Chemistry of Azidoquinones and Related Compounds

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1 Introduction

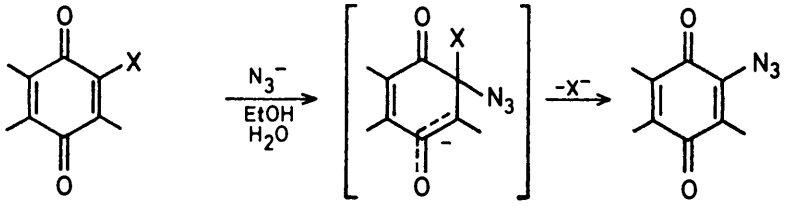
Azidoquinones constitute a remarkably versatile class of synthetically useful reagents. They are easily prepared and can function as penultimate precursors to a large variety of other compounds, among which are azidohydroquinones,[1,2] aminoquinones,[1-3] γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides,[4] 2-cyanocyclopent-4-ene-1,3-diones,[5] azepine-2,5-diones,[6] diacyl cyanides,[7] 3-cyano-2-aza-1,4-quinones,[8] 4-acetoxy-1,2-quinone-2-(*N*-acetyl)imines,[9] *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyanobuta-1,3-dienes,[9] 2-alkenyl-2,3-dihydroindole-4,7-diones,[10] benzo[*f*]indole-4,9-diones,[11] and cyanoketens.[12] Many of these compounds are themselves members of new or relatively unexplored classes of compound and should find synthetic utility in their own right. It is the purpose of this review to discuss the synthesis and chemistry of azidoquinones as well as certain of those compounds to which they are structurally and chemically related.

2 Synthesis of Azidoquinones

The literature contains over seventy examples of variously substituted mono-, di-, and poly-azido-1,4-benzo-, -1,4-naphtho-, and -1,2-naphtho-quinones. Almost without exception these compounds are prepared by the reaction of halogeno- or acetoxy-substituted quinones (1) with inorganic azide in aqueous alcohol, being generally obtained as highly coloured crystalline solids which are safely manipulated under normal laboratory conditions. One exception is tetra-azido-1,4-benzoquinone,[3,13,14] a beautiful deep-purple solid which is extremely shock and thermally sensitive and should be handled with *great caution*. The fact that

[1] L. F. Fieser and J. L. Hartwell, *J. Amer. Chem. Soc.*, 1935, **57**, 1482.
[2] H. W. Moore and H. R. Shelden, *J. Org. Chem.*, 1968, **33**, 4019.
[3] E. Winkelmann, *Tetrahedron*, 1969, **25**, 2427.
[4] H. W. Moore, H. R. Shelden, D. W. Deters, and R. J. Wikholm, *J. Amer. Chem. Soc.*, 1970, **92**, 1675.
[5] W. Weyler, jun., D. S. Pearce, and H. W. Moore, *J. Amer. Chem. Soc.*, 1973, **95**, 2603.
[6] H. W. Moore, H. R. Shelden, and W. Weyler, jun., *Tetrahedron Letters*, 1969, 1243.
[7] J. A. Van Allen, W. J. Priest, A. S. Marshall, and G. A. Reynolds, *J. Org. Chem.*, 1968, **33**, 1100.
[8] D. S. Pearce and H. W. Moore, unpublished results.
[9] D. S. Pearce, M. S. Lee, and H. W. Moore, *J. Org. Chem.*, in the press.
[10] P. Germeraad and H. W. Moore, *J. Org. Chem.*, in the press.
[11] P. Germeraad and H. W. Moore, *J. Org. Chem.*, in the press.
[12] H. W. Moore and W. Weyler, jun., *J. Amer. Chem. Soc.*, 1970, **92**, 4132.
[13] A. Korezynsky and St. Namylslowski, *Bull. Soc. chim. France*, 1924, **35**, 1186.
[14] K. Fries and P. Ochwat, *Ber.*, 1923, **56**, 1291.

quinones bearing halogeno-[15] as well as acetoxy-[16] groups are readily available translates to a versatile synthesis of azidoquinones (2). Yields are usually high, particularly when the leaving group is a halide ion.



X = Cl, Br, or OCOMe

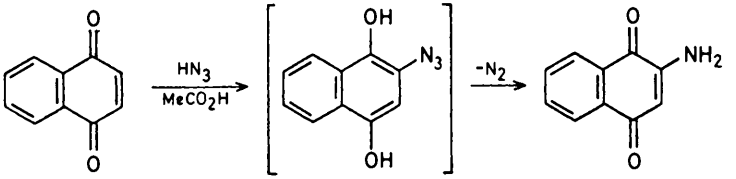
3 Reactions of Azidoquinones

A. Reduction.—Azidoquinones are reduced under a variety of conditions to the corresponding primary aminoquinones ($Na_2S_2O_4$, H_2/Pd–C, H_2/Pt_2O, H_2/Pt–C).[1,2,17–19] The scope of this reaction has not been extensively explored. However, it does appear to provide potentially one of the best methods of introducing an amino-substituent on to the quinoid nucleus. The yields are high and the conditions mild.

The mechanism of the sodium dithionite reduction is quite interesting in that the quinone nucleus is initially reduced to the hydroquinone which then apparently disproportionates to the corresponding aminoquinone and nitrogen. This latter step was proposed by Fieser and Hartwell[1] to explain the smooth conversion of 1,4-naphthoquinone (3) into 2-amino-1,4-naphthoquinone (4) upon its treatment with hydrazoic acid in glacial acetic acid. Subsequent investigations showed that azidohydroquinones do indeed undergo a thermally induced oxidation–reduction to the corresponding aminoquinones (5).[2,20] Whether this is an intra- or inter-molecular process is not clear and awaits further work. An implication that the latter is likely comes from the fact that the unsymmetrical diazide, 2,5-diazido-3-methyl-5-isopropyl-1,4-benzoquinol (6) gives 2-amino-5-azido-3-methyl-6-isopropyl-1,4-benzoquinone (7) and 2-amino-5-azido-6-methyl-3-isopropyl-1,4-benzoquinone (8) in the ratio of 2:1. Closer to a 1:1 mixture might be anticipated for an intramolecular reaction. The thermal decomposition of symmetrical diazidohydroquinones, (9) and (11), gives a

[15] H. W. Moore, D. L. Maurer, D. S. Pearce, and M. S. Lee, *J. Org. Chem.*, 1972, **37**, 1984.
[16] J. F. W. McOmie and J. M. Blatchly, *Org. Reactions*, 1972, **17**, 199.
[17] R. J. Wikholm and H. W. Moore, *Chem. Comm.*, 1971, 1070.
[18] Z. Cheng, K. Yuen, and C. C. Cheng, *J. Medicin. Chem.*, 1970, **13**, 264.
[19] Y. Watanabe, K. Nakajima, T. Seki, and H. Ozawa, *Chem. and Pharm. Bull. (Japan)*, 1970, **18**, 2208.
[20] H. W. Moore, H. R. Shelden, and D. F. Shellhamer, *J. Org. Chem.*, 1969, **34**, 1999.

specific reduction of only one azide group and provides an efficient route to 2-amino-5-azido-1,4-benzoquinones (10) and (12), respectively.



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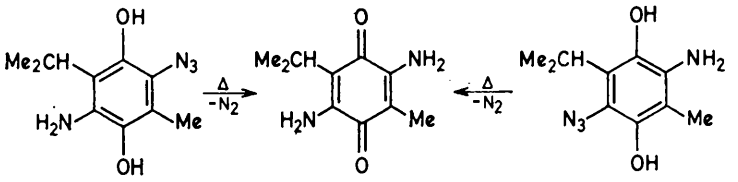

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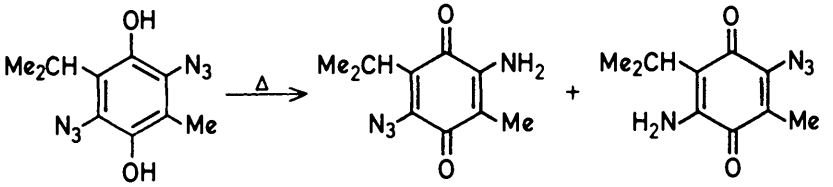
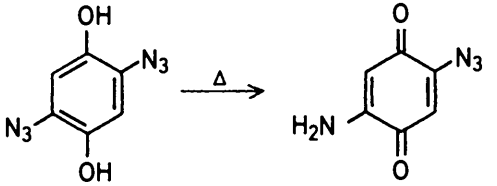


(6) (7) (8)



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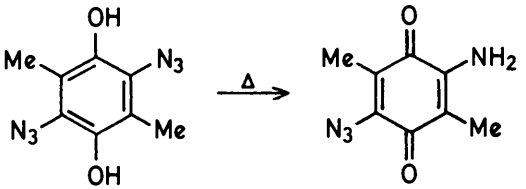
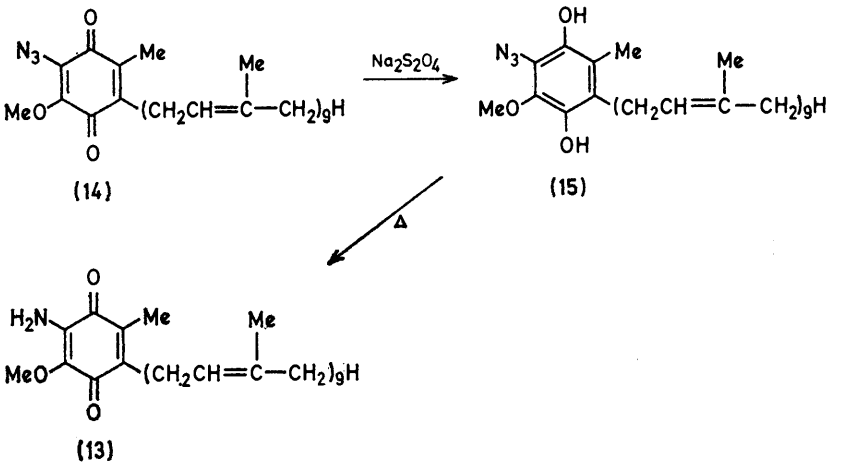


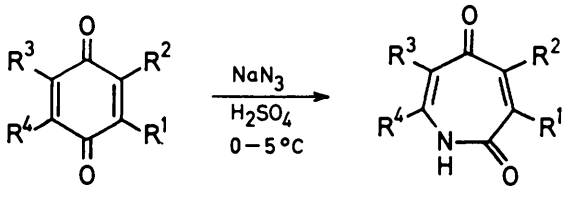
(11) (12)

An additional use of this reaction has recently appeared.[19] The naturally occurring aminoquinone rhodoquinone-9 (13)[21] was obtained from the azidoquinone (14) *via* sodium dithionite reduction to the azidohydroquinone (15) and subsequent thermal decomposition.



One can envisage other non-reductive routes to azidohydroquinones. For example, the 1,4-addition of hydrazoic acid to 1,4-benzo- and 1,4-naphthoquinones has been considered. As mentioned above, such an addition was proposed by Fieser and Hartwell[1] to explain the formation of 2-amino-1,4-naphthoquinone (4) from 1,4-naphthoquinone and sodium azide in glacial acetic acid. Under the same conditions, benzoquinone reacts to give a 35% yield of 2,5-diazidohydroquinone[20,22] (9). However, 2-methyl-1,4-naphthoquinone and 4-methyl-1,2-naphthoquinone failed to react.[1] Under strongly acidic conditions, cold concentrated sulphuric acid, the reaction takes an entirely different course; variously alkyl-substituted quinones (16a—e) react with hydrazoic acid to give azepinediones (17a—e) rather than azidohydroquinones.[23–25] Under the same conditions 2-hydroxy-1,4-naphthoquinone (18) undergoes a deep-seated rearrangement to 3-oxo-$\Delta^{1\alpha}$-isoindolineacetic acid (19).[26] Thymoquinone (20) reacts with sodium azide in trichloroacetic acid at 65 °C to give the butenolide (21).[2,27,28] It is shown below that this last reaction does involve the initial 1,4-addition of hydrazoic acid to the quinone giving an azidohydroquinone intermediate. Quinone mono- and di-imines appear to add readily hydrazoic

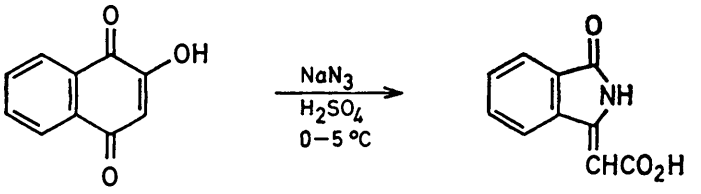
[21] R. Powls and F. W. Hemming, *Phytochemistry*, 1966, **5**, 1235.
[22] E. Oliveri-Mandala and E. Calderao, *Gazzetta*, 1915, **45**, 307.
[23] D. Misiti, H. W. Moore, and K. Folkers, *Tetrahedron* 1966, **22**, 1201.
[24] R. W. Richards and R. M. Smith, *Tetrahedron Letters*, 1966, 2361.
[25] G. R. Bedford, G. Jones, and B. R. Webster, *Tetrahedron Letters*, 1966, 2367.
[26] H. W. Moore and H. R. Shelden, *J. Org. Chem.*, 1967, **32**, 3603.
[27] A. H. Rees, *Chem. and Ind.*, 1964, 931.
[28] A. H. Rees, *Chem. and Ind.*, 1965, 1298.



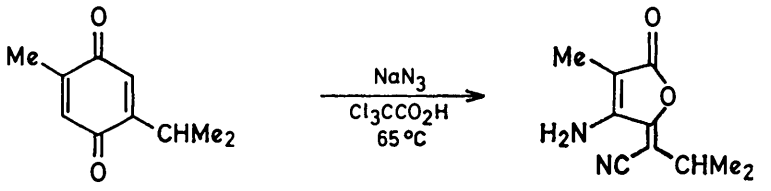
(16) (17)

	R^1	R^2	R^3	R^4
a;	H	Me	Me	Me
b;	H	$CHMe_2$	H	Me
c;	H	Me	—CH=CH—CH=CH—	
d;	H	Me	H	Me
e;	Me	Me	Me	Me

acid (NaN_3–$MeCO_2H$), giving the corresponding aryl azides in good yield (68—99%).[29] For example, 1,4-benzoquinonedibenzenesulphonimide (22) and 1,4-benzoquinonebenzenesulphonimide (24) react with sodium azide in aqueous acetic acid to give, respectively, (23) and (25) in greater than 90% yield.

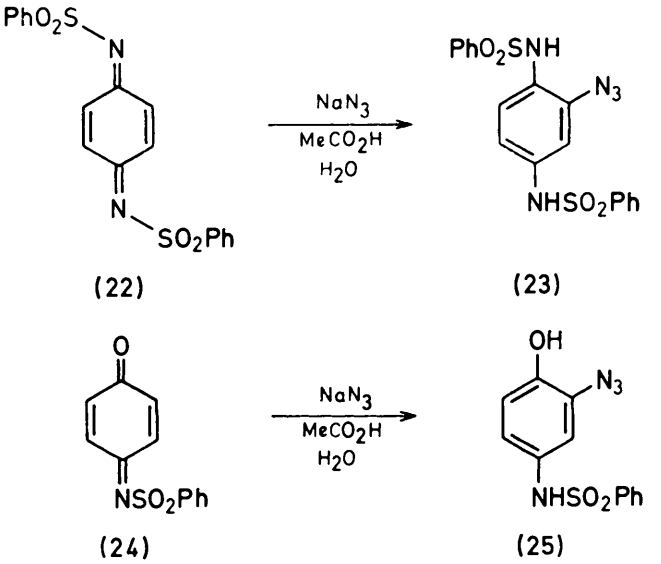


(18) (19)



(20) (21)

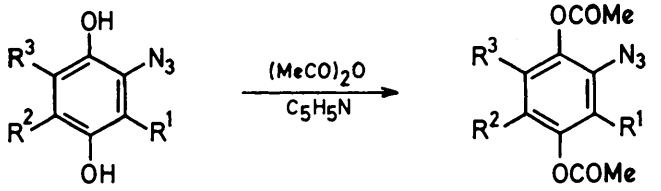
[29] R. Adams and W. Reifschneider, *Bull. Soc. chim. France*, 1958, 23.



(22) (23)

(24) (25)

B. Synthesis and Thermolysis of 1,4-Diacetoxyazidobenzenes.—The facile sodium dithionite reduction of azidoquinones to the corresponding hydroquinones not only provides a route to aminoquinones, but also potentially allows the synthesis of a large variety of other aryl azides by functionalization of the phenolic hydroxy-groups. For example, the diacetates (26) of a variety of mono- and di-azidoquinones have been prepared by the reaction of the corresponding azidohydroquinones (27) with acetic anhydride–pyridine.[9,20]

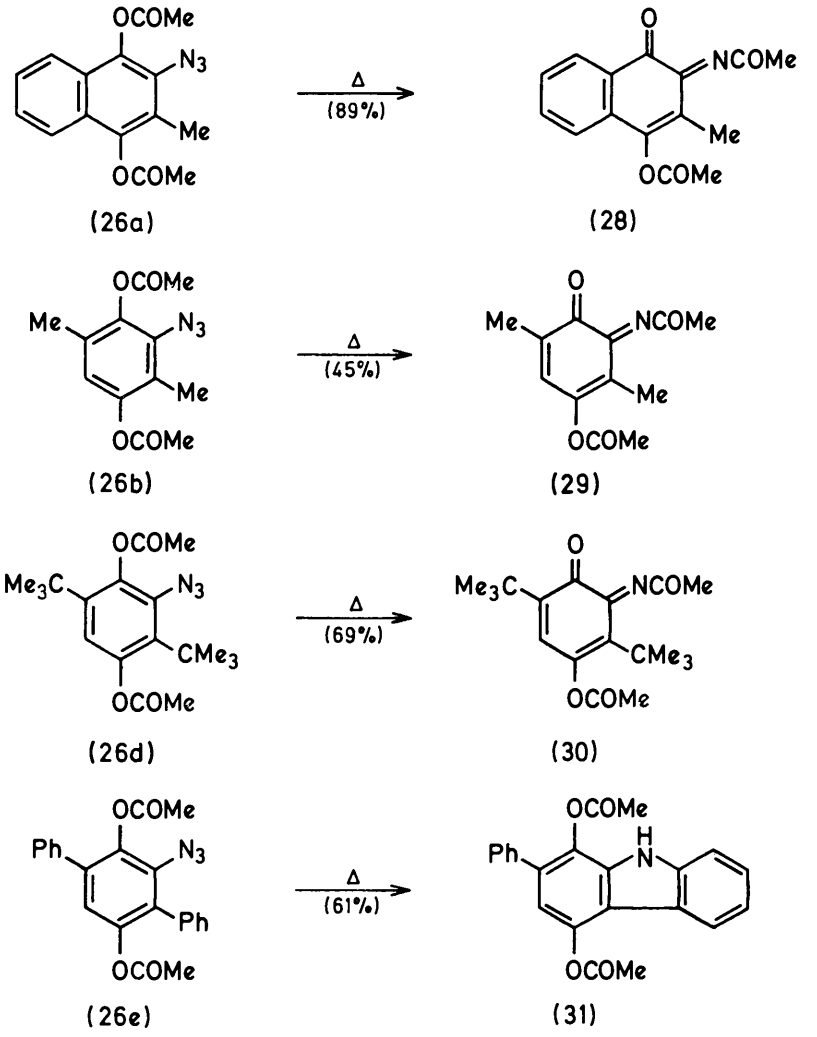


(27) (26)

	R^1	R^2	R^3
a;	Me	—CH=CH—CH=CH—	
b;	Me	H	Me
c;	H	Me	H
d;	CMe_3	H	CMe_3
e;	Ph	H	Ph
f;	H	N_3	H
g;	CMe_3	N_3	CMe_3
h;	N_3	—CH=CH—CH=CH—	
i;	N_3	$—CH_2—CH_2—CH_2—CH_2—$	
j;	N_3	Ph	H
k;	N_3	Me	Me

The thermal chemistry of certain of these 1,4-diacetoxyazidobenzenes has been studied.[9] The monoazides, (26a, b, and d) smoothly rearrange with nitrogen loss in refluxing chlorobenzene to the respective *N*-acyl-1,2-quinoneimines (28)—(30) whereas (26e) gives the carbazole (31) when decomposed under the same conditions.

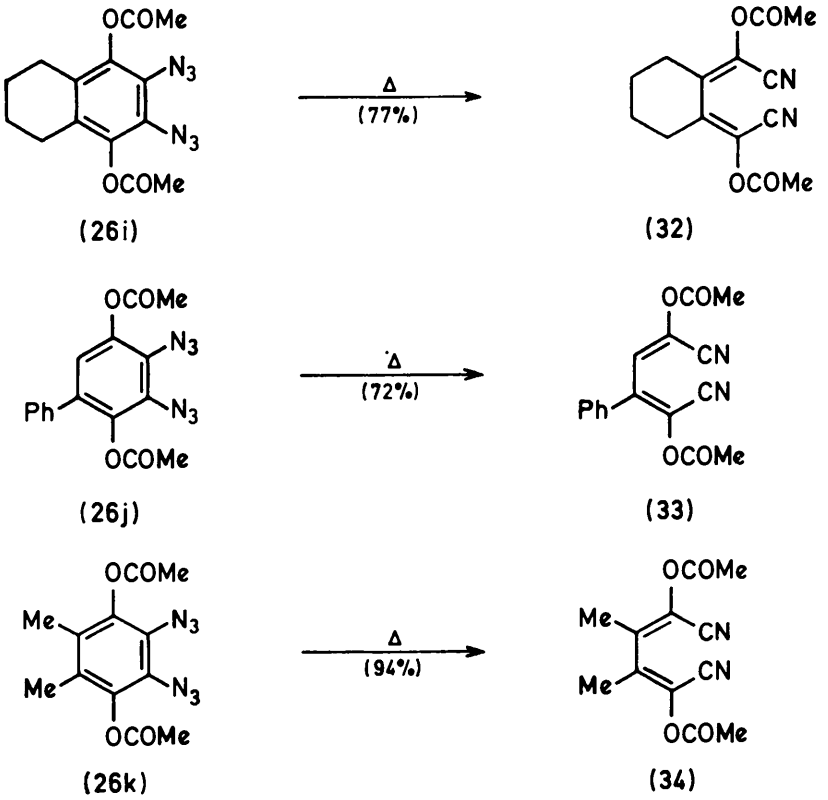
The formation of the *N*-acyl-1,2-quinoneimines is unusual since it involves an acyl migration to an azide nitrogen, a rarely observed process.[30] Other known



[30] W. Lwowski, 'Nitrenes', Interscience, New York, 1970, p. 72.

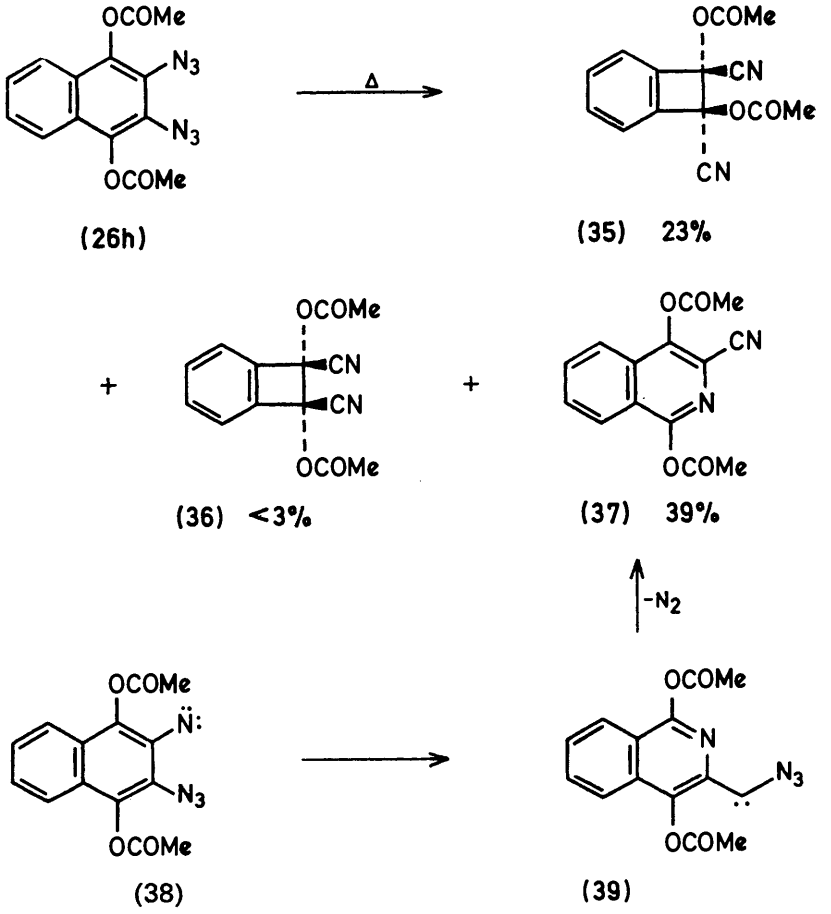
examples in which such a migration takes place are found in the photolytic decomposition of dimethyl diazidomalonate[31] and the pyrolytic decomposition of 2,2-diazido- and 2-azido-2-aryl-indane-1,3-dione.[32]

Unlike the monoazide series, the 1,4-diacetoxy-2,3-diazidobenzenes (26i—k) smoothly undergo thermally induced ring-cleavage in refluxing *o*-dichlorobenzene to give the *trans,trans*-1,4-diacetoxy-*cis,cis*-1,4-dicyanobuta-1,3-dienes (32)—(34), respectively.[9] These highly functionalized dienes, which can be regarded as the acylated cyanohydrins of bis-ketens, are masked 1,4-dicarbonyl moieties and may find according synthetic utility. The formation of 1,3-dienes from *o*-diazidobenzenes appears to be a general reaction, the first examples having been reported by Hall and Patterson.[33] Related transformations have been observed for the lead tetra-acetate oxidation of *o*-phenylenediamines.[34]



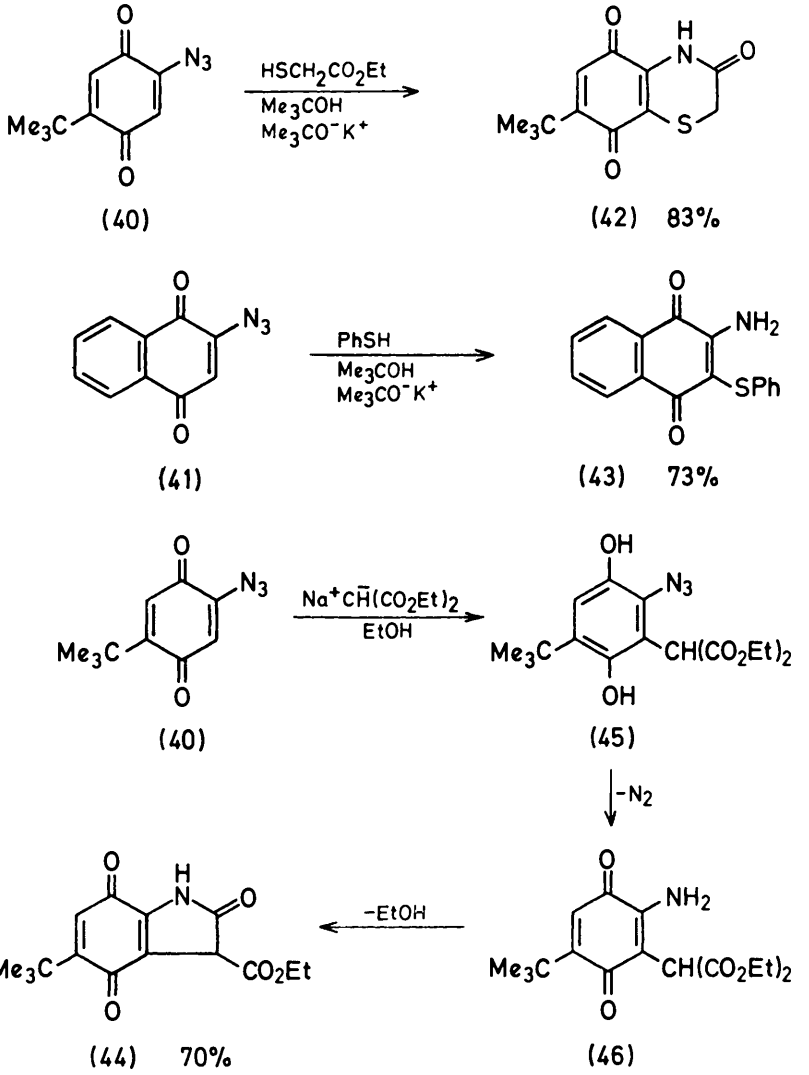
[31] R. M. Moriarty and P. Serridge, *J. Amer. Chem. Soc.*, 1971, 93, 1534.
[32] H. W. Moore and D. S. Pearce, *Tetrahedron Letters*, 1971, 1621.
[33] J. H. Hall and E. Patterson, *J. Amer. Chem. Soc.*, 1967, 89, 5856.
[34] K. Nakagawa and H. Onove, *Chem. Comm.*, 1965, 396.

A particularly interesting example of this pyrolytic cleavage was observed when 1,4-diacetoxy-2,3-diazidonaphthalene (26h) was thermally decomposed. The presumed intermediate quinodimethane collapsed to the *trans*- and *cis*-benzocyclobutenes (35) and (36). In addition, the unexpected isoquinoline (37) was isolated as the major product. The formation of 1,4-diacetoxy-3-cyanoisoquinoline (37) from (26h) is most intriguing and must result from a very deep-seated rearrangement. An attractive possibility for such a mechanism is based upon the fascinating gas-phase equilibrium of phenylnitrenes and α-pyridylcarbenes.[35] In the case at hand, the nitrene (38) could rearrange to the azidocarbene (39), which upon nitrogen loss would give (37).



[35] W. D. Crow and C. Wentrup, *Tetrahedron Letters*, 1968, 6149.

C. Reactions of Azidoquinones with Nucleophiles.—The reactions of azidoquinones with nucleophilic species have not received detailed study. This should be a worthwhile area for investigation since both quinone nuclei and azide groups are susceptible to nucleophilic attack. The former would give azidohydroquinones and their transformation products, *e.g.* substituted aminoquinones, and the latter could result in diazo-transfer reactions.[36] Examples related to each have been observed. 2-Azido-5-t-butyl-1,4-benzoquinone (40) and 2-azido-1,4-naph-



(40) (42) 83%

(41) (43) 73%

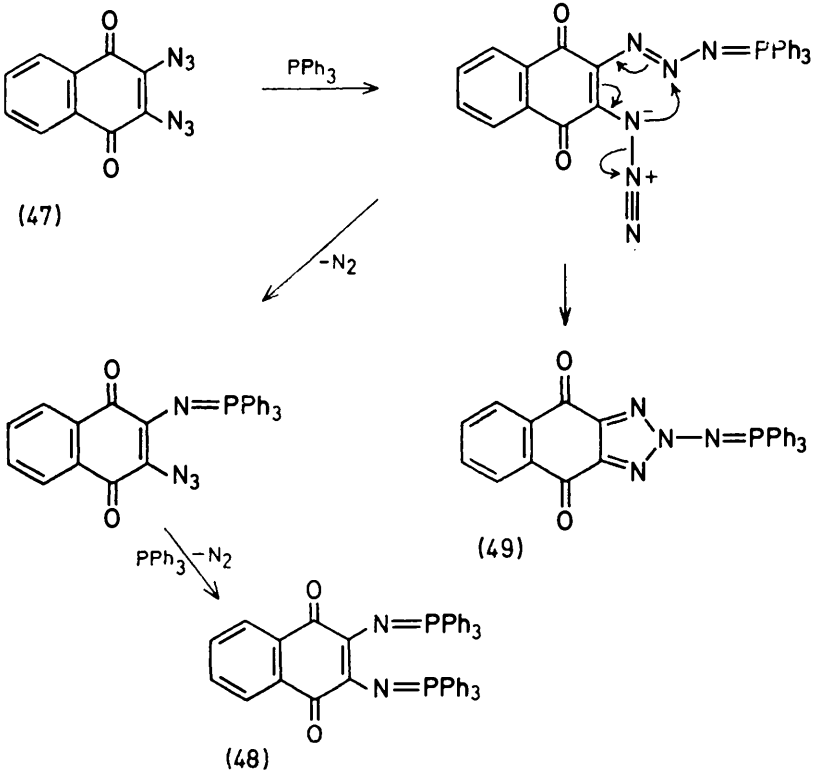
(40) (45)

(46) (44) 70%

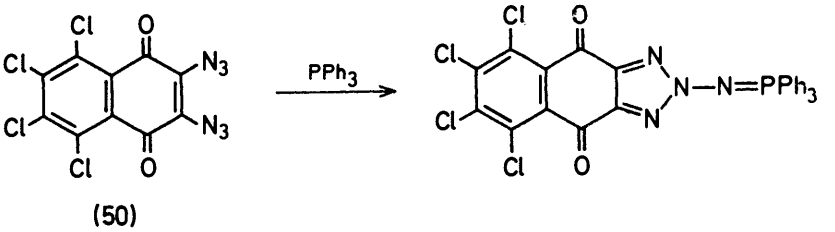
[36] M. Regitz, *Synthesis*, 1972. 351.

thoquinone (41) readily react with thiol nucleophiles. For example, the former reacts with ethyl mercaptoacetate to give the heterocyclic quinone (42) and the latter reacts with thiophenol to give the aminoquinone (43).[37] More interestingly, the enolate anion of diethyl malonate reacts with (40) giving a 70% yield of the indolequinone derivative (44), presumably arising *via* the azidohydroquinone (45) and aminoquinone (46) intermediates.[37]

Mosby and Silva[38–40] have investigated the reactions of certain 2,3-diazido-1,4-quinones with phosphines and phosphites. When two molar equivalents of triphenylphosphine were added to a solution of 2,3-diazido-1,4-naphthoquinone (47), 2,3-triphenylphosphoranylideneamino-1,4-naphthoquinone (48) and the interesting and unanticipated triazoline (49) were isolated. The ratio of these products was markedly dependent upon the solvent employed; in benzene the ratio (48):(49) was 1.0:0.8 whereas in dichloromethane it was 0.09:1.0. There



[37] G. Cajipe, D. Ratolo, and H. W. Moore, *Tetrahedron Letters*, in the press.
[38] W. L. Mosby and M. L. Silva, *J. Chem. Soc.*, 1964, 3990.
[39] W. L. Mosby and M. L. Silva, *J. Chem. Soc.*, 1965, 1003.
[40] W. L. Mosby and M. L. Silva, *J. Chem. Soc.*, 1965, 2727.



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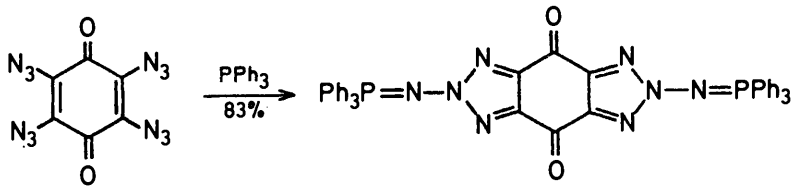

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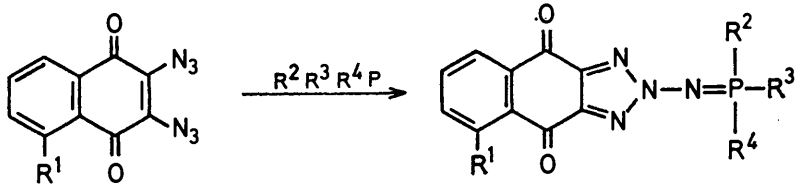
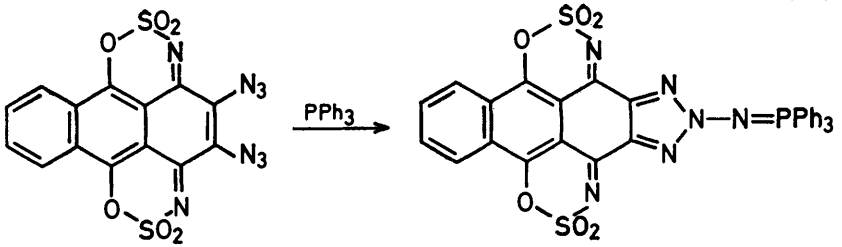


(52)

	R^1	R^2	R^3	R^4	*Yield* %
a;	NO_2	Ph	Ph	Ph	53
b;	NH_2	Ph	Ph	Ph	37
c;	NHCOMe	Ph	Ph	Ph	57
d;	H	Bu	Bu	Bu	21
e;	H	$C_5H_{10}N$	$C_5H_{10}N$	Ph	50
f;	H	$C_5H_{10}N$	$C_5H_{10}N$	C_5H_9N	49

appears to be a strong tendency for triazoline ring formation, since the other vicinal diazides (50), (51), (52a—f), (53), and (54) also gave the heterocyclic ring system upon reaction with phosphines. However, *o*-diazidobenzene (55) reacts with triphenylphosphine in a completely 'normal' fashion to give the mono- (56) and bis- (57) triphenylphosphoranylideneamino-compounds.

When one molar equivalent of triphenylphosphine was treated with 2,3-diazido-1,4-naphthoquinone (47) a 65% yield of the triazoline (49) along with a 7% yield of 2-azido-3-triphenylphosphoranylideneamino-1,4-naphthoquinone was obtained.[39] In contrast, when (47) was treated with one equivalent of trimethyl phosphite, (58) was formed in 87% yield and upon acid hydrolysis it



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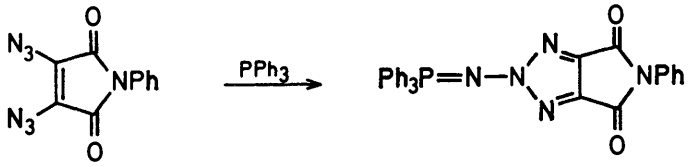

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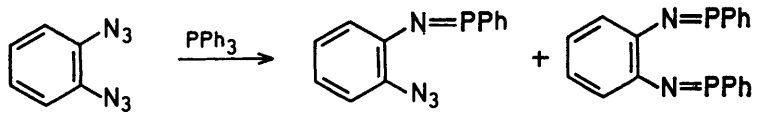
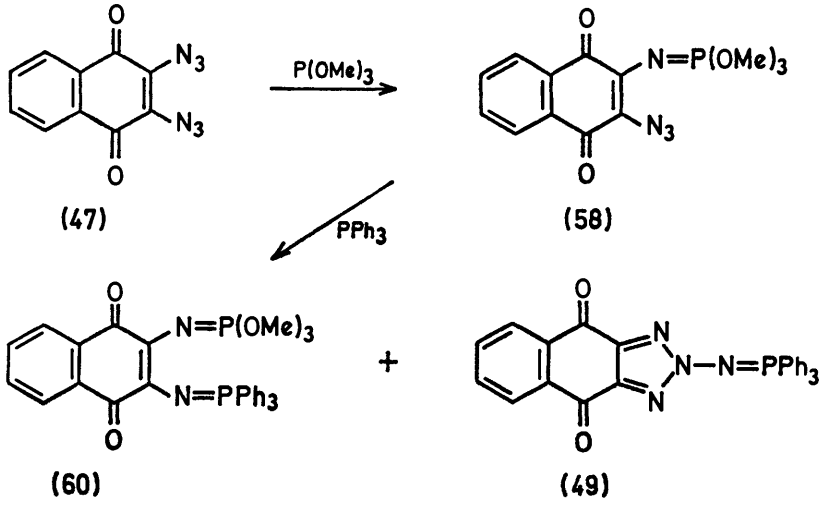
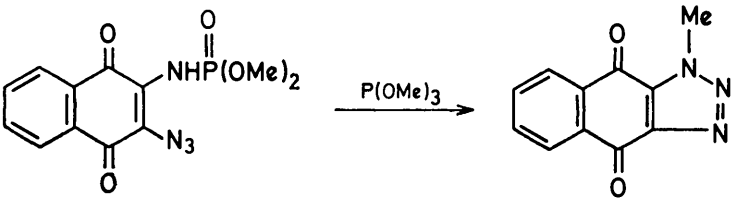


(55) (56) (57)

gave the phosphoramidate (59) in 84% yield.[40] Perchloro-2,3-diazido-1,4-naphthoquinone behaved similarly. The phosphorimidate (58) did not react with another equivalent of trimethyl phosphite but it did react with triphenylphosphine to give (60) and (49).



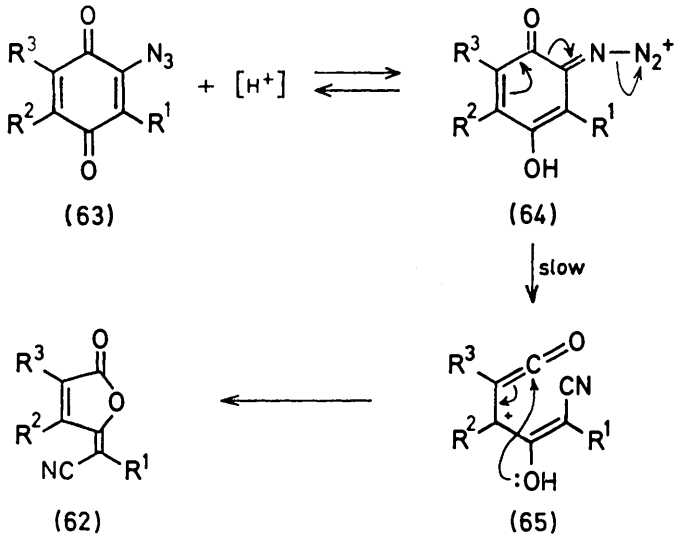
(47) (58) (60) (49)



(59) (61)

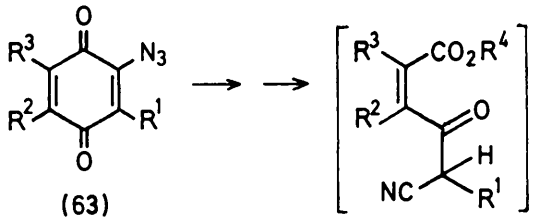
A most interesting transformation was observed when (59) was treated with one equivalent of trimethyl phosphite; a 33% yield of 1-methyl-1*H*-naphtho-[2,3-*d*]triazole-4,9-dione (61) was obtained. It is proposed[40] that (61) arises *via* a mechanism in which the azide group suffers the loss of the single terminal nitrogen, a reaction which appears to have no precedent in azide chemistry.

D. Acid-catalysed Rearrangements of Azidoquinones.—2-Azido-1,4-benzo- and -1,4-naphtho-quinones and certain 2,5-diazido-1,4-benzoquinones undergo a stereospecific rearrangement to γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides (62) when decomposed in cold (0—5 °C) concentrated sulphuric acid.[2,4,20] The general structures (62) and (63) illustrate the overall chemical transformation. This reaction generally proceeds in high yields and gives the butenolide in which the cyano-substituent is *trans* to the lactone oxygen. This reaction has been shown[4] to involve an initial protonation on that carbonyl oxygen which is in direct conjugation with the azide group to give the iminodiazonium ion (64). This intermediate suffers heterolytic cleavage with nitrogen loss in the rate-determining step to give (65), which then undergoes *o*-acylation to the butenolides (62). These butenolides (62) are actually masked active methylenes, *i.e.* (66), and should find synthetic utility as such.



(63) (64) (65) (62)

For R^1—R^3, see Table 1



(63) (66)

An example of this rearrangement is the synthesis of vulpinic acid, a natural product occurring in a number of lichens. Commercially available 2,5-diphenyl-1,4-benzoquinone (67) was converted into the natural product (68) as shown.

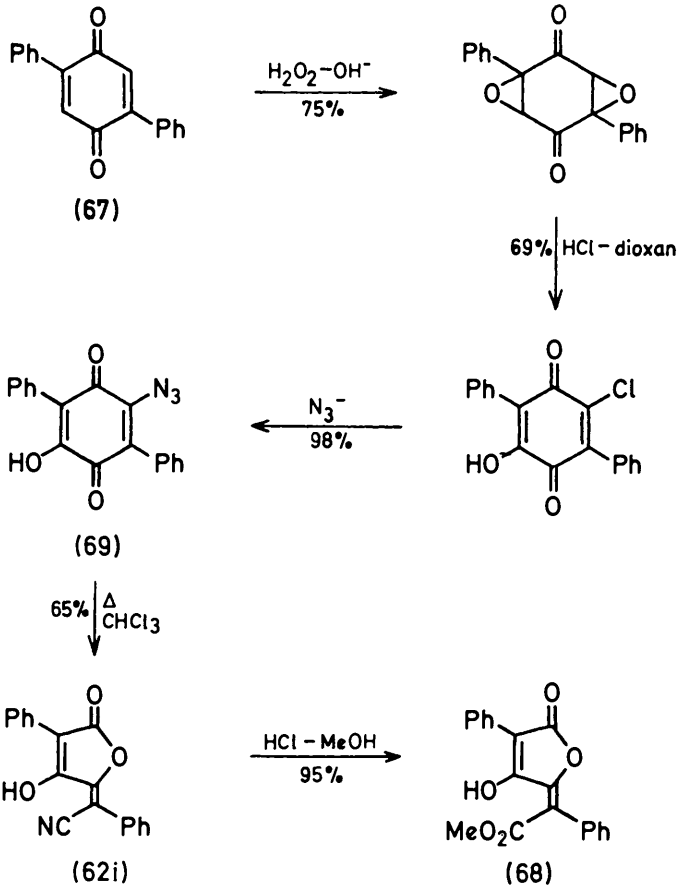
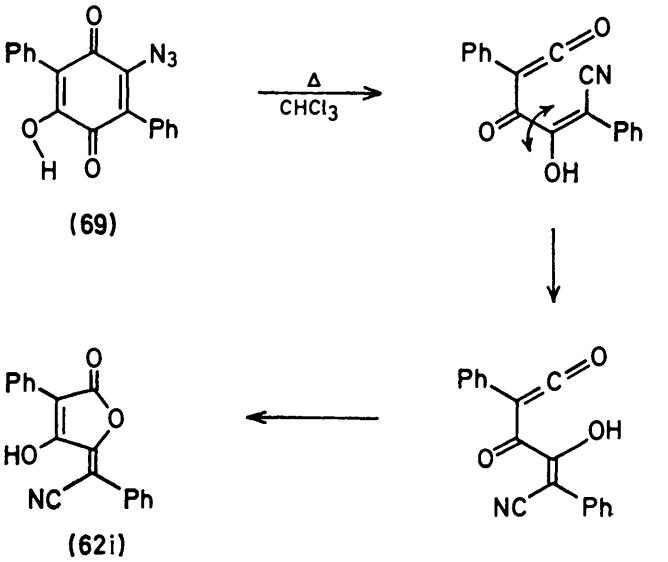


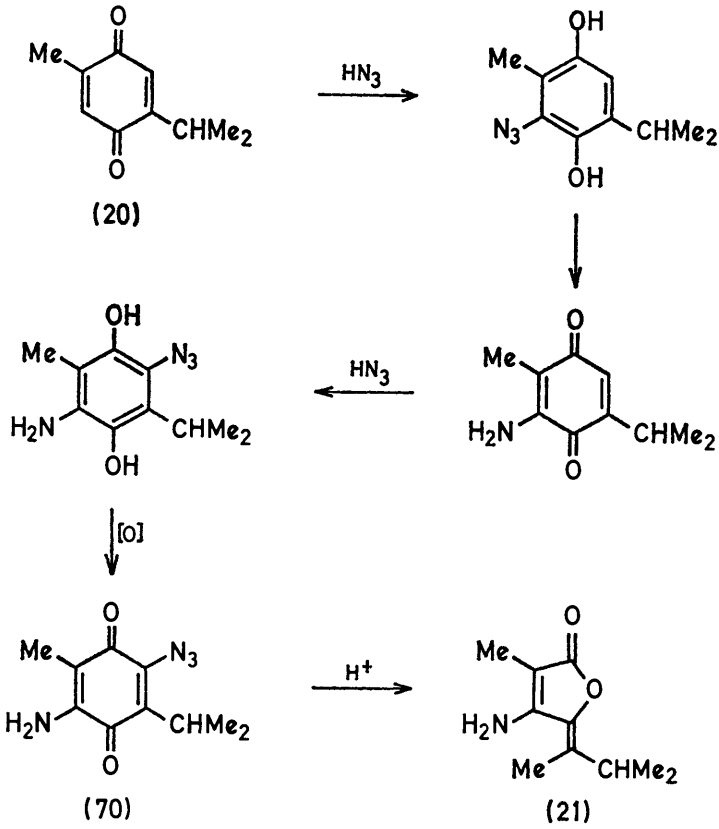
Table 1 *Substituents in compound* (62)

	R^1	R^2	R^3	*Yield* %
a;	H	Me	H	65
b;	H	CMe_3	H	95
c;	H	Ph	H	80
d;	H	NH_2	H	44
e;	Me	H	Me	70
f;	Ph	H	Ph	30
g;	Me	NH_2	$CHMe_2$	94
h;	$CHMe_2$	NH_2	Me	95
i;	Ph	OH	Ph	65
j;	H	N_3	H	73
k;	$CHMe_2$	N_3	$CHMe_2$	87
l;	Me	N_3	Me	87
m;	H	—CH=CH—CH=CH—		59
n;	Me	—CH=CH—CH=CH—		95
o;	CMe_3	H	CMe_3	87
p;	Br	CMe_3	H	86
q;	Me	H	$CHMe_2$	87

The conversion of (69) into (62i) required no external source of acid. Simply refluxing a solution of the azidoquinone (69) in chloroform for a few minutes induced its rearrangement to the butenolide in 65% isolated yield. Here, an intramolecular acid-catalysed process can be envisaged, as shown. This rearrangement is not simply a thermal process since, as is discussed below, azidoquinones thermally ring-contract to 2-cyanocyclopent-4-ene-1,3-diones.

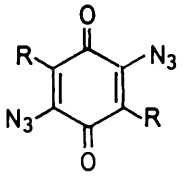


Earlier, it was pointed out that thymoquinone (20) rearranges to the butenolide (21) when treated with hydrazoic acid in trichloroacetic acid at 64 °C.[27,28] One of the key steps in this reaction has been shown to be an example of the acid-catalysed rearrangement of an azidoquinone, namely, the rearrangement of (70).[2]

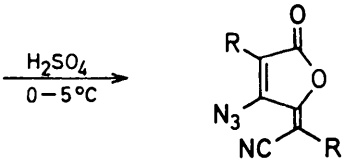


The rearrangement of azidoquinones to butenolides appears to be quite general. Exceptions which have been reported are for 2,5-diazido-1,4-benzoquinones (71) with bulky substituents (t-butyl and t-pentyl) in the 3- and 6-positions, and for 2-azido-3-vinyl-1,4-naphthoquinones (72). The former react to give the tetrazoles (73)[41] *via* the butenolide intermediate (74). The latter do not rearrange, but rather undergo ring-closure to the respective indolequinones (75).[11]

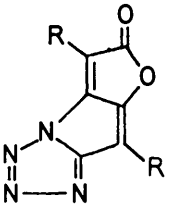
[41] W. Weyler, jun., P. Germeraad, and H. W. Moore, *J. Org. Chem.*, in the press.



(71)

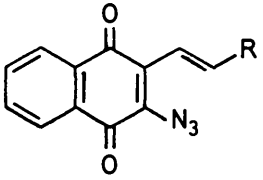


(74)

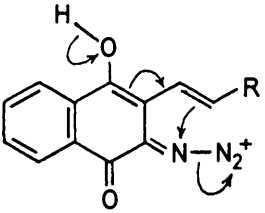


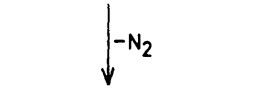
(73)

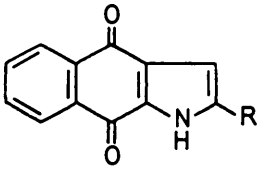
R = CMe_3 76%
R = CMe_2Et 80%



(72)



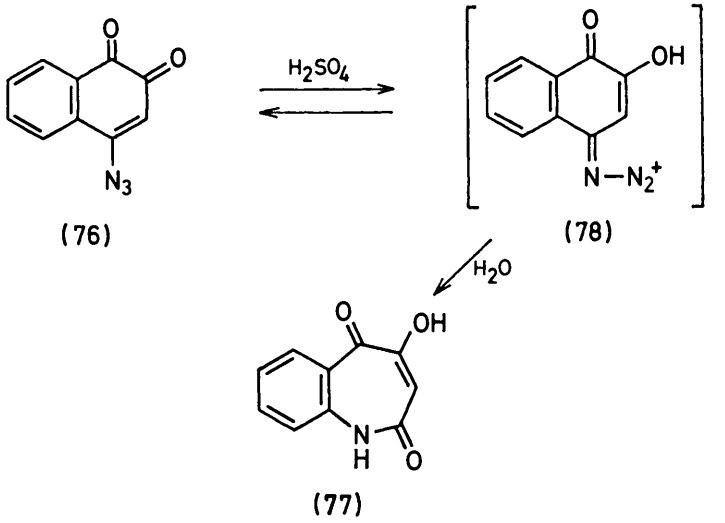




(75)

R = Me 67%
R = Pr 94%
R = Ph 24%

The chemistry of azido-1,2-quinones has barely received attention. The only known member of this series is 4-azido-1,2-naphthoquinone (76). Interestingly, this azide undergoes facile ring-expansion to 2,5-*H*-4-hydrozybenzoazepine-2,5-dione (77) when treated with cold concentrated sulphuric acid.[6] In passing, it is interesting to note the marked difference between chemistry of the iminodiazonium ions (64m) and (78); the former ring-contracts and the latter ring-expands.

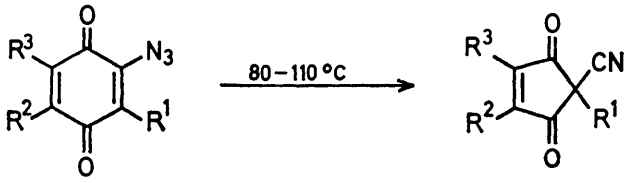


(76) (78) (77)

E. Thermal Rearrangements of 2-Azido-1,4-quinones.—Thermal decomposition of azidoquinones in refluxing benzene or toluene results in their smooth rearrangement to 2-cyanocyclopent-4-ene-1,3-diones (79).[5] This constitutes an efficient entry into this carbocyclic ring system which is of significant importance. For example, various natural products are 2-acylcyclopent-4-ene-1,3-diones, *i.e.*, linderone,[42] methyl-linderone,[42] lucidone,[43] methyl-lucidione,[43] calythrone,[44] and a number of hop constituents.[45] Various 2-substituted indane-1,3-diones show marked pharmacological activity as anticoagulants.[46] Pyrethrins[47] are among the most important natural insecticides and are related structurally to the cyclopentenedione ring system.[48] Indeed, even the prostaglandins,[49] which are of

[42] A. K. Kiang, H. H. Lee, and K. Y. Sim, *J. Chem. Soc.*, 1962, 4338.
[43] H. H. Lee, *Tetrahedron Letters*, 1968, 4243.
[44] R. O. Hellyer, *Austral. J. Chem.*, 1968, **21**, 2825.
[45] R. Stevens, *Chem. Rev.*, 1967, **67**, 19.
[46] R. Biggs and R. G. MacFarlane, 'Human Blood Coagulation', Oxford, 3rd Edn., Oxford University Press, Oxford, 1962.
[47] L. Crombie and M. Elliot, *Fortschr. Chem. org. Naturstoffe*, 1961, **19**, 120.
[48] R. A. Lee Mahiew, M. Carson, and R. W. Kierstead, *J. Org. Chem.*, 1968, **33**, 3660.
[49] R. Clarkson, *Progr. Org. Chem.*, 1973, **8**, 1.

pivotal biological importance, can be viewed as derivatives of the partially reduced cyclopentene-1,3-dione ring system. Of importance here is the fact that this basic ring system can be conveniently prepared in good yield from the readily available 2-azido-1,4-benzo- and -1,4-naphtho-quinones. The general structures (63) and (79) illustrate the synthetic scope of this transformation.



(63) (79)

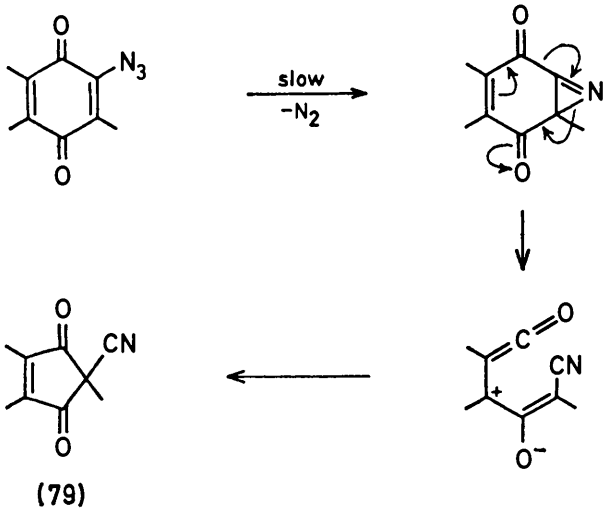
For R^1—R^3, see Table 2.

Table 2 *Substituents for compound* (79)

	R^1	R^2	R^3	*Yield* %
a;	Me	H	Me	92
b;	Ph	H	Ph	70
c;	Me	NH_2	$CHMe_2$	89
d;	$CHMe_2$	NH_2	Me	92
e;	$CHMe_2$	$CHMe_2$	Cl	31
f;	CMe_3	H	CMe_3	95
g;	Me	NH_2	Me	89
h;	NC_7H_{10}	H	CMe_3	78
i;	Br	H	CMe_3	75
j;	Me	CMe_3	H	80
k;	Me	Ph	Me	82
l;	Me	*p*-$MeOC_6H_4$	Me	87
m;	Me	*p*-$NO_2C_6H_4$	Me	65
n;	Me	—CH=CH—CH=CH—		95
o;	OMe	—CH=CH—CH=CH—		70

The mechanism of this reaction has been studied in some detail.[5] Based upon product analysis, activation parameters, and the absence of kinetic solvent effects and substituent effects, the mechanism shown in Scheme 1 has been presented.

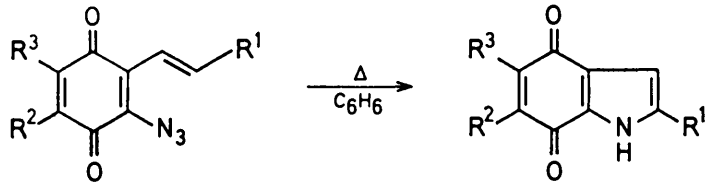
The synthetic limitations of this reaction thus far reported are for those azidoquinones in which the substituent adjacent to the azide group is a proton, a vinyl group, or a substituted amino-function. Those which are unsubstituted give a complex mixture of products upon pyrolytic decomposition, whereas those which are vinyl substituted are thermally converted into indolequinones,[11] *i.e.*,



(79)

Scheme 1

(80) → (81). The azidoquinones having an aryl- or alkyl-substituted amino-group in the 2-position pyrolytically decompose to give polynuclear heterocyclic quinones and are discussed later.

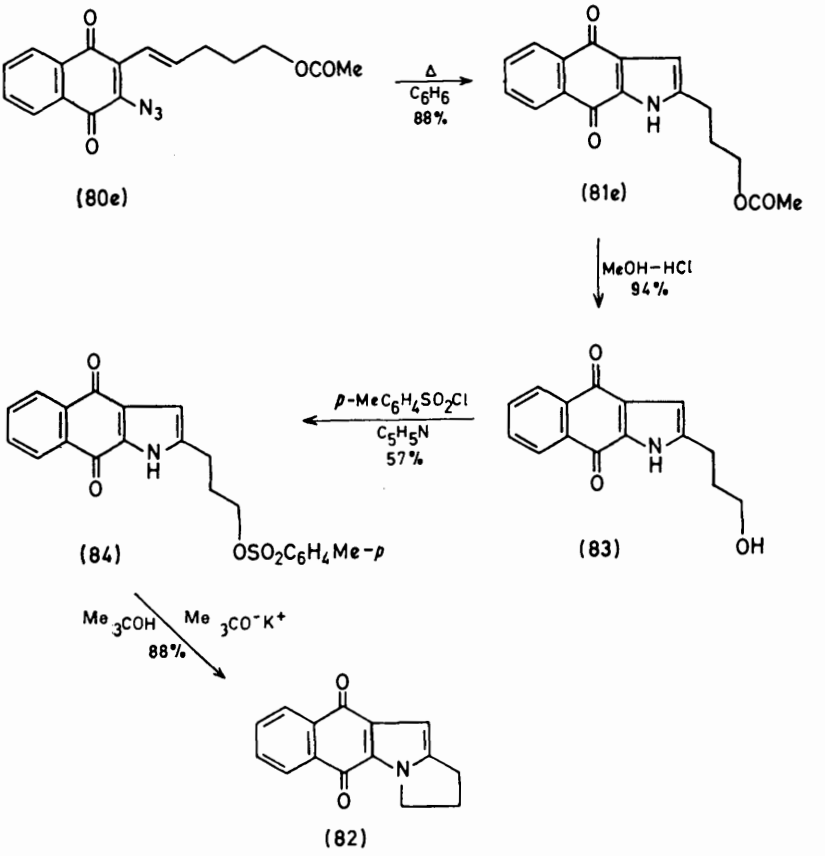


(80) (81)

	R^1	R^2	R^3	*Yield %*
a;	Me	—CH=CH—CH=CH—		90
b;	Pr	—CH=CH—CH=CH—		81
c;	$CH_2(CH_2)_8Me$	—CH=CH—CH=CH—		87
d;	Ph	—CH=CH—CH=CH—		92
e;	$CH_2(CH_2)OCOMe$	—CH=CH—CH=CH—		88
f;	Ph	Me	Me	66

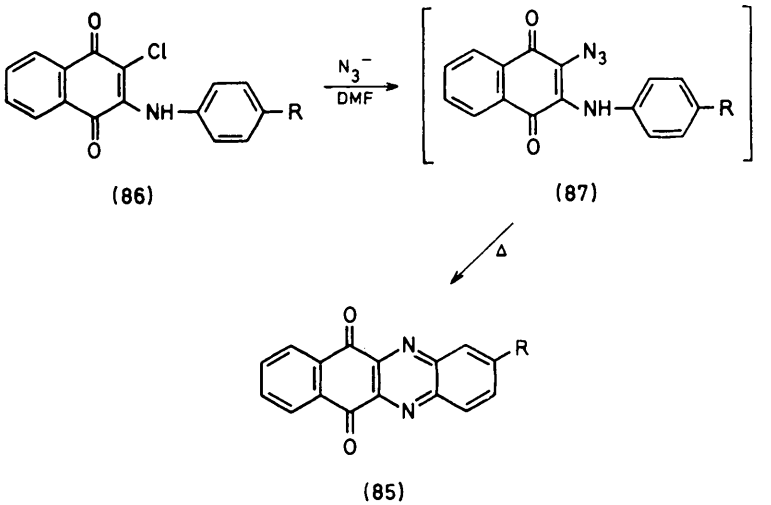
The synthesis of indolequinones as outlined above constitutes one of the best routes to this class of compound. An illustration of the synthetic utility of this reaction is the construction[11] of 6,7-benzo-2,3-dihydro-5,8-dioxo-1*H*-pyrolo-[1,2*a*]indole (82), the naphthoquinone analogue of the biologically important

mitosene ring systems.[50] Hydrolysis of 2-(3-acetoxypropyl)benzo[*f*]indole-4,9-dione (81e) in refluxing aqueous methanolic hydrogen chloride gave the alcohol (83) in 94% yield. Reaction of this alcohol with toluene-*p*-sulphonyl chloride in pyridine gave the tosylate (84) in 57% yield which upon reaction with potassium t-butoxide in t-butyl alcohol gave (82) in 88% yield.



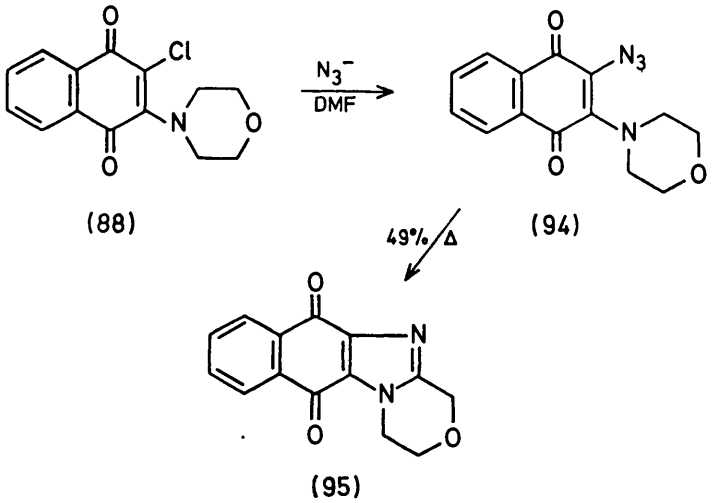
A most interesting reaction has been reported by Van Allen, Reynolds, and Adel[51,52] who have observed heterocyclic quinone (85) formation when 2-arylamino-3-chloro-1,4-naphthoquinones (86) are treated with sodium azide in dimethylformamide at 90—100 °C. The corresponding azidoquinones (87) are the presumed intermediates in this reaction and the products are assumed to arise by nitrene insertion followed by dehydrogenation.

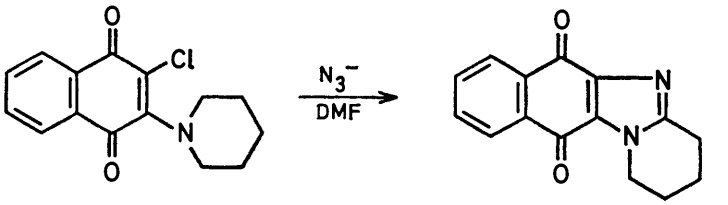
[50] G. R. Allen, jun., J. F. Poletto, and M. J. Weiss, *J. Org. Chem.*, 1965, **30**, 2997.
[51] J. A. Van Allen, G. A. Reynolds, and R. E. Adel, *J. Org. Chem.*, 1963, **28**, 520.
[52] J. A. Van Allen, G. A. Reynolds, and R. E. Adel, *J. Org. Chem.*, 1963, **28**, 524.



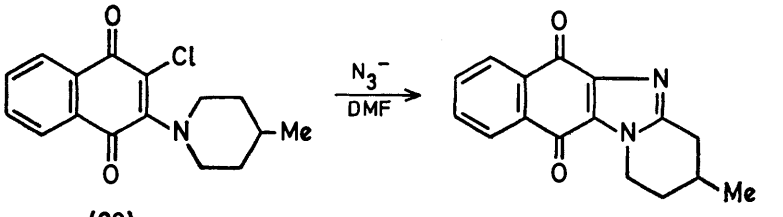
R = OMe (46%), Cl, Me, or OH

The same authors also observed that 2-chloro-3-alkylamino-1,4-naphthoquinones (88)—(93) react under the same conditions to give higher yields of heterocyclic quinones than the arylamino-derivatives. In one case an azidoquinone was isolated and shown to an intermediate, *i.e.*, 2-azido-3-morpholino-1,4-naphthoquinone (94) smoothly decomposed under thermal conditions to give 1,2,3,4,5,10-hexahydro-5,10-dioxo-2-oxa-4*a*,11-diazabenzo[*b*]fluorene (95) in 49% yield.

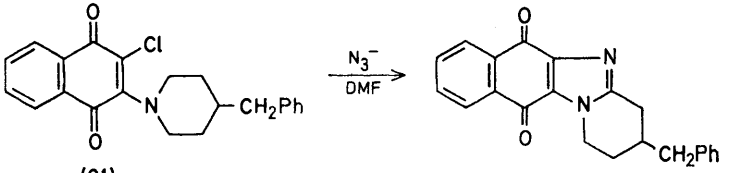



Cl
N
O
N_3^-
DMF
N
N
O

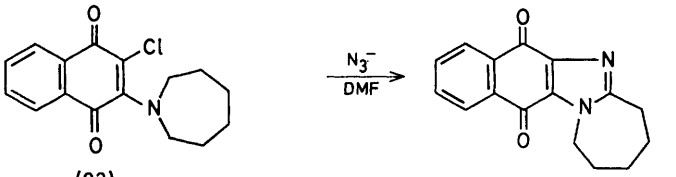
(89)


Cl
N
Me
O
N_3^-
DMF
N
N
Me

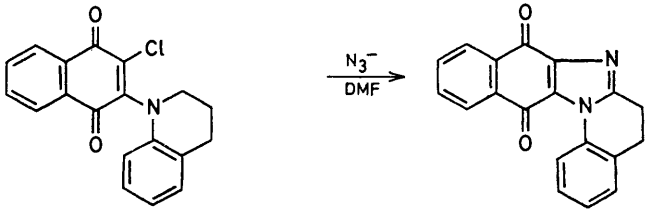
(90)


Cl
N
CH_2Ph
O
N_3^-
DMF
N
N
CH_2Ph

(91)


Cl
N
O
N_3^-
DMF
N
N

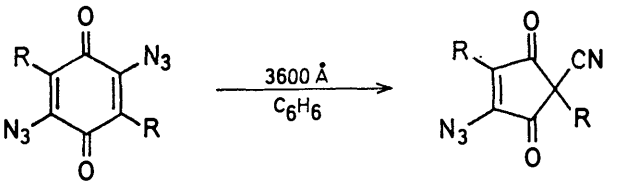
(92)


Cl
N
O
N_3^-
DMF
N
N

(93)

F. Photolysis of Azidoquinones.—Photolysis of azidoquinones in benzene with 3600 Å light results in transformations which are analogous to those observed for their thermal decompositions. That is, 2-azido-3-alkyl(aryl)-1,4-quinones ring-contract to 2-cyano-3-alkyl(aryl)cyclopent-4-ene-1,3-diones[53] and 2-azido-3-vinyl-1,4-quinones ring-close to the corresponding indolequinones.[11]

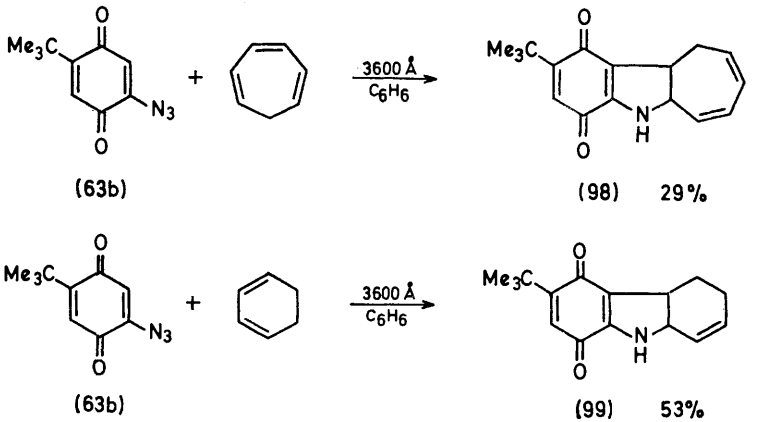
The photolytic ring-contraction has particular advantages for the synthesis of 4-azido-2-cyanocyclopent-4-ene-1,3-diones (96) from the corresponding 2,5-diazido-1,4-benzoquinones (97). As discussed below, these diazidoquinones also thermally ring-contract to the azidocyclopentene-1,3-diones. However, such products readily cleave under the reaction conditions giving two molecules of the correspondingly substituted cyanoketen. No such cleavage is observed when the photolytic ring-contraction is carried out in benzene with 3600 Å light.[12,54]



(97) (96)

R = CMe_3 (75%), $CHMe_2$(75%), or Me (65%)

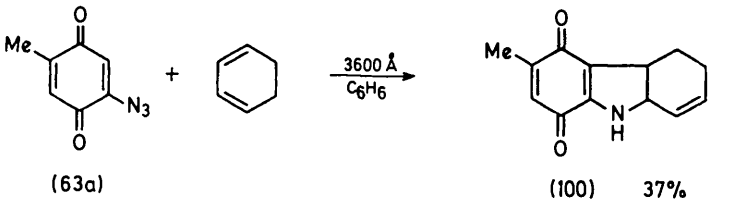
2-Azidoquinones which are unsubstituted at the 3-position decompose photolytically as well as thermally to give a complex mixture of products. However, if the photolysis is carried out in the presence of dienes, 2-alkenyl-2,3-dihydroindole-4,7-diones are obtained in generally good yields.[10] Specifically the heterocyclic quinones (98)—(102) have been prepared in this manner.



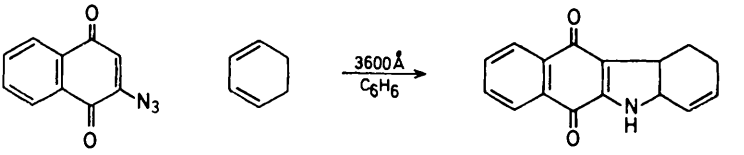
(63b) (98) 29%

(63b) (99) 53%

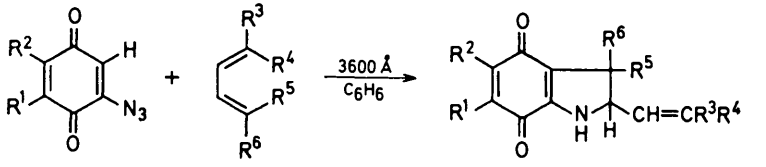
[53] P. Germeraad, W. Weyler, and H. W. Moore, unpublished results.
[54] H. W. Moore and W. Weyler, jun., *J. Amer. Chem. Soc.*, 1971, 93, 2812.



(63a) (100) 37%



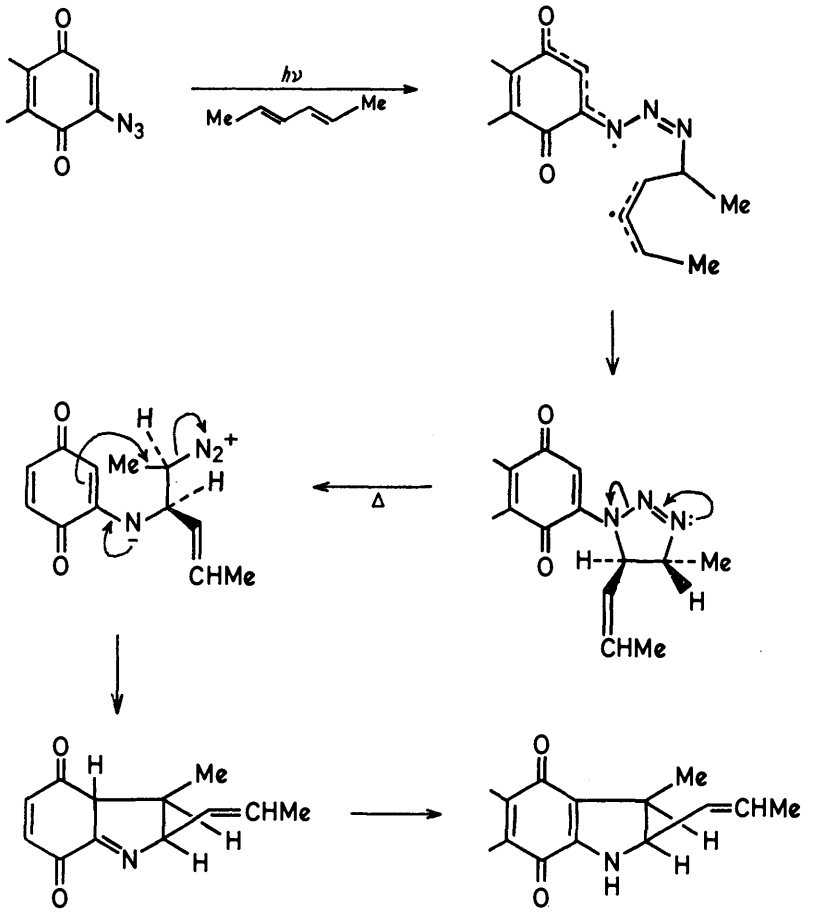
(63m) (101) 74%



(63) (102)

	R^1	R^2	R^3	R^4	R^5	R^6	*Yield* %
a;	H	CMe_3	Me	H	H	H	96
b;	H	CMe_3	H	Me	H	H	73
c;	H	CMe_3	Me	H	H	Me	66
d;	H	CMe_3	H	Me	Me	H	53
e;	H	Me	Me	H	H	H	40
f;	H	Me	H	Me	Me	H	84
g;	—CH=CH—CH=CH—		Me	H	H	H	72
h;	—CH=CH—CH=CH—		H	Me	Me	H	82

On the basis of kinetic and stereochemical studies, the mechanism shown in Scheme 2 has been presented. Pertinent data which are consistent are the facts that the rate of nitrogen evolution is dependent upon diene concentration and that regiochemistry and stereochemistry are nicely accounted for in terms of the proposed intermediates, *i.e.*, the reaction is regiospecific, giving only the 2-alkenyl isomer, and stereoselective, giving as the major isomer the one having a *cis* relationship between the substituents at the 2,3-positions regardless of the stereochemistry of the starting diene.



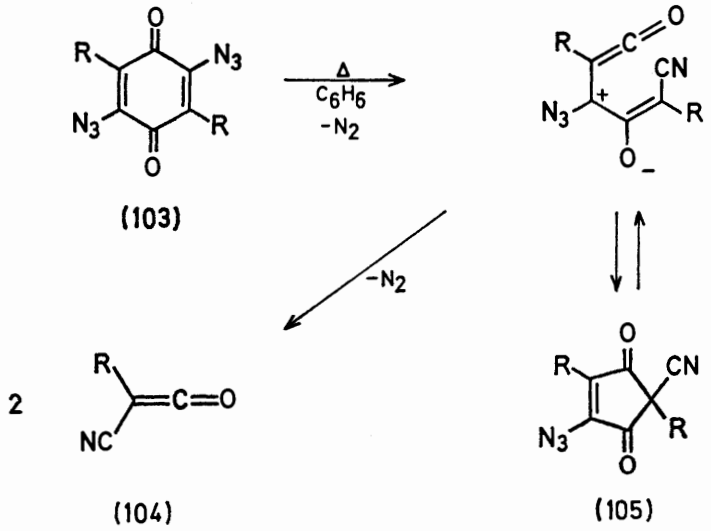
Scheme 2

One novel feature of this transformation is the photolytic cycloaddition of the organic azide to the carbon–carbon double bond of the diene. Such a reaction is certainly well known in the thermal chemistry of organic azides,[55] but appears to be without precedent under photolytic conditions. Cycloadditions of this type may be limited to those azides which can accept light of relatively low energy (> 3600 Å) such as the highly coloured azidoquinones. Light of higher energy may result in nitrene formation, thus leading to other products.

G. Thermal Cleavage of 2,5- and 2,6-Diazido-1,4-quinones.—It has been shown that the thermal ring-contraction of monoazidoquinones to 2-cyanocyclopent-

[55] G. L'Abbe, *Chem. Rev.*, 1969, 69, 345.

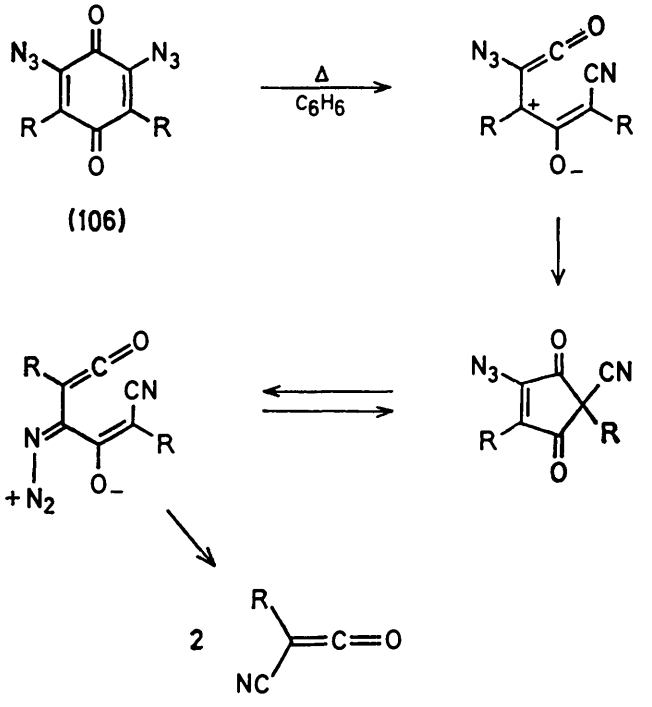
4-ene-1,3-diones (79) results from electrocyclic ring-closure of a zwitterionic intermediate (see Scheme 1). On the basis of this mechanism one would predict that 2,5-diazido-1,4-benzoquinones would thermally generate an analogous ring-opened intermediate which could partition itself between electrocyclic ring-closure and cleavage to two molecules of a cyanoketen. In fact, when 2,5-diazido-3,6-di-t-butyl-1,4-benzoquinone (103a) was refluxed for a few minutes in anhydrous benzene, t-butylcyanoketen (104a) was formed in >95% yield as a stable cumulene in solution.[12,56] When the reaction was closely monitored by t.l.c., 4-azido-2,4-di-t-butyl-2-cyanocyclopent-4-ene-1,3-dione (105a) was also detected. As pointed out earlier, photolysis of the diazidoquinone (103a) with 3600 Å light in benzene gave a 75% yield of the cyclopentenedione (105a) and no keten. However, (105a) was quantitatively converted into t-butylcyanoketen in refluxing benzene. The scope of this reaction has not yet been extensively probed, but it has been shown that t-pentyl, isopropyl-, methyl-, and phenyl-cyanoketen can be generated in an analogous fashion. The t-pentyl homologue, like t-butyl-cyanoketen, is stable in solution; the others are not and were isolated as their methyl esters by trapping with methanol.



a; R = CMe_3
b; R = CMe_2Et
c; R = CMe_2H
d; R = Me
e; R = Ph

[66] H. W. Moore and W. Weyler, jun., *J. Amer. Chem. Soc.*, 1970, 92, 4132.

2,6-Diazido-1,4-quinones (106) also thermally cleave to cyanoketens.[12] An initial ring-contraction to 2-cyano-4-azidocyclopent-4-ene-1,3-diones (105), the same intermediate as is formed from the 2,5-diazido-isomers, is followed by electrocyclic ring-opening and subsequent cleavage to give the ketens (104).

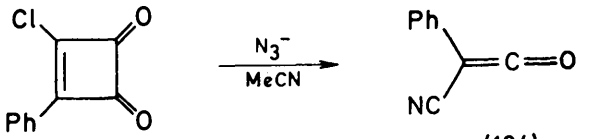


(106)

(104)

R = $CHMe_2$ or Me

Only two previous reports have appeared regarding the synthesis of cyanoketens. De Selms[57] and Schmidt and Reid[58] have independently reported the unique formation of phenylcyanoketen upon reaction of 2-halogeno-1-phenylcyclobut-1-ene-3,4-dione (107) with sodium azide.

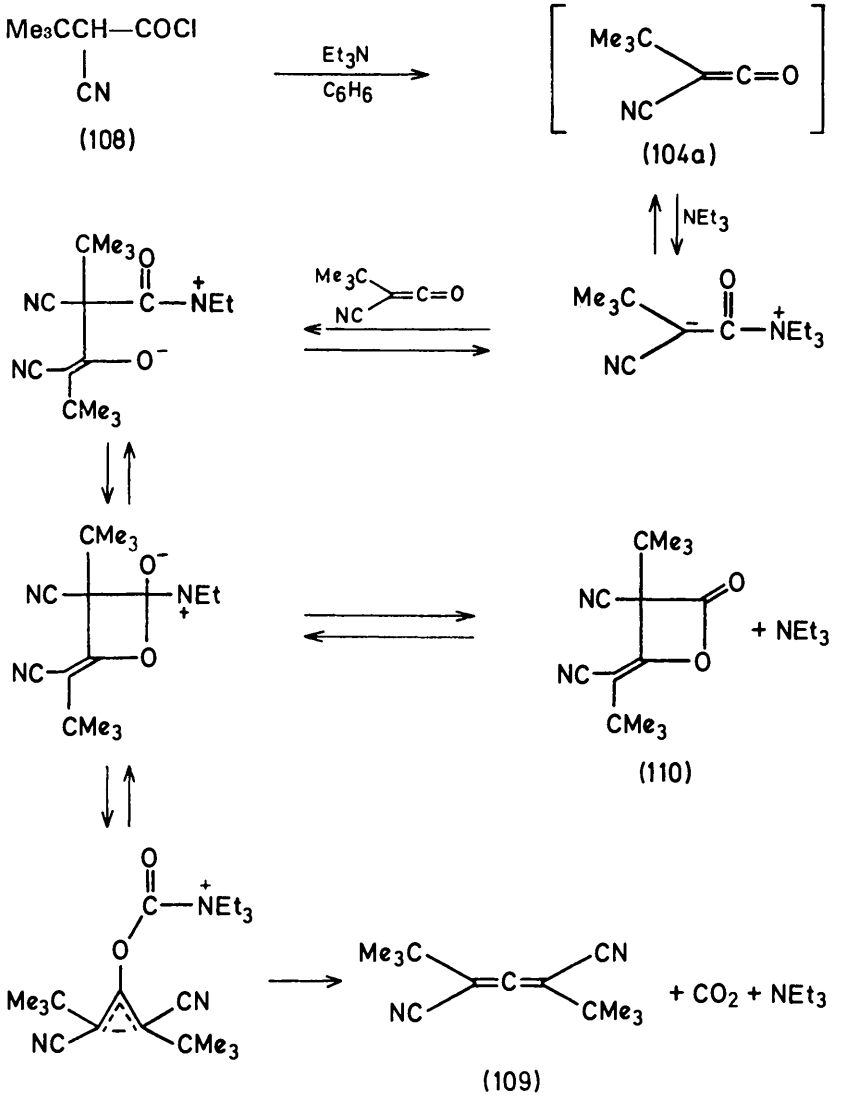


(107)

(104)

[57] R. C. De Selms, *Tetrahedron Letters*, 1969, 1179.
[58] A. H. Schmidt and W. Reid, *Tetrahedron Letters*, 1969, 2431.

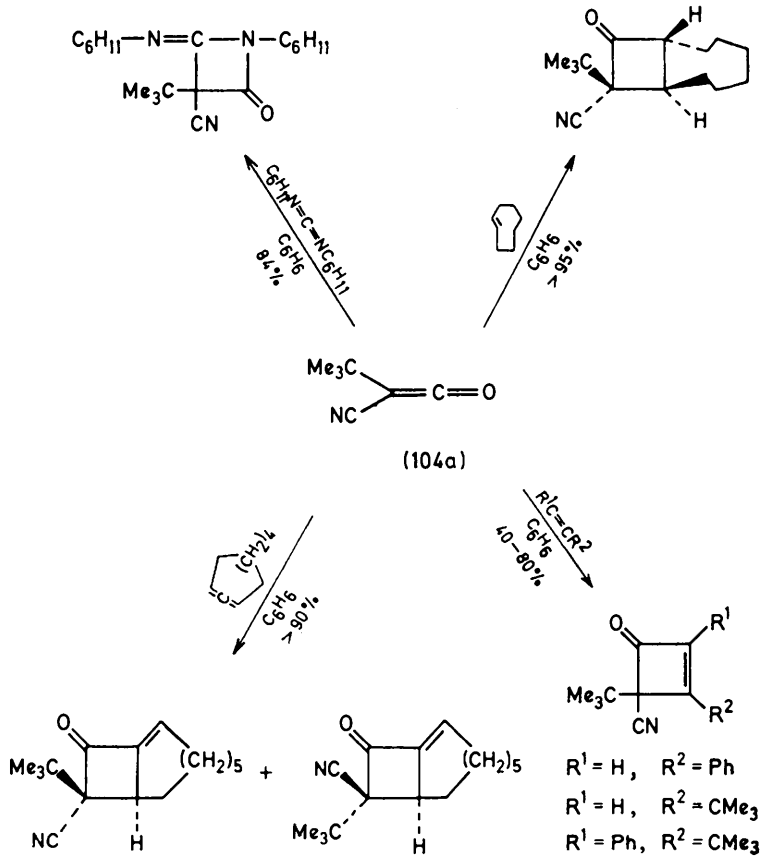
The generation of cyanoketens by the classical dehydrohalogenation of the corresponding acid chlorides may be difficult. This is certainly true for t-butylcyanoketen (104a) since reaction of a benzene solution of 2-cyano-3,3-dimethylbutyryl chloride (108) with a catalytic amount of triethylamine gives a good yield of 1,3-di-t-butylallene (109).[59] The same product was immediately formed when a solution of the keten was similarly treated. The reaction was shown to



[59] H. W. Moore and W. G. Duncan, *J. Org. Chem.*, 1973, **38**, 156.

involve a triethylamine-catalysed dimerization of t-butylcyanoketen to the β-lactone (110) which then reacted further with the amine, as indicated, to give the allene (109). On the other hand, when t-butylcyanoketen is generated by pyrolysis of 2,5-diazido-3,6-di-t-butyl-1,4-benzoquinone (103a) it is stable for days in benzene even at the reflux temperature.

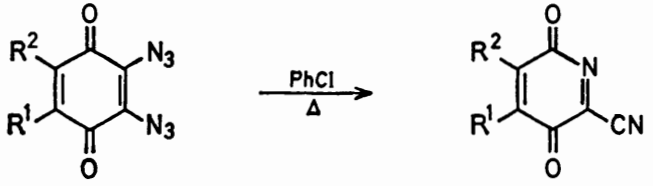
Even though t-butylcyanoketen is reluctant to self-condense in benzene, it quite readily undergoes cycloaddition to other substrates. Addition to alkenes,[12] alkynes,[60] allenes,[61] and carbodi-imides[12] have been reported, and selected examples are outlined in Scheme 3.



Scheme 3

[60] M. D. Gheorghiu, C. Draghici, L. Stanescu, and M. Avram, *Tetrahedron Letters*, 1973, 9.
[61] W. Weyler, jun., L. B. Byrd, M. C. Caserio, and H. W. Moore, *J. Amer. Chem. Soc.*, 1972, **94**, 1027.

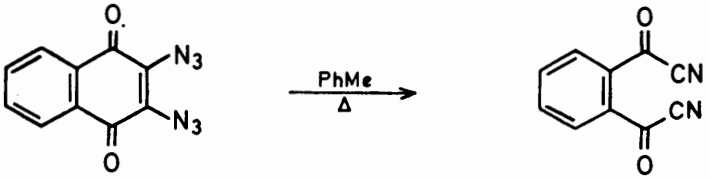
H. Thermal Rearrangement of 2,3-Diazido-1,4-quinones.—2,3-Diazido-1,4-quinones (111) undergo a fascinating rearrangement to 2-aza-3-cyano-1,4-quinones (112) when decomposed in refluxing chlorobenzene.[8] This reaction constitutes the first unambiguous synthesis of the new heterocyclic azabenzoquinone ring system. All other reported examples are hydroxy-derivatives which have several tautomeric possibilities, the azaquinone form being only one, and no evidence has been presented which would allow one to determine which isomer or isomers predominate.[62–66] In the azanaphthoquinone series one example has recently been described; 2-aza-3-phenyl-1,4-naphthoquinone has been prepared by two different routes.[32,67,68]



(111) (112)

	R^1	R^2
a;	CMe_3	H
b;	H	CMe_3
c;	Ph	H
d;	H	Ph
e;	Me	Me
f;	$-CH_2CH_2CH_2CH_2-$	
g;	$-CH=CH-CH=CH-$	

The conversion of 2,3-diazido-1,4-naphthoquinone (111g) into 2-aza-3-cyano-1,4-naphthoquinone (112g) warrants further comment. Van Allen, Priest, Marshall, and Reynolds[7] have reported that 2,3-diazido-1,4-naphthoquinone (111g) is pyrolytically converted into phthaloyl cyanide (113) in refluxing toluene.

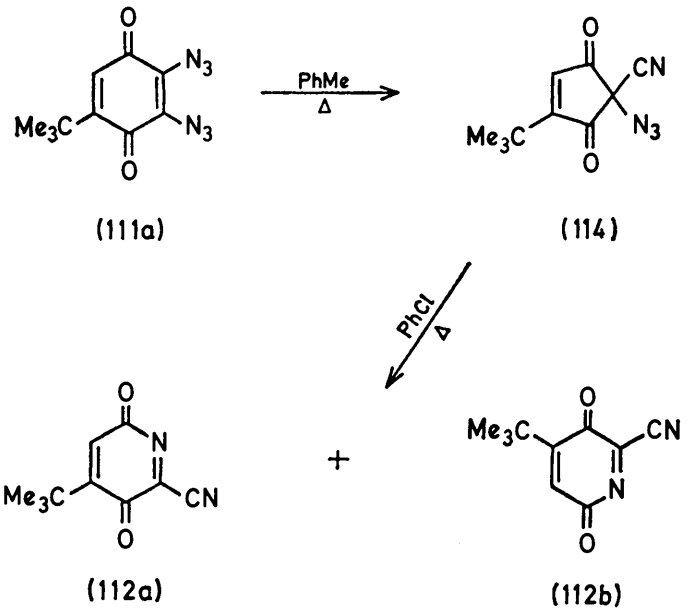


(111g) (113)

[61] H. J. Knackmuss, *Angew. Chem.*, 1973, **85**, 163.
[62] J. A. Moore and F. L. Marascia, *J. Amer. Chem. Soc.*, 1959, **81**, 6049.
[64] J. H. Boyer and S. Kruger, *J. Amer. Chem. Soc.*, 1957, **79**, 3552.
[65] H. Ost, *J. prakt. Chem.*, 1890, **27**, 260.
[66] R. Kudernatsch, *Monatsh.*, 1897, **18**, 613.
[67] K. Schenker, *Helv. Chim. Acta*, 1968, **51**, 413.
[68] I. Felner and K. Schenker, *Helv. Chim. Acta*, 1969, **52**, 1810.

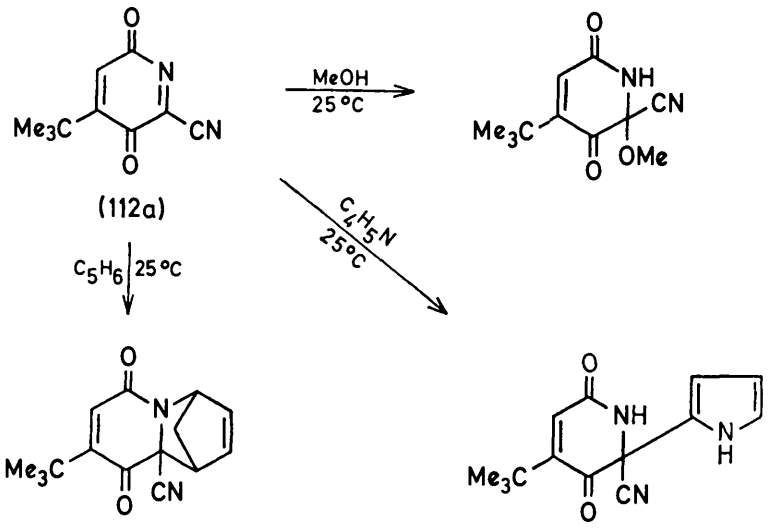
This has been confirmed, and it has been shown that, in addition, the azaquinone (112g) is also generated.[8]

The propensity of azidoquinones in general to undergo thermal ring-contraction to 2-cyanocyclopent-4-ene-1,3-diones suggested that such a process is also involved in the conversion of 2,3-diazidoquinones into azaquinones. Indeed, this was shown to be true. Thermolysis of 2,3-diazido-5-t-butyl-1,4-benzoquinone (111a) in refluxing toluene gave predominantly 2-azido-4-t-butyl-2-cyanocyclopent-4-ene-1,3-dione (114) in 80% yield. This compound, upon subsequent thermolysis in refluxing chlorobenzene, gave the azaquinones (112a) and (112b) as a 1:1 mixture. This last transformation finds a precedent in the previously reported conversion of 2-azido-2-phenylindane-1,3-dione into 2-aza-3-phenyl-1,4-naphthoquinone.[32]



(111a) (114) (112a) (112b)

The reactivity of the azaquinones centres around the very electron-poor imine double bond. This is illustrated for 2-aza-3-cyano-5-t-butyl-1,4-benzoquinone (112a), which readily undergoes nucleophilic additions as well as cycloadditions.



4 Reactions of Related Systems

A large number of cyclic azidoeneones and related compounds can be envisaged which might be chemically similar to the azidoquinones. A few of these are shown here [(115)—(125)], and some have received limited study.

It is also possible that reactions analogous to those described for azidoquinones might be induced from related vinylogous amides, such as aminoquinones, under oxidative conditions, *e.g.* the generation and chemistry of nitrenoid species from aminoquinones upon lead tetra-acetate oxidation.

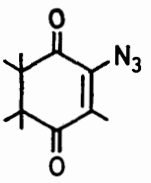
The following sections summarize the limited results in these areas.

A. Thermolysis and Pyrolysis of 4-Azido-1,2-pyridazine-3,6-dione.—4-Azido-1,2-dimethylpyridazine-3,6-dione (126) was subjected to pyrolytic and photolytic decomposition in the nucleophilic solvents methanol and diethylamine.[69] Its thermal decomposition in the alcohol at 130 °C gave a mixture of the amino-derivatives (127) and (128) in 25 and 10% yields, respectively. On the other hand, photolysis in methanol gave (129), (127), and (130) in 44, 20, and 5% yields, respectively. Thermolysis of (126) in diethylamine gave an 81% yield of 4-amino-5-diethylamino-1,2-dimethylpyridazine-3,6-dione (131). A nitrene intermediate has been suggested as the precursor of these products.

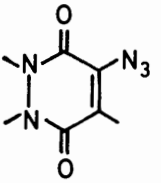
Formation of the ring-contracted product (130) is analogous to that observed for the thermolysis and photolysis of monoazido-1,4-quinones. As pointed out earlier, such a process in the quinone series is not facile when the position

[69] T. Sasaki, K. Kanematsu, and M. Murata, *Tetrahedron*, 1973, **29**, 529.

adjacent to the azide group is unsubstituted. This is apparently true also in the pyridazine series since (130) was formed in only 5% yield. Thus, 4-azido-5-alkyl (aryl)-1,2-pyridazine-3,6-diones should be prepared and their thermolysis and photolysis investigated.



(115)



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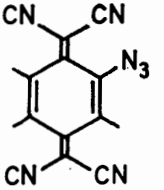

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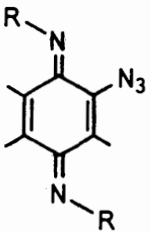

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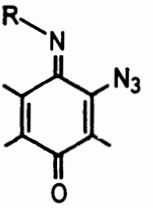

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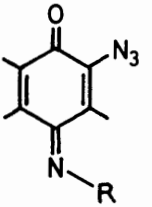

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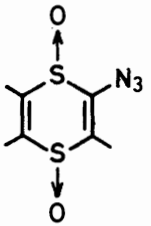

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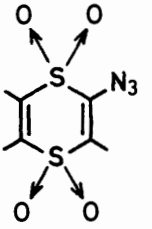

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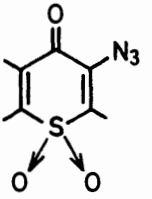

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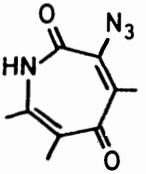
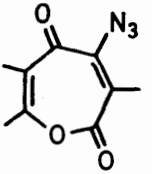
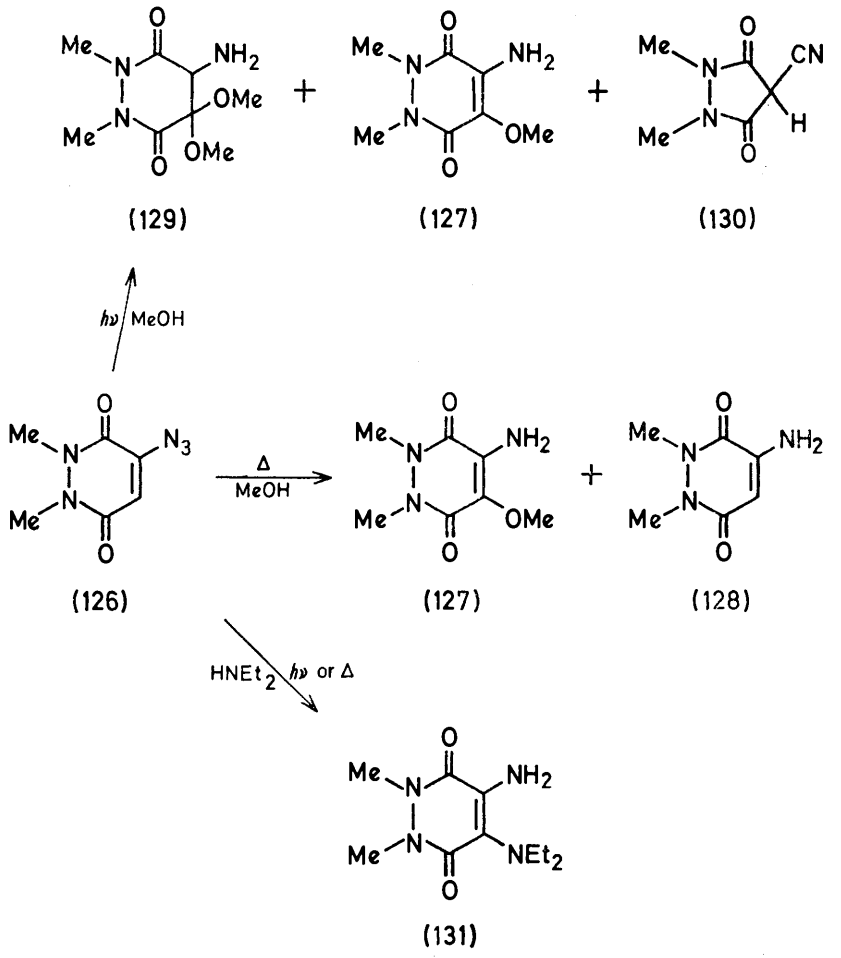


(124)



(125)

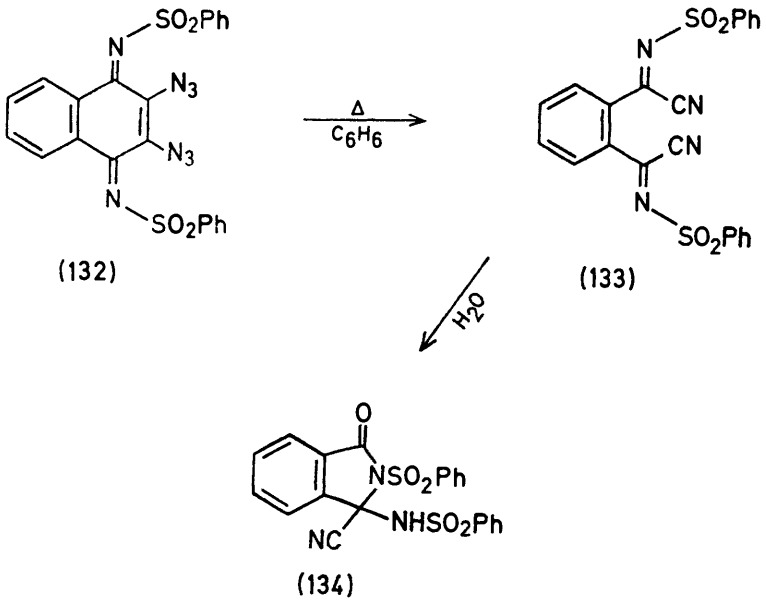


Unlike the azidoquinone series, (126) is reported to be stable in strong acid, even at 100°C.[69]

B. Thermal Cleavage of 2.3-Diazido-1,4-naphthoquinonedibenzenesulphonimide.— The thermal decomposition of 2,3-diazido-1,4-naphthoquinonedibenzenesulphonimide (132) in refluxing benzene gives phthaloyl cyanide dibenzenesulphonimide (133).[70] The α-cyanobenzenesulphonimide groupings in (133) are very reactive towards nucleophilic reagents. For example, water very readily

[70] H. W. Moore and M. S. Lee, *Tetrahedron Letters*, 1971, 3645.

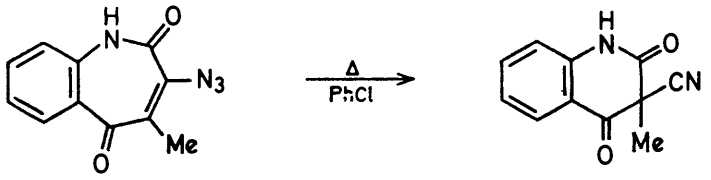
reacts with (133) to give the *N*-benzenesulphonyl-lactam (134) in 85% yield. This cleavage reaction finds analogy in the previously described thermolysis of 2,3-diazido-1,4-naphthoquinone (111g) to phthaloyl cyanide (113). As a result, it is possible that the readily available[71–76] azido-1,4-quinonedi-imines may be chemically similar to the azidoquinones, and their detailed study is thus warranted.



(132) (133) (134)

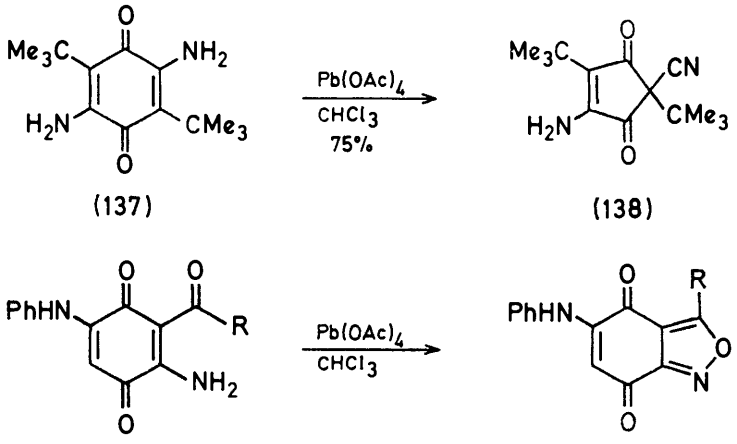
C. Thermal Rearrangement of 3-Azido-2,5*H*-azepine-2,5-diones.—2,5*H*-Azepine--2,5-diones are readily prepared from 1,4-benzo- and 1,4-naphtho-quinones upon their reaction with hydrazoic acid in cold concentrated sulphuric acid, *e.g.*, (16) → (17).[23–25] An azido-derivative in this series has recently been subjected to thermal decomposition,[77] and again ring-contraction was observed. Specifically, 3-azido-2,5*H*-4-methylbenzoazepine-2,5-dione (135) rearranged in 80% yield to the quinoline derivative (136) when a chlorobenzene solution was refluxed for two hours.

[71] R. Adams and D. C. Blomstrom, *J. Amer. Chem. Soc.*, 1953, **75**, 3405.
[72] R. Adams and W. Moje, *J. Amer. Chem. Soc.*, 1952, **74**, 5560.
[73] R. Adams and W. P. Samuels, *J. Amer. Chem. Soc.*, 1955, **77**, 5357.
[74] R. Adams and J. W. Way, *J. Amer. Chem. Soc.*, 1954, **76**, 2763.
[75] R. Adams and L. Whitaker, *J. Amer. Chem. Soc.*, 1956, **78**, 658.
[76] R. Adams and E. L. DeYoning, *J. Amer. Chem. Soc.*, 1957, **79**, 417.
[77] G. Landen and H. W. Moore, unpublished results.



(135) (136)

D. Lead Tetra-acetate Oxidation of Aminoquinones.—The reaction of primary amides with lead tetra-acetate has been investigated and found to parallel the Hofmann rearrangement.[78] Therefore, primary aminoquinones, being vinylogous amides, might be expected to react with lead tetra-acetate to give 2-cyanocyclopent-4-ene-1,3-diones *via* an intermediate nitreneoid species. That is, such reactions might be similar to those observed for the thermal reactions of azidoquinones. Limited studies indicate that there is some foundation for such an analogy. For example, 2,5-diamino-3,6-di-t-butyl-1,4-benzoquinone (137) gives a 75% yield of 4-amino-2,5-di-t-butyl-2-cyanocyclopent-4-ene-1,3-dione (138) upon lead tetra-acetate oxidation in chloroform.[79] Under the same conditions, the 2-amino-5-anilino-3-acyl-1,4-benzoquinones (139a—c) give good yields of the corresponding isoxazoles (140a—c).[79] This latter transformation is analogous to that observed when 2-acetyl-3-chloro-6-methoxy-1,4-benzoquinone (141) was treated with sodium azide to give the isoxazole (142).[80]

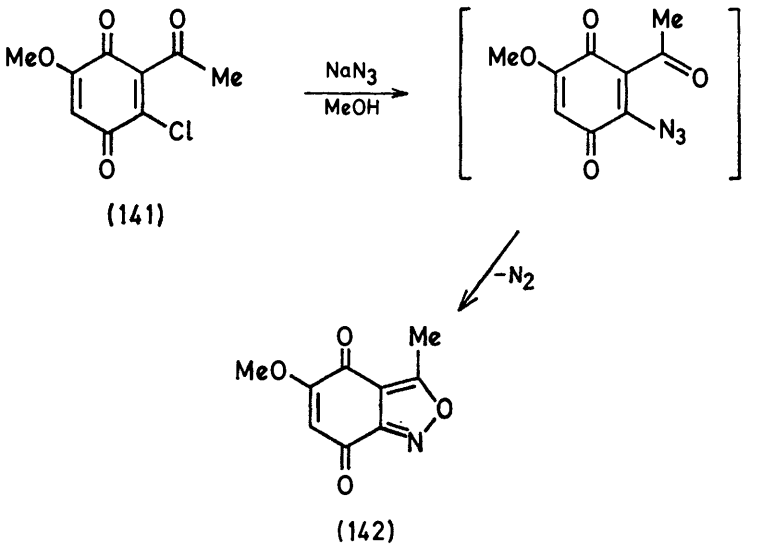


(137) (138)

(139) (140)

a; R = Me a; 75%
b; R = OMe b; 72%
c; R = NMe_2 c; 65%

[78] J. B. Aylward, *Quart. Rev.*, 1971, 407.
[79] H. W. Moore and W. Schäfer, unpublished results.
[80] W. Schäfer and Hj. Schlude, *Tetrahedron Letters*, 1967, 4313.



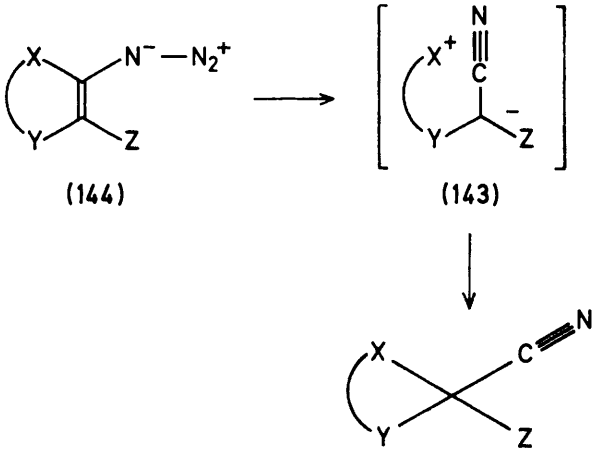
In the past thirty-five years alone well over one hundred and fifty richly substituted primary amino-1,4-benzo- and -1,4-naphtho-quinones have been reported in the literature. The plethora of such readily available starting materials along with the rich chemistry of the amino-group and the quinone nucleus should make a study of their oxidative rearrangements most worthwhile.

5 Conclusions

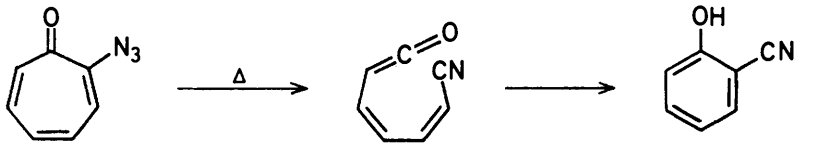
It is apparent from this review that the chemistry of azidoquinones and particularly of the related azidoeneones is still in its early stages of development. Many of their rearrangement, fragmentation, and cleavage reactions can be formally outlined according to Scheme 4. The penultimate precursor to the zwitterionic species (143) may be the azide (144), a nitrene, or an azirine. The group X is cation-stabilizing and Y and/or Z are anion-stabilizing substituents. Such a scheme adequately rationalizes the observed conversions of azidoquinones into γ-cyanoalkylidene-$\Delta^{\alpha,\beta}$-butenolides (62), 2-cyanocyclopent-4-ene-1,3-diones (79), 2-aza-3-cyano-1,4-quinones (112), and cyanoketens (104). It is also in agreement with the observed ring-contractions of 4-azido-1,2-dimethylpyridazine-3,6-dione (126) and 3-azido-2,5*H*-4-methylbenzoazepine-3,5-dione (135).

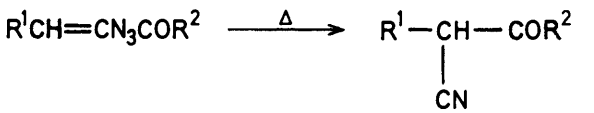
Certainly a large number of other cyclic and acyclic vinyl azides meeting the structural requirements outlined above should be investigated. Some such work has already been done and is outlined below.[81-84]

[81] J. D. Hobson and J. R. Malpass, *J. Chem. Soc.*, 1967, 1645.
[82] D. Knittel, H. Hemetsberger, R. Leipert, and H. Weidmann, *Tetrahedron Letters*, 1970, 1459.
[83] S. Sato, *Bull. Chem. Soc. Japan*, 1968, **41**, 2524.
[84] S. Maiorana, *Ann. Chim. (Italy)*, 1966, **56**, 1531.

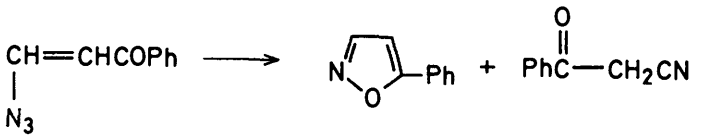


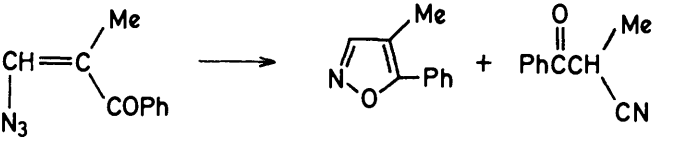
Scheme 4





	R^1	R^2	*Yield* %
a;	Ph	Ph	73
b;	Ph	4-MeC_6H_4	65
c;	4-MeC_6H_4	4-$CH_3C_6H_4$	74
d;	4-ClC_6H_4	4-$NO_2C_6H_4$	80
e;	4-MeC_6H_4	Me	75
f;	4-ClC_6H_4	Me	70
g;	2,4,6-$Me_3C_6H_2$	4-MeC_6H_4	74
h;	2,6-$Cl_2C_6H_3$	4-ClC_6H_4	45





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