QUINONE METHIDES

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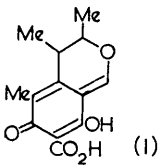
1. Introduction

THE reactive intermediates of organic chemistry have gained credence partly because many of them exist in stable forms, having the chemical properties required of the hypothetical species. This situation is well exemplified in the case of quinone methides, which, on paper, are derived from quinones by replacement of one of the carbonyl oxygens by a methylene, or substituted methylene, group. These compounds are also known as methylenequinones or quinone methines. Increased interest in their chemistry during the last few years has arisen largely from their probable involvement in biochemical processes, notably oxidative phosphorylation.

2. Stable Quinone Methides

This section is concerned only with *para*-quinone methides, as no members of the *ortho*-series have yet been obtained in a pure state. The chemistry of most of the natural products mentioned here has been covered in earlier reviews.[1]

Quinone methides occur in Nature both as fungal metabolites, familiar as a rich source of quinones themselves, and as wood pigments. Thus, various species of *Penicillium* elaborate citrinin (1),[2] pulvilloric acid (2),[3] and purpurogenone (3),[4] while fuscin (4) is obtained from cultures of *Oidiodendron fuscum* Robak.[5] Structural work on these compounds was



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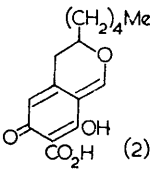

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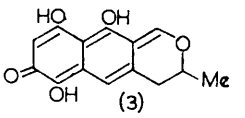
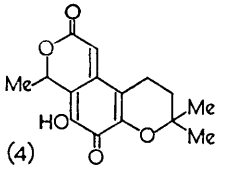


(3)

facilitated by the ease with which they undergo reversible addition reactions, giving colourless, phenolic products. Pulvilloric acid, for example, can be crystallised as a colourless ethanol adduct, which rapidly reverts to the yellow acid on keeping. It also forms a colourless adduct with sodium bisulphite. This behaviour is typical of quinone methides in general (see Section 4).

[1] R. G. Cooke and R. H. Thomson, *Rev. Pure Appl. Chem.* (*Australia*), 1958, **8**, 85; W. B. Whalley, "Progress in Organic Chemistry", ed. J. W. Cook, 1958, **4**, 72.
[2] J. P. Brown, A. Robertson, W. B. Whalley, and N. J. Cartwright, *J.*, 1949, 867.
[3] J. F. W. McOmie, M. S. Tute, A. B. Turner, and B. K. Bullimore, *Chem. and Ind.*, 1963, 1689.
[4] J. C. Roberts and C. W. H. Warren, *J.*, 1955, 2992.
[5] D. H. R. Barton and J. B. Hendrickson, *J.*, 1956, 1028.

Brazilein (5; R = H) and hæmatoxylein (5; R = OH) are the dyeing principles of redwood and logwood, respectively.[6]



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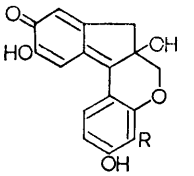

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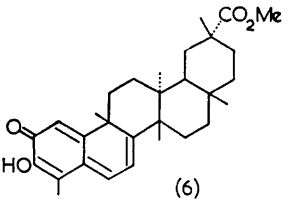
The orange wood-pigment pristimerin (6)[7,8] is the only member of the group which is prone to rearrange under the influence of acid. As might be expected from its structural resemblance to steroidal dienones, these skeletal rearrangements are of the dienone–phenol type, and involve initial migration of a methyl group to the terminus of the quinone methide system.[8]

In addition, there are the anhydro-base forms of the anthocyanins, which are responsible for some of the more brilliant colours of living plants. These pigments are all based upon the C_{15} unit (7), having the carbon skeleton of the flavones, and have been reviewed by Seshadri.[9]



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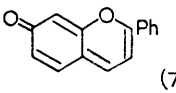
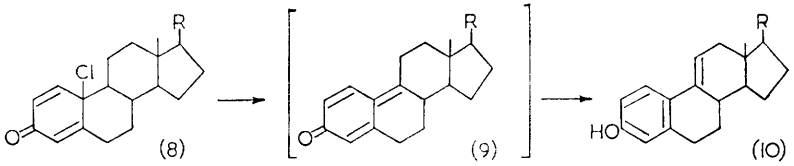


(7)

A feature common to all of these natural products is the isolation of the quinone methide chromophore from labile hydrogen atoms, which prevents tautomeric rearrangement of the colouring matter to a phenol.[10] This is achieved in most cases by the situation of a cyclic ethereal oxygen atom at the end of the conjugated system remote from the di-unsaturated carbonyl group. In the remaining compounds, carbon atoms terminating the chromophoric system do not bear hydrogen. These observations were first made by Grant and Johnson[10] in aid of their elucidation of the nature of the chromophore of pristimerin (6). An illustration of the instability of the quinone methide structure in rigid ring systems, when not isolated from labile hydrogen atoms, has been found in the steroid series. Elimination of

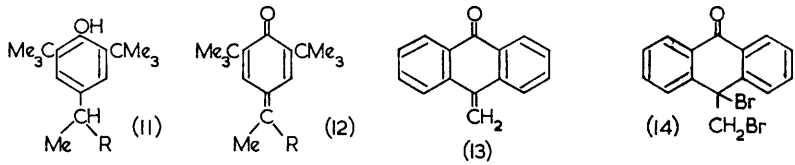
[6] R. Robinson, *Bull. Soc. chim. France*, 1958, 125.
[7] R. Harada, H. Kakisawa, S. Kobayashi, M. Musya, K. Nakanishi, and Y. Takahashi, *Tetrahedron Letters*, 1962, 603.
[8] A. W. Johnson, P. F. Juby, T. J. King, and S. W. Tam, *J.*, 1963, 2884.
[9] T. R. Seshadri, "Festschrift A. Stoll", Birkhauser, Basle, 1957, p. 318.
[10] P. K. Grant and A. W. Johnson, *J.*, 1957, 4079.

hydrogen chloride from 10β-chlorodien-3-ones (8), by means of calcium carbonate in refluxing dimethylformamide, gives $\Delta^{9(11)}$-phenols (10).[11]



The loss of a severe 1,3-diaxial interaction (11β-hydrogen and 13β-methyl) in going to the product (10) no doubt contributes to the ease of aromatisation of the transient intermediate (9).

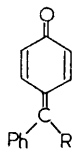
Simple quinone methides in which the terminus of the chromophore is linked to carbon atoms bearing hydrogen have, in fact, been isolated.[12] Oxidation of the phenols (11; R = Me or Et) gives the crystalline products (12; R = Me) and (12; R = Et). These two compounds show no tendency towards spontaneous aromatisation. They react with hydrogen bromide and alcohols, by 1,6-addition, to give the corresponding phenols.



10-Methyleneanthrone (13) is the sole example of a stable quinone methide having an unsubstituted methylene group.[13] The low probability of the central ring's becoming aromatic makes its quinone methide character negligible. The comparative isolation of the ethylenic bond from the carbonyl group in this molecule is shown by its typically olefinic behaviour in adding a molecule of bromine to give the dibromide (14).

Other monomeric quinone methides lacking tautomeric possibilities include fuchsone (15; R = Ph),[14] which is attacked by concentrated alkali giving the carbinol (16; R = Ph, X = OH). The related photoadduct (15; R = COPh) of benzoquinone and diphenylacetylene reacts similarly with hot alkali, but the resulting ketol (16; R = COPh, X = OH) is degraded under these conditions.[15] Catalytic hydrogenation gives the dihydro-derivative (16; R = COPh, X = H).

[11] J. S. Mills, T. Barrera, E. Olivares, and H. Garcia, *J. Amer. Chem. Soc.*, 1960, **82**, 5882.
[12] C. D. Cook and B. E. Norcross, *J. Amer. Chem. Soc.*, 1956, **78**, 3797.
[13] K. H. Meyer, *Annalen*, 1920, **420**, 135.
[14] A. Bistrzycki and C. Herbst, *Ber.*, 1903, **36**, 2335.
[15] H. E. Zimmerman and L. Craft, *Tetrahedron Letters*, 1964, 2131; D. Bryce-Smith, G. I. Fray, and A. Gilbert, *Tetrahedron Letters*, 1964, 2137.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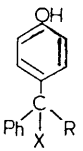
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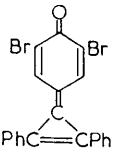
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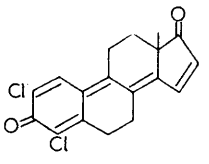
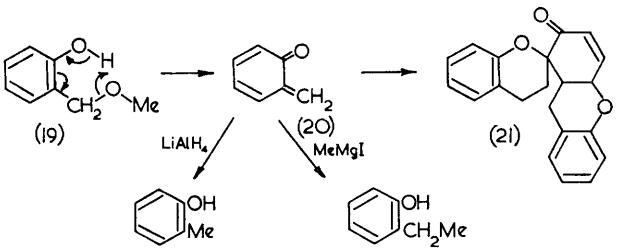

(18)

Further examples are the diphenoquinocyclopropene (17),[16] and the orange steroid (18), which results from chlorination, followed by dehydrochlorination, of œstrone.[17]

3. Reactive Quinone Methides

(a) **Simple Quinone Methides.**—Simple members of both the *ortho* and *para* series are very unstable molecules, which polymerise spontaneously. Some are nevertheless sufficiently stable, in dilute solution or at low temperatures, to allow studies of their properties. They are generally prepared either by oxidation of the corresponding cresols or by elimination of the appropriate elements from *ortho*- and *para*-hydroxybenzyl derivatives.

The parent compound of the *ortho* series, *o*-benzoquinone methide (20), is obtained[18] as a solid at liquid-nitrogen temperature by pyrolysis of *o*-methoxymethylphenol (19). On warming to −50°, the pyrolysate liquefies, and appears quire stable. Although spectral data are lacking, the chemical properties of the substance accord with its formulation as the monomer (20). Three reactions define the character of the product (Chart I).



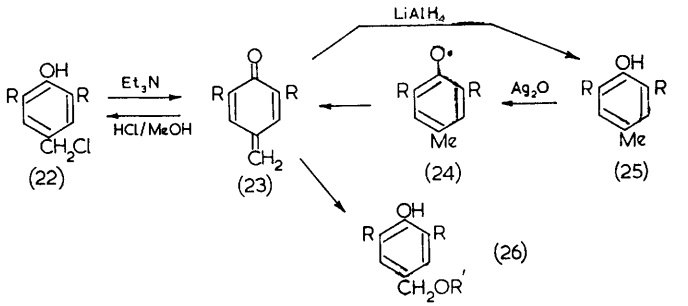
Reduction by metal hydride yields *o*-cresol; addition of methylmagnesium iodide, followed by hydrolysis, gives *o*-ethylphenol; and the colourless, solid trimer (21) is formed on warming to room temperature. Analogous trimers are obtained from ring substituted derivatives of *o*-benzoquinone methide.[19]

Attempts to prepare *p*-benzoquinone methide by pyrolysis of *p*-methoxymethylphenol were unsuccessful, this compound being stable up to 900°.

[16] A. S. Kende, *J. Amer. Chem. Soc.*, 1963, **85**, 1882.
[17] E. Schwenk, C. G. Castle, and E. Joachim, *J. Org. Chem.*, 1963, **28**, 136.
[18] S. B. Cavitt, H. Sarrafizadeh R., and P. D. Gardner, *J. Org. Chem.*, 1962, **27**, 1211.
[19] A. Merijan, B. A. Shoulders, and P. D. Gardner, *J. Org. Chem.*, 1963, **28**, 2148.

p-Hydroxymethylphenols are likewise more resistant to dehydration than their *ortho* isomers.[20] These differences may be due to the six-membered transition states available for the fragmentation of the *ortho* compounds.

Although the parent compound of the *para* series has not been isolated, Filar and Winstein[21] have studied its 2,6-dimethyl derivative (23; R = Me). This can be prepared either from the phenol (22; R = Me), by treatment with a base such as triethylamine, or by oxidation of mesitol (25; R = Me) with silver oxide. In the latter reaction, it is interesting that very little, if any, of the *ortho* isomer is formed.



The identity of the quinone methide (23; R = Me) is clear from its ultraviolet and infrared spectra. It is stable for days at room temperature in inert solvents at high dilution (10^{-5}M), but its disappearance becomes quite rapid as the concentration is increased. The di-t-butyl analogue (23; R = Bu^t) is rather more stable in solution, but again cannot be obtained pure. In both cases the reaction products are primarily dimeric (see p. 353). These *para*-quinone methides are attacked at the terminal methylene group by a variety of nucleophilic reagents, yielding the appropriate benzyl derivative (*e.g.*, 26; R′ = Me or COMe) by 1,6-addition.

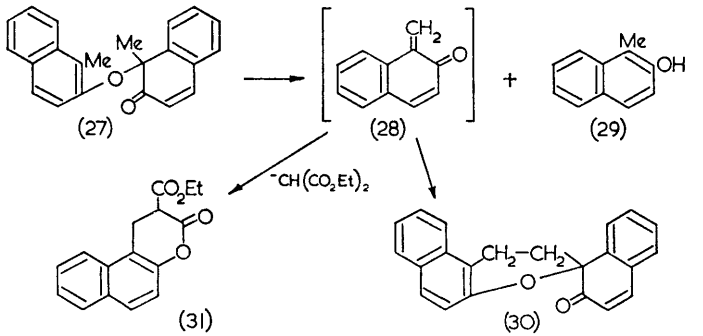
Attempts to prepare quinone methides of the naphthalene and phenanthrene series have met only with the formation of dimers.

Pummerer and Cherbuliez[22] have shown that dehydrogenation of 1-methyl-2-naphthol (29) leads to the dimer (27). This compound, when heated in xylene, disproportionates to the parent phenol (29) and the quinone methide (28), which, in turn, gives the stable dimer (30).

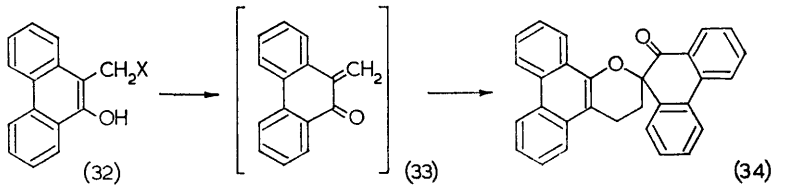
That the original dimer (27) does indeed give the intermediate (28) is substantiated by the work of Smith and Horner,[23] who found that the dihydrocoumarin (31) is formed when the dimer (27) is warmed with sodium malonate in dry ethanol (Chart III).

Condensation of phenanthr-9-ol with formaldehyde and dimethylamine under mild conditions[24] gives the unstable Mannich base (32; X = NMe_2).

[20] N. J. L. Megson, "Phenolic Resin Chemistry," Butterworths, 1958, p. 165.
[21] L. J. Filar and S. Winstein, *Tetrahedron Letters*, 1960, **25**, 9.
[22] R. Pummerer and E. Cherbuliez, *Ber.*, 1919, **52**, 1392.
[23] L. I. Smith and J. W. Horner, *J. Amer. Chem. Soc.*, 1938, **60**, 676.
[24] P. D. Gardner and H. Sarrafizadeh R., *J. Org. Chem.*, 1960, **25**, 641.

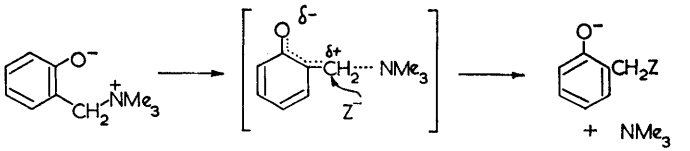


Loss of nitrogen occurs during attempts to purify it, and the high-melting dimer (34) is obtained. This material is also obtained from the reaction of phenanthr-9-ol with formaldehyde alone, indicating similar instability of the 10-hydroxymethyl derivative (32; X = OH). The reactivity of 10-methylene-9-phenanthrone (33) contrasts with the stability of 10-methyleneanthrone (13).



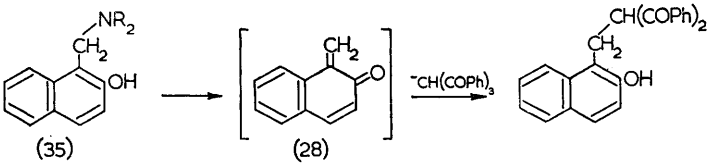
(b) **Quinone Methides as Chemical Intermediates.**—In addition to the cases in which quinone methides have been isolated, there are many reactions in which they are probably involved as transient intermediates.

It is well known that *ortho*- and *para*-hydroxybenzyl derivatives readily undergo nucleophilic substitution at the benzylic position. Thus, displacement of the amine moiety of Mannich base methiodides, by nucleophils such as methoxide, cyanide, and hydride ions, is facilitated by an anionic oxygen in the *ortho* position. Gardner and his co-workers[25] conclude that, although the reaction is bimolecular, the transition state closely resembles the quinone methide structure in its charge-separated state:



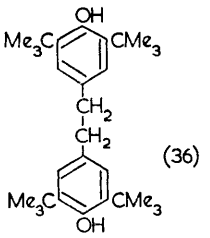
[25] P. D. Gardner, H. Sarrafizadeh R., and L. Rand, *J. Amer. Chem. Soc.*, 1959, **81**, 3364.

Similarly, the intermediate (23) is involved in the hydrolysis of the chloride (22), and in its reaction with sodium acetate in acetic acid to produce the corresponding benzyl acetate (26; R = COMe). A further example is the ready replacement of the substituted amino-group of the benzylamine (35) by active methylene compounds under basic conditions.[26] Side-chain *C*-alkylation of this type of phenol is thereby achieved by nucleophilic attack on the intermediate (28), in contrast to the more familiar mechanism of ring *C*-alkylation of phenoxide anions. Earlier work[23] (described on p. 351) in which the quinone methide (28), generated by other means, was shown to react with the malonate anion in the same way, substantiates this reaction path.



(35) (28)

The relatively stable phenoxyl radical (24; R = Bu^t), formed by one-electron oxidation of the hindered phenol (25; R = Bu^t), disproportionates to the parent phenol and the corresponding quinone methide (23; R = Bu^t).[27,28] The initial radical decay is bimolecular and the quinone methide reacts further, through the formation of free-radical intermediates, yielding equal amounts of the biphenylethane (36) and the stilbenequinone (37).



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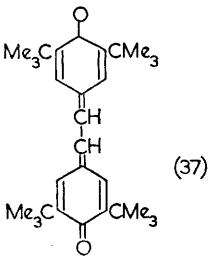
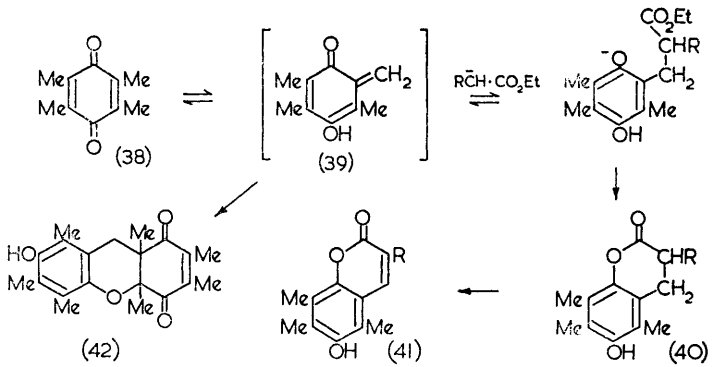


(37)

The suggestion that quinones having nuclear alkyl substituents might react in a tautomeric quinone methide form was originally made by Fuson, as an extension of the principle of vinylogy.[29] On this basis, a reasonable mechanism could be written for the mysterious condensation[30] of malonic ester with duroquinone (38) to give the coumarin (41; R = CO_2Et), involving initial attack of malonate ion on the tautomer (39). The enolate

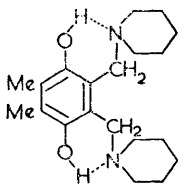
[26] H. Hellmann and J. L. W. Pohlmann, *Annalen*, 1961, **642**, 28.
[27] C. D. Cook and B. E. Norcross, *J. Amer. Chem. Soc.*, 1959, **81**, 1176.
[28] R. H. Bauer and G. M. Coppinger, *Tetrahedron*, 1963, **19**, 1201.
[29] R. C. Fuson, *Chem. Rev.*, 1935, **16**, 1.
[30] L. I. Smith and F. J. Dobrovolny, *J. Amer. Chem. Soc.*, 1926, **48**, 1693.

of methyl cyanoacetate adds similarly, giving the coumarin (41; R = CN), but acetylacetone does not condense.[31] Thus, cyclisation to the dihydrocoumarin (40) may be necessary to complete the reaction. The final dehydrogenation is brought about by the quinone.



The active form (39) is also responsible for the base-catalysed dimerisation of duroquinone (38),[32] biduroquinone (42) being formed by Diels–Alder addition of the tautomer (39) to the quinone (38). 2,3-Dimethylnaphthaquinone gives the same type of dimer under similar conditions.[33]

It has recently been found[34] that fully alkylated quinones readily undergo amination, involving this same tautomeric form, at carbon atoms adjacent to the nucleus. In the case of duroquinone, reaction with piperidine takes place at room temperature to give the bis-piperidino-derivative (43). The reaction proceeds by addition of piperidine to the tautomer (39), followed by oxidation of the resulting aminated quinol. Repetition of the process, with the new basic centre controlling the direction of the second tautomerisation, gives the observed product, which is stabilised by hydrogen bonding. This new type of amination is analogous to the well known nuclear amination of unsubstituted quinones.



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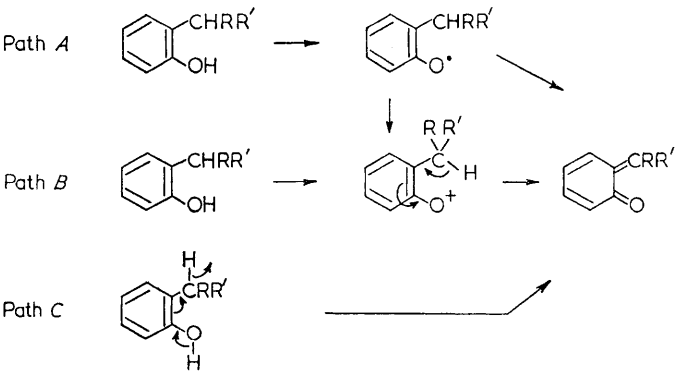
(c) **Quinone Methides as Biochemical Intermediates.**—Quinone methides are implicated as intermediates in a number of biochemical processes,

[31] L. I. Smith and E. W. Kaiser, *J. Amer. Chem. Soc.*, 1940, **62**, 138.
[32] L. I. Smith, R. W. H. Tess, and G. E. Ullyot, *J. Amer. Chem. Soc.*, 1944, **66**, 1320.
[33] K. Chandrasenan and R. H. Thomson, unpublished results.
[34] D. W. Cameron, P. M. Scott, and (Lord) Todd, *J.*, 1964, 42.

in which they are thought to arise either by tautomeric rearrangement of quinones or by oxidation of phenols.

Three mechanisms may be considered for the oxidation of *ortho*- and *para*-alkylphenols:

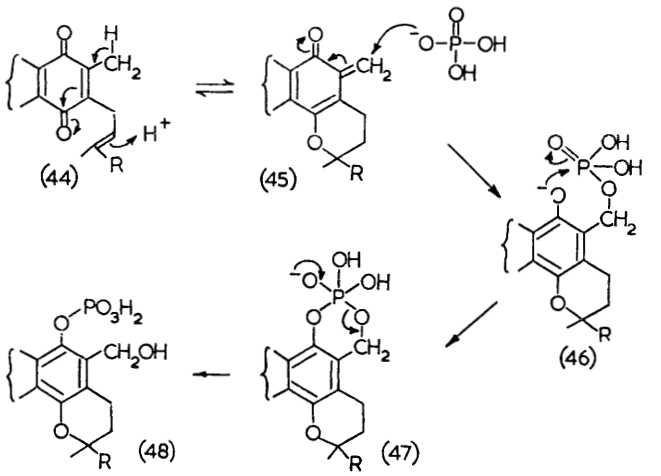


Chemical evidence, indicating that phenoxy-radical formation is the initial step in the majority of phenol oxidations,[35] points to one electron oxidation (Path *A*) as the most likely pathway. If an ionic process is involved, then in biological systems it could well be hydride abstraction from carbon (Path *C*). This has the advantage of yielding the quinone methide directly, perhaps by a concerted reaction, and the transformation could be brought about enzymically through the agency of pyridine nucleotide or quinonoid coenzymes. Recent work[36] indicates that enols are subject to two-electron oxidation. Thus, in both chemical and biochemical dehydrogenation of steroidal ketones, it is the enolic form of the substrate which undergoes hydride abstraction at the β-carbon atom. In addition, suitable enolic compounds are rapidly dehydrogenated[37] by high-potential quinones, reagents thought to function by accepting hydride ions.[38] In other enzymic dehydrogenations, for examples those mediated by pyridine nucleotides, the experimental evidence is markedly in favour of a mechanism involving direct transfer of a hydride ion.[39]

(i) *Oxidative phosphorylation.* Many lines of evidence point to the participation of quinones in the vital processes of electron transport along the respiratory chain and in the phosphorylations which accompany oxidation. Detailed schemes for the reaction cycles operating during oxida-

[35] H. Musso, *Angew. Chem. Internat. Ed.*, 1963, **2**, 723.
[36] H. J. Ringold, M. Hayano, and V. Stefanovic, *J. Biol. Chem.*, 1963, **238**, 1960.
[37] S. K. Pradhan and H. J. Ringold, *J. Org. Chem.*, 1964, **29**, 601.
[38] L. M. Jackman, "Advances in Organic Chemistry", ed. R. A. Raphael, E. C. Taylor, and H. Wynberg, 1960, **2**, 329.
[39] B. Pullman and A. Pullman, "Quantum Biochemistry", Interscience, 1963, p. 522.

tive phosphorylation have been suggested by Vilkas and Lederer,[40] taking advantage of structural features common to the tocopherol, Vitamin K, and ubiquinone groups. Quinones of these series have a methyl group at position 2 and a 3-substituent capable of participating in chroman ring formation, allowing rearrangement to the quinone methide (partial structure 45). Nucleophilic attack by phosphate anion at the terminal methylene group, followed by intramolecular migration of the phosphate group to the phenolic oxygen by way of the cyclic phosphate (47), complete the formation of the active quinol phosphates (48).

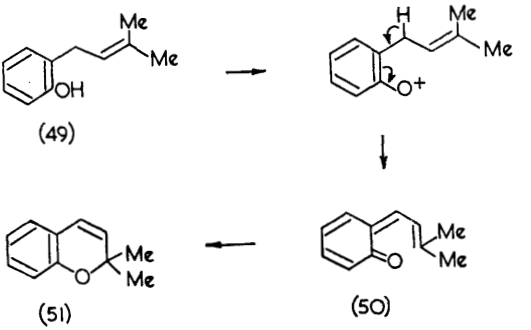


The ease of the transformation (44)→(45) is apparent from the ready formation of *ortho*-quinone methide-type dimers in both groups of vitamins.[41–43] In addition, the quinone methides (45) of the Vitamin K and uniquinone series have been trapped by reaction with acetyl chloride and acetic anhydride,[42] and styrene.[43] The suggestion has also been made[42] that 5-phosphomethyl-6-chromanols (46) are active phosphorylating species, generating metaphosphate on oxidation. However, there is, as yet, no direct evidence for the participation of quinone methides in oxidative phosphorylation.

(ii) *Biogenesis of* 2,2-*dimethylchromenes.* Ollis and Sutherland[44] have suggested the following mechanism for the biosynthesis of the ubiquitous

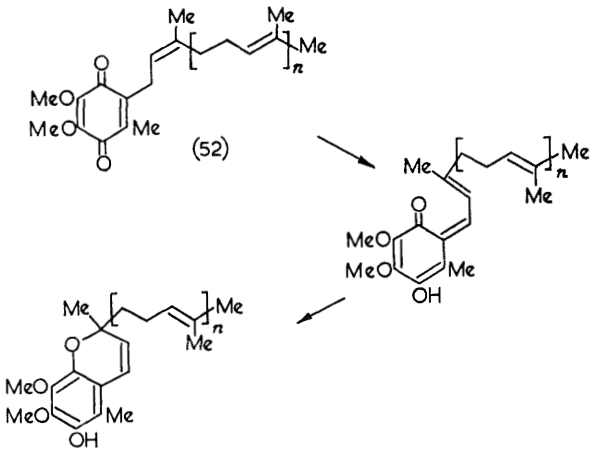
[40] M. Vilkas and E. Lederer, *Experientia*, 1962, **18**, 546.
[41] D. McHale and J. Green, *Chem. and Ind.*, 1964, 366.
[42] R. E. Erickson, A. F. Wagner, and K. Folkers, *J. Amer. Chem. Soc.*, 1963, **85**, 1535.
[43] P. Mamont, R. Azerad, P. Cohen, M. Vilkas, and E. Lederer, *Compt. rend.*, 1963, **257**, 706.
[44] W. D. Ollis and I. O. Sutherland, "Chemistry of Natural Phenolic Compounds", Pergamon Press, 1961, p. 84.

2,2-dimethylchromene system (51) from *o*-dimethylallylphenols (49):



While support for the formation of the quinone methide (50) is found in the occurrence of derivatives of the parent phenol (49) oxygenated at the benzylic position, these being presumed to arise by hydration of the intermediate (50), alternative processes may be considered for the oxidation of the phenol (49), as set out at the beginning of this section. Direct formation of the quinone methide (50), by hydride abstraction from the benzylic position, appears particularly attractive in this case.

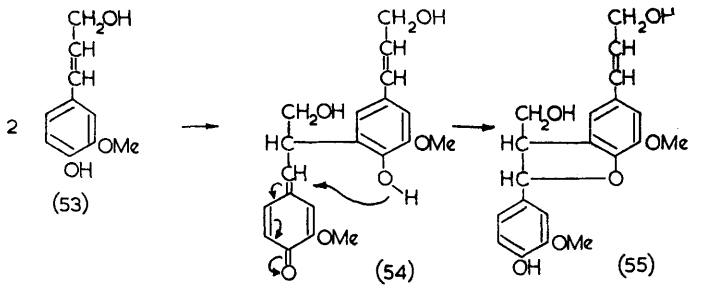
The mechanism proposed for the biosynthesis of 2,2-dimethylchromenes is analogous to that suggested for base-catalysed cyclisations of polyisoprenylated quinones such as the ubiquinones (52).[45]



(iii) *Lignin biosynthesis.* The part played by quinone methides in the biosynthesis of lignin has been uncovered by the work of Freudenberg.[46]

[45] B. O. Linn, C. H. Shunk, E. L. Wong, and K. Folkers, *J. Amer. Chem. Soc.*, 1963, **85**, 239.
[46] K. Freudenberg, *Fortschr. Chem. org. Naturstoffe*, 1962, **20**, 41.

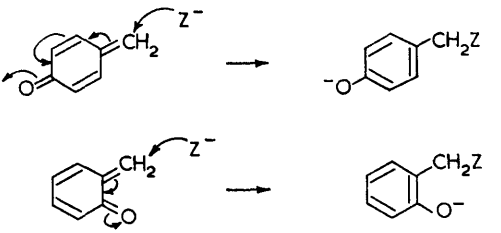
Both intermolecular and intramolecular additions of nucleophilic reagents to the quinonoid intermediates are involved. An illustration is the formation of dehydrodiconiferyl alcohol (55) by one-electron oxidation of coniferyl alcohol (53). Dimerisation of the mesomeric free radical produced yields the quinone methide (54), which cyclises as shown.



4. Reactions of Quinone Methides

Quinone methides are much more reactive than vinyl ketones, owing to the additional driving force of aromatisation which characterises all their reactions. These reactions can be divided into three main types, along the lines laid down by Hultzsch.[47] Many specific examples of these reaction types have already been mentioned.

(a) **Addition of Nucleophilic Reagents.**—The most characteristic property of quinone methides, both stable and unstable, is susceptibility to attack by nucleophils at the terminal methylene group:

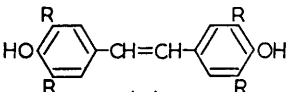


Reagents involved in these processes include alcohols, amines, carbohydrates, carboxylic acids, alkylmagnesium halides, hydrogen cyanide, metal hydrides, phenols, thiourea, water, and active methylene compounds. The net result is 1,4- or 1,6-addition of one molecule of the reagent, yielding a phenol. In the case of stable quinone methides, the addition is readily reversible, and this has been a useful guide in identifying the chromophoric system in the natural products.

[47] K. Hultzsch, *Angew. Chem.*, 1948, **60**, 179.

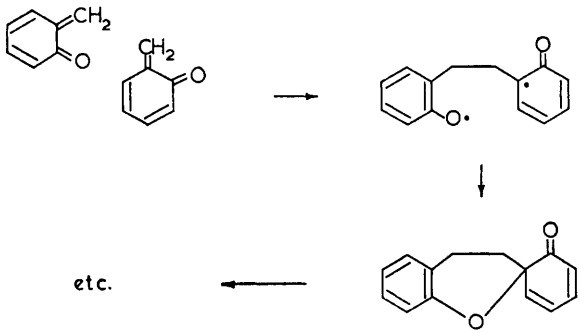
(b) **Polymerisation.**—Steric factors largely determine the stability of these compounds towards polymerisation, and simpler members of the group cannot be isolated in pure form when the terminal methylene group is unsubstituted. The *ortho* and *para* isomers give different products on polymerisation, the former yielding cyclic ethers and the latter undergoing tail-to-tail dimerisation.

(i) para-*Quinone methides.* Reactive members of the *para* series undergo a combined disproportionation and dimerisation, forming equal amounts of a stilbenequinone and a dihydroxybiphenylethane (see p. 353). They have also been found[48] to dimerise to dihydroxystilbenes of type (56).



(56)

(ii) ortho-*Quinone methides.* Simple compounds of the *ortho* series give dimers (*e.g.*, 30) or trimers (*e.g.*, 21) by a type of Diels–Alder reaction in which one molecule adds across a double bond of another.

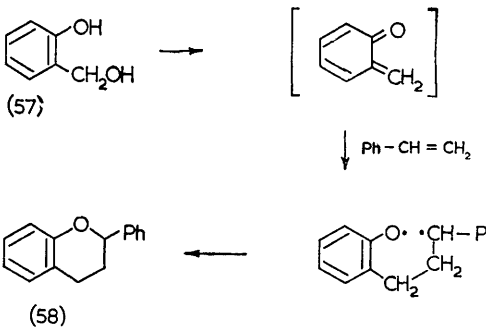


The reactions lead specifically to one of a number of possible types of product, as do dimerisations of $\alpha\beta$-unsaturated ketones and aldehydes.[49] The direction of addition can be rationalised on the basis of a stepwise rather than a synchronous mechanism, with formation of the most stable radical intermediates,[50] as indicated.

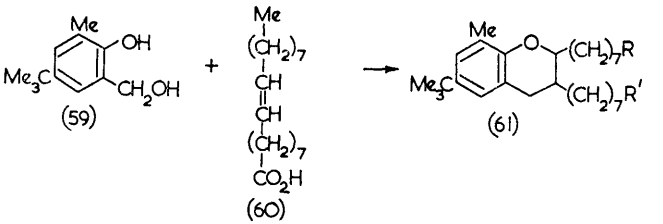
(c) **Addition of Olefins.**—Just as one molecule of a reactive quinone methide adds across a double bond of another, so will it combine with an olefin to give a chroman derivative. Thus, Hultzsch[51] has shown that *o*-

[48] H. Euler, E. Adler, and A. O. Caspersson, *Arkiv. Kemi*, 1943, **16***A*, No. 11, 1.
[49] K. Alder, H. Offermanns, and E. Ruden, *Ber.*, 1941, **74**, 926.
[50] J. D. Roberts and M. C. Caserio, "Basic Principles of Organic Chemistry", Benjamin, 1964, p. 268.
[51] K. Hultzsch, *Ber.*, 1941, **74**, 898; *J. prakt. Chem.*, 1941, **158**, 275.

hydroxymethylphenols react in this way with unsaturated compounds at high temperatures. An example of this is the formation of 2-phenylchroman (58) from saligenin (57) and styrene:



In the condensation of the phenolic alcohol (59) with oleic acid (60), both possible isomers (61; R = Me, R = CO_2H) and (61; R = CO_2H, R = Me) are obtained,[52] owing to the similar stabilities of the radical intermediates.



Reactions of this type are important industrially, since they are involved in the combination of drying oils with phenolic resins and perhaps also in vulcanisation.

Wakselman and Vilkas[53] have shown that the high temperatures of these reactions are necessary only for the formation of the quinonoid species, and not for their subsequent condensation with the olefins. Thus, substituted chromans can also be obtained by reaction of styrene or diphenylethylene at room temperature with *ortho*-quinone methides generated *in situ* from chloromethylphenols in basic media, or from hydroxymethylphenols by the action of acid.

The author thanks Professor R. H. Thomson for his helpful comments on the manuscript.

[52] G. R. Sprengling, *J. Amer. Chem. Soc.*,1952, **74**, 2937.
[53] M. Wakselman and M. Vilkas, *Compt. rend.*, 1964, **258**, 1526.