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ABSTRACT

Naphtho-1,2-quinone reacts with primary arylamines (without electron-withdrawing substituents) in methanol to give almost insoluble N-aryl-4-aminonaphtho-1,2-quinones, which show absorptions in the ultra-violet at ca. 250 nm. ($\log \epsilon = 4.4$), 280 nm. ($\log \epsilon = 4.15$), 340 nm. ($\log \epsilon = 3.8$) and 450-500 nm. ($\log \epsilon = 3.7$). Electron-donating substituents on the aryl ring give rise to bathochromic shifts of the first and last bands listed. The infra-red spectra of these substances show amino-group and carbonyl absorptions at ca. 3250 cm.^{-1} and 1680 cm.^{-1} respectively, suggesting that the tautomeric hydroxyquinone-imine is absent, as there is no evidence for intramolecular hydrogen bonding. The p.m.r. spectra of N-aryl-4-aminonaphtho-1,2-quinones dissolved in trifluoroacetic acid show absorptions at 1.6 τ and 2.0 τ (naphthalene protons), 2.1 - 2.8 τ (phenyl protons), ca. 3.2 τ (the 3 proton) and other signals corresponding to proton-containing substituents. In deuteriotrifluoroacetic acid the 3 proton is rapidly displaced by deuterium.

N-alkylarylamines undergo a corresponding reaction to give N-alkyl-N-aryl-4-aminonaphtho-1,2-quinones. These show similar spectroscopic properties to the materials described above, but are much more soluble in common organic solvents. Primary alkylamines react with naphtho-1,2-quinone to give many products, including the N-alkyl-4-aminonaphtho-1,2-quinone and an N,N'-dialkylaminonaphthoquinone-imine.

Treatment of benzo-1,2-quinone with a methanolic solution of sodium azide, or methoxide, or a nitrogenous organic base (e.g. 2-amino-2-methylpropane), yields the anion radical 4,5-dimethoxybenzo-1,2-semiquinone, possibly formed by a nucleophilic addition/oxidation sequence. In the absence of oxygen, it can be shown that methanolic sodium nitrite, sodium azide, potassium iodide or 2-amino-2-methylpropane reacts with benzo-1,2-quinone to

produce one form of the benzo-1,2-semiquinone radical (hyperfine splitting constants 3.86 gauss and 0.64 g.), which rapidly decays to a second form (h.s.c. 3.64 g. and 0.94 g.). Equilibria of the type $X^- + MeOH \rightleftharpoons MeO^- + HX$ may liberate enough methoxide to allow the latter to reduce the quinone, either by hydride or electron transfer. No thermodynamically feasible route for the reduction of the quinone by iodide has been found, though the spectroscopic evidence suggested that the products of treating the quinone with potassium iodide were iodine and catechol.

AN INVESTIGATION OF SOME 1,2-QUINONE CHEMISTRY

by

IAN DAVID BIGGS, B.A.

A thesis submitted for the degree of Doctor of Philosophy
in the University of St. Andrews

[1975]



TO MY MOTHER AND LATE FATHER

RESEARCH TRAINING

The candidate entered the University of York in October 1967 and graduated with First Class Honours in Chemistry in July 1970.

The candidate was admitted as a research student in the University of St. Andrews on 1st October, 1970 and was enrolled as a candidate for the Degree of Ph.D. in October 1971. The work which is embodied in this Thesis was carried out in the Departments of Chemistry of the Universities of St. Andrews and York under the supervision of Professor Lord Tedder.

CERTIFICATE

I certify that Ian David Biggs has spent eleven terms at research work under my direction and that he has fulfilled the conditions of Ordinance No. 12 and Resolution of the University Court, 1967, No. 1 so that he is qualified to submit the following Thesis for the Degree of Doctor of Philosophy.

Professor Lord Tedder

DECLARATION

I hereby declare that this thesis is of my own composition, that it describes work performed by myself, and that it has not previously been accepted in an application for a higher degree.

ACKNOWLEDGEMENTS

First of all may I thank my supervisor, Professor Lord J.M. Tedder, for his constant help and encouragement during the course of my research work. Gratitude is also expressed to Professor R.O.C. Norman and Dr. B.C. Gilbert for their enthusiastic supervision of the e.s.r. studies which I carried out at the University of York.

I thank Professor Tedder and Professor P.A.H. Wyatt for the provision of research facilities at the University of St. Andrews, and Professor Norman for permitting me to work at the University of York.

I also wish to thank friends and colleagues at the Universities of St. Andrews, York and Durham for helpful discussion and assistance.

The award of a Research Studentship by the Science Research Council is gratefully acknowledged.

Last but not least, may I thank Mrs. Eileen Duddy for typing this thesis.

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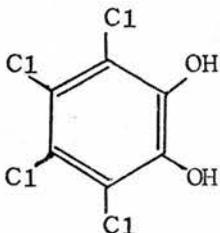
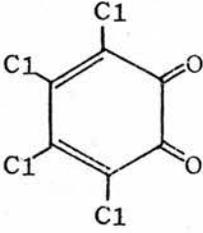
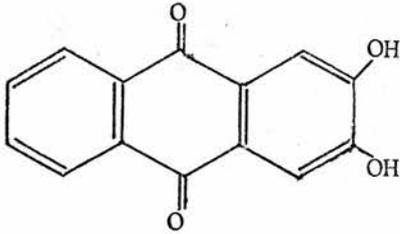
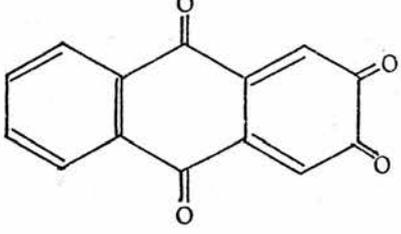
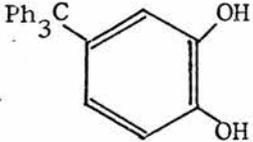
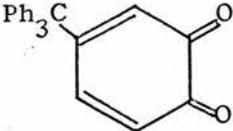
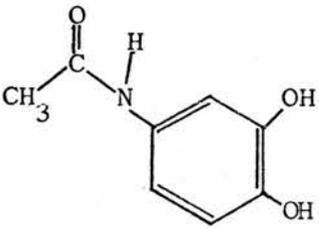
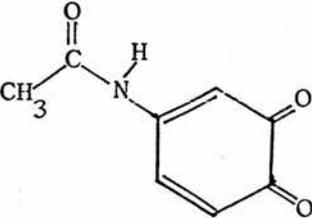
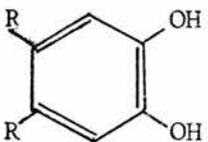
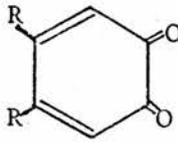
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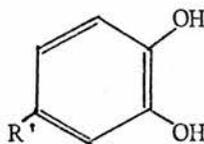
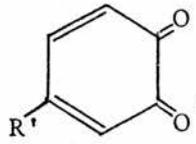
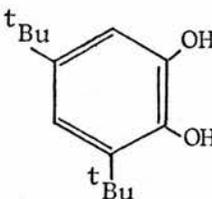
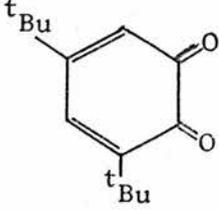
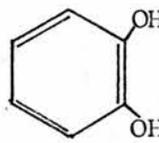
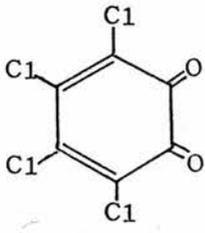
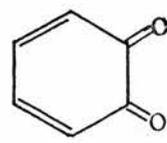
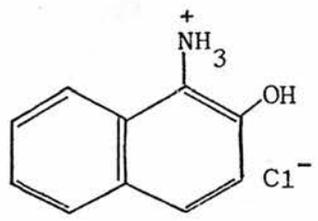
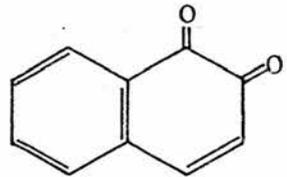
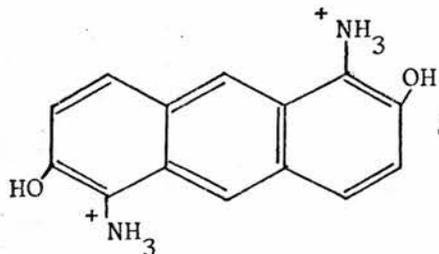
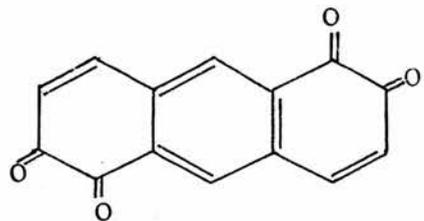
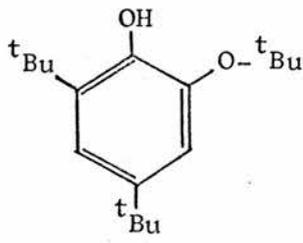
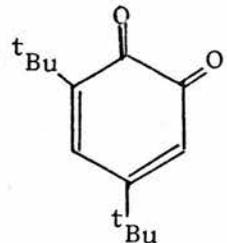
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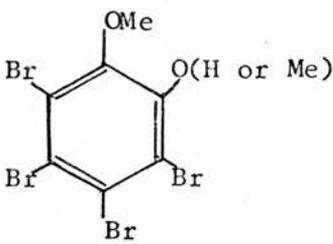
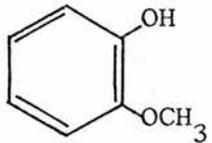
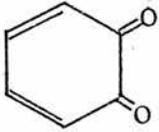
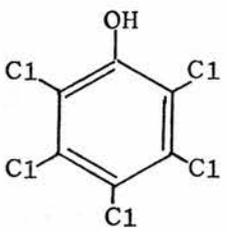
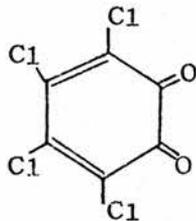
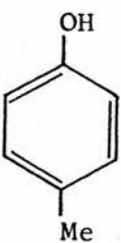
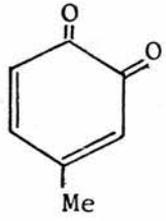
INTRODUCTION TO THE CHEMISTRY OF 1,2-QUINONES.¹

1. Preparation.

1,2-quinones are normally prepared by the oxidation of suitably substituted phenols. Known methods (for effecting this conversion) are listed below. The table is sub-divided according to the nature of the starting phenol.

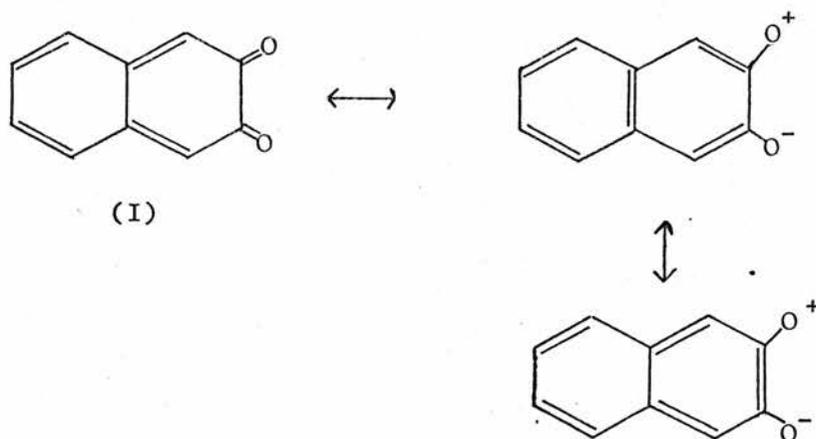
<u>Phenol</u>	<u>Oxidant</u>	<u>Product</u>	<u>Reference</u>
a) Catechols			
	Nitric acid		2
	Lead tetraacetate		3
	Lead dioxide		4
	Sodium dichromate		5
	Silver oxide	 R = H	6

<u>Phenol</u>	<u>Oxidant</u>	<u>Product</u>	<u>Reference</u>
	Silver carbonate/ Celite	 R' = H, Me, or tBu	7
	Oxygen/metal catalyst/base		8
			9
b) From aminophenols			
	Ferric chloride		10
	Sodium dichromate		11
c) From catechol ethers			
	Oxygen/cupric chloride/pyridine		12

<u>Phenol</u>	<u>Oxidant</u>	<u>Product</u>	<u>Reference</u>
	Nitric acid		13
	Sodium periodate		14
d) From other phenols			
	Nitric acid		15
	Fremy's salt		16

2. Properties of 1,2-Quinones.

1,2-quinones are normally reactive species. Symmetrical unsubstituted ones tend to be unstable at room temperature, e.g. benzo-1,2-quinone polymerizes rapidly at 20°C, and the isolation of naphtho-2,3-quinone (I) has yet to be accomplished. For such species resonance structures with an aromatic sextet (or '4n+2tet') can be drawn, but these have unfavourable charge distributions, e.g.



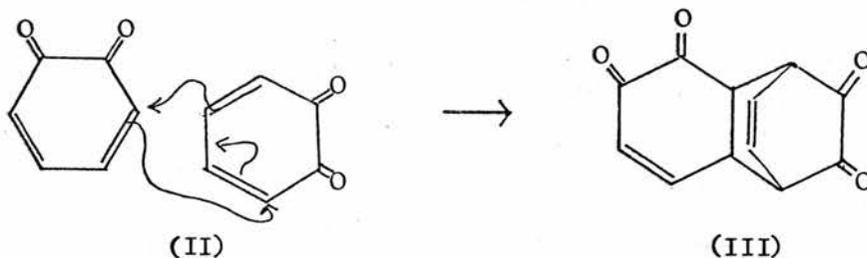
Substitution may or may not increase the shelf stability of the quinone. 5,6,7,8-Tetrahydronaphtho-2,3-quinone decomposes rapidly at room temperature,¹⁷ whereas 4,5-dimethylbenzo-1,2-quinone¹⁸ and the tetrahaloquinones¹⁹ (where halo is chloro or bromo) are stable. Naphtho-1,2-quinone can also be kept under normal conditions. In this case an aromatic sextet exists in the uncharged canonical form.

The reactions of 1,2-quinones can be classified as follows.

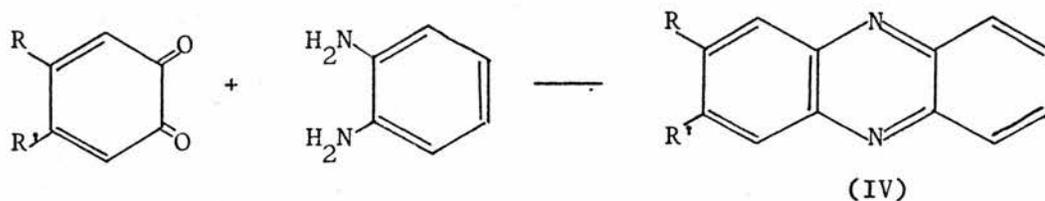
- a) Diels-Alder reactions.
- b) Condensations.
- c) Nucleophilic additions (so called).
- d) Oxidations.

Examples of such reactions.

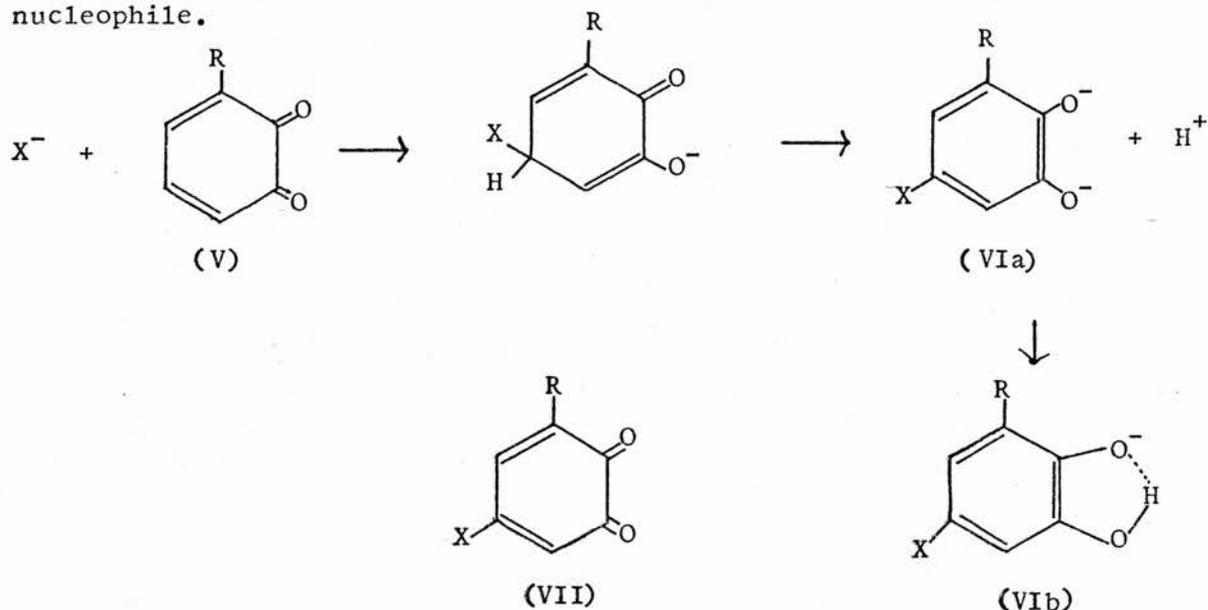
a. In Diels-Alder additions the quinone can act either as the diene or the dienophile. A consequence of this is that benzo-1,2-quinone (II) dimerizes in benzene to give (III).²⁰



b. In ethereal solution 1,2-diaminobenzene condenses with benzo-1,2-quinones to give phenazines (IV).^{21a,21b}



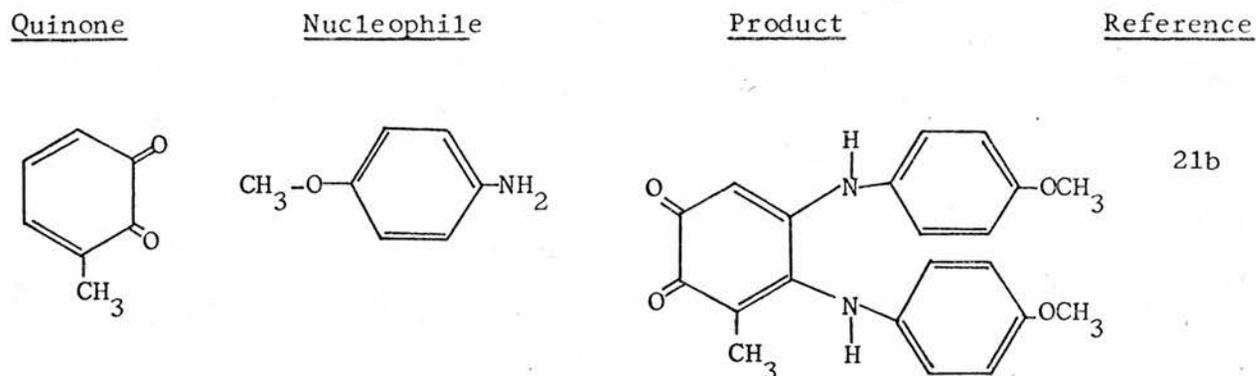
c. A quinone can be considered to consist of two 1-ene-3-one units joined together. As such it would seem vulnerable to 1,4-addition by a nucleophile.



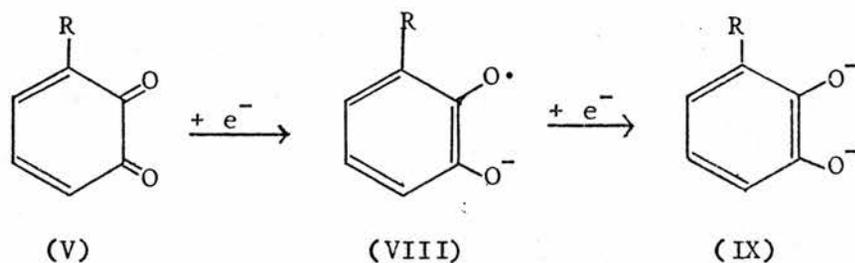
Further reaction may occur if the starting quinone (V) is capable of oxidizing (VI) to the quinone (VII).

Examples of these processes are given below.

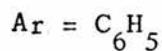
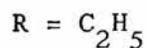
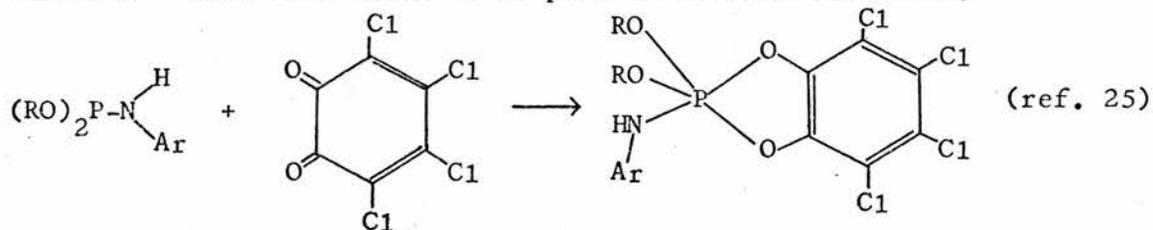
<u>Quinone</u>	<u>Nucleophile</u>	<u>Product</u>	<u>Reference</u>
			22



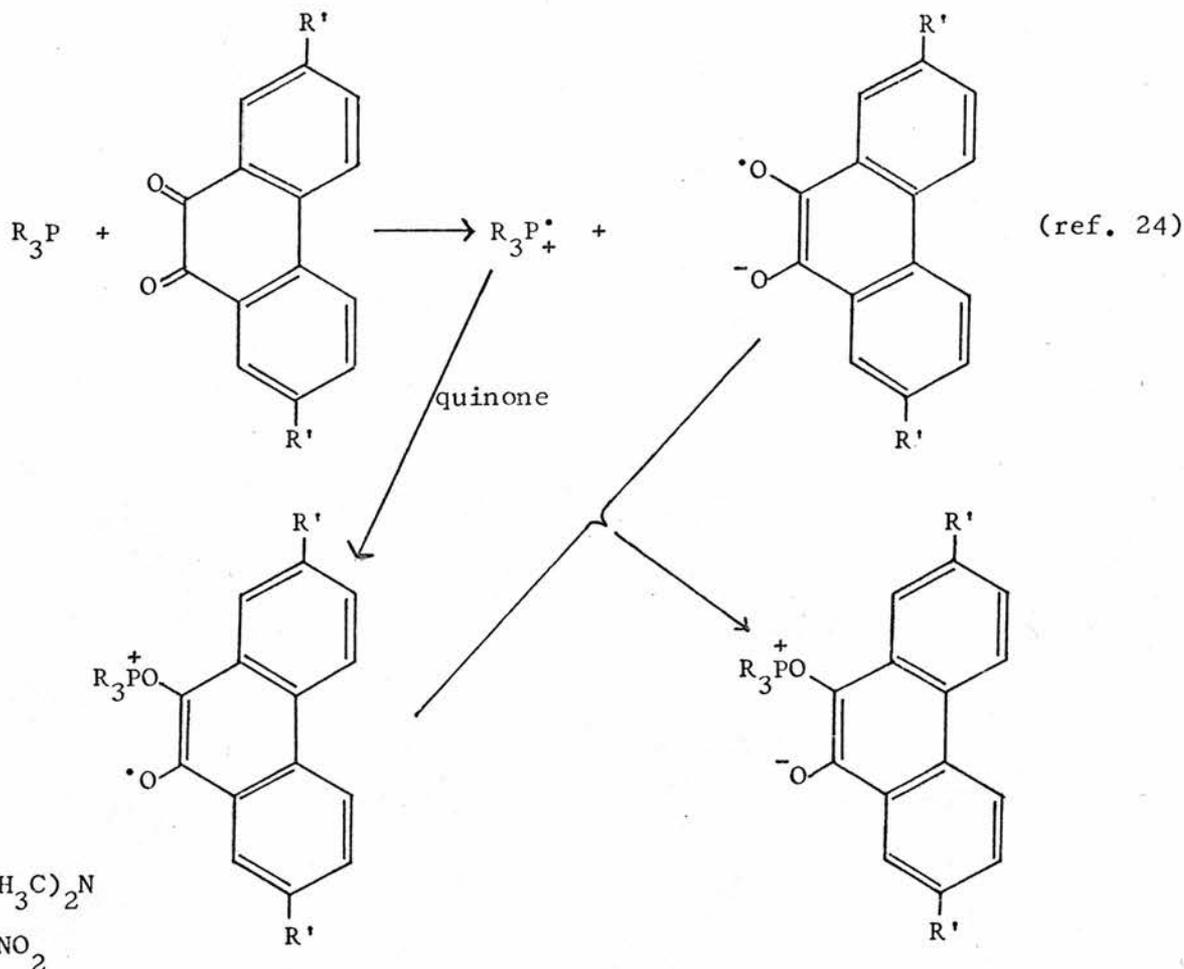
d. Reduction of a quinone is favoured energetically as the species generated is usually of an aromatic nature. Addition of one electron produces a semiquinone (VIII), which can be further reduced to the dianion of a catechol (IX).²³



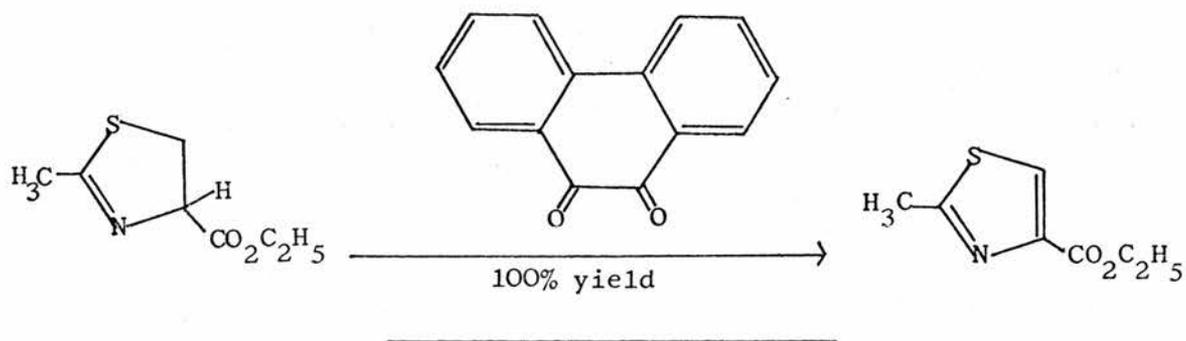
Trivalent phosphorus compounds are oxidized by 1,2-quinones with the formation of one or two phosphorus - oxygen bonds.^{24,25} In certain cases radicals²⁴ have been shown to be present in such reactions.



The following mechanism has been proposed to explain the formation of radicals.



These oxidative properties of quinones can result in complicated reactions (as mentioned in section c), but they can also be of synthetic value, e.g.²⁶



The work described in this thesis concerns the following:

1. The reactions of amines with naphtho-1,2-quinone. (This is an extension of the work by P.I. Smith on amines with benzo-1,2-quinone).

2. An investigation of radical formation occurring during potential 'nucleophilic addition' reactions.
3. An unsuccessful investigation of the reactions of some diazo-compounds with benzo- and naphtho-1,2-quinones.

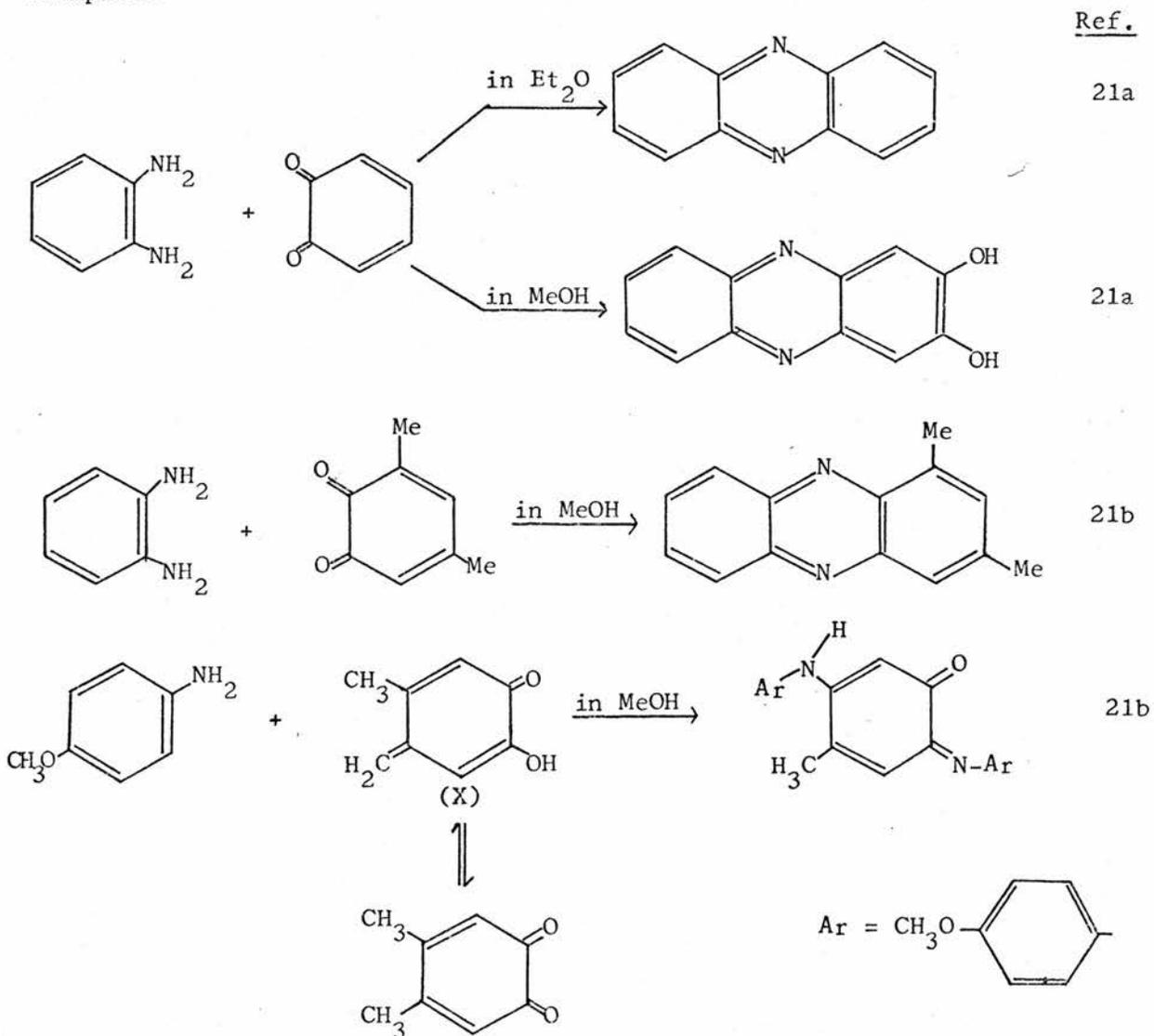
THE REACTIONS OF 1,2-QUINONES WITH AMINES

This topic may be divided into the reactions of aromatic amines and those of aliphatic amines.

1. Arylamines

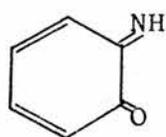
These normally react with 1,2-quinones by conjugate attack at the 4- or 5-position, and/or by condensation with one or both of the carbonyl groups. The type of attack is solvent dependent. In ether condensation or condensation plus conjugate addition occurs. In methanol quinones with unsubstituted 4- and 5-positions react by the addition mechanism, but if methyl groups are present in those positions, reaction may occur via the tautomeric form (X). The formation of hemi-acetals by the quinone in methanol is thought to be the reason for the different products.

Examples:

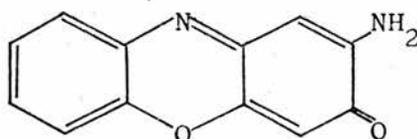


The product of conjugate addition is an amino-catechol, which may be oxidized to the amino-quinone by excess quinone, and further reaction with the amino-quinone can then take place.

If 2-hydroxyaniline is treated with benzo-1,2-quinone, one molecule of quinone oxidizes one mole of the amine to the quinonimine (XI), and this reacts with a second mole of the amine to give (XII).



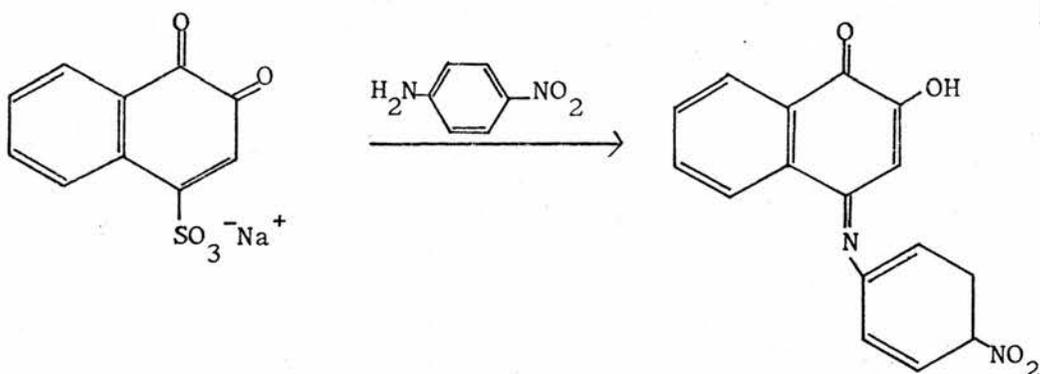
(XI)



(XII)

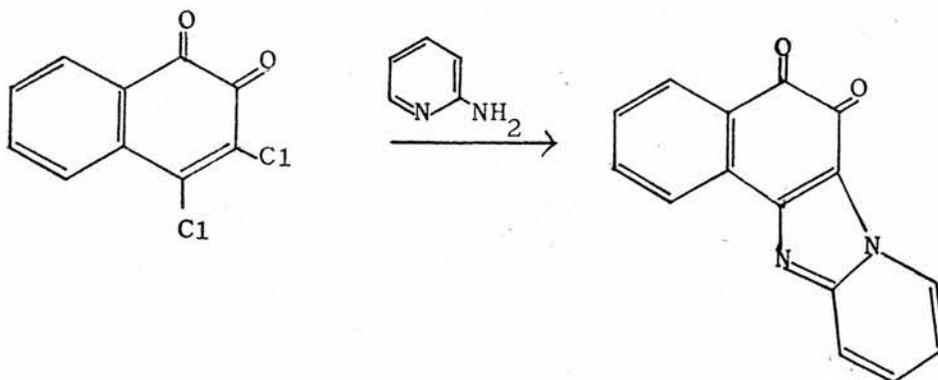
ref. 21a

In the case of naphtho-1,2-quinone, the bulk of the work has been on derivatives with a leaving group in the 4-position, but recently some work has been done on the unsubstituted compound.

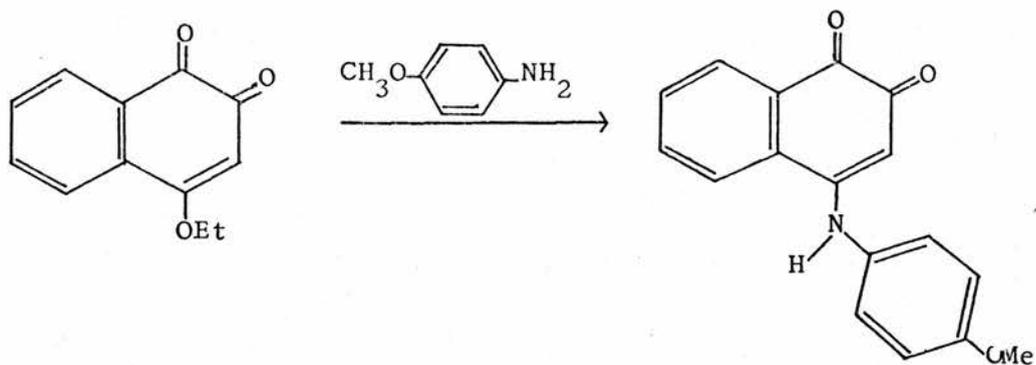


Ref.

27

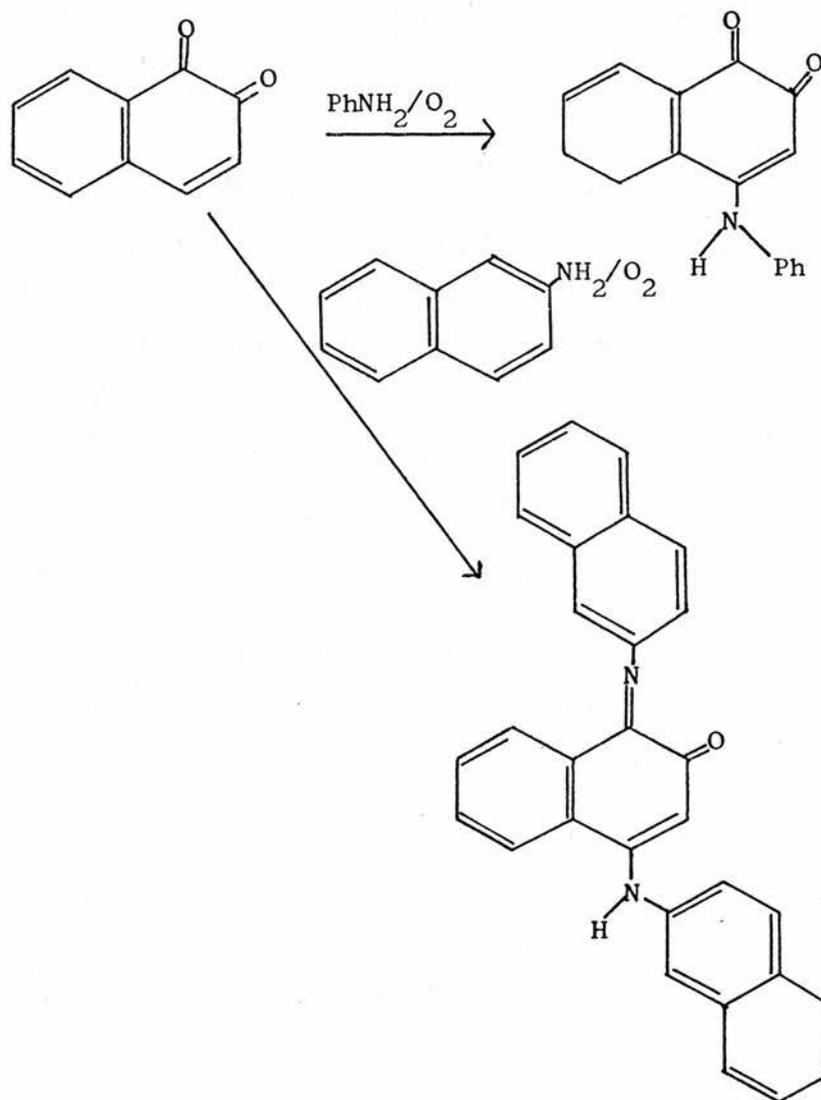


28



Ref.

29

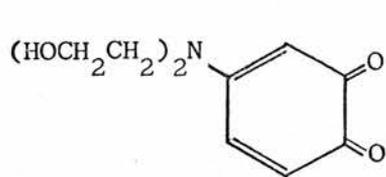


30

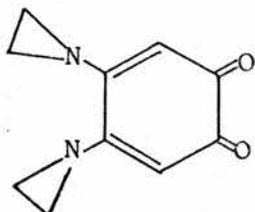
2. Alkylamines.

Several reactions of this type have been investigated, and various products obtained. In some cases the quinones were prepared in situ.

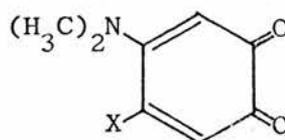
Silver oxide oxidation of catechol in the presence of N,N-di-(2-hydroxyethyl)amine,³¹ aziridine,³² and dimethylamine³² (separately) yields the products (XIII), (XIV) and (XV) respectively.



(XIII)



(XIV)

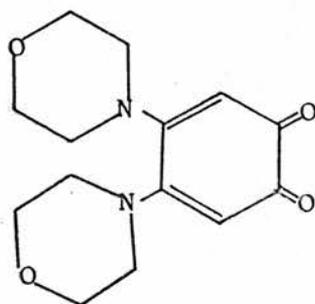


(XV)

(XVa) : X = H

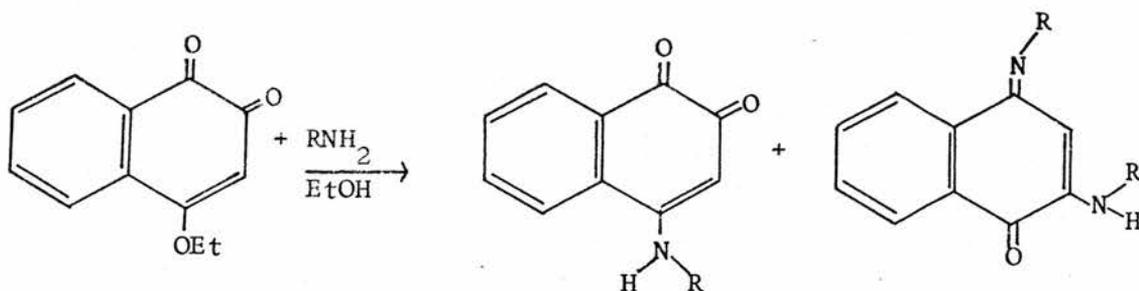
(XVb) : X = N(CH₃)₂

Morpholine reacts with benzo-1,2-quinone produced in situ by treating catechol with oxygen in the presence of a copper catalyst to yield 4,5-dimorpholinobenzo-1,2-quinone (XVI).³³

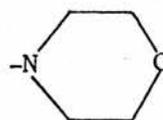
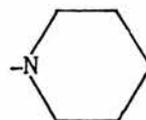
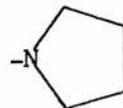
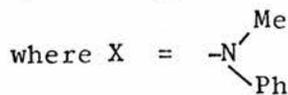
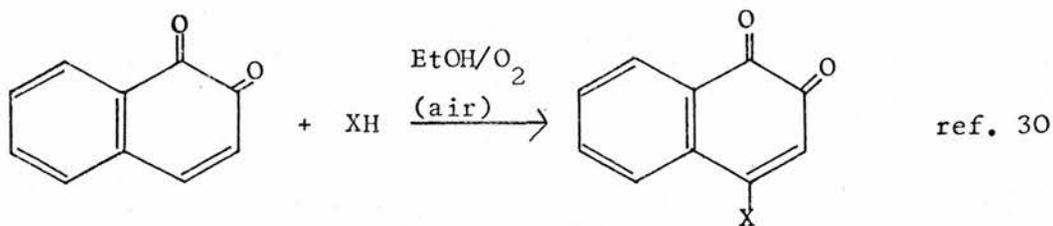


(XVI)

Naphtho-1,2-quinone has been treated with N-methylaniline and three cyclic secondary amines to give 4-substituted naphtho-1,2-quinones,³⁰ while 4-ethoxynaphtho-1,2-quinone reacts with primary alkylamines to give a mixture of the 4-amino-quinone and the 2-amino-1,4-quinone-imine.^{29,34}

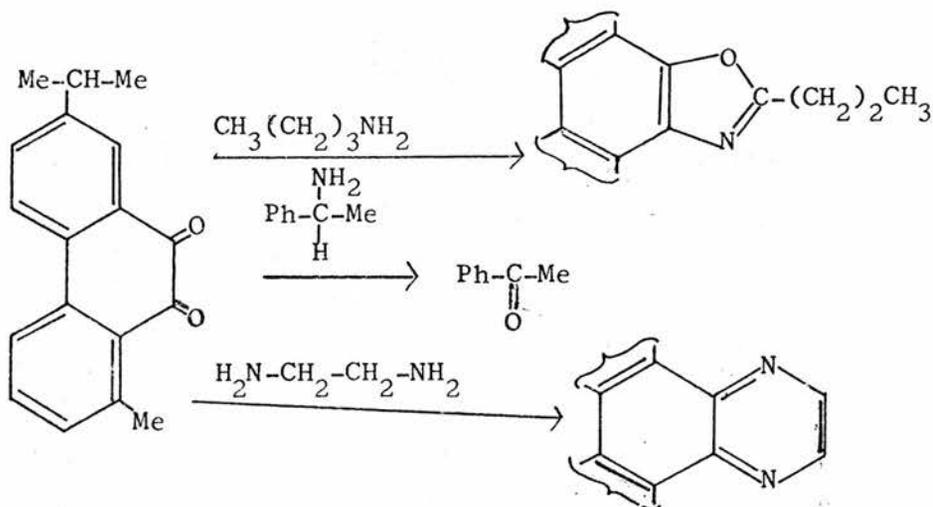


R = methyl or cyclohexyl



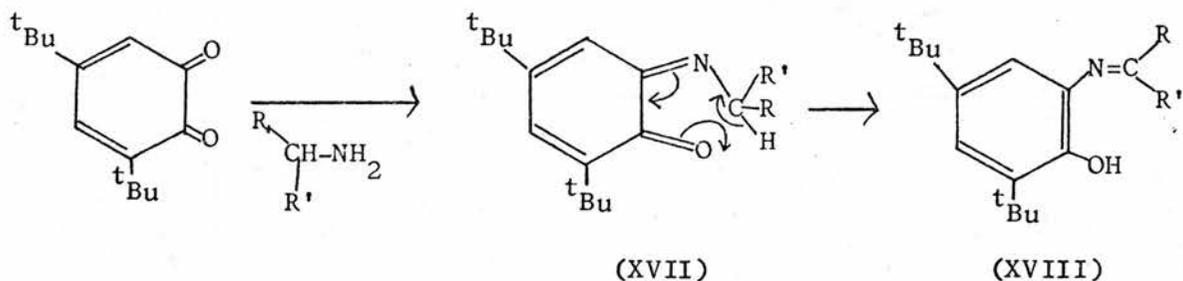
Where nucleophilic 1,4-addition is prevented, attack on the carbonyl group occurs.

McCoy and Day³⁵ investigated the reactions of alkylamines with phenanthrene-9,10-quinone and its 7-isopropyl-1-methyl derivative (known as retenequinone). With the latter, amines containing a methylene group adjacent to the nitrogen atom reacted to give oxazoles, whereas those with a secondary carbon next to the nitrogen underwent oxidation to ketones. Ethylene diamine was an exception - it condensed to give a pyrazine.

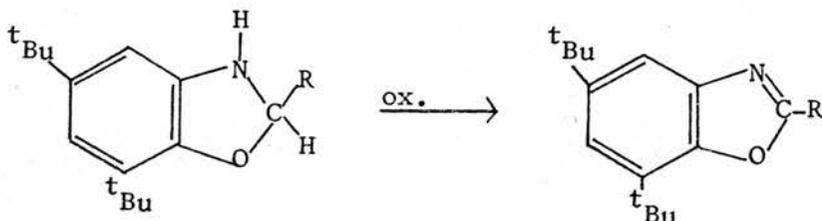


Phenanthrene-9,10-quinone itself reacted with n-butylamine to give intractable materials only.

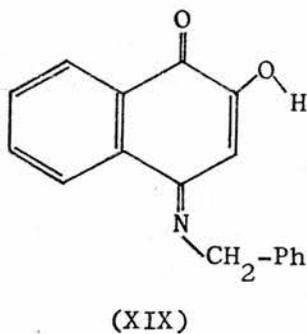
Corey and Achiwa³⁶ found that 3,5-ditertiarybutylbenzo-1,2-quinone condensed with aliphatic amines to give a quinonimine (XVII), which then rearranged to form an o-hydroxy anil (XVIII).



Where R (or R') is hydrogen, cyclization occurs to give an oxazolone, which can be oxidized by excess quinone to an oxazole.



Smith and Tedder³⁷ found that benzo-1,2-quinone oxidized benzylamine to benzaldehyde, indicating that the presence of an α -methylene group does not necessarily lead to a cyclic product. Benzylamine reacts with the sodium salt of naphtho-1,2-quinone-4-sulphonic acid to yield (XIX).²⁷



THE REACTIONS OF NAPHTHO-1,2-QUINONE WITH AMINES

General Procedure.

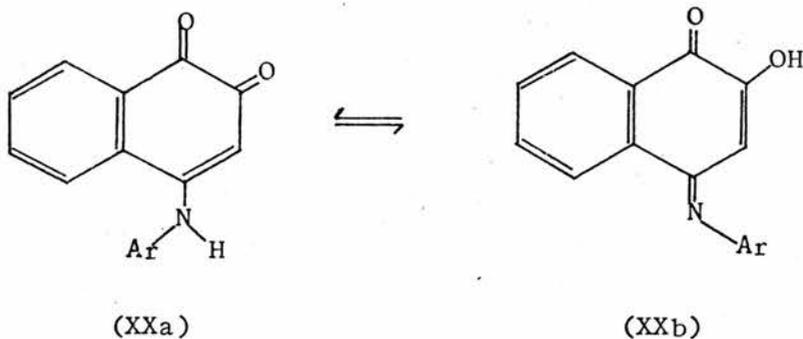
1. Primary Arylamines.

Solutions of the amine and the quinone in methanol were mixed and left to stand. A precipitate formed (except in the case of 2,6-dimethylaniline*) and was removed by filtration. Methanol or 2-methoxyethanol was used to recrystallize the precipitate, whose spectroscopic properties were investigated, and melting point determined.

As the use of diethyl ether in place of methanol resulted in the formation of different products when benzo-1,2-quinone was treated with amines,^{21a} it was originally intended to carry out similar experiments using naphtho-1,2-quinone, but the low solubility of this material in ether (1 g. in 1.5 l.) resulted in only one such experiment being performed. Tetrahydrofuran was used as solvent in one experiment.

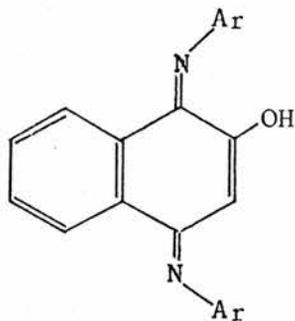
Results.

In each case the main product (the precipitate) was found to be that resulting from conjugate addition, followed by oxidation, i.e. (XXa) \rightleftharpoons (XXb).

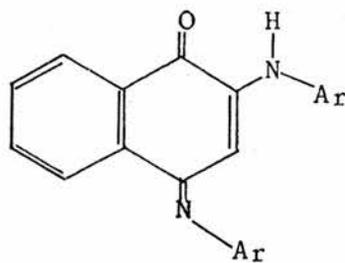


In the case of p-bromoaniline, a very small quantity of a second product was isolated. Mass spectral and infra-red spectroscopic studies suggested

* Chromatographic techniques suggested that some reaction had occurred, but no product could be identified.



(XXI)



(XXII)

Ar = p-bromophenyl

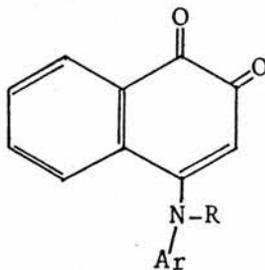
that the compound's structural formula was (XXI) or (XXII).

The reaction of p-toluidine with naphtho-1,2-quinone in tetrahydrofuran yielded a material whose mass spectrum was interpretable in terms of a similar structure, but thin layer chromatography showed that column chromatography had not succeeded in separating this substance from the normal addition product (XX). As the quantity of material was of the order of 0.01 g., further chromatography was not attempted.

The spectroscopic properties of the addition compounds will be discussed later.

2. Secondary Arylamines.

Methanolic solutions of the quinone and the amine were mixed and left to stand. No precipitate formed. Column chromatography or trituration was used to obtain the main product, and spectroscopic data indicated that it was of the type (XXIII).



(XXIII)

Compounds of this type were isolated from the reactions of N-ethyl- and N-methyl-anilines, and a derivative was prepared of the material obtained

from N-ethyl-4-methylaniline. Similar derivatives, prepared by the condensation of 1,2-diaminobenzene with the addition product, were obtained from (XXIII) where R = Me or Et.

3. Note. Tertiary Arylamines.

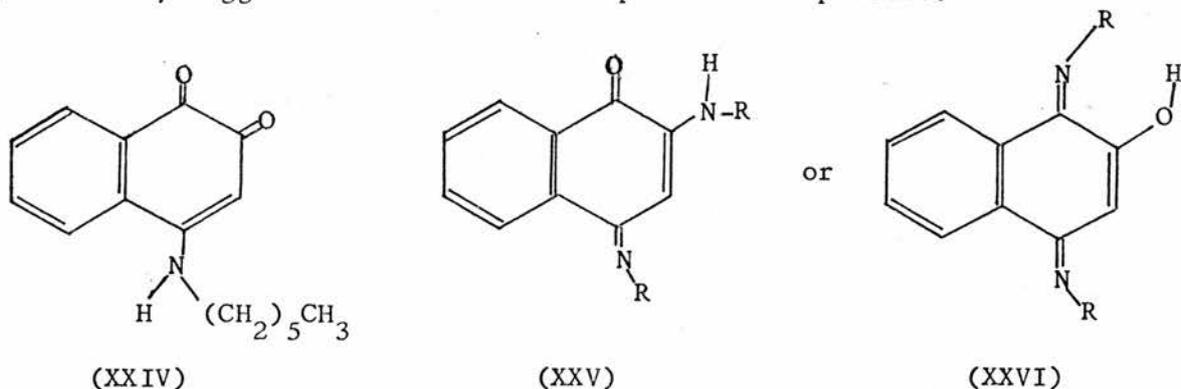
A reaction between N,N-dimethyl aniline and naphtho-1,2-quinone in ether was carried out, and investigated by thin layer and column chromatography. These indicated the presence of at least eight materials in the product solution, and that separating them would be extremely difficult, so no further work was done on this system. A similar experiment using methanol as solvent gave similar results.

4. Alkylamines.

The reaction was performed in methanol as for other varieties of amine. No precipitate formed after the mixture had stood for 24 - 48 hours, and the solvent was then removed under reduced pressure. Trituration (Ether, petrol, benzene) sometimes produced a precipitate. Thin layer chromatography demonstrated the presence of nine or more materials in the final mixture, the complete separation of which would have been extremely difficult.

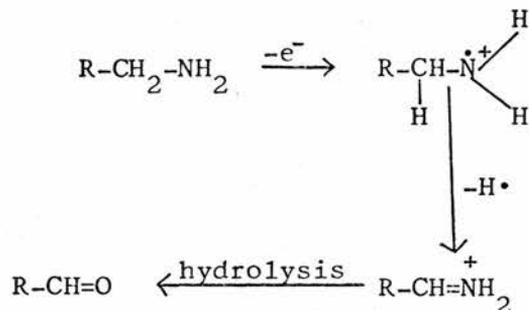
It proved possible to isolate a sample of (XXIV), and materials corresponding to (XXV) or (XXVI) where R = n-hexyl or cyclohexyl were identified by accurate mass measurements on the molecular ion.

In the cases of reactions involving n-octylamine and n-pentylamine, mass spectrometry suggested that similar compounds were present.



5. Other Experiments

a) An aliphatic amine with an α -methylene group might be oxidized according to the following mechanism.

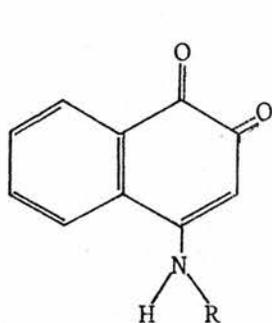


2-Amino-2-methylpropane can undergo the first, but not the second stage of this reaction, and its reaction with naphtho-1,2-quinone was therefore investigated. Products were obtained but could not be identified. The reaction between this amine and benzo-1,2-quinone was studied by e.s.r. spectroscopy, and that work is described on page 81 et seq.

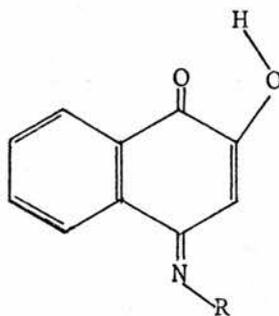
b) Treatment of naphtho-1,2-quinone with 1,2-diaminoethane in methanol gave a red precipitate within one hour. Concentration of the mixture under reduced pressure gave a material, from which trituration by methylene dichloride produced a yellow precipitate, which was demonstrated by chromatography to be a mixture, while the mass spectrum of the red material could not be interpreted despite the consideration of numerous theoretically possible products.

Infra-red Spectra.a) N-Aryl-4-aminonaphtho-1,2-quinones (XX and XXIII).

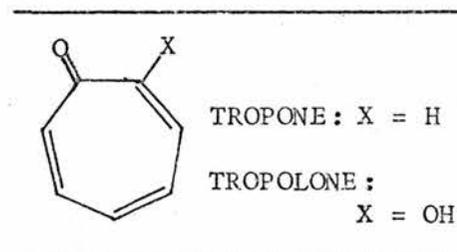
These were recorded using samples mullied in Nujol. The main peaks of interest are those corresponding to the N-H/O-H and carbonyl group absorptions. These, along with peaks occurring in the C=N and aromatic C=C regions, are listed in Table 1 (page 20).



(XXa)



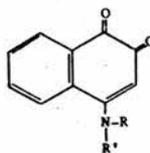
(XXb)



Both of the tautomers (XXa) and (XXb) are capable of forming intermolecular hydrogen bonds (N-H...O or O-H...O or N), while the quinone-imine system can also have an intramolecular hydrogen bond. Such intramolecular hydrogen bonds tend to reduce the frequency of both the O-H and carbonyl stretching vibrations, e.g. the free hydroxyl group in phenol absorbs at approx. 3600 cm.⁻¹^{38a} whereas the hydroxyl group of tropolone absorbs at 3100 - 3300 cm.⁻¹³⁹ Tropone has a carbonyl absorption at 1630 - 1650 cm.⁻¹³⁹ while the equivalent in tropolone is near 1600 cm.⁻¹³⁹ Similar phenomena are observed in ortho-hydroxyaryl ketones^{38a} and in anthra-9,10-quinones in which any of the 1,4,5 and/or 8 positions is substituted by hydroxyl. In these latter compounds the hydrogen-bonded carbonyl group absorbs at about 1635 cm.⁻¹, an ordinary carbonyl at approx. 1675 cm.⁻¹⁴⁰

With the exception of the derivative of p-amino-azobenzene, the carbonyl group absorption occurs in the range 1670 - 1690 cm.⁻¹ This

TABLE I
Positions of Absorption Peaks in Infra-red Spectra



R'	R	N-H/O-H	C=O	Others
Ph	H	3300(m, s)	1690(m, s)	1590, 1580(i, s)
	H	3200(w, b)	1690(m, s)	1610, 1590(i, fs)
	H	3290(w, b)	1680(m, s)	1605, 1580(i, fs)
	H	3340(w, s)*, 3200(w, b)	1670(m, s)	1570(i, b), 1510, 1520
	H	3300(w, s) 3280-3120(b)	1690(m, s) 1650(i, s)	1605, 1590, 1580(i, s), 1520(i, multiplet)
	H	3250(w, b)	1680(w, s)	1600, 1590-70(i, multiplet), 1515(i, fb)
	H	3300(m, b)	1690(i, s)	1590-70(i, doublet), 1540 → 1490(mult.)
	H	3200(w, b)	1680(m, s)	1600(i, fb)
	H	3200(w, b)	1685(m, s)	1610, 1580(m, s), 1520(i, fs)
	H	3300(w, b)	1690(m, s) †1670(m, s)	1610(i, s), 1560(i, s), 1540
Ph	Me	(3050 vw)	1685(i, s)	1630(i, s), 1560(i, s), 1580(i, fb)
Ph	Et	-	1690(i, s)	1620(i, fb), 1575(i, s), 1530(i, s)
n-hexyl	H	3330-3220(m, b)	1680(m, s)	1580(i, s)
n-pentyl	H	3220(w, fs) 3060(vw, fs)	1680(w, s)	1600, 1580(i, fb), 1530(i, b)
cyclohexyl	H	3320(w, s)	1660(m, s)	1600(m, multiplet)

* The primary amino group results in two N-H absorptions.

† Acetanilide has a carbonyl group at ca. 1670 cm.⁻¹ (Author's observation).

KEY: Where there are brackets after a given wavelength, the letters enclosed thereby indicate the intensity and width of the absorption.

i - intense; m - medium; w - weak; s - sharp; b - broad; f - fairly; v - very.

NOTE: Minor errors in calibration have not been corrected.

indicates that the compound is not intramolecularly hydrogen bonded and therefore almost certainly in the 1,2-quinonoid form. It is possible that the p-amino-azobenzene derivative existed as a tautomeric mixture, thereby giving two peaks in the region 1640 - 1700 cm.⁻¹

In the two tertiary amines the carbonyl absorption is more intense than in the secondary amines (i.e. N-arylamino-naphtho-1,2-quinones) described above. This may result from the bulkier amine function being less able to conjugate with the 2-carbonyl group.

b) Adducts formed from 2 Amine Molecules and 1 Quinone.

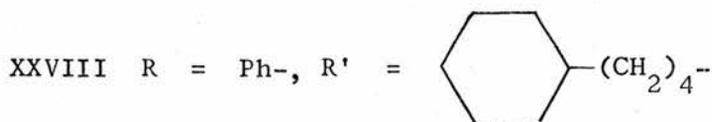
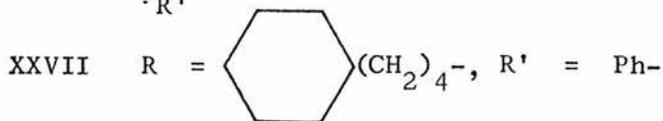
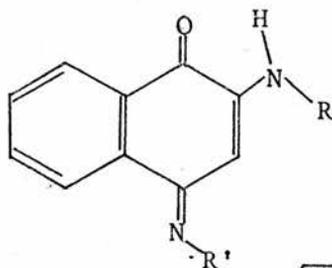
The infra-red spectra of these materials are noticeably different from those of the mono amine derivatives. The characteristic absorptions are detailed below. All samples were mullied in Nujol.

<u>Amine</u>	<u>NH/OH</u>	<u>C=O, C=N</u>	<u>Others</u>
n-hexylamine	3350(s,fi)	1645(fs,i)	1590(b,i), 1500(b,m)
4-bromo-aniline	3280(s,fi)	1650(s,i), 1645*	1610(s,i), 1580(fs,m), 1530(fs,m)
cyclohexylamine	3380(s,m)	1700(s,m), 1645(fb, i)	1590-70(b,m)
p-toluidine	3320(s,w)	(⁺ 1685), 1650(s,i)	1595(mult,i), 1520 (mult, i).

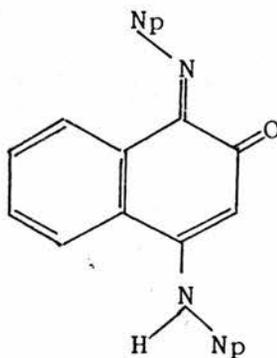
* shoulder

+ peak resulting from contamination by mono-arylamine-derivative.

For the cyclohexyl compound, Bullock et al.³⁴ obtained peaks at 3400 cm.⁻¹ and 1660 cm.⁻¹ using a sample in a potassium bromide disc. Other derivatives of alkylamines gave absorptions in the ranges 3335 - 3355 cm.⁻¹ and 1655-1660 cm.⁻¹ Replacement of one alkyl group by phenyl did not alter the carbonyl frequency, but (XXVII) had an N-H absorption at 3342, whereas (XXVIII)'s equivalent was at 3298 cm.⁻¹



Takada et al.³⁰ found that naphthyl-2-amine reacted with naphtho-1,2-quinone in ethanol to form a 2:1 adduct, to which they ascribed the structure (XXIX) on the grounds of the absence of an acetophenone type carbonyl absorption - presumably this means an absence of peaks in the range 1700-1680 cm.⁻¹



Np = 2-naphthyl

(XXIX)

Compounds having a structural formula of the type of (XXVII) or (XXVIII) would not be expected to show a carbonyl in that range, because of the N-H...O=C hydrogen bonding. Bullock et al.³⁴ prepared (XXVIII) from aniline and 4-(N-cyclohexylbutyl)aminonaphtho-1,2-quinone - the N.M.R. data for the product (XXVIII) are more consistent with the (XXVIII) type structure than the equivalent of (XXIX). Takada et al. can be correct for their compound of course. It therefore seems possible that the band near 1650 cm.⁻¹ is a combination of the C=O and C=N absorptions, unless the C=N bond has a frequency of the order of 1600 cm.⁻¹ or less.

Ultra-Violet and Visible Spectra.

Positions of absorption maxima and extinction coefficients are listed in Table 2 on page 24, while similar information for various related systems is given in the following tables (3,4,5).

Before considering the spectra it is worth noting that studies made using molecular models (of the space-filling kind) indicate that it is difficult, if not impossible, for 4-arylamino-naphtho-1,2-quinones to achieve the situation where the naphthyl ring and the phenyl ring are co-planar. The spectrum of N-phenylnaphthyl-1-amine,^{41,41b} a sterically similar system, is not the same as a combination of the spectra of aniline⁴¹ and naphthyl-1-amine,^{41b} indicating that there is some interaction between the various π -electrons. (As a contrasting example, 2,2'-dimethylbiphenyl has a spectrum resembling that of o-xylene, not biphenyl.⁴²)

Uncertainty also exists about the structure adopted by these compounds in alcoholic solution. They can exist in two tautomeric forms, either of which could be in equilibrium with a hemi-ketal type structure.

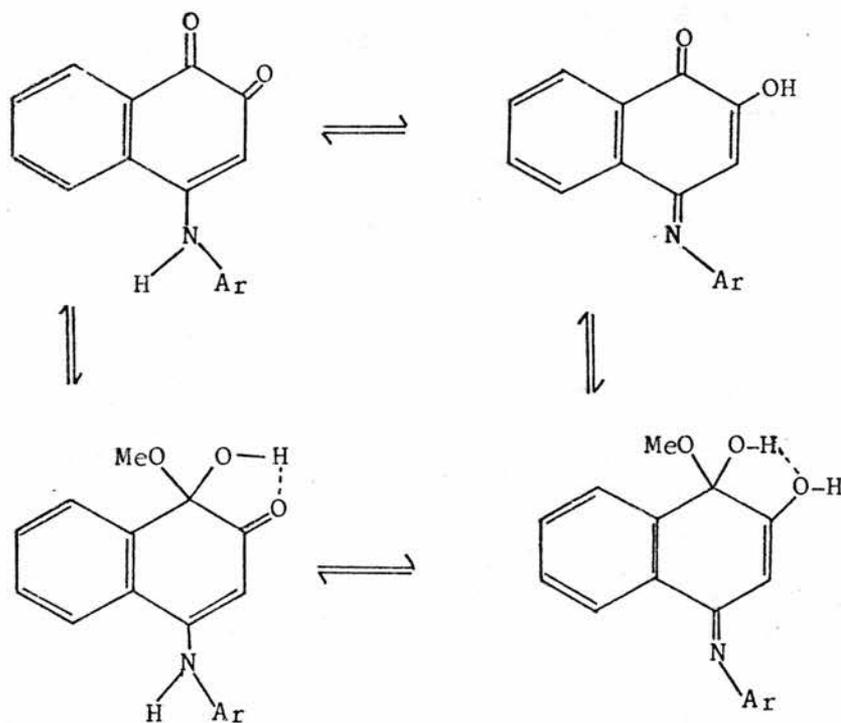
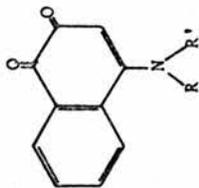


TABLE 2
Ultra-violet/Visible Spectra of 4-Aminonaphtho-1,2-quinones



SOLVENT: Methanol

	R	R'	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	λ_4	$\log \epsilon_4$
a	Ph	H	243	4.48	282	4.27	325 → 350(1)	3.80	459	3.69
b		H	242	4.40	277	4.16	325 → 345(1)	3.82	460 ± 10	3.72
c		H	240	4.33	277	4.14	325 → 345(1)	3.70	455	3.64
d		H	239	4.30	284	4.17	335	3.77	447	3.56
e		H	243	4.37	282	4.12	330	3.82	470	3.66
f		H	245	4.40	279	4.20	345	3.73	475	3.74
F		H	249	4.50	275	4.22	345	3.79	476	3.76
h		H	252	4.39	282	4.14	-	-	500	3.66
i		H	262	4.50	285	4.05	-	-	520	3.77
j		H	240	-	-	-	354	-	474	-
k	Ph	Me	244	4.31	272	4.06	322	3.81	456	3.83
l	Ph	Et	246	4.38	278	4.08	322	3.80	476	3.88
m	n-hexyl	H	238	4.27	275	4.23	325(1) +	3.64	445	3.68

+ Also an absorption at 300 nm. (i) with $\log \epsilon = 4.00$.

NOTES: 1. The minimum absorption in the range between λ_2 and λ_3 was very little less than the absorption at λ_3 . In the spectrum of 'h' and

'i' no shoulder was visible near 330 nm.

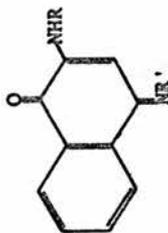
2. 'j' was too insoluble to allow determination of the extinction coefficients.

3. 'b' had a flat-topped peak over the range 450 → 470 nm.

4. (i) - shoulder or inflexion.

TABLE 3

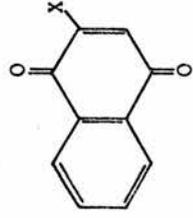
Ultra-Violet/Visible Spectra of 2-Aminonaphtho-1,4-quinone-imines



R	R'	Solvent	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	λ_4	$\log \epsilon_4$	λ_5	$\log \epsilon_5$	Reference
Me	Me	EtOH	238	4.41	270	4.18	280(1)	4.14	337	3.67	425	3.68	34
Butyl	Butyl	EtOH	238	4.40	272	4.12	280(1)	4.09	335	3.67	425	3.67	
Hexyl	$(\text{CH}_2)_3\text{-CH}_2$	EtOH	239	4.38	272	4.10	280(1)	4.08	338	3.66	425	3.66	
	Ph	EtOH	240	4.50	270(1)	4.20	280(1)	4.18	335	3.80	453	3.85	
	$(\text{CH}_2)_3\text{-CH}_2$	EtOH	252	4.27	-	-	280	4.40	340(1)	3.74	440	3.70	

TABLE 4

Ultra-violet/Visible Spectra of 1,4-Quinones



Substance	Solvent	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	λ_4	$\log \epsilon_4$	λ_5	$\log \epsilon_5$	λ_6	$\log \epsilon_6$	Reference
1,4-NQ	EtOH	240	4.34	251	4.34	260(i)	4.05	338	3.50					57
2-NH ₂ -1,4-NQ	EtOH					267	4.32	330	3.39			445	3.46	50
2-MeO-1,4-NQ	MeOH					280	4.29	340	3.49			420	1.64	58
2-HO-1,4-NQ	MeOH					275	4.14	335	3.44			400(i)	2.94	58
2-HO-1,4-NQ	95% EtOH/244(i) 4.23 5% HCl			249	4.28	278	4.18	333	3.47					57
Lapachol*				251.5	4.38	278	4.28	331	3.43	382(i)	3.17			59
Lomatol*				251.5	4.38	279.5	4.17	331	3.45	379(i)	3.18			
Isolomatol*	Possibly EtOH?			250.5	4.45	278.5	4.28	331	3.54	377.5(i)	3.15			
Lapachol Me-ether*				249.5	4.35	276.5	4.22	333	3.56	381.0(i)	3.05			
d-Lapachone*				248.0	4.41	281.0	4.18	332.5	3.43	373(i)	3.13			

* See page 36 for structural formulae.
NQ = Naphthoquinone.

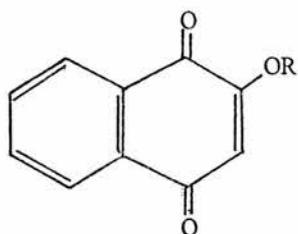
TABLE 4 (cont.)

X	Solvent	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	λ_4	$\log \epsilon_4$	λ_5	$\log \epsilon_5$	λ_6	$\log \epsilon_6$	Reference
	EtOH					272	4.51	325(1)	3.68			465	3.73	51
	EtOH	2375	4.20			275	4.30					465	3.69	50 (also 49)
	EtOH					280	4.43					480	3.76	50 (also 48)
	EtOH					275	4.43					490	3.66	50
	?											460	3.65	48
	EtOH					279	4.37					462	3.69	49
	EtOH					280	4.35	~330	~3.6			480	3.66	50
	95% EtOH	245	4.32			272	4.64	325(1)	3.80	390	3.24	490	3.84	52
	H ₂ O					280	4.64	320(1)	3.85	400(1)	3.23	485	3.87	52
	H ₂ O					284	4.50	325(1)	3.75			480	3.78	52
	EtOH											450	3.52	50

TABLE 5
Ultra-Violet/Visible Spectra of 1,2-Quinones

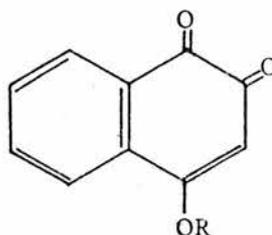
Substance	Solvent	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	λ_4	$\log \epsilon_4$	λ_5	$\log \epsilon_5$	λ_0	$\log \epsilon_0$	Reference
1,2-NQ	EtOH	2.50	4.35					340	3.40	400	3.40	500(i)	2.00	60
1-MeO-1,2-NQ	EtOH	2.50	4.07	254(i)	4.01	273(i)	3.78	339	3.26	403	3.29	490(i)	2.20	
β -Lapachone*	Possibly EtOH ?			256.5	4.45	282(i)	3.98	333	3.24	429.5	3.28			59
Br- β -Lapachone*				255.5	4.50	282(i)	3.93	333.5	3.22	425.5	3.27			
HO- β -Lapachone*				250.0	4.44	283.5(i)	3.88	331.2	3.20	431.0	3.27			

* See page 36 for structural formulae.



XXX a) R = H

b) R = CH₃



XXXI a) R = H

b) R = CH₃

Fieser⁴³ calculated that if

$$\frac{\text{S.E.P. of XXXa}}{\text{S.E.P. of XXXIa}} = \frac{\text{S.E.P. of XXXb}}{\text{S.E.P. of XXXIb}} \quad (\text{S.E.P.} = \text{standard electrode potential})$$

(a reasonable assumption), then the equilibrium constant for the reaction (XXXIa) \rightleftharpoons (XXXa) would be 502, which corresponds to a free energy difference of approximately 3.7 kcal.mol.⁻¹ (15.5 kJ mol.⁻¹). In this case a bond energy calculation would give a zero difference, whereas a similar calculation comparing a 4-aminonaphtho-1,2-quinone with a 2-hydroxy-naphtho-1,4-quinone-imine suggests the former has slightly more bond energy, but the difference is so slight (2 kcal.mol.⁻¹) as to be comparable with the error in the calculation. It is therefore not possible to decide (on these grounds) which tautomer is favoured.

Though the carbonyl groups will interact with hydroxylic solvents by hydrogen bonding, the spectrum of 1,2-naphthoquinone in methanol is similar to that of it in benzene,⁴⁴ except at wavelengths greater than 500 nm. where the weak $n \rightarrow \pi^*$ band appears at longer wavelength in the less polar solvent (a characteristic of that type of absorption⁴⁵). This indicates that ketalization is not an important effect.

Examination of the tables reveals that simple derivatives of naphtho-1,2- and -1,4-quinones show similar spectra, but the maxima at ca. 280 nm. and ca. 335 nm. have smaller extinction coefficients in the 1,2-quinones compared to their 1,4-analogues.

By examination of substituent effects, Singh et al.⁴⁶ have shown that the spectra of simple naphtho-1,4-quinones can be divided into benzenoid bands (240 - 245 nm. and 330 - 345 nm.) and quinoid bands (257 - 285 nm. and above 370 nm. - the latter band is weak and not well defined unless both the 2- and 3-positions are substituted). In addition there is the very weak $n \rightarrow \pi^*$ transition of the carbonyl groups in the visible region.

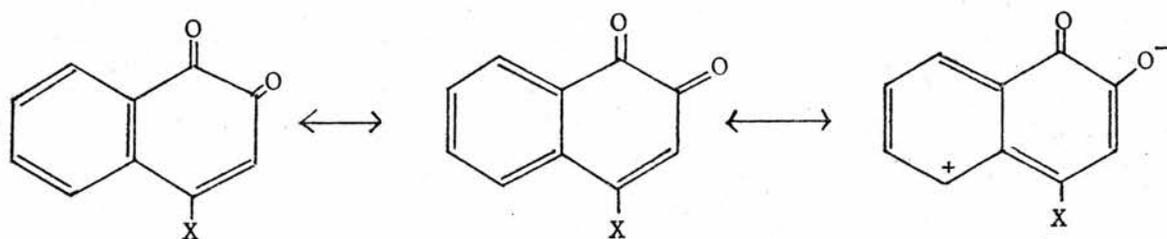
A limited amount of information has been published on the spectra of arylamino-naphthoquinones, both 1,2 and 1,4.⁴⁷⁻⁵² Harman et al.⁴⁷ investigated the variation of the spectra of 4-aminonaphtho-1,2-quinones with pH, by using aqueous buffer solutions as solutions. These gave spectra with similar wavelength maxima to alcoholic solvents, but the extinction coefficients were much larger in the buffer solutions. The values determined in the present work seem reasonable when compared with those of related compounds.

Comparison of the spectra of 2-arylamino-naphtho-1,4-quinones with those of 4-arylamino-naphtho-1,2-quinones reveals that the band at ca. 275 nm. is stronger in the former (as is the case for simple derivatives), but that the band at ca. 335 nm. is of approximately equal intensity in each type of compound - it may be slightly more intense in the 1,2-quinones but the limited amount of data on this band in the 1,4-quinones makes such a conclusion uncertain. This is a benzenoid band, but it is interesting to note that the band is more intense in N,N'-dialkyl-2-aminonaphtho-1,4-quinone-imines than in 2-hydroxynaphtho-1,4-quinone.

The absorption above 445 nm. is of similar intensity in both the arylamino-1,2- and 1,4-quinones, as is the band at ca. 240 nm. (In certain cases the 1,4-isomer does not show a peak at ca. 240 nm., e.g. 2-anilino-naphtho-1,4-quinone does not.) In the 1,2 case these two bands exhibit parallel bathochromic shifts as the electron-donating power of the

substituent(s) on the arylamino ring is increased. The short wavelength band is of similar intensity to the corresponding band in simple naphtho-1,2- and 1,4-quinones.

This is of interest because a substituent in the quinoid part is affecting the absorption of the benzenoid part. The simplest explanation is that the molecule is in the imino form, and that there is sufficient conjugation between the aryl ring and the imine double bond for resonance to occur with the benzenoid ring (in the quinone part of the molecule). Alternatively, in the amino form, an increase in electron-donation to the aryl ring by the substituent will allow the nitrogen's lone pair to conjugate better with the 2-carbonyl group, thereby reducing the 'electron drain' on the benzenoid ring that occurs via resonance of the type depicted below.



The effect should correlate roughly with the change in basicity of the aromatic amines which form the substituent. Table 6 on p. 32 demonstrates this, and it also shows the 'parallel' change of λ_1 and λ_4 . This explanation has a very 'weak link' - naphtho-1,4-quinone and 2-ethyl-naphtho-1,4-quinone both have two benzenoid bands at 245 and 251 nm.⁴⁶ whereas 2-methoxy compound has peaks at 242 nm. and 248 nm.,⁴⁶ - a hypsochromic effect, the reverse of what is expected for a substituent with a +M effect. (These figures are for solutions in chloroform.)

A third possible reason for the observed red shift is that the band originates from the overlap of the quinone part's benzenoid $\pi \rightarrow \pi^*$ band and a similar transition in the arylamino system. Such might occur if the

conformation of the molecule is such that the nitrogen lone pair resonates only with the phenyl ring. In this case the spectrum would resemble the sum of the spectra of naphtho-1,2-quinone and the arylamine. Arylamines absorb maximally in the range 230 nm. to 265 nm.,⁴¹ with extinction coefficients of the order of 10,000, which suggests that $\log \epsilon$ for the amino-quinone would be greater than 4.50. N-acetyl-p-phenylene-diamine absorbs at 261 nm.⁵³ whereas p-phenylene diamine has its maximum at ~ 230 nm.⁵³ Therefore one would expect a combination of $\pi \rightarrow \pi^*$ bands to have a longer wavelength maximum for the acetyl compound - in fact the reverse is the case.

TABLE 6

Ar	λ_1 (nm.)	λ_4 (nm.)	* pK _a ⁵⁴	λ_4 (eV)	I.P. of ArH ⁵⁵ (eV)
2,4-dichlorophenyl	239	447	2.05	2.77	9.12
2,4-dimethylphenyl	240	455	4.89	2.73	8.56
4-methylphenyl	242	460 \pm 10	5.1	2.70	8.82
phenyl	243	459	4.59	2.70	9.25
4-bromophenyl	243	470	3.8	2.64	8.98
4-methoxyphenyl	245	475	5.3	2.61	8.22
N-acetyl-4-amino-phenyl	249	476		2.60	
4-aminophenyl	252	500	6.2	2.48	7.70
4-dimethylamino-phenyl	262	520	6.59	2.38	

The comparison of λ_1 and λ_4 with the pK_a values reveals several anomalies. The 2,4-disubstituted phenyl ring probably has greater difficulty in achieving a suitable configuration than the other systems because of steric restrictions resulting from the bulk of the ortho-substituent. Secondly, the visible absorption in the p-bromo-derivative occurs at an unexpectedly large

$$* K_a = \frac{[ArNH_2][H^+]}{[ArNH_3^+]}$$

wavelength. This may be a characteristic of bromine-substituted aromatics. Bromobenzene absorbs at 210 nm., toluene at 206.5 nm.⁵⁶ Similarly, in calculating the absorption maxima in para-substituted acetophenones, the increment to be added to the base value is 15 nm. for a bromine substituent, and 10 nm. for a methyl group.⁵⁶

The visible transition could be considered as a charge-transfer, i.e. the electron density on the quinone part rises and that on the arylamino section declines. The energetics of this process can be considered as the difference in solvation energy of the ground and excited states, the ionization potential of the arylamino part, and the electron affinity of the quinone part. If the first remains roughly constant, and the last is constant, the variation in λ_4 should follow the change in ionization potential of the arylamine. The latter should follow the I.P.'s of the corresponding aryl hydrogen compound - it would be reasonable to expect the NH_2 group to lower the I.P. of each by a similar amount. The change in λ_4 does follow the change in I.P., though anomalies similar to those described above are observed.

The small amount of data available makes a comparison of the N-alkyl system with the N-aryl type difficult. In the 1,4-quinone case the visible absorption appears to increase slightly in intensity, accompanied by a bathochromic shift, of 15 nm., for replacement of methyl by phenyl. However N-(n-hexyl)4-aminonaphtho-1,2-quinone gives a value for the visible extinction coefficient approximately equal to the average of those for the N-aryl compounds. The change from n-hexyl to phenyl again results in a bathochromic shift, of 14 nm. Study of the data table for 2-aminonaphtho-1,4-quinone-imines reveals that a similar shift of 15 nm. occurs when the amino alkyl is replaced by phenyl, but a greater shift (28 nm.) occurs when

the same change is effected on the imino nitrogen. The short wavelength absorption is also effected by this substitution - an amino-phenyl group causes a bathochromic shift of 13 nm. relative to an amino-alkyl, whereas an imino-phenyl causes a shift of 1 - 2 nm. only. The comparable shift in the 4-amino-1,2-naphthoquinones is 5 nm.

These points suggest that the visible absorption originates in a $\pi \rightarrow \pi^*$ transition, the 'migrating' electron having max. electron density at the nitrogen, in the ground state. The fact that the p-amino-azobenzene derivative has a visible absorption at as short a wavelength as 474 nm. is indicative of the limited resonance in the system, as a fully conjugated planar N-(p-azobenzene)-4-aminonaphtho-1,2-quinone would be expected to have an absorption at much longer wavelength than the other listed derivatives owing to the massive increase in the length of the conjugated system.

The N-alkyl-N-aryl-4-aminonaphtho-1,2-quinones show generally similar spectra to their relatives without the alkyl group, but the long wavelength benzenoid band appears at slightly shorter wavelength (322 nm., a peak, as compared to an inflexion, centre 335 nm. in the N-phenyl compound). The change from N-methyl to N-ethyl causes a slight bathochromic shift in λ_1 , a larger one in λ_2 , and one of 20 nm. in the visible absorption maximum. However there is no effect on λ_3 , showing that this transition is un-influenced by the nitrogen atom's lone pair.

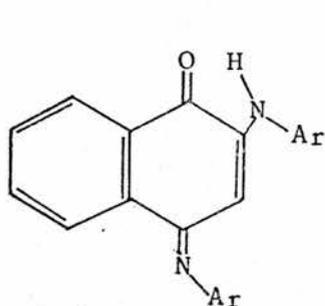
The adducts formed from one quinone molecule and two amine molecules gave spectra with the following characteristics (all wavelengths in nm.).

Amine	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	λ_4	$\log \epsilon_4$	λ_5	$\log \epsilon_5$
4-bromo-aniline	251	4.30	285	4.35			330(i)	3.80	462	3.76
n-hexyl-amine	239	4.29	272	4.16	307	3.88	345(i)	3.64	444	3.68
			278(i)	4.15						

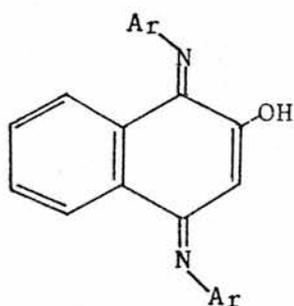
(The second compound may also have an ill-defined shoulder in the range 315 - 340 nm.).

The alkyl compound has a similar spectrum to the aminonaphthoquinone-imines in the table except in the visible region, where the spectrum resembles that of the mono-amine adduct. The compound is yellow in colour, whereas the mono-amine adduct is orange, and therefore should absorb at a shorter wavelength. It is therefore possible that the di-amine adduct was impure, or that some hydrolysis occurred in the solution used to determine the spectrum.

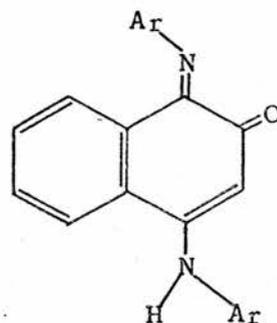
In comparison with the dialkylaminoquinone-imines the di-aryl compound shows similar features to those discussed earlier when the substitution of one alkyl group by phenyl was described, i.e. red shift of λ_1 accompanied by a slight decrease in intensity, single maximum near 280 nm. of increased intensity, and a shoulder near 335 nm. - these changes resulting from the 2-aminoaryl group, while both the aryl groups contribute to the bathochromic shift of λ_5 . This is consistent with the compound being (XXII) or (XXIb) and not (XXIa).



(XXII)

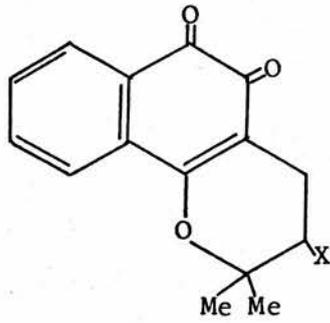


(XXIa)



(XXIb)

It is not possible on the above evidence to indicate which tautomer of the arylaminonaphtho-1,2-quinones predominates in methanolic solution, if one does - both might be present in reasonable amounts. The weaker 280 nm. absorption, the similarity of the spectrum of the aniline derivative to that of the N-alkyl aniline one, the shift in λ_1 when alkyl is replaced by aryl, and the size of the shift in λ_4 when aryl replaces alkyl all indicate that the 1,2-quinone form is favoured, but it is easier to explain the shift in λ_1 if the material is in the imino form.



β -LAPACHONE

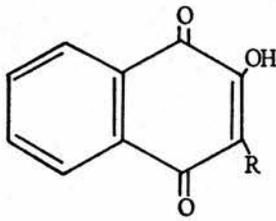
X = -H

BROMO- β -LAPACHONE

X = -Br

HYDROXY- β -LAPACHONE

X = -OH



LAPACHOL

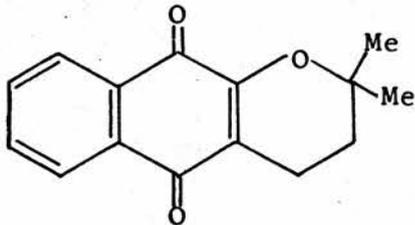
R = $-\text{CH}_2-\text{CH}=\text{CMe}_2$

LOMATIOL

R = $-\text{CH}_2-\text{CH}=\text{C} \begin{matrix} \text{Me} \\ \text{CH}_2\text{OH} \end{matrix}$

ISOLOMATIOL

R = $-\text{CH}_2-\text{C} \begin{matrix} \text{H} \\ | \\ \text{OH} \\ | \\ \text{C} \\ // \quad \backslash \\ \text{H}_2\text{C} \quad \text{Me} \end{matrix}$

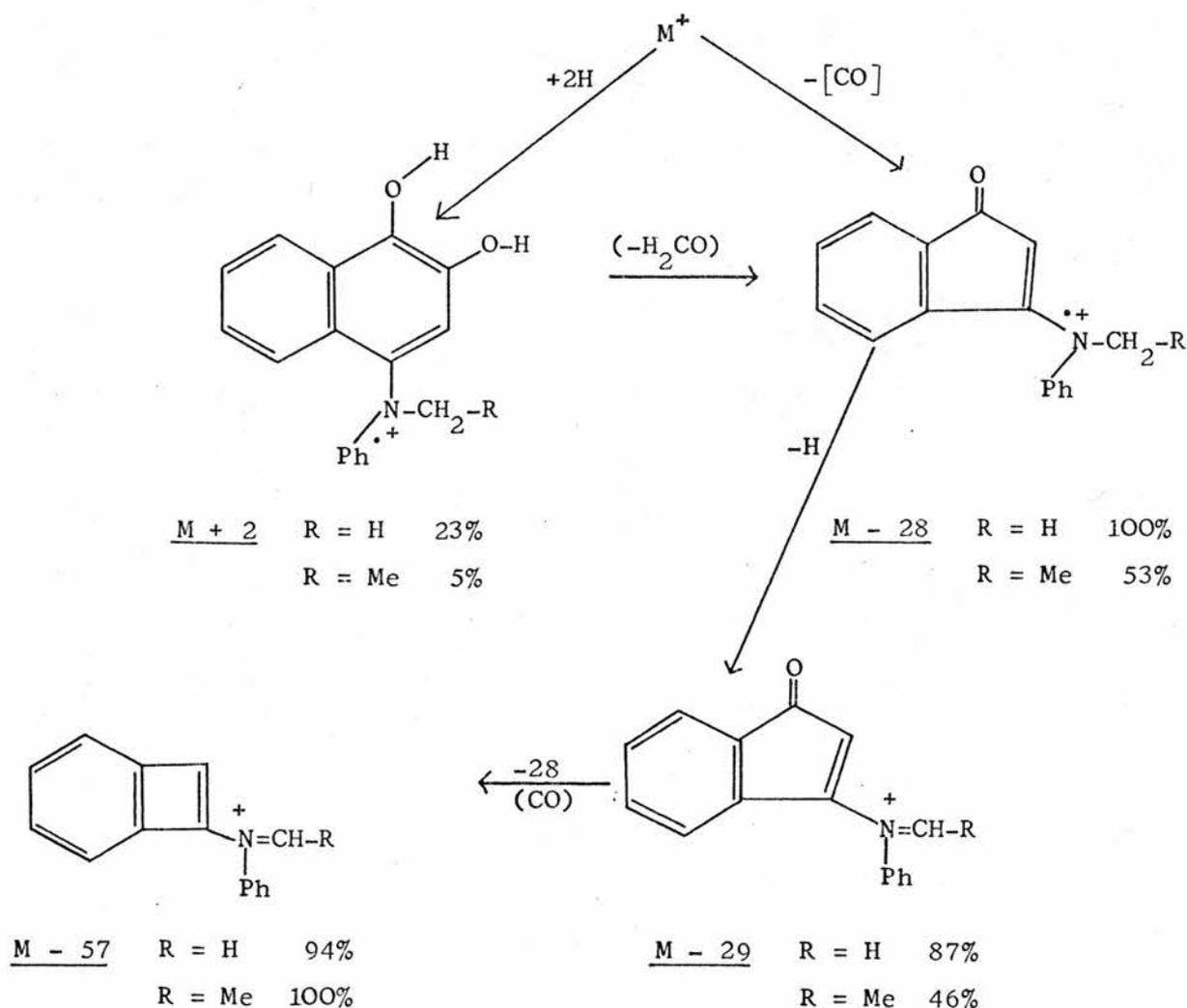


α -LAPACHONE

Mass Spectra.

Possible breakdown patterns for most of the compounds of the type (XX) are given in Appendix 1. The only notable feature they share is the loss of a mass of 28 during the first few breakdown processes, explainable as the elimination of carbon monoxide from the quinonoid ring.

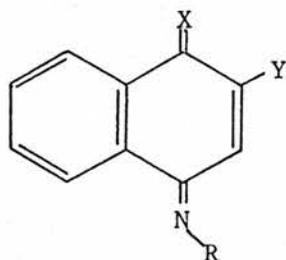
The two derivatives of secondary amines have similar spectra, showing large peaks at $M+2$, $M-28$, $M-29$ and $M-57$.



In addition in both cases the following ions are relatively intense.

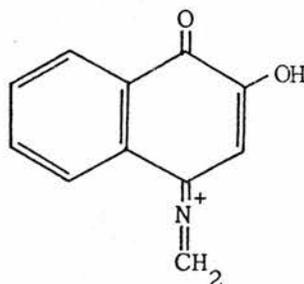
ion m/e	191	190	178	165	152	129	105	104	102	101	89	77
intensity R = H	8	11	22	21	11	10		25	30	21	18	55
R = Me												

The mass spectra of the n-alkylamine derivatives are very consistent. The breakdown pattern consists of the loss of methyl (or ethyl) followed by the break-up of the methylene chain to give an ion of m/e 186, which forms the base peak in each case. Accurate mass measurements showed that this ion's formula is $C_{11}H_8NO_2$, for which (XXXII) is a reasonable structure.



(XXV): X = O, Y = NHR

(XXVI): X = N-R, Y = OH

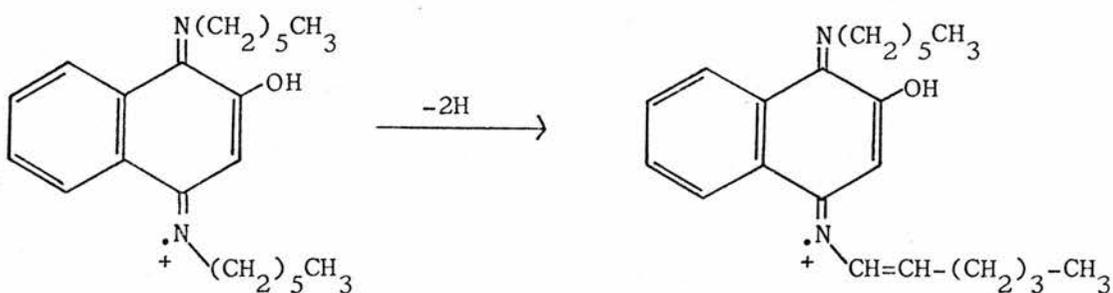


(XXXII)

Further breakdown follows a common pattern, illustrated by Table 7, which lists the peak heights as percentages of the height of the base peak.

The material corresponding to (XXV) or (XXVI) displays a similar breakdown pattern, one of the 'six-carbon' chains losing 4 carbon units and also 5 carbon units to produce large peaks, of which the latter breakdown gives the base peak, which corresponds structurally with (XXXII). This cleavage of the C-C bond adjacent to the N-C bond is typical of an alkyl-aryl amine.⁶¹

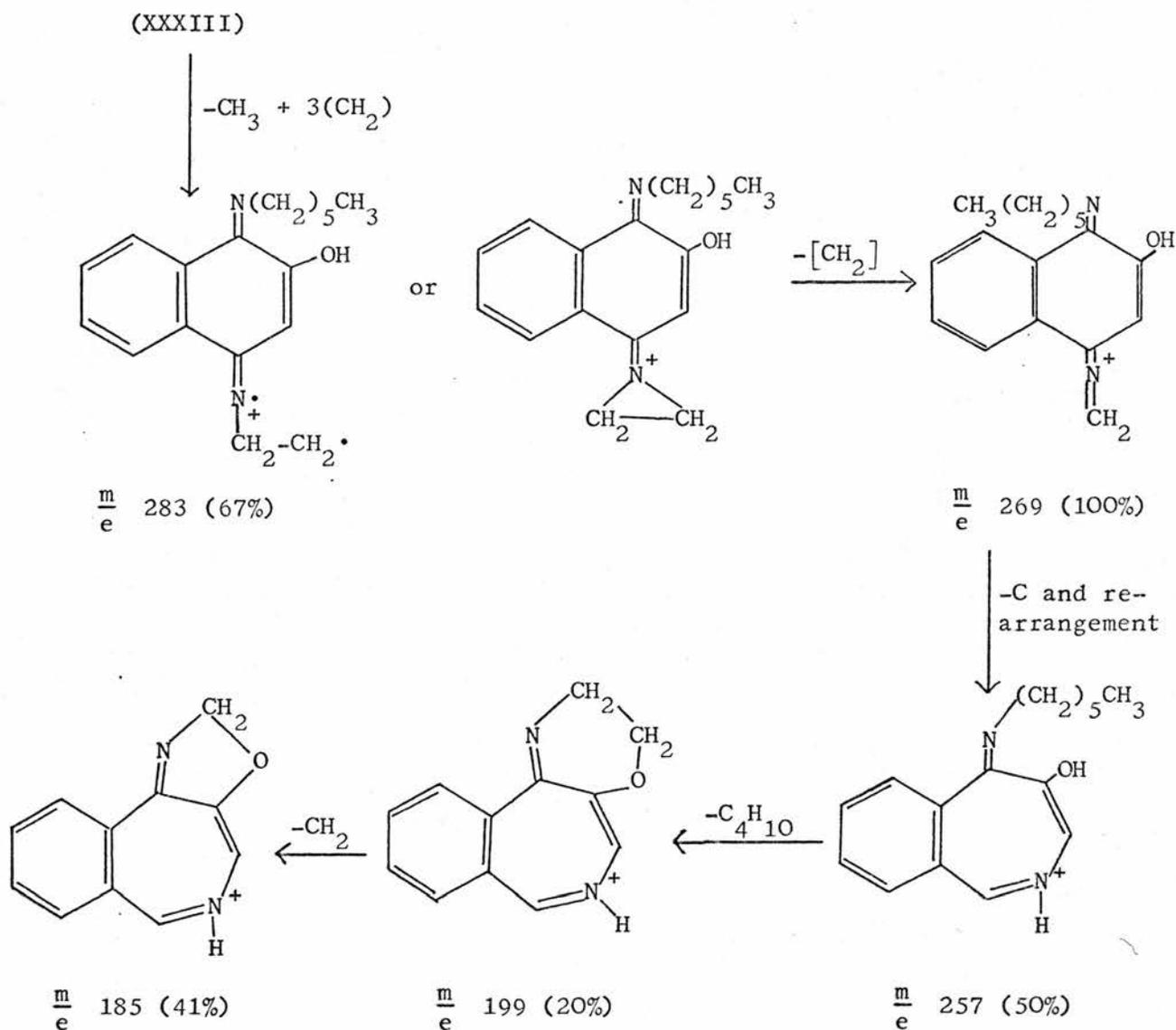
Possible Breakdown Pattern



(XXXIII)

$\frac{m}{e}$ 340 (86%)

$\frac{m}{e}$ 338 (53%)



These ions are derived from formula (XXVI). If the material exists in the (XXV) form, the corresponding ions of m/e 340, 338, 283 and 269 can be obtained by substituting $=\text{O}$ for $=\text{N}(\text{CH}_2)_5\text{CH}_3$ and $-\text{HN}(\text{CH}_2)_5\text{CH}_3$ for $-\text{OH}$ in the above formulae. The (alternative) ions of m/e 257, 199 and 185 are shown below.

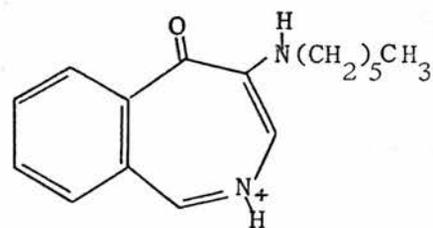
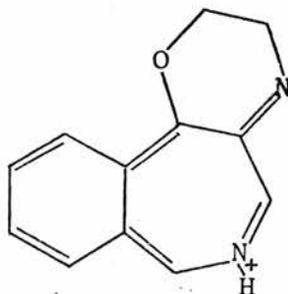
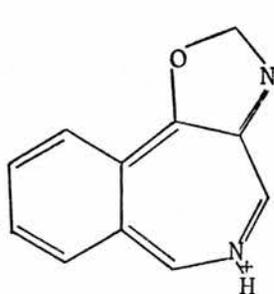


TABLE 7

Mass Spectral Peak Heights for N-alkyl-4-aminonaphtho-1,2-quinones

m/e	188	187	186	175	174	173	172	159	158	146	145	144
alkyl group	188	187	186	175	174	173	172	159	158	146	145	144
n-octyl } %	10.7	42.9	100.0	10.7	47.1	13.6	21.4	34.7	34.7	13.2	10.7	(3.6)
n-hexyl }	12.3	33.6	100.0	6.4	30.0	10.5	18.2	24.6	33.6	9.1	9.1	5.5
n-pentyl }	6.9	26.4	100.0	5.6	19.4	27.8	19.4	22.2	36.1	11.1	19.4	6.9

m/e	131	130	129	115	105	104	103	102	101	89	77	76	75
alkyl group	131	130	129	115	105	104	103	102	101	89	77	76	75
n-octyl } %	13.6	18.2	8.9	6.8	8.2	8.6	15.7	21.8	7.9	6.1	15.4	11.8	5.7
n-hexyl }	10.9	15.5	8.2	6.4	7.3	(4.6)	13.6	19.1	7.3	5.5	13.6	7.3	5.5
n-pentyl }	11.1	18.1	11.1	8.3	15.3	9.7	18.1	26.4	11.1	11.1	20.8	15.3	11.1

m/e	71	69	57	56	55
alkyl group	71	69	57	56	55
n-octyl } %	(2.1)	11.8	7.5	6.4	20.0
n-hexyl }	5.5	10.9	12.7	10.0	20.9
n-pentyl }	12.5	13.9	25.0	11.1	19.4

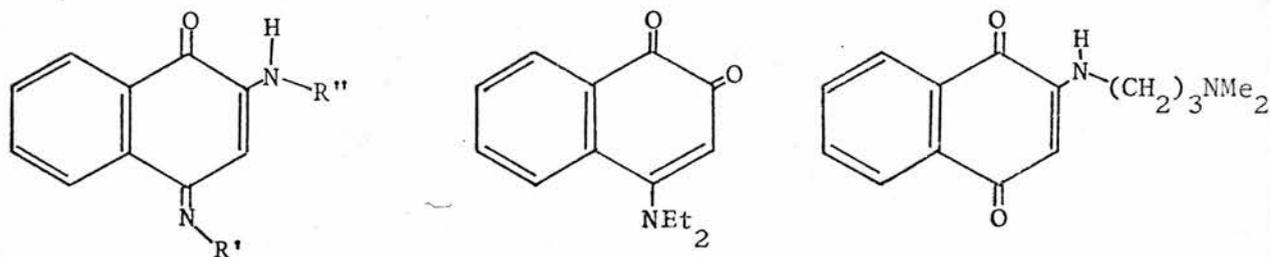
Proton Magnetic Resonance Spectra.

Details of the spectra are given in Table 8 (page 48).

The compounds derived from primary amines and naphtho-1,2-quinone proved to be almost insoluble in common organic solvents (e.g. benzene, chloroform), and the p.m.r. spectra were recorded using samples dissolved in trifluoroacetic acid. Even in this solvent the concentration was so low that an accurate integral could rarely be obtained.

4-(N-alkyl-N-arylamino)-naphtho-1,2-quinones are much more soluble in typical organic solvents, and spectra were recorded of these materials in deuteriochloroform as well as in trifluoroacetic acid.

Takada and Akiba³⁰ published the absorption position of the 3-proton in various 4-aminonaphtho-1,2-quinones, while Bullock et al.³⁴ studied the p.m.r. spectra of the following compounds.



R' and R'' - various hydrocarbon side chains

Tetramethylsilane was used as the internal reference.

N-Aryl-4-aminonaphtho-1,2-quinones.

Dissolution of these materials in TFA gave deep blackish-purple solutions, whereas the solids are mostly red-brown in colour (with the exception of those where the amine residue contains a substituent with a strong, positive mesomeric effect). This suggests that the spectra obtained are those of the protonated material.

The basic pattern of the spectra is listed below.

- (a) Two protons at τ 1.6,
- (b) two protons at τ 2.0,
- (c) n protons at τ 2.2 - 2.8, where n is the number of protons directly attached to the carbons of the phenyl ring,
- (d) 1 proton at τ 3.1,
- (e) groups of protons corresponding to any side chains on the phenyl ring.

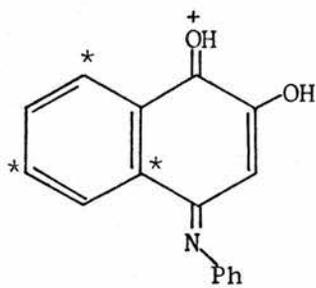
If deuteriotrifluoroacetic acid was used as the solvent, absorption (d) disappeared but otherwise the spectrum remained the same.

Possible singly protonated forms of (XX) are illustrated on page 43.

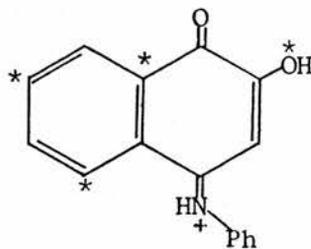
In the acidic medium the exchange of protons on oxygen and/or nitrogen would be extremely rapid, and therefore absorptions caused by such protons would not be observed. The integral indicates that the proton causing absorption (d) is on the naphthalene ring. As the use of deuteriated acid causes this absorption to disappear, the proton causing it must lie at a position vulnerable to electrophilic substitution. Structures (XXXIVc) and (XXXIVe) have no such position, and can therefore be eliminated. In addition the positive charge is localized on one atom in two structures, and they are therefore likely to be of higher energy than, for example (XXXIVb).

Examination of the p.m.r. spectrum of naphtho-1,4-quinone⁶² reveals certain similarities to the spectra under consideration, and an assignment can be made as follows.

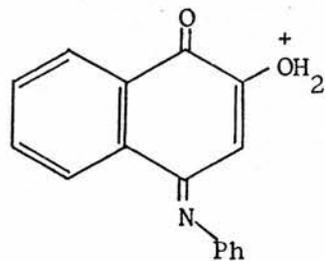
	τ	Proton position(s)
(a)	1.6	5 and 8
(b)	2.0	6 and 7
(c)	2.5 ± 0.3	on the phenyl ring
(d)	3.1	3



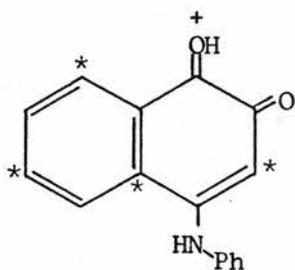
(XXXIVa)



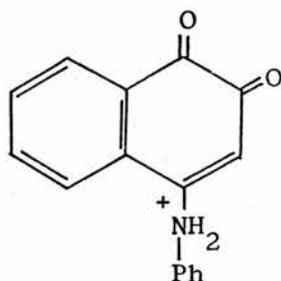
(XXXIVb)



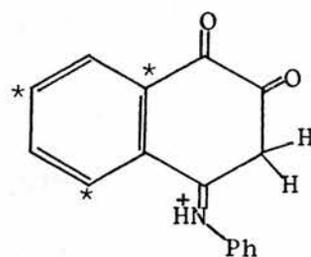
(XXXIVc)



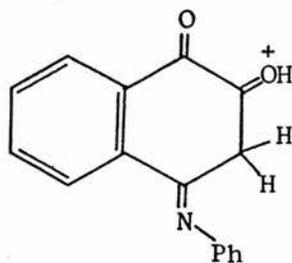
(XXXIVd)



(XXXIVe)



(XXXIVf)



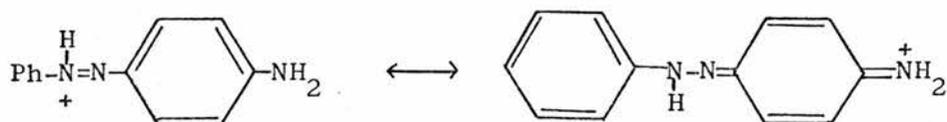
(XXXIVg)

In these diagrams an asterisk indicates that the positive charge can be delocalized on to the atom or atoms so marked.

Structures (XXXIVf) and (XXXIVg) can be described as the intermediates for an electrophilic substitution by a proton at position 3 of the 4-aryl-aminonaphtho-1,2-quinone and the N-aryl-2-hydroxy-naphtho-1,4-quinone-imine respectively. Each requires that two protons be present at position three, whereas the integral suggests that only one proton is present. It is therefore probable that proton exchange occurs via a di-protonated form, or that (XXXIVf/g) are present in equilibrium with another protonated form, the latter having the much greater concentration.

In structures (XXXIVa,b,d) the 3 position is activated to electrophilic substitution by either an amino or a hydroxyl group. Resonance results in a partial double bond between carbon and nitrogen in (XXXIVb) and (XXXIVd), and therefore the proton at position 5 will be deshielded, though less than it is in (XXXIVa).

On protonation the colour of the aminonaphthoquinones deepened from orange/brown to purple. This is reminiscent of the case of p-aminoazobenzene,⁶³ which changes from orange to violet on protonation.



Similarly in (XXXIVb) the charge can be delocalized over the benzene ring, the nitrogen atom and the 2-oxygen atom. This suggests that it is the main form in trifluoroacetic acid solution, though, of course, other forms could exist in equilibrium with it.

Note: Delocalization of the charge into the phenyl ring is not illustrated. This is because studies made using space-filling molecular models suggested that it is difficult for the molecule to achieve a conformation with the naphthalene and phenyl rings lying in the same plane.

N-Alkyl-N-aryl-4-aminonaphtho-1,2-quinones.

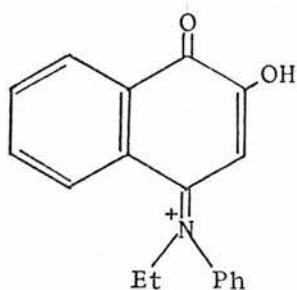
The spectra of these were recorded using samples dissolved in deuteriochloroform or trifluoroacetic acid. The exchange reaction of the 3-proton was investigated by adding trifluoroacetic acid to a solution of 4-(N-ethyl-N-phenylamino)-naphtho-1,2-quinone in deuteriochloroform.

The spectra of these materials in chloroform (deuteriated) can be assigned as below.

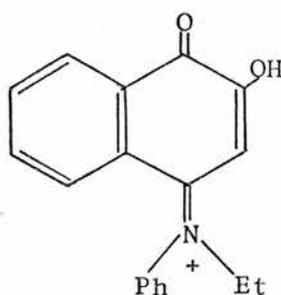
<u>τ</u>	<u>Integral</u>	<u>Assignment</u>
1.9	1	Proton 8
2.8	8	Phenyl protons + protons 5, 6 and 7
3.7	1	Proton 3

It will be noted that only one of the naphthalene ring protons absorbs below 2τ : - proton 8, which is deshielded by the neighbouring carbonyl group. Examination of molecular models of these compounds suggests that, if the amino lone pair orbital is to overlap with the naphthoquinone orbitals, either the alkyl group or the phenyl group must lie close to proton 5, resulting in its environment being very different from that of proton 8.

The complete replacement of deuteriochloroform by trifluoroacetic acid as the solvent results in a general downfield shift of the absorption peaks, while the sharp singlet at $\tau 3.7$ disappears. The multiplet (assigned to the phenyl protons and those at positions 5, 6 and 7) becomes wider, with a high field tail, and in the case of the ethyl compound, can be divided into two main areas with a deep cleft between them. In addition the ethyl compound shows two absorptions for both the methyl and the methylene groups. This can be explained by assuming that free rotation about the carbon-nitrogen bond is not possible, producing two isomers (XXXVa) and (XXXVb). In the spectrum of the methyl compound the methyl signal is a



(XXXVa)



(XXXVb)

large singlet with some tiny peaks at slightly higher field, suggesting that either rotation is unrestricted or that one of the two isomers is present in much greater concentration than the other.

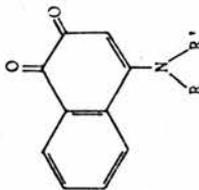
In the compounds derived from amines of the type ArNH_2 the proton at position 3 gave a sharp singlet in the p.m.r. spectrum when the compound was dissolved in trifluoroacetic acid. No such absorption was obtained from samples derived from secondary amines. Accordingly some 4-(N-ethyl-N-phenyl-amino)-naphtho-1,2-quinone was dissolved in deuteriochloroform, its spectrum recorded, and then one drop of trifluoroacetic acid was added to the solution and the spectrum recorded. This resembled the spectrum obtained using pure TFA, except that the methyl and methylene signals were not clearly visible as a 1:2:1 triplet and a 1:3:3:1 quartet respectively, and that an asymmetric doublet occurred at the high field side of the 'cleft multiplet'. The integral, though not very accurate, suggested that approximately two protons were causing this absorption. The spectrum in CDCl_3 showed an integral one in excess of the total number of protons in the compound. This can be explained by the presence of CHCl_3 in the solvent. Addition of 3 more drops of TFA resulted in the doublet changing into a very broad singlet, while the ethyl and methyl signals became much more like the normal absorptions of these groups. The change in shape of the 3-proton's absorption as the acid concentration was increased suggests that the high-field tail of the cleft doublet is caused by the 3-proton.

The spectrum containing the doublet had a total integral of approximately 11 protons for the cleft multiplet and the doublet. Allowing one proton for CHCl_3 , this leaves the compound with ten protons causing these absorptions. For the sample in pure TFA the integral was 9. It is therefore possible that one peak of the doublet is caused by a hydroxyl group, as in (XXXVa) and (XXXVb) above. In greater concentrations of TFA the hydroxyl proton will exchange rapidly with the acid protons, and the average environment of such a proton will be similar to that of the acid proton in pure TFA. This proton absorbs below 10τ , and therefore the absorption of the rapidly exchanging protons is not observed in the range $0 - 10\tau$.

The 4-(N-alkyl-N-arylamino)-naphtho-1,2-quinones dissolved in chloroform to give a red solution, whereas that in trifluoroacetic acid was nearly black. These results resemble those obtained with the aminoquinones derived from primary amines, and suggest that the N-alkyl equivalent of (XXXVb) is the main species in TFA solution, though exchange at the 3 position indicates that some other form is present. The increased basicity of the amino group resulting from the replacement of hydrogen by an alkyl substituent causes the faster exchange of the 3-proton, observed by the presence of the 'high-field tail' rather than a sharp singlet.

(Note: Bullock et al.³⁴ observed that the ethyl groups become non-equivalent when N,N-diethyl-4-aminonaphtho-1,2-quinone is dissolved in TFA, but do not give any details of the absorption due to the 3 proton.)

TABLE 8
4-Aminophtho-1,2-quinones; Proton Magnetic Resonance Spectra



All absorption positions are given in τ .
Integrals appear in brackets.

Key: br, broad; s, singlet; t, triplet; q, quartet.
TFA, F₃CCOOH; DTFA, F₃CCOOD.

Solvent	R	R'	Chemical Shifts (ppm)	Integration	Assignment
TFA	Ph	H	quartet 1.56	quartet 1.90	multiplet 2.28, multiplet 2.52
			broad 1.63(2)	broad 2.04(2)	broad 2.58
	Ph	H	br.mult. 1.63	br.mult. 2.0	AA'XX' pattern 2.20 and 2.62 (J = 8 Hz)
			br.mult. 1.58(2)	br.mult. 1.90(2)	AA'XX' pattern 2.50 and 2.76 (2:2)(J = 0 Hz)
	Ph	H	singlet 0.87	mult. 2.0	AA'XX' pattern 2.1 and 2.44 (J = 8 Hz)
			mult. 1.56		
	Ph	H	br.singlet 1.6		very br. mult. 2.0
	Ph	H	br.mult. 1.6	br.mult. 2.2	singlet 3.0
Ph	H	broad 1.6	broad 2.0	singlet 2.08, singlet 2.70, tiny peak 2.80	
Ph	H	broad 1.6	broad 2.0	slightly more complex but very similar to above	
DTFA	Ph	Me	broad mult. 1.95(1)	mult. 2.75(8)	very broad mult. 2.8(8)
CDCl ₃	Ph	Et	br.mult. 1.6	br.mult. 1.7	mult. 2.3(9)
CDCl ₃	Ph	Et	br.mult. 1.6	br.singlet 2.05	mult. 2.45
TFA	Ph	Me	br.mult. 1.6	br.singlet 2.05	br.mult. 1.6 → 1.9
TFA	Ph	Et	br.mult. 1.6	br.singlet 2.05	br.mult. 1.6 → 1.9
TFA	n-hexyl	H	br.mult. 1.6	br.singlet 2.05	br.mult. 1.6 → 1.9

as above but more complex
singlet 6.5(3)
1:3:3:1 quartet 6.0 (J = 7 Hz)(2), 1:2:1 triplet 8.68 (J = 7 Hz)(3)
s. 5.63(2)
q. 5.4, 9.6, 2, t. 8.1, t. 9.68
br. mult. 6.0, br. mult. 7.6 → 9.2, with large peaks at 8.1, 8.56, 9.06

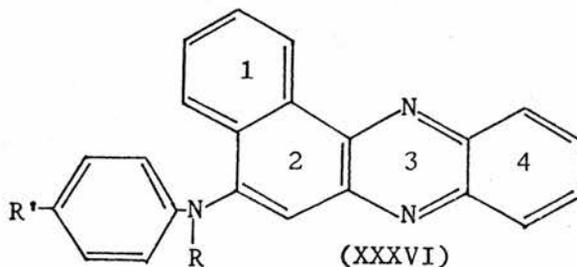
BENZO[a]PHENAZINESPreparation.

As stated earlier (p. 17), the adducts obtained by treatment of naphtho-1,2-quinone with a secondary arylamine were condensed with 1,2-diaminobenzene in order to confirm the presence of carbonyl groups. This condensation was carried out in methanol, and the resulting benzo[a]-phenazine was obtained by concentration and chromatography of the reaction mixture. Carbon tetrachloride and/or petrol were/ was used as solvent(s) for recrystallization.

NOTE: These compounds are also called naphthophenazines in the older literature. The use of different numbering systems also gives rise to problems.

Spectral Properties of Benzo[a]phenazines.Infra-red Spectra.

All three compounds have very similar spectra, those of (XXXVIa) and (XXXVIb) being virtually identical over the range $1650 - 1320 \text{ cm.}^{-1}$ (Note - includes Nujol peaks, therefore differences may be hidden). Each spectrum contains a very sharp and extremely intense absorption at $\sim 760 \text{ cm.}^{-1}$, ascribable to C-H bending in rings with 4 adjacent hydrogen atoms, which situation occurs in rings 1 and 4.⁶⁴



- A R = Me; R' = H.
 B R = Et; R' = H.
 C R = Et; R' = Me.

Details of the spectra in the region 1650 - 1320 cm.⁻¹

(XXXVI)	{	A	1615(w,s); 1595(fw,s); 1585(m,s); 1570(w,s); 1485(m,s);
			1400(m,s); 1355(fw,s); 1340(m,s)
		B	1615(w,s); 1585(m,s); 1575(fw,s); 1485(m,s); 1400(fw-m,s);
		1355(m,s); 1345(w,s)	
		*C	1615 ; 1580 ; 1500 ; 1485 ; 1405 ;
			1355

* Poorly resolved spectrum.

Ultra-violet/Visible Spectra.

Each of the three compounds shows four bands, while (XXXVIb) has an additional shoulder. Table 9 (p. 51) gives the data along with that for two other benzophenazines.

λ_1 and λ_3 undergo little change as the substituent is varied, and can be classified as $\pi \rightarrow \pi^*$ bands of the benzo-phenazine system. λ_4 and λ_7 undergo bathochromic shifts as the electron donating power of X is increased. It is interesting to note that the phenyl to tolyl change effects λ_7 considerably, whereas λ_4 changes very little. This suggests that λ_4 is a transition involving the phenazine system and the lone pair of the substituent, but not the aryl group of X, while the aryl group is conjugated with the lone pair and the benzophenazine system in the transition giving rise to λ_7 . (Similar steric restrictions apply to these compounds to those applicable to the 4-arylamino-naphtho-quinones).

Proton Magnetic Resonance Spectra.

Details are given in Table 10. The AA'XX' pattern in (XXXVIc) shows that group (iv) represents the protons of the aminoaryl group, while groups (i), (ii) and (iii) represent the benzophenazine protons.

TABLE 9

U.V./Vis. Spectra of Benzo[a]phenazines

Solvent: Methanol

λ in nm.

X	λ_1	Log ϵ_1	λ_2	log ϵ_2	λ_3	log ϵ_3	λ_4	log ϵ_4	λ_5	log ϵ_5	λ_6	log ϵ_6	λ_7	log ϵ_7	Ref.
H	224	4.63			277.5	4.72			380	4.06			400	4.08	65
MeO	225	4.55	232.5	4.56	277.5	4.60	295	4.49					415	4.09	
MeNPh	226	4.52			278	4.56	316	4.04					437	3.98	-
EtNPh	226	4.60			279	4.67	326	4.09			406(i)	3.87	446	4.04	-
EtNTo	225	4.55			279	4.60	327	4.09					460	4.07	-

To = p-tolyl. (i) indicates a shoulder.

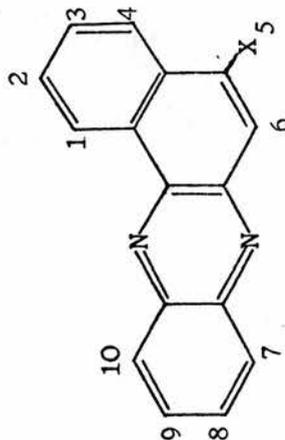


TABLE 10

P.M.R. Spectra of 5-(N-Alkyl-N-aryl)aminobenzo[a]phenazines

Sample (XXXVI)	Solvent	Aromatic protons				N-methyl protons	N-methylene protons	Methyl protons of N ethyl	p-Methyl protons
		(i)	(ii)	(iii)	(iv)				
A	TFA	d 0.75(1)	d 1.53(1)	complex m 1.8 → 2.8(12)	s 6.06(3)	-	-	-	
B	TFA	0.85(vw)	m 1.4 → 1.6	complex m 1.8 → 2.8	-	m 5.5	t 8.43	-	
B*	CCl ₄	sd 0.58(1)	m 1.6 → 2.0(2)	m 2.0 → 2.6(6.5)	m 2.75 → 3.40 (5.5)	q 6.00(2)	t 8.58(3)	-	
C	CCl ₄	sd 0.64(½-1)	m 1.7 → 2.0(2)	m 2.14 → 2.64(6)	AA'XX'q 3.04 → 3.30(4)	q 6.03(2)	t 8.62(3)	s 7.79(3)	
									J = 8 Hz
C	CDCl ₃	sd 0.80(1)	m 1.84 → 2.1	m 2.20 → 2.80	AA'XX'q 3.10 → 3.50	q 6.20(2)	t 8.93(3)	s 7.90(3)	
									J = 7 Hz
					(s 3.04)				
					(12)				

Integrals are given in brackets

Key: d - doublet
 sd - split doublet
 m - multiplet
 s - singlet
 vw - very weak

* The integral on this spectrum was not satisfactory
 Tetramethylsilane was used as the internal reference

The single proton at very low field is probably proton 1, as it is unique in having the C-H bond parallel and peri to a C-N \leftrightarrow C=N bond. Proton 6, the equivalent of proton 3 in 4-arylamino-naphtho-1,2-quinones, does not appear at higher field than the other aromatic protons. This results from the fact that it is now on the periphery of the benzenazine's ring current, whereas in the quinones proton 3 was in a vinylic position. The complex multiplets B and C could not be definitely assigned. In an attempt to simplify these portions of the spectra, the peak at 0.8 of (XXXVIc) was spin-decoupled while the spectrum of the other aromatic protons was recorded; no clearly observable difference could be found between this and the normal spectrum. A similar experiment using (XXXVIa) in TFA was equally unsuccessful.

Mass Spectra.

The main feature of note is the loss of methyl and ethyl substituents, followed by a common pattern of relatively small peaks, though the relative intensities within each group of peaks varied according to the substance. Table 11 (p. 54) lists those peaks with intensity (relative to the base peak - which varied from one compound to another) greater than 10%.

(Note. Table 11 reveals certain similarities. Superimposition of semi-transparent reproductions of the spectra shows up the resemblances to the full).

TABLE 11

Mass Spectra

A	<p>336 (22%), 335 (89%), 334 (100%), 320 (22%), 319 (27%), 305 (11%), 160 (21%), 100 (21%), 91 (11%), M + 1 M M - 1 M - CH₃ M - (H + CH₃)</p> <p>77 (29%), 76 (11%), 51 (18%) Ph⁺ C₆H₄⁺ C₄H₃⁺</p>
XXXVI B	<p>350 (20%), 349 (71%), 348 (31%), 335(20%), 334 (76%), 333 (10%), 332 (18%), 321 (20%), 320 (65%), 319 (35%), M + 1 M M - 1 M - CH₃ M - Et</p> <p>318 (18%), 305 (11%), 256 (23%), 231 (15%), 230 (13%), 229 (23%), 218 (10%), 217 (10%), 216 (11%), 201 (11%), 190 (18%), 127 (10%), 105 (16%), 104 (22%), 102 (23%), 91 (12%), 89 (10%), 78 (13%), 77 (100%), 76 (21%), 75 (19%), 63 (12%), 51 (49%)</p>
C	<p>364 (28%), 363 (100%), 362 (31%), 349 (25%), 348 (89%), 346 (17%), 335 (13%), 334 (31%), 333 (11%), 332 (19%), M + 1 M M - 1 M - CH₃ M - Et</p> <p>320 (15%), 319 (47%), 318 (12%), 305 (8%), 256 (14%), 231 (12%), 229 (14%), 119 (14%), 118 (11%), 102 (13%), M -(CH₃ + Et)</p> <p>91 (36%), 89 (12%), 77 (19%), 65 (22%), 51 (11%).</p>

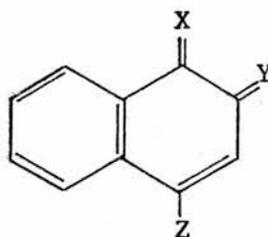
THE MECHANISM OF THE AMINE — QUINONE REACTION, AND SOME THOUGHTS ON

THE TYPES OF PRODUCT

The primary arylamines reacted to give the 4-arylamino-naphtho-1,2-quinones in yields varying from 29% to 76% (yield calculated on the basis that 1 quinone molecule reacts to give 1 aminoquinone). The production of arylaminoquinones in yields of greater than 50% indicates that an oxidizing agent other than naphthoquinone takes part in the reaction scheme, and a reasonable conclusion is that this agent is aerial oxygen. Takada and Akiba³⁰ drew the same conclusion after they had obtained a quantitative yield of 4-anilinonaphtho-1,2-quinone by reacting the quinone with aniline in ethanol at room temperature. (Note - their sample of product melted at 168-70°, the author's at 254-56°, Lit. value 258-61°C²⁷).

The low yields obtained by the author in certain cases can be explained by incomplete product isolation, or, in the case of the reaction involving 2,4-dichloroaniline, by the slowness of the reaction (29% yield after 9 days) - 2,4-dichloroaniline is a relatively poor base, and may therefore be a poor nucleophile. As 2,4-dimethylaniline gave a 76% yield within 24 hrs., it is thought that the steric effect of the ortho-substituent does not greatly hinder attack by the nitrogen atom at the 4 position of naphthoquinone.

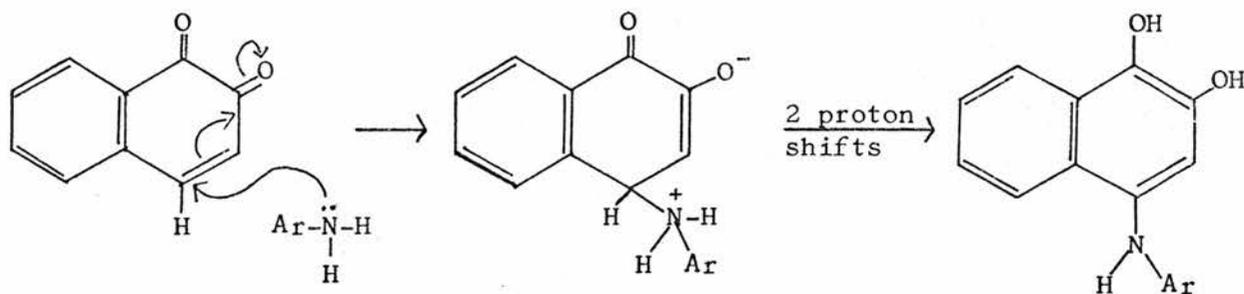
Various possible products of the quinone — amine reaction are shown below.



(XXXVII)

A	X = O; Y = Ar-N	}	Z = H	D	X = Y = O	}	Z = ArNH
B	X = Ar-N; Y = O			E	X = ArN, Y = O		
C	X = Y = Ar-N			F	X = O, Y = ArN		
		G	X = Y = ArN				

Products of types A, B and C (see XXXVII, p.55) could result from simple condensations of the amines with one or both carbonyl groups. Such imines⁶⁶ are vulnerable to hydrolysis, and so any water present in the solvent (or that generated during imine formation) could react with the product and convert it back to the starting materials. Furthermore such products retain the 1,2-quinonoid system, and therefore reactions leading to them are not likely to be as energetically favourable as those giving a product with an increased resonance energy. (Note. Lantz and Wahl⁶⁷ prepared several compounds of the B type by oxidising 1-arylamino-naphth-2-ol with sodium hypochlorite. Dissolution of the B materials in acetone followed by the addition of acid and, later, sodium acetate, resulted in the isolation of 4-arylamino-naphtho-1,2-quinones. Hydrolysis of the imine followed by conjugate addition of the amine and oxidation is an explanation for this process).



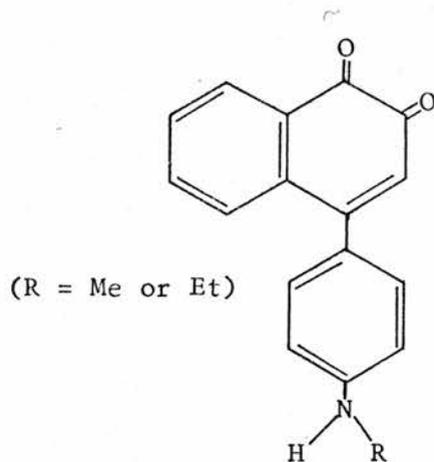
Nucleophilic attack at the 4-position, as illustrated above, leads to a naphthalene derivative, with an increased delocalization energy. (It might be possible to obtain a 4-arylamino-1,2-dihydroxynaphthalene by dropping a dilute solution of naphtho-1,2-quinone into a solution of an arylamine, the whole system being in an inert atmosphere.) The presence of oxygen, or unreacted quinone, means that the aminodihydroxy-naphthalene can be oxidised to the aminoquinone. In this compound delocalization of the nitrogen's lone pair into the carbonyl system effects some 'resonance' stabilization.

The low solubility of the 4-arylamino-naphtho-1,2-quinones in methanol means that, unless the reaction is carried out in very dilute solution, they will precipitate out and further reaction to form E, F or G is restricted to the product remaining in solution and to reaction with surface molecules of the precipitate.

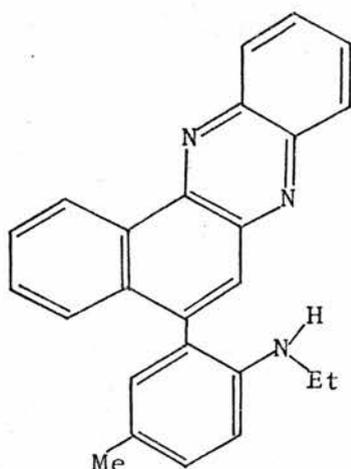
Takada et al.³⁰ found that heating a mixture of aniline and naphtho-1,2-quinone in ethanol resulted in an E product, whereas the same reaction at room temperature gave D. This is reasonable as the 4-anilino-quinone would be more soluble in the hot solvent - also the rates of nucleophilic addition, oxidation and condensation would be increased by the higher temperature.

(Note. Takada and Akiba³⁰ obtained 100% yield of a product of type E in the reaction of 2-naphthylamine with naphtho-1,2-quinone. No explanation is given - two possibilities are that the D type material (Ar = 2-naphthyl) is soluble, or that imine formation has a lower activation energy than attack at the 4-position, allowing a B compound to form. This subsequently could react with more amine to give the product E.)

In the case of a secondary amine, the condensation reaction is not possible, and nucleophilic attack occurs at the 4-position. Consideration was given to the possibility that the nucleophile reacted through the p-position of the phenyl ring, to give a product (XXXVIII). The p.m.r. spectra of these compounds did not contain a clearly visible AA'XX' pattern which (XXXVIII) would be expected to show, while N-ethyl-p-toluidine was found to react to give a product. Though this could not be isolated pure, its condensation product with o-phenylene-diamine was isolated. The p.m.r. spectrum of this benzophenazine was consistent with the formation of a carbon-nitrogen bond during the reaction of the naphthoquinone with



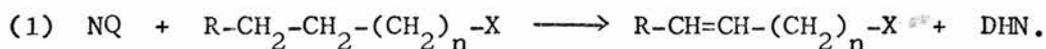
(XXXVIII)



(XXXIX)

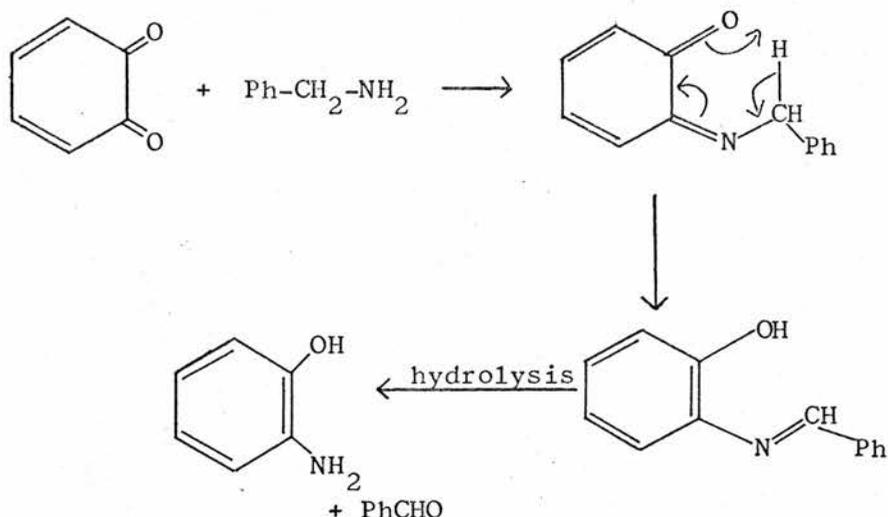
the N-ethyl-p-toluidine, and not with the benzophenazine having the structure (XXXIX) (an ortho addition product).

In the case of alkylamines oxidations can occur as well as addition and/or condensation reactions. Calculations (p. 60) indicate that the reaction (1) below has a negative free energy, and suggest that reaction (2) is similar (the amine \rightarrow imine + H_2 reaction has a positive enthalpy by bond energy estimates, but this is less than the free energy of reduction of naphtho-1,2-quinone and the process liquid \rightarrow liquid + gas will have a positive entropy change, so the overall free energy of (2) should be negative, at 25°C).



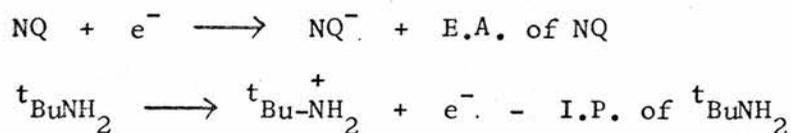
(NQ = naphtho-1,2-quinone, DHN = 1,2-dihydroxynaphthalene).

The imine formed would be very vulnerable to hydrolysis, to an aldehyde. (Benzaldehyde has been isolated as a product from the reaction between benzo-1,2-quinone and benzylamine³⁷ - the above oxidation mechanism is an alternative to the condensation - rearrangement - hydrolysis mechanism, illustrated on the next page.)



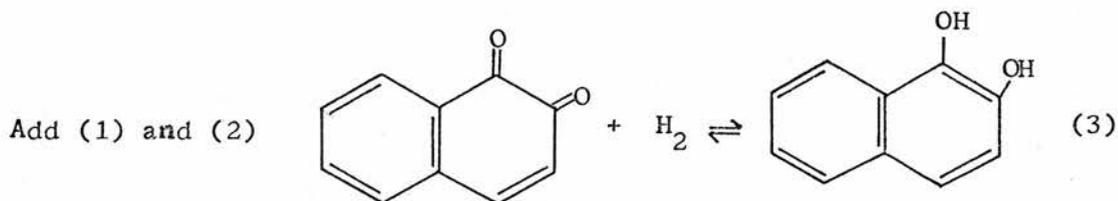
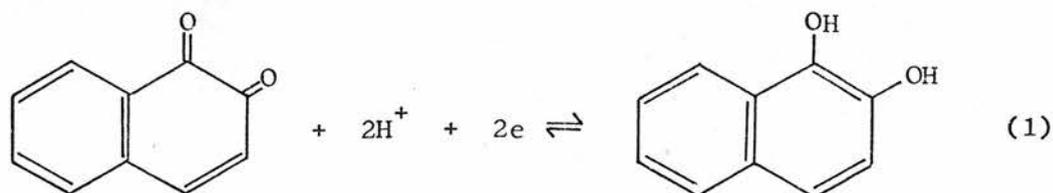
The numerous products resulting from reaction of an n-alkylamine with naphtho-1,2-quinone (n-hexyl, 12; n-octyl = n-pentyl, 11) were not all identified. Replacement of Ar by R in the listings of (XXXVII) materials gives 7 theoretical products, but materials such as A, B and C are likely to be easily hydrolysed. Further products could result from the presence of oxygen in the system, as the oxidation reaction might well yield a radical, dimerization of which could give a long conjugated system - some of the products detected by T.L.C. were blue or purple in colour, whereas the simple addition or addition/condensation compounds were red to yellow in colour.

A possible radical oxidation of an amine was mentioned in connection with the reaction between t-butyl amine and naphtho-1,2-quinone. The energetics of this system in the gas phase are as follows.



The electron affinity of naphtho-1,2-quinone has been calculated to be approximately 0.6 eV,⁶⁸ while the ionization potential of t-butylamine is 8.64 eV.⁵⁵ In solution each radical ion would be solvated, and the solvation energy thereby gained will affect the free energy of the reaction.

The difference in solvation energy between a quinone and its radical anion has been calculated to be approximately 3.6 eV^{68} for many quinones in CH_3CN . If the cation has a similar solvation energy, the total of the solvation energies and the quinone's electron affinity will still be less than the ionization potential of the amine. (Solvation energies in CH_3CN are generally less than those in water, and slightly smaller than those in methanol - see table on page 105). Naphthoquinone does absorb visible light (max. = 500 nm. = 2.48 eV), and so a radical reaction between an amine and a photo-excited naphthoquinone is much more likely than that between unactivated quinone and an amine*. Possible radical reactions between benzo-1,2-quinone and nucleophiles are discussed later (pp.96-117).



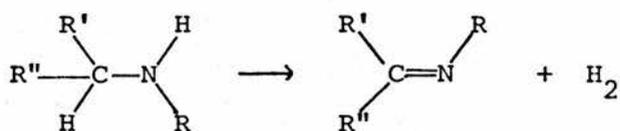
For (1) $E_1^{\circ} = 0.555 \text{ volts.}^{69}$

For (2) $E_2^{\circ} = 0.0 \text{ volts}$

For (3) $\Delta G^{\circ} = -zE^{\circ}F$, where $E^{\circ} = E_1^{\circ} - E_2^{\circ}$

$$\begin{aligned}
 \Delta G^{\circ} &= \frac{-2 \times 0.555 \times 96500}{4.184 \times 1000} \text{ kcal mol}^{-1} \\
 &= \underline{-25.6 \text{ kcal mol}^{-1}} \quad (-107 \text{ kJ mol}^{-1})
 \end{aligned}$$

* If the resulting radicals reacted further with a substantial release of free energy, then the unexcited radical route might occur.



Bond energy C-N	72.8	kcal	mol ⁻¹
Bond energy C-H	98.7	"	"
Bond energy N-H	93.4	"	"
Total bond energy lost =	<u>264.9</u>	"	"
Bond energy H-H	104.2	"	"
Bond energy C=N	<u>147.0</u>	"	"
Total bond energy gained =	<u>251.2</u>	"	"

∴ Overall loss of bond energy = 13.7 kcal mol⁻¹ (57.3 kJ mol⁻¹).

$$\Delta G_f^\circ \text{ for ethylene} = +16.28 \text{ kcal mol}^{-1} \quad ^{71}$$

$$\Delta G_f^\circ \text{ for ethane} = -7.86 \text{ " " } \quad ^{71}$$

$$\Delta G^\circ \text{ for } \text{C}_2\text{H}_6 \longrightarrow \text{C}_2\text{H}_4 + \text{H}_2 = +24.14 \text{ kcal mol}^{-1} \text{ (+ 101 kJ mol}^{-1}\text{)}$$

$$\text{Similarly } \Delta G_f^\circ \text{ for propene} = +14.99 \text{ " " } \quad ^{71}$$

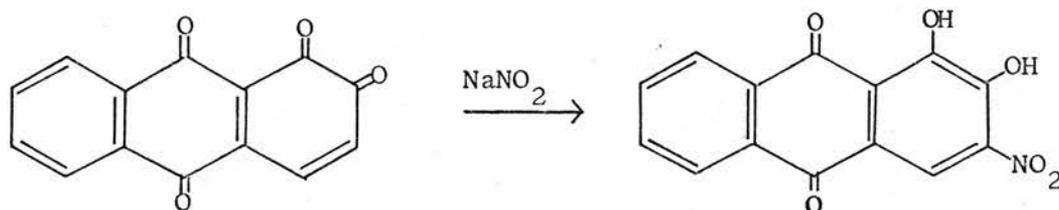
$$\text{and } \Delta G_f^\circ \text{ for propane} = -5.61 \text{ " " } \quad ^{71}$$

$$\Delta G^\circ \text{ for } \text{C}_3\text{H}_8 \longrightarrow \text{C}_3\text{H}_6 + \text{H}_2 = +20.6 \text{ " " (+86 kJ mol}^{-1}\text{)}$$

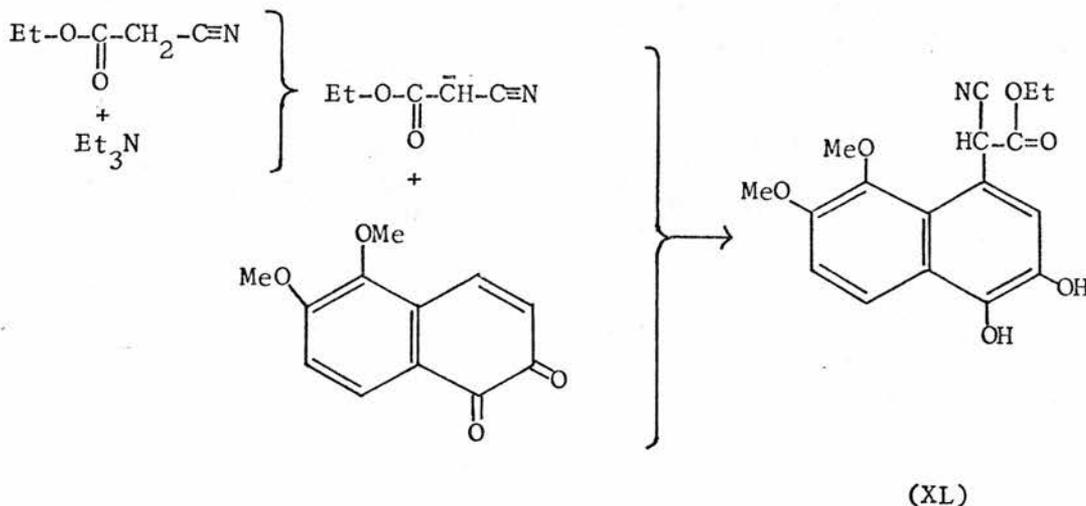
PREVIOUS WORK ON THE REACTIONS BETWEEN 1,2-QUINONES AND CHARGED NUCLEOPHILES

Reactions of this type have been carried out using isolated quinones and also by generating quinones 'in situ'.

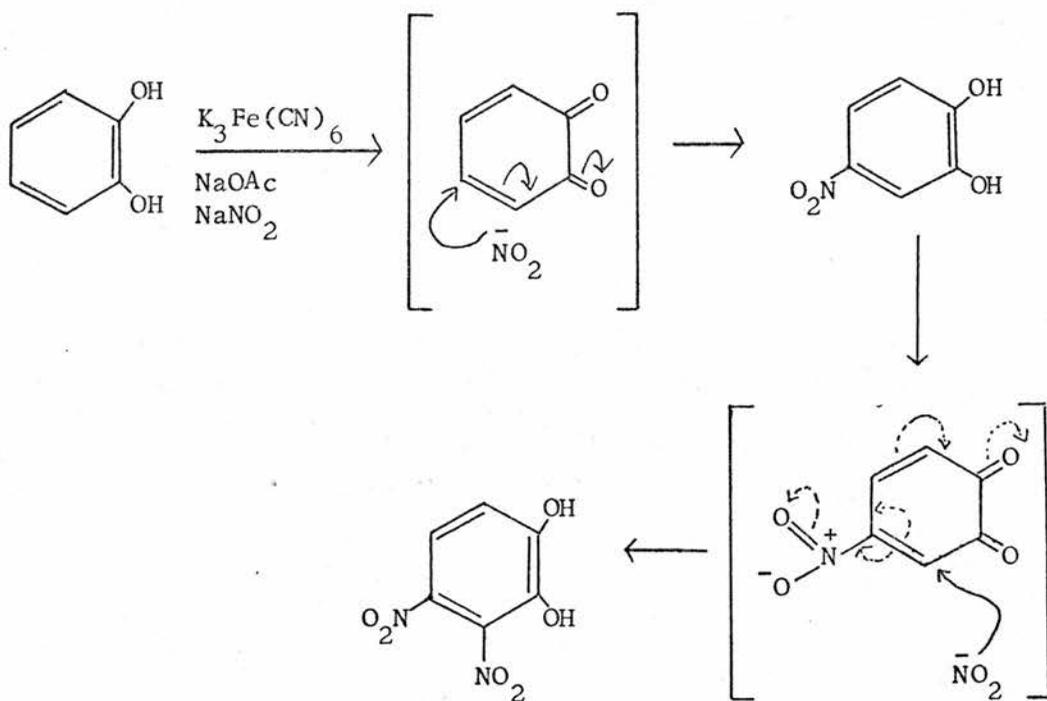
Gorelik⁷² treated anthra-1,2,9,10-diquinone with sodium nitrite and obtained 3-nitroalizarin.



During his syntheses of ring systems related to morphine Gates⁷³ reacted 5,6-dimethoxynaphtho-1,2-quinone with ethyl cyanoacetate and triethylamine to yield the catechol (XL), which was not isolated - instead it was oxidised to the corresponding quinone using potassium ferricyanide.



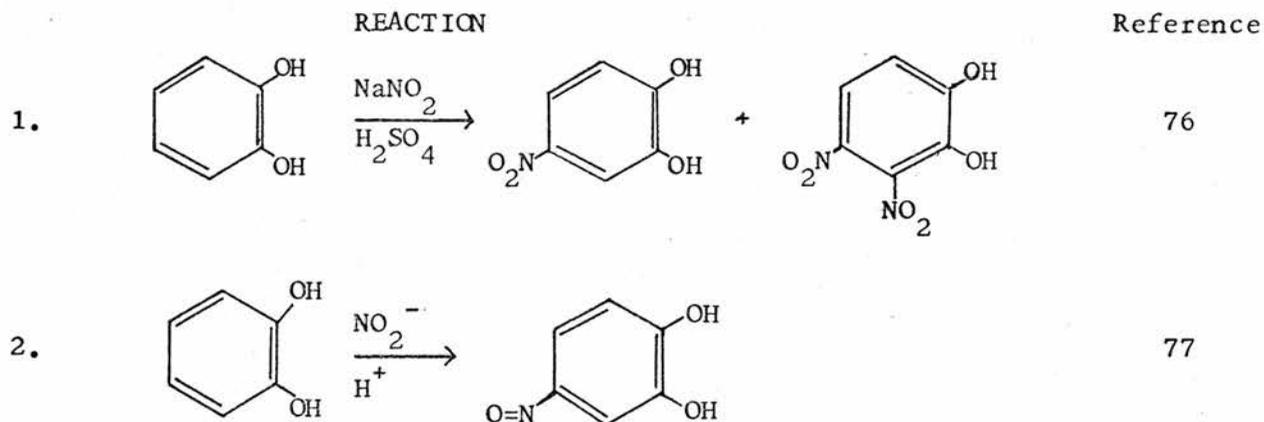
The use of 'in-situ' generated quinones is discussed by Wanzlick,⁷⁴ who, with others, showed that nitrite ion, catechol, and ferricyanide ion react together to yield 4-nitrocatechol. 3,4-Dinitrocatechol was obtained by replacing catechol by 4-nitrocatechol.



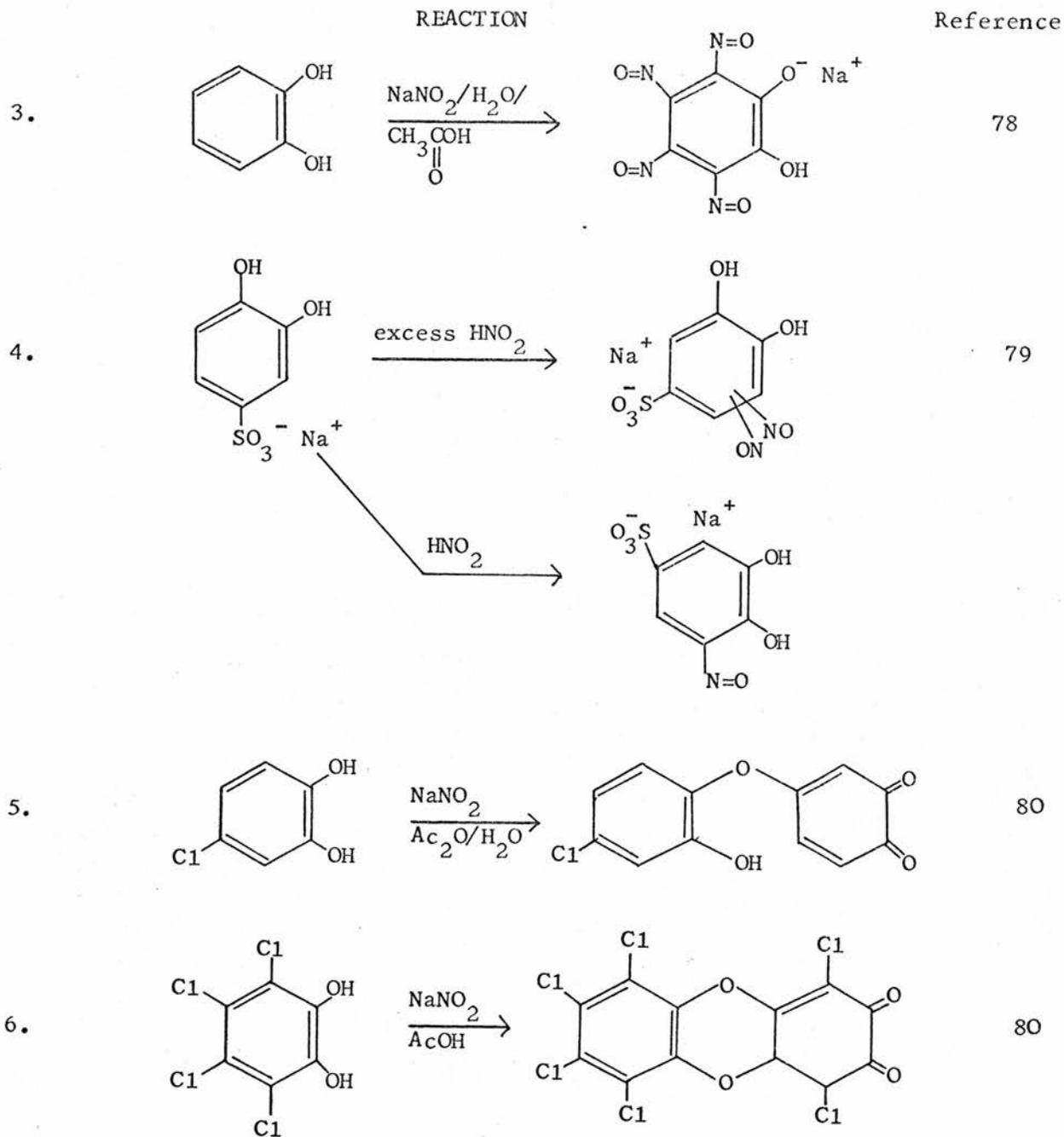
(Note. The presence of acetate ion (to act as a base, presumably) could complicate the reaction, as it can be shown that sodium acetate reacts with benzo-1,2-quinone in DMSO solution).

Wanzlick also discusses a peculiar reaction discovered by Benedikt,⁷⁵ who found that catechol reacts with nitrous acid to give 4-nitrocatechol.

Wanzlick thought that the nitrous acid oxidised the catechol to the quinone,* which then reacted with nitrite ion. Investigations of the reactions between catechols and nitrous acid have given various products, as shown below.



* A calculation on page 156 shows that this redox reaction is thermodynamically possible.



Reactions 2, 3 and 4 can be explained as typical nitrosation reactions, while the others involve oxidation steps as well. In connection with reaction 1 it is worth noting that N,N-dimethyl-p-anisidine reacts with nitrous acid to yield o-nitro-N,N-dimethyl-p-anisidine,⁸¹ and both catechol and N,N-dimethyl-p-anisidine are highly activated to electrophilic substitution.

The author's work consisted of an investigation into the reactions of isolated benzoquinone with various nucleophiles.

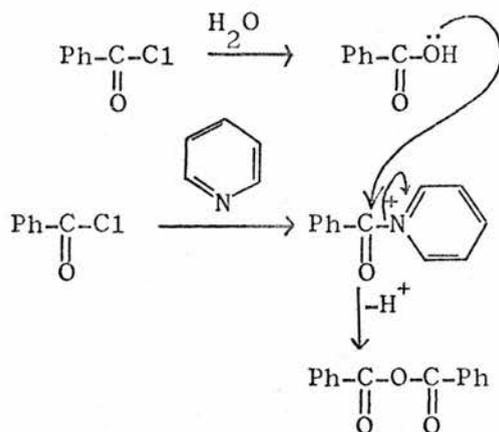
THE REACTIONS OF BENZO-1,2-QUINONE WITH ANIONS

In the present work early experiments were carried out according to the following procedure.

Solutions in dimethyl sulphoxide of benzo-1,2-quinone and the sodium salt of the anion under investigation were prepared, and mixed. After standing for some time, the mixture was poured into water and extracted with ether. The resulting ethereal extract was contaminated with dimethyl sulphoxide, and so the extract was treated with dilute sodium hydroxide solution, in which any phenolic products (and DMSO) would dissolve. After separation the basic layer was acidified with dilute hydrochloric acid, and was extracted with ether. The ethereal layer was separated, dried over magnesium sulphate, and concentrated under reduced pressure, yielding an oil. Once, in the case of sodium nitrite, the oil was treated with diazomethane; and once each in the cases of sodium azide and nitrite, the oils were treated with benzoyl chloride/pyridine in attempting to effect benzylation of any hydroxyl groups in the product(s).

This procedure can be criticized on the following grounds.

1. Dimethyl sulphoxide is an oxidant,⁸² and might react with any product formed by reduction.
2. While the triple extraction removed DMSO, it produced catecholate ions in the alkaline solution, where they would be vulnerable to aerial oxidation.⁸³
3. The use of pyridine would also produce anions of catechol. In addition the main product of benzylation seemed to be benzoic anhydride, formed in a side reaction discovered by Minunni.⁸⁴



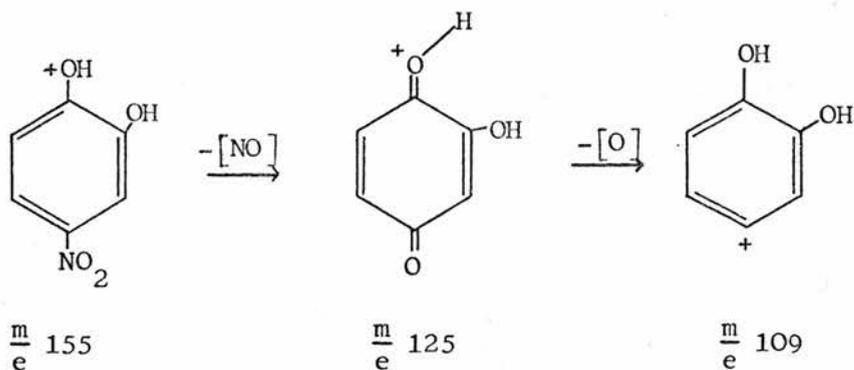
In the following sections the results obtained from the experiments described above, and descriptions of other simple experiments, are given.

Reaction with Sodium Nitrite.

The alkaline solution obtained by extraction was of a deep red colour, suggesting that 4-nitrocatechol might be present.⁸⁵ Mass spectra of the benzoylated and methylated products agreed with this, but also suggested that catechol was formed in the reaction (or work-up).

With methanol as solvent, the quinone/nitrite reaction was observed during the substrate mixing stage both in a nitrogen atmosphere with deoxygenated solvent and in ordinary solvent exposed to the air. There was no visible difference, nor was any change discerned when the 'nitrogen' system was moved into the air, suggesting that the air may not be involved. The addition of caustic soda to a similar solution gave rise to a deep red colour ($\lambda_{\text{max}} = 510 \text{ nm.}$), indicating the probable presence of 4-nitrocatechol.⁸⁵

The latter was isolated by vacuum sublimation of the product obtained from the quinone/nitrite reaction in methanol. The yellow sublimate was identified by its mass spectrum and the accurate mass value of the molecular ion (very little 4-nitrocatechol was obtained). The mass spectrum can be explained by the scheme illustrated below.



(Note. A green oil was also obtained during the sublimation. Accurate mass values of the molecular ion and the principal fragment showed that their formulae were $C_{15}H_{28}$ and $C_{10}H_{19}$ respectively. Grease, solvent impurity, and/or pump oil are thought to be likely sources of this material).

Sodium Azide.

The first reaction was carried out in DMSO, and no attempt to prepare a derivative of the product was made. The ether extract was concentrated to a syrup, which was partly soluble in chloroform. The chloroform - soluble part was chromatographed on a silica column, yielding two yellow eluates. Removal of the solvent gave two solids, whose infra-red spectra strongly resembled that of catechol, differing mainly in the presence of a peak at 2100 cm^{-1} (azide?⁸⁶). The first compound, in whose spectrum the azide absorption was more intense, melted over the range $85 - 93^{\circ}$, and showed peaks at the following $\frac{m}{e}$ values in the mass spectrum.

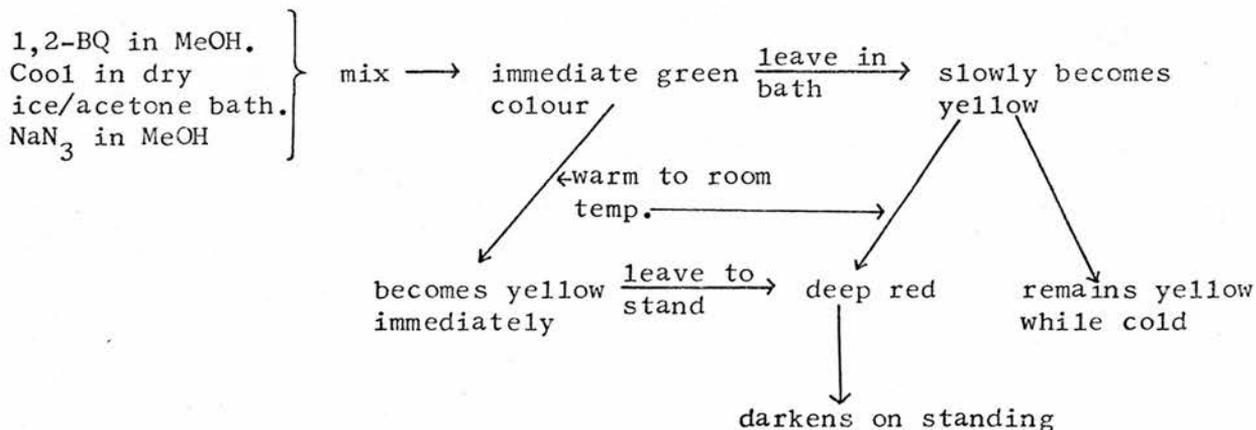
151, 124, 110 (very large), 92, 81, 64, 63. 151 could be the parent ion of azido-catechol, while the pattern from 110 downwards is extremely like that of catechol. The second compound melted over the range $99 - 103^{\circ}$.

Repetition of the reaction again produced a syrup, which was subjected to benzylation. The product thereof was chromatographed on a chloroform/silica column in the dark (to prevent photolytic reactions occurring). Two components (yellow and orange) were obtained. Removal of the solvent produced a yellow liquid and an orange solid, both of whose mass spectra

can be explained by the materials being benzoic anhydride/acid contaminated with di-(1,2-dihydroxyphenyl).

As the colour of the solution(s) changed on mixing the quinone with the azide, two qualitative experiments were performed to investigate the colour changes.

1. Solutions of benzo-1,2-quinone and sodium azide in acetonitrile were cooled to -35° and were then mixed. A green colour formed which lasted for at least 12 minutes at that temperature. On warming the colour became yellow and gradually darkened to brown.
2. A similar experiment in methanol produced the results shown in the chart below.



The presence of at least one transient intermediate is thereby demonstrated.

De-oxygenated solutions were used to react the quinone with azide in methanol/water. Ether extraction/drying/solvent removal yielded a tar, which was treated with pyridine and trimethylsilyl chloride. Filtration and solvent removal produced another tar, whose mass spectrum suggested the presence of 1,2-di(trimethylsilyloxy)benzene. Acidification of the aqueous layer followed by ether extraction/drying/solvent removal gave a third tar, which, (surprisingly) yielded a solid precipitate on the addition of ether. The mass spectrum thereof could not be explained. Accurate mass measurements on peaks

at 230 and 160 indicated formulae of $C_{10}H_4N_3O_4$ and $C_{10}H_8O_2$. The structure and origin of these ions cannot be deduced with any certainty whatever. Comparative experiments were performed using deoxygenated and normal systems. In both cases a transient green colour was observed, and no atmospheric effects were noted.

Sodium Cyanide.

One quinone/cyanide reaction was carried out in DMSO. The product's infra-red spectrum resembled that of catechol.

Sodium methoxide.

The quinone/methoxide system was studied qualitatively. Mixing solutions of the two substrates produced a green colour, which faded to brown/yellow, except on the surface, which remained green. During the half-hour following mixing the observations listed below were made.

1. The whole solution became green if it was stirred.
2. Blowing nitrogen through the green solution resulted in the colour becoming brown.
3. Re-exposure to the air resulted in the return of the green colour.

After $1\frac{1}{2}$ hours the solution remained brown. This suggests that aerial oxygen is involved in the reaction.

Sodium Iodide.

Mixing methanolic solutions of benzo-1,2-quinone and sodium iodide produced an immediate green colour, which rapidly changed to light brown.

A similar experiment using acetonitrile as solvent resulted in a very small amount of precipitate forming. This was filtered off and excess sodium iodide forced out of the filtrate by the addition of ether. The solvent was removed under reduced pressure, yielding a sticky black-brown solid. This partly dissolved in carbon tetrachloride to give a solution with

absorption maxima at 520 nm. and 278 nm. Iodine in that solvent has a single maximum at 520 nm.,^{*} while catechol absorbs maximally at 278 nm. in ethanol.⁴¹ The mass spectrum of the sticky solid was consistent with the material being a mixture of catechol and iodine.

Although these experiments are purely qualitative, it seems reasonable to draw the following conclusions.

1. Nitrocatechol can be detected, but catechol seems to be the product from the azide, cyanide, and iodide reactions.
2. Di-(1,2-dihydroxyphenyl) may be formed, though whether this occurs during the reaction or work-up cannot be stated.
3. Transient intermediates are present in the reactions.

The possibility that radicals were involved in these 'nucleophilic conjugate additions' was therefore investigated by electron spin resonance spectroscopy.

As electron spin resonance spectroscopy is not an 'everyday' analytical technique for many organic chemists, the following section is designed to provide a simple introduction to the topic. More detailed treatments are listed under ref. 87.

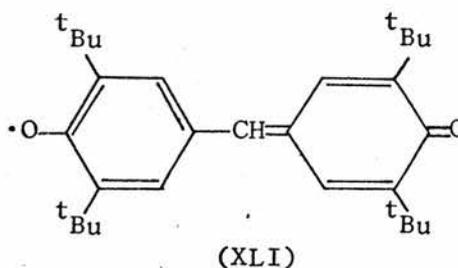
* Author's observation.

BASIC PRINCIPLES OF ELECTRON SPIN RESONANCE SPECTROSCOPY

In an atom (or molecule) the electron possesses spin angular momentum and a charge. In a normal closed shell species, e.g. helium or hydrogen fluoride, each electron is paired with a second electron of opposite spin, and the magnetic moments cancel out, making such substances diamagnetic.

In radicals, such as galvinoxyl (XLI) or certain transition metal ions (e.g. Mn^{VI}) there is at least one unpaired electron, and so the species has a finite magnetic moment, which can interact with an external magnetic field. The spin angular momentum can be positive or negative, and in the absence of an applied field these two states are of equal energy. Application of such a field removes this degeneracy, as the spins can align themselves with (low energy) or against (high energy) the field. It can be shown that the energy difference, E , between the two states is equal to $g\beta H$, where g is the splitting factor, β the Bohr magneton for the electron, and H the applied field in gauss. By irradiation of a paramagnetic sample with electromagnetic radiation of a suitable energy, transitions between the two energy levels can be caused. The frequency (ν) of such radiation can be calculated from the equation

$$h\nu = g\beta H$$



For a magnetic field of about 3000 gauss, such radiation occurs in the microwave region of the electromagnetic spectrum ($\lambda = 3 \text{ cm.}$, $\nu = 10 \text{ GHz}$).

Characteristics of an E.S.R. Spectrum.

The e.s.r. spectrum of a radical is characterized by the features listed below.

1. Its shape, i.e. the number of lines and their relative intensities.
2. The size of the hyperfine splitting constants.
3. Its 'g' value.

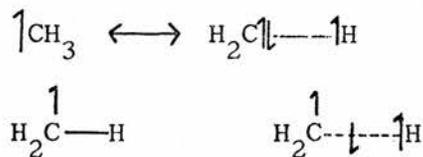
1 and 2 are discussed together below.

The shape of the spectrum is determined by the number and type of nuclear spins (in the radical) which interact with the spin of the electron. The e.s.r. spectrum of the free electron is a single line. In an atom the nuclear spin (value I) may lie in any of $2I + 1$ directions with respect to an external magnetic field. In the case of the hydrogen atom $I = \frac{1}{2}$ and the nuclear spin may be parallel or anti-parallel to that of the electron. In a field of 3000 gauss and at 300K the ratio of nuclei in the two states is given by

$$\frac{n^{+\frac{1}{2}}}{n^{-\frac{1}{2}}} = 0.9986, \quad 87a$$

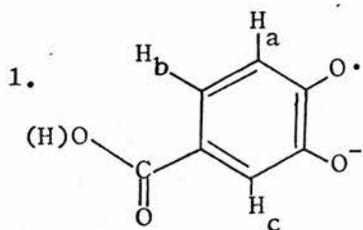
the two states having almost equal populations. The slight energy difference causes absorption to occur at different values of the magnetic field, and so the hydrogen atom shows a two line spectrum. The difference between the values of the magnetic field at which absorption occurs is called the 'hyperfine splitting constant'.

Interaction with a nucleus can occur only when the unpaired electron has a finite electron density at that nucleus. In theory this means that the electron must be in an orbital with s type character, but in practice electrons in π orbitals also interact via hyperconjugative/polarization mechanisms.

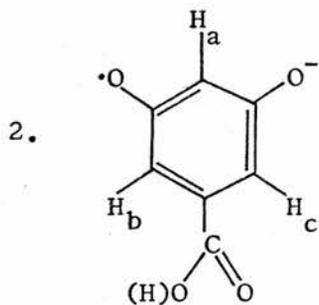
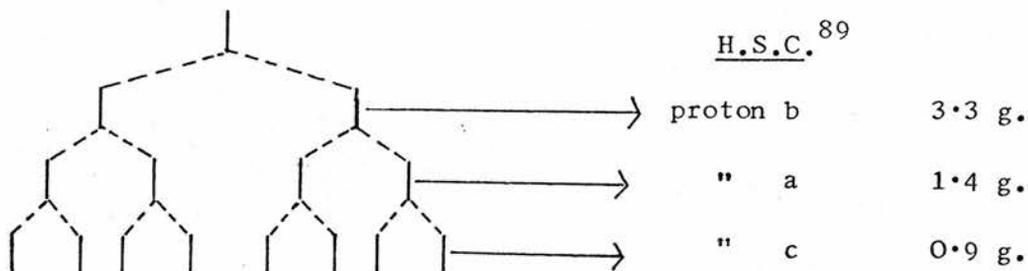


Direct interaction (i.e. when the electron is in an s type orbital) produces very large hyperfine splitting constants, (whereas π type interactions cause small splittings) e.g. $H\cdot$, h.s.c. = $506\cdot8$ gauss.^{87a}

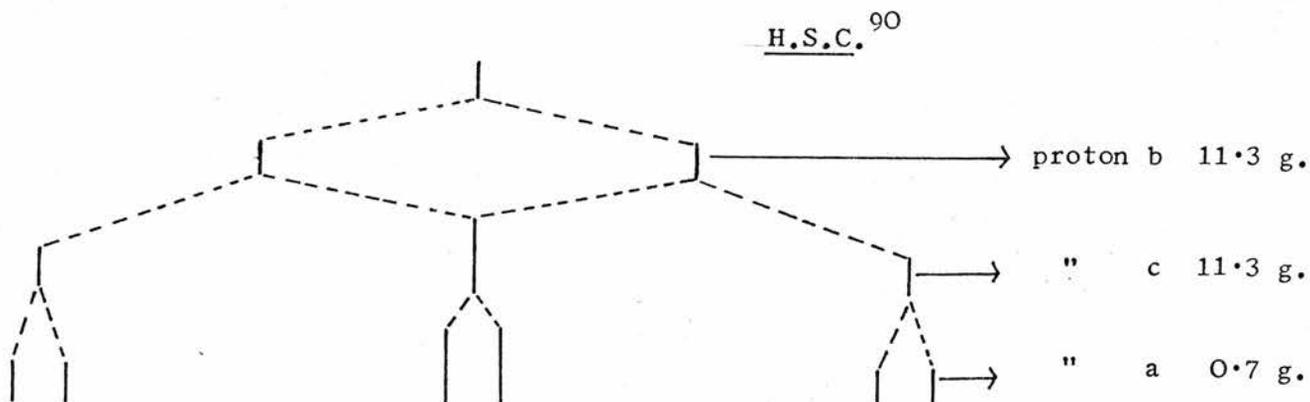
The number of interacting nuclei, their spin values, and the symmetry of the radical determine the number of lines in the spectrum. The following examples illustrate this.

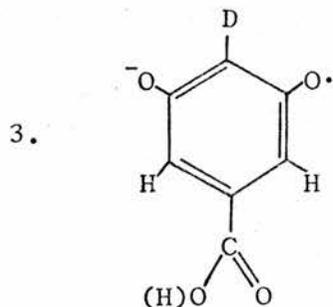


In this case the interacting nuclei are the protons, with $I = \frac{1}{2}$. The protons are all different from each other, and so an 8 line spectrum of intensity ratio 1:1:1:1:1:1:1:1 results.



This isomer of the above radical has two protons (b and c) in identical environments, resulting in the number of lines being reduced to six, and altering the line intensity pattern to 1:1:2:2:1:1





The substitution of deuterium for one of the hydrogen atoms in example 2 introduces a species with $I = 1$, resulting in three closely spaced lines in place of the two in the previous example. (Deuterium splittings are $\frac{2}{13}$ of hydrogen h.s.c.'s).⁸⁸



If a species contains n identical nuclei of spin $\frac{1}{2}$ capable of interaction with the unpaired spin, the intensity pattern can be obtained from Pascal's triangle.

n	Relative Intensities of lines		
0	1		
1	1	1	
2	1	2	1

etc.

'g' values.

$$h\nu = g\beta H \quad H = \frac{h\nu}{g\beta}$$

The above equations were obtained by consideration of the case of the free electron, in which the magnetic moment is caused by the charge and the spin angular momentum. In multi-atomic radicals rotational and orbital angular momenta also occur. These cause the e.s.r. spectra of radicals in the gas phase to be complex, but in solution the rotational effects are quenched. Orbital angular momentum has considerable effects in transition metal ion spectra, but only small results in the cases of organic radicals. In most organic radicals the unpaired electron will be in an orbital with some 'p' character (a pure 's' orbital has no orbital angular momentum and therefore need not be considered). A solitary (isolated) radical would have several orbitals of equal energy, but in solution interactions with the

surrounding molecules remove this degeneracy. Normally (at 300K) the highest occupied resulting orbital will have $M_L = 0$. Mixing-in of low-lying excited states and interactions with atoms having strong spin-orbit coupling introduce a small amount of orbital angular momentum. Therefore the above equations are slightly in error, and transitions occur at values of H differing from those calculated using $g = 2.00232$. By recording H and ν a 'g' value for a radical may be calculated. The deviation of this value from the free electron value (2.00232) is indicative of the size of orbital angular momentum effects in the radical. Where two radicals are present in the cavity, and one is of known g value, the g value for the other may be calculated using the first as a standard.

Theory of Calculation.

For a standard

$$h\nu = g_s \beta H_s$$

$$\therefore H_s = \frac{h\nu}{g_s \beta}$$

Similarly for the unknown

$$H_u = \frac{h\nu}{g_u \beta}$$

Let $H_u = H_s + \Delta H$ (ΔH positive if $H_u > H_s$)

$$\therefore H_s + \Delta H = \frac{h\nu}{g_u \beta}$$

$$\therefore g_u = \frac{h\nu}{\beta [H_s + \Delta H]}$$

Also $\frac{g_u}{g_s} = \frac{H_s}{H_u}$

As g_s , $h\nu$ and β are all known, and ΔH can be measured, it is possible to determine H_s , and hence, g_u .

E.S.R. WORK - PRACTICAL DETAILS

General Details.

An e.s.r. spectrometer consists of an electromagnet, the so-called 'cavity' at the centre of the magnet, a microwave generator with a waveguide to transmit microwaves to the cavity, and apparatus for recording the absorption of power by the sample which is at the centre of the cavity. A modulation frequency of 100 KHz is applied to the cavity. This causes the magnetic field to vary slightly and rhythmically, and results in the recording of the first derivative of the absorption spectrum. Improvements in the signal/noise ratio and the easier interpretation of poorly resolved spectra are benefits gained by recording the differential spectrum.

Polar solvents absorb microwave energy because of interactions between the molecular dipoles and the electric component of the radiation. In consequence it is necessary to use a sample container with a low volume in the irradiated zone. Normally a quartz tube with a thin, flat section at its centre (and known as an aqueous cell) is used.

The St. Andrews System.

The spectra were recorded using a Decca Spectrometer (Frequency = 9.27 GHz) with a Newport Magnet (Diameter = 9"). The field was normally set initially to 3300 gauss.

Freshly prepared solutions of the quinone and the nucleophile were mixed, and the resulting liquid was used to fill an aqueous cell, which was then fixed in position in the cavity. The spectrometer was then 'tuned', and an initial spectrum recorded. Scans were then run gradually at decreasing speeds and increasing modulation until no further (worthwhile) improvement in the resolution of the spectrum could be obtained. (This means that the resolved spectra obtained are those of radicals existing after an interval of many minutes).

The York System.

A Varian E3 Spectrometer (Frequency = 9.4 GHz, magnet diam. = 6") was used in conjunction with an aqueous cell, for 'static' work, or a mini-flow system. Flow techniques permit the recording of spectra of the first-formed radicals by allowing the reactants to mix just before they enter the e.s.r. cavity.⁹¹ Provided that the flow rate and reactant concentrations are suitable, a detectable concentration of the initial radical/radicals formed will be continually present in the cavity. The mini-flow system, designed by D.K.C. Hodgeman, is illustrated in figure 1. The flow rate can be adjusted by altering the heights of the reservoirs relative to that of the cavity. The cells used were modified aqueous cells, in which the tube below the flat cell portion had been replaced by two or three inlet tubes, which were arranged so that mixing of liquids flowing through them occurred immediately below the irradiated area (see figure 2).

The static work was performed in a manner similar to that described for the St. Andrews system. For the flow work freshly prepared solutions of the quinone and the nucleophile were poured into the reservoirs (250 ml. separating funnels), and deoxygenation was effected by bubbling nitrogen through them. The taps were then opened until the cell was full of liquid. The flow was terminated, and the machine 'tuned'. The taps were re-opened, and the flow rate and signal strength adjusted so that a satisfactory initial spectrum resulted. Adjustments were then made to the range of gauss scanned and the duration of a scan, so that the resolution of the spectrum could be improved.

In several cases a cell with three admission pipes was used: on these occasions nucleophile solution flowed through two and quinone solution through one. (The use of the three-tube system was necessitated because the only two-tube system suffered minor damage).

Sketch illustrating 'mini-flow' apparatus. The magnet coils on either side of the E.S.R. cavity are omitted, as is the connection to the microwave generator. Flexible plastic tubing was used to connect the reservoirs to the cell, and the cell to the residue container.

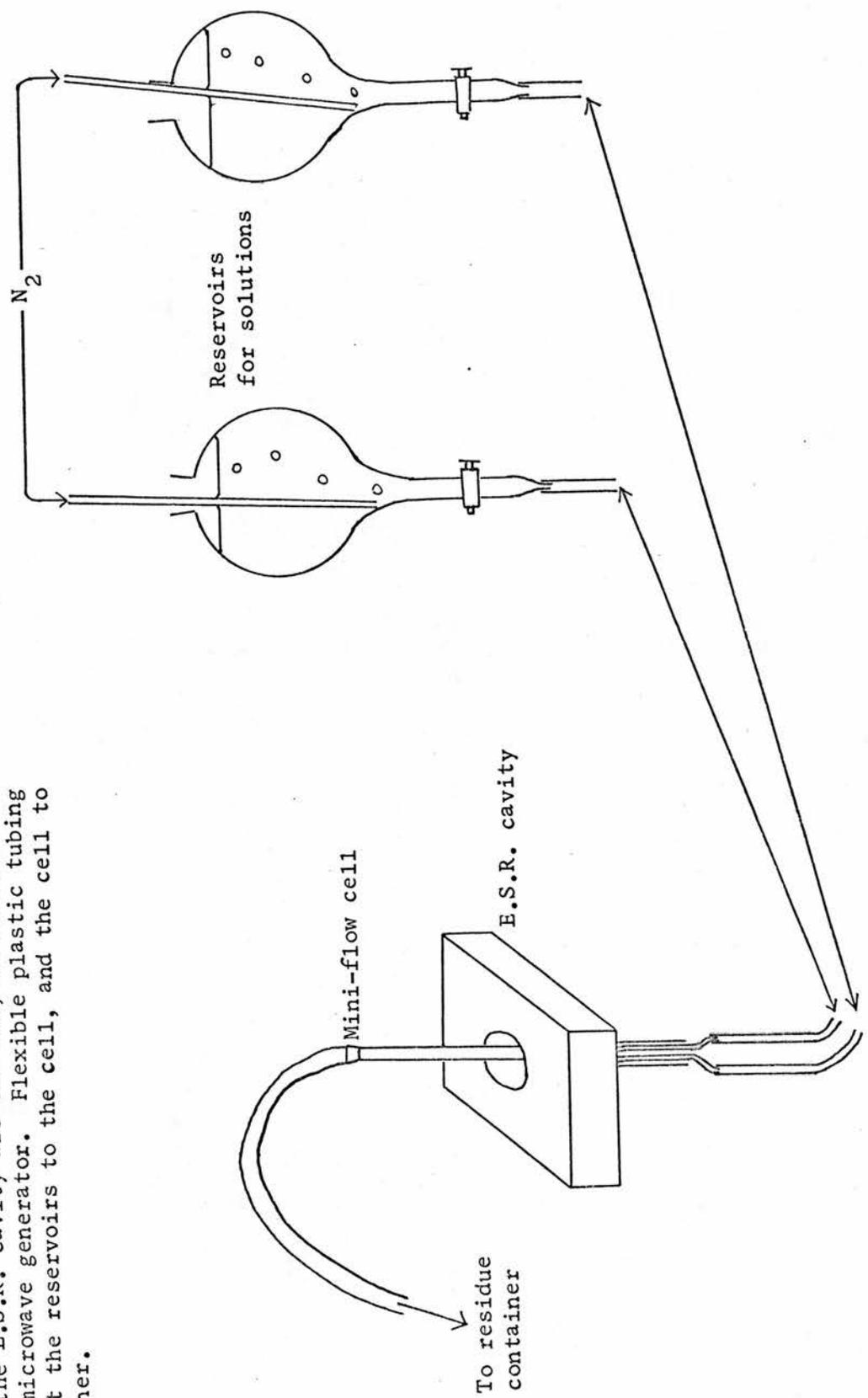


FIGURE 1 (Not to scale)

MINI-FLOW CELL

Designed by: D.K.C. Hodgeman

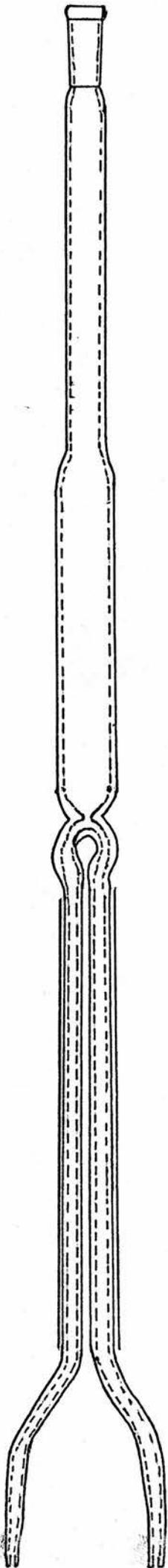


FIGURE 2 (Full scale)

Determination of hyperfine splitting constants.

At both York and St. Andrews the machine had been calibrated using Fremy's salt. The listed values of gauss/cm. for given scan methods were used.

Determination of g-factors.

An aqueous solution of Fremy's salt (potassium nitrosodisulphonate) in a fine capillary was attached to the (flat) face of the solution cell using vacuum grease, which also sealed the ends of the capillary. Scanning the spectrum then produced a super-imposition of the Fremy's salt spectrum (3 lines; ratio 1:1:1, $g = 2.0055 \pm 0.00005$, h.s.c. = 13.091 ± 0.0044)¹⁷¹¹⁷² on that of the radical in the cell.

E.S.R. STUDIES OF BENZO-1,2-QUINONE/NUCLEOPHILE REACTIONS

Details of Spectra Obtained from Static Systems

Nucleophile	Solvent for nucleophile	Solvent for quinone	Details of spectrum. (Hyperfine splitting constants are given in gauss)
Sodium azide	methanol	methanol	5 triplets (incomplete) H.S.C. 1.14 and 0.25
Diethyldihydro- pyrimidine	"	"	7 triplets H.S.C. 1.08 and 0.22
5,7-Dimethyl- dihydro- diazepine	"	"	7 triplets H.S.C. 1.15 and 0.24
Benzylamine	"	"	weak, complex spectrum
p-toluidine	"	"	very broad spectrum - precipitation of product caused difficulties
t-butylamine	"	"	7 triplets H.S.C. 1.14 and 0.25 or 1.21 and 0.26
N,N-dimethyl- aniline	"	"	complex, weak, very short-lived
Sodium acetate	DMSO	DMSO	asymmetric spectrum
Potassium carbonate	"	"	poorly resolved spectrum
Piperidine	-	methanol	weak, poorly resolved
Sodium nitrite	water	"	asymmetric
Sodium carbonate	"	"	very complex, 25-30 lines
Sodium nitrite	"	DMSO	'singlet'
Sodium nitrite	DMF	DMF	incompletely resolved triplet
t-butylamine	"	"	triplet H.S.C. 0.69
Potassium iodide	methanol	methanol	no observed signal
2,6-Dimethyl- aniline	-	"	" " "
N-methylaniline	-	"	" " "

Sodium methoxide - see following page.

Details of Spectra Obtained Using Sodium Methoxide and Benzo-
1,2-quinone

Stock Quinone Concentration	Vol. of Stock Q taken	Stock Methoxide Concentration	Vol. of NaOMe taken	Details of Spectrum
0.2M	X ml.	0.2M	X ml.	very complex (hints of presence of triplets)
0.2M	1 ml.	0.03M	10 ml.	app. [†] 27 lines
0.2M	1 ml.	0.1M	3 ml.	app. 21 lines
0.2M	1 ml.	0.2M	1.5 ml.	app. 27 lines
0.2M	2 ml.	$\frac{M}{18}$	1 ml.	very wide, app. 9 lines
0.2M	10 ml.	3M	1 ml.	very wide
0.2M	10 ml.	1M	1 ml.	7 triplets (not good). H.S.C. 1.12 and 0.22
unknown		unknown		3 triplets, H.S.C. 3.80 and 0.96
0.05M	3 ml.	0.28M	1 ml.	7 triplets, H.S.C. 1.16 and 0.25
0.01M	10 ml.	0.28M	0.6 ml.	very weak
0.2M	10 ml.	0.2M	*5 ml.	triplet evidence, spectrum suggests presence of more than one radical

* Methoxide added to quinone.

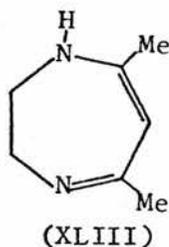
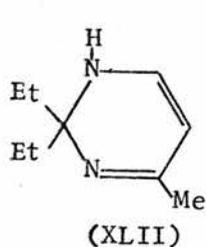
† app.: approximately.

Discussion of the Above Results.

Of the nucleophiles tested, N-methylaniline, 2,6-dimethylaniline and potassium iodide failed to give an e.s.r. signal, though a transient colour was observed when either of the latter two was mixed with benzo-1,2-quinone.

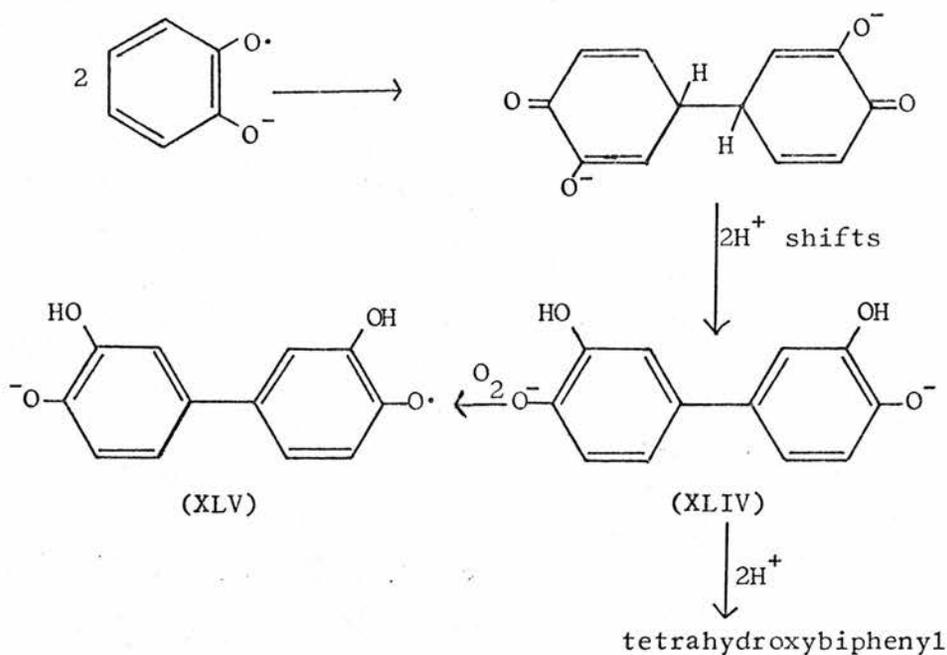
Only two types of resolved spectrum were obtained from systems using hydroxylic solvents. (Numerous non-resolvable spectra were produced). These are described below.

1. A 1:2:1 triplet of 1:2:1 triplets with h.s.c.'s of 3.80 g. and 0.96 g. This was produced using sodium methoxide in methanol, and is similar to the published^{83,92,93,94} spectra of the benzo-1,2-semi-quinone anion.
2. A 1:6:15:20:15:6:1 septet of 1:2:1 triplets, obtained by treating benzo-1,2-quinone in methanol with any of the following: sodium azide, sodium methoxide, 2-amino-2-methylpropane, 2,2-diethyl-1,2-dihydro-4-methylpyrimidine* (XLII), 2,3-dihydro-5,7-dimethyl-1,4-diazepine* (XLIII). (h.s.c. 1.14 g. and 0.25 g.).



The facts indicate that the radical species has a group of six equivalent protons and a set of two equivalent protons, and also that the nucleophile does not become incorporated into the radical. At first it was thought that the spectrum was one of a radical of the type (XLV), formed by the combination of a semi-quinone radical with a benzo-1,2-quinone molecule, or by the combination of two semi-quinone radicals followed by

*Thanks are expressed to Messrs. D.M.G. Lloyd and H. McNab for the supply of these compounds.



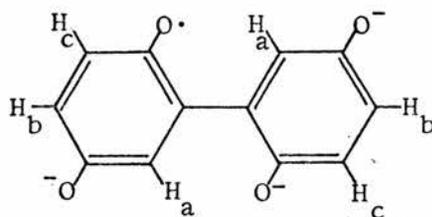
oxidation. The six ring protons could cause the larger splitting, while the smaller could be produced by the hydroxyl protons. Protonation of (XLIV) would yield tetrahydroxybiphenyl, whose possible presence in products obtained from the reaction of benzo-1,2-quinone with sodium azide has been discussed.

However structure (XLV) seems unlikely for the following reasons.

1. The six ring protons are not chemically equivalent, and therefore one would not expect them to produce identical hyperfine splittings.

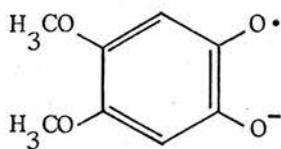
The known radical (XLVI)⁹⁵ contains 3 types of protons — each type has a different hyperfine splitting constant, as is indicated below.

<u>Proton Type</u>	<u>H.S.C. (in gauss)</u>
a	2.34
b	0.82
c	1.13



(XLVI)

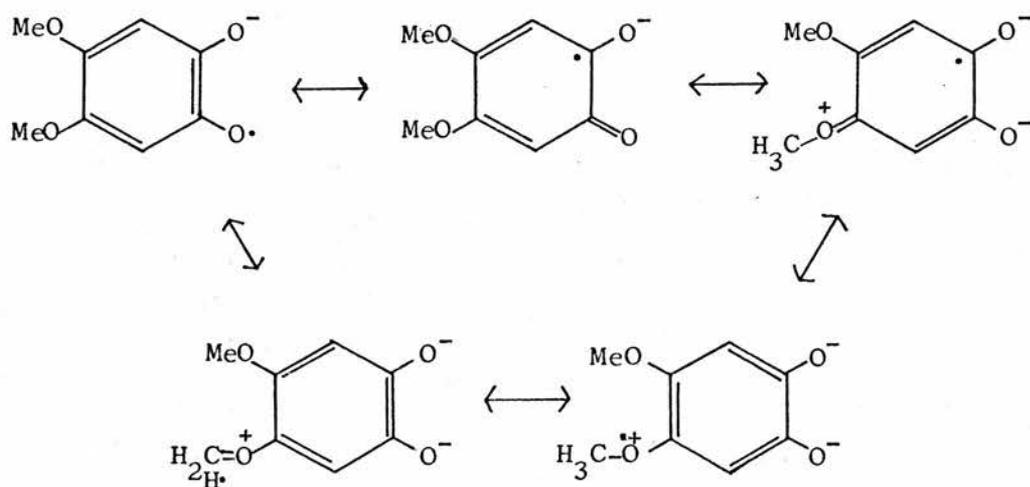
2. These spectra could be produced by using basic media (conc. $t\text{BuNH}_2$), and fewer than two hydroxyl protons might be present. Eaton⁹⁶ had previously obtained a heptet of triplets while working on methanolic benzo-1,2-semi-quinone, and attributed this result to the presence of 4,5-dimethoxybenzo-1,2-semiquinone (XLVII).



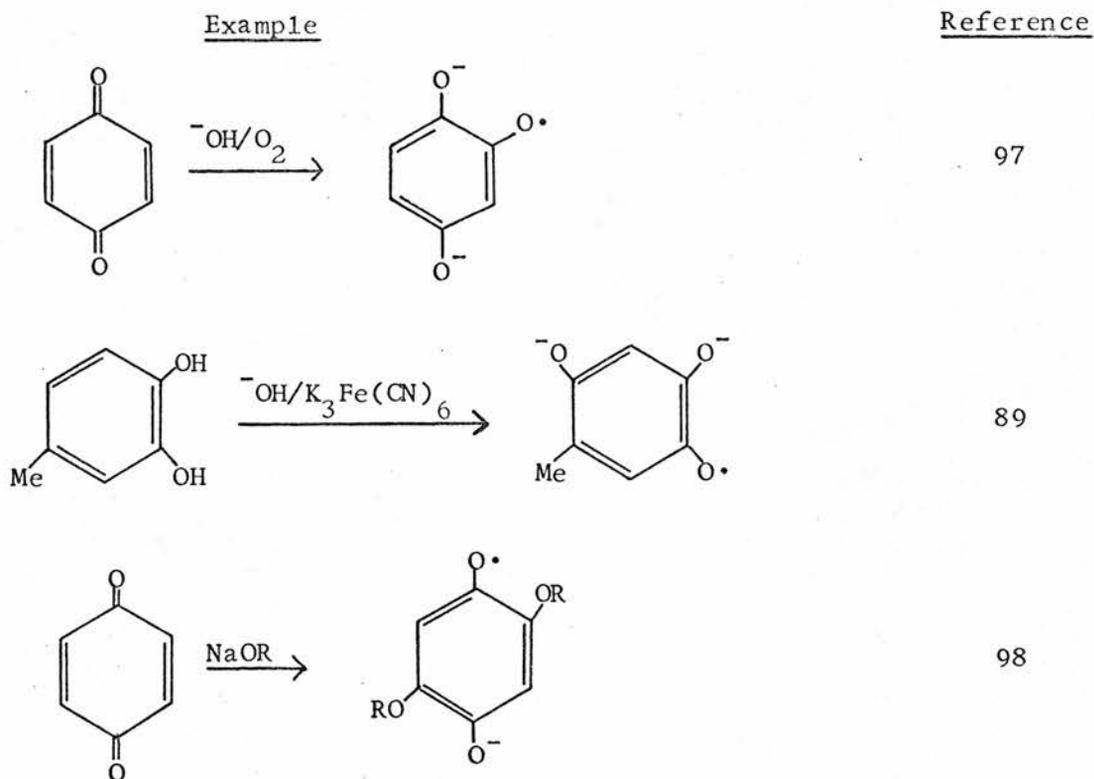
(XLVII)

The following evidence is in favour of this structure.

1. Six chemically equivalent (methyl) protons are present, and the ring protons are also equivalent.
2. The larger splitting is similar in size (1.12 g.) to that of the methoxy protons in 3- t butyl-5-methoxy-benzo-1,2-semiquinone; (1.1 g.⁸⁹). The methyl proton splitting results from the operation of a hyperconjugative mechanism, i.e.



3. Treatment of various quinones/dihydroxybenzenes with alkaline solutions has yielded hydroxylated/alkoxylated products (the hydroxylated ones ionize in alkaline solutions to give doubly charged anion radicals).



The data obtained by Reitz et al.⁹⁸ are very similar to figures for the species under investigation.

<u>R</u>	<u>H.S.C.</u>		<u>g value</u>
	Ring protons	Alkoxy protons	
CH ₃	0.28 g.	0.96 g.	2.00454
C ₂ H ₅	0.35 g.	1.06 g.	2.00456
cf.	0.22 g.*	1.04 g.*	2.0045*

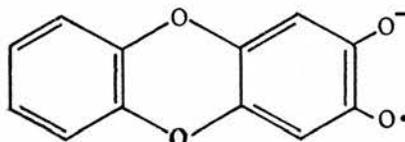
4. The radical species can be generated in an excess of methoxide ion. (Though it can also be formed using sodium azide in methanol).
5. The formation of such a species from benzo-1,2-quinone has been observed in methanol,^{96,99} but not in other solvents.

* See page 90.

Eaton⁹⁶ considered that metal ions catalysed the formation of this radical. The use of nitrogenous bases in its generation indicates that, while metals may cause catalysis, their presence is not necessary for the formation of (XLVII).

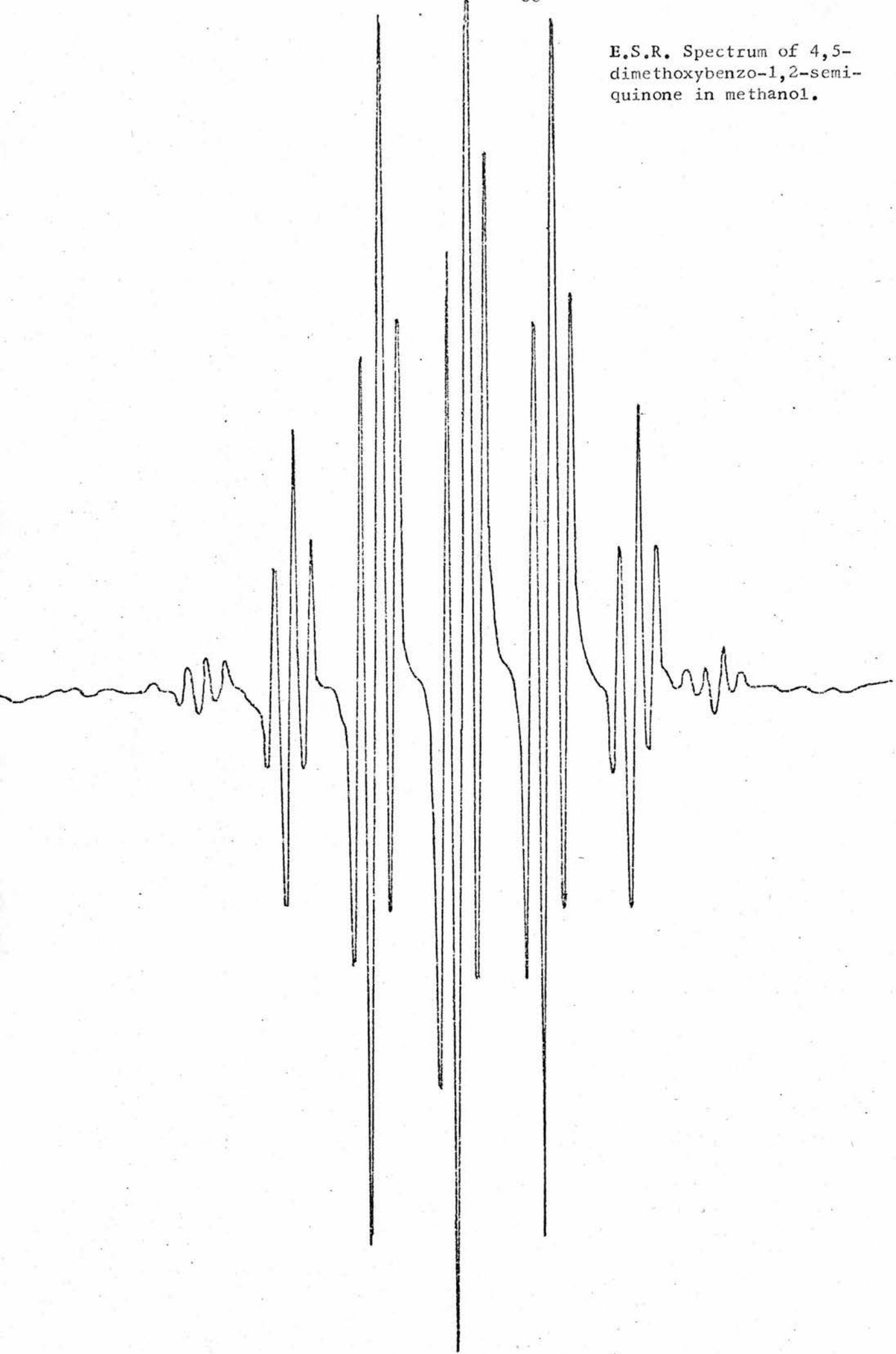
The mechanisms leading to the production of the unsubstituted semi-quinone and the dimethoxy semi-quinone are discussed later (pages 96-117).

The use of non-hydroxylic solvents did not normally result in satisfactory spectra, but one resolved triplet was obtained using N,N-dimethyl formamide as solvent and t-butylamine as the nucleophile. This triplet resembles that obtained by Hewgill, Stone and Waters⁸³ from the aerial oxidation of catechol in alkaline D.M.F. (H.S.C. 0.64 g., cf. 0.69 g.). The spectrum was ascribed to the radical (XLVIII).



(XLVIII)

E.S.R. Spectrum of 4,5-dimethoxybenzo-1,2-semiquinone in methanol.



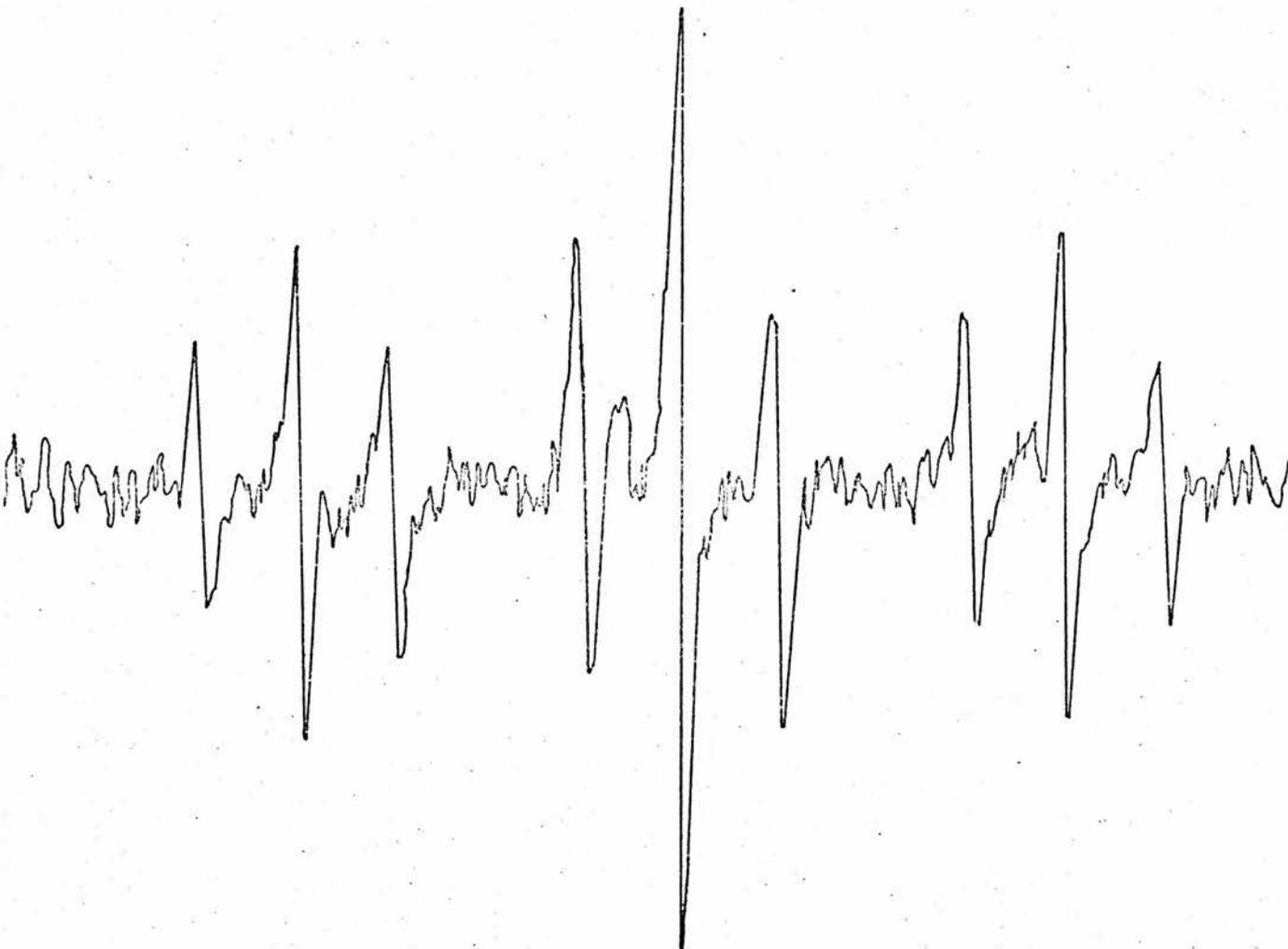
E.S.R. Flow System Results

Sodium Azide + Benzo-1,2-Quinone

<u>Solvent for NaN₃</u>	<u>[NaN₃]</u>	<u>[Quinone] in MeOH</u>	<u>Details of run and spectra</u>	<u>H.S.C. (in gauss)</u>	<u>g (if found)</u>
MeOH	0.011M	0.008M	Triplet of triplets	3.86 and 0.64	
MeOH	0.01M	0.005M	Superimposition of two triplets of triplets (+ 2 lines)	3.8 and 0.64 3.65 and 0.95	2.0041
H ₂ O	0.01M	0.007M	(1) slow flow - hint of presence of triplets (2) fast flow - superimposition of 2 triplets of triplets (3) static (termination of a flow). Triplet of triplets (4) Fremy's salt standard present, otherwise as (3)	3.64 and 0.94	2.0046

Other Nucleophiles + Benzo-1,2-Quinone

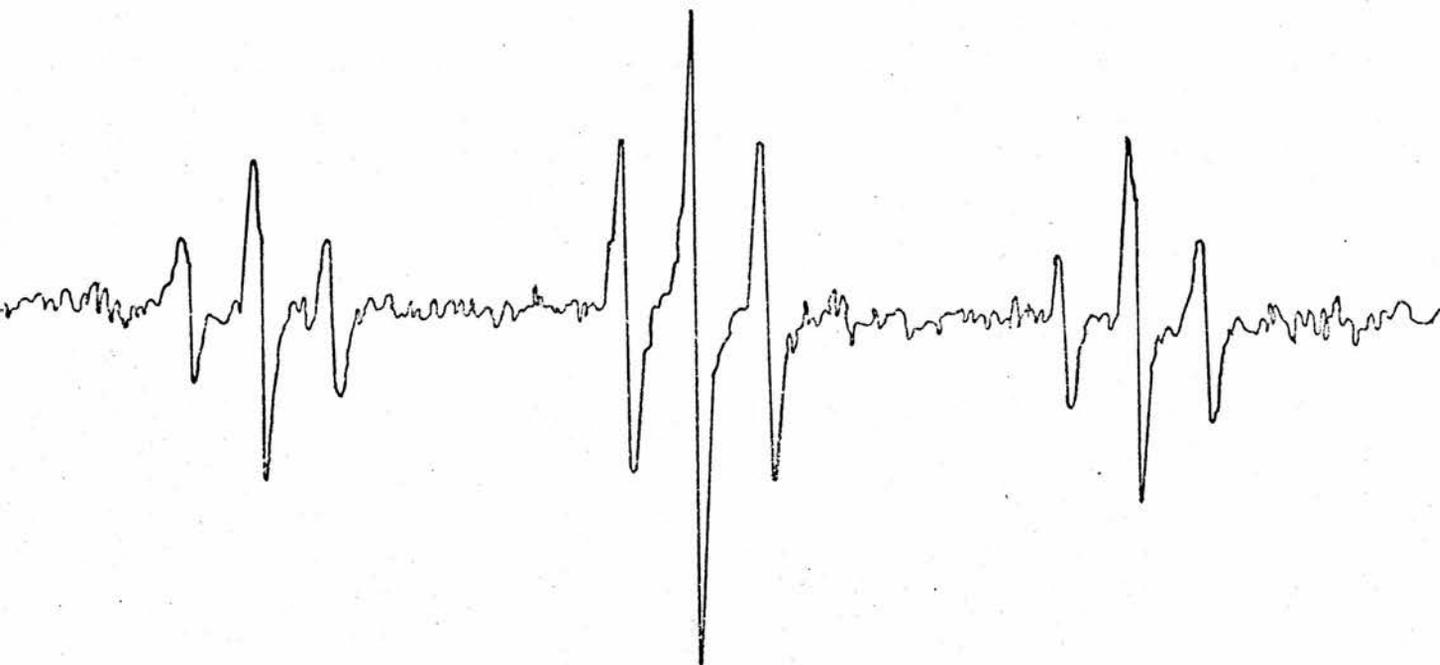
<u>Solvent for nucleophile</u>	<u>Nucleophile and concentration thereof</u>	<u>[Quinone] (in MeOH)</u>	<u>Details of run and spectra</u>	<u>H.S.C. (in gauss)</u>	<u>g (if found)</u>
MeOH	0.01M NaNO ₂	0.005M	1) Slow flow-superimposition of 2 triplets of triplets 2) Fast flow of quinone, normal nitrite; triplet of triplets plus other small lines	3.86 and 0.65 3.64 and 0.94 3.86 and 0.64	2.0040
H ₂ O	~0.01M NaHSO ₃	~0.007M	No spectrum obtained		
MeOH	0.01M KI	0.008M	Triplet of triplets	3.86 and 0.66	
MeOH	0.01M ^t Bu-NH ₂	0.005M	1) Flow. Triplet of triplets 2) Terminate flow-complex spectra were obtained	3.86 and 0.64	
MeOH	conc. ^t Bu-NH ₂	weak	3) Static experiment, open to the atmosphere. 7 triplets (a heptet of triplets)	1.04 and 0.22	2.0045



E.S.R. Spectra of benzo-1,2-semiquinone in methanol.

Lower spectrum: H.S.C. 3.86 g. and 0.64 g.

Upper spectrum: H.S.C. 3.64 g. and 0.94 g.



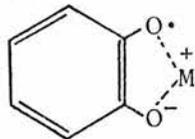
Flow System E.S.R. Spectra - Discussion

This system proved most valuable in investigating the reactions of nucleophiles with 1,2-quinones. Limitations on time prevented its use for further work. The results are summarized on pages 89-90.

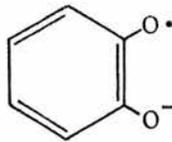
Methanolic solutions of sodium nitrite, sodium azide, potassium iodide and t-butylamine each reacted with benzo-1,2-quinone in methanol to give a radical whose spectrum consisted of a 1:2:1 triplet of 1:2:1 triplets. This indicates that the radical has two sets of two equivalent protons, as in the benzo-1,2-semiquinone radical anion. However the hyperfine splittings are different from those previously reported.^{83,92-4, 99,100} The points listed beneath are significant.

1. The h.s.c's were independent of the counter-ion (sodium, potassium, or an unknown species in the case of the amine reaction).
2. Certain complicated spectra can be analyzed as a superimposition of a triplet of triplets, with h.s.c's 3.65 g. and 0.95 g., g value 2.0046, on a triplet of triplets with h.s.c's 3.86 g. and 0.64 g., g value 2.0041. On cessation of the flow, the former spectrum remained, the latter having decayed away.
3. The solitary spectrum of the unsubstituted semiquinone obtained in the static system (using sodium methoxide) displayed h.s.c's of 3.80 g. and 0.96 g.
4. The superimposition spectra could be obtained in methanol and in a methanol/water mixture.

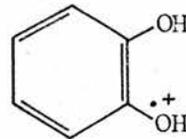
The hyperfine splittings of the benzo-1,2-semiquinone radical are known to be dependent on the solvent, the counter-ion, and the pH. The only systems possessing two sets of two equivalent protons are (IL), (L), and (LI).



(IL)



(L)



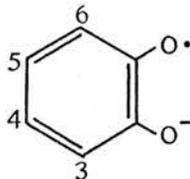
(LI)

(M⁺ is a metal ion)

(LI) was obtained by Smith and Carrington¹⁰⁰ in a strongly acid solution (pH ~ -1), and shows h.s.c.'s of 4.21 g. and 0.95 g. It seems extremely unlikely that such a species would exist in the presence of as strong a base as t-butylamine.

The solvent dependence is illustrated in Table 12.

Table 12



<u>Solvent</u>	<u>Counter-ion</u>	<u>H.S.C.</u> <u>(H4 and</u> <u>H5)</u> <u>(in gauss)</u>	<u>H.S.C.</u> <u>(H3 and</u> <u>H6)</u> <u>(in gauss)</u>	<u>Ratio</u> <u>of H.S.C.'s</u>	<u>Ref.</u>
H ₂ O	Na ⁺	3.75	0.77	4.87	100
H ₂ O	NH ₄ ⁺	3.77	0.76	4.96	99
MeOH	Na ⁺	?	?	4.05	96
EtOH	Na ⁺	3.65	0.95	3.84)	83
DMF	Na ⁺	3.55	1.16	3.06)	

The triplet of triplets obtained in the static experiment exhibited splittings of 3.80 g. and 0.96 g., which values are similar to those (3.64 g. and 0.94 g. in most cases, 3.55 g. and 1.0 g. in one case) obtained for the longer-lived triplet of triplets observed by the flow technique, and are also close to those published for the semiquinone in ethanol.⁸³

The mystery radical showed splittings of 3.86 g. and 0.64 g. (ratio 6.075). As both it and the 'normal' one were observable in pure methanol, it seems unlikely that the solvent is the cause of the different h.s.c's.

The effects of a change in counter-ion on both the hyperfine splitting constants and the g-factor of o-semiquinone have been studied.^{96,99} In aqueous solutions the alkali metals all gave the same values,⁹⁹ but group II metals gave the following results.⁹⁹

<u>Ion</u>	<u>H.S.C.</u> <u>(in gauss)</u>	<u>H.S.C.</u> <u>(in gauss)</u>	<u>g-factor</u>
Mg ²⁺	0.53	4.03	2.00423
Ba ²⁺	0.73	3.85	2.00400
Cd ²⁺	0.53	3.93	2.00347

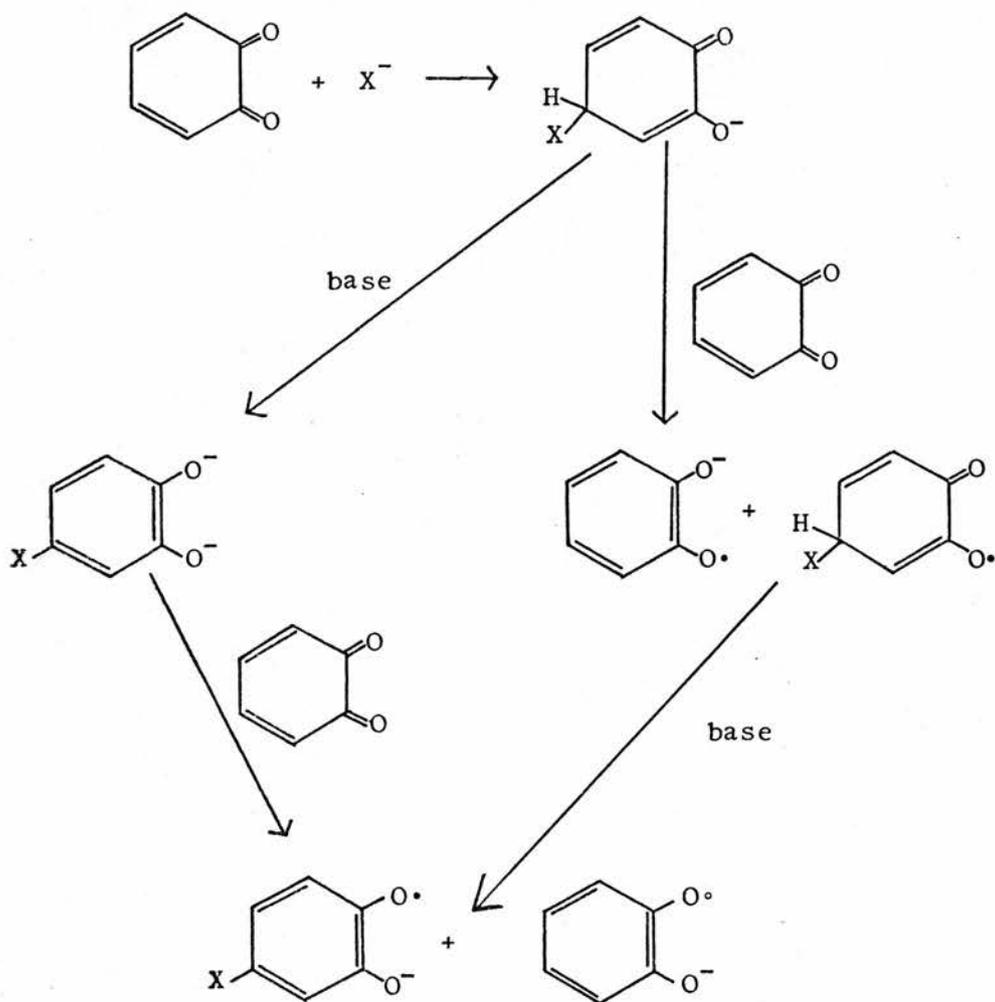
In less polar solvents, e.g. t-butyl alcohol or methyltetrahydrofuran, complexation of the metal ion by the semiquinone results in each line of the spectrum being split into several lines as a consequence of there being unpaired electron density at the nucleus of the metal ion. This effect has been observed where the metal ion was lithium or sodium.^{101,102} In the case of potassium the nuclear magnetic moment and the electron density at the nucleus are such that the product of these terms is much smaller than it is for lithium or sodium,¹⁰¹ and splittings caused by the metal ion were not observed when potassium was the semiquinone's counterion. Lucken¹⁰¹ observed that the addition of water to solutions of semiquinones in t-butyl alcohol caused the spectra to change to those of the 'free' anion radicals. No splittings caused by metal ions were observed during the present work, indicating that unchanging ion-pairs do not exist in the solution. Dr. Eaton informed the author that the data on benzo-1,2-semiquinone in methanol in the presence of alkali metal ions is no longer available.

It is possible that the initial radical formed is an excited semiquinone, as the hyperfine splitting constants indicate that the electron distribution differs from that in the 'normal' semiquinone; and that the former decays to give the latter, though whether some weak 'complexation' with a metal ion occurs in the normal radical is not clear.

POSSIBLE MECHANISMS OF SEMIQUINONE FORMATION

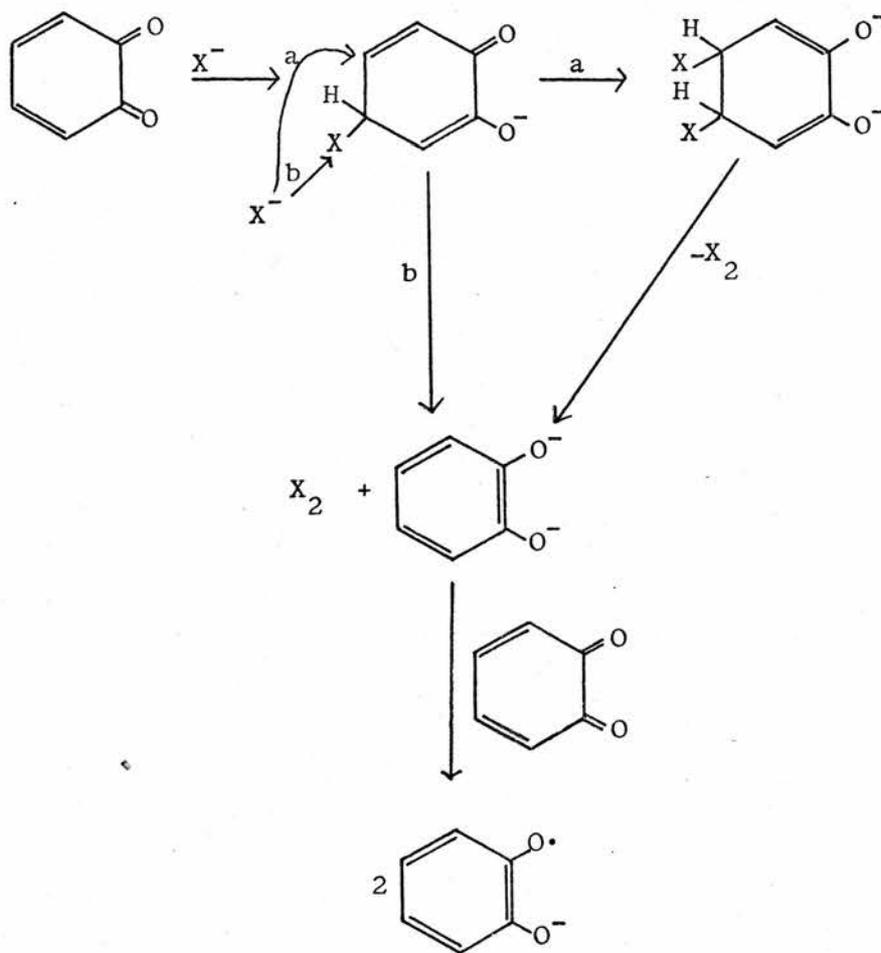
The benzo-1,2-semiquinone radical was first observed, using E.S.R. techniques, by Blois,¹⁰³ who reduced the parent quinone using alkaline sodium dithionite solution. The radical has also been 'prepared' by the aerial oxidation of alkaline solutions of catechol.⁸³

Studies^{97,104} have been made of the system quinol/benzo-1,4-semiquinone/benzo-1,4-quinone in alkaline solution, and processes similar to those described in references 97 and 104 can be envisaged in the case of the 1,2-quinone.



If the above scheme applied to the 1,2-quinone reactions, the e.s.r. spectra of the flowing reaction mixture should have revealed the presence of the unsubstituted semiquinone and also a substituted one, whereas only the two variants of the former were observed. If the quinone can oxidise the substituted catechol (anion) to the substituted quinone, then the resulting catechol (anion) might react with more unsubstituted quinone by disproportionation, producing two semiquinone radicals. For this to occur, the standard electrode potential of the substituted quinone must be lower than that of benzo-1,2-quinone. An amino group would be a suitable X, but nitro would not, as electron-withdrawing groups tend to raise the redox potential of quinones.¹⁰⁵

The above mechanism can be modified, as depicted below.



The oxidation of iodide or nitrite would yield iodine or dinitrogen tetroxide respectively, while azide would give N_6 , which would decompose immediately to three molecules of nitrogen. The energetics of these oxidations can be considered using redox potential data.

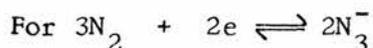
At pH 0, the standard electrode potentials for catechol/benzo-1,2-quinone and iodide/iodine are 0.795 v.¹⁰⁶ and 0.5355 v.¹⁰⁷ In neutral solution (pH7) the latter potential will not change very much, as hydrogen iodide is a very strong acid ($pK_a = -10$),¹⁰⁸ but the potential of the organic system varies according to the equation:

$$*E_{\frac{1}{2}} = E_o - 0.059 \text{ pH at } 25^\circ\text{C.}^{109}$$

*Polarographic $E_{\frac{1}{2}}$ potentials are normally equal to the redox potential under the same conditions in the absence of complexing agents.¹¹⁰

Therefore at pH7 the electrode potential of the catechol/quinone system is 0.382 v. A polarographic measurement¹¹¹ of $E_{\frac{1}{2}}$ at pH7 gave a value of 0.20 v. versus the saturated calomel electrode, which corresponds to a value of 0.44 v. versus the standard hydrogen electrode. Both of these potentials are below the standard potential of the iodide/iodine couple, and so the free energy of iodine plus catechol is greater than that of quinone with iodide (at pH7).

The case of the oxidation of azide to nitrogen is illustrated by the following calculations.



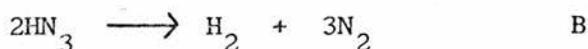
$$\text{Estimated } E^o = -3.3 \text{ v.}^{112}$$

$$\Delta G^o = -zE^oF = +2 \times 3.3 \times 96500/4,184 = +152.4 \text{ kcal mol}^{-1}$$

In neutral solution the reduction of benzo-1,2-quinone to catechol liberates free energy to the extent of $17.2 \text{ kcal mol}^{-1}$; therefore as both halves of the reaction proceed with the release of free energy such a reaction is possible. If the azide ion is protonated, the energetics of the reaction

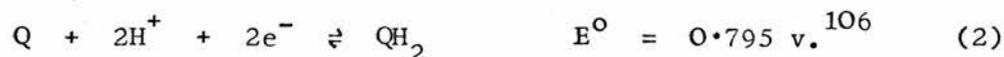
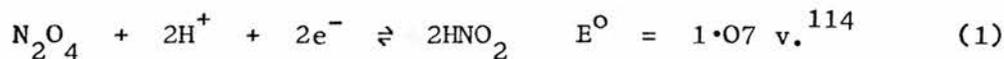


can be divided into

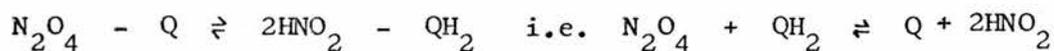


The free energy of the reaction A can be found using standard electrode potential data, and equals $-36.7 \text{ kcal mol}^{-1}$, while that for B equals $-157 \text{ kcal mol}^{-1}$ at 298°K (minus twice the standard free energy of formation of hydrazoic acid).¹¹³ The overall reaction releases $193.7 \text{ kcal mol}^{-1}$ of free energy, and is therefore thermodynamically possible. The addition of sodium azide solution to a solution of benzo-1,2-quinone did not produce observable effervescence, but on one occasion such solutions were mixed and the flask stoppered. Shortly afterwards the stopper was blown out of the flask. Nitrogen formation may therefore occur, but it does not seem to be the main reaction.

A calculation reproduced below shows that nitrogen tetroxide can be reduced by catechol, the products being nitrous acid and benzo-1,2-quinone.



Subtract (2) from (1).



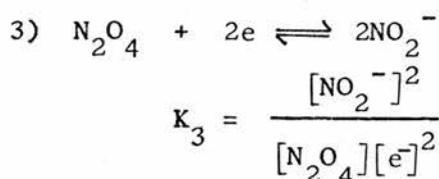
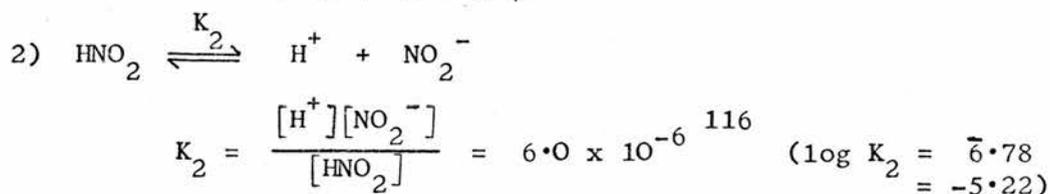
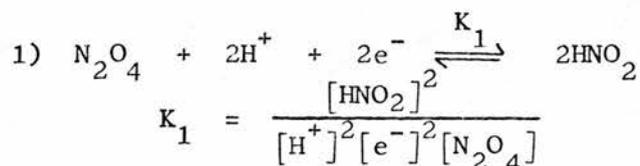
For reaction to proceed from left to right,

$$E_{\text{cell}}^\circ = +1.07 \text{ v} - (+0.795 \text{ v.}) = 0.275 \text{ v.}$$

$$\Delta G^\circ = -zE^\circ F = -2 \times 0.275 \times 96500 / (4.18 \times 1000) = -12.7 \text{ kcal mol}^{-1}$$

These figures are for reaction in acidic solution. Increasing the pH at which the reaction is performed will result in nitrite ions and catechol ions

being formed in the system. The calculation reproduced below shows that the oxidation of two nitrite ions to form one molecule of dinitrogen tetroxide requires $35.2 \text{ kcal mol}^{-1}$ of free energy. As the reduction of benzo-1,2-quinone at neutral pH supplies $17.2 \text{ kcal mol}^{-1}$ only, the quinone cannot oxidise nitrite to dinitrogen tetroxide, unless the disproportionation reaction and any subsequent reactions of the nitrogen oxide release sufficient free energy to give the overall process a negative free energy change. Methanol is known to react with nitrogen dioxide to give nitric acid and methyl nitrite.¹¹⁵ To demonstrate that such a scheme applied it would be necessary to prove the presence of these products. Nitric acid might well react with quinone radicals or dianions.



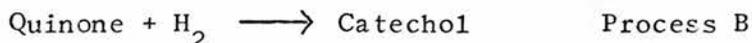
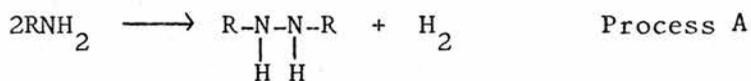
$$K_1 K_2^2 = \frac{[\text{HNO}_2]^2 [\text{H}^+]^2 [\text{NO}_2^-]^2}{[\text{H}^+]^2 [\text{N}_2\text{O}_4] [\text{HNO}_2]^2 [\text{e}^-]^2} = \frac{[\text{NO}_2^-]^2}{[\text{e}^-]^2 [\text{N}_2\text{O}_4]} = K_3$$

$$\therefore K_3 = K_1 K_2^2$$

$$\begin{aligned} \Delta G_3^0 &= -2.303RT \log K_3 = -2.303RT \log K_1 K_2^2 \\ &= -2.303RT \log K_1 - 4.606RT \log K_2 \\ &= \Delta G_1^0 - 4.606RT \log K_2 \end{aligned}$$

$$\begin{aligned}
 &= -zE_1^{\circ}F - 4 \cdot 606RT \log K_2 \\
 &= \frac{-2 \times 1 \cdot 07 \times 96,500}{4 \cdot 184 \times 1000} - \frac{4 \cdot 606 \times 1 \cdot 987 \times 298 \times (-5 \cdot 22)}{\times 1000} \\
 &= -49 \cdot 4 + 14 \cdot 2 \text{ kcal} \cdot \text{mol}^{-1} \\
 &= -35 \cdot 2 \text{ kcal} \cdot \text{mol}^{-1}
 \end{aligned}$$

The addition-elimination mechanism can also be applied to the reaction of t-butylamine with a quinone, the products being N,N'-di-t-butylhydrazine and catechol. Thermodynamically this system can be considered as:



Energetics of A

$$\text{Bond energy gained: H-H bond. } 104 \cdot 2 \text{ kcal mol}^{-1} \quad 70$$

$$\text{N-N bond } 39 \cdot 0 \text{ kcal mol}^{-1} \quad 70$$

$$\text{Temperature x Entropy of 1 mole of H}_2 \text{ at } 298^{\circ}\text{K} \quad \frac{9 \cdot 3}{152 \cdot 5} \text{ kcal mol}^{-1} \quad 117$$

The energy change (referred to subsequently as '?') due to entropy difference between the amine and the hydrazine is not known, but will probably be negative as di-t-butyl-hydrazine's bulky substituents could result in restricted rotation around certain bonds.

$$\text{Bond energy lost} = 2 \times \text{N-H} = 186 \cdot 8 \text{ kcal mol}^{-1}$$

$$\text{Overall energy change} = -152 \cdot 5 + 186 \cdot 8 + '?' = +34 \cdot 3 + '?' \text{ kcal mol}^{-1}$$

Energetics of B

$$\Delta G^{\circ} = -36 \cdot 7 \text{ kcal mol}^{-1}$$

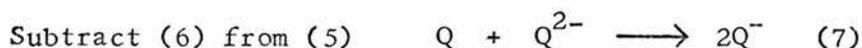
The entropic energy change '?' governs therefore whether such a reaction is possible if '?' is less than $2 \cdot 4 \text{ kcal mol}^{-1}$ the reaction is thermo-

dynamically allowed. However a reaction between two bulky species does seem somewhat unlikely, and a different mechanism whereby basic species such as ^tbutylamine can effect the reduction of a quinone in methanol is given later. A mechanism of the above type could occur in aprotic solvents, such as dimethylformamide, in which radical formation was observed when benzo-1,2-quinone was treated with ^tbutylamine.

The energy changes during the disproportionation of a quinone molecule with its 2-electron reduction product have not yet been considered. Heyrovsky and Zuman¹¹¹ give 2-electron process ' $E_{\frac{1}{2}}$ ' values for the catechol - quinone system at pH 7 and pH 9 (solvent presumably water), while Peover¹¹⁸ lists polarographic data for two separate 1-electron reductions of benzo-1,2-quinone in acetonitrile. In this solvent the energy gained by a quinone molecule reacting with one of the catechol dianion? to form two radicals is $13.6 \text{ kcal mol}^{-1}$ (56.9 kJ mol^{-1}).



$$E_{\frac{1}{2}}(5) = -0.31 \text{ v.}^{118} \qquad E_{\frac{1}{2}}(6) = -0.90 \text{ v.}^{118}$$



$$E_{(7)} = E_{\frac{1}{2}}(5) - E_{\frac{1}{2}}(6) = -0.31 \text{ v.} + 0.90 \text{ v.} = +0.59 \text{ v.}$$

$$\Delta G_{(7)}^{\circ} = -zE_{(7)}F = -1 \times 0.59 \times 96500/4184 \text{ kcal mol}^{-1} = -13.6 \text{ kcal mol}^{-1}$$

In aqueous solution the higher concentration of protons, resulting in catechol itself as the reduction product, may make the semiquinone unstable relative to quinone and catechol. The lack of polarographic data for the quinone system in methanol means that one cannot state which substance(s) will be stable (with respect to disproportionation) in that solvent. Methanol is much more acidic than acetonitrile, and is not much less

acidic than water (pKa values relative to water: H₂O 16, MeOH 16, RCH₂CN 25¹¹⁹). The semiquinone radical has been detected in alkaline alcoholic solution,⁸³ but under such conditions the low proton concentration and presence of oxygen could favour radical formation.

In considering the possible quinone/reductant reactions data for electrode potentials in aqueous solution was used. Fieser¹²⁰ observed that there was little difference between the standard redox potential of benzo-1,2-quinone and that of the same substance in acidified ethanol when the latter potential was measured against a hydrogen electrode in acidified ethanol. (Values 0.782 v. and 0.784 v. in H₂O and EtOH respectively). The lower concentration of protons in methanol and the smaller dielectric constant of that solvent will both effect the redox potential of the quinone. The proton concentration will have a smaller effect on the potentials of such species as azide, nitrite and iodide, whose conjugate acids are more acidic than catechol (see table below).

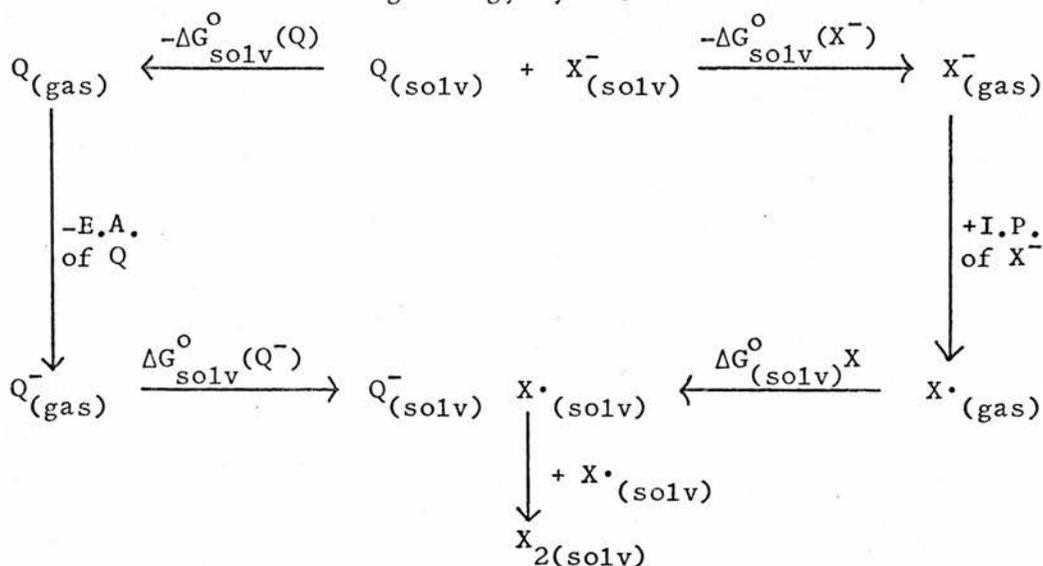
<u>Species</u>	<u>K_a</u>	<u>Temperature</u>	<u>Reference</u>
Catechol	1. 7.5 x 10 ⁻¹⁰	303K	121
	2. 8.37 x 10 ⁻¹³		
Nitrous acid	6.0 x 10 ⁻⁶	298K	116
Hydrazoic acid	1.8 x 10 ⁻⁵	298K	122
Hydroiodic acid	10 ¹⁰	298K	108

It therefore seems unlikely that a reaction will occur in methanol if it does not occur in water, unless disproportionation does occur in methanol and does generate sufficient free energy to cancel out that lost during the early stages of the reaction.

Published polarographic data does allow the consideration of the reaction between the quinone and iodide in acetonitrile. Iodide is initially oxidized in this solvent to the tri-iodide ion.¹²³ The E_{1/2} for this process

is -0.5 v. with respect to a silver/silver nitrate electrode, in acetonitrile.^{123*} Including the liquid junction potential, the Ag/AgNO₃ electrode has a potential of 0.337 v. with respect to an aqueous saturated calomel electrode.¹²⁴ This makes the potential for the iodide/tri-iodide system in acetonitrile -0.163 v. with respect to an aqueous S.C.E. The corresponding value for the 1-electron reduction of benzo-1,2-quinone to its anion is -0.31 v.¹¹⁸ As the oxidant has a lower potential than the reductant, the quinone cannot oxidise the iodide to tri-iodide.

An alternative method of considering a one-electron redox process is to make use of the following energy cycle.



KEY: Q a quinone

X⁻ a reductant

ΔG_{solv}° free energy of solvation (standard)

E.A. electron affinity

I.P. ionization potential

* Though it is not explicitly stated in ref. 123 that the reference electrode was in MeCN, the wording suggests that this was so.

Unfortunately values are not known for all the terms in the cycle, and others can only be estimated. Certain relevant data is given below. (In these tables all quantities are given in kcal mol⁻¹, and the temperature is 298 K).

<u>Ion Solvation Energies</u>				
Ion	$-\Delta H_{\text{solv}}^{\circ}$	$-\Delta G_{\text{solv}}^{\circ}$	Solvent	Reference
Iodide	67.3	64	H ₂ O	125
"		60.5 ± 1.3	MeOH	126, 127, 128
		56.4	MeCN	129
Azide	79		H ₂ O	130
Nitrite	98		H ₂ O	125

Ionization Potentials of Ions and one Amine

Ion	I.P.	Reference
Iodide	74.5	131
Azide	70	132
^t BuNH ₂	199	55
Ethoxide	200.1	133
Nitrite	<64.6	134
⁺ N=O-O ^{-*}	41.5	135

Electron Affinities of Radicals

Radical	E.A.	Reference
EtO	15.5	} 136
MeO	11.5	
NO ₂	ca. 55-57	137, 138

*It has been suggested^{135, 138} that sodium nitrite contains a proportion of the isomeric ion ⁺N=O-O⁻, as ionization experiments have shown the presence of some material of lower I.P. in sodium nitrite.

The difference between the electron affinity of some radicals and the ionization potential of the corresponding ions results from ionization producing a radical with a high energy geometry. Dissipation of this excess energy gives a ground state radical, whose electron affinity must therefore be less than the ionization potential. In a reaction system one would expect that the species would gradually alter their geometries during reaction, and therefore the energy change for the ionization of X^- could be considered as the electron affinity of X° .

Estimations of the difference in solvation energy between a quinone and its anion-radical in acetonitrile have revealed that this quantity is approx. 3.6 eV (83 kcal mol⁻¹) for many 1,4-quinones and phenanthra-9,10-quinone.¹³⁹ The electron affinity of a quinone can be estimated by use of the equation $E.A. = (E_{\frac{1}{2}} + 1.41)eV$, where $E_{\frac{1}{2}}$ is measured relative to the saturated calomel electrode.¹³⁹ This method can only give an estimate, as polarographic $E_{\frac{1}{2}}$ values are dependent on the nature of the supporting electrolyte used in the experiment, e.g. when 3,6-di-^tbutylbenzo-1,2-quinone was reduced in the presence of lithium chloride (0.1M) in dimethylformamide, the first one-electron $E_{\frac{1}{2}}$ value occurred at -0.15 v. relative to S.C.E. Use of tetraethylammonium perchlorate in place of lithium chloride altered the value to -0.50 v.¹⁴⁰ For benzo-1,2-quinone in acetonitrile, the first one-electron potential occurs at -0.31 v., corresponding to an approximate electron affinity of 1.1 eV (25.4 kcal mol⁻¹).

Unfortunately the data available limits the application of the energy cycle method to the system quinone plus iodide in acetonitrile.

$$\begin{aligned} \Delta G_{\text{solv}}^{\circ} (Q^-) - \Delta G_{\text{solv}}^{\circ} (Q) &= -3.6 \text{ eV} = -83 \text{ kcal mol}^{-1} \\ -E.A. \text{ of } Q &= -1.1 \text{ eV} = \underline{-25.4 \text{ kcal mol}^{-1}} \\ \text{Total} &= \underline{\underline{-108.4 \text{ kcal mol}^{-1}}} \end{aligned}$$

$$\begin{aligned} \Delta G_{\text{solv}}^{\circ} \text{ of } I\cdot \text{ (assumed}^*) &= 0.0 \text{ kcal mol}^{-1} \\ \Delta G_{\text{solv}}^{\circ} (I^{-}) &= 56.4 \text{ kcal mol}^{-1} \\ \text{I.P. of } I^{-} &= 74.5 \text{ kcal mol}^{-1} \\ \text{Total} &= \underline{\underline{130.9}} \text{ kcal mol}^{-1} \end{aligned}$$

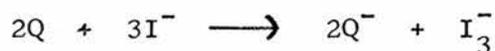
Free energy of combination of two iodine atoms to form one I_2 molecule (all species in the gas phase at 298K) = $\Delta G_f^{\circ}(I_2) - 2\Delta G_f^{\circ}(I\cdot) = 4.63 - 2(16.77)^{141} = \underline{-28.91} \text{ kcal mol}^{-1}$. The solvation energy of the iodine molecule is assumed to be small.*

Free energy of formation of tri-iodide ion = $-RT \ln K$, where

$$K = \frac{[I_3^{-}]}{[I_2][I^{-}]} = 725^{142}$$

$$\Delta G^{\circ} = -2.303RT \log 725 = \underline{-3.90} \text{ kcal mol}^{-1}$$

The overall free energy change for the reaction



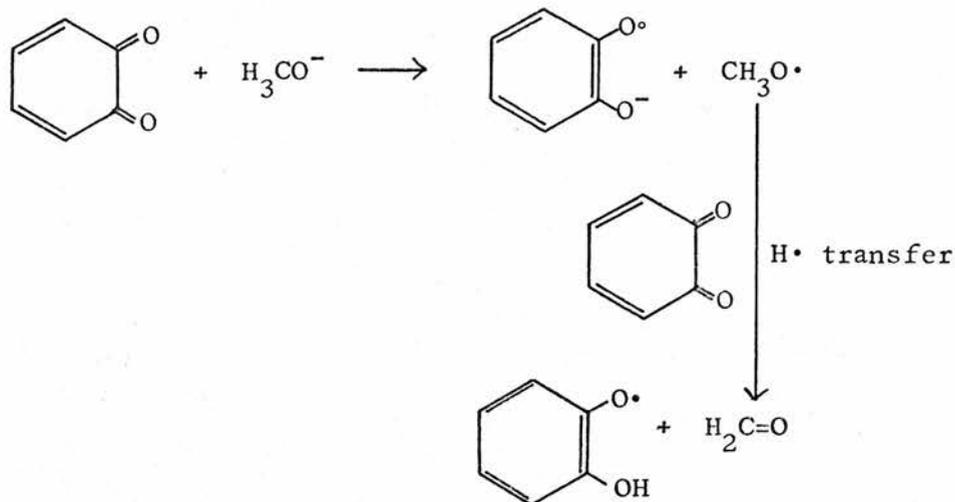
$$\text{is } 2(-108.4) - 28.91 - 3.90 + 2(130.9) = \underline{+12.2} \text{ kcal mol}^{-1}$$

The calculation agrees with the result from the polarographic data in indicating that benzo-1,2-quinone cannot oxidize iodide ion. This is in contrast to the observation that reaction between these species seemed to be rapid.

Electron transfer from t-butylamine to the quinone would generate two ions, and therefore two solvation energy terms would be needed to calculate the thermodynamic characteristics of such a reaction. The cation solvation energy would help to overcome the high ionization potential of the amine. (This assumes that the electron affinity of the t-butylamino radical does not differ greatly in numerical value from the ionization potential of the amine). However no radical cations derived from nitrogenous bases were detected during the e.s.r. work.

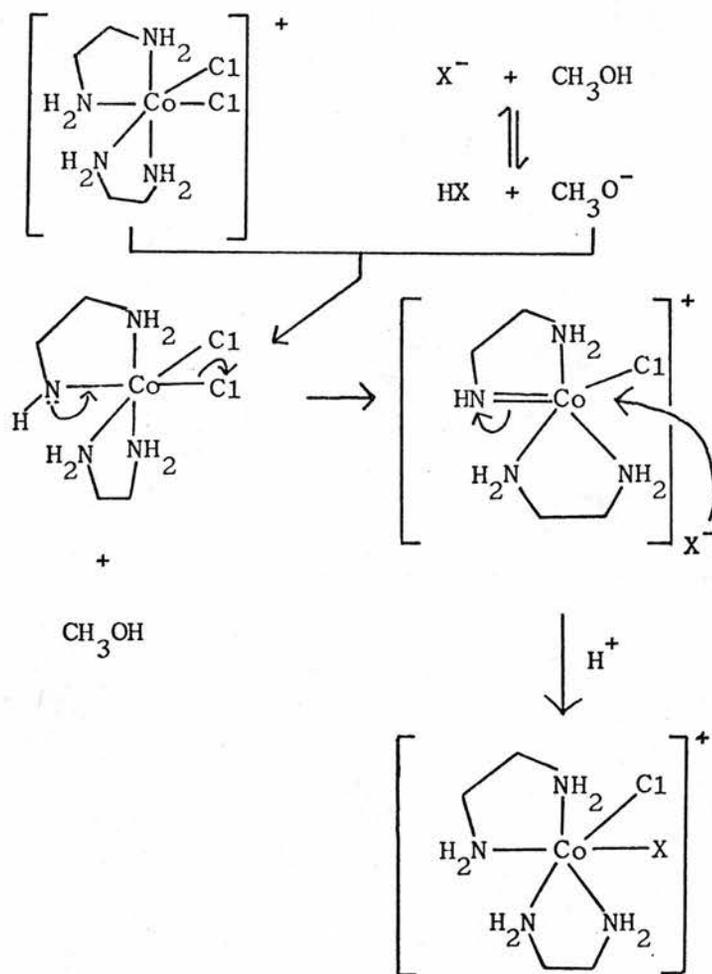
*The solvation energy of an uncharged species is likely to be much smaller than that of a charged one.

The low electron affinity values of the alkoxy radicals suggest that the corresponding anions might well be oxidized by the quinone through the electron transfer route. No methoxy radicals were detected, but this system was studied by the static method only.

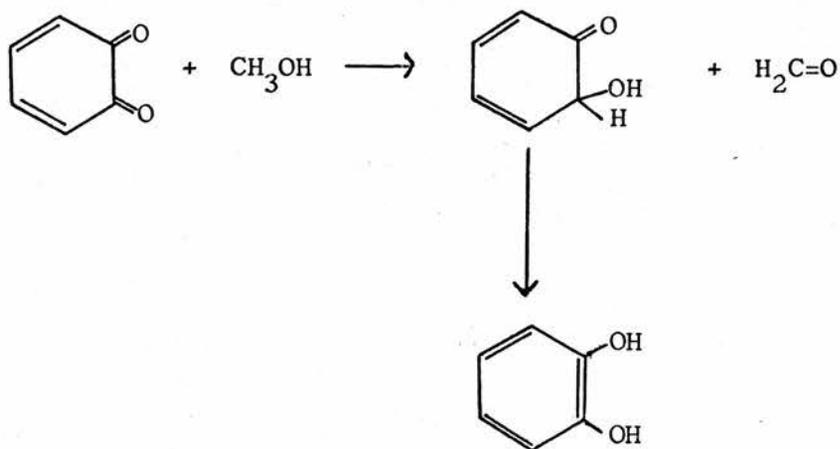


The methoxy radical could react further by transferring a hydrogen atom to a quinone molecule. An alternative mechanism for the reaction of basic species with benzo-1,2-quinone in methanol is discussed below.

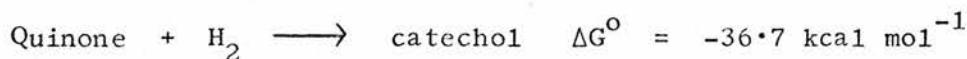
Studies¹⁴³ of substitutions on cobalt complexes in methanol solution showed that the mechanism depended on the ion effecting the substitution, and the following scheme was found to apply where the ion was azide, nitrite, or methoxide. The ion is depicted as X^- .



The possibility that methanol or methoxide ion is involved directly in semiquinone formation will now be considered.



This scheme depicts the interchange of a CHOH and a C=O group between benzo-1,2-quinone and methanol, forming formaldehyde and the keto tautomer of catechol. Enolization produces more resonance stabilization than is lost in the reaction, and, since on bond energy grounds ΔH ought to be approx. zero for formation of the keto tautomer, benzo-1,2-quinone can be reduced by methanol, in theory. The following calculation also demonstrates that the quinone/methanol reaction is thermodynamically possible.



$$\Delta G_f^\circ \text{ of methanol(gas)} = -38.69 \text{ kcal mol}^{-1} \quad 71$$

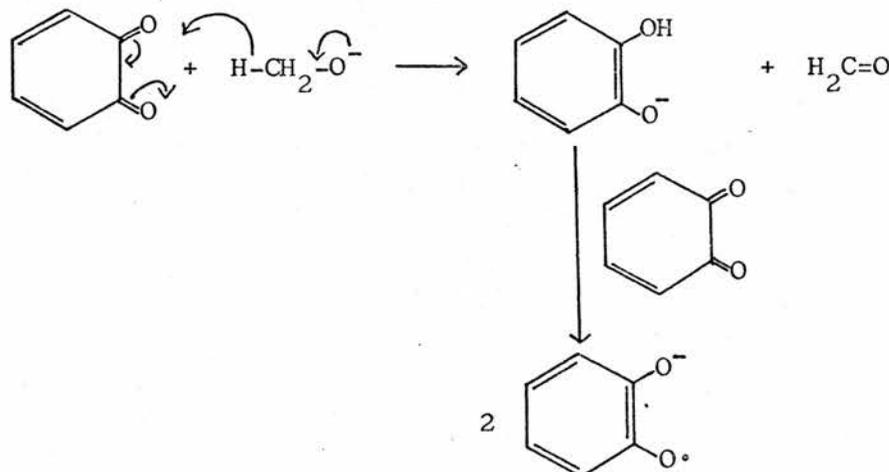
$$\Delta G_f^\circ \text{ of formaldehyde(gas)} = -26.2 \text{ kcal mol}^{-1} \quad 71$$

Therefore for quinone + methanol \longrightarrow formaldehyde + catechol,

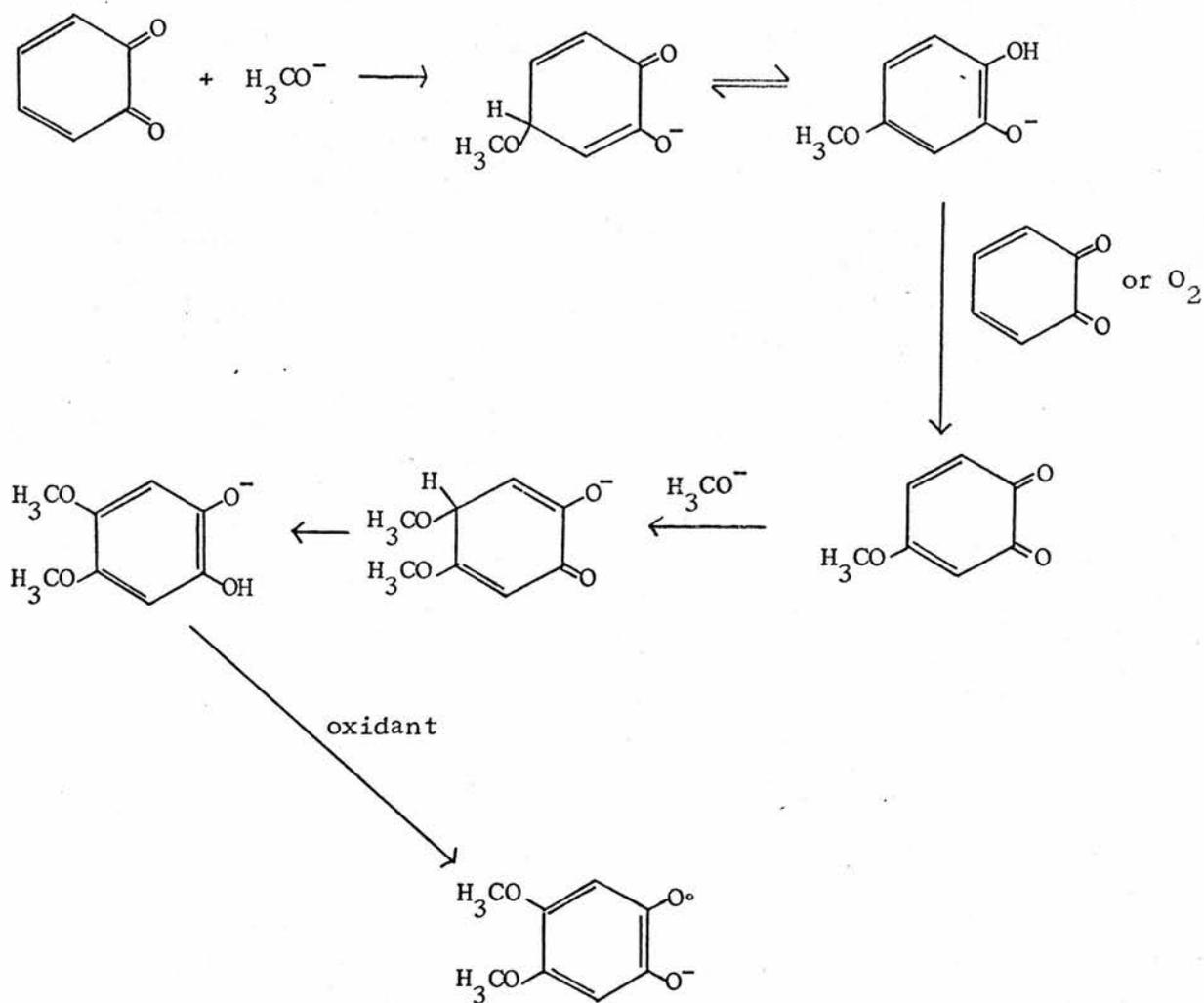
$$\Delta G^\circ = -24.2 \text{ kcal mol}^{-1}$$

In fact the u.v./visible spectrum of the quinone in methanol is not greatly different from that of it in benzene or chloroform,¹⁴⁴ indicating that this reaction is slow. The addition of a species such as azide or t-butylamine produces a green colour, and the u.v./visible spectrum is different from that of the original quinone.¹⁴⁴

In view of the results obtained in the cobalt substitution reactions, azide ion and nitrogenous bases might not react directly with benzo-1,2-quinone, but merely serve as proton abstractors, generating methoxide ion which goes on to react with the quinone, possibly by hydride transfer.



The disproportionation reaction was discussed earlier (page 102), but seems reasonable since Doskocil¹⁴⁵ found that the decomposition of benzo-1,2-quinone was catalysed by catechol. The detection of 4,5-dimethoxybenzo-1,2-semiquinone in the mixture resulting from the addition of solutions of azide or nitrogen bases to quinone solutions suggests that methoxide ion is present. A mechanism explaining the formation of this substituted semiquinone is shown below.

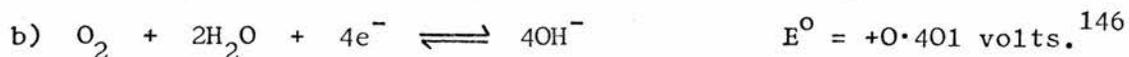


(A similar scheme using methanol itself can be drawn out - then the added nucleophile merely serves as a proton remover.)

Though nitrite ion is a stronger base than azide ion in water (see page 103 for dissociation constants of the acids), no dimethoxysemiquinone was detected in the solution containing the quinone/nitrite reaction. The static e.s.r. work on this system was performed using a water/methanol mixture, and so hydroxylated as well as methoxylated semiquinones could result. The asymmetric spectrum obtained may therefore have resulted from several different radicals being present. As hydrogen iodide is an exceedingly strong acid, one would not expect iodide ion to react with methanol to create a significant concentration of methoxide ion.

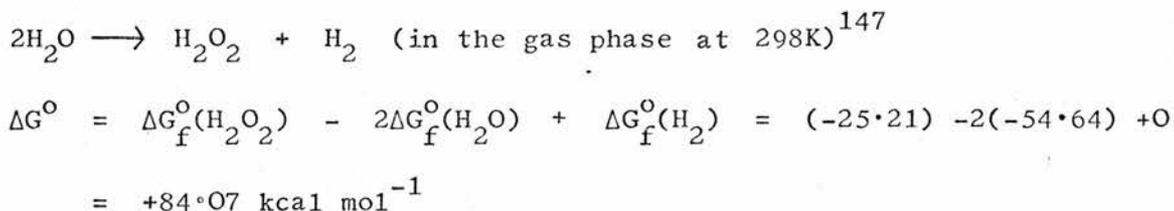
Oxygen was shown as a possible oxidant in the scheme depicting a mechanism for the formation of the dimethoxysemiquinone, as in all cases where this radical was detected the system had been exposed to the air. The preliminary experiments (page 69) had also suggested that oxygen could become involved in the quinone/methoxide reaction. For the flow system work, nitrogen was bubbled through the solutions before reaction commenced in order to remove oxygen. Even if some oxygen were present in the system, it would be necessary to generate from it a species capable of reducing the quinone, as it would seem unlikely that the other product e.g. iodine (as tri-iodide ion), or nitrogen dioxide, could reduce the quinone.

In aqueous solution oxygen can be reduced as follows:



If reaction a) occurred in aqueous or methanolic solution, by reaction of the oxygen with an added nucleophile, the water produced could not be reoxidised to oxygen, as the redox potential is much higher than that of the quinone

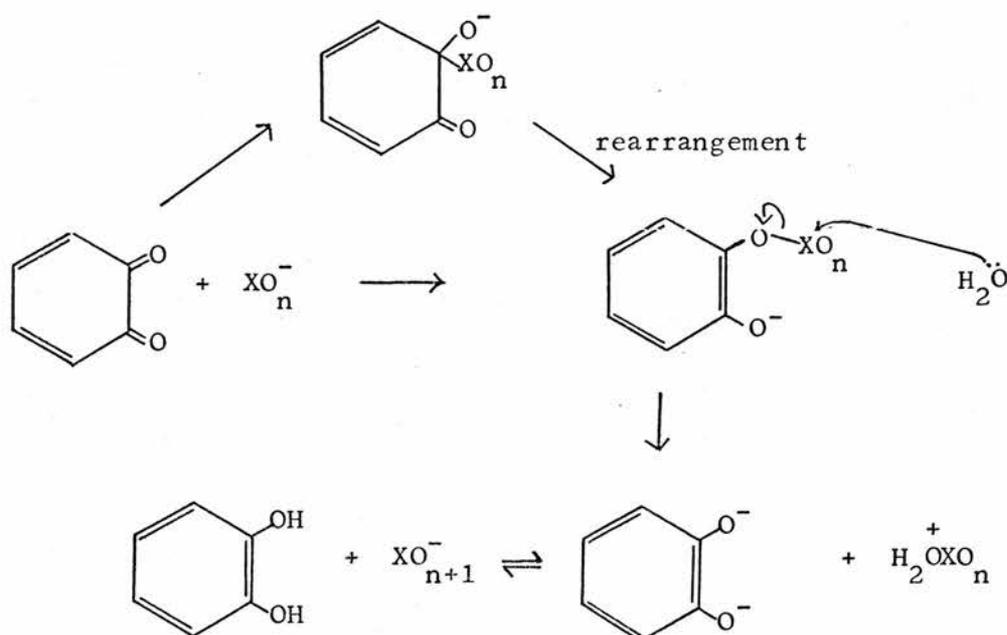
in neutral solution. The oxidation of water to hydrogen peroxide requires ca. 84 kcal mol⁻¹ (353 kJ mol⁻¹), as shown below.



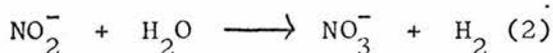
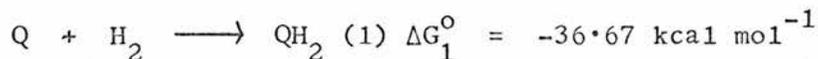
The free energy gained by reducing the quinone with the hydrogen would be 36.7 kcal mol⁻¹, and so benzo-1,2-quinone cannot oxidise water to hydrogen peroxide unless a subsequent reaction between the quinone and catechol liberates ca. 47 kcal mol⁻¹ of free energy. This figure is much larger than the calculated free energy of disproportionation in acetonitrile, and so makes the production of the peroxide seem very unlikely.

Reaction b) does produce hydroxide ions, which could react with methanol to yield methoxide ions, and radical formation could then occur as described above. However the initial reduction of oxygen occurs at a potential lower than that required to oxidise nitrite or iodide (0.763 v.¹⁴⁸ or 0.536 v.¹⁰⁷ respectively), and therefore the initial redox process needed to produce the hydroxide ions cannot occur.

A further redox reaction scheme can be envisaged as follows.



For the nitrite case, the thermodynamic characteristics can be calculated from:



$$\begin{aligned} \Delta G_2^{\circ} &= \Delta G_f^{\circ}(H_2) + \Delta G_f^{\circ}(NO_3^-) - \Delta G_f^{\circ}(NO_2^-) - \Delta G_f^{\circ}(H_2O) \\ &= 0 - 26.61^{149} + 8.9^{149} + 54.64^{147} \\ &= +36.93 \text{ kcal mol}^{-1} \end{aligned}$$

An alternative method of calculating the second free energy change using the redox potential for the system $NO_3^- + 3H^+ + 2e^- \rightleftharpoons H_2O + HNO_2$ ($E^{\circ} = 0.94 \text{ v.}^{150}$) and the dissociation constant of nitrous acid (6.0×10^{-6} ¹¹⁶) gives the value of $36.24 \text{ kcal mol}^{-1}$.¹⁵¹ In view of the small difference between the free energy gained by the reduction of the quinone and that needed to oxidise the nitrite to nitrate, it cannot be definitely stated that such a reaction can proceed in aqueous solution. In methanolic solution the possible products are methyl nitrate and the mono-anion of catechol. The latter might react with the quinone to give two semiquinone radicals. (The lack of thermodynamic data for methanolic solution prevents detailed consideration of this system).

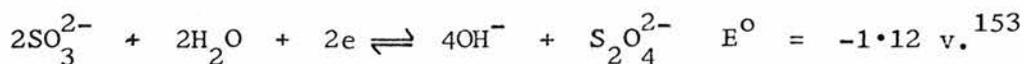
The reaction between aqueous sodium bisulphite and benzo-1,2-quinone was investigated using the flow e.s.r. technique alone. No radicals were detected. It is possible that rapid and complete reduction of the quinone to catechol occurs.



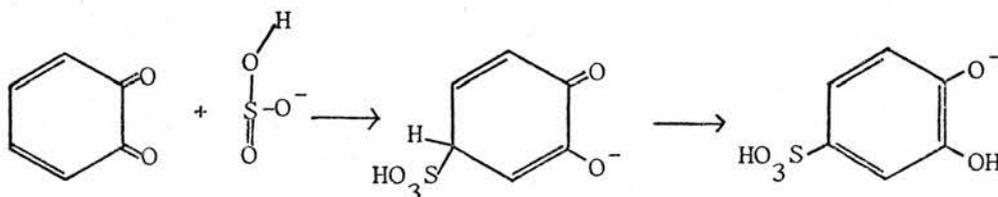
$$\begin{aligned} \Delta G^{\circ} &= \Delta G_f^{\circ}(H_2) + \Delta G_f^{\circ}(HSO_4^-) - \Delta G_f^{\circ}(H_2O) - \Delta G_f^{\circ}(HSO_3^-) \\ &= 0 - 179.94^{152} + 54.64 + 126.0^{152} \\ &= +0.7 \text{ kcal mol}^{-1} \end{aligned}$$

$$\begin{aligned}
 & \text{or } \Delta G_f^\circ(\text{H}_2) + \Delta G_f^\circ(\text{H}^+) + \Delta G_f^\circ(\text{SO}_4^{2-}) - \Delta G_f^\circ(\text{H}_2\text{O}) - \Delta G_f^\circ(\text{HSO}_3^-) \\
 & = 0 + 0 - 177.34^{152} + 54.64 + 126.0 \\
 & = +3.3 \text{ kcal mol}^{-1}
 \end{aligned}$$

The free energy needed to oxidise the bisulphite ion to bisulphate or sulphate is so much less than that gained by quinone reduction that it seems likely that the semiquinone could also be reduced by the bisulphite ion. However Blois detected the semiquinone in alkaline sodium dithionite solution, indicating that powerful reducing agents do not necessarily reduce the quinone completely to the dianion.



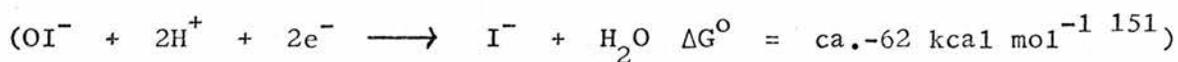
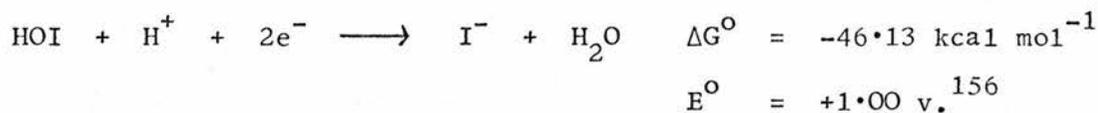
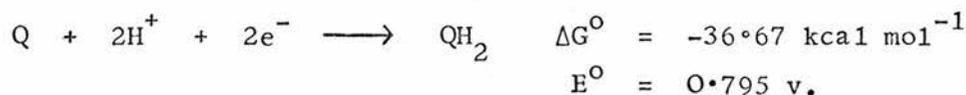
An alternative reaction is a nucleophilic addition of the bisulphite ion to the quinone, producing the sodium salt of 3,4-dihydroxybenzene-sulphonic acid.



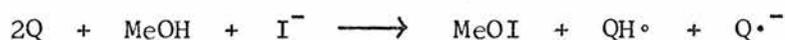
Provided this reaction is thermodynamically possible (which seems likely) and rapid, all the quinone could be removed from the system and the redox reaction necessary for radical formation would not be possible (in the absence of oxygen).

The scheme on page 113 can also be applied to the iodide/quinone reaction. In aqueous solution hypiodous acid is a weaker acid than catechol (K_a are ca. 10^{-12} at 25° ¹⁵⁴ and 1.41×10^{-10} ¹⁵⁵ at 20° respectively). Therefore the theoretical products would be catechol mono-anion and hypiodous acid. However, as can be observed by comparing the

redox potentials quoted below, the reaction will have a positive free energy and is not possible.

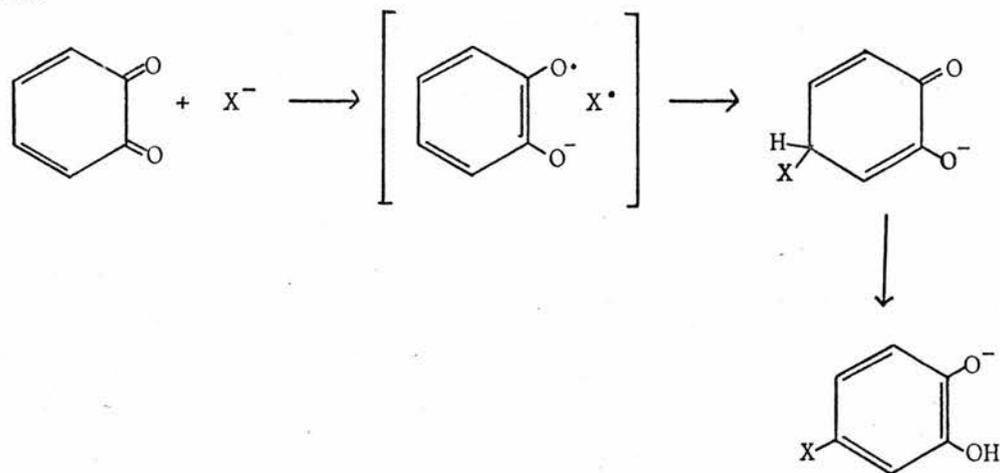


A possible reaction equation for a methanolic system is:



Methyl hypoiodite might react (like hypoiodous acid¹⁵⁷) as if it was I⁺ ion and methoxide ion. The former could react with iodide ion to produce iodine/tri-iodide ion, while the methoxide could deprotonate the uncharged semiquinone. This scheme is therefore another version of the charge transfer type reaction considered earlier, as the final products are the same.

Radicals are generated as transient intermediates in the system shown below.



The square brackets around the two radicals are meant to indicate that the radicals are trapped as a pair in the same cage of solvent molecules. In this case one would expect to obtain overlapping e.s.r. spectra of the semi-

quinone and of X^\bullet . Though some spectra contained extra lines, these did not fit a pattern and were usually of low intensity. If methoxide ion is converted to the methoxy radical (see page 108), flow e.s.r. studies of this system might show the presence of this radical.

Conclusions.

It is thermodynamically possible for benzo-1,2-quinone to oxidise azide ion to nitrogen, methanol to formaldehyde, and bisulphite ion to (bi)sulphate. The formation of dimethoxysemiquinone suggests that nitrogenous bases and azide ion generate methoxide ion in methanol, and that the latter ion reacts with the quinone. It seems possible that nitrite ion also reacts via this mechanism, since nitrite ion is more basic than azide ion. No mechanism for the oxidation of iodide ion by the quinone has been found.

If the presence of $\text{N}^+=\text{O}-\text{O}^-$ ion in sodium nitrite is conclusively proved, evidence may become available with regard to the redox properties of this ion, but until then its participation or non-participation in the quinone/nitrite reaction cannot be considered in detail.

As both nitrite ion and t-butylamine in dimethylformamide reacted with benzo-1,2-quinone to give radicals, some reaction path other than that involving methoxide ion must occur. Flow system e.s.r. studies of quinone/nucleophile reactions in aprotic solvents such as N,N-dimethylformamide or acetonitrile, combined with observations of the effects of adding oxygen or water to the system, would be useful in solving the problem of semiquinone formation.

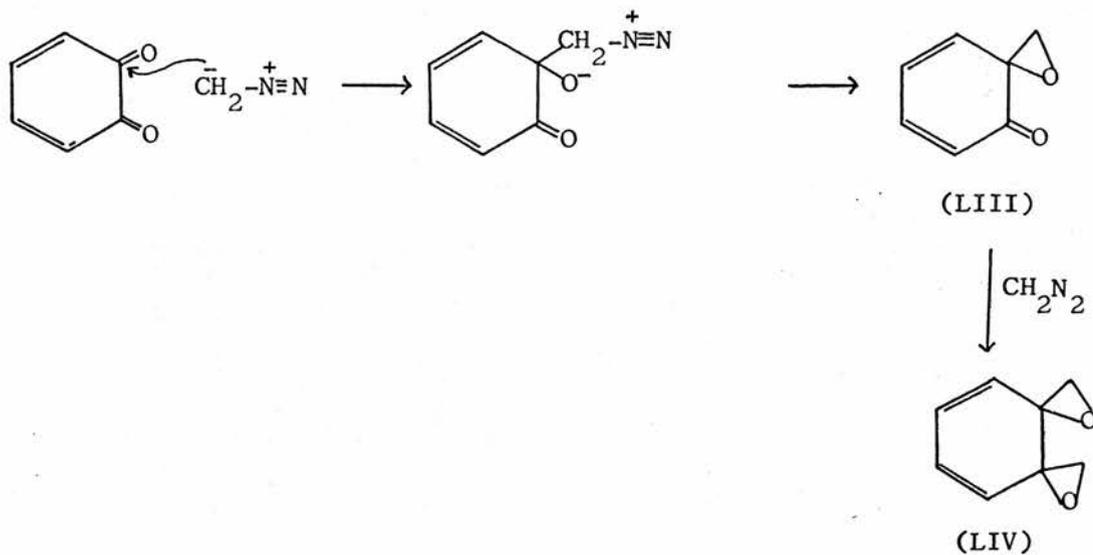
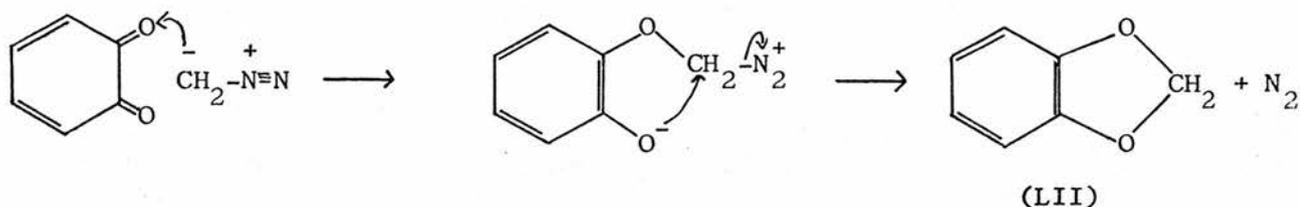
In addition product studies and further e.s.r. work on the bisulphite/quinone reaction would be of interest in explaining the absence of radicals noted during the present work.

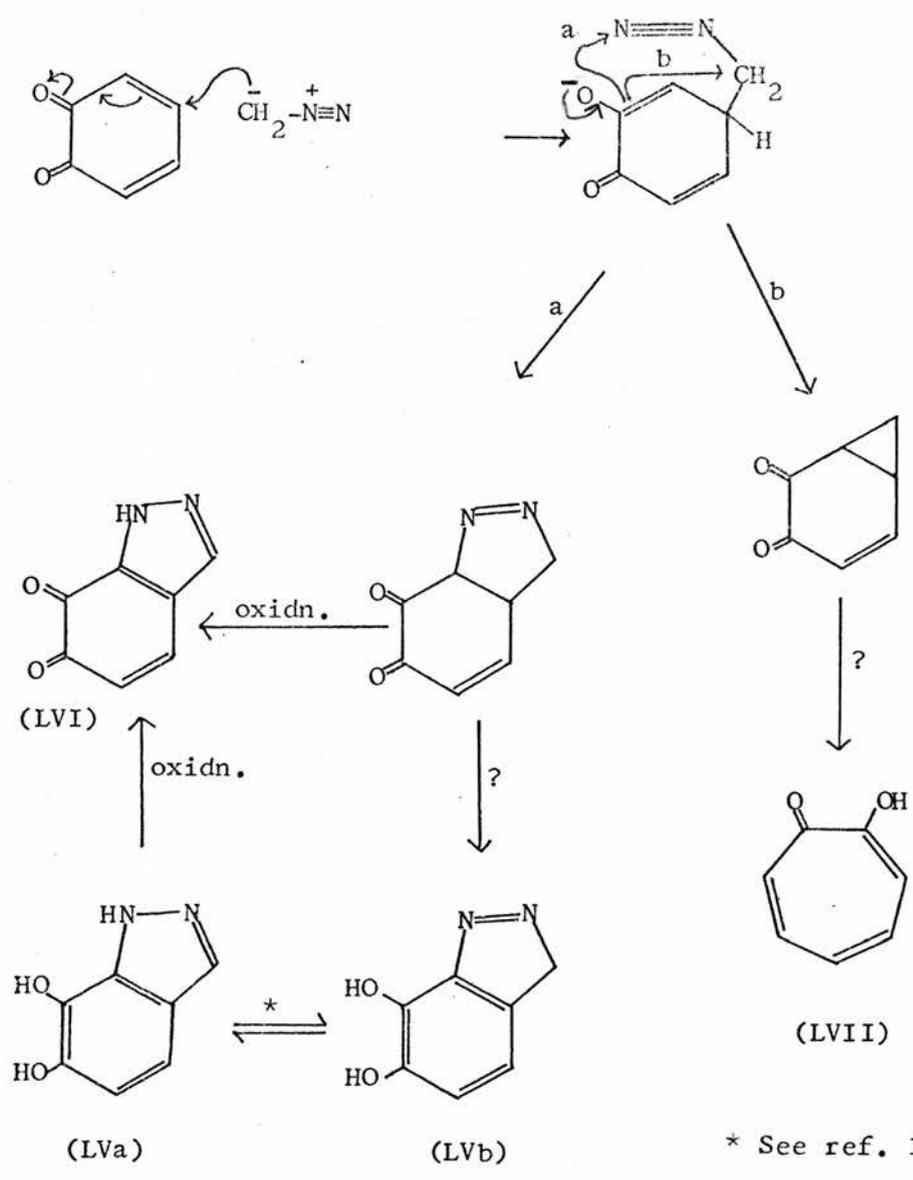
REACTIONS OF 1,2-QUINONES WITH DIAZO COMPOUNDS^{158,159}

The Reaction of Benzo-1,2-quinone with Diazomethane.

Although the reactions of diazomethane with various o-quinones have been investigated,¹⁵⁸ the product of the reaction between diazomethane and the unsubstituted quinone is not known.

Possible reaction schemes are illustrated below.





Compounds such as (LVa), (LVb) and (LVI) would probably be vulnerable to aerial oxidation - they resemble 5,6-dihydroxy indole, which can be oxidized by the air to form the natural dye melanin.¹⁶¹ If (LVII), tropolone, resulted, a relatively simple synthesis of tropolone might have been produced.

Excess diazomethane might react with the hydroxyl groups in (LVa), (LVb) and (LVII) to produce the methyl ethers of those compounds.¹⁶²

The Experiments themselves.

Ethereal diazomethane was distilled into a solution of benzo-1,2-quinone in chloroform, which was cooled in a cardice/acetone bath. A fluffy precipitate of pale colour (it appeared yellow) formed in the yellow solution which resulted. (Initial solution red). Some of the solid was filtered off and washed with petrol. On drying the precipitate became brownish-white in colour. The filtrate was cooled in cardice/acetone and more material precipitated. On filtration this gave a yellow powder which rapidly turned brown as the solvent evaporated from the filter. The remaining reaction mixture was irradiated with u.v. light (an attempt to effect the elimination of nitrogen from (LVa)-type products), the remaining precipitate was filtered, and the three solid samples dried. All three samples had similar mass spectra - the intense peaks suggested that the compounds were a mixture of catechol and its mono-methyl ether, though the first and third samples did have tiny peaks at 136 (the mol. wt. of (LIV)). The infra-red spectra (very crude - the author's technique being in its infancy) showed a strong absorption in the region $1650 - 1700 \text{ cm.}^{-1}$, which is inconsistent with the materials being a mixture of catechol and guaiacol only.

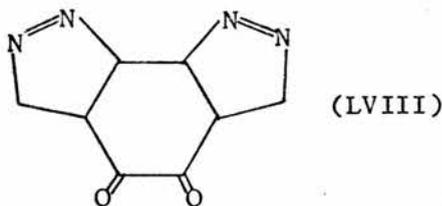
The experiment was repeated and acetic anhydride added to the reaction mixture. The low boiling solvents were evaporated under reduced pressure, pyridine and more acetic anhydride added, and the mixture left overnight. Ice and hydrochloric acid were added, and the mixture extracted with chloroform, which was further washed with hydrochloric acid. After drying, the chloroform solution was concentrated under reduced pressure - a dirty yellow-brown solid was obtained whose mass spectrum resembled that of pyridine/a pyridinium compound. The experiment was discarded.

Ethereal diazomethane was added to a solution of benzo-1,2-quinone in acetic anhydride. After standing overnight N/20 caustic soda solution was added. The mixture was extracted with ether. After evaporation of the latter no residue remained. The experiment was discarded.

A solution of benzoquinone in chloroform was added dropwise to a solution of diazomethane in ether. (Mole ratio 6 CH_2N_2 to 1 $\text{C}_6\text{H}_4\text{O}_2$). A precipitate formed in a yellow solution. Overnight the solid darkened slightly. Filtration produced a brown syrup, which became yellow on drying. The material darkened on heating, but did not melt below 300°C . Thin layer chromatography suggested the presence of two components. A silica column was made up and chloroform eluted a yellow solution, as did methanol - on concentration the latter gave a brown solid. T.L.C. indicated that neither the chloroform eluate nor the methanolic one contained only one component. Some of the chloroform solution was chromatographed further using a column of deactivated alumina. Comparison by T.L.C. of the eluates from the first and second columns showed that some change had occurred in the system during the column chromatography, and that the second column had not produced a single component. Nevertheless the I.R. and mass spectra of the yellow oil obtained by evaporation of the chloroform (2nd column) eluate were recorded. The mass spectrum had large peaks at 124 and 109, with a metastable peak at about 95.7 (95.8 is the required metastable for $124 \rightarrow 109$). This again suggests the presence of guaiacol, while a small peak at 138 suggests that veratrole (the dimethyl ether of catechol) is present. (There is a peak at 149, but this often appeared in spectra of that period and 149 is the m/e ratio of the most numerous fragment ion of dioctyl phthalate, used in vacuum pump oils, and therefore, in mass

spectrometers¹⁶³). The oil was distilled using a cold finger apparatus heated by an oil bath. Several drops of liquid were collected at 0.5 mm. pressure and with the bath at 200°C. The i.r. spectrum of the liquid³⁸ showed a broad absorption in the region 3200 - 3700 cm.⁻¹, with a small peak at 3400 cm.⁻¹, strong absorptions at 2940, 2920, and 2860 cm.⁻¹, ascribable to aliphatic C-H stretching, and a strong carbonyl absorption at 1715 cm.⁻¹. The peaks at 1370 and 1450 cm.⁻¹ (C-H bending) together with the peaks near 2900 cm.⁻¹ remind one of the spectrum of the hydrocarbon 'Nujol', and together with the carbonyl peak suggest that a saturated aliphatic ketone is present. A very weak absorption at 3050 cm.⁻¹ suggests that some aromatic C-H bonds are present, and a peak of medium intensity at 740 cm.⁻¹ is consistent with the material containing a 1,2-disubstituted aromatic.

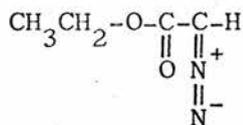
It is not possible to define the origin of the saturated ketone absorptions, though a compound such as (LVIII) might give rise to them.



Solvent contamination is another possibility. It is interesting to note the high boiling point of the liquid under reduced pressure - one would expect low-boiling ketones, such as acetone or diethyl ketone, to be sucked into the trap under such conditions. Guaiacol boils at 205°C and veratrole at 207°C at atmospheric pressure,¹⁶⁴ so one would expect a bath temperature of 150°C would suffice to distil them at 0.5 mm. pressure. If the material is a contaminant and also an aliphatic ketone, it must have large alkyl groups in order to have such a high boiling point.

Reaction of Benzo-1,2-quinone with Ethyl Diazoacetate.

Despite the difficulties (or because of them) encountered in the benzoquinone/diazomethane reaction, it was decided to try to react the quinone with ethyl diazoacetate (LIX), also called diazoacetic ester.



(LIX)

Ethyl diazoacetate was added to a solution of benzo-1,2-quinone in acetic anhydride. A yellow crystalline product formed in the flask. After filtration and drying the solid was identified by melting point and mixed melting point as the dimer of benzo-1,2-quinone.

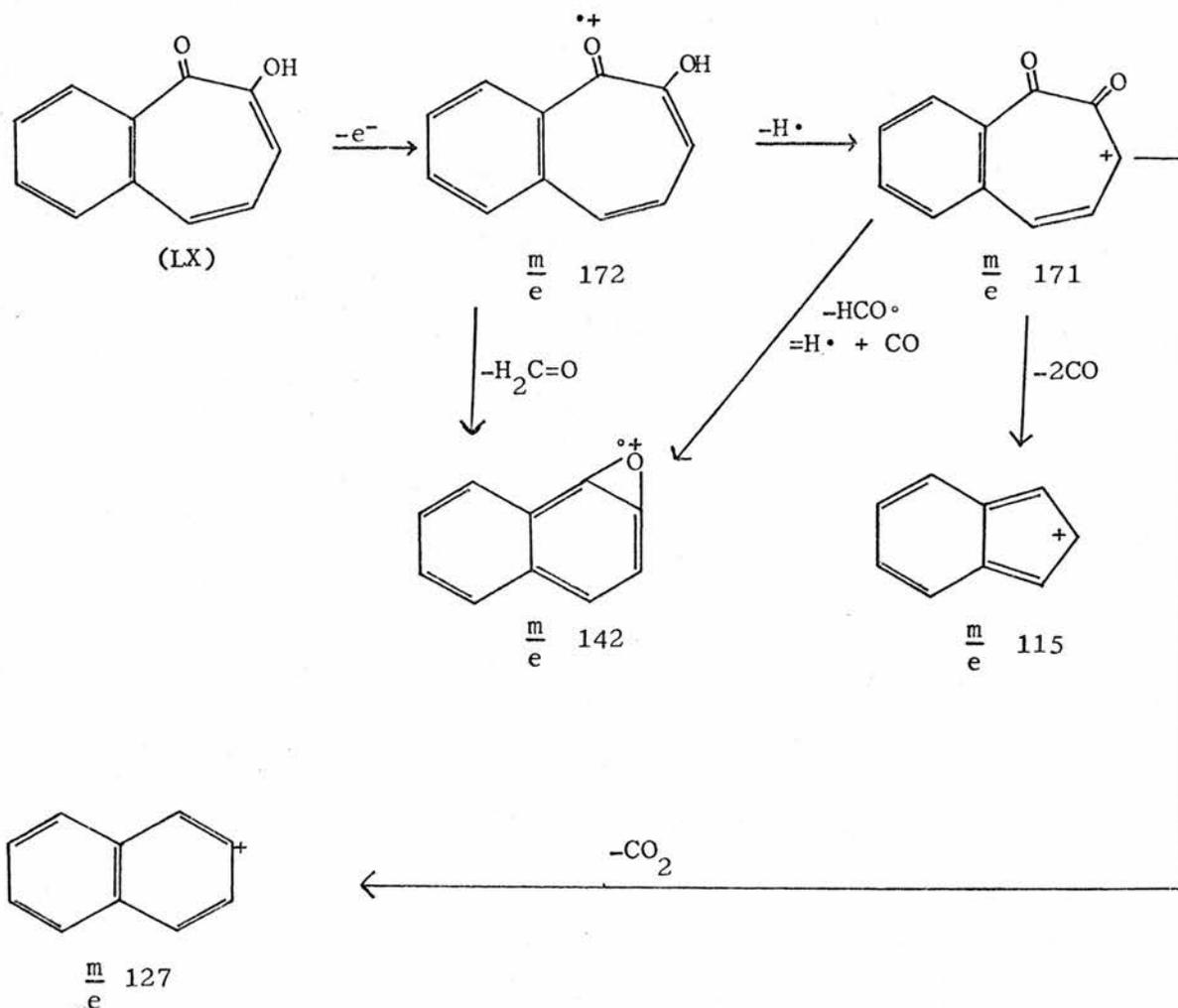
Two solutions of benzo-1,2-quinone in methanol were made up; to one was added diazoacetic ester. After 1½ hrs. thin layer chromatographic examinations of the two solutions and one of the ester indicated that no reaction had occurred. The reduced reactivity of the ester as compared with diazomethane is demonstrated, but the second experiment might have proved more fruitful if it had been left for a longer time.

Similar experiments were carried out using naphtho-1,2-quinone with both diazo-methane and ethyl diazoacetate.

Reaction of Naphtho-1,2-quinone with Diazomethane.

A solution in benzene of naphthoquinone was added dropwise to an ethereal solution of diazomethane, resulting in the formation of a clear orange solution. After standing overnight the solvent was removed under reduced pressure and the red oil obtained thereby was investigated by T.L.C. and infra-red spectroscopy. The former showed that three(+)

components were present, while the latter showed peaks characteristic of the O-H group (damp?) (broad, 3100-3700 cm^{-1}), aromatic C-H (3 peaks, 3000-3100 cm^{-1}), aliphatic C-H (3000-2800 cm^{-1}) and conjugated/quinonoid carbonyl (1680 cm^{-1}).³⁸ Column chromatography using chloroform as the eluent failed to effect separation of the components - this was shown by T.L.C. of the eluate. Treatment of the oil with hot acetone/ether resulted in the production of a brown solid on cooling; the infra-red spectrum of this solid showed a quinonoid carbonyl (1680 cm^{-1}) and a multiplet peak in the range 720-780 cm^{-1} , which may be assigned to aromatic C-H bending. Otherwise the spectrum was not very informative. The same applied to the mass spectrum, which was again dominated by the peak at 149. A peak at 172 might be due to (LX), which can also be used to explain peaks at 171, 142, 127 and 115, but not the large peak at 85, nor the carbonyl group absorption in the infra-red spectrum, as this would be expected to occur at ca. 1630 cm^{-1} .¹⁶⁵



Naphtho-1,2-quinone with Diazoacetic Ester in Methanol.

A mixture of the quinone with methanol was treated with the ester and was warmed on a water bath (max. temp. 65°C). A black solution formed. Overnight this was kept in the refrigerator. The work-up procedure 'branched' so often that the author considers the simplest description is provided by the flow chart on page 127.

Mass spectra were obtained of (LXI), (LXII) and (LXIII). That of (LXI) was worthless - it resembled what one would expect for the mass spectrum of polymerized hydrogen. That of (LXII) suggested a molecular weight of 298 or 297, and peaks occurred at 269, 241, 240, 190, 174, 173, 160, 159, 158, 149, 146. In the lower region a strange pattern emerged.

(135)	(137)				
(121)	123	125			
	109	111			
	95	97			
	81	83	85		
		69	71		
		55	57		
		41	43		

Bracketed peaks are relatively small.

This resembles the break-up of a methylenic chain - which seems unlikely for a product from the reaction under consideration. 'Background' is a probable explanation. A metastable peak at 243.6 indicated that the ion, m/e 297, gives the ion m/e 269. 298 is equal to the mol. wt. of a species formed from one quinone and two ester molecules after the loss of two molecules of carbon dioxide.

The mass spectrum of (LXIII) showed peaks at 191, 188, 170, 163, 158, 149, 102 and the pattern:

95	97	99		
81	83	85		
	69	71	73	
	55	57		
	41	43		

In the higher mass range 149 and 102 were far larger than the other peaks. Therefore no insight into the nature of either of (LXIII's) components was gained.

The infra-red spectra suggested that (LXIV) and (LXV) were the same substance; and the spectrum of (LXII) bore a resemblance to that of naphtho-quinone, notably around 1600 cm.^{-1} , though there were differences. The spectra of (LXVI), (LXVII) and (LXVIII) were not very informative.

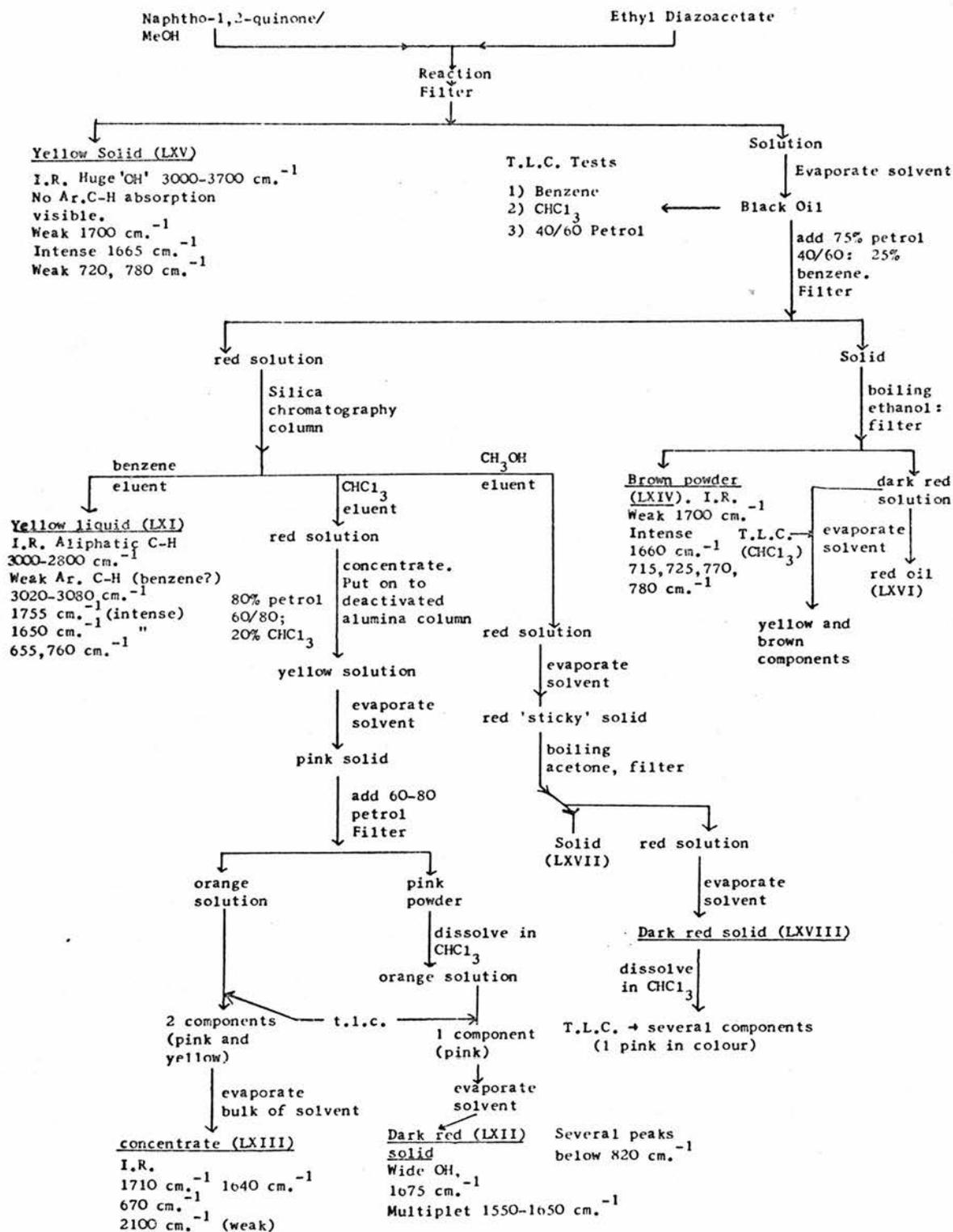
Naphtho-1,2-quinone and Ethyl Diazoacetate, in Chloroform.

Diazoacetic ester was added to a mixture of naphthoquinone and chloroform. The mixture was stirred overnight. Approximately one fifth of the volume of solution was then taken, concentrated under reduced pressure, and chromatographed on an alumina column. Changes in the eluate were monitored by periodically recording its u.v./visible spectrum.

The initial eluent was chloroform, and this produced a red solution, and three differing yellow solutions. The first and third yellow solutions were identified by I.R. spectroscopy as ethyl diazoacetate and contaminated naphtho-1,2-quinone respectively, while the intermediate yellow solution seemed to be a mixture of both starting materials. Insufficient red material was obtained to permit the production of a useful i.r. spectrum.

Further elution with methanol gave a dirty brown solid following solvent evaporation; the I.R. spectrum had a strong absorption in the $1620\text{-}1650\text{ cm.}^{-1}$ region, while the u.v. spectrum showed peaks at 250 nm., 275 nm.(i), 335 nm, and 400 nm. (i = inflexion), with intensity ratios 9:4:1:1. This suggests that the material was a naphthoquinone — see pages 24 - 28.

A silica column was made up, a quarter of the remaining solution (= 1/5 of the original volume) was concentrated and then chromatographed using chloroform. A red solution came off the column first. The I.R.



spectrum thereof showed an intense absorption at 1745 cm.^{-1} , and a slightly less intense band at 1650 cm.^{-1} . Further elution produced a yellow liquid, shown to be diazoacetic ester by I.R. spectroscopy, and a red-yellow solution, whose spectrum suggested that it was diazo-acetic ester with probably some naphthoquinone. The use of methanol gave a pinkish brown solid following evaporation of the solvent, but a useful I.R. spectrum of this material proved unobtainable.

From each column 0.7 g. of ethyl diazoacetate was recovered. This was from 2/5 of the solution, and represents 75% recovery.

Comments.

The above suggests that the diazo-compound reacted with the quinone in each system, with the possible exception of benzo-1,2-quinone and ethyl diazoacetate. Problems arose in the attempts to separate the reaction mixture into its components, and in the identification of the materials which were isolated. The mass spectra often suggested methylated catechols while infra-red techniques indicated that other substances were present.

EXPERIMENTAL

General Techniques.

Melting points were determined using a Gallenkamp Melting Point Apparatus, and are not corrected.

An A.E.I. MS9 mass spectrometer was used to obtain mass spectra and for the determination of accurate mass:charge ratios of ions.

The following instruments were used in the recording of p.m.r. spectra:

60 MHz Perkin-Elmer R10
90 MHz Bruker HX90 E
100 MHz Varian HA100

Ultra-violet/visible and infra-red spectra were recorded using a Unicam SP800 and Perkin-Elmer 257 spectrophotometers respectively.

Reactions of Naphtho-1,2-quinone with Primary Arylamines in Methanol.

In each case the quinone solution used contained 1 g. (0.63×10^{-2} moles) of quinone in 200-250 ml. of methanol. The amine was added neat or in methanol solution, and the methanolic washings of the amine container were added to the reaction mixture. After standing a precipitate formed. Unless otherwise stated, this was recrystallized from methanol.

Further details are given below for each amine (separately). Details of the ultra-violet/visible, infra-red and proton magnetic resonance spectra of the 4-arylamino-naphtho-1,2-quinones are given on pages 24, 20, and 48 respectively.

Aniline (1.22 g., 1.31×10^{-2} moles).

Within $1\frac{1}{2}$ hrs. of mixing a pale reddish-brown precipitate had formed. This was filtered off, and the filtrate left to stand overnight. Further solid precipitated, and was isolated by the same method. The combined solids, after drying over phosphorus pentoxide, had a mass of 1.08 g. (Yield, assuming 1 quinone molecule gives 1 arylaminoquinone, 69%). The solid was identified

as N-phenyl-4-aminonaphtho-1,2-quinone, M.P. decomp. 246-50^o, melt 254-56^oC,
lit. 258-61^oC.²⁷

Found: m/e 249.078727; C, 77.09%; H, 4.57%; N, 5.53%.

Calc. for C₁₆H₁₁NO₂: m/e 249.078973; C, 77.11%; H, 4.42%; N, 5.67%.

p-Toluidine (1.38 g. in 10 ml. methanol).

Mixing the components resulted in the development of a deep red colour. After standing overnight the mixture was filtered, yielding dull orange needles, which were washed with petrol and sucked dry (mass 0.40 g.). A further 0.1 g. of the solid was isolated from the filtrate later. (Total yield 31%). The material was concluded to be N-(4'-methylphenyl)-4-aminonaphtho-1,2-quinone on the basis of the spectral evidence, but an analytically pure sample could not be obtained, despite several recrystallizations.

C₁₇H₁₃NO₂ requires m/e 263.094623; Found: m/e 263.095255; M.P. 259^oC

Analysis	%C	%H	%N
C ₁₇ H ₁₃ NO ₂ requires:	77.57	4.94	5.32
Found:			
Recryst. from MeOH	78.42	5.15	5.15
" " "	76.65	4.87	5.01
" " MeOCH ₂ CH ₂ OH	76.75	5.00	5.12

2,4-Dimethylaniline (re-distilled, b.p. 100^oC at 13 mm. Hg; 1.57 g. in 5.5 ml. methanol).

An orange precipitate was observable within thirty minutes of mixing. Filtration on the following morning allowed a reddish-gold solid to be isolated. The mother liquor was evaporated to dryness under reduced pressure, treated with a little boiling methanol, and was filtered. This yielded more of the red solid, which was identified as N-(2',4'-dimethylphenyl)-4-aminonaphtho-1,2-quinone.

Mass: 1.33 g. (Yield 76%). M.P. decomp. 254°C, residue melts 264°C

Found: m/e 277.110367; C, 77.34%; H, 5.39%; N, 4.82%

$C_{18}H_{14}NO_2$ requires: m/e 277.110272; C, 77.98%; H, 5.42%; N, 5.05%

2,6-Dimethylaniline.

After standing for 18 hrs. the mixture was reddish brown. No visible change was observed during the following 3 days. Thin layer chromatography showed that some reaction had occurred, but column chromatography gave an unsatisfactory separation of the components of the reaction mixture and no product could be identified.

p-Anisidine (1.67 g. in 10 ml. MeOH).

The mixture rapidly became dark red, and the formation of a precipitate was observed. This was separated by filtration on the following day. The filtrate was concentrated under reduced pressure to a small volume. Sufficient hot methanol was added to dissolve the solid material in the residue (but not an excess, of MeOH). On cooling a precipitate formed. Infra-red spectroscopy showed that both solids were samples of the same material, of which more was obtained by repetition of the above process. Mass: 0.99 g.; Yield: 56%. The solid was identified as N-(4'-methoxyphenyl)-4-aminonaphtho-1,2-quinone. M.P. 238-40°C. (Lit. value 232°C).²⁷

Found: m/e 279.089747; C, 73.20%; H, 4.93%; N, 5.08%.

Calc. for $C_{17}H_{13}NO_3$: m/e 279.089537; C, 73.12%; H, 4.66%; N, 5.02%.

2,4-Dichloroaniline (1.03 g. in 30 ml. MeOH).

After the reaction mixture had stood for 2 days it was observed that a small amount of precipitate had formed. The stopper was removed from the reaction flask in order to allow aerial oxygen to participate in any oxidation reactions necessary for product formation. One day later the precipitate was

filtered off and dried (mass 0.41 g.). The solid was of a variegated orange-brown colour. A further 0.07 g. of this material was isolated on the following day, and after a further 6 days a yellow-brown solid (mass 0.1 g.) was isolated by filtration. The infra-red spectra of these three samples showed that all were samples of the same substance. (Yield 29%).

Recrystallization from 2-methoxyethanol gave a pale red solid, identified as N-(2',4'-dichlorophenyl)-4-aminonaphtho-1,2-quinone, M.P. (decomp.) 245-50°C.

Found: C, 60.22%; H, 2.97%; N, 4.43%.

$C_{16}H_9NO_2Cl_2$ requires: C, 60.38%; H, 2.83%; N, 4.40%.

p-Phenylene-diamine (4-aminoaniline) (1.40 g. in 25 ml. MeOH).

The mixture was shaken and became dark red in colour. Overnight shiny, black needles crystallized out of the reaction mixture. These were filtered off, dried and identified as N-(4'-aminophenyl)-4-aminonaphtho-1,2-quinone (mass 1.13 g.; yield 68%), m.p. > 360°C.

Found: m/e 264.090055; C, 72.09%; H, 4.67%; N, 10.88%.

$C_{16}H_{12}N_2O_2$ requires: m/e 264.089872; C, 72.73%; H, 4.55%; N, 10.61%

N,N-dimethyl-p-phenylene-diamine (1.82 g. in 20 ml. MeOH).

A dark red colour developed on adding the amine to the quinone. After 23 hrs. the deep purple solution was filtered and a black powder isolated. The filtrate was concentrated under reduced pressure, and the resulting black oil was treated with a small amount of boiling methanol. Filtration of the mixture obtained thereby yielded a black solid, whose infra-red spectrum was the same as that of the precipitate from the reaction mixture. (Total mass: 1.17 g.; yield: 64%). The solid was recrystallized and identified as N-(N',N'-dimethyl-4'-aminophenyl)-4-aminonaphtho-1,2-quinone, M.P. 239-241°C.

Found: m/e 292.121155

$C_{18}H_{16}N_2O_2$ requires: m/e 292.121170

p-Aminoacetanilide (1.90 g. in 30 ml. MeOH).

When the reaction components were mixed a red colour developed. After standing overnight the mixture was filtered and an orange-brown solid obtained. (Mass 0.87 g.; yield 45%). Recrystallization (various solvents tried - see below) gave a red solid, identified as N-(N'-acetyl-4'-amino-phenyl)-4-aminonaphtho-1,2-quinone; m.p. 311-313°C. (The sample recryst. from D.M.F. (N,N-Dimethylformamide)).

Found: m/e 306.100849

$C_{18}H_{14}N_2O_3$ requires: m/e 306.100435

Analysis results:

	%C	%H	%N	M.P.	Recryst. solvent
$C_{18}H_{14}N_2O_3$ requires:	70.59	4.58	9.15	-	-
Found: (i):	69.58	4.82	8.68	309-10°	MeOH
(ii):	67.26	4.81	8.44	319-20°	MeOH
(iii):	69.49	4.82	8.58	311-313°	D.M.F.
(iv):	69.58	4.78	8.78	312-313°	2-methoxyethanol

p-Aminoazobenzene (2.5 g. in 100 ml. MeOH, solution decanted off to separate small amount of insoluble material).

A reddish colour developed soon after mixing. After 1½ hrs. a precipitate was visible and the solution was a bright, intense red. On the next day filtration produced a pale purple solid. Standing for a further 12 days allowed more of this material to be isolated. (Mass 2.51 g.; yield 112%). Recrystallization gave a paler, red solid (M.P. decomp. above 205°C to give a black solid, M.P. 238-243°C) - identified as N-(4-phenylazophenyl)-4-aminonaphtho-1,2-quinone.

Found: C, 74.96%; H, 4.53%; N, 12.08%

$C_{22}H_{15}N_3O_2$ requires: C, 74.79%; H, 4.25%; N, 11.90%

p-Bromoaniline (2.27 g. in 70 ml. MeOH).

The mixture slowly became red and a precipitate was observable thirty minutes after commencement of the reaction. After standing overnight the mixture was filtered, the brown solid product washed with ether and sucked dry (mass 0.69 g.). The filtrate was concentrated under reduced pressure, and more solid obtained (mass 0.48 g.). The infra-red spectra of the two solids were similar. The remaining liquid was concentrated to a syrup.

Thin layer chromatography was used to compare solutions of the following in methylene dichloride:

- (i) The initial precipitate.
- (ii) The solid obtained by concentrating the reaction mixture.
- (iii) The syrup.
- (iv) naphtho-1,2-quinone.
- (v) p-bromoaniline.

The initial precipitate was found to have only one component, while the other solid contained two red components. The residual liquor contained several components in addition to the two red ones.

The initial solid was recrystallized from 2-ethoxy-ethanol and was identified as N-(4-bromophenyl)-4-aminonaphtho-1,2-quinone, M.P. (decomp.) 275-7°C.

Found: C, 58.15%; H, 2.93%; N, 4.24%

$C_{16}H_{10}NO_2Br$ requires: C, 58.54%; H, 3.05%; N, 4.27%

The syrup was dissolved in methylene dichloride and chromatographed on a silica column.

This process yielded:

- (a) Elution with methylene dichloride.
 - (i) An extremely small amount of fawn material.
 - (ii) A yellow solution which on concentration gave a tiny mass of a black solid.

(iii) A red solution which gave a sticky red solid when the solvent had been evaporated under reduced pressure. Trituration with 40/60 petrol allowed this substance to be filtered. (Mass 0.36 g.). An infra-red spectral comparison of this solid with p-bromo-aniline suggested that the latter constituted the bulk of the former. (See below for further work).

(b) Elution with $\text{CH}_2\text{Cl}_2/\text{MeOH}$ mixtures, with gradually increasing percentages of methanol (5% - 20%), yielded a brown solution. Concentration gave a purplish brown solid whose infra-red spectrum was not of scientific value.

The red solid obtained from eluate (aiii) was dissolved in methylene dichloride and chromatographed on an alumina column. This caused an orange band to separate from a blue-grey band. Collection and concentration of the orange eluate yielded an orange solid (mass < 10 mg.), which was identified as the mono-4-bromoanil of N-(4'-bromophenyl)-4-aminonaphtho-1,2-quinone. M.P. 237°C (shrinkage), $239-40^\circ\text{C}$ (fusion).

Found: m/e 481.944499

$\text{C}_{22}\text{H}_{14}\text{N}_2\text{OBr}_2$ requires: m/e 481.945417

Reaction of Naphtho-1,2-quinone with p-Anisidine in Diethyl Ether.

Naphtho-1,2-quinone (1.0 g.) was dissolved in ether (1500 ml.). To this solution were added a solution of p-anisidine (1.67 g.) in ether (30 ml.), and the ethereal washings of the amine container.

A small amount of solid precipitated out of solution overnight. The solution was evaporated to dryness under reduced pressure, and the resultant solid was recrystallized from methanol. Yield (1.09 g., 62%). The solid

melted alone (or in admixture with the product of the reaction in methanol) at 238-40°C, and was identified as N-(4¹-methoxyphenyl)-4-aminonaphtho-1,2-quinone.

Reaction of Naphtho-1,2-quinone with p-Toluidine in Tetrahydrofuran.

Solutions in tetrahydrofuran of the quinone (0.58 g. in 33 ml.) and the amine (0.84 g. in 12 ml.) were prepared and mixed. (Note. Approx. 0.03 g. of quinol was present as stabilizer). After 15 mins. a red colour was developing in the solution.

After 5 days the solvent was evaporated under reduced pressure. A reddish brown syrup was obtained. Trituration with ether gave a red-brown solid, which was filtered off and sucked dry. (Mass 0.57 g.). Thin layer chromatograms run in chloroform or methanol indicated that the material was the same as that obtained from the same reaction in methanol. Infra-red spectral evidence also supported this conclusion.

The ethereal filtrate was concentrated to a syrup, which solidified on the addition of a little fresh ether. T.L.C. showed that this material contained two red components, and so it was dissolved in chloroform and chromatographed using a silica column with chloroform as eluent. As the T.L.C. had shown that the slower moving component was the N-(4¹-methylphenyl)-4-amino-1,2-naphthoquinone, only the first component was removed from the column. Evaporation of the solvent gave a dark red solid (mass 10 mg.). T.L.C. indicated that 2 red components were still present. The small mass of material resulted in a decision not to re-chromatograph this solid, whose infra-red spectrum suggested that the mono-4-methyl-anil of N-(4¹-methylphenyl)-4-amino-naphtho-1,2-quinone was present.

The ethereal filtrate was concentrated and chromatographed on a silica column, using chloroform as eluent. A red component was eluted and the solvent evaporated under reduced pressure producing a red syrup which was

'recrystallized' from methanol. The resulting red solid had an infra-red spectrum resembling that of the impure anil.

Reaction of Naphtho-1,2-quinone with N,N-dimethylaniline in Diethyl Ether.

N,N-dimethylaniline (0.9 g.) was added to a solution of the quinone (0.50 g.) in diethyl ether (750 ml.). Over 6 days a very small amount of precipitate formed, and an attempt to filter this off merely dirtied the sinter. The solvent was evaporated under reduced pressure, yielding a red-brown liquid which smelt of N,N-dimethylaniline. T.L.C. of this using chloroform showed the presence of at least 6 components (pale brown, red-purple, orange, purple, purple, and brown - starting from the solvent front). Treatment of the red-brown liquid with chloroform followed by petrol produced a precipitate of a pale purple colour, and t.l.c. indicated that this contained at least three components. The precipitate was treated with chloroform and filtered on to a silica column, which was eluted with chloroform, but thin layer chromatography showed that the eluate contained many components (possibly 8).

As above but in Methanol.

N,N-dimethylaniline (1.8 ml.) was added to a methanolic solution of the quinone (1.02 g. in 250 ml.). After 5 days the solvent was evaporated and a black syrup obtained. Addition of ether precipitated a solid, which was filtered off. The ethereal filtrate was concentrated to a syrup. T.L.C. indicated that five components were present in the precipitate and 8 or 9 in the syrup. Some of the solid was chromatographed using a silica column and chloroform but little material was eluted. Dissolution of the syrup in chloroform followed by the addition of 40/60 petrol gave a blue-grey (with yellow patches) precipitate. This was dissolved in chloroform and

chromatographed on silica, but again little was eluted.

Reactions of N-alkyl-N-arylamines with Naphtho-1,2-quinone, and Condensations of the Resulting Alkylarylaminoquinones with o-phenylene-diamine.

These reactions are described below, and the relevant spectral data is given on pages 20, 24, 37 and 48 for the quinones and pages 49-53 for the benzophenazines.

Reaction of Naphtho-1,2-quinone with N-methylaniline.

The amine was redistilled (b.p. 106°C at water vapour pressure). Methanol (250 ml.) was added to naphtho-1,2-quinone (1.01 g.) and the mixture stirred until dissolution was complete. The same solvent was mixed with N-methylaniline (1.5 ml.) until the total volume was 10 ml., and this solution, followed by methanol (12 ml.) washings of the amine vessel, was poured into the quinone solution. A deep red solution resulted immediately.

After 4 days the solvent was evaporated under reduced pressure, on a luke-warm water bath. T.L. chromatograms of the concentrate using methanol and chloroform as eluents were obtained. These indicated that five components were present, the main one being of a bright red colour.

The methanolic concentrate was chromatographed on a silica column using methanol as eluent. This produced a very deep red solution, which after evaporation to dryness, gave a deep red syrup which solidified on treatment with ether. The solid was filtered off, washed with 40/60 petrol, and sucked dry (mass 0.85 g., yield 52%).

Recrystallization gave mainly green platelets, accompanied by some purplish brown material, identified as N-methyl-N-phenyl-4-aminonaphtho-1,2-quinone. M.P. shrinkage 160° , melt $165-69^{\circ}\text{C}$ (Lit. 173°).⁴⁷

The mass spectrum showed a peak for the dihydroxy compound rather than the quinone, and it was on this peak that an accurate mass measurement was made.

Found: m/e 265.110893

Calc. for $C_{17}H_{15}NO_2$: m/e 265.110277

Reaction of o-Phenylene-diamine with N-methyl-N-phenyl-4-aminonaphtho-1,2-quinone.

N-methyl-N-phenyl-4-amino-naphtho-1,2-quinone (0.4 g.) was dissolved in methanol (150 ml.) and thereto was added a solution of o-phenylene-diamine (0.18 g.) in methanol (10 ml.). Methanolic 'amine' washings were added, and the solution left for two days.

A small amount of precipitate had formed in the bottom of the flask. The mixture was cooled in the refrigerator for $1\frac{1}{2}$ hrs. and was then filtered. A dirty yellow brown solid was obtained (mass 0.04 g.). Further precipitate was removed from the sides of the flask (total mass 0.32 g.). The solid was recrystallized twice from carbon tetrachloride and was washed with petrol before drying. It was identified as 5-(N-methyl-N-phenyl)-aminobenzo[a]phenazine. M.P. $153-55^{\circ}C$.

Found: m/e 335.141705

$C_{23}H_{17}N_3$ requires: m/e 335.142240

Reaction of Naphtho-1,2-quinone with N-ethylaniline.

N-ethylaniline (3.4 ml.) and the methanol washings of the amine receptacle (10 ml.) were added to a methanolic solution of the quinone (2.02 g. in 500 ml.). After 5 days the mixture was concentrated to a syrup (under reduced pressure), which was dissolved in a little methanol. The addition of much ether precipitated a red solid, which was filtered off. (Mass 0.46 g.).

Concentration of the filtrate to a small volume resulted in red needles crystallizing from the solution. These were collected by filtration, dried, recrystallized first from methanol and were finally recrystallized from

2-methoxyethanol. These were identified as N-ethyl-N-phenyl-4-amino-naphtho-1,2-quinone, M.P. 172-74°C.

Found: C, 77.58%; H, 5.64%; N, 4.87%

$C_{18}H_{15}NO_2$ requires: C, 77.98%; H, 5.42%; N, 5.05%

Accurate mass measurement on the dihydroxy compound molecular ion in the mass spectrum showed: 279.126496; $C_{18}H_{17}NO_2$ requires: 279.125921.

(Note: $C_{18}H_{17}NO_2$ requires: C, 77.41%; H, 6.09%; N, 5.01%).

The filtrate (see beginning of 2nd paragraph) was investigated by T.L.C. This revealed the presence of approximately eight components, of which the major one corresponded to the solid described above. The addition of petrol to the filtrate yielded a sticky-black precipitate; the liquid was decanted off and the sticky mass dissolved in chloroform. T.L.C. showed that the petrol solution contained 7 components and the chloroform solution six. The petrol solution was concentrated and chromatographed on a silica column; this yielded a liquid identified as impure N-ethylaniline from its I.R. spectrum, and a small amount of a red solid - too little in fact to collect. The poor separation on the t.l.c. plate suggested that column chromatography would not be very successful, and elution was terminated.

The Reaction of o-phenylene-diamine with N-ethyl-N-phenyl-4-amino-naphtho-1,2-quinone.

The amino-quinone (0.33 g.) was dissolved in methanol (33 ml.?). To this solution were added a solution of the diamine (0.14 g.) in methanol (10 ml.) and methanol washings of the amine container. The colour of the solution faded slightly during the ensuing six hours.

After the mixture had stood overnight a sample was taken and the solvent evaporated under reduced pressure. Infra-red and mass spectra of the resulting orange syrup suggested that a condensation product had formed, so

the syrup and the remaining reaction mixture were combined and the solvent removed using a rotary evaporator. A thin layer chromatogram of the syrup in chloroform showed that the main component was orange in colour, while others were pink, colourless and brown. The syrup was chromatographed using a silica column with chloroform as eluent. Elution was halted when an orange solution had been collected. Concentration of this yielded a viscous orange syrup, which solidified on scratching. The yellow-orange solid was recrystallized from carbon tetrachloride and petrol, and identified as 5-(N-ethyl-N-phenyl)-aminobenzo[a]phenazine, M.P. 121.5 - 122.5°C.

Found: C, 82.21%; H, 5.45%; N, 12.24%

$C_{24}H_{19}N_3$ requires: C, 82.52%; H, 5.44%; N, 12.03%

Preparation of 5-(N-ethyl-N-(4'-methylphenyl))aminobenzo[a]phenazine.

Naphtho-1,2-quinone (1.00 g.) was dissolved in methanol (250 ml.). N-ethyl-p-toluidine (1.73 g.) was added to the quinone solution, as were the methanol washings (8 ml.) of the toluidine vessel. A red colour developed immediately, and this deepened to a red-black overnight. Evaporation of the solvent gave a red-black syrup, which did not solidify when triturated with ether or petrol. A chloroform solution of the syrup was chromatographed on a silica column. Several brown components of very small mass were eluted initially - these were discarded. A deep red eluate was then obtained. Evaporation of the solvent from this yielded a dark red viscous oil, which could not be crystallized from methanol. After the methanol had been evaporated under reduced pressure, the oil was dissolved in boiling carbon tetrachloride, and the resulting solution decanted from a sticky-black material left on the flask side. On cooling some solid formed in the CCl_4 solution, and was filtered off (mass 0.39 g.), but the infra-red spectrum of this material was unsatisfactory.

The remaining CCl_4 solution was concentrated under reduced pressure to an oil, which, after dissolution in methanol, was treated with a solution of o-phenylene-diamine (0.28 g.) in the same solvent. The mixture was left to stand overnight, and was then investigated by T.L.C. This suggested that an orange and a yellow component had formed. The reaction mixture was concentrated under reduced pressure, and the residue dissolved in methylene dichloride. This solution was chromatographed on a silica column, and the orange eluate obtained was concentrated to a syrup, which solidified on scratching with a glass rod (mass 0.64 g.). Recrystallization from carbon tetrachloride was unsuccessful, but petrol proved to be a suitable solvent for this purpose. The solid was identified as 5-(N-ethyl-N-(4'-methylphenyl))-aminobenzo[a]phenazine, M.P. 148-149°C.

Found: C, 82.66%; H, 6.01%; N, 11.86%

$\text{C}_{25}\text{H}_{21}\text{N}_3$ requires: C, 82.64%; H, 5.79%; N, 11.57%

Reactions of Naphtho-1,2-quinone with Alkylamines

Details of spectra are given on pages 20, 21, 24, 38-40 and 48.

n-Hexylamine.

A solution of the amine (0.67 g.) in methanol (5 ml.) was added to a methanolic solution of the quinone (1.00 g. in 240 ml.). After two days the black-brown solution had become red-brown, and the solvent was evaporated under reduced pressure. Treatment of the solid residue with methylene dichloride gave a red-brown precipitate, which was filtered off, washed with petrol, and sucked dry. (Mass 0.17 g.). The mass spectrum of this material suggested that both N-(n-hexyl)-4-aminonaphtho-1,2-quinone and that compound's mono-n-hexylimine were present.

A t.l.c. of the filtrate using chloroform as the eluent showed the presence of several components. Column chromatography of the concentrated filtrate was carried out. (Silica or alumina ?). Elution with 40% CH_2Cl_2 / 60% CCl_4 moved the bands down the column, but movement eventually seemed to cease. Concentration of the eluate yielded a very little yellow material. Elution with chloroform removed a purple solution, which on concentration gave an oil which smelt strongly of hexylamine. Some brown solutions were then eluted, but these contained very little material. The eluant was changed to methanol, and the resulting eluate yielded a khaki solid after solvent removal. The mass spectrum suggested that the amino-quinone-imine was the main constituent of this substance, which was dissolved in ether and chromatographed on a silica column, as t.l.c. had shown that ether was a suitable eluent for separating the amino-quinone-imine from the aminoquinone. A yellow solution was eluted from the column and evaporation of the ether gave a pale khaki solid, identified as the mono-n-hexylimine of N-(n-hexyl)-4-aminonaphtho-1,2-quinone. M.P. 62-64°C.

Found: m/e 340.250585

$\text{C}_{22}\text{H}_{32}\text{N}_2\text{O}$ requires: m/e 340.251451

The experiment was repeated in order to obtain more of the precipitated solid. In this case the solvent was evaporated from the reaction mixture and the residue treated with benzene. A solid was filtered off, the filtrate was concentrated, and then investigated by t.l.c. Chloroform revealed the presence of numerous components - in order, starting from the solvent front end: pink, blue, grey, grey, purple, orange, pale purple, grey-brown, pink-brown, blue, orange, brown. The first four components showed clearly separate spots, but the remainder formed a continuous stream to the starting point. Comparison with spots of the solids from the first experiment showed that the components of the solids moved parallel to the orange-brown zones near the start of the chromatogram.

The dried precipitate (mass 0.28 g.) was a brown solid. Part of this was dissolved in methylene dichloride and was chromatographed on a silica column. Chloroform eluted a minor black component, as did 95% CHCl_3 /5% MeOH (by volume). An orange component followed, from which a red-brown solid was isolated by solvent evaporation. This substance was identified as N-(n-hexyl)-4-aminonaphtho-1,2-quinone, M.P. 218-219°C. (Lit. 236-7°C).^{29,34}

Found: C, 74.13%; H, 7.68%; N, 5.23%

Calc. for $\text{C}_{16}\text{H}_{19}\text{NO}_2$: C, 74.71%; H, 7.39%; N, 5.45%

n-Pentylamine.

A solution of n-pentylamine (0.58 g.) in methanol (5 ml.) was added to a solution of the quinone (1.01 g.) in methanol (250 ml.). A red-brown colour slowly developed in the mixture. On the following day a small sample of the mixture was subjected to t.l.c.; this revealed the presence of several materials. In order from the solvent front the colours were blue, grey-purple, yellow, red-purple, yellow, purple, blue-grey, orange. The mixture was concentrated to a syrup after one more day, and the syrup was washed with petrol. The resulting yellow solution was decanted off, and ether added. Scratching the flask sides resulting in a red-brown solid forming. This was filtered off and sucked dry (mass 0.73 g.). Evaporation of the petrol solution gave a very little brown solid; while a thin layer chromatogram of the filtrate, after concentration and dissolution in methylene dichloride, revealed the presence of many compounds. (Colour pattern from solvent front - pink, blue, pale blue, pink-brown, pink-grey, blue, purple (very large area), an orange spot superimposed on the purple, yellow, pink and orange). The mass spectrum of the red-brown material showed a pattern suggestive of the presence of N-(n-pentyl)-4-aminonaphtho-1,2-quinone. The accurate mass of the molecular ion of this species is 243.125921, ($\text{C}_{15}\text{H}_{17}\text{NO}_2$), while the measured value was 243.125062. This is

closer to the accurate mass for $C_{13}H_{15}N_4O$, (243.124579) but that formula seems very unlikely for a product of the reaction under consideration.

n-Octylamine.

This experiment closely paralleled that described above, with octylamine (0.87 g.) replacing pentylamine. After one day the solvent was removed under reduced pressure. Ether, petrol/methylene dichloride, carbon tetrachloride/methylene dichloride and methylene dichloride all failed as triturating agents for the syrup obtained, though CH_2Cl_2 did produce a little solid. The solution in this solvent yielded a thin layer chromatogram suggesting little reaction had occurred, so the solution was left for three days and was then concentrated to a syrup. The procedure using petrol and ether (as described on page 144) was followed, and yielded very similar results to the pentylamine case. The t.l. chromatogram of the ether solution (using CH_2Cl_2 as eluent) was very similar to that from pentylamine - the colour pattern was virtually identical but the leading components moved faster from the octylamine mixture when the two systems were compared on the same t.l.c. plate. The mass of brown solid was 0.54 g. Part of this was dissolved in methylene dichloride, the solution was then filtered, and the filtrate was chromatographed using a silica column. Methylene dichloride, chloroform and chloroform/methanol mixtures eluted a few minor black components, while methanol eluted some reddish-brown material. The solid left by filtration was investigated by t.l.c. using ether as the eluent - this showed that two orange components were present. The mass spectrum of the original solid showed large peaks at 285 and 394 suggesting that both N-(n-octyl)-4-aminonaphthoquinone and its mono n-octylimine were present. Accurate mass measurements were made on the peaks at 285 and 186 (the major breakdown peak).

Found: m/e 285.172593; m/e 186.055964

$C_{18}H_{23}NO_2$ requires: m/e 285.172869

$C_{11}H_8NO_2$ " m/e 186.055499

1,2-Diaminoethane.

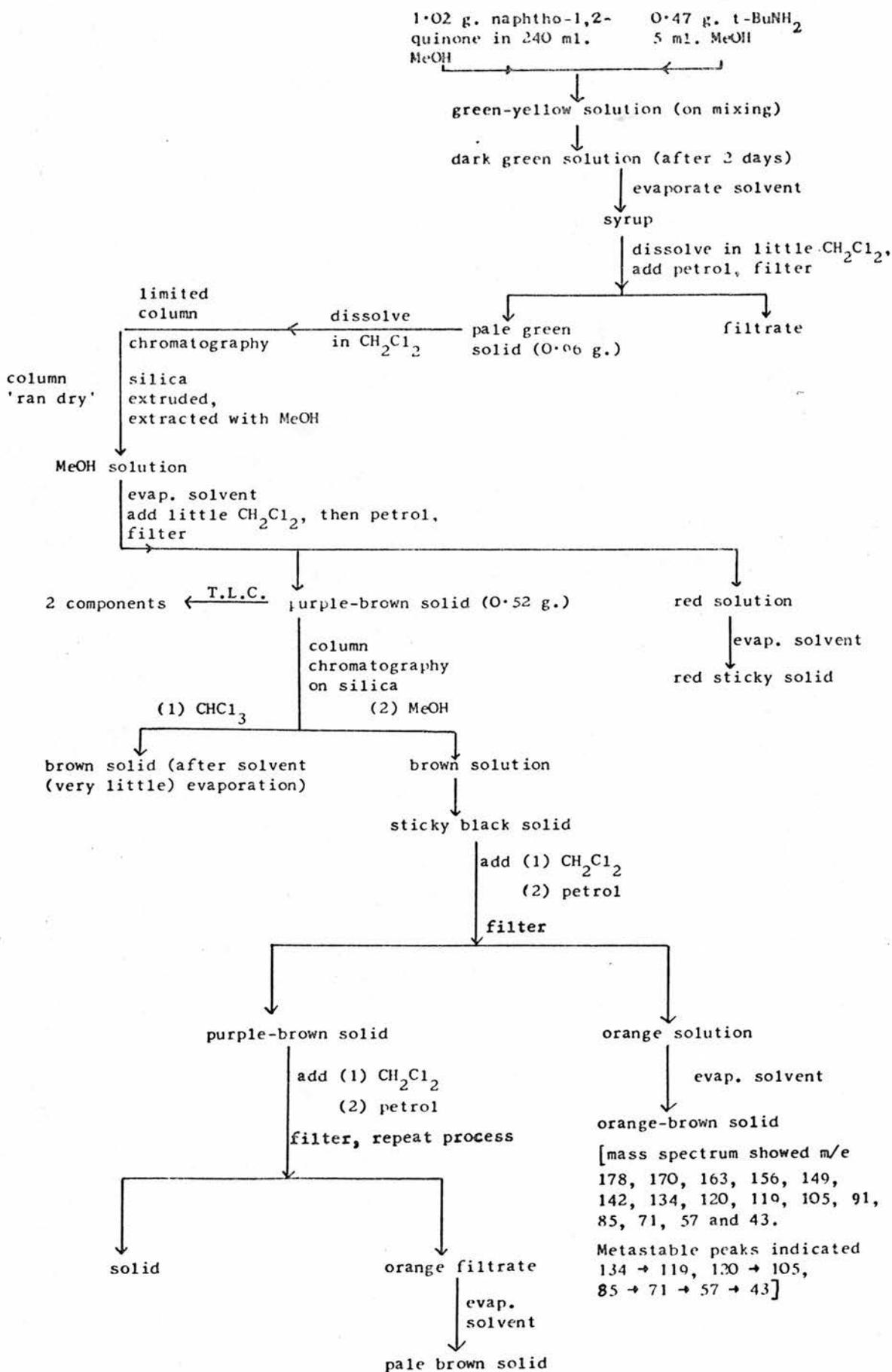
Ethylene-diamine (1.00 g.) was added to a solution of naphtho-1,2-quinone (1.12 g.) in methanol (250 ml.). After ten days a red precipitate was filtered off, washed with ether, and sucked dry. (Mass 0.24 g.). An N.M.R. spectrum of this solid in trifluoroacetic acid (60 mg. in 0.5 ml.) was extremely noisy, but showed absorptions in the regions $2.25 \pm 0.25\tau$ and $5 - 6\tau$. The filtrate was concentrated under reduced pressure to a syrup, which was dissolved in methylene dichloride. Thin layer chromatography of the CH_2Cl_2 solution using methanol as eluent showed the presence of 4 components (yellow, brown, yellow, brown). The addition of ether produced a yellow precipitate. Repetition of this process yielded a total of 0.44 g. of yellow solid. The infra-red spectrum of the yellow solid was not very good, but did indicate that the material was not recovered naphtho-1,2-quinone.

2-Amino-2-methylpropane (= ^tbutylamine).

This experiment became rather complex and is detailed in the diagram on the next sheet. No product could be identified.

Cyclohexylamine.

The amine (1.25 g.) was added to a solution of the quinone (1.03 g.) in methanol (225 ml.). The mixture was swirled and darkened in colour. After two days the solvent was evaporated under reduced pressure, and a little boiling methanol added to the residual syrup. Filtration yielded a little solid (black), whose infra-red spectrum contained no absorptions in the range $1620-2000 \text{ cm.}^{-1}$. No solid formed when the solution cooled. Thin layer chromatography using various solvents (CHCl_3 , petrol 40/60, CCl_4 , benzene, ether) revealed that at least 5 components (purple, yellow, red, brown, orange) were present. The methanol was evaporated from the solution



and the residue dissolved in benzene. Part of the solution thereby obtained was chromatographed using benzene on a column (silica or alumina?). Three components were eluted, and after solvent removal these were found to be a yellow solid, a dark greenish solid and a red solid. The green material showed mass spectral peaks at 178 and 149, and was not identified. Accurate mass measurements indicated that the yellow material contained the mono-cyclohexylimine of N-cyclohexyl-4-aminonaphtho-1,2-quinone.

Found: m/e 336.220613

Calc. for $C_{22}H_{28}N_2O$: m/e 336.220152

Similarly the red compound was shown to contain the parent aminoquinone.

Found: m/e 255.125422

Calc. for $C_{16}H_{17}NO_2$: m/e 255.125926

The Preparation of Benzo-1,2-quinone.

This compound was prepared by oxidising catechol with tetrachlorobenzo-1,2-quinone, which was obtained by the nitric acid oxidation of the corresponding catechol. The latter resulted from chlorination of catechol. These processes are described below.

Preparation of Tetrachlorocatechol.²

Chlorine, from a cylinder, was passed through a solution of catechol (100 g.) in glacial acetic acid (750 ml.). A Drechsel bottle was fitted between the cylinder and the reaction vessel to act as a trap for 'sucked-back' liquid and as a safety valve in the event of a blockage. Solid was found to form inside the tube through which the chlorine passed at levels below the surface of the reaction mixture. The use of a wide-bore tube in this part of the system reduced the risk of the pipe becoming completely

blocked. The flow of chlorine was terminated when white crystals of tetrachlorocatechol precipitated throughout the bulk of the solution. The mixture was cooled in ice for one hour and was then filtered using a sinter. Air was drawn through the solid to remove as much of the hydrogen chloride as possible. Yield: 143 g. (62%).

Oxidation of Tetrachlorocatechol.²

The yield of the above reaction was placed in a large beaker (much larger than the volume of solid). A solution of pure nitric acid (25 ml.) in glacial acetic acid (350 ml.) was slowly added to the solid and the mixture was stirred continuously. Much frothing occurred and a considerable volume of nitrogen dioxide evolved. Addition of the acid ceased when all the solid was seen to have dissolved. (Excess acid was found to lower the yield; insufficient acid produced an orange solid as the final product). The dark red solution was poured on to ice (1 litre) and the mixture stirred. Dark red tetrachlorobenzo-1,2-quinone precipitated out. After all the ice had melted, the product was collected by filtration using a large sinter, and was washed with water.

Note: The crystals of product may be very fine and can block the sinter.

Yield: From 50 g. of tetrachlorocatechol, 35 g. (70%).

Preparation of Benzo-1,2-quinone.⁹

During this preparation each solution used and the reaction mixture were protected by calcium chloride drying tubes.

Dry ethereal solutions of catechol (5.5 g. in 25 ml.) and tetrachlorobenzo-1,2-quinone (12.5 g. in 250 ml.) were cooled in a dry ice/acetone bath whose temperature was maintained in the range -25°C to -35°C .

The catechol solution was then added to the quinone solution, and the mixture stirred for two hours, using a magnetic stirring bead. The temperature was maintained at $-30^{\circ}\text{C} \pm 5^{\circ}\text{C}$. Red benzo-1,2-quinone precipitated, and was collected by filtration of the reaction mixture through a sinter. After being washed with dry ether, the product was placed in a dry tube, which was stoppered and stored in dry ice. (Cooling the tube prior to filling it with the quinone generally resulted in the condensation of water in the tube). The yield and colour of the product were found to be temperature dependent.

Yield	Colour	Temperature of dry ice/acetone bath
3.68 g. (68%)	dark red	-25°C to -30°C
2.00 g. (37%)	pale red	-30°C to -35°C

The pale red product was found to decompose less if stored for some time, than the darker material.

The Preparation of Diazomethane.¹⁶⁶

A solution of Diazald* (4.3 g.) in diethyl ether (26 ml.) was dripped into a solution of potassium hydroxide (1.0 g.) in ethanol (5 ml.) and water (1.6 ml.). The latter solution was in a distillation flask heated by a water bath maintained at ca. 65°C . Diazomethane/ether mixture distilled off, and, after condensation, was allowed to flow into a solution of the substance whose reaction with diazomethane was desired. When addition of the Diazald solution was complete, ether (5 ml.) was added dropwise and the water-bath was kept at 65°C until all the ether had distilled over.

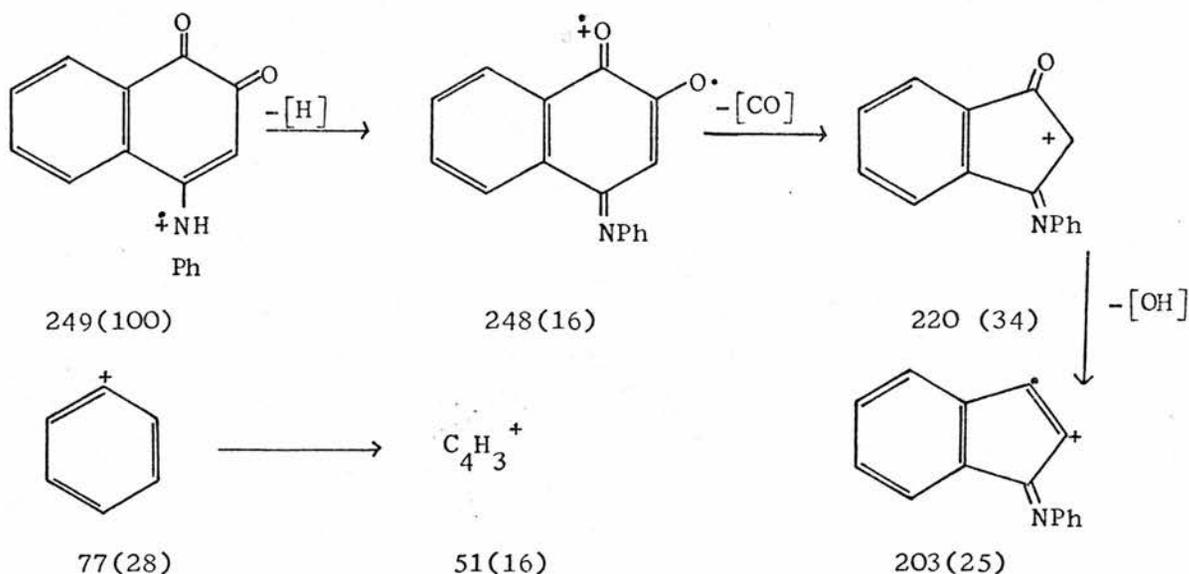
* Diazald is N-methyl-N-nitroso-p-tolylsulfonamide.

APPENDIX 1

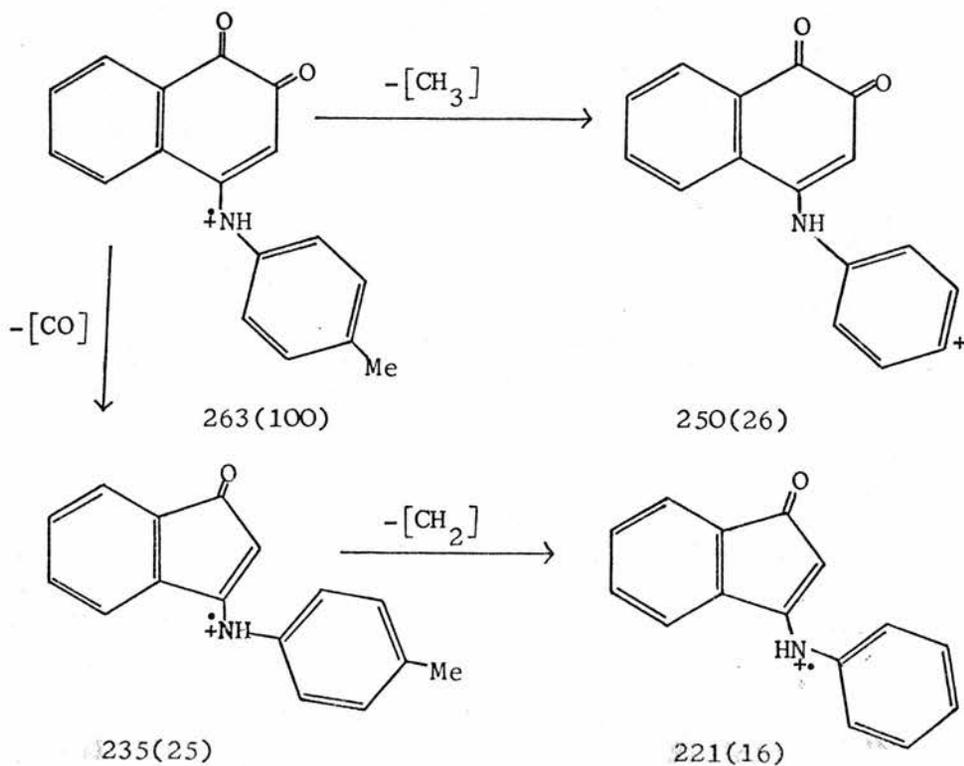
Possible Ions Formed During Mass Spectrometry
of N-aryl-4-aminonaphtho-1,2-quinones

The mass:charge ratio is given beneath each ion and the peak height, as a percentage of the height of the base peak, is given in brackets.

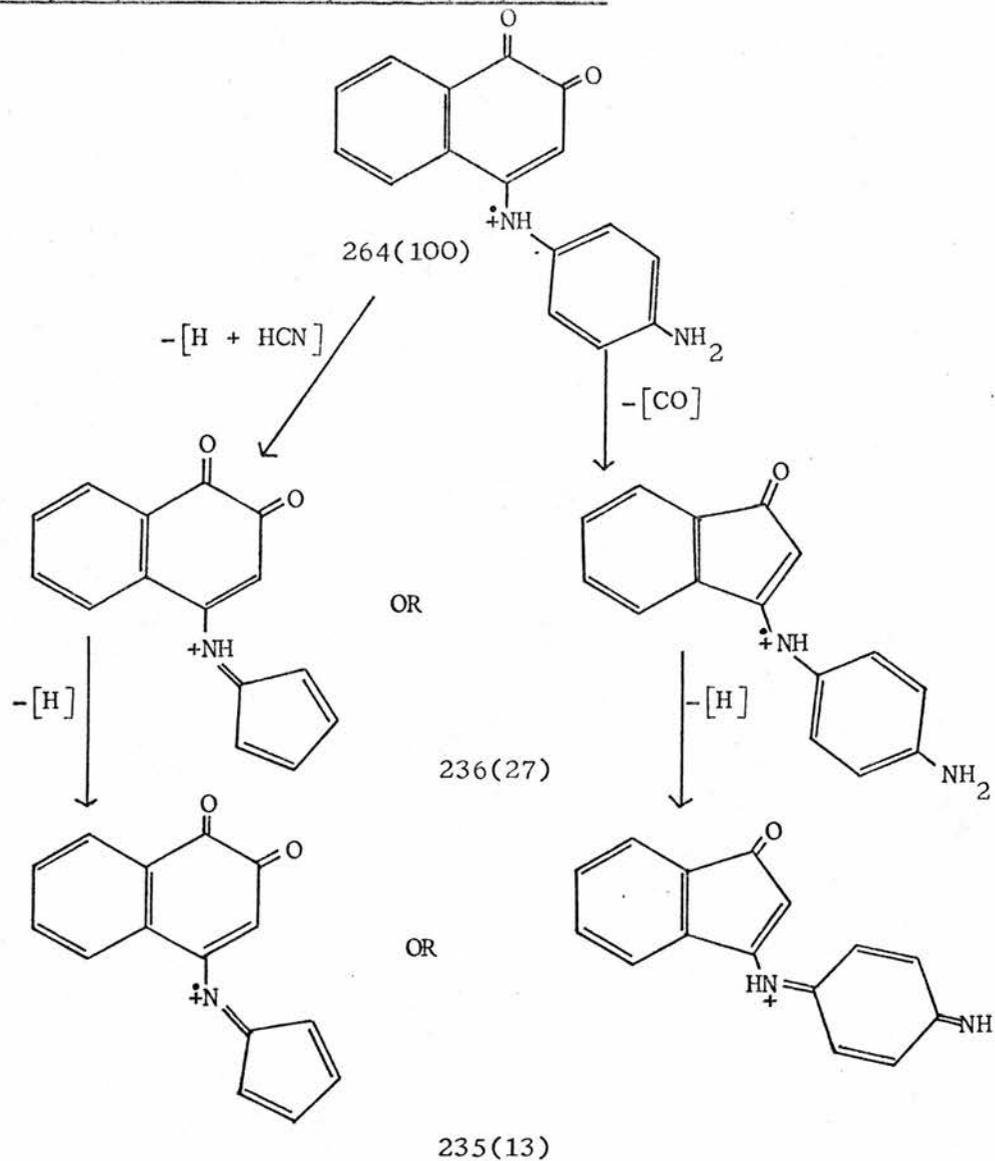
N-phenyl-4-aminonaphtho-1,2-quinone



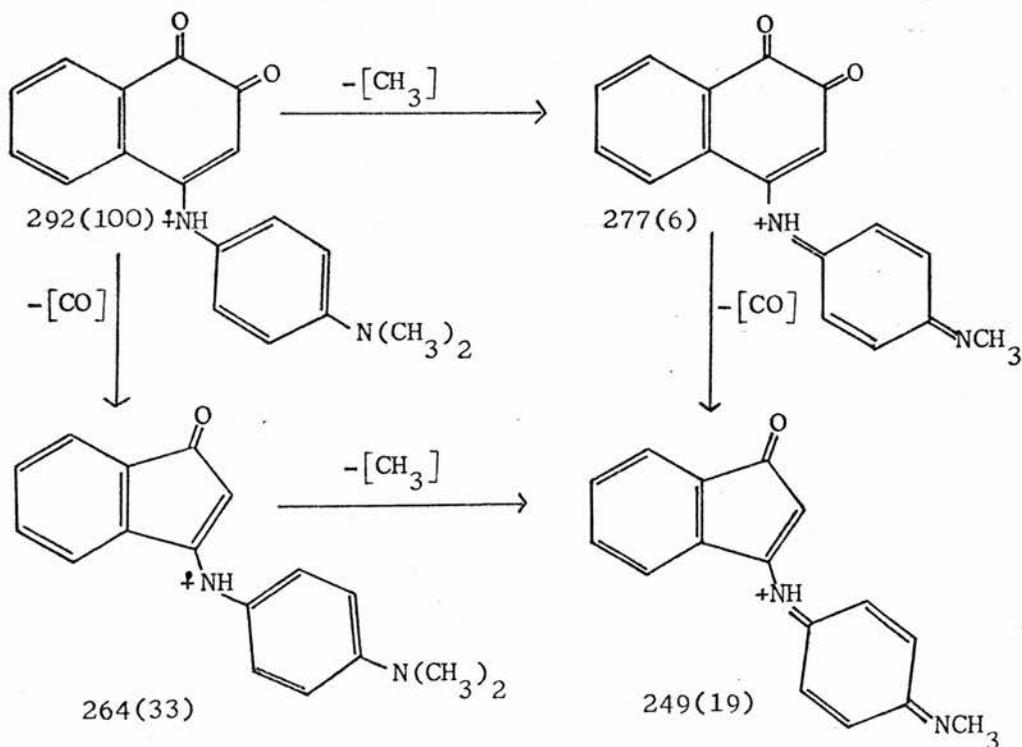
N-(4'-methylphenyl)-4-aminonaphtho-1,2-quinone



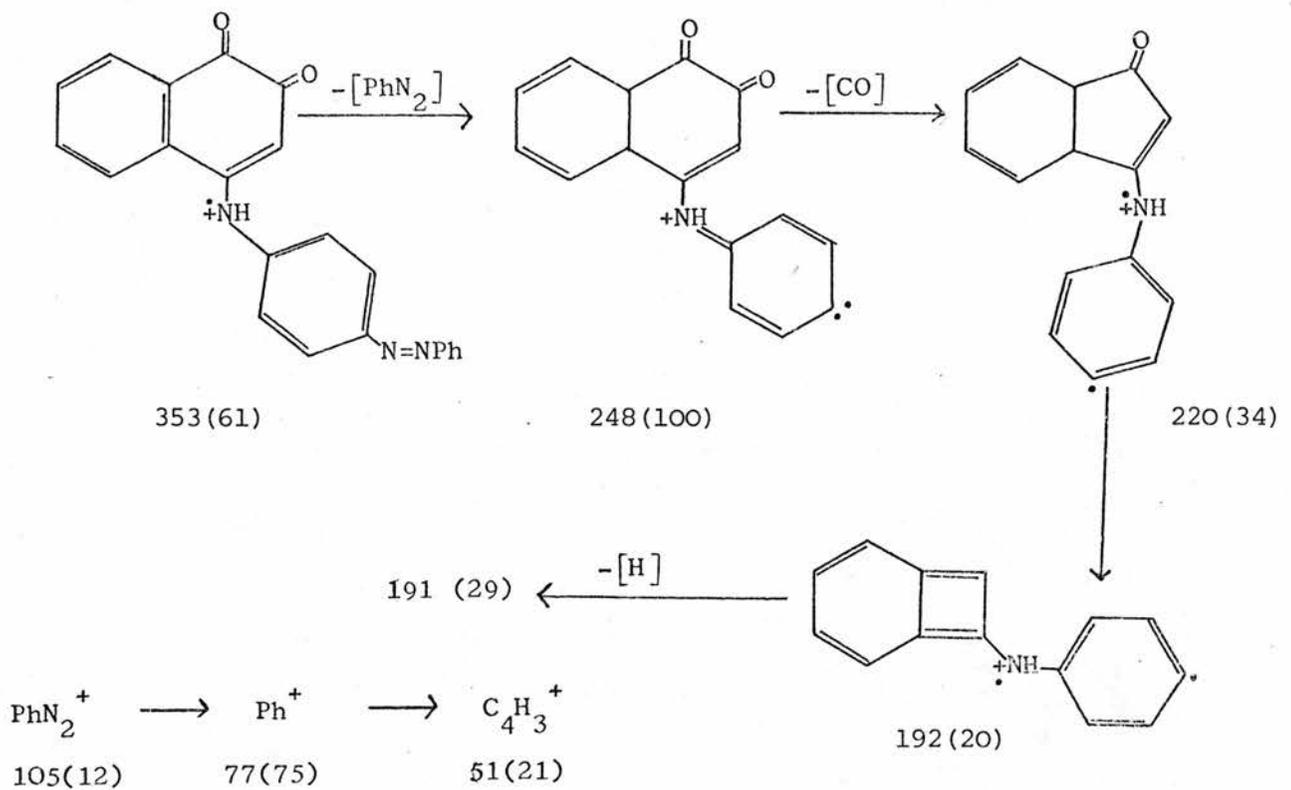
N-(4'-aminophenyl)-4-aminonaphtho-1,2-quinone



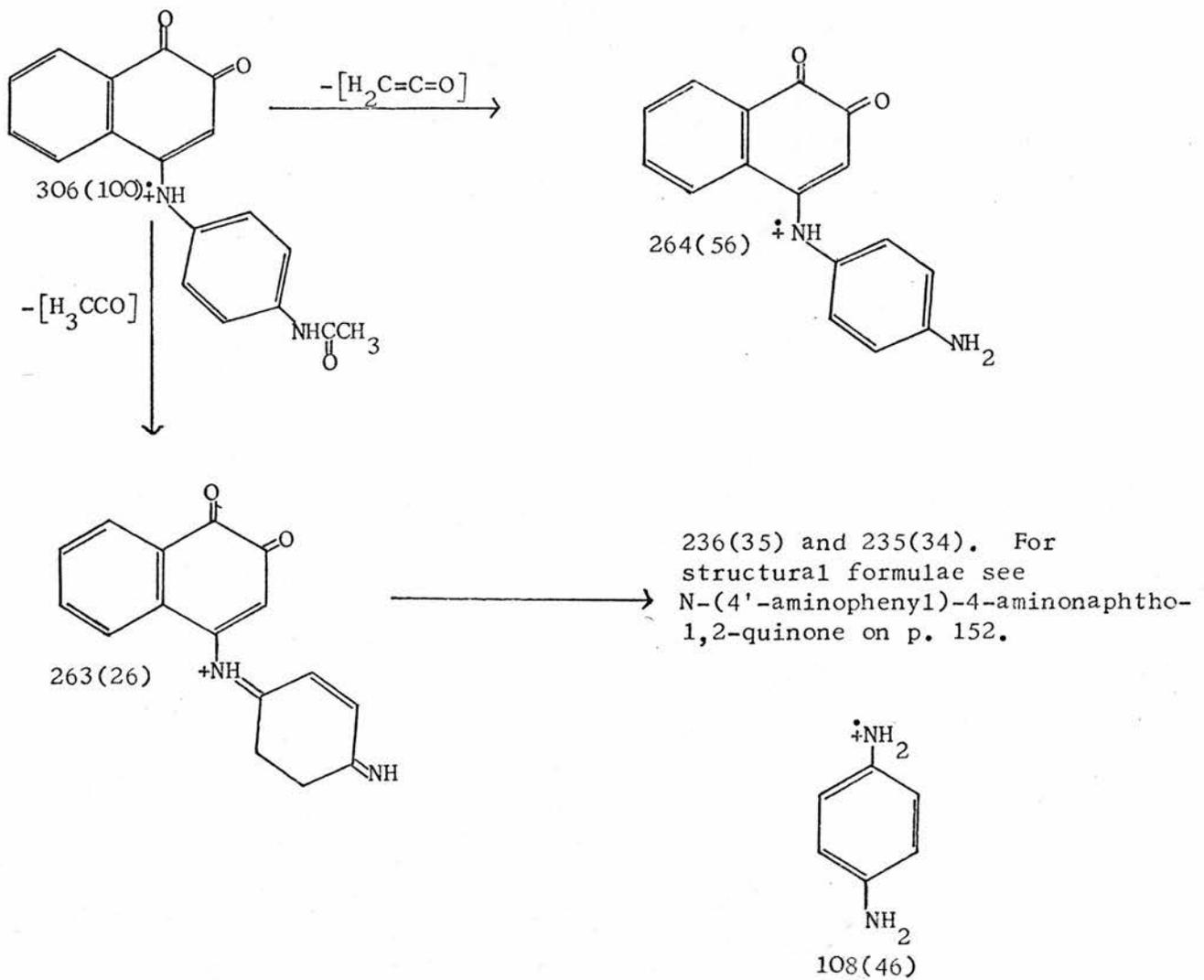
N-(N',N'-dimethyl-4'-aminophenyl)-4-aminonaphtho-1,2-quinone



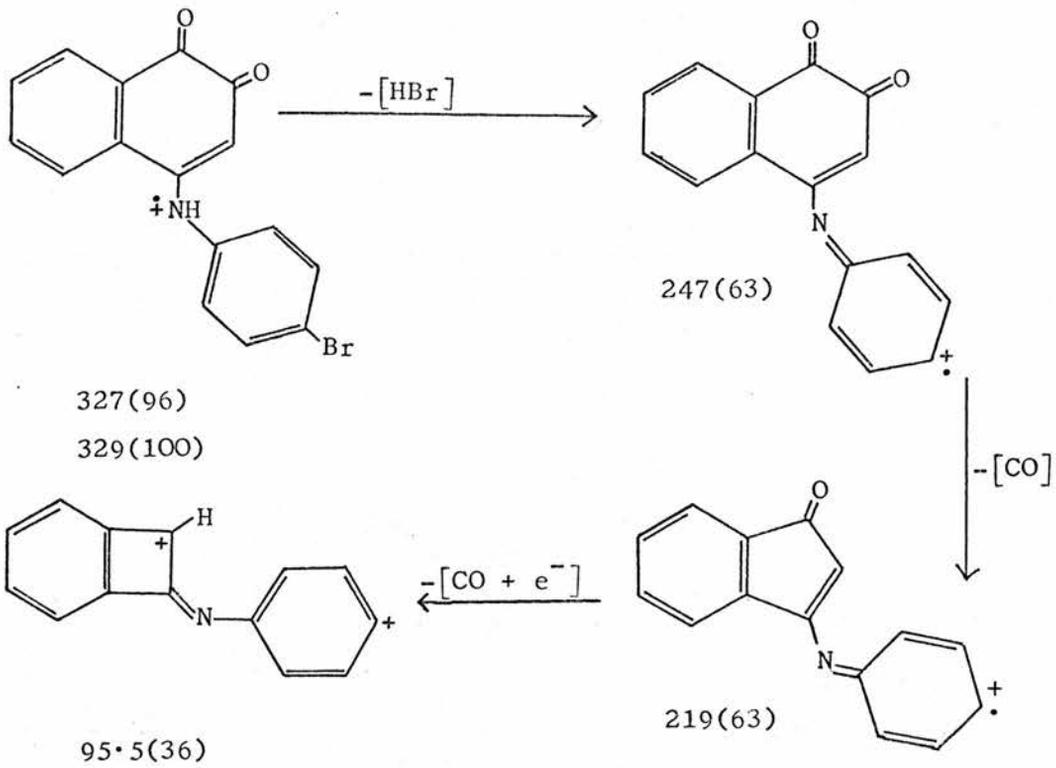
N-(4'-phenylazophenyl)-4-aminonaphtho-1,2-quinone



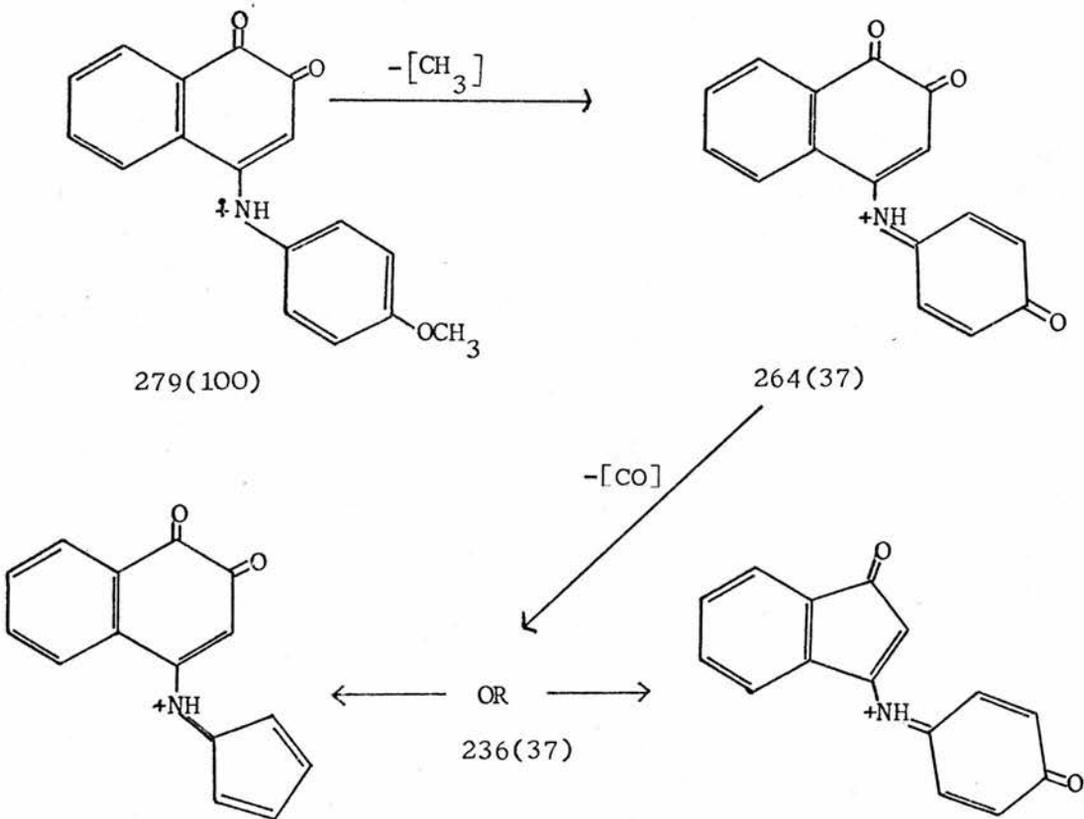
N-(N'-acetyl-4'-aminophenyl)-4-aminonaphtho-1,2-quinone



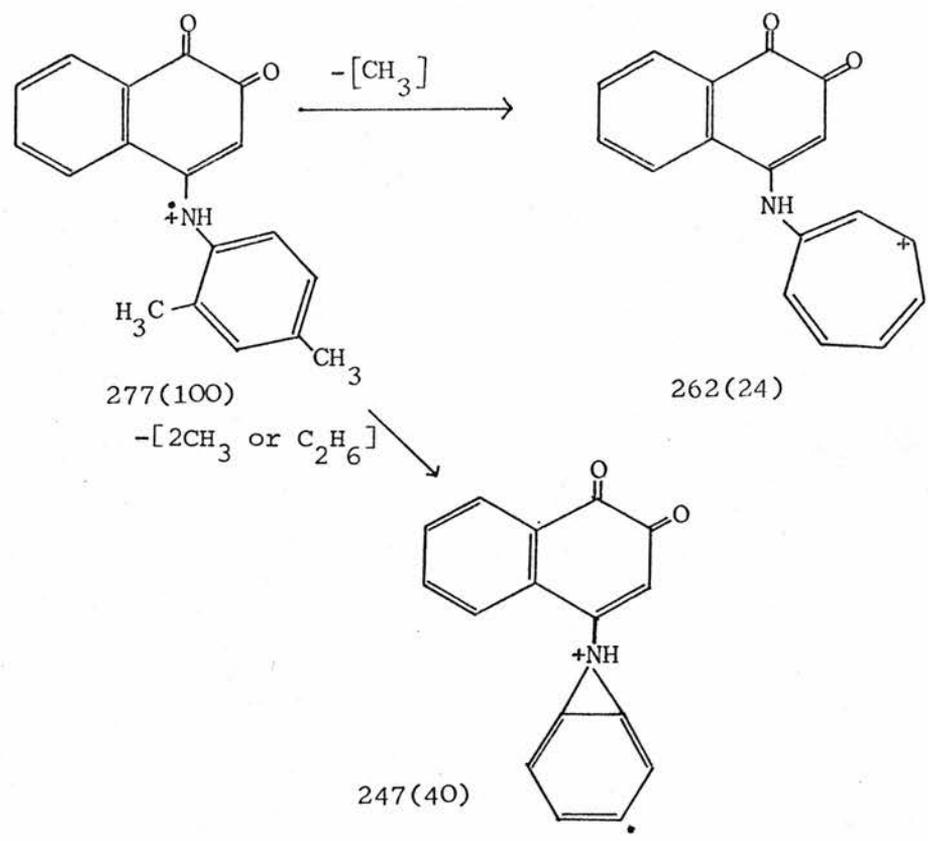
N-(4'-bromophenyl)-4-aminonaphtho-1,2-quinone



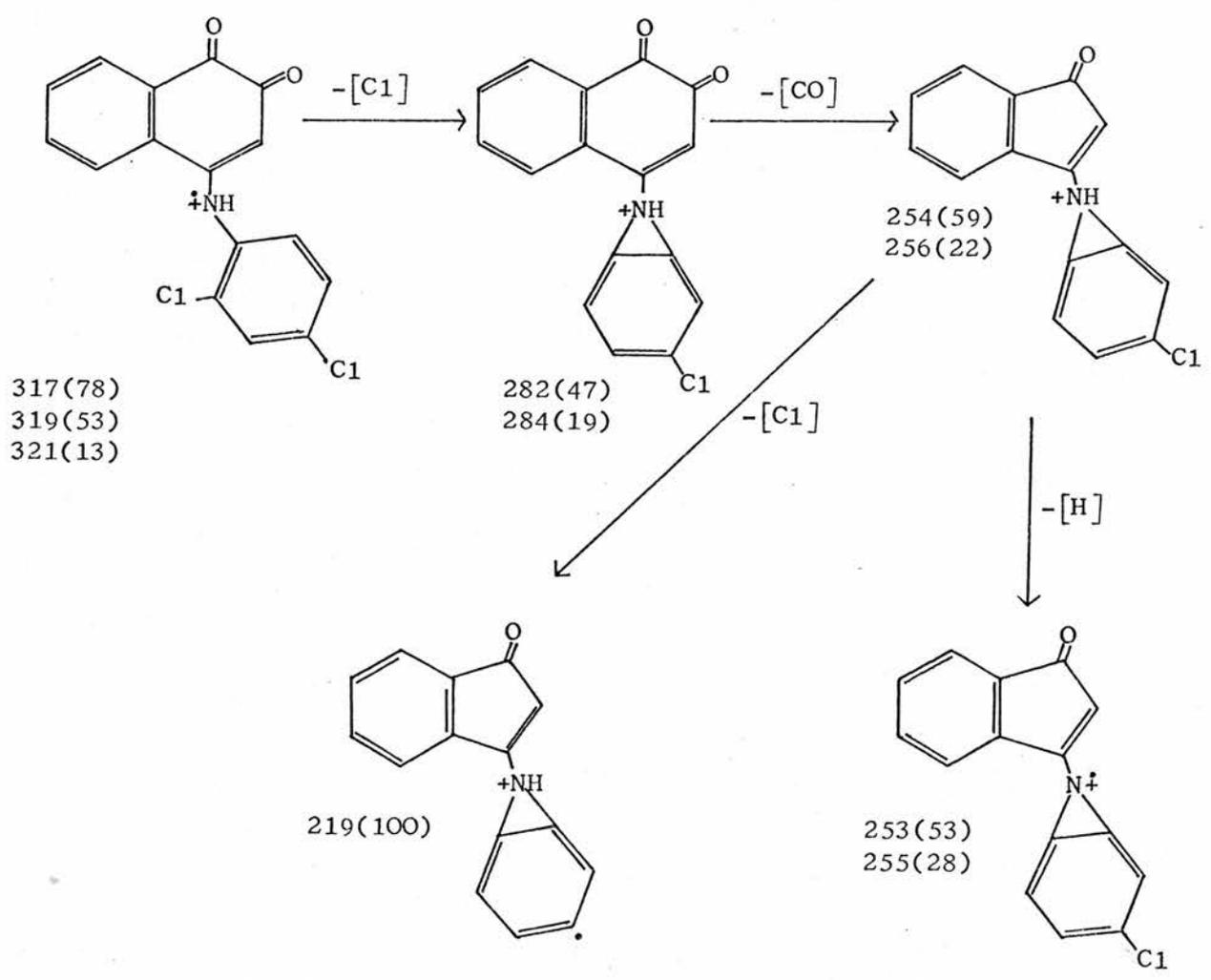
N-(4'-methoxyphenyl)-4-aminonaphtho-1,2-quinone



N-(2',4'-dimethylphenyl)-4-aminonaphtho-1,2-quinone

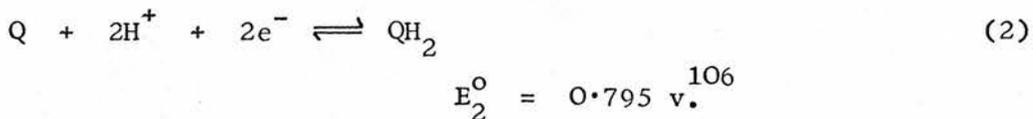
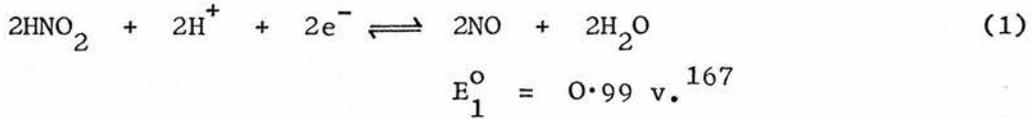


N-(2',4'-dichlorophenyl)-4-aminonaphtho-1,2-quinone

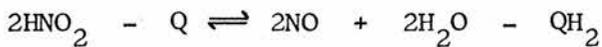


APPENDIX 2

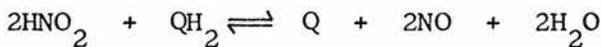
Thermodynamics of Possible Catechol/Nitrous
Acid Reaction.



Subtract (2) from (1)



Therefore



For reaction to proceed from left to right,

$$E_{\text{cell}}^{\circ} = E_1^{\circ} - E_2^{\circ} = 0.195 \text{ v.}$$

$$\Delta G^{\circ} = -zE^{\circ}F$$

$$= \frac{-2 \times 0.195 \times 96,500}{4,184}$$

$$= -8.99 \text{ kcal mol}^{-1} \quad (-37.64 \text{ kJ mol}^{-1})$$

APPENDIX 3

During the Spring of 1972 the author assisted in the design of some experiments suitable for use in schools. These are described in the article listed as ref. 168.

APPENDIX 4

Ultra-Violet Spectra of Some Aromatic Compounds

Substance	Solvent	λ_1	$\log \epsilon_1$	λ_2	$\log \epsilon_2$	λ_3	$\log \epsilon_3$	Ref.
Aniline	iso-octane	234	3.9	288	3.25			41a
Aniline	95% ethanol	234	3.87	283	3.13			53
Naphthyl-1-amine	ethanol	242	4.18	317	3.43	329	3.33	41b
N-phenyl-naphthyl-1-amine	ethanol	252	4.37	335	4.04			41b
4-Methylaniline	95% ethanol	235	3.90	290	3.10			169
4-Methoxyaniline	95% ethanol	235	3.95	300	3.13			169
Catechol	ethanol	214	3.78	278	3.42			170

All wavelengths are given in nm. The assignment to column numbers does not imply that all the figures in one column correspond to similar electronic transitions in the different molecules.

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