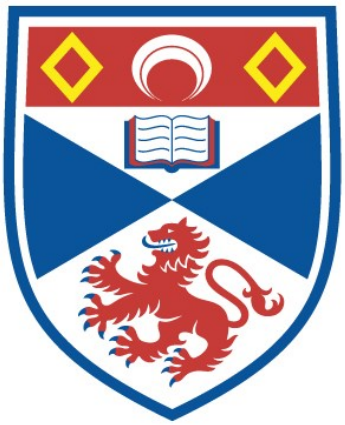
THE REACTIONS OF AROMATIC AMINES WITH 1,2-QUINONES

Peter Irvine Smith

A Thesis Submitted for the Degree of PhD
at the
University of St Andrews



1971

THE REACTIONS OF AROMATIC AMINES WITH 1,2-QUINONES

A THESIS

PRESENTED FOR THE DEGREE OF

DOCTOR OF PHILOSOPHY

OF

THE UNIVERSITY OF ST. ANDREWS

BY

PETER IRVINE SMITH

JUNE 1971

DECLARATION

I hereby declare that the following thesis is a record of experiments carried out by me, that the thesis is my own composition and that it has not been previously presented for a Higher Degree.

The research was carried out in the Chemistry Departments of the Universities of Dundee and St. Andrews under the joint supervision of Professor Lord Tedder and Dr. W.M. Horspool.

Peter I. Smith

CERTIFICATE

I certify that PETER IRVINE SMITH, B.Sc., 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

ACKNOWLEDGEMENTS

The author wishes to express his indebtedness for the advice and encouragement of Professor Lord Tedder and Dr. W.M. Horspool, under whose guidance this work was carried out.

Thanks are due to Professor A.D. Walsh for making available the facilities of the Chemistry Department of the University of Dundee, and to Professors Lord Tedder and P.A.H. Wyatt for the facilities of the St. Andrews University Chemistry Department. Thanks are also due to other members of the staff and research students at the two universities for helpful discussion, to the technical staff for services rendered, and to Mrs. Winton for typing the thesis.

Gratitude is expressed to the Agricultural Research Council for a grant to finance the work.

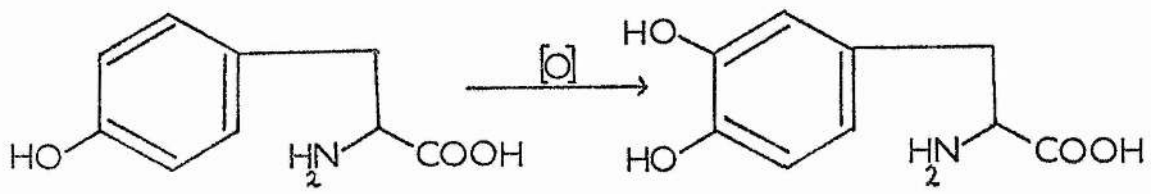
CONTENTS

Preparation of :-

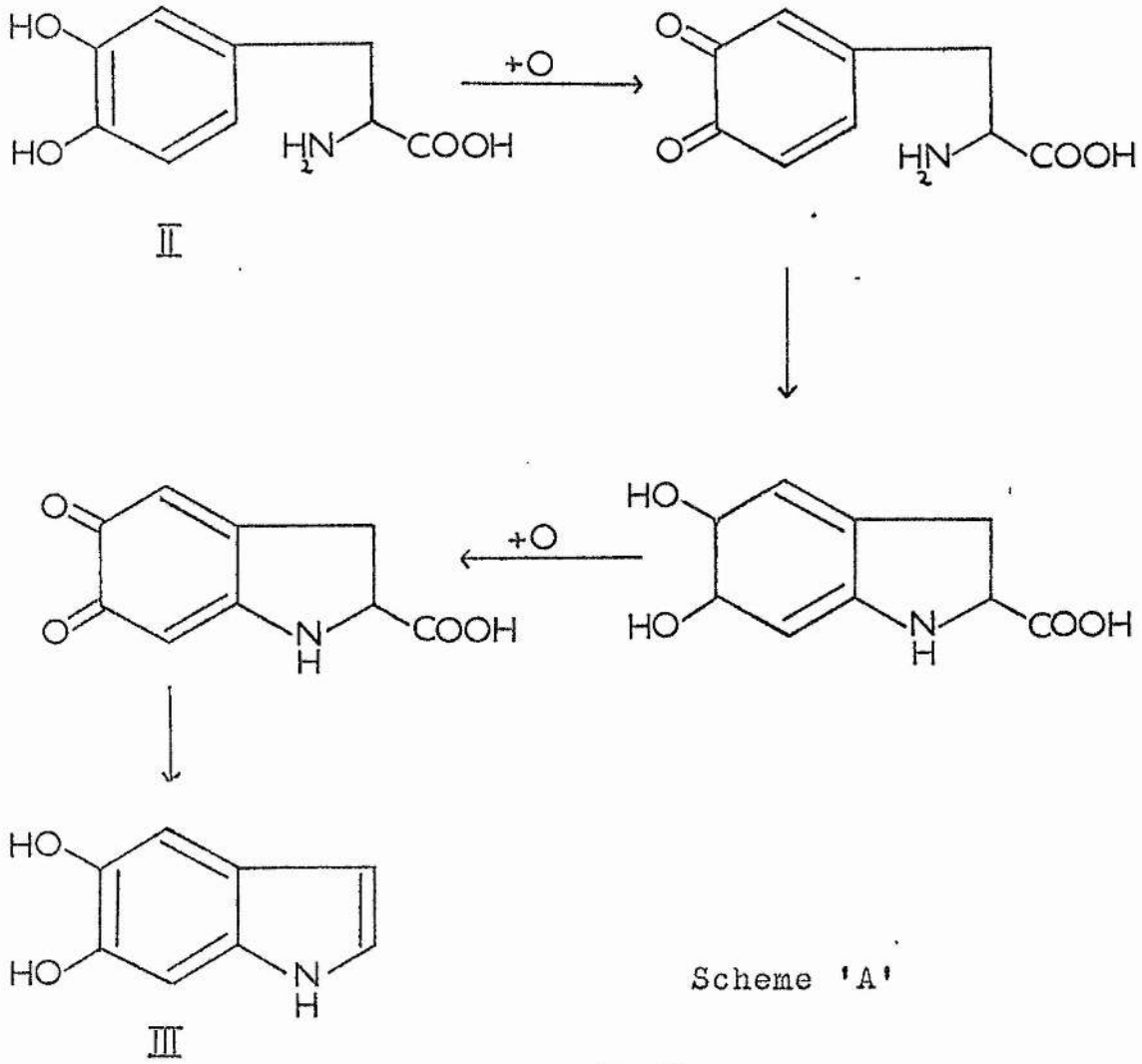
Reactions of o-phenylenediamine with :-

INTRODUCTION

The browning of foodstuffs of vegetable origin, such as bruised apples or bananas, is well known. This is caused, in part, by the formation of the brown pigment melanin. However, it is thought that an important part is played by the interaction of the amine groups of amino acids and proteins with o-quinonoid compounds generated by the action of enzymes on naturally occurring phenolic compounds such as adrenaline. The formation of the brown melanin pigments is basically due to this type of reaction, insofar as the first step involves intramolecular attack of an α-amino group of an amino acid on a 1,2-quinone nucleus. When Raper studied the formation of melanin, by the oxidation of tyrosine (I) and 3,4-dihydroxyphenylalanine (II) in the presence of tyrosinase[1], he found that one of the main intermediate products was 5,6-dihydroxyindole (III). This compound is also formed in vivo[2] and is readily oxidised by a non-enzymatic process to give melanin. The formation of (III) can be represented by Scheme 'A'.



I II

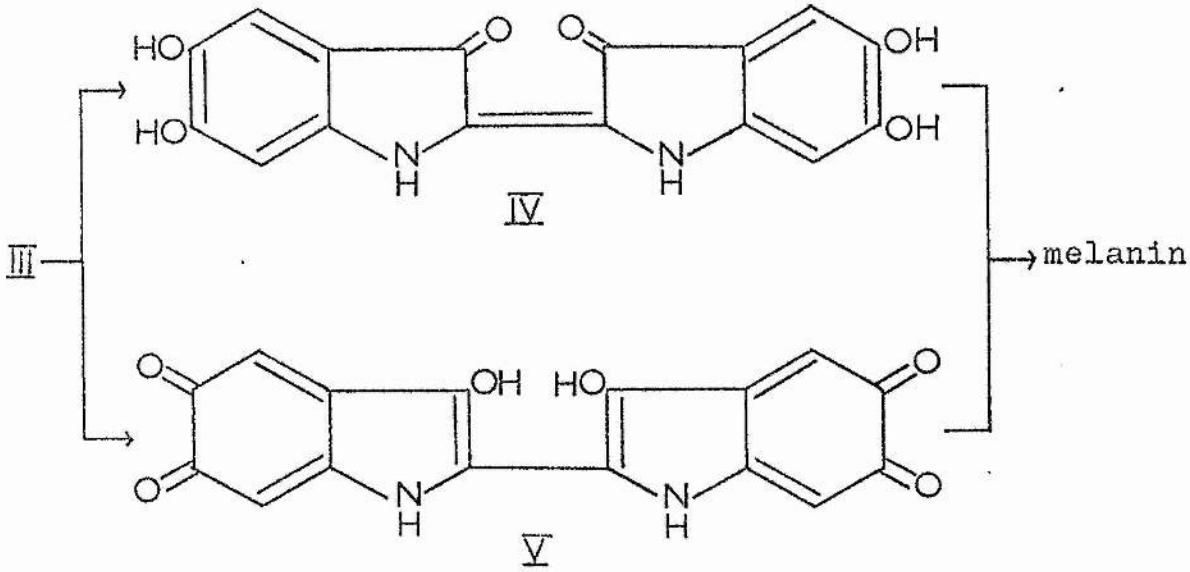


II

III

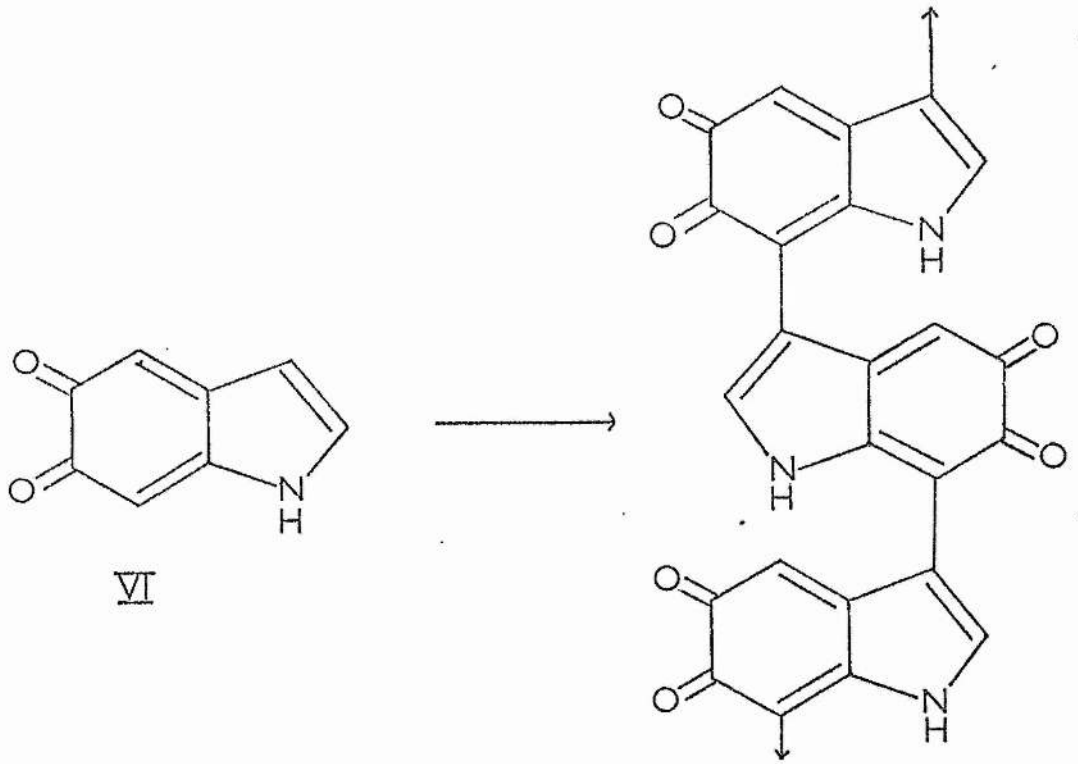
Scheme 'A'

It remained to determine how (III) was converted to melanin. Clemo and Weiss[3] suggested that further reaction first involved the formation of 5,5',6,6'-tetrahydroxyindigo (IV) and the corresponding di-o-quinone (V). These compounds condensing through one hydroxy and one keto group, either in the benzenoid or pyrrole ring, to give a chain structure. The main evidence in favour of this mechanism is that it would require the consumption



of 5.25 atoms of oxygen per molecule of (I) to give the melanin. This is in good agreement with a value of 5.23 found by Duliere and Raper[4]. The nitrogen content of (IV) is also in good agreement with that of several samples of natural melanins.

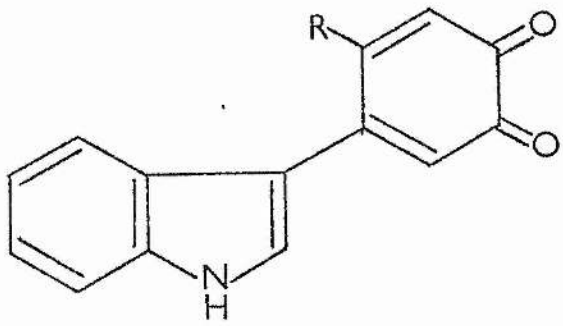
Bu'Lock and Harley-Mason[5] suggested that indole-5,6-quinone (VI) is the actual precursor of melanin, polymerisation occurring via the 3- and 7- positions to give a linear polymer (VII). These linear units would be cross-linked via the 2- position to the 4- position of another molecule. As evidence for this mechanism, work on the condensation of simple 1,2-quinones with simple indoles was carried out. It was found that 1,2-benzo-



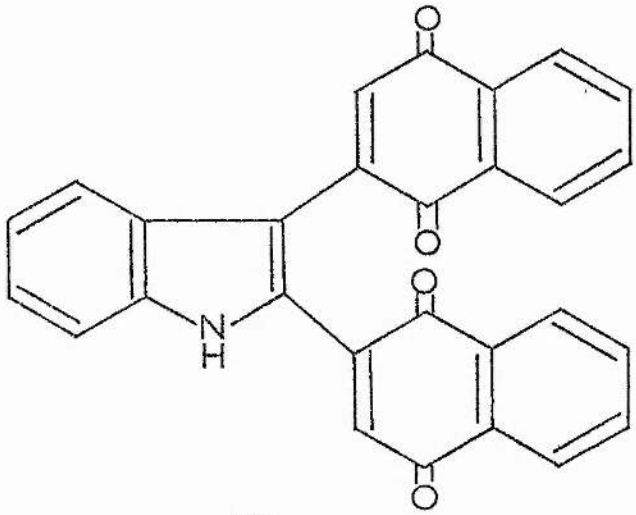
VI

VII

quinone, in aqueous ethanol, condensed with indole to give 4-3'-indolyl-1,2-benzoquinone (VIII). Similarly 4-methyl-1,2-benzoquinone yielded 4-3'-indolyl-5-methyl-1,2-benzoquinone (IX). Other examples are also given. Indole and 1,4-naphthaquinone yielded 2-3'-indolyl-1,4-naphthaquinone, analogous to (VIII), together with 2,3-di-(1,4-naphthaquino-2-yl)indole(X). This last product illustrating the way in which the linear chains of (VII) could become cross-linked. 5,6-Dihydroxy-1-methylindole yielded melanin-like products with all the quinones used by the authors. Substitution of indole



VIII, R=H; IX R=Me.



X

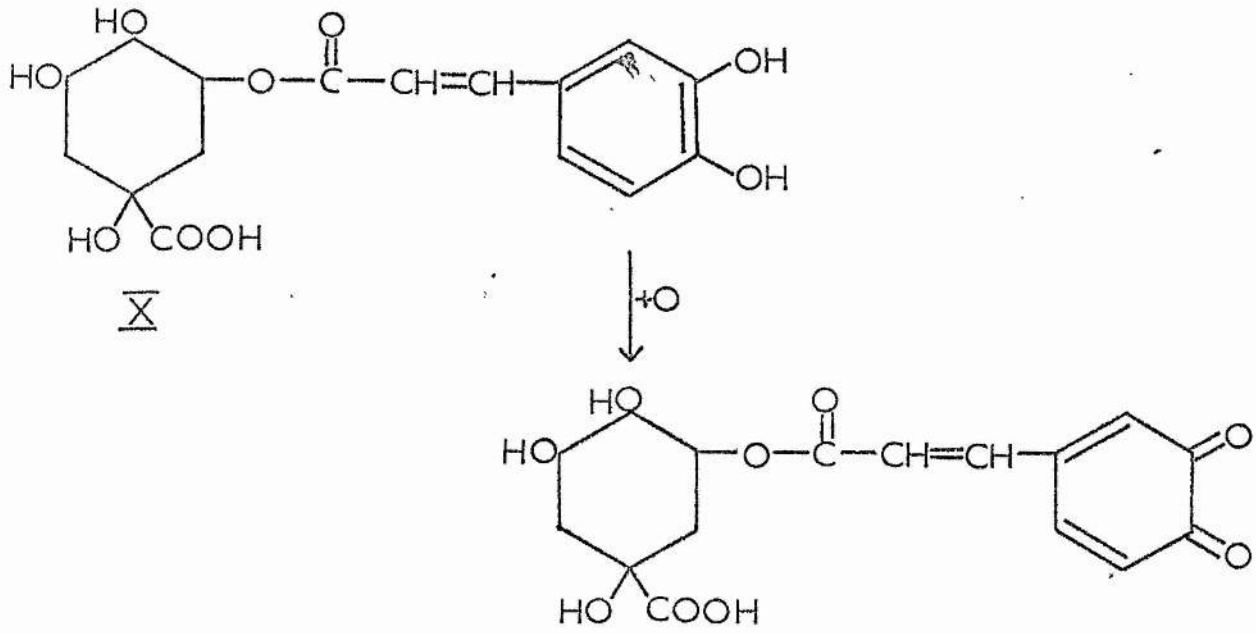
in the 3- position led to colourless adducts, of vastly different physical properties from the coloured adducts already described, which were not identified.

The reaction between amino acids and phenolic compounds in the presence of o-diphenol oxidase has been studied by several workers. James, Roberts, Beevers and DeHock[6] extracted a highly active polyphenolase from the

leaves of ATROPA BELLADONNA which oxidised catechol, adrenaline, N-methyladrenaline and other hydroxy compounds. If amino acids were added to a catechol-enzyme mixture, a rich red colour developed, which the authors claimed is due to the addition of one molecule of acid, via the amino group, to the 4 position of 4-hydroxy-o-quinone. It was believed that this condensation product was responsible for the observed secondary oxidation of the amino acids. Jackson and Kendal[7] treated tyrosine, catechol, and homocatechol with mushroom extract in the presence of proline, hydroxyproline, hydroxyproline ethyl ether, pyrrolidine, glycine, dimethylamine, and methylamine. The nitrogenous compounds with primary amino groups gave an orange-red colour, while secondary amino compounds gave an intense purple. It is believed that one molecule of nitrogenous compound reacts with one molecule of quinone, generated by action of the mushroom extract on the phenolic compound, to give a leuco base which air oxidises to the coloured form. Oxidation of any excess glycine present was also observed in agreement with the results of James et al. Mason and Peterson[8] obtained spectroscopic evidence for adducts when treating catechol, 4-methylcatechol, 3,4-dihydroxy-

phenylalanine or 5,6-dihydroxyindole with o-diphenol oxidase in the presence of compounds with terminal primary amino groups, aliphatic amino compounds, amino acids with secondary amino groups, and amino acids containing thio groups. They found that only compounds with thio groups and aromatic amines reacted with quinones derived from 3,4-dihydroxyphenylalanine and these adducts appeared to derive from 'indole-5,6-quinone' only.

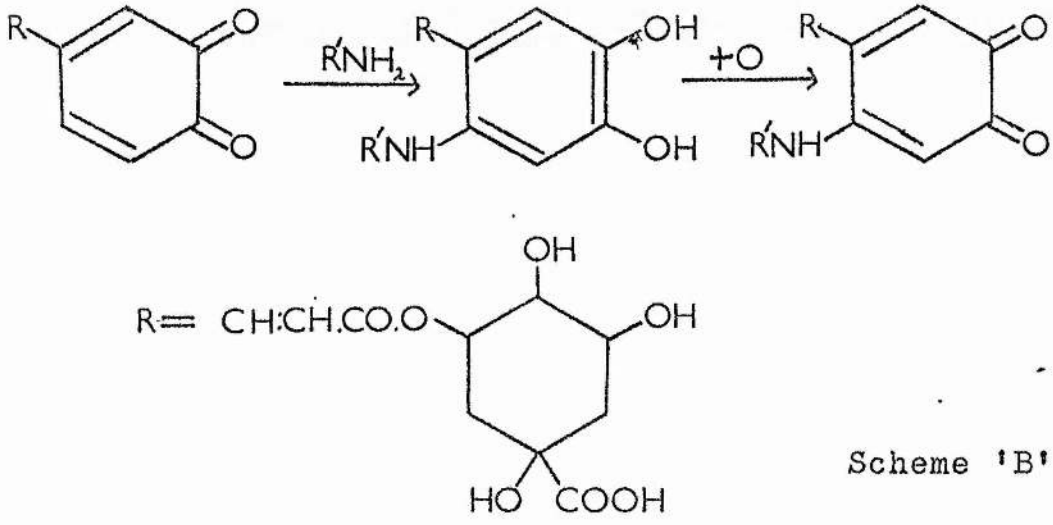
Pierpoint has carried out investigations on quinones of more biological significance. He treated chlorogenic acid (X) with tobacco leaf o-diphenol oxidase both alone and in the presence of various trapping agents.[9] A solution of chlorogenic acid and enzyme alone becomes brown with the uptake of oxygen, but correct amounts of benzenesulphinic acid or cysteine reduce oxygen uptake and prevent browning. Aniline, glycine and amino acids with secondary amino groups gave coloured products and increased the oxygen uptake by the system. Tertiary amines had no effect. Pierpoint suggested that the chlorogenic acid is first oxidised to the corresponding quinone (XI). This can then polymerise via the hydroxyquinone to give brown compounds. This has been suggested for aqueous solutions of β-naphtha-



X

XI

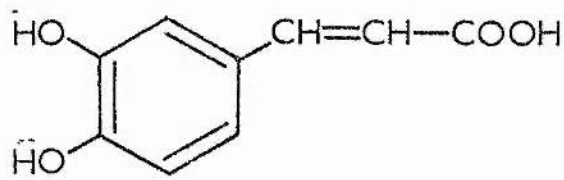
quinone[10] and o-quinone formed by the oxidation of catechol by mushroom o-diphenol oxidase[11]. The colouration and increased oxygen uptake in the presence of amines was postulated as being due to adducts obtained by attack at the 6 position of the quinonoid ring, scheme B. It



Scheme 'B'

is suggested that aniline reacts further to give the 2,6-di-anilinoquinone and possibly the anil.

In a later paper[12], Pierpoint extends his work to include unesterified caffeic acid (XII) and increases the range of amino acids studied. He finds both α- and ε-amino groups of amino acids react with the quinones



XII

from caffeic and chlorogenic acids to give coloured adducts. When peptides were used in place of amino acids, the terminal α-amino groups, and lysine ε-amino groups, reacted to give initially similar compounds to those obtained earlier though secondary reactions also occurred.

It will be seen that the work mentioned invariably used 'in situ' generated quinones and no isolation and characterisation of products was attempted. This thesis describes work carried out with freshly prepared crystalline 1,2-quinones and simple amines. This had the dual purpose of giving more insight into biologically important quinone/amine reactions and increasing our

knowledge of quinone chemistry.

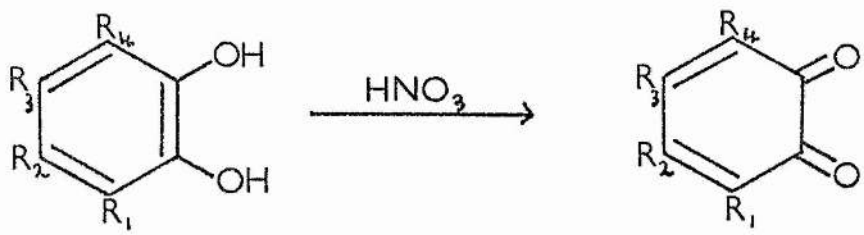
DISCUSSION

SECTION I

The Reactions of 1,2-Benzoquinone with Aniline and Substituted Anilines.

General Preparation of 1,2-Benzoquinones

The preparation of 1,2-benzoquinones is generally effected by the oxidation of the corresponding catechol or of a suitably substituted phenol. With catechols, only dehydrogenation is necessary, while with phenols, a second oxygen atom must be introduced into the aromatic nucleus in the 2-position. The first record of the preparation of a 1,2-benzoquinone was in 1887, when Zincke[13] prepared the tetrachloro- and tetrabromo- compounds by oxidation of the catechols with concentrated nitric acid. Several workers employed this method to prepare tetrasubstituted polyhalo- o-benzoquinones[13-18] and it has been used by later workers[19-25].



For example $R_1=R_2=R_3=R_4=Cl$ Ref. 13,21,32,58.

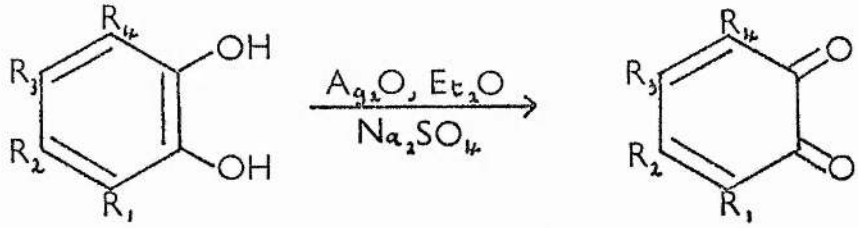
$R_1=Me$, $R_2=R_3=R_4=Cl$ Ref. 15.

See also references 13-27.

The early interest in highly substituted polyhalo- o-benzoquinones was probably due to their good shelf life compared with the instability of the less substituted

compounds. The use of nitric acid was extended by Cousin[28] who prepared tetrabromo- and tetrachloro-1,2-benzoquinones from the mono- and dimethyl ethers of the corresponding catechols.

In 1904, Willstäter and Pfannenstiel[29] first reported the use of silver oxide as an oxidising agent for catechols. This has been successfully used by many workers to prepare the more sensitive quinones. The general method involves shaking the catechol with freshly prepared silver oxide, in dry ether, in the presence of a dehydrating agent such as sodium sulphate.



For example, $R_1=R_2=R_3=R_4=H$. Ref. 29, 30, 34, 35.

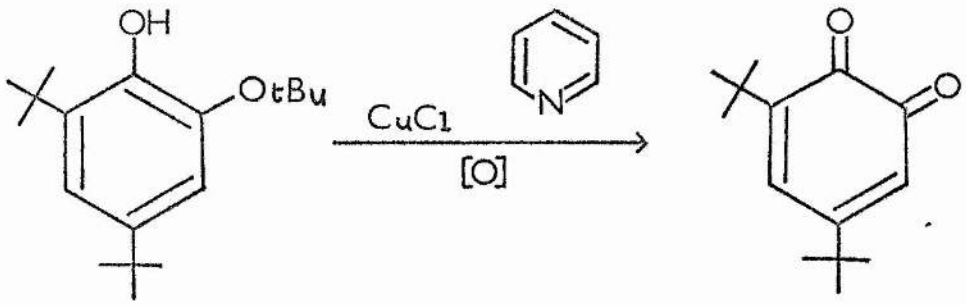
$R_1=R_4=H$, $R_2=R_3=Me$. Ref. 31.

See also references 29-43.

Other oxidising agents such as dichromate[31,44,45,46], lead dioxide[37,41,47,98], lead tetraacetate[48], sodium nitrate[49] and iodine[50,51] have been used occasionally.

Formation of o-quinones by air oxidation has been studied by several workers. Thus 3,5-diamino-1,2-benzoquinone[52], 4,5-diamino-1,2-benzoquinone[53], and 3,5-

diamino-6-hydroxy-1,2-benzoquinone[46] have been prepared by air oxidation of the corresponding catechols in ammonia solution. Metal salts in the presence of alkaline aqueous methanol have been used to catalyse air oxidation. Thus 3,5-ditertiarybutyl-catechol has been oxidised to the quinone[54,55], and 4-methyl-catechol has yielded the quinone as a transient product[56]. 3,5-Ditertiarybutyl-1,2-benzoquinone has been prepared from the catechol using a copper/amine complex as catalyst[57]. 3,5-Ditertiarybutyl-1,2-benzoquinone has also been prepared from 2-tertiarybutoxy-4,6-ditertiarybutylphenol by the action of a cuprous chloride/pyridine catalyst in an atmosphere of oxygen[62].

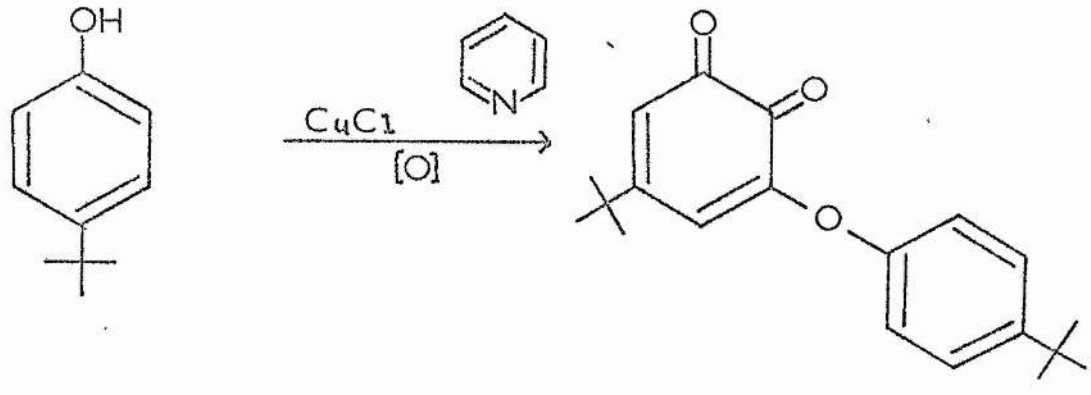


Horner and Dürckheimer[25,58,59] pioneered the use of o-chloranil as an oxidising agent for catechols. This is an extremely versatile reagent which can be used to prepare quinones, that have lower redox potentials and solubilities, at low temperature. Thus a solution of o-

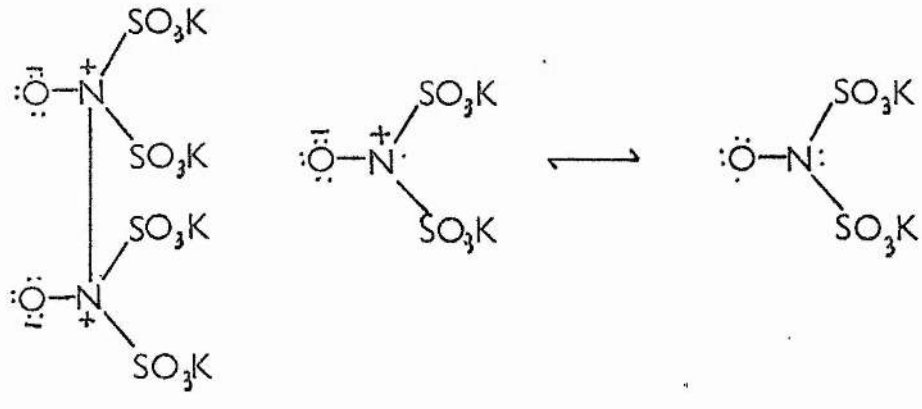
chloranil in dry ether will oxidise catechol in the same solvent, at -25 to -30°C, to give 1,2-benzoquinone which precipitates from the solution.

The oxidation of phenols to quinones can be effected by several reagents. Historically, the first use of this method was the preparation of 4-triphenylmethyl-6-chloro(or bromo)-1,2-benzoquinone from 2,6-dichloro-4-triphenylmethylphenol[60] (or the dibromo- compound) using nitric acid in acetic acid solution. Rocklin[61] has since applied this method to pentachloro- and pentabromo- phenols to give the corresponding tetrahalo-1,2-quinones. A wide range of solvents can be used and the concentration of nitric acid is not important as long as it is substantially in excess of the theoretical amount. Copper/amine catalysts have been used to oxidise phenols in an atmosphere of oxygen[63]. Thus 4-tertiarybutylphenol yields 3-(p-tertiarybutylphenoxy)-5-tertiarybutyl-1,2-benzoquinone when treated with a cuprous chloride/pyridine complex in an oxygen atmosphere. The same result can be obtained using cupric chloride in the place of the cuprous salt and morpholine in the place of pyridine.

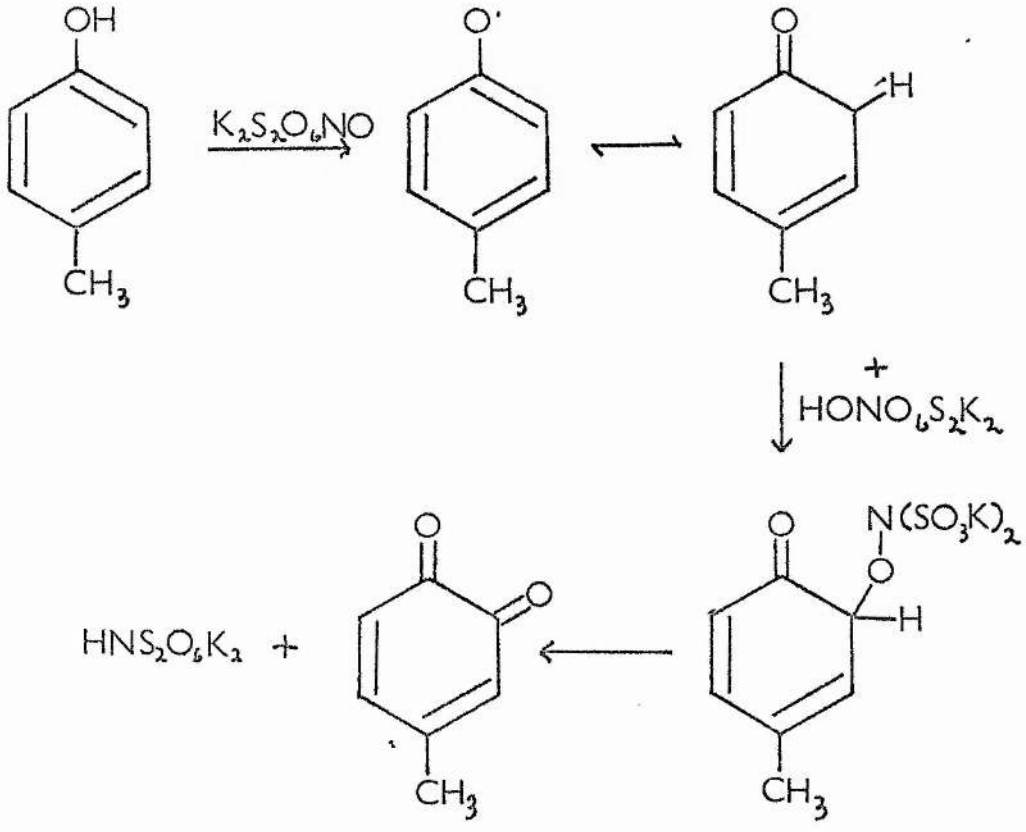
The most versatile and synthetically useful re-



agent for phenol oxidation is potassium nitrosodisulphonate (Fremy's salt). In the solid state, this is an orange/yellow dimer which is known to detonate spontaneously. However, if prepared by the method of Harvey and Hollingshead[64] and carefully dried, it can be stored indefinitely. Fremy's salt is used in buffered aqueous solution under which conditions it exists as a stable purple radical. The reagent was first used for 1,2-quinone synthesis by Teuber and Rau[65]. It has since

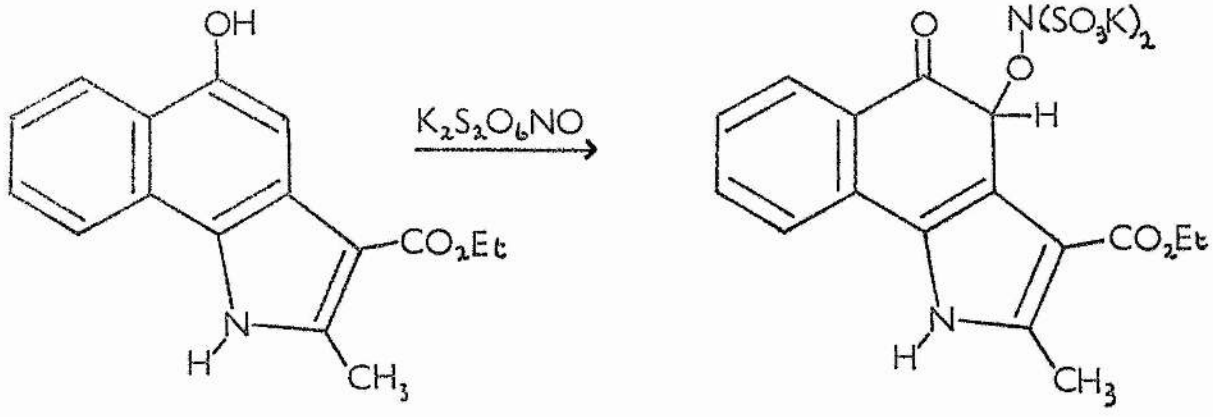


been shown to be widely applicable to p-blocked phenols[66-72], side chains being unaffected. It is necessary to employ p-blocked phenols, thus limiting its usefulness to 4-substituted 1,2-quinones, as 1,4-quinones will result if the para position is free. Teuber and Götz[68] showed that a three-step process was involved in the oxidation as suggested in scheme 'A'. This mechanism was substantiated by isolation



Scheme 'A'

of the intermediate (II) in the oxidation of (I)[69]. Further evidence in favour was obtained by using Fremy's salt



(I) (II).

with the nitroso group labelled with ^{18}O [73]. It was found that the labelled oxygen was incorporated into the quinone, though a certain amount of exchange with the solvent occurred in the preparation of o-quinones. (No such exchange was observed in the p-quinone system.)

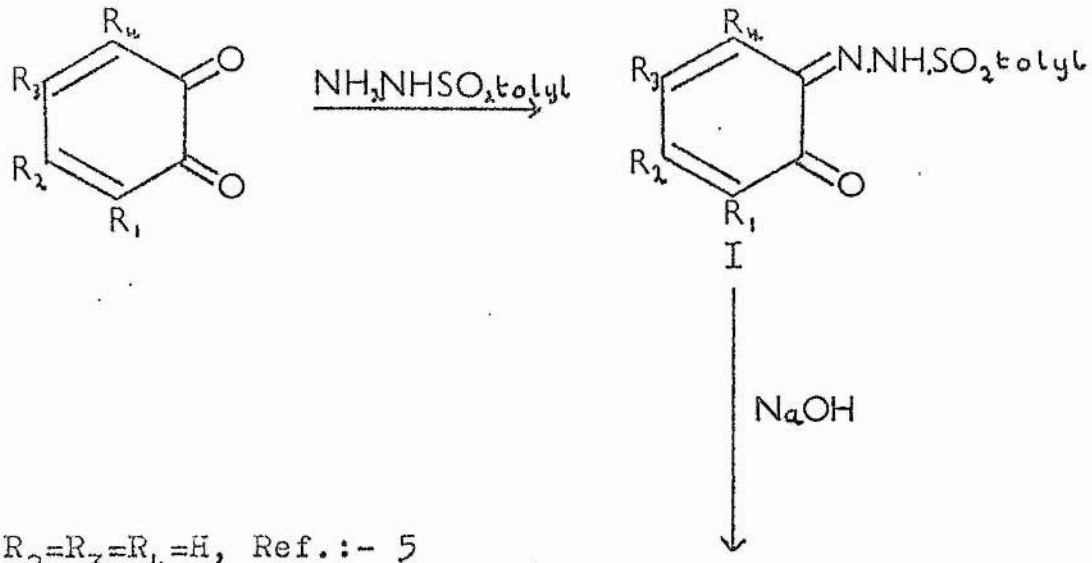
The work in this thesis used pre-prepared crystalline quinones throughout in contrast to earlier work in which quinones generated 'in situ' were often used. Except in one case, (4-methyl-1,2-naphthaquinone) these were prepared from the catechols by the method of Horner et al using o-chloranil, or from the phenols by the method of Teuber et al. Most 1,2-benzoquinones dimerise and polymerise if allowed to stand at room temperature.

However, it was found possible to store all the quinones used, for long periods, in solid carbon dioxide.

Previous work on the reactions of amines with 1,2-quinones

The presence of the conjugated carbonyl system in 1,2-benzoquinone allows two types of uncatalysed nucleophilic attack by amines to take place. These are direct attack on the carbonyl groups (i.e. at the 1 and 2 positions) and attack at the 4 and 5 positions to give Michael (conjugated) addition products. Both types of reaction are well known, the site of attack apparently depending mainly on the amine used.

Direct attack on the carbonyl groups is comparitively rare, having been reported only for α,β-diamines, hydrazine derivatives and primary aliphatic amines. Very little work has been done with the parent quinone, most workers having used the more stable substituted quinones. While hydrazine itself has been shown to reduce quinones[74], substituted hydrazines attack at one of the carbonyl positions to give hydrazones. Thus McPherson and Lucas[75] reacted benzoylphenylhydrazine with 1,2-benzoquinone to give benzoyl-o-hydroxyazobenzene. Several workers have reacted toluene-p-sulphonylhydrazine with various 1,2-benzoquinones to give hydrazones (I)[76,77,78]. Under the influence of base these decompose to give the diazo-oxides (II). Similar products (III) were obtained by



I

R_1=OMe, R_2=R_3=R_4=H, Ref.:- 5

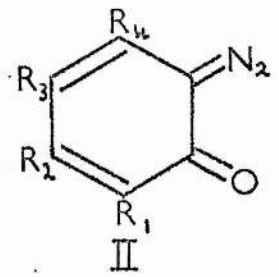
R_2=OMe, R_1=R_3=R_4=H, Ref.:- 5

R_2=Cl, R_1=R_3=R_4=H, Ref.:- 5

R_2=Me, R_1=R_3=R_4=H, Ref.:- 5

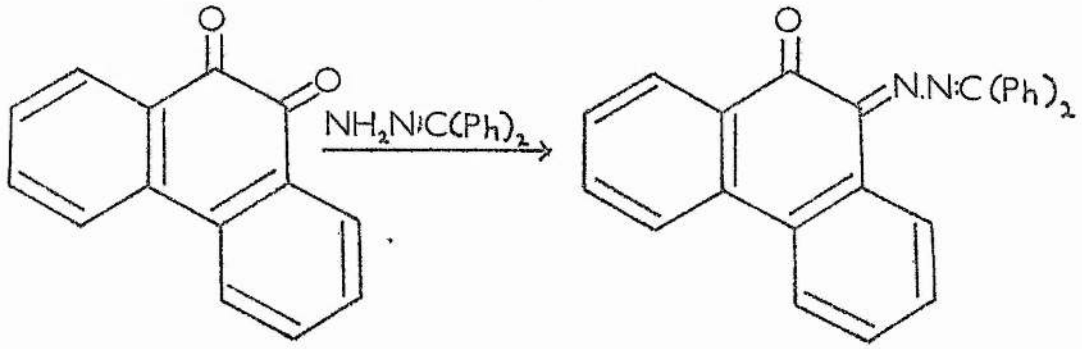
R_1=R_4=H, R_2=R_3=Me, Ref.:- 4

R_2=R_4=H, R_1=R_3=t-butyl, Ref.:- 3,4



II

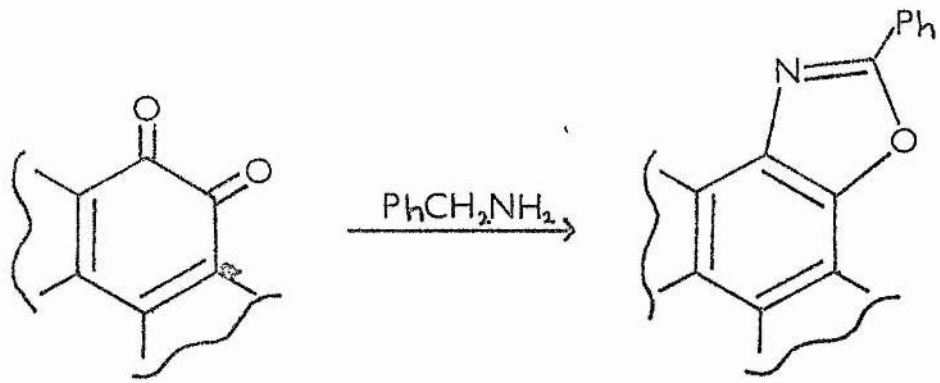
warming aromatic ketohydrazones with 1,2-quinones[79] in dry benzene or other hydrocarbon solvent.



III

Attack on the carbonyl function has also been

observed with primary aliphatic amines. McCoy and Day[80] obtained oxazoles (IV) when treating phenanthraquinone or retenequinone with primary aliphatic amines having two alpha hydrogen atoms. Similarly, Corey and Achiwa[81] obtained the oxazole by reacting benzylamine with 3,5-di-tertiarybutyl-1,2-benzoquinone. With other aliphatic

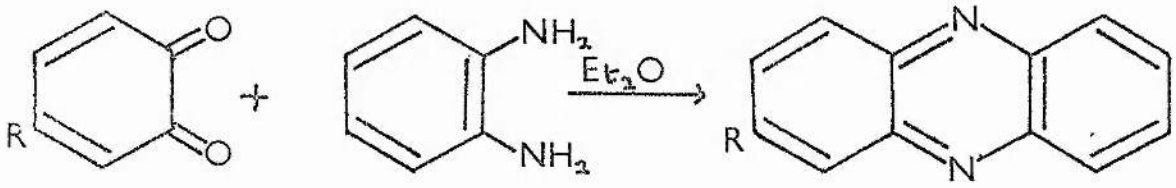


IV

amines, they obtained the Schiff's bases, which were not isolated, giving the corresponding aldehydes on acid hydrolysis. McCoy and Day similarly obtained benzaldehyde on hydrolysis of the intermediate in the retenequinone/benzylamine reaction.

In all these cases, only one carbonyl group has been attacked, probably for steric reasons. The only reports of double attack occurring are when diamines are used.

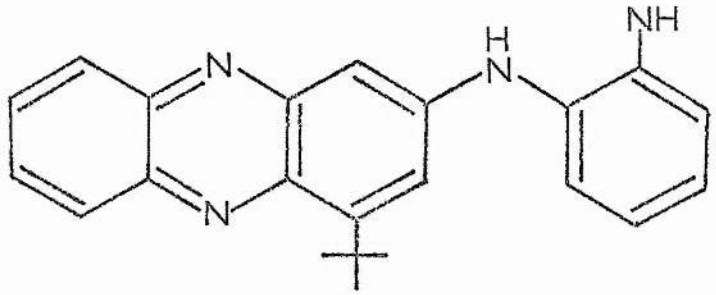
Ethylenediamine is known to form a pyrazine with retenequinone, but most work has been carried out with aromatic o-diamines such as o-phenylenediamine and its derivatives. Kehrmann and Mermod[82] treated 1,2-benzoquinone and 4-methyl-1,2-benzoquinone with o-phenylenediamine. The reactions were carried out in sodium-dried ether, in the presence of sodium sulphate to remove any water produced, giving good yields of phenazine and 2-methylphenazine (V)



R = H or CH_3 V

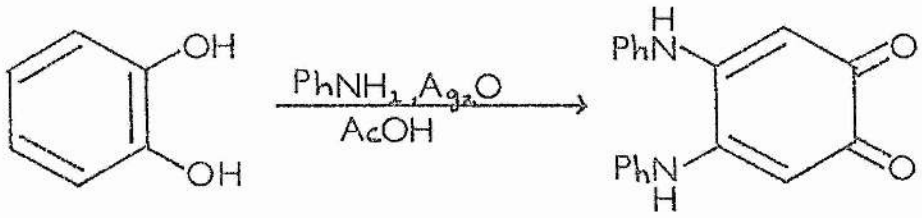
respectively. Many phenazine derivatives have since been made by the same general method in a variety of solvents refs. [83-96,63,67]. Occasionally, abnormal reactions occur. Thus, while dimeric 4,5-dimethyl-1,2-benzoquinone will react with pyrimidine derivatives to give diazophenazines, the monomer, with its higher redox potential, will not[94]. Similarly, 3,5-diacetamino-1,2-benzoquinone is reduced by o-diamines[82]. 5-Methoxy-3-tertiarybutyl-1,2-benzoquinone undergoes simultaneous attack at the carb-

onyl groups and at the 5 position to give 1-tertiarybutyl-3-(o-aminophenyl)aminophenazine (VI)[96].



VI

Attack at the 4 and 5 positions of 1,2-quinones can be brought about by various amines to give mono- or di-substituted quinones. Reactions reported have invariably been carried out using quinones generated in situ by several different means. Kehrmann and Cordone[83] treated a mixture of catechol and aniline in glacial acetic acid with silver oxide to give 4,5-dianilino-1,2-benzoquinone (VII). Maclaurin and Jackson[97] isolated several products from the reaction of aniline on o-chloranil in ethanol solution. They obtained dianilinodichloro-1,2-benzoquinone, ethyl alcohol-dianilinodichloro-1,2-benzoquinone and dianilinodichloro-1,4-benzoquinone-mono-anil. When the aniline dianilinodichloro-1,2-benzoquinone was recrystallized from petrol, dianilinodichloro-



VII

1,2-benzoquinone was obtained. This compound formed addition products with aniline and ethanol. Bernardi[98] obtained mono- and di-aryl derivatives of 1,2-benzoquinone using lead dioxide to oxidise catechol in the presence of aniline and substituted anilines. Di-p-methylanilino, di-p-chloroanilino and di-p-bromoanilino 1,2-benzoquinones have been prepared using sodium iodate to oxidise catechol [92,93,95]. 4,5-Dianilino-1,2-benzoquinone and the mono-anil have also been prepared by treating an aniline/catechol mixture, in acetone, with potassium ferricyanide[99].

Formation of quinones from catechols and phenols by enzymic oxidation has also been employed. Thus Wagreich and Nelson[100] treated catechol with tyrosinase in the presence of aniline to give 4,5-dianilino-1,2-benzoquinone. Similar products were obtained by Pugh and Raper[101] using tyrosinase to oxidise catechols and phenols. Deutscher and Wagreich[102] treated phenols and catechol

with tyrosinase in the presence of air and aniline to give unspecified dyes. The same products, which were presumably 4,5-dianilinoquinones, were obtained using p-chlorophenols in place of the unsubstituted compounds.

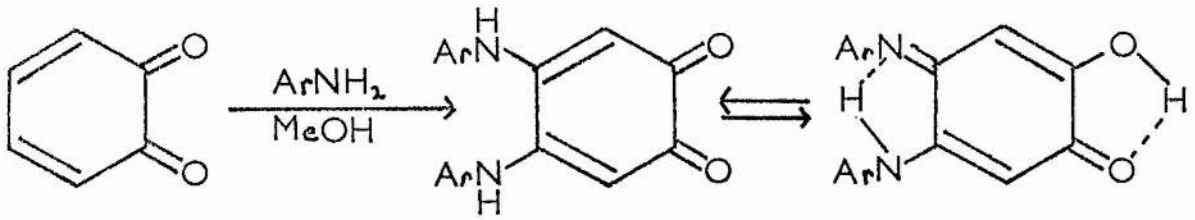
Aliphatic amines have also been added to 1,2-benzoquinones generated in situ. Thus König and Letsch[103] and Vasil'eva and Berlin[103] have obtained mono- and di-amino derivatives of o-benzoquinone by silver oxide oxidation of catechol in the presence of bis-2-hydroxyethylamine. Horner and Lang[104], using the same oxidising agent, obtained mono- and di- amino derivatives with ethylene-imine, dimethylamine and N-methylaniline. Brackman and Havinga[105] obtained 4,5-dimorpholino-1,2-benzoquinone by stirring catechol and morpholine together in an atmosphere of oxygen. The same product could be obtained from phenol in the presence of cupric nitrate.

Reaction of aniline and substituted anilines with 1,2-benzoquinone

Earlier workers have studied the reactions of aniline and its derivatives with in situ generated 1,2-benzoquinones (see references: 83,92,93,95,98,99,100,101,

102 and 103). This section of the present thesis describes a reinvestigation of the reaction using crystalline 1,2-benzoquinone that had been prepared previously by the method of Willstäter[29].

A solution of 1,2-benzoquinone and aniline in methanol was stirred for several hours then allowed to stand overnight. Addition of water precipitated red/brown 4,5-dianilino-1,2-benzoquinone having the same melting point as the product obtained by Barry et al[95]. The corresponding diarylamino compounds (VIII) were obtained when aniline was replaced by p-bromo-, p-chloro- or p-methoxyaniline. T.L.C. examination showed the presence



VIII

a) Ar=C_6H_5 b) Ar=p-OMe-C_6H_4 c) Ar=p-Cl-C_6H_4
d) Ar=p-Br-C_6H_4

of small quantities of the corresponding mono-anils of 2,5-diarylamino-1,4-benzoquinone (IX) which could not be

removed by crystallisation. Purification was effected by preparative scale T.L.C. on silica gel plates using chloroform as eluant. With o- and p-nitroaniline, no products were isolated presumably due to these compounds being weaker nucleophiles.

IX

a) Ar=Ph b) Ar=p-MeO-C_6H_4 c)Ar=p-Cl-C_6H_4 d) Ar=p-Br-C_6H_4

Table I

Compound	λ_{max}	logε	λ_{max}	logε	λ_{max}	logε	λ_{max}	logε
VIIIa	265	4.12	310	4.15	424	3.59	480	3.53
VIIIb	267	4.10	305	4.17	458	3.81	500	3.73
VIIIc	273	4.22	286	4.20	395	3.86	490	3.51
VIIId	277	4.15	285	4.15	392	3.84	500	3.24

Wavelength in mμ, ε in litre mole^{-1}cm^{-1}

The ultra violet spectra of the four diarylamino compounds are very similar having four absorption

maxima (Table I).

The infra red spectra show absorption characteristic of the N-H group at 3150-3250 cm^{-1} having no other readily assignable signals.

The n.m.r. spectra of compounds VIIIa-c are qualitatively similar (Table 2). Due to low solubility, it was not possible to record the spectrum of VIIId. The assignment of the absorptions are as follows: the singlet

Table 2

Compound	Aryl protons	Quinonoid protons	Alkyl protons
VIIIa	2.5-3.05τ (m,12H)	3.95τ (s,2H)	
VIIIb	2.7-3.2τ (m,10H)	3.95τ (s,2H)	6.20τ (s,6H)
VIIIc	2.8τ (s,10H)	3.95τ (s,2H)	

at 3.95τ, which integrates to two protons, is due to the protons of the quinonoid ring; the multiplets at 2.5-3.5τ and 2.7-3.2τ, in the spectra of VIIIa and VIIIb respectively, are due to superimpositions of the signals from the aryl protons and those carried by the nitrogen atoms, in VIIIc, the same protons give rise to a broad singlet; the methoxy protons of VIIIb are seen as a singlet at 6.20τ.

When ether was used as solvent instead of meth-

anol, the major products were different.

A solution of aniline and 1,2-benzoquinone in ether was allowed to stand for 24 hours. After filtration, the solvent was stripped under vaccuum to give a red solid which, on trituration with a little ether, yielded the brown mono anil of 2,5-dianilino-1,4-benzoquinone (IXa). The corresponding anils were obtained when p-chloro-, p-bromo- or p-methoxyaniline was used in place of aniline. The compounds were contaminated with small quantities of the diarylamino compounds (VIII) from which they were separated by T.L.C.

The ultra violet spectra, which are very similar, differ from those of the products obtained in methanol having only three maxima (Table 3). The infra red

Table 3

Compound	λ_{max}	logε	λ_{max}	logε	λ_{max}	logε
IXa	278	4.30	382	4.19	523	3.18
IXb	277	4.27	403	4.11	545	3.41
IXc	286	4.23	385	4.04	520	3.23
IXd	286	4.23	387	4.04	521	3.20

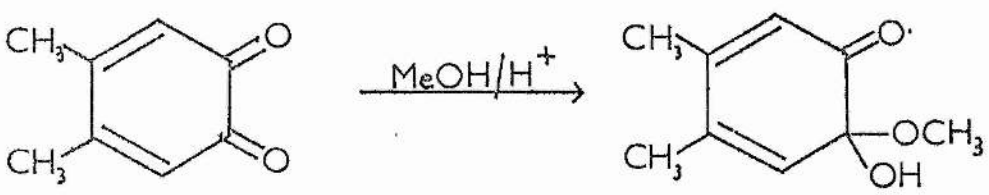
Wavelength in mμ, ε in litre mole^{-1}cm^{-1}

spectra show few readily assignable bands, with the exception of peaks at 3190-3300 cm^{-1} due to the N-H group.

N.m.r. spectra could only be obtained for IXa and IXb due to the low solubility of the other two compounds. In IXa, the protons of the aromatic rings and those on nitrogen give rise to a multiplet at 2.4-3.05τ correctly integrating to 17 protons. A corresponding multiplet at 2.7-3.3τ, integrating to 14 protons, is seen in the spectrum of IXb. A singlet at 3.86τ, integrating to 2 protons, in the spectrum of IXa is assigned to the quinonoid protons. These give rise to two singlets, at 3.88τ and 4.05τ, in a 1:1 ratio, in the spectrum of IXb. The methoxy protons of IXb are seen as two singlets at 6.20τ and 6.25τ. The two signals, which have the required overall integration of 9 protons and are in a 2:1 ratio, show that one group is in a slightly different environment from the other two. This is as expected from the structure of the product.

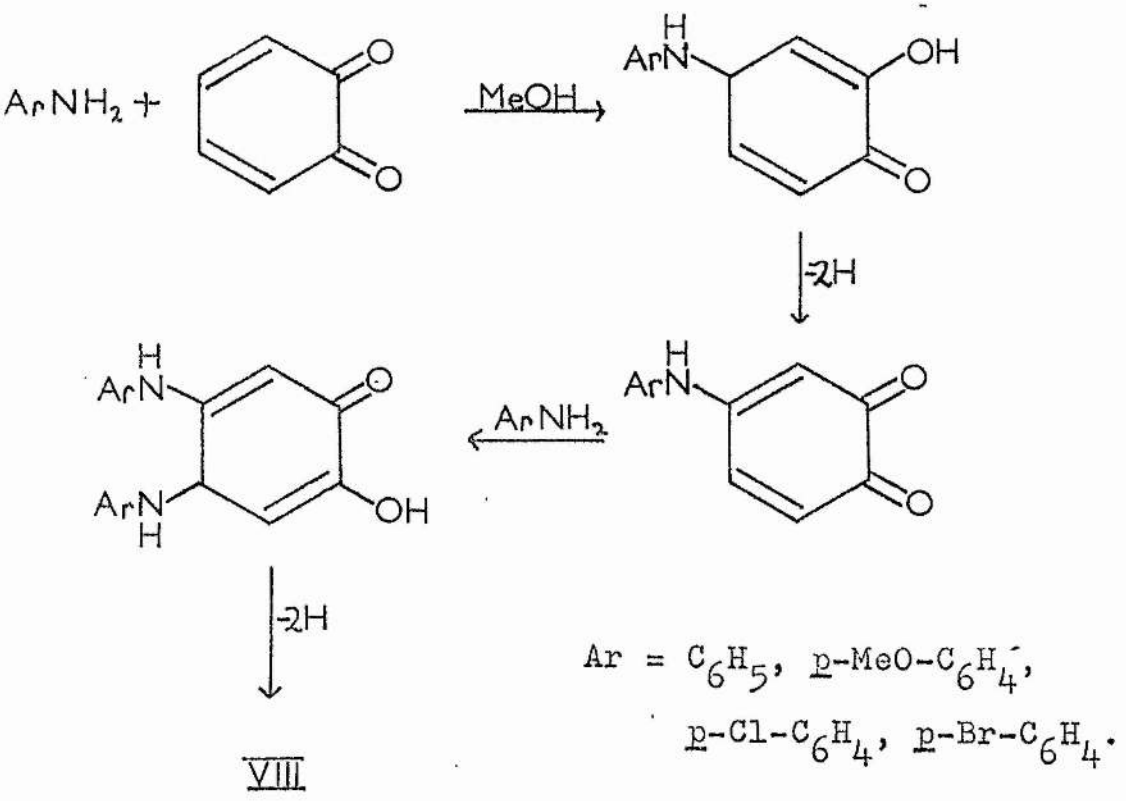
It is probable that the dramatic change in the proportions of the two types of product, with change of solvent, is due to acetal formation in methanolic solution. In ether, initial attack occurrs at the carbonyl

position to give the appropriate 1,2-benzoquinone monoanil, which probably remains as the anil hydrate. This makes attack at the remaining carbonyl group difficult, so that subsequent addition occurs at the Michael position. In methanol, acetal formation will make attack at the carbonyl groups unfavourable, so that we obtain mainly the adducts resulting from Michael addition. Hemiketals have previously been suggested as intermediates in nucleophilic attack on quinones. It is known that 1,2-benzoquinone reacts with aliphatic alcohols, in the presence of mineral acids as catalysts, to give substituted 1,4-benzoquinones[106,107,108]. Hemiketals are thought to be important intermediates in these reactions. Horner and Gowecke[106] provided good evidence for such intermediates, in acid catalysed reactions, by isolation of the hemiacetal (X) in 81% yield, from the reaction of methanol with 4,5-dimethyl-1,2-benzoquinone.



X

3:2 and 3:3 molar ratios of 1,2-benzoquinone to amine are required for the formation of adducts VIII and IX respectively. The 'extra' 2 moles of quinone required, above the stoichiometric amounts, are necessary to oxidise the initial adducts. Formation of VIII proceeds via an addition/oxidation process as shown in scheme 'B'.



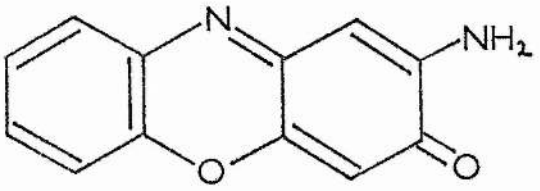
Scheme 'B'

Evidence for this scheme comes from the work of Adams, Hawley and Feldberg[109]. They reacted o-aminobenzoic acid and aniline with 4-methyl-1,2-benzoquinone (generated in

situ by electrochemical oxidation of the catechol) to give 1,4 addition products. By following the reaction electrochemically, they found it proceeded in a similar manner to that described in scheme 'B'. The first step was addition of the amine to the quinone to give the substituted 4-methylcatechol. This then underwent oxidation to give the corresponding quinone. They also found that substitution by the amines reduced the redox potential of the quinone, as is necessary for scheme 'B' to be viable. Formation of IX follows a similar route. In this case, the initial step is formation of the mono anil which then undergoes conjugate addition in a manner analogous to that set out in scheme 'B'.

Reaction of o-aminophenol with 1,2-benzoquinone

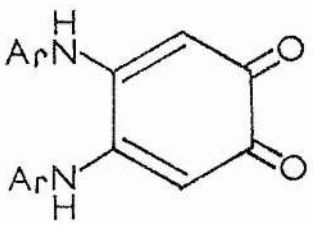
A solution of o-aminophenol in anhydrous ether was stirred for 24 hours with a solution of 1,2-benzoquinone in the same solvent. After filtering free of the polymer produced and stripping the solvent under vaccuum, the crude pruduct was chromatographed on alumina to give 3-aminophenoxaz-2-one (XI). This had an identical melting point and infra red spectrum to those published by Ikekawa et al[110]. The high resolution mass spectrometric



XI

measurement on the parent ion gave an m/e value of 212.0588 compared with a theoretical value of 212.0586.

The reaction was repeated using methanol as solvent in place of ether. After allowing the reaction mixture to stand overnight, the solvent was stripped under vacuum before adding a mixture of acetic anhydride and pyridine. After standing for two days, 4,5-di-(o-acetoxyanilino)-1,2-benzoquinone (XII) was filtered off as an orange solid.



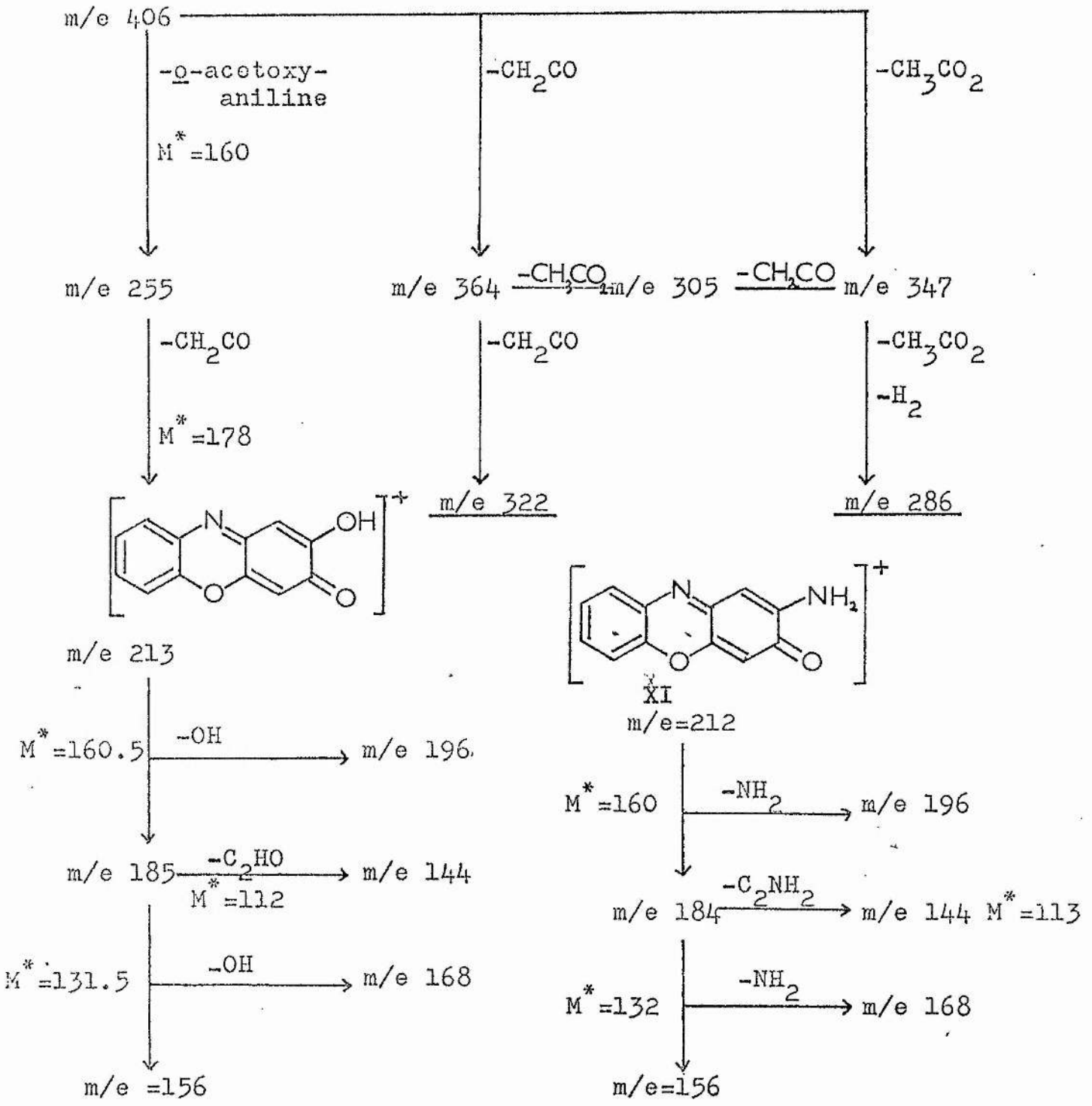
Ar = o-CH_3.CO.O.C_6H_4

XII

The ultra violet is similar to those of compounds VIIIa-d showing four absorption maxima at 246mμ

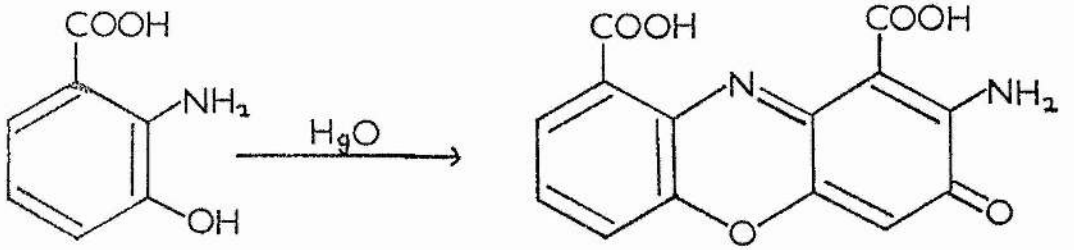
($\log\varepsilon$ = 4.18), 360mμ ($\log\varepsilon$ = 4.12), 450mμ ($\log\varepsilon$ = 3.96) and 500mμ (inflection). The infra red spectrum shows absorption at 1770 cm^{-1} (acetyl carbonyl) and 1640 cm^{-1} (quinonoid carbonyl) together with a broad absorption centred at 1160 cm^{-1} (C-O-C linkage). No strong N-H absorption is obtained presumably due to hydrogen bonding with the acetyl groups. The mass spectrum gives the major structural information. The parent ion, which is weak, was shown by high resolution to have an m/e ratio of 406.1163 compared with a theoretical value of 406.1165 for $C_{22}H_{18}N_2O_6$. The spectrum shows the expected losses of acetyl and acetoxy groups, but the first major fragmentation is loss of an o-acetoxyanilino group. The ion thus formed undergoes loss of acetyl and cyclisation to give the 3-hydroxyphenoxaz-2-one ion. Evidence for the last ion is obtained by comparison of the spectrum from this point with that obtained from 3-aminophenoxaz-2-one (XI) when the two are seen to be qualitatively almost identical. A breakdown scheme for the major ions obtained is given in scheme 'C'.

Compound XII is formed by Michael addition of o-aminophenol to the quinone, as shown in scheme 'B', followed by acetylation by the acetic anhydride/pyridine


m/e 406
-o-acetoxy-aniline
M* =160
-CH2CO
-CH3CO2
m/e 255
m/e 364
-CH3CO
m/e 305
-CH2CO
m/e 347
-CH2CO
M* =178
-CH2CO
-CH3CO2
-H2
m/e 322
m/e 286
m/e 213
XI
m/e=212
M* =160.5
-OH
m/e 196
M* =160
-NH2
m/e 196
m/e 185
-C2HO
m/e 144
M* =112
m/e 184
-C2NH2
m/e 144
M* =113
M* =131.5
-OH
m/e 168
M* =132
-NH2
m/e 168
m/e =156
m/e=156

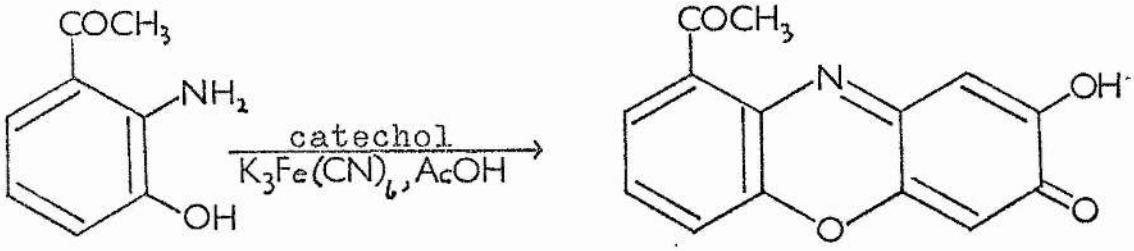
Scheme 'C'

mixture. XI is obtained by attack of a molecule of o-aminophenol on an other molecule that has previously been oxidised by 1,2-benzoquinone. XI has been obtained by other workers by direct oxidation of o-aminophenol with yellow mercuric oxide[111] and ultra violet light[110]. Eutenandt[112] has reported analogous products from the treatment of 3-substituted 2-aminophenols with oxidising agents. Thus, 2-amino-3-hydroxybenzoic acid (XIII) yields the 4,5-dicarboxylic acid of 3-aminophenoxaz-2-one (XIV) on treatment with mercuric oxide. If 2-amino-



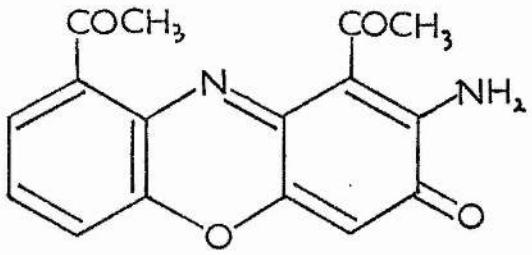
XIII XIV

3-hydroxy-acetophenone (XV) and catechol in acetic acid are treated with potassium ferricyanide, the product obtained is 3-hydroxy-5-acetyl-phenoxaz-2-one (XVI). This compound is formed by Michael addition of the aminophenol to 1,2-benzoquinone generated by ferricyanide oxidation of the catechol. If the oxidant is changed to tyrosinase, in an aqueous solution buffered to pH 6-8, 3-amino-4,5-



XV XVI

diacetyl-phenoxaz-2-one (XVII) is obtained. As tyrosinase is known to oxidise catechol to 1,2-benzoquinone, the product probably arises by an analogous manner to the formation of XI.



XVII

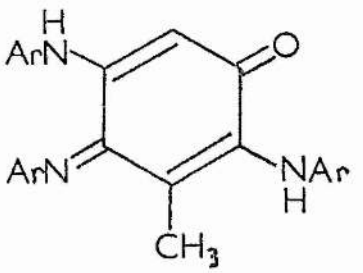
SECTION II

The Reactions of Alkyl Substituted 1,2-Quinones with Aniline and Substituted Anilines

Reactions of 3,5-dimethyl-1,2-benzoquinone with para-substituted anilines

The reactions of anilines with 1,2-benzoquinones having methyl groups in the 4 and/or 5 positions, where conjugate addition occurs, were studied in an attempt to force attack to occur at the carbonyl positions. p-Anisidine was used first as the methoxy protons give a convenient 'label' in the n.m.r. spectrum.

A solution of p-anisidine in methanol was added to a solution of 3,5-dimethyl-1,2-benzoquinone in the same solvent. After stirring for a few minutes, the flask was sealed and allowed to stand for three weeks. The crude product was filtered off and recrystallized from ethanol to give fluffy brown crystals of the mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-3(or 6)-methyl-1,4-benzoquinone (XVIIIa). When the



XVIII

a) Ar = p-MeO-C_6H_4

b) Ar = p-Cl-C_6H_4

reaction was repeated in ether, no isolable product was obtained.

XVIIIa has a sharp melting point and satisfactory C,H and N analysis. The infrared spectrum has an absorption at 3270 cm^{-1} showing the presence of the N-H group. The ultra violet spectrum is qualitatively similar to the spectrum of the mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone (IXb) having three major absorption maxima.

The n.m.r. spectrum shows a singlet at 8.37τ, integrating to three protons, due to the methyl group attached to the quinonoid nucleus. The protons of the three methoxy groups give rise to a close doublet at 6.25τ integrating to 9 protons in all. The two peaks are in the ratio of 2:1 showing two methoxy groups in a slightly different environment from the third as expected from the proposed structure. The single proton of the quinonoid ring gives a singlet at 3.9τ which integrates correctly, while the remaining protons give a multiplet at 2.4-3.3τ integrating to fourteen protons.

The mass spectrum gives a strong molecular ion at m/e 469, together with strong M+2 and M-1 ions. Loss of methyl gives rise to a fragment at m/e 454 while loss

of methoxy gives a fragment at m/e 438. The last two strong ions are the anisidine ion at m/e 123 and loss of methyl from this at m/e 108.

The reaction was repeated using p-chloroaniline in the place of p-anisidine giving the analogous product (XVIIIb). The product gave a satisfactory C, H and N analysis. The infra red spectrum shows the presence of N-H by a broad absorption at 3260 cm^{-1}. The ultra violet spectrum is very similar to that of the anil obtained from p-chloroaniline and 1,2-benzoquinone in ether (IXc).

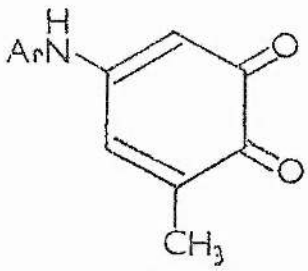
The n.m.r. spectrum showed a singlet at 8.30τ, integrating to three protons, due to the methyl group of the quinonoid ring. The proton of the quinonoid ring appears as a singlet, integrating to one proton, at 3.95τ. The remaining fourteen protons give rise to a multiplet at 2.6-3.3τ which integrates correctly.

The mass spectrum gives a strong parent with ions at m/e 481, 483, 485 and 487 in the ratio 27:27:9:1, as required for three chlorine atoms in the molecule. Loss of chlorine gives three strong peaks at m/e 445, 447 and 449 in the ratio 9:6:1.

The reaction of 3-methyl-1,2-benzoquinone with p-anisidine

The reaction of 3-methyl-1,2-benzoquinone with p-anisidine was carried out in order to gain further evidence for the structure of compounds XVIII. From the results obtained with unsubstituted 1,2-benzoquinone and aniline derivatives, the reaction of the 3-methylquinone with p-anisidine in ether would be expected to yield XVIIIa.

A mixture of 3-methyl-1,2-benzoquinone and p-anisidine, in the minimum quantity of ether, was stirred overnight. The crude product was filtered off and recrystallized from methanol giving dark needles which proved to be 4(or 5)-p-methoxyanilino-3-methyl-1,2-benzoquinone (XIX). When the solvent was stripped from the



XIX

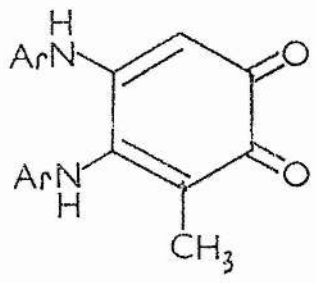
Ar = p-MeO-C_6H_4

filtrate, and the brown oil obtained chromatographed on alumina, a small quantity of XVIIIa was obtained as expected. This was identical to the sample from 3,5-di-

methyl-1,2-benzoquinone.

The infra red spectrum of XIX shows the presence of the N-H group by an absorption at 3160 cm^{-1}. The mass spectrum shows a strong molecular ion at m/e 243 and also a strong M+2 ion at 245. The loss of methyl from these gives strong peaks at m/e 228 and 230 respectively. The two peaks at m/e 123 and 108, which appear to be characteristic of p-anisidine substituted quinone rings, are also quite strong. Low solubility made it impossible to obtain an n.m.r. spectrum.

Though the reaction in ether did not yield the expected anil as the major product, the same reaction in methanol did yield the expected diarylamino compound. A solution of p-anisidine in methanol was added to a solution of 3-methyl-1,2-benzoquinone in the same solvent. After standing for 24 hours, filtration yielded the crude product. Recrystallization from methanol gave dark shiny



XX

Ar = p-MeO-C_6H_4

needles of 3-methyl-4,5-di-(p-methoxyanilino)-1,2-benzoquinone (XX).

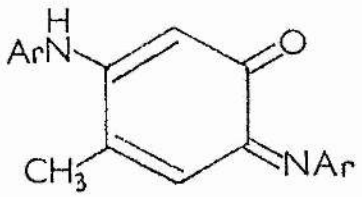
The product has a satisfactory C, H and N analysis. The presence of the N-H group is shown by an absorption at 3320 cm^{-1} in the infra red spectrum. The ultra violet spectrum is very similar to that of the dimethoxyanilino compound derived from benzoquinone itself (VIIIb) as expected from the structural similarity.

The n.m.r. spectrum showed a peak at 8.42τ, integrating to three protons, due to the methyl group on the quinonoid ring. The proton on this ring is seen as a further singlet, integrating to one proton, at 3.92τ. The two methoxy groups give rise to a singlet at 6.20τ integrating to six protons, while the remaining ten protons appear as two peaks at 3.07τ and 3.1τ which integrate correctly.

The mass spectrum shows a strong molecular ion at m/e 364. Strong peaks at m/e 349 and 333 come from loss of methyl and loss of methoxy respectively. The two peaks at m/e 123 and 108, due to anisidine and loss of methyl from ansidine, are also strong.

Reactions of 4,5-dimethyl-1,2-benzoquinone with para-substituted anilines

p-Anisidine was added to a solution of 4,5-dimethyl-1,2-benzoquinone in methanol. The mixture was stirred until all the amine had dissolved then set aside for 5 days. The purple solid obtained by stripping the solvent under reduced pressure was chromatographed on alumina to give the mono-p-methoxyanil of 5-(p-methoxyanilino)-4-methyl-1,2-benzoquinone (XXIa). When ether was used as solvent, no identifiable products were isolated.



XXI

a) Ar = p-MeO-C_6H_4

b) Ar = p-Cl-C_6H_4

The structure of the product, which had a satisfactory C, H and N analysis, was confirmed by spectroscopic means. The infra red spectrum has a strong absorption at 3320 cm^{-1} showing the presence of the N-H group. The n.m.r. spectrum shows a singlet at 7.65τ, integrating to three protons, due to the protons of the

methyl group remaining in the quinonoid ring. The two protons in the same ring give rise to two singlets at 3.42τ and 3.68τ each integrating to one proton. The two methoxy groups, which are in slightly different environments, give rise to a 1:1 doublet, centre 6.25τ, which integrates to six protons. The remaining nine protons give rise to a multiplet at 2.72-3.30τ which integrates correctly.

The mass spectrum shows a strong molecular ion at m/e 348 from which loss of methyl and methoxy groups give rise to ions at m/e 333 and 317 respectively. Loss of an anisidine group gives rise to an ion at m/e 226 while the anisidine group itself appears at m/e 123. The final major ion, at m/e 108, results from the elimination of a methyl group from anisidine.

The reaction was repeated replacing the p-anisidine by p-chloroaniline to give the analogous product (XXIb). The structure of the compound, which had a satisfactory C, H and N analysis, was again confirmed by spectroscopy. The infra red spectrum has a peak at 3305 cm^{-1} showing the presence of the N-H group. The n.m.r. spectrum shows a singlet at 7.70τ, integrating to three protons, due to the remaining methyl group of the quinonoid

ring. Only one of the ring protons now gives a clearly distinguishable signal, appearing as a singlet at 3.78τ. The other ring proton, together with the nine so far unaccounted for, makes up a multiplet at 2.6-3.5τ which integrates to ten protons as required.

The mass spectrum gives few strong ions. Strong molecular ions are seen at m/e 356, 358 and 360 in the approximate ratio of 9:6:1 as required for two chlorine atoms. Loss of one chlorine atom gives two peaks at m/e 321 and 323 in the ratio 3:1 in agreement with the presence of only one atom of chlorine.

Reactions of aniline and para-substituted anilines with 4-methyl-1,2-benzoquinone

A solution of p-anisidine in dry ether was added to a solution of 4-methyl-1,2-benzoquinone in the same solvent. After standing for 2 days, the crude product was filtered off and recrystallized from chloroform to give the dark brown mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone (IXb). This was identical in properties to that obtained from reacting 1,2-benzoquinone with p-anisidine in ether. When ether was replaced by methanol as solvent, the same product was

obtained. Replacement of p-anisidine by aniline and p-chloroaniline in turn yielded the corresponding anils (IXa) and (IXc) respectively in methanolic solution. All these products were identified by comparison with the samples obtained from 1,2-benzoquinone and the corresponding amine in ether.

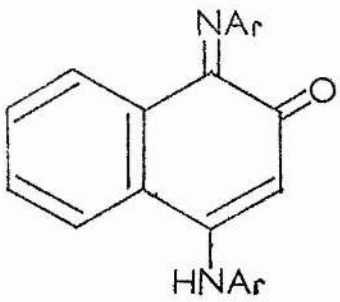
Reaction of p-anisidine with 4-ethyl-1,2-benzoquinone

A solution of p-anisidine in methanol was added to a solution of 4-ethyl-1,2-benzoquinone in the same solvent. After standing for 3 hours, the crude product precipitated was filtered off, a second crop was obtained after standing for 2 days. Recrystallization from methanol gave the dark brown mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone (IXb). The structure of the products was proved by comparison with a sample prepared from p-anisidine and 1,2-benzoquinone in ether.

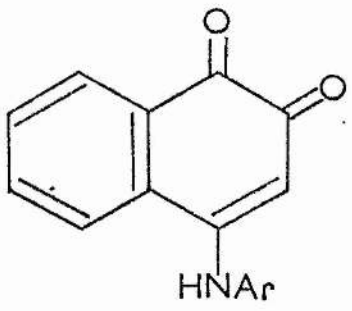
Reaction of p-anisidine with 4-methyl-1,2-naphthaquinone

A solution of p-anisidine in methanol was added to 4-methyl-1,2-naphthaquinone in methanol. After stirring for a short time and standing overnight, the crude product

was filtered off, a second crop being obtained after 24 hours. The product consisted of two components which were separated by column chromatography to give the mono-p-methoxyanil of 4-p-methoxyanilino-1,2-naphthaquinone (XXII) together with a small quantity of 4-p-methoxy-anilino-1,2-naphthaquinone (XXIII).



XXII



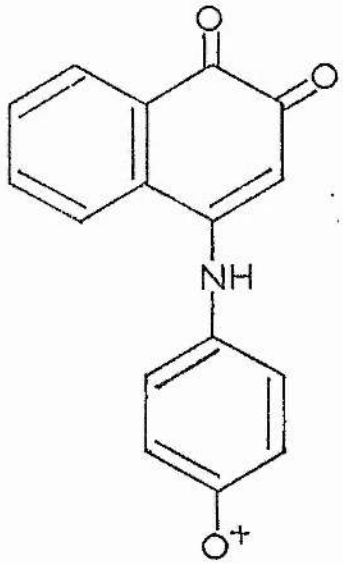
XXIII

Ar = p-MeO-C_6H_4

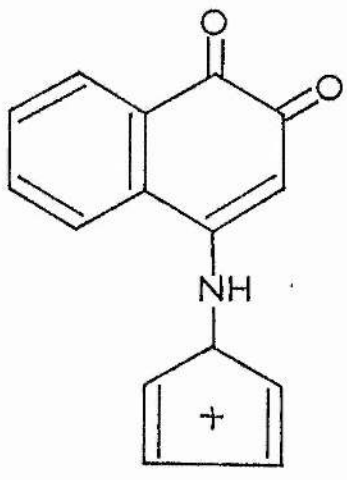
XXII has a sharp melting point. The infra red spectrum shows an absorption at 3310 cm^{-1} indicating the presence of the N-H group. The mass spectrum shows a strong parent ion which has an m/e value of 384.14738 under high resolution, as required for $C_{24}H_{20}N_2O_3$. Loss of methyl gives a strong ion at m/e 369. The next strong ion occurs at m/e 279 and is shown by high resolution to have the formula $C_{17}H_{13}NO_3$. This can only be explained by hydrolysis of the carbon-nitrogen double bond in the 1-position of the parent molecule, in the mass spectro-

meter. (The sample used was shown by t.l.c. to be free from compound XXIII). This ion eliminates methyl giving a further strong ion at m/e 264. It was not possible, due to low solubility, to obtain an n.m.r. of the compound.

The infra red spectrum of XXIII shows a broad N-H absorption at 3200 cm^{-1}. The mass spectrum shows a strong molecular ion which has an m/e value of 279.0895 under high resolution. This compares well with a theoretical value of 279.0897 for $C_{17}H_{13}NO_3$. The next major ion occurs at m/e 264 due to loss of methyl from the parent. A strong ion at m/e 236 is probably formed by elimination of CO from the remains of the anisidine ring giving a cyclopentadienyl ion as shown below.



m/e 264



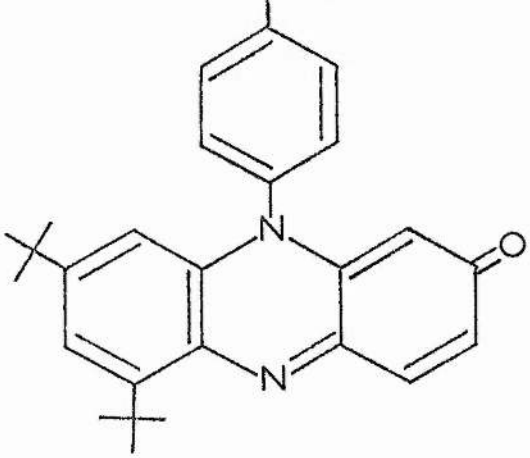
m/e 236

This compound is also too insoluble for an n.m.r. spectrum to be obtained.

Reaction of 3,5-ditertiarybutyl-1,2-benzoquinone with p-anisidine

Having observed elimination of methyl and ethyl groups from the 4-position of 1,2-quinones, the effect of substituting a tertiarybutyl group, which has no α-hydrogen, was tried to see if similar elimination would occur.

A mixture of 3,5-ditertiarybutyl-1,2-benzoquinone and p-anisidine in methanol was allowed to stand overnight. Purple crystals of 10-p-methoxyphenyl-6,8-ditertiarybutylphenaz-2-one (XXIV) were precipitated and filtered off.



XXIV

The infra red spectrum of XXIV does not show an absorption corresponding to N-H. A broad peak at 1250 cm^{-1} shows the presence of the C-O-C linkage. The n.m.r. spectrum shows 2 singlets at 8.3τ, integrating to eighteen protons, due to the two tertiarybutyl groups. The methoxy group gives rise to a singlet at 6.15τ which integrates to three protons. The remaining nine protons make up a correctly integrating multiplet at 2.5-3.2τ.

The mass spectrum shows a strong molecular ion having an m/e ratio of 414.231 by high resolution. This is as required for $C_{27}H_{30}N_2O_2$. Strong ions due to loss of methyl and methoxy are seen at m/e 399 and 383 respectively. Loss of ethane from these gives rise to two ions at m/e 369 and 353 respectively.

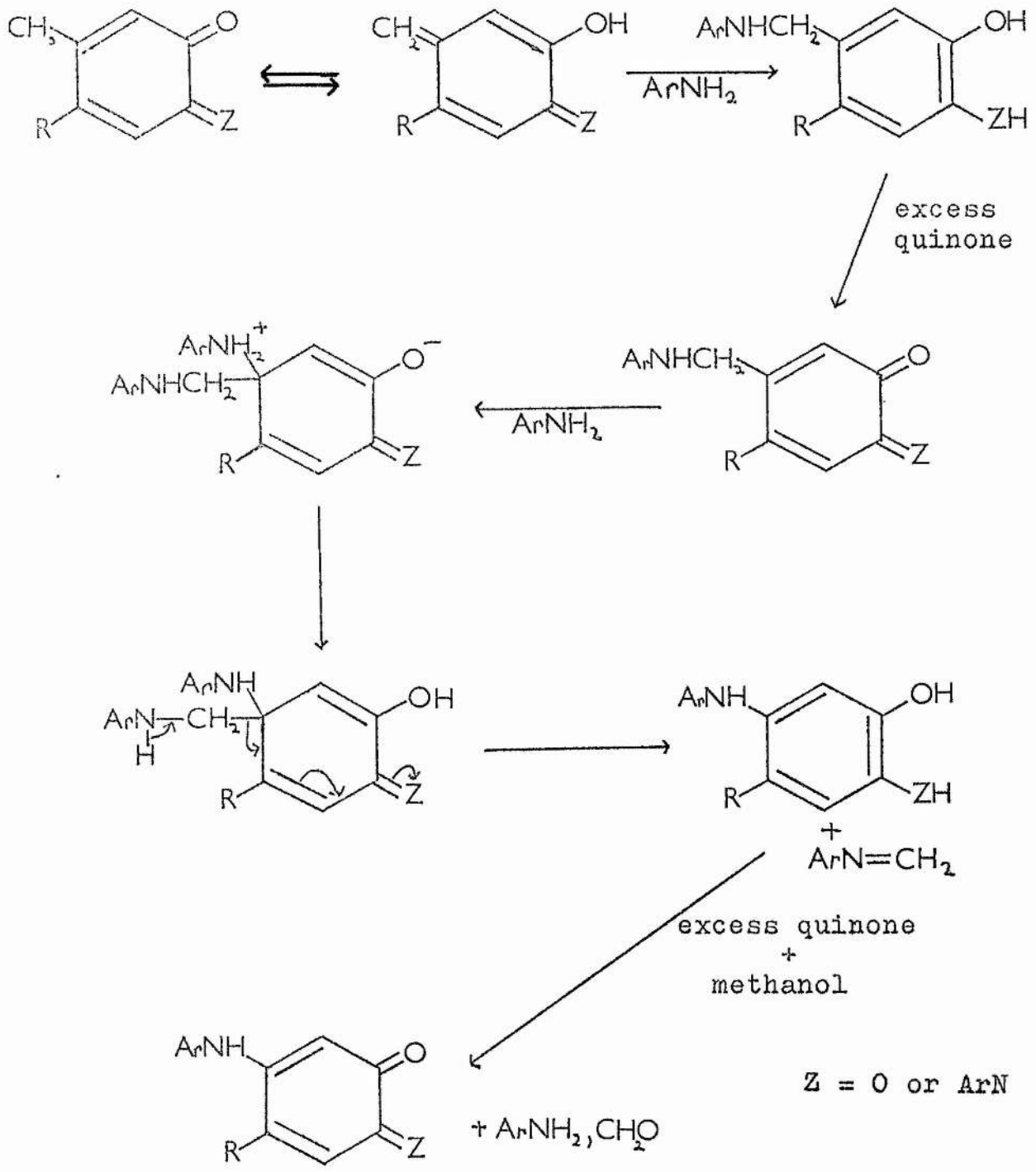
Mechanism of the dealkylation of substituted 1,2-quinones

Dealkylation of 1,2-benzoquinones, having methyl groups in the 4- and 5-positions, is readily brought about with anilines. Substitution by the amine at the dealkylated position always occurs. Displacement of an ethyl group also proceeds smoothly, but tertiary-butyl groups are not affected. In all cases where de-alkylation occurs, direct attack on one carbonyl group

also takes place giving an anil as the final product, e.g. XVIII.

The first step in the dealkylation is probably addition of the amine to a quinone methide or a quinone imine methide. This will have an arylaminomethyl group (Ar NH-CH_2-), which can be displaced, in the place of the methyl group, displacement of which seems inconceivable. The reaction path could then follow the route shown in scheme 'D'.

This route is supported by the observations previously noted. It is in agreement with the elimination of methyl and ethyl groups while a tertiarybutyl group, having no α-hydrogen, would not be expected to be displaced. The mechanism also predicts the elimination of secondary alkyl groups but this has not, as yet, been tested. Formaldehyde was detected in the reaction mixture by adding water, and distilling directly into a flask containing an alcoholic solution of dimedone in the presence of a catalytic amount of pyrimidine. After allowing to stand, long needles of the dimedone/formaldehyde addition product crystallized out. An attempt was made to synthesize 4-benzyl-1,2-benzoquinone in the hope of reacting this with p-anisidine.

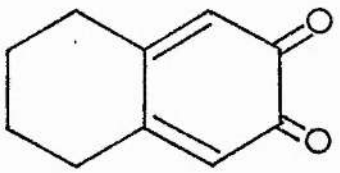


Z = O or ArN

Scheme 'D'

This would have given a much larger fragment which should have been detected as benzaldehyde. However, all synthetic routes tried failed to give the required quinone.

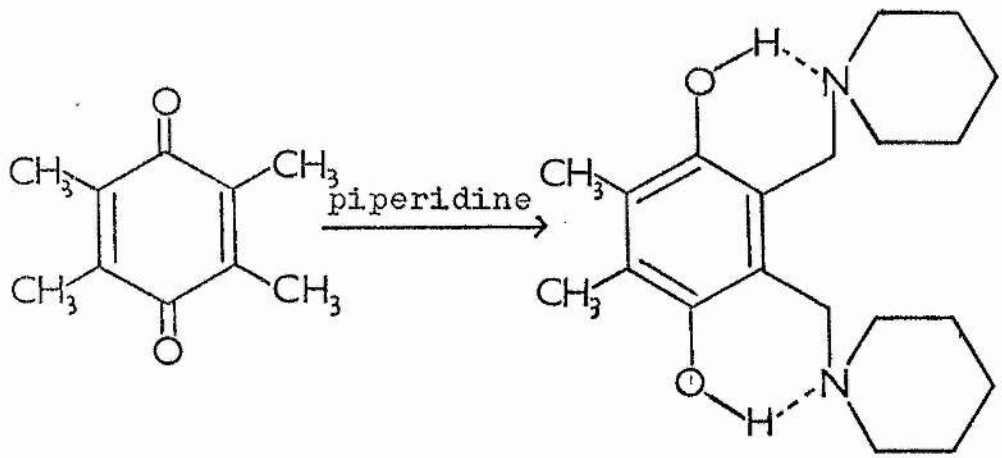
5,6,7,8-Tetrahydro-2,3-naphthaquinone (XXV) was synthesised and reacted with p-anisidine. The aim of this experiment was to cleave the ring between positions 5 and 10 with amination at position 10. It was hoped that by examination of the product, and in particular of the group at position 5, it would be possible to obtain further mechanistic evidence. A product was obtained from the reaction but it could not be thoroughly purified and though physical data were obtained on the impure product, identification was not possible.



XXV

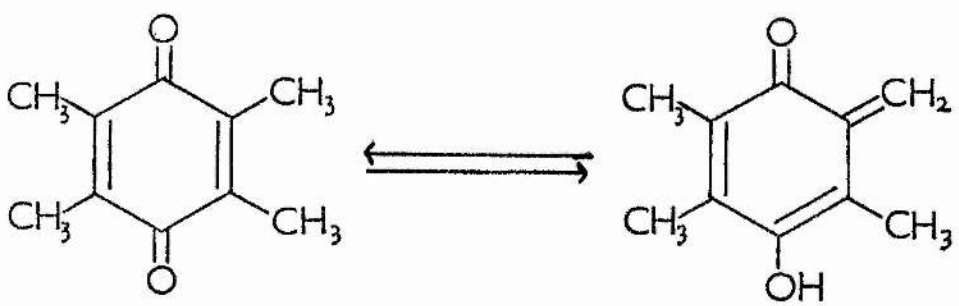
Though dealkylation has not been previously reported in the 1,2-benzoquinone series, evidence for the proposed mechanism is given in studies made with 1,4-benzoquinones. Cameron, Scott and Todd[113] obtained side

chain aminated products from methyl substituted 1,4-benzoquinones. Thus, duroquinone (XXVI), in the presence of excess piperidine, yields 2,3-dimethyl-5,6-bispiperidomethyl-quinol (XXVII) in 55% yield. Formation of



XXVI XXVII

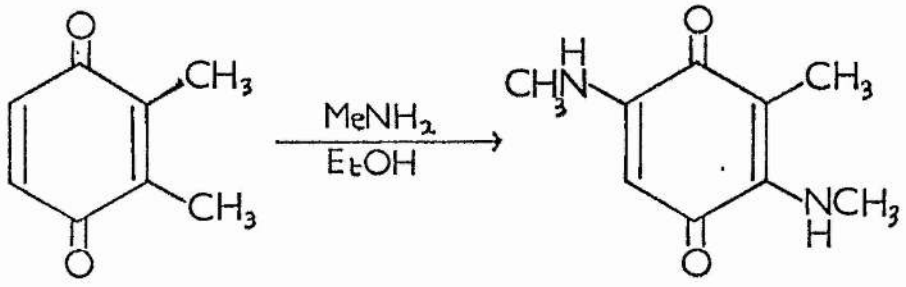
the product is thought to go via the tautomeric form (XXVIII) of duroquinone. This undergoes attack by the



XXVIII

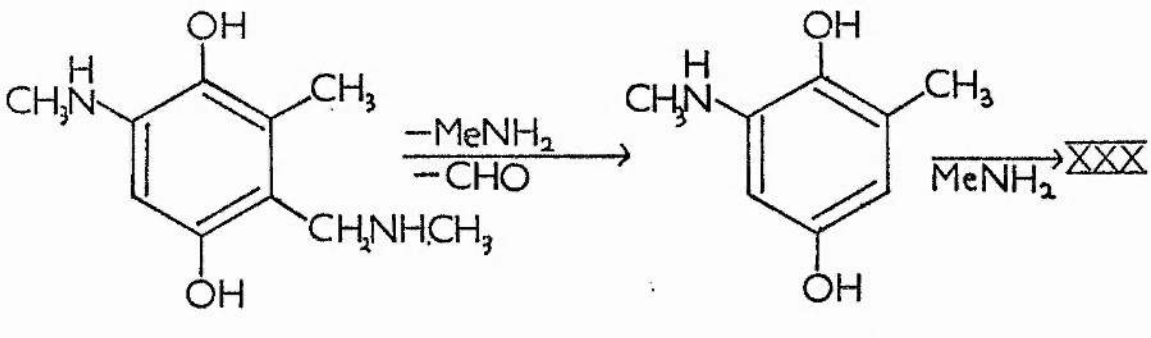
amine at the methylene group to give the 2-piperidomethyl-3,5,6-trimethyl-quinol. Oxidation and attack by a second molecule of amine then yields the product (XXVII). (In all cases reported, the quinol form, not the quinone, was obtained). This side chain amination gives good evidence for the possibility of a similar reaction occurring in the 1,2-benzoquinone series as required by the mechanism proposed.

Cameron and Scott[114] reported methyl elimination during amination of certain methyl substituted 1,4-benzoquinones using ethanolic methylamine. To obtain demethylation in this case, it is necessary to use quinones substituted in such a manner that direct attack on the nucleus to give the p-diamino quinone is not possible. Thus, o-xyloquinone (XXIX) with methylamine, yields 2-methyl-3,6-bismethylamino-1,4-benzoquinone (XXX). The mechanism proposed for the formation of the product is



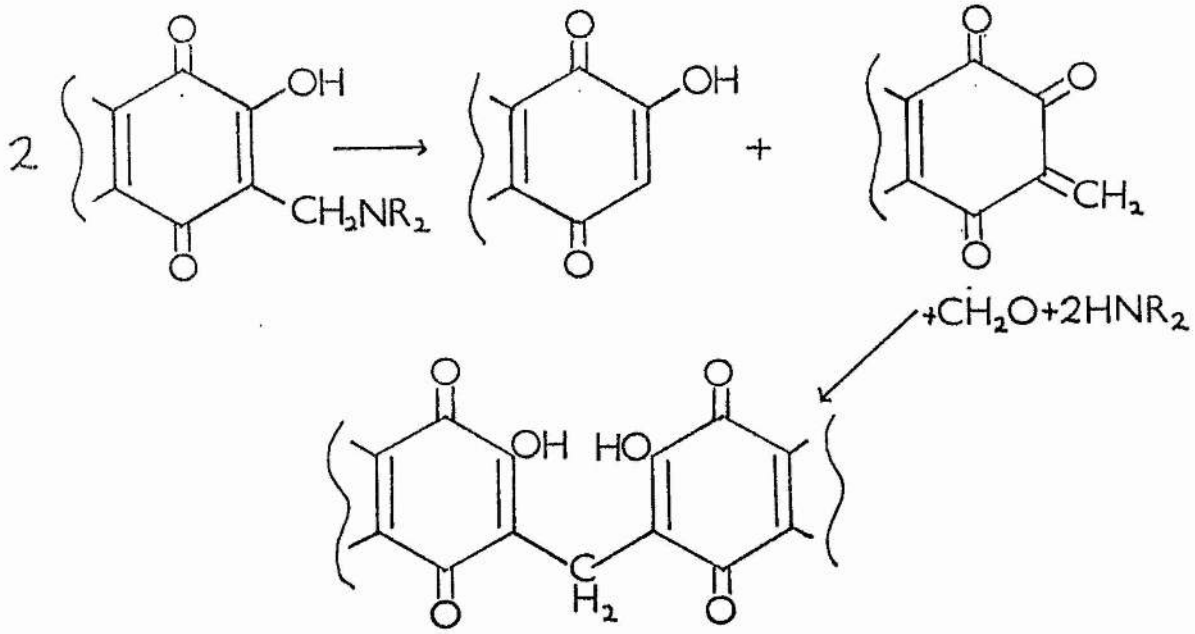
XXIX XXX

direct attack at the 6-position, giving nuclear amination, followed by side chain amination to give the intermediate quinol (XXXI). The authors then suggest that this undergoes a reverse Mannich to give the second quinol (XXXII) which, after oxidation to the quinone, undergoes nuclear oxidative amination to give XXX. The formation of diarylmethanes from naphthalic Mannich bases[115,116] is cited as evidence for the reverse Mannich stage. The formation of



XXXI XXXII

these diarylmethanes is thought[117] to involve decomposition of the base in two ways. Elimination of the amine to yield a quinone methide, and apparent reversal of the Mannich reaction to yield a naphthalic compound, formaldehyde and the corresponding amine. An addition reaction between the two fragments would then yield the diarylmethane as shown below for the case of lawsome, (2-hydroxy-1,4-naphthaquinone). These reactions pro-



ceed under a variety of conditions such as in weakly alkaline solution, acid solution[117] or just warming in ethanol in the absence of acid or alkali[116]. Formaldehyde would be formed by this mechanism as it would in the alternative scheme 'D'. This was detected by Cameron and Scott.

The conversion of XXXI to XXXII should not strictly be called a reverse Mannich reaction as true reversal of this reaction requires acid catalysis.

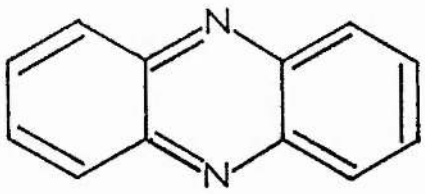
SECTION III

a) The Reactions of o-Phenylenediamine with 1,2-Benzoquinone and Methyl Substituted 1,2-Benzoquinones

b) The Reaction of Benzylamine with 1,2-Benzoquinone

Reaction of o-phenylenediamine with 1,2-benzoquinone

A solution of o-phenylenediamine in anhydrous ether was mixed with a solution of 1,2-benzoquinone, in the same solvent, in the presence of calcium sulphate as a drying agent. After filtration, concentration of the solution and chromatography on alumina yielded phenazine (XXXIII). This had an identical melting point and infra

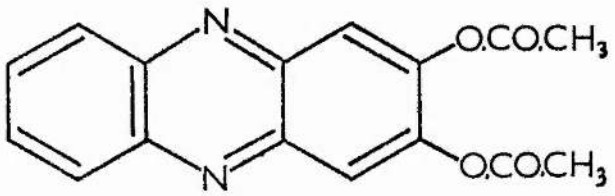


XXXIII

red spectrum to a sample prepared by the method of Morley[118]. The n.m.r. spectrum shows the expected AA'BB' system having two multiplets at 1.7-1.9τ and 2.1-2.4τ. The coupling between protons 1 and 2 is 7 c.p.s., and between 1 and 3 is 3.4 c.p.s., these values being in the region expected for ortho and meta coupling. The yield obtained was much lower than that of Kehrmann and Mermod[82], approximately 75% of unchanged diamine being recovered.

The reaction was repeated using methanol as solvent. The work up was modified in this case, acetic

anhydride and pyridine being added after removing the solvent from the reaction mixture. After standing for 2 days, yellow needles of 2,3-diacetoxyphenazine (XXXIV) were obtained. This compound melted at 238-40°C compared with a value of 230°C obtained by Fischer and Hepp[119]. The n.m.r. spectrum shows a singlet at 7.6τ, due to the six protons of the acetyl group, and a further singlet



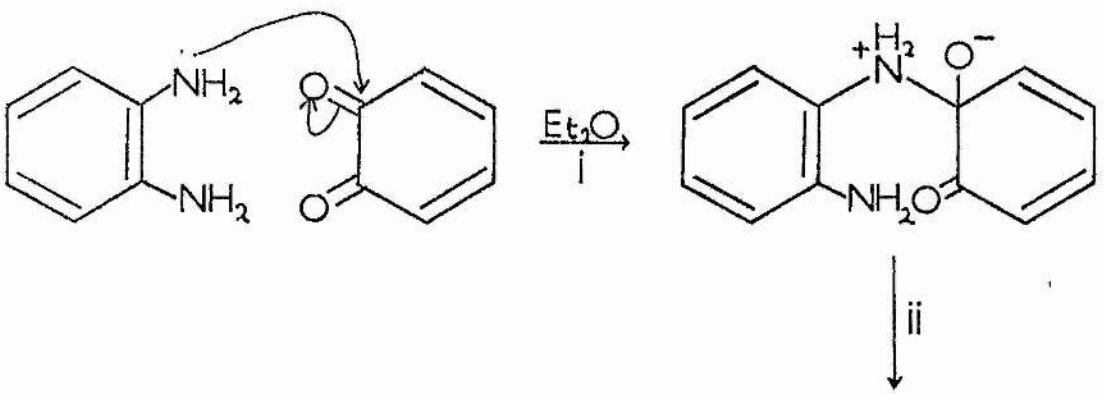
XXXIV

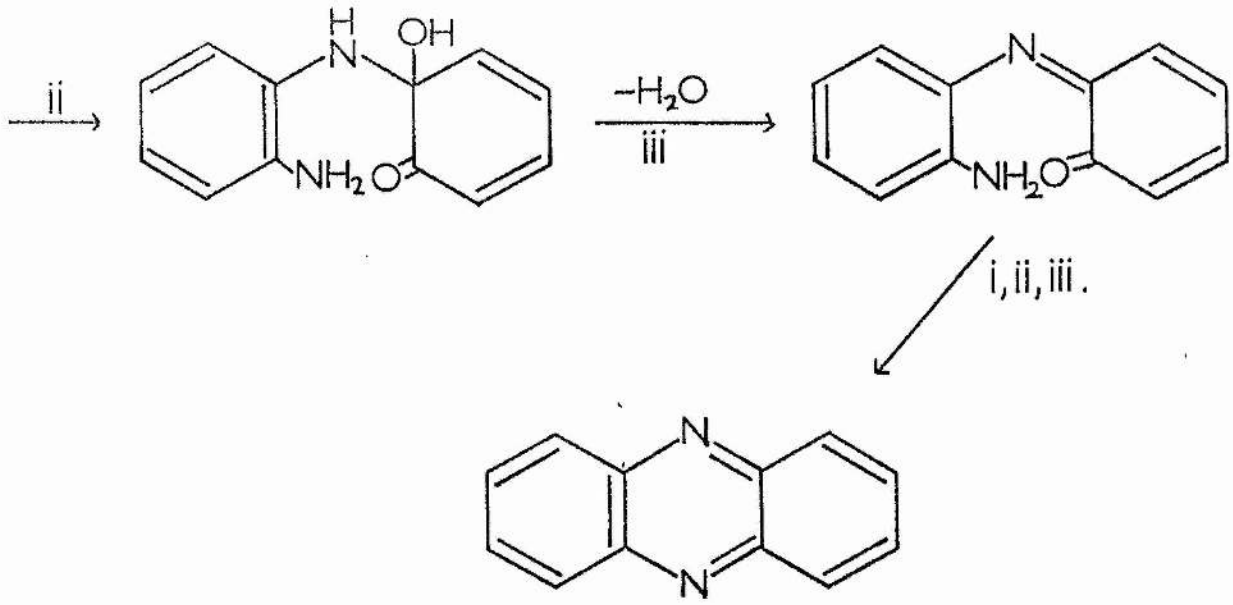
at 1.95τ due to the protons 1 and 4. The remaining four protons form an AA'BB' system with two multiplets at 1.7-1.9τ and 2.05-2.3τ, (J_{78} = 7c.p.s.; J_{68} = 3.4c.p.s.). The infra red spectrum supports the structure showing two strong overlapping bands at 1750 and 1775 cm^{-1} due to the carbonyl groups, and a broad absorption centred at 1180 cm^{-1} indicative of the C-O-C grouping. The mass spectrum shows the parent ion at m/e 296 with strong peaks at 254 (loss of $COCH_2$, M^* at 159.5), 212 (loss of the second $COCH_2$-group, M^* at 177), 184 (loss of CO, M^* at 131), 183, 166

(loss of H_2O), and 155 (loss of second CO, M^* at 131). Below this point, the spectrum shows the breakdown of the phenazine nucleus being closely comparable with the spectrum obtained for phenazine itself.

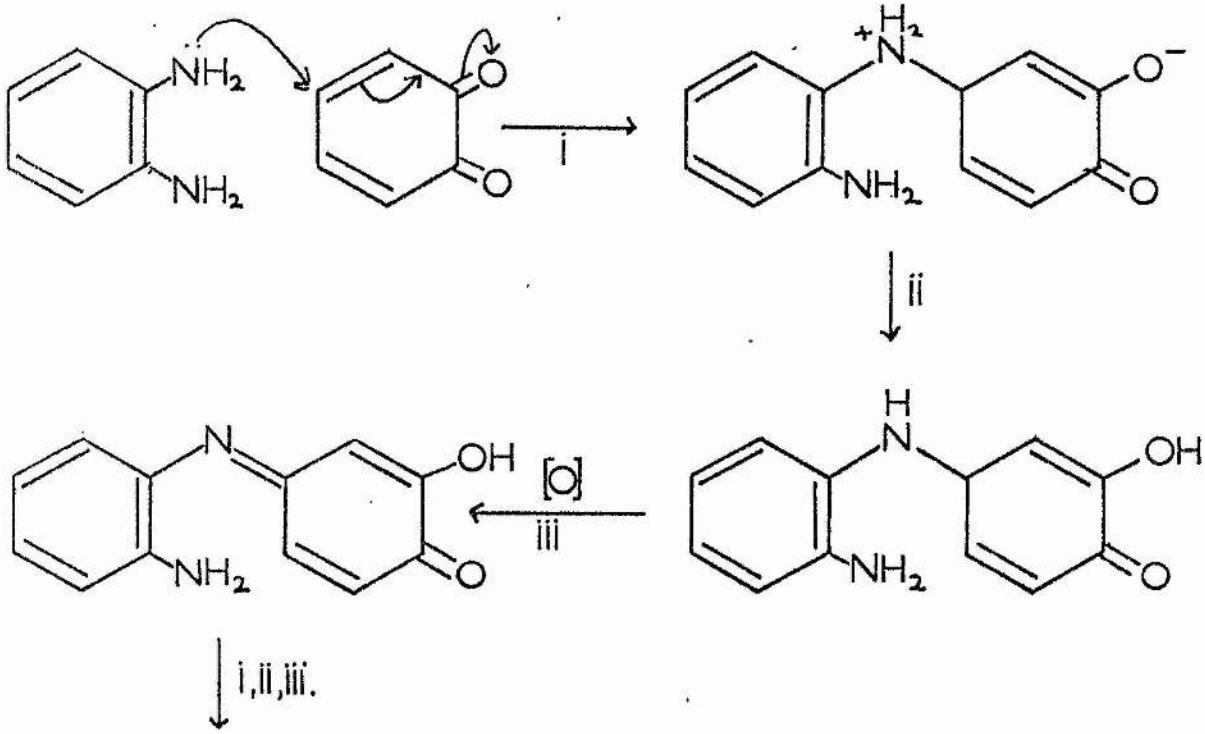
When an excess of o-quinone was used, a trace (<1%) of phenazine was detected in the reaction products, together with a large amount of the diacetate of catechol. When the reaction in ethereal solution was repeated using the acetylation work up technique, the product was mainly phenazine together with a trace of the diacetoxyphenazine and products of acetylation of the starting materials.

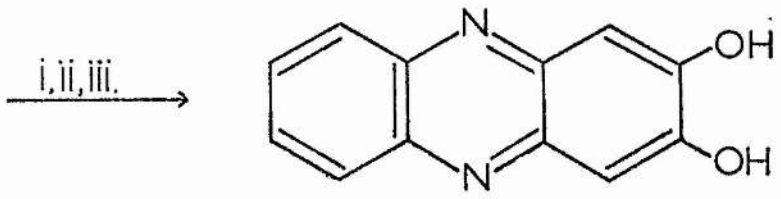
The different products obtained in the two different solvents are formed by attack by the amine at opposite ends of the 1,2-benzoquinone molecule. Thus the formation of phenazine may be represented by scheme 'E' and the formation of 2,3-diacetoxyphenazine by scheme 'F'.




ii
H
OH
N
NH2
O
-H2O
iii
N
NH2
O
i, ii, iii.
N
N

Scheme 'E'


NH2
NH2
O
O
i
+H2
N
O−
NH2
O
ii
H
N
OH
NH2
O
[O]
iii
N
OH
NH2
O
i, ii, iii.



Ac_2O
pyridine

XXXIII

Scheme 'F'

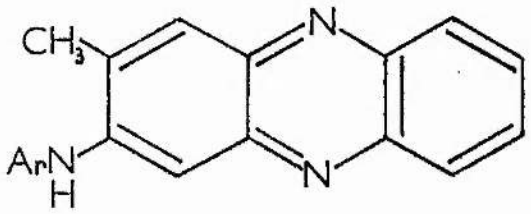
It will be seen that oxidation is necessary in the formation of XXXIII. This is brought about by the quinone present. The cause of the change of position of attack with changing solvent is probably due to acetal formation as described in section I.

The reaction of 4-methyl-1,2-benzoquinone with o-phenylenediamine

A mixture of 4-methyl-1,2-benzoquinone and o-phenylenediamine in methanol was allowed to stand for 24 hours. The crude red/brown product was filtered off and recrystallized from methanol to give 2-(2'-aminophenyl)-amino-3-methylphenazine (XXXV) as an orange solid.

The infra red spectrum shows a broad weak absorption at 3190 cm^{-1} due to the NH and NH_2 groupings present, broadening and low intensity being due to hyd-

rogen bonding. The mass spectrum shows a strong molecular ion which, under high resolution, had an m/e ratio of 300.13742. This compares well with a theoretical value of 300.13749 for $C_{19}H_{16}N_4$. The next major ion is at m/e 285 and arises from loss of methyl from the parent. Loss of the 2-aminoaniline group gives rise to a strong ion at m/e 194. The compound was not sufficiently soluble for an n.m.r. spectrum to be obtained.



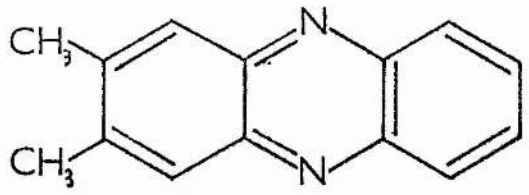
XXXV

Ar = o-NH_2-C_6H_4

The reaction of 4,5-dimethyl-1,2-benzoquinone with o-phenylenediamine

A solution of o-phenylenediamine in methanol was added to a solution of 4,5-dimethyl-1,2-benzoquinone in the same solvent. After standing overnight, filtration yielded the crude product which was recrystallized from methanol to give the almost colourless 2,3-dimethylphenazine (XXXVI).

The melting point of the recrystallized product



XXXVI

is 173°C, identical to that previously published[67]. The infra red spectrum is extremely simple as expected having no readily assignable absorptions. The mass spectrum shows a strong molecular ion which, under high resolution, is seen to have an m/e ratio of 208.0997 compared with a theoretical value of 208.1004 for $C_{14}H_{12}N_2$. The only other strong ion is seen at m/e 193 arising from loss of methyl from the parent.

The n.m.r. spectrum can be easily assigned. A singlet at 7.54τ integrating to six protons is due to the methyl protons. The four protons on carbon atoms 5, 6, 7 and 8 give rise to an AA'BB' system having two four line multiplets centred at 1.85τ and 2.3τ, (J_{57} = 3 c.p.s., J_{56} = 7 c.p.s.). The remaining two protons, 1 and 4, give rise to a singlet at 2.14τ. The multiplet centred at 1.85τ integrates to two protons and the remainder of the low field signals integrate to four. It is not possible to obtain individual integration for the singlet

and second multiplet.

The reaction of 3,5-dimethyl-1,2-benzoquinone with o-phenylenediamine

A solution of o-phenylenediamine in methanol was added to a solution of 3,5-dimethyl-1,2-benzoquinone in the same solvent. After stoppering the reaction flask, it was allowed to stand for two weeks. After this time, the solvent was stripped under reduced pressure, a mixture of acetic anhydride and pyridine added, and the whole left to stand for two days. N,N'-diacetyl-o-phenylenediamine was precipitated and filtered off before pouring the reaction mixture into ice water. This precipitated crude 1,3-dimethylphenazine (XXXVII) which was recrystallized from

XXXVII

methanol.

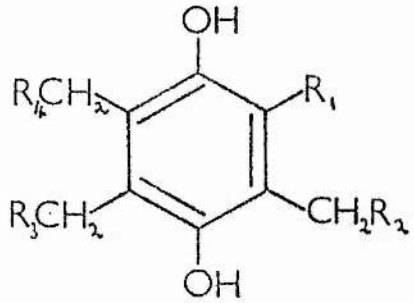
The product melts at 121-2°C compared with a published value of 123°C[67]. The infra red spectrum is feat-

useless as expected, having no readily assignable bands. The mass spectrum shows a strong molecular ion which high resolution spectrometry shows to have an m/e ratio of 208.0997 compared with a theoretical value of 208.1004 for $C_{14}H_{12}N_2$. The only major fragment ion occurs at m/e 193, being formed by elimination of methyl from the parent ion.

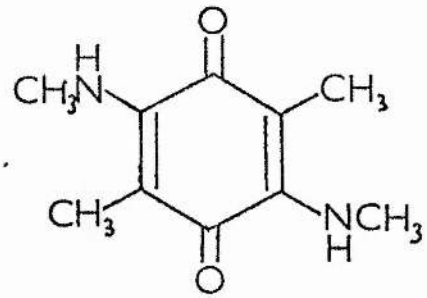
The n.m.r. spectrum shows two singlets at 7.17τ and 7.46τ, each integrating to three protons. A five line multiplet, centred at 1.82τ, integrating to two protons, is half of an AA'BB' system made up of protons 5, 6, 7 and 8. The other half of the AA'BB' signal and a doublet due to protons 2 and 4 are superimposed to give a multiplet centred at 2.28τ integrating to four protons.

We see from the results obtained with o-phenylenediamine and methyl substituted 1,2-benzoquinones, that the dealkylation observed using p-substituted anilines does not occur with the diamine. The type of reaction occurring in the 1,4-quinone system also changes with the amine used. Thus trimethyl-1,4-benzoquinone with piperidine yields 2-piperidino-3,5,6-trispiperidinomethylquinol [113] (XXXVIII, $R_1=R_2=R_3=R_4$=piperidyl), while methylamine gives 2,5-dimethyl-3,6-bismethylamino-1,4-benzoquinone[114]

(XXXIX). Similarly with duroquinone, piperidine yields



XXXVIII



XXXIX

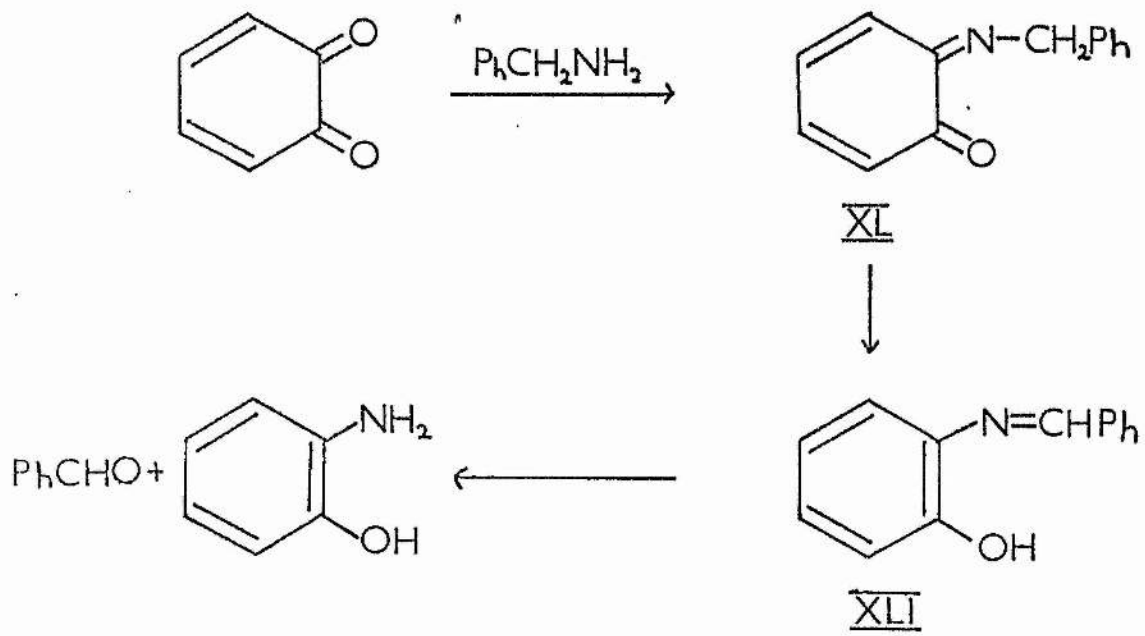
2,3-dimethyl-5,6-bispiperidomethylquinol[113] (XXVII), while methylamine again gives XXXIX, though in low yield[114]. In both cases, methylamine leads to demethylation whereas piperidine simply gives side chain alkylation.

In the case of 1,2-benzoquinone, attack occurs at the carbonyl groups in ether, but at the 4- and 5-positions in methanol. This can be accounted for by the acetal formation in methanol postulated in section I. Acetal formation is also expected in the substituted quinones, but in this case, the substitution at the 4- and/or 5- positions make direct carbonyl attack still the most favoured. If 3-methylquinone was reacted with o-phenylenediamine, solvent dependence should again be observed but this reaction has not been investigated.

Reaction of benzylamine with 1,2-benzoquinone

Benzylamine was stirred overnight with a solution of 1,2-benzoquinone in methanol. After filtering, the solvent was removed under reduced pressure and the oil obtained allowed to stand in the air for several hours. Subsequent chromatographic work up yielded benzaldehyde which was identified by comparison with an authentic sample and by preparation of the phenylhydrazone.

The most likely route for the formation of benzaldehyde is given in scheme 'G'. The first step is direct

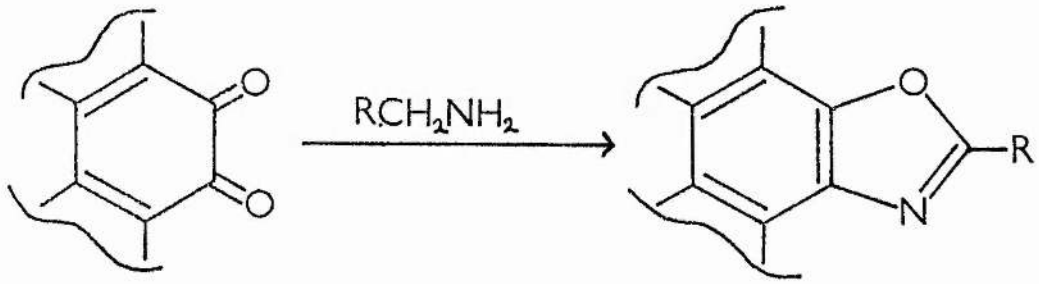


Scheme 'G'

attack at the carbonyl groups of the quinone by benzyl-

amine to give the Schiff's base (XL). This undergoes rearrangement to give the second Schiff's base (XLI) which readily hydrolyses to yield o-aminophenol and benzaldehyde.

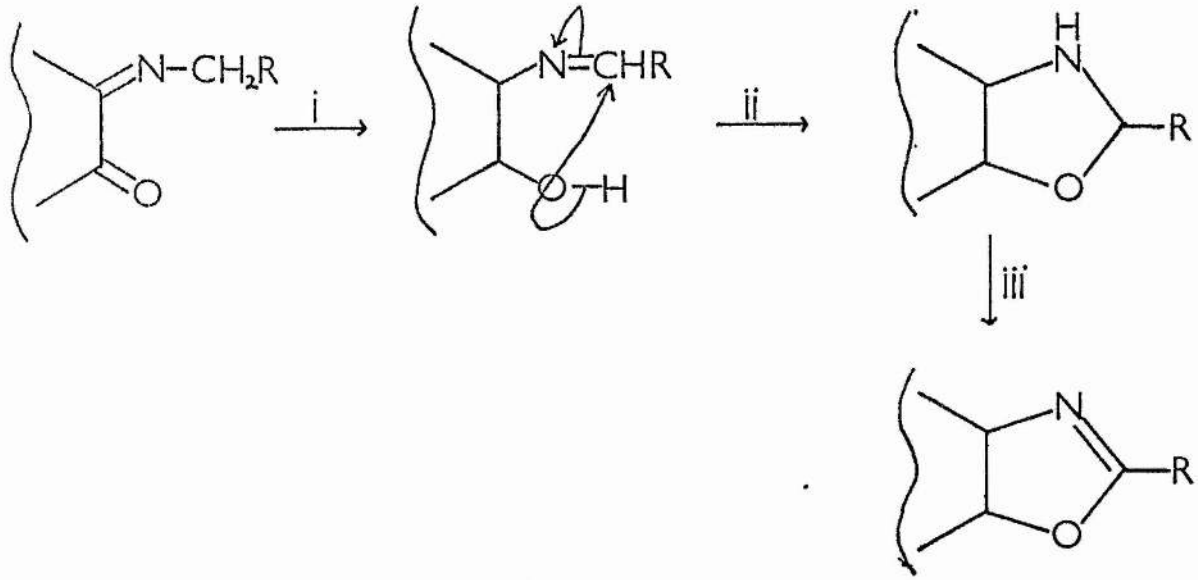
Evidence for this scheme is given by the work of McCoy and Day, and Corey and Achiwa. McCoy and Day reacted aliphatic amines, having two α-hydrogen atoms, with retenequinone and phenanthraquinone to give the corresponding oxazoles[80] (XLII). The reaction in this case is



XLII

thought to proceed via the Schiff's bases analogous to XL and XLI, cyclisation and dehydrogenation giving the oxazoles as shown below. As evidence for the formation of the first Schiff's base, the authors quote the formation of water which was detected when the reaction was carried out in dry toluene. When the quinone was replaced by the quinone imine, ammonia was liberated in the place of water. Evidence for the formation of the second Schiff's base (analogous to XLI) was obtained by adding acid, at the

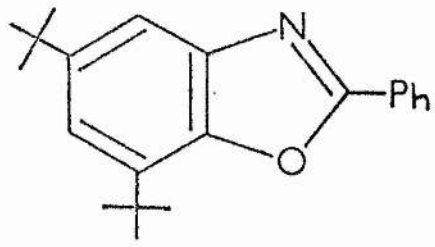
appropriate time, to the reaction mixture of the quinone and benzylamine to give benzaldehyde. Evidence for step



(ii) was obtained by condensing 9,10-aminophenanthranol with n-butyraldehyde or benzaldehyde to give the corresponding oxazoles. This reaction must go by the Schiff's base analogous to XLI. The dehydrogenation (step (iii)) is thought to proceed partially by oxidation with quinone and partially by air oxidation.

Corey and Achiwa[81] obtained aldehydes from the reactions of primary amines with 3,5-ditertiarybutyl-1,2-benzoquinone. The mechanism is postulated to follow a parallel route to that shown in scheme 'G'. However, the final hydrolysis step, which occurs spontaneously in the 1,2-benzoquinone system, requires acid hydrolysis in

this case and yields the N-protonated o-aminophenol. It is of interest to note that the method of these authors fails in the case of benzylamine, the oxazole (XLIII) being the major product with only a trace of benzaldehyde.



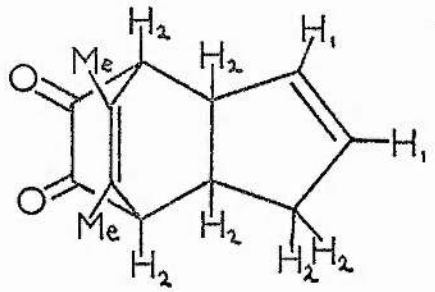
XLIII

SECTION IV

The Reaction of Cyclopentadiene with 4,5-Disubstituted 1,2-Benzoquinones

Reaction of cyclopentadiene with 4,5-dimethyl-1,2-benzoquinone

Freshly prepared cyclopentadiene was added to a solution of 4,5-dimethyl-1,2-benzoquinone in dry benzene. After stirring for two days, the reaction mixture was filtered and the solvent carefully removed at room temperature under reduced pressure to give a yellow oil. Chromatographic work up on a silica gel column yielded 8,9-dimethyltricyclo-$[5,2,2,0^{2,6}]$-undeca-4,5:8,9-diene-10,11-dione (XLIV).



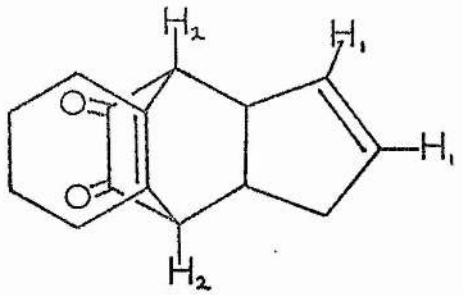
XLIV

The melting point of the adduct, which had a satisfactory analysis, was 195°C compared with a literature value of 212°C[119]. The melting point was not raised by repeated crystallization. The structure was confirmed spectroscopically. The infra red spectrum shows a broad carbonyl absorption centred at 1730 cm^{-1}. The mass spectrum supports the structure, showing a strong molecular

ion at m/e 202. Loss of a methyl group from the parent gives a peak at m/e 187. The base peak of the spectrum is at m/e 146 being due to elimination of C_2O_2 from the molecule. A further strong peak at m/e 131 is produced by loss of methyl from the base peak. The n.m.r. spectrum shows two singlets at 8.12τ and 8.22τ, having a total integration of six protons, due to the two methyl groups. The olefinic protons, H_1, give rise to two multiplets centred at 4.25τ and 4.55τ each integrating to one proton. The remaining six protons, H_2, appear as a multiplet from 6.4-8.0τ which integrates correctly.

Reaction of cyclopentadiene with 5,6,7,8-tetrahydro-2,3-naphthaquinone

Freshly prepared cyclopentadiene was stirred into a solution of 5,6,7,8-tetrahydro-2,3-naphthaquinone in dry benzene. After standing overnight, the solution was filtered and the solvent carefully stripped from the filtrate, at room temperature, under reduced pressure. The oil obtained was chromatographed on silica gel to yield tetracyclo-$[6,5,2,0^{2,6},0^{8,13}]$-pentadeca-4,5:8,13-diene-14,15-dione (XLV).



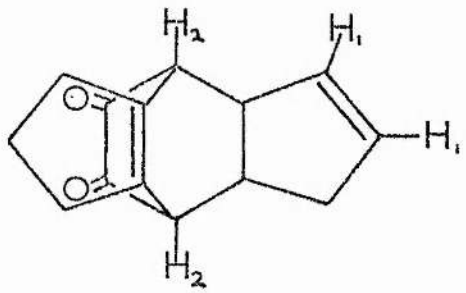
XLV

The compound melted sharply at 201°C. The structure was confirmed by spectroscopic means. The infra red spectrum shows broad carbonyl absorption at 1725 cm^{-1}. The mass spectrum shows a strong molecular ion which is shown, under high resolution, to have an m/e ratio of 228.1148 compared with a calculated value of 228.1150 for $C_{15}H_{16}O_2$. The first major fragment ion occurs at m/e 172, being formed by the characteristic loss of C_2O_2. Loss of ethylene and propyl from this ion gives rise to strong ions at m/e 144 and m/e 129 respectively. The n.m.r. spectrum shows two multiplets at 4.24τ and 4.55τ, each integrating to one proton, due to the olefinic protons, H_1. The remaining protons appear as a multiplet from 6.5-8.5τ integrating in all to fourteen protons. The bridge-head protons, H_2, can be distinguished as a narrow doublet at 6.8τ integrating

to two protons, while the protons of the cyclohexene ring can be observed as two broad multiplets centred at 7.95τ and 8.30τ, integrating to eight protons in all.

Reaction of cyclopentadiene with hydrin-5,6-quinone

Freshly prepared cyclopentadiene was stirred for 2 days with a solution of hydrin-5,6-quinone in dry benzene. After filtering the reaction mixture, the solvent was carefully stripped from the filtrate under reduced pressure at room temperature. The oil produced was chromatographed on a silica gel column to yield tetracyclo-[5,5,2,$O^{2,6}$,$O^{8,12}$]-tetradeca-4,5:8,12-diene-13,14-dione (XLVI).



XLVI

The compound melted at 162-3°C. The structure was confirmed by spectroscopic means. The infra red spectrum shows a broad carbonyl absorption centred at 1720 cm^{-1}. The mass spectrum shows a molecular ion which

is shown to have an m/e ratio of 214.0996 compared with a theoretical value of 214.0994 for $C_{14}H_{14}O_2$. The loss of C_2O_2 gives rise to a strong ion at m/e 158. The loss of methyl, ethyl and propyl groups from this ion gives rise to strong ions at m/e 143, 129 and 115 respectively. The n.m.r. spectrum shows two multiplets centred at 4.3τ and 4.6τ, each integrating to one proton, due to the olefinic protons, H_1. The bridge-head protons, H_2, appear as a broad singlet at 6.46τ, integrating to two protons. The remaining ten protons appear as a multiplet at 6.9-8.2τ which integrates correctly.

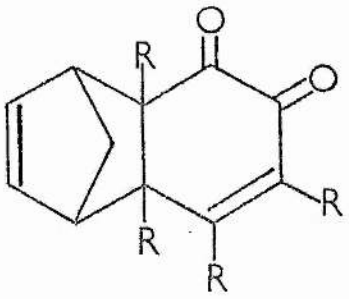
The infra red and n.m.r. spectra of the three compounds XLIV, XLV and XLVI are qualitatively similar. In the same way, the electronic spectra are almost identical, as shown in table 4. The electronic spectra are time-dependent, fading when allowed to stand. This is due to interaction of the carbonyl groups with the ethanol used as solvent, via the formation of acetals.

Table 4

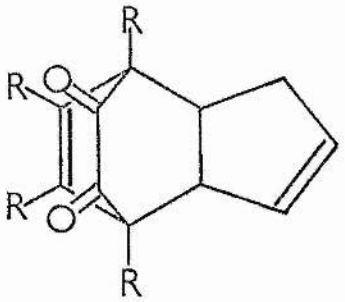
Compound	λ_{max}	ε_{max}	λ_{max}	ε_{max}	λ_{max}	ε_{max}
XLIV	230	1.88×10^3	283	1.66×10^3	452	2.67×10^2
XLV	230	1.67×10^3	285	1.06×10^3	450	2.7×10^2
XLVI	223	1.76×10^3	288	1.37×10^3	446	2.57×10^2

Wavelength in mμ, ε in litre $mole^{-1} cm^{-1}$

The adducts XLIV, XLV and XLVI reported above, are formed by Diels-Alder reactions of the quinones, acting as dienes, with cyclopentadiene which acted as the dienophile. It is now well known that 1,2-benzoquinones can react both as diene and dienophile in reactions with cyclopentadiene, giving methanonaphthaquinones (XLVII) and oxylindenes (XLVIII) respectively[121]. In a recent paper[122], Ansell et al have examined the n.m.r. spectra of the crude products obtained from the reactions of cyclopentadiene with 1,2-benzoquinones with various substituents. They find that, in almost every case, a mixture of the two types of adduct is obtained. In the case of 4,5-dimethyl-1,2-benzoquinone, they obtained 65% of adduct XLIV and 35% of the methanonaphthoquinone. This is not in agreement with our n.m.r. studies which show no



XLVII



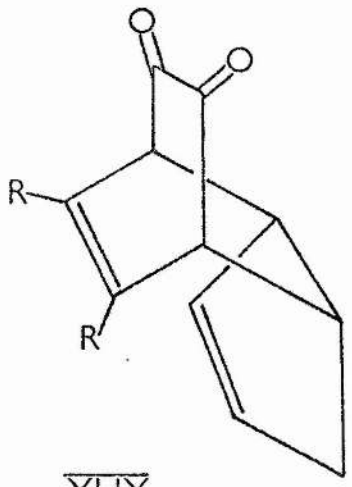
XLVIII

evidence for the methanonaphthaquinone. Though the n.m.r. spectra of the crude products obtained from 5,6,7,8-tetrahydro-2,3-naphthaquinone and indane-5,6-quinone were not obtained, our evidence suggests that disubstitution in the 4- and 5- positions leads to the oxylindene only. This is probably due to steric hindrance preventing the quinone acting as a dienophile. Ansell's results suggest that 4,5-dialkyl substituents depress the dienophilic activity of 1,2-benzoquinones. Thus 3,4,5-trimethyl-1,2-benzoquinone gives 70% of the oxylindene and the tetramethyl compounds give the oxylindene only.

Stereochemistry of the adducts

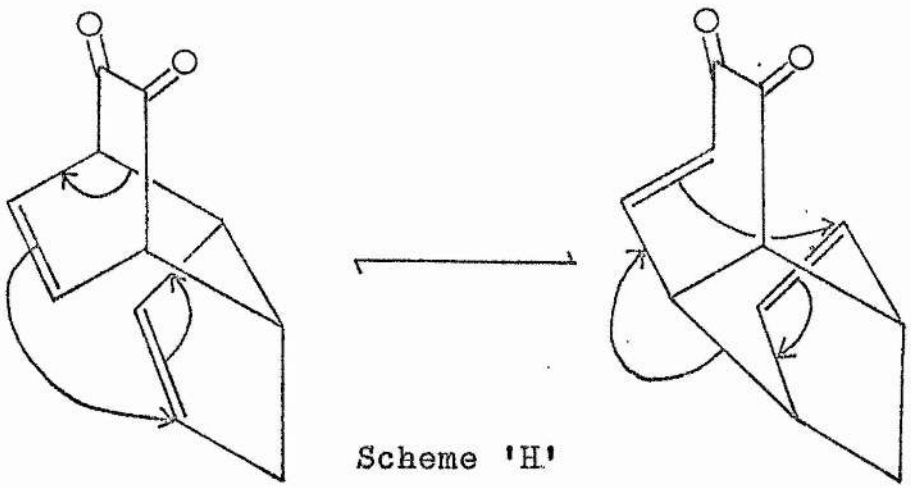
Diels-Alder reactions are known to proceed by a cis endo addition in general. This would give products with the structure shown below (XLIX). R_1 and R_2 are either ring residues or methyl groups. Chemical degrad-

ation of the adduct with $R_1=R_2=Me$[123] proved the structure to be as shown. The structure is also supported by the



XLIX

thermal interconversion of oxylindenes and methanonaphthaquinones which has been shown to proceed by an intramolecular mechanism[122] as shown in scheme 'H'. This can only occur if both adducts are in the endo-cis configuration.



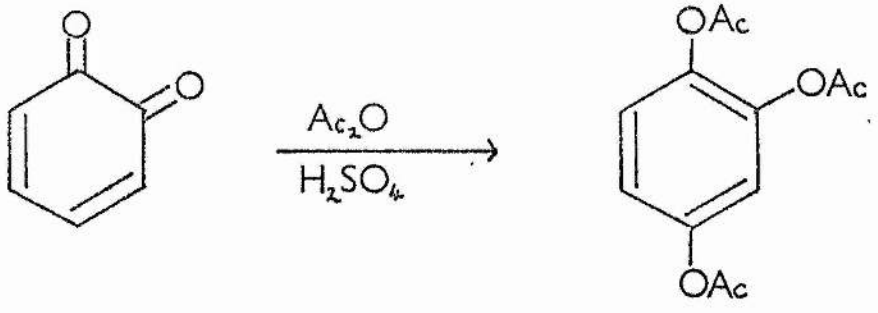
Scheme 'H'

SECTION V

Thiele-type Acetylation of 1,2-Benzoquinone

The reaction of 1,2-benzoquinone with acetic anhydride

1,2-Benzoquinone was dissolved in acetic anhydride and a few drops of concentrated sulphuric acid added. The colour was rapidly discharged, as reaction occurred, to give a yellow solution. After pouring into ice water and treating with bicarbonate to remove excess acid, the solution was extracted with chloroform. Drying the extract and stripping the solvent yielded the 1,2,4-triacetate of benzene (L) as a white solid.



I

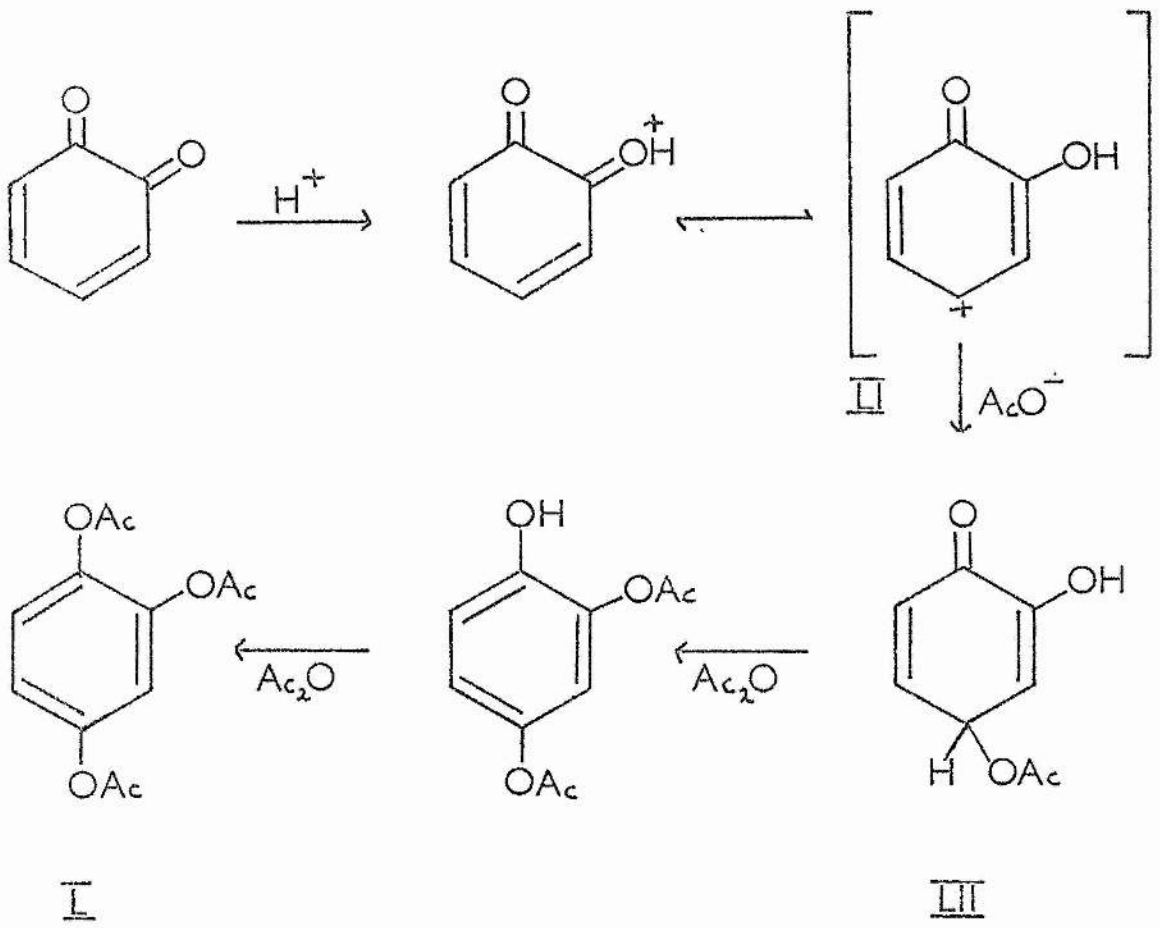
The product shows a strong carbonyl absorption in the infra red spectrum at 1770 cm^{-1}. A broad band centred at 1290 cm^{-1} indicates the presence of the -C-O-C- linkage. The mass spectrum shows a strong molecular ion at m/e 252. Loss of the three CH_2CO groups give peaks at m/e 210, 168 and 126 with metastable ions for each loss at m/e 175, 134 and 94 respectively. The n.m.r. spectrum

shows a multiplet at 2.8-3.0τ, integrating to three protons, due to the protons of the aromatic ring. A singlet at 7.75τ, integrating to nine protons, is due to the three methyl groups.

The spectroscopic data listed above show that the product is a triacetate of benzene but it is not possible to show whether the 1,2,3- or 1,2,4- isomer has been produced. To assign the structure unambiguously, the two isomers were synthesised and compared. The 1,2,3- isomer was prepared by the method of Heller[124] and had a melting point of 165-6°C. The 1,2,4- isomer was prepared by the method of Vliet[125]. This had a melting point of 93-5°C compared with the value of 92-4°C for our product. A mixture melted at 92-4°C showing that the compounds were identical and proving the product to be the 1,2,4-trisubstituted compound.

The acetylation, which is named the Thiele reaction after its discoverer[126], has been known for many years in the 1,4-benzoquinone system though there is no report of its being applied to 1,2-benzoquinones. The reaction also occurs with 1,2- and 1,4-naphthaquinones and can be brought about using boron trifluoride etherate as catalyst[127], though this is not as effective as sulph-

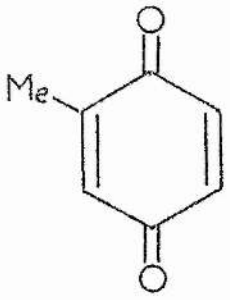
uric acid. A possible reaction mechanism is given below.



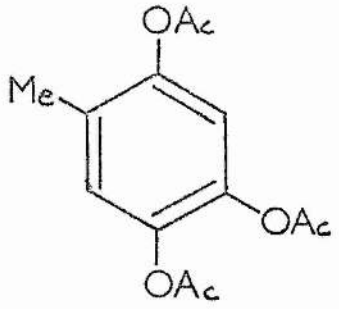
The first step involves protonation of one of the carbonyl groups. The protonated species produced undergoes attack by acetate ion, formally on the carbonium ion (LI), to give the mono-acetylated product (LII). Acylation of this compound, followed by aromatisation and acylation of the second hydroxy group, will yield the final product (L).

Application of the analogous mechanism to 1,4-quinones can successfully rationalize the products ob-

tained. For example, 2-methyl-1,4-benzoquinone (LIII), when treated with acetic anhydride and concentrated sulphuric acid, gives the 2-methyl-1,4,5-triacetate of benzene (LIV). The above mechanism requires protonation at

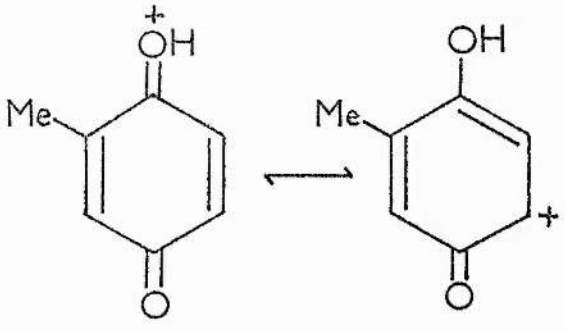


LIII

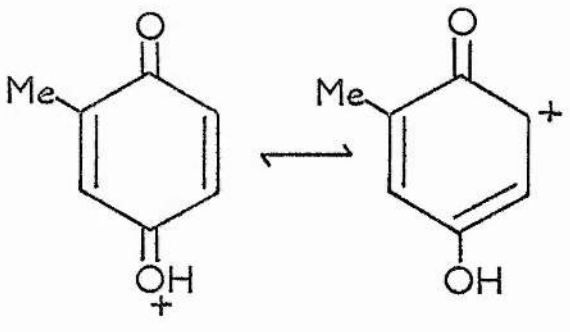


LIV

one carbonyl group to give the carbonium ions LV or LVI. Both are destabilized by proximity to a positively polarized carbonyl carbon. However, in LV, the methyl group



LV



LVI

tends to decrease the polarization at C(4) tending to stabilize the carbonium ion a little, while no such stab-

ilization of the ion LVI is possible. Attack by acetate ion at the more stable carbonium ion gives the observed product.

EXPERIMENTAL

General Experimental Procedure

Melting points were determined on a 'Gallenkamp' melting block and are uncorrected.

Infra-red spectra were run on Perkin Elmer 137 (sodium chloride prism), 157 or 257 (sodium chloride grating) instruments.

Ultra-violet spectra were obtained on a Unicam S.P.800 spectrophotometer in ethanol unless otherwise stated.

Nuclear magnetic resonance spectra were recorded in deuterochloroform solution on a Perkin Elmer 60 MHz spectrometer and measured with respect to internal tetramethylsilane.

Mass spectra were mainly recorded on an A.E.I./G.E.C. M.S.902 instrument, though a number were recorded on an M.S.12 instrument of the same manufacturer.

Preparation of Tetrachlorocatechol

Catechol (80g) was dissolved in glacial acetic acid (600cc) in a one litre conical flask immersed in a bath of cold water. A brisk stream of chlorine was passed until fine white needles of tetrachlorocatechol were precipitated (about one hour). The water bath was replaced by ice and the suspension cooled to $0^{\circ}C$ before filtering the product and sucking it dry at the pump. Yield :- 122g (69%) of fine white needles.

Preparation of Tetrachloro-1,2-benzoquinone

The whole of the tetrachlorocatechol prepared above was placed in a one litre beaker. A mixture of concentrated nitric acid (50cc) and glacial acetic acid (700cc) was added, with constant stirring, until all the solid had dissolved, giving a clear red solution. The product was precipitated by pouring into a two litre conical flask filled with ice. The dark red, powdery solid obtained was filtered off at the pump and sucked dry. It was used without further purification.

Preparation of Potassium Nitroso Disulphonate (Fremy's Salt)

A mixture of sodium bicarbonate (42g), sodium

nitrite (35g), distilled water (250cc) and crushed ice (500g) was placed in a beaker immersed in an ice/salt cooling bath, and equipped with a mechanical stirrer. Sulphur dioxide was blown through the solution with continuous stirring while maintaining the temperature around -2°C. After about 40 minutes the pH dropped to 2 and the originally colourless solution became a pale orange/brown. The sulphur dioxide supply was then cut off and the stirring continued for 10 minutes during which time the colour of the solution was discharged. Air was blown through the solution for 5 minutes, then 62.5cc of cold saturated sodium carbonate solution was added adjusting the pH to approximately 9. The cooling bath was removed and the solution stirred for a further 1½ hours during which time it warmed to room temperature.

Distilled water (500cc) and lead dioxide (180g) was added then the whole heated, with stirring, on an electric hot plate, between the limits 20-40°C for 30 minutes. The solution, which had become violet, was maintained at 40°C for a further 25 minutes. The stirrer was removed and the solution allowed to stand for 5 minutes before filtering to yield a violet filtrate with a pH of approximately 10. Carbon dioxide gas was rapidly bubbled

through the filtrate for 10 minutes, during which time lead carbonate was precipitated and the pH fell to 7. The precipitate was filtered off and the pH of the filtrate adjusted to about 9 by the addition of saturated sodium carbonate solution (15cc). Potassium nitrate (250g) was added and the solution stirred until it dissolved, during which time orange/yellow crystals of Fremy's salt began to appear. Precipitation was completed by cooling to $0^{o}C$ in an ice bath. The solid was filtered from the still violet mother liquor at the pump and washed with methanol and acetone before sucking as dry as possible. The product was thoroughly dried in a vacuum dessicator over solid caustic soda.

In our experience, the product, once thoroughly dry, could be stored for a period of months. The product was stored in a dark, screw-top jar containing a little caustic soda as dessicant. This was kept in the freezer compartment of the laboratory refrigerator. The compound did decompose before thoroughly dry on several occasions. The decomposition was highly exothermic, though at no time did detonation occur. If the product was in glassware when it decomposed, the glass invariably cracked, and on one occasion, when the product was on a

sheet of paper, the paper was charred. During decomposition, sufficient gas was given off to raise the lid of a large dessicator that was originally evacuated.

Preparation of 4-Ethyl-1,2-benzoquinone

A solution of p-ethyl phenol (0.98g) in ether was added to a solution of Fremy's salt (5.6g) in water (400cc) containing sodium acetate solution (16cc at 1.25M). The mixture was stirred for an hour, during which time the purple colouration of the Fremy's salt was replaced by the bright red colour of the quinone. The solution was extracted with 3x200cc of ether, the extract dried over magnesium suphate, and the solvent stripped to give the quinone as a bright red oil. The quinone was used in this crude state.

Preparation of 1,2-Benzoquinone

A solution of catechol (5.5g) in dry ether (25cc) was cooled to below -25°C in a flask protected by a drying tube. A solution of tetrachloro-1,2-benzoquinone (12.5g) in the same solvent (150cc) was similarly cooled. The two solutions were mixed and maintained at -25 to -30°C for 2 hours with stirring. The bright red powdery precip-

itate of 1,2-benzoquinone obtained was filtered off at the pump, washed with a little cold ether and transferred to a pre-cooled sample tube. Yield :- 3.7g. Decomposes before melting.

The compound was stored under cardice. Under these conditions it appeared stable indefinately. However, if allowed to warm to room temperature, it rapidly decomposed to the black polymer.

Preparation of 4-Methyl-1,2-benzoquinone

4-Methyl-catechol (20g) was dissolved in dry ether (50cc) in a flask fitted with a drying tube. The solution was cooled to -30°C before mixing with a similarly cooled and protected solution of tetrachloro-1,2-benzoquinone (40g) in the same solvent (350cc). The mixture was maintained at -30 to -40°C, with stirring, for 2 hours. 4-Methyl-1,2-benzoquinone was precipitated as orange crystals, which were filtered off at the pump, washed with ether, and stored under cardice.
Yield :- 14.4g.

Preparation of 3-Methyl-1,2-benzoquinone

Tetrachloro-1,2-benzoquinone (12.3g) was dissol-

ved in dry ether (150cc). 3-Methyl-catechol (6.2g) was dissolved in the same solvent (20cc). Both solutions were protected with calcium chloride tubes and cooled to -25 to -30°C. The solutions were mixed and maintained at -25 to -30°C with constant stirring for 1½ hours. The red/brown quinone that precipitated was filtered off, washed in cold ether, and stored under cardice.

Preparation of 4,5-Dimethyl-1,2-benzoquinone

A solution of 3,4-dimethyl-phenol (0.98g) in ether (20cc) was added to a solution of Fremy's salt (5.6g) in water (400cc). Sodium acetate (20cc, 1M) was added, and the whole vigorously stirred for 1 hour. The resultant solution was extracted with ether (5x200cc). The united extract was dried over magnesium sulphate, concentrated at room temperature under vacuum, and cooled in cardice/acetone to yield 0.44g of 4,5-dimethyl-1,2-benzoquinone. The quinone was recrystalised from methanol to give long, bright red needles. M.pt. 85-86°C (lit.[67] 106°C)

Preparation of 3,5-Dimethyl-1,2-benzoquinone

A solution of Fremy's salt (7.6g) in water (550cc) containing sodium acetate (30cc of 1M) was cooled

to 10°C. A solution of 2,4-dimethyl-phenol (1.35g) in ether (20cc) was added and the mixture stirred vigorously for 25 minutes while maintaining the temperature at 10°C. The resultant solution was extracted with ether (3x300cc), dried over magnesium sulphate in an ice bath, filtered, and cooled to cardice/acetone temperature. 0.68g of 3,5-dimethyl-1,2-benzoquinone was obtained as red crystals.

Preparation of 3,5-Ditertiary-butyl-1,2-benzoquinone

A solution of 2,4-ditertiary-butyl-phenol (2g) in ether (10cc) was added to a solution of Fremy's salt (5.5g) in water (400cc) containing sodium acetate (20cc of 1M). The mixture was vigorously stirred till the colour of the Fremy's salt had been discharged and replaced with the red of the quinone (about 3 hours). The whole was extracted with ether (2x200cc), the extract dried over magnesium sulphate, and the solvent stripped under vacuum to give a red oil. This was purified by chromatography on a silica gel column. Toluene eluted an unidentified orange oil, and chloroform eluted a green oil which yielded massive red needles of 3,5-ditertiary-butyl-1,2-benzoquinone on standing overnight.

M.pt. 111-112°C (lit.[41] 113°C).

Preparation of 4-Methyl-1,2-naphthaquinone

Concentrated sulphuric acid (125cc) was added with stirring and cooling to β-methyl-naphthalene (70g). The mixture was mechanically stirred for about an hour, to ensure thorough mixing of the two components, then set aside for 5 days. The resultant dark oil was poured into 125cc of water, with cooling under the tap, and the greyish-white 4-methylnaphthalene-1-sulphonic acid precipitated was filtered off after cooling to 0°C. The acid was taken into hot water (300cc) containing potassium chloride (75g), the hot solution filtered and allowed to cool. The potassium salt crystalised as fine needles which were filtered off at the pump, washed with acetone and air dried. Yield :- 55g, 43% of theoretical yield.

Potassium hydroxide pellets (150g) and water (30cc) were placed in an iron pot and the mixture heated until liquid. 30g of the potassium salt was stirred in and the mixture maintained just molten until frothing ceased. The mixture was cooled, diluted with 200cc of water, and neutralised with concentrated hydrochloric acid. The solution was extracted with ether, the ex-

tract dried over magnesium sulphate, and the solvent stripped under vacuum to give brown oil. The oil was vacuum distilled to give a pale yellow oil which rapidly crystalised to the almost colourless 4-methyl-1-naphthol on standing. B.pt. 180°C/22mm Hg, lit.[132] 179°C/25mm Hg. Yield :- 7.6g (42%).

Sulphanilic acid (10.5g), sodium carbonate (2.65g), and water (50cc) were placed in a 100cc conical flask and heated on a steam bath, with stirring, until all the acid had dissolved. The solution was then cooled in an ice bath to 10°C, at which point, sodium sulphanilate began to crystalise. A solution of sodium nitrite (3.7g) in water (10cc) was added and the resultant solution poured immediately into a mixture of concentrated hydrochloric acid (10.5cc) and ice (60g) in a 250cc conical flask. The solution, from which p-benzenediazonium suphonate separated on stirring, was allowed to stand in an ice bath for about 20 minutes.

Caustic soda (11g) was dissolved in water (60cc) and 4-methyl-1-naphthol (7.6g) was dissolved in the resultant warm solution. Ice (40g) was added, cooling the solution to about 5°C, after which the suspension of the diazonium salt (prepared above) was added. The solution

was stirred well then allowed to stand, without external cooling, for 1 hour, during which time a quantity of blood red solid precipitated.

The suspension was heated to about 50°C, when all the solid dissolved with the evolution of a little gas. About a tenth of a 23g sample of sodium dithionite was added and the mixture stirred until the frothing subsided. The remainder of the dithionite was then rapidly added and the mixture stirred to give a pinkish precipitate of 2-amino-4-methyl-1-naphthol. The suspension was strongly heated until it began to froth, cooled in an ice bath to 25°C, and filtered at the pump.

The crude product was taken into a beaker containing stannous chloride (0.2g), concentrated hydrochloric acid (5.3cc), and water (30cc) at 30°C. On stirring, most of the product dissolved. The solution was stirred for 5 minutes with activated charcoal (1g) then filtered at the pump. The resultant orange solution was treated with concentrated hydrochloric acid (5cc) and heated to boiling, a further 5cc of acid being added as the heating proceeded. The whole was transferred to an ice bath and allowed to cool undisturbed when a little 4-methyl-2-amino-1-naphthol hydrochloride separated.

When quite cool, 10cc of concentrated hydrochloric acid was added and the solution cooled to 0°C before filtering to yield the hydrochloride. The yield, after air drying, was 3.4g.

The product was dissolved in 1.5 litres of water containing 6cc of concentrated hydrochloric acid. After filtering, a filtered solution of ferric chloride (14.4g) in water (90cc) containing concentrated hydrochloric acid (3cc) was added in one go. In a few seconds fine yellow crystals of 4-methyl-1,2-naphthaquinone came down. These were filtered off, thoroughly washed with water, and dried overnight in a dessicator. The yield was 3.14g. The quinone polymerised before melting when heated.

Preparation of 5,6,7,8-Tetrahydro-naphtha-2,3-quinone

A mixture of o-dimethoxybenzene (16g), succinic anhydride (11g) and nitrobenzene (100cc) was placed in a round-bottomed flask equipped with a stirrer and a reflux condenser. Finely ground anhydrous aluminium chloride (30g) was added, a little at a time, with continuous stirring. The solution warmed appreciably and refluxed under the heat generated. When all the reagent had been added, the mixture was allowed to stand for 24 hours with

intermittent stirring. Dilute hydrochloride acid was added to the mixture, which was then steam distilled to remove nitrobenzene and excess o-dimethoxybenzene. β-3,4-Dimethoxybenzoyl propionic acid separated from the residue as a white solid and was filtered off after cooling on ice.

A mixture of granulated zinc (14g), mercuric chloride (1.4g), concentrated hydrochloric acid (2cc) and water (20cc) was shaken for 10 minutes. The zinc amalgam produced was washed with running water before use. The amalgam, β-3,4-dimethoxybenzoyl propionic acid and concentrated hydrochloric acid (22cc) was boiled under reflux for 4 hours. The solution was decanted from the remaining amalgam and ether extracted. The amalgam was thoroughly washed with ether and the washings added to the extract. The combined ethereal solution was dried over magnesium sulphate and the solvent stripped to give γ-3,4-dimethoxyphenyl butyric acid as a pale yellow oil which slowly solidified on standing.

12g of the acid was heated in the range 85-95°C under reflux with phosphorus pentoxide (100g) and phosphoric acid (100g) for an hour. The residue was diluted with water (400cc) and extracted with ether. The extract

was dried over magnesium sulphate and the solvent stripped to give 6,7-dimethoxy-1-tetralone as a colourless solid.

A mixture of granulated zinc (10g), mercuric chloride (0.8g), concentrated hydrochloric acid (0.8cc) and water (25cc) was shaken for 10 minutes. The amalgam produced was washed thoroughly with running water. It was added to a mixture of 6,7-dimethoxy-1-tetralone (8g) and 100cc of dilute hydrochloric acid (2 parts of water to 1 part of concentrated hydrochloric acid) which was then heated under reflux for 3 hours. The resultant mixture was diluted with water, filtered from the unchanged amalgam and ether extracted. The amalgam was washed with ether, the washings added to the extract, the ethereal solution dried over magnesium sulphate and the solvent stripped to give 2,3-dimethoxy-5,6,7,8-tetrahydro-naphthalene as a colourless oil.

The product was heated under reflux with 48% hydrobromic acid (25cc) in a stream of carbon dioxide for 5 hours. The solution was diluted with 100cc of water and extracted with ether. The extract was dried over magnesium sulphate and the solvent stripped to give a semi-solid consisting of crude 2,3-dihydroxy-5,6,7,8-tetrahydronaphthalene. The crude product was purified

by chromatography on a silica gel column using ether as eluant.

A solution of 2,3-dihydroxy-5,6,7,8-tetrahydronaphthalene (5g) in dry ether (10cc) was cooled to -30°C and added to a similarly cooled solution of tetrachloro-1,2-benzoquinone (7.4g) in dry ether (70cc). A further 20cc of ether was added and the mixture stirred for 2 hours at -25 to -30°C. The yellow precipitate of 5,6,7,8-tetrahydro-2,3-naphthaquinone was filtered off in a filter cooled to cardice temperature and rapidly transferred to a cardice cooled container. It was stored under cardice until required. If allowed to warm to room temperature, it decomposed in about 2 minutes giving 2,3-dihydroxy-5,6,7,8-tetrahydronaphthalene as the only identified product.

Preparation of Hydrin-5,6-quinone

Sodium metal (17g) was placed in a round bottomed flask through which a stream of nitrogen was blowing. Mercury (536g) was added in portions, the flask being heated after the first addition to initiate reaction. When addition was complete, the molten amalgam was poured on to an asbestos mat where it solidified. The solid was broken

up with a mortar and pestle and used immediately.

3,4-Dimethoxy-cinnamic acid (50g) was dissolved in a slight excess of 5M ammonium hydroxide solution. The 3% sodium/mercury amalgam prepared above was added portion-wise with continuous stirring. 5M Acetic acid was added from time to time to neutralise the ammonia liberated. On completion of the reaction, the aqueous solution was decanted from the remaining mercury, filtered and acidified with concentrated hydrochloric acid to give β3,4-dimethoxyphenylpropionic acid as a white solid. This was filtered off and recrystalised from benzene to give 40g of fluffy white crystals. M.pt. 96-7°C (lit.[131] 97°C).

β3,4-Dimethoxyphenylpropionic acid was dissolved in 300cc of benzene boiling under reflux. Phosphorus pentoxide (200g) was gradually added to the boiling solution with continuous mechanical stirring. After the final addition of phosphorus pentoxide, 100cc of benzene was added, then the whole boiled under reflux with stirring for 2 hours. The reaction mixture was mixed with ice which decomposed the red/blue phosphorus compound to give a yellow solution. This was extracted with a large volume of ether, the extract dried over magnesium sulphate, and the solvent stripped under vacuum to yield

the pale yellow 5,6-dimethoxy-hydrind-1-one. Yield :- 24g.

A mixture of granulated zinc (170g), mercuric chloride (17g), concentrated hydrochloric acid (25cc) and water (250cc) was shaken for 10 minutes. The zinc amalgam produced was washed in running water. The amalgam was placed in a 500cc round bottomed flask with sufficient dilute hydrochloric acid (1 part of concentrated acid to 2 parts of water) to just cover it. 5,6-Dimethoxy-hydrind-1-one (17g) was added and the whole boiled under reflux for 3 hours. 25cc of dilute hydrochloric acid (as above) was added after half an hour and one hour. Thereafter, 25cc of concentrated hydrochloric acid was added each half hour until completion. The resultant solution (complete with unchanged amalgam) was steam distilled, the distillate extracted with ether, the extract dried over sodium sulphate and the solvent stripped to give 5,6-dimethoxyhydrindene as a colourless crystalline solid. Yield :- 12g.

5,6-Dimethoxyhydrindene (12g) and hydriodic acid (91cc, Sp.gr. 1.7) were heated together under reflux in a current of carbon dioxide for 2 hours. After cooling, the mixture was diluted with water and extracted with ether. The ether layer was washed with dilute

sodium bicarbonate solution, dried over sodium sulphate and the solvent stripped to give an almost colourless oil. T.L.C. (silica gel/chloroform) showed this to consist of two components. These were separated on a silica gel column using chloroform as eluant. Two colourless solids were eluted the first, M.pt. 63°C, was not identified, the second was the required 5,6-dihydroxyhydrindene, M.pt. 113-4°C (lit.[131] 116°C).

5,6-Dihydroxyhydrindene (4g) was dissolved in dry ether (10cc) and cooled to -30°C. The solution was added to a similarly cooled solution of o-chloranil (7.0g) in the same solvent (70cc). The mixture was maintained at -25 to -30°C for 2 hours with continuous stirring. The orange precipitate of hydrin-5,6-quinone was filtered off at the pump and stored in cardice until required.

Preparation of Cyclopentadiene

Dicyclopentadiene was cracked by heating to about 170°C in a round bottomed flask equipped with a fractionating column. The cyclopentadiene (B.pt. 40°C) was collected and used immediately. It was not necessary to distil it further.

Preparation of 4-Chloro-1,2-benzoquinone

A solution of 4-chlorocatechol (7.2g) in ether (20cc) was cooled to -30°C and added to a solution of o-chloranil (12.5g) in the same solvent (100cc). The mixture was maintained at -25 to -30°C for 2 hours then the red/brown quinone produced was filtered off. The quinone decomposed to a black mass within a few minutes if allowed to warm to room temperature.

Preparation of 4,5-Dichloro-1,2-benzoquinone

A solution of 4,5-dichlorocatechol (8.9g) in ether (20cc) was cooled to below -30°C and added to a similarly cooled solution of o-chloranil (12.5g) in the same solvent (100cc). The mixture was maintained at -25 to -30°C for 2 hours. The 4,5-dichloro-1,2-benzoquinone was separated as a yellow precipitate and filtered off through a cooled sinter at the pump. After washing with a little cold ether, the product was stored under cardice. If allowed to warm to room temperature, the quinone rapidly decomposed to a black mass.

Preparation of Phenazine

A mixture of catechol (5g) and o-phenylene-

diamine (4.8g) was heated in a sealed tube at 190-200°C for 46 hours. The product was digested with water (80cc) at 60°C to give a black residue of 5,10-dihydrophenazine (5.2g). The product was placed in a flask equipped with an air condenser and an oxygen lead. The flask was heated to 220°C and a brisk stream of oxygen passed. Almost pure phenazine sublimed over as fluffy yellow crystals. A sample was recrystalised from ethanol to give 0.3g of yellow crystals. M.pt. 171-2°C (lit.[118] 176-7°C).

Reaction of 1,2-benzoquinone with o-phenylenediamine in dry ether

A solution of o-phenylenediamine (1.1g) in anhydrous ether (50cc) was added to a stirred solution of 1,2-benzoquinone (1.1g) in the same solvent (75cc). A little calcium sulphate was added to the solution which was then stirred for 24 hours, while protected by a calcium chloride guard tube. The solution was filtered and the solvent removed from the dark green filtrate, under vacuum at room temperature, to give a dark solid. This was dissolved in a little chloroform and chromatographed on alumina using chloroform as eluant. Phenazine

(69mg) was first eluted and recrystalised from ethanol. M.pt. 170-2°C, unchanged when mixed with an authentic sample. The I.R. spectrum was identical to that of an authentic sample. The N.M.R. spectrum showed two multiplets at τ1.7-1.9 and τ2.1-2.4. Unchanged o-phenylenediamine (0.75g) was also eluted.

In an other experiment, o-phenylenediamine (0.4g) in anhydrous ether (25cc) was added to a stirred solution of o-quinone (0.4g) in the same solvent (75cc). The mixture was stirred overnight before filtering off the polymer produced (0.14g). The solvent was stripped from the filtrate to yield a black solid which was taken into a mixture of pyridine (10cc) and acetic anhydride (10cc). After 2 days, the solution was filtered and the filtrate poured into 100cc of ice water. The resultant solution was extracted with chloroform (250cc), the extract washed with dilute hydrochloric acid, dried over calcium chloride and the solvent stripped at room temperature under vacuum to give a red oil. This was chromatographed on alumina using chloroform as eluant to yield phenazine (89mg).

Reaction of 1,2-benzoquinone with o-phenylenediamine in methanol

A solution of o-phenylenediamine (0.4g) in methanol (25cc) was added to a stirred solution of 1,2-benzoquinone (0.4g) in the same solvent (75cc). The bright red colour of the quinone solution turned almost black on mixing then faded to a red colour in about 30 seconds. The mixture was stirred over night then filtered to yield black polymer (13mg). The solvent was removed at room temperature under vacuum to yield a red/brown solid which was taken up in pyridine (10cc) and acetic anhydride (10cc). The solution was allowed to stand for 2 days then filtered to yield yellow needles of 2,3-diacetoxyphenazine (0.194g). A further 59mg was recovered when the filtrate was poured into 100cc of ice water. The product was recrystalised from a chloroform/benzene mixture to give plate-like pinkish yellow crystals. M.pt. 234°C (lit.[119] 230°C). (Found: C,65.4%; H,4.2%; N,9.3%. Calculated for $C_{16}H_{12}N_2O_4$: C,65.3%; H,4.1%; N,9.5%). The N.M.R. spectrum showed absorptions at τ1.7-1.9 (multiplet), τ1.95 (singlet), τ2.05-2.3 (multiplet) and τ7.6 (singlet) in the ratio 2:2:2:6. The mass spectrum showed major ions at m/e 296 (M^+), 254 (M^* for 296$\rightarrow$254 at 217.7), 212.

ν_{max}(nujol) 1775s, 1750s, broad absorption centre 1180s, complex absorption below 1000 cm^{-1}.

In experiments using an excess of quinone, the diacetate of catechol and trace quantities (<1%) of phenazine were detected.

Reaction of 4-methyl-1,2-benzoquinone with o-phenylene-diamine

A mixture of 4-methyl-1,2-benzoquinone (2.44g) and o-phenylenediamine (4.32g) in methanol was allowed to stand for 24 hours. The red/brown solid precipitated was filtered off (0.51g) and recrystalised from methanol to give 2-(2'-aminophenyl)-amino-3-methylphenazine as an orange solid M.pt. 360°C. M.wt. 300.13742, $C_{19}H_{16}N_4$ requiring 300.13749. [ν_{max}(nujol) 3190(weak, broad), 1620, 1610, 1599, 1565, 1545, 765, 740s cm^{-1}. The mass spectrum showed major ions at m/e 300(M^+), 285, 194, 150, 142. The product was too insoluble for an N.M.R. spectrum to be run]. The solvent was stripped from the filtrate under vacuum to give a brown solid. This was taken into a mixture of pyridine (10cc) and acetic anhydride (10cc). The resultant solution, which heated to boiling spontaneously, was allowed to stand for 24 hours.

N,N'-diacetyl-o-phenylenediamine 5.1g, M.pt. 185°C (lit.[128] 185-6°C) crystalised out and was filtered off. The filtrate was poured into ice water (200cc) and extracted with chloroform (3x200cc). The extract was washed with dilute hydrochloric acid, dried over magnesium sulphate and the solvent stripped to give a red oil which solidified on standing. This was dissolved in chloroform and examined by chromatography on a silica gel column. No identifiable products were isolated.

Reaction of 4,5-dimethyl-1,2-benzoquinone with o-phenylenediamine

A solution of o-phenylenediamine (1.08g) in methanol (10cc) was added to a solution of 4,5-dimethyl-1,2-benzoquinone in methanol (15cc). The mixture was allowed to stand overnight before filtering to yield 2,3-dimethylphenazine as a yellow solid (0.43g). The solvent was stripped from the filtrate to give a dark solid which was taken up in pyridine (10cc). Acetic anhydride (10cc) was added and the mixture allowed to stand for 36 hours. The N,N'-diacetyl-o-phenylenediamine (0.53g) that was precipitated was filtered off and recrystalised from benzene M.pt. 185-6°C (lit.[128] 185-6°C). The filtrate was

poured into ice water and the mixture filtered to yield a further 0.34g of the phenazine. The filtrate was extracted with chloroform (3x200cc), the extract washed with dilute hydrochloric acid, dried over magnesium sulphate and the solvent stripped to give a red oil. This was taken into chloroform and examined on a silica gel column. No identifiable products were isolated.

The 2,3-dimethylphenazine obtained waas recrystalised from methanol to give a pale solid M.pt. 173°C (lit.[67] 173°C). ν_{max}(nujol) 1500w, 867s, 755s cm^{-1}. The mass spectrum showed major ions at m/e 208(M^+), 193, 181, 138, 103, 77. The N.M.R. spectrum showed absorption at τ1.7-2.4 (multiplet, 6H), τ 7.54 (singlet, 6H). High resolution mass spectrum showed molecular weight 208.0997, $C_{14}H_{12}N_4$ requires 208.1004.

Reaction of 3,5-dimethyl-1,2-benzoquinone with o-phenylenediamine

A solution of o-phenylenediamine in methanol (10cc) was added to a solution of 3,5-dimethyl-1,2-benzoquinone (0.68g) in the same solvent (15cc). The reaction flask was stoppered and allowed to stand for 2 weeks. The solution produced was filtered to produce a trace amount

of unidentifiable black solid. The solvent was stripped from the filtrate to yield a brown oil which was taken into a mixture of pyridine (10cc) and acetic anhydride (10cc) and allowed to stand for 2 days. 0.37g of N,N'-diacetyl-o-phenylenediamine was filtered off. The filtrate was poured into ice water to give 1,3-dimethylphenazine (1.1g). This was recrystalised from methanol to yield dark shiny crystals M.pt. 121-2°C (lit.[67] 123°C). ν_{max}(nujol) 1625w, 1515w, 864s, 840m, 760s cm^{-1}. The mass spectrum showed major ions at m/e 209, 208(M^+), 207, 193, 181, 103, 91, 77. The N.M.R. spectrum showed absorptions at τ1.6-2.4 (multiplet, 6H), τ7.17 (singlet, 3H), τ7.46 (singlet, 3H). High resolution mass spectrum showed molecular weight of 208.0997, $C_{14}H_{12}N_2$ requires 208.1004.

Reaction of 1,2-benzoquinone with aniline in methanol

1,2-Benzoquinone (1.0g) and aniline (1.7g) were dissolved in methanol (40cc). The mixture was stirred for several hours then allowed to stand overnight. A small amount of solid came out of solution and precipitation was completed by the addition of water (40cc). The crude product was filtered off (0.87g) and recrystalised from chloroform to give 4,5-dianilino-1,2-benzoquinone as a

reddish-brown powder M.pt. 192-3°C (lit.[95] 193°C). The product was further purified by T.L.C. on silica gel before analysis. (Found: C,74.7%; H,4.8%; N,9.4%. Calculated for $C_{18}H_{14}N_2O_2$: C,74.5%; H,4.8%; N,9.7%). ν_{max}(nujol) 3150, 1620, 1580, 1540, 1520 cm^{-1}. The mass spectrum showed major ions at 290(M^+), 289, 261, (289→261, M^* at 235.7, loss of CO), 146 and 144. λ_{max}=265mμ, logε=4.12; λ_{max}=310mμ, logε=4.15; λ_{max}=424mμ, logε=3.59; λ_{max}=480mμ, logε=3.53. The N.M.R. spectrum showed absorptions at τ 2.5-3.05 (multiplet, 12H), τ 3.95 (singlet, 2H).

Reaction of 1,2-benzoquinone with aniline in ether

A mixture of 1,2-benzoquinone (1.1g) and aniline (3.75g) in dry ether (200cc) was stirred overnight in the presence of a little anhydrous calcium sulphate, protected by a calcium chloride tube. The resultant red solution was filtered and the solvent stripped under vacuum to give a red semi-solid. On treatment with a little ether this yielded a brown solid which was filtered off and washed with a little ether to yield the mono-anil of 2,5-dianilino-1,4-benzoquinone. This was recrystalised from chloroform and further purified by T.L.C. The purified products had a melting point of 205°C (lit.[130] 202-3°C). (Found:

C,78.8%; H,5.4%; N,11.5%. Calculated for $C_{24}H_{19}N_3O$: C,78.9%; H,5.2%; N,11.5%). ν_{max}(nujol) 3190, 1630m, 1600m, and 1580s cm^{-1}. λ_{max}=278mμ, logε=4.30; λ_{max}=382mμ, logε=4.19; λ_{max}=523mμ, logε=3.18. The mass spectrum showed major ions at m/e 365(M^+), 364, 336, (364 336 M^* at m/e 311, loss of CO), and 219. The N.M.R. spectrum showed absorptions at τ2.4-3.05(multiplet, 17H), τ3.86 (singlet, 2H).

Reaction of 4-methyl-1,2-benzoquinone with aniline

A solution of 4-methyl-1,2-benzoquinone (3.0g) in methanol (25cc) was added to a solution of freshly distilled aniline (4.6g, B.pt.183°C) in the same solvent (25cc). The mixture was allowed to stand for 4 days then filtered to yield the mono-(p-methoxy)-anil of 2,5-di(p-methoxy)-anilino-1,4-benzoquinone (1.61g). The solvent was stripped from the filtrate to give a brown oil. This was taken into a little chloroform and chromatographed on a silica gel column. A further 1.86g of the anil was obtained together with a brown oil consisting (T.L.C. on silica gel) of several components. This was chromatographed on an alumina column to give aniline (1.17g) as the only product which could be identified.

The crude anil was recrystalised from chloroform

to give dark fluffy crystals. The I.R. spectrum and melting point were identical to those of an authentic sample. The melting point was not depressed on mixing with an authentic sample.

Reaction of 1,2-benzoquinone with p-chloro-aniline in methanol

A solution of p-chloro-aniline (3.6g) in methanol was added to a solution of 1,2-benzoquinone (1.1g) in the same solvent (30cc). The mixture was stirred for 8 hours then the crude product filtered off. More product was isolated by the addition of water (40cc). Total recovery 0.67g. The product was recrystalised from chloroform to give fine dark red crystals of 4,5-di-(p-chloro-anilino)-1,2-benzoquinone, M.pt.209°C (lit.[95] 222-4°C). (Found: C,60.5%; H,3.3%; N,7.6%. Calculated for $C_{18}H_{12}Cl_2N_2O_2$: C,60.2%; H,3.3%; N,7.8%). ν_{max}(nujol) 3200, 1660m, 1610s, 1575s and 1540s cm^{-1}. The mass spectrum showed major ions at m/e 358(M^+), 323, 246, 217, 119, 105, 91. The N.M.R. spectrum showed absorptions at τ2.8 (broad singlet, 10H), τ3.95 (singlet, 2H). λ_{max}=273mμ, logε=4.22; λ_{max}=268mμ, logε=4.20; λ_{max}=395mμ, logε=3.86; λ_{max}=490mμ, logε=3.51.

There is a large discrepancy between our melting

point and the value given by Barry et al. These workers prepared the compound by in situ oxidation of catechol with sodium iodate in the presence of p-chloroaniline. Under these circumstances, we detected the presence of the quinone anil, i.e. the mono-p-chloroanil of 2,5-di-(p-chloroanilino)-1,4-benzoquinone, which has a substantially higher melting point. This may account for the discrepancy observed.

Reaction of 1,2-benzoquinone with p-chloroaniline in ether

A mixture of 1,2-benzoquinone (1.1g), p-chloroaniline (3.84g) and dry ether (190cc) was stirred for 2 days protected by a calcium chloride guard tube. The solution was filtered to give 0.14g of the crude product. The solvent was stripped from the filtrate at room temperature under vacuum to give a red solid which was taken up in a little chloroform and chromatographed on alumina. p-Chloroaniline (3.05g) and a further 0.2g of the product were isolated using chloroform as eluant. The crude product was recrystalised from chloroform to give deep red/brown crystals of the mono-p-chloroanil of 2,5-di-(p-chloroanilino)-1,4-benzoquinone. This was further purified by T.L.C. M.pt.239-40°C. (Found: C,60.6%; H,3.5%;

N,8.7%. $C_{24}H_{16}Cl_3N_3O$ requires: C,61.5%; H,3.4%; N,9.0%). ν_{max}(nujol) 3200, 1630m, 1610m, 1590s, 1580s, 1540m and 1510s cm^{-1}. The mass spectrum showed major ions at m/e 467(M^+), 432, 213, 199, and 178. λ_{max}=286mμ, logε=4.23; λ_{max}=385mμ, logε=4.04; λ_{max}=520mμ, logε=3.23. The anil was not sufficiently soluble for N.M.R. spectroscopy.

Reaction of 4-methyl-1,2-benzoquinone with p-chloroaniline

A solution of p-chloroaniline (6.35g) in methanol (20cc) was added to a solution of 4-methyl-1,2-benzoquinone in the same solvent (40cc). The flask was sealed and allowed to stand for 2 weeks. The crude product was filtered off (1.68g) and recrystalised from chloroform to give fine red/brown crystals of the mono-p-chloroanil of 2,5-di-(p-chloroanilino)-1,4-benzoquinone. (M.pt. was unchanged on mixing with an authentic sample. The I.R. and mass spectra were identical to those of an authentic sample). The solvent was stripped from the filtrate under vacuum to give a brown semi-solid. This was taken into chloroform and chromatographed on silica gel. The only product which could be identified was p-chloroaniline (2g).

Reaction of 3,5-dimethyl-1,2-benzoquinone with p-chloroaniline

A solution of p-chloroaniline (2.03g) in methanol (10cc) was added to a solution of 3,5-dimethyl-1,2-benzoquinone (0.72g) in the same solvent (10cc). The flask was sealed and allowed to stand for 2 weeks. The crude product was filtered off (0.19g) and recrystalised from methanol to give fine needle-shaped crystals of the mono-p-chloroanil of 2,5-di-(p-chloroanilino)-3(or 6)-methyl-1,4-benzoquinone. M.pt. 210-11°C. (Found: C,61.7%; H,3.7%; N,8.6%. $C_{25}H_{18}Cl_3N_3O$ requires: C,62.2%; H,3.7%; N,8.7%). ν_{max}(nujol) 3260(broad), 1620, 1600, and 1580cm^{-1}. The mass spectrum showed major ions at 481(M^+), 445, 343, 206. The N.M.R. spectrum showed absorptions at τ 2.6-3.3 (multiplet, H), τ 3.95 (singlet, H), τ 8.3 (singlet, H). $\lambda_{max}(CHCl_3)$=286mμ, ε=3.10x10^4; λ_{max}=402mμ, ε =1.67x10^4; λ_{max}=532mμ (shoulder).

Reaction of 4,5-dimethyl-1,2-benzoquinone with p-chloroaniline

A solution of 4,5-dimethyl-1,2-benzoquinone (0.7g) and p-chloroaniline (1.3g) in methanol (10cc) was allowed to stand for 24 hours. The crude product that was prec-

ipitated was filtered off (0.25g) and recrystalised from methanol to give dark shiny platelets of the mono-p-chloroanil of 4(or 5)-p-chloroanilino-5(or 4)-methyl-1,2-benzoquinone. M.pt. 176°C. (Found: C,63.7%; H,3.8%; N,8.0%. $C_{19}H_{14}Cl_2N_2O$ requires: C,63.8%; H,3.9%; N,7.9%). The mass spectrum showed major ions at m/e 356(M^+), 339, 321. The N.M.R. spectrum showed absorptions at τ2.6-3.5 (multiplet, 10H), τ3.78 (singlet, 1H), τ7.70 (singlet, 3H). ν_{max}(nujol) 3305, 1650, 1625, 1600, 1587 and 1575 cm^{-1}. $\lambda_{max}(CHCl_3)$=283mμ, ε =2.34x10^4; λ_{max}=490mμ, ε =6.25x10^3.

Reaction of 1,2-benzoquinone with p-anisidine in methanol

p-Anisidine (1.2g) was added to a stirred solution of 1,2-benzoquinone (0.5g) in methanol. The resultant deep red mixture was stirred overnight then filtered to yield crude 4,5-di-(p-methoxyanilino)-1,2-benzoquinone. The solvent was stripped from the filtrate under vacuum and the red oil produced taken into chloroform and chromatographed on alumina. The only product identified was p-anisidine (0.34g). The crude quinone was recrystalised from chloroform to give red crystals M.pt. 161°C. (Found: C,68.2%; H,5.1%; N,8.13%. $C_{20}H_{18}N_2O_4$ requires: C,68.6%; H,5.1%; N,8.0%). ν_{max}(nujol) 3250,

3180, 1660m, 1620s, 1590s and 1530s cm^{-1}. The mass spectrum showed major ions at m/e 350(M^+), 349, 319, 220 and 191. The N.M.R. spectrum showed absorptions at τ 2.7-3.2 (multiplet, 10H), τ 3.95 (singlet, 2H) and τ 6.2 (singlet, 6H). λ_{max} 267mμ, logε=4.10; λ_{max} 305mμ, logε=4.17; λ_{max} 458mμ, logε=3.81 and λ_{max} 500mμ, logε=3.73.

Reaction of 1,2-benzoquinone with p-anisidine in ether

A mixture of p-anisidine (1.8g) and 1,2-benzoquinone (0.5g) in 100cc of anhydrous ether was stirred overnight. A little crude product was filtered off then the solvent stripped from the filtrate at room temperature under vacuum to give a red solid. This was taken into chloroform and chromatographed on alumina. p-Anisidine (1.6g) and a further amount of the product was eluted. Total recovery 0.24g. The crude product was recrystalised from chloroform to give the dark brown mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone. M.pt. 202°C. (Found; C,71.0%; H,5.6%; N,9.3%. $C_{27}H_{25}N_3O_4$ requires: C,71.2%; H,5.5%; N,9.2%). ν_{max}(nujol) 3190, 1640m, 1610m, 1580s and 1515s cm^{-1}. The mass spectrum showed major ions at m/e 455(M^+), 440, 424, 298, 264, 255, 201 and 171. The N.M.R. spectrum showed absorptions at τ 2.7-3.3 (multi-

plet, 14H), τ3.88 (singlet, 1H), τ4.05 (singlet, 1H), τ6.2 (singlet, 6H), τ6.25 (singlet, 3H). λ_{max}277mμ, logε=4.27; λ_{max}403mμ, logε=4.11; λ_{max}545mμ, logε=3.41.

Reaction of 3-methyl-1,2-benzoquinone with p-anisidine in methanol

A solution of p-anisidine (1.83g) in methanol (10cc) was added to a solution of 3-methyl-1,2-benzoquinone (0.61g) in the solvent (10cc). The mixture was stirred for several minutes then allowed to stand for 24 hours, with occasional stirring. The crude product was filtered off (0.46g) and the solvent stripped from the filtrate under vacuum to give a brown solid. This was taken into a little chloroform and chromatographed on alumina. p-Anisidine (1.06g) was the only fraction identified. The crude product was recrystalised from methanol to give dark, shiny, needle-like crystals of 3-methyl-4,5-di-(p-methoxyanilino)-1,2-benzoquinone. M.pt. 142°C. (Found: C,69.1%; H,5.6%; N,7.6%. $C_{21}H_{20}N_2O_4$ requires: C,69.2%; H,5.5%; N,7.7%). ν_{max}(nujol) 3320, 1670m, 1610s and 1570 cm^{-1}. The mass spectrum showed major ions at m/e 364(M^+), 363, 349, 333, 123 and 108. The N.M.R. spectrum showed absorptions at τ3.07 (doublet, 10H), τ3.92 (singlet,

1H), τ 6.2 (singlet, 6H), τ 8.42 (singlet, 3H). λ_{max} 240mμ, $\varepsilon = 1.90 \times 10^4$; λ_{max} 304mμ, $\varepsilon = 1.66 \times 10^4$; λ_{max} 464mμ, $\varepsilon = 6.10 \times 10^2$. A shoulder was present on the 240mμ peak at 255mμ.

Reaction of 3-methyl-1,2-benzoquinone with p-anisidine in ether.

A mixture of 3-methyl-1,2-benzoquinone (2.27g) and p-anisidine (2.26g) was taken into a minimum quantity of dry ether and stirred overnight. The crude product was filtered off (1.0g) and recrystalised from methanol to give dark, needle-like crystals of 4(or 5)-p-methoxyanilino-3-methyl-1,2-benzoquinone. M.pt. >360°C. (Found: C,68.7%; H,5.4%; N,5.8%. $C_{14}H_{13}NO_3$ requires: C,69.1%; H,5.4%; N,5.8%). ν_{max} (nujol) 3160m, 1675, 1655, 1620, 1595, 1260, 1275s cm^{-1}. The mass spectrum showed major ions at m/e 245(M+2), 243(M^+), 230, 228, 200. λ_{max} 242mμ, $\varepsilon = 1.15 \times 10^4$; λ_{max} 268mμ (shoulder); λ_{max} 366mμ, $\varepsilon = 4.92 \times 10^3$; λ_{max} 508mμ, $\varepsilon = 4.86 \times 10^3$.

In another experiment, the solvent was stripped from the filtrate to give a brown oil. This was taken into chloroform and chromatographed on alumina. p-Anisidine was isolated together with the mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-3(or 6)-methyl-1,4-benzoquinone.

The I.R. and mass spectra of this compound were identical to those of a sample prepared from 3,5-dimethyl-1,2-benzoquinone. The melting points of the two samples were identical and unchanged on taking a mixture.

Reaction of 4-methyl-1,2-benzoquinone with p-anisidine in methanol

A solution of 4-methyl-1,2-benzoquinone (0.64g) in methanol (5cc) was added to a solution of p-anisidine (2.45g) in the same solvent (5cc). The mixture was allowed to stand for 3 days. The crude product was filtered off (1.03g) and recrystalised from chloroform to give the dark brown mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone. M.pt. 201°C. The I.R. and mass spectra were identical to those of an authentic sample. The melting point was unchanged on mixing with an authentic sample.

The solvent was stripped from the filtrate obtained from the isolation of the product to give a green oil. This was diluted with chloroform and chromatographed on alumina. The only product identified was p-anisidine (1.21g).

Reaction of 4-methyl-1,2-benzoquinone with p-anisidine in ether

A solution of p-anisidine (2.57g) in dry ether (50cc) was added to a solution of 4-methyl-1,2-benzoquinone (0.61g) in 50cc of the same solvent. The mixture was shaken, then allowed to stand for 2 days. The crude product (0.25g) was filtered off and the solvent stripped from the filtrate under vacuum to give a red oil. This was diluted with chloroform and chromatographed on alumina to give p-anisidine (2.22g) as the only fraction that could be identified. The crude product was recrystalised from chloroform to give the dark brown mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone. M.pt. 201°C. The mass and I.R. spectra were identical to those of an authentic sample. The melting point was unchanged on mixing with an authentic sample.

Reaction of 4-ethyl-1,2-benzoquinone with p-anisidine

A solution of p-anisidine (0.61g) in methanol (5cc) was added to a solution of 4-ethyl-1,2-benzoquinone in the same solvent (5cc). After standing for 3 hours, the crude product which was precipitated was filtered off. A further crop of crystals was obtained after standing for

2 days. Examination of the filtrate as before yielded only p-anisidine. The crude product was recrystalised from methanol to give the dark brown mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-1,4-benzoquinone. The I.R. spectrum was identical to that of an authentic sample. The melting point was identical to that of an authentic sample and was unchanged when the two samples were mixed.

Reaction of 3,5-dimethyl-1,2-benzoquinone with p-anisidine

A solution of p-anisidine (1.58g) in methanol (5cc) was added to a stirred solution of 3,5-dimethyl-1,2-benzoquinone in the same solvent (5cc). The mixture was stirred for 5 minutes, a further 10cc of methanol added, then the flask sealed and allowed to stand for 3 weeks. The crude product was filtered off (1.32g) and recrystalised from ethanol to give fluffy brown crystals of the mono-p-methoxyanil of 2,5-di-(p-methoxyanilino)-3(or 6)-methyl-1,4-benzoquinone. M.pt. 176-7°C. (Found: C,71.3%; H,5.7%; N,8.7%. $C_{28}H_{27}N_3O_4$ requires: C,71.6%; H,5.7%; N,8.9%). ν_{max}(nujol) 3270m, 1630m, 1595, 1510 and 1250s cm^{-1}. The mass spectrum showed major ions at m/e 471(M+2), 469(M^+), 468, 454, 438, 123 and 108. The N.M.R.

spectrum showed absorptions at τ8.37 (singlet, 3H), τ6.25 (doublet 2:1, 9H), τ3.9 (singlet, 1H), τ2.4-3.3 (multiplet, 14H). λ_{max}240mμ, ε=2.07x10^4; λ_{max}275mμ, ε=2.41x10^4; λ_{max}295mμ(inflection); λ_{max}409mμ, ε=2.41x10^4; λ_{max}550mμ (shoulder).

Reaction of 4,5-dimethyl-1,2-benzoquinone with p-anisidine

p-Anisidine (0.43g) was added to a solution of 4,5-dimethyl-1,2-benzoquinone (0.5g) in methanol (10cc). The mixture was stirred until the p-anisidine had dissolved then allowed to stand for 5 days. The solvent was stripped from the resultant solution to give a purple solid. This was taken into chloroform and chromatographed on alumina. The only product identified was the mono-p-methoxyanil of 5-p-methoxyanilino-4-methyl-1,2-benzoquinone (92mg). The crude product was recrystalised from ethanol to give shiny purple crystals M.pt. 138°C. (Found: C,72.9%; H,6.1%; N,8.1%. $C_{21}H_{20}N_2O_3$ requires: C,72.4%; H,5.8%; N,8.1%). The mass spectrum showed major ions at m/e 348(M^+), 333, 331, 317, 226, 123 and 108. The N.M.R. spectrum showed absorptions at τ7.65 (singlet, 3H), τ 6.25 (doublet, 6H) and τ2.8-3.7 (multiplet, 11H). ν_{max}(nujol) 3320m, 1655s, 1520s cm^{-1}. λ_{max}236mμ, ε=1.48x10^4;

λ_{max}276mμ, ε=2.04x10^4; λ_{max}295mμ(inflection); λ_{max}518mμ, ε=6.74x10^3; λ_{max}610mμ(inflection).

Reaction of 4-methyl-1,2-naphthaquinone with p-anisidine

A solution of p-anisidine (1,23g) in methanol (5cc) was added to a suspension of 4-methyl-1,2-naphthaquinone in the same solvent (15cc). The mixture was stirred until all the quinone had dissolved, the solution slowly becoming scarlet. The mixture was allowed to stand overnight. The purple granular crystals were filtered off and a second crop was recovered from the liquor after standing for a further 24 hours. Total recovery 1.25g. The crude product was taken into chloroform and the solution examined by T.L.C. on silica gel plates showing the presence of two components. The two products were separated on a silica gel column. Chloroform containing 5% acetone eluted the mono-p-methoxyanil of 4-p-methoxyanilino-1,2-naphthaquinone. M.pt. 218-9°C. (Found: M.wt. 384.14738 $C_{24}H_{20}N_2O_3$ requires 384.14738). ν_{max}(nujol) 3310m, 1650, 1590, 1500s cm^{-1}. The mass spectrum showed major ions at 384(M^+), 369, 279, 264, 167 and 149. λ_{max}($CHCl_3$) 252mμ, ε=1.94x10^4; λ_{max}278mμ, ε=2.09x10^4; λ_{max}330mμ(shoulder); λ_{max}504mμ, ε=6.66x10^3.

Elution with methanol eluted a small quantity of 4-p-methoxyanilino-1,2-naphthaquinone. M.pt. 204-5°C. (Found: M.wt. 279.0897, $C_{17}H_{13}NO_3$ requires 279.0895). ν_{max}(nujol) 3200(broad, weak), 1684, 1600, 1580, 1520 and 1500s cm^{-1}. The mass spectrum showed major ions at m/e 279(M^+), 264 and 236. λ_{max}244mμ, ε=1.71x10^4; λ_{max}278mμ, ε=9.98; λ_{max}346mμ, ε=3.46x10^3; λ_{max}474mμ, ε = 3.51x10^3.

Reaction of 3,5-di-tertiary-butyl-1,2-benzoquinone with p-anisidine

A mixture of 3,5-di-tertiary-butyl-1,2-benzoquinone (0.5g) and p-anisidine (0.33g) in methanol (10cc) was allowed to stand overnight. The purple crystals of 10-(p-methoxy)-phenyl-6,8-di-tertiary-butyl-phenaz-2-one obtained were filtered off (0.35g). M.pt. 192-3°C. ($C_{27}H_{30}N_2O_2$ requires 414.231, high resolution mass spectrum gives 414.231). ν_{max}(nujol) 1630m, 1600, 1570, 1500s, 1250 (broad, strong). The mass spectrum shows major ions at m/e 414(M^+), 399, 383, 369, 353 and 327. The N.M.R. spectrum showed absorptions at τ 2.5-3.2 (multiplet, 9H), τ 6.15 (singlet, 3H), τ 8.3 (doublet, 18H).

Reaction of benzylamine with 1,2-benzoquinone

Benzylamine (2.0g) was added to a solution of 1,2-benzoquinone (0.52g) in methanol (40 cc). The solution, which became brown on mixing, was stirred overnight. The solution was filtered free of the trace of black solid produced and the solvent removed under reduced pressure to give a brown oil. This was allowed to stand in the air when it became very hot after a few minutes. After standing for several hours, chloroform was added and the resultant solution chromatographed on an alumina column. Ether eluted benzaldehyde (0.93g).

The product had an identical infra red spectrum to an authentic sample. Further characterisation was carried out by preparing the phenylhydrazone of the product and an authentic sample. (Mann and Saunders, "Practical Organic Chemistry", page 339). The infra red spectra and the melting points of the two samples were identical. The melting points were unchanged when a mixture of the two samples was taken.

Attempted reaction of 5,6,7,8-tetrahydronaphthaquinone with p-anisidine

A solution of 5,6,7,8-tetrahydronaphthaquinone (3.8g) and p-anisidine (7.4g) in methanol (60cc) was stirred for 10 minutes then allowed to stand overnight. The solvent was stripped from the resultant dark solution under vacuum to give a brown oil which slowly solidified on standing. The solid was taken into chloroform and chromatographed on silica gel. p-Anisidine contaminated with a brown component (T.L.C. on silica) was eluted by chloroform. The mixture was taken up in chloroform and washed with dilute hydrochloric acid. The chloroform layer was dried and the solvent stripped to give a brown solid, more of which was obtained by elution of the column with methanol. The solid was recrystalised from methanol to give a brown powder. This melted at about 130°C over a wide temperature range. I.R., mass and N.M.R. spectra were obtained, but the product could not be identified.

Attempted reaction of hydrin-5,6-quinone with p-anisidine

A solution of p-anisidine (1.24g) in methanol (3cc) was added to a solution of hydrin-5,6-quinone in the same solvent (8cc). The bright red quinone sol-

ution became yelow/brown on mixing. The mixture was allowed to stand for three days. The solvent was stripped under vacuum to give a brown semi-solid which was taken into chloroform and chromatographed on silica gel. The only fraction that could be identified was p-anisidine.

Reaction of o-aminophenol with 1,2-benzoquinone in methanol

A solution of o-aminophenol (1.1g) in methanol (100cc) was added to a solution of 1,2-benzoquinone (1.1g) in the same solvent (100cc) and the mixture stirred overnight. After filtering off the insoluble black polymer, (0.09g), the solvent was stripped under vacuum to give a red solid. This was taken up in a mixture of pyridine (15cc) and acetic anhydride (20cc) and the solution allowed to stand for 2 days. The orange product which separated was filtered off and washed with a little ether to give 4,5-di-(o-acetoxyanilino)-1,2-benzoquinone (0.25g). The filtrate was poured into ice water (200cc) and extracted with chloroform (250cc). The extract was washed with dilute hydrochloric acid, dried over calcium sulphate and the solvent removed under reduced pressure to give a red oil. This was taken into chloroform and chromatographed on alumina. Chloroform eluted a little unidentified solid. 1:1

chloroform/methanol eluted 0.69g of o-acetamidophenol. M.pt. 201°C (from methanol). Lit.[123] 201°C.

The crude 4,5-di-(o-acetoxyanilino)-1,2-benzoquinone was recrystalised from methanol to give shiny, orange plates. M.pt. 211°C. (Found molecular weight: 406.1163, $C_{22}H_{18}N_2O_6$ requires: 406.1165). ν_{max}(nujol) 1770s, 1640, 1580 and 782 cm^{-1}. The mass spectrum showed major ions at m/e 406(M^+), 364, 347, 322, 305, 286, 255, (M^* 406-255 at 160), 213, (M^* 255-213 at 178), 185 and 156. λ_{max}246mμ, logε=4.18; λ_{max}360mμ, logε=4.12; λ_{max}450mμ, logε=3.96; λ_{max}500mμ (inflection). The compound was too insoluble for N.M.R. spectroscopy.

Reaction of o-aminophenol with 1,2-benzoquinone in ether

A solution of o-aminophenol (0.5g) in anhydrous ether (50cc) was added to a solution of 1,2-benzoquinone (0.5g) in the same solvent (150cc). The mixture was stirred for 24 hours then filtered free of the trace of black polymer produced. The solvent was removed from the filtrate under vacuum to give a dark red solid. This was treated with chloroform, leaving behind an unidentified red solid (0.14g). The chloroform soluble fraction, after filtering, was chromatographed on alumina with chloroform

as eluant to give 3-aminophenoxazone (0.17g) as the only identified product. M.pt. 250°C (lit.[110] 250-1°C). The I.R. spectrum was identical to that already published. The mass spectrum showed major ions at m/e 212(M^+), 184, 156 and 144. High resolution molecular weight found: 212.0588, $C_{12}H_{18}N_2O_2$ requires 212.0586.

Reaction of p-bromoaniline with 1,2-benzoquinone in methanol

A solution of p-bromoaniline (1.72g) and 1,2-benzoquinone (0.5g) in methanol (40cc) was stirred overnight. The crude product was filtered off (0.35g) and recrystalised from chloroform to yield bright red crystals of 4,5-di-(p-bromoanilino)-1,2-benzoquinone. M.pt. >300°C. The analysis sample was further purified by T.L.C. (Found: C,48.2%; H,2.8%; N,6.2%. $C_{18}H_{12}Br_2N_2O_2$ requires: C,48.2%; H,2.7%; N,6.2%). ν_{max}(nujol) 3200, 1610s, 1590s and 1530 cm^{-1}. The mass spectrum showed major ions at m/e 446(M^+), 417, 365 and 337. λ_{max}277mμ, logε=4.15; λ_{max}285mμ, logε=4.15; λ_{max}392mμ, logε=3.84; λ_{max}500m , logε=3.24. It was not possible to obtain an N.M.R. spectrum due to low solubility.

Reaction of p-bromoaniline with 1,2-benzoquinone in ether

A solution of p-bromoaniline (3.44g) and 1,2-benzoquinone (0.5g) in anhydrous ether (100cc) was stirred overnight protected by a calcium chloride tube. The solution was filtered free of the small amount of black polymer obtained and the solvent stripped under vacuum to give a red solid. This was taken into chloroform and chromatographed on acid-washed alumina. The mono-p-bromoanil of 2,5-di-(p-bromoanilino)-1,4-benzoquinone (0.13g) was eluted together with the original amine (1.92g). The anil was recrystalised from chloroform to give fine brown crystals. M.pt. $>300^{\circ}C$. A sample was further purified by T.L.C. before analysis. (Found: C,47.5%; H,2.7%; N,7.1%. $C_{24}H_{10}Br_3N_3O$ requires: C,47.8%; H,2.7%; N,7.0%). ν_{max}(nujol) 3300, 1615m, 1595m, 1575s and 1540 cm^{-1}. λ_{max} 286mμ, logε=4.23; λ_{max} 387mμ, logε=4.04; λ_{max} 521mμ, logε=3.20.

Reaction of 5,6,7,8-tetrahydronaphtha-2,3-quinone with cyclopentadiene

Freshly prepared cyclopentadiene (4cc) was added to a stirred solution of 5,6,7,8-tetrahydronaphthaquinone (1.5g) in dry benzene (175cc). The solution was

allowed to stand overnight during which time the colour faded to a pale yellow. The solution was filtered free of the yellow/grey solid deposited then the solvent carefully stripped at room temperature under reduced pressure. The orange oil obtained was taken into benzene and chromatographed on silica gel. Benzene gave a little unchanged diene then the solvent was changed to chloroform. This eluted the desired adduct but only the first portion was pure, the remainder being contaminated with other products. The column was finally eluted with methanol to give a brownish-yellow solid (M.pt. $>360^{\circ}C$) which was not further characterised. The tetracyclo-$\left[6,5,2,0^{2,6},0^{8,13}\right]$-pentadeca-4,5:8,13-diene-14,15-dione obtained had a melting point $201^{\circ}C$. ν_{max}(nujol) 1725 cm^{-1}. (Found: molecular weight: 228.1148, $C_{15}H_{16}O_2$ requires 228.1150). The mass spectrum showed major ions at m/e 228(M^+), 227, 200 and 172. The N.M.R. spectrum showed absorptions at τ 4.24 (multiplet, 1H), τ4.55 (multiplet, 1H), τ 6.8 (narrow multiplet, 2H) and τ 7.8-8.5 (multiplet, 12H). λ_{max} 285mμ, $\varepsilon = 1.58 \times 10^3$; λ_{max} 450mμ, $\varepsilon = 2.7 \times 10^2$.

Reaction of 4,5-dimethyl-1,2-benzoquinone with cyclopentadiene

Freshly prepared cyclopentadiene (1.0g) was added to a solution of 4,5-dimethyl-1,2-benzoquinone (0.6g) in dry benzene (200cc). The solution was mechanically stirred for 2 days during which time the original red colour due to the quinone slowly faded to give a yellow solution. After filtration, the solvent was carefully removed under vacuum at room temperature to yield a yellow oil. This was diluted with chloroform and chromatographed on a silica gel column to give 8,9-dimethyl-tricyclo-$[5,2,2,0^{2,6}]$-undeca-4,5:8,9-diene-10,11-dione (0.10g). M.pt. 194-5°C lit. 212°C. (Found: C,76.8%; H,7.2%, $C_{13}H_{14}O_2$ requires: C,76.9%; H,7.4%). ν_{max}(nujol) 1730 cm^{-1}. The mass spectrum showed major ions at m/e 202(M^+), 201, 146 and 131. The N.M.R. spectrum showed absorptions at τ 4.25 (multiplet, 1H), τ 4.55 (multiplet, 1H), τ 6.4-8.0 (multiplet, 2H), τ 8.12 and τ 8.22 (two singlets, 9H). λ_{max} 283mμ, $\varepsilon = 1.66 \times 10^3$; λ_{max} 452mμ, $\varepsilon = 2.67 \times 10^2$. Our melting point could not be raised to the published value by recrystalisation.

Reaction of cyclopentadiene with hydrin-5,6-quinone

Freshly prepared cyclopentadiene (9g) was added to a stirred solution of hydrin-5,6-quinone (1.0g) in dry benzene (150cc). The mixture was stirred for 2 days during which time the original bright red colour was slowly discharged to give a yellow solution. After filtering the reaction mixture, the solvent was carefully stripped at room temperature under reduced pressure to give a yellow oil. This was diluted with chloroform and chromatographed on a silica gel column. Chloroform first eluted dicyclopentadiene followed by the yellow crystalline solid tetracyclo-$[5,5,2,0^{2,6},0^{8,12}]$-tetradeca-4,5:8,12-diene-13,14-dione (0.20g). M.pt. 162-3°C. (Found molecular weight: 214.0996, $C_{14}H_{14}O_2$ requires 214.0994). ν_{max}(nujol) 1730 and 1710 cm^{-1}. The mass spectrum showed major ions at m/e 214(M^+), 186 and 158. The N.M.R. spectrum showed absorptions at τ 4.30 (multiplet, 1H), τ 4.60 (multiplet, 1H), τ 6.46 (singlet, 2H) and τ 6.9-8.2 (multiplet, 10H). λ_{max} 288mμ, $\varepsilon = 1.37 \times 10^3$; λ_{max} 446mμ, $\varepsilon = 2.87 \times 10^2$.

Thiele-type reaction with 1,2-benzoquinone

1,2-Benzoquinone (1.0g) was dissolved in acetic

anhydride (15cc) and a few drops of concentrated sulphuric acid were added. The bright red colour of the quinone solution rapidly faded to a pale orange/yellow colour. The product was poured into cold water (100cc), the resultant solution neutralised with sodium bicarbonate, extracted with chloroform (3x100cc), the extract dried over calcium chloride and the solvent removed at room temperature under vacuum. The resultant yellow oil gave a pale yellow solid (1.44g) on standing. This was recrystalised from ethanol to give the 1,2,4-triacetate of benzene as white solid. M.pt. 92-4°C (lit.[125] 96-7°C). The melting point was unchanged when mixed with an authentic sample and the I.R. spectra of the two were identical.

Preparation of the 1,2,4-triacetate of benzene

A mixture of concentrated sulphuric acid (1.2g) and acetic anhydride (18g) was placed in a 100cc beaker equipped with a thermometer and stirrer and surrounded by a cold water bath. 1,4-Benzoquinone (6g), which had been freshly recrystalised from benzene, was added, in small portions, with stirring, maintaining the temperature between 40°C and 50°C. When all the quinone had been added, the solution was left stirring, taking care not to allow

the temperature to rise above 50°C, until it began to cool. At this point, solid began to precipitate. The mixture was allowed to cool to room temperature and the product isolated by adding ice cold water (75cc). The white precipitate of the crude 1,2,4-triacetate of benzene was filtered off at the pump and recrystalised from a little ethanol. The product was dried over calcium chloride in an atmosphere of carbon dioxide. The freshly prepared product melted at 93-5°C (lit.[125] 96-7°C) but it decomposed over a period of days to grey solid.
Yield:- 10.3g.

Preparation of the 1,2,3-triacetate of benzene

A mixture of anhydrous sodium acetate (8.2g), pyrogallol (12.6g) and acetic anhydride (110cc) was heated under reflux at about 160°C for 2 hours. The mixture was allowed to stand overnight before adding water and filtering off the crude product at the pump. Yield:- 22.2g. A sample was taken and recrystalised from ethanol giving small white crystals M.pt. 165-6°C, (lit.[124] 165°C).

Attempted preparation of 4-benzyl-1,2-benzoquinone from p-benzylphenol

A solution of p-benzylphenol (1.8g) in ether (20cc) was added to a solution of Fremy's salt (7.6g) in water (550cc) containing sodium acetate solution (30cc, 1M). The mixture was cooled in an ice/salt bath and stirred vigorously for 4 hours. The resultant red solution was extracted with ether, the extract dried and the solvent stripped to give a red oil. This was chromatographed on a silica gel column using chloroform as eluant. The major product obtained was p-benzylphenol (1.3g), identified by I.R. spectroscopy.

Preparation of 1-amino-3-benzylphenol

A mixture of sulphanilic acid (105g), sodium carbonate (26.5g) and water (500cc) was heated with stirring until all the sulphanilic acid had dissolved. The solution was cooled in ice to 15°C at which point sodium sulphanilate began to precipitate. A solution of sodium nitrite (37g) in water (100cc) was added and the resultant solution poured at once into a mixture of concentrated hydrochloric acid (106cc) and ice (600g) in a 2 litre flask. The solution from which p-benzenediazonium

sulphonate separated on stirring was allowed to stand in an ice bath for about 20 minutes.

p-Benzylphenol (92g) was dissolved in the warm solution obtained by dissolving caustic soda (110g) in water (600cc) in a 5 litre beaker. The solution was cooled to about 5°C by the addition of ice (400g), then the suspension of p-benzenediazonium sulphonate, prepared above, was added. The mixture was stirred well before being allowed to stand for an hour without external cooling. The solution was a deep red at this stage indicating the presence of the azo dye, though this did not precipitate.

The dye solution was heated to 50°C, with stirring, on a steam bath. A little gas was evolved during this process. About one-tenth of a sample of 230g of sodium hydrosulphite was cautiously added, and the mixture stirred until frothing subsided. The remainder was now added, in one lot, while stirring continuously. The bright red colour of the solution rapidly faded to a pale yellow and fine needles of the almost colourless amino-phenol were precipitated. The reaction was brought to completion and the product digested by heating to 70°C, on a steam bath, with stirring. The solution was allowed

to stand for 3 hours then cooled in ice and filtered to yield fine crystals of 1-amino-3-benzylphenol.

Attempted preparation of 4-benzyl-1,2-benzoquinone from 1-amino-3-benzylphenol

1-Amino-3-benzylphenol (4.95g) and a few crystals of stannous chloride were dissolved in water (1.25 litres) containing concentrated hydrochloric acid (5cc). The solution was filtered then a filtered solution of ferric chloride (12g) in water (75cc) and concentrated hydrochloric acid (2.5cc) was added at once. Almost immediately a dark powdery precipitate separated. This was not the expected quinone but appeared to be p-benzylphenol.

Attempted preparation of 4-benzylcatechol from 1-amino-3-benzylphenol

Concentrated sulphuric acid (22cc) was cautiously added to water (15cc) in a 250cc conical flask. 1-Amino-3-benzylphenol (20g) was added together with ice (50g) and the whole thoroughly stirred to give a homogeneous paste. The mixture was cooled to about $0^{\circ}C$ in an ice/salt bath, and a cold solution of sodium nitrite

(7.2g) in water (16cc) was added in portions keeping the temperature below 5°C. The mixture was stirred for 5 minutes then allowed to stand for a further 5 minutes during which time it foamed somewhat.

Concentrated sulphuric acid (66cc) was cautiously added to water (60cc) in a 500cc round bottomed flask. The whole was heated to almost 100°C and the diazonium mixture slowly added in portions, care being taken to avoid excessive frothing. After all had been added, the solution was maintained at about 100°C for 5 minutes, then poured into a 500cc beaker cooled in an ice bath. The solution was stirred as it cooled, to yield a pale yellow solid which was filtered off and dried in a dessicator. The product, which was expected to be 4-benzylcatechol, had a molecular weight of 262 (by mass spectrometry). The I.R. spectrum showed a broad absorption from 2400 to 3600 cm^{-1} and a strong, sharp absorption at 2240 cm^{-1}. It was not further characterised.

The product was boiled under reflux for 2 hours with a mixture of concentrated sulphuric acid (50cc) and water (50cc). After standing overnight, the mixture was diluted with water and extracted with ether. The

ether extract was dried and the solvent stripped to give a brown oil which partially solidified on standing. The I.R. spectrum showed a broad absorption at 3100 to 3600 cm^{-1}, and a strong absorption at 1690 cm^{-1}. The absorption at 2240 cm^{-1} had completely disappeared. No further characterisation was attempted.

Attempted preparation of 4-benzylcatechol by acylation of 1,2-dimethoxybenzene

A mixture of benzoyl chloride (35.2g), 1,2-dimethoxybenzene (30g), carbon disulphide (130cc) and powdered anhydrous aluminium chloride (38.4g) was stirred under reflux (with cooling in ice for the first hour) for 8 hours. The resultant mixture was poured into ice water and the white precipitate of 3,4-dimethoxybenzophenone obtained was filtered off. More product was recovered by separating the organic layer and allowing the solvent to evaporate in a well ventilated hood overnight. The solid obtained was filtered, taken into ether, the solution water-washed, dried and concentrated under vacuum. The white needles precipitated were filtered off and washed with a little ether. M.pt. 98°C (lit.[129] 99°C). Total recovery 27.6g.

A mixture of granulated zinc (85g), mercuric chloride (8.5g), concentrated hydrochloric acid (12.5cc) and water (125cc) was shaken for 10 minutes. The amalgam obtained was washed in running water then placed in a 500cc round bottomed flask with dilute hydrochloric acid (200cc, 1 volume acid to 2 volumes water). 3,4-dimethoxybenzophenone (21.4g) was added and the whole brought to the boil under reflux. The mixture was refluxed for 4 hours, adding 3 portions of 25cc dilute hydrochloric acid at half-hourly intervals, then a final portion of 50cc concentrated hydrochloric acid after a further half hour. The solution was allowed to cool, separated from the remaining amalgam and ether extracted. The amalgam was washed with ether, the washings combined with the extract and the whole dried over magnesium sulphate. The solvent was stripped to give 1,2-dimethoxy-4-benzylbenzene as a colourless oil.

A mixture of 15g of the crude oil and hydriodic acid (147g, specific gravity 1.7) was boiled under reflux in a stream of carbon dioxide for 2 hours. The mixture was allowed to cool to room temperature, diluted with water and extracted with ether. The extract was washed with dilute sodium bicarbonate solution, dried over

magnesium sulphate and the solvent stripped to yield a brown oil. This was not the expected 1,2-dihydroxy-4-benzylbenzene and was not identified.

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