The Chemistry of the quinonoid compounds
Edited by Saul Patai

The chemistry of the quinonoid compounds

Part 1

Edited by

SAUL PATAI
The Hebrew University, Jerusalem

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CHAPTER 1

Theoretical and general aspects

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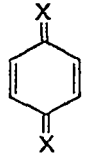
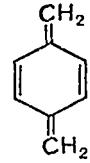
I. INTRODUCTION

Molecules possessing the quinonoid structure should, at first inspection, present no special problems to a student of structural chemistry. The alternating system of single and double bonds, including as it does exocyclic moieties, could be considered as a simple cross-conjugated system. This is true both if the exocyclic group is heteroatomic, as in the cases of quinones and quinonediimines **1**, or if the molecule is polyolefinic in nature such as quinododimethanes **2**.

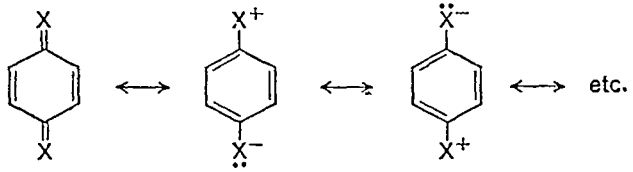


(1a) X = O
(1b) X = NH



(2)

Regarding these systems in this light would lead to the expectation that little novel chemistry would be found associated with the quinonoid function. In particular, the theoretical treatment developed for cross-conjugated olefins[1] or conjugated ketones[2] in earlier volumes of this series should be directly applicable here. There is, however, an obvious relationship between quinonoid and benzenoid functionalities. This can best be illustrated by the typical resonance description of the type shown below[3]:



Preceding even this resonance approach was the concept that an equilibrium might exist between quinones and cyclic aromatic peroxide structures[4,5], for example:

While this latter idea has little to recommend itself today, it is illustrative of the potential relationship between benzenoid and quinonoid structures that was, perhaps, too apparent to earlier workers. The following will, therefore, be considered: what is the relationship between quinonoid and benzenoid structures? To what degree can the quinonoid compounds be taken as 'aromatic'? As these two questions, particularly that concerned with the concept of aromaticity, are essentially theoretically derived, attention will be initially focused in section II on the various quantum chemical calculations applied to quinones. Section III will treat with the structural and spectral properties of quinones. It has been decided to deal initially with the quinones. A short summary on the quinododimethanes is given in section IV.

II. THEORETICAL TREATMENT OF QUINONES

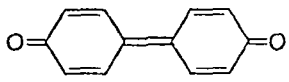
Most early calculations on quinones made use of simple Hückel Molecular Orbital calculations of the π energies[6]. In extending the basic Hückel approach from conjugated hydrocarbons to species, such as quinones, which contain heteroatoms, it becomes necessary to take into account

explicitly those electronic factors associated with the heteroatom. In particular these are the heteroatom one-centre coulombic integral and the two-centre carbon–heteroatom resonance integral. These expressions are usually developed in terms of the corresponding homoatomic parameters by incorporation into the Hückel matrix of the dimensionless terms h and k. The details of this type of parameterization and the relationship between h or k and experimentally obtained quantities is given in Streitwieser[6].

$$\alpha_X = \alpha_C + h\beta_{CC}$$

$$\beta_{CX} = k\beta_{CC}$$

Hückel calculations relying on these expressions have been applied to quinones by several groups of workers. In 1946, Coulson investigated several simple conjugated carbonyl-containing molecules[7]. The degree of bond fixation (as inferred from the calculated bond order) in 1,4-benzoquinone is much less than that obtained from glyoxal. The implication would be, of course, that a possible enhanced delocalization, perhaps associated with the contribution of relatively stable ionic structures, occurs in the quinone. It is of interest, however, that the formal carbon–carbon single bonds in 1,4-benzoquinone show a greater degree of fixation than the central bond of 1,3-butadiene. Diphenoquinone **3** shows the



(3)

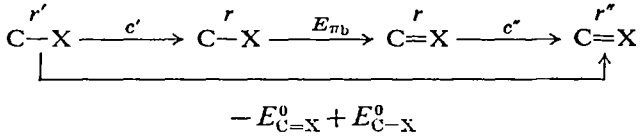
expected decrease of fixation relative to 1,4-benzoquinone; however, the degree of conjugation between the two rings is little different from biphenyl[8]. Also most interesting is the fact that 1,2-benzoquinone is predicted to be electronically equivalent to 2,4-hexadienedial as the bond between the carbonyl carbons in the quinone shows negligible π character[7]. If these quinones are examined in this light (i.e. relative to butadiene) it would appear that little delocalization is present. Other workers, however, did not reach the same conclusion. Bonino and Rolla, for example, determined that the average resonance energy per electron for 1,2- and 1,4-benzoquinone was intermediate in value to those obtained from olefins and benzenoid hydrocarbons[9,10].

Over the course of several years Kuboyama published a series of papers on Hückel calculations of quinones[11–13]. These calculations also showed pronounced alternation of bond orders for the benzoquinones[11,12]. This is in reasonable agreement with the results of Coulson[7]. (Variations in these results are no doubt due to the slightly different values of h and k employed.)

For systems in which aromatic rings are fused to the basic quinone unit, bond orders indicate the presence of a benzene ring. Thus, 1,2-naphthoquinone[12], 1,4-naphthoquinone[11], 9,10-anthraquinone[11] and 9,10-phenanthrene quinone[12] all show the presence of rings with six nearly equivalent bonds. This would again indicate limited delocalization. Kuboyama's calculations indicated that the lowest n–π^* transitions would be favoured by annellation of benzene units[11,12]. The corresponding π–π^* transitions should be similar for most systems[11], although diphenoquinone will behave in an exceptional manner[13]. A calculated dipole moment of 8·1 D was found for 1,2-benzoquinone[12]. This value is far too high even if certain empirical corrections are allowed. Hückel calculations often overemphasize charge separation (see section III.C).

The most complete treatment of quinones via the Hückel approach is that of Koutechký, Zahradník and Arient[14]. These workers have calculated the energy of 43 symmetrical quinones and related these quantities to spectroscopic and electrochemical results.

Because of the known tendency of simple Hückel calculations to overemphasize electron delocalization, it would be of value to determine the π energies of quinones via more complex means. The major failures of Hückel theory being the neglect of interelectronic interactions[15], these terms should be included in any advanced calculation. The modification of Roothaan's self-consistent field equations[16] as developed by Pople[17] and Pariser and Parr[18,19] has proved to be most effective in this regard. Dewar and his associates have carried out a series of studies on the ground-state properties of conjugated systems which are based on this approach[20-25]. A major distinction between the calculations of Dewar's group and those of other workers is the manner of empirically evaluating the two-centre resonance integrals. Following the suggestion of Dewar and Schmeising[26,27] these terms are obtained from parameters by means of the following thermocycle which treats all bonds as quasi two-centre (e.g. ethylene or formaldehyde) groupings.



$$-E^0_{C=X}+E^0_{C-X}$$

In this procedure E^0_{C-X} and r' refer to the bond energy and equilibrium bond length for an sp^2–sp^2 single bond between carbon and atom X while $E^0_{C=X}$ and r'' are the corresponding terms for a carbon–atom X double bond. The quantities c' and c'' are compression (elongation) energies needed to deform the equilibrium bond lengths to some distance r which

is associated with the bond in question. $E_{\pi b}$ is the π energy of the two-centre π system. From this term the resonance integral, β, can be obtained. The procedures for doing this, however, are more involved when a carbon–heteroatom bond is dealt with[23,25]. In the case of a carbon–carbon unit, the resonance integral can be obtained from a simple algebraic expression. The results of Dewar and Gleicher indicated that both 1,2- and 1,4-benzoquinone should be regarded as classical structures[23]. The calculated resonance energies of these species were zero within the limits of a few tenths of a kilocalorie per mole. A direct calculation by Dewar and Morita of the heat of atomization for 1,4-benzoquinone yielded a result within two-tenths of a per cent of the experimental value[25]. Calculations on the bond lengths of the two stable benzoquinones also indicated little electronic delocalization[23].

Dewar and Gleicher also considered the hypothetical molecule 1,3-benzoquinone[23]. Although no classical structure can be drawn for a *meta* quinone, a molecular orbital treatment can be directly applied. It was determined by self-consistent field theory that a singlet ground-state structure for this system would be less stable by two electron volts than its *ortho* or *para* counterparts. A diradical structure would be more plausible.

Other workers have also utilized various advanced molecular orbital techniques to study quinones. Kuboyama and Wada carried out self-consistent field calculations on 1,2-benzoquinone and 9,10-anthraquinone[28,29]. The results showed much less separation of charge than had been indicated by Hückel calculations[12]. The application of the results for 9,10-anthraquinone, however, led to poor correlation with the experimentally obtained electronic spectrum[29]. Newton, DeBoer and Lipscomb have also utilized self-consistent field theory to study the benzoquinones[30]. An ionization potential for 1,4-benzoquinone of 9·96 eV was determined by these workers. This is in reasonable agreement with the experimental value of 9·68 eV[31]. The calculation underestimates the dipole moment for 1,2-benzoquinone, however, yielding a value of 3·6 D[30]. The experimental value is 5·1 D[32]. Ionization potentials have also been determined for certain *para* quinones by Aussens and coworkers[33]. Calculated values of 9·53 and 9·10 eV were obtained for 1,4-benzoquinone and 9,10-anthraquinone. The corresponding experimental values are 9·68 and 9·34 eV[31]. A value of 9·21 eV was calculated for 1,4-naphthoquinone in agreement with the expectation that increased conjugation should lower the ionization potential[33]. These workers also calculated the transition energies and oscillator strengths for the two lowest singlet–singlet transitions of 1,4-benzoquinone and obtained values in good agreement with experiment[34].

Yonezawa, Yanabe and Kato have used variants of the Hückel approach to determine the extent of lone-pair electron localization on the oxygen atoms of quinones[35]. Localization decreased in the order 1,4-benzoquinone > 1,4-naphthoquinone > 9,10-anthraquinone. This parallels the p*K*s of these compounds[36].

Navangul has investigated the quinones by use of the electron gas model of molecules[37]. His results for charge densities and bond orders greatly differ from those obtained from Hückel calculations. Navangul has utilized his values of charge density to predict the course of electrophilic substitution in quinones[37]. The reactivity of quinones with respect to both electrophilic and nucleophilic substitution has been determined via Hückel calculation of localization energies by Hopff and Schweizer[38, 39].

III. PHYSICAL PROPERTIES OF QUINONES

A. *Thermochemistry*

The correlation between aromatic character (delocalization) and heats of combustion has frequently been invoked to assess the former. The determination of a resonance energy as a difference between experimental and calculated heats of combustion, heats of formation or bond energies is generally accepted. Criticism has been directed, however, toward the manner in which the calculated thermochemical quantities have been evaluated. Too often, as has been pointed out, a neglect of hybridization factors was general[26, 27].

The problem has been magnified by the uncertainty associated with the experimentally obtained thermochemical data. A heat of combustion of 684 kcal/mole was first obtained for 1,4-benzoquinone in 1886[40]. Since that time, more than a dozen additional studies have been carried out on these systems. Results have varied between 655 and 685 kcal/mole. Most recent workers have found values for the heats of combustion at the lower end of this range. Thus, Parks, Manchester and Vaughan have obtained a value of 656·84 kcal/mole for this quantity and a related value of 44·10 kcal/mole for the heat of formation[41]. Pilcher and Sutton have found corresponding values of 656·29 kcal/mole and 44·65 kcal/mole[42].

In the following discussion on the degree of delocalization (aromaticity) associated with quinones, the experimental thermochemical data utilized by each author will be given. Obviously, conclusions can be modified or even completely reversed by recourse to alternate results.

Early considerations of Pauling and Sherman[3] indicated that appreciable resonance energy should be encountered in both *para* and *ortho* quinone systems. A summation of empirical bond energies led to a predicted value

of 1407·0 kcal/mole for the heat of formation of 1,4-benzoquinone from gaseous atoms. This was compared with a value of 1393·8 kcal/mole obtained from a heat of combustion of 656·4 kcal/mole [43]. The difference of 13·2 kcal/mole is a substantial resonance energy equivalent to approximately one-third that of benzene[1]. Similar treatment for 9,10-phenanthraquinone and 9,10-anthraquinone provided values for the *total* resonance energy of approximately 110·7 kcal/mole. If the resonance energies associated with two benzene rings are subtracted from this value, a resonance energy of 32·3 kcal/mole is found for both systems. It would seem that the *ortho* and *para* quinone units are comparable in energy. A second conclusion would concern the effect of annellation of benzene rings: these results support the view that such annellation (apart from the resonance associated with benzene) will stabilize the basic quinonoid structure. The *total* resonance energy of these two polycyclic molecules is, however, greater than those currently accepted for the corresponding arenes themselves[44]. Equally high values for the resonance energies in these systems have not been reported by later workers. Franklin has, for example, published a value of only 7 kcal/mole for the resonance energy of 1,4-benzoquinone[45]. Wheland has also made use of the bond increment approaches of Franklin and Klages to obtain resonance energies of 4 and 3 kcal/mole for this molecule[44]. These results utilized a value of 671·5 kcal/mole for the heat of combustion in this system[46].

In view of the wide variance in reported values for the heats of combustion of quinones, the work of Magnus is particularly noteworthy[47]. Although, as shall be noted, several of his values appear high, a series of related molecules has been studied by a single worker under identical conditions. Table 1 contains these experimental values and those calculated

TABLE 1. Heats of combustion and resonance energies for some quinones[47]

Molecule	H_C (kcal/mole)		E_R (kcal/mole)
	exp.	calc.	
1,4-Benzoquinone	666·5	666·5	0
1,4-Naphthoquinone	1118·9	1158·2	39·3
9,10-Anthraquinone	1569·1	1649·9	82·8
9,10-Phenanthrenequinone	1556·6	1649·9	93·3
5,12-Naphthacenequinone	2026·2	2141·6	115·4
6,13-Pentacenequinone	2489·2	2633·3	114·1
1,2-Benz-7,12-anthracenequinone	1998·7	2141·6	142·9
1,2,7,8-Dibenzpyrene-3,6-quinone	2633·8	2845·8	212·1

by Magnus by means of a modified Klages approach[46]. As can be seen, no resonance stabilization is reported for *p*-benzoquinone. Polycyclic systems show resonance energies compatible with those of the aromatic portions of the molecules. Table 2 gives the resonance energies for some

TABLE 2. Comparative resonance energies in some acenes[47]

Molecule	E_R (kcal/mole)		
	Hydrocarbon	*p*-Quinone	Dihydroacene
Naphthalene	67·1	39·3	36·7
Anthracene	96·7	82·8	76·7
Naphthacene	129·6	115·4	106·8
Pentacene	—	144·1	—

acenes, *p*-quinones derived from these systems and the corresponding dihydroacenes. While the resonance energies of the *p*-quinones are less than those of the corresponding acenes, they are greater than those of the dihydro compounds. This is in keeping with the presence of some delocalization or resonance in the quinone systems. Part of this difference relative to the dihydroacenes must, however, be due to hybridization effects. Interestingly enough, if the resonance energies of the acenes and corresponding quinones are divided by the number of 'aromatic' double bonds, a nearly constant value is obtained (if 6,13-pentacenequinone is excepted). Unfortunately, the experimental heat of combustion for 1,4-benzoquinone obtained in this study is much higher than those heats obtained by other workers[41-43]. The same is true for 9,10-anthraquinone where Beckers has obtained an appreciably lower value[48]. Attractive as Magnus' conclusions are, therefore, some caution must be observed in utilizing them.

Direct calculations of the heats of atomization of 1,4-benzoquinone have been carried out by Dewar and coworkers[23, 25]. The value most recently obtained[25] corresponds to a heat of combustion of 667·7 kcal/mole, a value in excellent agreement with Magnus' findings. Dewar and Morita have also calculated a value of 670·4 kcal/mole for the heat of combustion of 1,2-benzoquinone[25].

B. Structure

The possibly high delocalization which may be present in quinonoid systems should strongly affect the ground-state structures of these same molecules. Molecular orbital calculations indicate, however, that appreciable alternation of bond lengths should be generally expected. Hückel

calculations, although dependent to a large degree upon choice of parameters, indicate that 1,4-benzoquinone should show a very distinct non-equivalence of carbon–carbon bonds. Coulson determined π-bond orders of 0·305 and 0·889 for the 1,2- and 2,3-bonds respectively[7]. Kuboyama's calculation of the same system yielded corresponding values of 0·345 and 0·873[11]. The π-bond order in benzene, which is defined by symmetry, has a value of 0·667. If anything, the Hückel approach will tend to underemphasize the extent of bond alternation within the ring by its neglect of electronic interactions[5]. Self-consistent field calculations upon 1,4-benzoquinone based upon methods utilizing two sets of semi-empirically obtained parameters led to values for the aforementioned bond orders in the ranges less than 0·15 and greater than 0·98[23]. The bond order of the carbon–oxygen bond in this molecule is indicative of appreciable double-bond character. The value from Hückel calculations is 0·795[7] while those from the self-consistent field calculation are greater than 0·85[23].

While the use of bond orders themselves is informative in a qualitative sense, it is the use of bond order–bond length relationships which will allow for a direct comparison of theoretical and experimental results. The earliest such relationship was developed by Coulson

$$r_{AB} = r' - \frac{r' - r''}{1 + k[(1 - P_{AB})/P_{AB}]}$$

where P_{AB} is the π-bond order of the A—B bond and r' and r'' refer to bond length for pure single and double bonds in the correct hybridization and k is some dimensionless parameter[49]. If k is assumed to be equal to unity, the expression is simplified to

$$r_{AB} = r' - P_{AB}(r' - r'')$$

Relationships of this type have been used in conjunction with both Hückel[49] and self-consistent field calculations[21]. The calculated bond lengths for 1,4-benzoquinone obtained from this equation are presented in Table 3. In the case of carbon–carbon bonds, r' was taken as 1·515 Å and r'' as 1·338 Å. The corresponding values for the carbon–oxygen bond were 1·397 Å and 1·210 Å.

The first structure determination on 1,4-benzoquinone was carried out by Robertson using X-ray diffraction[50]. His findings indicated strong alternation in carbon–carbon bond length with values of 1·50 Å and 1·32 Å while the exocyclic bonds were found to be only 1·14 Å. This is appreciably shorter than the pure double-bond value of 1·208 Å found in formaldehyde[51] and is only slightly longer than the bond length of 1·13 Å found in carbon monoxide[52, 53]. In a later X-ray study, however, Trotter

TABLE 3. Bond lengths in 1,4-benzoquinone (in Å)

A. Theoretical results

Bond			
C_1-C_2	C_2-C_3	C_1-O	Reference
1·461	1·358	1·248	7
1·454	1·361	—	11
1·490	1·341	1·237	23
1·499	1·339	1·239	23

B. Experimental results

Bond				
C_1-C_2	C_2-C_3	C_1-O	Method	Reference
1·50	1·32	1·14	X-Ray	50
1·52	1·31	1·15	Electron diffraction	55
1·49	1·32	1·23	Electron diffraction	56
1·477	1·320	1·222	X-Ray	54
1·481	1·344	1·225	Electron diffraction	57

found a value of 1·222 Å for the carbon–oxygen bond[54]. Electron diffraction has also been applied toward an elucidation of the structure of 1,4-benzoquinone. While Kimura and Shibata have obtained values similar to those of Robertson[55], Swingle has found bond lengths which are in particularly good agreement with those of Trotter[56]. Most recently this system has been re-investigated by Hagen and Hedberg[57]. The results of these workers, which are in accord with those of Trotter and Swingle, indicate a structure with little conjugation and in which the exocyclic carbon–oxygen bond is essentially little different from that of 1·22 Å found in acetone[58]. All of the above results are given in Table 3.

As can be seen, the most recent experimental results are in good agreement with the values calculated by the self-consistent field method. The experimental findings all support a planar structure for 1,4-benzoquinone. Some deviation from the idealized 120° angle associated with an sp^2 hybridized carbon was also noted. Robertson and Kimura and Shibata reported values for the $C_6-C_1-C_2$ angle which were approximately tetrahedral[50, 55]. Later workers, however, agree in assigning this angle a much larger value of about 117°[54, 56, 57].

The introduction of substituents in 1,4-benzoquinone has been reported to cause variable effects. Chu, Jeffrey and Sakurai have reported an X-ray determination of the structure of chloranil[59]. The system is found to be

planar and carbon–carbon bond lengths are all within 0·004 Å of those found by Hagen and Hedberg for the parent system[57]. Bond angles are also in excellent agreement. The carbon–oxygen distance in chloranil is only 1·195 Å, but, while this is somewhat shorter than that in 1,4-benzoquinone, it is not completely unexpected in view of chlorine's electron-withdrawing nature. This same bond shortening has been rationalized on the basis of spectroscopic studies[60].

A series of investigations on dihalogenated 1,4-benzoquinones by Rees, Haser and Weiss, however, indicate quite different results[61]. The molecules treated were 2,5-dibromo-1,4-benzoquinone, 2,5-dichloro-1,4-benzoquinone and 2,3-dichloro-1,4-benzoquinone. All these systems were stated to have structures which differed strongly from the parent molecule. The carbon–carbon bonds in the dibrominated compound have lengths between 1·377 Å and 1·451 Å. This increased equivalence of bond length is less observable for the chlorinated compounds. The 2,5-disubstituted compounds have carbon–oxygen bonds longer than 1·24 Å. The 2,3-dichloro compound is most like the parent system; however, this compound, as well as chloranil, is reported to be non-planar. These results must be regarded as exceptional.

A few structure determinations exist for polycyclic quinones. Recent X-ray determinations have been carried out for 9,10-anthraquinone. Murty has shown that the distances in the end rings, while they show variation, are distinctly in the range of those found in aromatic hydrocarbons[62]. The values in at least two instances are almost equivalent to the corresponding bonds in anthracene[63], but this must be fortuitous. Prakash[64] has refined Murty's results and reports an average value for bonds in the terminal ring of $1{\cdot}387 \pm 0{\cdot}005$ Å. This could well be expected if the terminal rings are only slightly perturbed *ortho* disubstituted benzene units. Prakash's refinement is also in excellent agreement with the results independently obtained by Lonsdale and coworkers[65]. Here again the bonds in the terminal rings are benzenoid in nature with an average value of $1{\cdot}392 \pm 0{\cdot}004$ Å. The bonds to the carbonyl carbon are again quite long, having values of 1·483 Å and 1·492 Å, respectively, from Prakash's and the Lonsdale group's results. While in general agreement, the reported lengths of the carbon–oxygen bond differ. (All results are shown in Table 4.) The above workers, however, have all conclusively shown that bond alternation does not extend to those portions of a polycyclic quinone for which benzenoid structures can be written. An earlier structure determination of 9,10-anthraquinone had reported complete bond alternation[66]. A second early X-ray structural determination by Sen is in good qualitative agreement with the more current work[67]. Unfortunately,

nothing is at present known on the effect of substituents on the structure of 9,10-anthraquinone. An attempt by Guilhem to study 1,5-dihydroxy-9,10-anthraquinone was abandoned when the experimental data proved too crude for bond-length elucidation[68].

TABLE 4. Bond lengths (Å) for two polycyclic quinones

A. 9,10-*Anthraquinone*

Bond	Murty[62]	Prakash[64]	Lonsdale[65] and coworkers	$r_{calc.}$[11]	$r_{anthracene}$[63]
$C_1—C_2$	1·366	1·385	1·391	1·399	1·368
$C_2—C_3$	1·410	1·388	1·383	1·398	1·419
$C_1—C_{13}$	1·391	1·382	1·391	1·403	1·436
$C_9—C_{13}$	1·478	1·483	1·492	1·451	1·399
$C_{11}—C_{12}$	1·372	1·401	1·404	1·413	1·428
$C_9—O$	1·224	1·213	1·244	—	—

B. 1,4-*Naphthoquinone*

Bond	r_{exp}[69]	$r_{calc.}$[11]	$r_{naphthalene}$[63]
$C_1—C_2$	1·465	1·453	1·364
$C_2—C_3$	1·310	1·362	1·415
$C_1—C_9$	1·445	1·450	1·421
$C_6—C_7$	1·370	1·397	1·415
$C_7—C_8$	1·420	1·400	1·364
$C_8—C_9$	1·375	1·403	1·421
$C_9—C_{10}$	1·390	1·412	1·418
$C_1—O$	1·215	—	—

An X-ray determination of the structure of 1,4-naphthoquinone has also been carried out[69] and these results are presented in Table 4 together with those for the corresponding hydrocarbon[63]. The purely quinonoid portion of the molecule possesses alternation of bond lengths. The results, however, are not completely satisfying. The $C_2—C_3$ bond is obviously too short and the $C_1—C_2$ and $C_1—C_9$ bonds are shorter than expected. The bonds in the aromatic portion show little equivalence.

In Table 4 the calculated bond lengths for 9,10-anthraquinone and 1,4-naphthaquinone are also reported. These were determined from the relationship previously described and are based on the bond orders obtained by Kuboyama in his Hückel calculation[11]. The agreement with experiment is reasonable in the case of 9,10-anthraquinone, particularly if the bonds to the carbonyl carbon are exempted from the discussion. This last bond is predicted to be far shorter than found. The average deviation

of the other calculated carbon–carbon bond lengths from experiment is only 0·012 Å. In the case of 1,4-naphthoquinone the corresponding deviation is 0·024 Å but this latter agreement cannot be considered acceptable.

C. Dipole Moments

It would be expected that any quinone with a symmetry less than D_{2h} would possess a permanent dipole. The simplest such molecule, 1,2-benzoquinone, is quite polar, having a dipole of 5·1 D in benzene[32]. The dipole moment of an *s-trans* propenal is 3·11 D[70]. If 1,2-benzoquinone is taken as a system of two joined *s-trans* propenal units, a value of 5·4 D can be predicted for the dipole. Such a result is to be expected if only limited delocalization is present. The annellation of benzene rings to the 1,2-benzoquinone unit causes only moderate changes in the value of the dipole moment. Thus, 1,2-naphthaquinone is reported to have a moment of 5·67 D[32] and several studies indicate that of 9,10-phenanthraquinone to be in the range 5·34–5·59 D[71–73]. Even in acenaphthenequinone, only a dipole moment of 6·0 D is found[73]. This last system, however, is appreciably different from the others in possessing the *s-cis* rather than the *s-trans* propenal unit and in being a derivative of a non-alternant hydrocarbon.

In the original study of 1,2-benzoquinone, Nakagura and Kuboyama attempted to correlate their dipole moment with HMO correlations. A calculated value of 7·5 D was obtained[32]. This should not be considered surprising in view of the often exaggerated charge separation found in such calculations. Their results, however, could be brought into agreement with experiment by subtracting 1·5 D as an empirical correction for adjacent carbonyl groups[74]. More sophisticated calculations by Béry have yielded a value of 4·85 D for 1,2-benzoquinone without recourse to such a correction[75].

Systems containing a *para* quinone structure will also, frequently, have permanent dipoles. As a case in point, 1,4-naphthoquinone shows a moment of 1·33 D in benzene solution[73] and an earlier report cited a value of 1·21 D in the solid phase[76]. At least one extended quinone system has also had its dipole moment reported: a value of 2·3 D has been reported for 5,11-naphthacenequinone[77].

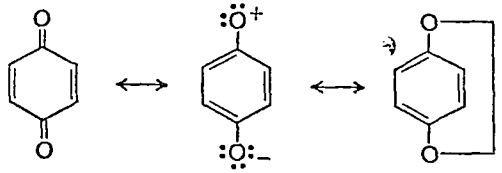
Values of 0·60–0·70 D were reported for 1,4-benzoquinone several decades ago[78–80]. Several 2,5-symmetrically substituted 1,4-benzoquinones were also shown to have moments of approximately 0·7 D[80]. The early structural work of Robertson had, by this time, eliminated the possibility of a permanent dipole in 1,4-benzoquinone by showing this molecule to be centro-symmetric[50]. Coop and Sutton rationalized these findings by

equating the unexpectedly high moment with an atom polarization associated with a carbonyl-bending mode[81] but some criticism of this explanation has been advanced. Kofod found a dipole moment of 0·83 D for 2,5-di-*t*-butyl-1,4-benzoquinone[82]. This was considered surprising as it had been presumed that a strained system would have a decreased, rather than increased, atom polarization[81]. (Possible non-planarity in this system was not considered in detail.) Meredith, Westland and Wright reported that the polarization of 1,4-benzoquinone was dependent upon both temperature and phase[76]; results, which, however, differ from those obtained earlier[79]. To explain these results, recourse was again made to a permanent moment caused by non-planarity. This would be particularly associated with an 8° out-of-plane deformation of both carbonyl groups[78], which seems highly unlikely (see section II.B). Paolini has equated the observed dipole in 1,4-benzoquinone with an induced deformation of the oxygen lone-pair electrons in the electric field[83]. Studies of the Kerr birefringence of 1,4-benzoquinone by Charney, however, have shown that there exists neither a permanent dipole nor an induced electron polarization large enough to cause a dipole moment greater than 0·15 D[84]. A similar conclusion has been reached by DiCarlo and Smyth as a result of an investigation of microwave absorption[85]. Both studies support the original explanation of atom polarization as the source of the experimental moment[81]. The dipole moment of 0·61 D for chloranil[73] can also be treated in the same way. Extension to other similarly symmetrical molecules should be possible. Studies on 9,10-anthraquinone have, however, produced variable results. Values for the dipole moment of 0·0 D[86], 0·71 D[76] and 0·27 D[73] have been published. A probable source of the experimental difficulties may reside in the limited solubility of this compound in most solvents.

D. Magnetic Susceptibilities

One of the often utilized criteria of aromatic character has been the enhanced magnetic susceptibility shown by benzoid compounds[87]. Compounds possessing delocalized electrons will exhibit a value for the susceptibility in excess of that predicted via a summation of Pascal-type constants. The magnetic susceptibility of 1,4-benzoquinone has been determined to be in the range $-38{\cdot}2$ to $-43{\cdot}2 \times 10^{-6}$ c.g.s. units per mole[88-95]. This general range appears to be independent of experimental conditions used and is in very good agreement with the value of $-40{\cdot}8 \times 10^{-6}$ c.g.s. units per mole obtained from Pascal constants[90]. At the very most, an exaltation of $2{\cdot}5 \times 10^{-6}$ c.g.s. units per mole may be found for 1,4-benzoquinone and the corresponding value for benzene is

$13{\cdot}7 \times 10^{-6}$ c.g.s. units per mole[87]. These results would seem to argue against extensive aromatic character in 1,4-benzoquinone. At least one set of workers, however, have claimed that canonical structures of the following type make equivalent contributions to the final hybrid[92].



A magnetic susceptibility equal to that of 1,4-benzoquinone has also been found for 1,2-benzoquinone[89].

Some reported values of magnetic susceptibility for polycyclic quinones are presented in Table 5. There are, in certain cases, large discrepancies

TABLE 5. Magnetic susceptibilities of some quinones and the corresponding hydrocarbons

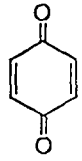
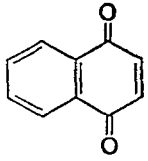
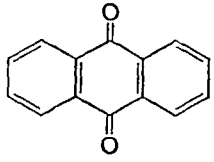
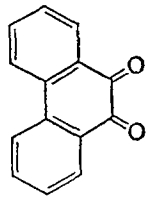
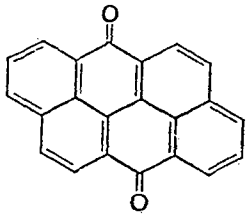
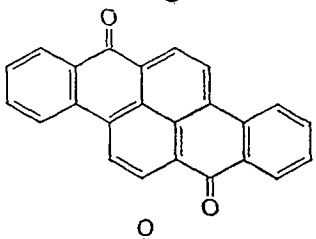
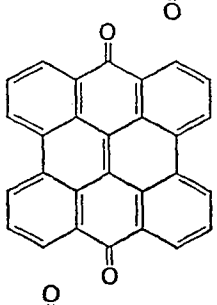
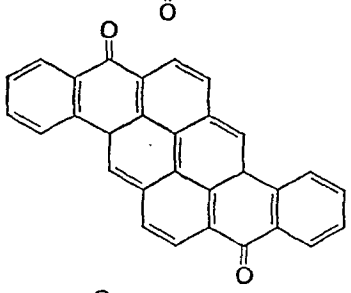
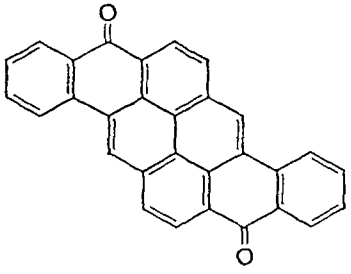
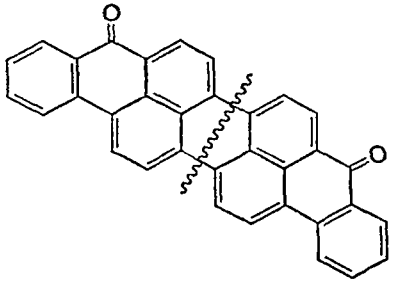
Compound	$\chi_M \times 10^6$ quinone	$\chi_M \times 10^6$ hydrocarbon	Reference
	−39·0 −42·4	−54·0 −58·0	93 95, 96
	−106·4	−123·9	95, 96
	−114 −147·6 −150·3	−159 −182·6 −179·1	93[a] 94 95, 96
	−113 −134·3	−155 −165	93 94, 95

TABLE 5. (*cont.*)

Compound	$\chi_M \times 10^6$ quinone	$\chi_M \times 10^6$ hydrocarbon	Reference
	−235	−285	93
	−212	−276	93
	−288	−238	93
	−335	−358	93
	−159	−320	93

[a] Y. Matsunaga, *Bull. Chem. Soc. Japan*, **39**, 582 (1956).

among the results of different workers. If, however, these values are compared with those obtained by the same workers for the corresponding hydrocarbons certain generalities appear. LeFevre and Murthy have pointed out that the magnetic susceptibility of 1,4-benzoquinone is 75 per cent that of benzene[96] and attribute this to a lessening of ring current effects[95]. The data in Table 5 support this conclusion. The studies of Akamata and Matsunaga on some polycyclic compounds are of particular interest[93]. In these larger systems the quinone portion of the molecule is, of course, a small fraction of the whole and an appreciable amount of the magnetic susceptibility, and presumably the electron delocalization, of the parent hydrocarbon can be maintained. Certain exceptions, however, merit attention. Violanthrone **4** shows 50 per cent of the magnetic susceptibility of the corresponding hydrocarbon while *meso*-naphthdianthrone **5** shows greater magnetic susceptibility than its



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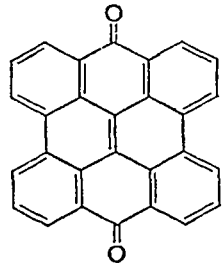


(5)

corresponding arene[93]. The former quinone is, in actuality, two fused benzanthrone units. The bonds joining the two units are essentially single in character and would, therefore, not contribute to any electron delocalization[97]. In the parent system electron delocalization through all nine rings should occur. The reverse should be observed in *meso*-naphthdianthrone. The corresponding hydrocarbon is composed of two isolated anthracene moieties connected by three purely single bonds. In the quinone delocalization through the centre of the system is now possible.

E. Reduction Potentials

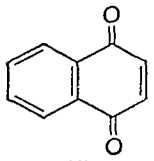
The facility with which quinones are reduced to the corresponding diphenols is of considerable interest. The biological activity of vitamin K, itself a 1,4-naphthoquinone, is, for example, due to its functioning as an oxidizing agent. The polarographic reduction of less complex quinones

has been the subject of investigation for over 40 years and Table 6 provides a summary of reported reduction potentials. Much earlier work was carried out by Fieser and associates[99-101]; however, several other groups of workers have also made substantial contributions to the field[105-107].

TABLE 6. Polarographic reduction potentials of some quinones

System	E_q^0(volts)	Reference
1,2-Benzoquinone	0·783	98
1,4-Benzoquinone	0·715	104
1,2-Naphthoquinone	0·576	104
1,4-Naphthoquinone	0·484	105
2,6-Naphthoquinone	0·758	99
Diphenoquinone	0·954	105, 100
1,2-Anthraquinone	0·490	98
1,4-Anthraquinone	0·401	106
9,10-Anthraquinone	0·154	105
1,2-Phenanthrenequinone	0·660	98
1,4-Phenanthrenequinone	0·523	106
3,4-Phenanthrenequinone	0·621	101
9,10-Phenanthrenequinone	0·458	98
	0·471	103
	0·460	105
	0·416	107
1,6-Pyrenequinone	0·612	106
1,8-Pyrenequinone	0·514	106
4,5-Pyrenequinone	0·474	106
4,5-Pyrenequinone	0·474	106
	0·424	107
1,2-Benz-5,6-anthracenequinone	0·430	99
	0·380	107
1,2-Benz-7,12-anthracenequinone	0·228	99
5,6-Chrysenequinone	0·465	99
6,12-Chrysenequinone	0·392	99
3,4-Benz-5,6-phenanthrenequinone	0·492	106
5,6-Picenequinone	0·451	106
	0·474	103
13,14-Picenequinone	0·503	106
1,2;5,6-Dibenz-5,6-anthracenequinone	0·446	106
1,2;5,6-Dibenz-4,14-anthracenequinone	0·292	106
1,2;7,8-Dibenz-5,6-anthracenequinone	0·445	106
1,2;7,8-Dibenz-7,14-anthracenequinone	0·302	106
1,2-Benz-3,8-pyrenequinone	0·438	106
1,2-Benz-3,6-pyrenequinone	0·441	106
1,2-Benz-4,5-pyrenequinone	0·442	106
1,2-Benz-6,12-pyrenequinone	0·443	106

With few exceptions, the data in Table 6 support the contention that fusion of a benzene ring to some basic unit tends to lower the reduction potential of the system. This would result from an increased ability to delocalize charge in the intermediate radical anion or dianion. It has been pointed out, however, that such fusion, particularly close to a carbonyl group, may have a converse effect for steric reasons[106]. Early work also indicated expected inductive effects with electron-donating groups lowering and electron-withdrawing groups raising the reduction potentials of substituted 1,2- and 1,4-naphthoquinones[104] and 9,10-phenanthrenequinones[98]. With regard to such electronic effects, it is of interest that Rieke and coworkers have reported the operation of a pronounced ring strain effect in the reduction of the following series of 1,4-naphthoquinones[108].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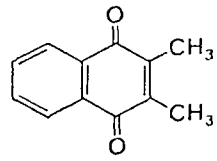
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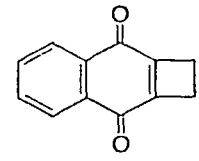
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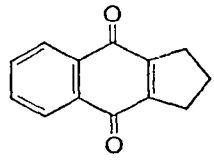
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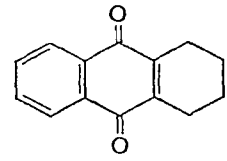

(10)

The observed ease of reduction was $\mathbf{6 \approx 8 < 9 < 7 \approx 10}$. The normal electron-donating effect of the alkyl groups can thus be shown to be effectively decreased by a corresponding ring strain phenomenon. These results can be nicely correlated with Hückel calculations which include Streitwieser's 'hybridization effect model'[109] as a means of introducing ring strain[108]. These experimental findings differ from the earlier results of Arnold and Zaugg[110] which were rationalized by recourse to the Mills–Nixon effect[111]. Substituents may also produce other types of steric effects. Newman and coworkers, in studying the reduction of substituted 9,10-phenanthrenequinones, noted that the reduction of 4,5-dimethyl-9,10-phenanthrenequinone was retarded relative to the 2,7-dimethyl isomer[112]. The decreased ease of reduction was equated to a 3·3 kcal/mole difference in strain energy between the quinones and corresponding hydroquinones due to the necessity of increased planarity in the latter

systems. The 4,5-dimethyl-9,10-phenanthrenequinone must itself be appreciably strained relative to the 2,7- isomer as determined from heats of combustion of the corresponding hydrocarbons[113].

Correlations of reduction potential data with other related experimentally observable results have been frequent. Examples include correlation with the rates of addition of bromine across the 9–10 bond of substituted phenanthrenes[114], rates of aromatic substitution[115], carbonyl-stretching frequency[116], ease of hydrogenation of the quinones[117] and ozonolysis of the corresponding hydrocarbons[118,119]. Correlations have also been based upon biological properties. Thus, Ikada has related the antibacterial activity of substituted 1,4-naphthoquinones with the corresponding reduction potentials[120]. An attempt by Iball, however, to correlate potentials with carcinogenic activity was less successful[121].

Various theoretical models have also been developed to correlate the reduction potentials of quinones. An early empirical relationship based upon resonance theory was discussed by Branch and Calvin[122]. Most later work in this area has, by contrast, been based upon simple Hückel molecular orbital approaches. Evans has developed a simplified method in which the effects of the heteroatoms are neglected[123]: the reduction potentials are considered as functions of the differences in resonance energy between the quinone and the corresponding dihydroxyaromatic compound, while the resonance energy of the latter is equivalent to that of the parent hydrocarbon. By assuming that the electrons of the carbonyl groups are completely localized in these bonds, Evans shows that the resonance energy includes no contribution from these groups or any otherwise isolated double bonds. Thus, for example, the resonance energy of 1,4-benzoquinone is zero, that of 1,2-benzoquinone equals that of butadiene, while 1,4- and 1,2-naphthoquinone are equivalent to benzene and styrene respectively. In correlating reduction potentials by this approach, Evans obtained separate correlations for *ortho* and *para* compounds[123]. These results, however, might be somewhat suspect in that the assumption of complete electron localization in the carbonyl bonds is too severe. Evans and coworkers have themselves re-examined the problem by recalculating the resonance energies for quinones in a 'normal' manner[124]. A double correlation was again obtained. While Gold has shown that a judicious adjustment of the Hückel parameters can lead to a single correlation[125], Basu, using a model based upon the particle in the box, also found separate correlations for the reduction potentials of *ortho* and *para* quinones[126]. While these separate correlations may not be artifacts of the calculation, it should be mentioned that Hückel and other simple molecular orbital methods frequently yield dual correlations which

coalesce into a single relationship when calculations which allow for interaction of electrons are utilized[127-129]. Hückel-type calculations have also been used to treat various substituted quinones. Kemula and Kygowski have correlated the reduction potentials of mono- and dichlorinated 9,10-anthraquinones with the calculated energy difference between the starting material and the radical anion form by the addition of one electron[130]. An attempt to treat hydroxyquinones in a similar manner, however, failed due to the method's inability to allow for hydrogen bonding[131].

Although the ease of reduction of quinones should be a function of some energy difference between quinonoid and benzenoid structures, simplifications can be introduced and some of the extensive calculation avoided. Maccoll showed that the ease of reduction of aromatic hydrocarbons could be correlated with the energy of the lowest unoccupied molecular orbital[132]. While this assumption was originally based upon the results of Hückel calculations, it has been shown to be equally valid for both hydrocarbon oxidation[133] and reduction[124] potentials using self-consistent field theory. Such correlations have been utilized in the correlation of quinone reduction potentials with reasonable success[36, 135].

Flaig and coworkers have also employed a Hammett relationship to correlate the reduction of various substituted 1,4-benzoquinones[136]. Somewhat unexpectedly, they found varying effects for different classes of substituents.

F. Infrared Spectroscopy

Appreciable data on the vibrational spectra of quinones exist in the literature. Complete normal co-ordinate analyses have been carried out for 1,4-benzoquinone[137] and 1,4-naphthoquinone[138]. Such studies, however, must be regarded as exceptional and recourse will be made to less detailed investigations. In the early Fifties several groups of workers examined the absorption associated with the stretching vibration of the carbonyl groups of unsubstituted quinones[139-141]. A few of these, based upon data obtained in mulls or as solid samples, are presented in Table 7.

The introduction of substituents into the quinones has been claimed to influence the position of the carbonyl-stretching frequency. Yates, Ardao and Fieser in a study of 22 1,4-benzoquinones noted an increase in the wavelength of this absorption with electron-donating groups[60]. It should be pointed out, however, that variations of only 48 cm^{-1} (carbon disulphide solution) and 30 cm^{-1} (mineral oil mulls) were dealt with. Flaig and Salfeld also examined 45 methyl and methoxy 1,4-benzoquinones[142].

Correlations of the carbonyl-stretching frequency were developed although a total variation of only 38 cm^{-1} was found. The variation of carbonyl-stretching frequency with substituents in other quinone systems is even smaller than the above. A variation of 22 cm^{-1} was observed for 10 1,2-benzoquinones[143] and only 12 cm^{-1} for a series of diphenoquinones[144].

TABLE 7. Stretching vibrations of some carbonyl bonds

Molecule	$\nu_{C=O}$ (cm^{-1})	Reference
1,4-Benzoquinone	1664	139
1,2-Benzoquinone	1667	143
1,4-Naphthoquinone	1664	140
9,10-Phenanthrenequinone	1683	140
9,10-Anthraquinone	1675	141
5,6-Chrysenequinone	1658	139
1,6-Pyrenequinone	1639	139
1,8-Pyrenequinone	1639	139
1,2-Benz-3,8-pyrenequinone	1645	140
Diphenoquinone	1623	140

Certain substituents in particular have apparently little effect on the carbonyl-stretching frequency. Chloranil and various dichlorinated 1,4-benzoquinones show a stretching frequency little different from the parent compound[145]. Various chlorinated 9,10-anthraquinones also show a consistent value for this frequency[146]. The introduction of the most subtle substituent, deuterium for hydrogen, causes a moderate effect in 1,4-benzoquinone-d_4 where a shift of 8 cm^{-1} has been observed in the carbonyl-stretching frequency[147]. No corresponding change for 9,10-anthraquinone-d_8 has been noted, however[148]. In addition to substituents affecting the carbonyl-stretching frequency by electronic or steric effects, closely neighbouring groups such as hydroxy or amino could become involved with the carbonyl oxygen atoms via hydrogen bonding[116]. It has been shown, however, that for certain *ortho*-hydroxy quinones there is no effect on the intensity of the carbonyl absorption[149].

Correlations of the carbonyl-stretching frequency with both theoretical calculations and with other experimentally observed data have been carried out. As previously mentioned in section III.D, correlations with reduction potentials are known[116]. Such empirical correlations are not completely inclusive, however, thus substituted 1,4-naphthoquinones, 9,10-anthraquinones and 9,10-phenanthrenequinones defined three separ-

ate relationships[150]. A similar result was obtained in correlating the carbonyl-stretching frequency with calculated values of the free valence index as obtained from the Hückel method[116]. (A very good single correlation between the free valence index and reduction potentials has, however, been noted[116].) The carbonyl-stretching frequencies for various methyl-substituted 1,2-benz-9,10-anthraquinones have also been correlated with their reduction potentials[151]. Although a good correlation was claimed, the particularly small variation found in stretching frequencies (3 cm^{-1}) does not make this an optimal system.

Berthier, Pullman and Pontis have calculated the force constants for several carbonyl compounds including quinones[152]. The force constants were derived from an expression involving both the bond order and the bond–bond polarizability of the carbonyl bond as obtained by Hückel calculation. General good agreement was obtained between the frequencies obtained from the calculated force constants and their experimental counterparts with the exception of 7,8-acenaphthenequinone. Later investigation has indeed shown, however, that this molecule should not be regarded as a true quinone[153]. This approach has also been extended to calculate the carbonyl-stretching frequencies of semiquinones[154], although a more simple relationship which relates the frequency solely to the bond order was utilized[155]. This simplification is justifiable. Deschamps has shown that the dependence upon the self-polarizability term should be relatively small[156].

More advanced calculations have also been utilized to evaluate the vibrational spectra of quinones. Bratoz and Besnainou have made use of a Pople–Pariser–Parr approach to determine the carbonyl force constants in 1,2- and 1,4-benzoquinone[157]. Their calculated force constants were within 3 per cent of the experimental values. A later calculation, in which the approach of Bratoz and Besnainou was appreciably simplified, also yielded reasonable results for the same systems[158]. Similar calculations have also produced reasonable values for the relative intensities of carbonyl absorptions[159].

Of the carbon–carbon and carbon–hydrogen vibrations associated with the most simple of quinones, very little need be said. Their absorptions, at least in the case of substituted 1,4-benzoquinones, seem generally invariant to substituents[145]. It has also been shown that none of these absorptions which characterize 1,4-disubstituted benzenes are associated with the corresponding 1,4-benzoquinone[160]. This must be regarded as further evidence against aromatic character being associated with quinones.

Finally, it must be mentioned that frequently the spectra of quinones show multiple absorption in the carbonyl region. At one point it was

suggested that this might be associated with vibrations of the carbon–carbon double bonds[161]. Various workers, however, have found a more plausible explanation by applying the concept of Fermi resonance as causing a splitting of the carbonyl absorption[162, 163]. In the case of 1,4-benzoquinone, extensive studies involving isotopic substitution and solvent effects have proved Fermi resonance to be the cause of the multiplicity in the 1650–1675 cm^{-1} region of the spectrum[164].

G. Ultraviolet Spectroscopy

Stevenson has studied the electron spectra of several 1,4-benzoquinones[165]. The parent molecule shows three well-defined absorptions in solution. An n–π^* transition occurs at 476 mμ while π–π^* transitions are encountered at 278 mμ and 244 mμ. Only the last of these is associated with an extinction coefficient of moderately high value. The π–π^* transition found at 278 mμ is symmetry-forbidden. The spectrum of 1,4-benzoquinone in thin film at 20 K has been investigated by Sidman[166] and distinct differences exist between the spectra. The n–π^* transition in the solid phase is split into several bands[166]. Sidman feels that this is indicative of the non-equivalence of the lone pairs of electrons on the oxygen atom. The π–π^* transition was also observed to take place at lower energy in the solid phase. A gas-phase spectrum of 1,4-benzoquinone is also available[5].

Certain similarities are observed among the electronic spectra of unsubstituted quinones. A low intensity transition in the 400–500 mμ range has been shown to be common for several quinones[167]. This has usually been associated with an n–π^* transition; however, certain quinones of acenes have been reported to show a π–π^* singlet–triplet transition in the same region[168]. These singlet–triplet transitions, however, are marked by a much more intense extinction coefficient. The previously mentioned paper of Hartmann and Lorenz[167] is invaluable in providing a compilation of spectra for thirteen unsubstituted quinones as well as diquinones and derivatives. Some additional spectra of important unsubstituted quinones have been reported by other workers[169–172]. The spectra of 1,4-naphthoquinone and 9,10-anthraquinone in the solid phase at 4 K have also been obtained[173].

The effects of ring substituents on the electronic spectra of quinones are complex. Stevenson[165, 174] has noted that substituents in 1,4-benzoquinone affect the symmetry-forbidden $^1B_g \leftarrow {}^1A_g$ transition at 278 mμ in a manner which parallels their behaviour in benzene[175]. Halogenated 9,10-anthraquinones, however, show spectra which differ only slightly from the parent molecule[167, 176]. Substituents which can directly interact with the

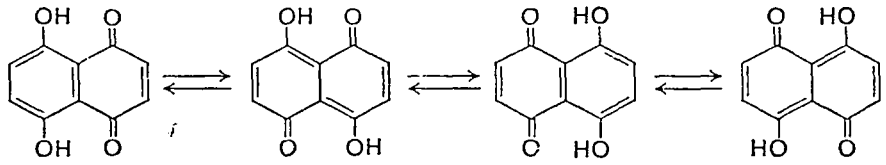
carbonyl groups by hydrogen bonding may profoundly affect the u.v. spectra of quinones. Thus, while β-amino-9,10-anthraquinones show spectra similar to the unsubstituted compound[167], α-amino-9,10-anthraquinones yield spectra indicative of severe perturbation of the energy levels via hydrogen bonding[177]. El-Sayed has predicted that the presence of heavy atoms in quinones should affect singlet–triplet absorption[178a]. Studies on 2,6-dihalo-1,4-benzoquinone have shown this prediction to be correct[178b].

Several workers have carried out theoretical calculations to correlate electronic spectra of quinones. Sidman obtained energies using a self-consistent field approach for both the n–π^* and π–π^* transitions in several carbonyl compounds[179]: results were within one electron volt of the experimental values. Leibovici and Deschamps, making use of self-consistent field calculations including configuration interaction with all singly excited states, have calculated the transitions for 1,4-benzoquinone[180]. Very good agreement with experiment was obtained for both the $^1B_{1g} \leftarrow {}^1A_g$ and $^1B_{2u} \leftarrow {}^1A_g$ transitions with differences of 0·2 eV and 0·01 eV respectively. Similar calculations have been carried out by these workers for 1,4-naphthoquinone, 1,4-anthraquinone and 9,10-anthraquinone[181]. The corresponding singlet–triplet transitions for these latter systems were also calculated for some acene quinones[182]. These agreed with the authors' earlier assignment of certain of these absorptions to π–π^* transitions rather than to the expected n–π^* transition[168]. Calculations of transition energies for charge-transfer complexes between quinones and *N,N,N',N'*-tetramethylphenylenediamine have also been carried out[183].

Edwards and Grinter[184] have attempted to calculate the transition energies for conjugated carbonyl systems using a molecule in molecules approach[185]. The 1,2-benzoquinone system was approximated by two acrolein units while 1,4-benzoquinone was treated both as two acroleins and as two ethylenes and two formaldehydes. In all cases agreement with experiment was poor. These authors obtained better results for 1,2-benzoquinone using a standard self-consistent field approach with configuration interaction with singly excited states[29,186]. Their calculations on 1,4-benzoquinone, 1,4-naphthoquinone and 9,10-anthraquinone yielded values for the transitions which were too high[185]. Similar results had been observed by other groups[181,187]. Edwards and Grinter have suggested that the inclusion of doubly excited states into the configuration interaction expression might improve the situation[186]. Leibovici and Deschamps, however, have noted that the polar nature of the excited state of quinones might necessitate a consideration of specific solvation energies, thus making direct comparisons between theory and experiment difficult[188].

H. Nuclear Magnetic Resonance Spectroscopy

The prior discussion of magnetic susceptibility (section III.D) attempted to show that little ring current is associated with the quinonoid structure. The results of n.m.r. studies also support this view. The protons of 1,4-benzoquinone show a signal at 6·67 δ (deuterocyclohexane) or 6·83 δ (deuteroacetone)[189]. Benzene itself shows absorption at 7·03 δ (carbon tetrachloride). The inclusion of a quinone moiety within a larger aromatic molecule also produces similar results. The signals in 1,4-naphthoquinone occur at 6·87 δ, 7·73 δ and 8·07 δ (deuterocyclohexane) and are associated with those protons at positions 2 and 3, 6 and 7, and 5 and 8, respectively[189]. The α and β protons of naphthalene absorb at 7·78 δ and 7·38 δ. While the aromatic absorptions in naphthalene and 1,4-naphthoquinone do not essentially differ, it should be pointed out that a 1,2-diacylated benzene will also produce signals in this region[190]. Similar results have been observed for 9,10-phenanthrenequinone[191]. A n.m.r. spectrum of 5,8-dihydroxy-1,4-naphthoquinone (naphthazarin) showed only a single absorption at 7·13 δ[192]. This was taken as showing a rapid equilibrium among the following structures.



These same workers were also able to develop a means of correlating the effects of substituents in the 1,4-naphthoquinone system[192].

IV. QUINODODIMETHANES

Current theory concerning electronic structure in polyolefinic compounds tends toward the conclusion that little delocalization is operative. Self-consistent field calculations on branched polyolefins indicated that the total π energy was a simple sum of the contributing parts[22,24]. While the quinododimethanes were not implicitly studied at that time, later calculations have indicated that such a conclusion had general validity[193]. Earlier Hückel calculations had indicated extensive delocalization in polyolefinic molecules[6]. Recently, however, the realization that calculated Hückel delocalization energies might require systematic corrections as a function of the number and types of bonds present has been proposed[194]. Incorporation of this argument within the framework of normal Hückel

calculations has yielded results which are frequently equivalent to those of more advanced calculations.

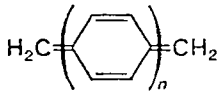
Early calculations on the quinododimethanes, however, were of the most simple type. These calculations, whether involving a molecular orbital or valence bond approach, were uniform in their predictions. Thus, Namiot, Dyatkina and Syrkin determined appreciable resonance energies for 1,2- and 1,4-benzenequinododimethane by both methods[195]. The molecular orbital approach was also applied to the hypothetical 1,3-benzenequinododimethane. While this is predicted to possess less resonance energy than its two isomers, significant stabilization was claimed[195]. Coulson and coworkers obtained results which tended to substantiate the above findings[196]. In the case of 1,4-benzenequinododimethane a very low separation between the singlet and triplet structures was predicted by molecular orbital theory[196]. Dyatkina and Syrkin also calculated similarly low energy barriers for other quinododimethanes, particularly for those systems where only a single classical structure can be drawn[197].

Experimental findings tend to contradict the prediction of moderate stability for simple quinododimethanes. Thus, for example, 1,2-benzenequinododimethane should be obtained from the thermal elimination of sulphur dioxide from 1,3-dihydroisothianaphthene 2,2-dioxide. While the quinododimethane has been trapped as a Diels–Alder adduct with anthracene, it has resisted isolation[198]. A similar failure was noted in the attempts to prepare 1,4-benzenequinododimethane via pyrolysis of the *p*-methylbenzyl radical[199]. Even those systems in which the quinododimethane moiety should be stabilized by the annellation of benzene rings have not been isolated at room temperature. Eliminations from various precursors have yielded 9,10-anthracenequinododimethane and 9,10-phenanthrenequinododimethane. Both have been trapped as Diels–Alder adducts[200, 201]. While still not yet isolated, these latter systems should be more stable than the parent benzenequinododimethanes. Cava, Shirley and Erickson have shown that naphtho[*a*]cyclobutene undergoes ring opening in the four-membered ring much more readily than the isomeric naphtho[*b*]cyclobutene[202], a result in complete agreement with the expected greater stability of 1,2-naphthalenequinododimethane to 2,3-naphthalenequinododimethane.

The relatively high stability accorded to 1,3-benzenequinododimethane by early calculations[195, 203] has been questioned in view of the hypothetical nature of the *meta*-quinonoid structure. Pullman, Berthier and Pullman explicitly showed the *meta*-quinododimethane structure to be diradical in character[204]. Such systems can be regarded as Schlenk hydrocarbons[205].

Their results were incorporated within a generalized treatment of radical and biradical chemistry[206].

Because of the low energy barrier between quinododimethanes and the corresponding biradical (which can maintain benzenoid character), much of the chemistry of quinododimethanes will be radical in nature. Seel calculated that the energy separation between singlet and triplet states for system **11** would decrease as n increased[207]. While these molecules them-



(11)

selves have not been studied, the tetraphenyl-substituted derivatives have been investigated in some detail. The radicals corresponding to these systems will be of a triarylmethyl type and should show appreciable stability[208]. In accord with Seel's prediction, the parent quinododimethane (**11**, $n = 2$) shows the characteristics of a diamagnetic molecule[209]. Chichibabin's hydrocarbon (**11**, $n = 2$)[210] has been shown to have about 2–5% radical character[211,212]. This is in very good agreement with the calculated singlet–triplet separation of 2·5 kcal/mole[197,213]. The higher members of this series exist as paramagnetic solids with up to 15% radical character where $n = 4$[214]. Seel has also suggested that the quinones analogous to molecule **11** should also show a similar relationship between singlet–triplet separation and the number of intervening six-membered rings[207]. Calculations on 1,4-benzoquinone and the corresponding quinodomethane and quinododimethane predict the ease of the last compound to assume a biradical structure as five powers of ten greater than that of the first[215]. This can be regarded as a consequence of the electronegativities of the exocyclic groups.

Advanced molecular orbital calculations on 1,4-benzenequinododimethane have been carried out by Béry and Bonnet using a Pariser–Parr treatment[216]. A non-equivalence of charge densities was noted. The bond orders obtained would predict extensive alternation of bond lengths with a value for the long bond of 1·464 Å. This is but little different from the central bond in 1,3-butadiene[217]. The results of these calculations also successfully correlate the electronic spectrum of the compounds[216].

Although relatively few measurements of the physical properties of simple quinododimethanes have actually been carried out, a combination of calculations plus experimental data on the more readily available tetraphenyl derivatives can provide a very general critique of the degree of aromatic character. Evans, deHeer and Gergely have calculated the

diamagnetic anisotropy of 1,4-benzenequinododimethane to be only 0·27 times that of benzene[218]. While the authors feel that this small value need not indicate essential localization of electron, this is the most obvious conclusion. The diamagnetic anisotropies have also been calculated for several quinododimethanes by Pullman and coworkers[219]. Experimental values for the magnetic anisotropies of certain tetraphenyl quinododimethanes are available[220]. The magnetic anisotropy of the tetraphenyl 1,4-benzenequinododimethane is only 3·74 times that of benzene in spite of the fact that four phenyl groups are present. It must be concluded that little electron delocalization is associated with the quinonoid portion of the molecule. Similar results are found for the tetraphenyl derivatives of 1,4-naphthalenequinododimethane and 9,10-anthracenequinododimethane[220].

The dipole moments for several quinododimethanes have been calculated as zero by Pullman's group, using the Hückel method[219]. In view of the uneven charge distribution predicted by one advanced approach[216] the experimental expectation is, however, by no means clear.

The gas-phase electronic spectra of 1,4-benzenequinododimethane was obtained by Tanaka[221]. A diffuse band in the range 2740–2770 Å was assigned to a singlet–singlet transition between the A_{1g} and B_{3u} states[221]. SCF calculations by Tanaka led to a value of 6·3 eV for this transition which was in poor agreement with the experimental value of 4·3–4·4 eV[222]. The calculated value of 4·5 eV obtained by Béry and Bonnet provides a far better correlation[216].

The electronic spectra of 1,4-benzenequinododimethane, 1,4-napthalenequinododimethane and 9,10-anthracenequinododimethane have been obtained as films at 77 K[223]. The three compounds show absorption at 3010 Å, 3100 Å and 2950 Å. This is in fair agreement with calculations although an expected hypsochromic shift is not observed[216]. Upon warming, the appearance of aromatic absorption accompanied by polymerization is noted. I.r. spectra under the same conditions have been obtained showing a vinylidene wag in the region 870–890 cm^{-1}[223]. The n.m.r. spectra for the same three compounds have been obtained at −80°C[224]. The ring hydrogens in 1,4-benzenequinododimethane produce a signal at 6·49 δ. If anything, this would be indicative of less ring current than is found in the corresponding quinone[189]. The exocyclic protons absorb at 5·10 δ and similar results are observed for the other quinododimethanes which also strongly resemble the corresponding quinones. In the 1,4-naphthalenequinododimethane and 9,10-anthracenequinododimethane the signals of the exocyclic protons are shifted due to the effects of ring currents from the aromatic units present.

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The Chemistry of the quinonoid compounds
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CHAPTER 2

The structural chemistry of quinones

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I. INTRODUCTION

Our aim in this review is twofold: first, we wish to describe the geometric features of quinone molecules, information which is thus far available almost exclusively from X-ray crystallographic structure analyses. These analyses also provide information on the architecture of the crystal, that is, how the crystal lattice is built up in a regular fashion from its constituent molecules. This brings us to our second aim—to outline the generalizations which can be made about the arrangements of the quinone molecules in their crystals. These arrangements are intimately related to intermolecular forces, so that an understanding of them provides a bridge between the structure and much of the chemistry of the molecules.

Since we are so dependent on the data obtained by X-ray crystallographers we start with some remarks on the significance of these data.

A. X-ray Crystallographic Results

Analysis of the structure of a crystal is carried out in two stages. The first stage is relatively rapidly and easily performed, and tells us which symmetry elements are present (space group), the dimensions of the unit cell and how many molecules there are in this cell. From these preliminary data it is sometimes possible to obtain an approximate picture of the shape of the molecule, some information on its symmetry and a general impression of the way in which the molecules are arranged in the crystal. For example, knowing the van der Waals radius of carbon (1·8 Å) and the fact that many of the quinones have a short crystal axis of <4 Å we can conclude that these molecules tend to pack parallel to one another with adjacent molecules markedly overlapped—an arrangement which leads to the development of infinite stacks of molecules, in a manner similar to the stacking of playing cards in a deck.

In the second stage of the analysis, the actual solution of the structure, lies the art of the crystallographer: here every atom in the crystal must be assigned approximate co-ordinates which are arrived at by various computational procedures, by considerations based on restrictions imposed by symmetry and unit-cell dimensions and by deduction hopefully based on chemical knowledge and intuition. These co-ordinates are then 'refined' by least-squares techniques to give the best possible structure which is determined both by the quality of the X-ray data and by the degree of sophistication of the method of refinement.

There are various ways of indicating the precision of the analysis. For our purpose this is best described in terms of the standard deviations of the atomic positions. During the years the attainable precision has

improved. Very roughly we can say that twenty years ago the standard deviations of atomic positions tended to be about 0·05 Å in a reasonable analysis; today, as a result of improved methods of data collection and the increasing speed and size of computers, the corresponding figure is often less than 0·01 Å. With this increase in precision additional types of information have become available. For instance, the positions of hydrogen atoms are now generally determined experimentally, where formerly they were deduced on the basis of chemical considerations. In addition, a good deal of knowledge is being acquired about the thermal motion of atoms and molecules in the solid and some information has in recent years been obtained from X-ray studies on the distribution of bonding-electron densities in molecules.

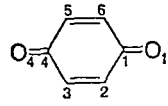
II. MOLECULAR GEOMETRY OF QUINONES

The majority of available results are for 1,4-benzoquinones, 1,4-naphthoquinones and 9,10-anthraquinones. We treat each of these groups separately, then turn to other molecules which do not belong to any of these categories. For comparison purposes we include some molecules which are not quinones, in a formal sense, but are closely related to them. The above groups of compounds may be usefully further subdivided: the introduction of —OH and $—NH_2$ substituents into the quinone moiety can affect not only the intermolecular interactions but also the molecular geometry, with the possibility of tautomerization as a limit. Even more drastic changes in the molecule may be found in the salts of the hydroxy- and amino-derivatives. Our subdivision is thus into two groups: one consists of hydroxy- and amino-substituted quinones and their salts, the second of all the other quinones. Finally we also consider two-component complexes of which one component is a quinone molecule.

In the following pages a number of tables of bond lengths and angles will be given. When a particular entry is omitted this implies that it is equal to a given entry, by symmetry. When the molecule has a centre of symmetry this is not stated specifically; when the symmetry is other than an inversion centre it is given.

A. Benzoquinones

The numbering system of benzoquinone is shown in **1**:



(1)

I. 1,4-Benzoquinones (not hydroxy- or amino-substituted)

In Table 1 we list the bond lengths and angles of 1,4-benzoquinones.

TABLE 1

(*a*) *Bond distances in* 1,4-*benzoquinones* (Å)

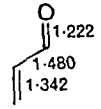
Compound	C_1-C_2	C_3-C_4	C_4-C_5	C_6-C_1	C_2-C_3	C_5-C_6	C_1-O_1	C_4-O_4	Reference
Unsubstituted	1·467	—	—	1·467	1·312	—	1·218	—	1
2,3-Dimethyl	1·47	1·48	1·44	1·47	1·33	1·30	1·21	1·22	2
2,5-Dimethyl[a, b]	1·502	—	—	1·480	1·347	—	1·224	—	3
	1·501	—	—	1·483	1·347	—	1·221	—	3
2,6-Dimethyl	1·484	1·458	1·461	1·483	1·336	1·336	1·224	1·229	4
2,3,5,6-Tetramethyl[a, b]	1·487	—	—	1·495	1·344	—	1·233	—	5
(duroquinone)	1·495	—	—	1·493	1·337	—	1·231	—	5
2-Chloro	1·505	1·473	1·487	1·479	1·346	1·340	1·226	1·227	6
2,3-Dichloro[b, c]	1·492	—	—	1·473	1·350	1·335	1·222	—	7
2,5-Dichloro[b]	1·503	—	—	1·470	1·340	—	1·222	—	7
2,6-Dichloro[b]	1·485	1·480	1·482	1·486	1·327	1·337	1·213	1·217	8
2,3,5,6-Tetrachloro[d] (chloranil)	1·477	—	—	—	1·342	—	1·195	—	9
2,3,5,6-Tetrachloro[b, d] at 110 K	1·489	—	—	1·491	1·344	—	1·211	—	10
2,5-Dibromo	1·431	—	—	1·451	1·377	—	1·241	—	11
2-Chloro-5-bromo[e]	1·457	—	—	1·461	1·389	—	1·277[f]	—	11
2-Methyl-5,6-dimethoxy	1·501	1·462	1·464	1·478	1·335	1·368	1·216	1·241	12
2-Methyl[f]	—	1·47	1·32	1·47	—	1·47	1·22	1·22	13

(*b*) *Bond angles* (°)

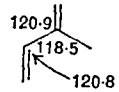
Compound	C_1 (at C_6, C_2)	C_4 (at C_3, C_5)	C_2 (at C_1, C_3)	C_3 (at C_2, C_4)
Unsubstituted	117·7	—	121·0	—
2,3-Dimethyl	119·0	120·0	120·7	118·9
2,5-Dimethyl[a, b]	118·6	—	123·4	—
	118·5	—	123·1	—
2,6-Dimethyl	119·5	117·8	119·0	122·4
2,3,5,6-Tetramethyl (duro-quinone)[a, b]	119·8	—	120·3	—
	119·6	—	120·3	—
2-Chloro	116·6	118·8	121·6	120·4
2,3-Dichloro[b, c]	117·1	—	121·0	—
2,5-Dichoro[b]	117·1	—	121·8	—
2,6-Dichloro[b]	115·4	117·6	122·4	121·3
2,3,5,6-Tetrachloro (chloranil)[d]	117·3	—	121·4	—
2,3,5,6-Tetrachloro at 110 K [b, d]	117·4	—	121·3	121·2
2,5-Dibromo	120·4	—	122·0	—
2-Chloro-5-bromo[e]	119·4	—	119·5	—
2-Methyl-5,6-dimethoxy	119·8	120·6	118·2	122·2
2-Methyl[f]	119	118	120	121

[a] Two symmetry-independent molecules.
[b] Results corrected for libration.
[c] Molecule on twofold axis which cuts C=C bonds.

The unweighted mean values of the room-temperature structures are shown in **2** and **3**. The average values for the unsubstituted C = C and



(2)



(3)

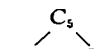
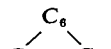
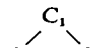
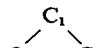
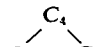
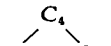
C—C bond lengths are 1·322 and 1·471 Å, respectively. The 'scatters' in these lengths

$$= \left(\sum_n (\bar{r} - r_i)^2/(n-1)\right)^{\frac{1}{2}}$$

are 0·02 and 0·01 Å respectively. For the system  , where X = Cl the corresponding values (length, scatter) are for C=C 1·338 (0·009) Å and for C—C 1·487 (0·01) Å. For X = Me these values are 1·342 (0·006) and 1·489 (0·010) Å, respectively. Thus within 0·02 Å the benzoquinone skeleton has *mmm* symmetry, even when unsymmetrically substituted.

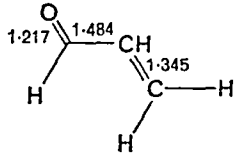
The average bond lengths of the O=C—C=C of the benzoquinone molecule agree to within 0·005 Å with the lengths of the corresponding

TABLE 1 (cont.)

					
—	121·4	121·3	121·0	—	—
121·0	120·4	121·8	119·3	119·8	120·2
—	122·3	121·3	120·2	—	—
—	122·3	121·4	120·1	—	—
122·5	118·9	120·4	120·1	120·8	121·4
—	119·9	119·8	120·4	—	—
—	120·1	120·7	119·7	—	—
120·4	122·2	121·8	121·6	120·7	120·5
—	121·8	121·3	121·6	—	—
—	121·0	121·9	121·0	—	—
120·0	123·2	121·9	122·7	121·3	121·1
—	—	121·4	—	—	—
—	—	121·5	121·1	—	—
—	117·9	120·8	118·4	—	—
—	121·1	120·9	119·6	—	—
118·8	120·5	119·3	120·9	119·5	119·9
121	121	—	—	—	—

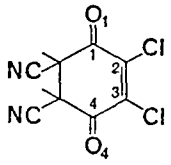
[d] Average values of C=C, C—C, C=O and angles.
[e] Cl and Br disordered.
[f] Not included in averaging.

bonds of acrolein **4**[14], as determined by electron diffraction. On the basis of this favourable match we may reasonably consider the quinone molecule to consist of two acrolein units.



(4)

It is of interest that if one of the ring double bonds is saturated the dimensions of the remaining O=C—C=C—C=O system are not much altered. Pointer and coworkers[15] describe the Diels–Alder adducts obtained from DDQ and cyclopentadiene and a cyclohexadiene. These adducts contain the system **5**, in which the bond lengths are (pentadiene adduct first): $C_1—O_1$, 1·19, 1·20; $C_4—O_4$, 1·25, 1·22; $C_1—C_2$, 1·48, 1·48; $C_3—C_4$, 1·48, 1·43; $C_2—C_3$, 1·30, 1·35 (Å).

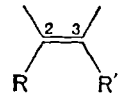


(5)

The ring systems in the unsubstituted quinone and its methyl-substituted derivatives are planar within the precision of the analyses. In the halo-substituted derivatives Rees[16] found that the halogen and oxygen atoms are displaced to opposite sides of the carbon ring and carry with them the carbon atoms to which they are attached. It is not clear that this suggested distortion of the carbon ring is significant; in the highly precise analysis of the structure of chloranil at low temperature the displacements of the carbon atoms from the mean plane of the ring were found to be less than the standard deviations in the atomic positions[10].

There are, however, effects which are more firmly established and deserve comment. First, we note that the average internal bond angle at C_1 (and at C_4) is smaller than the 120° expected for pure sp^2 hybridization; in fact, in Table 1 all but three entries for these angles are less than 120°. This is generally true of the angle 'opposite a double bond'; various interpretations have been given, some based on non-bonded interactions between the attached atoms (e.g. Bartell[17]) and others on the state of hybridization of the central atom. Further, as pointed out by Rabinovich,

Schmidt and Ubell[5], in-plane distortions, particularly of angles, occur more readily than out-of-plane ones: thus, in



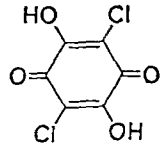
the steric repulsion between R and R′ tends to enlarge the angles $R—C_2—C_3$ and $C_2—C_3—R'$. In the methyl-dimethoxy-quinone these angles are about 123°.

Hirshfeld and Rabinovich[3] note that when the hydrogen attached to C_2 is replaced by a methyl the two ring bonds to C_2 are lengthened by 0·025 Å and the angle between them is decreased by 2°. These effects could be due, in part at least, to a change in hybridization at C_2 which is more symmetric when attached to three carbons than when attached to two carbons and a hydrogen.

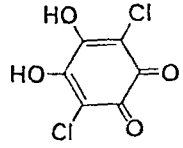
An additional point requires comment: the C=O length is appreciably shorter in the room-temperature structure of chloranil than in the other structures. However, the bond is of 'normal' length at 110 K at which temperature the molecular packing is essentially identical to that at room temperature; it therefore seems that the significance of the room-temperature length is questionable, possibly due to the fact that the bond lengths were not corrected for thermal motion. One is led to the same conclusion regarding the discrepancy in out-of-plane distortions in the structures at the two temperatures, as discussed above.

2. Hydroxy- and amino-substituted benzoquinones and their salts

The bond lengths and angles of these molecules are given in Table 2. These materials are discussed separately as the substituents may introduce qualitatively different influences on the molecular geometry. In some cases there is the possibility of tautomerization; thus, for example, 2,5-dihydroxy-3,6-dichloro-1,4-benzoquinone (**6**) could in fact be 4,5-dihydroxy-3,6-dichloro-1,2-benzoquinone (**7**). The names listed in Table 2



(6)



(7)

appear best to describe the materials. The hydrated materials can be 'true' hydrates or hydronium salts. Further, in the salts the question arises

as to whether charge delocalization occurs, causing a number of bonds to become equivalent and leading to an increase in the symmetry of the ion.

Except for the salts all molecules listed in Table 2 lie on a crystallographic inversion centre; in some of these cases chemically equivalent

TABLE 2. Bond distances and angles in hydroxy- and amino-1,4-benzoquinones and their salts

(*a*) *Bond distances* (Å)

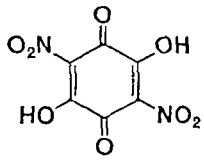
Compound	C_1-C_2	C_3-C_4	C_4-C_5	C_6-C_1	C_2-C_3	C_5-C_6	C_1-O_1	C_4-O_4	Reference
2,5-Dihydroxy-3,6-dichloro (chloranilic acid) (9)	1·501	—	—	1·445	1·346	—	1·222	—	18
Chloranilic acid dihydrate	1·512	—	—	1·446	1·345	—	1·229	—	19
Ammonium chloranilate monohydrate	1·535	—	—	1·407	1·401	—	1·243	—	20
2,5-Dihydroxy-3,6-dinitro ammonium salt (ammonium nitranilate)	1·551	—	—	1·434	1·436	—	1·221 1·218	—	21
Nitranilic acid hexahydrate	1·559	—	—	1·411	1·427	—	1·234 1·222	—	22
2,3,5,6-Tetrahydroxy	1·476	—	—	1·480	1·342	—	1·229	—	23
2,5-Diamino-3,6-dichloro (10)	1·522	—	—	1·409	1·383	—	1·237	—	24
2,5-Dihydroxy potassium salt	1·53	—	—	1·40	1·38	—	1·28 1·27	—	25
2-Hydroxy-3,5-dimethyl-6-chloromethyl (12)	1·471	1·474	1·503	1·475	1·340	1·339	1·225	1·214	26

(*b*) *Bond angles* (°)

Compound	C_1 (C_6 C_2)	C_4 (C_3 C_5)	C_2 (C_1 C_3)	C_3 (C_2 C_4)
2,5-Dihydroxy-3,6-dichloro (chloranilic acid) (9)	117·9	—	120·6	—
Chloranilic acid dihydrate	118·2	—	119·8	—
Ammonium chloranilate monohydrate	118·7	—	118·0	—
2,5-Dihydroxy-3,6-dinitro ammonium salt (ammonium nitranilate)	119·3 119·7	—	119·7 119·3	—
Nitranilic acid hexahydrate	118·5 119·4	—	119·4 118·5	—
2,3,5,6-Tetrahydroxy	119·6	—	120·9	—
2,5-Diamino-3,6-dichloro (10)	117·8	—	121·0	—
2,5-Dihydroxy potassium salt	120 119	—	119 120	—
2-Hydroxy-3,5-dimethyl-6-chloromethyl (12)	119·5	120·4	122·3	118·0

bonds which are not related by the centre of symmetry nevertheless have nearly the same lengths so that the molecule approximates a higher symmetry.

On the basis of the molecular geometries, the materials do not form a homogeneous group, and separate consideration must be given to the salts and non-salts. In this connexion we note that what we have listed as nitranilic acid **8** hydrate has dimensions closer to those of the salts and is in fact hydronium nitranilate. The non-salts are clearly 1,4-benzoquinones (C=C 1·350, C—C 1·488 Å) with C—OH about 1·32 Å and C—NH about 1·34 Å. The tetrahydroxy-*p*-benzoquinone has bond lengths similar to those of the molecules of Table 1 and does not show any marked effect due to the substituents. On the other hand, chloranilic acid, **9**, its dihydrate and the amino derivative **10** all have comparatively long O:C—C·OH bonds (ca. 1·51 Å), whilst the second C—C:O is significantly shorter (ca. 1·43 Å). Kulpe[24] suggests that the system is analogous to a coupled polymethine, **11**.



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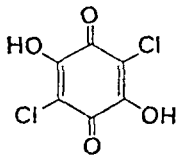

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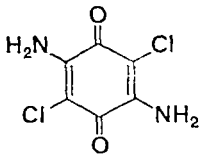
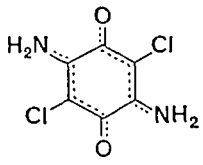


(10)

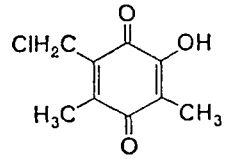
In the chloromethyl derivative **12** there are signs of steric interference: the methyl carbon attached to C_5 is 0·13 Å out of the mean plane and

TABLE 2 (cont).

C_5 / C_4 C_6	C_0 / C_5 C_1	C_1 / O_1 C_2	C_1 / O_1 C_6	C_4 / O_4 C_3	C_4 / O_4 C_5
—	121·2	118·2	123·8	—	—
—	122·0	117·6	124·2	—	—
—	123·5	116·1	125·2	—	—
—	121·1	114·5 114·5	125·9 126·3	—	—
—	122·1	114·6 114·8	126·9 125·8	—	—
—	119·5	119·8	120·6	—	—
—	121·2	117·6	124·8	—	—
—	120	118 116	122 124	—	—
119·8	119·8	118·8	121·6	120·3	119·3



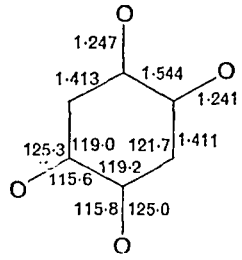
(11)



(12)

deviations of the ring from planarity appear to be significant. An additional manifestation of this hindrance is the fact that the angles $CH_3—C_5—C_6$ and $ClCH_2—C_6—C_5$ are about 124° whereas the exocyclic angles adjacent to them are near 116°.

The quinone frameworks in the salts all have symmetry approximating *mmm*, with the lengths of adjacent C—O bonds being almost equal. The O·C—C·O bonds are long, approaching the length of a $C(sp^2)—C(sp^2)$ single bond, while $C_2—C_3$ (double bond) is appreciably longer than those of materials previously discussed. These observations are also compatible with the 'coupled azomethine' picture[27,28]. The average dimensions of the four salts are shown in **13**.

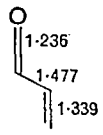


(13)

3. Benzoquinone molecular complexes

We shall now consider the molecular dimensions of the 1,4-benzoquinone fragment in its complexed form. The values are given in Table 3. For a fuller treatment of the structures of charge-transfer complexes see the recent review by Herbstein[29].

The average dimensions are given in **14** and **15** and match well the average values given in **2** and **3**. The calculated scatters in bond lengths,



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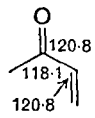


(15)

not including the chloranil complexes with hexamethylbenzene and [8-hydroxyquinolato-Pd(II)]$_2$, are: C=O, 0·07; C=C, 0·02; C—C, 0·02 Å. The high scatter in C=O bond length is reduced to a more reasonable value of 0·015 Å if the data from the structures phloroglucinol: (benzoquinone)$_2$ and *p*-chlorophenol: benzoquinone are also eliminated. The average C=O bond length with these four structures excluded is 1·219 Å in close agreement to that found for the uncomplexed benzoquinones. Even under these circumstances, however, the scatter for the complexed benzoquinones is higher than for the uncomplexed molecules.

Sakurai[31] has interpreted the difference between the lengths of the bonds C_1—C_2 (1·487 Å) and C_3—C_4 (1·447 Å) in triclinic quinhydrone as due to the effects of hydrogen bonding between benzoquinone and hydroquinone. A similar difference in bond length was also found in the structure of monoclinic quinhydrone analysed by Matsuda, Osaki and Mitta[43]. However, a more precise analysis of the monoclinic modification by Sakurai[30] shows that these bonds are equal in length (1·492, 1·488 Å). Moreover, in the structure of phenoquinone which shows the same hydrogen bonding pattern as hydroquinone, Sakurai[30] reports C_1—C_2 and C_3—C_4 bond lengths of 1·491 (0·011) and 1·478 (0·011) Å. The difference between these two lengths is equal to one standard deviation. Therefore the differences are probably not real in triclinic quinhydrone; moreover, the hydrogen bonding does not seem to exert an observable effect on the C—C bond lengths of the benzoquinone fragment.

On the basis of a series of crystallographic studies of barbiturates Craven and Vizzini[44] have noted that the C=O bond length is increased by ~0·01 Å if the oxygens participate in hydrogen bonding. It would be interesting to see if such an effect exists also in these complexes, but these analyses are not sufficiently precise to warrant such comparisons.

4. 'Modified' benzoquinones

In this section we turn to some quinone derivatives in which the carbonyl oxygen has been replaced by another function. The data for these compounds are listed in Table 4.

The data for TCNQ agree well with calculations using simple Hückel MO functions. The geometric features of the dicyanoethylene group are essentially identical to those found in tetracyanoethylene[45,46]. The molecule has approximately *mmm* symmetry. The only outstanding feature arrived at by comparing the bond lengths and angles with those of Table 1 is the relative shortness of the C—C bonds of the ring in TCNQ.

An interesting feature of the quinone oximes is their predilection to chromoisomerism, i.e. they tend to be dimorphic with the different forms

TABLE 3. Molecular dimensions of complexed 1,4-benzoquinones

(*a*) *Bond lengths* (Å)

Complex	C_1-C_2	C_3-C_4	C_4-C_5	C_6-C_1	C_2-C_3	C_5-C_6	C_1-O_1	C_4-O_4	Reference
1,4-Benzoquinone: phenol[a, b] (phenoquinone)	1·478	1·491	—	—	1·343	—	1·235	—	30
1,4-Benzoquinone: hydroquinone[a, b]									
(quinhydrone, triclinic)	1·487	1·447	—	—	1·335	—	1·234	—	31
(quinhydrone, monoclinic)[a, b]	1·492	1·488	—	—	1·339	—	1·224	—	30
1,4-Benzoquinone: resorcinol[a, b]	1·485	1·468	—	—	1·354	—	1·233	—	32
(1,4-Benzoquinone)$_2$:	1·48	1·51	—	—	1·38	—	1·25	—	33
	1·43	1·46	—	—	1·34	—	1·29	—	33
phloroglucinol[a, b, c]	1·48	1·52	1·44	1·47	1·38	1·30	1·26	1·30	33
1,4-Benzoquinone: *p*-chlorophenol[b]	1·50	1·43	1·46	1·46	1·34	1·34	1·17	1·23	34
1,4-Benzoquinone: (*p*-chlorophenol)$_2$ [a, b]	1·46	1·51	—	—	1·35	—	1·22	—	35
1,4-Benzoquinone: thymine	1·453	1·483	—	—	1·330	—	1·208	—	36
Fluoranil: pyrene	1·496	1·478	—	—	1·322	—	1·197	—	37
Chloranil: hexamethylbenzene[d, e]	1·400	1·435	—	—	1·343	—	1·327	—	38
Chloranil: tetramethyl-*p*-phenylenediamine	1·459	1·466	—	—	1·350	—	1·230	—	39
Chloranil: (tetramethylbenzidine)$_2$	1·478	1·496	—	—	1·331	—	1·209	—	40
Chloranil: (8-hydroxyquinoline)$_2$	1·47	1·51	—	—	1·30	—	1·20	—	41
Chloranil: [8-hydroxyquinolato-Pd(II)]$_2$	1·43	1·55	—	—	1·32	—	1·22	—	42

(*b*) *Bond angles* (°)

Complexes	C_1 (C_6 C_2)	C_4 (C_3 C_5)	C_2 (C_1 C_3)	C_3 (C_2 C_4)
1,4-Benzoquinone: phenol[a, b] (phenoquinone)	118·0	—	121·8	120·1
1,4-Benzoquinone: hydroquinone[a, b]				
(quinhydrone, triclinic)	118·9	—	119·9	121·2
(quinhydrone, monoclinic)[a, b]	117·8	—	120·6	121·5
1,4-Benzoquinone: resorcinol[a, b]	118·8	—	120·6	120·5
(1,4-Benzoquinone)$_2$:	123	—	118	119
phloroglucinol[a, b, c]	121	—	118	121
	120	124	123	113
(1,4-Benzoquinone)$_2$: *p*-chlorophenol[b]	118	118	118	124
1,4-Benzoquinone: (*p*-chlorophenol)$_2$ [a, b]	118	—	122	119
1,4-Benzoquinone: thymine	116·9	—	124·8	118·2
Fluoranil: pyrene	114·0	—	122·5	123·5
Chloranil: hexamethylbenzene[d, e]	120	—	115	125
Chloranil: tetramethyl-*p*-phenylenediamine	114·1	—	122·7	123·2
Chloranil: (tetramethylbenzidine)$_2$	114·7	—	122·3	123·5
Chloranil: (8-hydroxyquinoline)$_2$	117	—	125	118
Chloranil: [8-hydroxyquinolato-Pd(II)]$_2$	116	—	124	120

[a] Intermolecular hydrogen bond to O_1. [b] Intermolecular hydrogen bond to O_4.

[c] Asymmetric unit contains two formula units of benzoquinone constituted as follows: two crystallographically independent half-molecules, each lying on a centre of inversion, and one complete molecule at a general position. Thus the structural unit is best written as $C_6H_3(OH)_3:(C_3H_2O)_2:C_6H_4O_2$.

having different colours: a frequent combination is orange versus green. The question arises as to whether this colour difference is associated with tautomeric differences, since it has been shown that these oximes and the corresponding nitrosophenols interconvert in solution[47]. In fact, all the oximes listed here crystallize with their molecules in the quinone-oxime form, as can be seen by considering their bond lengths. However, in a number of cases it has been shown that the molecules of the two forms are geometric isomers about the C=N bond. Thus in the α-form of the oxime acetate the acetate group is *syn* to chlorine, whereas in the β-form it is *anti*. The (α)-2-chloro-5-methyl-derivative has the oxime group *syn* with respect to chlorine; the (β) form is probably *anti*[57]. The chloroethoxy-quinone has the oxime *anti* with respect to C=O, whereas in the propoxy derivative the relationship is *syn*.

In the oximes of 1,4-benzoquinone the scatter in the bond lengths is very large and it is probably inappropriate to average them for comparison to the previous groups. However, the analyses of the *ortho*-quinone oximes are more recent and relatively more precise. They give the averages shown in **17** and **18**. These agree fairly well with the corresponding dimensions of the 1,4-benzoquinones. We note the small angle 'opposite' the C=O bond.

Some other points deserve comment. The bond lengths of *p*-methoxy-indophenol-*N*-oxide (**16**)[56] are in good agreement with those calculated by use of Pople's SCF method. The bond orders obtained for the quinone ring by Mulder and Lugt[58] are (C_1 attached to O): C_1—O, 0·762; C_1—C_2,

TABLE 3 (cont).

C_5 / C_4 C_6	C_6 / C_5 C_1	C_1 / O_1 C_2	C_1 / O_1 C_6	C_4 / O_4 C_3	C_4 / O_4 C_5
—	—	121·1	120·9	—	—
—	—	120·1	121·0	—	—
—	—	121·5	120·7	—	—
—	—	119·6	121·6	—	—
—	—	122	114	—	—
—	—	117	122	—	—
120	118	120	119	117	119
121	121	119	123	123	119
—	—	122	119	—	—
—	—	123·0	120·0	—	—
—	—	122·7	123·3	—	—
—	—	119	121	—	—
—	—	123·0	122·9	—	—
—	—	122·6	122·7	—	—
—	—	125	118	—	—
—	—	124	120	—	—

[d] Not included in averaging.
[e] Calculated from reported parameters.

TABLE 4. Molecular dimensions of some benzoquinone derivatives

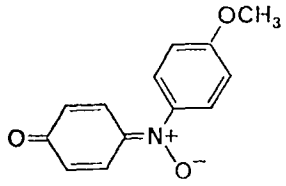
(*a*) *Bond lengths* (Å)

Compound	C_1-C_2	C_3-C_4	C_4-C_5	C_6-C_1	C_2-C_3	C_5-C_6	C_1-O_1	C_4-O_4	Reference
							(C_1=C)		
7,7,8,8-Tetracyano-quinodimethane (TCNQ)	1·446	—	—	1·450	1·346	—	1·374	—	48
								(C_4=N)	
2-Chloro-5-methyl-1,4-benzoquinone-4-oxime (α-form)	1·48	1·48	1·48	1·45	1·29	1·33	1·21	1·28	49
3-Methyl-1,4-benzo-quinone-4-oxime	1·47	1·46	1·46	1·44	1·33	1·34	1·20	1·25	50
2-Chloro-1,4-benzo-quinone-4-oxime acetate (β-form)[a]	1·48	1·51	1·46	1·54	1·33	1·38	1·21	1·37	51
(α-form)	1·47	1·53	1·48	1·49	1·32	1·35	1·20	1·29	52
							(C_1=N)	(C_2=O)	
4-Methoxy-1,2-benzo-quinone-1-oxime (α-form)	1·51	1·32	1·46	1·40	1·46	1·36	1·22	1·23	53
4-*n*-Propoxy-1,2-benzoquinone-1-oxime (β-form)	1·482	1·357	1·458	1·442	1·410	1·344	1·319	1·270	54
4-(2′-Chloroethoxy)-1,2-benzoquinone-1-oxime (α-form)[b]	1·502	1·358	1·457	1·435	1·430	1·345	1·306	1·253	55
							(C_1=N)		
p-Methoxyindophenol-*N*-oxide (**16**)	1·437	1·454	1·456	1·438	1·357	1·357	1·357	1·248	56

(*b*) *Bond angles* (°)

Compound	C_1 (centre of C_6, C_2)	C_4 (centre of C_3, C_5)	C_2 (centre of C_1, C_3)	C_3 (centre of C_2, C_4)
7,7,8,8-Tetracyanoquinodimethane (TCNQ)	118·3	—	121·0	—
2-Chloro-5-methyl-1,4-benzo-quinone-4-oxime (α-form)	114	114	123	121
3-Methyl-1,4-benzoquinone-4-oxime	114	116	121	122
2-Chloro-1,4-benzoquinone-4-oximeacetate (β-form)	115	121	125	110
(α-form)	116	117	120	117
4-Methoxy-1,2-benzoquinone-1-oxime (α-form)	120	122	114	120
4-*n*-Propoxy-1,2-benzoquinone-1-oxime (β-form)	119·2	122·7	118·7	119·6
4-(2′-Chloroethoxy)-1,2-benzo-quinone-1-oxime (α-form)[b]	119·6	122·1	117·0	120·5
p-Methoxyindophenol-*N*-oxide (**16**)	119·8	117·7	120·1	121·1

[a] Possible error in bond lengths ±0·07 Å.
[b] At −180°C.



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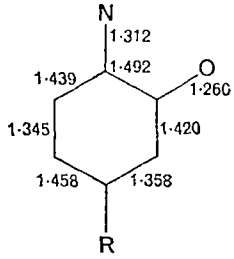

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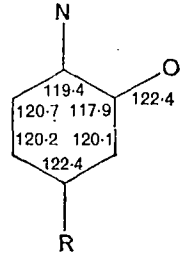


(18)

0·425; C_2—C_3, 0·849; C_3—C_4, 0·387; C_4—N, 0·593; C_4—C_5, 0·379; C_5—C_6, 0·853; C_6—C_1, 0·422.

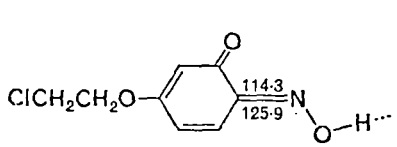
In several cases it is found that the two exocyclic angles at the C attached to N are not equal. Van Oijen and Romers[55] interpret this as resulting from steric repulsion between H and the oxime-oxygen, as in **19***. In the

* The authors quote F. L. Hirshfeld in support of this interpretation. In fact the paper cited suggests that the distortion may be due to repulsion between C_1 and the oxime oxygen. Dr. Hirshfeld (private communication) points out that there would be poorer overlap of σ orbitals on N and O in **19** as compared to **20**, and this should lead to a more strained bond in the former; in keeping with this the N—O bond lengths are 1·365 and 1·353 Å, respectively. The conformation in **19** is presumably stabilized by the intermolecular hydrogen bonding.

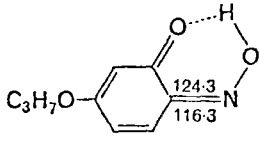
TABLE 4 (cont.)

C_5 / C_4 C_6	C_6 / C_5 C_1	C_1 / O_1 C_2	C_1 / O_1 C_6	C_4 / O_4 C_3	C_4 / O_4 C_5
		($C{=}C_1{-}C_2$)	($C{=}C_1{-}C_6$)		
—	120·7	121·0	120·7	—	—
				($N{-}C_4{-}C_3$)	($N{-}C_4{-}C_5$)
123	121	122	123	123	123
122	125	123	123	119	125
117	123	122	125	116	125
122	120	122	123	127	114
		($N_1{-}C_1{-}C_2$)	($N_1{-}C_1{-}C_6$)	($O_2{-}C_2{-}C_1$)	($O_2{-}C_2{-}C_3$)
118	120	115	123	122	122
119·9	120·9	124·3	116·5	118·8	122·6
120·4	120·3	114·3	125·9	120·3	122·7
121·0	120·2	118·4	121·7	121·1	121·2

case of the propoxy compound **20** [54], unlike that of **19**, the oxime group is *syn* to the carbonyl and the pattern of angles about the C=N bond is reversed. The oxime-hydroxyl participates in an intramolecular hydrogen

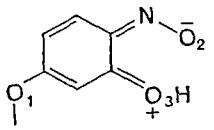


(19)

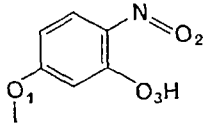


(20)

bond. Although the molecule apparently may be formally classified as an oxime, its absorption spectrum and pleochroism suggest a nitroso structure. If one considers the possibility of internal proton dissociation as in **21** and **22**, then the contribution from **22** can account for the nitroso absorption.



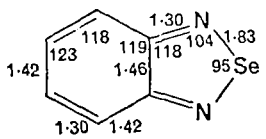
(21)



(22)

In fact the final electron density map which indicates that the hydrogen is midway between the two oxygen atoms is in accordance with this model. The C—O_3 bond length (1·270 Å) is intermediate between that of a normal carbonyl [average found for benzoquinones (1·222 Å)] and a C (arom)—O 1·36 Å [59], further adding weight to this argument.

The structures of three compounds closely related to the 1,2-benzoquinones have been analysed by Luzzati[60]. The dimensions of two of these molecules are given below (**23** and **24**); the molecules are planar and are



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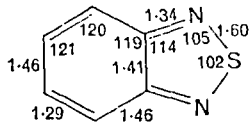


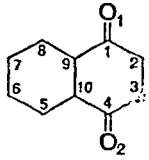
(24)

symmetric about the long molecular axis. The corresponding material with oxygen replacing sulphur and selenium was also treated; this is not described here because of the rather large probable error in atomic positions (±0·07 Å).

To complete this section on the benzoquinones we list their crystallographic constants in Table 5.

B. Naphthoquinones

The numbering systems for 1,4- and 1,2-naphthoquinones are given in **25** and **26**, respectively.



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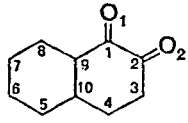
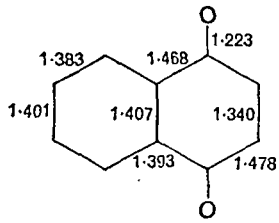


(26)

1. 1,4-Naphthoquinones (not hydroxy- or amino-substituted)

The molecular dimensions of this class of naphthoquinones are listed in Table 6. The mean values of the bond lengths, assuming mirror symmetry about the long molecular axis (mid-points of $C_2—C_3$ and $C_6—C_7$), are shown in **27**.



(27)

Many of the entries in the table for the 2-bromo-3-methyl compound differ rather drastically from average or expected values. The structure is disordered at the methyl and the bromine and the agreement factor (R index) is 0·16, which is rather high[68]. A set of atomic co-ordinates for the 2-chloro-3-methyl derivative has been published[72]. On the basis of cell constants and space group this structure appears to be isomorphous with the 2-bromo-3-methyl compound (see Table 9); however, bond lengths and angles calculated from the reported atomic co-ordinates are chemically unreasonable. The co-ordinates resemble those given for the bromo-methyl derivative if the following transformation is made (reported co-ordinates first): $z \rightarrow x$; $y \rightarrow y$; $1-x \rightarrow z$. The latter set of co-ordinates also failed to give reasonable molecular dimensions; consequently the structure is omitted from further discussion.

Comparison of the bond lengths with the average values for the 1,4-benzoquinones, **2**, reveals a number of interesting points. We note, first, that the framework $O_1—C_1—C_2—C_3—C_4—O_4$ is essentially identical in the two cases; thus, geometrically this system is little affected whether

Compound	a (Å)	b (Å)	c (Å)	β or α, β, γ (°)	Z[a]	Space group	Reference
1,4-BQ[b]	7·055	6·795	5·767	101·5	2	$P2_1/a$	1
2-Methyl-1,4-BQ	6·520	14·206	6·719	—	4	$Cmc2_1$	13
2,5-Dimethyl-1,4-BQ	4·013	9·366	9·738	93·50, 101·36, 98·57	2	$P\bar{1}$	3
2,3-Dimethyl-1,4-BQ	9·01	12·38	7·36	118	4	$P2_1/c$	2
2,6-Dimethyl-1,4-BQ	17·10	3·98	10·66	93·5	4	$P2_1/a$	4
2,3,5,6-Tetramethyl-1,4-BQ	6·924	8·851	9·536	119·74, 116·58, 72·03	2	$P\bar{1}$	5
2-Chloro-1,4-BQ	5·256	20·081	5·701	—	4	$P2_12_12_1$	6
2,3-Dichloro-1,4-BQ	5·650	—	21·220	—	4	$P4_12_12$	7
2,5-Dichloro-1,4-BQ	6·018	5·469	10·103	92·23	2	$P2_1/c$	7
2,6-Dichloro-1,4-BQ	9·061	5·500	17·740	126·5	4	$P2_1/c$	8
2,3,5,6-Tetrachloro-1,4-BQ	8·708	5·755	8·603	105·8	2	$P2_1/a$	9
2,3,5,6-Tetrabromo-1,4-BQ	8·624	6·173	9·027	74·2	2	$P2_1/c$	61
2,5-Dibromo-1,4-BQ	10·214	5·654	6·173	92·0	2	$P2_1/a$	11
2-Chloro-5-bromo-1,4-BQ	10·573	5·499	6·099	93·2	2	$P2_1/a$	11
2-Methyl-5,6-dimethoxy-1,4-BQ	28·008	3·948	16·445	102·53	8	$C2/c$	12
Chloranilic acid	10·025	5·544	7·566	122·9	2	$P2_1/a$	18
Chloranilic acid dihydrate	8·617	10·386	5·203	104·8	2	$P2_1/c$	19
Ammonium chloranilate monohydrate	16·988	4·780	14·101	118·01	4	$C2/c$	20
Ammonium nitranilate	4·712	7·000	7·847	111·14, 93·45, 102·24	1	$P\bar{1}$	21
Nitranilic acid hexahydrate	3·657	19·399	9·184	94·28	2	$P2_1/c$	22

oxime							
(α) 2-Bromo-5-methyl-1,4-BQ-4-oxime[c]	3·91	13·6	14·2	90	4	$P2_1/c$	49
(β) 2-Chloro-1,4-BQ-4-oxime acetate	7·14	19·88	6·80	113	4	$P2_1/n$	51
(β) 2-Chloro-5-methyl-1,4-BQ-oxime	19·3	3·80	38·6	120	4	A_2	57
(β) 2-Bromo-5-methyl-1,4-BQ-4-oxime	19·1	3·89	37·3	114·6	4	$P2/b$	57
3-Bromo-1,4-BQ-4-oxime	3·93	13·5	12·5	90·5	4	$P2_1/c$	50
3-Chloro-1,4-BQ-4-oxime	3·87	13·3	12·5	90	4	$P2_1/c$	50
p-Methoxyindophenol-*N*-oxide[d]	23·91	12·15	7·403	—	8	$Pbca$	56
(α) 4-Methoxy-1,2-BQ-1-oxime	17·11	3·80	10·67	—	4	$P2_12_12_1$	53
(β) 4-*N*-Propoxy-1,2-BQ-1-oxime[e]	10·64	12·57	6·63	95·5	4	$P2_1/c$	54
(α) 4-(2′-Chloroethoxy)-1,2-BQ-1-oxime	4·12	10·83	10·35	104·8	4	$P2_1/c$	55
(α) 4-(2′-Bromoethoxy)-1,2-BQ-1-oxime	4·34	10·8	20·9	105	4	$P2_1/c$	55

[a] Number of molecules per unit cell.
[b] BQ = benzoquinone.
[c] −140°C.
[d] −180°C.
[e] −120°C.

fused to a double bond or to an 'aromatic' ring. As to this latter ring ($C_5—C_6—\ldots—C_{10}$) it is seen to be essentially a benzene ring (the best available value for the length of the C—C bond in benzene is 1·392 Å *[73]). The $C_9—C_{10}$ bond shows no sign of its participation in a quinonoid ring. For further comparison we give the average values of the molecular dimensions of naphthalene, **28** (the molecule sits on a crystallographic inversion centre)[74].

* This value was obtained by X-ray diffraction. The neutron-diffraction value is 1·398 Å.

TABLE 6. Molecular dimensions

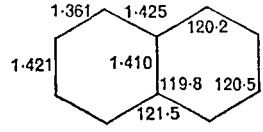
(*a*) *Bond lengths* (Å)

Compound	$C_1—C_2$	$C_3—C_4$	$C_1—C_9$	$C_4—C_{10}$	$C_2—C_3$
Unsubstituted	1·48	1·45	1·43	1·46	1·31
2-Bromo-	1·48	1·51	1·49	1·44	1·32
2-Iodo-	1·476	1·469	1·483	1·464	1·363
2,3-Dimethyl-	1·471	1·453	1·450	1·494	1·343
2,3-Dichloro-[b]	1·50	1·48	1·43	1·42	1·32
	1·48	1·47	1·49	1·49	1·34
2,3-Dibromo-	1·51	1·47	1·46	1·51	1·34
2-Bromo-3-methyl[b, c, d, e]	1·562	1·445	1·487	1·575	1·338
	1·576	1·444	1·458	1·445	1·341
2-Phenyl-[c]	1·471	1·481	1·491	1·439	1·355
2-Methyl-3-*N*-methyl-anilinomethyl-[f]	1·462	1·481	1·460	1·478	1·365
2,2′-Di(1,4-naphthoquinone)[g]	1·501	1·483	1·492	1·479	1·340

(*b*) *Bond angles* (°)

Compound	C_1 / C_9 C_2	C_4 / C_3 C_{10}	C_2 / C_1 C_3	C_3 / C_2 C_4	C_{10} / C_4 C_9	C_9 / C_1 C_{10}	C_1 / O_1 C_2	C_4 / O_4 C_3
Unsubstituted	121·5	123	120·5	117·5	117·5	118	118·5	118
2-Bromo-	116·5	119	124	118	121	119	121·5	115·5
2-Iodo-	118·1	120·4	122·1	119·1	120	119·5	120·6	116·2
2,3-Dimethyl-	121·5	120·8	119·8	120·7	117·7	119·5	119	120
2,3-Dichloro-[b]	117·5	117·5	122	120·5	122	119·5	125	113·5
2,3-Dibromo-	114	116	124	122	121	123	123	121
2-Bromo-3-methyl-[d]	121·3	108·9	107·8	139·9	118·4	123·4	122·4	126·7
	117·1	121·9	117·4	122·7	118·0	122·8	119·9	116·7
2-Phenyl-	120·4	120·1	118·1	121·5	120·0	119·8	119·9	117·1
2-Methyl-3-*N*-methyl-anilinomethyl-	120·1	120·4	121·5	119·0	119·0	119·9	120·5	119·9
2,2′-(1,4-naptho-quinone)	117·8	117·9	120·2	123·2	120·0	120·7	120·8	119·3

[a] Dimension not given in original paper.
[b] Two independent molecules in unit cell.
[c] Calculated from co-ordinates given in original paper.
[d] Not included in averaging.



(28)

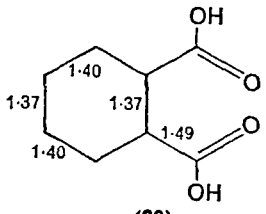
The dimensions of two other molecules are of interest in this context; the molecules are phthalic acid, **29** (point symmetry 2)[75] and tetrachlorophthalic anhydride, **30**[76]. In both cases the benzenoid dimensions of the ring are essentially maintained, while the bonds to the carbonyl carbon atoms are significantly longer.

of 1,4-naphthoquinones

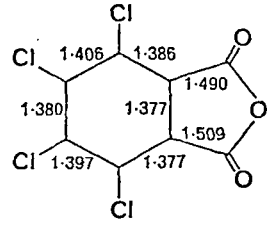
C_9—C_{10}	C_6—C_7	C_1—O_1	C_4—O_4	C_8—C_9	C_5—C_{10}	C_5—C_6	C_7—C_8	Reference
1·39	1·37	1·21	1·22	1·39	1·36	1·36	1·41	62
—[a]	1·42	1·19	1·25	1·40	1·39	1·36	1·42	63
1·393	1·411	1·228	1·243	1·365	1·421	1·356	1·366	64
1·405	1·374	1·243	1·238	1·401	1·390	1·390	1·396	65
1·36	1·36	1·23	1·22	1·41	1·39	1·37	1·38	66
1·43	1·40	1·18	1·20	1·44	1·43	1·40	1·43	66
1·42	1·43	1·17	1·19	1·41	1·42	1·37	1·37	67
1·384	1·510	1·134	1·218	1·450	1·469	1·288	1·377	68
1·383	1·352	1·279	1·176	1·509	1·377	1·364	1·446	68
1·362	1·409	1·291	1·244	1·332	1·385	1·365	1·399	69
1·403	1·449	1·223	1·219	1·382	1·366	1·371	1·370	70
1·404	1·385	1·220	1·224	1·391	1·396	1·385	1·392	71

C_1 O_1 C_9	C_4 O_4 C_{10}	C_9 C_1 C_8	C_{10} C_4 C_5	C_8 C_8 C_{10}	C_{10} C_5 C_9	C_8 C_7 C_9	C_5 C_6 C_{10}	C_7 C_6 C_8	C_6 C_5 C_7
119	118·5	—[a]	—[a]	119	119	121	121·5	119	118·5
121	124·5	—[a]	—[a]	122	117·5	118	122	118·5	120
120·5	123·2	119·2	121·1	120·4	118·4	119·4	120·6	121·5	118·1
119·5	119	—[a]	—[a]	119·5	122·2	117·5	118·2	123·2	119·6
117·5	128·5	—[a]	—[a]	117	120	122·5	121	118·5	120
123	123	—[a]	—[a]	117	120	123	121	118	119
116·2	124·1	123·4	112·0	113·2	129·4	121·7	112·7	117·9	124·4
122·9	121·3	115·7	120·1	121·5	121·8	109·2	120·5	128·0	118·8
119·6	122·6	121·8	118·9	118·4	121·1	124·8	119·4	114·9	121·3
119·4	119·7	119·9	120·1	121·0	120·9	121·5	120·5	118·4	119·6
121·3	122·7	119·1	120·4	120·1	119·6	119·6	119·7	120·1	120·8

[e] Disordered with respect to Br, Me.
[f] **34**.
[g] **33**.
[h] Angles averaged over two symmetry-independent molecules.

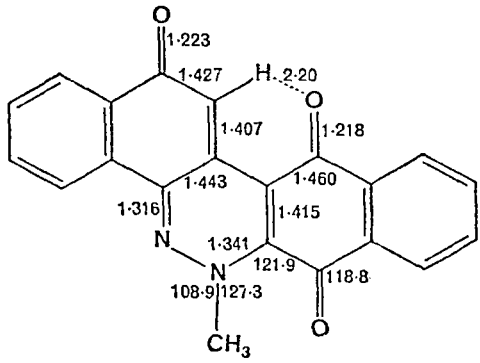


(29)



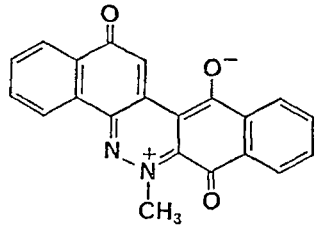
(30)

A 1,4-naphthoquinone derivative which has recently been analysed is **31**[77]. The molecule has some special features. In the central portion the



(31)

double bonds are slightly longer, single bonds shorter, than in the previously discussed quinones. This is interpreted as being due to intramolecular electron transfer from N to O, with contributions from resonance forms such as **32**. All ring atoms in the molecule lie in the same

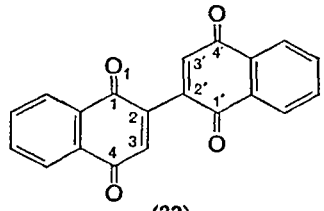


(32)

plane. However, the methyl and adjacent oxygen are overcrowded (C···O, 2·64 Å); as a result the methyl lies out of the ring plane and the angles between the two substituents are opened up from 120°.

Of the molecules listed in Table 6 all except the 2-phenyl derivative have naphthoquinone systems which are essentially planar; in the 2-phenylquinone a small deviation from planarity is reported. In this substance the phenyl ring is rotated 41° out of the best ring plane, probably to minimize the intramolecular O··· H (arom) contact. The external bond angles at C_2 are both about 121°, possibly indicating that most of the repulsion has been relieved by the rotation of the phenyl ring.

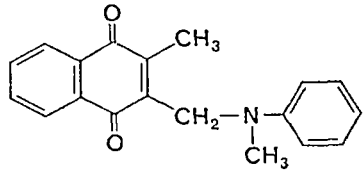
In the dinaphthoquinone **33** the external angle $C_1—C_2—C_2'$ is 117·7° and $C_3—C_2—C_2'$ is 122°. This suggests a tendency to decrease the distance



(33)

between C_2' and O_1, as has been reported for other quinones[3,78]. Here, too, the $C(sp^2)—C(sp^2)$ single-bond lengths vary according to the number of substituents other than hydrogen[3]. The internal angle at C_2 is about 3° larger than at C_3; this may also be associated with the degree of substitution at C_2. Finally, the $C_2—C_2'$ bond length (1·492 Å) is larger than usual $C(sp^2)—C(sp^2)$ single-bond lengths, suggesting little overlap of the π-electrons of the two halves of the molecule. This is consistent with the 47° twist about this bond between the two naphthoquinone moieties.

The structure of the anilino-derivative **34**[70] shows some interesting features. The dimensions of the quinone moiety are quite comparable to

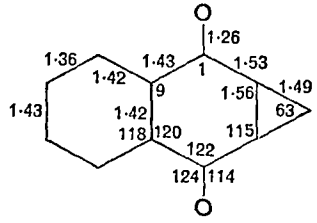


(34)

those of other quinones and to values calculated by MO methods; however, the $C_6—C_7$ bond is longer (1·449 Å) than the average value in **27**. The normals to the anilino and naphthoquinone planes make an angle of 3·5°. Of particular note is the mode of packing. The molecules stack along a twofold screw axis (*c*-axis) in such a way that the axis passes near the centre of gravity of the molecule; therefore the anilino part of one molecule

overlaps the naphthoquinone part of a neighbouring molecule in the stack, with a mean distance between planes of 3·39 Å, a value within the range found for many π-molecular complexes[79]. In such complexes anilines generally act as donors and naphthoquinones as acceptors; hence the packing arrangement suggests that this is a self-complexing molecule[80].

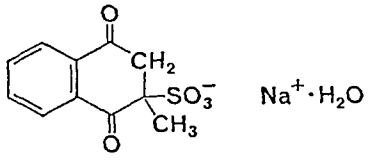
Grant and Speakman[81] analysed the structure of 2,3-dihydro-2,3-methylene-1,4-naphthoquinone (fewer than 200 reflexions were measured so that the analysis is only moderately precise). The molecule has a plane of symmetry normal to the molecular plane. Some of the dimensions are shown in **35**. Note that the two carbonyls are not parallel and that the



(35)

C_1—C_9 bond is short (1·43 Å) relative to that in the naphthoquinones; the latter possibly suggests that more conjugation between the carbonyl and the aromatic ring occurs here than in true quinones.

A second example in which the C_2—C_3 bond is saturated is provided by **36**[82]. In this case, too, the benzenoid ring geometry is near normal,

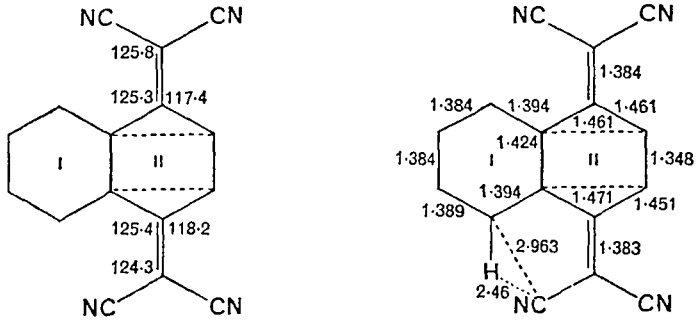


(36)

though with the 'fusing' bond (C_9—C_{10}) being rather long (1·423 Å). One carbonyl oxygen participates in octahedral co-ordination about the sodium ion. Both carbonyls are long (1·242, 1·238 Å) relative to those of quinones.

The structure of 11,11,12,12-tetracyano-1,4-naphthoquinodimethane (**37**) has recently been described[83]. In the benzenoid ring the bond lengths are all close to that of benzene (1·392 Å) except for that of the C_9—C_{10} 'fusing' bond which is 1·424 Å (compare naphthalene 1·418 Å and anthracene 1·428 Å). The exocyclic C=C bonds are 1·384 Å and are not

parallel, probably as a result of the overcrowding between cyano groups and the hydrogens of the benzenoid ring. The latter ring is essentially planar (plane I); atoms C_2, C_3, C_9, C_{10} also lie in a plane (II) which is 15·3° to I. The quinonoid ring is distorted into boat form. The $C{=}C{-}(CN)_2$ groups are near planar, tilted at 16·7 and 21·6° out of II and with the CNs all to the same side of the latter plane. The adjacent angles $C_9{-}C_1{=}C$, $C_{10}{-}C_4{=}C$, $C_1{=}C{-}CN$ and $C_4{=}C{-}CN$ are opened to relieve steric repulsion.

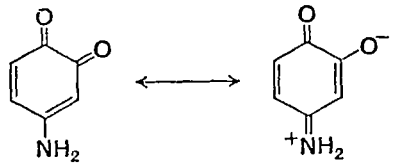


(37)

2. 1,2-Naphthoquinones

The dimensions of the molecules are given in Table 7. In all cases, except that of the methanol complex, the benzenoid sections are normal benzene rings (although we note the unreasonably short $C_7{-}C_8$ bond of the 3-chloro compound). For the first two compounds in the table the C—O bonds have the length expected for nearly 'pure' double bonds; the $C_3{-}C_4$, as well, is somewhat short compared to the 'double' bond $C_2{-}C_3$ of the 1,4-naphthoquinones. The single bonds $C_1{-}C_9$, $C_4{-}C_{10}$ and $C_2{-}C_3$ compare well with the corresponding bonds ($C_1{-}C_9$, $C_4{-}C_{10}$, $C_1{-}C_2$ and $C_3{-}C_4$) of the 1,4-naphthoquinones. However, in some respects the 1,2-quinones, particularly those which do not contain an amino group, differ substantially from the 1,4-quinones. Particularly striking is that the single bond $C_1{-}C_2$ is very long, a feature which has been noted earlier in other α-dicarbonyl compounds (see, for example, the complex between oxalic acid and acetamide where the length of the OC—CO bond is 1·53 Å [84]). This effect probably results from repulsion between the bond dipoles of the carbonyl bonds. Interestingly the exocyclic bond angles at the two carbonyls are such as to bring the two oxygens closer together; it may well be that this results from the tendency to equalize the '1...3' interactions, e.g. the interactions of C_1 and C_3 with O_2.

Introduction of the 4-amino substituent brings about some changes. $C_1—C_2$ and $C_2—C_3$ decrease, while $C_3—C_4$ and $C_2—O_2$ increase in length, all appreciably. The internal angle at C_2 appears to undergo slight expansion. These effects can be attributed to electron transfer from N to O_2 or, equivalently, to participation of the imino-alcohol structure **38**.



(38)

The shortening of $C_1—C_2$ is then associated with the change in the hybridization of O_2. The dimensions of the benzene ring appear to be unaffected by the introduction of the amino-substituent.

Benzocyclobutene-1,2-dione, which can be considered as a vinylog of both 1,2- and 1,4-naphthoquinones, has recently been studied[90]. The

TABLE 7. Molecular dimensions

(*a*) *Bond lengths* (Å)

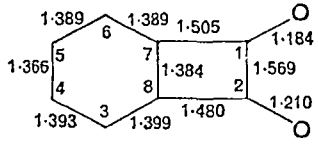
Compound	$C_1—C_9$	$C_4—C_{10}$	$C_1—C_2$	$C_3—C_4$	$C_1—O_1$
4-Amino-, hemihydrate	1·490	1·476	1·504	1·407	1·207
3-Chloro-	1·479	1·449	1·543	1·326	1·204
3-Bromo-[a]	1·476	1·466	1·568	1·326	1·202
3-Bromo-4-amino-, hydrate	1·478	1·471	1·517	1·384	1·211
3-Bromo-4-amino-, methanol complex[a]	1·475	1·464	1·471	1·386	1·253
3-Methyl-4-amino-, hydrate[a]	1·487	1·459	1·494	1·398	1·234

(*b*) *Bond angles* (°)

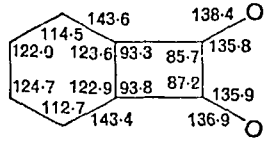
Compound	C_9 / C_{10} \ C_1	C_{10} / C_9 \ C_4	C_1 / C_9 \ C_2	C_4 / C_{10} \ C_3	C_1 / C_9 \ O_1	C_1 / C_2 \ O_1	C_2 / C_1 \ O_2	C_2 / C_3 \ O_2
4-Amino-, hemihydrate	119·4	118·3	119·2	122·1	120·5	119·5	116·5	124·4
3-Chloro-	118·6	121·4	118·9	122·2	123·6	117·5	121·3	123·5
3-Bromo-[a]	119·6	121·6	118·0	121·1	125·9	116·2	120·6	124·4
3-Bromo-4-amino-, hydrate[a]	119·6	120·2	119·0	120·4	122·6	118·3	117·6	124·4
3-Bromo-4-amino-, methanol complex[a]	119·2	120·0	119·5	118·7	121·4	119·0	117·5	125·0
3-Methyl-4-amino-, hydrate[a]	117·6	120·0	119·3	124·1	119·9	120·8	115·5	123·4

[a] Dimensions calculated from atomic co-ordinates given in original papers.

molecular dimensions are shown in **39** and **40**. Noteworthy features are the constancy of the bond lengths in the benzenoid ring, the smallness of



(39)



(40)

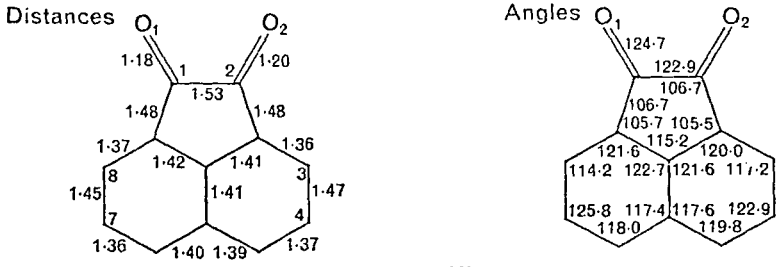
the internal angles at C_3 and C_6, which must be associated with the relief of the strain in the four-membered ring, the shortness of the carbonyl bonds and the length of C_1—C_2. Both rings are planar but slightly bowed with respect to one another (1·84°). Most of the strain in the system is relieved by deformation of the in-plane bond angles.

A second, comparable, molecule is acenaphthenequinone, **41**[91]. This analysis is less precise but again we see the long C_1—C_2 bond and short carbonyls. Bonds C_3—C_4 and C_7—C_8 are surprisingly long.

of 1,2-naphthoquinones

C_2—O_2	C_2—C_3	C_9—C_{10}	C_5—C_{10}	C_8—C_9	C_5—C_6	C_7—C_8	C_6—C_7	Reference
1·263	1·380	1·398	1·398	1·388	1·400	1·404	1·384	85
1·186	1·486	1·406	1·377	1·373	1·410	1·345	1·381	86
1·219	1·479	1·413	1·388	1·377	1·388	1·403	1·381	86
1·255	1·406	1·403	1·409	1·392	1·388	1·382	1·382	87
1·283	1·399	1·417	1·446	1·426	1·363	1·381	1·394	88
1·274	1·400	1·408	1·403	1·363	1·406	1·406	1·410	89

C_2 (C_1 C_3)	C_3 (C_4 C_2)	C_{10} (C_9 C_5)	C_9 (C_8 C_{10})	C_5 (C_6 C_{10})	C_8 (C_7 C_9)	C_6 (C_5 C_7)	C_7 (C_6 C_8)	C_9 (C_1 C_8)	C_{10} (C_4 C_5)
118·2	121·5	119·3	120·4	119·4	119·4	120·2	120·0	—	—
115·2	123·2	118·4	120·8	120·1	120·2	120·0	119·9	120·6	119·6
115·0	124·2	119·0	119·5	120·9	121·1	120·2	119·2	120·8	119·4
117·4	123·2	117·6	121·4	120·6	117·8	120·3	120·2	119·1	122·1
117·5	124·5	117·7	121·2	119·3	118·6	122·5	120·6	119·5	122·2
121·1	117·9	116·5	122·1	122·5	121·3	118·9	118·5	120·2	123·5



(41)

TABLE 8. Molecular dimensions of hydroxy-

(*a*) *Bond lengths* (Å)

Compound	C_1-C_2	C_3-C_4	C_1-C_9	C_4-C_{10}	C_2-C_3
2-Hydroxy-3-methyl-(phthiocol)	1·49	1·47	1·46	1·50	1·33
2-Hydroxy-3-chloro-	1·48	1·40	1·43	1·44	1·34
2-Amino-	1·487	1·448	1·486	1·485	1·349
2-Amino-3-chloro-	1·49	1·49	1·46	1·46	1·35
2-Amino-3-methyl-$\frac{1}{2}H_2O$[c]	1·50	1·47	1·47	1·46	1·35
	1·52	1·46	1·47	1·48	1·36
2-Amino-3-bromo-	1·52	1·40	1·45	1·50	1·34
2,5,8-Trihydroxy-3-methoxy-6-methyl-7-acetoxy- (cordeauxia quinone)[d]	1·48	1·48	1·49	1·38	1·40
5,8-Dihydroxy- (naphthazarin)[c] A	1·441	1·446	1·440	1·437	1·351
B	1·40	1·46	1·49	1·47	1·37
C I[c]	1·454	1·440	1·427	1·431	1·340
C II[c]	1·438	1·439	1·432	1·413	1·356
Tolypomycinone tri-*m*-bromobenzoate[b, e]	1·531	1·290	1·575	1·660	1·366

(*b*) *Bond angles* (°)

Compound	C_1 / C_9 C_2	C_4 / C_3 C_{10}	C_2 / C_1 C_3	C_3 / C_2 C_4	C_{10} / C_4 C_9	C_9 / C_1 C_{10}	C_1 / O_1 C_2	C_4 / O_4 C_3
2-Hydroxy-3-methyl-(phthiocol)	117	118	123	120	120	119	119	120
2-Hydroxy-3-chloro-	123	120	116	124	119	116	114	121
2-Amino-	117·5	118·9	121	121·9	119·9	120·7	119·7	120·9
2-Amino-3-chloro-	118	118	119	122	121	119	118	121
2-Amino-3-methyl-$\frac{1}{2}H_2O$[c]	119·0	120·5	121·0	119·5	120·0	119·0	118·0	119·0
	120·0	118·5	120·0	121·3	121·5	118·5	118·5	120·5
2-Amino-3-bromo-	121	118	116	125	119	118	116	124
2,5,8-Trihydroxy-3-methoxy-6-methyl-7-acetoxy- (cordeauxia quinone)	119	120	117	121	122	119	122	120
	120	121					117	113
5,8-Dihydroxy- (naphthazarin) A	119·0	119·2	121·9	120·6	120·0	119·5	119·7	118·5
B	123	119	119	122	119	118	119	122
C I	118·8	118·7	122·1	121·6	119·4	119·4	119·0	119·1
C II	119·0	119·8	121·1	121·0	119·7	119·2	—[f]	—[f]
Tolypomycinone tri-*m*-bromobenzoate	120·7	113·5	115·9	130·4	122·5	112·5	118·3	130·8

[a] Compounds are numbered so that hydroxyl- or amino-groups in the quinonoid ring are in position 2.
[b] Dimensions calculated from atomic co-ordinates given in original paper.
[c] Two symmetry-independent molecules in asymmetric unit.
[d] **43**. Compound name as given above does not correspond exactly to **43**, for reasons discussed in the text.

3. Hydroxy- and amino-substituted 1,4-naphthoquinones

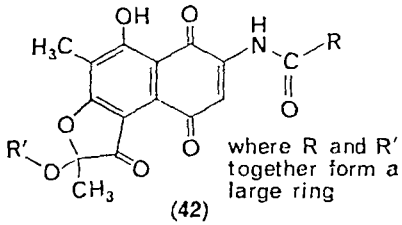
The molecular dimensions are given in Table 8. In the tolypomycinone derivative **42** the possible error in atomic co-ordinates is 0·2 Å; because of this rather low precision this molecule will not be discussed further. Of the remaining materials in the table those containing hydroxy groups in the 5- and 8-positions differ from the other substances. Thus, for example, the fact that in all three polymorphs of naphthazarin the molecule lies on

and amino-substituted 1,4-naphthoquinones[a]

C_9—C_{10}	C_6—C_7	C_1—O_1	C_4—O_4	C_8—C_9	C_5—C_{10}	C_5—C_6	C_7—C_8	Reference
1·39	1·36	1·22	1·22	1·38	1·38	1·38	1·39	92
1·44	1·39	1·26	1·27	1·39	1·38	1·44	1·40	93
1·385	1·387	1·208	1·224	1·408	1·403	1·373	1·387	94
1·40	1·35	1·23	1·24	1·41	1·39	1·42	1·41	95
1·41	1·40	1·23	1·25	1·41	1·41	1·41	1·40	96
1·39	1·40	1·23	1·23	1·40	1·42	1·40	1·40	96
1·41	1·39	1·21	1·22	1·40	1·38	1·41	1·40	97
1·37	1·32	1·32 1·26	1·30 1·39	1·37	1·41	1·41	1·39	98 98
1·422	—	1·309	1·296	—	—	—	—	99
1·42	—	1·33	1·30	—	—	—	—	100
1·452	—	1·304	1·303	—	—	—	—	99
1·443	—	1·303	1·313	—	—	—	—	99
1·365	1·452	1·178	1·196	1·301	1·332	1·411	1·508	101
C_1 O_1 C_9	C_4 O_4 C_{10}	C_9 C_1 C_8	C_{10} C_4 C_5	C_9 C_8 C_{10}	C_{10} C_5 C_9	C_8 C_7 C_9	C_5 C_6 C_{10}	C_7 C_6 C_8	C_6 C_5 C_7
123	120	—[f]	—[f]	120	120	118	119	121	120
122	118	—[f]	—[f]	121	117	120	121	120	119
122·7	120·2	—[f]	—[f]	118·7	120·3	120·2	120·3	120·2	120·0
122	120	—[f]	—[f]	121	118	120	121	118	119
123·0	120·0	—[f]	—[f]	122·5	119·5	118·5	118·5	120·5	121·5
121·5	120·5	—[f]	—[f]	121·5	119·0	119·0	119·5	120·0	120·5
122	117	—[f]	—[f]	118	118	118	121	122	117
118	119	119	120	121	118	121	119	118	123
123	127								
121·4	122·2	120·6	—	—	—	—	—	—	—
—[f]	—[f]	—[f]	—	—	—	—	—	—	—
122·3	122·3	121·1	—	—	—	—	—	—	—
121·2	121·9	121·2	—	—	—	—	—	—	—
120·9	115·5	118·9	122·1	127·5	114·9	120·9	124·5	111·1	120·7

[a] This material has three polymorphic forms A, B, C. In all, the molecules are centrosymmetric. Molecular dimensions of A and C are corrected for thermal motion.
[f] Results not given in paper.
[g] 42.

a crystallographic centre of symmetry shows that the two rings are equivalent, i.e. that the 'benzenoid' and 'quinonoid' rings are not distinguishable. These cases will be treated separately below.



(42)

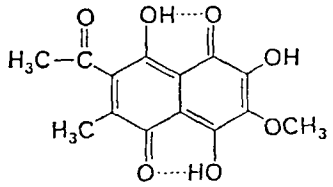
There remain five substances which are substituted in the 2-position by amino or hydroxy groups and which have no substituent in the second ring. It is conceivable that among these molecules some could be considered as 1,2-naphthoquinones or have bond lengths markedly modified by resonance interaction between the 2-substituent and the carbonyls. In four of the five substances no such effects are observed; the molecular dimensions are close to the average values for 1,4-naphthoquinones without the hydroxy or amino substituents. In these materials, too, the C_2—N (compare amino-phenol[102]) and C_2—O lengths are about 1·36 Å, indicating little double-bond character. Further, there is no consistent difference in length between C_1—O_1 and C_4—O_4. On the other hand, in these substances C_1—C_2 averages 1·503 Å which is rather long for a 1,4-naphthoquinone. The one molecule which consistently deviates from this generalization is the 2-hydroxy-3-chloro-quinone. In this compound C_1—O_1, C_4—O_4 and C_9—C_{10} are long and C_3—C_4 and C_1—C_2 (1·31 Å) are short. The angle O_1—C_1—C_2 has the unusually low value of 114° and C_1—C_2—C_3 is also small. These deviations from mean values suggest partial 1,2-quinone properties, although there is no lengthening of the C_2—C_3 bond.

Gaultier and Hauw[103] write of 'bifurcated' hydrogen bonds in 1,4-quinones with hydroxy or amino substituents in the 2-position. By this they mean that a hydrogen of the substituent participates both in an intramolecular hydrogen bond to O_1 and in an intermolecular hydrogen bond. Indeed, there are short N···O and O···O contact distances; the intramolecular ones are approximately 2·68 and 2·66 Å, respectively, and the intermolecular contacts fall in the ranges 2·85–3·05 Å and 2·64–2·79 Å, respectively. These are certainly ranges in which hydrogen-bonding interactions are known to occur[101]. In addition Gaultier and Hauw report that the crystalline 2-hydroxy-3-methyl- and 2-hydroxy-3-chloro-compounds have absorptions in their infrared spectra at 3335, 3260 and

2300 cm^{-1}, which are attributed to the two types of hydrogen-bonded networks. It seems, however, that the first two bands may be attributed to either inter- or intramolecularly bonded systems; the assignment of the 2300 cm^{-1} to the chelated system is not unequivocal[105]. Unfortunately, of the six examples which Gaultier and Hauw cite the critical hydrogen atom has been located in only one. Nevertheless, the circumstantial evidence in favour of their argument is strong; there is certainly intermolecular hydrogen bonding in all cases. This, together with consideration of the fate of the second hydrogen in the case of amino substituents, enables one to assign a position to the hydrogen with fair certainty. This hydrogen is indeed found to be within interacting distance of O_1; the use of 'bifurcated' might, however, be better confined to cases of intermolecular bonding only.

Gaultier and Hauw[97] find that in the amino-bromo-quinone the Br, NH_2 and O_1 are alternately above and below the mean plane of the carbon framework. In the amino-methyl compound[96] there appears to be a significant distortion of this framework from planarity. This distortion is different in the two symmetry-independent molecules and is apparently determined by intermolecular, particularly hydrogen-bonding, interactions.

We return now to the 5,8-dihydroxy-substituted molecules. For the cordeauxia quinone the dimensions suggest that the molecule is best described by structure **43**, so that the ring system is close to being centrosymmetric. Cradwick and Hall[99] point out that in naphthazarin the two phenolic hydrogens appear to be non-symmetrically placed with respect to their neighbouring oxygens. Thus the molecule can be pictured as shown for the cordeauxia quinone or in terms of the resonance hybrid **44**.



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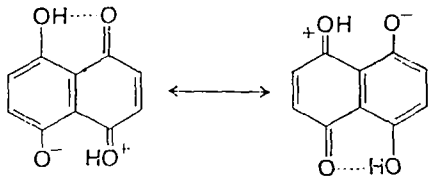


(44)

Unless stated otherwise all the molecules treated in this section have a carbon-ring skeleton which is planar within the significance of the data. To conclude the section of naphthoquinones we list the crystallographic constants in Table 9.

TABLE 9. Crystallographic constants of naphthoquinones (NQ)

Compound	Unit cell dimensions: Lengths a (Å)	b (Å)	c (Å)	Angles: β or α, β, γ (°)	Z	Space group	Reference
1,4-NQ	8·27	7·76	11·71	99·5	4	$P2_1/c$	62
2-Chloro-1,4-NQ	23·84	3·88	9·12	—	4	$P2_12_12_1$ or $P2_122_1$	106
2-Bromo-1,4-NQ	13·88	3·98	15·74	104	4	$P2_1/c$	63
2-Iodo-1,4-NQ	14·071	4·234	16·050	106·05	4	$P2_1/c$	64
2,3-Dimethyl-1,4-NQ	7·52	8·35	14·97	91·8	4	$P2_1/n$	65
2,3-Dichloro-1,4-NQ	18·18	8·29	7·35	112·5, 73, 117·5	4	$P\bar{1}$	66
2,3-Dibromo-1,4-NQ	15·17	3·97	15·83	—	4	$Pca2_1$	67
2-Chloro-3-methyl-1,4-NQ	7·43	8·30	14·79	87·5	4	$P2_1$	72
2-Bromo-3-methyl-1,4-NQ	7·46	8·42	14·87	88·3	4	$P2_1$	68
2-Phenyl-1,4-NQ	23·89	13·02	7·44	—	8	$Pbca$	69
2-Methyl-3-*N*-methyl-anilinomethyl-1,4-NQ	14·22	14·04	7·46	(γ) 104·2	4	$P2_1/n$	70
2,2′-di(1,4-NQ)	26·274	3·774	16·145	118·5	8	$C2/c$	71
3-Chloro-1,2-NQ	3·855	14·61	14·27	91·5	4	$P2_1/c$	86
3-Bromo-1,2-NQ	3·926	14·914	14·432	89·7	4	$P2_1/c$	86

2-Hydroxy-3-methyl-1,4-NQ	11·85	4·85	7·71	90·5	2	$P2_1$	92
2-Hydroxy-3-chloro-1,4-NQ	8·25	3·92	14·39	113·3	2	Pc	93
2-Amino-1,4-NQ	17·03	3·96	14·72	125·5	4	$P2_1/c$	94
2-Amino-3-bromo-1,4-NQ	15·18	3·93	15·92	110	4	$P2_1/c$	97
2-Amino-3-chloro-1,4-NQ	8·11	3·93	14·84	113	2	Pc	95
2-Amino-3-methyl-1,4-NQ.$\frac{1}{2}$ H_2O	17·06	3·91	30·95	116	8	$P2/c$	96
Cordeauxia quinone	7·58	10·84	3·90	97·2, 93·2, 101·2	1	P1	98
Naphthazarin A	3·743	7·622	14·549	97·7	2	$P2_1/n$	99
B	5·41	6·40	11·85	91·6	2	$P2_1/c$	100
C	7·906	7·324	14·05	96·6	4	$P2_1/n$	99
11,11,12,12-Tetracyano-1,4-NQ-dimethane	13·210	7·209	26·629	—	8	$Pbca$	83
Benzocyclobutene-1,2-dione	7·938	10·741	7·135	—	4	$Pbc2_1$	90
Acenaphthenequinone	7·81	27·0	3·851	—	4	$P2_12_12_1$	91

C. Anthraquinones

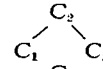
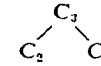
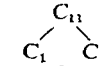
The numbering system of the 9,10-anthraquinones is given in **45**.

1. 9,10-Anthraquinones (not hydroxy- or amino-substituted)

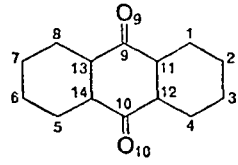
The molecular dimensions are listed in Table 10. Structures **46** to **49** are shown below.

TABLE 10. Molecular dimensions of

(*a*) *Bond lengths* (Å) Compound[b]	C_1-C_2 C_5-C_6	C_3-C_4 C_7-C_8	C_1-C_{11} C_5-C_{14}	C_4-C_{12} C_8-C_{13}	C_2-C_3 C_6-C_7
9,10-AQ	1·390	1·381	1·383	1·380	1·388
1-Chloro-9,10-AQ	1·45	1·44	1·38	1·37	1·38
	1·40	1·43	1·38	1·39	1·39
1-Bromo-9,10-AQ	1·41	1·41	1·36	1·34	1·37
	1·42	1·41	1·41	1·42	1·38
1,5-Difluoro-9,10-AQ[c]	1·41	1·41	1·40	1·43	1·42
	1·37	1·40	1·42	1·43	1·41
1,5-Dichloro-9,10-AQ	1·36	1·35	1·41	1·39	1·36
1,5-Dibromo-9,10-AQ	1·43	1·36	1·41	1·43	1·38
1,5-Diiodo-9,10-AQ	1·45	1·34	1·36	1·46	1·40
Anthrone[d]	1·376	1·360	1·389	1·412	1·364
10,10′-Dianthronyl[e]	1·37	1·40	1·40	1·39	1·39
	1·40	1·38	1·40	1·39	1·38
Dianthronylidene[f]	1·36	1·46	1·40	1·39	1·40
	1·35	1·41	1·40	1·41	1·42
10-Dicyanomethyleneanthrone[g]	1·39	1·46	1·41	1·37	1·45

(*b*) *Bond angles* (°) Compound					
9,10-AQ	120·3	120·0	120·2	119·8	118·9
1-Chloro-9,10-AQ	124	122	119	117	115
	121	120	119	119	120
1-Bromo-9,10-AQ	123	124	120	116	116
	122	122	119	119	119
1,5-Difluoro-9,10-AQ	124	119	118	120	116
	125	120	119	119	115
1,5-Dichloro-9,10-AQ	122	119	120	121	115
1,5-Dibromo-9,10-AQ	123	121	119	121	115
1,5-Diiodo-9,10-AQ	123	120	117	123	118
Anthrone	120·8	120·1	119·6	121·3	119·6
10,10′-Dianthronyl	121·0	121·1	119·5	119·7	119·9
	120·9	121·0	120·0	119·6	118·3
Dianthronylidene	120	118	120	119	120
	123	117	117	123	117
10-Dicyanomethyleneanthrone	121	120	119	119	121

[a] Dimensions related by an assumed inversion centre in the anthraquinone system are given in the same column. Where such an inversion centre in fact exists only one set of dimensions is given.
[b] AQ is anthraquinone.
[c] Asymmetric unit composed of two independent half-molecules, each on a centre of symmetry.

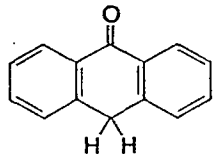


(45)

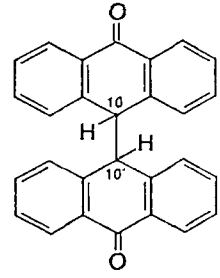
9,10-anthraquinones and related anthrones[a]

$C_{11}-C_{12}$ C_8-C_{13}	C_9-C_{11} $C_{10}-C_{14}$	C_9-C_{13} $C_{10}-C_{12}$	C_9-O_9 $C_{10}-O_{10}$	Reference	C_{12} C_4 C_{11} C_{13} C_8 C_{14}	C_9 C_{11} C_{13} C_{10} C_{12} C_{14}	C_{11} C_9 C_{12} C_{14} C_{10} C_{13}	C_{12} C_{10} C_{11} C_{13} C_9 C_{14}	C_9 O_9 C_{11} C_{10} O_{10} C_{14}	C_9 O_9 C_{13} C_{10} O_{10} C_{12}	C_{11} C_1 C_9 C_{14} C_5 C_{10}	C_{12} C_4 C_{10} C_{13} C_8 C_9
1·401	1·472	1·495	1·213	107	120·7	118·4	120·7	120·8	120·5	121·0	—	—
1·43	1·54	1·51	1·21	108	123	118	120	120	121	121	125	117
1·38	1·51	1·54	—		120	119	121	122	123	118	119	118
1·44	1·52	1·46	1·21	109	120	120	117	122	121	—	127	—
1·40	1·46	1·52	1·20		118	119	120	123	124	117	—	—
1·41	1·47	1·48	1·24	110	123	119	120	120	122	119	124	—
1·42	1·49	1·49	1·20		122	118	121	121	122	121	124	—
1·41	1·44	1·46	1·25	111	122	118	119	121	122	120	—	—
1·46	1·47	1·50	1·23	112	120	119	119	122	122	119	126	—
1·48	1·50	1·44	1·23	112	118	121	115	124	116	122	127	—
1·391	1·475	1·488	1·109	113	118·5	116·6	121·2	122·2	121·4	121·9	119·2	119·3
1·40	1·48	1·48	1·24	114	118·5	118·7	120·1	121·6	120·0	121·1	119·9	119·8
1·40	1·51	1·51	—		120·0	115·1	120·3	120·9	—	—	121·3	119·0
1·39	1·51	1·52	1·20	115	119	116	118	120	120	121	—	—
1·42	1·54	1·52	—		120	113	117	119	120	124	—	—
1·43	1·48	1·48	1·24	116	120	119	119	119	122	120·5	120	121

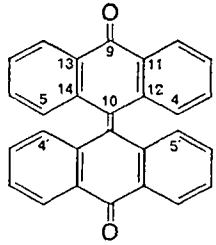
[d] 46. Disordered about a crystallographic centre.
[e] 47. Two anthrone units related by a twofold rotation.
[f] 48.
[g] 49. Molecule is symmetric about a mirror plane through C_9 and C_{10}.



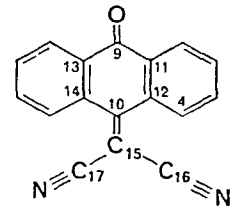
(46)



(47)

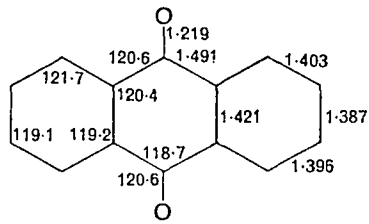


(48)



(49)

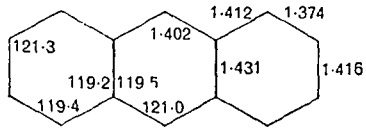
The averaged dimensions of the first six molecules of the table, based on an assumed symmetry *mmm*, are given in **50**. The outer rings are seen to be normal benzene rings except for slight elongation of the fusing bond



(50)

C_{11}—C_{12}. The C=O bond length is identical with that in the naphthoquinones (**27**). The C_9—C_{11} bond is of length approximately as expected for C(sp^2)—C(sp^2) single bonds. On the basis of these geometric features we may conclude that the molecule may be roughly considered as two benzene rings linked by two carbonyl groups which interact rather weakly with the rings. It is of interest that Harnik and Schmidt[115] described dianthronylidene **48** as being constructed of an isolated ethylenic bond (1·31 Å) attached by single bonds (1·53 Å) to normal benzene rings, which are in turn linked to carbonyl by single bonds (1·52 Å).

For comparison we give the molecular dimensions of anthracene **51** (these are averages over chemically equivalent bonds and angles[117]).



(51)

9,10-Anthraquinone and its difluoro derivative are essentially planar. In the cases of the other halogen derivatives the molecules are overcrowded because of interference between halogen and carbonyl oxygen. Thus, for a planar molecule with 120° bond angles the Br···O and I···O distances would be 2·5 and 2·6 Å, respectively, while the sums of the van der Waals radii are 3·3 and 3·5 Å. Two types of distortion result: an increase in bond angles hal—C_1—C_{11}, C_1—C_{11}—C_9 and O_9—C_9—C_{11} from 120° and distortion of the molecule from planarity. Angle C_1—C_{11}—C_9 is 126° in the two bromine-containing molecules and 127° in the diiodo compound. Angles hal—C_1—C_{11} and O_9—C_9—C_{11} are both greater than 120° for the overcrowded molecules; for example, the former angle is 123° in 1-bromo-anthraquinone and 125° in the diiodo derivative. Chetkina and Gol'der[112] find Br and O lying out of the mean plane of the dibromo compound by +0·04 and −0·19 Å, respectively. For the iodo compound the corresponding values are +0·16 Å (I) and −0·34 Å (O). The authors find that the ring carbon atoms are planar to within 0·03 Å. This is of the same order as the standard deviation of the carbon positions. We must conclude that the significance of the deviations from planarity is established for I and O, but not for Br or C. For the 1,5-dichloroquinone Bailey[111] finds a slight buckling of the central ring into the chair form, while the two outer rings are planar.

There is considerable overcrowding in dianthronylidene (**48**) and in molecules **47** and **49**. In dianthronylidene the benzene rings are planar and bent by 40° to the plane of the ethylenic system. This bending produces a separation of 2·9 Å between the overcrowded carbons (C_4···$C_{5'}$, C_5···$C_{4'}$). *Harnik and Schmidt*[115] suggest that this twist eliminates resonance interaction across C_{10}—C_{12} (and equivalent bonds) which thus have essentially single-bond character.

In 10,10′-dianthronyl (**47**) the bond lengths are all normal except for that of C_{10}—$C_{10'}$, connecting the two anthrone moieties, which is 1·60 Å (compare the 1·61 Å bond in di-*p*-anthracene[118]). The normals to the best planes of the two anthrone fragments lie at 143·3° to one another; C_{10} is 0·321 Å out of the best plane through its half molecule, indicating a

considerable pull towards the second half. Each anthrone moiety has a bend of 10·2° about the $C_9 \cdots C_{10}$ axis.

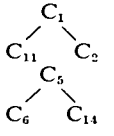
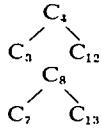
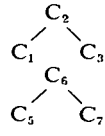
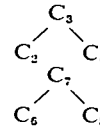
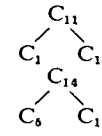
In the dicyanomethylene derivative **49** the overcrowding is between the carbons of the cyano groups (C_{16}, C_{17}) and H_4 and H_5. The strain is relieved by the opening-up of some angles and by out-of-plane distortion: angles $C_{16}—C_{15}—C_{10}$, $C_{15}—C_{10}—C_{12}$ and $C_{10}—C_{12}—C_4$ are 123°, 122° and 121°, respectively. The anthrone skeleton is butterfly shaped: $C_{11}—C_{12}—C_{13}—C_{14}$ is planar with the two benzene rings bent to the same side ('up') of this plane, both through angles of 14°, while C_9 and C_{10}

TABLE 11. Molecular dimensions of hydroxy-

(*a*) *Bond lengths* (Å)

Compound	$C_1—C_2$ $C_5—C_6$	$C_3—C_4$ $C_7—C_8$	$C_1—C_{11}$ $C_5—C_{14}$	$C_4—C_{12}$ $C_8—C_{13}$	$C_2—C_3$ $C_6—C_7$
1,2-Dihydroxy- (alizarin)[b]	1·40	1·41	1·35	1·36	1·31
	1·36	1·43	1·37	1·43	1·28
1,4-Dihydroxy-	1·479	1·451	1·576	1·443	1·440
	1·430	1·531	1·525	1·433	1·314
1,5-Dihydroxy- (anthrarufin)	1·399	1·365	1·395	1·379	1·397
	1·398	1·390	1·399	1·387	1·378
1,8-Dihydroxy-	1·43	1·44	1·49	1·38	1·34
	1·38	1·41	1·41	1·44	1·34
N,N'-Diphenyl-1,5-diamino-[c]	1·414	1·372	1·415	1·382	1·386
N,N'-Diphenyl-1,8-diamino-[d, e]	1·401	1·348	1·432	1·377	1·384
	1·348	1·401	1·377	1·432	1·384
1,5-Dihydroxy-4,8-dinitro-	1·395	1·383	1·385	1·368	1·351
1,1'-Diamino-4,4'-bianthraquinone[f]	1·378	1·412	1·430	1·411	1·374
	1·386	1·361	1·362	1·417	1·420

(*b*) *Bond angles* (°)

Compound					
1,2-Dihydroxy- (alizarin)	Angles not given				
1,4-Dihydroxy-	114·4	112·6	119·8	122·4	118·0
	114·6	109·5	123·5	124·5	118·7
1,5-Dihydroxy- (anthrarufin)	120·1	119·2	119·7	121·5	118·1
	119·7	119·4	120·3	121·0	119·2
1,8-Dihydroxy-	115·5	116·0	118·9	125·4	122·2
	115·8	114·8	123·4	122·5	118·2
N,N'-Diphenyl-1,5-diamino-[c]	118·1	119·7	121·6	120·2	118·4
N,N'-Diphenyl-1,8-diamino-[d, e]	117·6	120·8	121·3	120·6	118·8
	120·8	117·6	120·6	121·3	120·8
1,5-Dihydroxy-4,8-dinitro-	123·0	120·7	120·1	119·3	116·9
1,1'-Diamino-4,4'-bianthraquinone[f]	120·3	117·6	119·5	123·2	118·2
	120·4	120·9	121·8	117·2	116·8

[a] Molecules so named that a hydroxy or amino group is in the 1-position.
[b] Average value for three molecules.
[c] 53.

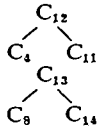
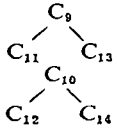
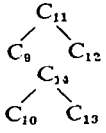
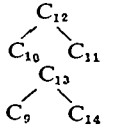
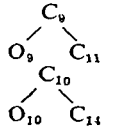
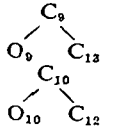
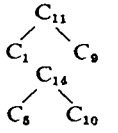
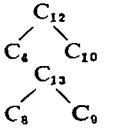
are both bent 'down'. Thus the central ring is in boat form. The carbonyl system and the dicyanomethylene group are both nearly planar; the former plane is bent by about 11° from the central ring plane, while the latter is tilted by 36·5° from this plane. The distances $C_{16}\cdots C_4$ and $C_{16}\cdots H_4$ are 2·84 and 2·22 Å, respectively.

2. Hydroxy- and amino-substituted 9,10-anthraquinones

The molecular dimensions are listed in Table 11. In the first two structures the probable errors in atomic positions are too high (e.g. $\sigma(x) = 0{\cdot}06$ Å

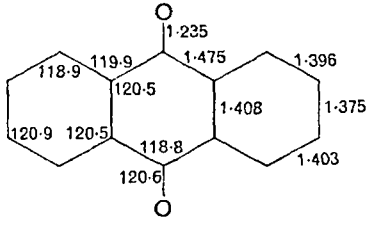
and amino-substituted 9,10-anthraquinones[a]

$C_{11}-C_{12}$ $C_{13}-C_{14}$	C_9-C_{11} $C_{10}-C_{14}$	C_9-C_{13} $C_{10}-C_{12}$	C_9-O_9 $C_{10}-O_{10}$	Reference
1·46	1·48	1·39	1·28	119
1·42	1·46	1·47	1·19	
1·286	1·390	1·623	1·286	120
1·332	1·507	1·616	1·293	
1·429	1·469	1·495	1·214	121
1·411	1·471	1·480	1·228	122
1·38	1·49	1·50	1·25	123
1·41	1·49	1·50	1·24	
1·409	1·449	1·510	1·256	124
1·402	1·467	1·495	1·250	125
1·402	1·495	1·467	1·218	
1·418	1·456	1·470	1·219	126
1·421	1·528	1·444	1·234	127
1·394	1·480	1·442	1·234	

							
Angles not given							
130·1	115·5	129·4	118·1	128·6	115·7	111·2	111·3
128·8	112·5	126·7	116·4	122·1	125·3	118·7	114·7
121·3	119·0	121·0	120·0	121·2	119·9	120·8	118·7
120·4	119·0	120·1	120·1	120·3	120·7	120·7	118·7
120·5	113·0	124·0	121·3	122·1	124·8	113·6	117·1
123·3	117·4	120·7	123·1	115·5	127·2	120·7	113·5
122·0	120·3	119·2	120·5	121·8	117·9	122·4	117·5
120·8	122·6	118·7	120·7	118·7	118·7	122·5	118·5
118·8	118·6	120·7	118·7	120·7	120·7	118·5	122·5
120·0	120·0	120·8	119·2	119·8	120·2	122·3	120·8
121·0	119·1	121·8	118·9	123·9	117·0	119·9	120·1
122·7	118·6	124·4	116·6	119·5	121·9	118·8	120·6

[d] 54.
[e] Molecule sits on twofold crystallographic axis which passes through the 9- and 10-positions.
[f] 55.

for the first) to enable consideration of the relatively small effects of substituents on molecular dimensions. In the remaining compounds the scatter is moderate and, assuming a skeleton with *mmm* symmetry, the averaged dimensions shown in **52** are obtained. Comparing with the

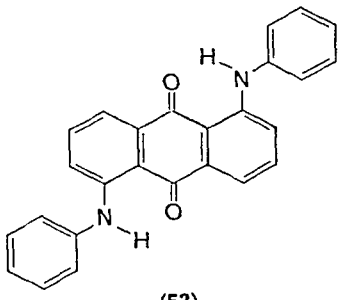


(52)

averages in **50** we find that introduction of the hydroxy or amino groups produces little significant difference except for a lengthening of the carbonyl bond. Again the molecules are planar with the outer rings possessing the geometric features of normal phenyl rings.

The $C_1—O_1$ length in the 1,5-dihydroxy derivative is given as 1·343 and 1·346 Å in the two analyses; in the dinitro compound this length is 1·336 Å. In these two compounds the $C_9—O_9$ length is about 1·22 Å. These values suggest that there is little, if any, tautomer present in which the hydrogen is on O_9 or O_{10}, nor is there substantial contribution from equivalent resonance structures. In the only one of these three structures in which the hydroxyl hydrogen was observed experimentally with certainty[122] there is no evidence for proton-delocalization or disorder, although Hall and Nobbs[121] argued for such an effect. The $C_1—O_1$ and $C_9—O_9$ lengths are consistent with this picture. The $O_1 \cdots O_9$ distance is in the range 2·59–2·62 Å, suggesting an intramolecular hydrogen bond[104].

In the two di(*N*-phenyl)amino derivatives (**53, 54**) and in the bianthraquinone (**55**) the $C_9—O_9$ is somewhat elongated (1·23–1·25 Å) and $C_1—N_1$ somewhat shortened (1·36 Å) suggesting some contribution



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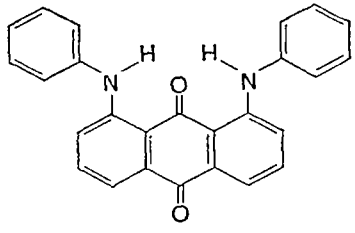

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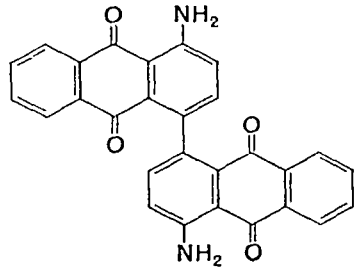


(55)

from resonance forms with a positive charge on N and a negative charge on O. The effect is most pronounced in the 1,8-diamino derivative **54** where $C_9—O_9$ is appreciably longer than $C_{10}—O_{10}$; we note that it is not possible to write a reasonable structure with a positive charge on N and a negative charge on O_{10}. In none of the structures has the amino-hydrogen been located experimentally, but the geometries are favourable for internal hydrogen bonding (except for O_{10} of **54**).

The lengths of the four C—O bonds in 1,8-dihydroxyanthraquinone[123] are $C_1—O_1$, 1·27 Å; $C_8—O_8$, 1·35 Å; $C_9—O_9$, 1·25 Å; $C_{10}—O_{10}$, 1·24 Å. These lengths can be rationalized in terms of participation of resonance structures in which $C_{10}—O_{10}$ is a carbonyl function, with the second carbonyl at the 1-, 8- or 9-position. However, it is not warranted to press this argument since the analysis is of rather low precision (R = 0·185).

Of the compounds listed in Table 11 only the bianthraquinone **55** has an anthraquinone framework which deviates significantly from planarity. Here each individual ring is essentially planar. The oxygens deviate by 0·113 Å from the planes of the rings to which they are attached. This may be due to a hydrogen bond to an amino group which is twisted out of plane. Each anthraquinone fragment is butterfly shaped with 6·1° between the two wings.

We conclude this section by listing the crystallographic constants of the anthraquinones (Table 12).

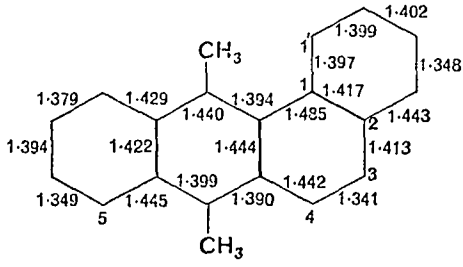
D. *Larger Fused-ring Quinone Systems*

By extrapolation of the conclusions drawn in the previous sections it is expected that as these molecules become larger they approach a state where the quinone ring is lost in a sea of aromatic rings; the molecular dimensions should thus more and more resemble those of the corresponding hydrocarbons. There seem to be but two systems in which this comparison can be made. One is the benzanthracene system: the structure of 9,10-dimethyl-1:2-benzanthracene (**56**) has been described[130].

TABLE 12. Crystallographic constants of anthraquinones and related compounds

Compound	Unit cell dimensions: Lengths a (Å)	b (Å)	c (Å)	Angles: β or α, β, γ (°)	Z	Space group	Reference
9,10-AQ	15·810	3·942	7·865	102·7	2	$P2_1/a$	107
1-Fluoro-9,10-AQ	24·35	3·88	16·47	96	4	$P2_1/c$	128
1-Chloro-9,10-AQ	7·90	3·99	17·09	96	2	$P2_1$	108
1-Bromo-9,10-AQ	7·86	4·03	17·06	95	2	$P2_1$	109
1-Iodo-9,10-AQ	7·90	4·24	17·04	92	2	$P2_1$	128
1,5-Dicarbomethoxy-9,10-AQ	24·34	6·21	19·44	94	8	$C2/c$ or Cc	128
1,5-Difluoro-9,10-AQ	18·13	3·83	16·48	114·8	4	$P2_1/c$	110
1,5-Dichloro-9,10-AQ	11·01	13·06	3·84	92·1	2	$P2_1/a$	111
1,5-Dibromo-9,10-AQ	11·24	13·43	3·96	91·4	2	$P2_1/a$	112
1,5-Diiodo-9,10-AQ	6·91	4·27	22·18	107·9	2	$P2_1/c$	112
1,4-AQ	13·83	9·65	7·35	96	4	$P2/m$	129
	8·40	5·93	19·82	99	4	$P2_1/c$	129
2-Chloro-1,4-AQ	21·74	5·80	8·74	—	4	$P2_12_12_1$ or $P2_12_12$	129
2,3-Dichloro-1,4-AQ	22·49	8·68	5·88	94	4	$P2_1/c$ or $P2/c$	129
2,3-Dibromo-1,4-AQ	20·50	5·76	9·48	92	4	$P2_1/c$	129
Phenanthraquinone	12·60	10·44	14·20	92	8	$C2/c$	129

dianthronylidene							
3:4-3′:4′-Dibenzo-dianthronylidene	14·7	11·5	7·6	103, 92, 101	2	P1 or $P\bar{1}$	115
10-Dicyanomethyleneanthrone	7·520	8·843	18·015	—	4	*Pnam*	116
1,2-Dihydroxy-9,10-AQ (alizarin)	21·04	3·75	20·12	104·5	6	*Pa*	119
1,4-Dihydroxy-9,10-AQ	20·56	6·06	10·53	125·2	4	$P2_1/a$	120
1,5-Dihydroxy-9,10-AQ	15·755	5·308	6·003	93·6	2	$P2_1/a$	121
1,8-Dihydroxy-9,10-AQ	5·76	5·76	31·45	—	4	$P4_1$ or $P4_3$	123
N,N′-Diphenyl-1,5-diamino-9,10-AQ	21·02	4·855	9·34	93·2	2	$P2_1/n$	124
N,N′-Diphenyl-1,8-diamino-9,10-AQ	21·312	9·205	4·855	—	2	$P2_122_1$	125
1,5-Dihydroxy-4,8-dinitro-9,10-AQ	10·17	10·49	6·015	94·6	2	$P2_1/a$	126
1,1′-Diamino-4,4′-bianthraquinone	12·996	8·500	17·636	—	4	*Pccn*	127



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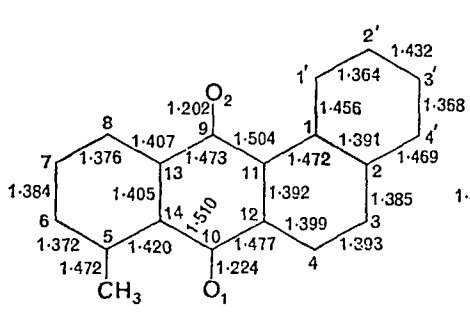
Ferrier and Iball have analysed the structures of 5-methyl-1:2-benzanthraquinone (57)[131] and of the 2′-methyl analogue **58**[132]. The bond lengths are shown below:



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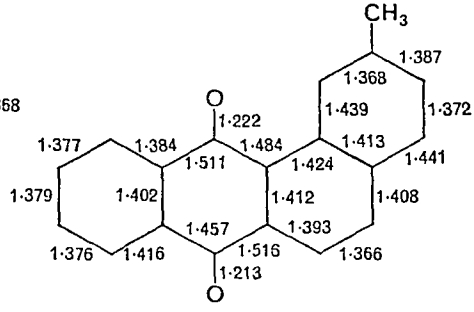
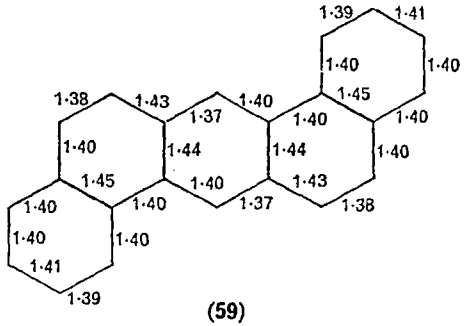


(58)

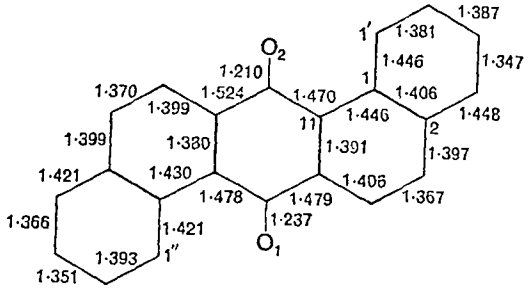
The lengths of the bonds in the quinone rings of both **57** and **58** are clearly distinguishable from those of the bonds of the other rings. In particular we note the long bond C_9—C_{11} and its equivalents. The carbonyl bond lengths are approximately the same as those of the quinones previously discussed. The bond lengths in this ring are approximately centrically related. In the hydrocarbon there is considerable variation (from 1·485 to 1·341 Å) of the lengths of the bonds of the benzenoid rings. It appears that there is a significant shortening of bonds C_1—C_{11}, C_4—C_{12}, C_{11}—C_{12} and their equivalents on passing from the hydrocarbon to the quinones, but since the differences between the two quinones are appreciable this point is not elaborated further. As compared to the hydrocarbon the quinones have the special feature of overcrowding involving O_2 and the H attached to $C_{1'}$. This brings about considerable distortion from planarity which affects the whole molecule, but particularly O_2, $C_{1'}$ and $C_{2'}$. The distortion pattern is markedly different between the two isomers.

A second case in which comparison with the parent hydrocarbon is possible is that of dibenzanthraquinone. Robertson and White[133] have given the structure of 1:2,5:6-dibenzanthracene (**59**). In this molecule the



(59)

lengths of the outer bonds scatter somewhat about 1·40 Å, while the fusing bonds, on the other hand, are about 1·44 Å in length. The structure of the corresponding quinone **60** has been solved by Entwhistle and coworkers[134]. Again we note the usual C=O bond lengths and the long



(60)

bonds to the carbonyls. The other rings do not differ appreciably from those of the hydrocarbon. However, in the three quinones discussed in this section the bonds $C_1—C_{1'}$, $C_2—C_{4'}$ and $C_1—C_{11}$, and their equivalents, are somewhat longer than is usual for aromatic systems. This effect is probably not primarily a result of overcrowding, which usually gives rise to smaller changes in bond lengths. The dibenzanthraquinone molecule is bent by 14·1° about the line connecting the two oxygens. The distances $O_2 \cdots C_{1'}$ and $O_1 \cdots C_{1''}$ are 2·851 and 2·824 Å, respectively.

The structures of a number of other large fused-ring quinones have been analysed. For reasons of space limitation and since no new principles seem to be involved in these molecular structures, we merely list them without description: anthanthrone[135], flavanthrone[136], pyranthrone[137], (α)indanthrone[138], violanthrone[139], isoviolanthrone[140]. We terminate this section with the crystallographic constants of these substances (Table 13).

Compound	Lengths			Angles	Z	Space group	Reference
	a (Å)	*b* (Å)	*c* (Å)	β or α, β, γ (°)			
1:2-BAQ[a]	10·96	11·70	19·23	96·8	8	Cc or C2/c	141
3-Methyl-1:2-BAQ	7·54	16·84	11·65	118·9	4	$P2_1/a$	141
4-Methyl-1:2-BAQ	11·80	15·50	3·99	117·8	2	$P2_1$	141
5-Methyl-1:2-BAQ	14·13	23·27	3·94	—	4	$P2_1nb$	141
6-Methyl-1:2-BAQ	13·12	13·69	7·68	103·0, 94·8, 83·1	4	P1 or $P\bar{1}$	141
8-Methyl-1:2-BAQ	10·37	16·91	7·57	100·5	4	$P2_1/c$	141
1′-Methyl-1:2-BAQ	31·78	3·94	23·84	120·4	8	Cc or C2/c	141
2′-Methyl-1:2-BAQ	20·67	4·06	7·77	90·8	2	$P2_1$	141
	7·87	16·53	22·35	113·5	8	$P2_1/c$	141
3′-Methyl-1:2-BAQ	21·93	30·75	3·95	—	8	P*n*2*a* or P*nma*	141
1:2-5:6-Di-BAQ	28·54	3·85	12·90	—	4	$Pca2_1$	134
Anthanthrone	20·9	3·86	33·2	92	8	$P2_1/c$	135
Flavanthrone	27·92	3·80	8·10	95	2	$P2_1/a$	136
Pyranthrone	22·05	3·84	21·16	90	4	$P2_1/n$	137
(α)Indanthrone	30·83	3·833	7·845	91·9	2	$P2_1/a$	138
Violanthrone	15·26	33·60	3·827	90·8	4	$P2_1$	139
Isoviolanthrone	15·21	3·825	33·12	90·8	4	$P2_1/c$	140

[a] BAQ = benzanthraquinone.

III. QUINONE PACKING MODES

We have mentioned in the Introduction the tendency of quinone molecules to stack in infinite one-dimensional arrays with the molecular planes lying nearly perpendicular to the stack axis. The crystal consists of a series of such stacks lying side by side with stack axes parallel to one another. In this section we treat two aspects of the molecular packing: the arrangement of molecules within the stack and the lateral contacts between molecules of neighbouring stacks.

A. Molecular Stacking

Planar aromatic molecules tend to arrange themselves in the crystal with molecular planes parallel. Typical interplanar distances are 3·53 Å (pyrene)[142] and 3·40 Å (coronene)[143]. We thus take the thickness of a planar conjugated π-electron system to be about 3·4 Å. Let us make a one-dimensional pile or stack of such molecules, lying with planes parallel and completely overlapped. The normals to the molecular planes are then parallel to the stack axis and the distance between equivalent points on adjacent molecules is 3·4 Å. If we allow neighbouring molecules to slip slightly with respect to one another then the normal plane-to-plane spacing remains 3·4 Å but the distance between equivalent points increases. If the angle between the normals to the molecular planes and the stack axis varies up to say 30° (that is, a given molecule is displaced by up to 2 Å with respect to its neighbour) then the repeat distance up to the stack varies from 3·4 to about 4 Å. Thus a crystallographic axial length of about 4 Å or less is diagnostic of one-dimensional stacking with adjacent molecules parallel and moderately to strongly overlapped.

Consideration of the tables of crystallographic constants of the quinones (not complexes) shows that of the 110 or so compounds listed, 50 have such short axes. Recalling that the remaining compounds include molecules which are non-planar and salts, which may be expected to pack differently, leads us to conclude that such a one-dimensional close-packing arrangement is a favourable one in the quinones.

Further, there are other molecular arrangements, corresponding to other crystallographic axial lengths, which are also associated with close-packed one-dimensional stacks. Thus consider that alternate molecules are related by a crystallographic inversion centre, by a twofold screw axis or by a glide plane perpendicular or near-perpendicular to the molecular plane. The molecules will then be parallel or near-parallel and, if they are close packed, then the repeat distance up the stack axis will be about twice that found in the previous group, that is between 6·8 and 8 Å. Finally, if the molecules lie parallel but sharply tilted to the stack axis,

the interplanar distance remaining 3·4 Å, then the repeat distance will fall in the approximate range 4·6–6 Å; in this case the overlap of adjacent molecules may be small.

Basic to consideration of the stacking type is the question of the overlap of neighbouring molecules; the crystal structure is determined by the minimization of the total energy of the crystal, which is a sum of intermolecular attractive and repulsive terms. In these terms the interactions between nearest neighbour molecules in a stack, and hence the intermolecular overlap, play an important role. In order to try to find out what forces are characteristic of interacting quinone molecules let us first consider molecules which have no bulky or polar substituents, for example the unsubstituted quinones.

We can consider the latter molecules as consisting of separate carbonyl groups and π-electron systems bound together—a model justified in the previous sections. Several types of arrangements in such systems have been recognized. In one type, exemplified by only a few structures which include those of chloranil[9] (Figure 1) and of 2,6-dichloro-1,4-benzouinqone[8]

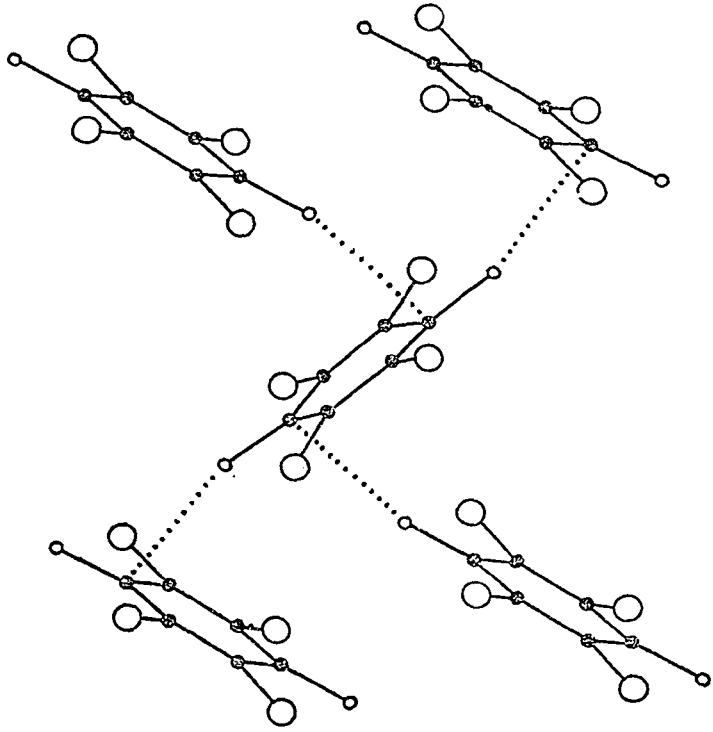


FIGURE 1. Intermolecular interactions in tetrachloro-1,4-benzoquinone. Reproduced with permission from H. A. Bent, *Chem. Rev.*, **68**, 587 (1968) after Chu, Jeffrey and Sakurai[9].

(Figure 2), the molecules pack in such a way[140] that a C=O group points towards the carbon of a C=O of a second molecule, inclined at a large angle to the first, and with an O···C separation of about 2·8 Å. Such structures are not compatible with plane-to-plane close packing.

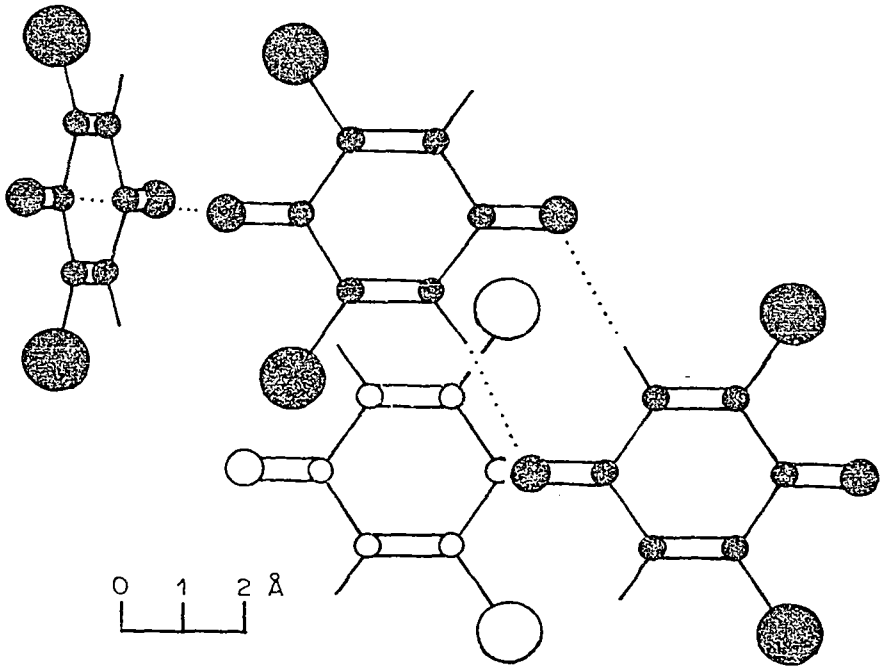


FIGURE 2. View of the structure of 2,6-dichloro-1,4-benzoquinone normal to the best plane of the molecule, showing the intermolecular overlap, and C—H···O (H···O, 2·46 Å) and C=O···C=O (O···C, 2·84 Å) contacts. Based on Rees[8].

A second type of packing arrangement, found for example in violuric acid[144] and later in tetrahydroxy-[23] and 2,6-dichloro-[8] 1,4-benzoquinones and in benzocyclobutene-1,2-dione[90], has the carbonyls of adjacent molecules overlapping in an antiparallel manner with a separation of about 3·1 Å (Figure 2). Here presumably the attractive force is largely due to dipole–dipole interaction.

A third and more prevalent type of arrangement is discussed by Prout and Wallwork[145]. It was first recognized for complexes involving quinones with aromatic electron donors and is found in the seven complexes listed first in Table 3, in perylene : fluoranil (Figure 3), and in the complex of bis-8-hydroxyquinolatopalladium(II) with chloranil, and a similar arrangement is found in pyrene : chloranil. In this arrangement the planes of

molecules of the two components are close packed and near parallel, but the mutual orientation of the molecules is such that a C=O of the quinone lies approximately over the centre of the aromatic ring (Figure 3). Prout and Wallwork[145] and also Gaultier and coworkers[146] discuss the occurrence of this type of packing in one-component systems where the quinone molecule contains a benzenoid ring (1,4-naphthoquinone[62] (Figure 4); 1,4-anthraquinone[107]; and 5,8-dihydroxy-1,4-naphthoquinone[123] although this molecule perhaps should not strictly be called a quinone).

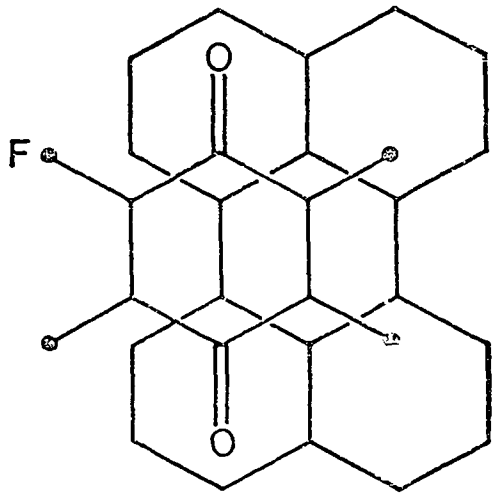


FIGURE 3. Overlap diagram of perylene: fluoranil complex. Reproduced with permission from F. H. Herbstein, after A. W. Hanson[37], *Perspectives in Structural Chemistry*, Vol. IV (Eds. J. D. Dunitz and J. A. Ibers), Wiley, New York, 1971.

The intermolecular interaction associated with this type of arrangement is probably a dipole-induced dipole one. It is of interest that seemingly analogous structures have been found for molecules containing a polarized C=C bond and an aromatic ring[145]. This is so for the complexes between tetracyanoquinodimethane and tetramethylphenylenediamine[147] and between tetracyanoethylene and naphthalene[148].

When there is no benzenoid ring in the molecule the C=C double bond of the quinone ring may act as the group which is polarized by the carbonyl dipole. In this case the carbonyl would lie over an adjacent quinone ring and between the two C=C double bonds (Figure 5), interacting with both. Such arrangements are found in 2,5-dimethyl- (Figure 16)[3] and 2,6-dimethyl-[149] 1,4-benzoquinones, and in the complex of 1,4-benzoquinone with thymine[36].

As always, the structure of the crystal is determined by compromise between various competing interactions. Thus, in many of the examples cited some intermolecular charge-transfer occurs, the spatial requirements

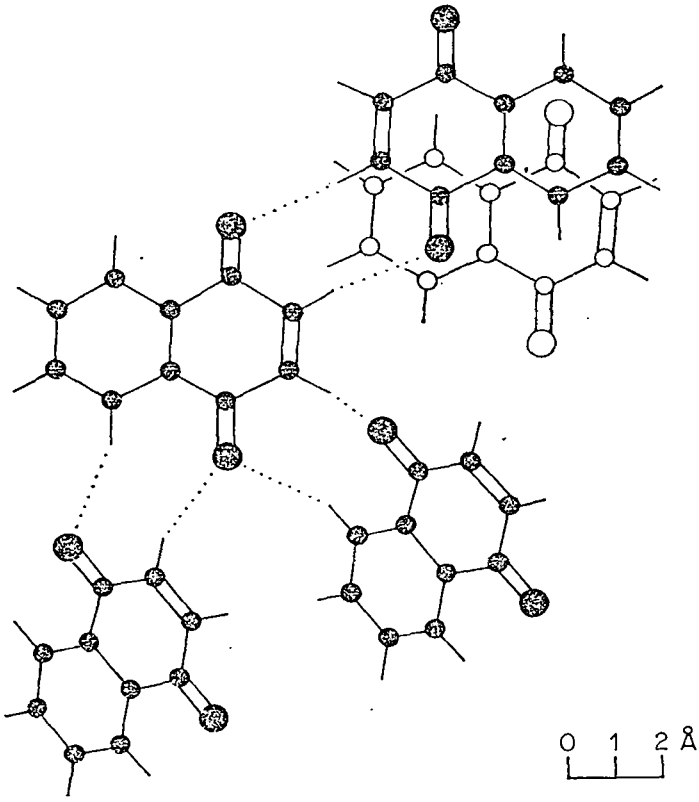


FIGURE 4. View of the structure of 1,4-naphthoquinone normal to the molecular plane, showing intermolecular overlap and C—H···O contacts. Based on Gaultier and Hauw[62].

for which may differ from those for optimal dipole-induced dipole interaction. Similarly, when bulky substituents are introduced into the molecule then the arrangement will tend to be such as to minimize interference between these substituents on adjacent molecules. In the 2,5- and 2,6-dimethylbenzoquinones this is achieved while the C=O to C=C interaction is maintained. In the case of 2,3-dimethyl-1,4-benzoquinone[2] (Figure 6), however, a completely new arrangement results: adjacent molecules are related by a centre of inversion so that the methyls do not overlap adjacent molecules at all. In this structure the carbonyls lie parallel and seemingly

within interacting distance, a feature which presumably introduces a repulsive dipole–dipole interaction. 2,3-Dimethyl-1,4-naphthoquinone packs in an analogous manner[65].

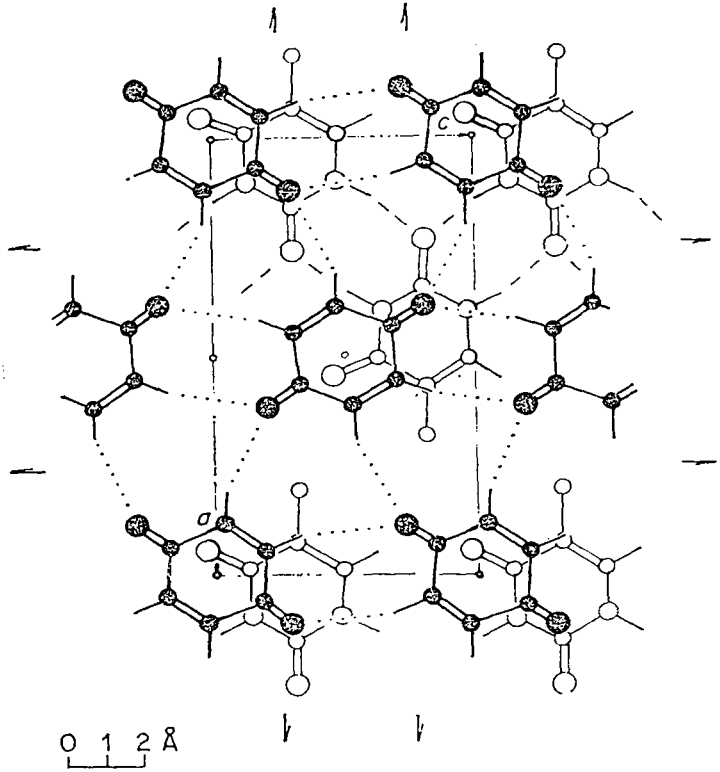


FIGURE 5. Thymine: 1,4-benzoquinone complex. View along the *b* axis showing a sheet of benzoquinone molecules (filled circles), and a neighbouring sheet of thymine molecules (open circles). The figure shows intermolecular overlap, C—H···O contacts and N—H···O hydrogen bonds.

There is a second structure type in which the carbonyls lie in a similar repulsive configuration; in this arrangement the adjacent molecules lie parallel and displaced with respect to one another in a direction perpendicular to the OC—CO axis. This type is found in 2-amino-[94] and in 2-amino-3-chloro-[95] 1,4-naphthoquinones, in 4-amino-1,2-naphthoquinone[85] and in 9,10-anthraquinone[107] (Figure 7).

In tetramethylbenzoquinone[5] and in the complex between hexamethylbenzene and chloranil[38] the overlap seems to be determined by the need of the bulky substituents to avoid one another (Figure 8).

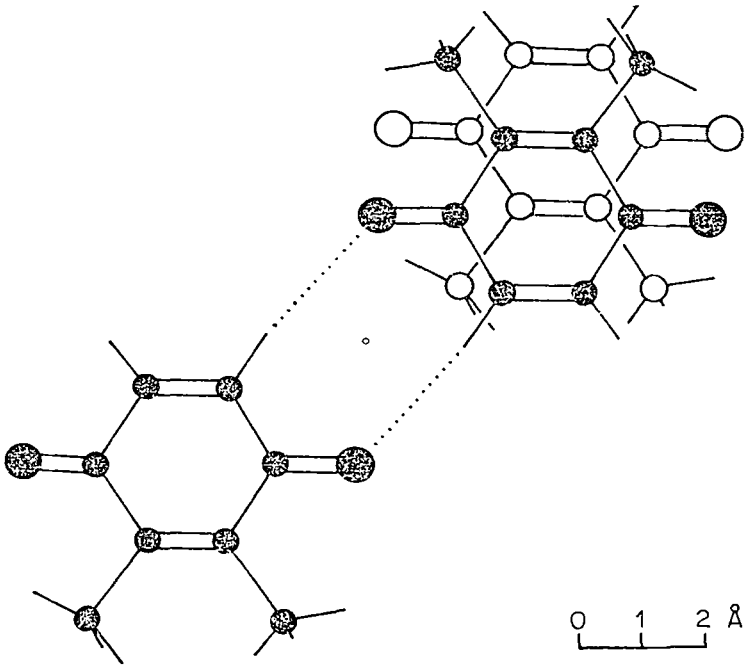


FIGURE 6. View of the structure of 2,3-dimethyl-1,4-benzoquinone normal to the molecular plane. The figure shows intermolecular overlap and C—H···O contacts. Based on Rabinovich[2].

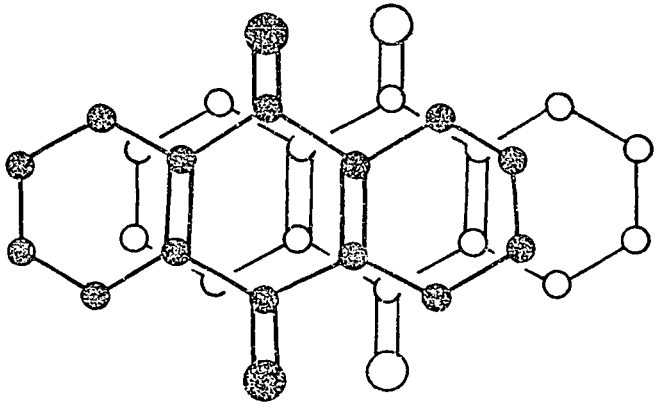


FIGURE 7. View of the structure of 9,10-anthraquinone normal to the molecular plane, showing intermolecular overlap. Based on Prakash[107].

We have thus far ignored lateral interactions. In the next section we will point out the tendency of quinone molecules to arrange themselves in a limited number of 'in-plane' geometries determined by lateral contacts.

The question then arises as to the compatibility of the intrastack overlap with the lateral environment. In 1,4-naphthoquinone overlap of carbonyl with the benzenoid ring is compatible with the 'in-plane' arrangement (Figure 4); on the other hand, in 1,4-benzoquinone overlap of C=O with two C=C bonds of a neighbouring molecule is not compatible with the environment. Instead the sheets of molecules are off-set, resulting in the interesting situation of practically no plane-to-plane molecular overlap (Figure 9).

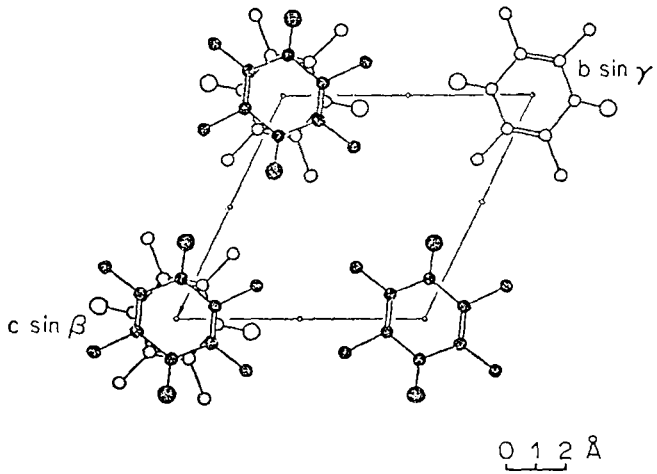


FIGURE 8. Packing arrangement of 2,3,5,6-tetramethyl-1,4-benzoquinone seen along [100]. For clarity, one of the two molecules has been omitted at (010) and at (011). Reproduced with permission from D. Rabinovich and G. M. J. Schmidt, *J. Chem. Soc.* (*B*), 144 (1967).

We have seen above that we can classify the overlap patterns and stacking modes of the smaller quinone molecules into a limited number of groups based on the type of carbonyl–π-electron interaction. As we move to the larger fused-ring systems we expect the packing arrangements to become dominated by the aromatic portions of the molecules. This question is referred to by Bolton and Stadler[139]. The large molecules flavanthrone, pyranthrone, violanthrone and isoviolanthrone all have crystallographic short axes of about 3·8 Å, and stack in plane-to-plane close packing with the normals to the molecular planes at 25–26° to the stack axis. This corresponds to an intermolecular overlap, as seen along the normals, which closely resembles that of graphite (Figure 10). The relationship between the stacks is not the same in the four compounds: in the first two the axes about which the molecules tilt (out of the *ac* plane)

are almost parallel for all stacks, with the molecules of alternate stacks having clockwise and anticlockwise tilts. In violanthrone and isoviolanthrone, however, the tilt axes (for tilt out of the *ab* plane) are not parallel for stacks alternating along *a*. This results in what Bolton and Stadler describe as a 'stacked ploughshare' arrangement.

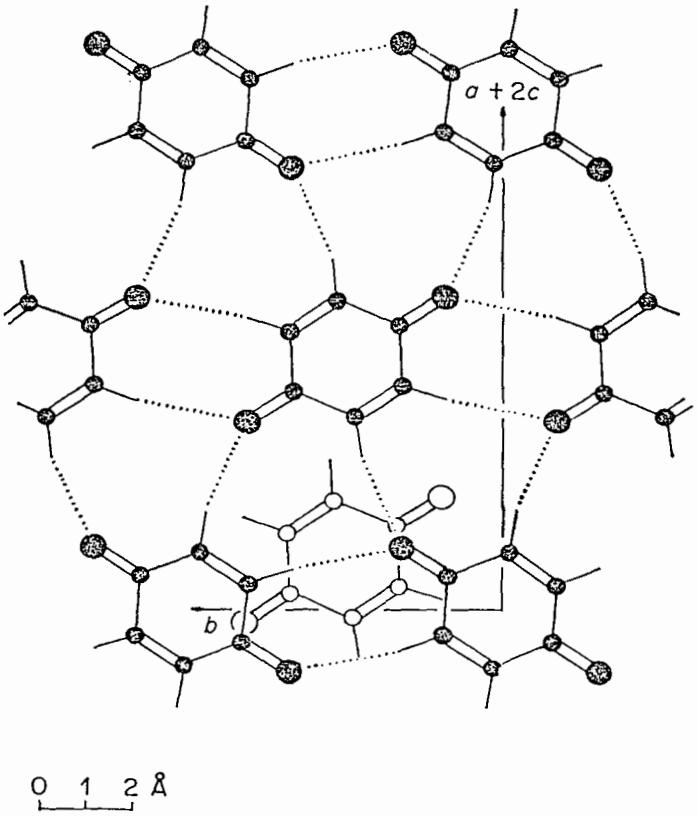


FIGURE 9. View of the structure of 1,4-benzoquinone normal to the molecular plane. Based on Trotter[1]. The figure shows the interlayer relationships and the C—H···O contacts.

B. Lateral Contacts

The most obvious of these contacts are hydrogen bonds of the type N—H···O and O—H···O, particularly with the acceptor atom being a carbonyl oxygen of the quinone ring. Such bonds are numerous in hydroxy- and amino-substituted quinones and in compounds containing suitable solvents of crystallization. The types of geometry which result are numerous and since, generally, the patterns are not specific to the quinones,

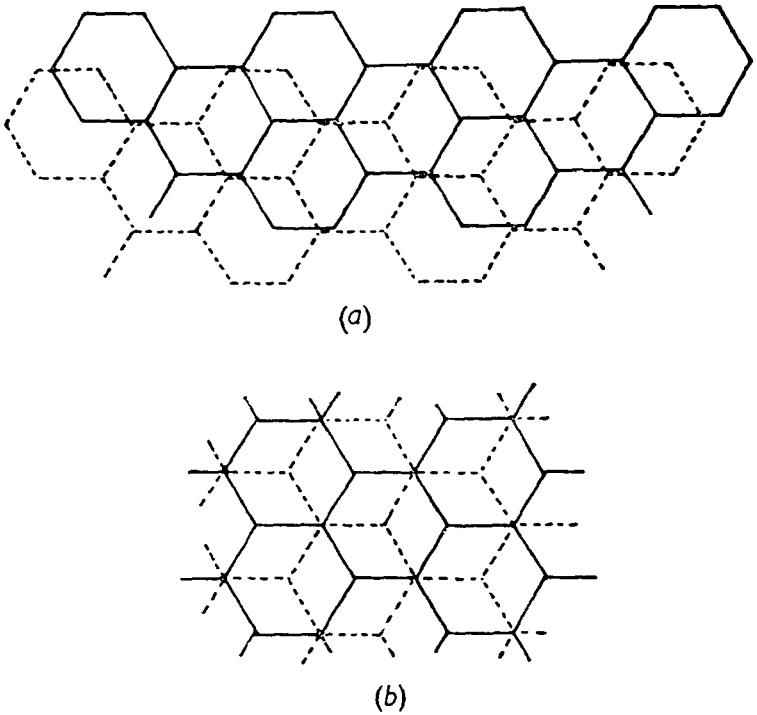


FIGURE 10. (a) The superposition of violanthrone molecules along the plane normals which is closely similar to (b) the stacking in graphite. Reproduced with permission from W. Bolton and H. P. Stadler, *Acta Cryst.*, **17**, 1015 (1964).

we do not consider them here. The question of bifurcated hydrogen bonds has been treated previously. Here we concentrate on some weaker, usually less obvious, types of lateral interaction.

1. C—H···O contacts

The existence of C—H···O interactions has frequently been postulated. The status of this postulate has recently been reviewed by Donohue[104] and by Sim[150]. Before embarking on this subject let us comment briefly on some geometrical aspects of conventional hydrogen bonds of the type X—H···O=C, where X is O or N. Frequently the strength of this bond is derived in terms of the shortness of the X···O distance. In fact, however, such a correlation may be misleading and a better indicator of the occurrence of hydrogen bonding is the existence of a constant geometric arrangement or pattern in a series of related materials. Thus, in X—H···O=C the X—H bond tends to lie in the plane of the carbonyl system and to point towards the lone-pair lobe on the acceptor oxygen

(assuming that the latter is sp^2 hybridized)[151]; we refer to this geometry as 'ideal'.

C—H···O=C interactions have been suggested in numerous quinones and short intermolecular C···O=C distances have been found in about half of the compounds we have listed. Gaultier and Hauw[96] refer to a number of quinones in this context.

We point out, first, that in the structure of 2,3-dimethyl-[2] (Figure 6), 2,6-dimethyl-[149] and 2,6-dichloro-[8] (Figure 2) 1,4-benzoquinones, in the related 2,6-dimethyl-γ-pyrone[152] and in 2-bromo-1,4-naphthoquinone[63] there is a common geometric pattern which can be interpreted in terms of C—H···O interactions. In these structures two adjacent molecules straddling a centre or psuedo-centre of inversion are coplanar, or nearly so, and have C—H bonds pointing towards the lone-pair lobes of the carbonyl oxygens. The distance between molecular centres (or pseudo-centres) is about 6·7 Å, and the CH···O and H···O distances are about 3·5 Å and 2·5 Å respectively. We refer to this as type-1 packing. Thus, in 2,3-dimethyl-1,4-benzoquinone (Figure 6) the molecular planes are offset by 0·1 Å and the distances from O to H and C in the type-1 ring are 2·57 and 3·61 Å, respectively. In the 2,6-dimethyl derivative the offset is 0·7 Å, and the corresponding distances 2·53 and 3·52 Å, respectively. Rees[63] gives 2·46 Å for the H···O distance in the 2,6-dichloro compound.

In 1,4-benzoquinone[1] (Figure 9) the molecules are arranged very nearly in planar sheets (all atoms are within 0·2 Å of the best plane). Along the 6·7 Å *b* axis neighbouring translationally equivalent molecules are connected by C—H···O= contacts in a type-1 pattern. Along this axis each molecule is thus connected to its two neighbours, generating an infinite planar ribbon. The distance between O and C in the type-1 ring is 3·50 Å. Adjacent ribbons are screw-axis related and are also interconnected by C—H···O= contacts, in a triangular pattern linking each molecule of one ribbon to two molecules of the adjacent ribbon (type-2); the C to O distance here is 3·38 Å. Thus each molecule acts as a hydrogen donor in four and as an acceptor in four C—H···O= contacts.

A very strong argument for this model comes from consideration of the structure of the thymine complex with 1,4-benzoquinone[36]. This is a layer structure in which each component is situated in a different layer, the two types of layer alternating. The structures of the thymine and benzoquinone layers are very similar to those of the planar sheets in the crystals of the pure components. Comparison of the benzoquinone sheet in the complex with that in the pure quinone (Figures 5 and 9, respectively) shows them to be practically indistinguishable, the *c*- and *a*-axes of the former corresponding to the *b*- and $(a+2c)$-axes of the latter. In the

complex the thymine molecules lie on a mirror plane, so that all its atoms are required by symmetry to lie in this plane. Since a sheet of benzoquinone molecules has completely different neighbouring sheets in the two materials, the in-sheet geometry must be determined by in-sheet, not out-of-sheet, forces.

1,4-Benzoquinone could, in principle, develop an infinite sheet structure based on the seemingly geometrically favourable type-1 contacts both within and between ribbons, as is done for example in its 1 : 1 complex with *para*-chlorophenol, which will be discussed later. That it does not do so may be due to repulsion between the lone pairs of oxygens[153] centrosymmetrically related in this type of contact (O···O distance about 4 Å), a repulsion which does not occur in type-2 contacts.

Trommsdorff and coworkers[13] have proposed a structure for the 2-methyl-1,4-benzoquinone crystal, based on some measured X-ray reflexions and on 'reasonable' molecular dimensions and intermolecular contacts. This structure is very similar to that of 1,4-benzoquinone, with the 6·72 Å *c*-axis of the methyl derivative corresponding to the *b*-axis of the unsubstituted quinone. Along this axis neighbouring molecules are connected in a type-1 pattern. Adjacent ribbons are screw-axis related; because of the methyl substituent there is only one type-2 ring per molecule so that on the average each oxygen participates in $1\frac{1}{2}$ C—H···O contacts.

In 1,4-naphthoquinone[62] (Figure 4) molecules are held in infinite sheets by two types of rings involving C—H···O= contacts. Centrosymmetrically related molecules participate in type-1 contacts, the hydrogen involved being that attached to C_2; the carbonyls in this ring each make only one contact with C—H. Screw-axis-related molecules make contacts similar to type-1, but involving the 'peri'-hydrogen of the benzenoid ring; each carbonyl participating makes two such contacts. Within the type-1 rings the molecules are offset by 0·7 Å and the CH···O distance is 3·57 Å; in the second type of contact the C(ar)H···O is 3·50 Å and the C(quinone)H···O is 3·25 Å.

Triclinic quinhydrone also has a sheet structure (Figure 11). Alternating hydroquinone and benzoquinone molecules form linear chains by O—H···O= hydrogen bonds. The benzoquinone molecules of adjacent chains are held together in a type-1 pattern parallel to the 6·77 Å *c*-axis (offset by 0·68 Å; CH···O= is 3·55 Å and H···O= is 2·62 Å). The hydroquinone molecules are held together in a similar pattern but involving phenolic instead of carbonyl oxygens as acceptor in the C—H···O contact (CH···O— is 3·46 Å and H···O— is 2·47 Å). In this way the sheet is developed, with each carbonyl oxygen as acceptor in one contact, and each hydroxyl group acting as a proton donor in an

O—H···O= bond and as proton acceptor in a C—H···O contact. The C—H···O— line points approximately along the bisectrix of the C—O—H angle.

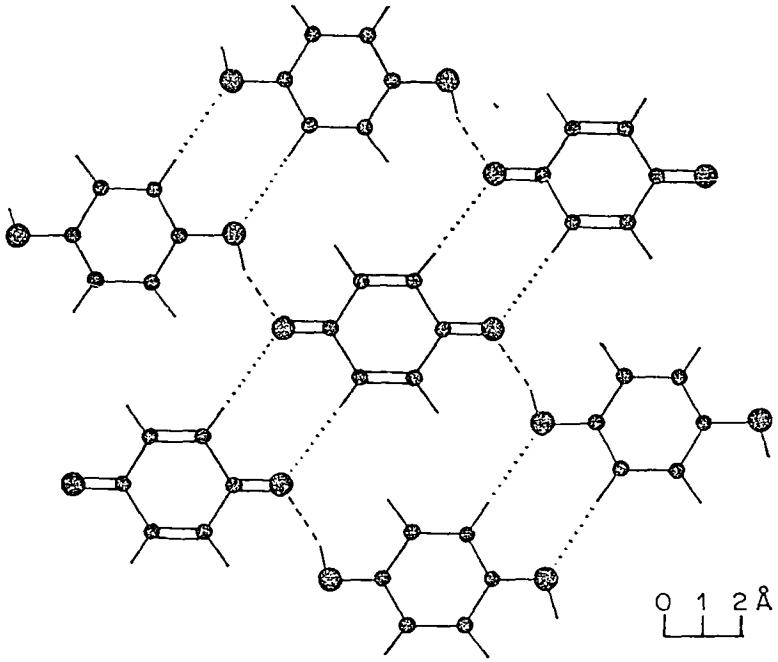


FIGURE 11. Triclinic quinhydrone. View of the layer structure normal to the central benzoquinone molecule. Based on Sakurai[31]. Figure shows C—H···O=, C—H···O— and O—H···O= contacts.

In the 1 : 1 complex of *para*-chlorophenol with 1,4-benzoquinone[34] (Figure 12) molecules of the two components are held together by O—H···O= hydrogen bonds, the molecules of the pair being almost coplanar. Two such pairs are linked to form a tetramer by C—H···O= contacts in a type-1 pattern (offset 0·70 Å; CH···O= is 3·64 Å) involving the carbonyls which do not participate in the O—H···O= hydrogen bonds. This thus generates sets of four approximately coplanar molecules which are held together by further type-1 contacts (offset 0·56 Å; CH···O= is 3·58 Å) along the 6·8 Å *a*-axis, between benzoquinone molecules, thus generating wide planar ribbons. The carbonyls in the centre of the ribbon participate in two type-1 contacts, while the outer carbonyls act as acceptors in one type-1 contact and in one O—H···O= hydrogen bond. The *para*-chlorophenol molecules of adjacent tetramers are connected by single C—H···O— contacts (CH···O— is 3·64 Å).

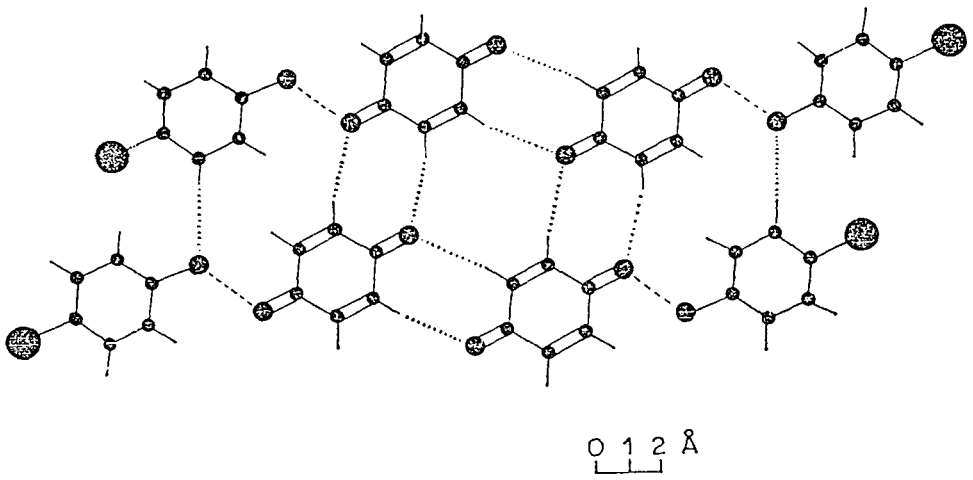


FIGURE 12. The complex *p*-chlorophenol : 1,4-benzoquinone (1 : 1). View of the layer structure. Based on Shipley and Wallwork[34]. Figure shows C—H···O=, C—H···O— and O—H···O= contacts.

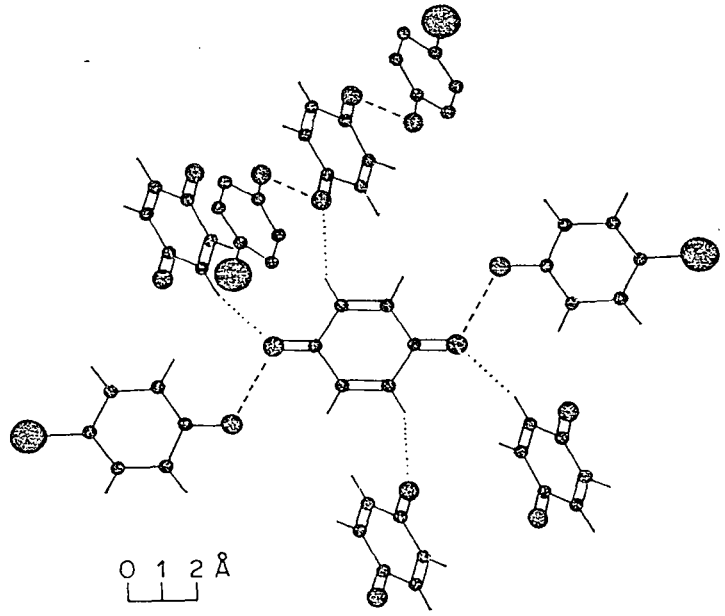


FIGURE 13. The complex *p*-chlorophenol : 1,4-benzoquinone (2 : 1). Packing environment seen normal to the plane of the central benzoquinone molecule. Based on Shipley and Wallwork[35]. Figure shows C—H··· O= and O—H··· O= contacts.

The environment of benzoquinone in its complexes with *para*-chlorophenol (1 : 2)[35] (Figure 13), with phenol (phenoquinone)[30] and with resorcinol[32] (Figure 14) are similar; nearly coplanar molecules of the two components are held together by O—H···O= hydrogen bonds in triplets in the first two complexes and in chains in the third. Quinone molecules related by a *c*-glide in the resorcinol complex form a continuous set of

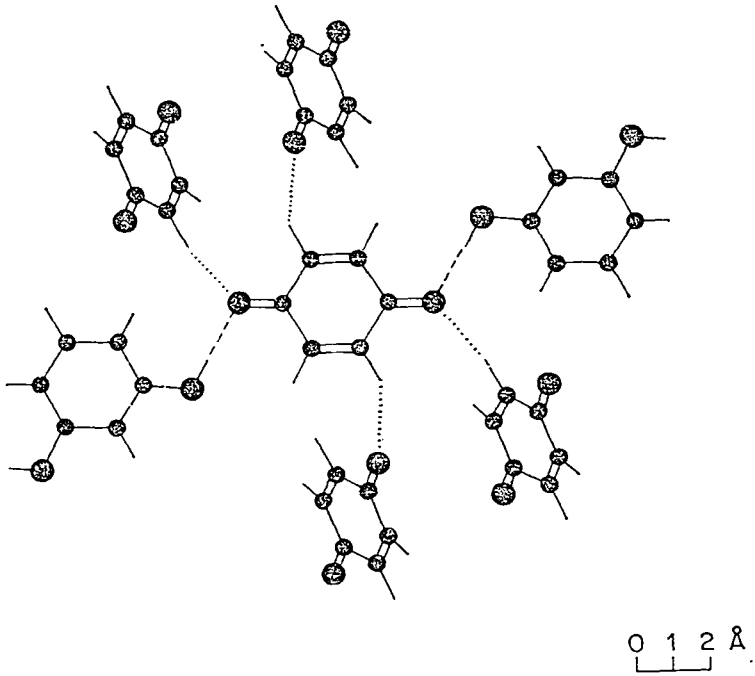


FIGURE 14. The complex resorcinol: 1,4-benzoquinone (1 : 1). Packing environment seen normal to the plane of the central benzoquinone molecule. Based on Ito, Minobe and Sakurai[32]. Figure shows C—H···O= and O—H···O= contacts.

single C—H···O= contacts with the CH···O= distance 3·33 Å and the H···O= distance 2·35 Å. These molecules are not coplanar, unlike the molecules discussed above. Each quinone molecule acts as a hydrogen donor in two such contacts, thus generating a chain in the *c*-direction. In addition, each quinone molecule acts as a hydrogen acceptor in two C—H···O= contacts in a second chain, as well as in two O—H···O= hydrogen bonds. In the chlorophenol complex the CH···O= distance is 3·36 Å, while in phenoquinone this distance is 3·32 Å with H···O being 2·23 Å. In the three systems under discussion the C—H···O= patterns have far from 'ideal' geometries based on the spatial orientation of

orbitals containing non-bonded electrons on oxygen. However, there is apparently compensation from the generation of a three-dimensional network of contacts.

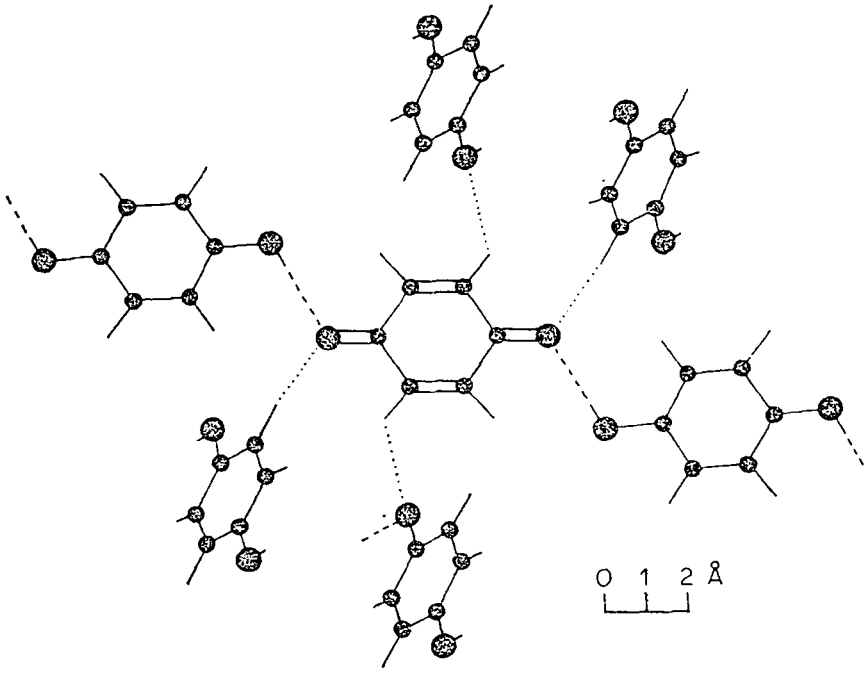


FIGURE 15. Monoclinic quinhydrone. Packing environment seen normal to the central benzoquinone molecule. Based on Sakurai[30]. Figure shows C—H···O=, C—H···O— and O—H···O= contacts.

The pattern of contacts in monoclinic quinhydrone[30] (Figure 15) is strikingly similar to those of the three complexes just described. In the quinhydrone the central benzoquinone molecule has single C—H···O— contacts to two hydroquinone molecules related to it by a pseudo-glide along [101] (compare the benzoquinone–benzoquinone contact in the *c*-direction in the resorcinol complex). The distances between equivalent points on the two molecules thus linked to the central benzoquinone are the [101] axis of the quinhydrone (11·50 Å) and the *c*-axis of the resorcinol complex (11·53 Å). The corresponding axes for the chlorophenol complex and for phenoquinone are 11·83 and 11·50 Å, respectively. In the quinhydrone only two CHs of the benzoquinone are involved in C—H···O contacts. Each carbonyl acts as a proton acceptor in one C—H···O= constant and in one O—H···O= hydrogen bond to hydroquinone

molecules. C(quinone)—H···O— is 3·19 Å with H···O— 2·48 Å, and C(arom)—H···O= is 3·44 Å with H···O= 2·54 Å.

As a final example of this type of contact we take 2-chloro-1,4-benzoquinone[6], the structure of which is in no way similar to that of the corresponding methyl derivative. No short chlorine···chlorine or chlorine···oxygen contacts are found, but there are C—H···O= contacts along the twofold screw-axis. Each molecule acts as a proton donor in two geometrically satisfactory and one geometrically poor contact, both with H···O distance of 2·43 Å. Each carbonyl acts as proton acceptor in one satisfactory and one poor contact (Figure 19).

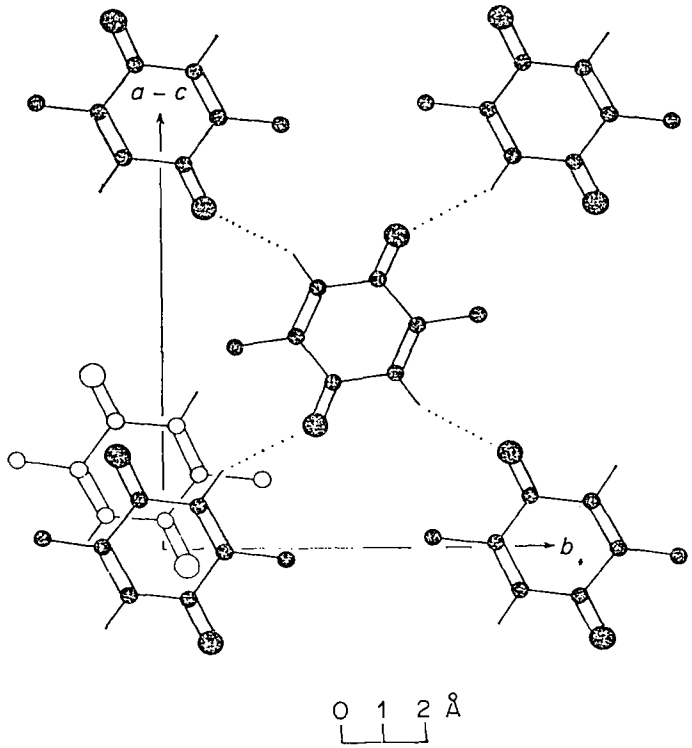


FIGURE 16. 2,5-Dimethyl-1,4-benzoquinone. View of the structure of the [101] layer. Based on Rabinovich and Schmidt[154]. Figure shows intermolecular overlap and the C—H···O= contacts.

In 2,5-dimethyl-1,4-benzoquinone[154], which is of space group $P\bar{1}$, the unit cell contains two crystallographically independent molecules, A and B, on centres of inversion (Figure 16). Rabinovich and Schmidt[154] noted that according to the distribution of intensities in the X-ray photographs

the molecular distribution approximates space group $P2_1/n$. The structure is a layer one, the layers lying parallel to (101) with spacing of about 3·3 Å. All atoms, except for the methyl hydrogens, lie within 0·1 Å of the best plane of the layer. Within the layer, molecules are related by pseudo-symmetry $P2_1/n$, and (101) is an approximate mirror plane; in the layer the angle between the *b*- and $(a-c)$-axes is 90·01°. In a given layer A and B, related by a pseudo-screw-axis parallel to *b*, are held together by a two-dimensional continuous net of C—H···O= contacts, one to each carbonyl (CH···O= is 3·44 Å and H···O= 2·48 Å). The geometry of these contacts is far from ideal but is apparently preferable to that of a type-1 contact in which the molecules would be connected into one-dimensional ribbons, adjacent ribbons being linked only by methyl–methyl contacts. If adjacent layers were offset in direction $(a-c)$ pseudo-monoclinic symmetry would result. However, apparently to allow the carbonyl to straddle the C=C bonds of a molecule in an adjacent sheet, the offset has a component along *b*, thus reducing the symmetry to triclinic.

When, as in the 1,2-quinones, the angle between the two carbonyl functions is acute, then other types of ring arrangements based on C—H···O contacts are possible. Such rings are found in benzocyclobutene-1,2-dione[90], in acenaphthenequinone[91] and in the isomorphous 3-chloro- and 3-bromo-1,2-naphthoquinones[86]. In the last-named compound (Figure 17) an infinite ribbon is built up by glide-plane-related molecules which are connected by contacts between the two carbonyls of one molecule and two CHs of the benzenoid ring of the neighbouring molecule. Clearly the pattern of contacts will vary with the angle between the carbonyls, and therefore with the size of the dione ring. In phenylcyclobutenedione[155] and cyclohexenylcyclobutenedione[156] the same patterns are found, involving approaches between C=O and C—H of the cyclobutenedione fragments (see also reference 150).

We conclude this section with two comments. First, the hydrogens on the double bonds in the quinone ring are slightly acidic and will thus have a higher tendency to participate in a C—H···O 'hydrogen bond' than will hydrogens on a non-activated olefinic bond. Second, C—H···N= interactions may be implicated in several systems (for example see references 157–159). Amongst the amino-substituted quinones, heterocyclic quinones and quinone oximes there are several cases suggestive of such interactions. However, in no case has this yet been clearly established, the main problem being that in most of the solved structures the dominant interaction is that of true hydrogen bonding; the C—H···N patterns may then be the result of other packing forces or may be so distorted as not to be recognizable.

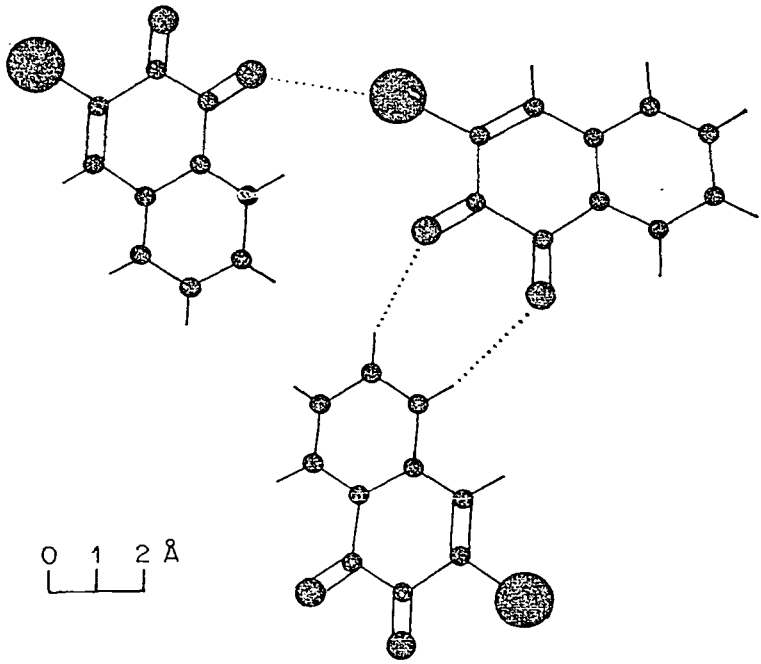


FIGURE 17. 3-Bromo-1,2-naphthoquinone. View normal to the reference molecule. Based on Courseille and coworkers[86]. Figure shows C—H···O= and Br···O=C contacts.

2. Halogen···carbonyl contacts

The existence of attractive interactions between bonded halogen atoms Cl, Br or I, and oxygen or carbonyl functions, whether in the same or different molecules, has clearly been established[160]. The interaction appears to be of the charge-transfer type with the halogen acting as acceptor. Gaultier, Hauw and Schvoerer[161] discuss this type of bond and its occurrence in a variety of benzoquinones, naphthoquinones and anthraquinones. As in hydrogen bonds the ideal arrangement appears to be that having the C—X (X = halogen) pointing towards the lone-pair electrons on the oxygen (assuming sp^2 hybridization). This results in a C—X···O angle of 160–170° (see, for example, Figure 17). The O···X distance is consistently less than the sum of the van der Waals radii of the halogen and oxygen atoms. The results given by Gaultier and coworkers are listed in Table 14.

On the other hand, the following compounds do not show this arrangement: 2-chloro-[162], 2,6-dichloro-[162] and tetrachloro-[9] 1,4-benzoquinone; 2-amino-[93] and 2-hydroxy-[95] 3-chloro-1,4-naphthoquinone, in both of

which the C—Cl···O angle is about 146° and the C···O distance about 3·7 Å, and in which the lateral packing is probably dominated by hydrogen bonds; 4-amino-3-chloro- and 4-amino-3-bromo-1,2-naphthoquinone[86], 2,3-dibromo-1,4-naphthoquinone[67] and 1-bromo-[111], 1-chloro-[109], 1,5-dichloro-[111], 1,5-dibromo- and 1,5-diiodo-[112] 9,10-anthraquinone. This last group tends to show short halogen–halogen, rather than halogen–carbonyl, contacts. Gaultier and coworkers[161] concluded that the naphthoquinones are most suited to give halogen–carbonyl interactions.

TABLE 14. Halogen–carbonyl contacts in quinones[161, 162]

Compound	C—X···O angle (°)	O···X (Å)	Reference
2,5-Dichloro-1,4-BQ	164	3·10	162
2,5-Dibromo-1,4-BQ	166	3·16	162
2-Chloro-5-bromo-1,4-BQ	157	3·21	162
2,3-Dichloro-1,4-BQ	164	3·01	162
2-Bromo-1,4-NQ	170	3·11	63
2-Iodo-1,4-NQ	168	3·21	64
2,3-Dibromo-1,4-NQ	168 166	3·15 3·22	67
2,3-Dichloro-1,4-NQ	169	3·28	66
3-Bromo-2-amino-1,4-NQ	167	3·20	97
3-Bromo-1,2-NQ	162	3·17	86
3-Chloro-1,2-NQ	160	3·22	86

BQ = benzoquinone; NQ = naphthoquinone

If we compare the O···X distances listed with the sum of the van der Waals radii (taking O···Br as 3·35 Å and O···Cl as 3·20 Å) we find a considerable shortening for the bromo derivatives and a lesser shortening for the chloro derivatives. Only two iodo-substituted materials have been studied, of which one shows this type of interaction, with considerable contraction in the O···I distance; however, there is insufficient information on iodo compounds. It does seem clear that bromine interacts with carbonyls more strongly than chlorine does: fluorine is probably not effective in such interaction.

No significant change in C=O and C—X lengths as a result of this interaction has been established, although Gaultier and coworkers[161] report a measurable shift in the carbonyl-stretching frequency.

We add some comments to those of Gaultier and coworkers[161]. Carbonyl–halogen contacts have not been observed to give rings across centres of inversion. Rather the contacts are between molecules related by a twofold screw-axis or a glide plane, and generate infinite but not planar sheets.

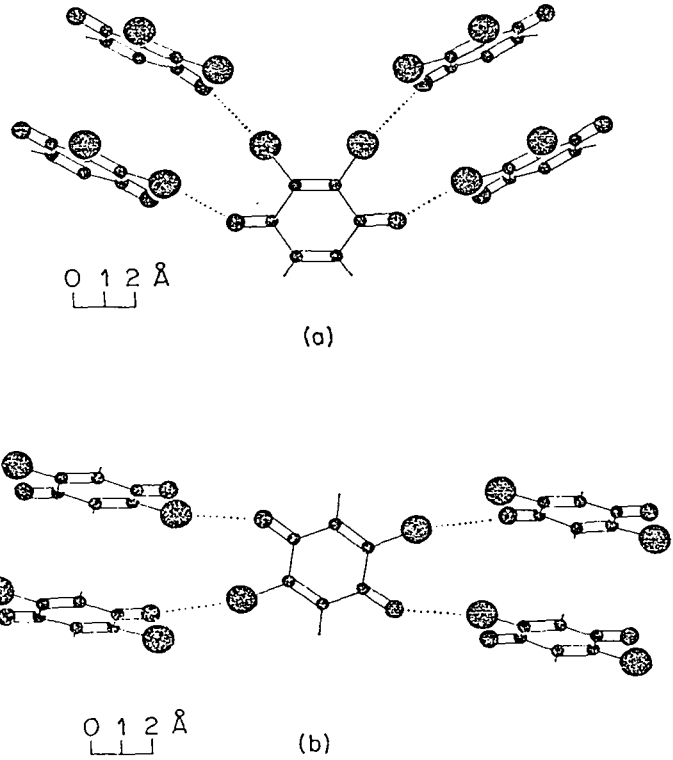


FIGURE 18. (a) 2,3-Dichloro-1,4-benzoquinone. (b) 2,5-Dichloro-1,4-benzoquinone. Packing arrangements seen along normals to planes of central molecules. After Rees[162]. Figure shows similarity of Cl···O=C contacts in the two structures.

Strong further argument for this interaction is provided by the near identity of pattern in different compounds. This is seen, for example, in the structures of 2,3- and 2,5-dichloro-1,4-benzoquinone (Figures 18a, b). It is noteworthy that in those cases where this type of contact is not observed we find other characteristic contacts present. Thus, we have noted the halogen–halogen contacts in the anthracene derivatives and the C—H···O contacts in 2-chloro- (Figure 19) and 2,6-dichloro-1,4-benzo-

quinone. Of special interest is the similarity of the Cl···O=C pattern shown in Figure 18 and C—H···O= pattern found in the 2-chloro-derivative (Figure 19).

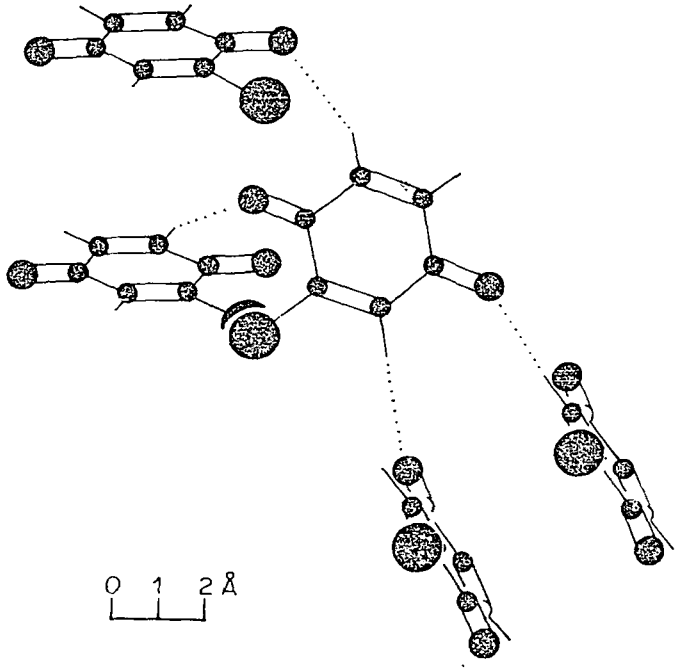


FIGURE 19. 2-Chloro-1,4-benzoquinone. Packing arrangement seen normal to plane of central molecule. Based on Rees[6]. Figure shows C—H···O= contacts.

3. Halogen···halogen contacts

The fact that halogenated materials tend to crystallize in structures in which there are close approach distances between halogen atoms is well established. In crystals of halogen molecules the intermolecular halogen···halogen distance tends to be less than the sum of the van der Waals radii of the contacting atoms[163]. Hillier and Rice[164] and Nyburg[165] have argued for some intermolecular electron delocalization or transfer in crystalline chlorine (see also Mason[166]). Sakurai and coworkers[167] have summarized the experimental evidence on electron delocalization in halogen-containing compounds. They recognized, further, two characteristic types of contacts between C—Cl bonds. In both, the chlorines are in close contact; in one, the bonds are near collinear and antiparallel, while in the second, the two bonds are nearly perpendicular to one another.

Green, Leser and Schmidt[168] have discussed the utilization of dichloro substitution to induce planar molecules to adopt face-to-face close packing (short crystal axis $\leqslant 4$ Å). It would seem then that there is a third common type of C—Cl contact in which these bonds are parallel and strongly overlapped. Here, however, a glance at the quinones is illuminative: of twenty halobenzoquinones and derivatives listed in this paper, only seven, all oximes, have short crystal axes of about 4 Å or less; of fourteen halo-naphthoquinones eight have such axes; and of twelve halo-anthraquinones nine have such axes. It seems probable that the efficiency of C—halogen bond interactions in inducing plane-to-plane close packing is dependent largely on the van der Waals interactions between the aromatic systems.

In addition to those quinones showing halogen···halogen close approach up a stack axis, there are a number of quinones having lateral contacts which may fit the classification of Sakurai and coworkers[167]. We list some of these materials:

2,5-dihalo-1,4-benzoquinones[11] (Cl···Cl, 3·83 Å; Cl···Br, 3·85 Å; Br···Br 3·83 Å).

2,6-dichloro-1,4-benzoquinone[8] (Cl···Cl, 3·33 Å), chloranilic acid (Cl···Cl, 3·34 Å), its dihydrate (Cl···Cl, 3·45 Å) and the monohydrate of its ammonium salt (Cl···Cl, 3·50 Å)[18-20].

(β)2-chloro-1,4-benzoquinone-4-oxime acetate[52] (Cl···Cl, 3·33 Å).

(α)5-(2′-chloroethoxy)-1,2-benzoquinone-2-oxime[55] (Cl···Cl, 3·57 Å).

1-chloro-[108] (Cl···Cl, 3·70 Å), 1-bromo-[109] (Br···Br, 3·66 Å), 1,5-dibromo- (Br···Br, 3·68 Å) and 1,5-diiodo- (I···I, 3·71 Å)[112] 9,10-anthraquinones.

In considering the lateral contacts we have come across cases where there are close halogen···halogen contacts and no close halogen···carbonyl contacts; cases where the reverse is true; and other cases where the two types of contact co-exist. Similarly the C—H···O interactions are sometimes complementary to, and sometimes competitive with, the other lateral interactions. The way in which a given system actually crystallizes must depend both on the relative energies associated with the different types of interaction and on the degree to which the various possible contacts have compatible spatial requirements. The study of the lateral contacts is obviously still in its infancy and much further research in this field remains to be done.

IV. ACKNOWLEDGMENT

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The Chemistry of the quinonoid compounds
Edited by Saul Patai

CHAPTER 3

Synthesis

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I. INTRODUCTION

Several chapters in this volume deal *inter alia* with the synthesis of quinones and to avoid excessive overlap this chapter is restricted to methods for the preparation of quinones from non-quinonoid precursors and to annellation methods in which an additional aromatic ring is built

onto an existing quinone ring. Otherwise transformation reactions whereby one quinone is converted into another are not considered. Quinones have been derived in numerous ways but the emphasis here is on general methods which give yields acceptable for synthetic purposes. Certain quinones which are very reactive and difficult to isolate can nevertheless be generated *in situ* and trapped efficiently. These reactions are also outside the scope of this chapter but their synthetic value should not be overlooked. The have been reviewed under the title *Syntheses with Nascent Quinones*[1] (see also reference 2).

II. OXIDATIVE METHODS

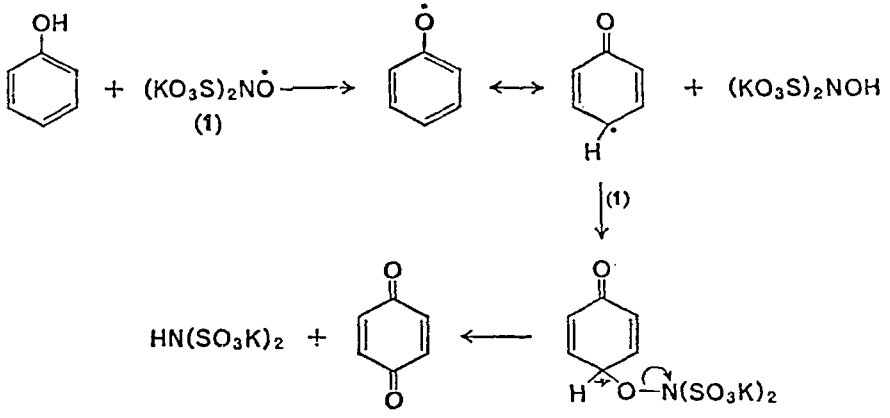
The vast majority of quinones have been prepared by oxidation, indeed this is the only completely general method. The substrate is usually a phenol or phenolic ether, an amine or a hydrocarbon. Many oxidants have been employed but in the discussion which follows only those of most practical value are considered. Quinols are the easiest to oxidize, and monohydric phenols and monoamines which require the introduction of one, and hydrocarbons which require the introduction of two atoms of oxygen, are progressively more difficult. However, since the use of Fremys' salt (potassium nitrosodisulphonate) was discovered[3], conversion of a monohydric phenol into a quinone has become a very easy process and this is frequently the method of choice. Accordingly it is considered first.

A. Monohydric Phenols

1. Fremy's salt

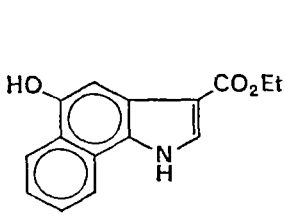
The Teuber reaction (recently reviewed[4]) for the oxidation of phenols has the advantages that it proceeds rapidly and efficiently under very mild conditions and side-reactions are rare. The disadvantages are that the reagent has to be prepared beforehand, an aqueous medium is necessary, it is not convenient for large-scale work, and occasionally it fails. Nevertheless for preparations under 10 g the advantages, compared to other methods, are overwhelming. The reagent is cheap and easily made, and an excellent method of preparation is available[5].

The oxidation is normally carried out in aqueous alcohol, aqueous acetone, etc., buffered with phosphate or acetate, at room temperature, two equivalents of reagent being required. Usually the purple colour of the radical, **1**, disappears almost immediately and the quinone may precipitate in a short time. The mechanism originally proposed by Teuber[6] is shown in Scheme 1. That the oxygen atom introduced is derived from the reagent was later confirmed[7] using ^{18}O-labelled Fremy's salt



SCHEME 1

and it was possible to isolate[8] the intermediate dienones in certain cases. Thus **3a** was obtained from **2** and converted into **3b** with acid. Scheme 1 can also be written for *o*-quinone formation and the large steric requirements of the intermediate dienone (see **3a**) may account for the occasional low yield, or failure. However, electronic factors are also important and electron-withdrawing substituents can inhibit the reaction completely[6, 221]. (Similar, but inferior, oxidations to *p*-quinones can be effected in organic solvents using organic nitroxides[24], chromyl chloride[43] and perchloryl fluoride[44].)



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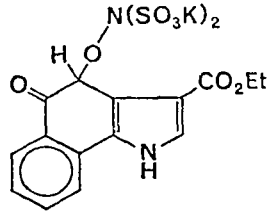
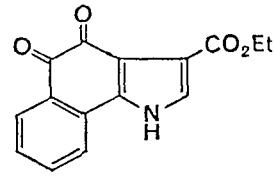
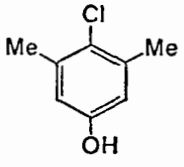


(3a)



(3b)

Normally a phenol with a free *para* position gives exclusively a *p*-quinone but if the *para* position is blocked an *o*-quinone results. Exceptionally, a *p*-chloro substituent[9] or a *t*-butyl group[20] may be eliminated during quinone formation [e.g. **4**→**5** (87%), **6**→**7** (65%)]. Certain α-naphthols give a mixture of *o*- and *p*-quinones (5-hydroxy-1,2- and 1,4-naphthoquinone from 1,5-dihydroxynaphthalene)[10] which may be ascribed to steric restriction of *p*-dienone formation by the *peri*-substituent. 3-Phenyl- and 2,3-diphenyl-7-hydroxy-benzofurans, -benzothiophenes and -indoles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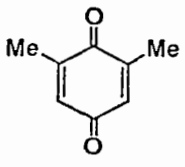
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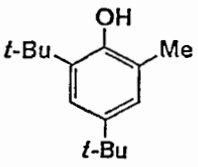
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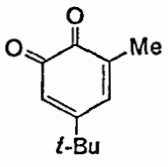
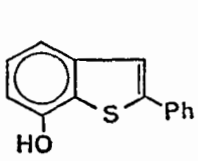

(7)

give mixtures of *o*- and *p*-quinones whereas the 2-phenyl analogues yield only *p*-quinones[21-23]. For example[23] **8** gives **9** (31%) but **10** yields both **11** (35%) and **12** (41%). This was attributed to the hindrance offered by the 3-phenyl group to the formation of the dienone **13**, the alternative intermediate **14** being favoured, but in view of the relatively low yield of **9** the explanation is unconvincing. 7-Hydroxy-1-methyl-2,3-diphenylindole forms an *o*-quinone as sole product[21] and, surprisingly, so does **15**[42].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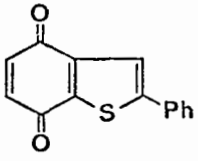
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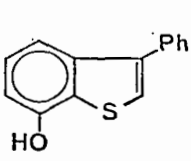
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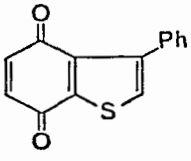
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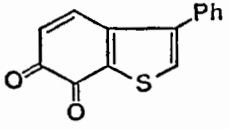
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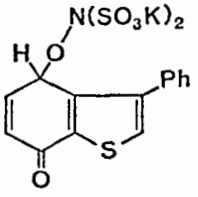
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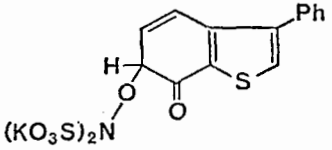
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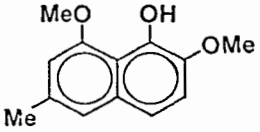
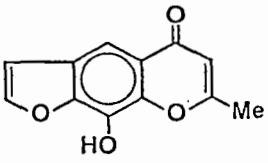

(15)

Teuber oxidized a large number of simple phenols[6,11] and naphthols[10] to the corresponding *o*- and *p*-quinones, usually in > 70% yield, sometimes almost quantitative. Numerous heterocyclic examples (e.g. **16** → **17**)[12] can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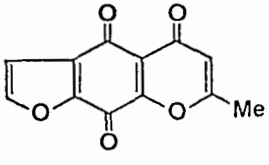
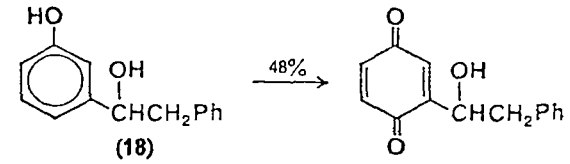

(17)

be found in recent reviews[4,13]. More complex phenols, such as **18**[15], **19**[15] and **20**[14] can also be selectively oxidized and in general, with the exceptions noted, substituents and side-chains are not attacked by Fremy's salt under the usual conditions. This virtue is further exemplified in the



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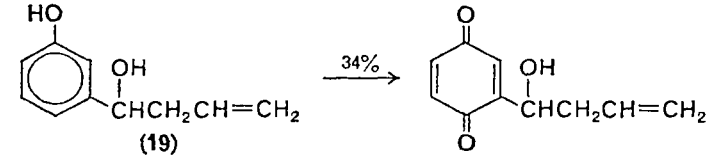

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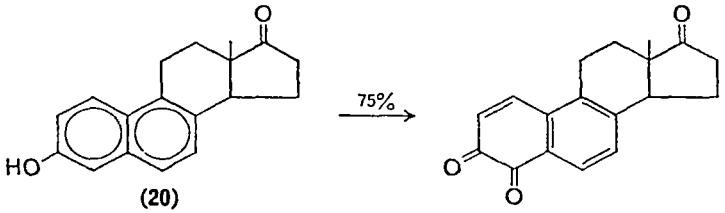
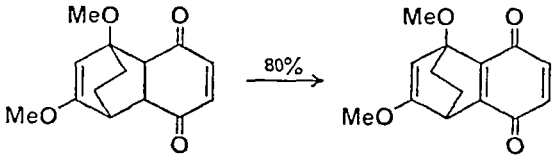


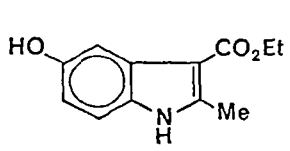
(20)

dehydrogenation of the enedione **21** to the quinone **22**; this could only be effected, with retention of the enol ether function, using the Teuber reagent[16].



(21) (22)

As mentioned previously, the Teuber oxidation is usually effected under neutral conditions or in the presence of phosphate or acetate buffer. These conditions are prescribed by the limited pH range within which solutions of Fremy's salt are stable and by the instability of many quinones in alkaline solution. Also *o*-quinones tend to be unstable under acid conditions and if prepared by Teuber oxidation < pH 7 further reaction may ensue. Thus the phenolic indole **23** gives the *o*-quinone **24** (85%) under the usual conditions but in acid solution the dimer **25** is slowly formed[17]. In the quinoline series further reaction of an *o*-quinone with the starting phenol is not unusual. Oxidation of the phenol **26** in neutral solution gave the quinolinoxyquinone **27** (60%) by nucleophilic displacement of chlorine from the quinoline-5,6-quinone initially formed[18]; in this case the normal product, **28**, could only be obtained when the



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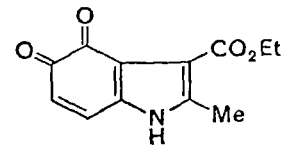

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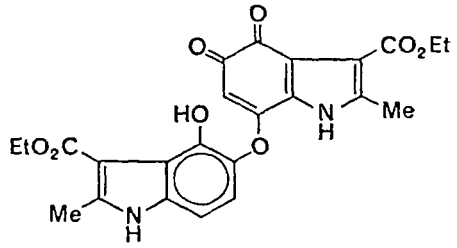
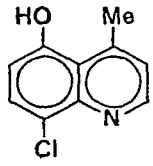


(25)

oxidation was effected at pH 4·5–4·7. On the other hand, the phenol **29** forms the dimer **30** (40%) when oxidized under acid conditions[18] while the isomer **31** results when the oxidation is effected in a neutral medium[19], an interesting example of the behaviour of a phenol as an ambident nucleophile.



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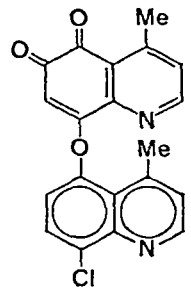

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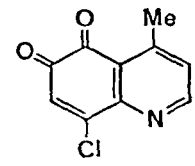

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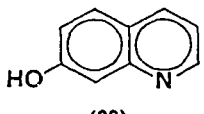

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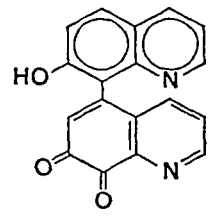

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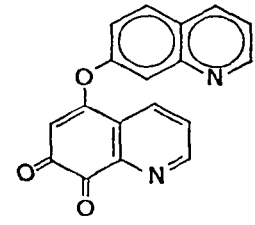
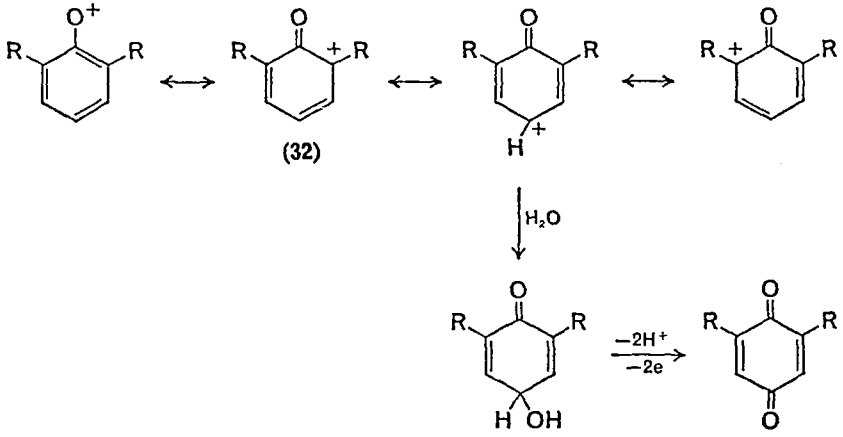


(31)

2. Other reagents

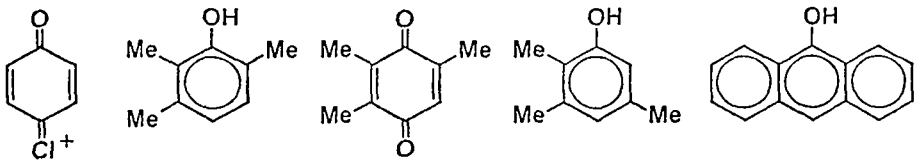
The oxidation of phenols is a complex subject[25], an important factor controlling the relative ease of oxidation being the redox potential[25, 107, 124]. Oxidants can be divided into 1-electron and 2-electron types, the former

generating aryloxy radicals which couple together (or with the Teuber reagent) leading, sometimes, to quinone formation (see below), while the latter produce cations **32** (with the charge localized predominantly in the ring) from which quinones arise by solvolysis and further oxidation (Scheme 2). However, 1-electron oxidants can also generate cations, in two steps, and both ferric chloride[40] and the hexachloroiridate anion[41], for example, will oxidize 2,6-dimethylphenol to 2,6-dimethylquinone, although the yields are low. Ionic oxidations are usually effected in acid solution or with reagents of high potential but as none of the available reagents have the scope of Fremy's salt they are considered here collectively.



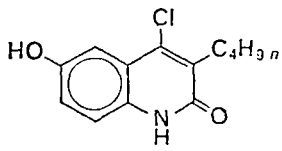
SCHEME 2

Formerly chromic acid was widely used for the oxidation of phenols but in the absence of a *p*-substituent (e.g. Hal, HO, NH_2) yields are usually poor. In the long list of phenols tabulated in Cason's review[26] the only successful oxidations of this type are those of highly alkylated derivatives such as **34** which gave **35** in 50% yield on treatment with dichromate and sulphuric acid[27]; however, under the same conditions, no quinone could



be obtained from the isomer **36**. 9-Anthranols (= 9-anthrones) (**37**) might be regarded as highly substituted phenols and these can also be

oxidized to quinones without difficulty. *o*-Quinones are rarely obtained in this way from phenols lacking *o*-substituents but 6-hydroxycarbostyrils[28] provide interesting exceptions; for example oxidation of **38** with chromic acid gave **39** (83%). However, such compounds can be regarded as 'internal' acylaminophenols and the reaction may proceed by hydration, and then further oxidation, of the quinoneimine or aza-*amphi*-quinone (**40**). Lead tetraacetate was equally effective[28].



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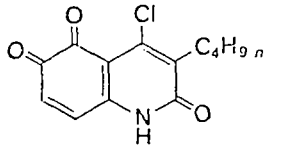

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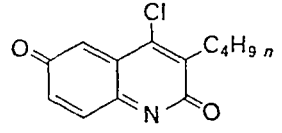
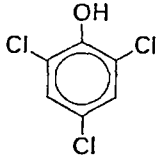


(40)

The presence of halogen *para* to the phenolic group is usually an advantage and yields are improved. Presumably the halogen atom increases the stability of the intermediate cation (see **33**), but is itself eliminated. Thus **41** affords **42** in 69% yield with chromium trioxide in acetic acid[29] and the same reagent converted **43** into **44** (82%)[30].



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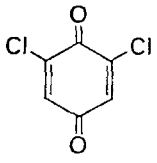

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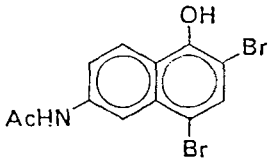

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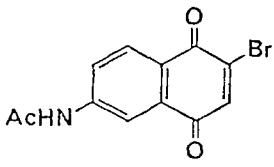
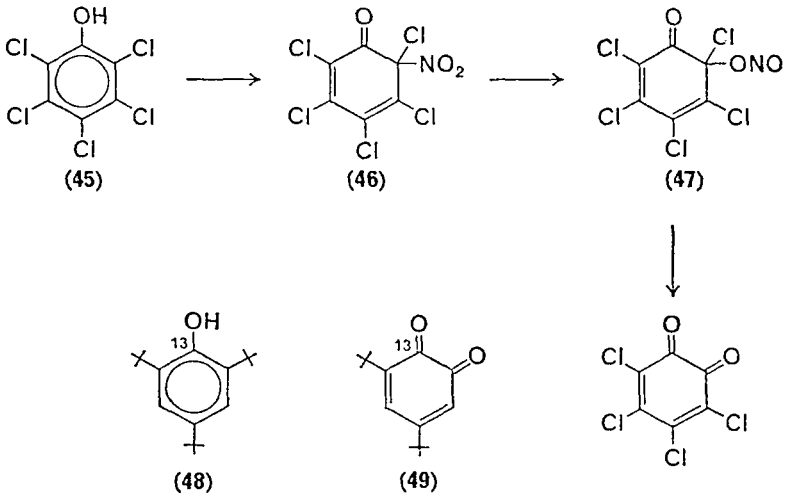


(44)

The oxidation of monohydric phenols with nitric acid is of little value unless they are highly substituted when reaction proceeds with elimination (mainly) of an *ortho* group. Thus the useful tetrachloro-*o*-benzoquinone can be prepared from pentachlorophenol, **45**, by treatment with fuming nitric acid to form a nitro-ketone, **46**, which rearranges to **47** and eliminates nitrosyl chloride[31]. Halogenated *o*-naphthoquinones can be prepared[32] similarly and the labelled quinone **49** was obtained (40%) in the same way from **48**[33].

Numerous other methods have been employed for the oxidation of monohydric phenols to quinones but mostly they have been applied only to very simple compounds and their synthetic value is generally low. Anodic oxidation may be an exception. There has been sporadic interest[135] in this method for many years but with limited success. However, it has been reported recently[31] that 2,6-dimethylphenol can be converted

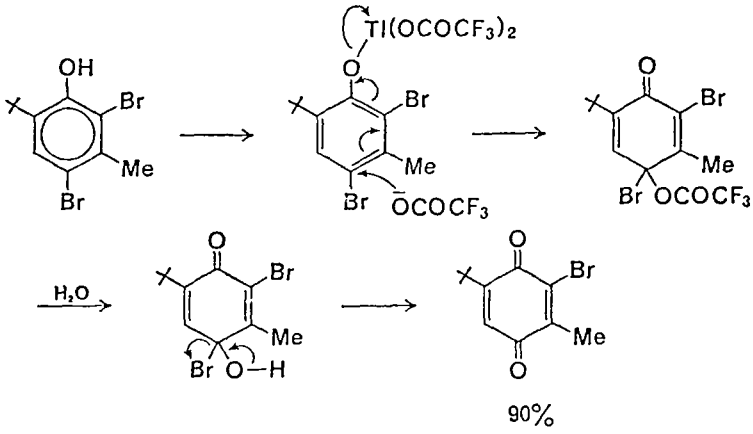


quantitatively into 2,6-dimethylquinone by anodic oxidation in *N*-sulphuric acid (PbO_2 anode) or in aqueous acetonitrile (Pt anode). The reaction is considered to proceed via the aroxyl radical to the cation (**32**; R = Me) and then solvolysis, and is potentially a useful quinone synthesis. The same phenol was also used as a substrate in a comparative study[40] of transition metal oxidants but only with titanium(III) chloride–hydrogen peroxide did the yield of 2,6-dimethylbenzoquinone exceed 50%. A number of polyalkylphenols have been oxidized to *p*-quinones using peracetic[35] or trifluoroperacetic[36] acid in fairly good yields. The reaction proceeds by electrophilic hydroxylation to form a quinol which is further oxidized. Quinones may also arise, along with other products, when phenols are treated with periodate[37] or lead tetraacetate[38]. A much more promising reagent is thallium(III) trifluoroacetate[39] which has been used to oxidize a series of *p*-halogeno- and *p*-*t*-butylphenols in high yields. *p*-Quinones are invariably formed, the substituent being eliminated. The reaction is illustrated for a *p*-bromophenol (Scheme 3). Extension to a wider variety of phenols would be welcome.

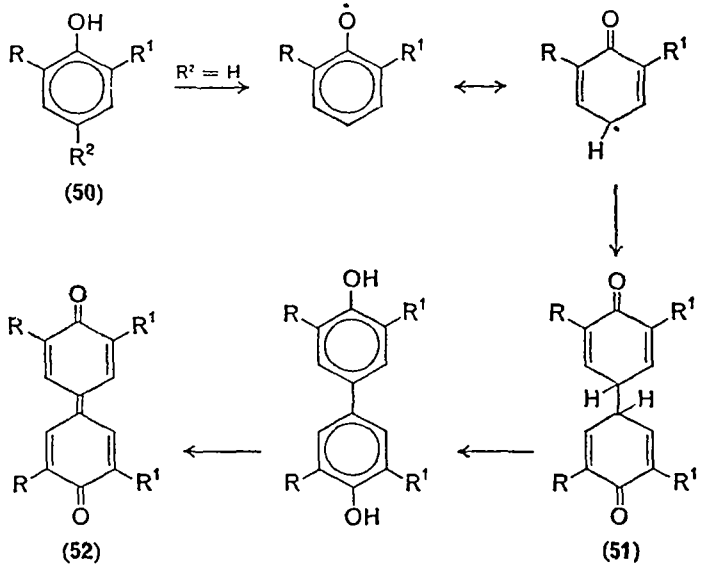
3. Formation of extended quinones

In addition to the conventional quinones discussed above extended quinones can also be formed from phenols by a process involving oxidation, coupling and further oxidation. Using 1-electron oxidants, the normal course of events is shown below (Scheme 4), high yields of 4,4′-dipheno-quinones (**52**)* being obtained with 2,6-disubstituted phenols. It is

* A mixture of geometrical isomers is produced when $R \neq R^1$ [48, 54].



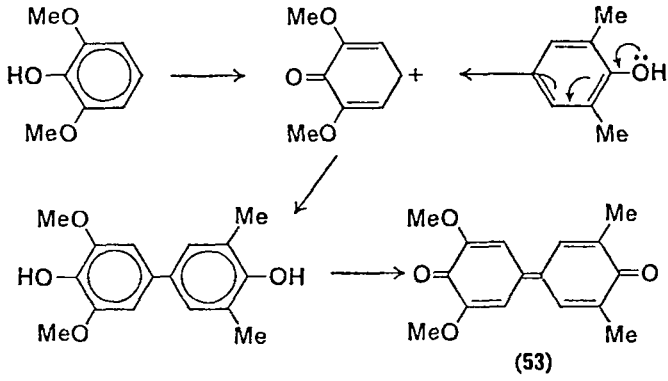
SCHEME 3



SCHEME 4

interesting that a stable tautomer of type **51** (R = *t*-Bu) could be obtained by oxidation of 2,6-di-*t*-butylphenol with alkaline ferricyanide[50]. Numerous reagents can effect this oxidation in some degree but in practice the best results (usually > 75%) have been obtained with ferric chloride[45], alkaline ferricyanide[46], silver oxide[47] and lead dioxide[48]. Stable aroxyl radicals[49] have also been used to good effect, and isopentyl nitrite[83], transition metal complexes[51] and oxygen in alkaline solution[50] are other alternatives. Silver

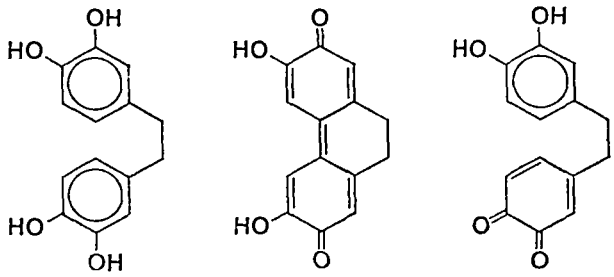
carbonate/Celite appears to be an excellent reagent but only three examples of its use have been reported[73]. Substituents *para* to the phenolic group may be eliminated in the course of diphenoquinone formation; oxidation of **50** (R = R^1 = *t*-Bu, R^2 = Hal[49], NO_2[52], CHO[53], CO_2H[53] and PhCHOH[65]) gives high yields of **52** (R = R^1 = *t*-Bu) in all cases. Synthesis of diphenoquinones by this method invariably gives symmetrical compounds (or geometrical isomers) but if 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) is used as oxidant the reaction may take the form shown[55] in Scheme 5. In this way the quinone **53**, for example, was obtained,



(53)

SCHEME 5

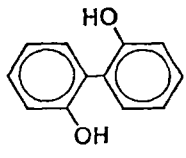
together with the two symmetrical analogues, by oxidizing a mixture of 2,6-dimethoxy- and 2,6-dimethylphenol[54]. An interesting intramolecular oxidation is the conversion of **54** to **55** with ferric chloride but the reaction may proceed by way of the *o*-quinone **56**[56].



(54) (55) (56)

In principle it should be possible to prepare *o*-diphenoquinones, **58**, by *ortho* coupling of suitable phenols. In fact this has only been achieved once[57] in the oxidation of 3,4-dimethoxyphenol with alkaline ferricyanide, under nitrogen, to give **58** (R = R^1 = OMe; R^2 = H) although the

quinone **58** (R = *t*-Bu; R^1 = H; R^2 = Me) is a transient intermediate when the phenol **59** reacts in alkaline solution to form a trimer[58]. Otherwise these reactive blue quinones have only been obtained[59] by ferricyanide oxidation of 2,2′-dihydroxybiphenyls (**57**) which should be fairly heavily substituted (in any case at 5,5′) to ensure adequate stability for **58**.



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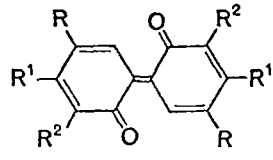

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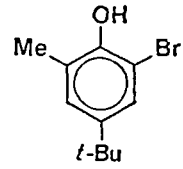
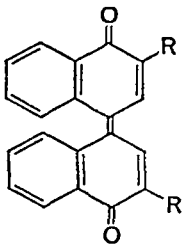


(59)

On the other hand 2,2′-binaphtho(**61**)- and 2,2′-bianthra(**62**)-1,1′-quinones are easily obtained by oxidation of 1-naphthols and 1-anthranols provided that position 4 is blocked. Ferric chloride[60] or alkaline ferricyanide[61] are the usual oxidants but a stable aroxyl radical[62], autoxidation in alkaline solution[61] and a copper–collidine (or pyridine) complex in the presence of oxygen[63] have also been employed. Thus 2-substituted-1-naphthols give red to violet quinones (**60**) while 4-substituted-1-naphthols give the blue isomers (**61**). 4-Methoxy-1-anthranol gives **62** (75%) simply by exposure to air in methanolic solution[64].



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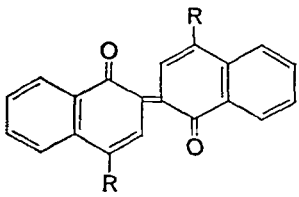

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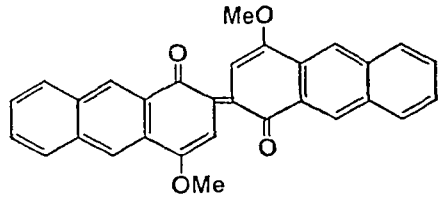
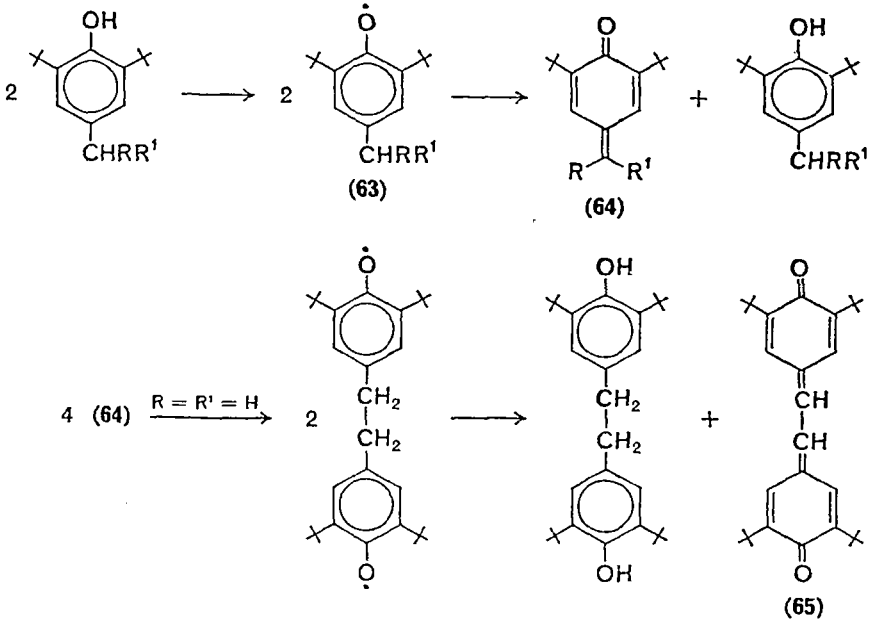


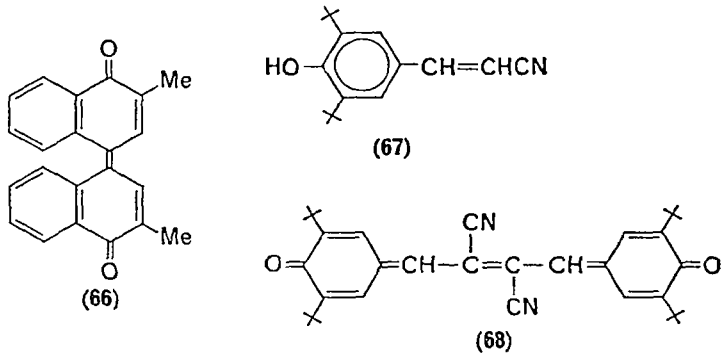
(62)

Hindered aroxyl radicals of the type **63**, i.e. having a *p*-alkyl substituent with an α-hydrogen atom, tend to disproportionate into a quinonemethide (**64**) and the original phenol. Dimerization of **64** then leads to the formation of a stilbenequinone (**65**)[66] (Scheme 6). The reaction is restricted mainly to the formation of symmetrical stilbenequinones from 2,6-dialkyl-4-methylphenols (and related naphthols), the usual oxidants being alkaline ferricyanide[67], silver oxide[68] or lead dioxide[69]. Fremy's salt[70] and a stable aroxyl radical[71] have also been used but even with excess oxidant yields seldom exceed 50%. However, in three cases silver carbonate/Celite



SCHEME 6

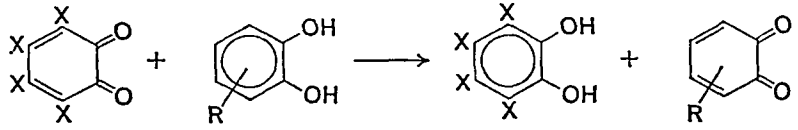
gave yields of >90%[73]. Silver oxide oxidation of 2,4-dimethyl-1-naphthol affords **66**[68] and by extension to *p*-hydroxystyrenes the more extended quinone **68** has been obtained[72] from **67** by treatment with excess alkaline ferricyanide or tri-*t*-butylphenoxyl.



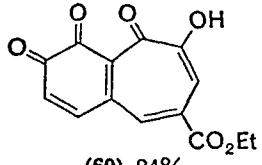
B. Catechols

The oxidation of catechols is an excellent method for the synthesis of *o*-quinones[26]. However, many *o*-quinones, especially *o*-benzoquinones, are sensitive to both electrophilic and nucleophilic attack and for such

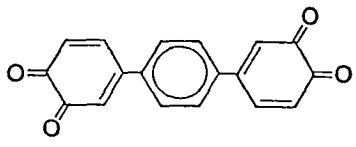
compounds mild conditions are essential. Reaction mixtures should be worked up without delay to avoid dimerization[81]. (Quinones of many types are potentially photolabile and it is good practice to prepare and store new quinones in the dark, until their stability has been established.) The classical method[26]—shaking with freshly prepared silver oxide in dry ether or benzene, in the presence of anhydrous sodium sulphate—works well, a recent improvement[73] being the use of silver carbonate/Celite. The absence of water is not essential, as formerly thought, for *o*-benzoquinone has recently been prepared (86% yield)[79] by shaking a chloroform solution of catechol with ceric sulphate in aqueous sulphuric acid. In chloroform solution the quinone is stable at pH 3 or lower, but begins to decompose at pH 4. Another excellent method[74] for the synthesis of *o*-quinones employs tetrachloro- or tetrabromo-*o*-benzoquinone (prepared by treatment of the tetrahalogenocatechols with nitric acid) as dehydrogenating agents, limited only by the redox potential of the catechol which must be lower than that of oxidant to permit the reaction (below) to



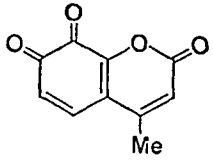
proceed. (An extensive list of redox potentials is available[75].) *o*-Quinones prepared in this way include **69**[76], **70**[77] and **71**[74] but the method failed



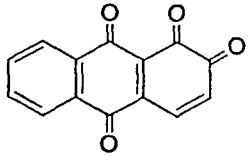
(69) 84%



(70) 94%



(71) 85%



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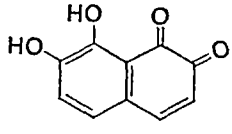


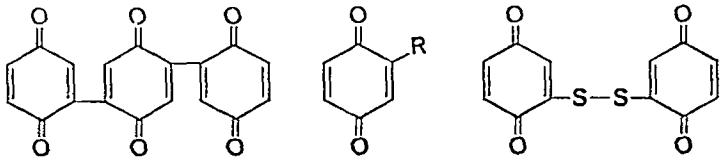
(73)

with alizarin and related compounds. High potential quinones of this type (**72**) are usually made of oxidizing alizarin, etc., with lead tetracetate[78]. Other reagents used in *o*-quinone synthesis include DDQ[82],

iodate (e.g. **73** from 1,2,7,8-tetrahydroxynaphthalene[80]), and periodate but the latter is mainly of interest for the oxidation of catechol monomethyl ethers (see section II.D).

C. Quinols

The oxidation of quinols is the easiest method of all for the preparation of *p*-quinones when the appropriate quinol is available. It requires the removal of two electrons and two protons from the quinol and the choice of reagent is therefore governed by redox potentials. In practice quinols are commonly oxidized with chromic acid, ferric ion or silver oxide which have long been used for this purpose[26], but many other oxidants are available[120]. Thus although the triquinone (**74**)[84] can be obtained from the triquinol in high yield using dichromate and sulphuric acid if the temperature is controlled, many quinones would not survive these conditions, and for very sensitive compounds (e.g. **75**; R = OMe, CN, Ac, CO_2Et) the use of silver oxide[85,86] or silver carbonate[73,87] is the method of choice. In many quinone syntheses where oxidation of a quinol is the final step, it is convenient to effect this with silver oxide without purification of the



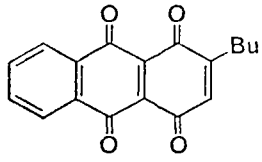
(74) (75) (76)

quinol. Quinones themselves can be used as mild oxidants, and in fact this occurs spontaneously in many 1,4-addition reactions of the form

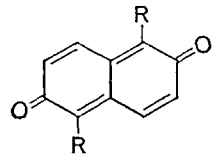
$$Q + HX \longrightarrow HQX \longrightarrow QX$$

where the substituted quinone (QX) is derived from the intermediate quinol (HQX) which is oxidized by the original quinone (Q), redox potentials permitting. An interesting example is the formation of **76** in quantitative yield[88] by oxidation of the biquinol with benzoquinone; there is no attack on sulphur. For quinones of higher potential, chloranil or DDQ are suitable oxidizing agents, or lead tetraacetate. The latter was used for the oxidation of 4,4′-dihydroxybiphenyl to diphenoquinone[91] and in the preparation of **77** from the corresponding quinizarin[92], while **78** (R = HO) was prepared[80] by oxidizing 1,2,5,6-tetrahydroxynaphthalene with tetrachloro-*o*-benzoquinone. The parent *amphi*-naphthoquinone (**78**; R = H) was obtained by oxidizing 2,6-dihydroxynaphthalene with active lead dioxide, prepared by treating lead tetraacetate with water[100].

For more robust quinones mixed nitrogen oxides[89,90] provide a convenient reagent and even nitric acid in ether may be used at low temperatures to give quinones in good yield[86].



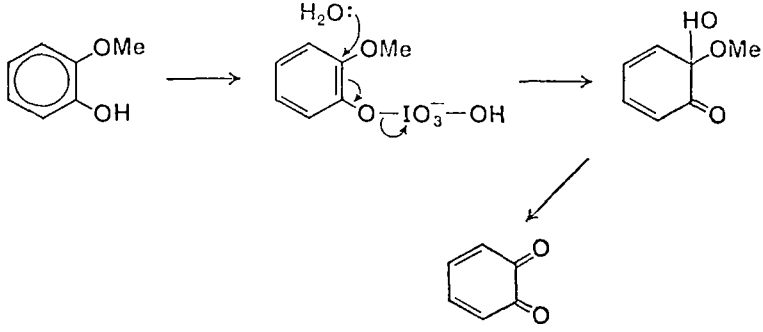
(77)



(78)

D. Catechol and Quinol Ethers

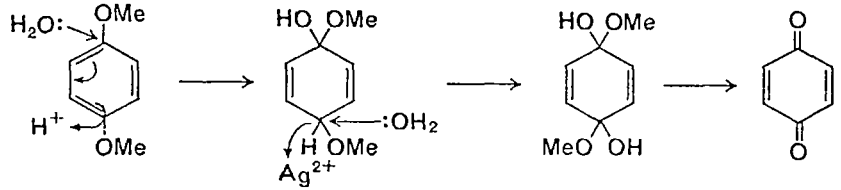
Although *o*- and *p*-quinones are often prepared by oxidation of catechols and quinols which have been obtained by demethylation of their ethers, this is not always necessary and quinones can often be obtained by direct oxidation of the ethers themselves. These reactions, in which demethylation may be accompanied by the introduction of oxygen, apply chiefly to quinol ethers, but there is a useful method for converting catechol mono-ethers into *o*-quinones which utilizes sodium periodate[93] in water or aqueous acetic acid. The reaction is regarded as a nucleophilic attack by water on a periodate ester (Scheme 7) to give a hemi-ketal, and thus a



SCHEME 7

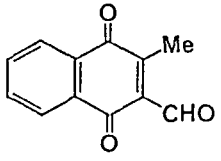
quinone. When guaiacol was oxidized in $H_2{}^{18}O$ the quinone was labelled but not the methanol[94]. When catechol was oxidized in the same way, however, the quinone was not labelled as the water removes the phenolic proton from the intermediate ester instead of attacking on carbon. Quinol and its mono-ethers behave in the same fashion but the reaction is mainly of interest for *o*-quinone synthesis. However, dimeric products may also arise[81c-e]. Nitrous acid will also convert guaiacols into *o*-quinones if the positions *o*/*p* to the hydroxyl carry bulky substituents, and *p*-quinones can be obtained similarly from 2,6-di-*t*-butylquinol mono-ethers[105].

Oxidative demethylation of quinol dimethyl ethers can be effected in high yield using argentic oxide in cold aqueous dioxan acidified with nitric acid[123]. Olefinic and aldehyde side-chains survive intact allowing the preparation of quinones such as **79**. *o*-Quinones can be obtained in moderate yield from catechol dimethyl (or methylene) ethers, provided there are substituents at positions 4 and 5. Studies in ^{18}O-enriched water established that the oxidation involves aryl–oxygen bond cleavage; a possible mechanism is shown in Scheme 8. Formerly oxidative demethylation of quinol dimethyl ethers was usually effected with nitric acid $< 30°$, or occasionally with chromic acid (other reagents are listed in



SCHEME 8

reference 95). The method is most successful with highly substituted ethers and high yields can be obtained. For example **80**[97] was prepared in ca. 90% yield from the corresponding quinol dimethyl ether by treatment with nitric acid, and **81** was formed in 96% yield by oxidation of hexamethoxybiphenylene[99].



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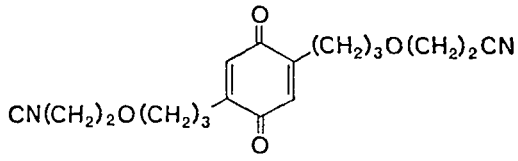

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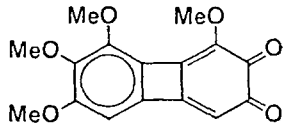
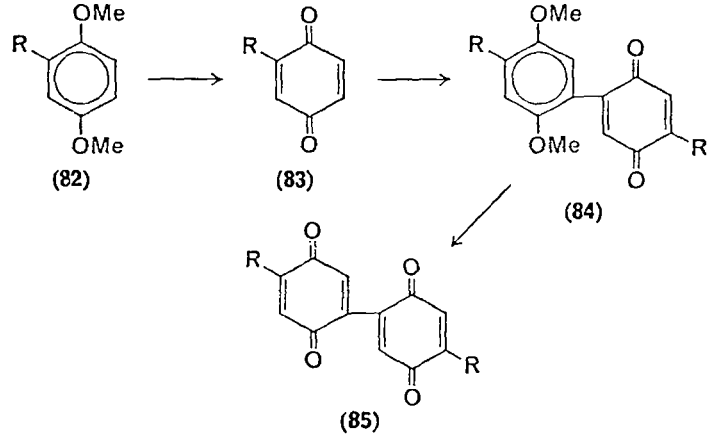


(81)

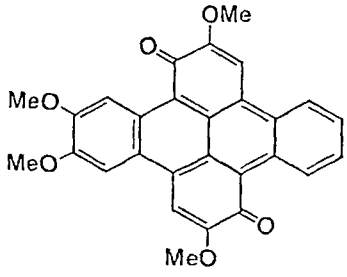
Quinol dimethyl ethers of type **82** (R = Hal, Me, Ph, OMe, AcNH, etc.) can be oxidized to dimeric compounds **84** or **85** using chromic acid[102] or cerium(IV) sulphate[103] in sulphuric acid, sometimes in good yield. The reactions presumably proceed by initial oxidative demethylation to give

83, followed by acid-catalysed arylation and oxidation to form **84**, further oxidative demethylation leading to the biquinone **85**. Alternatively **85** may arise by acid-catalysed dimerization of **83**.



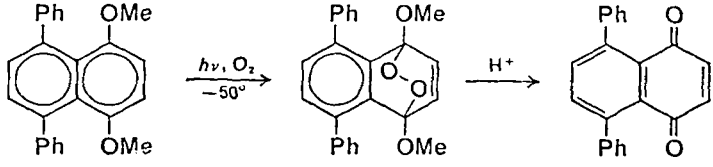
(82) (83) (84) (85)

Polymethoxybenzenes undergo oxidative coupling reactions fairly easily[95] and the products may undergo further oxidative demethylation. A good example is the formation of **86** in 76% yield by oxidizing 3,3′,4,4′-tetramethoxybiphenyl with chloranil in aqueous sulphuric acid[104].

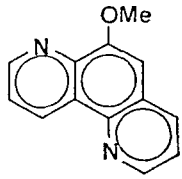


(86)

Photochemical oxidation of quinol dimethyl ethers is another way of obtaining quinones of the naphthalene and higher series, as the following example illustrates[220].



Phenol ethers can also be oxidized to quinones, with or without demethylation, one or both quinone oxygen atoms being introduced by the reagent[95]. While such oxidations can be useful for structure determinations they are not usually of much synthetic value, with certain exceptions, notably the formation of 2,6-dialkoxybenzoquinones by oxidation of pyrogallol ethers with nitric acid. 2,6-Dimethoxybenzoquinone can be obtained in yields up to 80% by treating 1,2,3-trimethoxybenzene in ethanol with nitric acid[101]. Another favourable case is the conversion of **87** into **88**, in 90% yield, with fuming nitric acid in sulphuric acid; isomeric 6-methoxyphenanthrolines can be oxidized in the same way[106].



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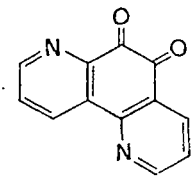
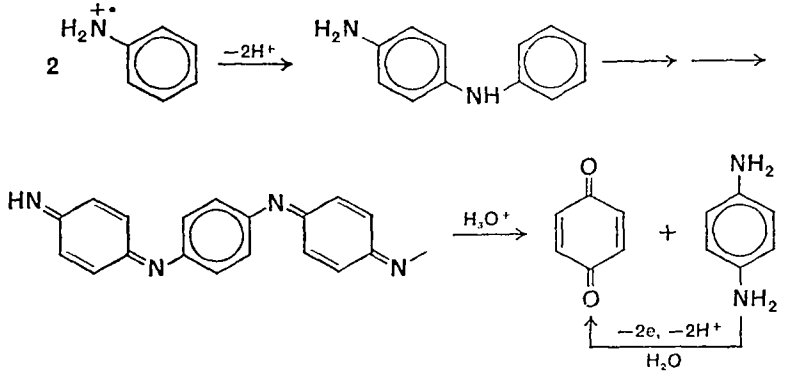


(88)

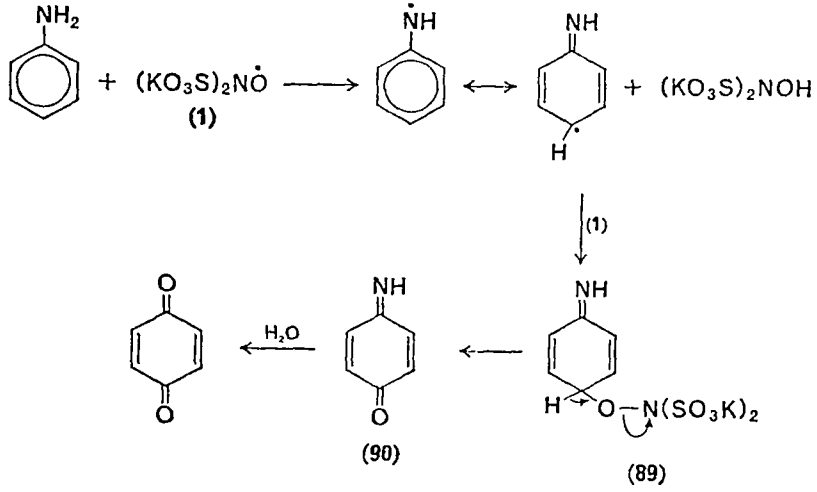
E. Aromatic Amines and Aminophenols

In general, simple amines are not oxidized to quinones as efficiently as phenols and until the advent of the Teuber reagent the yields obtained from amines lacking a *p*-substituent were usually poor. Nevertheless a commercial process for the manufacture of benzoquinone is based on the oxidation of aniline with manganese dioxide in sulphuric acid[108]. Very little is known about the mechanism of this process. Studies with other systems (anodic oxidation[121], hydrogen peroxide/peroxidase[122]) suggest initial oxidation to a radical-cation which dimerizes. Repetition of this process gives a polymer which at the quinone–imine oxidation level would undergo acid-catalysed hydrolysis to benzoquinone and *p*-phenylenediamine, and the latter would in turn be converted into quinone by further oxidation and hydrolysis (Scheme 9). Variations of this scheme have been suggested but the relevance of these ideas to the oxidation of aniline with manganese dioxide or dichromate in sulphuric acid is unknown. It is not difficult to write alternative mechanisms involving 2-electron oxidations but experimental data are lacking.

Anilines react with two equivalents of Fremy's salt (presumably as in Scheme 10) to give *p*-benzoquinones[109] although the reaction is not so generally useful as the corresponding oxidation of phenols. Yields are frequently excellent but other reactions may occur and the substituents present have an important influence. Significantly, oxidation of 5-amino-1-naphthol gives a high yield of 5-amino-1,4-naphthoquinone[116]. Surprisingly,

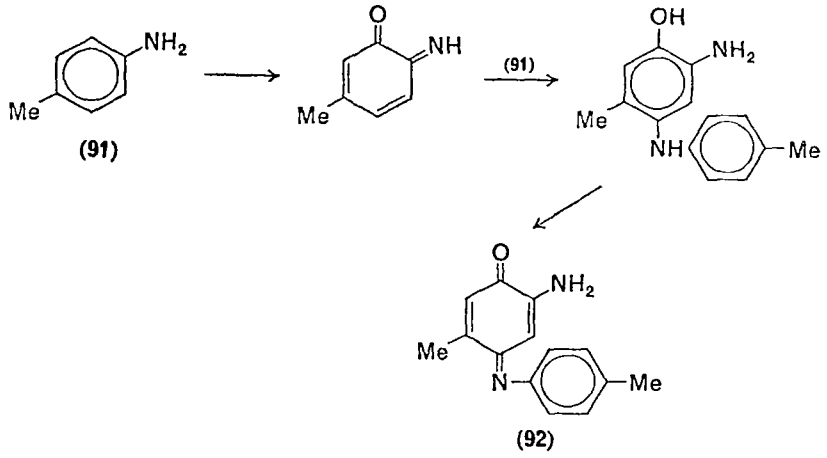


SCHEME 9

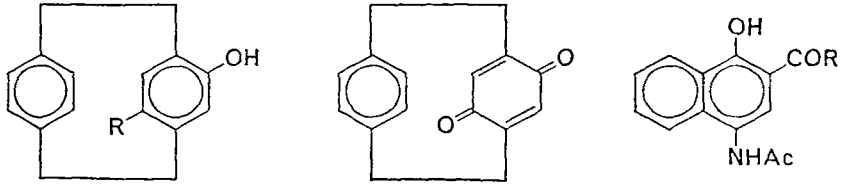


SCHEME 10

3,5-disubstituted anilines give virtually no quinone at all. This may be attributable, in part, to steric resistance to the formation of the intermediate **89** and to side-reactions occurring *ortho* to the amino group. Oxidation of the amino to a nitroso group has also been observed[109,110]. A quinone-imine (the 2,6-dimethyl homologue of **90**) was obtained[110] along with the quinone in the oxidation of 2,6-dimethylaniline, but *o*-quinones are not formed. Instead, where there is a blocking group in the *p*-position, the intermediate *o*-quinone-imine may undergo 1,4-addition with the original amine and the product, after oxidation, is a quinone-anil[109–111]. Thus *p*-toluidine **91** gives the anil **92** in 95% yield[110]. Very simple amines with a *free para* position may behave in the same way[110].



Using the older reagents[26], dichromate and sulphuric acid, or manganese dioxide, the oxidation proceeds more easily with *p*-substituted amines, the substituent (OMe, Hal, SO_3H, NO_2 and even Me) being eliminated. *p*-Diamines[119] and *p*-aminophenols are best, the intermediate mono- and di-imines being rapidly hydrolysed to quinones under aqueous acid conditions. The usual oxidants are chromic acid or ferric chloride. Occasionally the latter results in chlorination of the quinone[112] but this can be avoided by using ferric sulphate. For large-scale quinone preparations the best general procedure is to convert a phenol into its *o*- or *p*-amino derivative, most conveniently by coupling with diazotized sulphanilic acid and reduction of the azophenol with dithionite, followed by oxidation with chromic acid or ferric salts. Excellent procedures for both *o*- and *p*-quinones are available[113]*. This is also the method of second choice on occasions when the Teuber oxidation fails. For example, the 2,2-cyclophanequinone (**94**) could not be obtained from the phenol (**93**; R = H) using Fremy's salt (attributed to steric strain) but it was prepared without difficulty from the aminophenol (**93**; R = NH_2)[114]. *p*-Aminophenols can obviously be made in other ways and two which

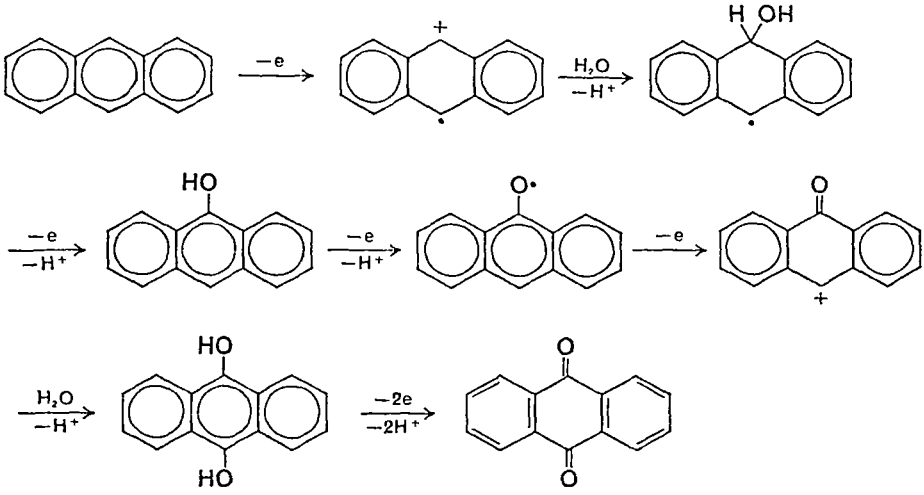


* *o*-Aminophenols, as distinct from *o*-aminonaphthols, may give phenoxazones on oxidation.

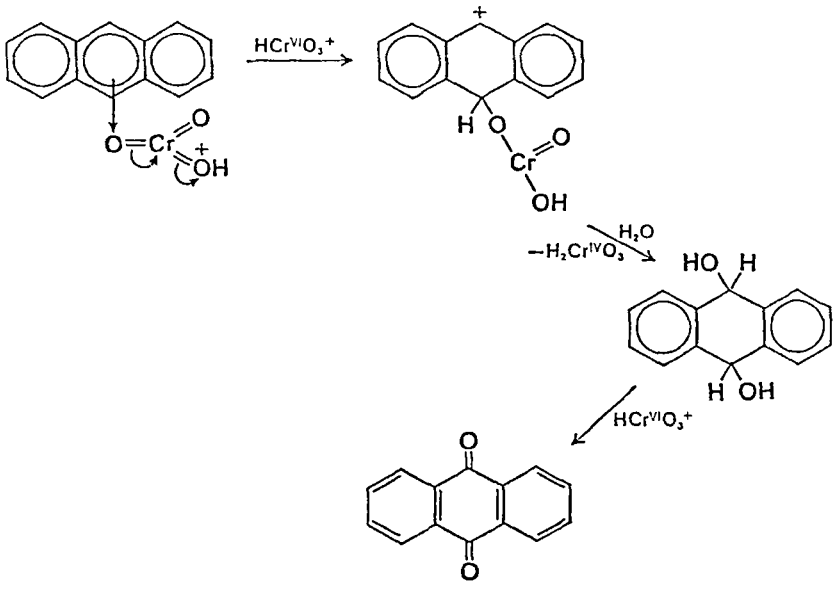
have been used involve nitrosation of a phenol[26] and electrolytic reduction of a nitro compound to a hydroxylamine followed by rearrangement[115]. Since nitrosophenols are tautomeric with quinone oximes their hydrolysis constitutes another, albeit unimportant, method of quinone synthesis[26, 117]. Nitric acid is not often used to oxidize aminophenols but gives excellent results with *N*-acetyl derivatives; thus both **95** (R = Me and Ph) give the corresponding acyl-1,4-quinones in ca. 90% yield[118].

F. Aromatic Hydrocarbons

Hydrocarbons provide a relatively unfavourable substrate for oxidation up to the quinone level and the method is limited in practice to a relatively few hydrocarbons which are readily available and form stable quinones. Generally yields are not high. Both chemical and electrochemical methods can be used and since the first step is the formation of a cation or radical-cation, the oxidation proceeds most easily in condensed polycyclic systems which permit extensive delocalization. The oxidation of anthracene to 9,10-anthraquinone is the most important example; manufacturing processes use nitric or chromic acids, a good laboratory process employs sodium chlorate[120] and many other oxidants have been utilized, besides anodic oxidation[135]. Alkyl derivatives can be oxidized similarly and likewise phenanthrene[125] and higher polycyclics. Periodic acid[126] in DMF has been used successfully to oxidize naphthacene, pentacene and benz[a]anthracene to the expected quinones in ~80% yield but there was little or no reaction with perylene and chrysene, and pyrene[127] gave 1,1′-bipyrenyl in >70% yield. The same reagent[126] converts naphthalene into 1,4-naphthaquinone in 70–76% whereas the conventional reagent, chromium trioxide in acetic acid, gives only a 32–35% yield[128]. Nevertheless the older process is a convenient way of making alkylated 1,4-naphthoquinones and yields can be improved by using a two-phase system of carbon tetrachloride and aqueous sodium dichromate/sulphuric acid[129]. ^{14}C-labelled 2-methyl-1,4-naphthoquinone was obtained in this way from the hydrocarbon in 50% yield[130]. There is no really useful laboratory process for converting benzene into benzoquinone; anodic oxidation[131] has been used, and with argentic oxide[96] in 6M perchloric acid the yield is 34%. Other simple benzenoid compounds have also been oxidized to quinones electrolytically but in low yield[135]. It is now well established[132] that electrolytic oxidation of aromatic hydrocarbons proceeds by a series of 1-electron transfer processes with intermediate solvolyses (see Scheme 11) but there are no comparable data on chemical oxidations with nitric and chromic acids. Indeed it is not known whether the oxygen introduced derives from water, from the reagent, or from both. Scheme 12 is



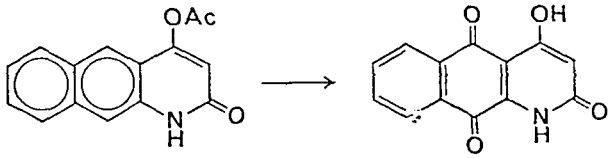
SCHEME 11



SCHEME 12

speculative[133]. On the other hand, peracid oxidations, e.g. conversion of durene into duroquinone using peracetic acid[134], presumably proceed by two electrophilic hydroxylations and final oxidation of the quinol.

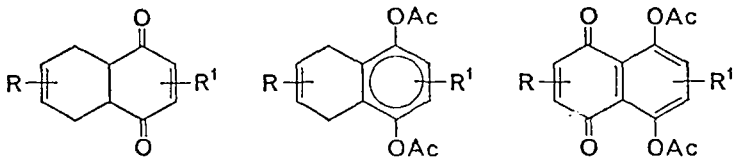
Analogous oxidations can also be effected with appropriate heterocycles as in the following example[153].



G. Miscellaneous Oxidations

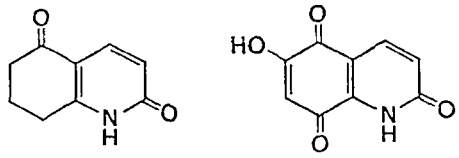
Quinones can be prepared by other oxidative methods which may be useful in special cases.

1. Naphthazarin (5,8-dihydroxy-1,4-naphthoquinone) derivatives (**98**) can be obtained[136] in good yields from Diels–Alder adducts (**96**) by aromatization with acetic anhydride to **97**, followed by oxidation with chromium trioxide in acetic acid at 0°. However, on scaling up, by-products were obtained and the yield of naphthazarin was poor[159].



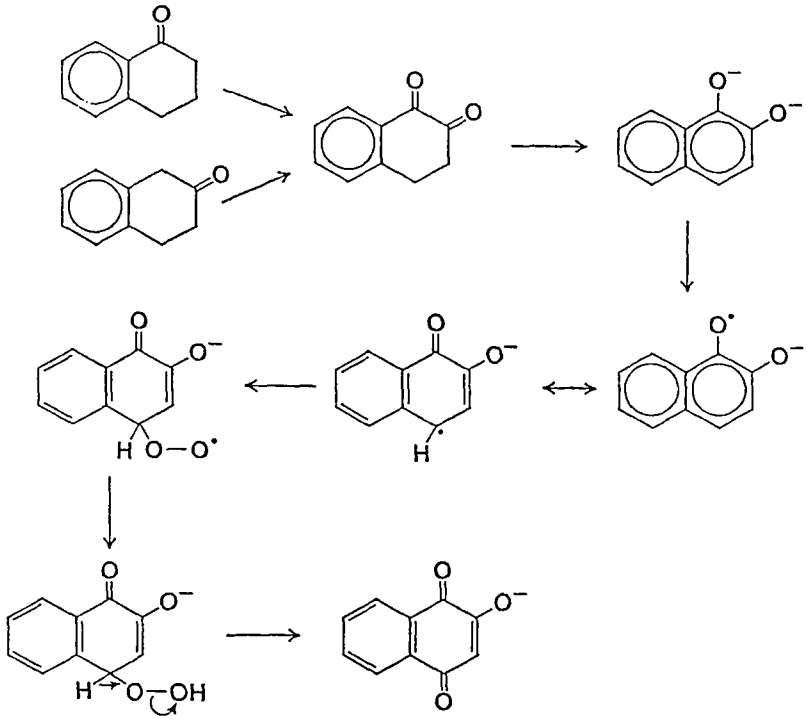
(96) (97) (98)

2. Both α- and β-tetralones can be converted rapidly into 2-hydroxy-1,4-naphthoquinones by autoxidation in *t*-butanol in the presence of potassium *t*-butoxide[137] and **99** can be converted into **100** in the same



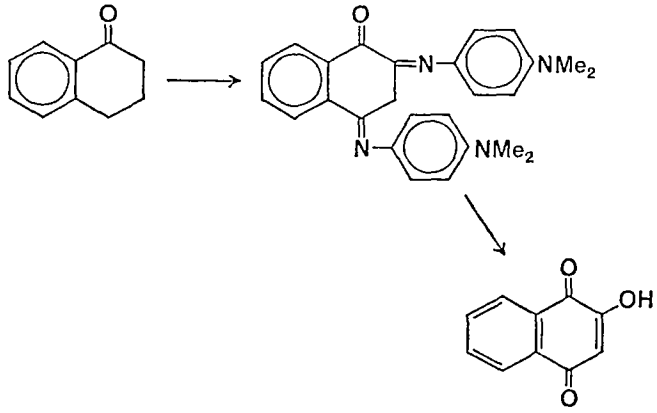
(99) (100)

way[211]. Two moles of oxygen are absorbed. The reaction proceeds by way of the α-diketone[138] which enolizes, and the dianion is then oxidized to the semiquinone which captures a molecule of oxygen to form a hydroperoxide, and hence the hydroxyquinone anion (Scheme 13). 1,2- and 1,3-Dihydroxynaphthalenes also autoxidize to 2-hydroxy-1,4-naphthoquinones under the same conditions. Yields (from tetralones) are moderate but usually better than those obtained by the older method[139] in which



SCHEME 13

an α-tetralone is condensed with *p*-nitrosodimethylaniline to give a dianil which is hydrolysed with acid, as shown below.

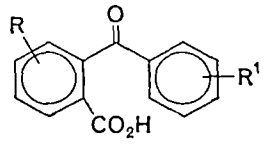


3-Methyltetralone-1 has been oxidized to 3-methyl-1,2-naphthoquinone and 2-hydroxy-3-methyl-1,4-naphthoquinone with selenium dioxide[140].

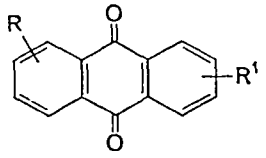
III. CYCLIZATION METHODS

A. o-Benzoylbenzoic Acids

This is a general procedure of technical importance for the manufacture of anthraquinones and is a widely used laboratory method for the preparation of these and higher polycyclic quinones[141]. The starting acids **101** are easily prepared from phthalic anhydrides by Friedel–Crafts condensations and the subsequent cyclization to **102**, an intramolecular

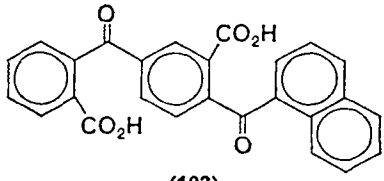


(101)



(102)

Friedel–Crafts reaction[147], is normally carried out by heating in sulphuric acid or, occasionally, polyphosphoric acid[151]. Cyclization of the acid chloride is also possible but seldom used. The cyclization *ortho* to a carbonyl group often proceeds with surprising efficiency[142]. Obviously the substitution pattern has an important influence and whereas in certain favourable cases isolation of the benzoylbenzoic acid may not be necessary, other cyclizations fail completely. Additional deactivating groups inhibit the reaction and to convert **103** into **104** the di-acid was heated with



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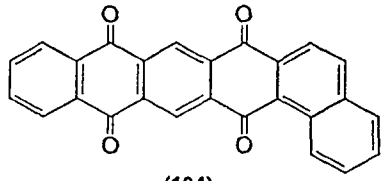
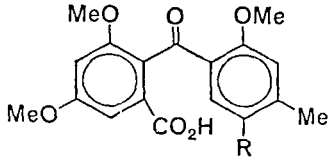
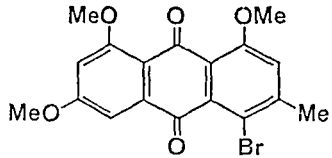


(104)

sulphuric acid in boiling benzoyl chloride[152]. Cyclization is also difficult or impossible when two *o*/*p*-directing groups are located *meta* to the site of cyclization, especially if a phenolic group is present, when sulphonation may become the main reaction. Thus cyclization of **105** (R = H) gave very poor yields of quinone but the difficulty was surmounted by introducing bromine (subsequently removed by reduction with hydriodic acid), followed by cyclization of **105** (R = Br) in oleum containing boric acid[143] to give **106**. A better solution to this problem is to reduce the benzoylbenzoic acid to a benzylbenzoic acid (**108**) followed by easy cyclization to an anthrone (**109**) and easy oxidation to the quinone. The reduction can be carried out under either acid[144,145] or alkaline[98] conditions. An

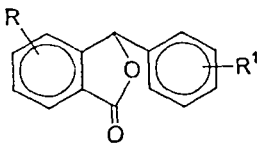


(105)



(106)

alternative is to start with an arylphthalide (**107**)[146]; these can be prepared by condensing *o*-phthalaldehydic acids with appropriate benzenoid compounds but this approach is restricted by the difficulty in preparing these acids.



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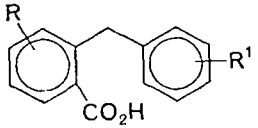

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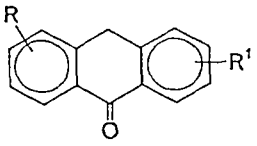
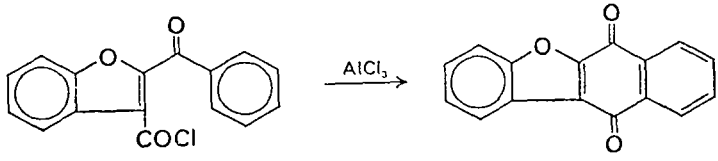
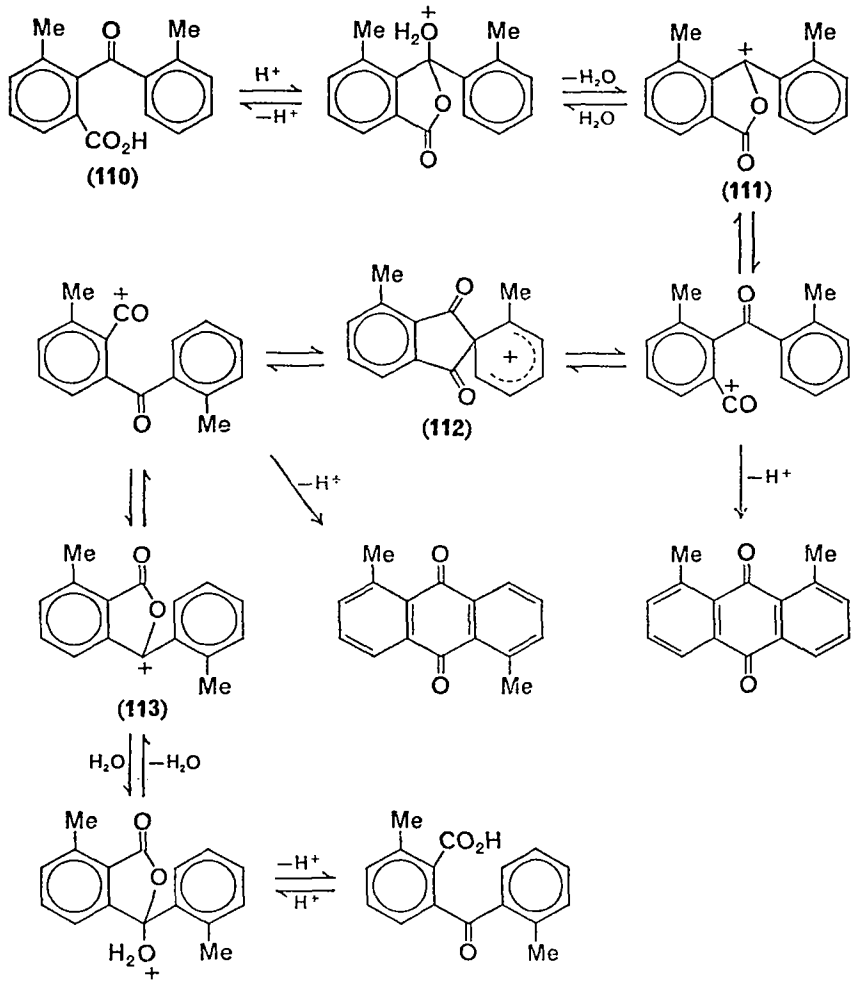


(109)

Unsymmetrical *o*-benzoylbenzoic acids may undergo Hayashi rearrangements[148]. This involves the reversible conversion of, for example, a 3-substituted-2-aroylbenzoic acid into a 6-substituted isomer, and the consequent formation of an anthraquinone which is an isomer of the normal product. The formation of a mixture of 1,5- and 1,8-dimethylanthraquinones from **110** is shown in Scheme 14[149]. The key intermediate is the spiro-cation **112** which can ring-open in two ways. In general the ratio of the final products depends upon the relative stabilities of cations such as **111** and **113**, the steric effects of *o*-substituents being important. The Hayashi rearrangement does not occur frequently but should be kept in mind when planning anthraquinone syntheses.

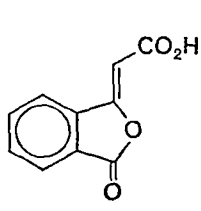
The benzoylbenzoic acid method is not confined to the preparation of simple anthraquinones as the following example[150] shows. In principle it





SCHEME 14

should be possible to apply this procedure to the synthesis of extended quinones, but practice has not proceeded far. The only example appears to be the preparation of 3,4-benzopyrene-1,5-quinone (**115**) by condensing the lactonic acid **114** with naphthalene in anhydrous hydrofluoric acid[154], this is a multiple Friedel–Crafts reaction in which *three* new carbon–carbon bonds are formed in one operation. The same quinone was also obtained by a more conventional process[155] in which the keto-ester **116** was converted into the di-acid **117** by a Stobbe condensation with *t*-butyl acetate and then cyclized.



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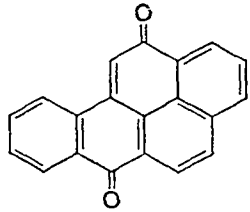

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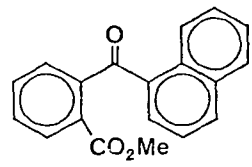

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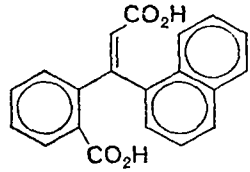
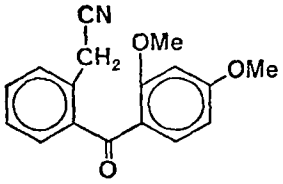


(117)

B. o-Benzoylphenylacetonitriles



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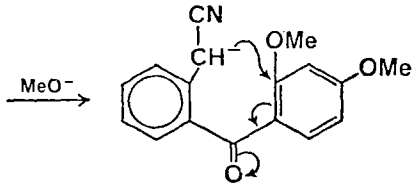

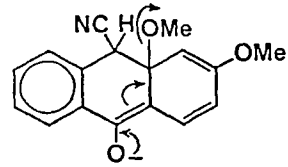

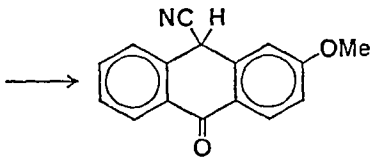

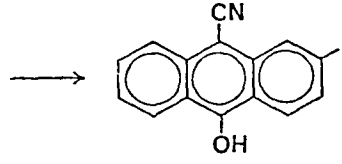

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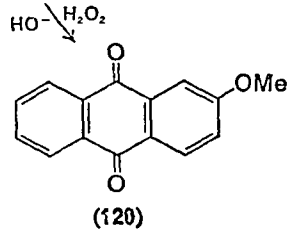
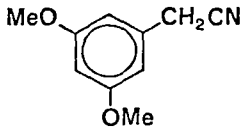


(120)

SCHEME 15

The *o*-benzoylbenzoic acid method for the synthesis of anthraquinones requires strong acid conditions and has other drawbacks already mentioned. An alternative procedure[156] allows cyclization to form an anthranol to be carried out under basic conditions, the synthesis being completed by oxidation. The required intermediate is an *o*-benzoylphenylacetonitrile carrying a methoxy group adjacent to the carbonyl function **118** (presumably other leaving groups could serve). Thus treatment of **118** in hot dimethyl sulphoxide with sodium methoxide under nitrogen gave the anthranol **119** in 95% yield, and this was quantitatively oxidized to the quinone **120** with alkaline hydrogen peroxide (Scheme 15). This new method has not been used extensively, as yet, but excellent yields have been obtained in all cases[156–158] and it need not be limited to the synthesis of anthraquinones. If suitably substituted, starting materials can be obtained easily by condensing an *o*-methoxybenzoic acid with a phenylacetonitrile in the presence of trifluoroacetic anhydride, e.g. **123** from **121** and **122**[157].



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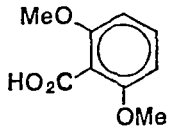

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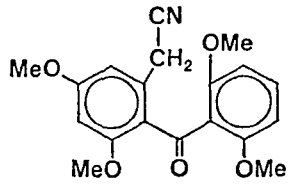
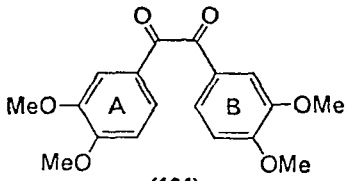


(123)

C. Scholl Reactions

These reactions, which have been reviewed[95,176], are mainly of use for the synthesis of higher polycyclic quinones, including vat dyes[177]. A simple example[178] is the formation of phenanthrene-9,10-quinone (25%) from benzil by heating with aluminium chloride, the yield improving if suitably located methoxyl groups are introduced (**124** → **125**, 86%)[179]. The reaction is usually regarded as an electrophilic substitution followed by oxidation*.



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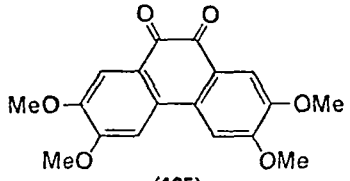
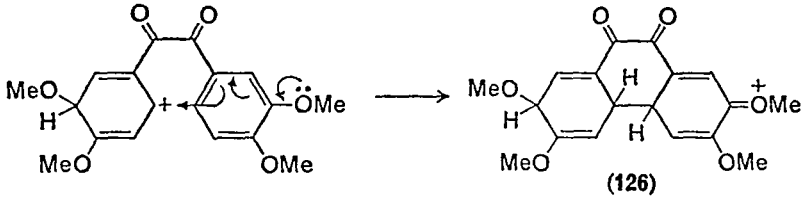


(125)

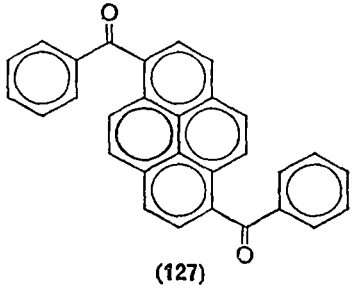
* There is evidence[176] that radical-cations are present in Scholl reactions and they may proceed, in part, by radical coupling or by radical substitution.

In the above case, ring A of **124** reacts, after protonation, with ring B to give **126** (the presence of hydrogen chloride or other protic acid is



(126)

necessary), hydride ion being subsequently removed by any available hydrogen acceptor. In this connexion hot nitrobenzene is a convenient solvent, although reactions can be carried out simply by baking with anhydrous aluminium chloride or heating in an aluminium chloride–sodium chloride melt. Other Friedel–Crafts catalysts are seldom used. Oxygenation is an advantage; in the conversion of the diketone **127** into pyranthrone **128** by heating in aluminium chloride–sodium chloride, the



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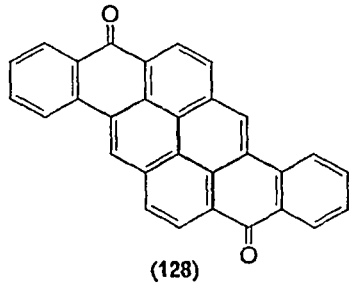
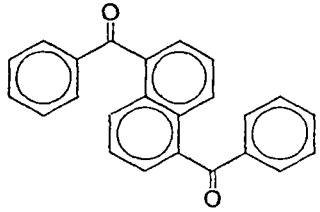


(128)

yield is increased from 25 to 80% by passing in oxygen[176, 180], and whereas 1,5-dibenzoylnaphthalene (**129**) does not cyclize under normal conditions[181] (i.e. *p*- to a carbonyl group) the quinone **130** is successfully formed if the mixture is oxygenated[177]. Manganese dioxide and other oxidants are occasionally added to the melt.



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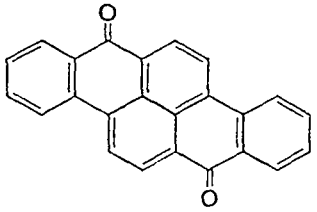
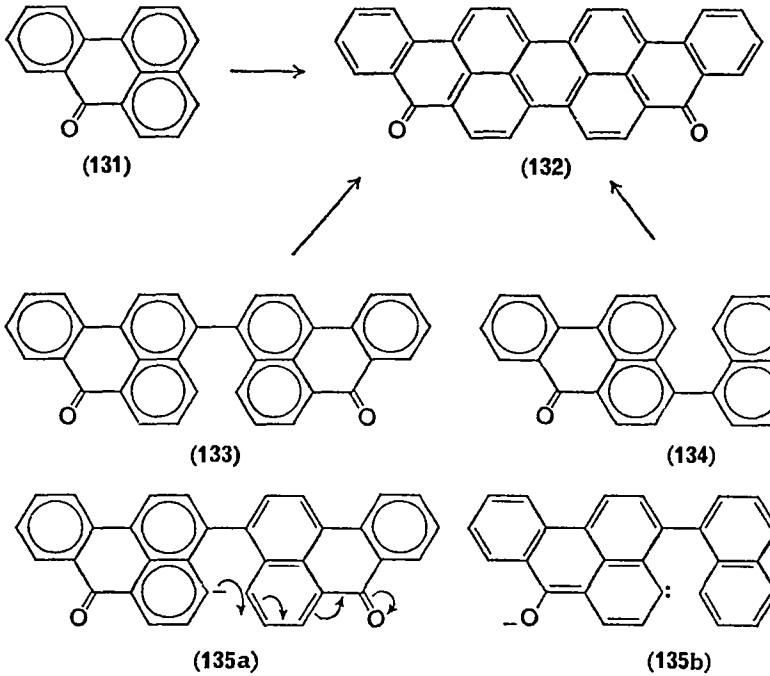


(130)

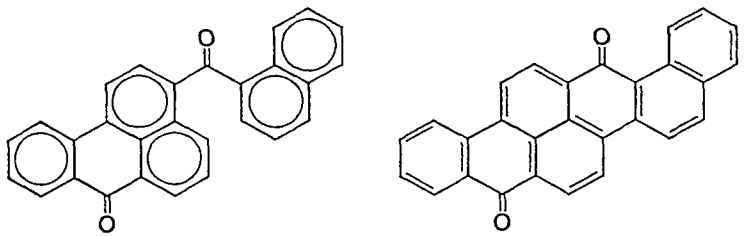
Large polycyclic quinones can also be prepared from diketones under basic conditions; both inter- and intramolecular C—C bond formation is possible, the products being similar to those obtained from Scholl

reactions[177]. Most examples involve benzanthrone derivatives, some of which are important commercial dyes. Thus fusion of *meso*benzanthrone **131** with potassium hydroxide and sodium acetate affords violanthrone **132** which can be derived also from both **133** and **134** by alkali fusion. It is suggested that a carbanion (e.g. **135a**)[182a] or a carbene anion (**135b**)[182b]



(131) (132) (133) (134) (135a) (135b)

is formed by removal of a proton from a carbon atom *o*- or *p*- (or equivalent) to a carbonyl group which then forms a new carbon–carbon bond by Michael addition, the reaction being completed by aerial oxidation. Obviously other reactions are possible and in the alkaline fusion of the benzoylbenzanthrone **136**, benzanthrone, 4-hydroxybenzanthrone, violanthrone and benzoic acid are formed, in addition to the quinone **137**, in low yield[183].

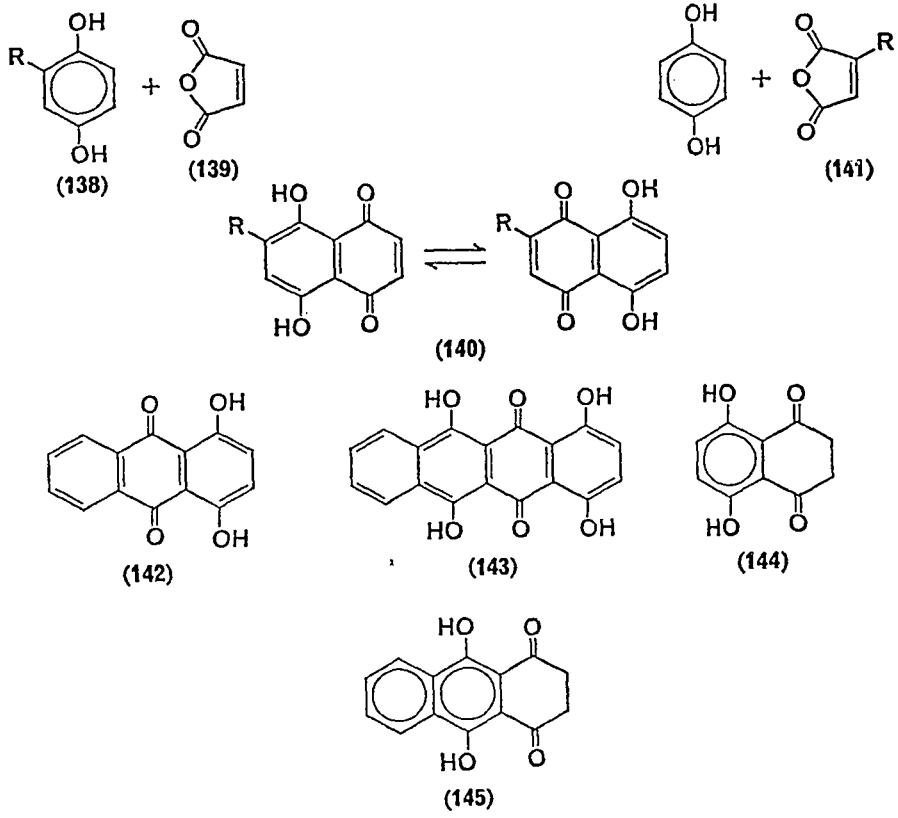


(136) (137)

IV. CONDENSATION METHODS

A. Quinols

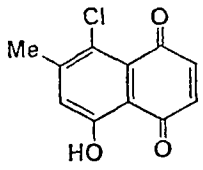
The principal reaction[160] under this heading is the condensation of quinols with cyclic anhydrides to give naphthazarins, quinizarins and related higher polycyclic quinones. In the simplest case naphthazarin itself (**140**; R = H) is obtained by condensing quinol with maleic anhydride, the reaction being an extension of the benzoylbenzoic acid synthesis in which formation of the keto-acid is immediately followed by cyclization under vigorous conditions. As naphthazarins are tautomeric there is a choice of starting materials, and **140** (R = Me), for example, can be derived either from toluquinol (**138**; R = Me) and maleic anhydride or by condensing methylmaleic anhydride (**141**; R = Me) with quinol[161]. If both **138** and **141** are unsymmetrical, mixtures result. By extension quinizarin **142** can be obtained from maleic anhydride and 1,4-naphthoquinol and the naphthacenequinone (**143**) from phthalic anhydride and the diketone **144**[160]. The latter can be prepared by condensing quinol with



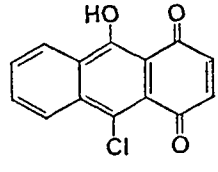
succinic anhydride in the same way[169]. Alternatively **143** could be derived from naphthoquinol and 3,6-dihydroxyphthalic anhydride, or from leucoquinizarin **145** and maleic anhydride. Quinol ethers and esters may also be used.

The reaction is usually carried out in a melt of anhydrous aluminium chloride–sodium chloride[160] and can be done rapidly on a small scale[162]. Yields seldom exceed 50% and may be very low. Alternatively the reaction has been done in hot tetrachloroethane[194] and in aluminium chloride–formamide[163], and the addition of boric acid has been found advantageous[163]. When diketones such as **144** and **145** are used, air should be excluded as they tautomerize to tetrahydroxy compounds which oxidize rapidly.

It is possible to condense *p*-chlorophenols in the same way[164]; **146a** was obtained[165] in modest yield from maleic anhydride and 2-chloro-5-hydroxytoluene and **146b** is the condensation product from maleic

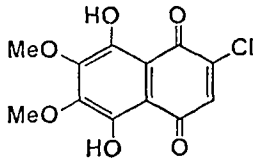


(146a)



(146b)

anhydride and 4-chloro-1-naphthol[189], but this variation has not been extended. However, it is worth noting that quinizarin can be synthesized[166] by heating phthalic anhydride with *p*-chlorophenol in sulphuric acid–boric acid, and presumably cyclization to a chloroanthraquinone occurs before the chlorine is displaced. Curiously, when 1,2-dihydroxy-3,4-dimethoxybenzene was condensed with chloromaleic anhydride in aluminium chloride–sodium chloride the product[167] (after methylation with diazomethane) was a mixture of the expected chlorodimethoxynaphthazarin **147** with **148** and **149**.



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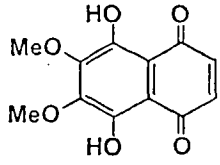

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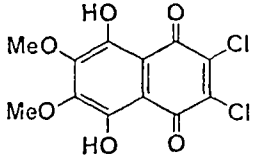
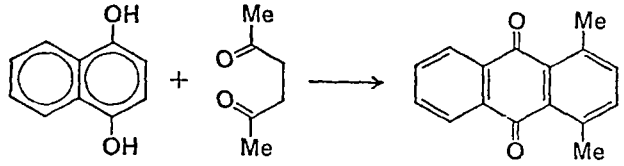


(149)

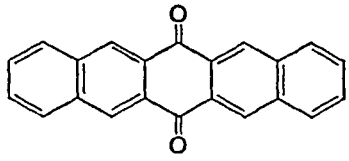
Phenols lacking a *p*-substituent fail to undergo this condensation but 1,5-dihydroxynaphthalene gave a small yield of the expected pentacenediquinone with phthalic anhydride[194, 195].

A related reaction, of limited value, is the condensation of 1,4-diketones with 1,4-naphthoquinol in acetic acid–hydrochloric acid to form anthraquinones[168]. An example is shown below.



B. Dialdehydes

Another 1,4-diketone condensation utilizes cyclohexane-1,4-dione as precursor to a quinone ring. Thus by reaction with two moles of phthalaldehyde in the presence of a base the pentacenequinone **150** is formed in good yield[169]. The reaction is probably general for aryl-*o*-dialdehydes[170]. Condensation on a 1 : 1 basis does not seem to have been



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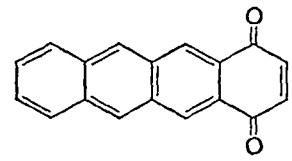
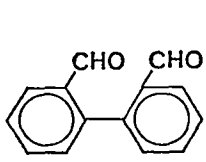


(151)

explored although it might be an easy route to quinones like **151** (cyclohexanedione and napthalene-2,3-dialdehyde) by condensation and oxidation. However, leucoquinizarin **145** has been condensed with naphthalene-2,3-dialdehyde to give 5,16-dihydroxyhexacene-6,15-quinone in high yield[196].

A seldom-used reaction for the preparation of certain *o*-quinones utilizes an intramolecular benzoin condensation. Originally[171] 9,10-phenanthrenequinone (**154**) was derived from biphenyl-2,2′-dialdehyde (**152**) under the usual conditions, warming in aqueous ethanol in the presence of cyanide ion, the initial benzoin **153** being oxidized by air to the final product. More recently, the reaction has been used to make the thiophene analogues **155** and **156**, from the appropriate dialdehydes in 50% and 72% yield, respectively[172].

Another benzoin condensation, useful for its special purpose, is an unusual double reaction leading to the formation of 2,3-dihydroxy-1,4-quinones. For example[173], isonaphthazarin, **157**, is obtained (60%) from phthalaldehyde and glyoxal. The reaction has been used for naphthoquinones[173], anthraquinones[174], indazolequinones[175] and benztriazolequinones[175]; yields are variable and seldom high.



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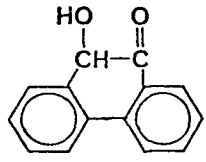

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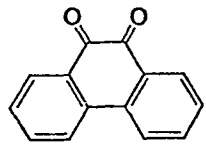

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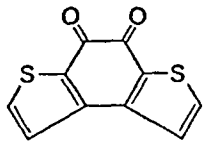

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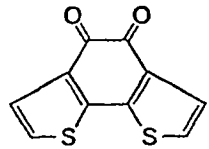

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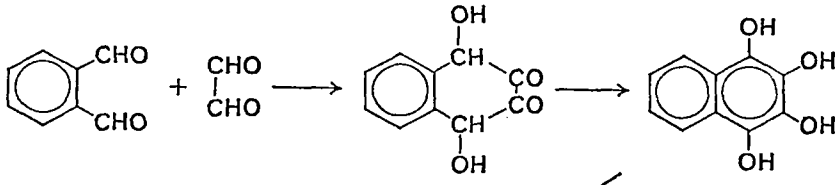
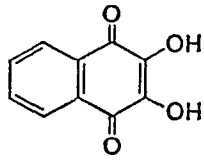




(157)

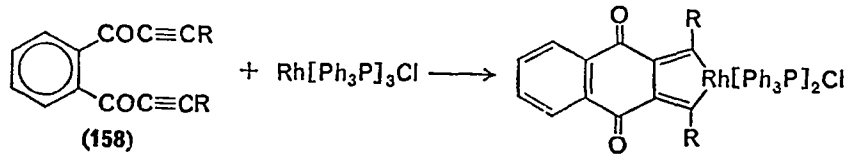
V. MISCELLANEOUS METHODS

Quinones have been obtained in numerous ways, many of which are of very limited preparative value and are not of general application. The few examples which follow were chosen because they illustrate different approaches to the synthesis of quinones, albeit somewhat specialized.

A. o-Bis-arylacetylenic Ketones[222]

Anthraquinones and naphthacenequinones can be prepared from rhodium complexes of *o*-bis-arylacetylenic ketones (**158**). The diketones (**158**; R = Ph, *p*-Tol, Me) (easily prepared from the corresponding diol[184] by oxidation with manganese dioxide[185]) on shaking with tris(triphenylphosphine) rhodium(I) chloride in benzene at room temperature form complexes **159** which, on heating with an acetylene,

yield anthraquinones **160**[185,188]. The mechanism of the reaction is not yet clarified but yields are in the range 30–90%. Similarly, naphthalenic analogues, **161**, provide naphthacenequinones, **162**, but heating is necessary to form the rhodium complexes[186,188].



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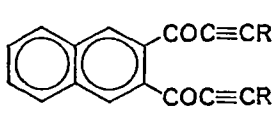

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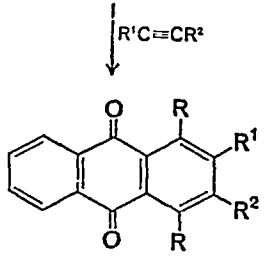

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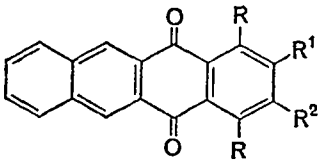
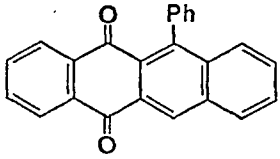


(162)

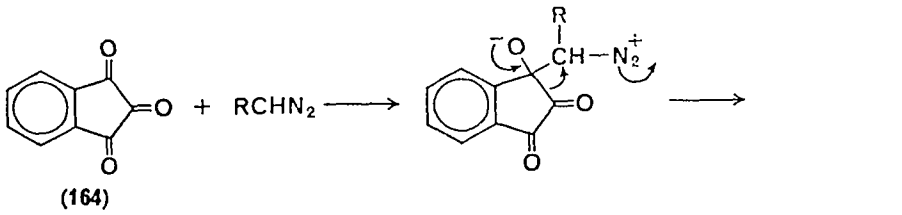
On heating **159** (R = Ph) at 280–290° in molten *trans*-stilbene the reaction takes a different course and the product is the tetracenequinone **163** (30%)[187]. The analogous pentacenequinone can be prepared, likewise, from **161** (R = Ph)[187].



(163)

B. Triketo-indanes

This reaction makes use of a well-known method for the ring expansion of cyclic ketones to synthesize hydroxynaphthoquinones (Scheme 16). Treatment of triketo-indane **164** with diazo-alkanes, in ether, in the usual way, gives the alkoxyquinones **166** in good yield (except with phenyldiazomethane) which can be hydrolysed to the hydroxyquinones **165** with cold alkali[190].



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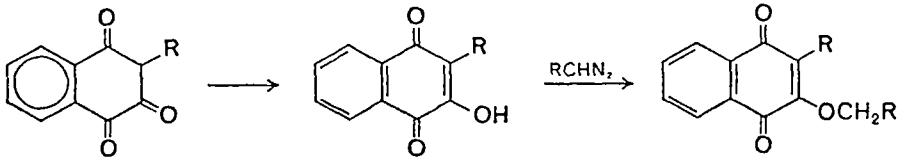
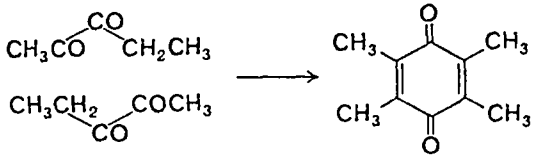


(165) (166)

SCHEME 16

C. *Ketones and Keto-esters*

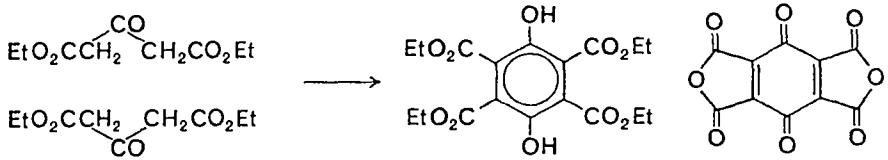
The preparation of benzoquinones from aliphatic precursors is of long standing. α-Diketones or α-keto-esters undergo aldol condensations in the presence of base, leading to quinones on dehydration, e.g. duroquinone **167** from 2,3-diketopentane and 2,5-dimethylbenzoquinone from



(167)

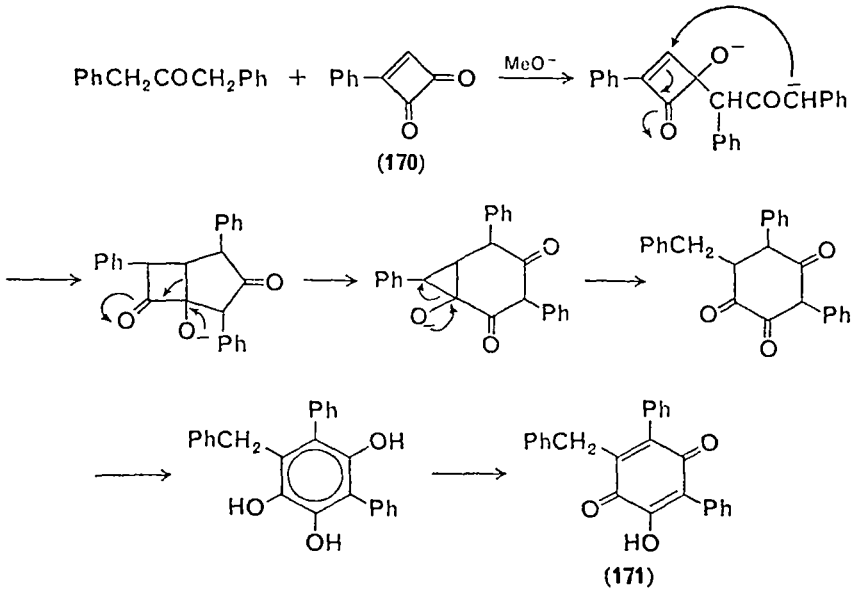
biacetyl[191]. Yields are usually poor but could probably be improved by careful control of conditions. Benzoquinone itself has been obtained from pyruvaldehyde[192].

By another old procedure[193] the quinol **168** was prepared from diethyl acetonedicarboxylate by conversion to its disodio derivative and reaction with iodine, again in poor yield. The corresponding quinone does not appear to have been made but the dianhydride **169** ($C_{10}O_8$) is known[194] as a benzene complex.



(168) (169)

A more unusual synthesis employs a cyclobutenedione to provide half the carbon atoms of a benzoquinone ring (Scheme 17)[197]. Addition of the dione **170** to a methanolic solution of dibenzyl ketone, containing excess sodium methoxide, initiates an exothermic reaction, the resulting highly substituted quinol being oxidized by air to the quinone **171** (50–60%).

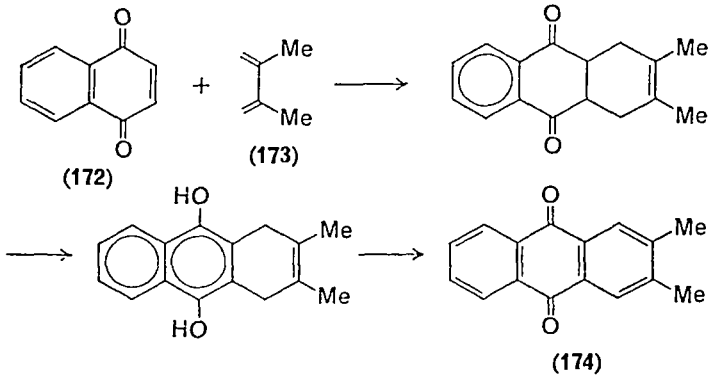


SCHEME 17

VI. ANNELLATION METHODS

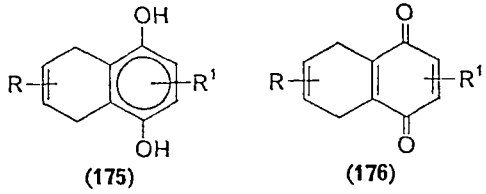
A. Diels–Alder Reactions

This well-known cyclo-addition reaction has been extensively reviewed[198] and attention will be confined to synthetic aspects[199]. There are three steps in quinone synthesis, addition of a conjugated diene to the starting quinone, aromatization of the adduct and oxidation of the resulting quinol, e.g. **172**+**173**→**174**[200]. It is a most useful method for fusing a benzene ring onto an existing quinone ring which has two adjacent positions unsubstituted, although addition may still take place even if substituents are present. Yields are usually good[199]. The addition shown above was effected in boiling ethanol but some reactions can take place at or below room temperature, and excess diene can serve as solvent. For large-scale reactions addition of a polymerization inhibitor[202] may be an

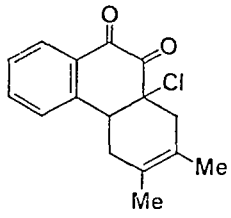


SCHEME 18

advantage, and sensitive *o*-quinones can be generated *in situ* by adding an oxidizing agent to a mixture of a diene and a catechol[203]. The Diels–Alder adduct need not be isolated. Aromatization and oxidation can be achieved in various ways. For anthraquinones this is usually effected by aeration in alkaline solution[200], while in naphthoquinone synthesis aromatization occurs rapidly on warming with hydrochloric acid (containing stannous chloride) and the quinol **175** is then oxidized to the naphthoquinone with acid dichromate. Alternatively, oxidation to the half-way stage **176** can



be effected with nitrous acid, followed by final dehydrogenation with chromic acid[201]. Aromatization can also be induced by chromatography on alkaline alumina[209] or simply on heating in a solvent[201] and if hot nitrobenzene is used as solvent for the Diels–Alder addition the complete reaction sequence (Scheme 18) can be completed in one step. The adducts formed from halogenated quinones readily aromatize by loss of hydrogen halide. The adduct **177**, from 3-chloro-1,2-naphthoquinone and 2,3-dimethylbutadiene, is converted into **178**[205] by warming with ethanolic sodium acetate, while the quinone **179** is formed from 10-methyleneanthrone and chloranil in boiling xylene[206]. Angular methoxy groups are usually eliminated spontaneously so that reaction of 2,3-dimethylbutadiene with 2,5-dimethoxybenzoquinone at 180° gives the anthraquinone **180** (together with 2,5-dimethoxyquinol), and so does **181**, the acetyl group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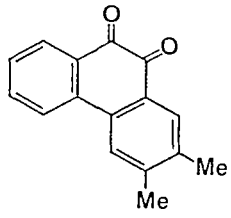
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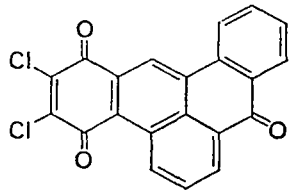
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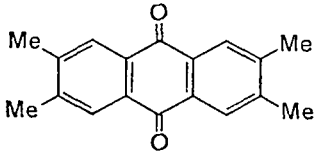
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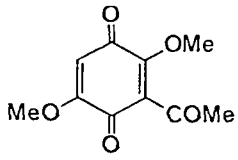
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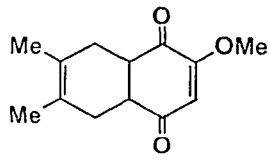
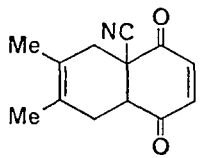

(182)

being also lost[209]. An important factor controlling Diels–Alder additions to *p*-benzoquinones is the more electronic nature of the substituents, reaction taking place preferably at the electron-deficient double bond. The following order of activation has been presented[209]: CN > COMe > CO_2Me > CF_3 > H > F ? > Cl > Me, OAc > NMePh, MeO, MeS. Thus addition of 2,3-dimethylbutadiene to methoxybenzoquinone affords **182** while cyanobenzoquinone gives **183**. More striking is the formation of **185** as well as **186** from **184**[210] and butadiene. However, steric factors are also important, arising from the number and size of potential angular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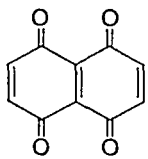
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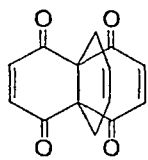
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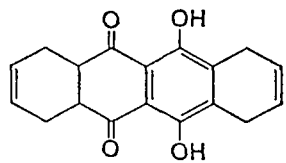
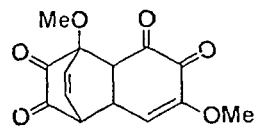

(186)

substituents, and from the 2,3-substituents, if any, on the diene which lead to non-bonded interactions in the *endo*-transition state and favour the formation of adducts with angular substituents[209]. Addition of butadiene to 2,3-dimethoxycarbonylbenzoquinone gives exclusively the adduct without angular substituents whereas substituted dienes give mixtures of adducts by addition to each side of the quinone ring.

o-Benzoquinones can behave both as dienophiles and as dienes, and this can be utilized in a novel synthesis of *o*-naphthoquinones. 3-Methoxy-1,2-benzoquinone forms the adduct **187** in various solvents and on oxidation with periodate it gives the quinone **188** in high yield[81c-e].



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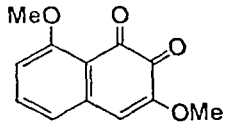
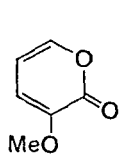


(188)

Less obvious components for Diels–Alder syntheses are α-pyrones and *o*-quinodimethanes. Addition of the pyrone **189** to benzoquinone takes place on heating in benzene in a sealed tube to give the lactone adduct **190** which can be converted to the quinone **191** on heating with activated



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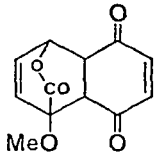

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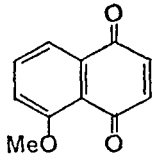
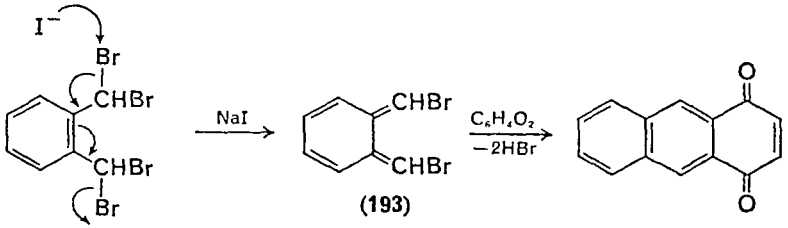


(191)

manganese dioxide in ethyl acetate[207]. An interesting synthesis of 1,4-anthraquinone starts from the tetrabromide **192**. By reaction with sodium iodide in dimethylformamide the tetra-ene **193** is formed which adds to

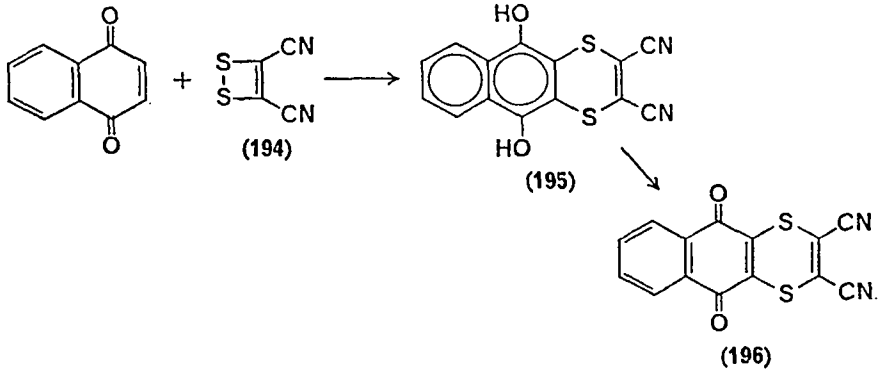


(192) (193)

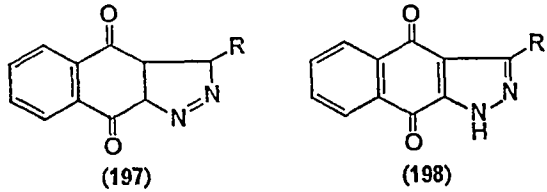
benzoquinone and spontaneously eliminates hydrogen bromide[208]. Finally the 1,2-dithietene (**194**) possesses a weak disulphide bond which readily breaks, the compound then behaving like a conjugated diene (cf. reference 212). On treating 1,2-dicyanoethylene-1,2-dithiol with excess 1,4-naphthoquinone it is oxidized to **194** when then adds to a second molecule of naphthoquinone to give the quinol **195** in high yield, and finally the dithia-anthraquinone **196** on oxidation with ferric chloride[213].

B. 1,3-Dipolar Cyclo-addition Reactions

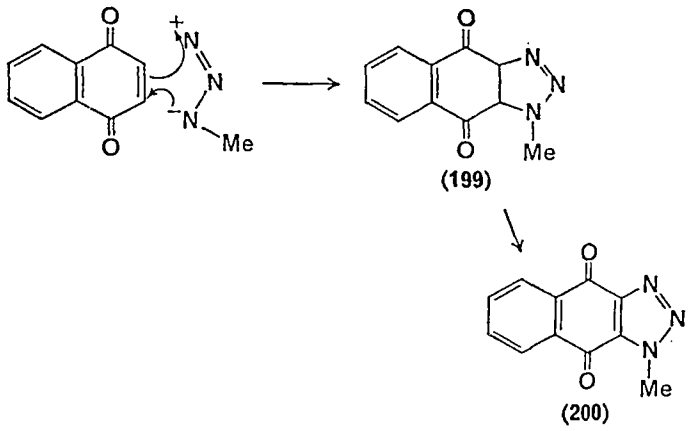
The choice of starting materials for this type of reaction is very wide (for reviews, see reference 214) but quinones have not been extensively



used as dipolarophiles. Diazoalkanes ($RCHN_2$) add rapidly to 1,4-naphthoquinone in ether to give the somewhat unstable adducts **197**; on attempted crystallization they isomerize and are oxidized by air to the indazolequinones **198**[215]. The reaction is applicable to *p*-quinones having adjacent



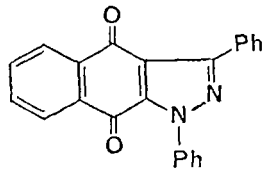
unsubstituted ring positions but unsymmetrical compounds give mixtures[216]. Azides behave similarly[216,217], the reaction of methyl azide with 1,4-naphthoquinone in a sealed tube giving the triazole **200**, the



initial adduct **199** being oxidized by the starting quinone[217]. *o*-Quinones react on oxygen with diazoalkanes to give the corresponding catechol

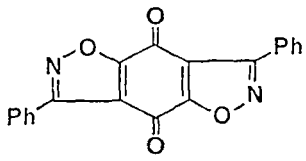
methylene ethers and their reaction with azides is ill-defined[217]. Pyrolysis of 2,5-diphenyltetrazole at 160–170° generates diphenylnitrilimine **201** which can be trapped by 1,4-naphthoquinone to give the naphthopyrazolequinone **202** in high yield, aromatization and oxidation occurring

(201)

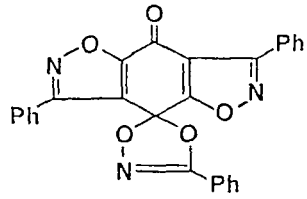


(202)

spontaneously[218]. Oxazole rings can also be fused onto quinone systems by 1,3-dipolar addition of nitrile oxides[219]. With benzoquinone in ether, benzonitrile oxide not only adds to both sides to give, after oxidation, the quinone **203** but some of the spiro-dioxazole **204** is also formed by



(203)



(204)

addition to a carbonyl group. Similar products were obtained from *o*-benzoquinone and from naphthoquinones.

The synthesis of heterocyclic quinones by 1,3-dipolar cyclo-addition is obviously capable of extension.

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The Chemistry of the quinonoid compounds
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CHAPTER 4

Identification and determination of quinones

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I. INTRODUCTION

As in other fields of chemistry, physical methods are preferentially used for the identification of quinones and therefore the main subject of this survey is the spectroscopy of quinones. Solutions to special problems in quinone chemistry, e.g. the distinction between the *p*- and *o*-structures, are indicated whenever possible and summarized in section VIII. Physical methods are also the most suitable for the quantitative determination of quinones, though chemical procedures will also be briefly discussed.

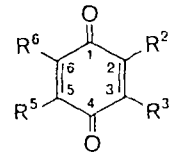
II. N.m.r. SPECTRA OF QUINONES

A. Proton Magnetic Resonance

1. 1,4-Benzoquinones

a. Chemical shifts. The chemical shifts of the quinonoid protons of *p*-benzoquinones (Table 1) as a rule are located between 6·3 and

TABLE 1. ^{1}H-n.m.r. spectra of *p*-benzoquinones



No.	Chemical shift (p.p.m.)				Coupling constants (Hz)	Solvent	Reference
	R^6 [a]	R^5 [a]	R^3 [a]	R^2 [a]			
(1)	H 6·72 s	H 6·72 s	H 6·72 s	H 6·72 s	$J_{23} = 10·22$ $J_{35} = 2·48$ $J_{25} = 0·13$ [b]	CCl_4	2, 3
(2)	H 6·70 nm	H 6·70 nm	H 6·58 m	CH_3 2·07 d	$J_{H_3-Me} = 1·6$	CCl_4	2, 3a
(3)	H 6·68 s	H 6·68 s	CH_3 2·02 s	CH_3 2·02 s	$J_{^{13}C-H(Me)} = 130$ $J_{23} = 1·3$ $J_{56} = 10·0$	CCl_4	2
(4)	H 6·53 q	CH_3 2·03 d	H 6·53 q	CH_3 2·02 d	$J_{23} = J_{56} = 1·6$	CCl_4	2
(5)	CH_3 2·03 d	H 6·50 m	H 6·50 m	CH_3 2·03 d	$J_{23} = J_{56} = 1·6$	CCl_4	2, 4
(6)	CH_3 2·00 s	CH_3 2·00 s	CH_3 2·00 s	CH_3 2·00 s	$J_{^{13}C-H(Me)} = 131$ $J_{23} = 1·3$	CCl_4	2
(7)	$(CH_3)_2CH$ 3·03 sp 1·13 d	H 6·40 s	H 6·40 s	$(CH_3)_2CH$ 3·03 sp 1·13 d	$J_{CH-Me} = 6·8$	CCl_4	4
(8)	H 6·47 s	$(CH_3)_2CH$ 3·00 sp 1·15 d	H 6·55 q	CH_3 2·02 d	$J_{CH-Me} = 7·0$ $J_{23} = 1·65$ $J_{6CH-6} = 1·25$	CCl_4	2
(9)	H 6·58 m	H 6·58 m	H 6·58 m	$C(CH_3)_3$ 1·30 s	—	CCl_4	2
(10)	H 6·47 s	$C(CH_3)_3$ 1·27 s	H 6·47 s	$C(CH_3)_3$ 1·27 s	—	$CDCl_3$	4
(11)	$C(CH_3)_3$ 1·27 s	H 6·49 s	H 6·49 s	$C(CH_3)_3$ 1·27 s	—	CCl_4	4
(12)	H 6·44 q	CH_3 1·98 d	H 6·48 s	$C(CH_3)_3$ 1·27 s	$J_{56} = 1·6$	CCl_4	4
(13)	$C(CH_3)_3$ 1·29 s	H 6·54 d	H 5·58 d	OCH_3 3·82 s	$J_{35} = 2·4$	$CDCl_3$	5
(14)	H 6·75 m	H 6·75 m	H 6·75 m	C_6H_5 7·38 m	—	CCl_4	5
(15)	H 6·95 s	C_6H_5 7·52 m	H 6·95 s	C_6H_5 7·52 m	—	$CDCl_3$	6
(16)	C_6H_5 7·41 m	H 6·81 s	H 6·81 s	C_6H_5 7·41 m	—	CCl_4	4
(17)	C_6H_5 7·20 m	C_6H_5 7·20 m	C_6H_5 7·20 m	C_6H_5 7·20 m	—	$CDCl_3$	5

TABLE 1 (*cont.*)

No.	Chemical shift (p.p.m.)				Coupling constants (Hz)	Solvent	Reference
	R^{6} [a]	R^{5} [a]	R^{3} [a]	R^{2} [a]			
(18)	H	H	H	Cl	$J_{56} = 9{\cdot}29$	CCl_4	3a
	6·96 m	6·87 m	7·05 m	—	$J_{35} = 2{\cdot}3$		
					$J_{36} = -0{\cdot}9$		
(19)	H	Cl	H	Cl	—	$CDCl_3$	6
	7·17 s	—	7·17 s	—			
(20)	Cl	H	H	Cl	—	CCl_4	3a
	—	7·00 s	7·00 s	—			
(21)	$C(CH_3)_3$	H	H	Cl	$J_{35} = 2{\cdot}4$	$CDCl_3$	5
	1·31 s	6·62 d	6·92 d	—			
(22)	Cl	H	H	CH_3	$J_{23} = 1{\cdot}6$	CCl_4	2
	—	6·92 d	6·58 m	2·13 d	$J_{35} = 2{\cdot}5$		
(23)	CH_3	Cl	Cl	CH_3	—	CCl_4	4
	2·21	—	—	2·21			
(24)	H	H	H	Br	$J_{56} = 10{\cdot}5$	CCl_4	2
	6·95	6·80	7·28	—	$J_{35} = 2{\cdot}6$		
					$J_{36} = -0{\cdot}6$		
(25)	H	Br	H	CH_3	$J_{23} = 1{\cdot}7$	CCl_4	2
	7·23 s	—	6·73 q	2·07 d			
(26)	Br	H	H	CH_3	$J_{23} = 1{\cdot}7$	CCl_4	2
	—	7·20 d	6·62 d/q	2·12 d	$J_{35} = 2{\cdot}5$		
(27)	H	Br	CH_3	CH_3	$J_{23} = 1{\cdot}3$	CCl_4	2
	7·20 s	—	2·08 m	2·08 m			
(28)	H	H	H	CF_3	—	CCl_4	2
	6·92 nm	6·92 nm	7·13 m	—			
(29)	H	CH_3	OH	CH_3	$J_{56} = 1{\cdot}7$	CCl_4	7
	6·53 q	2·06 d	—	1·93 s			
(30)	H	$(CH_3)_2CH$	OH	CH_3	—	CCl_4	7
	6·36	[c]	[c]	1·88 s			
(31)	OH	$(CH_3)_2CH$	H	CH_3	$J_{23} = 1{\cdot}7$	CCl_4	7
	[c]	[c]	6·38 q	2·03 d			
(32)	CH_3O	H	H	CH_3O	—	$CHCl_3$	8
	3·84	5·86	5·86	3·84			
(33)	H	CH_3	H	CH_3O	$J_{56} = 1{\cdot}5$	CCl_4	9
	6·40 q	1·98 d	5·74 s	3·74			
(34)	H	CH_3	CH_3O	CH_3O	$J_{56} = 1{\cdot}5$	CCl_4	9
	6·26 q	1·95 d	——3·88/3·90——				
(35)	CH_3O	H	H	CH_3	$J_{35} = 2{\cdot}5$	CCl_4	9
	3·74	5·70 d	6·39 m	2·00 d	$J_{23} = 1{\cdot}5$		
(36)	H	NH_2	H	NH_2	—	DMSO	10
	5·32	7·25–7·4	5·32	7·25–7·4			
(37)	H	$(CH_3)_2N$	H	$(CH_3)_2N$	—	$CDCl_3$	10
	5·32 s	3·19 s	5·32 s	3·19 s			
(38)	H		H		—	$CDCl_3$	10
	5·91 s	2·20 s	5·91 s	2·20 s			
(39)		H	H		—	$CDCl_3$	6
	2·16 s	5·95 s	5·95 s	2·16 s			

[a] s = Singlet, d = doublet, q = quartet, sp = septet, m = multiplet, nm = narrow multiplet.
[b] $^{4}J_{^{13}C,H} = -0{\cdot}20$; $^{3}J_{^{13}C,H} = 5{\cdot}27$.
[c] Not given in reference 7.

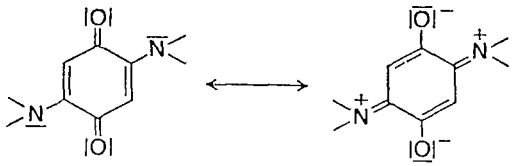
7·3 p.p.m., this being the typical region for α,β-unsaturated carbonyl compounds[1]. As a consequence of the relatively high symmetry of simple quinones their n.m.r. spectra are often of the first-order type. The chemical shifts of the usual substituents are separated from those of the quinonoid protons by several p.p.m. Long-range coupling with the protons of the substituents is very small and sometimes not even resolvable (see below). Thus, 2,6- or 2,5-substituted quinones with identical substituents form only one signal in the olefinic region. However, 2,6-substituted quinones with different substituents show an AB system, whereas monosubstituted quinones show only a narrow ABC pattern, whose components can be assigned by means of iterative computer calculations.

Quinones with alkyl and aryl substituents. Compared with the unsubstituted 1,4-benzoquinone **1** the quinonoid protons of all alkyl-substituted benzoquinones absorb at a higher field. This effect is small, but significant: proton 3 in toluquinone **2** absorbs at ca. 0·14 p.p.m. upfield compared to the protons of benzoquinone. Other methyl-substituted compounds show a similar behaviour, while their methyl groups have the typical chemical shift of olefinic methyl protons ($\delta \sim 2$ p.p.m.). The highest upfield shift for quinonoid ring protons (0·32 p.p.m.) was found in 2,6-di-isopropylquinone (**7**), whereas 2,6-di-*t*-butylquinone (**11**) absorbs by 0·09 p.p.m. at a lower field as compared to **7**. The phenyl groups of phenylbenzoquinone **14** and the diphenylquinones **15** and **16** shift the signals of the quinonoid protons downfield, and the greatest downfield shift (0·23 p.p.m.) was found for 2,5-diphenylbenzoquinone. This behaviour corresponds to the small positive Hammett σ_p constant of the phenyl ring (see below).

Quinones with halogen substituents. The quinonoid protons in the chloroquinones **18–20** are shifted to a lower field by about 0·3 p.p.m. Further substitution by alkyl groups (**21–22**), on the other hand, causes upfield shifts for the protons in the neighbourhood of the alkyl groups, whereas the other protons remain at their downfield position. The downfield shift in the bromoquinone **24** amounts to 0·56 p.p.m., while substitution by methyl groups (**25–27**) reveals the same pattern as for methyl substituted chloroquinones.

Quinones with methoxy and amino substituents. Introduction of a methoxy group (**32–35**) causes a large upfield shift of about 1 p.p.m. for the adjacent proton. This effect might be due to resonance participation by this substituent. As with chloroquinones the methoxy group influences only the neighbouring proton. Further substitution by methyl groups (**33–35**) shows that the proton next to the methyl group absorbs close to the normal position for methylquinones. The largest upfield shift has been

found in the aminoquinones **36** and **37**. The authors[10] explain this behaviour by assuming a quadrupolar merocyanine structure for such quinones:



b. Correlation of the chemical shifts with substituent constants. Mono- and 2,6-di-substituted benzoquinones are good examples for a correlation between Hammett σ values[11] and chemical shifts. One finds a good correlation of σ_p not only with the chemical shifts of *para* protons in substituted arenes, but also with the shifts of protons in the *ortho* position[12]. This reflects the resonance effect in σ_p, which should be nearly the same for the *ortho* as for the *para* position. Therefore, we tried to correlate the p.p.m. values of H_3 of the quinones **1**, **2**, **7**, **9**, **14**, **18**, **24**, **28**, **32**, **36** and **37** with the corresponding Hammett constants[5]. Figure 1 shows the result. A linear dependence between σ_p and the chemical shift of the protons H_3 exists for these quinones. The correlation factor is rather good (0·947 for 11 values). From this result we can conclude that the chemical shift of the ring protons in quinones is caused mainly by the resonance effects of the substituents.

However, a more accurate inspection of Figure 1 shows that the quinones **2**, **9**, **24** and **28** clearly deviate from the regression line. σ_p-Values for the methyl, *t*-butyl, Br and CF_3 groups seem to be inadequate for a correlation with chemical shifts of the *ortho* position. Some years ago, Schaefer and coworkers[13] defined the value $Q = P/Ir^3$ where P is the polarizability of a C—X bond, I the first ionization potential of X and r the distance between C and X. The authors showed that Q correlates very well with the chemical shifts of *ortho* protons in arenes. Unfortunately Q can be calculated exactly only for H, F, Cl, Br and I.

Therefore, Smith and coworkers[14] extended the concept of Schaefer and determined experimental Q values for other substituents. They showed that Q gives an excellent correlation with the chemical shifts of protons *ortho* to a substituent in a wide range of aromatic compounds.

Figure 2 represents an attempted correlation between Q values and the chemical shifts of the protons H_3 in the quinones **1**, **2**, **9**, **14**, **18**, **24**, **28**, **32** and **36** and demonstrates that Q is indeed a good ($r = 0{\cdot}978$) quantity to calculate the shifts of the olefinic protons in the quinone series[5].

Unfortunately, the theory and physical significance of Q are treated only very shortly by Schaefer and Smith. Therefore, no further conclusions should be drawn regarding the *ortho*-effect[15] from Figure 2 at this time. To summarize, the chemical shifts of *p*-benzoquinones follow the pattern of the usual substituent effects. No deviations could be detected and, accordingly, the double bonds in quinones seem to be fixed from the n.m.r. point of view[2].

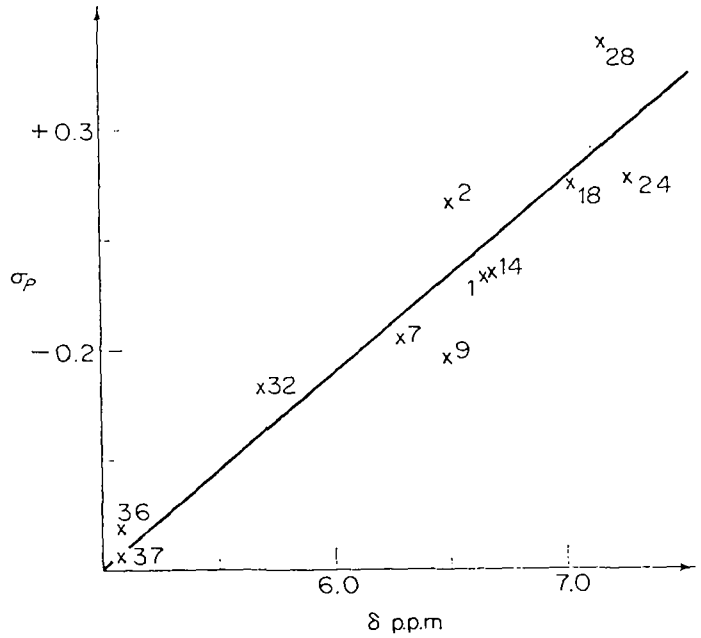


FIGURE 1. Hammett σ-values versus δH_3 of 2-substituted *p*-benzoquinones.

c. Coupling constants. 1,4-Benzoquinones having different substituents in the 2- and 6-positions reveal an AB quartet of the ring protons. In all compounds investigated so far the coupling constant (see **13**, **22**, **26** and **35**, Table 1) is 2·5 Hz. This is a typical value for coupling constants in the cyclohexadienone series[4]. Benzoquinones with different substituents in the 2- and 5-positions, on the other hand, show no significant coupling between the protons in the 3- and 6-positions (**8**, **12** and **25**). Their coupling constants, therefore, have to be smaller than 0·3 Hz[2].

Mono-substitution in benzoquinones (**2**, **9**, **14**, **18**, **24**, **28**) gives rise to an ABC system. Whereas the bromoquinone **24** and the chloroquinone **18**, for example, show the normal complex pattern of an ABC system,

other quinones, e.g. toluquinone **2**, reveal very simple spectra[3a]. In the latter compound the signals of the protons in positions 5 and 6 are only slightly separated, so that they appear as one broad unresolved line. From the analysis of the ABC spectra of the monosubstituted quinones the following coupling constants were determined:

$$J_{35} = 2{\cdot}2\text{–}2{\cdot}5 \text{ Hz}, \quad J_{56} = 10 \text{ Hz}$$

It is of interest that the small coupling constants J_{36} were found to be negative in the order of about $-0{\cdot}6$ Hz.

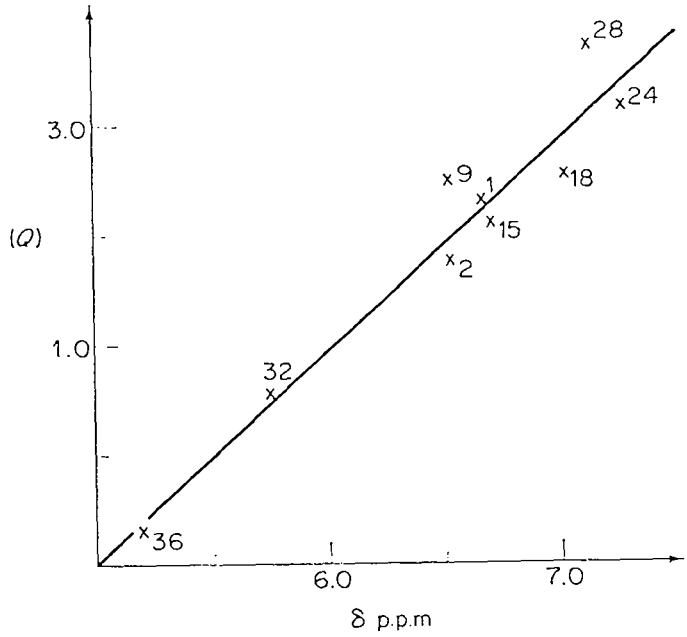
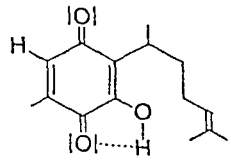


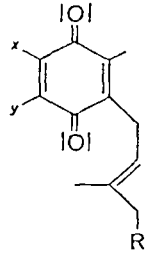
FIGURE 2. Q-values versus δH_3 of 2-substituted p-benzoquinones.

The values for the long-range coupling between methyl groups and the quinonoid protons are between 1·6 and 1·7 Hz. Apparently such methyl groups are coupled significantly only with the adjacent proton. Homoallylic coupling was observed in 2,3-dimethyl-benzoquinone ($J_{23} = 1{\cdot}3$ Hz)[2].

d. Application. In *p*-benzoquinone chemistry ^{1}H-n.m.r. spectroscopy was mainly applied to identify naturally occurring quinones and to distinguish between isomeric structures. Only a few examples may be quoted[8]. Wagner and coworkers[7] revised the structure of perezone, mainly on the basis of n.m.r. spectroscopy. The aromatic solvent-induced shifts (a.s.i.s.) in benzene and pyridine solutions relative to carbon

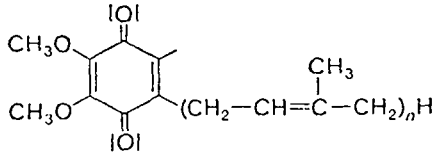


tetrachloride were used by Wilczynski and coworkers[9] to distinguish between the different forms of rhodoquinones:



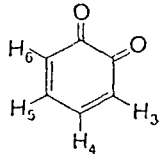
x, y = NH_2 and OCH_3
R = $-[CH_2CH=C(CH_3)-CH_2]_9H$

Careful integration has been used by Kofler and coworkers[16] to determine the length of the side-chain in compounds related to ubiquinone:



2. 1,2-Benzoquinones

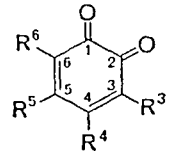
Little work has been done in n.m.r. spectroscopy of *o*-benzoquinones (see Table 2). Not even the n.m.r. spectrum of the unsubstituted *o*-quinone is published so far. According to our own measurements[5] the A_2B_2 system of this compound centres around 6·71 p.p.m., the resonance position of *p*-benzoquinone protons. The main lines form two quartet



(40)

signals (protons $H_{3,6}$ and $H_{4,5}$) which are centred at 7·09 and 6·34 p.p.m. The line separation in these quartets amounts to 4 Hz. On the basis of the investigation of the substituted *o*-quinones **41–48** it follows that the quartet at *higher* field belongs to the protons 3 and 6. This is in agreement

TABLE 2. ^{1}H-n.m.r. spectra of *o*-benzoquinones



No.	Chemical shift (p.p.m.)				Coupling constants (Hz)	Solvent	Reference
	R^6 [a]	R^5 [a]	R^4 [a]	R^3 [a]			
(40)	H	H	H	H	—	Et_2O	5
	6·34 m[b]	7·09 m	7·09 m	6·34 m			
(41)	H	CH_3	CH_3	H	$J_{34} = 1·1$	$CDCl_3$	4
	6·25 q	2·19 d	2·19 d	6·25 q			
(42)	$C(CH_3)_3$	H	CH_3	H	$J_{35} = 2·1$	$CDCl_3$	4
	1·26 s	6·63 m	2·16 m	6·18 m	$J_{Me-H} = 1·4$		
(43)	$C(CH_3)_3$	H	C_6H_5	H	$J_{35} = 2·3$	$CDCl_3$	4
	1·33 s	7·24 d	7·55	6·54 d			
(44)	$C(CH_3)_3$	H	$C(CH_3)_3$	H	$J_{35} = 2·4$	$CDCl_3$	4
	1·28 s	6·99 d	1·23 s	6·23 d			
(45)	$C(CH_3)_3$	H	$C(CH_3)_3$	C_6H_5	—	$CDCl_3$	5
	1·29 s	7·20 s	1·07 s	7·0–7·45 m			
(46)	$C(CH_3)_3$	H	$C(CH_3)_3$	Cl	—	$CDCl_3$	5
	1·26 s	7·20 s	1·48 s	—			
(47)	$C(CH_3)_3$	H	$C(CH_3)_3$	Br	—	$CDCl_3$	5
	1·27 s	7·20 s	1·50	—			
(48)	$C(CH_3)_3$	H	$C(CH_3)_3$	NO_2	—	$CDCl_3$	4
	1·30	7·07 s	1·35	—			

[a] s = Singlet, d = doublet, q = quadruplet, m = multiplet.
[b] Centre of the A_2B_2 system at 6·71 p.p.m.

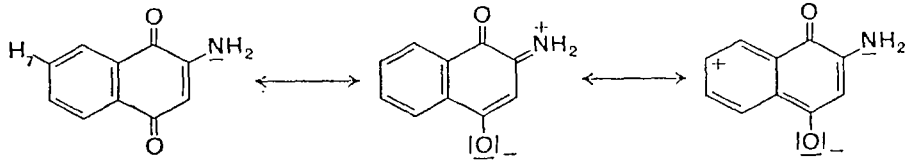
with the direction of the anisotropy of the carbonyl group, postulated by Karabatsos and coworkers[17a]. The influence of substituents in *o*-benzoquinones follows the rules found in the *p*-quinone series: alkyl substituents (**41**, **42** and **44**) shift the signals of the remaining protons to higher field, whereas the phenyl ring and the halogens (**43**, **45**, **46** and **47**) cause downfield shifts. The coupling constants in the asymmetrically substituted *o*-quinones (**42**, **43** and **44**) vary from 2·1 to 2·4 Hz, and the long-range coupling is again near 1·1 Hz. Meantime, the spectra of some simple *o*-benzoquinones (e.g. **40**) have been reported[17b].

3. 1,4-Naphthoquinones

a. Chemical shifts. The quinonoid protons of 1,4-naphthoquinone **49** (see Table 3) resonate at lower field (0·23 p.p.m.) than the protons in 1,4-benzoquinone. Whether this depends on 'ring current' effects or on the substituent effect of the benzene ring (cf. the spectra of the phenylquinones **14**, **15** and **16**) is doubtful[18] (cf. the general criticism of the ring current model by Musher[19]). The chemical shifts (Table 3) of the quinonoid

protons in 2-substituted naphthoquinones (**49–56**) obey the usual substituent rules. Some correlations, for instance, were found with σ_p[20], *ortho*-substituent effects[20] and redox potentials[20]. Substituents in the condensed benzene ring (**60**, **61** and **62**) exert only small effects on the resonance position of the quinonoid protons.

Since the benzenoid protons of naphthoquinones form complex patterns (A_2B_2 and ABCD spectra, see below) their exact resonance position is available only by computer analysis. The centres of these signals are found about 0·5 p.p.m. downfield relative to benzene. The signals of the benzenoid protons in naphthoquinones, therefore, are well separated from the quinonoid resonance position. Due to the electric-field effect and the magnetic anisotropy of the carbonyl group the signals of H_5 and H_8 in 1,4-naphthoquinones are shifted by ca. 0·3 p.p.m. to the lower field as compared to H_6 and H_7. It was found that in 2-substituted naphthoquinones the chemical shift of H_7 correlates with σ_p and somewhat better with the redox potential, whereas the signal position of H_5 is practically not altered. It seems that there could be a correlation between H_8 and σ_m. The phenomenon of a positive correlation between the chemical shift of H_7 and σ_p is explained[20] by an assumed interaction of **56** and its resonance contributors:

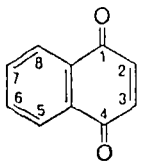


(**56**)

In the case of 2,3-substituted naphthoquinones (**57**, **58** and **59**) additivity of the substituent effects is observed.

b. Coupling constants. The vinylic proton–proton coupling constant J_{23} in 1,4-naphthoquinones amounts to 10 Hz. Whereas this coupling in the parent naphthoquinone is obtained from the $^{13}C-H$ satellite spectrum[2], it can be determined directly in asymmetric naphthoquinones as 6-acetyl-5,8-dihydroxy-1,4-naphthoquinone (**65**)[21], for instance. The bond connecting C-2 and C-3 in 1,4-naphthoquinone seems to have somewhat less double-bond character than the double bond in ethylene ($J = 11{\cdot}7$ Hz)[22]. Coupling constants of the quinonoid ring protons with alkyl groups (**50**, **60** and **64**) are in the same order as in alkyl-substituted benzoquinones (1·5–1·7 Hz). Long-range coupling was found to be 1·25 Hz in 2,3-dimethyl-1,4-naphthoquinone (**57**)[2]. In the case of symmetric naphthoquinones (**49**, **57** and **58**) the benzenoid protons form an A_2B_2 pattern. The coupling constants are nearly the same[20] as those in benzene itself.

TABLE 3. ^{1}H-n.m.r. spectra of 1,4-naphthoquinones

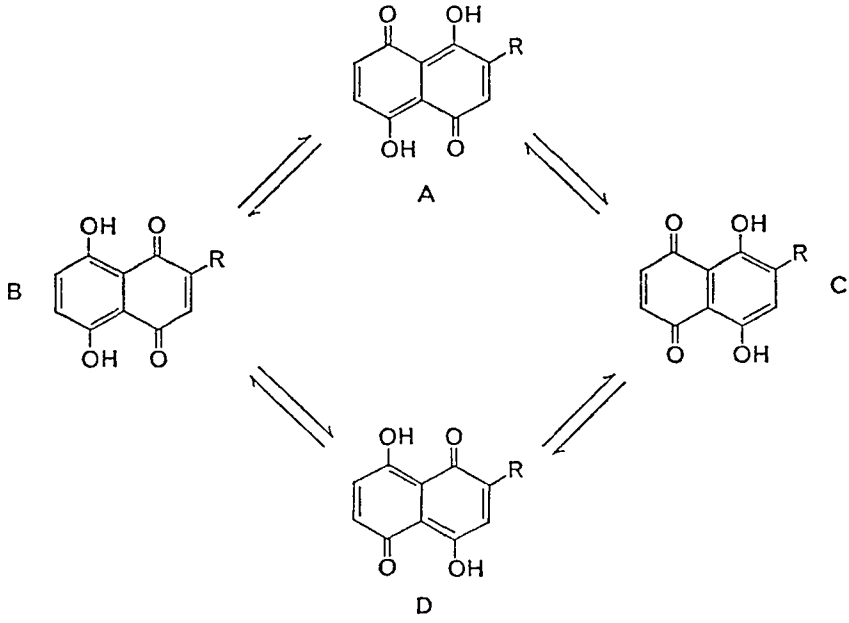
 No.	Chemical shift (p.p.m.)[a]						Substituents	Coupling constants (Hz)	Solvent	Reference
	H_2	H_3	H_5	H_6	H_7	H_8				
Un- (**49**) substituted	6·95	6·95	8·02	7·75	7·75	8·02		$J_{^{13}C-H} = 170$ $J_{23} = 10$ $J_{56} = 7·75$ $J_{57} = 1·3$ $J_{58} = 0·49$ $J_{67} = 7·45$	THF	2, 20[b]
2-Methyl (**50**)	—	6·81	7·98	7·71	7·71	8·03	Me: 2·13[c]	$J_{23} = 1·7$[c]	THF	20[b], 21
2-Phenyl (**51**)	—	7·06	8·04	7·75	7·76	8·12			THF	20[b]
2-Chloro (**52**)	—	7·26	8·03	7·78	7·78	8·11			THF	20[b]
2-Bromo (**53**)	—	7·55	8·03	7·79	7·78	8·11			THF	2, 20[b]
2-Hydroxy (**54**)	—	6·15	8·01	7·74	7·68	8·03			THF	20[b], 21
2-Methoxy (**55**)	—	6·21	8·00	7·71	7·69	8·02			THF	20[b], 21
2-Amino (**56**)	—	5·84	7·98	7·67	7·58	7·97			THF	20[b]

2,6-Di-methyl	(60)	—	6·73 q	7·78 m	—	7·38 d, q 7·52 d, q	7·87 s 8·00 s	Me (2): 2·17 Me (6): 2·50	J_{23} = 1·6	CCl_4	2
5-Hydroxy	(61)	6·97	6·97	—	7·25	7·6	7·7	OH: 11·93		$CDCl_3$	21
5-Hydroxy-7-methyl	(62)	6·91	6·91	—	7·08 d	—	7·41 d	OH: 11·83 Me: 2·42		$CDCl_3$	8
5,8-Di-hydroxy	(63)	7·13	7·13	—	7·13	7·13	—	OH: 12·43		$CDCl_3$	21
2-Ethyl-5,8-dihydroxy	(64)	—	6·84 t	—	7·20 d	7·20 d	—	OH (5): 12·45 OH (8): 12·60 Et: 1·24, 2·67	J_{23} = 1·5 J_{67} = 10	$CDCl_3$	21
6-Acetyl-5,8-dihydroxy	(65)	7·08	7·08	—	—	7·56	—	Ac: 2·75 OH (5): 13·08 OH (8): 12·15	J_{23} = 10	$CDCl_3$	21

[a] s = Singlet, d = doublet, t = triplet, q = quartet, m = multiplet.
[b] Line positions calculated by LAOCOON II.
[c] Taken from reference 20 ($CDCl_3$).

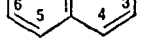
Therefore, on the basis of n.m.r. spectroscopy 1,4-naphthoquinones resemble *ortho*-disubstituted benzenes. No bond fixation in the benzenoid ring and no interaction between the two rings can be determined. Naphthoquinones, substituted in position 2 or by different groups in positions 2 and 3 (**59**), reveal ABCD spectra. Again the coupling constants are in the normal order of magnitude of disubstituted benzenes with only little dependence on the substituent[20].

c. Application. One of the most striking examples of application of n.m.r. spectroscopy in the naphthoquinone series is the naphthazarin system. In their extensive work Moore and Scheuer[21] investigated several mono-, di-, tri- and tetra-substituted naphthazarins and determined their tautomeric equilibria. Whereas naphthazarin **63** itself shows only one signal for quinonoid and benzenoid protons at 7·13 p.p.m., it follows clearly from the n.m.r. data that in the ethyl naphthazarin **64** the principal tautomer is B (in $CDCl_3$ solution). An acetyl group, on the other hand, causes C to be the predominant tautomeric form (**65**).



4. 1,2-Naphthoquinones

The centre of the AB system of H_3 and H_4 in the n.m.r. spectrum of 1,2-naphthoquinone (**66**) is situated at the resonance position of the quinonoid protons of 1,4-naphthoquinone as observed also with 1,4- and 1,2-benzoquinone. The investigation of 3- and 4-substituted 1,2-naphthoquinones (**67**, **68** and **69**, Table 4) reveals that H_3 resonates at higher field



		H_3	H_4	H_5	H_6	H_7	H_8	(Hz)		
Unsubstituted	**(66)**	6·48, 6·32 d	7·52, 7·36 d	——— 7·27–8·17 m ———				$J_{34} = 10$	$CDCl_3$	5[b]
3-Chloro	**(67)**	—	7·54	7·33–7·27 q	7·64–7·44 m	7·64–7·44 m	8·05–7·98 q		$CDCl_3$	23
4-Chloro	**(68)**	6·79	—	7·74–7·64 q	8·02–7·76 m	8·02–7·76 m	8·26–8·13 q		$CDCl_3$	23
3-Bromo	**(69)**	—	7·81	7·33–7·23 q	7·71–7·46 m	7·71–7·46 m	8·10–7·98 q		$CDCl_3$	23
6-Chloro	**(70)**	6·47, 6·37 d	7·39, 7·29 d	7·66–7·48 m	—	7·66–7·48 m	7·95–7·87 d	$J_{34} = 10$	$CDCl_3$	23[c]
6-Bromo	**(71)**	6·48, 6·38 d	7·37, 7·28 d	7·66–7·48 m	—	7·66–7·48 m	7·96–7·88 d	$J_{34} = 10$	$CDCl_3$	23[c]
6-Methyl-8-methoxy[d]	**(72)**	6·44, 6·27 d	7·38, 7·22 d	6·86 d	—	6·73 d	—	$J_{34} = 10$	$CDCl_3$	8[b]

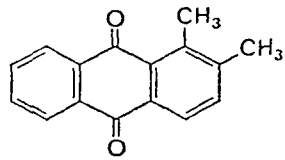
[a] m = Multiplet, d = doublet, q = quadruplet.
[b] In reference 8 the values for H_3 and H_4 of **66** and **72** should be reversed[24].
[c] In reference 23 the values for H_3 and H_4 of **70** and **71** should be reversed[25].
[d] MeO: 3·96, Me: 2·40 p.p.m.

than H_4, which is consistent with the results obtained for 1,2-benzoquinones. The coupling constant J_{34} in 1,2-naphthoquinones is 10 Hz and is independent of the nature of the substituents (**66**, **70**, **71** and **72**).

The aromatic protons of 1,2-naphthoquinones form ABCD systems (or ABC systems, if the aromatic ring is substituted). As one may conclude from the spectrum of 1,4-naphthoquinone, there is no observable coupling between the quinonoid and the aromatic protons.

5. 9,10-Anthraquinones

It is not intended to discuss the n.m.r. spectra of 9,10-anthraquinones in detail, since these compounds possess no quinonoid protons. Anthraquinone (**73**) itself shows the typical A_2B_2 pattern of an *ortho*-disubstituted aromatic compound. Interestingly, the centre of this A_2B_2 system is shifted to lower field (0·18 p.p.m.) relative to the A_2B_2 system of 1,4-naphthoquinone[5]. This result may be due to the second aromatic ring. The difference between the chemical shifts of H_5 and H_6 (0·5 p.p.m.) in anthraquinone is nearly twice as big as in the corresponding 1,4-naphthoquinone. The n.m.r. spectra of substituted anthraquinones can be calculated from the usual substituent parameters of aromatic compounds[26]. The solvent shift $\Delta^{CDCl_3}_{C_6H_6}$ was used to determine the positions of methyl groups in the anthraquinone series[27]. Thus, it was shown that in 2,3-dimethyl-9,10-anthraquinone the $\Delta^{CDCl_3}_{C_6H_6}$ value for the 1-methyl group is 0·17 p.p.m. and 0·6 p.p.m. for the 2-methyl group.

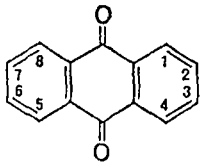


Steglich and Lösel[28] found another application of n.m.r. spectroscopy to polyhydroxy anthraquinones. The authors compared the n.m.r. spectra of the per(trimethylsilyl) ethers and the peracetates of these compounds: they could determine the position of *O*-substituents from the 'acylation shift'.

6. Phenanthraquinones

Since 9,10-phenanthraquinones have no quinonoid protons, their n.m.r. spectra reflect the normal aromatic n.m.r. pattern, depending on their specific substitution. The spectrum of the parent 9,10-phenanthraquinone (**77**) is of the ABCD type, whereas 2,7-dimethyl-9,10-phenanthraquinone shows an ABC spectrum (Table 6). Comparison of these two

TABLE 5. ^{1}H-n.m.r. spectra of 9,10-anthraquinones[a]



	No.	Chemical shift (p.p.m.)								Coupling constants (Hz)	Solvent	Reference
		H_1	H_2	H_3	H_4	H_5	H_6	H_7	H_8			
Unsubstituted	(73)	8·32	7·82	7·82	8·32	8·32	7·82	7·82	8·32		$CDCl_3$	5
1,2-Dihydroxy	(74)	—	—	7·21 d	7·56 d	———	8·30–7·70	———		$J_{34} = 8$	DMSO-d_6	29
1,3,5,7-Tetrahydroxy	(75)	—	6·51 d	—	7·04 d	—	6·51 d	—	7·04 d	$J_{23} = 3$	DMSO-d_6	29
1,8-Dihydroxy-3-methoxy-6-methyl[b]	(76)	—	6·67 d	—	7·35 d	7·60	—	7·08	—	$J_{24} = 3$	$CDCl_3$	29

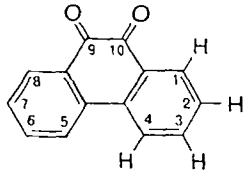
[a] d = Doublet.
[b] MeO: 3·99; Me: 2·48 p.p.m.

TABLE 6. ^{1}H-n.m.r. spectra of phenanthraquinones

Compound	No.	Chemical shift (p.p.m.)				Coupling constants (Hz)	Solvent	Reference
		H_1	H_2	H_3	H_4			
9,10-Phenanthraquinone	(77)	8·17	7·46	7·70	8·01	$J_{12} = 7{\cdot}85$ $J_{13} = 1{\cdot}65$ $J_{14} = 0{\cdot}4$ $J_{23} = 7{\cdot}3$ $J_{24} = 1{\cdot}3$ $J_{34} = 8{\cdot}0$	$CDCl_3$	30
2,7-Dimethyl-9,10-phenanthraquinone[a]	(78)	7·94	—	7·45	7·82	$J_{13} = 1{\cdot}85$ $J_{14} = 0{\cdot}35$ $J_{34} = 8{\cdot}4$	$CDCl_3$	30

[a] CH_3: 2·30 p.p.m.

spectra[30] permits a determination of the relative resonance position of protons: H_1 resonates at the lowest field, followed by H_4, whereas H_2 absorbs at the highest field. The coupling values of phenanthraquinones are in the order typical for *ortho*-substituted arenes.



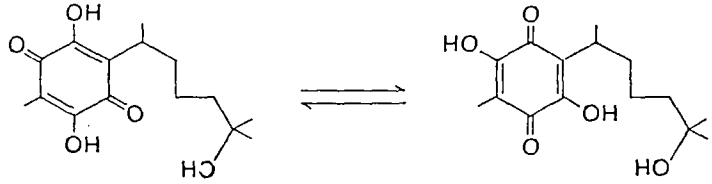
(77)

B. ^{13}C Magnetic Resonance (C.m.r.)

1. 1,4-Benzoquinones

In the first systematic c.m.r. study of *p*-benzoquinones[6] the chemical shifts of 17 derivatives have been assigned. The chemical shifts of the olefinic carbon atoms of these quinones cover the region from 110 to 160 p.p.m. (TMS scale; see Figure 3). A typical effect is the branching out of the chemical shifts of adjacent carbon atoms if one of these is substituted. The carbonyl resonances of 1,4-benzoquinones are found near 186 p.p.m., but may be shifted upfield in the case of chloro-substitution (**18**, **19**, **23** and **79**). A linear correlation holds for the chemical shift of the C=O group and polarographic half-wave potentials. The slope of the multiple regression line indicates that the oxygen atom is the reaction centre in the polarography of quinones. The ^{13}C chemical shift of C_3 and the proton chemical shift of H_3 again fit a linear correlation, indicating that the resonance position of both carbon and hydrogen atoms in quinones is caused mainly by the same effects.

Nathan and coworkers[31] applied c.m.r. spectroscopy to the problem of perezone structure (see section II.A.1.d). These authors assigned the resonance lines of perezone and of four derivatives as well. C.m.r. indicates that in 2,5-dihydroxy-quinones a rapid tautomerism occurs.



2. 1,2-Benzoquinones

In the olefinic region of the c.m.r. spectrum of *o*-benzoquinone[6] (**40**) two lines appear, the centre of which corresponds to the resonance

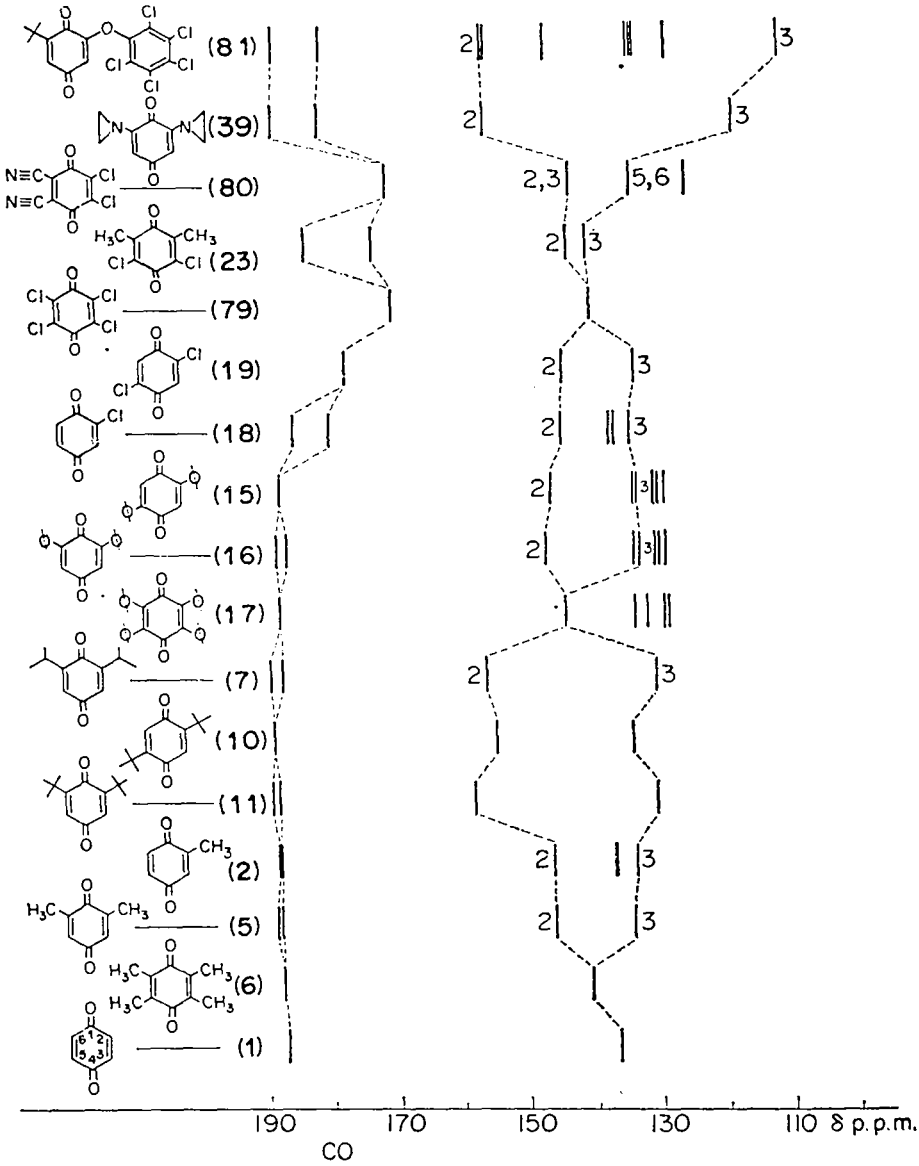


FIGURE 3. ^{13}C-chemical shifts of *p*-benzoquinones.

position of the *para* isomer. This agrees well with the results obtained by p.m.r. of these compounds (cf. section II.A.2). The assignment[6] (Figure 4) in *o*-benzoquinone c.m.r. is somewhat more difficult and, concerning C_4 and C_6, not unambiguous[17b]. Remarkable is the observed upfield shift of the carbonyl resonances with respect to 1,4-benzoquinones.

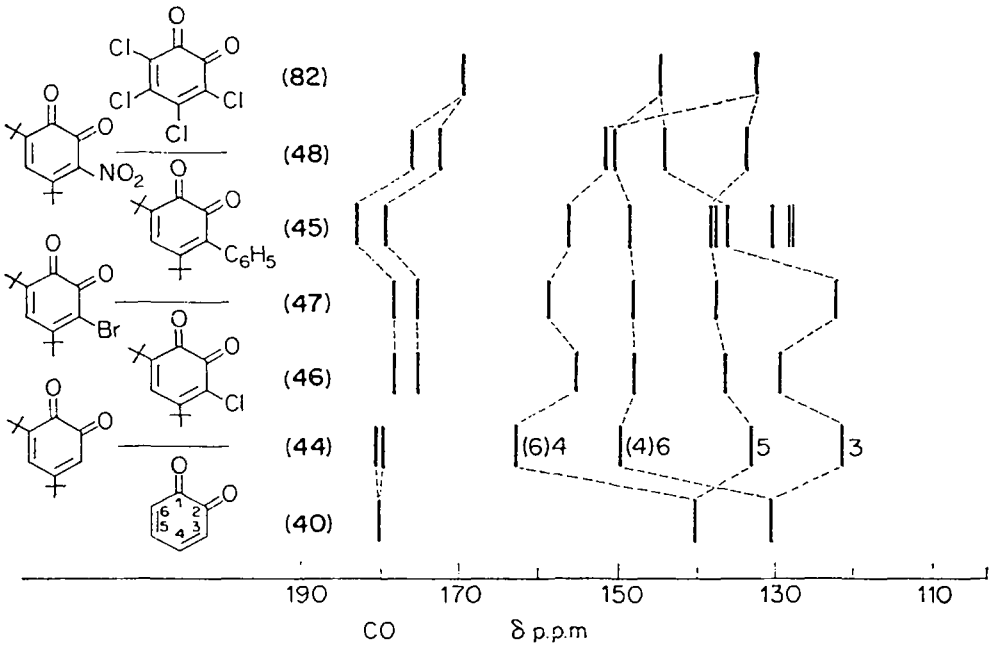
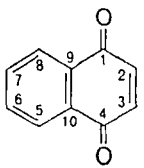
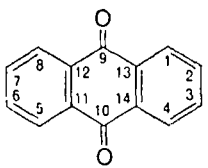


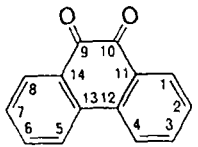
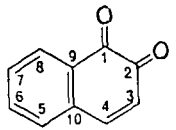
FIGURE 4. ^{13}C-chemical shifts of *o*-benzoquinones.

3. Condensed quinones

The complete c.m.r. spectra of naphtho-, anthra- and phenanthraquinones have not been published to date, although Lippmaa and coworkers[32] have reported on the carbonyl shifts of these quinones. In order to complete this survey we recently investigated the parent compounds by pulse Fourier transform spectroscopy[5]. The assignment of lines (Table 7), however, is rather difficult and in the case of 1,2-naphthoquinone and phenanthraquinone should be regarded only as tentative. In the case of 1,4-naphthoquinone (**49**) the quinonoid atom C_2 (and C_3) can be distinguished from the aromatic carbon atoms by the fact that only its signal shows no long-range proton coupling, if the spectrum is taken without a proton decoupling frequency. Carbon atom 9 (10) can be assigned by means of the off-resonance spectrum. Starting with the c.m.r. spectrum of naphthalene[33] (cf. Figure 5) we find that C_5 (C_8) is deshielded, whereas the other carbon atoms remain nearly at their positions. By the off-resonance spectrum and by comparison with 1,4-naphthoquinone the signals in the spectrum of 9,10-anthraquinone (**73**) are then readily assigned. Based on the line assignment in phenanthrene[33] we might ascribe the ^{13}C signals of phenanthraquinone **77** using the same order of sequence, with the sole exception that C_1 (C_8) is again deshielded by about

TABLE 7. C.m.r. spectra of naphtho-, anthra- and phenanthraquinones[5]

Compound	No.	Position of the carbon atom	Chemical shift (p.p.m.[a])	Solvent
	(49)	1, 4 2, 3 5, 8[b] 9, 10 6, 7[b]	184·8 138·5 133·9 131·8 126·2	$CDCl_3$
	(73)	9, 10 1, 4, 5, 8 11, 12, 13, 14 2, 3, 6, 7	181·1 134·1 133·7 127·3	$CDCl_3$

	(77)[b]	9, 10	180·3	$CDCl_3$
		1, 8	135·9	
		11, 14	135·7	
		12, 13	131·0	
		2, 7	130·4	
		3, 6	129·5	
		4, 5	123·9	
	(66)[b]	2	180·8	$CDCl_3$
		1	178·9	
		4	145·4	
		8	135·8	
		9	134·8	
		10	131·5	
		3	130·9	
		7	130·1	
		6	129·9	
		5	127·8	

[a] TMS scale.
[b] Assignment tentative.

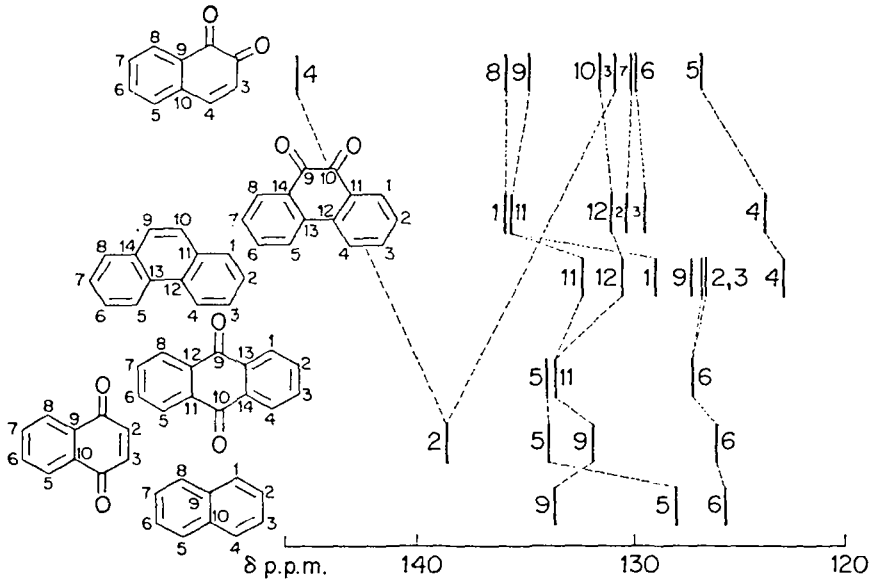


FIGURE 5. ^{13}C-chemical shifts of condensed quinones and of naphthalene and phenanthrene.

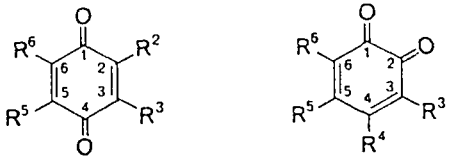
6 p.p.m. (cf. naphthalene and 1,4-naphthoquinone). Considering 1,2-naphthoquinone as a phenanthraquinone structure without one annelated ring, we might assign the ^{13}C signals of 1,2-naphthoquinone (**66**) in analogy to phenanthraquinone. The chemical shifts of the carbonyl carbon atoms of **49**, **66**, **73** and **77** are located between 179 and 184 p.p.m., the typical quinonoid region[6]. In summary, one important conclusion can be drawn from the c.m.r. spectra of these compounds: the aromatic carbon atoms approximately hold their resonance position relative to the unsubstituted hydrocarbons. On the basis of c.m.r. spectroscopy, therefore, the ring carbons reveal no typical quinonoid character.

III. I.r. SPECTRA OF QUINONES

A. General Remarks

Useful compilations of i.r. data are available for benzoquinones[4,8,34-36], naphthoquinones[8,37] and anthraquinones[8,38,39]. The following discussion will be restricted to the position of the double-bond vibrations near 6 μ, which should depend on the *p*- or *o*-structure. If the expected differences are modified only slightly by the substituents present, then characteristic areas for the absorptions of the *o*- and *p*-compounds will exist. Assignments may be rendered difficult by the *appearance of more than one*

absorption due to Fermi resonance, to the asymmetry of the molecule or to vibration coupling[40–43].



It should also be pointed out that differences in line numbers and positions may arise from using different experimental techniques (solution, film or KBr disc)[4]. The absorptions found for quinones in solutions are of somewhat higher frequencies than those measured in KBr. With few exceptions, the data included in the following tables are only those which have been obtained from compounds measured in solution. It is difficult to find a coherent series of solution spectra in the literature; a comprehensive systematic study of the i.r. spectra of quinones under standardized conditions would be highly desirable.

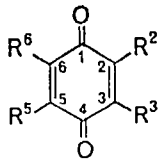
B. Benzoquinones

1. 1,4-Benzoquinones

a. Appearance of the spectra. For *p*-benzoquinones the frequencies of the C=O valence vibrations are generally located in the region of 1630 to 1700 cm^{-1} (Table 8), whereas the C=C valence vibrations give rise to absorptions near 1600 cm^{-1} [36,43]. A comprehensive analysis of the molecular vibrations of the parent benzoquinone **1** and its deuterated and ^{18}O-labelled derivatives and a complete assignment of the vibrational fundamentals has been carried out[42,44,45]. In solution the carbonyl absorption of *p*-benzoquinone falls at 1668–1671 cm^{-1}, which corresponds to an $\alpha,\beta;\alpha',\beta'$-di-unsaturated ketone[8]; there is another absorption of lower intensity at 1656–1657 cm^{-1} (Fermi resonance[40,44]). Many other *p*-benzoquinones also show two absorptions in the carbonyl region (see Figure 6). Often the absorption at highest frequency displays the highest intensity. Furthermore, pronounced shoulders on the lower frequency side of the main band (ca. 1640–1650 cm^{-1}) are sometimes observed (Figure 6).

b. Influence of the type of substituents. The influence of substituents on the C=O vibration frequency is determined not only by inductive and resonance effects, but also (by means of vibration coupling) by their mass (cf. the theoretical calculations of Bratož and Mirone[51]). This is demonstrated by a comparison of *p*-benzoquinone **1** and the deuterated compounds **83–87**. In the case of per-deutero-benzoquinone (**87**) there

TABLE 8. Carbonyl absorption of 1,4-benzoquinones



No.	R^6	R^5	R^3	R^2	$\tilde{\nu}_{C=O}$ [a] (cm^{-1})	$\bar{\tilde{\nu}}_{C=O}$ [b] (cm^{-1})	Solvent	Reference
(1)	H	H	H	H	1671, 1657	1664	CCl_4	46
					1668, 1656	1663[c]	CCl_4	42, 44
(83)	H	H	H	D	*1664*, (1652)	1664[c]	CCl_4	42, 45a
(84)	D	H	H	D	*1665*, 1641	1664[c]	CCl_4	45a
(85)[d]	H	D	H	D	1680, *1655*	1661[c]	CCl_4	45
(87)	D	D	D	D	1690, *1663*, 1648	1664[c]	CCl_4	42, 44
(2)	H	H	H	CH_3	1661	1661	CCl_4	35
(3)	H	H	CH_3	CH_3	*1656*, 1626	1641	CCl_4	35
(4)	H	CH_3	H	CH_3	1661, 1637	1649	CCl_4	35
(5)	CH_3	H	H	CH_3	1657	1657	CCl_4[e]	4
(88)	H	CH_3	CH_3	CH_3	1647	1647	CCl_4	35
(6)	CH_3	CH_3	CH_3	CH_3	1653, *1639*	1646	CCl_4	35
(7)	$CH(CH_3)_2$	H	H	$CH(CH_3)_2$	1660	1660	CCl_4[e]	4
(10)	H	$C(CH_3)_3$	H	$C(CH_3)_3$	1656	1656	CCl_4[e]	4
(11)	$C(CH_3)_3$	H	H	$C(CH_3)_3$	1670, *1660*	1665	CCl_4[e]	4
(12)	H	CH_3	H	$C(CH_3)_3$	1658	1658	CCl_4[e]	4
(15)	H	C_6H_5	H	C_6H_5	*1656*, 1652	1654	$CHCl_3$[e]	47
(16)	C_6H_5	H	H	C_6H_5	1670, *1655*	1662	CCl_4[e]	4
(17)	C_6H_5	C_6H_5	C_6H_5	C_6H_5	1667	1667	$CHCl_3$[e]	47
(18)	H	H	H	Cl	*1681*, 1660	1670	CCl_4[e]	47
(19)	H	Cl	H	Cl	1681	1681	CS_2	34
(20)	Cl	H	H	Cl	1695, *1653*	1674	CS_2	34
(89)	F	F	F	F	1705, 1668	1686	CCl_4	46
(79)	Cl	Cl	Cl	Cl	1696	1696	CCl_4	46
(90)	Br	Br	Br	Br	1689	1689	CCl_4	46

(95)	OC_6H_5	OC_6H_5	OC_6H_5	OC_6H_5	1681	1681	CCl_4	46
(13)	$C(CH_3)_3$	H	H	OCH_3	1684, *1651*	1667	CCl_4[e]	47
					1676, 1640	1658	KBr	48
(96)	$C(CH_3)_3$	H	H	OH	*1658*, 1653	1655	CCl_4	35
(97)	H	$C(CH_3)_3$	H	OH	1653	1653	CCl_4	35
(98)	H	H	CH_3	OH	*1667*, 1653	1660	CCl_4	35
(99)	H	CH_3	H	OH	1658	1658	CCl_4	35
(100)	CH_3	H	H	OH	1658	1658	CCl_4	35
(101)	H	H	CH_3	OCH_3	1669, *1653*	1661	CCl_4	35
(33)	H	CH_3	H	OCH_3	1681, *1653*	1667	CCl_4	35
(35)	CH_3	H	H	OCH_3	1683, *1656*	1669	CCl_4	35
(38)	H		H		1712 sh, 1660	1660	CCl_4	46
(39)		H	H		1686, 1643	1664	CCl_4	46
(102)	Cl		Cl		1670	1670	CCl_4	46
(103)	Cl			Cl	1680	1680	CCl_4	46
(104)	CN	CN	CN	CN	1698	1698	[f]	49
(105)	NO_2	CH_3	NO_2	CH_3	1677, 1639	1658	KJ	50

[a] The values printed in italics are those of the higher intensities, if indicated by the authors.
[b] The arithmetical average of the two values $\tilde{\nu}_{C=O}$ given.
[c] The arithmetical average of all $\tilde{\nu}_{C=O}$, weighted by their relative intensities.
[d] The tri-deuterated *p*-benzoquinone **86** has not been measured.
[e] Grating monochromator.
[f] Solvent not stated.

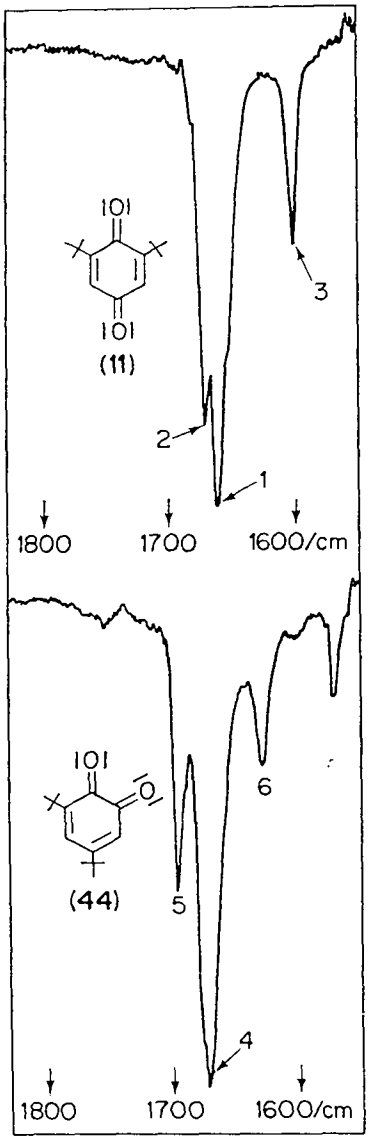


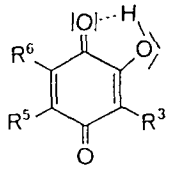
FIGURE 6. I.r.-spectra of **11** and **44** in the carbonyl region (CCl_4, grating monochromator; lines 1, 2, 4 and 5: $\tilde{\nu}_{C=O}$; lines 3 and 6: $\tilde{\nu}_{C=C}$).

are actually three absorptions (1690, 1663 and 1648 cm^{-1}) of comparable intensity. However, if the arithmetical average of the carbonyl absorptions ($\bar{\tilde{\nu}}_{C=O}$) weighted by their relative intensities is considered, all five quinones (**1**, **83–85** and **87**) show nearly the same value (ca. 1663 cm^{-1}), as would

be expected if Fermi resonance plays a role. For the other quinones in Table 8 the $\bar{\bar{\nu}}_{C=O}$ values are also given, although the intensities could not be taken into account.

In spite of the complexity of the substituent effects on the carbonyl vibration frequency some regularities exist. Generally, the carbonyl frequency is lowered with respect to the unsubstituted quinone **1** by electron-donating groups (alkyl, aryl, amino) and is raised by electron-withdrawing groups (halogen, CN, NO_2) (Table 8). However, the two main absorptions are not shifted by the same amount, so that sometimes they may coalesce into one absorption, or their intensities may become reversed. Therefore, the $\bar{\bar{\nu}}_{C=O}$ values may have some advantage when comparing i.r. spectra of quinones.

The effect of the methoxy group is not straightforward: 2-methoxybenzoquinone (**92**) absorbs in solution at higher wave numbers than benzoquinone **1** itself, considering the highest absorption bands or the $\bar{\bar{\nu}}_{C=O}$ values in both cases. The same is true for 2,6-dimethoxybenzoquinone (**32**), and for 2-methyl-6-methoxybenzoquinone (**35**). Only in the cases of multiple substitution (e.g. **94**) a weak shift of $\tilde{\nu}_{C=O}$ towards lower frequencies might be postulated from the observed values. However, these compounds have not been measured in solution. For hydroxybenzoquinones one might expect hydrogen bonding between the hydroxy and carbonyl groups:



This assumption is supported by the shift of the OH-stretching vibration to lower wave numbers. In the region of the carbonyl absorption no change is observed for monohydroxybenzoquinone **91** as compared to the parent benzoquinone **1**. However, there is a small shift in the pairs **2/99** and **2/100**. Larger shifts are found in polyhydroxyquinones and annelated quinones, especially of natural origin[8]. Moreover, in order to prove hydrogen bonding, one should compare the hydroxyquinone with the corresponding methoxyquinone. Then the shift $\Delta\bar{\bar{\nu}}_{C=O}$ towards lower wave numbers for the absorption at highest frequency is approximately 8 cm^{-1} per OH group (pairs **91/92**, **96/13**, **98/101**, **99/33**, **100/35**) with large deviations originating in the different types of substitution (see section III.B.1.c).

From their experimental data Kikot' and coworkers[46] calculated the average shifts ($\Delta\tilde{\nu}_{C=O}$) caused by various substituents in the carbonyl-stretch band of *p*-quinones relative to the parent compound **1** (Table 9).

TABLE 9. Average shifts ($\Delta\tilde{\nu}_{C=O}$) of *p*-benzoquinones[a] caused by various substituents X

X	F	Cl	Br	OC_6H_5	H	OC_2H_5	CH_3	N
$\Delta\tilde{\nu}_{C=O}$ (cm^{-1})	+8·5	+6·5	+4·5	+2·5	0	−2	−7	−6

[a] $\tilde{\nu}_{C=O}$ of **1** is taken as 1671 cm^{-1}. The increments refer to measurements in solution.

The influence of the substituents seems to be additive so that highly substituted quinones may undergo considerable lowering of their carbonyl frequency (e.g. duroquinone **6**: $\tilde{\nu}_{C=O}$ (calculated) = 1643 cm^{-1}, $\bar{\tilde{\nu}}_{C=O}$ (found) = 1646 cm^{-1}). The values of Table 9 should be regarded only as approximative: there may be deviations (e.g. **23**), especially for 2,6-isomers (e.g. **39**).

Josien and others[37,52] have found that $\tilde{\nu}_{C=O}$ of quinones is related linearly to the oxidation–reduction potentials of these compounds. The wave numbers versus potential diagrams show *positive* slopes. As in the case of the correlation of $\delta_{^{13}C=O}$ (n.m.r.) to polarographic half-wave potentials[6] (see section II.B.1), this dependence may be attributed mainly to the *inductive* effect of the substituents, which decreases the ionic character (B) of the C=O bond (A) for electronegative groups (NO_2, CN, halogen) and increases it in the case of electropositive groups (alkyl, NR_2).

(A) $\rangle C{=}\overline{O} \longleftrightarrow \rangle \overset{+}{C}{-}\overline{O}|^{-}$ (B)

The less ionic the character of the C=O bond, the higher the stretching frequency and the redox potential[6,37]. In the case of alkoxy, aryloxy and phenyl substituents resonance seems to cancel the inductive effect.

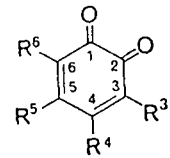
c. Influence of the position of substituents. An important problem in *p*-benzoquinone chemistry, which cannot be resolved by n.m.r. spectroscopy, is the distinction between the 2,5- and 2,6-isomers for a given pair of substituents. In the i.r. spectra both of solutions[46] and of the solids[43,46] the carbonyl-stretch frequencies of the isomers of disubstitution normally show the following order: $\bar{\tilde{\nu}}_{2,6} > \bar{\tilde{\nu}}_{2,5} > \bar{\tilde{\nu}}_{2,3}$ (e.g. **5**>**4**>**3**; **11**>**10**; **16**>**15**; **32**>**93**; **96**>**97**; **35**>**33**>**101**).

Furthermore, the 2,6- and 2,3-isomers usually show two (or three) bands, especially in KBr, whereas in the spectra of the 2,5-isomers only one symmetrical absorption is found[36]. However, exceptions are also known (two bands in **4**, **15**, **33**; one band in **5**, **7**, **100**).

2. 1,2-Benzoquinones

In the case of 1,2-benzoquinones (Figure 6 and Table 10) the absorption band of highest intensity (presumably the C=O stretching band) generally falls between 1645 and 1680 cm^{-1}. A weak absorption, which might correspond to the $\tilde{\nu}_{C=C}$ of *p*-benzoquinones, appears between 1620 and 1650 cm^{-1}. There is another weak band of unknown origin below 1600 cm^{-1}. The spectra of all *o*-benzoquinones investigated so far show an

TABLE 10. Carbonyl absorption of 1,2-benzoquinones



No.	R^6	R^5	R^4	R^3	$\tilde{\nu}_{C=O}{}^a$ (cm^{-1})	$\bar{\nu}_{C=O}{}^b$ (cm^{-1})	Solvent	Reference
(40)	H	H	H	H	1680, 1658	1669	Nujol	8
(106)	H	H	CH_3	CH_3	1675, 1646	1660	Nujol	8
(107)	*c*-C_6H_{11}	H	*c*-C_6H_{11}	H	1690, *1667*	1678	$CCl_4{}^c$	4
(42)	$C(CH_3)_3$	H	CH_3	H	1695, *1673*	1684	$CCl_4{}^c$	4
(43)	$C(CH_3)_3$	H	C_6H_5	H	1690, *1665*	1677	$CCl_4{}^c$	4
(44)	$C(CH_3)_3$	H	$C(CH_3)_3$	H	1695, *1670*	1682	$CCl_4{}^c$	4
(45)	$C(CH_3)_3$	H	$C(CH_3)_3$	C_6H_5	1683, *1661*	1672	$CHCl_3{}^c$	47
(46)	$C(CH_3)_3$	H	$C(CH_3)_3$	Cl	1695, *1680*	1687	$CCl_4{}^c$	47
(47)	$C(CH_3)_3$	H	$C(CH_3)_3$	Br	1694, *1678*	1686	$CHCl_3{}^c$	47
(48)	$C(CH_3)_3$	H	$C(CH_3)_3$	NO_2	1700, *1682*	1691	$CCl_4{}^c$	4

[a] The values printed in italics are those of the higher intensities, if indicated by the authors.
[b] The arithmetical average of the two values $\tilde{\nu}_{C=O}$ given.
[c] Grating monochromator.

absorption of medium intensity between 1675 and 1700 cm^{-1}, which is well separated from the main band (Figure 6, band 5)[1,53]. The influence of substituents seems to follow the same rules as in the *p*-series. Unfortunately, the i.r. data of only a few *o*-benzoquinones are known so far.

3. Distinction between o- and p-benzoquinones

Comparison of Tables 8 and 10 shows that the $\bar{\nu}$-values for *p*-quinones are located between 1640 and 1700 cm^{-1}, and those for *o*-quinones between 1660 and 1690 cm^{-1}. Though the *o*-quinones generally absorb

at higher wave numbers than the corresponding *p*-quinones, if the substituents are the same, there is no clear-cut range of $\tilde{\nu}_{C=O}$ or $\tilde{\nu}_{C=O}$ for each group of compounds. However, *o*-benzoquinones may be recognized by the well-separated band at the highest wave number[4,53]. Moreover, there are differences between both series of quinones in the weak absorption close to 1600 cm^{-1} (Figure 6).

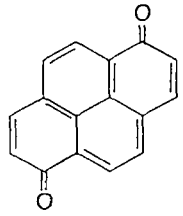
C. Condensed Quinones

The carbonyl frequencies of the *o*-series tend to be slightly higher than those of the *p*-series (Table 11), as was found for benzoquinones. However,

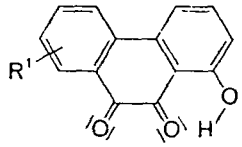
TABLE 11. Carbonyl absorption of some condensed quinones

No.	Compound	$\tilde{\nu}_{C=O}$ (cm^{-1})	Solvent	Reference
(49)	1,4-Naphthoquinone	1675	CCl_4	37
(66)	1,2-Naphthoquinone	1678, 1661	KBr	8
		1678	CCl_4	37
(73)	9,10-Anthraquinone	1675	Nujol	8
		1678	CCl_4	37
(77)	9,10-Phenanthraquinone	1684	CCl_4	37
(108)	1,2-Phenanthraquinone	1677	CCl_4	37
(109)	3,4-Phenanthraquinone	1668	CCl_4	37
(110)	5,12-Naphthacenequinone	1682	CCl_4	37
(111)	6,13-Pentacenequinone	1680	CCl_4	37
(112)	1,2-Benzanthra-9,10-quinone	1670	CCl_4	37
(113)	1,2,5,6-Dibenzanthra-9,10-quinone	1660	CCl_4	37

in both series of condensed quinones the frequency varies with the number and position of fused rings[37]. The carbonyl frequency is raised by the increase of fused rings in a quinonoid compound, as long as they are connected linearly (cf. **1**→**49**→**73**→**110/111**; **40**→**66**→**77**). The addition of fused benzene rings in an 'angular' way relative to one of the carbonyl groups decreases $\tilde{\nu}_{C=O}$ (cf. **73**→**112**→**113**; **66**→**109**). Quinones in which the C=O groups belong to different ring systems (extended quinones) have low C=O frequencies, e.g. 3,8-pyrenequinone (1640 cm^{-1})[54].



The effect of substituents on $\tilde{\nu}_{C=O}$ of condensed quinones follows the same rules as in the case of benzoquinones[37-39]. In some of the hydroxy compounds, especially in 1-hydroxy-9,10-phenanthraquinones and naphthazarin (**63**) considerable lowering of $\tilde{\nu}_{C=O}$ is observed (1639 and



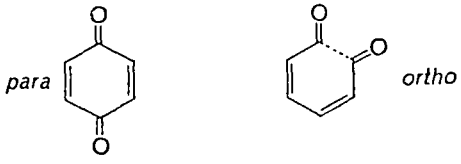
1623 cm^{-1}, respectively). According to Josien and coworkers[37] this effect is due mainly to resonance between two hybrid forms and not to normal hydrogen bonding (see also references 38 and 39):

For a compilation and discussion of i.r. data of naturally occurring fused quinones the reader is referred to the standard book of Thomson[8].

IV. U.v. SPECTRA OF QUINONES

A. General Remarks

p-Quinones contain a cross-conjugated π-system, whereas *o*-quinones may be considered as linear conjugated:



Therefore, considerable differences in the electron spectra of the two series are to be expected, and indeed can be detected even with the naked eye: *o*-quinones generally are dark red in colour while *p*-quinones tend to be yellow (see also Figure 7).

The charge-transfer absorption maxima of the molecular complexes of quinones with donor molecules offer additional possibilities of characterization in some cases[55]. Most u.v. spectra have been obtained in methanol, ethanol, hexane, cyclohexane, chloroform, CCl_4 or CH_3CN as solvents.

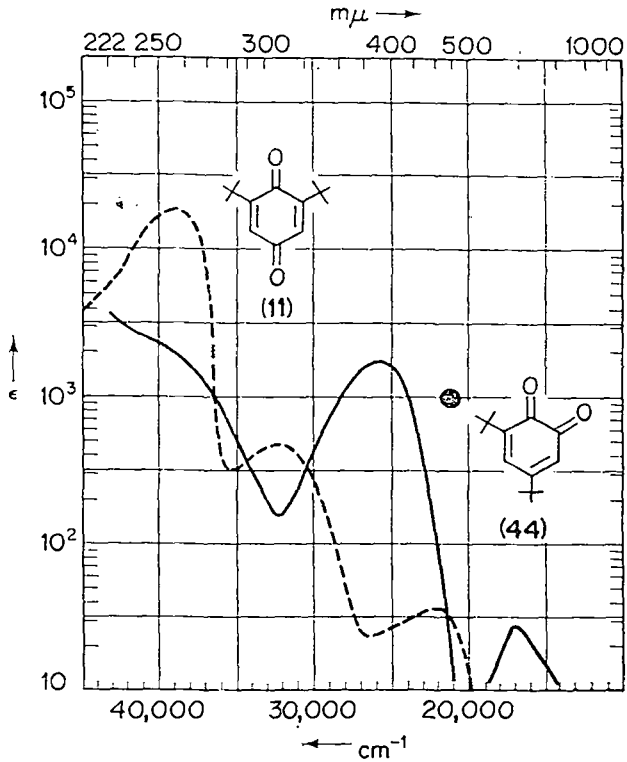


FIGURE 7. U.v.-spectra of **11** and **44** in cyclohexane.

Non-polar solvents are preferred for hydroxy-substituted quinones which otherwise would be ionized by the basic impurities nearly always present. The resulting 'alkali red-shifts' may lead to misinterpretation of the spectra, but, under controlled conditions in ethanol, can also be of diagnostic value (see section VI). For comparison of spectra obtained in different media the solvent shifts recorded by Flaig and coworkers[56] may be helpful.

B. Benzoquinones

1. 1,4-Benzoquinones

p-Benzoquinones *generally* cause three absorptions (Table 12): a band of strongest intensity (λ_{max} = 240–300 nm, $\log \varepsilon$ = 3·9–4·5), a medium band (285–440 nm, $\log \varepsilon$ = 2·4–3·2) and a weaker absorption in the visible region, λ_{max} = 420–460 nm ($\log \varepsilon$ = 1·2–2·1). These absorptions are attributed to singlet–singlet $\pi \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ [57,58], and $n \rightarrow \pi^*$ transitions[57,58], respectively. The very weak absorption of *p*-benzoquinone

1 at 535–540 nm is assumed to arise from $n \rightarrow \pi^*$ singlet–triplet transitions[57g,h]. The solvent shifts upon changing from non-polar to polar solvents are bathochromic for the $\pi \rightarrow \pi^*$ bands and hypsochromic for the $n \rightarrow \pi^*$ band[57b,h].

Only selected examples of substituted *p*-benzoquinones are collected in Table 12. For useful compilations of data and discussion of the corresponding spectra see Flaig[56], Thomson[8], Morton[58], Wallenfels[36] and others[57].

Mono-substitution of *p*-benzoquinone does not affect the first band and the visible band to any *significant* extent[57]. The second band, however, undergoes a more noticeable red-shift (Δ nm for Me: +27; Br: +50; MeO: +69; OH: +81 nm). Unfortunately, the spectra of only a few benzoquinones with electron-withdrawing substituents have been reported. Comparison of **11** and **118** reveals that the nitro group exerts no pronounced effect on the u.v. spectrum of *p*-benzoquinones (see section IV.B.2). The red-shift of the second band is less for the *second* substituent and then is greatest for 2,3-disubstituted derivatives. *Poly*-substitution results in further bathochromic displacement which in general cannot be reasonably calculated by additivity rules. Trommsdorff[57h], however, has found that the displacement of both $\pi \rightarrow \pi^*$ transitions for chlorine substitution is roughly proportional to the number of replaced hydrogen atoms. A quantitative treatment of the effect of substitution on frequencies and intensities of the absorption maxima has been given by Stevenson[57i] for the two $\pi \rightarrow \pi^*$ transitions. Since the $n \rightarrow \pi^*$ band is blue-shifted by substituents (see Table 12, compounds **2**, **3**, **5** and **18**) this absorption may be obscured by the red-shift of the second band.

2. 1,2-Benzoquinones

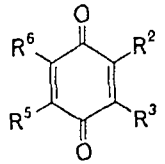
1,2-Benzoquinones also show three absorption bands (Table 13)[64–67]: a band of λ_{max} = 250–290 nm ($\log \varepsilon$ 2·6–4·1), a second band of somewhat lower intensity, λ_{max} = 370–470 nm ($\log \varepsilon$ 2·8–3·5) and a weak band in the visible region, λ_{max} = 500–580 nm ($\log \varepsilon$ 1·4–1·8). The absorptions probably can be attributed to $\pi \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ [67] transitions, respectively. As in *p*-benzoquinones, substitution causes red-shifts; the effect seems to be stronger for 3- than for 4-substitution, but the available data do not allow quantitative conclusions.

C. *Condensed Quinones*

1. General remarks

The spectra of condensed quinones naturally are more complex than those of benzoquinone itself, since both *quinonoid* and *benzenoid*

TABLE 12. U.v. spectra of *p*-benzoquinones



No.	R^6	R^5	R^3	R^2	Absorptions λ_{max}(nm) (log ε)			Solvent	Reference
(1)	H	H	H	H	246 (4·42)	288 (2·50)	439 (1·35)	$CHCl_3$	56
					242 (4·26)	285 sh (2·6)	434 (1·26)	Ethanol	56
							454 (1·22)		
							539 (−0·57)		57g
(2)	H	H	H	CH_3	249 (4·33)	315 (2·80)	436 (1·38)	$CHCl_3$	56
					255 sh (4·27)				
(3)	H	H	CH_3	CH_3	250 (4·26)	337 (3·05)	425 (1·55)	$CHCl_3$	56
					257 sh (4·20)				
(5)	CH_3	H	H	CH_3	255 (4·29)	319 (2·54)	429 (1·45)	$CHCl_3$	56
(18)	H	H	H	Cl	250 (4·35)	318 (3·10)	427 (1·25)[a]	Cyclohexane	59
(79)	Cl	Cl	Cl	Cl	287 (4·15)	362 (2·44)	[b]	CH_3OH	61a
					293 (4·41)	374 (2·37)	[b]	$CHCl_3$	57i

(115)	H	H	OCH_3	OCH_3	254 (4·17)	398 (3·17)	[b]	$CHCl_3$	56
(93)	H	OCH_3	H	OCH_3	278 (4·37) 284 (4·38)	370 (2·48)	[b]	$CHCl_3$	56
(32)	OCH_3	H	H	OCH_3	287 (4·28)	377 (2·78)	[b]	$CHCl_3$	56
(116)	H	OCH_3	OCH_3	OCH_3	291 (4·29)	418 (2·65)	[b]	$CHCl_3$	56
(94)	OCH_3	OCH_3	OCH_3	OCH_3	302 (4·23)	400 (2·42)	[b]	$CHCl_3$	56
(36)	H	NH_2	H	NH_2	336 (4·48)	488 (2·42)	[b]	DMSO	62
(117)	$N(CH_3)_2$	$N(CH_3)_2$	$N(CH_3)_2$	$N(CH_3)_2$	234 (4·25)	371 (3·94)	590 sh (2·50)[c]	*n*-Heptane[d]	36
(11)	$C(CH_3)_3$	H	H	$C(CH_3)_3$	254 (4·25)	318 (2·67)	446 (1·57)	CH_3OH	4
(118)	$C(CH_3)_3$	Br	NO_2	$C(CH_3)_3$	269 (3·94)	334 (2·80)	415 (2·02) 555 (1·70)	Cyclohexane	63

[a] Taken from Figure 3 of reference 60.
[b] Not stated in the reference quoted, since this maximum is partially obscured by the second maximum.
[c] This absorption seems not to be caused by $n \rightarrow \pi^*$ transition[36, 57].
[d] Taken from Figure 5 of reference 36.
sh = shoulder

No.	R^2	R^3	R^4	R^5	Absorptions λ_{max}(nm) (log ε)			Solvent	Reference
(40)	H	H	H	H		375 (3·23)	568 (1·48)	[a]	8
					254 (3·04)	368 (3·28)	587 (1·35)	Ether	68
(119)	H	H	CH_3	H	249 sh (3·32)	387 (3·23)	544 sh (1·48)	CH_2Cl_2	8
							570 (1·52)		
(120)	H	CH_3	H	CH_3	260 (3·19)	410 (3·20)	558 (1·66)	$CHCl_3$	64
(41)	H	CH_3	CH_3	H	260 (3·46)	400 (3·12)	555 (1·49)	$CHCl_3$	64
							570 (1·48)		
(121)	H	CH_3	CH_3	CH_3	265 (3·33)	425 (3·11)	545 (1·75)	$CHCl_3$	64
(82)	Cl	Cl	Cl	Cl	288 (3·49)	445 (3·28)	[b]	Cyclohexane	69
					250 (3·75)				
(122)	H	H	H	OCH_3	269 sh (2·66)	465 (3·26)	545 sh (1·78)	CH_2Cl_2	8
							575 sh (1·56)		
(123)	H	H	OCH_3	H	255 sh (3·75)	406 (3·21)	538 sh (1·66)	CH_2Cl_2	8
(124)	H	OCH_3	OCH_3	H	283 (4·09)	406 (2·82)	504 sh (1·60)	CH_2Cl_2	8
(125)	$C(CH_3)_3$	H	OCH_3	H	260 (3·8)[c]	398 (3·26)	545 (1·62)[c]	CCl_4	65
(44)	$C(CH_3)_3$	H	$C(CH_3)_3$	H	256 sh (3·50)	402 (3·28)	550 (1·77)	CH_3OH	4
(47)	$C(CH_3)_3$	H	$C(CH_3)_3$	Br	240 sh (3·79)	427 (3·30)	[b]	Cyclohexane	59
(48)	$C(CH_3)_3$	H	$C(CH_3)_3$	NO_2	253 (3·71)	393 (3·34)	[b]	CH_3OH	59

[a] Solvent not stated in reference.
[b] Absorption not measured or not observed.
[c] Taken from Figure 6, reference 65.

absorptions could be present according to n.m.r. data (see sections II A.3–6; II.B.3). Most naturally occurring and synthetic quinones (dyes) belong to this class of compounds. Only the spectra of the parent compounds (Tables 14 and 15) as well as general substituent effects will be discussed here. For further information several excellent reviews[8,70–74] should be consulted.

2. Compounds with *p*-quinonoid structures

In the spectrum of 1,4-*naphthoquinone* (**49**, Table 14) the bands at 245/251 and 335 nm are assigned to *benzenoid* $\pi \rightarrow \pi^*$ transitions[71,72]. These absorptions are shifted slightly by substituents (alkyl, OH, OMe, OAc, Cl) in the *quinonoid* ring (244–262; 333–341 nm)[72]. One of the *quinonoid* $\pi \rightarrow \pi^*$ transitions in **49** is found at 257 nm (shoulder, $\log \varepsilon$ 4·12) and is quite sensitive to substitution in the quinone ring (252–288 nm). A second quinonoid $\pi \rightarrow \pi^*$ transition in the 330–450 nm region is only of low intensity and, in the case of **49** and its 2-substituted derivatives, is not separated from the benzenoid band at 340 nm. Hydroxy-substitution shifts this quinonoid absorption bathochromically, so that it appears as an inflexion at 380 nm ($\log \varepsilon$ 2·87). In derivatives bearing methoxy and/or hydroxy groups in both positions 2 and 3 the red-shift of the quinonoid band is sufficient for complete separation from the benzenoid band (418–439 nm; $\log \varepsilon$ 3·12–3·17)[72]. The $n \rightarrow \pi^*$ absorption of the carbonyl groups in **49** is found at about 425 nm ($\log \varepsilon$ 1·51), but only in isooctane solution[72]. 1,4-Naphthoquinones substituted in the *benzene* ring frequently show coalescence of the benzenoid and quinonoid $\pi \rightarrow \pi^*$ transitions in the region of 240–290 nm and a red-shift of the characteristic benzenoid absorption close to 340 nm. Concerning the influence of the peri-hydroxy group and the alkali shift see references 8 and 72.

Although the 9,10-*anthraquinones* are important pigments, whose u.v. spectra are well investigated, the discussion will be restricted to some general features, since several surveys have been published[8,58,70,75–80]. Anthraquinone **73** itself (in ethanol) shows benzenoid $\pi \rightarrow \pi^*$ absorptions at 240–250 nm ($\log \varepsilon$ 4·5–4·7) and 332 nm ($\log \varepsilon$ 3·75), quinonoid $\pi \rightarrow \pi^*$ absorption at 260–270 nm ($\log \varepsilon$ 4·3)[8] and a long wavelength absorption near 405 nm ($\log \varepsilon$ 1·95), which might be assigned to a $n \rightarrow \pi^*$ transition[71].

Since in anthraquinone substituents can be introduced only in benzenoid rings an influence on the benzenoid $\pi \rightarrow \pi^*$ transitions would be expected. Indeed, electron-donating substituents in the 1-position (OH, OCH_3) cause a considerable red-shift in the visible region[8,73,77]. Surprisingly, however, some authors[8] assume that this red-shift does not involve the *benzenoid* absorptions at 320–330 nm but rather the anthraquinone

TABLE 14. U.V. spectra of linearly annelated 1,4-quinones

Compound	No.	Absorptions λ_{max}(nm) (log ε)					Solvent	Reference
		Benzenoid $\pi \rightarrow \pi^*$	Quinonoid $\pi \rightarrow \pi^*$	Quinonoid $\pi \rightarrow \pi^*$	Benzenoid $\pi \rightarrow \pi^*$	Quinonoid $n \rightarrow \pi^*$		
1,4-Benzoquinone	(1)	—	246 (4·42)	288 (2·50)	—	439 (1·35)	$CHCl_3$	56
1,4-Naphthoquinone	(49)	245 (4·34) 251 (4·37)	257 sh (4·12)	(340–450)[a]	335 (3·48)	425 (1·51)[b]	$CHCl_3$	72
9,10-Anthraquinone	(73)	243 (4·52) 252 (4·71)	263 (4·31) 272 (4·31)	(320–330)[d]	332 (3·75)	405 (1·95)[c]	Ethanol	8

[a] Normally obscured by the second benzenoid $\pi \rightarrow \pi^*$ transition.
[b] Found only in isooctane as solvent.
[c] Assignment tentative.
[d] Found only in hydroxy- or methoxy-substituted anthraquinones[66]; assignment tentative, see text.

TABLE 15. U.v. spectra of annelated 1,2-quinones

Compound	No.	Absorptions[a] λ_{max}(nm) (log ε)					Solvent	Reference
1,2-Benzoquinone	(40)		254 (3·04)		368 (3·28) q	587 (1·35) n	Ether	68
1,2-Naphthoquinone	(66)	249 (4·31)		337 (3·32) bz	400 (3·25) q	sh ca. 530 (ca. 1·7) n	CH_3OH	61b
9,10-Phenanthraquinone	(77)	256 (4·46)	265 (4·49)	322 (3·62) bz	410 (3·13) q	?	CH_3OH	61b

[a] Tentative assignments adopted by the present authors: bz = benzenoid $\pi \rightarrow \pi^*$ transition, q = quinonoid $\pi \rightarrow \pi^*$ transition, n = quinonoid $n \rightarrow \pi^*$ transition.

absorption at 400 nm. Some observations are not in agreement with this explanation and also a red-shift is not compatible with the $n \rightarrow \pi^*$ nature of the 400 nm transition. A preferred explanation similar to that first used by Moran[78] (see also reference 71) is that OH, NH_2[78], OCH_3 and $N(CH_3)_2$ shift the benzenoid band from 330 nm into or even beyond the region of the $n \rightarrow \pi^*$ transition (405 nm). At the same time one of the $\pi \rightarrow \pi^*$ absorptions of shorter wavelength migrates to the 330 nm area or, alternatively, a quinonoid $\pi \rightarrow \pi^*$ transition, originally masked in 9,10-anthraquinone (**73**) or its alkyl derivatives by the benzenoid 330 nm band, now becomes evident. For calculations of anthraquinone spectra using additivity rules see Scott[80] and other authors[70a].

3. Compounds with o-quinonoid structures

In 1,2-*naphthoquinone* **66** the benzenoid absorption at 250 nm is unchanged with respect to 1,4-naphthoquinone **49**. However, there are bands of medium intensity at 340 and 400 nm (benzenoid and quinonoid $\pi \rightarrow \pi^*$ transitions?) which are red-shifted with respect to 1,4-naphthoquinone. In non-polar solvents a weak absorption appears in the visible region > 500 nm[81] ($n \rightarrow \pi^*$ transition?)[67].

If one adopts the assignment of the absorptions of 9,10-*phenanthraquinone* **77** shown in Table 15, then there is good agreement with 1,2-naphthoquinone **66**[67].

V. IDENTIFICATION OF QUINONES BY POLAROGRAPHY AND E.s.r. SPECTROSCOPY

A. Introduction

Contrary to the spectroscopic methods described so far, in polarography and e.s.r. spectroscopy the quinones are reduced to semiquinones, either during (polarography) or before (e.s.r. spectroscopy) the measurement. By this, the sample is destroyed; however, the requirement on material is very low.

B. Polarography of Quinones

It was the merit of Conant and Fieser[82a, b] to introduce electrochemical methods into organic chemistry, measuring the standard redox potentials of quinones by potential controlled titration. Now it is usual to determine the standard redox potentials via the pH-dependence of the polarographic half-wave potentials of quinones[82c]. Since there is a parallelism between the first half-wave potential and the standard redox potential in most cases[83, 84a], we will not separately discuss the structural influences on these two quantities.

Although numerous workers have reported on the polarography of quinones, it is still difficult to collate a table of comparable data. Various authors use different solvents, concentrations, electrolytes, cell arrangements and reference electrodes. Therefore, we selected the data in Table 16 from the work of Peover[83] and supplemented them by our own measurements[6] which were run under comparable conditions.

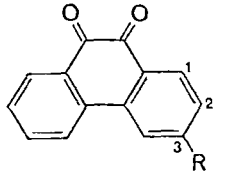
TABLE 16. Half-wave potentials of quinones in acetonitrile at 25° [a]

Quinone	No.	E_1	E_2	Reference
p-*Benzoquinones*				
Unsubstituted	(1)	−0·51	−1·14	83
Methyl	(2)	−0·58	−1·10	83
2,5-Dimethyl	(4)	−0·67	−1·27	83
2,6-Dimethyl	(5)	−0·66	−1·14	6
Trimethyl	(88)	−0·75	−1·35	83
Tetramethyl	(6)	−0·84	−1·45	83
2,6-Diisopropyl	(7)	−0·70	−1·26	6
2,5-Di-*t*-butyl	(10)	−0·73	−1·24	83
2,6-Di-*t*-butyl	(11)	−0·74	−1·35	6
2,6-Diaziridino	(39)	−0·73	−1·23	6
Phenyl	(14)	−0·50	−1·03	83
2,5-Diphenyl	(15)	−0·49	−1·05	6
Tetraphenyl	(17)	−0·57	−1·25	6
2-Chloro	(18)	−0·34	−0·92	83
2,5-Dichloro	(19)	−0·18	−0·81	83
2,6-Dichloro	(20)	−0·18	−0·81	83
Tetrachloro	(79)	+0·01	−0·71	83
Tetrafluoro	(89)	−0·04	−0·82	83
Tetrabromo	(90)	0·00	−0·72	83
2,3-Dichloro-5,6-dicyano	(80)	+0·51	−0·30	83
o-*Benzoquinones*				
Unsubstituted	(40)	−0·31	−0·90	83
4,6-Di-*t*-butyl	(44)	−0·58	−0·83	6
4,6-Di-*t*-butyl-3-phenyl	(45)	−0·51	−0·77	6
4,6-Di-*t*-butyl-3-chloro	(46)	−0·33	−0·62	6
4,6-Di-*t*-butyl-3-bromo	(47)	−0·37	−0·86	6
4,6-Di-*t*-butyl-3-nitro	(48)	−0·21	−0·48	6
Condensed quinones				
1,4-Naphthoquinone	(49)	−0·71	−1·25	83
1,2-Naphthoquinone	(66)	−0·56	−1·02	83
9,10-Anthraquinone	(73)	−0·94	−1·45	83
9,10-Phenanthraquinone	(77)	−0·66	−1·22	83

[a] Values in volts versus SCE, supporting electrolyte 0·1N NEt_4ClO_4.

We wish to make only a few comments on the results of polarography in quinone chemistry. An examination of Table 16 shows that electron-releasing substituents (alkyl and amino groups) lower the first half-wave potential with respect to the unsubstituted *p*-benzoquinone **1** whereas electron-withdrawing substituents (halogen and cyano groups) increase it. The same observation holds for condensed quinones. Phenyl groups seem to have no great disturbing effect on the half-wave potential[83]. It is remarkable that *o*-benzoquinones have *higher* (less negative) half-wave potentials than their *p*-isomers. This is also true for the pairs 1,4-/1,2-naphthoquinone and anthraquinone/phenanthraquinone.

Several attempts have been made to quantify the influence of substituents towards half-wave or redox potentials[82c,85]. Zuman[85] showed that a linear correlation exists for polarographic half-wave potentials and substituent constants taken from a modified Hammett equation. This correlation fits well in the case of monosubstituted benzo- and naphthoquinones. However, the half-wave potentials of polysubstituted quinones are lower than the values predicted by simple additivity of the substituent constants. Steric effects seem to be responsible for the deviations[85,86]. For seven 3-substituted phenanthraquinones the substituent effects on $E_{\frac{1}{2}}$



R = H, CH_3, C_2H_5, $CH(CH_3)_2$, $C(CH_3)_3$, CN, $COCH_3$, Br

could be correlated with the Hammett σ constants with a correlation coefficient of more than 0·995[87]. On the basis of a similar correlation of σ-values with redox potentials, Flaig and coworkers[82c] suggest that in some quinones the carbon atoms might be the reaction centres during polarography. The slope of the linear regression line obtained by plotting ^{13}C chemical shifts of the carbonyl groups versus polarographic values[6], however, shows that Flaig's assumption is not stringent.

Linear correlations also exist for i.r. absorption frequencies of the carbonyl groups of quinones and their polarographic values[82c]. However, the correlations are only good, if quinones with similar substituents are assorted.

Since in the polarographic reduction of a quinone one electron occupies the lowest empty orbital, a relation between polarography and u.v. spectroscopy of quinones is also expected. This prediction is correct and has been shown by several authors for the u.v. absorption of quinones[82c]

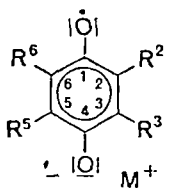
and for their charge-transfer complexes with electron-donor compounds[88] as well. Finally, several attempts are known to correlate polarographic half-wave potentials with the calculated energy of the lowest unoccupied orbital of quinones[83] and with the resonance energy obtained from MO theory[89-91].

In summary, polarography of quinones may be used as a powerful tool to determine quantitative relationships between their oxidative behaviour and several molecular properties.

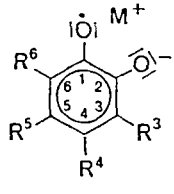
C. *E.s.r. Spectra of Semiquinones*

1. General remarks

p- and *o*-Semiquinones are relatively stable free-radical intermediates in the reduction of *p*- and *o*-quinones and in the oxidation of dihydroxybenzenes. Thus, their e.s.r. spectra may be used to identify and characterize the corresponding quinones. However, to obtain a well-resolved hyperfine structure, special experimental techniques are necessary[92].



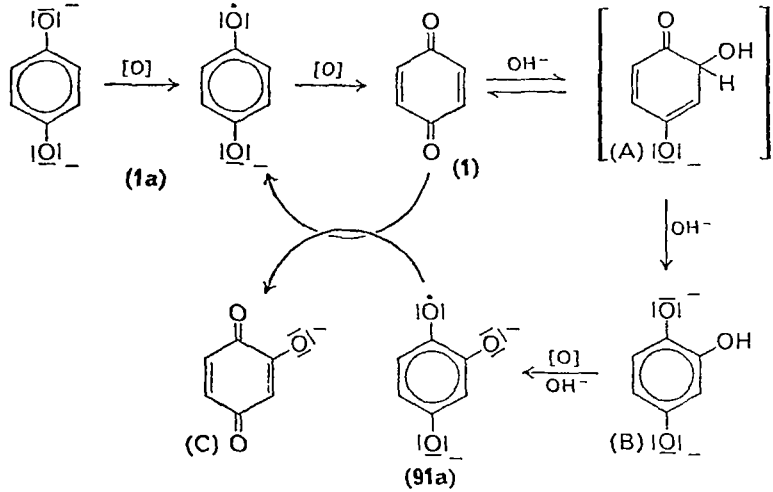
p-Semiquinone



o-Semiquinone

Ascorbic acid, zinc dust or sodium dithionite (in polar acidic solvents)[93], glucose or sodium dithionite[94] (in basic solvents) and alkali metals or amalgams (in ethereal solvents)[95] are used as reducing agents. The most universal method is the electrolytic reduction of the corresponding quinones. According to our own experience, mixing stoicheiometric amounts of the quinone and alkali metal salt of the corresponding dihydroxybenzene is a valuable method, especially for the isolation of stable *o*-semiquinones[95]. Reduction of quinones may be carried out in a flow system which is superior to the normal procedure if the semiquinones are unstable. It should be pointed out that even 'stable' semiquinones decompose readily, so that under stationary conditions the e.s.r. spectra of secondary products are frequently observed[96]. Under controlled conditions, these products may be of the hydroxy-semiquinone type[96a, b, d]. They are formed in *oxidizing* medium by coupled redox

processes, starting with either dihydroxybenzene or quinone. In the case of *p*-semiquinones the reaction proceeds in the following manner[96b]:

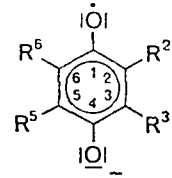


Addition of OH^- to the quinone **1** (A) leads to the trihydroxybenzene anion (B) which, on oxidation by air, produces the anion of the hydroxy-semiquinone **91a**. Depending on the concentration of **1** and of the alkali used, an electron transfer from **91a** to **1** may occur with the formation of equilibrium amounts of semiquinone **1a** and the anion (C) of hydroxy-quinone **91**[96b]. Since hydroxy-semiquinones show characteristic e.s.r. spectra (see Table 17), the reactions with alkali may be of diagnostic value for the parent quinones.

A serious problem is presented by the dependence of the coupling constants *a* on the polarity of the solvent[97] (Table 17). The changes in *a* may be in the order of several hundred mG for the protons and amount to several G in the case of other nuclei (e.g. **1a**)[94, 97–100]. These effects are caused by a change in the electronegative behaviour of the oxygen atoms and hence in the spin-density distribution of the odd electron within the molecule. The attraction between the protons of the solvent and the semi-quinone molecule may attain the strength of a stable complex by which the hyperfine structure is altered considerably[92]. Neutral semiquinones[114, 115] and (in *acidic* medium) even semiquinone cations[93, 116] may be formed. Due to restricted rotation of the hydroxy group, the e.s.r. spectra are frequently temperature-dependent[115, 117].

In *basic* medium ion-pair or even triple-ion formation between the semiquinone anion and the metal cation is observed[118]. This effect may complicate the spectrum by metal hyperfine splitting, in particular, if

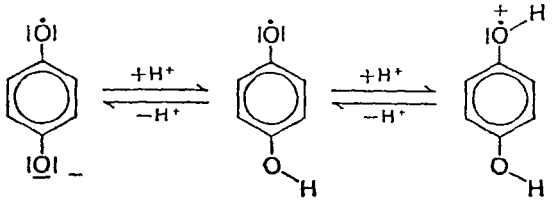
TABLE 17. E.s.r. spectra of *p*-semibenzoquinones



No.[a]	R^6	R^5	R^3	R^2	*g*-Value	Solvent and notes	Reference
	a (Gauss)						
(1a)	H	H	H	H			
	2·42	2·42	2·42	2·42[b, c]	—	DMSO[d]	94, 97, 98
	2·37	2·37	2·37	2·37[e]	2·00466	*f, g*	94, 101–104
	2·32	2·32	2·32	2·32	—	*d, h*	84
(2a)	H	H	H	CH_3			
	2·44	2·70	1·95	1·83	—	DMSO[d]	97
	2·56	2·72	1·98	1·90	—	*d, h*	84, 105
(3a)	H	H	CH_3	CH_3			
	2·59	2·59	1·71	1·71	—	*f, g*	106
(4a)	H	CH_3	H	CH_3			
	1·84	2·25	1·84	2·25	—	*f, g*	106
	2·00	2·24	2·00	2·24	—	*d, h*	84
(5a)	CH_3	H	H	CH_3			
	2·13	1·89	1·89	2·13	—	*f, g*	106
(88a)	H	CH_3	CH_3	CH_3			
	1·97	2·24	1·77	1·88	—	*f, g*	106
(6a)	CH_3	CH_3	CH_3	CH_3			
	1·90	1·90	1·90	1·90	2·0055	*f, g*	106
(10a)	H	$C(CH_3)_3$	H	$C(CH_3)_3$			
	2·07	0·06	2·07	0·06	—	*f, i*	107
	2·32	—	2·32	—	—	*d, h*	84
(18a)	H	H	H	Cl			
	2·21	2·45	2·21	—	2·0058	*f, g*	106
(19a)	H	Cl	H	Cl			
	2·03	—	2·03	—	—	*f, g*	106
(20a)	Cl	H	H	Cl			
	—	2·32	2·32	—	—	*f, g*	106
(89a)	F	F	F	F			
	4·14	4·14	4·14	4·14	2·0048	*f, g*	108
	3·95	3·95	3·95	3·95	—	Dimethoxy-ethane[d]	109a
(93a)	H	OCH_3	H	OCH_3			
	0·30	1·05	0·30	1·05	2·00454	*d, j*	96c, 110
(32a)	OCH_3	H	H	OCH_3			
	0·77	1·50	1·50	0·77	—	*d, k*	111
(126a)	H	$C_6H_5CH_2S$	H	$C_6H_5CH_2S$			
	0·91	0·79	0·91	0·79	—	Ethanol	112
(127a)	H	H	H	$P^+(C_6H_5)_3$			
	1·70	1·55	5·80	4·70	—	CH_2Cl_2	113
(91a)	H	H	H	OH[l]			
	1·34	4·98	0·60	—	—	*m*	96b

[a] Number of the parent quinone plus index *a* refers to the corresponding semiquinone.
[b] $a_{^{17}O} = 9{\cdot}46$ G, reference 98[a].
[c] $a_{^{13}C\text{-}1} = 2{\cdot}13$; $a_{^{13}C\text{-}2} < 0{\cdot}65$ G.
[d] Prepared by reduction of the quinone.
[e] $a_{^{13}C\text{-}1} = 0{\cdot}40$; $a_{^{13}C\text{-}2} = 0{\cdot}59$ G.
[f] Prepared by oxidation of the corresponding dihydroxybenzene.
[g] Alkaline alcohol.
[h] $CH_3CN/(C_4H_9)_4NClO_4$.
[i] Alkaline methanol or ethanol/water 50 : 50.
[j] Pyridine/2N KOH 50 : 50.
[k] 50% *t*-Butyl alcohol in water/0·1M NaOH.
[l] Dissociated in alkaline solution.
[m] Aqueous alkali; see text.

equilibria between pairs of different solvation exist. In addition, considerable solvent and temperature dependence of the e.s.r. spectra may result[118b,119].

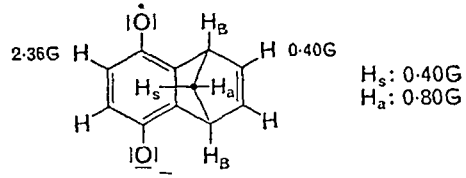


2. Hyperfine structure constants

a. p-*Semibenzoquinones.* The e.s.r. spectrum of the unsubstituted *p*-semibenzoquinone **1a** consists of five lines with the relative intensities 1 : 4 : 6 : 4 : 1. This pattern is caused by the coupling of the free electron to four equivalent protons, as expected on the basis of symmetry, if the odd electron is delocalized all over the ring. Moreover, using the ^{13}C- and ^{1}H-couplings, the complete spin-density distribution for **1a** (1,2-dimethoxyethane solution) could be satisfactorily computed[94] in accordance with MO calculations[92,94].

$$\rho_O = 17{\cdot}21\%, \quad \rho_{C_{1,4}} = 14{\cdot}87\%, \quad \rho_{C_{2,3,5,6}} = 8{\cdot}96\%$$

The value for ρ_O is in good agreement with the observed ^{17}O-coupling[98]. Substitution of alkyl groups or halogen atoms for one or more hydrogen atoms in **1a** does not basically alter the coupling constants of the ring protons, although the spectra are more complex because of a slight non-equivalence of the remaining protons. In addition, the substituents themselves may cause further splitting (e.g. β-protons of alkyl groups). In the case of alkyl groups small coupling with γ-protons (e.g. **10a**) may be observed under good resolution[107]. In bicyclic semiquinones, γ-proton couplings occasionally exceed the values found for *t*-butyl groups, whereas the bridge-head protons H_B do not show any splitting[120,121]. Here e.s.r. may be a valuable tool for the assignment of the *syn* or *anti* structure of a proton (H_s or H_a).



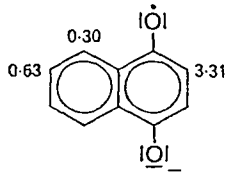
The coupling constants of fluorine in semiquinones are nearly twice the value obtained for protons[108,109]. The values of $a_{^{17}O}$ (enrichment) and of $a_{^{13}C}$ (natural abundance) in several fluorinated semiquinones were

found to be similar to those reported for unsubstituted semiquinones[109a]. However, the proton coupling constants observed in *partially* fluorinated semiquinones indicate that changes of up to 40% in spin density occur in the ring upon introduction of fluorine.

Semibenzoquinones with alkoxy or mercapto groups (Table 17) show stronger deviations of the *a*-values (spin-density distribution) as compared with the unsubstituted **1a**. The same holds for the phosphorus-containing compound **127a** which may be regarded as a zwitterion and not as a true semiquinone. There is also coupling of the free electron either with the heteroatom (e.g. phosphorus) or with the hydrogen atoms of alkyl groups connected to heteroatoms (e.g. oxygen and sulphur), giving insight into the mechanisms of the transfer of free-spin density to substituent atoms[96c, 110, 112, 122–124]. Contrary to the results based on chemical reactivity, it was concluded[112] that the S atom is essentially electron-releasing in its behaviour towards the aromatic ring. Therefore, it is not necessary to invoke the use of acceptor 3*d* oribtals by the S atom.

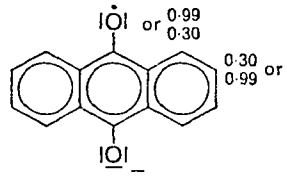
b. o-*Semibenzoquinones.* The e.s.r. spectrum of the *o*-semibenzoquinone **40a** shows a triplet of triplets with the relative intensity 1 : 2 : 1 ($a_I \simeq 3{\cdot}6$ G; $a_{II} \simeq 1{\cdot}0$ G). It must be concluded that two pairs of equivalent protons are present; from reasons of symmetry these are protons 3/6 and 4/5. On the basis of spin-density calculations[125] and by comparison of **40a** with specifically alkylated compounds (**41a**, **42a**, **44a**, **128a–130a**) it is seen that the higher value a_I belongs to the pair of hydrogen atoms 4/5. The relative amount of a_I/a_{II} is not altered considerably by the introduction of substituents, although the absolute values of the coupling constants within the pairs of protons H_3 and H_6 or H_4 and H_5, respectively, may change noticeably.

c. Condensed semiquinones. The spectra of condensed semiquinones are complex and have not been assigned unambiguously in all cases[93, 94, 97, 102, 126–132]. The coupling constants (in G) of the semiquinones of 1,4-naphthoquinone, 9,10-anthraquinone and 9,10-phenanthraquinone are given below:



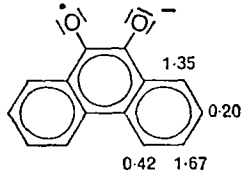
(49a)

DMSO, electrochemical reduction[97, 132]



(73a)

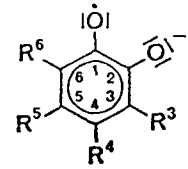
DMSO, electrochemical reduction[97]



(77a)

DMF, electrochemical reduction[126]

TABLE 18. E.s.r. spectra of *o*-semibenzoquinones

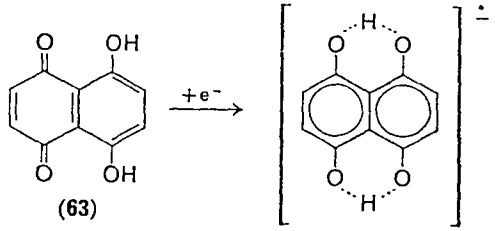


No.[a]	R^6	R^5	R^4	R^3	*g*-Value	Solvent and notes	Reference
	a (Gauss)						
(40a)	H	H	H	H			
	0·95	3·65	3·65	0·95	2·00441	[b, c]	101, 102, 125
	1·16	3·55	3·55	1·16	—	DMF[b]	106b
	1·02	3·58	3·58	1·02	—	DMF[d]	95
	1·50	3·30	3·30	1·50	—	[d, e]	84b
(119a)	H	H	CH_3	H			
	1·4	3·7	4·4	0·7	—	DMF/H_2O[b]	96a
(41a)	H	CH_3	CH_3	H			
	0·5	4·2	4·2	0·5	—	DMF[d]	95
(128a)	*n*-Propyl	H	H	*n*-Propyl			
	[f]	3·26	3·26	[f]	—	DMF[d]	95
(129a)	H	H	$C(CH_3)_3$	H			
	1·17	3·80	0·32	0·3	—	[b, g]	107
	1·40	3·90	0·30	1·16	—	[d, e]	84
(42a)	$C(CH_3)_3$	H	CH_3	H			
	< 0·03	2·50	5·35	0·35	—	[b, g]	107
(44a)	$C(CH_3)_3$	H	$C(CH_3)_3$	H			
	< 0·03	2·67	0·31	0·3	—	[b, g]	107
	—	3·20	0·32	0·6	—	[d, e]	84a
(130a)	CH_3	H	$C(CH_3)_3$	H			
	0·3	3·07	0·29	0·3	—	[b, g]	107
(131a)	H	H	COOH	H			
	1·4	3·3	—	0·9	—	DMF/H_2O[b]	96a

[a] Number of the parent *o*-quinone plus index *a* refers to the corresponding semiquinone.
[b] Prepared by oxidation of the dihydroxybenzene.
[c] Alkaline alcohol.
[d] Prepared by reduction of the quinone.
[e] $CH_3CN/(C_4H_9)_4NClO_4$.
[f] Additional unresolved hyperfine splitting.
[g] Alkaline methanol/water 50 : 50.

Comparison of the spin-density distribution in **73a** and **77a** to that of the unsubstituted semiquinones is impossible, since the quinone ring carbon atoms are 'blind', i.e. they bear no hydrogen atoms. However, in 1,4-naphthoquinone **49a**, the coupling constant for proton 2, and hence the spin density at carbon atom 2, is considerably higher than in the case of *p*-benzosemiquinone **1a**.

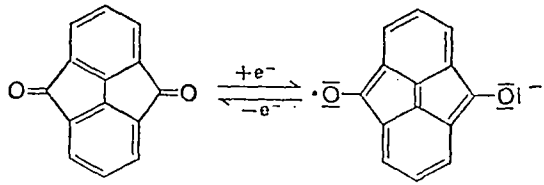
A series of hydroxy-substituted condensed semiquinones showing intramolecular hydrogen-bonding was investigated by Fraenkel and coworkers[131,133]. In the case of the semiquinone of naphthazarin **63** one single coupling constant for the ring protons (2·41 G, electrochemical



(63) (63a)

reduction) and for the OH-protons (0·52 G) was observed as one would expect for a completely symmetric molecule (with respect to the e.s.r. time scale). Hyperfine splitting of the ring protons and spin-density distribution are altered by deuteration of the OH-groups[133].

The e.s.r. spectra of annulene-semiquinones have attracted considerable interest. Thus, it was derived from the *a*-values and MO calculations that the semiquinone radical anion of dibenzo[c.d, g.h]pentaleno-4,8-quinone (A) should be described as a perturbed planar antiaromatic [12]annulene system, rather than as a [14]annulene, which could have been expected according to the formula (B)[134]. Concerning semiquinones derived from 1,6-bridged [10]annulenes see reference 135.



(A) (B)

3. *g*-Values

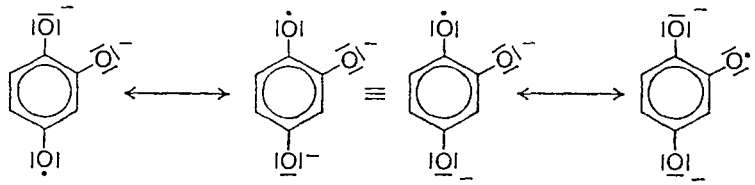
The *g*-values of semiquinones are more dependent on substituents than on the *o*- or *p*-structure. However, too few data are available to derive rules for the characterization of semiquinones. Moreover, the *g*-values depend on the solvent[136]. This phenomenon is interpreted qualitatively by assuming different solvations of the carbonyl oxygen atom of semiquinones by different solvents.

4. Characterization of quinones

According to the previous paragraphs characteristic sets of splitting parameters exist for protons in *p*- and *o*-semibenzoquinones. Therefore, characterization of a quinone or distinction between the *p*- and *o*-series, in principle, should be possible from the e.s.r. spectra, produced by

reduction of the quinone in question. This holds especially for the *o*-semiquinone system, showing a typical ratio of the hyperfine splitting parameters: $H_{4,5} : H_{3,6} \simeq 3 : 1$ (up to 10 : 1). In the *p*-semiquinone series the a_H-values are not changed significantly by alkyl or halogen substitution. However, in the case of other substituents one should anticipate considerable deviations. In the *p*-series the strong solvent effects on the *a*-values must also be taken into account.

For hydroxy-semiquinones in alkaline medium a spin-density distribution somewhere *between* that found for *p*- and *o*-semibenzoquinones is expected, according to the following mesomerism:



p-Semiquinone *o*-Semiquinone

However, the investigation of several hydroxy-semiquinones (e.g. **91a**, Table 17) shows[96b] that the spin-density distribution corresponds more to that in *o*-semibenzoquinones.

VI. CHEMICAL METHODS

A. General Remarks

The structure of quinones may be investigated by chemical degradation and derivatization processes[8]. Since these methods are often not selective and need large amounts of material which cannot be recovered, they are inferior to the physical methods discussed above. However, colour reactions are still valuable in controlling the purification of natural materials. Colours are formed or changed in reduction and addition reactions of quinones and in the formation of hydroxyquinone anions. These reactions are quickly performed in small samples and, moreover, can be combined with modern spectroscopic methods and separation techniques[137].

B. Colour Tests for Quinones

1. Anion formation from hydroxyquinones

Hydroxyquinones produce deep red to violet colours in alkaline solution[8] (Table 19; see also section IV under 'alkali shift'), or on treatment with methanolic magnesium acetate[138].

TABLE 19. Colour of hydroxyquinones in alkaline ethanol

Quinone	No.	Colour	$\lambda_{max}^{EtOH/OH^-}$ (nm)
1,4-*Benzoquinones*			
2,5-Dihydroxy	(114)	Bluish-red	505
2-Hydroxy-5-methyl	(99)	Red	493
2-Hydroxy-3,5-di-*t*-butyl	(132)	Violet-red	528[a]
2-Hydroxy-3,5,6-tri-chloro	(133)	Violet	542[a]
1,4-*Naphthoquinones*			
2-Hydroxy	(54)	Orange	459
5-Hydroxy	(61)	Violet	538
6-Hydroxy	(134)	Violet-red	520
2,3-Dihydroxy	(135)	Blue	650
2,5-Dihydroxy	(136)	Violet-red	490
3,5-Dihydroxy	(137)	Red	435
5,6-Dihydroxy	(138)	Blue	571
5,7-Dihydroxy	(139)	Violet	542
5,8-Dihydroxy	(63)	Blue	655
9,10-*Anthraquinones*			
1-Hydroxy	(140)	Red	500
2-Hydroxy	(141)	Orange-red	478
1,2-Dihydroxy	(74)	Violet-blue	576
1,3-Dihydroxy	(142)	Red	485
1,4-Dihydroxy	(143)	Violet	560
1,8-Dihydroxy	(144)	Red	513
1,4,5,8-Tetrahydroxy	(145)	Blue	630

[a] Reference 59, all other values reference 8.

Intense colours also appear on contact of hydroxyquinone spots on paper and thin-layer chromatograms with ammonia[137]. The hydroxyquinone anions responsible for these colours are sometimes formed as secondary products during the reaction of substituted quinones with alkali (e.g. 2,3-diallylnaphthoquinone[139], chloranil 79[140]).

2. Reduction and re-oxidation processes

Quinones are easily reduced to colourless or faintly coloured 'leuco' compounds by neutral or alkaline sodium dithionite, alkali borohydride, catalytic hydrogen, zinc and other reducing agents. Three tests are founded on the reduction reaction:

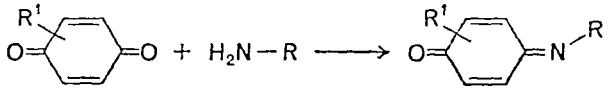
(i) The quinone is reduced, and the leuco compound is directly detected by its deep colour *in alkaline medium* (polycyclic quinones, but not naphtho- and benzoquinones)[141].

(ii) Reoxidation of the leuco compound by shaking with air restores the original colour[137] (non-hydroxylated benzoquinones and naphthoquinones react slowly).

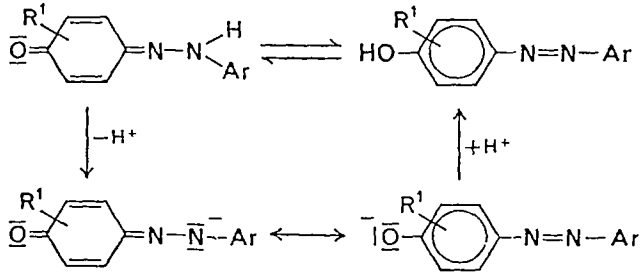
(iii) Reduction is accomplished by a second leuco compound, which in turn is oxidized to form a highly coloured oxidation product (leuco methylene blue spray for the detection of benzoquinones and naphthoquinones on paper and thin-layer chromatograms)[142].

3. Reactions with amines

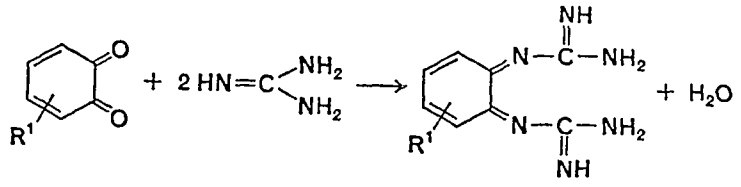
Quinones would be expected to react with amines by a normal condensation reaction to form quinone imines:



However, there are limitations for such a reaction with respect to the structure of the quinone and of the amine. *p*-Quinones with one hindered carbonyl group and aromatic anilines combine to highly coloured quinonemonoanils (R = aromatic group), which may be used for the identification of the quinone and of the amine as well. Mixtures are easily detected by thin-layer chromatography[143], however, in most cases long reaction times are necessary. For analytical use the reaction of quinones with arylhydrazines to form arylhydrazones (R = NH—Ar)[144] is recommended.



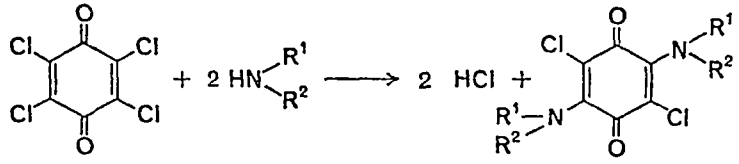
The hydrazones tautomerize into the corresponding hydroxyazoarenes; the equilibrium finally attained depends on the substituents in both rings and on the polarity of the solvent[145]. In alkaline solution only the mesomeric anion exists, and this is responsible for the deep colour observed[137, 144]. *o*-Quinones are often characterized by preparing the quinoxalines[146], but the reaction with guanidine carbonate may be useful with micro-gram amounts[147]. In this reaction a colourless diguanylquinone (A) is primarily formed, which on heating produces a coloured condensation product[147]. Deep colours are also formed by the reaction of



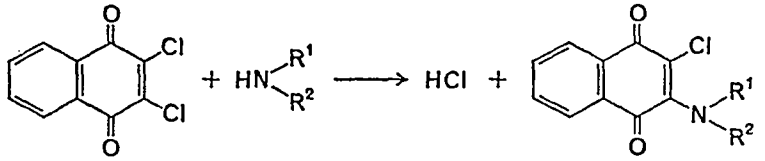
(A)

quinones with other amines, as with ethylenediamine[148] in neutral or alkaline solutions, and with indole[148], *N,N'*-diphenylbenzidine[149] or 3,4-dimethoxyaniline[150] in acidic solutions. It seems that only in the case of the indole reagent, leading to indolyl-quinones, is the chemistry of the reaction well established[151]. Formation of colour with ethylenediamine is specific for quinones and quinone-forming materials, except for anthraquinones and amino-substituted quinones. Compounds reacting with *N,N'*-diphenylbenzidine are 1,2-quinones, 1,4-benzoquinone, but also nitroso derivatives, chloramines, chlorimines and ether peroxides. The 3,4-dimethoxyaniline reagent is recommended by the authors[150] to be specific for inner-ring *o*-quinones (e.g. 9,10-phenanthraquinone (77), 9,10-retene-quinone, 5,6-chrysene-quinone).

Halogenoquinones react with primary and secondary amines as follows[36,152]:



(79)

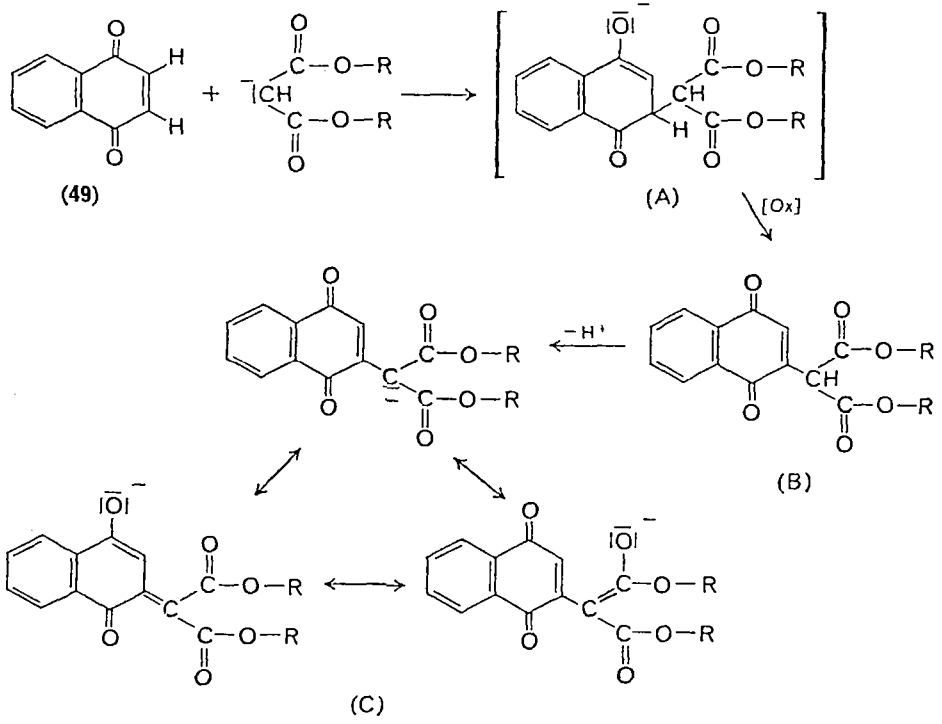


The resulting aminoquinones are well crystallized, showing sharp melting points and colours ranging from orange to violet and may be used for the characterization of halogenoquinones, as well as of primary and secondary amines.

4. Reactions with C—H acids

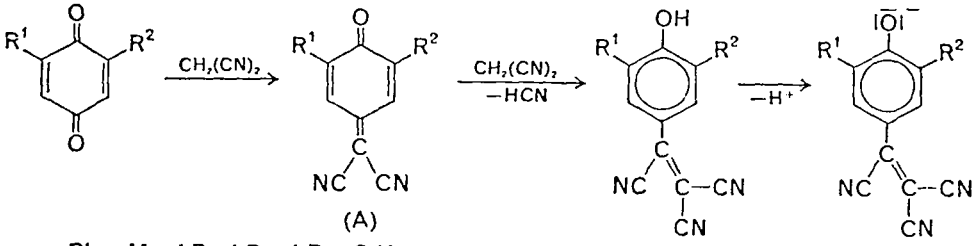
Non-hydroxylated quinones *having a free quinonoid position* can be detected by their reaction with active methylene compounds[153] (e.g.

acetoacetic ester, malononitrile, nitromethane[154], etc.) and ammonia in alcoholic solutions. This test was originally discovered and developed by Kesting[153]. Later it was also reported by Craven[155], without reference to the work of Kesting, and by Jeffreys[156], who cited neither Kesting's nor Craven's publications. Jeffreys showed that the anion of the reactive methylene group undergoes Michael addition (A). Subsequent oxidation produces a new quinone (B):



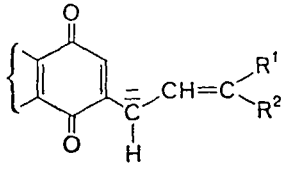
The blue-green or violet-blue colour which appears (Kesting test) is produced by the resonance stabilized anion (C) of this quinone (B). The test is also useful for spraying spots of quinones on thin-layer plates[137]. On treatment with acid, the primary adducts readily undergo ring-closure to benzofurans. The mechanism just outlined has been supported, in principle, by King and Newall[157] (see also Junek and coworkers[158]). In the presence of a hydroxy group the Kesting test may fail. On the other hand, an actual *free quinonoid* position is not essential, since alkoxy and halogen groups can be displaced by the reagent[159]. It should be pointed out, however, that phenanthraquinones or sterically hindered *p*-benzoquinones (e.g. 2,6-dialkyl-*p*-benzoquinones) also undergo condensation

at one of the carbonyl groups, at least when malononitrile is used as CH-active compound[160,161]. In this case dicyanoquinonemethides (A) are formed, which, in the presence of an excess of malononitrile (and piperidine as catalyst), give tetracyanovinylphenols (B)[161], whose anions (C) are highly coloured. For this reason, the reaction may be useful for the detection of 2,6-di-substituted *p*-benzoquinones.



R^1 = Me, *i*-Pr, *t*-Bu, *t*-Bu, C_6H_5
R^2 = Me, *i*-Pr, *t*-Bu, Cl, C_6H_5

The mesomeric anion of the Kesting test is similar to the anion produced by allyl-quinones in the Dam–Karrer test[162]. This latter anion is supposed



to be responsible for a transient blue-violet colour obtained when allyl-quinones are treated with alcoholic alkali[139]. The most widely used colour tests discussed in this section are summarized in Table 20.

VII. QUANTITATIVE DETERMINATION OF QUINONES

A. Physical Methods

In principle, all physical methods discussed in this review, as well as mass spectroscopy, are suitable for the quantitative determination of quinones. In practice, however, only n.m.r. spectroscopy, u.v. spectroscopy and polarography play a role since in these cases the measurements are rapid and easy and the evaluation is straightforward.

In proton-n.m.r. spectroscopy the peak areas of the quinone signals are determined quantitatively relative to a standard of known concentration, generally using an electronic integrator[163]. In ^{13}C-n.m.r., however, this procedure may be hampered by the extremely different relaxation times of individual carbon atoms and by the Overhauser

test	acetate in ethanol	quinones (Table 19); 2,3-diallylnaphthoquinones, chloroquinones	
Hydroquinone anion test	Reducing agents (KBH_4) + alkali in DMFA	Unsubstituted polycyclic *p*-quinones (e.g. **73**, ***110*** and ***111***) Not: naphtho- or benzoquinones	141
Reoxidation test	Reducing agents, air, alkali	All types of quinones; non-hydroxylated benzo- and naphthoquinones react slowly	8, 137
Methylene blue test	Leucomethylene blue (ethanol/acetic acid)	Coenzyme Q_{10}	142
Hydrazone test	2,4-Dinitrophenylhydrazine, alkali or ammonia	Benzoquinones and naphthoquinones (e.g. **1**, **49** and **50**)	137, 144
Ethylenediamine test	Ethylenediamine in water or petroleum ether	Quinones, hydroquinones, quinhydrones of the *p*-structure (e.g. **1**); naphthoquinones (e.g. **49** and **66**) Not: anthraquinones or amino-substituted quinones	148
Indole test	Indole/HCl in ethanol	*p*- and *o*-Quinones (e.g. **1**, **49**, **66** and **73**)	148
Kesting test	Active methylene compound (malononitrile, nitromethane, malonate, acetoacetate, benzoylacetate, cyanoacetate, acetylacetone, etc.) + base (NH_3, RONa, KOH) in ethanol	*p*- and *o*-Quinones with a free quinonoid position (e.g. **1**, **2**, **49**, **66** and **92**); alkoxy- and chloroquinones (e.g. **79**) without a free quinonoid position Not: anthraquinone **73** or phenanthraquinone **77**	137, 153–159
Dam–Karrer test	Alcoholic alkali (NaOR)	Allylquinones (vitamin K)	137, 162

effect, if proton decoupling is used[164]. In u.v. spectroscopy the Lambert–Beer law is used for the determination of the concentration of a quinone, if the molar extinction coefficient ε is known[165].

The importance of the visible region of the electron absorption spectrum for the determination of quinones is obvious (see sections IV and VI.B). In polarography the height of the plateau (diffusion current) of the first wave in the reduction of a quinone is proportional to the concentration of the quinone[166].

B. Chemical Methods

1. General remarks

Most of the reactions discussed in section VI may be used for the quantitative determination of quinones, by measuring either the oxidation equivalent or the intensity of a specific colour. Some examples may further illustrate these procedures.

2. Volumetric determinations

The easiest way of determination of a quinone seems to be the titration of the iodine liberated in acetic acid/NaJ with $Na_2S_2O_3$. According to our own experience, this procedure works well only in special cases (e.g. **1** and **79**) under carefully controlled conditions. Catalytic hydrogenation may be used instead.

Reduction of a quinone can also be effected by excess $NaBH_4$ in ethanol/NaOH in the presence of H_3BO_3, the excess of $NaBH_4$ being decomposed with 2N H_2SO_4 and the liberated H_2 measured[167]; Ti(III) is recommended by some authors[168]. In this case, the excess of reducing agent is detected either by polarography or visually by titration with $NH_4Fe(SO_4)_2$ and NH_4SCN in H_2SO_4 or HCl. Quinones can be detected volumetrically by reduction with hydrazine sulphate in $NaHCO_3$ or with hydroxylamine hydrochloride in Na_2HPO_4 to evolve N_2[169].

3. Colorimetric determinations

Coenzyme Q_{10} was analysed by comparing the change in absorption at $\lambda^{EtOH}_{275\,m\mu}$ of a Q_{10} preparation upon reduction with $NaBH_4$ (formation of the hydroquinone)[142]. Quantitative colorimetric determinations were also carried out with the following tests already described in section VI.B: 3,4-dimethoxyaniline[150]; 2,4-dinitrophenylhydrazine[144] (determination of 2-methyl-1,4-naphthoquinone **50** in urine). Finally, the Kesting reaction was employed to determine the quinone contents of drugs[170].

VIII. DISTINCTION BETWEEN *p*- AND *o*-QUINONES

According to the discussions in sections II–V it seems possible to distinguish between the *ortho*- and *para*-quinonoid structures by using a combination of physical methods, especially if the data of both species are available for a given substitution type.

The first indication for the structure may be taken from colour tests and from the u.v. spectrum since *o*-quinones absorb at higher wavelengths and with lower overall extinctions than the corresponding *p*-quinones. This statement holds even for the annelated quinones of Tables 14 and 15 as far as the quinonoid $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions are considered. For benzoquinones the second and especially the third band (section IV) may be used for the assignment of a compound to the *ortho* or *para* series. The unequivocal assignment, however, is possible only if substituents which absorb in the characteristic area are absent. This is also true for i.r. investigations. In this case position and intensity of the absorptions near 6 μ, recorded under good resolution, should be used as a criterion. *o*-Benzoquinones may be recognized by the well-separated carbonyl band at 1680–1700 cm^{-1}. However, it is advisable to assign the structure on the basis of the spectra of several similar compounds.

In favourable cases the ^{1}H-n.m.r. spectrum may be used in addition, especially in cases of a distinct regularity of substitution. Thus, unsymmetrical *o*-quinones are easily distinguished from symmetrical *o*- and *p*-quinones. The distinction between the latter, however, is difficult. ^{13}C.m.r. provides a convenient tool for the recognition of *o*-quinones. The usual range for the signals of the carbonyl carbon atoms of *p*-quinones is 180–190 p.p.m., whereas the carbonyl groups of *ortho* quinones show up at fields higher than 180 p.p.m. (TMS).

Since *o*-quinones normally give distinctly higher redox- or half-wave potentials and reveal pronounced tendency towards formation of a $[M+2]^{+\cdot}$ peak when compared with *p*-quinones, polarography and mass spectrometry (Chapter 5) are also useful tools to elucidate structural problems in quinone chemistry. In the case of low-substituted benzoquinones e.s.r. spectra of the corresponding semiquinones (section V.C.4) may be helpful, but care has to be taken, because of the solvent and temperature dependence of the spectra and the high possibility of measuring secondary and tertiary radicals.

As an example for the combined use of spectroscopic methods, the elucidation of the constitution of quinones of the vitamin K type and ubiquinone is illustrative[16,171]. ^{1}H-n.m.r. permitted the detection of the nature of the substituents whereas u.v. and i.r. spectra distinguished

between the positions on the quinone ring; the K_2 homologues were identified by X-ray diffraction.

Finally, it should be noted that chemical derivatization and degradation may also be erroneous. Quinoxaline formation, as an example, occurs not only with *o*-quinones, but also with some *p*-quinones[146]. In most cases, however, clear-cut results are obtained by a synoptic evaluation of all available spectroscopic data.

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The Chemistry of the quinonoid compounds
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CHAPTER 5

Mass spectra of quinones

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I. INTRODUCTION

The mass spectra of 1,4-[1] and 1,2-benzoquinone[2] reproduced in Figures 1 and 2, respectively, show two characteristic features of this class of compounds, namely (i) the stepwise loss of two molecules of carbon monoxide, which is a general observation in all the quinones, and (ii) the formation of peaks with two mass units higher than the molecular weight in the case of *ortho*-quinones and also in *para*-quinones having high redox potential.

The structure of the $[M-CO]^{+\bullet}$ and $[M-2\,CO]^{+\bullet}$ ions* will be dealt with before going into the appearance of the analytically important [M+2] peaks. This will be followed by a description of the mass spectra of benzo-, naphtho- and anthraquinones with special reference to the influence of substituents on the electron-impact-induced fragmentation.

Mass spectral studies of quinones are widely done in the field of natural products[3], because of the advantage that minute amounts of substance are sufficient for identification and structure elucidation.

* The symbols and abbreviations used in this article are those recommended in the journal *Organic Mass Spectrometry*, **2**, 249 (1969).

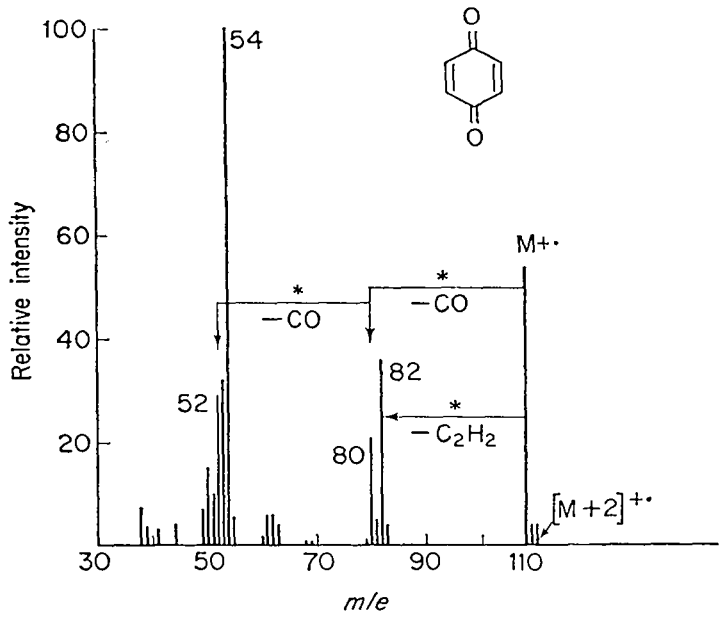


FIGURE 1. Mass spectrum of 1,4-benzoquinone.

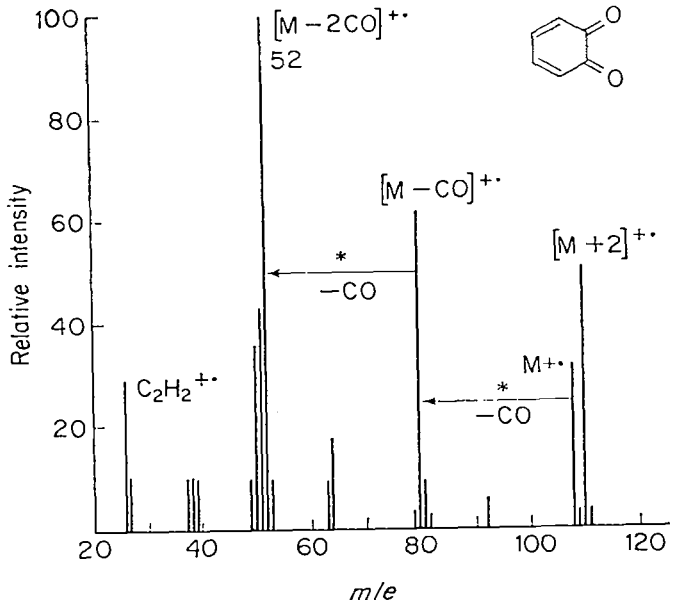
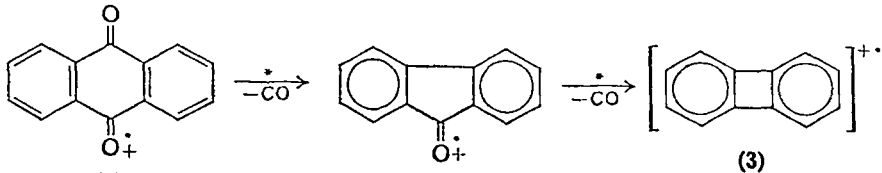


FIGURE 2. Mass spectrum of 1,2-benzoquinone.

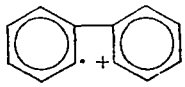
II. THE STRUCTURE OF $[M-CO]^{+\cdot}$ AND $[M-2\,CO]^{+\cdot}$ IONS

The structure of $[M-CO]^{+\cdot}$ and $[M-2\,CO]^{+\cdot}$ ions of quinones was first studied by Beynon and coworkers[4] with anthraquinone **1** (Figure 9) as an example. The authors described the $[M-CO]^{+\cdot}$ ion and the $[M-2\,CO]^{+\cdot}$ ion as fluorenone radical cation **2** and biphenylene radical cation **3**, respectively.



(1) (2) (3)

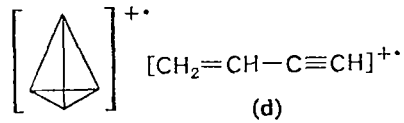
This interpretation would mean that every CO ejection should be accompanied by the formation of a new bond; however, successive elimination of two CO molecules may only prove the formation of one new bond, since the $[M-2\,CO]^{+\cdot}$ ion can also be represented with structure **3a**



(3a)

In the unsubstituted *para*-benzoquinone[1] the product of this decarbonylation process, $C_4H_4^{+\cdot}$ (*m/e* 52), is usually represented as ionized cyclobutadiene (**a**)[5].

(a) (b)

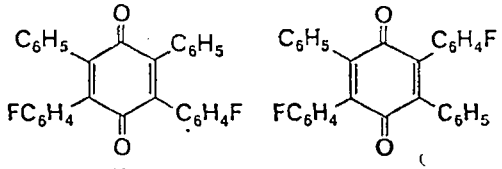


(c) (d)

The other alternative structures for $C_4H_4^{+\cdot}$ are the open species (**b**), the ionized tetrahedran (**c**) and the vinylacetylene ion radical (**d**) which can arise through a hydrogen shift*.

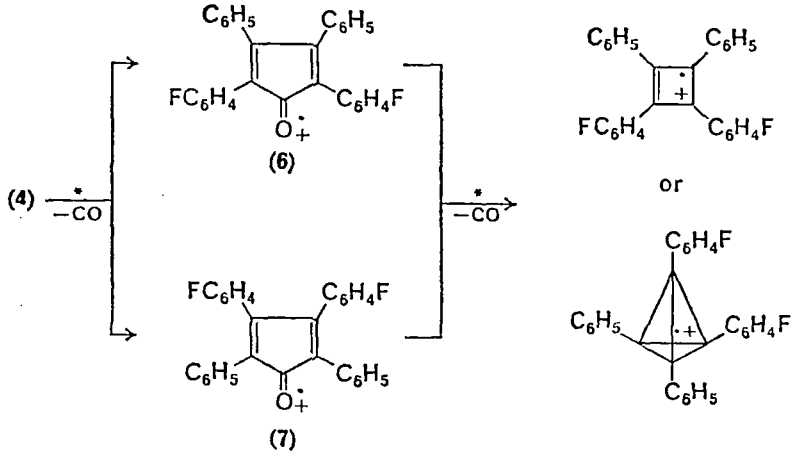
* For the formation of vinylacetylene in the thermolysis of benzoquinone see reference 6.

The structures of $[M-CO]^{+\cdot}$ and $[M-2\,CO]^{+\cdot}$ ions were investigated in an elegant study by Elwood and Bursey[7], using *p*-fluoro-substituted tetraphenylbenzoquinones **4** and **5**.



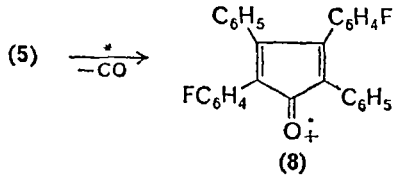
(4) **(5)**

The successive loss of two CO molecules from **4** results in a $[M-2\,CO]^{+\cdot}$ ion which decomposes further into unfluorinated, monofluorinated and difluorinated diphenylacetylene. The intensities of the corresponding metastable transitions lie in the ratio of 1 : 3·1 : 0·87. An almost similar ratio for the metastable peaks was observed in the decay of the $[M-CO]^{+\cdot}$ ion of the isomeric tetracyclones **6** and **7**[8]. This tends to show that **4**, after splitting off the first CO molecule, forms **6** and **7** which produce the same common $[C_4Ar_4]^{+\cdot}$ ion. From what is described so far, it is to be concluded that the C_4Ar_4 fragment must have a closed structure, since no two identical open structures $[C_4Ar_4]^{+\cdot}$ may be produced from both **6** and **7**. This closed structure must be either a cyclobutadiene or a tetrahedran.



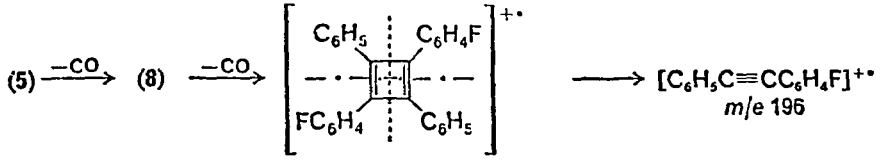
The quinone **5** after the expulsion of two CO molecules gives a C_4Ar_4 fragment which likewise decomposes further into diphenylacetylene as well as monofluoro- and difluorodiphenylacetylene. The intensities of the accompanying metastable peaks are, however, in the ratio 1 : 4·8 : 0·84.

A similar ratio of metastable peaks is found in the decomposition of the $[M-CO]^{+\cdot}$ ion obtained from **8**.

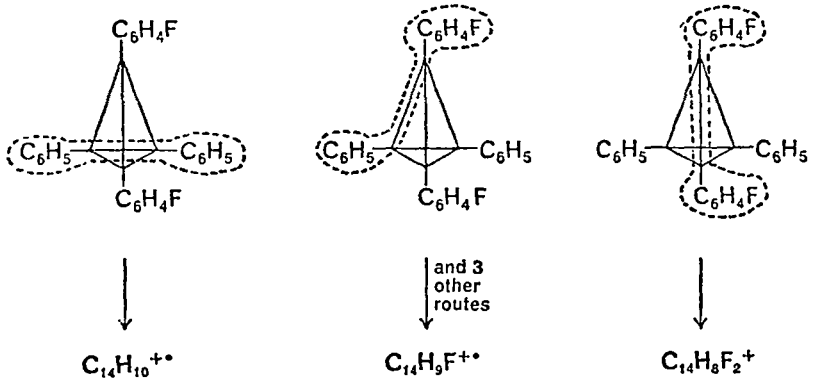


(8)

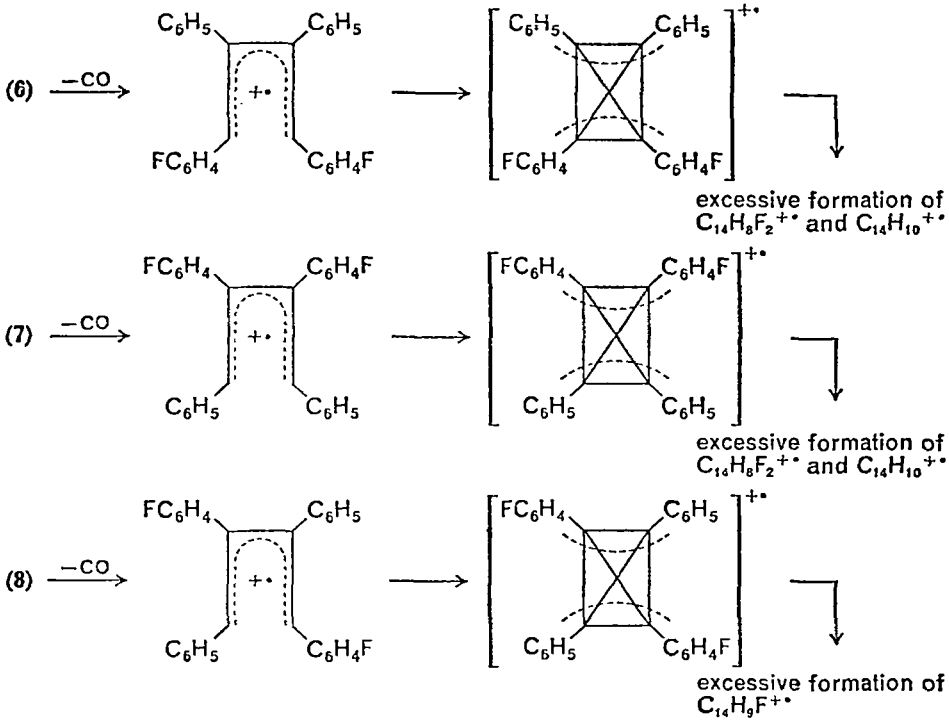
Should the $[M-2\,CO]^{+\cdot}$ ion from benzoquinones or the $[M-CO]^{+\cdot}$ ion of cyclopentadienones possess a cyclobutadiene structure, then from the $[C_4Ar_4]^{+\cdot}$ ion of **5** and **8** only a single acetylene, namely monofluorodiphenylacetylene (*m/e* 196), should result.



On the other hand, a tetrahedran structure permits the formation of all three diphenylacetylenes mentioned above. This model demands an



intensity ratio of 1 : 4 : 1, and the slight divergence between the experimental and the theoretically predicted results indicates either a distorted tetrahedran structure or some admixture of other structures. The last possibility is improbable because of the independence of the experimentally found ratio on temperature and electron energy. The discrepancy can be explained on the basis of a tetrahedran with unequal bond lengths as suggested by Bursey and Elwood[8].



The experimental results so far discussed are in conformity with a cyclopentadienone structure for the $[M-CO]^{+\bullet}$ ion and a distorted tetrahedran structure* for the $[M-2\,CO]^{+\bullet}$ ion derived from tetraphenylbenzoquinone. These results can without doubt be extended to other arylated quinones. It should, however, be considered, that the introduction of other substituents might consequently lead to the formation of different structures.

III. THE [M+2] PEAK

Quinones with high redox potential are reduced partially by the residual moisture present in the inlet system and ionization chamber[10-14]. When water is additionally introduced, it causes an increase in the intensity of the [M+2] peak[14]. Replacement of water adsorbed in the inlet system and ion source with D_2O leads to the appearance of [M+3] and [M+4] peaks[10-14]. An increase in the partial pressure of quinone diminishes the intensity of the [M+2] peak[14]. The maximum intensity of the $[M+2]^{+\bullet}$

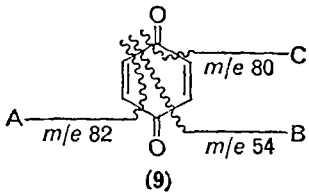
* A further study on the structure of $[C_4Ar_4]^{+\bullet}$ ions which supports these findings can be found in reference 9.

ion peak is often attained only after a long stay[11] in the inlet system (up to 60 min).

Table 1 shows that the formation of $[M+2]^{+\bullet}$ ions is more pronounced in *ortho*-quinones, which possess a considerably higher redox potential than the *para*-isomers. However, no simple relationship exists between the redox potential and the intensity of the $[M+2]^{+\bullet}$ ion peaks[13,14]. The mass spectra of more than thirty 1,2-naphthoquinones[11,13] known so far contain [M+2] peaks with similar intensities to those of the molecular ion peaks. The appearance of [M+2] peaks has been suggested[13] to differentiate 1,2-naphthoquinones from their 1,4-isomers. The presence of intense [M+2] peaks has also been noted in 2,6-naphthoquinone[15], dimeric 1,4-naphthoquinones[16], phenanthraquinone[15], diphenoquinones[14] and stilbene quinones[14].

IV. BENZOQUINONES

The *para*-benzoquinones generally give an intense molecular ion. Besides the expulsion of two CO molecules the elimination of alkynes and fission into two halves determines the fragmentation pattern[17]. The figure below shows the above behaviour for the parent compound **9**.

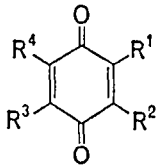
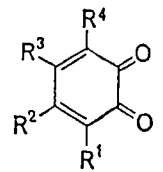


(9)

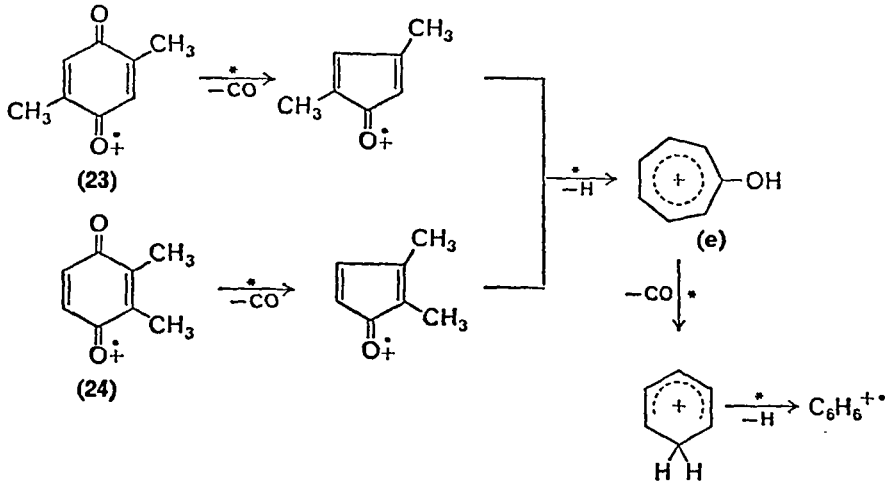
With the unsymmetrically substituted quinones fragmentation by path A leads exclusively to the elimination of alkynes with higher molecular weight[17]. For example, 2,3-dimethyl-1,4-benzoquinone gives an intensive peak at *m/e* 82 ($M^{+\bullet}-CH_3C{\equiv}CCH_3$) and 2,3,5-trimethyl-1,4-benzoquinone at *m/e* 96 ($M^{+\bullet}-CH_3C{\equiv}CCH_3$). The less-substituted alkyne (acetylene or propyne) is not eliminated in these cases. For the fragmentation pattern B, again the ejection of the more highly substituted neutral part is favoured. The corresponding metastable transitions show that in most cases this process comprises two steps, the elimination of an alkyne followed by CO.

The $[M-CO]^{+\bullet}$ ion of *para*-benzoquinones carrying two or more methyl substituents is stabilized through the loss of a radical leading to an ion with an even number of electrons. In the case of dimethyl derivatives the elimination of a hydrogen atom dominates. The ion so

TABLE 1. Relative intensities of the $M^{+\bullet}$ and $[M+2]^{+\bullet}$ ions of *ortho*- and *para*-quinones (related to the base peak = 100)

	Compound	$M^{+\bullet}$	$[M+2]^{+\bullet}$	Reference
	**(9)** $R^1 = R^2 = R^3 = R^4 = H$	100	12	12, 14
	(10) $R^1 = CH_3$, $R^2 = R^3 = R^4 = H$	100	7	12
	(11) $R^1 = OH$, $R^2 = R^3 = R^4 = H$	100	3	12
	(12) $R^1 = R^4 = OCH_3$, $R^2 = R^3 = H$	40	2	12
	(13) $R^1 = R^2 = R^3 = R^4 = Cl$	100	1	12
	(14) $R^1 = R^2 = R^3 = R^4 = D$	76	12	14
	(15) $R^1 = R^4 = t$-Bu, $R^2 = R^3 = H$	77	6	14
	**(16)** $R^1 = R^2 = R^3 = R^4 = H$	32	52	2
	(17) $R^1 = R^3 = R^4 = H$, $R^2 = CH_3$	100	92	11
	(18) $R^1 = R^3 = t$-Bu, $R^2 = R^4 = H$	5	37	14
	(19) $R^1 = R^3 = t$-Bu, $R^2 = H$, $R^4 = Br$	0	14	14
	(20) $R^1 = R^3 = t$-Bu, $R^2 = H$, $R^4 = NO_2$	0	33	14
	(21) $R^1 = R^3 = R^4 = H$, $R^2 = SCH_3$	2	100	11
	(22) $R^1 = R^2 = R^3 = R^4 = Cl$	15	4	14

formed is formulated as hydroxytropylium (e). This is supported by the subsequent decomposition of e which is exactly analogous to the fragmentation of the hydroxytropylium ion in the spectrum of benzyl alcohol[18].



The $[M-CO]^{+\cdot}$ ion of tetramethyl-1,4-benzoquinone (25)[17] (Figure 3) loses preferentially a methyl radical whereby the base peak appears at *m/e* 121. This fragment is similarly interpreted as a methyl-hydroxytropylium-ion (f) which disintegrates further into a stable $C_7H_7^+$ ion.

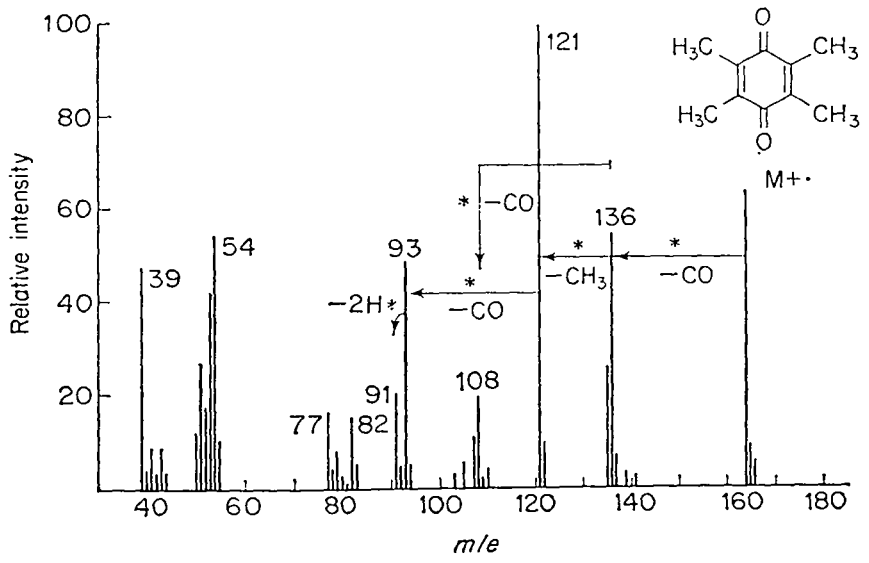
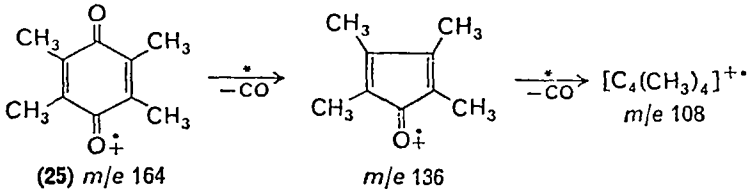
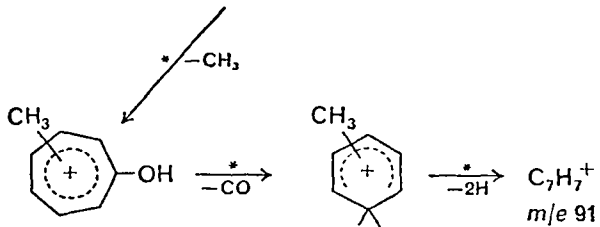


FIGURE 3. Mass spectrum of tetramethyl-1,4-benzoquinone.

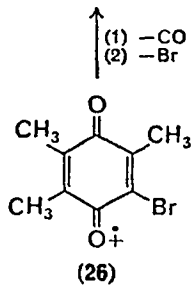
The same ion at *m/e* 121 is formed from trimethylbromo-1,4-benzoquinone (**26**)[17] through the elimination of CO and bromine.



(**25**) *m/e* 164 *m/e* 136

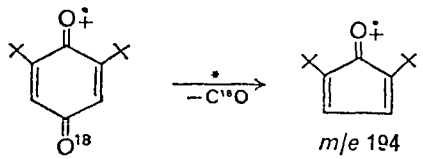


(**f**), *m/e* 121 *m/e* 93



(**26**)

The fragmentation of 2,6-di-*t*-butyl-1,4-benzoquinone (**15**)[14] is dominated by the breakdown of the *t*-butyl group, whereby paths A and B (formula **9**) are suppressed to a large extent. Studies with the ^{18}O-labelled compound **15a**[14] show that the unhindered CO group is eliminated first.

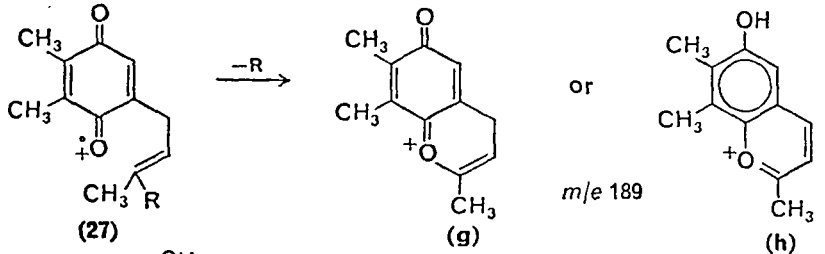


(**15a**), *m/e* 222 *m/e* 194

Mass spectrometry was found to be a powerful tool in the structure elucidation of plastoquinones, **27**[10], which play an important role in

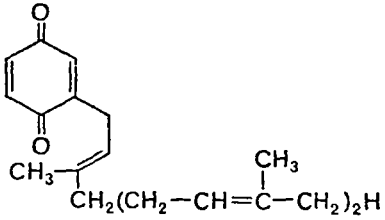
electron-transfer in chloroplasts. A series of plastoquinones investigated gave in each case a base peak at *m/e* 189 ($C_{12}H_{13}O_2$)[10,19,20].

The appearance of the same base peak in all cases shows that the 2,3-dimethyl-1,4-benzoquinone nucleus is always present and the differences are due only to the structure and length of the isoprenoid side-chain R. Through the breaking of R a stable pyrylium ion is formed (**g** and/or **h**). The behaviour of ubiquinones[21] (**28**) is reported to be similar.



(27) (g) (h)

$R = (CH_2-CH=\overset{CH_3}{\overset{|}{C}}-CH_2)_nH$



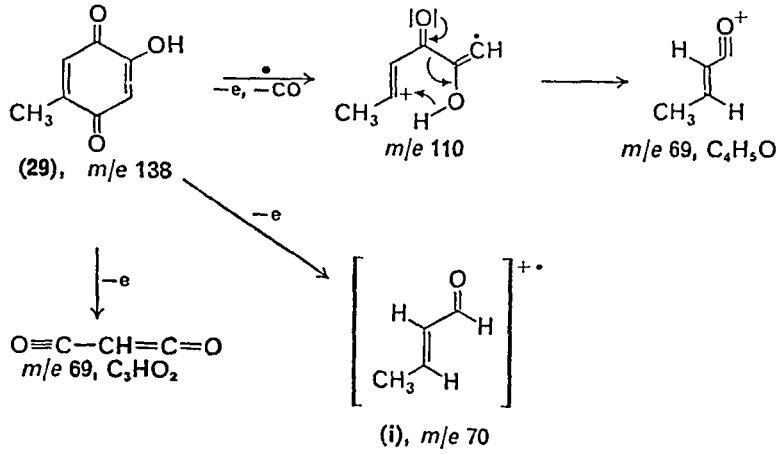
(28)

In the cases of hydroxy-1,4-benzoquinones[17] the breaking of the 1,2- and 4,5-bonds (or of the 3,4- and 1,6-bonds, respectively) is accompanied by a hydrogen shift. Deuterium-labelled experiments established that the OH group is the main source of the migrating hydrogen, as illustrated below in the example of 2-hydroxy-5-methyl-1,4-benzoquinone (**29**).

The ion **i** at *m/e* 70 results from the shift of two hydrogen atoms (Figure 4).

The behaviour of the hydroxyquinones **30** and **31** is analogous to that of **29**.

The spectra of methoxy-1,4-benzoquinones (**32**) present a more complicated picture[17]. The formation of ion **j** is typical for this class of compounds. Besides this, the formal elimination of two CO molecules and a methyl group, followed by a further loss of CO, can be generalized. Some natural quinone pigments contain dimethylallyl substituents[22,23].



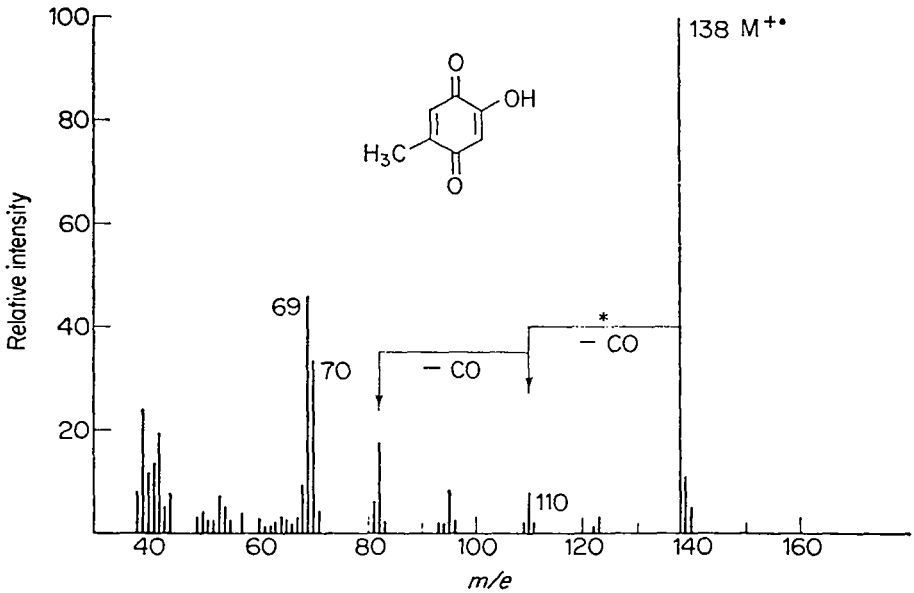
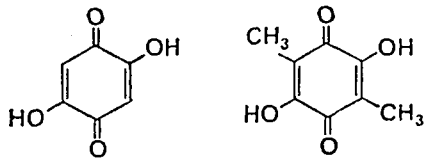
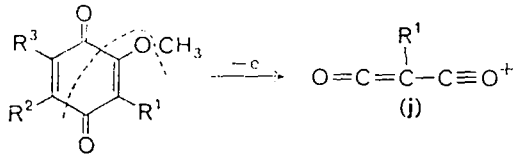


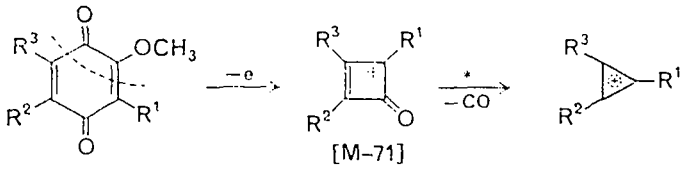
FIGURE 4. Mass spectrum of 2-hydroxy-5-methyl-1,4-benzoquinone.



(30) (31)

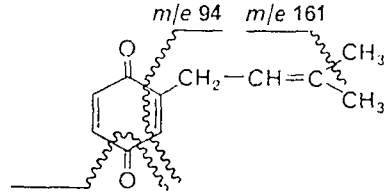


(32) (j)



[M–71]

A representative example is γ,γ-dimethylallylquinone (**33**), whose electron-impact induced fragmentation is shown below.



(33)

The unsubstituted *ortho*-quinone (**16**)[2] (Figure 2) is distinguishable from its *para*-isomer in the appearance of a strong [M+2] peak and a more pronounced CO elimination. The ejection of acetylene is nearly suppressed (Figure 2). The peaks at *m/e* 92, 64 and 63 are derived from the $[M+2]^{+\bullet}$ ion, since they are also formed from the molecular ion of 1,2-dihydroxybenzene[24].

V. NAPHTHOQUINONES

Exactly in the same way as *ortho*- and *para*-benzoquinone, the 1,2-[13] and 1,4-naphthoquinone[1] (Figures 5, 6) as well as 2,6-naphthoquinone[15] (Figure 7) show a stepwise loss of two CO molecules. In the recent past a large number of substituted 1,4-naphthoquinones have been examined[24–26], mainly to obtain basic concepts in structure-determination of naturally occurring naphthoquinones (pigments, vitamin $K_{1/20}$, etc.).

The appearance of peaks at *m/e* 104, 76 and 50 is characteristic[25] for naphthoquinones carrying only alkyl substituents in the quinonoid ring.

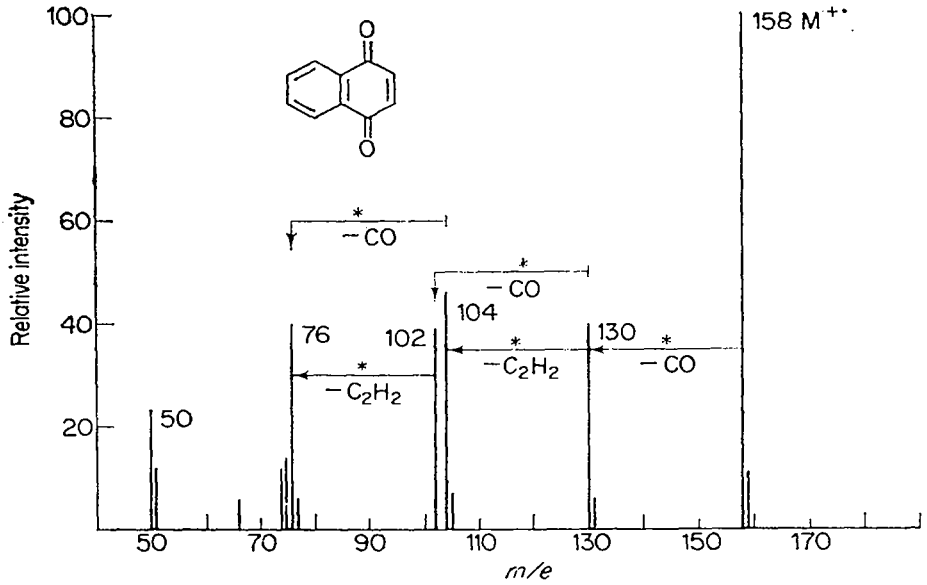


FIGURE 5. Mass spectrum of 1,4-naphthoquinone.

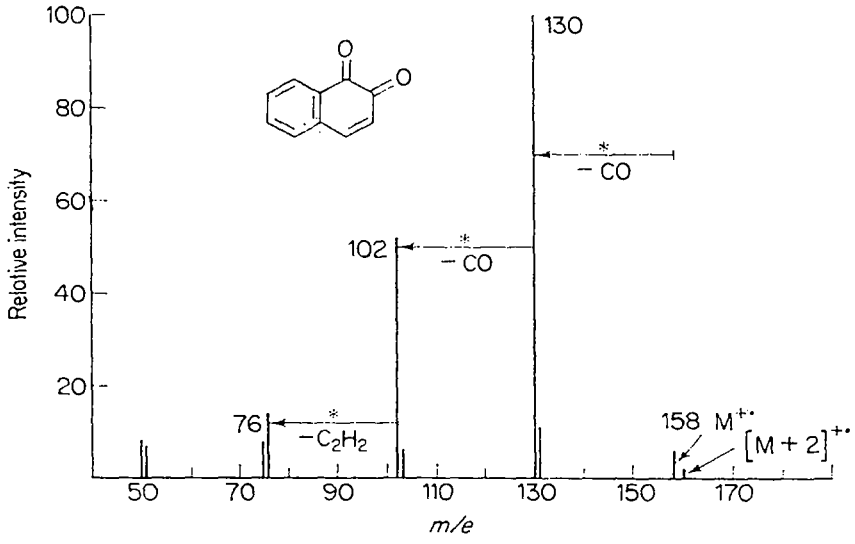


FIGURE 6. Mass spectrum of 1,2-naphthoquinone.

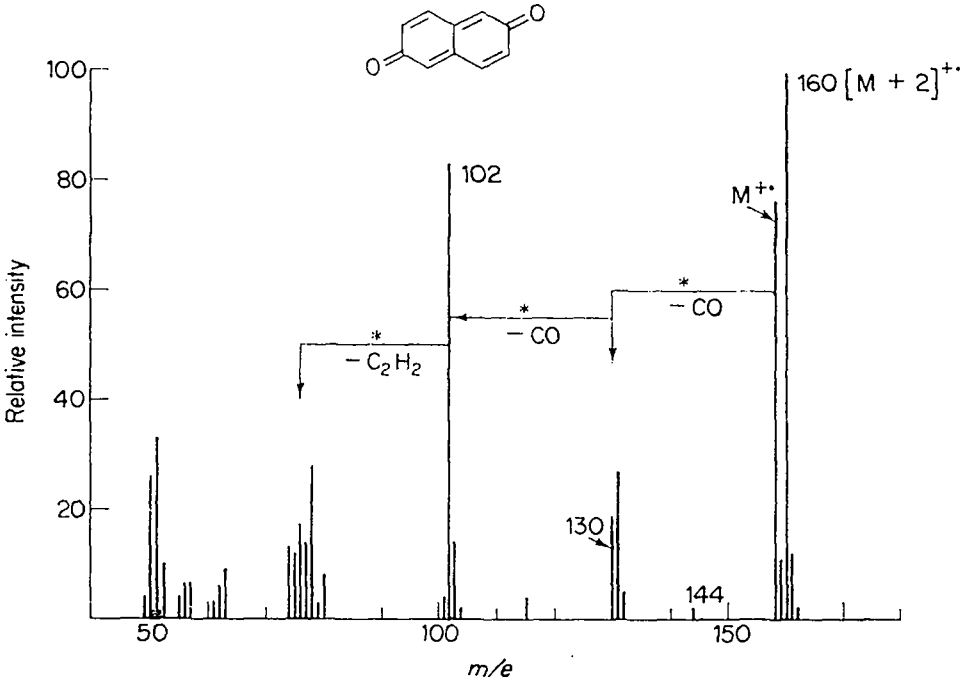
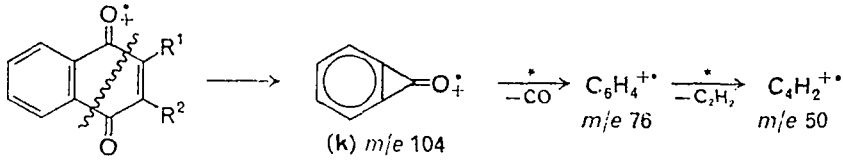


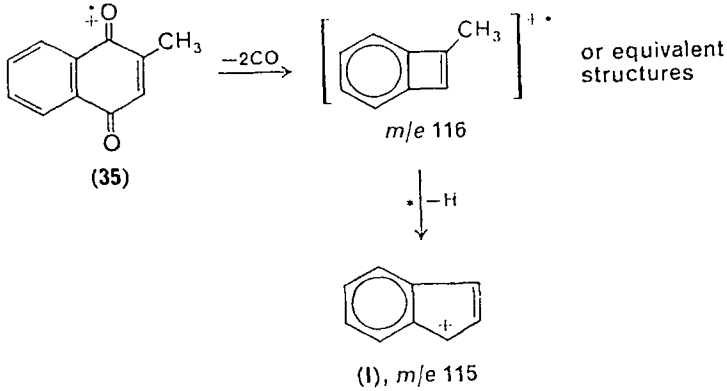
FIGURE 7. Mass spectrum of 2,6-naphthoquinone.

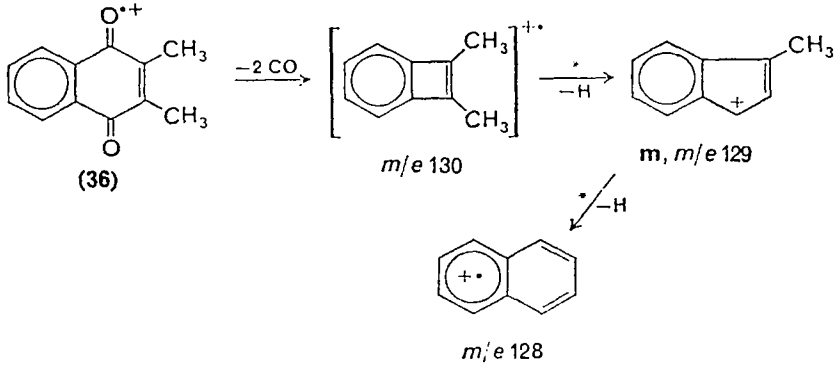
The $[M-2\,CO]^{+\cdot}$ *ion of 2-methyl-1,4-naphthoquinone* (**35**) *loses* a hydrogen and undergoes ring expansion giving another ion with an even number of electrons, for which a benzocyclopentadienyl structure (**l**) was suggested[25].



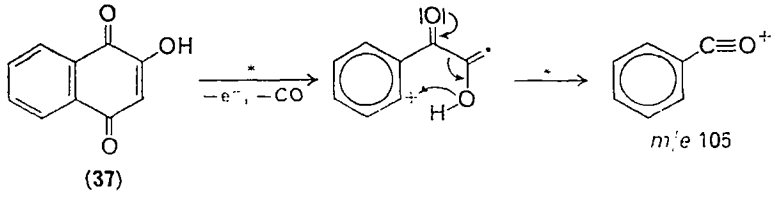
In a similar fashion the ion (**m**) at *m/e* 129 is obtained in the spectrum of 2,3-dimethyl-1,4-naphthoquinone (**36**). Interestingly enough this ion eliminates a further hydrogen atom giving a species with an odd number of electrons. A plausible explanation for this is the ring expansion to the stable naphthalene ion radical.

In naphthoquinones hydroxylated at position 2 or 3 the formation of a benzoyl cation is the dominating process[25], although examples[27] are known where this rearrangement is suppressed in the electron-impact-induced



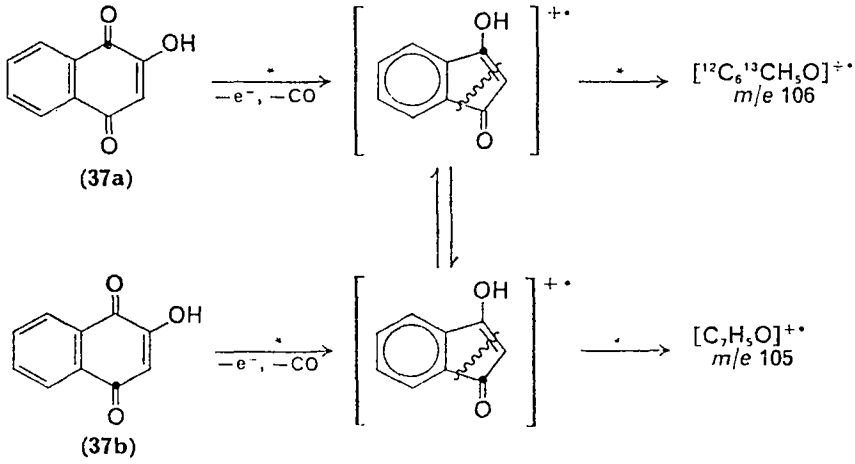


fragmentation. It has been proposed[25] that **37** (lawsone) first loses C-4 as carbon monoxide to form an ion which subsequently transfers its hydroxyl proton to the aromatic ring and decomposes to the benzoyl ion.



A re-examination[38] of the mass spectrum of **37** by ^{13}C-labelling in position 1 (**37a**) and 4 (**37b**) leads to the conclusion that most of the carbon monoxide (91%) expelled from the molecular ion of **37** involves C-2 with the enolic hydroxyl function. This clearly indicates that the above scheme, if operative at all, is not a major fragmentation process.

The 3-hydroxyindenone structure for the $[M-CO]^{+\bullet}$ ion is able to explain the data obtained from the labelled compounds **37a** and **37b**.



(37a) (37b)

If the benzenoid ring also contains hydroxyl groups, then the elimination of CO + H from the $[M-2\,CO]^{+\bullet}$ ion as well as from other fragments is observed[24,26]. This behaviour is to be expected because of the phenolic functional group[28].

A detailed study has been made with acetyl-1,4-naphthoquinones[27], which occur widely in the echinoderm pigments. The following rules for fragmentation apply for structural analysis[27]:

1. 2-Acetylnaphthoquinones with no substituents in position 3 can lose either the methyl group, followed by expulsion of CO (to give $M^{+\bullet}-43$), or ketene (to give $M^{+\bullet}-42$) from the molecular ion. Subsequent eliminations of carbon monoxide and acetylene from these initial $M^{+\bullet}-42$ and $M^{+\bullet}-43$ fragments lead to a characteristic 'doublet' pattern of abundant peaks (exemplified in Figure 8 for 2-acetylnaphthoquinone).

2. In 3-acetyl-2-hydroxynaphthoquinones the hydrogen-bonding between the hydroxy and the acetyl function favours the elimination of CO as the first fragmentation step, followed by loss of a methyl radical to give an abundant $[M-43]^{+\bullet}$ species. In addition, water and/or ketene can be lost from the $[M-CO]^{+\bullet}$ ion.

3. If the acetyl function is located in the benzenoid moiety of the molecule, a methyl group is lost first, followed by expulsion of carbon monoxide. Loss of ketene can be noted but is less pronounced than in the 3-unsubstituted 2-acetylnaphthoquinones.

4. Acetyl(methoxy)naphthoquinones exhibit in general the pattern expected for the unmethylated acetylnaphthoquinone derivative if the methoxyl and acetyl functions are attached to different rings. If both substituents are located in the quinonoid moiety, the vicinity of the two groups determines the breakdown of the molecule under electron impact.

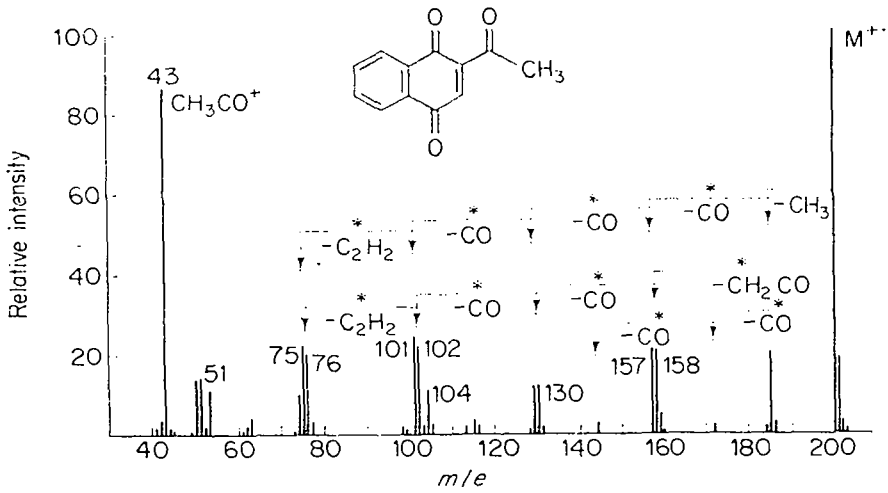
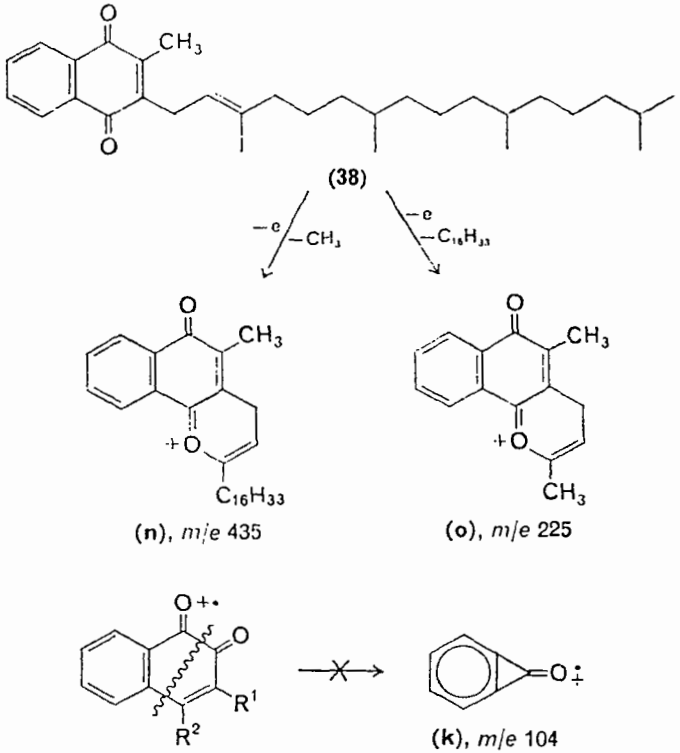


FIGURE 8. Mass spectrum of 2-acetyl-1,4-naphthoquinone

The 2-methyl-3-phythyl-1,4-naphthoquinone (**38**) (vitamin $K_{1/20}$)[26] gives upon electron impact an intensive ion peak at *m/e* 435 ($M^{+\cdot}-CH_3$) and the base peak at *m/e* 228. Through deuterium marking of the methyl group attached to the nucleus it is established that the expulsion of methyl occurs from the phythyl rest. Both ions mentioned above can at best be interpreted on the basis of cyclic oxonium structures (**n** and **o**; compare with **g** derived from structure **27** above).

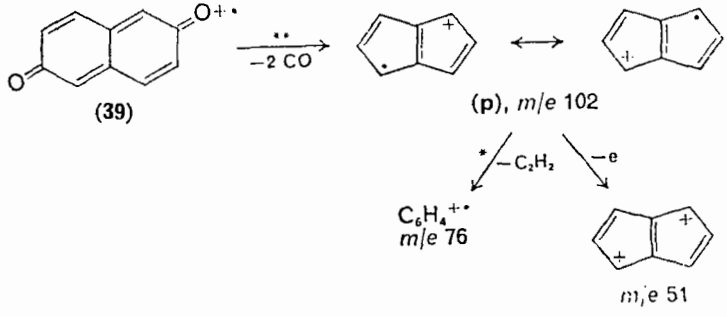
1,2-Naphthoquinone and its derivatives[13,29] give considerably less intense molecular peaks compared to the 1,4-isomers. Besides this, they give [M+2] peaks of the same order or more intense than the molecular peak. They are further distinguishable by the absence of the ion **k** (or its substituted analogues).

2,6-(or amphi-)Naphthoquinone (**39**) possesses a higher oxidation power[30] than the isomeric 1,2- and 1,4-naphthoquinones. A considerable amount of amphi-naphthoquinone is therefore reduced in the inlet system of the mass spectrometer[15] yielding an [M+2] peak of 100% relative intensity (Figure 7). Some of the peaks present in the mass spectrum of



39 are also seen in that of 2,6-dihydroxynaphthalene[15] (e.g. *m/e* 131) and correspond therefore to the $[M+2]^{+\bullet}$ ion.

The second decarbonylation step in the electron-impact-induced fragmentation of **39** is more pronounced than found in the 1,2- and 1,4-isomers. This indicates a relatively high stability of the resulting $[M-2\,CO]^{+\bullet}$ ion, which can be rationalized as ionized pentalene (**p**). Besides the expulsion of acetylene, **p** loses an electron, thus forming a double-ionized species at *m/e* 51.



VI. ANTHRAQUINONES

The successive elimination of two CO molecules from the ionized 9,10-anthraquinone (Figure 9), first reported by Beynon and coworkers[1,4] is a characteristic feature of the whole class of 9,10-anthraquinones.

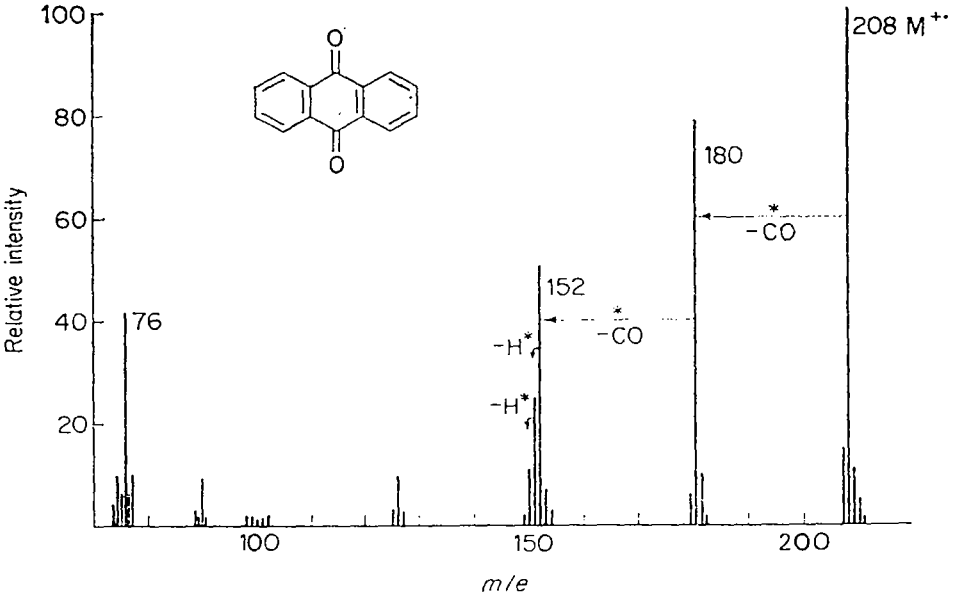
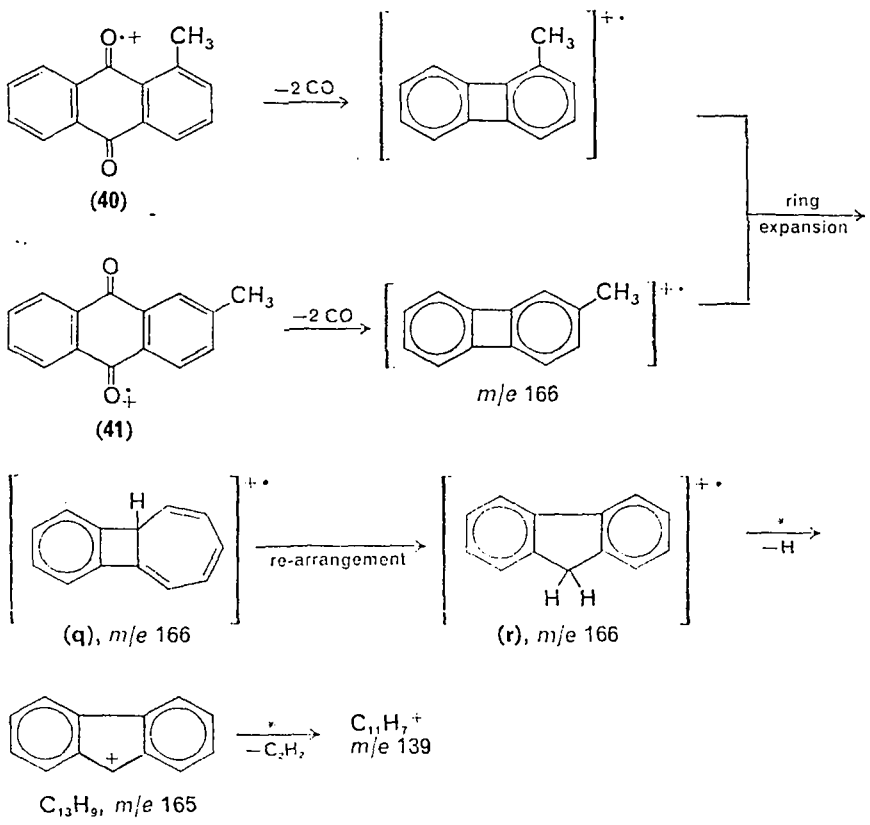


FIGURE 9. Mass spectrum of 9,10-anthraquinone.

The alkyl-substituted 9,10-anthraquinones[31] show in addition interesting hydrocarbon fragments. Thus for example **40** and **41** give $C_{13}H_9^+$ and $C_{11}H_7^+$ ions (Table 2), which is interpreted by intermediate formation of **q** through ring expansion of the $[M-2\,CO]^{+\cdot}$ ion and subsequent rearrangement to **r**.

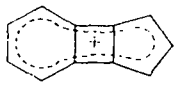
TABLE 2. Relative intensities of some characteristic hydrocarbon fragments in the mass spectra of **40**, **41**, **42** and **43**

Compound	*m/e*					
	166	165	164	163	139	69·5
(40) 1-Methyl-9,10-anthraquinone	26	100	17	21	32	3
(41) 2-Methyl-9,10-anthraquinone	31	100	14	19	25	3
(42) 1,2-Dimethyl-9,10-anthraquinone		100	10	16	24	3
(43) 1-Ethyl-9,10-anthraquinone		75	8	21	19	3

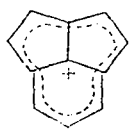


(40) (41)

The $[M-2\,CO]^{+\cdot}$ ions of 1,2-dimethyl-9,10-anthraquinone (**42**) and 1-ethyl-9,10-anthraquinone (**43**) also form $C_{13}H_9^+$ and $C_{11}H_7^+$ ions. Here, instead of a hydrogen, a methyl group is expelled from the corresponding homologue of **r**. The expulsion of acetylene from $C_{13}H_9^+$ leads to a $C_{11}H_7^+$ ion (*m/e* 139) of extraordinary stability. This loses an electron with the appearance of a peak at *m/e* 69·5 but shows no fragmentation. Structures **s**[4] and **t**[32] are proposed for the $C_{11}H_7^+$ ion, which is also often observed in the spectra of aromatic compounds.



s



t

A similar sequence of ring expansion and rearrangement of $[M-2\,CO]^{+\bullet}$ ion in the electron-impact-induced fragmentation of **42** and **43** leads to $C_{14}H_{10}^{+\bullet}$, formulated as anthracene (Table 3).

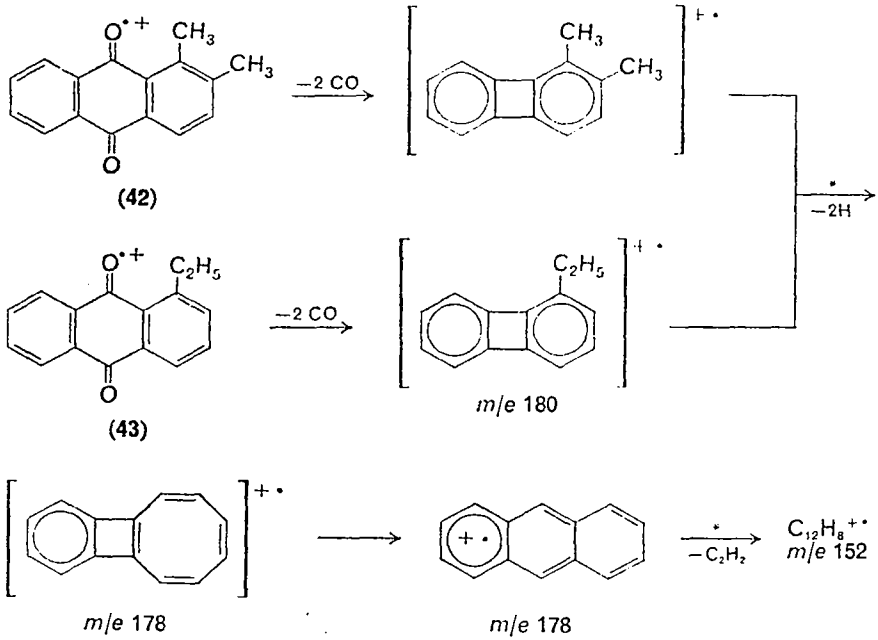


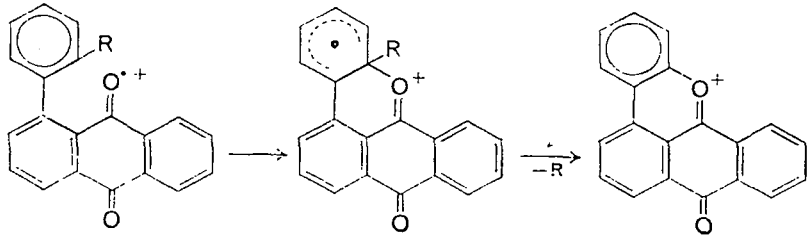
TABLE 3. Relative intensities of some characteristic ions in anthracene, **42** and **43**

Compound	*m/e*			
	180	178	152	89
Anthracene		100	10	3
(42) 1,2-Dimethyl-9,10-anthraquinone	10	48	35	2·5
(43) 1-Ethyl-9,10-anthraquinone	10	20	24	1

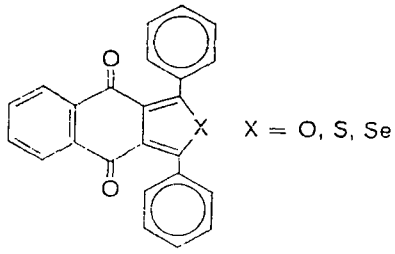
1-Aryl-substituted anthraquinones of type **44** show an intense $[M-R]^+$ peak[33], the driving force being the formation of a stable oxonium ion (**u**).

In the same manner the recently synthesized heteroanthraquinone derivates **45**[34] give rise to pronounced $[M-1]^+$ peaks.

In the spectra of 1-hydroxy- and 2-hydroxyanthraquinone (**46**, **47**)[1] besides the $[M-CO]^{+\bullet}$ and $[M-2\,CO]^{+\bullet}$ peaks, there appears also a $[M-3\,CO]^{+\bullet}$ peak through the usual breakdown of the phenolic hydroxyl

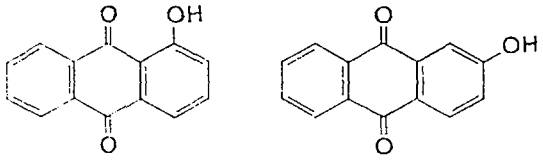


(44), R = H, CH_3, OCH_3, NO_2 (u), *m/e* 283



(45)

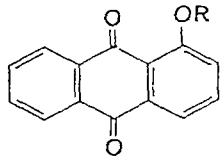
group. The subsequent expulsion of a hydrogen atom leads again to the $C_{11}H_7^+$ ion (structure **s** or **t**, see above). Probably as a result of chelating effects compound **46** eliminates considerably less CO and OH than its isomer **47**. This finding can be applied also to polyhydroxyanthraquinones.



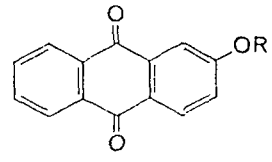
(46) (47)

Characteristic differences are also to be found between 1-methoxy- and 2-methoxyanthraquinone (**48**, **49**). Only the spectrum of the former shows $[M-OH]^+$ and $[M-H_2O]^{+\bullet}$ ions[1]. Although no ^{18}O-labelled studies are available, it is probable that the hydrogen atoms of the 1-methoxy group and the oxygen of the carbonyl function participate in these processes. In a similar way the $[M-H_2O]^{+\bullet}$ ion is obtained from 5-methoxynaphthoquinone[35].

Proximity effects are also observed in the spectra of other alkoxyanthraquinones[36]. For example the spectrum of 1-ethoxyanthraquinone (**50**) contains a strong $[M-CH_3]^+$ peak, which is absent in the case of

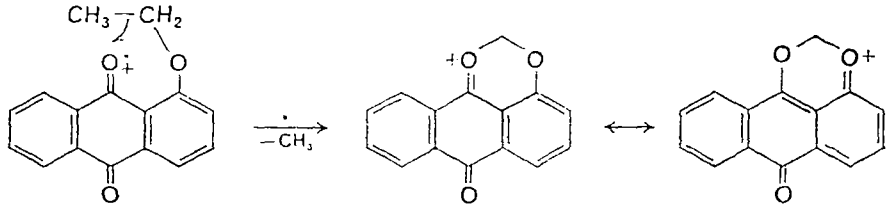


(48), R = CH_3
(50), R = C_2H_5



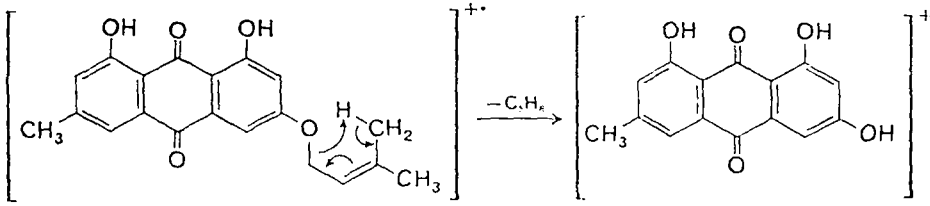
(49), R = CH_3
(51), R = C_2H_5

the 2-isomer **51**, where ethylene is eliminated instead. On the basis of deuterium-labelled experiments, the following mechanism has been proposed:



(50) *m/e* 237

The dimethylallyl ether **52**[22] is converted during the mass spectral decomposition, through a six-membered transition state into the molecular ion of emodin (1,3,8-trihydroxy-6-methylanthraquinone, **53**), which is recognizable from the fragmentation pattern below *m/e* 270.



(52), *m/e* 338 (53), *m/e* 270

The complex mass spectral fragmentation pattern of some other natural anthraquinones (e.g. rhodomycocinone, pyrromycinone) has been reviewed[37].

Finally the mass spectrum of 9,10-phenanthraquinone (**54**) (Figure 10)[1,16], an isomer of 9,10-anthraquinone, is treated briefly. Being an *ortho*-quinone, **54** gives an intense [M+2] peak and shows a more pronounced electron-impact-induced decarbonylation.

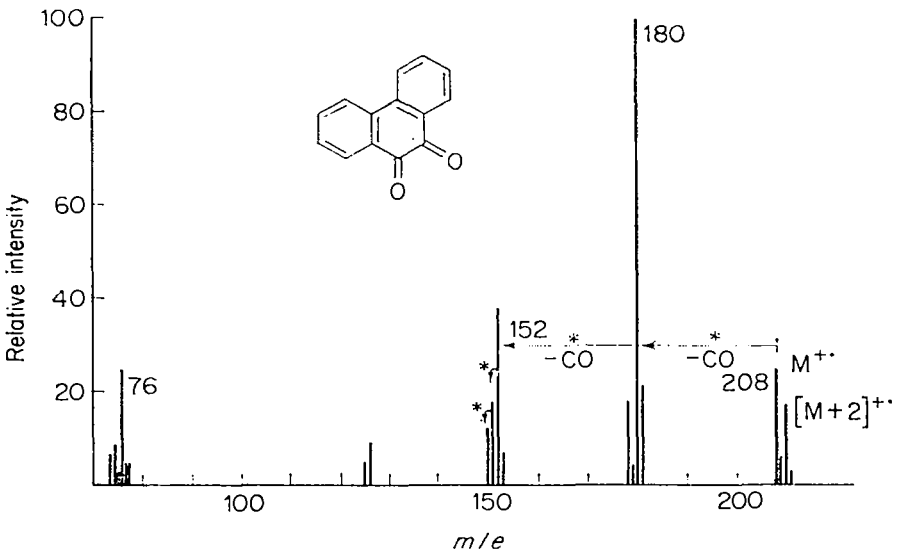


FIGURE 10. Mass spectrum of 9,10-phenanthraquinone.

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The Chemistry of the quinonoid compounds
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CHAPTER 6

Quinone complexes

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I. INTRODUCTION

The term 'complex' continues to have different connotations in chemistry. It has been taken to mean, experimentally, a substance formed by the interaction of two or more component molecules or ions which may have an independent crystal structure and which will reversibly dissociate into its components, at least partially, in the vapour phase and in solution[1]. This definition suggests that there is little or no contribution from covalent binding in the ground state. However, it must be recognized that there is a gradation from these weaker interactions to classical bonding. Moreover, in this present review we shall include a discussion of certain systems involving the interaction of quinones with metals in which dissociation is negligible.

An attempt has been made to divide complexes into organic and organometallic, and into electron donor–acceptor and hydrogen-bonded types. Inevitably there has been some overlap: thus quinhydrone-type complexes fall into both the latter two categories.

We have included under the heading 'quinone' certain quinonoid types exemplified by 7,7,8,8-tetracyanoquinodimethane (TCNQ).

II. ELECTRON DONOR–ACCEPTOR COMPLEXES

A. General

The formation of complexes both in the solid and in solution from components which may reasonably be classified as electron donors and electron acceptors has long been recognized. Very many organic acceptors are quinones; Pfeiffer[2] listed a large number in his monograph *Organische Molekülverbindungen* which was published in 1927. More recently, similar complexes in the vapour phase have been described.

Various theories were developed at an early stage in endeavours to account for the formation of such complexes. Their presence was often recognized by their colours, and many theories concerning the forces stabilizing the ground state of the complex were confounded by explanations as to the nature of the transition which gives rise to the colour (see reference 1). A major step forward was made by Mulliken, and is described in a series of papers[3] in the early 1950s. In terms of the valence-bond theory he proposed that the components of a complex are held together in the ground state by dispersion, dipolar, quadrupolar and such-like van der Waals forces (termed the 'no-bond' structure and written as $\psi(A, D)$) together with a structure in which one electron has been transferred from the donor to the acceptor component (termed the 'dative'

structure and written as $\psi(A^- - D^+)$). If the wave function for the ground state is written as ψ_N then:

$$\psi_N = a\psi(A, D) + b\psi(A^- - D^+) \quad (1)$$

Evidence has accumulated which suggests that the contribution of the dative structure (charge-transfer forces) to the ground state is usually small, i.e. $a \gg b$ in equation (1). Indeed, recent work has strengthened the view that the minor role of the dative structure in the ground state is more extreme than had been thought[4-7]. By contrast, in the simple case, there is an excited state ψ_E which is essentially the dative structure with some destabilization through a resonance contribution from the no-bond structure, thus

$$\psi_E = a^* \psi(A^- - D^+) - b^* \psi(A,D) \quad (2)$$

where $a^* \approx a$ and $b^* \approx b$ in equation (1). The transition $\psi_N \rightarrow \psi_E$ is essentially an intermolecular charge-transfer transition and is the origin of the electronic absorption and the consequent colour which generally characterizes these complexes*.

For most so-called weak complexes between neutral molecular donors and acceptors, the energy of interaction in the ground state is small, generally not more than a few kcal/mole. The weakness of the interaction is also reflected in the intermolecular separation which is often only a little less than the van der Waals separation. In the excited state, however, the coulombic attraction provides a stronger binding and a shortening of the intermolecular distance. A hypothetical pair of energy curves for such a relatively weakly interacting system is shown in Figure 1.

These complexes are not infrequently described as 'charge-transfer complexes. However, in the present chapter we shall restrict ourselves to the terminology 'electron donor–acceptor' or 'EDA' complexes.

Several books on, or containing large sections devoted to, EDA complexes have been published[1,8-12], as well as many reviews. A list of references to reviews up to ca. 1968 is given in a recent monograph[1].

B. Properties of Electron Donor–acceptor Complexes in Inert Solvents and in the Vapour Phase

There is now an extremely large amount of experimental data which substantiates the suggestion made several decades ago that these complexes are partly dissociated into the component species when dissolved in a

* In some complexes it appears that more than one electronic transition can occur, from different filled levels in the donor and/or to different vacant levels in the acceptor, see section II.B.1.

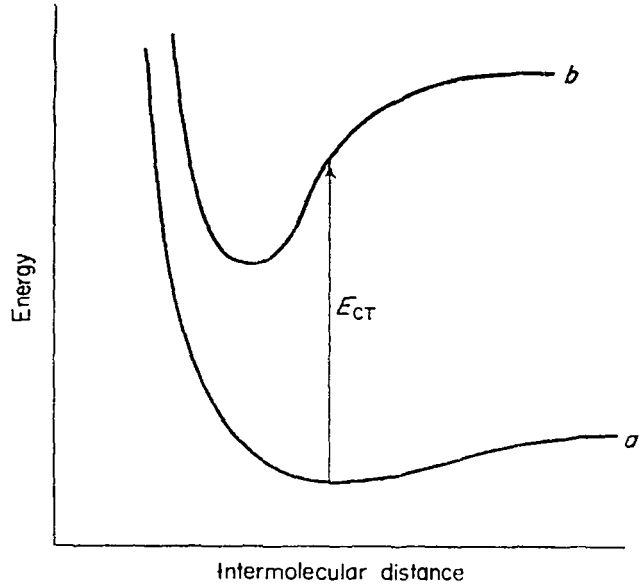


FIGURE 1. Hypothetical energy–intermolecular distance curves for a weak EDA complex; *a*, ground state; *b*, excited state.

third 'inert' medium*. The assumption has generally been made that a complex with 1 : 1 stoicheiometry is formed from the electron acceptor (A), i.e. the quinone, and the electron donor (D):

$$A + D \rightleftharpoons AD$$

However, there is growing evidence that in many cases this is an over-simplification which can lead to incorrect evaluations of the position of equilibrium and consequently of those parameters such as the molar absorption coefficient (molar extinction coefficient, ε) and oscillator strength (**f**) which are dependent on the prior evaluation of the position of equilibrium (see section II.B.2). In general, the experimental determination of the energy ($h\nu_{CT}$) of the intermolecular charge-transfer transition is, at most, only slightly affected by such problems (e.g. in the case of transitions corresponding to complexes of different stoicheiometry) and will be considered first.

* In some solvents ionization by complete electron-transfer occurs. The driving force for such processes is primarily the solvation of the ions so formed. Such reactions are discussed in section II.F of this chapter.

I. Energy of the charge-transfer transition

There is general agreement that the transition $\psi_N \rightarrow \psi_E$ is essentially a charge-transfer transition. Simple valence-bond treatment yields[13,14] for the energy of this transition

$$h\nu_{CT} = I^D - E^A - G_1 + G_0 + \frac{\beta_0^2 + \beta_1^2}{I^D - (E^A + G_1 - G_0)} \tag{3}$$

where I^D is the ionization potential of the donor, E^A is the electron affinity of the acceptor, G_0 is the energy of the no-bond function, G_1 is the coulombic attractive term of the dative state, β_0 and β_1 are the matrix elements for $(H_{01} - S_{01} W_0)$ and $(H_{01} - S_{01} W_1)$ respectively, where $W_0 = \int \psi_0 H \psi_0 \, d\tau$, $W_1 = \int \psi_1 H \psi_1 \, d\tau$, $H_{01} = \int \psi_0 H \psi_1 \, d\tau$ and S_{01} is the corresponding overlap integral $\int \psi_0 \psi_1 \, d\tau$.

For a series of complexes of a given acceptor with a range of donors, the practical limitation of the range of values of I^D is such that equation (3), which is a parabolic function of $h\nu_{CT}$ and I^D of the form

$$h\nu_{CT} = I^D - C_1 + \frac{C_2}{I^D - C_1} \tag{4}$$

in fact usually approximates to a linear function. This is sometimes written[15]

$$h\nu_{CT} = I^D - E^A + C \tag{5}$$

where C is essentially the coulombic term. Others have used the expression

$$h\nu_{CT} = I^D - E^A + C - P \tag{6}$$

which includes a polarization term (P) for the ground state. Many[16-19] have preferred just to write the parameters e and f for the experimentally observed linear correlation

$$h\nu_{CT} = eI^D + f \tag{7}$$

Mulliken and Person[20] in particular have emphasized that there is no theoretical justification for this apparent linearity. It only arises because of the relative magnitudes of the various terms in equation (3). Comparison of equation (3) with equation (7) shows that the parameter e has no direct physical significance. However, for many structurally related acceptors in complexes with a common group of donors, $e \approx$ unity and f is effectively the sum of E^A and the coulombic term in the simple valence-bond description (see section II.c).

Plots of $h\nu_{CT}$ against I^D have been used to provide estimates of ionization potential of other donors of unknown ionization potential. These estimates are obviously subject to the limitations indicated above

and are best restricted to comparisons within structurally related groups of donors. Estimates of I^D using data from more than one acceptor are advisable. In principle, some comparison of electron affinities of acceptors (E^A) can be made from $h\nu_{CT}$ data if the empirical linear relationships of the form of equation (7) are assumed to reflect differences in electron affinity in the term f (which will vary from acceptor to acceptor). The fact that this term involves coulombic and resonance interaction energies means that any argument which suggests that the term f is a measure of E^A is even more tenuous than those used to provide a measure of I^D. The problem is further aggravated by the fact that very few molecules used as organic electron acceptors have well-established values of electron affinity (see section II.C).

The general behaviour of the electron-accepting ability of quinones as reflected in the energies of the charge-transfer bands ($h\nu_{CT}$) follows a reasonably expected pattern (Table 1) (see also section II.C). An increase in the efficacy and number of electron-withdrawing groups of atoms in *p*-benzoquinone causes a decrease in $h\nu_{CT}$. Thus for hexamethylbenzene complexes $h\nu_{CT}$ is in the order: *p*-duroquinone > *p*-toluquinone > *p*-benzoquinone > chloro-*p*-benzoquinone > 2,3-dichloro-*p*-benzoquinone >

TABLE 1. Selected values of the lowest-energy intermolecular charge-transfer

Acceptor	*p*-Benzoquinone			Chloranil		
Donor	$h\nu_{CT}$	Solv.	Ref.	$h\nu_{CT}$	Solv.	Ref.
Benzene	32·8	*n*-hept	21	28·8	CCl_4	44
Toluene	31·7	*n*-hept	21	27·0	CCl_4	23
p-Xylene	31·2	*n*-hept	21	23·4	CCl_4	23
Mesitylene				23·3	CH_2Cl_2	22
Durene				20·9	CCl_4	23
Pentamethylbenzene				20·2	CH_2Cl_2	22
Hexamethylbenzene	24·0	CCl_4	105	19·4	CCl_4	23
Naphthalene	26·8	CCl_4	21	20·9	CCl_4	44
Anthracene	22·2	CCl_4	21	16·0	CCl_4	44
Phenanthrene	26·3	CCl_4	21	21·6	CCl_4	44
Perylene	19·0	$CHCl_3$	36	13·9	CCl_4	44
Pyrene	22·2	CCl_4	26	16·6	CCl_4	44
Triphenylene	26·7	CCl_4	105	20·7	CCl_4	44
Fluorene				20·0	CCl_4	44
Benz[*a*]anthracene				16·9	CCl_4	44
trans-Stilbene	25·8	$CHCl_3$	27	19·4	CCl_4	44
Benz-3,4-pyrene	20·0	$CHCl_3$	27	14·4	CH_3CN	28
Benz-1,2-pyrene				17·6	CH_3CN	28
Aniline	23·0	CCl_4	29	18·9	CCl_4	30
N,N,N',N'-Tetramethyl-*p*-phenylenediamine				11·5	C_6H_{12}	31

[a] DCNQ ≡ 2,3-dicyano-*p*-benzoquinone.
[b] DDQ ≡ 2,3-dichloro-5,6-dicyano-*p*-benzoquinone.

chloranil* > 2,3-dicyano-*p*-benzoquinone > 2,3-dichloro-5,6-dicyano-*p*-benzoquinone[31], although the order: fluoranil > chloranil > bromanil > iodanil is unexpected. Other comparisons of interest are chloranil > *o*-chloranil > *o*-bromanil[31]. *o*-Fluoranil is too reactive to enable measurements to be made[32].

The general pattern shown by *p*-benzoquinones is reflected in the 1,4-naphthoquinones and substituted naphthoquinones[33,34], the hexamethylbenzene complexes of which absorb at higher energies than those of the corresponding *p*-benzoquinones. Similarly 11,11,12,12-tetracyano-1,4-naphthoquinodimethane complexes[35] absorb at higher energies than those of 7,7,8,8-tetracyanoquinodimethane (TCNQ)[36,37]. Although TCNQ is often thought to be the strongest of the neutral organic electron acceptors, it is in fact weaker than 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) on the $h\nu_{CT}$ criterion. 2,3-Dicyano-5,6-dichloro-7-nitro-1,4-naphthoquinone is also weaker than DDQ despite its galaxy of

* chloranil≡tetrachloro-*p*-benzoquinone, likewise for fluoranil, bromanil and iodanil. Tetrachloro-*o*-benzoquinone will always be written as *o*-chloranil, likewise for the fluoro- and bromo-compounds.

transitions ($h\nu_{CT}/10^3 \times cm^{-1}$) for various EDA complexes in solution

DCNQ[a]			DDQ[b]			DCNNQ[c]			TCNQ[d]		
$h\nu_{CT}$	Solv.	Ref.	$h\nu_{CT}$	Solv.	Ref.	$h\nu_{CT}$	Solv.	Ref.	$h\nu_{CT}$	Solv.	Ref.
25·7	CH_2Cl_2	22	24·6	CH_2Cl_2	22						
23·8	CH_2Cl_2	22	22·7	CH_2Cl_2	22						
20·7	CH_2Cl_2	22	19·6	CH_2Cl_2	22						
21·0	CH_2Cl_2	22	19·6	CH_2Cl_2	22	21·7	$CHCl_3$	34			
18·5	CH_2Cl_2	22	17·2	CH_2Cl_2	22	19·4	$CHCl_3$	34			
18·2	CH_2Cl_2	22	16·8	CH_2Cl_2	22	19·4	CH_2Cl_2	33			
17·4	CH_2Cl_2	22	16·0	CH_2Cl_2	22	18·4	CH_2Cl_2	33			
17·9	CH_2ClCH_2Cl	37	15·9	CH_2ClCH_2Cl	37	19·0	CH_2Cl_2	33	17·9	$CHCl_3$	36
14·1	CH_2Cl_2	24	12·1	CH_2ClCH_2Cl	25	14·0	CH_2Cl_2	33	12·3	$CHCl_3$	36
19·0	CH_2ClCH_2Cl	37	17·1	CH_2Cl_2	25	18·9	CH_2Cl_2	33	18·7	$CHCl_3$	36
11·9	CH_2Cl_2	24	9·9	CH_2Cl_2	45	12·4	CH_2Cl_2	33	10·5	$CHCl_3$	36
13·7	CH_2ClCH_2Cl	37	11·8	CH_2ClCH_2Cl	37	13·4	CH_2Cl_2	33	13·1	$CHCl_3$	36
			16·1	CH_2Cl_2	25	14·7	CH_2Cl_2	33	17·4	$CHCl_2$	36
			16·0	CH_2Cl_2	25	18·0	$CHCl_3$	33			
			12·1	CH_2Cl_2	45	15·0	$CHCl_3$	33			
			14·6	CH_2ClCH_2Cl	25				15·8	$CHCl_3$	36
						13·6	CH_2Cl_2	33	11·6	$CHCl_3$	36
			12·8	CH_2Cl_2	45	15·4	CH_2Cl_2	33			
17·2	CH_2Cl_2	22	16·0	CH_2Cl_2	22	16·8	$CHCl_3$	34	15·8	$CHCl_3$	36
12·0	CH_2Cl_2	29							12·7	$CHCl_3$	36

[c] DCNNQ ≡ 2,3-dicyano-1,4-naphthoquinone.
[d] TCNQ ≡ 7,7,8,8-tetracyanoquinodimethane.

electron-withdrawing groups[33]. Tetracyano-*p*-benzoquinone gives the lowest reported energy for an EDA complex with a given donor[38,39]. Its pyrene complex in dichloromethane absorbs at 8860 cm^{-1}, compared with ca. 11,800 cm^{-1} for the corresponding complex of DDQ.

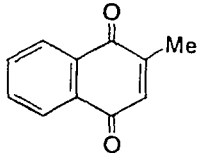
Menadione (2-methyl-1,4-naphthoquinone) (**1**) has been widely studied[40–43] as a complexing agent because of its biological interest, as vitamin K_3, and in its relation to vitamins K_1 (**2**) and K_2 (**3**), the ubiquinones (**4**) and α-tocophenylquinone (**5**). In fact it is a rather poor electron acceptor measured in terms of both the position of the charge-transfer bands of its complexes and the stability of the complexes in solution.

In Table 2 several examples of multiple intermolecular charge-transfer transitions are given. It is generally considered that these arise either from excitation of electrons in more than one level in the donor, e.g. from the highest and penultimate filled levels, or from transitions to more than one vacant level in the acceptor (or both). Thus the energy differences in transitions from the donor pyrene to the acceptors chloranil[44], DDQ[45] and 2,3-dicyano-*p*-benzoquinone[37] (~6600 cm^{-1}) are effectively independent of the acceptor (Table 2) which suggests that this is a measure of separation of the energies of the two highest filled levels in pyrene. With several complexes of TCNQ, two bands separated by 9300 cm^{-1} are observed[46] which suggests that in these cases the difference arises from transitions to the two lowest vacant orbitals in TCNQ. This is in reasonable agreement with the calculated energy separation of these two levels[47].

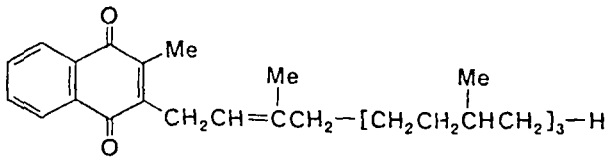
TABLE 2. Energies and energy differences (in $cm^{-1} \times 10^{-3}$) of EDA

Donor	Chloranil				DDQ [a]			
	ν	$\Delta\nu$	Solv.	Ref.	ν	$\Delta\nu$	Solv.	Ref.
Biphenyl	23·0 28·7	5·7	CCl_4	44	17·8 22·6	4·8	CH_2Cl_2	45
Naphthalene	20·9 26·0	5·1	CCl_4	44	16·3 20·6	4·3	CH_2Cl_2	45
Chrysene	18·5 21·5	3·0	CCl_4	44	15·9 21·1	5·2	CH_2Cl_2	46
Pyrene	16·6 23·1	6·5	CCl_4	44	11·8 18·4	6·6	CH_2Cl_2	37
Benz[*a*]anthracene	16·9 21·1	4·2	CCl_4	44	12·1 16·8	4·7	CH_2Cl_2	45
N,N,N′,N′-Tetramethyl-benzidine	11·4 17·8	6·4	$CHCl_3$	46				

[a] DDQ = 2,3-dichloro-5,6-dicyano-*p*-benzoquinone.
[b] TCNQ = 7,7,8,8-tetracyanoquinodimethane.



(1)



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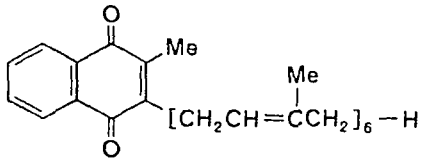

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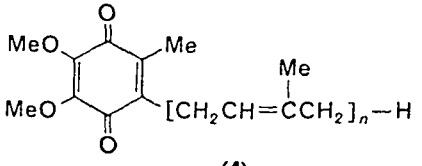

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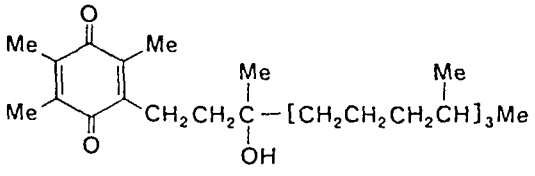


(5)

For the TCNQ–*N*,*N*,*N*′,*N*′-tetramethylbenzidine complex, three charge-transfer bands are observed[46], at 7700, 14,800 and 17,200 cm^{-1} in chloroform and may be assigned to the transitions indicated in Figure 2. It

complexes showing multiple charge-transfer transitions in solution

TCNQ[b]				2,3-DCNQ[c]				2,3-DCNNQ[d]			
ν	$\Delta\nu$	Solv.	Ref.	ν	$\Delta\nu$	Solv.	Ref.	ν	$\Delta\nu$	Solv.	Ref.
				17·9 22·8	4·9	CH_2Cl_2	37				
				13·7 20·6	6·9	CH_2Cl_2	37				
7·7 14·8 17·2	7·1 6·4	$CHCl_3$	46					9·5 16·0	6·5	$CHCl_3$	37

[c] 2,3-DCNQ = 2,3-dicyano-*p*-benzoquinone.
[d] 2,3-DCNNQ = 2,3-dicyano-1,4-naphthoquinone.

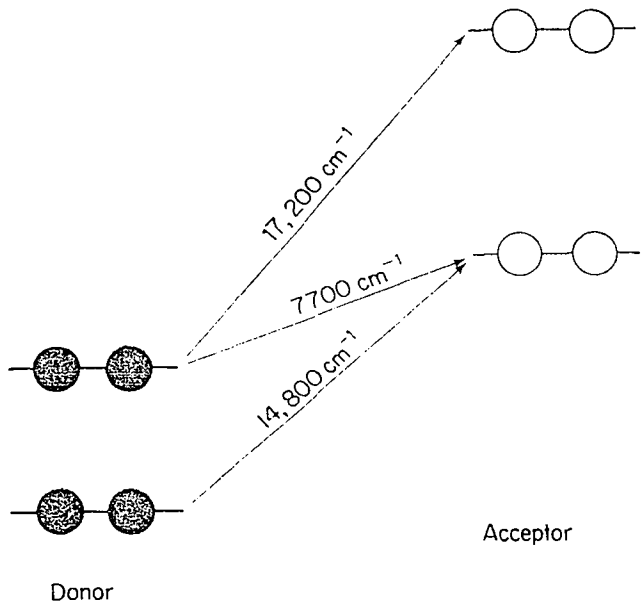


FIGURE 2. Proposed intermolecular transitions in the TCNQ–*N*,*N*,*N*′,*N*′-tetramethylbenzidine complex.

should be noted, however, that complexing may affect the molecular levels in the component molecules of the complex. This will usually be expected more in the stronger interactions and may be significant, for example, in TCNQ complexes[48]. For this reason care should be exercised in utilizing such charge-transfer measurements in estimating the separation of energy levels in the *un*complexed molecules. Observations of fine structure within the charge-transfer band for several quinone–donor complexes in solution have been reported[49–52]. The earliest of these[49], based on measurements using a conventional non-recording spectrophotometer, could not be reproduced in later experiments using a higher resolution recording spectrophotometer[17]. More recently, structure within the charge-transfer band has again been reported, from observations using a photographic spectrograph[50–52]. Independent attempts, using an Ebert 20 ft spectrograph with a resolution of ~3 Å for solutions, have shown no structure[53] *.

The energy of the intermolecular charge-transfer transition ($h\nu_{CT}$) in weak EDA complexes between neutral species is relatively insensitive to solvent polarity[55, 56]. Complexes of quinones are no exception (Table 3).

* A slight shoulder on a charge-transfer band of an EDA complex has recently been attributed to a vibrational component[54]. However, this complex does not involve a quinone.

Small differences in $h\nu_{CT}$ in various inert solvents have been generally accounted for in terms of McRae's theory[60]. It has been argued that the transition time is too short for there to be a significant reorientation of the solvent to stabilize the enhanced intermolecular dipole characteristic of the excited state, though the dipole in the ground state, which is enhanced over the normal charge-transfer contribution by polarization (see above), will be stabilized by solvation. However, the effect is not large.

TABLE 3. Dependence of charge-transfer band maximum (ν_{CT}) of substituted *p*-benzoquinone–hexamethylbenzene complexes on solvent

p-Benzoquinone derivative	$\nu_{CT}/cm^{-1} \times 10^3$							
	C_6H_{12}	Ref.	CCl_4	Ref.	CH_3CN	Ref.	EtOH	Ref.
H	24·4	150	24·0	105	25·3	57	24·5	57
Chloro	22·7	150	22·6	59	23·2	57	23·2	57
2,5-Dichloro	21·5	150	21·8	58	21·9	57	21·8	57
Trichloro	19·8	150	19·5	58	20·9	57	20·9	57
Tetrachloro	19·6	150	19·4	59	20·0	57	20·3	57
Tetrafluoro	21·1	58	20·6	58	21·1	57	21·7	57
2,3-Dichloro-5,6-dicyano	16·1	150	16·3	58	16·9	57	17·1	57

Little work has been reported on the absorption of quinone complexes in the vapour phase. This is because of the practical difficulties resulting from the low vapour pressure of quinones. Recently, however, the vapour-phase absorption spectra of anthracene–chloranil has been measured by Inokuchi and coworkers[61]. The optical cell was heated to 250° to obtain a sufficiently high vapour pressure. The maximum of the charge-transfer absorption was observed at 17,800 cm^{-1} compared with 16,400 cm^{-1} for the system in *n*-heptane solution. No estimates of the degree of association were made, hence no comparison of the intensity of absorption in the two phases could be made. In terms of equation (6), the coulombic energy was estimated to be 3·03 eV and the polarization energy (the term P in equation 6) to be 0·17 eV in *n*-heptane. This was based on an electron affinity value of 2·45 eV for chloranil[62].

There has been only one systematic study of the effect of pressure on $h\nu_{CT}$ for quinone complexes in liquid solution. This was by Ewald[63] who studied the spectroscopic behaviour of the system chloranil–hexamethylbenzene in methylcyclohexane, chloranil–naphthalene in dichloromethane and chloranil–pyrene in dichloromethane up to pressures of 6000 atm.

For a given solution there is a shift in the charge-transfer transitions to lower energy with increasing pressure. This is accounted for by a shortening of the intermolecular distance as the pressure is increased, so that because of the shapes and relative positions of the energy curves for the ground and excited states of this type of complex (Figure 1), the transition corresponding to a shorter intermolecular distance will be less.

Nothing so far has been said about the intensities of the charge-transfer spectra. Simple valence-bond theory predicts that for a given acceptor the intensity of the absorption should increase with increasing interaction. However, a direct determination of the intensity of absorption cannot be made without assumptions being made concerning the stoicheiometry and method of evaluating the degree of association of the components in the equilibrium mixture. This is the subject of the next subsection. As will be seen, there now appears to be some doubt concerning the published values of molar absorption coefficients (extinction coefficient, ε) for this type of system.

Fluorescence emission corresponding to the characteristic intermolecular charge-transfer absorption has been observed. This is the transition $\psi_E \rightarrow \psi_N$ (cf. equations 1 and 2). Most of the measurements have been made on complexes held in a solid glass at low temperatures[64, 65]. Such systems are strictly solid solutions in which presumably separated complexes are held in a random fashion in the solid matrix. The spectra reflect the absorption spectra of the first charge-transfer transition. In measurements of *p*-benzoquinone–aromatic hydrocarbon systems in solid matrices at $-180°$, Briegleb and coworkers[64] have observed the fluorescence emission of the complexes together with the phosphorescence of the *p*-benzoquinone.

Fluorescence-quenching of donors in systems with added quinones has been attributed in many cases to electron donor–acceptor complex formation[66–72].

2. Equilibrium constants[73]

The equilibrium quotient, K, expressed in terms of molar concentrations (K_c), mole fractions (K_x), molal concentration (K_m), or in moles/kg of solution (K_r), has been used as a measure of the position of the equilibrium between the components and the complex in solution. Apart from a few exceptional cases the activity coefficient ratio ($\gamma_{AD}/\gamma_A\gamma_D$) in the case of the formation of a complex of 1 : 1 stoicheiometry has been assumed to be unity.

In practice, for the relatively dilute solutions normally used, the error introduced by this assumption will probably be small.

The basic assumption usually made, that the complexes formed have a 1 : 1 stoicheiometry only, is far more disconcerting. Although one or two workers suggested at an early stage in the development of this field that there may be significant contributions from complexes with stoicheiometries other than 1 : 1, it is only relatively recently that the effect of such complexes, albeit usually in relatively low concentrations, has been fully appreciated. In this respect the paper by Deranleau[74] is important. In solutions where $[D] \gg [A]$, which is usually the case for experimental reasons, there can be a significant contribution from a species AD_2, particularly if both A and D interact via π-orbitals[75]. Consequently, the large volume of published values relating to the position of equilibrium of the 1 : 1 complex (e.g. K, $\Delta H^{\ominus}$, $\Delta S^{\ominus}$) must be treated with circumspection. For the same reason derived functions such as the molar absorption coefficient (ε) in the case of optical measurements, and relative chemical shift (Δ_0) in the case of n.m.r. measurements, may be seriously in error. As an example, Table 4 details the values of the equilibrium quotient (K) on the assumption of a 1 : 1 complex formation from measurements over the concentration range commonly used for optical measurements ($[D]_0 \approx 0{\cdot}03$–$0{\cdot}88$M), and for evaluations based on n.m.r. shift measurements ($[D]_0 \approx 0{\cdot}5$–$0{\cdot}7$M) *, for the system hexamethylbenzene-fluoranil in carbon tetrachloride[76]. Analyses of measurements made over a considerably wider range of concentrations, and based on the assumption that when $[D]_0 \gg [A]_0$ there may be measurable quantities of the termolecular complex AD_2, indicate values for the 1 : 1 association (K_1) which are considerably different from those above.

Consequently, there are large differences in the secondary quantities of molar absorption coefficient (ε) and relative chemical shift (Δ_0) (Table 4). The profiles of the intermolecular charge-transfer bands for these 1 : 1 and 2 : 1 complexes of hexamethylbenzene–fluoranil based on this analysis are shown in Figure 3. It is seen that, whereas there is a large difference in ε, the energies of the charge-transfer transitions as reflected in the wavelengths of the band maxima are little different for the two complexes.

Although such an analysis has been carried out for relatively few systems, there is good reason to suppose that existence of complexes between π-donors and π-acceptors with stoicheiometries other than 1 : 1 is not exceptional. However, there is some evidence that, for closely related complexes of a common acceptor, the earlier determined values of

* The subscript 'zero' following the square concentration brackets denotes the 'weighed-out' concentration of the species, i.e. free and complexed. In the case of these particular measurements where $[D]_0 \gg [A]_0$, the value of $[D]_0$ closely approximates to the equilibrium concentration of D.

TABLE 4. Association constants for 1 : 1 (K_1) and 2 : 1 (K_2) complexes between hexamethylbenzene (D) and fluoranil (A); also apparent values for the association constant (K) based on the assumption that only 1 : 1 association occurs, together with corresponding values of molar absorption coefficient (ε) and chemical shift Δ_0, in carbon tetrachloride at 33·5° [a]

Method	Rel. concn.	Range $[A]_0$/M	Range $[D]_0$/M	K/l mole^{-1}	ε/l mole^{-1} cm^{-1} [b]	Δ_0/Hz [c]
Optical	$[D]_0 \gg [A]_0$	$1{\cdot}65 \times 10^{-3}$	0·0074–0·72	$K_1 = 20 \pm 1$ $K_2 = 3 \pm 0{\cdot}5$	$\varepsilon_1 = 2700$ $\varepsilon_2 = 4400$	
N.m.r.	$[D]_0 \gg [A]_0$	$1{\cdot}6 \times 10^{-3}$	0·033–0·74	$K_1 = 20 \pm 1$ $K_2 = 3 \pm 0{\cdot}5$		$\Delta_0(1) = 170$ $\Delta_0(2) = 260$
Optical	$[D]_0 = [A]_0$	$(2{\cdot}1–5{\cdot}2) \times 10^{-3}$	$(2{\cdot}1–5{\cdot}2) \times 10^{-3}$	$K_1 = 20{\cdot}8 \pm 2$	$\varepsilon_1 = 2700$	
N.m.r.	$[D]_0 = [A]_0$	0·011–0·022	0·011–0·022	$K_1 = 19{\cdot}2 \pm 2$		$\Delta_0(1) = 190$
Optical	$[D]_0 \gg [A]_0$	$1{\cdot}5 \times 10^{-3}$	0·03–0·08	$K = 17{\cdot}1 \pm 2$	$\varepsilon = 3200$	
N.m.r.	$[D]_0 \gg [A]_0$	0·02	0·5–0·7	$K = 9{\cdot}6 \pm 0{\cdot}5$		$\Delta_0 = 260$

[a] Reproduced with permission from B. Dodson, R. Foster, A. A. S. Bright, M. I. Foreman and J. Gorton, *J. Chem. Soc.* (*B*), 1283 (1971).

[b] At 486 nm.

[c] ^{19}F shifts of the acceptor system measured at 56·462 MHz.

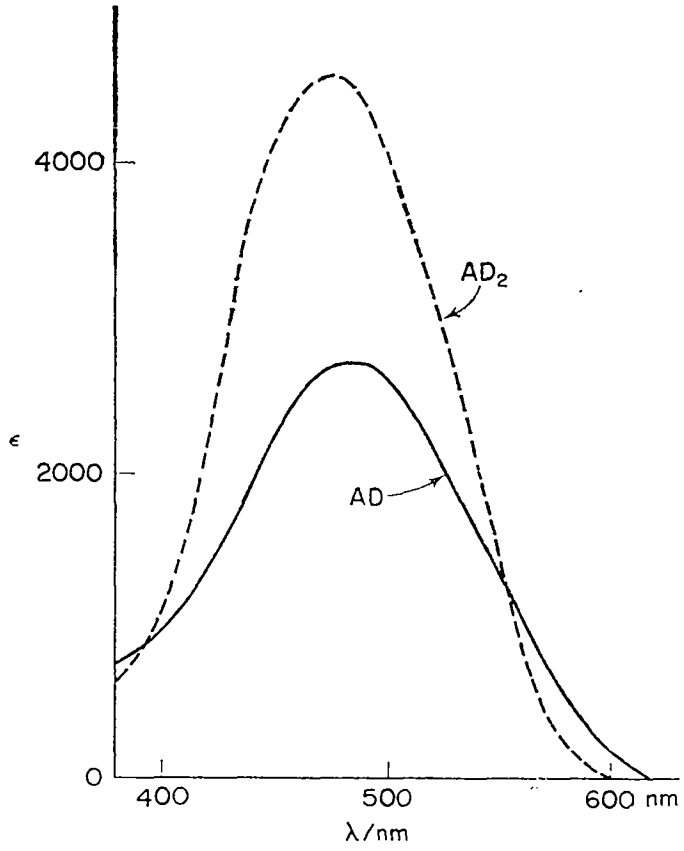


FIGURE 3. Fluoranil–hexamethylbenzene in carbon tetrachloride at 33·5°; absorption spectra of the AD and AD_2 complexes. [λ_{max} = 485 nm (ε = 2700) and λ_{max} = 475 nm (ε = 4600) respectively.] Reproduced with permission from B. Dodson, R. Foster, A. A. S. Bright, M. I. Foreman and J. Gorton, *J. Chem. Soc.* (*B*), 1283 (1971).

these parameters may at least be proportional to their correct values. Thus, for systems in which $[D]_0 = [A]_0$, the total concentration of species AD_2 and A_2D is minimized and for some systems under certain conditions can be demonstrated to be sufficiently small to be ignored. In such cases conventional determinations of equilibrium quotient will effectively measure K_1, the quotient for the 1 : 1 complex, only[76]. If these values are compared with K obtained under the usual condition namely $[D]_0 \gg [A]_0$, a direct proportionality is observed (Figure 4).

For the weaker interactions, where K_c is less than ca. 1 l/mole, there can be other serious complications to the evaluation of this and related parameters. If collisions between components are so orientated that an

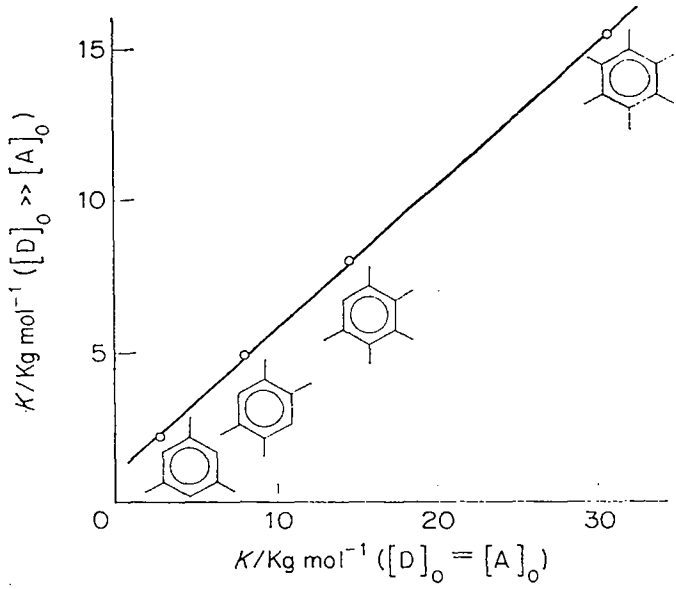


FIGURE 4. Plot of K for fluoranil–methylbenzene complexes in carbon tetrachloride, 33·5°, under the condition $[D]_0 \gg [A]_0$ against K for the same system under the condition $[D]_0 = [A]_0$.

intermolecular charge-transfer transition can occur (contact charge-transfer) then its contribution to the optical absorption will be wrongly attributed to a complex[77]. In the cases where complex formation is in fact small, the fractional contribution of this error can be large. Problems arise in any case in an analysis of the effect of random collisions[78–80], and on the concentration scale chosen[81,82], Murrell and coworkers[83] have suggested that the equilibria in solution should be thought of in terms of solvated species in which one or more solvent molecules are extruded in the process of complex formation. These complications will give rise to differences between the experimental and the correct values of the equilibrium constant, and the discrepancy will increase as the degree of complexing diminishes. A list of recent publications concerned with equilibrium parameters for EDA complexes in solution is given in Table 5. These are additional to those references given in Appendix 2 of reference 1.

C. *Electron Affinities of Quinones*

The involvement of quinones in EDA complex formation is a consequence of the fact that such molecules possess low-lying unoccupied electronic energy levels and are therefore ready acceptors of electrons.

TABLE 5. Recent determinations of association parameters for EDA complexes in solution

Acceptor	Donor	Solvent	Parameters	Reference
p-Benzoquinone	Benzene	CCl_4	K	84
p-Benzoquinone	Caffeine, theophylline		K	85
p-Benzoquinone, ubiquinone	Triethyl phosphate	CCl_4	K	86
p-Benzoquinones	Pyrazolones	Various	$K\,\Delta H^\circ$	87
Chloranil	Various	$CHCl_3$	K	88
Chloranil	Aromatic amines	$CHCl_3$	K	30, 89
Chloranil	Polar solvents	CCl_4	$K\,\Delta H^\circ$	90
Chloranil	Aromatic hydrocarbons	$C_6H_{11}Me$, CH_2Cl_2	K	63
Chloranil	2,2-Bis(*p*-hydroxyphenyl)propane	Acetone, dioxan	$K\,\Delta H^\circ\,\Delta S^\circ$	91
Chloranil	Benzene, heterocyclics	CCl_4	K	92
Chloranil	Methylbenzenes	CCl_4	K	93
Chloranil	*p*-Xylene	*n*-Heptane	K	94
Chloranil	Anthracene	$CHCl_3$	K	95
Chloranil	Aniline	Ether/iso-pr-alcohol	$K\,\Delta H^\circ\,\Delta S^\circ$	218
Fluoranil	Benzene, alkylbenzenes	Various	$K\,\Delta H^\circ\,\Delta S^\circ$	96
Fluoranil	Hexamethylbenzene	CH_2ClCH_2Cl	$K\,\Delta H^\circ\,\Delta S^\circ$	97
Fluoranil	Benzene, hexamethylbenzene	$CFCl_3$, CCl_4	K	98
Fluoranil	Alkylbenzenes	CCl_4	K	76
Fluoranil	Hexamethylbenzene	CCl_4	K	99, 75
Fluoranil	Alkylbenzenes	CCl_4	$K\,\Delta H^\circ$	100
2,3-Dichloro-5,6-dicyano-*p*-benzoquinone	Aromatic hydrocarbons		K	101
1,4-Naphthoquinones	Aromatic hydrocarbons	CH_2Cl_2	$K\,\Delta H^\circ\,\Delta S^\circ$	33

The electron affinity (E^A) of a given molecule provides a quantitative estimate of this tendency, and as a consequence considerable effort has been expended in attempts to determine values of the electron affinities of quinones. Unfortunately, direct estimates of these quantities are notoriously difficult to obtain. However, indirect estimates of the relative magnitudes of the electron affinities of series of related quinones can easily be estimated. As indicated above, one such method involves a study of the charge-transfer energy of the quinone-donor system, using the relationship[13,14] described by equation (4):

$$h\nu_{CT} = I^D - C_1 + C_2/(I^D - C_1) \tag{4}$$

For a series of complexes of the same type, C_2 is nearly constant, and C_1 may be approximated by the expression

$$C_1 = E^A + 4{\cdot}3 \text{ (eV)} \tag{8}$$

By plotting values of charge-transfer energy against I^D for a single acceptor with a series of donors, C_1 and thereby E^A may be determined. A value for the electron affinity of chloranil of 1·35 eV has been reported by this method[102].

A second approach uses the approximation

$$h\nu_{CT} = I^D - E^A + C \tag{5}$$

where C is a constant. This expression holds approximately for weak EDA interactions and implies that the changes in band positions of a given donor with a series of acceptors is a linear function of the electron affinity of the acceptor. In a simple application, for two acceptors, i and j:

$$h\nu_j - h\nu_i = E_i^A - E_j^A \tag{9}$$

and it therefore becomes possible to obtain values of electron affinities relative to some arbitrary reference acceptor. Based on a value of 1·8 eV for the electron affinity of iodine[103], an E^A of 2·6 eV for chloranil has been reported[104]. Essentially the same method has been used by Davis, Hammond and Peover[105]. Here, however, *p*-benzoquinone was used as the reference acceptor for which a direct magnetron determination of the electron affinity was available[62], giving a value of 1·40 eV. Values of the electron affinities for various mono-substituted quinones determined in this way are given in Table 6. Farragher and Page[62] have attempted to make direct determinations of the electron affinities of a number of quinones by the magnetron technique. Direct electron capture was, however, only observed for *p*-benzoquinone ($E^A = 1{\cdot}37 \pm 0{\cdot}08$ eV), chloranil ($E^A = 2{\cdot}45 \pm 0{\cdot}26$ eV) and possibly monofluoro-*p*-benzoquinone.

TABLE 6. Electron affinities of monosubstituted *p*-benzoquinones (E^A) based on electron affinity of 1·40 eV for *p*-benzoquinone[a]

Substituent	E^A/eV	Substituent	E^A/eV
$-NO_2$	2·06	$-Br$	1·59
$-CN$	1·83	$-I$	1·56
$-CF_3$	1·67	$-Ph$	1·48
$-CH_3CO$	1·65	$-H$	1·40
$-COOCH_3$	1·60	$-CH_3$	1·36
$-F$	1·52	$-OCH_3$	1·26
$-Cl$	1·58	$-N(CH_3)_2$	1·03

[a] Reproduced with permission from K. M. C. Davis, P. R. Hammond and M. E Peover, *Trans. Faraday Soc.*, **61**, 1516 (1965).

Electron affinities for some substituted naphthoquinones[34] obtained by the comparison technique, using chloranil ($E^A = 2{\cdot}46$ eV) as the reference acceptor[62], are listed in Table 7. Tetracyanoquinodimethane (TCNQ) has also been used as a reference acceptor, with an electron affinity of 1·7 eV[102], to obtain values of $1{\cdot}75 \pm 0{\cdot}05$ and $1{\cdot}99 \pm 0{\cdot}05$ eV for 2,3-dicyano-*p*-benzoquinone and 2,3-dicyano-5,6-dichloro-*p*-benzoquinone (DDQ) respectively[37].

TABLE 7. Electron affinities (E^A) of substituted 1,4-naphthoquinones[a] (based on an E^A for chloranil of 2·46 eV)

1,4-Naphthoquinone	E^A/eV
2,3-Dichloro	2·05
2,3-Dichloro-5-nitro	2·24
2,3-Dicyano	2·74
2,3-Dicyano-5-nitro	2·78

[a] From reference 34.

A second approach, which also yields relative orders of magnitude for electron affinities, is based on a molecular orbital treatment of EDA complexation[106-109]. Essentially, in this method, the energy of the charge-transfer transition of a given complex is equated to the difference between the energy of the lowest-unoccupied orbital of the acceptor ($\mathscr{E}^A = -E^A$)

and the highest-occupied orbital of the donor ($\mathscr{E}^{D}$). The charge-transfer energy may then be expressed as

$$h\nu_{CT} = \mathscr{E}^{A} - \alpha - \chi\beta \tag{10}$$

where α is the coulomb integral and χ is a function of $\mathscr{E}^{D}$. When $h\nu_{CT} = 0$ therefore

$$\mathscr{E}^{A} = -E^{A} = \alpha + \chi\beta \tag{11}$$

By plotting calculated values of χ against $h\nu_{CT}$ for a series of donors with a given acceptor, a straight-line graph is obtained having gradient $-1/\beta$ and intercept for $h\nu_{CT} = 0$ of $(\mathscr{E}^{A} - \alpha)/\beta$. In this way a value can be obtained for β in the expression

$$-\mathscr{E}^{A} = \alpha + \chi\beta \tag{12}$$

which allows an estimate to be made of the relative order of magnitude of the electron affinities for a series of acceptors. The method assumes that α is constant throughout such a series, and suffers from the inaccuracies inherent in any extrapolative method. Berger[110] has, however, applied this method to some quinone complexes, obtaining the results shown in Table 8.

TABLE 8. Estimated energies of the lowest unoccupied molecular orbital of some electron acceptors[a]

Acceptor	Energy of lowest unoccupied molecular orbital[b]
Tetracyanoquinodimethane	$\alpha + 0{\cdot}133 \pm 0{\cdot}08$
Bromanil	$\alpha + 0{\cdot}287 \pm 0{\cdot}20$
Chloranil	$\alpha + 0{\cdot}430 \pm 0{\cdot}10$
Iodanil	$\alpha + 0{\cdot}468 \pm 0{\cdot}15$

[a] From reference 110.
[b] α = coulomb integral.

The $h\nu_{CT}$ values for the complexes with two common donor species are given in Table 9. Disagreements between the valence-bond and molecular-orbital approach have also been noted for polynitrophenanthrenequinone acceptors[111].

A study of the luminescence spectra of quinone EDA complexes with methylbenzene donors[112] suggests the following relative order of electron affinities; fluoranil > hexafluoro-1,4-naphthoquinone > octafluoro-9,10-anthraquinone.

TABLE 9. Energies of the charge-transfer band ($h\nu_{CT}$) for some naphthalene and pyrene EDA complexes[a]

Acceptor	$h\nu_{CT}$/eV	
	Naphthalene	Pyrene
Tetracyanoquinodimethane	2·22	1·62
Bromanil	2·59	2·01
Chloranil	2·64	2·03
Iodanil	2·70	2·05

[a] From reference 110.

In the absence of more direct methods, possibly the most reliable estimates of acceptor electron affinities are to be obtained from polarographic studies. Under conditions where reversible, one-electron additiou to an acceptor A is observed, the process

$$A + e^- \rightleftharpoons A^-$$

yields an observable half-wave reduction potential ($E_{\frac{1}{2}}$) which, to a good approximation, is equal to the standard one-electron reduction potential (E_1). For aromatic hydrocarbons there is a linear relationship between E_1 and the electron affinity of the molecule[113]. This relationship has been discussed by other authors[114,115], and extended by Peover[116,117] to the quinone series in particular. Using calculated estimates of the energy of the lowest-unoccupied quinone molecular orbitals[118] a linear correlation was shown to hold between these values and the measured $E_{\frac{1}{2}}$ in aprotic solvents[119]. It was also evident from similar correlations for the second half-wave reduction potential corresponding to the process

$$A^- + e^- \rightleftharpoons A^{2-}$$

that the second electron is placed in the same molecular orbital as the first. The relation

$$h\nu = 2E_{\frac{1}{2}} + C \tag{13}$$

where C is a constant and $h\nu$ is the energy of a given electronic absorption has been shown[120] to hold for aromatic hydrocarbons, and for the quinones it has been demonstrated[121] that the measured $E_{\frac{1}{2}}$ is a linear function of the $n \rightarrow \pi^*$ excitation energy. It therefore seems reasonable to base a second method for the comparison of electron affinities, again relative to that for some arbitrary reference compound, on the relation

$$E_i^A - E_{ref}^A = E_{\frac{1}{2}i} - E_{\frac{1}{2}ref} \tag{14}$$

Peover[117,122] has argued that the relation

$$h\nu_{CT} = I^D - E_1 + (\Delta E_{sol} - \phi_{Hg} - E^0_{Hg:Hg^{2+}} - C) \qquad (15)$$

should hold to a good approximation for EDA complexes, where ΔE_{sol} is the solvation energy for the process

$$A^-_{(gas)} + A_{(sol)} \longrightarrow A_{(gas)} + A^-_{(sol)}$$

ϕ_{Hg} is the work function of mercury, and $E^0_{Hg:Hg^{2+}}$ is the absolute value of the saturated calomel electrode. A linear relation between estimates of E_1 and the charge-transfer absorption band was demonstrated for a series of quinones, and by estimating the likely contribution to $h\nu_{CT}$ from $\Delta E_{(sol)}$ for complexes with pyrene and *N,N,N',N'*-tetramethyl-*p*-phenylenediamine, probable upper and lower limits for the electron affinities of a number of quinones were obtained[122] (Table 10).

TABLE 10. Probable limits for the electron affinities (E^A) of quinone acceptors from charge-transfer absorption energies ($h\nu_{CT}$) and measured half-wave reduction potentials ($E_{\frac{1}{2}}$)[a]

Quinone	$E_{\frac{1}{2}}$/V [b]	$h\nu_{CT}$/eV (in dichloromethane)		E^A/eV	
		Pyrene	TMPD	Upper limits	Lower limits
9,10-Anthraquinone	−0·94	—	2·29	1·03	0·33
1-Hydroxy-	−0·77	...	2·12	1·20	0·50
1,8-Dihydroxy-	−0·64	...	1·87	1·33	0·63
1,4-Naphthoquinone	−0·71	...	2·10	1·26	0·56
2-Hydroxy-	−0·64	2·85	—	1·33	0·63
5-Hydroxy-	−0·52	—	1·89	1·45	0·75
9,10-Phenanthraquinone	−0·66	...	2·08	1·31	0·61
1,2-Naphthoquinone	−0·56	2·81	—	1·41	0·71
1,4-Benzoquinone	−0·51	2·74	1·89	1·46	0·76
Methyl-	−0·58	2·84	—	1·39	0·69
2,5-Dimethyl-	−0·67	2·93	2·10, 1·94	1·30	0·60
Chloro-	−0·34	2·51	1·67	1·53	0·83
2,6-Dichloro-	−0·18	2·32	1·52	1·79	1·09
2,5-Dichloro-	−0·18	2·32	—	1·79	1·09
Trichloro-	−0·08	2·15	1·48	1·89	1·19
Tetrachloro-	0·01	2·03	—	1·98	1·28
Tetrabromo-	0·00	2·03	...	1·97	1·27
DDQ	0·51	1·51	...	2·48	1·78

[a] Reproduced with permission from M. E. Peover, *Trans. Faraday Soc.*, **58**, 1656 (1962).

[b] Measured against saturated calomel electrode, from reference 116.

Care, however, has to be exercised in cases where hydrogen bonding may occur: hydroxy-naphthoquinones and hydroxy-anthraquinones exhibit anomalous $E_{\frac{1}{2}}$ values, due probably to intramolecular hydrogen bonding in aprotic solvents. In protic solvents the $E_{\frac{1}{2}}$ values for quinones generally are markedly affected by hydrogen bonding to the solvent[116]. The polarographic method has also been used to estimate affinities of polynitrophenanthrenequinones[111] (Table 11). Values based on the use of

TABLE 11. Half-wave reduction potentials and electron-affinities of polynitrophenanthrenequinones[a]

Acceptor	$E_{\frac{1}{2}}$(V S.C.E.)[b]	E^A/eV (Polarography)	E^A/eV (From CT band)
Phenanthrenequinone	−0·660	0·69	0·70
2,4,7-Trinitro-	−0·098	1·29	1·26
3,6-Dinitro-	−0·150	1·23	1·12
2,7-Dinitro-	−0·195	1·19	1·04
2,5-Dinitro-	−0·265	1·11	0·98

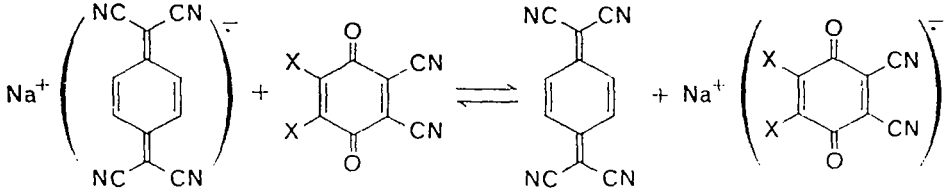
[a] From reference 111.
[b] *N*-*t*-butyl perchlorate used as supporting electrolyte.

the equation

$$h\nu_{CT} = I^D - E^A + C \tag{5}$$

and using 2,4,7-trinitrofluorenone as the reference acceptor, taking an E^A for this compound of 0·94 eV from a polarographic determination[111] are also quoted.

A technique which has been applied relatively recently to this problem involves a study of electron transfer between radicals in solution. The equilibrium constant for the reaction



may be expressed by the relation[123]:

$$-RT\ln K = E^A(\text{TCNQ}) - E^A(\text{quinone}) + \Delta\Delta G^{\ominus}_{solv}(\text{TCNQ, TCNQ}^{\cdot-})$$
$$= \Delta\Delta G^{\ominus}_{solv}(\text{quinone, quinone}^{\cdot-}) \tag{16}$$

in which $\Delta\Delta G^{\ominus}_{solv}$ is the difference in free energy of solvation between the

appropriate acceptor and its anion radical. If the two last terms are considered to be equal, then

$$-RT\ln K = E^{A}(\text{TCNQ}) - E^{A}(\text{quinone}) \tag{17}$$

For 2,3-dicyano-*p*-benzoquinone (X = H) and 2,3-dicyano-5,6-dichloro-*p*-benzoquinone (X = Cl) values of K were determined spectrophotometrically in acetonitrile at $20 \pm 1°$ of 30 and ~ 2000 respectively, yielding the relationships

$$E^{A}(\text{TCNQ}) - E^{A}(\text{2,3-dicyano-}p\text{-benzoquinone}) = -0{\cdot}09 \text{ eV} \tag{18}$$

and

$$E^{A}(\text{TCNQ}) - E^{A}(\text{2,3-dicyano-5,6-dichloro-}p\text{-benzoquinone}) = -0{\cdot}19 \text{ eV} \tag{19}$$

These types of study have led to a number of qualitative observations regarding the effect of substituent groups on the EDA complexing ability of an acceptor, and hence by inference on the electron affinity of the acceptor. Hammond[124] has reported a detailed study of monosubstituted quinones from which it is apparent that the electron affinity varies in relation to the Hammett σ_p values. Lepley and Thelman[125] have also discussed the effect of substituent groups in this context. It was generally concluded that the electron affinity of conjugated organic acceptor species will increase: (i) with the electron-withdrawing ability of the substituent; (ii) with the number of substituents present, depending on their respective positions in the molecule; (iii) the extent of conjugation in the molecule, ethylenic compounds being, for example, better acceptors than aromatic compounds. With particular reference to the quinone series, these observations require slight modification, in that the more powerful a quinone acceptor, the less pronounced is the effect of an extra substituent. This has been demonstrated for the naphthoquinone and benzoquinone series, the effect being more apparent for the latter compounds[34].

It will be clear from the foregoing pages that current knowledge of electron affinities of these organic species is not substantial. Relative orders of magnitude for acceptors of a given series, such as the quinones, are probably known with reasonable accuracy, particularly if estimated by the polarographic method. When measurements of absolute values are attempted however, large errors are likely to be encountered, since all such determinations depend on the accuracy to which the electron affinity of the reference compound is known. For this reason, therefore, such values quoted throughout this chapter have not been collected together in a single

table. Of all the determinations available, those of Farragher and Page[62] for *p*-benzoquinone and chloranil by the magnetron method are probably the best to date.

D. Solid Electron Donor–Acceptor Complexes

Solid complexes may generally be prepared by mixing solutions of the quinone and electron donor. Judicious choice of solvent will often lead to the direct precipitation of the complex. Purification may be achieved by recrystallization from hot solvent although in many cases where quinones of high electron affinity are mixed with donors of low ionization potential it is often preferable to avoid elevated temperatures. Slow evaporation of solvent will often provide good crystals. There is no obvious correlation between the ease of isolating a solid complex and the stability of the complex in solution.

1. Crystal structures

The crystal structures of a number of solid complexes of quinones with π-donors have been determined by X-ray diffraction (Table 12). In many systems where there is no hydrogen-bonding the complexes have a D : A stoicheiometry of 1 : 1. These are arranged in stacks of alternate D and A molecules, the molecules in a stack being parallel or near parallel (i.e. a zero or small intermolecular dihedral angle), with an average perpendicular intermolecular distance which is somewhat less than the van der Waals separation. In cases where the stoicheiometry is AD_2, the stacks usually contain the sequence –A–D–D–A–D–D–A–. In such arrangements the stacks are usually discontinuous in the sense that the molecules are grouped in D–A–D triads as might be expected. Examples of this are the 1 : 2 complexes of *p*-benzoquinone with phenol[135], with *p*-chlorophenol[136] and with *p*-bromophenol[136]. Within the stack the quinone molecule is by no means always centrally above the donor molecule (see also section III). For maximum charge-transfer interaction between *p*-benzoquinones and benzene donors a stacking angle of zero would be expected in which the donor and acceptor eclipse one another.

There appear to be two general arrangements of the molecules in one stack relative to those in adjacent stacks. Either the molecules in all stacks are coplanar (or near coplanar) or else the molecules in one stack are set at an angle to those in the adjacent stack (herring bone). The latter pattern appears in many systems in which there is hydrogen bonding (see section III). However, in these and other complexes the effects of other localized interactions may be observed. For example, for crystals of

TABLE 12. Some quinone complexes for which crystal structures have been determined

Acceptor	Donor	Notes	Ratio A : D	Dihedral angle	A–D distance (Å)	Reference
p-Benzoquinone	Hydroquinone	[a]	1 : 1	3·5°	3·22	135, 143
p-Benzoquinone	Hydroquinone	[b]	1 : 1	2·0°	3·19	239
p-Benzoquinone	*p*-Chlorophenol		1 : 1	3·0°	3·27 3·35	243
p-Benzoquinone	*p*-Bromophenol		1 : 1			243
p-Benzoquinone	*p*-Chlorophenol		1 : 2	6·0°	3·2	136
p-Benzoquinone	*p*-Bromophenol		1 : 2			136
p-Benzoquinone	Phenol		1 : 2	4·5°	3·23	135
p-Benzoquinone	Resorcinol		1 : 1	7·3°	3·1	138
p-Benzoquinone	Phloroglucinol		2 : 1	2·4 to 9·2°	3·18	241
p-Benzoquinone	Thymine		1 : 1	6·2°	3·16	137
Chloranil	Hexamethylbenzene		1 : 1	2·1°	3·5	126, 127, 128
Chloranil	Bis-(8-hydroxyquinolinato)-palladium(II)		1 : 1			308
Chloranil	8-Hydroxyquinoline		1 : 2			309
Chloranil	*N,N,N′,N′*-Tetramethylbenzidine	[c]	1 : 2	nearly 0°	3·162	139
Fluoranil	Perylene		1 : 1	within 1°	3·23	129

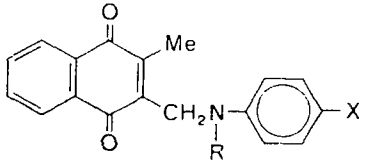
Chloranil	*N,N,N′,N′*-Tetramethyl-*p*-phenylenediamine	[c]	1 : 1	3·28	142, 143
Bromanil	*N,N,N′,N′*-Tetramethyl-*p*-phenylenediamine	[f]	1 : 1	3·31	132
7,7,8,8-Tetracyanoquinodimethane	*N,N,N′,N′*-Tetramethyl-*p*-phenylenediamine	[f]	1 : 1	3·27	144
7,7,8,8-Tetracyanoquinodimethane	Ditoluenechromium	[f]	1 : 1		145
7,7,8,8-Tetracyanoquinodimethane	Ditoluenechromium	[f]	1 : 2		133
7,7,8,8-Tetracyanoquinodimethane	Benzidine	[g]	1 : 1		134

[a] Monoclinic quinhydrone.
[b] Triclinic quinhydrone.
[c] Donor twisted. The structure of the corresponding 1 : 1 complex has also recently been determined (H. Kuroda, unpublished work). In this case the two rings of the donor are virtually coplanar.
[d] Self-complex.
[e] 'Monoclinic' lattice.
[f] Ionic lattice.
[g] Contains 1·8 molecules of dichloromethane per donor–acceptor pair.

p-benzoquinone-thymine which show the essential quinhydrone-like structure[137], the shortest interlayer intermolecular atomic distance is 3·19 Å between an oxygen atom in thymine and a carbonyl carbon atom in the quinone. A similar observation has been made in the *p*-benzoquinone-resorcinol complex[138]. This may represent a localized interaction and may account for the relatively large intermolecular dihedral angle in these complexes.

The structure of the 1 : 2 complex of chloranil with *N*,*N*,*N*′,*N*′-tetramethylbenzidine[139] comprises distinct groups in which one chloranil molecule is sandwiched between two benzene rings from two molecules of the donor. The second ring of each donor molecule is twisted 30·8° out of planarity relative to the other ring of the molecule. The structure of the corresponding 1 : 1 complex is at present being determined by Kuroda and coworkers.

Recently Prout and Castellano[140] have determined the structure of the self-complex of 2-methyl-3-*N*-methylanilinomethyl-1,4-naphthoquinone (**6a**), synthesized by Ledwith and coworkers[141]. This molecule contains a



(6)

	R	X
a	Me	H
b	Me	Cl
c	H	H
d	H	Me
e	H	CO_2Me

donor and an acceptor moiety separated by an 'insulating' methylene group. In the crystal lattice the molecules are placed to form stacks of alternate donor and acceptor groups in the manner of complexes formed from donors and acceptors in separate molecular species. The arrangement of molecules as seen projected down the *c*-axis is shown in Figure 5 (see also section II.E).

Certain neutral molecular species of donor and acceptor interact with complete electron-transfer to form lattices of ions. Some examples are listed in Table 12. Whereas the complexes of chloranil and bromanil with *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine[142, 143], though essentially ionic in character (see section II.D.4), follow the normal pattern of stacks of alternate components, other complexes, such as that formed from TCNQ and *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine[141] (Figure 6) or ditoluene-chromium[145], consist of alternate stacks of the two ionic species.

References to other structures involving hydrogen-bonding and metal-containing donors are made in sections III and IV respectively. For more

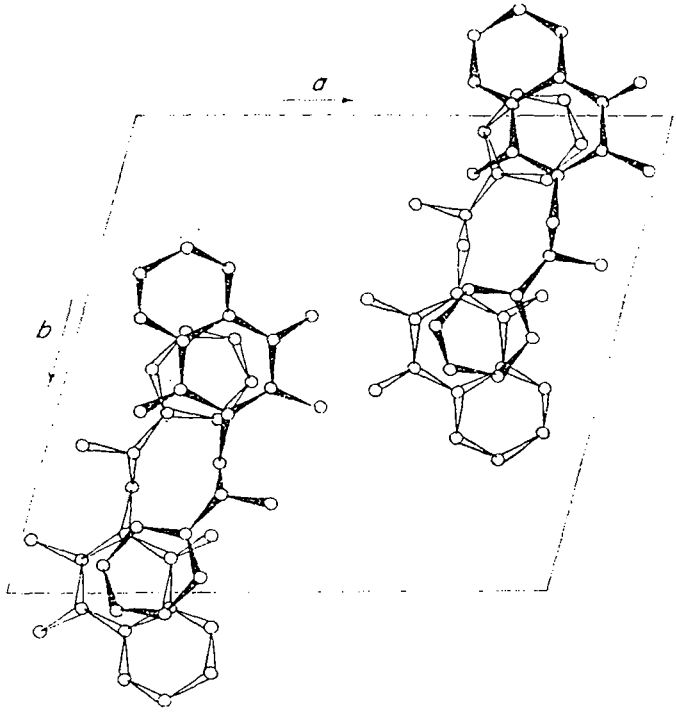


FIGURE 5. The crystal structure of 2-methyl-3-methylanilinomethyl-1,4-naphthoquinone projected down *c*. For clarity only the four molecules forming one unit-cell are shown. Reproduced with permission from C. K. Prout and E. Castellano, *J. Chem. Soc.* (*A*), 2775, Figure 1 (1970).

detailed descriptions of these and other systems and their relation to the structures of other EDA complexes, various reviews should be consulted[146–149].

2. Electronic absorption spectra

The electronic absorptions of solid complexes are often very similar to the corresponding absorptions in solution in an aprotic solvent as far as the lowest energy intermolecular charge-transfer transitions are concerned[46, 150]. On the other hand, with some quinone–donor interactions, there is no resemblance between the spectra in the two phases[46, 150–152]. In such cases the difference is generally attributed to complete electron-transfer in the solid phase, whereas in aprotic solvents a non-ionic molecular complex may persist. Evidence for such ionic solids includes their infrared absorption and their electrical and magnetic properties (see sections II.D.3 and II.D.4).

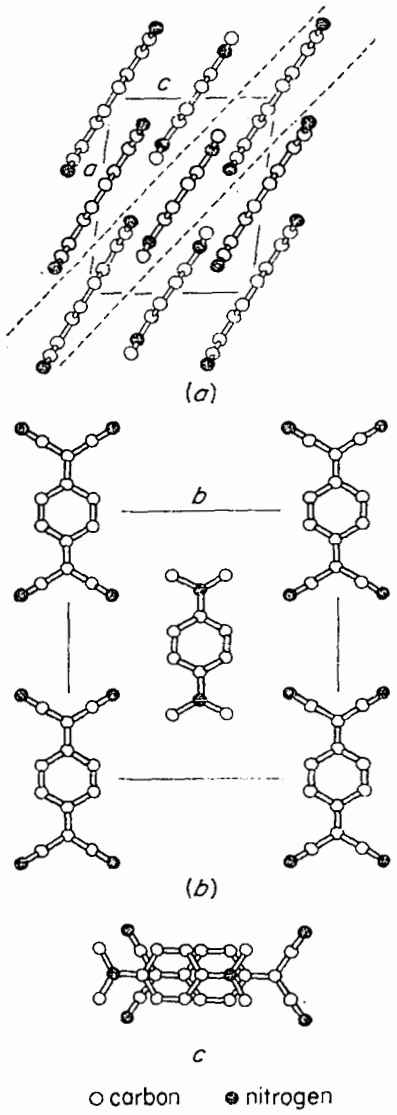


FIGURE 6. The crystal structure of the 7,7,8,8-tetracyanoquinodimethane–*N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine complex: (*a*) viewed along *b*, the heavily outlined molecules lie at $y = \frac{1}{2}$ and the rest at $y = 0$, the dotted lines define a sheet of molecules; (*b*) a sheet of molecules in plan; (*c*) overlapping molecules, viewed normal to their plane. Reproduced with permission from A. W. Hanson, *Acta Cryst.*, **19**, 610, Figure 3 (1965).

Single crystals of solid quinone complexes had been shown in 1952 by Nakomoto[153] to have a stronger absorption corresponding to the lowest-energy charge-transfer transition when polarized light with the electric vector perpendicular to the plane of the component molecules was used, compared with light polarized parallel to the molecular planes. It has since been shown that for benzoquinone and benzenoid components, the direction of maximum effect is the line joining the centres of the donor and acceptor in the complex, rather than the perpendicular to the molecular planes[154]. The polarization of this absorption has provided a strong argument for the intermolecular charge-transfer nature of the absorption[46,151-160]. This observation usually holds true for the lowest energy charge-transfer transition in solid quinone complexes[151,152]. Higher energy transitions, though in many cases intermolecular charge-transfer in nature, appear to involve mixing with local excitation in one or other component. This often leads to a diminished polarization. Thus in the fluoranil–perylene complex[155], the 14,200 cm^{-1} band has a polarization ratio in the sense indicated above for a first charge-transfer transition of >50, whereas the band at 28,700 cm^{-1} has a polarization ratio of ~ 2. In this case the higher energy band has been assigned as an intermolecular charge-transfer band with mixing of a $\pi \rightarrow \pi^*$ transition in perylene. In carbon tetrachloride solution the fluoranil–perylene complex shows only one charge-transfer band (at 14,400 cm^{-1}). By contrast, the fluoranil–pyrene complex shows two absorption bands in carbon tetrachloride solution (at 17,000 and 23,000 cm^{-1}) but only one band in the solid (16,800 cm^{-1}). It is suggested that the second transition is symmetry forbidden in the solid[155].

In solid chloranil-1,6-diaminopyrene, the lowest energy bands are observed at 18,500 and 24,500 cm^{-1} with opposing polarizations[158]. In solution in chloroform the same complex has absorption maxima at 9900 and 19,000 cm^{-1}. It appears that the lowest charge-transfer band is absent in the solid. By comparison, the two lowest bands of the corresponding bromanil complex in the solid (~ 7000 and $\sim 20{,}000$ cm^{-1}) agree well with those in chloroform solution (9260 and $\sim 19{,}000$ cm^{-1}) and likewise for the iodanil complex. It has been suggested[158] that the arrangement of donor and acceptor molecules in the chloroanil complex may be as in model *a* (Figure 7) for which calculations indicate that there is favourable overlap for charge-transfer from the a_u orbital of the donor but not that from the highest filled orbitals which are of b_g symmetry. Model *b* (Figure 7), where the opposite situation is favoured, could then represent the situation of the bromanil and iodanil complexes. The actual structure of these complexes has yet to be determined. The spectra of the

crystalline complexes of chloranil and TCNQ with benzidine and *N,N,N′,N′*-tetramethylbenzidine[156] each show two bands, both of which have been assigned to intermolecular charge-transfer transitions. The polarization of the second band is reversed by comparison with the lower energy transition. It has been suggested that the first band arises from a

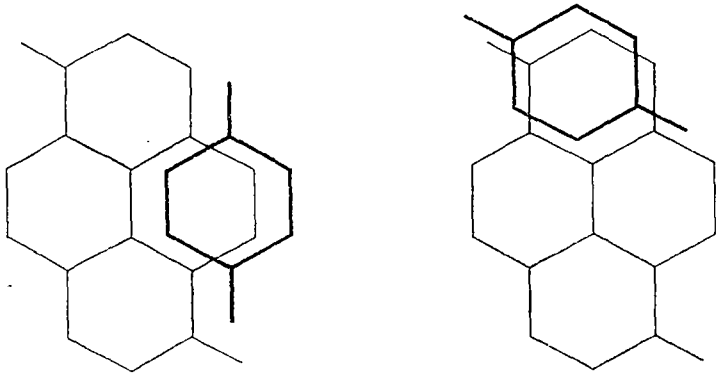


FIGURE 7. Models for the stacking of molecules of quinone–1,6-diaminopyrene complex. After reference 158.

transition from the highest filled level in the donor to the *nearest* acceptor molecule in the crystal lattice, whilst the second transition corresponds to a transition from the second highest filled level in the donor to the next nearest acceptor molecule. The crystal structure of the TCNQ–benzidine complex is at present being determined. This particular donor–acceptor pair is capable of forming inclusion compounds with certain molecules such as dichloromethane, dibromomethane and acetone[161].

Fluorescence spectra of the solid crystalline complexes of chloranil and of 2,5-dichloro-*p*-benzoquinone with durene have been measured[162]. The maxima correspond closely to the same systems measured in an *n*-propyl ether–isopentane glass at $-190°$ [64] and show the same mirror symmetry with the first absorption band.

3. Infrared spectra

In cases where only weak EDA complexes are formed, the infrared spectrum of the complex is essentially the sum of the spectra of the component molecules although some differences are to be expected and

are observed[163-168]. The most important of these is the red-shift of the carbonyl band of the quinone[166-168]. A red-shift of the —C=C— stretching frequency has also been observed. This has been taken as evidence of a degree of charge-transfer in the ground state (see section II.D.4). The spectrum of the chloranil–hexamethylbenzene complex is

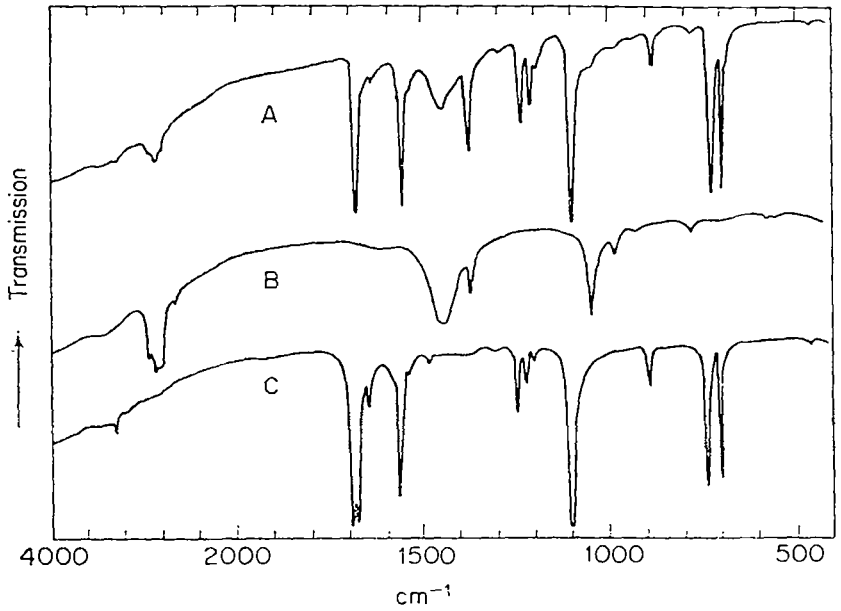


FIGURE 8. Infrared absorption spectra of powders in KBr disks: (A) chloranil–hexamethylbenzene complex; (B) hexamethylbenzene; (C) chloranil. Reproduced with permission from H. Yamada and M. Kawamori, *Spectrochim. Acta*, **27A**, 2425, Figure 1 (1971).

compared in Figure 8 with the absorption of the components[166]. The various absorptions corresponding to Figure 8 together with their assignments are listed in Table 13. Larger shifts are observed in quinones with phenols and hydroquinones. In these complexes hydrogen bonding as well as EDA complexing occurs.

Polarized infrared absorption spectra of single crystals of chloranil-hexamethylbenzene have been obtained recently[166] (Figure 9). The two components are stacked in columns almost perpendicular to the *a*-axis. Each component has a site symmetry C_i and consequently the *g*-vibrations should be, and in fact are, inactive in the complex. The details of the polarized spectra are summarized in Table 14. It is seen that many of the 'in-plane' absorption bands increase in intensity on complex formation in

TABLE 13. Infrared spectra of chloranil–hexamethylbenzene (HMB) complex, chloranil and HMB in KBr disks (cm^{-1}) [a]

Chloranil–HMB complex	Chloranil	Assignment	HMB	Assignment	
3336 vw	3355 w	Combination		[b]	
2996 w			2997 m	In	C—H Stretch
2924 m			2922 ms	In + out	C—H Stretch
2868 m			2867 m	In	C—H Stretch
2730 vw			2722 w		
1683 s	1695 vs 1683 vs	b_{1u} C=O Stretch			
1643 w	1651 m				
1561 s	1572 s	b_{2u} C=C Stretch			
1540 w	1548 w				
	1491 w				
1462 m			1460 ms	Out	CH_3 Deform.
1453 m			1453 ms	In	CH_3 Deform.
1387 m			1378 m	In	C_6 Skeleton
1308 w	1317 vw				
1250 m	1258 m	b_{1u} C—C Stretch			
1228 m	1236 m	b_{2u} C—C Stretch			

1206 w	1210 w				
1164 vw					
1110 s	1112 vs 1108 vs	b_{1u} C—Cl Stretch			
1075 w					
1060 w			1057 ms	In	CH_3 Deform.
			1046 (sh)	In	
993 w			995 w	Out	CH_3 Deform.
953 vw					
902 m	906 m				
794 w			795 w		
741 s	755 s	b_{2u} C—Cl Stretch			
711 s	715 s				
700 (sh)	706 w				
			592 vw		
			575 vw		
473 vw	471 vw				

[a] Reproduced with permission from H. Yamada and M. Kawamori, *Spectrochim. Acta*, **27A**, 2425 (1971).
[b] In: in-plane vibration; out: out-of-plane vibration.

the 'out-of-plane' direction (i.e. parallel to the *a*-axis). It is suggested that this enhancement is the result of delocalization moments due to electronic rearrangement during vibration of the complex—an idea previously considered in the case of halogen–aromatic hydrocarbon complexes[169, 170].

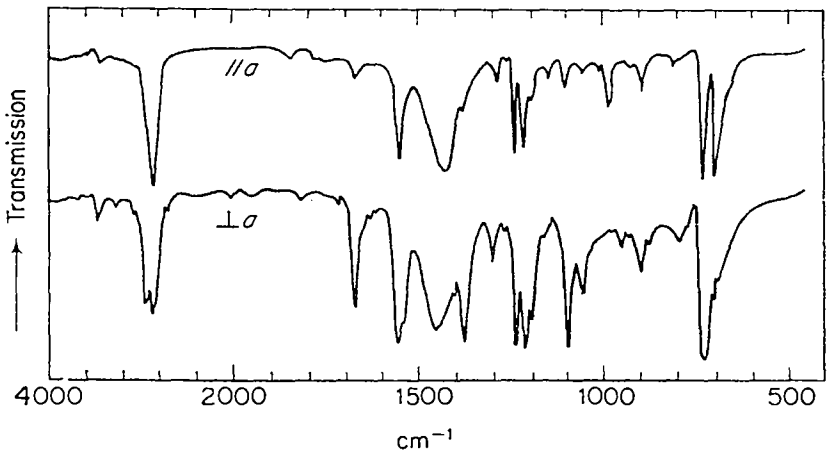


FIGURE 9. Polarized absorption spectra of a single crystal of the chloranil–hexamethylbenzene complex; (A), ||*a*, light polarized along *a*-axis (stacking axis); (B) ⊥*a* light polarized perpendicular to *a*-axis. Reproduced with permission from H. Yamada and M. Kawamori, *Spectrochim. Acta*, **27A**, 2425, Figure 2 (1971).

In contrast, those adducts which are formed by complete electron-transfer from the donor to the acceptor closely resemble the sum of the absorptions of the corresponding cation (D^+) and anion (A^-). This radical difference in the infrared spectra of the non-ionic and ionic complexes has been used frequently to determine the type of complex[171–175]. Some examples of these two types are given in Table 15.

4. Electrical properties

Quinones, and more particularly their EDA complexes, form part of the class of organic semiconductors. Although detailed accounts of the theory of semiconductors can be found elsewhere[176], a brief introduction is given here. In experimental terms, the resistivity (ρ) of a semiconductor is observed to vary with temperature, according to the expression

$$\rho_T = \rho_0 \exp(E_a/kT) \tag{20}$$

where E_a is the 'activation energy' for conduction and T is the absolute temperature. Semiconductors act as insulators at low temperatures, but

become increasingly conducting as the temperature is raised. In simple terms, in a metallic conductor the outer or valence electrons are readily separated from the parent metal atom and are able to move freely throughout the crystal, thereby carrying electrical current. In an insulator,

TABLE 14. Polarized infrared spectra of single crystal of chloranil–hexamethylbenzene complex (cm^{-1})[a]

∥ *a*-Axis	⊥ *a*-Axis		Assignment	
	3318 w	In[b]	C[c]	Combination
	2995 s	In	H	C—H Stretch
2947 vs	2923 s	In + out	H	C—H Stretch
	2872 m	In	H	C—H Stretch
1680 w	1679 s	In	C	C=O Stretch
	1635 w	In	C	
1555 s	1554 vs	In	C	C=C Stretch
1460 (sh)	1457 s	In	H	CH_3 Deform.
1440 s		Out	H	CH_3 Deform.
1390 w	1382 s	In	H	C_6 Skeleton
1298 w	1305 m		C, H	
1246 s	1245 s	In	C	C—C Stretch
1223 m	1222 s	In	C	C—C Stretch
1202 w	1201 m	In	C	
1113 w	1109 s	In	C	C—Cl Stretch
1059 w	1059 m	In	H	CH_3 Deform.
992 m	990 vw	Out	H	
899 m	900 m	In	C	
799 vw	799 w	In + out	H	
740 s	737 vs	In	C	C—Cl Stretch
709 s	711 m	Out	C	
701 (sh)	697 w		C	

[a] From reference 166.
[b] In: in-plane vibration; out: out-of-plane vibration.
[c] C: Chloranil vibration; H: HMB vibration.

on the other hand, the electrons are all tightly held by the atoms in the crystal matrix and conduction in this manner is not possible. The situation with regard to a semiconductor is in some ways intermediate between these two extreme cases. At low temperatures all the electrons are tightly bound to the atoms. As the temperature increases, however, some electrons are thermally excited to an energy state in which it is possible for the electron to move through the crystal. The process in some ways therefore is akin to ionization, although crystal forces render the energy requirements

TABLE 15. Infrared spectra of some *p*-benzoquinone complexes[a]

p-Benzoquinone	Donor (A : D)	Infrared[b]
2,3-Dichloro-5,6-dicyano-	Dibenzo[*c*,*d*]phenothiazine (1 : 2)	Ionic
2,3-Dichloro-5,6-dicyano-	1,6-Diaminopyrene	Ionic
2,3-Dibromo-5,6-dicyano-	Dibenzo[*c*,*d*]phenothiazine (2 : 3)	Ionic
Tetrachloro-	1,6-Diaminopyrene	Mol.
Tetrabromo-	1,6-Diaminopyrene	Mol.
2,3-Dichloro-5,6-dicyano-	Benzo[*c*]phenothiazine	Ionic
2,3-Dichloro-5,6-dicyano-	Dibenzo[*c*,*d*]phenothiazine	Ionic
2,3-Dichloro-5,6-dicyano-	Dibenzo[*c*,*d*]phenoselenazine	Ionic
Tetrachloro-	Tetramethyl-*p*-phenylenediamine	Ionic
Tetrachloro-	Durenediamine	Ionic
Tetrabromo-	Durenediamine	Ionic
2,3-Dichloro-5,6-dicyano-	Phenothiazine	Ionic
2,3-Dichloro-5,6-dicyano-	Phenoselenazine	Ionic
2,3-Dibromo-5,6-dicyano-	Phenothiazine	Ionic
2,3-Dibromo-5,6-dicyano-	Benzo[*c*]phenothiazine	Ionic
2,3-Dibromo-5,6-dicyano-	Dibenzo[*c*,*d*]phenoselenazine	Ionic
Tetrabromo-	Tetramethyl-*p*-phenylenediamine	Ionic
2,3-Dichloro-5,6-dicyano-	*N*-Methylphenothiazine	Ionic
2,3-Dibromo-5,6-dicyano-	*N*-Methylphenothiazine	Ionic
2,3-Dibromo-5,6-dicyano-	Phenoselenazine	Ionic
Tetrachloro-	*p*-Phenylenediamine	Ionic
2,3-Dichloro-5,6-dicyano-	*p*-Phenylenediamine	Ionic ?
2,3-Dichloro-5,6-dicyano-	Perylene	Mol.
Tetrachloro-	Tetramethylbenzidine	Mol.
Tetrachloro-	Dimethylaniline	Mol.
Tetrachloro-	Perylene	Mol.
Tetrabromo-	Tetramethylbenzidine	Mol.
2,3-Dibromo-5,6-dicyano-	Perylene	Mol.
2,3-Dibromo-5,6-dicyano-	Dibenzo[*c*,*d*]phenothiazine	Ionic
Tetrabromo-	Dimethylaniline	Mol.
Tetrachloro-	1,5-Diaminonaphthalene	Mol.
Tetrabromo-	*p*-Phenylenediamine	Ionic
2,3-Dichloro-5,6-dicyano-	Pyrene	Mol.
Tetrachloro-	Pyrene	Mol.
Tetrachloro-	Hexamethylbenzene	Mol.
Tetrachloro-	1,8-Diaminonaphthalene	Mol.
Tetrachloro-	*p*-Anisidine	Mol.
Tetrachloro-	Diethoxydinaphthostilbene (1 : 2)	Mol.
Tetrabromo-	Perylene	Mol.
2,3-Dibromo-5,6-dicyano-	Pyrene	Mol.

[a] From reference 173.
[b] Mol. = molecular-type structure as opposed to an ionic structure.

substantially less than would be the case for the free atom. Promotion of an electron in this manner necessarily leaves behind a site of positive charge, or 'hole'. It is essential to the theoretical treatment of semiconductor materials that the hole is also regarded as being mobile and is therefore a carrier of positive electrical charge. This behaviour is perhaps best thought of as being a consequence of the Heisenberg Uncertainty Principle, which does not allow of the localization of a charged 'particle' sharing random thermal motion with its environment on a particular site in the crystal. In the general case of a semiconductor crystal, electrical conduction is a consequence of hole and electron conduction, although there are cases where either holes or electrons separately carry the major part of the current. Where holes are the major carriers the crystal is described as a '*p*-type' semiconductor. In an '*n*-type' semiconductor electrons serve as the current carriers.

Promotion of a bound electron to form a 'hole–electron pair' may be achieved by illumination of the material with light of a suitable wavelength. This is termed 'photoconduction'. Photoconduction has been demonstrated for a number of quinones[177,178], including 7,7,8,8-tetracyanoquinodimethane[179]; although anthraquinone[180], fluoranil and *p*-benzoquinone[177] are not affected by light irradiation in this way.

The resistivities of many quinones have also been shown to be reduced markedly by 'doping' the sample in some manner with a species which acts as an electron donor. The resistivity of chloranil decreases on exposure to amine vapours[181], for example, and the photoconduction has also been shown to vary in the presence of donor materials[182]. Conversely, exposure of donor materials to the vapour of *p*-benzoquinone or anthraquinone can affect the conductivity of the donor[183]. In this example it was shown by electron paramagnetic resonance and optical reflexion studies that negative ions and ion-radicals had been formed at the semiconductor surface. Similar behaviour was observed for quinones adsorbed on to TlI or CdS semiconductors[184]. In some cases exposure to quinone can change not only the conductivity but also the nature of the host semiconductor. Tetrathiotetracene, for example is a *p*-type semiconductor which becomes *n*-type on exposure to *o*-chloranil[185].

The behaviour described above is almost certainly a consequence of the formation of small amounts of an EDA complex at the semiconductor surface. However, the observed behaviour cannot be related in any simple fashion to the properties of the supposed EDA complex. The photoresponse of chloranil on exposure to aliphatic amines is not markedly enhanced by irradiation with light of a frequency which corresponds to the charge-transfer absorption band of the amine–chloranil complex[186].

It has also been reported that the major photocurrent response of pyrene–quinone systems is only initiated by light of frequency higher than that of the first charge-transfer transition[187]. This type of behaviour seems to be fairly general for EDA complexes, and is dealt with in more detail below.

The electrical behaviour of pure EDA complexes, as opposed to crystals 'doped' with small amounts of such complexes, has caused even greater interest, doubtless because of the potential commercial value of these materials. Complexes of TCNQ[188], chloranil[189], *o*-chloranil, *o*-bromanil, *o*-iodanil[190] and DDQ[191] have been recognized as organic semiconductors for some time. The last mentioned quinone is of particular interest. With *p*-phenylenediamine the complex exhibits principally hole conduction and is paramagnetic, having an intense e.s.r. signal. With perylene and pyrene, on the other hand, diamagnetic complexes are formed in which conduction appears to be via electron carriers. For DDQ itself the resistivity depends on the mode of crystallization[191]. Crystals from benzene have lower resistivities than those obtained from dichloromethane, although studies at various temperatures suggest that the activation energy for conduction ($E_a = 0{\cdot}6$ eV) is not affected in this way. Numerous other accounts have appeared which report the semiconductor behaviour of specific quinone EDA complexes[192–195].

Most of the interest in quinone EDA semiconductors has been directed towards complexes of TCNQ. This compound forms three distinct types of EDA complex. The first type consists of weak EDA complexes in which the ground state is principally 'non-bonded', and the dative D^+-A^- state contributes little. In the second series the dative state is the principal contributor, and the complex may be regarded as a normal salt involving the anion-radical $(TCNQ)^{\bar{\bullet}}$. In these two respects TCNQ behaves much like other quinones. Classification of a given TCNQ complex as one or other of the above types can often be made from a study of the infrared spectrum (see section II.D.3). Matsunaga[172] has remarked that weak EDA complexes exhibit higher resistivities than those which have a dative ground state. Subsequent work suggests this statement is generally true[18,196], but that dative bonding is strictly speaking neither a necessary nor a sufficient condition for low resistivity[173]. The third type of complex which TCNQ can form may be formulated as $D^+(TCNQ)^{\bar{\bullet}}(TCNQ)^0$. These 'complex salts' which include neutral TCNQ molecules in the crystal lattice exhibit resistivities which are several orders of magnitude lower than the corresponding 'normal' salts which have values of 10^4–10^{12} ohm cm[197]. In addition, the resistivity of the complex salts varies with the direction of the current flow relative to the crystal axes[198].

In crystals of $[NHEt_3]^+(TCNQ)^{-\bullet}(TCNQ)^0$, for example, conductivities of 4·0, 0·05 and 0·001 $ohm^{-1}\,cm^{-1}$ have been reported for directions normal to the planes of TCNQ molecules, in the plane of TCNQ molecules, and normal to alternate layers of TCNQ and $NHEt_3^+$ molecules respectively[199] (Figure 10). Melby and coworkers[188] have given a very comprehensive

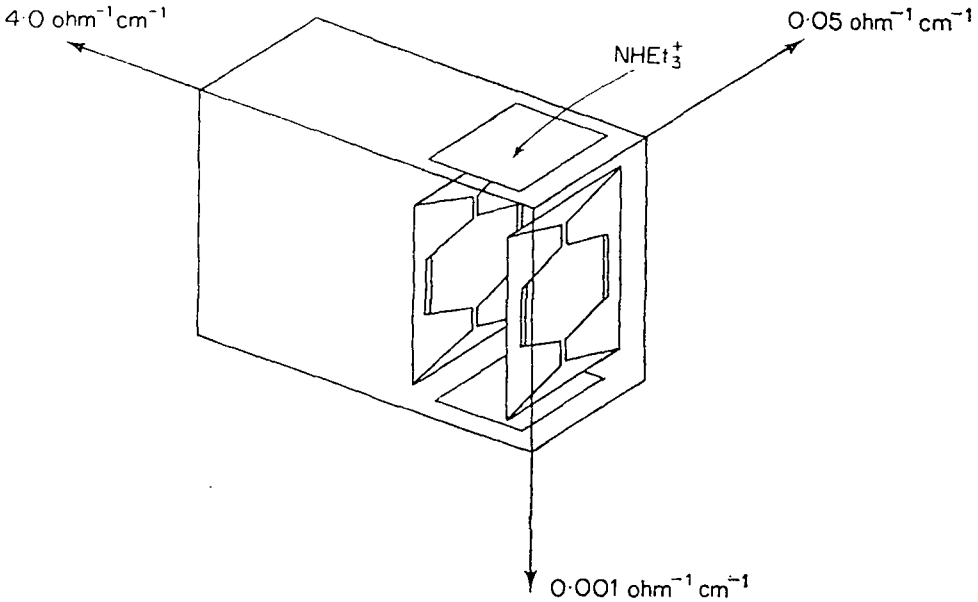
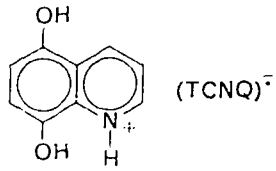


FIGURE 10. Crystal structure of $(NHEt_3^+)(TCNQ)^{-\bullet}(TCNQ)^0$ complex. Molecules of TCNQ are arranged in slightly offset stacks with $NHEt_3^+$ cations blanketing the ends of each pair. Conductivities appropriate to the crystal axes are marked. After reference 199.

account of the physical behaviour of the three types of TCNQ complexes, including details of their preparation. For the simple TCNQ salts the resistivities are isotropic and generally in the range quoted above, although exceptions are noted: the complex 7 has a resistivity of only 15 ohm cm.

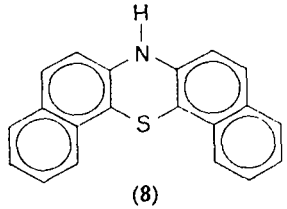


(7)

By contrast, the complex salts show consistently low resistivities with a pronounced crystal anisotropy, although the activation energy for

conduction does not appear to be anisotropic[200]. The same type of behaviour has been subsequently noted to be fairly general, for example in TCNQ complex salts with nitrogen bases[201].

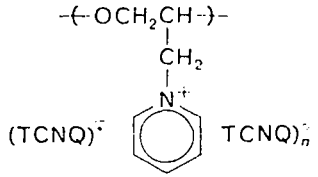
Quinone complexes, in some ways analogous to the complex salts of TCNQ, have been studied by Matsunaga[202]. 2,3-Dihalogeno-5,6-dicyano-*p*-benzoquinones complex with dibenzophenothiazine (**8**) to form dative



(8)

1 : 1 salts and a series of 2 : 1 $(D_2)^+A^-$ complexes similar to the TCNQ complex salts but with the donor–acceptor ratio reversed. Complexes having a 3 : 2 stoicheiometry $(D_3)^{2+}(A_2)^{2-}$ are also formed and the latter types have been shown to exhibit considerably lower resistivities than the 1 : 1 complexes in much the same way as has been observed for the TCNQ salts.

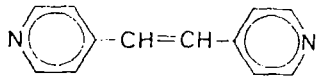
The large reduction in resistivity which arises from the inclusion of neutral TCNQ molecules into the crystal structure of TCNQ normal salts has led to attempts to enhance the conductivity of polymeric TCNQ complexes by similar methods. Poly(epichlorhydrin) complexes of the type **9** are semiconductors. Both the resistivity and activation energy of



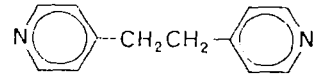
(9)

conduction of these complexes may be reduced by increasing the proportion of neutral TCNQ included[203]. The properties of copoly(styrene)-1-butyl-2-vinylpyridinium$(TCNQ)^-(TCNQ)^0$ have been described[204], and the expected enhancement of conductivity for TCNQ salts derived from **10** and **11** and related polymeric donors on addition of neutral $TCNQ^0$ has been observed[205].

A number of attempts have been made to generalize the conductivity behaviour of EDA complexes and related salts. In addition to the qualitative observations described above for normal and complex salts,



(10)



(11)

LeBlanc[206] has noted that the resistivity of normal TCNQ salts is related to the polarizability of the cationic species: the more polarizable the cation the higher the conductivity. This view is supported by studies on TCNQ salts involving cyanin dyes as cations, although it has been pointed out that the crystal structure, also a function of the cation polarizability, is likely to affect the conductivity of the material[207].

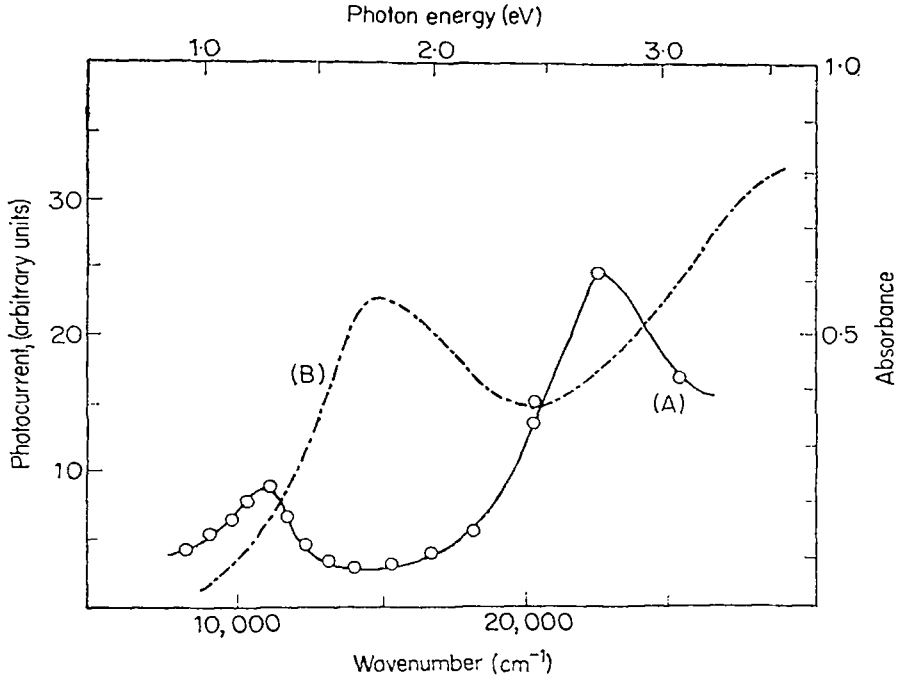


FIGURE 11. (A) Photocurrent and (B) absorption spectrum for the bromanil–pyrene complex. After reference 187.

It was mentioned earlier, albeit somewhat briefly, that the photoresponse of EDA complexes generally reaches a maximum for irradiation with light of higher energy than that corresponding to the first charge-transfer absorption band of the complex. This type of behaviour has been observed for a number of quinone EDA complexes with pyrene[187]. There appears (Figure 11) to be a small photocurrent produced by irradiation of

frequencies lower in energy than the charge-transfer absorption, the 'secondary' photocurrent, followed by the major photo-response, or 'primary' photocurrent, which occurs at energies higher than the charge-transfer transition band. It is argued that irradiation with frequencies corresponding to the charge-transfer band generates D^+A^- ion pairs in the crystal. The charges on the ions cannot move independently through the crystal in this state and are not, therefore, able to contribute to conduction. They may, however, be regarded as 'excitons', in the sense that, if sufficient additional energy is available to overcome the coulombic attraction of the charges, the electron present on the acceptor may be transferred to a 'distant' acceptor molecule, thereby generating a hole–electron pair, and electrical conduction becomes possible. This sort of approach has been applied by LeBlanc[206] to normal and complex TCNQ salts. In the normal case the unpaired electrons occupy fixed acceptor sites in the crystal. Transfer of one such electron to a distant acceptor produces a hole–electron pair and conduction becomes possible, the hole and the electron being now capable of independent motion. In the case of the normal salt this process effectively generates di-negative TCNQ ions in the crystal, and additional energy is therefore required in 'moving' the electron in order to overcome the resultant coulombic repulsion. It now becomes clear why the inclusion of neutral TCNQ molecules into the crystal, as in the complex salts, so dramatically increases the conductivity. The mobile electron can now be promoted to a remote $(TCNQ)^0$ site, and the coulombic repulsion energy for the process

$$\ldots\ldots D^+(TCNQ)^{\bar{\cdot}}\ldots\ldots(TCNQ)^0 \longrightarrow \ldots\ldots D^+(TCNQ)^0\ldots\ldots(TCNQ)^{\bar{\cdot}}$$

is considerably less than for

$$D^+(TCNQ)^{\bar{\cdot}}\ldots\ldots(TCNQ)^{\bar{\cdot}} \longrightarrow D^+(TCNQ)^0\ldots\ldots(TCNQ)^{=}$$

and the conductivity is thereby enhanced. In effect therefore, a low energy pathway is available in the crystal along which the charge carriers may move. The increased conductivity observed in crystals which are extensively hydrogen bonded can be accounted for in the same general terms[208, 209].

E. Miscellaneous Systems

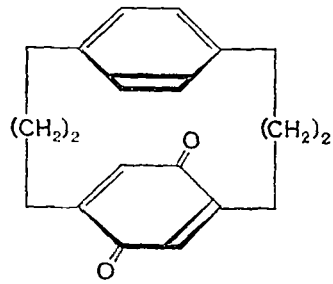
1. Quinhydrones

Quinhydrones are essentially complexes between hydroxy-aromatics and quinones in which the components, lying approximately parallel,

are hydrogen bonded in the molecular plane and held by polarization and such-like forces acting perpendicular to the molecular planes in the manner typical of EDA complexes. This two-directional binding can produce remarkably stable lattices. This, combined with their intense absorption in the visible region, undoubtedly accounts for their early observation. These systems are further discussed in section III.

2. Intramolecular complexes

Cram and Day[210] synthesized a quinone derived from [2.2]paracyclophane (**12**). The electronic spectrum includes a band at 29,400 cm^{-1} ($\varepsilon = 597$) which has been assigned as a transannular charge-transfer transition involving the benzene and quinone moieties which are rigidly fixed with respect to one another.



(12)

Somewhat different intramolecular complexes have been prepared by Ledwith and coworkers[141] (**6**). All are magenta black in the crystalline state. In solution, over the concentration range 40×10^{-4} to 8×10^{-4}M Beer's law is obeyed for the long waveband in each case. This absorption is therefore reasonably assigned to an intramolecular charge-transfer transition, which must be an 'across-space' transition because of the lack of conjugation throughout the molecule.

The crystal structure of the compound **6a** has been determined by Prout and Castellano[140] (see section II.D.1). The molecular configuration does not indicate a significant overlap of the donor and acceptor rings, and it is thought likely that in solution the interaction is between the nitrogen lone-pair orbitals and the quinone moiety, rather than the anilino group as a whole acting as the donor, i.e. an *n*- rather than a π-donor. In the solid phase the arrangement of adjacent molecules in the lattice suggests that inter- as well as intramolecular charge-transfer interactions are involved.

F. Involvement of Electron Donor–Acceptor Complexes in Organic Reactions

The possible role of EDA complexes in organic reaction mechanisms has been the source of many studies and considerable discussion, including several reviews[211–213]. At the outset it should be pointed out that there is a danger of the superficial presumption that an EDA complex is involved in a reaction if, on mixing the reactants, a colour characteristic of the complex is formed immediately and fades as the reaction proceeds to form the products. Although a complex may initially be formed from the reactants, it may not be on the reaction path. The fast reversible nature of the equilibrium will account for such behaviour even if the process is of the type

$$\text{Product} \xleftarrow{\text{slow}} \text{A} + \text{D} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \text{complex}$$

as opposed to

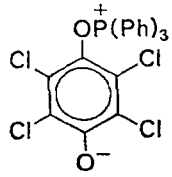
$$\text{A} + \text{D} \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} \text{complex} \xrightarrow{\text{slow}} \text{product}$$

The simplest type of chemical reaction is electron transfer from a donor to an acceptor. This may occur in the solid state to give an ionic structure. Such systems are often looked upon as EDA complexes in which the ground state is described in terms of equation (1) but where $b \gg a$, and described elsewhere as ionic complexes or salts. These complexes might well not be considered normally to be formed via the 'outer' EDA complex in the solid phase. However, there are examples of weak non-ionic ('outer') EDA complexes in solvents of low ionizing power being converted to separated ions by addition of other solvents which will solvate the ions sufficiently to favour electron transfer. For example chloranil–*N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine exists as a weak 'outer' complex in carbon tetrachloride but as the chloranil semiquinone-anion and the Wurster cation when the system is diluted with acetonitrile[214]. However, this ionization, though likely to proceed through the complex, could in principle be formed from the two components directly in the manner indicated above since there is always some dissociation of the complex in solution. Further studies[215] of the chloranil–*N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine complex in an ethyl ether–isopropyl alcohol mixture have shown that electron-transfer is not detected when a mixture of the components, of appropriate concentration for which the 'outer' complex is negligible at room temperature, is cooled directly to 193 K. However, if the system is first cooled to 77 K, at which there is considerable formation of the 'outer' complex, and then allowed to warm

up to 193 K, electron transfer does occur. This has been taken as reasonable evidence that at least in this case the reaction proceeds via the ('outer') EDA complex. In the crystalline state this complex may not have a simple ionic lattice[216].

The reaction of *p*-benzoquinone and its halo-derivatives, especially chloranil, with amines to form the corresponding 2-amino- and 2,5-diamino-quinone derivatives has long been known. Many of the aromatic amines form EDA complexes with the quinones immediately on mixing[217-219]. These represent another group of reactions in which the involvement of EDA complexes along the reaction path, though reasonable, has not been unambiguously established.

A similar situation occurs in the oxidation of *N*,*N*-dimethylaniline to crystal violet[220] where the initial formation of the complex is very obvious. The reaction of chloranil with triphenylphosphine to form the zwitterion **13** may likewise proceed through an EDA complex[221].



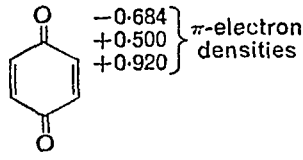
(13)

A number of polymerization reactions are catalysed by the addition of quinones and it has been suggested that some of these involve the formation of an EDA complex as the first step[222-229]. However, in some cases, for example *N*-vinylcarbazole plus chloranil, part of the reaction at least appears to be cationic, initiated by trace acidic impurities in the chloranil[222].

In most, if not all, of the above reactions, the participation of EDA complexes on the reaction path is not conclusive. Amongst some photochemical reactions the evidence is much stronger. Thus in the chloranil-catalysed polymerization of *N*-vinylcarbazole an increase in polymer yield was observed when the solution was irradiated within the charge-transfer band[222,224]. Where the charge-transfer absorption is at lower energies than all other absorptions of the components in the reaction, it is difficult to avoid the conclusion that photo-excitation of the EDA complex initiates polymerization via ionization, although at some stage an excited state of either the donor or the quinone acceptor may be involved (exciplex mechanism). A review of the participation of EDA complexes in polymers and polymerization involving both quinonoid and non-quinonoid acceptors is to be published[230].

III. HYDROGEN-BONDED COMPLEXES

In section II.C the effectiveness of quinones as acceptors in EDA complex formation was discussed, a behaviour which depends to some extent on the electron-withdrawing effect of the oxygen atoms. This effect generally leaves the π-system of the quinone electron-deficient, and the quinone oxygens correspondingly electron-rich; a situation which is exemplified by some recent calculations of the π-electron density distribution in *p*-benzoquinone **14** and other substituted quinones[231]. As a consequence the



(14)

quinone oxygens are good electron donors, and are therefore likely to be involved wherever possible in hydrogen bond formation. There seems to be little doubt that this tendency plays a large part in the chemistry of the quinones, although the extent of the involvement in any given case may be difficult to assess.

The quinhydrone system provides one example of a situation in which hydrogen bonding is likely to occur. The structure of the crystal was initially studied by Palacios and Foz[232] and later by Matsuda, Osaki and Nitta[233] in greater detail. The quinone and hydroquinone molecules are linked alternately by hydrogen bonds to form a zig-zag chain extending throughout the crystal (Figure 12). EDA interaction between quinone and hydroquinone molecules in adjacent hydrogen-bonded chains occurs. This approximately plane-to-plane juxtaposition of the two species accounts for the characteristic colour of quinhydrones. Earlier this colour had been used[234] as an argument in favour of a hydrogen-bonded *pair* suggested by Michaelis and Granick[235]. Hydrogen bonding contributes appreciably to the stability of the crystal[236]. The shift of the carbonyl-stretching frequency of *p*-benzoquinone in quinhydrone to lower energies relative to the free quinone has also been attributed to interactions of this type[237], an effect which has been shown to be general for quinones in association with the corresponding quinol[167] (Table 16). The coincidence of the stretching frequencies at about 1634 cm^{-1} for the quinhydrone systems reported in this work is probably fortuitous. The hydroxyl-stretching frequency also reflects the presence of hydrogen bonds in the quinhydrone. For quinhydrone itself the peak occurs at 3240 cm^{-1}. For

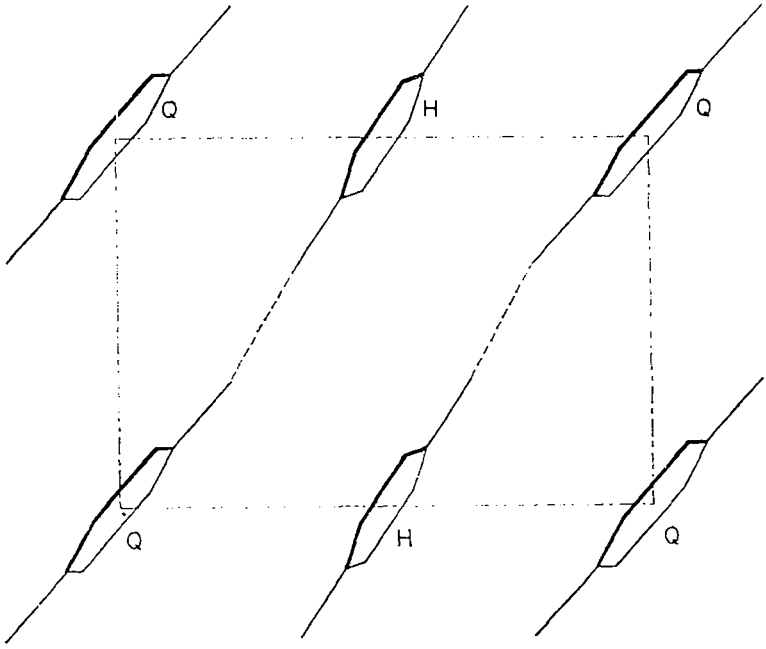


FIGURE 12. Arrangement of *p*-benzoquinone and hydroquinone molecules in a molecular sheet in monoclinic quinhydrone. After reference 233.

TABLE 16. Carbonyl-stretching frequencies of hydroquinone complexes of substituted *p*-benzoquinones[a]

Quinone	Carbonyl-stretching frequency/cm^{-1}	
	Free	Complexed
Chloranil	1692–1680	1634
Bromanil	1682–1673	1634
Trichloro-*p*-benzoquinone	1692–1681	1632
2,5-Dichloro-*p*-benzoquinone	1676	1632
Trichlorohydroxy-*p*-benzoquinone	1682–1660	1632
p-Benzoquinone	1663–1648	1634

[a] From reference 167.

other quinones in the presence of excess of the hydroquinone, two peaks are observed at 3250 and 3395 cm^{-1}, the latter being due to the free hydroquinone, the former to the hydrogen-bonded hydroquinone species.

The situation with regard to quinhydrone complexes in solution may

be rather different. It has been observed that the hydroxyl resonance absorption of quinhydrone in deuterochloroform solution is very similar to that of the free hydroquinone in the same solvent[238], which implies that such hydrogen bonding as occurs in the crystal does not persist in solution for this particular case.

Hydrogen bonding in crystalline quinone and quinone EDA complex systems has, however, been amply demonstrated by numerous X-ray crystallographic studies (Table 12). Quinhydrone crystallizes in both a monoclinic and a triclinic form. The work of Matsuda, Osaki and Nitta[233] mentioned above was concerned with the former case, Sakurai[239] has reported a similar study of the triclinic form which has essentially the same features. The component molecules are again linked by hydrogen bonds into zig-zag chains which are packed side by side to form molecular sheets. The two modifications appear to differ only in the alignment of the chains of molecules within the sheets. In both forms the perpendicular projection of the quinone molecule onto the adjacent hydroquinone shows that the carbonyl oxygen lies over the benzene ring of the hydroquinone. Prout and Wallwork[240] have commented on this aspect of many complexes analogous to quinhydrone as being due to a specific interaction between the carbonyl group and the π-electron system of the benzene ring.

The combination of charge-transfer forces and hydrogen bonding can be seen in the structures of many quinone complexes analogous to quinhydrone. The *p*-benzoquinone–resorcinol complex crystallizes in the same general way, with chains of hydrogen-bonded molecules packed into sheets allowing parallel overlap of the donor and acceptor rings[138]. The phloroglucinol–*p*-benzoquinone complex likewise crystallizes in the same way despite the complexity of the molecular arrangement[241]. This particular example is, however, unusual in that two different types of hydrogen bond are observed in the crystal, one having a C=O···H—O bond angle of 172°, rather different from the normally encountered angle of 120° (Figure 13). The infrared spectrum of this compound clearly shows the presence of the two types of hydrogen bond.

An interesting illustration of the relative influence of EDA and hydrogen-bonding interactions can be seen in studies of phenol-*p*-benzoquinone complexes. With hydroquinone, *p*-benzoquinone forms a complex having exclusively a 1 : 1 stoicheiometry. Phenol on the other hand complexes with a 2 : 1 phenol–quinone composition, which suggests that the stoicheiometry is largely determined by the availability of phenolic hydroxyl groups for hydrogen bond formation to the quinone carbonyls[135, 242]. *p*-Chlorophenol and *p*-bromophenol likewise form 2 : 1 complexes with *p*-benzoquinone in which each quinone is sandwiched

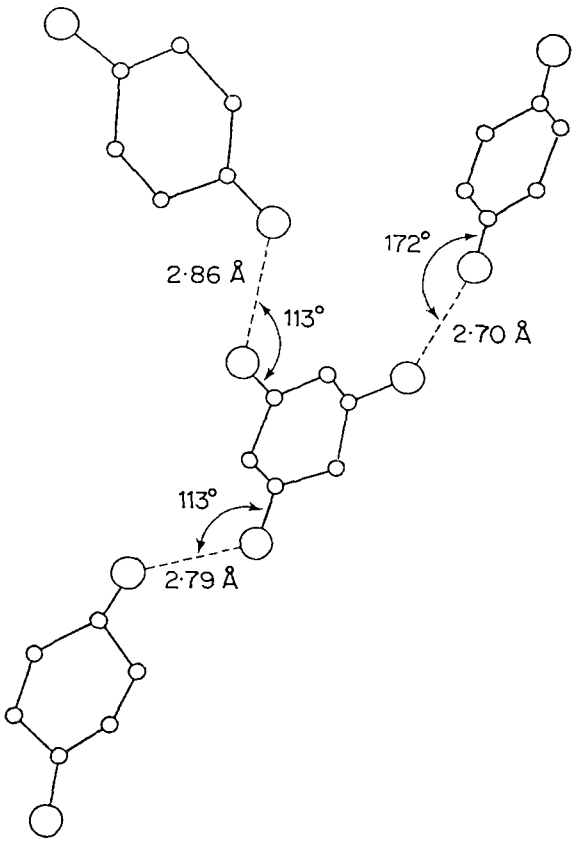


FIGURE 13. Hydrogen-bond lengths and bond angles in the structural unit of *p*-benzoquinone–phloroglucinol 2 : 1 complex. After reference 241.

between two phenol molecules in groups of three, each group being stacked in columns, with the axis through the centres of the three molecules of each group making an angle of about 13° to the column axis[136] (Figure 14). Hydrogen bonds link the molecules in a sideways direction to form infinite bands. The latter two phenols, however, also form 1 : 1 complexes with *p*-benzoquinone[243]. Here the phenol and quinone moieties are stacked alternately but with the normal to each molecular plane being tilted at 30° to the stacking axis. This arrangement again locates the quinone carbonyl group directly over the phenol ring. In the former example of the 2 : 1 complexes the charge-transfer interaction is limited to groups of three molecules, the loss of stability being, however, offset by the increased hydrogen bonding. In the 1 : 1 case, the extent of the hydrogen bonding is limited, but now the alternating arrangement of

donor and acceptor species allows the EDA interaction to extend throughout the molecular column. The authors observe therefore that, since complexes of both stoichiometries form under rather similar conditions, the energies of the two types of interaction must be approximately the same.

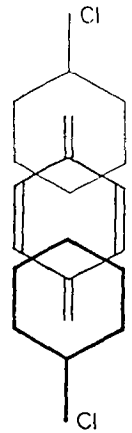
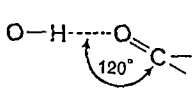


FIGURE 14. Overlap of *p*-chlorophenol molecules with *p*-benzoquinone in the 2 : 1 complex (the —OH groups are omitted for clarity). After reference 136.

A number of infrared studies of the interaction between methyl-substituted quinones and phenol in solution have appeared. In several cases it has been observed[244] that the phenol hydroxyl stretching band in the presence of quinone in carbon tetrachloride solution is asymmetric, apparently due to the presence of two overlapping symmetrical bands. From this and subsequent work[245,246] it was therefore concluded that two types of hydrogen bond were involved in these systems, the band at lower energies being ascribed to the normal hydrogen bond **15**, that at higher energies to species having structures of the type shown in **16**[247].



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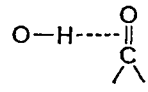


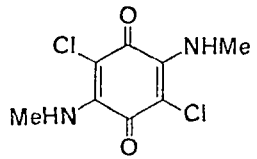
(16)

Fritzsche[248] also quotes one of the very few quantitative estimates of the strength of hydrogen-bonding interactions involving quinones. For the *p*-benzoquinone–phenol hydrogen bond $\Delta H^{\ominus} = -5{\cdot}05 \pm 0{\cdot}55$ kcal/mole, $\Delta S^{\ominus} = 15{\cdot}0 \pm 1{\cdot}9$ cal/mole deg^{-1} estimated from infrared studies.

Other authors have observed the effect of addition of phenol to the carbonyl-stretching band of *p*-benzoquinone in carbon tetrachloride[249].

The carbonyl band intensity increased, but without showing the shift to lower energies normally associated with hydrogen bonding. Since the addition of anisole, where hydrogen bonding is no longer possible, has the same effect on the quinone carbonyl band intensity, it was argued that EDA complexation and hydrogen bonding both affect the carbonyl absorption band in a similar manner.

Hydrogen bonding has also been demonstrated in pure quinones where suitable proton donor groups are present in the molecule. In crystals of **17** for example, the molecules are linked together by



(17)

N—H···O=C bonds[250]. The properties of anthraquinones in particular can be markedly affected by the presence of proton-donor substituents. Flett[251] has reported the effect of hydroxyl groups on the infrared spectral frequencies. In general, the hydroxyl-stretching frequency occurs at 3350 cm^{-1}. For 1-hydroxyanthraquinone, however, no hydroxyl frequency was detected in this region, whilst a carbonyl-stretching frequency was observed at lower energy than is normal for anthraquinones (Table 17).

TABLE 17. Carbonyl- and hydroxyl-stretching frequencies (ν) for hydroxyanthraquinones[a]

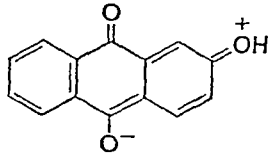
Quinone	ν/cm^{-1}		
	—OH	C=O	
1-Hydroxyanthraquinone	—	1673	1636
2-Hydroxyanthraquinone	3320	1673	
1,3-Dihydroxyanthraquinone	3380	1675	1635
1,4-Dihydroxyanthraquinone	—		1627
Anthraquinone	—	1676	

[a] From reference 251.

This behaviour was attributed to a weakening of the carbonyl and hydroxyl bonds due to strong intramolecular hydrogen bonding which can occur when the hydroxyl is immediately adjacent to the carbonyl group. This

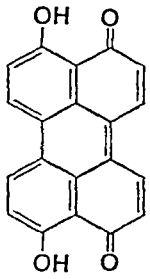
is also exemplified by a comparison of the melting points. 1-Hydroxyanthraquinone melts at 190°. However, for the 2-hydroxyl compound, where intermolecular hydrogen bonds are no longer precluded by the intramolecular bonds, the melting point is strikingly higher (302°)[251].

Other authors[252] have subsequently observed a very low intensity absorption at 2700 cm^{-1} due to an intramolecularly bonded hydroxyl group in analogous systems, and a similarly very weak absorption, again at 2700 cm^{-1}, for the case of 1-hydroxyanthraquinone itself[253]. The marked lowering in energy of the intramolecularly bonded carbonyl seems to be due to an altered electron distribution in hydroxyanthraquinones which may be represented by canonical structures such as **18**.



(18)

For the 1-hydroxy case such structures would be stabilized by intramolecular hydrogen bonding, which would account for the low energy carbonyl absorption. Recourse to such arguments seems to be necessary, since hydrogen bonding *per se* is not sufficient to account for the entire shift. 4,9-Dihydroxyperylene-3,10-quinone (**19**) is intramolecularly hydrogen bonded to the extent that the hydroxyl-stretching frequency is of extremely low intensity, yet the carbonyl-stretching frequency appears at energies not significantly different from **20**.



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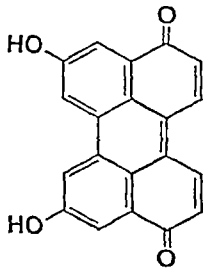


(20)

The intensity of the carbonyl absorption in anthraquinones, naphthoquinones and benzoquinones is not sensitive to the type of hydrogen bond formed in the way that the hydroxyl-stretching bond appears to be. The intensities in this case are reported to be rather a function of the symmetry of the quinonoid system[254].

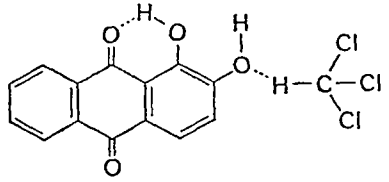
The presence of the intramolecular hydrogen bond of 1-hydroxyanthraquinone may also be inferred from the photo-excitation behaviour of this compound. In general, molecules having a hydroxyl group adjacent to a carbonyl may undergo a tautomeric process of the type illustrated below for 2-hydroxybenzophenone (**21**), a process which is

(21) (21a)

greatly enhanced by the intramolecular bond[255,256]. In such cases, a photo-excited triplet species may undergo rapid radiationless decay via the tautomeric mechanism and no emission is observed. In hydrogen-bonding solvents, however, solvent–solute intermolecular hydrogen bonding will compete with intramolecular bonding, thereby reducing the ability of the excited species to decay by the above mechanism, and phosphorescence may then be observed, the half-life of the excited triplet species being dependent on the particular solvent and the effectiveness with which it can disrupt the intramolecular bond[257]. With 1-hydroxyanthraquinone the phosphorescent emission is very weak and, unlike 2-hydroxybenzophenone, is almost insensitive to even strongly hydrogen-bonding solvents. This possibly reflects the strength of the intramolecular bond in this case, and the extent to which the resulting structure is preferred to species which are intermolecularly bonded to the solvent.

Polarographic studies of the hydroxyanthraquinones indicate that autoprotonation of the carbonyls occurs in aprotic solvents, a tendency which is particularly enhanced in cases where intramolecular hydrogen bonds of the type discussed above are present[258]. The effect of hydrogen bond formation on the electronic spectra of the hydroxyanthraquinone has also given rise to some interest. Weak absorptions at 510 nm for 1,5-dihydroxyanthraquinone and 580 nm for the 1,4-dihydroxy isomer in pyridine solution have been tentatively attributed to hydrogen bonding[259], and the red-shift of the absorption band observed for alizarin and histazarin in strongly alkaline media has been explained in terms of strong hydrogen bond formation to the appropriate anion[260]. Calculations carried out for the 1-hydroxy- and 1-aminoanthraquinone suggest[260] that the perturbation of the electronic absorption bands due to intermolecular hydrogen bonding is likely to be small, not more than ± 20 nm,

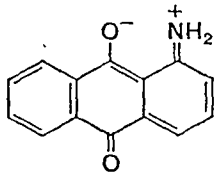
though there seems to be good evidence to attribute the appreciable blue-shift of the electronic absorption bands of 1,2-dihydroxyanthraquinone in chloroform solution to interactions of the type **22**[261]. For other hydroxy-anthraquinones, an intense absorption band in the visible region is



(22)

observed in ethanol solution. Beer's law is obeyed when carbon tetrachloride is used as the diluting solvent, which suggests that the absorption is a result of intermolecular hydrogen bonding with the solvent[261].

In addition to the observations outlined above for hydroxyanthraquinones, Flett[251] remarked that the carbonyl-stretching frequency of aminoanthraquinones was shifted to lower energies; the N—H stretch, however, was not greatly affected. This behaviour was attributed to contributions to the molecular ground state from such structures as **23**



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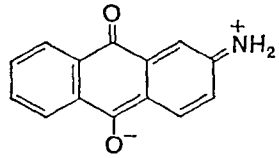

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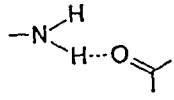
and **24** for the 1-amino- and 2-amino compounds rather than to hydrogen-bonding interactions. That such bonding does in fact occur in amino derivatives of quinones has been shown by X-ray crystallographic measurements[250] and by ultraviolet-visible spectroscopy[262]. Crystals of



(25)

2-aminoanthraquinone consist of infinite molecular columns connected by bonds of the type **25** in which only one of the two amino hydrogens is involved in the bonding[263], and a comparative study of the 1- and

2-aminoanthraquinones suggests that the behaviour of these compounds is in many ways similar to the corresponding hydroxy-substituted species[264]. For the 2-amino derivatives two carbonyl bands are observed in the solid phase at 1629 and 1670 cm^{-1}, only one of which persists, at 1680 cm^{-1} with a shoulder at 1671 cm^{-1}, on dilution with carbon tetrachloride[264]. This is presumably due to breakdown of intermolecular hydrogen bonding. In the case of the 1-amino derivative, however, the bands appear at 1688 and 1644 cm^{-1}, but are no longer influenced by the extent of dilution with the solvent, which argues for an intramolecular bond similar to that encountered in 1-hydroxyanthraquinone. A value of 3·3 kcal/mole has been estimated[265] for the energy of this interaction in amino-anthraquinones. However, other reports tend to support the view put forward by Flett[251]. A strong resonance interaction has been shown to exist between the amino and carbonyl groups for this series of compounds[266], and the pK_a values for the 1- and 2-amino derivatives do not appear to depend on the degree of hydrogen bonding.

Hydrogen bonding has been demonstrated in naphthoquinones. Crystalline 4,8-dihydroxy-1,5-naphthoquinone is extensively hydrogen bonded[267] and, in addition, the rather novel 'bifurcated' hydrogen bond[268] has been observed in certain cases. In hydrogen bonds of this type the hydrogen atom appears to be bound to three centres, and it has been suggested[269] that all naphthoquinones having an amino or hydroxyl group in the 1-position are likely to possess bifurcated hydrogen bonds in which a hydrogen atom from the substituent group is simultaneously bonded intramolecularly to the carbonyl, and intermolecularly to a second molecule, or to included solvent if present. The structure of 3-bromo-4-amino-1,2-naphthoquinone hydrate seems from X-ray analysis to be determined largely by hydrogen-bonding interactions. The naphthoquinone is midway between the 4-amino-2-keto and 4-imino-2-enol forms, the molecules being linked together by hydrogen bonds between the amino group and the carbonyl of a second molecule, and also by hydrogen bonds to included water molecules[270]. This particular naphthoquinone also forms a complex with methanol in which the quinone–methanol bonds are surprisingly strong. Differential thermal analysis of the crystalline complex shows[271] that methanol is not evolved from the crystal matrix below a temperature of 120°. The structure proposed for the complex is shown in Figure 15, in which there is thought to be a strong interaction between the hydroxyl groups of methanol and the bromine atom of the naphthoquinone ring. The same authors also propose a strongly hydrogen-bonded structure for the crystalline 3-methyl-4-amino-1,2-naphthoquinone hydrate[272].

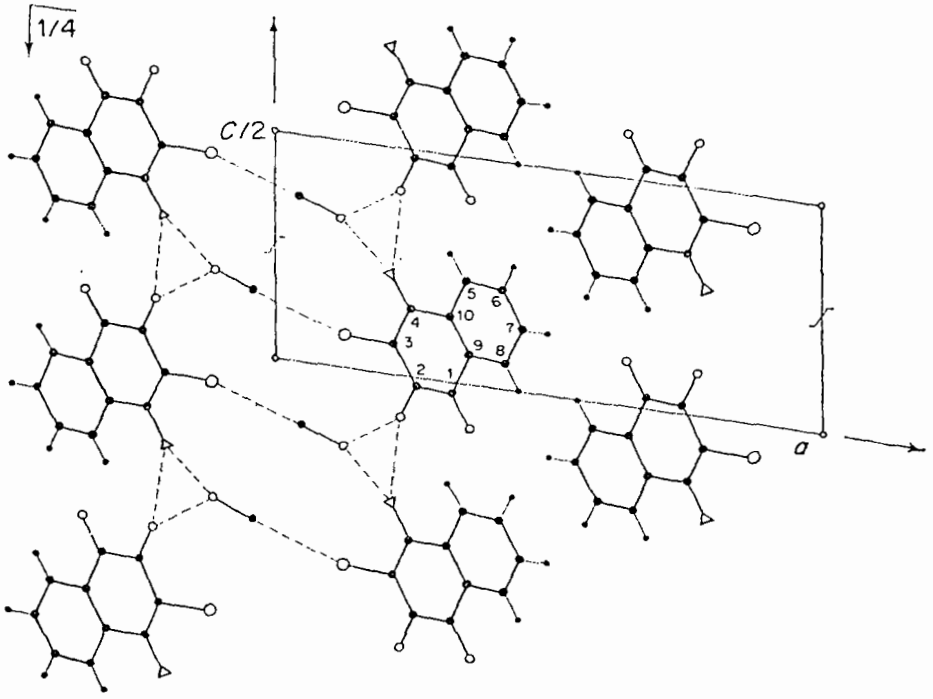


FIGURE 15. Structure of the methanol – 3-bromo-4-amino-1,2-naphthoquinone complex projected parallel to the [010] axis. Reproduced with permission from D. Chasseau, J. Gaultier and C. Hauw, *Compt. Rend. Ser. C.*, **270**, 1452 (1970).

IV. METAL COMPLEXES

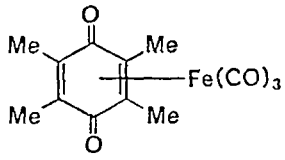
A. Introduction

In the present section, three distinct types of quinone complexes are discussed. *p*-Benzoquinones generally are capable of bonding to suitable metals via a π-orbital interaction to form stable organometallic species which are unlike those discussed hitherto in that the complex does not reversibly dissociate to any significant extent either in the vapour state or in solution. The acceptor properties of the quinonoid system are of some importance in such systems, for in the molecular-orbital description, electron donation from the metal to the low-lying acceptor orbitals ('back donation') has an important stabilizing effect. Secondly, the *o*-quinones behave as bidentate chelates with certain metals, the degree of dissociation of such species depending largely on the individual circumstances. The third type is exactly analogous to the EDA complexes discussed in section II. Here, however, the donor species is an organometallic com-

pound, such as ferrocene, the quinone associating in some way with the ligand which is already firmly bound to the metal.

B. Metal-bonded p-*Benzoquinone Complexes*

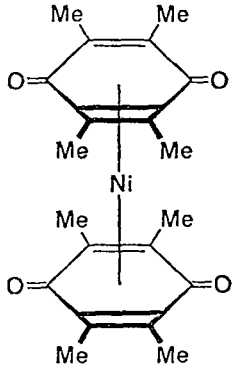
Possibly the earliest report of a quinone organometallic complex was of particular interest in that the synthesis of the material did not involve the use of the quinone as a reactant[273]. Dimethylacetylene and iron pentacarbonyl react together on exposure to sunlight to yield an orange crystalline material which produces durohydroquinone on treatment with acid and which slowly decomposes in air to liberate duroquinone. The product was therefore formulated as π-duroquinone-iron-tricarbonyl (**26**). 2-Butyne, 2-pentyne and 3-hexyne apparently behave in an analogous



(**26**)

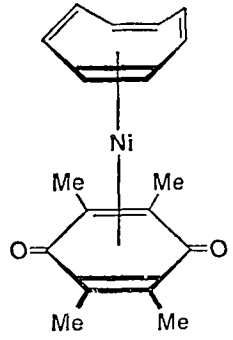
fashion, although with other metal carbonyls, $Cr(CO)_6$, $Mo(CO)_6$, $Mn_2(CO)_{10}$ or $Ni(CO)_4$, no isolable complexes were obtained[274].

This initial work, and a molecular-orbital treatment of π-bonded organometallic complexes by Brown[275], which suggested that many more such compounds might be realizable than had hitherto been thought, gave rise to considerable interest in this aspect of quinone chemistry, particularly with regard to the synthesis of metal–quinone complexes by more direct methods. The sandwich compound, bis-π-duroquinone–nickel, for example, was obtained[276] by refluxing duroquinone with $Ni(CO)_4$ (**27**). In this instance the compound is relatively stable,



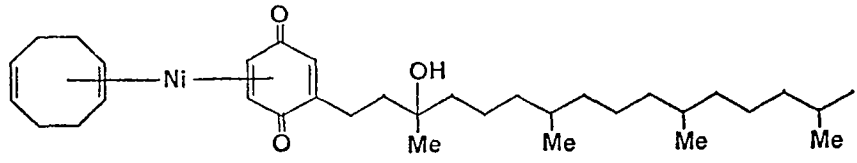
(**27**)

decomposing at 205° without melting. No analogous sandwich compounds are formed in this way from *p*-benzoquinone, methyl-*p*-benzoquinone or the various isomeric dimethyl-*p*-benzoquinones. The bis-π-duroquinone–nickel complex can be used as a precursor for a second series of compounds in which one of the quinone ligands has been replaced by a suitable olefin. For example, treatment with cyclo-octatetraene yields **28**[277].



(28)

The compound **29** made by treating tocopherylquinone (vitamin E-quinone) with $Ni(CO)_4$ and cycloocta-1,5-diene is of the same type, and

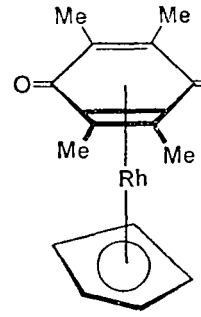


(29)

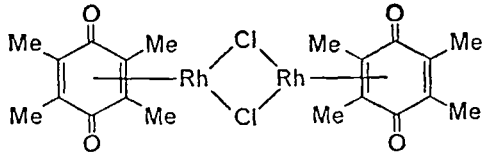
appears to be one of the earliest synthetic organometallic compounds involving a natural product[278]. A more detailed account of quinone–nickel complexes of the type discussed above can be found in an article by Schrauzer[279].

Complexes involving metals other than iron or nickel have also been reported. Reduction of rhodium and iridium trichlorides with ethanol in the presence of duroquinone gives rise to π-bonded duroquinone compounds. In the case of rhodium the product is extremely insoluble[280], and was therefore formulated as a chlorine-bridged polymer, the presence of π-bonded duroquinone being demonstrated by reaction with cyclopentadienyl sodium to yield duroquinonecyclopentadienylrhodium (**30**).

Iridium, on the other hand, forms a water-soluble complex having the approximate composition (duroquinone)$IrHCl_2$. With $[Rh(CO)_2Cl]_2$, duroquinone forms a dimeric product (**31**) by a slow reaction in benzene solution[281].

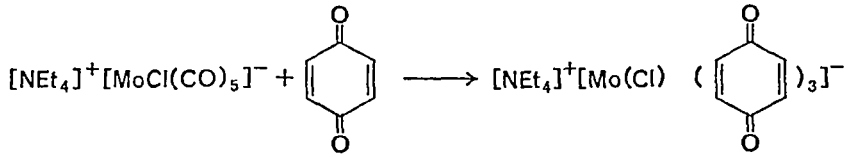


(30)



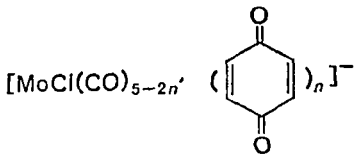
(31)

The displacement of metal carbonyl groups by quinones has been studied for the complex anions of molybdenum and tungsten. The following reaction yields **32** as a blue-black precipitate with evolution of carbon monoxide, from which hydroquinone and quinhydrone may be recovered



(32)

on heating in a sublimation apparatus at 200° [282]. Complete replacement of the metal carbonyls in this instance appears to reflect the enhanced π-electron acceptor potential of *p*-benzoquinone over that of carbon monoxide. Initial formation of the intermediate anion **33** will lead to even more rapid displacement of the remaining carbonyl groups, since the metal carbonyl bonds are weakened by the presence of the quinone.



(33)

Pentacyanocobaltate anion reacts with *p*-benzoquinone[283] to yield a product, formulated as $[(CN)_5Co$ (*p*-benzoquinone) $Co(CN)_5]^-$. Spectroscopic and electrochemical evidence suggest that the quinone fragment in this species is isoelectronic with hydroquinone dianion and with a greater degree of π-electron delocalization than expected for a quinone, which supports the supposition that this is a bridged compound. Compounds of the type $Pt(PPh_3)_2L$ have been prepared, where L = *o*- or *p*-quinones[284], likewise the series of compounds $M(NO)(PPh_3)_2L$ is known, where M = Co, L = 1,4-naphthoquinone; M = Rh; L = *p*-benzoquinone, chloranil, 1,4-naphthoquinone, 1,2-naphthoquinone or *o*-chloranil and M = Ir, L = *o*-chloranil[285]. π-Electron back-donation from the metal to the ligand appears to be the overriding factor which determines the stability of these compounds, an observation which is probably generally true for organometallic quinone complexes.

Involvement with the metal appears to modify to a significant extent the properties of the quinone when complexed. The carbonyl-stretching frequency is generally lowered, a consequence of the formation of dative π-bonds between the *d*-orbitals of the metal and the low-lying unoccupied molecular orbitals of the quinone ligand, i.e. the 'back-donation' referred to earlier[276, 286]. In addition, the carbonyl band generally appears as two peaks[282, 284, 285]. Schrauzer and Dewhirst[280] first reported such an observation for the duroquinone–cyclopentadienyl rhodium complex, which exhibits bands in the carbonyl-stretching region at 1580 and 1532 cm^{-1}, compared with 1629 cm^{-1} for duroquinone itself. It was proposed therefore[280] that the quinone fragment is to some extent non-planar in these complexes, in contrast to the normally planar quinone configuration of the methyl quinones[287–289]. The suggestion was supported by a molecular-orbital description of the complexes in which a repulsive metal–carbonyl oxygen interaction is apparent[280]. These considerations, and other evidence which suggests that the chemical behaviour of quinones when π-bonded to a metal is significantly different to that of the free state[290], have prompted a number of X-ray crystallographic studies on such systems in order to determine to what extent the quinone structure may in fact be distorted.

In an early study of duroquinone-cycloocta-1,5-diene nickel, Glick and Dahl[291] detected a slight distortion of the quinone fragment, in that the methyl groups incline slightly towards the nickel atom, whilst the carbonyl oxygens are inclined in the opposite direction, the carbonyl bond making an angle of about 6° with the plane defined by the four carbon atoms of the quinone-diene system (Figure 16). In cyclopentadienyl-2,6-di-*t*-butyl-*p*-benzoquinonerhodium[292] the quinone is even more strikingly distorted

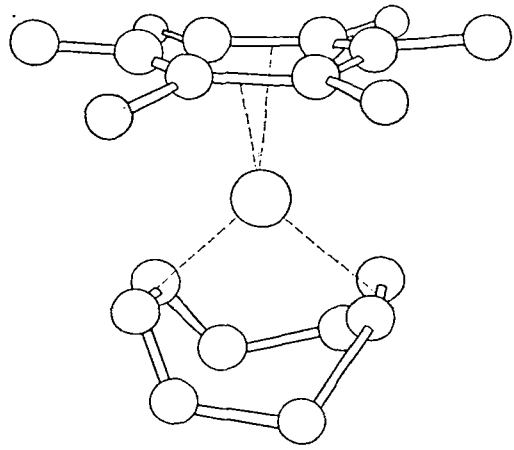


FIGURE 16. Structure of 1,5-cyclo-octadiene-duroquinone-nickel. Reproduced with permission from M. D. Glick and L. F. Dahl, *J. Organomet. Chem.*, **3**, 200, Figure 1 (1965).

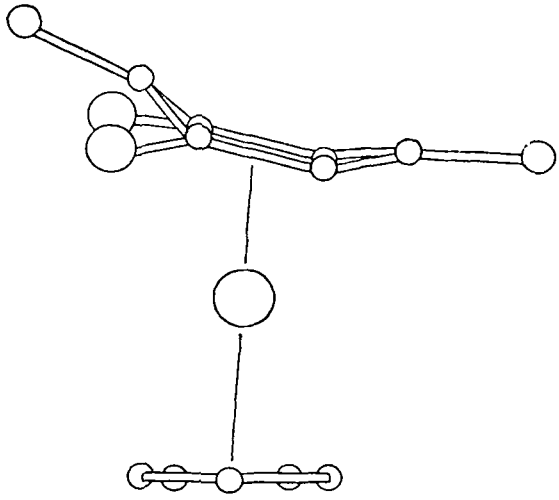


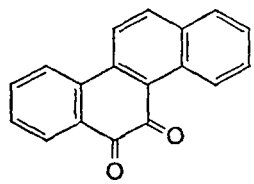
FIGURE 17. Structure of cyclopentadienyl-2,6-*t*-butyl-*p*-benzoquinonerhodium. After reference 293.

into a boat-shaped structure[293] (Figure 17). It has been argued that, in this case, the quinone is behaving rather as a di-olefin, since the carbonyl-stretching frequency is shifted only 33 cm^{-1} to low energies compared to the free quinone case[293]; for the corresponding duroquinone nickel compound the shift is 133 cm^{-1}, although such comparisons between different metals may be misleading[294].

Further work suggests that such distortion of the quinone fragment is probably general, rather than a consequence of steric effects such as might occur in the foregoing example. Cyclopentadienylduroquinonerhodium, in which steric effects are somewhat less, nevertheless shows significant distortion of the quinone ligand[295].

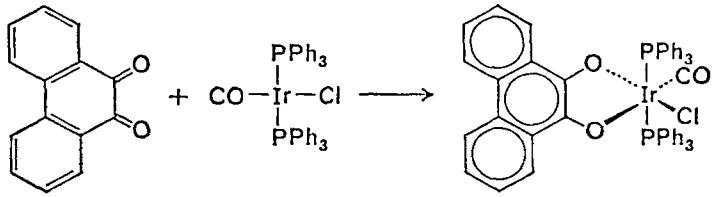
C. Metal-bonded o-Quinone Complexes

So far the discussion has centred on the formation of π-complexes of *p*-quinones with suitable metals. It is generally true that *p*-quinones bond to metals via a π-electron mechanism, although substituents in the quinone ring may modify this behaviour. For 1,2,5,8-tetrahydroxyanthraquinone, for example, it has tentatively been proposed that a chelate is formed with Pb^{2+} involving a quinone carbonyl and the neighbouring phenolic oxygen[296]. *o*-Quinones, on the other hand, generally form metal complexes by a quite different mode of bonding. The first extensive study of metal-*o*-quinone complexes was reported by Crowley and Haendler[297]. Of those studied, 9,10-phenanthrenequinone and 1,2-chrysenequinone (**34**) form a series of deeply coloured complexes with

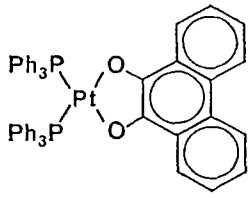


(34)

a range of transition metals, all of which are decomposed by polar solvents, and which can be prepared with stoicheiometries of 1 : 1, 2 : 1 or 3 : 1 (quinone : metal). The electronic absorption bands of the quinone are shifted to longer wavelengths, consistent with increased delocalization of the quinone electrons, and the stretching frequencies of the carbonyl bands are considerably shifted to low energies, all of which suggests that in *o*-quinones bonding to the metal is via the quinone oxygens. 9,10-Phenanthrenequinone also complexes photochemically with some iridium compounds to form a species which was formulated as **35** since in this case the product showed none of the infrared frequencies characteristic of the parent quinone[298]. A similar product is formed from 1,2-naphthoquinone. 9,10-Phenanthraquinone reacts in absence of light to form **36** where bonding is again via the carbonyl oxygens. *o*-Chloranil was reported in this work to react photolytically with $Ir(PPh_3)_2(CO)Cl$ to yield products

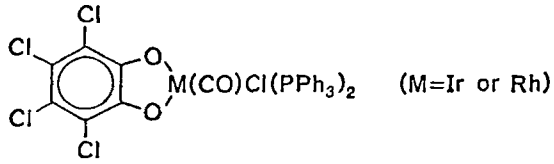


(35)



(36)

which were not identified, but which are not of the same type as those from 9,10-phenanthraquinone. Later workers[299] have, however, reported that this reaction occurs in the dark to yield complexes of the type **37**,



(37)

essentially the same process occurring with $(Ph_3P)_4Pt$ and $(Ph_3)_3Pd$. The oxidation potential seems to be crucial as far as this reaction is concerned; weakly oxidizing quinones do not behave in this way.

La Monica and coworkers[285] have remarked on the differences between the properties of *o*- and *p*-quinone metal complexes, of which the behaviour of the carbonyl-stretching frequency is the most striking. With both quinones the absorption shifts to lower energies on complexation relative to the free quinone, for the *p*-quinones the shift being approximately 20–100 cm^{-1} and for the *o*-quinones 250–300 cm^{-1}. N.m.r. studies also serve to distinguish the two cases, proton resonances of *p*-quinones undergo a high-field shift on complexation, whilst for the *o*-quinones the proton resonances are reported not be be greatly affected[285].

In general terms it may be concluded that *p*-quinones undergo metal complexation via the quinonoid π-electron system, whilst *o*-quinones rather chelate to the metal through the quinone oxygens. There seem to

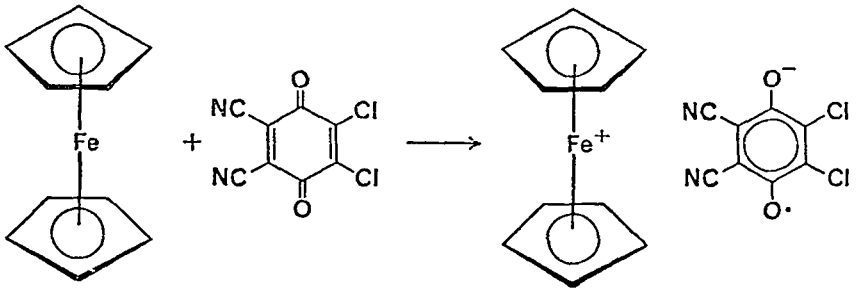
have been no reports to date of metal complexes of *o*-quinones which involve the olefinic π-electron system.

D. Organometallic EDA Complexes

Quinones may also form EDA complexes with organometallic compounds of a type exactly analogous to the complexes discussed in section II. Goan, Berg and Podall[300] first discussed the possibility of EDA complex formation with metallocenes, since a common method of preparing metallocinium salts consists of treating the metallocene with *p*-benzoquinone in the presence of a suitable organic acid, and it therefore seemed likely that EDA complexation with the quinone might be an intermediate stage in the reaction. Isolable complexes were obtained in a number of cases, for example nickelocene–*p*-chloranil (1 : 2) and cobaltocene–*p*-chloranil (1 : 2) and cobaltocene–*p*-chaloranil (1 : 1 and 1 : 2). Ferrocene behaves in a similar fashion, but the complexes in this case were not isolable. All of the complexes exhibit a charge-transfer absorption in the 430–450 nm region, and there is evidence from infrared studies of a possible degree of interaction between the quinone carbonyl and the metal. The actual extent of transfer of charge to the quinone, estimated from the intensity of the e.s.r. signal, appears to depend on the particular complex studied. 1:2-Cobaltocene–*p*-chloranil, for example, shows a strong signal, whilst for 1:2-nickelocene–*p*-chloranil the signal is rather weak. The 1 : 1 complexes show intermediate behaviour. On these grounds the 1:2-cobaltocene–*p*-chloranil complex was formulated as a radical ion salt, π-$(C_5H_5)_2Co^+$(chloranil)$^{\bullet}$(chloranil), and evidence for the presence of the metallocinium ion was obtained from the electronic absorption spectrum of the solution. For the 1 : 2 nickelocene complex a structure was proposed in which there is an EDA interaction between the hydroquinone anion and the quinone itself. Other workers[301] have also reported complexation between ferrocene, **38**, and 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) to form the metallocinium salts **39**. A similar reaction occurs with cobaltocene. For other quinones, metallocinium salts or EDA complexes are formed, depending on the oxidation–reduction potential of the donor–acceptor system. Generally, ferrocene requires a quinone of high electron-acceptor ability in order that the ferricinium salt is formed, with both *p*-benzoquinone and *p*-chloranil the EDA complex only is formed. Cobaltocene, on the other hand, is relatively readily ionized.

A catalytic effect of metallocene–quinone EDA compounds on hydrogen-exchange reactions involving, for example, acetylene has been reported[302].

Both components of the metallocene–quinone complex are necessary for the rate enhancement to be observed. However, the phenomenon is exhibited by other EDA complex systems[303].



(38) (39)

An interesting series of quinone complexes involving the copper, palladium or nickel chelate of 8-hydroxyquinoline as donor has been prepared[304-306]. This includes complexes having 2,5-diazido-3,6-dichloro-*p*-benzoquinone as the acceptor. A comparison of the charge-transfer band energies of such complexes of this latter quinone with those of *p*-chloranil or *p*-bromanil seems to suggest that the azido group is as effective as chlorine or bromine in activating the quinone system for EDA complex formation[305,307]. A crystal study of quinone complexes of the metal-8-hydroxyquinolinates has been undertaken[308], since there were grounds for believing that in the crystalline state an interaction of the metal of the 8-hydroxyquinoline complex and the functional group of the acceptor was involved, where, for example, the acceptor is chloranil, tetracyanoquinodimethane or benzotrifuroxan. In the bis-8-hydroxyquinolinatopalladium–chloranil (1 : 1) complex[308], an unusually short metal–chlorine distance (3·44 Å) was observed, and the orientation of donor–acceptor units in the crystal is not that which would maximize overlap of the π-electron systems (Figure 18). However, the metal-free 1 : 2 complex of chloranil with 8-hydroxyquinoline has a nearly identical arrangement of donor and acceptor molecules[309].

By contrast with the palladium bis-(8-hydroxyquinolinato)–chloranil system, copper bis-(8-hydroxyquinolinato)–tetracyanoquinodimethane 1 : 1 complex has a plane-to-plane structure with maximum overlap of the π-systems[310]. The π–π polarization and charge-transfer forces appear to dominate the molecular orientations with the copper atom in a square planar, rather than an octahedral, configuration. This atom therefore is coordinatively unsaturated.

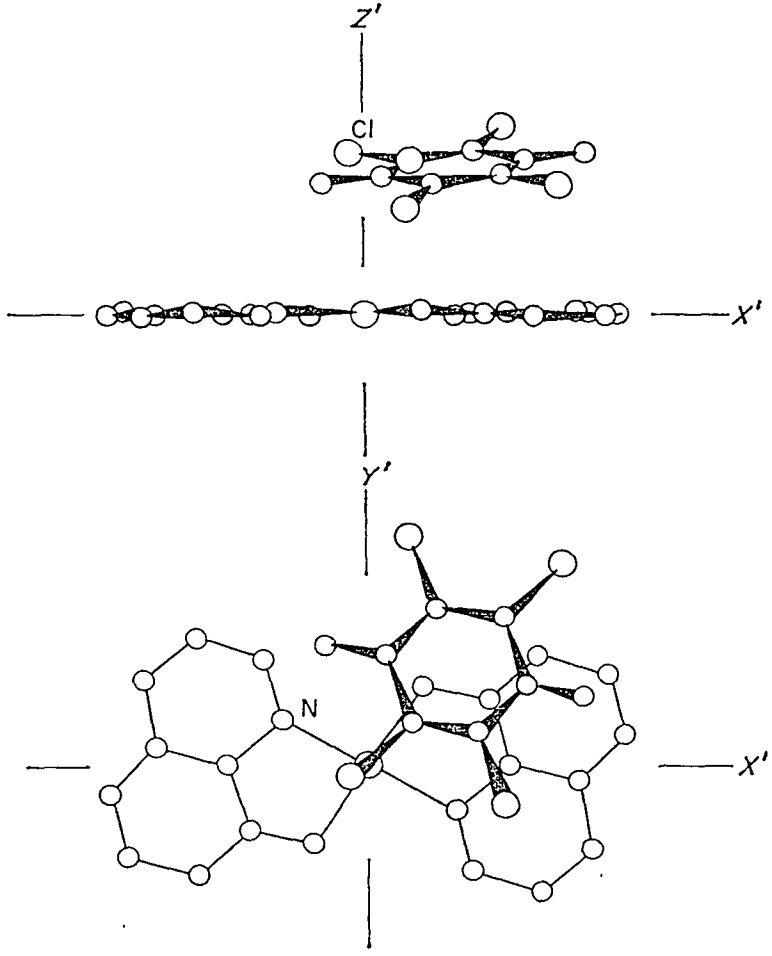


FIGURE 18. A chloranil molecule in the bis-8-hydroxyquinolinatopalladium-(II)chloranil complex projected parallel to, and perpendicular to, the least-squares best plane of the bis-8-hydroxyquinolinatopalladium. Reproduced with permission from B. Kamenar, C. K. Prout and J. D. Wright, *J. Chem. Soc.*, 4851, Figure 2 (1965).

V. ACKNOWLEDGMENT

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The Chemistry of the quinonoid compounds
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CHAPTER 7

Quinones as oxidants and dehydrogenating agents

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I. INTRODUCTION

The oxidizing properties of quinones were known around the turn of the century and quinones had been applied occasionally as dehydrogenating agents, but it was first pointed out in 1954 that quinones 'appear to represent neutral acceptors par excellence for hydride ion'[1]. This view was substantiated in numerous subsequent papers by Braude, Jackman, Linstead and their collaborators[2]. A stimulating account of that and related work was published[3] by Jackman in 1960 when the mechanism of hydrogen transfer from a donor molecule AH_2 to a quinone Q had been established to occur in a two-stage ionic process:

$$AH_2+Q \longrightarrow AH^+ + QH^-$$
$$AH^+ + QH^- \longrightarrow A+QH_2$$

During the past twelve years the scope of quinone dehydrogenation, previously largely limited to hydroaromatic compounds, has been extended to various other areas of organic chemistry. Numerous recent papers reflect the current interest in quinones as oxidants or dehydrogenating agents. Some selected quinones with high oxidation potential are now well established as reagents in organic chemistry[4].

The present chapter describes the use of quinones as oxidants and dehydrogenating agents in synthetic organic chemistry. Not included will be any light-induced dehydrogenations by quinones, as these are presented in the chapter on Photochemistry. Similarly, the quinone–hydroquinone system will not be discussed here, nor will there be a detailed discussion of those oxidations by quinones which frequently occur subsequent to nucleophilic addition reactions to quinones or of the role of quinones in electron transfer reactions in biological systems, as these are all treated in other chapters.

Quinones have found extensive use as dehydrogenating agents in steroid chemistry. Some mechanistically pertinent and recent examples

are discussed below in section III. For a comprehensive list of dehydrogenation reactions of steroidal compounds, however, the reader is referred to review articles[5-8], most notably to that by Walker and Hiebert on the use of 2,3-dichloro-5,6-dicyanobenzoquinone-1,4 (DDQ)[7].

The term quinones in this chapter covers *ortho*- and *para*-quinones as well as diphenoquinones. The term oxidation refers to electron transfer reactions not involving hydrogen transfer, while the term dehydrogenation refers to removal of hydrogen from a molecule with concomitant formation of a carbon–carbon double bond. However, the terms oxidation and dehydrogenation will be used indiscriminately in other cases, for instance in the conversion of an alcohol into an aldehyde. Also the removal of a hydrogen atom from a phenol by a quinone may be considered as an oxidation or a dehydrogenation.

General mechanistic features of quinone dehydrogenation are presented in section II.B, yet a brief discussion of the mechanism may, throughout the chapter, accompany the examples of quinone dehydrogenation, particularly those where the reaction takes a different course than expected, or when the reaction can be rationalized in terms of one-electron transfers rather than by hydride ion abstraction.

II. GENERAL FEATURES OF QUINONE DEHYDROGENATION

A. The Oxidation Potential

Attempts to correlate the rate of dehydrogenation with the oxidation potential (E_0) of the quinone applied apparently were first made by Dimroth and collaborators[9]. It was thus recognized that the nature of the substituents of the quinone has a pronounced effect on the reaction time in the dehydrogenation of hydrazo compounds[10]. 2,3-Dicyano-1,4-benzoquinone, (E_0 971 mV), for example, was found to react instantaneously with diarylsemicarbazides while methyl-1,4-benzoquinone (E_0 645 mV) reacted very slowly (20 hours for 50% conversion):

More recently, a similar relationship has been established between the rate of catalytic hydrogenation and the oxidation potential of quinones[11].

The oxidation potentials of a large number of quinones have been determined by various methods and data obtained before 1960 have been summarized by Clark[12]. Likewise, the polarographic half-wave potentials of various quinones have been determined[13]. It should be noted that

the oxidation potential depends, as well as on temperature and pH, on the nature of the solvent as illustrated by Table 1 for 1,4-benzoquinone and tetrachloro-1,4-benzoquinone (chloranil).

TABLE 1. Influence of solvent on the oxidation potential[12] (in mV)

Solvent	1,4-Benzoquinone	Chloranil
Benzene	711	742
50% acetic acid	696	712
Glacial acetic acid	650	675

Alkyl groups and other electron-donating substituents decrease the oxidation potential of quinones while halogens and other electron-withdrawing substituents have the opposite effect. The oxidation potentials of some selected examples of *ortho*-quinones, *para*-quinones, diphenoquinones and quinones of condensed aromatic compounds are given in Tables 2–5. E_0 values are given in millivolts.

TABLE 2. Oxidation potentials of *o*-benzoquinones[17, 18] (standard of reference: unsubstituted *o*-benzoquinone 795 mV)

1,2-Benzoquinone	E_0
4-Nitro-	895
4-Benzoyl-	ca. 895
4-Formyl-	883
4-Acetyl-	866
Tetrachloro-	830
Tetrabromo-	814
4-*t*-Butyl-	732
3,5-Di-*t*-butyl-	680
3,4,5-Trimethyl-	653
Tetramethyl-	627

Of the *p*-benzoquinones, only 1,4-benzoquinone, chloranil and DDQ are widely used as oxidants or dehydrogenating agents in synthetic organic chemistry. The synthesis of the high-potential tetracyano-1,4-benzoquinone was accomplished[14] some years ago; however, due to its high reactivity and moisture sensitivity, this quinone has not found the

TABLE 3. Oxidation potentials of *p*-benzoquinones (standard of reference: unsubstituted *p*-benzoquinone 711 mV (references 1, 3 and 12) or 699 mV (reference 19))

1,4-Benzoquinone	E_0	Remarks	Reference
2,3-Dichloro-5,6-dicyano-	ca. 1000		3
2,3-Dicyano-	971	In aqueous solution	12
2,5-Dibromo-	768	In benzene	12
Tribromo-	763	In benzene	12
Trichloro-	755	In benzene	12
Tetrabromo-	746	In benzene	12
Tetrachloro-	742	In benzene	12
2,6-Dichloro-	740	In benzene	12
Iodo-	737	In benzene	12
Methyl-	645	Reference, 699 mV	19
2,6-Dimethyl-	593	Reference, 699 mV	19
2-Methyl-5-isopropyl-	589		1
Trimethyl-	527	Reference, 699 mV	19
2,6-Di-*t*-butyl-	496	Reference, 699 mV	19
Tetramethyl	463	Reference, 699 mV	19

TABLE 4. Oxidation potentials of diphenoquinones

4,4′-Diphenoquinone	E_0	Reference
3,3′,5,5′-Tetrachloro-	ca. 1000	3
Unsubstituted	954	11
3,3′,5,5′-Tetramethyl-	845	11
3,3′,5,5′-Tetraisopropyl-	725	11
3,3′,5,5′-Tetra-*s*-butyl-	685	11
3,3′,5,5′-Tetra-*t*-butyl-	675	11

TABLE 5. Oxidation potentials of quinones of condensed aromatic compounds[12]

Quinone	E_0
1,2-Phenanthrenequinone	651[a]
1,2-Naphthoquinone	576
1,2-Anthraquinone	489[a]
1,4-Naphthoquinone	484
9,10-Phenanthrenequinone	471[a]
9,10-Anthraquinone	155[a]

[a] E.m.f.

anticipated[3] application as a dehydrogenating agent. Since many *o*-benzoquinones are prone to undergo Diels–Alder dimerization, only tetrahalo-*o*-quinones, particularly tetrachloro-*o*-quinone (*o*-chloranil) have found widespread use as dehydrogenating agents. Among the quinones of condensed aromatics, 9,10-phenanthrenequinone and its nitro derivatives are frequently used in the dehydrogenation of steroids.

Diphenoquinones have been applied only occasionally as oxidants although their fairly high oxidation potential and their ready availability should make them potentially useful as dehydrogenating agents[15,16].

B. Kinetics and Mechanism

Based on kinetic data obtained in studies of hydroaromatic compounds[1], triphenylmethanes[20] and allyl alcohols[21], the dehydrogenation by quinones has been found to be first-order in hydrogen donor and first-order in quinone. The rate of dehydrogenation is higher in polar solvents such as dimethylformamide, nitrobenzene or alcohols than in non-polar solvents such as benzene or phenetole. Radical-initiators were found to be without effect on the rate of reaction[1]. Electron-donating substituents in the hydrogen donor molecule enhance the rate of reaction[1].

It has been established for both the dehydrogenation of hydroaromatic compounds, dihydropyridines and diarylsemicarbazides that the rate of dehydrogenation increases as the oxidation potential of the quinone is increased and a linear correlation between the free energy of activation and the oxidation potential of *p*-benzoquinones has been found[1]. However, *o*-quinones react faster with hydroaromatic compounds than *p*-quinones of the same oxidation potential.

The mechanism for the dehydrogenation of hydroaromatic compounds put forward by Braude, Jackman and Linstead[1], and supported by a recent[22] investigation using tritium-labelled substrate, involves the transfer of a hydride ion to the quinone in the rate-determining step (reaction 1). In agreement with reaction (1) are the observed large isotope effects[20,22*]:

$$AH_2 + Q \xrightarrow{\text{slow}} AH^+ + QH^- \qquad (1)$$

Rapid proton transfer from the conjugate acid to the hydroquinone anion then leads to the dehydrogenated product A and the hydroquinone QH_2

* After completion of the manuscript, two pertinent papers dealing with the kinetics and mechanism of the dehydrogenation of hydroaromatic systems by DDQ appeared[260, 261]. The exceptional high reactivity of 1,4-cyclohexadiene was suggested to involve the simultaneous rather than a stepwise transfer of two hydrogens to the quinone.

(reaction 2):

$$AH^+ + QH^- \xrightarrow{\text{fast}} A + QH_2 \qquad (2)$$

Supporting this mechanism, the dehydrogenation of hydroaromatic compounds by low-potential quinones ($E_0 < 600$ mV) has been found to be subject to proton catalysis according to reactions (3–5) in which the protonated quinone QH^+ acts as an efficient hydride ion acceptor. *p*-Nitrophenol, picric acid and thymohydroquinone have been used as catalysts in the dehydrogenation by thymoquinone[1].

$$Q + H^+ \longrightarrow QH^+ \qquad (3)$$

$$AH_2 + QH^+ \longrightarrow AH^+ + QH_2 \qquad (4)$$

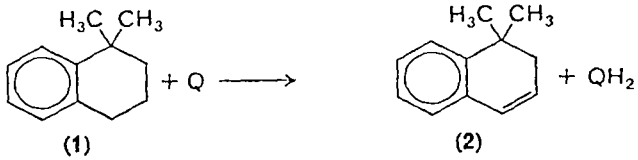
$$AH^+ \longrightarrow A + H^+ \qquad (5)$$

As to whether reaction (1) in the dehydrogenation of hydroaromatic compounds is preceded by formation of a substrate: quinone charge-transfer complex remains to be studied spectroscopically. However, charge-transfer complex formation certainly does precede the oxidation of amines and phenols by quinones.

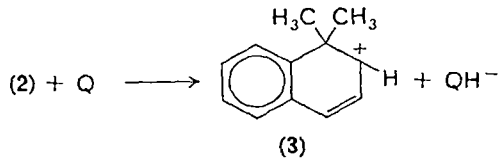
Further light has been shed on the mechanism of hydrogen transfer by a study of the dehydrogenation of *cis*-1,2-dideuterioacenaphthene by DDQ and *o*-chloranil[23]. In benzene solution, the dehydrogenation proceeds with predominantly *cis*-elimination. This result has been explained by the involvement of ion pairs which may collapse to give the hydroquinone and the *cis*-dehydrogenated product acenaphthylene-d_0 and acenaphthylene-d_2. Dissociation into the free ions leads to both *cis* and *trans* dehydrogenated products. Polar solvents such as dimethylformamide favour dissociation of the ion pair, thus affecting the *cis–trans* ratio.

The mechanism outlined above appears well substantiated for hydroaromatic compounds undergoing aromatization and for hydroethylenic compounds, such as bibenzyl being dehydrogenated to stilbene. The most convincing evidence for the involvement of ionic intermediates, however, may be seen in the aromatization of some *gem*-substituted hydroaromatic compounds by quinones (see section IV.C). For example, dehydrogenation of 1,1-dimethyltetralin (**1**) by *o*-chloranil or DDQ at 80°C in benzene gave 1,2-dimethylnaphthalene (**4**) as the result of a Wagner–Meerwein rearrangement (reactions 6–8)[24]. Since it has been established recently[22] that the rate-determining step in the conversion of tetralines into naphthalenes is the abstraction of a hydride ion from the α-position, the formation of **4** presumably involves the intermediacy of 1,1-dimethyl-1,2-dihydronaphthalene (**2**). Reaction (7) indeed has been verified by the dehydrogenation of **2** with 9,10-phenanthrenequinone[25].

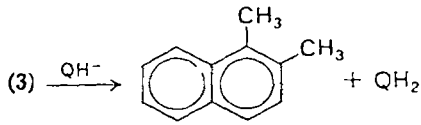
The dehydrogenation by 9,10-phenanthrenequinone was also found to give 1-methylnaphthalene. In agreement with the hydride ion mechanism of dehydrogenation, a methyl group is transferred to the phenanthrenequinone in an alternative reaction to the Wagner–Meerwein rearrangement of the intermediate cation 3.



(1) (2) (6)



(3) (7)



(4) (8)

The absence of carbon–carbon coupled dimerization products in the dehydrogenation of hydroaromatic compounds has been considered as supporting evidence for the involvement of ionic rather than of radical intermediates[1]. However, as has been shown subsequently[16,26], carbon–carbon coupled products may very well be formed by quinone dehydrogenation if carbon–carbon double bond formation is structurally impossible. Thus, the dehydrogenation of diphenylmethane by diphenoquinones gives tetraphenylethane in good yield and the result may be explained by a homolytic mechanism.

Actually, several examples are known in which the dehydrogenation by quinones does lead to stable free radicals[27,28]. In view of these reactions the proposal[27] to represent the hydride ion transfer (reaction 1) by two successive steps (reactions 9 and 10) appeared justified. Further refinement of the mechanism should take into account that high-potential

$$AH_2 + Q \longrightarrow AH^{\bullet} + QH^{\bullet} \quad (9)$$

$$AH^{\bullet} + QH^{\bullet} \longrightarrow AH^{+} + QH^{-} \quad (10)$$

quinones are strong electron acceptors. For example, 2,6-dichloro-1,4-benzoquinone reacts with *N,N,N′,N′*-tetramethyl-*p*-phenylenediamine to give, dependent on the nature of the solvent, via a charge-transfer complex,

the hydroquinone radical anion and the Wurster radical cation as the result of a one-electron transfer (reactions 11 and 12)[29]. The mechanism of

$$A+Q \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} [A:Q] \quad \text{charge-transfer complex} \tag{11}$$

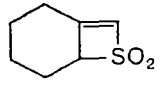
$$[A:Q] \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} A^{\cdot+}+Q^{\cdot-} \tag{12}$$

quinone dehydrogenation thus may depend on the structure of the substrate and, in particular, on the stability or reactivity of the intermediates.

III. DEHYDROGENATION OF ALIPHATIC COMPOUNDS AND STEROIDS

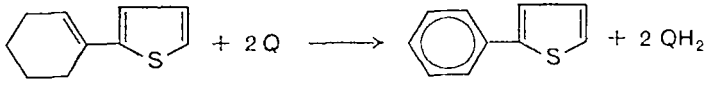
A. *Dehydrogenation of Hydrocarbons*

Saturated aliphatic hydrocarbons apparently resist dehydrogenation even by high-potential quinones. Thus, all attempts to dehydrogenate decalin with *o*-chloranil have been unsuccessful[30]. Activation of the substrate either by a phenyl substituent (see sections IV and V) or a carbon–carbon double bond generally is a prerequisite for quinone dehydrogenation. Furthermore, it appears to be essential that the olefinic hydrocarbon does not contain strongly electron-withdrawing substituents. For example, the sulphone (**5**) was recovered unchanged after



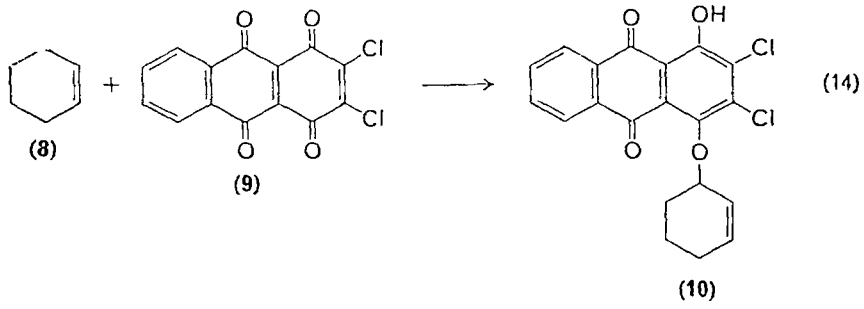
(5)

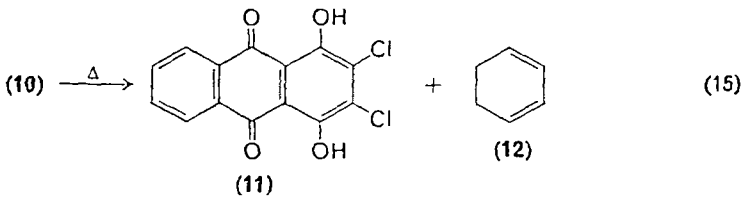
prolonged heating with chloranil in toluene[31]. By contrast, cyclohexene was dehydrogenated by *o*-chloranil at room temperature[30]. (However, the resulting 1,3-cyclohexadiene does undergo a subsequent addition reaction with *o*-chloranil.) Likewise, a mixture of dimethylcyclohexenes was found to undergo dehydrogenation by chloranil at elevated temperature to give a mixture of the three xylenes in 85% yield[32]. The dehydrogenation of the cyclohexenylthiophene **6** by chloranil proceeded smoothly in refluxing benzene to give 2-phenylthiophene **7** in 79% yield (reaction 13)[33].



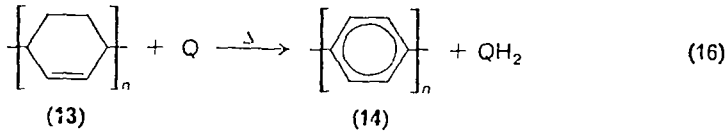
(6) (7) (13)

It is possible that the dehydrogenation of hydrocarbons by quinones generally involves intermediate hydrocarbon : quinone adducts which decompose thermally into the dehydrogenated product and the hydroquinone. For example, the reaction of cyclohexene **8** with the diquinone **9** gave the adduct **10** which, upon pyrolysis, gave the reduced quinone **11** and cyclohexadiene (**12**; reactions 14 and 15)[34]. The reaction of tetralin

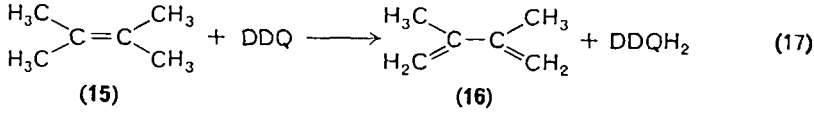




with the diquinone **9** was found to give an analogous adduct which, upon pyrolysis, gave 1,2-dihydronaphthalene[34]. Similar adducts of hydroquinone mono-ether structure **10** may also be involved in the dehydrogenation of poly(1,3-cyclohexadiene) (**13**) with chloranil in refluxing xylene. The poly-*p*-phenylene **14** was obtained in 90% yield after heating the reaction product to 450°C (reaction (16)[35].

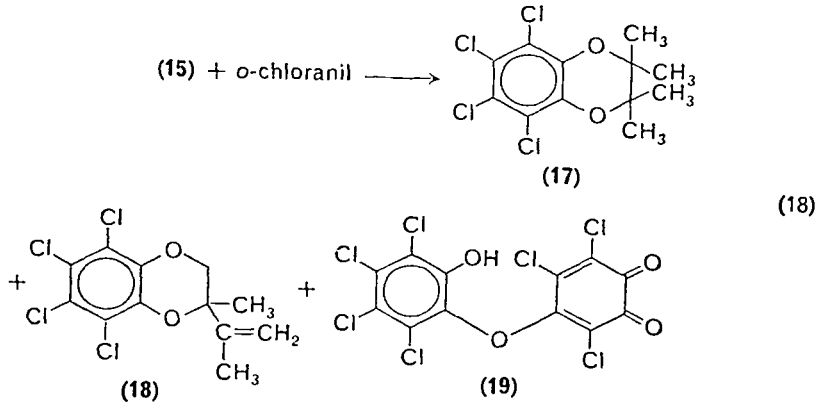


Earlier attempts to dehydrogenate linear olefins with chloranil in boiling xylene did lead to tetrachlorohydroquinone, though no pure products arising from the olefin were obtained[32]. Recently, however, some simple alkenes have been found to react smoothly with high-potential quinones[36]. Thus, DDQ reacts with tetramethylethylene (**15**) in methylene chloride, benzene or acetonitrile at room temperature to give 2,3-dimethylbutadiene (**16**) (reaction 17) which then is trapped by DDQ



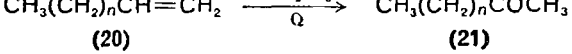
(15) (16) (17)

to give a Diels–Alder adduct. The reaction of *o*-chloranil with tetramethylethylene in benzene at room temperature gives compounds **17**, **18** and **19** (reaction 18)[37]. Though benzodioxanes frequently are formed from *o*-chloranil and olefins[30], it was verified that the benzodioxane **17** does



not derive by addition of *o*-chloranil to tetramethylethylene and 2,3-dimethylbutadiene (**16**) probably is not an intermediate in the formation of benzodioxane **18**. The formation of **17** and **18** has been rationalized by a homolytic mechanism in which the primary step consists of the abstraction of a hydrogen atom from tetramethylethylene by *o*-chloranil. *o*-Bromanil was found to react with tetramethylethylene in a similar fashion[37].

An interesting and preparatively significant palladium-catalysed oxidation of terminal olefins into methyl alkyl ketones requiring the presence of a quinone has been reported recently[38]. For instance, the reaction of 1-hexene (**20a**) with *p*-benzoquinone in the presence of palladium(II) chloride and water at room temperature gave butyl methyl ketone **21a** in 81% yield (reaction 19). In a similar fashion 1-dodecene



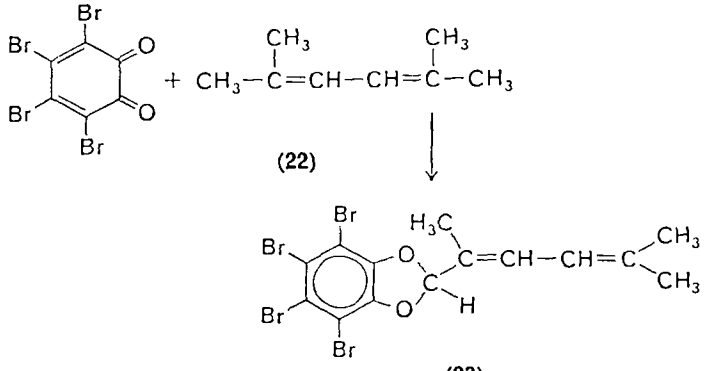
(19)

(20) (21)

a: $n = 3$
b: $n = 9$

20b was converted into 2-dodecanone **21b**. The quinone used in these oxidations should have an oxidation potential higher than that of palladium, suggesting that the role of the quinone is that of an oxidant for the regeneration of palladium(II).

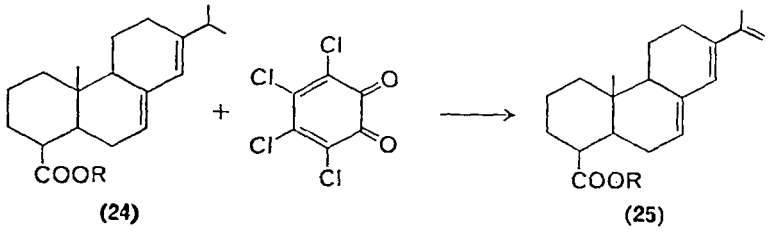
Conjugated dienes probably react with high-potential quinones more easily than simple olefins. The reaction of 2,5-dimethylhexa-2,4-diene (**22**) with *o*-bromanil has been found[39] to proceed smoothly at 0°C in benzene solution to give tetrabromocatechol and the dioxol **23** in 80% yield (reaction 20). *o*-Chloranil reacts with 2,5-dimethylhexa-2,4-diene



(22) (23) (20)

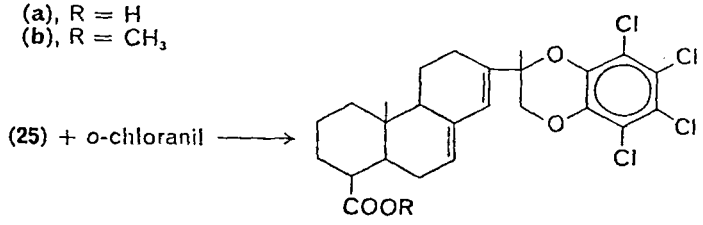
in a similar fashion to give the corresponding dioxol in 83% yield. Though the mechanism of the dioxol formation has not been elucidated, the reaction apparently involves the dehydrogenation by the tetrahalogen-*o*-benzoquinone. It has been suggested that the formation of **23** proceeds via a paramagnetic molecular complex since the reaction was found to be associated with the transient appearance of an e.s.r. signal.

Some other examples of dehydrogenative dioxol formation by reactions of *o*-quinones have been reported; however, the structural prerequisites for this reaction of dienes have not been established[39]. Hexa-2,4-diene, for instance, reacts with both *o*-bromanil and *o*-chloranil to give the benzodioxanes by Diels–Alder reaction of the diene with the *o*-quinone[39]. On the other hand, benzodioxane formation can be preceded by a dehydrogenation reaction if the introduction of a carbon–carbon double bond is structurally possible. Both abietic acid (**24a**) and its methyl ester (**24b**) react with *o*-chloranil to give the dehydrogenation adducts **26a** and **26b**, respectively (reactions 21 and 22)[40]. The formation of benzodioxanes **26** has been proposed to proceed by Diels–Alder addition to the isopropenyl group of the intermediate dehydroabietic acid **25**. This mode of reaction



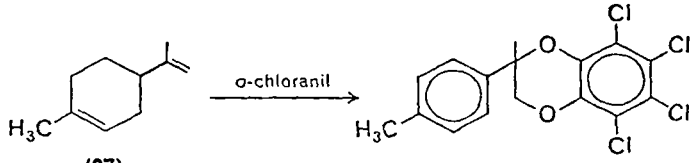
(24) (25) (21)

(a), R = H
(b), R = CH_3



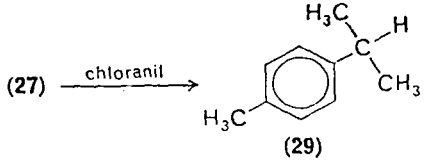
(26) (22)

is supported by the observation that limonene **27** in boiling xylene undergoes an analogous dehydrogenation–addition reaction with *o*-chloranil to give the benzodioxane **28** (reaction 23) which is also obtained from *p*-cymene and *o*-chloranil[40].

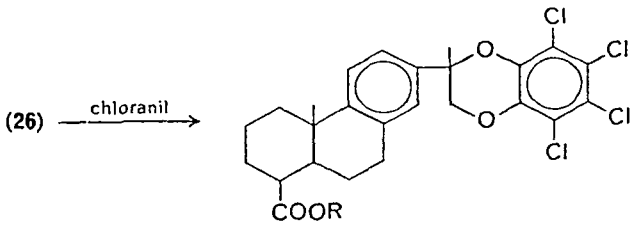


(27) (28) (23)

From a preparative point of view, *o*-quinones may not be the dehydrogenating agents of choice in reactions where the product is a dienophile. In those cases, halogenated *p*-benzoquinones may be used more advantageously. Thus, dehydrogenation of abietic acid **24a** with chloranil in boiling xylene does give—though in moderate yield—dehydroabietic acid **25a**[41]. Dehydrogenation of neat limonene **27** with chloranil has been claimed to give *p*-cymene (**29**; reaction 24)[42]. The formation of **29** involves both a dehydrogenation and an isomerization reaction. A similar dehydrogenative isomerization with concomitant aromatization is observed in the reaction of diene **26** with chloranil (reaction 25)[40].

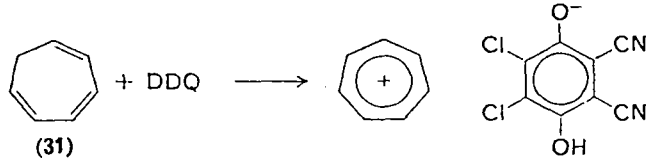


(29) (24)

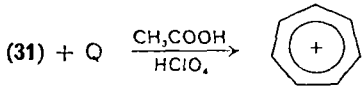


(30) (25)

The mechanism of the reactions of quinones with olefins resulting in the formation of a carbon–carbon double bond may be interpreted by the two-step ionic mechanism outlined in section II.B. Using cycloheptatriene **31** as the olefinic substrate, overall hydride ion transfer to the quinone can be demonstrated by the formation of stable tropyllium ion. Thus, reaction of DDQ with cycloheptatriene in methylene chloride gives a deep-coloured complex which was formulated as the tropylium dichlorodicyanoquinolate **32** (reaction 26)[27]. When the dehydrogenation is carried



(31) (32) (26)



(33) (27)

out in acetic acid in the presence of perchloric acid, tropylium perchlorate (33; 92% yield) is formed instantaneously (reaction 27)[27]. Tropylium picrate was prepared from cycloheptatriene in a similar fashion. Other quinones used successfully for the formation of tropylium perchlorate were *o*-chloranil (97%), chloranil (70%) and 1,4-benzoquinone (30%). It is conceivable that the lower yield in the case of 1,4-benzoquinone reflects acid-catalysed addition reactions of the quinone rather than the reduced efficiency as hydride ion acceptor due to the lower oxidation potential.

B. Oxidation of Allyl and Propargyl Alcohols

Simple saturated alcohols such as methanol or ethanol are stable towards oxidation by high-potential quinones at room temperature and

can be used as solvents in dehydrogenation reactions (see section V.B). Only under drastic conditions and upon prolonged contact may even saturated alcohols undergo oxidation by DDQ as has been observed with some steroidal alcohols[5,6].

Phenyl-substituted alcohols (see section V.A.3) and α,β-unsaturated alcohols, however, are readily oxidized by high-potential quinones to the corresponding carbonyl compounds. These reactions generally proceed smoothly at room temperature with equimolar amounts of reactants to give the α,β-unsaturated aldehydes or ketones in good yields[43]. Table 6

TABLE 6. Oxidation of allyl and propargyl alcohols by *o*-chloranil[43]

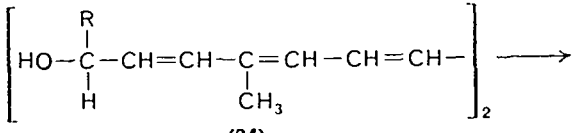
Alcohol	Reaction time (h)	Yield of carbony compound (%)
$C_6H_5CH{=}CH{-}CH_2OH$	15	100 [a]
$CH_3{-}CH{=}CH{-}\underset{\displaystyle OH}{\overset{\displaystyle H}{\underset{\displaystyle |}{\overset{\displaystyle |}{C}}}}{-}CH{=}CH{-}CH_3$	5	87
$C_6H_5{-}CH{=}CH{-}\underset{\displaystyle H}{\overset{\displaystyle CH_3}{\underset{\displaystyle |}{\overset{\displaystyle |}{C}}}}{-}OH$	48	72
$C_6H_5{-}C{\equiv}C{-}\underset{\displaystyle OH}{\overset{\displaystyle H}{\underset{\displaystyle |}{\overset{\displaystyle |}{C}}}}{-}CH{=}CH{-}C_6H_5$	0·17	91
$C_6H_5{-}C{\equiv}C{-}\underset{\displaystyle H}{\overset{\displaystyle CH_3}{\underset{\displaystyle |}{\overset{\displaystyle |}{C}}}}{-}OH$	18	57

[a] Cinnamaldehyde–tetrachloro-catechol complex.

lists some examples of allyl and propargyl alcohols undergoing oxidation with *o*-chloranil at room temperature in chloroform or carbon tetrachloride solution.

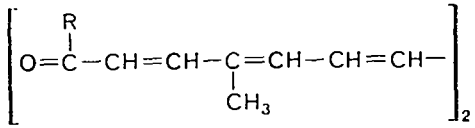
Attempts to oxidize the hexaene alcohol **34** with *o*-chloranil resulted in destruction of the polyene system, possibly by addition reactions to the

quinone. However, the hexaene dione **35** was obtained by oxidation of **34** with chloranil (reaction 28)[44].



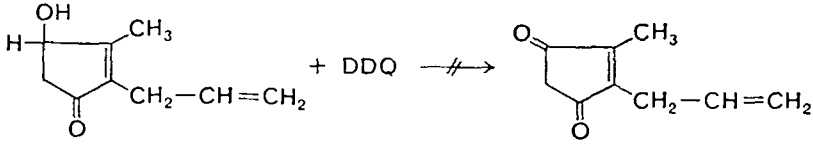
(34)

R = *t*-butyl



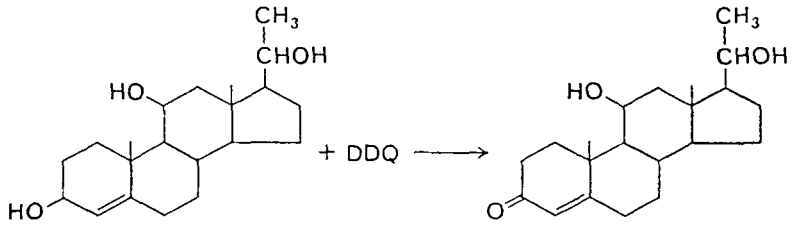
(35) (28)

Exceptions which may be due to structural peculiarities can be encountered in the generally facile oxidation of allyl alcohols by quinones. For example, the cyclopentenolone **36** was not oxidized by DDQ (reaction 29)[45].



(36) **(37)** (29)

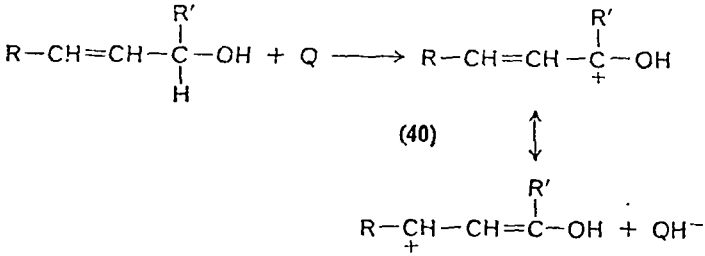
The major advantage of the oxidation of α,β-unsaturated alcohols by quinones lies in the remarkably high selectivity of the oxidant. This feature of quinone dehydrogenation has been preparatively exploited in the room temperature oxidation of numerous steroidal diols by DDQ in dioxan or benzene as illustrated by conversion of **38** into **39** in 70% yield (reaction 30)[46].



(38) **(39)** (30)

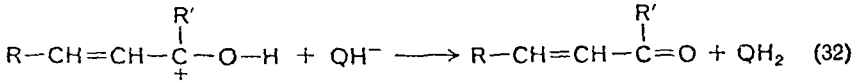
The selective oxidation of α,β-unsaturated alcohols can be explained by the two-stage ionic mechanism which in the first step leads to a resonance

stabilized cation **40** by rate-determining hydride ion transfer to the quinone (reaction 31). Thus, the reactivity will increase with extended



(31)

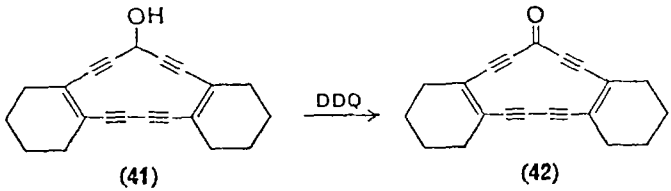
conjugation in the alcohol. It has been suggested that, in non-polar solvents, the cationic and anionic intermediates will remain associated as an ion pair, leading to products by rapid proton transfer (reaction 32)[43].



(32)

Kinetic evidence has been obtained in the oxidation of isotopically labelled steroidal allyl alcohols, which supports the ionic mechanism according to reactions (31) and (32)[21]. The observed higher rate of oxidation of equatorial allyl alcohols has been attributed to the overlap of the axial hydrogen with the π-electrons of the carbon–carbon double bond[21].

Oxidation of α,β-unsaturated alcohols by quinones proceeds faster than the dehydrogenations of olefinic hydrocarbons. Thus, the acetylenic ketone **42** was obtained, without concomitant aromatization, by reaction of the dipropargyl alcohol **41** with DDQ (reaction 33)[47].



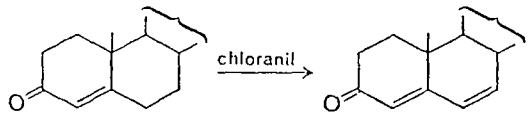
(33)

C. Dehydrogenation of Carbonyl Compounds

1. Monoketones

High potential quinones, particularly chloranil and DDQ, have found extensive application in the dehydrogenation of steroidal ketones. Comprehensive reviews of these reactions have been published[6,7], thus limiting the discussion here to some pertinent examples.

Interest in the dehydrogenation of steroid ketones was greatly stimulated by the discovery that steroidal 4-en-3-ones (**43**) were converted smoothly into the corresponding 4,6-dien-3-ones (**44**) upon treatment with quinones in a variety of solvents (reaction 34)[48]. Although chloranil in boiling



(43) (44) (34)

xylene or *t*-butanol gave the best yields of **44** most rapidly, other quinones such as 1,4-benzoquinone, 1,4-methylbenzoquinone, 2,6-dichloro-1,4-benzoquinone, 1,2-naphthoquinone and 1,4-naphthoquinone were also found to dehydrogenate selectively. It was suggested that the formation of **44** could be explained by hydride ion abstraction from the 7-position of the dienol **45**[48].

(45) (46)

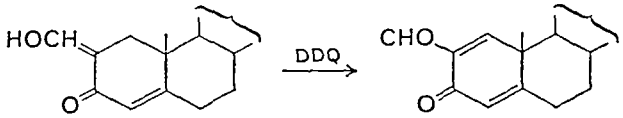
Interestingly, the dehydrogenation of steroidal 4-en-3-ones (**43**) by DDQ does not lead to 4,6-dien-3-ones (**44**) but gives, in high yields, 1,4-dien-3-ones (**47**) (reaction 35)[49]. A detailed mechanism study revealed

(43) (47) (35)

that the dehydrogenation of enones **43** can be catalysed by acids—DDQ itself may act as an acid—and that the observed differences between the reaction of DDQ and of chloranil may be rationalized by the dehydrogenation of the two different enols **45** and **46**[50]. Hydride ion abstraction from the 1-position of the 2,4-dien-3-ol (**46**), formed under kinetic control in the absence of acids or in the presence of weak acids, leads to the 1,4-dien-3-one (**47**). It was suggested that chloranil does not bring about this dehydrogenation because the oxidation potential of 2,4-dien-3-ol (**46**) is higher than that of chloranil. In the presence of strong acids the

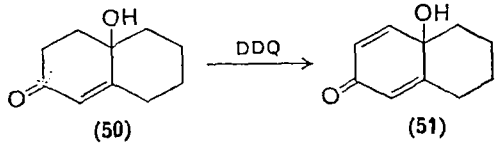
thermodynamically more stable 3,5-dien-3-ol (**45**) also becomes kinetically favoured to undergo hydride ion transfer to the quinone from the 7-position, thus giving rise to the 4,6-diene-3-one (**44**).

DDQ has been applied in recent years in numerous other instances in the dehydrogenation of steroidal ketones, and the mechanism involving enolization serves well to explain the selectivity of dehydrogenation[51–54]. Under prolonged drastic conditions, in refluxing dioxan in the presence of *p*-toluenesulphonic acid, excess DDQ converts steroidal ketones into steroidal phenanthrenes in a reaction which involves migration of methyl substituents[55]. Steroidal 2-hydroxymethylene-3-ones (**48**) are readily converted into 2-formyl-1,2-en-3-ones (**49**) by brief treatment with DDQ at room temperature (reaction 36)[7,56]. Likewise, the dehydrogenation of 2-hydroxymethylene-substituted octalones proceeds easily with DDQ to give the corresponding formyl-substituted cross-conjugated ketones[57,58].

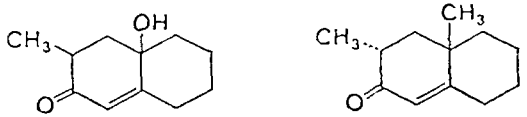


(48) (49) (36)

Few other examples of dehydrogenation of non-steroidal cyclic ketones have been reported thus far. For instance, dehydrogenation of the bicyclic γ-hydroxy α,β-unsaturated ketone (**50**) with DDQ gives the 4-hydroxycyclohexa-2,5-dien-1-one (**51**) (reaction 37)[59]. However, attempts

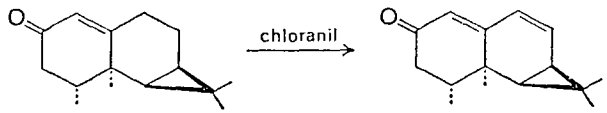


(50) (51) (37)



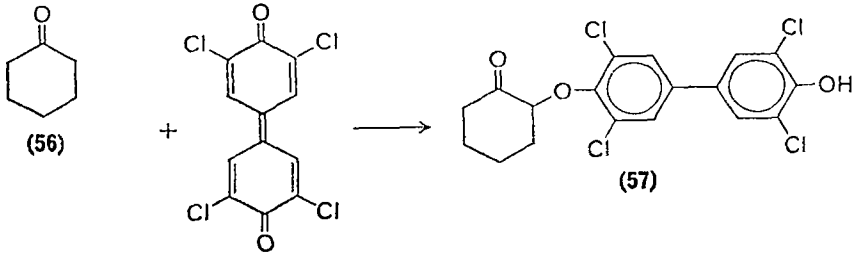
(52) (53)

to dehydrogenate the methyl-substituted octalone **52** were not successful[59]. Likewise, octalone **53** was found to be 'totally inert' towards DDQ in boiling benzene[60]. Steric reasons, presumably, are responsible for these failures. The tricyclic ketone **54** upon treatment with chloranil in boiling *t*-butanol gave the dehydrogenated ketone **55** (reaction 38), and its formation may be understood in light of the enol mechanism[61].



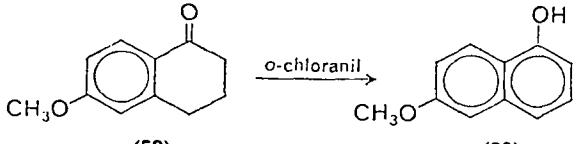
(54) (55) (38)

The reaction of cyclohexanone **56** with 3,3′,5,5′-tetrachloro-4,4′-diphenoquinone does not result in the formation of cyclohexenone but instead gives the addition product **57** (reaction 39)[62]. Adducts have also been obtained from substituted cyclohexanones as well as from pentan-2-one and tetrachlorodiphenoquinone. Since perchloric acid (but not peroxides or light) accelerates the formation of **57**, the reaction presumably involves the cyclohexanone enol and coupling of ionic intermediates.

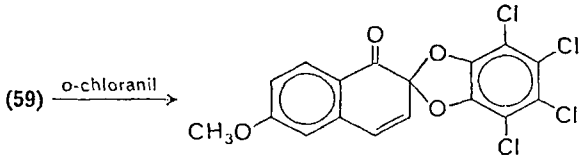


(39)

The dehydrogenation of the tetralone **58** with *o*-chloranil gives the naphthol **59** (reaction 40) which then rapidly undergoes further dehydrogenation with concomitant coupling to yield compound **60** (reaction 41)[63]. The mechanism of the formation of the naphthol **59** does not necessarily involve dehydrogenation of the tetralone enol but may proceed by hydride ion abstraction from the benzylic position of the tetralone **58**.

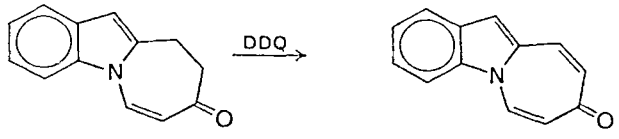


(58) (59) (40)



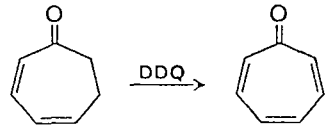
(60) (41)

The dehydrogenation of the dihydroazepinoindolone **61** to give the unsaturated compound **62** in 80% yield was easily accomplished by treatment with DDQ in boiling benzene (reaction 42)[64]. However,



(61) (62) (42)

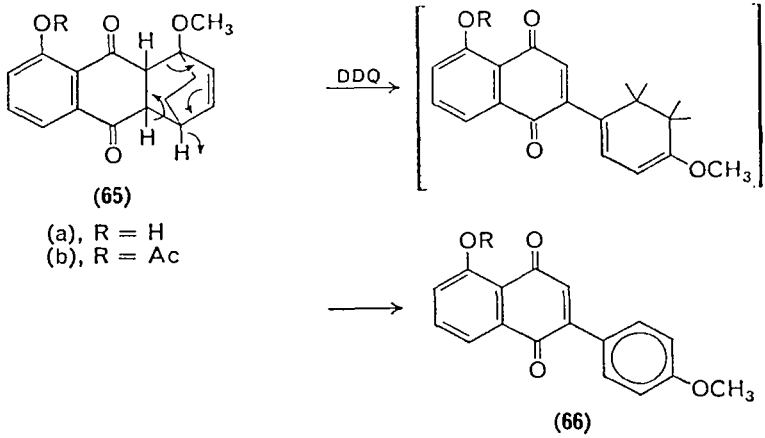
dehydrogenation of 2,4-cycloheptadienone **63** by DDQ gave tropone **64** in 10% yield only (reaction 43)[65]. It would be interesting to see whether, in the light of the proposed enol mechanism, acid catalysis of the dehydrogenation of **63** would improve the yield of tropone.



(63) (64) (43)

2. Diketones

Some unexpected results were obtained in the dehydrogenation of diketones. For example, treatment of the Diels–Alder adduct **65a** with excess DDQ in benzene gave the naphthoquinone **66a** in high yield (reaction 44)[66]. The analogous dehydrogenative rearrangement was

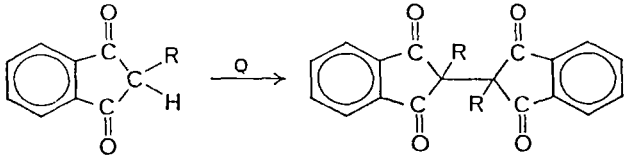


(65)
(a), R = H
(b), R = Ac

(66) (44)

observed in the reaction of DDQ with the acetoxy derivative **65b**. It appears conceivable that the carbon–carbon bond breakage is the result of hydride ion abstraction by DDQ as indicated in structure **65**.

The dehydrogenation of 2-arylindane-1,3-diones (**67**) by 1,4-benzoquinone in chloroform or benzene, and by DDQ in methanol, has been found to proceed rapidly and under mild conditions to give the dehydrodimers **68** (reaction 45)[26,67]. It has been suggested that this mode of



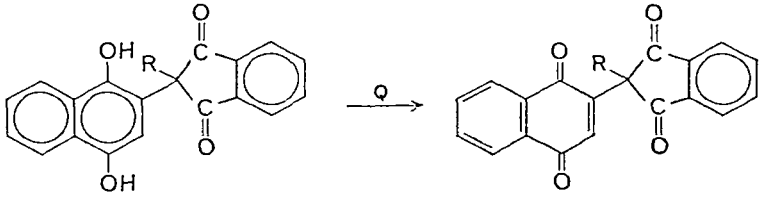
(45)

(67) **(68)**

R = phenyl; *p*-methoxyphenyl.

oxidative coupling occurs in a radical reaction which is preceded by a one-electron transfer from the enolate ion to the quinone[26].

The reaction of 2-arylindane-1,3-diones with 1,4-naphthoquinone ($E_0 = 482$ mV) does not give the oxidatively coupled dimers of structure **68** but yields Michael adducts **69** which subsequently undergo dehydrogenation by 1,4-naphthoquinone to give substituted naphthoquinones **70** (reaction 46)[68].

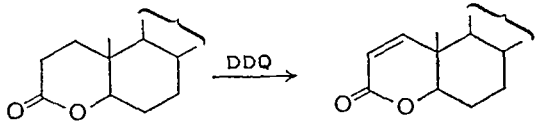


(46)

(69) **(70)**

3. Lactones and lactams

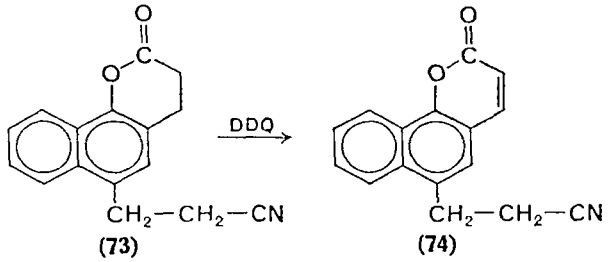
Probably due to less favourable enolization of lactones, the dehydrogenation of saturated lactones by quinones occurs less readily than dehydrogenation of cyclic ketones. For instance, only prolonged treatment of the steroidal lactones **71** with excess DDQ in boiling dioxan gave the α,β-unsaturated δ-lactones **72** (reaction 47)[69]. By contrast, the dehydrogenation of the lactone **73** containing a benzylic site was accomplished by



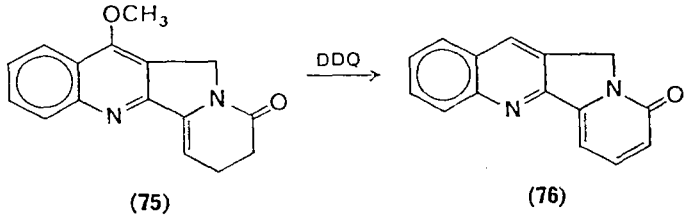
(47)

(71) **(72)**

DDQ and gave the dehydro-product **74** in 70% yield (reaction 48)[70]. Likewise, the dehydrogenation of the lactam **75** by DDQ in benzene to give compound **76** was reported recently (reaction 49)[71].



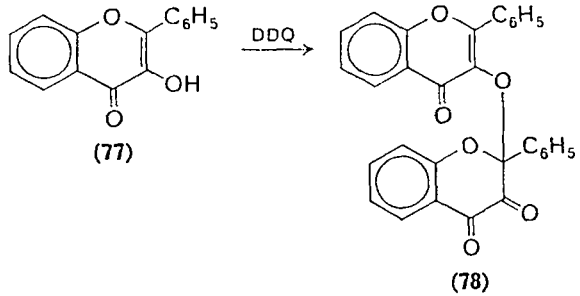
(48)



(49)

D. Dehydrogenation of Enols, Enol Ethers and Enol Esters

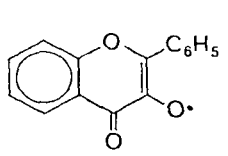
The dehydrogenation of the enolizable indane-1,3-diones by DDQ described in the preceding section was explained by a mechanism in which the quinone acted as a one-electron oxidizing agent. Further support for this mode of dehydrogenation may be seen in the reaction of DDQ with the enol flavonol (**77**). The oxidation in dioxan solution leads to a dehydro-dimer for which the carbon–oxygen coupled structure **78** has been proposed (reaction 50). Ionic dehydrogenation of flavonol could explain the



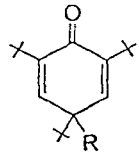
(50)

formation of **78** as well; however, the involvement of flavonoxy radicals **79** appears more likely since dimer **78** is also formed by oxidation of

flavonol with active manganese dioxide[72,73], and the flavonoxy radicals can be trapped to give the crystalline quinol ether **80** if this oxidation is carried out in the presence of 2,4,6-tri-*t*-butylphenoxy radicals[73].



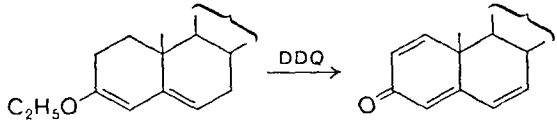
(79)



R = (79)

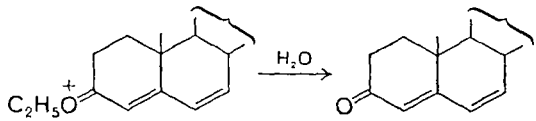
(80)

Most likely, dehydrogenation by quinones involving free radicals is limited to those enols for which carbon–carbon double bond formation is structurally impossible. The reaction of enol derivatives with high-potential quinones resulting in the introduction of carbon–carbon double bonds may be described best by the ionic dehydrogenation mechanism outlined in the preceding section. Thus, dehydrogenation of 3-ethoxy $\Delta^{3,5}$-steroids (**81**) with DDQ in the absence of water gives steroidal 1,4,6-trien-3-ones (**82**) whose formation may be rationalized by hydride ion transfer and subsequent hydrolysis (reaction 51)[74]. When the dehydrogenation is carried out in the presence of water, the cationic intermediate



(81) (82) (51)

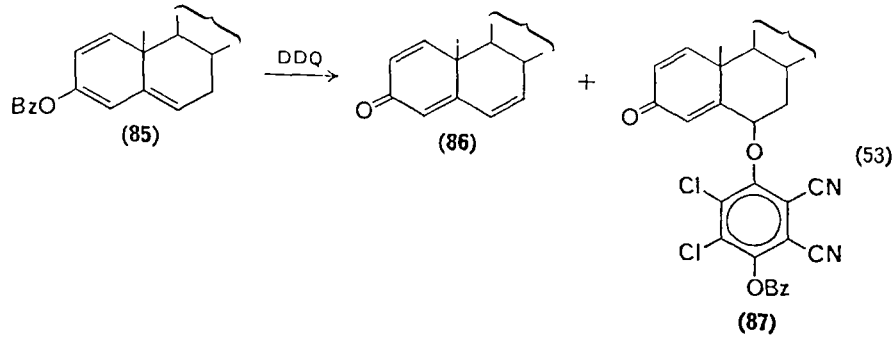
83 may undergo hydrolysis, thus giving rise to the 4,6-dien-3-ones (**84**) (reaction 52). A similar oxidative conversion of a steroidal enol benzoate



(83) (84) (52)

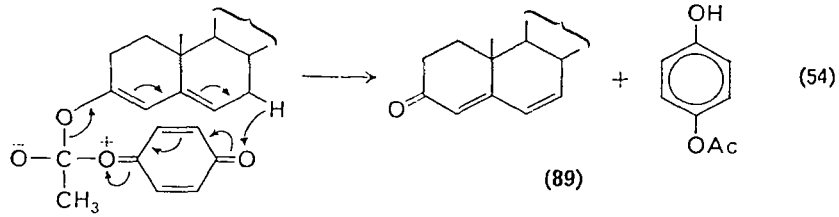
into a ketone by dehydrogenation with DDQ has been reported (reaction 53)[75]. The formation of compound **87** in reaction (53) has been suggested to involve an electrophilic addition of DDQ to the enol ester with concomitant transfer of the benzoyl group.

It is conceivable that the conversion of the enol benzoate **85** into the trienone **86** by DDQ is actually mediated by the acidic properties of the oxidizing agent. This assumption is supported by the observation that



(85) (86) (87) (53)

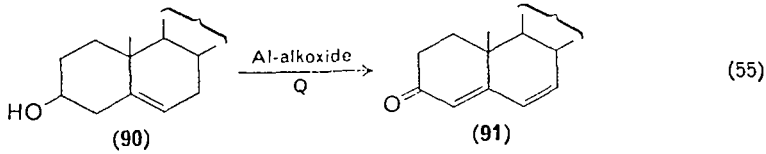
treatment of $\Delta^{3,5}$-3-acetoxycholestadiene by 1,4-benzoquinone in boiling toluene leaves the enol acetate unaffected. However, when this reaction is carried out in the presence of a small amount of anhydrous aluminium chloride, the enol acetate is converted into $\Delta^{4,6}$-3-ketocholestadienone (**89**). The mechanism of the formation of **89** has been suggested to involve 1,4-benzoquinone in a cyclic process as outlined in reaction (54)[76].



(88) (89) (54)

E. Quinones as Hydrogen Acceptors in the Oppenauer Oxidation

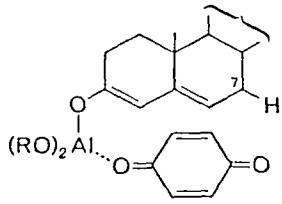
Oppenauer oxidation of Δ^5-3-hydroxysteroids (**90**) in the presence of 1,4-benzoquinone or 1,4-naphthoquinone has been found to give $\Delta^{4,6}$-3-keto-steroids (**91**) (reaction 55)[77]. This reaction, first reported in 1940, is remarkable in view of the Oppenauer oxidation of Δ^5-3-hydroxysteroids in the presence of non-quinonoid hydrogen acceptors, which leads to Δ^4-3-keto-steroids[78].



(90) (91) (55)

The mechanism of the conversion of **90** into the dienone **91** apparently involves, in the first step, the oxidation of the secondary carbinol group to give a Δ^5-3-keto steroid which undergoes further dehydrogenation in the presence of Al-alkoxide and quinone.

It has been convincingly suggested that the selective dehydrogenation of the intermediate Δ^5-3-keto-steroid involves coordination of the oxygen function of the quinone with the aluminium atom of the enolate **92**, thus making hydride transfer from the C-7 position of the steroid a sterically favoured process. In agreement with this rationalization, 1,2-naphthoquinone was found to be ineffective as hydride ion acceptor in the Oppenauer oxidation though its oxidation potential is higher than that of 1,4-naphthoquinone.



(92)

In contrast to the thermal dehydrogenation by either chloranil or DDQ, Δ^4-3-keto-steroids are not dehydrogenated by quinones under Oppenauer conditions. It has been reasoned that the intermediate aluminium $\Delta^{2,4}$-enolate is stable towards quinone dehydrogenation because of unfavourable steric arrangement[76].

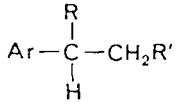
IV. DEHYDROGENATION OF HYDROETHYLENIC AND HYDROAROMATIC COMPOUNDS

In this section, dehydrogenations by quinones resulting in the aromatization of the hydrogen donor are described. A review of the aromatization of steroidal compounds by exhaustive dehydrogenation by quinones has been published recently[8], thus precluding treatment of this subject here. Included in the discussion below are reactions of aryl-activated $-CRH-CH_2-$ groups to which the term hydroethylenic had been previously applied[79].

A separate paragraph of this section deals with the quinone dehydrogenation of non-benzenoid hydroaromatic compounds.

A. Hydroethylenic Compounds

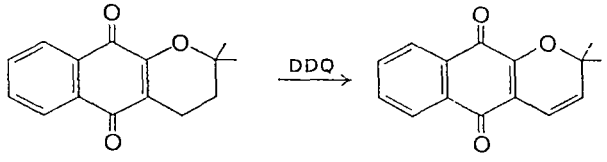
Aryl-substituted alkanes of structure **93** generally react quite slowly with chloranil even at elevated temperature, giving dehydrogenated products in low yields only[32]. By contrast, quinone dehydrogenation may be considered to be of preparative usefulness for the introduction of an



(93)

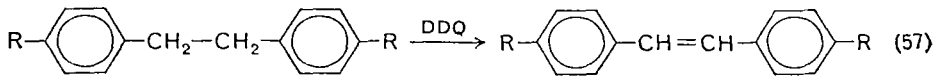
R, R′ = H; alkyl

α,β-double bond into the side-chain of a quinone. For instance, α-lapachone **94** is smoothly converted into the dehydrocompound **95** by treatment with DDQ in refluxing dioxan (reaction 56)[80].



(94) (95) (56)

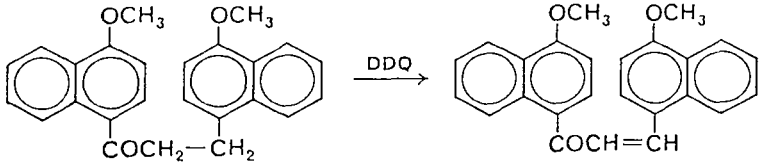
Dehydrogenation of bibenzyl **96a** with chloranil, DDQ, *o*-chloranil, *o*-bromanil, unsubstituted diphenoquinone, tetrachloro- or tetrabromodiphenoquinone in boiling benzene or boiling xylene gave stilbene **97a** always in about 10% yield only (reaction 57)[79, 81]. Substitution of bibenzyl



(96) (97) (57)

(a), R = H
(b), R = OCH_3

by electron-donating groups expectedly results in drastic enhancement of the dehydrogenation reaction. Thus, treatment of 4,4′-dimethoxybibenzyl (**96b**) with DDQ in boiling dioxan gave *trans*-4,4′-dimethoxystilbene (**97b**) in 83–85% yield (reaction 57)[82]. Likewise, the dehydrogenation of **98** may be enhanced by the methoxy substituent (reaction 58)[70].



(98) (99) (58)

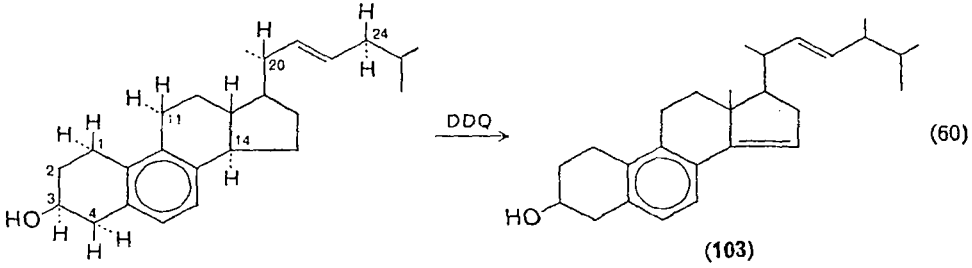
1,1,2-Triphenylethane (**100**) was dehydrogenated by chloranil in boiling xylene to give triphenylethylene (**101**; reaction 59)[83]. However, 1,1,2,2-tetraphenylethane resists quinone dehydrogenation, probably due to

steric hindrance, and also 1,1,1,2-tetraphenylethane was not attacked by DDQ in boiling benzene[84].

$$(C_6H_5)_2CH-CH_2C_6H_5 \xrightarrow{\text{chloranil}} (C_6H_5)_2C=CHC_6H_5 \qquad (59)$$

(100) (101)

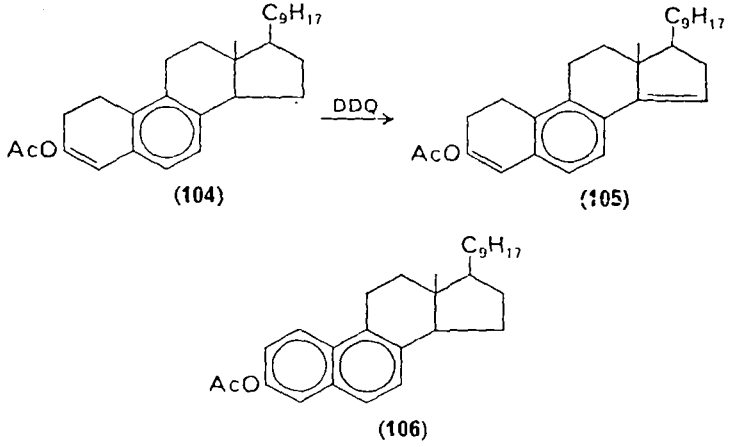
A remarkably efficient and selective dehydrogenation by DDQ, ascribed to stereoelectronic effects, has recently been described to occur with neoergosterols[85]. For instance, neoergosterol **102**, despite its numerous sites of possible attack by hydride ion acceptors, reacts with DDQ instantaneously at room temperature to give the dehydro-compound **103** in 80% yield (reaction 60). Neoergosterol acetate behaved similarly,



(60)

(102) (103)

giving the corresponding dehydro-compound in 86% yield. The preferential attack of DDQ at C-14 was also demonstrated by the conversion of the enol acetate **104** into the styrene **105** (reaction 61) rather than into the



(61)

(104) (105) (106)

aromatized compound **106**. The high specificity of hydride ion abstraction from C-14 has been explained by the favourable π-complex formation

of DDQ with the aromatic ring being the controlling factor. Inspection of Dreiding molecular models of neoergosterols reveals that the hydrogen at C-14 is almost perpendicular to the aromatic ring, 'thereby allowing maximal σ–π overlap in the transition state for hydride abstraction'[85].

B. Hydroaromatic Compounds

Kinetic and theoretical studies of hydroaromatic systems have contributed a wealth of information to the understanding of the mechanism of quinone dehydrogenation[1,86-89]. It has thus been concluded from the comparison of various hydrogen donors that the gain of resonance energy associated with the aromatization of the hydroaromatic compound will be reflected in the rate of dehydrogenation[86]. For instance, the case of dehydrogenation, established for both high-potential and low-potential quinones, has been found to decrease as follows:

1,4-dihydrobenzene > 1,4-dihydronaphthalene >
9,10-dihydroanthracene > 1,2-dihydronaphthalene,

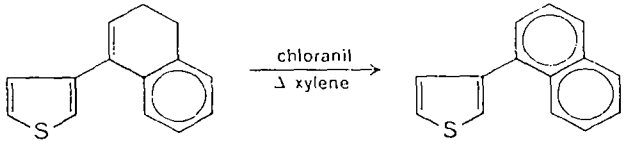
the relative rates being in the ratios 100 : 50 : 10 : 1 [86]. More pronounced differences in relative rates are observed in the dehydrogenation of a hydroaromatic compound by different quinones, as shown in Table 7 for the aromatization of 1,2-dihydronaphthalene.

TABLE 7. Relative rate of dehydrogenation of 1,2-dihydronaphthalene by different quinones at 100° [3]

Quinone	Relative rate
Chloranil	1
3,3',5,5'-Tetrachlorodiphenoquinone	1100
o-Chloranil	4200
DDQ	5500

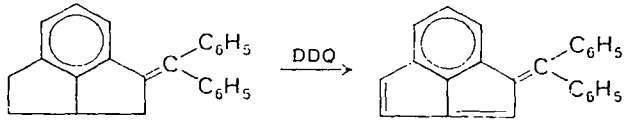
Thermal dehydrogenation of a hydroaromatic compound by a quinone apparently was first carried out on a preparative scale some forty years ago in the synthesis of pentacene[90]. Since then, quinone dehydrogenation of hydroaromatic compounds has been applied in numerous syntheses and its preparative significance becomes apparent in comparison with other thermal dehydrogenation methods. For example, dehydrogenation of 1,4-dihydroanthracenes with selenium gave only low yields of aromatized products; however, essentially quantitative yields of anthracenes were obtained when 1,4-dihydroanthracenes were treated with equimolar amounts of chloranil for one hour in boiling xylene[91]. Dihydrodibenzanthracenes aromatize smoothly upon treatment with DDQ [92]. Similar

high-yield dehydrogenations were observed in the synthesis of thiophen-substituted naphthalenes **108** (reaction 62)[93]. In the aromatization of tetrahydrophenanthrenes, both chloranil[94] in boiling xylene and DDQ[95] in boiling benzene have been found to bring about aromatization in good yields.



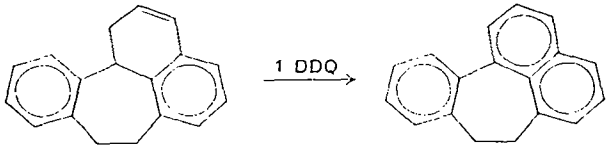
(107) (108) (62)

Dehydrogenation by DDQ of the tetrahydrocompound **109** gives the benzhydrylidene-cyclopent[cd]indene **110** (reaction 63)[96]. Indane itself

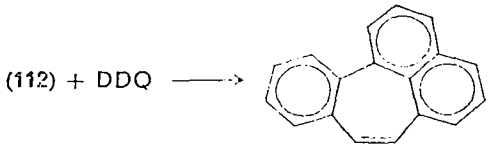


(109) (110) (63)

reacts with DDQ to give indene under conditions where, significantly, benzocycloheptene was found to be inert[89]. This indicates that ring size and, consequently, conformational factors do influence the rate of dehydrogenation of hydroaromatic compounds. Thus the reaction of the tetracyclic compound **111** with one molar equivalent of DDQ in benzene results in the dehydrogenation of the six-membered rather than the seven-membered ring to give compound **112** (reaction 64)[97]. Treatment of **111** with two molar equivalents of DDQ gives the benzocycloheptanaphthalene **113** (reaction 65). (Significantly, chloranil was found to be ineffective as a

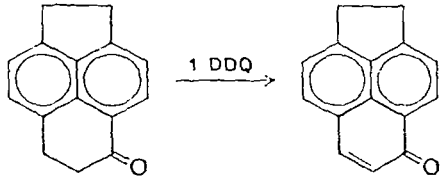


(111) (112) (64)

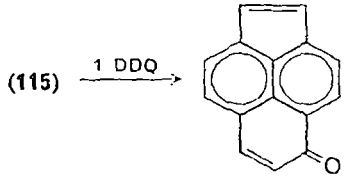


(113) (65)

dehydrogenating agent when used under the same conditions as DDQ.) A similar selective dehydrogenation involving different rings has been encountered recently[98]. Acenaphthene can be converted into acenaphthylene by dehydrogenation with either chloranil[32] or DDQ[23,79], however, treatment of compound **114** with one molar equivalent of DDQ gave the phenalenone **115** which, upon dehydrogenation with an additional molar equivalent of DDQ, then gave **116** (reactions 66 and 67). (It is not readily understood why the conversion of **114** into **116** could not be carried out when two molar equivalents of DDQ were applied directly.)

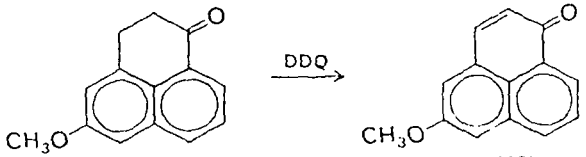


(114) (115) (66)



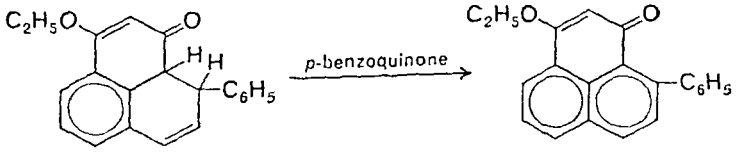
(116) (67)

Apparently the dehydrogenation of the phenalanone system generally proceeds with great ease. For instance, dehydrogenation of phenalanone **117** with DDQ in benzene gave the phenalenone **118** in 83% yield (reaction 68)[99]. The dehydrogenation of the dihydrophenalenone **119** to give the



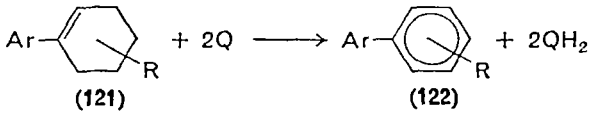
(117) (118) (68)

phenalenone **120** can be brought about even by unsubstituted 1,4-benzoquinone (reaction 69)[100].



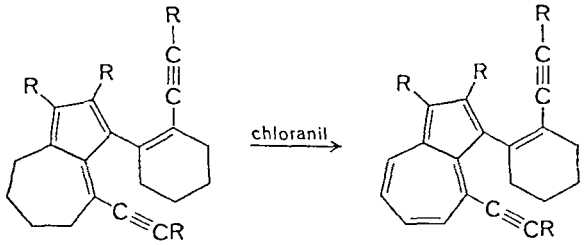
(119) (120) (69)

Aryl-substituted cyclohexenes **121** upon treatment with chloranil in boiling xylene are smoothly aromatized to give **122** (reaction 70)[101,102].



(121) (122) (70)

Some typical results are summarized in Table 8. Interestingly, the dehydrogenation of compound **123** with chloranil in boiling toluene gave, though only in 20% yield, the azulene **124** in which the cyclohexene ring was left intact (reaction 71)[103].



(123) (124) (71)

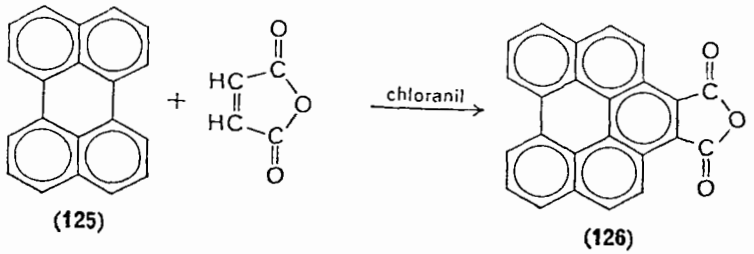
R = C_6H_5

TABLE 8. Dehydrogenation of aryl-substituted cyclohexenes with chloranil in boiling xylene[101]

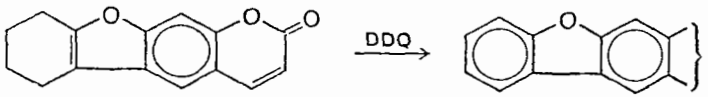
Cyclohexene	Product	Yield (%)
1-Phenyl-	Biphenyl	52
1-*o*-Tolyl	2-Methylbiphenyl	72
1-*p*-Biphenylyl-	Terphenyl	47
1-*p*-Biphenylyl-2-methyl-	2-Methylterphenyl	72
1-β-Naphthyl-	β-Phenylnaphthalene	72

Some remarkably smooth dehydrogenations by chloranil in boiling maleic anhydride have been reported. For instance, 1,12-benzoperylene-1′,2′-dicarboxylic anhydride (**126**) was obtained in quantitative yield by reaction of perylene **125** and maleic anhydride in the presence of chloranil. The intermediate maleic anhydride adduct was found to undergo dehydrogenation under the conditions of formation (reaction 72)[104].

Most recently, the aromatization of tetrahydrodibenzofurans by quinone dehydrogenation has been reported (reaction 73)[105]. However, striking

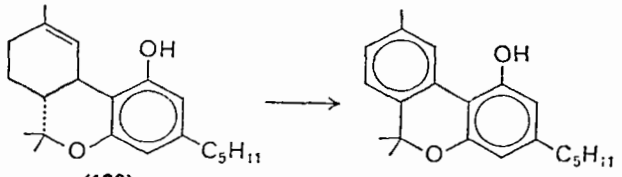


(125) (126) (72)



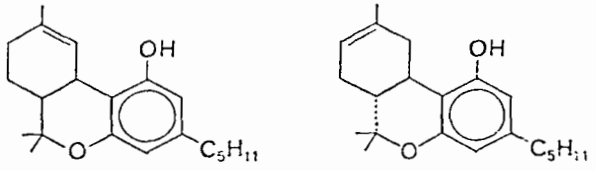
(127) (128) (73)

differences in reactivity of tetrahydrobenzopyrans have been encountered in the dehydrogenation of tetrahydrocannabinols (THC)[106]. For example, Δ^1-3,4-*trans*-THC (**129**) gives cannabinol **130** in 90% yield upon treatment with chloranil in boiling benzene (reaction 74). By contrast, Δ^1-3,4-*cis*-THC



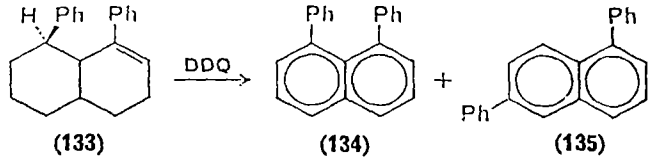
(129) (130) (74)

(**131**), for stereoelectronic reasons, remains unchanged even upon prolonged treatment with chloranil. Similarly $\Delta^{1(6)}$-THC (**132**) which lacks allylic activation of the benzylic hydrogen to be abstracted is not dehydrogenated by chloranil.



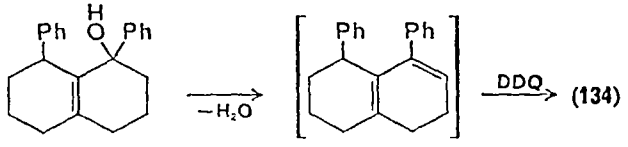
(131) (132)

Generally, the dehydrogenation of hydroaromatic compounds by quinones proceeds without skeletal rearrangement, unless we are dealing with 'blocked' hydroaromatic systems. The dehydrogenation of the octalin **133** by DDQ, however, gives, besides the expected 1,8-diphenylnaphthalene (**134**), the rearranged compound **135** (reaction 75)[107]. No



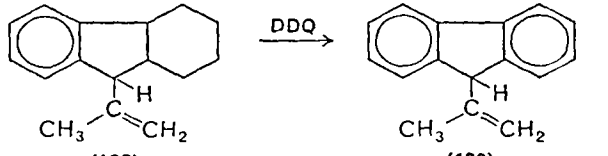
(133) (134) (135) (75)

such rearrangement was observed in the preparation of 1,8-diphenylnaphthalene (**134**) from the octalol **136** (reaction 76)[108]. The conversion of **136** into **134** is carried out with DDQ in boiling benzene and, most likely, the dehydrogenation steps are preceded by the elimination of water to give the hexahydro derivative **137** as an intermediate.

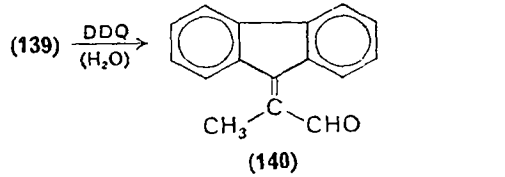


(136) (137) (76)

DDQ may offer the advantage of dehydrogenating hydroaromatic compounds at higher rates than other high-potential quinones. However, its high reactivity may also impair the selectivity of quinone dehydrogenation. For example, the reaction of DDQ with 9-isopropenyl-1,2,3,4-tetrahydrofluorene (**138**), particularly in refluxing benzene, does not stop at the stage of the aromatized compound **139** but yields the aldehyde **140** (reactions 77 and 78)[109]. Neither chloranil nor its *ortho*-isomer brings about this type of oxidation[109].



(138) (139) (77)



(140) (78)

C. 'Blocked' Hydroaromatic Compounds

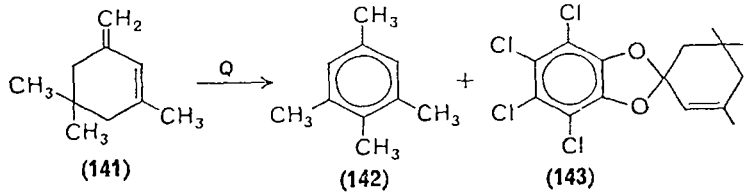
Dehydrogenation by quinones of hydroaromatic compounds containing *gem*-dialkyl or angular alkyl groups results in aromatization of the hydrogen donor with concomitant migration of an alkyl substituent[24, 25].

This type of Wagner–Meerwein rearrangement cannot be brought about by hydrogen atom abstraction and, therefore, represents the most important chemical evidence for the involvement of carbonium ion intermediates in quinone dehydrogenation.

As mentioned in section II.B, reaction of DDQ with 1,1-dimethyltetralin (**1**) in boiling benzene for two hours gives 1,2-dimethylnaphthalene (**4**) in almost quantitative yield (reactions 6–8). *o*-Chloranil also converts **1** into **4**, though the rate of reaction is only one-tenth of that of the DDQ reaction[24].

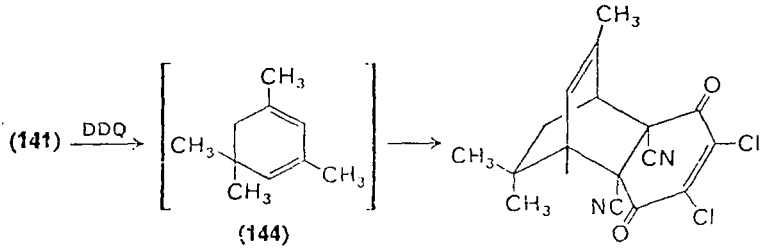
Similar alkyl group migrations may be brought about by phenanthrenequinone[8,25] at elevated temperature. Thus, 1,1-dimethyl-1,2-dihydronaphthalene (**2**) reacts with phenanthrenequinone in boiling anisole (190°C) to give a mixture of 1-methylnaphthalene and 1,2-dimethylnaphthalene (**4**). Interestingly, in this and other related aromatization reactions, a methyl group was found to be transferred to the quinone[8,25].

The choice of the quinone may be of critical importance in reactions of those blocked hydroaromatic compounds which contain a 1,3-diene system and, therefore, are prone to undergo Diels–Alder additions with dienophilic quinones. For instance, 1,5,5-trimethyl-3-methylenecyclohexene (**141**) yields isodurene **142** upon treatment with 3,3',5,5'-tetrachlorodiphenoquinone at 80°C or *o*-chloranil at 20°C (reaction 79)[24].



(141) (142) (143) (79)

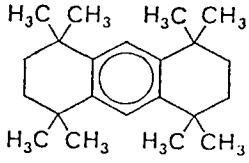
However, with the latter quinone, adduct **143** was formed as well. Attempts to aromatize **141** with DDQ gave in 80% yield, even at −10°C, a Diels–Alder adduct[21] whose *endo*-structure **145** was recently established (reaction 80)[110]. Apparently, the addition reaction by DDQ is preceded by the



(144) (145) (80)

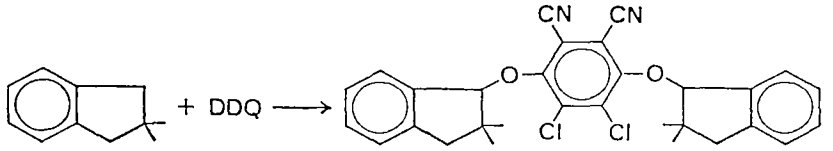
isomerization **141** to give **144**. Although the isomerization has not been investigated, it appears probable that the double-bond migration is catalysed by DDQ or occurs within the charge-transfer complex of **141** with DDQ.

In agreement with the ionic mechanism of quinone dehydrogenation in which attack occurs at the benzylic or allylic position of the blocked hydroaromatic compound, the octahydro-octamethylanthracene **146** was not aromatized by *o*-chloranil[24].



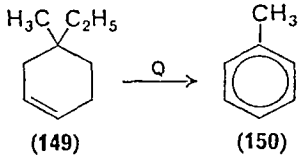
(146)

Attempts to bring about aromatization of 2,2-dimethylindane (**147**) by dehydrogenation with DDQ did not result in rearrangement but gave the hydroquinone diether **148** (reaction 81)[24]. The failure to achieve the



(147) **(148)** (81)

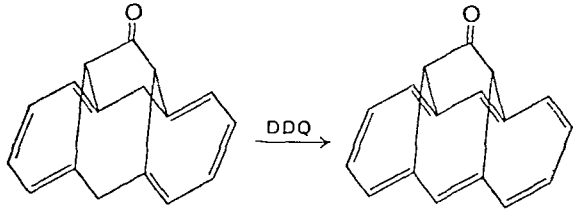
rearrangement has been attributed to unfavourable conformation of the methyl substituents. Similar hydroquinone diethers are known to be formed in the reaction of radicals with *p*-benzoquinone[111-113]. It is conceivable, therefore, that the formation of the diether **148** also involves radical rather than ionic intermediates. Hydrogen atom abstraction has been proposed recently to be the primary step in the gas-phase dehydrogenation of 4-ethyl-4-methylcyclohexene (**149**) by a polymeric quinone to give toluene **150** rather than *o*-ethyltoluene (reaction 82)[114].



(149) **(150)** (82)

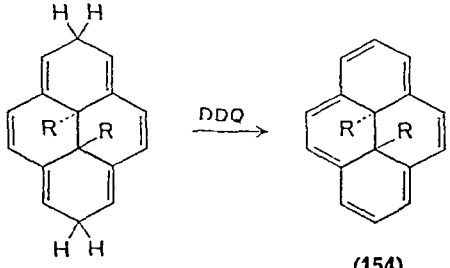
D. Non-benzenoid Hydroaromatic and Related Compounds

Dehydrogenation by high-potential quinones, particularly chloranil and DDQ, has proved to be useful in the recent syntheses of non-benzenoid aromatic and related compounds. For instance, treatment of the dihydro-[14]annulene ketone **151** with DDQ at room temperature in benzene gave the dehydro compound **152** in 90% yield (reaction 83)[115a,115b]. Similarly,



(151) (152) (83)

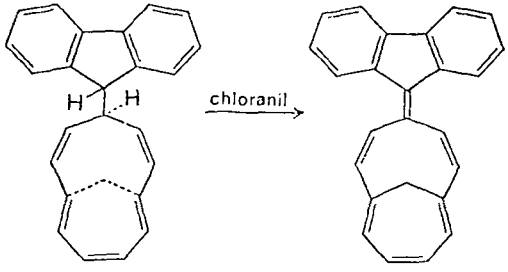
the tetrahydropyrene **153** was dehydrogenated by DDQ at room temperature to give the dihydropyrene **154** in 84% yield (reaction 84)[116,117].



(153) (154) (84)

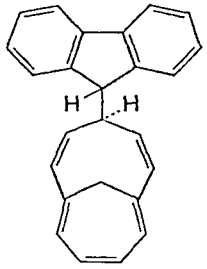
R = *n*-C_3H_7

Seemingly minute changes in the stereochemistry of the hydrogen donor may have dramatic effects on the dehydrogenation by quinones. For instance, compound **155** can be dehydrogenated by chloranil to give **156** (reaction 85); however, the isomer **157** resists dehydrogenation when

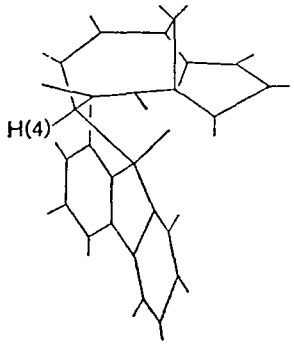


(155) (156) (85)

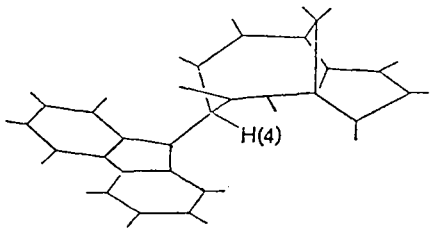
treated with chloranil under the same conditions[118]. Inspection of Dreiding molecular models reveals that in isomer **157** steric hindrance of the site of attack (H(4)) by the quinone accounts for the lack of reactivity[118].



(157)



(155)



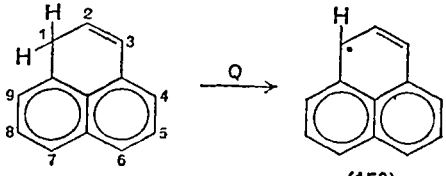
(157)

V. OXIDATION OF SUBSTITUTED AROMATIC COMPOUNDS

A. Benzylic and Arylallylic Oxidations

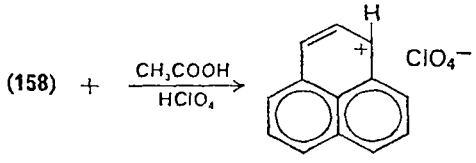
1. Phenalenes

Phenalene **158** reacts with a variety of quinones (DDQ, *o*-chloranil, chloranil, *p*-benzoquinone, 1,2-naphthoquinone, 1,4-naphthoquinone) in solvents such as benzene, methylenechloride, carbon tetrachloride, acetonitrile or nitromethane to give the phenalenyl radical (**159**; reaction 86)[27]. By contrast, oxidation of phenalene with either chloranil or



(158) (159) (86)

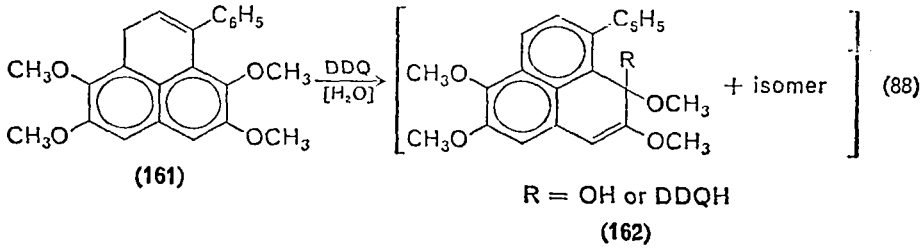
p-benzoquinone in acetic acid containing perchloric acid gives phenalenium perchlorate **160** in 75% and 81% yield, respectively (reaction 87). Treatment of 3,6,9-trimethyl-2,3-dihydrophenalen-1-ol with *o*-chloranil in



(160) (87)

boiling acetic acid containing perchloric acid resulted in dehydration and subsequent oxidation to give the corresponding trimethylphenalenium perchlorate in 89% yield.

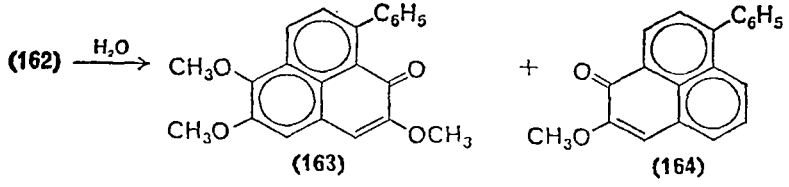
Clearly, the formation of phenalenyl radical under neutral conditions indicates that quinone dehydrogenation indeed can involve one-electron transfer or hydrogen atom abstraction reactions. Still, it may depend on the nature of the substituents attached to the phenalene molecule whether the reaction with the quinone will result in the formation of the phenalenyl radical or the phenalenium ion. Since methoxy substituents on the hydrogen donor would favour transfer of the hydride ion to the quinone, the oxidative conversion of the tetramethoxy-substituted phenalene **161** into the phenalenones **163** and **164** is probably best rationalized in terms of an ionic mechanism involving, by inadvertent participation of water, formation and subsequent hydrolysis of a hemiketal **162** (reactions 88 and 89)[119].



(161) (88)

R = OH or DDQH

(162)

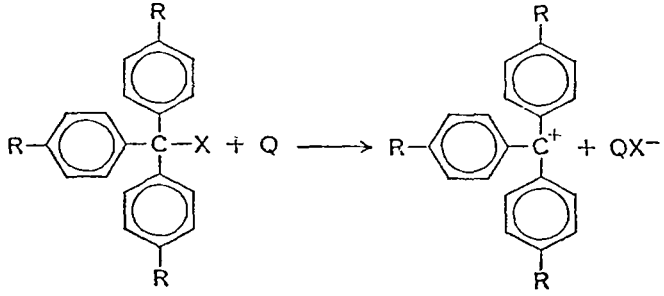


(163) (164) (89)

2. Arylalkanes and arylalkenes

As pointed out in section III.A, aryl substitution of alkanes and, more so, of alkenes, facilitates dehydrogenation by quinones. However, the compound to be oxidized should contain at least one benzylic hydrogen. For example, 1,1,1-triphenylethane was recovered unchanged after being treated with DDQ for 160 hours at 80°C.

As to whether the dehydrogenation of arylalkanes proceeds by overall hydride ion transfer or is better interpreted in terms of hydrogen atom abstraction may depend both on the nature of the substrate and the resulting intermediate. Thus, triphenylmethanes are dehydrogenated by quinones to triphenylmethyl cations. Of preparative interest is the oxidation of leuco triphenylmethane dyes by chloranil[120]. Using dimethylformamide as solvent, no 'over-oxidation' was observed even at 100°C[121]. In a kinetic study, the oxidation of deuterated triphenylmethanes such as leuco crystal violet (**165**) by a variety of quinones was found to follow second-order kinetics (reaction 90)[20]. Rates and isotope effects for some quinones are listed in Table 9.



(90)

(165) (166)

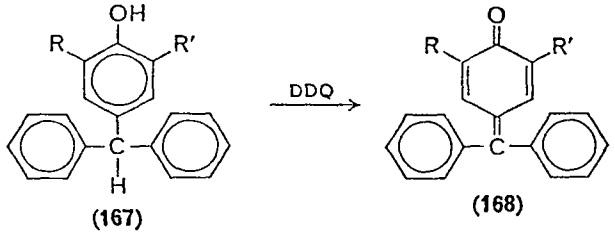
R = $N(CH_3)_2$; X = H or D

TABLE 9. Oxidation of leuco crystal violet by quinones in acetonitrile at 25°C

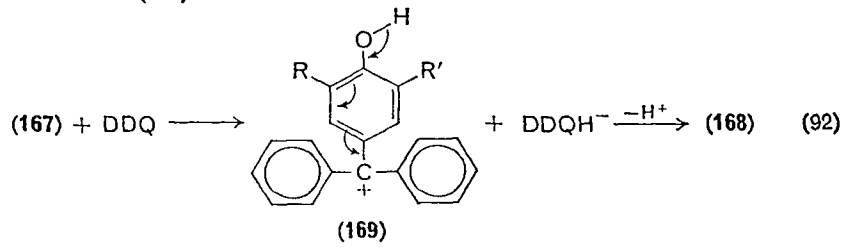
Quinone	k_H (M^{-1} s^{-1})	k_H/k_D
Chloranil	$1{\cdot}27 \times 10^{-1}$	11·4
Bromanil	$8{\cdot}14 \times 10^{-2}$	13·4
DDQ	$> 10^{5}$	6·96
Tetrachlorodiphenoquinone	$> 0{\cdot}5 \times 10^{-1}$	9·8

4-Hydroxytriphenylmethanes **167** react rapidly with DDQ in methanol solution to give substituted fuchsones **168** in high yield (reaction 91)[122]. The mechanism of this reaction has been explained to involve hydrogen

atom abstraction from the phenolic site, followed by disproportionation of the resulting phenoxy radical. However, in view of the easy formation of triphenylmethyl cations **166**, the formation of the fuchsones **168** may also be rationalized by an ionic mechanism (reaction 92). A similar

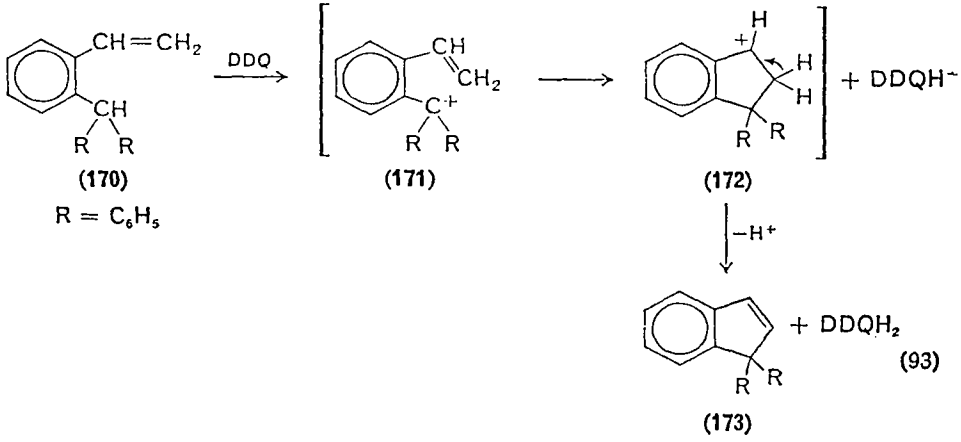


(91)



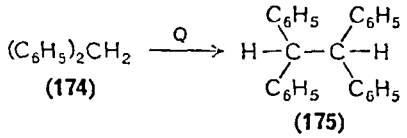
(92)

dehydrogenation of a triphenylmethane, though, with concomitant cyclization may account for the conversion of compound **170** into the ndene **173** (reaction 93)[123a,b].



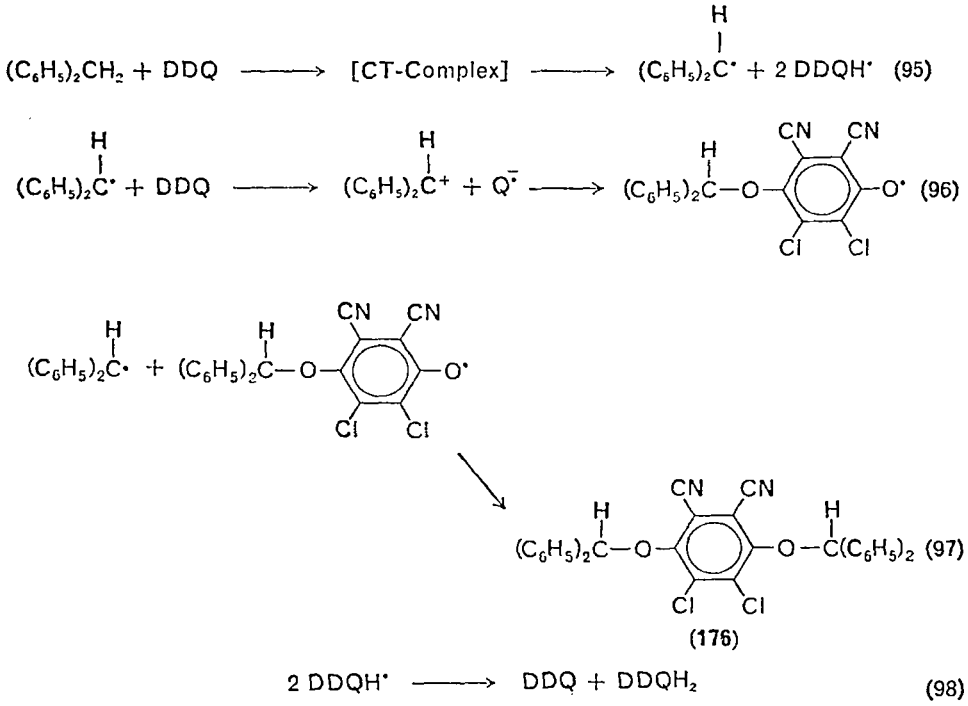
(93)

Diphenylmethane **174** was found to undergo oxidative coupling by 3,3′,5,5′-tetra-*t*-butyldiphenoquinone at 260°C, giving 1,1,2,2-tetraphenylethane (**175**) in 65% yield (reaction 94)[16]. Probably because of steric hindrance tetraphenylethane was not further dehydrogenated even by high-potential quinones.



(174) (175) (94)

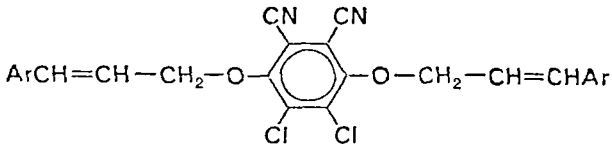
DDQ does not react with diphenylmethane in methanol solution; however, in the absence of solvent at 110°C, $DDQH_2$, and the hydroquinone di-ether **176** were formed in high yield. The formation of **176** and $DDQH_2$ was rationalized in terms of one-electron transfer reactions (95–98)[122]. On the other hand, the reaction of methyl-substituted benzenes with DDQ also leads to hydroquinone ethers whose formation has been explained by hydride ion transfer reactions[124].



(95) (96) (97) (176) (98)

Some interesting details about reactive intermediates have been obtained in the oxidation of 1-arylpropenes with DDQ. For example, under anhydrous conditions, 1-arylpropene **177** reacts with DDQ to give the hydroquinone di-ether **178** (reaction 99) which, upon treatment with a primary or secondary alcohol, rearranges to give the 1-arylallyl alkyl ether **179** in good yield (reaction 100)[125, 126, 126a].

$$ArCH{=}CHCH_3 + DDQ \quad \textbf{(177)}$$



(178)

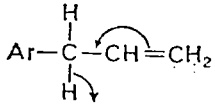
Ar = *p*-methoxyphenyl

$$\textbf{(178)} + ROH \xrightarrow[-DDQH_2]{} \underset{\textbf{(179)}}{ArCH(OR){-}CH{=}CH_2} + ArCH{=}CH{-}CH_2OR \qquad (100)$$

When the oxidation of 1-arylpropenes with DDQ is carried out in benzene or dioxan containing water, cinnamaldehydes **180** are formed (reaction 101)[109, 125, 127, 128]. Similar results were obtained with allylbenzenes[181]

$$\underset{\textbf{(177)}}{ArCH{=}CHCH_3} \xrightarrow[H_2O]{DDQ} \underset{\textbf{(180)}}{ArCH{=}CH{-}CHO} \qquad (101)$$

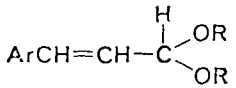
whose oxidation, obviously, is associated with allylic rearrangement (reaction 102). The formation of aldehydes may be explained by successive



(181)

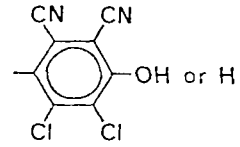
H_2O | DDQ

$$ArCH{=}CH{-}\overset{+}{C}H_2 \longrightarrow \xrightarrow[H_2O]{DDQ} \underset{\textbf{(180)}}{ArCH{=}CH{-}CHO} \qquad (102)$$

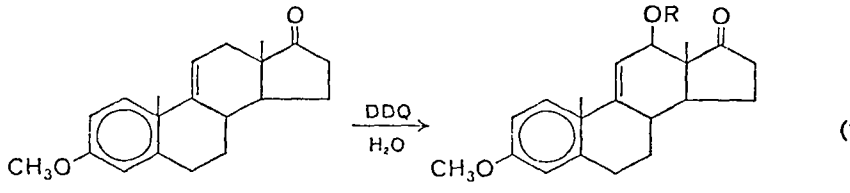


(182)

R =



hydride ion abstractions to give the acetal **182** which suffers hydrolysis. Evidence for hydride ion abstraction by quinones may be seen in the oxidation of $\Delta^{9(11)}$-oestrone methyl ether (**183**) by DDQ in wet benzene which gives, among the other products, the hydroxylated compound **184a** (reaction 103)[129a,b]. Oxidation of **183** in benzene containing methanol gives the methyl ether **184b**.

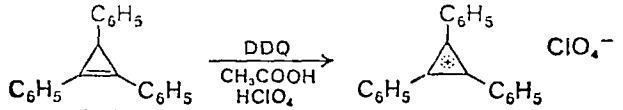


(103)

(183)

(184) (a), R = H
(b), R = CH_3

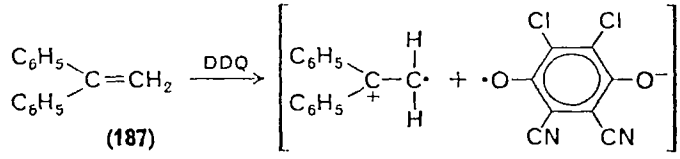
Hydride ion abstraction also occurs in the dehydrogenation of 1,2,3-triphenylcyclopropene (**185**) by DDQ which, when carried out in acetic acid containing perchloric acid, gives triphenylcyclopropenylium perchlorate (**186**) in 95% yield (reaction 104)[27].



(104)

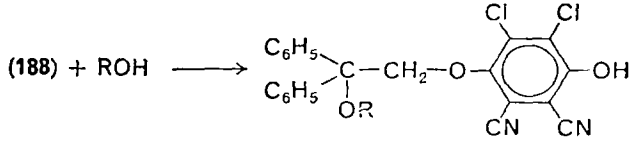
(185) (186)

Surprisingly, even 1,1-diphenylethylene **187** was found to react with DDQ in alcohol solution to give a DDQ : olefin : alcohol addition product **189** whose formation was proposed to involve radical ion intermediates (reactions 105 and 106)[122].



(105)

(187) (188)



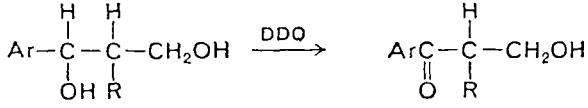
(106)

(189)

R = CH_3 or C_2H_5

3. Benzyl alcohols and benzyl ethers

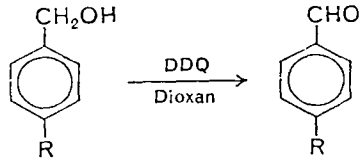
Introduction of an oxygen function into the benzylic position of an arylalkane greatly enhances the rate of hydride ion abstraction by quinones. Thus, benzyl alcohol is oxidized by *o*-chloranil to give benzaldehyde faster than ethylbenzene is dehydrogenated to styrene[130]. Still, from a preparative point of view, the dehydrogenation of phenyl-substituted carbinols by *o*-chloranil is slow. As a recent investigation[131] has shown, however, DDQ appears to be the reagent of choice for the oxidation of benzyl alcohols. For example, benzaldehyde was obtained in 39% yield by oxidation of benzyl alcohol with *o*-chloranil for three days at room temperature[130], while an 80% yield was achieved with DDQ in dioxan solution[131]. Likewise, oxidation of diphenyl carbinol with *o*-chloranil for seven days gave benzophenone in 42% yield, while DDQ in dioxan at room temperature gave an 80% yield of benzophenone after sixteen hours. Besides the high rate of oxidation, DDQ offers the advantage of selectivity, attacking benzylic alcohols with remarkable preference (reaction 107)[132].



(190) (191) (107)

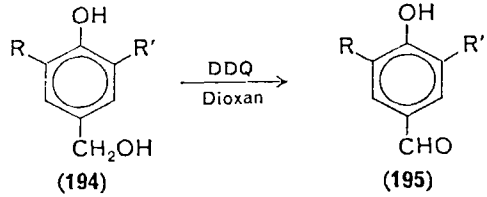
Ar = 3,4-dimethoxyphenyl
R = *o*-methoxyphenoxy

As may be expected, ring substitution by electron-donating groups enhances the rate of oxidation of benzyl alcohols, while electron-withdrawing groups drastically reduce the rate of oxidation. For example, oxidation of 4-methylbenzyl alcohol (**192**; R = CH_3) with DDQ at room temperature gives 4-tolylaldehyde (**193**; R = CH_3) in 93% yield after sixteen hours (based on the yield of $DDQH_2$) while oxidation of 4-phenylsulphonylbenzyl alcohol (**192**; R = $C_6H_5SO_2$) under similar conditions gives $DDQH_2$ in only 14% yield after five weeks (reaction 108). As shown



(192) (193) (108)

in Table 10, DDQ oxidizes 4-hydroxybenzyl alcohols **194** with remarkable ease, giving 4-hydroxybenzaldehydes **195** in excellent yields (reaction 109).



(194) (195) (109)

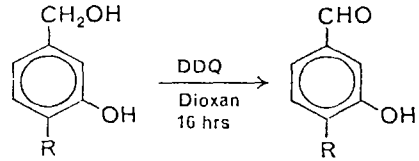
TABLE 10. Oxidation of 4-hydroxybenzyl alcohols **194** by DDQ at room temperature[a]

R	R'	Yield (%) of **195**
H	H	74
H	OCH_3	85
OCH_3	OCH_3	86
Cl	Cl	92
t-C_4H_9	*t*-C_4H_9	91

[a] Reaction conditions: addition of DDQ (4 mmol) to a solution of substrate (4 mmol) in dioxan (24 ml). Work-up after sixteen hours.

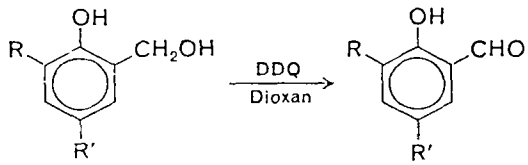
Similar results were obtained with 3-hydroxybenzyl alcohols **196** (reaction 110) and 2-hydroxybenzyl alcohols **198** (reaction 111; Table 11).

Secondary 4-hydroxybenzyl alcohols **200** (see Table 12) undergo oxidation by DDQ at room temperature in dioxan solution rapidly, giving 4-hydroxyketones **201** in yields around 90% (reaction 112).



(196) (197) (110)

R	Yield
H	83%
OCH_3	97%

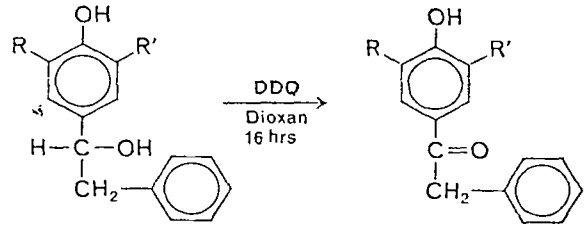


(198) (199) (111)

TABLE 11. Oxidation of 2-hydroxybenzyl alcohols **198** by DDQ in dioxan at room temperature

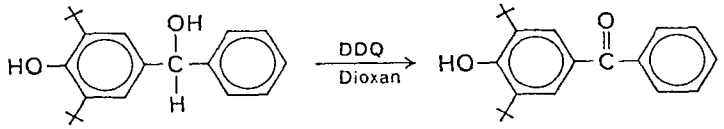
R	R′	Reaction time (h)	Yield of **199** (%)
H	H	16	57[a]
CH_3	t-C_4H_9	20	85
t-C_4H_9	t-C_4H_9	68	85

[a] Based on $DDQH_2$.



(200) (201) (112)

4-Hydroxydiphenyl carbinols, apparently, are still more reactive. Their oxidation to benzophenones by DDQ in dioxan at room temperature generally was completed within fifteen minutes (reaction 113).

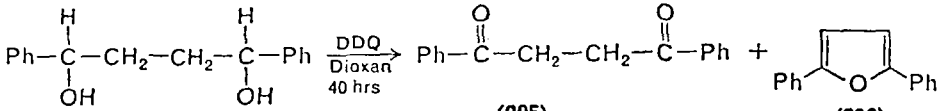


(202) (203) 95% (113)

TABLE 12. Oxidation of secondary 4-hydroxbenzyl alcohols **200**

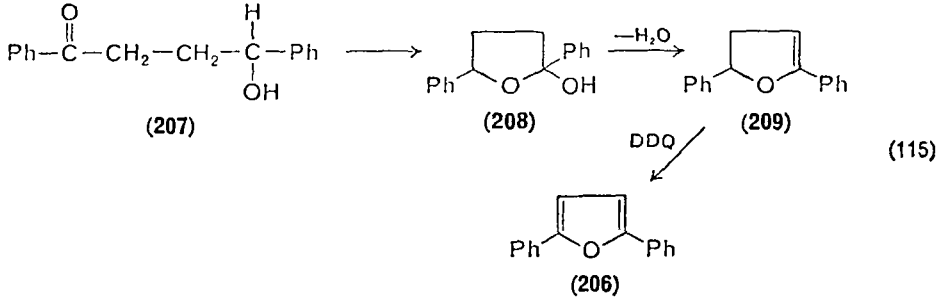
R	R′	Yield (%) of **201**
H	H	92
H	OCH_3	89
OCH_3	OCH_3	92
CH_3	CH_3	83
CH_2—CH=CH_2	OCH_3	88
t-C_4H_9	t-C_4H_9	90
Cl	Cl	82
C_6H_5	C_6H_5	89 [after 76 h]

Unexpectedly, oxidation of the phenyl-substituted diol **204** with DDQ gave the expected dibenzoyl ethane **205** in only 19% yield, while 2,5-diphenylfuran (**206**) was isolated in 66% yield (reaction 114). Presumably,



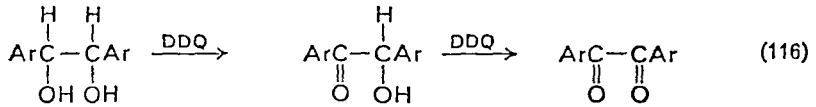
(204) (205) (206) (114)

the formation of **206** involves the dehydrogenation of 2,3-dihydro-2,5-diphenylfuran (**209**) (reaction 115).



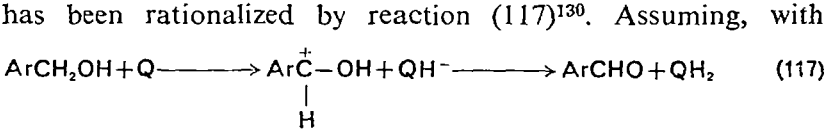
(207) (208) (209) (206) (115)

Hydrobenzoin (**210**; Ar = phenyl) upon oxidation with DDQ gives benzoin **211** rather than benzil **212**. By contrast, oxidation of hydrovanilloin (**210**; Ar = guajacyl) by DDQ rapidly gives vanillil **212** in 81% yield (reaction 116), indicating again that electron-donating ring substituents facilitate the oxidation of benzyl alcohols.



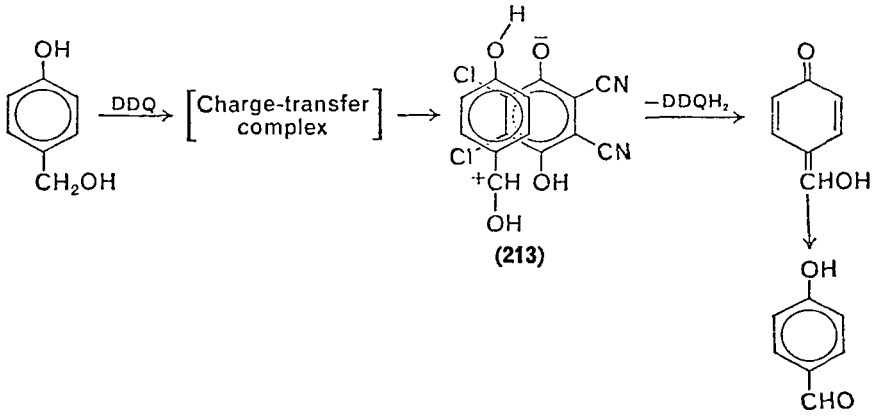
(210) (211) (212) (116)

The mechanism for the oxidation of benzyl alcohols by quinones in general has been rationalized by reaction (117)[130]. Assuming, with

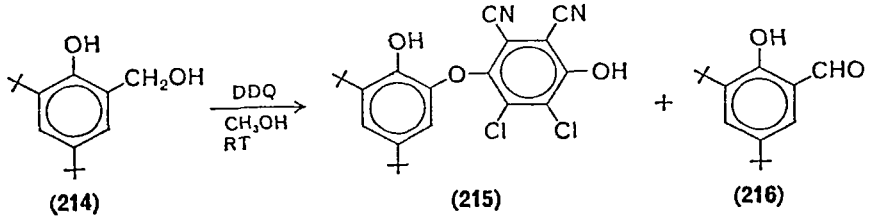


(117)

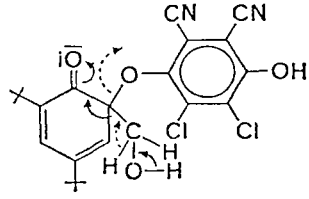
justification (see reaction 110), that the oxidation of hydroxybenzyl alcohols by DDQ in dioxan does not involve oxidation at the phenolic site, one conceivable mode of participation of the 4-hydroxyl group could be that of a proton donor within the intermediate ion pair **213** (reaction 118).



Experimental evidence suggests that the oxidation of hydroxybenzyl alcohols by DDQ in methanol solution (rather than in dioxan) does involve oxidation of the phenolic hydroxyl. For example, oxidation of 3,5-di-*t*-butylsalicyl alcohol (**214**) in dioxan gives 3,5-di-*t*-butylsalicyl aldehyde (**216**) in 85% yield, but oxidation of **214** in methanol solution gives **216** in only 35% yield, the major product (54%) being the substituted diphenyl ether **215** (reaction 119)[133]. The formation of **215** may be

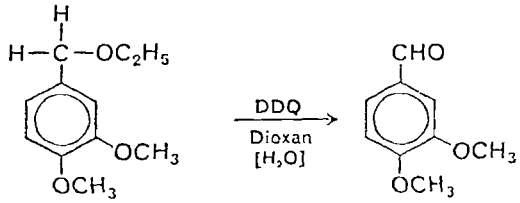


rationalized by phenolic oxidative coupling involving radicals to give **217** which subsequently aromatizes by loss of formaldehyde (solid arrows).



Aromatization by loss of the hydroquinone (dotted arrows) corresponds to the disproportionation of phenoxy radicals and would account for the formation of the salicylaldehyde **216**.

Benzyl ethers of structure **218** readily undergo oxidative cleavage when treated with DDQ at room temperature in dioxan (reaction 120)[128].



(218) (219) (120)

Mechanistic details of this oxidation by DDQ remain to be elucidated. Obviously the reaction requires the presence of water and, conceivably, intermediates analogous to those isolated in the oxidation of 1-aryl-propenes may be involved as well.

B. Oxidations Involving Phenols

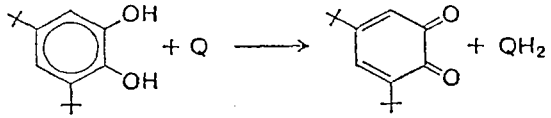
1. Dehydrogenation of aromatic dihydroxy compounds

Redox reactions are frequently encountered as secondary reactions in nucleophilic additions[134,135] to, or electrophilic substitutions[136] of, quinones leading to substituted hydroquinones whose oxidation potential is lower than that of the starting quinone. Apart from those unintentional, and often undesired, dehydrogenations, quinones are excellent oxidants of preparative significance for aromatic dihydroxy compounds. The oxidations are generally carried out in solvents in which one of the reaction products—often the hydroquinone—is essentially insoluble and precipitates. In which direction the reaction (121)

$$Q + Q'H_2 \rightleftharpoons QH_2 + Q' \qquad (121)$$

proceeds depends mainly on the relative oxidation potentials of the quinones Q and Q'. For example, 2,2',6,6'-tetramethoxy-*p*,*p*'-biphenol is oxidized by *p*-benzoquinone to give coerulignone and hydroquinone[137]. However, the higher potential *o*-bromanil oxidizes hydroquinone to give tetrabromocatechol and *p*-benzoquinone[138]. Likewise, lower potential catechols are converted into *o*-quinones by haloquinones. This type of redox reaction was applied some forty years ago in the intramolecular cyclization of laudanosoline by chloranil[139]; however, the preparative usefulness of this method was recognized much later when *o*-chloranil was found to convert catechols into *o*-quinones rapidly, conveniently and in high yield[140]. Numerous *o*-quinones have been prepared by this method as exemplified by reaction (122)[17,140,141]. It has been pointed out that the oxidation by *o*-chloranil also proceeds if the oxidation potential of

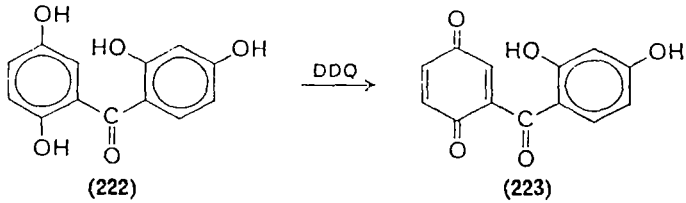
the dihydroxy compound to be dehydrogenated is higher than that of the oxidant, provided the oxidation product has low solubility and precipitates, thus affecting the equilibrium reaction (121)[17]. For example,



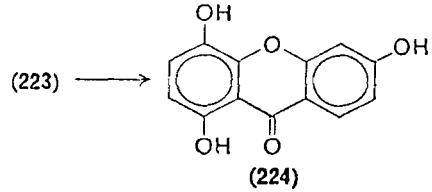
(220) (221) (122)

o-chloranil ($E_0 = 830$ mV) does convert 3-methoxy-5-formylcatechol ($E_0 = 839$ mV) into the corresponding *o*-quinone. During recent years the oxidation potentials of numerous catechols[17,18] and hydroquinones[142] have been determined, thus facilitating a prediction as to whether or not *o*-chloranil may act as an oxidant.

Unsubstituted *p*-benzoquinone has been used as oxidant for low-potential dihydroxy compounds[80] such as the catechol **220**[143]. A disadvantage of using *p*-benzoquinone may be seen in the required use of two molar equivalents of oxidant due to quinhydrone formation. This may be avoided by the use of high-potential quinones. For instance, reaction (122) proceeds instantaneously with one molar equivalent of DDQ in dioxan at room temperature[144]. Likewise, hydroquinone **222** is oxidized by DDQ in benzene at 0°C to give $DDQH_2$ and the quinone **223**, which then cyclizes to the xanthone **224** (reactions 123 and 124)[145].



(222) (223) (123)

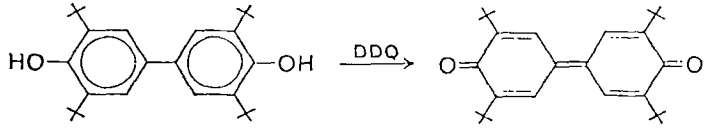


(224) (124)

DDQ in dimethyl sulphoxide, dimethylformamide or 1,2-dimethoxyethane has also been applied fully in the dehydrogenation of tetrahydroxyanthracenes to give new dihydroxyanthraquinones[146–149].

High-potential quinones rapidly dehydrogenate both 4,4′-dihydroxy- and 2,2′-dihydroxy-substituted biphenyls to the corresponding diphenoquinones. Addition of DDQ to a methanol solution of the substituted

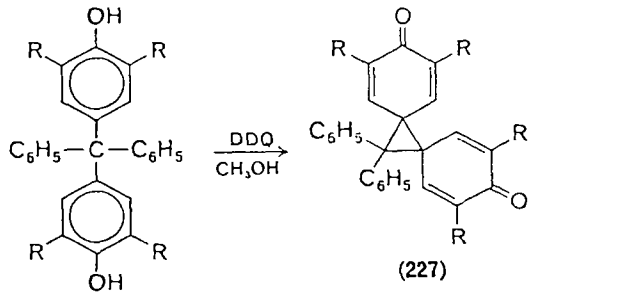
4,4′-dihydroxybiphenyl (**224**) instantaneously gives the diphenoquinone **225** in 98% yield (reaction 125). *o*-Chloranil has been applied in a similar fashion as dehydrogenating agent for various dihydroxybiphenyls[150-152].



(224) (225) (125)

Likewise, chloranil may be used for the dehydrogenation of 2,2′-dihydroxybiphenyls to give stable *o*-diphenoquinones[153]. Dehydrogenation of 4,4′-dihydroxystilbenes by DDQ in alcohol solution smoothly gives stilbenequinones[154].

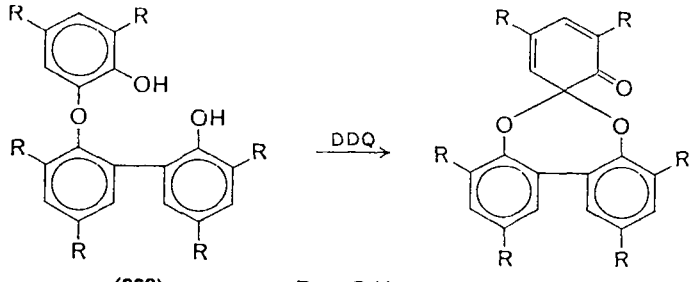
Several examples of spiro-cyclohexadienone formation involving intramolecular oxidative coupling of various aromatic dihydroxy compounds by high-potential quinones have been reported during recent years[63b,122,155,156]. DDQ, for example, rapidly oxidizes 4,4′-dihydroxytetraphenylmethanes (**226**) to bispiro-cyclohexadienones (**227**) in high yield (reaction 126)[122]. The oxidation of 2,4′-dihydroxydiphenyl ethers by



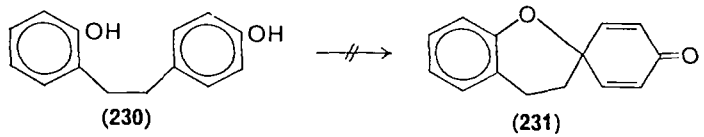
(226) (227) (126)

DDQ gives intramolecular coupling products of 1,3-benzodioxol-2-spiro-cyclohexadienone structure[156]. The dioxepin **229** was formed in high yield by oxidation of the dihydroxydiaryl ether **228** (reaction 127)[122].

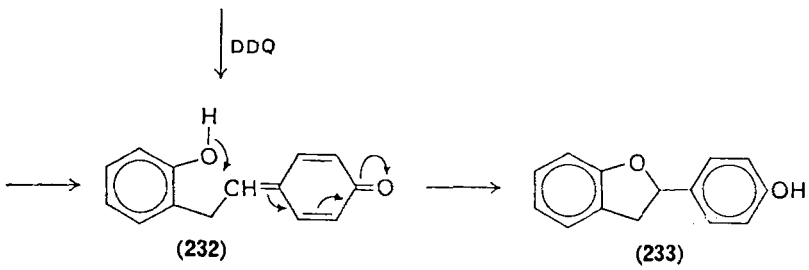
Attempts to prepare the spiro-dienone **231** by oxidation of the dihydroxy compound **230** with DDQ were not successful. Instead, dihydrobenzofuran **233** was formed, which underwent further dehydrogenation to **234** (reaction 129)[157]. The formation of **223** has been rationalized to involve the intermediate quinone methide **232** undergoing aromatization by intramolecular nucleophilic addition of the phenolic hydroxyl group. This finding suggests that, because of favourable steric orientation within the charge-transfer complex of the quinone with the hydrogen



(228) $R = C_6H_5$ (229) (127)



(230) (231) (128)

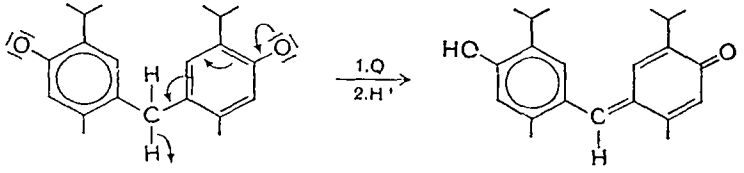


(232) (233) (234) (129)

donating '*p*-alkylphenol' **230**, quinone methide formation occurs as the preferred process over the oxidation of the second phenolic hydroxyl group. Provided the reaction (129) proceeds by primary attack of DDQ at the phenolic hydroxyl group, it appears reasonable to assume that quinone methide formation in this case does not involve the disproportion of free phenoxy radicals but involves DDQH (radical or anion) as the acceptor of the benzylic hydrogen.

The dehydrogenation reactions described above were all carried out with the neutral dihydroxy compounds. According to a recent report, an oxidation by chloranil was performed in alkaline solution[158]. Thus, the dianion of 4,4′-dihydroxy-5,5′-diisopropyl-2,2′-dimethyldiphenylmethane

(235) upon treatment with chloranil gave the quinone methide **236** in 80% yield (reaction 130). Most likely, this reaction does not involve



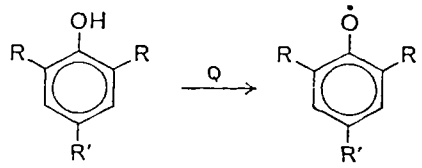
(235) (236) (130)

electron transfer from the phenolate ion but proceeds by hydride ion abstraction as indicated in structure **235**. An analogous hydride ion transfer was suggested[3] earlier to be a feasible mode of dehydrogenation of preformed enolate ions to give α,β-unsaturated ketones from saturated ketones.

2. Oxidation of monohydric phenols

Electron transfer reactions from hydroquinones to quinones have been known for many years; however, only during the past decade have quinones been added to the list of oxidants for monohydric phenols. The mechanism of oxidation, particularly that by DDQ, is still subject to discussion, but the uniqueness and preparative advantages of quinone dehydrogenation of phenols are obvious. Different from oxidations with metal oxides or alkaline potassium ferricyanide, oxidations of phenols by quinones are conveniently carried out in homogeneous organic solution.

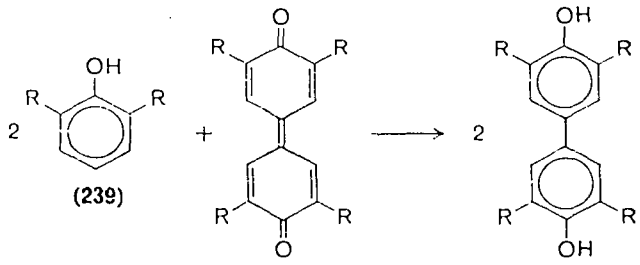
p-Benzoquinone has been used extensively in the oxidation of tocopherols and their model compounds, yielding dehydrodimers and trimers derived from *o*-quinone methide intermediates[159-162]. Since the oxidation of typical one-electron oxidants gives rise to the same products, benzoquinone most likely oxidizes tocopherols to the *o*-quinone methides via the corresponding phenoxy radicals. The reaction of *p*-benzoquinone with the tri-substituted phenol **237** was found to give the stable phenoxy radical **238** in 78% yield (reaction 131)[163].



(237) (238) (131)

R = *t*-butyl
R' = $(p\text{-}Me_2NC_6H_4)_2N$—

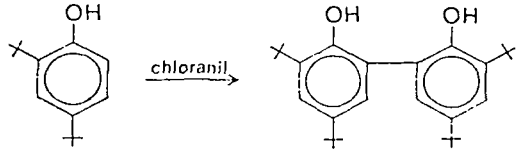
A remarkably simple high-yield synthesis of *p,p'*-biphenols has been found in the oxidation of 2,6-di-substituted phenols by their corresponding *p,p'*-diphenoquinones at elevated temperature (reaction 132)[164].



(239) (240) (241) (132)

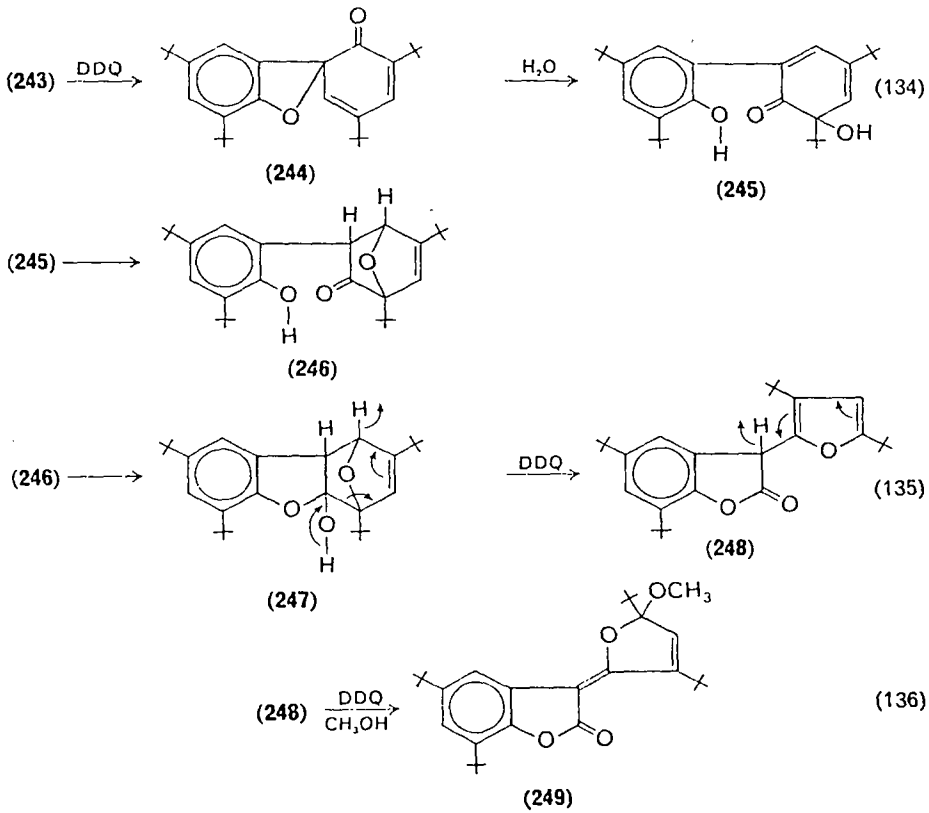
These oxidation–reduction reactions are catalysed by acids, tertiary amines and aluminium salts. It appears conceivable that catalysis by amines involves facilitated electron transfer from a phenol–amine complex while acid-catalysis may involve protonation of the diphenoquinone to give the conjugate acid which would be the more powerful oxidant. Redox reactions between diphenoquinones and phenols other than the parent phenols proceed as well but result, of course, in mixtures of biphenols[166].

The oxidative dimerization of 2,4-di-*t*-butylphenol (**242**) to give the *o,o'*-biphenol (**243**) can be brought about by chloranil at elevated temperature (reaction 133)[165]. The oxidation of 2,4-di-*t*-butylphenol by DDQ in



(242) (243) (133)

methanol, unexpectedly, results in the formation of a lactone by a reaction in which both water and methanol are incorporated in the product[165]. Originally, a seven-membered lactone structure was proposed for the oxidation product; however, recent evidence[167] suggests that the lactone has structure **249** and is formed by a sequence of reactions (134)–(136), involving oxidative coupling of biphenol **243** to give the spiroquinol ether **244** which then undergoes successive addition and dehydrogenation reactions. It has previously been stressed that oxidations by DDQ should be carried out in anhydrous solvents in order to avoid destructive hydrolytic displacement reactions of DDQ. However, numerous recently

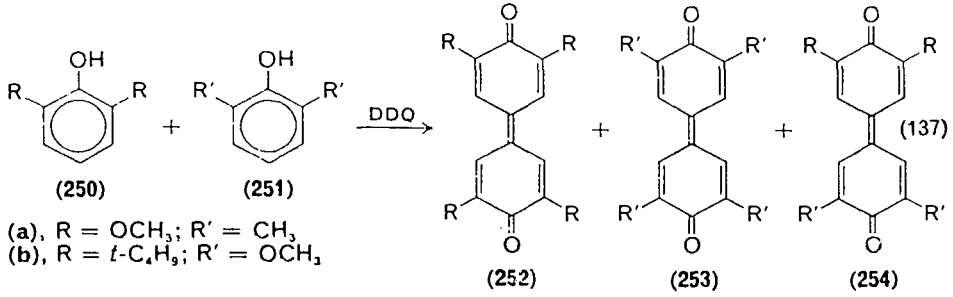


reported DDQ oxidations of preparative interest require the presence and participation of water in the reaction.

DDQ has been found to be a remarkably efficient oxidant for phenols[168]. Oxidation of 2,6-disubstituted phenols with one molar equivalent of DDQ gives diphenoquinones in good yields[168-170]. *p*-Benzoquinones may be formed as by-products in methanol solution[168]. Coupling reactions of DDQ with phenols give rise either to dihydroxydiphenyl ethers or to cyclohexadienones[122, 168].

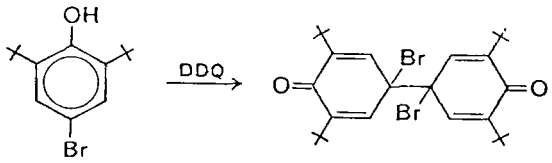
Significantly, DDQ was found to be the only oxidant to bring about oxidative cross-coupling of two different 2,6-disubstituted phenols (reaction 137)[169].

The formation of asymmetrically substituted diphenoquinones **254** by DDQ has prompted the suggestion that carbon–carbon coupled dimers in phenol oxidation derive by electrophilic substitution of phenoxonium ion intermediates[171]. It had been pointed out previously[172] that phenoxonium ion intermediates explain the formation of xanthones by DDQ oxidation of hydroxybenzophenones, and phenoxonium ions are possibly



(a), R = OCH_3; R' = CH_3
(b), R = t-C_4H_9; R' = OCH_3

involved in some other oxidations of phenols by DDQ in methanol solution, such as the oxidative dealkylation of hydroquinone monomethyl ethers[168] or the oxidative debromination of 4-bromo-tetramethylphenol to give duroquinone[168]. However, DDQ in methanol solution oxidizes 2,6-di-*t*-butyl-4-bromophenol (**255**) in high yield to the dehydrodimer **256** (reaction 138) which is also formed by typical one-electron oxidants.

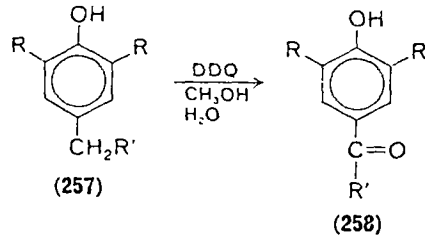


(255) (256) (138)

Likewise, 2,6-di-*t*-butyl-4-methylphenol in methanol is oxidized by DDQ to give a dehydrodimer rather than a quinol methylether which would be expected to be formed from the reaction of the solvent with an intermediate phenoxonium ion. Thus, experimental evidence suggests that DDQ can bring about the one-electron oxidation of phenols. One other explanation for the formation of asymmetrically substituted diphenoquinones **254** may be that DDQ, by virtue of its property as strong electron-acceptor, forms charge-transfer complexes with the two different (but still similar) phenols, whose rate of homolytic dissociation does not differ significantly.

DDQ oxidation in alcoholic solvents of phenols containing a methyl or methylene substituent in the 4-position results rapidly in high yield in the formation of 4-hydroxyphenyl carbonyl compounds (reaction 139; see Table 13)[168]. Analogous results were obtained in the oxidation of 6-hydroxytetralines[173] yielding 6-hydroxytetralones and in the oxidation of podocarpic acid derivatives[174].

It has been suggested that the benzylic oxidation of 4-alkylphenols involves quinone methide intermediates which undergo nucleophilic

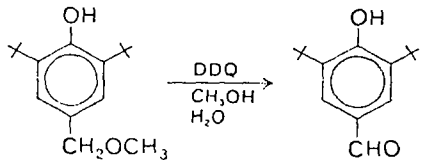


(257) (258) (139)

TABLE 13. Benzylic oxidation of phenols with two molar equivalents of DDQ in methanol[168, 173]

Phenol	Product	Yield (%)
Mesitol	3,5-Dimethyl-4-hydroxybenzaldehyde	83
Ionol	3,5-Di-*t*-butyl-4-hydroxybenzaldehyde	86
4-Benzylphenol	4-Hydroxybenzophenone	91
6-Hydroxytetralin	6-Hydroxytetralin-1-one	76

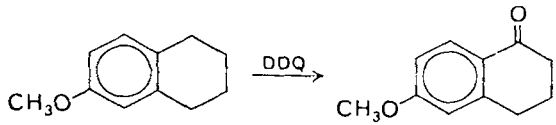
attack by the solvent. Indeed, quinone methides have been isolated in the dehydrogenation of steroidal phenols and, in certain cases, alkoxylation in the benzylic position can be achieved with one molar equivalent of oxidant[122, 173]. 4-Hydroxybenzyl ethers also undergo benzylic oxidation by DDQ in methanol solution to give the corresponding carbonyl compounds (reaction 140)[168, 173].



(259) (260) (140)

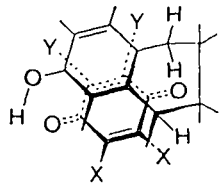
Concerning the mechanism of initial attack of DDQ on the 4-alkylphenol it has been proposed that, following charge-transfer complex formation, electron transfer followed by proton transfer gives rise to a phenoxy radical. Bimolecular disproportionation, either involving two phenoxy radicals or involving one phenoxy radical and the semiquinone radical DDQH, would then lead to the quinone methide[122]. Clearly, the formation of dehydrodimers by oxidation with DDQ supports this suggestion as one possible route to quinone methides. On the other hand, 6-methoxytetraline

(**261**) gives 6-methoxytetralin-1-one (**262**) in 70% yield by oxidation with DDQ in methanol (reaction 141), indicating that the 'attack by DDQ is



(**261**) (**262**) (141)

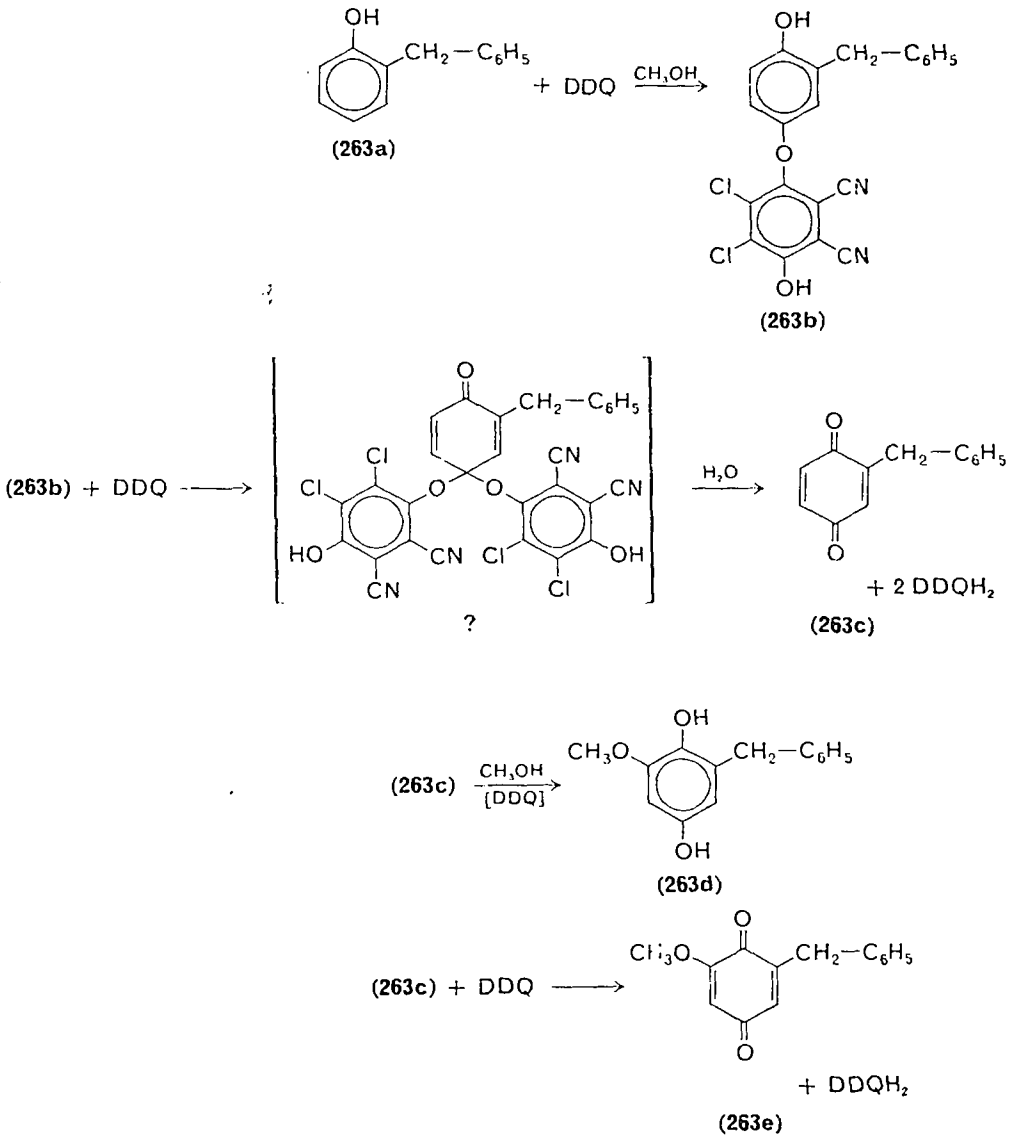
mounted at the benzylic carbon'[173]. The important prerequisite for the benzylic oxidation appears to be formation and proper orientation of a charge-transfer complex as indicated for 6-hydroxytetralin in structure **263**. A similar orientation of DDQ will be favoured in the case of



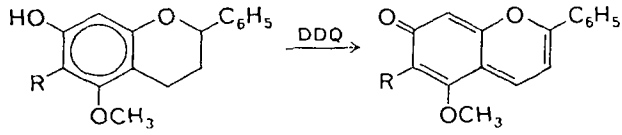
(**263**)

6-methoxytetralin. Significantly, unsubstituted tetralin upon reaction with DDQ in methanol at room temperature does not give any ketonic products[173]. It is furthermore worth noting that 4-benzylphenol upon oxidation with DDQ in methanol at room temperature is converted into 4-hydroxybenzophenone[168]; however, the oxidation of 2-benzylphenol **263a** under similar conditions does not give 2-hydroxybenzophenone but results in the formation of the 4,4'-dihydroxydiphenyl ether (**263b**) and the methoxy-substituted benzoquinone (**263e**)[262]. The formation of the latter was found to involve the oxidation of **263b** by DDQ and a DDQ-catalysed addition of solvent to the intermediate 2-benzylbenzoquinone **263c** as outlined in Scheme 1.

In the absence of the nucleophiles, the dehydrogenation of phenols containing a 2- or 4-alkyl substituent may give, dependent on the structure of the substrate, stable quinone methides[176]. Also, 7-hydroxy-substituted flavans **264**, upon treatment with DDQ in benzene, give quinone methides **264** (reaction 142)[177]. The involvement of the phenolic hydroxyl group in the dehydrogenation reaction is indicated by the fact that unsubstituted flavan resists dehydrogenation by DDQ[178]. It is conceivable also that the dehydrogenation of the hydroxychromans by DDQ in boiling benzene or toluene to give the hydroxychromenes[179], exemplified by the conversion of

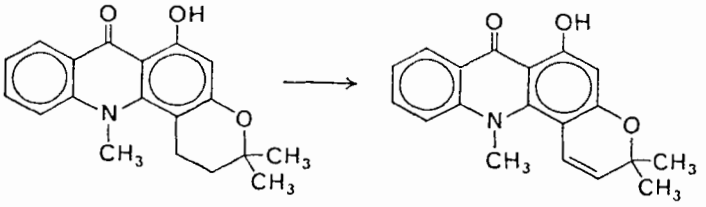


SCHEME 1. The oxidation of 2-benzylphenol by DDQ in methanol.



(142)

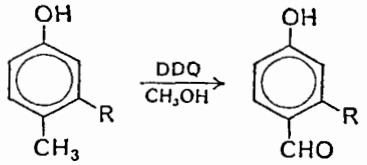
nordihydroacronycine[180] **265** into noracronycine **266** (reaction 143)[179], involves the intermediate formation and aromatization of the corresponding quinone methides. As pointed out above for the benzylic



(143)

(265) **(266)**

oxidation of 7-hydroxy- and 7-methoxytetralin, proper geometrical orientation of the hydrogen acceptor with the hydrogen donor may also be an important prerequisite for the facile conversion of hydroxychromans into hydroxychromenes. 2,2-Dialkylchromans containing a hydroxyl group in the 5-position rather than in the 7-position appear to be stable towards dehydrogenation by DDQ or chloranil[106, 181]. It is not readily understood, however, why 7-hydroxychroman is not dehydrogenated by DDQ in benzene[170]. Nor does it appear to be fully understood in which way the course of the dehydrogenation is influenced by the solvent. The 4-methyl-substituted phenol **267** is stable towards DDQ in benzene. Upon treatment with DDQ in methanol, however, the aldehyde **268** is formed (reaction 144). Also the nature of the product may change drastically

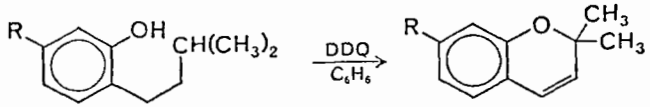


(144)

$R = COCH_2CH(CH_3)_2$

(267) **(268)**

with a change of solvent[170]. For example, 2-isoamyl-5-heptylphenol (**269**) upon treatment with DDQ in benzene gives the chromene **270** (reaction 145). When the oxidation is carried out in acetonitrile or dioxan, a mixture

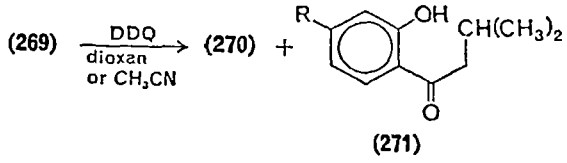


(145)

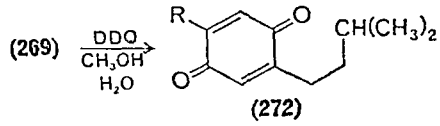
R = heptyl

(269) **(270)**

of chromene **270** and the ketone **271** is formed (reaction 146) while oxidation in methanol containing water gives the quinone **272** (reaction 147). These results are indicative of different mechanisms by which DDQ



(271) (146)

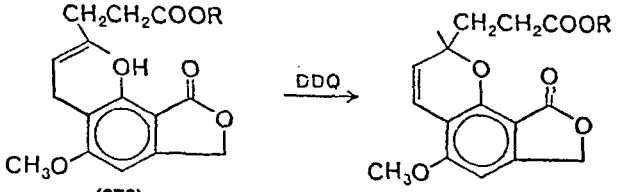


(272) (147)

can oxidize a phenol. The different products reflect the involvement of different intermediates and possibly, though not necessarily, different sites of attack by DDQ. In benzene, acetonitrile and dioxan, initial attack by DDQ may occur at the benzylic position in **269**, leading by a reaction involving water, possibly via an *o*-quinone methide, to an *o*-hydroxybenzyl alcohol, the dihydro precursor of the ketone **271**. Aromatization of the *o*-quinone methide by tautomerization would give an *o*-alkenylphenol, the dihydro precursor of the chromene **270**. By contrast, the formation of quinone **272** in methanol clearly does not involve any attack at the benzylic position in **269** but may be explained by initial hydrogen abstraction by DDQ from the phenol. As to whether quinone formation involves phenoxonium ions which react with the solvent or solvolysis of phenoxy radical coupling products remains to be investigated. The formation of the quinone **272** may be indicative of a preferred orientation of the hydrogen acceptor DDQ in the charge-transfer complex with the phenol **269** in methanol solution.

3. Oxidative conversion of 2-isoprenylphenols into chromenes

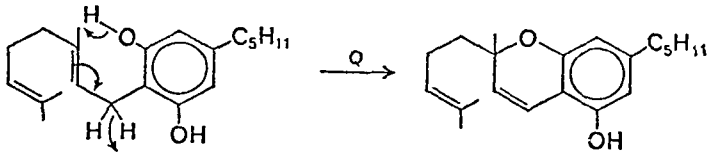
Recently, the dehydrogenation of 2-isoprenylphenols by quinones has received considerable attention. Both mycophenolic acid **273a** and its ethyl ester **273b** were found to undergo oxidative cyclization by treatment with DDQ in benzene to give mycochromenic acid **274a** and its ethyl ester **274b**, respectively (reaction 148)[182]. Numerous related examples of chromene formation have been reported, such as the conversion of cannabigerol **275** into D,L-cannabichromene (**276**) with either DDQ[179] or chloranil[106] (reaction 149), the dehydrogenation by DDQ of isoprenyl-substituted hydroxyxanthones to pyranoxanthones[181], the oxidative



(273)
(a), R = H
(b), R = C_2H_5

(247)

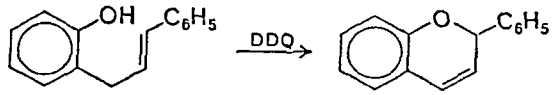
(148)



(275) (276)

(149)

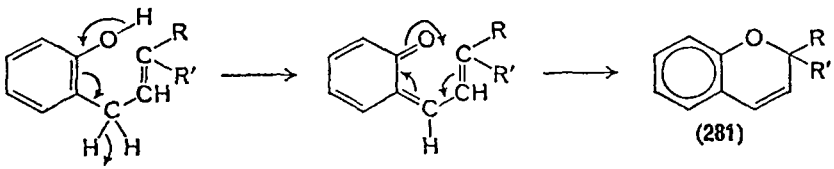
conversion of isoprenyl-substituted hydroxyisoflavones into the corresponding pyrano derivatives[183], the conversion of 2-cinnamylphenol **277** into flav-3-ene **278** (reaction 150)[178] or the oxidative cyclization of isoprenyl-substituted hydroxycoumarines[184].



(277) (278)

(150)

Most likely, the dehydrogenation of 2-isoprenylphenols by quinones involves the intermediate formation of *o*-quinone methides **280** (reaction 151), though the formation of chromenes may be rationalized in terms of



(279) (280) (281)

(151)

a cyclic mechanism involving hydride ion abstraction by the quinone from the benzylic position, double-bond migration and intramolecular nucleophilic reaction of the phenolic hydroxyl group (cf. reaction 149). Only recently, the conversion of mycophenolic acid **273a** into mycochromenic acid **274a** was accomplished[185] by oxidation with alkaline potassium ferricyanide, thus supporting the quinone methide route (reaction 151) to chromenes and suggesting that the *o*-quinone methide intermediate **280** can be formed not only by reaction (151) but via phenoxy radicals as well.

The dehydrogenation by DDQ in benzene has been extended to *o*-α,β-alkenyl phenols[170] and to *o*-α,β-alkenyl hydroquinones[186], but with these substrates the oxidative cyclization appears to be a less general mode of reaction.

VI. OXIDATION AND DEHYDROGENATION OF NITROGEN COMPOUNDS

A. Aliphatic and Aromatic Amines

It has been known for many years that amines react with high-potential quinones[138]; however, an insight into the nature of these reactions was first gained through the more recently accomplished isolation and characterization of defined products. The importance of charge-transfer complexes involved in amine–quinone interactions is now recognized and the spectroscopic investigation of their solvent-dependent dissociation has allowed some seemingly simple substitution reactions to be rationalized in terms of electron-transfer processes.

Primary and secondary amines readily undergo overall nucleophilic displacement reactions with halogen- or methoxy-substituted *p*-benzoquinones[187–190]. For instance, the reaction of *n*-butylamine with chloranil results in the rapid displacement of two chlorine substituents by the amine to give 2,5-bis-butylamino-3,6-dichloro-1,4-benzoquinone[187a]. No intermediate is observed when the reaction is carried out in cyclohexane solution and monitored spectroscopically under normal conditions[187b]. However, using rapid-scan spectrophotometry[191], and by carrying out the reaction in ethanol solution, the transient formation of the chloranil radical anion and the *n*-butylamine radical cation was verified, indicating that the displacement actually is preceded by the one-electron oxidation of the amine by the quinone. Aromatic primary amines may behave differently, since evidence for the involvement of radical ions in the reaction of chloranil with aniline has not been obtained[192].

The oxidation of tertiary amines by halogen-substituted benzoquinones has been the subject of several investigations. Aromatic tertiary amines and high-potential quinones often form solid molecular complexes[193, 194] which have been found to be paramagnetic[195]. It has been established by ultraviolet spectroscopy that the complex of *N,N,N',N'*-tetramethyl-*p*-phenylenediamine with 2,6-dichloro-1,4-benzoquinone in non-polar solvents dissociates into the neutral donor and acceptor molecules, while polar solvents favour dissociation into the radical cation and the radical anion[29, 196].

Aliphatic tertiary amines undergo irreversible oxidation by a variety of high-potential quinones[197,198]. Thus, triethylamine **282** smoothly reacts with chloranil to give the blue diethylaminovinylquinone **286** together with tetrachlorohydroquinone and triethylammonium chloride[197]. The mechanism for the formation of the vinylquinone **286** has been established to involve the dehydrogenation of triethylamine by chloranil to give the enamine **285** which then undergoes a displacement reaction with chloranil. It has been suggested[199] that the dehydrogenation reaction proceeds via the formation of the charge-transfer complex of triethylamine with chloranil **283** followed by one-electron transfer rather than by hydride ion transfer. Thus, the formation of the vinylquinone **286** may be rationalized in terms of the sequence of reactions (152)–(155).

$$\underset{(282)}{(C_2H_5)_3N} + Q \longrightarrow \underset{\text{charge-transfer complex}\ (283)}{[(C_2H_5)_3N;\ Q]} \qquad (152)$$

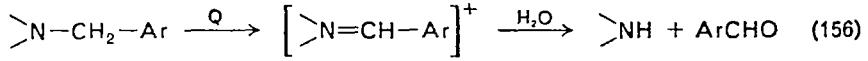
$$(283) \xrightarrow[\text{oxidation}]{\text{one-electron}} \underset{(284)}{(C_2H_5)_3N^{+\cdot}} + Q^{-\cdot} \qquad (153)$$

$$(284) + Q^{-\cdot} \xrightarrow[\text{transfer}]{\text{hydrogen}} \underset{(285)}{CH_2{=}CHN(C_2H_5)_2} + QH_2 \qquad (154)$$

$$(285) + Q \longrightarrow \underset{(286)}{\text{Cl-substituted quinone with CH=CHN(C}_2\text{H}_5\text{)}_2\text{ side chain}} + HCl \qquad (155)$$

Bromanil (E_0 746 mV) reacts with triethylamine in the same fashion as described above for chloranil (E_0 742 mV). By contrast, iodanil fails to dehydrogenate triethylamine, although its oxidation potential (E_0 737 mV) is only slightly lower than that of the bromo and chloro analogues. It has been suggested[197] that this lack of reactivity is to be attributed to the bulkiness of the iodo-substituents which prevent triethylamine from forming a charge-transfer complex with iodanil. Thus, both the oxidation potential and the shape of the quinone may determine whether or not a quinone will bring about the oxidation of an amine. Surprisingly, however, while 3,3′,5,5′-tetrachloro-4,4′-diphenoquinone dehydrogenates triethylamine (without subsequent displacement), unsubstituted 4,4′-diphenoquinone fails to do so, despite its high oxidation potential.

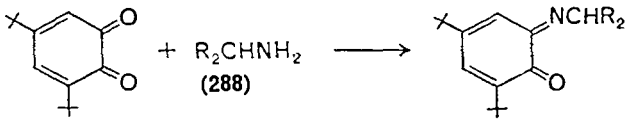
Tertiary amines not capable of forming enamines may also undergo dehydrogenation by quinones[197]. Thus, tribenzylamine or benzyldimethylamine react with chloranil to give benzaldehyde, presumably according to a mechanism which involves the hydrolysis of the intermediate shown in reaction (156).



(156)

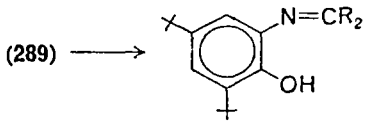
B. Conversion of Amines into Ketones

o-Benzoquinones generally undergo rapid nucleophilic addition rather than dehydrogenation reactions with amines[200]. However, 3,5-di-*t*-butyl-1,2-benzoquinone (**287**) has recently been found to be a remarkably efficient reagent for the rapid oxidative conversion of a primary amine of structure **288** into the corresponding ketone **291** under very mild conditions[201]. Due to the bulkiness of the *t*-butyl groups, the *o*-quinone **287** reacts with primary amines **288** to give the Schiff's bases **289** which spontaneously undergo tautomerization to the thermodynamically favoured Schiff's bases **290** (reactions 157 and 158). Acid-catalysed



(157)

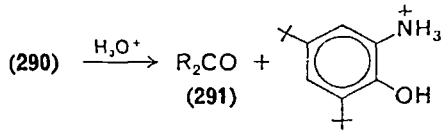
(287) (289)



(158)

(290)

hydrolysis of **290** affords the ketone **291** in yields as high as 97% (reaction 159). Some examples of the oxidation of amines by this method are listed in Table 14.



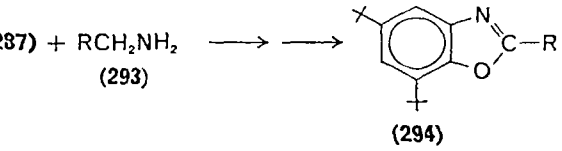
(159)

(292)

TABLE 14. Oxidative conversion of amines into ketones by 3,5-di-*t*-butyl-1,2-benzoquinone[201]

Amine	Ketone	Yield (%)
α-Phenylethylamine	Acetophenone	84
Benzhydrylamine	Benzophenone	90
Cyclohexylamine	Cyclohexanone	97
Cyclododecylamine	Cyclododecanone	97

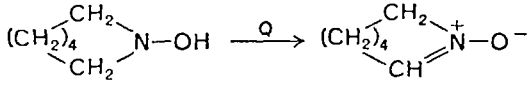
Primary amines of structure **293** cannot be converted into aldehydes by reaction with 3,5-di-*t*-butyl-1,2-benzoquinone in any useful yields because of favoured intramolecular addition reactions of the corresponding *ortho*-hydroxy-substituted Schiff's bases. Thus, the reaction of benzylamine with *ortho*-quinone **287** gave benzaldehyde in only 9% yield, while the benzoxazole **294** (R = phenyl) was obtained in 73% yield (reaction 160).



(160)

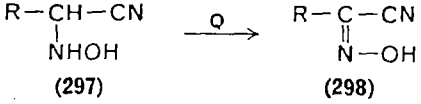
C. Hydroxylamines, Nitronic Acids and Hydrazines

Hydroxylamines containing an α-C—H group undergo dehydrogenation upon treatment with benzoquinone under rather mild conditions. For example, the cyclic hydroxylamine **295** reacts with benzoquinone in ether to give the imine *N*-oxide **296** (reaction 161)[202]. The dehydrogenation of



(161)

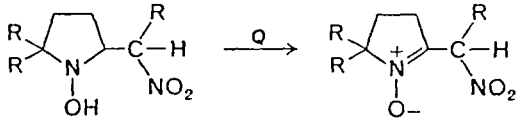
α-hydroxylaminonitriles **297** with benzoquinone proceeds smoothly in refluxing benzene to give α-cyanooximes **298** in good yields (reaction 162)[203].



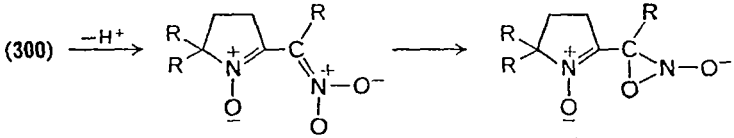
(162)

R = CH_3; C_2H_5; C_3H_7

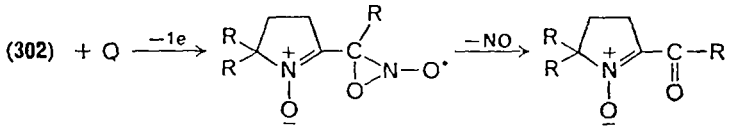
Surprisingly, the nitroalkyl-substituted cyclic hydroxylamine **299** was found to be stable towards chloranil. However, upon treatment with DDQ at room temperature, the β-nitrohydroxylamine **299** undergoes a most remarkable transformation to give nitric oxide and the ketonitrone **304**[204]. The mechanism for the oxidative elimination of nitric oxide has been suggested to involve a dehydrogenation step to give the intermediate **300** (reaction 163), deprotonation and one-electron oxidation of the *N*-hydroxy oxaziran anion **302** (reactions 164 and 165).



(299) R = CH_3 (300) (163)

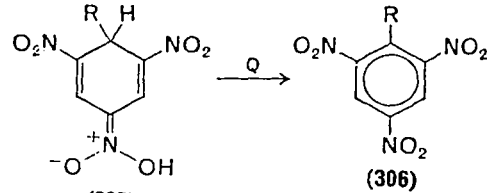


(301) (302) (164)

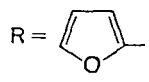


(303) (304) (165)

According to a recent report, nitronic acids of structure **305** undergo aromatization upon treatment with 1,4-benzoquinone (reaction 166)[205]. As to whether the primary step in the dehydrogenation consists in the removal of a hydride ion from the allylic position or involves protonation of benzoquinone by the nitronic acid has not been investigated.



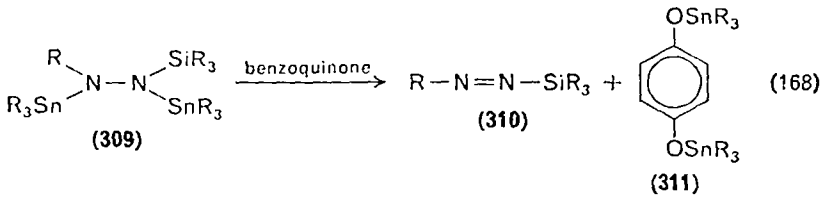
(305) (306) (166)



Arylhydrazines **307** are easily oxidized by benzoquinone[206] or diphenoquinone[207] (reaction 167); however, because of the instability of the resulting aryldiimides (diazenes)[208] **308**, this reaction has not been exploited

$$\underset{\textbf{(307)}}{ArNHNH_2} + Q \longrightarrow \underset{\textbf{(308)}}{ArN{=}NH} + QH_2 \qquad (167)$$

preparatively. Only recently, silylated and germylated trimethylstannylhydrazines have been found to undergo a remarkable oxidation by 1,4-benzoquinone which involves transfer of the organometal substituent to the quinone[209]. For example, hydrazines **309** are smoothly converted into the substituted diimides **310** upon treatment with equimolar amounts of 1,4-benzoquinone at room temperature (reaction 168). It has been suggested that

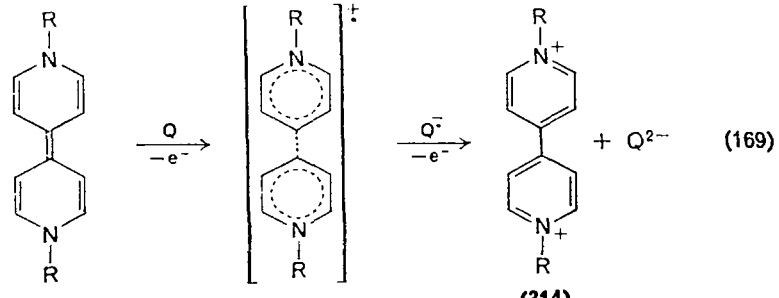


(309) **(310)** **(311)** (168)

the transfer of the trimethylstannyl groups to the quinone involves the intermediate formation of hydrazyl radicals since the oxidation of 1,2-diphenyl-1,2-bis(trimethylstannyl)-hydrazine with 1,4-benzoquinone gives *trans*-azobenzene rather than the *cis*-isomer which was expected to be formed if the transfer of the trimethylstannyl groups occurred in a concerted process.

D. Nitrogen Heterocycles

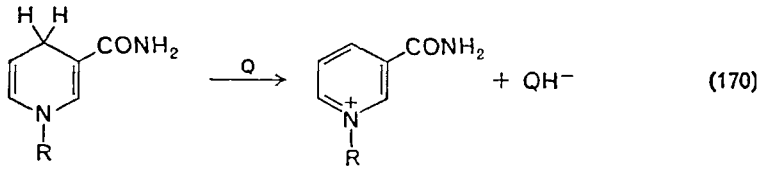
Nitrogen heterocycles generally readily undergo oxidation by quinones. As to whether the oxidation occurs as a one-electron transfer or involves the transfer of two electrons or a hydride ion depends on the structure of the nitrogen heterocycle, on the stoicheiometry of the reactants and on the oxidation potential of the quinone. Thus, 1,1′-dibenzyl-1,1′-dihydro-4,4′-bipyridyl (**312**) reacts with chloranil in a molar ratio of 1 : 1 to give the colourless bipyridinium salt **314** of the tetrachlorohydroquinone dianion (reaction 169)[210,211]. When the reaction between **312** and chloranil is carried out in a molar ratio of 2 : 1, the deep-violet radical cation **313** and the chloranil radical anion are formed. Quinones of lower oxidation potential such as phenanthrenequinone give the deep coloured salts **313** even when used in equimolar amounts.



(312) (313) (314) (169)

R = $-CH_2-C_6H_5$

Quinone dehydrogenation has been applied successfully to numerous other hydro derivatives of nitrogen heterocycles. The yields of dehydrogenated products are generally quite high and these reactions may be of both preparative and analytical value. Diethyl-1,4-dihydro-2,6-dimethylpyridine-3,5-dicarboxylate (the Hantzsch ester) is rapidly dehydrogenated in 97% yield by an equimolar amount of chloranil at room temperature[212,213]. Likewise, numerous *N*-substituted 1,4-dihydropyridines and 1,2-dihydropyridines, studied as model compounds of reduced diphosphopyridinium nucleotide, are readily dehydrogenated by various quinones, as exemplified by reaction (170)[214]. The rates of dehydrogenation increase



(315) (316) (170)

R = 2,6-dichlorobenzyl

with increasing oxidation potential of the quinone, however, the rate of dehydrogenation by 3,5-di-*t*-octyl-1,2-benzoquinone appears far higher than might be expected from its oxidation potential in comparison with that of the *para*-quinones (see Table 15). Also the nature of the 3-substituent of the 1,4-dihydropyridine may have a remarkable influence on the rate of dehydrogenation by one and the same quinone.

Dehydrogenation by high-potential quinones appears to be the most convenient synthetic method for the preparation of salts of nitrogen heterocycles[27]. DDQ and 9,10-dihydroacridine undergo reaction to give the acridinium 2,3-dichloro-5,6-dicyanoquinolate in 93% yield. Perchlorates of nitrogen heterocycles are most conveniently prepared by dehydrogenation

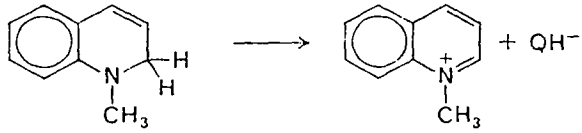
with high-potential quinones in acetic acid containing perchloric acid[27]. Thus, 5-methylphenanthridinium perchlorate was prepared in 94% yield by dehydrogenation of 5-methyl-5,6-dihydrophenanthridine with chloranil.

TABLE 15. Dehydrogenation of dihydropyridine **315** by quinones[214]

Quinone	Rate (l/mol min)
Duroquinone	5
1,4-Benzoquinone	800
Chloranil	12,000
3,5-Di-*t*-octyl-1,2-benzoquinone	~200,000

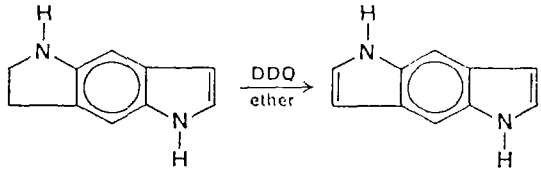
Unsubstituted benzoquinone was found to dehydrogenate hydro derivatives of nitrogen heterocycles only very slowly at room temperature[215]. Also, its use as dehydrogenating agent is limited because of its tendency to undergo nucleophilic 1,4-addition by the partially hydrogenated nitrogen heterocycle. However, tetrahalogen-substituted *p*-benzoquinones, most frequently applied in boiling xylene, readily dehydrogenate hydro derivatives of nitrogen heterocycles[216-218]. Thus, both dihydro-, tetrahydro- and hexahydrocarbazoles smoothly react with chloranil or bromanil to give the carbazoles in yields of 70–95%, reaction times ranging from one to twenty-four hours[216].

Dihydro derivatives of quinoline undergo dehydrogenation by chloranil very rapidly in dioxan solution, even at room temperature[212]. 1,2-Dihydroquinoline is thus converted into quinoline. In analogy with other *N*-alkyl-substituted compounds, 1,2-dihydro-1-methylquinoline (**317**) reacts with quinones to give the salts **318** (reaction 171)[212].

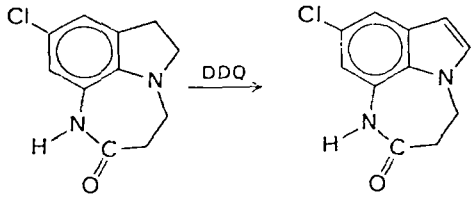


(317) (318) (171)

Hydro derivatives of indoles can be dehydrogenated by both chloranil[219] and DDQ[220] as exemplified by the conversion of **319** into the dehydro compound **320**. The dehydrogenation of the tricyclic compound **321** by DDQ in boiling benzene does not lead to an unsaturated lactam but gives the dehydro derivative **322** (reaction 173)[221].

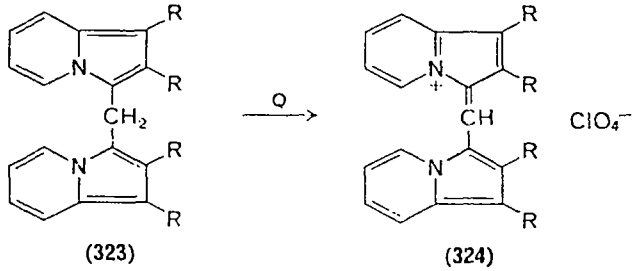


(319) (320) (172)

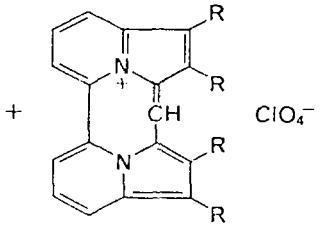


(321) (322) (173)

One interesting example of intramolecular coupling has been observed in the dehydrogenation of the tetramethylmethylene-3,3′-indolizine (**323**) which, upon treatment with chloranil in acetonitrile or methanol, followed by perchloric acid, yields the indolizinium perchlorate **324** and the cyclodehydrogenated compound **325**[222]. It has been established that **324** is not the precursor of **325** and it has been suggested that the cyclodehydrogenation involves a one-electron transfer rather than hydride ion transfer from the base **323** to the quinone.



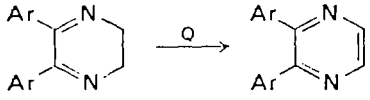
(323) (324)



(325) (174)

R = CH_3

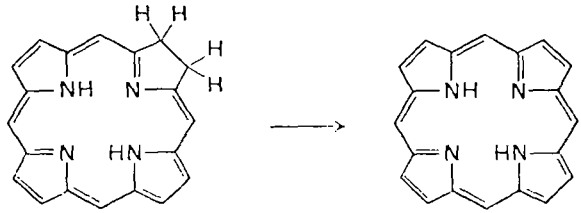
Heterocyclic compounds containing more than one nitrogen atom in the same ring undergo dehydrogenation by high-potential quinones in high yields. Reaction of the dihydropyrazines **326** with chloranil in boiling xylene gives 2,3-diarylpyrazines **327** in yields of up to 97% (reaction 175)[223]. DDQ was applied as dehydrogenating agent in the preparation



(326) (327) (175)

of unsubstituted pyridazine from tosylated dihydropyridazine[224]. Phenanthrenequinone may be the more suitable dehydrogenating agent when high-potential quinones 'over-oxidize' the nitrogen heterocycle, as has been observed in the dehydrogenation of 4,5-dihydro-2,4,5-triphenylimidazole[3]. Most recently, however, DDQ was used successfully in the dehydrogenation of 1,2-dihydro-1,4-diazacycl-[3,2,2]azine to give the heteroaromatic compound in 75% yield[259].

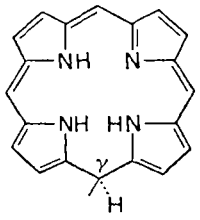
In the dehydrogenation of hydroporphines, including their copper derivatives, the oxidation potential of the quinone may be of particular importance as far as selectivity is concerned[225-227]. Phenanthrenequinone dehydrogenates chlorin **328** only incompletely, even at 140°C for ten hours[225]. By contrast, porphin **329** is formed smoothly by dehydrogenation of chlorin with either *o*-chloranil for ten minutes at 130°C, or DDQ for two minutes at 80°C (reaction 176). Treatment of octaethyl-tetrahydroporphin with excess *o*-chloranil yields octaethyl-chlorin which may then



(328) (329) (176)

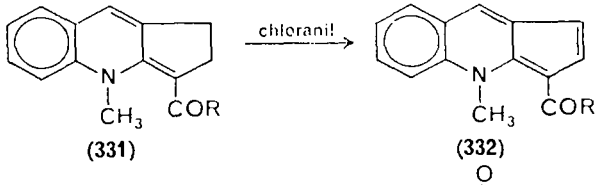
be dehydrogenated by DDQ at room temperature to give octaethylporphin[226,227]. By using the appropriate molar equivalents of DDQ, either the chlorin or the porphin can be obtained in high yield by dehydrogenation of either the tetrahydro, hexahydro or octahydro derivatives of porphins. DDQ has also found application in the dehydrogenation of

hydro derivatives of tetrazaporphin[228], and has been applied most recently in the successful dehydrogenation of a thiaphlorin to give the corresponding thiaporphin[229]. Phlorins (**330**) are easily converted into porphins by dehydrogenation with chloranil (reaction 177)[230].

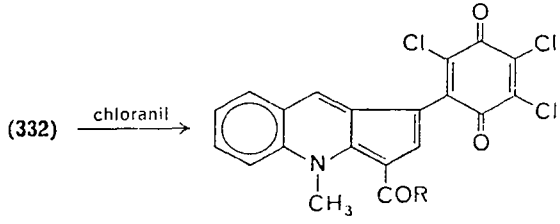


(330) ⟶ (329) (177)

Though chloranil and DDQ have been applied most frequently in the dehydrogenation of nitrogen heterocycles, only few examples have been described in which the totally dehydrogenated product undergoes subsequent reaction with the quinone. Attempts to dehydrogenate the substituted 1,2-dihydroquinindine **331** with chloranil to compound **332** gave, instead, the blue-green coloured trichloro-substituted *p*-benzoquinone **333** in 64% yield (reactions 178 and 179)[231]. Similar examples of secondary

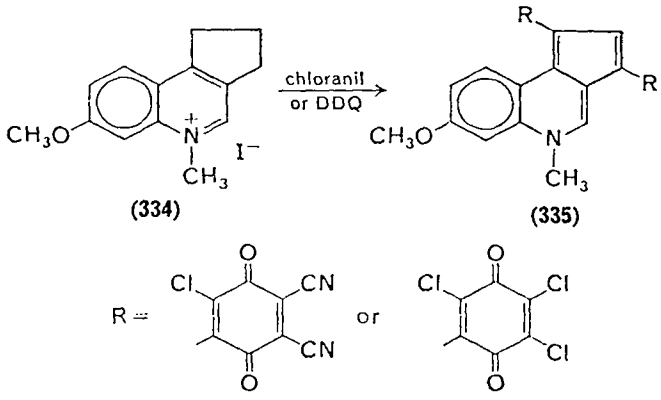


(331) (332) (178)



(333) (179)

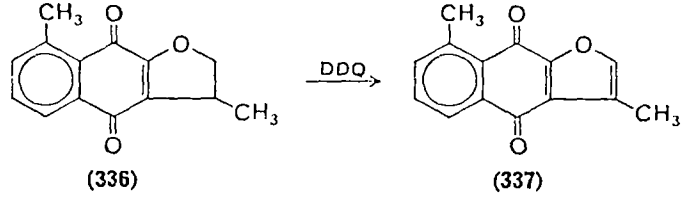
reactions have been encountered in the reaction of the methiodides such as **334** with both chloranil and DDQ which leads to the di-substituted compound **335** (reaction 180)[232]. It has been suggested[232] that the formation of **333** and **335** involves electrophilic substitution by the quinone of the reactive aromatic dehydrogenation product. The reaction of the free base of **334** with DDQ was found to give a stable charge-transfer complex.



(180)

VII. DEHYDROGENATION OF OXYGEN AND SULPHUR HETEROCYCLES

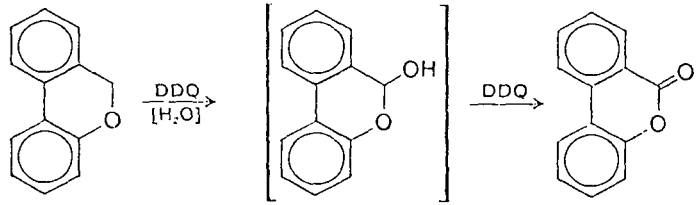
Although the non-bonding electrons in oxygen heterocycles should facilitate hydride ion abstraction, double-bond activation of the site to be attacked appears to be necessary for the efficient dehydrogenation by quinones. Even then, success or failure of a reaction appear difficult to predict. Thus, reaction of 2,5-dihydro-3-phenylfuran with chloranil in boiling ethylene glycol gave 3-phenylfuran in 10% yield only[233]. Better yields were obtained in the dehydrogenation of dihydronaphthofurandiones by DDQ, as in the conversion of **336** into **337** (reaction 181); however, prolonged reaction time in refluxing benzene was required[234]. DDQ was used successfully in the dehydrogenation of chromanes into chromenes[80,179]; however, unsuccessful attempts to dehydrogenate chromanes by DDQ have also been reported[181].



(181)

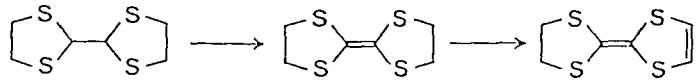
The oxidation of the dibenzopyran **338** with DDQ resulted in the formation of benzocoumarin **340** and an ether dimer (reaction 182)[235]. Most likely, both products derive from the same intermediate **339** whose formation requires the presence of water. Since the dibenzopyran **338** contains a benzyl ether group, it may be the nature of this function which

facilitates the oxidation of **338** (see section V.A.3). Likewise, dehydrogenation of 6-methoxyflavanone with chloranil in boiling xylene to give the substituted flavone in 60–70% yield[94] is probably facilitated by a similar phenyl group activation.



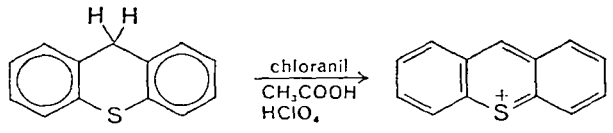
(338) (339) (340) (182)

Although tetrahydrothiophenes have been reported[236] to resist dehydrogenation by chloranil, sulphur heterocycles appear to be more prone to undergo dehydrogenation by quinones than their oxygen analogues. Thus, thioacetals are dehydrogenated by DDQ, as shown by the conversion of **341** into **342** and **343** (reaction 183)[176]. Dihydrothiophenes react with



(341) (342) (343) (183)

chloranil in boiling ethylene glycol to give thiophenes in excellent yields[237]. Quinone dehydrogenation in acetic acid containing perchloric acid also provides a convenient method for the preparation of heterocyclic salts. For instance, thioxanthene **344** was converted by chloranil into thioxanthylium perchlorate **345** in 87% yield (reaction 184)[27].



(344) (345) (184)

The reaction of DDQ with a thiadiazole in dioxan was reported to give a cyclic thionyldiamide[238]. The reaction obviously requires the presence of water in the solvent; however, the mechanism of the oxygen transfer remains to be elucidated.

Most recently, a benzothiepin was prepared by dehydrogenation of a dihydrobenzothiepin with DDQ in benzene at room temperature[239].

Although we are dealing with a sulphur heterocycle, in this particular instance the substrate is better classified as a hydroaromatic compound.

VIII. OXIDATION OF ORGANOMETALLIC COMPOUNDS

A. Grignard Compounds and Organolithium Compounds

Grignard compounds undergo oxidative dimerization according to reaction (185) upon treatment with quinones but this reaction has not been exploited synthetically, apparently because of the inconsistent

$$\mathrm{ArMgX} \xrightarrow{Q} \mathrm{Ar{-}Ar} \qquad (185)$$

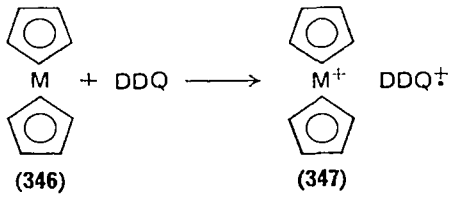
yields of coupling products obtained. Still, even low-potential quinones may act as electron acceptors. Thus, phenylmagnesium bromide upon treatment with duroquinone gives biphenyl, among other products, though in low yield[240]. Quarterphenyl was obtained in 44% yield from 4-biphenylmagnesium bromide by oxidation with *p*-benzoquinone[241].

The yields of dimerization products are probably low because of competing addition reactions to the carbonyl groups of the quinones. This conclusion may be drawn from a more recent study of the reaction of Grignard reagents with diphenoquinones[242]. Thus, phenylmagnesium bromide was oxidized by 3,3′,5,5′-tetramethyldiphenoquinone to give biphenyl in 27% yield. Tetraphenyldiphenoquinone gave biphenyl in 38% yield, while tetra-*t*-butyldiphenoquinone gave biphenyl in up to 94% yield. The yield of biphenyl was low in the oxidation of phenyllithium with tetra-*t*-butyldiphenoquinone, presumably because phenyllithium does add even to *o*,*o*′-di-*t*-butyl-substituted quinonoid carbonyl groups[243].

B. Metallocenes

Metallocenes readily undergo one-electron oxidation by quinones, giving the corresponding metallocinium ions in excellent yields. Thus, benzoquinone in organic solvents in the presence of acid is a convenient oxidant for the conversion of ferrocene into the ferricinium ion[244]. The reaction of ferrocene and of cobaltocene **346** with DDQ in benzene solution gives the corresponding metallocinium salts **347** in high yields (reaction 185a)[245].

As to whether a metallocene by reaction with a quinone in neutral organic solvents gives a π-complex or gives, as the result of complete electron transfer, the metallocinium ion depends on the relative oxidation–reduction potentials of the donor and acceptor compounds. Thus,



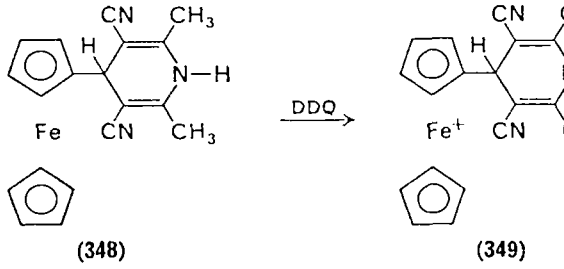
(185a)

(346) (347)

M = Fe or Co

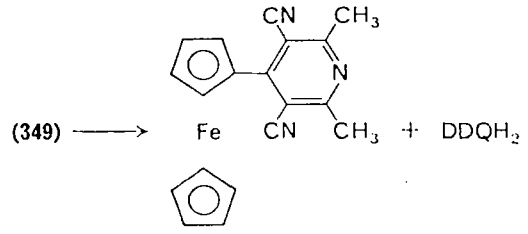
chloranil in benzene gives a π-complex with ferrocene (polarographic half-wave potential $E_{\frac{1}{2}}+0{\cdot}30$ V), but gives the metallocinium salt with cobaltocene ($E_{\frac{1}{2}}-1{\cdot}16$ V)[245,246].

It is worth noting that one-electron transfer from the metallocene to the quinone proceeds much more easily than possible dehydrogenation reactions. For instance, bis(tetrahydroindenyl) iron was oxidized by DDQ to give the corresponding metallocinium compound rather than the dehydrogenated aromatized compound[245]. Likewise, DDQ reacted with the ferrocenyl-dihydropyridine **348** in acetonitrile at room temperature by one-electron transfer to give the metallocinium quinolate **349** which slowly changed into $DDQH_2$ and the ferrocenylpyridine **350** (reactions 186 and 187)[247].



(186)

(348) (349)



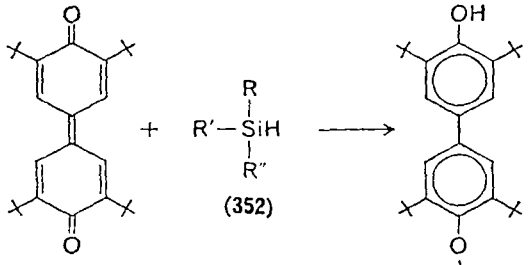
(187)

(350)

C. *Oxidative-Reductive Additions to Quinones by Organosilicon and Organophosphorus Compounds and Metal Complexes*

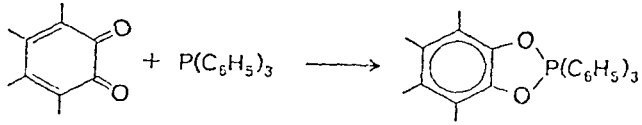
Tetra-*t*-butyldiphenoquinone reacts with silicon hydrides **352** at elevated temperature to give addition products of structure **353** (reaction

188)[248]. Though the mechanism of this reaction has not been investigated, hydride-ion rather than hydrogen-atom transfer from the silane to the quinone appears to be the most probable mode of dehydrogenation preceding the coupling reaction.



(351) (352) (352) e.g. R = H; R′ = R″ = C_6H_5 (353) (188)

Triphenylphosphine and related phosphorus compounds undergo addition reactions to both *o*- and *p*-quinones in which phosphorus is oxidized to the penta-covalent state[249]. The mechanism of the reaction of chloranil with triphenylphosphine resulting in the formation of a phenoxy-*O*-phosphonium radical cation has been found to involve oxidation of the chloranil–triphenylphosphine charge-transfer complex by chloranil[250]. *o*-Quinones react with triphenylphosphine to give penta-covalent phosphor compounds of structure **356** (reaction 189). An analogous oxidative addition has been achieved recently by reaction of low-valent transition metal complexes with *o*-chloranil[251].



(354) (355) (356) (189)

IX. HYDROGEN TRANSFER IN STRONGLY ACIDIC MEDIA

Quinones in acidic media such as sulphuric or trifluoroacetic acid give rise to the mono- or di-protonated conjugate acids QH and QH_2^{2+}, respectively, (reactions 190 and 191).

$$Q + H^+ \longrightarrow QH^+ \quad (190)$$

$$QH^+ + H^+ \longrightarrow QH_2^{2+} \quad (191)$$

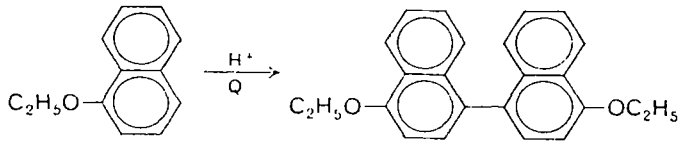
Even those conjugate acids which derive from low-potential quinones are strong oxidants which readily accept either electrons or hydride ion from otherwise non-reactive substrates. For example, triethylsilane in trifluoroacetic acid (TFA) reduces protonated *p*-benzoquinone to give hydroquinone according to reaction (192).

$$Q \xrightarrow{TFA} QH^+ \xrightarrow{R_3SiH} QH_2 \qquad (192)$$

Anthraquinone was thus converted into anthraquinol, and anthra-1,4:9,10-diquinone was reduced by triethylsilane in trifluoroacetic acid to give quinizarin[252].

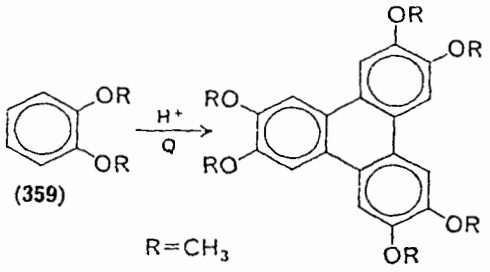
Di-protonated 4,4′-diphenoquinone has been reported to oxidize proton complexes of aromatic hydrocarbons to give the corresponding radical cations. Other quinones, such as *p*-benzoquinone, 1,2-naphthoquinone and anthraquinone in sulphuric acid were found to react similarly[253-255].

Protonated quinones may be used as oxidants in preparatively important coupling reactions such as the Scholl reaction. For instance, the oxidative coupling of 1-ethoxynaphthalene (**357**) to give 4,4′-diethoxy-1,1′-binaphthyl (**358**) may be brought about in sulphuric acid by quinones such as *p*-benzoquinone or 9,10-phenanthrenequinone (reaction 193). It has been suggested that the mechanism of biaryl formation involves radical cations resulting from electron transfer from the aromatic substrate to the oxidant[256].

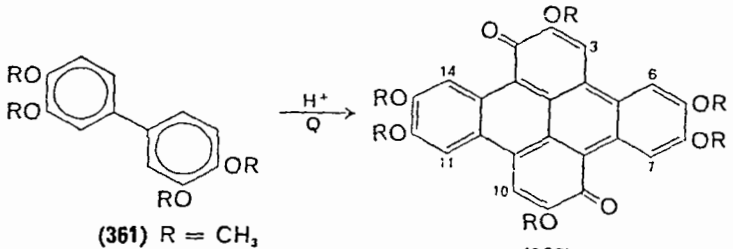


(357) (358) (193)

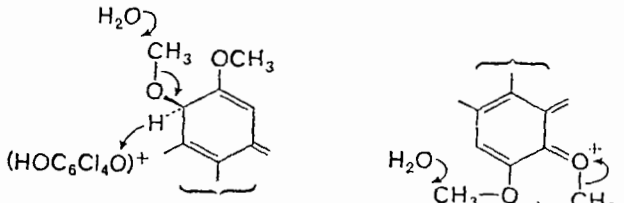
Protonated high-potential quinones, for example, chloranil in 70% v/v aqueous sulphuric acid, have been found to bring about, in high yield, the oxidative trimerization of veratrole **359** to give the hexamethoxytriphenylene **360** (reaction 194)[257]. It has been established that the formation of **360** proceeds via the intermediate tetramethoxybiphenyl **361** which undergoes a further coupling reaction with veratrole. The oxidation of tetramethoxybiphenyl **361** by protonated chloranil gives, in 76% yield, the dibenzonaphthacenequinone **362** whose formation has been suggested to involve a series of hydride ion transfers to the conjugate acid of chloranil (reaction 195)[258]. The precursor of **362** is the corresponding octamethoxy-substituted dibenzonaphthacene which, upon



(359) (360) (194)



(361) R = CH_3 (362) (195)



(363) (364)

treatment with chloranil in aqueous sulphuric acid, undergoes oxidative demethylation. It has been suggested that the oxidative demethylation involves protonation of the octamethoxy-substituted dibenzonaphthacene as indicated in partial structure **363** followed by removal of a hydride ion, reaction with water and an intramolecular transetherification step as shown in partial structure **364**.

X. ACKNOWLEDGMENT

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The Chemistry of the quinonoid compounds
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CHAPTER 8

Rearrangements of quinones

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I. INTRODUCTION

The discussions in this chapter deal primarily with reactions of benzo- and naphthoquinones in which the quinoid nucleus has undergone molecular rearrangement. Discussions of the rearrangements of variously substituted quinones which do not intimately involve the quinoid nucleus have not been included.

An appreciable amount of fragmentary results has appeared concerning the rearrangements of hydroxyquinones. The principal pathway for molecular reorganization of this class of compounds, under either oxidative or hydrolytic conditions, is ring contraction to five-membered cyclic ketones or lactones. Depending upon the reaction conditions as well as the quinone involved, these ring-contracted compounds can either be isolated as stable products or are formed as intermediates which subsequently undergo further reaction.

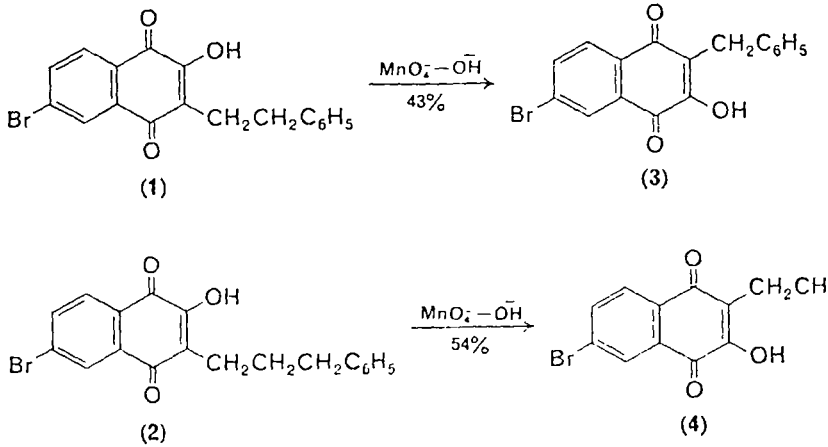
Azidoquinones undergo facile rearrangements induced by the action of heat or acid. The principal products again arise via ring contraction reactions. However, a number of cleavage and fragmentation reactions which are of synthetic utility and mechanistic interest have also appeared.

Very little has appeared on ring expansion reactions of quinones. The only example of such a reaction which has received any systematic study is the rearrangement of alkyl-substituted quinones to azepinediones induced by the action of hydrazoic acid in strongly acidic media.

II. REARRANGEMENTS OF HYDROXYQUINONES

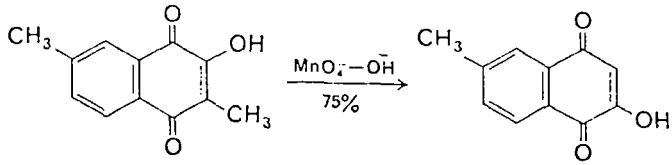
A. *Oxidative Rearrangements of Hydroxyquinones*

A most remarkable oxidative rearrangement of 2-hydroxy-3-alkyl or alkenyl-1,4-naphthoquinones (Hooker oxidation) to the next lower homologue by the action of alkaline permanganate was reported by Hooker in 1936[1]. Hooker concluded that the quinone ring was cleaved and that it subsequently closed in a different manner resulting in a transformation in which the alkyl and hydroxyl groups exchange places as a result of the oxidation. Fieser and coworkers[2,3] in a paper published the same year as Hooker's original work showed that such a transposition does indeed occur. They observed the oxidative rearrangement of 2-hydroxy-3-β-phenylethyl- (**1**) and 2-hydroxy-3-γ-phenylpropyl-6-bromo-1,4-naphthoquinone (**2**) to, respectively, 3-hydroxy-2-benzyl- (**3**) and 3-hydroxy-2-β-phenylethyl-6-bromo-1,4-naphthoquinone (**4**). In addition, 2,6-dimethyl-3-hydroxy-1,4-naphthoquinone (**5**) rearranged to 2-hydroxy-6-methyl-1,4-naphthoquinone (**6**) in high yields.



(1) (3)

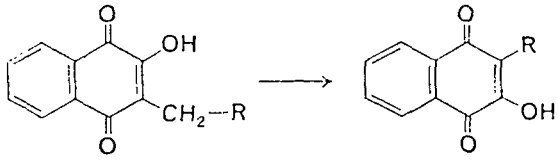
(2) (4)



(5) (6)

Fieser and Fieser later reported[4] that a large variety of 2-hydroxy-3-alkyl and alkenyl-1,4-naphthoquinones **7** react with hydrogen peroxide–sodium carbonate to give the ketol-keto acids **10**. Subsequent oxidation of these colourless acids by the action of copper sulphate and alkali converted them into the corresponding hydroxynoralkylnaphthoquinones **15** in high yields. In addition, Shemyakin and coworkers[5–7] have isolated the triketo acids (**12**, $n = 1$, R = H, and **12**, $n = 1$, R = C_6H_5) from the corresponding ketol-keto acids and have shown that they are converted to the hydroxyquinones **15** under Hooker oxidation conditions. The Russian workers also claimed that the intermediate **13** undergoes decarboxylation only in the presence of the oxidizing agents. On the basis of these results, the mechanism **7**–**15** has been proposed for the Hooker oxidation[4,5].

TABLE 1. Hooker oxidation of 2-hydroxy-3-alkyl or alkenyl-1,4-naphthoquinones



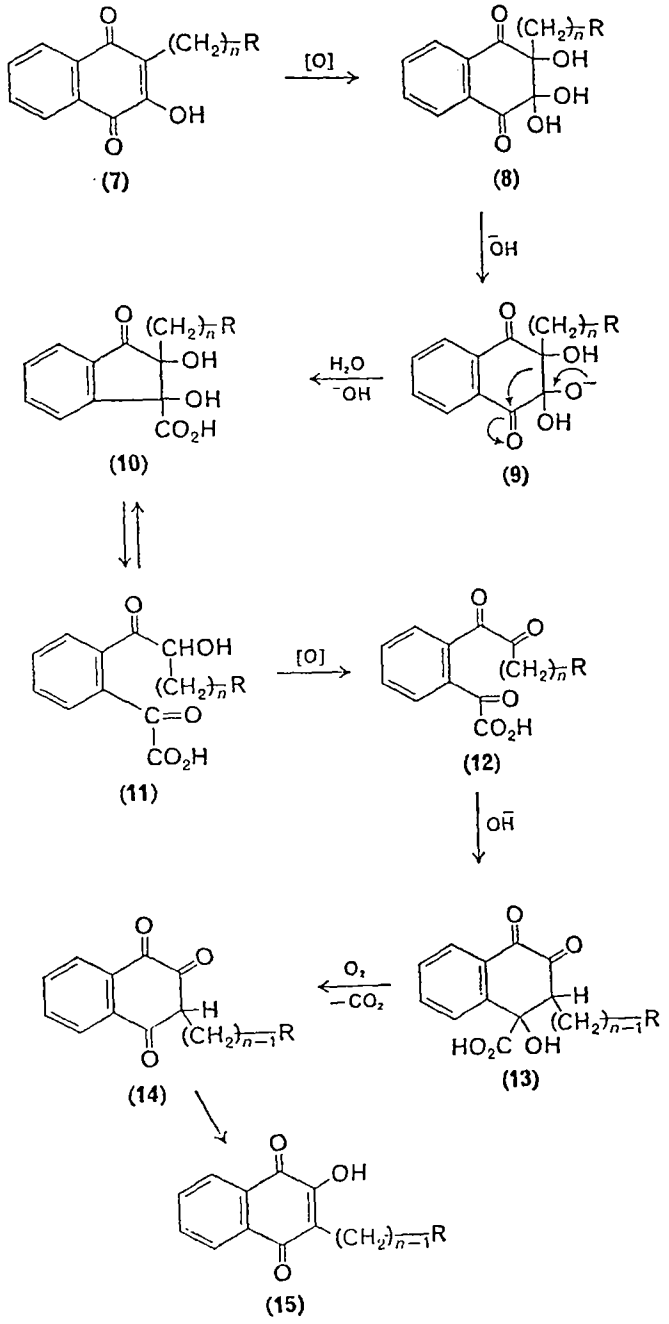
R	Oxidizing agent	Yield	Reference
$-CH{=}C(CH_3)_2$	$KMnO_4/\bar{O}H$	35	1
$-CHC(CH_3)_2OH$	$KMnO_4/\bar{O}H$	72	1
$-CH_2CH(CH_3)_2$	$KMnO_4/\bar{O}H$	67	1
$-(CH_2)_2C_6H_5$	$KMnO_4/\bar{O}H$	78	1
$-CH_2C_6H_5$	$KMnO_4/\bar{O}H$	78	1
$-C_6H_5$	$KMnO_4/\bar{O}H$	70	1
$-(CH_2)_5CH_3$	$KMnO_4/\bar{O}H$	85	1
$-(CH_2)_4CH_3$	$KMnO_4/\bar{O}H$	96	1
$-(CH_2)_3CH_3$	$KMnO_4/\bar{O}H$	91	1
$-(CH_2)_2CH_3$	$KMnO_4/\bar{O}H$	89	1
$-CH_2CH_3$	$KMnO_4/\bar{O}H$	88	1
$-CH_3$	$KMnO_4/\bar{O}H$	80	1

TABLE 1 (*cont.*)

R	Oxidizing agent	Yield	Reference
$-H$	$KMnO_4/\bar{O}H$	43	1
$-CH{=}CH_2$	$KMnO_4/\bar{O}H$	68	1
$-CH{=}CHCH_2$	$KMnO_4/\bar{O}H$	30	1
$-CH{=}CHCO_2H$	$KMnO_4/\bar{O}H$	—	1
$-CH{=}C(CH_2OH)(CH_3)$	$KMnO_4/\bar{O}H$	—	1
$-CH(CH_3)_2$	$H_2O_2-\bar{O}H/CuSO_4$	76	4
$-(CH_2)_7CH(CH_3)_2$	$H_2O_2-\bar{O}H/CuSO_4$	79	4
$-C_{16}H_{33}$-*n*	$H_2O_2-\bar{O}H/CuSO_4$	49	4
$-C_{14}H_{29}$-*n*	$H_2O_2-\bar{O}H/CuSO_4$	91	4
$-C_6H_{10}-C_6H_{11}$-*trans*	$H_2O_2-\bar{O}H/CuSO_4$	89	4
$-CH_2-$cyclopentyl	$H_2O_2-\bar{O}H/CuSO_4$	57	4
$-$Cyclopentyl	$H_2O_2-\bar{O}H/CuSO_4$	44	4
$-(CH_2)_2C_6H_{10}C_6H_{11}$-*cis*	$H_2O_2/CuSO_4$	67	4
$-(CH_2)_2$cyclohexyl	$H_2O_2-\bar{O}H/CuSO_4$	93	4
$-(CH_2)_3$cyclohexyl	$H_2O_2-\bar{O}H/CuSO_4$	86	4
$-(CH_2)_2C_6H_4OC_6H_5$-*p*	$H_2O_2-\bar{O}H/CuSO_4$	86	4
$-CH_2C_6H_4OC_6H_5$-*p*	$H_2O_2-\bar{O}H/CuSO_4$	91	4
$-(CH_2)_8C_6H_5$	$H_2O_2-\bar{O}H/CuSO_4$	72	4
$-(CH_2)_6C_6H_5$	$H_2O_2-\bar{O}H/CuSO_4$	51	4

An investigation of the Hooker oxidation of 2-hydroxy-3-alkyl or alkenyl-1,4-benzoquinones has not appeared. However, a number of very interesting reports on the oxidative rearrangements of hydroxybenzoquinones under other conditions have been described.

A unique example of the oxidative rearrangement of a hydroxybenzoquinone concerns the conversion of polyporic acid, 2,5-dihydroxy-3,6-diphenyl-1,4-benzoquinone (**16**) to pulvinic acid dilactone (**17**). Polyporic acid **16** occurs with pigments of the pulvic acid series, e.g. **17**, in certain lichens, and labelling experiments have shown the latter are derived from the quinone[8]. For example, pulvinic acid dilactone **17** and calycin **18** are found in *Pseudocyphellaria crocata* and both have been shown to incorporate labelled polyporic acid **16** efficiently[9]. Chemical analogy for this biosynthetic transformation has been provided by the oxidation of polyporic acid with lead tetraacetate[10] (28%) and dimethyl sulphoxide/acetic anhydride[11,12] (95%). An analogous transformation of atromentin **19** to the dilactone **20** by the action of hydrogen peroxide in acetic acid[13] or dimethyl sulphoxide/acetic anhydride[12] (55%) has also appeared.


(7)
(8)
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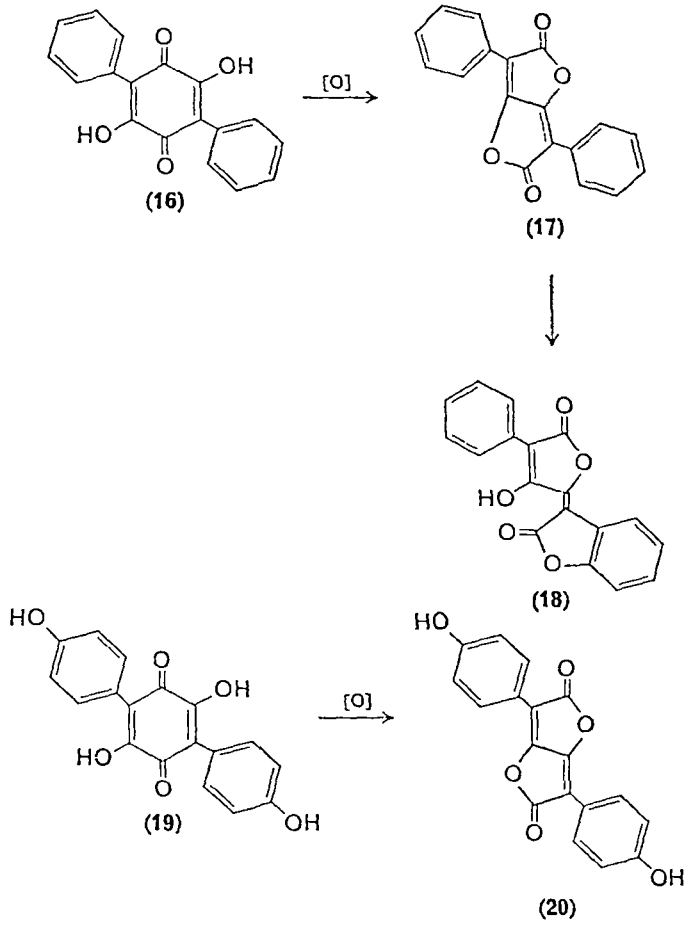
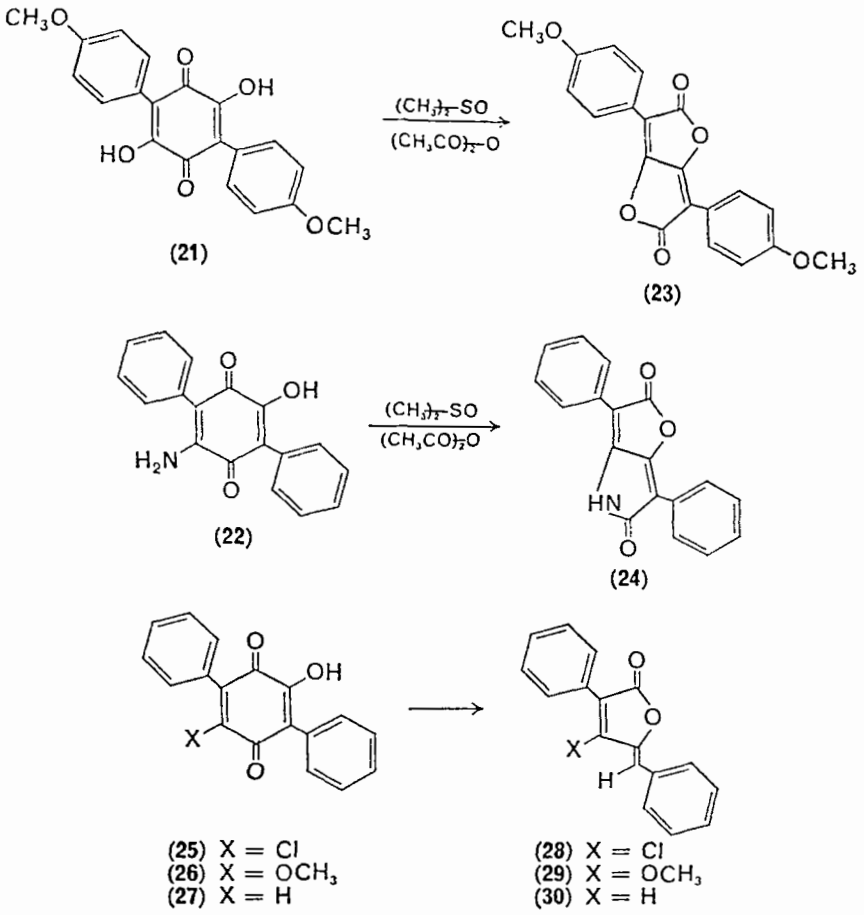
(14)
(15)
[O]
$\bar{O}H$
H_2O
$-\bar{O}H$
O_2
$-CO_2$
$(CH_2)_nR$
$(CH_2)_{n-1}R$
OH
CO_2H
HO_2C
CHOH
C=O



The scope of the above transformations induced by the action of dimethyl sulphoxide/acetic anhydride has been explored[12]. In addition to polyporic acid **16** and atromentin **19**, 2,5-*bis*-(*p*-methoxyphenyl)-3,6-dihydroxy-1,4-benzoquinone (**21**) and 2,5-diphenyl-3-hydroxy-6-amino-1,4-benzoquinone (**22**) are converted to the respective products **23** (90%) and **24** (30%) by the action of these oxidizing conditions.

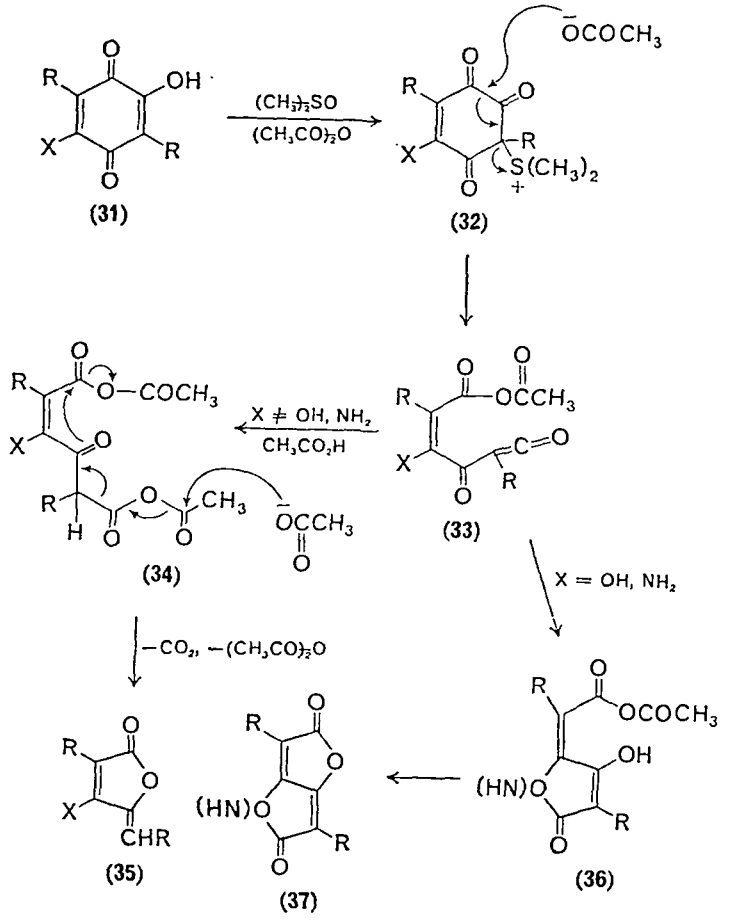
To gain some insight into the mechanism of this rearrangement three additional 2-hydroxy-3,6-diphenyl-1,4-benzoquinones (**25–27**) were subjected to the oxidative conditions. All of these quinones, which are substituted at the 5-position with a substituent other than a hydroxyl or an amino group, react with decarbonylation and rearrangement giving the γ-arylmethylene-$\Delta^{\alpha,\beta}$-butenolides (**28–30**) in 60–70% yield[11,12].



The mechanism for these oxidative rearrangements is envisaged as depicted below[12]. The key intermediate in these transformations is the ketene **33**. The dilactones **17**, **20** and **23** and the lactone-lactam **24** are viewed as arising from the ketene intermediate **33** by intramolecular addition of the protic substituent (OH or NH_2) originally at the quinone C-5 position to the ketene functionality followed by intramolecular alcoholysis of the anhydride linkage to form the bicyclic structures. For those quinones in which the protic C-5 substituent is missing, **25**, **26** and **27**, the ketene, **33**, can be converted to the β-ketoanhydride **34** by addition of acetic acid. Decarboxylation and subsequent ring closure initiated by acetate ion would then give the observed γ-arylmethylene-$\Delta^{\alpha,\beta}$-butenolides, (**28**–**30**).

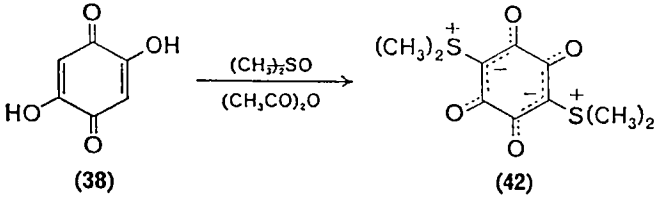
The proposed sulphonium salts **32** were not isolated. However, products consistent with their existence were formed in high yield when hydroxyquinones which are unsubstituted at the position adjacent to the hydroxyl

groups were subjected to the oxidation conditions. 2,5-Dihydroxy- (**38**), 2-hydroxy-5-phenyl- (**39**), 2-hydroxy-5-methyl-1,4-benzoquinone (**40**) and 2-hydroxy-1,4-naphthoquinone (**41**) all smoothly react with dimethyl

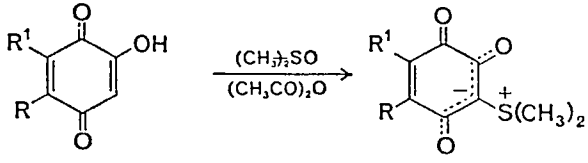


sulphoxide/acetic anhydride to give respectively the sulphonium ylids **42**, **43**, **44** and **45**. These products are visualized as arising from the sulphonium salt intermediate **32**, which loses the acidic ring proton to give the ylids. Recently, the naturally occurring dihydroxyquinone, bovinone, was converted to the corresponding dimethylsulphonium ylid in an analogous manner[14].

The mechanisms of the lead tetraacetate oxidation[10] of polyporic acid (**16**) and the hydrogen peroxide oxidation[13] of atromentin (**19**) may be analogous to that described above. This is illustrated below for the atromentin case.

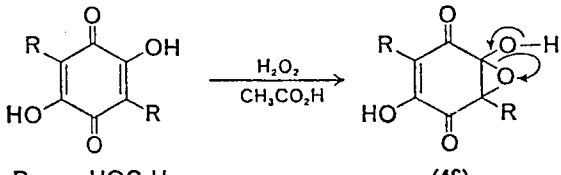


(38) (42)

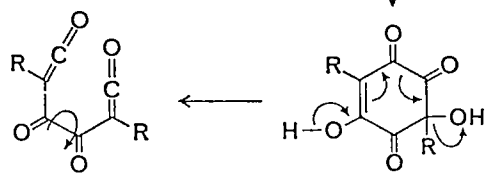


(39), (40), (41) (43), (44), (45)

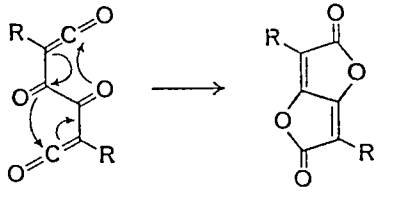
	R	R^1
(39), (43)	C_6H_5	H
(40), (44)	CH_3	H
(41), (45)		



R = *p*-HOC_6H_4 (19) (46)



(48) (47)

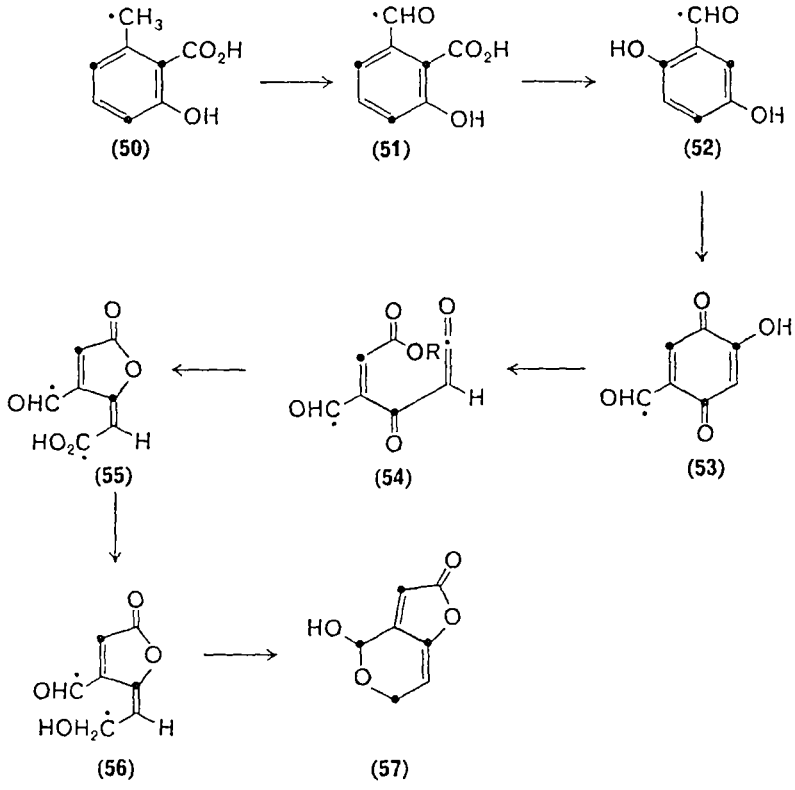


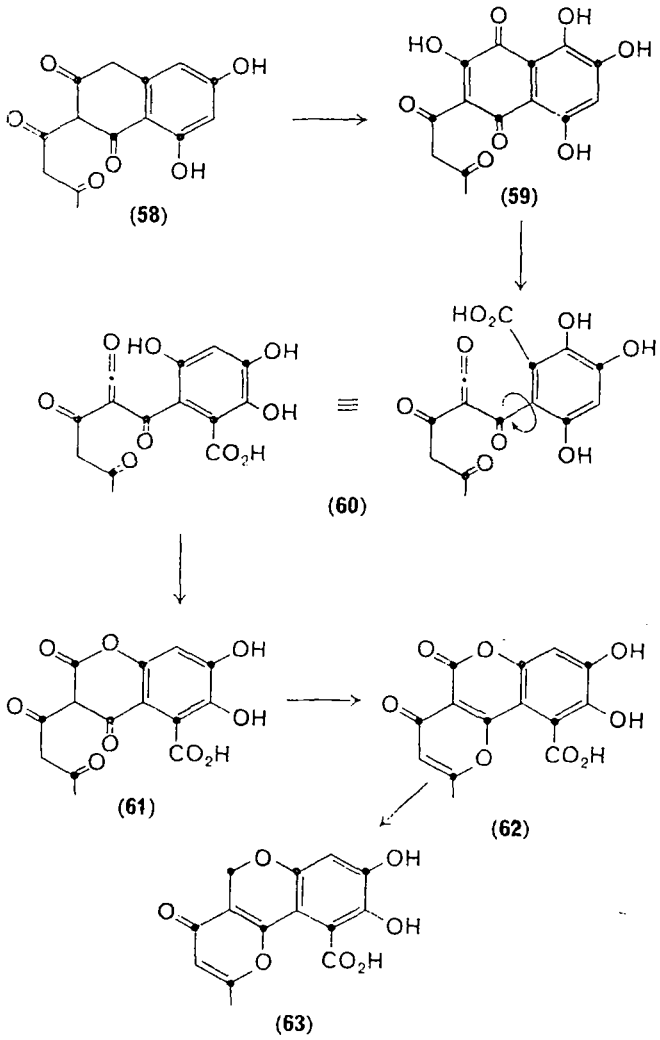
(49)

R = *p*-HOC_6H_4

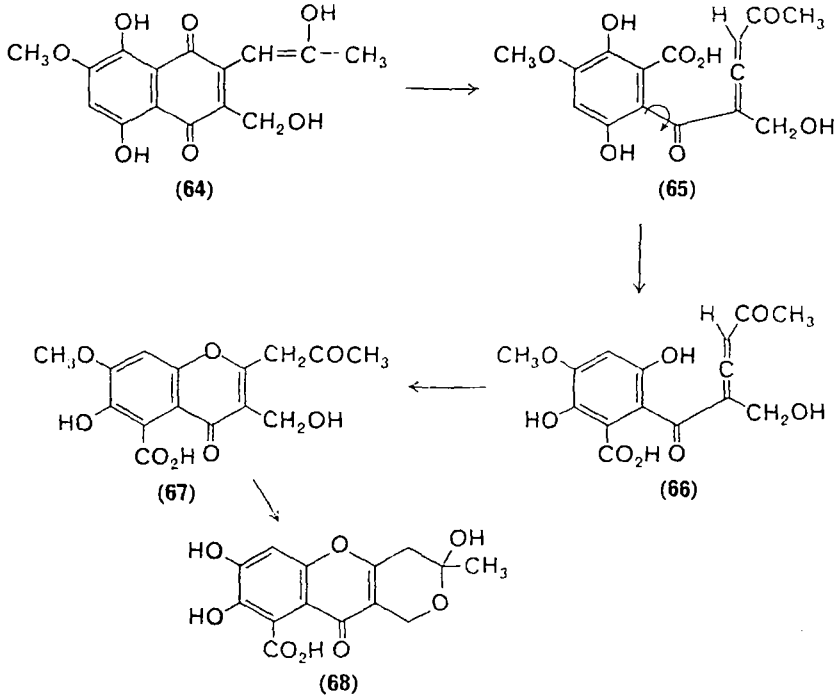
(20)

The above oxidative rearrangement of the hydroxy-diaryl-benzoquinones provides an efficient *in vitro* pathway to the pulvinic acid derivatives, a sequence possibly paralleling the biosynthetic scheme. The ubiquity of hydroxyquinones in nature[15] as well as phenolic compounds[16] which may be oxidized to hydroxyquinones suggests a number of possible biosynthetic schemes involving analogous oxidative cleavages of quinone nuclei. Tenuazonic acid[17], penicillic acid[18], patulin[19], citromycetin[20], aflatoxin[21], brevifolin and brevifolin carboxylic acid[22], to mention only a few, can all be viewed as arising from ketene intermediates which could be formed via oxidative cleavage of hydroxyquinone precursors. Biosynthetic studies for several of the above compounds have been reported[18-21] and their labelling pattern, starting from radioactive precursors, has been established. The oxidative cleavage of hydroxyquinone precursors can adequately explain these results. This proposal is illustrated below for the biosynthetic conversion of 6-methyl-salicyclic acid (**50**) to patulin **57** and the acetate-derived intermediate **58** to citromeycetin **63**.



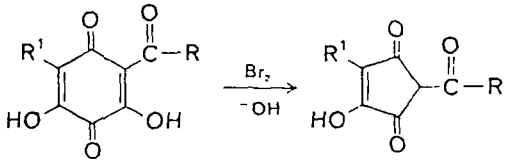


Extension of these concepts to vinylogous hydroxyquinones would lead to allene intermediates. An interesting speculative application of a possible allene biosynthetic intermediate in nature arises in the biosynthesis of fulvic acid (**68**) from the quinone, fusarubin (**64**). Fulvic acid, citromycetin and fusarubin are metabolites of similar mould species and their biosynthesis by various polyacetate cyclizations has been suggested[23]. The notion that fulvic acid arises from fusarubin via cleavage of the latter's quinone ring giving an allene intermediate **65** seems plausible.



(64) (65) (66) (67) (68)

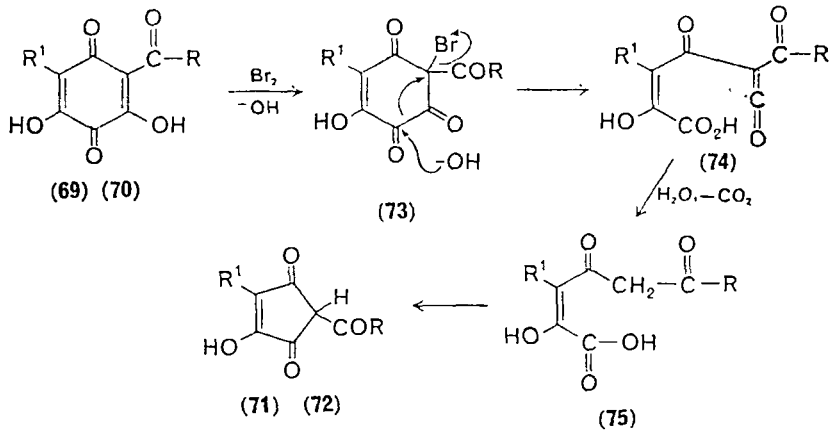
Sodium hypobromite (Br_2, $\bar{O}H$) has found limited use as a reagent for accomplishing the oxidative rearrangement of certain 2-acyl-3,5-dihydroxy-1,4-benzoquinones to 1,4-cyclopentenediones. Humuloquinone (**69**)[24,25] and cohumuloquinone[26] (**70**), constituents of hops, have been converted to isohumulinic acid (**71**) and isocohumulinic acid (**72**), respectively, by the action of bromine under alkaline conditions.



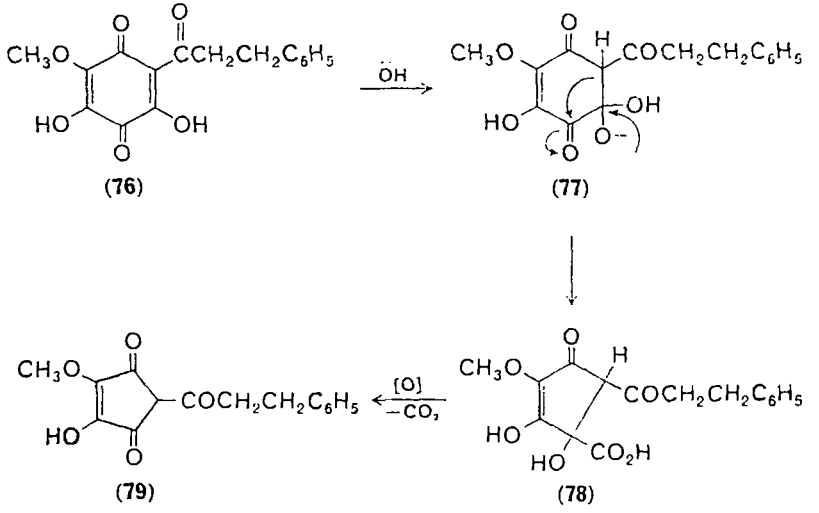
(69), (70) (71) (72)

(**69**), (**71**) R = $-CH_2CH(CH_3)_2$
R' = $-(CH_2)_2CH(CH_3)_2$
(**70**), (**72**) R = $-CH(CH_3)_2$
R' = $-(CH_2)_2CH(CH_3)_2$

The mechanism of this transformation has not been investigated. However, a possible mechanistic sequence which is analogous with the above discussion of the rearrangements of hydroxy-diarylbenzoquinones follows.

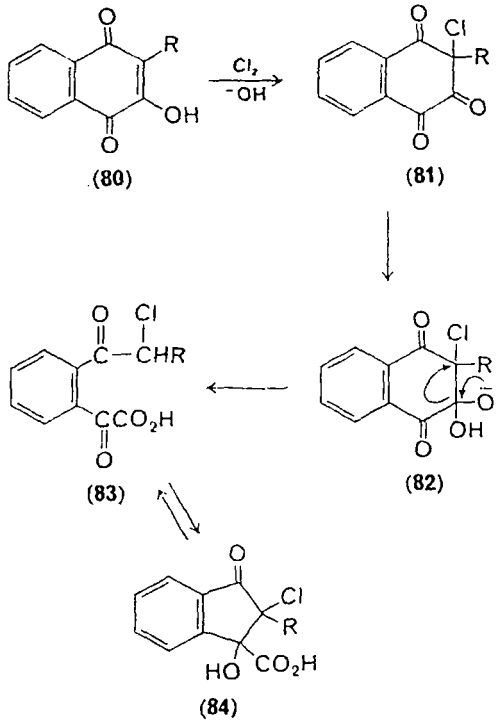


It is interesting that dimethyldihydrolinderone **79** was not detected in the reaction of the quinone **76** with alkaline bromine[27]. Instead, the degradation products, 3-phenylpropanoic acid and benzylacetone, were isolated. Such products can be envisaged as arising via base hydrolysis of the intermediate **75** ($R = -CH_2CH_2C_6H_5$, $R^1 = OCH_3$). The desired ring-contracted cyclopentenedione **79** was obtained in good yield when the quinone **76** was subjected to hydrolytic conditions (2N NaOH, $2\frac{1}{2}$ h). This transformation occurs either in the presence or absence of O_2 and, as a result, the authors proposed that the starting quinone functioned as an oxidant and the ring contraction itself was envisaged as a benzylic acid type rearrangement giving the intermediate **78** which suffered oxidative decarboxylation.



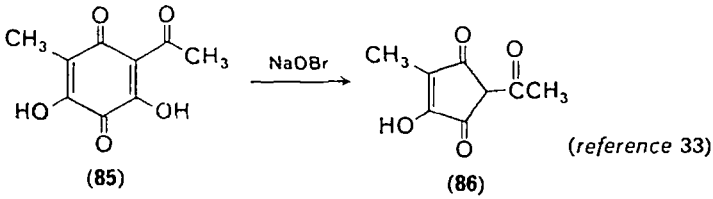
A number of other oxidative–hydrolytic rearrangements of certain quinones and quinone oxides in which the initial or intermediate compounds themselves act as oxidants have been studied[5]. In all of these cases, the reactions take an especially complicated course, usually resulting in a variety of products. For example, 2-chloro-3-hydroxy-1,4-naphthoquinone when refluxed with aqueous alkali undergoes a long sequence of oxidative–hydrolytic changes resulting finally in the formation of phthalide-3-carboxylic acid, phthalonic and phthalic acid[28, 29].

A synthetically useful reaction for the preparation of halogeno acids of type (**83** ⇄ **84**) from 2-alkyl or aryl-3-hydroxynaphthoquinones by the action of hypochlorous acid has been reported[4, 30–32], and evidence for the following mechanistic scheme was presented.

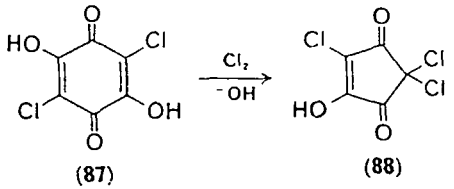


Other selected examples of oxidative ring contractions of quinones induced by the action of halogens under hydrolytic conditions follow[33–36].

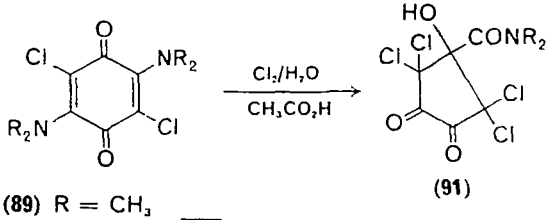
6-Hydroxy-6-alkoxy-1,3-diphenyl-4-aryl-3-cyclohexene-2,5-diones (**92**) undergo ring contraction to 1-alkoxycarbonyl-2,4-diphenyl-5-aryl-1,4-cyclopentadiene-3-ones (**95**) when heated in acetic anhydride[37]. The cyclohexene-2,5-diones (**92**) are in turn prepared by the addition of



(85) (86) (*reference* 33)



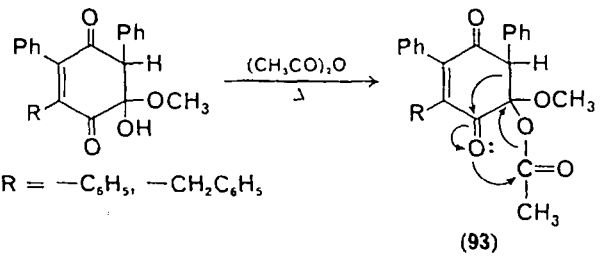
(87) (88) (*references* 34, 35)



(89) R = CH_3

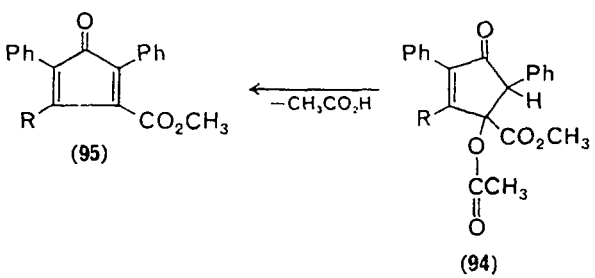
(90) NR_2 = 

(91) (*reference* 36)



(92) R = $-C_6H_5$, $-CH_2C_6H_5$

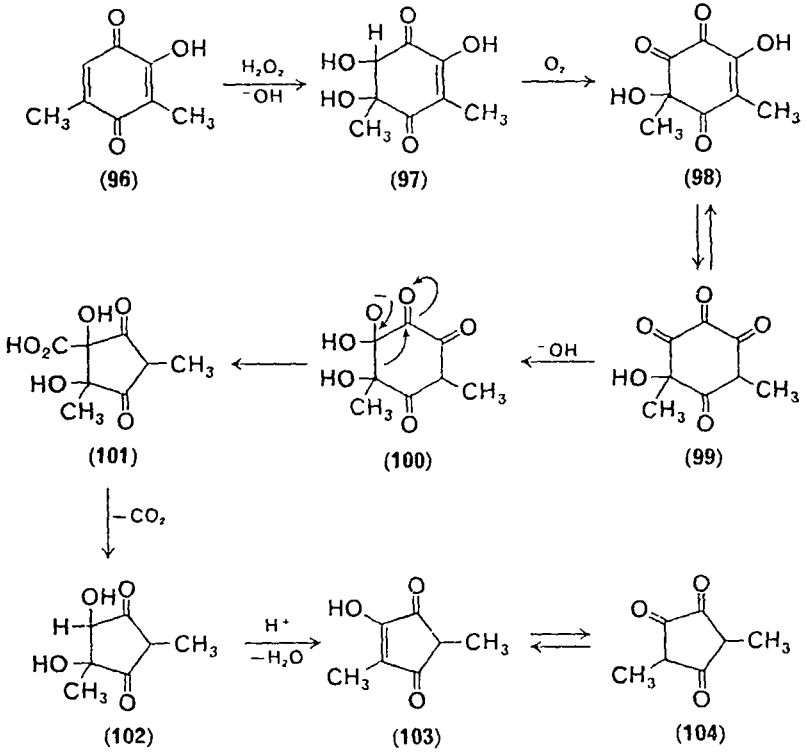
(93)



(94) (95)

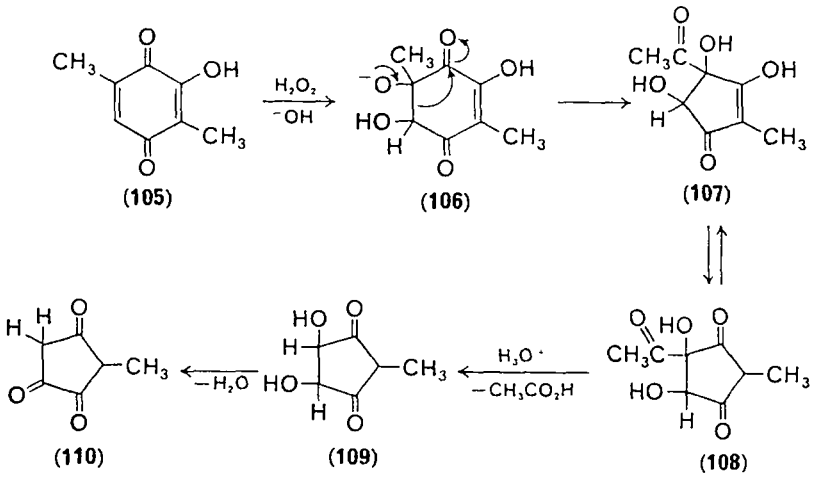
methanolic Br_2 to the corresponding quinones followed by reductive debromination.

The oxidative rearrangements of simple alkyl-substituted hydroxyquinones by the action of alkaline H_2O_2 has been extensively studied by Corbett[38-41]. 2-Hydroxy-3,5-dimethyl-1,4-benzoquinone (**96**) was shown to react with alkaline H_2O_2 in the presence of O_2 to give 2,4-dimethyl-4,5-dihydroxy-1,3-cyclopentanedione (**102**) which was isolated as the trione **104** after acid-catalysed dehydration. The oxidation was shown to consume oxygen and CO_2 was detected as a product. The following mechanism, which was based upon extensive spectroscopic and kinetic studies, was suggested.

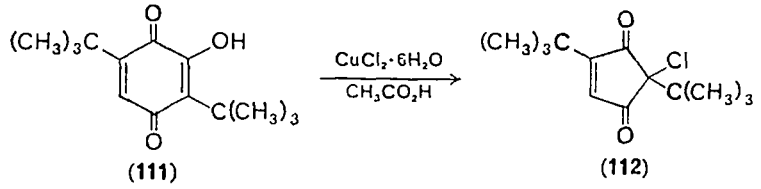


When the 6-position is substituted with a methyl substituent, the reaction takes a slightly different course. No O_2 is consumed and the product is the acylated cyclopentanedione. For example, 2-hydroxy-3,6-dimethyl-1,4-benzoquinone (**105**) rearranges to **108** by the action of alkaline H_2O_2. The product arises via a benzylic acid rearrangement of the intermediate glycol **106**. The cyclopentanedione **108** was not isolated in pure form, but was detected spectroscopically. However, deacylation

and dehydration of **108** by the action of HCl gave the trione **110** in 70% isolated yield. Analogous transformations were reported for 2-hydroxy-6-methyl-, 2-hydroxy-5,6-dimethyl- and 2-hydroxy-3,5,6-trimethyl-1,4-benzoquinone.



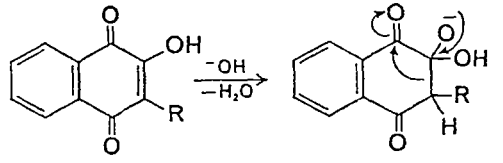
Finally, mention should be made of the recently observed rearrangement of 2-hydroxy-3,6-di-*t*-butyl-1,4-benzoquinone (**111**) to 2-chloro-3,4-di-*t*-butyl-1,3-cyclopentenedione (**112**) by the action of $CuCl_2 \cdot 6H_2O$ in hot glacial acetic acid[42]. The scope of this interesting ring contraction has not yet been explored. However, 2-hydroxy-3-methyl-1,4-naphthoquinone and 2-hydroxy-5-chloro-3,6-diphenyl-1,4-benzoquinone appear to undergo analogous transformations[43].



B. Base-induced Rearrangements of Hydroxyquinones

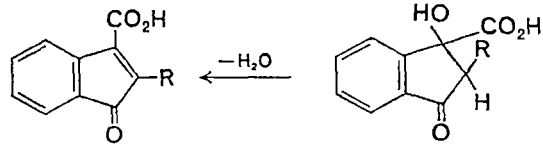
A rearrangement of hindered 2-hydroxy-3-alkyl-1,4-naphthoquinones to 2-alkylindenone-3-carboxylic acids induced by dilute aqueous alkali has been reported[44–48]. 2-Hydroxy-3-cyclohexyl- (**113**) and 2-hydroxy-3-*t*-butyl-1,4-naphthoquinone (**114**) rearrange in high yields to respectively **117** and **118** when heated with 5% aqueous alkali in the absence of oxygen. The mechanism is regarded as a benzylic acid rearrangement of the

hydrated hydroxyquinone **115** to the intermediate 3-hydroxyindanone-3-carboxylic acid (**116**) which then suffers a base-catalysed dehydration. The colourless intermediate **116** was isolated when the reaction was conducted in a buffer of pH 9·2.



(**113**) R = C_6H_{11}
(**114**) R = $C(CH_3)_3$

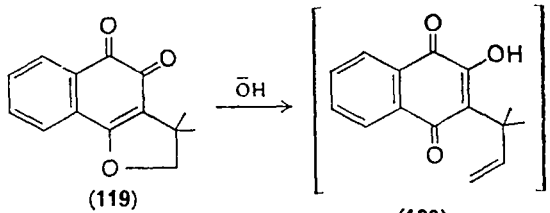
(**115**)



(**117**) R = $-C_6H_{11}$
(**118**) R = $-C(CH_3)_3$

(**116**)

The base-catalysed rearrangement of dunnione **119** to allodunnione **122** can be considered as involving an analogous transformation[49,50].



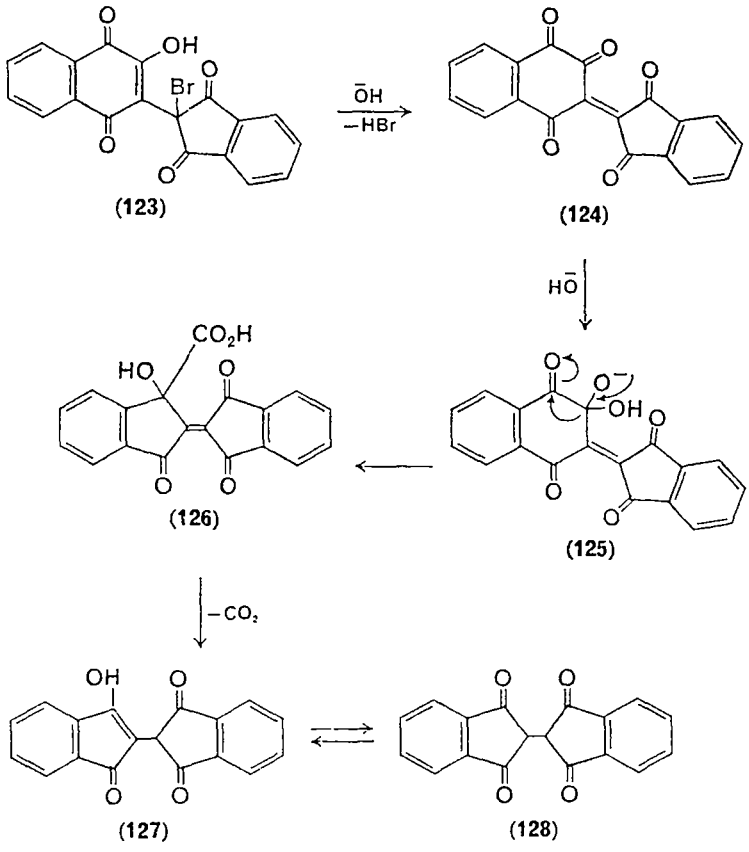
(**119**)

(**120**)

(**122**)

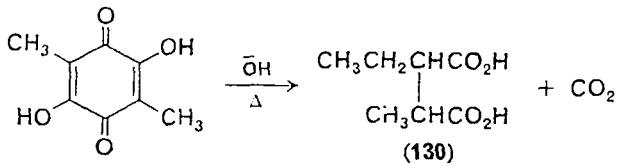
(**121**)

Still another example of such a rearrangement is the observed conversion of the hydroxynaphthoquinone **123** to bindone **128** by the action of ethanolic KOH[51].



(123) (124) (125) (126) (127) (128)

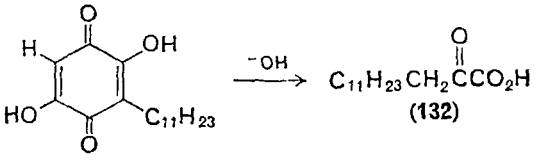
The rearrangements of hydroxy-1,4-benzoquinones induced by the action of alkali appear to be much more complex. 2,5-Dialkyl-3,6-dihydroxybenzoquinones when heated with alkali give succinic acids and carbon dioxide, e.g. α-ethyl-β-methyl-succinic acid (**130**) was obtained from 2,5-dihydroxy-3,6-dimethyl-1,4-benzoquinone (**129**)[52].



(129) (130)

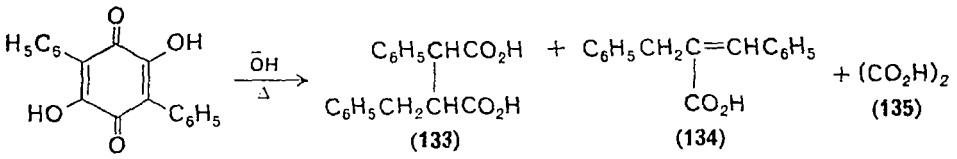
In contrast to the above, ambelin[53] (**131**) and its homolgoue rapanone[54] have been reported to yield the corresponding α-keto-acids, e.g. **132** from ambelin.

Still a third pathway has been reported for polyporic acid **16** which gives a mixture of α-benzyl-β-phenylsuccinic acid (**133**) *cis*- and *trans*-α-benzylcinnamic acid (**134**) and oxalic acid **135** upon base hydrolysis[55].

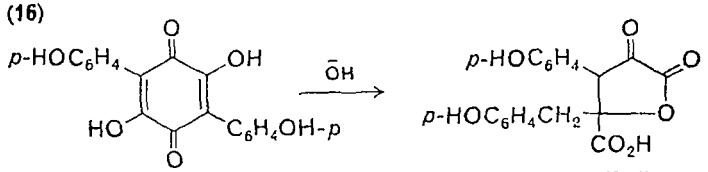


(131) **(132)**

Under similar conditions, atromentin **19** gives the lactone **136** which has been shown to give the corresponding cinnamic acid on boiling in 50% alkali[55].



(16) **(133)** **(134)** **(135)**

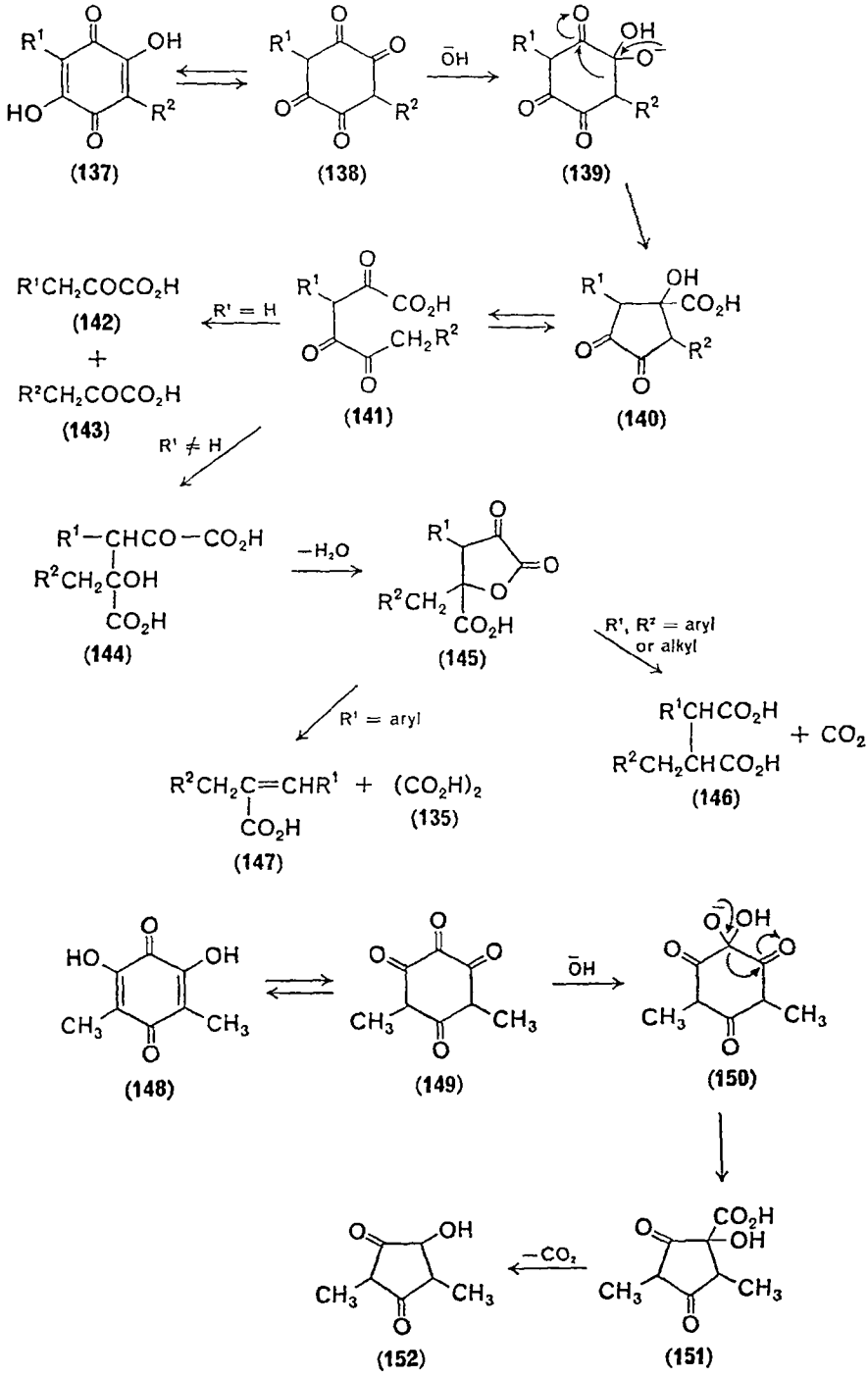


(19) **(136)**

Corbett and Fooks[56] have recently reported a detailed study of the reactions of 2,5-dihydroxy-1,4-benzoquinones with alkali and have suggested the reaction scheme (**137–147**) which explains all the available data.

In a manner analogous to the above, 2,6-dihydroxy-1,4-benzoquinones have also been shown to undergo a base-induced benzylic acid rearrangement followed by decarboxylation of the resulting hydroxydioxocyclopentanecarboxylic acid to give 4-hydroxycyclopentane-1,3-diones[57]. This transformation is illustrated below for 2,6-dihydroxy-3,5-dimethyl-1,4-benzoquinone (**148**) which gives **152** in >90% yield.

The formation of hydroxycyclopentane-1,3-diones by the alkaline degradation of 2,6-dihydroxy-1,4-benzoquinones is analogous to the conversion of humuloquinone **69** into dihydrohumulic acid[24] and to the


(137)
(138)
(139)
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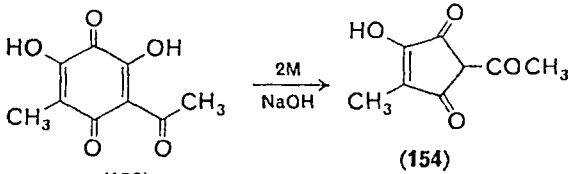
(141)
(140)
(144)
(145)
(146)
(147)
(135)
(148)
(149)
(150)
(151)
(152)

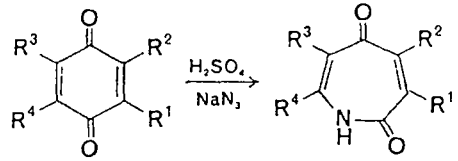
conversion of 3-acetyl-2,6-dihydroxy-5-methyl-1,4-benzoquinone (**153**) to the cyclopentenedione **154** by the action of 2M-alkali[58].



(153) (154)

III. REARRANGEMENTS OF QUINONES UPON REACTION WITH HYDRAZOIC ACID AND ORGANIC AZIDES

A variety of alkyl- and aryl-substituted 1,4-benzo- and 1,4-naphthoquinones undergo ring expansion to 2,5-*H*-2,5-azepinediones (**156**) (60–80%) induced by the action of NaN_3 in cold (0–5°) conc. H_2SO_4[59-62]. Under these conditions (Schmidt reaction), the reaction takes place at the least hindered carbonyl and the NH group has inserted in such a manner that it is attached to the more substituted carbon atom. Such a product would be expected for a typical Schmidt reaction involving one of the carbonyl groups of the quinone[63].

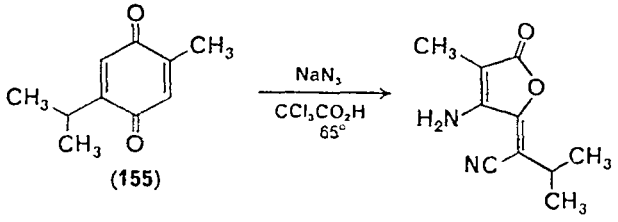


(155) (156)

R^1	R^2	R^3	R^4
H	CH_3	CH_3	CH_3
H	$CH(CH_3)_2$	H	CH_3
H	CH_3		
H	CH_3	H	CH_3
CH_3	CH_3	CH_3	CH_3

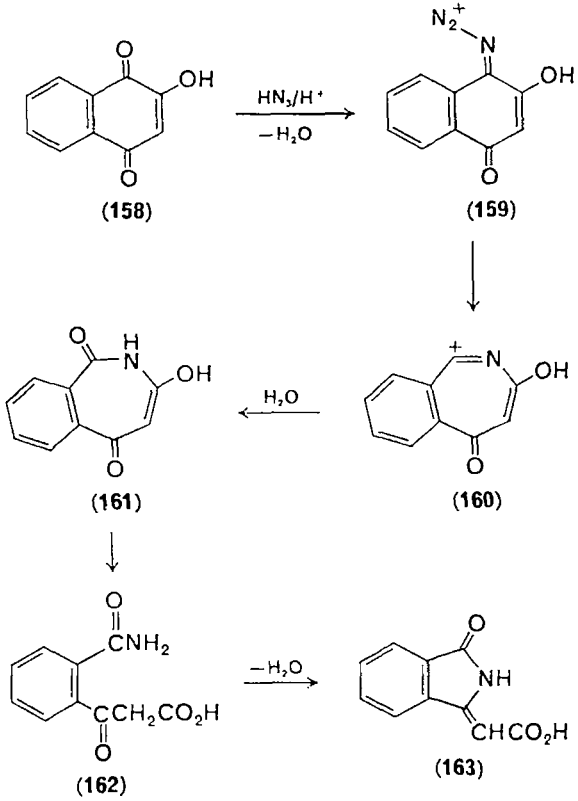
The reaction conditions employed to obtain the azepinediones (NaN_3, H_2SO_4, 0–5°) appear to be very critical since several of the above quinones **155** have been previously subjected to the Schmidt reaction using other solvents and acids and quite different products were reported. For example, 2-methyl-1,4-naphthoquinone is reported to be unreactive at 40° in acetic acid with sodium azide. However, under the same conditions 1,4-naphthoquinone gives an 87% yield of 2-amino-1,4-naphthoquinone[64]. More surprising is the fact that thymoquinone **155** reacts with sodium azide in trichloroacetic acid at 65° to give the ring-contracted butenolide **157**[65,66]. The mechanism of this reaction has been investigated[67] and shown to be

an example of an acid-catalysed rearrangement of an azidoquinone intermediate which will be discussed later.



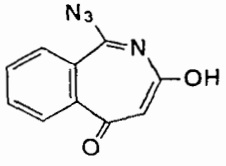
(155) (157)

2-Hydroxy-1,4-naphthoquinone (**158**) reacts with sodium azide in cold concentrated sulphuric acid to give ultimately 3-oxo-$\Delta^{1\alpha}$-isoindolineacetic acid (**163**) in good yield[68]. This transformation can be envisaged as an initial ring expansion to give **161** which subsequently undergoes hydrolytic rearrangement to **163**. Consistent with this reaction sequence was the fact that the cation **160** could be trapped with excess azide ion to give **164** which could also be converted to **163** in nearly quantitative yield by the



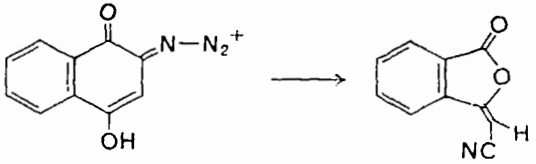
(158) (159) (161) (160) (162) (163)

action of concentrated H_2SO_4 followed by addition of water. In addition, the acid **162** was shown to give **163** by the action of cold concentrated H_2SO_4.



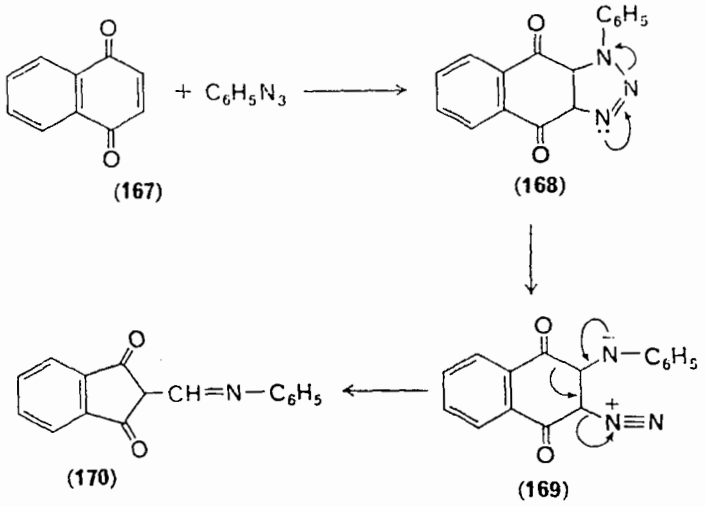
(164)

Another mechanism for this transformation can be considered which involves the intermediate iminodiazonium ion **165**. However, as will be shown later, intermediates of this type rearrange to γ-cyanoalkylidene-$\Delta^{\alpha\beta}$-butenolides, i.e. **166**.

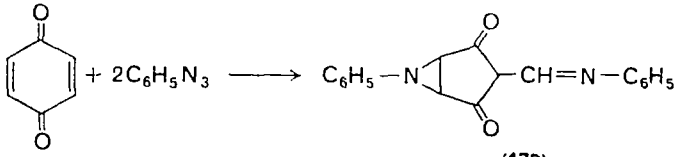


(165) (166)

Very little work has appeared on the reactions of quinones with organic azides. Wolff[69,70] has observed the ring contractions of 1,4-naphthoquinone (**167**) and 1,4-benzoquinone (**171**) to respectively **170** and **172** induced by the action of phenyl azide. Such transformations probably involve the pyrolytic rearrangement of the intermediate triazoles, e.g. **168**.



(167) (168) (169) (170)



(171) (172)

IV. REARRANGEMENTS OF AZIDOQUINONES

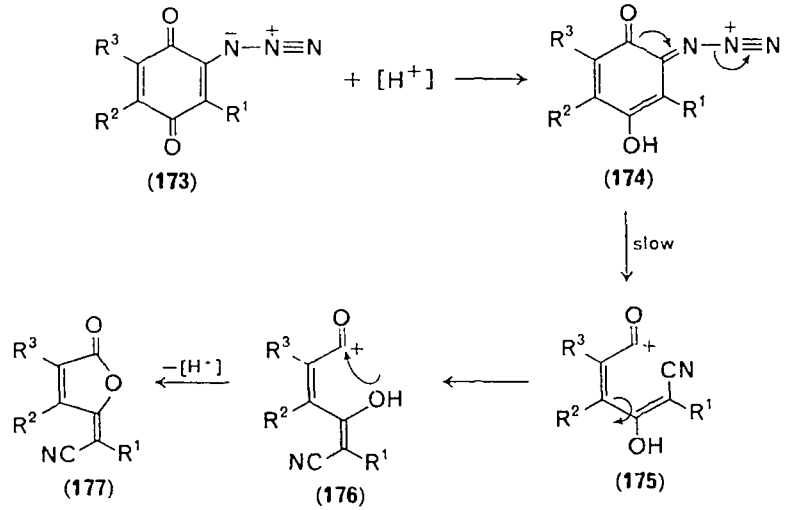
Until recently, very little had appeared in the literature concerning the chemistry of azidoquinones. This is somewhat surprising in view of their ease of formation, relative stability and the fact that they are structurally related to vinyl and acyl azides, both of which have been extensively studied[71–74]. These compounds undergo a remarkable variety of rearrangement and fragmentation reactions and thus function as synthetic intermediates to γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides[75–77], azapinediones[78], 2-cyano-1,3-cyclopentenediones[79], cyanoketenes[80,81], acyl cyanides[82], aminoquinones[67], cyanoazaquinones[83] and 1,4-diacetoxy-1,4-dicyano-1,3-butadienes[83].

A. Acid-catalysed Rearrangement of Azidoquinones

The decomposition of azido-1,4-quinones (**173**) in cold concentrated sulphuric acid results in a stereospecific rearrangement to γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides (**177**) (44–95%)[75–77,84,85]. The intermediate iminodiazonium ions **174** ($R^1 = CH_3$, $R^2,R^3 =$  ; $R^1 = H$, $R^2 = CH_3$; $R^1 = -H$, $R^2 = -C(CH_3)_3$) were detected spectroscopically and shown to follow first-order kinetics in their decomposition. The mechanism (**173–177**) is in strict accord with the experimental data.

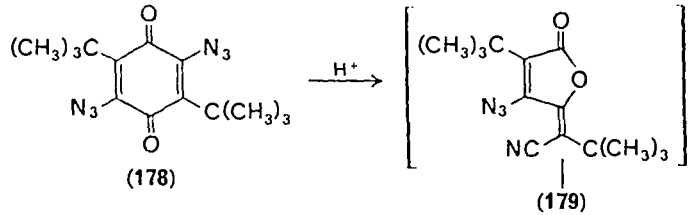
The above rearrangement appears to be quite general and has worked for all azidoquinones thus far investigated. The only modification in the structure of the products was observed when 2,5-diazido-3,6-di-*t*-butyl-1,4-benzoquinone (**178**) was subjected to the reaction[86]. In this case, the tetrazole **180** was isolated in high yield and is viewed as arising from the butenolide **179** via cycloaddition of the azide to the cyano moiety. When the tetrazole is refluxed for a short time in aqueous ethanol it is quantitatively converted to the interesting lactone-lactam **181**.

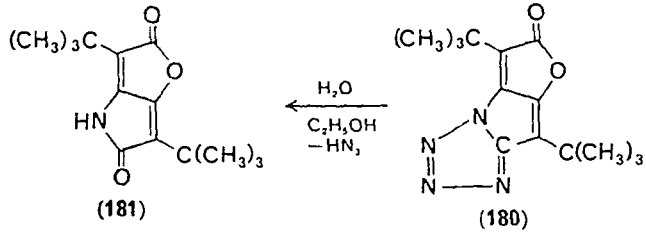
Earlier it was mentioned that thymoquinone **155** reacts with excess sodium azide in trichloroacetic acid at 65° to give the butenolide **157**[65,66]. This transformation can now be explained by the sequence of reactions (**155–157**) which has been established experimentally[67].

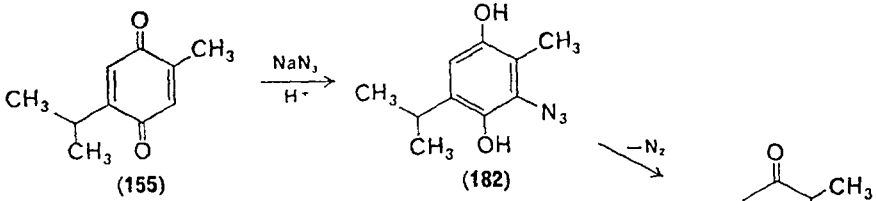


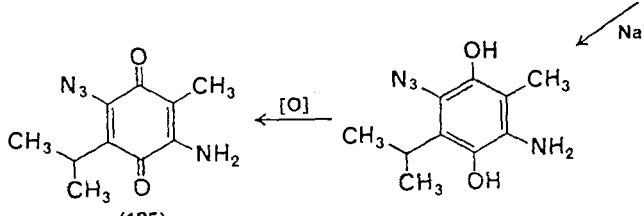
	R^1	R^2	R^3	Yield
a	H	$C(CH_3)_3$	H	95
b	H	C_6H_5	H	80
c	H	CH_3	H	65
d	CH_3	H	CH_3	70
e	CH_3	H	$CH(CH_3)_2$	87
f	H			59
g	CH_3			95
h	C_6H_5	H	C_6H_5	30
i	C_6H_5	OH	C_6H_5	65
j	CH_3	NH_2	$CH(CH_3)_2$	94
k	$CH(CH_3)_2$	NH_2	CH_3	95
l	H	NH_2	H	44
m	CH_3	N_3	CH_3	77
n	H	N_3	H	73
o	$CH(CH_3)_2$	N_3	$CH(CH_3)_2$	87
p	Br	$C(CH_3)_3$	H	86
q	$C(CH_3)_3$	H	$C(CH_3)_3$	87

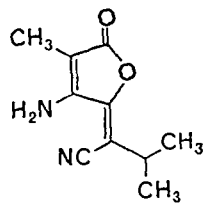
Only one example of an acid-catalysed rearrangement of an azido-1,2-quinone has been reported, and here ring expansion to an azepinedione is observed rather than ring contraction[78]. Specifically, 4-azido-1,2-naphthoquinone (**186**) rearranges in 82% yield to 2,5-*H*-4-hydroxybenzo-azepinene-2,5-dione (**189**) by the action of cold concentrated H_2SO_4.

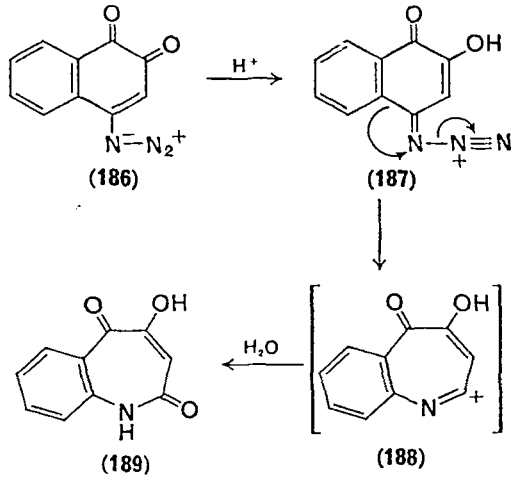

(178)
H+
(179)


H2O
C2H5OH
−HN3
(181)
(180)


NaN3
H+
(155)
(182)
−N2
(183)


NaN3/H+
[O]
(185)


H+
(157)

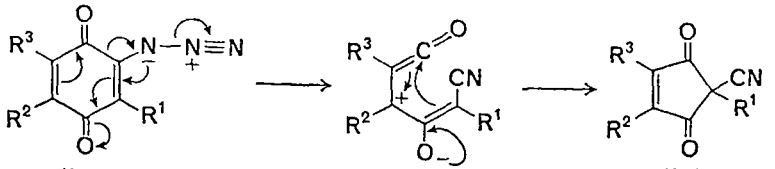


B. Thermal Rearrangement of Azidoquinones

The thermal decomposition of azido-1,4-quinones has also been investigated[79–82]. Here, ring contraction to the 2-cyano-1,3-cyclopentenediones (**192**) is observed rather than to the butenolides **177**. Like the acid-catalysed rearrangements, this reaction also appears to be very general and the diones **192** are formed in good to excellent yield (31–96%). The general structures **190** and **192** illustrate the overall chemical transformation as indicated by the following mechanistic scheme.

The intermediacy of the zwitterionic species **191** is only tentatively proposed. One can envisage this reaction as proceeding via a nitrene, an azirene or by a concerted process. However, the decomposition of 2-azido-3,6-di-*t*-butyl-1,4-benzoquinone (**190f**) does show a solvent-dependent product ratio which is consistent with the zwitterion intermediate. Decomposition of the quinone in refluxing benzene gives the cyclopentenedione **192f** and the butenolide **177g** in a ratio of 19 : 1. When the decomposition is carried out in refluxing methanol the ratio of **192f** to **177g** changes to 7 : 13[86]. Since the products are not interconverted under the reaction conditions, this change in observed product ratio may be a reflexion of stabilization by methanol solvation of the intermediate zwitterion.

The complexity of this mechanistic problem is further illustrated by the isolation and identification of two additional products in the decomposition of 2-azido-3,6-diphenyl-1,4-benzoquinone (**190g**). In addition to the major product **192g**, the butenolide **177h** and the quinone **193** were obtained. Again compounds **192g** and **177h** are not interconverted under the reaction conditions and, as a result, they could

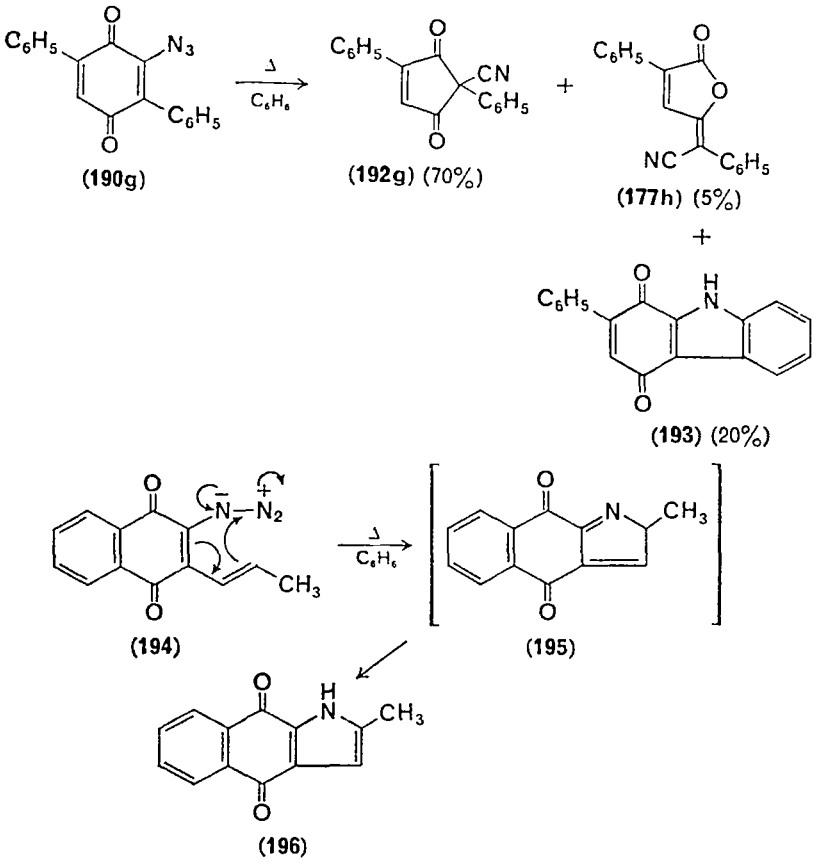


(190) (191) (192)

	R^1	R^2	R^3	Yield
a	CH_3			95
b	OCH_3			70
c	Cl			35
d	CH_3	H	CH_3	92
e	$CH(CH_3)_2$	$CH(CH_3)_2$	Cl	31
f	$C(CH_3)_3$	H	$C(CH_3)_3$	97
g	C_6H_5	H	C_6H_5	70
h	CH_3	NH_2	CH_3	96
i	CH_3	NH_2	$CH(CH_3)_2$	89
j	$CH(CH_3)_2$	NH_2	CH_3	92
k	NC_7H_{10}	H	$C(CH_3)_3$	78
l	Br	H	$C(CH_3)_3$	75
m	$C(CH_3)_3$	CH_3	H	82

reasonably come from **191** by respectively C- or *O*-acylation while **193** appears to result from a nitrene insertion or a concerted process. A concerted process for the formation of **193** seems more reasonable since no insertion products were observed for those quinones having an isopropyl or *t*-butyl substituent adjacent to the azide group, both of which could give 5-membered ring formation by nitrene insertion into an sp^3 C—H bond. In addition, when 2-azido-3-propenyl-1,4-naphthoquinone (**194**) was decomposed in refluxing benzene the indolequinone **196** was formed in 90% yield[87]. As a result, a substituent in the 3-position having an alkene double bond in direct conjugation with the azide group appears to favour heterocyclic ring formation rather than ring contraction.

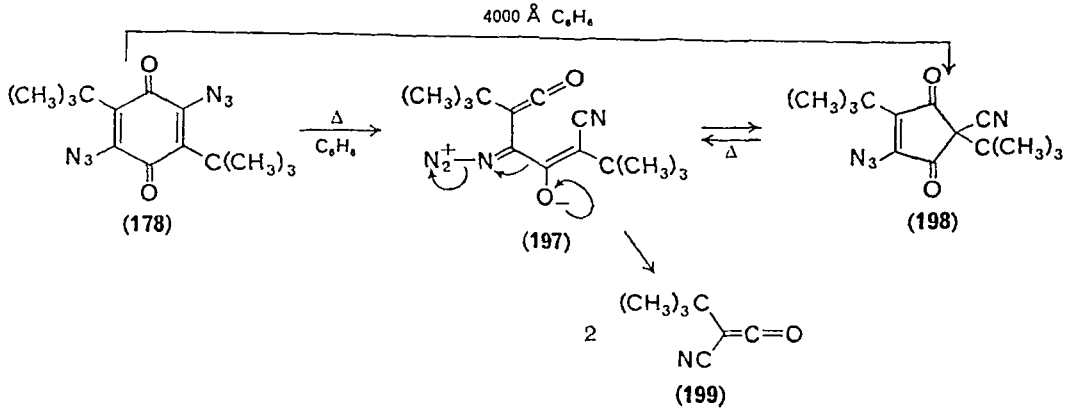
On the basis of the mechanism presented above one would predict that 2,5-diazido-1,4-benzoquinones would pyrolytically generate the ring-opened intermediate **191** ($R^2 = N_3$) which could partition itself between electrocyclic ring closure to the corresponding 2-cyano-4-azido-1,3-cyclopentenedione and cleavage to two molecules of a cyanoketene. In fact, when 2,5-diazido-3,6-di-*t*-butyl-1,4-benzoquinone (**178**) was decomposed in refluxing benzene *t*-butylcyanoketene (**199**) was formed in



>95% yield[80]. When the reaction was closely monitored 2,4-di-*t*-butyl-2-cyano-4-azido-1,3-cyclopentenedione (**198**) was detected. Photolysis of the quinone **178** in benzene (4000 Å) gave the cyclopentenedione **198** in 75% yield. No ketene products were detected. However, **198** quantitatively was converted to *t*-butylcyanoketene in refluxing benzene. The scope of this cleavage reaction has not yet been extensively explored. However, it has been shown that *t*-pentyl-, phenyl-, isopropyl- and methylcyanoketene can be generated in an analogous way. The *t*-pentyl homologue, like *t*-butylcyanoketene, is stable in solution; the others are not and were isolated as the methyl esters (65–82%) obtained by trapping the ketenes with methanol.

The thermal decomposition of 2,6-diazido-3,5-di-isopropyl-1,4-benzoquinone (**200**) in methanolic chlorobenzene provides a particularly interesting example with reference to the mechanism of the fragmentation reaction presented above. The only product observed from this reaction

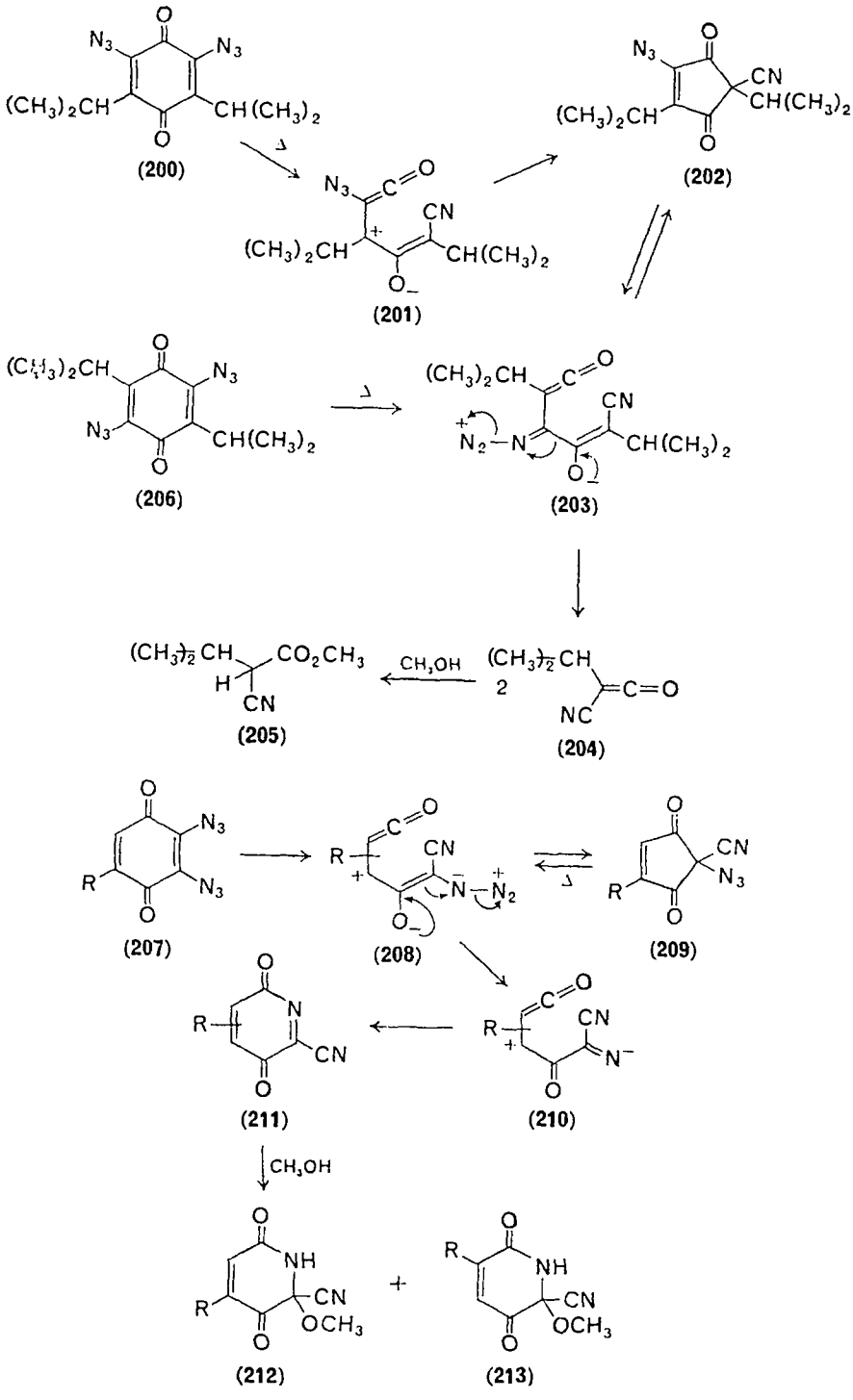
was the ester **205** (75%)[88]. The same ester was formed in 82% yield when 2,5-diazido-3,6-di-isopropyl-1,4-benzoquinone (**206**) was thermally decomposed under similar reaction conditions. Thus, both quinones give isopropylcyanoketene **204**. An analogous result was obtained when



2,6-diazido-3,5-dimethyl and 2,5-diazido-3,6-dimethyl-1,4-benzoquinone were decomposed in refluxing methanolic chlorobenzene. These results may be explained with reference to the mechanism presented above for the formation of *t*-butylcyanoketene **199**. That is, in order for the ketene **204** to be generated from the quinone **200**, the following mechanistic change should take place, **200** → **201** → **202** → **203** → **204**. A much more direct pathway is available starting with the 2,5-isomer, i.e. **206** → **203** → **204**.

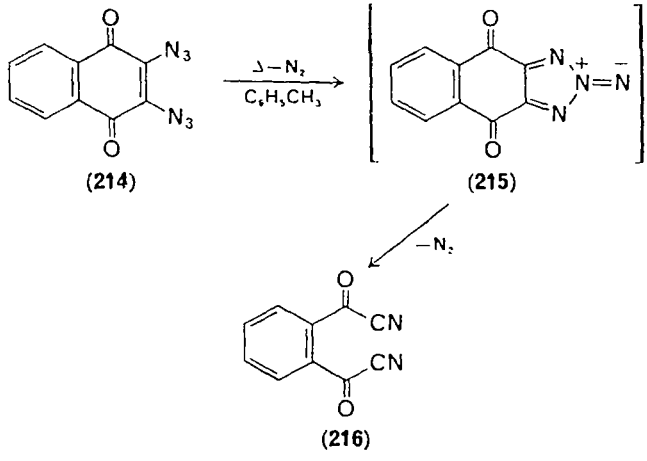
Again, based upon a ring-opened intermediate such as **208** one would predict that 2,3-diazidoquinones could partition themselves between ring contraction to 2-azido-2-cyano-1,3-cyclopentenediones and nitrogen loss to the intermediate **210** which upon subsequent bond formation would give 2-aza-3-cyano-1,4-quinones. To test this possibility, 2,3-diazido-5-*t*-butyl- (**207a**) and 2,3-diazido-5-phenyl-1,4-benzoquinone (**207b**) were decomposed in refluxing toluene (110°)[89]. Under these conditions, the major products are the corresponding ring-contracted diones, respectively **209a** and **209b**. When the quinone **207a** or the dione **209b** were decomposed in refluxing chlorobenzene (132°) the isomeric mixture of the azaquinones **211** was formed; these were isolated as the methanol adducts **212** and **213** in 50% yield as a 1 : 1 mixture.

It is interesting to point out that 2,3-diazido-1,4-naphthoquinone (**214**) has been reported to cleave to phthaloyl cyanide **216** after 10 minutes in refluxing toluene[82]. The 2,3-diazido-1,4-benzoquinones reported above require about one hour in refluxing toluene and give the cyclopentene-



(a), R = $-C(CH_3)_3$
(b), R = C_6H_5

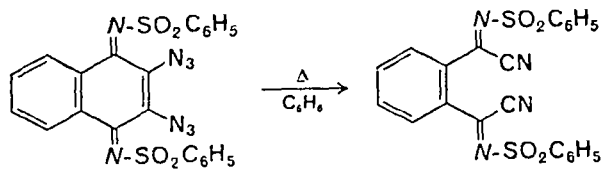
diones **209a, b**. There is a minor product formed in these reactions which may be the corresponding diacyl cyanide. However, identification remains to be established.



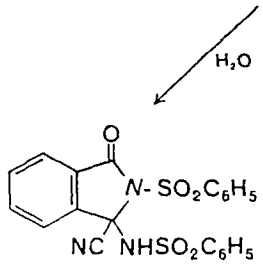
(214) (215) (216)

The cleavage of **214** to phthaloyl cyanide **216** may be favoured over ring contraction for the following reason. Ring contraction of azidoquinones appears to involve the zwitterionic intermediate **191**, the formation of which may be assisted by interaction of the 5,6-double bond. In the naphthoquinone series this would involve disruption of the aromatic ring. Such a process is not prohibitive, as evidenced by the fact that various monoazidonaphthoquinones do undergo pyrolytic conversion to indanediones. However, the adjacent azide groups in **214** can directly interact via the intermediate **215** and result in cleavage without disruption of the aromatic nucleus.

A reaction analogous to that reported for 2,3-diazido-1,4-naphthoquinone was recently observed for 2,3-diazido-1,4-naphthoquinonedibenzenesulphonimide (**217**)[90]. This diazide thermally cleaves to phthaloyl cyanide-dibenzenesulphonimide (**218**) after several hours in refluxing anhydrous benzene. The α-cyano-benzenesulphonimide moieties in **218** are very reactive towards hydrolytic reagents. For example, water readily reacts with **218** to give the *N*-benzenesulphonyllactam **219** in 80% yield.



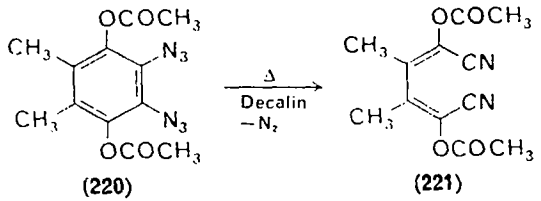
(217) (218)



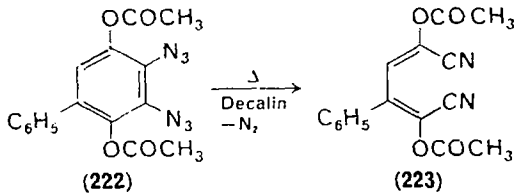
(219)

C. *Thermal Rearrangement of Azidohydroquinone Derivatives*

Azidoquinones are conveniently reduced to azidohydroquinones by the action of aqueous sodium dithionite[67]. These compounds undergo an interesting disproportionation reaction giving the corresponding amino quinone when gently heated in an inert solvent[67, 91]. Reaction of the quinols with acetic anhydride catalysed by a small amount of pyridine gives the corresponding diacetate. 2,3-Diazido-5,6-dimethyl- (**220**) and 2,3-diazido-5-phenyl-1,4-benzoquinol diacetate (**222**) were prepared in this manner and then pyrolysed in refluxing decalin[89]. These diazides undergo a smooth, high yield (75–91%) cleavage when slowly added to refluxing decalin giving the corresponding dienes, respectively, *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyano-2,3-dimethyl-1,3-butadiene (**221**) and *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyano-2-phenyl-1,3-butadiene (**223**). These unique dienes are diketene equivalents and may be of synthetic utility as 1,4-dicarbonyl moieties. This cleavage reaction finds precedent in the reported cleavage of 2,3-diazidobenzene to muconononitrile[92].



(220) (221)

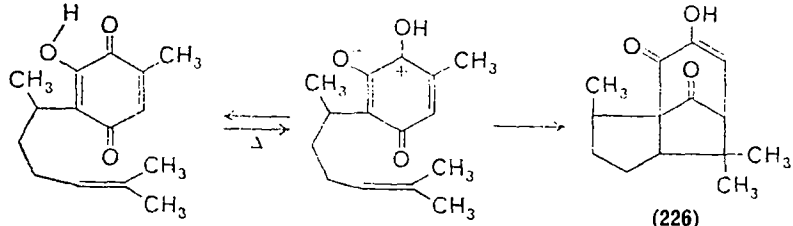


(222) (223)

V. MISCELLANEOUS REARRANGEMENTS OF QUINONES

A. Intramolecular Cycloaddition of Perezone

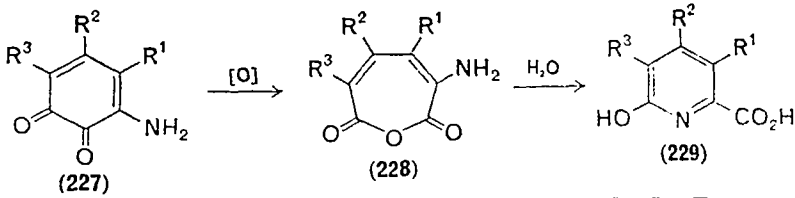
An especially fascinating thermal rearrangement has been reported for the naturally occurring hydroxyquinone, perezone **224**. This compound is converted on simple thermolysis in refluxing tetralin into the pipitzols **226**[93–95]. Woodward[95] has interpreted this rearrangement as a symmetry allowed $[4\pi^2+2\pi^2]$ cycloaddition. This reaction is viewed as the addition of a pentadienyl cation moiety in **225** to the 2π electron alkene group in the side-chain.



(224) (225) (226)

B. Baeyer–Villiger Oxidations of 3-Amino-1,2-Benzoquinones

An interesting rearrangement of certain 3-amino-1,2-benzoquinones to 6-hydroxypicolinic acids has been reported[96]. Baeyer–Villiger oxidation of the aminoquinones **227a, b, c** with a peroxy organic acid apparently gives an unisolated derivative of muconic acid anhydride **228a, b, c**. Hydrolysis of these anhydride intermediates with water causes their isomerization to the corresponding hydroxypicolinic acids **229a, b, c**. These transformations provide an *in vitro* model for the enzymatically observed conversion of 3-hydroxyanthranilic acid to quinolinic acid, nicotinic acid and picolinic acid[97].

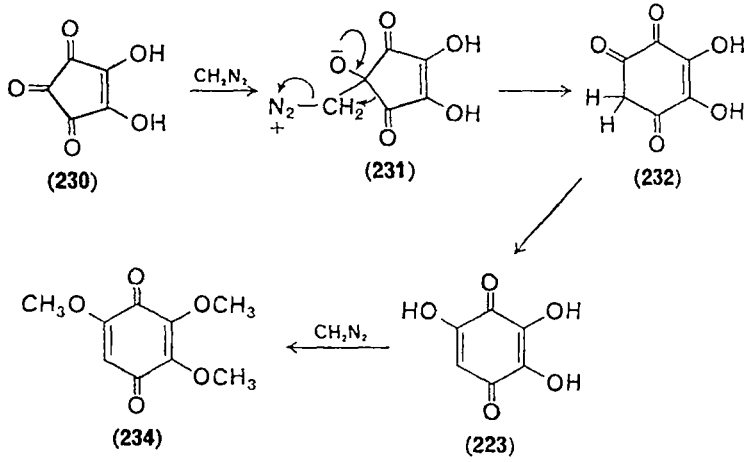


(227) (228) (229)

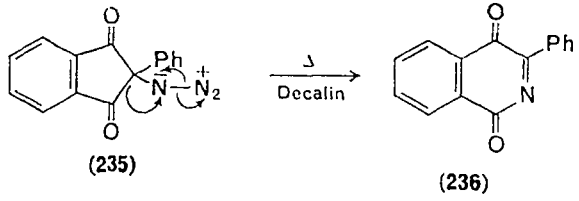
	R^1	R^2	R^3	Yield
a	H	H	H	16
b	CO_2H	H	H	11
c	NH_2	CH_3	H	16

VI. REARRANGEMENTS RESULTING IN THE FORMATION OF QUINONES

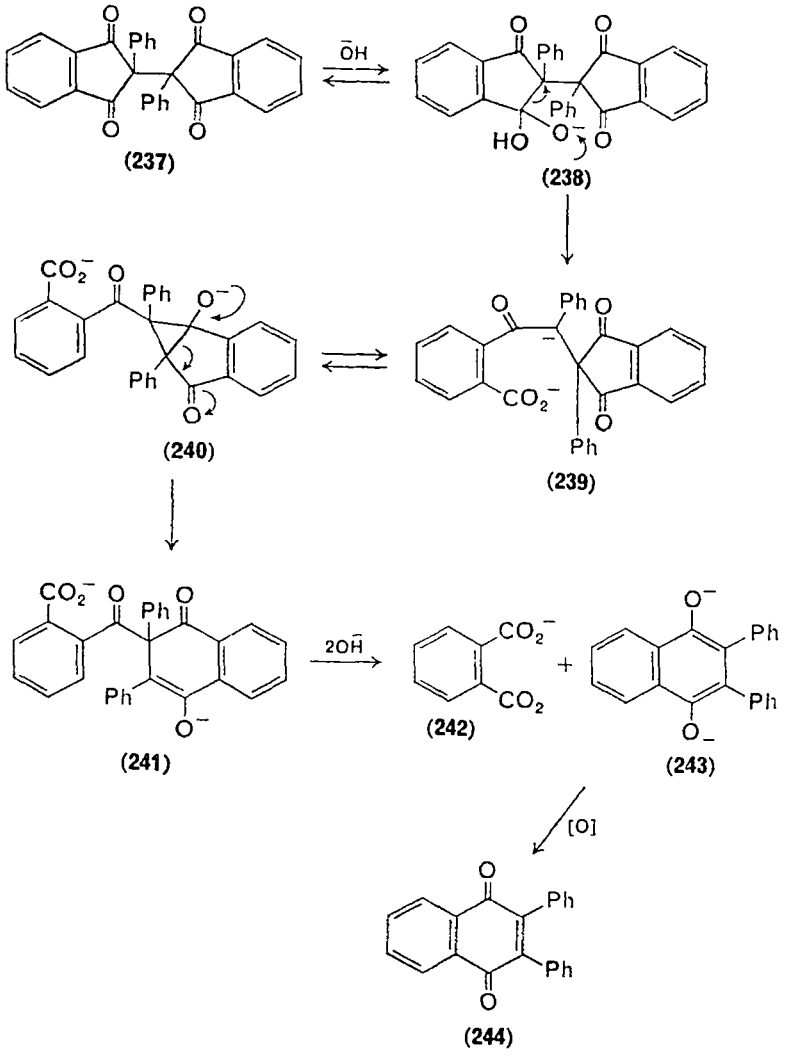
Very few rearrangements have been reported which directly result in the formation of the quinone nucleus. Croconic acid **230** reacts with excess ethereal diazomethane to give trimethoxy-1,4-benzoquinone (**234**) rather than the simple methylated product[98]. Ring expansion followed by tautomerization and successive methylation adequately explains this transformation.



An example somewhat analogous to the above is the recently reported thermal rearrangement of 2-azido-1,3-indanediones to azanaphthoquinones[99]. For example, 2-azido-2-phenyl-1,3-indanedione (**235**) decomposes in refluxing decalin to give 3-phenyl-2-aza-1,4-naphthoquinone (**236**).

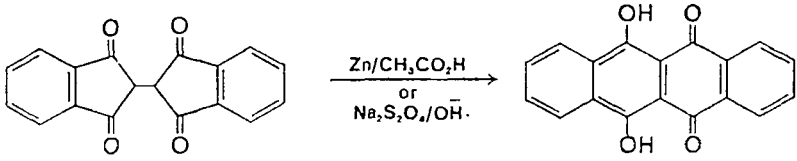


An unusual hydrolytic rearrangement of 2,2′-diphenyl-2,2′-diindane-1,1′,3,3′-tetrone (**237**) to 2,3-diphenyl-1,4-naphthoquinone (**244**) and phthalic acid induced by the action of sodium methoxide or sodium hydroxide has been reported[100]. The authors have proposed the following mechanism to account for this transformation.



(237) (238) (239) (240) (241) (242) (243) (244)

Another related ring expansion is that of 2,2′-biindan-1,1′,3,3′-tetrone (**245**) in the presence of zinc dust in acetic acid, or sodium dithionite in aqueous alkali to form dihydroxynaphthacenequinone (**246**)[101–103].



(245) (246)

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The Chemistry of the quinonoid compounds
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CHAPTER 9

Photochemistry of quinones

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I. INTRODUCTION

The first light-induced reaction of a quinone, the photodimerization of thymoquinone, was described[1] in 1857, after which there was a gap of about 40 years until Ciamician and Silber undertook their classical work on the photochemistry of carbonyl compounds, including quinones, particularly with respect to reactions involving oxidizable substrates[2,3]. Mainly qualitative work was described during the next 50 years, and this served to establish the broad limits of light-induced reactions between quinones and various substrates, although in most cases only the major product was isolated; this work was reviewed[4] in 1947.

The advent of refined spectroscopic and chromatographic techniques enabled a much more systematic study to be undertaken, and this, together with parallel work on the photochemistry of many other systems, particularly ketones, led to a much clearer picture of the gross features of many of the light-induced reactions of simple quinones, although there were still many points of controversy when the topic as a whole was last reviewed[5], in 1967. Some of these have now been resolved. The photochemistry of *ortho*-quinones was reviewed[6], *inter alia* with that of α-diketones, in 1969. Recent developments are now summarized annually[7].

As a consequence of the general principles which emerged from the early studies, and the experience gained later in handling quinones carrying progressively more complex substituents, emphasis has recently been shifting towards studies of the *in vitro* photochemistry of quinones which are of importance *in vivo*[8], e.g. in processes such as electron-transport. It is already becoming apparent that for some systems, e.g. the ubiquinones, there are appreciable differences from the phenomena observed for the model compounds studied previously, and that data for a much wider range of simple quinones carrying substituents such as alkoxy groups are now required.

Some 200 papers on quinone photochemistry have appeared during the last five years, and their contents form the main part of this chapter. Although many have dealt with purely organic aspects, there has been a considerable shift of emphasis from product analysis through e.s.r. spectroscopy of short-lived free radical intermediates to a study of the nature and kinetics of decay of the initially excited molecules, the limits of this now being in the nanosecond region as a result of developments in laser flash photolysis. The most recently applied new technique is chemically induced dynamic nuclear polarization (CIDNP), which has provided definitive evidence for the presence of caged radical pairs in certain light-induced reactions of 9,10-phenanthraquinone.

Light-induced reactions of quinones can be either intermolecular, usually involving reaction of the excited quinone with a ground-state substrate such as another quinone molecule, an olefin, or a hydrogen-donor, or intramolecular or potentially intramolecular, usually involving reaction of the excited quinonoid moiety with an appropriate part of an attached side-chain; reactive side-chains vary in complexity from the methyl groups of duroquinone to the polyisoprenoid systems found in many naturally occurring quinones.

The primary step in light-induced reactions of quinones is absorption of electromagnetic energy, giving an excited singlet state which can undergo intersystem crossing to yield the triplet state, which is probably responsible for the subsequent chemical reactions, at least for those systems which have been studied from this point of view. Evidence concerning excited states is given in section II.

Reaction of an excited quinone with an olefin usually results in cycloaddition, either 1,2- across the carbon–oxygen or carbon–carbon double bonds of simple *para*-quinones, or 1,2- across one carbonyl group and/or 1,4- across both in the case of *ortho*-quinones. These reactions are discussed in section III. Reactions involving addition of benzene are described in section IV.

Under conditions which are unfavourable for cycloaddition, the predominant chemical reaction in the presence of hydrogen donors is abstraction of hydrogen from the substrate by the excited quinone, leading, usually by ground-state free radical reactions, to the hydroquinone and dehydrogenation products of the substrate, or to 1 : 1 quinone–substrate adducts which are normally isolated as the corresponding hydroquinones. These reactions are discussed in section V. Some miscellaneous reactions, which do not conform to these patterns, are covered in section VI.

Cycloaddition and hydrogen-abstraction reactions of simple quinones often provide models for potentially intramolecular reactions involving side-chains, and the latter are described in section VII.

Light-induced reactions of 4,4′-diphenoquinones and of quinone methides and quinone imines have attracted much less attention, and are briefly described in sections VIII and IX respectively.

Much more information is available for *p*-quinones than for *o*-quinones, and *p*-quinones are therefore discussed first in each section or sub-section. Evidence relating to mechanisms is presented as appropriate throughout the text.

The abbreviations Q, $Q^{\cdot-}$, $QH^{\cdot}$ and QH_2 are used to indicate, respectively, the quinone, the semiquinone anion radical, the neutral semiquinone and the hydroquinone.

II. SPECTRA AND EXCITED STATES

A. Spectra

The main features of the absorption spectra of *p*- and *o*-quinones in relation to their photoreactivity are discussed in this section.

The electronic absorption spectrum[9] of 1,4-benzoquinone in hexane contains three main bands, λ_{max} 2400, 2760 and 4560 Å, with ε 19,500, 340 and 20, due, respectively, to allowed π–π^*, 'forbidden' π–π^*, and 'forbidden' n–π^* singlet–singlet transitions[10]; the latter band shows appreciable fine-structure[11,12]. There is also a very weak band (ε ca. 0·25) at 5390 Å due to the 'strongly forbidden' n–π^* singlet–triplet absorption[12–14]. The origins and natures of these bands have been analysed in some detail[10,15], the most recent data[16,17] being for the crystal at 4·2 K.

The 4560 Å band is shifted to shorter wavelengths when the spectrum is measured[18–20] for solutions in water and alcohols with which the quinone can hydrogen bond, and the very weak absorption in the 5390 Å region cannot be observed. The π–π^* bands are also slightly affected, but in the opposite sense[21].

1,4-Benzoquinone forms π-complexes with benzene and its homologues[22–27], and charge-transfer bands are observed; a semi-empirical molecular orbital treatment has been described[28]. Photochemical activity with respect to potentially reactive substrates is not inhibited under these conditions and benzene is commonly used as an 'inert' solvent.

Progressive introduction of alkyl groups into the 1,4-benzoquinone nucleus causes the 2760 Å band to move to longer wavelengths and the 4560 Å one to move to shorter wavelengths[9,29], with the result that whereas the lowest excited state of 1,4-benzoquinone is of n, π^* character, that of duroquinone has π, π^* character. This is reflected in their photochemistry, e.g. cycloaddition of alkenes to 1,4-benzoquinone occurs across a carbonyl group giving oxetans, whereas the reaction with duroquinone occurs at a carbon–carbon double bond to give cyclobutanes (section III.B). However, the long-wavelength n–π^* singlet–triplet transitions can still be detected in some cases[18], e.g. at 5280 Å (ε 0·20) and 5190 Å (ε 0·22) for, respectively, toluquinone and 2,5-dimethyl-1,4-benzoquinone, both in heptane.

A similar shift occurs when halogeno substituents are introduced, and for chloranil, the most extensively used of the halogeno-1,4-benzoquinones, the lowest triplet probably has π,π^* character[30,31], although, unlike duroquinone, it is photoactive in hydrogen-abstraction reactions, processes usually considered to involve n,π^* states.

Parallel shifts in absorption result from the introduction of hydroxy and alkoxy substituents[9], methoxy-1,4-benzoquinone, photochemically the most extensively studied member of this series, showing typical

π,π^* reactivity in yielding cyclobutanes and cyclobutenes when irradiated in the presence of alkenes and alkynes (sections III.B and D). The most pronounced effects are observed for the amino-1,4-benzoquinones, in which the visible absorption band is shifted to much longer wavelengths and becomes of the charge-transfer type, resulting in extremely low reactivity towards hydrogen-donor solvents, although potentially intramolecular reactions involving alkylamino substituents have been described (section VII.H). The spectra of alkyl-, chloro-, hydroxy- and methoxy-1,4-benzoquinones have been analysed in detail[32].

1,4-Benzoquinones carrying electron-accepting groups form progressively stronger π-complexes with aromatic compounds as the electron affinity of the quinone increases, and the spectroscopic properties of these complexes have been studied, particularly in relation to the determination of equilibrium constants[23,33]. Chloranil is almost completely complexed[34] in benzene and the solution is stable to irradiation with visible light. Analogous data have been given[22] for fluoranil (tetrafluoro-1,4-benzoquinone), which is photoactive by virtue of the n–π^* transition in the 3380 Å region[35].

Chloranil also forms complexes with donors such as tetrahydrofuran[36], although these do not preclude hydrogen abstraction reactions. Even relatively low-potential 1,4-benzoquinones such as the 2,5-diethoxy- and 2,5-bis(methylamino)-derivatives are capable of forming π-complexes[37] with appropriate donors, and this must be considered in any detailed analysis of their photochemistry.

The electronic spectra of 1,4-naphthoquinone[10,38,39] and its simple derivatives[38,39] are more complex than those of 1,4-benzoquinones since absorption by the benzenoid moiety is involved in addition to that by the enedione system, and in the overall assessment both chromophores interact. The spectrum of 1,4-naphthoquinone in hexane has λ_{max} 2460, 3300 and 4250 Å, with ε 24,000, 3200 and 50 respectively[9], the most important absorption from the photochemical point of view being that in the visible region at 4250 Å assignable to an n–π^* singlet–singlet absorption; the extremely weak n–π^* singlet–triplet absorption appears at 4910 Å for a solution in heptane[14]. Overlapping of the π–π^* and n–π^* absorptions is probably responsible for the fact that 1,4-naphthoquinone gives both cyclobutanes and cyclobutenes, and products which may be derived from oxetans and oxetes when it is irradiated in the presence of, respectively, alkenes and alkynes (sections III.B and D).

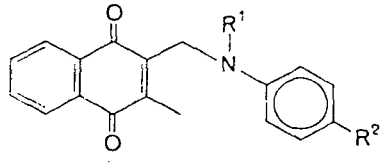
The effect of alkylation of 1,4-naphthoquinone at $C_{(2)}$ and $C_{(3)}$ is similar to, although less pronounced than, that in the 1,4-benzoquinone series. The vapour-phase spectrum of 2-methyl-1,4-naphthoquinone has

been described[40]. The introduction of alkyl substituents into the benzenoid moiety has little effect on the main features of the spectrum of 1,4-naphthoquinone, although with the 5-methyl and related homologues there exists the possibility of intramolecular hydrogen abstraction from the substituent (section VII.A).

Peri-interaction is strongly apparent in juglone (5-hydroxy-1,4-naphthoquinone), the hydroxy group causing a pronounced red-shift of the benzenoid absorption and, by virtue of the strong intramolecular hydrogen bond, preventing intermolecular photoreduction by hydrogen donors (section V.D). The effect on the spectrum is even more marked[41] for naphthazarin (5,8-dihydroxy-1,4-naphthoquinone).

A 5-methoxy group has a much less pronounced effect, whilst both the spectrum and the photoreactivity of the 5-acetoxy compound are very similar to that of 1,4-naphthoquinone itself. The presence of hydroxy and alkoxy substituents in the quinonoid ring causes changes similar to those observed for the 1,4-benzoquinones. Thus the lowest excited state of 2-methoxy-1,4-naphthoquinone appears to be π,π^* in character, since cycloaddition of alkynes gives cyclobutenes exclusively; reduction of the interaction of the oxygen *p* electrons with the quinonoid π-system increases the importance of the n,π^* state relative to the π,π^*, as shown by the formation of both cyclobutenes and oxete-derived products when 2-acetoxy-1,4-naphthoquinone is irradiated in the presence of alkynes (section III.D).

Dialkylamino substituents, such as piperidino, at $C_{(2)}$ have similar, but more pronounced effects, although they do not inhibit potentially intramolecular reactivity (section VII.H). Intramolecular charge-transfer is to be expected with simple aminoquinones, but it has also been observed[42] for systems such as **1** in which the amino and quinonoid moieties are separated by an insulating group.

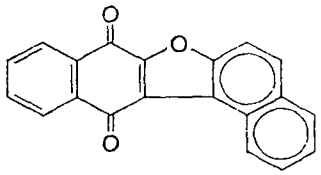


(1)

The polycyclic systems **2** and **3**, which are related to the 2-alkoxy-1,4-naphthoquinones, have a significant intramolecular charge-transfer contribution to their π–π^* absorption bands[43].

9,10-Anthraquinone absorbs[18,29] weakly in the visible region at 4050 Å, and this band, of n–π^* character, is predominantly responsible for

hydrogen-abstraction reactions. Simple alkyl substituents[44,45] do not appreciably alter the spectrum in this region, and, with the exception of intramolecular hydrogen-abstraction reactions involving methyl and



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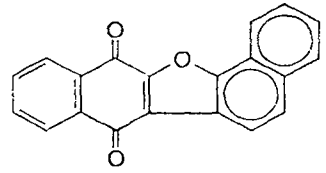
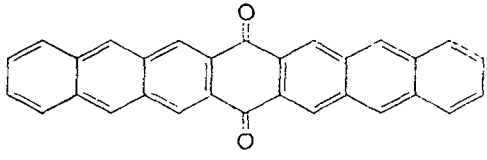


(3)

related substituents at the α-positions (section VII.A), also have little effect on the photochemistry. Hydroxy and alkoxy substituents have a more pronounced effect[29,39,46], and, as in the 1,4-naphthoquinone series, hydroxy groups in the α-positions suppress the photoreactivity, possibly as a consequence of photoenolization[47] (e.g. **6** ⇌ **7**, p. 476) or because the longest wavelength visible absorption is of the charge-transfer type[46]. Amino substituents behave similarly, and the longest wavelength bands of both 1- and 2-piperidino-9,10-anthraquinone in neutral solution are charge-transfer in character[48,49], but, at least for the 1-piperidino compound, this effect is destroyed by protonation of nitrogen and the absorption then becomes of the n–π^* type which restores the more normal photoreactivity. The effects of electron-donor substituents on the relative spacings of the n, π^* and π, π^* levels have been discussed[50].

The spectra of the higher acenequinones have been examined in much less detail, although the n–π^* singlet–singlet absorptions of the linear systems up to and including heptacene-7,16-quinone (**4**) have been described[51]. However, the photochemistry of these compounds has not been discussed.



(4)

Comparatively little information is available for *o*-quinones[6,52], and, with the exception of 9,10-phenanthraquinone, their photochemistry has not been extensively studied.

The simple *o*-quinones such as 1,2-benzoquinone and 1,2-naphthoquinone[10] show weak (ε 10–100) n–π^* singlet–singlet bands in the visible

region, the absorption envelope often being broad[53] and extending beyond 6500 Å. The visible absorption spectrum of 1,2-benzoquinone in ether shows three bands[54], at 5650, 5870 and 6100 Å (ε 21·5, 22·5 and 22·5 respectively), but this fine-structure is lost[53] in benzene solution due to π-complexing and the band then extends beyond 7000 Å. The longest wavelength band of 9,10-phenanthraquinone occurs in the 5000 Å region, and is also due to an n–π^* singlet–singlet transition[18].

B. Excited States

As indicated in section A, the generally most important absorption band in relation to photoreactivity is that at the longest wavelength, and for simple quinones this lies in the region 4000–5000 Å (ε 20–100). It is due to an n–π^* singlet–singlet ($S_0 \rightarrow S_1$) transition, or, in some cases, e.g. duroquinones, to the corresponding π–π^* transition, and provides the most convenient route, by intersystem crossing ($S_1 \rightsquigarrow T_1$), to the first triplet state which, as far as evidence is available, is the one primarily responsible for the subsequent chemical reactions. The $S_1 \rightsquigarrow T_1$ process generally occurs with high[52, 55, 56] efficiency (0·8–1·0) and completely outweighs direct $S_0 \rightarrow T_1$ excitation which can only be selectively effected in a few favourable cases (e.g. 1,4-benzoquinone in heptane[14]), and even then with such poor efficiency (ε ca. 0·2) as to render it useless for preparative work.

When the 'strongly forbidden' $S_0 \rightarrow T_1$ transition can be observed it does, however, provide an easy means of determining the energy of the first triplet state, e.g. 53 kcal/mole for 1,4-benzoquinone in heptane and 58 kcal/mole for 1,4-naphthoquinone in heptane[14]. For 1,4-benzoquinone this represents a first singlet–triplet splitting of ca. 6 kcal/mole, since from the readily observed absorption in the 4500 Å region the energy of S_1 is about 59 kcal/mole.

When the $S_0 \rightarrow T_1$ absorption cannot be directly observed, the energy of T_1 can be obtained from the phosphorescence emission spectrum, which arises from the $T_1 \rightarrow S_0$ transition, and which also gives a measure of the lifetime of the triplet state. Observations have been made for crystalline quinones and for quinones trapped in glassy matrices, both at low temperature, and for 'normal' solutions, although choice of solvent is often crucial. Thus phosphorescence was not detected for solutions of 1,4-benzoquinone in n- and cyclo-paraffins, but it was observed for a solution in 9 : 1 hexane–toluene, although the emission was here attributed to the quinone–toluene complex[57]; a more recent analysis[58] shows that for excitation of solutions of 1,4-benzoquinone in methylbenzenes at $-180°$ with light of wavelength near the charge-transfer maximum, the emission

contains both charge-transfer fluorescence of the complex and $^3(\pi^*, n)$ phosphorescence of the quinone.

Less precise data on triplet energy levels can be obtained from quenching experiments, provided that suitable quenchers are available, e.g. 1,3-dienes are often appropriate in terms of energy considerations, but are difficult to use because of competing ground-state reactions such as Diels–Alder addition.

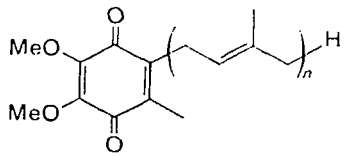
The value of the triplet energy obtained for a given compound often varies somewhat with the method of determination and, for the same method, with the conditions, e.g. the 0–0 phosphorescence band for 1,4-benzoquinone in the crystal[58] at $-180°$ corresponds to 52·4 kcal/mole, in solution in di-*n*-propyl ether[58] at 20° to 51·8 kcal/mole and in the vapour phase[59–61] to 53·5 kcal/mole. Values of 50 kcal/mole [62, 63] and 53 kcal/mole [14] have also been reported for 1,4-benzoquinone. However, the overall spread is as yet not of great importance in attempts to assess the energetics of light-induced reactions of quinones since other, even less precise, data are involved.

The lifetime of $^3(n, \pi^*)$ 1,4-benzoquinone is reported[58] to be less than 3×10^{-5} s in the crystal at $-180°$, and $6{\cdot}8 \times 10^{-5}$ s in di-*n*-propyl ether at 20°.

In appropriate cases, the kinetics of triplet decay can be determined by flash photolysis. Flash photolysis[64] of 1,4-benzoquinone in solvents such as water, ethanol and benzene does not reveal a transient in the 4900 Å region (where the triplet of duroquinone absorbs) and a similar lack of absorption is observed for toluquinone in ethanol and 1 : 1 ethanol–water, but the transient can be detected for solutions of toluquinone in water and benzene; in water it decays according to first-order kinetics, but the decay in benzene is too fast to allow kinetic analysis. 2,5-Dimethyl-1,4-benzoquinone does not show a 4900 Å transient in ethanol, but it does in 3 : 1 water–ethanol, and again the decay is first-order. Both 2,3-dimethyl- and trimethyl-1,4-benzoquinone show transients in the same region for solutions in ethanol[64], and the corresponding transient for duroquinone has been long known, although only recently has it been assigned with certainty to the triplet state[64, 65]. Progressive introduction of methyl groups into the nucleus of 1,4-benzoquinone thus enhances the lifetime of the triplet, from less than 10 ns for the parent compound to 9000 ns for duroquinone, both in ethanol[64].

2,3-Dimethyl- and 2,5-dimethyl-1,4-benzoquinone have[14] first triplet levels at 51·6 kcal/mole and it has been assumed[66] that duroquinone has the same value. The singlet–triplet crossing efficiency for duroquinone is approximately unity.

The first triplet level of ubiquinone-6 (**5**; $n = 6$) has been estimated[67] to lie in the region 29–42 kcal/mole, which is particularly low, although it is paralleled by a very low $S_1 \rightsquigarrow T_1$ efficiency (ca. 0·04) and an unusually



(5)

short lifetime. Since the short lifetime is observed for solutions in cyclohexane and in benzene it appears that decay by a hydrogen-abstraction process is not necessarily responsible, and it has been suggested[67] that the isoprenoid chain has a profound influence. An alternative view is that the properties of the triplet are affected by the methoxy groups, although preliminary work[68] suggests that the energy and lifetime of the 2,6-dimethoxy-1,4-benzoquinone triplet are similar to those of duroquinone; corresponding studies with other methoxy-1,4-benzoquinones are planned[68].

The unusually short lifetimes of the triplets of 1,4-benzoquinone and toluquinone[64] and related compounds[68] in benzene, which is a very poor hydrogen donor, have not been adequately accounted for, although effects similar to those described[69] for the quenching of triplet benzophenone are worthy of consideration.

The transient at 5000 Å observed during the flash photolysis of chloranil in ethanol has been assigned[70] to the triplet. It has been suggested[30,31] that the lowest triplet of chloranil has π,π^* character, and a similar assignment has been made[57] for the structureless luminescence observed from the complexes of chloranil, bromanil and fluoranil with toluene in hexane solution.

The first triplet energies of the dichloro-1,4-benzoquinones are very similar to that of 1,4-benzoquinone itself (ca. 52 kcal/mole). Thus the absorption spectra[16] of crystals of 2,3-, 2,5- and 2,6-dichloro-1,4-benzoquinones at 4·2 K give values of 53·1, 53·0 and 52·4 kcal/mole respectively; the emission spectra[60] of the 2,5- and 2,6-dichloro-compounds in the vapour phase indicate 55·1 and 53·0 kcal/mole respectively. 2,6-Dichloro-1,4-benzoquinone has also been studied[71] in ligroin solution at 25°, the absorption spectrum giving a first triplet level of 53·2 kcal/mole, identical with that obtained[71] under the same conditions for 1,4-benzoquinone itself and for 2,6-dibromo-1,4-benzoquinone. The corresponding level[71] for 2,6-di-iodo-1,4-benzoquinone is appreciably lower, at 47·2 kcal/mole.

No heavy-atom perturbation of the singlet–triplet transition was observed[71].

The first triplet level of 1,4-naphthoquinone is at 58 kcal/mole when measured by absorption[14], a value in agreement with that determined from the vapour-phase emission spectrum[72]; the emission spectrum at 77 K has also been measured[73]. The corresponding level for 2-methyl-1,4-naphthoquinone, determined from the vapour-phase emission spectrum[40], is at 58·0 kcal/mole.

The first triplet level of 9,10-anthraquinone is slightly higher than that of 1,4-naphthoquinone, being at 62·4 kcal/mole in non-polar media, and at 63·3 kcal/mole in polar media[62], and a value of 63·0 kcal/mole has been obtained from the phosphorescence spectrum[63, 74]. It is of interest that the phosphorescence emission[75] of 9,10-anthraquinone in the crystal at 77 K is at appreciably longer wavelength than it is in rigid solution at the same temperature, and its lifetime is also much longer (e.g. 100 ms in the crystal, 3·3 ms in methylcyclohexane or ethanol); this lifetime effect is considerably greater than that observed for other quinones. The nature of the emission also depends on the medium, and for various crystalline matrices at 77 K the phosphorescence maxima[76] lie in the range 4860–4990 Å, corresponding to first triplet levels in the range 58·9–57·4 kcal/mole, considerably below those determined for glassy matrices at 77 K, (62·4 kcal/mole in methylcyclohexane–isopentane[62]; 63·3 kcal/mole in ether–isopentane–ethanol[77]).

The phosphorescence emission spectra of 1-methyl-9,10-anthraquinone[78], 2-chloro-9,10-anthraquinone[79], and of 1-chloro- and 1,4-, 1,5- and 1,8-dichloro-9,10-anthraquinones[80] have been described.

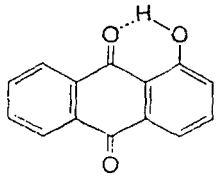
The presence of a steady-state concentration of triplet 9,10-anthraquinone can be detected by irradiating a benzene solution of the quinone in the 3000–4000 Å region and observing the ^{1}H n.m.r. spectrum of the ground-state molecules, for which most of the normal absorption lines are changed to emission as a result of Overhäuser effects[81].

The $S_1 \rightsquigarrow T_1$ intersystem crossing efficiency for 9,10-anthraquinone has been inferred to be unity from the quantum yield for photoreduction[55, 82], but a determination[56] based on the sensitized *cis–trans* isomerization of olefins indicates a value of 0·9.

Most recently, the luminescence of 9,10-anthraquinone in 1,1,2-trichlorotrifluoroethane has been examined[83]. At 77 K it consists only of phosphorescence (previously not observed for *solutions* of the quinone) *and* delayed thermal fluorescence, which arises from $T_1 \rightsquigarrow S_1$ intersystem crossing, the reverse of the 'normal' $S_1 \rightsquigarrow T_1$ process which was previously thought to be unidirectional. Hydrogen-abstraction by excited 9,10-anthraquinone

has until now been considered to involve the first triplet state exclusively, and the pseudo-first-order rate constants obtained[83] for this reaction in 1,1,2-trichlorotrifluoroethane, combined with the unity quantum yield of reduction, are too high to be accounted for solely on the basis of abstraction by singlet anthraquinone, but they do not preclude the possibility that a small fraction of the reaction does involve the singlet. In the case of 9,10-anthraquinone, the singlet–triplet splitting is about 4 kcal/mole, and it is suggested[83] that the possibility of singlet reactivity should not be overlooked for other systems with similar small splittings, particularly when the reaction quantum yield is low; there may be significant singlet population at room temperature even with singlet–triplet splittings as high as 14 kcal/mole.

9,10-Anthraquinones carrying 1-hydroxy or 1-amino substituents have low quantum yields for reduction in the presence of hydrogen donors[84], and this is paralleled by their lack[85,86] of phosphorescence at 77 K, which indicates the absence of the $T_1 \rightarrow S_0$ process, and the very short (ca. 10^{-8} s) lifetimes of their excited states under these conditions (cf. triplet 9,10-anthraquinone, ca. 10^{-3} s), phenomena which can be attributed[47] to deactivation via photoenolization, e.g. **6** ⇌ **7**.



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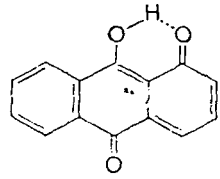


(7)

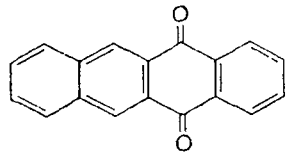
2-Hydroxy-9,10-anthraquinone shows phosphorescence[86], but 2-amino-9,10-anthraquinone does not[85], possibly because the excited state is of the charge-transfer type (cf. reference 49).

A similar phenomenon has been observed for 1-methyl-9,10-anthraquinone[87], but 2-methyl-9,10-anthraquinone behaves normally[87], as do the halogeno-9,10-anthraquinones[84,85,88].

The trend to a progressively higher first triplet level in the series 1,4-benzoquinone, 1,4-naphthoquinone and 9,10-anthraquinone is not continued by 5,12-naphthacenequinone (**8**), for which a value of only 55·8 kcal/mole has been reported[62].

Less information is available about the energy levels of *o*-quinones. Phosphorescence emission could not be detected[75] for 1,2-naphthoquinone. The first triplet level of 1,2-anthraquinone has been estimated[52] to be at 47 kcal/mole. The corresponding level for 9,10-phenanthraquinone[89] is

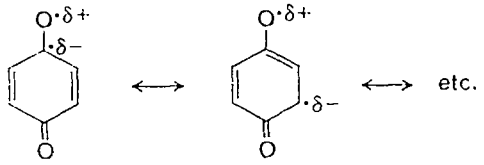
at 48·8 kcal/mole, determined from the emission spectrum in alkanes at 77 K, and the singlet–triplet crossing efficiency is unity[52,90]. However, it has also been reported[75] that in rigid solution 9,10-phenanthraquinone



(8)

shows a weak phosphorescence maximum, with a lifetime of about 5×10^{-3} s, at 5440 Å, indicating a triplet energy of 52·6 kcal/mole, but this may not be the lowest level since a more recent determination[91], based on the 0–0 band for phosphorescence at 77 K in either isopentane–methylcyclohexane or ethanol, indicates a value of $50 \pm 0{\cdot}5$ kcal/mole.

Absorption of electromagnetic energy by the quinone causes promotion of an n or π electron, depending on the quinone, from its ground-state orbital to an antibonding orbital, resulting in uncoupling of an electron pair. If, as is normally the case, excitation is to the singlet state, the uncoupled electrons retain their opposed spins, but intersystem crossing to give the triplet state (or, rarely, direct $S_0 \rightarrow T_1$ excitation) results in the spin of one electron being reversed. Both these states can be regarded as having diradical character in which delocalization over the remainder of the conjugated system is possible, and for which there will be an overall dipole. Thus n–π^* excitation of the carbonyl group will give a system of the type



whilst π–π^* excitation will give an analogous system, but with the dipole in the opposite sense. Similar structures can be written for excited *o*-quinones.

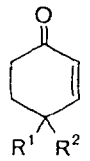
The majority of cases for which definitive evidence is available indicate that reactions involving the carbonyl group proceed via the n,π^* triplet state, and the excited quinone would therefore be expected to show electrophilic character. This is certainly so for cycloaddition[92,93] of 9,10-phenanthraquinone to olefins, and it also appears to be true for

hydrogen-abstraction reactions, e.g. hydrogen α- to oxygen is readily abstracted[94] whereas that α- to a cyano group is not[95].

However, diradical states with dipoles in the opposite sense from those indicated above may be involved under some conditions, since an examination of the situation for αβ-unsaturated carbonyl compounds other than quinones has led to the suggestion[96] that the direction of polarization may be governed by the energetics of the possible reaction pathways following excitation, and the immediate environment of an excited quinone will therefore be of particular importance. Further, it has been reported[97] that dipolar representations of the excited states of 4,4-diarylcyclohex-2-enones (**9**) give a poor guide to the prediction of the products of their photorearrangement, and the simple diradical representation

$$C{=}C{-}\dot{C}{-}\dot{O} \quad \longleftrightarrow \quad \dot{C}{-}C{=}C{-}\dot{O}$$

is preferred. On this basis, the n,π^* excited state involved in both cycloaddition to, and hydrogen-abstraction by, the carbonyl group of a *p*-quinone can be considered to have appreciable weighting from the canonical form **10**, and the π,π^* state responsible for 2+2 cycloaddition to the carbon–carbon double bond to have appreciable weighting from the form **11**. Analogous considerations apply to *o*-quinones.



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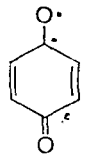

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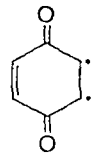


(11)

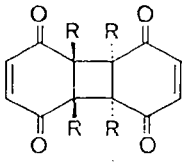
In determining the feasibility of a light-induced reaction of a quinone, the energy of the lowest excited state involved, the strengths of the bonds broken and formed and changes in stabilization of the quinonoid system must be taken into account, and in the latter context it should be noted that many of the photoreactions of quinones lead to the generation of benzenoid aromatic systems.

III. CYCLOADDITION REACTIONS

A. Dimerization

Quinone photodimers are probably formed by addition of excited quinone to ground-state quinone. Only dimers of *p*-quinones have been described, and the factors which govern whether or not dimerization will

occur, whether solid-state or solution conditions will be required, and whether the dimer will be an *anti*-cyclobutane, e.g. **12** (R = H) from 1,4-benzoquinone[98] in molten maleic anhydride or benzophenone, or in a mixture[99] of benzophenone and benzil at 70°, a *syn*-cyclobutane, e.g. **13** from solid 2,3-dimethyl-1,4-benzoquinone[100], or a spiro-oxetan, e.g. **14** from solid 2,5-dimethyl-1,4-benzoquinone[101], have not been clearly established.



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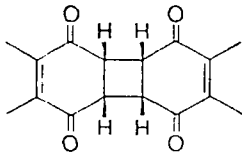

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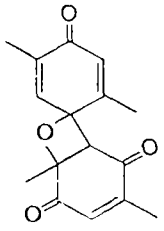
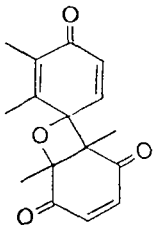


(14)

Studies[102,103] of molecular packing in cystalline quinones indicate that dimerization is unlikely if the potentially reacting centres are more than about 4·3 Å apart, but otherwise they do not provide a generally useful guide, e.g. the arrangement of the 2,3-dimethyl-1,4-benzoquinone molecules suggests that both the *anti*-cyclobutane dimer **12** (R = Me) and the spiro-oxetan **15** should be formed, but in practice the *syn*-dimer **13** is obtained[100] in good yield. A possible explanation is that different crystalline modifications were used by the two groups of workers, but, since the photodimerization of 2,3-dimethyl-1,4-benzoquinone has been effected with the same result at different times in several laboratories, an alternative, and more probable, explanation is that excitation of molecules in the crystal causes appreciably enhanced molecular motion, as has been suggested[104] for the solid-state photodimerization of *trans*-cinnamic acid.

Solid-state dimerization of 2,3-dichloro-1,4-benzoquinone gives[105] the *anti*-dimer **16** and, as with 1,4-benzoquinone itself, the yield is very low. It is of interest that the photodimerization of the dichloroquinone is thermally reversible.



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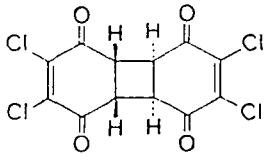
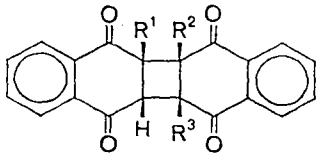


(16)

2,6-Diphenyl-1,4-benzoquinone gives an unidentified, probably cyclobutane-type, dimer[106] when irradiated in solution in benzene; its photochemistry in other solvents is quite different (see section VII.B).

The crystal structure[103] of 1,4-naphthoquinone indicates that it should be stable in the solid state, but the *syn*-dimer **17** ($R^1 = R^2 = R^3 = H$) has since been obtained[107] in 15% yield by irradiation of the crystal, although the conditions are fairly critical. The *anti*-dimer **18** ($R^1 = R^2 = R^3 = H$) is the major product when the quinone is irradiated in solution in acetic anhydride[107]; it is formed with equal efficiency when the quinone, in solution in benzene, is selectively excited to either its n,π^* or π,π^* singlet state[108]. Several new reactions of the dimer **18** ($R^1 = R^2 = R^3 = H$), which support the structure assigned to it, have been described[109-111].



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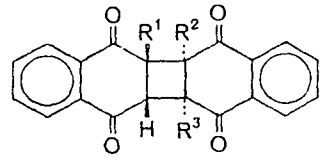
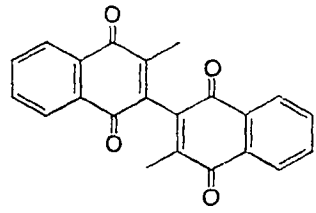


(18)

Contrary to an earlier report[112], solid-state dimerization of 2-methyl-1,4-naphthoquinone gives both the head-to-head (**17**; $R^1 = R^2 = Me$, $R^3 = H$) and head-to-tail (**17**; $R^1 = R^3 = Me$, $R^2 = H$) *syn*-dimers[113]. When irradiated in solution in acetone or adsorbed on silica gel (a new condition for this type of reaction) it yields the corresponding *anti*-dimers **18** ($R^1 = R^2 = Me$, $R^3 = H$) and **18** ($R^1 = R^3 = Me$, $R^2 = H$), together with a dehydrodimer **19** and an unidentified oxetan dimer[113].

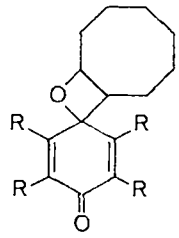


(19)

B. Simple Alkenes and Related Compounds

The products from these reactions are analogous to those described in the preceding section in that they are frequently cyclobutanes and spiro-oxetans, although dihydrodioxins also result from 4+2 cycloaddition to *o*-quinones.

For 1,4-benzoquinone, the order of efficiency of spiro-oxetan (**20**; R = H) formation with *cis*-cyclo-octene is in the order[114] of quinone excitation n–π^* (4500 Å) ≥ π–π^* (2900 Å) ≫ π–π^{**} (2400 Å), the lowest triplet state being n, π^*. For chloranil, the lowest triplet state may contain both n, π^* and π, π^* contributions since with *cis*-cyclo-octene it yields[115] both the spiro-oxetan **20** (R = Cl) and the bis-cyclobutane **21**, although the proportions are dependent on the quinone : alkene ratio.



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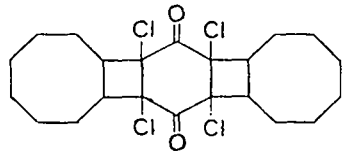
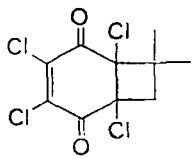


(21)

When irradiated in the presence of isobutene, chloranil gives[31] the cyclobutane **22** and the trichloroquinone **23**. The latter may arise by thermal loss of hydrogen chloride from **22** with concomitant ring-opening, or via intramolecular transfer of a hydrogen atom in a diradical intermediate such as **24** followed by elimination of hydrogen chloride. The formation of adducts such as **22** may be a consequence[31] of the dipolar character of the π, π^* excited state of chloranil, electron-deficiency at carbon rendering it electrophilic at the ethene linkage; polarization in the opposite sense is suggested for 1,4-benzoquinone.



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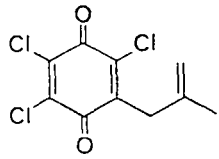

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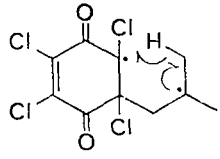
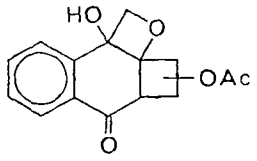


(24)

The lowest triplet state of duroquinone appears to be entirely of π, π^* character, since with a variety of alkenes it yields[116,117] cyclobutanes exclusively.

The change in character of the lowest excited state from n, π^* to π, π^* by introduction of an alkoxy group into the quinonoid nucleus is reflected in the formation of the novel spirocyclic system **25** by irradiation[118] of 2-methoxy-1,4-naphthoquinone in the presence of vinyl acetate; compound **25** is formed from the initial cyclobutane adduct **26** by a second light-induced step.

Photoaddition of *cis*-cyclo-octene to 9,10-anthraquinone is unusual in that a bis-spiro-oxetan is formed; it results from further addition to the initial mono-adduct and can be obtained in 90% yield[119].



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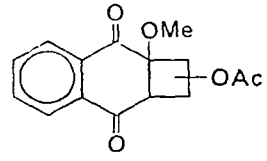
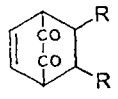


(26)

The relationship between thermal and photochemical cycloaddition of alkenes to 1,2-benzoquinones is of interest from the point of view of mechanism. Thermal addition of an alkene RCH=CHR can yield a bicyclo-octene **27** or a dihydrodioxin **28**. Perturbational molecular



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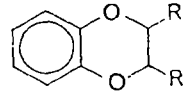
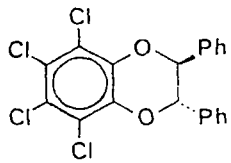


(28)

orbital treatment[120] indicates that dihydrodioxin formation is more favourable than bicyclo-octene formation and, in agreement with this, dihydrodioxins are generally the major products isolated. Concerted thermal cycloaddition is Woodward–Hoffmann allowed, and under these conditions tetrachloro-1,2-benzoquinone yields the dihydrodioxins **29** and **30** almost exclusively when treated in the dark with, respectively, *trans*- and *cis*-stilbene.



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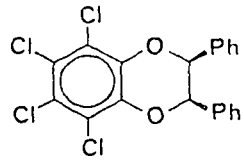
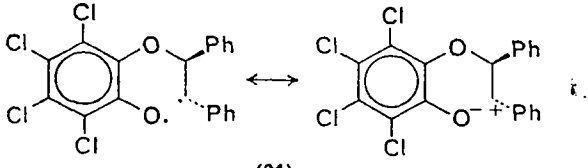


(30)

Irradiation[121] of a mixture of tetrachloro-1,2-benzoquinone and *trans*-stilbene in benzene, at a temperature too low for thermal addition, with light of wavelength greater than 4000 Å, gives 88% of the *trans*-dihydrodioxin **29** and 12% of the *cis*-compound **30**; *cis*-stilbene, which could have been formed by quinone-sensitized photoisomerization of the *trans*-isomer, is not a precursor of the *cis*-dihydrodioxin **30**. It has been suggested[121] that the light-induced formation of **29** may be a non-concerted process involving singlet quinone, steric control resulting from charge correlation in an appreciably dipolar intermediate **31**, but perturbational

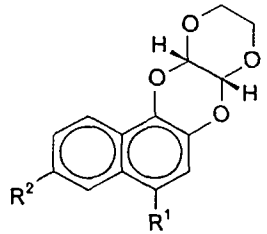
molecular orbital treatment[120] indicates that a concerted photocycloaddition should still be possible even when the thermal addition is highly stereoselective.



(31)

Similar irradiation[122] of tetrachloro-1,2-benzoquinone in the presence of *cis*-stilbene gives only traces of **29** and **30**, in the ratio 1 : 5, the major product being a 1 : 1 quinone–benzene adduct (see section IV); the reason for this marked difference has not been elucidated. However, compounds **29** and **30** are the major products, still in the ratio 1 : 5, when either acetonitrile or acetone are used as solvents.

Photoaddition of dihydro-1,4-dioxin to a range of 1,2-naphthoquinones in benzene gives[123] the *cis*-1,4-dioxans **32** (R^1, R^2 = variously H, Cl, Br, *t*-Bu), although the nature of the intermediate has not been established.

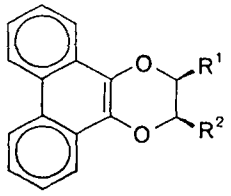


(32)

Most of the recent investigations of this type of reaction have been with 9,10-phenanthraquinone. Addition of stilbene, 1-phenylpropene and 2-butene gives mixtures of the corresponding *cis*- and *trans*-dihydrodioxins **33** and **34** regardless of which geometrical isomer of the olefin is used initially[124,125] and it has been suggested[124] that an equilibrating diradical (**35** ⇌ **36**) is involved, **35** giving the *cis*-dihydrodioxins and **36** the *trans*, a view supported by the increasing proportion of *trans*-compound formed as the reaction temperature is raised.

The cleanest reactions of this type, giving dihydrodioxins, are observed with the stilbenes. More products are formed when simpler alkenes are used, although dihydrodioxins still predominate. Thus photoaddition of either *cis*- or *trans*-2-butene to 9,10-phenanthraquinone gives[125] the dihydrodioxins **33** ($R^1 = R^2 = Me$) and **34** ($R^1 = R^2 = Me$), together with

the spiro-oxetan **37** (R = Me) and at least two minor products which probably arise via hydrogen-abstraction reactions (see section V.A). The dihydrodioxins **33** ($R^1 = R^2 = Me$) and **34** ($R^1 = R^2 = Me$) are



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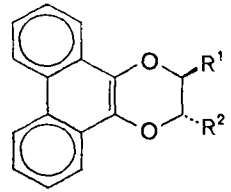

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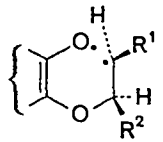

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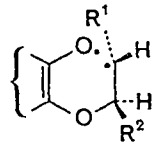
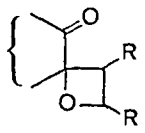


(36)

formed in the ratio 57 : 43 regardless[126] of which geometrical isomer of 2-butene is used, and quenching experiments indicate that triplet, probably n,π^*, phenanthraquinone is involved, suggesting that addition occurs stepwise and again indicating that the lifetimes of the intermediate diradicals **35** ($R^1 = R^2 = Me$) and **36** ($R^1 = R^2 = Me$) are sufficiently long to allow equilibration to occur prior to cyclization. The absence of *cis*-4-octene in the olefin recovered after irradiation[126] of 9,10-phenanthraquinone in benzene in the presence of the pure *trans*-isomer indicates that the cycloaddition is not reversible.



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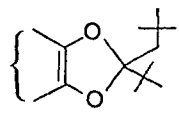
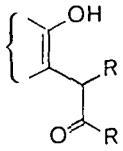


(38)

The dioxole **38** has been isolated[127] from the products of irradiation of 9,10-phenanthraquinone in 1,2-di-*t*-butylethylene. It is probably formed[127] by phenanthraquinone-sensitized rearrangement of the spiro-oxetan **37** (R = *t*-Bu), although it has been shown[91] that the spiro-oxetans are photolabile in the absence of a sensitizer, dissociating to their original components and also yielding the dihydrodioxin, the dioxole and, via ring-opening to give **39** followed by dehydration of the derived hemiacetal, the dihydrofuran **40**.

Analogous rearrangement products have been obtained from irradiations of 9,10-phenanthraquinone in the presence of α-chlorostilbene[127] and the cyclic enamide[127,128] **41**, although in the latter case the dihydrodioxin



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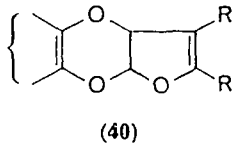
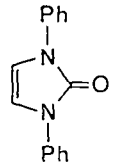


(40)

(as **33**) is the major component; photoaddition of the enamide **42** also gives the corresponding dihydrodioxin[129].

Irradiation of 9,10-phenanthraquinone in the presence of the chloroethylenes ($C_2H_{4-n}Cl_n$, $n = 1, 2, 3, 4$) indicates[92] that the proportion of



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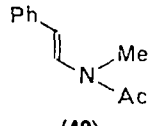
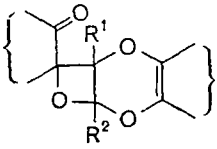


(42)

spiro-oxetan, relative to dihydrodioxin, increases as n increases, and that for trichloroethylene the spiro-oxetan is favoured at $+70°$ whereas the dihydrodioxin is favoured at $-23°$. In some cases there is elimination of hydrogen chloride from the spiro-oxetan and dihydrodioxin to give the corresponding olefins from which the new dihydrodioxin systems **43** and **44** are formed by 4+2 photocycloaddition of another molecule of quinone; dioxoles, e.g. **45** from *trans*-1,2-dichloroethylene, are also formed in some cases.



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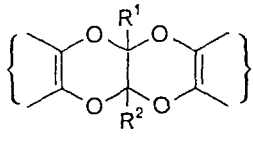
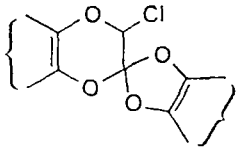


(44)



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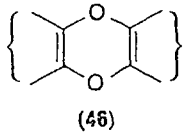


(46)

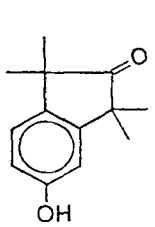
Photoaddition of 2-chloroindene occurs analogously to give both the dihydrodioxin and the spiro-oxetan, but only **46**, formed by loss of hydrogen bromide from the dihydrodioxin, was isolated when the substrate was 9-bromophenanthrene[92].

The rate of addition of 9,10-phenanthraquinone to alkyl-substituted ethylenes is about 100 times that of addition to the corresponding chloroethylenes, again indicating the electrophilic character of the excited quinone.

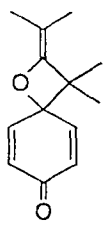
Much more work with these systems is required before a comprehensive rationale can be presented. The reversibility of some of the reactions presents additional problems.

C. *Dienes and Trienes*

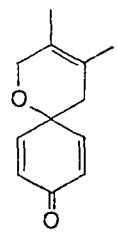
Many of the reactions with dienes parallel those described in the preceding section in so far as 2+2 or 4+2 cycloaddition of the quinone to only one of the double bonds of the diene is involved, although for some systems the products probably arise by rearrangement of the initial adducts. Thus irradiation of a mixture of 1,4-benzoquinone and tetramethylallene in benzene (Pyrex filter) gives a 78% yield of the indanone **47**, which may arise from the initial spiro-oxetan **48** by a quinone-sensitized rearrangement[130].



(47)



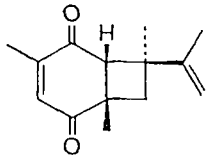
(48)



(49)

In contrast to the formation of spirodihydropyrans[131], e.g. a high yield of **49** from 1,4-benzoquinone and 2,3-dimethyl-1,3-butadiene, irradiation of a benzene solution of 2,5-dimethyl-1,4-benzoquinone and the same diene with light of wavelength greater than 4000 Å gives a mixture of ten products, of which only one, a cyclobutane of structure and probable stereochemistry **50**, and representing 45% of the total product, has been identified[31]. This may reflect greater π,π^* character in the excited state of the quinone, as suggested for chloranil, which with 1,3-butadiene under similar conditions gives a 72% yield of the cyclobutane **51** as a mixture of stereoisomers, and with 2,3-dimethyl-1,3-butadiene also gives[31] a cyclobutane of structure and probable stereochemistry **52** in 33% yield; the

major product (42%) of the latter reaction is, however, the trichloroquinone **53** which is stated[31] to arise from the adduct **54** produced by a mechanism (as **24**) analogous to that suggested for compound **23** (section III.B), although no evidence is presented for the existence of **54**, and loss of hydrogen chloride from **52** as indicated by **55** would provide an alternative mechanism, analogous to that suggested in section III.B for the transformation **22** → **23**.



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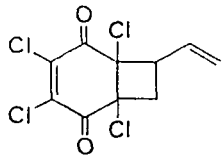

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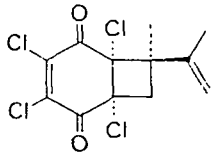

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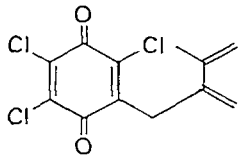

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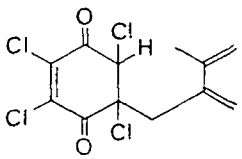

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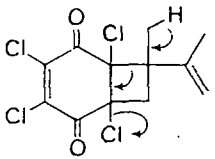
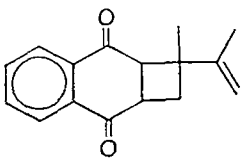


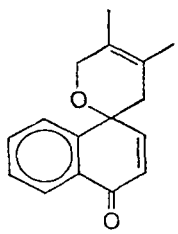
(55)

Ultraviolet irradiation of an ethereal mixture of duroquinone and cyclopentadiene is reported[131a] to give 30% of the Diels–Alder *exo*-monoadduct, but no evidence is presented to support this unusual stereochemistry.

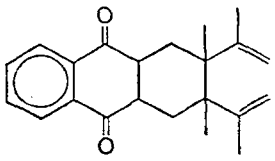
1,4-Naphthoquinone adds tetramethylallene to give[130] the benzologue of compound **47**, although in much lower yield. In the presence of 2,3-dimethyl-1,3-butadiene it behaves as if its lowest excited state has both π,π^* and n,π^* character, giving[31] a 2 : 1 mixture of the cyclobutane **56** and the spirodihydropyran **57**, together with a 1 : 2 quinone–diene adduct **58**.



(56)



(57)

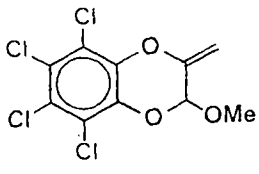


(58)

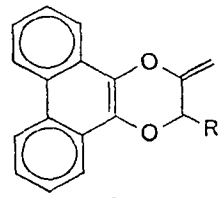
Irradiation of 1,4-naphthoquinone and cycloheptatriene in benzene gives a 1 : 1 spiro-oxetan adduct, but the positions of the double bonds in the resulting cycloheptadiene moiety have not been established[132].

9,10-Anthraquinone does not add to either buta-1,3-diene or its 2,3-dimethyl homologue since these dienes have triplet levels lower than that of the quinone and they therefore act as quenchers[119].

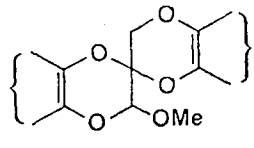
Tetrachloro-1,2-benzoquinone adds to methoxyallene when irradiated in benzene to give[93] the dihydrodioxin **59**, but this compound is also formed in the dark, and it is not clear whether the reaction really is light-catalysed. However, the addition of 9,10-phenanthraquinone to the allene probably is a light-induced process and spectroscopic analysis indicates that when the allene is in twofold excess in benzene the adduct **60** (R = OMe) is formed exclusively, although only about 60% was isolated. With an excess of quinone, further addition to the exocyclic double bond of **60** (R = OMe) occurs, giving **61** as an additional product[92].



(59)

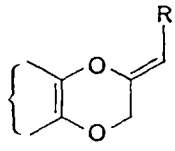


(60)

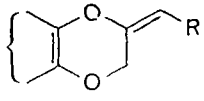


(61)

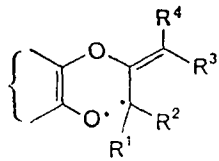
Allenes of the form $CH_2{=}C{=}CHR$, where R is methyl or methylthio, but not methoxy, also yield the adducts **62** and **63**, together with unidentified compounds which may be formed via hydrogen-abstraction reactions, but the adducts **60** (R = Me or SMe) are still the major products[93].



(62)



(63)

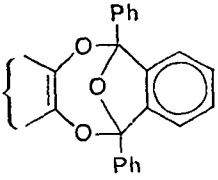


(64)

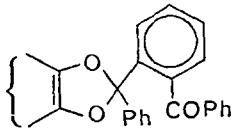
The rate of photocycloaddition of 9,10-phenanthraquinone to allene and its methyl homologues increases[133] as the degree of methyl substitution increases, indicating the electrophilic character of the excited quinone and also the stabilizing effect of the substituents R^1 and R^2 in the proposed diradical intermediate **64** (cf. references 124, 126, 129), although electrophilic character probably outweighs the effect of radical stabilization since monoalkoxy- and monoaryloxy-allenes add even more rapidly[133].

The quantum yield for formation of adduct **60** (R = OMe) from methoxyallene is 0·53 although the quantum yield of disappearance of the quinone is 0·98, both figures being independent of allene concentration and thus indicating that neither reversible addition nor appreciable deactivation of excited quinone occurs[133], although it is difficult to reconcile these quantum yields with the statement[93] that the adduct **60** (R = OMe) is the sole product, unless the experimental conditions were different. In contrast, the addition of ethoxyallene appears to be reversible[133]. No adduct is formed with cyanoallene[133], although the quinone is slowly consumed ($\Phi_{-Q} = 0{\cdot}09$). This again suggests that the electrophilic character of the excited quinone is important, more so than the stabilization which could equally well be achieved in the diradical **64** (R^1 = CN, R^2 = H), although the effect of ground-state complexing remains to be assessed.

Irradiation of 9,10-phenanthraquinone in benzene containing 1,3-diphenylisobenzofuran gives the dihydrodioxocin **65** by 4+4 cycloaddition, and the dioxole **66** by a process involving cleavage of the furan ring[134]. Related systems behave analogously.



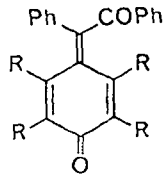
(65)



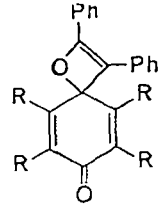
(66)

D. Alkynes

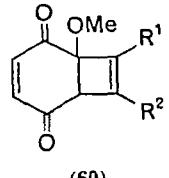
In contrast to 1,4-benzoquinone, which adds diphenylacetylene to give the quinone methide **67** (R = H), probably[135,136] via the spiro-oxete **68** (R = H), methoxy-1,4-benzoquinone gives the cyclobutene **69** ($R^1 = R^2$ = Ph) in 50% yield; 2-butyne adds analogously, giving **69** ($R^1 = R^2$ = Me) together with polymeric material[137].



(67)

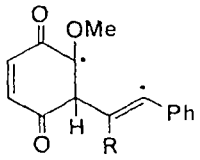


(68)

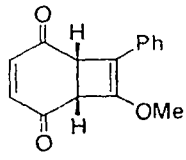


(69)

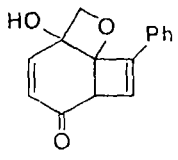
Phenylacetylene and 1-phenylpropyne add stereoselectively[137-139] to methoxy-1,4-benzoquinone to give the adducts **69** (R^1 = Ph, R^2 = H) and **69** (R^1 = Ph, R^2 = Me) respectively, the former in 80% yield. These reactions may reflect π, π^* activity in the excited quinone, the direction of addition being controlled by stabilization in a diradical intermediate such as **70**. Over-irradiation of these products causes isomerization[118], e.g. the adduct **69** (R^1 = Ph, R^2 = H) yields a mixture of **71** and **72**.



(70)



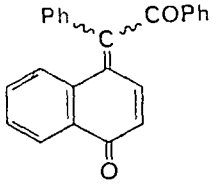
(71)



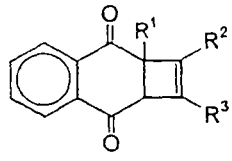
(72)

Despite the fact that addition of olefins to chloranil yields cyclobutanes (sections III.B and C), addition of diphenylacetylene, by irradiation in benzene with light of wavelength greater than 4000 Å, gives[31] the quinone methide **67** (R = Cl) and in this respect the reactivity of the excited chloranil system parallels that of the 1,4-benzoquinone one.

1,4-Naphthoquinone shows both types of reactivity towards diphenylacetylene, addition occurring cleanly[140] in acetonitrile to give a 4 : 1 mixture of the quinone methide **73** (both geometrical isomers are formed) and the cyclobutane **74** (R^1 = H, R^2 = R^3 = Ph). The latter compound and its methyl analogue (**74**; R^1 = H, R^2 = R^3 = Me) have been prepared independently[141] and a more detailed study[142] has shown that increasing the degree of methyl- or phenyl-substitution of the acetylenic component increases the proportion of quinone methide; acetylene itself gives the parent cyclobutene (**74**; R^1 = R^2 = R^3 = H) exclusively, although in poor yield[142].



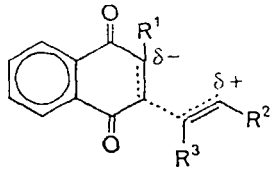
(73)



(74)

2-Acetoxy-1,4-naphthoquinone behaves analogously[140], although the ratio of the two types of adduct may be nearer to 1 : 1 and the overall rate of addition is less; the position of the acetoxy group in the corresponding quinone methide (as **73**) has not been established.

Photoaddition of diphenylacetylene to 2-methoxy-1,4-naphthoquinone is more rapid and there is no evidence for reaction at a carbonyl group; with light of wavelength greater than 4000 Å in acetonitrile as solvent, the adduct **74** (R^1 = OMe, R^2 = R^3 = Ph) was obtained in 76% yield[138,140], again suggesting predominantly π,π^* reactivity. Dipolar character in the excited state is indicated by the fact that addition of *p*-methoxyphenylphenylacetylene and *p*-cyanophenylphenylacetylene in each case gives[139] a mixture of the two possible cyclobutanes **74** (R^1 = OMe, R^2 = *p*-MeO·C_6H_4, R^3 = Ph *and* R^1 = OMe, R^2 = Ph, R^3 = *p*-MeO·C_6H_4) and **74** (R^1 = OMe, R^2 = Ph, R^3 = *p*-NC·C_6H_4 *and* R^1 = OMe, R^2 = *p*-NC·C_6H_4, R^3 = Ph) with the first indicated member of each pair predominating, possibly as a consequence of the greater stabilization of the dipole to be expected in the intermediate **75**, although the effect in the cyano-case is marginal, suggesting that the excited quinone is only weakly electrophilic and that stabilization of the intermediate diradical **76** may be of greater importance; a more pronounced orientational effect, in the direction indicated above, is observed[139] for the methoxyphenyl compound when the solvent is changed from acetonitrile to benzene.



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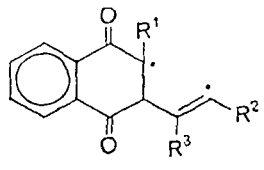
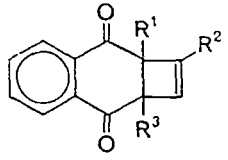


(76)

The proportion of cyclobutene formed by addition of acetylenes carrying, variously, hydrogen, methyl and phenyl groups is much greater for 2-methyl-1,4-naphthoquinone than it is for 1,4-naphthoquinone itself, and cyclobutenes are formed almost exclusively from 2,3-dimethyl-1,4-naphthoquinone[142]. This trend appears to parallel that described previously (section III.B) for the photoaddition of alkenes to 1,4-benzoquinone and its methyl homologues. For 2-methyl-1,4-naphthoquinone the ratio of quinone methide to cyclobutene is temperature-dependent[142]; the quinone methide is formed by addition to the 4-carbonyl group and the orientation of the cyclobutene appears to be governed by stabilization in the intermediate diradical **76** (R^1 = Me, R^2, R^3 = variously H, Me, Ph), the isomer derived from the most stabilized intermediate predominating to the extent of at least 6 : 1.

As in the 1,4-benzoquinone series, further irradiation of the cyclobutenes causes rearrangements of the type **77** → **78**, sometimes reversibly[143].

Cyclobutene-formation is not expected from 9,10-anthraquinone, and the quinone methides **79** are formed in yields of 40–90% with propyne, 2-butyne, phenylacetylene and diphenylacetylene[142]; there is evidence that addition of the latter compound may occur quantitatively[119].



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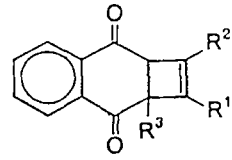
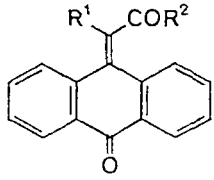


(78)

Tetrachloro-1,2-benzoquinone reacts photochemically with diphenylacetylene in acetone or acetonitrile (but not in benzene: see section IV) to give a mixture which may contain the polycyclic compound **80**, possibly formed by thermal addition of the quinone to the initial 1 : 1 photoadduct[122].



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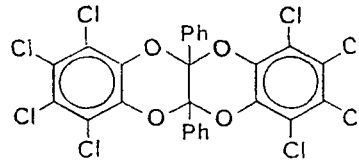
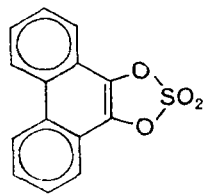


(80)

More detailed investigations will be required in order to elucidate the controlling factors.

E. Miscellaneous

Irradiation of 9,10-phenanthraquinone in benzene containing sulphur dioxide gives[144] the dioxathiole dioxide **81**, but the quinone does not react with triphenylphosphine in dry benzene[145]. However, if the benzene is wet, a compound formulated as the zwitterion hydrate **82** is formed in 63% yield; the initial step may be a reaction of the excited quinone with water[145] (section V.F).



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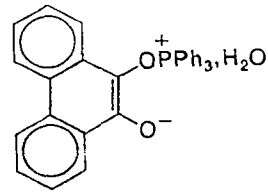
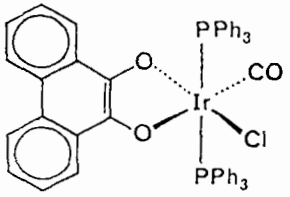


(82)

Photoaddition of 9,10-phenanthraquinone to the iridium compound $(Ph_3P)_2Ir(CO)Cl$ gives the cycloadduct **83**; 1,2-naphthoquinone behaves analogously[146]. Photoexcitation here appears to have the effect of increasing the oxidation potential of the quinone, since the addition fails in the dark but can be effected purely thermally with *o*-quinones of higher potential[147].

Photooxidation of 9,10-phenanthraquinone with oxygen in benzene or acetonitrile affords the anhydride **84** in unspecified yield[148].



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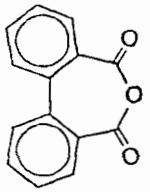


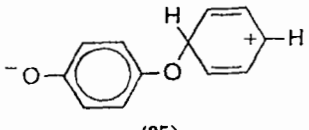
(84)

IV. ADDITION TO BENZENE

The role of benzene in quinone photochemistry is still something of an enigma and the mechanism or mechanisms by which it reacts with excited quinones are little understood except for systems containing acids.

Until 1966 benzene was considered to be an inert solvent for light-induced reactions of quinones initiated by visible light, but it was then reported[149] that irradiation of hydroxymethyl-1,4-benzoquinone in dry benzene with tungsten filament light gave phenoxymethyl-1,4-benzoquinone, although in low yield (see section VII.C for a discussion of the mechanism of this reaction). Further examples of the reactivity of benzene have since appeared[149a].

1,4-Benzoquinone is stable to irradiation with visible light in benzene solution and the absorption spectrum indicates the presence of the expected π-complex. However, when trifluoroacetic acid is present, *p*-phenoxyphenol is formed in good yield[150]. It is possible that the zwitterion **85** is produced by excitation of the π-complex and that its reversion to the starting materials is prevented by protonation; appropriate deprotonation then gives the phenoxyphenol.



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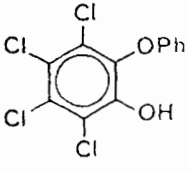


(86)

Irradiation of tetrachloro-1,2-benzoquinone in benzene containing *trans*-stilbene with light of wavelength greater than 4000 Å results in quantitative 4+2 cycloaddition of the olefin[121] (section III.B), but with *cis*-stilbene only traces of the stereoisomeric cycloadducts are formed, and the major product[122] is the ether **86**; a similar result is obtained when diphenylacetylene is present instead of *cis*-stilbene, but only a trace of the ether is formed when the quinone is irradiated in benzene alone. No explanation is available, although a side-reaction, e.g. Diels–Alder carbocycloaddition, between the quinone and the alkene or the alkyne to give a product which could lead to the formation of hydrogen chloride would put the reaction in the same category as that described in the preceding paragraph.

9,10-Phenanthraquinone is readily[151] photoreduced by benzene, and under nitrogen with light of wavelength longer than 3800 Å it gives[152] 13% of the phenyl ether analogous to **86**, together with the quinhydrone (10%) and biphenyl (19%). An addition–rearrangement sequence may be involved, but the formation of biphenyl strongly suggests the presence of phenyl radicals[152], although *direct* abstraction of hydrogen from benzene is unlikely.

Further work in this area could be profitable, particularly from a synthetical point of view.

V. REACTIONS INVOLVING ABSTRACTION OF HYDROGEN FROM SUBSTRATES

The basic principles of these reactions, which normally involve removal of hydrogen, either directly[152a], as H$^{\bullet}$, or indirectly via electron-transfer[152b] followed by proton-transfer, to give the neutral semiquinone, QH$^{\bullet}$, and a substrate radical from which the products are derived by ground-state reactions, have been described previously[5]. Recent work has provided further clarification of the mechanisms involved.

In general, *p*-quinones are reduced to the hydroquinone and the substrate is dehydrogenated, hydrocarbons yielding olefins or dehydrodimers and alcohols giving the corresponding aldehydes and ketones; 1 : 1 addition products, either acylhydroquinones or hydroquinone monoesters, predominate when the substrates are aldehydes. The formation of 1 : 1 adducts, either ketols or the hydroquinone monoethers or monoesters, is more common with *o*-quinones.

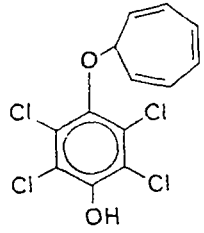
A. Hydrocarbons

Flash photolysis or continuous irradiation of duroquinone in cyclohexane or liquid paraffin with light of wavelength greater than 3300 Å

causes only slight dehydrogenation of the solvent; the trace of the hydroquinone which is formed acts as an inhibitor, facilitating deactivation of the excited quinone[153]. Flash photolysis in benzene or liquid paraffin produces a species which shows broad structureless absorption in the 4900 Å region and decays by a first-order process. It is formed in less than 10^{-7} s, which excludes the possibility of its being an isomer[153,154] (see section VII.A) or any other chemically different species; this, together with the results of quenching and related experiments, indicates that the transient is due to the triplet state of the quinone[64,65] and that the triplet is also the photoactive species[154].

The apparent anomaly[5] that singlet duroquinone is active in hydrogen abstraction has therefore been removed. However, the fact[153] that duroquinone is stable in cyclohexane when irradiated with light of wavelength greater than 3300 Å may be a consequence of the intensity of the light used, since it has been reported[155] that no change occurs with low-intensity light in the region 3000–4000 Å. This might suggest[65] that photoactivity at high light intensity is a consequence of the formation of an excited or higher triplet state. A further complication arises from concentration effects: duroquinone is reported[156] to be photoinert at 10^{-2}–10^{-3} molar in benzene, toluene, xylene and hexane.

Chloranil gives the ether **87** when irradiated in benzene containing cycloheptatriene[157]; scavenging of cycloheptatrienyl radicals by ground-state quinone may be involved.



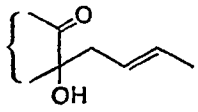
(87)

Electron spin resonance studies have shown that the triplet state of ubiquinone-6 (**5**; $n = 6$) in methylcyclohexane at 77 K decays by abstraction of hydrogen to give a neutral semiquinone[67].

The kinetics of photoreduction of 9,10-phenanthraquinone in the presence of toluene, ethylbenzene, isopropylbenzene and *t*-butylbenzene at 20, 40 and 60° have been studied, the rate of the reaction increasing progressively with temperature, although there is a slight anomaly with isopropylbenzene. The reactivity of the excited quinone with respect to abstraction of hydrogen from these substrates is greater than that of

triplet benzophenone, and lies between those of chlorine and fluorine atoms[151]. The major product is 9,10-dihydroxyphenanthrene; the others have not been identified.

The formation of dihydrodioxins and oxetans by irradiation of 9,10-phenanthraquinone in the presence of alkenes has been discussed in section III.B, but additional 1 : 1 adducts are formed when the alkene possesses readily abstractable, particularly allylic, hydrogen atoms. Thus with either *cis*- or *trans*-2-butene the ketols **88** and **89** are formed; analogous products are obtained from isobutene, 2-methyl-1-butene and 2,3-dimethyl-2-butene[125]. It has been suggested[125] that these compounds



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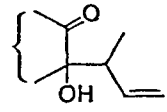
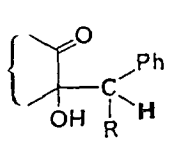


(89)

arise by combination of the neutral phenanthrasemiquinone radical with the allylic radical, in this case $MeCH{=}CH\dot{C}H_2 \leftrightarrow Me\dot{C}HCH{=}CH_2$, derived from the substrate, a mechanism the same as that previously proposed[158-160] to account for the formation of analogous ketols from 9,10-phenanthraquinone and toluene and related compounds.

The validity of this mechanism has recently been established[161-163] for toluene, ethylbenzene, diphenylmethane and similar compounds by means of CIDNP. Thus u.v. irradiation of a solution of 9,10-phenanthraquinone in the hydrocarbon concerned ($PhCH_2R$) in the cavity of a ^1H n.m.r. spectrometer causes enhancement of the resonance due to the proton **H** in the product **90**, the enhancement disappearing as soon as the u.v. irradiation is cut off, thus confirming the intervention of a solvent-caged pair (**91**) of unlike radicals, viz. the neutral semiquinone and the benzylic radical $Ph\dot{C}HR$ derived from the substrate. The reversibility[160] of the reaction under the influence of u.v. (but not visible) light has also been confirmed[164]: irradiation of the ketol **90** in the cavity of the spectrometer again causes enhancement of the signal due to the proton **H**. The ketols also dissociate thermally by the same mechanism, but the process is not reversible; the products are the quinhydrone and the dehydrodimer $(PhRCH{-})_2$ of the substate[164].



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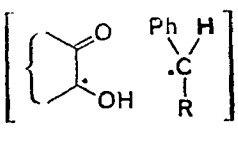


(91)

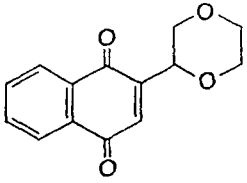
B. Ethers

It is generally accepted that the initial chemical step in light-induced reactions between *p*-quinones and ethers is abstraction of hydrogen from a position α- to the ether linkage to give the corresponding pair of radicals. The presence of the neutral benzosemiquinone radical in a system of this type has now been confirmed by e.s.r. spectroscopy, without resort to a flow technique, for 1,4-benzoquinone in the presence of 1,2-dimethoxyethane[165].

Duroquinone appears to be stable to irradiation in diethyl ether or tetrahydrofuran when its concentration is in the region 10^{-2}–10^{-3} molar, but some reaction occurs in dioxan, although the products have not been identified[156].

Fluoranil gives the corresponding neutral semiquinone when it is irradiated at 3380 Å in dioxan or tetrahydrofuran, but its e.s.r. spectrum is only detectable[35] in the presence of a trace of a proton acid such as trifluoroacetic.

Irradiation of 1,4-naphthoquinone in 1,4-dioxan with visible light gives[166] a 50% yield of the quinone **92**, which probably arises by ground-state oxidation of the initial 1 : 1 adduct by 1,4-naphthoquinone. It is the first dioxan-*p*-quinone adduct to be identified.



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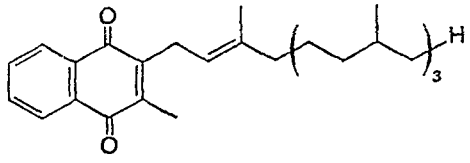
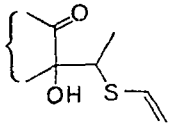


(93)

E.s.r. spectra accumulated by repetitive scanning indicate that phylloquinone **93** gives the corresponding semiquinone anion radical when it is irradiated in outgassed 1,4-dioxan[167], but the other products have not been identified.



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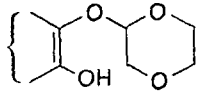

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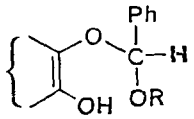


(96)

9,10-Phenanthraquinone gives the dihydrodioxin, by 4+2 cycloaddition, as the major product when it is irradiated in benzene containing ethyl vinyl sulphide, but the ketol **94**, as a mixture of stereoisomers, is

also formed[125], reactivity here resembling that with hydrocarbons (section V.A) rather than ethers which normally give phenanthrols, e.g. **95** from 9,10-phenanthraquinone and 1,4-dioxan[94]. Some aspects of the kinetics of the latter and related reactions have been described[151], but of greater importance is the report[168] that CIDNP is observed for the proton **H** in the products **96** formed from 9,10-phenanthraquinone and the ethers $PhCH_2OR$ ($R = CH_2Ph$, CH_2CH_2OPh, Ph and p-$C_6H_4OCH_2Ph$), thus establishing that the adducts are formed by cage-controlled radical pairing rather than by a concerted cyclic mechanism[5].

A convincing explanation for the differing modes of radical–radical combination, giving ketols from 9,10-phenanthraquinone and hydrocarbons and ethyl vinyl sulphide, but phenanthrols from the quinone and ethers, is still required.

C. Alcohols

As with ethers, the first chemical step involves abstraction of hydrogen from the α-position of the alcohol[5] and pulse radiolysis studies[169] of methanol solutions have now provided further evidence that the ultimate oxidation products arise by oxidation of the resulting hydroxyalkyl radicals by ground-state quinone:

$$R\dot{C}HOH + Q \longrightarrow RCHO + QH^{\bullet} \rightleftharpoons Q^{\bullet-} + H^{+}$$

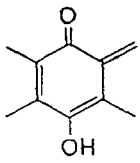
rather than by disproportionation[5]; dissociation of the neutral semiquinone radical is suppressed in acidic or non-polar media[170]. The alkoxide is involved in basic media[169].

A mechanism of this type accounts for the 'proton ejection' detected by pH measurements during intermittent visible-light irradiation of 1,4-benzoquinone in methanol or ethanol[171], an investigation which provided e.s.r. evidence for the presence of the semiquinone. It also lends general support to the suggestion[5] that light-induced cleavage of glycols of the form $ArRC(OH)-C(OH)RAr$ in the presence of quinones involves ground-state oxidation of radicals $ArR\dot{C}(OH)$, since it has now been demonstrated that pinacols of the form $Ar_2C(OH)-C(OH)Ar_2$ are only cleaved, ultimately to Ar_2CO with concomitant formation of the hydroquinone, when the pinacol is excited and thereby caused to dissociate; no reaction occurs when the quinone is selectively excited[172].

Nanosecond laser flash photolysis of 1,4-benzoquinone and its methyl homologues has been described[64], with particular reference to transient products absorbing in the 4900 Å region, where assignments for duroquinone systems have until recently (see below) been particularly confused. No

transient was detected for 1,4-benzoquinone in ethanol or water, or for toluquinone in ethanol or aqueous ethanol. 2,5-Dimethyl-1,4-benzoquinone did not show a transient in ethanol, but it did in 3 : 1 water–ethanol, its decay being first-order and its lifetime proportional to the concentration of water. The transient for 2,3-dimethyl-1,4-benzoquinone was longer-lived and could be detected in ethanol, whilst those of trimethyl-1,4-benzoquinone and duroquinone were progressively longer still; they decay to give the semiquinone[64].

Earlier flash photolytic work established that the 4900 Å transient observed for duroquinone in ethanol and 2-propanol is not due to the singlet[154, 173] and isomeric structures were suggested for it, e.g. **97** (references 153, 154) and **98** (reference 173). Evidence that it is really due to triplet duroquinone has been obtained[154, 174] and this assignment has since been confirmed[65, 156, 175].



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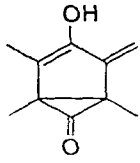


(98)

It is of interest that the lifetimes of the triplet states of the methyl homologues of 1,4-benzoquinone in ethanol appear to be enhanced by the presence of water, since it has been reported[175] that water quenches the triplet of duroquinone in 2-propanol. Both durohydroquinone and diduroquinone (see section VII.A) inhibit the photoreduction of duroquinone by alcohols[153, 175] and it has been suggested[175] that the hydroquinone acts as a hydrogen-source:

$$^3Q + QH_2 \longrightarrow 2\,QH^{\bullet} \longrightarrow Q + QH_2$$

The quantum yield[176] for disappearance of duroquinone in ethanol is 0·2. At a concentration not greater than 10^{-3} molar in 2-propanol the quantum yield[156] is 0·39 and the products are durohydroquinone and acetone exclusively, suggested to arise by simple disproportionation of the corresponding first-formed radicals; diduroquinone and three unidentified products appear at higher concentrations[156]. However, pulse radiolysis studies[169] indicate that duroquinone is capable of oxidizing hydroxymethyl radicals to formaldehyde and similar oxidation of 2-hydroxy-2-propyl radicals would therefore be expected, particularly since benzhydryl radicals ($Ph_2\dot{C}OH$) can be oxidized to benzophenone by ground-state duroquinone[177].

Irradiation of chloranil in methanol or ethanol gives the corresponding hydroquinone together with hydroxytrichloro-1,4-benzoquinone[178,178a]. The latter may be formed by attack of alcohol on the excited quinone followed by cleavage of the resulting alkoxytrichloro-1,4-benzoquinone; phenoxytrichloro-1,4-benzoquinone is formed when the quinone is irradiated in the presence of phenol[178a]. The chloranil–ethanol system, which has been reported to give predominantly the hydroquinone and acetaldehyde, has been studied[70] by flash photolysis at 3470 Å; the transient absorbing at 5000 Å is assigned to the triplet quinone and, as with duroquinone and 9,10-anthraquinone, the initial step in the dehydrogenation of the alcohol is probably[179–182] abstraction of hydrogen rather than electron-transfer.

Flash photolysis of a flowing chloranil–ethanol system in the cavity of an e.s.r. spectrometer[183] has provided further evidence for the presence of the semiquinone anion radical, which decays by a second-order process. The corresponding anion radical from fluoranil has also been detected[35] by e.s.r. for solutions in methanol, ethanol and 2-propanol. It probably arises by dissociation, $QH^{\bullet} \rightleftharpoons Q^{\bullet-} + H^{+}$, of the neutral semiquinone formed by direct abstraction of α-hydrogen rather than by electron transfer from the oxygen of the alcohol, although the relative importance of the latter process has yet to be determined with certainty.

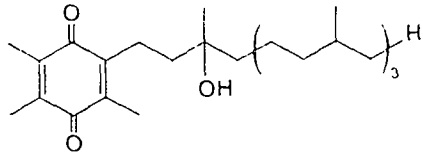
Laser flash photolysis of ubiquinone-6 (**5**; $n = 6$) in ethanol or 2-propanol and in ethanol–cyclohexane mixture shows that little ubisemiquinone is formed by reaction of the triplet with the alcohol, a conclusion supported by e.s.r. work[67]. The absorption spectra of the ubisemiquinone anion radical and the neutral semiquinone have been determined[184] by pulse radiolysis of methanol solutions containing, respectively, sodium hydroxide and sulphuric acid; in neutral and acidic media the quinone is reduced[169] by the hydroxymethyl radical:

$$Q + \dot{C}H_2OH \longrightarrow QH^{\bullet} + HCHO$$

and in basic media by the corresponding anion, $\dot{C}H_2O^{-}$. Disproportionation of ubisemiquinone-6 anion radical is slower than disproportionation of either benzosemiquinone or durosemiquinone anion radicals, possibly for steric reasons[169].

α-Tocopherolquinone **99** is consumed in ethanol, by irradiation at 2537 Å, with a quantum yield of $1{\cdot}1 \pm 0{\cdot}4$, giving the corresponding hydroquinone and a dihydrobenzofuran (section VII.C), flash photolysis suggesting the presence of the semiquinone in ethanol and the semiquinone anion radical in alkaline aqueous ethanol[167]; a transient possibly

due to a quinone methide was also detected. Phylloquinone **93** behaves similarly (see also section VII.B).



(99)

Photooxidation of alcohols sensitized by 9,10-anthraquinone sulphonates has continued to attract attention, particularly in relation to the phototendering of fabrics by anthraquinone dyestuffs. Relationships between phototendering and absorption spectra[185], fluorescence spectra[186] and free-radical formation[187] were described several years ago and the topic has recently been reviewed[188]. The photochemistry of dyes has also been reviewed[189].

The quantum yield of photoreduction of sodium 9,10-anthraquinone-2-sulphonate by alcohols in aqueous media is unity, and the initial chemical step is again considered to be direct transfer of a hydrogen atom from the α-position of the alcohol to the excited quinone[190,191]. The rate of the reaction is pH-dependent[192] and the triplet state of the quinone is involved[193]; at high concentrations, e.g. 4 molar, of primary and secondary alcohols in water, the quantum yield of photoreduction is approximately unity[190,192-195a].

At a quinone concentration of about 10^{-4} molar in an aerobic aqueous solution of an alcohol, the steps generally accepted to be involved are:

$$Q \xrightarrow{h\nu} Q^*$$

$$Q^* \longrightarrow Q$$

$$Q^* + RCH_2OH \longrightarrow QH^{\bullet} + R\dot{C}HOH$$

$$2\,QH^{\bullet} \longrightarrow QH_2 + Q$$

$$QH^{\bullet} + O_2 \longrightarrow Q + HO_2^{\bullet}$$

$$2\,HO_2^{\bullet} \longrightarrow H_2O_2 + O_2$$

$$Q + R\dot{C}HOH \longrightarrow QH^{\bullet} + RCHO$$

$$O_2 + R\dot{C}HOH \longrightarrow RCH(OH)O_2^{\bullet}$$

$$RCH(OH)O_2^{\bullet} + HO_2^{\bullet} \longrightarrow RCHO + H_2O_2 + O_2$$

$$2\,RCH(OH)O_2^{\bullet} \longrightarrow 2\,RCO_2H + H_2O_2$$

$$RCH(OH)O_2^{\bullet} \longrightarrow RCHO + HO_2^{\bullet}$$

Similar reactions occur when glycols and sugars are the substrates[196]. At higher concentrations of quinone and at low concentrations of alcohol, other reactions involving the water and leading to the formation of hydroxyanthraquinone sulphonates become of significance[193] (see section V.F).

Sodium 9,10-anthraquinone-2,6- and -2,7-disulphonates photooxidize methanol, ethanol and 2-propanol in anaerobic aqueous media to give the corresponding carbonyl compounds; the 1,8-disulphonate is inactive[197].

The longest wavelength absorption of 1-piperidino-9,10-anthraquinone in neutral ethanol is predominantly of the charge-transfer type and the quinone is therefore reduced[49, 198] only slowly. In an acidified medium, the nitrogen is protonated and n,π^* excitation occurs, leading to more rapid photoreduction. 1-Piperidino-9,10-anthraquinone reacts with aqueous alkaline 2-propanol by abstraction of hydrogen, but the 2-piperidino-quinone is thought to react by electron transfer from the hydroxyl oxygen to the excited charge-transfer state. In neutral solution, the 1-piperidino-compound abstracts hydrogen much more rapidly than does the 2-piperidino-isomer[49].

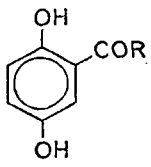
The case of photoreduction of a mixture of two quinones by an alcohol has been treated mathematically[199] and an overall kinetic scheme deduced for the twenty-four reaction steps considered, one of which is the now generally accepted oxidation of the hydroxyalkyl radical by ground-state quinone. The scheme has been applied[200] to the photoreduction of a mixture of 2-*t*-butyl-9,10-anthraquinone and 9,10-phenanthraquinone by ethanol.

The quantum yield of photoreduction of 9,10-phenanthraquinone, probably as the triplet, by 2-propanol in benzene at 4350 Å, giving 9,10-dihydroxyphenanthrene and acetone, is independent of the intensity of the incident light and increases with increasing concentration of alcohol, reaching a maximum of 1·6 in the pure alcohol[201]. This observation is reminiscent of an earlier one[202] that quantum yields of up to 4 can be obtained for photoreduction of the quinone in ethanol and, again, it suggests that the neutral semiquinone, possibly in a vibrationally excited state[201], is capable of abstracting hydrogen from the alcohol. This intermediate semiquinone can be stabilized as a relatively long-lived blue-green cation complex when the reducing medium is aqueous ethanol containing salts of divalent magnesium, calcium and zinc[203].

The 9,10-phenanthraquinone-2-propanol system appears to be somewhat anomalous in that the rate of photoreduction of the quinone is appreciably less at 40° than it is at either 20 or 60°; this result is stated[151] to be reproducible.

D. Aldehydes

Irradiation of 1,4-benzoquinone with visible light in acetaldehyde gives the ketone **100** (R = Me) as the predominant product; only a trace of the ester **101** (R = Me) is formed[204]. Acetyl radicals are produced by abstraction of formyl hydrogen from the aldehyde by the excited quinone and the products arise via scavenging of these radicals by ground-state quinone. With benzaldehyde as substrate, the ketone **100** (R = Ph) is still the major product, but the ester **101** (R = Ph) is formed in significant yield[205]. Electrophilic character of the derived aroyl radical, $ArC\dot{O}$, may be important, since *p*-formyl-, *p*-cyano- and *p*-trifluoromethyl-benzaldehyde all give the corresponding esters (**101**; R = *p*-$OHCC_6H_4$, *p*-NCC_6H_4 and *p*-$F_3CC_6H_4$) as the predominant products; benzaldehydes carrying electron-donor substituents at the *para*-position give radicals which appear to have nucleophilic character[205], since the main products are ketones (**100**; R = Ar).



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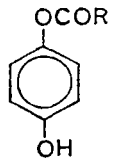

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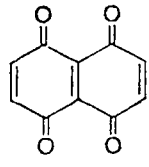


(102)

Electron-affinity of the quinone is also important, since 2,3-dicyano-1,4-benzoquinone, 1,4-benzoquinone-2,3-dicarboxylic anhydride and 1,4:5,8-naphthodiquinone (naphthazarinquinone, **102**), in which there are equal numbers of carbon and oxygen sites available for competitive scavenging to give either ketones (as **100**) or esters (as **101**), all give esters exclusively[206].

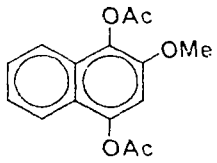
Irradiation of 1,4-benzoquinone in cinnamaldehyde gives the ester **101** (R = COCH=CHPh) as the only adduct, suggesting that not only the electron affinity of the quinone but also the ionization potential of the acyl radical may be important and that whenever the balance between these two factors is appropriate for electron transfer to occur from the radical to the quinone to give a radical ion pair ($Q^{\bar{\cdot}}$, $R\overset{+}{C}O$), both oxygen atoms of the quinone will be involved in the most stabilized (aromatic) system which can be produced and this will lead to ester formation. In support of this argument, irradiation of 1,4-benzoquinone in acraldehyde gives the ester (**101**; R = $CH{=}CH_2$) exclusively[206], although with crotonaldehyde both the ketone (**100**; R = CH=CHMe) and the ester

(**101**; R = CH=CHMe) are formed, in equal amounts, suggesting that the methyl group enhances the nucleophilic character of the acyl radical so that both direct and electron-transfer attack can occur competitively[206].

1,4-Naphthoquinone yields 2-acetyl-1,4-dihydroxynaphthalene when irradiated in acetaldehyde[207], but 5-hydroxy-1,4-naphthoquinone (juglone) is inert[206], presumably due to intramolecular deactivation of the excited state by the strongly hydrogen-bonded hydroxy group; 5-acetoxy-1,4-naphthoquinone gives the expected mixture of 2- and 3-acetyl-5-acetoxy-1,4-dihydroxynaphthalenes[206].

E. Anhydrides and Amides

Irradiation of 2-methoxy-1,4-naphthoquinone in acetic anhydride with light from a medium-pressure mercury arc filtered through Pyrex glass gives a mixture of the hydroquinone diacetate **103** and hydroxyketone **104**. It is suggested[208] that the quinone is reduced by abstracting hydrogen from the anhydride and that the resulting hydroquinone is then acylated in the normal way; the hydroxyketone **104** may arise from the ester **103** by a photo-Fries rearrangement.



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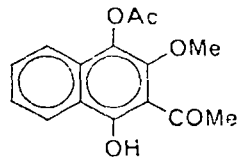


(104)

Irradiation of 1,4-benzoquinone and sodium 9,10-anthraquinone-2-sulphonate severally in the presence of dimethylformamide and *N*-ethylacetamide gives the semiquinones, detected[171] by e.s.r., possibly via abstraction of hydrogen α- to nitrogen since disodium 9,10-anthraquinone-2,6- and -2,7-disulphonates have been reported[197] to yield enamides ($R^1CONHCH{=}CHR^2$) when irradiated in anaerobic aqueous solutions of *N*-ethylacetamide and *N*-(*n*-propyl)propionamide, and a range of *N*-alkylamides ($R^1CONHCH_2R^2$) has been converted[209] into the corresponding *N*-acylamides ($R^1CONHCOR^2$) by irradiation in the presence of oxygen and either 2-methyl-9,10-anthraquinone or disodium 9,10-anthraquinone-2,6-disulphonate.

The photoreduction of 1-piperidino-9,10-anthraquinone in the presence of polyamides has been examined[198] in relation to the phototendering of nylon and related fibres by anthraquinone dyestuffs.

F. Water

Water can often be used as an inert solvent for substrates of high reactivity such as primary and secondary alcohols (section V.C), but it is not always inert under conditions where no other material is available for reaction with excited quinone. Thus 1,4-benzoquinone yields 1,2,4-trihydroxybenzene as the primary product when its aqueous solution is irradiated[210,211] with u.v. light, although hydroquinone has also been isolated[211a], in 37% yield.

Nanosecond laser flash photolysis of aqueous 1,4-benzoquinone does not reveal a transient in the 4900 Å region due to the triplet, but a transient showing first-order decay can be observed[64] for toluquinone; transients can also be detected for aqueous solutions of 2,3- and 2,5-dimethyl-1,4-benzoquinone, trimethyl-1,4-benzoquinone and duroquinone. No neutral semiquinone has been detected for aqueous trimethyl-1,4-benzoquinone, although it can be readily observed when ethanol is present[64].

Irradiation of sodium 9,10-anthraquinone-2-sulphonate in water with visible light was at first[212] thought to yield 2-hydroxy-9,10-anthraquinone, but it was later shown[213] that a mixture of hydroxy-9,10-anthraquinone-2-sulphonates was formed, the composition of the mixture being identical with that obtained by treating the aqueous quinone with Fenton's reagent[213-215]. Hydroxylation occurs mainly at the α- and β-positions of the unsulphonated ring and in aqueous sodium hydroxide is predominantly at the β-position. At high quinone and low oxygen concentration, monohydroxylation predominates and occurs exclusively in anaerobic media; dihydroxylation predominates at low quinone and high oxygen concentration[215]. It has been suggested[214] that the excited quinone abstracts hydrogen from the water to give the neutral semiquinone and a hydroxy radical, which then attacks ground-state quinone; a similar suggestion has been made[216] for the 1-sulphonate and the 2,6- and 2,7-disulphonates. However, although the results obtained with Fenton's reagent support the view that hydroxy radicals are involved, direct abstraction of a hydroxylic hydrogen atom is not energetically favourable and evidence has recently been obtained[193,217,217a] which suggests that at quinone concentrations greater than 10^{-3} molar there is appreciable interaction between excited quinone and ground-state quinone, giving, by electron transfer, a cation radical and an anion radical, the latter having been detected by e.s.r. The production of hydroxy radicals then becomes, more favourably, an

essentially ionic process in which there is electron transfer from hydroxyl ion to the quinone cation radical. The overall, simplified, sequence is then:

$$Q^* + Q \longrightarrow Q^{\bullet-} + Q^{\bullet+}$$

$$Q^{\bullet-} + Q^{\bullet+} \longrightarrow 2\,Q$$

$$H_2O \rightleftharpoons HO^- + H^+$$

$$Q^{\bullet-} + H^+ \longrightarrow QH^\bullet$$

$$2\,QH^\bullet \longrightarrow QH_2 + Q$$

$$2\,Q^{\bullet-} \longrightarrow Q^{2-} + Q$$

$$Q^{\bullet+} + QH^\bullet \longrightarrow 2\,Q + H^+$$

$$Q^{\bullet+} + HO^- \longrightarrow Q + HO^\bullet$$

$$Q + HO^\bullet \longrightarrow (QOH)^\bullet$$

$$(QOH)^\bullet + Q \longrightarrow QOH + QH^\bullet$$

where $(QOH)^\bullet$ represents the quinone-hydroxy radical adduct and QOH the hydroxyquinone derived from it by removal of a nuclear (α- or β-position) hydrogen atom. An additional series of steps, accounting for the formation of hydrogen peroxide, can be envisaged for systems containing oxygen:

$$Q^{\bullet-} + O_2 \longrightarrow Q + O_2^{\bullet-}$$

$$2\,O_2^{\bullet-} \longrightarrow O_2^{2-} + O_2$$

$$QH^\bullet + O_2 \longrightarrow Q + HO_2^\bullet$$

$$2\,HO_2^\bullet \longrightarrow H_2O_2 + O_2$$

$$(QOH)^\bullet + O_2 \longrightarrow QOH + HO_2^\bullet$$

Reactions such as these account for the kinetics observed over the pH range 3–11 (the rate increases with increasing pH), but they do not account for them outside this range. An additional equation

$$Q^{\bullet+} + X \longrightarrow Q + X^{\bullet+}$$

in which X is not defined has been introduced[193] to cover this.

Some doubt has recently been cast[68] on the validity of the step involving electron transfer from ground-state to excited quinone and the above scheme may therefore require revision. However, an alternative, and energetically acceptable, mechanism for the formation of the hydroxy radical involves electron transfer from the hydroxyl anion to the excited quinone, a suggestion made[218] over 20 years ago and since supported[219–223] for a variety of 9,10-anthraquinones in aqueous media (see also section VI).

2-Piperidino-9,10-anthraquinone in alkaline aqueous ethanol is reduced by electron-transfer from hydroxide and ethoxide to the charge-transfer state of the quinone[224].

9,10-Phenanthraquinone appears to be photoreduced in aqueous benzene, but no product has been characterized[145] and the role of the benzene is uncertain.

VI. MISCELLANEOUS SYSTEMS

Irradiation of a mixture of 1,4-benzoquinone and 2-methyl-3-nitrocyclohexene in benzene gives[224a] a low yield of 4-(2-methyl-3-cyclohexenyloxy)-2-nitrophenol, possibly via transfer of $\dot{N}O_2$.

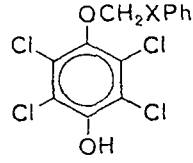
1,4-Benzoquinone, chloranil, 9,10-anthraquinone and 9,10-phenanthraquinone photosensitize[225] the decarboxylation of α-substituted acetic acids:

$$R{-}X{-}CH_2CO_2H \longrightarrow R{-}X{-}CH_3{+}CO_2$$

where X = O, S or NH. The reaction may involve excitation of a substrate–quinone complex, followed by transfer of a nonbonding electron from X to the quinone and subsequent proton transfer to the resulting semiquinone anion radical:

$$RXCH_2CO_2H, Q \xrightarrow{h\nu} \dot{R}\overset{+}{X}CH_2{-}CO{-}O{-}H{\cdot}Q \longrightarrow RX\dot{C}H_2{+}QH^{\bullet}$$

The intervention of radicals such as $RX\dot{C}H_2$ is supported by isolation of the ethers **105** (X = O or S) from decarboxylations of $PhXCH_2CO_2H$ sensitized by chloranil; the radicals are probably scavenged by ground-state quinone.



(105)

Photoexcited fluoranil abstracts hydrogen from chloroform and dichloromethane to give the neutral semiquinone, which has been detected[35] by e.s.r., but the other products have not been identified.

Chloranil acts as a photosensitizer for the dimerization of 9-vinylcarbazole to *trans*-1,2-dicarbazolylcyclobutane. The rate of dimerization is enhanced by the presence of oxygen. A cation–radical chain mechanism, initially involving electron transfer from the enamine to the excited quinone, may be involved[226]. Several benzoquinones, 1,4-naphthoquinones

and 9,10-anthraquinones act as photosensitizers for the cleavage, to monomer, of 1,3-dimethyluracil photodimers[226a], and a CIDNP study of the cleavage of thymine dimers by sodium 9,10-anthraquinone-2-sulphonate indicates that electron transfer from dimer to quinone is involved[226b] (cf. reference 152b).

In contrast to the clean reactions between *o*-quinones and $(Ph_3P)_2Ir(CO)Cl$ (section III.E), chloranil gives a mixture of unidentified products[146].

The generation of free radicals in systems containing sodium 9,10-anthraquinone-2-sulphonate and the disodium 2,6-disulphonate (sections V.E and F) is further supported by the ability of these quinones to act as sensitizers for the polymerization of methyl acrylate and methacrylate[227].

Irradiation of several 9,10-anthraquinone mono- and disulphonates in aqueous hydrogen chloride produces chlorine and chloroanthraquinones in which the sulphonyl groups have been replaced by chlorine[228, 229], a known ground-state chlorination reaction in this series. Aqueous hydrogen bromide is similarly oxidized[229].

Flash photolysis indicates that in aqueous media at pH 6·5, triplet 9,10-anthraquinone-2,6-disulphonic acid will accept electrons from a variety of anions (X^{n-}), such as halide, carbonate, sulphate, nitrate, phosphate, acetate and hydroxide, according to the scheme:

$$Q + X^{n-} \xrightarrow{h\nu} Q^{\bullet-} + X^{\bullet(n-1)-}$$

Electron transfer from bromide and iodide is less efficient than that from chloride due to heavy-atom facilitation of the $T_1 \rightarrow S_0$ process[230].

Irradiation of a solution of 2-methoxy-9,10-anthraquinone in aqueous acetonitrile containing ammonia gives a 70% yield of 1-amino-2-methoxy-9,10-anthraquinone[230a], the rate of amination being accelerated by oxygen (see also section VII.D).

Some studies related to those involved in biological electron transfer have been described, e.g. the conversion of zinc chlorin to zinc porphin by irradiation in the presence of *o*- and *p*-quinones[231, 232], proton-ejection from tetraphenylporphin in the presence of 1,4-benzoquinone[233] and photobleaching and related reactions of chlorophyll-*a* in the presence of 1,4-benzoquinone, substituted 1,4-benzoquinones and 1,4-naphthoquinones[234–237], but the role of excited quinones under these conditions may be minimal.

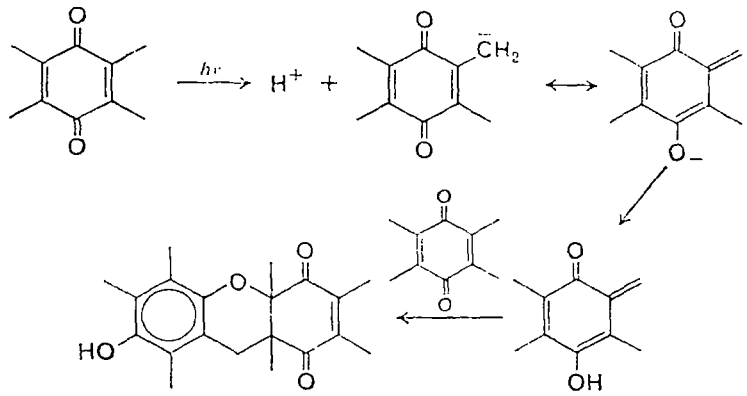
Visible-light irradiation of 3,5-di-*t*-butyl-1,2-benzoquinone in oxygenated methanol gives a low yield of 2,4-di-*t*-butyl-4-carboxymethyl-2-buten-4-olide[237a].

VII. REACTIONS INVOLVING SUBSTITUENTS

Several reactions involving abstractions of hydrogen from the side-chains of quinones have been reviewed previously[5] and interest in the photochemistry of these and related systems has continued. Considerable progress has been made in some areas, particularly that of the *t*-butyl-1,4-benzoquinones and the concept of spirocyclopropane intermediates, either as such or as diradicals or zwitterions, which has arisen particularly in connexion with these systems may well be applicable to a much wider range of quinones provided that there is an abstractable hydrogen atom at the β-position of the side-chain. However, the factors governing many of the reactions are still far from clear. There are no examples involving *o*-quinones.

A. Saturated Substituents

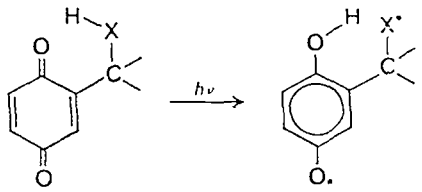
The photochemistry of duroquinone has attracted a great deal of attention and the isomeric quinone methide structure **97** has frequently, and erroneously, been assigned to the 4900 Å transient observed during its flash photolysis in alcohols (section V.C), which leads to the hydroquinone and diduroquinone **106**, the ground-state dimer of the quinone methide. The most recent results[64] in this area favour *proton* loss from $^3(\pi, \pi^*)$ duroquinone in ethanol and related polar media to give an anion from which the tautomer, and hence diduroquinone, can readily be obtained:



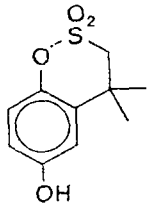
(106) (97)

A mechanism of this type is consistent with the absence of the dimer **106** when the photolysis is carried out in non-polar media, since ionization would not be favoured under these conditions[64].

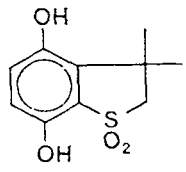
Evidence for analogous ionic intermediates in the photolysis of other alkylquinones has not been obtained, and abstraction of a hydrogen *atom* from the β-position of the side-chain, via a favourable six-membered transition state, is generally preferred (X = CR^1R^2 or O):



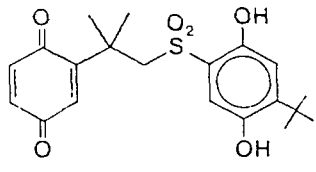
Support[238] for this comes from the irradiation of *t*-butyl-1,4-benzoquinone in the presence of sulphur dioxide at $-50°$, giving the systems **107–110**, all of which can be accounted for by scavenging of the primary alkyl radical **111** by sulphur dioxide to give the radical **112** which then cyclizes, or gains hydrogen to form the sulphinic acid from which **109** and **110** can be derived by normal addition to ground-state quinone. 2,5-Di-*t*-butyl-1,4-benzoquinone behaves similarly.



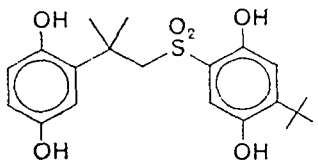
(107)



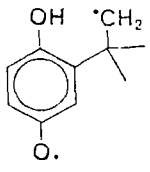
(108)



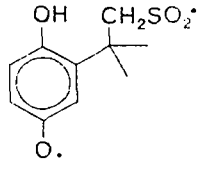
(109)



(110)



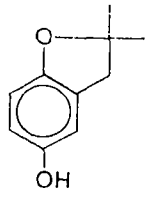
(111)

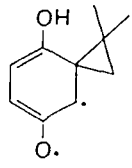


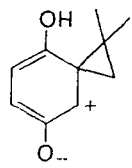
(112)

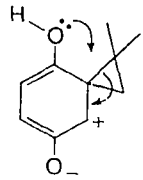
The dihydrobenzofuran **113**, containing a rearranged side-chain skeleton, is also formed, by a competitive process in which the diradical **111** probably undergoes intramolecular cyclization to yield the spirocyclopropane **114**; electron-demotion to give the zwitterion **115** followed by ring-opening (as **116**) of the cyclopropyl carbonium ion system is envisaged to complete the process.

Dihydrobenzofuran formation need not be concomitant with ring-opening, however, since irradiation of *t*-butyl-1,4-benzoquinone in ethanol gives[239,240] both the dihydrobenzofuran **113** and the ether **117** (R = Et),

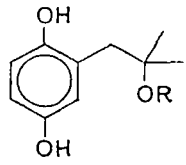

(113)

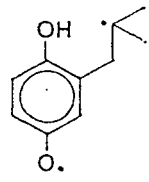

(114)

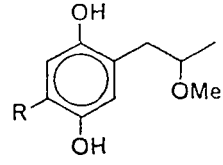

(115)


(116)

the production of the latter compound suggesting that, when appropriate, solvent participation can compete. Analogous ethers are formed[241] when the quinone is irradiated in methanol and in 2-propanol, but when 2-methyl-2-propanol is used the major product is the alcohol **117** (R = H), possibly arising from reaction with water since the yield is reduced when the irradiation is carried out in the presence of anhydrous magnesium sulphate and increased (to 72%) when the solvent is aqueous 2-methyl-2-propanol.


(117)

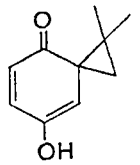

(118)


(119)

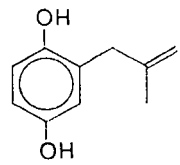
Further support for this mechanism comes from the observation[240] that both *t*-butyl- and isobutyl-1,4-benzoquinone give the same ether (**117**; R = Et) when they are irradiated in ethanol, the diradical **118** from the isobutyl compound cyclizing to the same intermediate spirocyclopropane (**114**) as that formed from the *t*-butyl isomer. Similarly, irradiation[240] of 2,5-di-*n*-propyl-1,4-benzoquinone and 2-isopropyl-5-methyl-1,4-benzoquinone (thymoquinone) in methanol gives, respectively, the ethers **119** (R = *n*-Pr) and **119** (R = Me) in which the alkoxylated side-chains have identical carbon skeletons.

Direct spectroscopic evidence for the intervention of diradical **114** or zwitterionic **115** species is not available and flash photolysis experiments with *t*-butyl-1,4-benzoquinone have given transients with lifetimes too short to be reliably studied with the equipment currently available[68]. However, it appears that neither the diradical nor the zwitterion is an essential intermediate since, for example, the ether **117** (R = Et) can

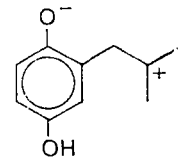
also be obtained by irradiating *t*-butyl-1,4-benzoquinone in 1,2-dimethoxyethane at −80°, cutting off the light and then adding ethanol and allowing the system to warm to room temperature, which indicates the presence of a long-lived reactant. It has been suggested[242] that this may be the spirocyclopropane **120**, from which the olefin **121**, which is also formed, could be derived via the abnormal Claisen rearrangement and the other products via spontaneous (to give **122**) or reactant-assisted ring-opening.



(120)

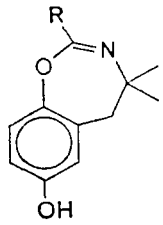


(121)

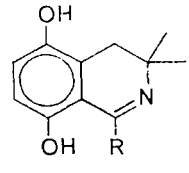


(122)

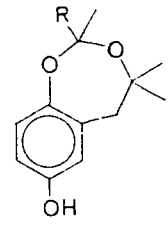
Mechanisms of this type also account for the formation of cyclic addition compounds, often in high yield, when *t*-butyl-1,4-benzoquinone is irradiated with visible light in the presence of acetonitrile or benzonitrile[242], giving **123** (R = Me or Ph) and **124** (R = Me or Ph), acetone[242], giving **125** (R = Me) and **126**, and acetaldehyde[241], giving the dioxepin **125** (R = H); under the latter conditions the dihydrobenzofuran **113** and the alcohol **117** (R = H) are also formed, but addition of water to the acetaldehyde completely suppresses formation of the dioxepin and the alcohol becomes the major product[241].



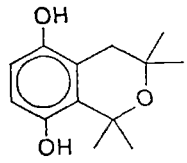
(123)



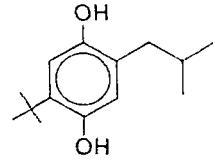
(124)



(125)



(126)

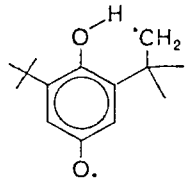


(127)

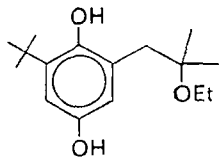
2,5-Di-*t*-butyl-1,4-benzoquinone gives analogous compounds when irradiated in the presence of alcohols and acetic acid[239], nitriles[242], acetone[242] and acetaldehyde[241]. However, when it is photoreduced with visible light in 1,2-dichloroethane, the yield of the hydroquinone **127**,

with one rearranged side-chain, is very much temperature-dependent[212], being about 10% at −40° and about 90% at 60°; no explanation has been offered.

In contrast to the above reactions, which usually proceed cleanly and in good yield, comparable irradiation of 2,6-di-*t*-butyl-1,4-benzoquinone in acetaldehyde causes extremely slow consumption of the quinone, ultimately yielding several, unidentified, products[241]. This may be a consequence of buttressing by the 6-*t*-butyl group rendering the initial abstraction of hydrogen from the 2-*t*-butyl group, giving the diradical **128**, strongly reversible, but, unless there are appreciably different solvation effects, it does not explain why this quinone readily yields the ether **129** when it is irradiated[241] in ethanol. Such solvation effects are not readily apparent in the ground state: the absorption spectra of the three *t*-butyl-1,4-benzoquinones are very similar in ethanol[239] and acetaldehyde[241].



(128)



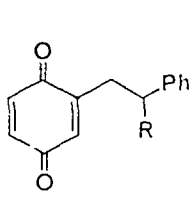
(129)

Irradiation of the above *t*-butyl-1,4-benzoquinones in benzene gives tars and low yields of the corresponding hydroquinones, dihydrobenzofurans (as **113**) and alkenes (as **121**), together with a range of related compounds[241].

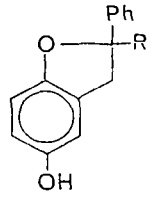
It is clear that the cleanest and synthetically most useful reactions of the *t*-butyl- and analogous 1,4-benzoquinones are to be expected in polar media which can facilitate the formation and reactions of (probably) zwitterionic species. However, higher yields of some products can be obtained in benzene solution when the radical resulting from abstraction of β-hydrogen from the side-chain is more stabilized. Thus the phenethylquinones **130** (R = H and Ph) give the dihydrobenzofurans **131** (R = H and Ph) in yields of 20 and 17% respectively when irradiated with visible light[243], although the mechanism may be different, e.g. these products would also be expected if the abstraction were *inter*molecular.

Photooxidation of 1- and 2-methyl-9,10-anthraquinones with air in acetic acid gives[228] the corresponding carboxylic acids and dehydrodimers (viz. $2\,QCH_3 \rightarrow QCH_2CH_2Q$), the formation of the latter indicating the intervention of the derived alkyl radicals. When irradiated in alcoholic

solution, however, 1-methyl-9,10-anthraquinone suffers photoenolization (to **132**) with participation of the hydroxyl hydrogen of the alcohol[87].

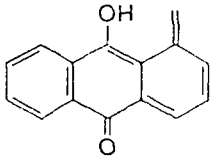


(130)

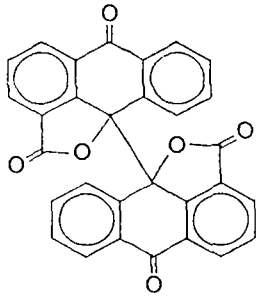


(131)

When oxygenated benzene is the solvent, the products are 9,10-anthraquinone, its 1-carboxylic acid and the bis-lactone **133**; again, photoenolization may be involved[244].



(132)

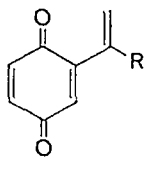


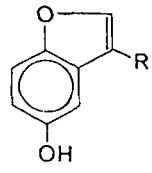
(133)

B. Olefinic and Benzenoid Substituents

Earlier work in this area[5] showed that irradiation of alkenyl-1,4-benzoquinones frequently resulted in cyclization to give benzofurans, chromenols and dihydronaphthalenes, sometimes in high yield. These studies have been continued, but the most significant trend has been towards an examination of the products obtained, under both anaerobic and aerobic conditions, from the irradiation of naturally occurring quinones carrying more complex side-chains.

Irradiation of isopropenyl-1,4-benzoquinone **134** (R = Me) with visible light gives a good yield of the benzofuran **135** (R = Me), and it was suggested[149] that this might arise via *inter*molecular abstraction of hydrogen from the allylic methyl group to give the radical **136** followed by cyclization and isomerization, but a favoured mechanism involved intramolecular cycloaddition (cf. section III.B) to give the spiro-oxetan **137** which then rearranged as shown.


(134)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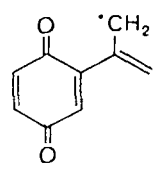
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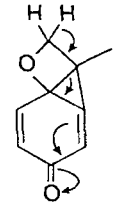
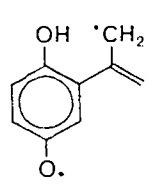
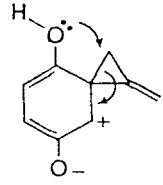

(137)

The advent of the spirocyclopropane intermediate (section VII.A) has since provided an attractive alternative pathway via the diradical **138** and the spiro-compound **139**, as shown. The effect of other R groups in **134**

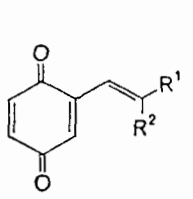

(138)


(139)

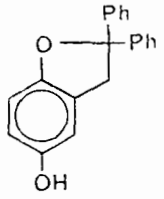
has therefore been examined[245,246]. Vinyl-1,4-benzoquinone (**134**; R = H gives only dark amorphous material, but the phenyl compound **134** (R = Ph) gives the corresponding benzofuran **135** (R = Ph), although in lower yield than the methyl analogue, indicating that the reaction is very much substituent dependent, but that an abstractable hydrogen atom in the side-chain is not a prerequisite. Irradiation of the deuteriomethyl compound **134** ($R = CD_3$) readily gives the corresponding benzofuran (**135**; $R = CD_3$) *without* scrambling of the label, thus making intermediates such as **136** and **138** seem unlikely, and lending indirect support to the pathway involving the cycloadduct **137**. It may be significant that the sp^2 hybridization of the α-carbon atom in the isopropenyl systems increases the O···H distance in the transition state for intramolecular hydrogen abstraction compared with that in *t*-butyl-1,4-benzoquinone, although adoption of the *s-trans* conformation may be a more important factor.

Both *cis*- and *trans*-styryl-1,4-benzoquinones (**140**; $R^1 = H$, $R^2 = Ph$ and $R^1 = Ph$, $R^2 = H$) afford[243] only amorphous material when irradiated in benzene with visible light, but the diphenyl compound (**140**; $R^1 = R^2 = Ph$) gives a low yield of the dihydrobenzofuran **141**.

Irradiation of plastoquinone-1 (**142**) in benzene under nitrogen gives[247] the naphthoquinone **143**, the chromenol **144** and the benzoxepin **145**, and these products are also formed, together with a mixture of two stereoisomeric dimers **146**, when the solvent is 2-propanol; the maximum yield

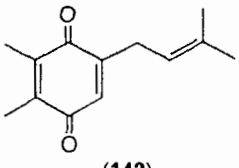


(140)



(141)

of any one of these products is about 10%. In contrast, irradiation in methanol gives 64% of the dihydrobenzofuran **147** (R = Me), and in aqueous acetonitrile 86% of the related hydroxy compound **147** (R = H);



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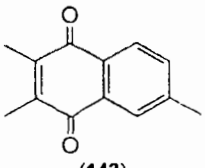

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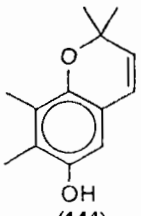

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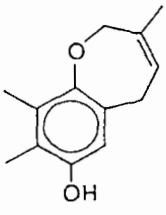

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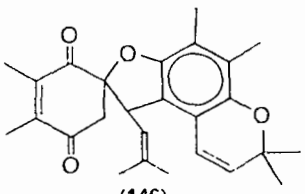

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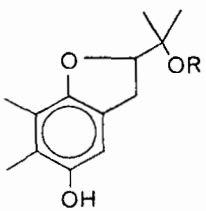

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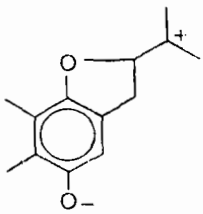

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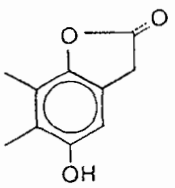
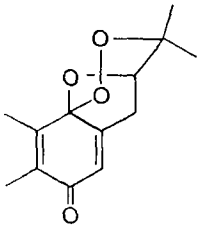


(149)

it is suggested[247] that these may arise from the zwitterion **148**, the formation of which would, as for the *t*-butyl-1,4-benzoquinones (section VII.A), be favoured by the polar media. A dimer isolated from the products of irradiation of plastoquinone-1 in benzene has been characterized by X-ray crystallography[247a].

The peroxide **150** is the major product when plastoquinone-1 is irradiated in benzene or 2-propanol under oxygen and interaction of the zwitterion **148** with ground-state oxygen may be involved; the coumaranone **149** is also formed. The peroxide **150** is not obtained when the solution contains methylene blue or eosin, suggesting that it is not derived from singlet oxygen by a stepwise pathway, but this experiment does not rule out the possibility of a concerted process (cf. the photooxidation of compound **162** described in this section, and also section VII.F).



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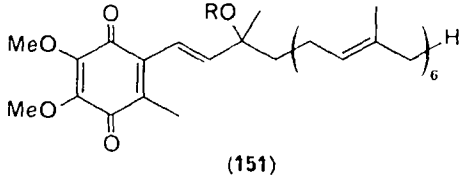

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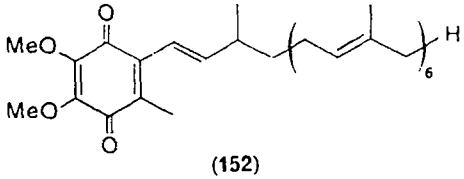
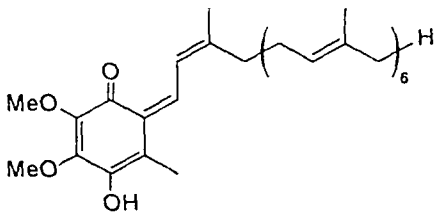


(152)

Pulse radiolysis[169,184] of ubiquinone-6 (**5**; $n = 6$) in methanol has given the absorption spectra of the semiquinone anion radical and the neutral semiquinone and flash photolysis[67] in alcohols and hydrocarbons has allowed the transient due to the triplet to be identified, but no other products have been characterized.

Further investigation of the photochemistry of ubiquinone-7 (**5**; $n = 7$) in methanol and ethanol has shown[248] that the ethers **151** (R = Me and Et) are formed rather than the iso-ubiquinone **152** previously suggested[249]; conjugate addition of the alcohol to a quinone methide intermediate **153**, possibly formed as suggested for duroquinone methide (section VII.A), may be involved, although the intervention of zwitterions has not been excluded. When the irradiation is carried out in aerated alcohols the products are the corresponding chromenol **154** and demethylated compounds[250,251], as previously reported[252,253]. These substances are also formed when the quinone is exposed to air and sunlight in the absence of solvent, but they are accompanied[251] by the alcohol **151** (R = H), the hydroperoxide **151** (R = OH) and a mixture of two uncharacterized



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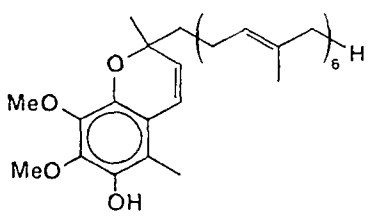
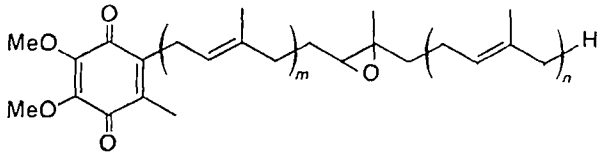


(154)

epoxides **155** ($m+n=6$). Photoreduction of ubiquinone-7 under more biological conditions has been described[254], but chemical details are lacking.



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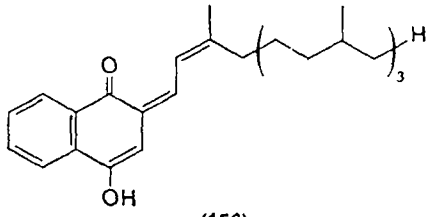
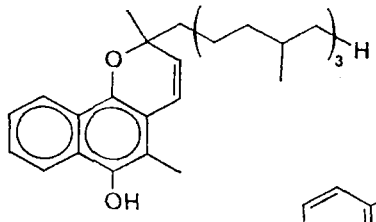


(156)

Phylloquinone, **93**, and the ubiquinones, **5**, are structurally similar to plastoquinone-1, **142**, with respect to the first five carbon atoms of the side-chain and their photochemistry is also similar in several respects. Irradiation of phylloquinone in a hydrocarbon medium causes fluorescence from an unidentified species which is not affected by oxygen[255]. Electron spin resonance indicates that the semiquinone anion radical is formed when outgassed dioxan is the solvent[167] and flash photolysis shows that the same species is present in ethanol, together with, possibly, the quinone methide **156**; this is present as its enolate anion in 10% aqueous ethanol at pH > 10. The neutral quinone methide **156** is probably also formed in dioxan and heptane. The chromenol **157** is a product of irradiation in benzene or 2-propanol[256,257].

The hydroperoxide **158** (R = OH) is formed when phylloquinone is irradiated in oxygenated hexane at 3600 Å and at 7000 Å when methylene blue is present[258], suggesting that it arises via an ene-reaction with singlet oxygen. The hydroperoxide itself is unstable at 3600 Å and is cleaved[258] to the ketone **159** (phytone). The same hydroperoxide can be obtained in greater than 50% yield by methylene blue-sensitized oxidation in 2-propanol[247].

The ketone **159**, the hydroperoxide **158** (R = OH) and the corresponding alcohol (**158**; R = H), and the coumaranone **160**, presumably derived by photocyclization of a side-chain fragmentation product, have



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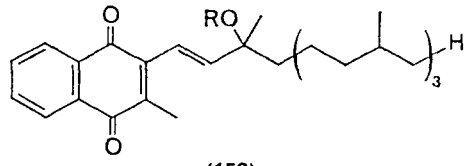

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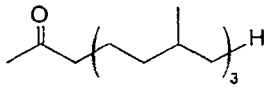

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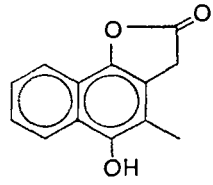

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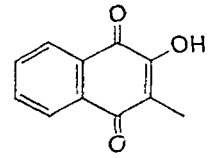
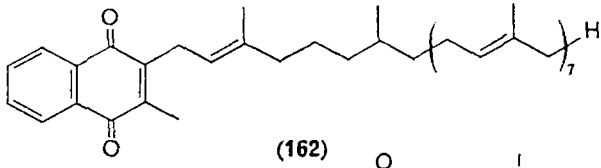


(161)

been obtained by photooxidation of phylloquinone in benzene[259,260], and these products, together with phthiocol, **161**, are also formed in ethanol and when the quinone is irradiated in air in the absence of solvent[260,261].

Irradiation of the polyunsaturated system **162** in oxygenated hexane with light of wavelength 3600 Å gives 8% of the expected 3′-hydroperoxide, and 50% of the ketone **163**, indicating that oxygenation occurs with high specificity at $C_{(3)}$ of the side-chain despite the availability elsewhere of suitable sites for attack. This suggests that if singlet oxygen is involved, it remains in close proximity to the nucleus of the quinone sensitizer rather than diffusing away; a concerted process may be involved[258].



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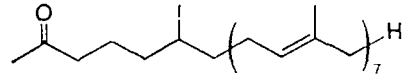
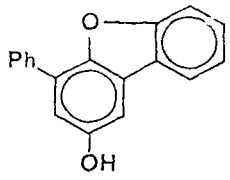


(163)

In contrast to irradiation in benzene, which yields a dimer (section III.A), irradiation[106] of 2,6-diphenyl-1,4-benzoquinone in acetonitrile, methanol or acetic acid leads smoothly and rapidly to the dibenzofuran **164**; intramolecular charge-transfer, facilitated by the polar medium, may be involved, and for the photocyclizations in methanol and acetic acid there is potential similarity with the proton-assisted photoadditions of benzene discussed in section IV.



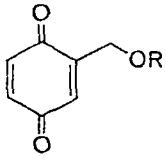
(164)

C. Hydroxy-bearing Substituents

Unlike other simple 1′-hydroxyalkyl-1,4-benzoquinones which are inert to the solvent when irradiated with visible light in benzene, and give high yields of the corresponding acylhydroquinones (**100**) by an oxidation–reduction process[5], hydroxymethyl-1,4-benzoquinone (**165**; R = H) gives[149] a low yield of the phenoxymethyl compound **165** (R = Ph), and it has been suggested that attack of the alkoxy radical **166** on the solvent may be involved. An intramolecular path (as **167**) for rearomatization is then possible. However, this is not supported by the results[245,246] of irradiation of the quinone in hexadeuteriobenzene, which yields the pentadeuteriophenoxy compound **165** ($R = C_6D_5$) without incorporation of deuterium into the quinonoid ring. Intermolecular hydrogen transfer from an intermediate such as **167** might therefore be involved. However, the presence of a methyl group *ortho* to the hydroxymethyl group has a pronounced effect: irradiation of a benzene solution of 2-hydroxymethyl-3-methyl-1,4-benzoquinone gives 30% of the aldehyde **168** (R = Me), with no evidence for the formation of a phenoxy product; both the 5- and 6-methyl homologues of hydroxymethyl-1,4-benzoquinone give low yields of the corresponding phenoxymethyl compounds, but the aldehydes were not detected[245,246]. No satisfactory interpretation is available.

Support for a pathway involving the formation of alkoxy radicals (as **166**) comes from studies[262,263] with side-chain-substituted 1′-hydroxyalkyl-1,4-benzoquinones (**169**) in which at least one of the substituents R^1 and R^2 is potentially a good leaving-group. Thus irradiation of the quinone **169** ($R^1 = H$, $R^2 = CH_2Ph$) in benzene with visible light gives

2,5-dihydroxybenzaldehyde (**168**; R = H), its benzyl homologue **168** (R = CH_2Ph), a dibenzyl homologue and a trace of toluene; the deuterio analogue **169** (R^1 = D, R^2 = CH_2Ph) behaves similarly, and with retention



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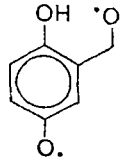

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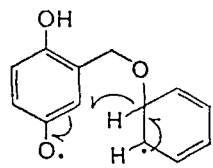

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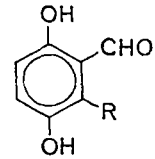
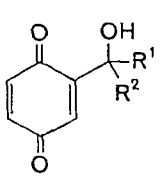


(168)

of deuterium, indicating that abstraction of the α-hydrogen is not important. The diphenylmethyl compound **169** (R^1 = H, R^2 = $CHPh_2$) is similarly cleaved to 2,5-dihydroxybenzaldehyde, and 1,1,2,2-tetraphenylethane is also formed. This product in particular is indicative of the intervention of free radicals, and fragmentation following excitation of the quinonoid nucleus is suggested to occur as shown in **170**.



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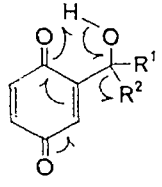

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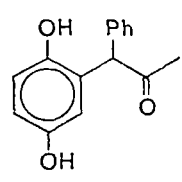

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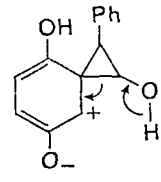
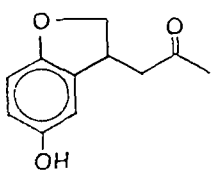


(172)

A similar cleavage, giving 2,5-dihydroxyacetophenone (**100**; R = Me), occurs with the quinone **169** (R^1 = Me, R^2 = CH_2Ph), but the major product is the isomer **171**, the formation of which can be explained on the basis of a spirocyclopropane zwitterion **172** resulting from intramolecular abstraction of hydrogen from the benzylic position[262].

The allyl analogues **169** (R^1 = H or Me, R^2 = $CH_2CH{=}CH_2$) are similarly cleaved, but the methyl compound **169** (R^1 = Me, R^2 = $CH_2CH{=}CH_2$) is unusual in that it also gives 6% of the dihydrobenzofuran **173**, which cannot be accounted for by the spirocyclopropane mechanism. A route involving intramolecular cycloaddition to give a spiro-oxetan **174** followed by a two-step dienone-phenol rearrangement (as **174** and **175**) has been proposed[262].



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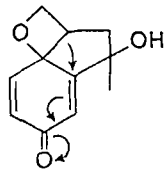

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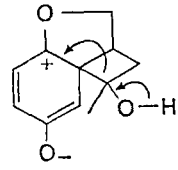
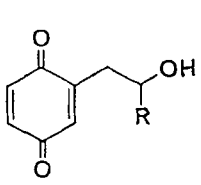
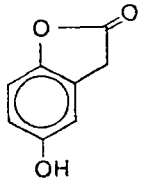


(175)

2′-Hydroxyalkyl-1,4-benzoquinones behave more simply[243], presumably because the hydrogen atom α- to the hydroxy group (i.e. at the β-position of the side-chain) can be readily abstracted intramolecularly through a six-membered transition state. Thus 2′-hydroxyethyl-1,4-benzoquinone (**176**; R = H) gives the coumaranone **177**, although in low yield, and its methyl homologue **176** (R = Me) affords over 70% of 2,5-dihydroxyphenylacetone (**178**). The spirocyclopropane zwitterion route will account for thsee products.



(176)



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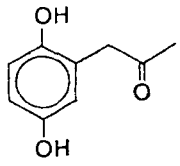
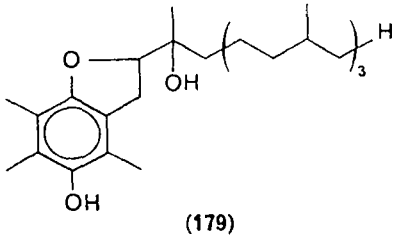


(178)

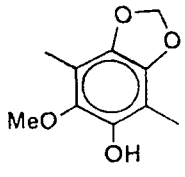
The only example of a 3′-hydroxyalkyl system to be studied is α-tocopherolquinone (**99**), and this yields the dihydrobenzofuran **179** when it is irradiated in ethanol[167], again indicating the importance of an abstractable hydrogen atom at the β-position of the side-chain.



(179)

D. Methoxy Substituents

Despite the availability of a potentially abstractable β-hydrogen atom, irradiation of 2,5-dimethoxy-3,6-dimethyl-1,4-benzoquinone does not[264] yield the benzodioxole **180**. This may be due to the excited state being essentially π, π^* in character. However, 2-bromo-3-methoxy-1,4-naphthoquinone, which, due to the steric effect of the bromine, exists in the favourable conformation **181**, does yield the corresponding dioxole **182**, together with the triester **183**, when it is irradiated in acetic anhydride[208]. It has been suggested[208] that intramolecular hydrogen abstraction to give the diradical **184** is followed by electron-transfer giving the zwitterion **185** from which the products arise, but an alternative mechanism, consistent with that previously described for *t*-butyl-1,4-benzoquinones (section VII.A), would involve the spiro-oxiran zwitterion **186**.



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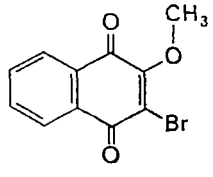

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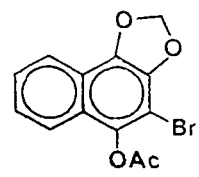
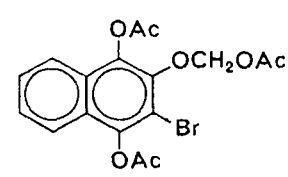


(182)



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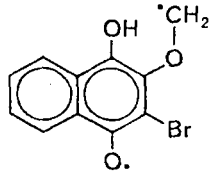

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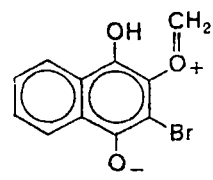

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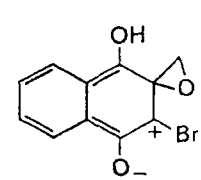
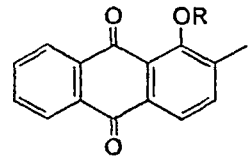


(186)

Irradiation of 1-methoxy-2-methyl-9,10-anthraquinone (**187**; R = Me) in acetic acid with sunlight gives[226] the corresponding phenol (**187**; R = H), and although no studies relating to the mechanism have been described, it is possible that an acetal analogous to **183** may be involved.



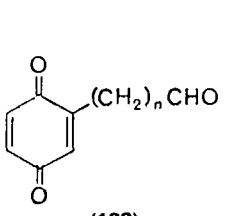
(187)

Ultraviolet irradiation, through Pyrex, of 1-methoxy-9,10-anthraquinone in aqueous acetonitrile containing ammonia gives a 96% yield of 1-amino-9,10-anthraquinone; replacement of the methoxy group of 2-methoxy-9,10-anthraquinone occurs to the extent of only 25%, the major (70%) product being 1-amino-2-methoxy-9,10-anthraquinone (see also section VI). Both reactions occur cleanly under air or nitrogen, and are not retarded by the presence of 2,6-di-*t*-butylphenol. The first singlet state of the quinone may be responsible[230a].

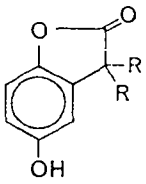
E. Formyl-bearing Substituents

In view of the particularly facile abstraction of formyl hydrogen from aldehydes and the very specific nuclear scavenging of acetyl radicals by 1,4-benzoquinone (section V.D), an attempt has been made[265] to combine these processes into an intramolecular cyclization reaction by using quinones of the form **188**. However, the only cyclic products obtained from irradiations with visible light in benzene involved the 1-carbonyl

group of the quinone and not $C_{(3)}$. Formyl-1,4-benzoquinone (**188**; $n = 0$) gives 2,5-dihydroxybenzoic acid and 2,5-dihydroxybenzaldehyde, 1,4-benzoquinonylacetaldehyde (**188**; $n = 1$) gives the coumaranone **189** (R = H), and β-1,4-benzoquinonylpropionaldehyde (**188**; $n = 2$) gives the dihydrocoumarin **190**. These compounds may be formed by quinone photooxidation of the corresponding lactols; the lactol **191** was isolated from the products of the latter irradiation.



(188)



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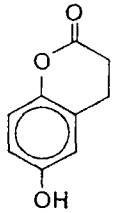
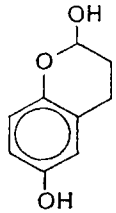
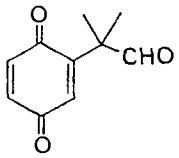


(190)



(191)



(192)

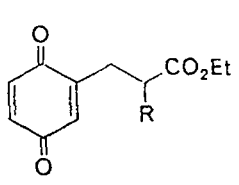
The quinone **192** behaves similarly in that it gives the coumaranone **189** (R = Me) and the related lactol, but differently in affording 25% of 3-methylbenzofuran-5-ol (**135**; R = Me), which represents a new fragmentation process; it is suggested[265] that intramolecular abstraction of formyl hydrogen is followed by loss of carbon monoxide and isomerization to give isopropenyl-1,4-benzoquinone (**134**; R = Me), a known[149] precursor of the benzofuranol. The 1,4-naphthoquinone analogous to **192** behaves in the same way[265].

F. Ester-bearing Substituents

Ethyl β-1,4-benzoquinonylpropionate (**193**; R = H) behaves analogously to other systems carrying abstractable methylene hydrogen at the β-position (section VII.A) in that it gives[243] the dihydrobenzofuran **194**, possibly by an analogous mechanism, although this would require opening of the three-membered ring of the zwitterion **195** in the least favourable direction, with the positive charge developing α- to the ethoxycarbonyl group; this could be offset to some extent by participation of the hydroxy group.

The diester **193** (R = CO_2Et) behaves unusually in that it is stable to visible light in rigorously degassed benzene, but yields ethanol and

45–50% of the coumarin **196** (R = CO_2Et) when a catalytic amount of oxygen is present[246, 266]. Oxygen suppresses the formation of the dihydrobenzofuran **194** from the monoester **193** (R = H), but does not induce



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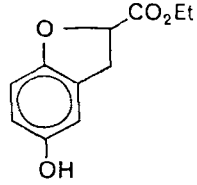
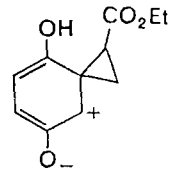
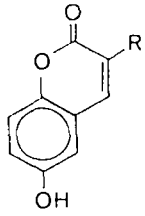


(194)



(195)

formation of the corresponding coumarin (**196**; R = H). Photostability of the diester **193** (R = CO_2Et) in the absence of oxygen may be due to reversibility of abstraction of hydrogen from the β-position of the side-chain, or to the fact that abstraction of hydrogen from positions α- to electron-accepting groups appears to be an inherently difficult process for photoexcited quinones[5]. A possible explanation of coumarin formation involves an ene-reaction (as **197**) with singlet oxygen produced in the immediate neighbourhood of the quinone (cf. section VII.B, reference 258) to give the hydroperoxide **198** which then decomposes, as shown, by two intramolecular hydrogen-transfer processes, one regenerating oxygen and the other, facilitated by the acidic character of the hydrogen α- to the ethoxycarbonyl groups, completing the formation of the αβ-unsaturated diester **199** which contains a *cis*-cinnamate system and would therefore readily cyclize, with elimination of ethanol, to give the coumarin.



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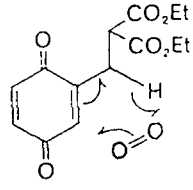

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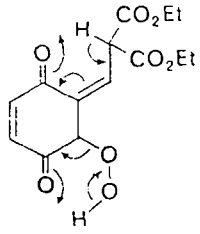
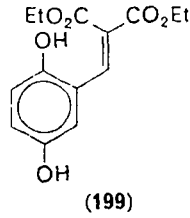


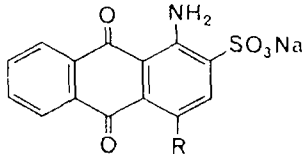
(198)



(199)

G. Halogeno Substituents

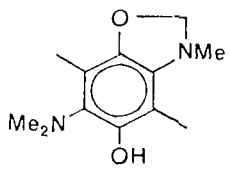
The bromoanthraquinone **200** (R = Br) is stable to primary aliphatic amines, and to piperidine, in aerated aqueous ethanol in the dark and when irradiated with unfiltered light from a high-pressure mercury vapour lamp, but suffers substitution, giving the aminoanthraquinones **200** (R = NHAlk or piperidino), when irradiated with light of wavelength greater than 4200 Å. The reaction is promoted by solvents such as alcohols and acetonitrile, but fails in the absence of oxygen[267].



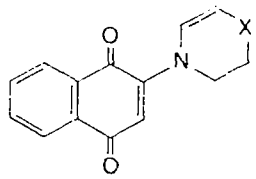
(200)

H. Amino, Diazonium and Azido Substituents

It has been suggested[240] that the formation[264] of oxazolines, e.g. **201**, from the corresponding dialkylamino-1,4-benzoquinones proceeds by a mechanism analogous to the spirocyclopropane zwitterion one described in section VII.A. The related 2-piperidino- and 2-morpholino-1,4-naphthoquinones have been reported[268] to yield the corresponding dehydro-compounds **202** (X = CH_2 or O), but, in view of the isolation[264] of oxazolines from analogously-substituted 1,4-benzoquinones, further investigation is needed.



(201)

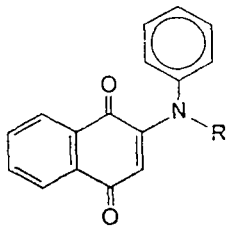


(202)

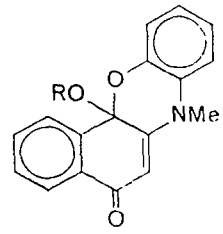
Irradiation of a benzene solution of 2-acetyl-6-anilino-3-methylamino-1,4-benzoquinone gives a mixture of 4-acetyl-6-anilino-5-hydroxybenzoxazole and 2-acetyl-3-amino-6-anilino-1,4-benzoquinone, the former being the major product[268a].

A cyclization reaction which may be related to that observed for 2,6-diphenyl-1,4-benzoquinone (section VII.B) occurs[269] with 2-arylamino-1,4-naphthoquinones (**203**). 2-Anilino-1,4-naphthoquinone (**203**; R = H) is stable, but the *N*-methyl compound (**203**; R = Me) gives **204** (R = H)

when irradiated in aqueous tetrahydrofuran, and its methyl ether (**204**; R = Me) when the solvent is methanol; as expected for a hemiacetal, **204** (R = H) gives **204** (R = Me) when treated with methanol in the dark. The presence of a methoxy group at the *para* position of the phenyl ring has little effect, but the yield of the photocyclization product is significantly enhanced by a methoxy substituent at the *meta* position, suggesting that intramolecular electrophilic attack by an n,π^* excited carbonyl system is involved[269].

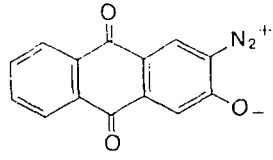


(203)



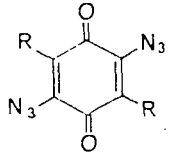
(204)

Irradiation of the diazonium compound **205** in aromatic solvents gives the corresponding 2-aryl-3-hydroxy-9,10-anthraquinones[270], but this type of reaction is not peculiar to quinones.



(205)

The diazido-1,4-benzoquinones (**206**; R = Me or *t*-Bu) give[271] the corresponding cyclopentenediones **207** in useful yield when they are irradiated in benzene at 3600 Å, and 2,3-diazido-1,4-naphthoquinone affords[272] the dinitrile **208**.



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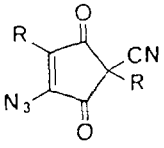

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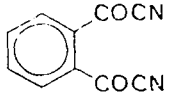
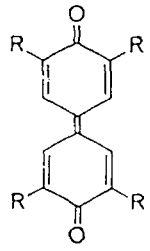


(208)

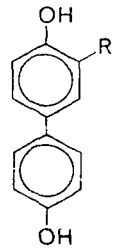
VII. 4,4′-DIPHENOQUINONES

Irradiation of 4,4′-diphenoquinone (**209**; R = H) in acetaldehyde with visible light gives results similar to those obtained with 1,4-benzoquinone[204] in that the hydroquinone **210** (R = H) and the ketone **210** (R = Ac) are

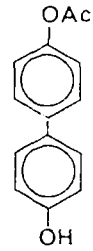
formed, but different in that the yield of hydroquinone monoacetate **211** is significantly larger (8% instead of less than 1%), possibly reflecting a greater contribution from the electron-transfer mechanism (section V.D) consequent upon the higher oxidation potential of the diphenoquinone[245, 273]. Irradiation in benzaldehyde gives analogous products.



(209)



(210)



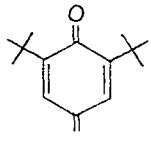
(211)

Similar irradiation of the tetramethyldiphenoquinone **209** (R = Me) gives an 80% yield of the corresponding hydroquinone, together with a little biacetyl which may be formed by dimerization of acetyl radicals[245, 273]. The tetra-*t*-butyldiphenoquinone **209** (R = *t*-Bu) is unchanged even after prolonged irradiation under similar conditions[245, 273] and there is here a possible parallel with the low photoreactivity of 2,6-di-*t*-butyl-1,4-benzoquinone (section VII.A).

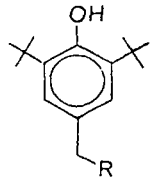
IX. QUINONE METHIDES AND QUINONE IMINES

The photochemistry of quinone methides and imines has been much less extensively studied than that of the quinones themselves, but there are obvious parallels in reactivity.

Irradiation of the di-*t*-butylquinone methide **212** in diethyl ether with light of wavelength 3660 Å gives the cresol **213** (R = H) as a minor product, and the 1 : 1 adduct **213** (R = MeCHOEt) as the major one. Irradiation in 1,3-cyclohexadiene gives the corresponding adduct (**213**; R = 2,4-cyclohexadienyl). Reorganization of the carbon skeleton of a *t*-butyl group was not observed[274]. 10-Methyleneanthrone forms an analogous adduct with diethyl ether[274].

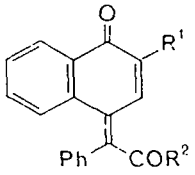


(212)

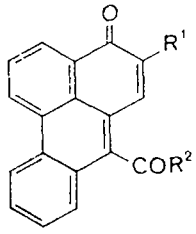


(213)

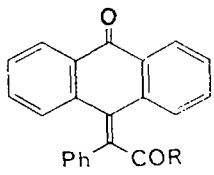
Irradiation of the naphthoquinone methides **214** (R^1 = H or Me, R^2 = H, Me or Ph) causes *cis–trans* isomerism and dehydrocyclization to give the corresponding benzanthrones **215**. The 10-methyleneanthrones **216** (R = Me or Ph) give analogous dehydrocyclization products almost quantitatively when irradiated in benzene at 3660 Å in the presence of oxygen or iodine as hydrogen-acceptors[142].



(214)



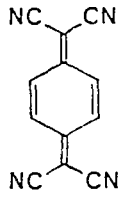
(215)



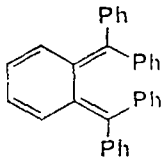
(216)

The formation of the semiquinodimethane anion radical of the tetracyanoquinodimethane **217** solubilized in aqueous surfactants is enhanced by daylight[275], again suggesting an increase in oxidation potential as a result of excitation (cf. section III.E). Irradiation of **217** in toluene or *p*-xylene results in 1,6-addition of a benzyl or *p*-methylbenzyl group, probably by pairing of the radicals resulting from electron- followed by proton-transfer in the excited π-complex; both reactions are accelerated by the presence of trifluoroacetic acid[275a].

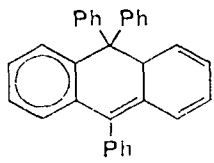
Irradiation of the tetraphenyl-1,2-benzoquinone dimethide **218** at −185° with light of wavelength 5300 Å causes cyclization[276] to the dihydroanthracene **219**.



(217)



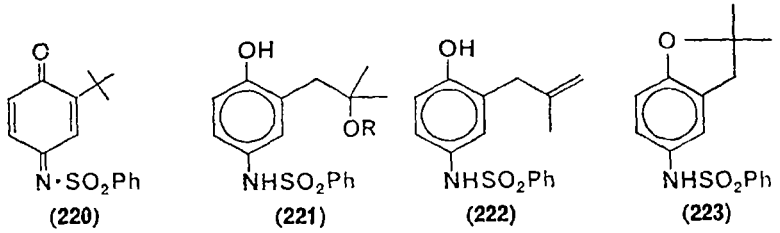
(218)

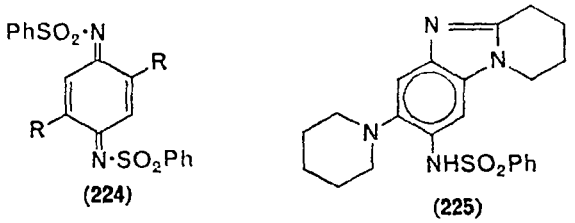


(219)

In contrast to the methide **212**, irradiation of the benzenesulphonimide **220** does cause reorganization of the side-chain[277]. Thus in ethanol it gives the ether **221** (R = Et), and in acetic acid the corresponding ester (**221**; R = Ac) together with the olefin **222** and the dihydrobenzofuran **223**. These results parallel those obtained for *t*-butyl-1,4-benzoquinone

(section VII.A), and suggest that the mechanism is analogous. The dibenzenesulphonimide **224** (R = *t*-Bu) behaves similarly[277].





Exposure of a chloroform solution of the dipiperidino compound **224** (R = piperidino) to sunlight rapidly affords the benzimidazole **225** as its benzenesulphonate salt; the dimethylamino compound behaves analogously[278]. These photocyclizations are probably similar to those observed for the alkylamino- and related 1,4-benzoquinones (section VII.H).

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The Chemistry of the quinonoid compounds
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CHAPTER 10

Radiation chemistry of quinones

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I. INTRODUCTION

Considerable progress has been made in recent years in the quantitative understanding of chemical processes occurring subsequent to the irradiation of water, dilute aqueous solutions and organic liquids by γ-rays or high-energy electrons[1-24]. While the use of radiation for syntheses falls considerably short of initial expectations[25], it has provided an extremely powerful technique for the elucidation of organic reaction mechanisms[26]. Not only have novel transients been characterized by pulse radiolysis[27] and *in situ* electron spin resonance techniques[28] but accurate data have been obtained for the rates of their formation and decomposition[29,30]. The purpose of

this chapter is to discuss critically the radiation chemistry of quinones. Radiolytic investigations involving quinones, hydroquinones and semiquinones as starting materials, intermediates or transients as well as products will be discussed. Our treatment will not, however, include work in which quinones are used only as specific radical or excited state scavengers. Results of analogous photo- and electrochemical experiments will only be cited when they substantiate or contradict the proposed structure and mechanism of radiolytically formed transients.

The prominent function of quinones in vitamins, particularly A, E, D and K, as well as in the electron transfer processes and photosynthesis provided much of the impetus for their radiolytic investigation[31]. Additionally many organic dyes contain quinonoid structures. Investigations of the radiation chemistry of dyes in early work centred around their possible use as chemical dosimeters; while subsequent research shed light on the mechanistic aspects of radiation-induced oxidations and reductions, particularly those related to dying and colour sensitizing in photochemistry, photography and biology[32]. Of the numerous quinones only some two dozen have been investigated quantitatively[30]. As a consequence of the explosive growth of modern radiation chemistry and the availability of pulse radiolytic facilities to organic and biochemists, considerable progress is to be expected in the near future. It is our hope that this chapter will stimulate activity in the area of mechanistic radiation chemistry in general and that of quinones in particular. Basic differences in the radiation chemistry of aqueous and non-aqueous solutions necessitate a separate treatment. Since the theory, experimental techniques and interpretation of radiation chemistry is treated in numerous recent monographs and textbooks[1-24], only the most essential concepts will be summarized in section II. The spectra of the transient species derived from quinones, semiquinones and hydroquinones in aqueous and non-aqueous solutions are summarized in the Appendix.

II. FUNDAMENTALS OF RADIATION CHEMISTRY

Radiation chemical changes are initiated most commonly by high-energy γ-ray sources (cobalt-60 or caesium-137), electron generators (Van de Graaff) or linear accelerators. For quantitative studies, a knowledge of the amount of energy absorbed by the irradiated sample is required. The absorbed energy or irradiation dose is generally expressed in units of rad or eV/g. One *rad* is equivalent to 100 erg/g or 10^{-5} joule/g and equals $2{\cdot}4 \times 10^{-6}$ cal/g and $6{\cdot}24 \times 10^{13}\,\rho$ eV/cm^3 (ρ = density in g/cm^3). The *absorbed dose rate* equals the absorbed dose per unit time, e.g. rad/min or

rad/h. The yield of products relative to the amount of radiation is expressed by the *G-value*. $G(X)$ and $G(-X)$ refer to the number of molecules of product X formed or decomposed, respectively, on irradiation per 100 eV of absorbed energy. For solution studies, substitution of the appropriate units into the above definition gives the following useful expression[33]:

$$G(X) = \frac{(X \text{ in moles litre}^{-1})\ (9{\cdot}65 \times 10^8)}{(\text{absorbed dose in rads})\ \rho}$$

The energy of a given radiation source is determined by dosimetry[2].

Pulse radiolysis, the radiation chemical analogue of flash photolysis, affords the direct determination of the absorption spectra or conductance of transients in the milli to picosecond (10^{-3}–10^{-12} s) ranges as well as their rates of formation and decomposition[27].

Particularly convenient is the broad absorption spectrum of the hydrated electron, $\varepsilon_{715\,nm} = 1{\cdot}85 \times 10^4\ M^{-1}\,cm^{-1}$, since measurements of its rate of absorbance decrease in the presence of different solutes afford the direct determination of rate constants for the reaction of e^-_{aq} with a large variety of compounds[31].

The net chemical result of the irradiation of water is the formation of the following species:

$$H_2O \longrightarrow e^-_{aq} + {}^{\bullet}H + {}^{\bullet}OH + H_2 + H_2O_2 + H_3O^+ \qquad (1)$$

The yields of these species with respect to the absorbed energy are known with considerable accuracy[35]: $G_{e_{aq}^-} = 2{\cdot}8 \pm 0{\cdot}1$, $G_{\bullet H} = 0{\cdot}6 \pm 0{\cdot}1$, $G_{\bullet OH} = 2{\cdot}8 \pm 0{\cdot}1$, $G_{H_2} = 0{\cdot}45$, and $G_{H_2O_2} = 0{\cdot}71$. Furthermore, by the judicious use of scavengers it is possible to simplify the system such that it contains exclusively the hydrated electron, e^-_{aq}, the hydrogen atom, $^{\bullet}H$ or the hydroxyl radical, $^{\bullet}OH$ (Table 1). When it is desirable to study exclusively the reaction of e^-_{aq} with solutes, advantage can be taken of equation (21) by saturating the triply distilled water with H_2 and, concurrently, of equation (12) by making the solution alkaline. Alternatively, the system can be simplified to contain primarily e^-_{aq} by adding methanol (equation 22) and adjusting the pH to ca. 10 (equation 12). In order to investigate the reactions of $^{\bullet}H$ with solutes, the triply distilled water is made acidic (equation 2) and is saturated with hydrogen (equation 21). Hydroxyl radical reactions are studied in the presence of nitrous oxide since the reaction given in equation (10) not only eliminates e^-_{aq} but doubles the amount of hydroxyl radicals in the system. This reaction is, therefore, very conveniently employed in radiation-induced hydroxylation studies.

The radiation chemistry of organic liquids differs from that of water since in addition to ionization (formation of electrons and positive ions)

TABLE 1. Selected rate constants for the primary species in water[a]

Reaction	Equation no. used in this chapter	Rate constant[b] ($M^{-1}\,s^{-1}$)	pH
$e^-_{aq} + H_3O^+ \rightarrow {}^\bullet H + H_2O$	(2)	$(2{\cdot}07 \pm 0{\cdot}08) \times 10^{10}$	2·1–4·3
$e^-_{aq} + e^-_{aq} \rightarrow H_2 + 2OH^-$	(3)	$(0{\cdot}9 \pm 0{\cdot}15) \times 10^{10}$ [c]	10·9
$e^-_{aq} + H_2O_2 \rightarrow {}^\bullet OH + OH^-$	(4)	$(1{\cdot}23 \pm 0{\cdot}14) \times 10^{10}$	7
$e^-_{aq} + {}^\bullet H \rightarrow H_2 + OH^-$	(5)	$(2{\cdot}5 \pm 0{\cdot}6) \times 10^{10}$	10·5
$e^-_{aq} + {}^\bullet OH \rightarrow OH^-$	(6)	$(3{\cdot}0 \pm 0{\cdot}7) \times 10^{10}$	10·5
$e^-_{aq} + {}^\bullet O^- \rightarrow 2OH^-$	(7)	$(2{\cdot}2 \pm 0{\cdot}6) \times 10^{10}$	13
$e^-_{aq} + H_2O \rightarrow {}^\bullet H + OH^-$	(8)	$16{\cdot}0 \pm 1{\cdot}0$	8·4
$e^-_{aq} + O_2 \rightarrow {}^\bullet O_2^-$	(9)	$(1{\cdot}88 \pm 0{\cdot}2) \times 10^{10}$	7
$e^-_{aq} + N_2O \rightarrow N_2 + {}^\bullet OH + OH^-$	(10)	$(8{\cdot}67 \pm 0{\cdot}6) \times 10^{9}$	7
${}^\bullet H + {}^\bullet H \rightarrow H_2$	(11)	$1{\cdot}5 \times 10^{10}$	0·1–1·0
${}^\bullet H + OH^- \rightarrow e^-_{aq} + H_2O$	(12)	$1{\cdot}8 \times 10^{7}$	11–13
${}^\bullet H + {}^\bullet OH \rightarrow H_2O$	(13)	$(0{\cdot}7\text{–}3{\cdot}2) \times 10^{10}$	3
${}^\bullet H + O_2 \rightarrow {}^\bullet HO_2$	(14)	$2{\cdot}6 \times 10^{10}$	0·4–3·0
${}^\bullet H + H_2O_2 \rightarrow {}^\bullet OH + H_2O$	(15)	$(9{\cdot}0 \pm 1) \times 10^{7}$	2·1
${}^\bullet H + H_3O^+ \rightarrow H_2^+ + H_2O$	(16)	$2{\cdot}6 \times 10^{3}$ [d]	3·5–11
${}^\bullet H + N_2O \rightarrow N_2 + {}^\bullet OH$	(17)	$\sim 1{\cdot}2 \times 10^{4}$ [d]	3·5–11
${}^\bullet OH + {}^\bullet OH \rightarrow H_2O_2$	(18)	5×10^{9}	7
${}^\bullet OH + OH^- \rightarrow {}^\bullet O^- + H_2O$	(19)	$3{\cdot}6 \times 10^{8}$ [e]	---
${}^\bullet OH + H_2O_2 \rightarrow H_2O + {}^\bullet HO_2$	(20)	$4{\cdot}5 \times 10^{7}$	7
${}^\bullet OH + H_2 \rightarrow {}^\bullet H + H_2O$	(21)	$(6{\cdot}0 \pm 2{\cdot}0) \times 10^{7}$	7
${}^\bullet OH + CH_3OH \rightarrow {}^\bullet CH_2OH + H_2O$	(22)	$4{\cdot}8 \times 10^{8}$	7
$H_3O^+ + OH^- \rightarrow 2H_2O$	(23)	$1{\cdot}43 \times 10^{11}$ [f]	7

[a] References 29 and 30.
[b] Determined by pulse radiolysis unless stated otherwise.
[c] Rate constant, k, defined by $d(X)/dt = k(X)^2$, where $X = e^-_{aq}$ (equation 3), $X = {}^\bullet H$ (equation 11) and $X = {}^\bullet OH$ (equation 18).
[d] Determined photochemically.
[e] Determined by competition kinetics.
[f] Determined by T-jump technique.

singlets and triplets are formed either by initial excitation or by electron neutralization[36–38]. Conditions may be adjusted in such a way that the dissolved solute either accepts an electron forming a radical anion, $A^{\bullet -}$, or gives up an electron forming a radical cation, $A^{\bullet +}$. Under suitable conditions the rates of successive electron transfer processes between several dissolved solutes have, in fact, been observed[39]. The number of possible reactions which can occur in organic liquids therefore far exceeds that which occurs in the radiolysis of water. In organic liquids, hydrogen atoms, for example, rarely combine to form molecular hydrogen, a common

reaction in water (equation 11), but rather preferentially abstract hydrogen from or add to a solvent molecule.

It is evident that reasonable care must be exercised in designing radiation chemical experiments. However, the available compilation of rate constants for the reactions of radiolytically generated species with several thousand inorganic and organic compounds, radicals and excited states[29,30] considerably facilitates the execution of fruitful experiments.

III. RADIATION-INDUCED REACTIONS OF QUINONES IN AQUEOUS SOLUTIONS

Radiation chemical techniques have been applied successfully in investigations of the oxidation–reduction system of hydroquinone and benzoquinone and their substituted analogues. The hydrated electron and hydrogen atom are the reducing and the hydroxyl radical and hydrogen peroxide are the oxidizing agents present subsequent to the deposition of energy. By the use of different scavengers (Table 1) it is possible to adjust conditions such that only one of these species predominates.

Several radiation chemical studies have been carried out in aqueous air or oxygen-saturated solutions[40]. Oxygen removes the reducing radicals (equations 9 and 14) by converting them to oxidizing species ($O_2^{\bullet-}$ and $HO_2^{\bullet}$). The pH of the solution determines the nature of the oxidizing species:

$$H_2O_2^+ \underset{\leftarrow}{\xrightarrow{pK=1{\cdot}0\pm0{\cdot}4}} H^+ + HO_2^{\bullet} \underset{\leftarrow}{\xrightarrow{pK=4{\cdot}5}} O_2^{\bullet-} + 2\,H^+$$

In an air-saturated solution the oxidizing species are, therefore, the hydroxyl radical, $^{\bullet}OH$ (which above pH 12 exists primarily as $O^{\bullet-}$), hydrogen peroxide, H_2O_2 (which again above pH 12 ionizes to HO_2^-) and the protonated, neutral or ionized form of the perhydroxyl radical ($HO_2^{\bullet}$). Each can react with quinones and indeed some quinones have shown a certain degree of selectivity towards these oxidizing species. Perhaps it is not superfluous to re-emphasize the special importance of controlling and varying such experimental conditions as scavengers and pH in these reactions since many of the quinones exist in different extents of protonation with consequent differences in their reactivities.

A. *Simple Aromatic Quinones*

The radiation chemistry of simple aromatic quinones will be discussed initially in considerable detail since, to some extent, the behaviour of more complex quinones is analogous.

Pulse irradiation of a nitrous-oxide-saturated aqueous 5×10^{-3}M solution of *p*-benzhydroquinone resulted in the formation of two transients[41]. Chart I summarizes the proposed reaction paths. The first

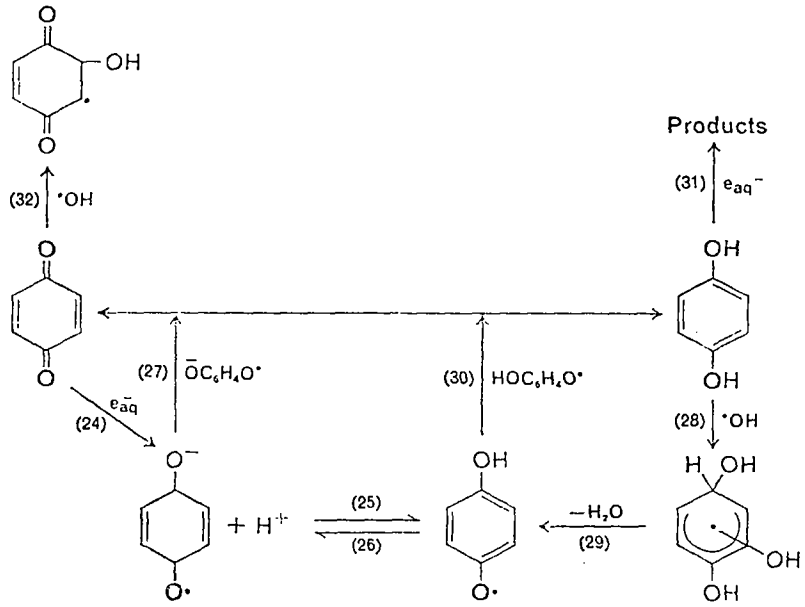


CHART I

transient was observed 1 μs after the pulse. On a longer time scale a second transient formed. The rate of build-up of the second transient, determined at 425 nm, obeyed first-order kinetics and was found to be independent of the concentration of the first transient (Figure 1). These transients have been assigned to the hydroxyl adduct of *p*-benzoquinone (equation 32) and the *p*-benzsemiquinone anion radical (equation 24). The independently determined rate constants for the reactions of e_{aq}^- and •OH with *p*-benzoquinone and *p*-benzhydroquinone (Table 2) afforded the design of the experimental conditions required for the substantiation of the assigned structures. Since e_{aq}^- reacts considerably faster with *p*-benzoquinone than with *p*-benzhydroquinone, and since the reaction of the hydroxyl radical with the quinone is an order of magnitude slower than with the hydroquinone, in an aqueous solution of 1×10^{-3}M quinone and 1×10^{-2}M hydroquinone all the e_{aq}^- and •H react with benzoquinone and all the •OH reacts with hydroquinone, consequently at neutral pH the single species present is the semiquinone radical anion. At pH 2 in the

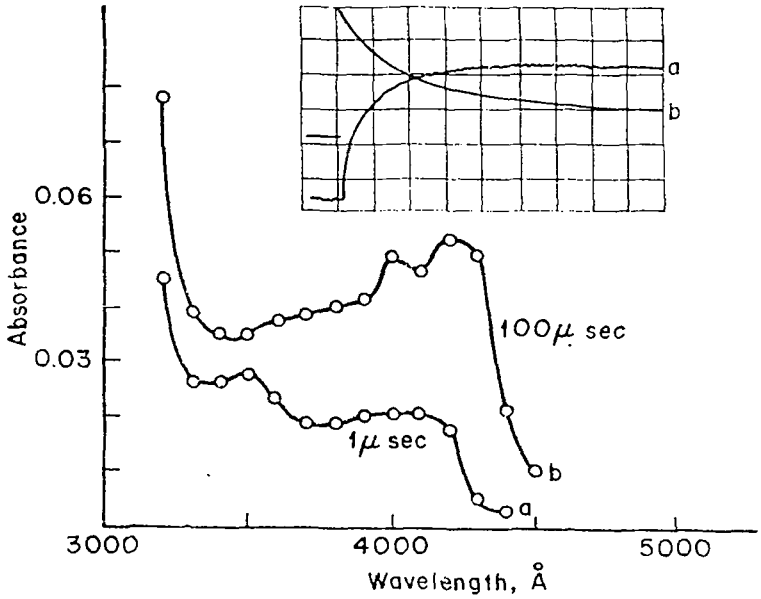


FIGURE 1. Transient absorption spectra after pulse radiolysis of 5×10^{-3}M hydroquinone saturated with nitrous oxide. Curve a, absorption immediately after the pulse; curve b, absorption after 100 μs delay. Inset, oscillogram showing: a, transition from the $^{\bullet}OH$ adduct to the semiquinone ion ($\lambda = 4100$ Å); b, decay of the semiquinone ion. Ordinate, percentage absorption, 2·6 per cent per large division; abscissa, (a) build-up, 20 μs per large division; (b) decay, 1 ms per large division. Reproduced with permission from G. E. Adams, B. D. Michael and E. J. Land, *Nature*, **211**, 293 (1966).

same aqueous system a different spectrum is obtained which was assigned to the protonated form of the semiquinone, $HOC_6H_4\dot{O}$. The absorption changes at 430 nm (maximum difference between the two forms) afforded the determination of the protonation equilibrium (Figure 2)[41]. The assigned structures of the semiquinone radical anion and the semiquinone are supported by previous flash photolytic determinations of the absorption spectra of a number of semiquinones in their different ionization states[44,45]. Additionally, the observed salt effects on the rate constant for the decay of the transient produced in the pulse radiolysis of neutral nitrous-oxide-saturated solutions of *p*-benzhydroquinone (equation 27) gave a good Brönsted plot with a slope of +1, thereby substantiating the postulated unit charge on the semiquinone anion radical[41].

The initial product of the reaction of hydroxyl radical with *p*-benzhydroquinone is the trihydroxycyclohexadienyl radical (equation 28)[41]. The point

TABLE 2. Rate and equilibrium constants for the reactions of quinones, hydroquinones and their intermediates[a]

Reaction	Equation no.	Rate constant
p-Benzoquinone + e^-_{aq}	(24)	$1{\cdot}25 \times 10^{9}$ [b] $2{\cdot}7 \times 10^{10}$ [c]
p-Benzhydroquinone + e^-_{aq}	(31)	$< 10^{7}$
p-Benzoquinone + •OH	(32)	$1{\cdot}2 \times 10^{4}$
p-Benzhydroquinone + •OH	(28)	$1{\cdot}2 \times 10^{8}$
Protonation of *p*-benzsemiquinone anion radical	log (25)/(26)	$pK = 4{\cdot}0$
Disproportionation of *p*-benzsemiquinone anion radical	(27)	$1{\cdot}7 \times 10^{8}$
Disproportionation of *p*-benzsemiquinone radical	(30)	$1{\cdot}1 \times 10^{9}$
Water elimination from •OH adduct of *p*-benzhydroquinone	(29)	pH-dependent

[a] Reference 41 unless stated otherwise.
[b] Reference 42.
[c] Reference 43.

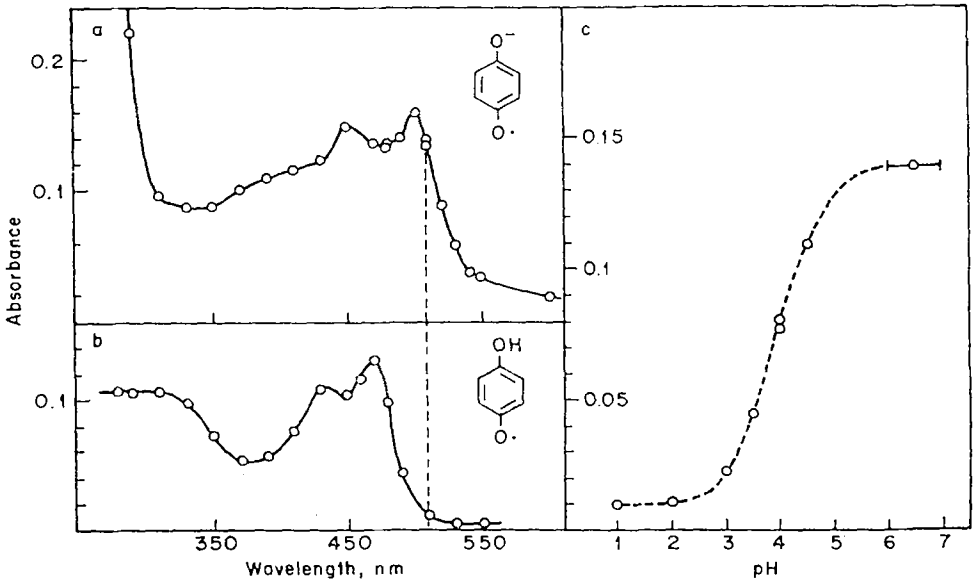


FIGURE 2. Transient spectra from the pulse radiolysis of an aqueous solution containing 1×10^{-3}M *p*-benzoquinone and 1×10^{-2}M hydroquinone (O_2 free) 1 μs after the pulse. (a) Neutral solution, (b) pH 2, (c) pK curve of semiquinone. Reproduced with permission from G. E. Adams and B. D. Michael, *Trans. Faraday Soc.*, **63**, 1171 (1967).

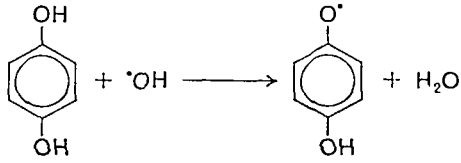
of hydroxyl radical attack is somewhat ambiguous since absorption spectroscopy does not distinguish between the different isomers. Comparison of the spectral and kinetic properties of the transient trihydroxycyclohexadienyl radical with transients obtained in the irradiation of aqueous nitrous-oxide-saturated solutions of 1,2- and 1,3-dihydroxybenzene (catechol and resorcinol) suggests that attack occurs primarily, but not exclusively, at the 1-position forming the geminal 1,1,4-trihydroxycyclohexadienyl radical[41]. The recently developed *in situ* electron spin resource observations of radicals with millisecond lifetimes, generated by high-energy radiation, can establish the structures and rate constants for the formation of the different isomeric trihydroxycyclohexadienyl radicals[28].

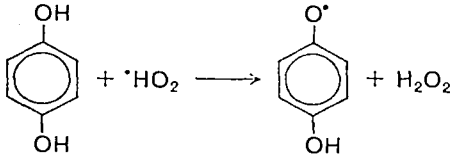
The semiquinone is formed from the trihydroxycyclohexadienyl radical by water elimination (reaction 29)[46]. This is apparently a well-substantiated reaction and will be discussed at some length in part B.

Both the semiquinone anion radical (reaction 27) and its protonated form (reaction 30) could disproportionate to form mixtures of the quinone and the hydroquinone; however, the former reaction requires that the electron affinity of the semiquinone anion radical be greater than that of *p*-benzoquinone. The rate constant for the former (at neutral pH) is an order of magnitude slower than that for the latter at pH 2 (Table 2). This difference in rates is in agreement with the spectral assignment of the species[41] since reaction (27) would undoubtedly be slower than that between two uncharged radicals (reaction 30). It is conceivable that the slower reaction at neutral pH could involve disproportionation between the semiquinone anion radical and the semiquinone radical rather than between the two negatively charged radical species.

The steady-state radiation chemistry (Co-60 irradiations) of aqueous air-saturated solutions of 2,5-dichloro-*p*-benzhydroquinone, 2,5-dimethyl-*p*-benzhydroquinone, 2,5-dimethyl-*p*-benzoquinone, 1,2,4-trihydroxybenzene, 3,6-dihydroxy-*p*-benzhydroquinone and 4-*t*-butyl-1,2-dihydroxybenzene has provided important information on the role of the perhydroxy radical ($HO_2^{\cdot}$) in the oxidation–reduction processes of quinones and hydroquinones[47,48]. Subsequent to the formation of the oxidizing species, $^{\cdot}HO_2$, $^{\cdot}OH$ and H_2O_2 (equations 1, 2 and 14), reactions (33–39) can be envisaged.

Four different mechanisms have been postulated to account for the radiation-induced oxidation of these substituted quinones and hydroquinones[40,47]. In mechanism I, the reaction sequence is equations (1), (2), (14) and (33) followed by either (34) or (35) and terminated by (36). Using this reaction scheme good agreement was obtained between the calculated


(33)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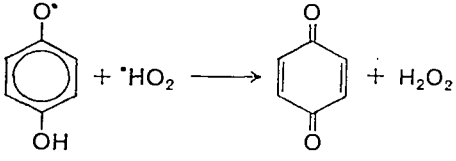
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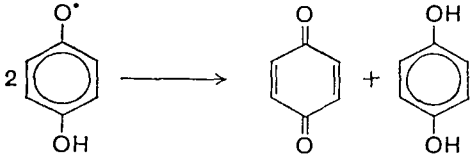
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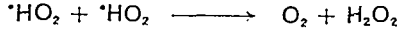
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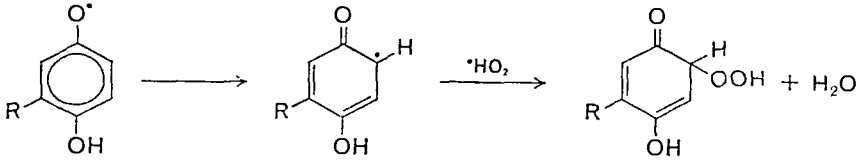
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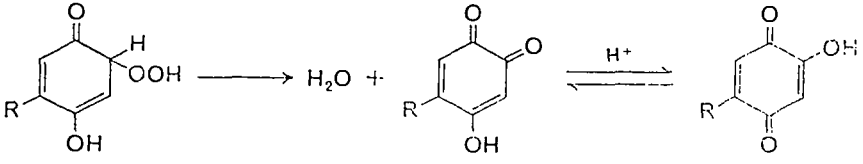

(39)

and observed yields for the radiation-induced oxidation of 2,5-dimethyl-*p*-benzhydroquinone and 1,2,4-trihydroxybenzene[47]. In mechanism II, the perhydroxy radical oxidizes the semiquinone radical (equations 1, 2, 14, 33 and 35) but is not a strong enough oxidizing agent to react with the hydroquinone, i.e. reaction (34) does not take place. The radiation-induced oxidation of 4-*t*-butyl-1,2-dihydroxybenzene is an example of this case since the observed yields are compatible with the material

balance equations derived from this mechanism[48]. In mechanism III, the perhydroxy radical is unable to oxidize either the hydroquinone or the semiquinone radical, i.e. reactions (34) and (35) do not occur and hence the steps subsequent to equations (1), (2), (14) and (33) are disproportionation of the perhydroxy radical and of the semiquinone radical (equations 36 and 37). The reaction of 2,5-dichloro-*p*-benzhydroquinone is an example of this mechanism[40]. In mechanism IV the perhydroxy radical acts as a hydroxylating agent and the reaction sequence is equations (1), (2), (14), (33), (34), (36), (38) and (39). Since hydroquinone and its monosubstituted derivatives readily react with the perhydroxy radical, the extent of hydroxylation depends on the rates of these competing processes and the ratio of hydroquinone to semiquinone radical. The observed yields for *p*-benzhydroquinone, 2-chloro-*p*-benzhydroquinone, 2,5-dihydroxytoluene and 1,2,4-trihydroxybenzene were found to be consistent with this mechanism[40]. Additional research of this type would allow the accumulation of sufficient data to test the validity of a relationship between the oxidation–reduction potential of substituted hydroquinones and their radiolytic yields or their reactivity with the perhydroxy radical. Although the transient absorption of pulse radiolytically generated $^{\bullet}HO_2$ and its anion, O_2^-, have been reported[49], no absolute rate constants are available for its reactions with dissolved organic compounds.

B. Formation of Semiquinones from p-Hydroxy-substituted Aromatic Compounds

It was noted in the previous section that the trihydroxycyclohexadienyl radical, formed by $^{\bullet}OH$ attack, readily eliminates water to form the semiquinone[41,46] (equations 28 and 29 in Chart I, Table 2 and Figure 1). This process is apparently general and the driving force for it is the gain in potential energy resulting from the rearomatization of the cyclohexadienyl radical[26]. It should be possible, at least in principle, to generate semiquinones from *p*-hydroxy-X-substituted aromatic compounds by hydroxyl radical attack followed by elimination of XH from the substituted hydroxycyclohexadienyl radical. The importance of this reaction lies in the interpretation of radiation and, indeed, chemically and biochemically induced hydroxylation[50].

The best substantiated process is the hydroxyl radical induced denitration of *p*-nitrophenol[51]. In the *in situ* e.s.r. examination of irradiated nitrous-oxide-saturated (equation 17) aqueous solution of *p*-nitrophenol a 1 : 4 : 6 : 4 : 1 e.s.r. quintet with a hyperfine splitting of 2·3 Gauss and $g = 2{\cdot}0044$ was observed (Figure 3)[28]. The e.s.r. parameters for this

FIGURE 3. E.s.r. spectrum of *p*-benzosemiquinone radical ion obtained from an N_2O-saturated solution of 10^{-3}M *p*-nitrophenol at pH 11·8. Reproduced with permission from K. Eiben and R. W. Fessenden, *J. Phys. Chem.*, **75**, 1186 (1971).

radical correspond unambiguously to the *p*-benzsemiquinone anion radical. Chart II illustrates the proposed mechanism which involves the initial formation of the nitro-substituted hydroxycyclohexadienyl radical (equation 40) which can lose HNO_2 to give the semiquinone (equation 41) or disproportionate to 4-nitro-1,2-dihydroxybenzene and *p*-nitrophenol (equation 42). Analytical determinations of the yields of nitrite ion, the total yields of quinone, subsequent to oxidation of hydroquinone to *p*-benzoquinone (equation 43), and the yields of 4-nitro-1,2-dihydroxybenzene have substantiated the proposed mechanism (Table 3)[51]. It is seen that the yields of nitrite ion are equal to that of *p*-benzoquinone and that the addition of nitrous oxide (equation 10) doubles the yields indicating that $^{\bullet}OH$ is indeed a necessary precursor. The hydrogen ion concentration clearly influences the extent of denitration. At pH 8, 31% of the reaction goes via denitration while at pH 5 only 14% denitration occurs. This fact has been rationalized by postulating that while the preferred site for the $^{\bullet}OH$ attack on *p*-nitrophenolate ion (pK of

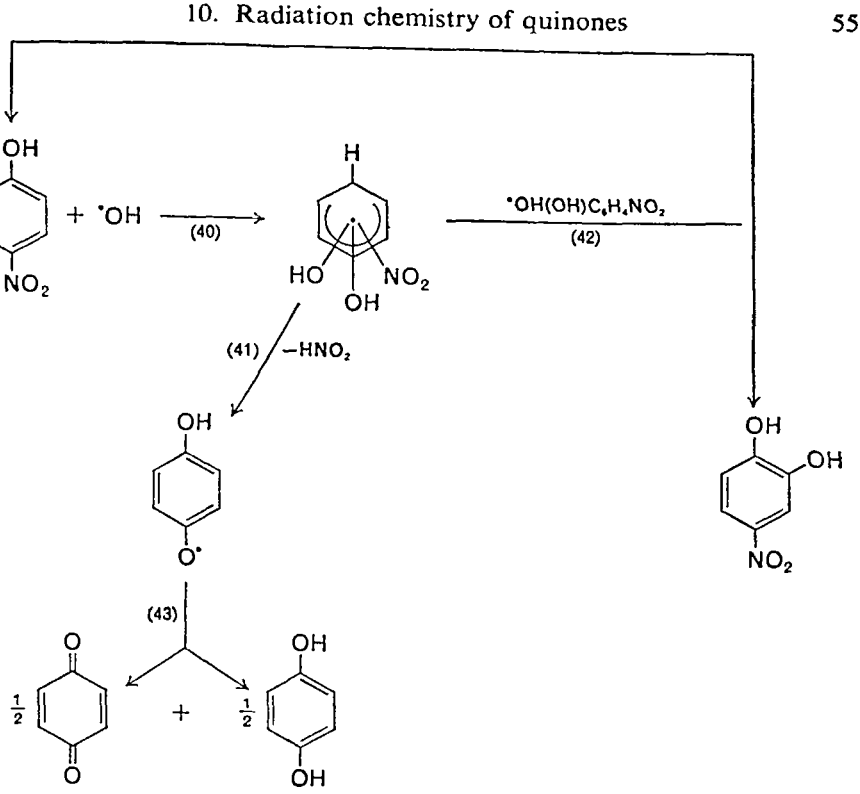


CHART II

TABLE 3. Yields of products in irradiated aqueous solutions of *p*-nitrophenol[a]

pH	Gas	Concentration (M)	$G(NO_2^-)$ [b]	*G*(*p*-Benzoquinone) [b]	*G*(4-nitro-1,2-dihydroxybenzene) [b]
5	N_2	5×10^{-4}	0·30	0·33	1·88
5	N_2	2×10^{-2}	0·39	—	2·42
5	N_2O	5×10^{-4}	0·66	0·65	3·84
8	N_2	5×10^{-4}	0·68	0·70	1·50
8	N_2	2×10^{-2}	0·77	—	1·94
8	N_2O	5×10^{-4}	1·32	1·42	2·98

[a] Reference 51; dose = 5×10^{17} eV/ml.
[b] *G* is the radiation chemical yield (see section II for its definition).

p-nitrophenol is 7·15) is the *ortho* position, electrophilic attack by ·OH occurs with equal ease at both the *ortho* and *para* positions of the unionized molecule[51].

The presence of hydroquinone in irradiated aqueous solutions of *p*-bromophenol[52] can be rationalized by an analogous process in which the bromo-substituted hydroxycyclohexadienyl radical loses HBr.

The formation of phenols on irradiation of aqueous solutions of chlorobenzene[53], fluorobenzene[54], anisole[55] and nitrobenzene[56] can also be rationalized by elimination of HCl, HF, CH_3OH and HNO_2 from the substituted hydroxycyclohexadienyl radicals. Although the intermediate in these cases is the phenoxyl radical, rather than the semiquinone, the driving force for all these processes is the resonance energy gained from the formation of stable aromatic structures.

Hydroxyl radicals generated in the Ti/H_2O_2 system also produced *o*- and *p*-benzoquinones in the presence of *o*- and *p*-nitrophenol[51].

Since biological hydroxylation of phenolic compounds *in vivo* readily occurs and since semiquinones have important roles in electron transfer processes, quantitative radiolytic investigations of many hydroxy-substituted aromatic systems are to be expected.

C. Complex Quinones and Dyes

Since the application of radiation techniques to mechanistic bioorganic chemistry is in its infancy, it is not surprising that only a few of the complex quinones have been examined to date. In some cases, such as ubiquinone for example, the lack of solubility necessitated the use of methanol or ethanol instead of water. Although the electron reductions of these compounds are similar in water and in alcohol, it is felt that the overall differences in the radiation chemistry of aqueous and non-aqueous solvents warrant their separate discussion.

The oxidation–reduction processes of sodium 9,10-anthraquinone-2-sulphonate in water have been investigated recently[57]. The proposed mechanism is entirely analogous to that of the benzoquinone–hydroquinone system (Chart III). The rate constant for the reaction of hydrated electrons with sodium 9,10-anthraquinone-2-sulphonate (equation 44)

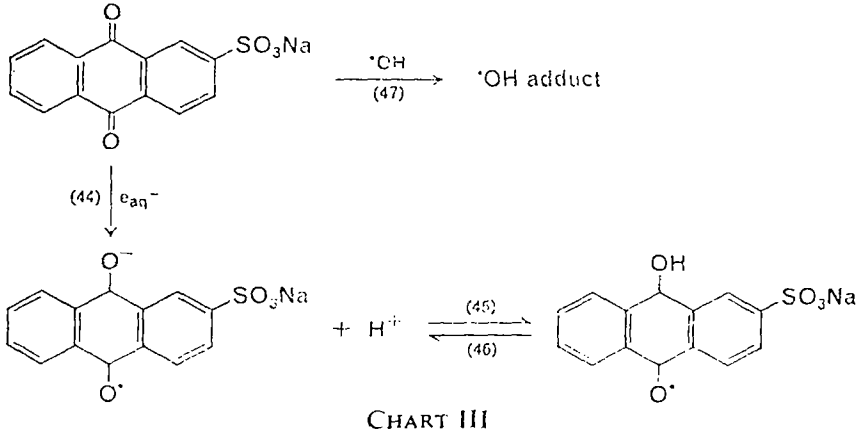


CHART III

has been determined to be $2{\cdot}8 \times 10^{10}\ M^{-1}\,s^{-1}$. In the presence of 10^{-1}M HCOONa all the hydroxyl radicals and hydrogen atoms are converted to $CO_2^{\bullet-}$ which then transfers an electron to the anthraquinone. The anthraquinone anion radical has a transient absorption maximum at 500 nm. With decreasing pH this absorption maximum decreases with the concomitant increase of another band at 390 nm. The latter band is due to the formation of the protonated anion radical (equation 45). The pK (log 45/46) for the equilibrium has been determined to be 3·25[57].

The rate constant for the reaction of hydroxyl radical with sodium 9,10-anthraquinone-2-sulphonate (equation 47) has been determined to be $5{\cdot}6 \times 10^9\ M^{-1}\,s^{-1}$. A transient with an absorption of 460 nm was observed which is, most probably, a hydroxyl adduct[57].

Many of the organic dyes have quinonoid structures or are sufficiently closely related to quinones to warrant a treatment of their radiation chemistry in this volume. Since a comprehensive review of the radiation chemistry of organic dyes has appeared recently[32], the obtained data will only be discussed in an illustrative fashion.

Most of the early work centred around observing, and in some cases quantitatively determining, the extent of bleaching of a suitable chromophore as a function of absorbed radiation dose[23]. Using pulse radiolysis rate constants for the reaction of reducing and oxidizing radicals with the dyes as well as disproportionation have been determined[32, 58-61]. Table 4 summarizes the data for methylene blue, fluorescein and eosin. Different extents of protonation of the dyes at given pH values, of course, have to be considered. The dissociation constants for methylene blue, for example, have been determined spectrophotometrically to be[58]:

$$MB^+ \underset{}{\overset{pK_1=0}{\rightleftharpoons}} MBH^{2+} \overset{pK_2=-5{\cdot}1}{\rightleftharpoons} MBH^{3+}$$

In neutral solutions the hydrated electron reduces methylene blue:

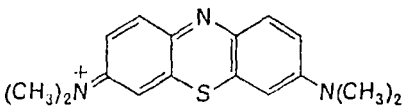
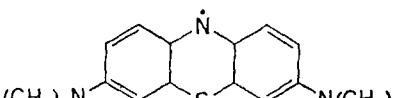
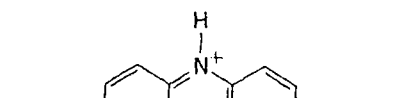
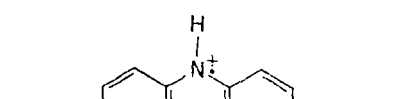
$$MB^+ + e_{aq}^- \longrightarrow MB^{\bullet} \qquad (48)$$

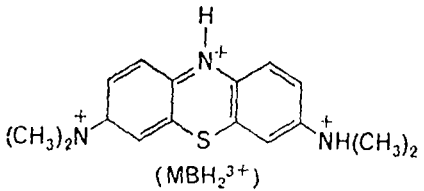
Formate radicals (found in the presence of sodium formate) also react with MB^+ to form $MB^{\bullet}$. The $MB^{\bullet}$ radicals subsequently disproportionate by a second-order process:

$$2MB^{\bullet} + H_2O \longrightarrow MB^+ + MBH + OH^- \qquad (49)$$

In acidic solutions rate constants for reduction of the protonated species have been determined (Table 4). Although the data did not allow the determination of the dissociation constants for transient semiquinones, it indicated that they are weaker acids than those from which they were derived by electron addition[58]. More recent spectroscopic evidence[62, 63]

TABLE 4. Rate constants for radiation-induced reactions of dyes in aqueous solutions

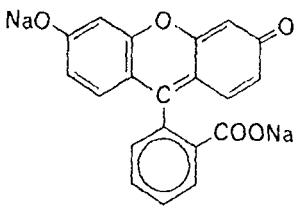
	Rate constant, $M^{-1} s^{-1}$				
	e^-_{aq}	$CO_2^{\cdot-}$	$^{\cdot}COOH$	$^{\cdot}OH$	Semiquinone decay
Methylene blue[a]					
 (MB^+)	$2{\cdot}5 \times 10^{10}$	$5{\cdot}6 \times 10^9$	$\sim 2 \times 10^{10}$		
 ($MB^{\cdot}$)					$2MB^{\cdot} \rightarrow$ (pH = 7·8) 3×10^9
 (MBH^{2+})			$\sim 10^9$		
 ($M\dot{B}H^+$)					$2M\dot{B}H^+ \rightarrow$ (4N H_2SO_4) $\sim 1{\cdot}6 \times 10^9$



(MBH_2^{3+})

~ 7×10^{8}

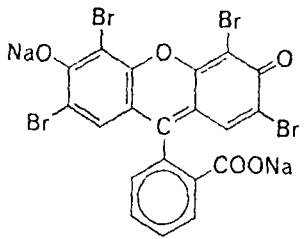
Fluorescein[b]



(Fl)

$1{\cdot}4 \times 10^{10}$ $2{\cdot}5 \times 10^{7}$ $3{\cdot}0 \times 10^{9}$ $2\dot{F}l \rightarrow$ (pH = 10·4 $2{\cdot}0 \times 10^{7}$

Eosin 4[c]



(Eo)

$2{\cdot}2 \times 10^{10}$ $2{\cdot}5 \times 10^{8}$ $1{\cdot}4 \times 10^{9}$ $2\dot{E}o \rightarrow$ (pH = 9·0) $1{\cdot}6 \times 10^{7}$

[a] Reference 58. [b] Reference 61. [c] Reference 60.

indicates that the species present at pH 6 is $MBH^{+\bullet}$ rather than $MB^{+\bullet}$[64] and that the pK of $MBH^{+\bullet}$ is ca. 9[63].

Reaction of the hydroxyl radical with dyes can involve ring addition forming substituted cyclohexadienyl radicals or attack at a functional group[32]. In any event, these processes need not necessarily lead to colour bleaching. Direct pulse radiolytic observation of the formation of transient intermediates formed by hydroxyl radical attack on fluorescein and eosin[60,61] afforded the rate constants for these processes. The hydroxyl radical adduct of fluorescein eliminates water forming a species which subsequently reacts to give a product with an absorption maximum at 500 nm. The products of these reactions under different conditions (Table 4) have been elucidated in some cases and are discussed by Grossweiner[32].

In addition to oxidation and reduction, fluorescein and eosin undergo chemiluminescence[65]. The proposed mechanism involves triplet–triplet interactions leading to a loosely bound triplet–singlet complex which reacts with e^-_{aq} to generate the excited singlet state of the monomer and the dye semiquinone[65].

Radiolysis of dye–biopolymer complexes has been examined recently in an effort to understand the influence of binding on rate processes[66–69]. In many instances the rate constants for the reaction of hydrated electrons with dyes bound to polymers are markedly different from those for the unbound analogues. These results have recently been reviewed[32] and, therefore, are not reiterated here.

D. Pulse Radiolytic Investigations of Electron Transfer Processes

Coenzyme Q, or ubiquinone, is involved in the mitochondrial electron transfer chain. One of the requirements for a compound to be included as an obligatory member of the electron transfer system is, of course, that it must undergo oxidation–reduction at a rate commensurate with the overall enzyme activity[31]. The experimental verification of this point presents, however, considerable difficulties. It is likely that the turnover of the total coenzyme Q is different from that localized in the immediate vicinity of the sites of oxidation and indeed from that of its reactivity in aqueous alcoholic media. Nevertheless, the technique of pulse radiolysis offers a means whereby electron transfer processes can conveniently be investigated directly. Inevitably such studies have been carried out initially on simple model systems, extrapolation of which to complex biological macromolecules may be less than straightforward. The principles of the method can be understood in terms of the following

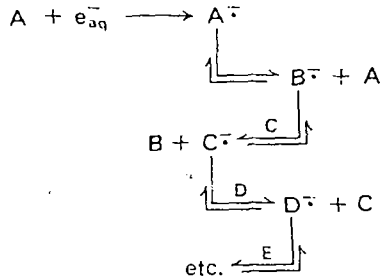
competition scheme:

$$A + e^-_{aq} \xrightarrow{k_{50}} A^{\cdot -} \quad (50)$$

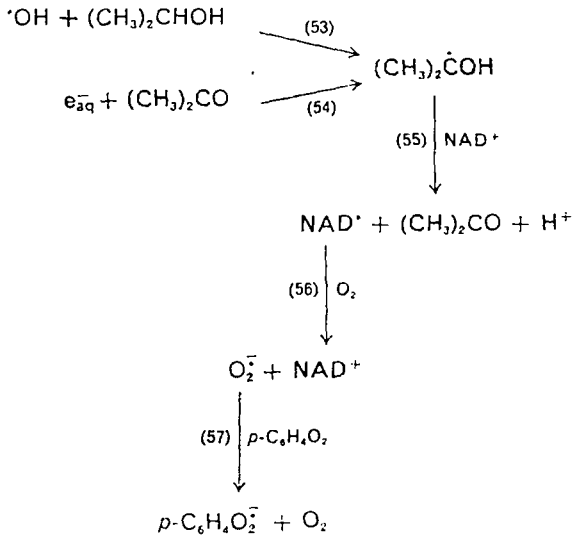
$$B + e^-_{aq} \xrightarrow{k_{51}} B^{\cdot -} \quad (51)$$

$$A^{\cdot -} + B \xrightarrow{k_{52}} B^{\cdot -} + A \quad (52)$$

If $k_{50}[A] \gg k_{51}[B]$ all of the electrons will react with A to form the anion radical $A^{\cdot -}$. Furthermore, if the electron affinity of B is greater than that of A, a subsequent electron transfer with a rate constant of k_{52} will occur. The requirement for the direct pulse radiolytic observation of reaction (52) is a suitable difference in the transient absorption spectrum of $A^{\cdot -}$ and $B^{\cdot -}$. Such conditions prevail for many organic transients for which electron transfer processes have been determined[39]. Under suitable conditions it is perfectly feasible to observe quantitatively chain electron transfer processes of the type:



The following scheme has been proposed for the recently observed multiple electron transfer processes involving acetone, nicotinamide adenine dinucleotide (NAD^+), oxygen and *p*-benzoquinone[70]:



The system for irradiation consisted of 1·0M acetone, 1·0M isopropanol, $2{\cdot}0\times10^{-2}$M NAD^+, $2{\cdot}5\times10^{-4}$M oxygen and $2{\cdot}0\times10^{-5}$M *p*-benzoquinone. Under these conditions, each individual step was shown to occur[70]. The high concentrations of acetone and isopropanol ensured the scavenging of all radiolytically generated radicals to form the alcohol radical, $(CH_3)_2\dot{C}OH$ (equations 53 and 54). When NAD^+ was added to isopropanol and acetone (equation 55), the spectral properties of the new transient ($\lambda_{max} = 400$ nm) corresponded to that of the NAD radical ($NAD^\bullet$). In the absence of oxygen this radical was rather long-lived (over hundreds of μs). In the presence of oxygen, however, it decayed exponentially with a rate constant, k_{56}, of $1{\cdot}9\times10^9$ M^{-1}. This rate constant is in reasonable agreement with the value directly determined for $NAD^\bullet + O_2$. Finally, when *p*-benzoquinone is also present a new transient is formed (equation 57) on a 200 μs time scale, the spectral properties of which correspond to the semiquinone radical anion[70].

The above study clearly illustrates the inherent potential of pulse radiolysis. It is significant that electron transfer involving oxygen in biological molecules has been demonstrated. Future studies of other multicomponent systems may well approach the complexity of biological electron transfer mechanisms.

IV. RADIATION-INDUCED REACTIONS OF QUINONES IN NON-AQUEOUS SOLUTIONS

The radiation chemistry of solutes in organic liquids depends, to a large extent, on the polarity of the solvent[4]. In the more polar solvents, such as alcohols, the electron becomes solvated. The lifetime of the solvated electron, e_s^-, in alcohols is, however, considerably shorter than that in water since in the absence of scavengers or impurities it is rapidly neutralized by

$$e_s^- + ROH_2^+ \longrightarrow {}^\bullet H + ROH \qquad (58)$$

When a solute, *S*, is present in sufficient concentration to compete with reaction (58) electron transfer occurs:

$$e_s^- + S \longrightarrow S^{-\bullet} \qquad (59)$$

resulting in the formation of anion radical, $S^{-\bullet}$. The anion radical may be neutralized by ROH_2^+ (equation 60), react with the solvent (equation 61) or transfer its charge to an available second solute S_1 (equation 62):

$$S^{-\bullet} + ROH_2^+ \longrightarrow \dot{S}H + ROH \qquad (60)$$

$$S^{-\bullet} + ROH \longrightarrow \dot{S}H + RO^- \qquad (61)$$

$$S^{-\bullet} + S_1 \rightleftharpoons S_1^{-\bullet} + S \qquad (62)$$

In less polar solvents the formation of excited states predominates over ionic processes. Both ionizations (forming electrons, e^-, and positive ions) and direct excitation occur:

$$S \xrightarrow{\text{(excitation)}} S^* \tag{63}$$

The excited molecules may dissociate or react with neutral radical ions. Additionally, in non-polar solvents the electron may be neutralized by an excited cation to produce superexcited states (equation 64) or undergo dissociative capture (equation 65) prior to its being solvated:

$$e^- + R^{+*} \longrightarrow R^{**} \tag{64}$$

$$e^- + RX \longrightarrow R^{\cdot} + X^- \tag{65}$$

The radiation chemistry of non-polar liquids involves a greater number of excited states and is generally more complex than that in analogous photochemical processes. Nevertheless many analogies exist between radiation and photo-excitation systems and useful studies are being carried out using both techniques.

Electron transfer processes have been determined for duroquinone[71] and ubiquinone[72] and steady-state and pulse radiolytic investigations have been carried out for a number of quinones in cyclohexane and in benzene[73-75]. These processes will be discussed consecutively in the following sections.

A. Radiolysis of Duroquinone and Ubiquinone in Methanol

Rate constants for the reaction of the solvated electron with *p*-benzoquinone, duroquinone and ubiquinone have been determined by following the rate of decay of e_s^- in methanol at 630 nm (no other transient absorbs at this wavelength) in the presence of different concentrations of these solutes[72]. The rate constants, calculated after taking into consideration the lifetime ($t_{\frac{1}{2}} \sim 1$ μs) of e_s^- in methanol, are given in Table 5. The rate constant for the reaction of e_s^- with ubiquinone can be considered to represent the upper limit for the bimolecular rate of electron transfer to coenzyme Q (ubiquinone) *in vivo*. Apparently all of these quinones are reacting at diffusion-controlled rates which are not dependent on the solvent (see Table 2 for the rate constant of *p*-benzoquinone with electrons in water).

The absorption spectrum of the ubiquinone transient in a methanolic solution of 1×10^{-2}M NaOH is different from that in methanolic 1×10^{-2}M sulphuric acid (Figure 4)[76]. By analogy to the irradiation of other quinones, ubisemiquinone anion radical and neutral ubisemiquinone radical have

TABLE 5. One-electron reactions in biochemical systems[a]

Reaction	Rate constants		
	Ubiquinone	Duroquinone	*p*-Benzoquinone
$e^-_{MeOH} + Q \rightarrow Q^{\cdot}$	$1{\cdot}7 \times 10^{10}$ M^{-1} s^{-1}	$\sim 10^{10}$ M^{-1} s^{-1}	3×10^{10} M^{-1} s^{-1}
$^{\cdot}CH_2OH + Q \rightarrow HCHO + QH^{\cdot}$	$1{\cdot}4 \times 10^{9}$ M^{-1} s^{-1}	$1{\cdot}0 \times 10^{9}$ M^{-1} s^{-1}	$3{\cdot}2 \times 10^{9}$ M^{-1} s^{-1}
$^{\cdot}CH_2O^- + Q \rightarrow HCHO + Q^{\cdot}$	$2{\cdot}0 \times 10^{9}$ M^{-1} s^{-1}	$3{\cdot}3 \times 10^{9}$ M^{-1} s^{-1}	—
$2\ QH^{\cdot} \rightarrow Q + QH_2$	$4{\cdot}8 \times 10^{7}$ M^{-1} s^{-1}	$4{\cdot}4 \times 10^{8}$ [b] M^{-1} s^{-1}	$7{\cdot}3 \times 10^{8}$ M^{-1} s^{-1}
$QH^{\cdot} \rightarrow Q^{\cdot} + H^+$	$1{\cdot}0 \times 10^{4}$ s^{-1}	$7{\cdot}4 \times 10^{3}$ s^{-1}	—

[a] Data taken from reference 72.
[b] With an $\varepsilon_{410\ nm}$ for DQH$^{\cdot}$ of 3500 M^{-1} s^{-1}.

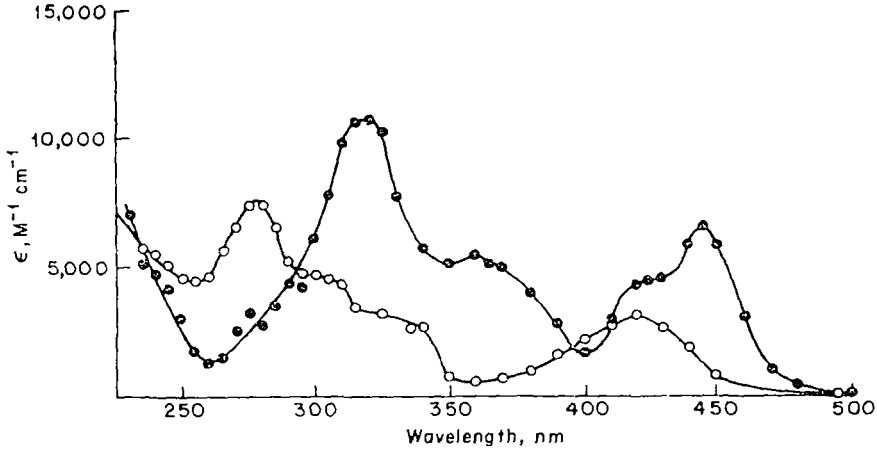


FIGURE 4. Absorption spectrum of ubisemiquinone. Anionic form (●), neutral form (○); ε is the molar extinction coefficient. Reproduced with permission from E. J. Land, M. Simic and A. J. Swallow, *Biochim. Biophys. Acta*, **226**, 239 (1971).

been assigned to these spectra (Chart IV) since in strongly acidic methanolic solution the following reactions take place 'instantaneously':

$$e^-_5 + H^+ \longrightarrow H^{\cdot} \qquad (66)$$

$$^{\cdot}H + CH_3OH \longrightarrow H_2 + \dot{C}H_2OH \qquad (67)$$

Making the assumption that the rate constant for the protonation of ubisemiquinone anion in methanol, k_{67}, is $(3 \pm 1) \times 10^{10}$ M^{-1} s^{-1}, the pK

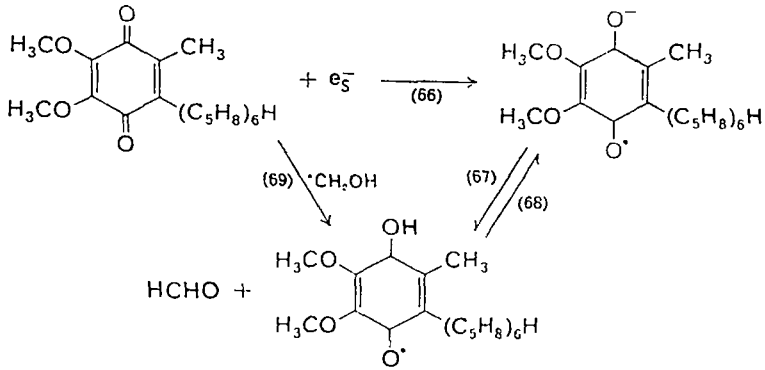


CHART IV

for this process, $\log k_{67}/k_{68}$, has been estimated to be $6{\cdot}45 \pm 0{\cdot}15$. The ubisemiquinone radical disproportionates at a rate which is an order of magnitude slower than the corresponding values obtained for duroquinone or *p*-benzoquinone (Table 5)[72]. These rate differences can be rationalized in terms of steric hindrance caused by the isoprene side-chain in ubiquinone.

B. *Radiolysis of p-Benzoquinone, Duroquinone and Ubiquinone in Cyclohexane and Benzene*

Pulse-irradiation of duroquinone in benzene and in cyclohexane results in the formation of a transient with absorption maxima at 490 and 410 nm, respectively (Figure 5)[73,77]. There has been some question as to the structure of this transient. Initially, by analogy with the transient spectrum obtained on flash photolysis of duroquinone in liquid paraffin[44], this absorption was ascribed to duroquinone triplet, but subsequently it was reassigned to a photo-isomer of duroquinone. In a recent work, Land has marshalled evidence in favour of the transient being due to triplet–triplet absorption[77]. These arguments were based on the fact that the rate of the first-order decay of the transient absorption at 490 nm is increased with increasing concentration of anthracene (a known triplet quencher) and that the rate of transient decay at 490 nm is exactly paralleled by that of the formation of anthracene triplet at 422·5 nm (Table 6).

The proposed mechanism for the formation of duroquinone triplets in cyclohexane and benzene involves electron and positive ion scavenging by the solute and by the solvent, followed by geminate neutralization[77] (equations 58, 59 and 64).

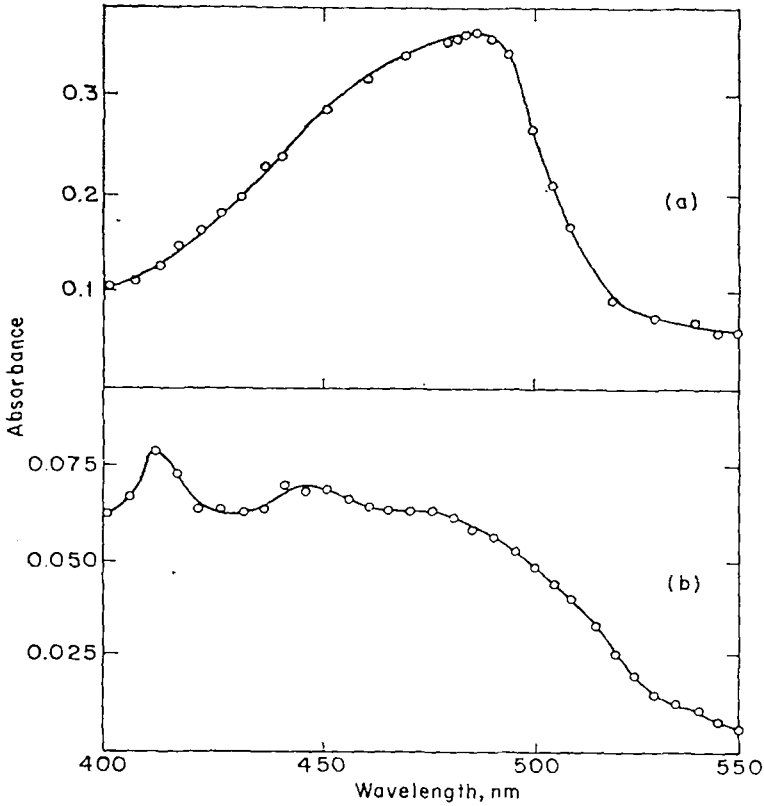


FIGURE 5. Transient spectra immediately (< 1 μs) after pulse radiolysis of duroquinone in benzene and cyclohexane. (a) 10^{-2}M duroquinone in benzene, dose $\approx$ 5000 rad; (b) 10^{-2}M duroquinone in cyclohexane, dose $\approx$ 11,000 rad. Path length = 2·5 cm. Reproduced with permission from E. J. Land, *Trans. Faraday Soc.*, **65**, 2815 (1969).

An earlier steady-state radiolytic investigation of *p*-benzoquinone in cyclohexane is in agreement with this mechanism[74,75]. The determined *G*-value for *p*-benzoquinone consumption (10·6) was found to be equal to the sum of the quinone-containing product yields as required by the material balance: G(*p*-benzoquinone) = G(monocyclohexylquinone) + 2G(*p*-benzhydroquinone); for monocyclohexylquinone $G = 4{\cdot}4$ and for *p*-benzhydroquinone, mostly as quinhydrone, $G = 3{\cdot}1$. In addition, cyclohexene ($G = 1{\cdot}0$), bicyclohexyl ($G = 0{\cdot}15$) and hydrogen ($G = 3{\cdot}1$) are formed[74]. These products can be formed by scavenging of hydrogen atoms or cyclohexyl radicals or by the reaction of the excited quinone with the solvent. Using tritium-labelled cyclohexane, no tritiated quinone was found in irradiated solutions and in the photolysis, no cyclohexene or

TABLE 6. Pulse radiolytic rate constants for the duroquinone–anthracene system in benzene and cyclohexane[a]

[Anthracene], M	10^{-5} k, s^{-1}			
	Decay[b]		Formation[c]	
	Benzene	Cyclohexane	Benzene	Cyclohexane
3×10^{-5}	2·6	2·2	≈3	≈3
10^{-4}	5·9	—	6·2	—
3×10^{-4}	>10	—	>10	—

[a] Data taken from reference 77; [duroquinone] in benzene = 10^{-3}M and in cyclohexane = 10^{-2}M: dose ≈ 1000 rad in benzene and ≈ 3500 rad in cyclohexane.
[b] At 490 nm.
[c] At anthracene triplet absorption maximum, 430 nm in benzene and 422·5 in cyclohexane.

bicyclohexyl could be detected. These results led to the postulation that the radiolysis of *p*-benzoquinone in cyclohexane involves cyclohexyl radical scavenging (with $G = 3{\cdot}4$), deactivation of excited cyclohexene molecules (with $G = 2{\cdot}3$) and the reaction of cyclohexene with hydrogen ($G = 1{\cdot}0$)[74,75].

The decrease in the yield of duroquinone [G(-duroquinone)] in irradiated cyclohexane solutions was equal to the sum of the yields of hydrogen, cyclohexene and bicyclohexyl, and the yields of these products are lower than those in pure cyclohexane. These results are interesting since duroquinone is photochemically inert in cyclohexane and its affinity for methyl radical is some twentyfold less than that of *p*-benzoquinone. Additionally, no change in duroquinone concentration was found in irradiated benzene solutions[74,75]. The implication of these results is that duroquinone is both an electron and a cyclohexyl radical scavenger.

A transient absorption spectra, with an absorption maximum centred around 440 nm, was observed in the nanosecond irradiation of ubiquinone in cyclohexane and in benzene[78]. The half-life in the former solvent, determined by laser photolysis, was 650 ns and that in benzene, studied by pulse radiolysis, 450 ns. In order to establish the nature of this transient, its energy level and the extinction coefficient effects of triplet donors and acceptors were investigated. Addition of neither 1×10^{-2}M biacetyl nor 1×10^{-3}M anthracene in cyclohexane appreciably decreases the lifetime of the ubiquinone transient, suggesting that if any ubiquinone triplet is present, its energy lies below that of biacetyl ($E_T = 236$ kJ mole^{-1} in cyclohexane) and anthracene ($E_T = 176$ kJ mole^{-1} in cyclohexane.)

Conversely, the anthracene triplet lifetime, observed in 10^{-2}M solutions of anthracene in cyclohexane at 420 nm, decreased markedly on the addition of 2×10^{-4}M ubiquinone, which substantiates that the triplet energy of anthracene is indeed greater than that of ubiquinone. Unequivocal evidence was obtained for the presence of ubiquinone triplet by observing the sensitized triplet formation of β-carotene ($E_T = 94$–121 kJ mole^{-1} in cyclohexane) in irradiated cyclohexane solutions of 2×10^{-4}M β-carotene and 1×10^{-3}M ubiquinone. In the absence of ubiquinone no transient absorption due to β-carotene triplet was observed, indicating that its formation, in the presence of ubiquinone, must be due to energy transfer from the ubiquinone triplet donor. These and similar experiments in benzene suggest that the triplet energy level of ubiquinone lies between 123–170 kJ mole^{-1}, a value considerably smaller than those for other quinones[78]. The significance of this result is that energy transfer from chlorophyll to plastoquinone, which is structurally similar to ubiquinone, may be energetically favourable during photosynthesis.

Using biphenyl triplet as the standard, $\varepsilon_{440\,nm} = 19{,}000$ M^{-1}cm^{-1} and $\varepsilon_{430\,nm} = 13{,}000$ M^{-1}cm^{-1} have been determined for the ubiquinone triplet in cyclohexane and in benzene, respectively[78].

It is worth mentioning that the lifetime of ubiquinone triplet in benzene and in cyclohexane, like the lifetime of other quinone triplets, is anomalously short compared to other triplets. At present, the insufficient information on the mechanism of triplet decay precludes excessive speculation on the significance of this point.

The fact that quinones act both as radical and electron scavengers points out the inherent dangers of using these compounds to determine total radical yields, i.e. for the reaction, organic liquid + *p*-benzoquinone → hydroquinone, since G(hydroquinone) is not necessarily equal to G(total radical yield).

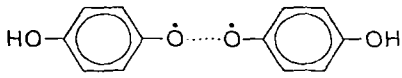
C. Irradiations in the Solid State

Steady-state irradiations of organic compounds in suitable matrices at liquid nitrogen or lower temperatures has provided a convenient technique for investigation of free radicals and excited states by absorption or electron spin resonance spectroscopy.

Solid hydroquinone has two crystalline modifications. The less stable β-form can accommodate large amounts of rare gases, forming the so-called clathrates of hydroquinone. At room temperature there is a slow release of the gas from the hydroquinone clathrate with the concomitant formation of the more stable α-form. Recent γ-irradiation of the β-hydroquinone resulted in the inhibition of the polymorphic phase

transition[79]. Although no mechanism has been suggested, this work is significant since it represents the first instance in which radiation-induced phase transition inhibition has been observed.

A radical pair, formed in an X-ray irradiated single crystal of the clathrate complex of hydroquinone, has been reported to be due to a phenoxyl radical pair in which the unpaired electron is delocalized over the whole phenoxyl radical[80],



V. APPE

Absorption spectra of quinone

Compound	Solvent	Suggested species
Benzoquinones and related compounds		
p-Benzoquinone	Water (pH 2)	Semiquinone$^{\bullet}$
	Water (neutral)	Semiquinone$^{\bullet-}$
	Water	$^{\bullet}$OH Adduct
	Water	Trihydroxycyclohexadienyl radical(s)
	Water	Dihydroxycyclohexadienyl radical(s)
	Water	*p*-Hydroxyphenoxyl radical (semiquinone$^{\bullet}$)
p-Benzhydroquinone	Water	*p*-Hydroxyphenoxyl radical (semiquinone$^{\bullet}$)
4-*t*-Butyl-*o*-benzoquinone	Water (0·8M H_2SO_4)	Neutral molecule
4-*t*-Butyl-1,2-dihydroxybenzene	Water (0·8M H_2SO_4)	Neutral molecule
2,5-Dichloro-*p*-benzoquinone	Water	Neutral molecule
2,5-Dichloro-*p*-benzhydroquinone	Water	Neutral molecule
2,5-Dichloro-3,6-dihydroxy-*p*-benzoquinone	Water	Neutral molecule
2,5-Dichloro-3,6-dihydroxy-*p*-benzhydroquinone	Water	Neutral molecule
2,5-Dihydroxy-*p*-benzoquinone	Water	Neutral molecule
1,2-Dihydroxybenzene (catechol)	Water	*o*-Hydroxyphenoxyl radical (semiquinone$^{\bullet}$)
1,3-Dihydroxybenzene (resorcinol)	Water	*m*-Hydroxyphenoxyl radical (semiquinone$^{\bullet}$)
2,5-Dimethyl-*p*-benzoquinone	Water	Neutral molecule

DIX

hydroquinones and their transients[a]

λ_{max} or λ, Å [b]	ε, $M^{-1}\,cm^{-1}$ [b]	Comments	Reference
4150	$5500\ M^{-1}$	$pK = 4{\cdot}0$	41
4250	$7{\cdot}3 \times 10^3\ M^{-1}$		41
4150	$6600\ M^{-1}$		41
<3200			41
3200			46 and reference 8 cited therein
4280		Narrow, very strong	81
<3900		Very broad, strong	
4060		Narrow, strong	
4020		Narrow, strong	
4280		Narrow, very strong	81
<3900		Very broad, strong	
4060		Narrow, strong	
4020		Narrow, strong	
2600	3600 ± 20		48
2790	2380 ± 20		
4000	930 ± 25		
2600	715 ± 10		48
2790	2750 ± 20		
4000	5 ± 5		
2720	19,650 ± 300		47
2980	354 ± 30		
2720	860 ± 20		47
2980	4500 ± 50		
5120	398 ± 12		47
	0		47
2460	1285 ± 60		47
2570	4680 ± 120		
2880	21,180 ± 580		
≈3500		Very broad, strong	81
3600		Narrow, strong	
4300		Narrow, strong	81
4080		Narrow, weak	
<4000		Very broad, strong	
2570	19,500 ± 500		47
2880	257 ± 10		

Compound	Solvent	Suggested species
2,5-Dimethyl-*p*-benzoquinone	Water (pH 2)	Semiquinone$^{\bullet}$
	Water (pH 7)	Semiquinone$^{\bullet -}$
2,5-Dimethyl-*p*-benzhydroquinone	Water	Neutral molecule
Diphenoquinone	Water	*p*-(4-hydroxyphenyl)phenoxyl radical
Hydroxy-*p*-benzoquinone	Water	Neutral molecule
Tetrachloro-*p*-benzoquinone (chloranil)	Ethanol	Triplet
		Semiquinone$^{\bullet}$
	Cyclohexane	Triplet
Tetrafluoro-*p*-benzoquinone (fluoranil)	Chloroform	Neutral molecule ($n\pi^*$)
		Neutral molecule ($\pi\pi^*$)
	Tetrahydrofuran	Neutral molecule
Tetramethyl-*p*-benzoquinone (duroquinone)	Water (pH 2)	Semiquinone$^{\bullet}$
	Water (pH 7)	Semiquinone$^{\bullet -}$
	Water (ethanol, H_2SO_4)	Semiquinone$^{\bullet}$
	Isopropanol	Neutral molecule
	Water/isopropanol (75/25, v/v)	Neutral molecule
	Liquid paraffin	Semiquinone$^{\bullet}$
	Liquid paraffin	Semiquinone$^{\bullet -}$
	Liquid paraffin	T–T
	Benzene	T–T or isomer
	Benzene	T–T
	Cyclohexane	T–T
	Cyclohexane	Neutral molecule
	Cyclohexane	T–T
	Cyclohexane	
	Cyclohexane	Semiquinone$^{\bullet}$

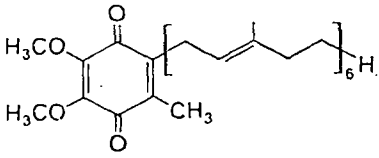
λ_{max} or λ, Å [b]	ε, $M^{-1}\,cm^{-1}$ [b]	Comments	Reference
4150		$pK = 4{\cdot}6 \pm 0{\cdot}1$	82
4400			82
2570	343 ± 10		47
2880	3265 ± 12		
≈6300		Very broad, strong	81
4500		Narrow, strong	
4000		Broad, very strong	
2460	$10{,}800 \pm 200$		47
2570	$14{,}200 \pm 350$		
2880	450 ± 12		
5000		Transient reacts with solvent yielding semi-quinone•	83
4400			
4200			
5000			
ca. 3380	ca. 200		83
ca. 2580	ca. 27,500	Two overlapping maxima at 2640 and 2530 Å	84
Two bands		Longest λ band is very intense	84
4300		$pK = 5{\cdot}1 \pm 0{\cdot}1$	82
4450			82
3000	$G\varepsilon = 52{,}300$	Also $G\varepsilon_{5000\,Å} = 735$,	71
4200	$G\varepsilon = 37{,}300$	shoulder at 4050 Å; single absorbing species	
34,000 cm^{-1}	$(1{\cdot}44 \pm 0{\cdot}02) \times 10^2$	Not λ_{max}	86
34,000 cm^{-1}	$(1{\cdot}12 \pm 0{\cdot}02) \times 10^2$	Not λ_{max}	86
4100			43
3200			
4350			44
4600			44
4900			
3400	$G\varepsilon = 7800$	Second species present	71
4850	$G\varepsilon = 16{,}000$	(DH• and/or D^- ?)	
4900	9800	Naphthalene, anthracene and diphenyl used as donors or acceptors	77
4900	4700		
3310	251		75
4180	24·0		
4330	25·1		
3400	$G\varepsilon = 2200$	Also $G\varepsilon_{4900\,Å} = 2200$	71
4400	$G\varepsilon = 3230$		
4300	7400		85
4200			73

Compound	Solvent	Suggested species
Benzoquinones and related compounds (cont.)		
	Cyclohexane	Radical ion, triplet, or biradical
	Tetrahydrofuran	Semiquinone$^{\bullet}$
Tetramethyl-*p*-benzhydroquinone (durohydroquinone)	Water/isopropanol (50/50, v/v)	Neutral molecule
	Isopropanol	Neutral molecule
1,2,4-Trihydroxybenzene	Water	Neutral molecule
Anthraquinone	Benzene	Triplet
9,10-Anthraquinone-2-sulphonate (sodium salt)	Water	Semiquinone$^{\bullet}$
	Water	Semiquinone$^{\bullet-}$
	Water	$^{\bullet}$OH adduct
9,10-Anthraquinone-2,6-disulphonate	Water (pH 2)	Semiquinone$^{\bullet}$
	Water (pH 7)	Semiquinone$^{\bullet-}$
2-*t*-Butyl-9,10-anthraquinone	Ethanol	Neutral molecule
2-*t*-Butyl-9,10-anthrahydroquinone	Ethanol	Neutral molecule
2-Piperidinoanthraquinone	Benzene	Triplet
	Benzene	Semiquinone$^{\bullet-}$
1,4-Naphthaquinone	Water (pH 2)	Semiquinone$^{\bullet}$
	Water (pH 7)	Semiquinone$^{\bullet-}$
2-Methyl-1,4-naphthaquinone	Water (pH 2)	Semiquinone$^{\bullet}$
	Water (pH 7)	Semiquinone$^{\bullet-}$
9,10-Phenanthraquinone	Ethanol	Neutral molecule
	Ethanol	Semiquinone$^{\bullet}$
		Semiquinone$^{\bullet-}$ (?)
	Tetrahydropyrane	Neutral molecule
	Tetrahydropyrane	Quinone^{2-}, $2Na^{+}$

λ_{max} or λ, Å [b]	ε, $M^{-1}\,cm^{-1}$ [b]	Comments	Reference
3200			
4600			73
4100	$G\varepsilon = 13{,}600$	Also $G\varepsilon_{3200\,Å} = 4300$, $G\varepsilon_{3600\,Å} = 3800$, $G\varepsilon_{4900\,Å} = 2800$	71
34,000 cm^{-1}	$(16{\cdot}48 \pm 0{\cdot}33) \times 10^2$	Not λ_{max}	86
34,000 cm^{-1}	$(16{\cdot}50 \pm 0{\cdot}20) \times 10^2$	Not λ_{max}	86
2570	350 ± 10		47
2880	3235 ± 25		
4400		Broad, weak (apparent peak at 3800 Å)	57
3600			
3900	11,900	$pK = 3{\cdot}25$	57
5000	8200		57
3900	8200		
4600	3900		57
3100	18,000		
3900		$pK = 3{\cdot}2 \pm 0{\cdot}1$	82
3950			82
5250			
4360	8	λ_{max} (?)	87
4360	2600	λ_{max} (?)	87
5300			57
3460			57
3740			
4950			
5600			
3800		$pK = 4{\cdot}1 \pm 0{\cdot}1$	82
3900			82
3700		$pK = 4{\cdot}7 \pm 0{\cdot}1$	82
4050			82
4360	1200	λ_{max} (?)	87
3855			87
5450			87
3125	4070		88
3990	1700		
3310	8050		83
3810	12,800		
4770	1500		

Compound	Solvent	Suggested species
	Tetrahydropyrane	Semiquinone$^{\bullet}$, Na^+
	Tetrahydropyrane	Dimagnetic dimer^{2-}, $2Na^+$
Acenaphthaquinone	Tetrahydropyrane	Neutral molecule
	Tetrahydropyrane	Quinone^{2-}, $2Na^+$
Alicyclic quinones and dyes		
Acridine	Methanol	Neutral molecule
	Methanol	Semiquinone$^{\bullet}$
	Ethanol	Semiquinone$^{\bullet}$
	Benzene	Semiquinone$^{\bullet}$
	Benzene	T-T
Camphoroquinone	Benzene	Triplet
	Carbon tetrachloride	Triplet
	Isopropanol	Triplet (short-lived)
		Hydrogen adduct
		Free radical (long-lived)

λ_{max} or λ, Å [b]	ε, M^{-1} cm^{-1} [b]	Comments	Reference
3310	15,400		88
4990	5700		
4400	4650	See cited reference for postulated structure	88
6700	4900		
3010	7500		88
3120	6500		
2100	15,300		88
3750	ca. 3000		
ca.2500			89, 90
3500			
5640			
2780			89, 90
ca.4800			
ca.5200			89, 90
3520			89, 90
5570			
4400		Intense	89–91
3140		Probably single initial transient, transitions are assigned	92
4040			
6380			
7060			
7960			
9160			
10,700			
$\lesssim$2000		Probably single initial transient, transitions are assigned	92
2800			
3160			
5000			
5900			
6380			
7050			
7960			
9160			
10,680			
$\lesssim$2200		Hydrogen adduct* absorbs mainly at 3200 Å, u.v. absorption at ca. same λ as triplet	92
2760			
3200			
~5000			
6300			
7020			
7900			
9080			
10,600			

Compound	Solvent	Suggested species
Ubiquinone 	Methanol	Neutral molecule
	Methanol (H_2SO_4)	Semiquinone$^{\bullet}$
	Methanol (H_2SO_4)	Semiquinone$^{\bullet}$
	Methanol (NaOH)	Semiquinone$^{\bullet-}$
	Methanol (NaOH)	Semiquinone$^{\bullet-}$

[a] See the cited reference for the method of determination and experimental conditions.
[b] Unless specified otherwise.

VI. ACKNOWLEDGMENTS

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λ_{max} or λ, Å [b]	ε, M^{-1} cm^{-1} [b]	Comments	Reference
2740	15,150		31
4200	3000 (2900, 3100)	$\varepsilon_{4100\ Å}$ = 3500 (E. J. Land, unpublished results)	72
4200	3000	$\varepsilon_{2740\ Å}$ = 7400	76
4450	7200 (6400, 8000)	$\varepsilon_{2740\ Å}$ = 2500	72
4450	6400	Also $\varepsilon_{4150\ Å}$ = 8000, lower value probably more correct	76

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The Chemistry of the quinonoid compounds
Edited by Saul Patai

CHAPTER 11

Fragmentation reactions of quinones

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I. INTRODUCTION

This chapter is concerned with reactions of 1,2- and 1,4-benzoquinones, 1,2- and 1,4-naphthaquinones, 9,10-anthraquinones and 9,10-phenanthrenequinones in which two or more carbon–carbon bonds of the quinone ring are broken and where, as a consequence, fragments are formed. This includes reactions where a one-carbon fragment is lost provided the carbon atom of the fragment was originally part of the quinone ring. Often reactions of this type involve ring-contraction and loss of carbon dioxide. Ring-opening reactions which give acids or acid derivatives are also included because many of the reactions are closely related to the ring-contraction reactions, and because it is only necessary to decarboxylate the acids to release carbon atoms that were originally part of the quinone rings. Photochemical reactions are not discussed.

Most fragmentations are the result of hydrolytic or oxidative processes and for convenience these are considered in separate sections. Some reactions, often those involving alkaline oxidizing agents, cannot be readily classified in this way because both hydrolytic and oxidative processes are involved[1]. Such reactions are considered together with other oxidations unless it is clear that oxidation merely modifies the products of what are essentially hydrolytic processes.

In many cases the reactions discussed are complex and, as extensive mechanistic studies have not been made, their mechanisms are often not known with any certainty. Some of the schemes that have been suggested to explain the reactions are included here, partly in the hope that the reader will be tempted to seek evidence that will help us to understand these reactions more fully.

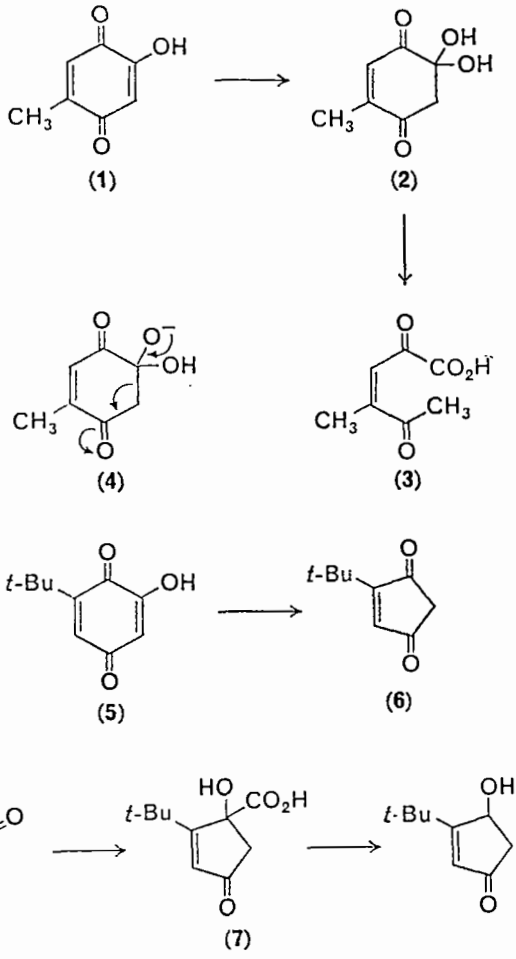
II. BENZOQUINONES

A. *Hydrolytic Reactions*

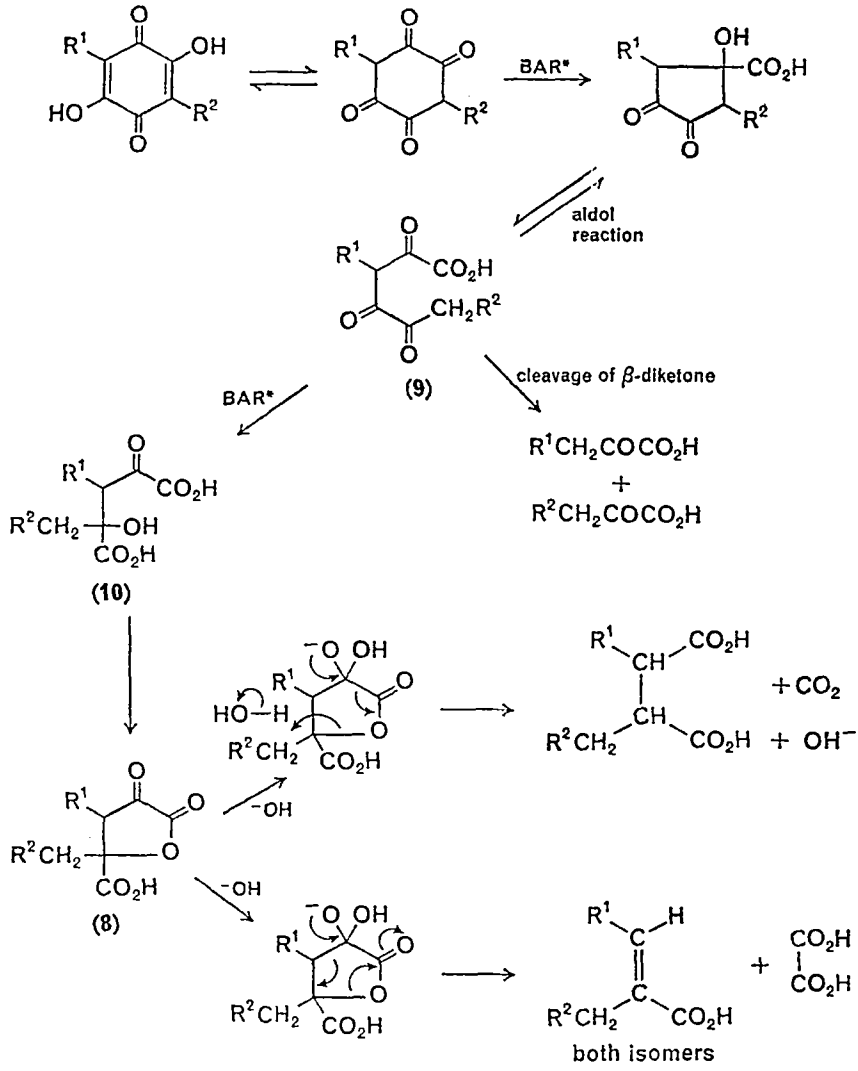
When many benzoquinones, including 1,4-benzoquinone itself, are treated with alkali, complex reactions occur which result in the formation of hydroquinols and amorphous polymeric materials known as 'quinone humic acids'[2,3]. Hydroxybenzoquinones, however, tend to undergo ring-opening or ring-contraction reactions when treated with alkali. One of the simplest reactions of the former type is the hydrolytic cleavage of 2-hydroxy-5-methyl-1,4-benzoquinone (**1**)[4]. At self-pH this quinone hydrates to the diol **2** and at higher pH the diol ring-opens to give the diketo acid **3**. The reaction presumably proceeds via anion **4**. The reaction between 2-hydroxy-6-*t*-butyl-1,4-benzoquinone (**5**) and alkali in the presence of air is much more complicated[5]. Numerous products are obtained, one of the simplest of which is the dione **6**. This almost certainly arises by decarboxylation of the hydroxyl acid **7** and oxidation of the resulting alcohol. It has been suggested[5] that the hydroxyl acid is formed by a benzilic acid rearrangement of the *o*-quinone tautomer of **5**. Another possibility is that **5** ring-opens like **1** and that the diketo acid produced cyclizes to give hydroxyl acid **7**. Diketo acids of a similar type are known to cyclize in this manner, especially in the presence of base[6].

2,5-Dihydroxybenzoquinones react with alkali by three main pathways. These lead to the formation of (i) α-keto acids, (ii) succinic acids and carbon dioxide and (iii) αβ-unsaturated acids and oxalic acid. Corbett and Fooks have carried out kinetic studies on some of these reactions and suggested[7] that the various products are formed by the pathways outlined in Scheme 1. In support of this it is known that alkylated γ-lactones of the

type **8** react with alkali to give dialkylsuccinic acids and carbon dioxide[8] and that the lactone (**8**; $R^1 = R^2 = p\text{-}HOC_6H_4$) reacts with alkali to give the appropriate cinnamic acids[9]. Two aspects of Scheme 1 merit comment.



Firstly, a possible alternative route for the conversion of the starting material to the triketo acid **9** is via a cleavage reaction similar to that of quinone **1** discussed above. Secondly, Thomson[10] has questioned whether γ-lactones of the type **8** could be formed under the reaction conditions. Although γ-hydroxy acids do not normally cyclize under basic conditions, compounds of the type **10** may be able to lactonize by an elimination–addition mechanism. Thus **10**, being a β-hydroxyketone, may dehydrate under the basic conditions to give an $\alpha\beta$-unsaturated ketone system, and



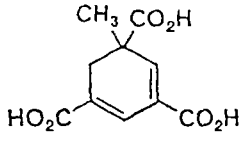
*BAR = benzilic acid rearrangement

SCHEME 1

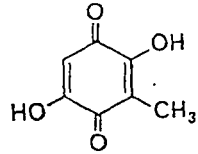
the carboxylate anion may then add conjugatively to this system to produce the γ-lactone.

The type of products obtained when 2,5-dihydroxybenzoquinones are degraded with alkali depends largely on the nature of the other substituents. 2,5-Dihydroxybenzoquinone gives pyruvic acid and its self-condensation product **11** as the only products[7], but the methyl derivative **12** gives αβ-dimethylsuccinic acid as well as the α-keto acids α-oxobutyric acid

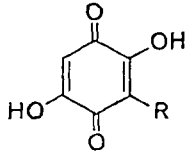
and pyruvic acid (together with **11**)[7]. Alkaline degradations of the two naturally occurring alkyl derivatives embelin **13**[11] and rapanone **14**[12] give α-keto acids **15** and **16** respectively; no other acids were isolated.



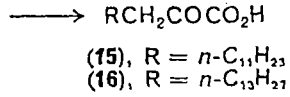
(11)



(12)

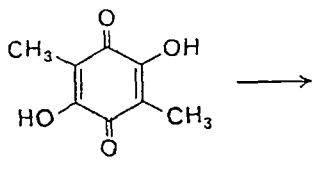


(13), R = n-$C_{11}H_{23}$
(14), R = n-$C_{13}H_{27}$

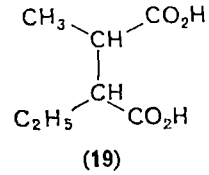


(15), R = n-$C_{11}H_{23}$
(16), R = n-$C_{13}H_{27}$

The dialkyl derivatives **17** and **18** react to give succinic acids **19** and **20**[7,8], but the diphenyl derivative **21** (polyporic acid) gives oxalic acid and both geometrical isomers of the cinnamic acid **22** in addition to the succinic acid **23**[9]. The related diaryl derivative atromentin (**21**; p-HOC_6H_4 in place of each Ph) behaves similarly[9].



(17)



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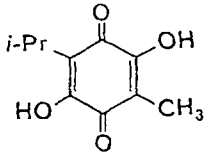

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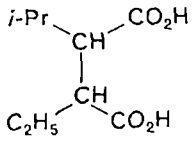
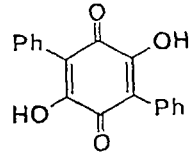


(20)



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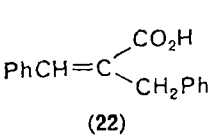
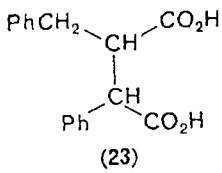


(22)



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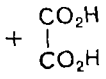
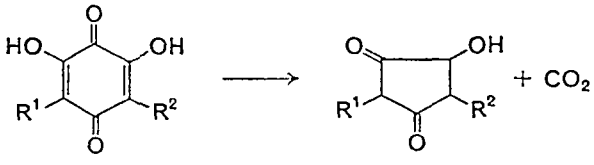
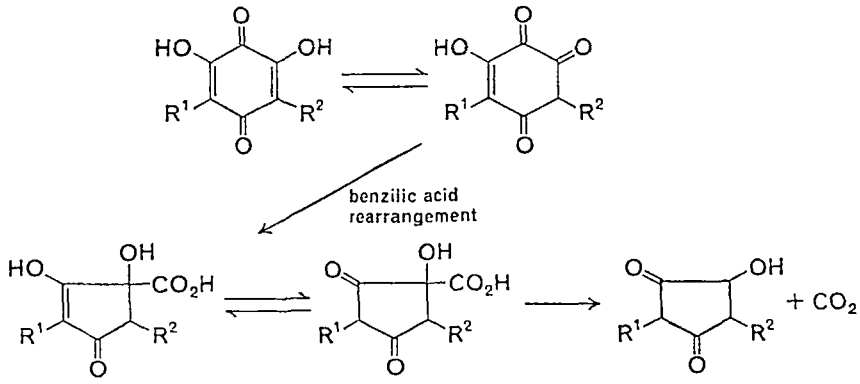


2,6-Dihydroxybenzoquinones, in contrast to 2,5-dihydroxybenzoquinones, usually undergo ring-contraction reactions when treated with alkali giving cyclopentane derivatives and carbon dioxide. Thus, the 3-methyl derivative **24** gives[13] the dione **25** and the 3,5-dimethyl derivative **26** gives[13] the dione **27**. Corbett has made kinetic studies on these reactions and proposed that the products are formed by the pathways in Scheme 2[13]. 3-Acetyl-2,6-dihydroxy-5-methyl-benzoquinone (**28**) undergoes a similar reaction giving the dione **29**[14].



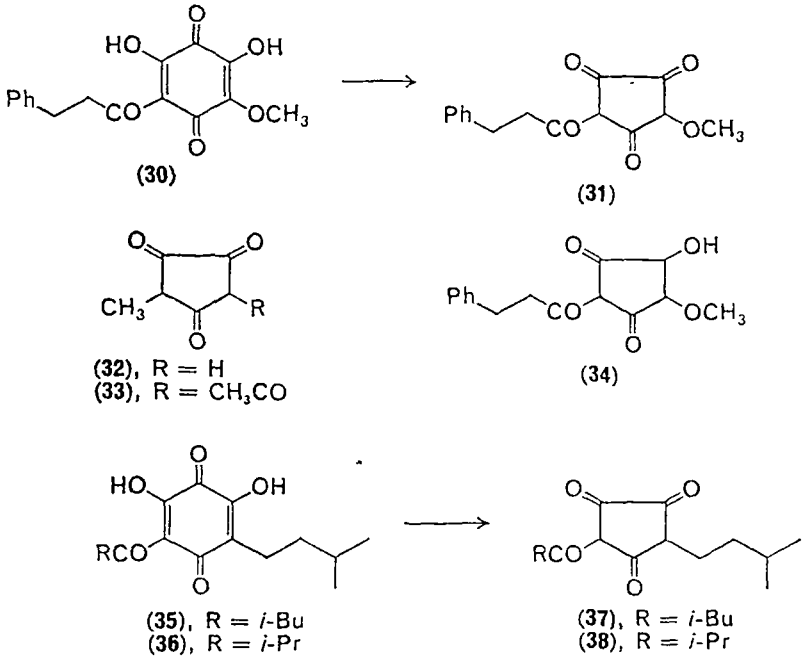
(**24**), R^1 = Me, R^2 = H
(**26**), R^1 = R^2 = Me
(**28**), R^1 = CH_3CO, R^2 = Me

(**25**), R^1 = Me, R^2 = H
(**27**), R^1 = R^2 = Me
(**29**), R^1 = CH_3CO, R^2 = Me



SCHEME 2

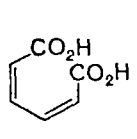
Treatment of quinone **30** with alkali gives the trione **31**[15] and the reactions of **24** and **28** with alkali give as minor products the triones **32**[13] and **33**[14]. These products are probably formed by oxidation of **34**, **25** and **29**. Unreacted quinone starting material might be the oxidizing agent[15] or the oxidation might occur during the work-up[13]. Similar conversions have been effected using an alkaline oxidizing agent, namely alkaline sodium hypobromite. Treatment of humuloquinone **35** and cohumuloquinone **36** with this reagent gives isohumilic acid **37**[16] and isocohumilic acid **38**[17] respectively.



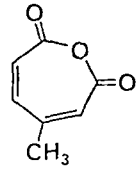
B. Oxidation Reactions

Benzoquinones are oxidized by many reagents. In some cases all or most of the carbon atoms originally present in the quinone ring are present in one major product, but in other reactions, especially those involving the use of vigorous oxidizing agents, the carbon skeleton of the quinone ring is extensively degraded. For convenience these are discussed separately, the former type being considered first.

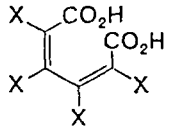
1,2-Benzoquinones tend to behave like α-diketones when treated with peracids and undergo Baeyer–Villiger type oxidations[18]. The initial products are the cyclic anhydrides but these may be hydrolysed under the reaction conditions to give the diacids. 1,2-Benzoquinone itself reacts with peracetic acid to give *cis,cis*-muconic acid (**39**)[19,20] and 4-methyl-1,2-benzoquinone reacts with monoperphthalic acid to give the anhydride **40**[21]. When tetrabromo-1,2-benzoquinone is treated with monoperphthalic acid the tetrabromomuconic acid **41** initially formed cyclizes to the tribromomuconic acid lactone **42**[22,23]. A similar reaction occurs when tetrachloro-1,2-benzoquinone is treated with monoperphthalic acid except that in this case tetrachloromuconic acid **43** is the major product and the lactone **44** is only a minor product[24].



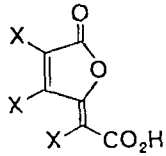
(39)



(40)

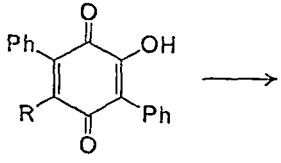


(41), X = Br
(43), X = Cl

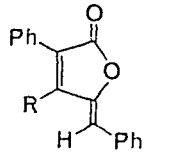


(42), X = Br
(44), X = Cl

Several oxidation reactions of hydroxybenzoquinones result in the formation of γ-lactones. Thus, the 3,6-diphenyl-2-hydroxybenzoquinones **45, 46** and **47** react with dimethyl sulphoxide and acetic anhydride to give the γ-lactones **48, 49** and **50**[25]. These products may be formed[26] via a Baeyer–Villiger type of oxidation as shown in Scheme 3.

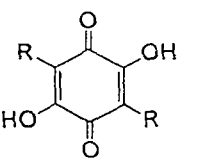


(45), R = H
(46), R = Cl
(47), R = OCH_3

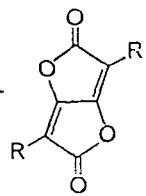


(48), R = H
(49), R = Cl
(50), R = OCH_3

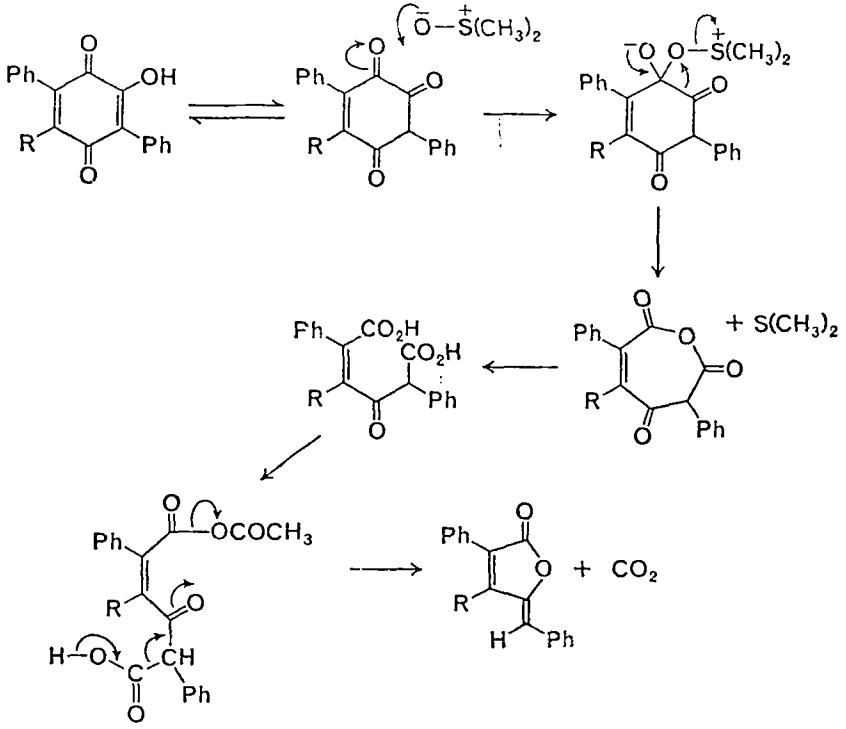
Atromentin **51** reacts with hydrogen peroxide under acidic conditions to give the di-γ-lactone **52**[9], presumably by oxidative cleavage of the *o*-quinone tautomer of **51** and cyclization of the resulting diacid. Oxidation of polyporic acid **53** under similar conditions gives only a trace of the corresponding lactone[9], but this conversion can be carried out efficiently using lead tetraacetate[27] or dimethyl sulphoxide and acetic anhydride[25].



(51), R = *p*-HOC_6H_4
(53), R = Ph

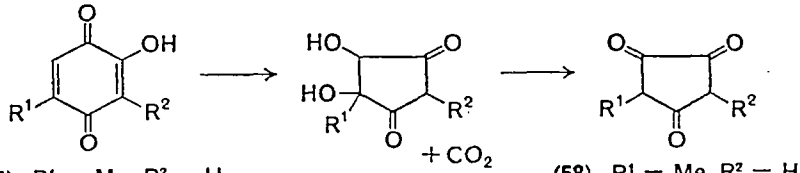


(52), R = *p*-HOC_6H_4



SCHEME 3

Hydroxybenzoquinones are prone to undergo ring-contraction reactions with loss of carbon dioxide when treated with alkaline oxidizing agents. Thus, treatment of the 2-hydroxybenzoquinones **54** and **55** with alkaline hydrogen peroxide in the presence of oxygen gives the dihydroxycyclopentandiones **56** and **57** and these on treatment with acid lose water to give the triones **58** and **59**[28]. These products are probably formed by the reactions outlined in Scheme 4[28]. The reactions follow a different course,

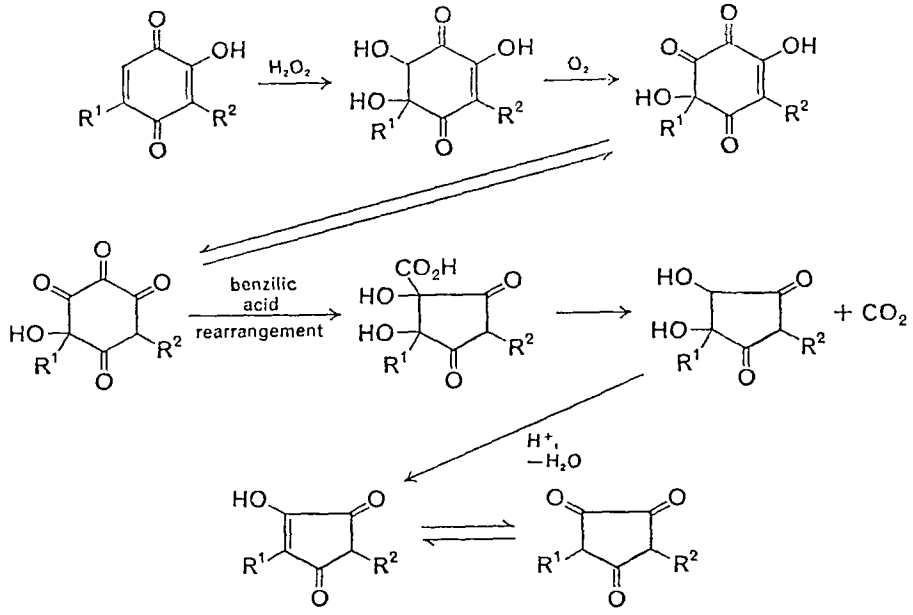


(**54**), R^1 = Me, R^2 = H
(**55**), R^1 = R^2 = Me

(**56**), R^1 = Me, R^2 = H
(**57**), R^1 = R^2 = Me

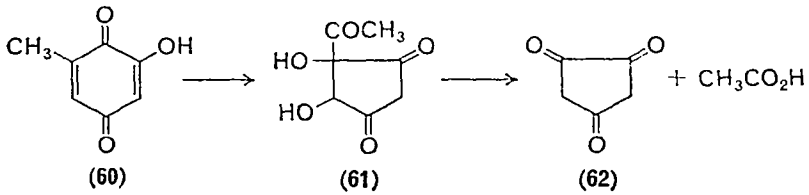
(**58**), R^1 = Me, R^2 = H
(**59**), R^1 = R^2 = Me

however, when a 6-methyl substituent is present. 6-Methyl-2-hydroxybenzoquinone (**60**) reacts with alkaline hydrogen peroxide to give the cyclopentane derivative **61**, and this, on acid treatment, undergoes

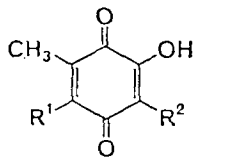


SCHEME 4

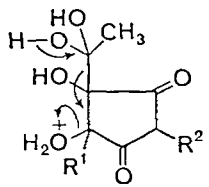
deacetylation and dehydration giving cyclopentane-1,2,4-trione (**62**)[28]. The related quinones **63**, **64** and **65** behave similarly giving acetic acid and the expected methyl-substituted cyclopentanetriones[28]. These products may be formed by the reactions shown in Scheme 5[28]. A possible mechanism for the loss of acetic acid is shown in **66**.



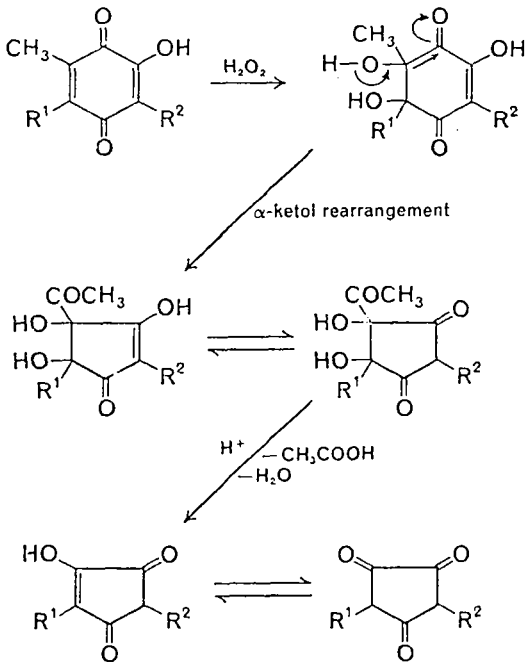
(**60**) (**61**) (**62**)



(**63**), $R^1 = H$, $R^2 = CH_3$
(**64**), $R^1 = CH_3$, $R^2 = H$
(**65**), $R^1 = R^2 = CH_3$

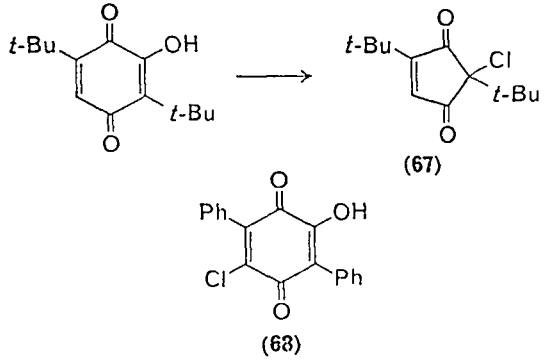


(**66**)



SCHEME 5

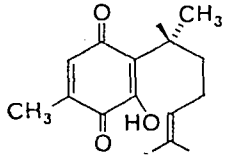
It has recently been reported[29] that 3,6-di-*t*-butyl-2-hydroxybenzoquinone undergoes an oxidative ring-contraction reaction when treated with cupric chloride and acetic acid giving the cyclopentane derivative **67**. A one-carbon fragment is formed but its precise nature and origin are not clear; no mechanism has been suggested for this reaction. The quinone **68** undergoes a similar reaction[29].



(67)

(68)

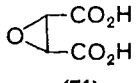
Benzoquinones are extensively degraded by vigorous oxidizing agents. In a few instances small acids containing several carbon atoms which were originally part of the quinone ring have been isolated. For example, ozonolysis of 1,4-benzoquinone gives formic, glyoxalic, oxalic, mesoxalic and maleic acids[30], and the products of ozonolysis of perezone **69** include the diketo acid **70**[31]. The alkaline potassium permanganate oxidation of 1,2-benzoquinone gives oxalic acid[32] and the action of alkaline hydrogen peroxide on 1,2-benzoquinone gives the epoxy acid **71**[33]. In most instances,



(69)

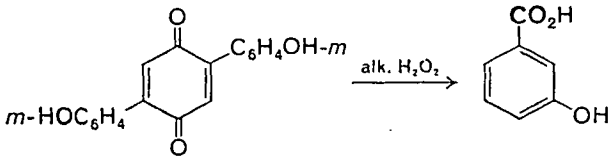
$CH_3COCOCO_2H$

(70)

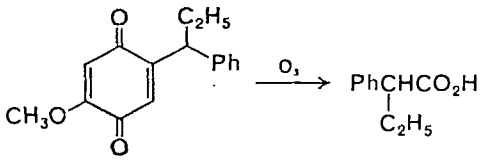


(71)

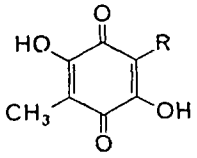
however, no attempts have been made to isolate the small acids and only the acids derived principally from the side-chains have been isolated. Reactions of this type have been widely used for the degradation of natural benzoquinones or their derivatives. The oxidizing agents most commonly employed for this purpose are potassium permanganate and alkaline hydrogen peroxide. The following reactions are illustrative.



(reference 34)



(reference 35)

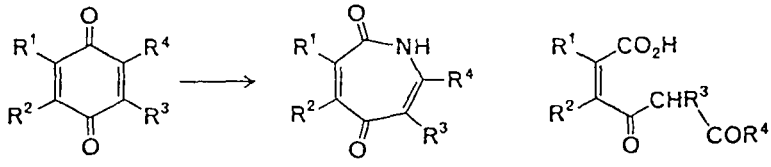


$R = n\text{-}C_9H_{17}$ $\xrightarrow[\text{in acetone}]{KMnO_4}$ $n\text{-}C_9H_{17}CO_2H + CH_3CO_2H$ (reference 36)

$R = n\text{-}C_{21}H_{43}$ $\xrightarrow[\text{or } KMnO_4 \text{ in pyridine}]{\text{alk. } H_2O_2}$ $n\text{-}C_{21}H_{43}CO_2H$ (reference 37)

C. Other Reactions

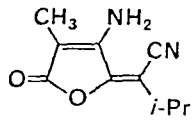
The alkylbenzoquinones **72a–d** undergo the Schmidt reaction when treated with sodium azide in sulphuric acid[38–41]. The only products obtained from quinones **72a–c** are the 1*H*, 2*H*, 5*H*-azepin-2,5-diones (**73a–c**)[40,41] but the reaction with **72d** affords two products, the major one being the dione **73d** and the minor one the dione **73e**[40]. The structures of these products indicate that the quinones are preferentially attacked at the less hindered, more basic, carbonyl function and that the larger adjacent group migrates preferentially. When **72a**, **72b** and **72d** were treated with hot alkali they were hydrolysed, presumably via the diketo acids **74**, to mixtures of ketones and acids[40]. Quinone **72a** gave acetone, methyl ethyl ketone and mesaconic acid (α-methylfumaric acid), **72b** gave acetone and methyl *i*-butyl ketone, and **72d** gave methyl ethyl ketone, diethyl ketone and mesaconic acid.



(72) (73) (74)

	R^1	R^2	R^3	R^4
a	H	Me	H	Me
b	H	Me	Me	Me
c	Me	Me	Me	Me
d	H	*i*-Pr	H	Me
e	H	Me	H	*i*-Pr

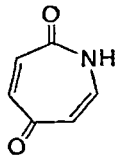
Treatment of thymoquinone **72d** with hydrazoic acid in trichloroacetic acid gives the lactone **75**[42]. No mechanism has been suggested for this reaction.



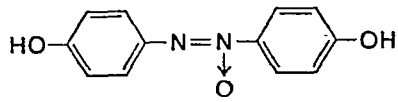
(75)

Contrary to an earlier report[43], treatment of 1,4-benzoquinone monooxime (the tautomer of *p*-nitrosophenol) with tosyl chloride and pyridine

does not give the Beckmann rearrangement product **76**, but the azoxy compound **77**[44]. Attempts to carry out a Beckmann rearrangement of 1,4-benzoquinone di-oxime were also unsuccessful[43].



(76)



(77)

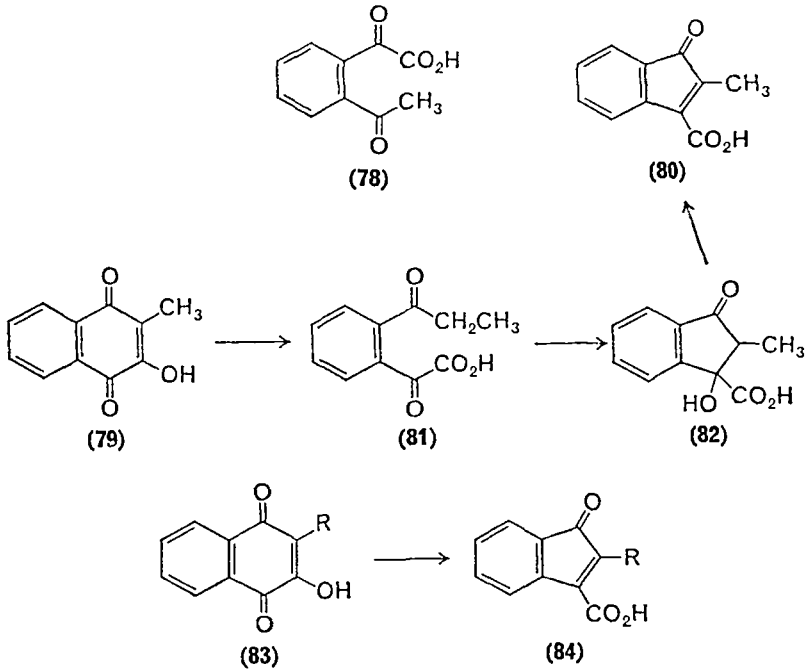
III. NAPHTHAQUINONES

Many of the fragmentation reactions of naphthaquinones, like those of benzoquinones, result from initial attack on the carbon–carbon 'double bonds' of the quinone ring. The fact that in naphthaquinones one of these 'double bonds' is fused to a benzene ring has two consequences. Firstly, there are only two positions on the quinone ring that can bear substituents, and this restricts the types of fragmentations that can occur. For example, there can be no reactions analogous to those of 2,5- and 2,6-dihydroxybenzoquinones. Secondly, the reaction products are often less labile than those obtained in the benzoquinone series and the extent of degradation is less. For example, oxidation reactions employing vigorous conditions usually only proceed as far as a phthalic acid.

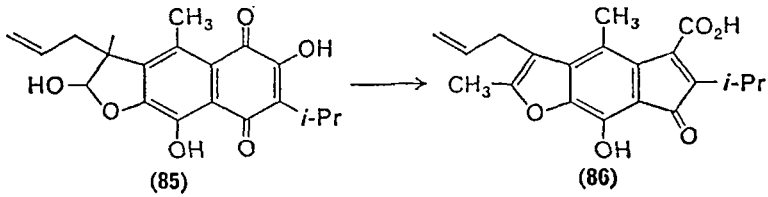
A. Hydrolytic Reactions

1,4-Naphthaquinone and 2-alkylnaphthaquinones are scarcely affected by base in the absence of an oxidizing agent[45]. 2-Hydroxynaphthaquinone reacts, however, giving the diketo acid **78**[46]. This reaction is analogous to the cleavage of the benzoquinone **1** to the acid **3** and is believed to occur by a similar mechanism. 2-Methyl-3-hydroxynaphthaquinone (**79**) gives the indenone acid **80** as well as the diketo acid **81** when treated with alkali[6]. The indenone acid **80** is formed by cyclization of acid **81** to acid **82** and dehydration of the latter. Many 2-alkyl- and 2-aryl-3-hydroxynaphthaquinones behave in a similar manner when treated with alkali and give indenone acids as the main products. Thus quinones **83a–f** give the acids **84a–f**[47–49] and the natural quinone coleon-A **85** gives the acid **86**[50].

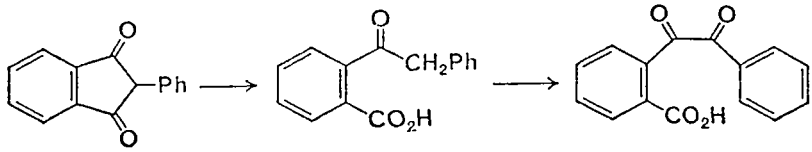
When oxygen is present 2-phenyl-3-hydroxynaphthaquinone (**83f**) reacts with alkali to give 2-phenylindan-1,3-dione (**87**) as the main product, and *o*-carboxybenzil **88** and the indenone acid **84f** as minor products[49].



	R	Reference
a	*i*-Pr	47
b	*t*-Bu	47, 48
c	C_6H_{11}	48
d	$-CMe_2CH=CH_2$	47
e	$PhCH_2$	49
f	Ph	49

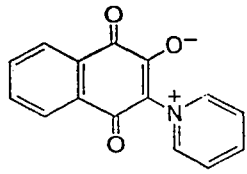


In this case instead of all the hydroxyl acid intermediate similar to **82** dehydrating to give **84f**, some was oxidatively decarboxylated to give the dione **87**, and this, being a β-diketone, was partially hydrolysed under the reaction conditions to give the keto acid **89** which rapidly oxidized to the zilben **88**.



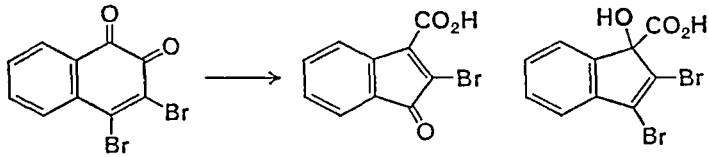
(87) (89) (88)

2,3-Dihydroxynaphthaquinone[51] and 2-amino-3-hydroxynaphthaquinone[52] are, in contrast to 2-hydroxynaphthaquinone, scarcely affected by alkali. Shemyakin and Shchukina have studied the conditions necessary for the hydrolytic cleavage of carbon–carbon double bonds and have concluded that cleavage will occur most readily when the bond is highly polarized[1]. This is the case with 2-hydroxynaphthaquinone. In the 2-amino-3-hydroxy derivative the polarization is not sufficient to promote ready cleavage and it is totally absent in the 2,3-dihydroxy derivative and 1,4-naphthaquinone itself. On prolonged treatment with alkali, the quinone **90** gives, amongst other products, phthalic acid[53]. 2-Chloro-3-hydroxynaphthaquinone reacts with alkali but oxidation–reduction reactions occur between intermediates and this reaction is best considered in the section on oxidation reactions.



(90)

3,4-Dibromo-1,2-naphthaquinone (**91**) reacts with alkali to give the acid **92**, the reaction presumably proceeding via the benzilic acid rearrangement product **93**[52]. The corresponding dichloro compound behaves similarly[54].



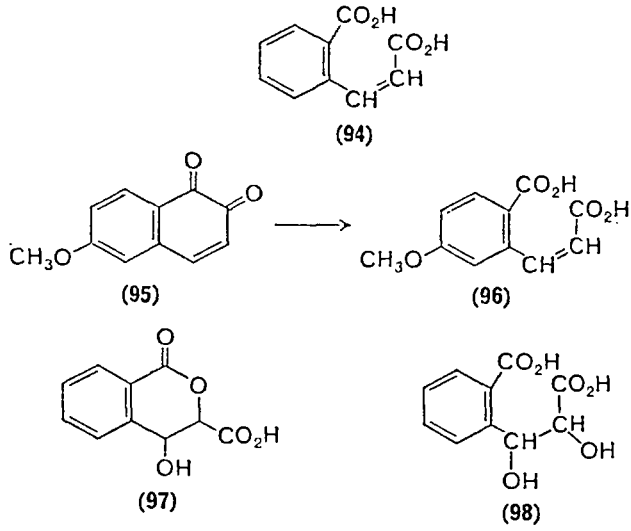
(91) (92) (93)

B. Oxidation Reactions

As in the corresponding section on benzoquinones, reactions which give products retaining all or most of the carbon atoms of the original

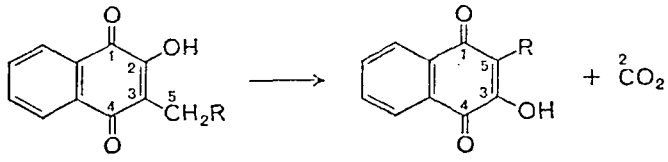
quinone ring will be discussed before those resulting in extensive fragmentation.

1,2-Naphthaquinones, like 1,2-benzoquinones, undergo Baeyer–Villiger type oxidations. Thus 1,2-naphthaquinone reacts with perbenzoic acid to give the cyclic anhydride of the diacid **94**[22,55] and with peracetic acid[19] or with hydrogen peroxide in acetic acid[56] to give the diacid **94** itself. Treatment of 6-methoxy-1,2-naphthaquinone (**95**) with peracetic acid or with monoperphthalic acid gives the diacid **96**[57]. A formally related reaction is that between 1,2-naphthaquinone and chlorine in sodium carbonate solution[58]. This gives the lactone **97** which is presumably formed via the hydroxylated *o*-carboxylcinnamic acid (**98**).



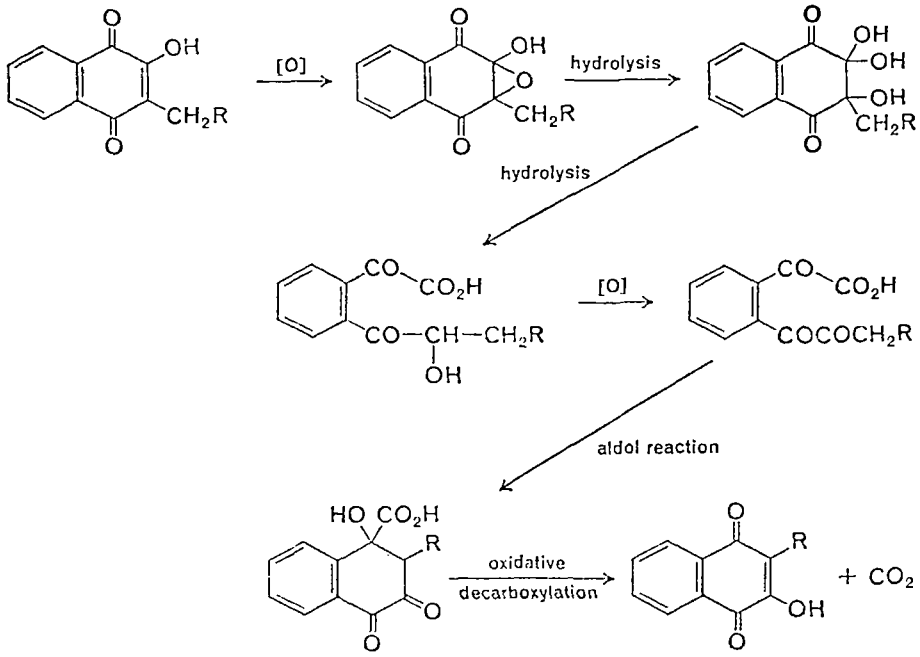
An important general reaction of 3-alkyl-2-hydroxynaphthaquinones is the Hooker oxidation[59–62]. This takes place in high yield when the substrates are treated with cold alkaline potassium permanganate or with hydrogen peroxide and cupric sulphate and results in the transformation shown overleaf, the carbon atom expelled being present originally in the quinone ring. Some of the many examples of this reaction are the conversions of quinones **99a–d** to quinones **100a–d**. The course of the reaction is as outlined in Scheme 6[63,64].

Attempts to gain insight into the mechanism of the Hooker oxidation prompted investigations into the oxidation of 3-alkyl-2-hydroxynaphthaquinones under other conditions. It was found that treatment of the 3-methyl derivative **99a** with cold alkaline potassium permanganate until



(99) (100)

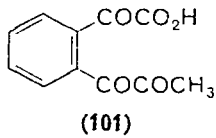
	R	Reference
a	CH_3—	60
b	$CH_3(CH_2)_n$— (n = 1–6)	60
c	$(CH_3)_2C{=}CHCH_2$—	59
d	$C_6H_5CH_2$—	60



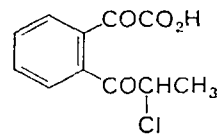
SCHEME 6

the colour disappears gives the triketo acid **101**[65]. Several substrates were oxidized to hydroxyl acids using hydrogen peroxide in sodium carbonate[64,66]. Quinones **102**[64], **103**[64] and **104**[66], for example, gave acids **105**, **106** and **107**. When the 3-methyl derivative **99a** was treated with

chlorine water the chloro acid **108** was obtained[67]. Chloro acids are also obtained when 3-alkyl-2-hydroxynaphthaquinones are treated with sodium hypochlorite[64].



(101)



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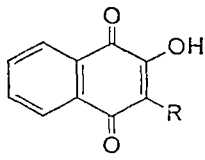
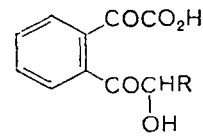
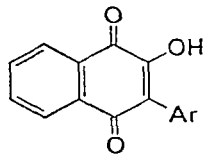


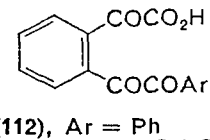
(102), R = CH_3
(103), R = $(CH_3)_2C{=}CHCH_2$
(104), R = $PhCH_2$



(105), R = CH_3
(106), R = $(CH_3)_2C{=}CHCH_2$
(107), R = $PhCH_2$
(115), R = Ph
(116), R = β-$C_{10}H_7$



(109), Ar = Ph
(110), Ar = o-$CH_3C_6H_4$
(111), Ar = β-$C_{10}H_7$

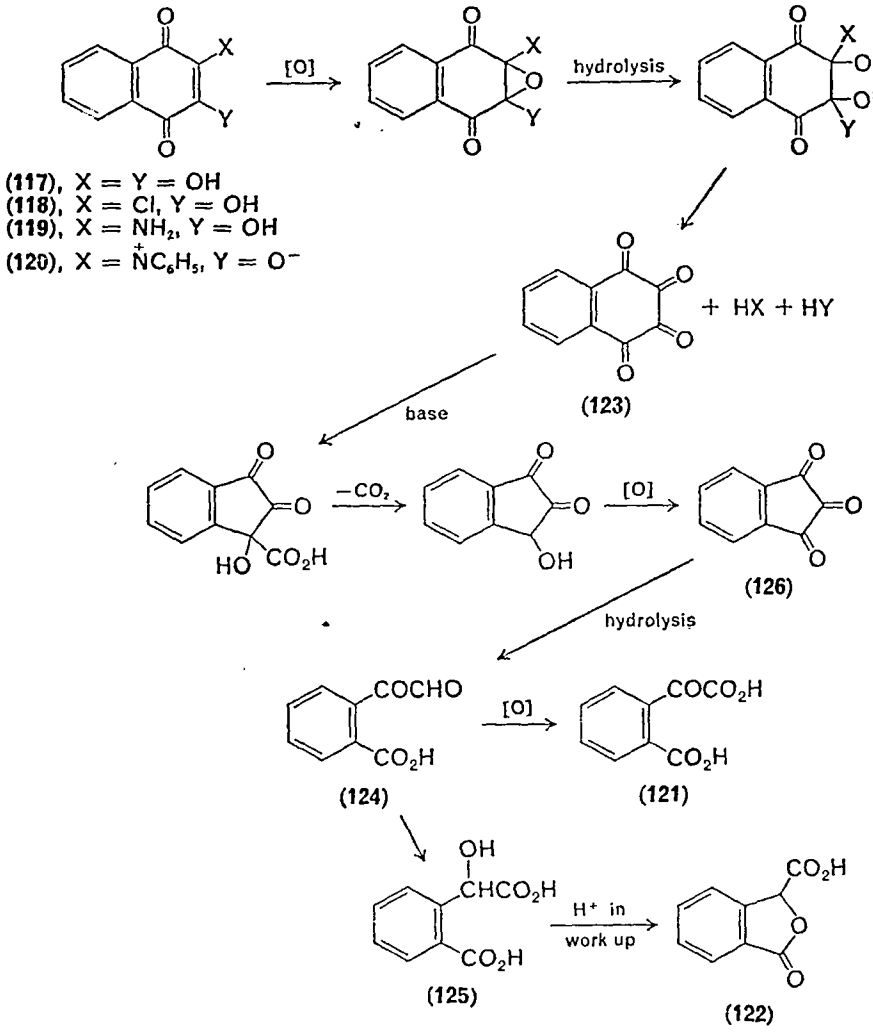


(112), Ar = Ph
(113), Ar = o-$CH_3C_6H_4$
(114), Ar = β-$C_{10}H_7$

2-Aryl-3-hydroxynaphthaquinones clearly cannot undergo the Hooker oxidation and when quinones **109**, **110** and **111** are treated with cold alkaline potassium permanganate the reactions shown in Scheme 6 proceed to the triketo acid stage, acids **112**, **113** and **114** being the products[68]. Oxidation of quinones **109** and **111** with hydrogen peroxide in the presence of sodium carbonate gives the hydroxyl acids **115**[66] and **116**[64].

If alkaline solutions of the disubstituted quinones **117–120** are boiled in the presence of oxygen, phthalonic acid (**121**), phthalide-3-carboxylic acid (**122**) and phthalic acid are formed. Shemyakin and coworkers[51,52] have studied these reactions and concluded that phthalonic acid **121** and phthalide-3-carboxylic acid **122** arise as a result of the reactions shown in Scheme 7, in which all the substrates react initially to give the tetraketone **123** which then breaks down to give the acids **121** and **122**. The degradation

of the 2-chloro-3-hydroxyquinone (**118**) may partly proceed by hydrolysis to the 2,3-dihydroxyquinone (**117**) which then breaks down as in Scheme 7. It is not clear how the phthalic acid is produced.

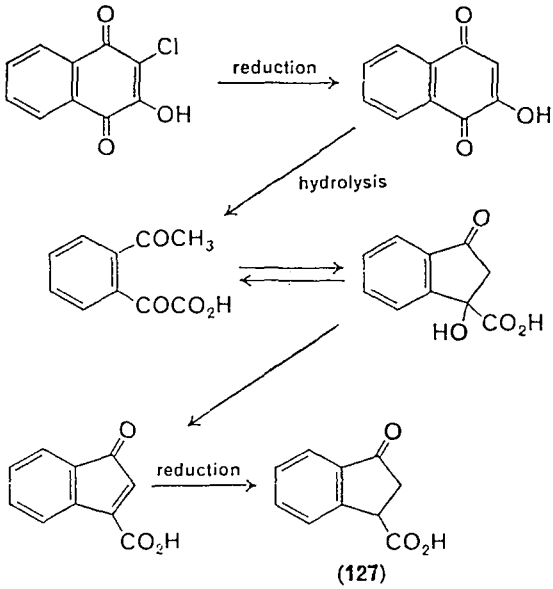


SCHEME 7

The conversion of **124** to **125** is an internal Cannizzaro reaction and requires more vigorous alkaline conditions than the other transformations. Consequently when a *neutral* solution of 2,3-dihydroxynaphthaquinone (**117**) is boiled in the presence of oxygen no phthalide-3-carboxylic acid

(**122**) is obtained and the final products are phthalonic acid **121** and ninhydrin **126**[51].

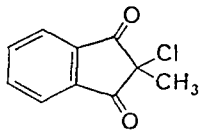
2-Chloro-3-hydroxynaphthaquinone (**118**) reacts with alkali to give low yields of phthalic acid and the acids **121** and **122** even in the absence of oxygen[52]. This is possible because this quinone is a fairly strong oxidizing agent and the reductive–hydrolytic processes shown in Scheme 8 occur in parallel with the oxidative–hydrolytic processes of Scheme 7. As a result of this the indanone acid **127** is a major product[69].



(**127**)

SCHEME 8

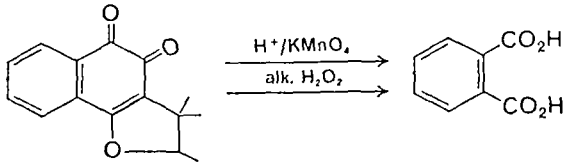
Moore and Wikholm[29] have recently reported that 2-hydroxy-3-methylnaphthaquinone undergoes an oxidative ring-contraction when treated with cupric chloride in hot acetic acid to give the dione **128**. It is not known how this is formed.



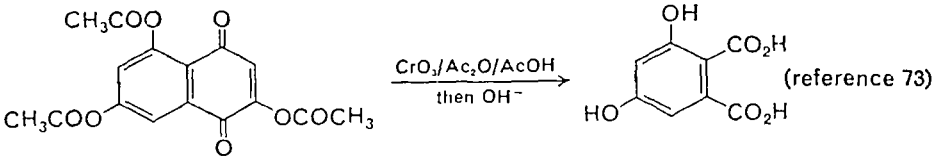
(**128**)

With vigorous oxidizing agents naphthaquinones are usually oxidized to phthalic acids. For example, 1,2-naphthaquinone is oxidized to phthalic acid by hydrogen peroxide in hot acetic acid[32] and by hot aqueous

potassium permanganate[70], and 1,4-naphthaquinone is oxidized to phthalic acid by potassium permanganate in acid solution[71]. Reactions of this type have been widely used to degrade natural naphthaquinones or their derivatives. The following examples are illustrative.



(reference 72)



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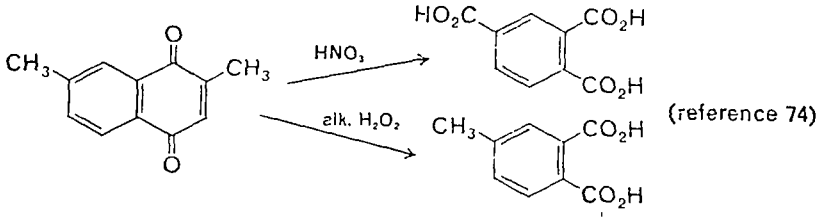

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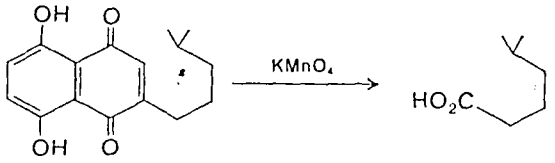
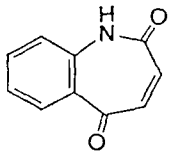


(reference 75)

C. Other Reactions

1,4-Naphthaquinone undergoes the Schmidt reaction when treated with sodium azide in sulphuric acid, to give the benzazepindione **129**[40]. 2-Methylnaphthaquinone reacts under similar conditions to give the three benzazepindiones **130**, **131** and **132** in a ratio of 4 : 2 : 1[39–41]. Base-catalysed hydrolysis of **132** gives acetone and *o*-acetylbenzoic acid[40].



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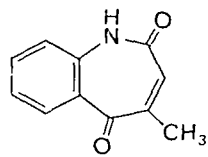

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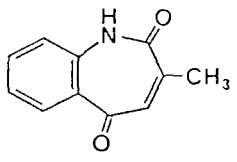

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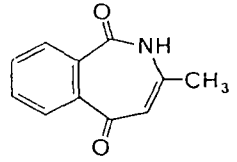
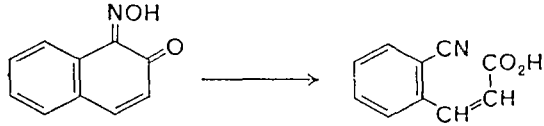
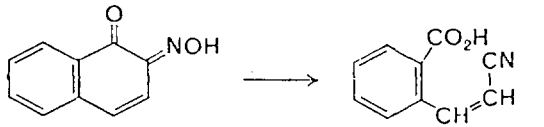


(132)

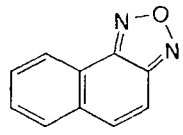
1,2-Naphthaquinone 1-oxime (**133**) (the tautomer of 1-nitroso-2-naphthol) undergoes a Beckmann fragmentation when treated with tosyl chloride or phosphorus pentachloride and gives the cinnamic acid derivative **134**[43,76]. 1,2-Naphthaquinone 2-oxime (**135**) (the tautomer of 2-nitroso-1-naphthol) undergoes a similar reaction when treated with phosphorus pentachloride, tosyl chloride and pyridine, or hydrogen chloride in acetic acid and acetic anhydride to give the benzoic acid derivative **136**[43,76]. Under similar reaction conditions 1,2-naphthaquinone dioxime cyclizes to the furazan **137**[43]. The mono- and di-oximes of 1,4-naphthaquinone do not rearrange when treated with hydrogen chloride in acetic acid and acetic anhydride[43].



(133) (134)



(135) (136)



(137)

IV. ANTHRAQUINONES

Most of the fragmentation reactions of benzoquinones and naphthaquinones result from initial attack at a carbon–carbon 'double bond' of the quinone ring. Since in 9,10-anthraquinones both 'double bonds' are fused to benzene rings, these quinones cannot undergo analogous reactions, they are more stable and there are fewer types of fragmentation reactions.

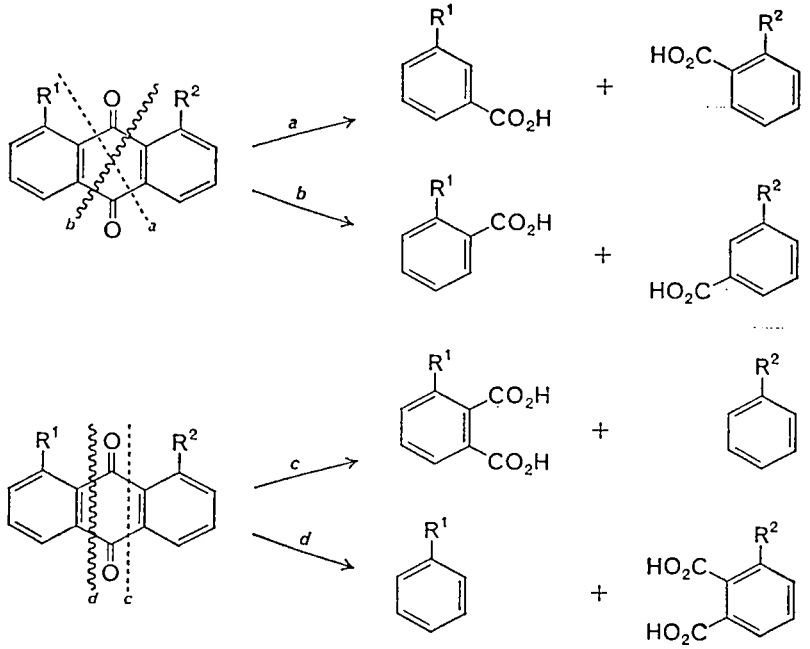
A. Hydrolytic Reactions

Anthraquinone is unaffected by aqueous base but it is cleaved to benzoic and phthalic acids when treated with fused potassium hydroxide at 250°[77]. Under similar conditions 1,1′-bianthraquinone is cleaved to benzoic acid, diphenic acid and biphenyl-3,3′-dicarboxylic acid[78]. Schneider tried to bring about cleavage under milder conditions and found that anthraquinone is cleaved in good yield by a suspension of potassium hydroxide in an inert solvent at 250°[79]. A suspension of sodamide in refluxing toluene or xylene, a reagent that cleaves many non-enolizable carbonyl compounds[80], is without effect on anthraquinone[81,82], but 1,8-dimethoxyanthraquinone is cleaved in low yield when treated with the reagent in refluxing ethylbenzene[82]. The current reagent of choice for cleaving anthraquinones is that formed by adding water (3 equivalents) to potassium *t*-butoxide (10 equivalents) in an inert solvent. Although it was reported[83] in 1948 that this reagent cleaves anthraquinone efficiently under substantially milder conditions than those mentioned above, it is only recently that its action on substituted anthraquinones has been investigated. Many anthraquinones, including methoxy- and chloroanthraquinones, have been cleaved in high yield by treatment with the reagent in refluxing 1,2-dimethoxyethane[84–86], and anthraquinone-2-carboxylic acid and several benzanthraquinones have been cleaved using the reagent in dioxan at 150°[87]. In some cases cleavage can conveniently be effected at 20°. The results are summarized in Table 1.

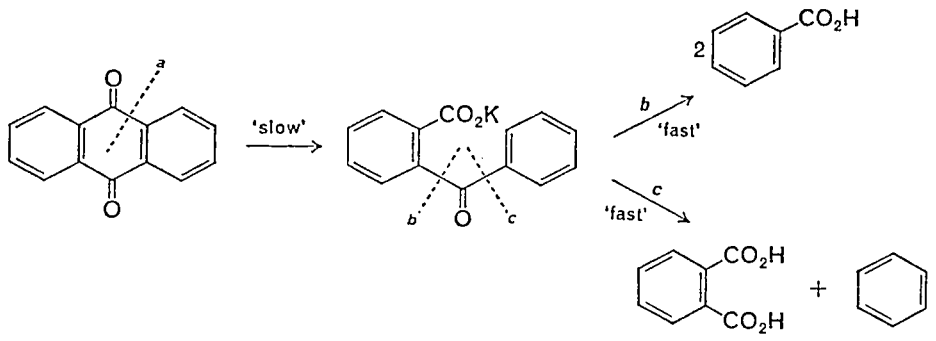
In general anthraquinones could be cleaved in two ways (*a* and *b*, Scheme 9), each of which affords a pair of benzoic acids in equal yield, and two ways (*c* and *d*) each of which affords a phthalic acid and a neutral fragment. Thus a maximum of four benzoic acids and two phthalic acids could be obtained. These cleavages are shown in Scheme 9 using a 1,8-disubstituted quinone as an example.

The cleavage reactions almost certainly take place in two distinct stages (Scheme 10), the first being cleavage at one carbonyl group to give a salt of a benzophenone-2-carboxylic acid (or acid amide if sodamide is the cleavage reagent) and the second cleavage of this salt[84]. The mechanisms of the cleavage steps are probably similar to that of the cleavage of benzophenone, which is believed to be as outlined in Scheme 11[88].

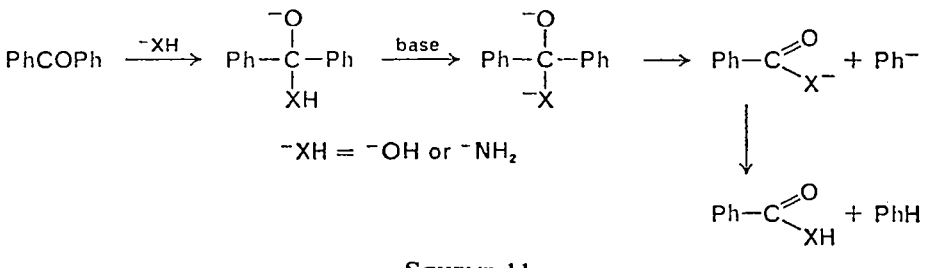
The results in Table 1 can be rationalized in terms of reactions like Scheme 10 by assuming that substituents affect the initial cleavages in the same way that they affect the cleavages of benzophenones[88]. As an example consider the cleavage of 1-methoxyanthraquinone. The results obtained from the cleavages of the three monomethoxybenzophenones show that *o*-methoxybenzophenone is cleaved the most rapidly and that cleavage of



SCHEME 9



SCHEME 10



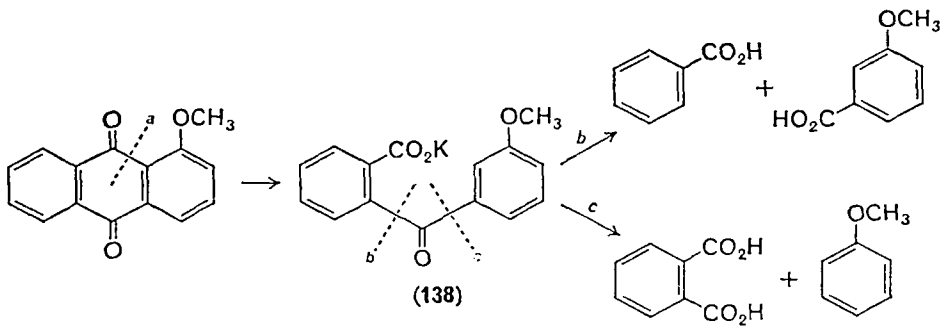
SCHEME 11

None	2 h, 85°	60	Benzoic	97	84
	4 h, 85°	98	Phthalic	3	
1-Methoxy	2 h, 20°	85	Benzoic	44	
			3-Methoxybenzoic	50	84
			Phthalic	6	
2-Methoxy	2 h, 85°	31	Benzoic	50	
			3-Methoxybenzoic	16	86
			4-Methoxybenzoic	34	
1,2-Dimethoxy	2 h, 85°	98	Benzoic	46	
			3,4-Dimethoxybenzoic	44	84
			Phthalic	7	
1,3-Dimethoxy	2 h, 85°	94	Benzoic	47	
			3,5-Dimethoxybenzoic	44	84
			Phthalic	6	
1,4-Dimethoxy	2 h, 85°	98	Phthalic	93	84
1,5-Dimethoxy	2 h, 85°	97	3-Methoxybenzoic	100	84
1,8-Dimethoxy	4 h, 20°	89	2-Methoxybenzoic	49	
			3-Methoxybenzoic	49	84
			3-Methoxyphthalic	2	
2,6-Dimethoxy	6 h, 85°	33	3-Methoxybenzoic	22	84
			4-Methoxybenzoic	78	

2-Chloro	2 h, 85°	97	Benzoic	39	
			3- and 4-Chlorobenzoic	39	84
			Phthalic	22	
1-Methyl	4 h, 85°	~1	Complex mixtures obtained. Benzoic acid was a major component in all cases	—	85
2-Methyl	7 h, 85°	~2			
2-Ethyl	4 h, 85°	~2			
2-*i*-Propyl	4 h, 85°	~1			
2-*t*-Butyl	4 h, 85°	55	Benzoic	49	
	8 h, 85°	89	3-*t*-Butylbenzoic	24	85
			4-*t*-Butylbenzoic	27	
2-Carboxyl	16 h, 150°	56	Benzoic	62	
			Phthalic	28	87
			Iso- and Terephthalic	7	
			Trimellitic	3	
Benz {*b*}-	16 h, 150°	94	Benzoic	56	
			2-Naphthoic	44	87
Dibenz {*a*, *c*}-	16 h, 150°	84	Benzoic	20	
			Phthalic	61	87
			Phenanthrene-9-carboxylic	19	
Tetrabenz {*a*, *c*, *h*,*j*}-	16 h, 150°	48	Phenanthrene-9-carboxylic	93	
			Phenanthrene-9,10-dicarboxylic	7	87

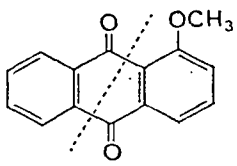
[a] Reactions run at 20° were carried out using 1,2-dimethoxyethane as the solvent. Reactions run at 85° were carried out in refluxing 1,2-dimethoxyethane. Reactions run at 150° were carried out using 1,4-dioxan as the solvent.

this compound is virtually exclusively at the bond nearer the methoxyl group[88]. Consequently, 1-methoxyanthraquinone would be expected to cleave initially at *a*, Scheme 12, to give **138**. Since an *o*-carboxyl substituent favours cleavage of the neighbouring bond more than a *m*-methoxy group, **138** cleaves mainly at *b* to give benzoic acid and 3-methoxybenzoic acid, and to only a small extent at *c* to give phthalic acid and anisole.

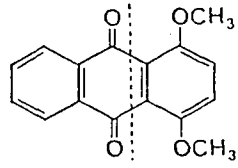


SCHEME 12

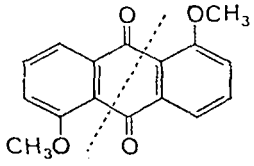
The most extensively studied group of compounds are the methoxyanthraquinones[84,86]. It can be seen from the results in Table 1 that those quinones containing only α-methoxy substituents are cleaved more readily than anthraquinone whereas those containing only β-methoxy substituents are cleaved less readily. The effect of an α-methoxy substituent is the greater, for substrates which contain both types are cleaved more readily than anthraquinone. An α-methoxy substituent not only facilitates cleavage of the substrate but, as noted previously, also strongly favours cleavage at the neighbouring bond. Hence the nature of the acids produced in cleavages of α-methoxyanthraquinones is very largely determined by the number and relative positions of the α-methoxy substituents. The patterns of cleavage observed are summarized in (**139**)–(**143**). It will be noted that these patterns are generally characteristic. The 1,5- and 1,8-dimethoxy derivatives, for example, can be readily distinguished.



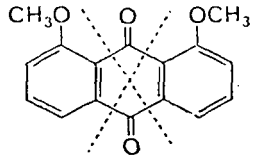
(139)



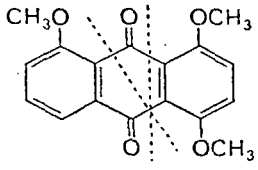
(140)



(141)

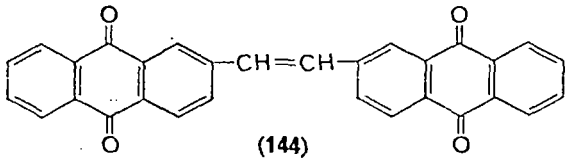


(142)



(143)

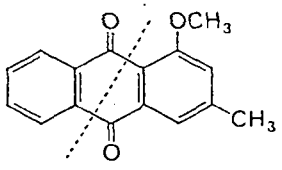
Very little cleavage occurs when 1-methyl-, 2-methyl-, 2-ethyl- and 2-*i*-propylanthraquinone are treated with the butoxide–water reagent[85]. The main reaction products are 'dimers'. The 2-methyl derivative, for example, reacts to give compound **144**. The 'dimers' are probably formed by mechanisms in which the initial steps are removal of a proton from a benzylic position, followed by transfer of one electron from the resulting carbanion to another quinone molecule giving a radical, which then reacts further. 2-*t*-Butylanthraquinone, which cannot form an analogous carbanion, can be cleaved in high yield by the butoxide–water reagent[85].



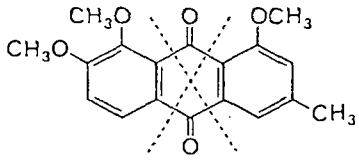
(144)

The permethyl ethers of many naturally occurring hydroxyanthraquinones contain both α-methoxy and β-alkyl (commonly β-methyl) substituents[89]. 1-Methoxy-3-methylanthraquinone (**145**) and nataloe-emodin (**146**) and frangula-emodin (**137**) trimethyl ethers are all cleaved in fairly good yield when treated with the butoxide–water reagent, the patterns of cleavage being those indicated in the formulae[86]. These results indicate that α-methoxy substituents facilitate cleavage to such an extent that cleavage is a major reaction even when a β-methyl substituent is present. Cleavage reactions of this type should, therefore, prove useful for degrading derivatives of natural anthraquinones. This type of degradation has advantages over the oxidation reactions discussed in the following section. Thus, all the carbon atoms of the quinone ring can be recovered in relatively large fragments, and, if the substrate is labelled with ^{14}C, the

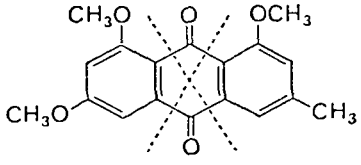
amount of activity present in each carbonyl group can in most cases be readily determined.



(145)

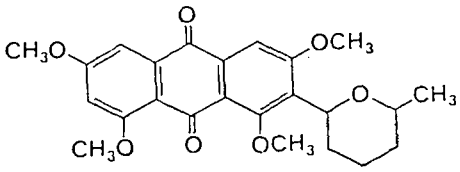


(146)

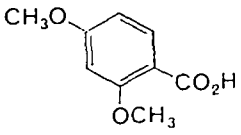


(147)

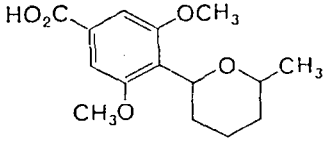
In connexion with biosynthetic work, Holker and Webster have recently shown that avermutin tetramethyl ether (**148**) is cleaved by the butoxide–water reagent to give, amongst other products, the acids **149–151**[90].



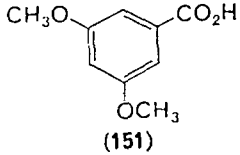
(148)



(149)



(150)

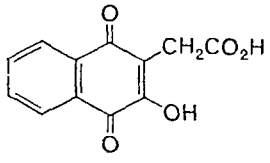


(151)

B. Oxidation Reactions

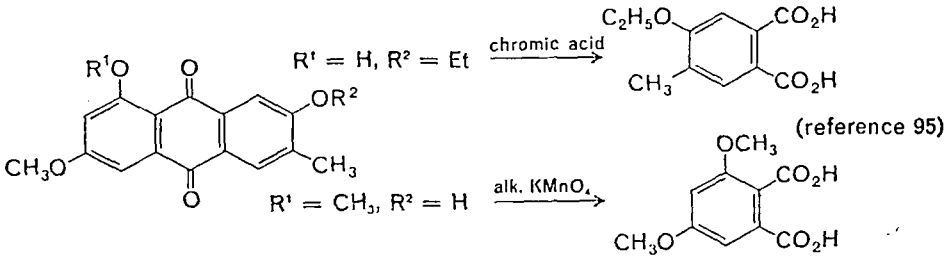
Anthraquinones are generally much more resistant to oxidation than are benzoquinones and naphthaquinones. Indeed, the β-methyl group in some substituted anthraquinones can be oxidized to a β-carboxyl group by chromic acid without causing breakdown of the quinone ring[91]. If, however, one ring bears hydroxyl substituents, oxidation of that ring is facilitated. For example, 1-hydroxy-, 1,2-dihydroxy- and 1,2,3-trihydroxy-anthraquinone give phthalic acid when oxidized with nitric acid[92]. Some

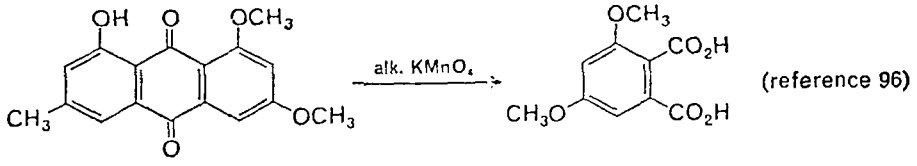
polyhydroxyanthraquinones can even be oxidized by air in the presence of alkali. Thus, under these conditions 1,2,4-trihydroxyanthraquinone gives phthalic acid[93] and 1,2,3-trihydroxyanthraquinone gives the naphthaquinone **152**[94].

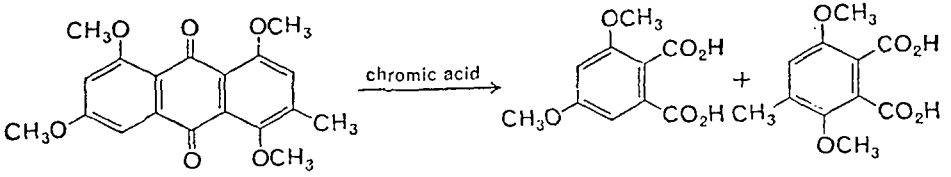


(152)

Many natural anthraquinones or their derivatives have been oxidized to give phthalic acids. The reagents most commonly used for this purpose are alkaline potassium permanganate and chromic acid. The following examples are illustrative.



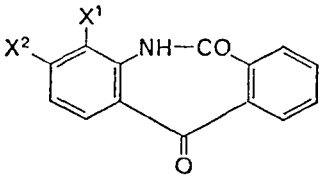




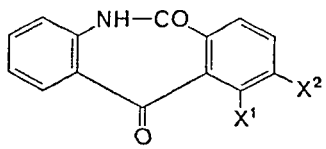
(reference 97)

C. Other Reactions

Anthraquinone undergoes a Schmidt reaction when treated with sodium azide and sulphuric acid giving the lactam **153**[98,99]. Several substituted anthraquinones have been shown to undergo similar reactions. 1-Amino- and 2-aminoanthraquinone give the lactams **154** and **155** respectively[98], and 1-chloro- and 2-chloroanthraquinone give the lactams **156** and **157**[100]. 1-Nitroanthraquinone gives the lactam **158**[100].



(153), $X^1 = X^2 = H$
(156), $X^1 = Cl$, $X^2 = H$
(157), $X^1 = H$, $X^2 = Cl$
(158), $X^1 = NO_2$, $X^2 = H$



(154), $X^1 = NH_2$, $X^2 = H$
(155), $X^1 = H$, $X^2 = NH_2$

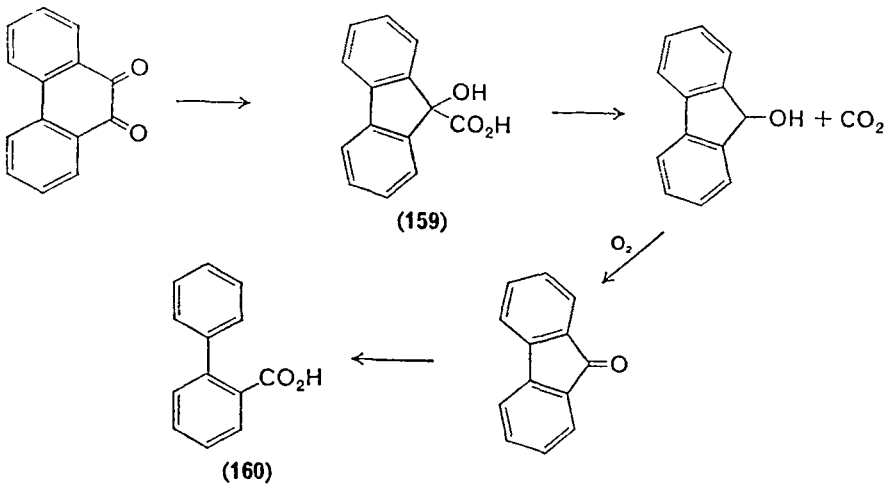
Anthraquinone mono-oxime undergoes a Beckmann rearrangement when treated with acetyl chloride and phosphorus pentachloride to give the lactam **153**[43].

V. PHENANTHRENEQUINONES

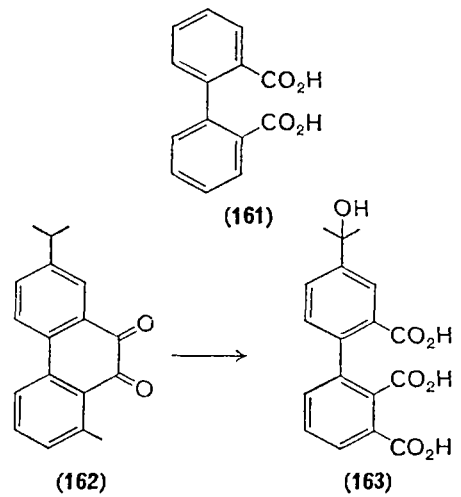
In phenanthrene-9,10-quinones both carbon–carbon 'double bonds' of the quinone rings are fused to benzene rings. This greatly limits the types of fragmentation reactions that occur.

Phenanthrene-9,10-quinone undergoes a benzilic acid rearrangement when it is warmed with aqueous alkali and gives the hydroxyl acid **159**[101]. When the same quinone is treated with the butoxide–water reagent in the presence of oxygen a high yield of biphenyl-2-carboxylic acid (**160**) is obtained[84]. This is almost certainly formed by the reaction sequence shown in Scheme 13.

Phenanthrene-9,10-quinones are readily oxidized to diphenic acids. For example, phenanthrenequinone itself is oxidized to diphenic acid (**161**) by chromic acid[102], alkaline hydrogen peroxide[32,103] and hydrogen peroxide in acetic acid[101], and retenequinone **162** gives the acid **163** when treated with potassium permanganate in aqueous pyridine[105]. The use of hydrogen peroxide often gives lactones in addition to diphenic acids. Thus, oxidation of the phenanthrenequinone **164** with hydrogen peroxide in acetic acid gives the lactone **165** as well as the diphenic acid **166**[106]

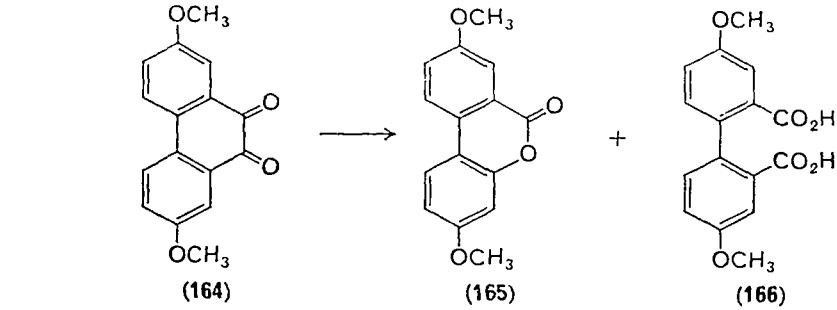


SCHEME 13

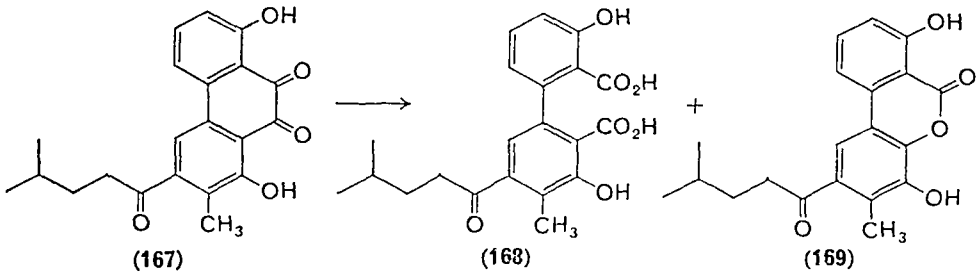


and oxidation of the naturally occurring phenanthrenequinone **167** with alkaline hydrogen peroxide gives the diphenic acid **168** and the isomeric lactones **169** and **170**[107].

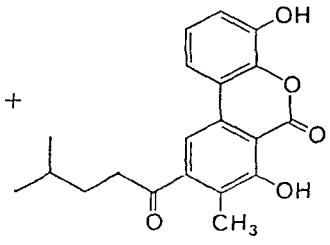
Phenanthrenequinone reacts with sodium azide in sulphuric acid to give phenanthridone **171** and carbon dioxide[108]. Under similar conditions retenequinone **162** gives the phenanthridone **172**[108].



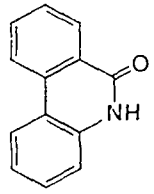
(164) (165) (166)



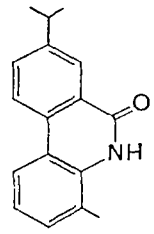
(167) (168) (169)



(170)

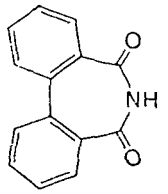


(171)

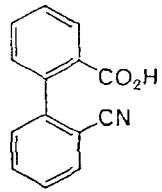


(172)

Phenanthrenequinone mono-oxime undergoes a Beckmann rearrangement when treated with hydrogen chloride in acetic acid and acetic anhydride to give the imide **173**[109] and when treated with benzenesulphonyl chloride and pyridine it gives the acid **174**[110].



(173)



(174)

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CHAPTER 12

Syntheses and uses of isotopically labelled quinones

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I. THEORETICAL INTRODUCTION

A. Absolute Rate Theory of Isotope Effects

According to equilibrium statistical mechanics[1-47], absolute rate theory of chemical reactions[2,3] and Redlich–Teller product rule[16,17], and in agreement with the Bigeleisen–Mayer reduced partition function ratios[4,18], the theoretical equation which relates through vibrational frequencies the ratio of rate constants of two isotopic molecules, k_1/k_2, with the force constants and geometry of reactants and of the transition complex has the form (1)[19,20]:

$$\frac{k_1}{k_2} = \frac{(\nu^{\neq})_{1L}}{(\nu^{\neq})_{2L}}\left[\prod_{i=1}^{3N-\nu}\frac{u_{2i}}{u_{1i}}\frac{\sinh(u_{1i}/2)}{\sinh(u_{2i}/2)}\left(\frac{\sigma_1}{\sigma_2}\right)\Bigg/\prod_{i=1}^{3N^{\neq}-(\nu+1)}\frac{u_{2i}^{\neq}}{u_{1i}^{\neq}}\frac{\sinh(u_{1i}^{\neq}/2)}{\sinh(u_{2i}^{\neq}/2)}\left(\frac{\sigma_1}{\sigma_2}\right)\right] \quad (1)$$

$$= (\mathrm{TIF})(\mathrm{TDF})$$

Here, $\sinh(u_i/2) = \frac{1}{2}[\exp(u_i/2) - \exp(-u_i/2)]$, $u_i = hc\omega_i/kT$, k is Boltzmann's constant, h is Planck's constant, c is the light velocity, ω_i is the fundamental (normal) frequency of the molecule, $\nu_{1L}^{\neq}$ is the imaginary frequency corresponding to the coordinate of the reaction, σ_1, σ_2 are symmetry numbers, $\neq$ denotes the transition state complex, N is the number of atoms in a polyatomic molecule, y equals 5 for linear molecules and 6 for nonlinear molecules, and the symbols (TIF) and (TDF) denote temperature-independent and temperature-dependent factors. In (1) the ratio of transmission coefficients is omitted and the motion of the reacting system along the reaction coordinate has been treated classically.

Equation (i) is valid for all isotopes and in the case of heavy isotopes with small differences between their masses it approaches the well-known Bigeleisen–Mayer expression (2)[3,4]:

$$\frac{k_1}{k_2} = \frac{(\nu^{\neq})_{1L}}{(\nu^{\neq})_{2L}}\left[1 + \sum_{i=1}^{3N-6} G(u_i)\,\Delta u_i - \sum_{i=1}^{3N^{\neq}-7} G(u_i^{\neq})\,\Delta u_i^{\neq}\right] \quad (2)$$

where $G(u_i) = \frac{1}{2} - 1/u_i + 1/[\exp(u_i) - 1]$, $\Delta u_i = (u_{1i} - u_{2i})$; the subscript 1 refers to the lighter molecule and $u_i = h\nu_{2i}/kT$ refers to the frequency of the heavier molecule. Function $G(u_i)$ was introduced and tabulated for different values of u by Bigeleisen and Mayer[3,18]. Expression (2) can be

further simplified[5, 21–23] for $u_i < 2\pi$, that is for small ν_i or high temperatures:

$$\frac{k_1}{k_2} = \frac{(\nu^{\pm})_{1L}}{(\nu^{\pm})_{2L}}\left[1 + \frac{1}{24}\left\{\sum_{i=1}^{3N-6}(u_{1i}^2 - u_{2i}^2) - \sum_{i=1}^{3N^{\pm}-6}(u_{1i}^{\pm 2} - u_{2i}^{\pm 2})\right\}\right]$$

$$= \frac{(\nu^{\pm})_{1L}}{(\nu^{\pm})_{2L}}\left[1 + \frac{\hbar^2}{24(kT)^2}\{a_{ii} - a_{ii}^{\pm}\}(m_{1i}^{-1} - m_{2i}^{-1})\right] \tag{3}$$

Expression (3) has summation over $3N-6$ degrees of freedom both in the substrates and in the transition complex, since the Wigner tunnel correction (4) discussed in section A.2 has been included in the transition complex part of formula (3). It has also been presumed that the isotopic

$$Q_1/Q_2 = \left[1 + \frac{1}{24}(u_{2iL}^{\pm 2} - u_{1iL}^{\pm 2})\right] \tag{4}$$

molecules are labelled in one position and $a_{ii} = (a^{xx} + a^{yy} + a^{zz})$ is the sum of the Cartesian force constants at the place of isotopic substitution. Approximate expression (3) results directly from more general expansion in powers of u of the logarithm of the reduced partition function f[5, 23].

From equations (1), (2) and (3) it follows that the k_1/k_2 ratio tends to the ratio of the frequencies of decomposition, $(\nu_{1L}^{\pm}/\nu_{2L}^{\pm})$, when $h \to 0$, since expressions $\sinh(u_{1i}/2)/\sinh(u_{2i}/2)$ both in numerator and denominator of (1) reduce to the ratios (ν_{1i}/ν_{2i}) and $(\nu_{1i}^{\pm}/\nu_{2i}^{\pm})$ correspondingly. From expression (3) it follows that the high-temperature kinetic isotope effect should approach the ratio $(\nu_{1L}^{\pm}/\nu_{2L}^{\pm})$ according to the $1/T^2$ law. At lower temperatures equations (1) and (2) require the kinetic isotope effect to diminish with temperature according to the $1/T$ law. Expression (3) shows that the kinetic isotope effects reflect the changes in force constants at the isotopic atom in going from the initial to the transition state of the reaction. Weakening of the force constants around the isotopic atom in the transition state makes the value in square brackets larger than unity and, consequently, the molecule possessing the lighter isotope (subscript 1) reacts faster than the heavier one ('normal isotope effect'). In the opposite situation of strengthening of the force constants around the isotopically substituted atom in the transition state, the numerical value of the expression in the square brackets is lower than unity and may outweigh the pre-exponential factor, thus leading to the 'inverse isotope effect'. The latter situation frequently occurs in the so-called 'secondary isotope effects' for which the theoretical pre-exponential factor $(\nu_{1L}^{\pm}/\nu_{2L}^{\pm})$

is very close to unity. Anomalous temperature dependences of theoretical isotope effects were discussed by Stern and Wolfsberg[7-10, 24].

I. Two- and three-centre reactions

a. Two-centre reactions. In the one-bond approximation[3, 4, 25, 26] the equations (1), (2) and (3) reduce to expression (5).

$$\frac{k_1}{k_2} \approx \left[\frac{\sinh(u_{1i}/2)}{\sinh(u_{2i}/2)}\right] \approx \left(\frac{\nu_{1L}^{+}}{\nu_{2L}^{+}}\right)[1 + G(u_i)\,\Delta u_i]$$

$$\approx \left(\frac{\nu_{1L}^{+}}{\nu_{2L}^{+}}\right)\left[1 + \frac{1}{24}\left(\frac{h}{2\pi kT}\right)^2 (f_{X-m_i})(m_1^{-1} - m_2^{-1})\right] \qquad (5)$$

where f refers to the force constant of the isotopic $X-m_i$ bond. From the one-bond treatment of isotope effects for the isotopes of hydrogen it follows that at relatively low temperatures the major portion of the effect arises from the difference of the zero-point energies of the harmonic X—H and X—D oscillators. Taking the value 2900 cm^{-1} for the stretching frequency of the C—H bond one finds 4·15 and 3·0 kcal/mole for the zero-point energies of the C—H and C—D bonds respectively. The difference $\Delta E_0 = (h\nu_H/2 - h\nu_D/2)$ equals 1·15 kcal/mole which in zero-point approximation leads to a factor of 7 in rate at 300 K[27]. Inclusion of the Boltzmann excitation term (sinh approximation) gives slightly lower values. For instance, taking $\omega_{C-H} = 2985$ cm^{-1} and $\omega_{C-D} = 2191{\cdot}68$ cm^{-1} one finds that at 273·2, 283·2 and 313·2 K the calculated values of k_H/k_D are respectively 8·07, 6·97 and 5·88. For tritium k_H/k_T are 19·65, 12·81 and 2·414 at 273·2, 313·2 and 998·2 K, respectively[20].

In many reactions the experimental deuterium and tritium kinetic isotope effects are in agreement with one-bond model calculations, but experimental kinetic deuterium isotope effects may vary in magnitude from 1 to 16 or even more. Some small hydrogen isotope effects have been explained by the assumption that the carbon–hydrogen bond is not broken in the rate-controlling step of the reaction, as, for example, in the nitration of toluene[60]. Other small experimental deuterium isotope effects have been explained by invoking a triangular transition state in which the A—H bond is not completely broken in the transition state but is bent, the hydrogen atom being at the same time attached to two skeletal carbon atoms in the molecule.

b. Three-centre reactions: $AH + B = A + HB$. Deuterium isotope effects smaller than those calculated according to the one-bond method are explained by considering the equilibrium between the one-bond oscillator

and a linear three-centre transition state in which only stretching vibrations are taken into account[27,28].

$$\begin{matrix} k_1 & & k_2 \\ \mathrm{A}\cdots & \mathrm{H} & \cdots\mathrm{B} \\ x_\mathrm{A} & x_\mathrm{H} & x_\mathrm{B} \end{matrix}$$

(1)

Three-centre transition state model

Following the method of Herschbach, Johnston, Pitzer and Powell (H.J.P.P.)[27-29] one approximates the potential in which particles A, H and B move by the function (6) with the interaction term β, and one eliminates

$$V = \tfrac{1}{2}k_1(x_\mathrm{H}-x_\mathrm{A})^2+\tfrac{1}{2}k_2(x_\mathrm{B}-x_\mathrm{H})^2+\beta(x_\mathrm{H}-x_\mathrm{A})(x_\mathrm{B}-x_\mathrm{H}) \qquad (6)$$

from the general solution of the vibrational secular equation the antisymmetric stretching vibration, corresponding to the reaction coordinate, by putting $(k_1k_2-\beta^2)=0$. In the case of a symmetrical transition state, when $k_1=k_2$, the central hydrogen atom does not participate in the motion in the symmetrical mode of vibration and the isotope effect is as large as in the one-bond approximation. If $k_1 \gg k_2$ or $k_2 \gg k_1$, that is when the transition state is substrate-like or product-like, and if, additionally, $\nu_\mathrm{s}^{\neq}$ is comparable to the frequency of the substrate one-bond oscillator, then the contribution of the temperature-dependent part to the total theoretical isotope effect might be negligible and the 'classical' isotope effect is caused mainly by the temperature-independent factor, which in the H.J.P.P.[29] approach to the problem is close to unity. When the ratio of the imaginary frequencies $(\nu_{1\mathrm{L}}^{\neq}/\nu_{2\mathrm{L}}^{\neq})$ is replaced by the ratio of 'zero frequencies' of the antisymmetric vibration (ν_1^*/ν_2^*) of two isotopic three-centre transition complexes, the value of the pre-exponential (TIF) factor for hydrogen isotopes is close to unity[27,28].

In the more detailed consideration of the reaction of the type[30]

$$\mathrm{AH}+\mathrm{B} \longrightarrow [\mathrm{A}\cdots\mathrm{H}\cdots\mathrm{B}]^{\neq} \longrightarrow \mathrm{A}+\mathrm{HB} \qquad (7)$$

where A and B are not atoms but molecular fragments, one takes into account also the two real bending vibrations in the initial state and two bending modes in the transition state: $\mathrm{A}\cdots\mathrm{H}\cdots\mathrm{B}$. In the symmetrical 'hydrogen-bonded' transition state the two bending vibrations might be greater than in the initial normal molecule, their contribution to the zero-point energy differences $\Delta E_0^{\neq}$ might be large and $(E_\mathrm{D}-E_\mathrm{H}) = \Delta E_0 - \Delta E_0^{\neq\prime}$ will be smaller than the value obtained for the stretching vibration alone. In the practical treatment of the deuterium and tritium isotope effects in

hydrogen transfer reactions one frequently takes into account three real vibrations in the initial state and only two bending vibrations in the transition state. Within the framework of such approximation the values of the pre-exponential factors permitted by equation (1) should be found in the case of deuterium to be between 0·5 and 1·41 and closer to unity than to the possible extreme values $(2)^{\frac{1}{2}}$ or $(\frac{1}{2})$. Calculation of isotope effects according to the simple equation (8) should reproduce the experimental isotope effects in reactions and experimental conditions in which

$$k_1/k_2 = \exp(\Delta E_0/RT) \tag{8}$$

the tunnel effects do not operate. Finally, the (highly unrealistic) upper extreme value of the deuterium isotope effect calculated according to the scheme which takes into account one stretching and two (in-plane and out-of-plane) deformation vibrations in the initial state, and neglects the negative contribution of the transition state, gives values for k_H/k_D equal 12·1 at 40·0°C and 18·5 at 0°C. Inclusion of terms corresponding to vibrations of the transition state of the hydrogen transfer reactions diminishes the theoretical deuterium isotope effect to a value close to the one obtained in the one-bond treatment of the kinetic isotope effects.

2. Tunnelling in isotopic chemical reactions[30–41]

According to quantum mechanics and numerous experimental observations[30–45], there is a certain probability that microscopic particles will penetrate the potential energy barriers when their individual energies, E_i, are less than the height of the barrier, V_0 (E_0) which they encounter on their path. Expressions for probability of crossing the barrier by the particle of mass m and energy E have been derived by solving the stationary Schroedinger equation (9) for different shapes of energy barriers, $V(x)$[30–45].

$$\frac{d^2\psi}{dx^2} + \frac{8\pi^2 m}{h^2}[E - V(x)]\psi = 0 \tag{9}$$

The expression for the likelihood of the particle penetrating through the one-dimensional, rectangular potential barrier of the width l in the simplest case when $2m(V_0 - E)l^2/\hbar^2 \gg 1$ is given by[42–45]

$$G(E) \approx \exp\{-(2/\hbar)\sqrt{[2m(V_0 - E)l^2]}\} \tag{10}$$

The expression for the likelihood of crossing the potential barrier approximated by an inverted parabola, $V(x) = V_0 - V_0 x^2/a^2$ whose base equals $2a$ is given by equation (11)[33, 43] while (12) defines the curvature of

$$G(E) = \{1 + \exp[2\pi(V_0 - E)/h\nu_l]\}^{-1} \tag{11}$$

the barrier at the top. Expression (11) follows also from the relations derived for the more realistic symmetrical Eckhart potential, more closely resembling the potential barrier found in chemical reactions[31,35,36]. From

$$\nu_t = E_0^{\frac{1}{2}}/\pi a(2m)^{\frac{1}{2}} \tag{12}$$

relations (10), (11) and the de Broglie relation assigning a wavelength $\lambda = (\hbar/mv)$ to a particle of mass m and velocity v it follows that the largest deviations from classical behaviour should be observed for particles of low masses (electron, proton, deuteron), narrow energy barriers and large $(V_0 - E)$ differences. Protons moving with thermal velocities (at ordinary temperatures) have the wavelength of 10^{-8}–10^{-9} cm which is similar to the width of the barriers found in chemical reactions. Substituting the value 0 for $\hbar$ in expressions (10) and (11) one obtains the classical value 0 for the permeability of the barriers for particles having energy E less than V_0.

a. Relations between the classical and quantum mechanical treatments of the reaction rates. Classically only those molecules $N(E_0)$ from the total assembly, N_{tot}, which have a total energy equal to or greater than its height $E_0(V_0)$ are able to pass the potential barrier. Therefore the classical expression for the reaction rate constant is obtained by multiplying the collision rate by the factor q equal to the fraction,

$$q = N(E_0)/N_{tot} = \exp(-E_0/kT)$$

of molecules with $E_i \geqslant E_0$ from the total number of molecules. The quantum mechanical expression for q (13) takes into account the finite value of the permeability, G, of the potential barrier for particles with energies $E < E_0$, as well as the partial reflexion of particles having $E > E_0$. Insertion of expressions for G into (13) and further integration leads to theoretical relations for the quantum mechanical reaction velocity

$$q = \frac{1}{kT}\int_0^\infty G \exp(-E/kT)\,\mathrm{d}E \tag{13}$$

constant. Integration of expression (13) in the case of a parabolic potential barrier, assuming that $G = 1$ for $E > E_0$ gives

$$q = \frac{1}{\beta - \alpha}(\beta \exp(-\alpha) - \alpha \exp(-\beta)) \tag{14}$$

where

$$\alpha = E_0/kT \quad \text{and} \quad \beta = 2\pi^2 a\sqrt{(2mE_0)}/h \tag{15}$$

The observed heat of activation E_0^* is given by equation (16) and expression (17) gives the ratio of E_0^* to the classical height of the barrier E_0.

$$E_0^*/R = -\mathrm{d}\log(q)/\mathrm{d}(1/T) \tag{16}$$

$$E_0^*/E_0 = [\beta/(\beta-\alpha)] \times [(\beta-\alpha-1)\exp(-\alpha)+\exp(-\beta)]/[\beta\exp(-\alpha)-\alpha\exp(-\beta)] \tag{17}$$

When $\exp(-\alpha) \gg \exp(-\beta)$, equation (17) simplifies to

$$E_0^*/E_0 = 1-[1/(\beta-\alpha)] \tag{18}$$

One can solve the quantum mechanical problem of the reaction rate by deriving the first- and further-order quantum mechanical corrections to the corresponding classical and semiclassical relations[20, 33, 41]. The true rate constant will be the product of the classical rate constant k_{cl} and the quantum mechanical correction Q:

$$k_{\mathrm{qu}} = Qk_{\mathrm{cl}} \tag{19}$$

Then, by definition, the quantum correction to the reaction velocity constant equals

$$Q = \exp(E_0/kT)\int_0^\infty (1/kT[\exp(-E/kT)]\,G(E)\,\mathrm{d}E \tag{20}$$

Insertion of expression (11) into (20) and integration gives

$$Q = \frac{\pi\alpha/\beta}{\sin(\pi\alpha/\beta)} - \frac{\alpha\exp(\alpha-\beta)}{\beta-\alpha}\left\{1-\left[\frac{\beta-\alpha}{2\beta-\alpha}\exp(-\beta)\right]+\ldots\right\} \tag{21}$$

If $\exp(\alpha-\beta) \ll 1$, that is for small $\nu_l(u_l)$ or large (E/kT), the first term of (21) is used as a tunnel correction to the reaction velocity:

$$Q_l = (\pi\alpha/\beta)/\sin(\pi\alpha/\beta) = (u/2)/\sin(u/2) \tag{22}$$

where $u = (2\pi\alpha/\beta) = (h\nu_l/kT)$. The second part of expression (21) can be similarly expressed in terms of u_l:

$$\frac{\alpha}{\beta-\alpha}\exp(\alpha-\beta) = \frac{u_l}{(2\pi-u_l)}\exp\left[\frac{-E_0}{kT}\left(\frac{2\pi-u_l}{u_l}\right)\right] \tag{23}$$

One neglects the term (23) when $u \ll 2\pi$. Expansion of (22) into powers of u gives

$$Q = 1+u^2/24+7u^4/5760+\ldots \quad (u<2\pi) \tag{24}$$

The first two terms of the expansion (24) correspond to Wigner's quantum correction to the classical passage of a particle of mass m over a col in

the energy surface of n dimensions (25)[37]. The difference between the

$$Q = \frac{v_{qu}}{v_{cl}} = 1 - \frac{1}{24}\sum_{n}(hi\nu_i/kT)^2 \tag{25}$$

experimental (quantal) activation energy E^* and the classical activation energy E_0 can be found by differentiating (19):

$$(E^*_{qu} - E_{cl}) = kT^2\,\mathrm{d}(\ln Q)/\mathrm{d}T = kT[(u_i/2)\cot(u_i/2) - 1] \tag{26}$$

Similarly the departure of the apparent pre-exponential factor A^* from the classical one is found to be

$$\begin{aligned} A^*/A &= (k_{qu}/k_{cl})\exp[(E^* - E)/kT] \\ &= [(u/2)/\sin(u/2)]\exp[(u/2)\cot(u/2) - 1] \end{aligned} \tag{27}$$

From relations (17), (18), (22), (26) and (27) it follows that the experimental activation energy E^* should be less than the height of the barrier E_0 and should decrease with decreasing temperature. Also, the pre-exponential factor A^* should be less than the classical A due to the curvature of the plot $\log k_{exp}$ against $1/T$[30,40]. From expressions (10) and (11) it follows that the tunnel corrections are mass-sensitive and, therefore, deuterium and tritium kinetic isotope effects should be a good test of the theoretical quantum mechanical predictions for tunnelling and its consequences. The following general predictions can be made.

Experimental kinetic isotope effects k_H/k_D and k_H/k_T should be at low temperatures greater than theoretical isotope effects calculated with equation (1), which has no correction for tunnelling.

Differences of the activation energies $(E^*_D - E^*_H)$ and $(E^*_T - E^*_H)$ should be larger than the appropriate differences of zero-point energy.

The ratios (A^*_H/A^*_D) and (A^*_H/A^*_T) should be smaller than the limits predicted by the transition state theory in the absence of tunnelling. Abnormal low values for (A^*) are more marked for hydrogen than for deuterium compounds. Values of (A^*_H/A^*_D) smaller than 0·5 should serve as the evidence of tunnelling.

3. Relative tritium and deuterium isotope effects

If we consider that the differences in zero-point energies of isotopic substrates and transition states determine the observed kinetic isotope effect then the numerical relation between deuterium and tritium isotope effects takes the form (28)[16,47].

$$k_H/k_T = (k_H/k_D)^{1.442} \tag{28}$$

Equation (28) is valid for relatively low temperatures (0–100°C), at which most of the X—H_i oscillators are in their lowest vibrational state. Relation (28) neglects the pre-exponential entropy factor, the correction for tunnelling, the ratio ($\nu^{\neq}_{L,H}/\nu^{\neq}_{L,D,T}$) of frequencies of crossing over the potential barrier by light- and heavy-activated complexes and the fact that not all normal modes of vibration are shifted by $\sqrt{2}$ and $\sqrt{3}$ upon substitution of proton by deuterium and tritium respectively. Taking into account the neglected terms, the equation relating tritium and deuterium isotope effects can be written in the general form as[41]

$$k_H/k_T = (k_H/k_D)^r \tag{29}$$

where r equals $1{\cdot}442 \pm 0{\cdot}11$. The estimated departures $\pm 0{\cdot}11$ from the Swain value 1·442 also cover the uncertainties introduced by tunnel effects. The power s in equation (30), relating the tunnelling correction for tritium–protium and deuterium–protium has, in Wigner's approximation,

$$Q_H/Q_T = (Q_H/Q_D)^s \tag{30}$$

the value 1·333 for very small u_H and the value 1·58 for very large u_H. Thus departures of r from the value 1·442 are expected when the observed isotope effects k_H/k_D are determined mostly by the dependence of the tunnelling correction Q on the masses of the hydrogen isotopes.

B. Experimental Methods of Determining Kinetic Isotope Effects

In the ratio k_1/k_2 of the rate constants of two isotopic molecules with different isotopic composition k_1 usually refers to the molecule having the lighter isotope and k_2 refers to the molecule with the heavier isotope. Theoretically it is possible to determine the isotope effect by carrying out two reactions, one with molecules highly enriched with the isotope under consideration and the second with molecules with known natural isotopic composition. Because of the high cost of production of pure isotopes and the limited accuracy of absolute rate determinations, the direct method is practically limited to deuterium isotope effects. The most common methods used in kinetic isotope effect determinations are the competitive methods which were reviewed by Bigeleisen and Wolfsberg[1, 19, 20a]. Only methods which have been used in studies with quinones will be surveyed here.

1. Chemical competitive method

In this method two isotopic compounds, S_1 and S_2 both compete with a chemically different compound B, all three reacting with compound C.

Equations (31)–(33) are the simplest schemes illustrating this method.

$$S_1 + C \xrightarrow{k_1} X_1 \tag{31}$$

$$S_2 + C \xrightarrow{k_2} X_2 \tag{32}$$

$$B + C \xrightarrow{k_B} Y \tag{33}$$

If the reaction is first-order in each of the reactants, processes (31)–(33) are described by the differential equations (34)–(36), where s_{0i} and b_0 are

$$\mathrm{d}(x_1)/\mathrm{d}t = k_1(s_{01} - x_1)\,[c_0 - (x_1 + y)] \tag{34}$$

$$\mathrm{d}(x_2)/\mathrm{d}t = k_2(s_{02} - x_2)\,[c_0 - (x_2 + y)] \tag{35}$$

$$\mathrm{d}(y)/\mathrm{d}t = k_\mathrm{B}(b_0 - y)\,[c_0 - (y + x_1,\ x_2)] \tag{36}$$

the initial concentrations of the species S_i and B, x_i and y are concentrations at time t_i of the product X_i and Y. In the experiment in which species S_1 and B are compared we have therefore

$$\mathrm{d}(x_1)/[k_1(s_{01} - x_1)] = \mathrm{d}(y)/[k_{1\mathrm{B}}(b_0 - y)] \tag{37}$$

For reactions (32) and (33) one obtains

$$\mathrm{d}(x_2)/[k_2(s_{02} - x_2)] = \mathrm{d}(y)/[k_\mathrm{B}(b_0 - y)] \tag{38}$$

Integration of equations (37) and (38) and further transformations lead

$$\frac{k_1}{k_2} = \frac{\ln(1 - f_{\mathrm{B}2\mathrm{exp}})}{\ln(1 - f_{\mathrm{B}1\mathrm{exp}})} \frac{\ln(1 - f_{S_1})}{\ln(1 - f_{S_2})} \tag{39}$$

to (39), where the sign 1 or 2exp means first and second experiment,

$$f_{S_1} = (x_1/s_{01}), \quad f_{S_2} = (x_2/s_{02}) \quad \text{and} \quad f_{\mathrm{B}i\,\mathrm{exp}} = (y_i/B_{i\,\mathrm{exp}})$$

are the degrees of conversion of the species S_1, S_2 and B in the two competitive experiments and k_1 and k_2 are the rate constants defined by equations (31) and (32). When $f_{S_1, S_2} \ll 1$ and $f_{\mathrm{B}i\,\mathrm{exp}} \ll 1$ then equation (39) simplifies to

$$k_1/k_2 = (f_{\mathrm{B}2\mathrm{exp}} f_{\mathrm{B}1\mathrm{exp}})\,(f_{S_1}/f_{S_2}) \tag{40}$$

Equation (40) is applied when S_1, S_2 and B are used in considerable excess.

2. Isotopic competitive methods

The isotopic competitive method is the most general method of kinetic isotope effect determinations. In this method two isotopic molecules, S_1 and S_2, compete with each other in reaction with other types of species B, C etc., or in their own unimolecular decomposition. The observed fractionation R_0/R_t of the isotopic molecules in the course of the reaction

can be related with the ratio of the rate constants k_1/k_2 and with the degree of decomposition or degree of the reaction of the isotopic compounds.

a. Analysis of the product after a known amount of conversion. In certain cases, for instance in decarboxylation processes[19], it is easy to separate the product from the reaction mixture at a known amount of reaction. If reactions (41) and (42) are first-order in the isotopic molecules,

$$S_1 + B + C + \ldots \xrightarrow{k_1} X_1 + Y + \ldots \tag{41}$$

$$S_2 + B + C + \ldots \xrightarrow{k_2} X_2 + Y + \ldots \tag{42}$$

S_i, and arbitrary-order in the other reactants, differential equations (43) and (44) will apply:

$$\mathrm{d}(x_1)/\mathrm{d}t = k_1(s_{01} - x_1)(B)^b(C)^c \tag{43}$$

$$\mathrm{d}(x_2)/\mathrm{d}t = k_2(s_{02} - x_2)(B)^b(C)^c \tag{44}$$

Dividing equation (43) by (44), integrating the differential equation obtained in the limits $0, x_2$ and $0, x_1$ and rearranging, one obtains (45)

$$\frac{k_1}{k_2} = \frac{\log\{1 - [(1+R_0)/(1+R_t)]\,f\}}{\log\{1 - [(1+R_0)/(1+R_t)](R_t/R_0)\,f\}} \tag{45}$$

where $R_0 = (s_{02}/s_{01})$, $R_t = (x_2/x_1)$ and $f = (x_1 + x_2)/(s_{01} + s_{02})$ is the fraction of the reaction. When $x_2 \ll x_1$ and $s_{02} \ll s_{01}$ equation (45) simplifies to (46):

$$k_1/k_2 = \log(1-f)/\log[1 - (R_t/R_0)f] \tag{46}$$

When $f \ll 1$, (46) approximates to (47):

$$(k_1/k_2) \approx (R_0/R_t) \tag{47}$$

In this method it is recommended to work at small reaction percentages.

b. Analysis of the substrate after a high amount of conversion. Let us assume that the two isotopic species, S_i, disappear according to the exponential laws (48):

$$S_{t1} = S_{01}\exp(-k_1 t), \quad S_{t2} = S_{02}\exp(-k_2 t) \tag{48}$$

and the fraction-reacted f is given by the relation (49):

$$(1-f) = (s_{t1} + s_{t2})/(s_{01} + s_{02}) \tag{49}$$

Then the relation (50) can be derived:

$$(1 - k_2/k_1) = \ln(R_{0s}/R_{ts})/\ln[(1-f)(1+R_{0s})/(1+R_{ts})] \tag{50}$$

where $R_{0s} = (s_{02}/s_{01})$ and $R_{ts} = (s_{t2}/s_{t1})$ are the isotopic ratios of the isotopic substrates under consideration at zero time of conversion and

after fraction f of the chemical species S has reacted. Equation (50) transforms into equations (51) or (52) when the isotopic species, S_2, is found in the reacting mixture at the tracer level†:

$$(1-k_2/k_1) = \ln(R_{0s}/R_{ts})/\ln(1-f) \tag{51}$$

$$k_1/k_2 = [\ln(1-f)]/[\ln(1-f)+\ln(R_{ts}/R_{0s})] \tag{52}$$

Equations (51) and (52) are used in studies with radioactive isotopes and with molecules containing ^{13}C, ^{15}N and ^{18}O at the natural abundance level. In the very precise works with ^{13}C and ^{18}O at the natural abundance level, formula (50) is used. In this method the reactions are carried to at least 50–60% of completion.

The equations relating kinetic isotope effects with the isotopic composition of substrates, products, or both as well as those applying for more complicated chemical processes where in the course of the reaction both intramolecular and intermolecular isotopic competition and fractionation occur, are given in references 4, 19, 20a and 60.

3. General remarks

If in the course of the reaction studied there are no isotopic exchanges between products, intermediates and reactants and the isotopic inhomogeneity within the molecule is easily determined, then the isotopic competitive methods are the most sensitive, since the two isotopic reactions are carried out in exactly the same physical conditions. Moreover, the precision of the mass spectrometric determinations of the isotopic composition of the samples is very high (in the case of $^{18}O/^{16}O$ and $^{13}C/^{12}C$ ratios sometimes better than 0·01‰[48-50]). In the case of samples containing ^{14}C, the composition can sometimes be determined with an accuracy approaching 0·2% but usually an error of 0·5% is considered acceptable[51]. In determinations of the relative specific activity of samples containing tritium the precision attained is sometimes 1–2% but measurements carried out with an accuracy better than 5% are still classified as good[52-55]. The problems of isotopic inhomogeneity[4, 19], are important when working with compounds having natural isotopic abundances but do not exist with artificially labelled substances.

C. Tracer Studies with Isotopes

A rich literature[56-63b] covers the theory of tracer applications of isotopes and isotopically labelled compounds. A short formal description of the isotopic exchange reactions is given below.

† In this case: $s_{02} \ll s_{01}$; $s_{t2} \ll s_{t1}$; $(1+R_{0s}) \approx 1$; $(1+R_{ts}) \approx 1$ and the denominator of equation (50) approximates $\ln(1-f)$.

I. Kinetics of isotope exchange reactions

Consider the simple example of the exchange of isotopes X and X^* taking place between molecules AX and BX,

$$AX+BX^* = BX+AX^* \tag{53}$$

If there are no isotope effects and the transfer of isotope X^* from BX^* to AX and from AX^* to BX proceeds at the same rate, then at a tracer concentration of X^* in the system, the rate with which the concentration of X^* in chemical species AX changes is given by equation (54), where R

$$\mathrm{d}(ax)/\mathrm{d}t = Ry - Rx \tag{54}$$

is the rate, expressed in g atom/s, with which X exchanges at equilibrium between compounds AX and BX, $a = (AX)$ is the total concentration of AX molecules, $b = (BX)$ is the total concentration of BX molecules, $x = (AX^*)/[(AX)+(AX^*)]$ and $y = (BX^*)/[(BX)+(BX^*)]$ are fractions of the isotopically labelled species AX and BX. Integration of (54) leads to equation (55), where $F = (x/x_\infty) = x(a+b)/r$ is the degree of exchange, t is the time of exchange and $r = ax+by$.

$$-\ln(1-F) = [R(a+b)/ab]\,t = \rho t \tag{55}$$

Formula (55) has been derived without any particular assumption about the explicit functional dependence of R on concentrations of exchanging species and is of general validity. In the case of tritium and deuterium isotope exchanges, when the force constants in the chemical species AX and BX differ very much, $(x_\infty/y_\infty) = \alpha \neq 1$, and, at equilibrium, the relation

$$x_\infty = \left(\frac{ax+bx}{a+b}\right)$$

has to be replaced by

$$x_\infty = \frac{\alpha(ax+bx)}{\alpha a+b}$$

and the equation describing the exchange will be (56). Derivations of equations describing the kinetics of isotopic exchanges involving large kinetic and thermodynamic isotope effects are given in the monograph by Melander[60].

$$\ln[1-x/x_\infty] = -[R(\alpha a+b)/ab]\,t \tag{56}$$

II. SYNTHESES OF LABELLED QUINONES

A. Syntheses of ^{13}C-Labelled Quinones

Synthesis of ^{13}C-labelled quinones has been undertaken in connexion with interpretation of the low intensity lines present in the electron spin

resonance spectra of semiquinones, the ring-carbon atoms of which contain ^{13}C on the natural abundance level[64–71], and also for the elucidation of the nature of the electronuclear ^{13}C hyperfine interactions in the semiquinone ions[64,65].

1. Synthesis of ^{13}C-labelled *p*-benzoquinones

a. Synthesis of p-*benzoquinone*-1-^{13}C. Das and Venkataraman[66–68,70] obtained (in 10 steps) labelled 1-^{13}C-benzoquinone with about 50 at% isotope abundance of ^{13}C in the 1-position in an overall yield of 2%, starting from $Ba^{13}CO_3$, enriched in ^{13}C to about 48%.

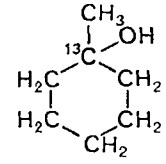
Ethyl acetate-1-^{13}C (**2**) was first prepared in four steps by adapting well-established preparative methods of ^{14}C-labelled compounds[19,72,73,84,85].

$$\begin{aligned} Ba^{13}CO_3 &\xrightarrow{H_2SO_4} {}^{13}CO_2 \xrightarrow[\text{anhydrous ether}]{CH_3MgI} CH_3{}^{13}COOH \\ &\xrightarrow{NaOH} CH_3{}^{13}COONa \longrightarrow CH_3{}^{13}COOC_2H_5 \end{aligned} \qquad (57)$$

(**2**)

The labelled sodium acetate was converted to ethyl acetate by refluxing with triethyl phosphate[74] at 170–220°C (yield: 90·7%). 1-Methylcyclohexanol-1-^{13}C (**3**) was prepared in 53% yield from the Grignard reagent of pentamethylene dibromide with ethyl acetate-1-^{13}C[75].

$$CH_3{}^{13}COOC_2H_5 \xrightarrow[\text{anhydrous ether}]{BrMg(CH_2)_5MgBr} \qquad (58)$$

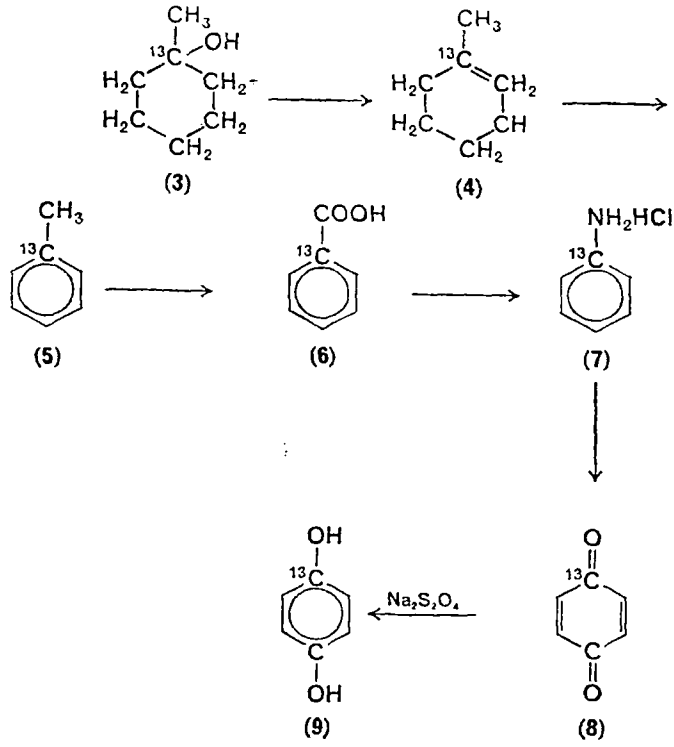


(**3**)

The iodine-catalysed dehydration of **3** to 1-methylcyclohexene-1-^{13}C (**4**) was carried out at 135–140°C using a Podbielniak column[75] with glass coils (yield: 40·1%). The dehydrogenation of **4** to toluene-1-^{13}C (**5**) was performed at 450°C using 30% platinum-on-asbestos (or palladium) catalyst in 67·7% yield. Toluene **5** was oxidized with an aqueous solution of potassium permanganate and sodium hydroxide to benzoic-1-^{13}C acid (**6**). This was converted to aniline-1-^{13}C hydrochloride (**7**) by Schmidt reaction using an excess of sodium azide (yield: 85·4%).

p-Benzoquinone-1-^{13}C (**8**) was obtained by oxidation of **7** with MnO_2 in dilute sulphuric acid (yield: 51·6%). The presence of one ^{13}C atom in the ring with an enrichment of about 50% was confirmed by observing the hyperfine structure[67] in the e.s.r. spectrum of the semiquinone ion prepared from the labelled *p*-benzohydroquinone-1-^{13}C (**9**).

p-Benzoquinone-1-^{13}C was also synthesized in four steps with an overall yield of 16% by condensing acetone-2-^{13}C (**10**) with sodium

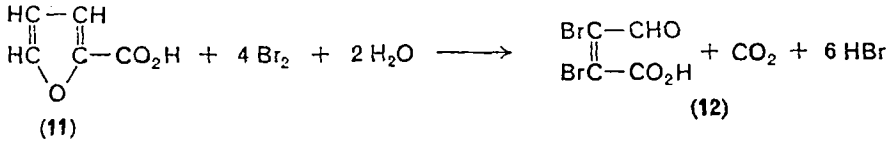


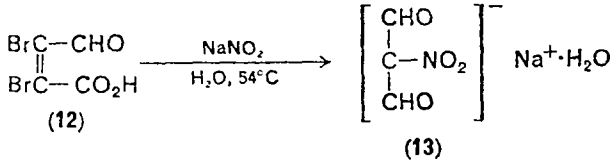
(59)

$$CH_3{}^{13}CO_2Ba \xrightarrow[490\text{–}510^\circ C]{\text{pyrolysis}} CH_3{}^{13}C(=O)CH_3 \qquad (60)$$

(10)

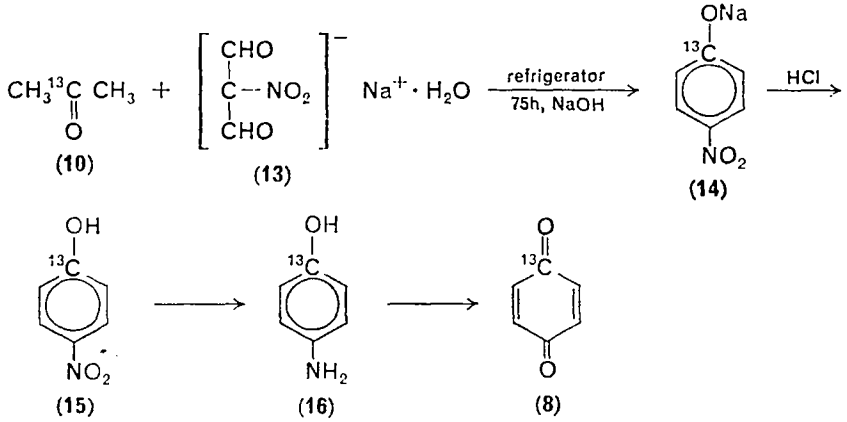
nitromalonaldehyde **13**[71,76–78]. Nitromalonaldehyde **13** was obtained from the aldehydo-acid **12** which in turn was prepared from furoic acid **11**. *p*-Nitrophenol-1-^{13}C (**15**) was prepared in 36·8% yield by condensing **10** with sodium nitromalonaldehyde monohydrate **13**. **14** was obtained from





(61)

the reaction mixture by addition of NaOH pellets. *p*-Aminophenol **16** was prepared from **15** by reduction with Sn and HCl (yield: 96·4%). *p*-Benzoquinone-1-^{13}C was prepared from **16** by oxidation with sodium

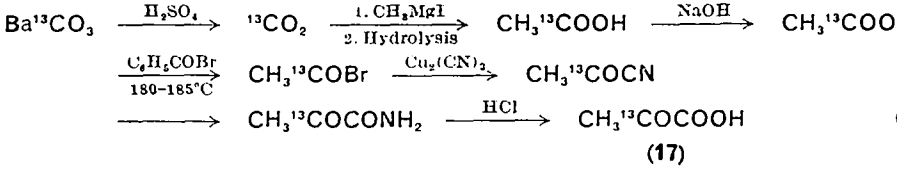


(62)

dichromate. The yield of the oxidation step was 47·4%, and the overall yield based on sodium acetate-1-^{13}C was 16%. The intensity measurements of the e.s.r. spectra of the semiquinone showed that the isotopic abundance of ^{13}C in the 1-position of the final product was 54 ± 3 at% in agreement with the 56·3 at% in the starting material sodium acetate-1-^{13}C.

b. Synthesis of p-*benzoquinone*-1,3,5-^{13}*C*. Synthesis of *p*-benzoquinone labelled with ^{13}C in positions 1, 3 and 5 was performed by condensation of pyruvic-2-^{13}C acid (**17**)[68,79-83].

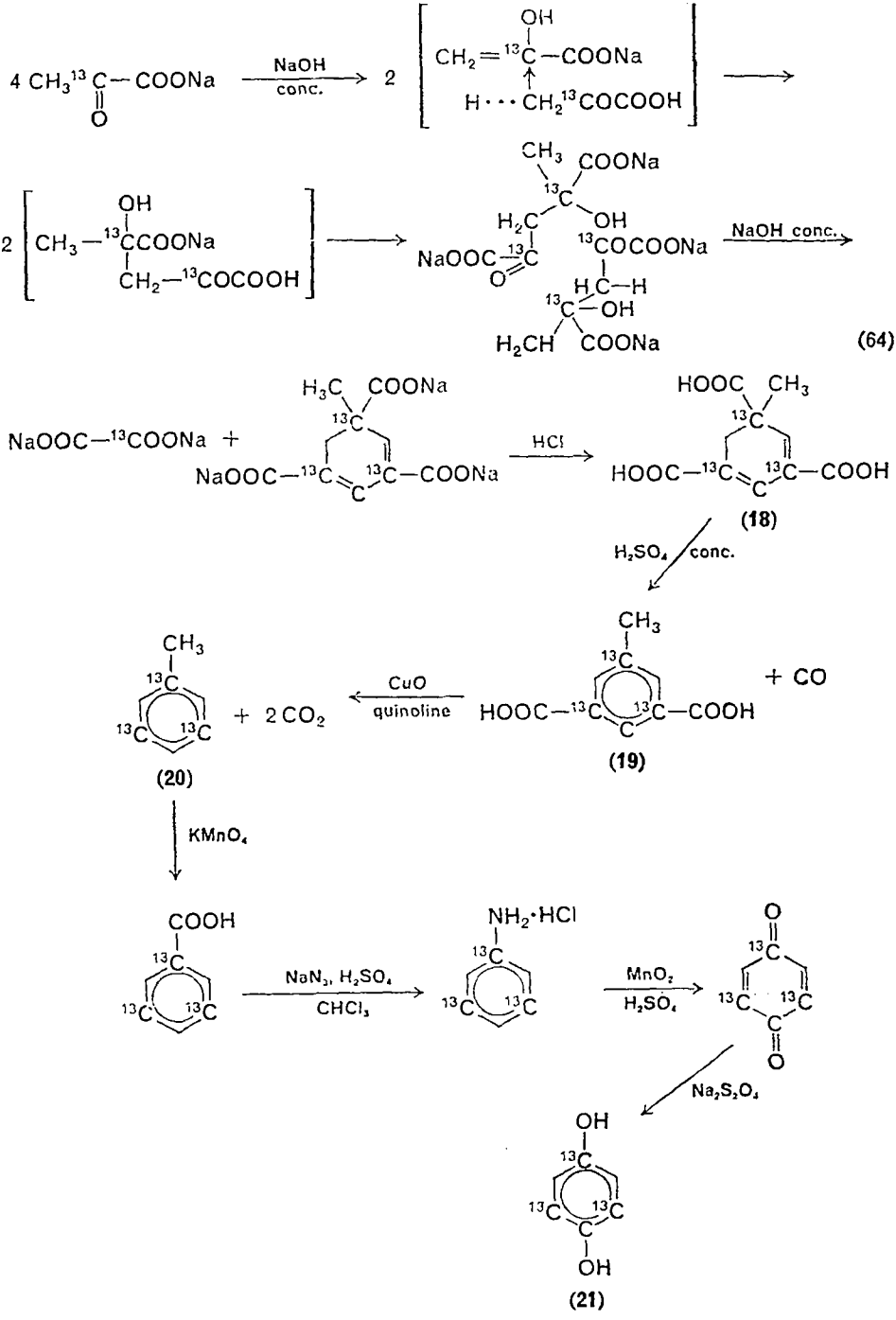
Pyruvic acid labelled in the keto-group was synthetized according to sequence (63):



(63)

If in the last step the concentration of the hydrochloric acid was higher than 2N or if the pyruvamide was hydrolysed at a higher temperature than 70°C, acetic acid appeared as a side-product.

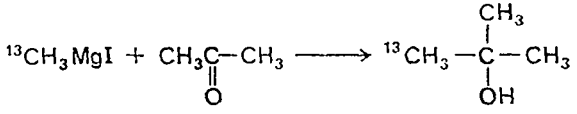
The condensation of the ^{13}C-labelled pyruvic acid (**17**) to methyl-dihydrotrimesic-1,3,5-$^{13}C_3$ acid (**18**) has been performed according to the method of Hughes and Reid[69], who also described the formation of uvitic-1,3,5-$^{13}C_3$ acid (**19**) and synthesis of toluene-1,3,5-$^{13}C_3$ (**20**) by decarboxylation of **19**. Transformation of **20** to *p*-benzohydroquinone-1,3,5-$^{13}C_3$ (**21**) has been carried out using the same sequence of reactions as in the case of *p*-benzoquinone-1-^{13}C.


NaOH conc.
NaOH conc.
HCl
(18)
H_2SO_4 conc.
CuO quinoline
+ CO
+ $2CO_2$
(19)
(20)
$KMnO_4$
NaN_3, H_2SO_4 $CHCl_3$
MnO_2 H_2SO_4
$Na_2S_2O_4$
(21)

(64)

2. Synthesis of 2-t-[β-^{13}C]butylhydroquinone

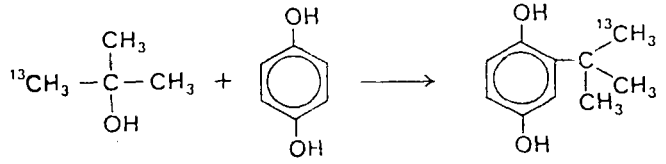
This has been performed[86-88] by alkylation of hydroquinone with *t*-butyl alcohol-β-^{13}C (**22**). The latter was obtained from the Grignard reaction of methyl iodide-^{13}C (having 48·1 at% excess of ^{13}C) with acetone:



(65)

(22)

The method of Young and Rogers was used for the reaction of **22** with hydroquinone[89], adding an aqueous solution of the labelled alcohol to



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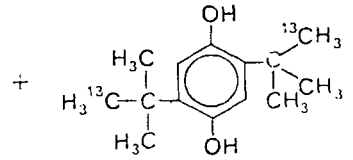


(66)

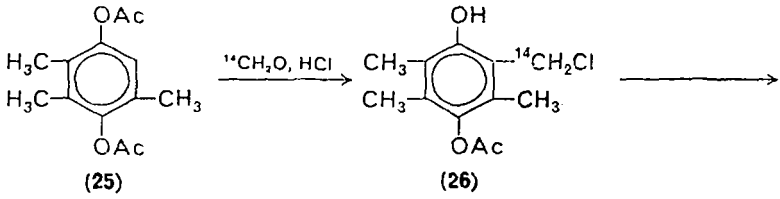
(24)

the vigorously stirred mixture of hydroquinone, phosporic acid and xylene heated to 115°C. After 30 min the hot xylene layer was removed and the hot acid phase was extracted with more xylene. The xylene was removed *in vacuo* to yield a crude mixture of 2,5-di-*t*-butylhydroquinone (27%) (**24**) and 2-*t*-butyl-β-^{13}C-hydroquinone (**23**) in 30% yield. The separation of the labelled compounds was achieved by chromatography on a silic acid–celite column using chloroform as the eluent.

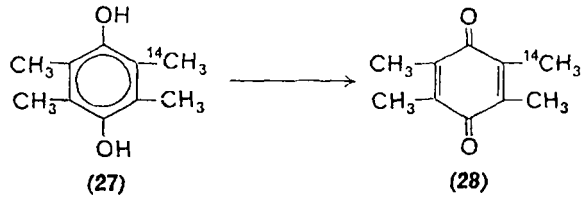
B. Syntheses of ^{14}C-Labelled Quinones

1. Synthesis of tetramethyl-$^{14}C_1$-*p*-benzoquinone (28)

Duroquinone-α-^{14}C was obtained according to reaction scheme (67)[72, 90, 91]. 2-Chloromethyl-^{14}C-3,5,6 trimethyl-4-acetoxyphenol (**26**), prepared in 89% yield by chloromethylation of trimethylhydroquinone diacetate (**25**) with formaldehyde-^{14}C[90-92] was reduced by lithium aluminium hydride to tetramethyl-^{14}C-hydroquinone (**27**). Oxidation of **27** with ferric sulphate gave a quantitative yield of duroquinone-α-^{14}C (**28**).

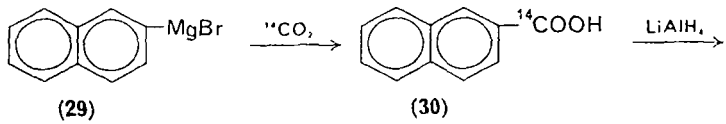


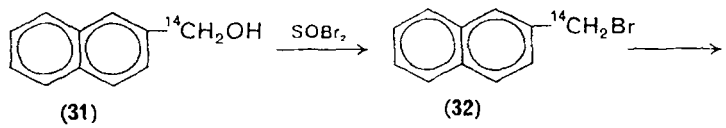
(67)

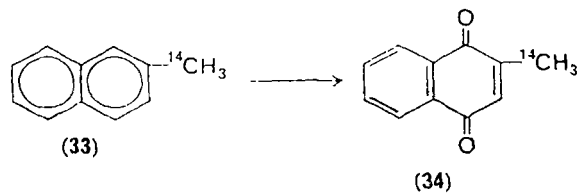


2. Synthesis of ^{14}C-labelled naphthoquinones

a. Synthesis of 2-methyl-^{14}C-1,4-naphthoquinones. Synthesis of ^{14}C-labelled menadione (vitamin K_3) (**34**) has been achieved by the following scheme[93, 94]:



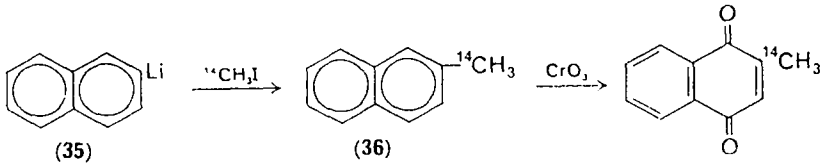




(68)

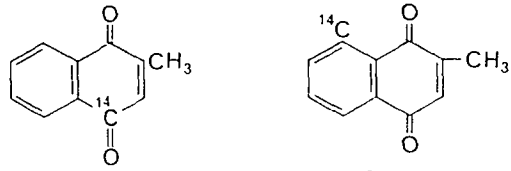
2-Naphthoic acid-carboxyl-^{14}C (**30**) was obtained in 70% yield from **29** and reduced to **31**, which in turn was converted to 2-bromomethyl-^{14}C-naphthalene (**32**). Reduction of **32** with $LiAlH_4$ yielded **33**, which was

oxidized with chromic oxide[94] to 2-methyl-^{14}C-1,4-naphthoquinone (**34**). The overall yield of vitamin K_3 was 23%. Vitamin K_3 (**34**) has also been synthesized using methyl-^{14}C iodide as a labelled starting material[72,95].



(35) (36) (34) (69)

b. Synthesis of ring-labelled 2-methyl-1,4-naphthoquinones. The detailed directions for the synthesis of 2-methyl-1,4-naphthoquinone-4-^{14}C (**36**), using the method of Li and Elliot[96] and of 2-methyl-1,4-naphthoquinone-8-^{14}C (**37**) performed according to Collins[97], are given by Murray and Williams[72]. The reaction schemes have also been reviewed by Mikluhin[59] and by Crompton and Woodruff[73].

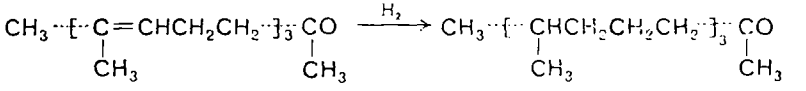


(36) (37)

3. Synthesis of vitamin K_1 labelled with ^{14}C

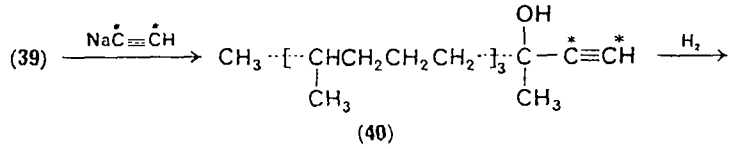
Labelled chemically pure compounds with vitamin K activity, especially vitamin K_1 and labelled menadione, are important tools for the elucidation of their functions, mode of action and metabolic pathways in living organisms[98–101]. Carbon ^{14}C can be introduced separately into vitamin K_1 either by the synthesis of a labelled naphthoquinone ring, or by introducing isotopic carbon into the 2-methyl group of the menadione used for the condensation reaction, or by labelling the phytyl chain in the 3-position. Reaction schemes used for the synthesis of simple naphthoquinones labelled with ^{14}C in various positions are described by Murray and Williams[72]. Methods used for the synthesis of labelled isoprenoid chains have been reviewed by Isler and coworkers[98].

a. Synthesis of ^{14}C-labelled isophytol. The reactions below illustrate the synthesis of isophytol labelled in the 1- and 2-position:



(38) (39) (70)

The unsaturated C_{18} ketone **38** was hydrogenated to give the saturated ketone **39**. Ethynylation of the latter with uniformly ^{14}C-labelled sodium acetylide in liquid ammonia followed by partial hydrogenation of the triple bond yields isophytol **41**. Phytol, **42**, can be prepared in three steps



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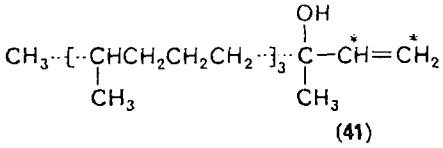
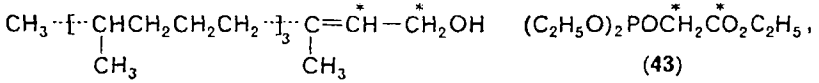
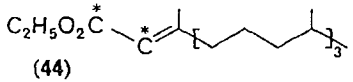


(41) (71)

from isophytol **41** or independently by reaction of **39** with the doubly labelled **43**, followed by reduction of the ester **44** with lithium aluminium hydride[98–102]:



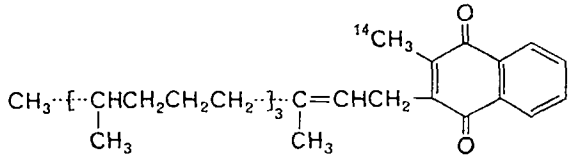
(42) (43)



(44)

The condensation of the isophytol with 2-methyl-1,4-naphthohydroquinone is catalysed by boron trifluoride. Oxidation of the condensation product by air or by silver oxide produces chain-labelled vitamin K_1.

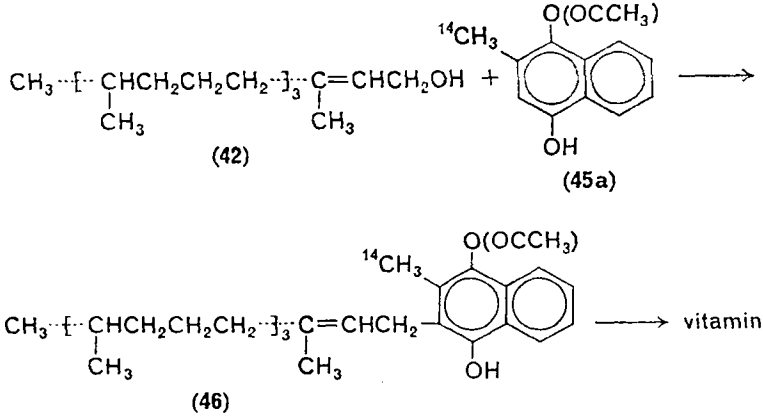
b. Synthesis of vitamin K_1 labelled in the methyl group. Racemic vitamin K_1 (**45**) labelled with ^{14}C in the 2-methyl group was synthesized by



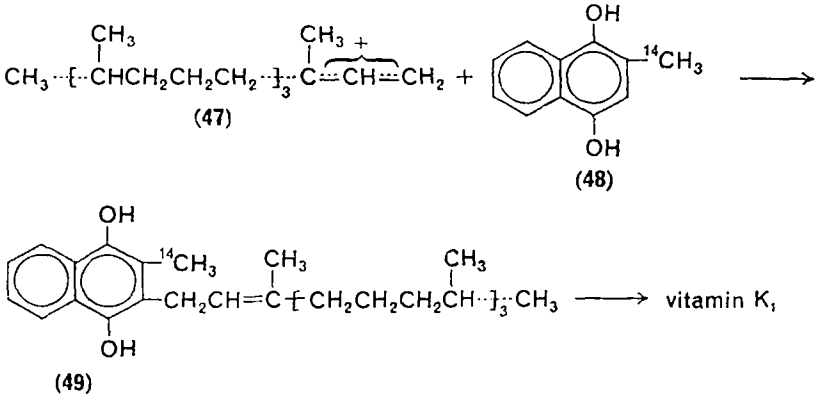
(45)

condensing 500 mg of 2-methyl-^{14}C-1,4-naphthohydroquinone (prepared from ^{14}C-labelled vitamin K_3) with 400 mg of isophytol **41** in dioxan with boron trifluoride as catalyst[103, 104]. Vitamin K_1 was obtained, by oxidation of the hydroquinone **49**, as a clear yellow oil, 20% based on **48**. The

purity of the product has been tested by subjecting quinone to reductive acetylation[98-103] when the diacetate obtained accounted for 96·0% of the vitamin K_1 radioactivity used. Better overall yields of unlabelled vitamin K_1 (as high as 66%) were obtained[105] from menadiol 1-monoester (**45a**) using boron trifluoride etherate, aluminium chloride or potassium acid sulphate as catalysts. The condensation product **46**, dihydrovitamin K_1 1-monoacetate, was first hydrolysed and then oxidized to the quinone, vitamin K_1.

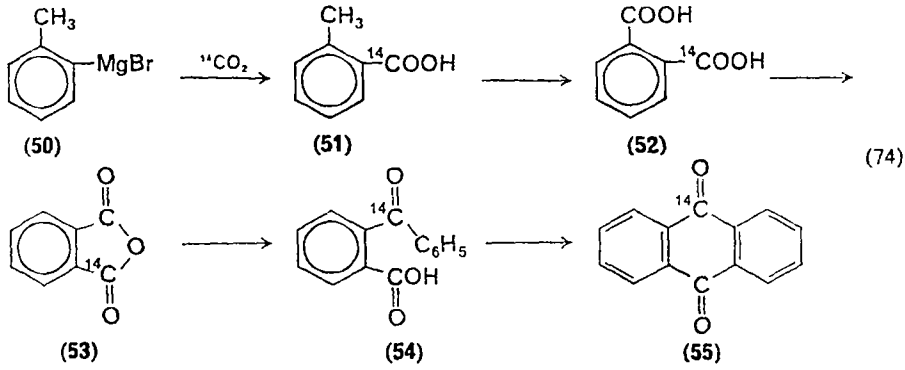


It is possible that electrophilic displacement by both phytol and isophytol may proceed through the same cationoid intermediate **47** yielding the hydroquinone of vitamin K_1, **49**.



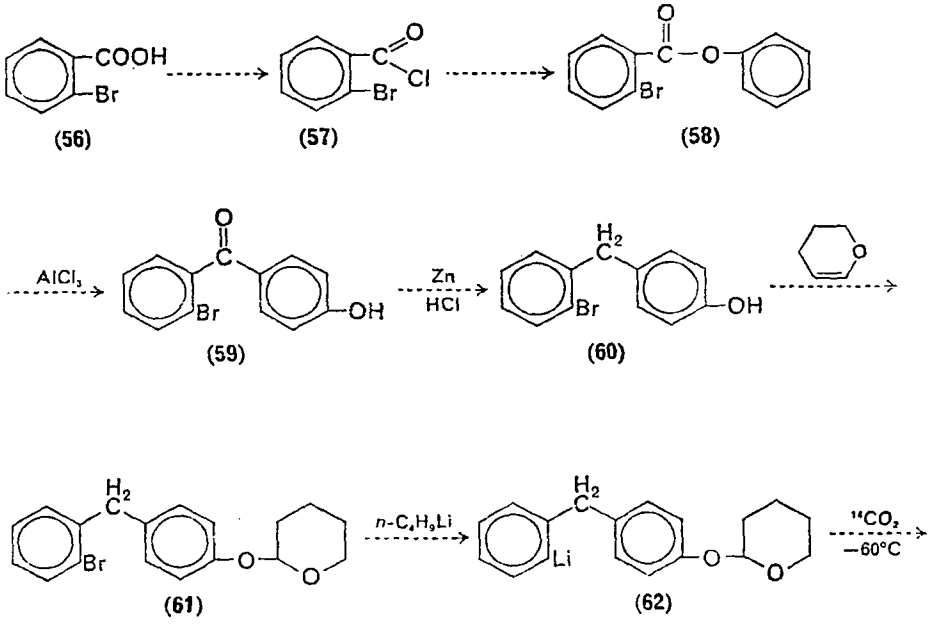
4. Synthesis of ^{14}C-labelled anthraquinones

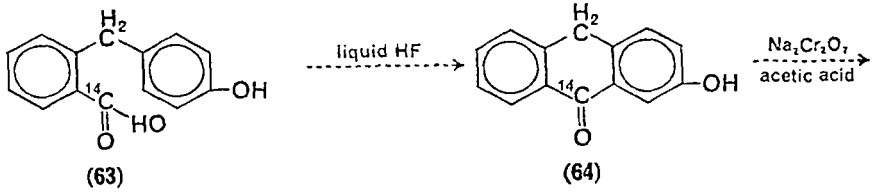
a. Synthesis of anthraquinone-9-$^{14}C_1$. Anthraquinone-9-$^{14}C_1$ (**55**) has been prepared as a labelled intermediate in the synthesis of anthracene-9-$^{14}C_1$[106]:

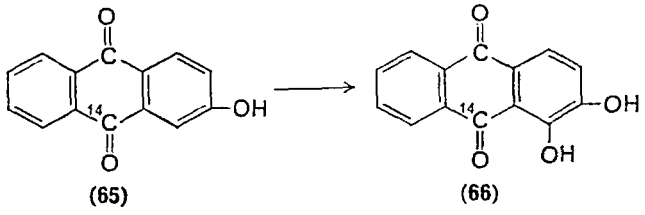


Carboxyl-labelled *o*-toluic acid (**51**) was prepared from **50** and oxidized to **52** by potassium permanganate. The anhydride **53** was obtained by refluxing **52** with thionyl chloride and gave **54** by Friedel–Crafts reaction. Ring closure to **55** has been achieved by heating **54** in 96% sulphuric acid at 120°C for 1 h[109].

b. Synthesis of 1,2-*dihydroxy anthraquinone*-9-^{14}C. The synthesis of labelled alizarin **66** is shown in the following reaction scheme[107]:







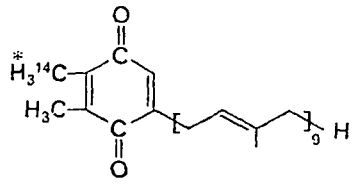
(75)

o-Bromobenzoyl chloride (**57**) is esterified with phenol. The Fries rearrangement[108] of **58** gave 2-bromo-4'-hydroxybenzophenone (**59**) which was reduced to 2-bromo-4'-hydroxydiphenylmethane (**60**). The hydroxyl group is protected in the next step by formation of a cyclic acetal with dihydropyran[110]. The halogen–metal interconversion with **61** and butyllithium yields the organolithium compound **62**, which was carbonated with labelled carbon dioxide. Ring closure of **63** gave 2-hydroxy-9-anthrone (**64**) in 88–100% yield[111], which was oxidized to 2-hydroxyanthraquinone (**65**) in practically quantitative yield. Conversion of **65** to alizarine **66** by hydroxylation has been achieved with high yield using an excess of potassium chlorate and sodium hydroxide.

5. Biosynthesis of ^{14}C-labelled quinones

a. Biosynthesis of phytoquinones. Threlfall, Whistance and Goodwin[112] studied the incorporation of ^{14}C and tritium activity into terpenoid quinones synthesized by maize shoots, incubated during 24 h with continuous illumination, in water containing 50 Ci of L-Me-^{14}C methionine and 300 Ci of L-Me-^{3}H methionine[112]. They found that in the isolated plastoquinone **67**, ubiquinone **68** and phylloquinone **69** all the ^{14}C and tritium radioactivity was in the methyl or methoxyl groups on the quinonoid ring. Ubiquinone **68** contained 26% of the ^{14}C activity in the methyl group and the remaining activity in the methoxyl groups. Phylloquinone **69** also had the activity in the ring-attached methyl group which was formed by transfer of an intact $^{14}CH_3$ group from methionine. It is suggested that in the cases of phylloquinone and plastoquinone the methylation takes place in the chloroplast, whereas methylation of ubiquinone occurs elsewhere within the cell. Possible mechanisms for

C- and *O*-methylation have been proposed. Unfortunately, the yield of the labelled compounds based on the L-[Me-^{14}C, ^{3}H]-methionine radioactivity used is very low (under 1%).



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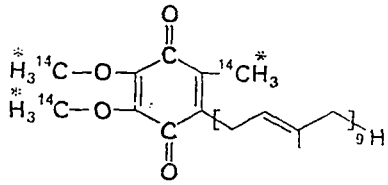
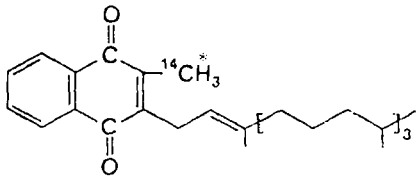
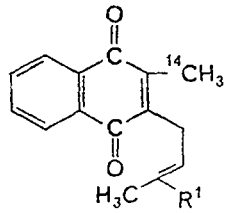


(68)

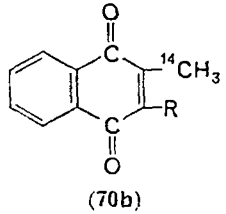


(69)

Guérin, Azerad and Lederer[113] have found that vitamin $K_2(45)H$ (**70**) with ^{14}C-labelled 2-methyl group is synthesized by *Mycobacterium Phlei* from L-methionine-$^{14}CH_3$. It has been proved that the isoprenoid chain of the vitamin contains no radioactivity and that the total activity of the molecule is localized in the 2-methyl group. Phthalic acid obtained by oxidation of the labelled vitamin $K_2(45)H$ showed only 0·24% of the total activity of the vitamin $K_2(45)H$. This excludes incorporation of the methyl group of the L-methionine-$^{14}CH_3$ into those eight atoms of the anthraquinone ring system which are transformed by oxidation into phthalic acid.



(70a)



(70b)

(In **70b** R is an isoprenoid chain consisting of 45 carbon atoms or 9 units of isoprene, one of which is saturated.)

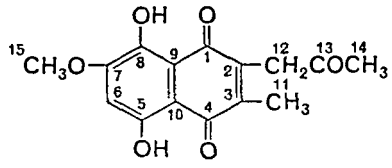
Martius and Billeter[114], using vitamin K_1 labelled with tritium in the nucleus, with ^{14}C in the side-chain, demonstrated that animals are able to replace the phytyl group of the vitamin K_1 by a geranyl-geranyl group, thus producing vitamin $K_2(20)$.

Later Martinus and Leuzinger[114, 115] showed that the anaerobic heterotrophic bacteria *Fusiformis nigrescens* can use 1,4-naphthoquinone in the vitamin K synthesis, by transmethylation of a CH_3 group from methionine into the 2-position of naphthoquinone and attaching the isoprenoid chain in the 3-position.

b. Naphthaquinone biosynthesis[116]. Gatenbeck and Bentley[116] have shown that Me-^{14}C-methionine (**71**), 1-^{14}C acetate or 2-^{14}C malonate added to the growth medium of *Fusarium javanicum* are converted into labelled javanicin **72**. The percentages of incorporation are 0·83, 0·70 and 0·07%, respectively.

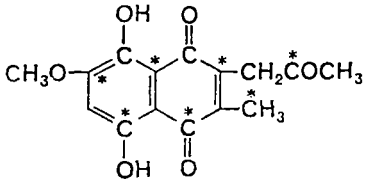
$^{14}CH_3SCH_2CH_2CH(NH_2)COOH$

(71)

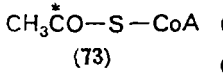


(72a)

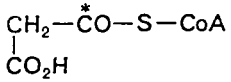
Degradation of labelled javanicin revealed that the label is incorporate only in the methoxyl group (position 15). According to the authors the methyl group (position 11), is formed not by transmethylation but by the reduction of the carboxyl group. The remaining carbon atoms labelled with an asterisk in **72b** originate from the carbonyl groups of the labelled acetyl-CoA (**73**) and malonyl-CoA (**74**).



(72b)



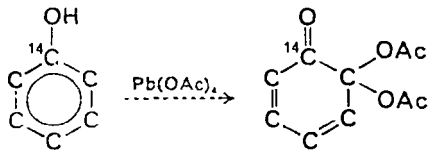
(73)



(74)

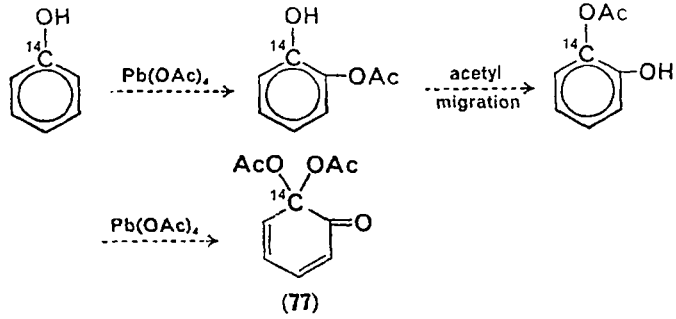
6. Synthesis of ^{14}C labelled o-benzoquinone diacetate

Billek, Swoboda and Wessely[117] synthesized *o*-benzoquinone diacetate (**76**) labelled with ^{14}C predominantly at the C-1-position by treating ^{14}C-labelled phenol with lead tetraacetate. Besides the main product



(75) (76) (76)

2,2-diacetoxycyclohexa-3,5-dienon-1 (**76**), obtained in 95% yield, oxidation leads also to the formation of the 2-^{14}C isomer (**77**) in about 5% yield.

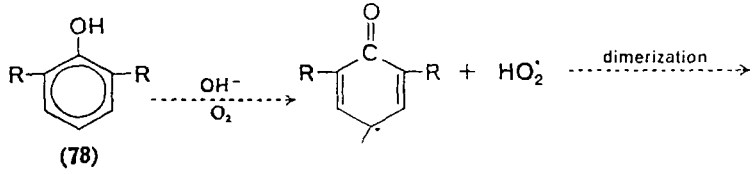


(77)

(77)

7. Synthesis of uniformly ^{14}C-ring-labelled 3,3′,5,5′-tetra-t-butyldiphenoquinone

Uniformly ^{14}C-ring-labelled diphenoquinone (**79**) was synthesized in the presence of oxygen from uniformly ^{14}C-ring-labelled 2,6-di-*t*-butylphenol (**78**). The reaction[118] takes place at 37°C in *t*-butyl alcohol solution



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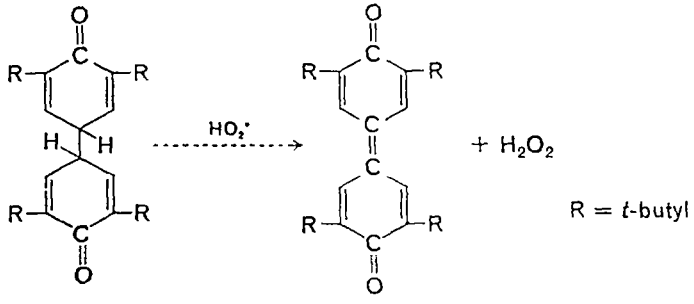


(79)

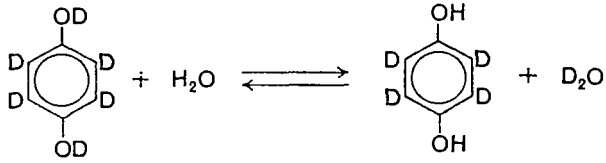
of KOH. The final yield of the purified dark-red crystalline product **79** was 64% having a specific activity of 2·4 mCi/mmole.

C. Synthesis of Tritium- and Deuterium-labelled Quinones

1. Synthesis of deuterium-labelled *p*-benzoquinone

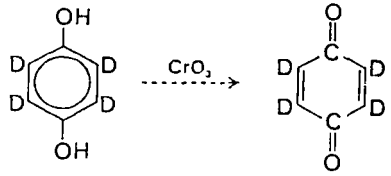
Deuterium-labelled 1,4-hydroquinone has been obtained[119, 120] by hydrogen exchange taking place between heavy water and *p*-benzohydroquinone at high temperatures (170°C, 40–50 h) in the presence of sodium

hydroxide. In the product so obtained the labile oxygen-bound deuterium was replaced by hydrogen through re-exchange (79a) at room temperature.



(79a)

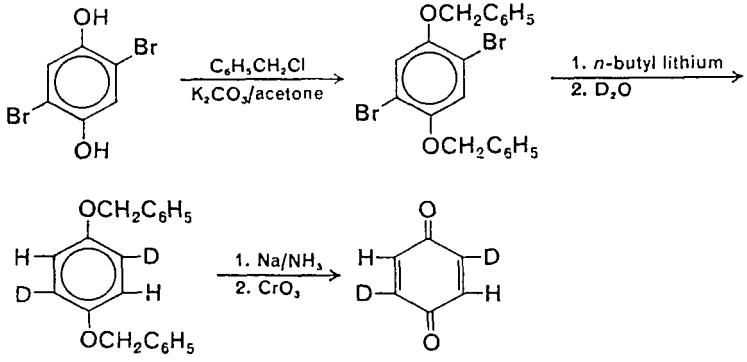
The heavy 1,4-benzoquinone was obtained by oxidation of the heavy hydroquinone with dichromate solution according to the usual method[121, 122]. The authors did not notice any transfer of deuterium from



(79b)

either the ring-labelled *p*-benzohydroquinone or the *p*-benzoquinone to the solvent during the oxidation process.

Charney and Becker[122b] prepared *p*-benzoquinone-d_4 by carrying out three subsequent isotopic exchange reactions between fully deuterated 3·4M sulphuric acid and hydroquinone at 100°C during 36 h. The labelled hydroquinone was oxidized with chromic oxide[122] to *p*-benzoquinone-d_4. The final yield of the purified *p*-benzoquinone was 55%. The authors[122c] have also obtained *p*-benzoquinone-2,5-d_2 and *p*-benzoquinone-2,6-d_2 by applying the reaction scheme (79c). *p*-Benzoquinone-d_1 was obtained[122c], starting from the commercially available monobromohydroquinone, by applying a similar sequence of reactions.

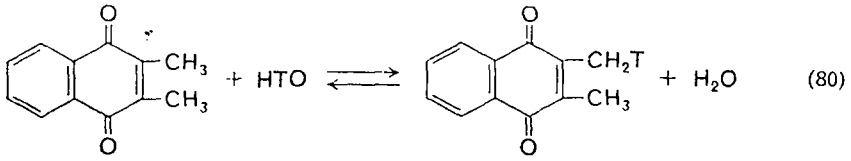


(79c)

2. Synthesis of deuterium- and tritium-labelled methylquinones

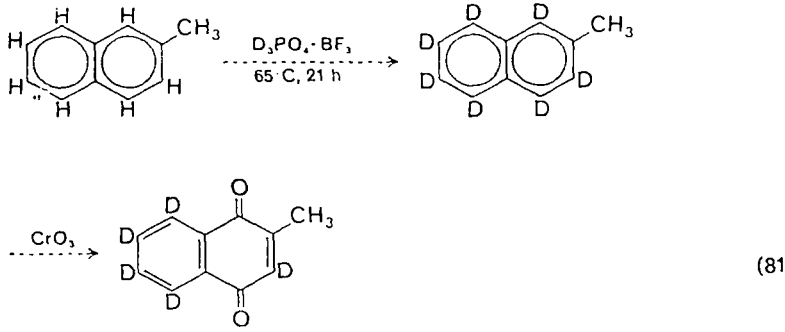
Clark and coworkers[123] and Lapidot and coworkers[125] investigated the base-catalysed hydrogen isotope exchange between methyl quinones

(duroquinone, 2,3-dimethylnaphthoquinone and other quinones including vitamin $K_1(20)$) and D_2O or tritiated water in dioxan solutions. Such studies can furnish data for choosing the best conditions for synthesis of labelled methylquinones. For example, in the case of a solution of 2,3-dimethylnaphthoquinone in a dioxan-tritiated water mixture using triethylamine as catalyst, isotopic equilibrium was reached after 10 h of refluxing. The dependence of the rate of the hydrogen exchange and the



dependence of the type of the side-reactions occurring during isotopic exchange on the nature of the base, temperature and pH have been observed.

Synthesis of 2-methyl-1,4-naphthoquinone-3,5,6,7,8-d_5 has been achieved by treatment of 2-methylnaphthalene with phosphoric acid-d_3-boron trifluoride reagent in cyclohexane and subsequent oxidation of the 2-methylnaphthalene-1,3,4,5,6,7,8-d_7 with chromic acid[93, 99] (reaction 81).

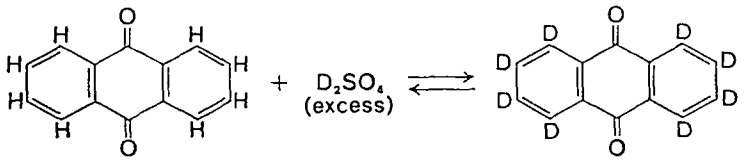


Condensation of the 2-methyl-1,4-naphthohydroquinone-3,5,6,7,8-d_5 with phytol catalysed with boron trifluoride gave vitamin $K_1(20)$-5,6,7,8-d_4[99, 124].

3. Synthesis of partially and fully deuterated 9,10-anthraquinone

Using sulphuric acid-d_2 as a deuterating agent, Lunelli and Pecile[126] prepared 9,10-anthraquinone-d_8 (**80**). The hydrogen exchange takes place to an appreciable extent at high temperatures and high concentrations of deuterated sulphuric acid. Under such severe experimental conditions sulphonation of the compound also occurs which, however, could be overcome by taking into account the reversibility of the sulphonation

reaction at low concentrations of sulphuric acid. Anthraquinone (2 g) in the form of a solid cylinder, deuterium oxide (5·4 ml) and deuterium



(82)

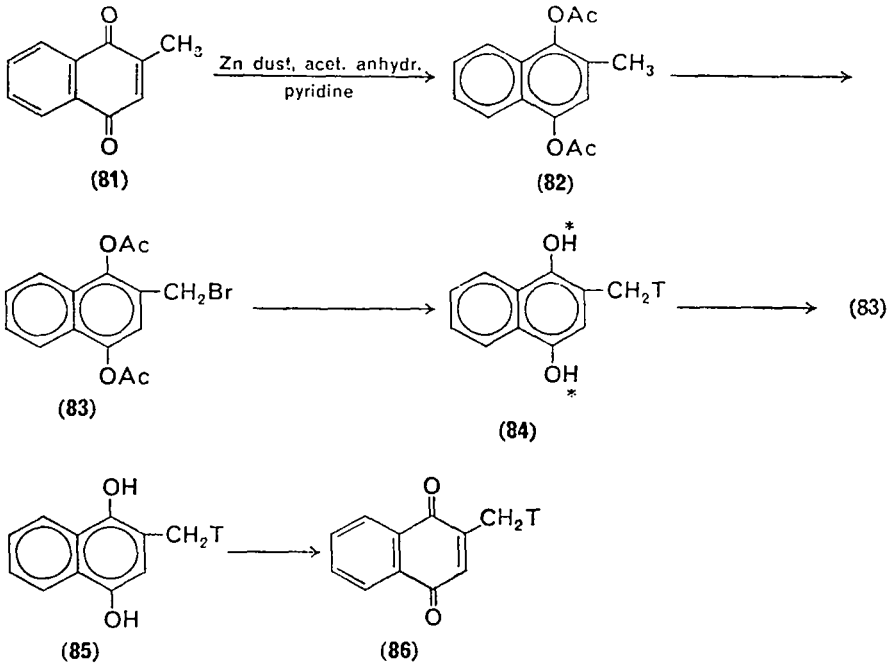
(80)

sulphate (6·6 ml) are placed in a small glass apparatus filled with dry nitrogen in a dry box. The apparatus is then immersed in liquid nitrogen, evacuated, sealed and heated for 2·5 h with a small flame. The water evaporates during heating from the bottom (the reaction bulb) of the apparatus and condenses in a side-arm cooled by flowing water. The condensate flows down to the bottom through a thin tube connecting the side-arm with the reaction volume of the apparatus. In this way, after reaching a steady state, the circulation of the water causes the formation of a concentration gradient of the sulphuric acid as well as a temperature gradient in the reaction mixture moving from the bottom to the surface. Closer to the bottom, where the acid is concentrated, hydrogen exchange and sulphonation occur, while at the top of the reaction volume desulphonation of anthraquinone and exchange between sulphuric acid and water take place. After purification 1·8 g of the labelled product was obtained by Lunelli and Pecile[126]. The procedure was repeated two or more times to attain full deuteration and the final yield was 1·4 g (70%). Mass spectrometric analysis of the product showed 95·4% of anthraquinone-d_8 and 4·6% of anthraquinone-d_7.

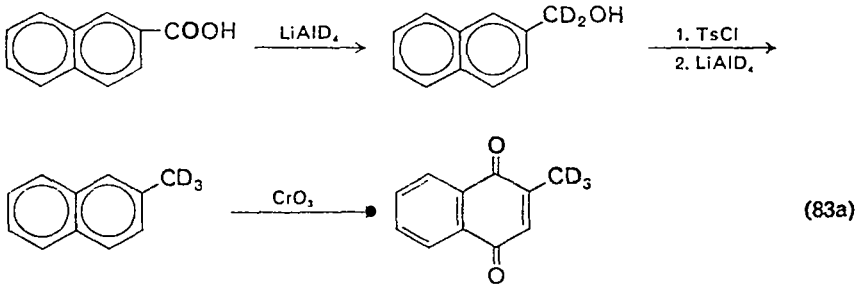
4. Synthesis of 2-methyl-T-1,4-naphthoquinone and 2-methyl-d_3-1,4-naphthoquinone

Synthesis of menadione labelled with tritium presumably in the 2-methyl group (**86**) has been carried out by Billeter and Martius[114]. The diacetate of 2-bromomethyl-1,4-naphthohydroquinone (**83**) was obtained by reduction of menadione **81** to menadiol diacetate **82** followed by side-chain bromination with *N*-bromosuccinimide and dibenzoyl peroxide. **83** was tritiated by a mixture of hydrogen and tritium, using a Pd-black catalyst in dioxan solution in the presence of triethylamine, and subsequently reduced by lithium aluminium hydride to give **85**, which in turn was oxidized with Ag_2O. The labelled product (**86**) was chromatographed, and 19% yield of tritium-labelled menadione was recovered with a specific activity of 46·5 μCi/μmole.

Introduction of deuterium into the 2-methyl group of the menadione[99] was achieved by Di Mari, Supple and Rapoport according to the reaction



scheme (83a). 2-Naphthoic acid was reduced with lithium aluminium deuteride[127]. 2-Naphthylmethanol-α-d_2 was converted to the *p*-toluenesulphonate, and directly reduced with $LiAlD_4$ to 2-methyl-d_3-naphthalene,



(83a)

the oxidation of which with chromic acid yielded 2-methyl-d_3-1,4-naphthoquinone.

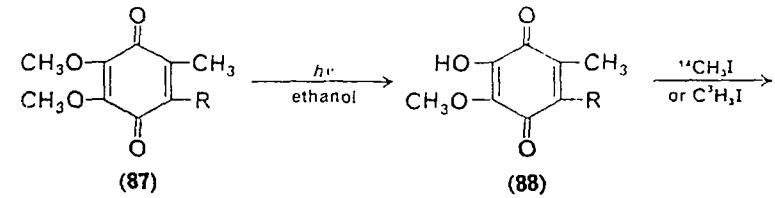
5. Synthesis of tritium-labelled vitamin K_1

Tritium-labelled vitamin K_1 was prepared by condensing tritium-labelled menadione with isophytol according to the method of Isler and Doebel[103]. Tritiated menadione (30 mg) was first hydrogenated over

palladium catalyst in dry dioxan solution and then mixed with 0·01 ml of BF_3-etherate in 0·5 ml of dry dioxan and 100 mg of isophytol in 0·5 ml of dry dioxan. All operations were carried out in an atmosphere of hydrogen. The reaction mixture was kept at 50°C for 10 min. The condensation product, hydroquinone of vitamin K, was oxidized with 100 mg of silver oxide for half an hour. After extraction with heptane, followed by chromatography, 35 mg of labelled phylloquinone were obtained (44% yield).

6. Synthesis of ^{3}H- and ^{14}C-methoxyl-labelled ubiquinone

2-Methoxyl-^{14}C- and 3-methoxyl-^{14}C-mixtures, and 2-methoxyl-^{3}H- and 3-methoxyl-^{3}H-mixtures of labelled ubiquinone (**89a, b**) have been obtained by methylation with labelled methyl iodide or labelled diazomethane[128], the photochemically obtained mixtures of approximately equal amounts of the 2- and 3-hydroxyubiquinone (**88**). Photolysis of ubiquinone **87** in

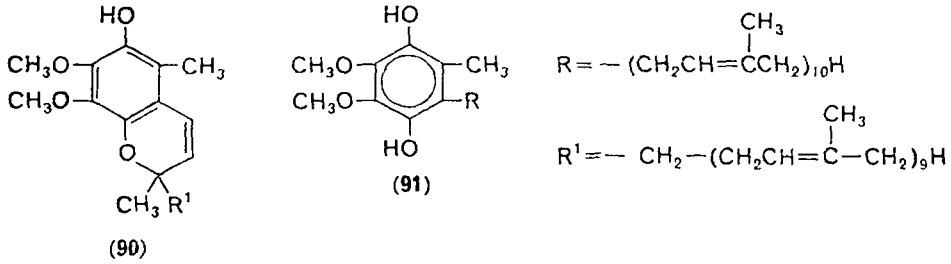


(87) (88) (89a) (89b)

(84)

$$R = (CH_2-CH=C-CH_2)_{10}H \quad (CH_3 \text{ on } C)$$

absolute ethanol yields at least eight products such as ubichromenol **90**, hydroubiquinone **91** and hydroxyubiquinone **88**. Hydroxyubiquinone **88**



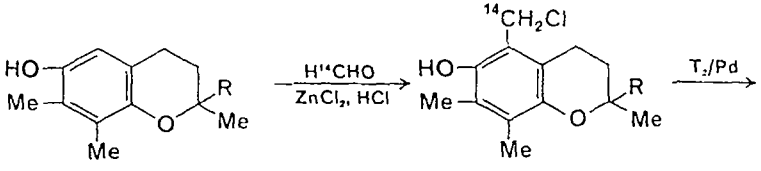
(90) (91)

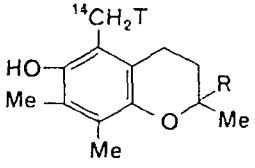
was converted to methoxyl-^{3}H ubiquinone by reaction with methyl-^{3}H-iodide and anhydrous potassium carbonate in dry acetone.

In similar experiments with methyl-^{14}C iodide the ubiquinone-methoxyl-^{14}C was obtained in 55% yield.

7. Synthesis of DL-α-tocopherol labelled with tritium and ^{14}C [129]

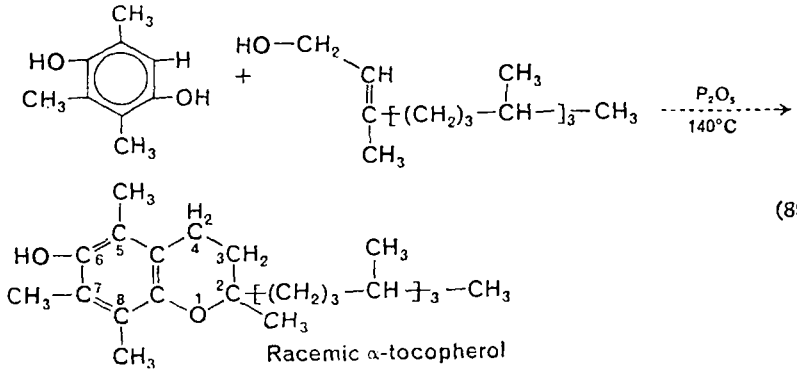
DL-α-Tocopherol-5-methyl-^{14}C was prepared by reduction of 5-chloromethyl-^{14}C-tocopherol, obtained by reacting DL-γ-tocopherol[129a] with ^{14}C-labelled paraformaldehyde and HCl. Tritium-labelled DL-α-tocopherol-5-methyl-T (**94**) of very high specific activity was synthesized using a modification in which the reduction of the unlabelled chloromethyl compound was carried out with tritium gas in dioxan using a mixed catalyst consisting of equal parts of palladium on charcoal and palladium on calcium carbonate.





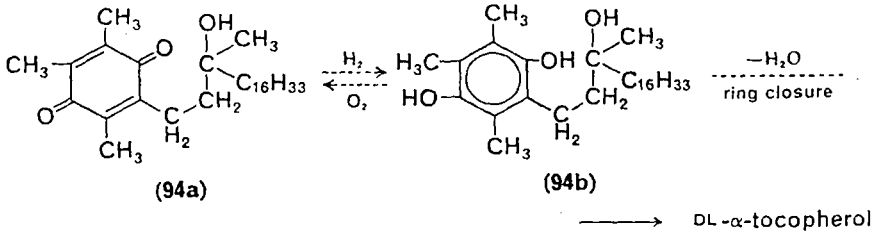
(85)

Doubly labelled tocopherol was prepared by reduction of 5-*chloromethyl*-^{14}C-tocopherol with tritium gas according to scheme (85). Commercial synthetic tocopherols ('antisterility' vitamin E) are obtained by condensation of trimethylhydroquinone with phytol or phytylbromide according to reaction scheme (85a)[129b-g]. Oxidation of thetocopherol with



(85a)

ferric chloride ($FeCl_3$) or silver nitrate ($AgNO_3$) yields tocopherylquinone **94a** which in turn can be reduced to tocopheryl-hydroquinone **94b**[129g] with zinc in glacial acetic acid or palladium in alcohol. The original



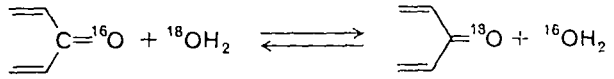
tocopherol can be regenerated by the reduction (and cyclization) of the quinone **94a** with reducing agent in strong acid solution[129g].

Condensation of phytylbromide with trimethylhydroquinone proceeds in benzene solution in the presence of $ZnCl_2$ or HCOOH. Better yields are obtained if monoesters of trimethyl hydroquinone are used for the reaction[129b, c, d].

D. Synthesis of Oxygen-labelled Quinones†

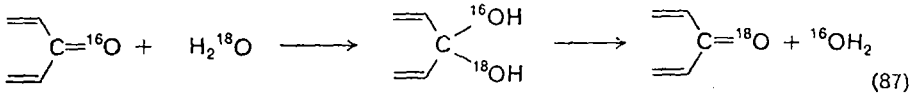
1. ^{18}O exchange in benzoquinones

It has been found that heavy oxygen of water exchanges with light oxygen of *p*-benzoquinone at room temperature[59, 130]:



(86)

The isotope equilibrium was reached after 10 days in neutral medium. (At the same time in acidic medium 70% exchange was found.) The exchange proceeds by addition of a molecule of water to the double bond of the carbonyl group:



(87)

† The reader of this section is referred to references A–H and 1–71 on oxygen isotope methodology, i.r., n.m.r. and e.s.r. spectroscopy, and also on ^{17}O and ^{18}O applications in physical and life sciences, in the catalogue of ^{18}O- and ^{17}O-labelled compounds edited by the Research Products Dept. of Miles Laboratories Inc., Elkhart, Indiana 46514, U.S.A.

I.r. spectra of deuterated and ^{18}O-labelled quinones are reviewed in the book of S. Pinchas and I. Laulicht, *Infrared Spectra of Labelled Compounds*, Academic Press, London and New York, 1971.

The isotope exchange reaction (86) can be used for synthesis of ^{18}O labelled quinones. Becker, Ziffer and Charney[122a] prepared *p*-benzoquinone-$^{18}O_2$ and *p*-benzoquinone-d_4-$^{18}O_2$ by shaking 1·3 ml of a benzene solution containing 100 mg of the quinone with 0·5 g heavy water enriched up to 90% in ^{18}O at room temperature for about 10 days[122a]. The relatively slow ^{18}O isotope exchange in the case of *p*-benzohydroquinone was studied quantitatively at 140–170°C in neutral, acid and basic solutions. In neutral and acid medium the exchange proceeds with an activation energy equal to 18 kcal/mole, while the base-catalysed exchange is stated to proceed with an activation energy of 27 kcal/mole[130].

2. Synthesis of ^{18}O-labelled naphthoquinones

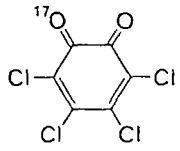
Di Mari, Snyder and Rapoport have established[100,101] that the initial rate of the acid-catalysed ^{18}O exchange between ^{18}O-enriched water and the 1,4-naphthoquinone is 50 times faster at room temperature than the ^{18}O exchange with 2,3-dimethyl-1,4-naphthoquinone. This difference between the unhindered and the hindered carbonyl-^{18}O-exchange was utilized for the synthesis of selectively labelled phylloquinones. *Phylloquinone-4-^{18}O* was prepared by condensing phytol with menadione-4-^{18}O, obtained by the direct exchange of 2-methyl-naphthoquinone with ^{18}O-enriched water in tetrahydrofuran solvent. The condensation reaction was catalysed by boron trifluoride-etherate and proceeded without loss of isotope. Synthesis of *phylloquinone-1-^{18}O* was achieved by preparing uniformly ^{18}O-labelled menadione at the temperature of refluxing tetrahydrofuran, preferential washing out of ^{18}O from the 4-position, and converting the 1-^{18}O-menadione into the corresponding phylloquinone[101]. Synthesis of *phylloquinone-1,4-$^{18}O_2$* was carried out by direct ^{18}O-exchange of the phylloquinone itself with an $H_2{}^{18}O$–dioxan mixture at reflux during 3 h, when phylloquinone enriched up to 7·0% of ^{18}O was obtained.

^{18}O-labelled phylloquinones have been used subsequently by Snyder and Rapoport[101] to test the different mechanisms proposed to explain the role of these quinones in oxidative phosphorylation, to eliminate those mechanisms which involve the intermediacy of quinone methides and to impose additional restrictions on other allowable mechanisms[99–101].

3. Synthesis of ^{17}O-labelled quinones

Broze, Luz and Silver[131,132] prepared ^{17}O-labelled tetrachloro-*o*-benzoquinone (**95**), acenaphthenequinone (**96**), 9,10-phenanthraquinone (**97**), tetrafluoro-*p*-benzoquinone (**98**), tetrabromo-*p*-benzoquinone (**99**) and 2,3-dichloro-1,4-naphthoquinone (**100**) by exchange reactions between the parent quinones and ^{17}O-enriched water with 4–10 at% of

^{17}O. The isotope exchange of ^{17}O was carried out in dioxan–water (20 : 1). The concentration of the carbonyl compound was between 0·2 and 0·4M. Except in the case of compounds **95** and **96** HCl was added to the reaction mixture. The exchange with **95** and **98** was carried out at room temperature for 1 and 2 days respectively. The exchange with compounds **96**, **97**, **99** and **100** was performed at 60°C for 1–4, 3, 7 and 3 days, respectively. The kinetics of the ^{17}O exchange between water and the quinones **95**–**100** has not been studied, nor has the position of the equilibrium attained in the exchange been determined.



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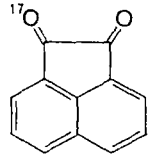

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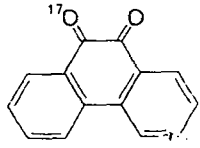

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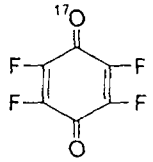

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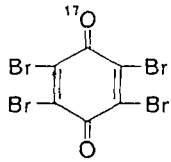

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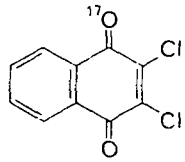
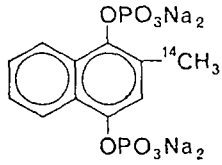


(100)

E. Synthesis of Labelled Drugs[133–158]

Introduction. Laboratory and clinical (metabolic) investigations[133–153] have shown that tetrasodium 2-^{14}C-methyl-1,4-naphthaquinol diphosphate (**101**, menadiol diphosphate), one of the earlier chemical radiosensitizers in the radiotherapeutic treatment of some malignant[134] tumours, enters

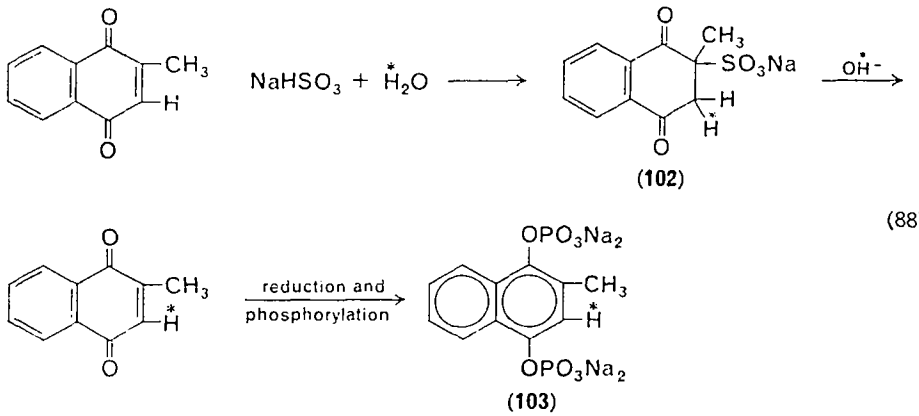


(101)

malignant cells to a much greater extent than normal cells. It localizes mostly along the growing edge of the tumours, and to a lesser extent in muscle and some other organs concerned with detoxification, excretion and vitamin K function. Uptake of the Synka-Vit (a synthetic K vitamin,

commercial name of **101**) by the bone marrow is less than by the tumour, by a factor of 5. This preferential concentration of compound **101** in some tumours and fast-growing tissues gave the idea to several research groups[62,133-152] of further developing radioactive drugs which are already used for the hospital treatment of human malignancies and allied diseases. Tritium was found to be the most promising isotope for cancer internal radiotherapy. It is produced in nuclear reactors in practically 100% pure chemical T_2 form, is relatively cheap and readily available. Its low energy β-emission (maximum energy of the β-particles is $18{\cdot}7 \pm 0{\cdot}1$ keV, their mean energy is $5{\cdot}73 \pm 0{\cdot}003$ keV, the ranges in tissues corresponding to the mean and maximum energies are 1 and 6 μ respectively; the half-life is $12{\cdot}43 \pm 0{\cdot}04$ years) ensures that only the cell in which the labelled molecule was fixed will be affected by the radiation. In the next section some of the methods which have been used to incorporate tritium into the non-labile positions of Synka-Vit are described. Tritium-labelled compounds of specific activities as high as 83 Ci/mM have been synthesized for use in radiochemical therapy.

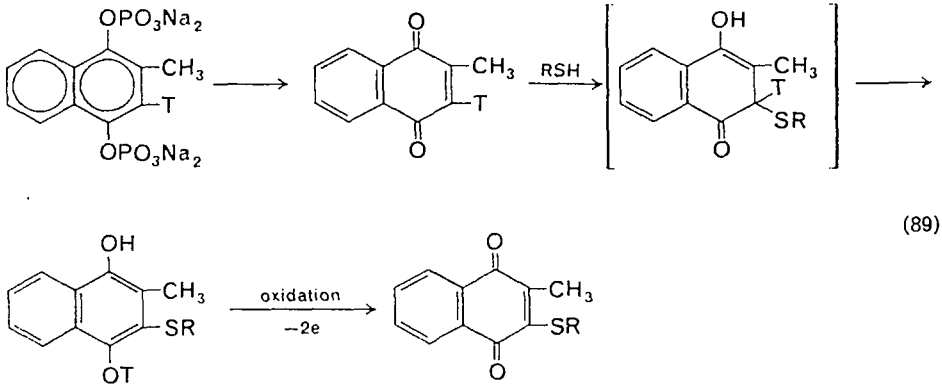
a. Synthesis of tetrasodium 2-methyl-1,4-naphthoquinol-3-T diphosphate[137,140]. Synka-Vit (**103**), labelled with tritium in the 3-position of the hydroquinone system, was obtained by the intermediate formation of the adduct **102** with sodium hydrogen sulphite in the presence of tritiated water according to reaction scheme (88)[137]. Quinone was regenerated by



(88)

tritium-labelled alkali. The specific activity of the drug, **103**, labelled by this method was relatively low due to tritium–hydrogen exchange processes. Higher specific activity has been achieved by reductive dehalogenation of tetrasodium 2-methyl-3-bromo-1,4-naphthaquinol diphosphate in aqueous solution, using tritium gas in the presence of palladium–oxide

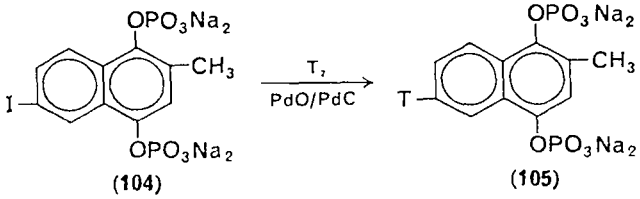
and palladium–charcoal. However, the atom in the 3-position is lost by the quinone during the fixation of the molecule to the cell, as shown in (89).



(89)

b. Synthesis of tritium-labelled Synka-Vit by the Wilzbach method[140,154–156]. Incorporation of tritium into the vitamin K substitute has also been achieved by direct exposure of the dry sodium salt **103** to practically pure tritium gas for a period of 1–3 weeks according to the Wilzbach exchange technique. Subsequent purification procedures showed that much of the original radioactivity of the vitamin K was associated mainly with the water of crystallization, and the tritium activity in non-exchangeable positions was relatively low. Moreover, some highly radioactive by-products associated with the vitamin gave toxic effects, especially damage to the bone marrow. The maximum specific activity obtained after 32 days of irradiation was less than 1 Ci/mM.

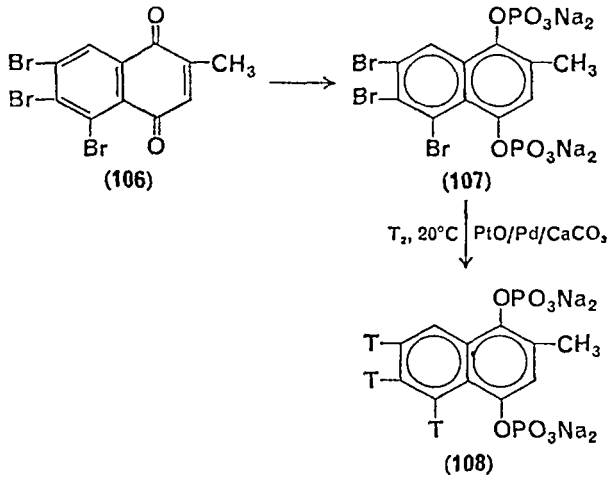
c. Synthesis of 2-methyl-6-tritio-1,4-naphthoquinol bis-disodium phosphate (TRA72)[140,142]. The radioactive drug TRA72 (**105**) was obtained by reductive dehalogenation of tetrasodium 6-iodo-2-methyl-1,4-naphthaquinol diphosphate (**104**). The reduction by tritium gas was rapid and quantitative. Radiochemically pure drug TRA72 of specific activity 28 Ci/mM was obtained. This corresponds to nearly 1 atom of tritium per molecule. Maximum theoretical specific activity for pure TRA72 equals 29·1 Ci/mM.



(104) (105)

(90)

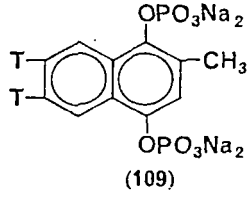
d. Synthesis of 2-methyl-5,6,7-tritrito-1,4-naphthoquinol bis-disodium phosphate. To fulfil the need for a drug with higher specific activity, the synthesis of 2-methyl-5,6,7-tritritio-1,4-naphthoquinol bis-disodium phosphate (**108**) was performed by reductive dehalogenation of the 5,6,7-tribromo-2-methyl-1,4-naphthoquinol bis-disodium phosphate (**107**)[141,142].



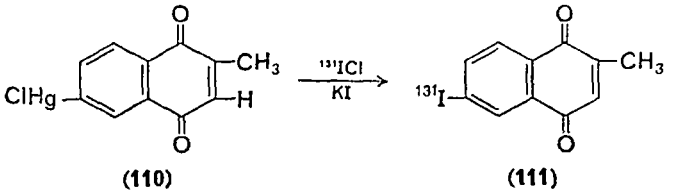
(91)

The specific activity of the drug (**108**, TRA119) was as high as 83 Ci/mM. The radiochemical purity of the product as determined by the dilution method and confirmed by chromatography was 100%[143].

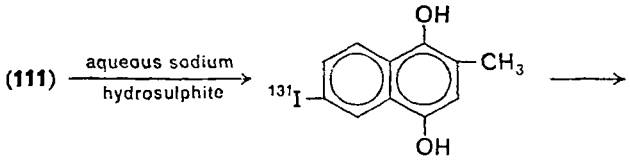
Since 1964 the radioactive drug of specific activity 58·2 Ci/mM, named TRK219, structure **109**[145,146,148,149], has also been produced.

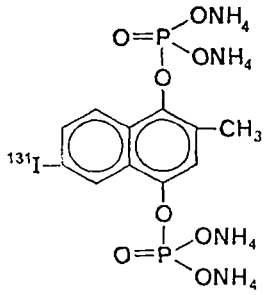


e. Synthesis of 6-^{131}I-iodo-2-methyl-1,4-naphthoquinol bis-diammonium phosphate[149–151]. This has been accomplished by treating 2-methyl-6-chloromercury-1,4-naphthaquinone (0·5 g) with 10 mCi of ^{131}I-iodine monochloride. The labelled product, 6-iodo-2-methyl-1,4-naphthaquinone (**111**) was used after purification for the preparation of the radioactive drug (**112**, 6-^{131}I-iodo MNDP) as shown in reaction (93). The compound **112** was used for the purpose of tumour localization by radioisotope scanning method.



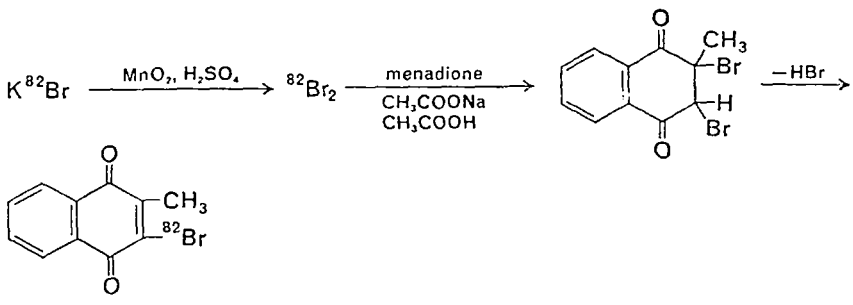
(110) (111) (92)





(112) (93)

f. Synthesis of 2-*methyl*-3-^{82}*Br-bromo*-1,4-*naphthoquinone*[135,136]. This has been carried out according to scheme (94). Radioactive bromine was added to menadione in the presence of sodium acetate and acetic acid at liquid air temperature. The contents were warmed to 50°C in a water bath and further acetic acid was added. After 3 h water was added to precipitate the labelled quinone **113**.

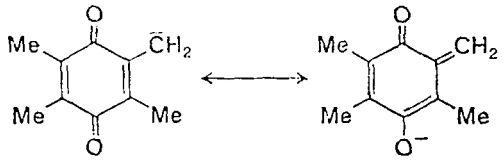


(113) (94)

III. TRACER APPLICATIONS OF LABELLED QUINONES

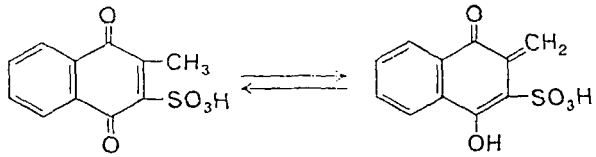
A. Hydrogen-Isotope Exchange in Methylquinones

Discussing the problems of reactivity of quinones and their derivatives[59,159–162], various authors included in the reaction schemes intermediate anions of the quinone methide type **114** as the transient species, or postulated the existence of the tautomeric forms such as **117**.



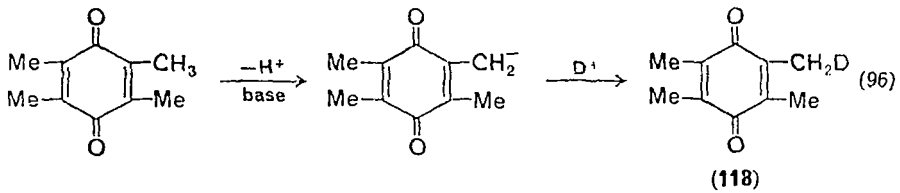
(114) (115)

(95)



(116) (117)

Formation of the intermediates **114** and **117** requires removal of a proton from the methyl group of the corresponding methyl quinones. Addition of deuterium to the methylene group of one of these intermediates should lead to the formation of methyl-labelled quinones. Experimental



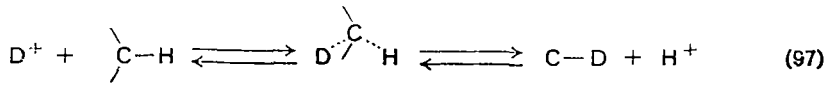
(118)

(96)

evidence[123] for such reaction schemes has been obtained in the case of duroquinone **118**, 2,3-dimethylnaphthoquinone and perhydrovitamin K, which were found to incorporate deuterium into C—H bonds when heated under reflux for several hours in dioxan–D_2O solutions with triethylamine or potassium carbonate as catalysts. Similar exchange reactions have been used for synthesis of tritium-labelled methyl quinones.

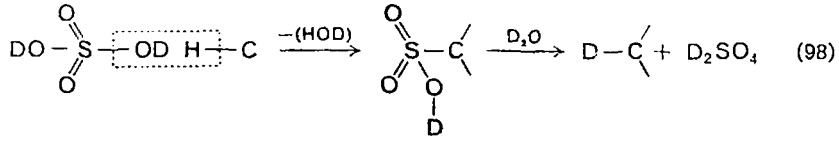
The multistep high-temperature exchange between concentrated deuterosulphuric acid, D_2SO_4, and 9,10-anthraquinone has been utilized for synthetic purposes; however, its kinetics and mechanism have not been studied in detail[126].

Exchange of ring hydrogens proceeds probably either through a bimolecular replacement mechanism (97):



(97)

or through sulphonation followed by desulphonation (98):

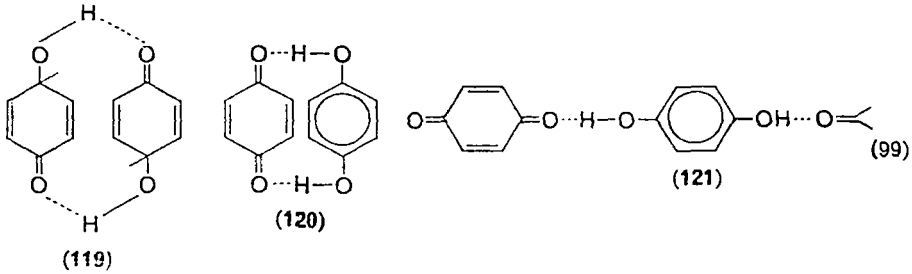


(98)

B. Quinone–Hydroquinone Exchange Reactions

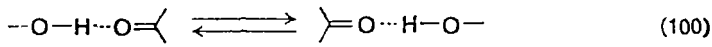
1. Hydrogen bonding in benzoquinhydrone[163, 164]

It was thought for some time that in the benzoquinhydrone complex the hydrogen bond binding the complex is symmetrical and that the two constituent molecules lose their identity through the formation of the symmetrical resonance hybrid **119**[90, 163]. Later it was found that in 'dimeric' structures such as **120**, or in long chains of the type **121**, the hydrogen is located closer to one of the oxygen atoms, but the potential energy curve may have two minima and hydrogen can jump from one



(119) (120) (121) (99)

minimum into another. In the latter case the transition (100) should be possible, and quinone nuclei are transformed into hydroquinone or *vice*



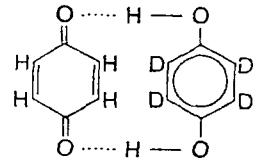
(100)

versa with a rate dependent on the potential barrier between the two minima. The final mixture should contain equal quantities of both indistinguishable forms. Gragerov and Miklukhin[119, 120] approached the problem of the hydrogen bond in the quinhydrone complex by studying the exchange between benzoquinone and hydroquinone-2,3,5,6-d_4 in the

labelled quinhydrone **122**. The authors found that there is no exchange between benzoquinone and the hydroquinone-2,3,5,6-d_4 nucleus in the

$C_6H_4O_2 \cdots C_6D_4(OH)_2$

(122)



(123)

solid quinhydrone complex kept at room temperature for 24 h or for 6 h at 70°C. Similarly, labelled quinhydrones **123** or quinhydrones with deuterium-labelled benzoquinone **124** when kept at 100°C for 3 h showed,

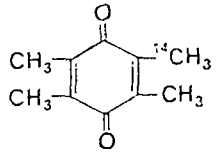
$C_6D_4O_2 \cdots C_6H_4(OH)_2$

(124)

after subsequent thermal decomposition *in vacuo* and separation by sublimation at 10^{-4} mm Hg into the two components, the retention of heavy hydrogen in the original positions. According to the authors, this shows that hydrogen is located in the quinhydrone complex near the oxygen of the hydroquinone moiety and that hence there is no nuclear deuterium exchange after the complex has been formed.

2. Exchange in duroquinhydrone

Bothner-By[90] investigated the problem of exchange in duroquinhydrone using tetramethyl-$^{14}C_1$-*p*-benzoquinone (**125**) or durohydroquinone-α-^{14}C as labelled molecules. The separation of the duroquinhydrone into its components after the exchange process has been completed was effected by thermal decomposition of the quinhydrone samples *in vacuo* and sublimation of the more volatile quinone at 90°C.



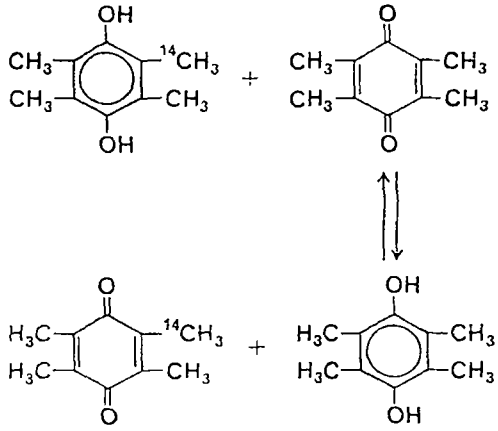
(125)

This author found that there is no detectable exchange of the total duroquinone moiety between duroquinone and durohydroquinone in the *solid* duroquinhydrone complex at 25°C during 24 hours but there is a rapid exchange between the quinone and the hydroquinone in *solution* prior to precipitation of the complex. The formulation of quinhydrones as

symmetrical resonance hybrids is incompatible with these experimental results and the earlier observations reported by Gragerov and Miklukhin are confirmed.

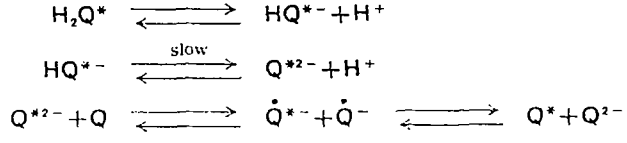
3. Duroquinone and durohydroquinone exchange in buffered methanol solution

A rapid electron and labile hydogen exchange reaction between duroquinone and durohydroquinone observed previously in the process of preparation of the quinhydrone complex has been studied quantitatively by Bothner-By at 25°C in methanol solution saturated with potassium biphthalate[91].



(101)

The exchange reaction (101) proceeds in methanol solution at a measurable rate with a half-life of the order of minutes. This solvent has been chosen because duroquinone can be partially extracted from it by means of pentane (after the addition of a few drops of water to cause immiscibility). The rate of the exchange reaction was found to be nearly independent of the quinone concentration and first-order with respect to the hydroquinone. The author has suggested that the exchange proceeds through the intermediate oxidation state, which is a 'semiquinone free radical' formed rapidly from duroquinone and doubly charged durohydroquinone anions. The proposed path of the exchange is represented in scheme (102), where H_2Q^* represents the radioactive durohydroquinone. Q represents inactive duroquinone, $^{\bullet}Q^-$ represents a semiquinone radical, etc. In the relatively acid solution the concentration of the doubly charged

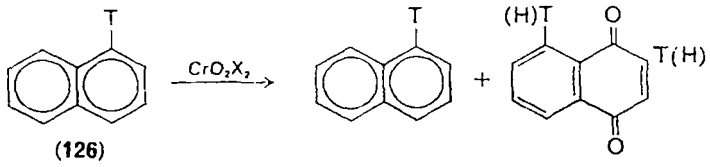


(102)

anion would be extremely low, and its rate of formation may be assumed to be rate-controlling. Low initial concentrations of singly charged hydroquinone anions in the solution and the low second ionization constant for hydroquinones suppress the rate of the exchange reaction observed.

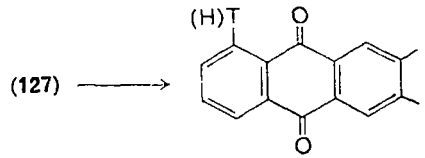
C. *Tritium Shift in the Oxidation of Naphthalene to 1,4-Napthoquinone with Chromyl Reagents*[165, 166]

Sharpless and Flood showed in a recent preliminary report[165] that the quinone **127**, obtained in the course of the partial oxidation of 1-^{3}H,1-^{14}C naphthalene (**126**) with chromyl acetate or chromyl chloride in CCl_4, contains tritium in the 2-position:



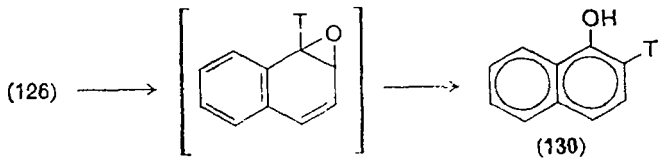
(126) (127) (103)

The location of the tritium has been determined by Diels–Alder reaction of the quinone **127** with 2,3-dimethylbutadiene, followed by air oxidation (reaction 104), when the hydrogen atoms bound to the 2- and 3-carbons of **127** are removed. The ratio of the total tritium radioactivity to the



(128) (104)

total ^{14}C radioactivity, ^{3}H/^{14}C, in the compound **128** was found to be 26–31% less than in the quinone **127**. In the absence of a tritium shift the ^{3}H/^{14}C ratio should be nearly the same in both **127** and **128** compounds. The authors have suggested that the migration of tritium proceeds through the intermediate of the epoxide type **129** without participation of a



(129) (130) (105)

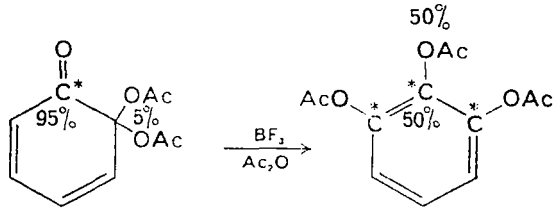
protonic exchange mechanism. They have found also that in the partial oxidative destruction of the naphthaquinone **127** by chromyl acetate (in CCl_4) the $^3H/^{14}C$ ratio in the unreacted quinone which was recovered decreased slightly (from 0·70 to 0·67).

D. ^{18}O Studies of the Oxidative Fission of Hydroquinone Ethers with Argentic Oxide

Silver(II) oxide (AgO) oxidizes selectively dimethyl ethers of naphtho- and benzohydroquinones in acidic media. *p*-Quinones are formed at room temperature in high yield. The reactions are accomplished most efficiently in dilute acidified aqueous dioxan solution[167]. When 2,3-dimethyl-1,4-dimethoxynaphthalene was oxidized with AgO in the presence of $H_2{}^{18}O$ and H_3PO_4, the product, 2,3-dimethyl-1,4-naphthoquinone, was found to be enriched with ^{18}O[167]. Carbon monoxide, obtained by the pyrolysis of the labelled naphthoquinone at 600°C, was only slightly less enriched with ^{18}O (1·65%) than the initial acidic water milieu which contained 1·70% of ^{18}O. A control experiment carried out with 2,3-dimethyl-1,4-naphthoquinone for 5 min in the same reaction conditions, including silver oxide, showed after isolation an unchanged content of ^{18}O (0·28%), close to the natural abundance[167,168]. Therefore it was assumed that the oxidative demethylation of hydroquinone ethers by AgO proceeds through *aryl–oxygen bond fission.*

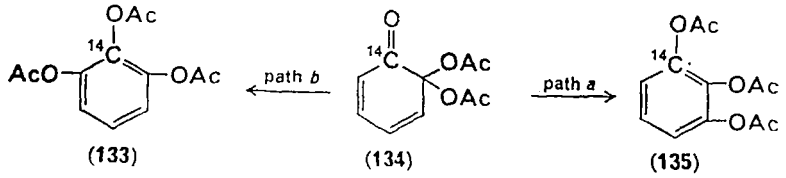
E. The Diketone–Phenol Rearrangement

The 2,2-diacetate of *o*-benzoquinone **131** undergoes in the presence of, for example, BF_3 in ether or in acetic acid anhydride the diketone–phenol rearrangement[117,169,170]. Localization of the ^{14}C activity in the resulting pyrogallol triacetate (**132**) revealed[117] that the C-1 and C-3 atoms together contain 50% of the labelled carbon while the remaining 50% of the activity was found at the C-2 carbon atom:



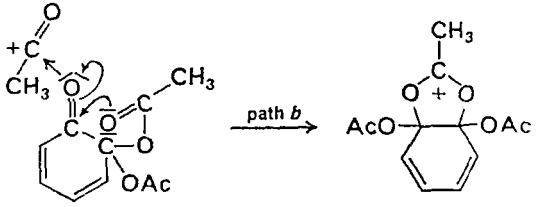
(131) (132) (106)

Thus, in the presence of BF_3 the rearrangement proceeds in two directions:



(133) (134) (135) (107)

It is suggested[117,170] that the rearrangement is initiated by attack by arc acetylium cation $CH_2\overset{+}{C}O$ on the carbonyl oxygen and formation of positive charges at the ring carbons. In the next step, intramolecular migration of the acetyl group takes place through the formation of an 'acetate bridge'. Accepting the possibility of the formation of an intermediate acetoxonium-ion (**137**) it follows that the acetoxy group can migrate in both directions with equal probability[117].



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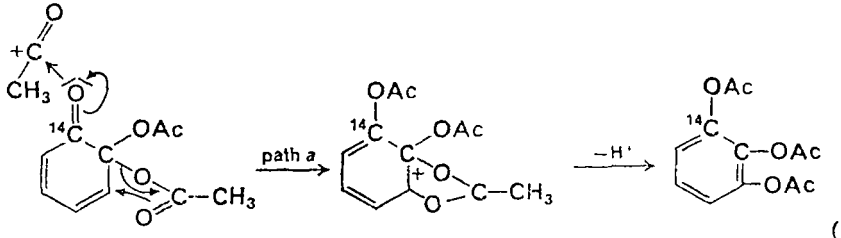
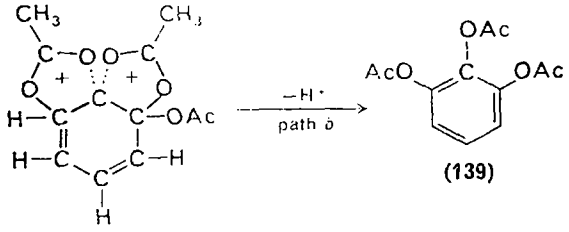


(109)

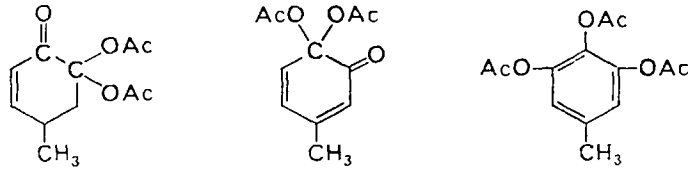
One can visualize also a reaction scheme in which attack by the $CH_3\overset{+}{C}O$ cation on the carbonyl oxygen leads to the transient species **138**, which then transforms into isotopic isomer **139** upon proton abstraction. Aromatization ends the migration process similarly as in the case of path *a*[117].

When $Ac_2{}^{18}O$ was used to convert 4-methyl-*o*-benzoquinone diacetate (**140**) and 5-methyl-*o*-benzoquinone diacetate (**141**) into 5-methylpyrogallol (**142**) in both cases one-third of the ^{18}O enrichment was found in the central hydroxyl group and two-thirds in the two peripheral hydroxyl groups[171]. In view of the absence of kinetic and tracer studies



(138) (139) (110)

concerning the inter- and intra-molecular acetoxy exchange in the reacting mixture and the preliminary state of the research itself[170,171], the interpretation of this distribution of the label in the pyrogallol triacetate obtained should be postponed.



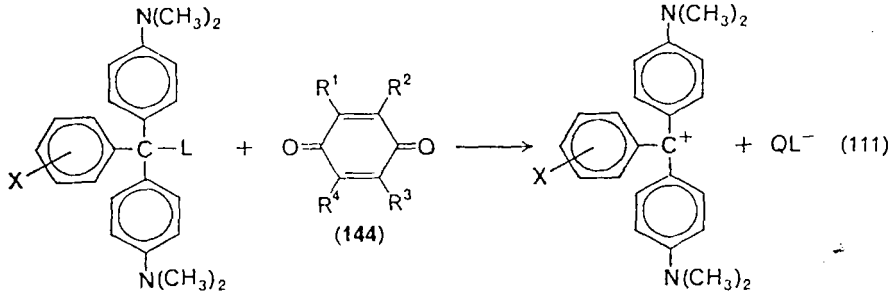
(140) (141) (142)

IV. ISOTOPE EFFECT STUDIES WITH QUINONES

So far isotope effect studies with quinones have been directed mainly towards the elucidation of the structure of the transition states of hydrogen transfer processes. The possibilities of the method are, however, much broader. For instance, ^{13}C-isotope effect studies of the mechanism of the catalytic reduction of quinones by carbon monoxide are currently being investigated by Russian groups[172–176]. Many other as yet untouched problems could be investigated using isotopic techniques. The results presented in this section are very promising and indicate that in spite of experimental difficulties the fundamental problems of quantum mechanics concerning the motion of hydrogen in the course of chemical changes can be treated by studying deuterium and tritium isotope effects.

A. Isotope Effects in the Quinone Oxidation of Leuco-Triphenylmethane Dyes

Lewis and his students[177–180] studied the oxidation of substituted leuco-malachite greens **143** by chloranil and other quinones **144**.



(143) (144) (145) (111)

The following substituents, both in **143** and **144**, have been investigated:

(1a) X = *p*-$N(CH_3)_2$, L = H or D
(1b) X = *o*-(OCH_3), L = H or D
(1c) X = *m*-Cl, L = H or D
(1d) X = H, L = H or D
(1e) X = *p*-NO_2, L = H

(2a) $R^1 = R^2 = R^3 = R^4 = Cl$
(2b) $R^1 = R^2 = R^3 = R^4 = Br$
(2c) $R^1 = R^2 = R^3 = R^4 = I$
(2d) $R^1 = R^2 = Br$, $R^3 = R^4 = Cl$
(2e) $R^1 = R^4 = Br$, $R^2 = R^3 = Cl$
(2f) $R^1 = R^3 = Br$, $R^2 = R^4 = Cl$
(2g) $R^1 = R^4 = Cl$, $R^3 = R^2 = F$
(2h) $R^1 = R^2 = Cl$, $R^3 = R^4 = CN$

The reaction was found to be first-order in each of the reagents[177], independent of acid concentration and, in the case of acetonitrile solvent, also independent of water or oxygen content. The authors have concluded that the oxidation by quinones takes place by a one-step hydride-transfer mechanism ('although the argument lacks rigour'). Only in the case of methanol solvent was the oxidation process complicated by the solvolysis of tetrachloro-*p*-benzoquinone.

Chloranil is quite stable in acetonitrile and the overall oxdiation rate follows second-order kinetics almost up to completion. When excess of chloranil was used the reaction was first-order. Some of the data characterizing the temperature-dependence of the deuterium isotope effect observed in the oxidation of the leuco-crystal violet (1a) by chloranil (2a) in methanol solvent are given in Table 1. The data obtained fit quite precisely the Arrhenius equation (112), but side-reactions introduced into the experiment result in a substituent-, isotope- and temperature-dependent error, so that the authors could draw no conclusions concerning the structure of the transition complex.

$$k_H/k_D = 0{\cdot}345\,[\exp(1933/RT)] \qquad (112)$$

The oxidation reaction was also investigated in acetonitrile, which is a better solvent than methanol (regarding both solubility and stability) of

TABLE 1. Deuterium isotope effects in the oxidation of 4,4′,4″-tris(dimethylamino)triphenylmethane (1a) by tetrachloro-*p*-benzoquinone (2a) in methanol

T (°C)	$k_H \times 10^2$ ($M^{-1} s^{-1}$)	k_H/k_D
2·7	9·68	11·3
14·7	19·8	9·9
29·9	43·2	8·2
44·7	89·5	7·1

all reagents and products. The effect of substituents on the rate constants in the oxidation of leuco-triphenylmethane dyes with chloranil (2a) and bromanil (2b) is shown in Table 2. Rate constants and deuterium isotope

TABLE 2. Rate of oxidation of substituted leuco-malachite greens by chloranil and bromanil in acetonitrile, at 25°C

X in compound **143**	Oxidant	k_H ($M^{-1} s^{-1}$)	k_H/k_D
H	Chloranil	$2·05 \times 10^{-2}$	11·4
H	Bromanil	$1·26 \times 10^{-2}$	—
o-OCH_3	Chloranil	$1·81 \times 10^{-2}$	11·9
o-OCH_3	Bromanil	$1·40 \times 10^{-2}$	12·7
m-Cl	Chloranil	$1·06 \times 10^{-2}$	11·8
p-$(CH_3)_2N$	Chloranil	$1·27 \times 10^{-1}$	11·4
p-$(CH_3)_2N$	Bromanil	$8·14 \times 10^{-2}$	13·4

effects in the oxidation of leuco-crystal violet (1a) with different substituted quinones at 25°C in acetonitrile are shown in Table 3. The first five reactions listed in Table 3 give experimentally satisfactory kinetic results while the other entries are less reliable because of side-reactions, too fast kinetics or other experimental difficulties. The value 6·96 obtained for the deuterium isotope effect in the oxidation of the leuco-dye with 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (2h) was determined by two different methods which gave nearly coincident data. Partial oxidation (up to 68·2%) of a mixture of deuterated and undeuterated leuco-crystal violet with quinone and analysis of the residual leuco-dye for protium content by the kinetic method (using oxidation with excess of chloranil) resulted in the value $k_H/k_D = 6·99 \pm 0·07$. It should be noted that the competitive method should give good results even with fast reactions because both

deuterated and undeuterated compounds are reacting in exactly the same experimental conditions. The deuterium isotope effect in the same reaction was determined also by the chemical competitive method (see section

TABLE 3. Rates of oxidation of leuco-crystal violet (1a) with substituted quinones in acetonitrile, at 25°C

Substituted *p*-benzo and other quinones	k_H ($M^{-1}s^{-1}$)	k_H/k_D
Tetrachloro (2a)	$1{\cdot}27 \times 10^{-1}$	11·4
Tetrabromo (2b)	$8{\cdot}14 \times 10^{-2}$	13·4
2,3-Dibromo-5,6-dichloro (2d)	$9{\cdot}29 \times 10^{-2}$	11·8
2,5-Dibromo-3,6-dichloro (2f)	$8{\cdot}07 \times 10^{-2}$	11·8
2,6-Dibromo-3,5-dichloro (2e)	$8{\cdot}46 \times 10^{-2}$	12·0
2,5-Dichloro	1×10^{-2}	—
2,5-Dichloro-3,6-difluoro (2g)	$2{\cdot}1 \times 10^{-2}$	13·2 ± 2·5
Tetrachloro-*o*-benzoquinone	3·21	3·1
2,3-Dichloro-5,6-dicyano (2h)	10^5	6·96
$OCl_2H_2C_6—C_6H_2Cl_2O$ [181-2]	$7{\cdot}5 \times 10^{-1}$	9·8
$OBr_2H_2C_6—C_6H_2Br_2O$ [181-2]	3·23	12·9
Tetraiodo (2c)	$4{\cdot}4 \times 10^{-2}$	11·6

I.B.1). In the particular case under consideration, the comparison of the relative rates of the oxidation of two leuco-dyes, leuco-crystal violet (1a, L = H) and leuco-4″-nitro malachite green (1e, L = H), on the one hand, and the deuterated analogue (1a, L = D) and the nitro compound (1e, L = H), on the other, yielded a value of k_H/k_D equal to 6·96, in agreement with the first set of experiments. The relative rates of reaction have been determined by a spectrophotometric method not requiring the direct analysis of the isotopic composition of the material used.

The data shown in Table 4 illustrate the temperature dependence of the separate constants as well as the temperature dependence of the

TABLE 4. Temperature dependence of the rate constant and of the deuterium isotope effect in the oxidation of leuco-crystal violet with chloranil

T (°C)	$k_H \times 10^2$ ($M^{-1}s^{-1}$)	$k_D \times 10^2$ ($M^{-1}s^{-1}$)	k_H/k_D
9·96	5·23 ± 0·22	0·380 ± 0·004	13·7
14·88	7·45 ± 0·02	0·515 ± 0·007	14·7
19·83	9·96 ± 0·37	0·738 ± 0·012	13·1
24·91	12·7 ± 0·4	1·08 ± 0·05	11·8
29·84	15·4 ± 0·3	1·40 ± 0·01	11·01
35·44	19·4 ± 0·7	1·96 ± 0·006	9·9

deuterium isotope effect in the oxidation of leuco-crystal violet (1a) by tetrachloroquinone in acetonitrile.

The results obtained in methanol solution presented in Table 1 show that the observed isotope effect is large, strongly temperature-dependent and indicates the existence of large tunnelling in the process studied. The quantitative interpretation of the data was not undertaken by the authors because of the relatively large spread of the experimental data, the temperature dependence of which was approximated by the linear relationship:

$$\log(k_H/k_D) = -0{\cdot}4622 + 0{\cdot}4226(10^3/T) \tag{113}$$

The data listed in Table 2 indicate that the solvent does not introduce drastic effects. The temperature dependence of the experimental rate constants of the oxidations of leuco-crystal violet in methanol and acetonitrile solvents are expressed correspondingly by the Arrhenius equations (114):

$$\left.\begin{aligned} k_H^{MeOH} &= 1{\cdot}8 \times 10^6 \exp(-9180/RT) \\ k_D^{MeOH} &= 5{\cdot}0 \times 10^6 \exp(-11080/RT) \\ k_H^{MeCN} &= 1{\cdot}2 \times 10^5 \exp(-8130/RT) \\ k_D^{MeCN} &= 2{\cdot}92 \times 10^6 \exp(-11520/RT) \end{aligned}\right\} \tag{114}$$

The temperature dependence of the observed deuterium isotope effect obeys (with the exception of the value at the lowest temperature) the Arrhenius equation (115) and suggests even larger tunnelling than in the

$$k_H/k_D = 0{\cdot}041\,[\exp(3390/RT)] \tag{115}$$

case of the oxidation carried out in methanol solution. The pre-exponential factor, $A_H/A_D = 0{\cdot}041$, is estimated with an experimental error of about 40%. Thus it has been demonstrated that experimental data in acetonitrile deviate strongly from the 'classically' allowed temperature dependence of the primary deuterium isotope effect (116) where $A_H/A_D \geqslant 0{\cdot}5$.

$$\log(k_H/k_D) = \log(0{\cdot}5) + \frac{1904}{2{\cdot}303}\Big/RT \tag{116}$$

The estimated low value of the pre-exponential factor, $A_H/A_D = 0{\cdot}0415$, is as small as in the fluoride-catalysed bromination of 2-carbethoxycyclopentanone[183]. The value $\log_{10} A_D^*/A_H^* = 1{\cdot}38 \pm 0{\cdot}07$, obtained by Bell and coworkers[183], corresponds to the ratio $A_H/A_D = 0{\cdot}0417$.

The existence of tunnelling in the chloranil oxidation of leuco-crystal violet was also documented[41] by Lewis and coworkers by determining the

tritium isotope effect in the oxidation of the tritium compound (1a; L = T) at 35·5°C and comparing the obtained value with the deuterium isotope effect at the same temperature. The tritium isotope effect, $(k_{\mathrm{H}}/k_{\mathrm{T}})$, equals 20·4 ± 1·3; the deuterium isotope effect, $(k_{\mathrm{H}}/k_{\mathrm{D}})$, equals 9·90 at this temperature. Equation (117), correlating the tritium and deuterium isotope effects, thus gives the value $r = 1{\cdot}31$, which deviates from the value $r_{\mathrm{s}} = 1{\cdot}442$ in the direction expected for tunnelling. However, it is

$$(k_{\mathrm{H}}/k_{\mathrm{T}}) = (k_{\mathrm{H}}/k_{\mathrm{D}})^{r} \tag{117}$$

frequently stated that the tunnel effect can be extensive without much deviation from the Swain equation (28). Lewis and coworkers[184] deduced from the rate and isotope effect data obtained in the studies of the oxidation of the leuco-triphenylmethane dyes the imaginary frequency $\nu_{i\mathrm{H}}^{\neq} = 1080$–$1150\ \mathrm{cm}^{-1}$ which corresponds to a correction of about 3 in the deuterium isotope effect. The authors assumed in the course of their calculations that $\nu_{i\mathrm{H}}^{\neq} = (2)^{\frac{1}{2}} \cdot \nu_{i\mathrm{D}}^{\neq}$. The ratio $(Q_{\mathrm{H}}/Q_{\mathrm{D}})$ calculated with Wigner's approximate first quantum correction (118) amounts at 0°C to

$$Q_{\mathrm{H}}/Q_{\mathrm{D}} \approx 1 + \tfrac{1}{24} h^2 \Delta(\nu^2)/(kT)^2 \tag{118}$$

the value $Q_{\mathrm{H}}/Q_{\mathrm{D}} = 1{\cdot}679$ if the frequency $\omega_{\mathrm{H}} = 1080\ \mathrm{cm}^{-1}$ is used. If this frequency, describing the potential energy barrier, is also used for the calculation of the shape of the one-dimensional truncated parabola with a height corresponding to $E = 8{\cdot}150$ kcal/mole then the formula (119), relating the imaginary frequency $\omega_i^{\neq}$ with the parameters of the inverted

$$\omega_{i\mathrm{t}} = (E_0^{\frac{1}{2}})/\pi a (2m)^{\frac{1}{2}} c \tag{119}$$

parabola, gives the width $2a = 0{\cdot}8087 \times 10^{-8}$ cm. The reaction barrier in the leuco-dye oxidation is therefore narrower than the barrier in the proton transfer reactions. This is so because in hydride transfer reactions the electron-deficient atom can approach the transferable hydrogen without electron repulsion (characteristic of nucleophilic substitution)[179].

The data presented in Table 3 show the relative insensitivity of the isotope effect to substitution in the leuco-dye, in agreement with the experimental and theoretical rules suggested by Swain[185] for hydride transfer reactions. Lewis noted nevertheless[184] a slight increase of the isotope effect on replacing the hydrogen in the *o*-position by an *o*-methoxy group and replacing the chloranil by bromanil, thus revealing a small steric influence on the deuterium isotope effect. The data presented in Table 3 indicate that the more powerful oxidizing agents react more rapidly and the results show smaller deuterium isotope effects. This is clearly seen in the case of oxidation with dichlorodicyanoquinone, for which the ratio $k_{\mathrm{H}}/k_{\mathrm{D}} = 6{\cdot}96$ was found. Faster rates of oxidation and

smaller deuterium isotope effects are caused by markedly reduced activation energies in the oxidation process. According to equation (21) of section I.A.2 the tunnel correction Q diminishes with reduction of the reaction potential barrier E_0.

Conclusions. The experimental deuterium and tritium isotope effects presented in this section show that the carbon–hydrogen bond is broken in the rate-determining step of the oxidation of triarylmethanes by quinones. The observed large isotope effects are consistent with the nearly symmetrical transition state in which the hydrogen is transferred about half the distance to the product[180] (although an alternative suggestion was presented by Lewis[179]). Faster oxidation reactions are accompanied by slightly smaller isotope effects. This can be explained in terms of increasing reagent-like character of the transition state resulting in a lower activation energy and, consequently, in smaller kinetic isotope effects.

The unusual behaviour of the low-temperature Arrhenius plot of the experimental deuterium isotope effects leading to differences in the activation energy of 3·35 kcal/mole and a very low ratio of the pre-exponential factor (0·041) can hardly be accounted for in terms of the usual absolute rate theory. The large value, 10–13, of the deuterium isotope effect and the unusually large differences in the activation energy would require one to consider all three frequencies in the initial state and their complete loss in the transition state of the oxidation reaction. But this extreme assumption about the change in bonding on passing from reactants to the transition state cannot explain the very low ratio of the Arrhenius pre-exponential factor $(A_H/A_D) = 0{\cdot}041$. Therefore it is necessary to reject the 'classical transition state' explanation and admit the existence of the large quantum-mechanical tunnelling in the oxidation of triarylmethanes. Assuming that the potential barrier separating substrates and products of the reaction has the form of a truncated two-dimensional parabola and using Bell's method one finds from the amount of tunnelling the barrier dimensions given by Perry[180] (Table 5).

TABLE 5. Barrier dimensions in the oxidation of leuco-crystal violet by chloranil

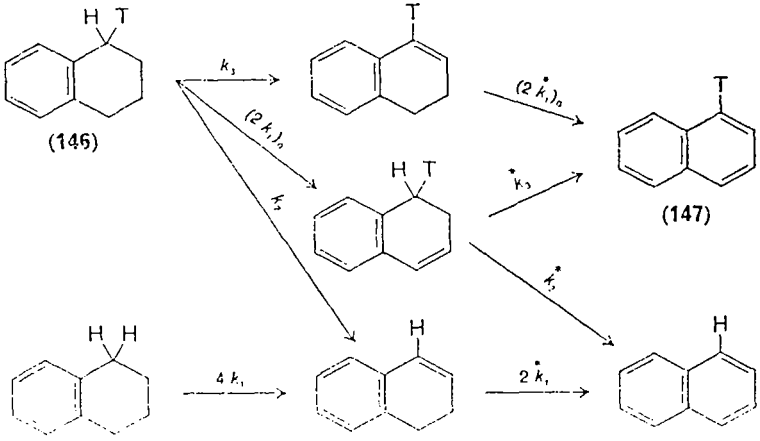
E_H (kcal/mole)	E_D (kcal/mole)	a (Å)	E_H^*/E_H	E_D^*/E_H
12·21	12·45	0·485	0·72	0·95

E_H^* and E_D^* are the observed Arrhenius (experimental) activation energies; E_H and E_D are the classical true potential barrier heights for hydrogen and deuterium.

Other observations, such as, for example, the tendency towards increasing the deuterium isotope effect with decrease in the rate constant, are also consistent with the presence of a large amount of tunnelling in the quinone oxidation reactions studied.

B. *Tritium Isotope Effects in the Oxidation of 1,2,3,4-Tetrahydro-1-^{3}H Naphthalene to 1-^{3}H Naphthalene by 2,3-Dichloro-5,6-Dicyano-Quinone (DDQ)*

Fast kinetics caused some difficulties in determination of the parameters characterizing the hydrogen isotope effects of deuterium and tritium in the course of the oxidation of the triphenylmethane dyes (reaction 111) with 2,3-dichloro-5,6-dicyanoquinone (2 h). An attempt was made recently[186] to determine the hydrogen isotope effect in the oxidation of tritium-labelled tetralin (1,2,3,4-tetrahydro-1-^{3}H-naphthalene, (**146**) and of 6-^{3}H-tetralin with DDQ at reflux temperature of the benzene solvent. The authors did not notice any measurable tritium isotope effect in the quinone oxidation of 6-^{3}H-tetralin to 2-^{3}H-naphthalene. Measuring tritium enrichment of the recovered starting tetralin in the course of its conversion to naphthalene, it has been found that the unlabelled tetralin molecules react 1·42–1·66 times faster than tetralin molecules labelled with tritium in the 1-position. The authors also found that 1,2-dihydro naphthalene with natural isotopic composition oxidizes with DDQ to naphthalene in refluxing benzene medium $2{\cdot}44 \pm 0{\cdot}11$ times faster than the 1,2-dihydro-1-^{3}H-naphthalene. It is suggested that the oxidation of tetralin to naphthalene proceeds according to the approximate reaction scheme (120) which takes into account the hydrogens in the 1- and 4-positions of the tetralin molecule. Besides the reactions presented in scheme (120) some side-processes also probably occur, since the authors did not

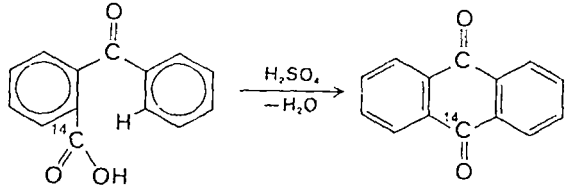


(120)

obtain the material balance in their experiments and total recovery was only about 80%. The lack of quantitative yields and the analytical difficulties introduce large uncertainties in the determination of the degree of conversion of the labelled tetralin into the intermediate dihydronaphthalene and into the final product, naphthalene. Moreover, the separation method used might itself also change the isotopic composition of labelled chemicals. The quantitative interpretation of the experimental results presented by the authors is therefore difficult. Nevertheless, some qualitative conclusions can be drawn. For instance, one obtains for the intramolecular tritium isotope effect, defined by the ratio of rate constants k_3/k_2 or k_3^*/k_2^*, the value 16·6 at 80°C, neglecting in the first approximation the departure of the values of the secondary isotope effects of tritium from unity. The deuterium isotope effect k_H/k_D calculated according to the Swain or Lewis relation should be about 8·54–7·02 at 80°C. This means that the rupture of the carbon–hydrogen bond takes place in the rate-determining step of the oxidation of tetralin with 2,3-dichloro-5,6-dicyanoquinone and that the hydrogen abstraction is accompanied by large tunnelling. The above qualitative conclusions should be confirmed by quantitative studies of the deuterium isotope effects in the quinone oxidation reactions of the tetralin labelled with deuterium in different positions.

C. ^{14}C Isotope Effect in the Condensation of o-Benzoylbenzoic Acid-Carboxyl-^{14}C to Anthraquinone-9-^{14}C

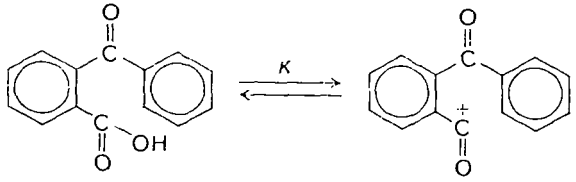
Ropp studied the ^{14}C isotope effect in the condensation of carboxyl-labelled *o*-benzoylbenzoic acid **148** to anthraquinone **149**[187]. The author



(148) (149) (121)

has found that at 80°C the experimental isotope effect, k_{12}/k_{14}, in reaction (121) is 1·03–1·04. This value is much smaller than the theoretical ^{14}C isotope effect in the ^{14}C—O bond rupture. Ropp explains the small value of the experimental ^{14}C isotope effect by suggesting that the condensation step leading to ring closure and formation of the new ^{14}C—^{12}C bond is

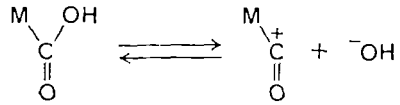
preceded by an equilibrium between the *o*-benzoylbenzoic acid and the corresponding acylium ion **150**:



(122)

(150)

The isotope effect on the equilibrium constant K of such a reaction can be calculated by considering the model (123):



(123)

Ropp makes the first step in the approximate theoretical treatment of equilibrium (123) by assuming that the isotopic equilibrium constant for ^{14}C in this process is equal to the ratio of the partition functions f_i corresponding to the isotopic C_i—OH bond, lost during the formation of the ionic structure **150**. Assuming a rather low frequency (850 cm^{-1}) for the C—OH bonds he finds that the K_{12}/K_{14} ratio equals 1·035 at 80°C in agreement with the reported experimental isotope effect. Ropp stated further that there are no (or only very small) isotope effects in the subsequent formation of the new C—C bond. The explanation presented by Ropp is very plausible but it is not a decisive one. Strict calculation in harmonic approximation gives at 80°C the value $1{\cdot}035_2$ for the ratio of the reduced partition functions of the isotopic ^{12}C—^{16}O and ^{14}C—^{16}O bonds. However, the experimental error with which the ^{14}C isotope effect has been determined is too large to be used for a quantitative test. A more complete theoretical approach to the problem would require one to consider also the four-centre coordinate of the reaction[188] which takes into account the simultaneous C—H and C—OH bond rupture and C—C and H—OH bond formations in the elimination of the water molecule.

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The Chemistry of the Quinonoid Compounds
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CHAPTER 13

Biological reactions of quinones

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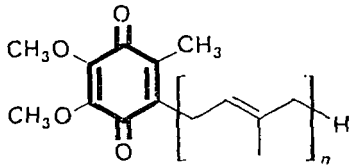
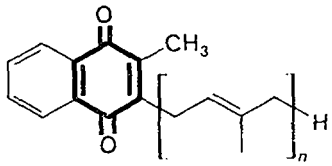
I. INTRODUCTION

Biologists are well acquainted with the meaning of the term 'quinone'. It connotes to them materials such as the ubiquinones, **1**, the menaquinones, **2**, alizarin, **3**, and diosquinone, **4**, which contain in their

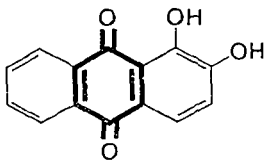
constitution either a 1,4-diketocyclohexa-2,5-dienoid moiety or a 1,2-diketocyclohexa-3,5-dienoid moiety (note emphasized portions of structures **1**–**4**). An excellent compendium of the structures and chemical properties of the naturally occurring substances of this type has been provided by Thomson[1].



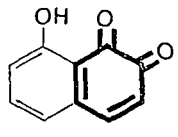
(1), $n = 0 \rightarrow 10$



(2), $n = 0 \rightarrow 12$



(3)



(4)

Less evident is the meaning of the term 'biological reaction'. Formally, an article on the 'biological reactions of quinones' would comprise a record of all the chemical transformations that could be wrought on each and every known quinonoid compound by any whole cell or cellularly derived system. Such a record would be enormously bulky, however, and would not necessarily increase our understanding of the fundamental biological significance of quinones. A more productive approach would be to focus only on those quinonoid materials which biological systems synthesize themselves, and then set out the functional roles these materials play *in the system that produces them*. Such will be the approach used in this chapter. We will start by reviewing the pathways used by cells to make quinonoid materials. Since this is an area wherein much is known and to which the present authors have contributed, it will be covered quite extensively. Thereafter, we will attempt to gather together what is known about the biological ends these syntheses serve. Apart from a few isolated areas, data on this topic are scant. Indeed, it is one of the goals of this chapter to stimulate biosynthetic chemists to think more teleologically. One final introductory comment—since we plan to consider only those situations in which the quinone is functionally involved in the cell that produces it, we will not be dealing with several important topics such as

menaquinones (vitamin K) and blood clotting, tocoquinone and ageing, the mode of action of the various quinonoid drugs, and microbial and insect controlling agents. Fortunately, the first two items have been the subject of recent reviews[2–4].

II. THE BIOSYNTHESIS OF QUINONES

Nature has devised a surprising number of biosynthetic routes to quinones. Chemists and biochemists have risen to the challenge of elucidating these pathways with great success. A limited number of typical examples of these achievements will be covered in this chapter. For the sake of classification, three major categories will be considered. The distribution of each pathway in nature will be summarized at the beginning of each heading or sub-heading.

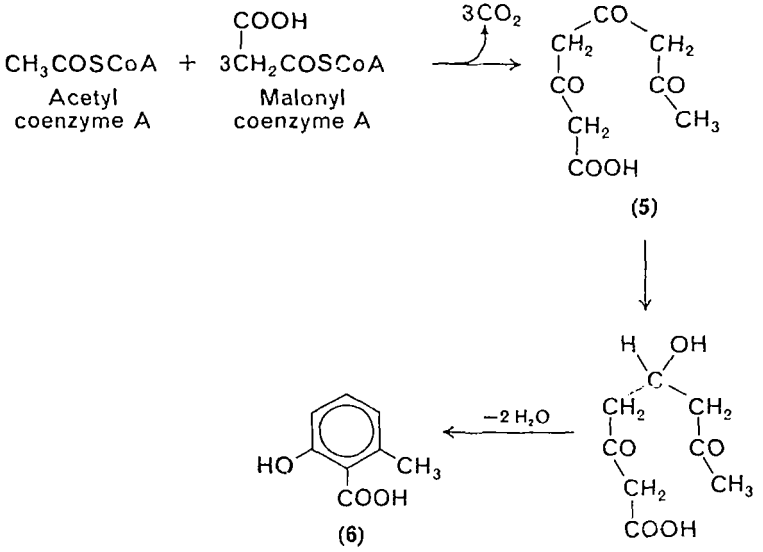
A. De Novo *Quinonoid Synthesis from Simple Aliphatic Acids ('Polymalonate' Condensations)*

Benzoquinones: fungi, insects
Naphthoquinones: fungi, plants, sea urchins
Anthraquinones: fungi, plants
Miscellaneous: fungi, *Streptomyces*

A well-explored pathway for the biosynthesis of aromatic compounds consists of the formation of a 'polyketomethylene' chain (e.g. **5**) which then undergoes cyclization and subsequent modification (for review, see references 5 and 6). Construction of the chain is usually initiated by a molecule of acetic acid, probably activated as its coenzyme A (CoA) derivative, which condenses in sequence with a number of molecules of malonic acid, again probably as the CoA derivative*. Each malonate molecule loses one CO_2. The prototypic reaction is the formation, from one acetate and three malonate units, of 6-methylsalicylic acid (**6**), a typical 'secondary metabolite' of fungi. This whole process is catalysed by a multi-enzyme system, 6-methylsalicylic acid synthase, which has

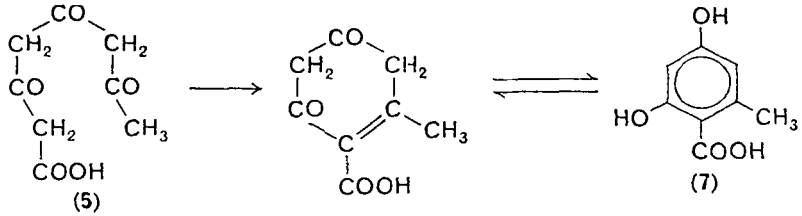
* The malonyl CoA is generally regarded as being derived through the action of acetyl CoA carboxylase: that is, the biotin-dependent carboxylation of acetyl CoA. However, in *Penicillium islandicum* (which also produces acetate-polymalonate-derived anthraquinones), the malonate moiety of the acidic polysaccharide, islandic acid (glucose : malonic acid, ca. 1 : 1), can be derived by oxidative α-decarboxylation of oxaloacetate[7]. It is not clear whether this 'alternate' route to malonate is generally employed for synthesis of the acetate-polymalonate products.

been extracted from *Penicillium patulum* in a stable form and has been studied in detail by Lynen and coworkers[8].



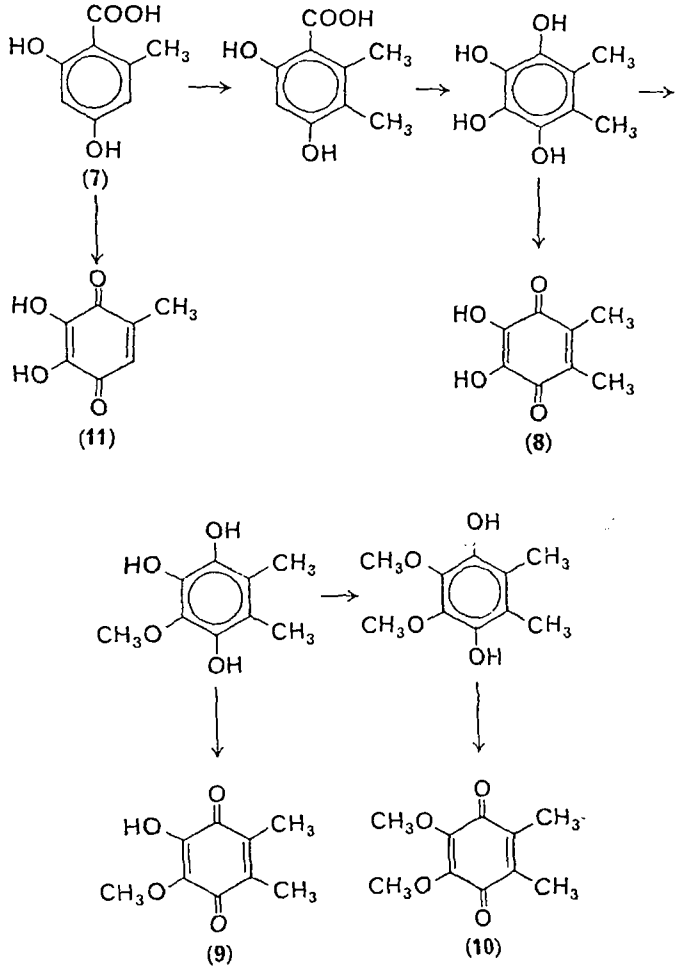
Assembly of aromatic compounds by this pathway does not take place in animals, but, to take the case of 6-methylsalicylic acid, this compound is formed by the 'acetate-polymalonate' pathway in a variety of fungi, in the bacterium *Mycobacterium phlei*[9], and in chloroplasts of dark-grown barley leaves[10].

If the polyketomethylene intermediate **5** does not undergo a reductive step, simple cyclization leads to orsellinic acid **7**, another commonly found mould secondary metabolite.



A frequently encountered feature of secondary metabolism and one that gives rise to many quinones is the modification of a basic skeleton by further biosynthetic manipulation. Thus, by methylation (in which *S*-adenosyl methionine serves as the methyl donor), hydroxylation and

oxidation, simple benzoquinones such as 2,3-dihydroxy-5,6-dimethyl-1,4-benzoquinone (**8**) and 2-hydroxy-3-methoxy-5,6-dimethyl-1,4-benzoquinone (**9**) and aurantiogliocladin (**10**) are produced from orsellinic

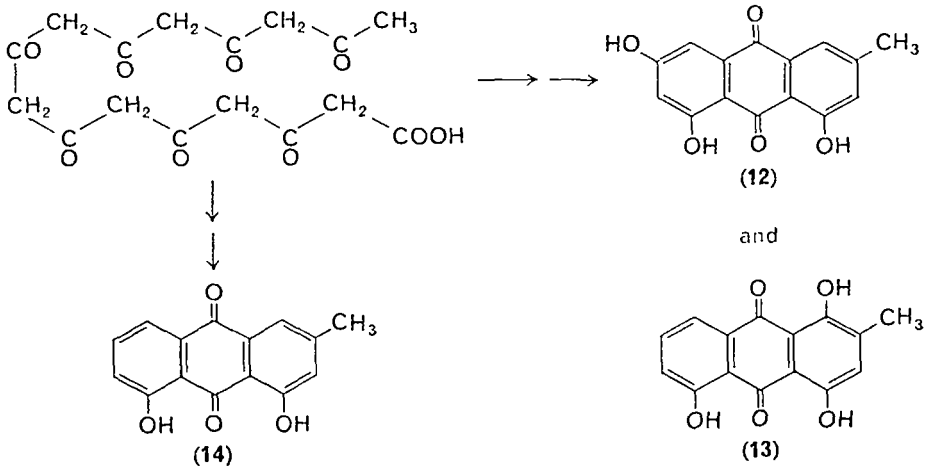


acid **7** by the fungus *Gliocladium roseum*[11,12]. 3,4-Dihydroxy-2,5-toluquinone (**11**) and its 3-methyl ether (fumigatin) are also examples of benzoquinones derived from orsellinic acid[11].

Cyclization of polyketomethylene chains and subsequent oxidation, etc., are not restricted to the formation of benzenoid compounds. In fact, some very early experiments substantiating the 'polyacetate' hypothesis*

* The need for malonate as the chain-extending unit was not recognized until 1961. Before that date the simple term 'polyacetate' was used.

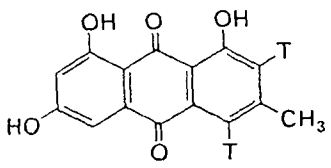
were concerned with anthraquinone biosynthesis*. Thus, in *Penicillium islandicum*, a chain of 16 carbons eventually gives rise to emodin **12**, its dimer skyrin, and islandicin **13**[14]. At some unknown stage the terminating carboxyl group is lost, hence these compounds contain only 15 carbons. This type of process also goes on in plants. Thus chrysophanol **14** and emodin **12** are acetate-polymalonate products of *Rumex alpinus*, *Rumex obtusifolius* and *Rhamnus frangula*[15-17].



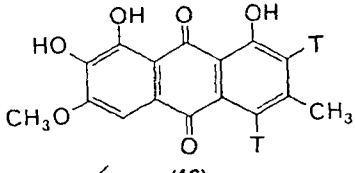
In an interesting study which sheds light on the decarboxylation reaction so frequently found in anthraquinone biosynthesis, Steglich[18,19] has used intact young sporophores of *Dermocybe sanguinea* to study the late stages of anthraquinone biosynthesis in this mushroom. The 6-mono-β-D-glucoside of emodin **15** labelled with tritium was well converted to dermoglaucin **16** and dermocybin **17** whereas endocrocin (**18**, ^{14}C-label) was converted to dermolutein **19** and dermorubin **20**. There was apparently no decarboxylation of endocrocin to the neutral compounds; thus decarboxylation may occur at a pre-aromatic stage.

Simple fungal naphthoquinones such as javanicin, **21**, are also derived from polyketomethylene compounds, the reduction of the terminal carboxyl to methyl being a unique feature in this case[20]. In plants, plumbagin **22** and 7-methyljuglone **23** arise from acetate[21] (presumably by

* Anthraquinones are often produced in very substantial amounts, e.g. the dry mycelium of *Helminthosporium gramineum* contained 30% of its weight of a mixture of polyhydroxyanthraquinones[13].



(15)
(as 6-β-glucoside)



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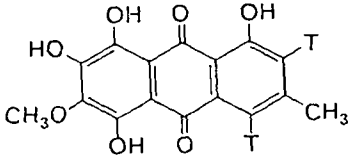

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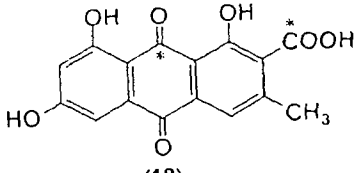

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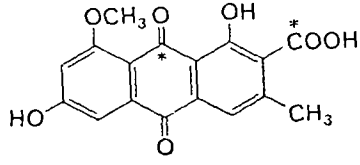

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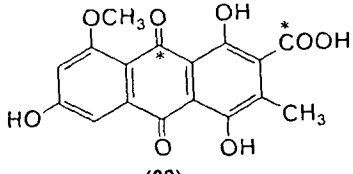
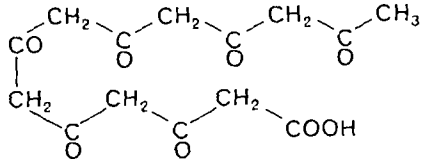
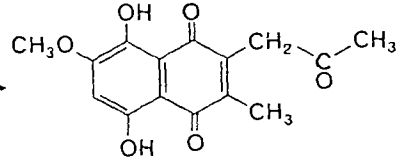


(20)

* = ^{14}C





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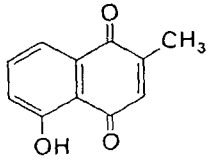

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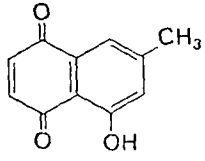
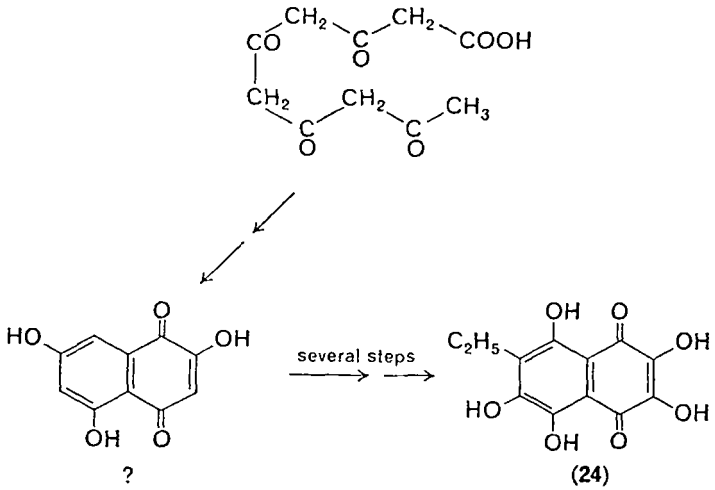
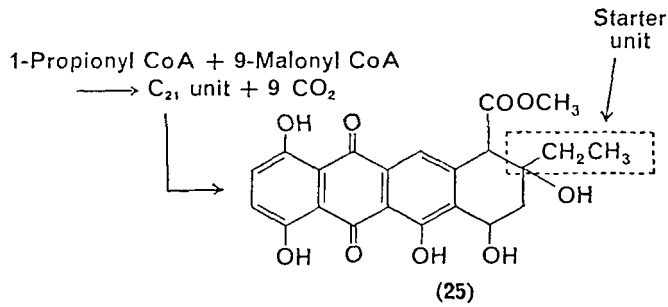


(23)

the acetate-polymalonate mechanism) and there is good evidence that echinochrome A, **24**, is derived in the sea urchin, *Arbacia pustulosa*, from a basic acetate skeleton[22].

A variation of this basic pathway is the use of 'starter' units other than acetate. For example, condensation of one propionyl and nine malonyl units gives rise to ε-pyrromycinone (**25**) in various Actinomycetes[23]. A

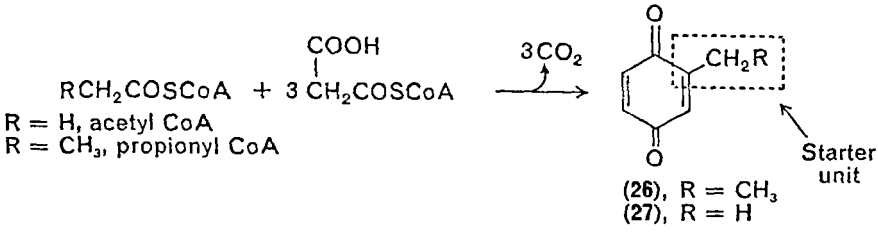




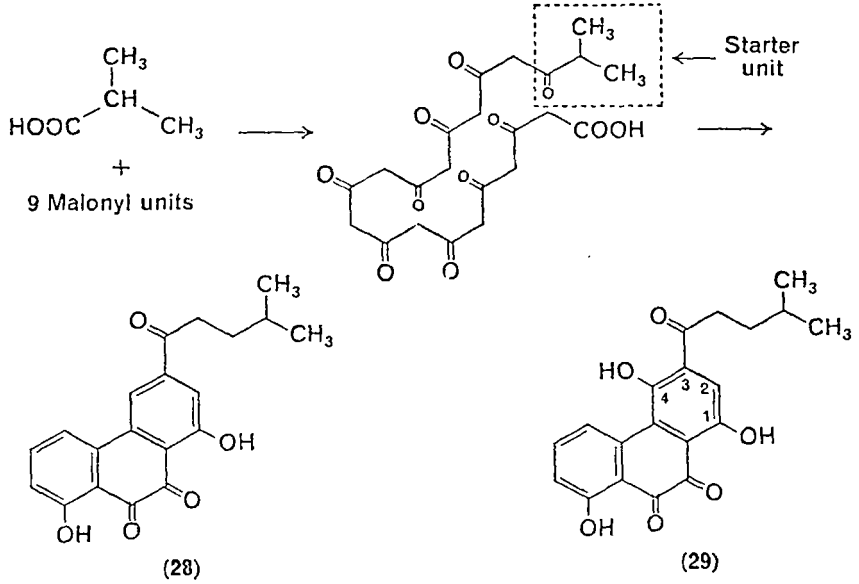
simpler case is the use of a propionate-polymalonate pathway in the biosynthesis of ethyl *p*-benzoquinone (**26**) in the defensive secretion of the beetle *Eleodes longicollis* (for more details, see p. 728). In this same secretion, methyl *p*-benzoquinone (**27**) is apparently derived by the acetate-polymalonate pathway, while, remarkably, benzoquinone itself is biosynthesized from the aromatic ring of tyrosine or phenylalanine[24] (see

section II.B.1 for details of this pathway)*. It is not clear whether symbiotic micro-organisms play a role in these syntheses.

In another case of quinone biosynthesis, this time an *ortho* system, isobutyrate apparently functions as the starter of a chain, extended



presumably by malonate units. The quinone is the *ortho*-phenanthrene-quinone, piloquinone (**28**), produced by *Streptomyces pilosus*. Valine also functions as a source of the branched starter unit[26,27]. The accompanying 4-hydroxy-piloquinone (**29**) has the extra OH group in correct alignment for the proposed pathway.



* Also note the use of a propionate plus methylmalonate condensation in the biosynthesis of macrolide antibiotics[25].

B. Quinones Derived from Aromatic and Pre-aromatic Cyclic Precursors

Many quinones can be traced back to shikimic acid and hence finally to carbohydrate. Shikimate is the key compound for the biosynthesis of many aromatic compounds which are 'primary' metabolites (e.g. the amino acids, phenylalanine, tyrosine, tryptophan) and, in addition, serves as a precursor for many secondary metabolites.

There are several pathways to quinones, all of which diverge from shikimate. For ease of discussion, they will be identified by means of critical intermediates: *p*-hydroxybenzoate, homogentisate, *o*-succinylbenzoate and phenylpyruvate.

1. The role of *p*-hydroxybenzoate

Benzoquinones:	animals, plants, bacteria, fungi, insects, *Tetrahymena*
Naphthoquinones:	plants

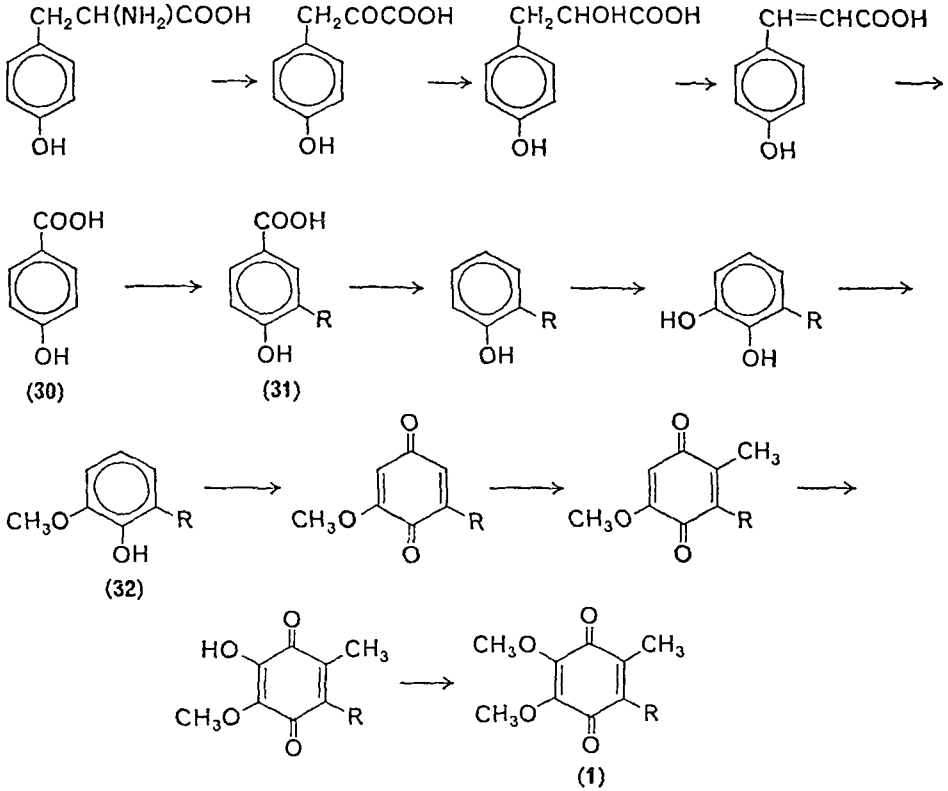
The discovery of ubiquinone **1** and related isoprenyl quinones and the elucidation of their biological function[28] stimulated considerable interest in the role of quinones in mammalian metabolism. Isoprenoid naphthoquinones had, of course, been investigated at a much earlier date in connexion with the menaquinone (vitamin K) problem. Despite the general structural resemblance of vitamin K and ubiquinone, it soon became apparent that ubiquinone was not a vitamin in mammals; unlike vitamin K, it could be biosynthesized by animal tissues*. Since animals do not have the capability for *de novo* synthesis of aromatic compounds†, it was logical to suspect a role for the 'essential' aromatic acids‡. Phenylalanine and tyrosine were shown to be precursors of ubiquinone in

* Several reviews have covered the subject of the biosynthesis of ubiquinone and other isoprenoid quinones[29-33]. Morton's classic text[33] covers much of the basic (pre-1965) material relating to the biologically active quinones and related compounds. For this reason, only early references of particular interest will be cited here. An effort will be made, however, to cover the most recent literature.

† They are unable to make shikimate or other hydro-aromatic derivatives to serve as precursors to the aromatics. On the other hand, hydro-aromatic compounds such as cyclohexanecarboxylate if added to the diet can be dehydrogenated (to benzoate in this case). The one exception to this statement is the ability to form by dehydrogenation (aromatization) of ring A of a steroid oestrogen.

‡ Since tyrosine, phenylalanine and tryptophan are important protein components and cannot be synthesized by the animal these amino acids have to be supplied in the diet as 'essential' components.

animals; however, only the ring-carbon atoms were used[34]. A similar situation was found for *p*-hydroxybenzoate (**30**)[35]. Our present understanding[36-40] of the pathway from phenylalanine and tyrosine through *p*-hydroxybenzoate is shown*. As would be expected from general



biosynthetic considerations the *O*- and *C*-methyl groups were found to be derived from the methyl group of methionine and the isoprene side-chain from mevalonate. In the course of the reactions from *p*-hydroxybenzoate the carboxyl group is lost and three other oxygen atoms are introduced onto the benzenoid nucleus. In the bacterium *Pseudomonas desmolytica* the oxygen atoms which carry the methyl groups are derived from oxygen gas[42].

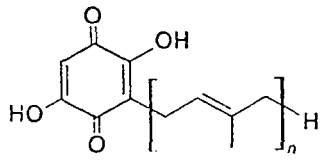
* Cyclohexanecarboxylic acid has been found to serve as a precursor of the quinone ring of ubiquinone in rat liver slices; this presumably involves dehydrogenation to benzoate which is also known to function as a ring precursor in the same way as *p*-hydroxybenzoate[41].

The pathway in animals is beginning to be clearly defined. Radioactivity from *p*-hydroxybenzoate is incorporated into 3-polyprenyl-4-hydroxybenzoate (**31**) in rat liver homogenates or slices[43]. In addition, 6-methoxy-2-nonaprenylphenol (**32**) has been well-characterized from neutral lipids of rat liver and when labelled with tritium was converted to ubiquinone by intact rats[44].

Olson and his colleagues have also completely characterized 5-demethoxyubiquinone-9 from rat liver slices, refuting a suggestion that their earlier reports were in error[45,46]. Although alternatives to the route shown above may exist, both in bacteria and animals, it appears to be generally correct in the major features.

While the *p*-hydroxybenzoate required as an ubiquinone precursor is derived from the essential amino acids in animals, it is generally assumed to arise directly from shikimic and chorismic acids in bacteria[47–49] and fungi[50]. Much of the bacterial work has centred on *Rhodospirillum rubrum*, a photosynthetic anaerobe which does not readily assimilate shikimate. However, this latter compound is efficiently utilized by *Escherichia coli* and, as will be seen later, radioactivity is incorporated into both ubiquinone and menaquinone.

It will be of interest to see whether this biosynthetic pathway is used in the formation of the recently discovered 2,5-dihydroxy-1,4-benzoquinones (**33a** and **b**) which have relatively short prenyl side-chains[51–52].

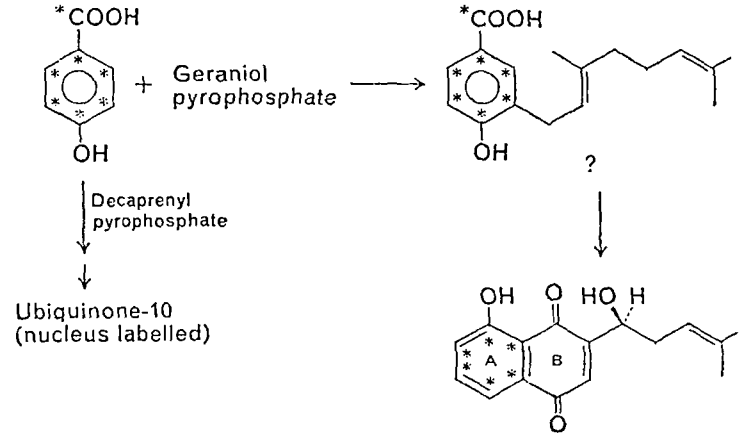


(33)

(a), $n = 3$, helveticone (fruiting bodies of *Chroogomphys helveticus*)
(b), $n = 4$, bovinone (fresh sporophores of *Boletus* [*Suillus*] *bovinus*)

Although the major biological role of *p*-hydroxybenzoate is presumably as a precursor to the ubiquinones, it also has a restricted role in the biosynthesis of the plant naphthoquinone, alkannin **34**. The side-chain of this material contains 6 carbon atoms rather than the 5 that would be expected from addition of mevalonate to a preformed naphthoquinone nucleus. However, it has been shown in *Plagiobothrys arizonicus* that the A-ring is derived from *p*-hydroxybenzoate, and *all* of the remaining carbons from 2 moles of mevalonate[53]. Possibly the *p*-hydroxybenzoate is first alkylated by a C-10 side-chain (i.e. by geraniol pyrophosphate), this

step then corresponding in essential detail to the ubiquinone biosynthetic pathway.

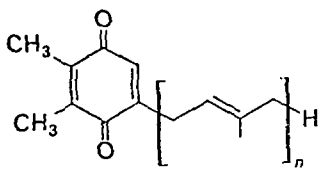


(34)

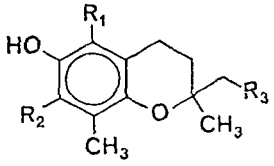
2. The role of homogentisate

Benzoquinones: plants
Naphthoquinones: plants

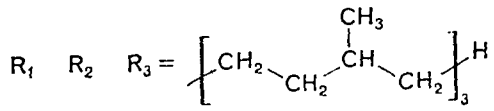
Kofler in 1946 isolated a quinone (Kofler's quinone) from alfalfa which was later rediscovered and named plastoquinone[54]. The plastoquinones are a group of 2,3-dimethyl-5-polyprenyl-1,4-benzoquinones (**35**) found in higher plants and algae. They share a common biosynthetic pathway with the tocopherols (**36a–39a**) and tocotrienols (**36b–39b**). Although



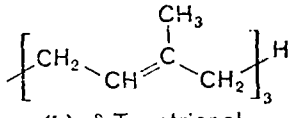
(35), $n = 4$



(36)–(39)

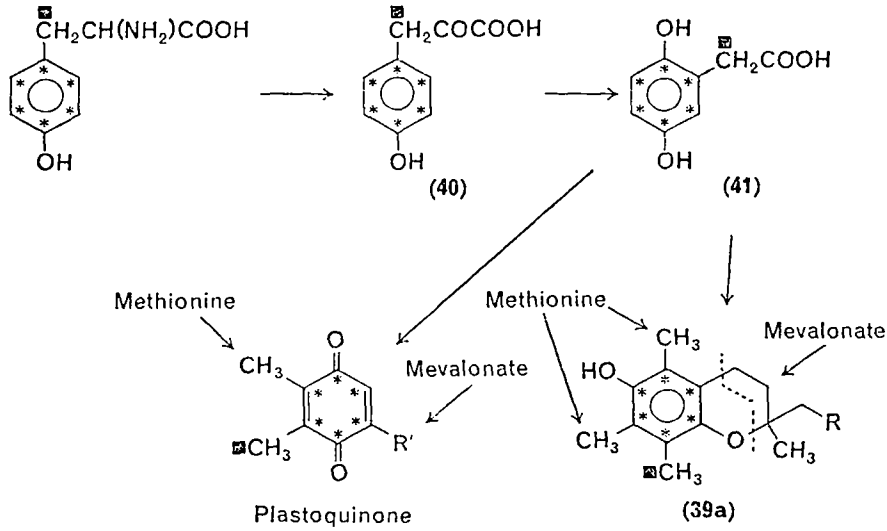


(36), H	H	(a), δ-Tocopherol	(b), δ-Tocotrienol
(37), CH_3	H	(a), β-Tocopherol	(b), β-Tocotrienol
(38), H	CH_3	(a), γ-Tocopherol	(b), γ-Tocotrienol
(39), CH_3	CH_3	(a), α-Tocopherol	(b), α-Tocotrienol



these latter materials are chromanols rather than quinones, they will be considered briefly here since they are probably derived from quinones.

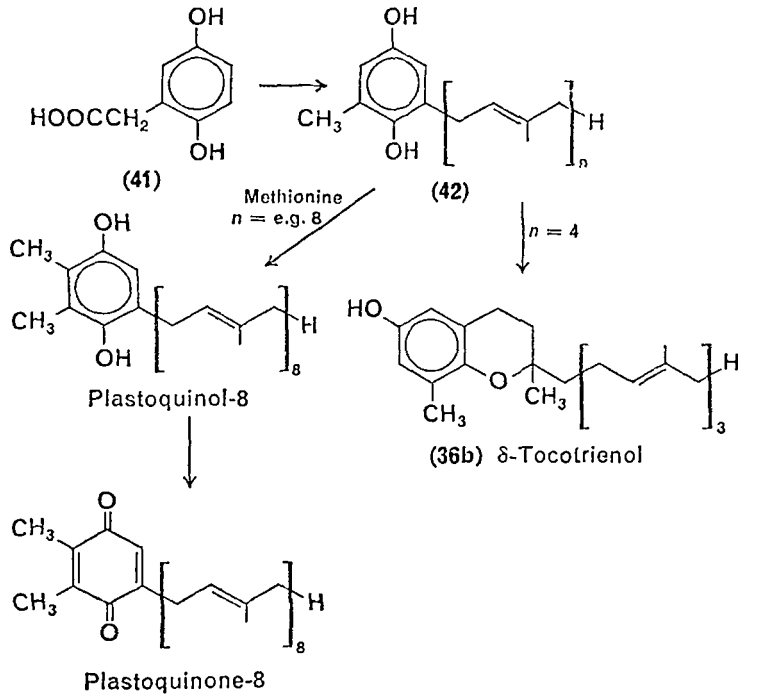
A key observation in the investigation of the biosynthesis of these two groups of compounds was the finding that one methyl group was derived from C-3 of the side-chain of tyrosine or phenylalanine[55]; a sharp contrast to ubiquinone biosynthesis where *all* of the side-chain carbons of tyrosine are lost. Furthermore, the benzenoid ring was derived from the ring system of either phenylalanine or tyrosine so that these amino acids contribute a C_6–C_1 fragment. Evidence that *p*-hydroxyphenylpyruvate **40** and homogentisate **41** are also involved has been obtained in a variety of plants[56]. The second methyl group of a plastoquinone and the second and/or third methyl of a tocopherol are derived from methionine[31]. Hence, the biosynthetic origins of these materials are, in outline, as follows*:



The exact sequence between homogentisate and the first intermediate with the methyl group (derived from the side-chain) is not known. The following materials, and their glucosides, are said not to be involved: gentisate, gentisaldehyde, gentisylalcohol and toluquinol[31]. The first step,

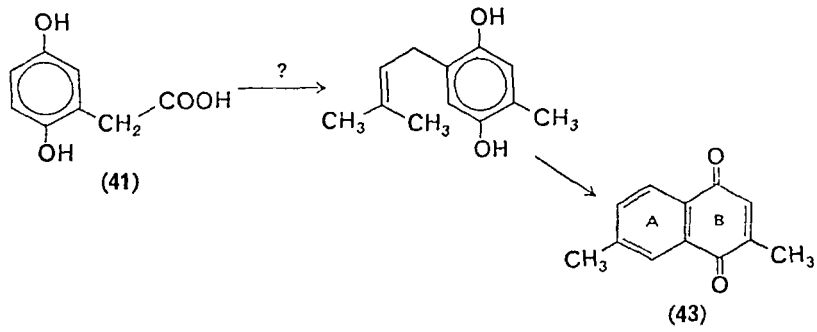
* The results summarized here for two labelling patterns were, of necessity, obtained in separate experiments.

therefore, may be sequential or concomitant prenylation and decarboxylation to form 3-polyprenyltoluquinols (**42**). Thus:



The chromanol (**36b**; δ-tocotrienol) may be regarded as the parent of both the tocotrienol and tocopherol series; alternate pathways are possible and for a more comprehensive discussion reference 31 should be consulted.

An apparently related pathway leads to the naphthoquinone, chimaphilin **43** in *Chimaphila umbellata*[57,58]. In this case, the quinonoid ring and attached methyl arise from a C_6–C_1 unit derived from tyrosine, as discussed

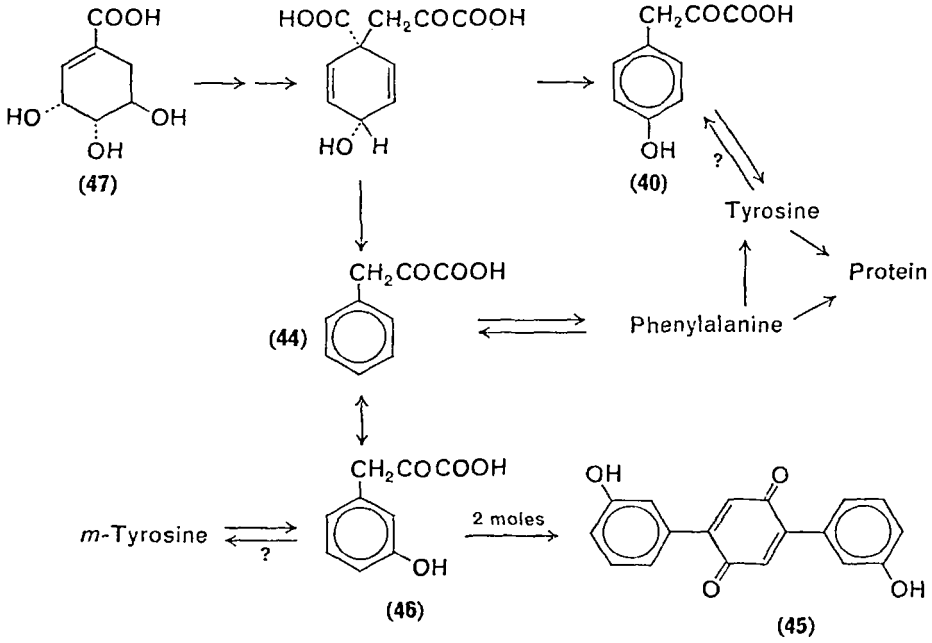


above, while the four atoms of the A-ring and the attached methyl originate in mevalonate. Note that in chimaphilin, the single prenyl unit must be added *para* to the CH_2COOH group, rather than *meta* as in plastoquinone biosynthesis.

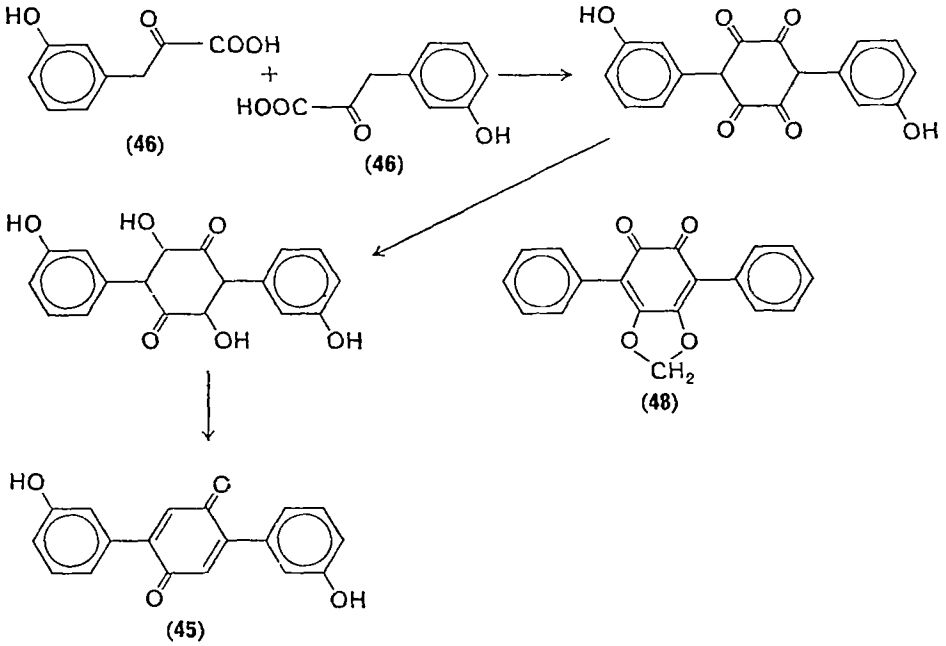
3. The role of phenylpyruvate

Terphenylquinones: fungi

Although *p*-hydroxyphenylpyruvate **40** is a precursor for homogentisate, as indicated in the previous section, some quinones are apparently formed directly from phenylpyruvate **44**. This is the case for the terphenylquinone, volucrisporin **45**, produced by cultures of the Imperfect Fungus, *Volucrispora aurantiaca*[59]. The results of feeding experiments with a variety of labelled precursors are consistent with the following biosynthetic map. An essential step in it is the hydroxylation reaction leading to the formation of *m*-hydroxyphenylpyruvate (**46**). The intermediate stages



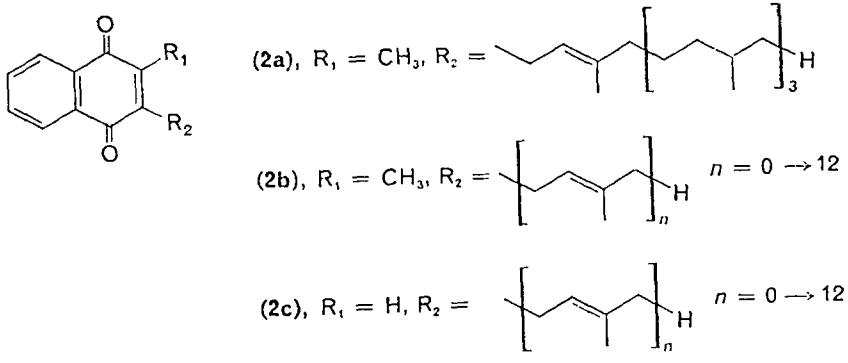
between *m*-hydroxyphenylpyruvate and the final product are not completely understood, but indirect evidence supports the scheme as shown. The related substance, phlebiarubrone **48**, is biosynthesized in a similar fashion from phenylalanine[60].



4. The role of succinylbenzoate in biosynthesis of naphthoquinones and anthraquinones

Naphthoquinones: bacteria, plants
Anthraquinones: plants

A novel pathway leading to naphthoquinones and anthraquinone biosynthesis has emerged as a result of interest in the biosynthesis of phylloquinone (**2a**, ≡vitamin K_1) and the menaquinones (**2b**, ≡vitamin K_2). The natural occurrence of, and structural variation possible in, these materials have been reviewed[1].

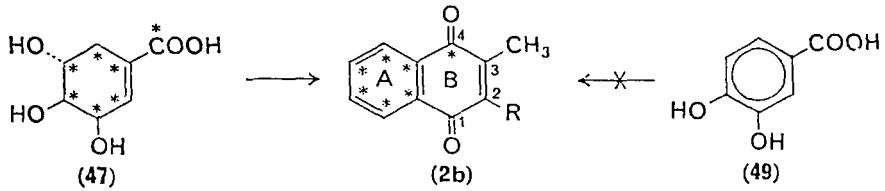


Three broad structural aspects have to be recognized in considering the biosynthesis of phylloquinone or a menaquinone type.

(i) *The methyl group at C-3.* The occurrence of desmethylmenaquinones (**2c**) suggested that these materials could act as substrates for methyl transferases. Direct evidence for the utilization of labelled methionine has been obtained for MK-9 * in *Bacteroides melaninogenicus* (= *Fusiformis nigrescens*)[61], for MK-9 (II-H_2) in *Mycobacterium phlei*[62] and *Mycobacterium smegmatis*[63], and for MK-8 in *E. coli*[64]. Furthermore, labelled DMK-9 has been converted to MK-9 (II-H_2) in a cell-free extract prepared from *M. phlei*[65].

(ii) *The isoprene side-chain at C-2.* With the realization of the prime role of mevalonate in the biosynthesis of isoprenoid compounds, it was logical to assume this material was the precursor for the side-chains of materials such as plastoquinone, ubiquinone, phylloquinone and menaquinone. The utilization of mevalonate for the production of the isoprenoid portions of phylloquinone[67,68] and menaquinone[69] has been demonstrated.

(iii) *The naphthalene nucleus.* Tentative evidence for a role of shikimate **47** in menaquinone biosynthesis in *E. coli* was obtained in 1964[70,71]. At that time, it was also suggested that protocatechuate **49** was involved. Independent work with *E. coli* and *M. phlei* confirmed the role of shikimate and provided unambiguous proof that all seven carbon atoms of this acid were incorporated[72,73]. No evidence has been obtained, however, to support a role for protocatechuate or its aldehyde in menaquinone



(47) (2b) (49)

biosynthesis[72–77]. The utilization of shikimate has also been studied in *Bacillus megaterium* with analogous results[74], and work in *M. phlei* with [1,2-^{14}C]- or [5-^{3}H]-shikimate shows that the ring junction of the naphthoquinone system originates from the ethylene carbons of shikimate, as shown previously[75,76]. In those bacteria such as *E. coli* which contain both

* In accordance with recommended practice[66], the following abbreviations will be used in this section:

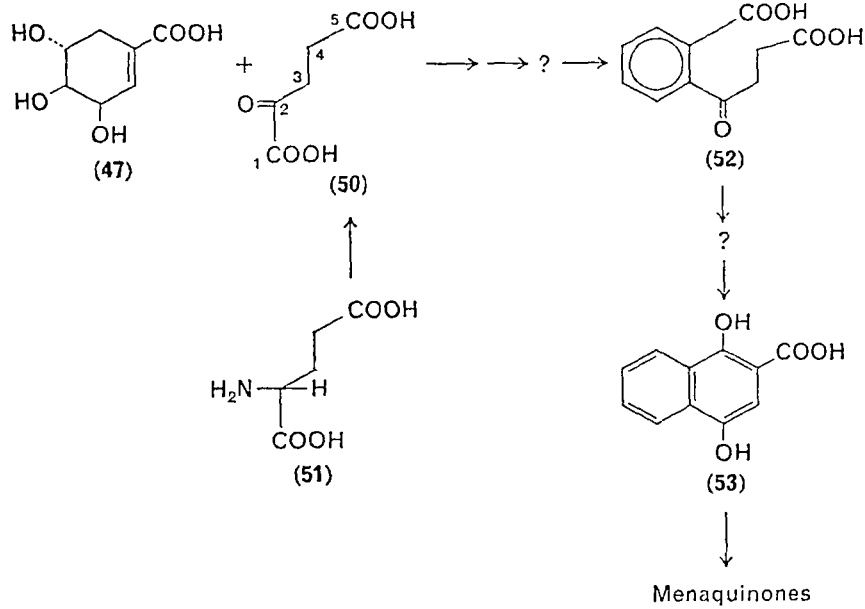
MK = menaquinone; DMK = desmethylmenaquinone at C-3.

MK-*n* = menaquinone with side-chain of *n*-prenyl units at C-2.

MK-*n* (II-H_2) = dihydromenaquinone with side-chain of *n*-prenyl units in which the second, counting from the nucleus, is saturated.

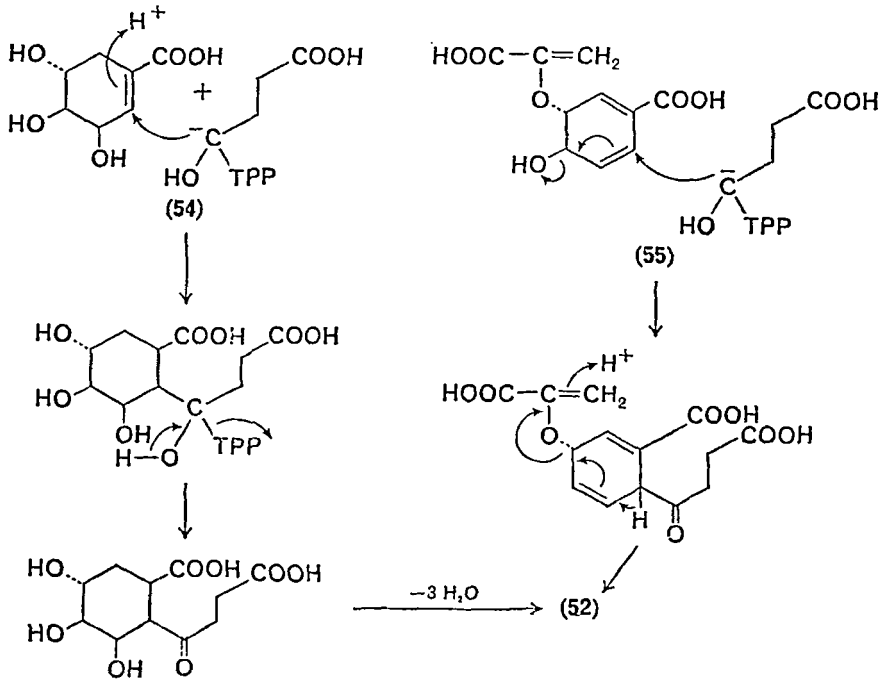
ubiquinone and menaquinone, administration of labelled shikimate leads to label incorporation into both types of compound.

To complete the menaquinone structure a precursor for the remaining three carbon atoms, C-1, C-2 and C-3, of the B-ring had to be discovered. After considerable effort, indirect evidence that the 'missing' three carbon atoms originate in 2-ketoglutarate (**50**) was obtained, both for lawsone biosynthesis in plants[78] (see later) and for menaquinone biosynthesis in bacteria[73,79]. This conclusion depended on tracer experiments with labelled glutamate, **51**, a substance which was presumed to undergo deamination to the keto compound. Thus, the general outline for biosynthesis of the naphthalene nucleus of menaquinones appears to involve a novel condensation of shikimate and 2-ketoglutarate. At some stage both the carboxyl groups of the ketoglutarate component are lost, leaving behind the original C-2, C-3 and C-4 of 2-ketoglutarate. Furthermore, succinylbenzoate (4-[2′-carboxyphenyl]-4-oxobutyrate) (**52**) has been shown to function as a menaquinone precursor in bacteria[73,80]. It seems likely that this oxobutyrate derivative could undergo a cyclization to 2-carboxy-1,4-naphthoquinol (**53**) as indicated below; compound **53** would then be decarboxylated, prenylated, methylated and oxidized to give the final menaquinone.



In the mechanism of decarboxylative coupling of the shikimate/ketoglutarate moieties originally postulated, 2-ketoglutarate is first converted

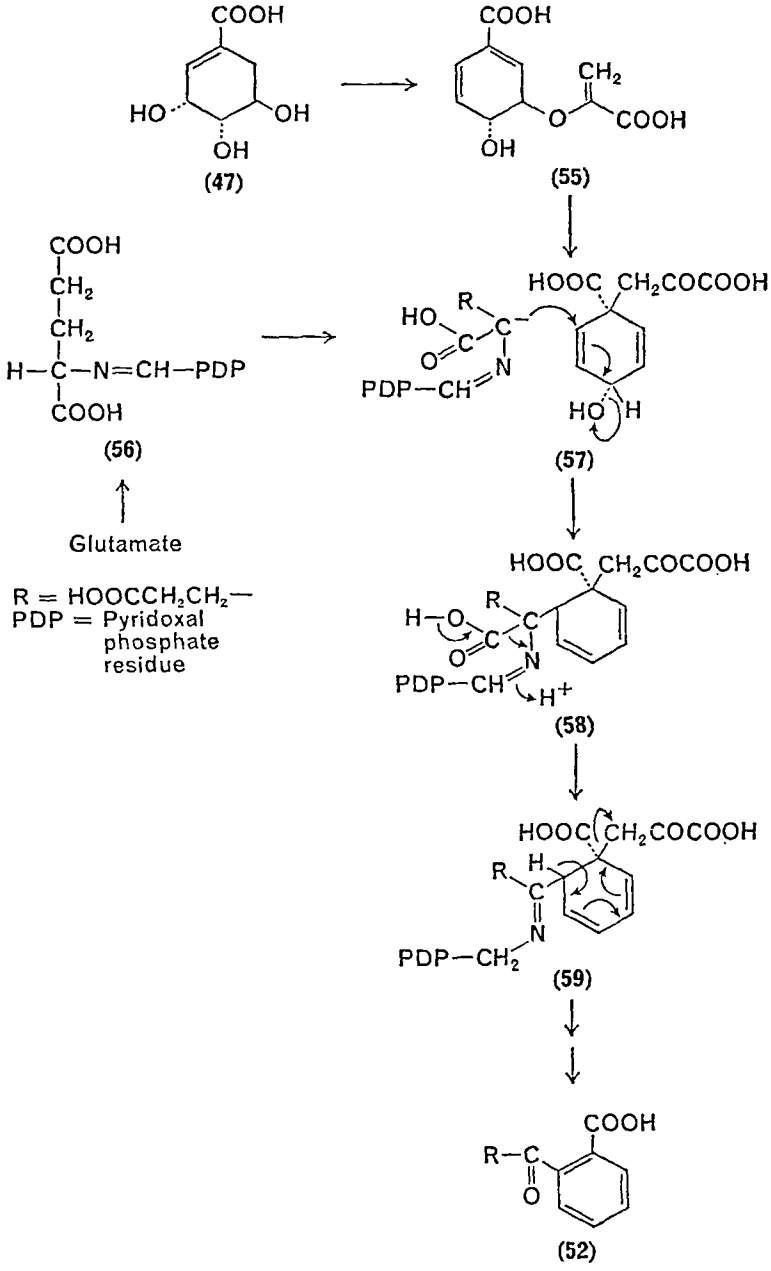
to the thiamin pyrophosphate (TPP) complex of succinic semialdehyde **54** exactly as in the initial reaction of the 2-ketoglutarate dehydrogenase system[73,78,79]. The addition of this material to shikimate would then be analogous to the Michael reaction. The French group, on the other hand, suggest[80] that the TPP anion is added to chorismate **55**.



An alternative coupling mechanism (**47** → **55** → **56** + **57** → **58** → **59** → **52**) wherein the anion of the pyridoxal pyrophosphate complex of *glutamate* **56** adds to prephenate **57** has recently been considered[81]. It was evoked to explain the fact that in the lawsone biosynthetic system (see later) glutamate is more efficiently incorporated than ketoglutarate.

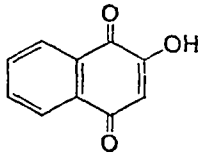
Another controversial matter concerns the possible role of 1-naphthol as a menaquinone precursor. It has been claimed that this material was incorporated into the menaquinone components of *Bacillus megaterium*[74], and *Staphylococcus aureus*[69]. We have not been able to repeat the result with *B. megaterium* and have also failed to incorporate labelled 1-naphthol into the menaquinones of *E. coli* and *M. phlei*[73]. The French group found no incorporation of [1-^{14}C]-1-naphthol in *B. megaterium*, *M. phlei* and three other bacteria, but it was incorporated by a mutant strain of *Aerobacter aerogenes*[75]. This latter strain appears anomalous since it also

incorporates 2-methyl-1,4-naphthoquinone and 1,4-naphthoquinone itself, in contrast to *M. phlei* and *E. coli*[73]. Other workers have similarly failed with a variety of microorganisms (including *B. megaterium*) and plants[82].



Mechanistically, 1-naphthol is not at the correct oxidation level to be involved in the hypothetical scheme, and in our view it is not to be regarded as a direct menaquinone precursor. Furthermore, the oxygen atoms of the quinone functions of *M. phlei* menaquinone are derived from water rather than oxygen gas[83]. If 1-naphthol were an intermediate, the introduction of the second oxygen would, of necessity, be by an aromatic hydroxylation. Since these reactions require molecular oxygen, a role for 1-naphthol is inconsistent with the origin of the oxygen atoms from water.

The shikimate pathway is involved in the biosynthesis of phylloquinone in plants[84], but evidence for the role of ketoglutarate or glutamate has not yet been reported. The simple plant naphthoquinones, lawsone **60** and juglone **61**, are also biosynthesized by this route. Indeed, as mentioned above, much of its detail has been worked out using the lawsone- and juglone-producing systems as models.



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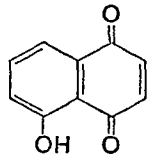
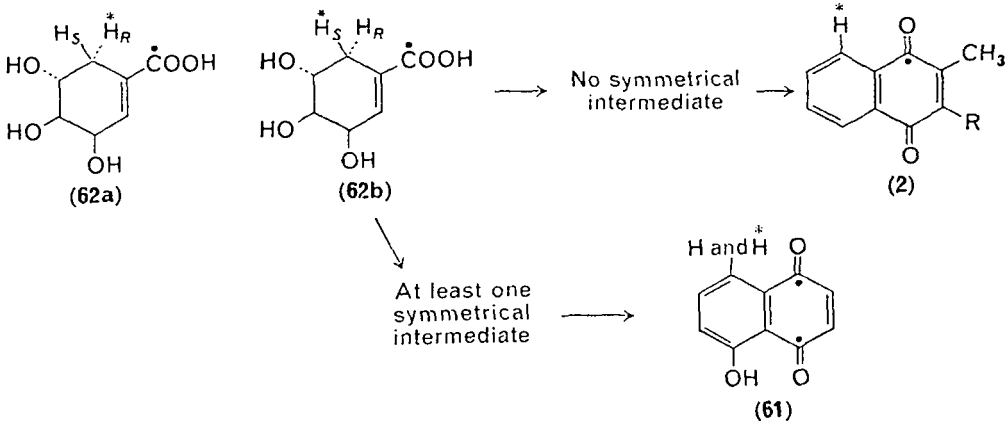


(61)

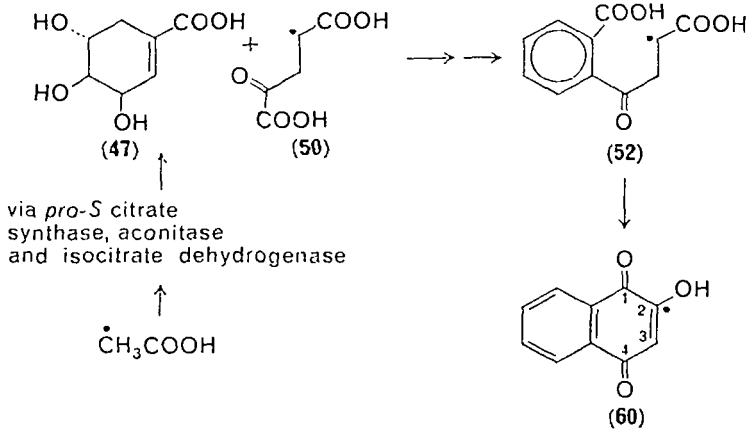
Although the precise structures of the intermediates between the succinylbenzoate **52** and the various products have not yet been determined, some information on their symmetry is available. Thus the stereochemistry of hydrogen elimination from the prochiral C-6 position of shikimate has been studied for juglone biosynthesis in *Juglans regia* and MK-7 biosynthesis in *Bacillus megaterium*[85]. In both cases, using (6*R*)-[7-^{14}C, 6-^{3}H]-shikimate (**62a**) the naphthoquinone contained no tritium. Hence, the *pro*-6*R* hydrogen is eliminated*. Using the corresponding 6*S* tritium-labelled material (**62b**) most of the isotope was retained during MK-7 biosynthesis, but only about half of the tritium in juglone biosynthesis†. From these data, it was concluded that no symmetrical intermediate was involved in menaquinone biosynthesis, but one was in juglone biosynthesis. Using a somewhat different approach, the problem has been examined in the lawsone-producing system[89]. 2-^{14}C-Acetate, fed to *Impatiens balsamina*, was found to label C-2 predominantly: a situation

* For nomenclature, see reference 86.

† It should be noted that this observation is compatible with a role for chorismate since retention of the *pro*-6*S* hydrogen also occurs in its formation[87, 88].



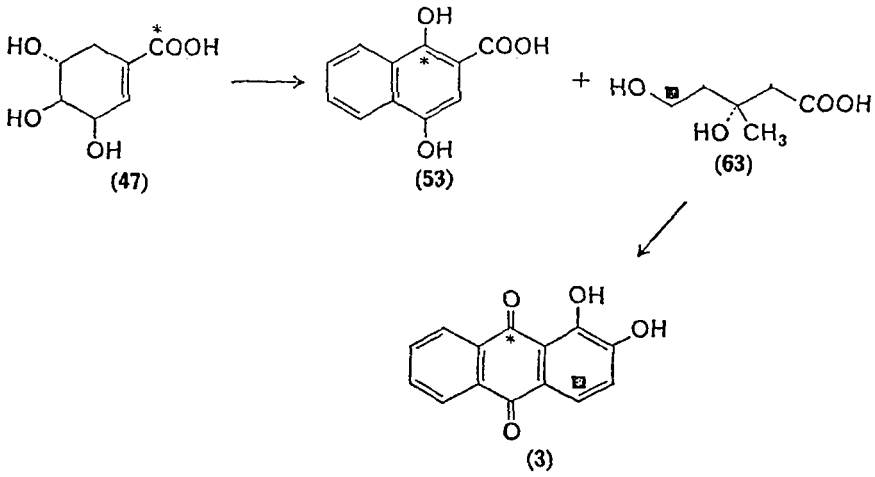
which can only occur if no symmetrical intermediates are involved. The pathway of the methyl group of acetate into C-2 of lawsone is shown below*.



A further interesting development has been the finding that some plant anthraquinones are derived by an extension of this pathway. Thus, carboxyl-labelled shikimate **47** and [5-^{14}C]-mevalonate **63** were incorporated specifically into alizarin **3** [76,90-92]. The biosynthetic sequence shown below explains the observed labelling pattern. Label from the carboxyl group of shikimate was not randomized between the two carbonyl functions, consistent with involvement of non-symmetrical intermediates.

* This finding also indicates that C-1 of lawsone derives from the carboxyl group of shikimate.

The succinylbenzoate **52** is known to be an intermediate in the biosynthesis of pseudopurpurin **64** in plants[80]; it also yields anthraquinones in tissue cultures of *Rubria* species[93].



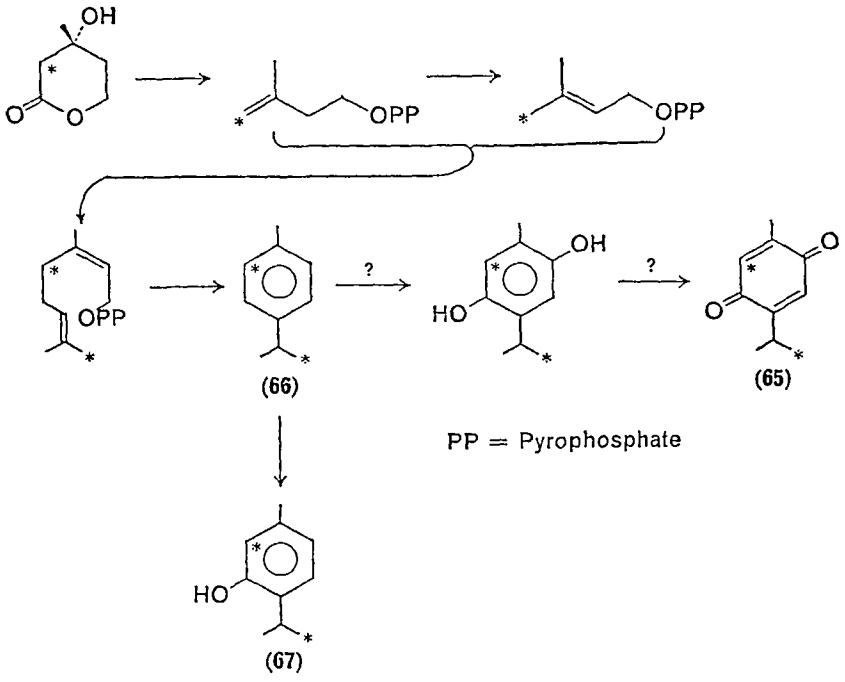
C. *Quinones Derived Wholly from Mevalonate*

Benzoquinones: fungi, plants
Naphthoquinones: plants

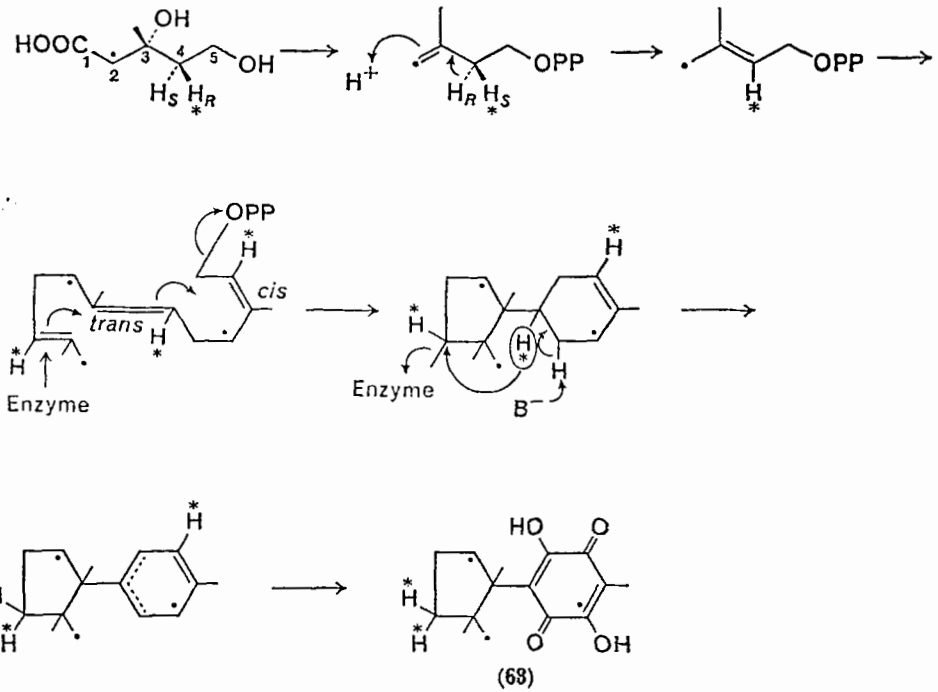
The structures of some naturally occurring quinones are in harmony with the 'Empirical Isoprene Rule'[94], and are clearly related to terpenes and hence, ultimately, to mevalonate. Thymoquinone **65** and its quinol occur in some plants and are probably derived from *p*-cymene **66**. This latter monoterpene is a likely precursor for thymol **67**, a phenol which has been shown to be labelled, with the anticipated isotope pattern, on administration of [2-^{14}C]-mevalonate to *Orthodon japonicum*[95].

At the sesquiterpene level, the fungal benzoquinone, helicobasidin **68** (from *Helicobasidium mompa*) has been shown to be derived from labelled acetate and mevalonate with the anticipated labelling pattern[96,97]. Of

several possible hypotheses, it now appears that a direct cyclization of *trans-cis*-farnesyl pyrophosphate takes place[96]. The reaction is more complex than originally proposed since helicobasidin incorporates two of the three possible *pro-R* hydrogen atoms from C-4 of mevalonate[98]. Since the six-membered ring is fully substituted, a hydrogen transfer must

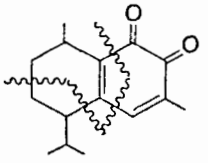


have occurred: this is postulated by Adams and Hanson to take place in an enzyme displacement step as shown below[99]:



(68)

Although no feeding experiments have yet been recorded, it is clear that many other quinones, both 1,4- and 1,2- systems, derive from terpenoid precursors and hence mevalonate. Some of these are shown below, e.g. mansonones A and B (**69** and **70**), tanshinone I (**71**) and coleon A (**72**).



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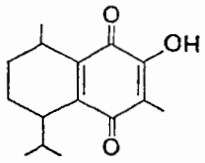

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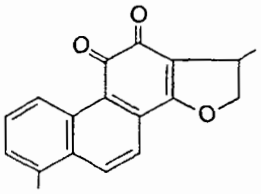

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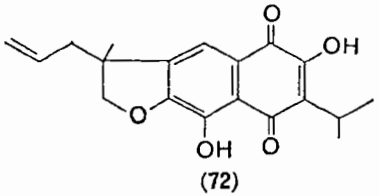
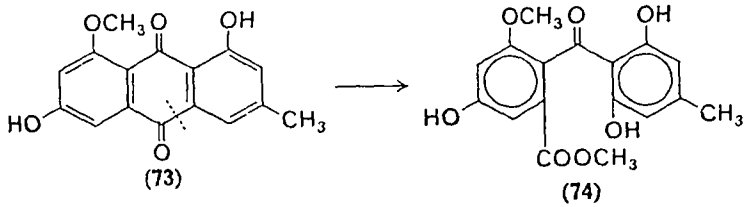


(72)

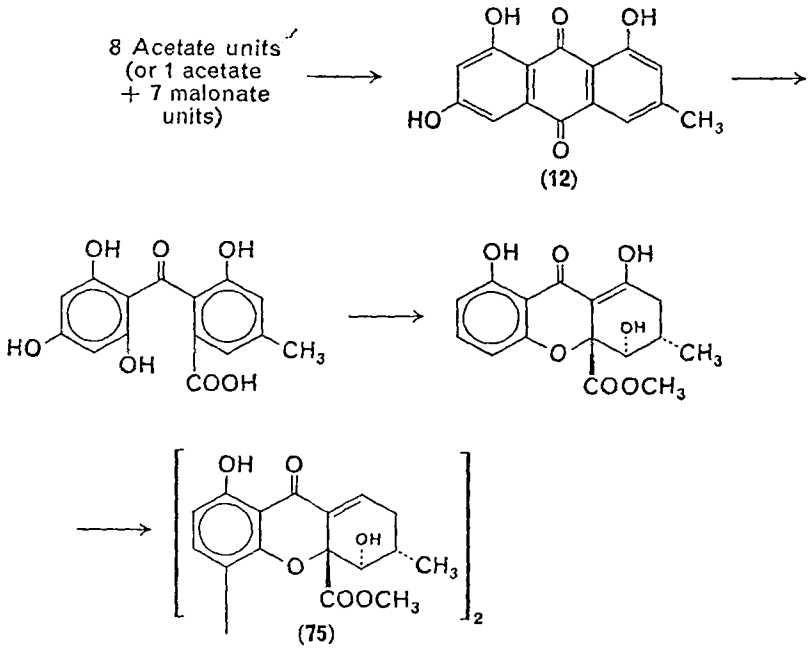
D. Quinones as Intermediates in Formation of Other Secondary Metabolites

In several cases, quinones function as intermediates in the biosynthesis of other secondary metabolites, some of which, such as the tetracyclines and aflatoxins, have considerable importance. This possibility was first considered in structural terms, namely a similarity between the anthraquinone, questin **73** and the benzophenone, sulochrin **74**. That questin in



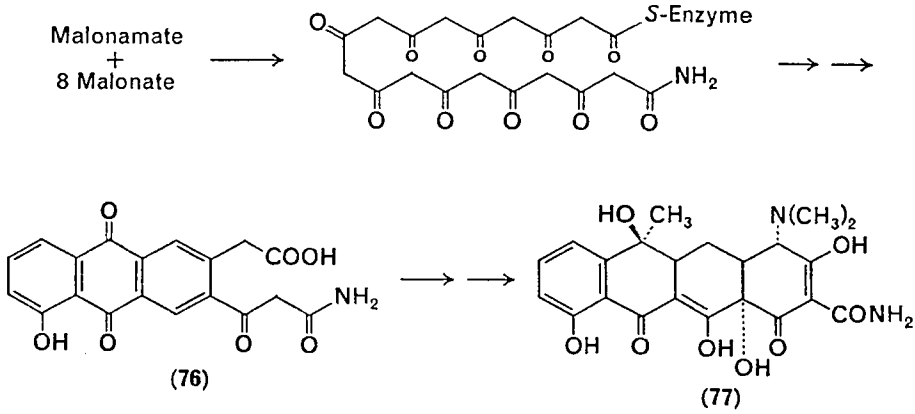
(73) (74)

fact yields sulochrin has been demonstrated directly in *Penicillium frequentans*[100] and *Aspergillus terreus*[101]. A similar type of cleavage takes place in the biosynthesis of the various ergochromes from emodin **12** in *Claviceps purpurea*. The reactions yielding ergochrome BB (**75**) are shown below[102,103]:



(12) (75)

Anthraquinone derivatives are intermediates in the formation of the important antibiotics, the tetracyclines, e.g. protetrone **76**[101] in the tetracycline **77** bisynthetic sequence shown below*. Quinones are also apparently



(76) (77)

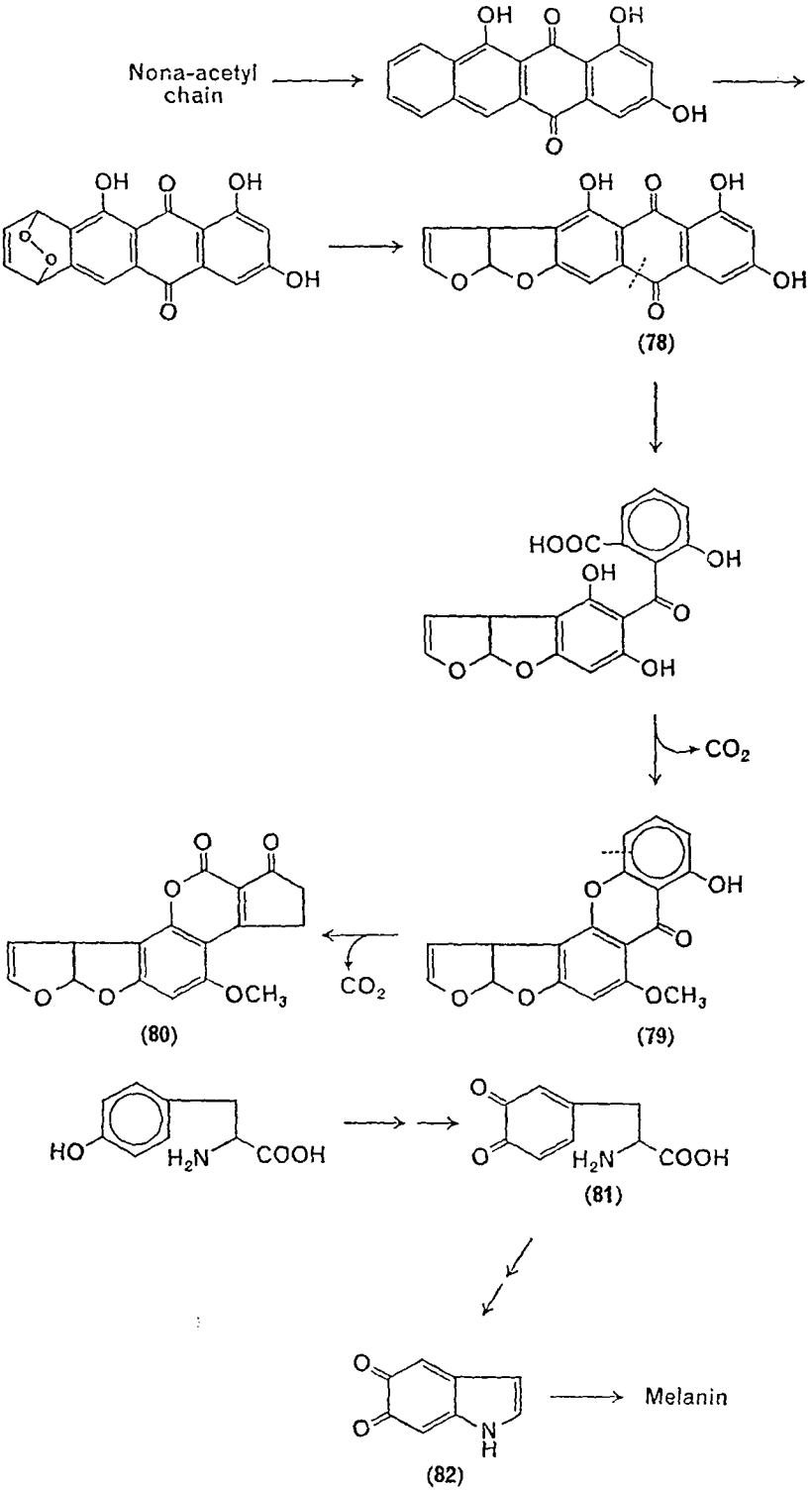
involved as intermediates in the biosynthesis of a group of interesting difurans. To account for the observed results in the biosynthesis of aflatoxins in *Aspergillus flavus*, the following pathway has been proposed[105]. The quinonoid species versicolorin A (**78**) together with its methyl ether and sterigmatocystin (**79**) has been encountered in *Aspergillus versicolor*. The final product of the sequence below is aflatoxin B_1 (**80**). Recent work on sterigmatocystin **79** in *A. versicolor* by Tanabe and coworkers[106] lends credence to this scheme of Büchi.

Although not specifically a secondary metabolite, it is convenient to note at this stage that melanin, the black polymeric pigment found in the skin, the retina and various other specialized tissues, is synthesized from tyrosine via Dopa quinone (**81**) and indole 5,6-quinone (**82**) as shown below.

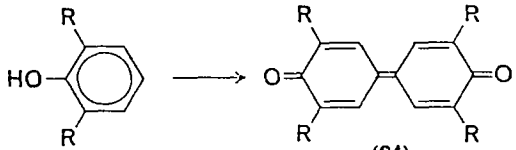
E. Polymeric Quinones

Many examples of naturally occurring polymeric quinones are known; it is likely that these are produced by the 'phenolic coupling' reaction although little direct experimental evidence is available[107]. However, unpurified enzyme preparations from *Polystictus versicolor* are reported to convert 2,6-dimethylphenol (**83**, R = CH_3) or 2,6-dimethoxyphenol (**83**, R = OCH_3) to 3,5,3′,5′-tetramethyl-diphenoquinone (**84**, R = CH_3)

* The role of malonamate as a starter unit is unique. Although generally accepted as correct, the evidence on this point is not wholly definitive.

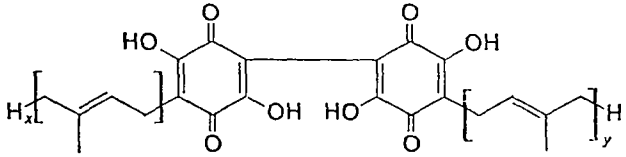

Nona-acetyl chain
OH
O
OH
OH
O
OH
OH
O
OH
O
O
OH
O
OH
O
O
OH
(78)
HOOC
OH
OH
O
O
O
OH
CO2
O
O
O
OH
O
O
O
OCH3
CO2
O
O
O
OCH3
(80)
(79)
HO
H2N
COOH
O
O
H2N
COOH
(81)
O
O
N
H
Melanin
(82)

or 3,5,3′,5′-tetramethoxy-diphenoquinone (coerulignone) (**84**, R = OCH_3), respectively[108].



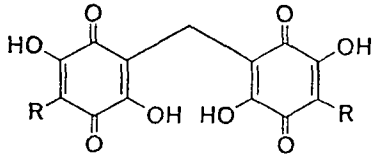
(**83**) (**84**)

Thomson's prediction[109] that the isolation of many more biquinones can be expected is being borne out. For instance, in the benzoquinone field, diboviquinones (e.g. **85** and **86**) have been isolated[110] from *Boletus* (*Suillus*) *bovinus* as well as a new member of the regular boviquinone series (boviquinone-3, nomenclature as for ubiquinone and menaquinone).



(**85**), $x = 3, y = 4$
(**86**), $x = y = 4$

Furthermore, these authors have found compounds (**87**, **88** and **89**) in which two quinone units are linked at the 6,6′-position through a methylene group; in this case, of course, more than a simple phenolic coupling is presumably involved.

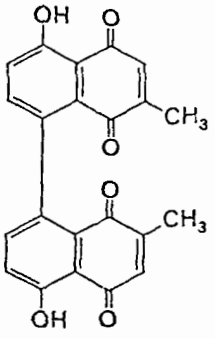


R = prenyl as in (**85**) and (**86**)

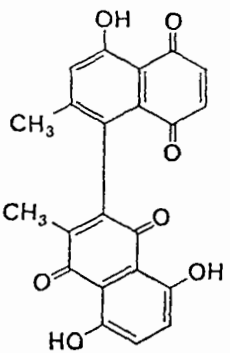
(**87**), $x = y = 3$ (**88**), $x = 3, y = 4$ (**89**), $x = y = 4$

Diospyros species are good sources of naphthoquinone derivatives and several new binaphthyls have been reported from extracts of *Diospyros kaki*, e.g. maritinone **90** and hydroxyisodiospyrin **91**[111]. Similarly, a blue pigment isolated from extracts of the sapwood of *Diospyros buxifolia* has been identified as 8,8′-dihydroxy-4,4′-dimethoxy-6,6′-dimethyl-2,2′-binaphthyl-1,1′-quinone (**92**)[112].

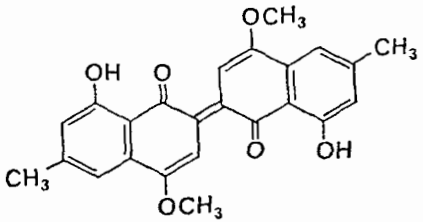
Other sources of naphthoquinones ('spinochromes') and of binaphthoquinones are various sea urchin species. From *Spatangus purpureus*,



(90)

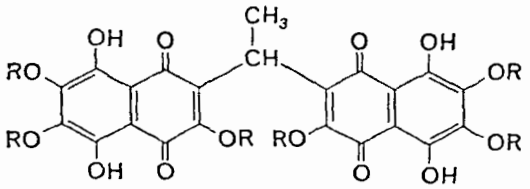


(91)



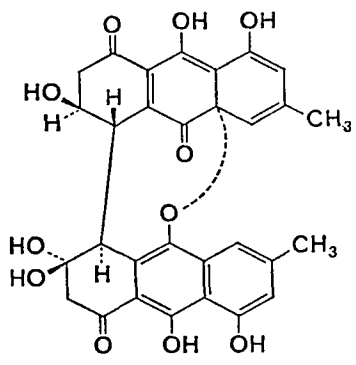
(92)

Mathieson and Thomson isolated four pigments, two of which were biquinones (**93**, **94**)[113]. The quinone units were linked by a $CH_3CH<$ group, reminiscent of the methylene linkage in the methylene diboviquinones.

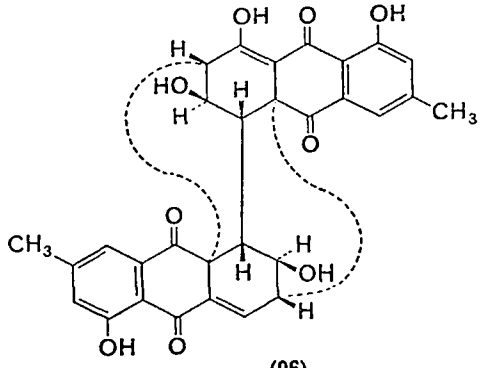


(**93**), R = H (**94**), R = CH_3

Some materials, previously reported as monomeric quinones, are now known to be polymeric. Thus, (−)-flavoskyrin, a pigment of *Penicillium islandicum*, is now formulated as **95** and is related to (−)-rugulosin **96**; it is, in fact, converted to the latter by the action of pyridine[114]. (−)-Rugulosin has been isolated from *P. islandicum* and *Myrothecium verrucaria*; the enantiomer, (+)-rugulosin, was well known as a metabolite of *Penicillium rugulosum*. The stereochemistry of these cage structures is not easily shown. In formula **96** the 'cage' is imagined to be

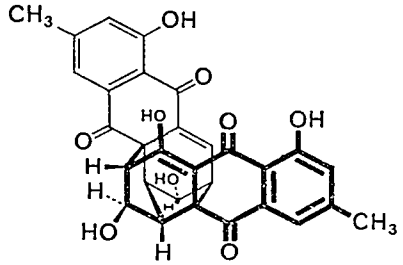


(95)



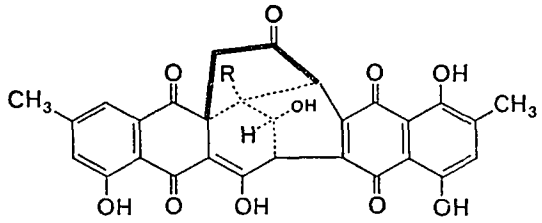
(96)

opened up by stretching two of the three bonds linking the anthraquinone units; the two anthraquinone units are then roughly coplanar. A more accurate representation of the stereochemistry of (−)-rugulosin is **97** [115].



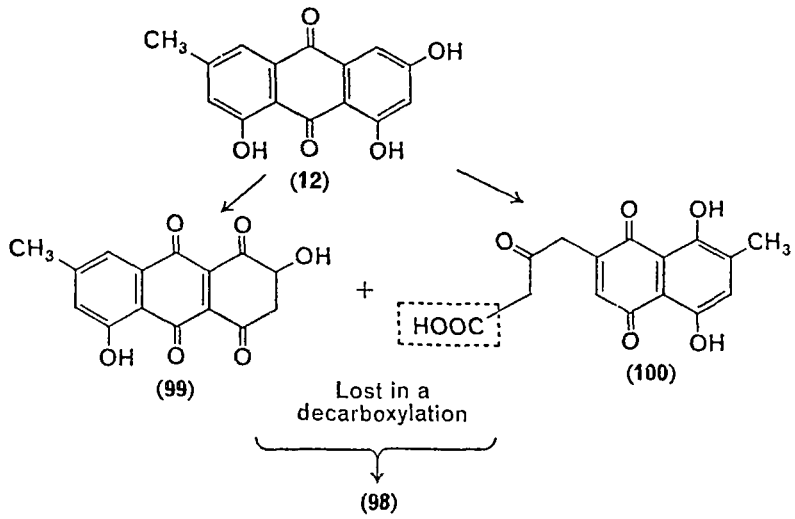
(97)

Although not strictly a dimer, the revised structure for the principal colouring matter from *Penicillium purpurogenum*, purpurogenone **98**, is of interest[116]. It has been suggested that this molecule originates from 2 molecules of emodin (**12**) (or of its carboxylic acid, endocrocin **18**) by a



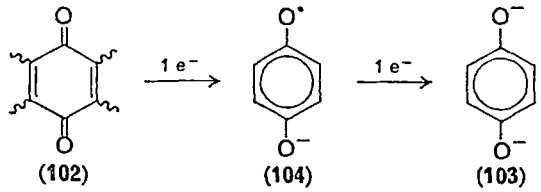
(**98**), R = OH
(**101**), R = H

complex series of reactions. A Michael addition between two systems such as **99** and **100** would be a key step. A deoxypurpurogenone, **101**, has also been isolated as a minor pigment from this fungus[117].



III. THE FUNCTIONAL SIGNIFICANCE OF QUINONES

The most important reaction of quinones as far as biology is concerned is their reversible reduction to the corresponding hydroquinone (**102–103**). This is a relatively mild chemical process, being accomplished by such gentle laboratory reagents as bisulphite and Fe^{2+}. When the reducing agent is a single electron donor, the reaction can be viewed as a two-stage process, the semiquinone, **104**, being the intermediate. Since quinones and



hydroquinones are highly conjugated species, their mutual interconversion can be followed very effectively by ultraviolet spectrometry. Moreover, since semiquinones possess an unpaired electron in their structure, their presence can be detected through the use of electron paramagnetic resonance (e.p.r.) spectrometry. Both of these techniques have been used extensively in the study of quinones in biology.

Analysis of the various quinonoid structures mentioned in the previous sections reveals compounds of two distinct classes. Firstly, there are the

biochemist's compounds, materials such as the menaquinones, the ubiquinones and the plastoquinones which even the most esoteric molecular biologist would have no trouble recognizing. Such is the case because the biological role of these substances is fairly well established, albeit sometimes not totally in molecular terms. Most of the text of this section will therefore be devoted to them (Part A). This class of material is also connoted by the term 'primary metabolite'.

On the other hand, there are in section II many examples of what the organic chemist refers to as 'natural products'. Also known as 'secondary metabolites', these materials are characterized somewhat negatively by having no firmly established role to play in the cell that makes them. True, many secondary metabolites have distinct and often profound effects on cells other than those from which they come: the inventory of any pharmaceutical company bears cogent witness to this fact. Recently, however, some wisps of insight have come into this field and these will be considered in Part B.

A. The Quinones that are Primary Metabolites

It is a well-known fact that the principal energy-yielding reactions of the biosphere are associated with the phenomena of photosynthesis and respiration. In the former, the energy radiated by the sun is trapped by green plants and by the photosynthetic bacteria and converted into the standard energy currency of cells, adenosine triphosphate (ATP), and reduced nicotinamide adenine dinucleotides (NADH/NADPH). This potential energy is subsequently used to synthesize 'energy-rich' tissue components such as carbohydrates, fatty acids and amino acids from simple, fully oxidized precursors such as carbon dioxide, nitrate, etc. These materials eventually act as foodstuffs for non-photosynthetic species. Creatures such as man degrade them oxidatively and in so doing recover, in the form of NADH, the reducing power they contained. In the process of respiration, the NADH is used to reduce molecular oxygen. Thereby ATP is generated for the use of the non-photosynthetic organism (energetically speaking therefore, the non-photosynthetic organism has vicarious communion with the sun!). In both photosynthesis and respiration, the potential energy form that is transduced into metabolically useful energy is a redox potential gradient. Discharge of this gradient by a series of coupled chemical redox reactions leads to the synthesis of ATP. Since the redox gradient discharge necessarily involves electron movements, the series of coupled reactions is frequently referred to as an electron transport chain.

As will be amplified in the following section, the redox reaction, quinone $\rightleftharpoons$ hydroquinone, constitutes one of the elements of the electron transport chain found both in photosynthesis and in respiration. For ease of discussion, procaryotes (organisms such as bacteria and the blue-green algae whose cells lack nuclei) and eucaryotes (organisms such as animals, plants, fish, fungi, green, brown and red algae, etc., whose cells possess nuclei) will be considered separately.

1. Photosynthesis in eucaryotes[118–123, 126]*

Photosynthesis in green plants and the eucaryotic algae is conducted in special, membrane-encompassed, subcellular organelles called chloroplasts. These relatively large bodies have been the subject of much electron microscopy and the details of their structure are now well known[124]. The operational unit appears to be the thylakoid disc.

Chemical analysis of whole chloroplasts indicates that several quinonoid species are present[29, 122, 125, 126]. Plastoquinones, **35**, are the major constituents and the entities believed to be obligatorily involved in photosynthesis; phylloquinone and several tocopherolquinones have also been found, but have been attributed no definite role to date. Some doubt exists as regards which specific member(s) of the plastoquinone family is (are) involved naturally. The prenylogue with nine isoprene units (PQ-9 $\equiv$ PQ-A)† is the member most frequently encountered and the substance most commonly used in experimental work. Different chain lengths and derivatization states have been encountered, however. Thus materials with phytyl side-chains, hydroxylated side-chains (the PQ-C/D group and PQ-Z), ester functions in the side-chain (PQ-B and PQ-Z) and monomethyl quinols have been isolated, while PQ-C and -B have all been further fractionated[29, 126–129].

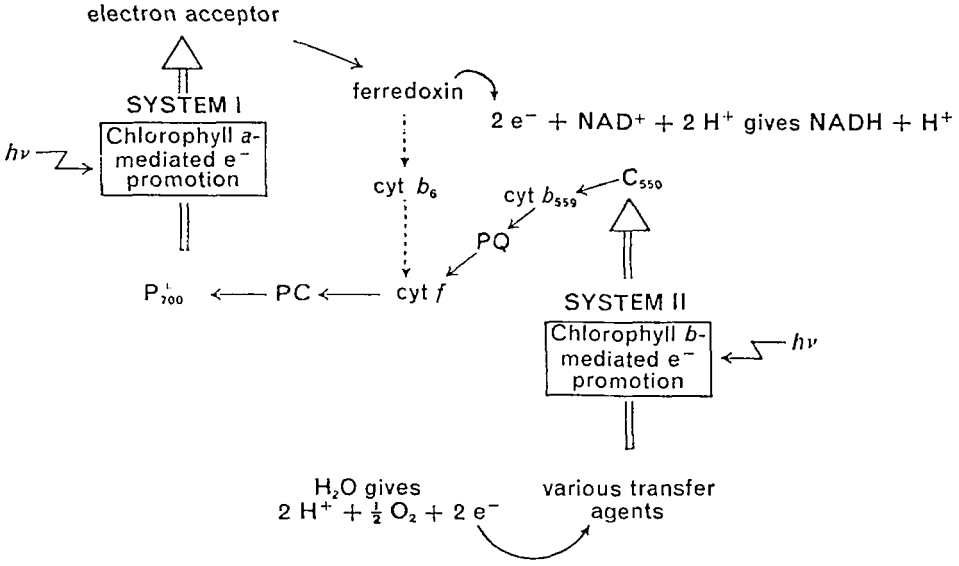
It seems clear that methods such as partition chromatography, gel filtration and mass spectrometry, which were so effective in the fields of menaquinone multiplicity, will be needed to resolve fully the question of plastoquinone composition[130, 131]. Moreover, these analytical methods will need to be applied very judiciously if their results are to have real biological function significance. Cognizance will need to be taken of the facts, established by Lichtenthaler[132], that (i) plastoquinone pools are

* Since consideration is concentrated on the role of quinones in these various processes, a series of review references is provided for those readers seeking more complete coverage of the topic.

† PQ = plastoquinone. PQ-*n* = plastoquinone with *n*-prenyl units in the side-chain.

associated with two distinct chloroplastic subfractions, the photoactive lamellae and the photoinert plastoglobuli and (ii) plastoquinone levels fluctuate widely with the age and physiological state of the chloroplast.

The general context in which the plastoquinones operate in photosynthesis is shown in Figure 1, but this scheme is far from being the final



PC = plastocyanin; PQ = plasto-quinone; cyt = cytochrome.

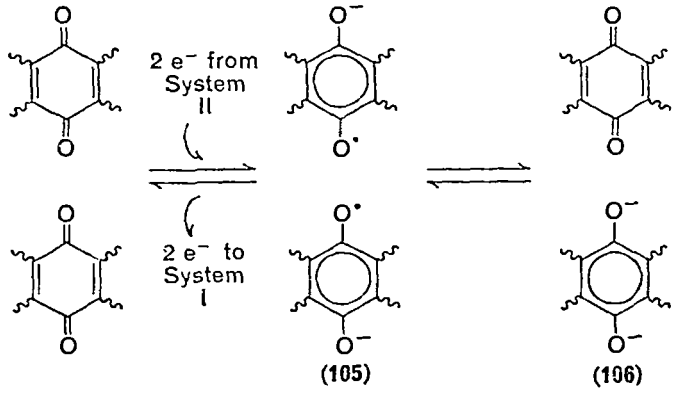
FIGURE 1. Note how the 2-electrons extracted from water are eventually made available for the reduction of NAD^+.

word. It has suffered many alterations and expansions since it was first introduced in 1963[133]; many more can be expected. Notwithstanding the general air of uncertainty, the basic principles are easily appreciated. Starting from the right-hand side, light of short wavelength (< 680 nm) activates chlorophyll *b* * molecules causing electrons to be excited and consequently transferred to an acceptor species referred to cryptically as C_{550} (this is the compound *Q* of former literature)[134]. By this simple process the necessary redox gradient is established. In response to the redox pressure it creates, electrons flow into the oxidized chlorophyll *b* via various transfer agents from water. Meanwhile, the electrons donated by chlorophyll *b* to C_{550} tumble down the redox gradient that consists in

* Chlorophyll *b* is the agent in green plants; chlorophyll *c* is the agent in the brown algae, chlorophyll *d* in the red algae.

part of a low potential form of cytochrome b_{559}[135,136], plastoquinone, cytochrome f[137] and plastocyanin. At this point, the electrons serve to discharge the oxidizing pole of another photo-established redox gradient. This second photo promotion involves chlorophyll a (in all species), long wavelength light (> 700 nm) and the electrons are eventually donated to NAD. The electron passage from reduced C_{550} to oxidized P_{700} is coupled in a way not yet fully understood to the synthesis of ATP*.

Many of the details of the electron transport chain through the plastoquinone pool have been worked out by Witt and coworkers[123,139,140]. Firstly, they have established that the electron transport chain does not exist as a series of single, isolated 'wires' made up of a single representative of each of the constituent molecules. Chains interact with each other and it appears that one of the major sites of interaction is located at the plastoquinone level. Siggel and coworkers[139] suggest that at least ten individual chains can feed into a common plastoquinone pool. On the basis of the analysis of kinetic data, they propose that electrons enter this pool as a pair from two coupled System II centres. The first-formed product is a plastosemiquinone twin **105** which subsequently disproportionates with the formation of a plasthydroquinone anion, **106**. This latter entity migrates through the pool to the appropriate acceptor



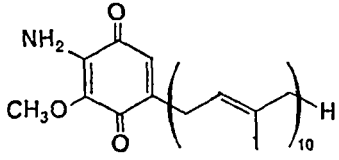
* This overall pathway can be short circuited if and when cytochrome b_6 feeds electrons from ferredoxin to cytochrome f. This pathway, leading to the direct conversion of actinic energy into ATP, is called cyclic photophosphorylation.

We also note at this time that the scheme described above has been amended somewhat by Arnon[138]. The amendation is not as yet generally accepted. It considers System I to be divided into two; one part executing cyclic photophosphorylation exclusively, the second part coupling in the manner we have described with System II.

location, reforms the plastosemiquinone twin and discharges its two-electron complement, presumably to a pair of single-electron acceptors. The scheme neatly explains how single and paired electron redox agents can operate in consort. The pool concept also helps to rationalize the observed fact that plastoquinones are found in great molar excess relative to the cytochromes, etc.

2. Photosynthesis in procaryotes[141–143]

Several species of bacteria (green and purple) and the blue-green algae can also harness the energy of sunlight to the synthesis of ATP and the generation of a reduced nicotinamide derivative. This they do, not in chloroplasts, but in specialized cell membrane locations isolable as chromatophores. Ubiquinone **1** is the main quinonoid material found in the electron transport chain of bacteria, although it is not exclusive[29, 122, 126]. Thus *Rhodospirillum rubrum* contains the substance rhodoquinone **107**, vitamins K_2 (**2b**) are found in various photosynthetic bacteria, and species of *Chlorobium* contain the compound, chlorobiumquinone **108**, unusual in that it contains a keto grouping in the side-chain. Also, the length of the polyprenyl side-chain found in the ubiquinone alters from one



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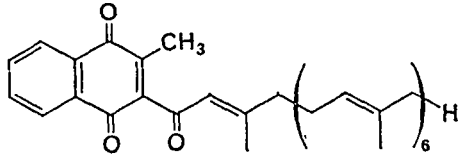


(108)

organism to another: ubiquinone-7 through ubiquinone-10 being common. Mixtures are also found within the same organism. Thus, *R. rubrum* has been shown to contain ubiquinone-1 through ubiquinone-10[144].

In some ways, the photosynthetic process is simpler in bacteria than in green plants since bacteria do not possess an analogue of Photosystem II, i.e. they do not oxidize water to molecular oxygen. In some other ways, however, they are much more complex. There is thus not the same degree of uniformity from one organism to another as is found in eucaryotes,

and multiple pathways are not uncommon. The review by Frenkel established these points effectively[142]. Moreover, the production of reduced NAD can be accomplished in at least two ways. For the present purpose, however, it is sufficient that we note the general pattern of events (Figure 2).

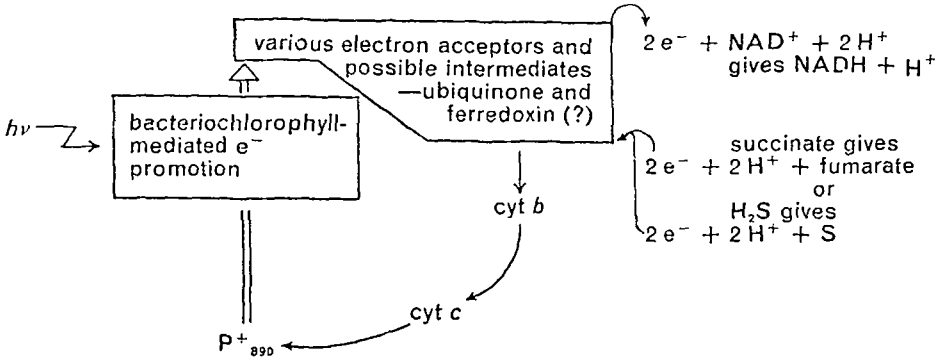


FIGURE 2. Note how the 2-electrons extracted from substrates such as succinate etc. are eventually made available for the reduction of NAD^+.

As in eucaryotic photosynthesis, a primary photo event creates an oxidizing agent and a reducing agent and thereby sets up a redox gradient. The photoactivator is a set of specially situated bacteriochlorophyll molecules: the species P_{890}. The reducing pole of the redox gradient is coupled directly to the oxidizing pole via a series of ATP-producing reactions. Ubiquinone is one of the electron carriers in this chain and it has been suggested recently that in *Rhodopseudomonas spheroides* ubiquinone is in fact one of the primary electron acceptors[145]. NADH (or NADPH) is formed either in the photoreduction manner described for eucaryotes, using electrons derived from substrates such as succinate or hydrogen sulphide, or by an ATP-catalysed reversal of oxidative phosphorylation (see later). In these organisms, it is not certain as yet whether the ubiquinone functioning in the photophosphorylation process is spatially distinct from that functioning in respiration.

3. Respiration in eucaryotes[122, 126, 146–154]

Ubiquinones are also implicated in the electron transport chain associated with eucaryotic respiration. This process is conducted in special subcellular organelles, the mitochondria. In view of what has been discussed above, it will be no surprise to learn that side-chain length

variability is found in the mitochondrial quinones. Ubiquinone-10 is the predominant form found in vertebrates, but ubiquinone-6 through ubiquinone-9 are found as major forms in yeasts and plants[29, 122, 126]. Beef heart muscle, the tissue used extensively in respiration investigation, appears to produce ubiquinone-10 exclusively. It is interesting to note that sometimes ubiquinones with shorter chain lengths markedly out-perform the natural material in *in vitro* experiments[155].

Respiration involves the overall oxidation by molecular oxygen of the reducing equivalents that have resulted from metabolic degradation of ingested foodstuff. The principal source of these equivalents is the citric acid cycle. Pyruvate, isocitrate, malate and 2-ketoglutarate dehydrogenases yield reduced NAD while succinate dehydrogenases yield reduced flavin adenine dinucleotide (FAD). Both these entities can also be formed from fatty acid degradation (hydroxy fatty acyl CoA dehydrogenase, NADH; fatty acyl CoA dehydrogenase, $FADH_2$). The $NAD^+/NADH$ system has a standard electrode potential of $-0{\cdot}32$ volts, the $FAD/FADH_2$ system has a corresponding value of $-0{\cdot}19$ volts, while the $\frac{1}{2}O_2/OH^-$ system records a value of $+0{\cdot}82$ volts. The redox gradient between the former two and the latter one is spanned by a series of reactions which involve cytochromes of the *a*, *b* and *c* type. The reader will notice that there is no immediate external energy input to the process of respiration.

Until recently, the general consensus of bioenergetic opinion was that ubiquinone fitted into the electron transport chain on the substrate side of cytochrome *b*. It was seen to act as a kind of chemical electron transport interface between the various flavoprotein dehydrogenases and the chain of cytochromes which accomplished the eventual reduction of oxygen (Figure 3). As with the pools of plastoquinone in photosynthesis, the ubiquinone molecules were considered to diffuse freely in the lipophilic medium of the membrane. In support of this role for ubiquinone in respiratory electron transport was the fact that pentane extraction of lyophilized mitochondria yielded a product which, when warmed and resuspended in buffer, was not able to conduct electron transport. Viability could, however, be restored by addition of ubiquinone-10 or a lower prenylogue[156]. Moreover, methods of mitochondrial fractionation have been developed which allow four complexes to be isolated which together are able to conduct electron transport in its entirety[157]. It was found that complex I reduced ubiquinones at the expense of NADH, complex II reduced ubiquinone at the expense of succinate, and complex III reduced cytochrome *c* at the expense of reduced ubiquinone*.

* Complex IV reduced oxygen at the expense of reduced cytochrome *c*.

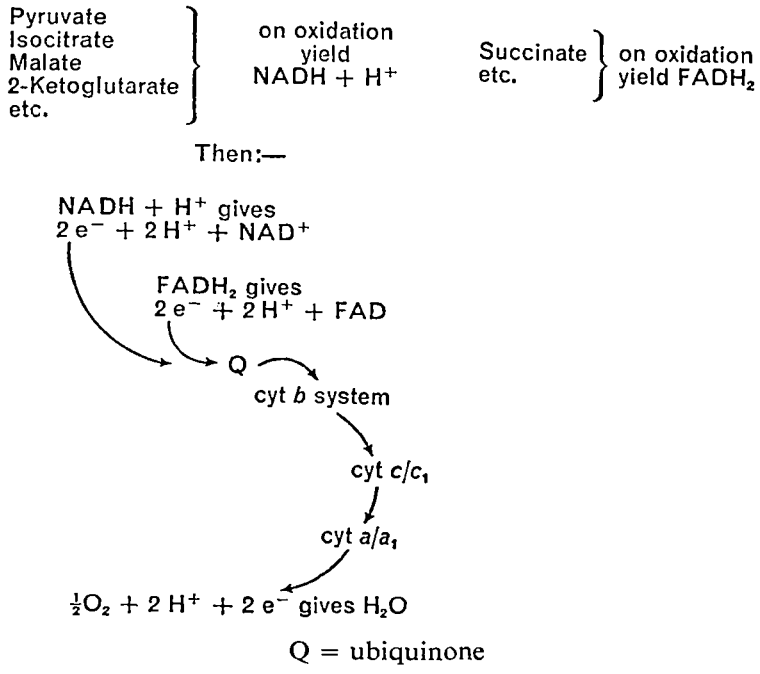


FIGURE 3.

Recent work on several fronts has demonstrated that such a simple representation is inadequate. The reviews by Slater[153] and Chance[154] indicate just how complex the situation has become. Of greatest significance to the quinonoid issue, and therefore the only topic we will consider here, is the finding in several laboratories that under certain conditions succinate dehydrogenase can be coupled to the cytochrome *b* ensemble in the absence of ubiquinone[158–161]. Further evidence that the electron path from succinate to oxygen does not actually pass through ubiquinone is the observation[162,163] that ubihydroquinone may be a NADH-sensitive, conformational-altering activator of succinate dehydrogenase. This activator role for ubiquinone would provide a possible explanation for the fact that in restitution experiments with pentane-extracted beef heart mitochondria, the succinate dehydrogenase complex could be reconstituted equally well with ubiquinones-2 through -10, while the NADH dehydrogenase was quite specific for ubiquinones-7 through -10[164,165]. Thus once again uncertainty rises vis-à-vis the obligatory nature of ubiquinone's involvement in electron transport[166]. This time, however, the question is not so far-reaching since there seems no doubt that ubiquinone is required to link NADH dehydrogenation with cytochrome *b* reduction[167].

Nothing comparable to the Witt–Siggel–Stiehl[123,139,140] analysis of the electron flow into the plastoquinone pool has yet been done for the ubiquinone pool in respiration. It is, however, known that free radicals, presumably semiquinones, are involved[168].

4. Respiration* in procaryotes[122, 147, 205]

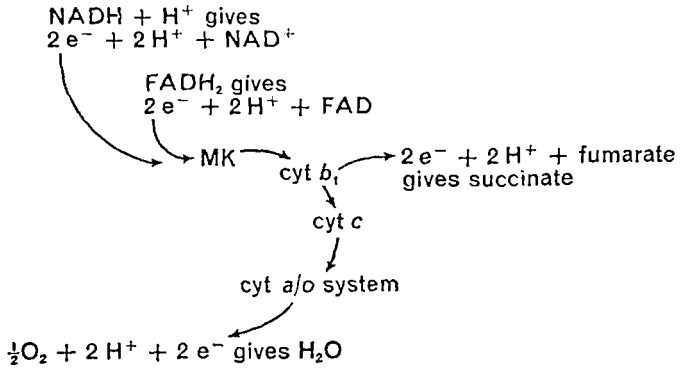
We have seen earlier that procaryotes have no chloroplasts yet some of them can conduct photosynthesis; likewise they have no mitochondria, but they can respire. The respiratory centres are found bound to the cytoplasmic membrane. Two quinone types are found in such centres, menaquinones and ubiquinones[29,122,126]. In general, the menaquinones are found in Gram-positive species while the ubiquinones are found in Gram-negative ones[169]. Some of the enterobacteria, e.g. *E. coli*, contain both ubiquinones and menaquinones. As in the case of the eucaryotic respiratory quinones, they exist in a high molar excess relative to the other electron transport chain components and exhibit some structure diversity. For instance, hydrogenated menaquinone side-chains have been found in *Mycobacterium phlei*[170] and species of *Streptomyces*[171,172]. The full range of ubiquinones from ubiquinone-1 to ubiquinone-8 has been found in *E. coli*[144].

Where an organism contains only a single quinone type, the general trend of the experimental analysis to date is that the quinone participates in the electron transport chain in a manner analogous† to that described above for the eucaryotes, i.e. it acts as a collection funnel for the electrons derived from the action of the various NAD- and FAD-linked dehydrogenases of the cell. The experimental evidence has been obtained from pentane-extraction/quinone-replacement studies, reduction extent and time course examinations and work with chain inhibitors. The general pattern proposed by Kröger and Dadák[174] for *Bacillus megaterium* can be taken as typical for several bacteria (Figure 4). Note how, in the absence of molecular oxygen, after the electrons have passed from the menaquinone pool through cytochrome *b*, they can be used to reduce fumarate. All NADH-forming substrates seem to have equal access to the menaquinone pool; a measure of compartmentalization was found in a similar

* The term 'respiration' is used here a little loosely to preserve the continuity of the discussion. It must be noted, however, that many bacteria are able to use materials other than molecular oxygen as the terminal oxidant of the electron transport chain, e.g. the nitrogen-fixing bacteria, the anaerobes, etc.

† The bacterial cytochromes differ somewhat from the eucaryotic type. In particular, a cytochrome *o* acts in consort with the cytochromes of the *a* type in the final reduction of oxygen[173].

study as far as the demethylmenaquinone pool was concerned in *Hemophilus parainfluenzae*[175]. E.p.r. signals possibly emerging from menasemiquinonoid species have been detected in *Mycobacterium phlei*[176]. Whether or not this scheme is oversimplified remains to be seen.



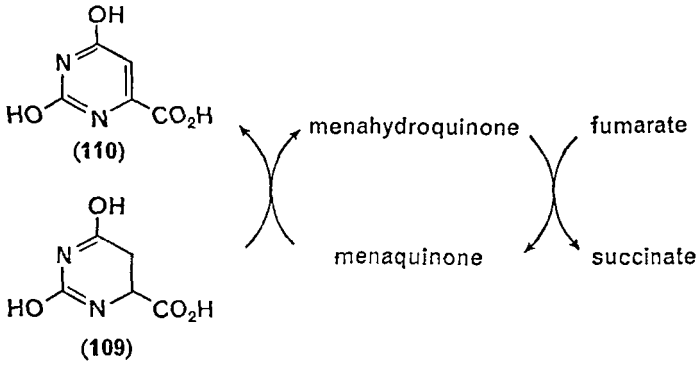
MK = menaquinone

FIGURE 4.

In organisms where ubiquinones and menaquinones co-exist, the roles of the two species seem to be divided. Some ten years ago, work by Kashket and Brodie[177] suggested that in *E. coli* menaquinones were exclusively associated with NADH oxidation, while ubiquinones took care of succinate oxidation. Recent work has revised the nature of this division of labour. In a detailed study using *E. coli* mutants lacking the power to make menaquinones and/or ubiquinones, Cox, Gibson and coworkers[178,179] showed that menaquinones were needed for anaerobic growth, while ubiquinones were needed for aerobic growth. Thus the entire responsibility for electron transport *into oxygen* was attributable to ubiquinone. Inhibitor studies, however, constrained these workers to conclude that ubiquinone was not functioning as a single, isolated component of the chain, but as an obligatory part of *two* iron–ubiquinone complexes. One of these was situated before cytochrome *b*, the other on the oxygen site of that cytochrome. E.p.r. studies suggest that ubisemiquinones participated[180]. Thus the low seven-eighths of the iceberg of complexity are beginning to show in procaryotic respiration!

The function of menaquinone in *E. coli* was more conclusively defined by the same study. Its principal role was not as a component of the respiratory chain, but as a cofactor in that step of pyrimidine biosynthesis leading

from dihydroorotate **109** to orotate **110**. This oxidation is conducted at the expense of fumarate, thus:

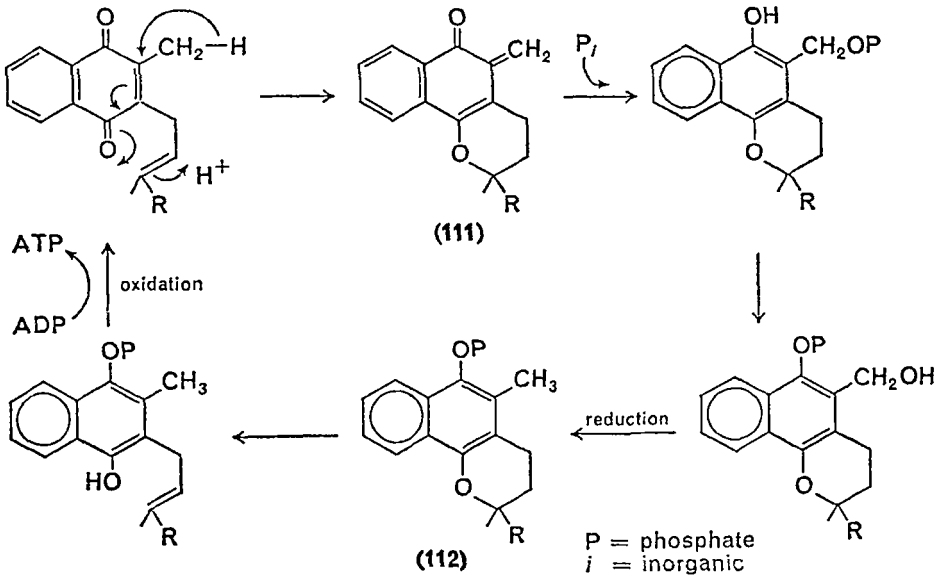


A similar pattern of menaquinone/ubiquinone function was found by Kröger and coworkers[181] to pertain in another enterobacterium, *Proteus rettgeri*. Thus, ubiquinone was shown to be on the *direct* path for electron transport from succinate, formate and NADH to oxygen and was situated at a point on the substrate side of cytochrome *b*. The menaquinone component was shown to be involved in the anaerobic discharge of reduced NAD (and formate) into fumarate through the action of the enzyme fumarate reductase. Further metabolism of the succinate so formed presumably required the succinate dehydrogenase/ubiquinone/cytochrome chain.

The involvement of menaquinones in anaerobic growth, demonstrated by Cox and Gibson and coworkers and by Kröger and coworkers is in harmony with the known fact that facultative anaerobes which contain both ubiquinone and menaquinone form higher relative proportions of menaquinone when grown anaerobically[182].

There is a tradition in the discipline of physics that if an hypothesis is simple and theoretically beautiful, the chances are that it is based on reality. Some years ago, such an hypothesis was proposed in relation to quinones and oxidative phosphorylation[183], the process in respiration whereby the energy derived from the redox gradient is actually converted into ATP (see reference 184 and 185 for the early history of this hypothesis). It was applicable to procaryotes and eucaryotes, but since most investigative work was performed with *M. phlei*, it will be considered here. The scheme involved the formation of a quinone methide **111** which picked up inorganic phosphate (P_i) and eventually transferred this unit to ADP as shown. The scheme was supported by the finding that 6-chromanyl

phosphates such as **112** could reduce cytochrome *c* and convert ADP to ATP when incubated anaerobically with appropriate extracts of *M. phlei*[186]. Despite its inherent plausibility and beauty, the weight of experimental evidence[187] is now against this scheme. Current thoughts on the mechanism of oxidative phosphorylation are contained in references 152–154.



(111)

(112)

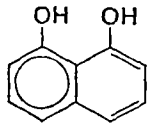
B. The Quinones that are Secondary Metabolites

Two observations emerge from Part A of this section which are particularly striking. Firstly, the structures of plastoquinones, ubiquinones and menaquinones are markedly alike. They all possess polyprenyl side-chains and can be deemed formally substituted benzoquinones. Secondly, and with the exception of chlorobiumquinone and rhodoquinone, there is little species specificity. The same ubiquinone which powered the muscles of a Caesar's conquering hand provides the lowly alga with its energy needs. This latter feature is a characteristic of all primary metabolites. In contrast thereto, secondary metabolites exhibit great species specificity sometimes even being strain-specific. It is this fact, maybe more than any other, that has made the problem of determining their function so difficult.

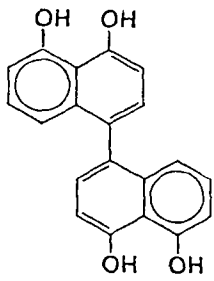
An interesting avenue of exploration has opened up with the demonstration that quinones are found in the defensive secretions of several arthropods[188a, b]. By far the most spectacular defence mechanism is that

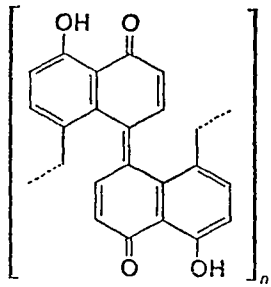
of the bombardier beetles[189]. When threatened, these creatures jet onto their assailant a concoction of benzoquinones in hydrogen peroxide! Several substitution patterns are found in the benzoquinone armoury of the arthropods, viz. ethyl; 2,3-dimethyl; 2,5-dimethyl; 2,3,5-trimethyl; methoxy; 2-methoxy-3-methyl[188b]. Recently 6-methyl, 6-ethyl, 6-propyl and 6-butyl-1,4-naphthoquinones have been identified in the defensive secretions of the tenebrionid beetle, *Argoporis alutacae*[190].

Along similar lines of function should be considered the 'fungal melanins'[191]. The sporophores of species of *Daldinia* are darkly coloured due to the investment of their cell walls with quinonoid polymers such as **113**[192]. This polymer can be formed by phenol coupling of 1,8-dihydroxynaphthalene (**114**).



(114)





(113)

Not all the secondary metabolites, however, can be considered to have a defensive or structural role. In an attempt to rationalize the existence of the phenomenon itself, Bu'Lock[193] proposed that secondary metabolism is the organism's response to exhaustion of a specific nutrient from the environment. This nutritional deficiency causes a 'dislocation' in the organism's primary metabolic process, a 'dislocation' which takes the form of momentarily elevated levels of a few primary metabolites such as acetate, mevalonate, shikimate, etc. These elevated pool sizes trigger the production of secondary metabolite synthases and secondary metabolism is under way. In this manner, the organism protects itself from undue over-accumulation of any primary metabolite. Bu'Lock's ideas have been amplified in two recent reviews by Weinberg[194,195]. While this concept of secondary metabolite function has much to commend it, and may, in fact, be correct in many situations, it is not the complete answer. Many secondary metabolites, both quinonoid and otherwise, are formed before any nutritional deficiency can possibly be felt, e.g. lawsone production in developing cultured root tips of *Impatiens balsamina*[196]. For such materials, our search for functional significance must continue.

IV. EPILOGUE

It is apparent that quinones play a variety of roles in our overall life cycle and that interest in their biological function has stimulated basic chemical research in several areas. The use of quinones, in fact, dates to antiquity and the recorded and verifiable history of these compounds is perhaps longer than that of any other group of naturally occurring compounds. Quinones came to man's attention in two ways—as pigments and as drugs.

As drugs, the use of crude preparations of various plants as purgatives has been recorded for well over 4000 years. Rhubarb, which contains various anthraquinones, is described in the Chinese herbal, *Pen-king*, believed to date from 2700 B.C.[197]. The use of senna was introduced by the Arabs who described its properties as early as the 9th century[198]. Its use survives today even in Europe and the United States and many other plant extracts have been used for the same purpose.

As pigments, two materials stand out, henna and madder. Henna is a paste of powdered leaves of *Lawsonia inermis* and has been used since antiquity as a cosmetic. It was considered indecent in ancient Egypt not to dye the fingernails with the orange-red colour of this preparation and many mummies have been found so decorated. It has also been used to dye parts of the hands, feet, hair and beard, as well as the manes of horses. Henna is believed to be the 'camphire' of *The Song of Solomon*[199] and was also used in the preparation of Moroccan leather[200]. The active principle is 2-hydroxynaphthoquinone (lawsone). Even in 1972, henna preparations are still used to dye hair (in the United States)[201]; to the younger hairdressers who are 'into ecology', it has the advantage of being a natural substance unassisted by chemistry!

Madder, a preparation of the root of *Rubia tinctorum* and other plants, contains the anthraquinone, alizarin. Cloth dyed with madder (which has not faded) has been found on Egyptian mummies, and it is also said to have been used to dye the cloaks of Libyan women in the days of Herodotus[202]. Madder was also used as a drug (to treat amenorrhea) by the ancients and in the Middle Ages.

A recent investigation of human bones from the cemetery at Qumran has provided evidence that the diet of this Dead Sea community included the madder plant. Alizarin has long been known to have a selective affinity for bone-forming areas of the skeleton and when growing animals are fed on madder, or subject to alizarin injection, the extremities of the long bones are particularly stained. Seven of ten skeletons from Qumran were likewise stained and a definite identification of alizarin was possible by infrared spectometry. It is known that madder root was made into

garlands by Jews from the second century B.C. to the second century A.D. as a preventive against witchcraft. Arabs still make a sherbet drink of madder which protects against the 'evil eye'. The concrete evidence for the dietary use of madder by the Essenes identifies a cultural custom persisting for at least 2000 years[203].

Madder was a major commercial dyestuff of considerable importance until the present century. The chemical synthesis of alizarin from anthracene by Graebe and Liebermann in 1868 and the development of a viable commercial process by Sir William Perkins (1869) are, of course, milestones in the history of organic chemistry. Synthetic alizarin was placed on the market in 1871 (for historical review, see Fieser[204]).

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The Chemistry of the Quinonoid Compounds
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CHAPTER 14

Electrochemistry of quinones

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I. INTRODUCTION

Simple quinone–hydroquinone couples are perhaps the most thoroughly studied organic redox couples. Discussions of the quinhydrone electrode are included in most instrumental analysis and elementary physical chemistry textbooks and can be found in some freshman chemistry books. The half-reaction (1) is presented as a typical reversible couple whose

$$Q + 2\,H^+ + 2\,e^- \rightleftharpoons QH_2 \qquad (1)$$

potential is rapidly established at an electrode surface and obeys the Nernst equation.

$$E = E^0 + \frac{RT}{2F}\ln\frac{a_Q}{a_{QH_2}} + \frac{RT}{2F}\ln a_{H^+}^2 \qquad (2)$$

In these equations and throughout this chapter, Q represents the oxidized, or quinoidal form, QH_2 represents the hydroquinone form, and a_i is the activity of the ith species. The remaining terms in equation (2) have their usual significance. Under ordinary polarographic or potentiometric conditions equilibrium behaviour is observed for equation (1) and potentials of quinhydrone couples readily give solution pH values. But when the electrode kinetics of quinhydrone couples are examined closely, non-textbook complexities are evident.

Since quinone couples are easily studied and often readily available, they have been used as test cases for experimental verification of various theoretical models. Thus a wide range of ideas and methodologies have been applied to the interpretation of the electrochemical behaviour of quinone couples. Approaches to the study of quinone electrochemistry range from classical Tafel plots to pure voltammetry to synthetic organic chemistry. The outline chosen for this review is primarily mechanistic in nature. Contributions to the understanding of the kinetics and mechanisms of quinone and hydroquinone electrode reactions are reviewed. Both homogeneous and heterogeneous reactions are included. Electrode reactions of *ortho* and *para* quinones are emphasized; the isoelectronic quinonediimines, the phenylenediamines and their derivatives are mentioned only in passing. Purely analytical applications are not included.

The literature coverage is not intended to be complete, the emphasis being on the last fifteen years although an attempt has been made to include the important early polarographic papers. The pioneering potentiometric studies of Michaelis, Fieser and others are not dealt with as this work is well covered in the monograph by Clark[1]. Literature coverage for this chapter extends into early 1972.

The electrochemistry of quinones has been reviewed previously. The relevant chapters in the books by Kolthoff and Lingane[2] and by Brezina and Zuman[3] are excellent introductions to the older polarographic literature. The latter is especially strong on the analytical applications to physiological and biological samples. Quinones are also covered in the comprehensive text by Heyrovsky and Kuta[4], in the book on non-aqueous electrochemistry by Mann and Barnes[5] and in the monograph by Adams[6]. The chapter by Peover[7], who has made major contributions to modern quinone electrochemistry in non-aqueous solvents, is quite useful in this area. The biennial reviews in *Analytical Chemistry* by Wawzonek and more recently by Pietrzyk[8-13] contain sections on quinones and are an extremely useful and complete source of references.

None of these reviews contains an extensive survey of the kinetic and mechanistic aspects of the quinone electrode reactions and it is hoped that this chapter will fill that void.

II. HALF-WAVE POTENTIALS

A. Aqueous Solutions

Quinone reductions at the dropping mercury electrode (d.m.e.) are often electrochemically reversible and consequently polarographic half-wave potentials ($E_{\frac{1}{2}}$) of quinones are good approximations to potentiometric formal standard potentials, $E^{0\prime}$ values. These terms are related by the familiar equation (3) at 25°C where the potentials are given in volts.

$$E_{\frac{1}{2}} = E^{0\prime} - \frac{0{\cdot}06}{n} \log \sqrt{\frac{D_{ox}}{D_{red}}} \tag{3}$$

If the ratio of the diffusion coefficients of the oxidized and reduced forms of a couple is within 10% of unity, as is usually the situation for quinone couples, we have equation (4).

$$E_{\frac{1}{2}} = E^{0\prime} \pm 0{\cdot}001 \text{ V} \tag{4}$$

The polarographic experiment is less tedious than the potentiometric one and $E_{\frac{1}{2}}$s for a great variety of quinones in various mixed solvents are scattered throughout the chemical literature. The variety of experimental conditions (solvent, pH, supporting electrolyte, buffer components, etc.) makes a summary of $E_{\frac{1}{2}}$ data in aqueous solutions impracticable here. The monograph by Zuman[14] contains an outstanding compilation of the older $E^{0\prime}$ and $E_{\frac{1}{2}}$ data in the chapter on quinoidal compounds. Recent reports which contain extensive $E_{\frac{1}{2}}$ data on quinones in aqueous solution include the following series: 121 pyrocatechols[15], 27 pyrocatechols[16],

104 substituted 1,4-naphthoquinones[17], 35 sulphonyl derivatives of benzohydroquinone[18], 43 benzoquinones[19], 15 thio- and phenylsulphonyl benzoquinones[20], 25 benzohydroquinones[21], 12 halogenated and sulphonated 9,10-dihydroxyanthracenes[22], 23 substituted amino derivatives of benzoquinone[23] and 26 aminoquinones and quinone thioethers[24].

B. Non-aqueous Solutions

Table 1 in the Appendix to this chapter lists half-wave potentials for quinones in non-aqueous solvents. The first value listed usually corresponds to the reduction potential for the simple one-electron process (5),

$$Q + e^- \rightleftharpoons Q^{\cdot -} \tag{5}$$

to form the semiquinone anion. A second electron can be added to most quinones at more negative potentials and other waves may be present as well. The potentials for these waves are given in Table 1 when they are available.

Many of these $E_{\frac{1}{2}}$ values are referenced against an aqueous saturated calomel electrode (s.c.e.). Unfortunately, due to the variable liquid junction potentials which are encountered with this electrode in non-aqueous solvents, the aqueous s.c.e. is recognized as a poor choice for a non-aqueous reference electrode. The Ag/Ag^+ couple is often used as a basis for a non-aqueous reference electrode and is a superior choice to the s.c.e. However, when $E_{\frac{1}{2}}$ values are measured in non-aqueous solvents, some attempt should be made to relate the potential of the reference electrode used to the aqueous s.c.e. so that a comparison with the literature is possible. Best values for the half-wave potentials in Table 1 are difficult to determine because the reference electrode and liquid junction potentials cannot be compared in many cases. The half-wave potentials in this table have been rounded off to the nearest 0·01 V. Different experimenters working on the same system have obtained no better agreement than this. However, internal precision for a given series of quinones may well be better than 0·01 V and this information is not contained in Table 1. Also, in some cases the $E_{\frac{1}{2}}$s of simple derivatives of heterocyclic quinones are not given even though the data are available in the literature. The reader is referred to the literature on the parent compound in these cases.

Table 1 is organized in the following general manner. Simple quinones and their derivatives are given first, followed by the more complex hydrocarbons and then some heterocycles. The table is not meant to be an exhaustive listing (especially for the heterocycles), but does represent a

thorough literature search through 1971 and is a good entry into the literature for systems not discussed explicitly in this chapter.

C. Substituent Effects

Substituent effects on reversible half-wave potentials of quinone/hydroquinone couples have been elegantly treated by Zuman in a 1962 paper[14,25]. Half-wave potentials and $E^{0'}$ values for several series of benzo-, naphtho- and polycyclic quinones were shown to correlate with substituent constants using a modified Hammett equation:

$$\Delta E_{\frac{1}{2}} = \rho_{\pi,Q}\,\sigma_{P-X} \tag{6}$$

In this equation $\Delta E_{\frac{1}{2}}$ is the shift in half-wave potential relative to the unsubstituted quinone, $\rho_{\pi,Q}$ is the proportionality or reaction constant in volts and σ_{P-X} is the total polar substituent constant. The latter term is based on the acid dissociation constants of a series of substituted benzoic acids,

$$\sigma_{P-X} = \log(K_{XC_6H_4CO_2H}/K_{C_6H_5CO_2H}) \tag{7}$$

and contains contributions from both polar and resonance effects. For a quinone/hydroquinone couple polar effects would be predominantly operative in the quinone form, while resonance effects would be more important in the aromatic hydroquinone or semiquinone forms. Perhaps the most spectacular success of equation (6) is afforded by the correlation of the one-electron $E_{\frac{1}{2}}$s of quinones in acetonitrile solutions[26] shown in Figure 1[14]. The reaction constant, $\rho_{\pi,Q}$, for these data is 0·53 V and a range of almost 1·4 V is covered. Because the electrode process in this solvent is a simple one-electron step, this reaction constant can be viewed as an intrinsic parameter of the electron transfer process. In aqueous solutions much lower proportionality constants are obtained (ca. 0·2–0·3 V) and substituent effects are not always additive in a series of polysubstituted quinones. As Zuman has pointed out[14], care must be taken in interpretation of $\Delta E_{\frac{1}{2}}$ values in aqueous solutions because acid–base dissociation constants of substituted quinones and hydroquinones will be influenced by the substituents. In order to apply equation (6), the experimenter must establish that the $E_{\frac{1}{2}}$ versus pH dependence is identical for each member of the series under the experimental conditions of the study. For further details the reader is referred to Zuman's monograph[14].

D. Molecular Orbital Correlations

Simple molecular orbital theory was used to interpret potentiometric E^0 values of quinones several years ago with some success[27–30]. Following

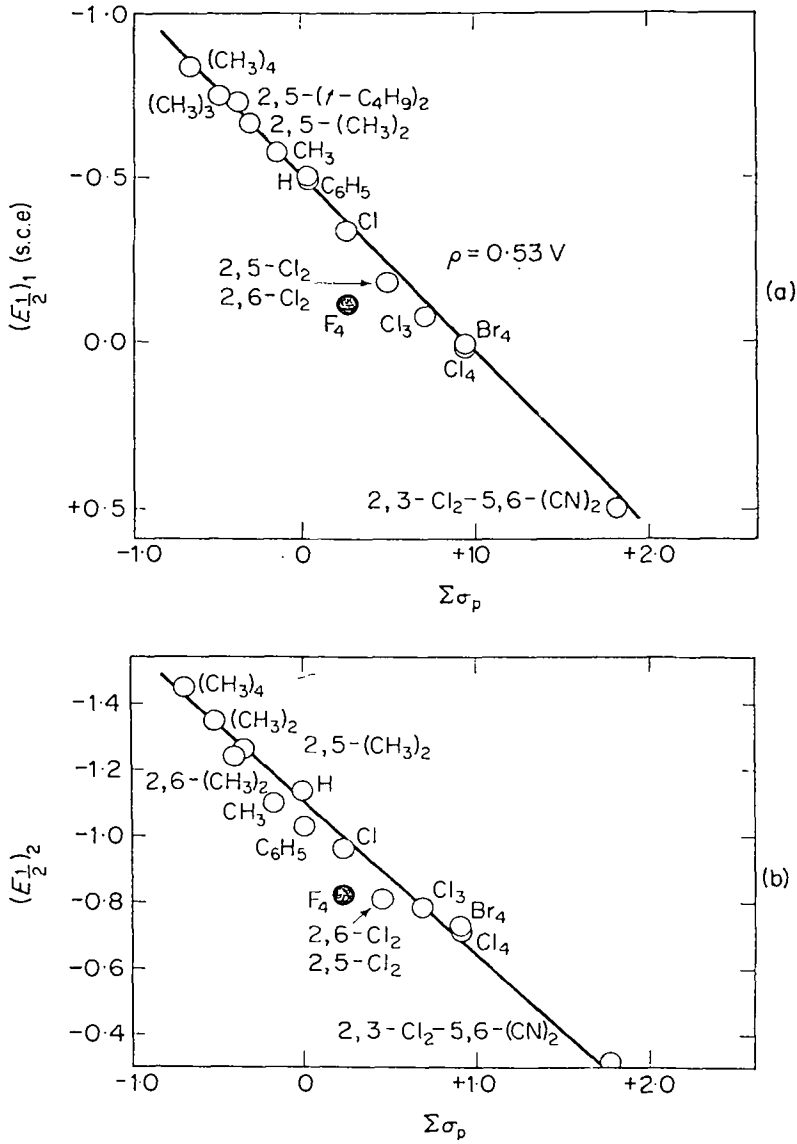


FIGURE 1. Relation of half-wave potentials for the reduction of substituted *p*-benzoquinones in acetonitrile solution to the sum of the Hammett substituent constants $\Sigma\sigma_{p-X}$. Half-wave potentials from reference 26; supporting electrolyte 0·1M $N(C_2H_5)_4ClO_4$. Value for tetrafluoroderivative (full point) deviates. (a) first wave; (b) second wave. (Reproduced with permission from P. Zuman, *Substituent Effects in Organic Polarography*, Plenum Press, 1967, Figure VIII-6, p. 287.)

Maccoll[31], who first demonstrated the relationship between electron affinities and polarographic $E_{\frac{1}{2}}$ values, equation (8) is readily derived[32].

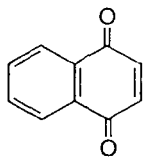
$$E_{\frac{1}{2}} = -E_{m+1} + C \tag{8}$$

Here the half-wave potential is equal to $-E_{m+1}$, the negative of the energy of the lowest unoccupied molecular orbital (l.u.m.o.), plus a constant which includes the difference in solvation energies of the neutral molecule and its radical anion. If this last term is constant, $\Delta E_{\frac{1}{2}}$ for a series of quinones should be given by $-\Delta E_{m+1}$. This relation has been demonstrated experimentally by Peover[33,34] for a limited series of unsubstituted quinones in acetonitrile. The half-wave potential of the second one-electron wave correlates with E_{m+1} as well, thus indicating that both the first and second electrons are added to the l.u.m.o. in the electrode processes.

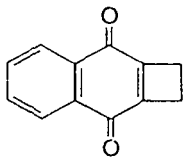
Dewar's semi-empirical molecular orbital procedure has been applied to the calculation of redox potentials for 25 quinone/hydroquinone couples[35]. The calculated values show good correlation with potentiometric $E^{0'}$ values in 95% ethanol, 0·1M LiCl, 0·1M HCl solutions.

Correlation of $E_{\frac{1}{2}}$s for substituted quinones with molecular orbital calculations has not been as successful. Hydroxyl derivatives in particular exhibit half-wave potentials more positive than those predicted by theory[36]. In some of these cases there is evidence that the electrode processes involve inter- and intramolecular hydrogen bond formation, thus invalidating a simple application of m.o. theory. The half-wave potentials for the first and second one-electron waves of a series of mono- and disubstituted chloroanthraquinones correlate with the energies of the l.u.m.o., but with different slopes[37]. In this series it appears that interactions of the chloro substituents with the reducible group are weaker in the semiquinone than in the quinone.

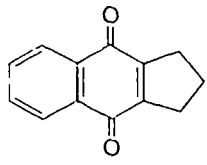
Ring-strain effects on half-wave potentials are nicely illustrated in a series of substituted 1,4-naphthoquinones[38]. Strain in the cyclobutane derivative induces more *p* character and less *s* character in the bonding of the carbons in the 2,3-positions and decreases the ability of the α-carbons to donate electron density to the quinone framework. Thus the half-wave potential of the cyclobutane derivative is almost the same as that of the parent naphthoquinone where there are no α-carbons to donate electron density. The strain-free cyclohexane derivative, on the other hand, has a half-wave potential almost identical with that of 2,3-dimethyl-1,4-naphthoquinone.



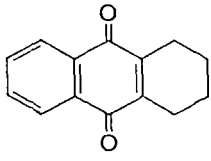
$E_{\frac{1}{2}} = -0.685$ V



-0.695 V



-0.748 V



-0.854 V

E. Spectroscopic Correlations

The most thoroughly interpreted correlation of quinone half-wave potentials is that between the maximum frequency of donor→quinone charge-transfer absorption bands (ν_{CT}) and polarographic $E_{\frac{1}{2}}$ values due to Peover and coworkers[26, 39, 40]. Quinones readily serve as acceptors in charge-transfer complexes with aromatic hydrocarbon donors such as anthracene, pyrene, hexamethylbenzene and others. The energy of the long wavelength absorption of the resulting complex can be approximated by the Mulliken equation,

$$h\nu_{CT} = I_D - E_A + \text{constant} \tag{9}$$

where I_D is the ionization energy of the donor molecule and E_A is the electron affinity of the acceptor. Using this equation, Peover and coworkers showed that ν_{CT} and $E_{\frac{1}{2}}$ values for equation (5) in non-aqueous solvents permitted estimates of relative electron affinities of quinones. Since the electron affinity of *p*-benzoquinone was known from gas-phase measurements, absolute values of E_A were determined for 13 mono-substituted quinones[26]. The principal assumption underlying the measurement is that solvation energies are similar throughout the series under study. For simple quinones in which a large fraction of the charge is localized on the oxygen atoms the approximation should be a good one. This assumption is usually necessary when spectroscopic $E_{\frac{1}{2}}$ correlations are made and has been discussed by Peover[41]. Other correlations of this type have been demonstrated for a series of high-potential quinones[42].

Various additional spectroscopic correlations have been proposed. A sampling of these involves the correlations of quinone half-wave potentials with the following parameters: the energy of the long wavelength $n \rightarrow \pi^*$ transition of 12 *para* and 3 *ortho* quinones[43], the shift ($\overline{\Delta\nu}$) of the O—H

stretching mode in some methyl-substituted benzohydroquinones[44], the p.m.r. chemical shifts of H_7 and H_3 in 2- and 2,3-disubstituted naphthoquinones[45], the energies of the absorption bands of the radical anions[46], the e.s.r. hyperfine splitting constant of the amine nitrogen in a series of aminosemiquinones[24] and the activation energies for the decay of a photoexcited state[47].

III. ELECTROCHEMISTRY IN NON-AQUEOUS SOLVENTS

In aprotic non-aqueous solvents quinones are reduced in two successive one-electron steps which are electrochemically reversible under usual polarographic conditions:

$$Q \underset{}{\overset{e^-}{\rightleftharpoons}} Q^{\bullet -} \overset{e^-}{\rightleftharpoons} Q^{2-} \qquad (10)$$

The first clear demonstration of semiquinone formation in the first polarographic wave was given by Wawzonek and coworkers[48]. In this early work, benzoquinone, duroquinone, 2-methylnaphthoquinone and anthraquinone were studied in acetonitrile (MeCN) and *N*,*N*-dimethylformamide (DMF) and the effect of proton sources on the positions and heights of the two waves noted. Several years later the first observation of an e.s.r. signal from an electrochemically generated radical ion was made by Austen and coworkers[49] who observed the spectrum of the radical anion of anthraquinone after freezing an electrolysis solution. These simple experiments have been refined and repeated for many quinone systems under a variety of experimental conditions in the last fifteen years.

The straightforward polarographic behaviour of quinones in aprotic solvents can be altered by any perturbation on the diffusion layer concentrations of Q, $Q^{\bullet -}$ or Q^{2-}. Acid–base, ion-pairing and complex formation equilibria are the principal perturbations on those concentrations which have been studied. These effects can simply shift the first or second quinone reduction waves in a Nernstian manner or can completely eliminate waves and replace them with new diffusion or kinetically controlled processes. For the most part the electrochemistry of quinones and hydroquinones in non-aqueous solvents involves these diffusion layer chemical reactions. The electron transfer reactions appear to be very fast, and when attempts have been made to measure them, diffusion-controlled reactions have been indicated[31]. Furthermore, adsorption seems to be minimal in these solvents for most simple quinones and does not come into play unless biologically important quinones with large molecular weights are examined.

A. Proton Donor Effects

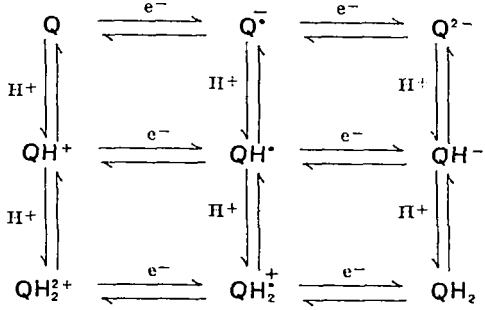
1. General considerations

As electrons are added to the quinone structure (equation 10), the electron density on the oxygen atoms and the basicity of the molecule increases dramatically. Each of the species in equation (10) is capable of accepting one or two protons. For *p*-benzoquinone, the fully reduced dianion is a relatively strong base, the pK_as of *p*-benzohydroquinone being 10·35 and 11·4. The pK_as of the semiquinone oxidation state are much smaller. For $QH^{\bullet}$ a pK_a of ca. 4·0 has been determined by pulse radiolysis and e.s.r. measurements in aqueous solutions[50-52]. The pK_a of QH_2^+ has not been reported, but this species is stable in strongly acid media such as $AlCl_3$–$MeNO_2$ mixtures[53] and concentrated sulphuric acid[54]. The quinoidal structure is more difficult to protonate and few reports of K_as for QH^+ species are in the literature. Biedermann has estimated $pK \approx -1$ for protonated *p*-benzoquinone from shifts of less than 1 mV in the potentiometric $E^{0\prime}$ value in concentrated acid solutions[55]. However, there is some dispute over this value since quinone species which are stable in concentrated acid solutions give pK values considerably lower on a Hammett acidity function scale[56,57]. Badoz-Lambling and Demange-Guérin report that *p*-benzoquinone is not protonated in DMF by perchloric acid on the basis of spectrophotometric studies[58].

In non-aqueous solvents, in which a wide range of hydrogen ion activity is possible, the role of proton donors and proton availability in quinone redox processes becomes clearly evident. Potential shifts of almost 1 V can occur for a reduction of a given quinone by variation of the type and amount of proton donor present in non-aqueous solvents. Incidentally, these results were anticipated, in part, by Müller who studied the quinhydrone couple in weakly buffered aqueous solutions[59-61]. He found that both the amounts of buffer components present and the rates at which they act as proton donors or acceptors would effect the position of the Q and QH_2 waves. In a novel experiment, the addition of the enzyme carbonic anhydrase, which catalyses the acid–base proton transfer reactions in carbonate buffers, converts an irreversible Q/QH_2 polarographic wave (pH 7·5, carbonate buffer) into a reversible one[61].

If each possible protonated form is considered, a nine species array of electrochemical pathways is possible (equation 11). The Q/QH_2 couple has been analysed in terms of this array previously by Jacq[62] and by Jeftic and Manning[63]. If we ignore the unlikely intermediacy of the QH_2^{2+} species, there are five possible pathways from Q to QH_2. By the addition of proton donors of varying acid strength, each of

these routes can be demonstrated in the electrode reactions of most quinones.



(11)

2. Protonation of $Q^{-\cdot}$ and Q^{2-}

In their early experiments Wawzonek and coworkers[48] observed that addition of water to DMF solutions shifted the second one-electron wave of several quinones to more positive potentials and did not markedly alter the first one-electron wave. These results indicate that rapid protonation of Q^{2-} is taking place in the diffusion layer. If stronger proton donors than water are employed, it is possible to protonate $Q^{-\cdot}$ at potentials of the first wave. This was first demonstrated by Given and Peover[64], who studied anthraquinone reduction in the presence of phenol and benzoic acid. With the latter proton donor, the first wave is increased at the expense of the second until a single two-electron wave is observed at a 5 : 1 ratio of acid to quinone. This behaviour is interpreted by postulating protonation of $Q^{-\cdot}$ to form $QH^{\cdot}$, which is reduced at the potential of the first wave (equation 12). This is the mechanism originally suggested by

$$
\begin{aligned}
Q + e^- &\rightleftharpoons {}^{-}Q^{\cdot} \\
Q^{-\cdot} + HA &\rightleftharpoons QH^{\cdot} + A^- \\
QH^{\cdot} + e^- &\xrightarrow{\text{fast}} QH^- \\
Q^{-\cdot} + QH^{\cdot} &\longrightarrow Q + QH^-
\end{aligned}
\qquad (12)
$$

Hoijtink and coworkers for the reduction of aromatic hydrocarbons in the presence of HI[65]. The fourth reaction represents a solution electron transfer step which will be thermodynamically favoured if $QH^{\cdot}$ is readily reduced at the potential of the first wave. This reaction was initially suggested by Austen and coworkers[49]. The calculations of Hoijtink for hydrocarbons show that the electron affinity of the protonated radical

anion is greater than that of the parent hydrocarbon and thus one two-electron reduction occurs. This pathway has been shown to be operative in several quinone reductions including stilbene quinones[66], α-tocopheryl-quinone[67], ubiquinone-1[68] and 2-methylnaphthoquinone[69] in addition to the simple ones[64].

3. Disproportionation reactions

Reactions other than those contained in equation (11) are possible in the presence of proton donors, e.g. disproportionation and dimerization. Umemoto has found that the Hoijtink mechanism (equation 12) does not describe the reduction of anthraquinone (AQ) in the presence of a large excess of water[70]. In 50% water–DMF mixtures, the anthraquinone reduction wave has almost reached a two-electron height, although the semiquinone species has an appreciable lifetime in solution. A kinetic analysis of the decay of the e.s.r. signal indicated that the radical species decays via a disproportionation reaction:

$$\begin{aligned} AQ^{\cdot-} + AQ^{\cdot-} &\rightleftharpoons AQ + AQ^{2-} \\ AQ^{2-} + 2\,H_2O &\rightleftharpoons AQH_2 + 2\,OH^- \end{aligned} \qquad (13)$$

Disproportionation reactions for $AQ^{\cdot-}$ and AQH have also been discussed by Kuwana and coworkers[71,72] who report absorption spectra of anthraquinone reduction products in LiOH solutions using optically transparent electrodes[71].

Solvent effects on the $E_{\frac{1}{2}}$s of AQ in DMF/H_2O mixtures have been correlated with the $\Delta\lambda_{max}$ of the absorption bands of $AQ^{\cdot-}$ and AQ^{2-} in the visible region[73]. Marked blue-shifts are observed, which are consistent with strong hydrogen bonding between the anions and water.

4. Preprotonation reactions

If the proton donor is a sufficiently strong acid, quinone reduction occurs via the protonated species, QH^+. For simple benzoquinones, addition of acids such as perchloric acid, *p*-toluenesulphonic acid and chloroacetic acids results in the appearance of a 'prewave' which is proportional to the concentration of the acid. These prewaves occur at potentials as much as 0·6 V more positive than the simple one-electron reduction of the corresponding quinone. This potential shift is too large to be explained by a rapid follow-up protonation of $Q^{\cdot-}$ in the diffusion layer and suggests prior protonation of the quinone (equation 14).

$$Q + H^+ \underset{k}{\overset{k_1}{\rightleftharpoons}} QH^+ \xrightarrow{2e^-,H^+} QH_2 \qquad (14)$$

Although the inequality, $k_1[H^+] \ll k_{-1}$, obtains under most polarographic conditions, reduction may proceed via QH^+ if $k_1[H^+]_{x_2}$ is large, where $[H^+]_{x_2}$ is the concentration of hydrogen ions in the diffuse double layer. These 'QH^+ waves' in non-aqueous media have been reported for simple quinones[63, 74–77], benzopyrenequinones[78], biologically important quinones[67–69] and others. Reduction via QH^+ is similar to the mechanism proposed by Vetter[79] for quinone reduction in acidic aqueous solutions which is discussed below. Significantly, the non-aqueous QH^+ waves have roughly the same appearance and position for mercury, platinum and carbon electrodes[75]. The involvement of adsorbed hydrogen atoms in the electrode process is therefore unlikely. However, in the presence of excess acid on electrodes such as platinum the reduction process can be complicated by the simultaneous evolution of hydrogen[67, 75].

The QH^+ wave is dependent on both the pK_a of the proton donor and the basicity of the quinone. By introducing electron-donating substituent groups on the quinone ring, Cauquis and coworkers have clearly demonstrated the intermediacy of the QH^+ species[77]. For 2,6-dimethoxybenzoquinone and 3,3′,5,5′-tetramethoxybiphenylquinone, the QH^+ species are readily prepared in acetic acid–acetonitrile solutions and their u.v. and visible absorption spectra obtained. For these quinones the two-electron QH^+ waves have a log slope of 30 mV and shift by 30 mV per decade increase in acid concentration. These results are consistent with a reversible two-electron reduction of QH^+ to QH_2.

The value of $-E_{\frac{1}{2}}$ for the QH^+ wave in methyl cellosolve solutions is directly proportional to the pK_a of the proton donor. For a series of proton donors including chloracetic acids and chlorophenols, the $E_{\frac{1}{2}}$ for QH^+ was found to shift by ca. -50 mV per unit increase in pK_a[80, 81]. Similar dependences have been reported in DMF solutions by Demange-Guérin[82] and by Kheifets and coworkers[83, 84].

While the intermediacy of the QH^+ species is well established, the kinetics of the reduction process (equation 14) have not been worked out. In general the QH^+ wave is somewhat drawn-out and exhibits kinetic character. (The term 'kinetic character' is used in the sense that the flux of an electroactive species at the electrode surface, and hence the current, is limited by the rate of a chemical reaction which is slow on the time scale of the electrochemical measurement.) Even the well-behaved systems studied by Bessard, Cauquis and Serve[77] (see above) exhibit kinetic character when the time scale of the electrochemical experiment is decreased. Thus the experimental current function of 3,3′,5,5′-tetramethoxybiphenylquinone in $HClO_4$ solutions decreases at fast sweep rates[77]. Similar behaviour was observed for the duroquinone QH^+ wave

in acetonitrile[75]. On the other hand, the current function of the unsubstituted benzoquinone on both mercury and platinum electrodes was found to be constant at sweep rates up to 500 V/s[75]. Slow heterogeneous steps, both electron transfer and adsorption, as well as slow protonation reactions, are possible kinetic complications in these QH^+ electrode reactions.

The QH^+ wave has been exploited by several workers for the analytical determination of acids. For example, Takamura and Hayakawa[80,81,85] have been able to analyse mixtures of acids, e.g. acetic and perchloric acids, which give separate QH^+ polarographic waves. In the presence of excess quinone these waves are proportional to the acid concentrations. This procedure has also been used in unbuffered aqueous solutions for the determination of trace acidic components[86].

5. Reduction of hydroxylquinones

Hydroxy derivatives of quinones fall into a somewhat special category since mechanistic complications not encompassed by equation (11) are possible. These molecules can function as proton donors themselves, and if the hydroxyl substituent is α to the carbonyl group, intramolecular hydrogen-bond formation can stabilize the intermediate semiquinone species. This latter behaviour is well documented in the e.s.r. literature[87]. Thus half-wave potentials for α-hydroxylquinones are more positive than those of the parent compounds by up to 0·4 V and do not correlate with Hammett substituent constants or simple molecular orbital calculations[33,34,36,88].

By far the most thoroughly studied α-hydroxylquinone is 1-hydroxy-9,10-anthraquinone, HOAQ. Piljac and Murray[89] studied the effect of proton donors on the electrochemistry of HOAQ and its conjugate base (OAQ^-) in several non-aqueous solvents and came to some interesting conclusions. Reduction of OAQ^- in the absence of added proton donors occurs in a two-electron, one-proton step in which protons are supplied by the media:

$$OAQ^- + HS + 2\,e^- \rightleftharpoons HOAQ^{2-} + S^- \qquad (15)$$

Addition of the weak proton donor, phenol, results in the appearance of two new diffusion-controlled waves at potentials more negative than the reversible one-electron reduction of HOAQ and more positive than the two-electron reduction of OAQ^- (equation 15). The first of these waves

is assigned to the reduction of a heteroconjugate acid–base dimer via the following reactions:

$$\begin{aligned} C_6H_5OH + OAQ^- &\rightleftharpoons [C_6H_5OH\cdots OAQ]^- \\ [C_6H_5OH\cdots OAQ]^- + e^- &\longrightarrow HOAQ^{\cdot-} + C_6H_5O^- \\ [C_6H_5OH\cdots OAQ]^- + C_6H_5O^- &\longrightarrow [C_6H_5OH\cdots OC_6H_5]^- + OAQ^- \end{aligned} \quad (16)$$

The overall reaction is

$$OAQ^- + 2\,C_6H_5OH + e^- \longrightarrow [C_6H_5OH\cdots OC_6H_5]^- + HOAQ^{\cdot-} \quad (17)$$

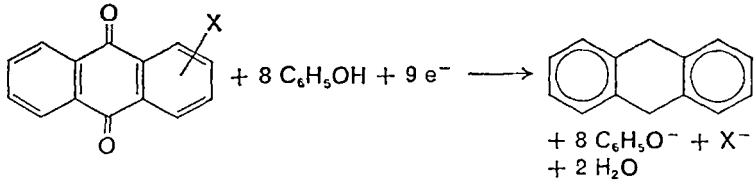
The second wave is due to reduction of unreacted OAQ^-; i.e.

$$\begin{aligned} OAQ^- + e^- &\longrightarrow OAQ^{2-} \\ OAQ^{2-} + [C_6H_5OH\cdots OC_6H_5]^- &\longrightarrow HOAQ^{\cdot-} + 2\,C_6H_5O^- \end{aligned} \quad (18)$$

In equations (16)–(18), the homoconjugate acid–base dimer, $[C_6H_5OH\cdots OC_6H_5]^-$, is a product of the reductions. This species can also act as a proton donor, e.g. equation (18), but is a weaker acid than phenol. Splitting of the second wave in the reduction of HOAQ in the presence of phenol is attributed to follow-up protonation reactions by both C_6H_5OH and $[C_6H_5OH\cdots OC_6H_5]^-$. These results of Piljac and Murray[89], which are supported by spectroscopic in addition to polarographic data, represent one of the most detailed analyses of proton donor effects in non-aqueous electroorganic chemistry.

6. Carbon–oxygen bond scission

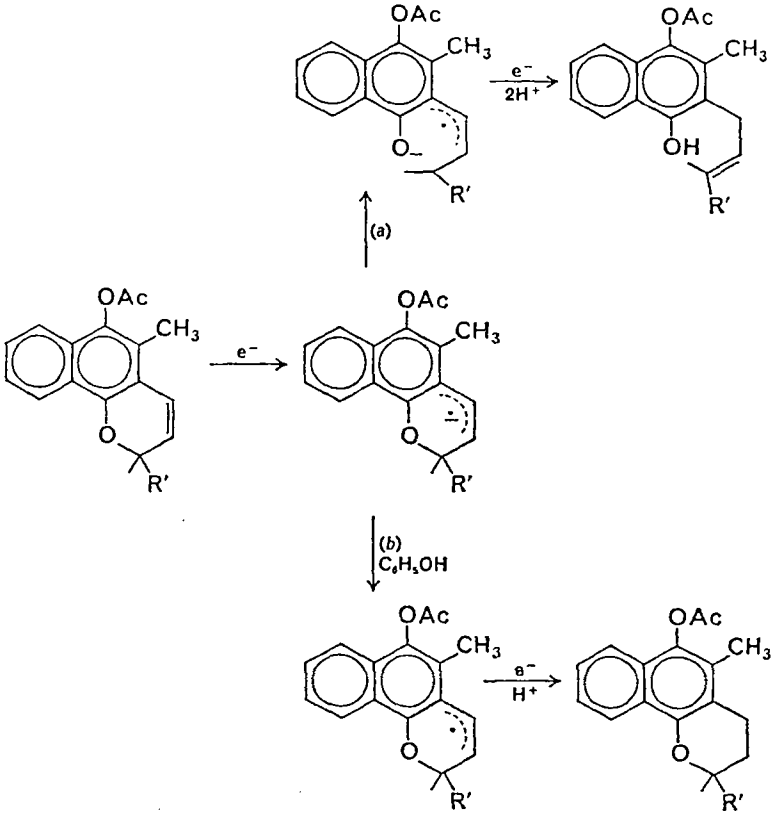
Finally, scission of carbon–oxygen bonds has been reported for some quinones by reduction at very negative potentials in the presence of an excess of proton donor. For example, electrolysis of anthraquinone–phenol solutions in DMF–tetraethylammonium iodide at −2·15 V versus s.c.e. gives a 60% yield of 9,10-dihydroanthracene[90]. Similar products were obtained for some halogen derivatives of anthraquinone by Bezuglyi and coworkers[91] who report the following stoicheiometry in DMF solutions.



(19)

Phyllochromanol acetates are reduced via two routes (equation 20) in DMF[92]. In the absence of added proton donor, C—O bond fission occurs

(route *a*) to yield the hydroquinone form, while in the presence of a hundredfold excess of phenol the chromanol ring remains intact during the reaction. In the absence of added proton donors (route *a*) protons are presumably supplied by residual water and/or the supporting electrolyte.



(20)

B. Oxidation of Hydroquinones

All of the oxidative pathways from QH_2 to Q contained in equation (11) have been postulated for various hydroquinone oxidations in non-aqueous solvents. In the presence of excess tetrabutylammonium hydroxide both protons are removed from simple hydroquinones and separate one-electron waves are observed for oxidation of the Q^{2-} and $Q^{\cdot-}$ species[75,82]. In these strongly basic solutions, this apparently simple behaviour is complicated considerably by autooxidation of the quinone[69] and by precipitation of a QH^- salt[82,93]. The solubility product

$K_{sp} = [NBu_4^+][QH^-]$, is $10^{-4.5}$ for the tetrabutylammonium salt of the monoanion of *p*-benzohydroquinone in DMF[82,93]. Thus, as QH_2 is titrated with NBu_4OH in acetonitrile, all voltammetric waves decrease until the end-point is reached. Past the end-point the precipitate dissolves according to equation (21).

$$NBu_4QH + OH^- \longrightarrow NBu_4^+ + Q^{2-} + H_2O \tag{21}$$

1. Oxidation of QH^-

Oxidation of QH^- can be observed by the use of a non-hydroxylic base such as pyrrolidine[75], 2,6-lutidine[76] or pyridine[69]. In these solutions a new wave appears at potentials ca. 0·7 V more positive than the corresponding QH_2 oxidation wave. This wave has been assigned to oxidation of a QH^- species (equation 22). The analysis is similar to that for the QH^+ wave

$$\begin{aligned} QH_2 + B &\underset{k_1}{\overset{k_1}{\rightleftharpoons}} BH^+ + QH^- \\ QH^- &\rightleftharpoons QH^{\bullet} + e^- \\ QH^{\bullet} &\rightleftharpoons Q^{\bullet -} + H^+ \\ Q^{\bullet -} &\xrightarrow{\text{fast}} Q + e^- \end{aligned} \tag{22}$$

discussed above; i.e. if $k_1[B]_{x_2}$ is large, oxidation can proceed via QH^-.

2. Oxidation of QH_2

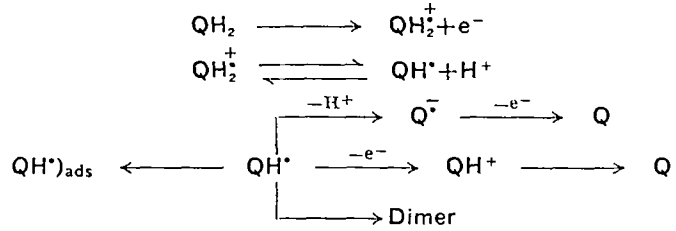
Oxidation of the fully protonated hydroquinone occurs via an irreversible two-electron process (equation 23). The products of the

$$QH_2 \longrightarrow Q + 2H^+ + 2e^- \tag{23}$$

oxidation are the corresponding quinone and protons, which are readily detected in the cyclic voltammetric experiment by the appearance of a QH^+ wave on the reverse potential sweep. This behaviour was originally reported by Turner and Elving[94] for pyridine solutions and is general for aprotic solvents[74,75].

Kinetic character has been reported for QH_2 oxidation waves although this point has been disputed. The linear sweep voltammetry current functions for some simple hydroquinones have been reported to decrease at fast sweep rates and give apparent *n*-values less than two[75]. Similar behaviour has been observed for 2-methylnaphthohydroquinone[69]. These results suggest the existence of a kinetically significant one-electron intermediate in the QH_2 oxidation process, i.e. $QH^{\bullet}$ or its equivalent in

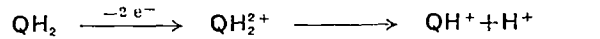
the following oxidation scheme:



(24)

Several possible routes are available to a one-electron intermediate as indicated by equation (24). A reduction wave which has been observed in the cyclic voltammograms of simple hydroquinones has been tentatively assigned to an intermediate dimeric species[75]. This interpretation has been challenged by Parker and Eberson[75] who found that the limiting current constant for QH_2 oxidation at a platinum rotating disk electrode was constant at angular velocities up to 500 rad/s and indicated a two-electron process. Furthermore, the limiting current was not decreased by the addition of a tenfold excess of 2,6-lutidine. Eggins[96] has recently re-interpreted the data of Parker and Eberson in terms of a one-electron transfer. More experimental work over a wider concentration range appears to be necessary to settle this issue.

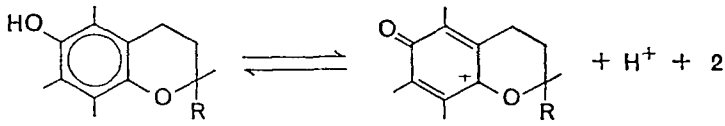
The role of protons in QH_2 oxidations is clearly indicated by the effect of acids on the oxidation of 3,3′,5,5′-tetramethoxybiphenylhydroquinone[77]. The addition of 10^{-2}M $HClO_4$ results in the increase of the linear sweep voltammetry current function by ca. 40%, although the limiting current at a rotating disk electrode remains constant. This suggests an increase in reversibility and implicates protons in a rate-determining step in the oxidation process. Cauquis and coworkers[77] suggest that the oxidation proceeds via the QH_2^{2+} species in the presence of protons; i.e.



(25)

3. Oxidation of tocopherols

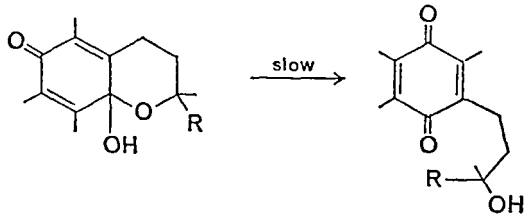
In some cases the two-electron hydroquinone oxidation process becomes electrochemically reversible. This is nicely demonstrated by α-tocopherol and the model compound, 2,2,5,7,8-pentamethyl-6-hydroxychroman, which produce reversible two-electron cyclic voltammograms in acetonitrile solutions[97–99].



(26)

R = $C_{16}H_{33}$ or CH_3

The resulting carbonium ion is rapidly attacked by water to give an electroinactive species which opens to give an electroactive quinone[98] (equation 27). This latter reaction has been studied in detail and has been shown to involve both general acid and base catalysis[99].



(27)

C. Metal Ion Effects

Small amounts of metal ions can have striking effects on the current-potential curves of quinones in non-aqueous solvents. Both the semiquinone and the quinol dianion species can complex and/or form ion pairs with metal ions. The usual result is to shift the first or second one-electron wave to more positive potentials, but in some cases the behaviour becomes more complicated.

Peover and Davies have studied the effect of metal perchlorates on the reduction of anthraquinone in DMF solutions[100]. The radical anion, $AQ^{\bullet-}$, forms a 1 : 1 complex with Li^+ but not with Na^+ K^+, NEt_4^+ or NBu_4^+. The dianion AQ^{2-} is complexed by all these cations, which shifts the second reduction wave to considerably more positive potentials. The order of complexing strength is $Li^+ > Na^+ > K^+ > NEt_4^+ > NBu_4^+$. Similar results were indicated for *p*-benzoquinone and chloranil. Ion-pair formation is more prevalent in acetonitrile solutions, but the tetraalkylammonium salts, $NR_4^+Q^{\bullet-}$, were also found to be completely dissociated in this solvent.

Metal ions have similar effects on the reduction of 1,2-naphthoquinone and 1,4-naphthoquinone in DMF, DMSO, CH_3CN, propylene carbonate and acetone[101]. The effect of complex formation is more pronounced with the *ortho* quinone and increases in the order,

$$K^+ < Na^+ < Li^+ < Mg^{2+} < Zn^{2+}$$

With the divalent cations the two one-electron waves are merged into one drawn-out two-electron process. The solvent effect operative in these systems has been recently interpreted in terms of solvent donicity[102].

In the above systems the $NR_4^+Q^{\bullet-}$ salts were found to be completely dissociated at polarographic concentration levels. This is not always the

case; for example, the tetrabutylammonium salt of a pyracylene semiquinone appears to be associated in DMSO[103].

Cyclic voltammograms and reverse current chronopotentiograms of *p*-benzoquinone at hanging mercury drop and platinum electrodes in the presence of lithium ions present features more complex than suggested by the above polarographic results. In DMSO, chronopotentiometric results indicate that addition of LiCl causes the second one-electron wave to disappear, although the first wave retains its one-electron character[104]. In addition, a small wave appears at potentials between the original one-electron waves. Controlled potential electrolysis indicates that severe electrode filming occurs at potentials corresponding to the first wave. Similar results were obtained by Eggins[105] who reported deposition of a yellowish-blue film on a platinum electrode in acetonitrile solutions containing 0·1M $LiClO_4$. A large anodic stripping wave was observed which was attributed to oxidation of adsorbed LiQH.

D. Change–transfer Complexes

Polarographic half-wave potentials of quinones have been combined with spectral absorption maxima of charge-transfer complexes to estimate electron affinities of electron acceptors (see section II.E above). In addition, Peover[106] has developed the theory for determination of charge-transfer complex formation constants from shifts in the polarographic half-wave potentials. The theory was applied to several strong charge-transfer complexes, including those of chloranil and dicyanodichlorobenzoquinone with the donor molecules, hexamethylbenzene and pyrene. Comparison of spectroscopic and polarographic methods revealed that the latter technique can provide a direct method of obtaining formation constants when one of the components is electroactive.

IV. ELECTROCHEMISTRY IN AQUEOUS SOLUTIONS

A. Electrochemical Kinetics

The quinone/hydroquinone couple presents a 'non-textbook' complexity when the electrochemical kinetics are examined in detail in aqueous solutions. The 3×3 array of reactants, intermediates and products which are interrelated by electron and proton transfer steps (equation 11) must again be taken into consideration. Indeed all nine of these species (and one more) have been proposed by different authors in electrode schemes in aqueous solutions, sometimes within relatively narrow pH regions. In addition, the likelihood of adsorbed species in aqueous solutions should be considered, thus adding a third dimension to the above scheme (equation

11). Finally, the concept of partial charge-transfer at electrode surfaces has been applied to the Q/QH_2 couple, further refining the above scheme[107].

For aqueous solutions, the literature on the Q/QH_2 kinetics divides between work on mercury and work on platinum and other solid electrodes. The solid electrode results will be discussed first.

I. Kinetics at solid electrodes

The electrochemical reduction of benzoquinone was first studied by Haber and Russ[108] at the turn of the century. In spite of the incorrect conclusion that quinone reduction proceeds via hydrogen ion reduction, this paper was well ahead of its time. Thirty-three years later Rosenthal, Lorch and Hammett[109] published a careful study of Tafel plots* for quinhydrone solutions in the pH region 1–8. These workers measured reaction orders at low overvoltages and found first-order dependence on both Q and QH_2. However, the Tafel slopes were not constant and definitive mechanistics conclusions were not reached.

In an important paper in the early fifties, Vetter presented Tafel plots at platinum electrodes that extended into the limiting current regions for quinhydrone solutions between pH 0·2 and 7·2[79,110]. The limiting currents were shown to be purely diffusion controlled. Vetter's conclusion that two different consecutive charge-transfer reactions occur over a wide pH region has gained wide acceptance in the modern literature. The electrochemical reaction orders which were established for Q, QH_2 and H^+ indicated a change of mechanism between pH 5 and 6. Below pH 5 the order of electron and proton transfer for Q reduction is H^+, e^-, H^+, e^- (HeHe); while for pH greater than 6, the order is e^-, H^+, e^-, H^+ (eHeH) Thus the two mechanisms are:

$$\begin{aligned}
Q + H^+ &\rightleftharpoons QH^+ \\
QH^+ + e^- &\longrightarrow QH^\bullet \\
QH^\bullet + H^+ &\rightleftharpoons QH_2^{+\bullet} \\
QH_2^{+\bullet} + e^- &\longrightarrow QH_2
\end{aligned} \qquad pH < 5 \qquad (28)$$

$$\begin{aligned}
Q + e^- &\longrightarrow Q^{-\bullet} \\
Q^{-\bullet} + H^+ &\rightleftharpoons QH^\bullet \\
QH^\bullet + e^- &\longrightarrow QH^- \\
QH^- + H^+ &\rightleftharpoons QH_2
\end{aligned} \qquad pH > 6 \qquad (29)$$

* Tafel plots represent the familiar linear dependence of overvoltage on the logarithm of the current.

Similar mechanisms have been advanced for quinone reduction on mercury electrodes (see section IV.A.2 below) and in non-aqueous solvents (see sections III.A.2 and II.A.4). In a recent paper Dohrmann and Vetter[111] have reached nearly identical conclusions for the duroquinone/durohydroquinone couple in aqueous–methanol buffers at gold electrodes. For this system the transition between the HeHe and eHeH mechanisms occurs between pH 3·1 and 6·6.

Vetter's mechanism has been disputed by Loshkarev and Tomilov[112] who found a zero-order dependence on hydrogen ion in the benzoquinone reduction on platinum. A direct rate-determining two-electron transfer over a wide pH range was proposed (equation 30). Similar results were

$$Q + 2\,e^- \longrightarrow Q^{2-} \xrightarrow{H^+} QH_2 \qquad (30)$$

obtained for 9,10-anthraquinone-2-sulphonate. Under controlled conditions a minimum in the exchange currents occurred at approximately pH 3, although the exchange currents measured by these workers tended to decrease with time due to adsorption of quinhydrone decomposition products and other impurities from solution.

The exchange current was also found to be markedly dependent on electrode material and the electrode pretreatment[113]. The following order of decreasing electrochemical activity was found although the order could be altered by differing electrode pretreatment: graphite > platinized graphite $\gg$ Au > Rh > Pd > Ir > Pt. For graphite nearly Nernstian behaviour was observed for the complete current-potential curve, while oxidized platinum gave the most irreversible behaviour. In general, cathodic polarization in H_2SO_4 increased the observed exchange current density for a particular electrode material. Surface platinum oxide formation has also been implicated as the cause of anomalous behaviour in the oxidation of QH_2 in weakly basic solutions[114].

Exchange current densities for the Q/QH couple which were constant with time and considerably higher than those reported by previous workers were found in carefully purified solutions by a second group of Russian workers[115]. The low exchange currents of previous workers[79, 112, 113] were attributed to adsorption of impurities, the supporting electrolyte or oxygen after anodic electrode pretreatment. A minimum in the exchange current pH profile was again found at approximately pH 4. The results support Vetter's mechanisms, equations (28) and (29), although the exact order of proton and electron transfer steps is not clearly stated in their papers. Adsorption of Q and QH_2 is indicated by the non-integral dependence of the exchange currents on the Q and QH_2 concentrations.

These workers extended their studies and quantitatively determined the dependence of the exchange current on the concentration of species which are adsorbed on the platinum electrode surface[116]. The decrease of the exchange current was linearly related to the logarithm of the concentration of the additive for a series of anions ($F^- < Cl^- < Br^-$), cations ($K^+ < NH_4^+ < Rb^+ < Cs^+ < NMe_4^+$) and neutral organic molecules (hexyl alcohol < isoamyl alcohol < phenylacetic acid). In these series the species least strongly specifically adsorbed (i.e. KF) was the least effective in lowering the observed exchange current. Double-layer corrections were discussed but not taken explicitly into account. It was further demonstrated by radioisotope measurements that the exchange current decreases linearly with the amount of adsorbed bromide ion on the electrode. These results readily rationalize the lack of agreement between exchange currents reported in the presence of different 'inert' supporting electrolytes. Unfortunately, double-layer parameters are not generally available for platinum electrodes so that true exchange current densities could not be determined.

Adsorption effects have also been noted by Gileadi in the current-potential curves of hydroquinones at platinum electrodes[117,118]. At QH_2 concentrations greater than approximately 0·1M 'self-inhibition' of the electrode process occurs and limiting currents are not observed. Adsorbed intermediates and products were invoked to rationalize these results. A similar phenomenon has been observed in acetonitrile solutions at high concentrations of quinhydrone; see Figure 7 in reference 75.

Finally, a novel experiment due to Peover[119] will be mentioned here, although it was carried out in a non-aqueous solvent. He applied a triangular wave to a platinum electrode directly in the cavity of an e.s.r. spectrometer and measured the resulting e.s.r. signal which was in phase with the electrode potential. The system was chloranil in acetonitrile and the resulting spectrum was ascribed to the semiquinone species in the vicinity of the electrode surface. Radical species in the bulk of the solution were not detected since they were not being modulated at the frequency of the triangular wave. The resulting spectrum was broadened and shifted downfield in accord with expectations for a semiquinone species specifically adsorbed on the electrode surface.

2. Kinetics at mercury electrodes

Although many polarographic studies on quinone systems exist in the literature, surprisingly few papers are devoted to the electrochemical kinetics of the quinone/hydroquinone couple. The intermediacy of the semiquinone species was apparent to polarographic workers[120-122], but

early studies were carried out under diffusion-controlled conditions and no meaningful kinetic information was obtained.

Quinone/hydroquinone couples present electrochemically more reversible behaviour on mercury than on most solid electrodes because the heterogeneous electron exchange rates are greater and adsorption forces tend to be weaker on mercury. Hale and Parsons[123] analysed polarographic waves for several quinhydrone solutions (benzoquinone, naphthoquinone, anthraquinone, 9,10-phenanthraquinone and 1,2-benzoanthraquinone) in aqueous and alcoholic acetate buffer solutions (pH $\approx$ 4). Apparent heterogeneous rate constants of the order of 10^{-3} cm/s were measured under these conditions using Koutecky's analysis[124] and assuming a two-electron form for the waves. Free-energy differences between the various species in equation (11) were estimated from data in the literature and free energies of activation were obtained from the experimental rate constants using Marcus' theory[125] in order to obtain a free-energy profile for the Q/QH_2 reaction pathway under the experimental conditions. In agreement with Vetter's mechanism[79], they concluded that at pH 4 the reaction proceeds via successive electron transfers with nearly equal free energies of activation.

These results were questioned in a later paper by Galli and Parsons[126] who were not able to obtain agreement between the kinetic analysis of the polarographic waves and the results of a Sluyter's impedance plane analysis[127]. This small-amplitude relaxation technique indicated diffusion control at rates up to 10^3 greater than those reported previously[123]. The double-layer capacity was found to be dependent on the presence of quinhydrone and the couple behaved in a manner typical for the case of weak adsorption of reactants. Galli and Parsons attribute the irreversible behaviour in the polarographic case to adsorption effects[126].

Adsorption of quinone and hydroquinone species at the mercury electrode interface has been firmly established by several studies. Benzoquinone and benzohydroquinone have been shown to adsorb simultaneously by a chronopotentiometric[128] and a quasi-thermodynamic method[129]. In the latter the surface tension of a d.m.e. in a Q/QH_2 solution was determined by means of the drop-weight method at open circuit. By neglecting the surface excess of hydrogen ions adsorbed from the phosphate buffer solutions (pH = 6·4–7·6), relative surface excesses were estimated for total quinone, oxidized components and reduced components. (See Frumkin and coworkers[130] for comments on this paper.) The sum of the quinone, semiquinone and hydroquinone surface concentrations was constant for various ratios of Q to QH_2:

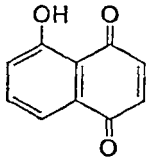
$$\Gamma_{QH_2}+\Gamma_{QH}+\Gamma_{Q}\approx 1{\cdot}2\times10^{-10}\ \text{mole/cm}^2 \qquad (31)$$

where Γ_i is the relative surface excess of the ith species. The sums $\Gamma_Q + \frac{1}{2}\Gamma_{QH}$ and $\Gamma_{QH_2} + \frac{1}{2}\Gamma_{QH}$ were found to vary linearly with the potential, i.e. with the Nernstian ratio, $\log([Q]/[QH_2])$.

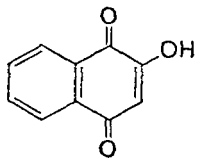
A definitive study of the electrode kinetics of a quinone couple at mercury in aqueous solutions has not appeared in the literature. The effects of pH, buffer components and temperature on the reversibility of voltammetric quinone waves have not been reported. It appears to this author that the intermediacy of the semiquinone species and its associated acid–base reactions must be taken into consideration in the analysis along with adsorption of the quinone, semiquinone and hydroquinone species.

In addition to the results of Mollers and Janenicke[128] and Plieth[129], there is more evidence for adsorption of complex quinone species at the mercury/solution interface. A careful double-step chronocoulometric study of the adsorption of anthraquinone-2-sulphonate (AQS) on Hg from fluoride, nitrate and thiocyanate electrolytes has been reported by Anson and Epstein[131]. The amount of specifically adsorbed AQS was decreased by co-adsorption of nitrate and thiocyanate ions, although neither nitrate nor thiocyanate was desorbed by co-adsorption of AQS. Changes in the ϕ_2 potential due to the presence of the negatively charged adsorbed AQS ion were detected by monitoring the half-wave potentials of the irreversible $Co(NH_3)_6^{3+}$ and CrO_4^{2-} reductions.

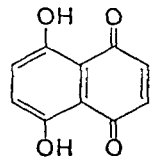
Adsorption phenomena of three hydroxynaphthoquinones at mercury electrodes in neutral phosphate buffers have been analysed in some detail[132–134]. The quinones studied were juglone (**1**), lawsone (**2**) and naphthazine (**3**). Only juglone, of these three quinones, gives polarographic adsorption prewaves. This is one of the smallest molecules whose



(1)



(2)



(3)

polarographic behaviour is well described by the Brdicka theory, which ascribes the presence of a prewave to strong equilibrium adsorption of the hydroquinone form in preference to the oxidized or quinone form[135, 136]. However, chronopotentiometric measurement of surface concentrations revealed that both the quinone and hydroquinone forms are strongly adsorbed at prewave potentials for the juglone/hydrojuglone couple[133]. Furthermore, the adsorption isotherms are almost identical for the juglone and lawsone couples. The variation of surface concentrations with

electrode potential (Γ versus $E_{1/2g}$) for both these systems is quite similar to the behaviour of the benzoquinone system discussed above[128, 129]. However, the rate of adsorption of juglone is slow on the polarographic time scale (less than ca. 4 s), thus formally creating a situation analogous to the requirements of the Brdicka theory. This is not the case for lawsone adsorption. The appearance of a prewave, therefore, is associated with the slow rate of quinone adsorption and not with a large difference in free energy of adsorption in these systems[133]. To complicate matters further, the total surface coverages were found to be somewhat greater than unity for the juglone/hydrojuglone couple in the vicinity of the prewave. This suggests bilayer adsorption and was tentatively ascribed to charge-transfer complex formation between the protonated semiquinone species and adsorbed quinone (equation 32)[133].

$$Q + H^+ + Q)_{ads} \xrightarrow{e^-} Q{\leftarrow}QH^{\bullet})_{ads} \qquad (32)$$

Bimolecular complexes have also been postulated as intermediates in the reduction of 1,4- and 2,7-dihydroxyanthraquinone in weakly basic solution[137].

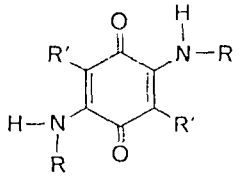
Adsorbed charge-transfer complexes have also been invoked to explain the unusual enhancing effect of anthracene and other hydrocarbons on the polarographic maximum of methylbenzoquinone[138, 139]. Charge-transfer complexes are seen to form between adsorbed aromatic hydrocarbon and the quinone substrate. As the π-system of the adsorbed hydrocarbon is increased, the height of the polarographic maximum increases.

Extensive adsorption of the biologically important quinone, ubiquinone-6, occurs in aqueous methanol solutions at the hanging mercury drop electrode[140]. Surface concentrations are almost independent of solution concentration between 7×10^{-6} and 9×10^{-5}M and are close to the saturation limit, $4{\cdot}3 \times 10^{11}$ mole/cm^2. At higher concentrations reversible polarographic behaviour is observed[141]. Adsorption of monohalogen-substituted 9,10-anthraquinones has been reported[142].

A more detailed description of the hydroquinone adsorption process has been sought by Lorenz and coworkers who have applied Lorenz's theory[107] of partial charge-transfer reactions at electrode surfaces to the Hg–QH_2 interaction[143]. For pH > 5, the amount of adsorption was found to be pH and potential dependent and QH_2 was found to be partially dissociated in the adsorbed state. Dissociation of adsorbed QH_2 was increased by an increase in the electrode potential. For example at pH $\approx$ 6, the average adsorbed species is $QH_2)_{ads}$ at $-0{\cdot}7$ V versus s.c.e. and $QH_{1{\cdot}7})_{ads}$ at $-0{\cdot}2$ V versus s.c.e. Thus the charge on the electrode induces a predissociation of QH_2 on the electrode surface. In another paper,

Gaunitz and Lorenz have determined that the desorption process for hydroquinone at negative potentials is diffusion-controlled at frequencies up to more than 10^5 s^{-1} [144].

A complete kinetic description of the interactions between the electron transfer, proton transfer and adsorption steps in quinone/hydroquinone couples remains to be presented. A brute-force approach would be to examine many quinone couples in the light of the details now understood about simple quinones. One such attempt has been made by Huntington and Davis[24] who measured apparent heterogeneous rate constants (k_s) for a series of aminoquinones and sought correlations with the hyperfine splitting constant of the corresponding semiquinones. The compounds studied were derivatives of **4**. The apparent $\log k_s$ values were found to



R′ = H; R = Me, Et, Pr, *i*-Pr, *t*-Bu, $-CH_2CH{=}CH_2$
R′ = Me; R = *t*-Bu

(4)

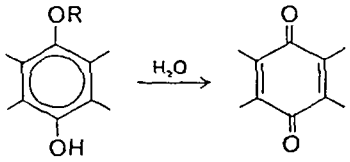
increase monotonically with the splitting constant of the nitrogen proton. However, the heterogeneous rate constants were determined at one pH value and include possible variations in proton transfer rates, adsorption isotherms and the stabilities of semiquinone intermediates. Refinements in the kinetic measurements in studies of this type should lead to a more detailed picture of the heterogeneous kinetics and electron-transfer transition states at electrode surfaces.

B. Coupled Chemical Reactions

Since the heterogeneous kinetic steps in Q/QH couples are often diffusion-controlled, chemical reactions coupled to the electron-transfer steps have readily observable effects on the electrochemical behaviour. Modern electroanalytical methods such as cyclic voltammetry[145] provide techniques for producing unstable species in solution where their kinetic behaviour can be followed. Examples of chemical reactions which are coupled to the Q/QH_2 system on the time scale of electrochemical experiments are briefly summarized in the following paragraphs.

The oxidation of ether and ester derivatives of hydroquinones, i.e. **5**, at solid electrodes presents features similar to the Q/QH_2 couples discussed above. A significant difference is that the oxidations are usually highly

irreversible and take place at more positive potentials than the corresponding hydroquinones. The overall electrode process involves two-electrons to yield the quinone (equation 33), which is readily detected in



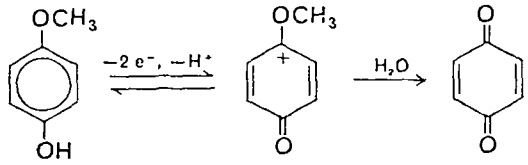
$$+ \text{ROH} + 2\text{H}^+ + 2\text{e}^- \qquad (33)$$

(5)

cyclic experiments. It should be mentioned here that many examples of reactions of this general type exist in the older electroorganic literature[146]. Constant current electrolysis of phenols often leads to substituted quinones as intermediates or products of the electrode reaction.

Chambers and coworkers have studied several phosphate ($R = PO_3H_2$) and sulphate ($R = SO_3H$) ester derivatives of various hydroquinones at carbon paste electrodes over a wide pH range[147–150]. These workers stressed the intermediacy of one-electron intermediates and proposed mechanisms similar to Vetter's[79] in terms of the order of proton- and electron-transfer steps. However, diffusion-controlled electron-transfer rates were postulated with irreversible chemical reactions following the first and second electron-transfer steps. In strongly acidic solutions, these esters undergo reversible two-electron, one-proton transfers followed by rapid hydrolysis reactions. In these solutions the behaviour is further complicated by specific adsorption of the reduced form[148,150].

Similar electrode reactions have been described for 4,4′-dihydroxydiphenyl ether, *p*-methoxy- and *p*-ethoxyphenol in sulphuric acid solutions[6,151,152]. The monograph by Adams[6] should be consulted for

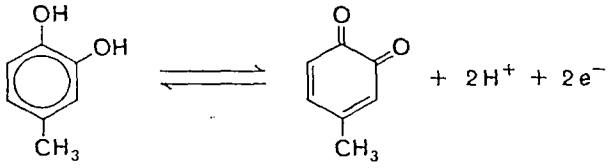


$$+ \text{CH}_3\text{OH} + \text{H}^+ \qquad (34)$$

more details on these oxidations as well as the analogous reactions for aminophenols and phenylenediamines.

Electrochemical techniques have proved to be versatile and convenient for the measurement of rates of addition of nucleophiles to quinones[6]. The procedure is to generate the appropriate quinone substrate from the hydroquinone and measure the apparent electrochemical *n*-value as a

function of electrolysis time. The following reaction scheme has been shown to apply to several benzoquinones[153, 154].



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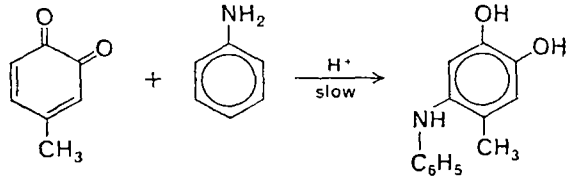

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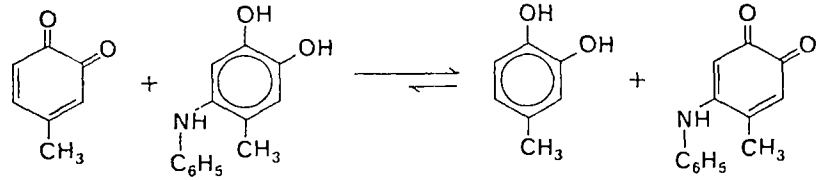
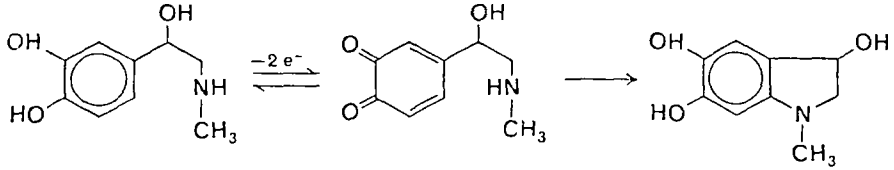


(37)

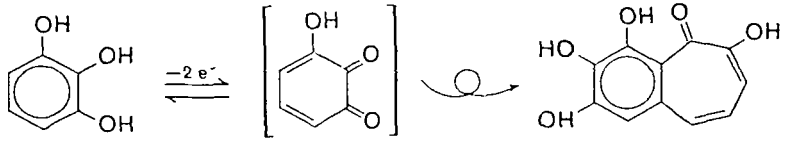
At short times (compared to the lifetime of the initial electrode product) a two-electron oxidation is observed which undergoes a transition into a four-electron process as the equilibrium (equation 37) is established in the diffusion layer. (This is the nuance of the e.c.e. mechanism or the e.c.c. mechanism[153]. In electrochemical parlance, an e.c.e. mechanism refers to a sequence in which a chemical reaction occurs between two heterogeneous electron-transfer steps. The same overall reaction can be realized in the e.c.c. mechanism if an homogeneous electron-transfer reaction follows the first two steps of the e.c.e. mechanism.) Similar reactions occur for a series of catechloamines, whose quinoidal forms undergo intramolecular 1,4 Michael additions[155]. This reaction is given below (equation 38) for



(38)

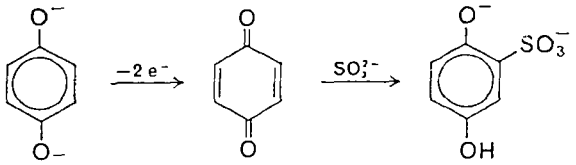
the cyclization of adrenalinequinone to leucoadrenochrome. The catecholamines studied in addition to adrenaline were noradrenaline, α-methyladrenalines, dopamine and isoproterenol.

The electrochemical oxidation of pyrogallol involves an initial two-electron step followed by rapid, complex reactions to form purpurogallin[156]. Kalousek polarography indicated that the initial electron-transfer step was reversible. Chemical oxidation of pyrogallol is believed to involve a dipolar dimerization of the intermediate *ortho* quinone[157].



(39)

The electrochemical oxidation of *p*-benzohydroquinone in neutral sodium sulphite solutions appears to involve 1,4-addition reactions. Two two-electron waves are observed at carbon paste electrodes corresponding to formation of the monosulphonate and disulphonate derivatives, equations (40) and (41)[158].



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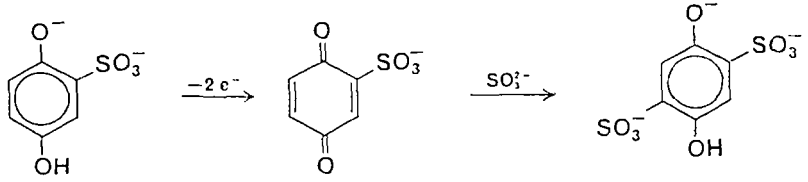
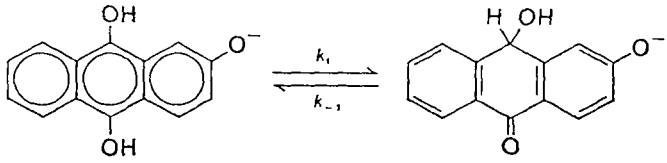


(41)

In this case the initial addition product is not more easily oxidized than the simple hydroquinone and the e.c.e. or e.c.c. pathway is not followed. Sulphonated benzohydroquinones are also formed in concentrated sulphuric acid solutions[159]. Up to ca. 10M H_2SO_4, oxidation occurs via oxygen protonated hydroquinone, QH_3^+. At higher acid strengths sulphonation of the benzene ring occurs and the behaviour becomes complex[159].

Several papers have dealt with the tautomerism of 2-substituted anthrohydroquinones since the original report of this equilibrium by Gill and Stonehill[160–164]. Freshly prepared aqueous solutions of anthrohydroquinones exhibit diffusion-controlled oxidation waves which are time-dependent due to a slow tautomerism of the ionized form (equation 42). The equilibrium constant for this reaction is pH-dependent and obtains a maximum value in the neighbourhood of pH 9. The tautomeric oxanthrol

form is itself polarographically reducible at a potential ca. 0·5 V more negative than reduction of the corresponding quinone. Thus polarograms of the quinone exhibit a diffusion-controlled wave followed by a

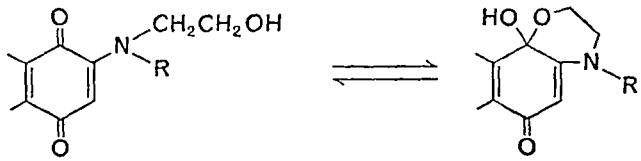


(42)

kinetically controlled wave[161]. Equilibrium rate constants for this process have been determined for several anthrahydroquinones substituted in the 2-position[164].

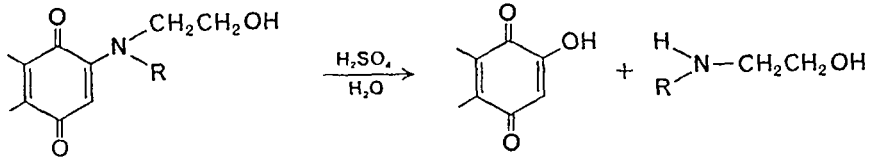
The use of borate buffers alters these reactions by complex formation with the hydroxy groups[163]. This is a well-known property of borate buffer solutions; for a good example of this effect see the work of Hofmann and Jaenicke on the oxidation of 1,2,4-trihydroxybenzene in basic borate buffers[165].

The polarographic behaviour of a series of amino-substituted quinones has been reported by Berg and coworkers[166–168]. β-Hydroxyalkylamino-benzoquinones give two polarographic waves over a wide pH range. The normal quinone, which is reduced at the more positive potential, is in equilibrium with a quinol formed by an intramolecular addition reaction (equation 43). The structure of this cyclization product has been recently



(43)

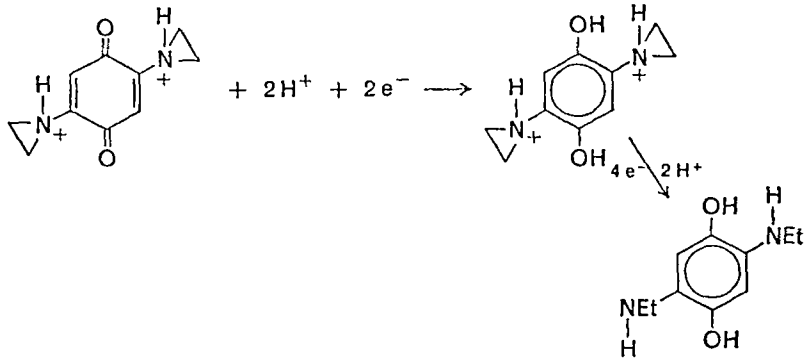
confirmed[169]. In sulphuric acid solutions the quinone form is hydrolysed to 2-hydroxybenzoquinone via equation (44)[168].



(44)

Berg and Wayner[170] have also studied the reduction of some ethylene-iminobenzoquinones. These quinones are reduced in two steps, initially to the hydroquinones followed by catalytic hydrogen waves at very negative potentials.

Photochemical reactions of quinones are also easily coupled to their electrode reactions[171–174], sometimes inadvertently. Quinones exhibit



(45)

strong $n \rightarrow \pi^*$ bands in the ultraviolet or visible region of the spectrum. Irradiation of quinones with light of this wavelength causes reactions of the following type to occur:

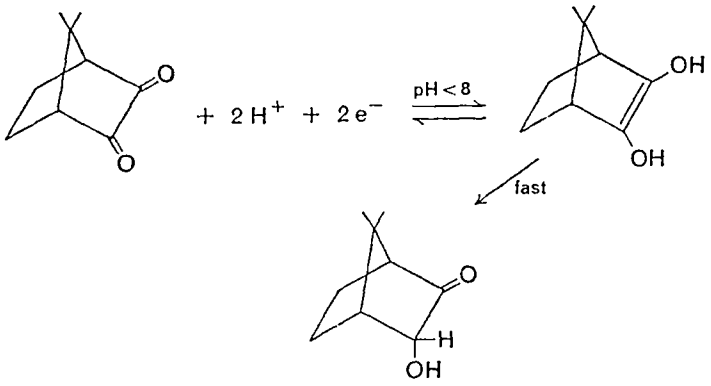
$$\begin{aligned} Q + h\nu &\longrightarrow Q^* \\ Q^* + H_2O &\rightleftharpoons QH^{\bullet} + HO^{\bullet} \\ 2\,QH^{\bullet} &\rightleftharpoons QH_2 + Q \end{aligned} \qquad (46)$$

Quinone solutions are accordingly sometimes unstable in the presence of ordinary laboratory light. Also 'photocatalytic' currents are readily observed in the presence of the proper radiation. These latter techniques have been coined 'Photopolarography' and were initially employed by Berg and coworkers[171]. Hydroxylation of the parent quinone is sometimes observed, presumably arising from reactions of the $HO^{\bullet}$ radical[175]. Electrochemical observation of this latter species has been recently claimed[176].

Hydroxyl radicals have also been invoked in the reactions of quinones in basic aqueous and aprotic solutions[177]. The reactions of quinones in these solutions have been followed by polarography, cyclic chronopotentiometry and e.s.r. spectroscopy. Reaction is initiated by an electron transfer between Q and OH^- followed by disproportionation reactions (equation 47). Further reactions occur, including formation of electroinactive polymers[177].

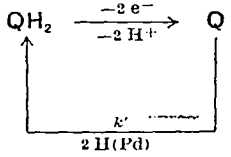
$$\begin{aligned} Q + OH^- &\rightleftharpoons Q^{\bullet -} + {}^{\bullet}OH \\ 2\,Q^{\bullet -} + 2\,H^+ &\longrightarrow Q + QH_2 \end{aligned} \qquad (47)$$

The polarographic reduction of camphorquinone has been studied in aqueous solutions[178]. This compound represents an interesting comparison for typical quinone reductions since its behaviour corresponds to that of an α,β-diketone (equation 48). Above pH 12 one-electron reduction and dimer formation is observed[178].



(48)

Rates of rapid microheterogeneous catalytic hydrogenation reactions of quinones have been measured polarographically. Oxidation of hydroquinone in the presence of palladium catalyts yields electrochemical currents according to the following scheme and rates of hydrogenation can be conveniently determined under a wide variety of conditions[179].



(49)

V. APPENDIX: HALF-WAVE POTENTIALS OF QUINONES IN NON-AQUEOUS SOLVENTS

TABLE 1

Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
p-Benzoquinone	0·48	S.c.e.	DMF	TEAP	25	180
p-Benzoquinone	0·54, 1·23	S.c.e.	DMF	TEAP	25	34
p-Benzoquinone	0·15, 0·81	Ag/AgCl	DMF	TEAP	19	36
p-Benzoquinone	0·54[f], 1·33[f]	S.c.e.	MeCN	TEAP	—	77
p-Benzoquinone	0·51, 1·17	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone	0·51, 1·14	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone	0·10, 0·84	HgPool	MeCN	TEAP	—	48
p-Benzoquinone	0·60, 1·32	S.c.e.	MeCN	TBAP	—	181
p-Benzoquinone	−0·04, 0·47	HgPool	MeCN	TBAI	—	182
p-Benzoquinone	0·15, 0·89	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone	0·35, 1·2	S.c.e.	DMSO	TEAP	—	104
p-Benzoquinone	0·40, 1·24	S.c.e.	DMSO	TEAP	25	183
p-Benzoquinone	0·38, 1·17	S.c.e.	DMSO	TEAI	25	103
p-Benzoquinone	0·52[f], 1·04[f]	S.c.e.	PC	TEAP	—	63
p-Benzoquinone	0·51[f]	S.c.e.	NB	TEAP	—	63
p-Benzoquinone	0·4	S.c.e.	$MeNO_2$	TMACl	26	184
p-Benzoquinone	0·18[f]	Ag/Ag^+	Py	$LiClO_4$ (0·5M)	25	94
p-Benzoquinone, fluoro-	0·374, 1·05	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, chloro-	0·34, 0·97	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, chloro-	0·34, 0·92	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, bromo-	0·325, 0·95	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, iodo-	0·33, 1·05	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, 2,5-dichloro-	0·18, 0·81	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, 2,6-dichloro-	0·18, 0·81	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, trichloro-	0·08, 0·78	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, tetrafluoro-	0·04, 0·82	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, tetrachloro-	−0·01, 0·71	S.c.e.	MeCN	TEAP	25	34

p-Benzoquinone, tetrachloro-	−0·20, −0·04	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, tetrachloro-	0·02, 0·90	S.c.e.	DMF	TEAP	25	34
p-Benzoquinone, tetrachloro-	−0·33	Ag/AgI	$CHCl_3$	TBAP (0·5M)	25	106
p-Benzoquinone, tetrachloro-	−0·35, 0·43	Ag/AgI	CH_2Cl_2	TBAP (0·5M)	25	106
p-Benzoquinone, tetrachloro-	−0·08, 0·73	S.c.e.	DMSO	TEAP	25	183
p-Benzoquinone, tetrabromo-	0·00, 0·72	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, cyano-	0·120, 0·83	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, 2,3-dicyano-	−0·31, −0·05	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, 2,3-dicyano-5-chloro-	−0·41, −0·08	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, 2,3-dichloro-5,6-dicyano-	−0·51, 0·30	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, 2,3-dichloro-5,6-dicyano-	−0·50, −0·12	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, 2,3-dichloro-5,6-dicyano-	−0·81, −0·02	Ag/AgI	$CHCl_3$	TBAP (0·5M)	25	106
p-Benzoquinone, 2,3-dichloro-5,6-dicyano-	−0·78, 0·02	Ag/AgI	CH_2Cl_2	TBAP (0·5M)	25	106
p-Benzoquinone, 2,3-dicyano-5-phenylsulphonyl-	−0·52, −0·20	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, 2,3-dicyano-5-chloro-6-phenylsulphonyl-	−0·62[a], −0·20	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, nitro-	−0·405, 0·32	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, methyl-	0·58, 1·12	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, methyl-	0·58, 1·10	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, methyl-	0·580	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, methyl-	0·17	HgPool	MeOEtOH	LiCl(0·25M)	25	186
p-Benzoquinone, 2,5-dimethyl-	0·67, 1·27	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, 2,5-dimethyl-	0·68, 1·34	S.c.e.	DMF	TEAP	25	34
p-Benzoquinone, 2,6-dimethyl-	0·665	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, 2,6-dimethyl-	0·660	S.c.e.	MeCN	TBAP	25	187
p-Benzoquinone, trimethyl-	0·75, 1·35	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, trimethyl-(3′-methyl-3′-hydroxybutyl)-	0·8, 1·4	S.c.e.	MeCN	TEAP	22·5	67
p-Benzoquinone, tetramethyl-	0·84, 1·45	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, tetramethyl-	0·84	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, tetramethyl-	0·76	S.c.e.	DMF	TEAP	25	180
p-Benzoquinone, tetramethyl-	0·33, 1·05	HgPool	MeCN	TBABr	—	48

TABLE 1 (*cont.*)

Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
p-Benzoquinone, tetramethyl-	0·73, 1·53	S.c.e.	DMSO	TEAP	25	183
p-Benzoquinone, trifluoromethyl-	0·306, 0·98	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, 2-methyl-5-isopropyl-	0·665	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, 2-methyl-6-*t*-butyl-	0·685	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, *i*-propyl-	0·590	S.c.e.	MeCN	TBAP	25	187
p-Benzoquinone, 2,6-di-*i*-propyl-	0·675	S.c.e.	MeCN	TBAP	25	187
p-Benzoquinone, 2-*i*-propyl-6-*t*-butyl-	0·700	S.c.e.	MeCN	TBAP	25	187
p-Benzoquinone, *t*-butyl-	0·610	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, 2,6-di-*t*-butyl-	0·730	S.c.e.	MeCN	TBAP	25	187
p-Benzoquinone, 2,5-di-*t*-butyl-	0·715	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, 2,5-di-*t*-butyl-	0·73, 1·24	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, 2,5-di-*t*-butyl-	0·15, 0·71	HgPool	MeCN	TBAI	—	182
p-Benzoquinone, 2,5-di-*t*-amyl-	0·725	S.c.e.	MeCN	TBAP	25	185
p-Benzoquinone, phenyl-	0·49, 1·11	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, phenyl-	0·50, 1·03	S.c.e.	MeCN	TEAP	25	34
p-Benzoquinone, 2,5-dihydroxy	0·01	Ag/AgCl	DMF	TEAP	19	36
p-Benzoquinone, tetrahydroxy-	0·32	Ag/AgCl	DMF	TEAP	19	36
p-Benzoquinone, methoxy-	0·615	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, 2,6-dimethoxy	0·74[f], 1·48[f]	S.c.e.	MeCN	TEAP	—	77
p-Benzoquinone, 2,5-dimethoxy	0·43, 0·97	Ag/AgCl	DMF	TEAP	19	36
p-Benzoquinone, carbomethoxy-	0·315, 0·91	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, acetyl-	0·306, 0·98	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, *N*,*N*-dimethylamino-	0·745, 1·28	S.c.e.	MeCN	TEAP	25	26
p-Benzoquinone, 2,5-bis(trimethylsilyl)-	−0·04, 0·51	HgPool	MeCN	TBAI	—	182
p-Benzoquinone, 2,6-bis(trifluoromethylthio)-	0·01, 0·43	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, tris(trifluoromethylthio)-	−0·15, 0·09	S.c.e.	MeCN	$LiClO_4$	—	42
p-Benzoquinone, tetrakis(trifluoromethylthio)-	−0·23	S.c.e.	MeCN	$LiClO_4$	—	42

p-Benzoquinone, trifluoromethylsulphonyl-	−0·15, 0·12, 0·38	S.c.e.	MeCN	$LiClO_4$	—	42
o-Benzoquinone	0·31, 0·90	S.c.e.	MeCN	TEAP	25	34
o-Benzoquinone	0·220	S.c.e.	DMSO	TBAI	25	102
o-Benzoquinone, 4-*t*-butyl-	0·455	S.c.e.	MeCN	TBAP	25	185
o-Benzoquinone, 3,5-di-*t*-butyl-	0·560	S.c.e.	MeCN	TBAP	25	185
1,4-Naphthoquinone	0·71, 1·25	S.c.e.	MeCN	TEAP	25	34
1,4-Naphthoquinone	0·70, 1·33	S.c.e.[h]	MeCN	TEAP (0·05M)	25	101
1,4-Naphthoquinone	0·85, 1·55	S.c.e.	MeCN	TBAP	—	181
1,4-Naphthoquinone	0·685	S.c.e.	MeCN	TEAP	—	38
1,4-Naphthoquinone	0·60	S.c.e.	DMF	TEAP	25	180
1,4-Naphthoquinone	0·63, 1·35	S.c.e.[i]	DMF	TEAP (0·05M)	25	101
1,4-Naphthoquinone	0·63, 1·35	S.c.e.	DMF	TBAP	—	188
1,4-Naphthoquinone	0·31, 0·96	Ag/AgCl	DMF	TEAP	19	36
1,4-Naphthoquinone	0·72, 1·63	S.c.e.	DMF	TEAP	25	34
1,4-Naphthoquinone	0·69, 1·18	S.c.e.[j]	Me_2CO	TEAP (0·05M)	25	101
1,4-Naphthoquinone	0·58, 1·29	S.c.e.[k]	DMSO	TEAP (0·05M)	25	101
1,4-Naphthoquinone	0·55, 1·29	S.c.e.	DMSO	TBAI	25	103
1,4-Naphthoquinone	0·67, 1·05	S.c.e.[l]	PC	TEAP (0·05M)	25	101
1,4-Naphthoquinone, 2-methyl-	0·78	S.c.e.	MeCN	TEAP	25	48
1,4-Naphthoquinone, 2-methyl-	0·77, 1·28	S.c.e.	MeCN	TEAP	25	34
1,4-Naphthoquinone, 2-methyl-	0·27, 0·94	HgPool	MeCN	TBABr	—	48
1,4-Naphthoquinone, 2-methyl-	1·10	Ag/Ag^+ (0·01M)	MeCN	TEAP	—	69
1,4-Naphthoquinone, 2-methyl-	0·69	S.c.e.	DMF	TEAP	25	180
1,4-Naphthoquinone, 2-methyl-	0·20, 1·02	HgPool	DMF	TBABr	—	48
1,4-Naphthoquinone, 2-methyl-	0·34, 1·05	HgPool	DMF	$NaNO_3$	—	48
1,4-Naphthoquinone, 2,3-dimethyl-	0·846	S.c.e.	MeCN	TEAP	—	38
1,4-Naphthoquinone, 2,3-cyclobutano-	0·695	S.c.e.	MeCN	TEAP	—	38
1,4-Naphthoquinone, 2,3-cyclopentano-	0·748	S.c.e.	MeCN	TEAP	—	38
1,4-Naphthoquinone, 2,3-cyclohexano-	0·854	S.c.e.	MeCN	TEAP	—	38
1,4-Naphthoquinone, 2,3-(3,4-diphenylcyclobutano)-	0·40, 0·86	S.c.e.	DMF	TBAP	—	188
1,4-Naphthoquinone, 2-amino-	0·92, 1·40	S.c.e.	MeCN	TEAP	25	34
1,4-Naphthoquinone, 2-hydroxy-	0·64, 1·20	S.c.e.	DMF	TEAP	25	34

TABLE 1 (*cont.*)

Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
1,4-Naphthoquinone, 5-hydroxy-	0·51, 1·17	S.c.e.	DMF	TEAP	25	34
1,4-Naphthoquinone, 5-hydroxy-	0·13, 0·70	Ag/AgCl	DMF	TEAP	19	36
1,4-Naphthoquinone, 5-hydroxy-	0·52, 0·99	S.c.e.	MeCN	TEAP	25	34
1,4-Naphthoquinone, 5,8-dihydroxy-	0·05, 0·67	Ag/AgCl	DMF	TEAP	19	36
1,2-Naphthoquinone	0·20, 0·67	Ag/AgCl	DMF	TEAP	19	36
1,2-Naphthoquinone	0·51, 1·12	S.c.e.[i]	DMF	TEAP (0·05M)	25	101
1,2-Naphthoquinone	0·56, 1·02	S.c.e.	MeCN	TEAP	25	34
1,2-Naphthoquinone	0·58, 1·18	S.c.e.[h]	MeCN	TEAP (0·05M)	25	34
1,2-Naphthoquinone	0·46	S.c.e.	DMSO	TBAI	25	103
1,2-Naphthoquinone	0·49, 1·18	S.c.e.[k]	DMSO	TEAP (0·05M)	25	101
1,2-Naphthoquinone	0·57, 1·01	S.c.e.[j]	Me_2CO	TEAP (0·05M)	25	101
1,2-Naphthoquinone	0·55, 0·92	S.c.e.[l]	PC	TEAP (0·05M)	25	101
9,10-Anthraquinone	0·43, 1·05	HgPool	MeCN	TBABr	—	48
9,10-Anthraquinone	0·94	S.c.e.	MeCN	—	—	39
9,10-Anthraquinone	0·98[f], 1·50[f]	S.c.e.	MeCN	TEAP	—	63
9,10-Anthraquinone	1·04, 1·69	S.c.e.	MeCN	TBAP	—	181
9,10-Anthraquinone	0·94, 1·45	S.c.e.	MeCN	TEAP	25	34
9,10-Anthraquinone	0·34, 1·10	HgPool	DMF	TBABr	—	48
9,10-Anthraquinone	0·32, 0·92	HgPool	DMF	TEAI	—	189
9,10-Anthraquinone	0·32, 0·99	HgPool	DMF	TEAI	—	64
9,10-Anthraquinone	0·38, 1·04	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone	0·33, 0·9	HgPool[n]	DMF	TEAI	—	191
9,10-Anthraquinone	0·33, 0·95	HgPool	DMF	TEAI	—	192
9,10-Anthraquinone	0·30, 0·57	HgPool	DMF	LiCl (1M)	—	191
9,10-Anthraquinone	0·85, 1·43	S.c.e.	DMF	TEAP	20	70
9,10-Anthraquinone	0·93[f], 1·63[f]	S.c.e.	DMF	TEAP	—	63
9,10-Anthraquinone	0·90, 1·54	S.c.e.	DMF	TEAP	25	193

9,10-Anthraquinone	0·82, 1·44	S.c.e.	DMF	TEAP	—	194
9,10-Anthraquinone	0·98, 1·74	S.c.e.	DMF	TEAP	25	34
9,10-Anthraquinone	0·98, 1·69	S.c.e.	DMF	TEAI	25	34
9,10-Anthraquinone	0·86, 1·48	S.c.e.	DMF	TEAI (0·05M)	25	196, 197
9,10-Anthraquinone	0·97	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone	0·94	N.c.e.	DMF	TEAP	—	200
9,10-Anthraquinone	0·55, 1·17	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone	0·97, 1·43	S.c.e.	PC	TEAP	—	63
9,10-Anthraquinone	0·78, 1·45	S.c.e.	DMSO	TBAI	25	103
9,10-Anthraquinone, 1-amino-	0·46, 1·04	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1-amino-	0·44, 0·96	HgPool	DMF	TEAI	—	192
9,10-Anthraquinone, 1-amino-	0·42, 0·98	HgPool	DMF	TEAI	—	189
9,10-Anthraquinone, 1-amino-	0·49, 0·80	HgPool	DMF	LiCl	—	189
9,10-Anthraquinone, 1-amino-	1·06	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-amino-	0·54, 1·09	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 2-amino-	1·13	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1,2-diamino-	0·63, 1·13	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,4-diamino-	1·16	N.c.e.	DMF	TEAP	—	200
9,10-Anthraquinone, 1-bromo-	0·83, 1·45	S.c.e.	DMF	TEAI (0·05M)	25	197
9,10-Anthraquinone, 2-bromo-	0·78, 1·44, 2·31	S.c.e.	DMF	TEAI (0·05M)	25	197
9,10-Anthraquinone, 2-bromo-	0·90	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1-carbamoyl	0·94	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-carbamoyl	0·90	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1-chloro-	0·29, 0·88	HgPool	DMF	TEAI	—	189
9,10-Anthraquinone, 1-chloro-	0·83, 1·46, 2·23	S.c.e.	DMF	TEAI (0·05M)	25	196, 197
9,10-Anthraquinone, 1-chloro-	0·90	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-chloro-	0·78, 1·43, 2·50	S.c.e.	DMF	TEAI (0·05M)	25	196, 197
9,10-Anthraquinone, 2-chloro-	0·90	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-chloro-	0·24, 0·81	HgPool	DMF	TEAI	—	198, 199
9,10-Anthraquinone, 1,2-dichloro-	0·76, 1·43, 2·26	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,3-dichloro-	0·75, 1·42, 2·21	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,4-dichloro-	0·79, 1·46, 2·32	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,5-dichloro-	0·79, 1·46, 2·35	S.c.e.	DMF	TEAI (0·05M)	25	196

TABLE 1 (*cont.*)

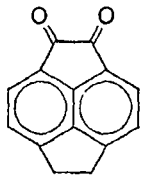
Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
9,10-Anthraquinone, 1,5-dichloro-	0·25, 0·85	HgPool	DMF	TEAI	—	189
9,10-Anthraquinone, 1,6-dichloro-	0·74, 1·43, 2·30	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,7-dichloro-	0·74, 1·43, 2·28	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,8-dichloro	0·79, 1·46, 2·23	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,8-dichloro-	0·25, 0·86	HgPool	DMF	TEAI	—	189
9,10-Anthraquinone, 2,3-dichloro-	0·71, 1·35, 2·45	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 2,6-dichloro-	0·70, 1·32, 2·53	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 2,7-dichloro-	0·72, 1·36, 2·64	S.c.e.	DMF	TEAI (0·05M)	25	196
9,10-Anthraquinone, 1,4-diacetoxy-	0·46, 0·85	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 2-ethyl-	1·12, 1·69	S.c.e.	DMF	TEAI	25	34
9,10-Anthraquinone, 2-ethyl-	0·41, 0·70	HgPool	DMF	LiCl	—	201
9,10-Anthraquinone, 2-ethyl-	1·00	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1,2-diethyl-	0·82	S.c.e.	DMF	TEABr	—	199
9,10-Anthraquinone, 1-fluoro-	0·83, 1·47	S.c.e.	DMF	TEAI (0·05M)	25	197
9,10-Anthraquinone, 1-fluoro-	0·92	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-fluoro-	0·77, 1·46	S.c.e.	DMF	TEAI (0·05M)	25	197
9,10-Anthraquinone, 2-fluoro-	0·93	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1-hydroxy-	0·20, 0·80	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1-hydroxy-	0·16, 0·73	HgPool[n]	DMF	TEAI	—	191
9,10-Anthraquinone, 1-hydroxy-	0·10, 0·54	HgPool	DMF	LiCl (1M)	—	191
9,10-Anthraquinone, 1-hydroxy-	0·77, 1·39	S.c.e.	DMF	TEAP	25	34
9,10-Anthraquinone, 2-hydroxy-	0·39, 0·64, 0·82, 1·10	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 2-hydroxy	0·54, 0·81	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 2-hydroxy-	0·64, 1·26	S.c.e.(Na)	DMF	TEAP	—	89
9,10-Anthraquinone, 2-hydroxy-	0·77, 1·20	S.c.e.(Na)	MeCN	TEAP	—	89
9,10-Anthraquinone, 2-hydroxy-	0·74, 1·20	S.c.e.(Na)	PC	TEAP	—	89

9,10-Anthraquinone, 1,2-dihydroxy-	0·43	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,4-dihydroxy-	0·06, 0·72	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,4-dihydroxy-	0·07, 0·58	HgPool[n]	DMF	TEAI	—	191
9,10-Anthraquinone, 1,4-dihydroxy-	0·42, 0·55, 0·90	HgPool	DMF	LiCl (1M)	—	191
9,10-Anthraquinone, 1,4-dihydroxy-	0·29, 0·88	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,4-dihydroxy-	0·56	N.c.e.	DMF	TEAP	—	200
9,10-Anthraquinone, 1,5-dihydroxy-	0·03, 0·54	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,5-dihydroxy-	0·24, 0·72	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,8-dihydroxy-	0·04, 0·74	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,8-dihydroxy-	0·27, 0·93	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,8-dihydroxy-	0·64, 1·42	S.c.e.	DMF	TEAP	25	34
9,10-Anthraquinone, 1,2,4-trihydroxy-	0·18, 0·73	HgPool[m]	DMF	TEAI	19	36
9,10-Anthraquinone, 1,2,5,8-tetrahydroxy-	0·30	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,4,5,8-tetrahydroxy-	0·12	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1-iodo-	0·84, 1·34, 1·44	S.c.e.	DMF	TEAI (0·5M)	25	197
9,10-Anthraquinone, 1-iodo-	0·93	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-iodo-	0·78, 1·37, 1·48	S.c.e.	DMF	TEAI (0·05M)	25	197
9,10-Anthraquinone, 1-methoxy-	0·43, 0·89	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1-methoxy-	1·01	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 2-methoxy-	0·39, 0·93	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,4-dimethoxy-	0·50, 1·04	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,4-dimethoxy-	0·71, 1·04	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,5-dimethoxy-	0·54, 1·04	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 1,5-dimethoxy-	0·71, 1·05	Ag/AgCl	DMF	TEAP	19	36
9,10-Anthraquinone, 1,8-dimethoxy-	0·50, 1·06	HgPool[m]	DMF	TEAI	25	190
9,10-Anthraquinone, 2-methyl-	1·00	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1,4-dimethyl-	1·08, 1·57	S.c.e.	MeCN	TEAP	—	202
9,10-Anthraquinone, 1,4,5,8-tetramethyl-	1·27, 1·73	S.c.e.	MeCN	TEAP	—	192
9,10-Anthraquinone, 1-nitro-	0·07, 0·70, 0·98	HgPool	DMF	TEAI	—	192
9,10-Anthraquinone, 1-nitro-	0·76	S.c.e.	DMF	TEABr	—	198, 199
9,10-Anthraquinone, 1-nitro-2-carboxy-	0·86	S.c.e.	DMF	TEABr	—	199
9,10-Anthraquinone, 1,2-diphenyl-	0·32	HgPool	DMF	TEABr	—	198
9,10-Anthraquinone, 2-sulphonate (Na)	0·91, 1·40	S.c.e.	MeCN	TEAP	25	34

TABLE 1 (*cont.*)

Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
9,10-Anthraquinone, 2-sulphonate (Na)	0·98, 1·64	S.c.e.	DMF	TEAI	25	34
9,10-Anthraquinone, 2-sulphonate (Na)	0·33, 0·97	HgPool	DMF	TEAI	—	189
1,4-Anthraquinone	0·75, 1·25	S.c.e.	MeCN	TEAP	25	34
9,10-Phenanthraquinone	0·12, 0·69	HgPool	DMF	TEAI	—	64
9,10-Phenanthraquinone	0·30, 0·76	Ag/AgCl	DMF	TEAP	19	36
9,10-Phenanthraquinone	0·70	S.c.e.	DMF	TEAP	25	203
9,10-Phenanthraquinone	0·66, 1·22	S.c.e.	MeCN	TEAP	25	34
9,10-Phenanthraquinone	0·66	S.c.e.	MeCN	TBAP	RT	46
9,10-Phenanthraquinone	0·24	S.c.e.	MeCN	$LiClO_4$	RT	46
9,10-Phenanthraquinone	0·54, 1·28	S.c.e.	DMSO	TBAI	25	103
9,10-Phenanthraquinone, 2,4,7-trinitro-	0·10	S.c.e.	MeCN	TBAP	RT	46
9,10-Phenanthraquinone, 2,4,7-trinitro-	−0·08	S.c.e.	MeCN	$LiClO_4$	RT	46
9,10-Phenanthraquinone, 3,6-dinitro-	0·15	S.c.e.	MeCN	TBAP	RT	46
9,10-Phenanthraquinone, 3,6-dinitro-	−0·06	S.c.e.	MeCN	$LiClO_4$	RT	46
9,10-Phenanthraquinone, 2,7-dinitro-	0·20	S.c.e.	MeCN	TBAP	RT	46
9,10-Phenanthraquinone, 2,7-dinitro-	−0·04	S.c.e.	MeCN	$LiClO_4$	RT	46
9,10-Phenanthraquinone, 2,5-dinitro-	0·26	S.c.e.	MeCN	TBAP	RT	46
9,10-Phenanthraquinone, 2,5-dinitro-	−0·01	S.c.e.	MeCN	$LiClO_4$	RT	46
5,12-Naphthacenequinone	1·13, 1·65	S.c.e.	MeCN	TBAP	—	181
1,2-Benz-9,10-anthraquinone	0·66, 1·19	S.c.e.	DMF	TEAP	—	194
6,13-Pentacenequinone	1·23, 1·55	S.c.e.	MeCN	TBAP	—	181
1,6-Benzopyrenequinone	0·57[f], 0·77[f]	S.c.e	MeCN	TEAP	—	63
3,6-Benzopyrenequinone	0·60[f], 0·86[f]	S.c.e.	MeCN	TEAP	—	63
6,12-Benzopyrenequinone	0·58[f], 0·90[f]	S.c.e.	MeCN	TEAP	—	63
Benzocyclobutadienequinone	1·20	S.c.e.	MeCN	TEAP	25	204
1,2-Acenaphthaquinone	0·81, 1·66	S.c.e.	DMSO	TBAI	25	103
Diketopyracene (**1**)	0·91, 1·73	S.c.e.	DMSO	TBAI	25	103

Pyracycloquinone (**2**)	0·74, 1·30	S.c.e.	DMSO	TBAI	25	103
4,8-Dibenzopentalenoquinone (**3**)	0·90, 1·63	S.c.e.	DMSO	TBAP	—	205
Triptycenequinone (**4**)	0·64, 1·25	HgPool	DMF	KNO_3	—	206
12,15-Dihydro-12,15-dioxo-2,3:6,7-dibenzotriptycene (**5**)	0·67, 1·28	HgPool	DMF	KNO_3	—	206
9,10-Dihydroanthrylenenaphthoquinone (**6**)	0·09, 0·47	HgPool	DMF	LiCl	—	206
Naphthotriptycenequinone (**7**)	0·94, 1·40	HgPool	DMF	KNO_3	—	206
12,15-Dihydro-12,15-dioxo(2,3-6,7-13,14)-tribenzotrypticene (**8**)	0·81, 1·35	HgPool	DMF	KNO_3	—	206
12,15-Dihydro-12,15-dioxo-2,3:6,7-dibenzo-13,14-naphthotriptycene (**9**)	0·82, 135	HgPool	DMF	KNO_3	—	206
(**10**)	0·66, 1·34	HgPool	DMF	KNO_3	—	206
(**11**)	0·63, 1·26	HgPool	DMF	KNO_3	—	206
Biphenylquinone	0·23, 0·52	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone	0·24, 0·41	S.c.e.	MeCN	TEAP	25	34
Biphenylquinone, 3-methyl-	0·28, 0·62	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3-*t*-butyl	0·30, 0·64	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′-dimethyl-	0·34, 0·64	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′-di-*t*-butyl-	0·36, 0·72	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′,5,5′-tetramethyl-	0·44, 0·77	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′,5,5′-tetraisopropyl-	0·45, 0·80	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′,5,5′-tetra-*t*-butyl-	0·50, 0·90	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′-dimethyl-5,5′-di-*t*-butyl-	0·47, 0·83	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′-diisopropyl-5,5′-di-*t*-butyl-	0·48, 0·86	S.c.e.	MeCN	TBAP	—	207
Biphenylquinone, 3,3′,5,5′-tetramethoxy-	0·51	S.c.e.	MeCN	TEAP	—	77
Dibenzoquinone (**12**)	0·35, 0·65, 0·88	S.c.e.	MeCN	TEAP	25	208
Dibenzoquinone (**12**)	0·38, 0·74, 1·29	S.c.e.	DMF	TEAP	25	208
Dibenzoquinone (**12**), 5,5′-dimethyl-	0·55, 0·72, 1·08	S.c.e.	MeCN	TEAP	25	208
Dibenzoquinone (**12**), 5,5′-dimethyl-	0·57, 0·77, 1·48	S.c.e.	DMF	TEAP	25	208
Dibenzoquinone (**12**), 5,5′-dimethyl-	0·50, 0·66, 1·23	S.c.e.	DMSO	TEAP	25	208
Triquinone (**13**)	0·49, 0·67, 0·73, 1·05	S.c.e.	MeCN	TEAP	25	208



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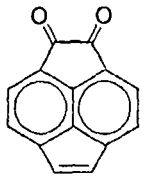

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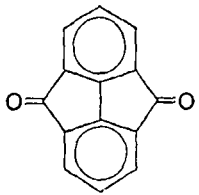

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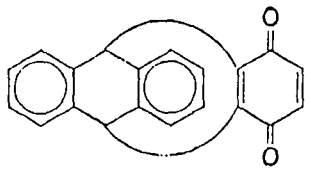

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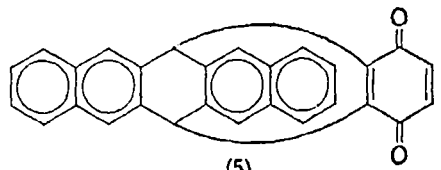

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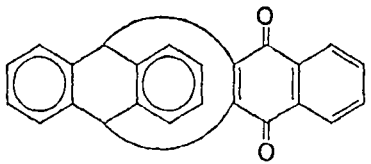

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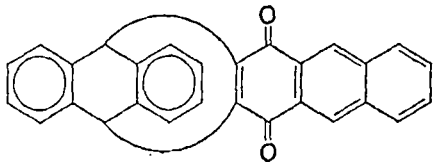

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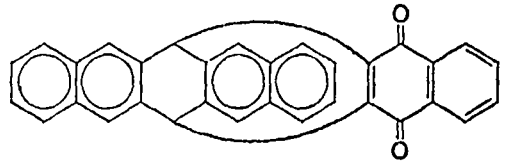

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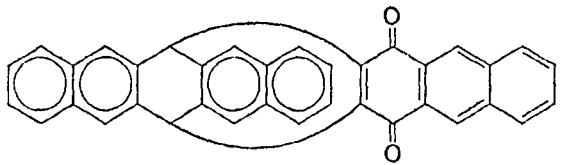

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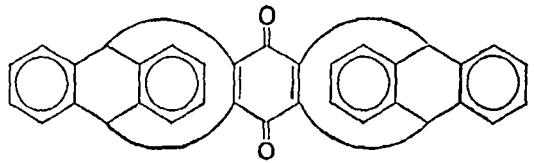

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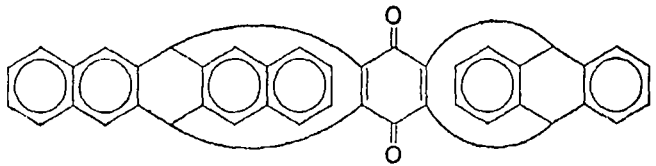


(11)

TABLE 1 (*cont.*)

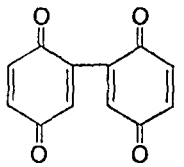
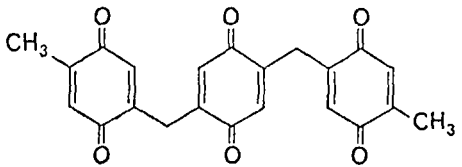
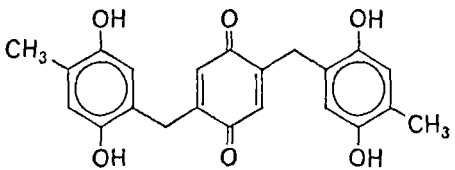
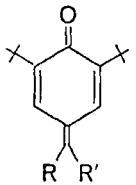
Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
Triquinone (**13**)	0·51, 0·71, 1·20	S.c.e.	DMF	TEAP	25	208
Triquinone (reduced) (**14**)	0·32, 0·68	S.c.e.	DMF	TEAP	25	208
 (**12**)						
 (**13**)						
 (**14**)						
Stilbenequinone, 3,3,5,5′-tetra-*t*-butyl-	0·04, 0·33	HgPool	DMF	TEAP	25	66
Stilbenequinone, 3,3′,5,5′-tetramethyl-	0·02, 0·17	HgPool	DMF	TEAP	25	66
Methylenequinone (**15**, R = H, R′ = CH_3)	1·28, 2·01	S.c.e.	DMF	TEAP	25	209
Methylenequinone (**15**, R = R′ = CH_3)	0·81, 1·42	S.c.e.	DMF	TEAP	25	209
Methylenequinone (**15**, R = CH_3, R′ = C_2H_5)	1·41,	S.c.e.	DMF	TEAP	25	209
Methylenequinone (**15**, R = R′ = C_5H_6)	1·11, 1·41	S.c.e.	DMF	TEAP	25	209
Methylenequinone (**15**, R = H, R′ = CH_2Br)	1·52	S.c.e.	DMF	TEAP	25	209
Methylenequinone (**15**, R = H, R′ = CN)	0·26, 0·50	S.c.e.	DMF	TEAP	25	209
Ubiquinone-1	0·84, 1·6	S.c.e.	MeCN	TEAP	—	68

TABLE 1 (*cont.*)

Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
α-Tocopherylquinone	0·56	S.c.e.	MeCN	$LiClO_4$	—	97
Vitamin E quinone	0·75	S.c.e.	DMF	TEAP	25	180
Benzimidazole-4,7-quinone (**16**)	0·44	S.c.e.	DMF	TEAP	—	210
Benzimidazole-4,7-quinone, 1-methyl-	0·67	S.c.e.	DMF	TEAP	—	210
Benzimidazole-4,7-quinone, 1-methyl-2-phenyl-	0·41	S.c.e.	DMF	TEAP	—	210
Benzimidazole-4,7-quinone, 1-methyl-2-dimethylamino-	0·67, 1·29	S.c.e.	DMF	TEAP	—	210
Benzimidazole-4,7-quinone, 1-methyl-2-chloro-	0·60	S.c.e.	DMF	TEAP	—	210
Benzimidazole-6,7-quinone, 1-methyl-	0·54	S.c.e.	DMF	TEAP	—	210
Benzimidazole-6,7-quinone, 2-phenyl-	0·38	S.c.e.	DMF	TEAP	—	210
Benzimidazole-6,7-quinone, 1-methyl-2-phenyl-	0·56	S.c.e.	DMF	TEAP	—	210
Benzimidazole-6,7-quinone, 1-methyl-2-chloro-	0·54	S.c.e.	DMF	TEAP	—	210
Benzimidazole-6,7-quinone, 1-methyl-2-dimethylamino-	0·64	S.c.e.	DMF	TEAP	—	210
Benzimidazole-5,6-quinone, 1-methyl-2-dimethylamino- (**17**)	0·71, 0·91	S.c.e.	DMF	TEAP	—	210
Benzimidazole-5,6-quinone, 1-methyl-2-(*p*-dimethylaminophenyl)-	0·48	S.c.e.	DMF	TEAP	—	210
Benzimidazolone-5,6-quinone, 1,3-dimethyl- (**18**)	0·63, 1·09	S.c.e.	DMF	TEAP	—	209
Benzimidazolone-4,7-quinone, 1,3-dimethyl-	0·59, 1·22	S.c.e.	DMF	TEAP	—	210
Naphth[2,5-*d*]imidazole-4,9-quinone, 1-methyl (**19**)	0·87	N.c.e.	DMF	TEAP	—	200, 211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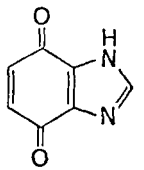
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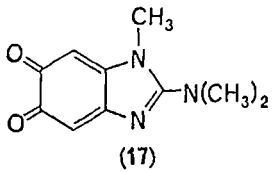
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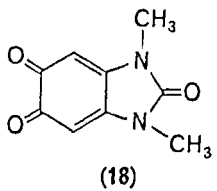
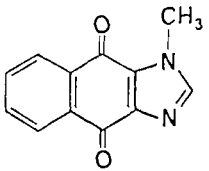
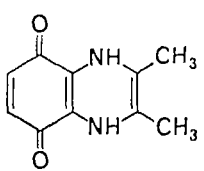
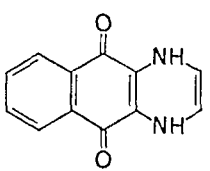
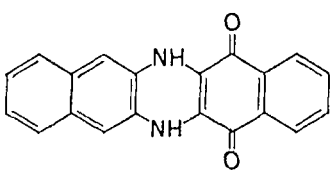
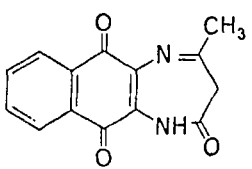
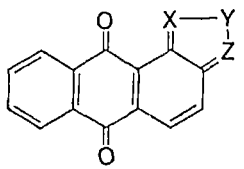
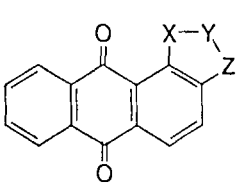

(18)

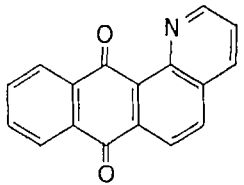
Naphth[2,5-*d*]imidazole-4,9-quinone, 1-methyl, 5,8-dihydroxy-	0·56	N.c.e.	DMF	TEAP	—	200
Naphth[2,5-*d*]imidazole-4,9-quinone, 1-methyl, 5-amino-8-hydroxy	0·59	N.c.e.	DMF	TEAP	—	200
Naphth[2,5-*d*]imidazole-4,9-quinone, 1-methyl, 5,8-diamino-	1·17	N.c.e.	DMF	TEAP	—	200
Quinoxaline-5,8-dione, 2,3-dimethyl-(**20**)	0·60, 1·37, 2·15	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione (**21**)	0·73, 1·37, 1·90	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione, 2-methyl-	0·76, 1·37, 1·96	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione, 2,3-dimethyl-	0·79, 1·45, 2·07	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione, 2-(*p*-dimethyl-aminostyryl)-	0·71, 1·36, 1·71	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione, 2,3-diphenyl-	0·81, 1·51, 2·14	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione, 2-hydroxy-3-phenyl-	0·49, 1·22, 2·08	S.c.e.	DMF	TEAP	—	211
Benzo[*g*]quinoxaline-5,10-dione, 2,3-dihydroxy-	0·59, 1·10	S.c.e.	DMF	TEAP	—	211
Dibenzo[*b*, *i*]phenazine-5,14-dione (**22**)	0·87, 1·53, 1·77	S.c.e.	DMF	TEAP	—	211
(**23**)	0·62, 1·36	S.c.e.	DMF	TEAP	—	211
(**24**: X = N, Y = O, Z = N → O)	0·19, 0·86	S.c.e.	DMF	TEAP	—	194, 195
(**24**: X = N, Y = O, Z = N)	0·27, 0·97	S.c.e.	DMF	TEAP	—	194, 195
(**24**: X = N, Y = S, Z = N)	0·42, 0·97	S.c.e.	DMF	TEAP	—	194, 195
(**24**: X = N, Y = Se, Z = N)	0·43, 1·01	S.c.e.	DMF	TEAP	—	194, 195
(**24**: X = N, Y = NC_5H_6, Z = N)	0·57, 1·13	S.c.e.	DMF	TEAP	—	194, 195
(**25**: X—Y—Z = S—N=N)	0·43, 1·10	S.c.e.	DMF	TEAP	—	194, 195

TABLE 1 (*cont.*)

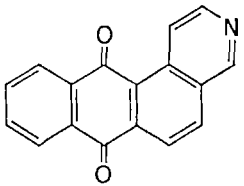
Name	$-E_{\frac{1}{2}}$ (V)	Reference electrode[a]	Solvent[b]	Supporting electrolyte[c, d]	T[e] (°C)	Reference
 (19)						
 (20)						
 (21)						
 (22)						
 (23)						
 (24)						
(25: X—Y—Z = N=N—S)	0·57, 1·06	S.c.e.	DMF	TEAP	—	194, 195
(25: X—Y—Z = N=N—NCH_3)	0·67, 1·19	S.c.e.	DMF	TEAP	—	194, 195
(25: X—Y—Z = S—$C(CH_3)$=N)	0·67, 1·35	S.c.e.	DMF	TEAP	—	194, 195
(25: X—Y—Z = N=$C(CH_3)$—S)	0·79, 1·21	S.c.e.	DMF	TEAP	—	194, 195
(25: X—Y—Z = N=CH—NH)	0·76, 1·10	S.c.e.	DMF	TEAP	—	194, 195
(25: X—Y—Z = N=CH—$N(CH_3)$)	0·88, 1·18	S.c.e.	DMF	TEAP	—	194, 195
(26)	0·69, 1·07	S.c.e.	DMF	TEAP	—	194, 195
(27)	0·62, 1·22	S.c.e.	DMF	TEAP	—	193, 194



(25)



(26)



(27)

[a] Abbreviations: s.c.e., saturated calomel electrode; n.c.e., normal calomel electrode; s.c.e. (Na) saturated NaCl calomel electrode; HgPool, mercury pool electrode.

[b] Abbreviations: DMF, *N*,*N*-dimethylformamide; MeCN, acetonitrile; DMSO, dimethyl sulphoxide; PC, propylene carbonate; NB, nitrobenzene; $MeNO_2$, nitromethane; Me_2CO, acetone; MeOEtOH, 2-methoxyethanol.

[c] Abbreviations: TEAP, tetraethylammonium perchlorate; TBAP, tetra-*n*-butylammonium perchlorate; TBAI, tetra-*n*-butylammonium iodide; TEAI, tetraethylammonium iodide; TMACl, tetramethylammonium chloride, TBABr, tetra-*n*-butylammonium bromide; TEABr, tetraethylammonium bromide.

[d] Concentration: 0·1M unless specified otherwise.

[e] No entry implies that the temperature was not given in the literature; room temperature is assumed.

[f] Peak potential, linear sweep voltammetry.

[g] Graphite electrode.

[h] −0·40 V versus $E_{\frac{1}{2}}$ ferrocene.

[i] −0·46 V versus $E_{\frac{1}{2}}$ ferrocene.

[j] −0·47 V versus $E_{\frac{1}{2}}$ ferrocene.

[k] −0·44 V versus $E_{\frac{1}{2}}$ ferrocene.

[l] −0·38 V versus $E_{\frac{1}{2}}$ ferrocene.

[m] −0·51 V versus s.c.e.

[n] −0·50 V versus s.c.e.

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The Chemistry of the Quinonoid Compounds
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CHAPTER 15

Polymeric quinones

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I. INTRODUCTION

This chapter considers the natural occurrence, synthesis, properties, and theoretical and practical importance of quinones incorporated into macromolecular structures or polymeric systems.

The presence of the macromolecular or polymeric structure confers new, distinctive, and sometimes unusual, properties on the quinone function as exemplified by changes in reactivity, electrochemical behaviour and in the development of semiconductor and catalytic properties.

Discussion is confined mainly to polyquinones in which there exists an *ortho* or *para* relationship of the carbonyl groups, but for the special case of conjugated polyquinones it has been extended to include polymers of quinonoid structure where the functional groups may also be —C=N—, or —C=C—.

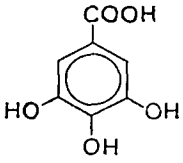
II. NATURALLY OCCURRING QUINONE POLYMERS

A. General

Simple quinone and quinonoid molecules, their reduction products and derivatives, are widely distributed in nature. In numerous cases such molecules can become polymerized, condensed or otherwise bound into macromolecular structures and they have been recognized through their chemical and physical properties, or from their occurrence in the products of degradation reactions. Thus mono-, di- and triquinones are found in moulds and fungi and quinone derivatives of perylene and coronene are present in certain aphids and plants[1]. Plants of the genus *Hypericum* contain red fluorescent pigments, which on ingestion cause animals to become light-sensitive, and which have been shown to be derivatives of *bis*-anthraquinone[2]. More highly polymerized structures which contain quinone groups, or groups readily convertible to quinones, include the tannins, lignins, humic acids, coals, melanins and other less definable components of plants and animals. These various groups of natural polymers will be considered in turn.

B. Tannins

The tannins are water-extractable constituents of the leaves, bark, roots and heartwood of various trees and plants, which are used for converting hides into leather[3,4]. As obtained, they are complex mixtures containing polyhydroxyphenols or derivatives thereof, and in many cases consist of polymeric condensed ring systems but the precise structures of the tannins are largely unknown. A molecular weight of 600–2000 appears necessary for satisfactory tanning action. Alkali fusion and dry distillation of tannins yield a variety of decomposition products mainly phenolic in character. These include catechol, pyrogallol, resorcinol, hydroquinone, *p*-hydroxybenzoic acid, gallic acid, **1**, and ellagic acid, **2**.



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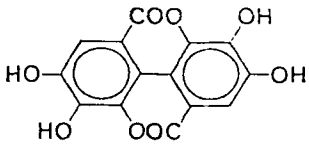

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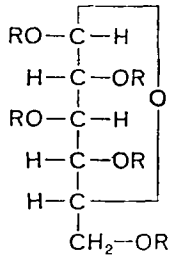
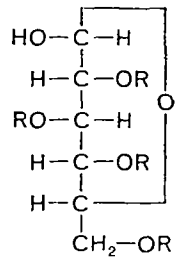




(R = 3,4,5-trihydroxybenzoyl)

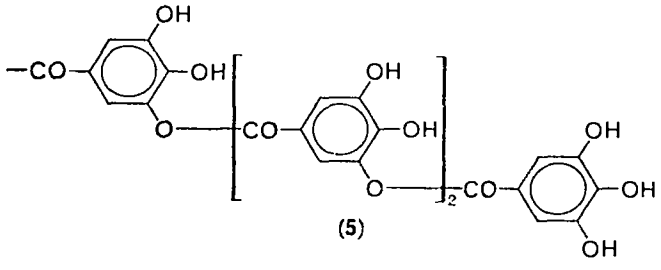
(3) (4)

Two main groups of tannins are recognized: the hydrolysable tannins, which are esters of a sugar, usually glucose, with one or more trihydroxybenzene carboxylic acids and the condensed tannins which are derivatives of flavanols. The former are those in which the complex molecule is hydrolysed by acids and enzymes to simpler units; the latter on similar treatment with acids are converted into more complex insoluble coloured products called phlobaphens.

Considerable progress has been made in elucidating the structure of gallotannin, an important hydrolysable tannin present in nut galls and sumach[4]. Paper chromatography[5] revealed that Chinese gallotannin is a mixture of closely related galloylglucose derivatives, which analysis showed to be octa- or nona-galloylglucose compounds. Elegant degradation work by Haworth and coworkers[6] showed this gallotannin to be based on units of β-penta-*O*-galloyl-D-glucose (**3**) and 2,3,4,6-tetra-*O*-galloyl-D-glucose (**4**). The additional gallic acid residues are linked to the base unit by depside bonds (for example **5**).

Exact knowledge of the structures of the condensed or flavanoid tannins is scanty. Freudenberg[7] proposed in 1920 that the basic unit of their structure was catechin, **6**, and this has been supported by isolation of catechin derivatives and dimers from degradative reactions. A variety of polycondensation mechanisms and structures have been proposed, a common feature being the presence of *o*-dihydroxybenzene units[3,4].

The tannins are amorphous substances which give deep colorations with ferric salts, are precipitated from solution by potassium dichromate, lead acetate and by alkaloids, and which precipitate gelatin from solution. The ability of tannins to form durable, and in many cases irreversible, compounds with proteins is the basis of their tanning action. The mechanism of the tanning action has not been clearly elucidated and may in part be related to quinone formation in the tannin with subsequent condensation with free hydroxyl or amino groups present in the hide



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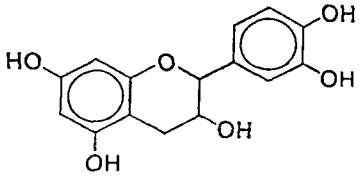
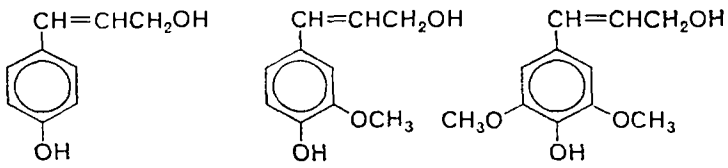


(6)

proteins. Thus, it has been found that when gelatin was treated with phenols under aerial oxidizing conditions the resultant precipitate became insoluble in boiling water as well as in dilute acids and alkalis[8]. Against the view that quinones are intermediates in the tanning process can be set the report[9] that optimum conditions for benzoquinone tanning require alkaline solutions of about pH 8–10, whereas tanning is normally carried out under acidic conditions. Present views are that tanning occurs by a hydrogen-bonding process with the amide groups of the protein and it has been shown[10] that tanning compounds able to form quinonoid resonance structures which favour hydrogen bonding are good tanning agents, whereas those condensates in which resonance cannot occur are poor tanning agents.

C. Lignins

The lignins[11,12] are complex three-dimensional macromolecular structures which form the cell walls of plants and the 'woody' tissue of trees. On the basis of extensive degradation and other studies they are considered to be polymers built up from a variety of primary monomeric units which include *p*-coumaryl alcohol, 7, coniferyl alcohol, 8, and sinapyl alcohol, 9.



(7) (8) (9)

Although the object of much research the chemical structure of lignin is still uncertain. The complexity of the structure apparently derives less from the multitude of component units than from the variety of ways in

which these units may be linked together[13]. Certain tentative structures for lignin have been proposed by Freudenberg[14,15] and by Adler[16,17] in which *ortho*-related hydroxyl, methoxyl and ring carbonyl groups are present, and consequently provide pathways for quinone generation.

Lignins prepared by hydrolytic methods which involve some aerial oxidation have been shown to contain quinone groups. Thus, a lignin in a very early stage of decomposition was found to possess infrared absorption bands at 1648 and 1668 cm^{-1} indicative of *o*-quinone groups[18]. These disappeared on reduction with sodium dithionite. The initial and reduced lignins had the same electron spin resonance spectra and approximately the same concentration of free radicals (10^{16}–10^{17} spin/g). The oxidized lignin liberated iodine from potassium iodide solution which was not due to peroxide but might be due to quinone action.

The amount of quinone carbonyl groups in various lignins has been determined by selective reduction methods. Values of quinone carbonyls present range from 0 to 1·1 meq/g[19]. Further support for the presence of quinone or quinone precursor groups in lignins derives from the production of quinone nitropolycarboxylic acids as red-coloured products by the stepwise oxidation and hydrolysis of condensed lignin with aqueous nitric acid at 100°C[20–22]. The ammonium salts of these quinone nitropolycarboxylic acids have been used as plant growth stimulants.

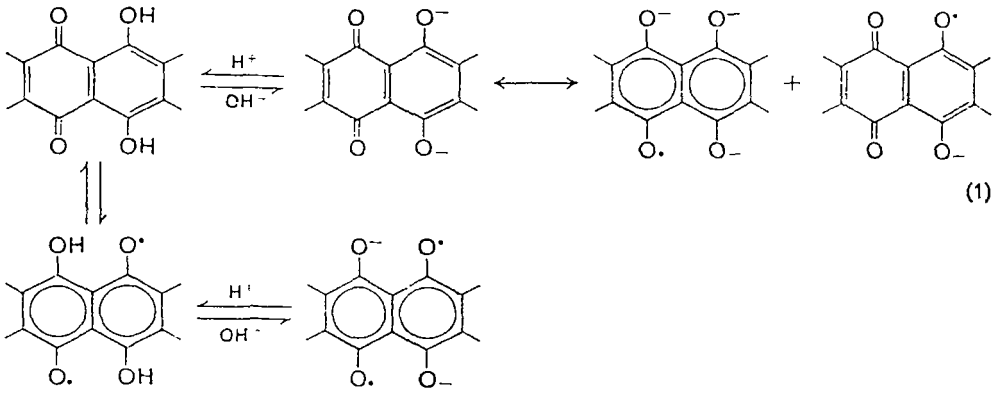
D. Humic Acids and Coal

Humic acids occur in soil[23,24] and may be generally defined as that polymer constituent of the organic matter present which has become resistant to microbial attack. Humic acids derive from decomposing plant matter—in the main from lignin. It is suggested that biological oxidation causes decomposition of the side-chains of the lignin macromolecule, together with demethylation and oxidation to quinone structures which can then polycondense with plant phenols, amino acids and other nitrogenous materials available in the soil[25].

Generally, the humic acids are regarded as amorphous, three-dimensional polymers of high molecular weight, built up of essentially aromatic and quinonoid rings, which also carry numerous acidic groups such as carboxyl and phenolic hydroxyl. Because of their properties humic acids contribute to soil stability and influence plant growth. The presence of acidic groups confers strong ion-exchange and chelating properties on them and they readily form complexes with metals and silicates[26]. Commercial humic acids and sodium humate are obtained from oxidized coals such as forms of lignite and bituminous coals.

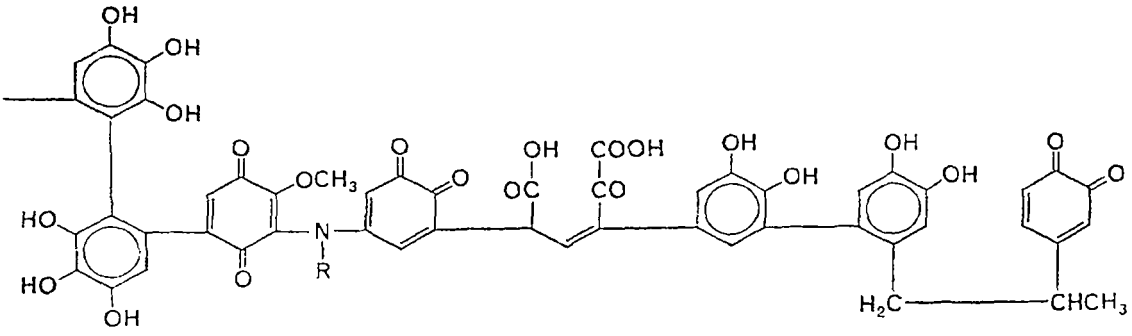
There is considerable evidence indicating the presence of quinone groups in humic acids. Thus humic acids derived from coal have been shown to give two main polarographic reduction waves with similar characteristics to polynuclear quinones[27]. Close similarities of the i.r. spectra of humates to those of hydroquinone polymers have been reported[28]. Comparison of the i.r. absorption spectra of solid sodium *p*-diphenoquinhydrone and of sodium humate have also revealed close similarities.

The presence of stable free radicals in soil humic acids has been established by e.s.r. measurements[29]. Conversion to the sodium salts increased the free-spin concentration by a factor of about 25, whilst acidification returned the free-spin content to about the original value. The e.s.r. results were interpreted as showing that humic acid contains quinhydrone and/or hydroxyquinone species which characteristically increase in radical content on addition of base (reaction 1).



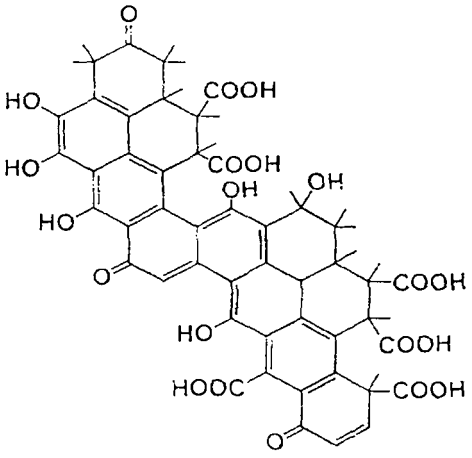
(1)

It is generally considered that no one specific structural formula will adequately represent humic acid. However, a number of structures have been proposed by Flaig, Kononova, Felbeck, Finkle and others, which account for many of the properties of the humic acids, and therefore are worthy of mention. Flaig's[25,30] proposed structure, **10**, is based on the assumption that lignin is the precursor of soil humic acids as mentioned above. The alternative structures of Fuchs[31a], **11**, and Dragunov[31b], **12**, for certain humic acids containing quinonoid groups, or *o*- or *p*-dihydric phenols in the reduced state, have been discussed by Kononova[31c], who considered the latter to be more consistent with the known facts. Felbeck[32] considered that heterocycles form an important part of the macromolecular structure and proposed structure **13**.

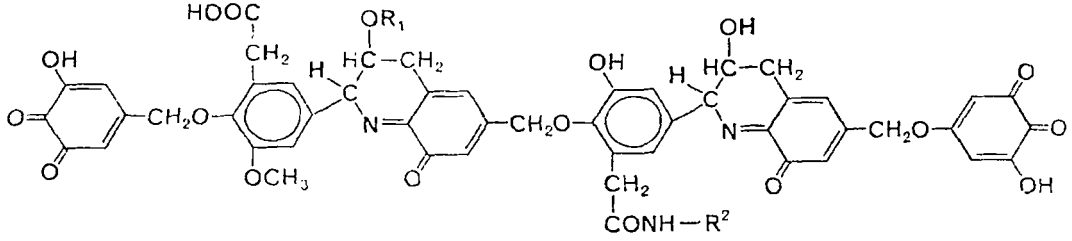


R = aminoacid residue

(10)

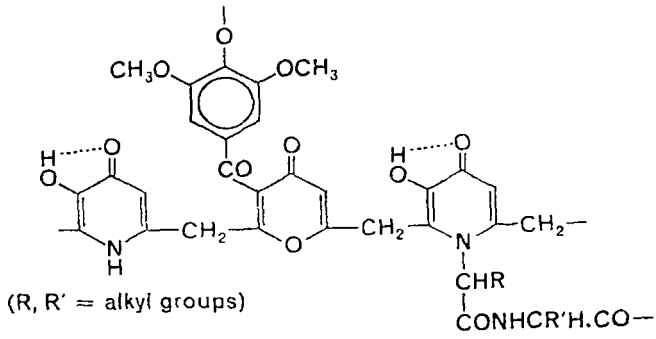


(11) Fuchs humic acid



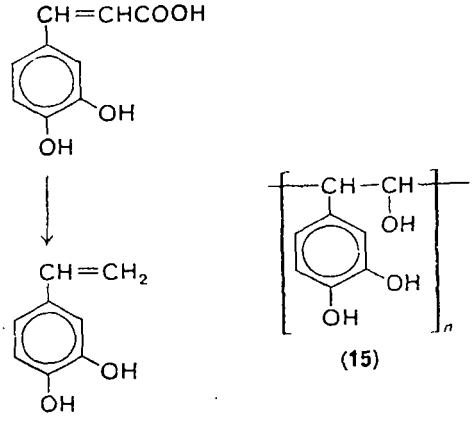
R_1 and R_2 are carbohydrate residues

(12) Dragunov humic acid



(13)

Finkle[33] found that decarboxylation of certain plant cinnamic acid derivatives to hydroxystyrene derivatives, **14**, was brought about by *Aerobacter*, and drew attention to the fact that polymers, **15**, based on this monomer had properties very similar to those of the humic acids.



The variety of postulated structures for the humic acids, as in the case of other naturally occurring polymeric quinones, underlines the difficulty in establishing firm evidence of structure. The presence of quinonoid groups, however, is a common feature of the proposed structures, and probably explains the ability of humic acids to bind amino compounds present in the soil, as well as making a contribution to their metal-complexing properties.

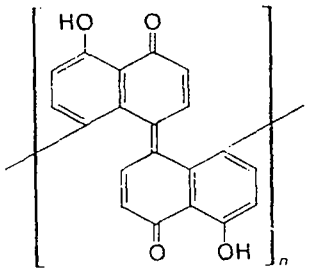
Coals also contain quinones and quinonoid groups and their presence has been established by a number of investigators[34,35]. The most convincing evidence comes from the polarographic study of oxidized coal products[27] or solvent extracts[36] in which two distinct reduction waves

can be identified which are characteristic of simple quinones. Other evidence is provided by examination of i.r. spectra of coal extracts before and after reductive acetylation[35,37] in which there is clear evidence of quinone hydrogen-bonded carbonyl absorption near 1600 cm^{-1}. Other supporting evidence is based on measurements of the X-ray diffraction pattern of coal, which are markedly similar to those of an 'artificial' coal prepared by coprecipitation of three polynuclear quinones from sulphuric acid solution[38]. The quinone content of certain lignite coals of Central Asia has been found to lie between 2–3·3 mg/g[39] on the basis of the quinone carbonyl groups present.

E. Other Natural Quinone Polymers

The melanins form another group of natural polymers of ill-defined structure which are believed to be complex aggregates of quinonoid pigment and several enzyme systems in a protein matrix[40]. They form the brown pigmentations of skin and hair, and occur in the cuticle and epidermis of insects[41]. The formation of melanins apparently can proceed through the intermediate formation of *o*-quinone structures such as 1-methylindole-5,6-quinone[42].

A black quinonoid polymer has been shown to be[43] a constituent of the cell-wall material of *Daldinia concentrica* sporophores. The powder which was obtained after exhaustive extraction of the ground sporophores with solvents was found to undergo reversible bleaching by reducing agents, but even in the reduced state no alkali soluble phenols could be removed. It was suggested that the cell-wall polysaccharides contained non-acetylated aminosugar residues which were cross-linked with monomeric or polymeric quinone oxidation products of the general structure **16**.



(16)

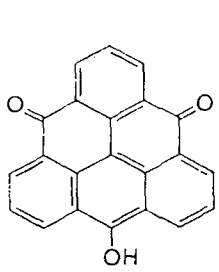
Recently[44], a hexachloro polynuclear quinone has been isolated from Australian soil as a crystalline red pigment thought to arise from the decomposing roots of eucalyptus.

III. POLYNUCLEAR AND CONJUGATED POLYQUINONES

A. Introduction

The polynuclear quinones were among the earliest group of polyquinone systems studied. This was because of their prominence as intermediates in the preparation of polynuclear aromatic hydrocarbons[45] and dyestuffs[46]. More recently, studies have centred on their generation during the coking of coals and the role they play in the coking mechanism[47]. Polynuclear quinones and conjugated polyquinones have been widely utilized for experimental and theoretical studies of the semiconductor, electronic and catalytic behaviour of conjugated quinone systems[48,49]. Certain quinonoid polymers such as the polyphenoxazines are thermally stable.

The materials considered in this section are those in which *ortho* or *para* quinone or quinonoid groups form integral units within a system of essentially aromatic or heteroaromatic rings which are annellated linearly or angularly. Three structural types can be distinguished. (i) Those in which the quinone groups form part of an extended polynuclear system. In some cases the two carbonyl groups exhibiting quinonoid properties may be linked by a series of conjugated double bonds forming a π-electron system, as in 12-hydroxytriangulene-4,8-quinone (**17**) and isodibenzanthrone (**18**). (ii) Those in which the quinone groups are regularly linked



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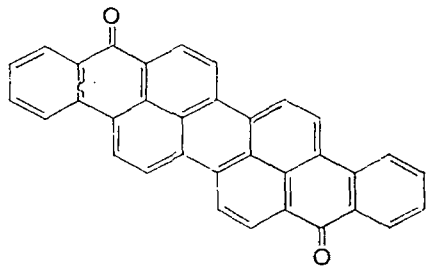


(18)

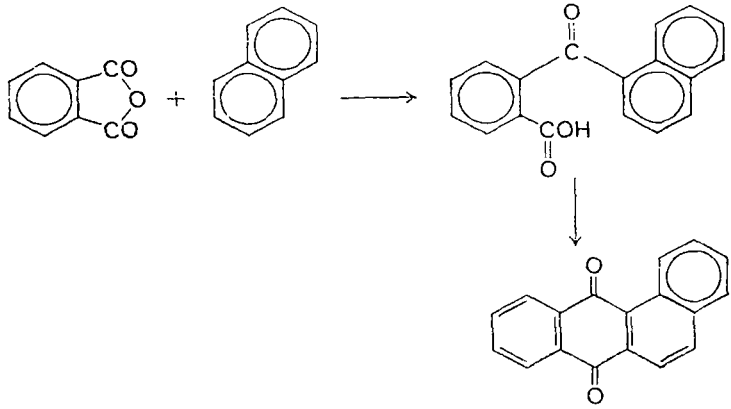
through conjugated bonds. (iii) Those in which quinonoid groupings form the prominent structural units. These structural groups are considered in more detail below.

B. Polynuclear Polyquinones

Several synthetic routes are available for the preparation of fused polynuclear quinones, the most important being the condensation of phthalic anhydride, pyromellitic dianhydride and similar aromatic anhydrides with various aromatic systems. Other methods involve

oxidation of the corresponding aromatic hydrocarbon, or its hydroxyl and amino derivatives, and by application of the diene synthesis utilizing butadiene and its analogues as the diene component.

In the presence of aluminium chloride, phthalic anhydride will condense with a wide range of aromatic hydrocarbons usually to form carboxy diaryl ketones which are then fully cyclized to the corresponding polynuclear quinone by heating with concentrated sulphuric acid (equation 2). The number of *p*-quinone groups in the system in some cases can be increased by using two or more moles of phthalic anhydride.



(2)

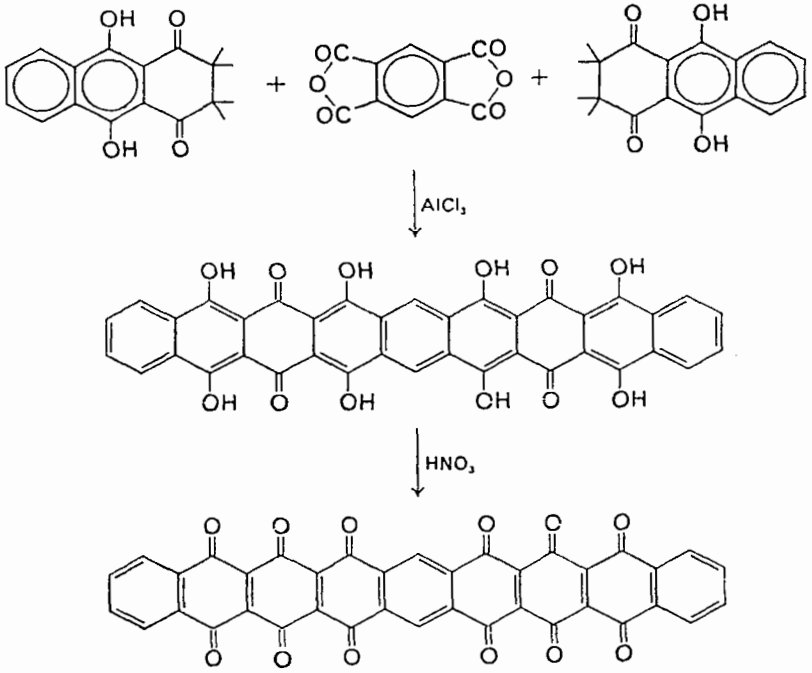
Condensation with hydroxy hydrocarbons proceeds more readily than with hydrocarbons, and milder condensing agents such as boric acid can be employed. Thus, by using pyromellitic dianhydride and leucoquinizarin a polynuclear hexaquinone, **19**, can be prepared[50].

Another variant[51] is condensation of dihydroanthracene tetracarboxylic acid dianhydride with benzene, followed by cyclization and oxidation to give the triquinone **20**.

Pohl and his group[52] have applied the anhydride condensation reaction to the preparation of a wide range of polynuclear quinone polymers. The chemical structures of the polymers were not characterized but they were considered to contain mainly quinone **21** and carbonyl groups (e.g. ketone, carboxyl) and only low amounts of lactone groups as in **22**.

These polymers were black, insoluble, infusible materials and contained a few p.p.m. of the metal of the catalyst used. They exhibited important semiconductor properties (see section VI.C).

Oxidation of hydrocarbons may also be used for preparing polynuclear quinones[45]. Thus chromic acid oxidation of isodibenzoanthrone **23** gives the triquinone indoquinoneanthrene **24** which can be further reacted with hydrazine to form the quinonoid diazine **25**.



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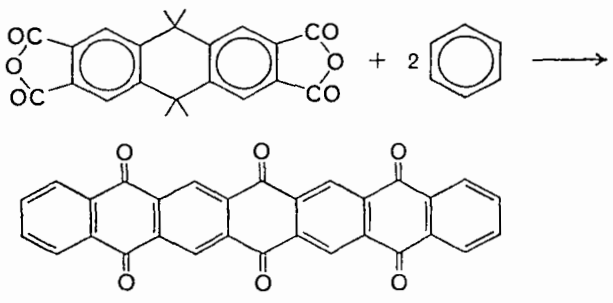

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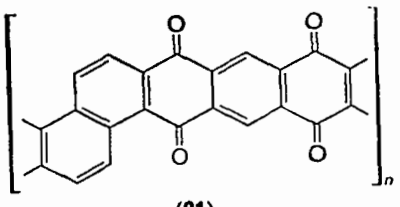

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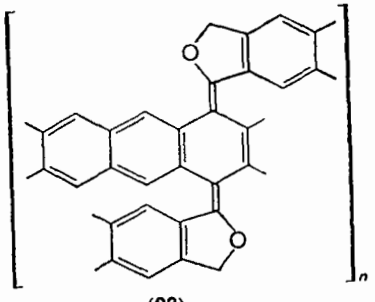

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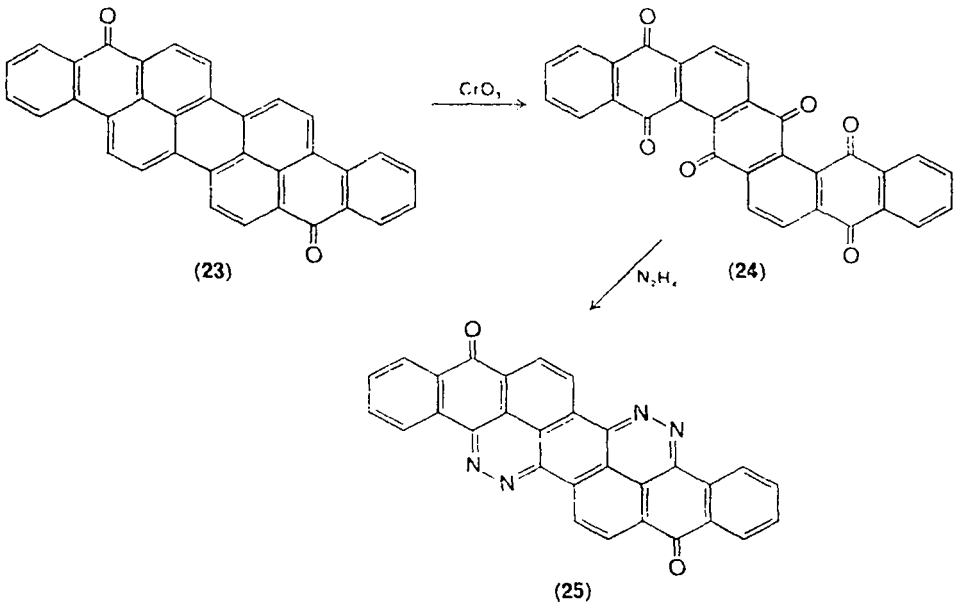


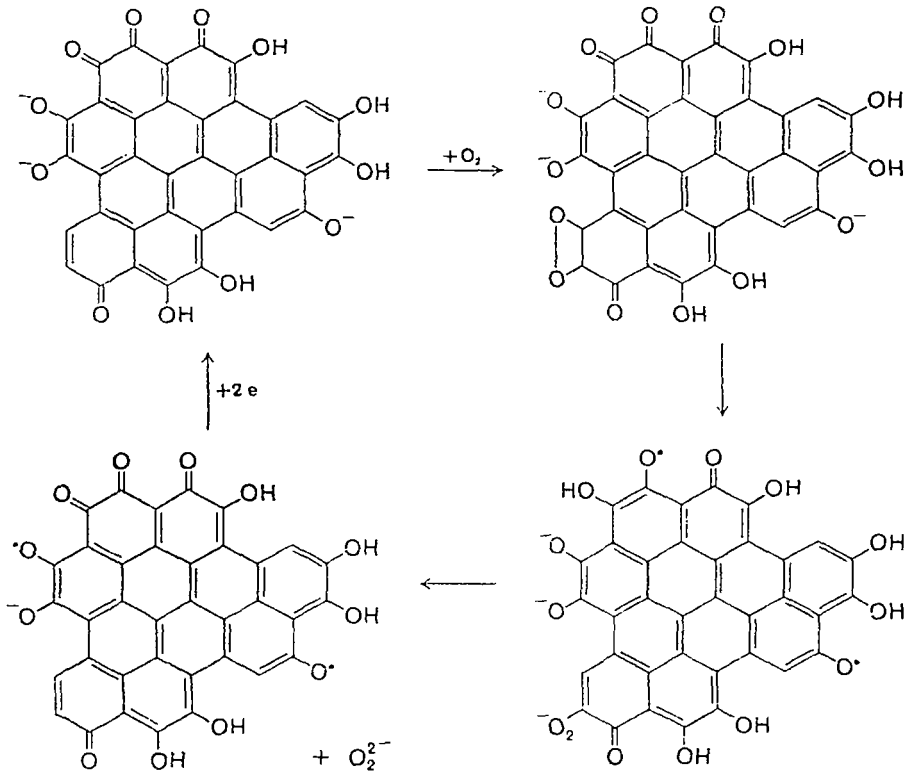
The pyrolysis and coking of coals are thought to involve formation of polynuclear quinone type compounds[47], and the formation of quinone and quinonoid groupings during the preparation of carbon blacks and activated carbons is commonly adduced to explain the reactions they will bring about. The presence of structures such as **26** in H-carbons (i.e. those active carbons that adsorb mineral acid but not alkali) has been proposed to explain its behaviour as an oxygen electrode in alkaline solutions[53].

Some polynuclear quinones have been prepared by condensation reactions. 1,4-Naphthoquinone, for example, on heating with pyridine and glacial acetic acid in nitrobenzene forms the triquinone, triphthaloylbenzene (**27**)[54]. The diene synthesis has been applied to the preparation of polynuclear quinones[55] and is of general application where quinonoid double bonds are exposed.

C. Conjugated Polyquinones

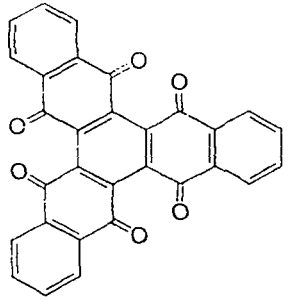
Conjugated polyquinones exhibit unusual properties such as photodynamism[2], photochromism[56] and semiconduction[52] and consequently their synthesis has received increasing attention.

Dimeric and polymeric quinones which are linked through double bonds have been studied by a number of workers. Apparently the first such dimeric quinone, **30**, was described by Hunt and Lindsey[57], who prepared it from the tetramethoxystilbene derivative **28** by demethylation



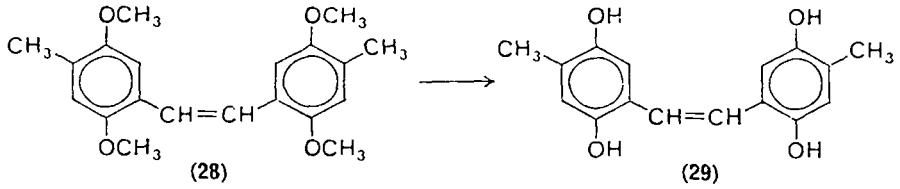
(26)

(After Garten and Weiss[53])

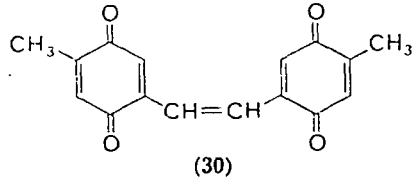


(27)

with pyridinium chloride to give the tetrahydroxy compound **29** which was oxidized to the diquinone by means of silver oxide in dimethoxyethane. The diquinone was unstable to light and air, and the i.r. spectrum and electrochemical behaviour indicated ring conjugation.

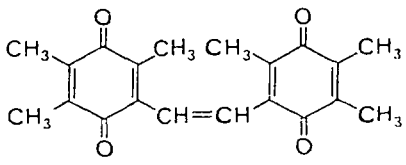


(28) (29)



(30)

Forster and Manecke[58] examined the synthesis of the corresponding fully methylated diquinone **31** using the Wittig reaction to prepare the stilbene derivative **32**. However, on demethylation cleavage occurred into 4,6,7-trimethyl-5-hydroxybenzofuran (**33**) and trimethylhydroquinone.



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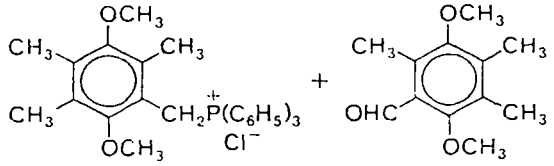

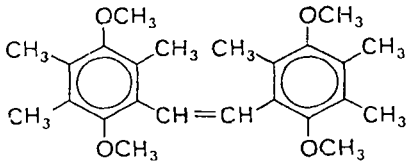

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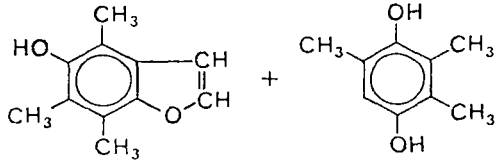
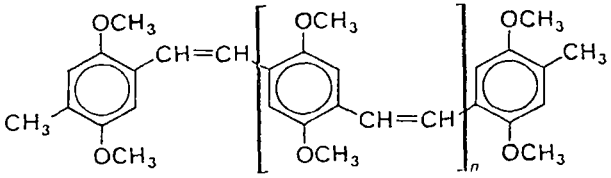
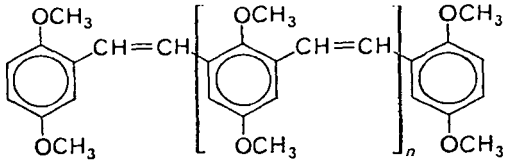


(33)

The Wittig reaction was also employed[59] to prepare a series of oligomers ($n = 1$–4) and polymers of the general formula (3), and also oligomers ($n = 0, 1$) and a polymer of the general structure (4).



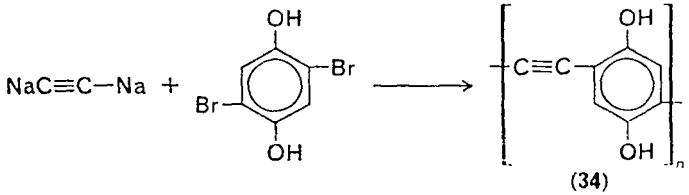
(3)



(4)

However, because of side-reactions and difficulty in obtaining complete demethylation, the corresponding hydroquinone compounds could not be fully characterized. The hydroxy analogue of formula (3) ($n = 1$) was air sensitive and rapidly darkened to a black-brown colour.

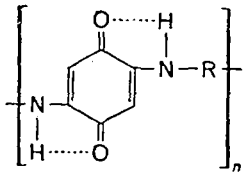
A polyethynylhydroquinone (**34**) has been prepared by reacting disodium acetylide with 2,5-dibromohydroquinone[60]. The polymer was an insoluble black powder which could be reversibly oxidized and reduced and also showed semiconductor properties.



(34)

Berlin and coworkers[61] have studied a series of conjugated quinones prepared by reacting aromatic diamines with *p*-benzoquinone or chloranil in hot ethanol or dimethylformamide with an acid acceptor present (sodium acetate) to give polymers of the general structures **35** and **36**, which can also exist in a tautomeric form such as **37**. The polymers were obtained as brown to black powders which were soluble in concentrated sulphuric acid and formic acid to give deep-blue or violet solutions. They had considerable solubility in dimethylformamide, but solubility in other solvents was poor. The dimethylformamide-soluble polymers would react with cupric acetate to give copper-containing polymers believed to have the chelated structure **38**[61]. The polyphenyleneaminoquinones exhibit a narrow electron spin resonance line of high intensity corresponding to 10^{17}–10^{18} free electrons per gram and are semiconductors. In contrast, polyaminoquinones prepared from aliphatic diamines show no paramagnetic properties.

Other conjugatively linked quinones which have been studied by Berlin and coworkers are the polyarylenequinones (**39**)[62] and the polyphenylazoquinones (**40**)[63]. Both series are prepared by reacting *bis*-diazotized aromatic diamines such as *p*-phenylenediamine, benzidine, substituted benzidines and 4,4′-diaminostilbene with benzoquinone or



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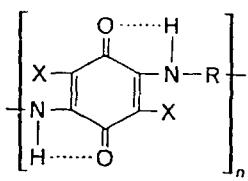
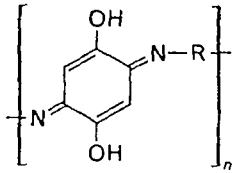


(36)

(R = $-C_6H_4-$, $-C_6H_4C_6H_4-$ etc.)
(X = Cl, CH_3COO-)



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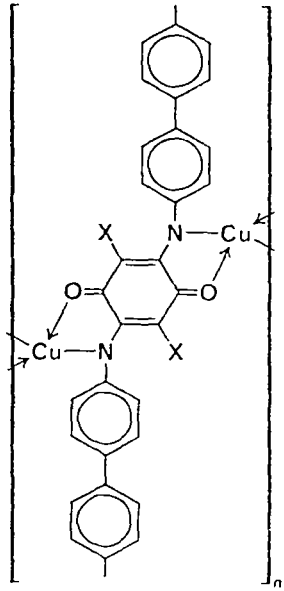

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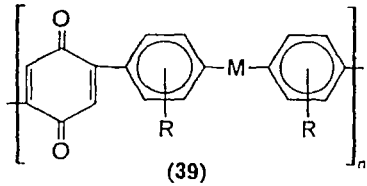
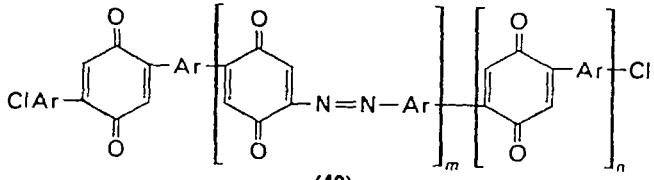


(39)

M = $-CH=CH-$, or is absent
R = H, $-HSO_3$, $-CH_3$



(40)

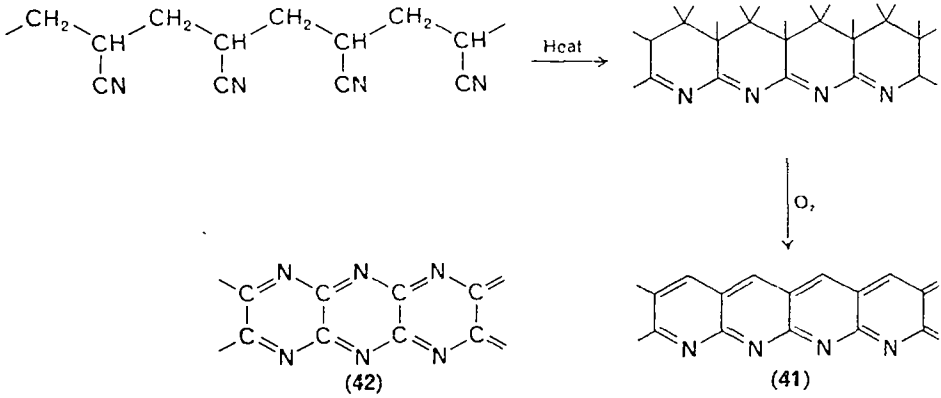
Ar = Arylene group

chloranil. Thus, with benzoquinone polymer structure **40** is thought to arise, the azo groups being retained due to incomplete decomposition of the diazo compound. In other cases, such as when benzidine-3,3′-disulphonic acid is used, structures of substantially the polyarylenequinone type are obtained and only very low amounts of nitrogen are retained.

D. Quinonoid Polymers

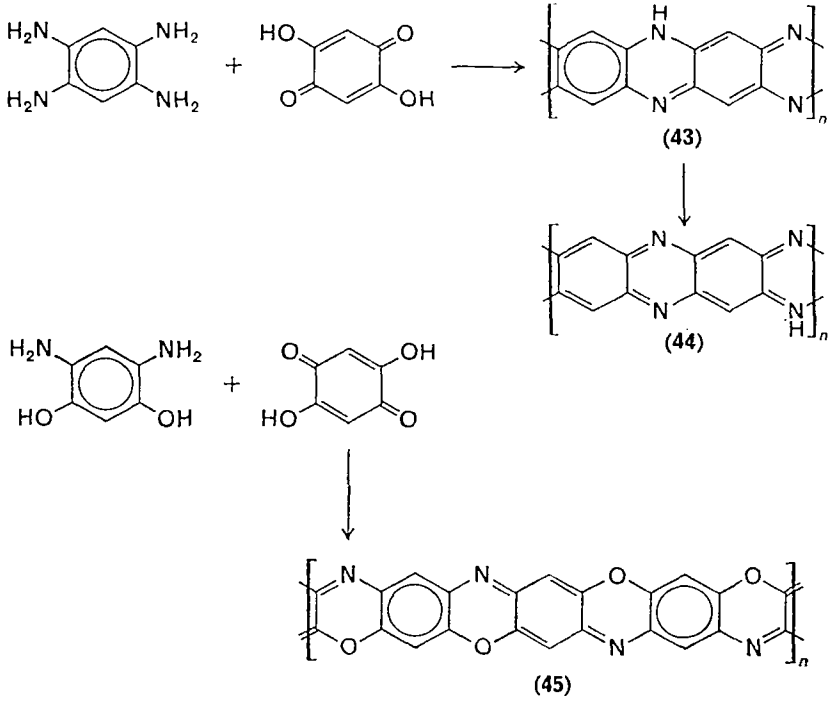
Quinonoid polymers are those polymers which exhibit quinonoid structures or possess quinonoid properties. A wide range of such polymers both aromatic and heteroaromatic has been reported in the literature. However, in this section only quinonoid polymers which illustrate special methods of preparation or which exhibit properties of particular interest, such as thermal stability or semiconductivity, will be considered.

The high thermal stability of graphitized polyacrylonitrile fibre is well established[64], but if pyrolysis of the fibre is carried out in air at lower temperatures (400–500°C) black polymers, believed to have structure **41** and containing nitrogen in the ring, are obtained[65]. These polymers contain free electrons and exhibit semiconducting and catalytic properties which are discussed more fully in section VI. The orthoquinonoid structure is similar to that proposed for paracyanogen[66], **42**.



A number of the so-called 'ladder' polymers possess quinonoid structures. Examples of these are the polyhydroquinoxalines (**43**), the polyquinoxalines (**44**) and the polyphenoxazines (**45**) prepared by Stille and coworkers[67].

The polyhydroquinoxaline **43** is believed to be the first product of the condensation of stoicheiometric amounts of the hydrochloride of 1,2,4,5-tetraminobenzene and 2,5-dihydroxy-*p*-benzoquinone in solvents such as dimethylacetamide, hexamethylphosphoramide and polyphosphoric acid.

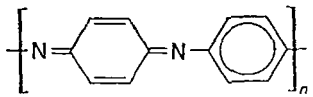


The structure of the black polymer formed was assumed by analogy with the product of the simple monomeric reaction. Oxidation on heating the polymer in air was assumed to give the polyquinoxaline **44**. A rather similar series of reactions provided the polyphenoxazines. In this case 4,6-diaminoresorcinol was condensed with 2,5-dihydroxy-*p*-benzoquinone (or its diacetate) in hexamethylphosphoramide.

Aniline black is a deep-black polymeric product obtained by oxidation of aniline with potassium dichromate or potassium chlorate[46b]. In an alternative preparation cyclohexa-1,4-dione was condensed with *p*-phenylenediamine and then aerially oxidized[49]. Although its structure has not been established it is thought to be a conjugated polymer of the type shown, **46**. The chemistry of aniline black was examined by Willstater and coworkers and by Green and coworkers who showed that there were several distinctive oxidation stages involving progressive oxidation from a colourless leuco compound through to an ungreenable aniline black[46b]. Similar quinonoid polymeric dyes which also contain sulphur are obtained by oxidation of aniline, diphenylamine and triphenylamine with sulphuric acid[68]. Aniline black has been shown to possess free electrons, giving both narrow line and broad line e.s.r. signals[61]. Its semiconductor properties

have been studied, as well as its catalysis of hydrogen peroxide decomposition and dehydrogenation of hydrocarbons (see section VI).

Structurally similar polymers, **47**, have been prepared by heating 1,4-naphthoquinone with toluenediisocyanate in the absence of air at 250°C[52].



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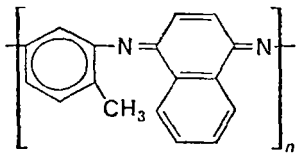
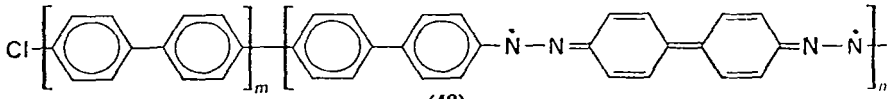


(47)

Another group of conjugated polymers which probably possess quinonoid structures in the chain are the polyazophenylenes studied by Berlin and coworkers[69]. These were prepared by treatment of *bis*-diazotized benzidine or substituted benzidines with ammoniacal cuprous salts.



(48)

Brick-red to brown polymers were obtained, **48**, which were soluble in concentrated sulphuric acid but not very soluble in organic solvents. Chlorine apparently formed the chain end groups. Most of the polyazophenylenes are of high thermal stability and survive temperatures of 300°C. The e.s.r. spectrum showed three types of signal, and the polymers had high free-electron spin values ranging from 10^{18} to 10^{19} spins/g. The quinonoid structure of the polymer chain was deduced from the i.r. absorption spectrum. Some rather similar polymers have been obtained by replacing benzidine in the reaction by 4,4′-diaminodiphenylmethane or by 4,4′-diaminobenzil[70].

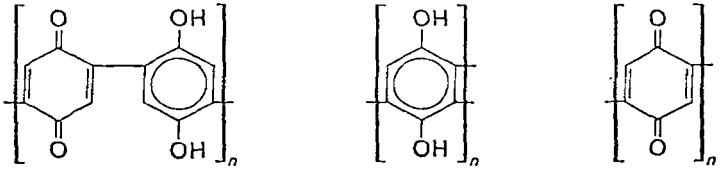
IV. POLYMERIC QUINONES

A. Polymers with Directly Linked Quinone Groups

Treatment of mono-, di- or polyhydric phenols or of aminophenols in alkaline solution with aerial oxygen, potassium persulphate solution or hydrogen peroxide at temperatures below 60°C yields dark-brown amorphous polymers[71]. 1,2-Benzoquinone under similar treatment likewise gives amorphous polymers. These polymers were called 'synthetic humic acids' because of the similarities of their properties, such as redox

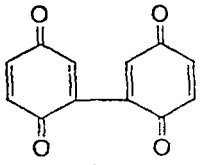
character, solubility in alkali and precipitation by acids, and of their chlorinated and nitrated products, with one another and with the natural humic acids.

The structure of these polymers was investigated by Erdtman[72], and later with coworkers[73], who established that they contained directly linked hydroquinone and quinone groups as well as diphenylene oxide structures. The polymeric products were usually prepared by shaking a suspension of *p*-benzoquinone in alkaline solution (sodium hydroxide or sodium acetate) in an inert atmosphere for a prolonged period, then acidifying with mineral acid and extracting the hydroquinone with ether. The moist polymers were easily soluble in alkali, giving green or brown solutions which readily absorbed oxygen from the air to form deep-brown solutions. Erdtman proposed that the alkali polymerized *p*-benzoquinone had a linear or three dimensional structure based on units such as series (5).



(5)

Directly linked di-, tri- and tetraquinones (**49–51**) which were separately synthesized were shown to yield typical synthetic humic acids when treated with alkali.



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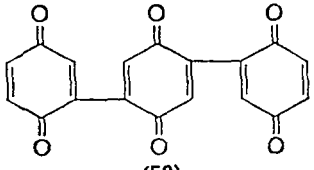

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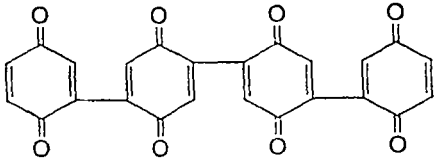

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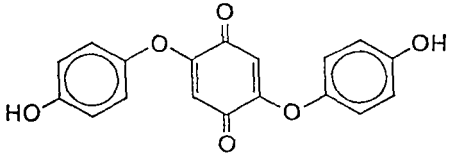
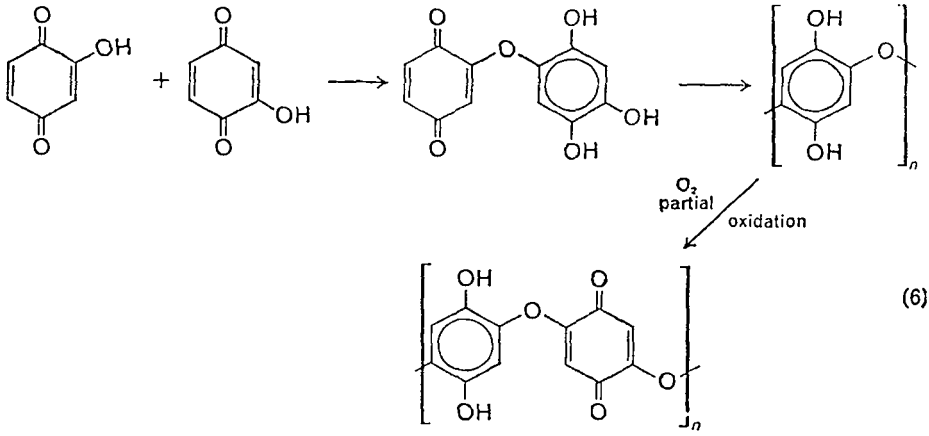


(52)

Diels and Kassebert[74] obtained a quinone trimeride, **52**, from benzoquinone by the action of pyridine, but in view of the ready alkaline hydrolysis of this compound to hydroquinone and 2,5-dihydroxyquinone,

Erdtman[73] has discounted the possible existence of this structural unit in the polymers.

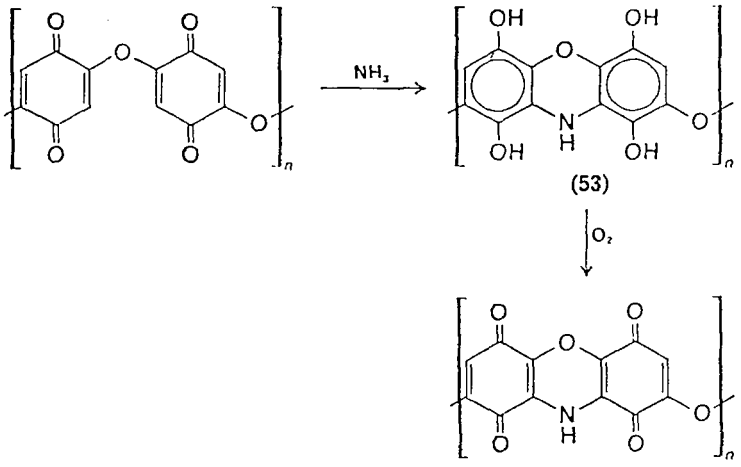
It has been established that a primary product of alkali treatment of *p*-benzoquinone is 2-hydroxy-*p*-benzoquinone[75], and Flaig[76] has proposed that since hydroxy-*p*-benzoquinone is not stable in aqueous solution it undergoes polycondensation by the reactions shown (6). Flaig[76] also



(6)

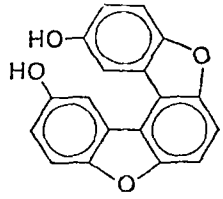
showed that when oxidation of hydroquinone was carried out in strong ammonia solution a polymer containing nitrogen was obtained, which was considered to have structure **53** on the basis of its nitrogen analysis.

Attention has also been drawn to the ring-opening effect of alkaline oxidation on 4,6-di-*t*-butylpyrogallol[77] to yield 2,4-di-*t*-butyl-4-oxalocrotonic acid which could also be involved in the formation of the synthetic humic acids.



Mineral acids will also cause dimerization and polymerization of quinones[72]. Thus the main product from *p*-benzoquinone is an amorphous mixture of at least partly quinonoid substances. Erdtman[78] has proposed that they are formed mainly by 2,5 (or 2,6) condensation of the quinone nuclei and that the trimeride which is also found to be present owes its formation to a competing reaction involving 2,4-condensation followed by dehydration to the stable product **54**. The alternative structure **55** was eliminated on the basis of direct comparison with an authentic sample.

Shand and Thomson[79] have pointed out that ring cyclizations of diquinones **56**→**57** not only proceed under acid conditions but also thermally and by u.v. irradiation.



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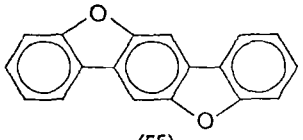

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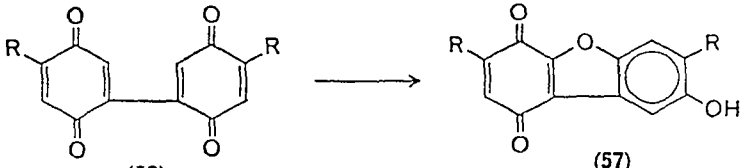
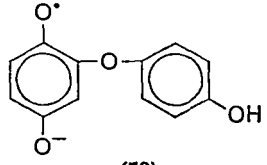


(56) (57)

The exact mechanisms of the hydroquinone and quinone polymerizations have not yet been established. However, there are certain lines of evidence which point to the intermediate formation of semiquinone anions which subsequently dimerize and polymerize by free-radical combination processes. It is well known that phenols will undergo a wide variety of coupling reactions under oxidative conditions which are similar to those of semiquinone radicals[80]. Thus, when aqueous sodium hydroxide is added to an alcoholic solution of *p*-benzoquinone (or duroquinone) in the presence of air a dark-green–yellow solution results which exhibits a strong paramagnetic signal (e.s.r.) thought to be due to formation of a semiquinone species, possibly that of hydroxybenzoquinone[81]. Anderson and coworkers[82] have made a more detailed e.s.r. study of the development of paramagnetic semiquinone free radicals produced by aerial oxidation of hydroquinone in alcoholic potassium hydroxide. The results suggested that the radicals dimerize or otherwise react in concentrated

solution to form radicals linked through oxygen, whilst dibenzosemiquinone radicals are produced from the benzoquinone under reducing conditions. The primary coupling products suggested are **58** and **59**, including their various possible substituted versions depending on the starting material, the reaction mechanism and the displacement of substituents.



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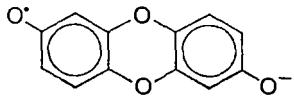
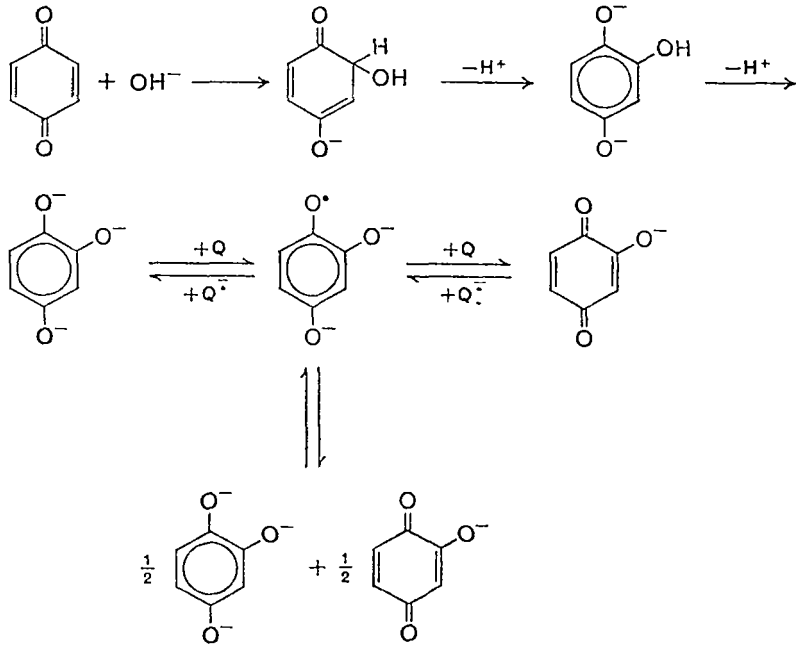


(59)

On the basis of a kinetic study of the reactions of *p*-benzoquinone with alkali at 22°C Eigen and Mathies[83] have put forward the reaction scheme shown (7). An initial reaction between the quinone and hydroxyl ions is



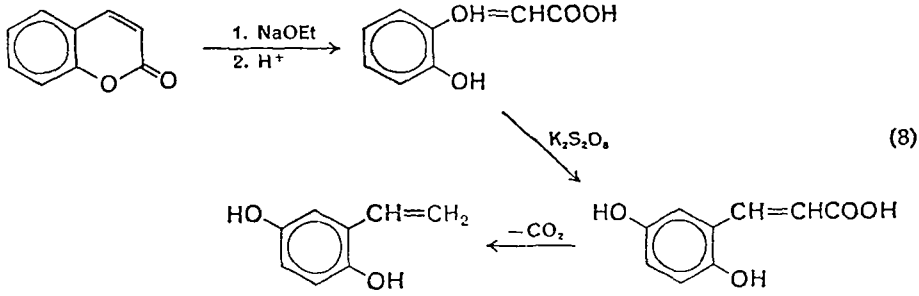
(7)

(Q = benzoquinone)

thought to result in formation of hydroxyhydroquinone, which then undergoes redox reactions with the *p*-benzoquinone leading to the formation of *p*-benzosemiquinone, hydroxy-*p*-benzoquinone and hydroxy-*p*-benzosemiquinone. These reactive intermediates could be expected to link up to form polymeric products of the types described above.

B. Polymerized Quinones

Quinones are well-known inhibitors of free-radical polymerization of vinyl monomers[84], although apparently anthraquinone has little affect on the molecular weight of the chain in styrene polymerization[85]. Vinyl hydroquinone is sensitive to aerial oxidation and consequently radical polymerization of it tends to be hindered by the presence of the quinone, and only low molecular weight polymer is obtained[86]. Much higher degrees of polymerization can be attained by protecting the hydroxyl group with another group which can readily be removed after polymerization. Suitable groups which have been used are acetyl[86], benzoyl[86], methyl[87], tetrahydropyranyl[88], methoxymethyl[89] and 1-ethoxyethyl[90], although in the last two instances formaldehyde and acetaldehyde are liberated in the hydrolysis stage, and may further react with the polymer. The initial synthesis of vinyl hydroquinone[86] was carried out by the series of reactions shown (8) but alternative routes have been reported[91].



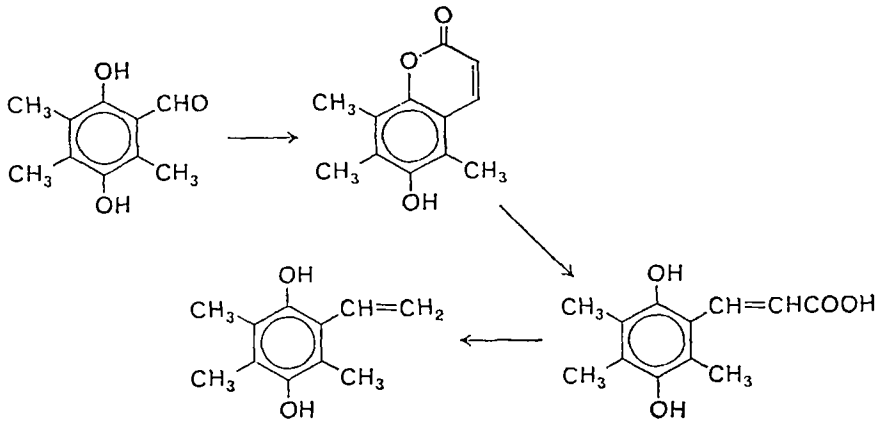
(8)

Polyvinylhydroquinone is not very hydrophilic and therefore copolymers of vinylhydroquinone dibenzoate with α-methylstyrene and divinylbenzene have been prepared which could be sulphonated to confer a greater degree of hydrophilic character on them[92]. Since methylated and other substituted quinones show a greater stability towards inorganic oxidants than the unsubstituted benzoquinone, various synthetic methods have been developed to incorporate these into a polymeric matrix[93–95], which are shown in the reaction sequences (9–11).

Spinner and coworkers[96] circumvented the necessity to attach the polymerizable double bond directly to the hydroquinone, by linking the latter to the styrene molecule via a sulphone bond. The hydroxyl was protected by a pyranyloxy group during the polymerization reaction (12).

Manecke and coworkers[97] found that neither 2-methyl-3-vinyl naphthoquinone nor 2,3-dimethyl-5-vinyl naphthoquinone could be polymerized when converted to the corresponding diacetates. However, when the

latter was converted to the epoxide the product could be readily polymerized. The oxide bridge was then removed by treating with potassium iodide in aqueous acetic acid (reaction 13).



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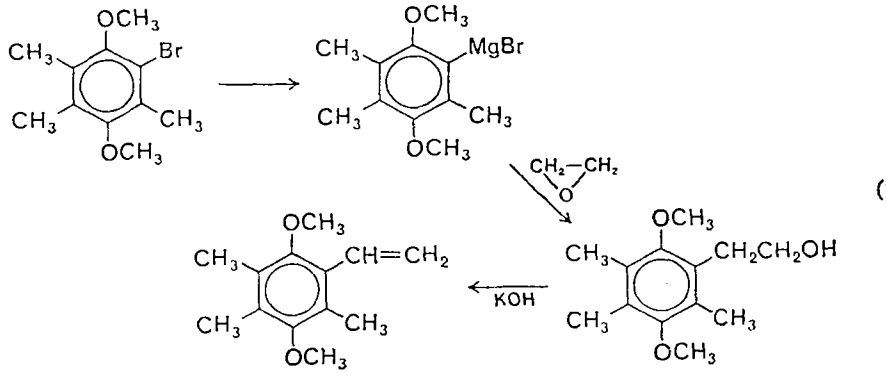

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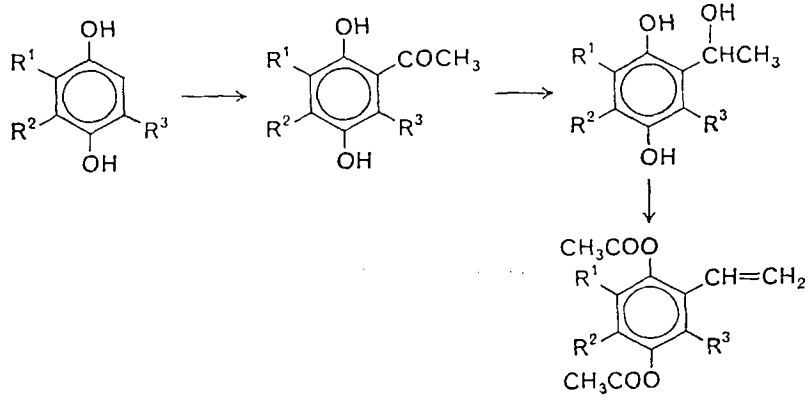

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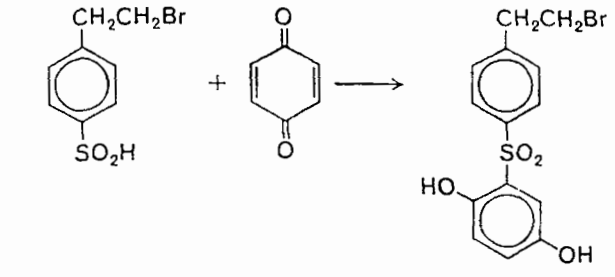

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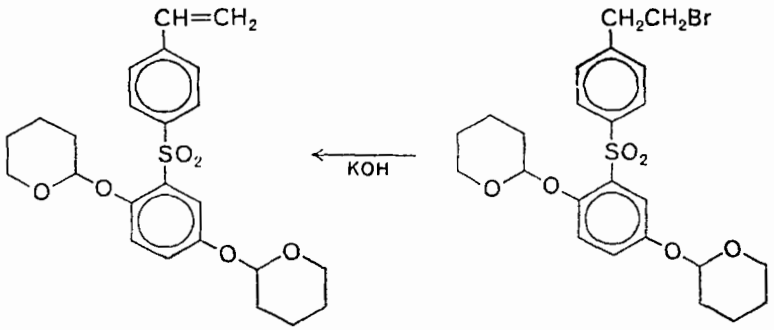

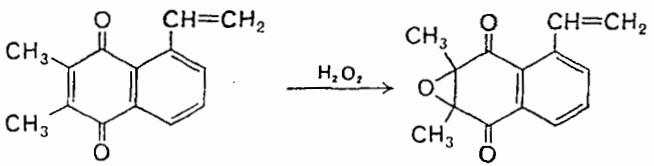

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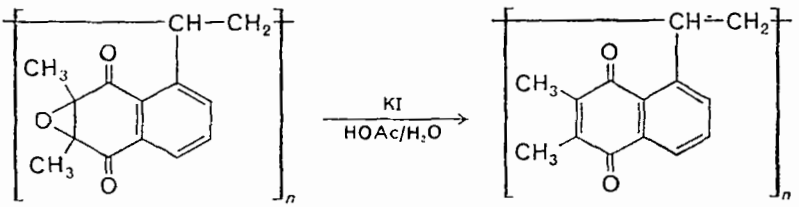
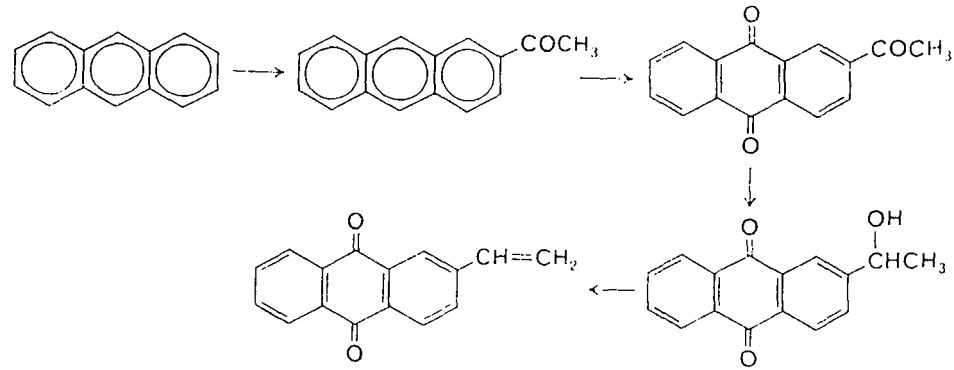
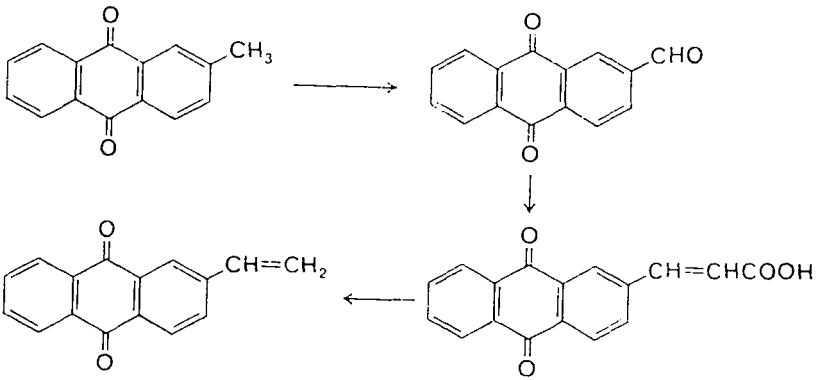


Routes have also been examined to the polyvinylanthraquinones. 1-Vinylanthraquinone has been prepared by Diels–Alder addition of 1,3,5-hexatriene to 1,4-naphthoquinone and subsequent oxidation, but was found to be thermally non-polymerizable[98]. Several routes to 2-vinylanthraquinone have been reported[96]. The simplest method involves

dehydrogenation of 2-ethylanthraquinone by passage over palladized asbestos at 600°C. Oxidation of 2-methylanthraquinone to the aldehyde, conversion to the 2-acrylic acid followed by decarboxylation to 2-vinylanthraquinone is an alternative route.



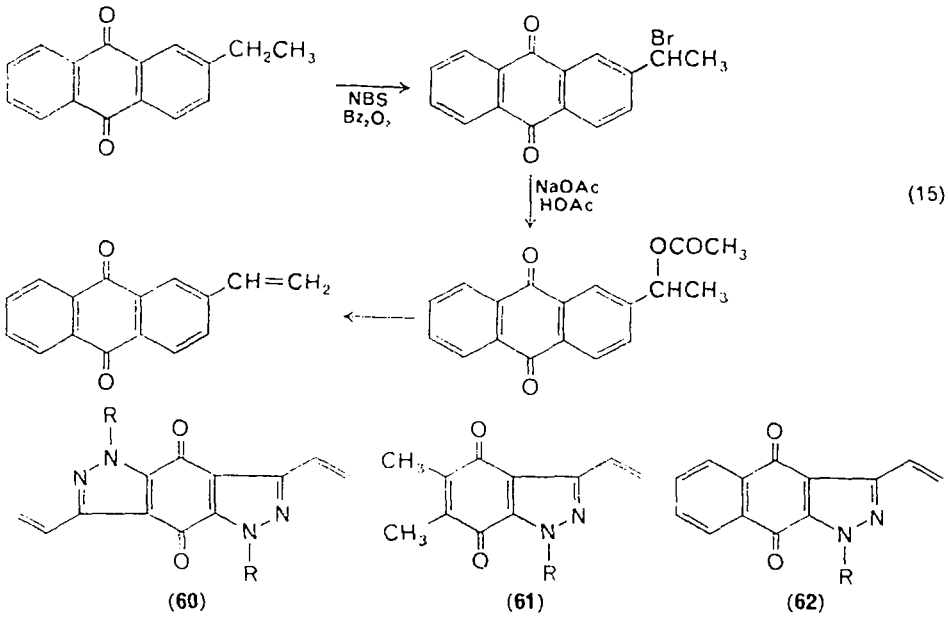


(14)

Manecke and Storck[100] prepared 1- and 2-vinylanthraquinone from anthracene or from anthraquinone by a variety of routes (reaction 14). They also used 2-ethylanthraquinone as starting material which they converted to the vinyl compound by the reaction sequence (15).

2-Vinylanthraquinone readily undergoes radical polymerization with high conversions and can be copolymerized with styrene and divinylbenzene. The copolymers can be sulphonated to improve their hydrophilic character[100].

Polymers and copolymers based on various vinylpyrazoloquinones have been reported by Manecke and coworkers[101]. Thus 1,3-dipolar addition of vinyl diazomethane to benzoquinone, 2,3-dimethylbenzoquinone and naphthoquinone gave the vinyl pyrazoloquinones (**60–62**, R = H) which could be copolymerized. The polymers and copolymers



could be *N*-sulphalkylated ($R = (CH_2)_3SO_3K$) to give water-swellable polyquinones by treatment with propane sultone. The water-swellable copolymers obtained were claimed to be very stable chemically and thermally.

Some typical values of redox and ion-exchange capacities of polymerized quinones are given in Table 1.

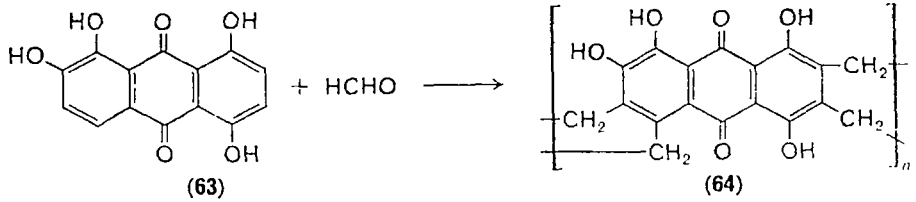
TABLE 1. Typical redox and ion-exchange capacities of polymerized quinones

Polymer	Redox capacity (meq/g dry resin)	Ion-exchange capacity (meq/g dry resin)	Reference
Sulphonated copolymer of vinylhydroquinone, α-methylstyrene and divinylbenzene	5·7	3·9	139
Sulphonated copolymer of 2-vinylanthraquinone, styrene and divinylbenzene	4·8	2·0	100
Sulphoalkylated copolymer of 3-vinylpyrazolonaphthoquinone and 3,6-divinyl-*bis*-pyrazolobenzoquinone	5·0	2·7	101

C. Polycondensed Quinones

The preparation of polymeric quinones by polycondensation reactions provides an alternative synthetic method which is versatile and prolific.

A very widely applied method utilizes the acid- or base-catalysed condensation of *o*- or *p*-dihydric phenols, or hydroxyquinones, such as quinalizarin (**63**) and chrysazin, with formaldehyde. The degree of cross-linking can be controlled by varying the molar ratio of formaldehyde, and by adding phenol or resorcinol to the reaction mixture as a diluent and cross-linking agent. Thus two- or three-dimensional networks of the types **64** and **65** can be obtained. Treatment with oxidants such as ferric or ceric salt solutions converts the polymers to the polyquinone form, which can be reduced again with sodium dithionite solution.



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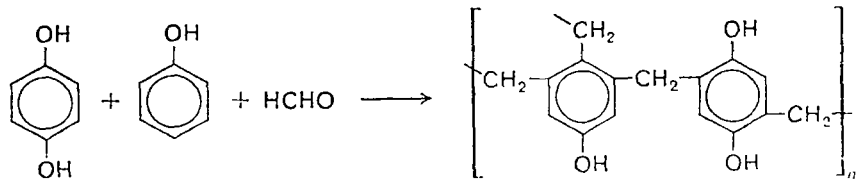


(65)

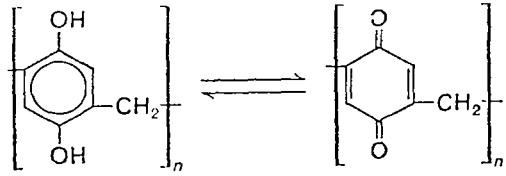
The earliest report of the condensation of phenol and formaldehyde with polyhydroxy benzenes was that of Griessbach and coworkers[102] who described a regeneratable redox resin. Condensates of phenol–formaldehyde–hydroquinone have been studied in detail by Manecke and coworkers[103,104]. By using phenolsulphonic acid as one component, water-swellable polymers were obtained[105]. A range of quinones and hydroxy quinones such as juglone, 2-hydroxyanthroquinone, alizarin, anthrarufin, quinalizarin, chrysazin and purpurin have been utilized[103,106]. Formaldehyde as such, or in the form of paraformaldehyde or hexamethylene triamine, has been most commonly used as the cross-linking agent. Other aldehydes such as acetaldehyde, paraldehyde, benzaldehyde, furfural and glyoxal may be used to replace all or some part of formaldehyde in the condensation[107]. Practical conditions for the preparation

of hydroquinone–resorcinol–formaldehyde polymers have been examined[108]. Macroporous polycondensates with improved redox reaction kinetics (i.e. faster acting) have been obtained by Shostak and Ergozhin[109]. Some typical redox capacities of polycondensed quinones are given in Table 2.

TABLE 2. Typical redox capacities of polycondensed quinones

Polycondensate components	Ratio	Redox capacity (meq/g dry resin)	Reference
Hydroquinone	1		
Phenol	1	6·8	103
Formaldehyde	3		
Juglone	1		
Phenol	1	4·5	103
Formaldehyde	3		
Hydroquinone	1		
Resorcinol	1	4·4	108
Formaldehyde	2		

A convenient way of preparing methylene- and dimethylene-linked quinone polymers has been reported by Hunt and Lindsey[110] in which 1,4-di(chloromethyl)-2,5-dimethoxybenzene was directly condensed with 2,5-dimethoxybenzene by refluxing the two compounds together in glacial acetic acid. Subsequent demethylation gave the polyhydroquinone which could be reversibly oxidized to the polyquinone form (reaction 16). By treating 1,4-di(chloromethyl)-2,5-dimethoxybenzene with a sodium dispersion in dioxan the dimethylene-linked polymer was obtained which could likewise be demethylated and oxidized to the polyquinone (reaction 17).



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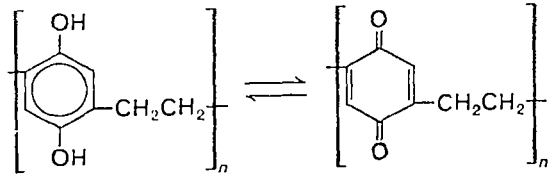
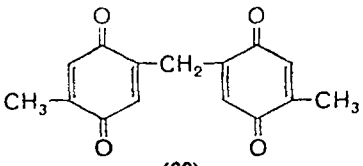


(17)

Because of the difficulties of studying the properties of the formaldehyde condensation products directly, a number of studies have been carried out on low molecular weight dimeric, trimeric and tetrameric quinones with analogous structures to those of the polymer chain unit (see section V.B). Thus Lindsey and coworkers[110] synthesized the polymer model compounds **66** to **71** by direct condensation of the mono- or *bis*-2,5-chloromethyl-1,4-dimethoxybenzene with 1,4-dimethoxybenzene or derivatives to form dimers and trimers. Demethylation gave the corresponding hydroxy compounds which could be oxidized with acid ferric ammonium sulphate, or by refluxing with ethanolic benzoquinone.



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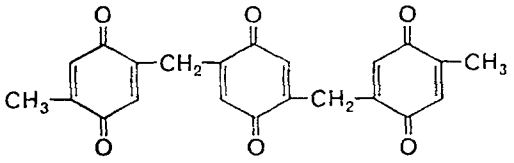

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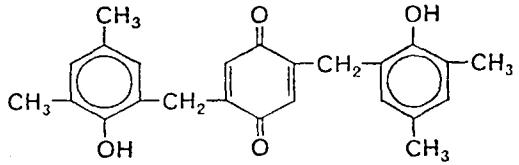

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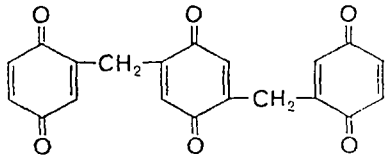

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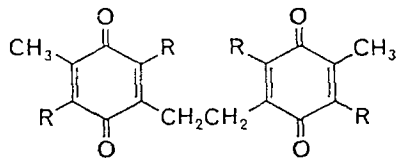
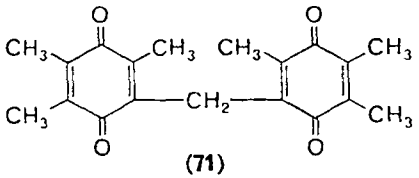


(R = CH_3— or Br)

(70)



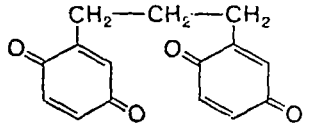
(71)

Manecke and Forster[104] similarly synthesized oligomers by controlled condensation of phenol, hydroquinone and formaldehyde to give chain segments carrying hydrogen, methyl or chloro substituents. These compounds were also used for potentiometric studies (see section V.B).

A series of model chain units (**72–74**) corresponding to the polyvinylquinone system were synthesized by Moser and Cassidy[111], and were examined spectroscopically and potentiometrically (see section V.B).

Another route to the polyquinones has utilized a polypeptide chain as backbone with hydroquinone groups pendant to it[112]. Thus polycondensation of 4-(2,5-diacetoxybenzyl)-oxazolidine-2,5-dione (**75**) by

treatment with alkali in dioxan gave the protected hydroquinone polymer **76**, which on hydrolysis gave the polyhydroquinone **77**.



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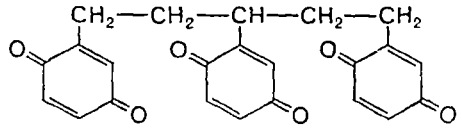

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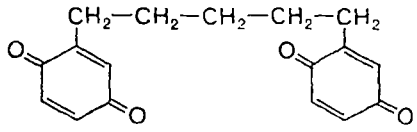
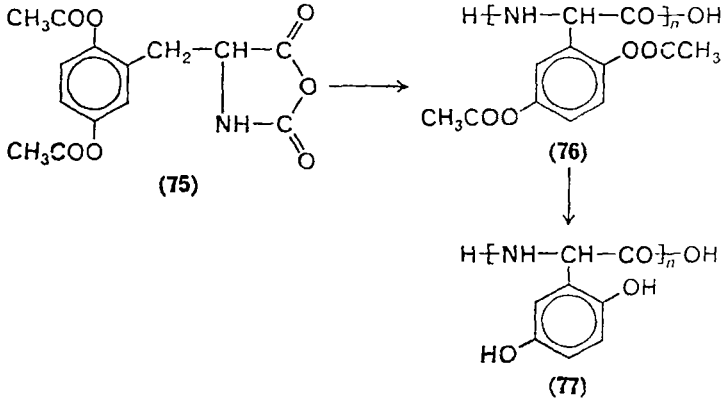


(74)

The 3,4-dihydroxyphenyl polymer was prepared by a similar route. The 2,5-dihydroxy polymer was hygroscopic whilst the 3,4-dihydroxy polymer was not. Copolymers were prepared by copolycondensation with the *N*-carboxy anhydride of γ-benzyl glutamate. Conversion to identifiable polyquinones was not reported[112].

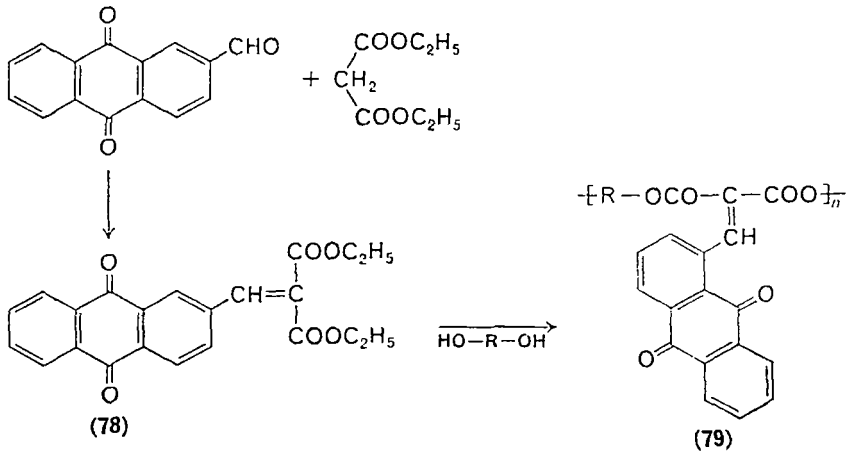
A polyester chain carrying pendant anthraquinone groups has been reported[113]. Initially 2-formylanthraquinone was reacted with diethyl-malonate to give diethyl anthraquinonyl-2-methylenemalonate (**78**), which readily condensed with aliphatic diols and glycerol to give a polyester polyquinone of structure **79**.

Haas and Schuler[114] showed that peroxidation of the diacetate of allyl hydroquinone provided the epoxide derivative which could be poly-condensed under the catalytic action of zinc chloride–aluminium isopropoxide to give poly-3-(2,5-diacetoxyphenyl)propylene oxide. The



(75) (76) (77)

acetate groups were removable by alkaline hydrolysis to give the polyhydroquinone, which was susceptible to aerial oxidation under these conditions.



(78) (79)

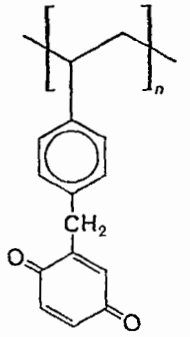
D. *Polymer Supported Quinones*

Quinones and hydroquinones have been attached to a variety of polymer frameworks by chemical reaction, often under mild conditions. The main difficulties are achieving high reaction yields and the avoidance of side-reactions, particularly cross-linking.

One of the earliest reports of this synthetic approach was that of Sansoni[115], who converted polyaminostyrene to the diazonium salt which was then reacted directly with *p*-benzoquinone. Dyestuffs such as methylene blue and thionine could be similarly attached. The reactions of aryldiazonium salts with benzoquinone have been studied by Brassard and L'Ecuyer[116]. Dorfner[117] extended the scope of the reaction by coupling diazotized polyaminostyrene with *p*-benzoquinone, 1,4-naphthoquinone and anthraquinone. Hydroquinone has also been utilized in this reaction to give polymers of high redox capacity, stable to strong oxidants and reducible by alkaline dithionite[118]. The polyquinone form was found to oxidize Fe^{2+} and methylene blue.

Kun[119] developed alternative methods of bonding the quinone system to the polystyrene matrix. Conventional gel and macroreticular styrene-divinylbenzene polymers were chloromethylated with chloromethyl ether using a Friedel–Crafts catalyst, and the chloromethylated polymer treated with hydroquinone, benzoquinone or 1,4-dimethoxybenzene in the presence of further Friedel–Craft's catalyst. The dimethoxy compound was subsequently demethylated by means of hydriodic acid. The polyquinones so obtained were of the type **80** and **81**. The polystyrene backbone

renders the polymers hydrophobic in character, and they were made more hydrophilic by limiting the initial amount of hydroquinone reacting with the polymer and converting the surplus chloromethyl groups to hydrophilic quaternary groups, e.g. by reaction with trimethylamine **82**[120]. An alternative method was sulphonation of the hydroquinone groups[121].



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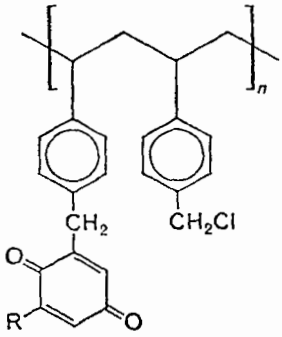

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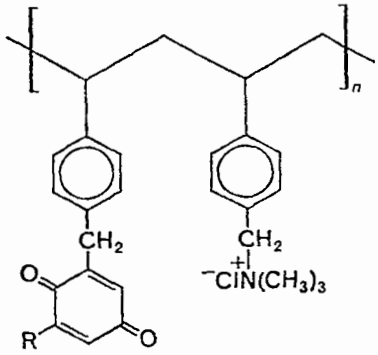
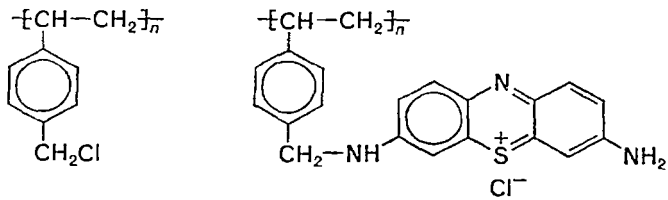


(82)

Russian workers have described the preparation of similar polyquinones from chloromethylated polystyrene and styrene-disopropenylbenzene copolymer[122]. A commercial polymeric quinone with a structure approximating to **82** (R = *t*-butyl) has been marketed[123].

Manecke and Kossmehl[124] have reacted a chloromethylated crosslinked polystyrene with thionine and with trimethylthionine to prepare blue-coloured polymers containing quinonoid dye structures **83**, and possessing good redox capacities (ca. 4 meq-g).

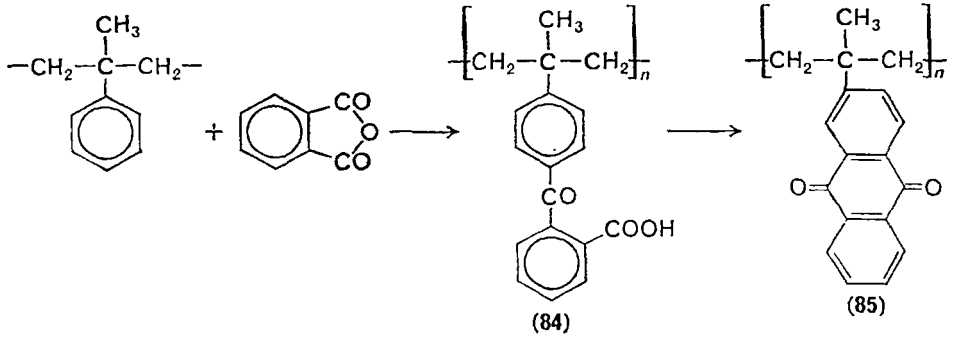
Reaction of phthalic anhydride with poly-(α-methylstyrene) in the presence of aluminium chloride gave poly[*p*-(*o*-carboxybenzoyl)-α-methylstyrene] (**84**) which on heating in syrupy phosphoric acid cyclized to



(83)

give the poly[2-(α-methylvinyl)-anthraquinone] polymer (**85**). The low redox capacity of the product (0·5 meq/g) indicated that only a low introduction of anthraquinone groups had occurred[124].

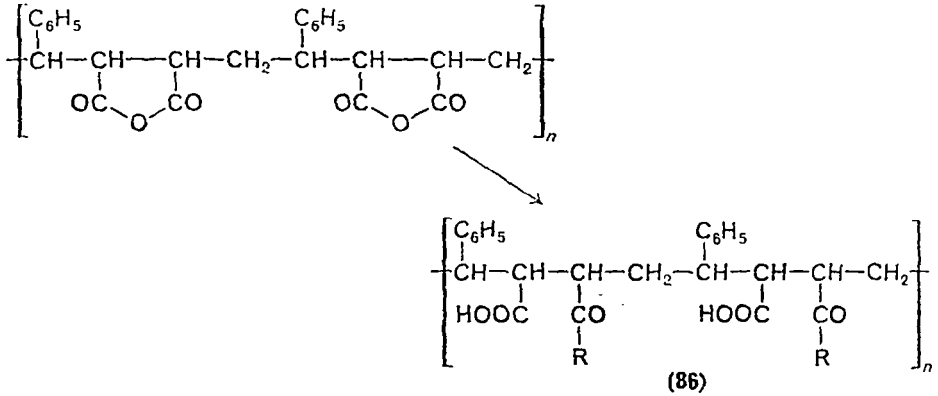
Kern and Schulz[125] utilized a styrene–maleic acid copolymer which they reacted with β-aminoanthraquinone in tetrahydrofuran in an autoclave at 160°C for six hours. A pale-yellow polymer of the general structure **86** was obtained which was soluble in tetrahydrofuran, pyridine and dimethylformamide and possessed oxidizable–reducible groups. A quinonoid grouping was introduced into the polymer by reaction with 7-amino-phenthiazone-2.



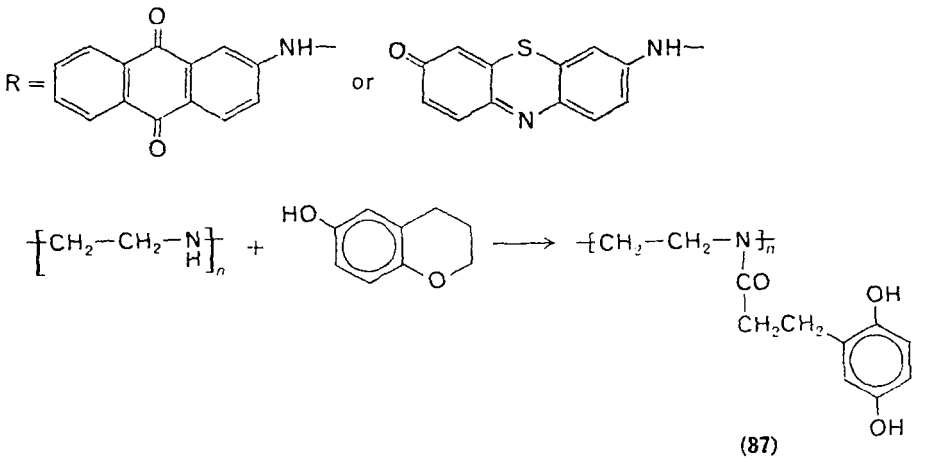
(84) (85)

An interesting route to the polyquinones was developed by Taylor[126], who reacted 6-hydroxy-3,4-dihydrocoumarin and similar compounds with poly(vinylamine) and poly(ethylenimine) by refluxing the components together in aqueous methanol. Polymers of the general structure **87** were obtained which were stable to alkalis and were proposed for use as anti-fogging or antistain agents in photographic emulsions.

Polyvinyl alcohol[127,108] and polyacrylic acid[127] have also been used as supports for anthraquinone and benzoquinone groups. Thus in acidified methanolic or dimethyl sulphoxide solution 2-formylanthraquinone condenses with polyvinyl alcohol to give a polyacetal structure carrying pendant anthraquinone groups (**88**). These groups were reducible by solutions of titanous salts or sodium dithionite, and reoxidizable with air.

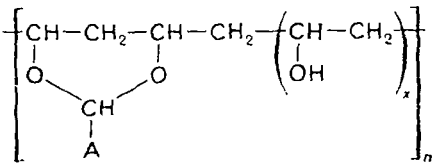


(86)



(87)

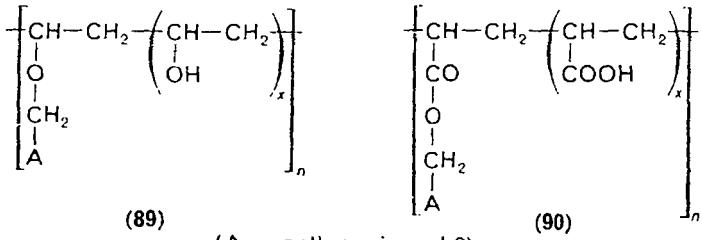
The acetal bonds were rather easily cleaved by acids. Izoret[127] has also described polyquinones prepared by reacting the tosylate of 2-hydroxymethylanthraquinone with polyvinyl alcohol to give **89**, and by reacting 2-hydroxymethylanthraquinone with polyacrylic acid to give polymers of the type **90**. Tetrachlorobenzoquinone has been reacted with a sodium



(88)

(A = anthraquinonyl-2)

derivative of polyvinyl alcohol to give a polyquinone of good redox capacity[128].



(89) (90)

(A = anthraquinonyl-2)

Kamogawa[129] methylolated polyacrylamide and an acrylamide-vinylpyridine copolymer with formaldehyde under alkaline conditions. The products were reacted with hydroquinone or phenothiazine to give redox polymers which could be potentiometrically titrated with ceric sulphate solutions.

V. ELECTROCHEMICAL BEHAVIOUR OF POLYQUINONES

A. The Polymeric Quinone–Hydroquinone Electrochemical System

The reversible electrochemical behaviour of the quinone–hydroquinone system can be represented by the following series of reaction equations:

$$Q + e \rightleftharpoons Q^- \quad \text{(semiquinone anion)} \qquad \text{(A)}$$

$$Q^- + e \rightleftharpoons Q^{2-} \quad \text{(quinol dianion)} \qquad \text{(B)}$$

$$Q^{2-} + 2H^+ \rightleftharpoons H_2Q \quad \text{(quinol)} \qquad \text{(C)}$$

Reactions (A) and (B) can occur as discrete steps under aprotic conditions whilst reaction (C) requires the presence of a proton donor (usually water). Under certain conditions (e.g. strongly alkaline solution) the semiquinone anion may also exist as a metastable species in aqueous media[130].

Consequently, the electron acceptor ability of a quinone may be determined in two ways: (i) by measurement of its electron affinity and (ii) by measurement of its standard oxidation–reduction potential (E^0). Electron affinity measurements are valid for aprotic media and are more usefully considered under section VI, whereas oxidation–reduction potentials are generally determined under aqueous or partially aqueous conditions.

The standard oxidation–reduction potential (E^0) of a quinone–hydroquinone system under aqueous conditions can be measured potentiometrically and provides a measure of the free-energy change ΔG^0 accompanying the interconversion of the two species. These quantities are related by equation (D)

$$\Delta G^0 = -nFE^0 \qquad \text{(D)}$$

When the conversion takes place in solution the free-energy change is dependent on a number of factors such as pH of the solution, the molecular and electronic structures of the oxidized and reduced forms, as well as environmental effects such as interactions with the solvent and other species present[131].

At moderate concentrations of hydrogen ions the quantitative effect of pH on the mid-point potential (E_m) of a simple quinone–hydroquinone system is described by the modified Nernst Equation (E)[132]

$$E_m = E^0 + 0{\cdot}0591 \ln [H^+] \qquad \text{(E)}$$

The characteristic mid-point oxidation–reduction potential (E_m) of the simple system at a specified hydrogen ion concentration can be readily determined by potentiometric titration, and hence the standard oxidation–reduction potential established.

In principle a polymeric quinone should behave similarly and on potentiometric titration can be expected to follow a typical two-electron titration curve (curve 1, Figure 1). The titration is normally carried out in a half-cell with addition of the oxidant to the polymeric hydroquinone, which is either in solution or in suspension. In some cases, due to sluggish response of the system, a mediator (e.g. isopropylhydroquinone) is added which will rapidly establish equilibria with both polymer and electrode. Considerable detail on the methods of measurement has been given by Cassidy and Kun[133].

However, contrary to expectation the measured potentiometric titration curve for many polymeric quinones deviates considerably from the typical two-electron shape (curves 2 and 3, Figure 1)[100,111]. The curve can be used to determine three characteristic potentials of the polymer system, the mid-point potential (E_m) at the 50% oxidation stage and the two index potentials E_{i_1} and E_{i_2} which represent the differences between the mid-point potential and the 25% (E_{25}) and 75% (E_{75}) oxidation potentials. That is, $E_{i_1} = E_{75} - E_m$ and $E_{i_2} = E_m - E_{25}$. For a symmetrical two-electron titration curve $E_{i_1} = E_{i_2} = 14{\cdot}1$ mV[132b]. The titration curves for the polymeric systems are frequently non-symmetrical with wide variations in the values of E_{i_1} and E_{i_2}[133,134].

The cause of the non-symmetricality of these titration curves has been ascribed to a number of individual 'polymer effects' such as semiquinone formation, complexation with the oxidant or reductant, quinhydrone formation, dimerization and tautomerism (e.g. formation of quinone-methide structures). Another cause may be associated electrode effects[134].

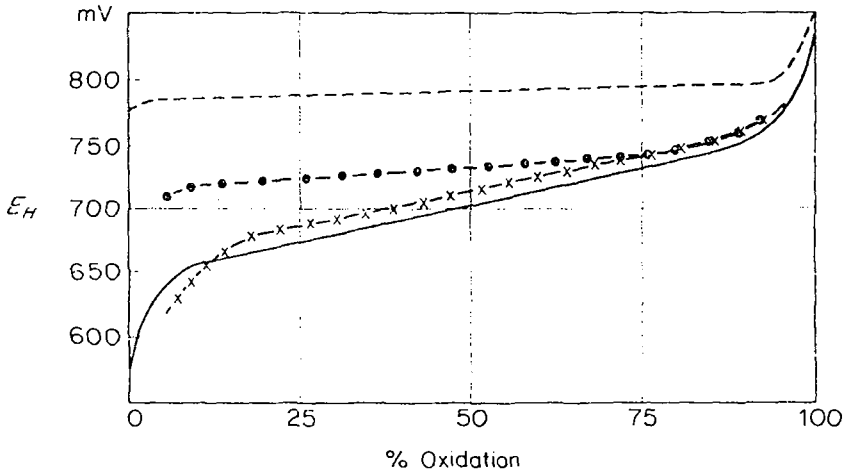


FIGURE 1. Potentiometric titration curves. (1) ——, Typical two-electron curve; (2) – – –, sulphonated polyvinylhydroquinone; (3) – · – · –, poly-2,5-dihydroxy-4′-vinyldiphenylsulphone; (4) —x—x—, hydroquinone–phenol–formaldehyde polymer (1 : 1 : 2).

Cassidy and coworkers[111, 133b] have described the striking colour change which occurs when a sulphonated polyvinylhydroquinone is oxidatively titrated. On first addition of oxidant a pink colour appears which intensifies up to the mid-point of the titration, and then becomes more and more yellow, finally giving the clear yellow of polyvinyl-*p*-benzoquinone at completion of the oxidation. The origin of these colour changes has been discussed[133b].

Apart from variation in the shape of the potentiometric titration curve, the measured mid-point potential of a polymeric quinone is found to be much higher than that measured for the corresponding monomeric reference quinone system[135]. As pointed out by Lindsey[136] and by other workers[133, 135, 137], the oxidation–reduction mid-point potentials of polymeric quinones are dependent on a number of factors, the more important of which can be broadly classified as structural, configurational and environmental. These are expanded in more detail in Table 3, though it should be recognized that the classification shown is arbitrary to some extent since some factors (e.g. semiquinone formation) can obviously fall into more than one category.

Structural features of polymeric quinones which affect the electrochemical behaviour of the system as a whole arise from the structure of the functional quinone unit, the type of nuclear substituent on the ring and the nature of the bridging groups since these, as in simple substituted quinones, materially affect the electron affinity of the unit. It is known, for

TABLE 3. Factors affecting mid-point potentials of polymeric quinones

1. Structural:	(i) Nature and degree of bridging groups
	(ii) Type and degree of nuclear substitution
	(iii) Nearest-neighbour interactions
	(iv) Molecular weight of polymer
	(v) Electrostatic field effects
	(vi) Complexation or addition of cations or anions
	(vii) Presence of non-functional chain members (copolymers)
	(viii) Solubility of polymer system
	(ix) Side-reactions (e.g. xanthene formation)
2. Configurational:	(i) Stereochemical disposition of quinone groups
	(ii) Chain coiling—uncoiling
	(iii) Semiquinone formation
	(iv) Inter- and intra-chain quinhydrone formation
	(v) Internal hydrogen bonding
	(vi) Steric effects
	(vii) Charge-transfer complexes
3. Environmental:	(i) Hydrogen ion concentration
	(ii) Nature of titration solvent medium
	(iii) Presence of neutral salts
	(iv) Differences in composition of macromolecular and bulk solvent phases
	(v) Type and normality of oxidant or reductant
	(vi) Presence of a mediator
	(vii) Electrode effects
	(viii) Liquid junction potentials

example, that increasing the degree of methyl substitution of *p*-benzoquinone results in a fall in the oxidation–reduction potential and similarly with increasing polynucleicity[47]. Helfand[138] has pointed out that in some polyquinones interactions between neighbouring quinone groups may be quite strong, as shown by deviation in the shape of the titration curve of the polymer compared to that of a suitable monomer model. Helfand[138] developed, on a mathematical basis, a theoretical treatment of polymeric quinone titrations and showed that above a certain limit the degree of polymerization did not affect the course of the titration. Below this limit the observed behaviour depended on the degree of reduction of the polyquinone system. Electrostatic field effects may be important where the

polymer chain is also a polyelectrolyte (e.g. is sulphonated)[139]. The properties of polyelectrolytes are known to differ from both non-polymeric electrolytes and non-ionized polymers. Their properties mainly depend on the average electrostatic potential of the polyelectrolyte macromolecule, its contribution to the electrostatic free energy of the system and its effect on the average dimensions of the macromolecule. Because of the coulombic forces present, polyelectrolyte systems incorporating quinone groups can be expected to exhibit a modified E_m value. Indeed, it has been experimentally shown[139] that the effect of a sulphonated polystyrene matrix is to raise the E_m of the copolymeric quinone. When the quinone was non-bonded to the sulphonated matrix only a small positive increase in E_m occurred. In the presence of molar potassium chloride the mid-point potential of the sulphonated polyvinylhydroquinone fell to that of the monomeric system. It was not confirmed that this was due to an electrostatic screening effect since other salts did not bring about this effect[139].

Other structural effects arising from complexation, presence of non-functional chain members, occurrence of irreversible side-reactions and effects arising from the molecular weight and solubility of the polymer system have been considered as influencing the redox behaviour of the polyquinone system[133, 139].

Configurational features which exert an effect on the interconversion of the bonded quinone–hydroquinone couple arise in the polymeric system because of the greater degree of regularity and lower degree of flexibility of the macromolecular structure compared with a random association of monomeric units[136]. Thus, in the polymer there are inherent constraints placed on the spatial orientation of the quinone groups which may arise from primary bonding (cross-links) or from secondary bonding (hydrogen bonds, charge-transfer interactions, quinhydrone formation) or through purely steric factors (bulky substituents). Consequently, the degree of electronic interaction between the polymer chain structure and each individual quinone group, causing variation in electron-acceptor ability, will be related to the degree of flexibility of the chain and the orientational freedom of the quinone group. These factors can also tend to stabilize semiquinones when formed by hindering delocalization of the unpaired electron, and preventing dismutation or dimerization of the semiquinone. Variation in the value of E_m may be associated with coiling and uncoiling of the polymer chain during change in the ratio of reduced and oxidized groups along the chain in the course of titration[93, 139].

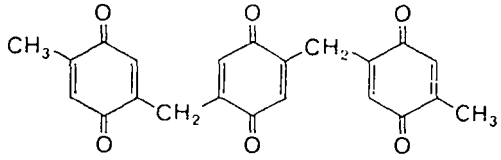
Many of the environmental factors influencing redox behaviour which are listed in Table 3 are valid for both monomeric and polymeric quinones. However, the macromolecular environment can bring about concentration

and species alterations within the macromolecular cells compared to the bulk solvent phase, which can lead to variation in the solute and solvent interaction between monomeric and polymeric quinone groups[136,140]. Neutral components of the solvent phase may also affect the potential, for example the depressing effect of potassium chloride on the E_m value of a sulphonated polyvinylhydroquinone system already mentioned. Other aspects of environmental effects have been discussed by Cassidy and Kun[133]. Evidence has been presented that adsorption of the oxidized polymer on to the electrode during potentiometric titration is responsible for increased potentials. In the presence of detergent the monomer value was approached[131].

Table 4 shows some representative E_m values for different polymers measured under varied conditions.

B. Electrochemical Behaviour of Polyquinone Chain Segments

As indicated in the previous section, the potentiometric titration curve for many polyquinones deviates considerably from the shape of a normal two-electron curve. An important approach to the study of the factors causing this deviation has been based on examination of the electrochemical behaviour of oligomeric quinones which have analogous structures to the polymeric quinone.



+ 6e (18)

The synthesis and redox behaviour of a variety of di-, tri- and tetrafunctional *p*-hydroquinone, 1,4-naphthoquinone and 9,10-anthraquinone systems have been reported but have not been systematically studied[45,141]. Apparently the first systematic studies were published by Hunt, Lindsey, Savill and Peover[110,142], who studied the electrochemical behaviour of mono-, di-, tri- and polyfunctional quinones with structures corresponding to those thought to be present in polyquinones derived from hydroquinone–formaldehyde and hydroquinone–phenol–formaldehyde condensates. Polarographic reduction of the quinone segments in aqueous–ethanolic solutions established that two-electron additions were made successively to each quinone unit. Thus reaction (18) showed a two-electron step and a complex four-electron wave, which could be analysed into two two-electron components (Table 4, No. 12). The titration curves for both the methylene-bridged diquinone and the two triquinone molecules revealed larger index potentials than for normal two-electron addition

TABLE 4. E_m Values of monomeric and polymeric quinone–hydroquinone systems

Quinone or polyquinone	Conditions[a]	E^0_m (mV)	Reference
1. Polyvinylhydroquinone, linear sulphonated	0·4N H_2SO_4 Neutral salt absent	789	86
2. Copolymer of vinylhydroquinone and α-methylstyrene, linear	0·106N H_2SO_4 + LiCl	643	139
3. Isopropylhydroquinone	0·106N H_2SO_4 + LiCl	630	139
4. Copolymer of vinylhydroquinone and α-methylstyrene, linear, sulphonated	1M KCl + H_2SO_4 (1 ml per 250 ml)	646	139
5. As 4	As 4 but neutral salt absent	849	139
6. Isopropylhydroquinone	As 4 but neutral salt absent	636	139
7. Poly(vinyl-3,4,6-trimethylhydroquinone)	In 90% acetic acid	420 (approx.)	93
8. Tetramethylhydroquinone	1 : 1 Acetic acid–0·5N H_2SO_4	456	93
9. Polycondensate of hydroquinone, phenol and formaldehyde (1 : 1 : 3)	N-H_2SO_4	628	142
10. Chain segment corresponding to 9, (68)	Polarographic	650	142
11. Poly-(2,5-dihydroxy-*p*-phenylenemethylene)	N-H_2SO_4	730	142
12. Trimeric quinone, chain segment corresponding to 11 (18)	Polarographic	624, 652 703	142
13. Sulphonated poly(2-vinylanthraquinone)	0·1N H_2SO_4 + mediator	178	100
14. Anthraquinone 2-sulphonic acid	In 50% aqueous acetic acid	183	100
15. 2-Isopropyl anthraquinone	In 50% aqueous acetic acid	124	100
16. Polyvinylpyrazolonaphthoquinone (*N*-sulphoalkylated)	Polarographic	130	101
17. 4-Quinonyl-4′-isopropyldiphenylsulphone	1 : 1 Acetic acid + 0·085N H_2SO_4	740	96
18. Poly-(2,5-dihydroxy-4′-vinyldiphenylsulphone)	In 80% acetic acid	753	96

[a] Potentiometric titration, except where stated.

and the mid-point potentials were much more positive than the reference monomer 2,5-dimethyl-*p*-benzoquinone. The central quinone nucleus (reaction 18) was considered to undergo the first two-electron addition, the high reduction potential being due to the strong electronegative

character of the two adjacent quinonyl groups and the much lower reduction potential of the third group resulting from the lower electronegativity of the adjacent hydroquinone group[142].

These electrochemical studies led to the conclusion that the anomalous redox behaviour observed during titration of polyquinones linked through methylene bridges could be qualitatively interpreted in terms of nearest-neighbour interactions, whilst the redox behaviour of the di- and triquinone segments suggested that other interactions in addition to nearest neighbours might be important. The shapes of the curves for the corresponding polymeric quinones significantly deviated from the theoretical shape for a two-electron process (index potentials of 35 mV compared to the normal value of 14 mV). However, the form of the polymer titration curve and its mid-point potential was not thought to have direct meaning since it was statistically dependent on factors such as extent of hyperconjugation between the methylene bridge protons and the quinone–hydroquinone nuclei which in turn appeared to depend on steric factors. Consequently, as reduction of the polymer proceeded those quinone groups having the most positive redox potential would be reduced first.

In aprotic solvents such as acetonitrile reduction of the same mono-, di- and triquinones proceeded by one-electron additions with formation of multiradical structures[142]. The spread in the first half-wave potentials of the three overall reduction steps was greater than the corresponding spread of the two-electron potentials in the protic solvent. E.s.r. measurements of the partially reduced quinone species indicated delocalization of the unpaired electron between directly coupled quinones but charge-transfer between quinones linked through a methylene bridge did not occur to any appreciable extent.

Similar studies of model monomer, dimer and trimer molecules related to hydroquinone–phenol–formaldehyde polymers by Manecke and coworkers[135,143] showed that benzyl-type substituents lowered the oxidation potential with respect to the reference *p*-hydroquinone by 47 ± 4 mV. The effects of both methyl- and benzyl-type substituents on the hydroquinone were claimed to be additive.

For *bis*-hydroquinone systems bridged by a *p*-xylylene grouping ($-CH_2-C_6H_4-CH_2-$) the symmetrical potentiometric curve deviated only slightly from the shape expected for a normal two-electron change. However, the corresponding *tris* hydroquinone oligomer gave an asymmetric curve with considerably steeper slope. Manecke[135] claimed that only relatively small interaction effects occurred in the oligomer systems which were inadequate to explain the potentiometric behaviour of the polymers.

Moser and Cassidy[111] also carried out electrochemical studies on oligomeric hydroquinone chain analogues of polyvinylhydroquinone (72–74). During potentiometric oxidation the hydroquinone groups appeared to react independently, which differed from that found for sulphonated polyvinylhydroquinone. When oxidized in aqueous acetic acid (1%) the *bis* and *tris* compounds developed a red colour which attained its maximum intensity at the mid-point. This behaviour was similar to that found for polyvinylhydroquinone polymers, and was thought to arise through quinhydrone formation.

Mills and Spinner[144] have made a detailed analysis of the redox behaviour of difunctional hydroquinone–quinone systems in which they show that the two overall oxidation potentials of the system are related to fundamental 'internal' oxidation potentials by a characteristic tautomeric equilibrium constant. The 'internal' oxidation potentials could be derived from the data available for the simple quinone–hydroquinone analogues and consequently made it possible to calculate the overall oxidation potential of specified dimeric hydroquinones. The analysis also permitted a direct numerical evaluation of intramolecular inductive effects due to nearest-neighbour interactions. The shapes and positions of the titration curves of the dimeric hydroquinones were related to the different values of the interaction effects. The possibility of analysing and predicting redox behaviour in monomeric, oligomeric and polymeric *p*-hydroquinone–quinone systems was envisaged by application of these methods.

C. Reaction Kinetics of Polymeric Quinones

The utilization of polymeric quinones as practical oxidation–reduction agents has focused attention on the necessity of ensuring that electron or hydrogen transfer at the polymeric redox sites should occur at reasonably fast rates. Since the presence of the polymer matrix complicates the reaction kinetics it is useful initially to consider the factors which influence transfer reactions with monomeric quinones.

The specific reaction rate constant of a simple monomeric quinone for a given substrate depends on a number of factors which include nature of solvent, pH, temperature and nature of the intermediate and other species present. Vetter[145] and Hale and Parsons[146] have measured the rate constants for the reduction of *p*-benzoquinone under carefully controlled conditions. Both authors found that the reduction proceeded by two one-electron transfers of almost equal activation energy. Hale and Parsons also established that the value of the free energy of activation was consistent with the Hush[147]–Marcus[148] theory of electron-transfer

reactions. Variation in the rate constant with the molecular size of the quinone was ascribed to the change in the free energy of formation of the semiquinone.

A number of correlations of the redox reaction rate with the oxidation–reduction potentials of the reactants has been reported. Gershinowitz[149], for example, deduced a theoretical relationship between reaction rate and the free energy of formation of the activated state which could be written in the form

$$0{\cdot}03 \log (k_1/k_1') = E_{OB} - E_{OD}$$

where k_1 and k_1' are the specific reaction rate constants for the reaction between the substance A and the oxidizing agents B and D. E_{OB} and E_{OD} denote the normal oxidation–reduction potentials of B and D. This equation was identical with that derived from experimental results by Conant and Pratt[150]. Other linear free-energy equations have been derived which are applicable to the dehydrogenation reactions of *o*- and *p*-quinones[151, 152], but these are useful for special cases only. The more general and more detailed theory developed by Marcus[153] which relates reaction rate with the free-energy changes occurring has been shown to give calculated results in agreement with the experimental measurements.

Braude and coworkers[151, 152] measured the rate constants of hydrogen transfer from organic substrates, such as dihydroaromatics, dihydropyridines, hydrazobenzenes, etc., to quinones of high electron-affinity of varied structures which included *o*-, *p*- and polynuclear quinones. In the majority of cases the hydrogen-transfer reaction was shown to be bimolecular and to obey a second-order rate equation up to at least 80% completion. The reaction was considered to proceed by a two-step heterolytic mechanism involving a rate-determining transfer of hydride ion from the hydrocarbon to the quinone followed by rapid proton transfer between the resulting conjugate acid of the aromatic hydrocarbon and the hydroquinone anion. In some cases a charge-transfer complex was formed between the reactants which led to a modification of the reaction kinetics[152]. Wallenfels and Gellrich[154] obtained rather similar results when they measured the rate constants for hydrogen transfer from various dihydropyridines to a restricted group of quinones.

Whilst the factors discussed above are generally relevant to the oxidation–reduction reactions of all types of quinones, the immobility and separation of functional quinone groups within a polymer matrix introduce additional factors affecting the reaction rate. Apparently the most important factors are the diffusion rates of the reactants and the internal equilibration rate.

Consideration[136] of literature evidence strongly suggests that in polymeric quinones the rate of the oxidation–reduction reaction is dependent on diffusion controlled processes similar to those operative in the case of ion-exchange resins[155]. These are (i) diffusion of reducing species in, and oxidized species out, through the Nernst film covering the redox beads, (ii) diffusion of the same species through the polymer network to and from the redox sites, or alternatively electron and proton migration to and from the reaction sites, (iii) electron plus proton transfer at the redox site. Diffusion of reactants into and within a polymeric matrix is linked to the swelling and hydrophilic properties of the polymer. Manecke has pointed out that the behaviour of a sulphonated anthraquinone polymer is completely analogous to that of a normal cation-exchanger based on polystyrene[135]. Kun and Kunin[121] have examined the redox kinetics of a series of polymers of the general structures previously shown (**81**, **82**, $R^1 = Cl$, $R^2 = H$), in which the degree of cross-linking was varied and the polymers were prepared with a macroreticular structure. They found that on increasing the hydrophilic character of the matrix, that is by making $R^1 = -N(CH_3)_3Cl$ or $R^2 = HSO_3$, the reaction rates and the available redox capacities significantly increased. Also, decreasing the particle size increased the reaction rate, which is similar to the observation of Sansoni[115]. Although the macroreticular structure of the polymer complicated interpretation of the results, Kun and Kunin[121] concluded that the low rates observed and the marked effect of introducing ionic groups indicate the rate-controlling step to be particle diffusion rather than Nernst-film diffusion. Similar results have been reported by Russian workers[156].

Oxidation–reduction reactions in solution can be catalysed by addition of other species. The oxidation of $Fe^{2+} \rightarrow Fe^{3+}$ for example is accelerated in the presence of chloride ions[157]. Luttinger and Cassidy[139] found that in the presence of 1 M potassium chloride the rate of oxidation of a sulphonated polyvinylanthraquinone by ceric ion (Ce^{4+}) was increased tenfold over that observed in the absence of neutral salt. No effect was noted in the presence of sodium acetate, sulphate or citrate anions, H^+, sulphuric or acetic acid. Manecke and Bahr[105] similarly found that addition of dimethylbenzoquinone or potassium chloride to the titration cell led to higher oxidation rates of a polymer, prepared by condensation of hydroquinone, phenolsulphonic acid and formaldehyde, with Ce^{4+}. In subsequent studies[100] on sulphonated polyvinylanthraquinone polymers it was found that on addition of a mediator such as anthraquinone-2-sulphonic acid to the solution, the reaction between the oxidant and polymer proceeded more rapidly and the potential of the polymer was established in a shorter time

on titration. The theory and utilization of mediators have been discussed by Cassidy and Kun[133].

The rate of equilibration of the polymeric quinone system can also exert an influence on the apparent rate of reaction. Cassidy and coworkers[133,158] established that there is an immediate stoicheiometric oxidation of the hydroquinone groups in a linear polymeric hydroquinone during electromeric titration, whereas attainment of a steady electrode potential for the system was comparatively slow. A similar behaviour has been observed[159] in the case of sterically hindered quinones such as 2,5-di-*t*-butyl-1,4-benzoquinone. Cassidy and Kun[133] and Moser[160] have postulated that in the polymer matrix where the hydroquinone groups are permanently separated, there is initially a rapid localized oxidation (*b*) followed by a much slower redistribution of electrons within the macromolecular structure (see Figure 2 (*c*)) and thence a slow redistribution of

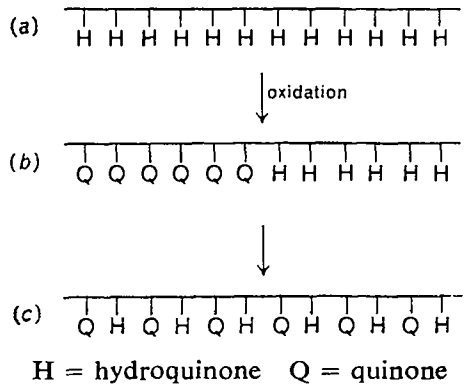


FIGURE 2. Equilibration stages.

electrons between different macromolecules (*d*). It is very probable that the rates of processes (*c*) and (*d*) are increased by the presence of certain salts or mediators.

VI. ELECTRONIC PROPERTIES OF POLYMERIC QUINONES

A. General

The electron acceptor–donor relationship of the quinone–hydroquinone system is fundamental to its distinctive electrochemical behaviour as well as the remarkable solid-state properties shown when incorporated into a macromolecular solid. Such materials are characterized by semiconductive and photoconductive properties and by catalytic activity.

The ability of a quinone in its ground state to accept electrons is quantitatively expressed as its electron affinity value. The electron affinity of a quinone can be defined as the energy liberated when an electron adds to the molecule in the gaseous state and is normally expressed in electron volts (eV). However, since direct measurement in the gas phase has attendant difficulties[161], electron affinity values of quinones are more usually indirectly determined from charge-transfer spectra[162] or from the linearly related first half-wave reduction potential of the quinone measured polarographically under aprotic conditions[163]. Pullman[164] has shown that the electron affinity of a quinone bears a simple relationship to the calculated energy of its lowest empty molecular orbital. It is therefore possible to calculate electron affinities from quantum mechanical data.

Similarly, the electron donor ability of an aromatic system can be represented quantitatively by its first ionization potential, which can be defined as the energy required to remove the most weakly bound electron of the molecule in the gaseous state. The first ionization potentials of molecules can be directly related to the energy of the highest filled molecular orbitals which are also calculable by quantum mechanical methods[165]. The presence of oxygen and nitrogen atoms can reduce the ionization potential of a molecule, whilst the ability of quinone to be converted to semiquinone forms stabilized by unpaired electron delocalization can provide a more mobile π-electron system which is reflected in the electrical and catalytic behaviour of the solid.

Information on the electronic transitions and interactions of coupled quinones may be obtained by studying their visible and u.v. spectra.

B. *Electronic Spectra*

The electronic spectra of *p*-benzoquinone and its derivatives were studied by Orgel[166] who identified the three absorption maxima at 410, 282 and 250 mμ as arising respectively from $n \rightarrow \pi^*$, $\pi \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions. The effect on the electronic spectrum of incorporating quinone groups into a macromolecular or polymeric structure has received little systematic study. Pullman and Diner[167] carried out some semiempirical molecular orbital calculations for polyquinones of increasing polynucleicity, which they used to interpret the spectral behaviour of the quinones. Existing data showed that an increase in the number of quinone functions in a linearly fused ring system led to a hypsochromic shift (blue-shift) of the longwave absorption band. In the case of angularly fused polyquinones a bathochromic effect (red-shift) occurred. The molecular orbital calculations indicated that in some polyquinones (e.g. heptacene diquinone) the *n*-electron energy level fell below that of the

π-electron level, and consequently the longwave absorption band was due to a $\pi \rightarrow \pi^*$ transition and not $n \rightarrow \pi^*$. These results explained the observed shifts of the longwave band.

The light absorption properties of molecular arrays of π-electron systems when linked, particularly in polymers, have been the subject of theoretical discussion[168,169]. However, this has mainly been applied to polynucleotides and linked quinones have not been considered. Experimental studies of the spectra of quinones linked by methylene and ethylene bridges have been made by Lindsey and coworkers[110]. The data showed that in these systems ring interactions caused marked deviations from the oscillator-strengths-sum rule leading to intensity losses and hypochromism. Moser and Cassidy[111] found that when the quinone groups were linked by a chain of three or more methylene groups there was little interaction between the π-electron systems.

C. Semiconductor and Photoconductor Properties

As already indicated in section III, there are a number of polyquinones and quinonoid polymers which exhibit semiconductor and photoconductor properties. These can be grouped as follows:

1. Crystalline polynuclear quinones and analogues.
2. Polyacenequinones.
3. Polyaminoquinones.
4. Polyarylenequinones.
5. Polyphenylazoquinones.
6. Polysemiquinones.
7. Polymeric dyestuffs such as aniline black.
8. Polyarylenes.

The syntheses and inferred structures of these polymers have been discussed in section III. The majority are characterized by high free-electron spin values and by relatively low resistivity values which vary exponentially with temperature. The semiconductor properties can also apparently confer unusual chemical reactivity on functional groups attached to the polymers, and enable the polymers to form unusually stable charge-transfer complexes with strong electron donors or acceptors[170,171]. Some of the polyquinones have been shown to be photoconductive[171].

The e.s.r. spectra of nearly all the above conjugated polymers, either as prepared or after further heat treatment, display a characteristic narrow line, the intensity of which corresponds to free-electron spin concentrations of 10^{16} to 10^{21} spin/g. The e.s.r. signal is little affected by oxygen for polymers which have not been heated above 300–400°C, but for polymers

heated above 500°C line broadening and a decrease in the free-spin concentration occur. In addition to the narrow e.s.r. line the spectra of some of the polymers, such as the polyaminoquinones, show broad absorption lines of great intensity, which disappear abruptly on cooling to 80 K. This behaviour is analogous to that of antiferromagnetic substances and has also been observed in nucleic acid preparations. The observed behaviour was suggested to be due to the presence of a single system of strongly interacting unpaired electrons constituting an orderly array of magnetic dipoles[172].

TABLE 5. Paramagnetic and semiconductor properties of polyquinones

Type of polyquinone	Electron free spins (per g)	Resistivity (ohm cm)	E_a Conduction activation energy (eV)	Reference
Polynuclearquinones (e.g. violanthrone)	—	10^{10} (288 K)	—	173
Polyacenequinones	10^{18}	10^{3}–10^{7} (300 K)	0·15–0·42	174
Polyaminoquinones	10^{17}–10^{18}	10^{10}–10^{16} (300 K)	0·88–1·0	69
Polyarylenequinones	9×10^{17}	10^{10}–10^{20} (300 K)	0·7–1·25	61, 69
Polysemiquinones	6×10^{19}	10^{9} (473 K)	1·00	175
Aniline black polymer	—	10^{10} (300 K)	—	52

In Table 5 the main data relating to the various groups of polyquinones listed above are summarized. It will be noted that the resistivities of the polymers vary between 10^3 and 10^{20} ohm cm at around room temperature. These values lie well insider the range usually classified as insulators and only at the lower resistivity end ($R < 10^{10}$ ohm cm) can the polymers strictly be called semiconductors.

On the basis of the limited amount of data yet available it appears that the electrical properties of these polymers depend on both the structure of the macromolecule and the structure of the material[171]. Conducting polymers are distinguished by macromolecules possessing an extended conjugated π-electron system which permits extensive charge delocalization over the macromolecule. As the number of π-electrons increases the ionization potential will tend to decrease and the electron affinity increase.

There will also be an increase in the polarizability of the system, in which strong internal polarization can be induced by the presence of hetero-atoms (e.g. oxygen, nitrogen, metals), edge-atom substituents or possibly by different sized macromolecules in the layer planes. Most of these expected features should confer improved electrical properties on the polymer, particularly as the conjugated system becomes more extended.

The dependence of electrical behaviour on the bulk structure of the polymeric material has been shown in a number of ways, particularly from the improvement resulting from a more ordered packing of the macromolecules[177] and from increasing pressure on the material[174]. Dulov and coworkers[179] have shown that introducing methylene bridges into the polymer chain improves the conductivity, which they interpret as arising from the improved flexibility of the polymer chain which enables closer and more ordered packing of the macromolecules to occur and thereby improves interlayer transfer of charge. Longer bridges such as $-CH_2CH_2-$ were found to restrict the conjugation path length and conductivity was reduced. Semiconducting polymers show enormous increases in conductivity with pressure, increased pressure leading to a reduction in the activation energy. The basis of this effect has been discussed[178].

Possible semiconduction mechanisms in organic polymers have been widely discussed. Two which have received considerable attention are the 'biradical' theory and the 'charge-transfer' theory.

The biradical theory propounded by Berlin[180] assumes that biradicals are formed in the longest conjugated macromolecular structure through local unpairing of π-bonds, followed by singlet–triplet transitions by thermal excitation, the double radicals remaining stabilized by non-coplanarity of structure or other steric factors. The formation of biradicals on heat treatment of the polymer explains the increase in the electron free-spin concentration and the improved conductivity due to decrease in the conduction activation energy. This theory has received further support from quantum mechanical calculations[181].

That donor–acceptor action promotes electrical conduction in polymers has been verified experimentally[174]. This lends weight to the theory[182] that charge-transfer states are present in the polymers giving rise to radical-ion centres. The charge-transfer either can occur between two neighbouring macromolecules or it can involve charge capture by more remote molecules, traps or crystal defects. Formation of polarized states involving charge-transfer is thought to be promoted by (i) an extensive conjugated π-electron system, (ii) polydispersity, which produces differences in electron affinity and ionization potential between the

macromolecules, (iii) polarization of the molecules, (iv) disorder and structural defects in the material, which permit local interactions between molecules and the formation of traps[171].

Photoconductivity in solids arises when light of a wavelength corresponding to a fundamental absorption band is absorbed by the material. Excitons or excited states are generated which lead to increased numbers of current carriers and improved conductivity. Some of the polyquinones have been shown to be photoconductive, and in most cases the photoconductivity has been shown to be electronic in origin[183]. Thus polyacenequinone polymers were found to be photoconductive[174].

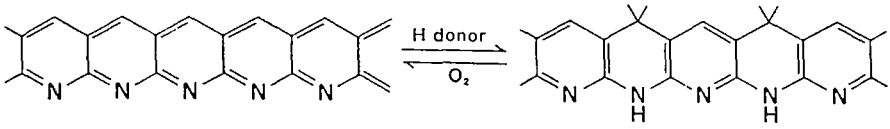
D. Catalytic Properties

Many of the conjugated quinone and quinonoid polymers described in section III have been shown to possess catalytic properties. Thus, the decomposition of hydrogen peroxide is catalysed by pyrolysed polyacrylonitrile[184], polyaminoquinones[185] and aniline black[186]; the decomposition of formic acid is catalysed by pyrolysed polyacrylonitrile[187], polyquinones[188], aniline black[188], polyquinoxalines[188], etc. Other reactions catalysed by these types of polymers are dehydrogenations and dehydrations[49, 188, 189], autoxidations[189, 190], decomposition of hydrazine and nitrous oxide[188, 189] and isomerizations[49, 188].

In some of these studies it has been possible to demonstrate a direct correlation between the catalytic activity of the organic polymer and the electron free-spin concentration as determined by e.s.r. measurements[49, 188, 191]. The catalytic activity of inorganic semiconductors is usually interpreted as a property which arises from their ability to function as conductive matrices for electrons and holes. A similar theory has been applied to the polymer catalysts, the semiconduction mechanism operating through the extended system of conjugated double bonds present in the polymer[192].

The work of Manassen, Wallach and Khalif[49], however, provides strong evidence that it is the presence of quinonoid groups and not extended π-electron systems which are essential for the catalysis of dehydrogenation reactions. They showed that if vapour-phase dehydrogenations (such as cyclohexene $\rightarrow$ benzene) are carried out over a thermostable polymer containing quinone units, hydrogen transfer from the substrate to the polymer occurs. Thus, the red polymer prepared by treating diazotized benzidine with benzoquinone, during the catalytic hydrogen transfer reaction changed in colour to yellow-brown and the characteristic quinone carbonyl absorption band at 1660 cm^{-1} in the i.r. spectrum disappeared. After aerial re-oxidation this band reappeared

together with the red colour. Similar results were established for pyrolysed samples of polyacrylonitrile and polycyanoacctylene, and aniline black. All three catalysts were considered to function by hydrogen atom abstraction from the substrate leading to conversion of quinonoid to hydroaromatic structures, e.g. reaction (19). In the case of pyrolysed polyacrylonitrile, acidic sites were also thought to be present on the catalyst leading to hydride ion transfer.



(19)

The catalytic polymers apparently did not liberate hydrogen, nor transfer hydrogen to the substrate and, when in the reduced condition, could be regenerated by air at about 140°C with formation of water. Catalysed reactions could be carried out in an air stream which maintained the activity of the catalyst. Non-quinonoid-type polymers and compounds were shown to be catalytically inactive. The correlation between dehydrogenation activity and electron spin values can be expected for the quinonoid polymer where semiquinone structures are possible, whereas there is no fundamental reason for a correlation with semiconduction properties.

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The Chemistry of the Quinonoid Compounds
Edited by Saul Patai

CHAPTER 16

Non-benzenoid quinones

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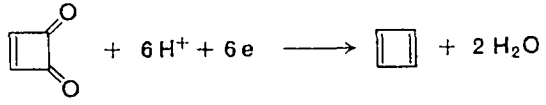
I. INTRODUCTION

Your reviewer, who is not an expert in the field covered, accepted the editor's invitation to produce a review of compounds that might reasonably be covered in this area. He defined the limit of the enquiry by excluding compounds where the carbonyl groups were attached to six-membered or extended six-membered rings and which might be thought to be benzenoid in character. He sought a reasonable definition of this class of compounds and the most comprehensive one was provided by Professor Trost who defined a non-benzenoid quinone as any dicarbonyl species whose two-electron reduction product would generate a non-benzenoid aromatic.

On reflexion the author considered that the use of the word 'aromatic' was unduly restrictive in this context since it implied the reduction product would have to conform to Huckel's $4n+2$ electron rule whereas there were compounds that might legitimately be included in this class whose reduction products did not conform to the rule. He therefore modified the latter part of the definition to 'any dicarbonyl species whose two-electron reduction product would generate a cyclic non-benzenoid structure containing conjugated double bonds'.

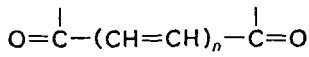
Thus we can write the following equation for the reduction of cyclobutenequinone



where two electrons are required for the reduction of the quinone. This definition gives the classes of compounds discussed in sections II and III, viz. the simple even- and odd-membered ring systems.

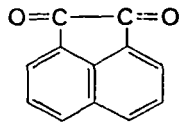
Other dicarbonyl systems still conforming to the above general definition can be generated by considering the ways in which carbonyl groups can become cross-conjugated. The requirements for this type of system are (i) that both carbonyls should be directly joined to one another

or through a mobile electron system and (ii) that each carbonyl should be attached to a carbon containing mobile electrons. Thus we can generate a further class of compounds from the system



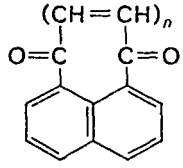
and any conjugated system capable of linking across the free valences would produce the type of system we have in mind.

For example, we can take the acenaphthene quinone system

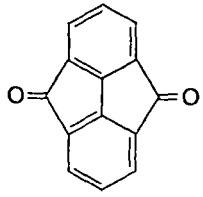


which could be extended by a many-fold extension of the aromatic ring in various ways.

We might also construct further systems from the generating formula



in which we could build up 1,2-, 1,4-, 1,6-, 1,*n*-mobile-electron carbonyl systems attached to an aromatic system. Apart from the simple ring systems discussed in sections A and B we can get larger ring systems such as



All these other types of dicarbonyl systems are discussed in section IV.

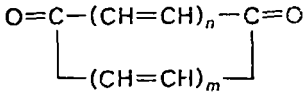
Having limited the class of compounds in the above way your reviewer then attempted to write an interesting but not exhaustive review of compounds in this class. He decided to indicate synthetic methods but not to give a detailed account of them; he would note chemical properties

of interest; he would observe the physical properties of these compounds especially in relation to physical properties normally met with in the quinone system such as oxidation–reduction potentials, colour and the ability to form radical ions and, while recording these properties, would indicate but not include calculations of a theoretical nature. He hopes he has neither overestimated nor underestimated work in this area and would apologize to any worker in this area who feels his work may have been misrepresented.

II. EVEN-MEMBERED RINGS

A. Generating Formula

The quinones in this class may be regarded as being generated from the system



in which either n or m, but not both, may be zero.

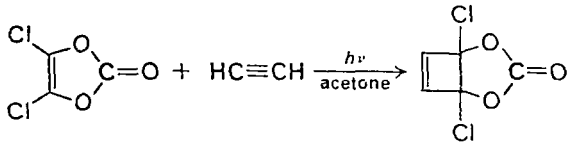
The case $n = 0$, $m = 1$ generates cyclobutenequinone, i.e. the class of four-membered rings. For the situation $n+m = 2$ we have the case $n = 2$, $m = 0$ which yields *ortho*-benzoquinone and $n = 1$, $m = 1$ yields *para*-benzoquinone. If we now take the situation $n+m = 3$ then we generate the eight-membered ring which can have either a 1,2- or a 1,4-dicarbonyl function. If we take the situation $n+m = 4$ then we generate a ten-membered ring with a 1,6 dicarbonyl function and larger symmetrical rings will produce 1,8 and 1,10 cases and so on.

If instead of —C=C— we take —C≡C— then new possibilities are introduced, though whether or not such compounds would strictly belong to the class we have in mind is not clear.

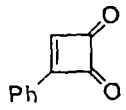
B. Four-membered Rings

1. Cyclobutenequinone and derivatives

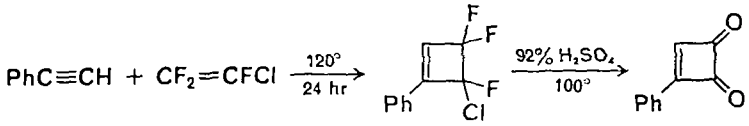
a. Preparation. The parent compound of this class cyclobutenequinone or cyclobutenedione has only recently been prepared by the following route[1].



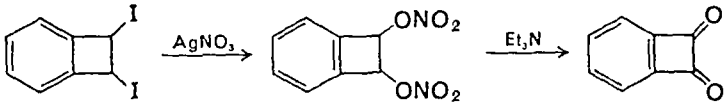
The cycloadduct is a rather unstable liquid (B.P. 41–42°C at 0·05 Torr) formed in 10–15% yield. Hydrolysis of the adduct at 60° in 60% acetone–water gives cyclobutenedione as a light-yellow solid (M.P. 40–41°C). The compound



was prepared[2] by the following route

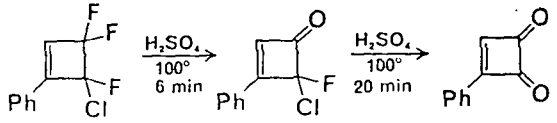


The benzo compound was formed[3] through the route

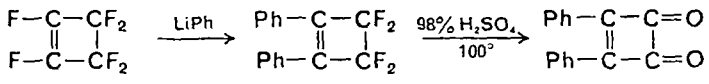


A later paper[4] gives more generalized procedures for preparing cyclobutenedione derivatives.

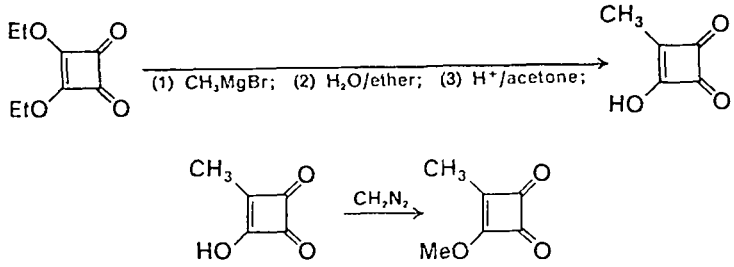
In these syntheses the cycloadducts of perhaloethylenes with phenylacetylene were used as starting materials. Thus, from trifluorochloroethylene and phenylacetylene heated in a sealed tube at 125° for 20 h there was obtained 1,1,2-trifluoro-2-chloro-3-phenylcyclobutene which was then hydrolysed.



The synthesis of the diphenyl compound has been described by the following route[5]

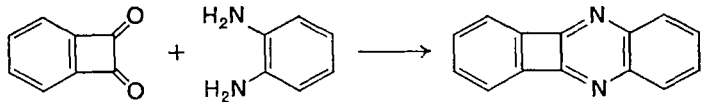


The methylcyclobutenedione and its methoxy derivative have been prepared according to the schemes below[6]

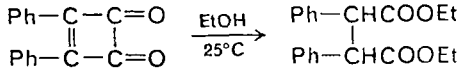


b. Chemical properties. The following by no means exhaustive series of reactions of cyclobutenedione and its derivatives was noted:

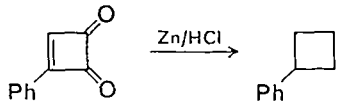
Condensation[4]:



Esterification[5]:

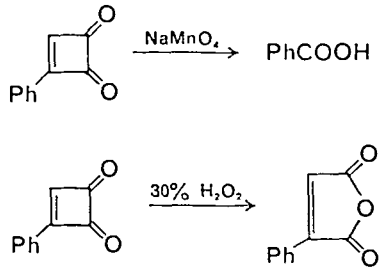


Reduction[4]:

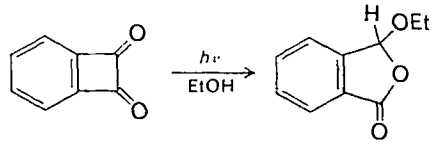


However, phenylcyclobutenedione is apparently not reduced[3] by reagents such as hydrogen over platinum to the corresponding hydroxy compound.

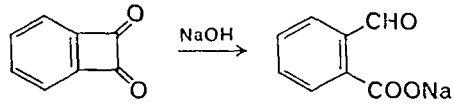
Oxidation[4]:



Photolysis[7]:

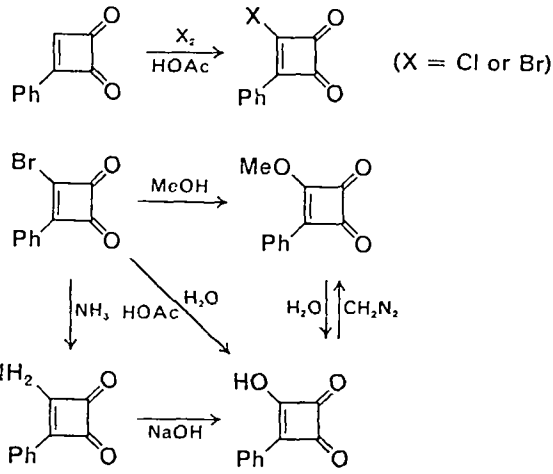


Ring opening[3]:



Blomquist and La Lancette[8] report that with phenylcyclobutenedione and diphenylcyclobutenedione treatment with hydroxide results in cleavage of the 2,3-bond.

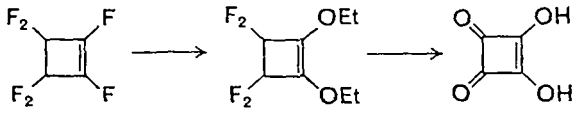
Substitution[4]:



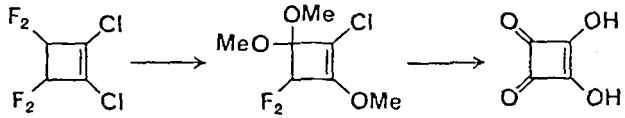
c. Physical properties. The physical properties of these compounds are mildly quinonoid in character. Thus phenylcyclobutenedione separates as yellow crystals and has a u.v. spectrum with a maximum of 287 mμ in ethanol. Heats of combustion, resonance energies, dipole moment data and acid dissociation constants of this compound and its derivatives are also recorded[4].

2. Squaric acid

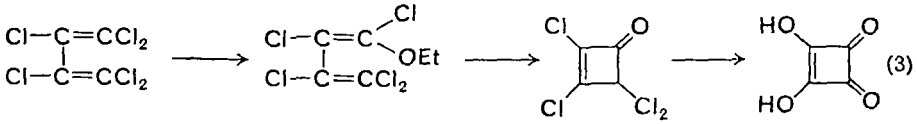
a. Preparation. The properties of this compound have been the subject of review[9] and the following preparative methods described.



(reference 10) (1)



(references 11, 12) (2)

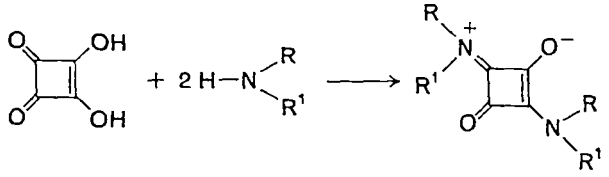


(3)

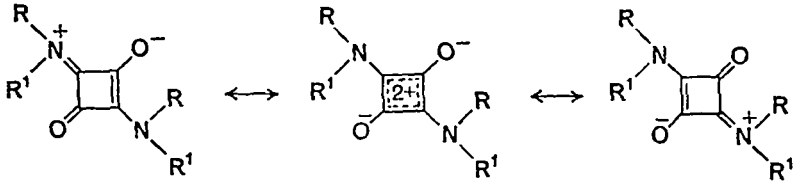
(reference 9)

b. Chemical properties. Again, without being exhaustive, a selection of reactions is described.

Condensation[13]: Gauger and Manuke report the condensation products of squaric acid with primary and secondary amines to produce a new class of betainic squaric acids



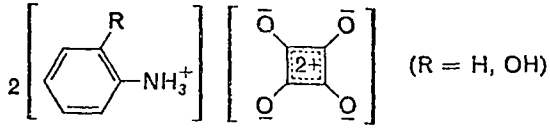
The product formed can be written in further resonance forms



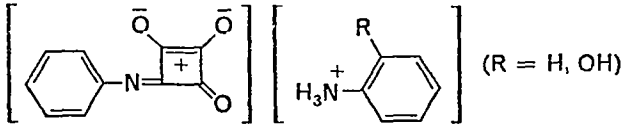
(R = H, alkyl or aryl) (R¹ = aryl)

The structure of these compounds has been confirmed by i.r., n.m.r. and mass spectroscopic measurements.

As intermediates the following squarates were isolated,



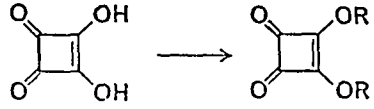
as well as the compounds



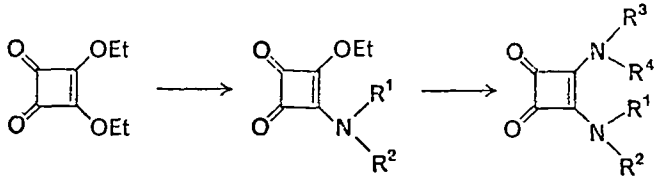
and these compounds were transformed into the corresponding squaric acid 1,3-bisamides by stepwise condensation.

A further paper[14] describes the preparation of copper chelates of the squaric acid 1,3-bisamides with aromatic substituents containing donor groups in the *ortho* position.

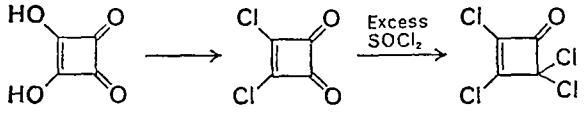
Esterification[9]: diethyl and dibutyl esters are formed by the reaction of the acid with excess alcohol,



the diesters reacting with amides to give squaramides, e.g.

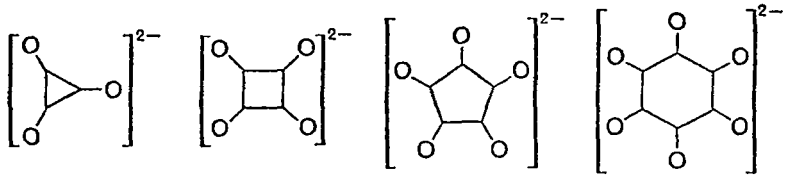


Halogenation[15]: the reaction of squaric acid with thionyl chloride and catalytic amounts of *N,N*-dimethylformamide has been recorded.



c. Physical properties. Squaric acid is a white dibasic acid. A precise determination of the ionization constants of squaric acid has been made

and values of pK_1 1·2 and pK_2 3·5 recorded[16]. A large number of substituted squaric acids have also been studied and their pK's recorded[17]. An extended account of the properties of the ions $C_nO_n^{-m}$ has been given[18].



The series is of interest, though the existence of the three-membered ring compound has not been recorded.

Results from simple LCAO-MO calculations on anions of the $C_nO_n^{-m}$ group correlate with observed properties of known members of this group. Calculations have also been carried out on a large number of theoretically possible anions with related but more complex structures.

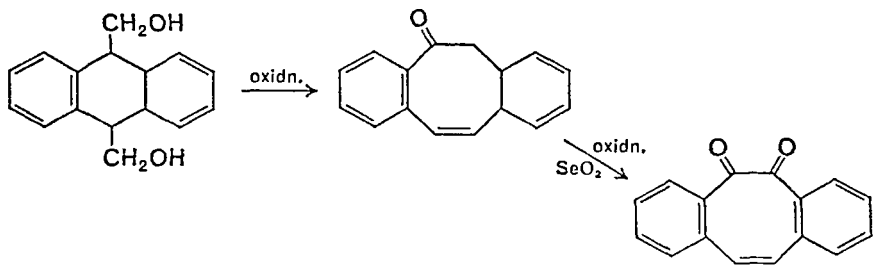
In a subsequent paper[19] the infrared spectra of solid $K_2C_4O_4$ and $K_2C_5O_5$ and the Raman spectra of their aqueous solutions were studied. Spectra indicate planar symmetrical structures (D_{4h} and D_{5h}) for the ions. Vibrational assignments were made on the basis of these structures and a normal coordinate treatment was carried out using a Urey–Bradley force field. The resulting force constants supported the view that these ions constituted members of an aromatic series.

In subsequent papers[20,21] complexes of these ions with divalent and trivalent metal ions were prepared and characterized.

C. Eight-membered Ring Systems

1. Cyclooctatrienequinone

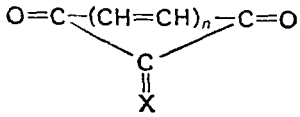
An article has been written which contains a very good account of the theory of such compounds and of attempts that have been made to prepare them[22]. In this paper the following synthesis is reported:



III. ODD-MEMBERED RINGS

A. Generating Formula

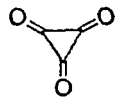
These compounds may be regarded as being generated from the formula



where n can be 0, 1, 2, 3, etc., the larger rings producing dicarbonyl systems with 1,2-, 1,4- and 1,6-function respectively. In accord with our earlier definitions, the only restriction is that X must not produce an immobile electron system on the carbon attached to the two carbonyls and we have chosen to regard compounds where X is oxygen as belonging to this class.

B. Three-membered Ring Systems

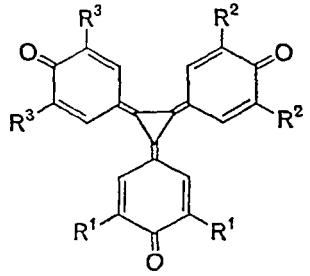
The generating compound of this class is cyclopropanetriquinone



which has not been prepared as yet. However, triquinocyclopropanes, which are an approach to this system, are known[23].

1. Cyclopropanetriquinone derivatives

a. Preparation. Triquinocyclopropanes are generated from the corresponding tris-(*p*-hydroxyaryl)cyclopropenium salts[23]. When these are dissolved in benzene and treated with potassium hexacyanoferrate(III) solution, deprotonation and oxidation occur simultaneously, the benzene layer turning deep-blue and producing



where R^1, R^2 and R^3 are alkyls.

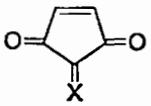
b. Chemical properties[23]. Treatment of the blue-green solutions of the triquinocyclopropanes with hydroquinones resulted in orange solutions. The electronic spectra of the solutions indicated that the products were diarylquinocyclopropenes and this was confirmed by a quantitative preparative experiment.

c. Physical properties. The compounds are soluble in non-polar solvents and insoluble in polar solvents. All the compounds are highly coloured and the i.r., n.m.r. and u.v. spectra all support the proposed symmetrical structure.

C. Five-membered Ring Systems

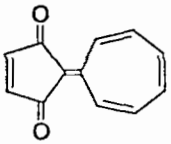
1. Cyclopentenequinone and derivatives

The parent compound in this class may be regarded as

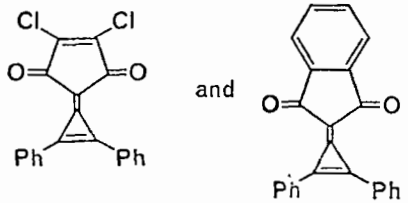


in which quinonoid properties are achieved by the attachment of a mobile electron system as X.

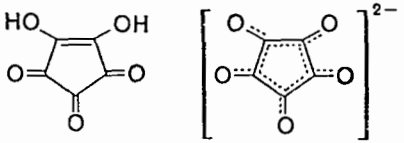
An example of this class is fulvalmixene-1,4-quinone, of which the synthesis has been described[24]. The substance crystallizes in red plates



whose absorption spectrum has been recorded. It undergoes addition at the 2,3-position. In the same class we record the compounds[25]



a. Croconic acid. Croconic acid is a yellow substance which has been known for a long time[26]. A structural investigation[27] suggests the formulae

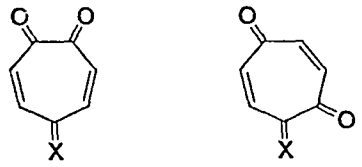


for the acid and the ion and a comparison between this species and squaric acid has been noted earlier in this review. The reduction of croconic acid either by hydriodic acid and red phosphorus or electrochemically gives the pinacol of croconic acid[28].

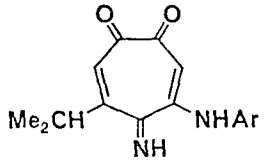
D. Seven-membered Ring Systems

1. Cycloheptadienequinone and derivatives

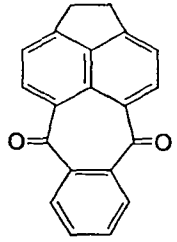
The parent compounds in this class may be regarded as



in which quinonoid properties are again achieved by the attachment of a mobile electron system as X. The compounds thus have the possibility of both 1,2- and 1,4-function. An interesting member of this class recorded in the literature[29] was the compound

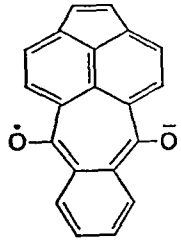


a. 5,12-*Dihydroacepleiadene*-5,12-*dione*[30]. This was the best example available of a seven-membered ring showing quinonoid properties. The compound 5,12-dihydroacepleiadene-5,12-dione undergoes reactions leading to the formation of stable radical ions in a manner similar to pyracylo-quinone to be discussed in the subsequent section.

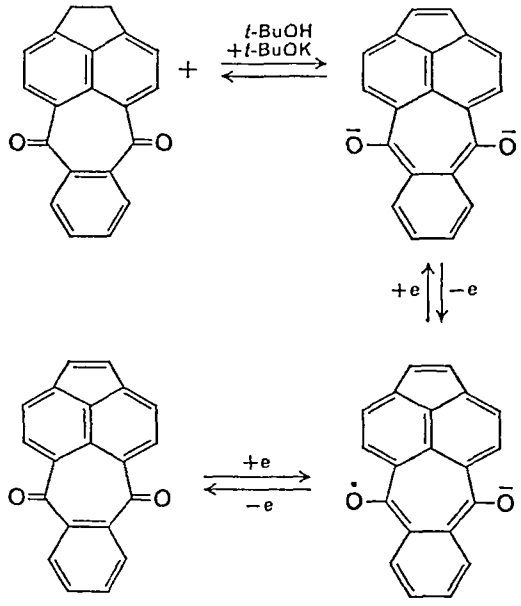


Treatment of a 1×10^{-2}M solution of the above dicarbonyl compound in dimethyl sulphoxide with a $2{\cdot}5 \times 10^{-2}$M solution of potassium *t*-butoxide

solution gives a deep-blue solution containing a paramagnetic species as evidenced by a strong e.p.r. signal.



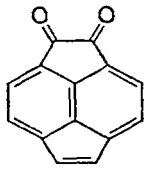
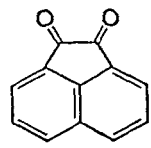
An identical e.p.r. signal was obtained when a 1×10^{-2}M solution of 5,10-dihydroacepleiadylene-5,10-dione in dimethyl sulphoxide was treated with 2×10^{-2}M potassium *t*-butoxide in dimethyl sulphoxide. The total investigation gave evidence for the equilibrium scheme below.



IV. OTHER DICARBONYL SYSTEMS

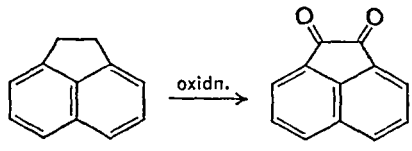
A. 1,2-Dicarbonyl Systems

The compounds which we will discuss in this class are pyracyloquinone and acenaphthenequinone

I. Acenaphthenequinone

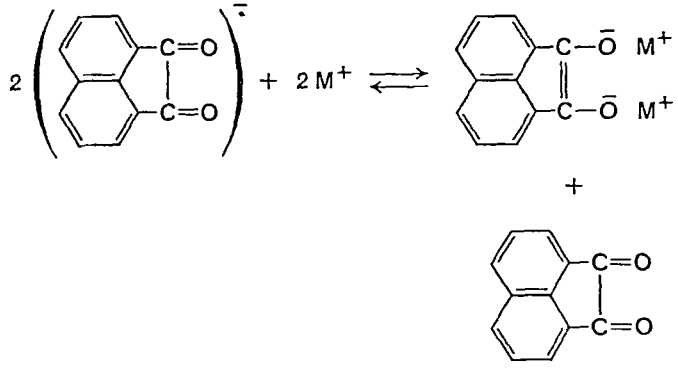
a. Preparation. This compound is well known and the reaction



is recorded in most organic texts. Heilbron records information on bromo[31a], hydroxy[31b] and nitro[31c] derivatives of acenaphthenequinone. A definitive synthesis has also been described[32]. Acenaphthenequinone can be prepared from acenaphthene by oxidation with chromic acid, calcium permanganate or by air in the presence of catalysts in various solvents.

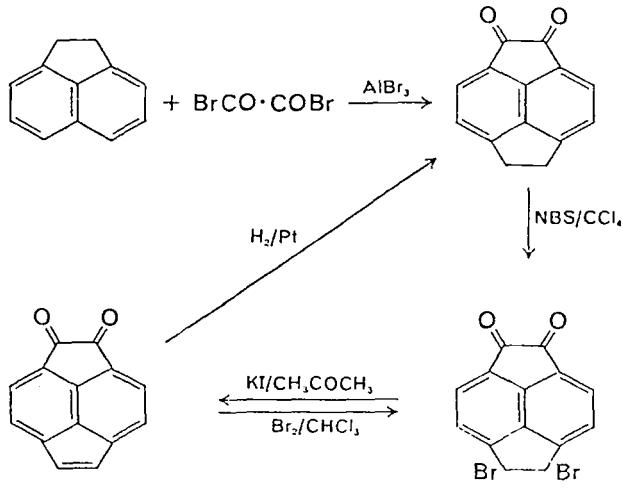
b. Chemical properties. Structures have been assigned to the products of the reaction of acenaphthenequinone with ethylene glycol[33] and the reactions of acenaphthenequinone and ammonium acetates in the presence of aryl aldehydes have been recorded[34].

c. Physical properties. Acenaphthenequinone is capable of forming radical ions and the equilibrium between these radical ions and metal ions has been determined, it being possible to measure an equilibrium constant for the reaction[35].



2. Pyracyloquinone

a. Preparation. Following a preliminary report on pyracyloquinone[36] a definitive account of the synthesis and chemistry of this interesting compound has been given[37]. The following synthetic and reactive scheme is described:



The diketopyracene was prepared by Friedel–Crafts acylation with oxalyl bromide. The compound does not tautomerize under acidic or basic conditions to dihydroxypyracylene or a derivative. Bromination with *N*-bromosuccinimide followed by debromination with iodide ion produced pyracyloquinone.

b. Chemical properties. Attempts to reduce pyracyloquinone chemically to a derivative of pyracylene all failed. Among methods used were trimethyl phosphite, zinc in acetic acid, zinc in acetic anhydride and sodium and lithium in liquid ammonia followed by acetylation or alkylation with methyl iodide.

Pyracyloquinone undergoes Diels–Alder reactions with both cyclopentadiene and with 2,6-diphenyl-3,4-benzofuran. Irradiation of pyracyloquinone produces either acenaphthene-5,6-dicarboxylic anhydride or acenaphthylene-5,6-dicarboxylic anhydride, depending on reaction conditions.

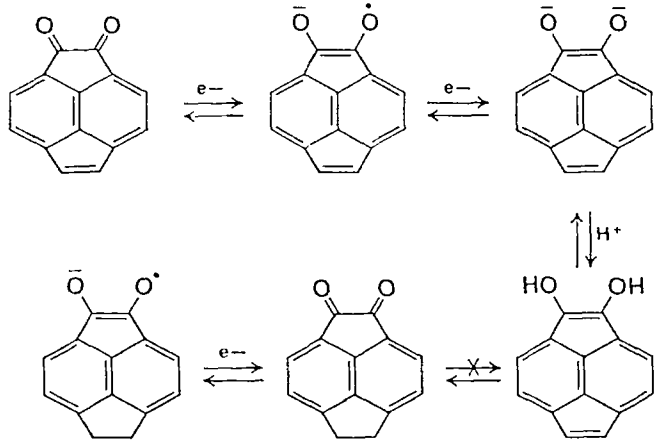
c. Physical properties. The spectral properties of pyracyloquinone are in complete agreement with the above structure. The i.r. spectrum shows a pair of peaks at 1735 and 1685 cm^{-1} due to the diketone moiety. The energy separation between these peaks is about 30 cm^{-1} less than any of the diketopyracene derivatives. This decreased energy is associated with

increased strain in the diketo bridge. The u.v. spectrum of the pyracyloquinone contains the following peaks.

max. mμ	log ε
230	4·47
247	4·19
307	4·25
314	4·23
346	3·85

This spectrum agrees well with one predicted from theoretical calculation.

In an earlier paper the formation of radical ions from pyracyloquinone by treatment of the substance with 0·1 M potassium tertiary butoxide in dimethyl sulphoxide was described[38] and also the following equilibrium system:

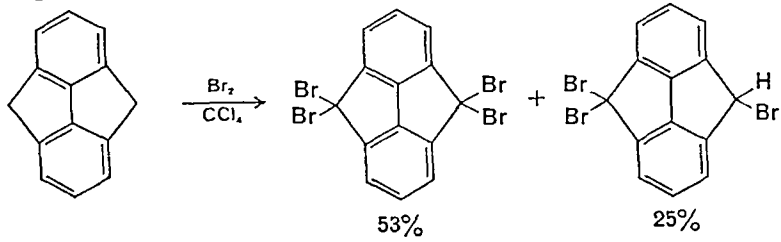


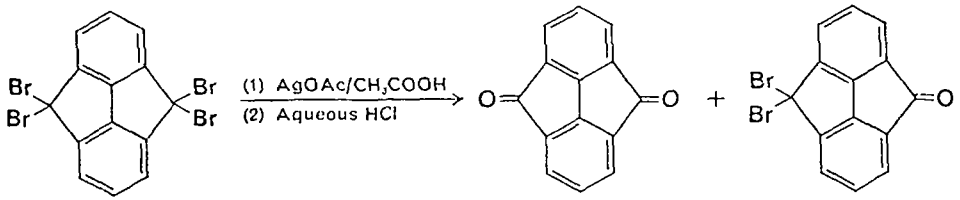
B. Other Dicarbonyl Systems

The compound discussed in this class is the dibenzo[*cd*,*gh*]pentaleno-4,8-quinone[39].

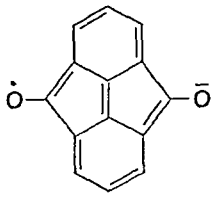
1. Dibenzo[cd,gh]pentaleno-4,8-quinone

a. Preparation.





b. Properties. Electrolytic reduction of the dibenz[*cd*,*gh*]pentaleno-4,8-quinone in DMSO containing 0·1 M tetra-*n*-butylammonium perchlorate produced the radical ion



V. ACKNOWLEDGMENT

The author wishes to thank Professor B. M. Trost for assistance in the preparation of this review.

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31a. I. Heilbron in *Dictionary of Organic Compounds*, Vol. 1, Eyre and Spottiswoode, London, 1965, p. 415.
31b. Reference 31a, Vol. 3, p. 1638.
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The Chemistry of the Quinonoid Compounds
Edited by Saul Patai

CHAPTER 17

The addition and substitution chemistry of quinones

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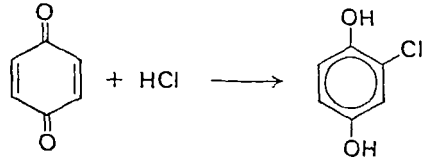
I. INTRODUCTION

From the very beginnings of modern organic chemistry the chemistry of the quinones has formed a lively section of our discipline. Wöhler himself carried out a 1,4-reductive addition reaction (equation 1) quite typical of the chemistry to be described in the present chapter[1]. In our day, the prolific Fieser continues to add to his extensive contributions to quinone chemistry[2].



(1)

Between these two reference points has come an army of scientists producing a bewildering array of synthetic and mechanistic facts and speculation. Even in the more limited areas of addition and substitution chemistry the scientific scope is both broad and deep. Consequently, a great many very difficult choices have had to be made in preparing this chapter. While every effort has been made to treat all of the major areas of activity, in a number of cases only one or two leading papers have been dealt with in detail. Where this course has been necessary, those papers with the greatest mechanistic detail have been discussed and checked to see that adequate references to other aspects of the work are provided.

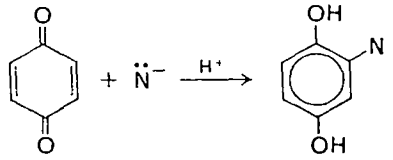
The general pattern selected for the chapter has been to treat most of the non-quinonoid reactants in separate subsections. While the details of the mechanisms are very similar in many cases, and a unified treatment is attractive, the best and most complete studies are still centred on discrete and rather narrow areas. The encouragement of research to examine the interrelationships to be found in this old, but partially tilled, field is certainly a desirable objective. Within each of the sections there are basically three major subsections: (i) a very brief historical introduction, (ii) a detailed discussion of the current mechanistic picture, and (iii) a summary of the synthetic scope of the reaction type. Where a particular area has received detailed treatment, some in more than one subsection, some further sections have been included for clarity. Finally, in a few cases a brief note or two has been added at the end of a section. These notes are simply a recognition that an interesting piece of work has been reported, but not yet studied in sufficient detail for discussion.

Mention should be made of two other aspects of this review. First, benzo-, naphtho-, 1,2- and 1,4-quinones have been included where data are available. The higher, polycyclic quinones do not show addition and substitution chemistry of the types treated here (with exceptions such as carbonyl reactions) and, therefore, are largely omitted. Second, the rather large patent literature: after a careful study of the actual patents it was decided that relatively little is lost by not citing these materials. Much of the patent literature is related to practical modifications and improvements in such industries as dyes, photography, plastics, etc.

II. NUCLEOPHILIC ADDITION CHEMISTRY OF QUINONES

A. Scope and Mechanism

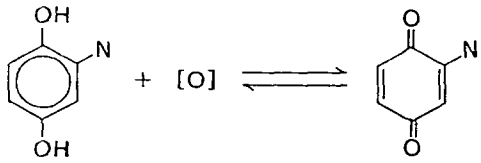
The vast majority of the reactions of quinones can be characterized as 1,4-reductive additions of the Michael type (equation 2). The initial hydroquinone product **1** is, of course, susceptible to oxidation by air,



(2)

(1)

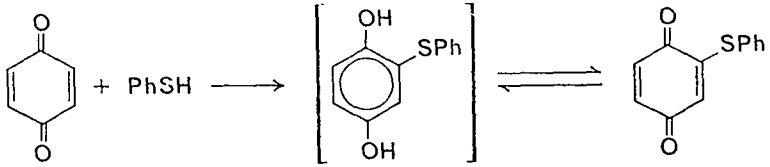
added oxidant, or (with electron-donating substituents) the quinone starting material (equation 3). The nature of the new substituent (N) introduced will determine, in large measure, the details of such subsequent



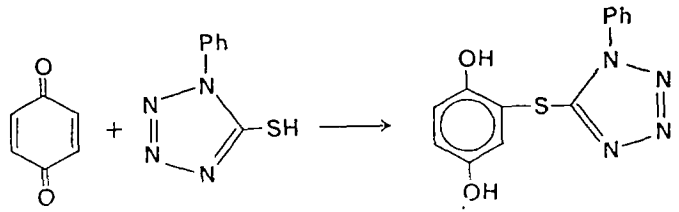
(3)

chemistry. The presence of the phenolic hydroxyl group (or the carbonyl group of the oxidation product, **2**) also leads to many important following reactions.

The addition of hydrogen chloride has already been cited as one of the earliest reported quinone addition reactions[1]. The addition of sulphur nucleophiles has been studied extensively and can lead either to oxidized (equation 4) or reduced (equation 5) product under appropriate circumstances[3,4]. The addition of amines and anilines to quinones usually

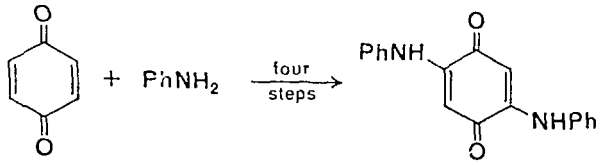


(4)



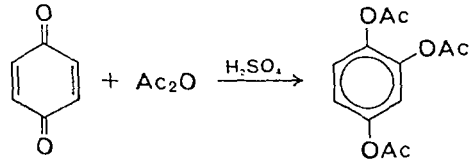
(5)

produces an easily oxidized substituted hydroquinone. In fact, the usual product is the result of a sequence of two additions each followed by oxidation (equation 6)[5]. Yet another widely used and extensively studied



(6)

addition reaction is the Thiele acetylation (equation 7)[6]. While the Thiele is an electrophilic reaction, it shows characteristics of the nucleophilic reactions rather than the diazonium arylations to be discussed in section VI.

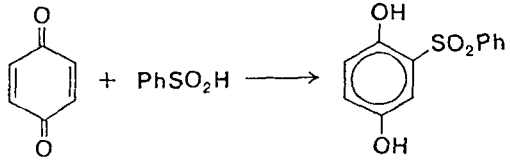


(7)

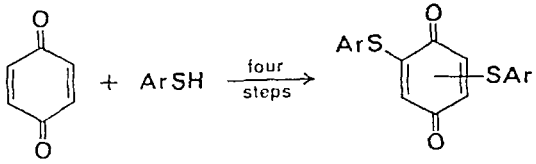
B. Sulphur Addition

1. Historical introduction

The earliest mention of a reaction between a sulphur compound and a quinone appears to be Bongartz's observation that in the absence of solvent 1,4-benzoquinone will oxidize thioglycolic acid and itself be reduced to hydroquinone[7]. Soon afterward examples of the addition of the two most common sulphur nucleophiles appeared in the literature; i.e. sulphinic acids (equation 8)[8–10] and thiols (equation 9)[11,12]. In the



(8)



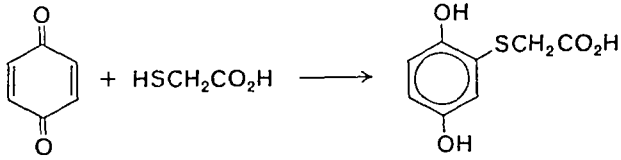
(9)

latter example a mixture of isomeric products was obtained; this situation will be discussed in some detail in connexion with the mechanism of the

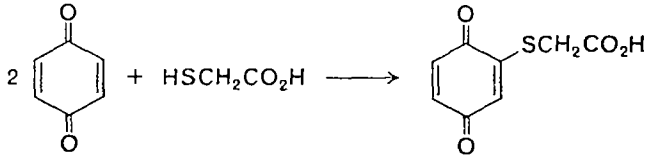
reaction (see section II.B.2.b). The reaction between 1,4-benzoquinone and thiophenol (along with hydrogen chloride and aniline) played an important role in the early development of a clear picture of valence in organic molecules[12-16].

2. Mechanistic studies

There are relatively few mechanistic studies of the addition of sulphur nucleophiles to quinones, but those reported form a rather complete picture. The first really modern study with definite mechanistic implications is that of Snell and Weissberger[3]. By varying the relative proportions of quinone and thiol they were able to obtain either oxidation state of the product (equations 10 and 11). With other thiols it was not possible to stop

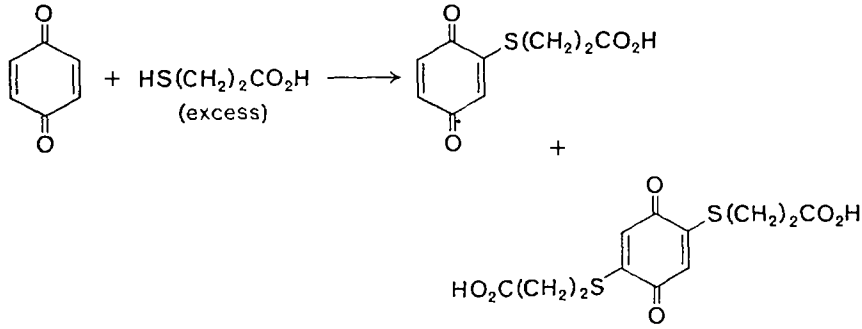


(10)



(11)

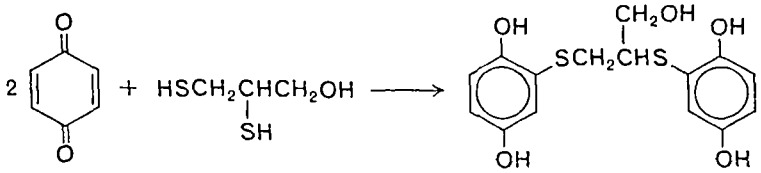
at the hydroquinone monosubstitution product, even with an excess of thiol (equation 12). All of these observations are consistent with the general mechanistic picture presented in section II.A (equations 3, 4 and 6) and the observations of Posner[12].



(12)

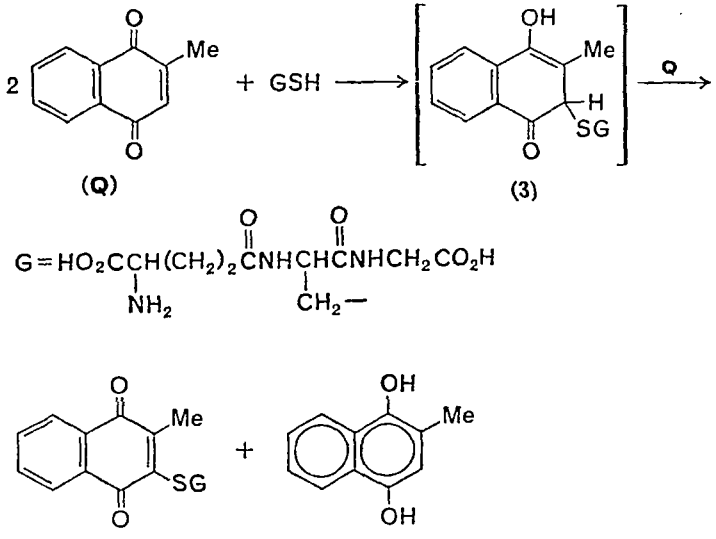
More recently, this generally accepted mechanism received some additional support from Zuman and Zumanová[17]. In a polarographic study of 2,3-dimercaptopropanol the formation of an insoluble mercury

salt produced an anodic wave useful for the study of several related reactions, including those with oxidants. When 1,4-benzoquinone was added no disulphide was formed and reaction with two moles of 1,4-benzoquinone (equation 13) was suggested to account for the disappearance of the wave.



(13)

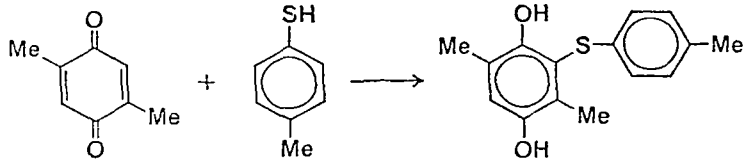
On the other hand, the reductive addition followed by cross-oxidation mechanism has been severely criticized in one instance[18]. The case presented in this paper states that in earlier work the substituted hydroquinone had not actually been isolated during the course of the reaction[3,19,20]. In fact, Snell and Weissberger present strong evidence of the formation of the substituted hydroquinone when equimolar amounts of 1,4-benzoquinone and thioglycolic acid are employed (i.e. loss of colour and formation of a lactone). When the reactant ratio was 2 : 1 (quinone : thiol) the substituted quinone was obtained as the product. Admittedly, the yields obtained by Snell and Weissberger were not high and the strength of their argument suffers from that deficiency. Also, it appears that the redox data presented by Nickerson and collaborators[18] argue for their proposed mechanism of substitution (equation 14). Since the products predicted by both groups are the same, the essential question is whether (i) the intermediate **3**



(14)

enolizes to a substituted naphthohydroquinone, or (ii) the intermediate **3** transfers hydrogen directly to a second molecule of 2-methyl-1,4-naphthoquinone. The observation of a small difference in redox potentials between the quinone starting material and the hydroquinone corresponding to the product, coupled with the lack of any appreciable cross-oxidation, is very important. It may well be that the bulky glutathionyl group (G) makes significant changes in the ability of the product to be reduced and to enolize.

In our own studies we have found that the addition of aryl thiols to 1,4-benzoquinones results in only small differences in redox values[21]. However, these differences are very important and lead to quite striking equilibrium results. The most significant results for the present discussion are, (i) a methyl group adjacent to the sulphide linkage severely inhibits the following cross-oxidation and (ii), so great is this inhibition that the postulated hydroquinone intermediate becomes the principal product (equation 15). We feel that this reaction, and those of the other methylated



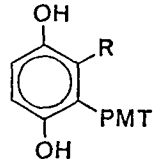
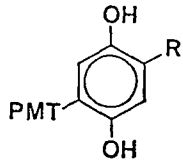
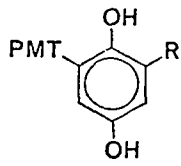
(15)

1,4-benzoquinones, is convincing evidence for the reductive addition mechanism; however, it does make the situation with 2-methyl-1,4-naphthoquinone all the more puzzling. The influence of the glutathionyl chain deserves more detailed study.

The first solid evidence of the correctness of the assumed ionic mode of addition of acidic thiols (see section IV.B) came from a study of 1-phenyl-5-mercaptotetrazole (HPMT). As indicated earlier (equation 5), very little cross-oxidation occurs and the substituted hydroquinone is isolated in good yield[4]. Our electrochemical results are also consistent with this synthetic observation[21]. When HPMT is added to monosubstituted 1,4-benzoquinones, the product distribution is consistent with a nucleophilic addition mechanism[22]. The original assignment of structure in disubstituted 1,4-benzoquinones was made by Posner on the basis of logical arguments[12]. The results of Gates and collaborators[22], using n.m.r., suggest that the earlier assignments are correct. The data presented in Table 1 offer some evidence for nucleophilic addition when compared with the predictions one makes from a consideration of the resonance possibilities of the ground state and intermediates for each of the three

possible orientations. We have recently re-examined Posner's original work, improved Gates' yields in some cases, and found general agreement with both reports[23].

TABLE 1. Product orientation in the addition of 1-phenyl-5-mercaptotetrazole (HPMT) to monosubstituted 1,4-benzoquinones[22]

R	Yield (%)		
			
OMe		88	
4′-C_6H_4OMe		80	
Me		25	13
n-$C_{15}H_{31}$		48	12
4′-C_6H_4Me		10	30
Ph		10	46
PMT	28	20	26
4′-$C_6H_4NO_2$			82
4′-C_6H_4Ac [a]			36
Ac	74		8
CO_2Me	91		

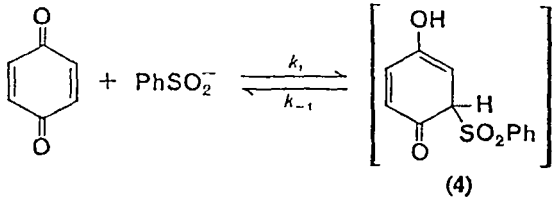
[a] A second minor product found but not identified.

The complete lack of kinetic studies in the thiol addition area is both notable and lamentable; however, two recent studies of sulphone formation (equation 8) are instructive[24, 25]. The rate law below pH 5·7 was shown to be:

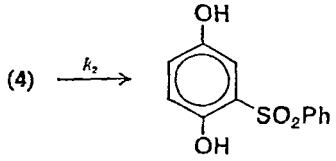
$$v = k[C_6H_4O_2]\,[PhSO_2^-]$$

At higher pH's, serious competing side-reactions made rate measurements difficult. The pH–rate profile shows a distinct change of slope at pH 3·5 to 4·0. The reactions below pH ca. 3·1 are subject to general-acid catalysis and show no kinetic isotope effect. At higher pH (ca. 4·0–5·7) the reactions are general-base-catalysed and exhibit an isotope effect that increases with pH.

The mechanism proposed involves two steps as shown in equations (16) and (17)[24]. At pH's below 3·1 the addition step (k_1) would be rate-determining; while above pH 4·0 the loss of a proton by the intermediate



(4) (16)



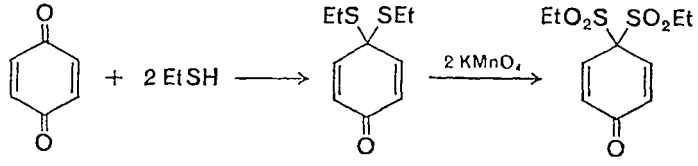
(17)

4 becomes kinetically significant. The observations reported for catalysis and isotope effect as well as the pH–rate profile all support these proposals. A later study extended these results to a series of 4-substituted arylsulphinic acids and showed an excellent Hammett correlation[25]. The negative ρ obtained ($-1{\cdot}55$ at pH 3·50) and the observation that it changes very little with pH are both consistent with the proposed mechanism. The essentially quantitative yields of reduced (i.e. substituted hydroquinone) product obtained in these reactions are quite expected from our electrochemical studies[21].

3. Synthetic survey

While detailed mechanistic studies of the addition of organic sulphur nucleophiles to quinones have been limited, a substantial number of significant synthetic reports are to be found. The intention in the present section (and analogous sections throughout the chapter) is to illustrate the breadth of past work and to furnish leading references to the type of synthesis under discussion.

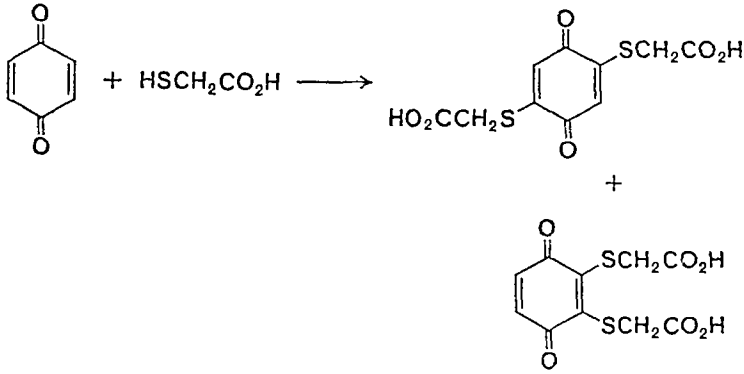
In 1927 Récsei reported some truly amazing addition and oxidation reactions of 1,4-benzo- and 1,4-naphthoquinone with ethyl mercaptan[26]. He maintained that carbonyl addition took place and that the adduct obtained could be oxidized to a disulphone with potassium permanganate (equation 18). The true course of these reactions has not been demonstrated,



(5) (18)

but Snell and Weissberger showed that a better yield of the alleged 'sulphone', **5**, could be obtained with ferric chloride and that the elemental analysis of **5** does not fit the proposed structure[3].

The addition of thioglycolic acid to 1,4-benzoquinone has already been mentioned[3,19]. The reaction first appeared in the chemical literature in 1930 when the formation of two isomeric disubstitution products was reported (equation 19)[27].

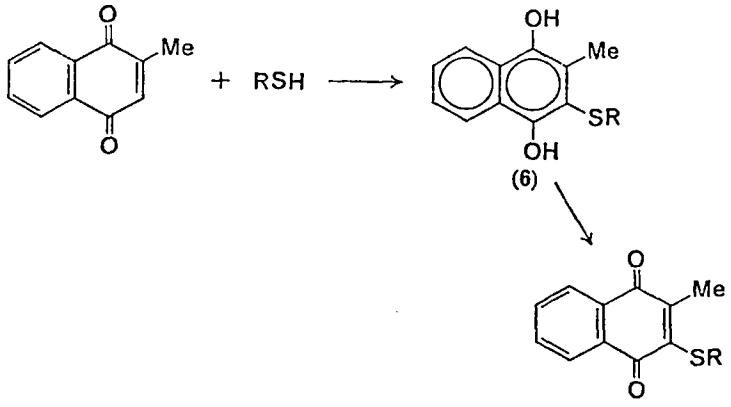


(19)

The addition of thiophenol to 1,4-benzoquinone has been considerably expanded and a number of *ortho*- and *para*-substituted phenylmercapto-1,4-benzoquinones prepared[28]. A few related 1,4-naphthoquinone and 1,4-dihydroxy-9,10-anthraquinone derivatives are included. The proposed structures are based on analogy with Posner's work[12], but are probably correct as suggested by Gates[22]. Some significant improvements in yields are reported under various modified reaction procedures.

As one part of their continuing search for compounds of potential medicinal importance (specifically antihaemorrhagic or bacteriostatic activity) Fieser and Turner investigated the addition of a variety of thiols to 2-methyl-1,4-naphthoquinone (equation 20)[20]. It was not demonstrated that the substituted hydroquinone **6** is formed during the course of the reaction; a fact later pointed out by Nickerson and collaborators[18]. However, Fieser was surely confident of its presence, since he suggests the *in situ* oxidation of the products as the optimum synthetic method (see section II.B.2).

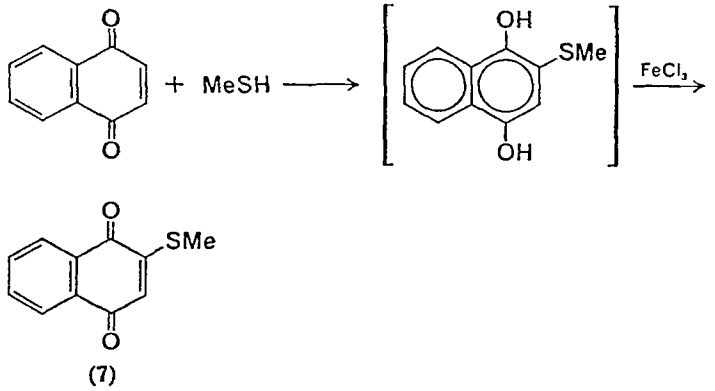
The obvious importance of alkyl and aryl sulphides of 1,4-naphthoquinones has led to the development of preferred synthetic routes. For example, Little, Sproston and Foote found that the yield of 2-methylmercapto-1,4-benzoquinone (**7**) could be doubled by adding ferric chloride when the first crystals of product appeared (equation 21)[29]. If the oxidant was added at the beginning of the reaction, no quinonoid product was



(20)

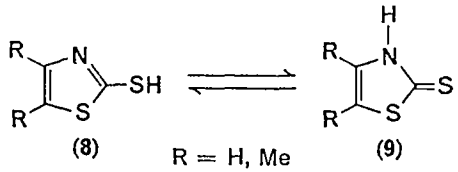
R = $PhCH_2$, HO_2CCH_2, $HO_2CCH(CH_2)_2$ (NH$_2$), n-$C_{16}H_{33}CH$ (CO$_2$H)

obtained. Fieser and Brown modified this method slightly and prepared a large number of mono- and disubstituted 1,4-naphthoquinone sulphides[30]. In this same study a very useful method of achieving either addition or substitution was found (see section VIII.D).

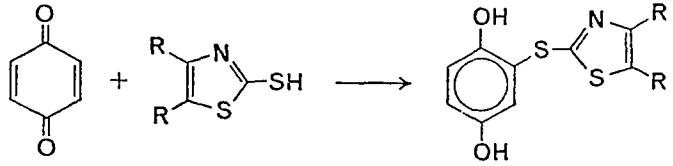


(21)

The addition of a heterocyclic mercaptan to 1,4-benzoquinone by Gates and his colleagues has been mentioned[4,22]. In an earlier study the question of sulphur versus nitrogen attack was answered for the related 2-mercapto-thiazoles[31]. These compounds can exist in either the mercapto (**8**) or the thione (**9**) form (equation 22). All three heterocycles added smoothly to give good yields of the hydroquinone sulphide (equations 5 and 23).

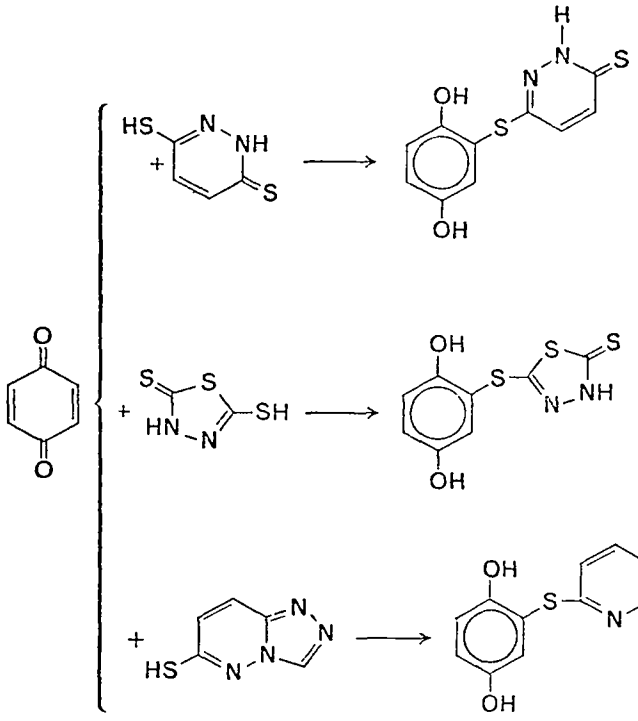


(22)



(23)

More recently a series of complex heterocycles were shown to add to 1,4-benzo- and 1,4-naphthoquinone in high yield (equations 24–26)[32]. The hydroquinone products can be oxidized with lead tetraacetate and a second addition carried out.



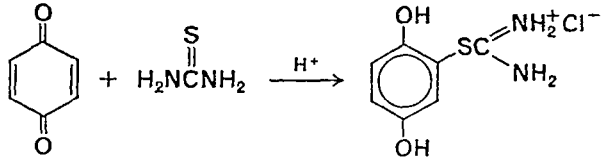
(24)

(25)

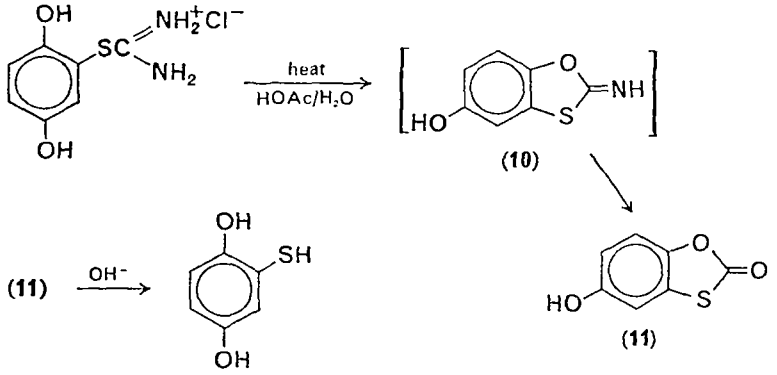
(26)

A related question of the mode of addition of ambident reactants is found in the cases of thiourea and cysteine. The first of these was mentioned by Schubert[19], who found it possible to isolate the hydrochloride salt at

moderate temperatures in acidic solution (equation 27). A more detailed study by Burton and David showed that the reaction could be achieved with several different quinones and that the product from 1,4-naphthoquinone is not as unstable as Schubert claimed[33]. They further found that the thiouronium salts can be cyclized to 5-hydroxy-1,3-benzoxathiol-2-ones* (**11**) and subsequently to 2-mercaptohydroquinone (equation 28). The presumed imino intermediate, **10**, was not isolated, nor was any definite evidence for it advanced.



(27)



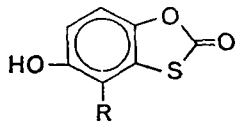
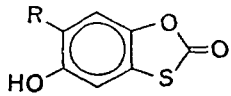
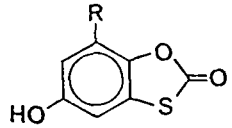
(28)

Definitive studies of the addition of thioureas to quinones have recently been published by Lau and collaborators[34,35]. They found that a large number of substituted 1,4-benzoquinones will add thiourea in excellent yield when an excess of the latter reagent and a strongly acidic medium are used. Examples of both the thiouronium salts (several cases) and the imino salts corresponding to **10** (a few cases) were isolated, purified and characterized. The decomposition problems reported by earlier workers occurred only from heating in weak acid solution or from failure to undergo cyclization (for example, with 1,4-naphthoquinone and 2,5-diacetyl-1,4-benzoquinone). Sterically very crowded molecules, like 2,5-di-*t*-butyl-1,4-benzoquinone, are simply reduced to the hydroquinone without addition.

* Incorrectly named 2′-hydroxy-4,5-benzothioxol-2-ones by Burton and David.

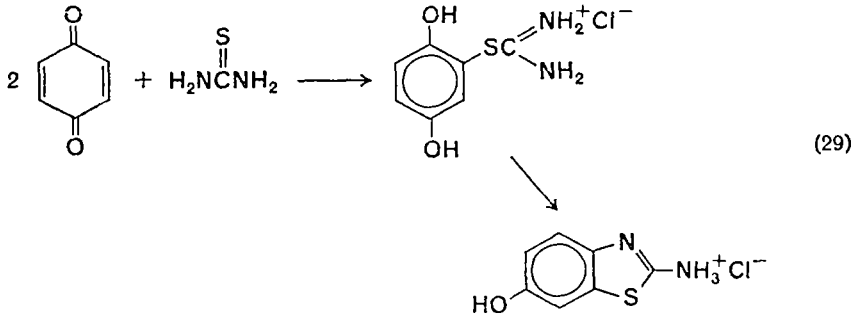
In addition to 1,4-benzoquinone and its di- and trisubstituted derivatives, a series of monosubstituted 1,4-benzoquinones were studied and the distribution of products determined. The data presented in Table 2 may

TABLE 2. Product orientation in the addition of thiourea to monosubstituted 1,4-benzoquinones[34]

R	Yield (%)		
			
Me		7	82
n-C_8H_{17}			99
n-$C_{18}H_{37}$			96
Ph		3	90
PhS		2	96
Cl	12	13	53
Ac	79		11

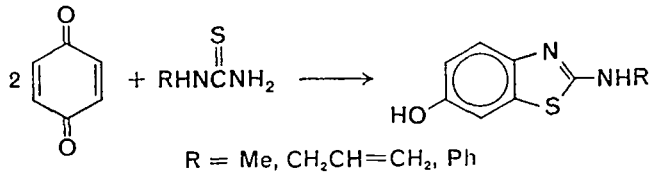
be compared with those of Gates (Table 1) presented earlier (see section II.B.2). The most striking point in the comparison is the shift of reactivity from 2,5- to 2,6-orientation for electron-releasing groups. This effect may be associated with the excellent hydrogen-bonding ability of the thiourea, but its impressive magnitude surely warrants further study. The overall reaction represents the preferred route to the 5-hydroxy-1,3-benzoxathiol-2-ones.

A later study by Lau and Gompf showed that the addition of thiourea to an excess of a quinone proceeds through the thiouronium salt to 2-amino-6-hydroxybenzothiazoles (equation 29)[35]. The yields, while not as high as in the benzoxathiol cases, are entirely satisfactory. With



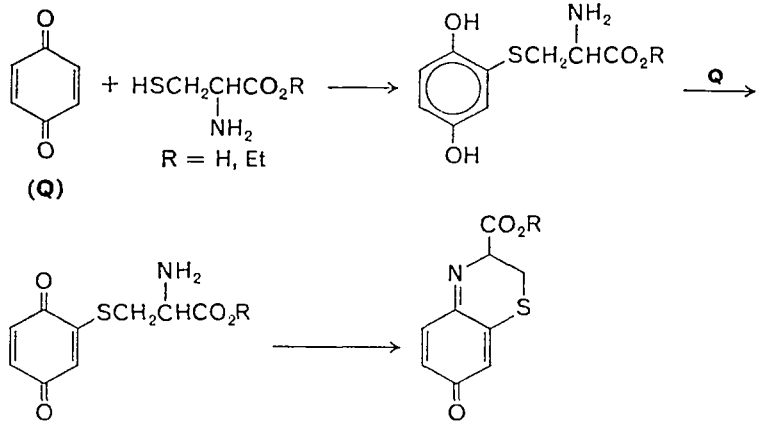
(29)

1,4-naphthoquinones only this second mode of cyclization is successful. The reaction has also been extended to some *N*-substituted thioureas (equation 30).



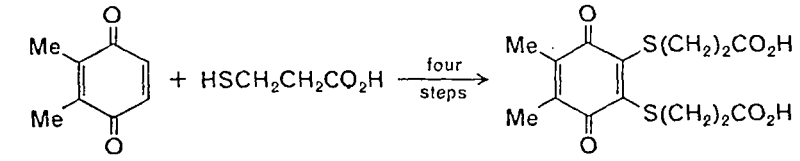
R = Me, $CH_2CH{=}CH_2$, Ph (30)

The naturally occurring α-amino acid cysteine presents orientation and reactivity problems similar to those of thiourea. Furthermore, the related structure present in certain enzymes makes such questions especially important (see section VIII.D). The reaction of cysteine involves initial addition of the thiol to the quinonoid ring[36]. This addition is followed by cross-oxidation and cyclization via dehydration (equation 31) and the yields reported are quite acceptable. Similar results were obtained with 2-methyl-, 2,5-dimethyl-1,4-benzoquinone and 1,4-naphthoquinone[37]. The addition reaction took place with 2-methyl-1,4-naphthoquinone, but the cyclization step was not reported[33].



(31)

In the process of establishing the structure of the active (antibiotic) component of gonyleptidine, Fieser and Ardao examined the addition of β-thiopropionic acid[38]. Sequential addition and oxidation should lead to completely substituted quinones which possess both increased chemical stability and molecular weight (for example, equation 32). In practice the yields were poor. The major component of gonyleptidine was shown to be 2,3-dimethyl-1,4-benzoquinone by alternate procedures (see sections II.D and V.A.3).

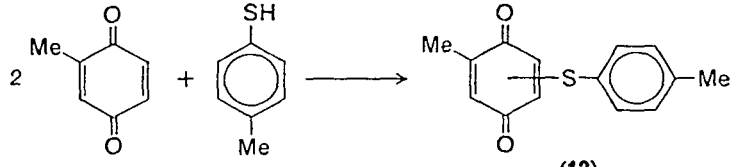


(32)

(and other simple quinones)

(and related products)

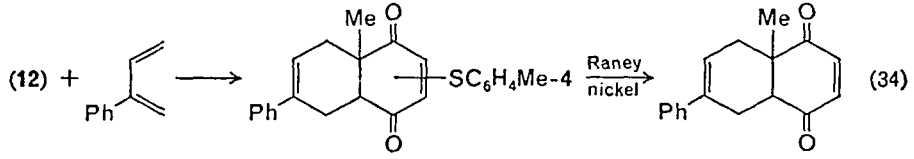
The synthesis of alicyclic compounds of rather complex structure has been accomplished using the Diels–Alder reaction (see section V.A.3) with quinones bearing an arylmercapto substituent for its protective and directive influence[39]. An addition reaction between *p*-toluenethiol and 2-methyl-1,4-benzoquinone was carried out with the usual results (equation 33). Following the Diels–Alder reaction of **12** with 2-phenylbutadiene,



(33)

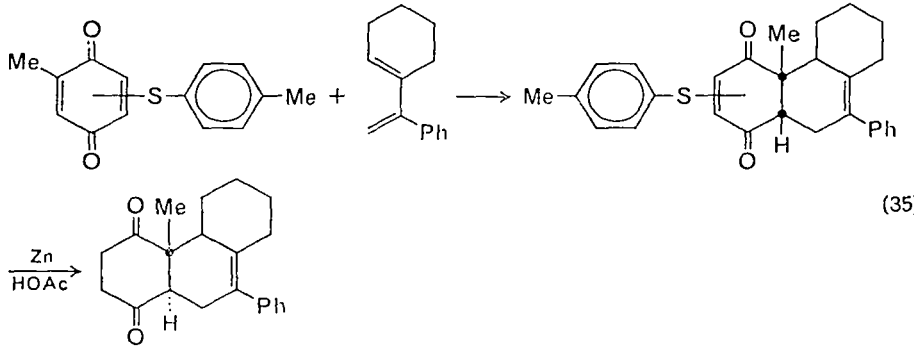
(12)

the sulphide substituent was removed with Raney nickel (equation 34). When zinc and acetic acid were the reactants in the desulphurization, the



(34)

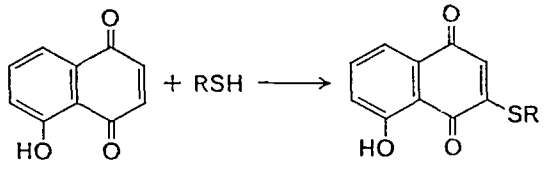
alkene linkage was also reduced and the *cis* ring-fusion product isomerized to the *trans* configuration (equation 35)[40]. The simpler methylmercapto group was also examined and found to be satisfactory for these functions.



(35)

The addition of excess methylmercaptan to 2-methyl-1,4-benzoquinone followed by ferric chloride produced a product distribution similar to our findings with thiophenol and excess 1,4-benzoquinone[23,41].

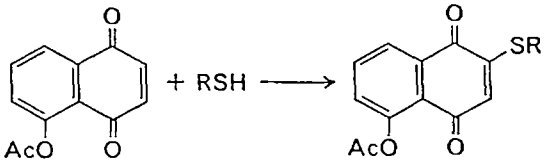
Not only has the addition of thiols been of interest in the synthesis and identification of natural products, but the study of thiol additions to quinonoid natural products has also received some attention. As part of his detailed study of the chemistry of juglone (**13**) Thomson added both thioglycolic acid and *p*-toluenethiol to the parent compound and its acetate, with very interesting results (equations 36 and 37)[42]. The complete



(36)

(13) (14)

R = HO_2CCH_2, 4-MeC_6H_4

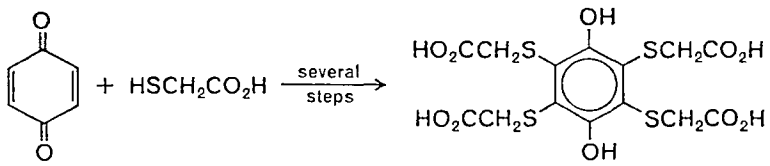


(37)

(15)

change of orientation (the yields were reasonably high in all four cases) was explained on the basis of radical addition to juglone acetate resulting in the 2-substituted mercapto product **15**. The 'normal' ionic addition to juglone itself produces the 3-substituted mercapto product **14**. There will be more to say about sulphur radical additions to quinones in section IV.B.

Thomson and Blackhall continued the study of thioglycolic acid addition using a series of simpler quinones[43]. They found this thiol, as had others earlier[3,19,20], to be very reactive in such additions. With the exception of 1,4-naphthoquinone and possibly 2-methyl-1,4-benzoquinone, sequential cross-oxidation and addition took place readily and only the completely substituted hydroquinone was obtained (e.g. equation 38).



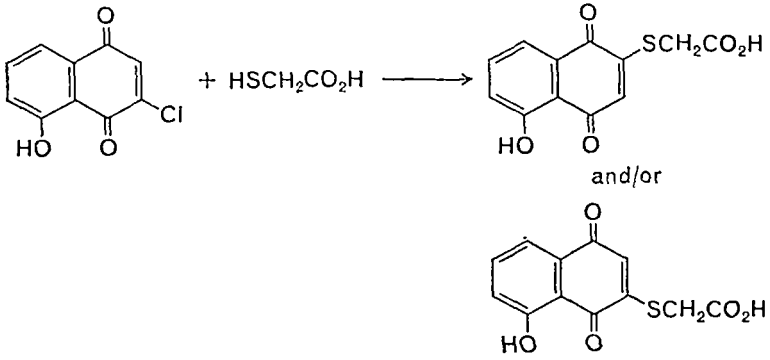
(38)

It was also found that 3-mercaptopropanoic acid behaves similarly, but 4-mercaptobutanoic acid is considerably less reactive. It was found that the reactivity of the thiols roughly paralleled their acidity; i.e.

$$HS(CH_2)_3CO_2H \approx PrSH < PhSH < HS(CH_2)_2CO_2H < HSCH_2CO_2H$$

The solvent employed also plays a significant, but only poorly defined role.

Rothman has also studied the reactions of juglone and juglone acetate with thioglycolic acid and questioned the suggested radical versus ionic pathway[44]. His chief concern was with the assignment of structure for the addition products claiming that displacement of halogen does not necessarily lead to product with the same structural arrangement (equation 39). His own structure proof led to exactly the opposite product orientations and eliminated the need for the proposed radical mechanism.



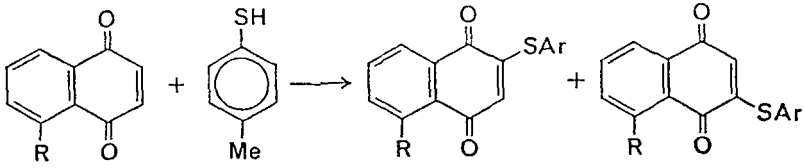
(39)

The third (and apparently the final) round in this controversy is Thomson's[45]. He and McLeod showed that for *p*-toluenethiol the original[42] structural assignments were correct. This was accomplished by basic hydrolysis to 2- and 3-hydroxyjuglones whose structures were established independently. Similar reactions with the thioglycolic acid adducts were not successful because of extensive decomposition and they admitted this extremely reactive thiol could be an exception. The study of the addition of *p*-toluenethiol was expanded to include a variety of 5-substituted-1,4-naphthoquinones (equation 40). The results shown in Table 3 clearly indicate the unusual character of juglone acetate. Thomson thus presents the first specific experimental evidence for competing ionic and radical addition of thiols to quinones[42, 45].

In the past few years, a number of interesting reactions involving sulphur nucleophiles and quinones have appeared. The following brief notes and equations will illustrate these observations:

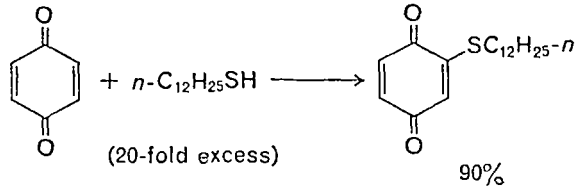
(1) The long alkyl chains (fattails), so useful in many technological applications, can be introduced in excellent yield (equation 41)[46].

TABLE 3. The addition of *p*-toluenethiol to 5-substituted 1,4-naphthoquinones[45]

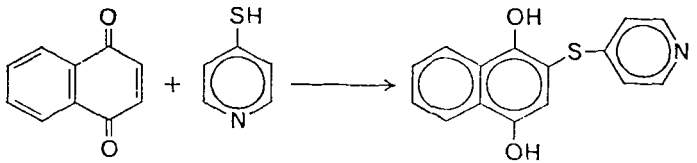


R	%	%
OH		90
AcO	80	80[a]
MeO		73
Me	10	75
AcNH		72
Cl	12	49

[a] See text.

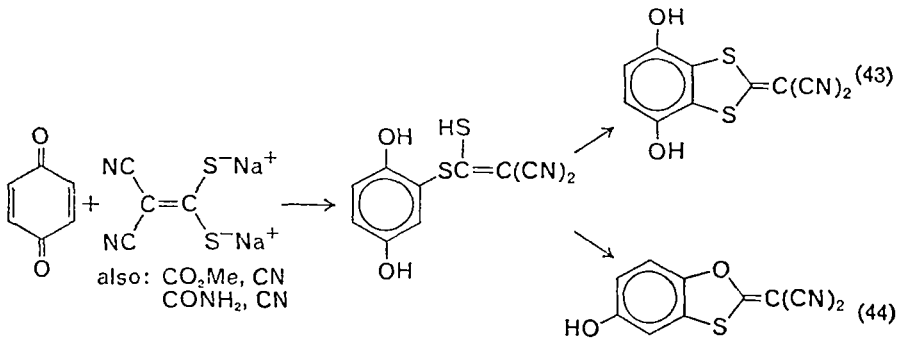


(2) The long list of important nitrogen–sulphur heterocyclic combinations has been expanded by addition of 2- and 4-mercaptopyridines to 1,4-naphthoquinones (equation 42)[47]. It was shown that, in most cases,

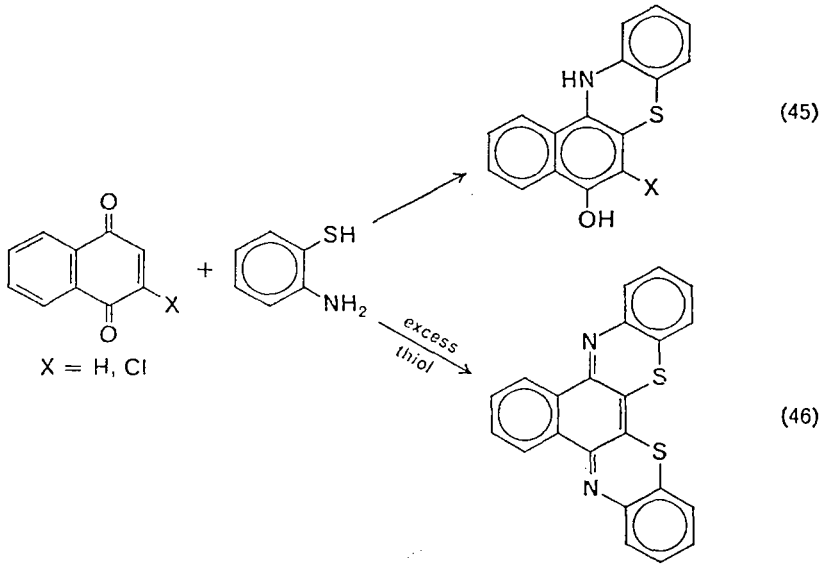


either the mono- or disubstituted product could be obtained under appropriate conditions.

(3) The addition of thioacetic acid enol salts bearing strong electron-withdrawing substituents in the α-position can lead to different heterocyclic products depending on the reaction conditions (equations 43 and 44)[48]. While no mechanistic detail is given, the displacement of sulphur by oxygen (equation 44) is noteworthy and resembles the thiourea examples given earlier[34,35].



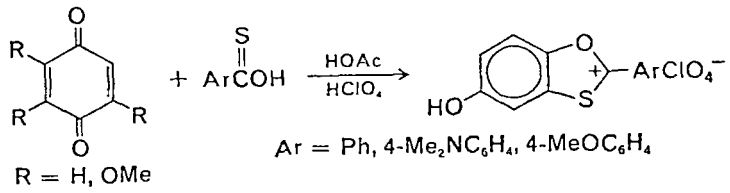
(4) The compound *o*-aminobenzenethiol, with its obvious similarities to many natural systems, will add to 1,4-naphthoquinone to form heterocyclic systems (equations 45 and 46)[49]. When the appropriate groups are



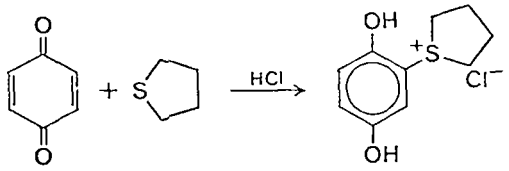
present substitution will take place (see section VIII.D) but, as indicated in equation (45), addition is the preferred route with either hydrogen or chlorine as the substituent.

(5) Nearly quantitative yields of heterocyclic perchlorate salts can be obtained from the addition of aryl monothioacetic acids to 1,4-benzo- and 1,4-naphthoquinones (equation 47)[50].

(6) For a wide variety of quinones and thioethers it has been shown that in acidic media the corresponding hydroquinone sulphonium salt can be obtained in high yield (e.g. equation 48)[51].

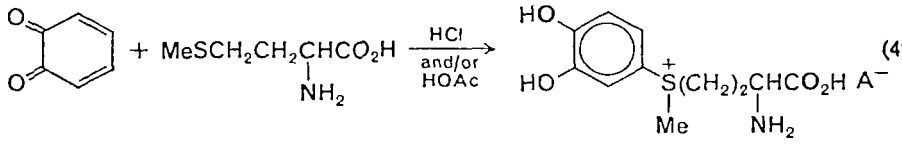


(47)



(48)

(7) The formation of sulphonium salts has also been studied with DL-methionine (as well as its *N*-acetyl derivative and methyl ester[52]). With 1,2-benzoquinone the structure of the product was established by the usual techniques: elemental analysis, spectral comparison, etc. (equation 49). The methionine residues of ribonuclease-A also showed this chemistry in acid solution.

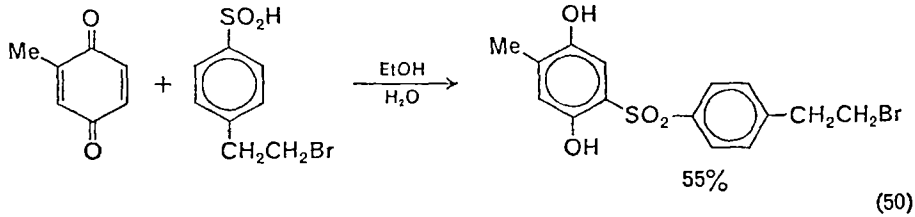


(49)

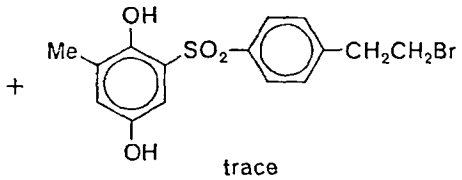
The second major area of synthetic interest in discussing sulphur nucleophiles and quinones is the addition of sulphinic acids (equation 8). After the initial work by Hinsberg[8–10], this field of quinone chemistry lay totally bare for over forty years. With the advent of the sulpha drugs an intense interest resumed and many compounds were prepared with little new chemistry being added[53–58].

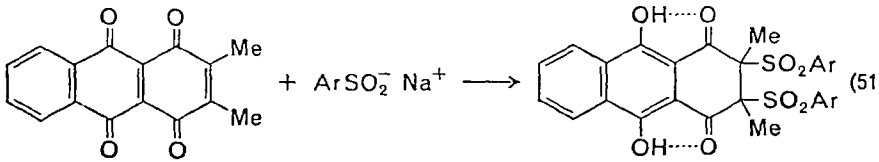
In 1963, as part of their studies of the synthesis and properties of redox polymers, Spinner and his collaborators reported an interesting orientation effect (equation 50)[59]. This situation seems strange since we have, in many attempts, found only the 3,4′-dimethyl isomer in the analogous addition of *p*-toluenesulphinic acid[21]. This problem is currently under active study.

A very interesting and unusual 2,3-addition of sulphinic acids to quinones has been reported (equation 51)[60]. Very strong intramolecular hydrogen bonding in the product, **16**, is assumed to explain the observed reaction.



(50)



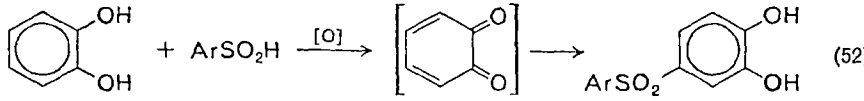


(51)

Ar = Ph, 4-MeC_6H_4, 3-$NO_2C_6H_4$ **(16)**

4. Nascent quinones

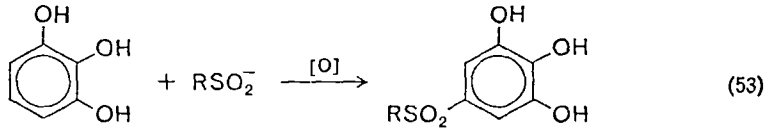
The pioneering work of Hinsberg and Himmelschein on the addition of sulphinic acids to quinones contained an example of synthesis via nascent quinones (equation 52)[10]. This technique of *in situ* preparation or



(52)

the nascent quinone has been applied most frequently to the less stable 1,2-quinones, but examples of 1,4-quinones are also be be found. The following examples of nascent quinones reacting with sulphur nucleophiles are drawn from a recent review[61].

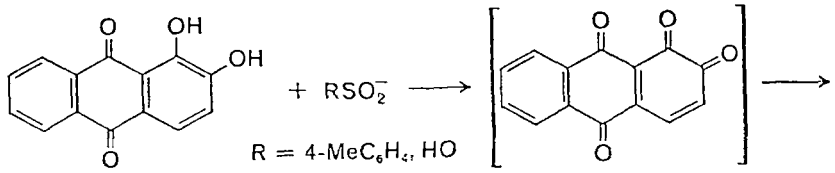
(1) Pyrogallol reacts with either benzenesulphinic acid or sulphite under oxidative conditions (equation 53)[62].



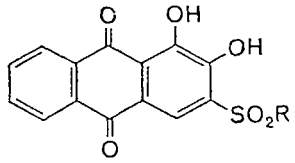
(53)

R = Ph, HO

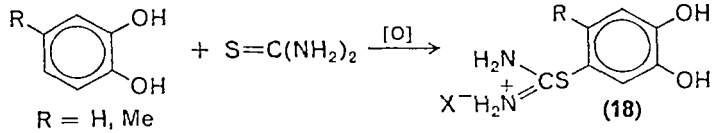
(2) An unexpected product orientation results in the case of the di-quinone formed from alizarin (equation 54)[61]. The intermediate quinone **17** is only known in solution[63].



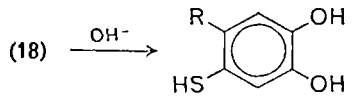
(54)



(3) The addition of thiourea to a nascent 1,2-benzoquinone has been reported to produce greater than a 90% yield (equation 55)[64,65]. It has also been shown that the product salt **18** can be hydrolysed by base to the corresponding mercaptan (equation 56)[65].



(55)



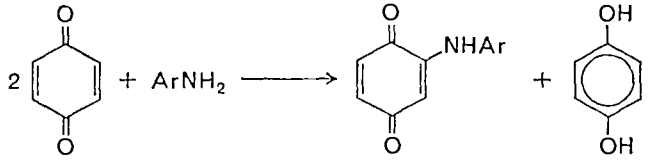
(56)

C. *Nitrogen Addition*

1. Historical introduction

The ability of compounds containing basic nitrogen to undergo Michael addition with a variety of quinones was observed and amply documented in the late 19th and early 20th centuries[66–80]. The culmination of these efforts is the synthetic *tour de force* of Suida and Suida[5]. In this single paper they reported the preparation and characterization of 50 addition products of 1,4-benzoquinone and various substituted anilines (equation 57). The study included some *N*-methylaniline derivatives and a brief look at 2-methyl-1,4-benzoquinone. Finally, the competition between

addition and substitution (see section VIII.B) was recognized in the case of several chloroquinones (e.g. equation 58).



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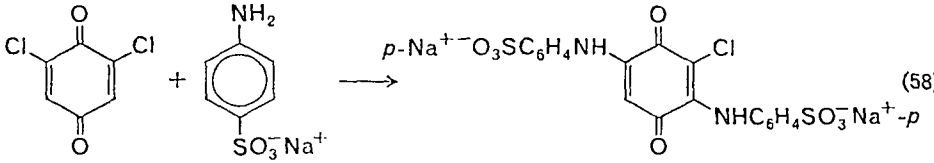
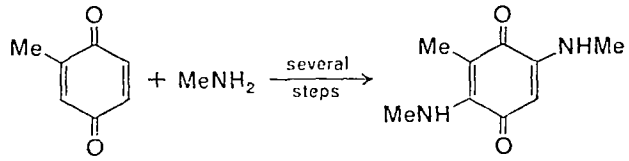


(58)

The possibility that nitrogen addition chemistry might be important in protein work was recognized. An early example deals with a very clinical concern—the bactericidal properties of quinones[82,83]. Cooper and Haines showed that a portion of the disinfectant activity of several quinones could be attributed to reaction with amino acids rather than with proteins. A rough set of kinetic experiments showed a strong positive salt effect for the reaction of 1,4-benzoquinone, but only a slight effect with 2-methyl-1,4-benzoquinone.

The method of choice for preparing dimethoxy quinones has also revealed structural detail of nitrogen addition products[84,85]. The method of synthesis does not demand the product structure shown in equation (59), but it was established by reliable methods. The structure of the product **19** is interesting in that the usual *para* orientation expected from a

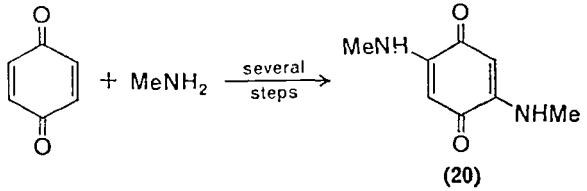


(59)

(19)

methyl group either does not occur or rearranges to allow the *para* arrangement for the two methylamino groups.

The interaction of alcoholic solutions of methylamine with methyl- and methoxy-substituted 1,4-benzoquinones has produced other unexpected chemistry[86]. The most interesting aspects of this study will be discussed in connexion with nitrogen substitution chemistry (see section VIII.B). The expected 2,5-bis(methylamino)-1,4-benzoquinone (**20**) is obtained in the simplest case (equation 60).



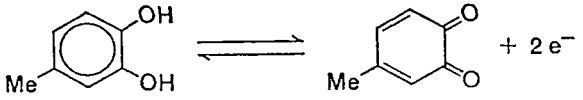
(60)

(20)

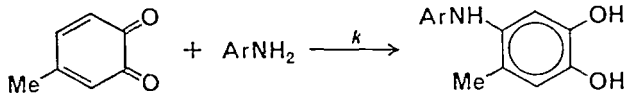
2. Mechanistic studies

In spite of the rather large amount of synthetic effort that has been expended on the addition of amines to quinones, relatively few purely mechanistic studies have been reported. The analytical difficulties in such studies are real and account, in part at least, for their scarcity. It should be noted that many of the reports cited in sections II.C.3 and 4 make important contributions to our understanding of the reaction mechanism.

The first study of the detailed mechanistic path for the addition of amines to quinones involved the electrochemical study of 1,2-benzoquinone generated *in situ*[87]. Using chronoamperometry, cyclic voltammetry and chronopotentiometry it was possible to obtain rate and equilibrium data that are consistent with the following reaction sequence (equations 61–64).

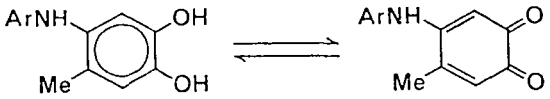


(61)

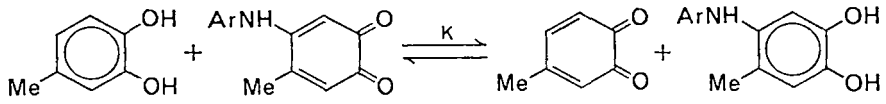


(62)

Ar = Ph, 2-$HO_2CC_6H_4$



(63)

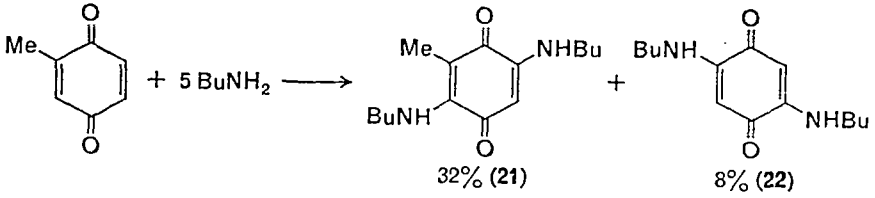


(64)

Second-order rate constants $k = 7{\cdot}8 \times 10^4$ and $5{\cdot}5 \times 10^3$ ($s^{-1}M^{-1}$), for aniline and *o*-aminobenzoic acid respectively, were obtained and the equilibrium constant K was found to be very small ($\approx 10^{-4}$) for both

anilines. The curve-fitting procedures used leave no doubt that the equilibrium constant is very significant and that for aniline addition the nitrogen-substituted catechol is practically non-existent.

The combination of thin-layer chromatography and polarography has proved to be of value in these studies[88]. The system 2-methyl-1,4-benzoquinone and *n*-butylamine was chosen because the reaction rates are suitable for study by standard kinetic techniques. The products found, both with excess amine (equation 65) and excess quinone (equation 66), are consistent with earlier experience. The product analyses for the



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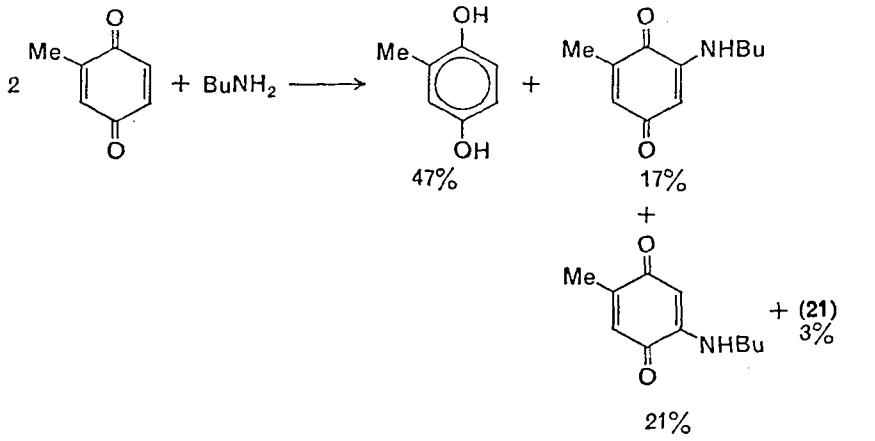
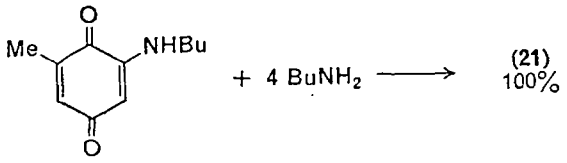
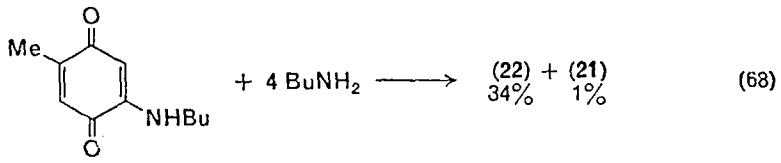


(66)

reactions of 3- and 4-butylamino-2-methyl-1,4-benzoquinone (equations 67 and 68) are also of interest. In both reactions a significant amount of methyl group displacement was observed (see section VIII.B.2) and a large amount of unidentified by-product was obtained. Excellent material balance was found over the course of these reactions and reactivity index calculations (superdelocalizability by the ω-technique[88a]) were used to discuss the observed reactivity.



(67)



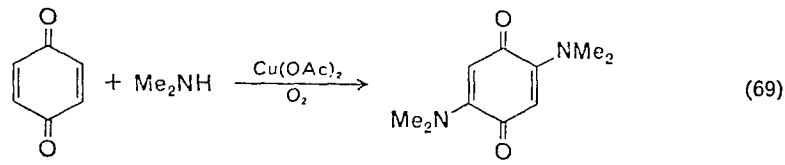
The techniques developed in the study just cited have continued to be employed: for example, the ω-technique calculations have been used for a more detailed analysis of the reactivity of 1,4-benzoquinones with amines[89]. The first step is the addition of the amine; both reactivity indices and resonance energy calculations indicate that this involves nucleophilic 1,4-attack.

The effect of alkyl groups in the amine on the rate of reaction is important[90]. With 1,4-benzoquinone the primary amines Me, Et, Pr, *i*-Pr, Bu, *s*-Bu and *t*-Bu all gave bis(alkylamino)-1,4-benzoquinones. The secondary amines Me_2, Et_2, Pr_2 and Bu_2 gave only mono-dialkylamino-1,4-benzoquinones. In the latter case the reaction rate decreased with increasing size of the alkyl groups.

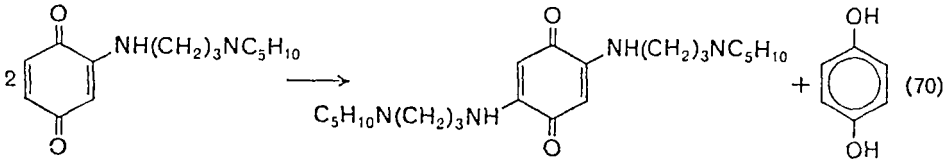
The most recent mechanistic study of the addition of amines to quinones made use of rapid-scan spectrophotometry[91]. The work presented by Yamaoka and Nagakura deals mostly with substitution chemistry (see section VIII.B.1), but they did show that an electron transfer from the amine to the quinone occurs prior to the formation of the final product, 2,5-bis(butylamino)-1,4-benzoquinone. They were unable to observe a spectrum for 2-butylamino-1,4-benzoquinone.

3. Synthetic survey

Some of the post World War II work was simply routine syntheses in an effort to explore and exploit physiological properties of the nitrogen-substituted quinones[92,93], but some useful synthetic and mechanistic information was also obtained. First, it was found that in cases where the 2,5-disubstituted product is desired, the use of an added oxidant greatly improves the conversion of the starting quinone and simplifies the purification (equation 69)[94]. The technique, while useful, appears to be quite limited as it was unsuccessful with methylamine, aniline and ammonia.

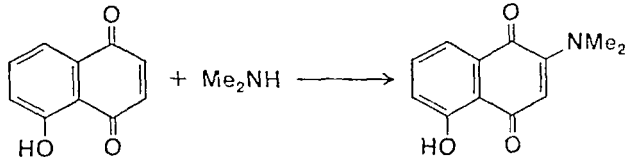


In a synthetic study, where both the mono- and the 2,5-dialkylamino-1,4-benzoquinones were isolated, it was found that the former can undergo disproportionation to the latter (equation 70)[95]. This observation could bear on the unusual orientation cited earlier.



(70)

The reactions of quinonoid natural products with amines have been studied and have contributed to our understanding of addition chemistry. Thomson's work with juglone sulphur chemistry has already been described[42] (see section II.B.3). Less success was achieved with direct nitrogen addition and dimethylamine gave only a 34% yield (equation 71).

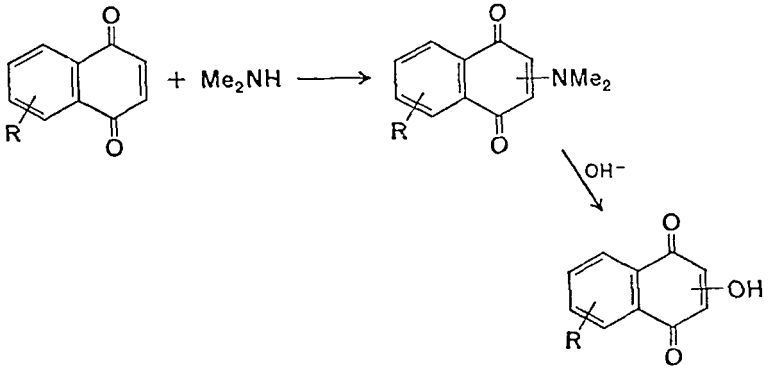


(71)

The 3-isomer was also prepared, but only by substitution (see section VIII.B.2). When aniline was added to juglone acetate the yield was somewhat better (66%) and the expected 3-anilino product was obtained. Unlike *p*-toluenethiol, aniline reacts with various 5-substituted 1,4-naphthoquinones to give only the 3-anilino product[45]. The reaction with 5-acetamido-1,4-naphthoquinone, like juglone, gave only black amorphous material.

The addition of dimethylamine to juglone (equation 71) has been expanded to a series of 1,4-naphthoquinones with substituents in the aromatic ring[96]. The product distribution was determined after hydrolysis to the corresponding hydroxy quinone (equation 72). The results shown in Table 4 are interesting, especially the very strong methyl effect, but the most significant questions are still not answered because of the low overall yields.

In the course of preparing compounds for biological testing, an added oxidant, cerium(III) chloride, has been used[97] (equation 73). Several of the substituted 2-naphthylamines reacted very poorly and sulphuric acid proved a good catalyst, but no detailed study of the effect was made. The general observations of the substituent effect on reactivity were consistent with nucleophilic addition; i.e. 6-bromo > 8-nitro > 1-bromo ≈ 1,6-dibromo > 1-nitro.



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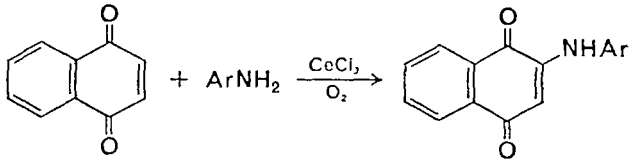


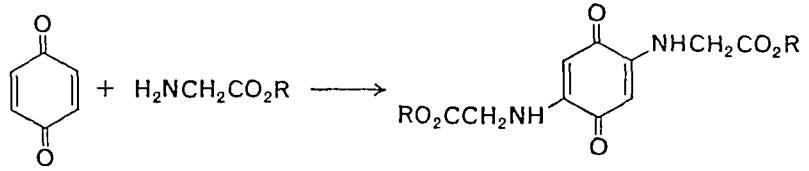
(73)

Ar = various halo and nitro substituted 2-naphthyls

TABLE 4. Product distribution in the addition of dimethylamine to 5- and 6-substituted 1,4-naphthoquinones (equation 72)[42, 96]

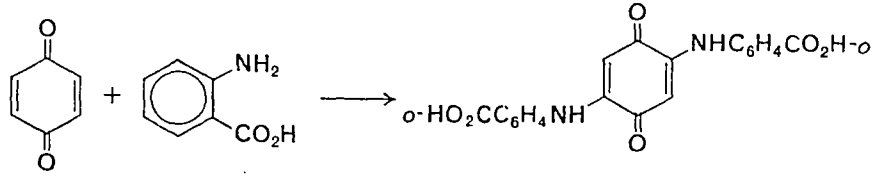
Substituent (R)		Product (%)		Total yield (%)
5	6	2	3	
OH	—	100	0	34
AcO	—	0	0	0
MeO	—	50	50	42
Me	—	Trace	~100	Not given
—	Me	~100	Trace	55

The application of polarographic methods to the study of quinones and their reactions has been very productive. In the field of nitrogen addition, amino acids and peptides have been shown to undergo reversible redox reactions at the dropping mercury electrode[98]. The earlier work on the interaction of amino acids and quinones[82, 83] has been followed by the synthesis of some peptide-like derivatives of 1,4-benzoquinone (equation 74)[99]. Three other amino acid esters were used and the product obtained in reasonable yield.



(74)

The addition of anthranilic acid to 1,4-benzoquinones is interesting in that a recent study failed to agree with a number of earlier reports[100]. Only in the case of 2,3-dimethoxy-1,4-benzoquinone was the mono-addition product obtained and several previously reported reactions did not produce useful products. The observed reaction is the normal one shown in equation (75). Reaction with 2-methyl-1,4-benzoquinone did



(75)

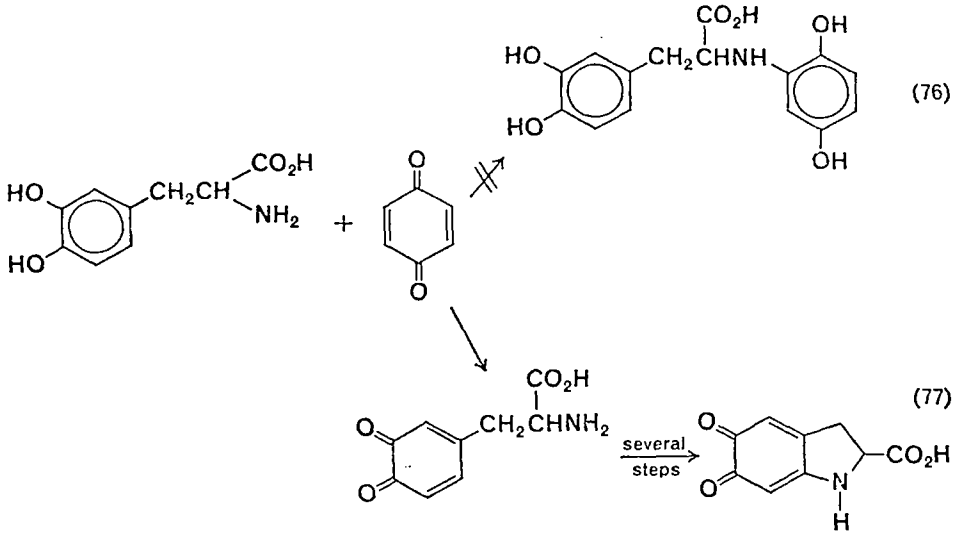
not give crystalline products, nor did *N*-ethylanthranilic acid. The example of 2,3-dimethoxy-1,4-benzoquinone is also limited in that neither the methyl ester nor the *N*-methyl derivative of anthranilic acid reacted. These observations deserve closer attention in view of the heterocyclic compounds for which they might serve as precursors and their relationship to the natural amino acids.

More recently, the important problem of model systems for the fixation of nitrogen in soils and the formation of humic acids has been studied polarographically[101]. Earlier studies suggested the formation of 2-hydroxy-1,4-benzoquinone as a key intermediate in aqueous-ammonia solutions. The experimental results of Lindbeck and Young make it clear that, depending on pH and ammonia concentration, 2-amino- and/or 2,5-diamino-1,4-benzoquinone must be considered significant intermediates in any proposed mechanism. The stability of organic nitrogen in soils has also been studied by examining the acid hydrolysis of quinone–α-aminoacid adducts[102]. The nature of these reactions led to the suggestion that such compounds play an important role in stability considerations.

Interest in the chemistry of amino acids and quinones continues and a recent report contained some important rate studies[103]. The optimum pH for the reaction of 1,4-benzoquinone and glycine was determined. A wide range of amino acids was studied and the rates of addition are

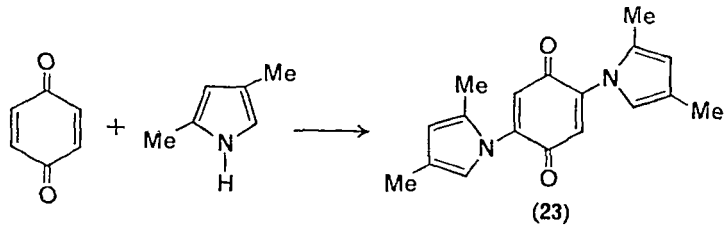
quite similar. However, the ability of the *N*-substituted quinone products to catalyse ascorbic acid oxidation varied with substituent.

Of particular significance to the future direction of the chemistry just described is the question of what actually happens to quinones and amino acids under physiological conditions. A first effort in this area has been made in the study of 3,4-dihydroxyphenylalanine (dopa)[104]. The rate of addition (equation 76) is not fast enough to be significant, but oxidation followed by intramolecular cyclization does occur (equation 77).



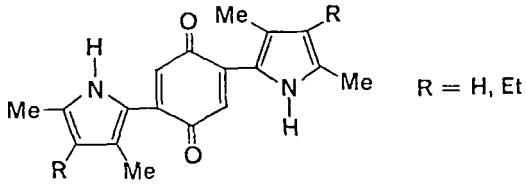
A more detailed synthetic study of the use of added inorganic oxidant for 2,5-diamino-1,4-benzoquinones further revealed the nature of the reaction[105]. The failure of the reaction with diisopropyamine is of significance and was explored to some extent. Other fairly bulky secondary amines produce quite good yields of product (e.g. di-*n*-propyl-, methyl-isopropyl- and benzylmethylamine). This steric hindrance is very clearly demonstrated in substitutions (see section VIII.B.1). The weakest base in the series, morpholine, gave the highest yield (96%). Finally, while 1,4-naphthoquinone gave an excellent yield of 2-(1-piperidyl)-1,4-naphthoquinone with piperidine, 1,2-naphthoquinone did not react.

The reaction of substituted pyrroles with 1,4-benzoquinones is especially interesting in that it leads to carbon–carbon bond formation! An early report suggested the expected nitrogen addition product (equation 78)[106]. A study of the i.r. spectra of the product thought to be **23**, and its 3-ethyl analogue, showed N—H vibrations that clearly indicate the bonding



(78)

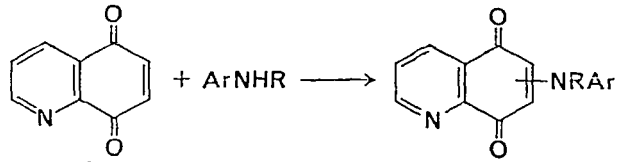
(23)



(24)

cannot be with nitrogen[107]. The alternative structure, **24**, offers an explanation of the compound's colour and behaviour with acid. Finally, this understanding has been applied to provide a better picture of the important pyrrole–quinone dyes[108].

The two interesting research lines of substituent effects and added oxidants have received detailed attention in the chemistry of 5,8-quinoline-quinone (**25**)[109]. The addition of aniline to this quinone and its alkyl derivatives had been studied some years before[110]. Several substituted anilines were added to this quinone and the relative amounts of the 6- and 7-isomers determined (equation 79). As expected, the 6-isomer is the



(79)

(25)

major product in all experiments. Table 5 shows the very significant improvement in yield obtained with cerous chloride as the oxygen carrier. While the yield should be higher with the quinone starting material not being used up as an oxidant, the change in several cases is greater than can be expected on this basis alone. An impressive example of this effect is the reaction of *p*-nitroaniline with 1,4-naphthoquinone, where the product yields are 1% and 81% in the absence and presence of cerous chloride (0·1 mole) respectively. Furthermore, the relative amount of

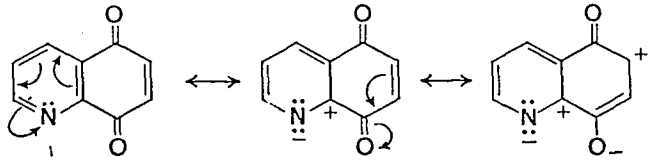
TABLE 5. Product distribution in the addition of anilines to 5,8-quinolinequinone (equation 79)[109]

Aniline	Yield, % (without $CeCl_3$)		Yield, % (with equivalent $CeCl_3$)	
	6-isomer	7-isomer	6-isomer	7-isomer
p-Toluidine	30	24	68	Trace
p-Chloroaniline	19	13	68	Trace
N-Methylaniline[a]	28	5	62	0

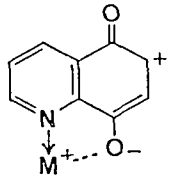
[a] Quinone : aniline = 1 : 10.

the 6-isomer increases dramatically in the presence of the metallic salt, suggesting that cerous chloride enhances the reactivity of the 6-position.

The observed isomer distributions with 5,8-quinolinequinone can be understood in terms of the 8-carbonyl group being bound to the α-position of the pyridine ring and hence more electron-deficient than the 5-carbonyl group in the β-position. The lower electron density is then transferred to



the 6,7-double bond as shown and leads to electron deficiency and observed preferential attack at the 6-carbon. The catalysis by the positive cerous ion is understood as involving structure **26**; its relationship to chelated 8-quinolinol (**27**) is noteworthy. Experiments dealing with the relationship between addition and substitution in this system are also discussed and will be treated later (see section VIII.B).



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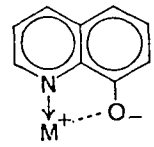
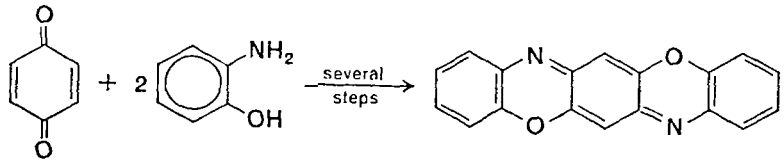


(27)

A number of relatively limited studies involving the addition of amines to quinones have appeared in recent years.

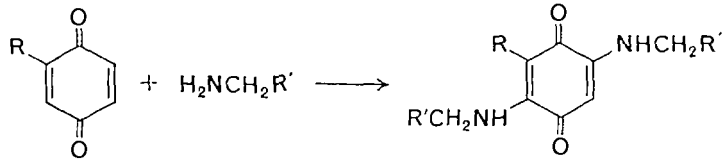
(1) Valuable heterocyclic systems can be prepared by condensing quinones with *o*-aminophenol (equation 80). The use of ^{13}C-labelled



(80)

1,4-benzoquinone allowed demonstration that the first step is addition of the amino group to the quinone ring rather than to the carbonyl group or cross-oxidation followed by condensation[111].

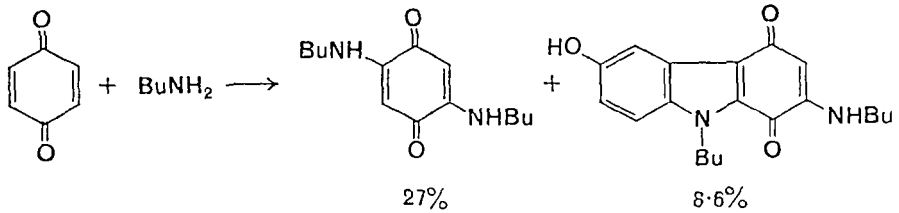
(2) Amino alcohols have been reported to add to quinones if care is taken to prevent polymerization (equation 81)[112]. More limited success was achieved with 2-methyl-1,4-benzoquinone and 1,4-naphthoquinone.



(81)

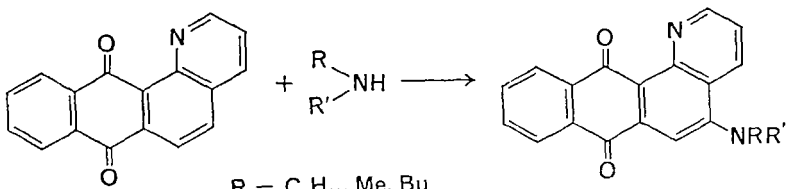
R = H, Me R' = CH_2OH, CH_2CH_2OH, CH(Me)OH

(3) An interesting new compound has recently been obtained from the addition of butylamine to 1,4-benzoquinone (equation 82)[113].



(82)

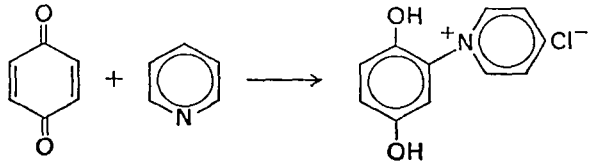
(4) For obvious reasons the anthraquinones do not usually undergo addition reactions of the type under discussion. An interesting exception was found in naphtho[2,3-*h*]quinoline-7,12-dione (equation 83)[114]. Thiophenol also added at the 5-carbon atom.



(83)

R = C_6H_{11}, Me, Bu
R' = H, Me
R and R' = $(CH_2CH_2)_2O$

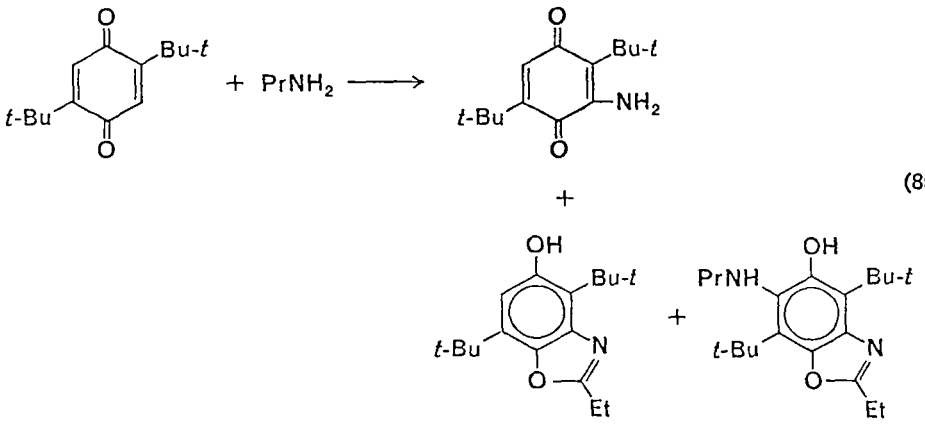
(5) The addition of pyridine to 1,4-benzoquinone leads to the pyridinium salt in moderate yield (equation 84)[115]. A variety of solvents is useful and a small amount of water seems to favour the reaction. The catalyst of choice is hexachlorocyclotriphosphazatriene.



(84)

(6) Methods have been worked out in which 1,4-benzoquinone is useful as a qualitative and quantitative chromatographic reagent for both primary and secondary amines, including amino acids. Applications in thin-layer[116] and paper[117] chromatography are presented.

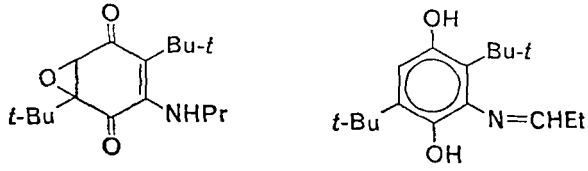
(7) The reaction between 2,5-di-*t*-butyl-1,4-benzoquinone and propylamine has been shown to lead to some unexpected products[118]. When the reaction is carried out in the dark, under nitrogen and with the amine as solvent, the products shown in equation (85) are found. Air was passed



(85)

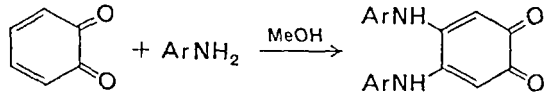
through the reaction just prior to work-up and a large amount of unreacted starting quinone was recovered. The same reaction carried out in the presence of air gave the products shown along with a 20% yield of the following epoxide. The enamine **28** was suggested as an intermediate in the anaerobic reaction (equation 85).

Because of the rather unstable nature of 1,2-benzoquinone the usual method for studying its chemistry is *in situ* oxidation or the nascent quinone technique (see section II.C.4). Recently an effort was made to verify the usefulness of this method by starting with the quinone itself[119].



(28)

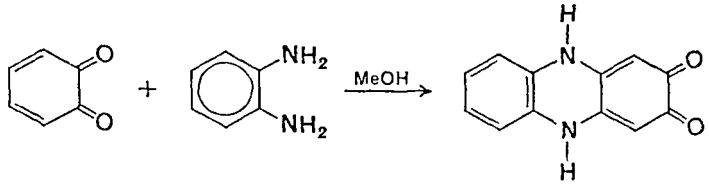
The reaction with various anilines gave the expected product (equation 86). No reaction was observed with 4-nitroaniline and *o*-phenylenediamine



(86)

Ar = 2-$AcOC_6H_4$, 4-$MeOC_6H_4$, 4-BrC_6H_4, 4-ClC_6H_4

gave cycloaddition (equation 87). The failure of this latter reaction to



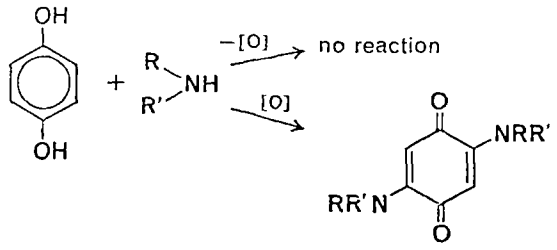
(87)

produce phenazine was attributed to the formation of hemiacetals by methanol and the quinone carbonyl groups. In ether solution phenazine was obtained, although in poor yield.

4. Nascent quinones

The idea of *in situ* preparation of quinones for nitrogen addition does not appear to have as long a history as in the case of sulphur. However, Harger observed in 1924 that hydroquinone reacted with a variety of primary and secondary amines only under aerobic conditions (equations 88 and 89)[120]. Even earlier Kehrmann and Cordone had shown that the oxidation of catechol in the presence of aniline leads to 4,5-dianilino-1,2-benzoquinone (equation 90)[75].

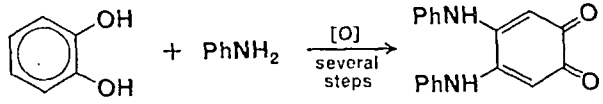
More recently, the addition of secondary amines to nascent quinones has been examined quite successfully[121]. The addition of dimethylamine and ethyleneimine produced reasonable yields of 4,5-disubstituted 1,2-benzoquinone product, but *N*-methylaniline gave an excellent yield of 4-*N*-methylanilino-1,2-benzoquinone.



(88)

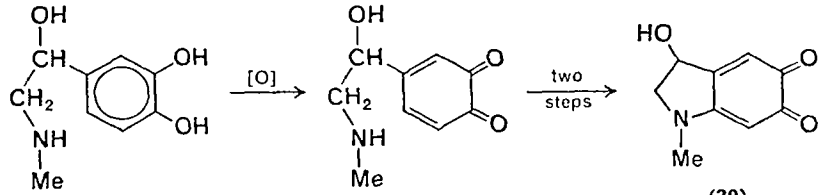
(89)

R or R' = H, Me, Et, *i*-Bu, *s*-Bu, Am, allyl, $PhCH_2$



(90)

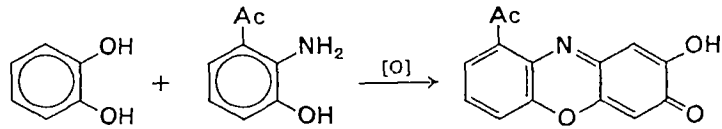
An interesting example of intramolecular addition of amines to quinones has been studied in the formation of adrenochrome (**30** in equation 91)[122]. The intermediate (**29**) can be detected in the early stages of the reaction[61].



(91)

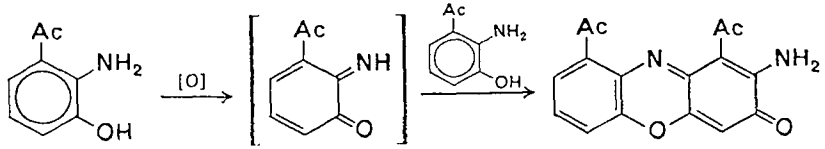
(29) (30)

A bifunctional reagent of the *o*-aminophenol type can undergo condensation with either catechol or itself under oxidative conditions. The former path has been important in the study of insect pigments and leads to 2-hydroxy-3-phenoxazones (equation 92)[123]. The latter leads to 2-amino-



(92)

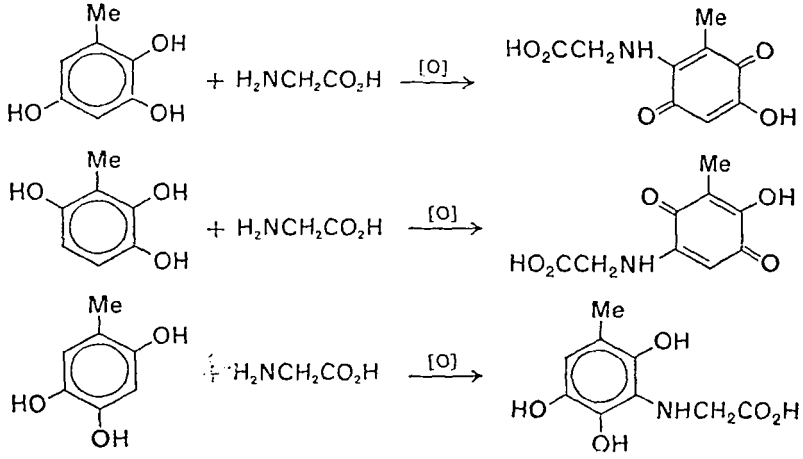
3-phenoxazones (equation 93) and has been important in several natural product syntheses[124]. The earlier literature of this field has been reviewed[125].



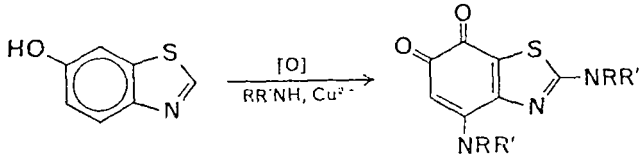
(93)

An effort has been made to evaluate the reactivity of protein towards nascent quinones[126]. Of the compounds studied, 3-*n*-pentadecyl-1,2-benzoquinone, formed by silver oxide oxidation, was found most reactive toward γ-globulin, bovine fraction II. The three isomeric methyl derivatives of this quinone were only slightly less reactive, while the 4,5-dimethyl and 4,5,6-trimethyl derivatives were completely unreactive.

In a related study, conducted polarographically, glycine was allowed to react with the quinones that result from the oxidation of 2,3,5-, 2,3,6- and 2,4,5-trihydroxytoluene[127]. The pattern of addition and subsequent reaction was shown to be influenced rather strongly by the substitution in the starting material (equations 94–96).

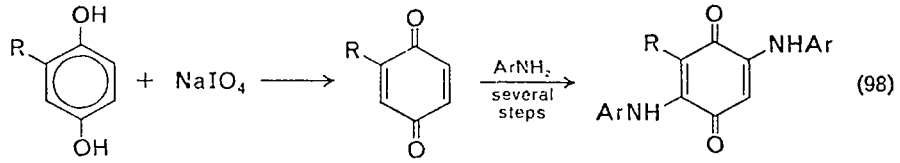


A very unusual and interesting modification of the nascent quinone route involves the oxidation of 6-hydroxybenzothiazole followed by amine addition and re-oxidation (equation 97)[128]. Clearly, a great many questions remain to be answered about these reactions.



R, R' = Me, C_5H_{10}, $(CH_2CH_2)_2O$

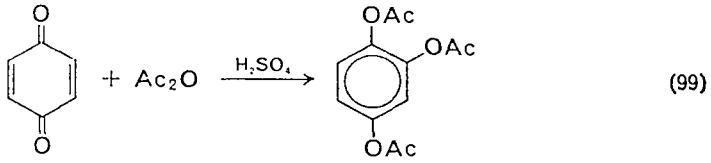
The experiments described earlier involving an added oxidant are, of course, examples of nascent quinone syntheses[94, 95, 97, 105, 109]. Recently, sodium periodate has been found to be an excellent reagent for such reactions (equation 98)[129]. Yields of 80–90% were found.



D. Thiele Acetylation

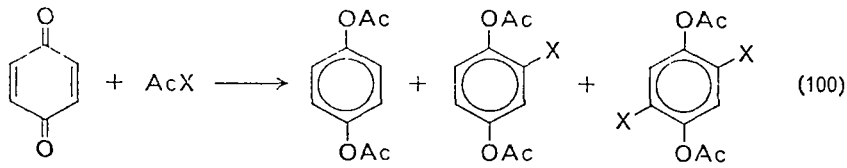
1. Historical introduction

The treatment of quinones with acetic anhydride under acidic conditions produces a combination of addition and esterification (equation 99)[130].



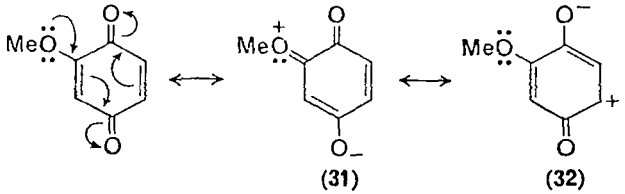
The reaction has been very widely used for the synthesis of new quinones and hydroquinones, the proof of structure of quinonoid materials, and to facilitate the isolation and purification of natural products. The reaction is usually known as the Thiele acetylation. Our interest is chiefly concerned with mechanistic questions and because of the simplicity and generality of the reaction a reasonably clear picture has been formed. This state of affairs is very fortunate because the Thiele reaction, while properly considered electrophilic, is closely related to the reductive, nucleophilic reactions of quinones. Why the acetylium ion and monosubstituted 1,4-benzoquinones lead to a product orientation predicted by nucleophilic considerations deserves some serious study.

A reaction closely related to the Thiele acetylation is that of quinones with carboxylic acid halides. The reaction was observed and reported long before Thiele's first publication (equation 100)[131,132]. It was recognized that both mono- and dihalogenated hydroquinone diacetates are formed, although the proposed sequence of steps does not appear to be correct in view of later studies.

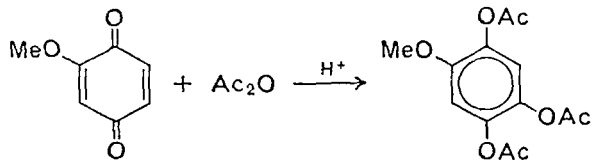


2. Mechanistic studies

The mechanistic study of the Thiele reaction began very early in the development of physical organic chemistry. In an effort to apply the new electronic theory to quinonoid systems, Erdtman presented the relative reactivities and product orientation for several alkyl- and methoxyl-substituted 1,4-benzoquinones[133]. His general observations and conclusions for electron-donating substituents have been verified in later studies. For example, 2-methoxy-1,4-benzoquinone would be expected to have structures **31** and **32** as principal resonance contributors and thus to react as indicated in equation (101). In fact, 2,4,5-triacetoxyanisole (**33**) is obtained in quantitative yield under very mild conditions.

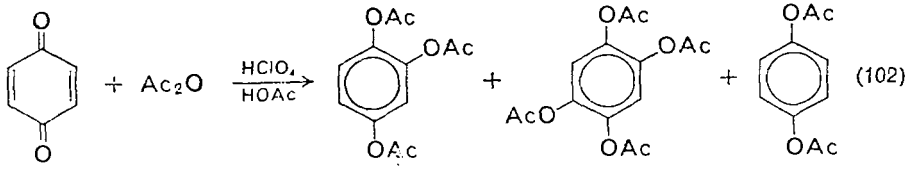


(31) (32)



(33) (101)

A series of papers giving a kinetic picture of the Thiele acetylation of 1,4-benzoquinone and 2-methyl-1,4-benzoquinone has appeared[134]. From these studies it is clear that the mechanism of the reaction is more complicated than that employed by Erdtman, although he suggested that this was likely to be the case. The limitations of the earlier proposal are obvious from the change in products with the composition of the reaction medium. In nearly pure acetic anhydride the 1,2,4-triacetoxybenzene (**34**) obtained by Thiele is the sole product, but in 50 vol. % acetic acid : acetic anhydride, two additional significant products (**35** and **36**) are found (equation 102). These additional products, the kinetics, the



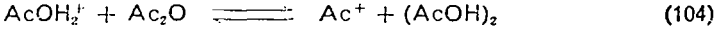
(34) (35) (36) (102)

thermodynamics and the behaviour of the solvent system all contribute evidence for the presence of the acetylium ion **37**.

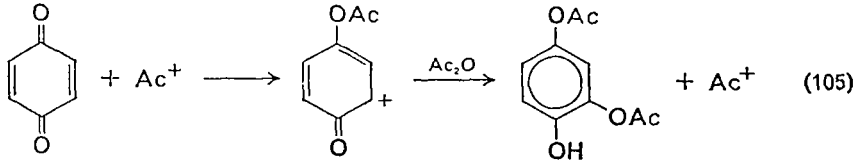
(37)

The suggested mechanism (equations 103–107) is capable of accounting for all of these observations. The quinonoid cross-oxidation product **40**

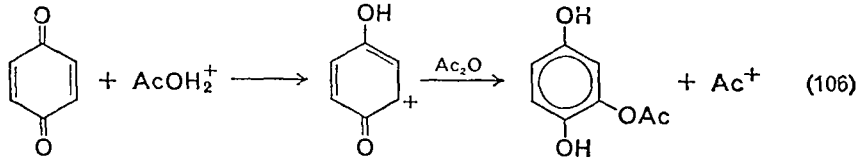
(103)



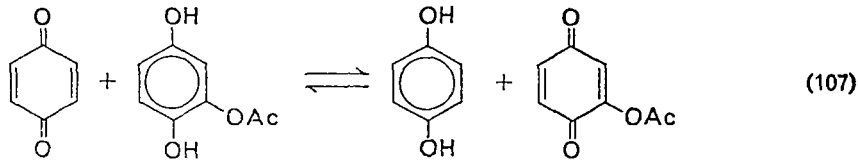
(104)



(38) (105)



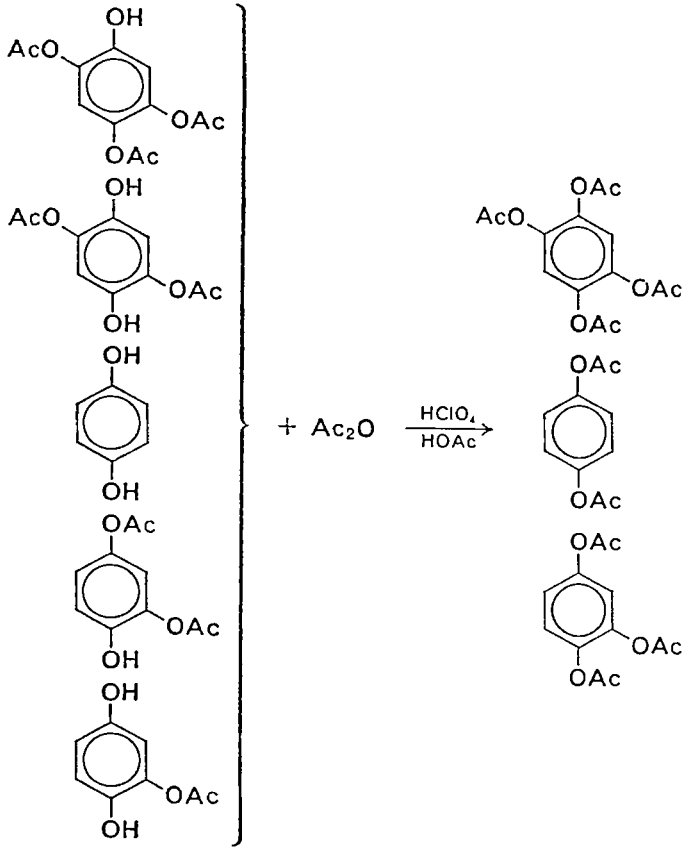
(39) (106)



(107)

(40)

can now react similarly to the original quinone. When the initial products of this second generation Thiele acetylation (hydroquinone, **38** and **39**) have all hydroxyl groups acetylated, the observed products are obtained (equation 108). An analogous, but somewhat more complicated, scheme was worked out for the Thiele acetylation of 2-methyl-1,4-benzoquinone. The presence of any significant concentration of 2-acetoxyhydroquinone in the reaction mixture has been questioned[135]. Burton and Praill do not offer any explanation for the presence of 1,2,4,5-tetraacetoxybenzene (**35**) and 1,4-diacetoxybenzene (**36**). The observation of analogous multiple addition products in other very rapid reactions (see sections II.B and II.C) suggests that the cross-oxidation reaction is able to compete, even with aggressive reagents.

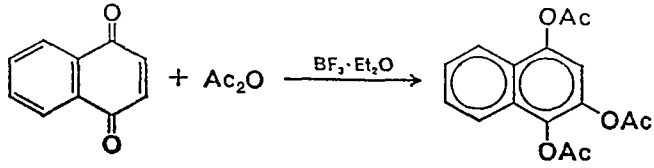


(108)

A rather detailed theoretical treatment of the reactivity of quinones has been published[136]. Standard methods of calculating localization energies were employed and the influence of both resonance and Coulomb integrals was evaluated. The agreement between prediction and observed experimental results is quite good, but many more data are needed. The discussion of various examples of addition mechanisms is excellent and especially informative in the case of the Thiele acetylation.

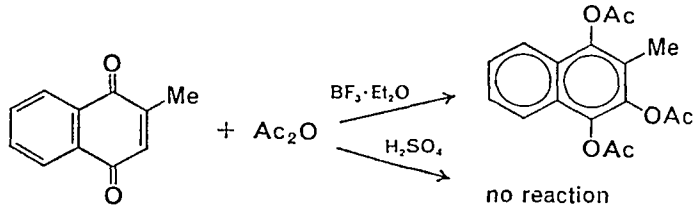
3. Synthetic survey

In the past 25 years the synthetic literature of the Thiele acetylation has provided a good preparative route to hydroxyquinones and a number of isolated, but intriguing reactions. As one aspect of an enormous synthetic study of potential antimalarial drugs, Fieser and his collaborators introduced the use of boron trifluoride etherate as the acidic catalyst (equation 109)[137-139]. The Thiele acetylation of naphthoquinone, using



(109)

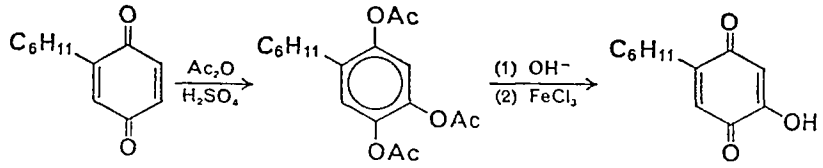
sulphuric acid, had been successfully carried out by Thiele himself[140]. Of greater interest is the ability of BF_3 to catalyse the acetylation of 2-methyl-1,4-naphthoquinone (equation 110); with sulphuric acid the



(110)

reaction does not occur[141]. It has also been shown that perchloric acid, used earlier for kinetic studies, is a very fine catalyst for preparative applications. Burton and Praill go so far as to claim: 'there appears little doubt that for preparative purposes perchloric acid is probably the most efficient catalyst for the Thiele acetylation'[142].

McLamore applied the Thiele acetylation with sulphuric acid to the synthesis of hydroxy alkyl-1,4-benzoquinones (e.g. equation 111)[143].

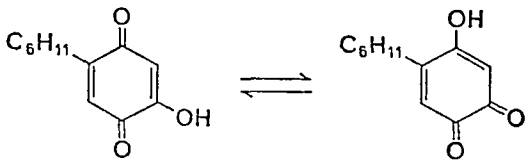


(111)

C_6H_{11} = cyclohexyl

(41)

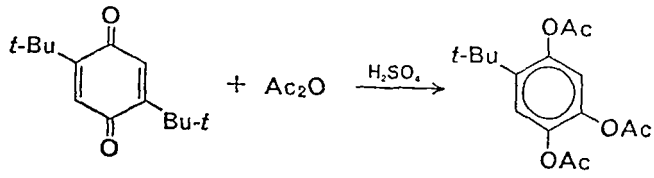
The structure of the product **41** was demonstrated by two independent syntheses, but the question of tautomerism (equation 112) was not treated.



(112)

The use of BF_3 was not reported in this study and comparison is made with the 2-alkylnaphthoquinones that are said not to undergo the Thiele reaction: nevertheless, some hindered benzoquinones were acetylated.

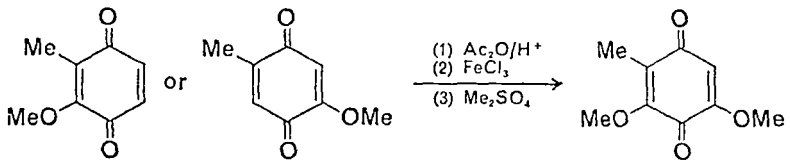
The most interesting of the reactions is that of 2,5-di-*t*-butyl-1,4-benzoquinone (equation 113). The structure of product **42** was simply deduced from the elemental analysis, but it is reminiscent of some nitrogen dealkylations (see section VIII.B).



(113)

(42)

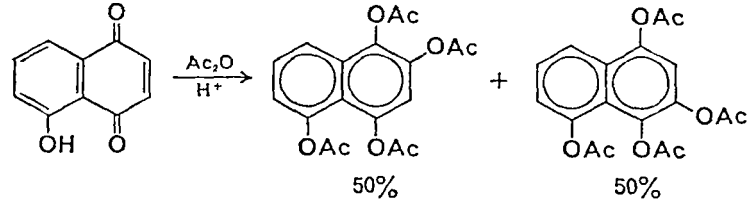
The Thiele reaction has been used in conjunction with dimethyl sulphate for the synthesis of methoxy quinones[85]. Both 2-methyl-3-methoxy- and 2-methyl-5-methoxy-1,4-benzoquinone react to produce the same product (equation 114).



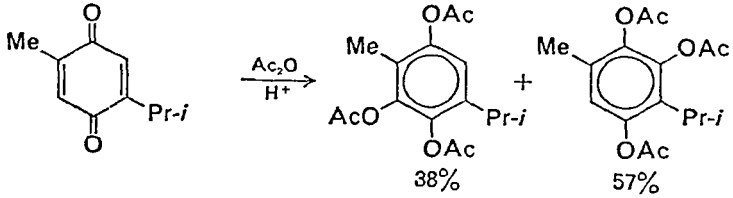
(114)

The structure of the antibiotic gonyleptidine, and associated minor companions, was demonstrated in part, using the Thiele reaction[38]. From several lines of evidence, gonyleptidine proved to be chiefly 2,3-dimethyl-1,4-benzoquinone accompanied by smaller amounts of 2,5-dimethyl- and 2,3,5-trimethyl-1,4-benzoquinone. As expected, the 2,3-dimethyl isomer underwent the Thiele reaction very rapidly and nearly quantitatively, while the 2,3,5-trimethyl homologue was recovered from the reaction mixture unchanged. Fieser was interested in the fact that 2,5-dimethyl-1,4-benzoquinone, unlike 2,5-dimethoxy-1,4-benzoquinone, produces a very high yield of 1,3,4-triacetoxy-2,5-dimethylbenzene with BF_3 as the catalyst. It was known from earlier work that sulphuric acid produces an even higher yield of product.

The large number of studies and the variety of applications of the Thiele acetylation have provided a good deal of understanding of the scope and mechanism of the reaction. However, the same studies have provided a number of conflicting reports; for example, regarding the question of orientation in unsymmetrically substituted quinones. In 1967 only two examples of more than one isomeric product had been reported (equations 115 and 116)[96,133]. Questions of the most suitable catalyst,



(115)



(116)

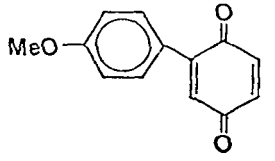
optimum yields and conflicting reports of 'unreactive' quinones led Wilgus and Gates to summarize the literature and attempt some definitive experiments[144].

Probably the most significant result of this study was the extension of the Thiele reaction to quinones having electron-withdrawing substituents. Both 2-acetyl- and 2-carbomethoxy-1,4-benzoquinone gave only the 1,3,4-triacetoxy product: the latter in poor yield. Only 2-(4'-nitrophenyl)-1,4-benzoquinone gave significant amounts of all three isomeric products. The minor isomeric product was isolated in the cases of 2-methyl- and 2-phenyl-1,4-benzoquinone and the yields determined. In general, the orientation pattern as a function of quinone substituent shown in Table 6 is similar to that found in thiol addition (see section II.B.2). The isomer distribution does not appear to be strongly influenced by the catalyst

TABLE 6. Isomeric yields for the Thiele reaction of monosubstituted 1,4-benzoquinones[144]

Substituent	Acetoxy group position (%)			Catalyst
	3	5	6	
Ac	92			H_2SO_4
Ac	78			BF_3
CO_2Me	34			H_2SO_4
Me		78	15	H_2SO_4
Me		89	11	BF_3
4'-$NO_2C_6H_4$	18	56	19	H_2SO_4
4'-MeO-3',5'-$Cl_2C_6H_2$		65	35	H_2SO_4
Ph	21	52		H_2SO_4
Ph	31	62		BF_3

employed (perchloric acid was not examined), but the overall yields and ease of isolation are probably improved with $BF_3 \cdot Et_2O$. It is very likely that the milder the catalyst the better; however, note the complete failure of the reaction with 2-(4′-methoxyphenyl)-1,4-benzoquinone (see also reference 145) and the outstanding success with 2-(4′-methoxy-3′,5′-dichlorophenyl)-1,4-benzoquinone (equations 117 and 118). It seems clear that competing Friedel–Crafts reactions are important.



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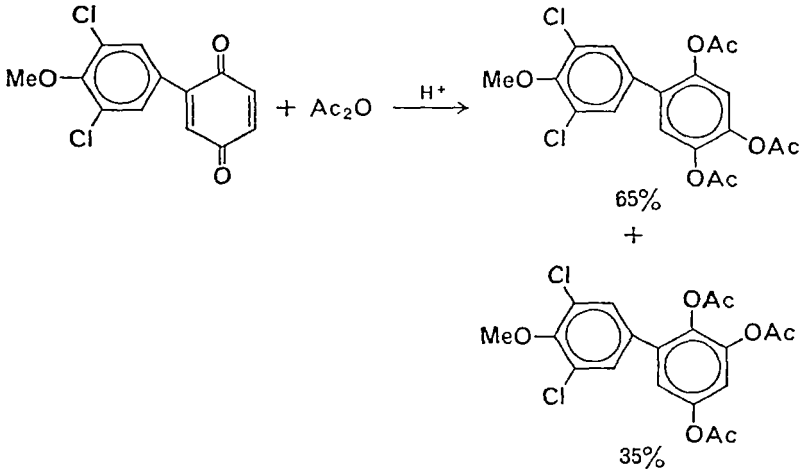
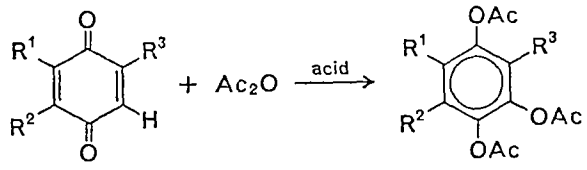


(118)

The scope of the Thiele reaction is still under active investigation with much emphasis on halo- and alkoxyquinones (equation 119). It was found sometime ago that 2,6-dichloro- and 2-bromo-3,5-dimethoxy-1,4-benzoquinone fail to undergo the Thiele acetylation. Recently, detailed studies of the Thiele acetylation of haloquinones produced the results in Table 7[146]. It is apparent that steric effects are important and may overbalance the activating electronic effect of the electron-withdrawing substituent.

The strong electronic deactivating influence of the methoxy group makes it an interesting substituent for detailed study. The earlier reports that 2,5- and 2,6-dimethoxy-1,4-benzoquinone fail to react with acetic anhydride in the presence of sulphuric acid have been confirmed[147]. The more powerful catalyst, perchloric acid, also fails to cause either these two compounds or 2,3,5-trimethoxy-1,4-benzoquinone to undergo Thiele acetylation. The

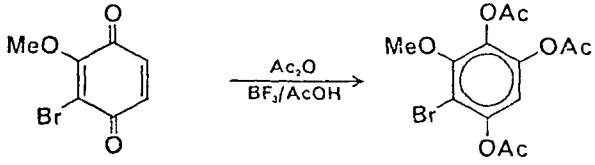
TABLE 7. Thiele acetylation of various halo-1,4-benzoquinones[146]



(119)

Substituent(s)			Yield (%)	
R^1	R^2	R^3	BF_3	$HClO_4$
Br	H	H	42	28
I	H	H	35	—
Cl	H	Cl	60	60
Br	Br	H	47	—
Br	H	Br	33	40
H	Br	Br	49	12
I	H	I	10	23
Br	Br	Br	4	0

various combinations of bromo and methoxy groups and their effect on the Thiele reaction sheds some light on the general mechanistic picture (equations 120–122). The six trisubstituted (bromo, methoxy) 1,4-benzo-



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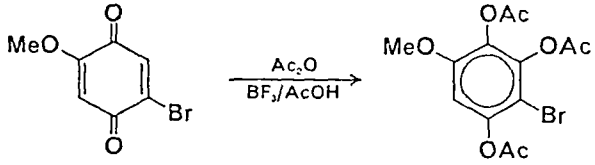

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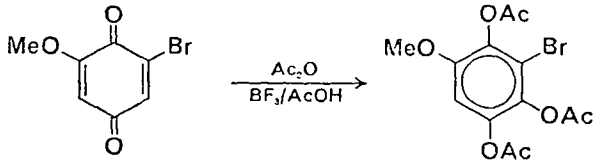
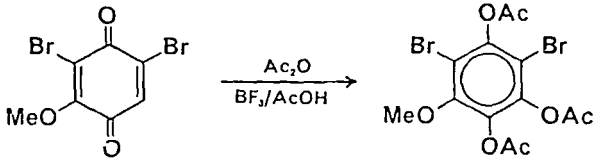


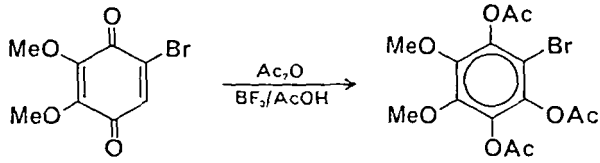
(122)

quinones were also prepared and subjected to Thiele conditions. Only the two shown in equations (123) and (124) underwent reductive acetylation. The other four compounds also failed to react with perchloric acid as the catalyst. This evidence seems to confirm completely the hypothesis that

Thiele acetylation, and presumably the other nucleophilic quinone addition reactions, does not occur *ortho* to an alkoxy group (for an extreme case resulting in an exception, see section V.A).

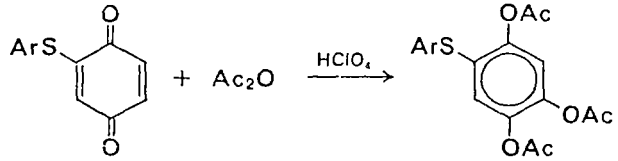


(123)



(124)

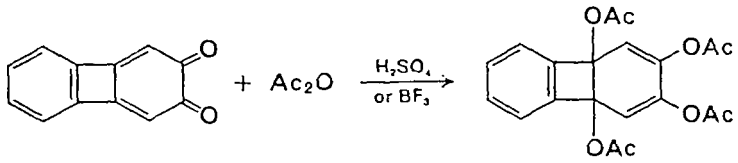
One study of the analogous alkylthio groups has been made and only starting material or resinous product was found[148]. However, the arylthio groups did lead to the expected triacetates (equation 125).



(125)

Ar = Ph, 4-MeC_6H_4 and 4-ClC_6H_4

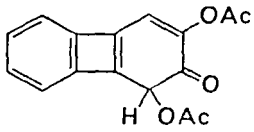
Very little has been written about the Thiele acetylation of 1,2-quinones. An exceptional case and an unexpected product have been reported for a biphenylene quinone[149]. The structure of the tetraacetate, **43**, is supported by chemical and physical data. This unusual structure is rationalized on



(126)

(43)

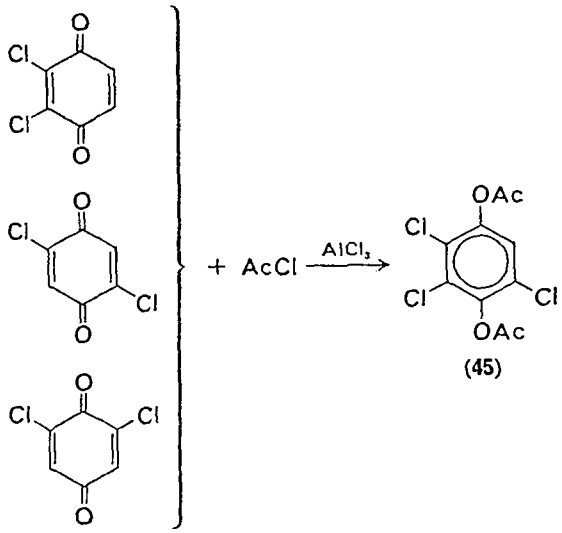
the basis that normal Thiele acetylation would have to involve an intermediate like **44** with an unstable benzocyclobutadiene structure.



(44)

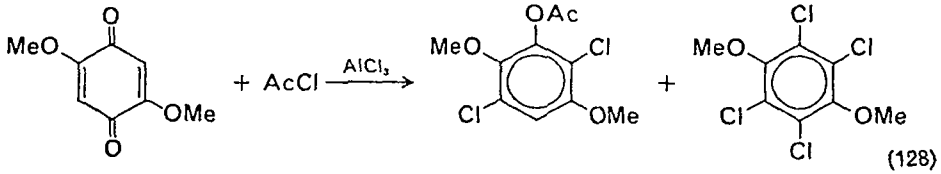
4. Reactions of acetyl halides

This reaction, which bears some resemblance to the Thiele acetylation, does not appear to be very general since the dimethoxy- and dichloro-1,4-benzoquinones fail to react with acetyl chloride, even on boiling[150]. When aluminium chloride is added, in much greater than catalytic amount, the three dichloro isomers studied do react (equation 127). The three reactions lead to a common, but non-Thiele product (**45**). Similar reactions



(45) (127)

of 2,5-dimethoxy- and 2,5-diethoxy-1,4-benzoquinone lead to products even further removed from simple addition (equations 128 and 129)[151,152].



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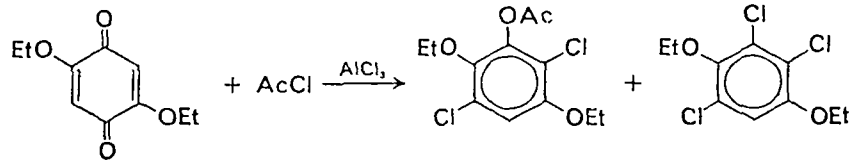
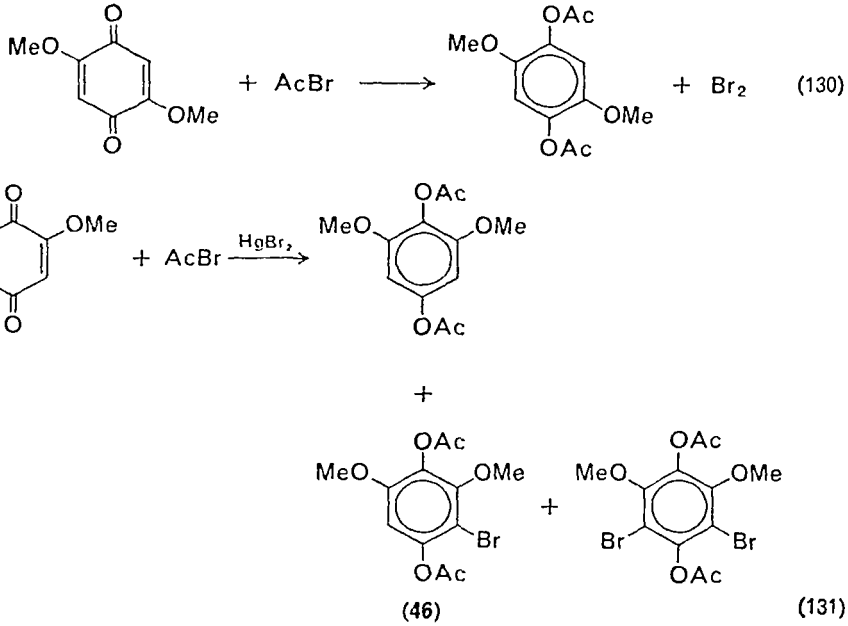


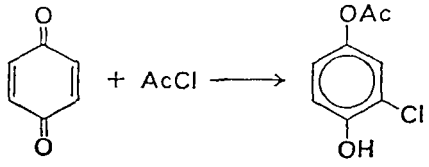
(129)

No reaction was observed with 2,6-dimethoxy-1,4-benzoquinone. Thiele himself used the Lewis acid zinc chloride to a limited extent, but this has been shown to be a poor synthetic system by later workers.

Quinones with certain substituents can undergo reversible addition reactions and an investigation of this process bears on the mechanism of the reactions of quinones and acid halides. Asp and Lindberg were able to verify nearly all the observations of Oliverio and collaborator[150,151], and they extended the study to the reactions of acetyl bromide (equations 130 and 131)[153]. When the hydrolysis of the monobromo addition product **46** was attempted, it lost hydrogen bromide and regenerated the starting quinone (equation 132). The expected 3-bromo-2,6-dimethoxyhydroquinone could be obtained in ether solution (equation 133) but decomposed when concentration under reduced pressure was attempted.



In an effort to find a more useful preparative route to the haloquinones, Cason and collaborators found some very significant facts concerning the addition of acetyl chloride[154]. They reasoned that simple addition, leading to 2-chloro-4-acetoxyphenol (**47**), might be observed under carefully controlled conditions (equation 134). Such a reaction should not lead to a



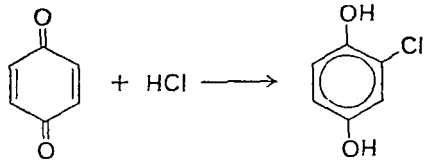
(134)

(47)

dichloro product and thus represents an ideal route to pure monochloroquinones or hydroquinones. Actually, with purified acetyl chloride and dry equipment, no reaction took place. Upon addition of a small amount of acetic acid, a vigorous reaction took place and formed the usual mixture of mono- and dichloro products.

Cason's conclusion, that the simple addition of hydrogen chloride and subsequent acetylation is the probable reaction mechanism, has received substantial support[155]. The products originally described by Schulz[132] were verified (equation 100) as was the extremely slow rate under anhydrous conditions. The suggested mechanism is shown in equations (135) through (138); followed by the acetylation of the phenolic products (**48–50**). Additional evidence for this hypothesis includes: (1) The isolation of 2-chlorohydroquinone under certain conditions, and (2) The chlorine content of the mixed products corresponds to that calculated for a quantitative yield of monochloro product. The mechanism for reaction-

(135)



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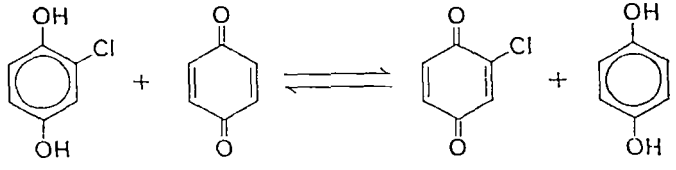
(48)



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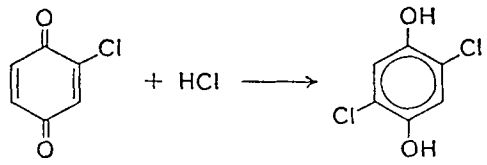


(138)

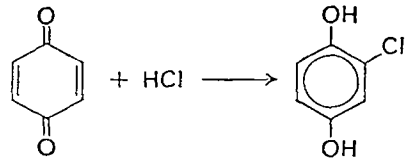
(50)

with 2-methyl-1,4-benzoquinone is probably similar, but the role of the acid is clouded by the observation of a different isomeric product with water from that found earlier with zinc chloride.

E. Addition of Inorganic Substances

1. Halogen and hydrogen halides

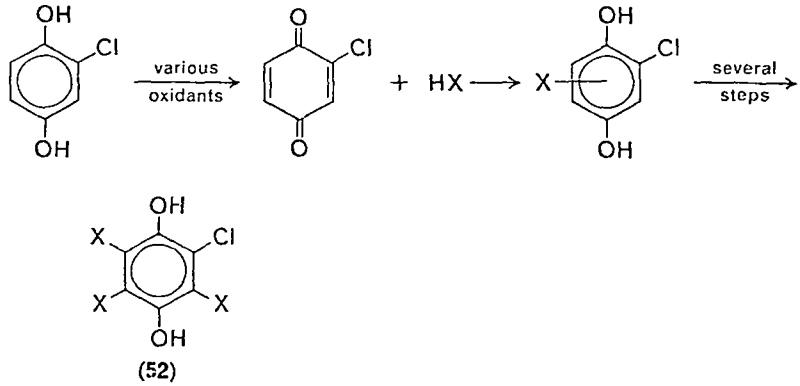
a. Historical introduction. Interest in the interaction of hydrochloric acid and 1,4-benzoquinone (equation 139) dates from the very beginning of modern organic chemistry[1]. A later and thorough synthetic study



(139)

(51)

showed that the initial reductive addition product **51** could be oxidized and subjected to successive additions of either HCl or HBr (equation 140)

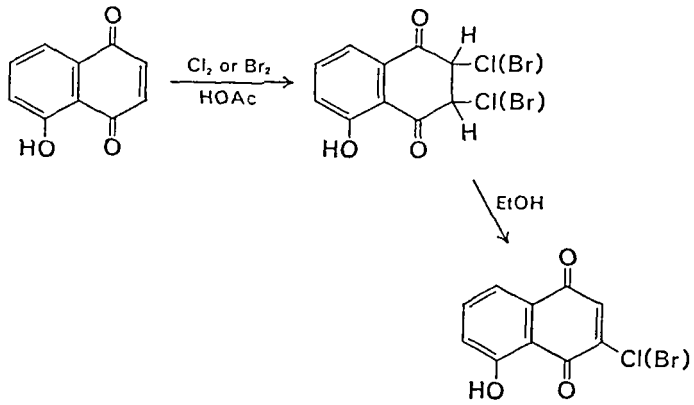


(140)

(52)

to produce eventually the tetrahalo-1,4-benzoquinone (**52**); for example, chloranil (X = Cl). Levy and Schultz also attempted the reductive addition of HF, HI and HCN to 1,4-benzoquinone[156]. Hydrogen iodide in chloroform solution caused the reduction of the quinone to hydroquinone; hydrogen fluoride and hydrogen cyanide in the same solvent produced no identifiable addition products.

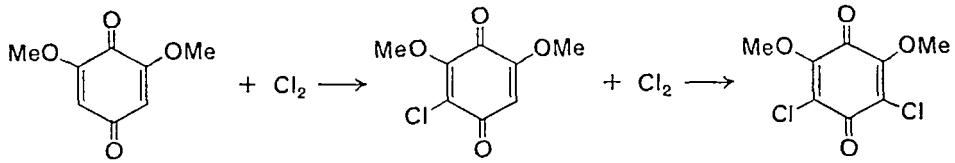
A substantial number of papers concerned with the synthesis of halogenated quinones appeared in the late 19th century and the results have been carefully reviewed[157–164]. During the first half of the 20th century little of synthetic significance was achieved, although there were reports (some conflicting) of the application of these reactions for the preparation of specific halogenated quinones[165–168]. One exception to this undistinguished record comes from the field of natural products. Thomson showed that juglone can be halogenated, followed by dehydrohalogenation to produce 3-halojuglone (equation 141)[169]. One should be warned of a



(141)

number of earlier papers where this reaction was said to lead to the 2-halojuglones[170]. The dihalojuglones can be obtained by treating the 3-halo compounds with additional halogen in acetic acid. When juglone acetate is halogenated and then treated with anhydrous sodium acetate, the 2-halojuglone product is obtained[42]. These substituent effects are clearly related to those described for thiols and anilines (see sections II.B.3 and C.3).

When this route was attempted on 2-methyl-5-hydroxy-1,4-naphthoquinone (plumbagin) the reactions were slow and produced mixtures[96]. On the other hand, Huisman has used the direct halogenation of substituted 1,4-benzoquinones for the preparation of useful synthetic intermediates (for example, equation 142)[171].

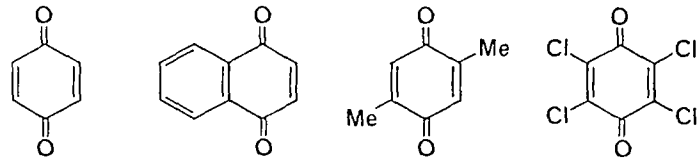


(142)

The varying reports and uncertain results led Cason and his students to make a careful study of the synthesis and especially the isolation and purification of chlorinated 1,4-benzoquinones[154]. The study included 2-methyl-1,4-benzoquinone and its 3-, 5- and 6-chloro derivatives (the latter with HBr or HCl) as well as 1,4-benzoquinone. With the exception of the preparation of 5-chloro-2-methyl-1,4-benzoquinone reported previously[172], the direct addition of hydrogen halides proved to be an entirely unacceptable method for obtaining pure haloquinones.

b. Mechanistic studies. Like the synthetic studies, mechanistic work on the quinone–hydrogen chloride reaction began very early. Clark suggested a mechanism that seems unnecessarily complicated[173] and Michael argued against 2-halohydroquinone as the initial product[174]. The troublesome presence of higher halogenated quinone products makes simple reductive 1,4-addition followed by a cross-oxidation equilibrium attractive. A rather detailed study of the kinetics of HCl addition in methanol is also convincing evidence for the current mechanism[175].

The kinetics of the addition of bromine to 1,4-quinones have been described and the not unexpected very slow electrophilic and very fast acid-catalysed reactions were found[176]. For example, 2-methyl-5-isopropyl-1,4-benzoquinone shows the following rate values in acetic acid: $k(\text{NaOAc}) < 0{\cdot}01$, $k(H_2SO_4)$ ca. 100. The rate of the second addition of bromine is extremely slow, even in the presence of sulphuric acid ($k < 5 \times 10^{-4}$). The following comparative rates (with added H_2SO_4) for various quinones were given:



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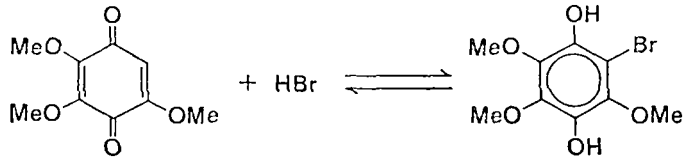
All of these rate data were rationalized on the basis of significant resonance contributors to the quinone nucleus.

The interesting anomalous behaviour of certain methoxy quinones has been mentioned before (see section II.D.3). Neither 2,5- nor 2,6-dimethoxy-1,4-benzoquinone is reactive toward hydrogen chloride or bromide[153]. However, once prepared indirectly, the 2-halo-3,6-dimethoxyhydroquinones are quite stable, while the 3,5-dimethoxy isomers decompose readily[177]. In an effort to understand this strange effect, Lindberg studied the reaction of hydrogen bromide with 2,3,5-trimethoxy-1,4-benzoquinone[178]. He found what appears to be the first example of a reversible

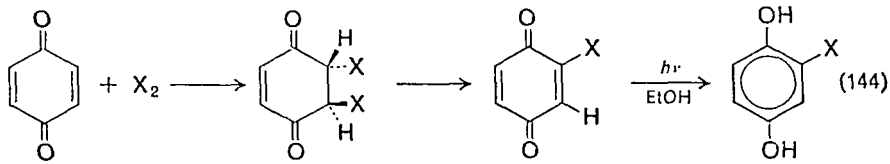
hydrogen halide addition to a quinone (equation 143). The product **53** is formed and can be converted to a diacetate known from independent synthesis. The chlorinated monomethoxy-1,4-benzoquinones are also known to be sensitive[179].



(143)

(53)

There has been some conflict in the literature concerning the configuration of the dichloride produced by addition of chlorine to 1,4-benzoquinone[180,181]. In the most recent study of this particular question, the spectral evidence earlier employed to suggest a *cis* product that isomerizes to the *trans* product was re-examined[182]. It was possible to isolate and characterize the intermediate and end products of the reactions of dichlorides that occur in alcohol. On the basis of this evidence it has been concluded that only the *trans*-dichloride (or dibromide) is formed in these additions, but elimination to the monohaloquinone can occur. This is then followed by photochemical reduction to the observed monohalohydroquinone (equation 144).



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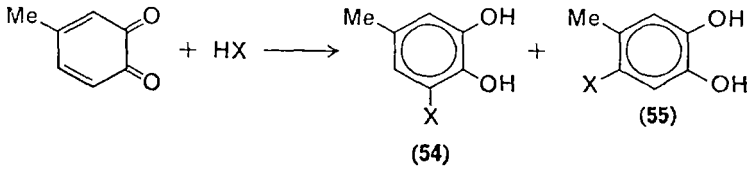
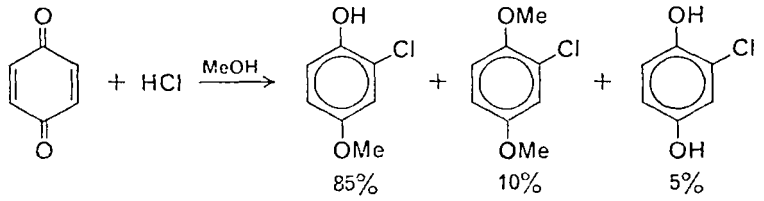
If there were any doubts concerning the detailed mechanism of hydrogen chloride addition to quinonoid systems, they were put to rest by the recent elegant kinetic study of Adams, Hawley and Feldberg[87]. Using chronoamperometry, cyclic voltammetry and chronopotentiometry it was possible to show that the addition of HCl to 4-methyl-1,2-benzoquinone (generated electrochemically) is dependent on both the rate of addition and the equilibrium constant for the subsequent cross-oxidation.

This same *ortho* quinone was the substrate for a study with HCl or HBr in a series of solvents[183]. A combination of thin-layer chromatography and u.v.–visible spectroscopy allowed the determination of the amounts of the two isomeric products (equation 145). An excellent correlation was found with the more polar solvents favouring 1,4- over 1,6-addition (i.e. **54** > **55**).



(145)

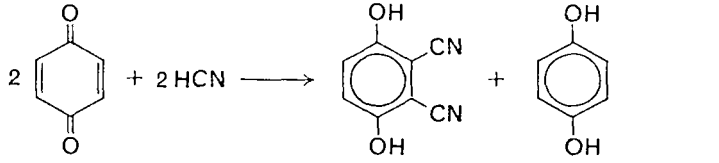
It has been found quite recently that when HCl addition is carried out in methanol this solvent enters into the reaction to a very significant extent (equation 146). Moderately sophisticated theoretical calculations (e.g. extended Hückel) gave a good interpretation of the observed results.



(146)

2. Hydrogen cyanide

Thiele and Meisenheimer made the interesting observation that, unlike the apparently similar hydrogen halides, hydrogen cyanide yields only a diaddition product with 1,4-benzoquinone—that being the 2,3-isomer (equation 147)[184]. No monoaddition product could be isolated. A

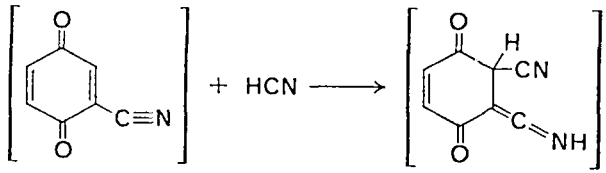


(147)

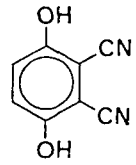
reasonable explanation of this experimental fact is the presence, in the first-step product, of a strong electron-withdrawing group which also offers an attractive conjugated system for 1,4-addition (equation 148). Allen and Wilson pointed out that this reaction is very sensitive to temperature and only succeeds in a very narrow range (20–30°C)[185].

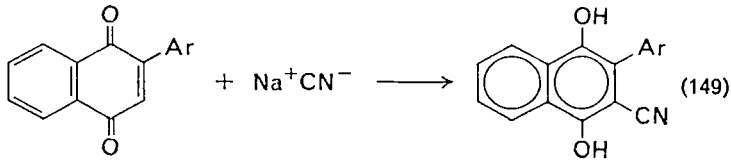
In some cases it is possible to add sodium cyanide to quinones (equation 149)[186]. The best results were obtained with 2-(*p*-nitrophenyl)-1,4-naphthoquinone. No cyanohydroquinones were obtained from 1,4-benzo-, 1,4-naphtho- or 2-methyl-1,4-naphthoquinone.

The reaction of 1,4-benzoquinone with cyanide forms the basis for an extremely sensitive quantitative determination of that anion[187]. The reaction is very rapid at a concentration of as little as 0·2 μg/ml. The



(148)





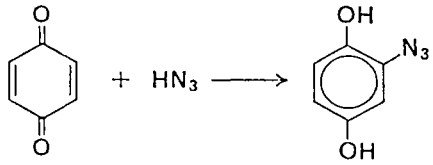
(149)

Ar = Ph, 4-MeC_6H_4, 4-$MeOC_6H_4$, 4-$O_2NC_6H_4$

fluorescence of the 2,3-dicyanohydroquinone, presumed to be produced, is proportional to cyanide concentration over the range 0·2 to 50 μg/ml. A wide variety of other quinone derivatives was tested, but all gave inferior results.

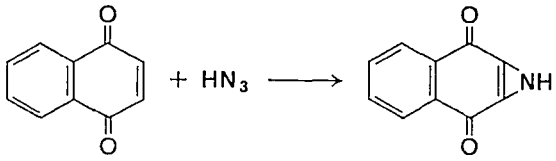
3. Hydrazoic acid

In 1915 Oliveri-Mandalá and Calderaro disproved the earlier report that hydrazoic acid reacts with 1,4-benzoquinone to produce only nitrogen-free product[188,189]. In fact, the addition takes place in a manner very similar to HCl addition (equation 150); the nitrogen-free product reported previously is quinhydrone.



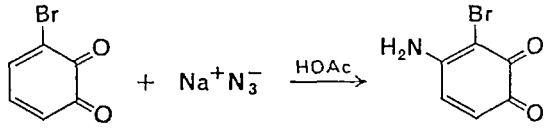
(150)

In the naphthoquinone series a similar situation occurred when an early report suggested an especially interesting structure for the addition product (equation 151)[190]. Fieser and Hartwell re-examined the reaction and showed that the product was actually 2-amino-1,4-benzoquinone[191]. The



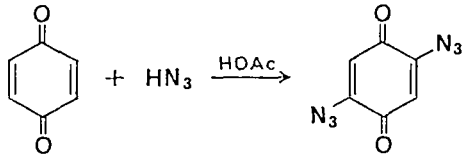
(151)

suggested mechanism was simply 1,4-addition followed by a redox reaction between the azido group and the quinone. The difference in oxidation potential between 1,4-naphthoquinone and 1,4-benzoquinone can explain the observed difference in product. Efforts to test this hypothesis by isolating the expected intermediate, 2-azido-1,4-naphthoquinone, failed, but the scope of the reaction was examined. It was found that 1,2-naphthoquinone gave the 4-amino derivative, but both 2-methyl-1,4- and 4-methyl-1,2-naphthoquinone were unreactive toward HN_3. With 3-bromo-1,2-benzoquinone, only addition at the 4-position is observed (equation 152).



(152)

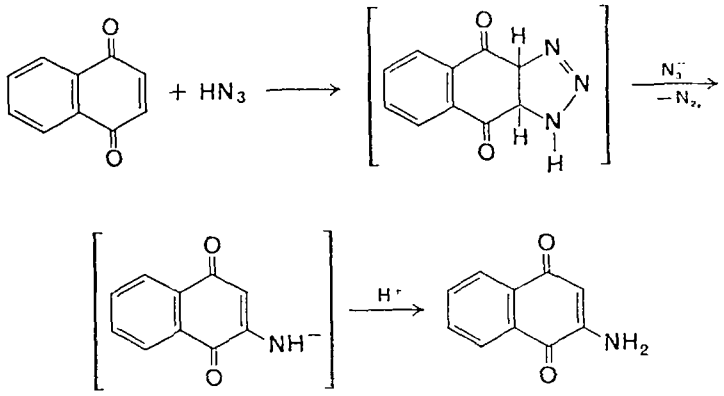
Fieser and Hartwell also carried out the addition of sodium azide and 1,4-benzoquinone in acetic acid[191] and agreed with Oliveri-Mandalá[189]. Recent work has shown that the product is actually 2,5-diazido-1,4-benzoquinone (equation 153) and that the original work in benzene does produce 2-azidohydroquinone (equation 150)[192].



(153)

The mechanism of these reactions has also been discussed briefly by Dean and collaborators[193]. They favour initial triazole formation followed by proton abstraction by azide with loss of nitrogen, which leaves the amide anion to take up a proton to form a product (equation 154). It would seem that this is a much more attractive explanation of the failure of 2-methyl-1,4-naphthoquinone to react.

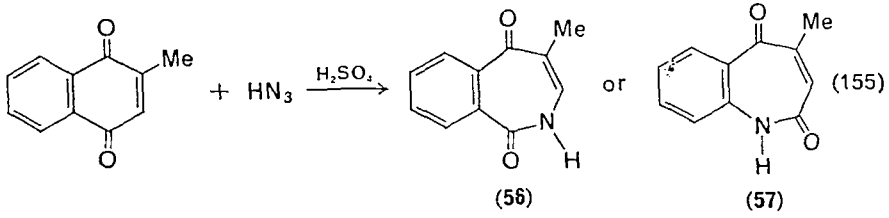
The reaction between hydrazoic acid and quinones in sulphuric acid solution has been studied and the simple quinones led only to decomposition products[194]. With 2,5-dimethyl- and 2-methyl-5-isopropyl-1,4-benzoquinone, however, it was possible to isolate pure products with



(154)

analyses consistent with the addition of HN[195]. The products did not show the properties of amines and evidence of imide structure was sought. The ease of hydrolysis of the compounds is consistent with an imide structure, but no compelling evidence was presented.

In more recent work it has been demonstrated that quinones undergo the Schmidt reaction upon treatment with hydrazoic acid and sulphuric acid (equation 155)[196]. This reaction presents a very valuable synthetic entry to the 2,5- H-2,5-azepindiones and thus the structure of the product (**56** or **57**) is of special importance. The spectroscopic character of N—H



(155)

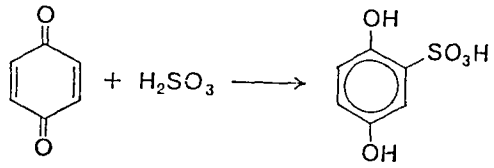
(56) (57)

and C—H protons led Folkers and collaborators to suggest **56** as the correct structure; i.e. preferential migration of the least hindered end of the quinone. This assignment has been re-examined and the alternate structure, **57**, found to be in better agreement with the spectra and a chemical rearrangement product of known structure[197].

4. Sulphur anions

The reactions of sulphite and related anions with quinones have been of practical importance in photography for a long time and fundamental research on the subject has accompanied this interest[198,199]. These first experiments verified the general assumption that the quinone formed in

the developing process oxidized aqueous sulphur dioxide to sulphuric acid. Dodgson also found strong evidence for a second reaction: i.e. the addition of sulphite to the quinone (equation 156)[198]. The hydroquinone



(156)

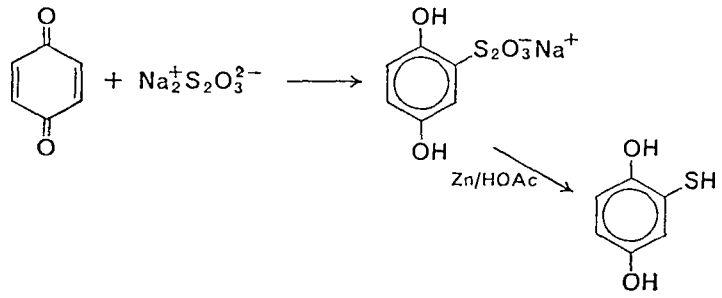
(58)

sulphonic acid **58** was isolated and characterized. The amounts of sulphate and sulphonic acid were shown to provide a reasonable material balance for the quinone employed. The expected effect of increased hydroxide concentration, i.e. increased base leads to increased sulphonic acid formation, was substantiated with experimental evidence. It was also observed that above an equivalent amount of base, sulphate production remained constant while less and less sulphonic acid was found. This was attributed to the destruction of quinone by base. Similar results were obtained with a series of substituted 1,4-benzoquinones. Again the effect of hydroxide ion was found, although it generally required more excess base than in the case of 1,4-benzoquinone. The more highly substituted quinones were also somewhat more resistant to attack by base. Substitution as well as addition was observed with chlorinated quinones.

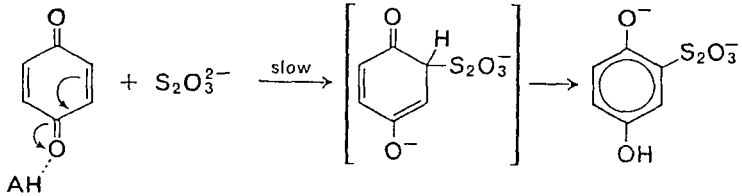
A kinetic study of the inhibition of the autoxidation of several hydroquinones by sulphite has shown that the oxidation of hydroquinone by oxygen is most consistent with the rate data and the product distribution[200]. The hydrogen peroxide formed in the first step appears to be responsible for the oxidation of sulphite to sulphate. The rate laws are not first-order, but to a good approximation the assumption that sulphite acts to remove quinone by one or two additions fits the observations. Of special interest to organic chemists is the observation that thiols (e.g. cysteine, thioglycolic acid, thiocresol, etc.) act in a manner very similar to sulphite; the products of their reaction with quinones have been discussed (see section II.B.3). An elaborate spectrophotometric study of the reactions of various quinones with sulphite has been published[201]. Apart from showing that the system is exceedingly complex little of interest to the organic chemist is presented. The addition of sulphite to nascent quinones was mentioned in section II.B.4.

The addition of sodium thiosulphate to 1,4-benzoquinones has been used as a preparative route to mercaptohydroquinones (equation 157)[202].

The first report that 2-methyl-1,4-benzoquinone gave only the 2,5-addition product was later corrected; in fact, the 2,6-isomer is the major product[203]. A careful kinetic study of this reaction has been conducted[201]. The yield of product in the pH range 1–5 in aqueous solution was quantitative and the rate law is: $v = k$[quinone][thiosulphate]. The data at various acidities show general-acid catalysis and a linear relationship between the rate constant and the redox potential. The fact that the addition is very dependent upon the redox potential is reasonable in view of the reductive nature of the addition. The energy and entropy of activation (4·0 kcal/mole and −39 e.u. at pH 3·19) are certainly reasonable when compared with the values for additions to other α,β-unsaturated carbonyl compounds. The picture obtained is quite consistent with the widely held mechanistic view of such additions (equation 158). A marked increase in rate was found with



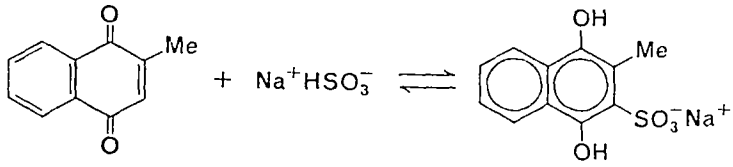
(157)



(158)

increasing fraction of ethanol in the aqueous solvent. This observation is also consistent with the mechanism presented. As the polarity of the solvent decreases the increased opportunity for hydrogen bonding enhances the catalytic effect of acetic acid buffer.

It was found that 2-methyl-1,4-naphthoquinone readily dissolves in aqueous bisulphite and that such a solution possesses excellent anti-haemorrhagic activity[205]. The reaction was considered an example of normal 1,4-addition (equation 159). It was found that the quinone itself is very much less active, as are other 2-methyl-1,4-naphthoquinones with substituents in the 3-position.

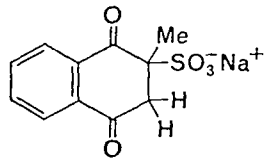


(159)

(59)

The usefulness of the sulphonate led at once to an active effort to establish its structure with certainty[206]. When 2-methyl-1,4-naphthoquinone was added to concentrated aqueous potassium bisulphite, two different salts were obtained. One showed the remarkable activity desired and the other showed less than one-tenth as much. Through a series of chemical interconversions and an independent synthesis, the inactive salt was shown to be the expected product **59**. The active isomeric salt is converted to **59** by heat.

The most likely structure for the active salt **60** was proposed on the basis of comparison of its u.v. spectrum with model compounds[207]. The



(60)

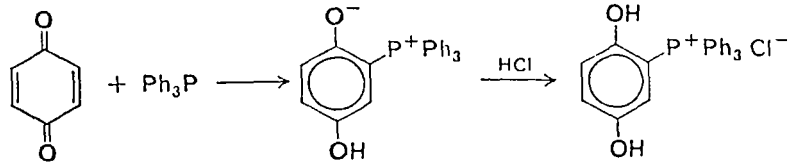
similarity of the spectrum of **60** with that of 2-methyl-1,4-naphthoquinone-2,3-oxide is very impressive. The chemical facts concerning the active salt are also best understood in terms of this structure.

Unsubstituted 1,4-naphthoquinone and 1,4-anthraquinone have also been studied in bisulphite solution[208–210]. In addition to the 2-sulphonate salt, two distinct complexes were also observed and in some cases isolated. On the basis of i.r. spectral data and the characteristics of their reactions with various nitrogen-containing carbonyl reagents, these complexes are described as 1,2- and 1,4-adducts in equilibrium. Their stability is attributed to their resonance possibilities.

5. Aryl phosphorus compounds

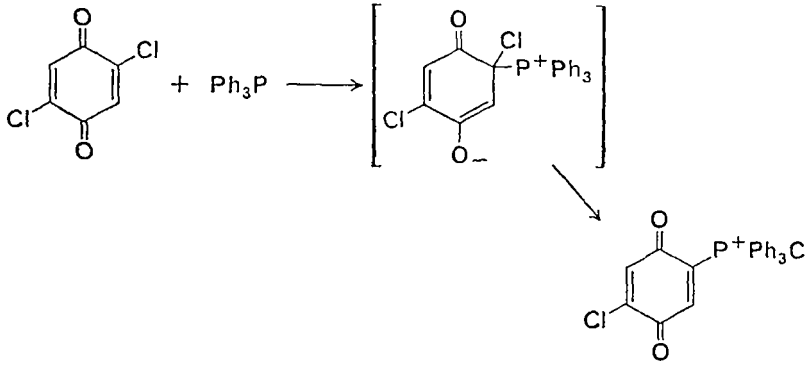
Much of the chemistry of quinones and phosphorus compounds has involved carbonyl addition (see section III), but examples of nuclear addition have also been presented. While ruling out a carbon-to-phosphorus bond in the reaction of chloranil with triphenylphosphine, Ramirez and Dershowitz offer convincing evidence for such a bond in the case of

1,4-benzoquinone (equation 160)[211]. The u.v. spectra of these phosphonium salts, as well as a substantial number of chemical transformation, are all best understood in terms of these structures.



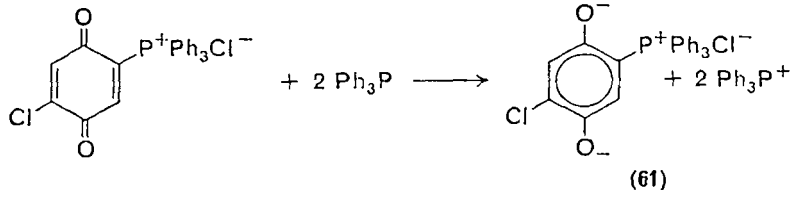
(160)

The intermediate case of 2,5-dichloro-1,4-benzoquinone is of special interest. Two points came to light immediately: (i) pure adduct formed quantitatively only when a 3 : 2 ratio of phosphine to quinone was employed, and (ii) the adduct had a chloride ion associated with it. Like chloranil, reaction with this quinone resulted in the oxidation of two moles of triphenylphosphine and the formation of oxygen-to-phosphorus bonds. Like 1,4-benzoquinone, ring attachment also occurred. In this instance it also results in the displacement of a chloride ion (equation 161).



(161)

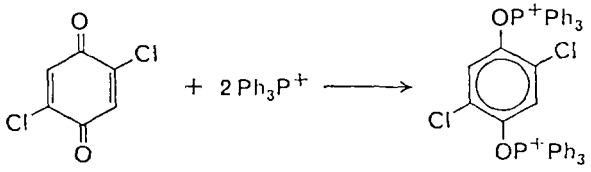
This new quinone (one of the observed products) with its positively charged group should have a high oxidation potential and thus accomplish the next required step (equation 162). Finally, the reduction of the second



(162)

(61)

mole of quinone and the formation of the other observed product (equation 163) occurs. The two products (**61** and **62**) behave as a single material

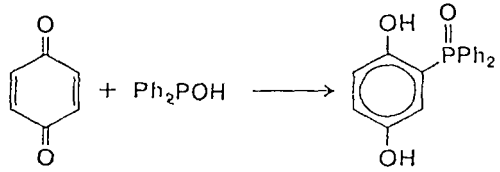


(163)

(62)

until they are hydrolysed in aqueous methanol. Again, the chemical and spectral evidence for these structures is impressive. On the basis of a detailed study of the i.r. spectra of the adducts of different quinones with several tertiary phosphines, the conclusion that there must be substitution on the quinone ring and quaternarization of the phosphorus atom was reached[212].

A report of a very similar addition of a secondary phosphine oxide to 1,4-benzoquinone has appeared (equation 164)[213]. The yield of adduct is high and the authors see no reason to suspect other than a simple addition.

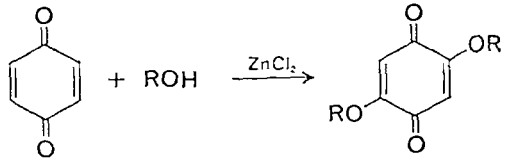


(164)

F. Oxygen Addition

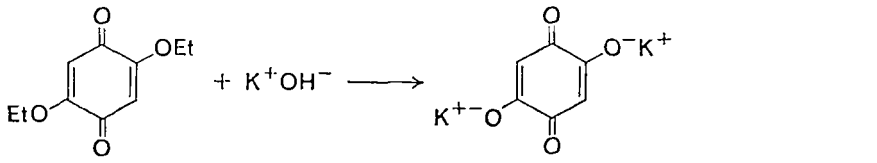
1. Alkoxyquinones and related compounds

The importance of quinonoid materials in aqueous and sometimes basic solutions (for example, physiological and photographic) has created an interest in their reactions with oxygen nucleophiles. It was recognized very early that the direct treatment of quinones, having little substitution, with strong bases led to extensive decomposition. Thus, it was of some significance when an indirect preparation of such compounds was found (equations 165 and 166)[214]. The first reaction for the preparation of alkoxy derivatives is also of value. In an attempt to apply this method to 2-methyl-1,4-benzoquinone a modest yield of the 5-methoxy derivative and none of the desired 3,6-dimethoxy product was obtained (equation 167)[215].



(165)

R = Me, Et, Pr



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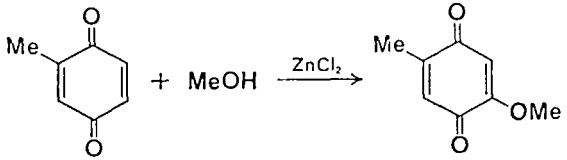
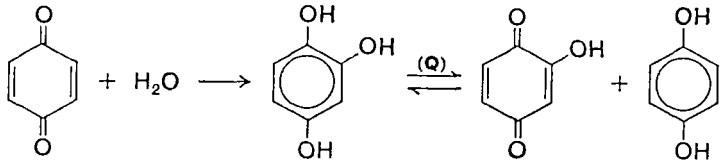


(167)

The direct reactions of quinones with water are of great interest and generally very difficult to study. The products from the aqueous decomposition of 1,4-benzoquinone and 1,2-naphthoquinone have been shown to be the corresponding hydroxy quinone and hydroquinone (equation 168)[216, 217]. A similar mechanism has been proposed for the decomposition



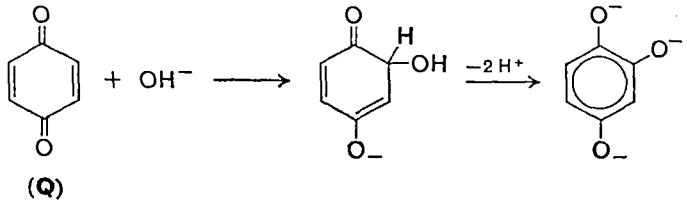
(168)

(Q)

of 1,2-benzoquinone[218] and a polarographic study of this quinone has shown that two molecules of 1,2-benzoquinone do produce one of catechol and one of some new substance[219]. However, the second product is not the required hydroxylated quinone; furthermore it is polarographically inactive and other means of characterizing it had to be found. A kinetic study of the decomposition showed that it is autocatalytic. The mechanism of decomposition of 4-methyl-1,2-benzoquinone appears to be the same, but it is considerably slower.

The most convincing evidence concerning the course of the alkaline decomposition of 1,4-benzoquinone was the isolation of 2-hydroxy-1,4-benzoquinone[220]. However, the mechanism was still better understood when Eigen and Matthies published their kinetic studies[221]. Their analysis

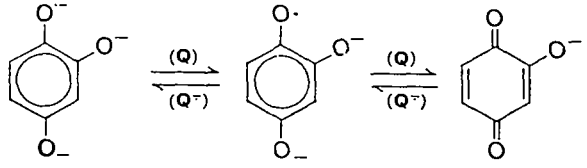
of the reactions takes into account the intermediate semiquinone. It is the characteristic spectrum of that species that allowed the flow determination of kinetic and equilibrium data. On the basis of these data the following reaction scheme was defended. First, the addition reaction (equation 169).



(169)

(Q)

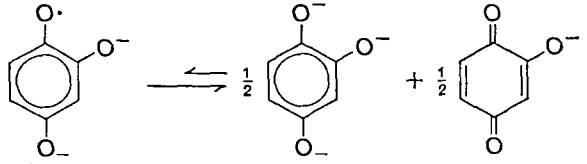
Second, the oxidation equilibria (equation 170).



(170)

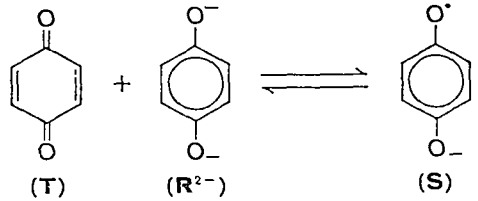
$(Q^{\cdot-})$

Third, the disproportionation (equation 171).



(171)

Two other studies of the semiquinone equilibrium and the mechanism of hydroxide attack have appeared. The first of these reports an extensive study of the factors that affect the equilibrium between quinone–hydroquinone and semiquinone (e.g. equations 172 and 173)[222]. The effect of various nuclear substituents, the effect of pH and the effect of reversible 1,2-carbonyl addition are all discussed.

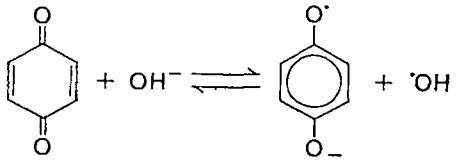


(172)

(T) (R^{2-}) (S)

$$K' = \frac{[S]^2}{[T][R^{2-}]} \qquad (173)$$

In the second paper, two of the current pictures of the hydroxide decomposition of 1,4-benzoquinone are examined[223]. One of these mechanisms is that of Eigen and Matthies already discussed[221]; the other is a more recent suggestion[223a] (equations 174 and 175). A careful selection



(174)

$$2 \cdot OH \longrightarrow H_2O_2 \qquad (175)$$

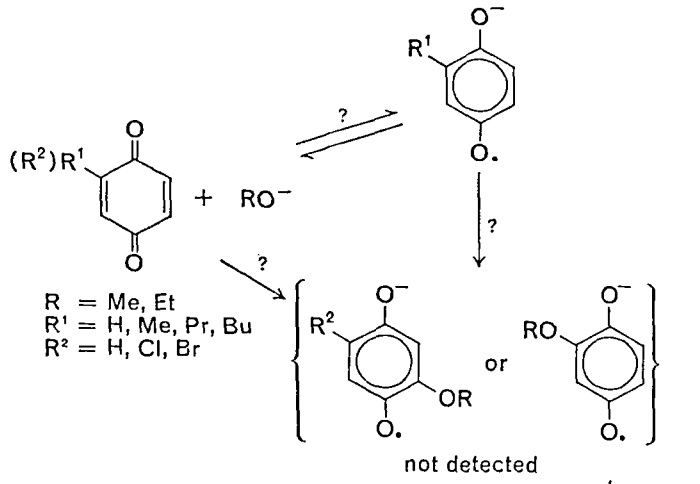
was made of experimental conditions for the detection of hydrogen peroxide. The complete failure to find any in such systems is taken as evidence against this later scheme. The failure of tetrasubstituted quinones to produce semiquinone anions as required by the above proposal is also presented as an argument in favour of Eigen's proposal.

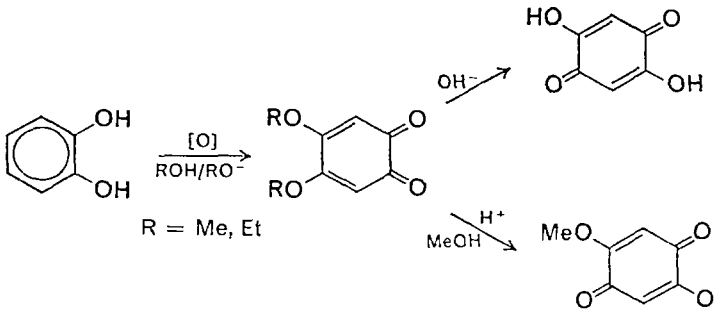
Interest in the reactions of quinones with hydroxide and alkoxide ions continues. A variety of 1,4-benzoquinones, with hydroxide and alkoxide ions, have been shown to be first-order in base and quinone[224]. The rates were measured both by following the loss of base (potentiometrically) and the increase of radical (e.s.r.): good agreement was found. When a similar study was conducted in the presence of various proteins, a catalytic effect was found[225]. A higher mobility of hydroxide ion at the water–protein interface was suggested as the explanation.

A recent study of the kinetics of alkoxide reactions with 1,4-benzoquinone, and several alkyl and halo derivatives, centred on the formation of the semiquinone[226]. It was not possible either to detect the expected monoalkoxy semiquinone intermediates or to decide whether the first semiquinone is an intermediate or the product of a concurrent reaction (equations 176 and 177). Stopped-flow spectrophotometry was used to follow the semiquinone formation. In the short reaction times studied, alkyl 1,4-benzoquinones showed only semiquinone formation, but hydrogen or halogen substitution produced dialkoxy semiquinone.

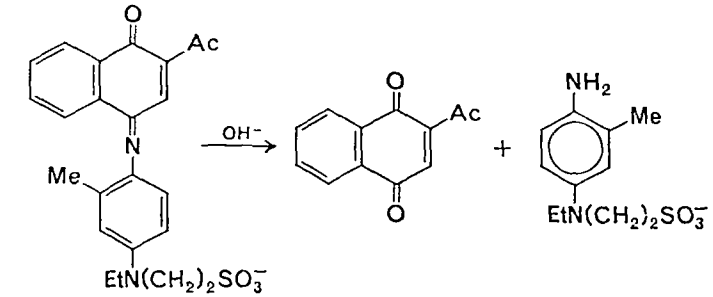
A recent report of the use of nascent 1,2-benzoquinone is interesting for the product structure and subsequent conversion to substituted 1,4-benzoquinones (equations 178 and 179)[227]. Similar chemistry is observed with 4-methylcatechol.

As a part of a study of the bleaching of imine dyes, Reeves and Tong found it necessary to study the decomposition of 2-acetyl-1,4-naphthoquinone in basic aqueous solution[228]. This quinone is one product of the

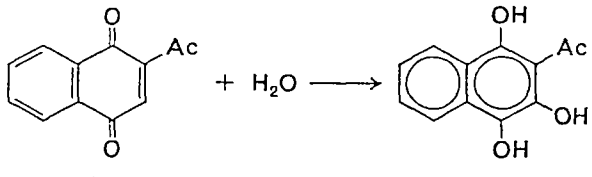




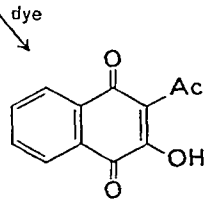
hydrolysis of the dyes studied (equation 180). The product of its reaction with water can cause a serious side-reaction with the original dye (equation 181). The most significant observation for our present concern was that **63** alone in pH 9·2 buffer does not decompose in the simple fashion suggested as the first step of equation (181). Compounds **63** and **64** would be expected to establish the cross-oxidation equilibrium shown in equation (182). Compound **63** has completely disappeared within 30 seconds. However, the yields of compounds **65** and **66** are 42% and 28% respectively rather than the expected equal amounts and they appear over a period of



(180)

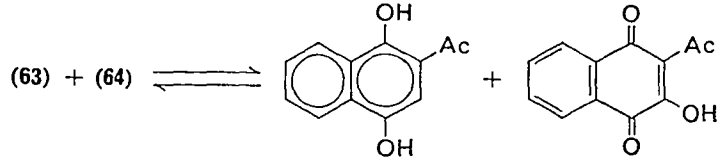


(63) (64)



(181)

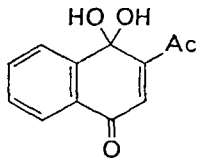
+ leuco dye

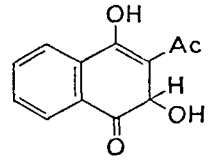


(182)

(65) (66)

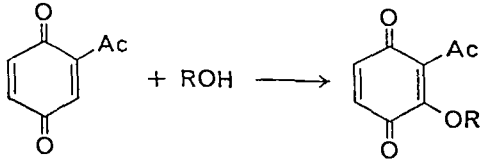
about 10 minutes. Spectral evidence indicates that at least two intermediates must intervene between reactants (**63** and **64**) and products (**65** and **66**). The following intermediates are suggested. The conversion of the latter intermediate (**67**) could well be the slow product-forming step.





(67)

The addition of alcohols to 2-acetyl-1,4-benzoquinone has been studied and the expected 2,3-orientation observed (equation 183)[220]. Excellent



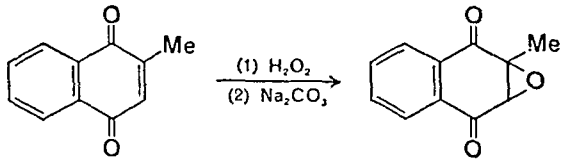
(183)

R = Me, Et, *i*-Pr, Bu, allyl, C_6H_{11}, CH_2Ph

yields were obtained for a broad range of alcohols when equimolar reactants were used in dry benzene. Poor yields of the initial hydroquinone adduct were obtained when the alcohol was used as solvent. No reaction was found with *t*-butyl alcohol.

2. Epoxyquinones and their chemistry

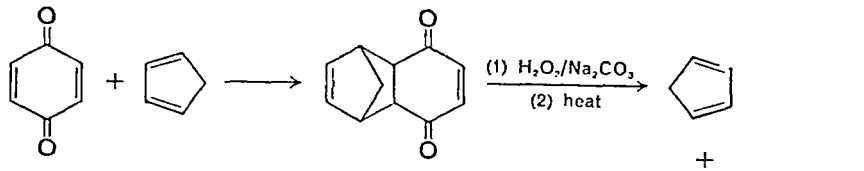
It has been known for a long time that the double bonds of quinonoid nuclei can be epoxidized. The method most widely used was worked out by Fieser and his students (equation 184)[230]. This preparative method has



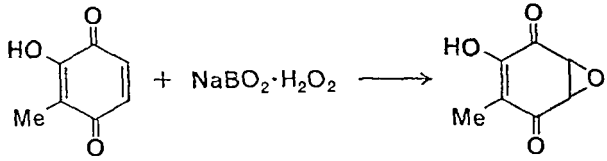
(184)

been applied to a great many quinones including 5,8-quinolinequinone and its 6-alkyl derivatives and excellent yields are obtained[110]. A promising alternate route to quinone epoxides is sodium hypochlorite in aqueous dioxan[231]. The yields of product appear quite satisfactory and the reagent is faster, safer and cheaper than 30% peroxide.

The synthesis of 1,4-benzoquinone epoxides is a good deal more difficult. An indirect method devised by Alder and collaborators involves the formation of the mono- adduct with cyclopentadiene and thermal reversal of that reaction after epoxidation (equation 185)[232]. The generality of this method suffers from the orientation of the Diels–Alder adducts and the thermal instability of some quinone epoxides. In an effort to find a milder epoxidation reagent Rashid and Read found sodium perborate to be excellent[233]. They were particularly interested in the synthesis of terreic acid (**68** in equation 186). A number of other sensitive quinone epoxides were prepared in low yield; e.g. 1,4-benzoquinone and juglone.



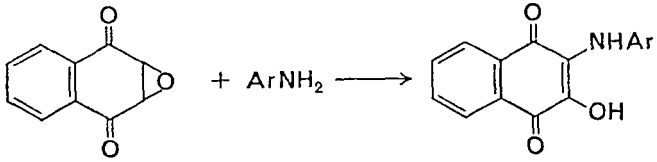
(185)



(186)

(68)

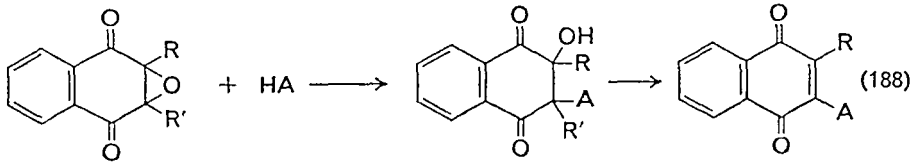
The quinone epoxides have proved to be useful intermediates for the synthesis of 2,3-disubstituted quinones in which one of the substituents is a hydroxy or alkoxy group. For example, a series of 2-anilino-3-hydroxy-1,4-naphthoquinones have been prepared by this route (equation 187)[234]. The yields are only fair and in the nitro cases poor (3-NO_2 = 4-NO_2 = 5%, 2-NO_2 = 0).



(187)

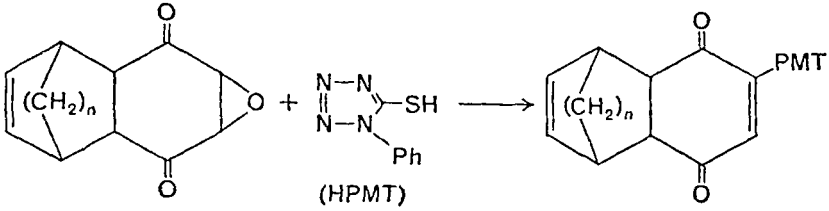
Ar = 2-ClC_6H_4, 4-ClC_6H_4, 2,4-$Cl_2C_6H_3$, 2-$MeOC_6H_4$, 4-$MeOC_6H_4$, 4-$HO_2CC_6H_4$, 4-$H_2NO_2SC_6H_4$, 3-$O_2NC_6H_4$, 4-$O_2NC_6H_4$

As part of a synthetic search for bacterial growth inhibitors various substituted 1,4-naphthoquinone epoxides were treated with aniline, *n*-butanethiol and hydrogen halides (equation 188)[235]. When either R or R′ is hydrogen, the yield of quinone product is satisfactory, but when both groups are alkyl the second step does not occur.



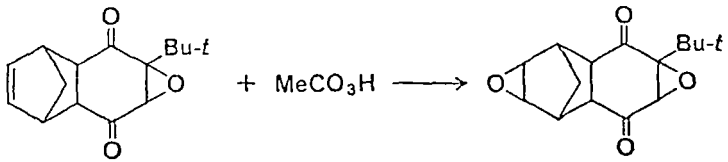
(188)

The chemistry of epoxides of quinone Diels–Alder adducts has been studied by Gates and colleagues. Through an n.m.r. study of the cyclopentadiene adducts of various 1,4-benzoquinones and their epoxides the *cis–endo* configuration of the Diels–Alder product was confirmed[236]. Similar results were found with 1,3-cyclohexadiene adducts. The configuration of the epoxide was shown to be *exo*. The ring-opening reaction with 1-phenyl-5-mercaptotetrazole (HPMT) was carried out (equation 189). The configuration of the 2-thioether enediones corresponds to the



(189)

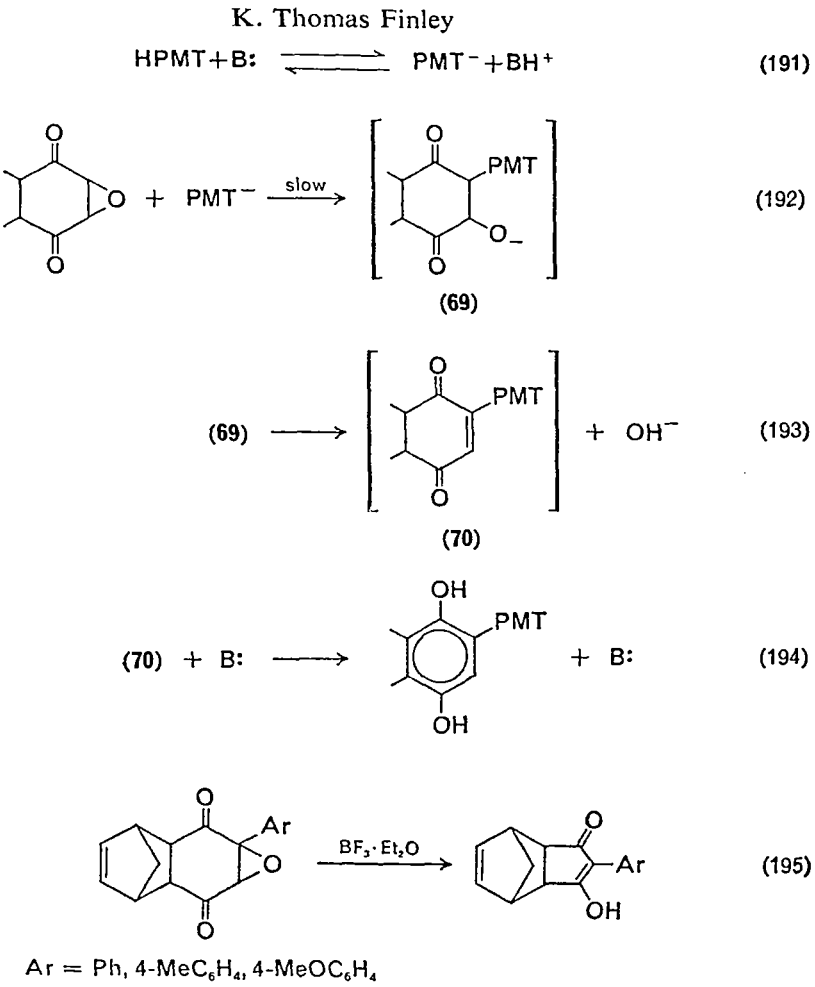
Diels–Alder adduct. Finally, it was found that peracetic acid is a useful reagent for preparing diepoxides (equation 190).



(190)

A kinetic study of the reaction of the epoxides described above with HPMT has been carried out in basic buffered ethanol solution[237]. The following reaction mechanism is consistent with the observations (equations 191–194). The effect of substitution on the rate of ring opening is similar to that found in halide displacement and large negative entropies of activation were found (−28 to −32 e.u.). Both of these effects could arise from participation of the carbonyl groups in the reaction, but comparison of the rate of ring opening of cyclohexene oxide by HPMT and data for other similar nucleophilic reactions argue against such participation.

A rather interesting ring-contraction reaction occurs when cyclopentadiene quinone adduct epoxides bearing aryl substituents are treated with acids (equation 195)[238]. Analogous reactions occur with strong proton acids and with the double bond reduced and with 1,3-cyclohexadiene adducts. The structures of the products were convincingly demonstrated with spectral and chemical evidence and the yields were fair to excellent with the choice of acid apparently very important.



III. THE CARBONYL CHEMISTRY OF QUINONES

A. Introduction

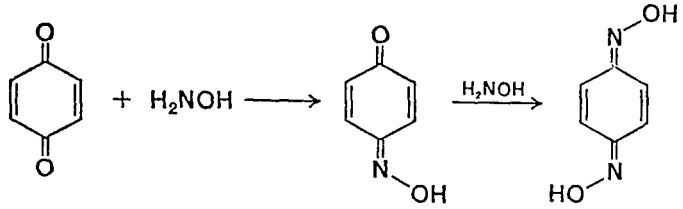
As might be expected, the carbonyl group plays a significant role in quinone chemistry. However, some aspects of this chemistry are rather closely related to another quinone addition reaction and have been treated in that section; for example

Thiele acetylation, section II.D.
Radical addition, section IV.B.
Hydroboration alkylation, section IV.C.4.
1,2-Quinone cycloaddition, section V.A.4.
Diazo cycloaddition, section V.B.

Enamine addition, section V.C.1.
Active methylene compounds, section VII.
Substitution chemistry, section VIII.D.

The present section is designed to discuss those features of quinone chemistry that relate chiefly to the carbon–oxygen double bonds.

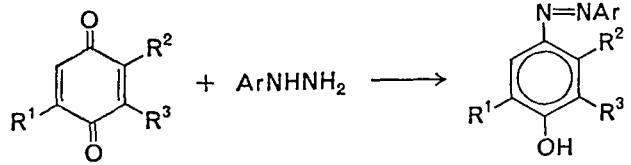
The earliest studies that deal exclusively with the chemistry of the quinonoid carbonyl group are those of Kehrmann and collaborators who examined the formation of oximes (equation 196)[239-242]. Either the mono- or the dioxime can be obtained with monosubstituted or 2,5-disubstituted



(196)

1,4-benzoquinones. The monooximes of the less hindered carbonyl group are obtained in the monosubstituted case and are the only product with 2,6-disubstituted and trisubstituted 1,4-benzoquinones. A review of the earlier literature is included[239]. Tetrasubstituted 1,4-benzoquinones did not form oximes under these conditions. The large number of nitrogen-containing carbonyl reagents provide additional examples[243-247] and a very early kinetic study is available[248].

The work of Borsche[245,246] was developed by Smith and Irwin as an important tool in demonstrating the structure of substituted quinones[249]. They realized that the addition of an arylhydrazine to a quinone and the addition of an aryldiazonium salt to a phenol may lead to isomeric products if the other substituents are the same (equations 197 and 198)*.



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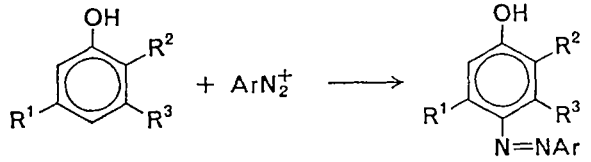
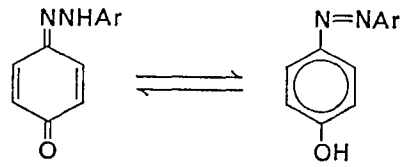


(198)

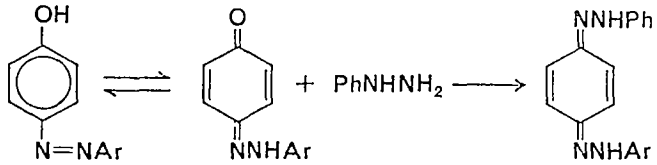
* This argument assumes that the quinone monohydrazone exists in the azo form (equation 199). Some recent studies of this equilibrium and the factors that influence it have appeared[250, 251].



(199)

The scheme worked very well with *p*-nitrophenylhydrazine and *p*-nitroaniline. In most cases the yields were excellent and the conversions to isomeric *p*-aminophenols and then to identical 1,4-benzoquinones were smooth. Formation of the monohydrazone derivatives with 2,4-dinitrophenylhydrazine was satisfactory, but the subsequent cleavage was not. It was found that duroquinone reacted very satisfactorily, unlike the earlier reports of attempted oximation.

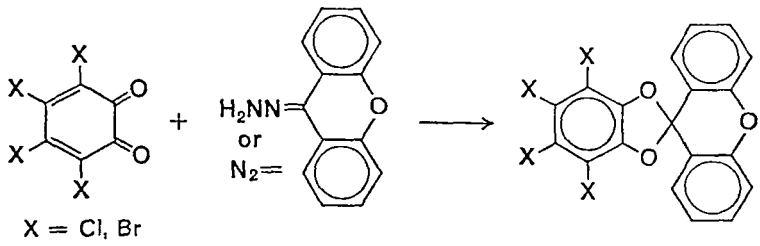
In the process of examining the question of azo–hydrazone tautomerism, a more detailed picture of the steric requirements for quinone carbonyl addition reactions was obtained[252]. A series of nine arylhydrazines, with a variety of halo and nitro substituents, reacted smoothly with 1,4-benzoquinone, 2-methyl-1,4-benzoquinone and 2-methyl-5-isopropyl-1,4-benzoquinone. Chloranil, anthraquinone and β-methylanthraquinone reacted only with those hydrazines substituted in neither or one *ortho* position. When one *ortho* position is substituted, the hydrazones show chemical and physical properties quite unlike those resulting from the less substituted quinones. Typical of this difference is the interesting reaction between phenylhydrazine and *p*-arylazophenol (equation 200). The highly hindered quinones and hydrazines failed to undergo this reaction, which incidentally clearly demonstrates the tautomerism of the starting material.



(200)

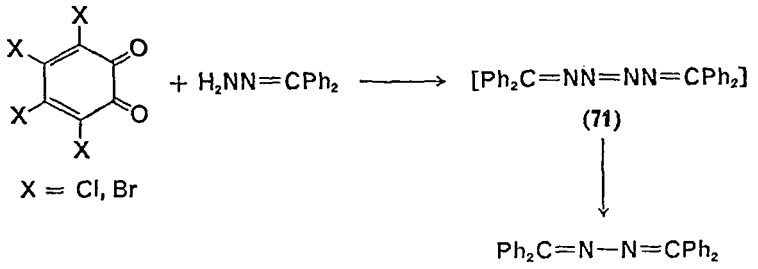
The rate of oxime formation has been studied in some detail with respect to both steric and electronic effects[253]. The steric influence of the rest of the quinone molecule has been used as a diagnostic tool in structure determination (see section V.A.1). A more recent study has involved the calculation of Hückel molecular orbital parameters for various substituted quinone monooximes and a discussion of the rates of dioxime formation by these compounds[254].

The reactions of 1,2-quinones with polyaryl hydrazones and diazo compounds (equation 201) have been studied quite extensively[255,256].



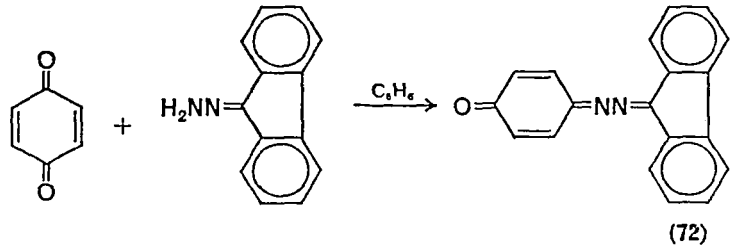
X = Cl, Br (201)

The corresponding hydroquinone is also a product of the reaction when a hydrazone starting material is used. This fact, along with other evidence, suggests that the diazo compound is an intermediate, if it is not a reactant[257]. Early experiments with tetrahalo-1,2-benzoquinones and benzophenone hydrazone produced benzophenone azine and the corresponding hydroquinone (equation 202); the intermediate **71** was suggested[258]. Similar



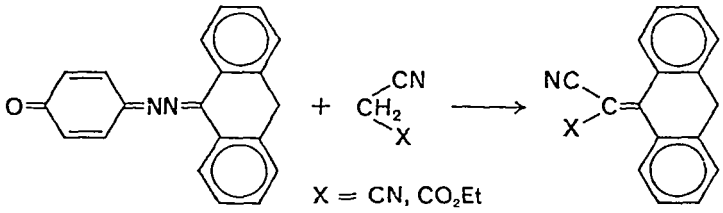
X = Cl, Br (202)

chemistry was observed between 1,4-benzoquinone and fluorenone hydrazone in ethanol; however, in benzene the quinone imine **72** is formed (equation 203)[258]. A reactant ratio of 1 : 2 produces the quinone bisimine



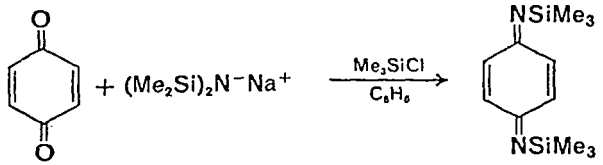
(72) (203)

and other hydrazones (e.g. xanthone and benzophenone) show somewhat similar, but not identical, chemistry. The monoimine has been shown to be an intermediate of some promise in the synthesis of certain alkenes (equation 204)[259]. Finally, using ether as the solvent, the original reaction (equation 201) has been extended to a series of substituted benzophenones[260] and other modifications explored[261–264].



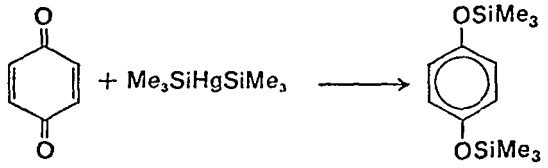
(204)

An interesting silicone-containing compound has been prepared (equation 205)[265]. The product is very reactive (light, air and moisture), but can be purified by sublimation.



(205)

Two groups announced almost simultaneously the reductive silylation of quinones with bis(trimethylsilyl) mercury (equation 206)[266,267]. The

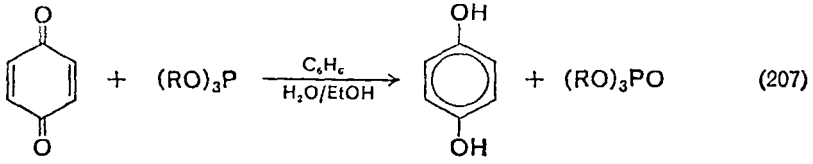


(206)

reaction takes place with 1,2- and 1,4-naphthoquinone as well as simple ketones such as acetone and cyclohexanone. The yields for the quinones are quite satisfactory. Some evidence is presented for a radical intermediate, but the possibility of a molecular reaction leading directly to product is also presented[267].

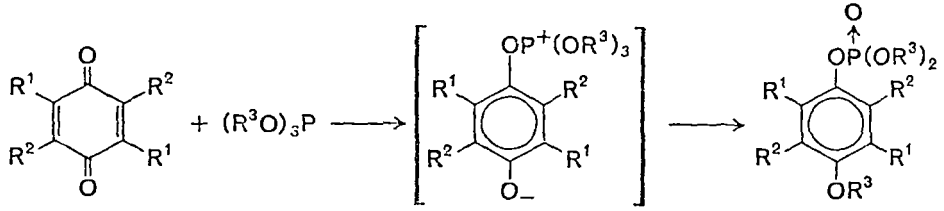
B. Addition of Tertiary Phosphines and Related Compounds

A very active area of quinone carbonyl chemistry has involved their interaction with tertiary phosphines. In the first paper of an extensive and detailed study Ramirez and Dershowitz[211] reviewed and criticized the earlier work in the field. Much of the chemistry studied deals with redox questions and will not be treated in this chapter, but both carbonyl and nuclear addition and substitution reactions of interest also emerged (see section II.E.5). For example, it was shown that, in the presence of water, the trialkyl phosphites can serve as efficient reducing agents for quinones (equation 207)[268]. However, when the reaction is carried out in anhydrous



(207)

benzene, the proposed intermediate **73** can undergo the rearrangement reaction shown in equation (208). The product, **74**, can be hydrolysed to the hydroquinone mono-ether. Dialkyl phosphites undergo very similar reactions with chloranil, which are accelerated by light (360–370 nm)[269].



R^1 = H, Cl, Me
R^2 = H, Cl
R^3 = Me, Et

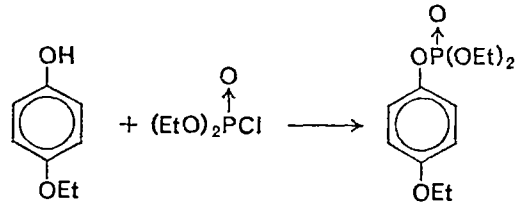
(73) (74)

(208)

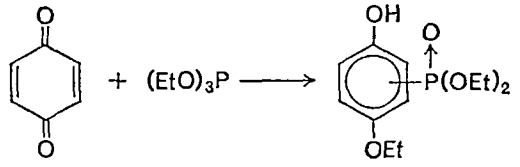
A more detailed report of this useful *O*-alkylation procedure revealed evidence of a stepwise intermolecular mechanism and the intermediate **73**[270]. This intermediate is analogous to that strongly suggested by the evidence from experiments in the triphenylphosphine case (see section II.E.5). It also allows a sensible explanation of the reduction cited above and the formation of very small amounts of diether.

The reactions of trialkyl phosphites with 1,4-benzoquinones bearing few substituents also lead to the hydroquinone mono-ethers under anhydrous conditions[271]. In the presence of water reduction again takes place. Duroquinone, the least potent oxidizing agent of the quinones examined, is not reduced.

These studies of the structure of adducts formed by quinones and trialkyl phosphites have been questioned and a somewhat deeper understanding of the reaction obtained[272]. The product obtained by Kukhtin and colleagues from the reaction of triethylphosphite and 1,4-benzoquinone did not have the same properties as that reported by Ramirez and Dershowitz. The product was also different from that obtained in an independent synthesis (equation 209). On the basis of this evidence, the structure **75** was proposed for the reaction product (equation 210). Identical products are obtained when the crude product is washed with base before vacuum distillation. Some additional interesting facts came out of this study: (i) the product obtained in the absence of base is a



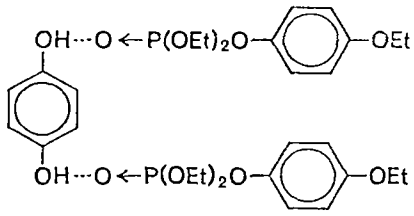
(209)



(210)

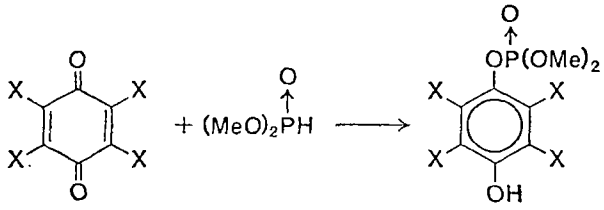
(75)

complex (**76**) that distils without decomposition over a one degree range, (ii) a similar reaction takes place with 1,4-naphthoquinones, and (iii) only the reaction with chloranil gave e.s.r. evidence of radicals.



(76)

Nishizawa has studied the related reaction of *O,O*-dimethyl phosphonate with 1,4-benzoquinone and chloranil (equation 211)[273]. With chloranil,

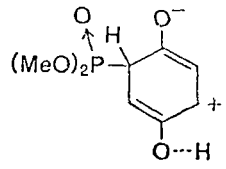


X = H, Cl

(211)

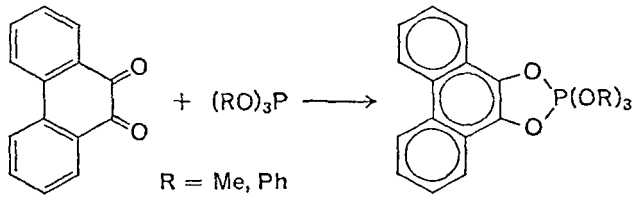
his product is identical to that obtained by Ramirez and Dershowitz[270]; however, he prefers a ring substituted intermediate (**77**) that rearranges rather than tautomerizes.

In a related area Ramirez and his students have studied the reactions of trialkyl and triaryl phosphites with α-diketones including 1,2-quinones[274]. Crystalline 1:1 adducts were obtained with 9,10-phenanthrenequinone (equation 212) and biacetyl. The assignment of the



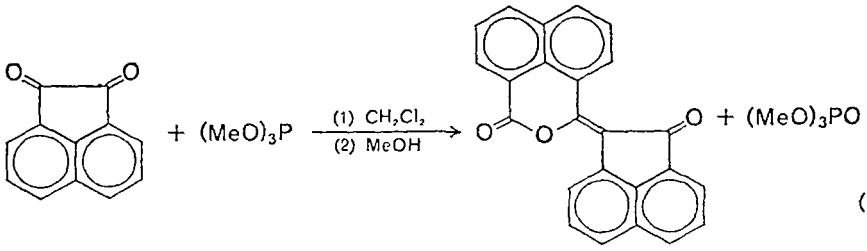
(77)

unusual structure containing a pentacovalent phosphorus was made on the basis of spectral and dipole moment studies. The structures of these and related compounds have been discussed in detail and supported in a later publication[275] and by other authors[276].



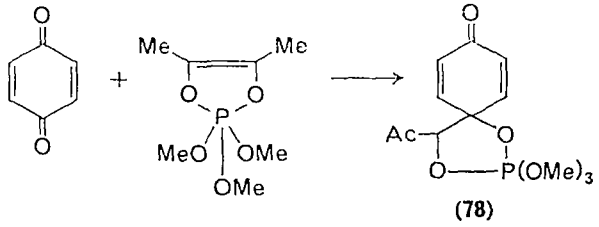
R = Me, Ph (212)

The chemistry of these adducts, especially their reactions with other quinones, is interesting. When two moles of acenaphthenequinone react with trimethyl phosphite a 2:1 adduct is formed. The adduct is cleaved in hot methanol to give the enol lactone shown in equation (213)[277]. Similar reactions occur with biacetyl and a combination of these two α-dicarbonyl compounds[278].



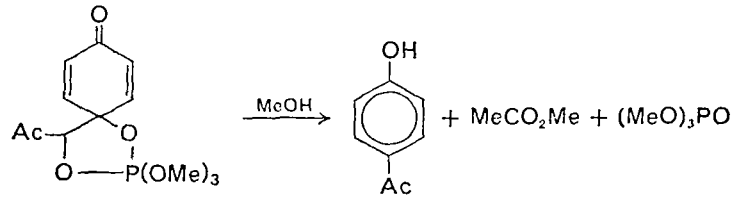
(213)

The reversible addition of simple inorganic ions to quinone carbonyl groups has played a significant role in our understanding of certain quinone reaction mechanisms (see section VIII.D). Recently the irreversible nucleophilic addition of carbon to a quinone carbonyl group has been reported[279]. The addition takes place between 1,4-benzoquinone and a pentaoxyphosphorane of the type we have been discussing (equation 214). The product **78**, like most of the pentacovalent phosphorous compounds, is sensitive to water, but can be recrystallized and undergoes an



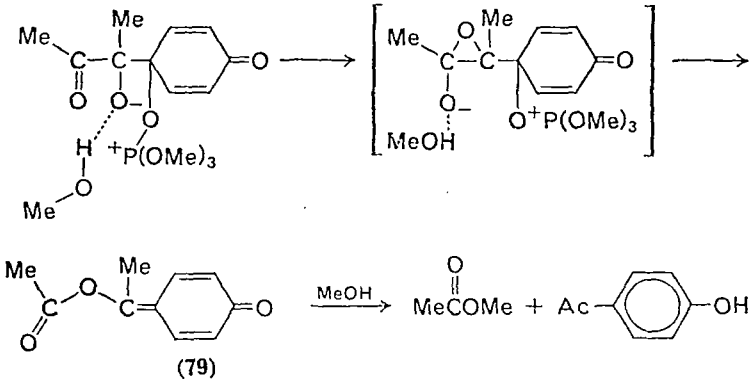
(78) (214)

interesting decomposition (equation 215). These studies have been expanded since the preliminary communication and the mechanism of the



(215)

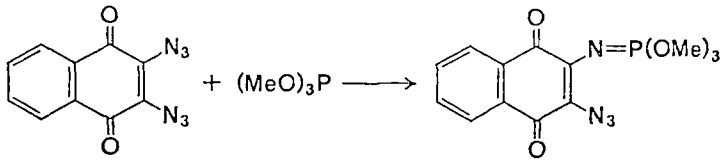
rearrangement explored[280]. Based on the facts obtained from the methanolysis of intermediate **78**, an enol-acetate intermediate (**79**) is proposed (equation 216). Hydrogen bonding by the methanol is clearly indicated because the reaction is much slower in ethanol and does not take



(79) (216)

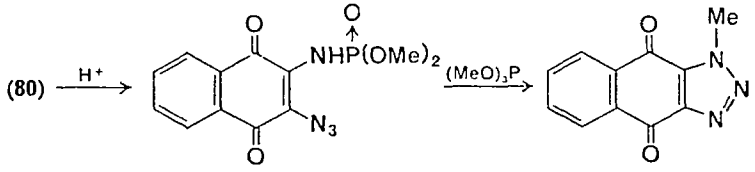
place in *t*-butyl alcohol. The loss of the stable trimethyl phosphate provides an efficient driving force for the reaction. This reaction also was observed with 1,4-naphthoquinone.

When phosphites are given a choice between carbonyl and azido groups as reactive sites in 2,3-diazido-1,4-naphthoquinone the latter is favoured[281]. In only one instance was a useful product obtained; the usual result being a very low yield and intractable oil mixtures (equation 217).



(80) (217)

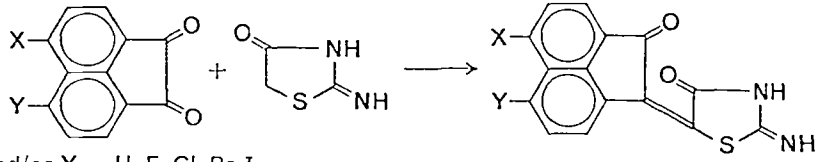
Compound **80** can be hydrolysed with acid to give **81** which also reacted with trimethyl phosphate to give a fair yield of a known heterocycle (**82** in equation 218). This reaction, and a similar one involving triphenylphosphine, is curious because it appears to involve the loss of a single nitrogen atom from an azide group.



(81) (82) (218)

C. *Brief Notes*

(1) In hot acetic acid pseudothiohydantoin will condense with acenaphthenequinone and various halogen derivatives in excellent yield (equation 219)[282]. As was pointed out above, acenaphthenequinone is in fact an α-diketone.

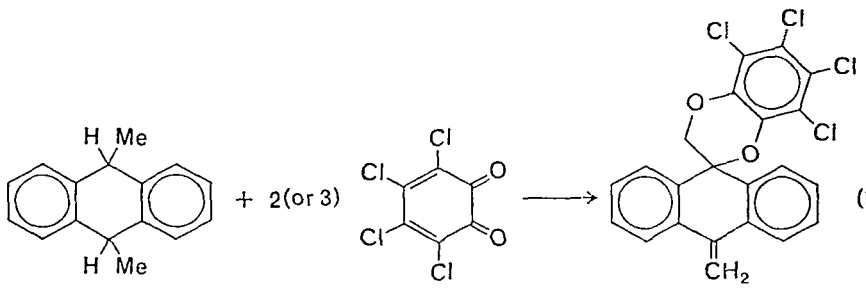


X and/or Y = H, F, Cl, Br, I (219)

(2) A good deal of interest exists concerning the quinodimethanes or *p*-xylylenes. One recent method that combines their synthesis and evidence for their existence involves the use of high-potential quinones (equation 220)[283]. The spectra, elemental analysis and ozonolysis products all confirm the product structure, **83**.

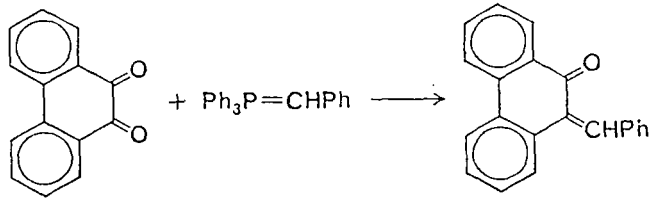
(3) The Wittig reaction of ylides has been applied to quinones (equation 221)[284, 285].

Under slightly different conditions the product undergoes what appears to be a subsequent Michael addition with a second mole of ylide followed by cyclization (equation 222).

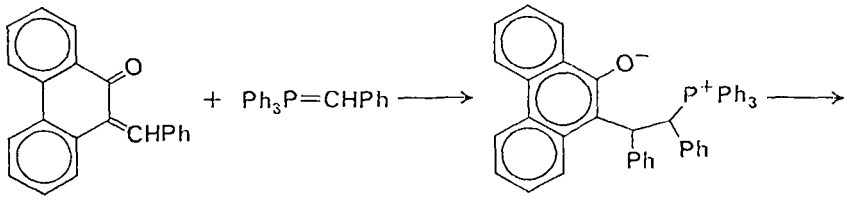


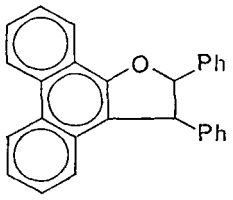
(220)

(83)



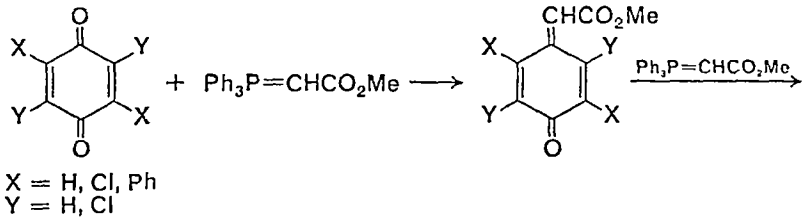
(221)

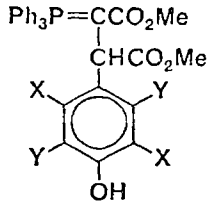




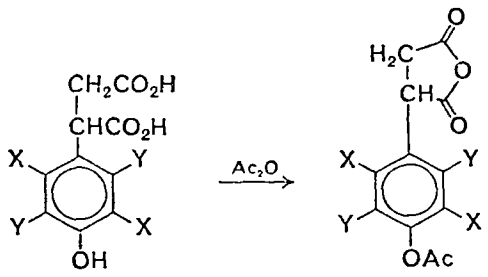
(222)

The application of the Wittig reaction to quinones has been expanded considerably by Bestmann and Lang who studied the addition of a methyl acetate residue to 1,4-benzoquinone[286]. As indicated in equation (223), quite similar chemistry was found in the initial phases of the reaction sequence. Further treatment of **84** produced *p*-hydroxyphenyl dicarboxylic acid derivatives (equations 224 and 225). In this same study it was shown that the Wittig reaction of 1,2-benzoquinones can lead to cyclic diethers analogous to those described earlier in this section (equation 226). A final note concerning the Wittig reaction with 1,2-quinones involves an interesting diene ylide and leads directly to cyclized product (equation 227)[287].





(84) (223)



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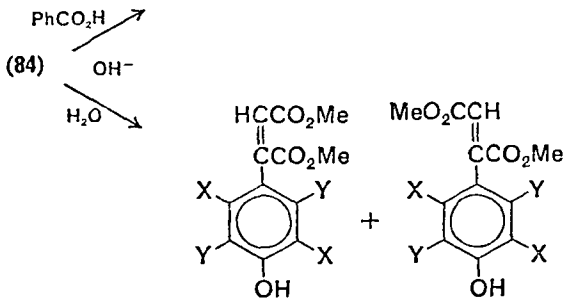

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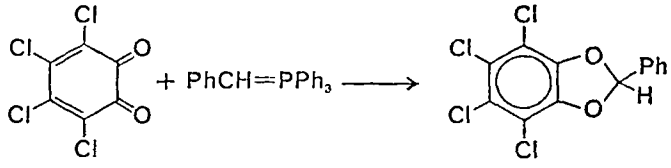

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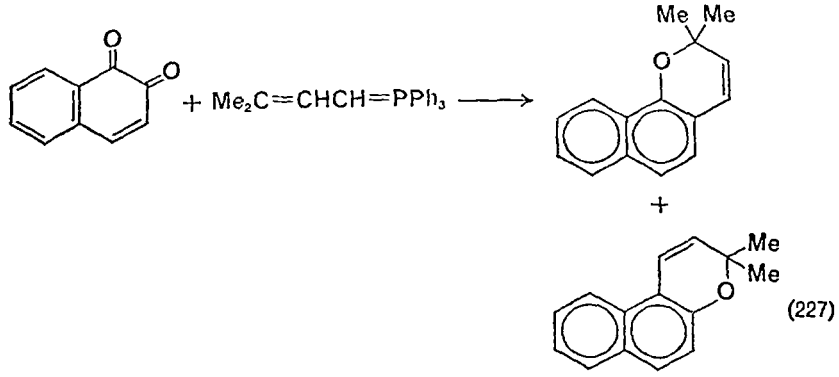
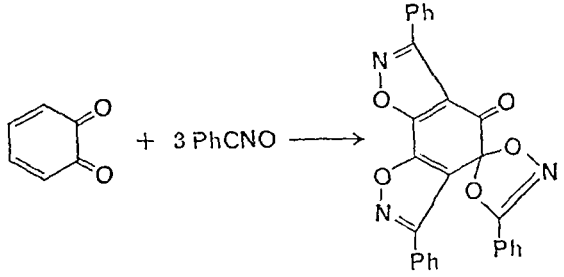


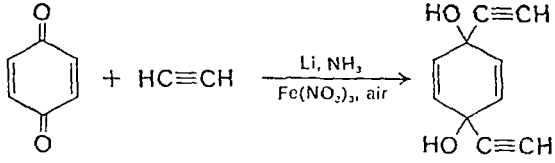
(227)

(4) Benzonitrile oxide will add to 1,2-quinones to produce rather complex heterocycles of the type shown in equation (228)[288]. The product shown is the only one found with 1,2-benzoquinone, but with 1,2-naphtho- and 9,10-phenanthrenequinone it was possible to isolate intermediates in which only the carbonyl groups had been attacked. These results are contrary to an earlier report by Awad and collaborators[289].



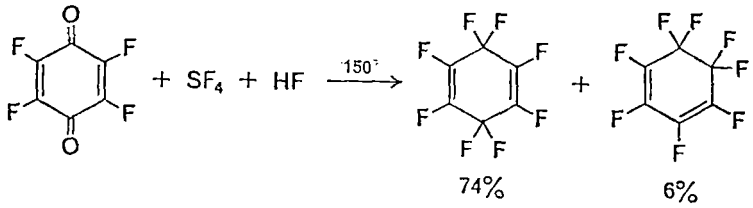
(228)

(5) The yield in the addition of acetylene to the carbonyl groups of 1,4-benzoquinone has been improved (> 70%) through the use of lithium amide (equation 229)[290].



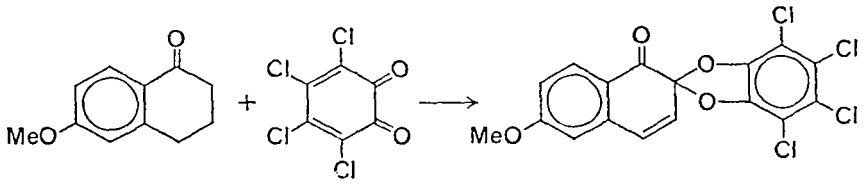
(229)

(6) The synthesis of perfluorocyclohexadienes can be accomplished by the treatment of fluoranil with a mixture of hydrofluoric acid and sulphur tetrafluoride (equation 230)[291].



(230)

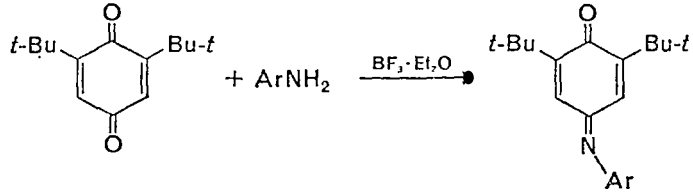
(7) A surprising reaction, formally related to the synthesis of cyclic diethers from diazo compounds, is the reaction of tetrachloro-1,2-benzoquinone with 6-methoxy-1-tetralone (equation 231)[292]. In a later and more



(231)

detailed study it was shown that the reaction is fairly general for tetralones and naphthols and that the most likely reaction pathway involves the dehydrogenation of the tetralone to a naphthol[293].

(8) An interesting exception to the normal mode of aniline addition to quinones (see section II.C) leads to a very useful preparation of highly hindered azomethine dyes (equation 232)[294]. In the case of *p*-phenylene-



(232)

diamine either the mono- or the bis-dye can be prepared. Electron-donating substituents facilitate the reaction and only the highly hindered quinones can be used.

IV. THE ADDITION OF RADICALS TO QUINONES

A. Polymerization Chemistry

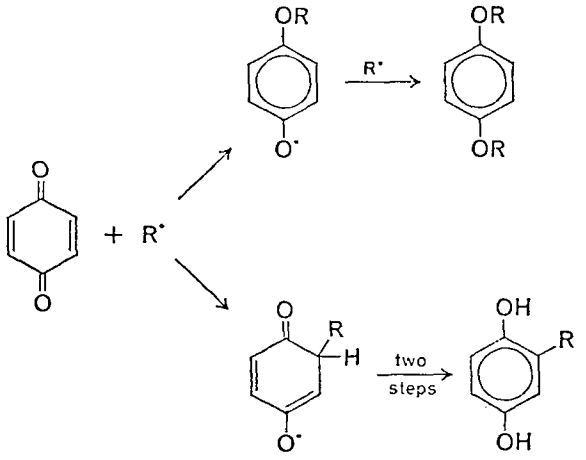
A sizeable literature concerning the chemistry of radicals and quinones has centred on quinones as inhibitors in radical polymerizations. Most of these studies have been concerned with the kinetics and the nature of the polymeric product, but some insight on quinone chemistry has been obtained. With styrene, the fate of the quinone was first thought to

involve either reduction or incorporation in the polystyrene being formed[295]. These ideas were discredited by the yellow colour of the product, the fact that the product(s) are formed at a time when essentially no polymer is formed and finally, its retention in solution at the later polymerization stage. It was then suggested that the quinone must be consumed by reaction with some simple, non-polymeric material[296]. Admittedly, it was not possible to obtain a pure sample of any reaction product.

The relationship between inhibition and copolymerization has been discussed and the suggestion made that slight changes in resonance stabilization of the intermediate radicals control the type of reaction observed[297]. The comparison made was of the difference between maleic anhydride (a superb copolymer participant) and 1,4-benzoquinone (a strong inhibitor) and these observations in spite of the compounds' obvious formal similarity in structure. This line of argument is in accord with radical addition to the quinone as an important step in inhibition.

Somewhat similar conclusions were reached by Price from a study of polystyrene formation in the presence of chloranil[298]. The isolated polymer contained one chloranil residue per polymer molecule and essentially none when the chloranil was added after polymerization, but before isolation. However, in this case there was no evidence of inhibition and it was concluded that chloranil acted as a chain-transfer agent.

On the basis of kinetic data for the inhibition and retardation of the rate of peroxide-initiated polymerization of styrene, Cohen also suggested a combination of carbon and oxygen alkylated products (equations 233 and 234)[299]. The alkylhydroquinone is, of course, free to be re-oxidized and to serve as an inhibitor again.

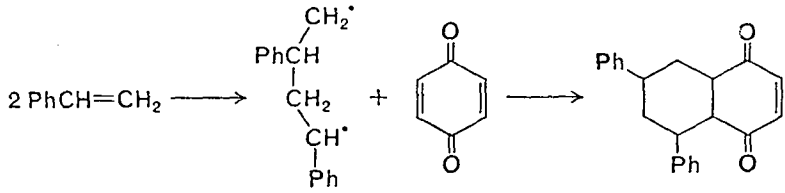


(233)

(234)

In a study designed, in part, to examine the chemical fate of the quinone inhibitor, the monomer allyl acetate was chosen[300]. The short chain length in this polymerization should result in a large number of quinone fragments being attached to the polymer. In a careful examination of the reaction mixture, no quinone could be recovered or found in solution. Cleavage of the polymer with hydriodic acid or cleavage of various polymer fractions gave hydroquinone product. These observations showed that all of the quinone is bound in the polymer. Examination of the u.v. and visible spectra showed that a combination of carbon and oxygen alkylation is most probable.

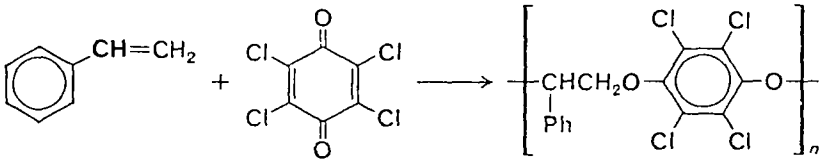
The first report of the isolation of a quinone inhibitor product occurred in the thermal polymerization of styrene[301]. This product corresponded approximately to two molecules of styrene and one of 1,4-benzoquinone. These observations were interpreted in the Diels–Alder fashion shown in equation (235).



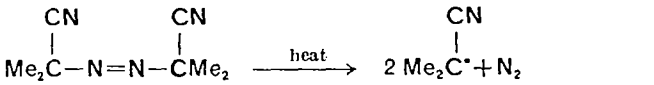
(235)

It has been shown that chloranil will copolymerize with styrene in the presence of benzoyl peroxide[302]. The polymeric product contains three moles of styrene to two moles of chloranil. Degradative experiments with hydrobromic acid yielded strong evidence that the quinone is bound to the polymer by hydroquinone ether linkages (equation 236). Thus, at least in this particular case, oxygen attack is observed. Of course, this is not an example of inhibition.

The polymerization of methyl methacrylate can be conveniently initiated with α,α'-azoisobutyronitrile through the thermally generated 2-cyano-2-propyl radicals (equation 237)[303]. The importance of inhibitor–initiator termination and especially of carbon–oxygen bond formation

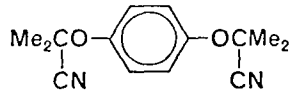


(236)



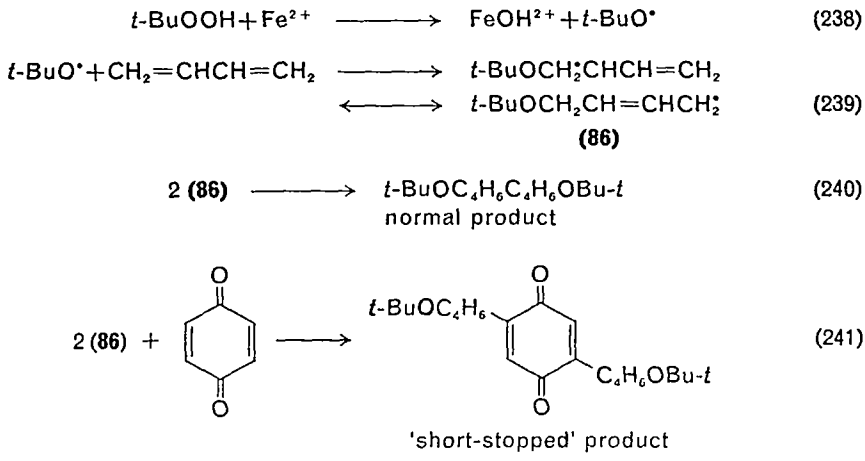
(237)

with quinones was established by the formation of the hydroquinone di(cyanoalkyl)ether (**85**).



(85)

A somewhat different view of the stage at which inhibition takes place is based on evidence supplied by Kharasch and colleagues[304]. When *t*-butyl hydroperoxide and ferrous salts initiate the polymerization of 1,3-butadiene at low temperature, it is possible to inhibit completely the reaction with quinones (equations 238–241). The use of either 1,4-benzoquinone or hydroquinone alone led to a sluggish reaction and the need for large amounts of ferrous ion. Quinhydrone produced a very rapid reaction.



t-BuOOH + Fe^{2+} ⟶ $FeOH^{2+}$ + *t*-BuO• (238)

t-BuO• + CH_2=CHCH=CH_2 ⟶ *t*-BuOCH$_2$CHCH=CH_2

⟷ *t*-BuOCH$_2$CH=CHCH$_2$ (239)

(86)

2 **(86)** ⟶ *t*-BuO$C_4H_6C_4H_6$OBu-*t* (240)

normal product

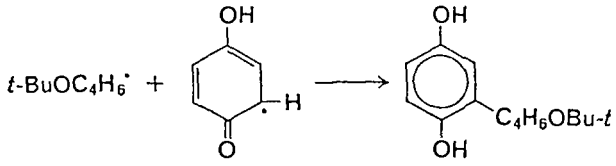
2 **(86)** + ⟶ *t*-BuOC_4H_6 C_4H_6OBu-*t* (241)

'short-stopped' product

The following scheme was proposed to account for these observations (equations 242–244).

It was found that 2-methyl-1,4-benzoquinone reacts in a similar fashion, but its semiquinone combines with only one *t*-butoxybutylene radical. Finally, chloranil was shown to terminate through reaction of the oxygen of the semiquinone (equation 245).

These results are consistent with the earlier work of Breitenbach and Renner[302] showing the formation of a copolymer of styrene and chloranil. More recently Kice has arrived at the same conclusion in the polymerization of methyl methacrylate[305]. He found evidence for very little copolymerization when 1,4-benzoquinone is the inhibitor.



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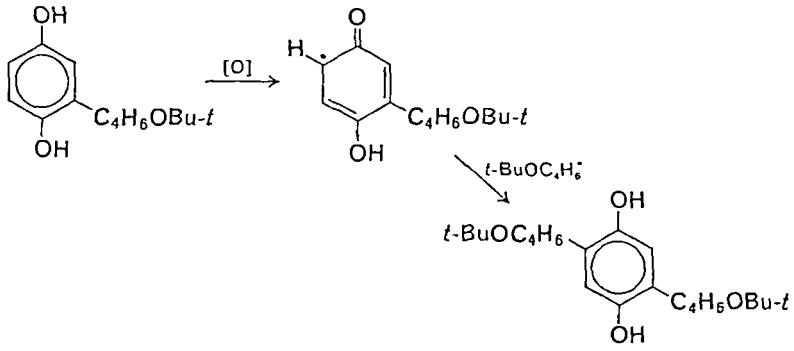
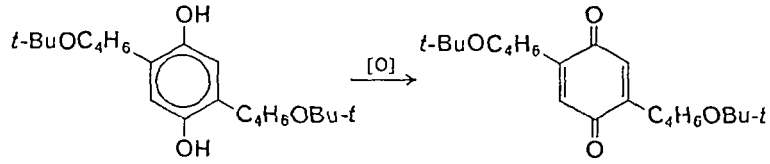


(243)



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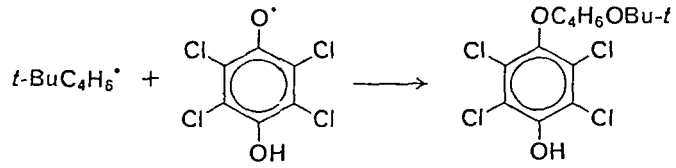


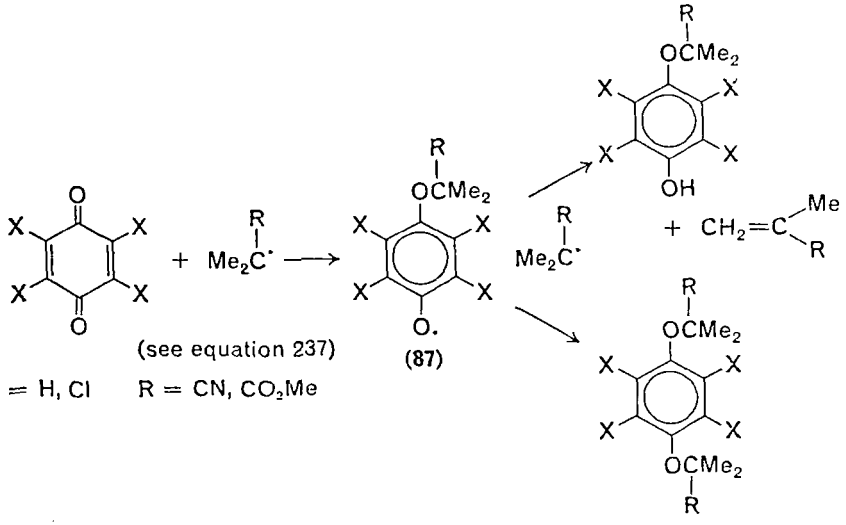
(245)

The studies cited thus far appear to be correct, but give a misleading impression of the fate of 1,4-benzoquinone in polymerization reactions. The polymerization kinetics for both styrene and methyl acrylate appear to be best understood in terms of 1,4-benzoquinone, as well as chloranil, being incorporated in the small amount of polymer formed during the induction period or inhibition phase[306, 307]. The evidence once again points to reaction at oxygen.

B. Mechanism of Reaction with Simple Radicals

Interest in the effect of quinones on polymerization has stimulated study of the reactions of smaller, less complicated radicals. The widely used initiator α,α'-azoisobutyronitrile and its carbomethoxy analogue

have been generated in the presence of several quinones (equations 246 and 247)[308]. The aliphatic disproportionation products (methyl methylacrylate or methylacrylonitrile) were not isolated, but can be accounted

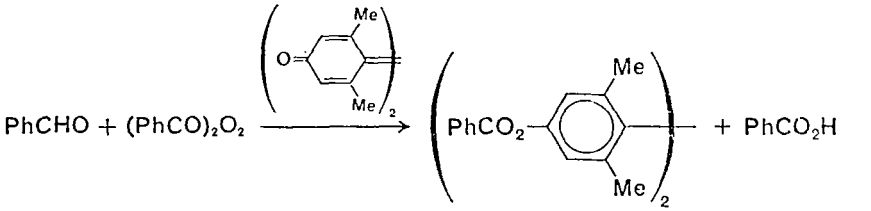


(246)

(247)

for by the high molecular weight material formed. The yields of the hydroquinone ethers were satisfactory considering the complexity of the system. Under similar conditions 2-methyl-1,4-naphthoquinone does not react.

A product isolated from the benzoyl peroxide oxidation of benzaldehyde, with a quinonoid retarder, is also consistent with the oxygen attack hypothesis (equation 248)[309].



(248)

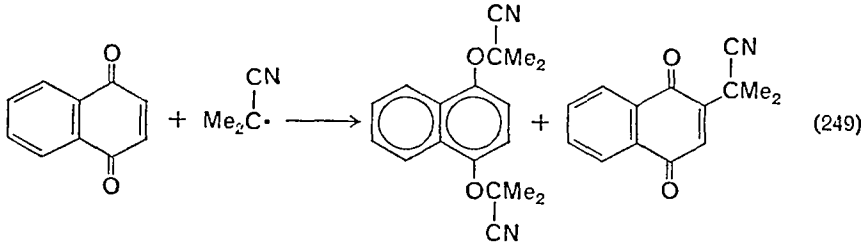
The study of quinones and 2-cyano-2-propyl radicals has been extended to a series of substituted quinones[310]. The data in Table 8 are given in crude yields because of difficulties in separation and purification. There is some correlation between the redox potential of the quinone and the extent of its reaction with the radical. Steric effects obviously play a role in some cases (e.g. 2,5-di-*t*-butyl-1,4-benzoquinone). The unreliability of the yield data reduces the strength of the argument, but there does seem

TABLE 8. Product yield and redox potentials for the reaction of 2-cyano-2-propyl radicals and 1,4-benzquinones[310]

Quinone substituent(s)	Yield (%)			Quinone redox	Phenol[b] critical oxidation
	Monoether	Diether	Dimer[a]	Potential (V)	Potential (V)
Cl_4	17	67	44·1	0·703	—
2,5-$(AcO)_2$	23	32	18·0	—	—
None	56	10	25·7	0·711	1·089
2-Me	31	46	26·0	0·653	1·037
2,6-Me_2	8·6	41	37·6	0·600	0·985
2,5-Me_2	5·9	35	47·5	0·597	0·985
2-Me-5-*i*-Pr	1·0	32	49·2	0·589	—
2,5-$(EtO)_2$	2·3	26	57·8	0·480	0·619
2,5-*t*-Bu_2	0	0	—	0·554	—
Me_4	0	0	67·0	0·466	—

[a] Tetramethylsuccinonitrile.
[b] Of the corresponding monohydric phenol; e.g. 1,4-benzoquinone–phenol.

to be a correlation between ratio of mono : di ethers and the critical oxidation potential of the corresponding monohydric phenol. This potential can be supposed to be a measure of the stability of the aryloxy radical, **87**. The polycyclic quinones react only slightly, if at all, as would be expected from their redox potentials. A small amount of ring addition is found with 1,4-naphthoquinone and 2,5-dimethyl-1,4-benzoquinone as well as ether formation (equation 249).

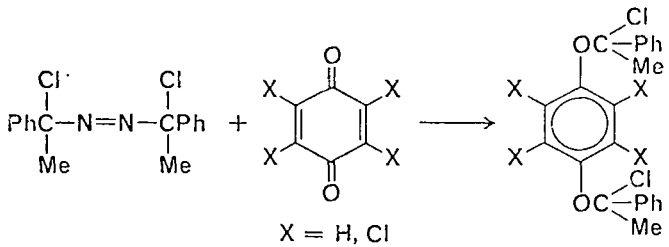


(249)

The conflicting evidence regarding product structure in quinone termination of polymerization reactions (i.e. carbon–carbon versus carbon–oxygen bond formation) has been explained as the result of our using incomparable studies of very reactive radicals (Me· and Ph·) and much less reactive radicals (growing polymer chains). A detailed study of the methyl affinities of quinones adds strength to this argument[311,312].

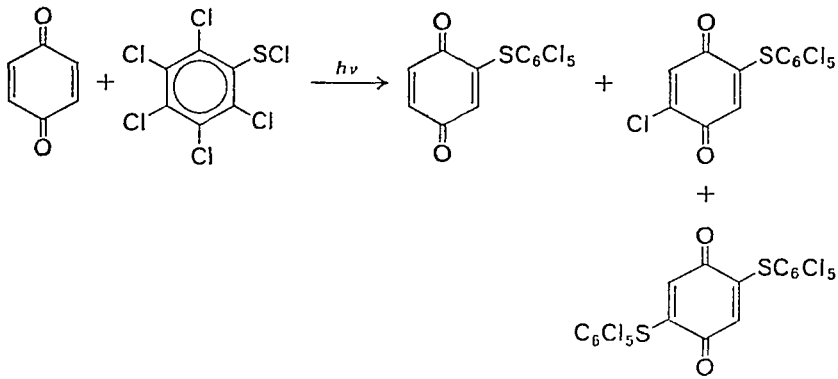
Szwarc and collaborators suggest that the isolation of products may not give unambiguous answers concerning the initial point of radical attack. They prefer to apply a kinetic argument based on the rate of reaction of methyl radicals with various substituted quinones. It was found that predictions based on both electronic and steric effects are consistent only with the observed rates for carbon–carbon bond formation; i.e. ring addition. It was also determined that styryl radicals are less than half as reactive as methyl radicals under the conditions employed.

A few reports of the reactions of various radicals with quinones have appeared, but none of these could be considered detailed studies. For example, the thermal decomposition of bisazo compounds to form radicals has been expanded slightly (equation 250)[315]. The ether products hydrolysed readily in aqueous ethanol to give the appropriate hydroquinone and acetophenone.



(250)

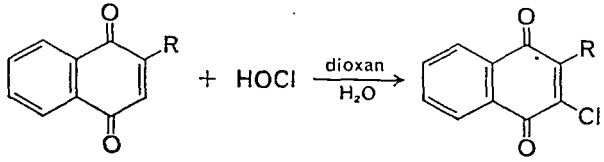
Earlier the possibility of radical addition of thiols was mentioned as a possible alternative to nucleophilic addition (see section II.B.2). While such a mechanism has been invoked, the only promising work is that of Kharasch and Ariyan with sulphenyl chlorides (equation 251)[314]. The



(251)

reaction does not take place in the dark, but no e.s.r. signal was found. The structure of the disubstituted quinones was assumed to be 2,5.

Aqueous hypochlorous acid has been reported to cause the epoxidation of quinones, but a careful examination of such reaction mixtures revealed that no reaction takes place[315]. When solution is obtained with added dioxan, the quinone is converted to the chloro derivative in good yield (equation 252). With peroxide-free solvents very low yields were obtained.



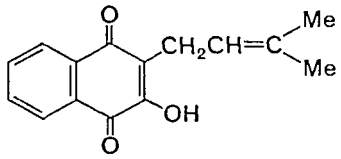
R = H, Me (252)

The *in situ* generation of hypochlorous acid converted 1,4-naphthoquinone to an approximately equimolar mixture of 2-chloro- and 2,3-dichloro-1,4-naphthoquinone.

C. Alkylation

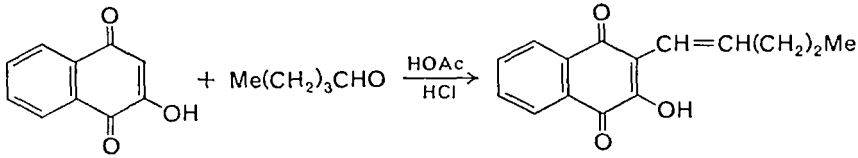
1. Historical introduction

The naturally occurring quinonoid compound lapachol **88** has held a great deal of interest for synthetic organic chemists over a very long



(88)

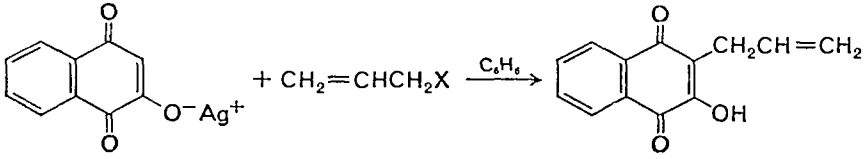
period of time[2,316]. Some of the earliest work was concerned with the structure of the alkyl side-chain and introduced the useful aldehyde alkenylation reaction (equation 253)[317].



(253)

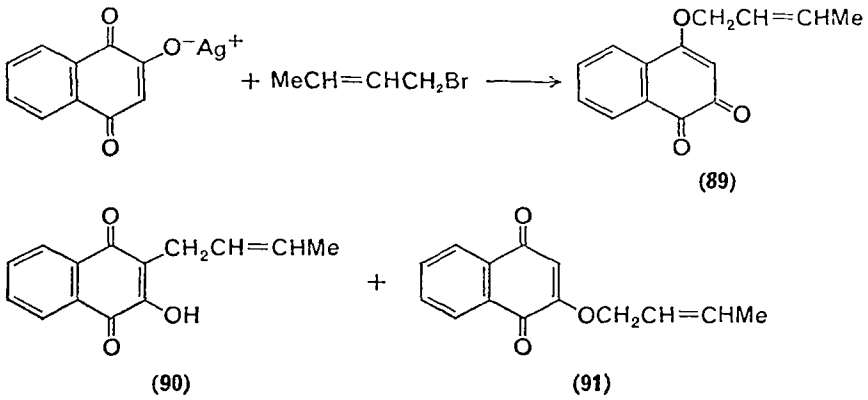
In his studies of the tautomeric equilibrium of *ortho*- and *para*-quinones, Fieser found that very reactive unsaturated and benzylic alkyl halides react with the silver salt of 2-hydroxy-1,4-naphthoquinone to produce 2-alkyl-3-hydroxy derivatives (equation 254)[318]. The reaction was regarded

as 1,2-addition followed by the elimination of silver halide. Alkylation on oxygen also takes place in most instances. The detailed reasons for the amounts of *O*- and *C*-alkylation are undoubtedly more complex than the reactivity of the halide.



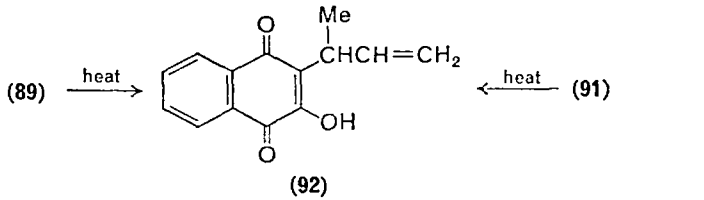
(254)

The alkylation of the silver salt of 2-hydroxy-1,4-naphthoquinone has also been used as a synthesis of lapachol[319]. The question of direct alkylation versus Claisen rearrangement was answered by the synthesis of the two possible *O*-crotyl ethers of 2-hydroxy-1,4-naphthoquinone (equation 255). The Claisen rearrangements of both **89** and **91** produce a



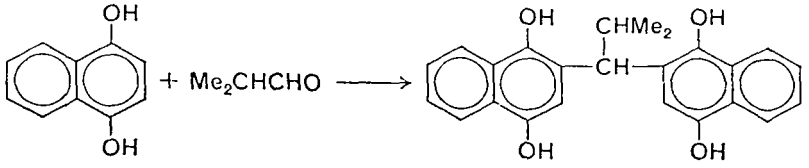
(255)

single compound, **92**, that is isomeric with the direct alkylation product, **90**. The change of structure in the Claisen rearrangement was already known[320] and the facts require a direct alkylation of the quinonoid ring.



(256)

The aldehyde alkenylation reaction (equation 253) is not general; 1,4-naphthoquinone is reduced and then converted to a product containing two hydroquinone residues (**93** in equation 257)[321]. Hooker had



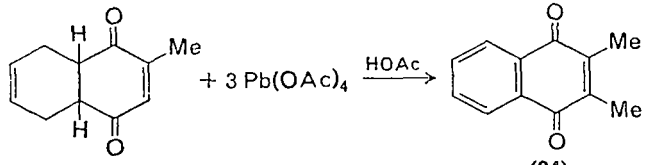
(257)

(93)

already reported that under certain conditions two moles of quinone can condense with aldehydes. In view of the rather extensive subsequent literature concerning these compounds, including their synthesis by independent routes, there seems to be little question of the correctness of the structures. It is probably significant that Fieser fails to mention Raudnitz and Puluj in the eleven posthumous Hooker papers he completed, wrote or edited[322].

2. Acyl peroxide alkylation

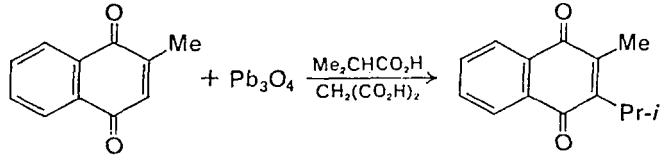
Fieser and his students have made extensive contributions to the techniques available for the alkylation of quinones. One of the earliest, perhaps one of the most important, is the remarkable methylation with lead tetraacetate (equation 258)[323]. The structure of product **94** was definitely



(258)

(94)

established and the generality of the reaction explored. The addition of an active-hydrogen compound permits smooth alkylation of 1,4-naphthoquinone under mild conditions and in quite reasonable yields. It is also possible to employ higher homologues of the lead salt and thus to introduce longer alkyl chains. These lead salts can be generated *in situ* (equation 259).

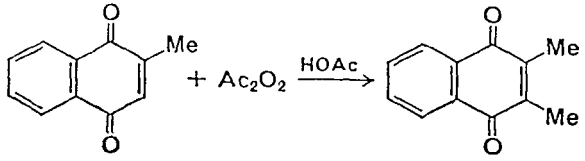


(259)

(95)

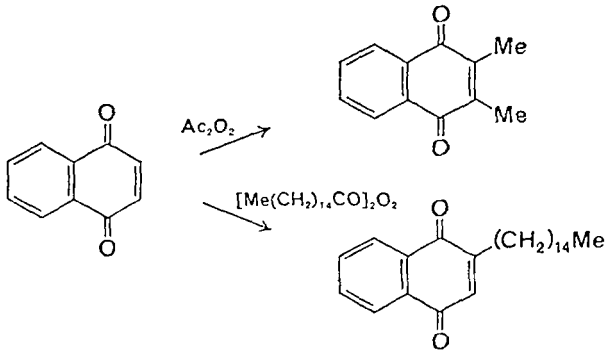
Treatment of 2-isopropyl-1,4-naphthoquinone with lead tetraacetate also produces **95**. It is interesting to note that the introduction of a methyl group adjacent to a larger alkyl group is subject to much more steric retardation than the reverse process (e.g. equation 259).

A later study of this methylation by lead tetraacetate, and alkylation with higher homologues, produced some interesting mechanistic evidence[324]. When 2-methyl-1,4-naphthoquinone is heated at 90–100°C in acetic acid with excess lead tetraacetate, no reaction occurs. Upon addition of a wide variety of materials gas is evolved, usually vigorously, and 2,3-dimethyl-1,4-naphthoquinone is formed. Included in the list of promoters are water, alcohols and hydrocarbons (e.g. benzene and cyclohexane). All of these, except *t*-butyl alcohol, promote the decomposition of lead tetraacetate to carbon dioxide and a neutral, flammable gas, thought to be ethane. Several of the observations concerning the reaction suggest that it might be related to the Kolbe reaction and led Fieser and Oxford to study alkylations with diacyl peroxides (equation 260). It was



(260)

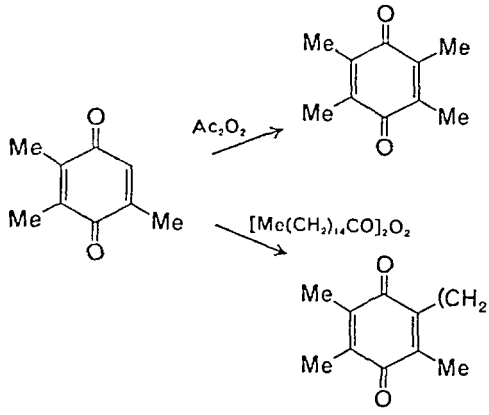
found that the method could be applied for the introduction of a wide variety of alkyl groups including some alkenyl or cycloalkenyl groups. The reaction is subject to a steric effect that makes it somewhat more selective with the higher acid peroxides (equations 261 and 262).



(261)

(262)

Alkylation can also be accomplished in the 1,4-benzoquinone series (equations 263 and 264). Methoxy groups appear greatly to reduce the reactivity of the quinone while hydroxy and bromo groups (on the basis of limited study) seem to enhance reactivity. The bromine atom may serve a very useful synthetic role as a blocking group (equation 265). The results obtained with dibenzoyl and dicinnamoyl peroxides were not promising, but might be improved by changing the experimental conditions.



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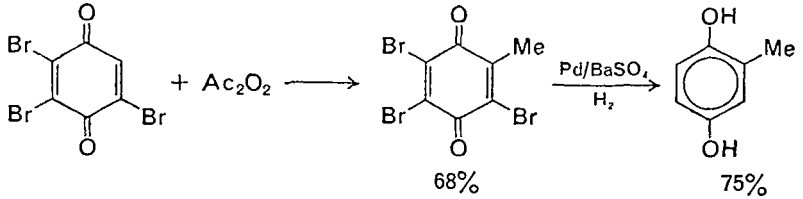
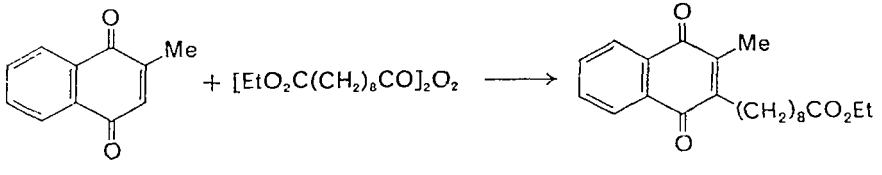
(264)



(265)

Finally, it is not necessary to purify the peroxides to achieve quite acceptable product yields. In general, the reagent was prepared by the reaction of the appropriate acid chloride with excess sodium peroxide in ligroine.

A large number of applications of the peroxide alkylation method, some with important extensions, have been made by Fieser and collaborators. For example, the introduction of alkyl groups ending in other functional groups has been accomplished (e.g. equation 266)[325]. The synthetic aspects of structure determination for some interesting natural products have been achieved (e.g. equation 267)[326]. It may be



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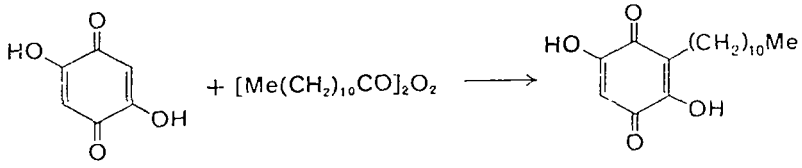
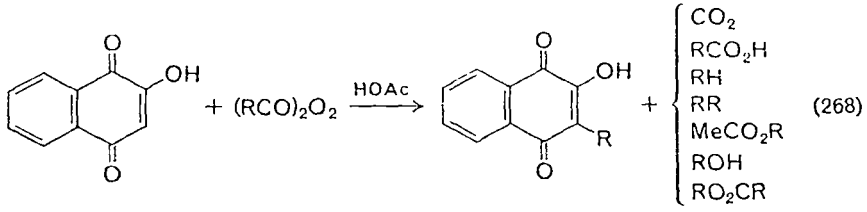


(267)

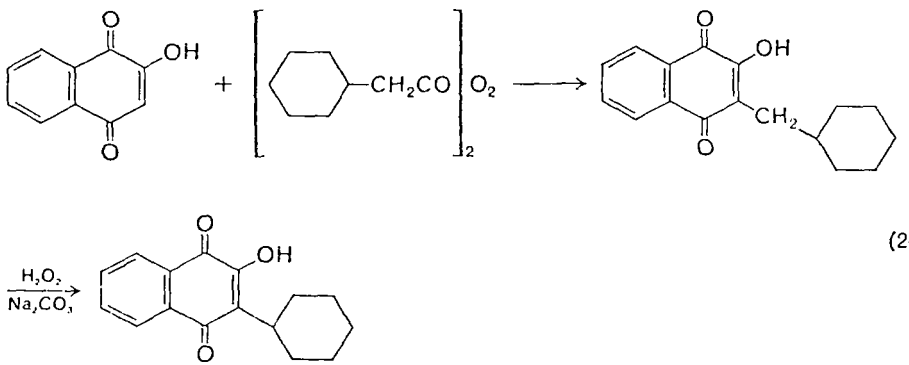
noted that there are limitations of unknown extent in this alkylation procedure; Fieser and Chamberlin reported low yields and difficulty in obtaining crystalline product, especially in cases involving long, unsaturated hydrocarbon chains.

The magnificent effort made to find naphthoquinones with antimalarial activity was, to a very large extent, centred on the alkylation reactions with acyl peroxides[327]. While the main purpose of this work was the synthesis, characterization and testing of potential drugs, the observations made are useful in understanding the alkylation reaction. Some of the by-products have been identified (equation 268) and clearly



(268)

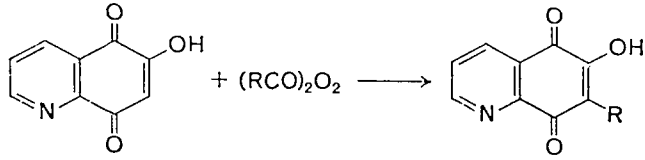
conform with the expected radical process. Four major structural limitations were found: peroxides of α-carbon branched chain, cycloalkane, aromatic and benzylic carboxylic acids all gave very low yields, if they reacted at all. A wide variety of substituents and functional groups may be included in the rings and chains without interfering with the peroxide alkylation. The compounds cited above as being difficult to prepare directly were usually obtained in quite reasonable yield by the synthesis of the next higher homologue and the application of the Hooker oxidation (equation 269)[322,328].



(269)

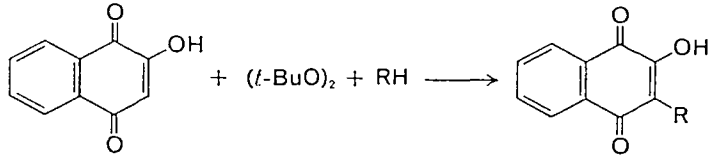
The heterocyclic quinones 6(or 7)-chloro- and 6-hydroxy-5,8-quinolinequinone have been alkylated using the diacyl peroxide method (equation

270)[329-332]. A very wide range of R groups has been employed and the yields have been fair to good in most cases. The 7-hydroxy isomer has also been used in one instance.



(270)

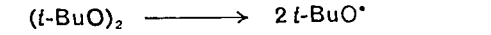
A very interesting recent kinetic study has led to the synthetic complement of Fieser's alkylation reaction[333]. The decomposition of *t*-butyl peroxide in the presence of a hydrocarbon and 2-hydroxy-1,4-naphthoquinone leads to the 3-alkyl-2-hydroxy-1,4-naphthoquinone (equation 271). The chief synthetic limitation of this reaction lies in the fact that



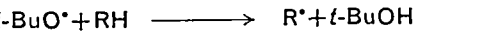
(271)

several products will be formed if hydrogen abstraction from the hydrocarbon leads to more than one radical. For simplicity in the kinetic study, cyclohexane and potential benzylic radicals were chosen and they gave excellent yields of product. The 3-alkyl products obtained in these model cases are just those most difficult to prepare by the earlier route.

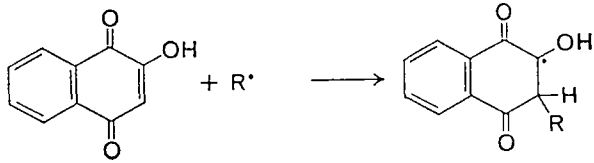
The proposed mechanism involves the radical-chain process shown in equations (272) to (276) (plus the usual termination reactions). The rate of decomposition of *t*-butyl peroxide was studied both with an excess and with less than a stoicheiometric amount of 2-hydroxy-1,4-naphthoquinone. In the former case the observed rate was very much faster than that of the peroxide alone. With a limited amount of quinone, two rates were found: a fast initial rate when the quinone was present and a second



(272)

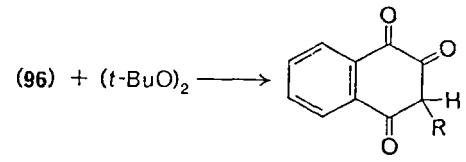


(273)

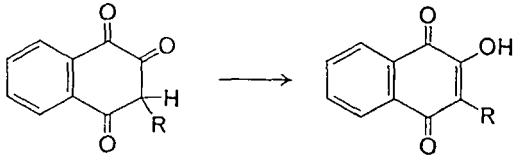


(274)

(96)



(275)



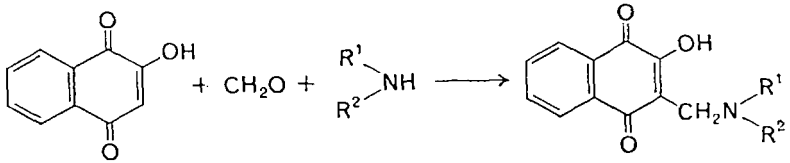
(276)

slower rate close to that of the peroxide alone. These observations are consistent with the proposed mechanism which requires the following rate expression for peroxide loss (equation 277):

$$-\frac{d\,[\text{peroxide}]}{dt} = k[\text{peroxide}] + k[\mathbf{96}]\,[\text{peroxide}] \tag{277}$$

3. Related alkylation reactions

As yet another aspect of their antimalarial search, the Harvard–Abbott team investigated the application of the Mannich reaction (equation 278)[334]. Amines that gave the most satisfactory results were primary,

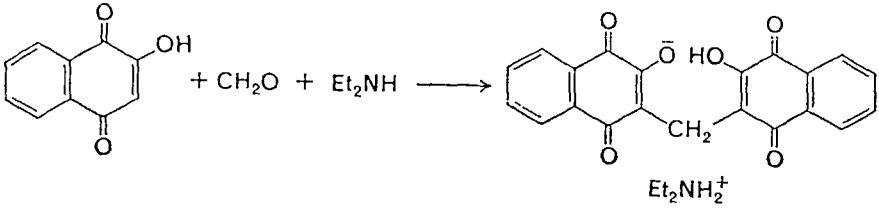


(278)

R¹, R² = H, alkyl, heterocyclic ring

secondary and alicyclic. Most of the products were stable enough to be recrystallized in the usual manner, but in some cases, e.g. when R^1 and R^2 make up a morpholine ring, the purification was effected by solution in dilute hydrochloric acid and precipitation with cold sodium acetate solution. Some very strange observations were made in this study; for example, dimethylamine and piperidine gave excellent yields of product while diethylamine gave only the salt of 3,3′-methylene-bis-2-hydroxy-1,4-naphthoquinone (**97** in equation 279). Both mono- and diammonium salts appear to be formed.

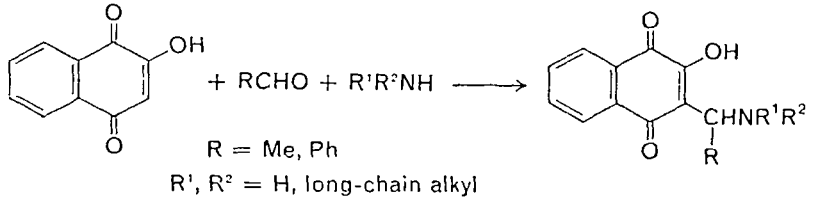
A later study was directed at placing bulkier groups on the nitrogen in order to improve the antimalarial activity[335]. Under milder conditions than reported earlier excellent yields of products were obtained with



(279)

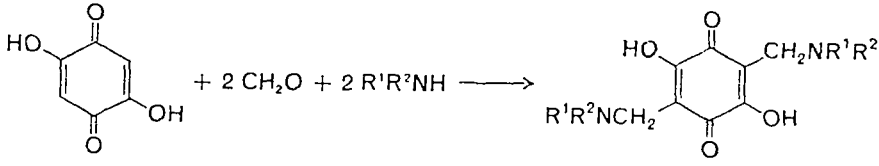
(97)

C_8–C_{18} *n*-alkyl primary amines. The products yielded crystalline hydrochlorides that were recrystallized from ethanol. The higher secondary amines gave only analogues of **97** and anilines gave insoluble products that were not characterized. It was found that acetaldehyde and benzaldehyde can be used in place of formaldehyde, while propionaldehyde and crotonaldehyde cannot (equation 280). The reaction took place very



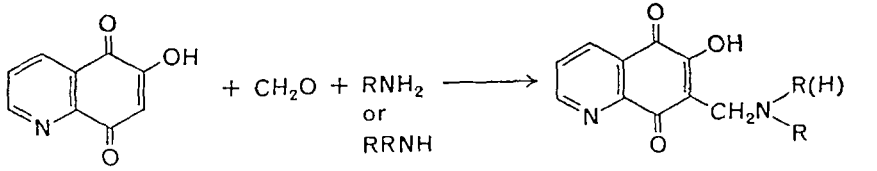
(280)

readily with 2,5-dihydroxy-1,4-benzoquinone and gave the 3,6-bis product (equation 281).



(281)

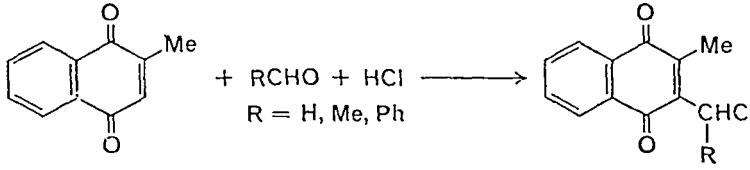
The Mannich reaction of primary and secondary amines has been applied to 6-hydroxy-5,8-quinolinequinone with reasonable success (equation 282)[329]. Once again diethylamine showed abnormal behaviour and failed to produce the expected product.



(282)

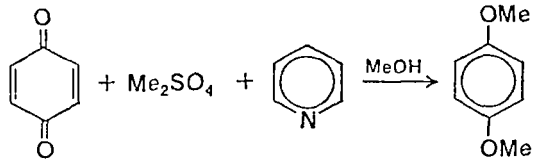
A somewhat similar reaction has been used to prepare chloromethyl derivatives of 1,4-naphthoquinones (equation 283)[336]. The scope of the reaction is severely limited because 1,4-benzoquinones prefer to add HCl

rather than chloroalkylate and very few aldehydes are useful. In fact, only certain combinations of quinone and aldehyde appear to react cleanly. The 2,3-bis-chloromethyl product is obtained from 1,4-naphthoquinone and formaldehyde.



(283)

An example of reductive *O*-methylation of quinones has been reported[337]. The reaction (equation 284) is not general and roughly the yield is a function of the redox potential of the quinone as indicated in Table 9.

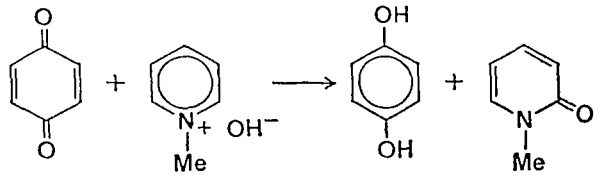


(284)

TABLE 9. Reductive methylation of quinones[337]

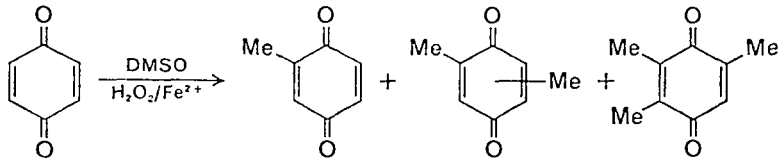
Quinone	Redox potential (V)	Yield (%)
1,4-Benzoquinone	0·711	74
2,5-Diphenyl-1,4-benzoquinone	0·673	79
2-Methyl-1,4-benzoquinone	0·657	60
2-Methyl-5-isopropyl-1,4-benzoquinone	0·589	30
1,2-Naphthoquinone	0·576	10
1,4-Naphthoquinone	0·483	14
2,3,5,6-Tetramethyl-1,4-benzoquinone	0·480	0
2,5-Dimethoxy-1,4-benzoquinone	0·470	0
2,5-Dihydroxy-1,4-benzoquinone	0·434	0
Retenequinone	0·410	0
Anthraquinone	0·155	0

It was shown that no reduction occurs in the absence of dimethyl sulphate and that no reaction takes place without pyridine. The known Decker reaction suggests that *N*-methylpyridinium hydroxide is the reducing agent[338]. When 1,4-benzoquinone was treated with this reagent alone it was reduced to hydroquinone and *N*-methyl-2-pyridone was isolated (equation 285).



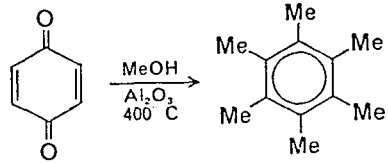
(285)

When 1,4-benzoquinone in dimethylsulphoxide solution is treated with an equimolar amount of hydrogen peroxide in the presence of ferrous ion, a mixture of various methyl-1,4-benzoquinones is produced in low yield (equation 286)[339]. This interesting reaction requires extensive modification if it is to have any synthetic utility.



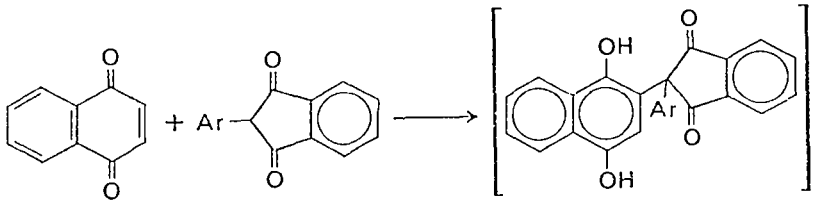
(286)

In an effort to find a simple preparation of pentamethylbenzene, 1,4-benzoquinone in methanol was treated with alumina at high temperature (equation 287)[340]. The only product characterized was hexamethylbenzene. Once again, this reaction could be of great importance if greater control of it could be established.



(287)

Finally, an exotic alkylation reaction has been reported recently (equation 288)[341]. The naphthohydroquinones formed initially are rather unstable and were not isolated, but could either be oxidized or acetylated to stable products.

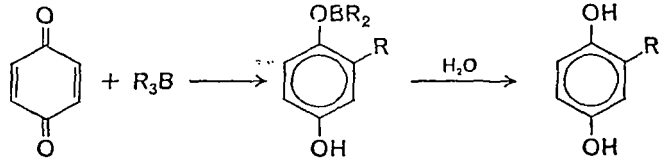


(288)

Ar = Ph, 4-MeC_6H_4, 4-$NO_2C_6H_4$, 4-ClC_6H_4

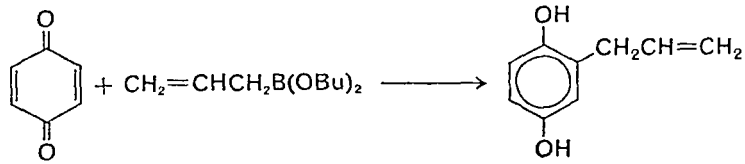
4. Hydroboration

In view of the extensive use of alkylboranes in organic synthesis, it is not surprising that they have been applied to the alkylation of quinones[342,343]. The reaction at first appeared to be restricted to 1,4-benzoquinones. Actually, only 1,4-benzoquinone itself was investigated carefully. There is every reason to believe that a wide variety of functional groups might be introduced and that conditions might be found under which more highly substituted quinones will react satisfactorily. The isolation of the monodialkylborinic acid ester of the alkylhydroquinone (**98**) offers some mechanistic information (equation 289). The quinol ester, probably formed initially, may rearrange under the influence of a second mole of trialkylborane acting as a Lewis acid.



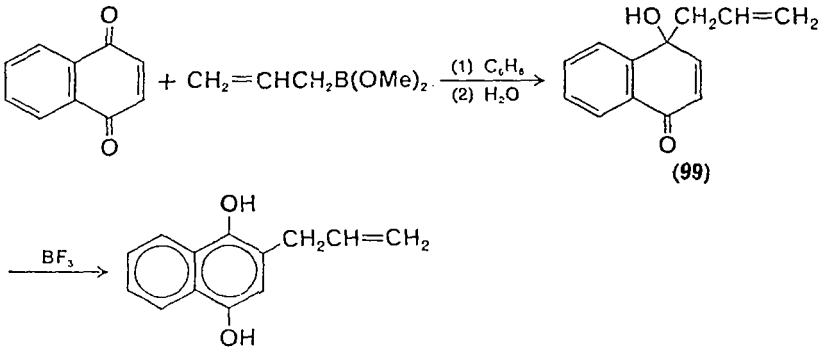
(98) (289)

A study of the reaction of boric acid esters has added to the synthetic range of quinone hydroboration (equation 290)[344]. The reaction takes



(290)

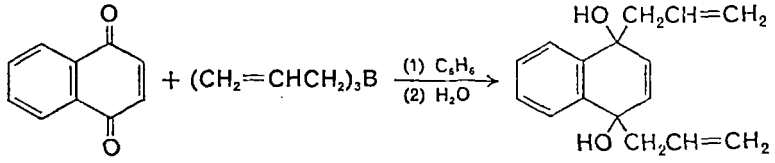
place smoothly and the yield is quite good. A similar reaction with 1,4-naphthoquinone, under milder conditions, allows the isolation of an intermediate, **99**, of mechanistic significance (equation 291). The structure



(99) (100) (291)

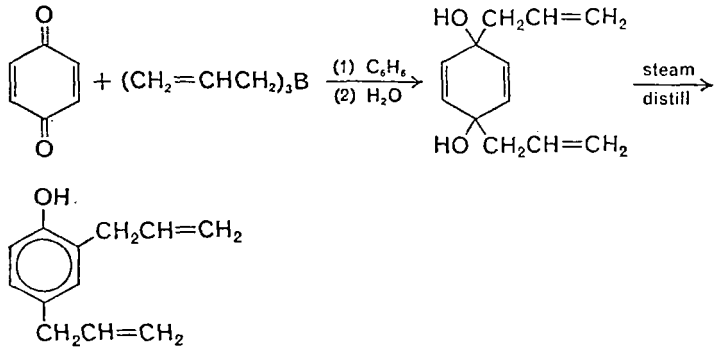
of **99** was determined from its i.r. spectrum. In refluxing benzene the final product, **100**, is obtained directly. Apparently the boric ester acts as the Lewis acid.

The reactivity of triallylborane towards quinones is somewhat greater than the trialkylboranes and both 1,4-benzoquinone and 1,4-naphthoquinone give a good yield of the di-1,2-carbonyl addition product (equation 292). When the analogous 1,4-diallyl-1,4-dihydroxy-2,5-cyclohexadiene



(292)

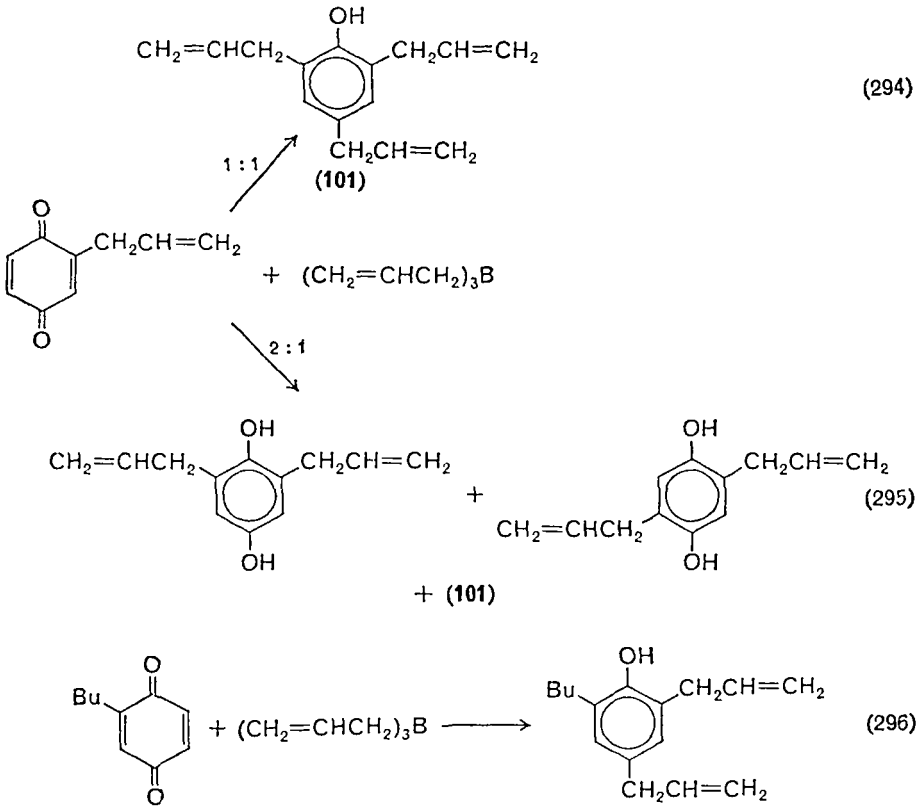
(actually either of the two separated geometric isomers *cis*-major, *trans*-minor) is steam distilled, the known compound 2,4-diallylphenol is formed (equation 293).



(293)

Questions related to hydroboration of substituted 1,4-benzoquinones have been studied in a few cases (i.e. *n*-butyl and 2-allyl-1,4-benzoquinone with triallylborane)[344,345]. The nature of the reaction appears to depend strongly on the ratio of reactants (equations 294 and 295). The overall yield (75% and 67% respectively), while not quantitative, are high enough for the product distribution to be a reasonably accurate estimate of the reaction outcome. The butyl group led only to 4,6-diallyl product (equation 296)[345]. Reaction with 1,2-naphthoquinone gave the bis-carbonyl addition product analogous to equation (292).

Until recently the hydroboration of 1,4-naphthoquinone had not been studied as extensively as 1,4-benzoquinone[346]. It was found that, in addition to alkylation, a significant amount of reduction (15–20%) takes place and complicates the separation and purification of product.



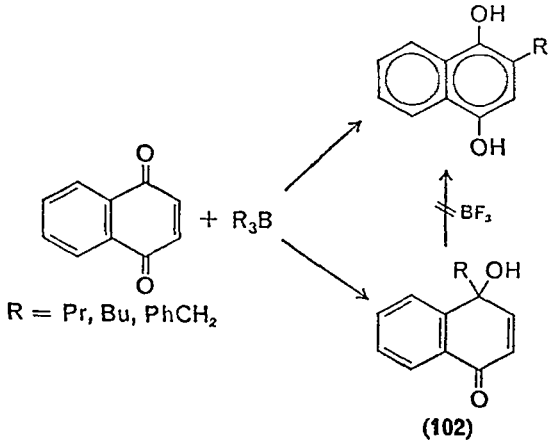
(294)

(295)

(296)

This problem can be overcome most easily by simply oxidizing the products at once and isolating the desired quinone. The 1,4-naphthoquinones appear to react by a 1,4-addition mechanism because the product of 1,2-addition to the carbonyl group (**102**) is not converted to the 2-alkyl-1,4-naphthalenediol by boron trifluoride. This difference from earlier work with allylboranes suggests two different reaction paths (equations 297 and 298). The reactions of 1,4-benzoquinone and 1,4-naphthoquinone with dibenzylborinic anhydride were studied (equation 299). The yields were only fair and 1,4-naphthoquinone gave a little **102** as well as 2-benzyl-1,4-naphthalenediol.

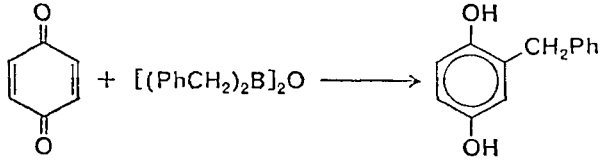
A recent study sheds additional light on the mechanism of alkylation with trialkylboranes[347]. Kabalka offers evidence that the alkylation is a radical process by showing that iodine, and to a smaller extent galvinoxyl, inhibits the addition of triethylborane to 1,4-benzoquinone. He pictures the mechanism as a radical addition to the carbon–carbon double bond (equations 300–302). A consequence of this hypothesis is that the so-called



(297)

(298)

(102)



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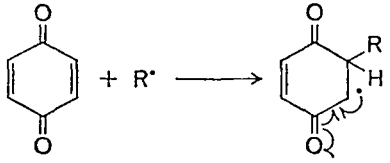
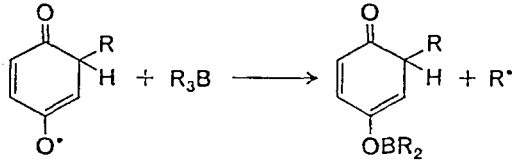
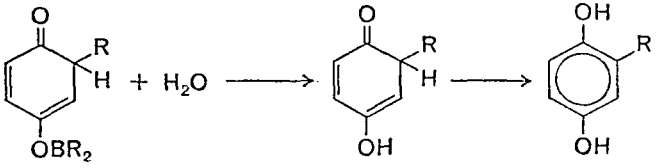


(300)

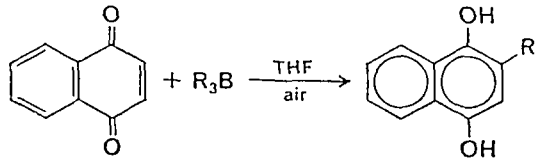


(301)



(302)

unreactive quinones (see, however, references 344–346) simply suffer from short chain lengths and require more efficient initiation. This point was demonstrated by the excellent yields of 2-alkyl-1,4-naphthalenediols obtained when air was passed through the reaction mixture (equation 303).



R = Et, Bu, C_6H_{11} 85–95% (303)

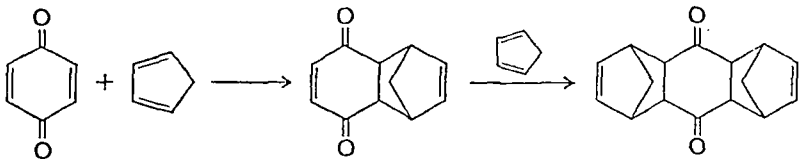
V. CYCLOADDITION TO QUINONES

A. The Diels–Alder Reaction

1. Historical introduction

A wide variety of quinones have been used in the diene synthesis developed by Diels and Alder. The synthetic facts in the earlier literature have been systematically reviewed and will not be treated here[348]. Our main concern is with quinonoid dienophiles which have provided understanding of the mechanistic details of this important synthetic tool. Current synthetic efforts have been included where they are somewhat different from the earlier reports. An important current review will appear shortly[348a].

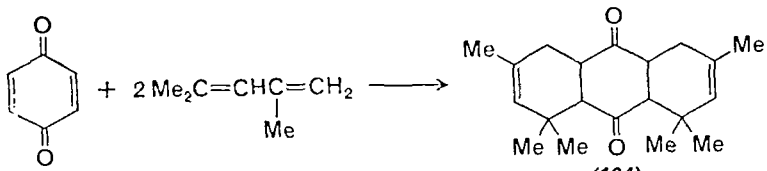
A quinone Diels–Alder reaction of particular interest had actually been carried out more than twenty years before Diel's and Alder's papers began to appear[349], but was not correctly understood until their reinvestigation (equation 304)[350,351].



(304)

(103)

I have found only one early example of a quinone Diels–Alder reaction not mentioned by Butz and Rytina. The rate of oxime formation was used as evidence for the structure of a Diels–Alder adduct (equation 305)[253]. It was found that the product obtained formed a monooxime in two hours and a dioxime very slowly. On this basis the structure **104** was chosen because one carbonyl group is much more hindered than the other.

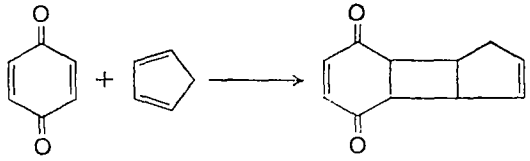


(305)

(104)

2. Mechanistic studies

Some of the earliest serious mechanistic studies of the Diels–Alder reaction involved the kinetics of addition of 1,4-benzoquinone to cyclopentadiene (equation 304)[352]. Both of the reaction steps are second-order and the rate of the first is about 100 times that of the second in benzene at 25°C. In a later and more detailed study of these reactions Wassermann examined the thermochemistry as well as the kinetics[353]. The question of a reasonable explanation of the observed 1,4-, rather than 1,2-addition, was approached first from a thermochemical point of view. The calculated and observed heats of formation were in excellent (perhaps fortuitous) agreement, assuming only about 10 kcal of ring strain in the product (**103**). From these data it was possible to calculate the gas-phase heats of reaction for both the observed 1,4-addition (first half of equation 304) and the hypothetical 1,2-addition (equation 306). Both of these reactions



(306)

proved to be exothermic (24 kcal and 19 kcal respectively). While the absolute values of the heats of reaction are approximate, there is no thermodynamic reason to prefer one path over the other.

An additional examination of the earlier kinetic study was also carried out. The various probable competing reactions were considered and conditions selected where they were unlikely to interfere and where the yield of expected product (**103**) was essentially quantitative. A wide variety of catalysts and inhibitors were examined along with light and magentic fields; no change in rate was observed. Wassermann concluded that a radical chain reaction was very improbable. The temperature dependence of rate in both benzene and ethanol followed the Arrhenius equation and gave activation energies of 14·2 kcal (benzene) and 12·7 kcal (ethanol).

The kinetic results require that the 1,4-addition and/or the 1,2-addition be described by only the Z and E constants of the Arrhenius equation. This requirement allowed Wassermann to consider the various steric situations that would be best suited for 1,4- as contrasted with 1,2-addition. From these models and calculations, it was shown that the Z values for the two modes of reaction could not be very different and therefore those constants cannot be used to explain the predominance of 1,4-addition.

A final effort to explain the observed reaction product on the basis of the activation energy(E) required a consideration of the induced dipole in cyclopentadiene as a result of the quinone carbonyl groups. The resulting values showed clearly that orientation for 1,4-addition produces larger induction energies than those for 1,2-addition. Wassermann reasoned that the repulsive forces for the two modes of addition should not be very different and thus the activation energy for 1,2- should be greater than for 1,4-addition. Calculated rate constant ratios for the two reactions appeared to be sufficient to explain the observed exclusive formation of **103**.

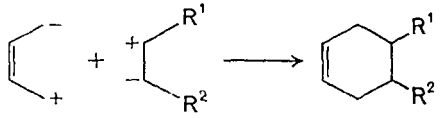
The Diels–Alder reaction possesses kinetic characteristics that make it suitable for a comparison study of gas- and solution-phase mechanisms. Wassermann has compared his studies of quinone–cyclopentadiene additions in solution to several analogous gas-phase studies[354]. The observed kinetics produce temperature-independent Arrhenius A values* of the order of 10^6 l/mole s. Because these values are several orders of magnitude lower than either the gas- or solution-phase bimolecular collision frequencies (ca. 10^{11} l/mole s), it follows that only a small fraction of the collisions of molecules with sufficient energy result in reaction. The so-called 'normal' and 'slow' bimolecular reactions[355] were discussed and evidence offered that the collision frequencies in the gas- and solution-phases can be of the same order of magnitude for both reaction types. The most significant conclusion relative to the Diels–Alder reaction is that the reason for the large difference between the Arrhenius A and the collision frequency is the complicated structure of the reactants rather than restricted electronic transitions. This study offered rather strong additional support for the importance of transition-state geometry which became significant at a much later date in the development of physical organic chemistry.

The Diels–Alder reaction is known to be reversible and Wassermann has studied the resulting equilibria in several systems involving quinone dienophiles[356]. His results show once again that both the heat of reaction and the statistical probability of reaction are very similar in the gas-phase and hydrocarbon solution.

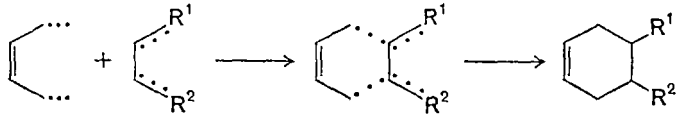
The question of the exact electronic distribution in the Diels–Alder reaction has been a source of study and debate for a long time and quinones have played a modest role in that story. Two early formulations suggested that (i) two ionic resonance contributors were involved (equation 307)[357], or (ii) the diene served as an electron donor at both ends and the dienophile

* In Wassermann's earlier papers the symbol Z was used in place of A.

accepted electrons at both carbon atoms (equation 308)[358]. The scheme shown in equation (308) cannot be applied when the dienophile is



(307)



(308)

substituted unsymmetrically. The authors of the ionic proposal studied a series of dienophiles in which the electronegativity of the substituents R^1 and R^2, as well as their location, was varied[359]. The diene employed, bicyclohexenyl, was also used as the solvent (5-fold excess). This latter experimental detail proved to be very wise, especially with the quinones where the excess not only drives the equilibrium toward product, but reduces subsequent dehydrogenation. The results shown in Table 10

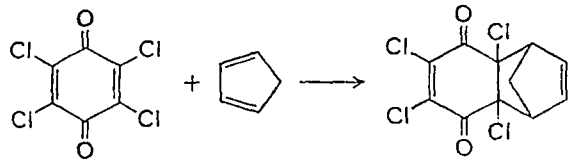
TABLE 10. Adducts of bicyclohexenyl with various dienophiles[359]

Dienophile	Temperature (°C)	Yield (%)
Maleic anhydride	80	95
1,4-Benzoquinone	80	85
1,4-Naphthoquinone	100	99
Fumaric acid	200	80
Benzalacetone	180	76
Dibenzalacetone	180	95
Cinnamic acid	180	75
β-Nitrostyrene	80	95

clearly indicate that neither the yield nor the reaction temperature can be correlated with symmetrical and unsymmetrical dienophiles. This observation was taken as support for the ionic mechanism as presented in equation (307). There appears to be no evidence for a change in reactivity over the series of quite different electronic situations.

As the amount of mechanistic detail concerning the Diels–Alder reaction has grown, it has become increasingly apparent that not only the electronic, but also the geometric situation in the transition state is

very important. An interesting kinetic approach to this aspect of the reaction has been provided in the addition of cyclopentadiene to selected quinones[360]. The addition of cyclopentadiene to chloranil (equation 309)



(309)

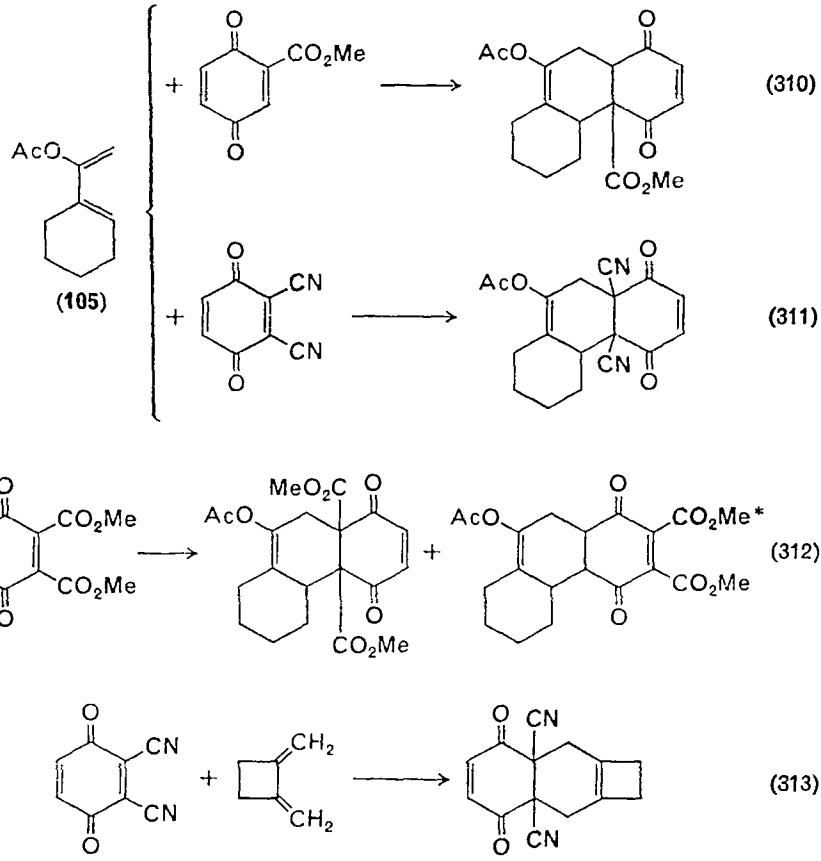
may be compared with equation (304). The greater bulk of the chlorine atoms relative to hydrogen should cause variation in the Arrhenius equation constants A and E unless the transition state is non-planar. The data in Table 11 show essentially no variation in A and only a slight range of E

TABLE 11. Arrhenius parameters for the reaction of cyclopentadiene with various dienophiles[360]

Dienophile	log A (A in l/mole s)	E (kcal)
Chloranil	6·2 ± 0·5	14·5 ± 0·5
1,4-Benzoquinone	6·5 ± 0·4	11·6 ± 0·6
1,4-Naphthoquinone	4·8 ± 0·9	10·0 ± 1·0
Cyclopentadiene-benzoquinone (**103**)	5·5 ± 0·9	13·2 ± 1·0
Acraldehyde	6·1 ± 0·3	13·7 ± 0·5
Cyclopentadiene	6·1 ± 0·4	16·4 ± 0·6

values. The latter variation is far too small to argue convincingly for a planar transition state.

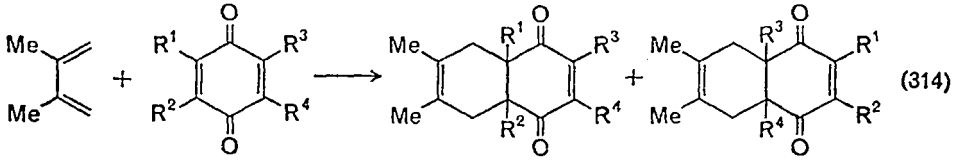
Any proposed mechanism for the Diels–Alder reaction must account for the rather specific nature of orientation observed when unsymmetrically substituted dienophiles are employed. An explanation has been advanced that takes both steric and electronic effects into account, but it is somewhat limited[361]. This limitation was not serious until the reactions of 1,1′-acetoxyvinylcyclohexene (**105**) with quinones bearing electron-withdrawing substituents were reported (equations 310 and 311)[362]. These examples show clearly that, with sufficient electronic activation, a large amount of steric interaction can be overcome. There are, however, limits and two carbomethoxy groups produced the mixture of isomers shown in equation (312). The extraordinary reactivity of 2,3-dicyano-1,4-benzoquinone was also illustrated by its rapid reaction with 1,2-dimethylenecyclobutane (equation 313)[363].



At about the same time a spectrophotometric study of the reactions of 1,4-benzoquinone and 1,4-naphthoquinone with cyclopentadiene, isoprene and piperylene produced some very significant information about the mechanism[364]. It was possible to follow the formation of the expected adducts in all cases, including both the mono- and diadducts of 1,4-benzoquinone. However, with 1,4-benzoquinone, absorption was found in the 290 nm region preceding the formation of each adduct and decreasing as the adduct formed. Because known molecular compounds between quinones and aromatics absorb in this region, it was felt that evidence of significant intermediates had been obtained. These absorptions were not observed with 1,4-naphthoquinone: perhaps this is the result of a more rapid rate of conversion of the intermediate to the adduct.

* Isolated as the hydroquinone.

The reactions of **105** with a variety of unsymmetrically substituted 1,4-benzoquinones have been observed and the product structures determined[365-367]. From these studies has come a somewhat better picture of the electronic and steric requirements of the reaction. In their general discussion of the Diels–Alder reaction of 1,4-benzoquinones, Ansell and colleagues report the reactions of simpler dienes, such as 2,3-dimethylbutadiene, with mono-, di-, tri- and tetrasubstituted 1,4-benzoquinones[368]. The general situation (equation 314) is that a symmetrical diene and an



(314)

unsymmetrically substituted 1,4-benzoquinone can form isomeric monoadducts (**106** and **107**). The results of a representative sample of the large number of examples studied are shown in Table 12. The additions to the tetrasubstituted 1,4-benzoquinones are especially interesting in that they

TABLE 12. Adducts of 2,3-dimethylbutadiene and various substituted 1,4-benzoquinones[368]

1,4-Benzoquinone substituent(s)	Angular groups	Yield (%)
Me	H, H	61
MeO	H, H	30
Cl	H, H	42
CO_2Me	H, CO_2Me	95
CN	H, CN	85
COMe	H, COMe	86
2,3-$(CN)_2$	CN, CN	96
2,3-$(CO_2Me)_2$	H, H/CO_2Me, CO_2Me	25, 25
2-Me, 3-NO_2	H, H	35
2-OAc, 5-Me	OAc, H	36
5-Cl, 2,3-$(CN)_2$	CN, CN	88
5-Me, 2,3-$(CO_2Me)_2$	CO_2Me, CO_2Me	76
2-CO_2Me, 3,5-Me_2	Me, H	23
5-MeO, 2,3-Me_2	Me, Me/MeO, H	20, 13
2-CO_2Me, 3,5-$(Me)_2$	Me, CO_2Me	81
2,6-$(CO_2Me)_2$, 3,5-Me_2	Me, CO_2Me	90
Me_4	Me, Me	87
$(MeO)_4$	MeO, MeO	95

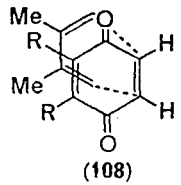
show that even the unreactive tetramethoxy-1,4-benzoquinone can be made to form an adduct in excellent yield if the product has the required thermal stability.

The general agreement of these data with the earlier ideas expressed by Ansell is clear. An electron-withdrawing group attached to the carbon–carbon double bond of a quinone does activate the dienophile. The balance between steric and electronic effects is apparent, especially in the relationships between cyano and carbomethoxy groups. An order of activating effect was proposed: $CN > COMe > CO_2Me > CF_3 > H > F > Cl > Me > OAc > NMePh > OMe > SMe$. The study also included some examples of 1,3-butadiene addition and in these data (Table 13) a third

TABLE 13. Comparison of Diels–Alder products from 1,3-butadiene and 2,3-dimethylbutadiene and various 1,4-benzoquinones[368]

1,4-Benzoquinone substituent(s)	1,3-Butadiene		2,3-Dimethylbutadiene	
	Angular groups	Yield (%)	Angular groups	Yield (%)
CO_2Me	H, H	6	H, CO_2Me	95
CO_2Me	H, CO_2Me	65	—	—
2,3-$(CN)_2$	H, H	16	CN, CN	96
2,3-$(CN)_2$	CN, CN	62	—	—
2,3-$(CO_2Me)_2$	H, H	70	H, H	25
2,3-$(CO_2Me)_2$	—	—	CO_2Me, CO_2Me	25

influence on product structure was observed. If an *endo*-transition state is assumed, it is reasonable to expect the arrangement shown in structure **108** to be less probable than the transition state leading to product with angular R substituents. In a similar manner, transition states with 1,3-butadiene and a 2,3-disubstituted quinone should be more probable than **108**. Thus, a second steric effect must be considered in predicting the

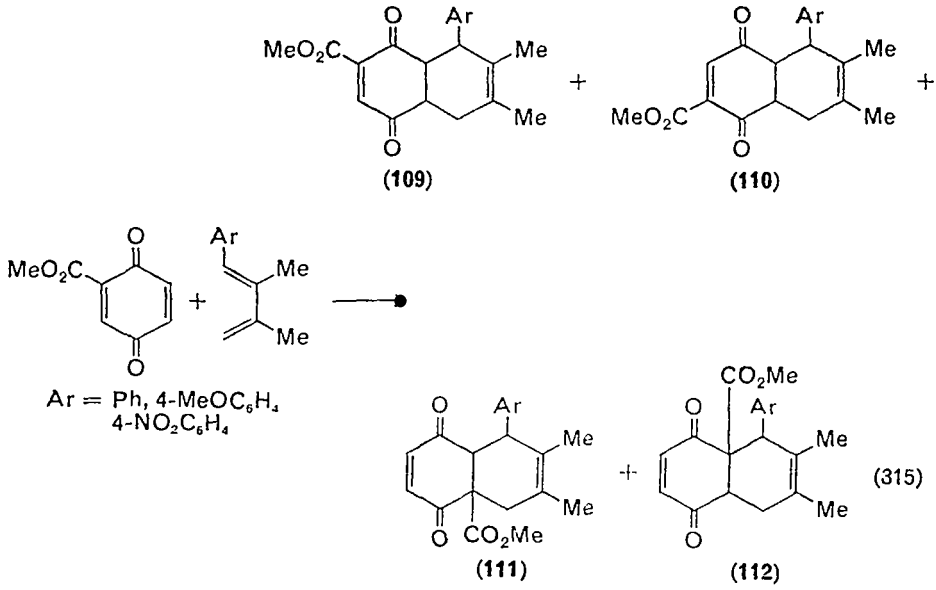


(108)

major product of the Diels–Alder reaction of an unsymmetrical benzoquinone. In the limited number of examples that have been studied, the observed facts are in accord with the predictions of this effect; e.g. 2,3-dicarbomethoxy-1,4-benzoquinone gives mixtures of products with

isoprene, 1-vinylcyclohexene and 1,1′-acetoxyvinylcyclohexene, as well as 2,3-dimethylbutadiene.

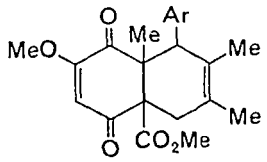
Finally, Ansell and Clements have examined the other aspect of these orientation questions; i.e. the relative orientation of substituents[369]. When an unsymmetrical 1,4-benzoquinone and an unsymmetrical diene undergo a Diels–Alder reaction, there are four possible isomeric products that can result (equation 315). The factors that determine the 'side of



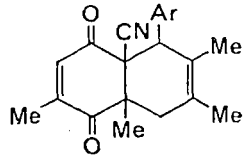
addition' (i.e. **109–110** versus **111–112**) have just been discussed; now we are interested in a choice between the individual members of the pairs of structures. The diene chosen allows variation in the electronic situation while holding the steric factor quite constant. The 2,3-dimethyl groups in the diene are useful for the interpretation of the n.m.r. spectra of the products. The specific quinone shown in equation (315) (2-carbomethoxy-1,4-benzoquinone) was found to give a single product in high yield with each of the three dienes. As would be expected, neither **109** nor **110** was obtained in any case. The n.m.r. spectra of the adducts clearly indicated structure **112**, where Ar = 4-$MeOC_6H_4$, 4-$NO_2C_6H_4$ and Ph.

A series of di- and trisubstituted 1,4-benzoquinones were studied to examine electronic and steric effects in the dienophile on the product orientation. It was found that the electronic natures of the diene and the dienophile have no effect on the orientation of product involving a single angular group. In each case (angular group = Me or CO_2Me) the arrangement of angular and aryl groups is *ortho* relative to the newly formed ring.

The trisubstituted quinones gave products **113** and **114**. All of these data are consistent with a transition state in which both bonds are partially



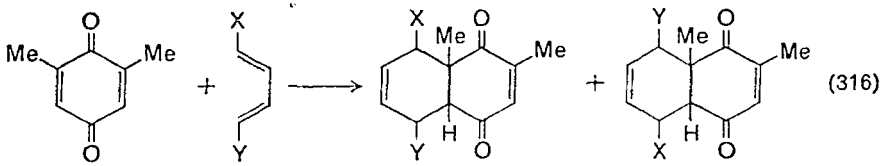
(113)



(114)

and unevenly formed, thus possessing some diradical character. The structure of product **113** requires that a radical centre be more stabilized by hyperconjugation with a methyl group than by delocalization to a carbonyl. This situation is explained on the basis of steric inhibition of resonance. This explanation is made more convincing by the lowered i.r. frequency of the carbonyl group. With the related cyano example **114** no such problem exists because of the group's linear structure.

Recently, an effort has been made to obtain more detail concerning the Diels–Alder transition state through a study of product orientation when unsymmetrical 1,4-disubstituted 1,3-butadienes react with 2,6-dimethyl-1,4-benzoquinone (equation 316)[370]. Two cases were studied: 1-acetoxy-1,3-pentadiene (X = AcO, Y = Me) and methyl sorbate (X = CO_2Me, Y = Me). Schmidt suggests that these reactants allow the comparison of



(316)

(115) **(116)**

methyl with an electron-donating group (acetoxy) and an electron-withdrawing group (carbomethoxy) while keeping the steric situation approximately the same.

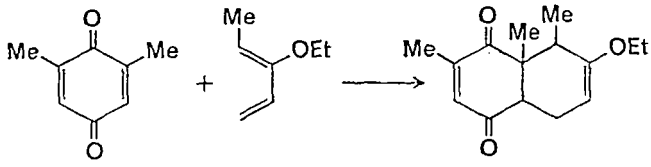
The results, with satisfactory total product yield, showed:

X = AcO **115** : **116** 4 : 1

X = CO_2Me only **115** could be found

Thus, while the carbomethoxy group has a more powerful directive effect than the acetoxy group, both electron-donation and electron-withdrawal influence the geometry of the transition state in the same direction. These results further suggest that the polarities of reactants are not the most significant considerations in predicting the nature of a Diels–Alder transition state.

This work has been expanded to include the methoxy group: an even stronger electron-donating substituent than acetoxy (equation 316; X = MeO, Y = Me)[371]. The only product found was **115**. Finally, 3-ethoxy-1,3-pentadiene and 2,6-dimethyl-1,4-benzoquinone produced only **117**, showing the lack of influence of a non-terminal group when a terminal group other than hydrogen is present (equation 317). This last



(117) (317)

experiment also shows the importance of methyl versus hydrogen as a directing influence in the Diels–Alder reaction and leads to the following scale of directive importance:

$$MeO = MeO_2C > AcO > Me > H$$

The kinetics of the two earlier reactions (equation 316: X = AcO and MeO_2C, Y = Me) have also been reported[372]. Selected rate data and thermodynamic parameters are given in Tables 14 and 15. The three

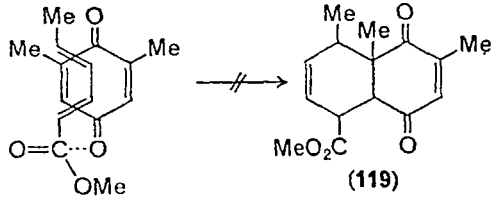
TABLE 14. Rates of addition of substituted 1,3-pentadienes to 2,6-dimethyl-1,4-benzoquinone (equation 316)[372]

Product	X	T (°C)	k, 1/mole s ($\times 10^5$)
(115)	AcO	140·4	1·17
(116)	AcO	140·4	1·34
(115)	CO_2Me	140·0	0·955
(115)	AcO	159·2	3·32
(116)	AcO	159·2	3·38
(115)	CO_2Me	159·0	2·80
(115)	AcO	176·0	8·44
(116)	AcO	176·0	6·92
(115)	CO_2Me	178·0	7·40

adducts are formed at very similar rates and the fourth possibility (**116**: X = CO_2Me or **117**) is not found even in trace amounts. The large negative entropy values require the highly oriented transition state that would result from an arrangement such as **118** if any of the missing product **119** were found (equation 318).

TABLE 15. Thermodynamic parameters for the addition of substituted 1,3-pentadienes to 2,6-dimethyl-1,4-benzoquinone (equation 316)[372]

Product	X	Activation energy (kcal/mole)	Entropy of activation (e.u.)
(115)	AcO	21·75 ± 0·82	−29·36 ± 1·92
(116)	AcO	18·33 ± 0·63	−37·32 ± 0·48
(115)	CO_2Me	21·91 ± 1·01	−29·44 ± 2·33



(118) (119) (318)

Liu and Schmidt suggest, on a preliminary basis, an unsymmetrical transition state in which the less hindered carbon atom of the dienophile takes the lead in σ bond formation. The bond formation is preferably initiated by that carbon atom of the diene possessing the higher electron density. The distribution of isomers in the case of 1-acetoxy-1,3-pentadiene (equation 316: X = AcO) is explained on the basis of the rigid structure of the transition state as indicated by the large negative entropy of activation.

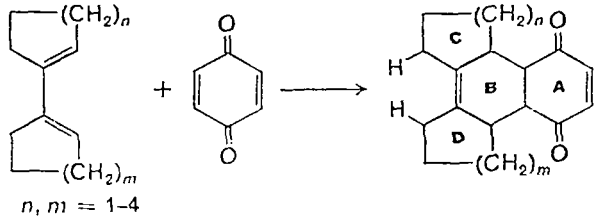
Three recent studies of more limited scope bear on the details of Diels–Alder chemistry involving quinones.

(1) The *para*-localization energy technique of Hückel molecular orbital calculations has been applied to both 1,2- and 1,4-benzoquinones[373]. This approach allowed the explanation of the dienophilic character of the carbon–carbon double bonds of these types of molecules.

(2) A detailed thermostudy of the Diels–Alder reaction of 1,4-benzoquinone with 2,3-dimethyl-1,3-butadiene and isoprene has been reported[374]. Two distinct steps can be observed and it can be shown that they correspond to the formation of the mono- and di-adduct. When the reaction is carried out at higher temperature, the *cis–cis* to *trans–trans* isomerism can be observed. Finally, when the reactants are present in equimolar amounts, a second exothermic effect corresponding to the isomerization of ketone to hydroquinone is found.

(3) A recent series of papers has dealt with retro-Diels–Alder reactions that occur under electron bombardment in the mass spectrometer[375–377].

From the organic chemist's point of view the most important finding is related to the conformation of the newly formed ring. The types of Diels–Alder adducts studied are shown in equation (319) (the syntheses of such adducts have been reported)[378]. With small **C** and **D** rings (m, n = 1 or 2), a special type of retro-Diels–Alder reaction took place involving the two allylic hydrogens shown. The most abundant ions were those of the retro-Diels–Alder bicyclodiene and hydroquinone. With larger **C** and **D**

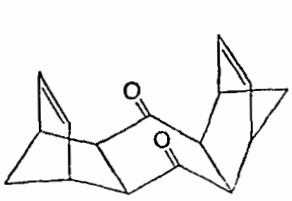


(319)

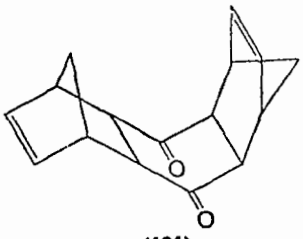
rings (n, m = 3 or 4), the adduct was very much more stable and the molecular ion became the most abundant. These observations are explained on the basis of changes in the conformation of the **B** ring brought about by different size **C** and **D** rings. The conformational changes brought about by smaller **C** and **D** rings bring the allylic hydrogens into a more favourable position relative to the quinone carbonyl groups. When the remaining quinone carbon–carbon double bond is reduced, only a normal retro-Diels–Alder reaction is observed. If the quinone double bond is part of an aromatic ring (i.e. 1,4-naphthoquinone was the original dienophile), both paths are observed. Thus, it appears that each of these structural features plays a significant role in the retro-Diels–Alder reaction in the mass spectrometer.

The stereochemistry of the Diels–Alder reaction has been of concern to chemists since the reaction first began to find very wide application. Of special interest at this point is the stereochemistry of the adduct formed when two moles of cyclopentadiene add to 1,4-benzoquinone. This adduct was assumed to possess the *endo–cis–endo*-configuration (**120**) for a very long time[379]. Both Winstein and Cookson and their colleagues have published convincing evidence that the *endo–trans–endo*-configuration (**121**) is correct[380,381].

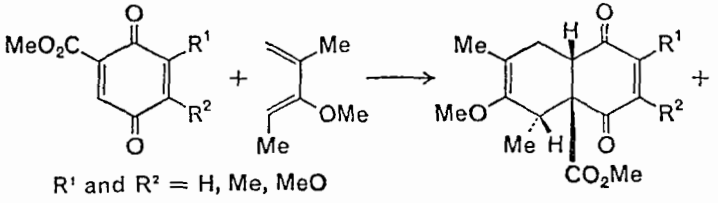
Several Diels–Alder adducts of substituted 1,4-benzoquinones were prepared in an attempt to determine their stereochemistry using n.m.r. spectroscopy (equation 320)[382]. The gross structural features were assigned in all but one case; however, it was not possible to determine the complete stereochemistry.



(120)

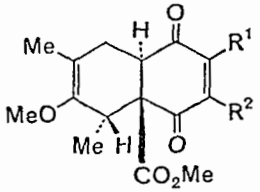


(121)

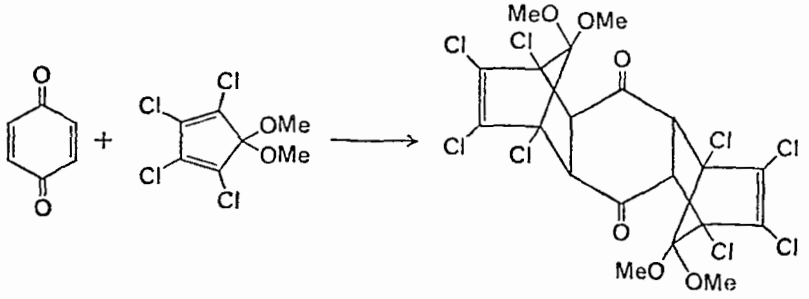


R^1 and R^2 = H, Me, MeO

(320)



The stereochemistry of the Diels–Alder adduct of 1,4-benzoquinone with two moles of 1,2,3,4-tetrachloro-5,5-dimethoxycyclopentadiene has been investigated, using variable-temperature n.m.r. spectroscopy (equation 321)[383]. The results strongly suggest the planar cyclohexadione ring shown, but do not rule out two boat conformations, if they are still in rapid equilibrium at $-100°C$.

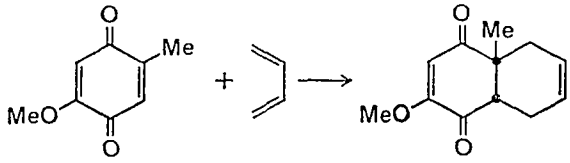


(321)

In view of the very large amount of study devoted to the mechanism of Diels–Alder reactions involving quinones, it is rather surprising that no Woodward–Hoffman treatment has appeared. The importance of this fresh approach to the interpretation of cycloaddition reactions requires its application here.

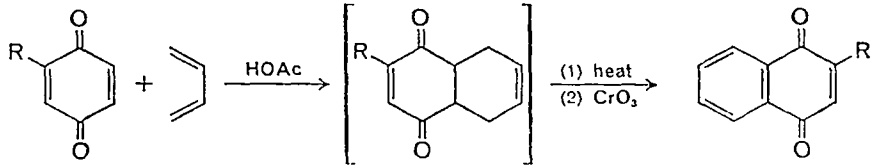
3. Synthetic survey

Since the earlier review[348], a dramatic example of the significance of quinone Diels–Alder reactions in recent synthetic organic chemistry is given by Woodward. He and his collaborators launched the first successful total synthesis of a non-aromatic, naturally occurring steroid (*dl*-$\Delta^{9(11),16}$-bisdehydro-20-norpogesterone), with such a reaction (equation 322)[384].



(322)

The work of Fieser and collaborators in the synthesis of potential antimalarial drugs has provided many useful synthetic techniques; among them a significantly improved diene synthesis of naphthoquinones (equation 323)[137]. Acetic acid is a very desirable solvent in that it avoids

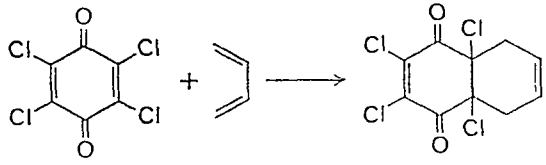


(323)

(122)

the use of pressure equipment and the need to work up the intermediate **122**. This procedure has been refined by later studies[385].

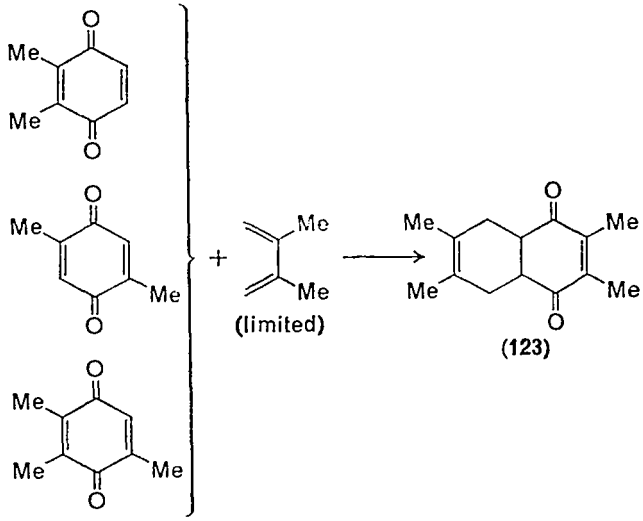
The addition of simple dienes to chlorinated 1,4-benzoquinones has been reported (equation 324)[386]. A number of slightly more complicated



(324)

dienes were used successfully (e.g. isoprene, 2,3-dimethylbutadiene and 1-acetoxy-1,3-butadiene); a number of chlorinated dienes, 2-lauroxybutadiene, 1,4-diphenylbutadiene, etc. did not add to chloranil. It was found that 2,5-dichloro-1,4-benzoquinone can also act as a dienophile although the isolated adducts were quite unstable to light. In benzene solution they could be converted to 2-chloro-1,4-naphthoquinones.

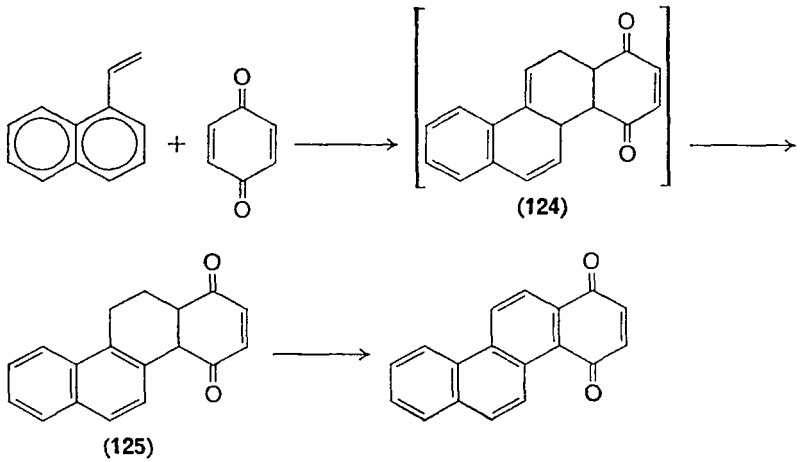
As a part of the separation and characterization of the components of the antibiotic gonyleptidine, Fieser and Ardao employed the difference in reactivity of various methylated 1,4-benzoquinones (equation 325)[38].



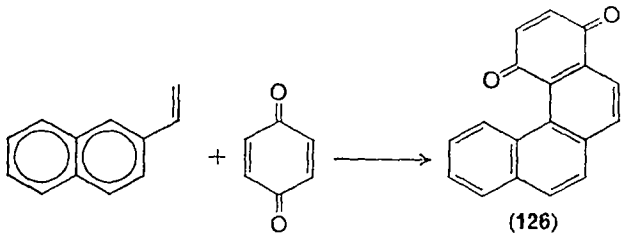
(325)

The product **123** is not affected by the hydrosulphite reduction of the other two quinones which can then be removed by basic extraction.

The general interest in polycyclic aromatic compounds has prompted the study of Diels–Alder reactions of 1- and 2-vinylnaphthalene with quinones (equations 326 and 327)[387,388]. The initial adduct **124** can be isolated or oxidized *in situ* depending upon the experimental conditions employed[388]. An analogous hydrogenated intermediate could not be isolated in the case of 5,6-benzophenanthrene-1,4-quinone (**126**). The

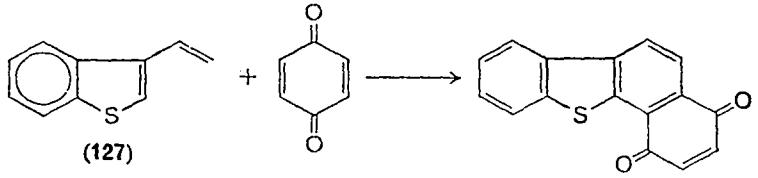


(326)



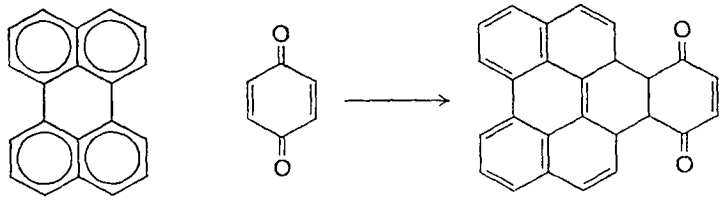
(126) (327)

reaction of 1-vinylnaphthalene with 1,4-naphthoquinone took place satisfactorily, but 2-vinylnaphthalene failed to produce the expected adduct. Styrene, 1-propenylnaphthalene and other similar compounds failed to react. In an analogous reaction, 3-vinylthionaphthene (**127**) reacts with 1,4-benzoquinone in excellent yield (equation 328)[389].



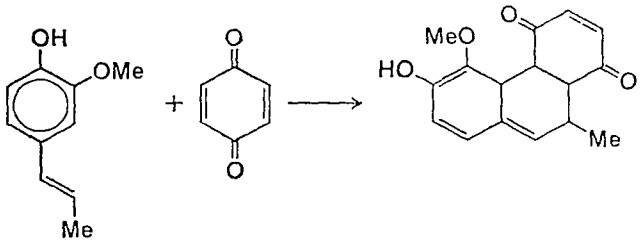
(127) (328)

The interest in polycyclic aromatic systems and their synthesis via Diels–Alder reactions of quinones continues (equation 329)[390]. The bis-adduct can also be isolated and an analogous reaction with 1,4-naphthoquinone takes place.

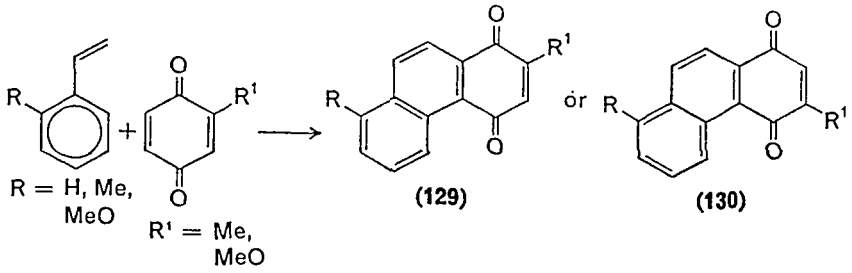


(329)

Vinyl aromatic systems are more generally useful as dienes with substituted 1,4-benzoquinones and the introduction of a methoxy group can activate the diene so that reaction with 1,4-benzoquinone itself is possible (for example, equations 330 and 331)[391]. The present application

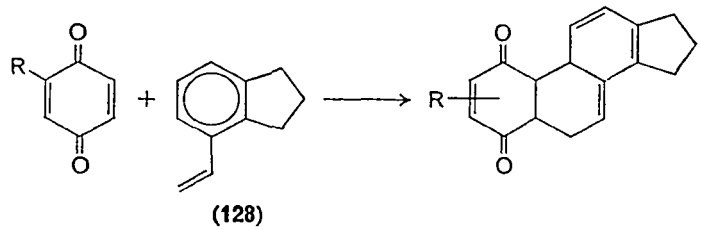


(330)



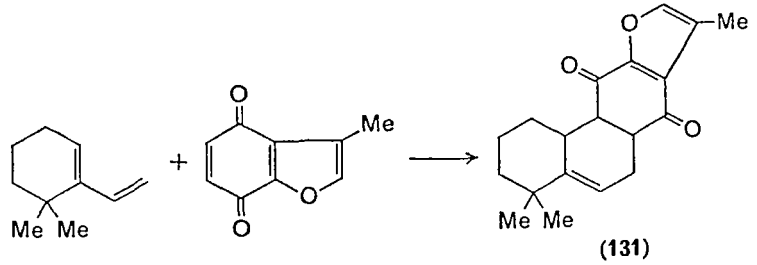
(331)

of this information is in the synthesis of compounds related to the steroids by reaction with 4-vinylindane (**128** in equation 332). In this particular instance, 1,4-benzoquinone does react, but an attempt to introduce an angular methyl group using 2-methyl-5-methoxy-1,4-benzoquinone produced only starting material after heating for eight days.



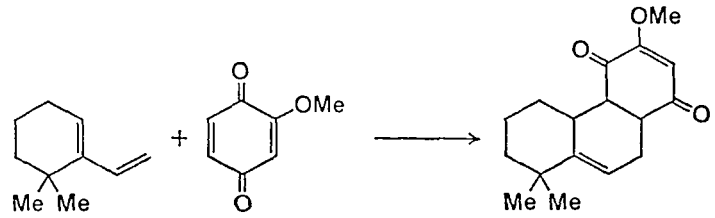
(332)

A somewhat similar reaction was used as the starting point for the synthesis of an important series of natural compounds (equation 333)[392].



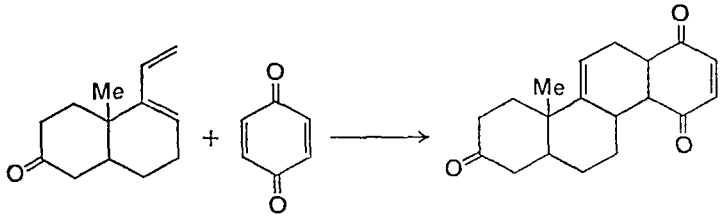
(333)

The fact that only a single product (**131**) was obtained and that it was the structure shown, called into question Lora-Tamayo's earlier structural assignments; e.g. product **129** was claimed in equation (331) when R = H or Me and R^1 = MeO. The result obtained with 2-methoxy-1,4-benzoquinone added strength to the argument (equation 334). A careful re-examination of the earlier work showed that in both cases (i.e. R = H or Me and R^1 = MeO) the product actually obtained has structure **130**[393].



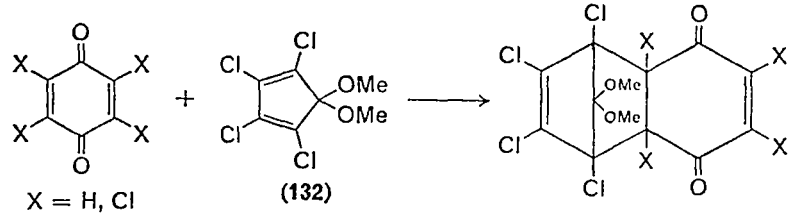
(334)

Another steroid synthesis involves the **D**-ring and allows the introduction of angular groups (equation 335)[394]. Related reactions, and much subsequent chemistry, provide entries to a variety of 'natural' and 'inverted' *cis–cis* steroids.



(335)

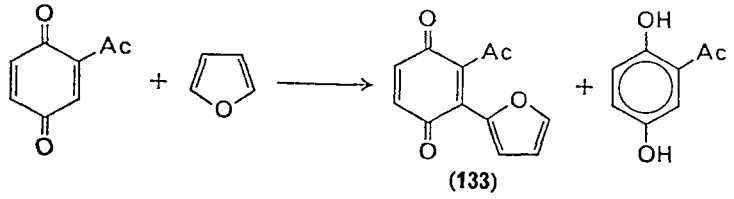
An effort has been made to prepare some interesting chlorinated 1,4-naphthoquinones by the Diels–Alder reaction of **132** with various 1,4-benzoquinones[395]. The project failed at a later point, but yielded some interesting new compounds in the cyclization step (equation 336). The



(336)

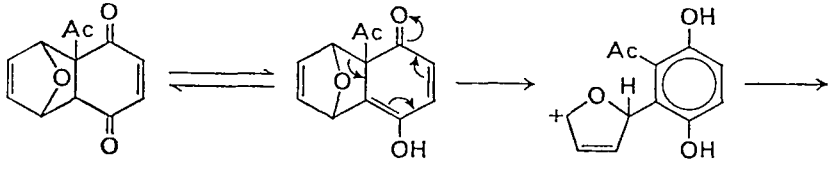
failure of the reaction with 2,5-dichloro-1,4-benzoquinone and chloranil is consistent with an earlier report[395a]. Additional verification of that study and some new adducts were obtained with cyclopentadiene.

In contrast to the chemistry of the cyclopentadienes, furan was found to add to 2-acetyl-1,4-benzoquinones in an abnormal fashion (equation 337)[396]. It was suggested that the 2-acetyl-3-(2-furyl)-1,4-benzoquinone (**133**) might be formed by a dienone-phenol rearrangement of the normal adduct in its enol form (equation 338). The substituted hydroquinone **134** could react with the starting quinone to produce the observed products. The actual quinone product **133** undergoes a normal Diels–Alder reaction with 1,3-butadiene (equation 339)[397].



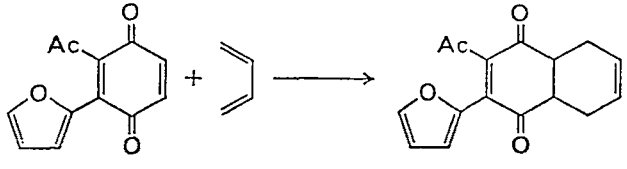
(337)

(133)



(338)

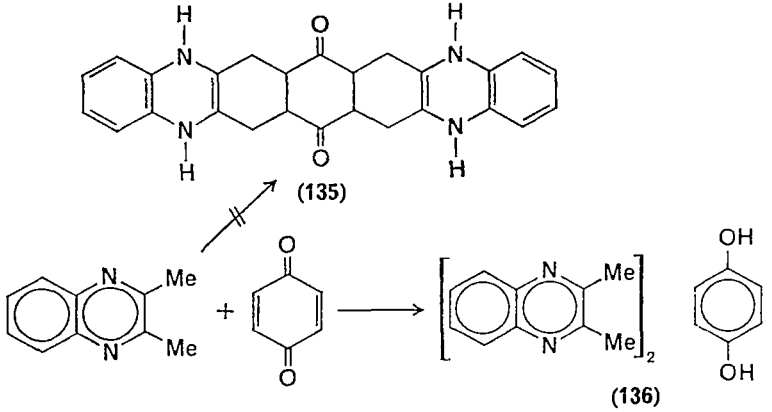
(134)



(339)

(133)

An interesting and prevalent error in Diels–Alder chemistry of quinones is the alleged adduct (**135**) of 2,3-dimethylquinoxaline and 1,4-benzoquinone[398]. Two groups recognize the formation of a complex, **136**, at nearly the same time (equation 340)[399,400]. The source of the hydroquinone was



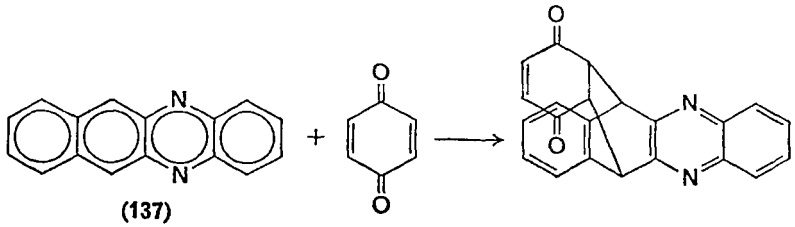
(340)

(135)

(136)

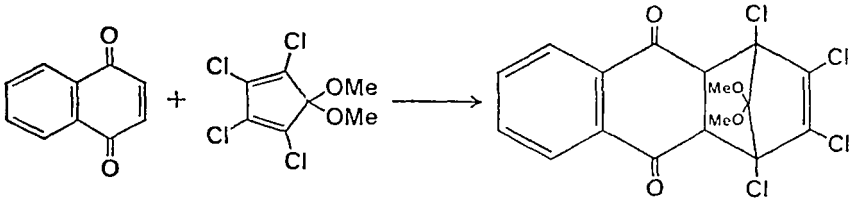
not determined, but the polymeric by-product suggests hydrogen abstraction from the quinoxaline.

A heterocyclic system vaguely related to that just discussed is benzo[b]-phenazine (**137**); this compound has been shown to react with the dienophile 1,4-benzoquinone (equation 341)[401].



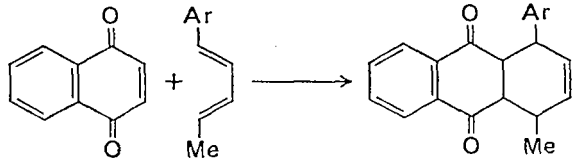
(137) (341)

It has been possible to prepare certain substituted anthraquinones by the Diels–Alder reaction of 1,4-naphthoquinone with 5,5-dimethoxy-1,2,3,4-tetrachlorocyclopentadiene (equation 342)[402]. The removal of the bridgehead carbon atom could be carried out in several different ways to lead to a number of products.



(342)

In recent years a method for the preparation of 1-aryl-1,3-pentadienes has been developed and used to prepare the little studied 1-methyl-4-arylanthraquinones (equation 343)[403]. The initial product **138** can be



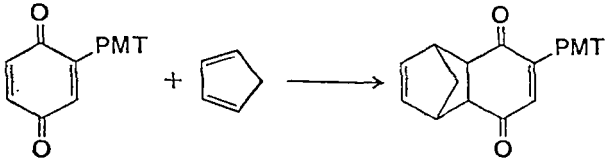
(138) (343)

Ar=Ph, 4-MeC_6H_4, 4-ClC_6H_4, 4-$MeOC_6H_4$, 2- or 4-$O_2NC_6H_4$, 4-Me-3-$O_2NC_6H_3$

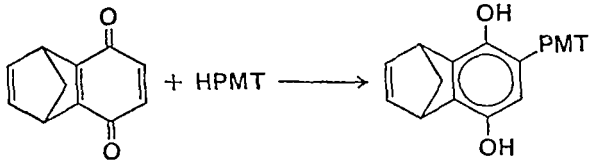
oxidized *in situ* to the substituted anthraquinone. Conditions have been found for analogous preparations of 2-methyl- and 2,3-dimethyl-1-arylanthraquinones[401].

In their study of the addition of 1-phenyl-5-mercaptotetrazole (HPMT) to various 1,4-benzoquinones, Gates and collaborators carried out some

interesting new Diels–Alder reactions[4]. The three dienes used (2,3-dimethylbutadiene, 1,3-cyclohexadiene and cyclopentadiene) added smoothly and in good yield to 2-(1′-phenyl-5′-tetrazoylthio)-1,4-benzoquinone (e.g. equation 344). Similarly, the quinones prepared from the Diels–Alder adducts without a thio substituent add HPMT (equation 345). The

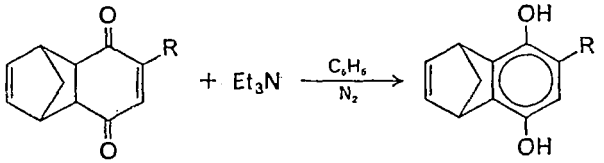


(344)



(345)

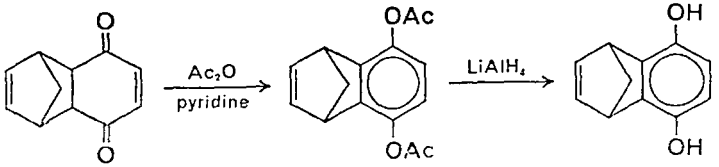
preparation of this last quinone reactant represents the most significant contribution of this study to Diels–Alder chemistry. The adducts of cyclopentadiene, unlike those of the other two dienes, do not undergo acid-catalysed aromatization to the corresponding hydroquinone, which can be oxidized by the usual reagents. It was found that the cyclopentadiene adducts are converted to their hydroquinones by treatment with triethylamine in benzene, preferably under anaerobic conditions (equation 346). The yields, with the exception of the 1,4-benzoquinone adduct, are



(346)

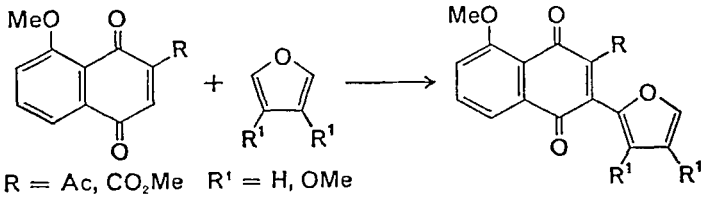
R = H, Me, Ph, PMT

quite satisfactory. The parent compound can be prepared in high yield by reductive acetylation and lithium aluminium hydride cleavage of the initial adduct (equation 347)[405].



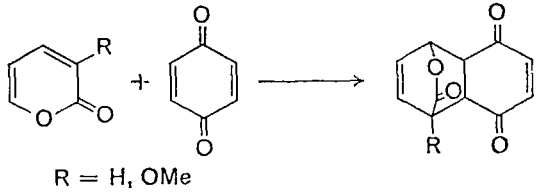
(347)

In a continuation of the study of the 'abnormal' addition of furans to quinones with electron-withdrawing groups, 2-carbomethoxy- and 2-acetyl-8-methoxy-1,4-naphthoquinone were prepared[406]. Both of these quinones failed to undergo the usual Diels–Alder reaction with either furan or 3,4-dimethoxyfuran (equation 348). A potentially useful synthesis of



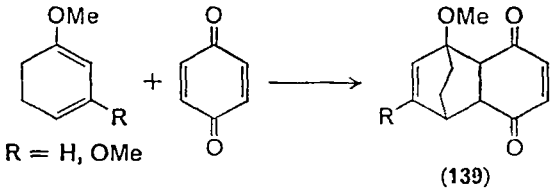
(348)

1,4-naphthoquinones involves the addition of α-pyrones to 1,4-benzoquinones followed by decarboxylation (equation 349).



(349)

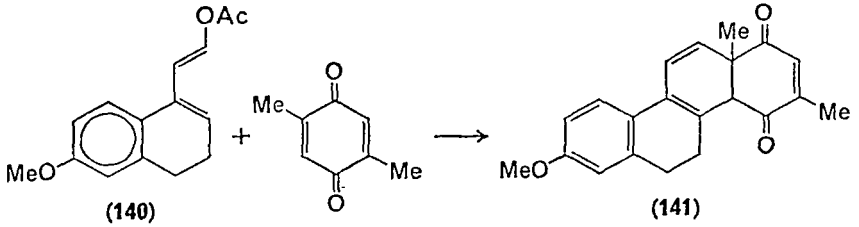
The availability of a reasonable synthetic route to 1-methoxycyclohexa-1,3-dienes has made possible the study of their Diels–Alder reactions with quinones (equation 350)[407]. The initial adduct **139** can undergo a variety



(350)

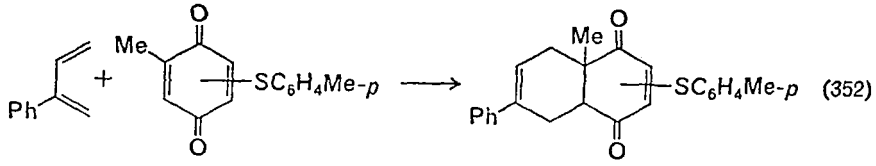
of interesting reactions, including photochemical formation of cage compounds, acid-catalysed loss of the bridge and the formation of derivatives of dibenzofuran. Substituted 1,4-benzoquinones have also been successful dienophiles. Procedures have been worked out for converting a number of mono- and di-adducts related to **139** to polycyclic aromatic quinones[408].

The ability to introduce an angular methyl group in the 16-position in certain steroids is very desirable and one possible route to such materials is shown in equation (351)[409]. The elimination of acetic acid to give the observed product **141** is consistent with other observations of the 1-acetoxy-diene, **140**.



(351)

Still another route to the introduction of an angular methyl group involved the addition of *p*-toluenethiol to 2-methyl-1,4-benzoquinone (see section II.B.3) and its subsequent removal (equation 352)[39]. The

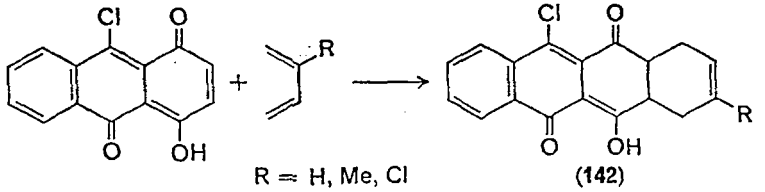


(352)

presence of an angular methyl group, rather than the angular thio group, was demonstrated by comparison of the u.v. spectra of the adduct with appropriate model compounds[41].

A brief survey of the possible routes to the synthesis of halogenated anthraquinones, along with their merits and drawbacks, has been presented[410]. The general conclusion, that using halogenated cyclopentadienone acetal is the preferred route[402], has been emphasized with additional synthetic work[411].

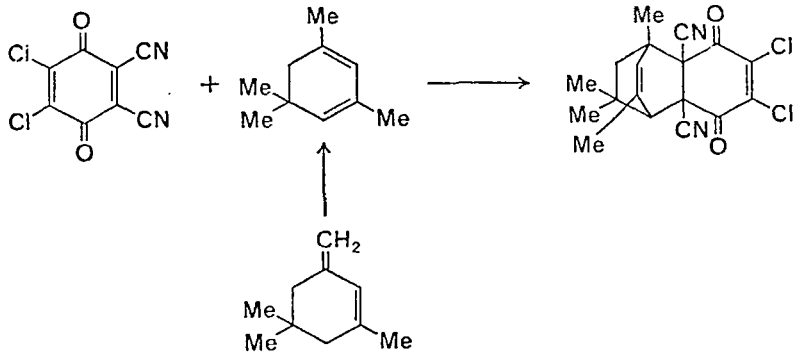
The Diels–Alder reaction of 1,3-dienes with certain chlorohydroxyanthraquinones provides an approach to compounds related to the tetracyclines (equation 353)[412]. The halogenated cyclopentadienone acetals have also been used in this approach. The various initial adducts (e.g. **142**) can be dehydrogenated to hydroxynaphthacenequinones.



(353)

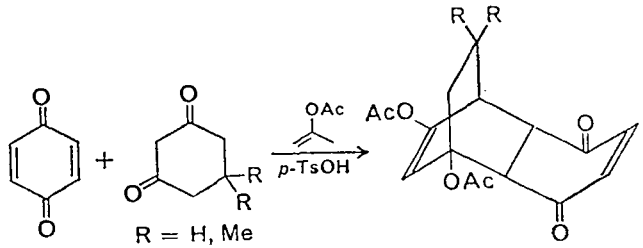
The tetrasubstituted quinone 2,3-dichloro-5,6-dicyano-1,4-benzoquinone has been used extensively as a dehydrogenating agent, but not in the diene synthesis. Recently the detailed structure of its Diels–Alder adduct with 1,5,5-trimethyl-3-methylenecyclohexene has been reported[413].

Under the reaction conditions the diene isomerized to 1,1,3,5-tetramethylcyclohexa-2,4-diene and the latter forms the adduct (equation 354). The structure was established by X-ray structure analysis.



(354)

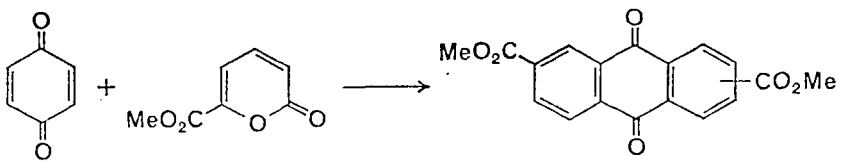
It has been shown that cyclic bis enol acetates can be generated *in situ* and that, in the presence of 1,4-benzoquinone, Diels–Alder adducts are formed (equation 355)[414]. Isophorone reacts to give an approximately



(355)

equimolar mixture of the two expected products. Other α,β-unsaturated carbonyl compounds (e.g. crotonaldehyde) gave only tars. The structure and chemistry of the adducts are described in some detail.

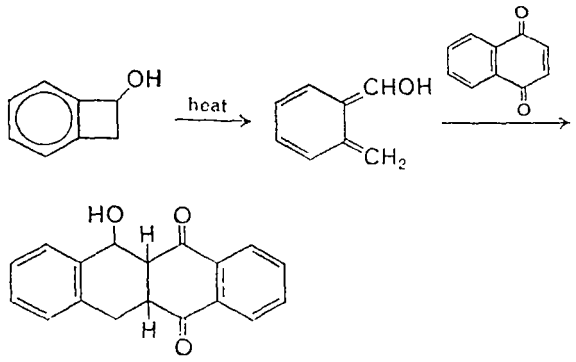
A recent extension of the Diels–Alder reaction between 1,4-benzoquinone and pyrones involves the use of the 5-carboxylic esters (equation 356)[415]. The product obtained was homogeneous, but the specific structure



(356)

of the product (2,6- or 2,7-dicarbomethoxy) was not determined. The presumed intermediates before decarboxylation were not isolated.

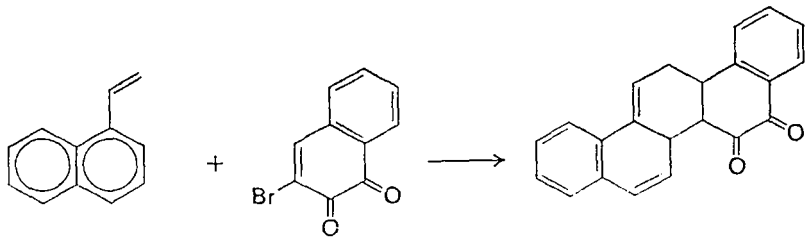
The thermolysis of benzocyclobutenol generates an interesting hydroxy-1,2-quinone dimethide that will react with 1,4-naphthoquinone (equation 357)[416]. The yield in this reaction was very good while the comparable photochemical reaction gave a complex mixture.



(357)

4. Diels–Alder reactions of 1,2-quinones

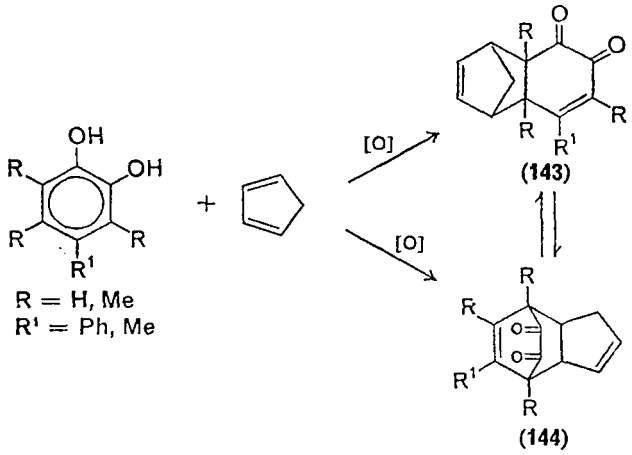
Compared to the enormous literature of the Diels–Alder chemistry of 1,4-quinones, relatively few 1,2-quinones have been studied until recently. The problems are, to some extent, illustrated by the study of the structure of picenequinone[417]. One suggestion for the structure of picenequinone is that expected from the Diels–Alder reaction between 1-vinylnaphthalene and 1,2-naphthoquinone after dehydrogenation (equation 358). Using 1,2-naphthoquinone only tar was obtained, but with 3-bromo-1,2-naphthoquinone dehydrobromination and dehydrogenation could be accomplished *in situ* and a reasonable yield of material corresponding to picenequinone was obtained.



(358)

In the past few years the interest in cycloaddition reactions of 1,2-quinones has grown very rapidly. Two English groups have played a major role in these studies: Ansell (Queen Mary College, London) and Horspool (Dundee) and their collaborators have published extensively and the latter has written a general review of the field[418].

Much of the Diels–Alder chemistry of the 1,2-benzoquinones is concerned with cyclopentadiene adducts. A recent study of these reactions by Ansell begins with a detailed review of the field[419]. The chief problem was the structure of the adduct; i.e. whether the quinone acts as a diene[420,421] or a dienophile[422,423] (equations 359 and 360). The correct explanation of

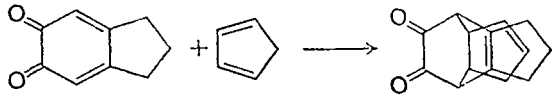


(359)

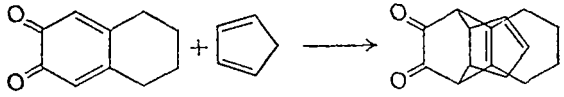
(360)

these differing views was suggested by Ansell and Gosden[424]. As shown above, the two adducts (**143** and **144**) can be interconverted thermally via a Cope rearrangement. This mechanistic picture has been supported by a number of subsequent studies[419]. It seems clear that many 1,2-benzoquinones act as dienophiles and give the kinetically controlled product. The chief exceptions are those quinones with substantial steric demands (e.g. tetramethyl- and 3,6-dimethyl-1,2-benzoquinone). In many of the cases studied an interesting interplay of steric and electronic effects could be seen.

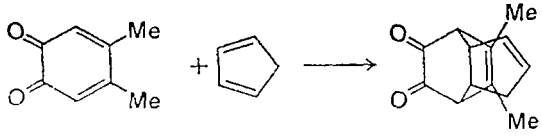
A still more recent study involved some bicyclo 1,2-quinones and shows that substitution in the 4,5-positions of the quinone also results in diene behaviour (equations 361–363)[425].



(361)



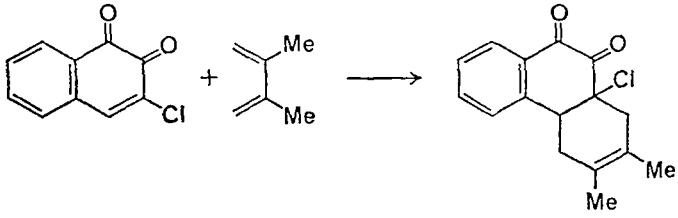
(362)



(363)

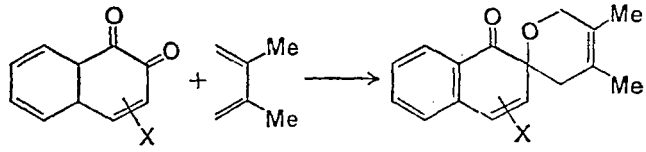
The study of Diels–Alder chemistry of 1,2-quinones has continued at a brisk pace as the following brief notes indicate.

(1) The reaction of 3-chloro-1,2-naphthoquinone with 2,3-dimethylbutadiene has been reinvestigated[426,427]. The structure originally reported for the 1:1 adduct was confirmed and is the usual Diels–Alder product (equation 364). Various other 3- and 4-substituents on the quinone ring



(364)

were re-investigated[428,429] or examined for the first time[430]. With halogen located in the 4-position, a carbonyl addition product was obtained (equation 365). The 3-methoxy derivative gave the normal Diels–Alder



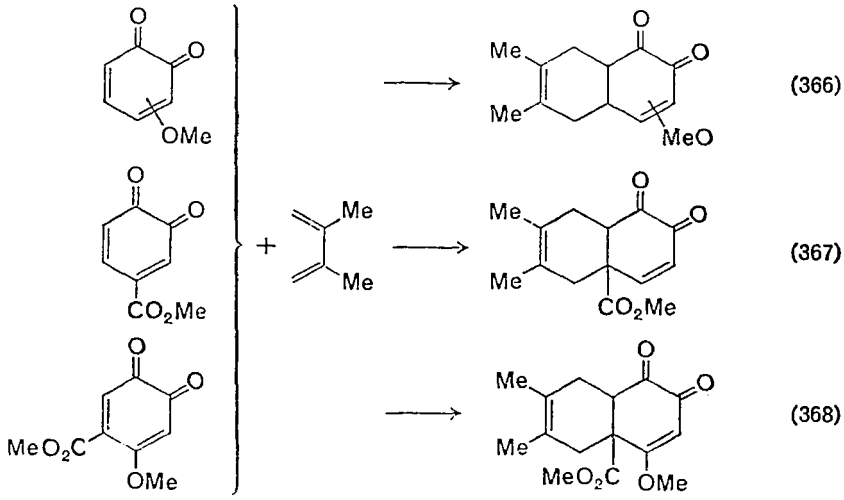
(365)

X = 4-Cl, 4-Br, 3-MeO, 3, 4-Cl_2 (145)

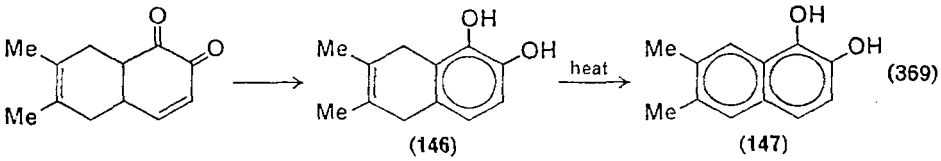
adduct and the spirodihydropyran (**145**) in the ratio of 3 : 1. Strong electron-withdrawing groups (4-cyano, 3-carbomethoxy and 3-nitro) all undergo the normal Diels–Alder reaction. The example of 3-nitro-1,2-naphthoquinone is especially interesting in that it is unusual to find a product with an angular nitro substituent. The mechanism and the product structures have been reported in some detail[431].

(2) The 1,2-benzoquinones are even more sensitive than the 1,2-naphthoquinones and very few successful Diels–Alder reactions have been reported until recently; exceptions are cyclopentadiene[419] and dimerization. Using a large excess of diene (10–25 molar), it has been shown that a large number of such quinones will react with simple acyclic dienes[432]. The yields vary, but are often quite good. Two of the quinones, 4-cyano and 4-carbomethoxy, could not be isolated and were prepared *in situ* by oxidation of the corresponding catechol in the presence of the diene. In the 4-cyano case, only nickel peroxide was effective, while a variety of oxidants were used to generate the 4-carbomethoxy-1,2-benzoquinone (silver oxide was the best).

The adducts from unsymmetrical mono- and disubstituted quinones showed dienophilic reactivity of the more electron-deficient carbon–carbon double bond (e.g. equations 366–368). The initial adducts shown were, in

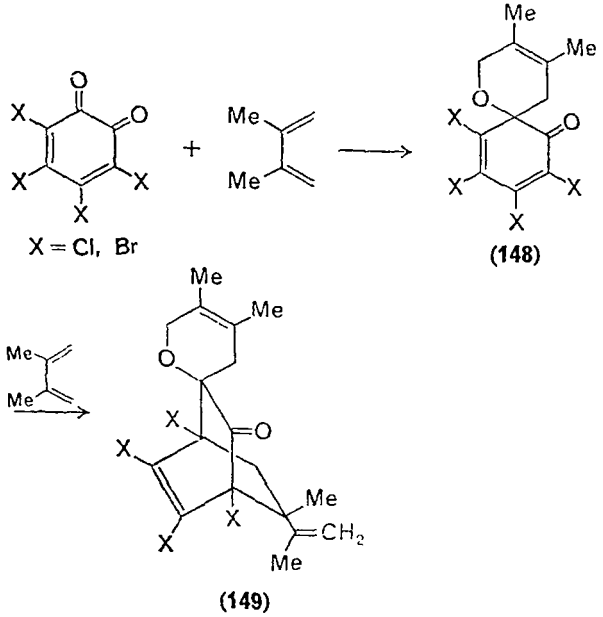


most cases, not the only product isolated. Usually, at least a part of the adduct aromatized and often purification (sublimation) caused dehydrogenation (**146** and **147** in equation 369). Trimethyl- and trichloro-1,2-benzoquinones were also studied and of the four substrates, 3,4,5-trimethyl-1,2-benzoquinone decomposed too rapidly to allow adduct formation. The other three substrates gave adducts of the mono-substituted alkene linkage.



(146) (147)

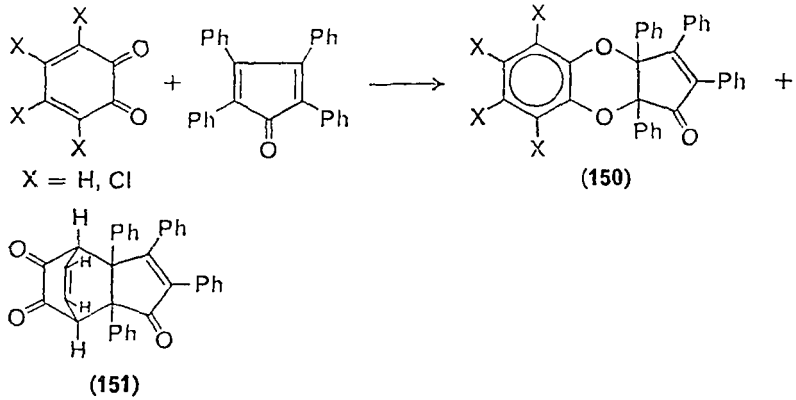
These studies have been expanded to the tetrahalo-1,2-benzoquinones and interesting new chemistry has been reported[433]. An earlier investigation of the reactions of such quinones with 2,3-dimethylbutadiene found a 1:2 adduct, for which an incorrect structure was proposed[434]. Re-investigation showed that with equimolar reactants at 0°C, a 1:1 adduct is formed in high yield. The i.r. spectra of the 1:1 adduct showed a single α,β-unsaturated carbonyl group and by analogy with earlier work[430] a spirodihydropyran structure (**148**) was assigned (equation 370). Such a system retains the 1,2-benzoquinone's diene system and reacts with a



(370)

second mole of 2,3-dimethylbutadiene to produce the same 1:2 adduct **149** found by Horner and Merz[434] with excess diene. The structure of the product **149** was assigned on the basis of its ability to undergo a Cope rearrangement and the spectra (i.r. and n.m.r.) of the rearranged product.

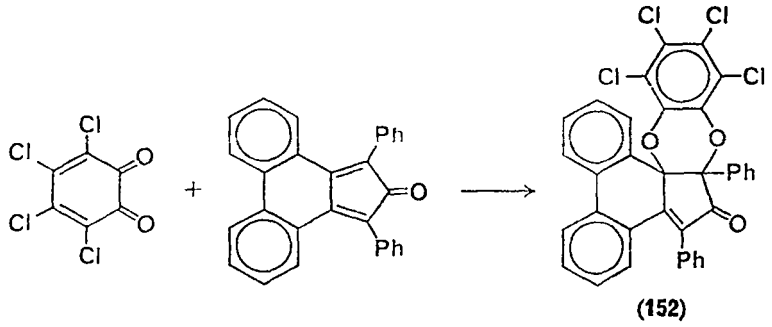
(3) The compound, 2,3,4,5-tetraphenylcyclopenta-2,4-diene-1-one (tetracyclone), is well known as a fine electron-deficient diene in Diels–Alder syntheses, but rarely does it act as a dienophile. Recent examples of such behaviour have been reported with 1,2-benzoquinone and its tetrachloro derivative (equation 371)[435]. Tetrachloro-1,2-benzoquinone gives only a very high yield of the dioxan derivative (**150**; X = Cl).



(371)

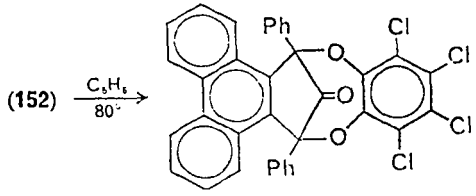
Further examination of the reaction of tetrahalo-1,2-benzoquinones with various cyclopentadienones revealed that dioxan formation is, by far, the most common reaction[436]. A variety of substituent patterns were used and it was concluded that steric effects are of much greater significance than electronic effects. The only instance of the quinone acting as a carbon diene (**151**) is the unsubstituted case reported earlier[435].

Other dioxan-type cycloaddition reactions have been reported between tetrahalo-1,2-benzoquinones and, for example, 2,5-dimethyl-3,4-diphenylcyclopentadienone[437]. Of special interest is the example shown in equation (372). The expected initial adduct **152** undergoes a very facile rearrangement to an eight-membered ring containing two oxygen atoms and a carbonyl bridge (equation 373).



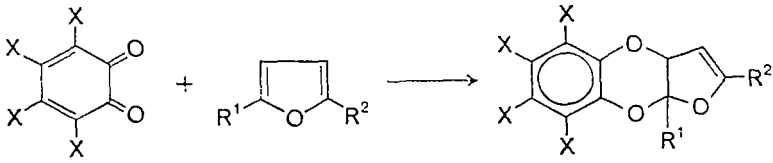
(372)

(152)



(373)

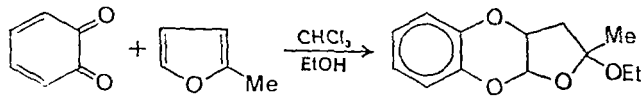
(4) Still another unusual aspect of 1,2-benzoquinone Diels–Alder chemistry is illustrated by reactions with various furans. The ability of furans to act as dienes is well known, but the observed mode of reaction with 1,2-benzoquinones is as a dienophile (equation 374)[438]. An interesting



(374)

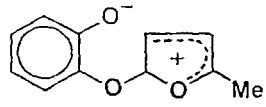
X = H, Cl R^1 = H, Me, Ph R^2 = H, Ph

piece of mechanistic detail was found when the reaction was carried out in chloroform (containing the usual ethanol stabilizer) and ethanol was incorporated in the product (equation 375). This observation, and some



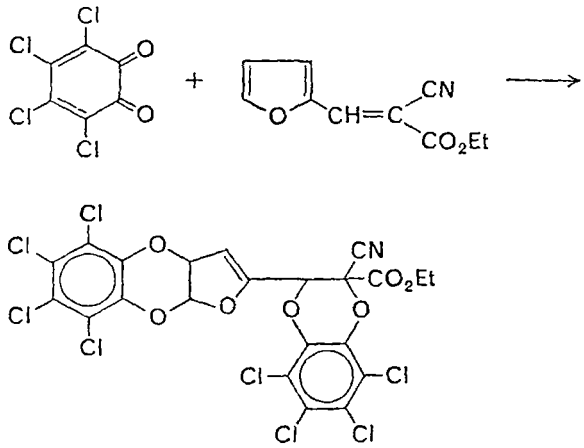
(375)

related experiments, suggest a two-step mechanism rather than a concerted cycloaddition. Electrophilic attack of the quinone on the furan to produce a stabilized carbonium intermediate (**153**) was suggested.



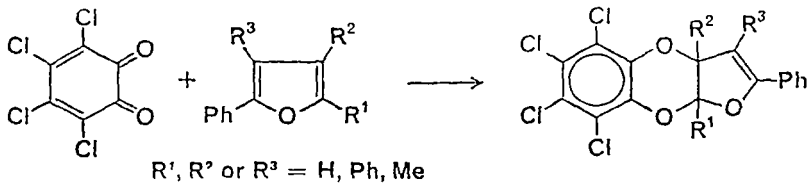
(153)

A series of furans with 2-vinyl side-chains and tetrachloro-1,2-benzoquinone react with interesting results[439]. Even though the vinyl group was substituted with strong electron-withdrawing groups, the addition usually took place on the furan ring (equation 374: X = Cl; R^1 = H; R^2 = —CH=CYZ, with Y = H, CN, CO_2Et and Z = CN, NO_2, CO_2Et, COPh). A single exception was found in which the vinyl side-chain also acted as a dienophile (equation 376).



(376)

Further study with furans containing various combinations of methyl and phenyl substituents has confirmed the generality of the dioxan-forming reaction (equation 377)[440]. Some additional evidence for the

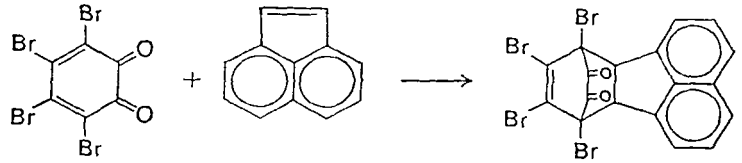


(377)

R^1, R^2 or R^3 = H, Ph, Me

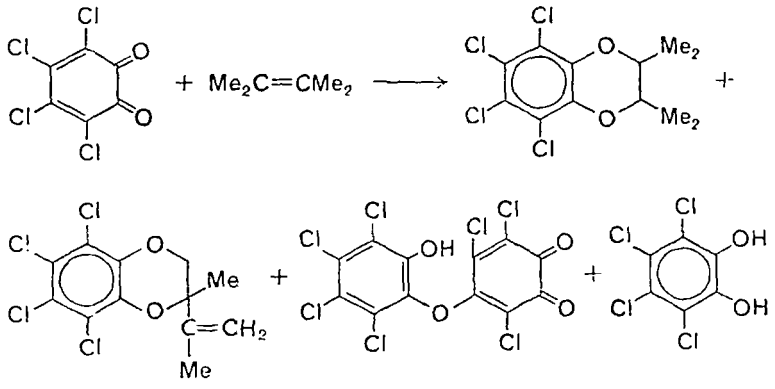
two-step carbonium ion intermediate mechanism is presented and once again steric effects appear to outweigh electronic effects in determining the structure of the product.

(5) Finally, two reports have been made of relatively unactivated double bonds entering into reactions with tetrahalo-1,2-benzoquinones. The first involves acenaphthylene and the quinone as a diene (equation 378)[441].



(378)

The second is the addition of 2,3-dimethyl-2-butene to tetrachloro-1,2-benzoquinone and leads to several products besides the expected dioxan derivative (equation 379)[442]. The preliminary experiments reported suggest



(379)

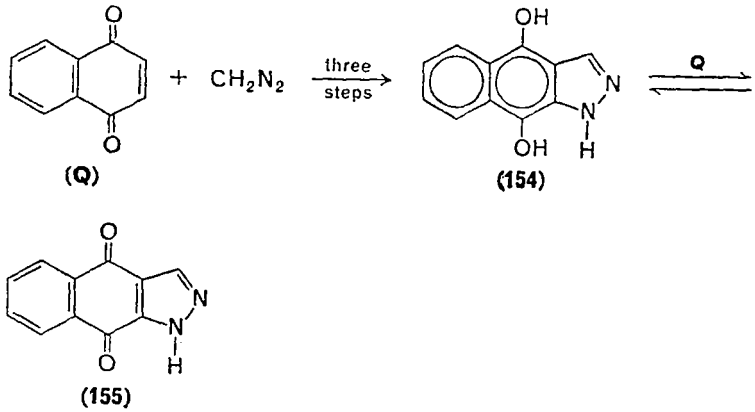
that two competing reaction paths are operating: (i) direct cycloaddition leading to the benzodioxan, and (ii) an allylic radical sequence leading to the other products. Tetrabromo-1,2-benzoquinone gives similar products.

B. Cycloaddition of Diazo Compounds

The first observation of the addition of diazomethane to 1,4-benzo- and 1,4-naphthoquinone was made in the last years of the 19th century[443,444]. It was more than thirty years later, after Diels and Alder had rekindled the

interest in cycloaddition chemistry, that Fieser re-examined and expanded the field[445]. The additional study was motivated both by the feeling that von Pechmann did not understand the structure of the product and the desire to explore the possible synthesis of cyclopropane derivatives of quinones and hydroquinones.

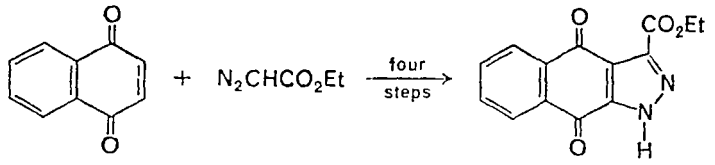
Fieser and Peters found that von Pechmann's elemental analyses were not quite correct and that the addition of diazomethane follows the well-established pathway; i.e. reductive addition, isomerization, enolization and cross-oxidation (equation 380). The intermediate **154** and product



(380)

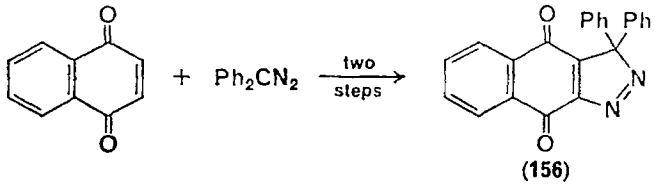
155 are interesting in that the hydroquinone is yellow and the quinone is colourless under most circumstances. The evidence, including electrochemical data, leaves no doubt that the structures are correct.

Ethyl diazoacetate and diphenyldiazomethane also add cleanly to 1,4-naphthoquinone. The former adds slowly allowing ample time for the cross-oxidation reaction to take place (equation 381). Thus, in contrast to



(381)

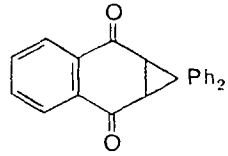
diazomethane, no intermediate is isolated. The addition of diphenyldiazomethane was carried out in an effort to prevent rearrangement to a pyrazole ring. Chemical evidence shows that the product does contain a cyclic azo arrangement (equation 382). The pyrolysis of **156** did lead to some product that was tentatively assigned a fused cyclopropyl structure.



(382)

(156)

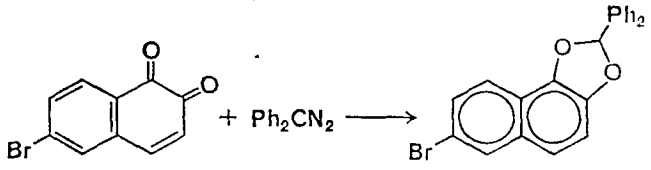
This pyrolysis has been carefully re-examined and the correct structure **156a** and mechanism determined[446, 447].



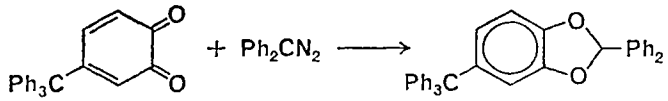
(156a)

The use of dialkylazomethanes produced even less satisfactory results. It was found that 1,4-benzoquinone also adds diphenyldiazomethane, but the chemistry of the product appeared less interesting and was not pursued.

This study of the addition of diazo compounds to quinones has included the 1,2-naphthoquinones[448]. With diazomethane only resinous products were obtained and this was thought to be connected with the relatively low stability of the starting quinone. The use of the more stable 6-bromo-1,2-naphthoquinone failed to produce crystalline product and only starting material could be obtained with the milder reagent ethyl diazoacetate. The conclusion, that the alkene linkages of 1,2-quinones are not reactive toward diazo compounds, is clearly supported by the reactions of diphenyldiazomethane with the heterodiene system (equations 383 and 384).

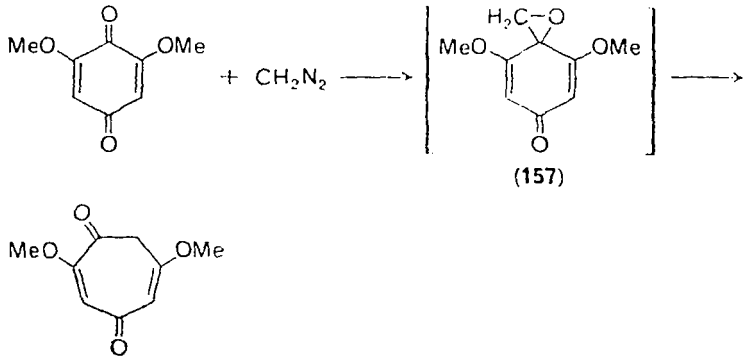


(383)



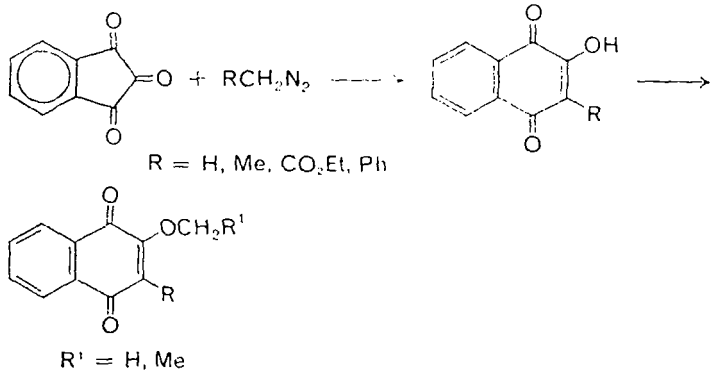
(384)

An interesting ring enlargement reaction of quinone with diazomethane has been reported[449]. It was suggested that the intermediate **157** may be involved (equation 385). A related ring enlargment of trioxoindan has



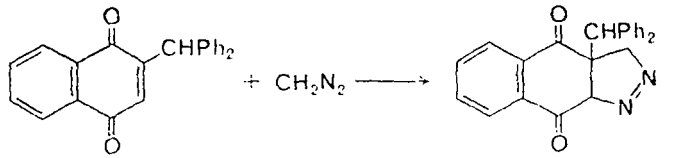
(385)

been shown to produce quite reasonable yields of substituted 2-hydroxy-1,4-naphthoquinones (equation 386)[450]. In certain cases, the actual product isolated was a 2-alkoxy derivative.



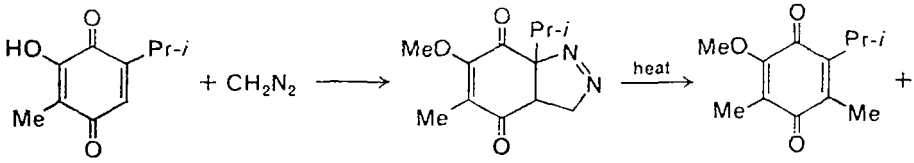
(386)

Fieser and Hartwell succeeded in stopping the reaction sequence at the pyrazoline stage by using the so-called 'blocked' quinone 2-diphenylmethyl-1,4-naphthoquinone (equation 387)[448].

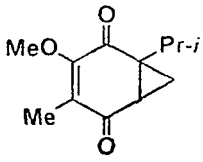


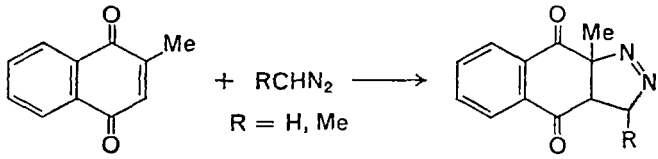
(387)

A continuation of this work with blocked quinones produced a cyclic azo compound that pyrolysed to a fused cyclopropyl derivative (equation 388)[193]. When this work was extended to a re-examination of 2-methyl-1,4-naphthoquinone and diazomethane, several conflicting literature reports were resolved[451]. The addition takes place in the expected manner (equation 389) and the adduct exhibits chemistry analogous to that found



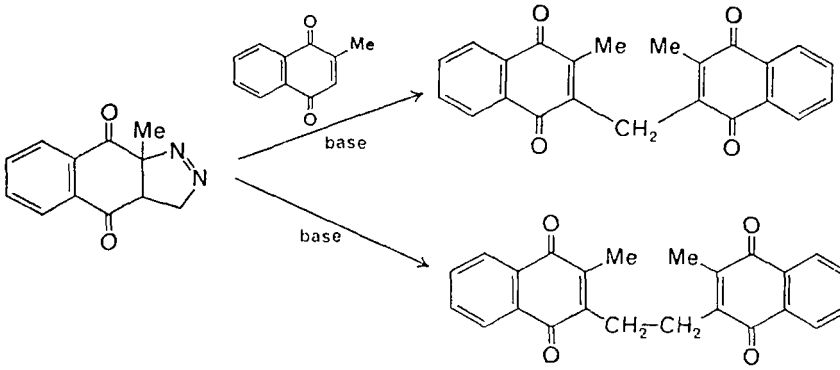
(388)





(389)

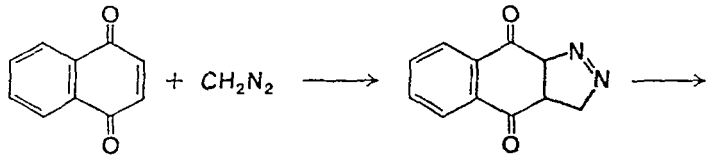
for 2-hydroxythymoquinone. Diazoethane also added in the expected manner; diphenyldiazomethane did not react under the same conditions. The base-catalysed dimerization of adducts of this general structure provides a convenient route to methylene and dimethylene diquinones (equations 390 and 391)[452].



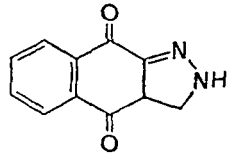
(390)

(391)

A recent extension of this quinone addition has resulted in the isolation of the expected initial adduct (**158** in equation 392)[453]. This compound is quite unstable and is easily converted to a yellow isomer that had generally been pictured as a 1,4-naphthalenediol derivative. Evidence is presented for believing that **159** is the correct structure.

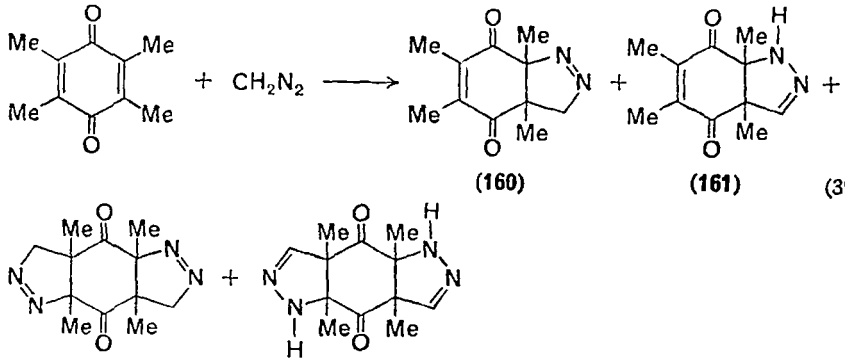


(158) (392)



(159)

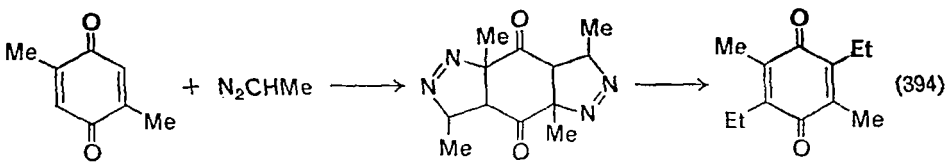
The logical extreme case of a blocked quinone in the present sense would be 2,3,5,6-tetramethyl-1,4-benzoquinone (duroquinone). A re-investigation of the report that diazomethane adds to the carbonyl group showed that quite normal cycloaddition takes place[454,455]. Four products were isolated under the reaction conditions given earlier (equation 393). The conversion of **160** to **161** and **162** to **163** can be achieved under mild conditions. Pyrolysis leads to fused cyclopropane systems.



(160) (161) (393)

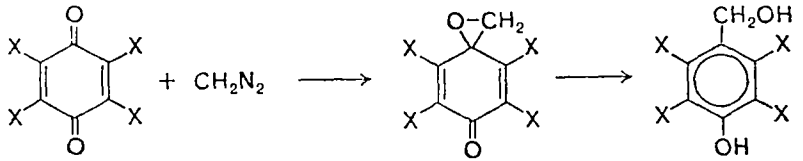
(162) (163)

Simpler quinones have also been employed in these reactions and the cycloaddition product can lose nitrogen to produce alkylated product as well as fused cyclopropyl derivatives (equation 394)[456].



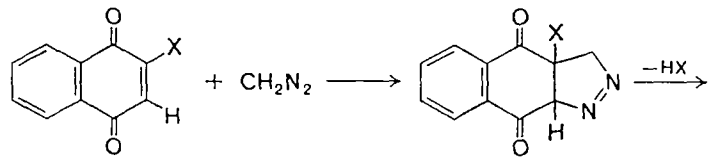
(394)

It has been shown recently that diazomethane adds to a carbonyl group in quinones with all of the hydrogens replaced by electronegative groups (equation 395)[457]. The epoxy product **164** is useful for the synthesis

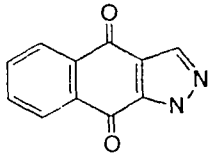


X = F, Cl, Br, I, OMe, O_2CMe **(164)** (395)

of certain types of benzyl alcohols. The 1,4-naphthoquinones bearing similar 2,3-substituents also show this chemistry. When one of the substituents is hydrogen, ring addition takes place and subsequent elimination occurs readily (equation 396).



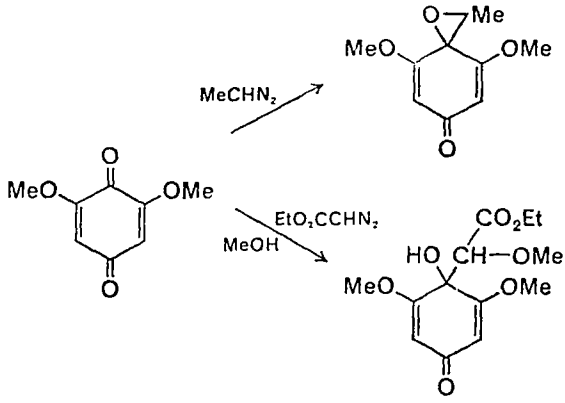
X = Cl, Br, SMe, SOMe, SO_2Me (396)



A later and closely related study showed that carbonyl addition of diazomethane and diazoethane also occurs with 2,6-dimethoxy-1,4-benzoquinone[458]. The exact nature of the product depends on the substitution pattern of the quinone and the diazo compound employed (e.g. equations 397–400).

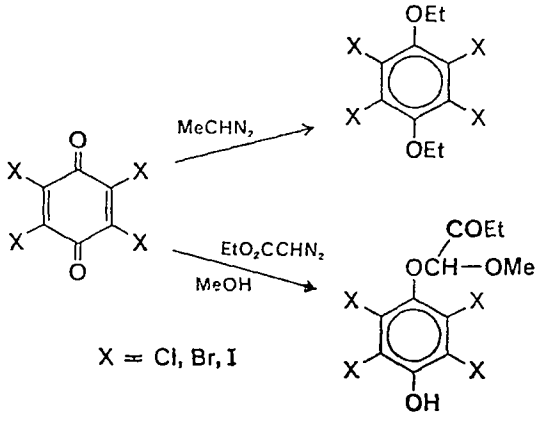
Earlier reports of the addition of diazomethane to 1,4-naphthoquinone have been re-examined, the structure of the adduct revised and a new product identified (equation 401)[459]. The general structure of **166** was consistent with its spectra and formation from **165** and dimethyl sulphate or diazomethane. The alternative structure **167** was not ruled out.

Awad and collaborators have expanded their studies to include the 1,4-benzoquinones[460]. With 2-methyl-1,4-benzoquinone, diazomethane and diazoethane each produced a single product (**168** in equation 402).



(397)

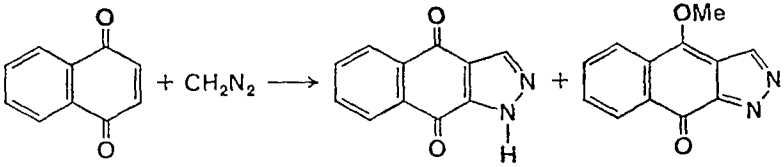
(398)



X = Cl, Br, I

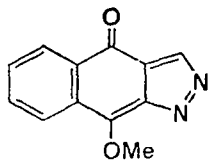
(399)

(400)

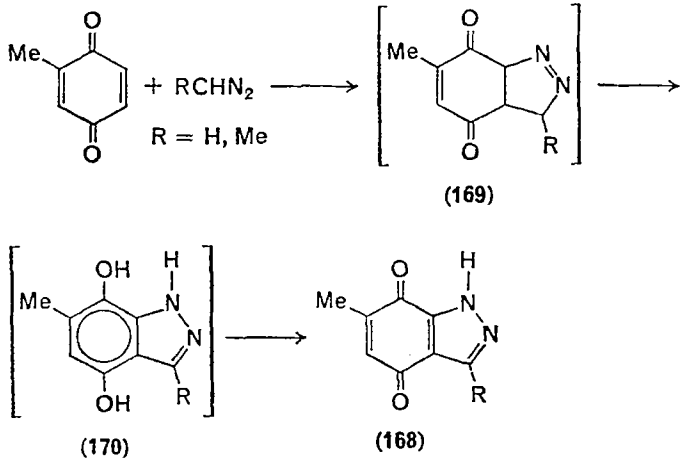


(165) (166)

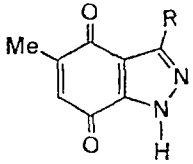
(401)



(167)

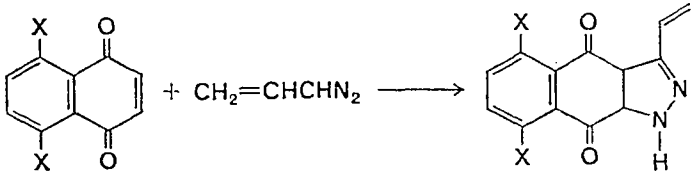


Neither of the suggested intermediates (**169** and **170**) was isolated. The possible isomeric product **171** was considered (as were the appropriate



isomeric intermediates) but no evidence favouring one or the other is presented. The oxidized state of the product **168** is attributed to atmospheric oxygen, because no 2-methylhydroquinone could be found in the reaction mixture.

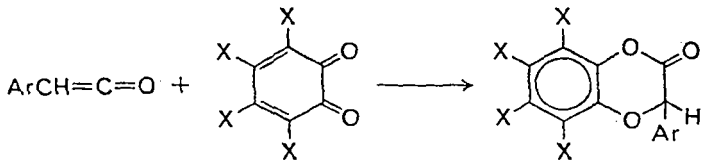
The addition of vinyldiazomethane to substituted 1,4-naphthoquinones has been reported recently (equation 403)[461].



Until recently only a single study of the reaction 1,2-quinones with diazoalkanes had been added to the early work of Fieser and Hartwell[448,462]. Fair yields of cyclic lactones were obtained from the

ketoketenes formed in the pyrolysis of acyldiazomethanes (equations 404 and 405). A variety of aryl groups, stearoyl and two bis-diazomethanes were used.

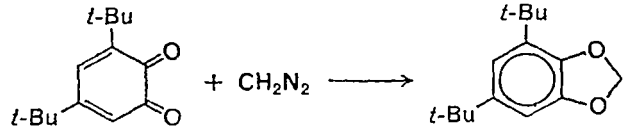
(404)



(405)

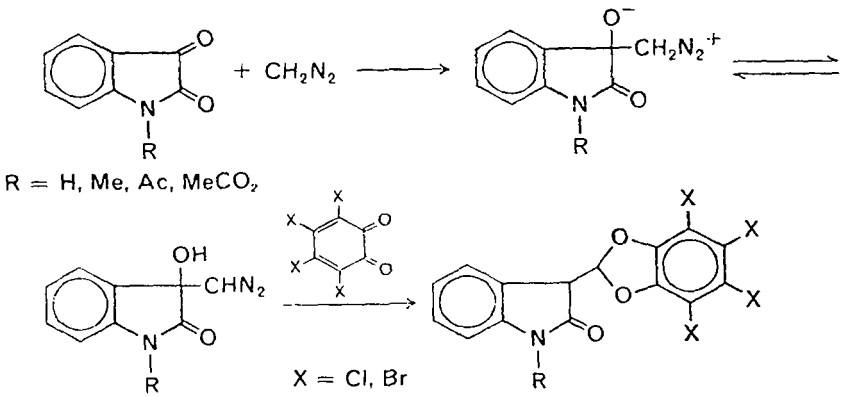
X = Cl, Br

With diazomethane itself the cyclic diether first reported is the usual product (equation 406)[463]. These products are also familiar from our earlier discussion of carbonyl hydrazone addition (see section III).



(406)

The tetrahalo-1,2-benzoquinones have been used to trap intermediate 1:1 addition products of diazomethane and α-dicarbonyl compounds (equation 407)[464]. Similar chemistry was found for a series of indanediones.

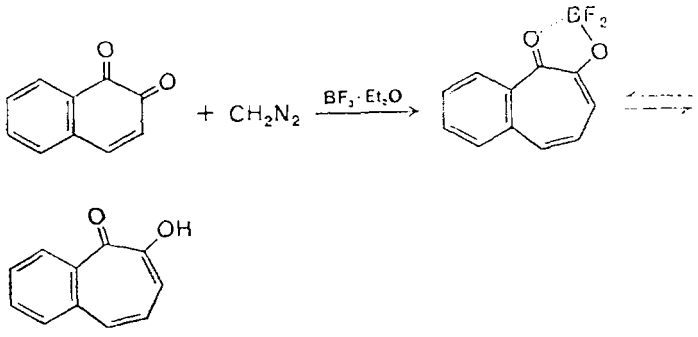


R = H, Me, Ac, $MeCO_2$

(407)

X = Cl, Br

A ring enlargement reaction starting from a 1,2-quinone has been reported (equation 408)[465]. The intermediate boron complex can be isolated and the overall yield is a respectable 24%.

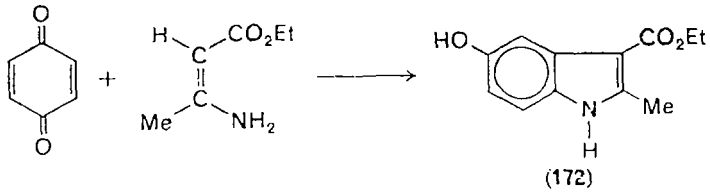


(408)

C. The Addition of Enamines

1. Nenitzescu condensation

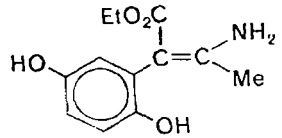
The pharmacological activity of several naturally occurring 5-hydroxyindoles has resulted in extensive study of the general method for their synthesis first published by Nenitzescu[466]. The original reaction (equation 409) has been modified extensively[467–470]. Some of this work, while



(409)

(172)

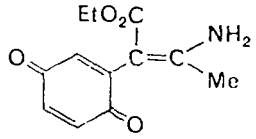
emphasizing synthetic variations, has also produced useful mechanistic information. An early proposal[468] suggested an intermediate, **173**, that cyclizes to product in some unspecified manner. A more elaborate picture of this mechanism has been presented[471], but with little solid evidence. The variation of yield with substitution seemed to these authors to be consistent with the proposed mechanism. A modification has been offered



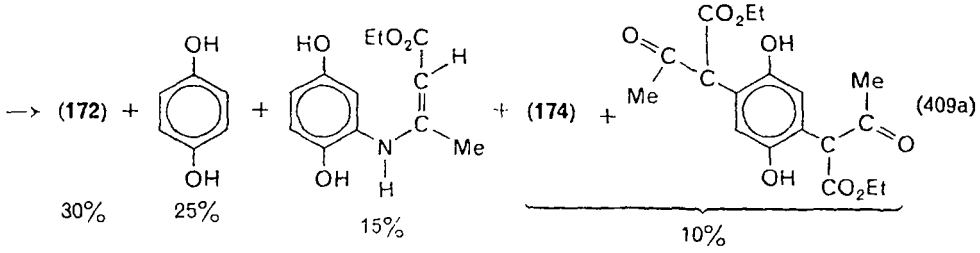
(173)

in which both the hydroquinone **173** and its oxidation product **174** are intermediates[472]. At about the same time a careful product isolation and characterization study provided a good deal of experimental support for such a path (equation 409 with some additional products)[473]. The high

total yield (some experiments were as high as 95%) is important. Similar results were found with 2-methyl-1,4-benzoquinone.

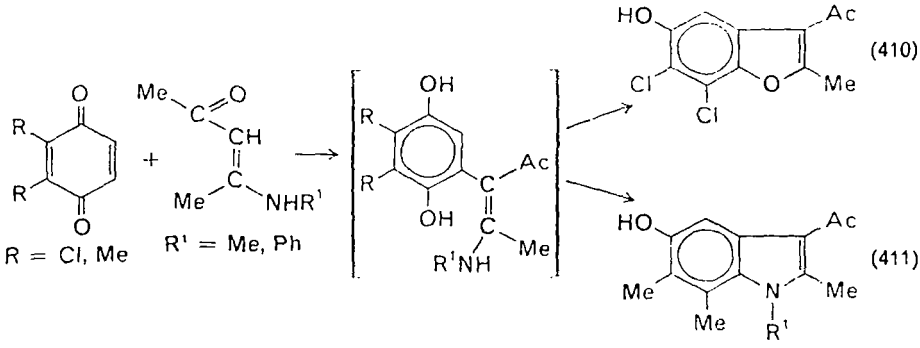


(174)



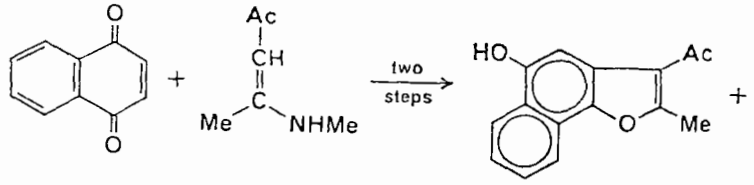
(409a)

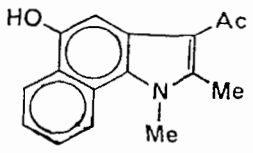
The Nenitzescu condensation can also represent a valuable method for the synthesis of substituted benzofurans. Grinev and collaborators have made an impressive contribution to our understanding of both paths. As a part of their continuing study of the addition of a monoimine of acetylacetone to 1,4-benzoquinones, the influence of substituents in the quinone was studied[474]. As indicated in equations (410) and (411) the electronic nature of substituents in the quinone has a very strong effect on the direction of the cyclization and hence on the structure of the observed product. The direction of the effect is certainly in accord with electronic expectations, but the magnitude of the effect is surprising. When 1,4-naphthoquinone is used in the reaction, the nature of the nitrogen substituent is significant in determining the product (equation 412). With acetylacetone *N*-phenylimine and 1,4-naphthoquinone only the indole was obtained (i.e. **175** with *N*-Ph rather than *N*-Me).



(410)

(411)

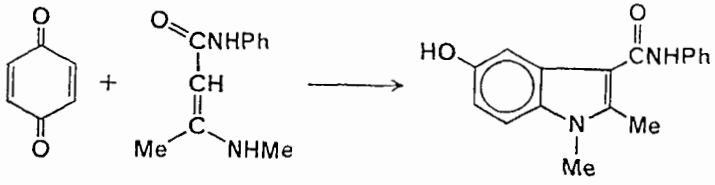




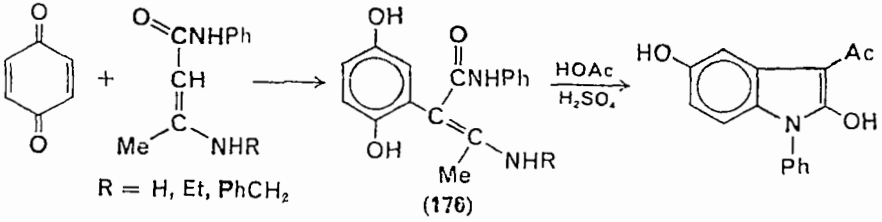
(175)

(412)

The synthesis of variously substituted indoles has been accomplished via the addition of the anilides of β-amino- and N-alkyl-β-aminocrotonic acids to 1,4-benzoquinone[475]. The nature of the substituent on nitrogen has a marked effect on the reaction and its outcome, as indicated by equations (413) and (414). An intermediate analogous to **176** was postulated in the N-Me case, but could not be isolated.



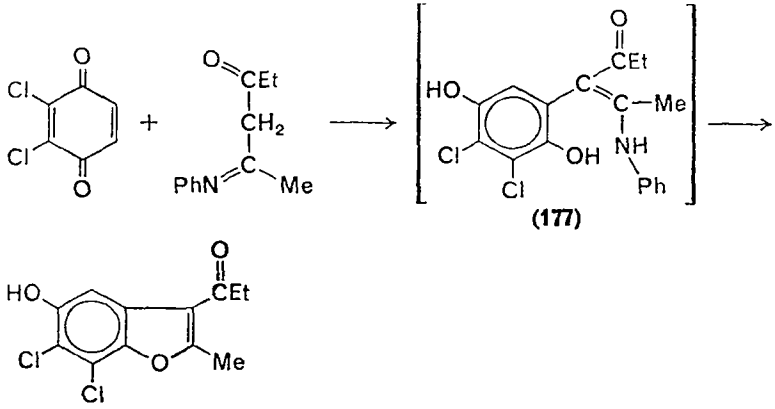
(413)



(176)

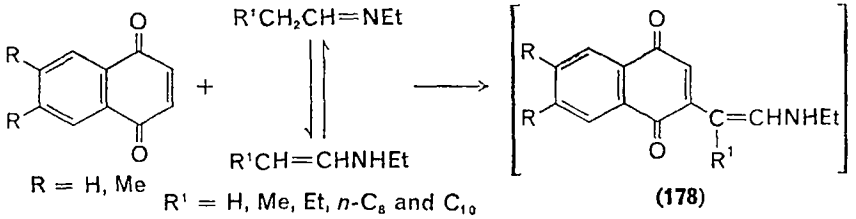
(414)

The Michael addition of 1,4-benzoquinones and the monoimines of 1,3-diketones can lead, by subsequent cyclization, to either indoles or furans. The question of whether the enamine and/or the enol system engages in the second reaction step has been studied (equation 415)[476]. The intermediate **177** was not isolated and none of the isomeric 2-ethyl-3-acetyl-5-hydroxy-6,7-dichlorobenzofuran was obtained. Thus, it may be suggested that the carbonyl imino group is always involved and the molecule eliminated (H_2O or $PhNH_2$) is significant.

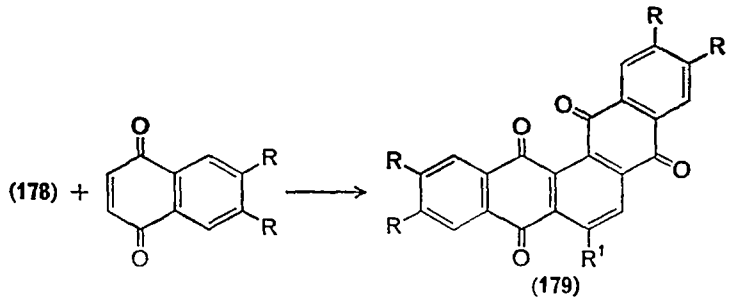


(415)

An interesting combination of the Michael and Diels–Alder reactions of enamines and quinones occurs when the Michael product reacts with additional quinone. This sequence leads to polycyclic compounds in quite reasonable yields (equations 416 and 417)[477]. Both the intermediate **178**



(416)



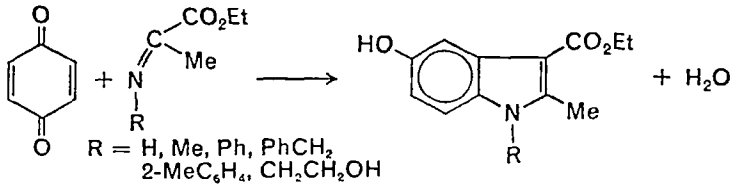
(417)

and the isolated product **179** presumably require the oxidation of an intermediate by the excess of quinone present. The significant intermediate, **178**, was not isolated and the overall yield is strongly dependent on the nature of R^1; i.e. the aldehyde from which the enamine is prepared. Finally, the presence of acid seems to be required.

A continuation of these studies showed that both 5- and 6-methyl-1,4-naphthoquinones react but the product mixture could only be

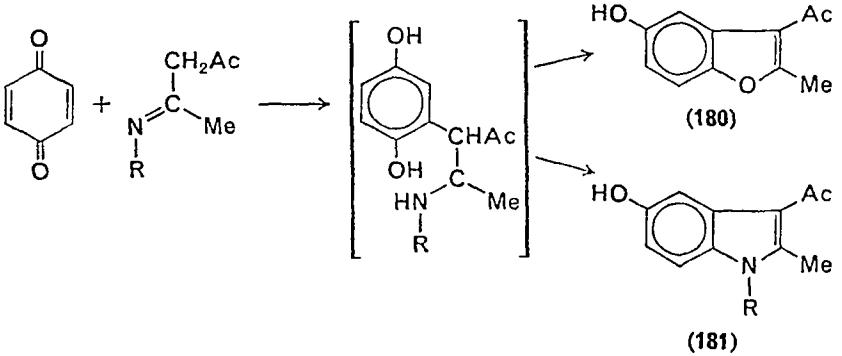
separated by paper chromatography[478]. The condensation of 1,4-anthraquinone occurred but less readily; 5,8-quinolinoquinone did not react.

In some cases the yields of indole in these reactions is quite small and methods have been sought to improve the outcome. One beneficial approach is the azeotropic distillation of the water formed in the reaction (equation 418)[479]. It appears that the water reacts with the enamine to release ammonia or amines that cause the polymerization of the quinone.



(418)

A somewhat more detailed study of the effect of imino nitrogen substituents has been made[480]. Several *N*-substituted monoimines of acetylacetone were allowed to react with 1,4-benzoquinone under the same conditions and the product(s) determined (equations 419 and 420).



(419)

(420)

The product distribution is given in Table 16. The relationship between product and basicity of amine is striking; i.e.

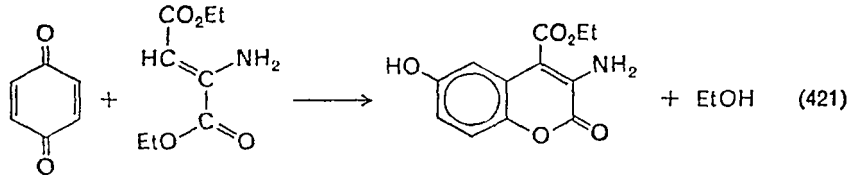
p*K* 3·3–4	benzofurans
p*K* 4·6–5	mixture
p*K* 8–10	indoles
still weaker bases	no reaction

The synthetic utility of the Nenitzescu condensation has been greatly expanded by Domschke and collaborators[481]. Much of this work deals with benzofuran synthesis, but coumarins (equation 421)[482] have also been prepared.

TABLE 16. Product distribution in the reactions of monoimines of acetylacetone with 1,4-benzoquinone (equations 419 and 420)[490]

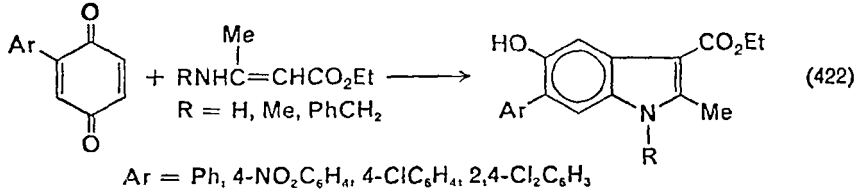
R	Product (180) %	(181) %
n-Bu	39	
CH_2CO_2Et[a]	×	×
CH_2CH_2OH[a]	×	×
CH_2Ph[a]	×	×
Ar(XC_6H_4)		
4-Me		37
4-MeO		50
2-MeO		12
4-Me_2N		58
4-AcNH		57
4-Br	0	0
4-NO_2	0	0

[a] Total yields are in the range 20–49%. Both products are present, but individual yields were not recorded.



(421)

Finally, aryl-substituted quinones have been used in the synthesis of indoles by the Nenitzescu route, but the yields have been very disappointing (equation 422)[483].

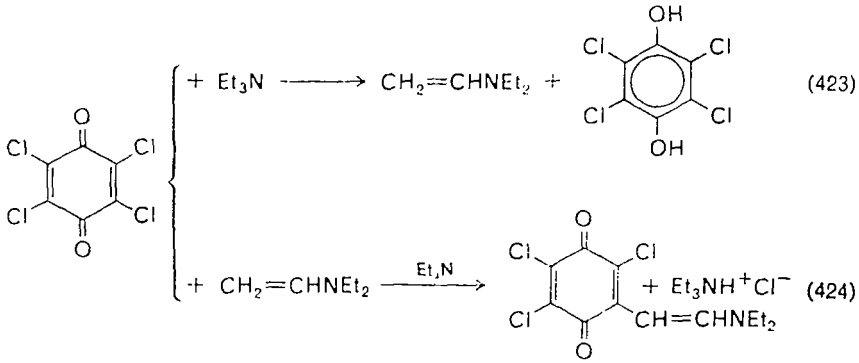


(422)

Ar = Ph, 4-$NO_2C_6H_4$, 4-ClC_6H_4, 2,4-$Cl_2C_6H_3$

2. The oxidation of tertiary amines

While examining the oxidation of tertiary amines with quinones, the following important reaction was discovered[484]: a solution of triethylamine and chloranil in benzene turned green, then blue, and finally a colourless crystalline product precipitated. The colourless compound was shown to be triethylamine hydrochloride and tetrachlorohydroquinone was isolated from the reaction mixture. The blue compound was also obtained in a crystalline form and shown to have the molecular formula $C_{12}H_{12}O_2NCl_3$. These data and i.r. spectra suggested the structure **182** and the following reactions were proposed (equations 423 and 424).

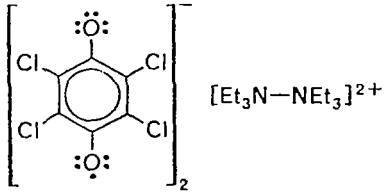


(182)

A thorough evaluation of the scope of the reaction revealed that for practical synthetic applications it is rather limited. Aside from chloranil and bromanil, only the 2,5- and 2,6-dichloro (and presumably the trichloro, di- and tribromo quinones) give any useful product. A wide variety of tertiary amines was tried, with few giving satisfactory results (*N*-ethylpiperidine is an exception). Some of the amines that did react in both steps (e.g. tri-*n*-butylamine) gave products that were quite reactive and consequently difficult to purify. Some speculations concerning the mechanistic details are given; for example, the available evidence suggests that the formation of a sufficient concentration of suitably activated molecular complexes is as important to the reaction's success as is a suitable redox potential.

A more detailed study of the absorption spectra of chloranil and aliphatic amines has revealed some useful facts about enamine formation[485]. As expected, solutions of ethylamine or diethylamine and chloranil show changing u.v. spectra with time and shortly produce the corresponding *N*-substituted 2,5-diamino-3,6-dichloro-1,4-benzoquinone (see section VIII). However, when a suspension of chloranil is shaken with pure triethylamine, a dark-green precipitate forms. This dark-green solid shows u.v.

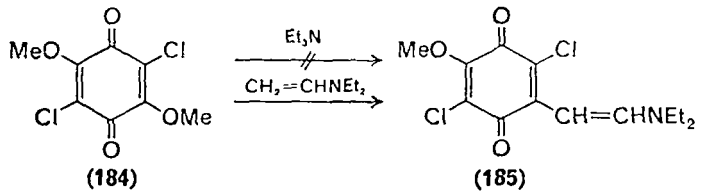
and e.s.r. spectra that are very similar to those of the product of sodium iodide and chloranil. This latter material is generally accepted as the sodium salt of chloranil semiquinone. The spectra of both products in methanol, ethanol and triethylamine are very similar, their i.r. spectra being virtually identical. There seems little doubt that the dark-green solid contains the chloranil semiquinone anion **183**. The detailed nature of the cation was not determined, but on the basis of preliminary data, it may have the structure shown. The addition of acid to this salt, **183**, regenerates



(183)

pure chloranil, showing that no substitution has taken place at this stage. The salt appears to be quite stable in the absence of solvent, but in acetone its spectrum changes with time until 2,3,5-trichloro-6-(2′-diethylaminovinyl)-1,4-benzoquinone (**182**) is produced. Foster argues against a charge-transfer complex and suggests **183** as the first phase of the reaction described by Henbest and collaborators.

In the further study of the reactions of quinones and tertiary amines, a useful example has been found in 2,5-dichloro-3,6-dimethoxy-1,4-benzoquinone[486]. This quinone, **184**, does not oxidize triethylamine to an enamine, but if the enamine is formed it undergoes the substitution reaction readily (equation 425). Such a reaction, with its deep-blue

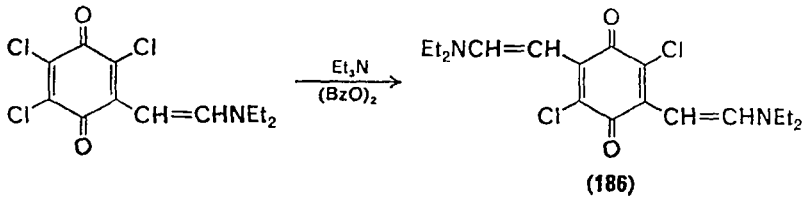


(425)

(184) **(185)**

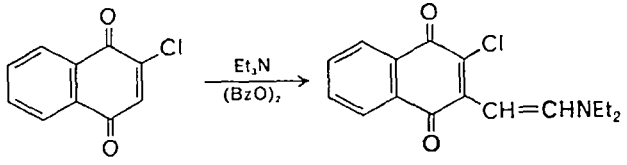
product **185**, represents a very useful test for the presence of enamines. Using quinone **184**, a number of oxidizing agents were tried with triethylamine; for example, enamines were formed with benzoyl peroxide and with *N*-bromosuccinimide, but were not formed either with MnO_2 or with 1,4-benzoquinone. The enamine used in equation (425) was generated by added benzoyl peroxide and it was found that the amount of blue quinone **185** formed is proportional to the peroxide added up to a peroxide : quinone ratio of 1 : 1.

The use of an added oxidant, like benzoyl peroxide or *N*-bromosuccinimide, provides a useful synthetic route. In several instances a reaction failed because the quinone failed to generate the enamine, not because of the substitution step (for example, equations 426–428).

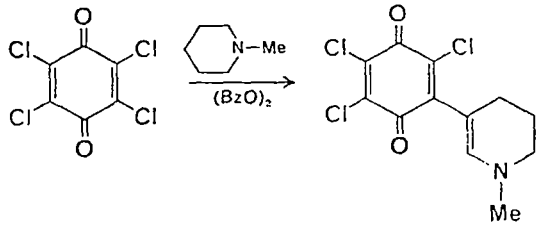


(426)

(186)

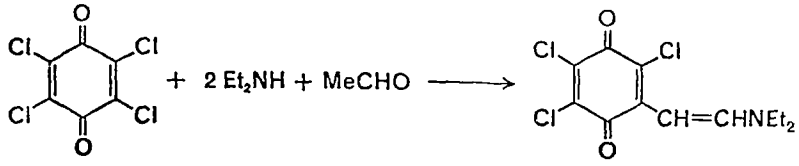


(427)

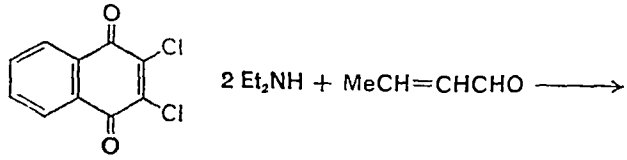


(428)

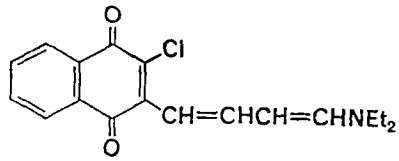
In an effort to confirm the structure of the chloranil–triethylamine adduct, another useful new synthetic approach was developed[487]. Upon simply mixing chloranil, diethylamine and acetaldehyde, a rapid reaction took place and the desired product was obtained in excellent yield (equation 429). The disubstituted product **186** can also be prepared by further additions of acetaldehyde and diethylamine. A wide variety of secondary amines is useful in this reaction and those quinones that react well with primary amines generally react with acetaldehyde and secondary amines as shown in equation (429). A complication is found with dimethylamine in that a substantial amount of direct substitution takes place and the yield of desired vinylamino compound decreases. It appears that acetaldehyde may be the only practical carbonyl reactant. Higher aldehydes gave blue solutions, but the products were difficult to purify. A reaction mixture of chloranil, acetone and morpholine led only to substitution of morpholine for chlorine. One interesting exceptional case was crotonaldehyde (equation 430). The yield of **187** was only 20%, but it could be



(429)



(430)



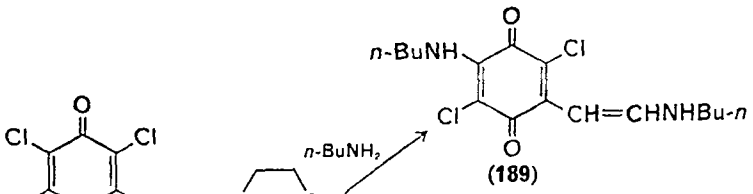
(187)

increased to 80% when the presumed intermediate **188** was prepared externally.

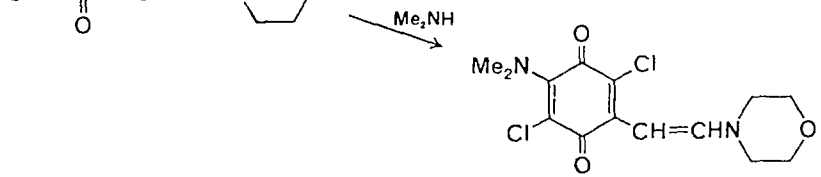
$CH_2{=}CHCH{=}CHNEt_2$

(188)

The dialkylaminovinylquinones undergo the usual nucleophilic substitution reactions of quinones (see section VIII). An interesting and exceptional reaction is illustrated in equations (431) and (432). It appears



(431)



(432)

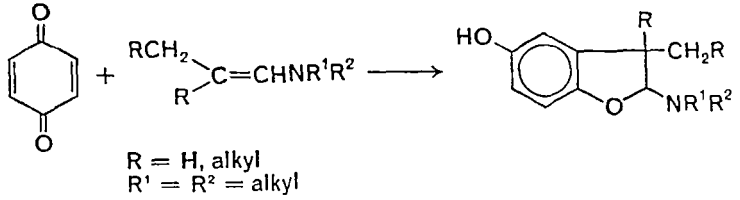
that the disubstitution product **189** arises from the preliminary substitution of the 2-chloro group by butylamine. This presumed intermediate has been thought to allow an *ortho* quinoneimine form that can lead to the

second substitution. Some comparison experiments were carried out in the substitution of chloro and methoxy quinones by primary and secondary amines. This aspect of quinone chemistry will be treated in section VIII.

3. Brief notes

Enamines and quinones have been shown to undergo several interesting reactions that deserve our notice, but have not been studied in much detail.

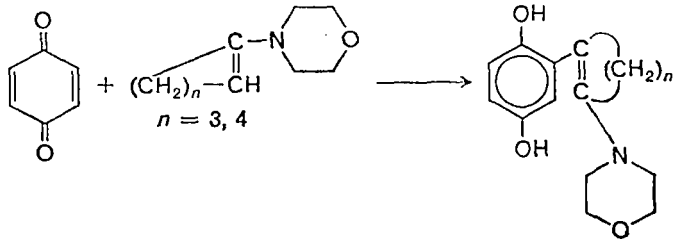
(1) A group under the direction of Brannock has made a number of contributions to our knowledge of enamine chemistry. As a part of their general survey of the enamine–carbonyl reaction, they prepared several dihydrobenzofuranols (equation 433)[488].



(433)

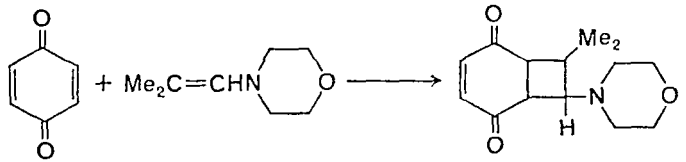
R = H, alkyl
$R^1 = R^2$ = alkyl

(2) A study similar to that just cited has been carried out by Shvedov and Grinev[489]. They found that excellent yields of the initial addition product of 1,4-benzoquinone and certain enamines can be obtained by working in benzene at ice temperature (equation 434). In addition to the



(434)

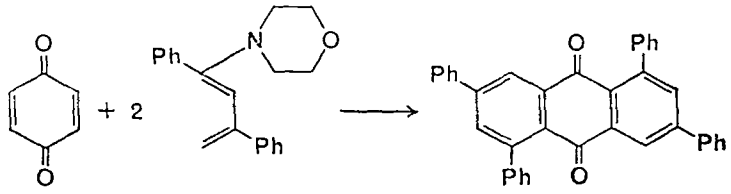
enamines of cyclic ketones, some aliphatic aldehydes gave similar results. The morpholine enamines seemed to be very superior. One exceptional case was found in the isobutyraldehyde enamine (equation 435). The structure of product **190** was assigned tentatively.



(435)

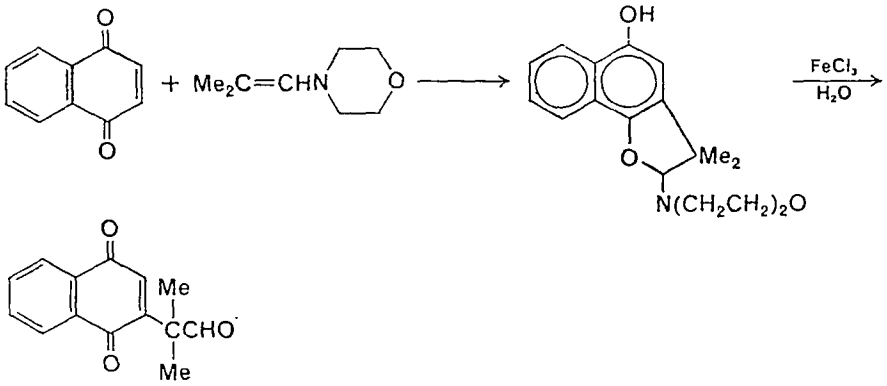
(190)

(3) Domschke has shown that 1,4-benzoquinone and enamines can undergo a Diels–Alder reaction and produce substituted anthraquinones (equation 436)[490]. The required dienamines were prepared by the condensation of two moles of morpholine–acetophenone enamine with the loss of one imino group. The expected intermediate (initial adduct) was not isolated.



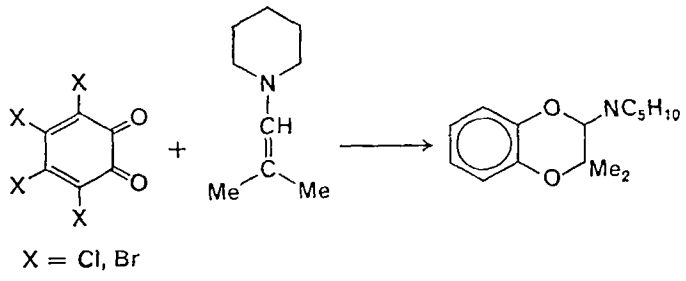
(436)

(4) It has been shown that a variety of oxidants will convert certain coumarins to quinones bearing a formylalkyl substituent (equation 437)[491]. The yields are better than 70%, but to be successful at least one of the positions *ortho* to the phenolic hydroxy group must be substituted.



(437)

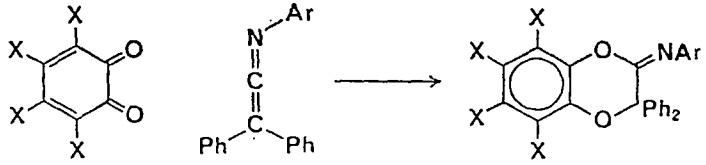
(5) Enamines will react with 1,2-quinones in a fashion reminiscent of the Diels–Alder reaction (equation 438)[492,493]. The yields are, with a few exceptions, good or excellent. Several other 1,2-quinones were used and the enamine can involve cycloalkenes and other secondary amines.



X = Cl, Br

(438)

(6) Diphenylketenimines with *N*-aryl substituents also react with 1,2-quinones to provide an interesting series of aryliminolactones (equation 439)[494]. The yields are uniformly high.

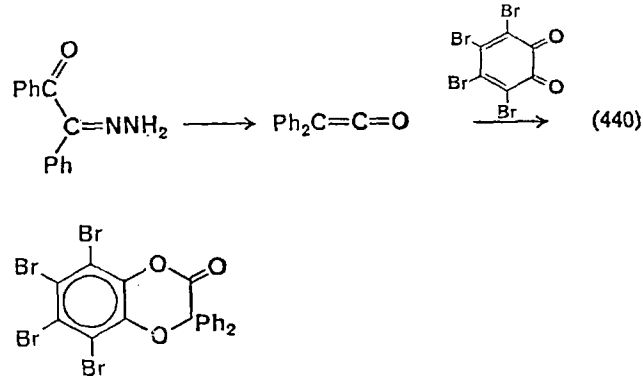


(439)

X = Cl, Br; Ar = Ph, 2- or 4-MeC_6H_4, 4-$MeOC_6H_4$

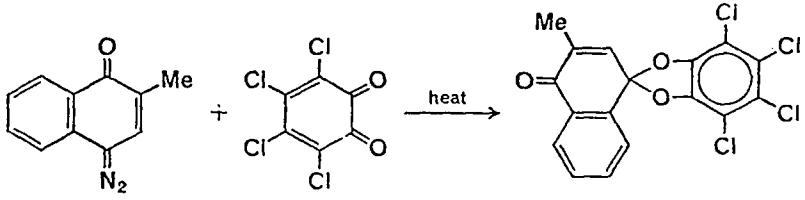
D. Related Cycloaddition Reactions

The 1,2-quinones undergo cycloaddition reactions with ketenes to form cyclic lactones[495,496]. The reaction (equation 440) allows capture of



(440)

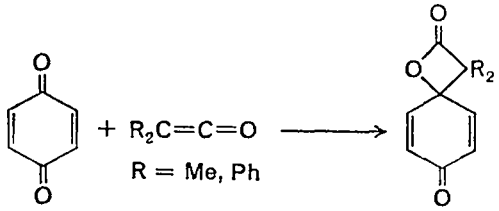
ketenes formed as unstable intermediates in the thermolysis of diazo ketones. In cases where no Wolff rearrangement takes place (e.g. 2-methyl-1,4-naphthoquinone diazide), the carbene forms a monoacetal with the quinone (equation 441).



(441)

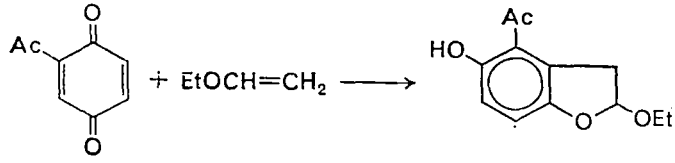
The reaction of diphenylketene with 1,4-benzoquinone was reported in 1907[497] and recently the analogous chemistry of dimethylketene was investigated[498]. Both ketenes gave a spirolactone when one equivalent was

used (equation 442). Two equivalents of the ketene led to a low yield of the bis-spirolactone when R = Ph, but R = Me gave only polymer.



(442)

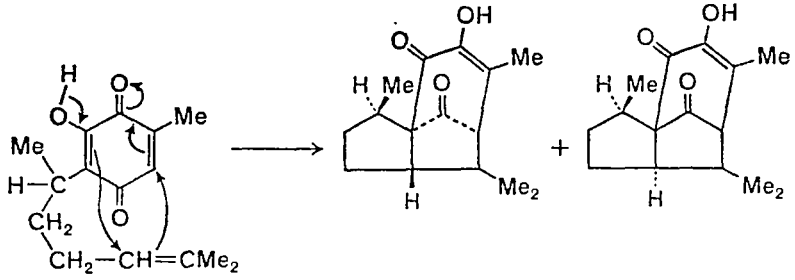
A variety of α,β-unsaturated ethers undergo cycloaddition reactions with 2-acetyl-1,4-benzoquinone to form derivatives of benzofuran (equation 443)[499]. This study has been greatly expanded recently and a



(443)

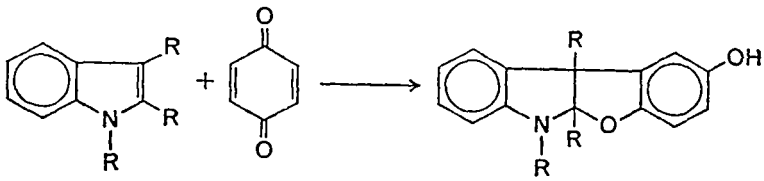
number of additional enols examined[500, 501]. Enol esters and cyclic enol ethers can be used and 2-carbomethoxy-1,4-benzoquinone is also a suitable reactant. The nitrogen heterocycles, pyrrole and imidazole, are also capable of similar addition reactions when strong electron-withdrawing groups are present in the quinone.

An interesting 1,3-cycloaddition of a hydroxy 1,4-benzoquinone has been invoked to explain the relationship of the observed products and the newly characterized parent compound perezone (equation 444)[502].



(444)

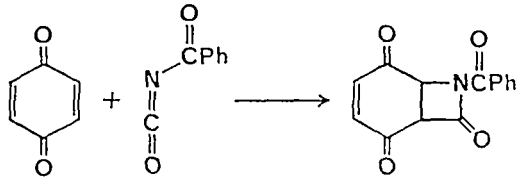
The indoles with alkyl substituents in the 3-position are known to undergo cycloaddition reactions with 1,4- and 1,2-quinones (equation 445)[503, 504]. The reaction is known to be strongly acid-catalysed, quite general and subject to some steric hindrance. The more recent study has investigated in some detail the mechanism and especially the formation of 2:1 adducts.



R = H, Me

(445)

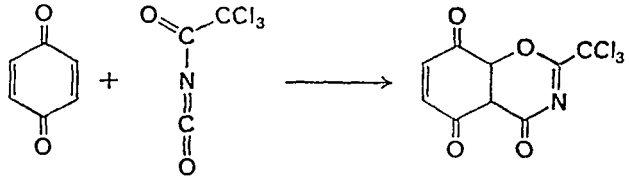
The number of 2,3-cycloadditions found in quinone chemistry is somewhat limited, but a potentially useful example has been reported in isocyanate chemistry[505]. Both 1,4-benzo- and 1,4-naphthoquinone react with benzoyl isocyanate (equation 446). The product **191** can undergo



(446)

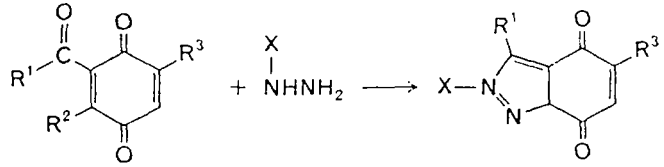
(191)

epoxidation and saponification. In the case of 1,4-naphthoquinone, the latter reaction provides a reasonable route to the fairly stable 2-carboxy-1,4-naphthoquinone. The reaction between 1,4-benzoquinone and trichloroacetyl isocyanate takes the Diels–Alder route (equation 447). No product was obtained with 1,4-naphthoquinone and this isocyanate.



(447)

Several five-membered nitrogen heterocycles fused to dihydro-1,4-benzoquinones have been prepared in good yield (equation 448)[506].

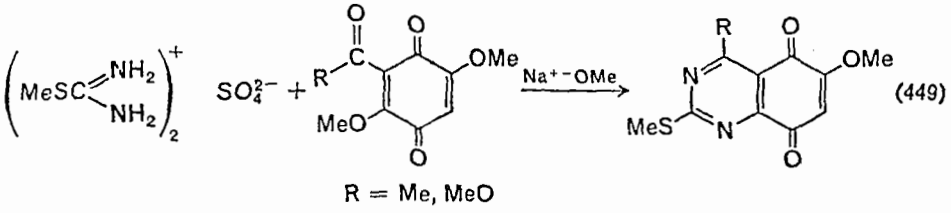


R^1 = Me, MeO
R^2, R^3 = Cl, MeO, NH_2, NHR, NHAr

X = Me, Ph, 4-$NO_2C_6H_4$, Ac, PhCO, 4-Me or 4-$NO_2C_6H_4SO_2$, OH (O in product)

(448)

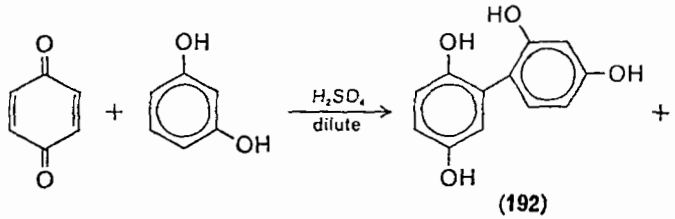
Once again a strong electron-withdrawing group in the quinone is needed. A similar reaction with *S*-methylthiuronium sulphate leads to six-membered heterocycles (equation 449).



(449)

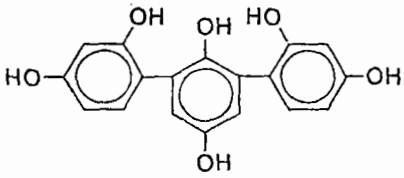
VI. ELECTROPHILIC ARYLATION OF QUINONES

The preparation of quinonoid compounds bearing aryl substituents is an important synthetic goal for both practical and theoretical reasons. An early experimental effort in this area consisted of the acid-catalysed reactions of phenols with quinones (e.g. equation 450)[507]. The mono-substitution product **192** was not correctly named and the orientation of



(192)

(450)

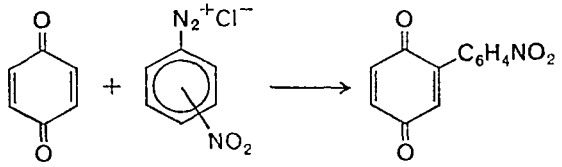


(193)

the disubstitution product **193** was not specified, but the chemistry and the gross structures have recently been verified[508]. The latter work has included a re-investigation of pyrogallol and 1,4-benzoquinone[509]. The same coupling products were obtained, along with self-condensation products.

In recent years it has become clear that the preferred route to aryl-substituted quinones is via diazonium intermediates. The first efforts in this area involved *p*-nitrosophenol or the 1,4-benzoquinone monoxime[510,511]. Several experimental difficulties caused very low yields. The patent literature provided a very important improvement by showing

the efficacy of sodium acetate in an alcoholic reaction medium. This lead was developed by Marini-Bettolo and collaborators who prepared *m*- and *p*-nitrophenyl-substituted 1,4-benzoquinones (equation 451) and studied their conversion to other derivatives[512]. In later papers it was shown that



(451)

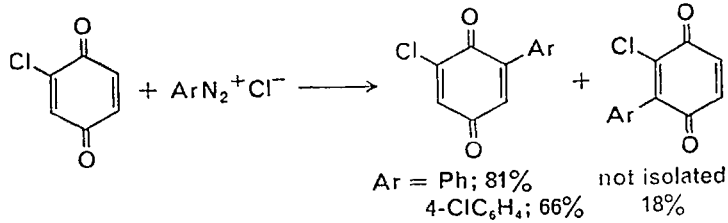
copper powder could increase the yield very sharply, at least for 1,4-naphthoquinone[513]. The range of anilines that could be used was expanded and it was found that hydroquinone is also a suitable starting material for arylation[514].

Over the last forty years the synthesis of a large number of aryl-substituted quinones using this route, with major and minor variations, has been reported[145,186,327g,331,514a-517]. However, in 1958 L'Écuyer and his students (notably Brassard) began publishing a series of detailed synthetic and mechanistic studies of quinone arylation with diazonium salts. In the first paper of the series, a careful search for optimum reaction conditions was made[518]. The following conclusions were reached:

Solvent: water	Buffer: 2 mole $Na^+{}^-OAc$/mole reactant
Concentration: 0·1M	Temperature: gradually rising from 10–15°C to ambient
pH: 5	Anion: Cl^-, Br^-, PO_4^{3-}, SO_4^{2-}, but not NO_3^-

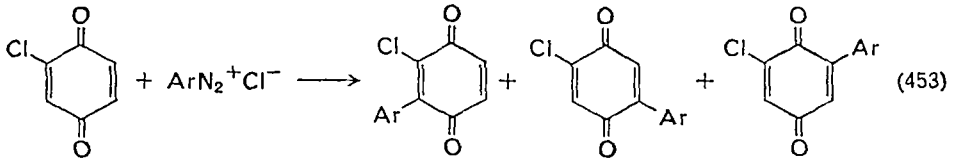
Excellent yields of product were obtained using these general principles with a wide variety of substituted anilines. These monosubstituted quinones can be converted to 2,5-diarylated-1,4-benzoquinones (symmetrical or unsymmetrical) in lower, but still satisfactory yields, by simply repeating the diazonium salt procedure[519]. While only the one product was reported in each case, the modest yields suggest that the isomeric products may also be formed.

The study of the influence of substituents in the quinonoid ring began with 2-chloro-1,4-benzoquinone (equation 452)[520]. The structures of both



(452)

the products found and the missing isomer were demonstrated by the synthesis of more highly chlorinated derivatives by unambiguous routes. This product distribution study has been re-examined and expanded to include the *p*-nitrophenyl case[521]. The earlier discussion of nucleophilic addition showed the effect of quinone substitution, but not of nucleophile substitution (see sections II.B.2 and II.D.2). However, our own observations show that for thiol addition, *para* substituents have only minor effect on the product ratio[522]. In the current study, of electrophilic addition, all three isomers were found in significant yield (equation 453). Clearly

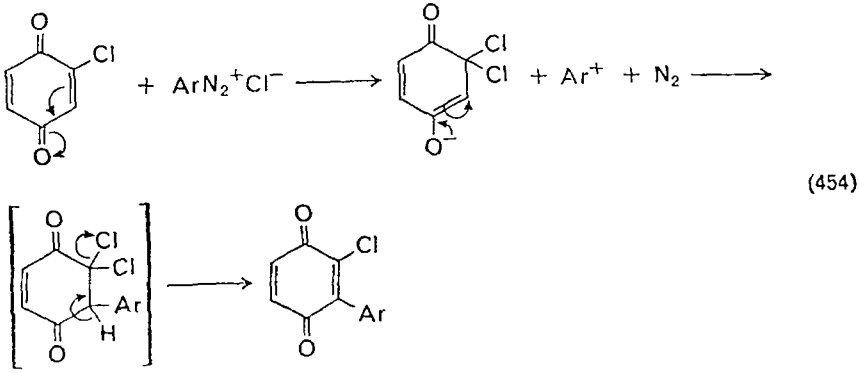


Ar = Ph;	8%	75%	17%
4-ClC$_6$H$_4$;	28%	35%	37%
4-NO$_2$C$_6$H$_4$;	41%	19%	40%

(453)

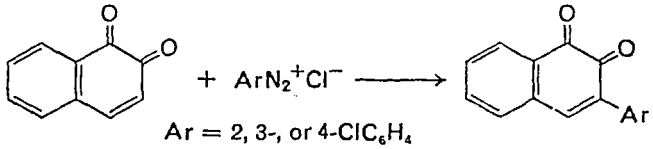
the substituent in the diazonium salt plays an important role in product determination. An earlier report of the addition of a wide variety of substituted aryldiazonium salts to 2-methyl-1,4-benzoquinone also produced only the 2,5-disubstituted product[523]. The yields varied over a very broad range, but this was attributed to the difficulty of isolation, rather than to the substituent. The structure of the product obtained was verified by a careful independent synthesis of all three possible isomeric products[524]. Certain of these studies make contributions to our understanding of the synthetic applications of hydrogen chloride addition to aryl-substituted quinones[520, 521].

On the basis of these studies, an ionic mechanism is presented (equation 454)[521]. A later study of the arylation of 1,2-naphthoquinone produced



(454)

only the 3-aryl isomer (equation 455)[525]. The yields were poor, but the results prompted the consideration of a modified reaction mechanism (equation 456).



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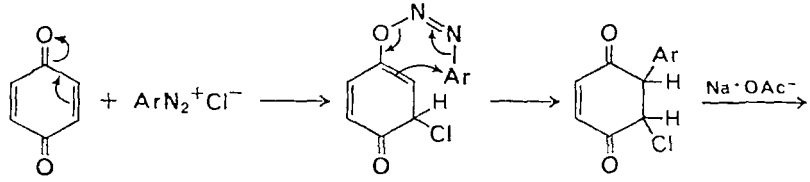
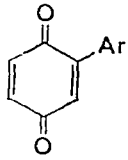
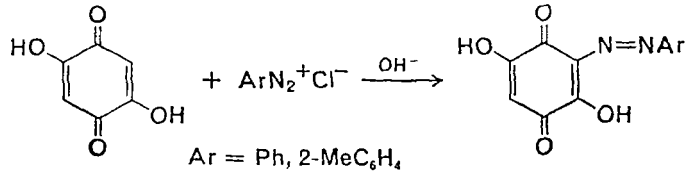


(456)

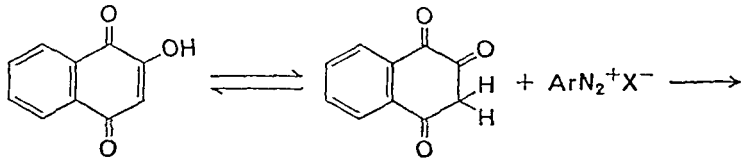


The reaction of diazonium salts with certain quinones can result in coupling rather than arylation. This competing reaction is observed with 2,5-dihydroxy-1,4-benzoquinone (equation 457)[526]. Similar behaviour has



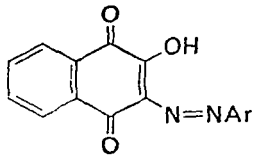
(457)

been observed with 2-hydroxy-1,4-naphthoquinone[327g, 527]. The success of the coupling reaction may be attributed to the tautomeric triketo form **194** which has an active methylene group (equation 458). The presence of

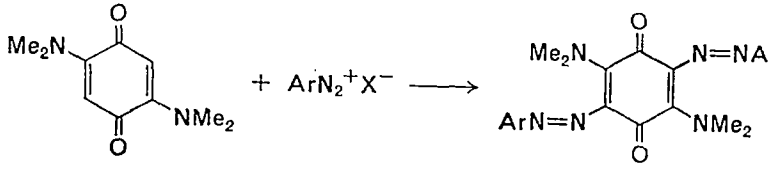


(194)

(458)

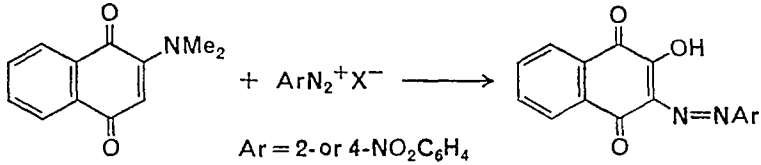


other electron-donating substituents on the quinone also promotes diazo coupling (equation 459). In the case of 2-dimethylamino-1,4-naphthoquinone the product isolated, in excellent yield, is 2-hydroxy-3-arylazo-1,4-naphthoquinone (equation 460). It was shown that under the same



(459)

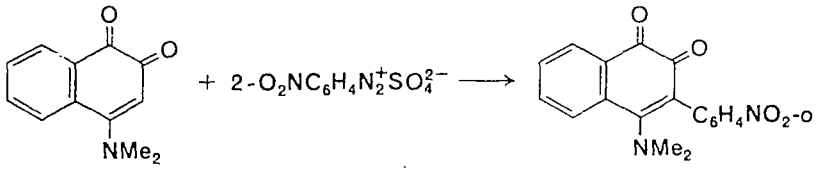
Ar = 2- or 4-$NO_2C_6H_4$, 2,5-$Cl_2C_6H_3$



(460)

Ar = 2- or 4-$NO_2C_6H_4$

conditions, but in the absence of the diazonium salt, the dimethylamino group is very readily hydrolysed. The isomeric starting material, 4-dimethylamino-1,2-naphthoquinone, has been prepared and its reactions with diazonium salts studied[528]. The only example of arylation found with this new substrate was with *o*-nitrobenzenediazonium sulphate in the presence of an excess of quinone (equation 461).



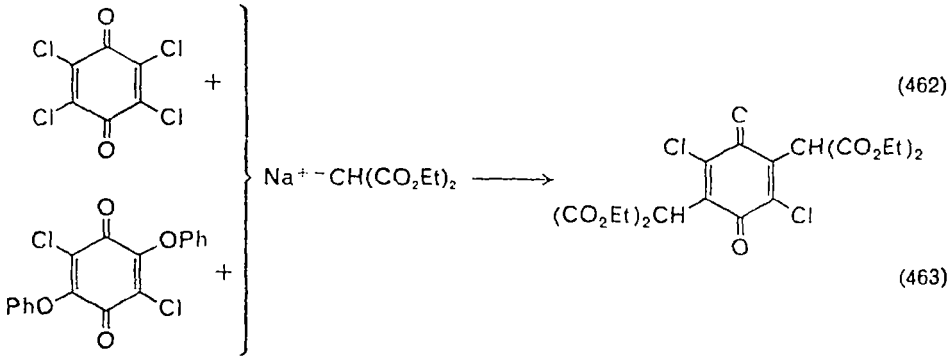
(461)

In acidic media both quinones gave the same diazonium coupling products (equation 460) and in acetate buffer 2-dimethylamino-1,4-naphthoquinone gave the 3-aryl derivatives.

VII. ACTIVE METHYLENE ANIONS AND QUINONES

A. Historical Introduction

The α,β-unsaturated carbonyl system of quinones should provide interesting examples of the Michael condensation of active methylene compounds. However, the strongly basic conditions associated with these reactions produce chiefly tars, and the early workers found very poor yields of products even with completely halogenated quinones (equations 462 and 463)[529,530].



(462)

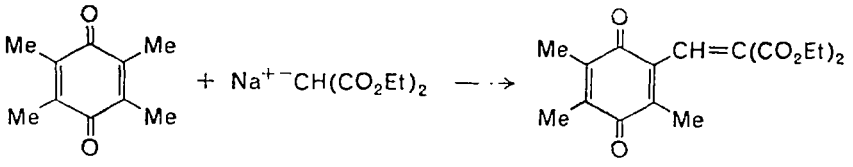
(463)

In 1926 Smith reported the first results of what was to become for him and his students a very detailed study of quinones and metal enolates[531]. Bamberger and Blangey had already reported their discouraging results with another organometallic reagent and quinones[532]. When the Grignard reagent, methylmagnesium iodide, was added to simple quinones, very large numbers of products were formed. Even though they succeeded in isolating and identifying six solid reaction products in the case of 2,5-dimethyl-1,4-benzoquinone, less than half the starting material was accounted for and the general outlook was very unpromising.

B. The Work of Lee Irvin Smith

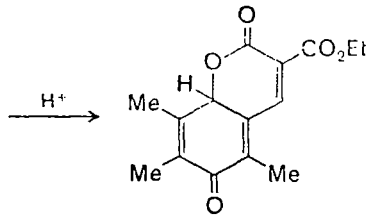
Smith began his work feeling that the presence of hydrogen on the quinonoid ring was responsible for the large number of products and he also wished to avoid the ambiguity of the Würtz–Fittig path for halogenated quinones. Thus, he chose to study first the reaction of diethyl sodiomalonate with duroquinone. The reaction was carried out in dry benzene to avoid the formation of diduroquinone. When an inert atmosphere is used, one of the products is durohydroquinone, accompanied by equivalent amounts of a red sodium salt of **195** that resists further purification. When this salt is treated with acid, a yellow compound, **196**, is obtained. An extensive series of chemical reactions of **196** led Smith and Dobrovolny[531] to suggest the following structures (equation 464).

One especially interesting point in the experimental evidence concerning the structure of **195** is the oxidation of a hydroquinone diacid dimethyl ether related to it (equation 465). All of the evidence clearly requires the highly substituted benzaldehyde shown, but **197** could not be oxidized to a benzoic acid derivative. While this seems strange, some other examples are cited and Smith later synthesized **197** by a completely independent route[533].



(464)

(195)



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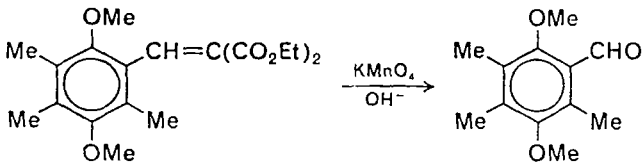
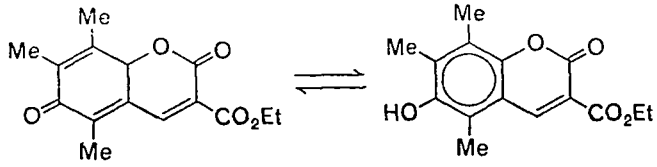


(465)

(197)

The yellow colour of the lactone **196** caused Smith and Dobrovolny to use the structure shown, but their use of the tautomeric structure (**198** in equation 466) for all of the methylation and acetylation products clearly showed they felt the latter better described the chemical nature of the product (equation 464). In a later study, Smith and Denyes showed that a



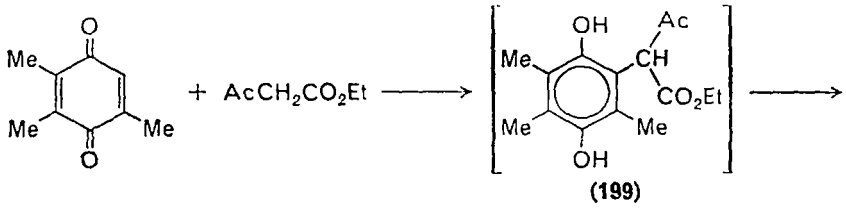
(466)

(196) (198)

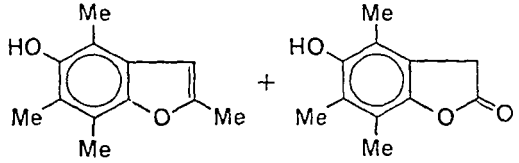
large number of chemical transformations were best explained on the basis of 3-carbethoxy-5,7,8-trimethyl-6-hydroxycoumarin (**198**) and that none required the tautomeric form **196**[534]. Some other examples of yellow coumarins are given.

The single reaction described thus far, using duroquinone as the substrate, is quite different from the usual quinonoid addition reaction in that a methyl group attached to the quinone is the reactive site. Smith and MacMullen wished to remove the particular limitation of duroquinone without returning to the state described in an earlier paper; 'It may be

noted, however, that benzoquinone, when treated with malonic ester in exactly the same way as duroquinone, gives only a hopeless tar'[535]. They cite some earlier reports of the addition of acetoacetic ester to quinone; however, the structures of the products were not satisfactorily demonstrated. The reaction between 2,3,5-trimethyl-1,4-benzoquinone and acetoacetic ester allows both the methyl group reaction, observed earlier, and the more usual 1,4-addition. Actually, only the latter reaction was observed and this produced two products (**200** and **201** in equation 467).



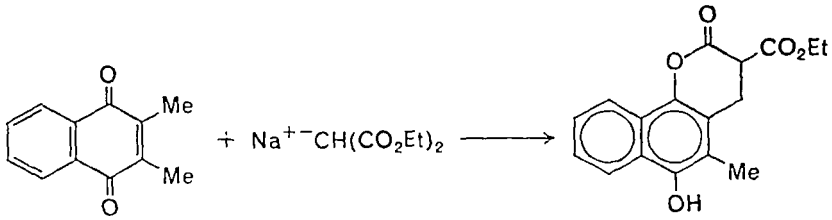
(199) (467)



(200) **(201)**

The most reasonable way to explain the products is simply 1,4-addition to yield the intermediate **199** (not isolated) which then undergoes ring closure and the usual two cleavages of β-keto esters. When diethyl sodiomalonate was used, only **201** was produced, offering additional evidence of the correctness of the proposed reaction scheme. The chemical properties of both **200** and **201** were entirely consistent with the structures assigned and the latter was synthesized by an independent route. It is especially significant that no coumarin derivatives were obtained, even when the reaction was run under exactly the same conditions applied earlier to duroquinone.

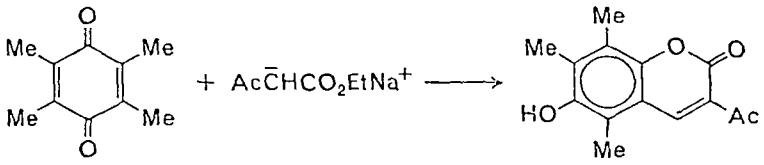
An obvious extension of the work with duroquinone would be 2,3-dimethyl-1,4-naphthoquinone and its reaction with diethyl sodiomalonate has been studied (equation 468)[536]. Two facts about this work are of



(202) (468)

interest in view of the obvious similarity to the earlier work: (i) the naphthoquinone proved to be very much more difficult to work with than duroquinone, and (ii) the α-naphthocoumarin (7,8-benzocoumarin, **202**) product was very resistant to ring opening.

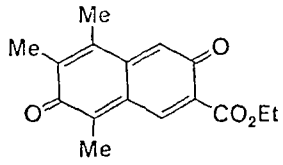
Another logical extension is the reaction of ethyl sodioacetoacetate with duroquinone (equation 469)[537]. The product, 5,7,8-trimethyl-3-acetyl-6-



(469)

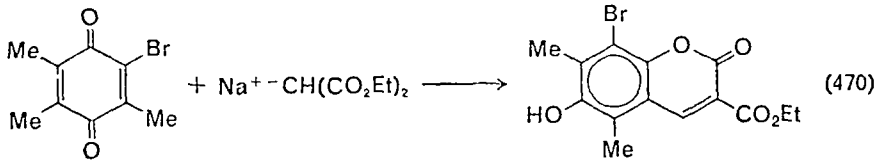
(203)

hydroxycoumarin (**203**), showed chemical properties similar to the compounds reported previously. The structure **203** was demonstrated in the usual manner including independent synthesis. The hope of finding the *amphi*-naphthoquinone **204** that might result from a reasonable alternate pathway was not realized.



(204)

The next step in the exploration of the active methylene chemistry of quinones by Smith and his students involved offering a substitution pathway for the reaction[538]. Again, the earlier literature was reviewed and found to be intriguing, but sketchy. The reaction between diethyl sodiomalonate and 2-bromo-3,5,6-trimethyl-1,4-benzoquinone did not follow the substitution path and produced only one of the three possible isomeric coumarins (equation 470). The coumarin ring proved to be very difficult



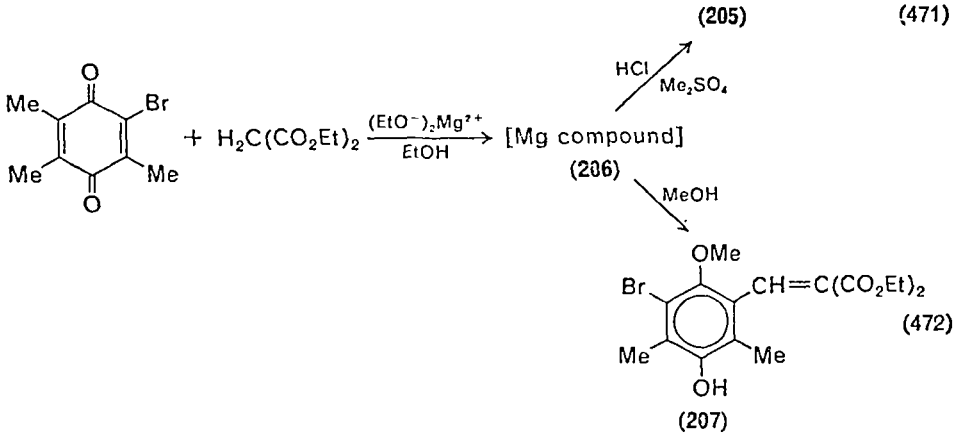
(470)

(205)

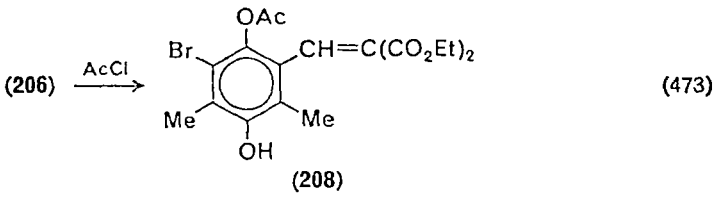
to open and thus synthesis appeared to be the best approach to structure determination. In a very pleasant display of candour, Smith and Johnson

reported that their selection of the first route was made because 2,5-dimethyl-1,4-benzoquinone was the most available starting material. The synthesis was carried far enough to offer good evidence that the actual product **205** did not have the *para*-dimethyl structure. The use of 2,6-dimethyl-1,4-benzoquinone in a similar synthesis led, after some difficulties, to a derivative of **205** and was considered to demonstrate the correctness of that structure.

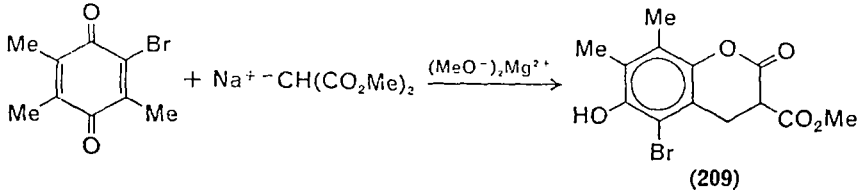
The reaction of the bromoquinone just described did not produce very good yields and the material balance was also poor under the usual conditions. A method was found under which not only could the yield of **205** be greatly improved, but a new series of related compounds could be prepared from a common intermediate, **206**. A very tentative structure assignment was made for the first member of the new series (**207** in equation 472). It was also found that freshly distilled acetyl chloride



converted the magnesium compound into a new derivative, tentatively assigned structure **208** in equation (473).



A thorough re-investigation of the reaction between 2-bromo-3,5,6-trimethyl-1,4-benzoquinone and dimethyl sodiomalonate revealed that, in the presence of magnesium methoxide, the hydrocoumarin **209** is produced (equation 474)[539]. It should be noted that the structure of **209**

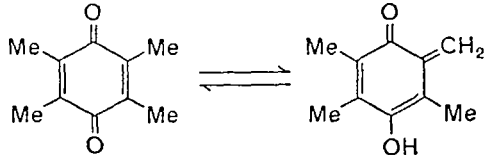


(474)

(209)

is that of the third isomeric possibility; i.e. the *ortho*-dimethyl derivative. This structure was demonstrated by two independent syntheses and comparison of X-ray powder diagrams of the product with those of authentic 3-carbomethoxy-5-bromo-6-hydroxy-7,8-dimethylcoumarin. This demonstration of the correct structure of the chief reaction product and its derivatives allowed Smith and Wiley to show that the 'new series' of compounds obtained from the magnesium compound **206** were, in fact, identical with them.

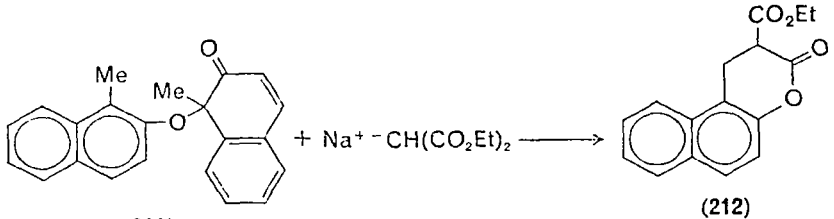
It had been felt for some time in Smith's laboratory that the addition of active methylene compounds to the methyl groups of quinones probably involved the methylene tautomer (**210** in equation 475). A trapping



(475)

(210)

experiment provided the first experimental evidence for this mechanism[540]. Evidence had been presented earlier for the existence of an *ortho*-methylene quinone as a transitory intermediate[541]. Smith and Horner reasoned that, if such intermediates were formed, and if they reacted with diethyl sodiomalonate more rapidly than with each other, a dihydrocoumarin would be formed. When dehydro-α-methyl-β-naphthol (**211**) was warmed with diethyl sodiomalonate, the hydrocoumarin **212** was isolated (equation 476). The yield of **212** was not good because of the difficulty of isolating it

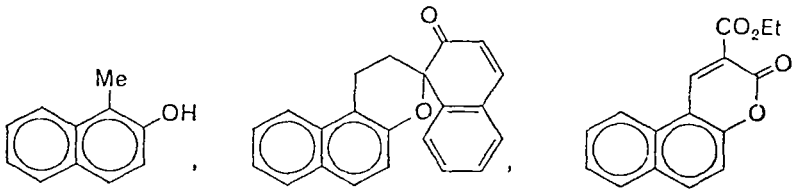


(476)

(211)

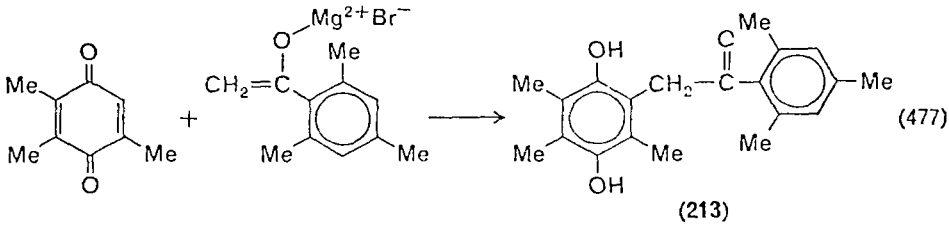
(212)

from the other products; e.g.:



However, the evidence of an *ortho*-methylene quinone intermediate is quite convincing.

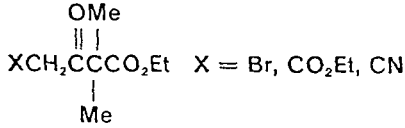
A class of weakly basic metallic enolates, that offer attractive possibilities for addition to quinones, are the bromomagnesium compounds derived from ketones and Grignard reagents. With the enolate of acetomesitylene, addition to 2,3,5-trimethyl-1,4-benzoquinone took place smoothly (equation 477)[542]. For steric reasons, it is not surprising



(477)

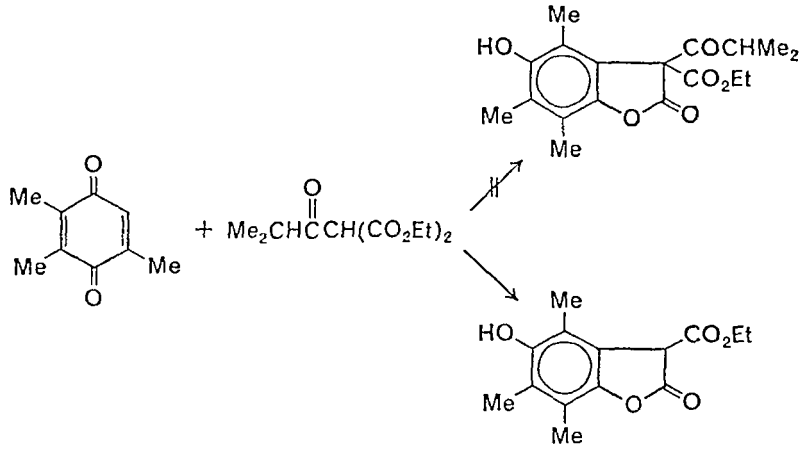
(213)

that the initial adduct **213** does not cyclize. Several other metallic enolates of this type were tried and either did not form or did not react with the quinone; for example, an acylmalonic ester did add to the quinone, but



the product had lost the acyl group during formation (equations 478 and 479). Efforts to re-introduce the acyl group proved unsuccessful so, while the synthesis demonstrated additional interrelationships among previously prepared compounds, the aim of extending the scope of the reaction was not realized.

The sodium enolates of a variety of active methylene compounds were allowed to react with duroquinone and 2,3,5-trimethyl-1,4-benzoquinone[543]; Table 17 summarizes the results of these studies. It seems clear that there are quite definite limitations on the simple addition reactions, although the reasons are not so clear. In the case of addition to

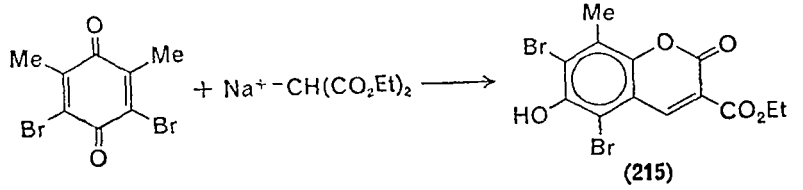


(478)

(479)

a methyl group of duroquinone (or to the *ortho*-methylene tautomer) the ease of the loss of an alkoxy group and the resulting cyclization appears to be an essential aspect of the reaction.

The compound, 3,5-dibromo-2,6-dimethyl-1,4-benzoquinone, appeared to offer an entirely new system with respect to the arrangement of alkyl and halogen groups; thus, its reaction with diethyl sodiomalonate was examined (equation 480)[544]. The additional bromine on the quinonoid



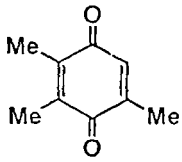
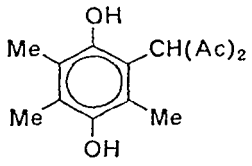
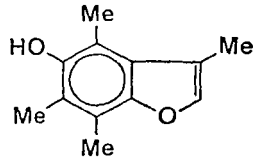
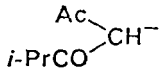
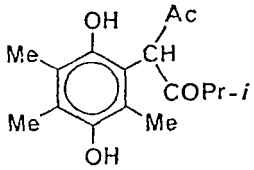
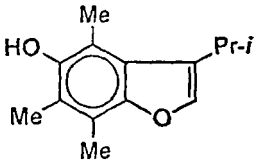
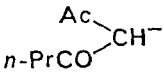
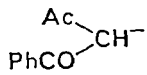
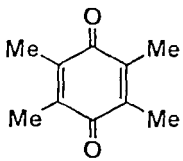
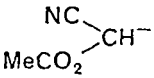
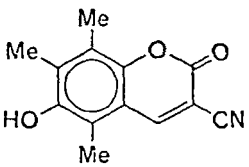
(480)

(215)

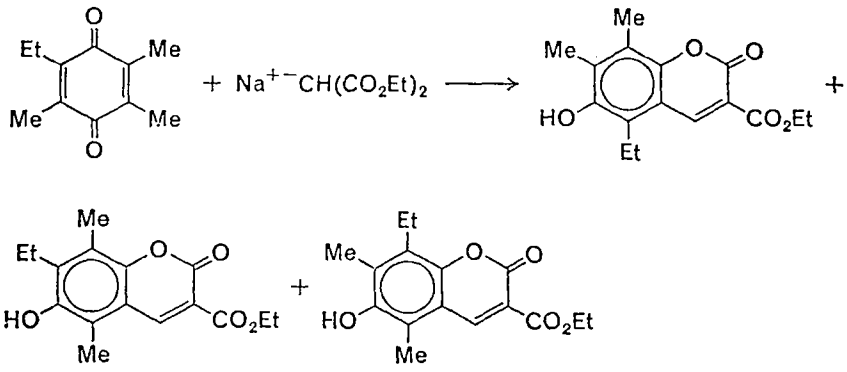
ring made the selection of solvent and other experimental conditions much more critical and, at best, substantially increased the effect of side-reactions. Unlike the earlier example of a coumarin with a single ring bromine, this product **215** underwent ring-opening reactions with great ease. The structure of **215** was demonstrated by a consideration of its chemical behaviour and an independent synthesis of the dimethyl ether of its ring-opened derivative.

The very strong directive effect of the bromine in 2-bromo-3,5,6-trimethyl-1,4-benzoquinone[538] promoted interest in the range of such effects. Therefore, the reaction of diethyl sodiomalonate with 2-ethyl-3,5,6-trimethyl-1,4-benzoquinone was carried out[545] after it was demonstrated that 2,3,5,6-tetraethyl-1,4-benzoquinone is inert. It was expected

TABLE 17. Some additions of active methylene enolates to methylated 1,4-benzoquinones[543]

1,4-Benzoquinones	Enolate	Products
	$(Ac)_2CH^-$	  (214)
		 (214) + 
		None
		None
	$(PhCO)_2CH^-$	None
		
	$(Ac)_2CH^-$	None
	$(PhCO)_2CH^-$	None

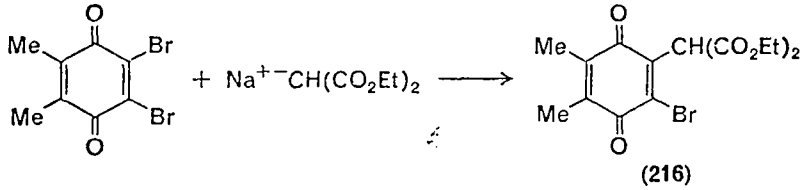
that three isomeric coumarins should be formed upon acid treatment of the initial adduct (equation 481). The yields of products in both steps are excellent but the separations extremely tedious. It was felt that two pure materials had been obtained, but so little material was available that the synthesis of the three expected products was undertaken. When the three



(481)

isomeric coumarins, of known structure, were in hand, thermal analysis showed that both of the isolated fractions were mixtures. The effect of the ethyl group on orientation in active methylene addition is negligible[516].

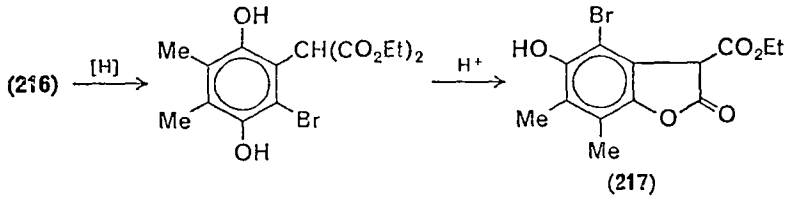
The reaction of 5,6-dibromo-2,3-dimethyl-1,4-benzoquinone with diethyl sodiomalonate has been studied (equation 482)[517]. Unlike the



(482)

(216)

brominated quinones reported previously, the *ortho*-dibromo arrangement leads to substitution of one or, after longer reaction times, two bromine atoms. The quinonoid product **216** is easily reduced to the corresponding hydroquinone which in turn is cyclized with acid to the isocoumaranone (**217** in equation 483). The synthesis of a key derivative of **217**, together

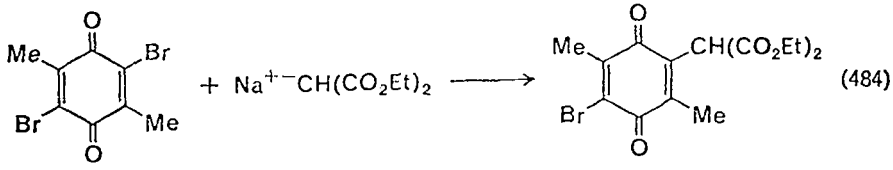


(483)

(217)

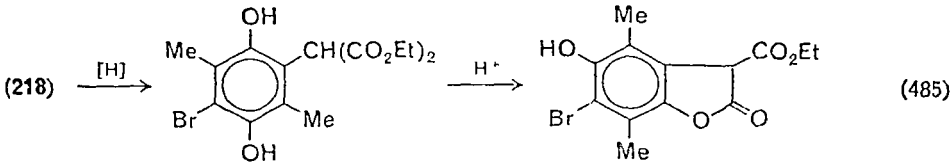
with the usual chemical evidence, determined the structure. These findings clearly require that the *ortho*-dibromo grouping exert a stronger mutual influence in these reactions than that directed toward the *meta*-methyl groups.

The reactions of *ortho-* and *meta*-dibromodimethyl quinones with active methylene compounds proved sufficiently interesting that the *para* isomer was also treated with diethyl sodiomalonate[548]. The chemistry observed exactly followed that of the *ortho*-dibromo isomer[547] (equations 484 and 485). The disubstituted product is also obtained, but in poor



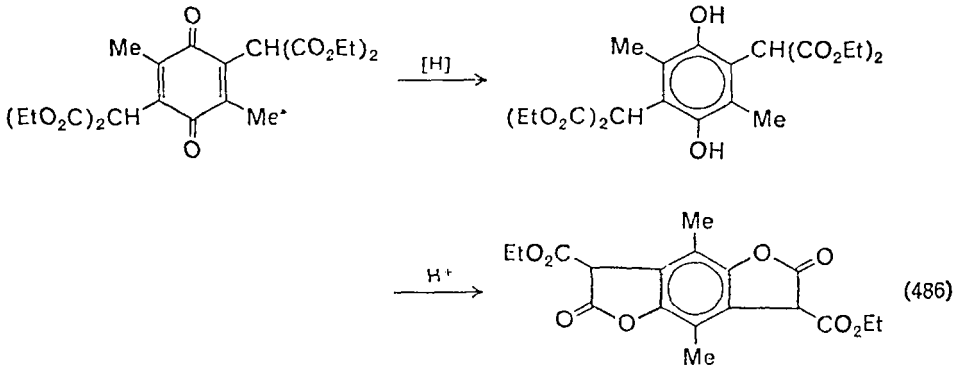
(484)

(218)



(485)

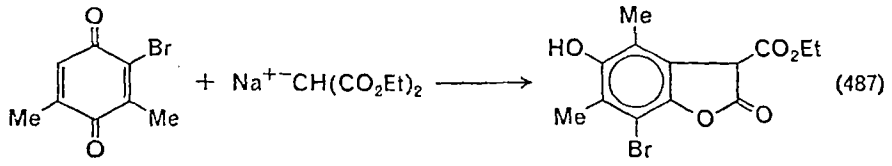
yield and under much more strenuous conditions. This disubstitution product can be converted to a difurano compound (equation 486). In neither the *ortho-* nor the *para*-dibromo case could any evidence of a coumarin be found; i.e. only substitution for bromine took place.



(486)

The observed reactions of the three isomeric dibromo-dimethyl-1,4-benzoquinones and 2-bromo-3,5,6-trimethyl-1,4-benzoquinone can be rationalized in terms of the principal resonance contributors. A description of this analysis has been presented and its application to the more general case of anionic reagents and hetero conjugated systems pointed out[549].

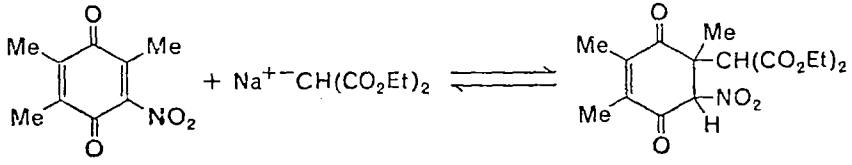
An interesting combination experiment was carried out by Smith and Wiley when they reacted 2-bromo-3,5-dimethyl-1,4-benzoquinone with diethyl sodiomalonate (equation 487)[550]. In principle, this quinone can



(487)

undergo three different modes of reaction: (i) bromine substitution, (ii) methyl group addition, or (iii) Michael (1,4-) addition. As shown in equation (487), only the third option is taken, shedding some light on the relative energetics of the three paths.

The reactions of active methylene enolates with replaceable groups other than bromine are of interest in considering the electronic influence of substituents on the course of the reaction. The very strong electron-withdrawing nitro group and electron-donating amino group were selected for study[551]. The results were indeed very different; 2-nitro-3,5,6-trimethyl-1,4-benzoquinone undergoes simple 1,2-addition of diethyl sodiomalonate at the double bond bearing the nitro group; i.e. behaves like a nitroalkene (equation 488). The properties of **219** are quite consistent with the proposed

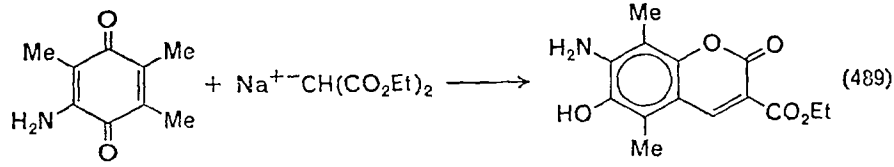


(488)

(219)

structure; e.g. formed reversibly, acidic, colourless, *cis* and *trans* forms, etc. Dimethyl sodiomalonate formed a completely analogous adduct, but ethyl sodioacetoacetate and the bromomagnesium enolate of aceto-mesitylene produced only oils and resins.

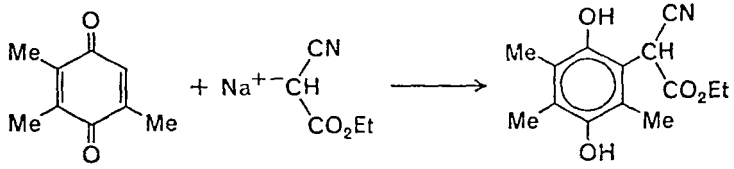
The reaction of 2-amino-3,5,6-trimethyl-1,4-benzoquinone with diethyl sodiomalonate followed a course related to the corresponding bromo-quinone (equation 489). The high yield suggests that once again only a



(489)

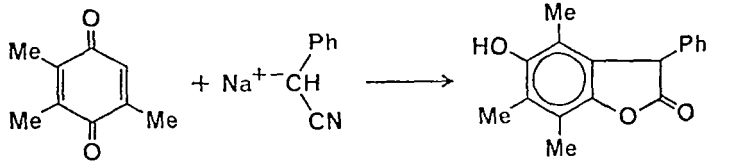
single isomer is formed, but the methyl group *para* to the amino group is attacked. This is in contrast to the earlier observation of attack at the methyl group *ortho* to the bromine atom. The structure of the product was demonstrated by the synthesis of a derivative.

In an attempt to study the range of active methylene enolates that can successfully react with quinones, Smith and Dale carried out the following reactions with 2,3,5-trimethyl-1,4-benzoquinone (equations 490–492)[552].

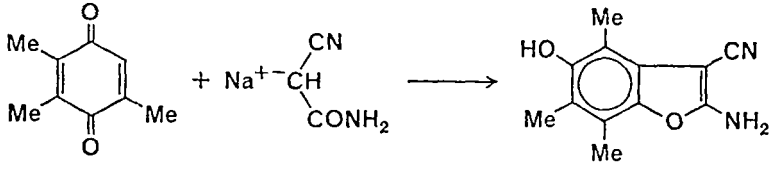


(490)

(220)



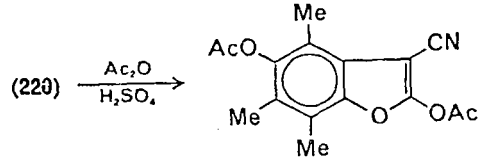
(491)



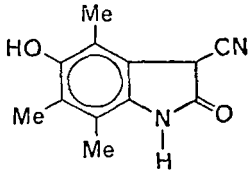
(492)

(221)

Treatment of **220** with acetic anhydride and sulphuric acid produced cyclization (equation 493). Structure **222** was not rigorously excluded as a

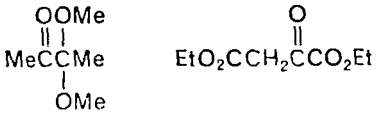


(493)



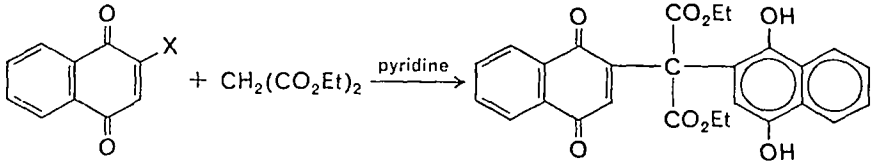
(222)

possible alternative for **221**. Determined efforts were made to add two other enolates to this quinone, but without success:



C. Recent Studies

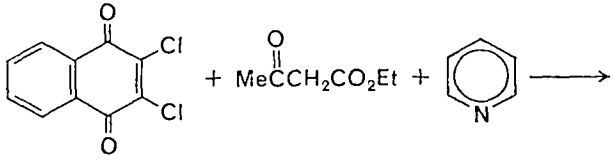
With the conclusions of Smith's efforts, others have continued to explore these condensations of quinones with active methylene compounds. One area, relatively unexplored so far, concerns the reactions of 1,4-naphthoquinones. Pratt and his students began with a not too surprising result (equation 494)[553]. The yield was markedly improved by



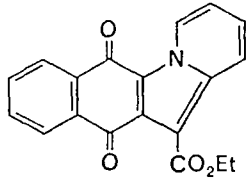
(494)

using the potassium sulphonate salt in a substitution reaction (15–40%). Diethyl malonate does not appear to be a typical reagent as Pratt's further work suggests.

The reaction of 2,3-dichloro-1,4-naphthoquinone with ethyl acetoacetate and pyridine provides an interesting heterocyclic quinone **223** in good yield (equation 495)[554]. Related active methylene compounds give



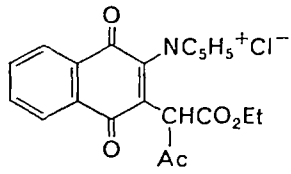
(495)



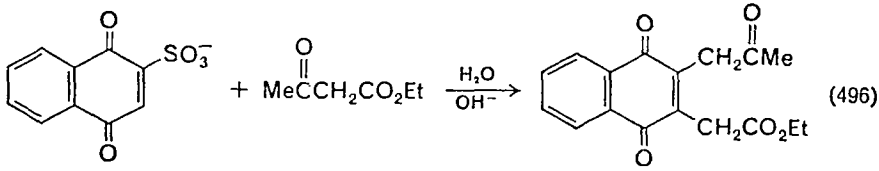
(223)

the same or analogous products; e.g. ethyl benzoylacetate yields **223** and methyl acetoacetate yields the corresponding methyl ester. Quinoline will take the place of pyridine in the reaction. The possible mechanisms presented depend on the logical intermediate **224**, but no experimental evidence is given.

An interesting sidelight on these studies is the reaction of 1,4-naphthoquinone-2-sulphonate with ethyl acetoacetate in aqueous alkali (equation 496). The two different modes of cleavage are not explained. The same



(224)

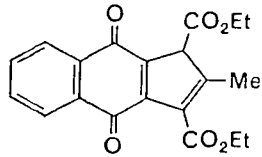


(496)

(225)

reaction takes place with 2-bromo-1,4-naphthoquinone and the unsubstituted quinone.

Ten years later Reynolds and his collaborators undertook a careful re-investigation of this unexpected chemistry[555]. Actually, the structure **225** had been questioned much earlier and the alternative structure **226**



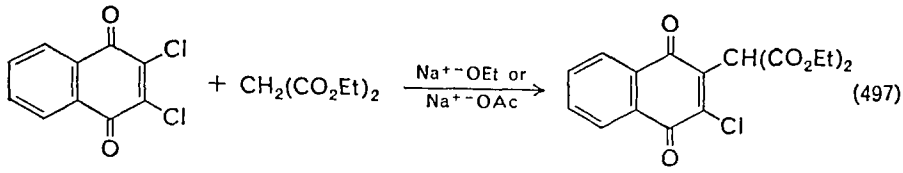
(226)

proposed[556]. The twofold objective of this study was:

(1) To improve the yield of product (**225**, **226** or ?).

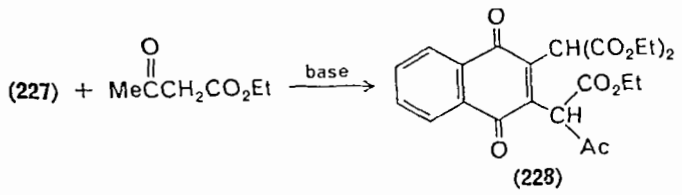
(2) To use modern instrumentation to determine the correct structure.

A careful product study, in which reactant concentration, base and time were varied, revealed that competing cyclization of the initial adduct was the cause of low yields of the desired cleavage product. The following synthesis was devised to avoid the cyclization (equations 497–499). Both of the intermediates (**227** and **228**) could be isolated, but the preferred method used them *in situ*. A massive instrumental attack was made on the final product structure. The results of mass spectra, molecular weight

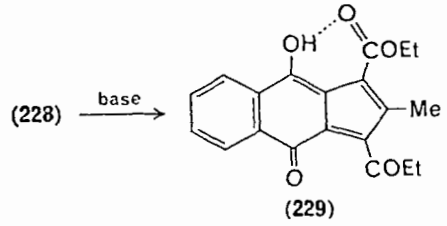


(497)

(227)



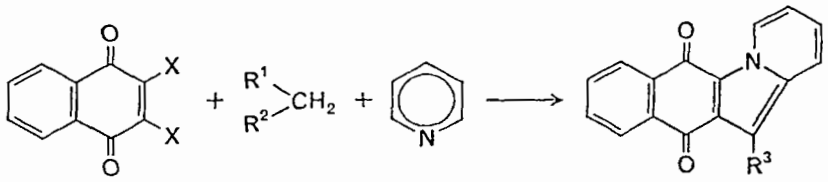
(498)



(499)

determination (vapour pressure osmometry), absorption spectra (i.r., u.v., visible and n.m.r.), polarography and non-aqueous titration were strikingly consistent with structure **229**.

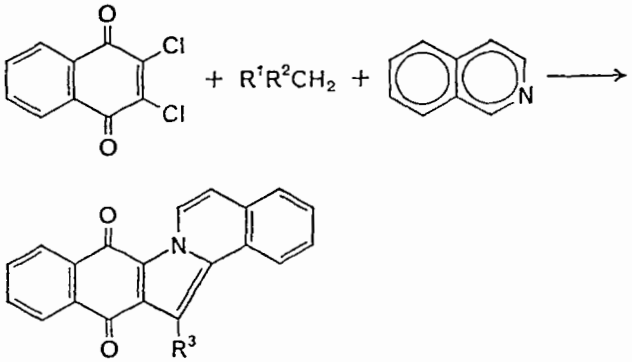
The range of active methylene compounds that exhibit quinonoid addition and substitution reactions involving heterocyclic bases is quite large (equation 500)[557]. The yields vary from trace to very good for



(500)

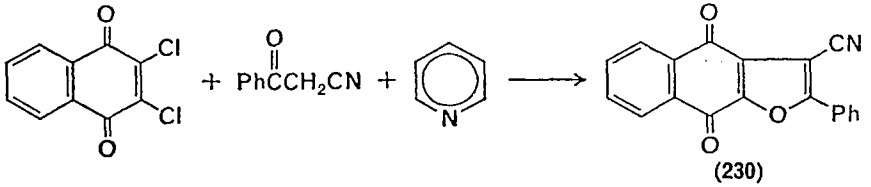
X = H, Cl
R^1, R^2 = Ac, CN, CO_2R, Ph, EtCO, Me, NO_2, PhCO
R^3 = CO_2R, Ac, PhCO, CN, Ph, Me

pyridine, but when isoquinoline is used, the yields are generally superior (equation 501).



(501)

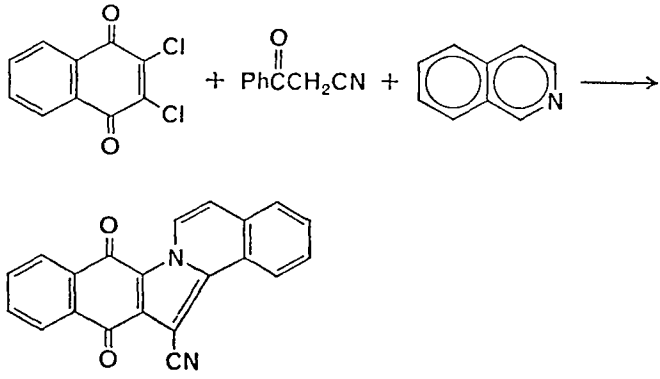
An exception to the entry of nitrogen bases into these reactions was found in the case of benzoylacetonitrile (equation 502)[558]. This example



(502)

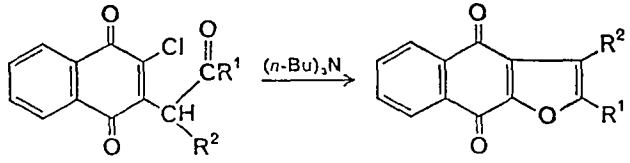
(230)

is very surprising because when isoquinoline is used in place of pyridine the more usual product, including the base in its structure, is found (equation 503). The same furan **230** is produced if 2-hydroxy-3-bromo-



(503)

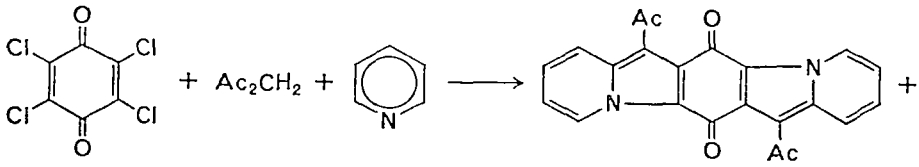
1,4-naphthoquinone is used, but the yield drops substantially. A series of active methylene enolates displaced one chlorine of 2,3-dichloro-1,4-naphthoquinone and these intermediates could be cyclized to 2,3-di-substituted-4,5-phthaloylfurans (equation 504).



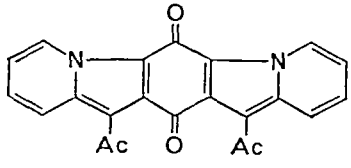
(504)

R^1 = Ph, Me R^2 = CN, Ac, PhCO, CO_2Et, H

Condensations of active methylene compounds and chloranil in the presence of pyridine have also been conducted with analogous results (equation 505)[559]. It was also found that with a limited amount of pyridine a single displacement–cyclization sequence can be achieved, thus opening the way for the synthesis of unsymmetrical compounds related to **231** and **232**.

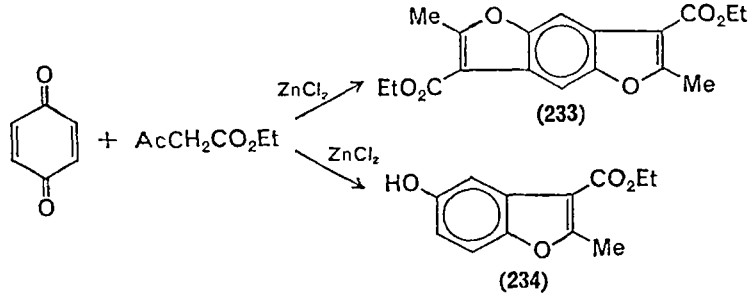


(231) (505)



(232)

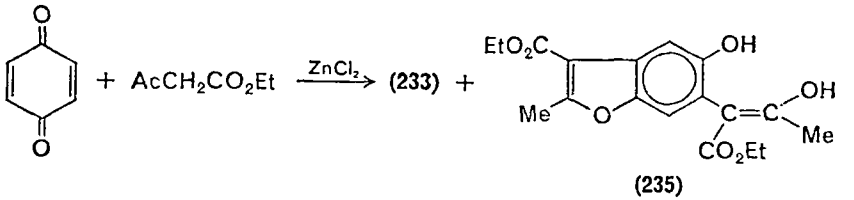
A detailed study of the reactions of ethyl acetoacetate with 1,4-benzoquinone in the presence of Lewis acids has shown that the relative amounts of mono- and diaddition can be controlled by regulating the concentration of quinone[560–563]. The slow addition of quinone can produce the monofuran in 80% yield (equations 506 and 507). Similar control can be achieved in the addition of ethyl benzoylacetate.



(233) (506)

(234) (507)

In another study of this addition, the effect of lower reaction temperature was investigated[564]. When the reaction is carried out at 80–85°C and with very low concentration of quinone, only the benzofuran (**234**) is obtained. At 41–45°C, and a low quinone concentration, the difuran (**233**) and a new product (**235**) are formed (equation 508). At 38°C only **235** is produced;

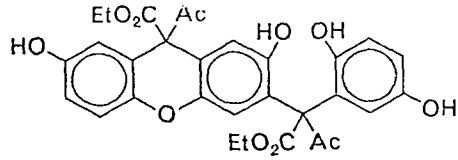


(233) (508)

(235)

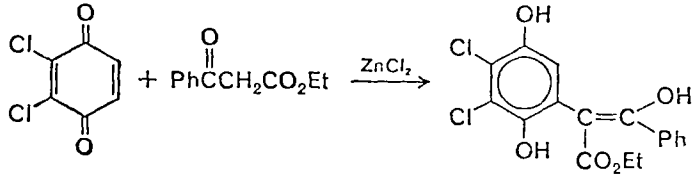
the same result can be achieved by lowering the zinc chloride concentration. If the concentration of quinone is increased at the lowest temperatures

studied, a new product (**236**) is formed. This material shows chemical and physical properties that indicate a dibenzopyran derivative.



(236)

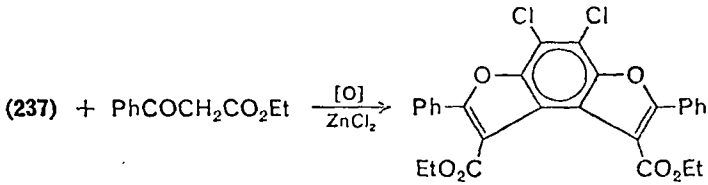
With 2,3-dichloro-1,4-benzoquinone and ethyl benzoylacetate, it was possible to isolate the proposed intermediate **237** in good yield by working at less than 60°C (equation 509). The intermediate could be oxidized to the



(509)

(237)

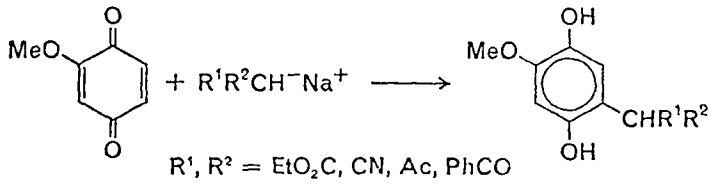
corresponding quinone, which underwent further reaction with ethyl benzoylacetate to form the previously prepared difuran (equation 510).



(510)

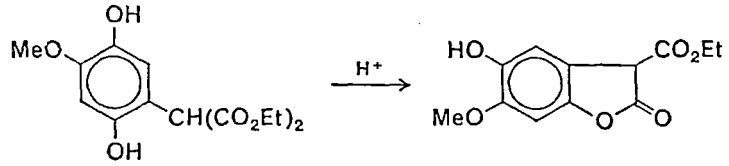
The several stable enols suggested need additional experimental verification, but the general situation is clear. The outcome of these reactions depends heavily on: (i) the concentration of quinone, (ii) the concentration of Lewis acid, (iii) the temperature and (iv) the nature of the active methylene compound.

A series of active methylene compounds have been added to 2-methoxy-1,4-benzoquinone (equation 511)[565]. All the primary adducts were isolated, but that from ethyl acetoacetate was unstable. Subsequent

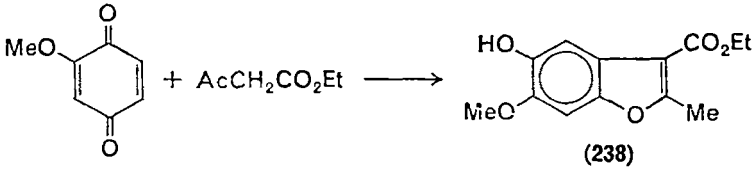


(511)

treatment with acid caused ring closure of the usual kinds (e.g. equation 512). The major product isolated from the reaction of ethyl acetoacetate was the benzofuran (**238** in equation 513).



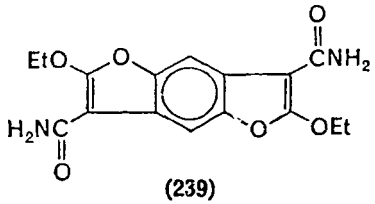
(512)



(513)

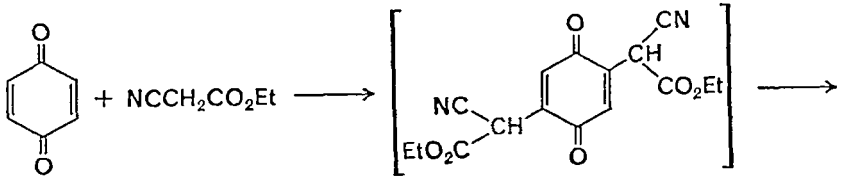
(238)

Jeffreys found several minor products in the preparation of the adduct with ethyl cyanoacetate. One of these, **239**, was the same as that found, but given a different structure, in an earlier re-investigation of the Craven

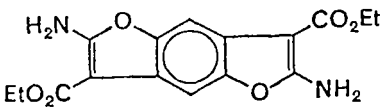


(239)

reaction[566,567]. Still another re-investigation of this particular example has been reported[568]. On the basis of spectral data, especially comparisons with compounds known to contain certain structural features, it now appears that the elusive structure is **240** in equation (514).

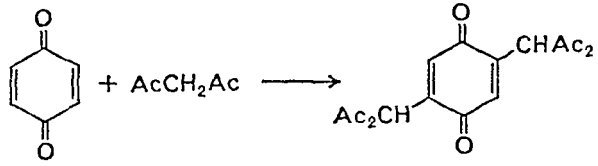


(514)

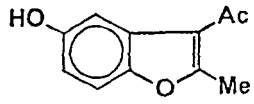


(240)

Some earlier reports also bear on the most probable pathway for these reactions[569,570]. The reaction of 1,4-benzoquinone with acetylacetone produced a quinone with the characteristics of a simple bisaddition product (equation 515). An n.m.r. study strongly suggests that these

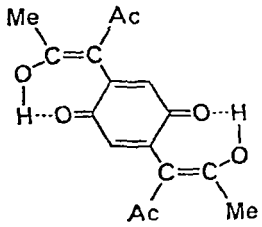


(515)



(242)

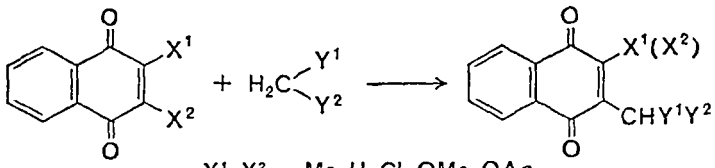
simple adducts exist in the doubly enolized form **241** [571]. However, when the excess acetylacetone, used as the solvent, was recovered, a new crystalline



(241)

product, **242**, was obtained. All of the chemical and physical data are consistent with the proposed structure **242**.

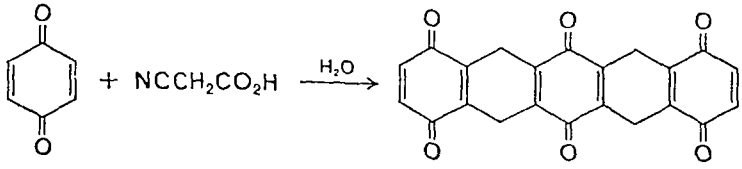
Interest in the Craven reaction continues and a recent report has made its synthetic range somewhat clearer (equation 516)[572]. When 1,2-naphthoquinone is used, the 4-substituted product is obtained.



(516)

X^1, X^2 = Me, H, Cl, OMe, OAc
Y^1, Y^2 = CN, CO_2Et

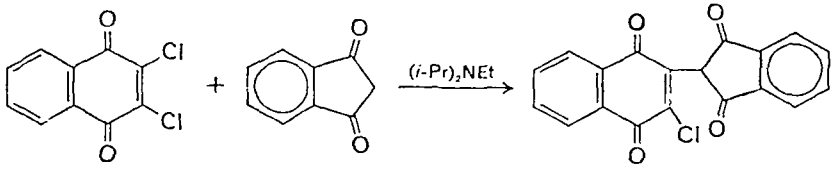
In 1960, Junek reported that in aqueous solution without excess base, cyanoacetic acid and 1,4-benzoquinone form a surprising triquinone (**243** in equation 517)[573]. With more highly substituted quinones, normal addition products are obtained.



(517)

(243)

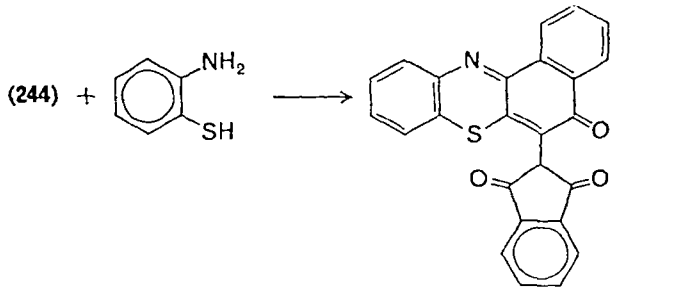
A less usual active methylene compound, 1,3-indandione, also reacts with 2,3-dichloro-1,4-naphthoquinone (equation 518)[574]. The product



(518)

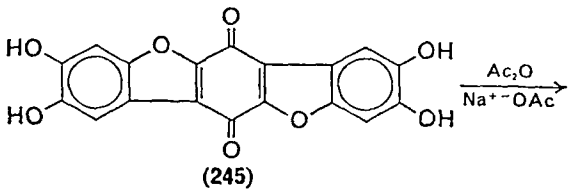
(244)

244 is obtained in excellent yield and undergoes additional substitution reactions including the formation of a phenothiazine with *o*-aminobenzenethiol (equation 519). This reaction is closely related to the furan and lactone cyclizations described earlier in the Nenitzescu condensation.

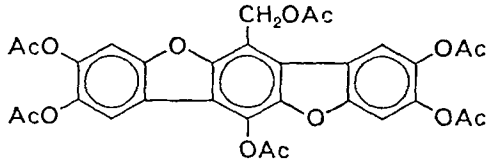


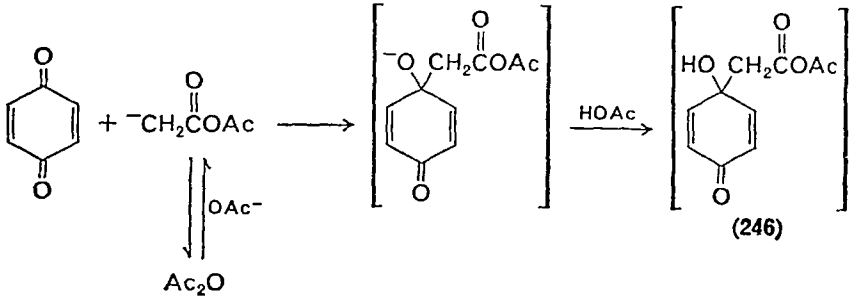
(519)

In attempting to prepare the hexaacetate of thelephoric acid **245**, it was discovered that an intermediate Perkin condensation has taken place (equation 520)[575]. This route only became clear after rather extensive studies of simpler quinones (especially 2,5- and 2,6-dimethoxy-1,4-benzoquinones) by Lounasmaa[576]. The mechanism is essentially that proposed earlier by Bloom for the reaction of 9,10-phenanthrenequinone with acetic anhydride in the presence of sodium acetate[577]. The initial addition of the α-carbanion of acetic anhydride to the quinone (equation 521) is followed by dehydration and hydrolysis (equation 522). After this fairly normal Perkin condensation, decarboxylation and the reductive addition of acetic anhydride occur (equation 523)[578]. The decarboxylation

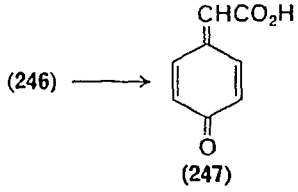


(245) (520)





(521)



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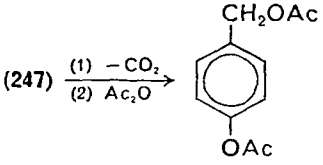
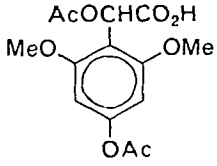
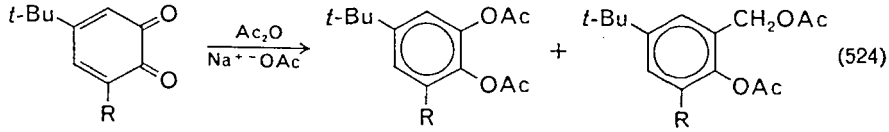


(523)

reaction did not occur spontaneously and it was possible to isolate the key intermediate (**248**)[579]. This reaction also takes place with 1,2-benzoquinones (equation 524), but in very low yield[580].

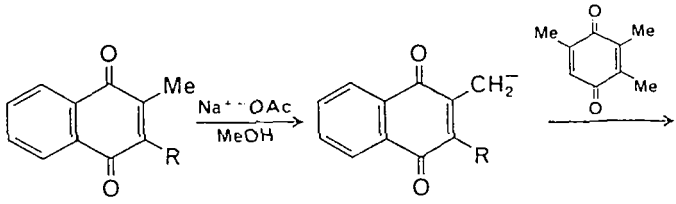


(248)

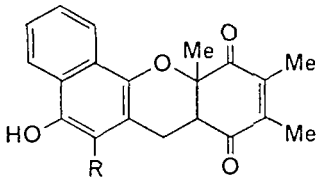


R = Me, *t*-Bu (524)

Recently the reactions of carbanions derived from alkyl quinones with a second quinone have been examined. The use of mildly basic conditions makes it possible to control subsequent reactions and isolate an initial 1,4-cycloaddition product (**249** in equation 525)[581]. With stronger base,

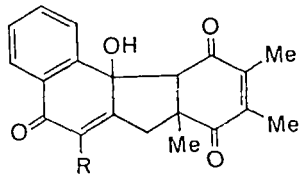


R = H, Me (525)



(249)

ring opening and oxidation are rapid and an unsymmetrical methylenediquinone forms. A previously unreported competing reaction leads to a 1,3-cycloaddition product containing a fluorene ring structure (equation 525 with additional product **250**). It is interesting that the isomeric

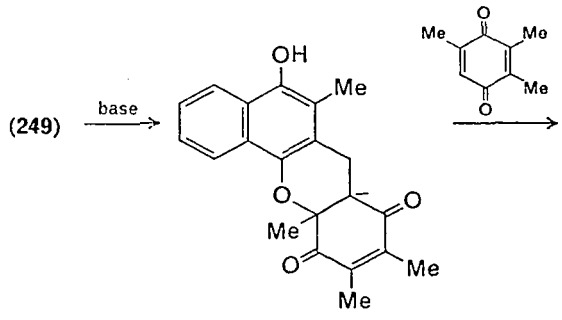


(250)

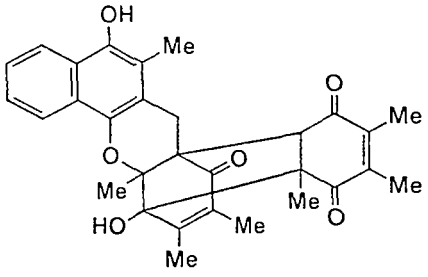
structures of **249** and **250** (where R = H) are not present in these reactions and it is possible to account directly for as much as 70% of the carbanion produced.

In a later study it was found that **249** (R = Me) in weak base also forms a carbanion that will react with a second molecule of 2,3,5-trimethyl-1,4-benzoquinone (equation 526)[582]. Only the single isomer (**251**) is

produced and both the structures and stereochemistry of the addition have been demonstrated.

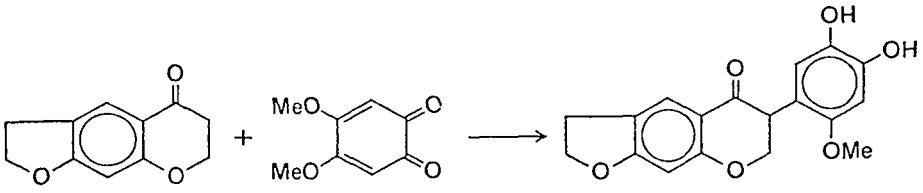


(526)

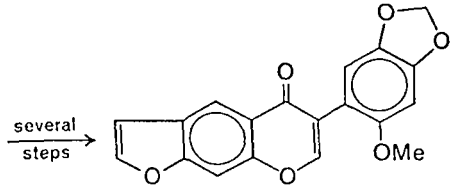


(251)

A final recent example of the use of carbanion–quinone reactions comes from the synthesis of natural products[583]. The total synthesis of dehydroneotenone (**253**) has been accomplished by the condensation of the furobenzopyran (**252**) with 4,5-dimethoxy-1,2-benzoquinone (equation 527).



(527)



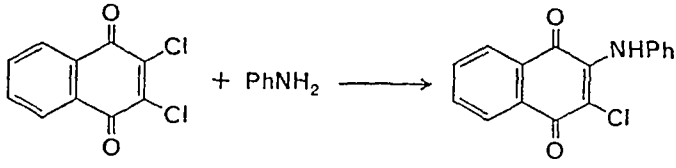
(253)

VIII. THE SUBSTITUTION CHEMISTRY OF QUINONES

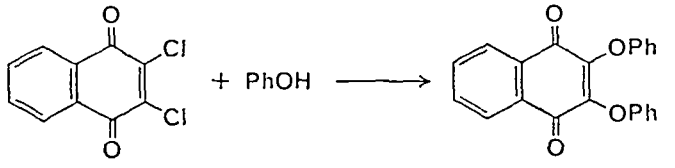
A. Historical Introduction

A large number of substituted quinones can be conveniently prepared via a suitable nucleophilic substitution reaction of a quinone bearing some relatively labile group. The vast majority of these reactions are displacements by amines offering a complement to the nitrogen addition studies previously discussed (see section II.C).

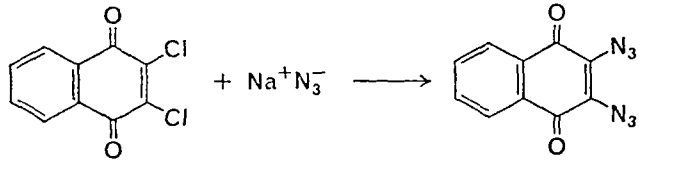
From the earliest days, a key synthetic intermediate in quinonoid chemistry has been 2,3-dichloro-1,4-naphthoquinone (see section VII.C). Among the first reports of syntheses involving this substrate are those that suggest the broad potential scope of quinone substitution chemistry. The following will provide some typical examples (equations 528–530)[584-586]. Furthermore, the sequential introduction of 2,3-nitrogen



(528)



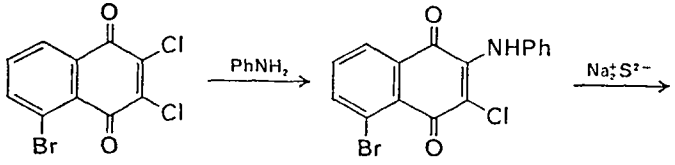
(529)

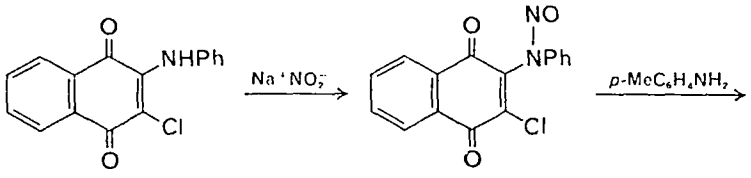


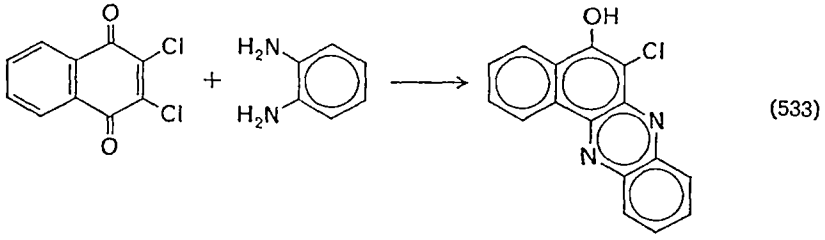
(530)

substituents makes it possible to prepare a large number of additional interesting compounds (equations 531 and 532)[587,588]. Diamines generally react with the two chlorine atoms in 2,3-dichloro-1,4-naphthoquinone, one amino group at a time. An interesting exception is *o*-phenylenediamine (equation 533)[589]. As the introduction to a synthetic report, Buu-Hoï has given a fine brief review of these early studies[590].

The massive study of aryl-nitrogen addition chemistry already mentioned (see section II.C.1) suggested the importance of competitive substitution in certain cases[5]. For example, depending on the relative

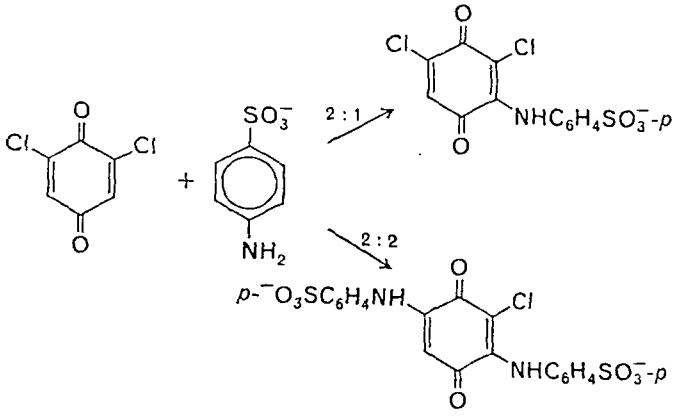






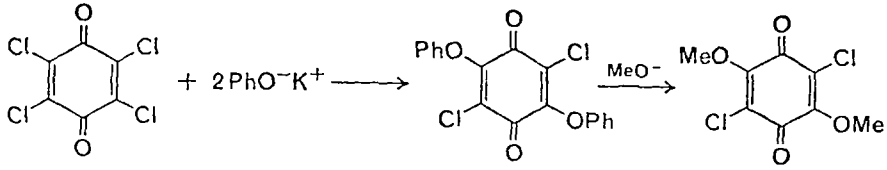
proportions of reactants, the following reactions occur (equations 534 and 535). An equivalent amount of 2,6-dichlorohydroquinone is also found in both reaction product mixtures.

Some of the early substitution chemistry of quinones involved nucleophiles other than nitrogen. Before the turn of the century, a number of studies of oxygen substitution had been made[591-593] (e.g. equation 536[530]). It was also found that the phenoxy groups could be displaced by aniline and that under slightly more severe conditions all four chlorine atoms can be replaced.



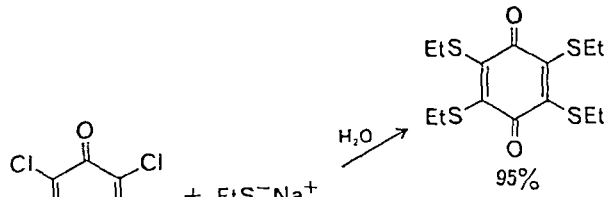
(534)

(535)



(536)

Several early reports of the substitution of quinones by sulphur nucleophiles have been recorded[594,595]. The most important outcome of these studies was an appreciation of the importance of solvent in determining the reaction outcome (equations 537 and 538). While substitution and



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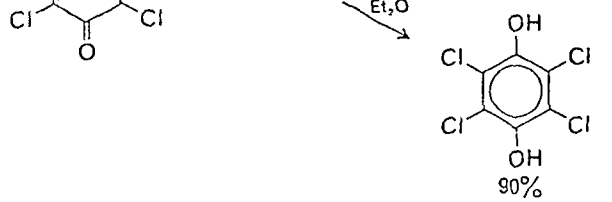


(538)

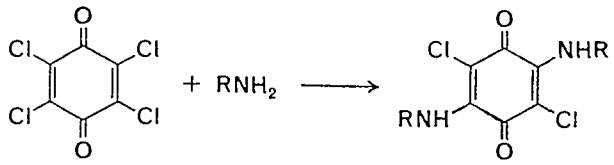
reduction were not the only reactions observed in water and ether respectively, the yields change in such a dramatic manner that the significance of the observation cannot be doubted.

Numerous additional contributions to the synthetic literature of quinonoid substitution chemistry were made in the late 19th and early 20th centuries[68,596–599].

B. Nitrogen Substitution

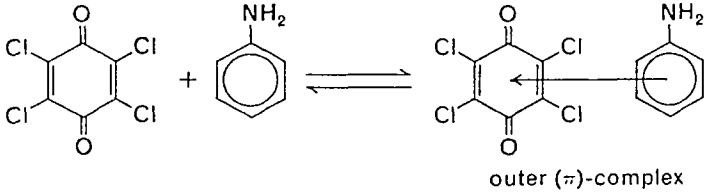
1. Mechanistic studies

While the application of nitrogen substitution chemistry to the synthesis of quinonoid compounds has a long and abundant history, the serious mechanistic study of these reactions is a recent activity of the physical-organic chemist. The question of the importance of charge-transfer complexes as intermediates in such substitution reactions is a central concern. In 1968 Das and Majee claimed that, for simple amines (equation 539), the observed spectra are those of product rather than

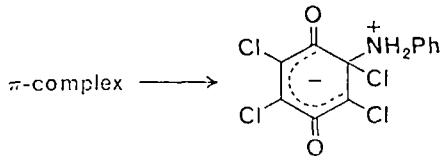


R = Et, *n*-C_6H_{13}, C_6H_{11} (539)

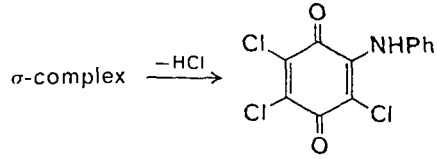
charge-transfer[600]. The experimental evidence is unconvincing and a later, detailed study has been presented[601]. For the system of chloranil and various substituted anilines evidence for both outer- and inner-complex formation was obtained. It was not possible to state positively that the outer-complex actually takes part in the reaction, but the inner-complex is certainly an intermediate in the substitution reaction. The following reaction mechanism is suggested (equations 540–542). The details of the second substitution are not as clear and two alternatives are presented. Still, the essential characteristics of the reaction mechanism are clear.



outer (π)-complex (540)

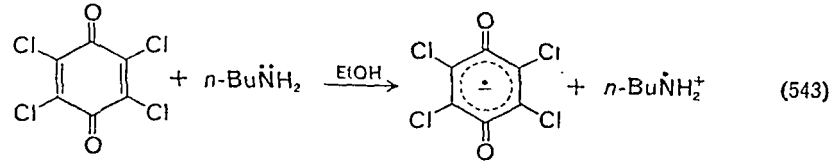


inner (σ)-complex (541)



(542)

In a recent study by Tamaoka and Nagakura[91] (see section II.C.2) using rapid scan spectrophotometry, the occurrence of electron transfer, prior to the substitution itself, was demonstrated (equation 543). Spectra of the chloranil–butylamine system and related kinetics suggest the following sequence of steps (equation 544). The monoaminated intermediate was not detected in this particular reaction, but was in other quite



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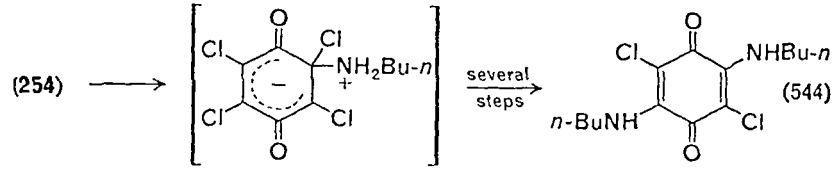
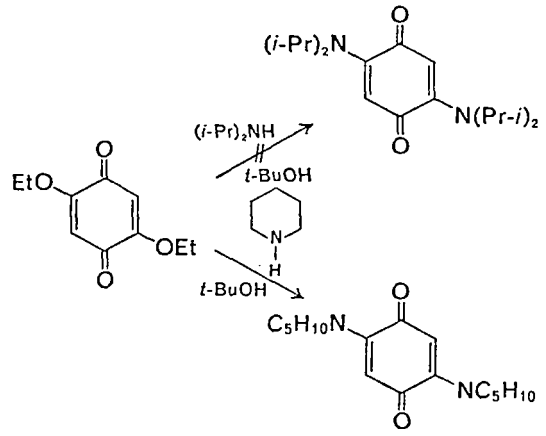


(544)

similar systems. The general outline of the above mechanistic scheme was applied to a broad range of quinones and amines. With the less polar solvent ethyl ether, the quinone anion radical was not observed in systems that clearly showed this step in ethanol.

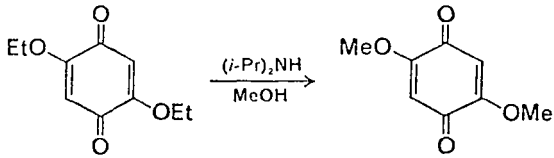
A number of synthetic papers record observations bearing on nitrogen substitution mechanisms in quinonoid compounds. An interesting observation relative to the substitution of alkoxy groups by amines was made during a study of the steric limitations of diisopropylamine in addition reactions (see section II.C.3)[105]. When 2,5-diethoxy-1,4-benzoquinone is treated with diisopropylamine in refluxing *t*-butyl alcohol no reaction takes place in three days, while under these conditions piperidine readily replaces the ethoxy groups (equations 545 and 546). However, when methanol is used as the solvent, a quantitative conversion to 2,5-dimethoxy-1,4-benzoquinone is achieved, if diisopropylamine is present (equation 547).

The striking effect of cerous ion on the addition products formed between anilines and 5,8-quinolinequinone has already been discussed (see section II.C.3)[109]. Pratt included some significant substitution



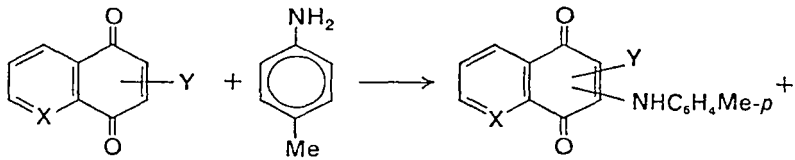
(545)

(546)



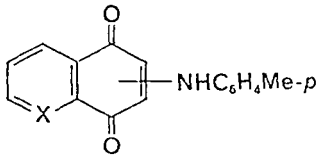
(547)

reactions in his study. Halogen and methoxy groups were examined in both the heterocyclic quinone and 1,4-naphthoquinone (equation 548).



X = CH, N
Y = Cl, Br, OMe

(255)



(256)

(548)

The approach used (i.e. monosubstituted quinone substrates) allows a discussion of the competition between addition and substitution. Some typical results are presented in Table 18. As would be expected, the halogenated quinones react mostly by addition. The low reactivity of the 7-position in 5,8-quinolinequinone is re-emphasized by the complete absence of substitution in the 7-chloro derivative. The addition of cerous

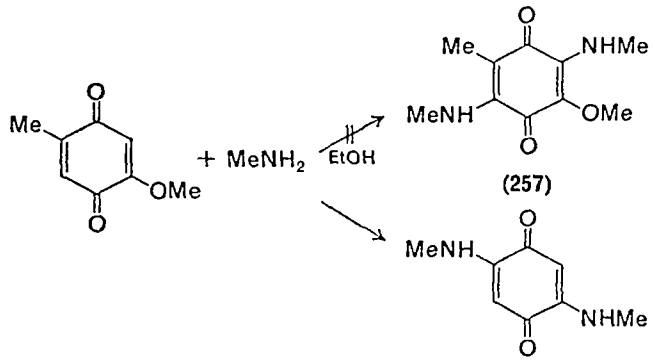
ion again exerts its strong catalytic effect on the 6-position of the heterocyclic quinone. Not only do the overall yields increase, but substitution becomes essentially the only reaction with 6-chloro-5,8-quinolinequinone. With 2-halo-1,4-naphthoquinones the effect of cerous ion is not very great. The low reactivity of the methoxy group is clearly demonstrated as is the powerful catalysis of the cerous ion.

TABLE 18. Addition versus substitution products of *p*-toluidine and quinones (equation 548)[109]

	Yield, % (without $CeCl_3$)		Yield, % (with equivalent $CeCl_3$)	
	Addition (255)	Substitution (256)	Addition (255)	Substitution (256)
5,8-quinolinequinone				
6-Chloro-	76	7		94
7-Chloro-	69	0	87	0
6-Methoxy-	0	0		93
7-Methoxy-	0	0	33	22
1,4-naphthoquinone				
2-Chloro-	75	14	62	27
2-Bromo-	58	26	47	33
2-Methoxy-		<10		80[a]

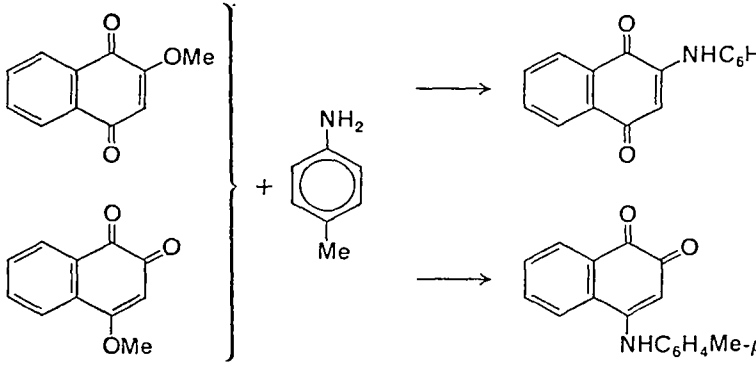
[a] 0·1 equivalent $CeCl_3$.

One of the most unexpected observations in quinone chemistry is the substitution of a methyl group by nitrogen[86]. In demonstrating the structure of spinulosin, a product of mould metabolism, Anslow and Raistrick attempted the reaction of alcoholic methylamine with 2-methyl-4-methoxy-1,4-benzoquinone. Instead of the expected addition product **257** they found that both the methyl and methoxy groups had been displaced by methylamine (equations 549 and 550). The displacement of a methoxy group by an amine was already a known process. Fieser had used the reaction as part of the characterization of isomeric methoxynaphthoquinones (equations 551 and 552)[602]. Even the surprising methyl substitution reaction was not completely unknown at the time (equation 553)[597,598] but had not been explored. The case of methylamine and 3,6-dibromothymoquinone is exceptional in that the 'normal' substitution of bromine takes place and the methyl group is unaffected.

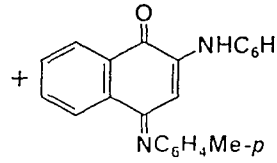


(549)

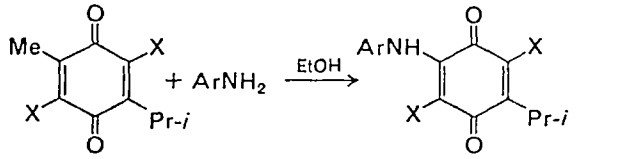
(550)



(551)



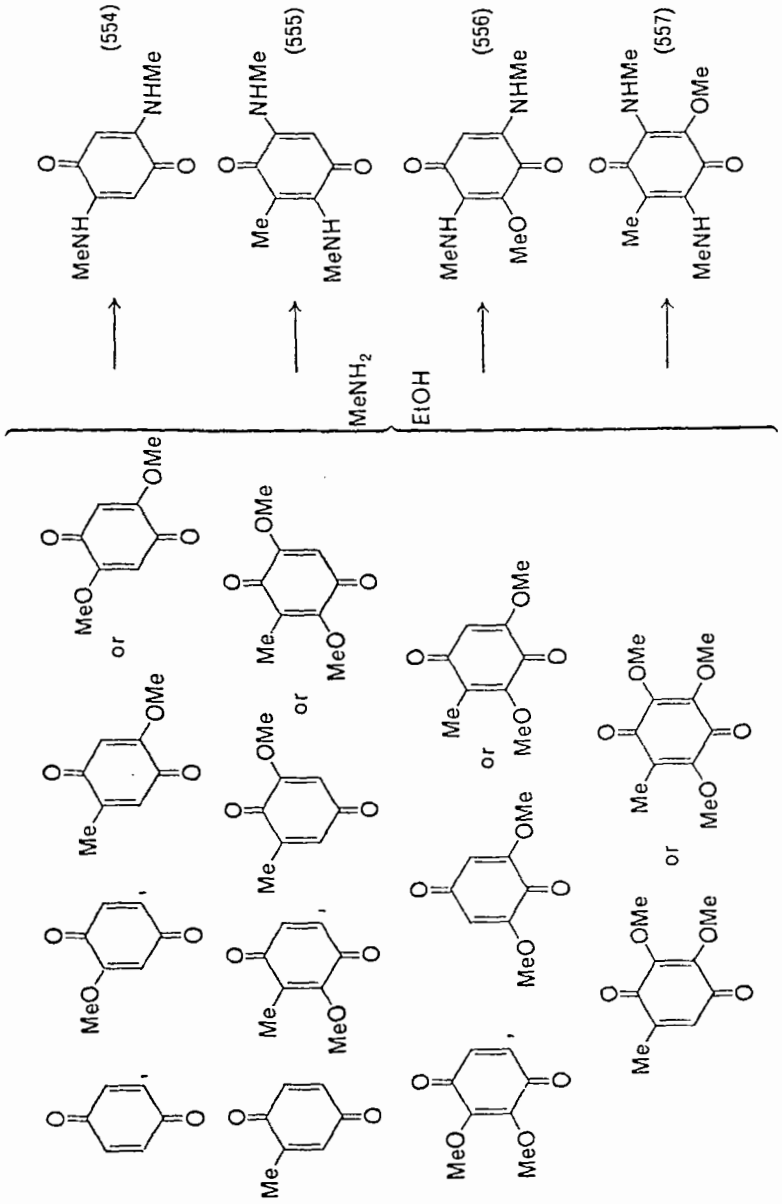
(552)



(553)

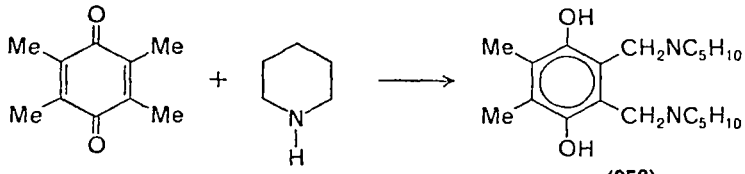
X = Cl, Br Ar = Ph, 3- or 4-MeC_6H_4, 4-$MeOC_6H_4$

Thirteen 1,4-benzoquinones, variously substituted with methyl and methoxy groups, were allowed to react with alcoholic methylamine and the products determined (equations 554–557). All of the reactions gave the bismethylamino product and the *para* orientation. The yield, in most cases, was that expected from the relative proportion of addition and substitution. It is interesting to note that addition *ortho* to a methoxy group is avoided


(554)
(555)
(556)
(557)
MeNH
NHMe
Me
MeO
OMe
or
$MeNH_2$
EtOH

(see section II.D.3) in all cases except 2,6-dimethoxy-1,4-benzoquinone. In this case the tendency toward *para* nitrogen orientation overcomes the low reactivity of the three position. A series of nine 1,4-benzoquinones containing methyl, methoxy and hydroxy groups was also examined, but no methyl group displacement was found.

Another important new quinone–amine reaction has been found in the process of side-chain amination (equation 558)[603, 604]. In addition to the

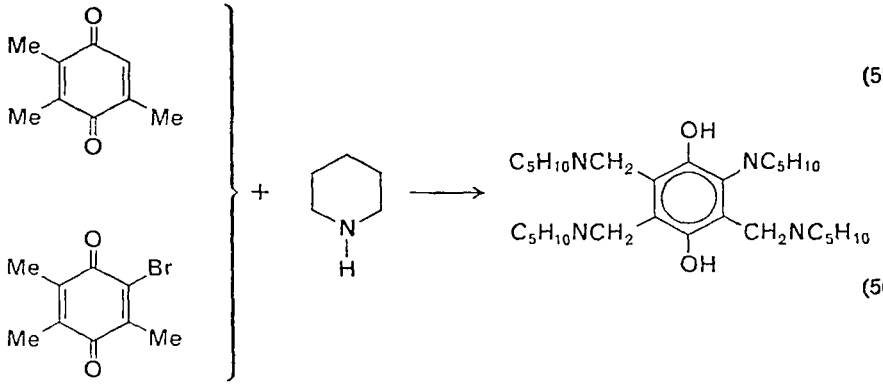


(558)

(258)

2,3-bispiperidinomethyl product **258**, a low yield of 2-methyl-3,5,6-trispiperidinomethylhydroquinone was obtained. The latter product, or duroquinone, can be converted, in low yield, to the tetrakispiperidinomethyl derivative by prolonged treatment. The structure of **258** is consistent with its spectral characteristics and it was synthesized by an independent route.

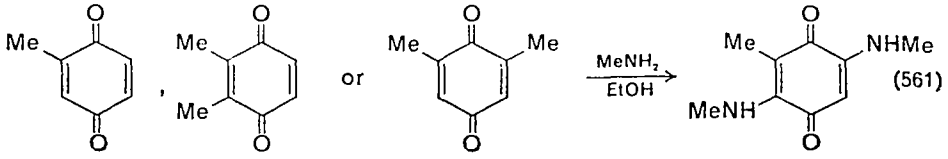
The reaction is fairly general with respect to quinones and primary or secondary amines. With quinones that are not fully alkylated, addition or substitution takes place as well as side-chain amination (equations 559 and 560).



(559)

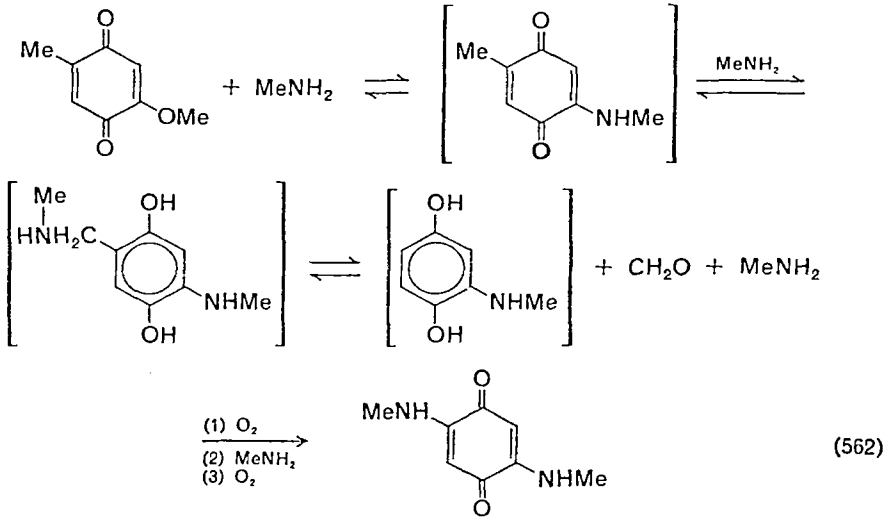
(560)

The relationship between side-chain amination and methyl group substitution by amines has been discussed[605]. The data presented earlier suggest that direct addition or substitution will take place as long as the two amino groups can be *para* to one another. However, if such an arrangement is not possible by simple routes, the displacement of a methyl group occurs (compare equation 561 with equations 559 and 560). The mechanism



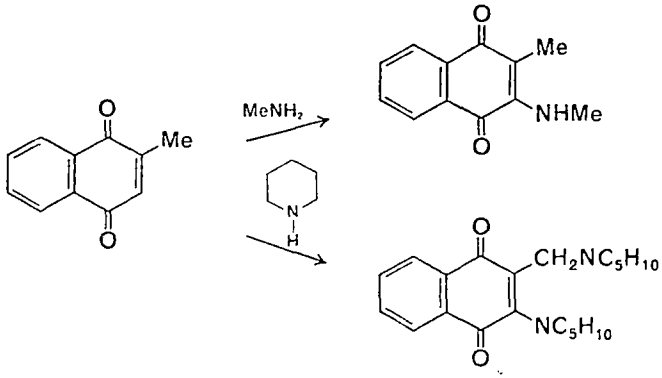
(561)

suggested for this entire reaction type takes into account the oxygen uptake and the formation of formaldehyde (equation 562). The several



(562)

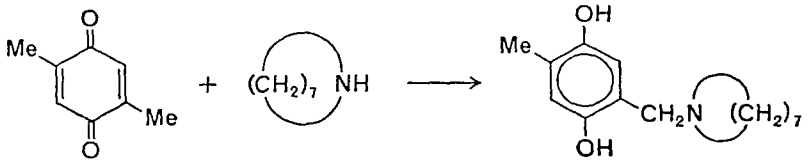
equilibria may well be unfavourable, but the final irreversible step assures the observed product. The reverse Mannich reaction is also a reasonable proposal, although attempts to isolate intermediates were not successful. It was also shown that analogous reactions occur with other amines; e.g. piperidine and cyclohexylamine. Finally, it appears that methylamine is a much weaker nucleophile for side-chain amination than is piperidine (equations 563 and 564).



(563)

(564)

The relationship between nuclear and side-chain amination has been studied with respect to both quinone and amine structure[606]. The first system in which the side-chain reaction is clearly preferred suggests the importance of steric effects (equation 565). The bis side-chain amination



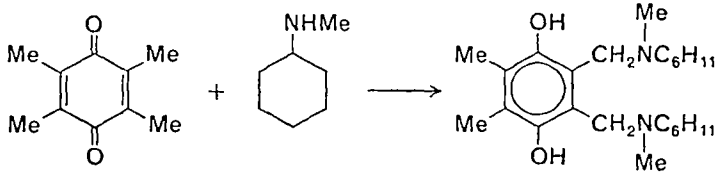
(565)

product was also formed. The reactions of the homologous series of polymethyleneimines and 2,5-dimethyl-1,4-benzoquinone were carefully re-examined and two interesting trends were found. The data in Table 19 suggest both the steric effect and the very impressive change in redox potential with ring size.

TABLE 19. Side-chain versus nuclear amination of 2,5-dimethyl-1,4-benzoquinone[606]

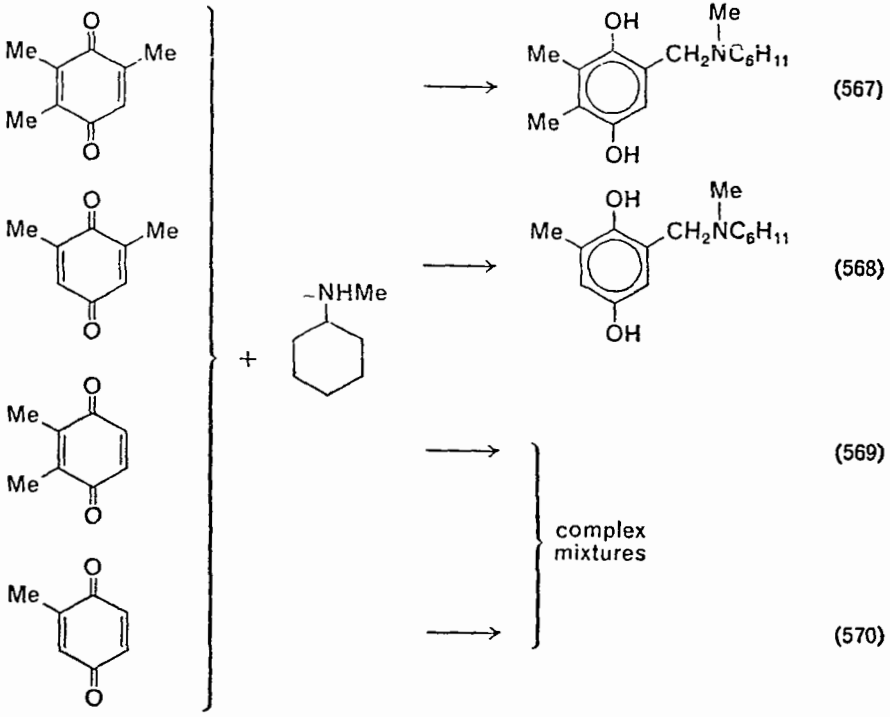
$(CH_2)_xNH$	Side-chain product (%)	Oxidation state of nuclear product
4	0	Q
5	Trace	1 : 1 Q : HQ
6	20–30	HQ
7	100	

A more detailed study was made with *N*-methylcyclohexylamine. As would be expected, this amine reacted with 2,5-dimethyl-1,4-benzoquinone to give only the side-chain amination product (equation 566). When

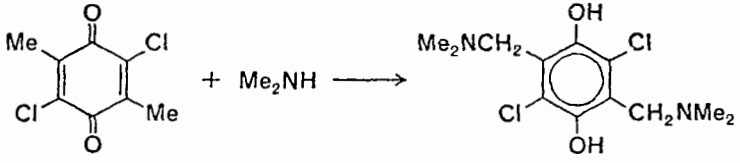


(566)

duroquinone was used, the bis side-chain amination product, analogous to those found earlier, was obtained. The remaining methylated 1,4-benzoquinones present some interesting observations (equations 567–570). The reaction with 1,4-benzoquinone itself gave a poor yield of a bis-*N*-methylcyclohexylamino adduct (probably the 2,5-isomer).

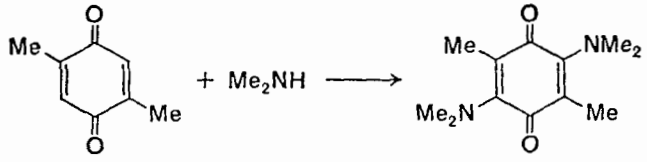


Finally, the compound 2,5-dichloro-3,6-dimethyl-1,4-benzoquinone provided an unexpected and interesting picture of side-chain amination versus nuclear substitution (equation 571). The product structure **260**



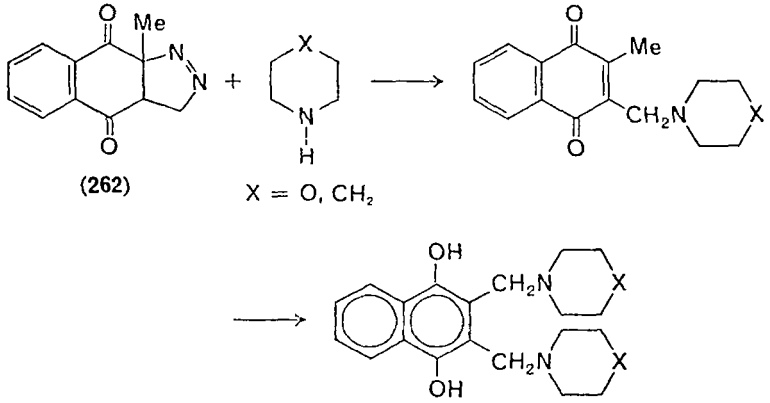
(259) **(260)**

should be contrasted with that obtained from the addition of dimethylamine to 2,5-dimethyl-1,4-benzoquinone (**261** in equation 572). With methylamine the dichloro quinone **259** undergoes a trace of substitution for chlorine, but side-chain amination is by far the major process.



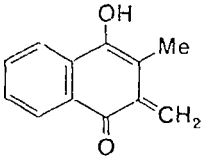
(261)

Another group of English chemists has recently published a detailed study bearing on the mechanism of side-chain amination[607]. When the quinone–diazomethane adduct (**262**) is treated with secondary amines, products clearly related to such reactions are obtained (equation 573).



(262) X = O, CH_2 (573)

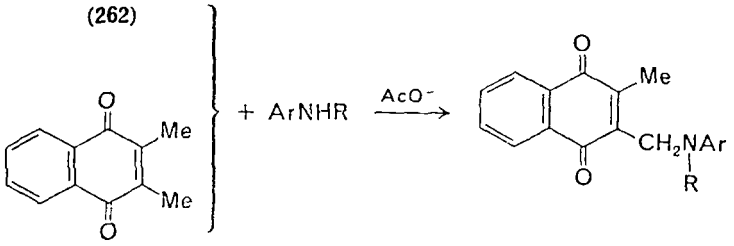
The two amines behave differently, as befits their different basicity. Only the first step was observed with morpholine, although there is no reason to doubt that the second will occur under more strenuous conditions. With piperidine, only the bisaminomethyl product was obtained unless short reaction times and lower temperatures were used. An intermediate quinone methide (**263**) was suggested for this ring opening[608] as well as



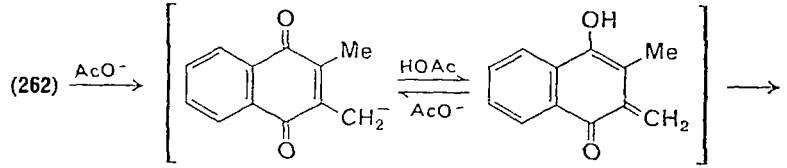
(263)

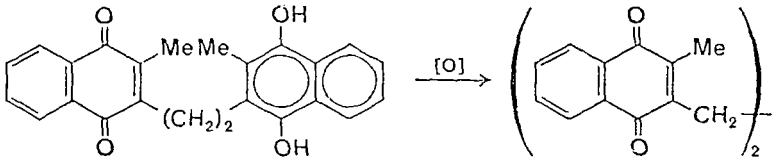
for the side-chain amination reaction[601]. It was found that a series of anilines could also participate in either of these reactions if acetate ion is present (equations 574 and 575).

The decomposition of **262** under basic conditions, but in the absence of primary or secondary amines, leads to an ethylenediquinone (equation 576). Several different possible mechanistic paths were considered in the light of available experimental evidence. The sequence involving Michael addition of the carbanion **264** to the quinone methide **263** seems most plausible. The equilibrium between **263** and **264** is certainly a central aspect of the mechanism and competitive experiments (with limited aniline concentration) show that base concentration has strong influence. If the



Ar = Ph, 4-MeC_6H_4, 4-$NO_2C_6H_4$, 4-ClC_6H_4, 4-$MeO_2CC_6H_4$
R = H, Me

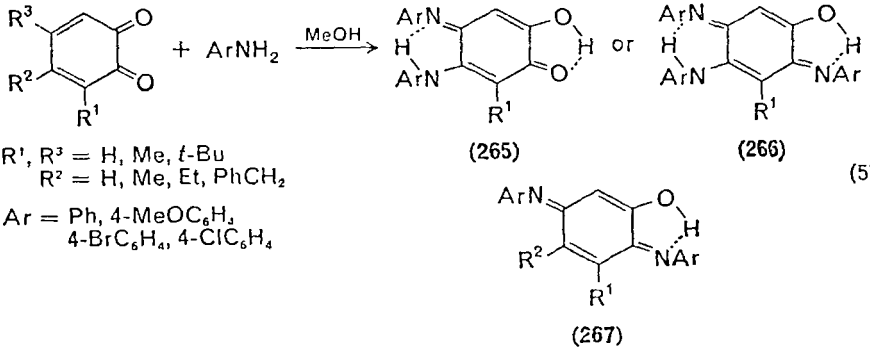




(576)

acetate concentration is low, the arylaminomethylquinone is favoured (equation 574); at high acetate concentration, the ethylenediquinone is favoured (equation 576).

Within the past two years the displacement of alkyl groups from 1,2-quinones has been observed (equation 577*)[609]. The scope of the reaction has been expanded and the mechanism investigated[610]. The data



(577)

R¹, R³ = H, Me, *t*-Bu
R² = H, Me, Et, $PhCH_2$

Ar = Ph, 4-$MeOC_6H_4$, 4-BrC_6H_4, 4-ClC_6H_4

* Other tautomeric forms are possible, but these are preferred on the basis of the expected strong intramolecular hydrogen bonding.

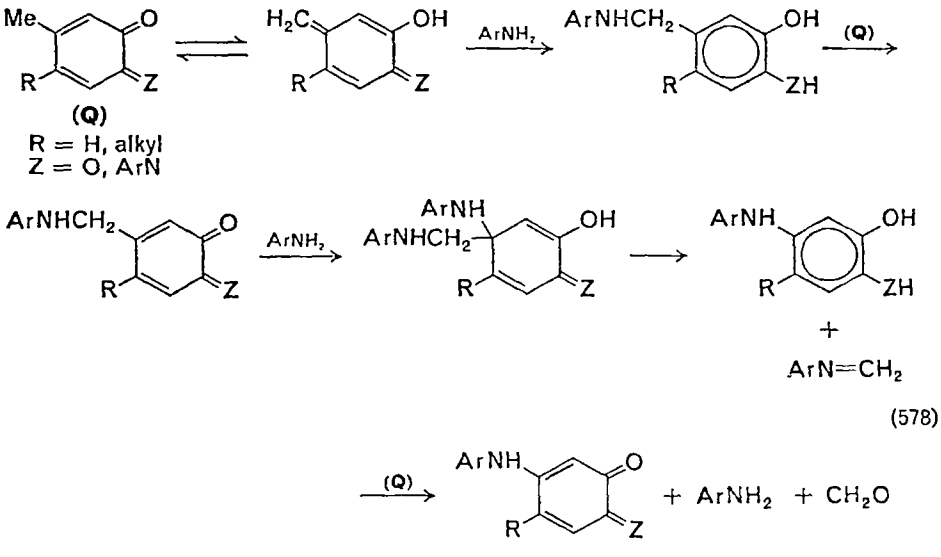
in Table 20 indicate the major product obtained with various quinone structures. Several important features of this reaction are clear: (i) ethyl or benzyl groups are displaced as well as the methyl group, (ii) alkyl groups in the three position are not displaced, (iii) when two groups are present, only one (*para* to a carbonyl group) is displaced and (iv) the product of a displacement reaction is a mono-anil.

TABLE 20. Principal product of the reaction of anilines with alkyl-substituted 1,2-benzoquinones (equation 577)[609, 610]

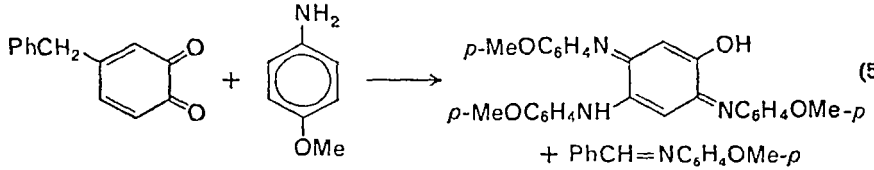
R^1	R^2	R^3	X in 4-XC_6H_4	Major product
H	H	H	H, MeO, Cl, Br	(265)
Me	H	H	MeO	(265)
H	Me	H	H, MeO, Cl	(266)
H	Et	H	MeO	(266)
Me	H	Me	MeO, Cl	(266)[a]
H	$PhCH_2$	H	MeO	(266)
H	Me	Me	MeO, Cl	(267)[a]

[a] One of two possible structural isomers.

The mechanism of this reaction was carefully studied. Both oxygen and solvent were ruled out as being directly involved in the reaction although the latter appears to be important in solvating the transition state. The following mechanism was proposed (equation 578). The required formaldehyde was found in the recovered solvent. The case of benzyl group



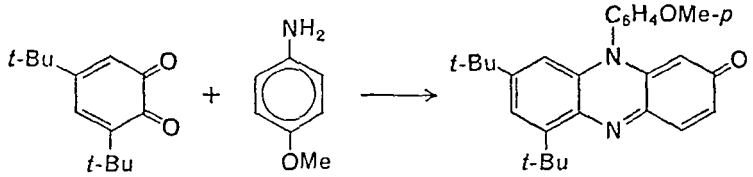
displacement is important because *N*-benzylidene-*p*-anisidine (**268**) was obtained in the same yield as the quinonoid product (equation 579).



(579)

(268)

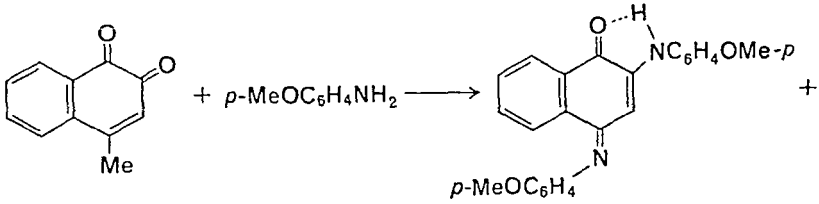
No alkyl group displacement was found in the case of 3,5-di-*t*-butyl-1,2-benzoquinone. This observation could be the result of steric hindrance, but it is also the predicted result on the basis of the suggested mechanism (equation 578). The product that does form has not been completely characterized, but appears to be **269** on several grounds (equation 580).



(580)

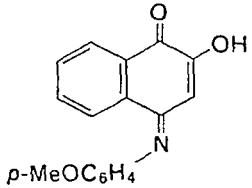
(269)

Finally, 4-methyl-1,2-naphthoquinone and *p*-anisidine produce two products and both involve methyl group displacement (equation 581).



(270)

(581)



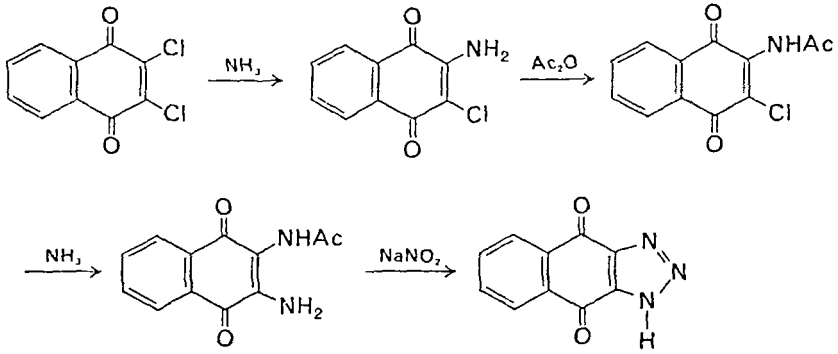
(271)

It is possible that product **271** might be formed by the hydrolysis of product **270**, but under more vigorous conditions than those of the

displacement such a hydrolysis did not occur. It follows that, at least in this case, methyl group displacement precedes or occurs concurrently with anil formation.

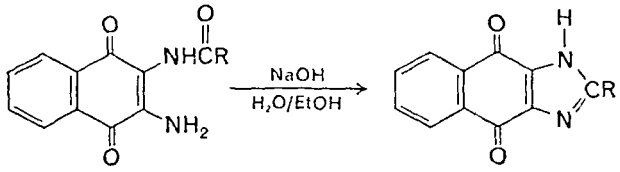
2. Synthetic survey

Fieser, in his wide-ranging studies of heterocyclic quinones electronically analogous to carbocyclic systems (see sections II.E.3 and V.B), has made interesting use of a modification of the *N*-nitroso method (equation 582)[611]. Chloranil was also used to prepare the analogous system



(582)

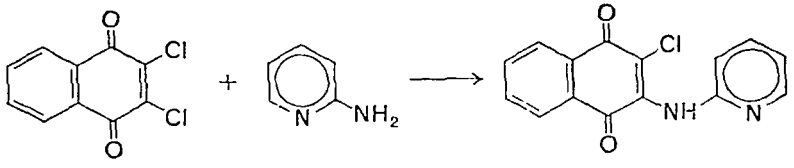
containing two triazole rings. A closely related sequence of reactions has been used to prepare imidazoles of similar structure (equation 583)[234,612].



(583)

R = alkyl

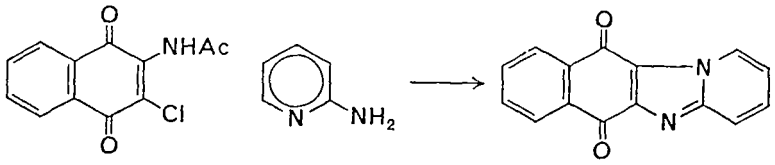
The reaction of 2-aminopyridine with 2,3-dichloro-1,4-naphthoquinone has been reported (equation 584)[613] and the structure of the product **272**



(584)

(272)

confirmed through subsequent conversion to a polycyclic benzimidazole prepared independently (**273** in equation 585)[614]. This latter preparation is a further application of the method of Fries and Billig[588]. The benzimidazole structure proposed (**273**) has now been revised.

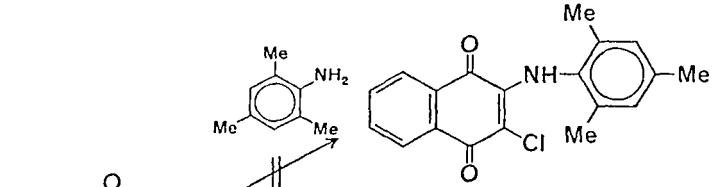


(585)

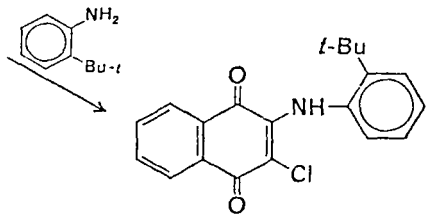
(incorrect structure, see reference 619)

(273)

The possibility that halogen displacement reactions might be useful for the qualitative identification of primary and secondary amines led Buu-Hoï to examine the question of steric limitations[615]. Not unexpectedly, the reaction of either 2,3-dichloro-1,4-naphthoquinone or chloranil took place with anilines having one *ortho* substituent, but not with both *ortho* positions occupied (equations 586 and 587). The reactions with chloranil



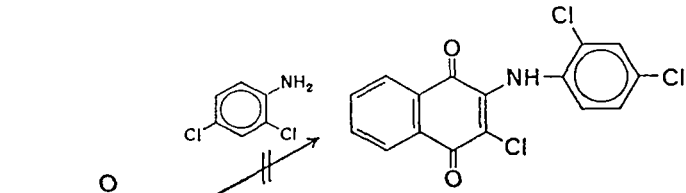
(586)



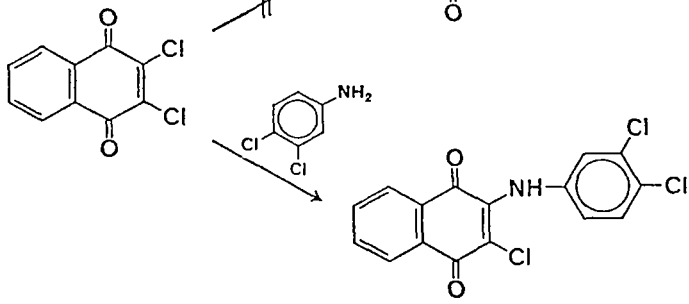
(587)

produced the 2,5-dianilino derivatives. It has been found recently that the interplay of steric and electronic effects is very strong in these reactions. For example, even a single *ortho* electron-withdrawing substituent will prevent the reaction (equations 588 and 589)[616].

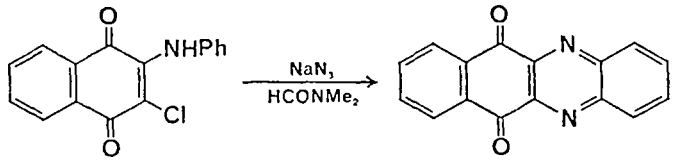
An important modification of the techniques for converting 2,3-dichloro-1,4-naphthoquinone to heterocyclic quinones has been presented by Reynolds and collaborators. In studies of the chemistry of benzo[b]-phenazine and related compounds, the 6,11-quinone (**274**) is a key intermediate[617]. The treatment of 2-anilino-3-chloro-1,4-naphthoquinone with sodium azide in dimethylformamide produced the required compound (equation 590). The presumed intermediate azide was not isolated in this case, but was in a later example (**275**).



(588)



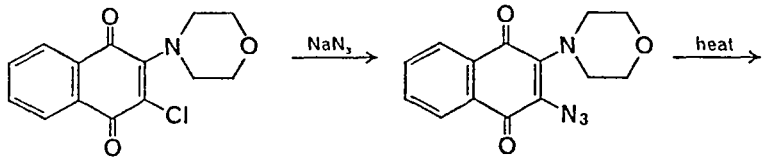
(589)



(590)

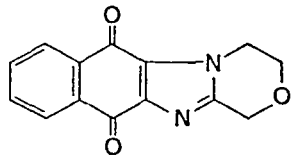
(274)

The reaction proved to be quite general both for anilines and a series of saturated heterocyclic amines (e.g. equation 591)[616]. The preparation

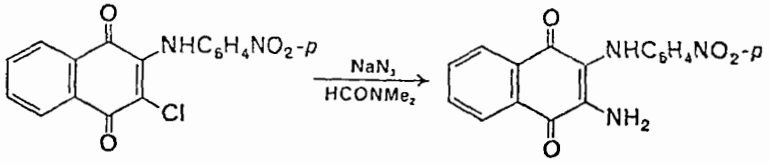


(275)

(591)



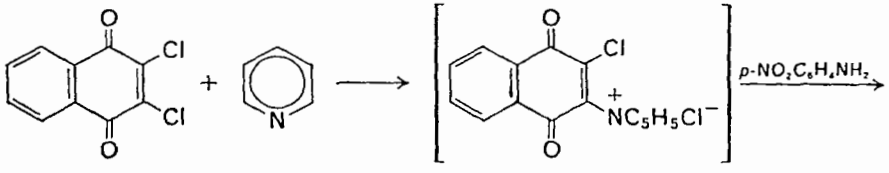
of 2-(4-nitroanilino)-3-chloro-1,4-naphthoquinone (**276**) had to be accomplished indirectly. When this compound was treated with sodium azide in dimethylformamide, the chlorine was replaced by an amino group and no cyclization took place (equation 592). On closer inspection, products analogous to **277** were found for other cyclizations involving an anilino group.



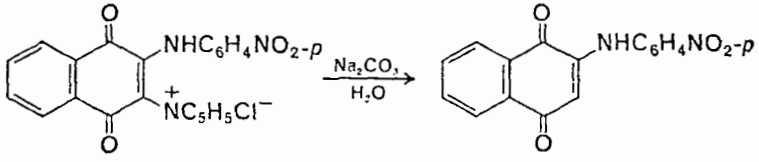
(592)

(276) (277)

While trying to prepare **276**, Reynolds and Van Allan attempted unsuccessfully to repeat the reported direct substitution of 2,3-dichloro-1,4-naphthoquinone by *p*-nitroaniline[584]. They found that under more vigorous conditions an interesting reductive loss of chlorine occurred (equation 593)[618]. The initial pyridinium salt was not isolated, because on

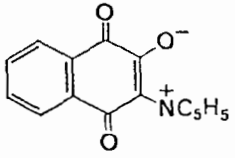


(593)



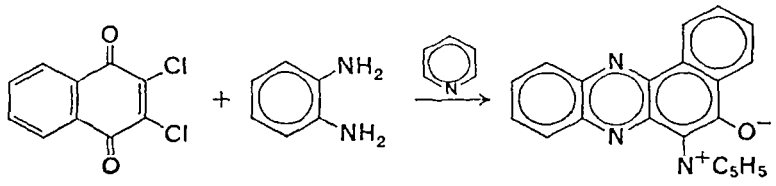
(278)

attempted recrystallization, from water or ethanol, the internal salt **279** was obtained (equation 594). The second pyridinium salt **278** was purified and its structure established.

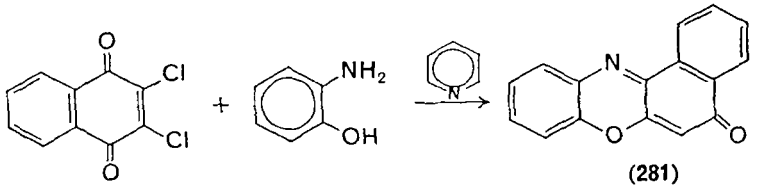


(279)

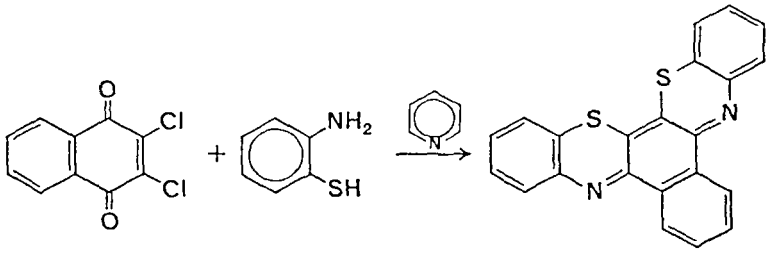
The condensation of *ortho* bifunctional aromatic amines with 2,3-dichloro-1,4-naphthoquinone in pyridine has led to some interesting new heterocyclic syntheses (equations 594–596)[618]. All three of these reactions are of interest beyond their indication of the scope of this condensation. The reaction product with *o*-phenylenediamine in pyridine (**280**) is



(280) (594)

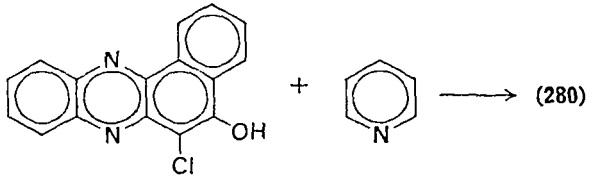


(281) (595)



(282) (596)

similar to that formed from the same reactants in ethanol (**283**) and can be obtained from the latter (equation 597). The reaction with *o*-aminophenol

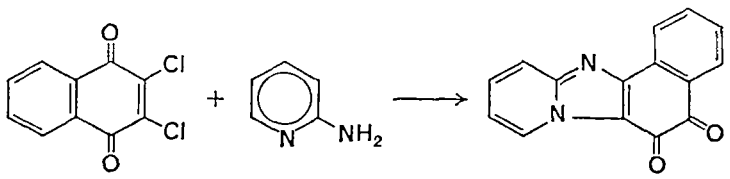


(280) (597)

(283)

is again noteworthy for its facile reduction of the chloro group (**281**). Finally, under all conditions studied, *o*-aminobenzenethiol produced the disubstitution product (**282**).

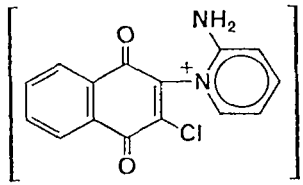
The structure of the products just described (i.e. all angular) caused Reynolds and Van Allan to re-examine the reaction of 2,3-dichloro-1,4-naphthoquinone with 2-aminopyridine (equation 598; see also equation 585)[618]. The authors of the earlier report[614] had eliminated structure **284** from consideration because they could not observe a reaction with *o*-phenylenediamine. Reynolds and Van Allan achieved this reaction as well as the conversion of **284** to an anhydride with sodium peroxide,



(598)

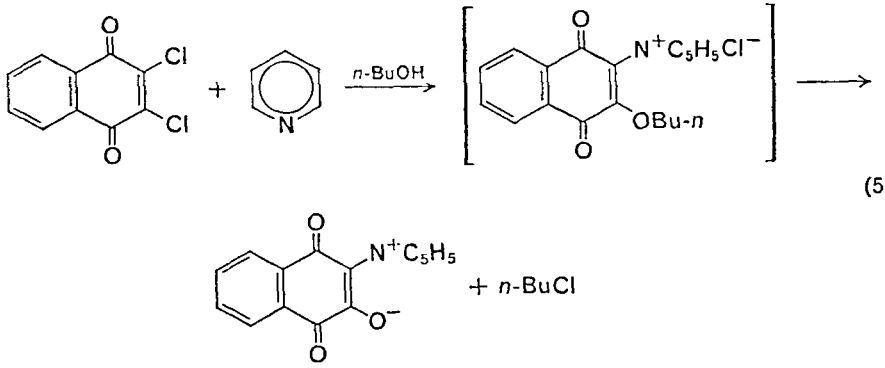
(284)

leaving no doubt of its *ortho* quinonoid structure. The alternative arrangement of nitrogen atoms was considered, but **284** was preferred because the ring nitrogen of 2-aminopyridine is known to quaternize more readily than the amino group, hence intermediate **285** is suggested.



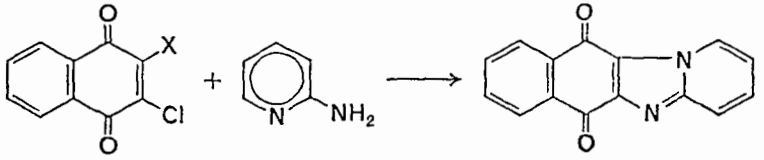
(285)

The reaction of 2,3-dichloro-1,4-naphthoquinone with two equivalents of pyridine in anhydrous butanol is interesting (equation 599)[618]. The intermediate is speculative, but seems entirely reasonable. On the basis of this experiment, it is possible to see the probable similarity of mechanism in the several examples.



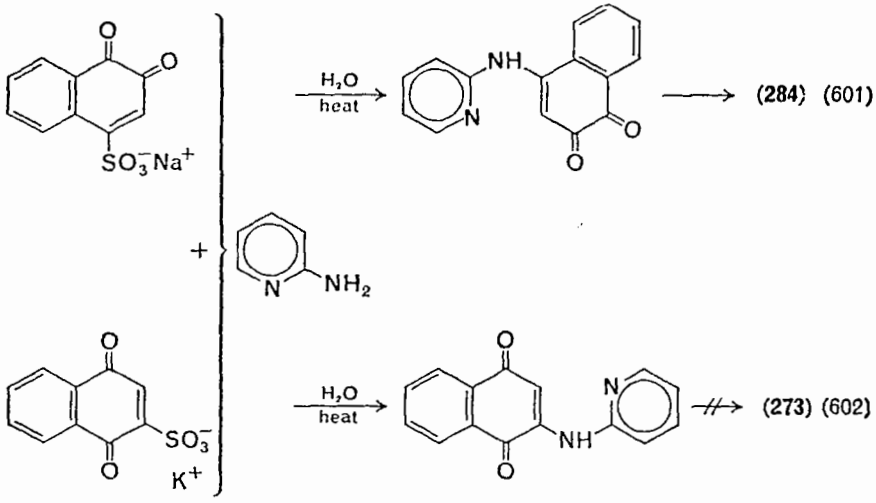
(599)

Actually another group of chemists had demonstrated the angular structure of **284** some years earlier[619]. Mosby had also shown that by using different leaving groups on the quinone it is possible to prepare the linear system **273** in equation 600[620]. Some mechanistic speculations are presented, but the subtle structure changes and the marked changes in product they bring about demand more detailed study. In a later paper, Mosby and Silva present still another curious aspect of these systems



X = OH, EtO, OAc (273) (600)

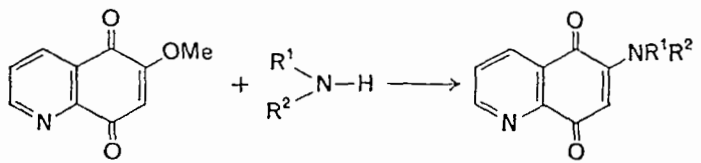
(equations 601 and 602)[621]. It should also be noted that both of the initial substitution products are formulated as *N,N*-diaryl secondary amines rather than pyridinium salts. Clearly, much work remains to be done in this important reaction series.



(284) (601)

(273) (602)

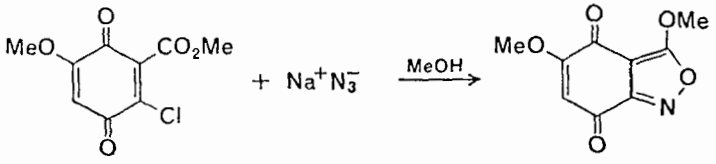
The displacement of oxygen functions by nitrogen nucleophiles has also played a significant role in quinone substitution chemistry. A variety of amines have been used to displace the ether linkage of 6-methoxy-5,8-quinolinequinone (equation 603)[622]. The yield of product obtained in most cases is very good, but the *p*-toluidine reaction is slow and gives only 40% of the theoretical yield.



(603)

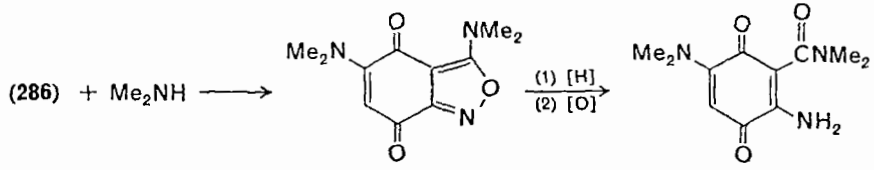
R^1 = Et, *n*-C_6H_{13}, 4-MeC_6H_4
R^2 = H, Et
R^1, R^2 = $(CH_2)_5$

An interesting azide substitution and subsequent cyclization has been reported (equation 604)[623]. A variety of substituted quinones can be prepared from **286** (e.g. equation 605).



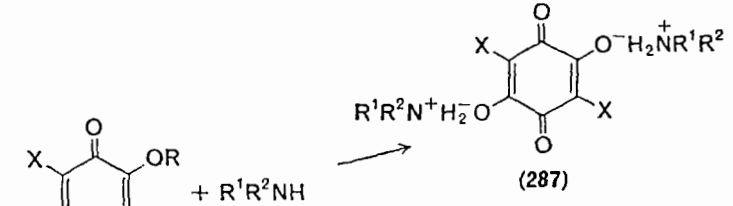
(604)

(286)



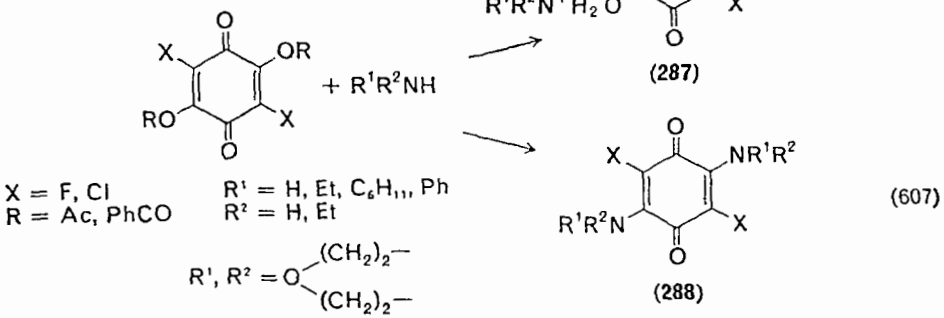
(605)

The esters of certain halogen hydroxy-substituted 1,4-benzoquinones can be regarded as mixed anhydrides since, for example, chloranilic acid is more acidic than the carboxylic acids. Thus, the competition between aminolysis and substitution (equations 606 and 607 respectively) is of



(606)

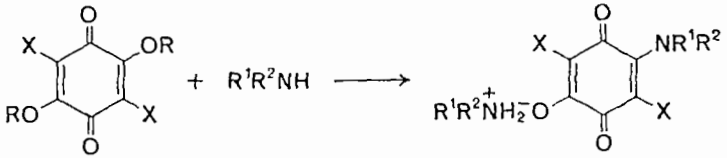
(287)



(607)

(288)

interest[624]. Mixed products (**289**) were also found under appropriate conditions (equation 608). It is especially interesting to note that the two



(608)

(289)

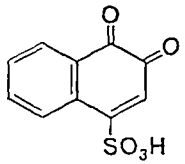
reactions proceed independently; when the salts (**287** or **289**), or the corresponding free acids, were treated with amines under different conditions no conversion to the substitution products (**288**) could be observed.

Both the basicity of the amine and the nature of the ester influence the product distribution. The amines studied showed the following decrease in substitution reaction:

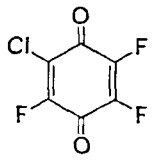
aniline > cyclohexylamine > morpholine > diethylamine

The mixed product **289** was important except with diethylamine where aminolysis was essentially the only reaction with either ester. Except for aniline, higher temperatures tend to favour aminolysis; with aniline only substitution was found. The diacetate of fluoroanilic acid was allowed to react with ammonia and cyclohexylamine in hopes of learning about the ease of substitution of the fluorine atoms. However, only aminolysis was observed.

Two new reagents for the identification of amino acids and protein residues have been introduced (**290** and **291**)[625, 626]. It has been found possible to make a classification scheme practical using the substitution chemistry of these quinones.



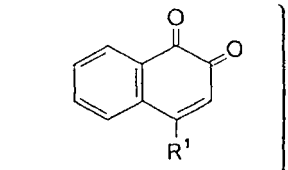
(290)



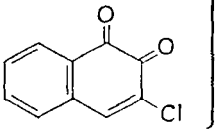
(291)

The reactions of a series of acid hydrazides with various naphthoquinones have been reported and the substitution chemistry is informative[627]. With 1,2-naphthoquinones having 4-substituents, substitution takes place; with a 3-substituent, addition takes place (equations 609 and 610). Addition, rather than substitution, is also observed with 2-chloro-1,4-naphthoquinone.

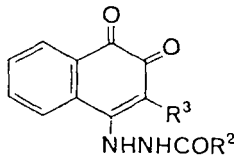
In a study of substitution reactions between molecules containing more than one site for addition and/or substitution, the following interesting observation was made. The reaction of ethylenediamine with chloranil gives a heterocycle that must be the result of a rather complex reaction sequence (**292** in equation 611)[628]. On the other hand, reaction between ethylenediamine and 2,5-dimethoxy-1,4-benzoquinone produces only simple substitution (equation 612). Clearly, there is a great deal to be learned about this 'simple' system. Several other bifunctional amines were studied and the expected reactions (i.e. analogous to equation 612) were found.



R^1 = H, Cl, SO_3^- Na^+



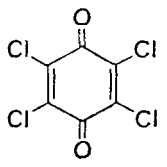
+ R^2CNHNH_2 ⟶



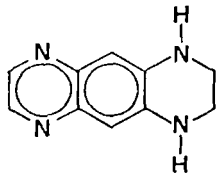
R^2 = Me, $PhCH_2$, 4-HOC_6H_4, 4-$NO_2C_6H_4$, 4-NC_5H_4
R^3 = H, Cl

(609)

(610)

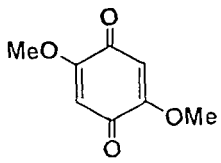


+ $H_2NCH_2CH_2NH_2$ ⟶

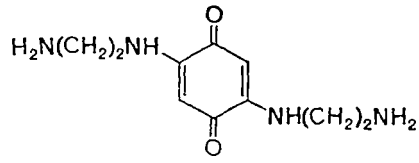


(292)

(611)



+ $H_2NCH_2CH_2NH_2$ ⟶

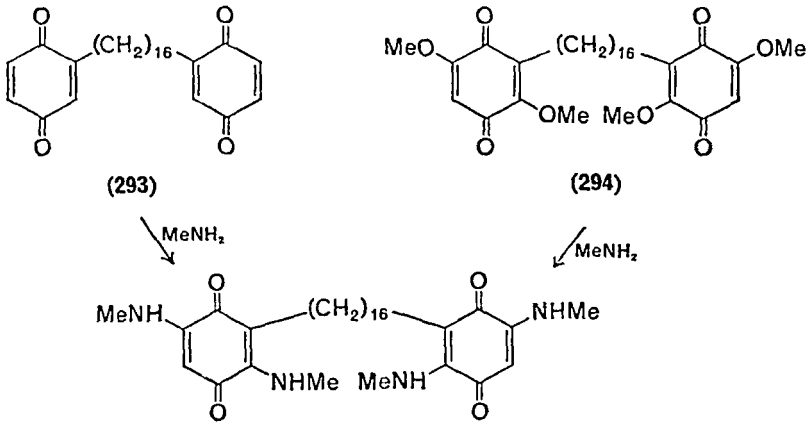


(612)

The substitution of various quinonoid groups by nitrogen continues to be of considerable practical importance. One report of the synthesis of a large number of substituted 1,4-naphthoquinones for growth inhibitory testing includes a fine, brief survey of many of the most useful methods[235]. In addition to the synthesis of potentially useful drugs[629–631] an interesting characterization of a natural product has been reported (equation 613)[632]. The synthetic quinone **293** was obtained by Friedel–Crafts and oxidative reactions. The natural quinone **294** was derived from the isolated natural product by reduction of an alkene and methylation of two hydroxy groups.

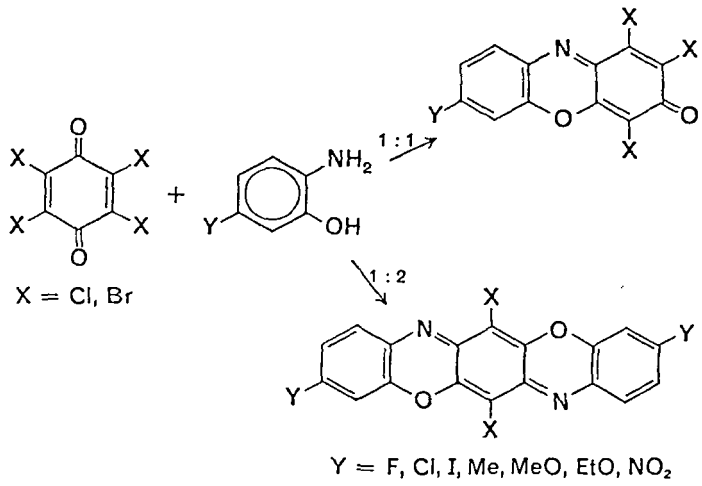
The work of Reynolds and Van Allan with bifunctional aromatics in heterocyclic synthesis[618] has been expanded to the benzoquinone series[633].

When chloranil or bromanil reacts with various 4-substituted *o*-aminophenols, either mono- or diadducts can be obtained by changing reactant



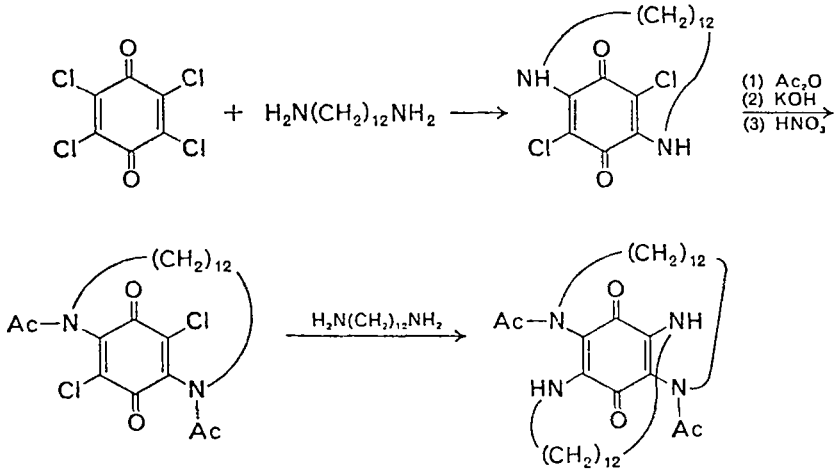
(293) (294) (613)

ratios (equations 614 and 615). Similar results were obtained with *o*-aminothiophenol or its zinc salt.



(614) (615)

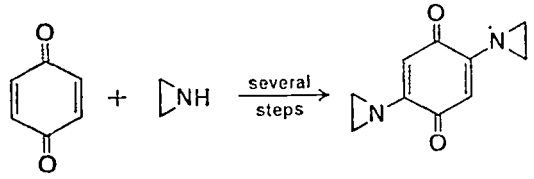
The synthetic problems associated with interlocking rings and related topological considerations have fascinated organic chemists for a long time and very recently quinone substitution chemistry provided an interesting fresh approach[634]. When a single 1,4-benzoquinone has both the 2,5-substituents and the 3,6-substituents locked in rings, the total system is, in fact, a Möbius-strip with one twist. Such a molecule has been prepared (equation 616).



(616)

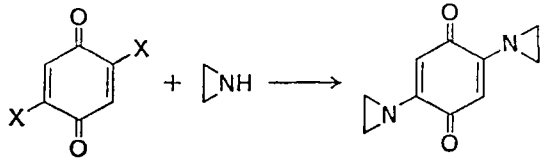
C. Substitution by Ethylenimine

The observation that quinones and hydroquinones bearing ethylenimino substituents are effective cytostatic agents has caused a great deal of synthetic effect in this particular nitrogen substitution area[635-637]. As with other imines, normal Michael addition of ethylenimine followed by oxidation is a useful route to some quinone derivatives (equation 617).



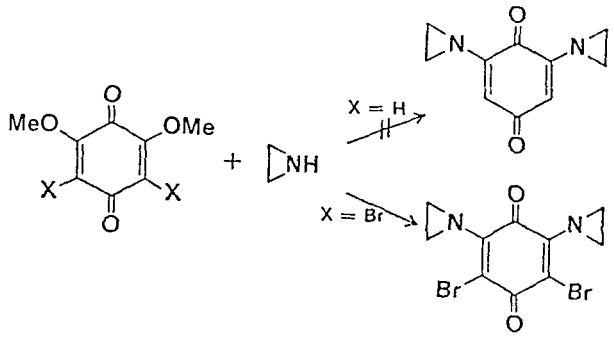
(617)

More often, substitution chemistry, of the type discussed in this section, is the preferred route (equation 618).



(618)

The examples of 2,5-dichloro- and 2,5-dimethoxy-1,4-benzoquinone are interesting in view of a study of 2,6-dimethoxy-1,4-benzoquinone[638]. This *meta* isomer shows no substitution reactivity toward ethylenimine, but its 3,5-dibromo derivative reacts smoothly under the same conditions (equations 619 and 620). The two bromine atoms in **295** can be replaced

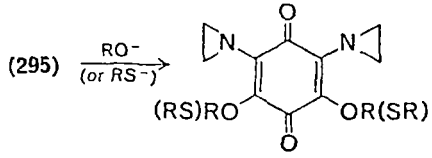


(619)

(620)

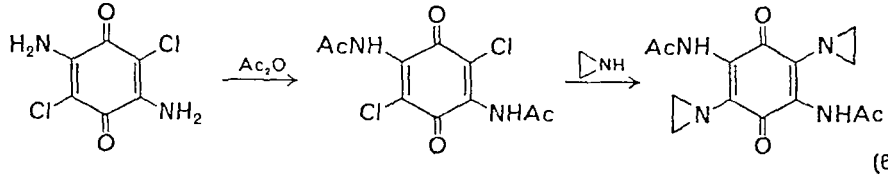
(295)

by alkoxy or thioalkoxy groups (equation 621). A rationalization of this observation on the basis of resonance contributors is presented. It is



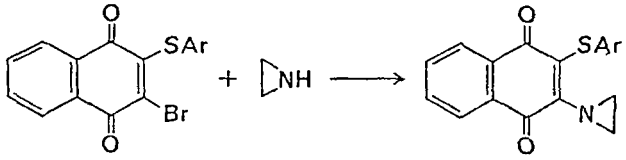
(621)

important to note another experimental observation. In the closely related structure, 2,5-diamino-3,6-dichloro-1,4-benzoquinone, the halogen atoms are unreactive toward nitrogen substitution. This limitation, which we have seen several times before, can be overcome by acetylation (equation 622). The synthesis of quinones with adjacent arylmercapto and



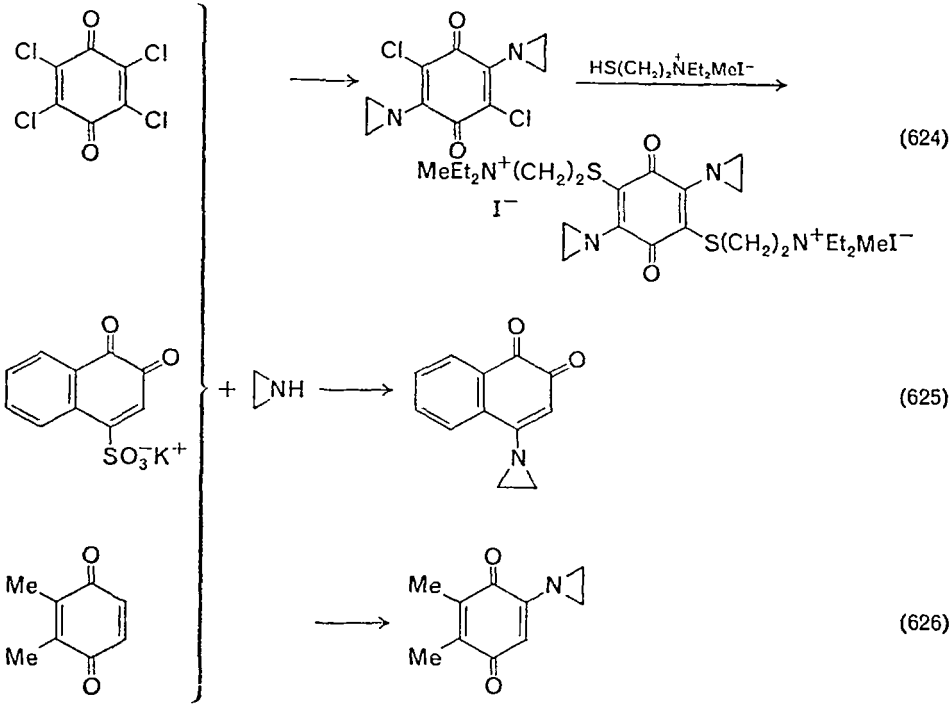
(622)

ethylenimino groups has also been carried out in the 1,4-naphthoquinone series (equation 623)[639].



(623)

Gauss and Petersen have continued to make synthetic contributions in the ethylenimino-substituted quinones[640–642]. A hydrophilic quinone type, derivatives of 1,2-quinones and monoethylenimino 1,4-quinonoid compounds have been prepared (equations 624–626). Satisfactory conditions

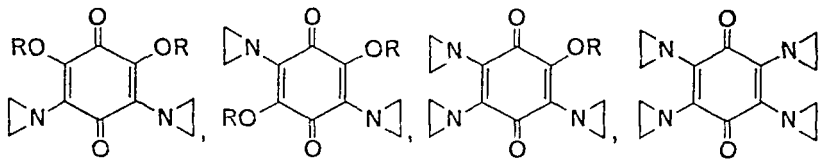


(624)

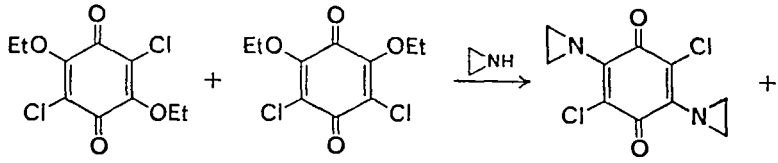
(625)

(626)

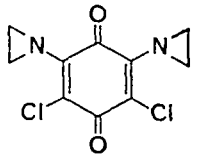
have been found for the selective introduction of ethylenimino groups on alkoxy-substituted 1,4-benzoquinones; for example, the following have been prepared:



Berlin and Makarova, in detailed studies of the preparation and properties of the ethylenimino-substituted 1,4-benzoquinones, have shown that the chemistry possesses a great deal of interesting detail[643]. Both 2,5-diethoxy-3,6-dichloro- and 2,6-diethoxy-3,5-dichloro-1,4-benzoquinones react smoothly with a cold alcohol solution of ethylenimine to yield the corresponding diethylenimino dichloro products. Furthermore, it was found that both products can be prepared conveniently from a mixture of starting materials because of the difference in their solubilities (equation 627). The slightly soluble **296** precipitates first and further cooling provides the somewhat more soluble isomer **297**.



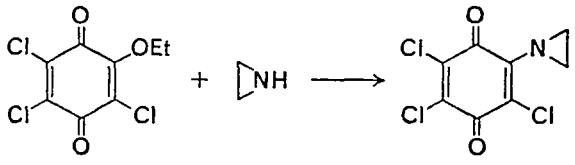
(296)



(297)

(627)

In a closely related study these same chemists found a method for the preparation of 2-ethoxy-3,5,6-trichloro-1,4-benzoquinone (see section VIII.D) and through this intermediate one of the limited number of examples of monoethylenimino quinones (equation 628)[644]. Further amine



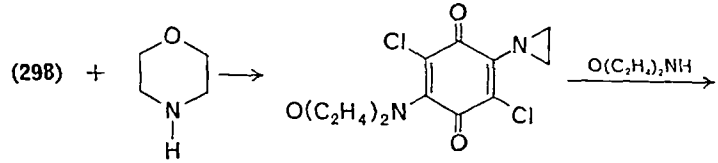
(298)

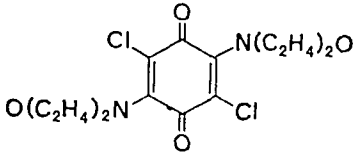
(628)

substitution chemistry is possible with this product (**298**) and a number of unusual quinones can be prepared (e.g. equation 629).

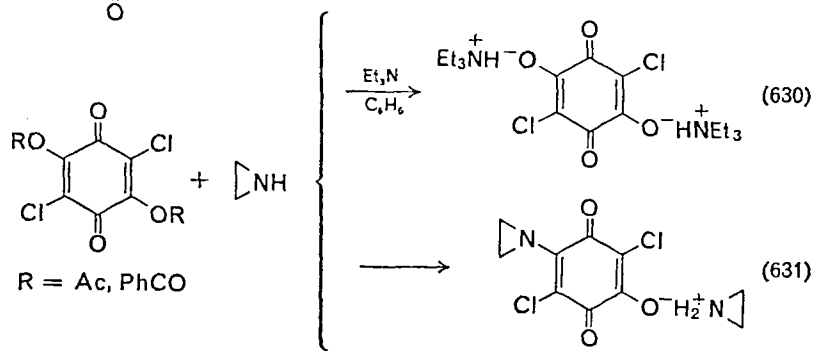
The study of competitive substitution and aminolysis of chloranilic salt esters discussed earlier (see section VIII.B.2) was actually preceded by a related exploration of the reactions of ethylenimine[645]. In the presence of triethylamine, a benzene solution of ethylenimine reacts with either the acetate or benzoate of chloranilic acid to give the bistriethylammonium salt of chloranilic acid; i.e. aminolysis results (equation 630). When triethylamine alone was the reagent, monoaminolysis took place. Mixed product resulted with ethylenimine alone; i.e. both monosubstitution and monoaminolysis were found (equation 631). In all cases the halogen atoms were unaffected and the benzoate was significantly less reactive than the acetate.

Fluoranil is a particularly important synthetic intermediate because the fluorine atoms are quite easily and selectively replaced (see also section VIII.D)[646, 647].





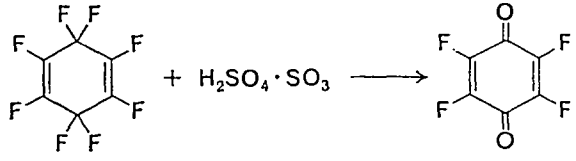
(629)



(630)

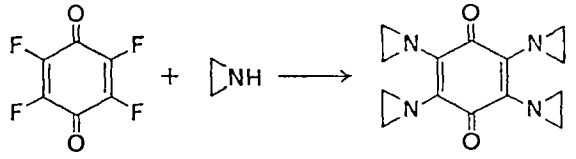
(631)

An interesting preparation of fluoranil has been reported (equation 632)[648]. The problem of obtaining perfluoro-1,4-cyclohexadiene, except



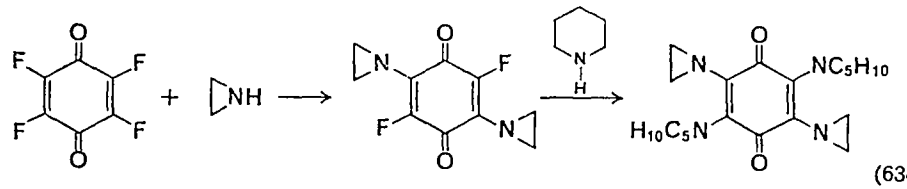
(632)

from fluoranil, may seriously limit the application of this reaction[291]. Unlike most amine substitution reactions, the tetraamino derivatives can be prepared directly from fluoranil (equation 633)[649]. At lower temperatures



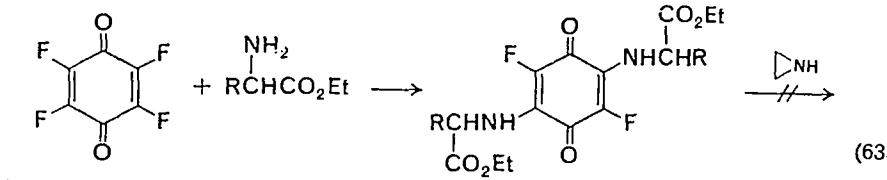
(633)

disubstitution takes place; this reaction can be followed by substitution of another amine (equation 634). In an attempt to obtain analogous compounds containing the esters of α-amino acids, only disubstitution was



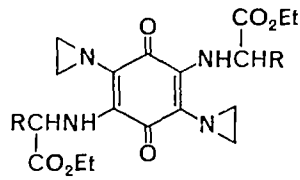
(634)

found and subsequent reaction with ethylenimine does not take place (equation 635). The desired product **299** was obtained, in low yield, by



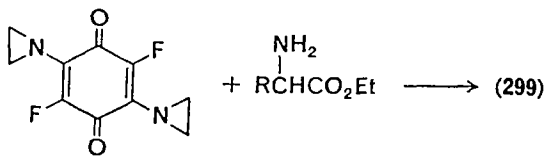
(635)

R = H, Me, $PhCH_2$



(299)

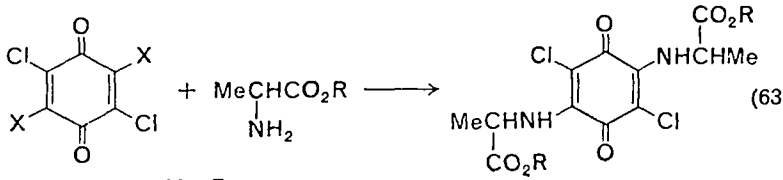
the reverse reaction sequence. The failure of the ethylenimino groups to be opened or displaced is unique and **300** represents the sole direct route to a large class of tetranitrogen-substituted 1,4-benzoquinones (equation 636).



(636)

(300)

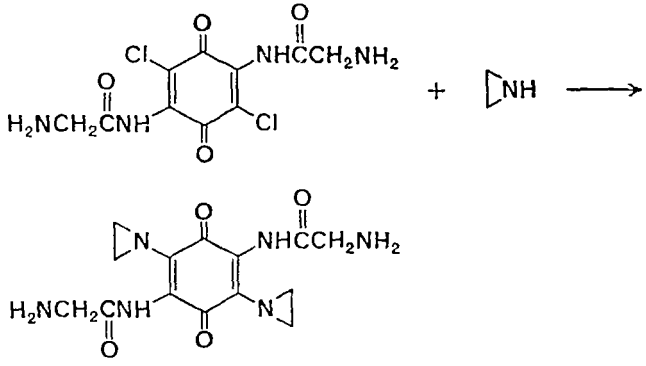
Some earlier studies are related to this discussion. It has been reported that when chlorine atoms or ethylenimino groups are present, they can be displaced by esters of α-amino acids (equation 637)[650]. A supplementary technique for preparing tetranitrogen-substituted 1,4-benzoquinones in



(637)

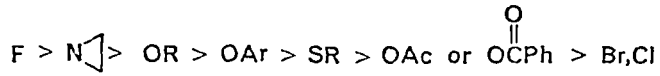
X = Cl, NC_2H_4 R = Me, Et

which two ethylenimino substituents are included, involves amide formation (equation 638)[651]. The peptide-like character of these compounds

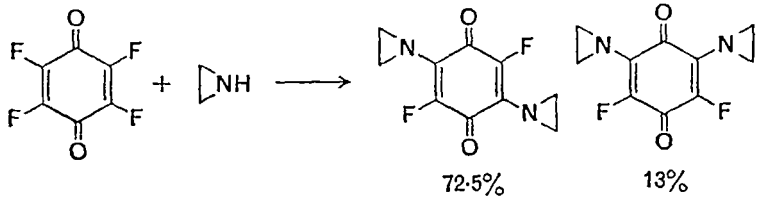


(638)

is apparent (see section II.C.3). A survey of the literature shows the ease of displacement of quinonoid substituents by amines:

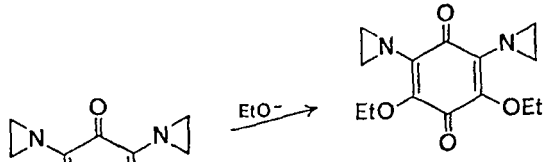


A further useful aspect of the reaction of fluoranil with ethylenimine is the discovery that a small amount of the 2,6-isomer is formed and can be conveniently obtained because of its greater solubility (equation 639)[652].

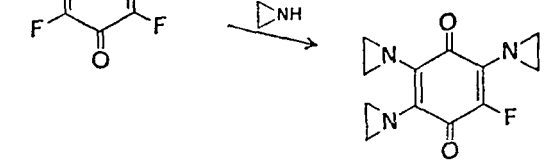


(639)

It was also learned that its subsequent reactions proceed much more easily than those of 2,5-diethylenimino-3,6-difluoro-1,4-benzoquinone (equations 640 and 641).

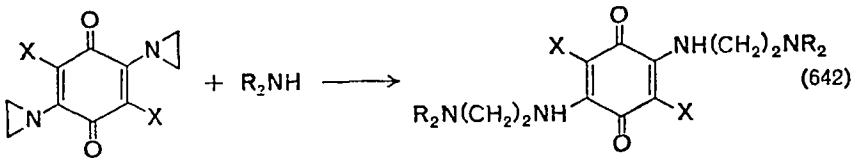


(640)



(641)

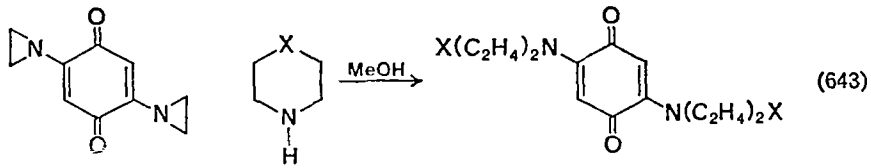
The ethylenimino-substituted quinones themselves have shown some interesting chemistry. In a study of the reactions of such compounds with secondary amines, ring opening was often observed (equation 642)[653].



(642)

X = H, Cl, OEt
R_2 = Me-Ph, Et_2, C_5H_{10}, $(C_2H_4)_2O$

The other substituents attached to the quinonoid ring have an effect on the ease of the reaction. Longer reaction times and poorer yields were found where X = OEt than when X = Cl. This effect can be understood on the basis of the resonance contributors involved. With 2,5-diethylenimino-1,4-benzoquinone, and either piperidine or morpholine in methanol, the alternate path of ethylenimino displacement was found (equation 643).



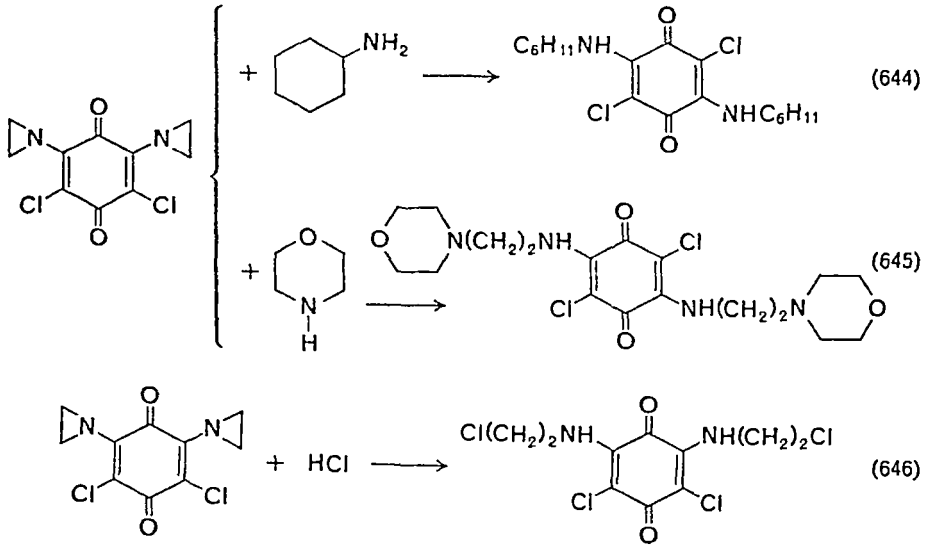
(643)

X = CH_2, O

A similar study was conducted with primary amines and only substitution was observed (often in excellent yield)[654]. Once again, the presence of an ethoxy group on the quinonoid ring led to a less favourable reaction, while chlorine enhanced the reactivity. As would be expected, the basicity of the amine plays an important role in determining the rate of reaction.

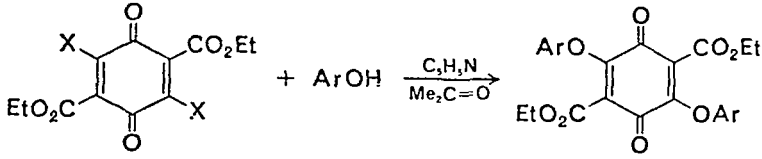
The potential synthetic usefulness of these substitution reactions is clear and an effort to make use of them revealed an interesting rearrangement (equation 644)[643]. The rearrangement even takes place along with ring opening (equation 645). The yields of rearranged products are much lower than in direct preparation from the 2,5-isomer. A complex series of addition–elimination reactions is offered as a possible mechanism.

Finally, it has been shown that hydrochloric acid causes simple ring opening (without rearrangement) to the 2-chloroethylamino derivative (equation 646)[650].



D. Oxygen and Sulphur Substitution of Quinones

The large amount of work that has been expended on the substitution chemistry of quinones by nitrogen should not completely obscure the valuable studies of oxygen and sulphur nucleophiles. An early synthetic effort, the aryloxy displacement of halogen, provided valuable synthetic intermediates (equation 647)[655].

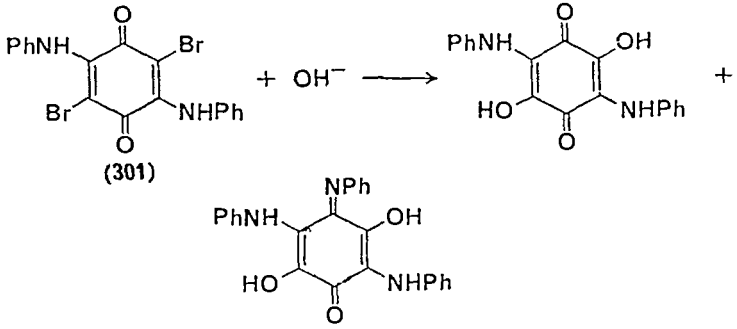


X = Cl, Br

Ar = Ph, 2-, 3- and 4-MeC_6H_4, 2- and 4-$MeOC_6H_4$, 4-ClC_6H_4

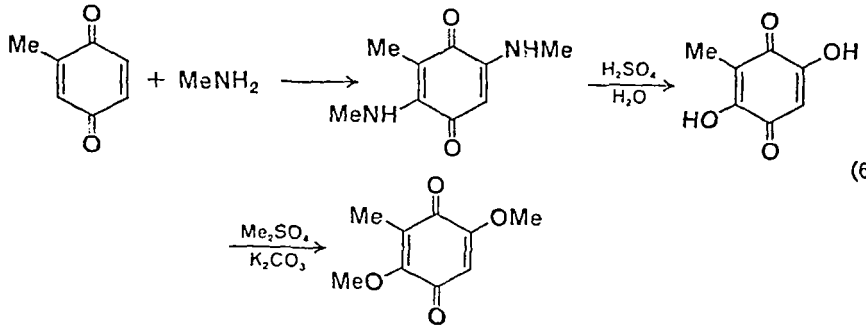
In the process of establishing the structure of a dibromodianilino quinone, its reaction with hydroxide ion led to a somewhat surprising result (equation 648)[656]. None of the expected bromanilic acid was obtained. Furthermore, bromanilic acid was unaffected by either aniline or hydroxide ion. The structure of **301** had been demonstrated earlier by its synthesis from 2,5-diphenoxy-3,6-dibromo-1,4-benzoquinone and aniline[530]. The ease with which quinonoid groups are displaced by hydroxide ion was suggested as:

PhO > Br > NHPh > OH



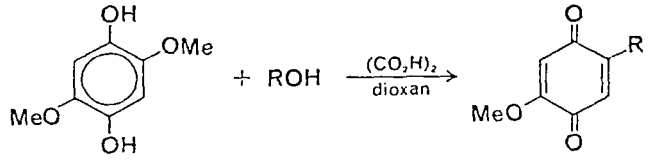
(648)

The preparation of the three dimethoxy-2-methyl-1,4-benzoquinones has been referred to earlier (see sections II.C.1 and II.D.3)[85]. The 3,6-dimethoxy isomer was made using an acid-catalysed hydrolysis (equation 649). Actually this compound had been made by the same method much earlier, but its correct structure was not known[84].



(649)

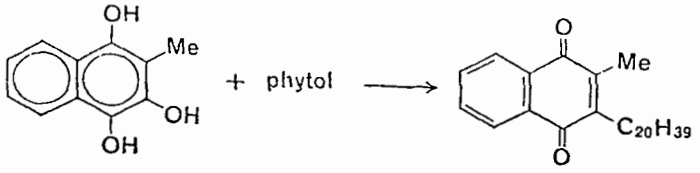
Fieser and Gates discovered an interesting and useful alkylation reaction that involves the displacement of a hydroquinone methoxy substituent and concurrent oxidation (equation 650)[657]. These allylic



(650)

R = phytyl ($C_{20}H_{39}$)
farnesyl ($C_{15}H_{25}$)
geranyl ($C_{10}H_{17}$)
PhCH=CHCH$_2$

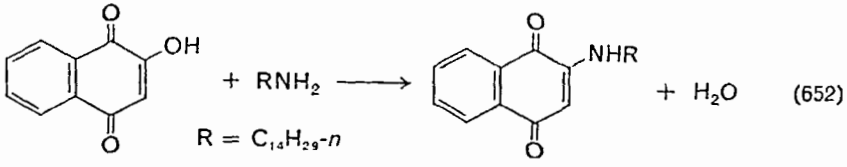
alcohols are capable of replacing a hydroxy group and 1,4-naphthalenediols are also suitable substrates. For example, the reaction of phytol and 2-methyl-1,3,4-naphthalenetriol (phthiocol hydroquinone) constitutes an interesting synthesis of vitamin K_1, (**302** in equation 651).



(651)

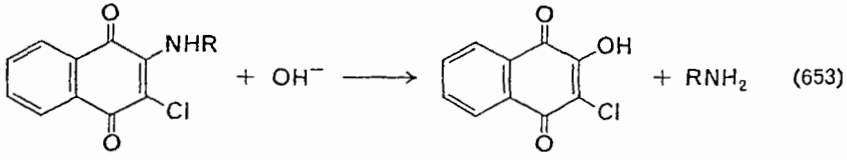
(302)

An interesting bit of oxygen–nitrogen substitution information came out of efforts to prepare naphthoquinone antimalarials of the lawsone type. Attempts to add amines resulted in displacement of hydroxide (equation 652)[335]. An alternate route also failed showing the marked



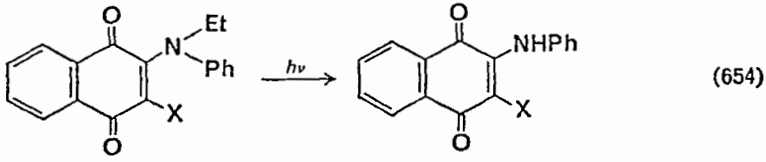
(652)

difference often found between benzo- and naphthoquinones (equation 653).



(653)

The interaction of 2,3-substituents on the 1,4-naphthoquinone ring and its effect on basic hydrolysis has been studied in more detail as the result of an interesting photochemical dealkylation (equation 654)[658]. Treatment



(654)

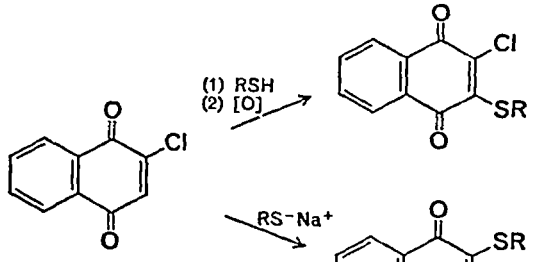
(303)

X = Cl, Br

(304)

of either chloro or bromo **303** with hydroxide results in the smooth displacement of halogen. The simple anilino compounds (**304**) are hydrolysed to 3-halolawsone as reported above for the amine analogues[335]. The *N*-acetyl compounds related to **304** were prepared and showed properties similar to those of the *N*-ethyl derivatives.

A great many alkyl and aryl mercapto-substituted quinones have been made by addition reaction (see section II.B), but substitution routes are also important. The inhibition of enzymes has played a vital role in motivating this chemistry from the earliest days. Fieser and Brown showed that either addition or substitution can be achieved under the

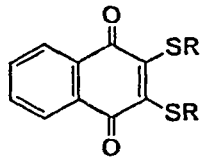


(655)

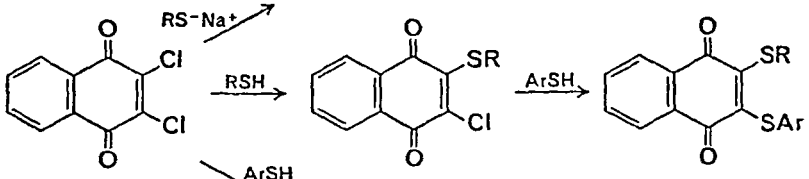
(656)

R = Me, Et, ... $C_{12}H_{25}$-*n*, $PhCH_2$

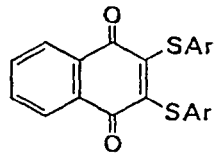
proper conditions (equations 655 and 656)[30]. They also developed useful modifications with 2,3-dichloro-1,4-naphthoquinone (equations 657–659).



(657)



(658)



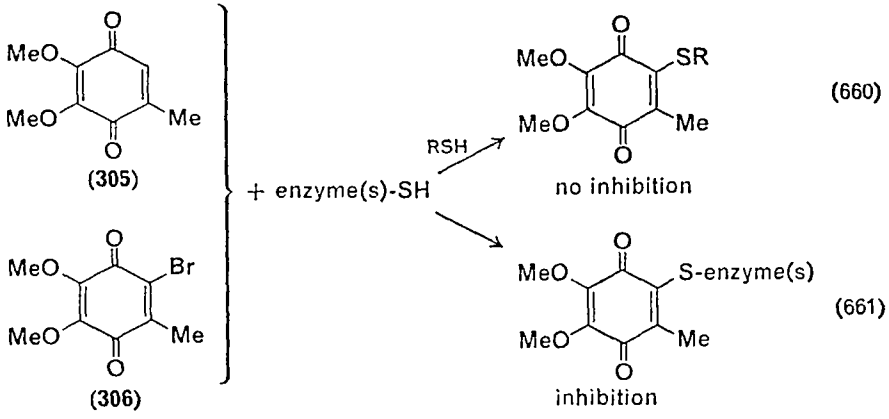
Ar = Ph, 2- or 4-ClC_6H_4, 3- or 4-MeC_6H_4, 2-$C_{10}H_7$

(659)

While these are valuable synthetic methods and appear to be quite general, the yields of symmetrical 2,3-dialkylmercapto-1,4-naphthoquinones are quite low in the examples given. A change of solvent (methanol to benzene–methanol), a reduction of reaction temperature

(refluxing methanol to 15°C) and the potassium salt instead of the sodium salt brought about a marked improvement[659]. Only *n*-propylmercaptide gave a really poor yield (15%), probably because of its low solubility.

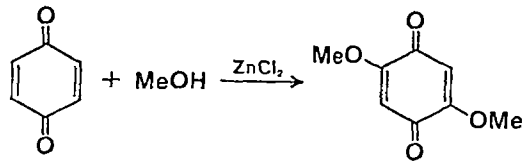
It has been found that two simple 1,4-benzoquinones (**305** and **306**) cause marked inhibition of oxidation and phosphorylation in beef-heart mitochondria[660]. When compounds containing mercapto groups (e.g. cysteine or glutathione) are added to the system, the inhibition can be prevented and at least partly reversed. The suggested cause of both inhibition and protective action is reaction between the quinones and mercapto groups of the enzymes and cysteine or glutathione (equations 660 and 661). The observed spectral changes are also consistent with the reactions shown.



$$R = CH_2CHCO_2H,\ CH_2CHNHCCH_2CH_2CHCO_2H \quad (NH_2;\ O;\ NH_2;\ CNHCH_2CO_2H;\ O)$$

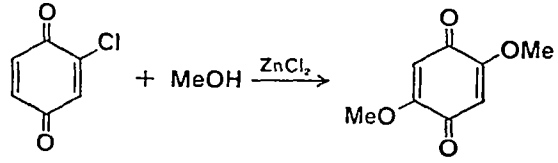
A second and more detailed study dealt with addition reactions of the type associated with quinone **305**[661]. It was shown that heart-muscle enzymes are inhibited by a series of alkyl- and or methoxy-substituted 1,4-benzoquinones. The quinone must have at least one unsubstituted position, not adjacent to a methoxy group, for inhibition to take place. No evidence for methoxy group substitution was reported.

The direct introduction of methoxy groups into a quinone has been accomplished (equations 172 and 662)[180, 214, 215, 662], but both early and later investigators were only partially successful; i.e. 2,5-dimethoxy-1,4-benzoquinone and 2-methyl-5-methoxy-1,4-benzoquinone. In a recent

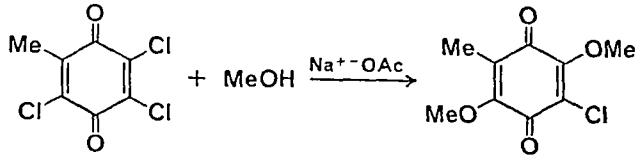


(662)

attempt to prepare chloromethoxy-1,4-benzoquinones, the following substitution reaction was found (equation 663)[662]. Such compounds have been prepared by base-catalysed displacement of chlorine by methanol (equation 664)[171].

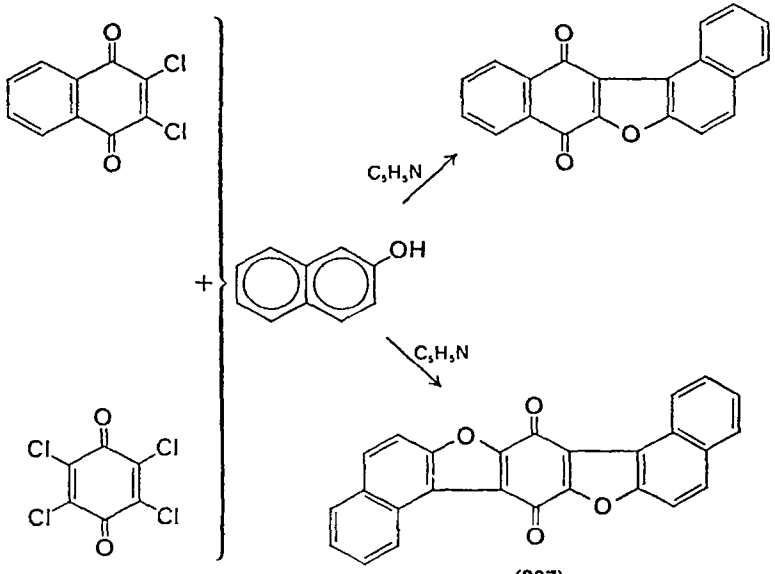


(663)



(664)

Certain examples of phenolic condensation with quinones constitute useful routes to polycyclic furans (equations 665 and 666)[663–665]. The evidence for these structures is adequate, as is that for the initial product

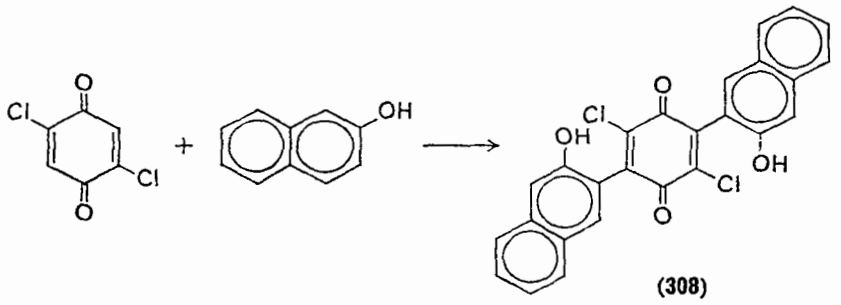


(665)

(666)

(307)

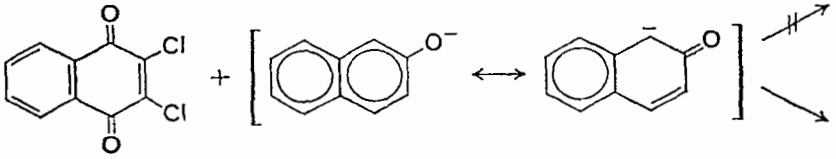
of the condensation of 2-naphthol and 2,5-dichloro-1,4-benzoquinone (**308** in equation 667). The structure of **308** raises some interesting questions



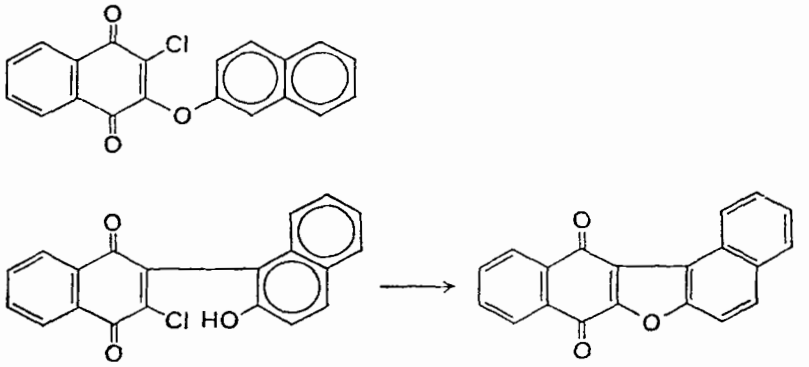
(667)

(308)

about the mechanism of the reaction; a short period of refluxing in pyridine converts **308** to **307**. One proposed intermediate is the ether formed by *O*-alkylation of the naphthol anion (equation 668)[666]; however, the most recent study has shown the presence of an intermediate analogous to **308** (equation 669)[667]. Not only is this pathway consistent with the



(668)

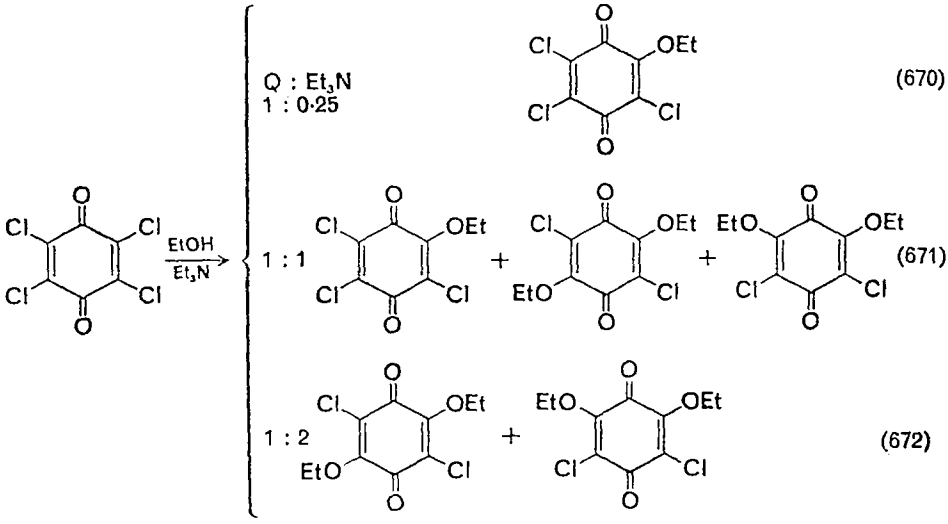


(669)

intermediates found here and in the earlier study[665], but it provides a much more satisfactory explanation of the final cyclization step.

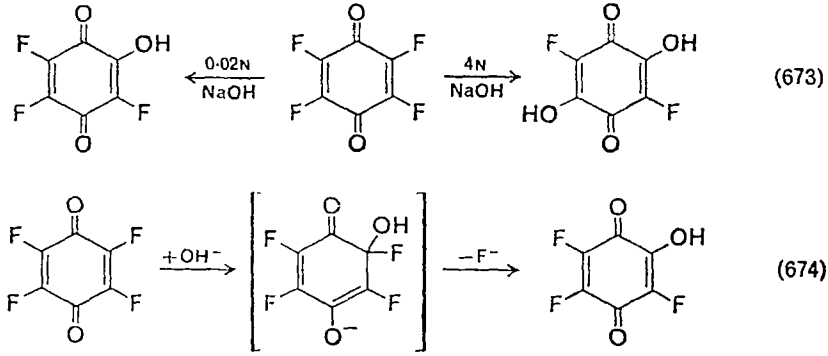
The general interest in the combination of halo and alkoxy substituents on quinonoid rings has produced the following interesting data (equations 670–672)[643]. The two isomeric diethoxy products can be separated quite

efficiently by fractional crystallization and the optimum condition for the preparation of the monoethoxy compound is described[644].



(670) (671) (672)

The utility of fluoranil as a substrate for nitrogen substitution has already been presented (see section VIII.C). The reactions of fluoranil with oxygen nucleophiles are also impressive[668]. A comparison of the four haloanils shows that, with a wide range of nucleophiles, all four fluorine atoms can be replaced; two is the maximum for most combinations of nucleophiles and chlor-, brom- or iodanil. An exception to this generalization is the reaction of fluoranil with hydroxide ion, where either one or two fluorine atoms can be displaced under appropriate conditions (equation 673). The kinetics of the hydrolysis of fluoranil was studied and a simple addition–elimination mechanism proposed (equation 674).

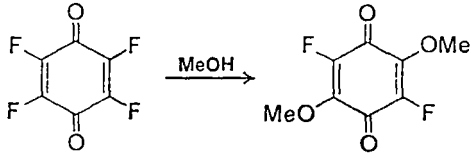


(673) (674)

(309)

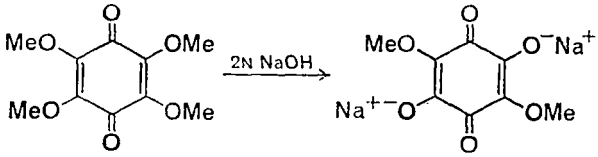
Catalysis by the acetate ion was also observed and explained by a similar pathway.

The nucleophilic substitution of fluorine by methoxide also takes place under mild conditions and in good yield. Simply dissolving fluoranil in methanol results in disubstitution (equation 675). With methoxide ion,



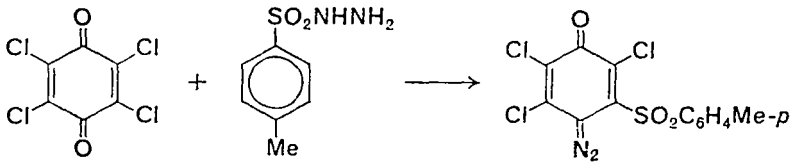
(675)

an excellent yield of tetramethoxy-1,4-benzoquinone is obtained. This last compound reacts very smoothly with hydroxide (equation 676). The reaction of fluoranil with phenoxide ion is very rapid even at low temperatures and produces tetraphenoxy-1,4-benzoquinone[669].



(676)

An interesting, and apparently quite complex, reaction has been reported between halogenated 1,4-benzoquinones and tosylhydrazine (equation 677)[670]. The mechanism of the reaction is not at all clear, but

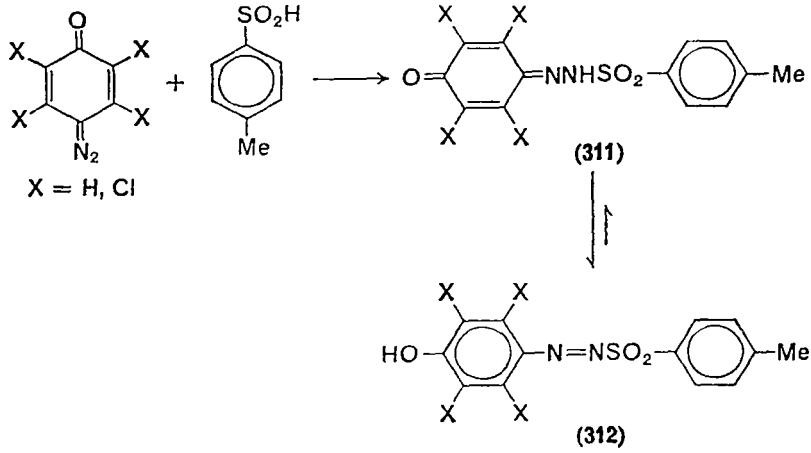


(677)

(310)

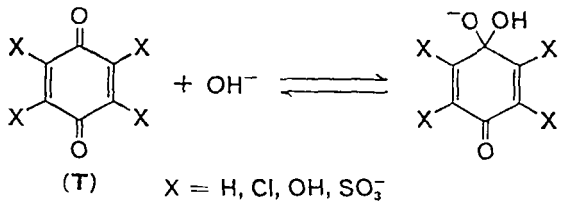
seems to be closely associated with the diazide formation. An attempt to prepare **310** by reaction between the diazide and sulphinic acid produced the hydrazone **311** by addition (equation 678). Several hydrazones were shown to exist chiefly as the sulphonylazophenol tautomer **312**.

The intermediate usually suggested for the nucleophilic substitution of quinones (**309**) appeared to receive some experimental support from a study of the u.v. spectra of chloranil in basic solution[671]. The spectrum of chloranil in ice-cold 2N sodium hydroxide is quite different from that of 2-hydroxy-3,5,6-trichloro-1,4-benzoquinone. This last compound is obtained in a nearly quantitative yield upon cold acidification of the basic solution. This interpretation has been seriously questioned by Bishop



(678)

and Tong[672]. They studied the u.v. spectra of several quinones at very short reaction times as a function of pH. At a given pH, no change in the spectrum could be observed between 12 and 300 ms and acidification completely regenerated the starting material. The reaction was thus described as the reversible 1,2-addition of hydroxide to the carbonyl group (equation 679). The data at various pHs allowed formation constants to be calculated by



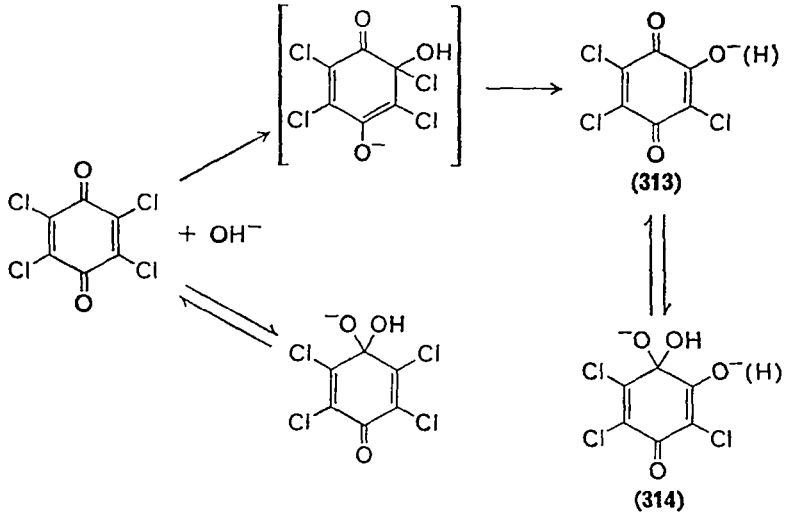
(679)

following formula:

$$K_c = \frac{(T{\cdot}OH)}{(T)(OH^-)}$$

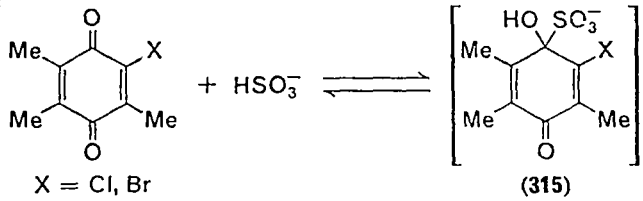
The consistency of the calculated values is an excellent argument for the proposed equilibrium, as is the observed reversibility.

In the case of 2-hydroxy-3,5,6-trichloro-1,4-benzoquinone, Bishop and Tong argued that the product must be formed very rapidly from chloranil and that the observed spectrum is really that of 1,2-carbonyl addition (**314** in equation 680). If this were not the case, their observation, that putting the final product (**313** after acidification) into basic solution produces the same spectrum, would not be possible.



(680)

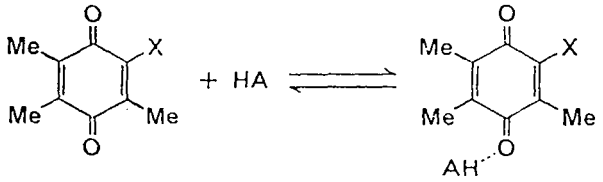
In large measure the above analysis grew from an earlier and more detailed study of the substitution of quinone halides by the sulphite anion[673]. The substrate, 2-halo-3,5,6-trimethyl-1,4-benzoquinone, was chosen so that competing 1,4-addition might be avoided. It happily turned out that the selection also avoided the complication of a redox reaction between quinone and bisulphite. An unexpected complication analogous to that described above with hydroxide was found; i.e. 1,2-carbonyl addition (equation 681). The α-hydroxysulphonate (**315**) was not isolated



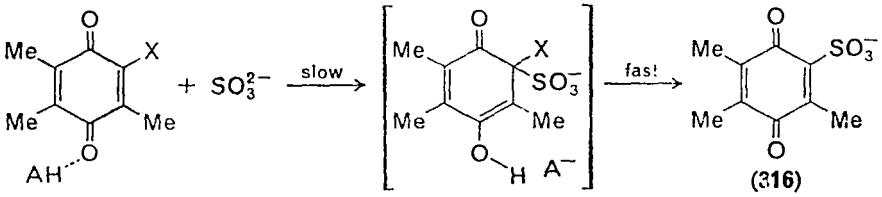
(681)

in a form pure enough for rigorous structure determination, but the u.v. spectrum is quite suggestive. For example, similar spectra were obtained with duroquinone and 3,5,6-trimethyl-1,4-benzoquinone where substitution does not take place. The complete reversibility of the reactions and the favourable comparison with formation constants for aldehydes and ketones argue for structure **315**. These equilibria must be taken into account in kinetic studies of the substitution reactions, except in the case of 2-iodo-3,5,6-trimethyl-1,4-benzoquinone. In this instance the rate of disappearance of quinone is equal to the rate of release of iodide. The observation requires

either that the rate of substitution is much faster than the rate of adduct formation or that the equilibrium lies far to the quinone carbonyl side. The interpretation of the kinetic data shows that both adduct formation and substitution are general-acid-catalysed. The proposed mechanism is the addition–elimination typical of many carbonyl reactions (equations 682–684). The product **316** also forms a bisulphite adduct by 1,2-addition



(682)

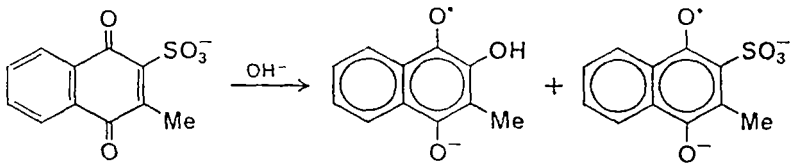


(683)

(684)

to the carbonyl group. All three quinones (2-iodo, 2-bromo and 2-chloro) gave the same product and a crude sample showed $-SO_3^-Na^+$ in the i.r. Thus, it was assumed to be **316**.

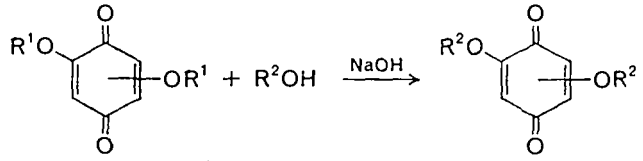
The rate of semiquinone ion radical formation with the haloanils and iodide ion has been studied[674]. The reaction is first-order in quinone and second-order in iodide. The reaction rate varies in the following order: F > Cl > Br > I. In another nucleophilic substitution reaction, evidence has been presented that the displacement takes place on the ion radical (equation 685)[675].



(685)

Yet another study reported a series of e.s.r. spectra of quinones in alcohol or dimethyl sulphoxide solutions[676]. There was no doubt from the

spectra that rapid exchange of alkoxy groups occurs in alcoholic solution (equation 686) and this conclusion was supported by product isolation.

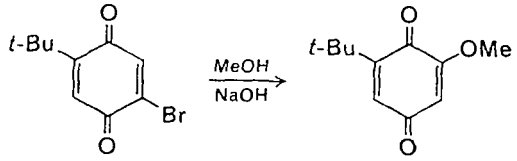


(686)

R^1, R^2 = Me, Et, *n*-Pr, *i*-Pr

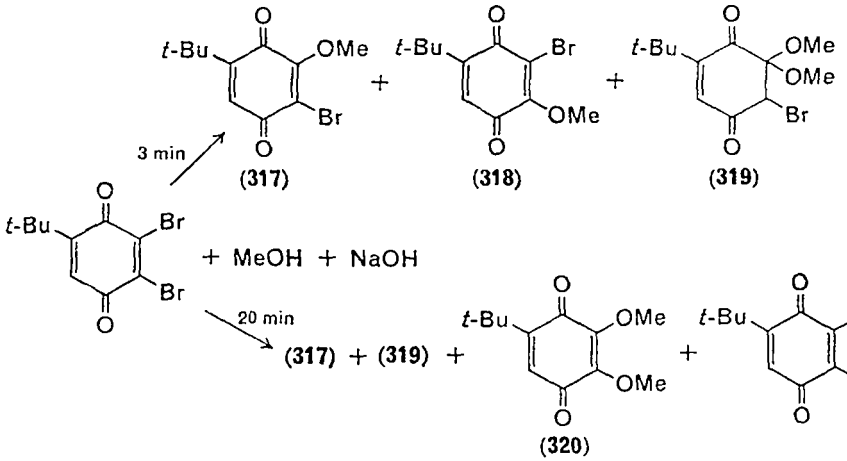
The e.s.r. signal arises from the subsequent reduction of the quinone to the semiquinone. Evidence is presented for a two-equivalent reduction involving hydride transfer.

The extension of this study to halogen displacement demonstrated an interesting rearrangement reaction (equation 687). With 3-bromo-5-*t*-butyl-1,4-benzoquinone a mixture of rearranged and normal substitution



(687)

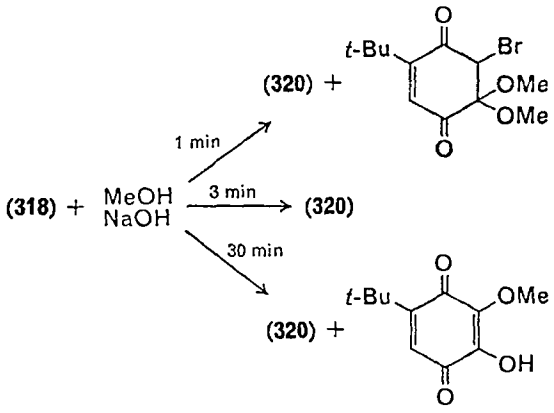
product (2:1) was obtained. The mechanism of the rearrangement was investigated in the quinone 2,3-dibromo-5-*t*-butyl-1,4-benzoquinone. Strong evidence was obtained for a variety of products and intermediates at different reaction times (equations 688 and 689). It was also shown that



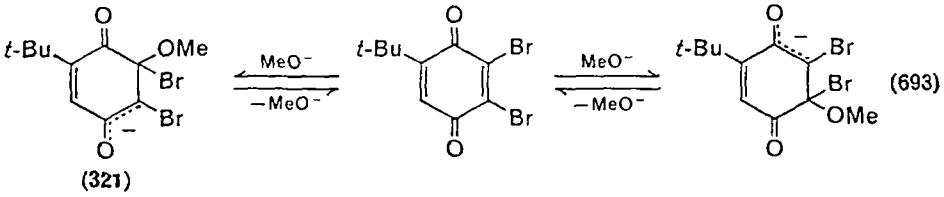
(688)

(689)

318 is converted to **320**. These experiments also produced useful intermediates for mechanistic speculation (equations 690–692). These observations seem best explained by the establishment of equilibria (equation



693) and preferential solvation of **321**. The structures of these intermediates and products were satisfactorily established. The importance of solvation

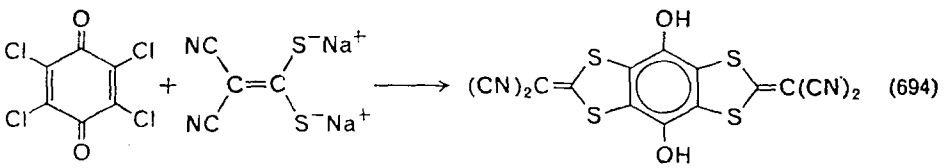


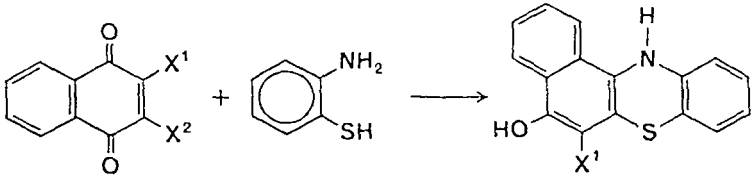
(321)

was demonstrated by adding dimethyl sulphoxide and observing the shift from mostly C-3 attack (methanol) to C-2 attack (DMSO).

Two recent reports of heterocyclic syntheses by quinonoid addition also contain useful substitution chemistry (equations 694 and 695)[48,49].

The lignin found in hardwood is known to be paramagnetic and 2,6-dimethoxy-1,4-benzoquinone appears to be the structural precursor of the paramagnetic species[677]. A combination of e.s.r. and u.v. spectra of basic solutions of this quinone showed that the semiquinone radical is formed in quite high concentration. Preceding the observation of the e.s.r.

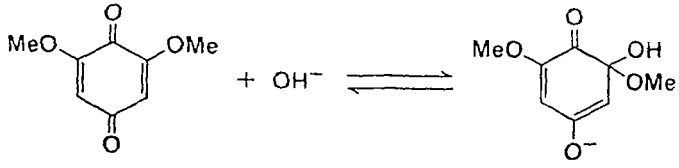




(695)

X^1 = Cl, MeO, Me, NHAc
X^2 = H, Cl

signal, an equilibrium between the quinone and base is rapidly established (equation 696). The proposed mechanistic path for subsequent conversion



(696)

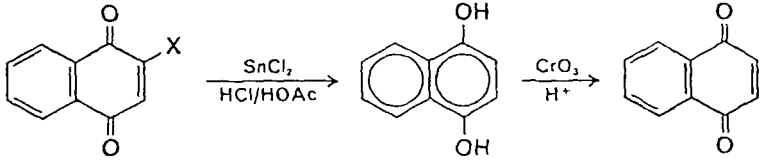
(322)

to semiquinone and substitution product is essentially that of Eigen and Matthies (see section II.F.1)[221], except that the conversion of **322** to product is the rate-determining step. This situation is not unexpected since **322** cannot enolize rapidly as could the unsubstituted 1,4-benzoquinone studied earlier.

E. Other Substitution Reactions

A few reports of significant experiments are found that do not fit any of the major areas of interest within quinone substitution chemistry.

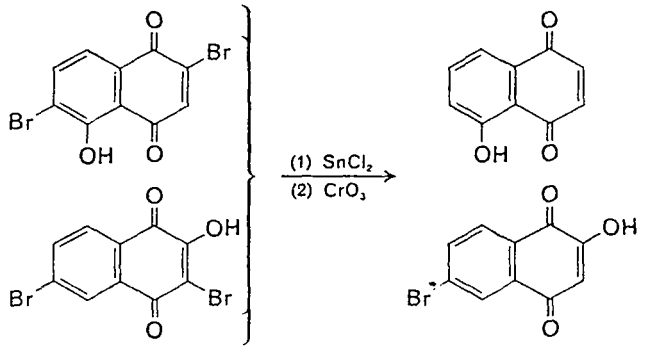
For example, Bruce and Thomson have evaluated the range of substituents that can be removed directly from 1,4-naphthoquinones[678]. The general method involves reductive elimination of the substituent with acidic stannous chloride followed by chromic acid reoxidation (equation 697). The intermediate, 1,4-naphthalenediol, was usually not isolated.



(697)

The following groups were removed in fair to excellent yield: Cl, Br, NHPh, SR, SAr, SO_2Ar, SO_3H. Hydroxy groups were removed in some cases, although in poor yield. Hydriodic acid was also used for the direct

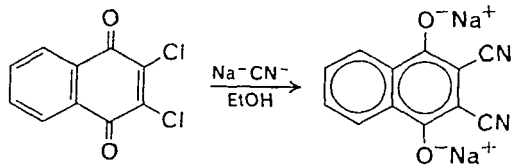
elimination of halogen. This reagent appears satisfactory for 2-alkyl-3-halo-1,4-naphthoquinones, but in the other cases the two-step process gave superior yields. One interesting observation is that halogen in the benzenoid ring is also removed if that ring is phenolic (equations 698 and 699).



(698)

(699)

In view of the very extensive studies of 2,3-dichloro-1,4-naphthoquinone substitution chemistry that have been reported, Reynolds and Van Allan were surprised to find in 1964 that cyanide had been neglected[679]. What would appear to be a very simple substitution reaction, in fact turns out to be quite complicated (equation 700). It seemed most reasonable that



(700)

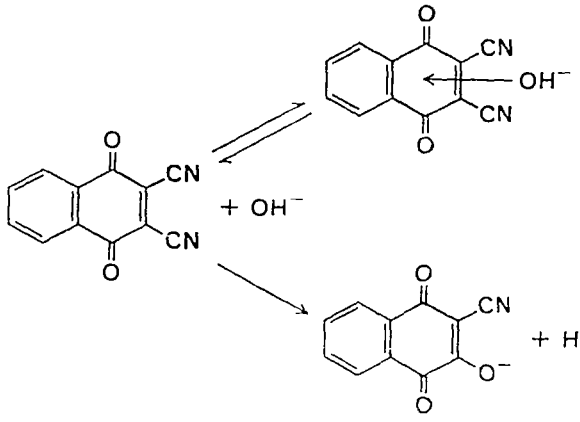
(323)

the direct substitution product was reduced by cyanide, and when 2,3-dicyano-1,4-naphthoquinone was treated with aqueous sodium cyanide it went into solution immediately as **323**. The quinone acts as a strong π-acid and also undergoes substitution by hydroxide (equations 701 and 702).

The reactions of 2,3-dipiperidino-1,4-naphthoquinone with dry hydrogen halides have been reported[680]. In one case the hydrogen bromide salt was isolated and is assumed to be an intermediate in the other reactions (equation 703).

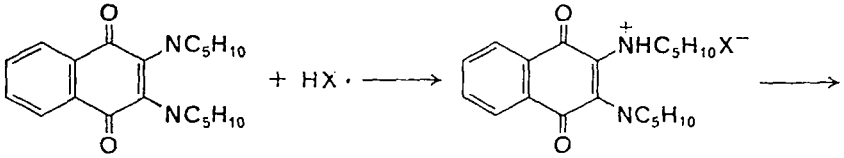
A synthetically useful dealkylation reaction has been found in the combination of halodi-*t*-butyl-1,4-benzoquinones and anhydrous

hydrohalogen acids (equation 704)[681]. An analogous reaction occurs with 3-chloro-2,6-di-*t*-butyl-1,4-benzoquinone.



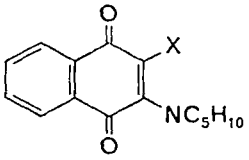
(701)

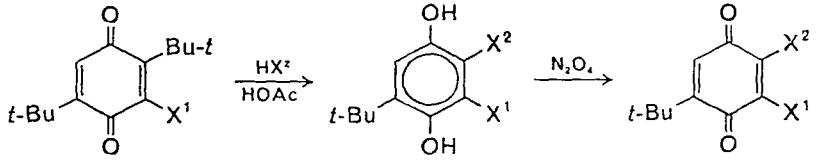
(702)



X = F, Cl, Br

(703)

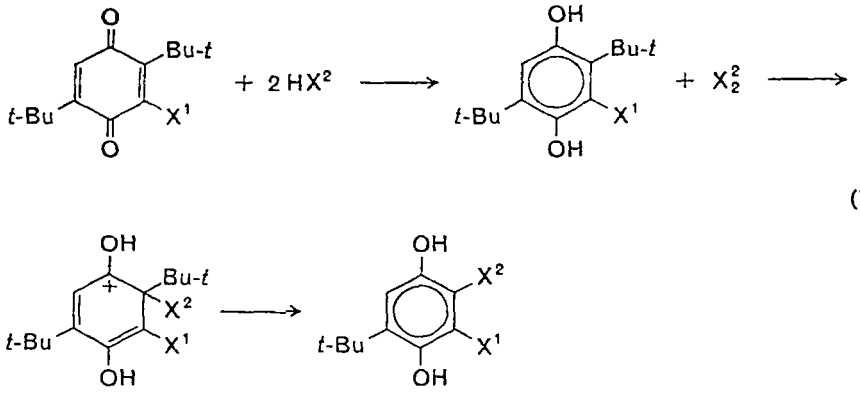




(704)

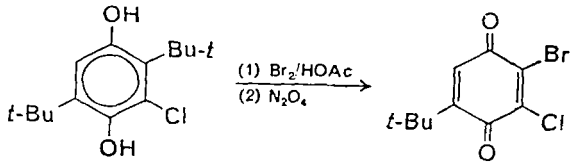
X¹, X² = Cl, Br

The mechanism suggested as accounting for the dealkylation consists of an initial redox reaction followed by electrophilic substitution (equation 705). In support of this proposal it was found that with excess cyclohexene present an excellent yield of 1,2-dibromocyclohexane is obtained; thus supporting the first step. The second step was tested by allowing



(705)

3-chloro-2,5-di-*t*-butylhydroquinone to react with bromine in acetic acid. After treatment with nitrogen oxide, 2-bromo-3-chloro-5-*t*-butyl-1,4-benzoquinone was obtained in high yield (equation 706).



(706)

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The Chemistry of the Quinonoid Compounds
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CHAPTER 18

Quinone methides

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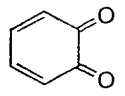
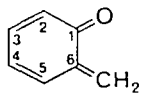
I. INTRODUCTION

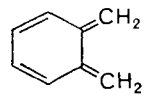
The name quinone methide is derived from a structural analogy between this class of compound and the quinones. If one oxygen atom of a quinone is replaced by a methylene group, a quinone methide results; such compounds have also been called quinomethanes[1], methylenequinones and quinomethines. If both oxygen atoms of a quinone are replaced by methylene groups, the so-called quinodimethanes result[2,3]; in this case the name quinone dimethide, analogous to quinone methine, has not become popular[2]. Quinone methides are listed as cyclohexadiene derivatives in the Subject Index of *Chemical Abstracts*.



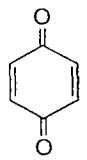
o-Benzoquinone



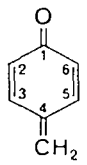
o-Benzoquinone methide (6-methylene-2,4-cyclohexadien-1-one)



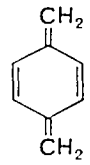
o-Benzoquino-dimethane



p-Benzoquinone

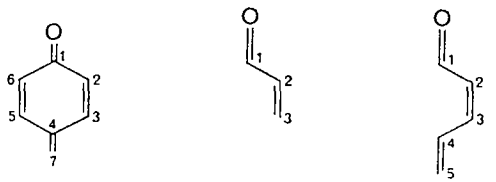


p-Benzoquinone methide (4-methylene-2,5-cyclohexadien-1-one)

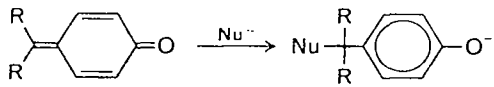


p-Benzoquino-dimethane

Being vinylogous carbonyl systems, quinone methides should be compared with α,β-unsaturated ketones and with ketones having longer conjugated groups.



Such compounds behave as ambifunctional electrophilic reagents: in addition to the usual electrophilic reactivity of the carbonyl group, the conjugated centre 3, 5 or 7 can enter into reaction as in the Michael reaction. A special situation arises with the quinone methides from the transition of the quinonoid to a benzenoid system on addition of a nucleophile at C-7. This carries with it a large gain in energy owing to the



aromatic structure of the product; examples of this favoured mode of reaction are given in the section on reactions of quinone methides. All other modes of addition are disfavoured in comparison with this type.

Quinone methides assume a position between quinones and quinodimethanes. The similarities and differences arising from the analogous topologies can be seen in the HMO description. Figure 1 shows the

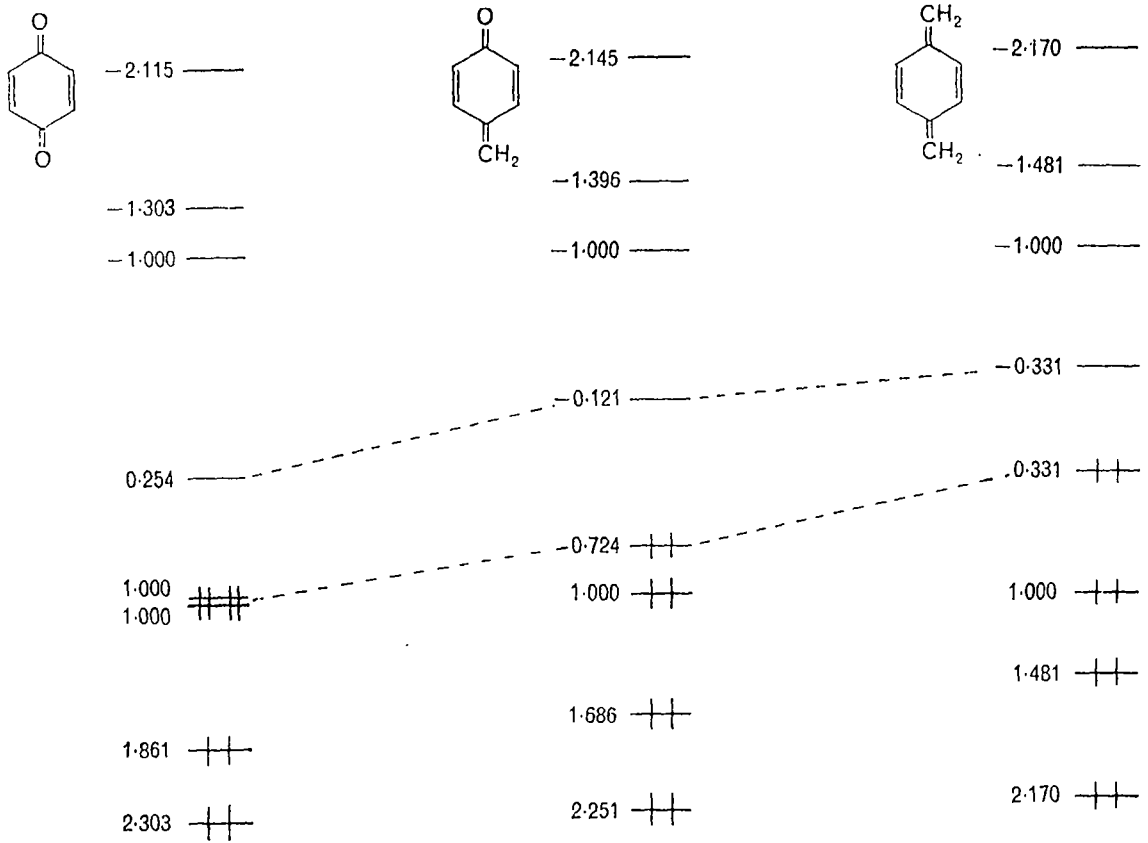


FIGURE 1. Energy levels and occupation of the Hückel molecular orbitals for three *p*-quinonoid π-systems (heteroparameters $\alpha_O = \alpha_C + 1{\cdot}0\beta_{CC}$, $\beta_{CO} = \beta_{CC}$). The numerals are the eigen values x_i in the expression $\varepsilon_i = \alpha + x_i\beta$ of the corresponding MO with index *i*.

π-molecular orbitals for *p*-quinonoid systems. The lowest unoccupied molecular orbital (LUMO) of *p*-benzoquinone lies at a particularly low level and indicates well-developed reactivity of this molecule as an electrophile, and the LUMO is also relatively low for the quinone methide. According to Fukui[4] the electron distribution in the extreme orbitals is determinant for a comparison of kinetic reactivity. Figure 2 shows, on

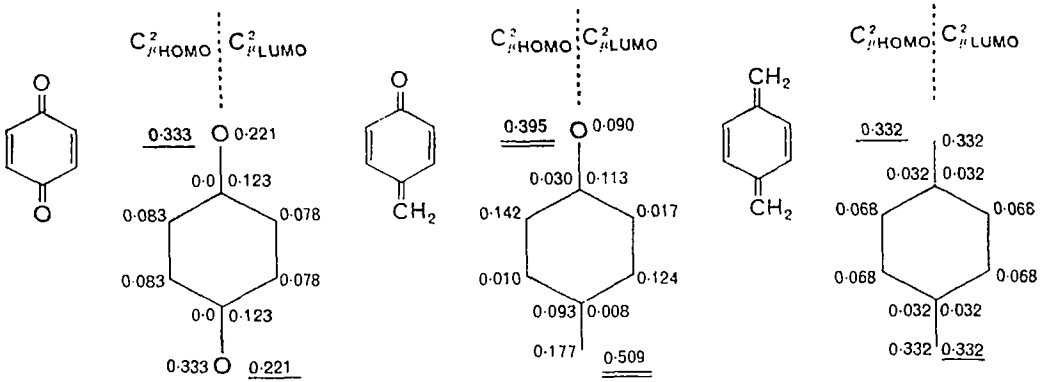


FIGURE 2. Squared coefficients C^2 at the centre μ in the highest occupied molecular orbital (HOMO), figures to the left of the atomic centre) and in the lowest unoccupied molecular orbital (LUMO, figures to the right of the atomic centre). Particularly large values are underlined.

the right of the atoms, the squared coefficients of the LUMOs of the three quinonoid systems. Quinone methide, placed in the middle, shows an exceptionally high value at the *exo*-carbon atom of the methylene group, so this centre is characterized by particularly high electrophilicity and, as the reactions described in section XI will show, quinone methides are susceptible to attack by nucleophilic reagents.

The electron distribution in the highest occupied molecular orbital (HOMO) is determinant for the nucleophilic reactivity of the quinonoid systems. Figure 2 shows the squared coefficients of the HOMOs to the left of the atoms; here too the quinone methide system shows a particularly high value, so that the oxygen atom of quinone methides should be readily attacked by electrophiles.

The π-charge distribution shown in Figure 3, according to HMO, indicates that in the quinone methide system the attack of an electrophile is supported by the negative charge on the oxygen atom, and the same is true for the attraction of a nucleophile by the positively charged *exo*-carbon atom of the quinone methide. In the quinone the attack of an

electrophile is favoured only by coulombic attraction, and in the non-polarized quinodimethane there is no control of the attacking reagents by charge interaction.

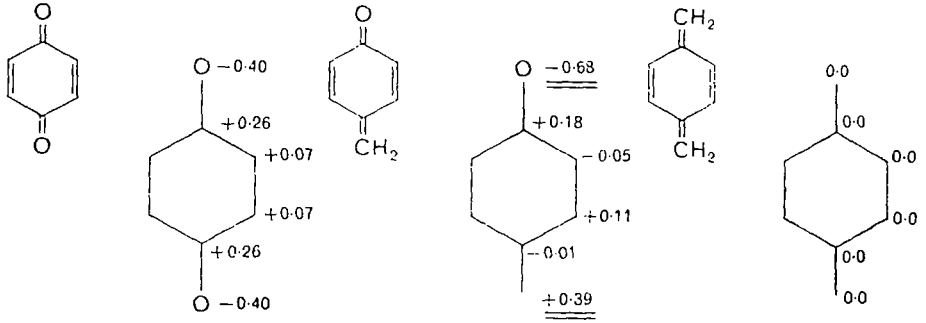
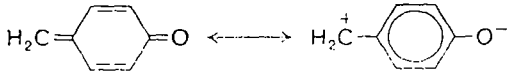
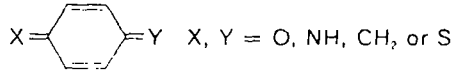


FIGURE 3. Distribution of the effective charge in the π-systems of three *p*-quinonoid systems according to the HMO model (cf. Figure 1).

The quinone methides thus assume a special position. There, high reactivity towards electrophiles as well as towards nucleophiles is displayed in high electron densities in the limiting orbitals and also in suitable polarization corresponding to the formulation of the two most important valence-bond resonance structures[5,6].



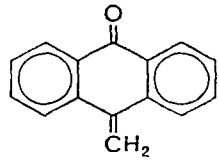
The reactivity of quinonoid systems is further influenced by the interchange between the initial quinonoid structure and the possible benzenoid structure of transition states or end products. In Coppinger and Bauer's calculations[7] the relative stabilities of *p*-quinonoid systems (**1**) are defined as the difference between the quinonoid ground state and a benzenoid transition state; they find that the stability increases with increasing electronegativity of X and Y.



(1)

The reactivity of unsubstituted quinone methides is generally so high that they cannot be isolated under normal conditions: in the absence of a compound with which they can react the molecules react with one another, forming dimers, trimers and polymers. These reactions will be described in section 12.

The quinone methide can, however, be isolated if the benzenoid character of the ring in the quinonoid system is weak, as, for example, in the methyleneanthrone (2)[8].

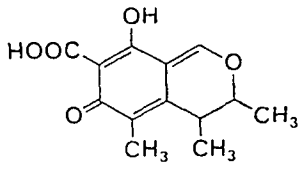


(2)

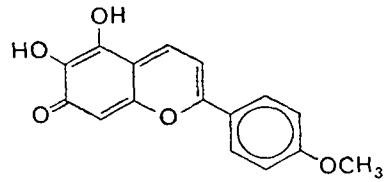
In spite of its arbitrariness, the quinone methides treated in this section are limited to those showing the quinone methide reactivity discussed above. The molecular diagrams displayed in Figure 4 for fuchsone (3), diphenoquinone (4) and stilbenequinone (5) show that only slight relationship exists between these molecules or their derivatives and quinone methides: the fuchsone derivatives lead into the class of triphenylmethane dyes and the diphenoquinones are better regarded as phenylogous quinones.

The importance of quinone methides in the chemistry of phenolic resins has been treated in several reviews[9-11].

The natural occurrence of quinone methide structures is mainly in the vegetable kingdom. They play a large part in the chemistry of lignin[12] and they are found also among wood pigments and other vegetable dyes.



Citrinin



Carajurone

Citrinin and carajurone are two typical examples. Naturally occurring quinone methides have been described previously in several reviews[12-16] and will therefore not be discussed further in this chapter.

II. PREPARATIVE METHODS

Syntheses of quinone methides are usually started from the corresponding phenols. The different synthetic routes described here will explain their division among the later sections. The routes displayed in Scheme 1 for *p*-benzoquinone methide are representative for all quinone methides and are valid for both *para*- and *ortho*-quinonoid systems in general.

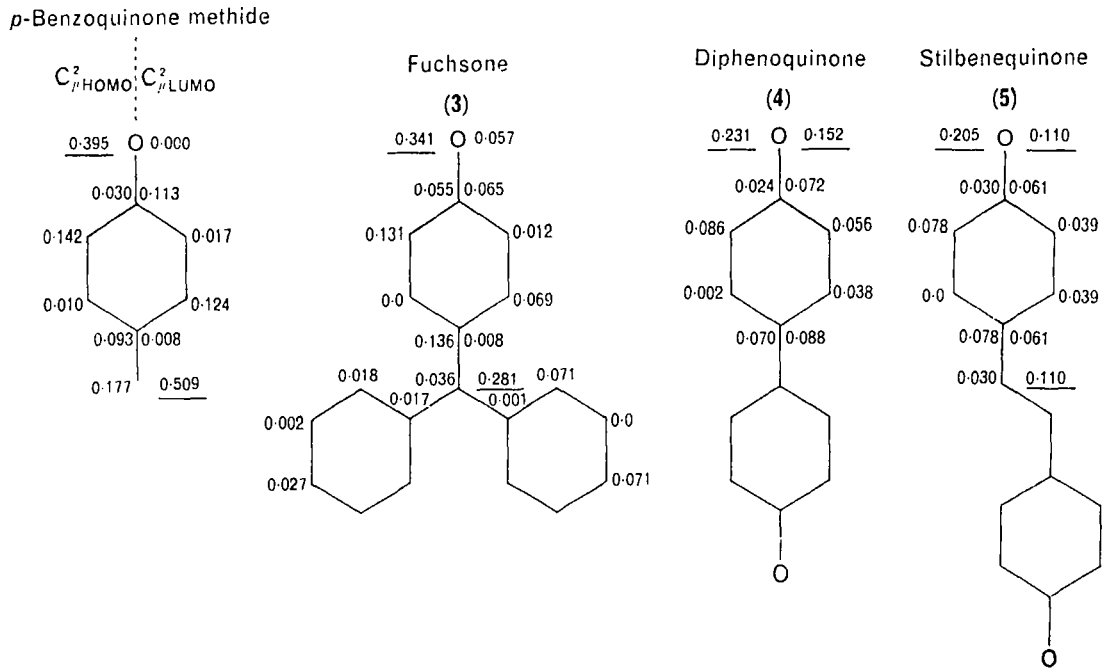
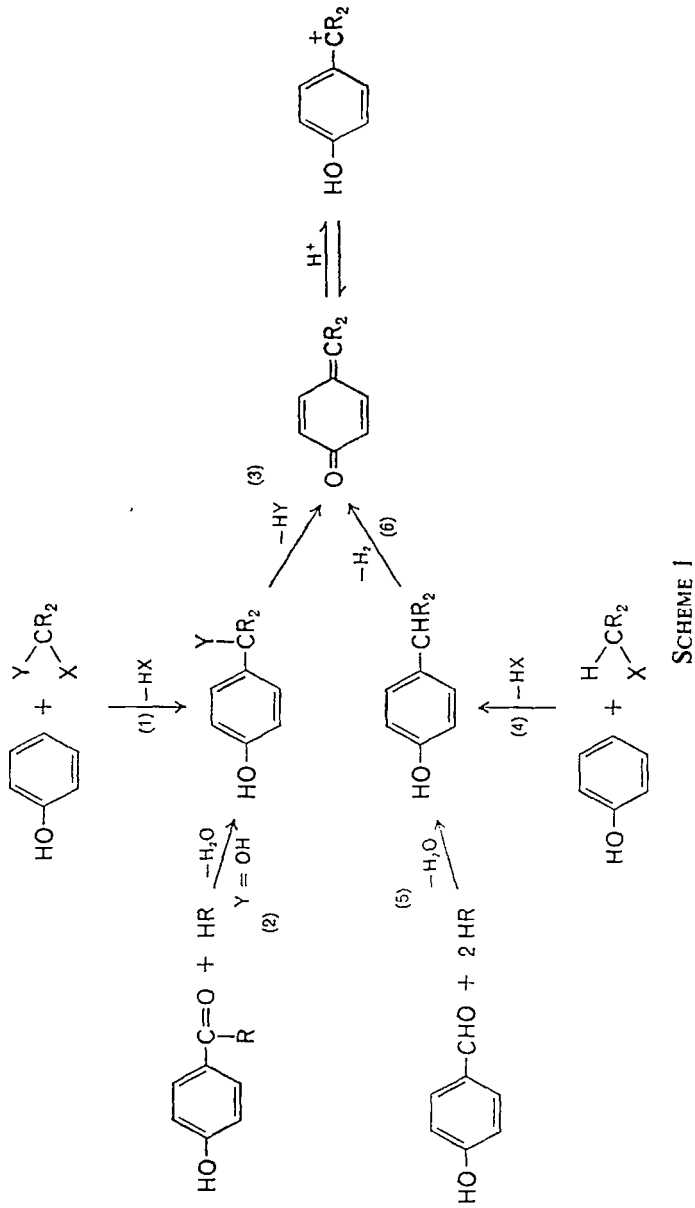


FIGURE 4. Squared coefficients in HOMO and LUMO of *p*-quinonoid systems. For symbolism see Figure 2.



SCHEME 1

Reactions of type (1) are electrophilic aromatic substitutions of a phenol. When the group Y is suitable the subsequent elimination (3) leads spontaneously to formation of the quinone methide, but when Y = OH more forcing conditions are necessary.

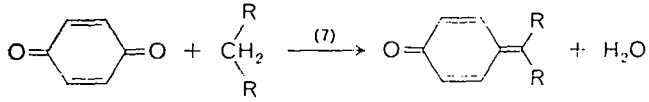
In reactions of type (2), addition of HR to the carbonyl group of an aromatic hydroxy-ketone leads to the same intermediate as in type (1). In this case, RH is often replaced by the metallated derivative, e.g. the Grignard compound RMgBr.

As in route (1), reactions of type (4) employ electrophilic aromatic substitution for synthesis of the intermediate, but this is dehydrogenated to the quinone methide in a subsequent oxidation step (6).

In reactions of type (5), aromatic hydroxy-aldehydes are converted into derivatives which are subsequently oxidized in step (6).

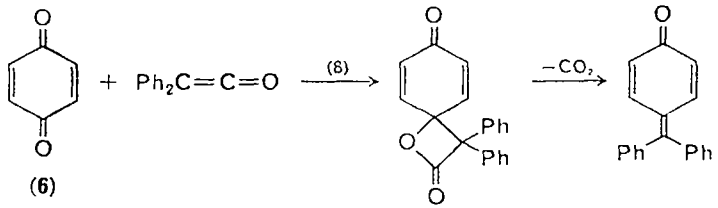
The quinone methides are not often isolated themselves but are obtained as salts indicated on the extreme right of Scheme 1. These salts are usually readily deprotonated and this step can be regarded as part of the elimination process (3).

The possibilities for synthesis of quinone methides from quinones are greatly limited by the low electrophilicity of the carbon atom of the quinone carbonyl group (cf. the squared coefficient of these atoms in the LUMO of *p*-benzoquinone displayed in Figure 2). It is only rarely that quinones can be condensed with CH-acidic components in a reaction shown in general form as type (7).



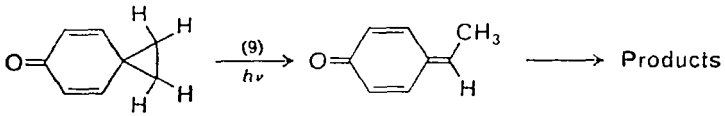
R = Electron-attracting group

The most favoured electrophilic attack on the oxygen atom of a quinone is utilized in reactions of type (8) which involve treatment with diphenylketene. The quinone methides are formed by elimination of CO_2 from the spirans such as **7** formed from **6**.



(6) **(7)**

This type of reaction (8) proceeds by ring opening of a spirocyclohexadienone. In reactions of type (9) it is a photochemical ring cleavage that leads similarly to quinone methides, although these are formed only as intermediates (**9**).

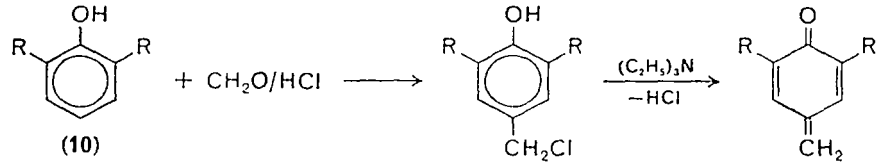


(**8**) (**9**)

In the following sections the reactions of types 1–9 of Scheme 1 are discussed individually. The formation of one quinone methide by alteration of another is treated in the section on reactions.

III. SYNTHESIS BY ELECTROPHILIC AROMATIC SUBSTITUTION OF PHENOLS AND SUBSEQUENT ELIMINATION

Chloromethylation of the phenol (**10**, R = *t*-butyl) and subsequent elimination of hydrogen chloride by triethylamine at −15° lead to orange-red solutions of the quinone methide (**11**, R = *t*-butyl)[17–19]. Although **11** cannot be isolated since dimerization and other reactions

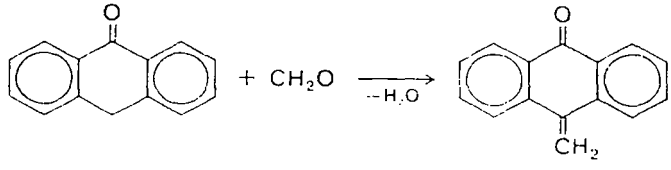


(**10**) (**11**)

R = CH_3 or *t*-butyl

occur on concentration of the solutions[18], the dilute solutions can be preserved for several days in the dark[19]. The dimethyl derivative (**11**, R = CH_3) can be prepared analogously in solution[17].

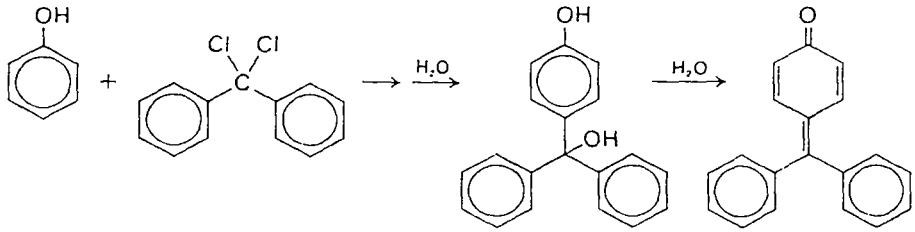
A further quinone methide without substituents on the methylene group can be obtained by condensing anthrone with formaldehyde under catalysis by base[8, 19–21]. In this case elimination of water follows spontaneously. The resulting quinone methide, **12**, named methyleneanthrone, is stable and can be isolated as colourless crystals.



(**12**)

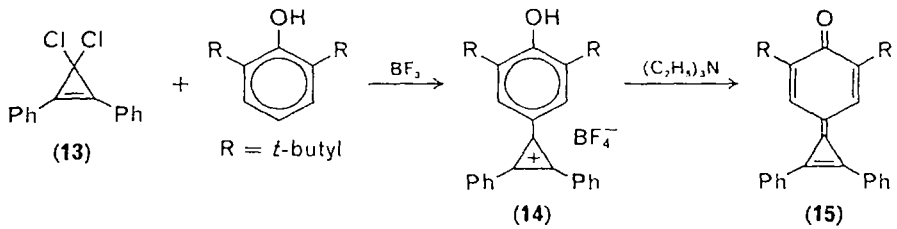
Condensation of anthrone with aldehydes is very generally applicable[22], but the resulting methyleneanthrones retain few properties of quinone methides, as will be discussed in the section of reactions.

Ketones are as a rule too feebly electrophilic to be able to attack phenols. However, numerous quinone methides, in particular fuchsone derivatives, have been prepared by condensing ketone dichlorides with phenols and then eliminating water from the resulting alcohols[22-30]. The synthesis of fuchsone itself from benzophenone dichloride and phenol may be formulated as an example[31]. However, electrophilic aromatic



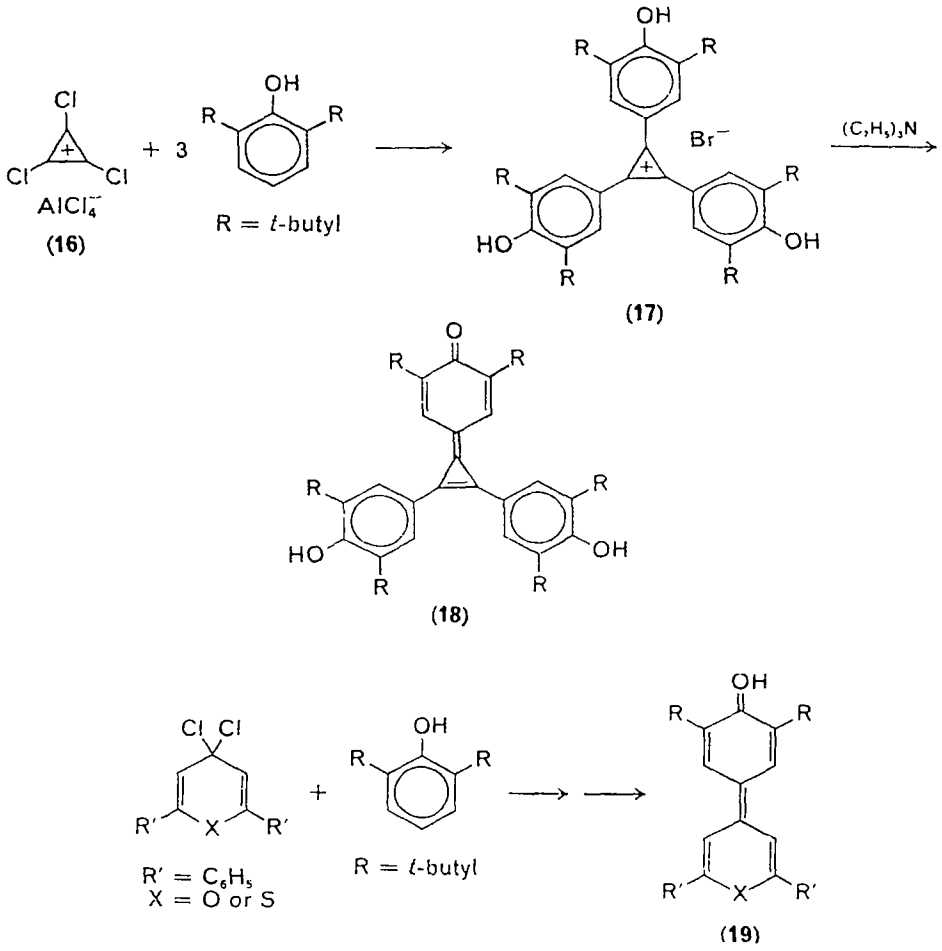
substitution of phenols by ketone dichlorides must generally be catalysed by addition of a Lewis acid; in such syntheses of fuchsone derivatives the whole range of Friedel–Crafts catalysts has been utilized for activation of the ketone dichlorides[32,33].

The dichloride **13**, which can be easily prepared from diphenylcyclopropenone and phosgene, reacts rapidly with phenols if catalysed by boron trifluoride[33]; being cyclopropenylium derivatives, the resulting salts, **14**, are particularly stable, but they can be deprotonated by triethylamine to the red quinone methides **15**[34].



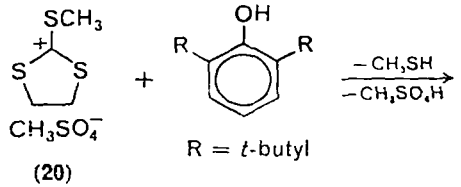
In the following reaction, three phenol nuclei are substituted by the trifunctional cyclopropenylium salt **16**; the product can be isolated as the bromide **17**, which on dehydrobromination leads to the red quinone methide **18**[35].

The quinone methides **19** can be obtained by analogous treatment of phenols with the dichlorides from pyrone and thiapyrone[36].

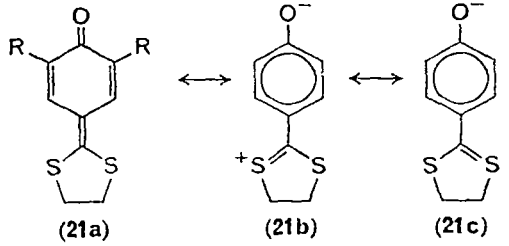


Ring substitution of phenols by resonance-stabilized carbenium ions is very generally applicable. For example, reaction of the dithiolanium salt **20** with 2,6-di-*t*-butylphenol affords, after spontaneous loss of methanethiol, a good yield of the very stable quinone methide **21**[37]. The structure of this resonance-stabilized product is reflected in the dipolar limiting formulae, e.g., **21b** and **21c**; this weakens the electrophilicity of the *exo*-carbon atom of the quinone methide, decreasing its reactivity, so that this quinone methide is stable and can be isolated. The same holds for examples **15**, **18** and **19**.

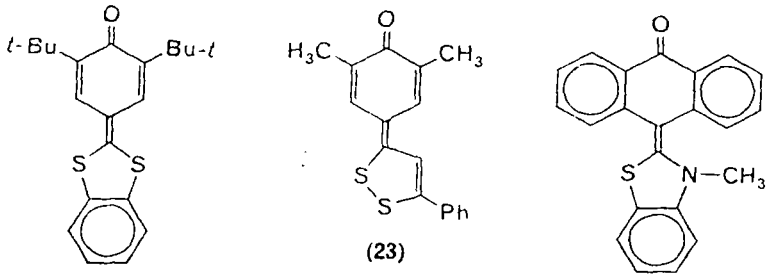
To the same group of compounds belong the quinone methides **22**, **23** and **24** prepared, respectively, from 1,3-benzodithiolium salts[37], 1,2-dithiolium salts[38–40] and benzothiazolium salts[41].



(20)

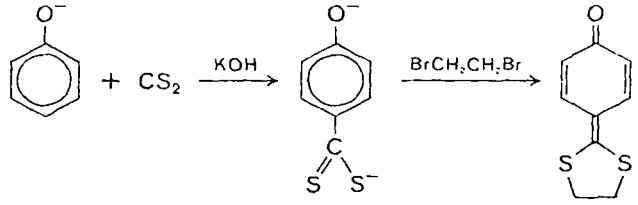


(21a) (21b) (21c)



(22) (23) (24)

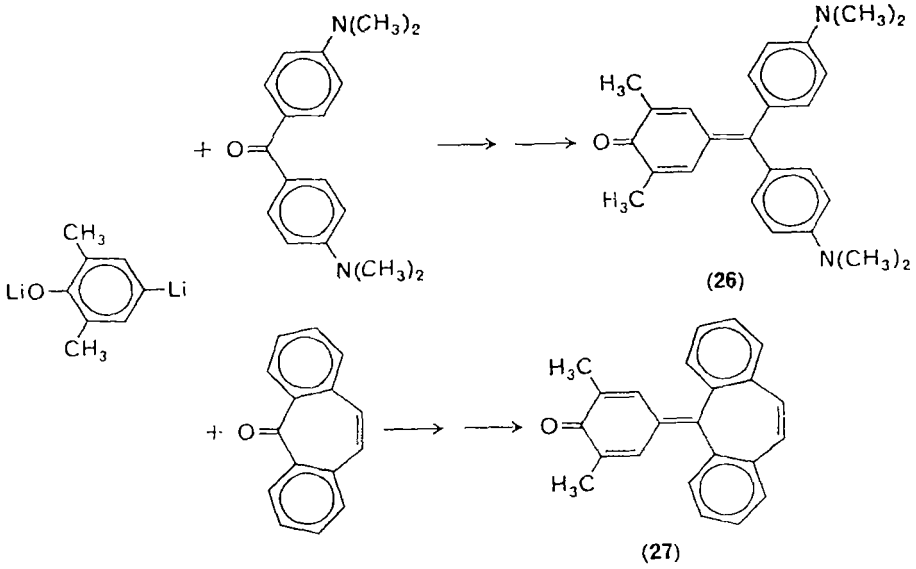
Reaction of phenoxides with carbon disulphide as electrophile also leads to ring substitution[42]. This results in the anions of *p*-hydroxydithiobenzoic acids, which can be alkylated by, e.g., 1,2-dibromoethane. The quinone dimethides **25** obtained in this way have the same type of structure as was formulated above in **21**.



(25)

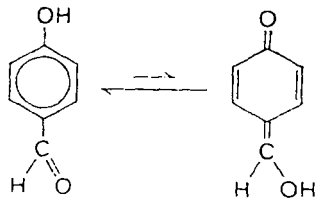
In their synthetic principle the following reactions of metallated aromatic compounds with carbonyl compounds also belong to this

section. The phenolic component is so strongly activated by replacement of a hydrogen atom by lithium that it reacts even with relatively unreactive ketones. The result is alcohols that are converted by loss of water into quinone methides such as **26**[43] and **27**[44].



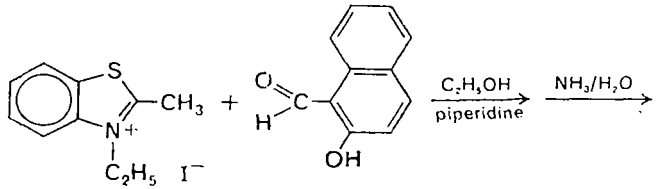
IV. SYNTHESIS FROM AROMATIC HYDROXY-ALDEHYDES AND -KETONES

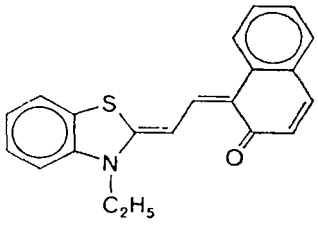
Hydroxybenzaldehyde can be formulated in a tautomeric form as hydroxy-quinone methide, thus:



Condensation of such aldehydes with CH-acidic components leads to blocking of the tautomerism and thus to fixation of the quinonoid structure. Of the numerous quinonoid dyes prepared in this way[45–53] only one, the annexed violet benzothiazole derivative, can be formulated here as example[54].

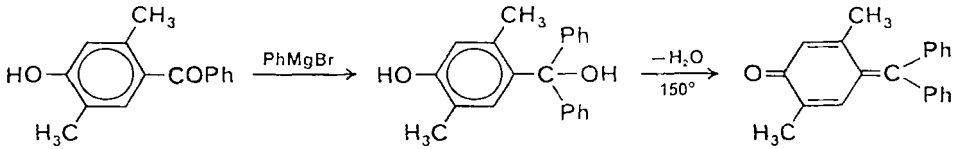
Interaction of aromatic hydroxy-ketones with organometallic compounds occurs by a similar type of condensation[22,29,55]. Loss of water



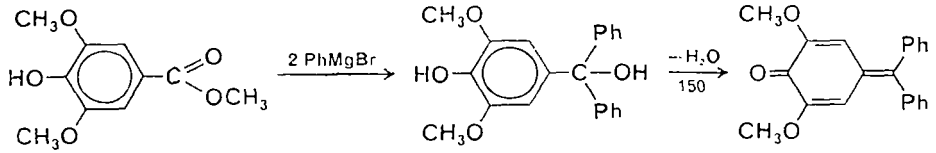


Violet

from the resulting alcohol leads to quinone methides, e.g. the annexed fuchsone derivative[56].



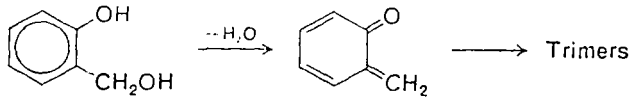
In the next synthesis the alcoholic intermediate is obtained from a hydroxybenzoic ester by successive Grignard reactions and its dehydration leads to another fuchsone derivative[57].



Elimination of water at a high temperature, as formulated for the last two reactions, is often used in the synthesis of quinone methides, and particularly of fuchsones[58-60]. This elimination of water is also an important step in other methods of quinone methide synthesis and is stressed in the next section, even though this separation is somewhat arbitrary.

V. SYNTHESIS BY ELIMINATION AND DEPROTONATION

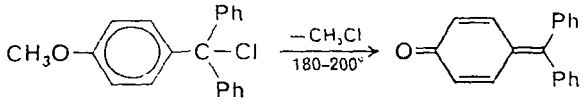
When *o*-hydroxybenzyl alcohol was pyrolysed and the products trapped at −196°, the presence of *o*-benzoquinone methide **28** could be proved spectroscopically[61]. When warmed, it was converted into trimers which had been known for some time[62,63]; their formation will be discussed in the section on reactions.



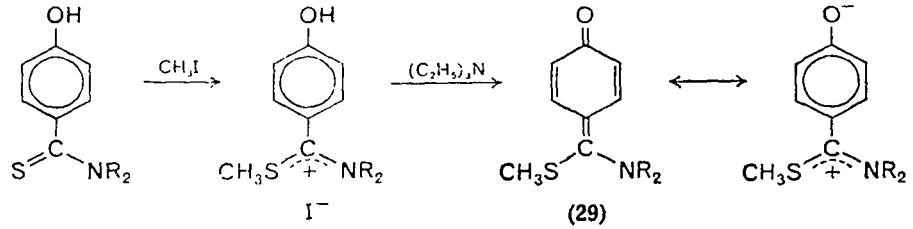
(28)

Elimination of hydrogen chloride was described in section I. Removal of hydrogen bromide from appropriate hydroxybenzyl bromides should also lead to quinone methides, but often only products of further reaction could be isolated[64–67].

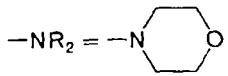
In the fuchsone series alkyl halide can also be removed at elevated temperature, an example being afforded by the synthesis of fuchsone itself from *p*-methoxy-α,α-diphenylbenzyl chloride[1].



In the synthesis of donor-stabilized quinone methides of type **29**, deprotonation of the intermediate cations is the last step; the intermediate salts can be isolated[68]. Here both the salts and the quinone methides owe their stabilization to conjugation of the carbenium centre with electron-



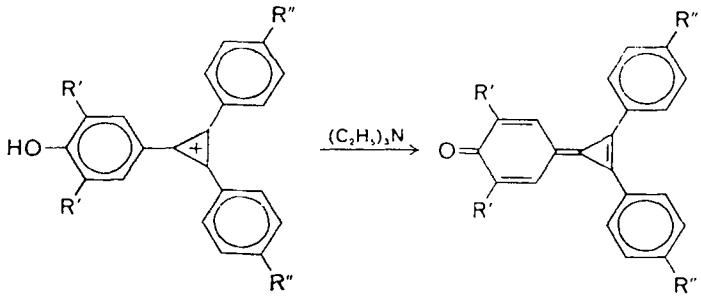
(29)



shifting substituents; there is a 'push–pull' stabilization of the quinone methide system due to the attractive effect of the oxygen atom and the

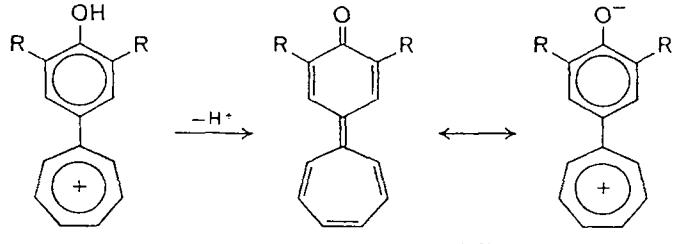
shift by the donor substituents. Further development of this idea leads to push–pull stabilization of the corresponding quinodimethanes[69].

Similar stabilization occurs with the quinone methides **30**, obtained from (hydroxyaryl)cyclopropenylium salts[70,71] as mentioned above.



R' = H or Br
R'' = H or OH (30)

Synthesis of **32** from the (hydroxyaryl)tropenylium salts **31** belongs to the next section since dehydrogenation is involved, but it may be mentioned here that the easy deprotonation of the salts again affords resonance-stabilized, deeply coloured quinone methides[44,72–76].

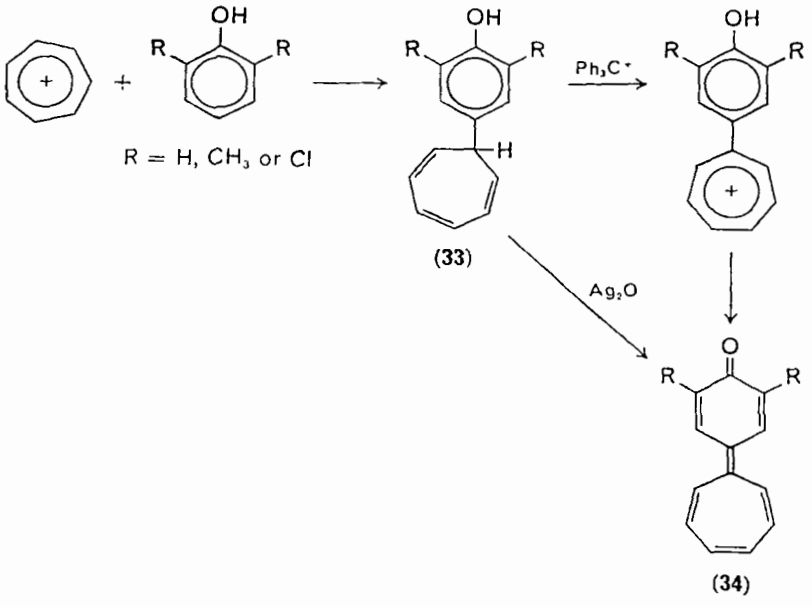


(31) (32)

R = H, CH_3, or *t*-butyl

VI. SYNTHESIS BY ELECTROPHILIC AROMATIC SUBSTITUTION OF PHENOLS AND SUBSEQUENT OXIDATION

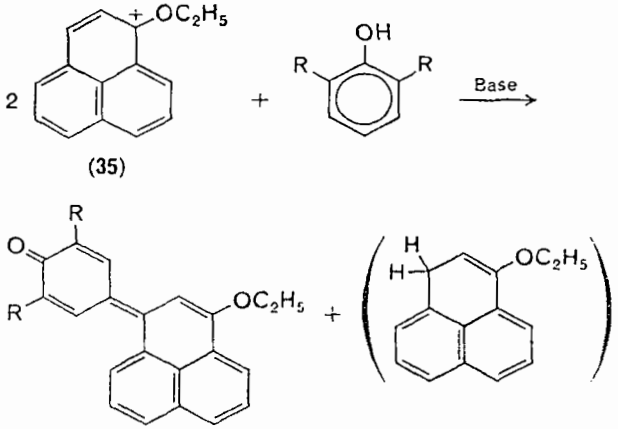
Numerous synthetic routes to tropylidenephenols (**33**) provide a connexion to the last example in the preceding section. Reaction of most 2,6-di-substituted phenols with tropylium salts stops at the intermediate hydrogenated stage **33**, and the subsequent dehydrogenation to quinone methides **34** is then effected either by using an excess of the tropylium salt or by isolating the phenolic **33** and treating it with a triphenylcarbenium salt or other oxidizing agent such as silver oxide[44,72–76].



(33)

(34)

The ethoxyphenalenium salt **35** is also able to substitute phenols, and in this case the product is oxidized spontaneously to the blue quinone methide **36** by a second molecule of the carbenium salt **35**[77].

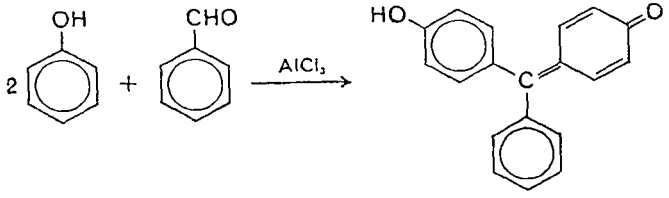


(35)

(36)

Phenols can also be substituted by using aldehydes as the electrophile, particularly if the reaction is catalysed by a Lewis acid. The following synthesis of benzaurin **37** is effected in this way; the intermediate product is not isolated but is at once dehydrogenated[78]. As this example shows,

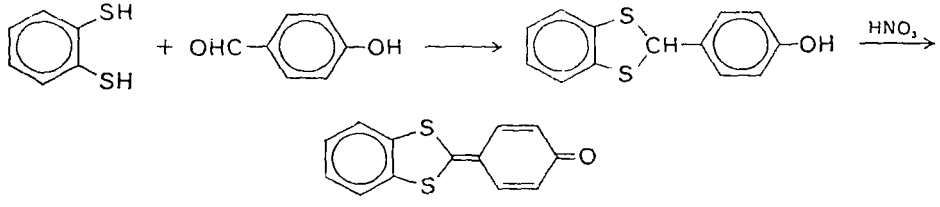
this type of synthesis leads into the fuchsone series and the triphenylmethane dyes, and very many further reactions of this type are described in the literature[79-81].



Benzaurin (37)

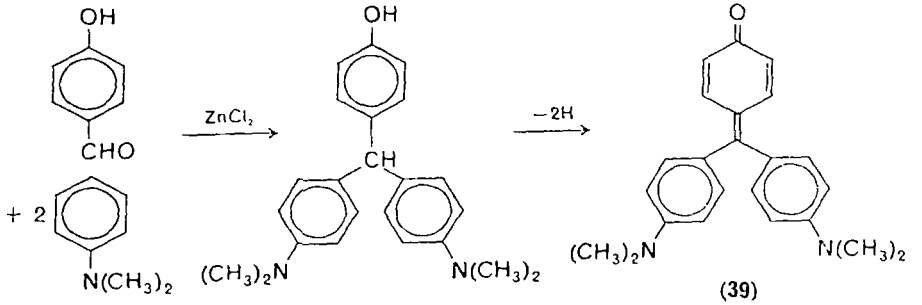
VII. SYNTHESIS FROM AROMATIC HYDROXYALDEHYDES BY OXIDATION OF THEIR DERIVATIVES

The synthetic principle underlying this section can be seen most clearly in the formulae below showing preparation of the push–pull stabilized quinone methide **38**[82]. Oxidation of the mercaptal of the aromatic aldehyde by nitric acid occurs by way of a nitrate.



(38)

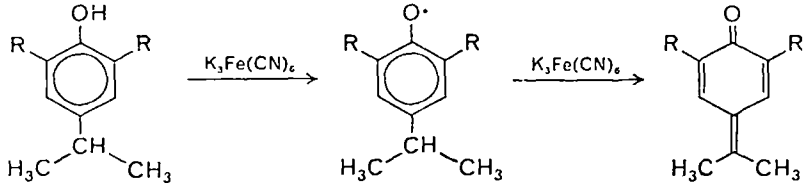
Further, preparation of the fuchsone derivative **39** and analogous triphenylmethane dyes proceeds through derivatives of aromatic hydroxyaldehydes that are very easily oxidized[83].



(39)

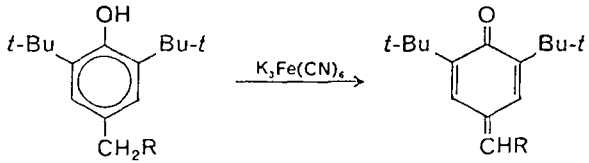
VIII. SYNTHESIS BY OXIDATION OF (HYDROXYARYL)METHYL COMPOUNDS

Potassium hexacyanoferrate(III) has been found particularly valuable as an oxidizing agent for preparation of a variety of quinone methides from (hydroxyaryl)methyl derivatives, as illustrated[84]. This oxidation should be formulated as occurring through aryloxyl radicals[85], and these can themselves act as dehydrogenating agents[86]. The general applicability of



R = *t*-butyl

oxidation by potassium hexacyanoferrate(III) is illustrated by the variety of substituents R listed under the following formulae for the 2,6-di-*t*-butyl case[87–89]. The reaction can, however, be effected by very many other oxidizing agents, and silver oxide[17,90], lead oxide[91–94] and choranil[95]

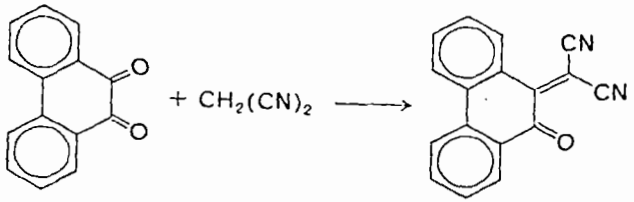


R = CH_3, C_2H_5, iso-C_3H_7, *n*-C_4H_9, C_6H_5, CH_2OH, COOH, CN, or piperidine

inter alia, have each been used with success. Very often, however, formation of stilbenequinones or related dimerization products occurs as a side-reaction, and this applies also to oxidation by potassium nitrosodisulphonate[96].

IX. SYNTHESIS FROM QUINONES

Condensation of the carbonyl group of quinones with CH-acidic compounds, which is often used for synthesis of methylene derivatives in other series, rarely succeeds, owing to the low electrophilicity of the quinone carbonyl atom (see section I). However, in special cases, such as phenanthraquinone and 1,2-acenaphthenequinone, reaction with malonodinitrile affords quinone methides **40** and **41** carrying the two cyano-groups[97]; in these two cases the quinonoid character is weakened, the relationship to 1,2-quinones being obvious.



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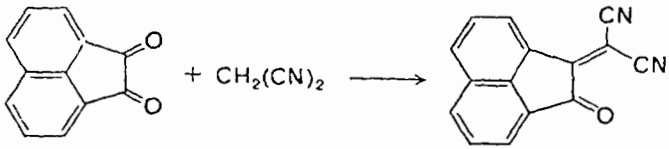
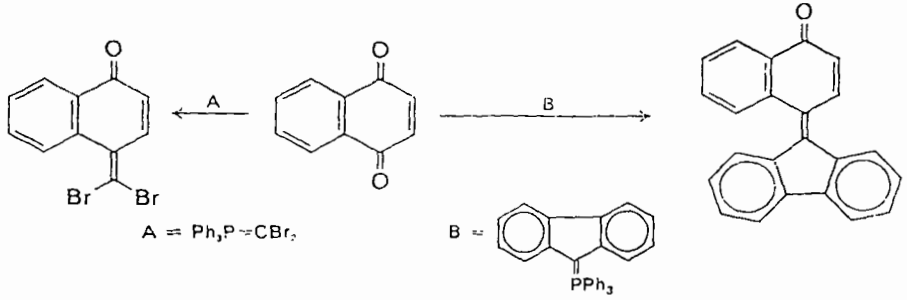
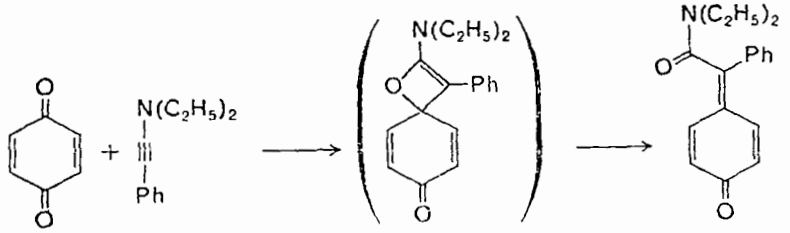


(41)

Synthesis of methylene derivatives from carbonyl compounds by the Wittig reaction can be carried out in the quinone series, as illustrated here for the formation of two quinone methides from 1,4-naphthoquinone[98].

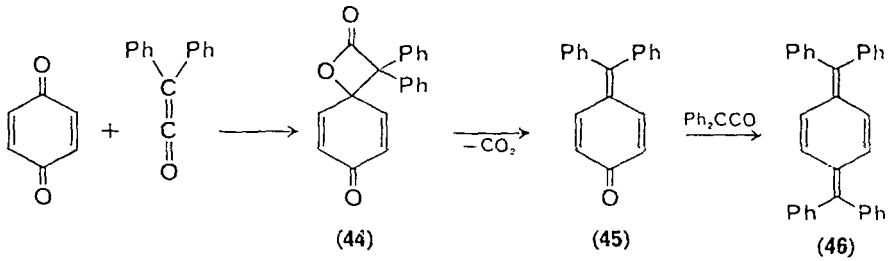


It is also possible to cause reaction between the carbonyl group of quinones and very reactive ynamines. For instance, *p*-benzoquinone and *N*,*N*-diethyl-2-phenylethynylamine afford the quinone methide **43**, whose formation is most simply formulated as occurring through the intermediate **42** with subsequent ring-opening[99].

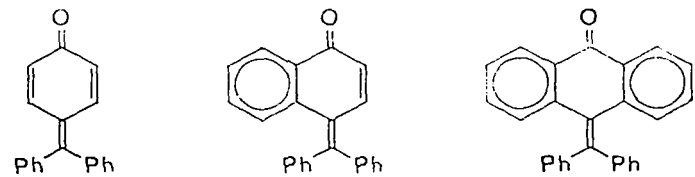


(42) (43)

In these reactions, electrophilic attack on the oxygen atom of the quinone system plays a considerable part in the further course of the reactions, but in the earlier syntheses of quinone methides and quinodimethanes from quinones and diphenylketene attack by the electrophilic ketene on the oxygen atom of the quinone is the cause of the first reaction step[100]. The lactone **44**, for instance, can be isolated and gives the quinone methide **45** by loss of CO_2. When two equivalents of diphenylketene are used both carbon groups of the quinone react, yielding quinodimethanes such as **46**[100].



The fuchsone derivatives prepared in this way show a striking hypsochromic shift of the longest wavelength band in the series benzo-, naptho- and anthra-quinone methide, i.e. the colour becomes paler as the size of the conjugated systems increases. The hypsochromic shift is still more marked with the corresponding quinodimethanes, so much so that this



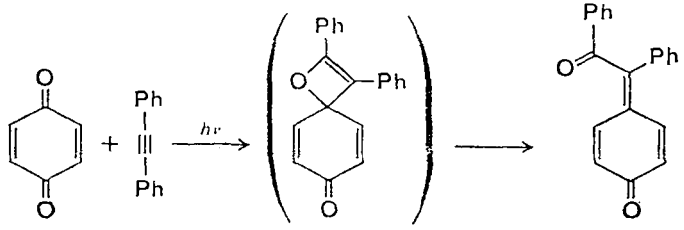
unusual effect led Staudinger to doubt the quinonoid structure of tetraphenylanthraquinone dimethane[101]. The shifts can, however, be explained by MO calculations[102, 103], in which the decrease in quinonoid character through the series benzo-, naphtho- and anthra-quinone is seen to play a significant role.

X. PHOTOCHEMICAL SYNTHESES

As a monocyclic four-electron process the addition of the triple bond of an ynamine to the carbonyl double bond of a quinone described in the preceding section should be thermally unfavourable[103, 104]; it will be made

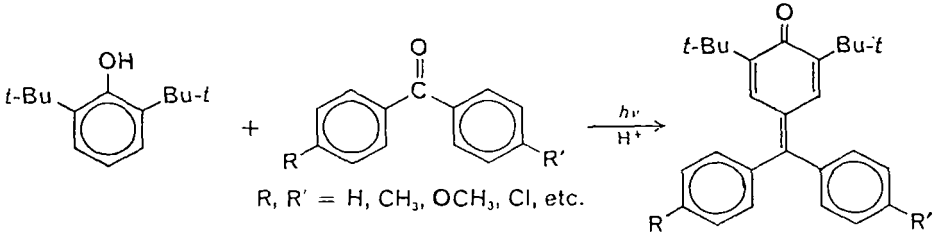
much easier by polarization of the two components and can proceed through polar intermediates.

The Woodward–Hoffmann rules for cyclic transition states[103,104] stipulate that a photochemical process is favourable when the thermal process is unfavourable, and a suitable example of this is provided by photochemical addition of tolane to *p*-benzoquinone, as illustrated[105,106].

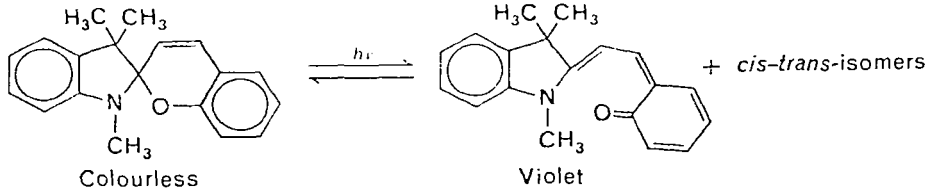


As in the thermal reaction of the ynamine this reaction also is most simply formulated as involving a spirocyclic intermediate.

Photochemical activation is also utilized in synthesis of the series of fuchsone derivatives shown below[107].

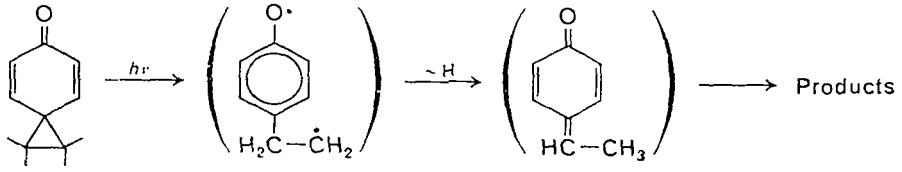


In the chemistry of photochromic dyes light energy can be used to open a spiran system, and quinone methides are often formed as chromophores; a violet indole derivative and its isomers exemplify the principle[108,109].



Of particular interest is the photochemical cleavage of a cyclopropane ring involved in a spiro-junction. Quinone methides are obtained from the

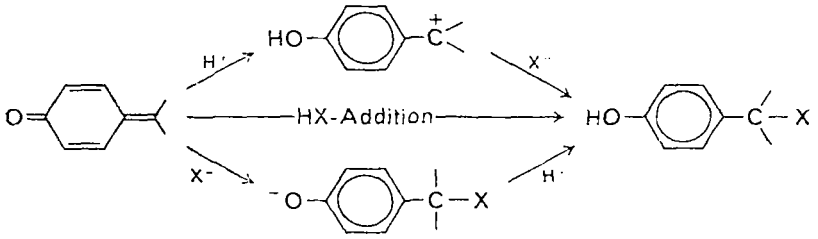
diradicals formed as intermediates, but under the reaction conditions further reactions set in to give the products isolated[110,111].



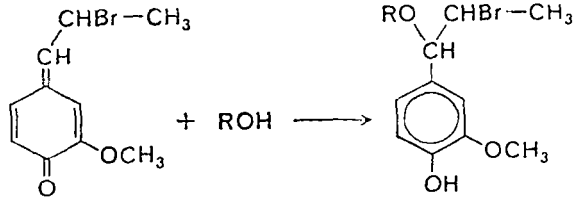
XI. GENERAL REACTIONS

As mentioned in the Introduction, quinone methides constitute a rather unstable and thus reactive class of compound. This great reactivity results from the higher energy potential of the quinonoid than of the corresponding aromatic structure.

Being vinylogous carbonyl compounds, the quinone methides are especially amenable to addition reactions of Michael type (cf. the scheme below). The addition occurs stepwise in both cases, i.e. addition of the



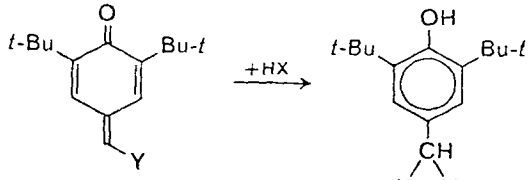
electrophile precedes that of the nucleophile or *vice versa*, but in both cases the ring becomes aromatic in the first step. The rate of addition of alcohols to quinone methides depends to a substantial extent on the acid strength of the alcoholic component[112]: the more easily the proton is removed, the faster is the addition. This, however, implies that in such cases addition of the proton to the nucleophilic centre of the methide (i.e. to its oxygen atom) is the important step. Higher alcohols add extremely



ROH: PhOH > Sugar > H_2O > CH_3OH > C_2H_5OH

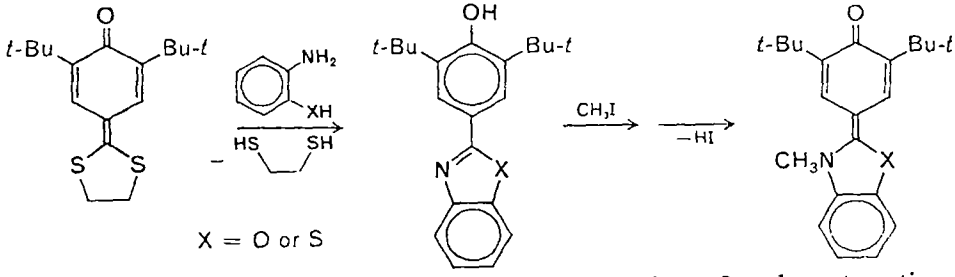
slowly but, as shown in the scheme, their reaction is greatly accelerated by traces of acid[113,114].

The same dependence on the acid strength of a component HX is found with the quinone methides **47a** and **47b**[115]: the nucleophilicity of the oxygen atom of the methide is further increased by the donor substituents Y. On the other hand, when the substituent is an electron acceptor, as in **47c** and **47d**, the quinone methide reacts only with very strong nucleophiles[115] and it is then the electrophilicity of the carbon atom at the other end of the conjugated system that determines the reaction since the nucleophilicity of the oxygen atom is too greatly weakened to be effective.



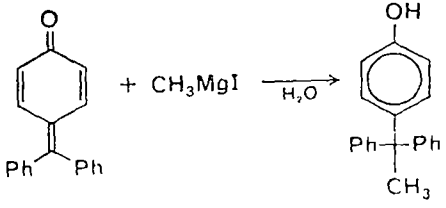
(47a) Y = $N(CH_3)_2$
(47b) Y = OCH_3
(47c) Y = CN
(47d) Y = COOH

Nucleophilic substitution is also the basis for conversion of a 2,6-di-*t*-butylbenzoquinone methide containing a 1,3-dithianylidene group into other methides by *o*-amino-phenol or -thiophenol[116]. The sulphur substituents are removed as 1,2-ethanedithiol owing to the more strongly nucleophilic amino-group[116] and the resulting phenolic compound can be

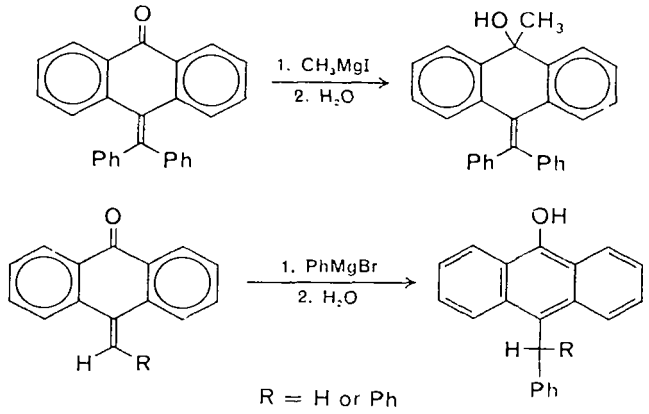


converted by alkylation into its ammonium salt, whereafter deprotonation restores the quinone methide system.

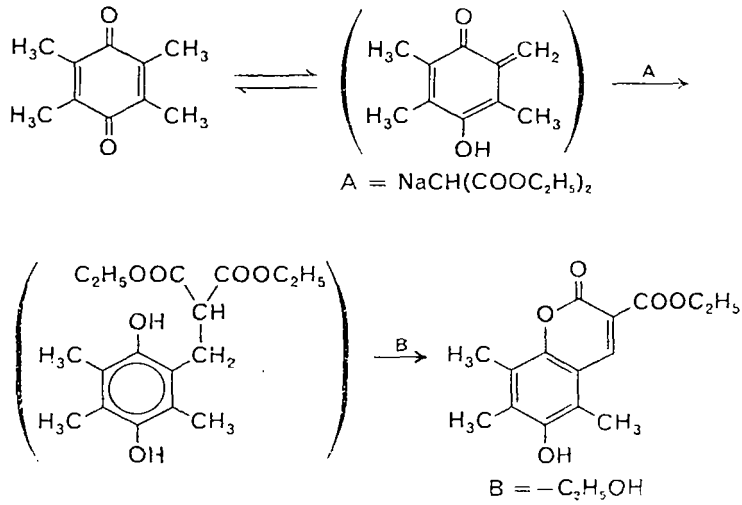
1,6-Addition of Grignard reagents to quinone methides occurs, as expected, with formation of the phenolic system, as illustrated for diphenyl methide[117].



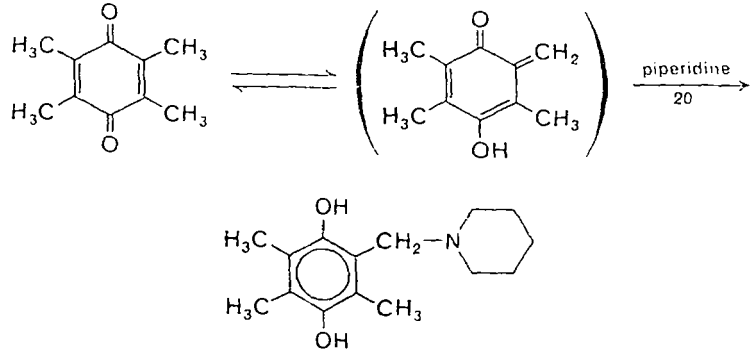
The corresponding 1,4-naphthoquinone methide reacts analogously, but methylmagnesium bromide reacts with 9,10-anthraquinone methide by 1,2-addition to the carbonyl group[117]; here the less pronounced quinonoid (or benzenoid) character of the central ring of the anthracene system makes itself felt, but in other cases 1,6-addition of phenylmagnesium bromide can still occur[118]. The two modes of addition are shown in the formulae.



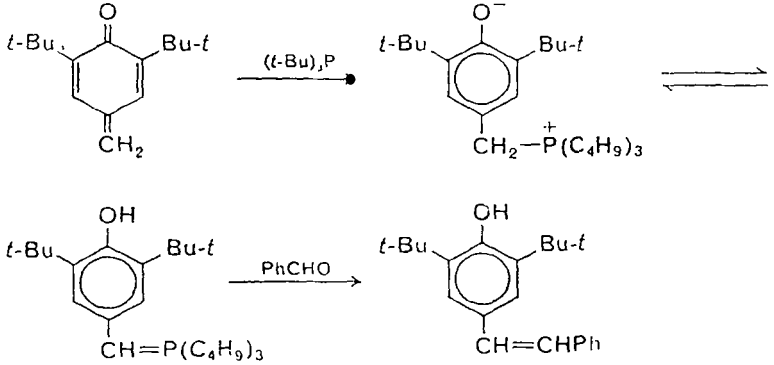
Addition of CH-acidic compounds to quinone methides follows the HX scheme[119]. It plays a large part in the chemistry of duroquinone; *o*-quinone methides, which can be formulated as the enolic form of the quinone, are assumed as intermediates[120,121], with the results illustrated in the following reaction sequence.



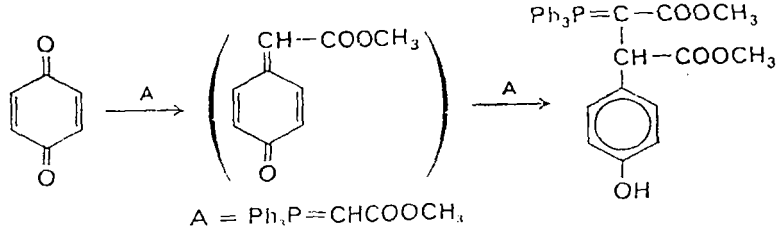
Duroquinone can be readily aminated in the side-chain at room temperature and this great reactivity is again attributed to the *o*-quinone methide. After oxidation of the resulting diphenolic product to its quinone analogue, further amino groups can be introduced[122].



Interaction of tributylphosphane and a quinone methide affords a good yield of the phosphonium betaine; this cannot be isolated but it can be trapped by the Wittig reaction with benzaldehyde[123]. The ready addition of phosphanes or phosphites to quinone methides is also involved in transformations and dimerizations of the latter[124].

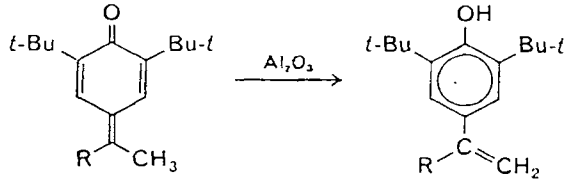


In section IX, on the syntheses of quinone methides from quinones, the Wittig reaction with quinones was cited. That synthesis fails with methyl trimethylphosphoranylideneacetate and *p*-benzoquinone because



the intermediate quinone methide reacts with a second molecule of Wittig reagent and that adduct is stabilized by prototropy[125].

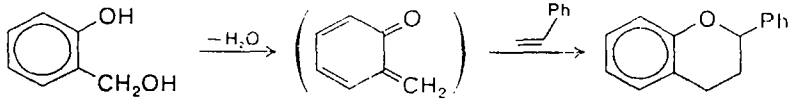
An analogous prototropy is shown by 2,6-di-*t*-butylbenzoquinone methide and its 7-methyl and 7-phenyl derivatives, the reaction being catalysed by alumina[126].



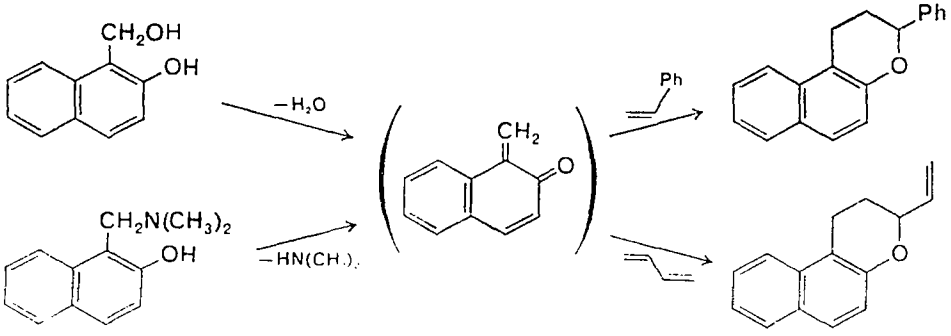
XII. CYCLOADDITION REACTIONS

Transition from the quinonoid to the corresponding benzenoid structure can be achieved particularly easily with *o*-quinonoid systems by a bond shift during the course of a Diels–Alder reaction, and this is the driving force for the great tendency of *o*-quinone methides to dimerize.

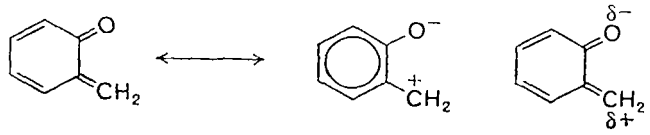
On formation of *o*-quinone methide by dehydration of *o*-hydroxybenzyl alcohol in the presence of an olefin, addition of the latter occurs[127,128], yielding flavan if the olefin is styrene. The same reaction



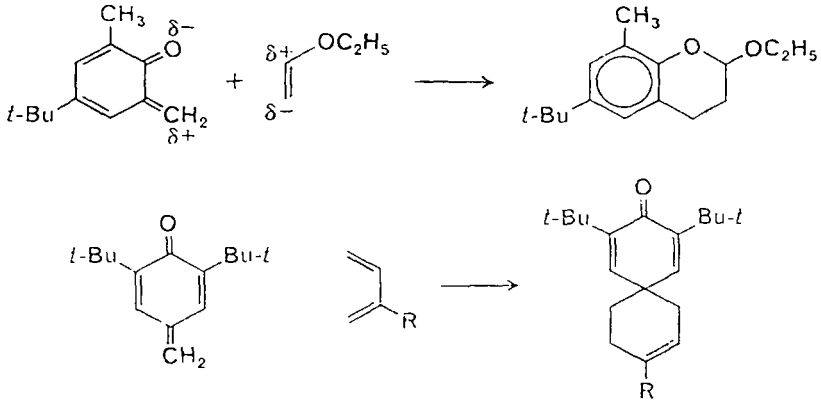
occurs with *o*-naphthoquinone methide obtained by either of the two methods illustrated[129]; the products formed on use of styrene and butadiene are both shown.



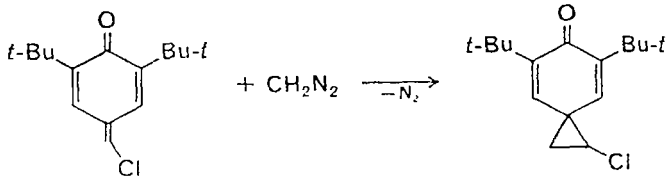
In all cases the *o*-quinone methide acts as a heterodiene component, and the high regiospecificity corresponds to polarization of the methide in the manner shown. This is particularly clear in the reaction with ethyl vinyl ether, which is quantitative[130].



p-Quinone methides can not react as the diene components, for with these compounds the *exo*-methylene group behaves as the dienophile; this can be exemplified by the behaviour of 2,6-di-*t*-butyl-*p*-benzoquinone methide with substituted butadienes[131].

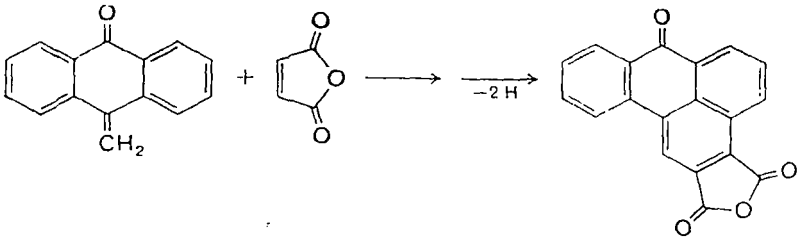


The methylene group also acts as dienophile in reactions with diazomethane, for spirocyclopropyl derivatives are formed in very good yield, as shown here for a 7-chloromethide[132].

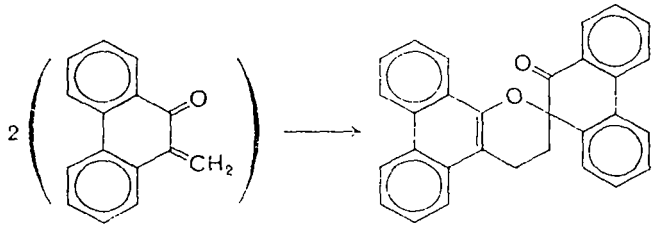


However, in the case of methyleneanthrone the double bond next to the methylene group can enter into the reaction; thus, after addition of maleic anhydride and dehydrogenation the product is found to be a benzanthrone derivative[132,134].

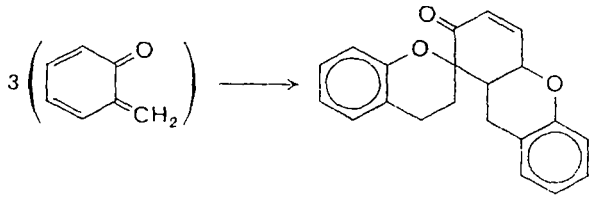
In the absence of a suitable addendum, the considerable tendency of an *o*-quinone methide to add to a heterodiene system leads to dimerization,



one molecule acting as heterodiene and another as dienophile. Phenanthraquinone methide provides such an example[135,136]. Very often,

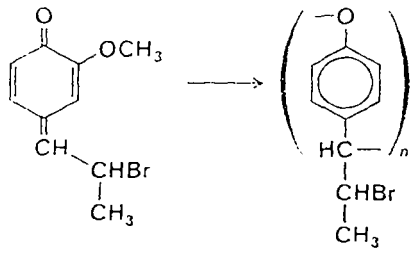


however, trimeric products are formed in attempts to prepare quinone methides, such as that shown from *o*-benzoquinone methide[63,137]. Indeed a large number of compounds described in the early literature as quinone



methides are really dimers or, more often, trimers[138]; colour alone allows a decision between the yellow quinone methides and their colourless oligomers.

Self-addition of *p*-quinone methides leads to polymeric 1,6-adducts[112].



XIII. ACKNOWLEDGMENT

We thank Dr. Klaus-Peter Paul for his help in compilation of the references.

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The Chemistry of the Quinonoid Compounds
Edited by Saul Patai

Subject Index

For *o*- and *p*-quinones *see* 1,2- and 1,4-compounds, respectively