THE STUDY OF FREE RADICALS BY ELECTRON SPIN RESONANCE

A Thesis submitted for
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by

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NOTE

For the author's Oxford B.A. Part II thesis, preliminary work was carried out on the oxidation of some 15 monohydric phenols, and the results were the subject of a preliminary communication (Proc.Chem.Soc., 1962, 253). After a part of the e.s.r. spectrometer, which had been damaged in transit, was replaced, much improved resolution was obtained, and at the start of the author's D.Phil. work all previous results were repeated. Thus every result quoted in the present thesis was obtained during the author's D.Phil. course, although experience had been previously gained in the operation of the spectrometer and the use of the flow apparatus.

PART 1

INTRODUCTION

1.1. INTRODUCTION

This thesis is presented in five Parts, which may briefly be described as follows. Part 1 is an introductory section in which a brief account is given of electron spin resonance (e.s.r.) and the e.s.r. spectrometer. Also described is the general experimental technique; in particular, the flow apparatus used to obtain most of the radicals described in this work. The other Parts are concerned with the four main groups of compounds from which radicals have been obtained and investigated. These groups of compounds have a common feature in that they are all aromatic compounds with one or more oxygen-containing functional groups (*i.e.* -OH, =O).

Part 2 describes the radicals obtained by the oxidation of monohydric phenols; Part 3 the oxidation of resorcinols to produce the *meta*-semiquinones. In both cases the radicals were observed using the flow system. The shorter Part 4 describes a few examples of the production of secondary radicals from catechol and substituted quinols, giving some insight into the reaction mechanism of the further reactions. Although Part 5, which describes the oxidation of substituted catechols, contains information on quite a large number of spectra, this section is relatively the most incomplete. This is because the spectra obtained

were in many cases either unanalysable or analysable only after simplifying assumptions were made. Several secondary radicals, such as the semiquinones from substituted 1,2,4-trihydroxybenzenes and pyrogallols, have been detected during the oxidation of catechols and have been successfully characterised.

The emphasis of the work has been mainly on the detection and characterisation of radical intermediates in organic reactions. The discussion of the e.s.r. results has been almost entirely qualitative, and suffers as a result. There are several examples in this work where qualitative trends or interesting results have been observed, but it has not been within the ability of the author to perform the necessary quantitative calculations.

It would seem that, for organic chemists untrained in the quantitative theoretical aspects of the subject, the value of e.s.r. lies in its use for the detection and characterisation of radical intermediates in organic and biological reactions, thus giving valuable information to help in the elucidation of the mechanisms involved in the reactions.

1.2. ELECTRON SPIN RESONANCE

Electron spin resonance (e.s.r.) spectroscopy is a technique by which molecules possessing electrons with unpaired spins may be directly investigated. The present work is concerned solely with the investigation of organic aromatic monoradicals in solution and the following discussion will be centred primarily on those aspects of e.s.r. which deal directly with this. The detailed theory of e.s.r. and the rigorous interpretation of the information which can be derived from the experimental results depend on a detailed knowledge of wave mechanics. Whenever possible a simple qualitative description of e.s.r. theory is given below, and for the detailed derivation of the basic expressions reference may be made to the many reviews and theoretical papers which are quoted below.

1.2.1. BASIC PRINCIPLES.

As its name implies e.s.r. spectroscopy depends basically on the fact that an electron has a spin. In an external magnetic field the spin of an unpaired electron can acquire two orientations, either in the same or in the opposite direction to the field, corresponding to two energy states, $-\frac{1}{2}g\beta H$ and $+\frac{1}{2}g\beta H$ (where H is the external magnetic field, β the Bohr magneton, and g the spectroscopic splitting factor).[1] If radiation of energy $h\nu$ (where ν is

the frequency) equal to the difference between the two energy levels is applied, transitions from one energy level to the other will occur. Since more electrons are present in the lower level more transitions will occur from the lower to the higher level and energy will be absorbed from the applied field of frequency ν. The resonance condition will therefore be $h\nu = g\beta H$.

If the molecular orbital of the unpaired electron embraces nuclei having magnet moments interaction will occur between the electron and nuclear spins, and this will give rise to the feature on which almost all e.s.r. studies of organic free radicals in solution depend - hyperfine structure (hfs). The magnetic moment of a nucleus with a spin of $I = \frac{1}{2}$ (i.e. the hydrogen nucleus) can align itself either parallel or antiparallel to the magnetic moment of the electron spin, and the original two energy levels are now split into four. Of the four possible transitions only two are allowed, namely those in which the nuclear spin does not change. Thus interaction with one nucleus of spin $\frac{1}{2}$ produces two transitions and the spectrum consists of two absorption lines of equal intensity. For interaction with two equivalent protons, each electron spin level is split into three with a doubly degenerate level in the centre, and three equidistant spectral lines of intensity 1:2:1 are obtained. If the protons were not equivalent each proton would split the

electron levels by different amounts and four spectral lines of equal intensity would be observed, although the separation between adjacent lines would not all be equal.

Interaction with n equivalent nuclei of spin I results in (2nI + 1) hyperfine lines; for the more usual case of $I = \frac{1}{2}$, (n + 1) equally spaced lines are produced with relative intensities proportional to the coefficients of a binomial expansion in n. The value of the splitting caused by a particular nucleus is called the (hyperfine) coupling constant, $\underline{a}$, of that nucleus.

1.2.2. Hfs AND SPIN DENSITY.

(i) Ring proton hfs. Since hfs is caused by interaction of the electron with a nucleus the coupling constant should depend on the unpaired electron density on the given nucleus. McConnell[2] has shown that there is a direct relationship between a proton coupling constant, $\underline{a}_H$, and the unpaired electron density ρ_C on the carbon atom adjacent to the proton, thus: $\underline{a}_H = Q_{C-H}\rho_C$, where Q_{C-H} is a constant, called for simplicity the Q-factor.

Now electrons in pure p-, d- and f-orbitals have no density at the nucleus so the unpaired electron must have a certain amount of s-orbital character. The radicals dealt with in the present work are derived from aromatic molecules, the free electron moving in a π-orbital which has a node in the molecular plane; at first

sight, therefore, it would appear to have no unpaired electron density in this plane. To overcome this apparent anomaly the concept of $\sigma - \pi$ configurational interaction has been used by several authors,[3,4] although the approach by McConnell and Chesnut is more amenable to a simple qualitative discussion. If we consider a $>\dot{C}H$ part of an aromatic system, we have a σ-bonding orbital formed from a C sp^2 and H 1s orbital. Perpendicular to the plane of the σ-bond is the p_π-orbital of the C atom which contains the unpaired electron. The two possible arrangements of the electron spin orientations are shown by arrows in Fig.1.1. Because the C sp^2 electron tends to orient its spin parallel to that of the p_π -electron the second arrangement is slightly preferred and thus there results a small unpaired spin density at the C sp^2 and H 1s orbitals, which latter gives rise to hfs.

The constant Q_{C-H} in the equation above has been calculated by Jarrett,[3d] who found $|Q_{C-H}| \sim 28$ Oe. Since the sum of all the spin densities in a one-electron hydrocarbon radical system is unity the constant Q_{C-H} should be identical with the total proton splitting <u>i.e.</u> $\sum_{i=1}^{N} a_{H_i} = |Q_{C-H}| \sum_{i=1}^{N} \rho_{C_i} = |Q_{C-H}|$, where N is the number of carbon atoms to which hydrogen atoms are attached. This has been found to be the case with, for example, the naphthalene anion,[5] the overall width of the spectrum being ca. 28 Oe. More

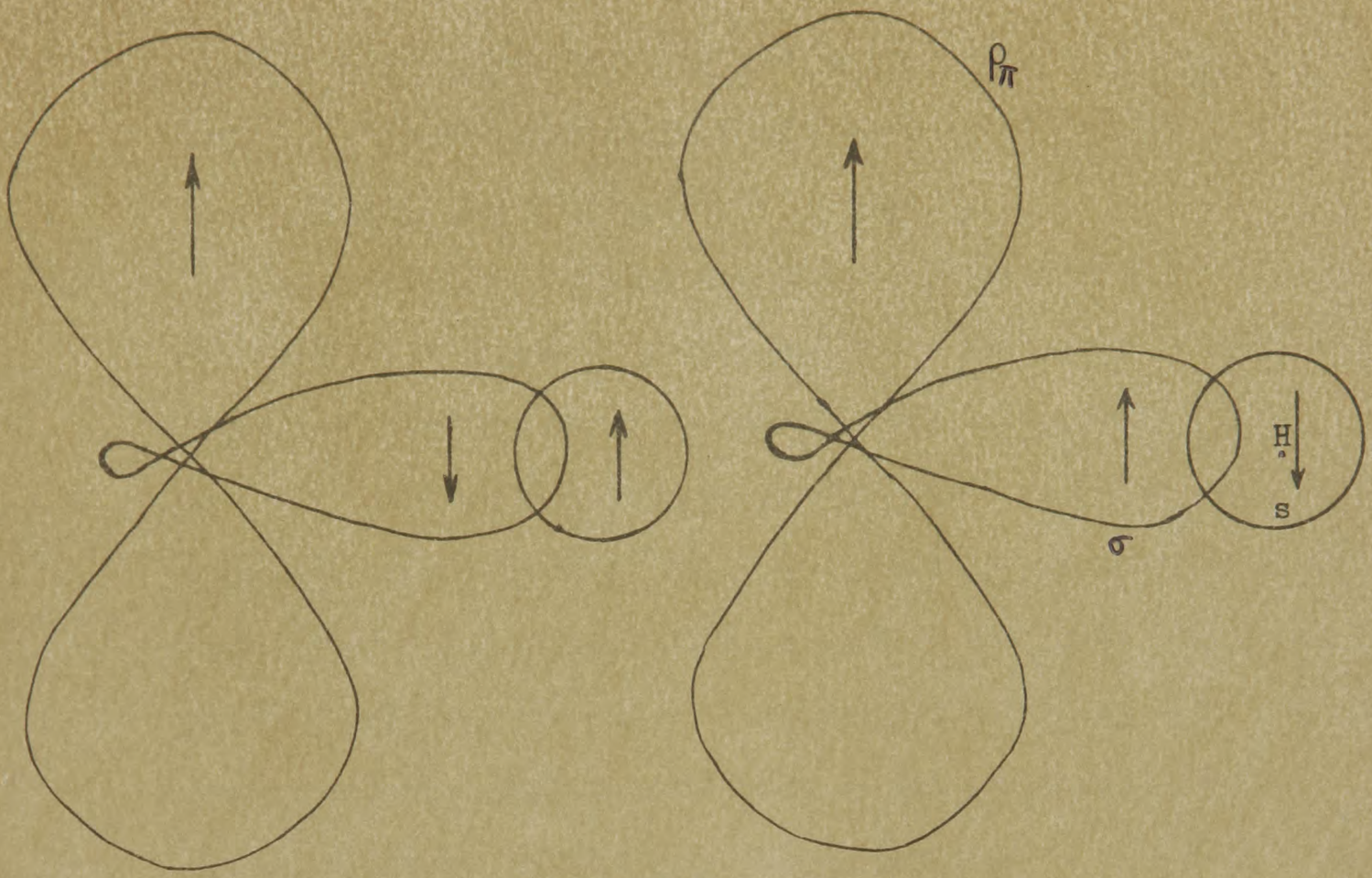


Figure 1.1

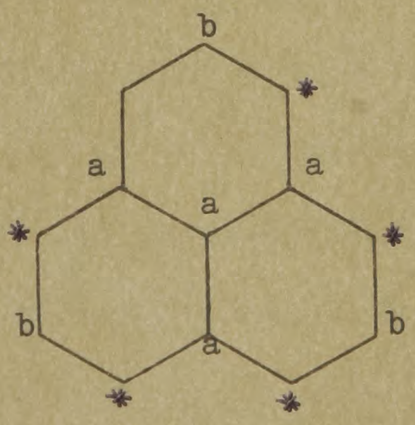


Figure 1.2

recently it has been the practice to take the value for $|Q_{C-H}|$ as 23.7 Oe, from theoretical considerations and a comparison with the splitting observed in the methyl radical.[6]

Good agreement between electron densities obtained from experimental coupling constants and those calculated by the simple Hückel M.O. theory[7] has been achieved for radicals from even-alternant hydrocarbons such as naphthalene[8] and perylene[9] (alternant hydrocarbons are those in which the atoms can be starred in such a way that each starred atom is bonded to unstarred atoms; even and odd refer to the number of conjugated carbon atoms). In the case of odd-alternant systems such as the perinaphthenyl free radical, however, simple M.O. theory predicts that the unpaired electron density at the positions marked a and b (Fig. 1.2) should be zero. In fact a finite hfs from protons at positions b is observed in the e.s.r. spectrum.[10] To explain this and similar observations it has been pointed out[4] that hyperfine interaction may be either positive or negative, and, in general, it is necessary to calculate not the unpaired electron density but the spin density, which may be positive or negative depending on the polarization of the electron spin.

The valence bond method predicts the presence of negative spin densities in odd-alternant hydrocarbon radicals[4a,11], but

in order to obtain negative spin densities by the molecular orbital theory the simple Hückel method has to be modified to include interaction of the electrons with one another.[4] As shown above, under the influence of the unpaired electron, orbitals with previously balanced spins become partly uncoupled i.e. an electron density appears having a spin opposite to that of the unpaired electron. In this way, owing to the different projections of the spins the electrons have densities of opposite sign. The spin density at a carbon atom is obtained by adding the spins, either α or β, of all the electrons at the atom. If there is an excess of α- over β-spins the spin density is positive, and if not, it is negative. For example, in the allyl radical:

$$\underset{a\ \ b\ \ c}{\dot{C}H_2\text{-}CH\text{=}CH_2} \longleftrightarrow \underset{a\ \ b\ \ c}{CH_2\text{=}CH\text{-}\dot{C}H_2}$$

it can be shown[12] by V.B. theory that carbon atoms a and c have spin = $\frac{2}{3}\alpha$ and carbon atom b has spin = $\frac{1}{3}\beta$, i.e. a negative spin density.

Because a π-electron on a carbon atom induces a little unpaired spin of opposite direction at an attached proton the Q-value in the above equation has been shown[4] to have a negative value.

Evidence for the existence of positive and negative spin densities can be obtained from n.m.r. studies on paramagnetic

substances. The chemical shift, ΔH, at the proton and the spin density, ρ_C, at the adjacent carbon atom, are related[4,13] by $\Delta H \propto Q\rho_C$ and the sign of the spin density is determined by the direction of the chemical shift at the proton. The review by Morozova[14] quotes several examples of this use of n.m.r.

(ii) Methyl-proton hfs. Hfs is observed experimentally from the protons of a methyl group attached to an aromatic system. As the carbon atom of the methyl group has sp^3 configuration with no free p-orbital to take part in the π-bond system of the ring, some other mechanism has to be invoked whereby the unpaired electron can move out from the ring system onto the protons of the methyl group. This could take place by at least two mechanisms[15]: one is hyperconjugation, the other an inductive effect where the only effect of the methyl group is to make the adjacent ring carbon more electropositive, the electrons in the ring readjusting themselves without any transfer of charge between the ring and the methyl group.

The hyperconjugative mechanism can be explained by treating the three hydrogen atoms of the methyl group as a single group.[16] Three combinations of the three hydrogen 1s-orbitals can be formed, two of which have π-symmetry and can combine with the aromatic π-system.

An equation analogous to that used for ring protons may be

used for α-proton splitting, in which the coupling constant of the methyl protons is given by[17] $a_{H-CH_3} = Q_{C-CH_3}\rho_{C-CH_3}$ where ρ_{C-CH_3} is the spin density on the carbon atom to which the methyl group is attached. In this case the Q-factor is usually given the value[18] +27.2 Oe. Experimental evidence for the difference in sign for the Q-factors has also been found using n.m.r.[19]

1.3 THE E.S.R. SPECTROMETER

On substituting values for the constants in the equation $h\nu = g\beta H$, it can be seen that the ratio ν/H is approximately equal to 3 when ν and H are expressed in Mc/s and Oersteds (Oe) respectively. Thus for a spectrometer working with a magnetic field of the order of 3000 Oe the frequency of the radiation necessary to produce resonance would be approximately 9000 Mc/s (ca. 3 cm. wavelength). This frequency falls in the microwave region of the electromagnetic spectrum.

In the e.s.r. spectrometer a klystron generates a microwave field of frequency ca. 9000 Mc/s, which is applied to a resonant cavity which contains the sample under investigation, and which is situated between the poles of an electromagnet. The cavity is connected to one arm of a microwave bridge, another arm of which contains a crystal detector, and this bridge can be balanced in the absence of any electron resonance. When energy is absorbed as a

result of resonance, and the d.c. magnetic field is varied slowly through the value required for resonance, the bridge becomes unbalanced and this is sensed by the crystal detector.

The cavity also contains a set of coils which provides 100 kc/s modulation of the d.c. magnetic field at the sample position. The e.s.r. signal information then appears as an a.c. modulation on the microwave energy reflected from the sample cavity to the crystal detector. The signal is then amplified, phase detected, and applied to an oscilloscope or graphic recorder.

The spectrometer used in the present work was a Varian V-4500 model employing a 6 in. magnet and 100 kc/s frequency modulation.

1.4 GENERAL EXPERIMENTAL TECHNIQUE

1.4.1 RECORDING SPECTRA

The basic procedure for operating the e.s.r. spectrometer will not be given as it has been adequately described elsewhere.[20] It is worth noting, however, the precautions necessary to obtain the best spectrum from a free radical sample, these are as follows:

a) If too much microwave power is delivered to the sample the signal will be saturated and broad lines will result. If too little is used, the maximum sized signal will not be obtained.

b) The amplitude of modulation should be as low as possible when observing spectra of free radicals with narrow line

widths and small splittings. If the modulation amplitude is too high broadening of the signal occurs[21] and many important features of the spectrum may be missed completely.

c) When a spectrum is being run a slow sweeping of the magnetic field is preferable, although also time consuming. If the signal is run through too rapidly the derivative curve (an e.s.r. signal is presented as the first derivative of the absorption signal) may be partially integrated and distortion will occur.

d) The cavity should be placed in the position of maximum magnet field homogeneity.

e) Low concentrations of radicals should be used to prevent spin-spin broadening.

In the investigation of stable free radicals most of the above optimum conditions can be achieved with care. However, when unstable free radicals in solution are being observed by the technique described below, these conditions cannot always be obtained and a balance has to be struck between obtaining a signal on the one hand too small and on the other hand too distorted.

1.4.2. THE FLOW APPARATUS

Free radicals with comparatively long lifetimes may be examined in the e.s.r. spectrometer in the normal way. A minimum time of

about two minutes is required between producing a free radical solution and observing the spectrum in the spectrometer. The examination of unstable free radicals in solution requires either the production of the radicals *in situ* by, for example, an electrochemical process,[22] or the use of a flow system. Two flow systems have been described in the literature: one, a very simple system used for detecting the relatively stable p-semiquinones,[23] and the other a very complex system used for reactions of biological interest.[24] Hitherto little work has been done on the detection of quite unstable radicals produced in solution as intermediates in chemical reactions. The flow apparatus described below was designed in this laboratory[25] and has proved effective in detecting radicals produced by the oxidation of phenols and resorcinols (see Parts 2 and 3 below), by the reduction of aromatic nitro compounds,[26] and by the further reaction of the hydroxyl radical produced *in situ*.[25]

Two open reservoirs are connected by tubing to a mixing chamber which is attached to a Varian aqueous sample tube as shown in Fig.1.3. The two reacting solutions mix at A; the volume between mixing and reaching the flat portion of the cell is *ca.* 0.05 ml. The maximum flow rate obtainable is 5 ml. $sec.^{-1}$, thus radicals with lifetimes $\geqslant 10^{-2}$ sec. may be observed with this simple apparatus.

The conditions mentioned in the previous section for observing

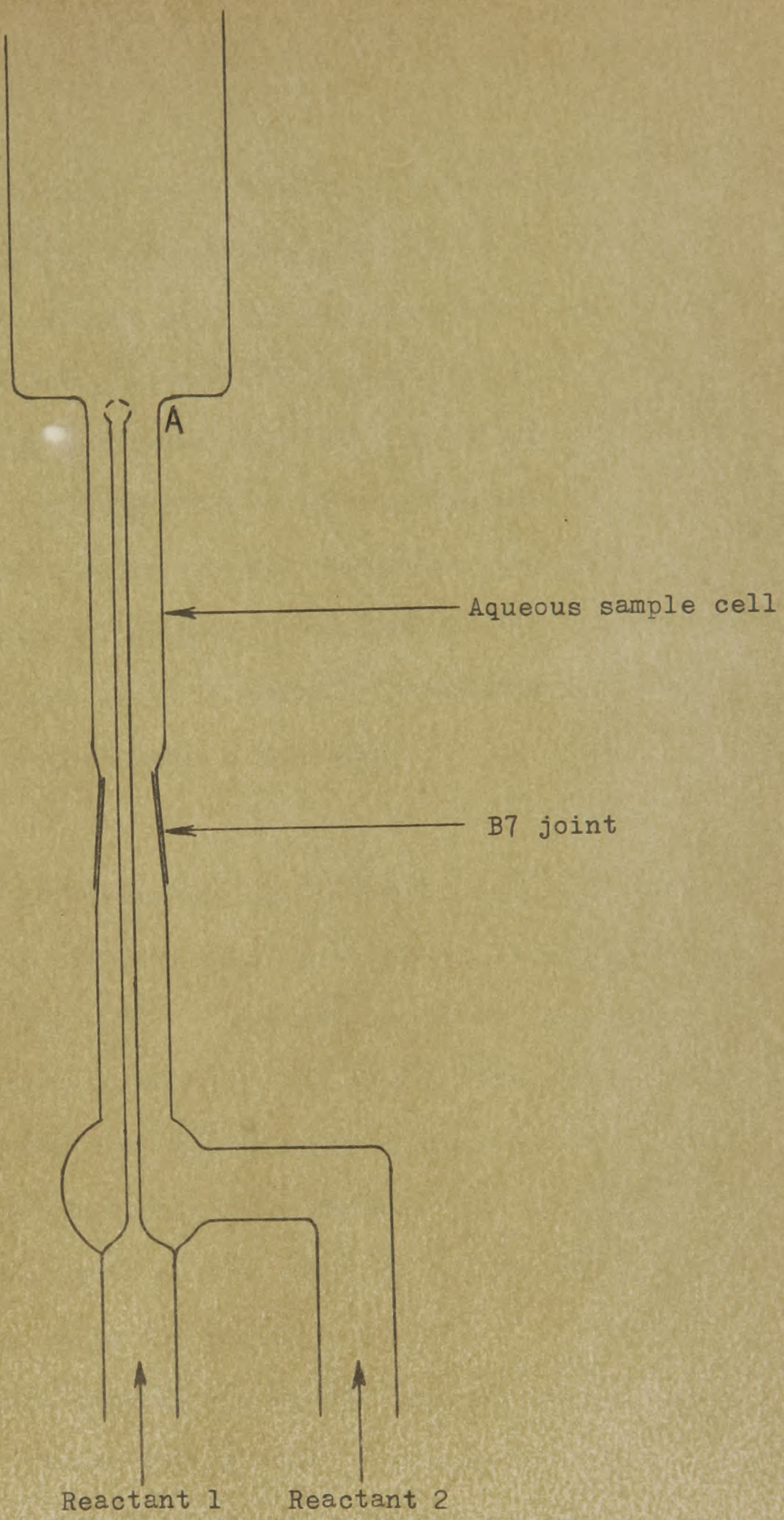


Figure 1.3

the optimum e.s.r. spectrum are difficult to attain using the flow technique. Although the initial concentration of the reagents might be 10^{-2}M it is evident that the mean concentration of the radicals under observation is usually several powers of ten smaller, and so relatively high microwave power and modulation amplitudes have to be used for the production of measureable spectra. As a result there is in some cases evident modulation broadening and asymmetry with respect to the horizontal base line of the spectra. Also the signal-to-noise ratio is somewhat lower than is usual with the spectra obtained from stable radicals.

1.4.3. CALIBRATION

The magnetic field sweep was calibrated using potassium nitrosyl disulphonate (Frémy's salt) in alkaline solution, which produces the radical dianion $NO(SO_3)_2^{2-}$. The spectrum from this radical consists of three lines 13 Oe apart and of relative intensities 1:1:1 (from interaction with the nitrogen nucleus I = 1). The calibration was also frequently cross-checked with an ethanolic solution of p-benzosemiquinone or a concentrated sulphuric acid solution of perylene (i.e. the perylene cation).

Calibrations were carried out on the same day as the unknown spectra were run. It was noticed that calibrations were slightly different depending on whether the spectrum was run from high to

low field or vice versa. A spectrum run in one direction must therefore be calibrated from a standard spectrum run in the same direction.

In every case the quoted coupling constants in this work are the average from several spectra of the same radical. The coupling constants are estimated to have a maximum error of 3%.

1.4.4 ANALYSIS OF SPECTRA

Little can be said concerning the method of analysing e.s.r. spectra. In some cases, when the radical has few interacting nuclei, the pattern of spectral lines is obvious by inspection. For example, the spectrum of the p-carboxyphenoxy radical is a simple triplet of triplets - a large triplet arising from interaction with the two equivalent ortho-protons, and a smaller triplet from interaction with the two equivalent meta-protons.

In the case of, say, the 2,4,6-trimethylphenoxy radical, however, the e.s.r. spectrum might be expected to consist of a quartet from the three p-methyl protons, each line of which being split into a septet from the six equivalent o-methyl protons giving 4 x 7 = 28 lines, each of these being further split into triplets from the two meta protons, giving in all a maximum number of lines of 3 x 28 = 84. In fact only 39 lines (see Part 2) are observed in the spectrum obtained experimentally. This is due to the

accidental overlapping of several lines in the spectrum, which occur if, say, the ortho and para coupling constants are in some simple ratio such as 2:3, 3:4 etc. Thus the pattern of lines is no longer analysable by inspection, and inspired guesswork, trial and error, and experience gained from analysing spectra of similar radicals must be used. Theoretical spectra, obtained by considering the most likely combinations of the coupling constants of the interacting nuclei in the radical concerned, are then constructed until a theoretical reconstruction is found which most nearly fits the one obtained experimentally.

Care must always be taken to ensure that lines of low intensity on the extreme wings of a spectrum are not accidentally missed. In the case of the spectrum of the 2,4,6-trimethylphenoxy radical mentioned above, the ratio of the first line to the largest centre line is 1:184. In cases such as this the spectrum must be deliberately overmodulated so that the larger lines go off-scale but the smaller wing lines are discernable.

PART 2

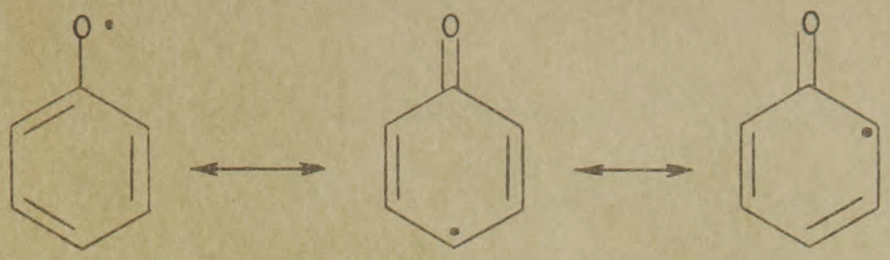
OXIDATION OF MONOHYDRIC PHENOLS

2.1 INTRODUCTION

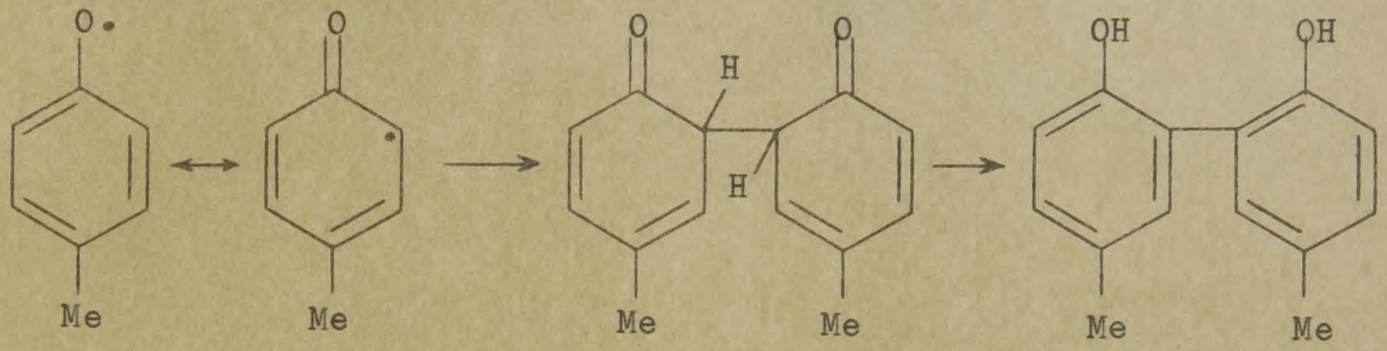
The initial product of the oxidation of a monohydric phenol, ArOH, by a one electron oxidising agent is a phenoxy radical, ArO• (I). Subsequent reactions of these phenoxy radicals have been well documented[27]; dimerisation may occur, i.e. p-cresol giving 2,2'-dihydroxy-5,5'-dimethyldiphenyl (II)[28], or the coupling of the phenoxy radical with another radical, such as a peroxy radical ROO•, present in the system, i.e. 2,4,6-trimethylphenol with benzoyl peroxide giving 4-benzoyloxy-2,4,6-trimethylcyclohexa-2,5-dienone (III)[29].

Many hindered phenols (i.e. phenols containing bulky groups such as t-butyl in the two positions ortho to the hydroxyl group) produce phenoxy radicals which are relatively stable. These hindered phenols have been very extensively studied by two groups of workers collaborating with Müller[30] in Germany and Cook[31] in the U.S.A. It has been found that phenoxy radicals containing bulky substituents having no α-hydrogen, thus making nuclear dimerisation impossible, are relatively stable, either in the absence of air (i.e. IV, R=t-Bu, OMe, CN, etc.)[31,30a,32], or in the presence of air (i.e. V).[33]

Previous e.s.r. investigations of phenoxy radicals have been hitherto concerned with those derived from highly substituted



(I)



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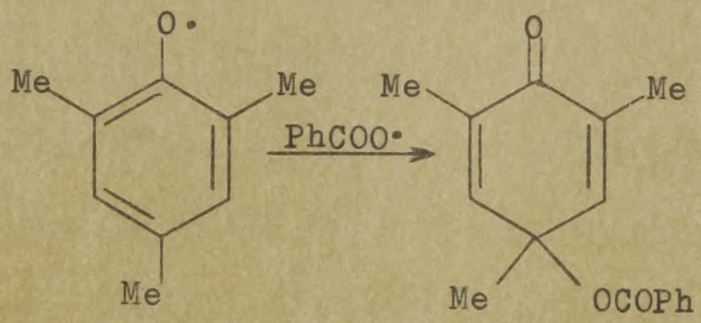

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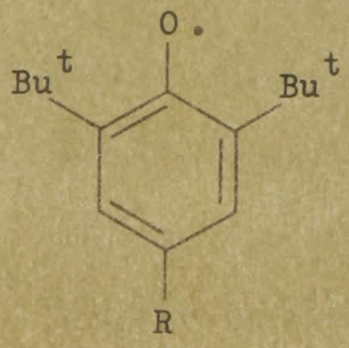

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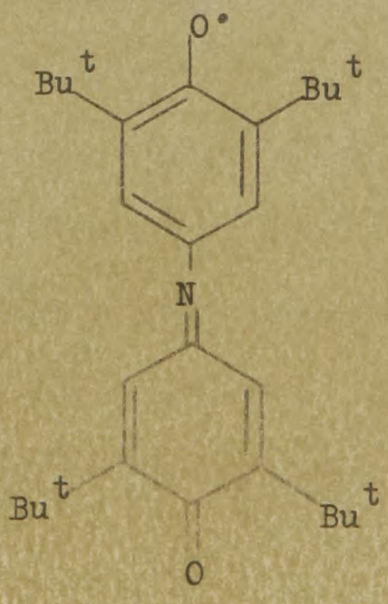


(V)

phenols. Müller and colleagues[30b] obtained in 1958 the first well resolved spectrum of a phenoxy radical - that from 2,4,6-tri-t-butylphenol - and have since reported[30] the e.s.r. spectra of a large number of substituted phenoxy radicals, mainly 4-substituted-2,6-di-t-butylphenoxy radicals. The phenols were oxidised with aqueous alkaline ferricyanide or with a suspension of lead dioxide in benzene. The oxidation and filling of the e.s.r. sample tube were performed under nitrogen.

Scott[34] has examined a number of phenoxy radicals by a freezing technique, which involves freezing the oxidant and solvent in a sample tube, adding more solvent containing the dissolved phenol, freezing again and placing the tube in the spectrometer. The solvent melts and the formation of radicals may be observed. He found that phenols with at least one bulky ortho-group gave detectable free radicals. 2,4,6-Trisubstituted phenols with no α-hydrogen in either the ortho- or para-positions gave primary radicals only, in agreement with Müller's work. Phenols with bulky groups in two positions and a group containing α-hydrogen in the third gave primary radicals immediately and secondary radicals after varying periods of time. Secondary radicals only were detected with phenols containing less than two bulky groups - the primary radicals being too unstable to be observed by this method.

Another technique, due to Pannell[35], involves the oxidation of phenols by t-butoxy radicals formed within the e.s.r. spectrometer by ultraviolet irradiation of cooled solutions containing t-butylperoxide. All the phenols investigated were 2,6-di-t-butylphenols.

With all phenols except those having no α-hydrogen in the 2-, 4- or 6-positions the formation of secondary radicals or the rapid decay of the primary radical cannot be prevented by any of the three methods mentioned above, with consequent complication or non-appearance of the e.s.r. spectrum of the primary phenoxy radical. The least substituted radical hitherto observed by e.s.r. is the 2,6-di-t-butylphenoxy radical, although the spectrum is rather poor.[35]

To obtain spectra of the less substituted phenoxy radicals and of the radical from phenol itself a system must be devised in which the radicals are examined in the e.s.r. spectrometer a very short time after being formed, and then quickly removed to prevent secondary reactions. This state of affairs is realised using the flow system described in Part I, and an account is given below of the formation and e.s.r. spectra of some 50 phenoxy radicals.

2.2. EXPERIMENTAL

The flow apparatus used was the one described in the previous Part. Ceric sulphate (10^{-2}M) in M-sulphuric acid was used as the oxidant. The phenol (10^{-2}M) was dissolved in water or aqueous sodium hydroxide. Aqueous acetone was previously used to effect solution of those phenols which were insoluble in water, but it was found that better spectra were obtained by dissolving these phenols in a slightly alkaline solution and then mixing this solution with the oxidant in an excess of acid.

Maximum flow rates of *ca* 5 ml. sec.$^{-1}$ were needed in most cases to observe a satisfactory spectrum. This was necessary in the case of most of the less-substituted phenols because of the very small lifetime of the radicals produced. It has been estimated[36] that the unsubstituted phenoxy radical has a lifetime of *ca* 1 millisec; thus with the flow system used, which is estimated to observe radicals *ca* 10^{-2} sec. after formation, only a small proportion of the phenoxy radicals produced will be observed. The maximum flow rate is also necessary because in some oxidations insoluble products are formed, but with a sufficiently high flow rate deposition can be made to occur well beyond the spectrometer cell.

Materials used

The ceric sulphate used was the B.D.H. product: ca 85% 'low in rare earths'. All the phenols, with the exception of those described below, were commercial products. All were purified by recrystallisation or distillation.

p-Iodophenol: prepared by the method of Vogel[37] from p-aminophenol using ¼ quantities. Product recrystallised from pet. ether (80-100°); m.p. 93° (lit. 94°), yield 18 g. (65%).

2,6-Diethylphenol: prepared by the method of Moffett and Seay[38] from the corresponding amine using ¼ quantities; b_{10} 104°, yield 13 g. (52%).

p-Phenoxyphenol: prepared by the method of Southwick[39] from the corresponding amine using double quantities. Product recrystallised from water; m.p. 81° (lit. 81-2°), yield 4.5 g. (63%).

2.3. RESULTS AND ANALYSIS OF SPECTRA

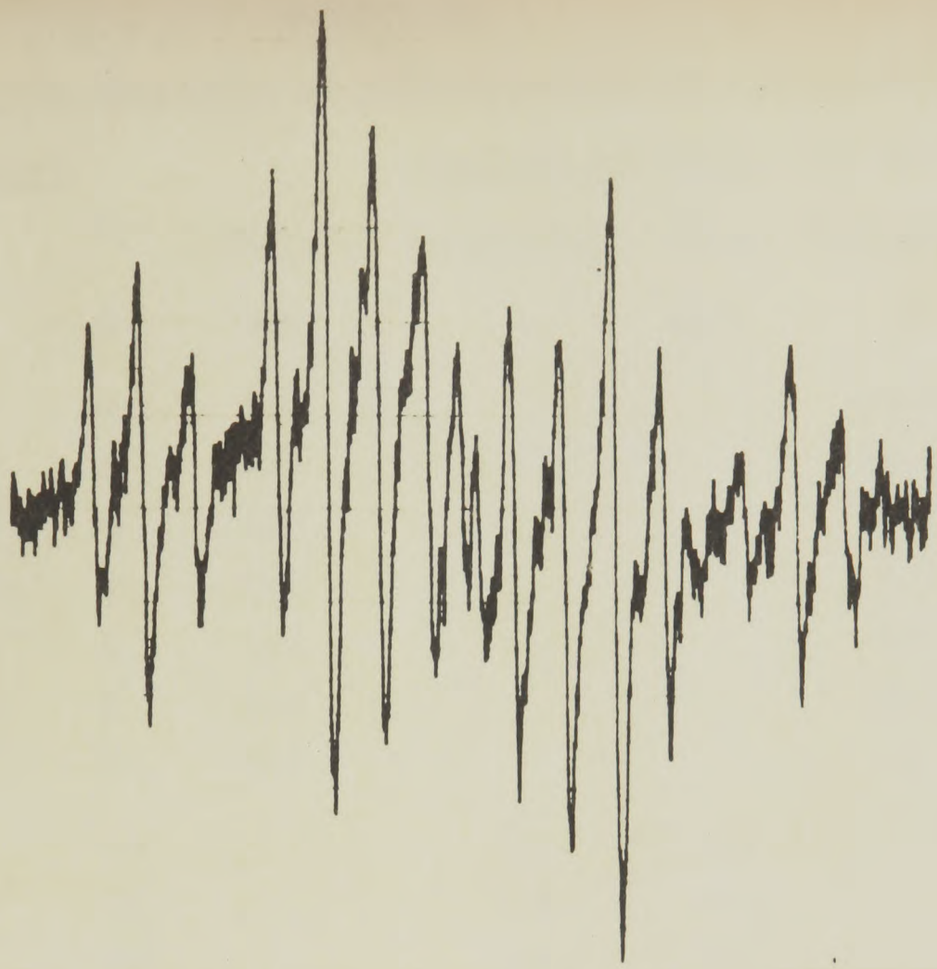
2.3.1. PHENOL

The first spectrum obtained was that from the oxidation of phenol itself, and is shown in Fig.1A. The spectrum contains 16 lines; the number of lines expected from the phenoxy radical itself, if there were no accidental overlap of lines, would be 3 (from the two ortho-protons) x 3 (meta-protons) x 2 (para-protons) = 18 lines. From the previous work on the e.s.r. of substituted phenoxy radicals mentioned above it was found that the coupling constants for the ortho-, meta- and para-protons were of the order of 6, 2 and 10 Oe respectively; the spectrum from the phenoxy radical itself can be analysed by taking coupling constants of $a_{H(2,6)}$ = 6.65 Oe, $a_{H(3,5)}$ = 1.8 Oe and $a_{H(4)}$ = 10.1 Oe, as shown in Figs.1B and C.

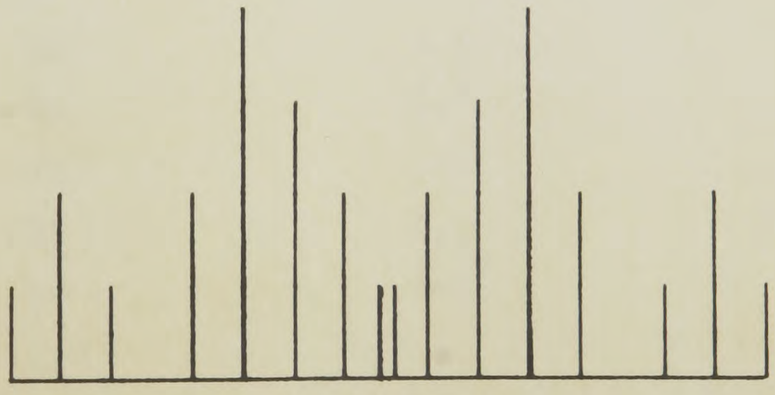
2.3.2. ALKYL-SUBSTITUTED PHENOLS

Four main groups of alkyl-substituted phenols were investigated 4-alkyl-, 2,6-dialkyl-, 2,6-dimethyl-4-alkyl- and 2-alkylphenols. The coupling constants obtained are listed in Table 1, and representative spectra together with reconstructions are shown in Figs. 2-5.

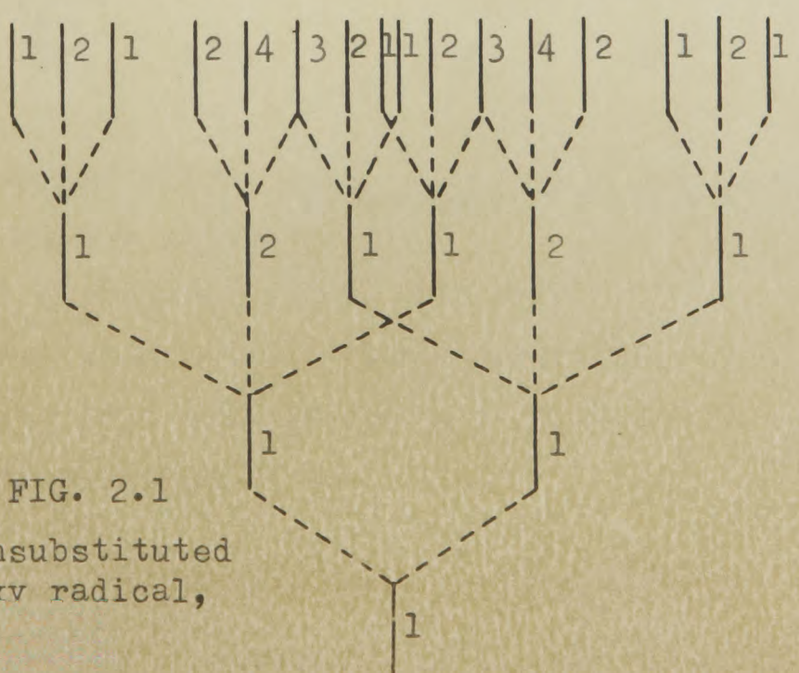
In the 4-alkyl-substituted series it was found that when the substituent contained either one or no α-hydrogen atom (i.e. Bu^s, Bu^t) the spectra were poorly resolved and consisted of broad lines



(A)



(B)



(C)

FIG. 2.1

The unsubstituted phenoxy radical,

TABLE 2.1.

Coupling constants of alkyl-substituted phenoxy radicals

Substituent			Coupling Constants (in Oe.)[a]				
2	4	6	$\lvert a_H(2,6)\rvert$	$\lvert a_{Alkyl}(2,6)\rvert$	$\lvert a_H(4)\rvert$	$\lvert a_{Alkyl}(4)\rvert$	$\lvert a_H(3,5)\rvert$
H	H	H	6.6_5		10.1		1.8
H	Me	H	6.0			11.9_5	1.4_5
H	Et	H	6.0			10.1_5	1.5
H	Pr^n	H	6.1			8.7	1.4_5
H	CH_2Ph	H	6.1			8.7	1.4_5
H	Pr^i	H	6.1			6.0	$\leqslant 1.4$[b]
H	Bu^s	H	6.0			4.[illegible]	$\leqslant 1.4$[b]
H	Bu^t	H	6.0			-	$\leqslant 1.4$[b]
Me	H	Me		6.5	9.5		1.6_5
Et	H	Et		5.7	9.3_5		1.6_5
Pr^i	H	Pr^i		3.7	9.5		1.8
Bu^t	H	Bu^t		-	9.6[c]		2.0[c]
Me	Me	Me		6.0		11.9_5	1.4
Me	Et	Me		6.0		9.1	1.4_5
Me	Pr^n	Me		6.0		8.3	1.3_5
Me	CH_2Ph	Me		6.0		8.5	1.3_5
Me	Bu^t	Me		6.1[d]		-	1.8[d]
H	H	Me[e]					
H	H	Et[e]					
H	H	CH_2Ph[e]					
H	H	Pr^i	5.8_5	4.0	9.7		1.8

a absolute values given, $\lvert a_{Alkyl}(2,6)\rvert$, $\lvert a_{Alkyl}(4)\rvert$, $\lvert a_H(3,5)\rvert$ probably positive, others negative.

b values not accurately known, see text.

c values taken from ref. 35 for comparison.

d values taken from ref. 34 for comparison.

e spectra not analysed.

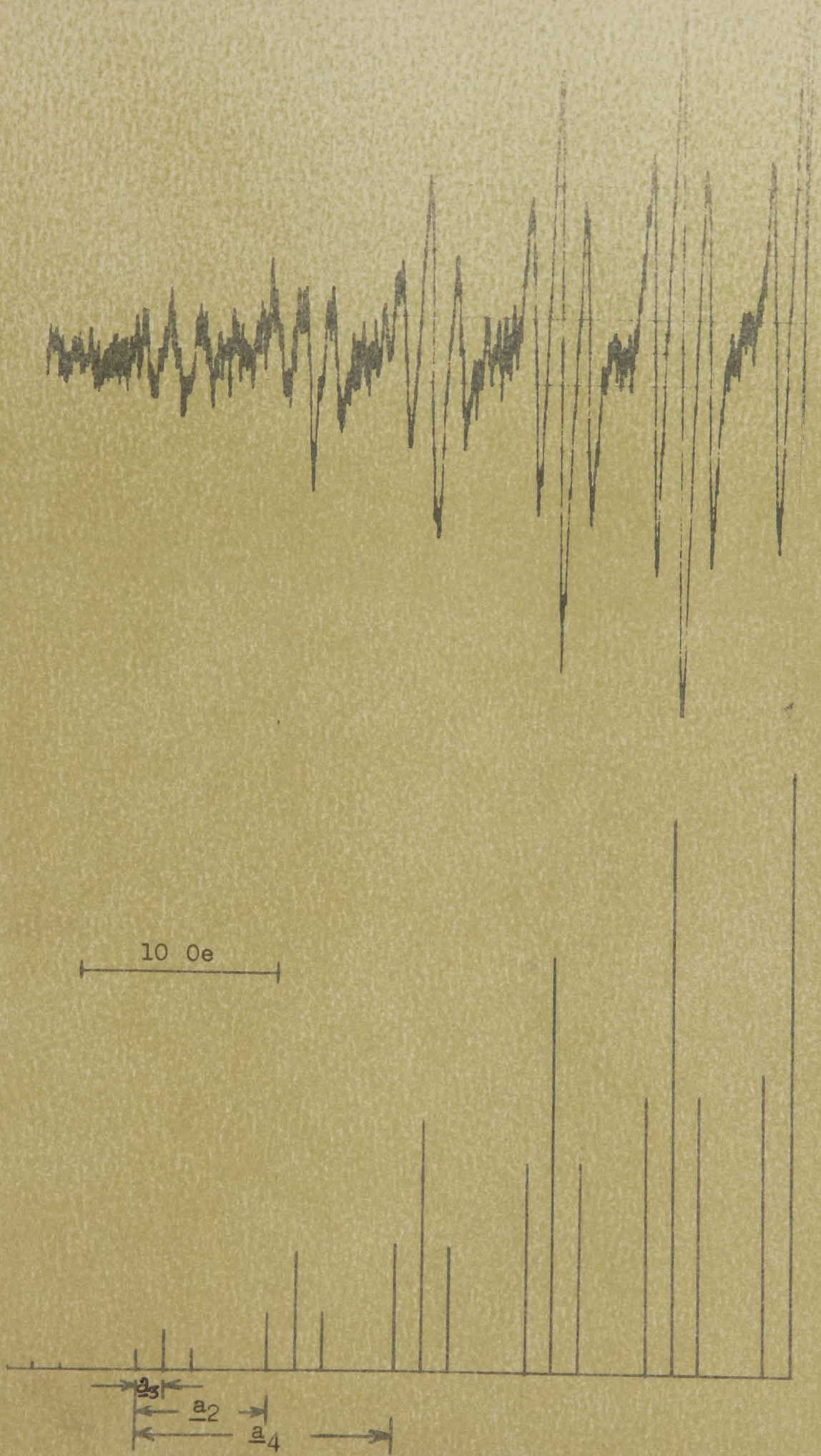


FIG.2.2 2,4,6-Trimethylphenoxy (half-spectrum)



FIG. 2.3. 2,6-Dimethyl-4-n-propylphenoxy

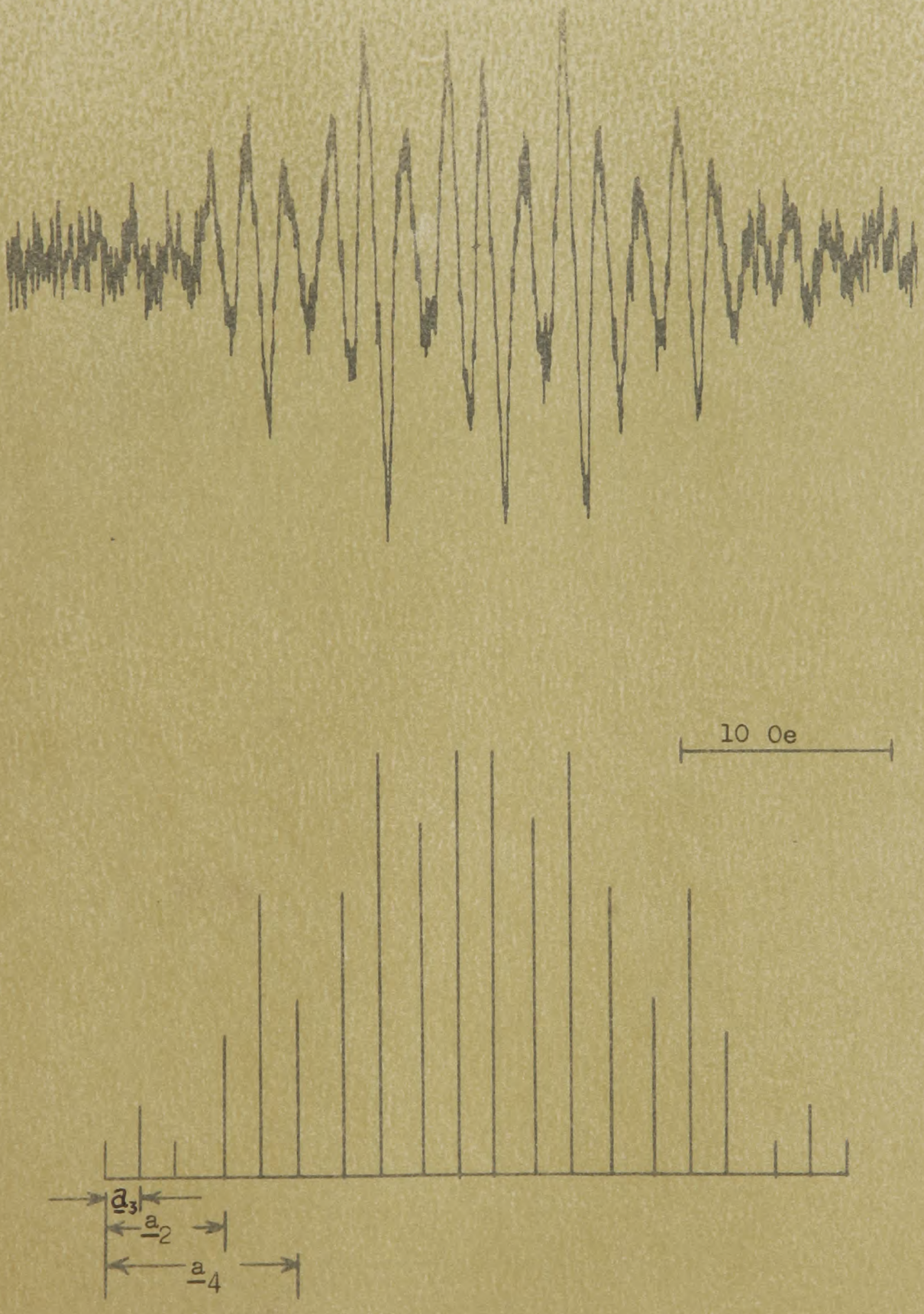
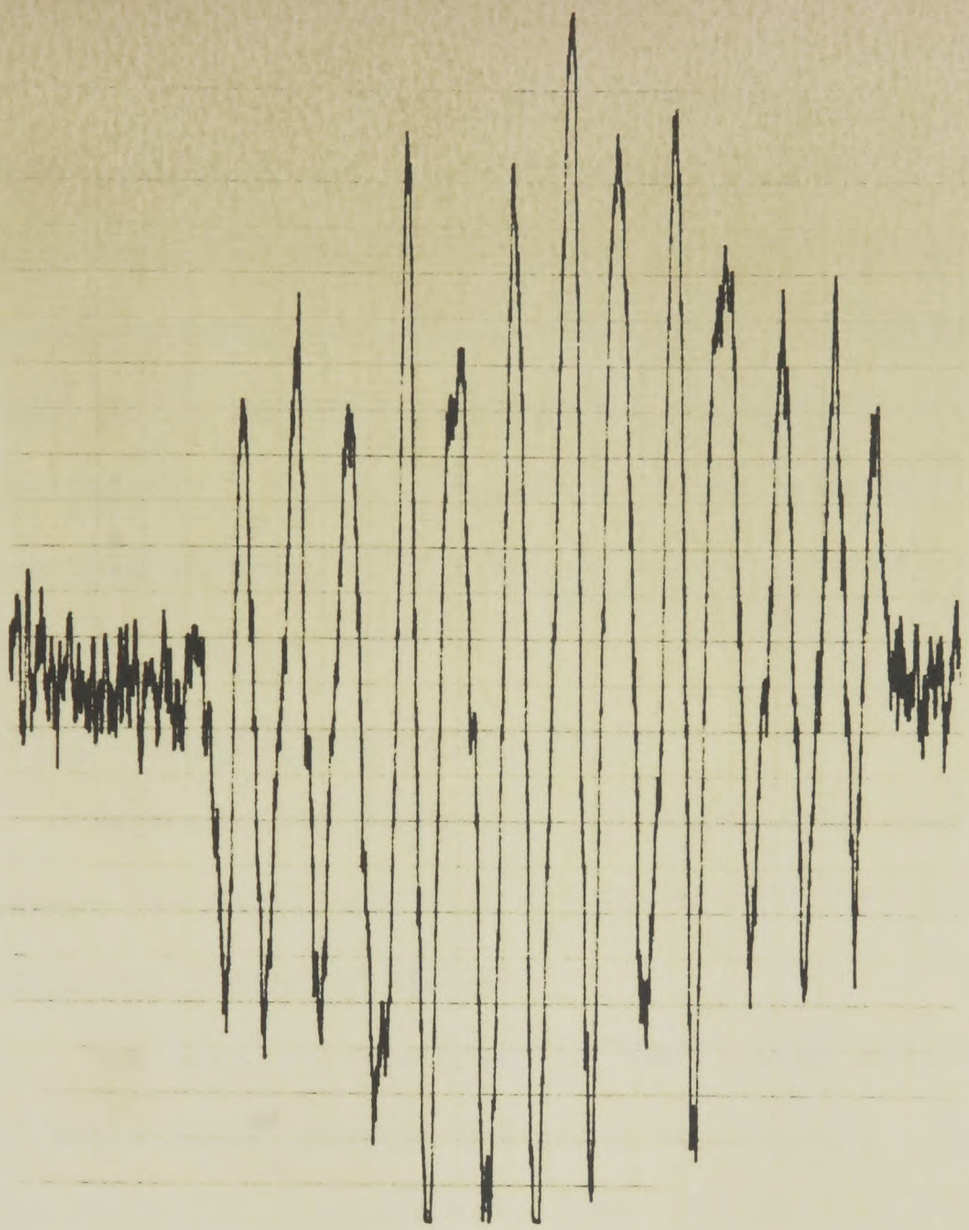
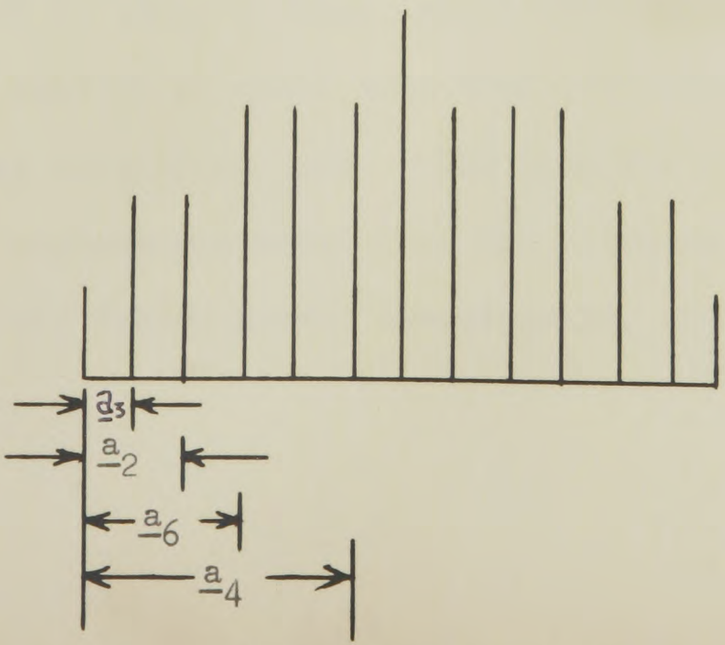


FIG. 2.4 2,6-Diethylphenoxy



10 Oe



2.5 2-i-Propylphenoxy

from which only the coupling constants of the ortho-protons and para-α-protons could be obtained with any accuracy. The 2-alkylphenols produce radicals in which both the ortho-protons (at the ring and in the substituents) and the meta-protons are no longer equivalent. Only the spectrum of the 2-i-propylphenoxy radical has been analysed successfully, although fairly well resolved spectra were obtained.

2.3.3. OTHER SUBSTITUTED PHENOLS

This section deals with all substituted phenols investigated except the alkyl-substituted (above) and the alkoxy-substituted, which are discussed below.

The coupling constants of the phenoxy radicals for a variety of substituted phenols are given in Table 2. The phenols with the following para-substituents: $-CO_2H$, $-CO_2Et$, -COMe, $-SO_3Na$, gave almost identical spectra consisting of a simple triplet of triplets (i.e. Fig.6). No splitting was observed due to protons contained in these groups; these have been observed by others[40] but are usually so small that they would not have been detected under the conditions used. The spectrum of p-nitrophenoxy (Fig.7) gave an obvious splitting from the nitrogen atom of the nitro group.

Of the fluorophenols investigated, the ortho- (Fig.8) and para-

TABLE 3.2.

Coupling constants of substituted phenoxy radicals

Substituent			Coupling constant (in Oe)[a]					
2	4	6	$a_H(2,6)$	$a_{Alkyl}(2,6)$	$a_H(3)$	$a_H(5)$	$a_H(4)$	$a_R(4)$
H	CO_2H	H	6.8		2.2	2.2		
H	CO_2Et	H	6.8		2.3	2.3		
H	COMe	H	7.0		2.3	2.3		
H	CHO	H	6.8		2.2	2.2		
H	SO_3Na	H	6.8		2.2	2.2		
H	NO_2	H	7.0		2.3,	2.3_5		2.3_5[b]
H	CN	H[c]						
H	F	H	6.5		1.6	1.6		27.4[d]
H	Cl	H	5.7		1.7	1.7		1.7[e]
H	Br	H[c]						
H	I	H[c]						
Me	CO_2H	Me		6.8	2.2	2.2		
Me	COPh	Me		7.0	2.2	2.2		
Cl	NO_2	Cl	1.1_5[e]		1.1_5	1.1_5		1.1_5[b]
H	H	CO_2H	7.5		2.2[f]	1.3[f]	10.8	
H	H	F	6.0_5	17.0[d]	2.1[f]	1.5[f]	10.1	
meta-CO_2H			7.5[f]	6.6_5[f]	2.0		10.1_5	
meta-F[c]								
α- and β-naphthol[c]								

a see note a Table 1

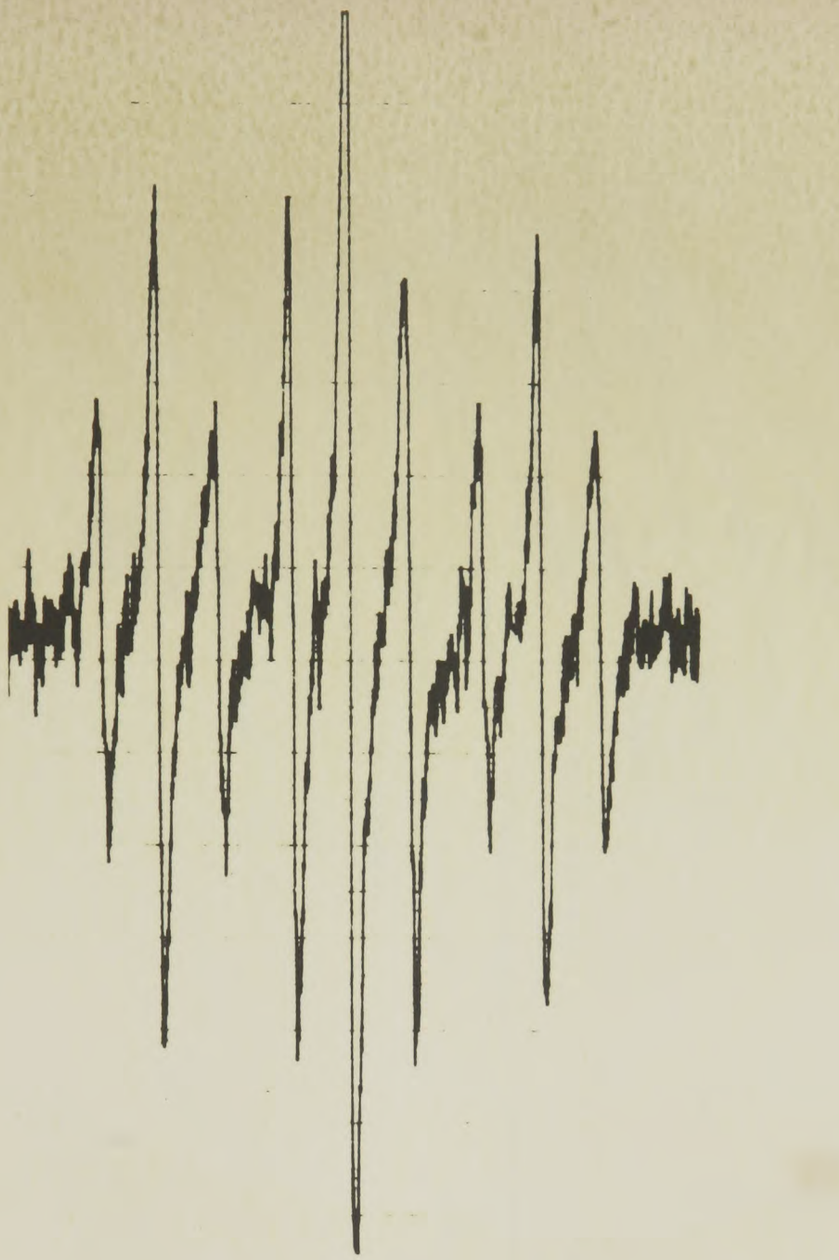
b coupling constant for N

c spectra not analysed

d coupling constant for F

e coupling constant for Cl

f coupling constant not conclusively assigned between two possible positions.



10 Oe

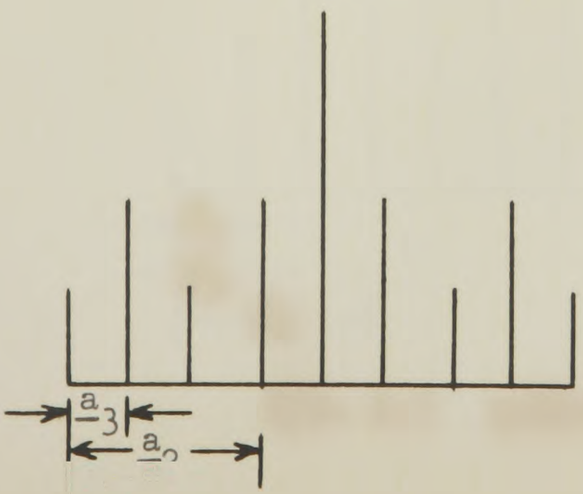


FIG. 2.6

Radical from
4-hydroxybenzene
sulphonic acid

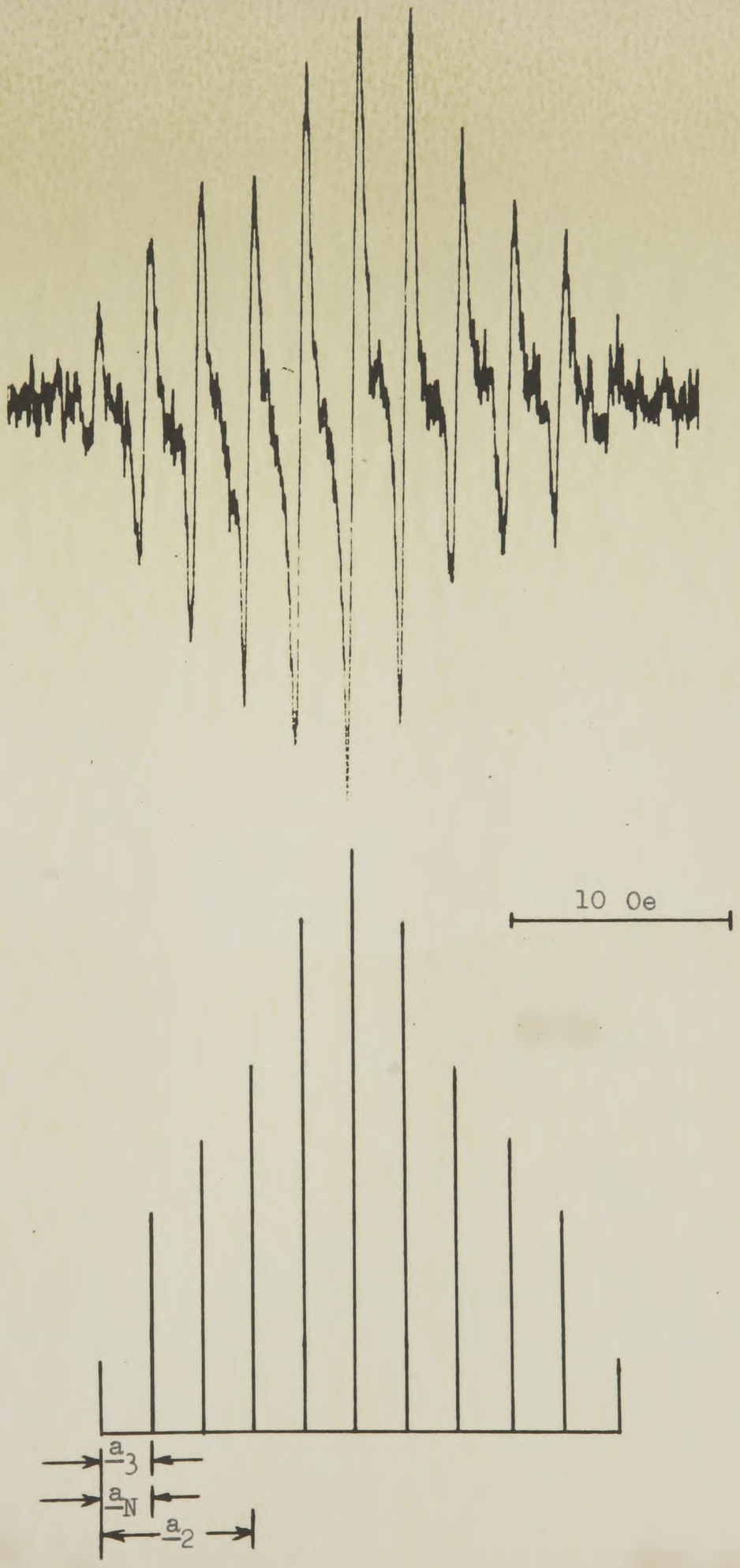


FIG. 2.7 p-Nitrophenoxy

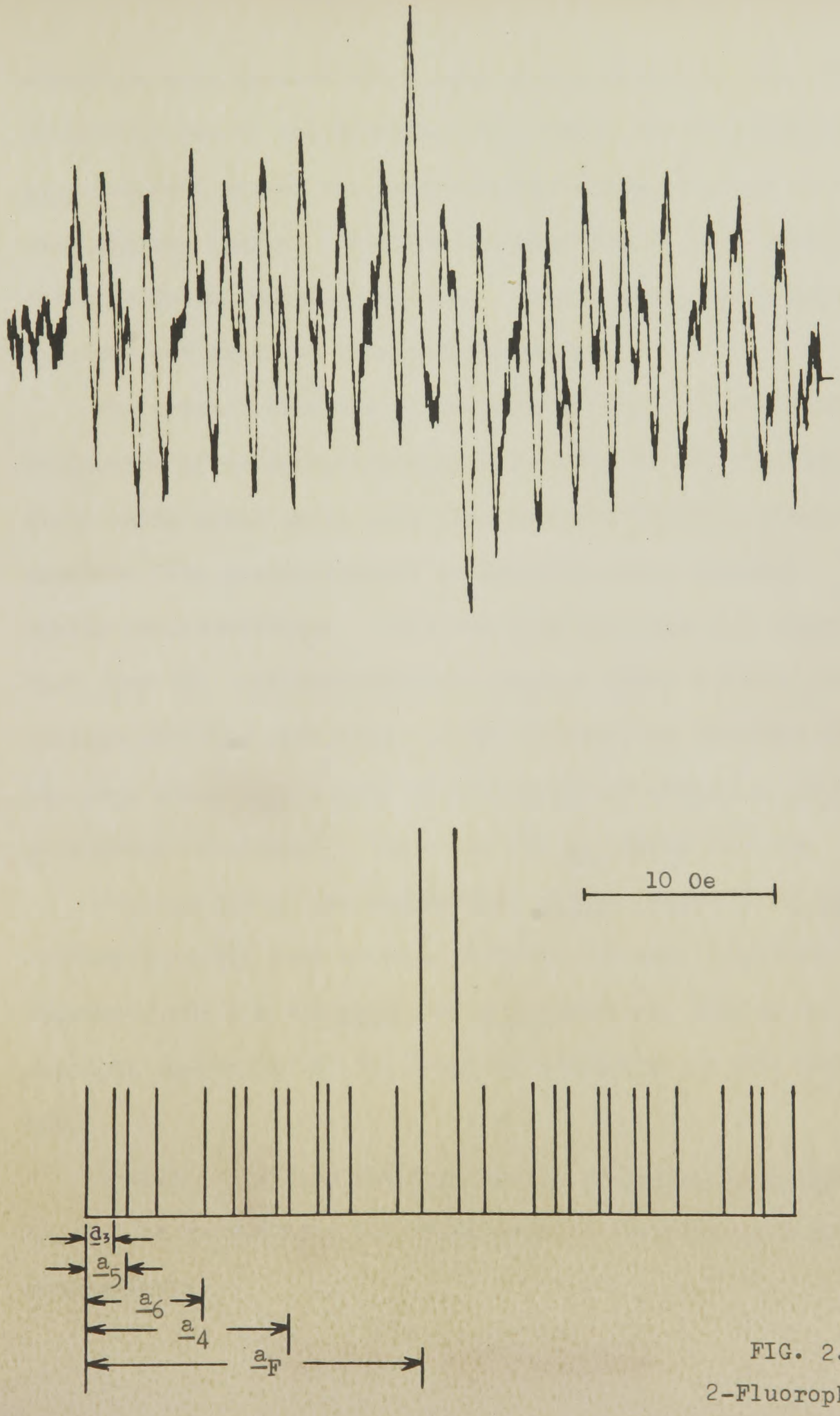


FIG. 2.8.

2-Fluorophenoxy

compounds gave spectra which were characterised by very large splittings due to the fluorine atom ($I=\frac{1}{2}$), the splitting from the para-compound having the exceptionally large value of 27.4 Oe; probably the largest splitting observed for an atom directly attached to the benzene nucleus. Only a poor, badly resolved spectrum was obtained from m-fluorophenol.

The spectra from the chlorophenols were only analysable on the assignment of an appreciable splitting due to the chlorine nucleus ($I=\frac{3}{2}$) which would split each line into four further lines. The spectrum from p-chlorophenol is shown in Fig.9 together with a likely reconstruction. This chlorine splitting and especially that from the 4-chlororesorcinol radical (Part 3 below) are the largest chlorine splittings so far observed in aromatic systems. The only other observation of a chlorine splitting is that from p-chloronitrobenzene[41], the value for a_{Cl} being 0.17 Oe.

The spectra of the unsymmetric ortho- (Fig.10) and meta-carboxylic acids were readily analysed and gave different coupling constants for the two meta- and ortho-protons, respectively. A definite assignment of the coupling constants has not been carried out.

Spectra were also obtained on the oxidation of p-cyanophenol and α- and β-naphthols but these spectra have not been analysed successfully.

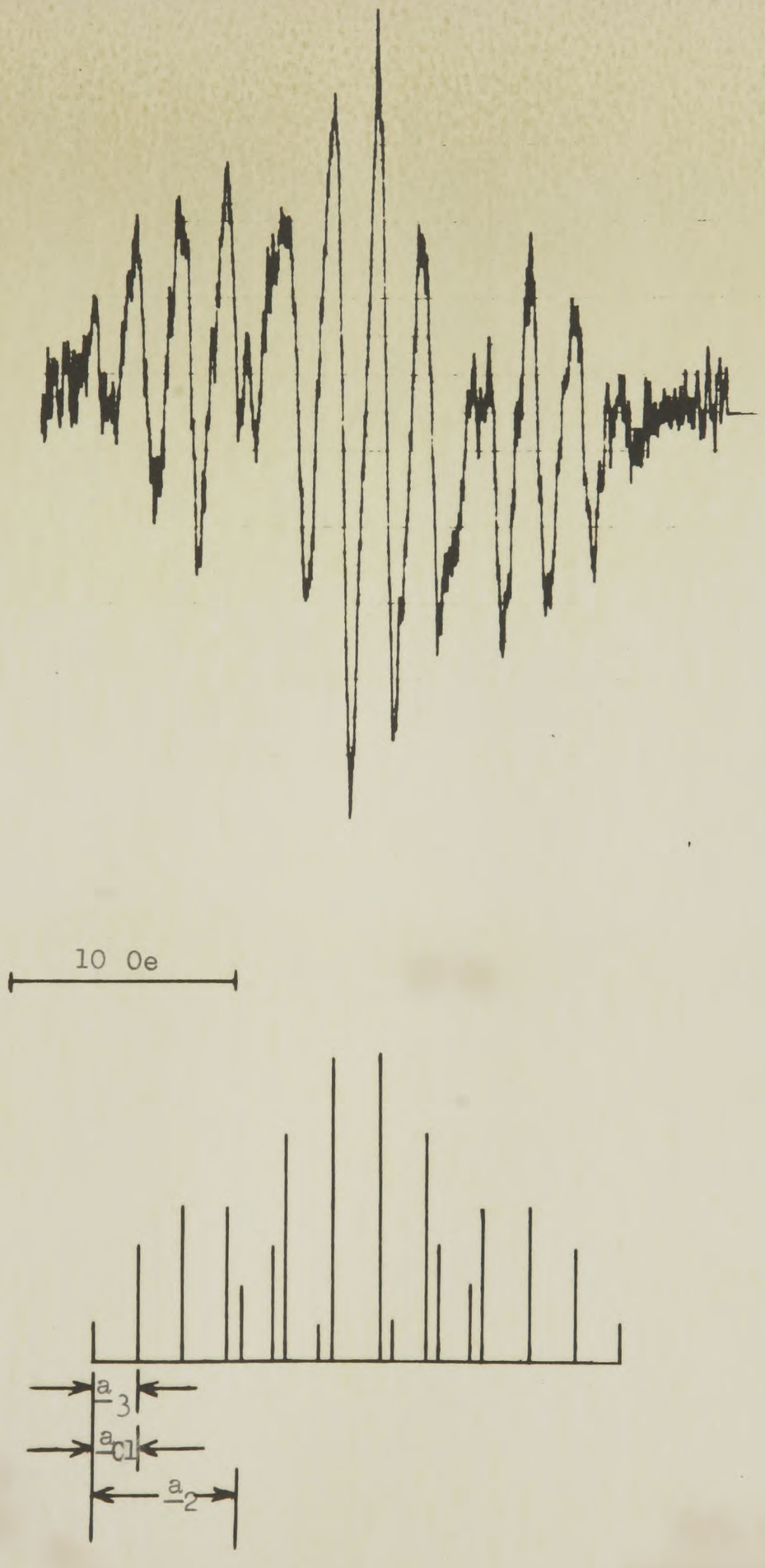


FIG. 2.9. 4-Chlorophenoxy

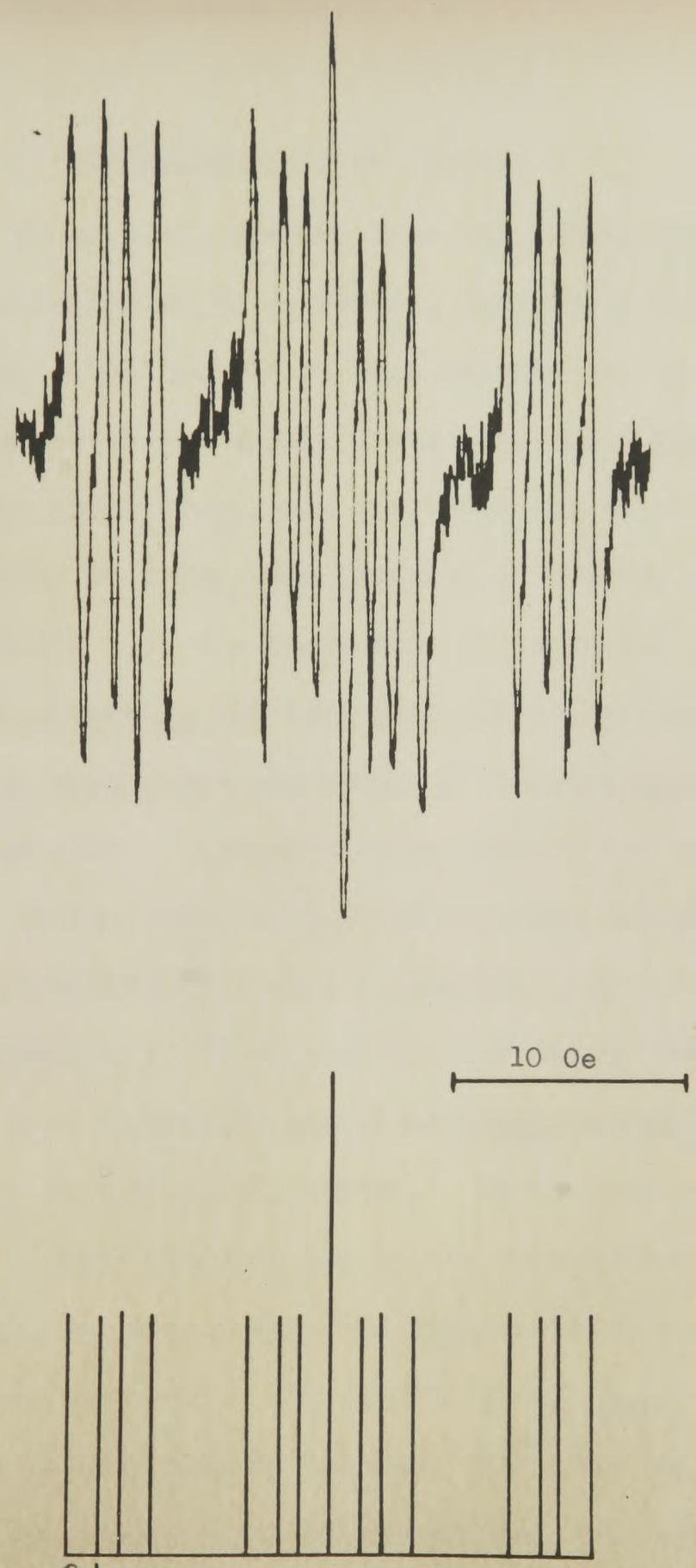


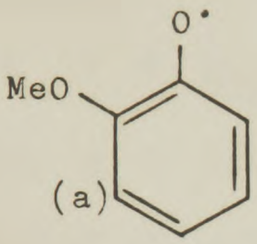
FIG. 2.10.

2-Carboxyphenoxy

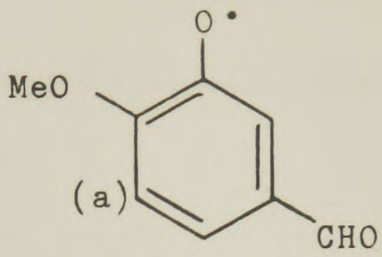
2.3.4. ALKOXY-SUBSTITUTED PHENOLS

In general, spectra from the alkoxy-substituted phenoxy radicals tended to be broader than those from the radicals described above. The phenols in this section may be divided into two groups - those with the alkoxy group *para* and *ortho* to the hydroxy group. In the first group, the splitting due to the alkoxy-protons were observed in every case (except, of course, in the *p*-phenoxyphenoxy radical). It was found that the coupling constants of the ring protons were *ca* 20% less than those for the unsubstituted radical, and in many cases the coupling with the *meta*-protons could scarcely be detected. Representative spectra are shown in Figs. 11-13.

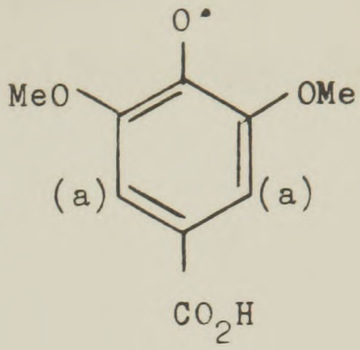
In the group of *o*-methoxyphenols investigated, the radical from guaiacol (VI) gave a spectrum (Fig. 14) which could be interpreted on the basis of a splitting from the methoxy protons and from protons at positions *ortho* and *para*, and at *one* position *meta*, to the phenolic group. As the spectrum from the radical (VII) shows coupling due to the same number of protons as (VI), it appears likely that the *meta*-coupling observed is due to the proton adjacent to the methoxy group (*i.e.* at position marked (a)). This is confirmed by the fact that when the radical contains two methoxy groups (*i.e.* VIII) coupling due to both *meta*-protons appear.



(VI)



(VII)



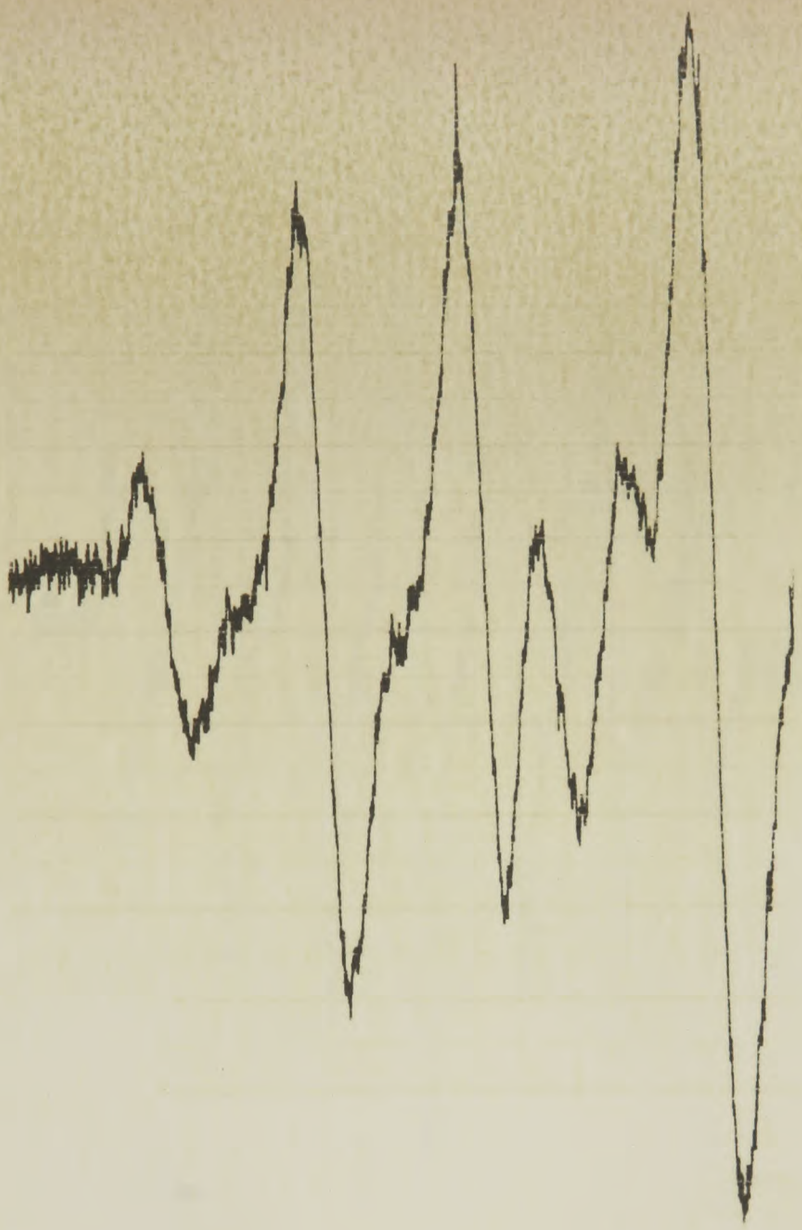
(VIII)

TABLE 2.3.

Coupling constants of alkoxy-substituted phenoxy radicals

Substituent					Coupling constants (in Oe)							
2	3	4	5	6	$a_{H(2)}$	$a_{H(6)}$	$a_{O.Me(2,6)}$	$a_{Me(2,6)}$	$a_{H(3)}$	$a_{H(5)}$	$a_{H(4)}$	$a_{O.Me(4)}$
H	H	OMe	H	H	5.0	5.0			?	?		2.0
H	H	OCH_2Ph	H	H	4.9	4.9			?	?		2.1
H	H	OBu^n	H	H	4.6	4.6			?	?		2.3
H	H	OPh	H	H	5.2	5.2			.5	0.5		-
H	Bu^t	OMe	H	H	3.9[a]	5.8[a]						2.1
Bu^t	H	OMe	H	H		5.4			0.6[b]	?		1.9
Bu^t	H	OMe	Bu^t	H		4.0			?	-		2.0
Me	H	OMe	H	Me				4.7	?	?		2.0
OMe	H	H	H	H		4.2	1.8		1.8[b]	?	8.3	
OMe	H	CHO	H	H		4.3	2.2		2.2[b]	?		
OMe	H	H	CHO	H		5.4	1.8		1.8		7.8	
OMe	H	H	H	OMe			1.5		1.5	1.5	8.3	
OMe	H	CO_2H	H	OMe			1.6_5		1.6_5	1.6_5		

a,b coupling constants not conclusively assigned between two [a]ortho and [b]meta-positions.



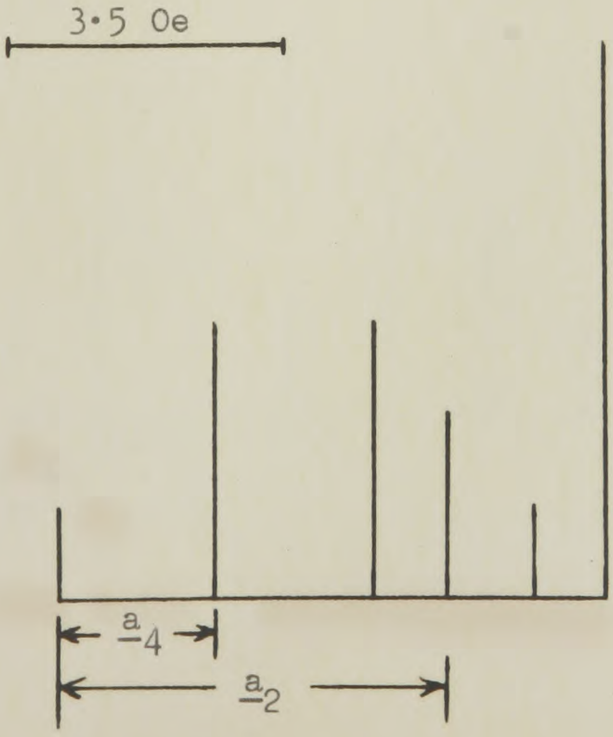
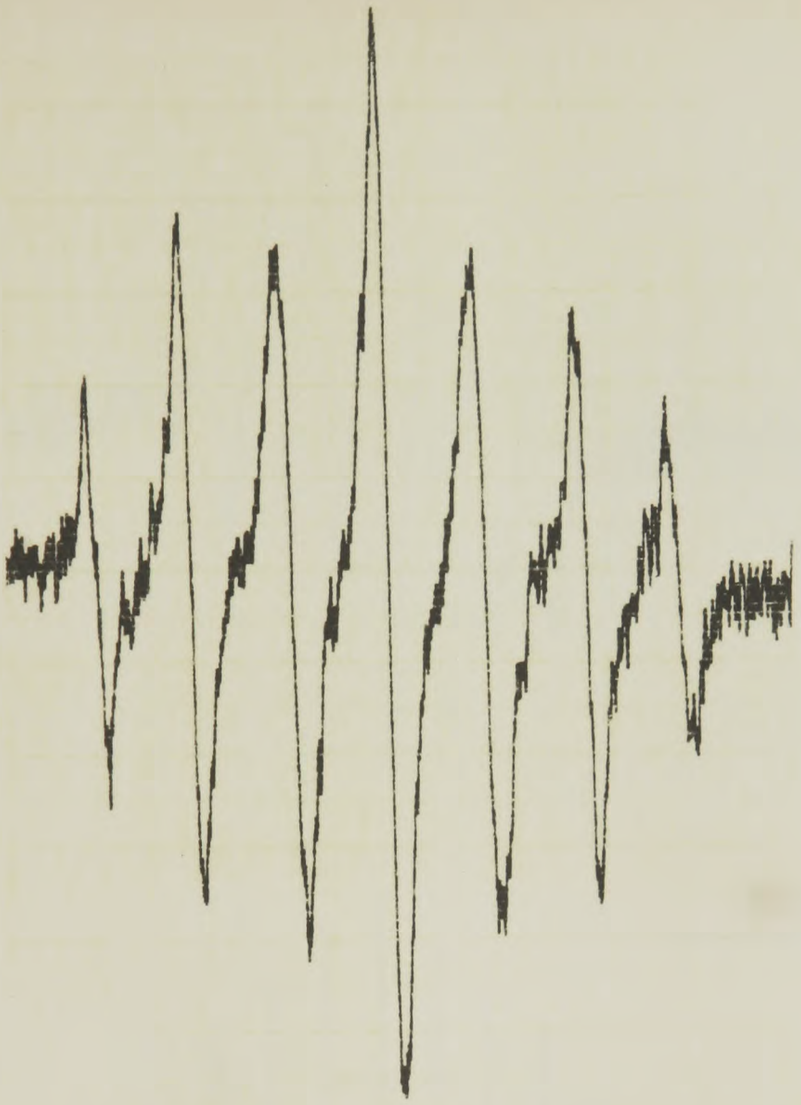


FIG. 2.11.

4-Methoxyphenoxy
(half spectrum)



7 Oe

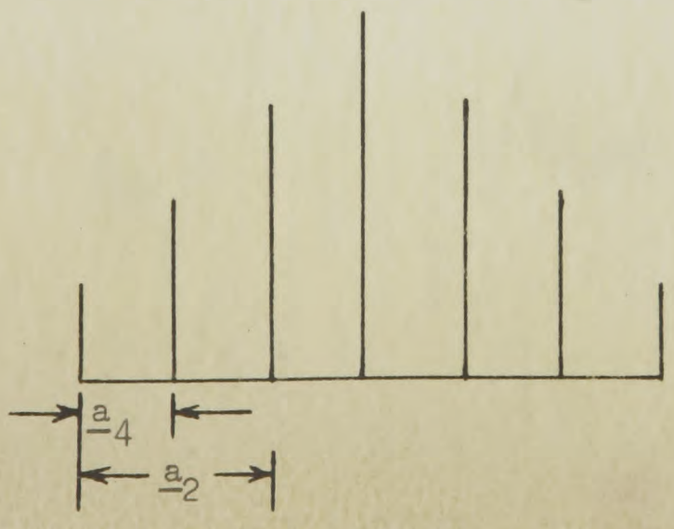


FIG. 2.12. 4-n-Butoxyphenoxy

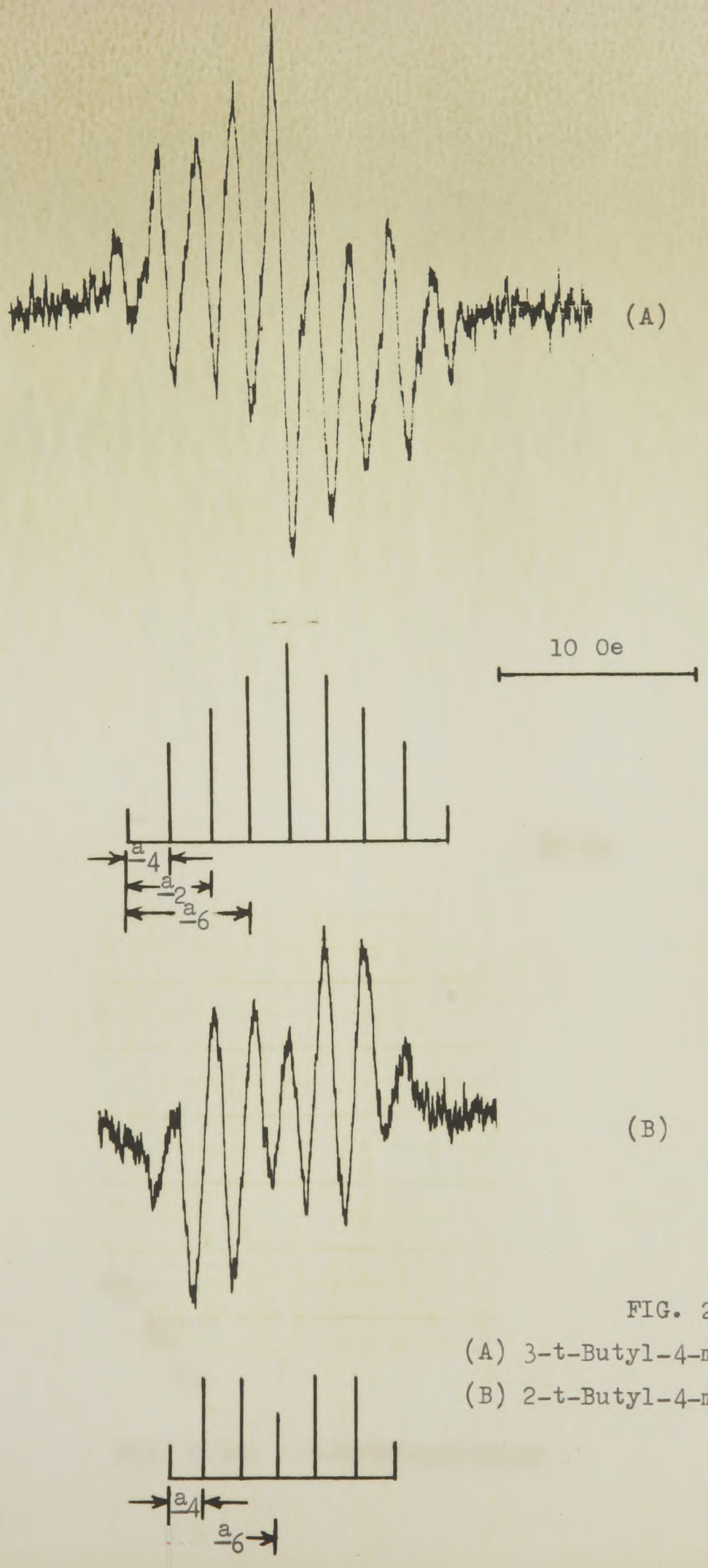


FIG. 2.13.

(A) 3-t-Butyl-4-methoxyphenoxy

(B) 2-t-Butyl-4-methoxyphenoxy

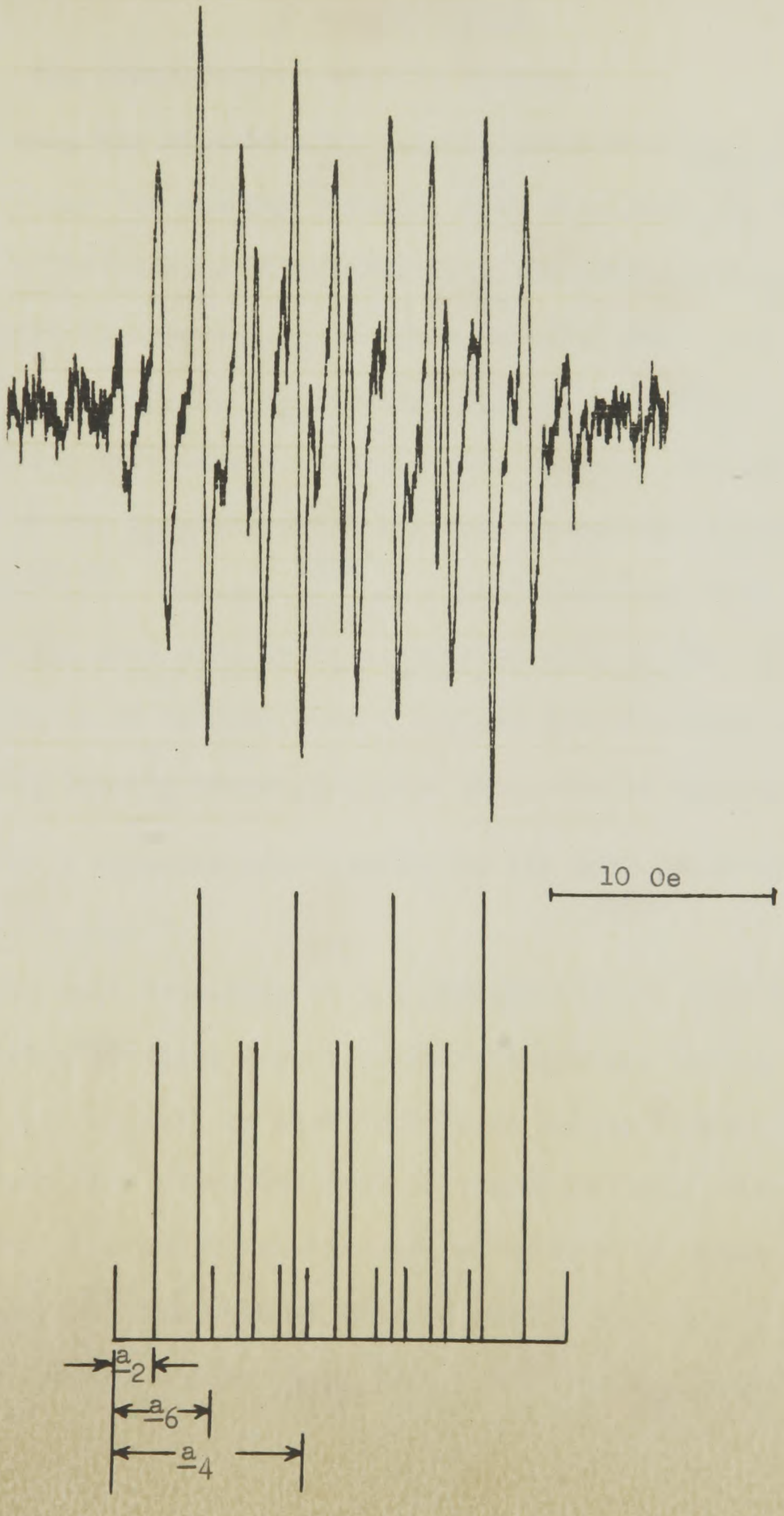


FIG. 2.14. 2-Methoxyphenoxy

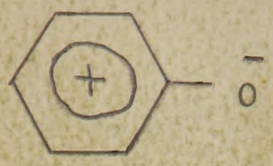
2.4 DISCUSSION

2.4.1 THE UNSUBSTITUTED PHENOXY RADICAL

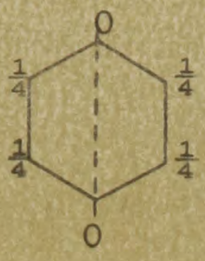
Using the experimental couping constants, $a_{H(i)}$, given in Table 1 for the phenoxy radical, spin densities ρ_i at carbon atom C_i (i = 2-6) can be calculated from the expression $a_{H(i)} = Q_{C-H}\rho_i$ (see Part 1), where Q_{C-H} is taken as -23.7 Oe. The values found are $\rho_2 = \rho_6 = 0.28$, $\rho_4 = 0.42$, $\rho_3 = \rho_5 = -0.075$. The sign of the latter indicates a negative spin density, the existence of which at the meta-positions has been proved by theoretical calculations.[42,43] The sum $\sum_{i=2}^{i=6} \rho_i = 0.83$ indicates that a total of 17% of the spin density is associated with C_1 and the oxygen atom. As there is no nucleus with a nuclear spin directly attached to C_1 the spin density associated with this atom is unknown: it may be there is a negative spin density of the same order of magnitude as that at C_3/C_5.

The spin densities of the phenoxy radical have been theoretically calculated by three groups of workers; their values are given in Table 4. It will be seen that their values differ considerably both from each other and from the experimentally obtained values.

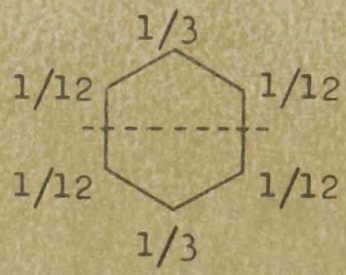
The simplest model has been considered by Symons[44], who suggests that the phenoxy radical may be regarded as a derivative of the benzene cation (i.e. IX). The two e_{1g} levels of the



(IX)

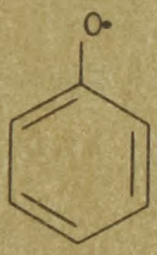


(a)

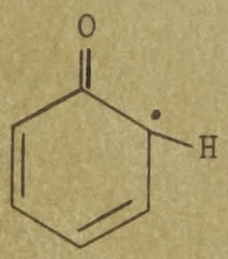


(s)

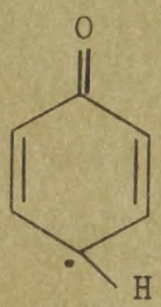
(X)



(a)

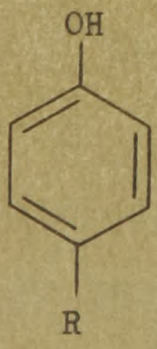


(c)

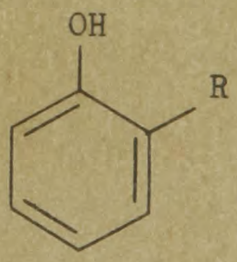


(b)

(XI)



(a)



(b)

(XII)

TABLE 2.4

Calculated and experimental spin densities for PhO·

	ρ_2	ρ_3	ρ_4	$2(\rho_2+\rho_3)+\rho_4$
Experimental	0.28	-0.075	0.42	0.83
Symons	0.08	0.08	0.25	0.57
Schug et al	0.32	-0.21	0.28	0.50
Atherton et al	0.15	-0.02	0.34	0.60

molecular orbitals for benzene are as shown (X). As the $-O^-$ group would probably repel the paired electrons, which would thus occupy the antisymmetric orbital (a), the unpaired electron would therefore half-fill the symmetric level (s). Thus spin densities of $\frac{1}{12}$, $\frac{1}{12}$ and $\frac{1}{3}$ are predicted for the ortho-, meta- and para-positions respectively.

Schug and colleagues[43] use an extension of the V.B. method applied to substituted aromatic radicals. The radical is decomposed into sets of fragment structures, each of which is treated by the standard V.B. method. By simple averaging of the fragment values the approximate spin density for the entire molecule can be obtained. Their values for the phenoxy radical differ greatly from the experimental values, especially as they obtain $\rho_2 > \rho_4$.

Atherton, Land and Porter[42] use a far better approach in which

they stress the point that the electronegativity of the oxygen atom should be taken into account. By including contributions from excited doublet states having three singly occupied orbitals, they find values which, although smaller than the experimental, correctly assess ρ_3 as a small negative value and give $\rho_4 > \rho_2$.

The values of the spin densities for the phenoxy radical should give an indication of the relative reactivities of the various positions in the molecule to reaction with other free radicals. Thus in a reaction of the phenoxy radical with a radical R• the ratio $\rho_4 : \rho_2$ = 1:0.6 should indicate the relative proportions in which the structures XI(b) and (c), respectively, combine with R• to form XII(a) and (b) (after hydrogen migration).

An experiment of this kind has been carried out by Mulcahy and Williams[45], who reacted phenoxy radicals with methyl radicals in a stirred flow reactor. The products (mainly p- and o-cresol and anisole) were analysed by v.p.c. and the relative reactivities of the ortho- and para-positions and the oxygen atom were obtained, after correction for secondary methyl attack. They found the relative reactivities of the positions were para:ortho:oxygen = 1:0.55:0.17. These are in fairly good qualitative agreement with the ratio of the spin densities given above, although an accurate value of the spin density on oxygen cannot be obtained.

2.4.2 ALKYL-SUBSTITUTED PHENOXY RADICALS

The spin densities at the ring positions calculated for the 4-methyl-, 2,6-dimethyl- and 2,4,6-trimethyl-phenoxy radicals are shown in Table 5. To determine spin densities at carbon atoms with attached methyl groups a value for Q_{C-CH_3} of +27.2 Oe was taken.

TABLE 2.5

Spin densities for methyl-substituted phenoxy radicals

	ρ_2	ρ_3	ρ_4	$2(\rho_2+\rho_3)+\rho_4$
phenol	0.28	-0.075	0.42	0.83
p-cresol	0.25	-0.06	0.44	0.82
2,6-dimethylphenol	0.24	-0.07	0.40	0.74
2,4,6-trimethylphenol	0.22	-0.06	0.44	0.76

It will be seen that the introduction of a para-methyl group to the phenoxy radical causes very little change in the total spin density at the ring positions. The introduction of two methyl groups at the ortho-positions does however cause some 10% decrease. It may be worth noting here that comparisons such as these above depend on the use of accurate values of both Q_{C-H} and Q_{C-CH_3}. The values employed for these constants vary considerably. Comparisons are more likely to be valid when they involve the use of just one

constant, i.e. in comparing unsubstituted ring positions, such as those discussed below.

A feature of all the alkyl-substituted phenoxy radicals investigated is that on changing the substituent in a particular series there is practically no change in the spin densities of the unsubstituted positions i.e.

p-alkyl-	$\underline{a}_{H(2,6)} \sim 6.0$ Oe	$\underline{a}_{H(3,5)} \sim 1.45$ Oe
2,6-dialkyl-		$\underline{a}_{H(3,5)} \sim 1.70$ Oe $\underline{a}_{H(4)} \sim 9.5$ Oe
2,6-dimethyl-4-alkyl-	($\underline{a}_{H(2,6)} \sim 6.0$ Oe)	$\underline{a}_{H(3,5)} \sim 1.4$ Oe

Considering the α-proton coupling constants of the alkyl groups, there is a general trend throughout, in that coupling constants decrease in the sequence

$$Me > Et > Pr^{n} \sim CH_2Ph > Pr^{i} > Bu^{s} \quad (> Bu^{t}).$$

This can only be in small part due to a change in spin density at the position of the substituent, the main change being probably associated with the magnitudes of the constants $Q_{C\text{-}Alkyl}$, which obviously depend to a large extent on the mean conformation of the substituent group $-CH_2R$ or $-CHR_2$. This has been shown to be the case for the 2,6-di-t-butyl-4-cyclohexylphenoxy radical.[46] In this radical the α-proton is constrained to lie near the plane of the aromatic ring, such a conformation showing a smaller coupling

(4.5 Oe) than one where there is free rotation of the cyclohexyl ring, since the coupling of the α-proton would depend on $\cos^2\theta$, where θ is the dihedral angle between the aliphatic C-H bond and the symmetry axis of the 2p orbital on the adjacent carbon atom.

The ratio of the coupling constants for the α-protons of the methyl, ethyl and isopropyl groups appears to have the reasonably constant value 1:0.8:0.5 (*i.e.* p-R-phenoxy 1:0.8:0.5, p-R-nitrobenzene anion[26] 1:0.85:0.5, p-R-2,6-di-t-butylphenoxy[34] 1:0.83). If there is no change in the relative spin densities at the substituted carbon atoms values of $Q_{C\text{-}Alkyl}$ can be estimated to be $Q_{C\text{-}Et} \sim 0.8\ Q_{C\text{-}CH_3}$ and $Q_{C\text{-}Pr^i} \sim 0.5\ Q_{C\text{-}CH_3}$.

2.4.3. CARBOXY-, CARBONYL- ETC. SUBSTITUTED PHENOXY RADICALS

It will be seen (Table 2) that electron-attracting groups, such as $-CO_2H$, -CHO and $-NO_2$, substituted in the *para*-position, cause a general increase in the coupling constants of both the *ortho*- and *meta*-protons compared with the unsubstituted phenoxy radical (*i.e.* $a_{H(2)} \sim 6.9$, $a_{H(3)} \sim 2.3$ Oe, *cf.* 6.6 and 1.8 Oe for PhO•). The *p*-alkyl substituents discussed above generally cause a decrease in the coupling constants of the unsubstituted positions. These changes could well indicate variations of spin density by an inductive effect. It is interesting to note that

those radicals with a lower spin density at the ortho-positions, i.e. the alkyl phenoxy radicals, are formed from the more easily oxidised phenols, while those with a higher spin density are formed from less easily oxidised phenols. This is reasonable since for electron transfer to an oxidant, $-O\cdot C_6H_4\cdot R \longrightarrow \cdot O\cdot C_6H_4\cdot R + e$, an electrophilic substituent R should, by electron pull from the oxygen atom, both increase the electronic charge in the ring and decrease the ease of formation of the radical from the corresponding anion. However, as the spin density on the oxygen atom and at the para-position in every case (except for methyl-substitution) is unknown, definite conclusions are difficult to make.

In contradiction to the above reasoning, it would appear, from the fact that in all the simple para-substituted phenoxy radicals investigated the relationship

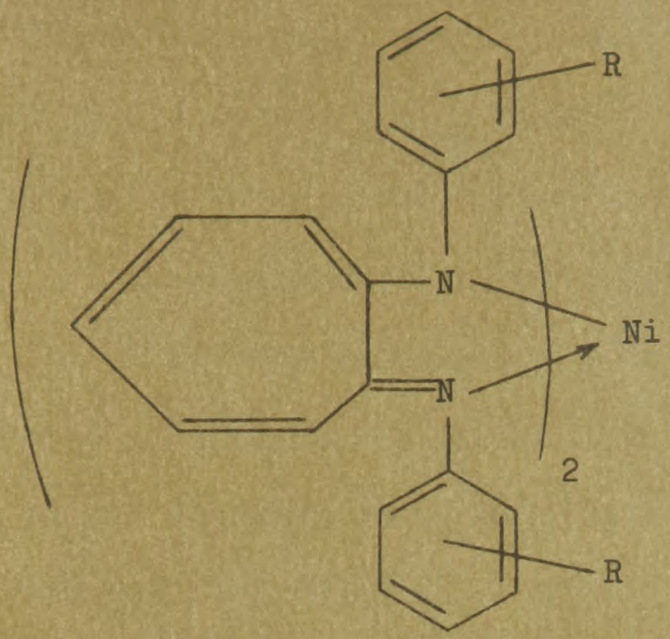
$$a_{H(2)} + a_{H(3)} = -4.5 \pm 0.2 \text{ Oe}$$

holds good, that the total spin density at the ortho- and meta-positions remains constant; the only effect of the para-substituent being to cause a redistribution of this spin density. A similar relationship has been found for the para-substituted nitrobenzene anions.[22,26]

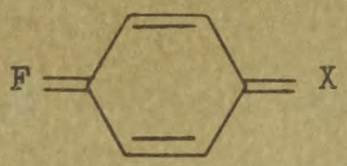
2.4.4 HALOGENO-SUBSTITUTED PHENOXY RADICALS

The fluorine coupling constants in the o- and p-fluorophenoxy radicals have the large values of 17.0 and 27.4 Oe respectively; these values are 2.55 and 2.7 times the coupling constant for the corresponding hydrogen atom in the unsubstituted phenoxy radical. Fluorine splitting has been obtained by other workers and the values of the ratio a_F/a_H are as follows: tetrafluoro-p-benzosemiquinone[47] 1.75, p-fluoronitrobenzene[22] 2.1, p-fluoroacetophenone anion[48] 2.05. Thus using an expression $a_F \sim Q_{C-F}\rho_C$ similar to that used for a proton attached to the aromatic ring, and assuming that the spin density at the carbon atom in question is not changed on substitution by fluorine (the spin densities at the unsubstituted position in the last two examples above are little changed), various values for Q_{C-F} are obtained i.e. $Q_{C-F} = (2.2\pm0.5)\ Q_{C-H}$.

Eaton and colleagues[49] have investigated a series of unsubstituted (R=H) and fluorosubstituted (R=F) nickel (II) N,N'-diphenyl aminotroponeimineates (XIII) by n.m.r., using the proton contact interaction shifts to determine coupling constants. The signs of the latter can also be determined by this approach. Again assuming that the introduction of a fluorine atom causes little or no effect on the spin density at the carbon atom concerned, they find the following values of Q_{C-F} for para-, meta- and ortho-



(XIII)



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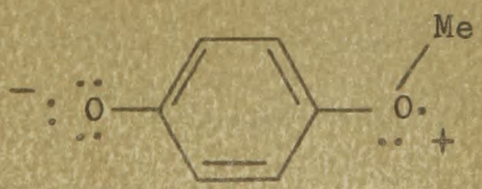


(XV)

fluoro compounds: +47.2, +4.0, +41.1 Oe. It therefore seems that the value of Q_{C-F} depends on the position of substitution in the phenyl ring, and that the expression $\underline{a}_F = Q_{C-F}\rho_C$ is unsatisfactory

They suggest an expression $\underline{a}_F = Q_{C-F}\rho_C + (Q_{F-C}{}^A)\phi_{C-F}\rho_C$, where the first term represents the contribution due to the positive spin density on the carbon atom inducing a negative spin density at the fluorine atom, analogous to the $\sigma - \pi$ interaction in an aromatic C-H fragment. The second term represents a contribution due to a positive spin density on a p_π -orbital of the fluorine atom itself, produced as a result of conjugation involving such structures as XIV; $(Q_{F-C}{}^A)$ is a constant and ϕ_{C-F} is the double bond order of the C-F bond. Having first calculated values for ϕ_{C-F} by M.O. theory, Eaton uses the experimental results for the p- and m-fluoro compounds (assuming that ρ_C, the spin density at the carbon atom to which the fluorine is attached, is the same as the spin density at that position with just an hydrogen atom attached) and finds $(Q_{F-C}{}^A) = +848$ Oe and $Q_{C-F} = -147$ Oe. He then calculates, using these Q-values, the coupling constants, $\underline{a}_F$, for the meta-fluoro compound and obtains good agreement.

Until the bond orders can be calculated, the results obtained for the fluorine splittings in the phenoxy radical cannot be used

in an expression such as the above. The assumption that the spin density at the carbon atom to which the fluorine is attached is the same as the spin density at the corresponding unsubstituted atom probably does not hold good. It can be seen from the present work that in the 2-fluorophenoxy radical the coupling constant of the proton at position 6 has been reduced by some 10% from the value in the unsubstituted phenoxy radical.

No doubt a similar relationship holds good for chloro-substituted radicals, although apart from the present work only one example of chlorine splitting has been hitherto reported; Ayscough and colleagues[41] having observed a splitting of 0.17 Oe in p-chloronitrobenzene. Probable splittings of 1.7 and 1.1 Oe for p-chloro and 2,6-dichloro-phenoxy have been observed in the present work (an even larger chlorine splitting is reported for 4-chlororesorcinol - Part 3).

It seems likely that appreciable chlorine splittings will only be observed in radicals in which the proton coupling constants in the corresponding unsubstituted radicals are relatively large, since the chlorine nucleus has a magnetic moment some 3½ times smaller than that of the proton. Hitherto recorded aromatic proton coupling constants have not been greater than ca 5 Oe,

whereas the para-proton coupling constants in the phenoxy radical is ca 10 Oe and that at position 4 in the radicals from resorcinol ca 11.4 Oe.

2.4.5 ALKOXY-SUBSTITUTED PHENOXY RADICALS

The results shown in Table 3 indicate that methoxy and similar groups decrease the ring coupling constants very much more than do the alkyl group. A similar effect has been found by Colowell[50], who has investigated several methoxy-substituted p-benzosemiquinones. The decrease in spin density at the unsubstituted positions in the ring can probably be explained by assuming that much of the spin density is associated with the two oxygen atoms and that structures such as XV are important.

PART 3

OXIDATION OF RESORCINOLS AND FORMATION OF meta-SEMIQUINONES

3.1 INTRODUCTION

The oxidation of resorcinols has been hitherto little investigated by e.s.r. The only reported observation of e.s.r. spectra are those of Adams and colleagues[51], who oxidised resorcinol and a few of its substituted compounds in air in an alkaline solution of water, acetone, ethanol or mixtures thereof. In view both of the fact that their spectra were not analysed for definite radical species, and of the work reported below, it would appear that the spectra were of some secondary oxidation products.

Resorcinol and some 15 of its substituted compounds have been oxidised, using the flow apparatus, both in alkaline solution with potassium ferricyanide and in acid solution with ceric sulphate. The results obtained in both cases are given below, and in the case of alkaline oxidation it seems highly probable that the species being observed are the meta-benzosemiquinones. This is the first time that the detection of the latter radicals has been reported, although the spectra of many para-[50,52] and of a few ortho-semiquinones[51] are well known.

3.2 EXPERIMENTAL

Essentially the same technique was used as for the production of phenoxy radicals (Part 2). The resorcinol (10^{-2} M) was oxidised in the flow apparatus with (i) a solution of potassium ferricyanide (10^{-2} M) in ca. 10^{-1} M aqueous sodium hydroxide, and (ii) a solution of ceric sulphate (10^{-2} M) in ca. 1 M sulphuric acid.

The resorcinols were dissolved in water or in as low a concentration of alkali as was necessary to effect solution. More concentrated alkaline solutions increased the likelihood of spurious peaks appearing in the e.s.r. spectra, although even with a very low concentration these occasionally appeared (i.e. the two spurious peaks in Fig. 2). These are possibly due to the formation of secondary radicals produced from oxidation products.

Materials used

The resorcinols were commercial products except for those described below. All were recrystallised before use.

4,6-Dibromoresorcinol: prepared by the method of Kohn and Löff[53] using 10 g. resorcinol. Product recrystallised from water; m.p. 110° (lit. 110-112°), yield 18 g. (75%).

4,6-Diiodoresorcinol: prepared by the method of Nicolet and Sampey[54]

using the same quantities. Product recrystallised from benzene; m.p. 145° (lit. 145°), yield 13 g. (79%).

2,4,6-Tribromoresorcinol: prepared by the method of Davis and Hill[55] using $\frac{1}{10}$ quantities. Product recrystallised from water; m.p. 111° (lit. 111-112°), yield 30 g. (95%).

3.3. RESULTS AND ANALYSIS OF SPECTRA

In general the spectra obtained by the acid oxidation of the resorcinols tended to be less well resolved than those from alkaline oxidation. The former spectra were also somewhat asymmetric about the horizontal base-line (i.e. Fig. 4). The coupling constants obtained from resorcinols by oxidation with alkaline ferricyanide and with acid ceric sulphate are given in Tables 1 and 2 respectively.

3.3.1 RESORCINOL

The spectra obtained by both the alkaline and the acid oxidation of resorcinol are shown in Figs. 1 and 4 respectively. Both can be seen to consist of a large triplet splitting, each line of which is split into a further doublet of doublets. This indicates interaction of the free electron with two equivalent protons and with a further two non-equivalent protons. These interacting nuclei could well correspond, in the case of the radical from alkaline oxidation, to the ring protons of meta-benzosemiquinone, in which the proton at positions 4 and 6 would be equivalent. In the spectrum of the radical produced by acid oxidation it would also seem likely that the observed splittings are due to the ring protons, although in this case the simple meta-semiquinone anion

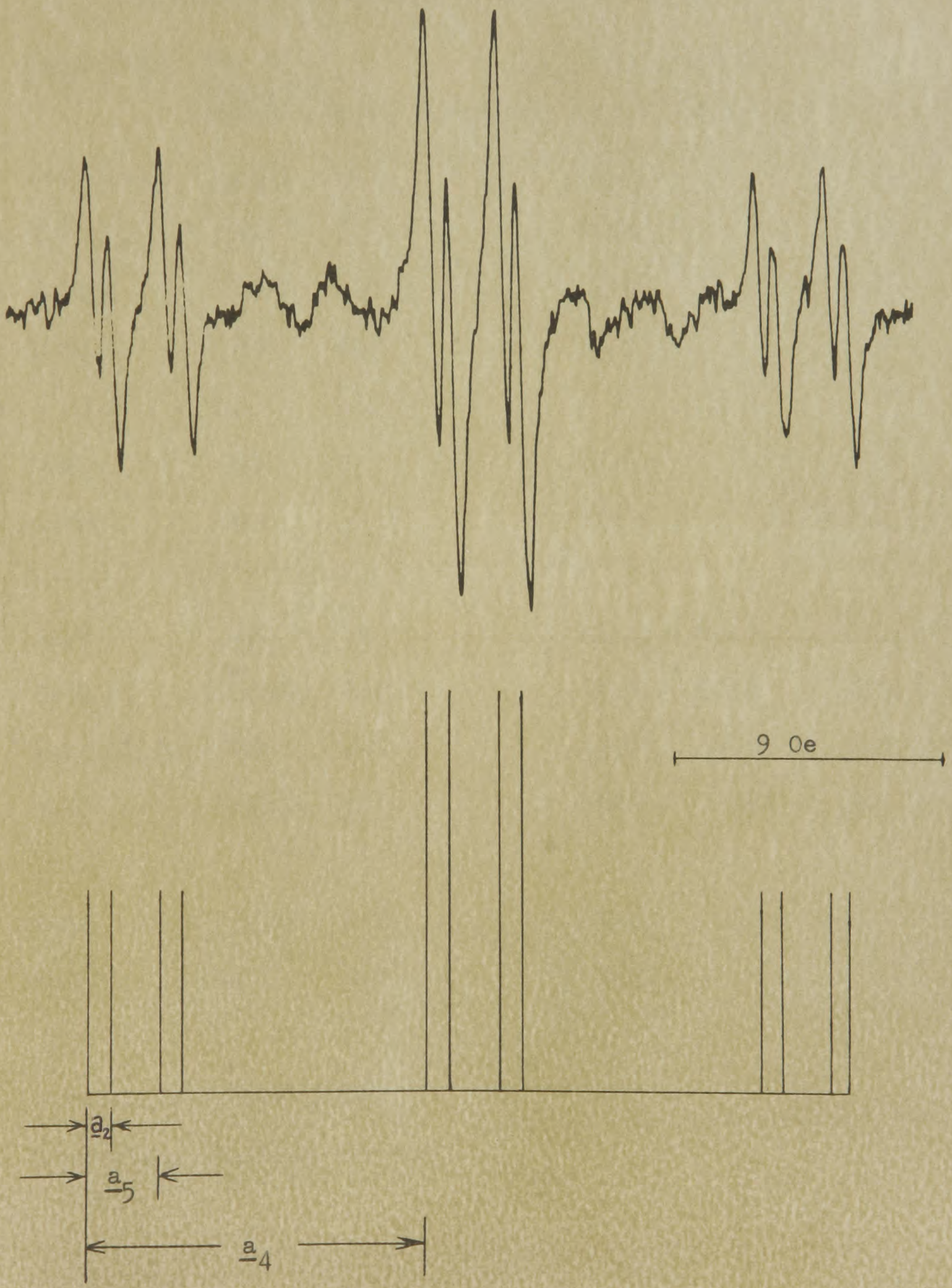


FIG. 3.1. Alkaline oxidation of resorcinol

TABLE 3.1.

Alkaline oxidation of substituted resorcinols

Resorcinol	No. of spectral lines	Coupling constants (Oe)[a]					
		$a_{H(2)}$	$a_{Alkyl(2)}$	$a_{H(4,6)}$	$a_{Alkyl(4)}$	$a_{H(5)}$	$a_{Alkyl(5)}$
Resorcinol	3x2x2	0.7		11.2_5		2.4	
2-CO_2H	3x2			11.2_5		2.3_5	
4-CO_2H	2x2x2	0.7		11.0		2.3	
5-CO_2H	3x2	0.7		11.3			
2-Me	3x6		1.0	10.9_5		2.2	
2-NO_2	3x2			11.5		2.6	
4-Et	4x2	?		10.5_5	10.5_5	2.3	
4-CH_2Ph	4x2x2	0.7		10.4	10.4	2.3	
4-$(CH_2)_5CH_3$	4x2	?		10.0	10.0	2.3	
4-Cl	2x5x2	0.7		9.8	2.0[b]	2.0	
5-Me	3x4x2	0.8		11.1_5			2.3_5
5-OH	4	7.5		7.5			

a absolute values given

b coupling constant for Cl.

TABLE 3.2.

Acid oxidation of substituted resorcinols

Resorcinol	No. of spectral lines	Coupling constants					
		$\underline{a}_{H(2)}$	$\underline{a}_{Alkyl(2)}$	$\underline{a}_{H(4,6)}$	$\underline{a}_{Alkyl(4)}$	$\underline{a}_{H(5)}$	$\underline{a}_{Alkyl(5)}$
Resorcinol	3x2x2	3.8		9.8		2.2_5	
2-CO_2H	3x2			10.6_5		2.5	
4-CO_2H	2x2x2	4.6		9.9_5		1.9	
5-CO_2H	3x2	3.9_5		9.8_5			
2-Me	20		5.3	8.9		1.8_5	
2-NO_2	3x2x3	0.5[b]		10.7		2.6	
4-Et	4x2x2	3.2		10.0	10.0	2.0_5	
4-CH_2Ph	22	3.2		9.1_5	8.1_5	2.1	
4-$(CH_2)_5CH_3$	4x2x2	3.2		8.6	8.6	2.0	
4-Cl[c]							
5-Me	16	4.0		9.5_5			2.0
5-OH[c]							

a absolute values given

b coupling constant for N

c poor spectra obtained

would be unlikely to exist in acid solution (see discussion).

In order to prove that the observed splittings were due to the ring protons, and to unambiguously assign each splitting, resorcinols blocked at each ring position in turn with the carboxy group were oxidised and the e.s.r. spectra obtained (see section 3.3.2.). Deuterium substitution is the method usually used to assign splittings, but this frequently involves complicated syntheses, and, in the case of the flow method where several grams of compound may be needed to obtain one spectrum, high cost. Although the introduction of a carboxy group was found to cause small changes in the coupling constants of the phenoxy radicals (Part 2), it was thought unlikely that the relative magnitudes of the coupling constants concerned would be appreciably altered; in fact in the resorcinol carboxylic acids very little change in the values of the coupling constants of the unsubstituted positions occurred.

3.3.2. RESORCINOL CARBOXYLIC ACIDS

On alkaline oxidation of the resorcinol 5-carboxylic acid, the spectrum shows a large triplet, and a doublet of 0.7 Oe (Fig.2). The 2-carboxylic acid similarly shows a triplet, and a larger doublet of 2.35 Oe (Fig. 3). The 4-carboxylic acid shows a large doublet

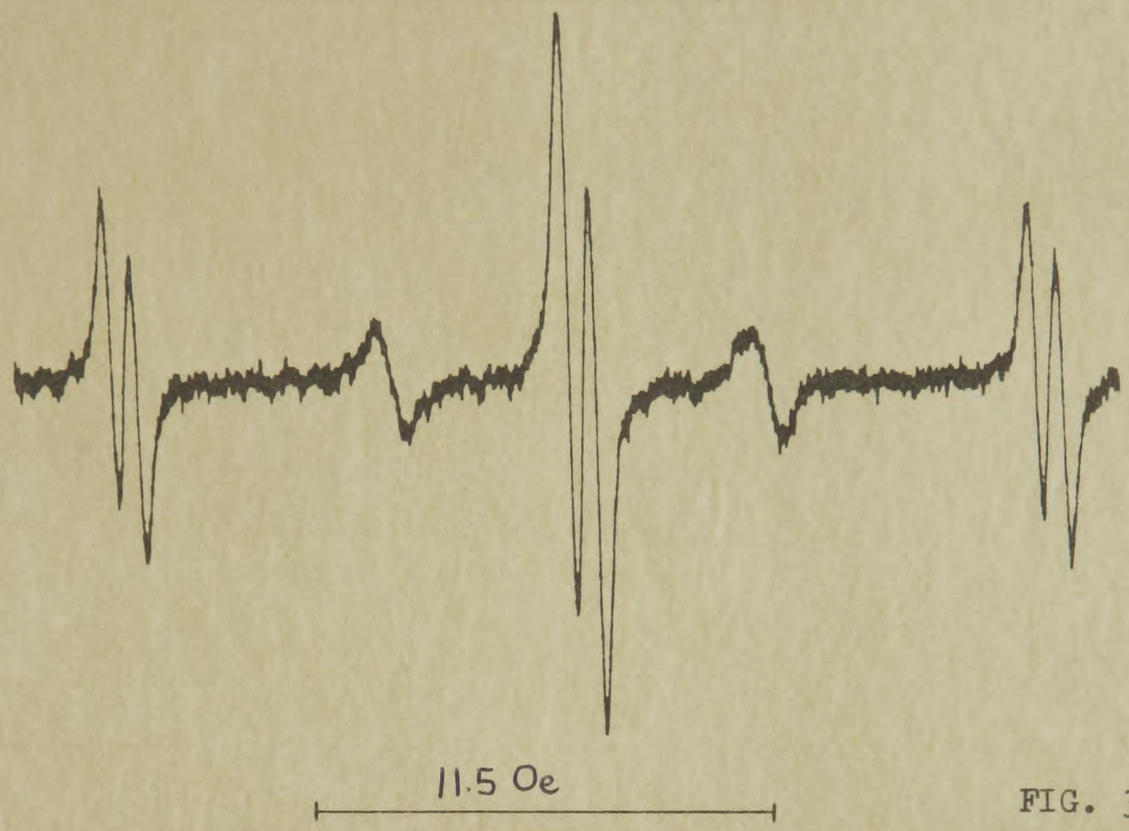


FIG. 3.2.

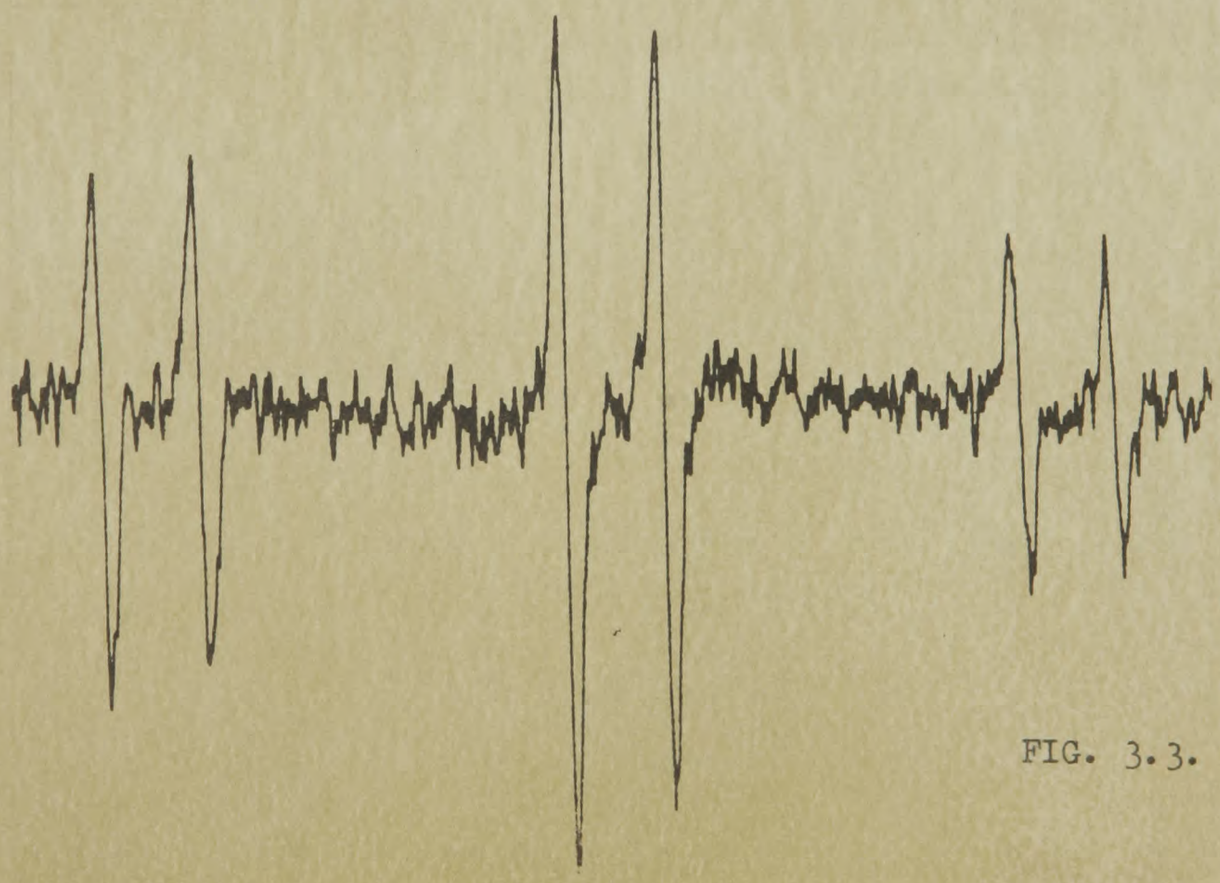


FIG. 3.3.

Alkaline oxidation of resorcinol 5-carboxylic acid (Fig. 2) and resorcinol 2-carboxylic acid (Fig. 3).

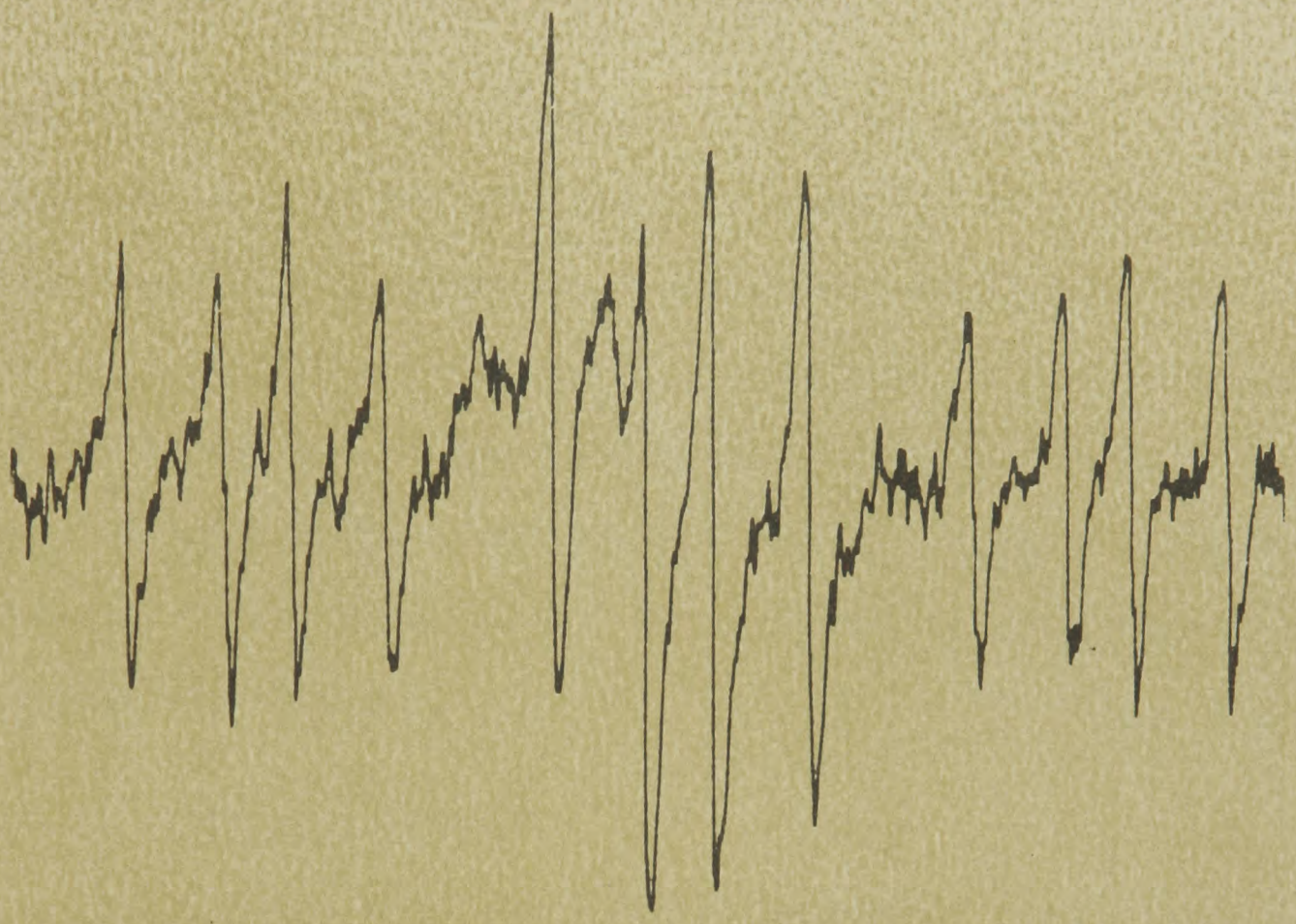


FIG. 3.4.

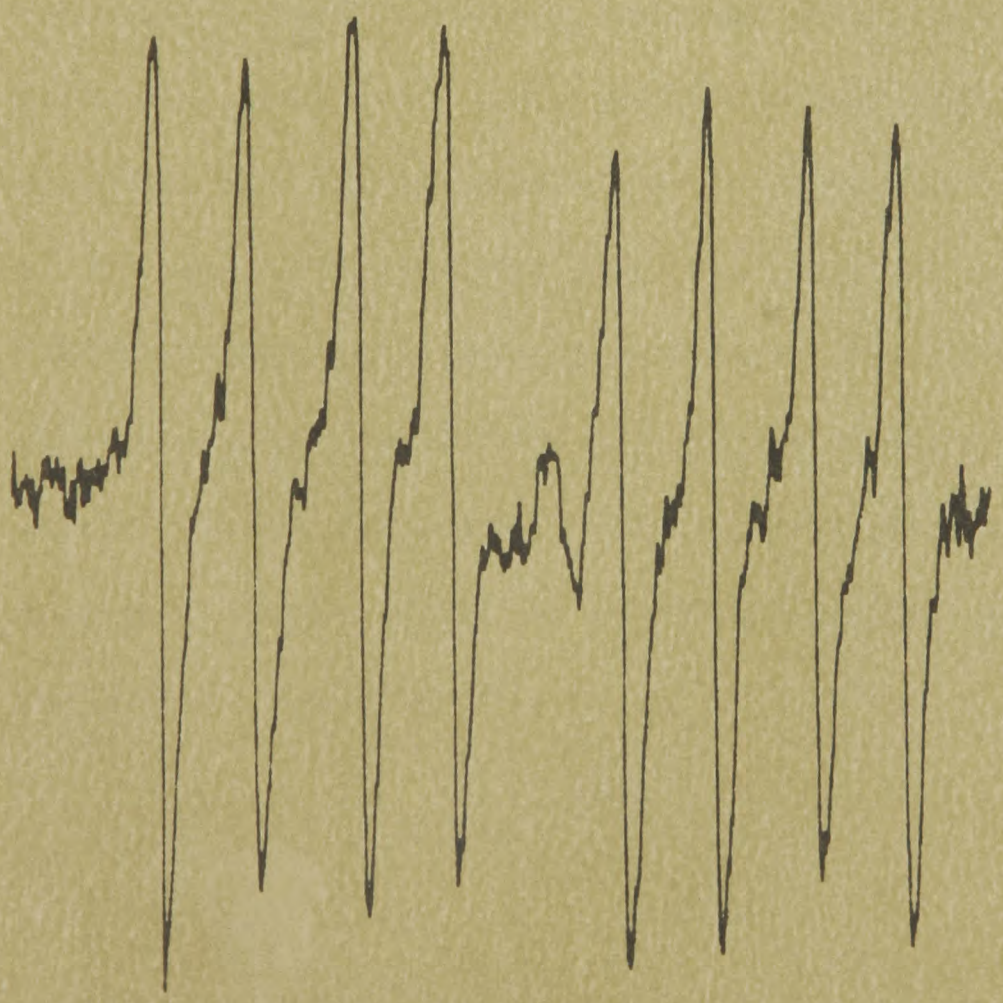


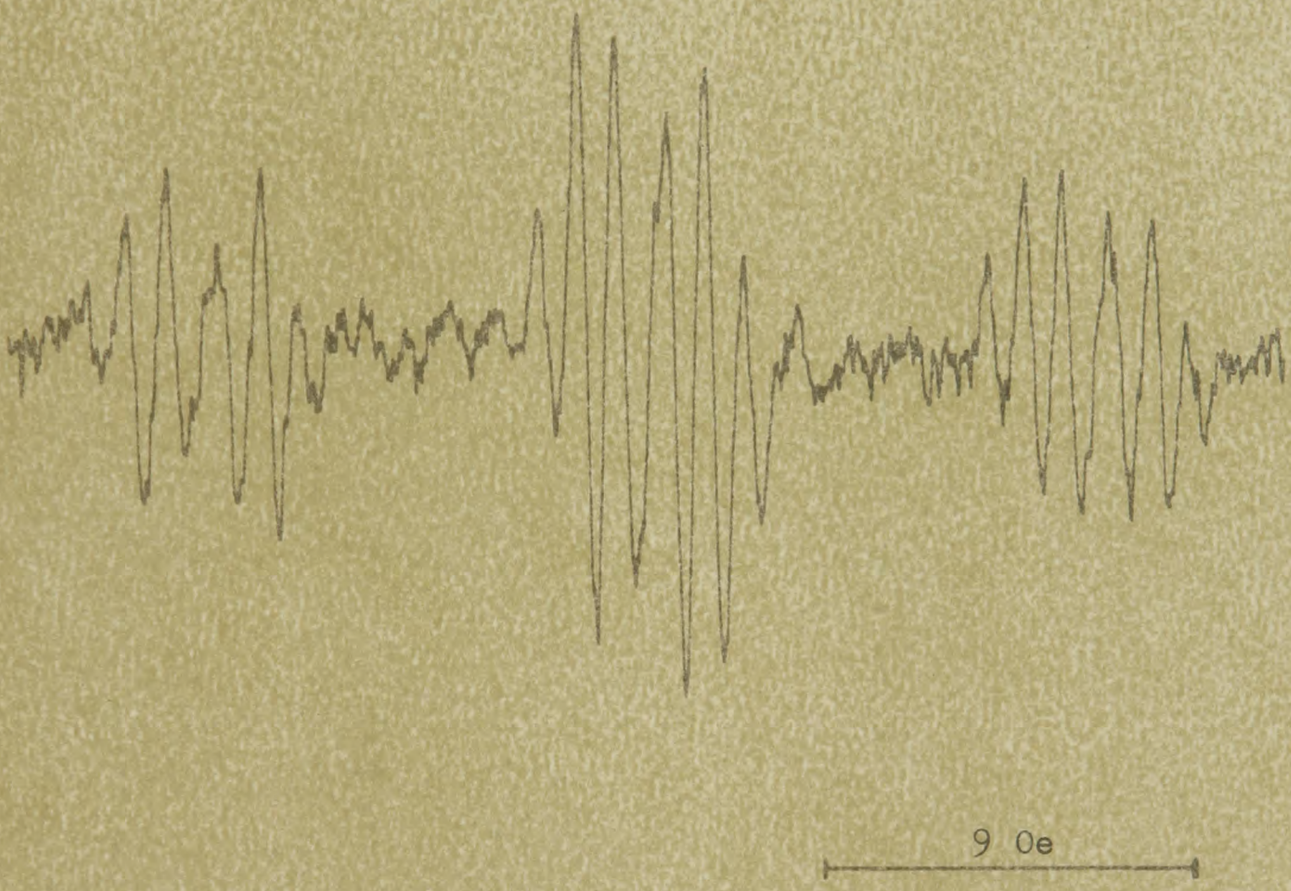
FIG. 3.5.

Acid oxidation of resorcinol (Fig. 4) and resorcinol 4-carboxylic acid (Fig. 5).

and two further smaller doublets of 2.3 and 0.7 Oe. These results indicate that the two doublets of 2.4 and 0.7 Oe in the spectrum from the alkaline oxidation of resorcinol can be assigned to the 5- and 2-positions respectively. Similarly in the acid oxidation of the 2- and 5-carboxylic acids the spectra each consist of a triplet and a doublet, but in this case the larger of the two is assigned to the 2-position. The 4-carboxylic acid shows three sets of doublets (Fig. 5).

3.3.3. ALKYL-RESORCINOLS

The spectra of 2- and 5-methylresorcinol (Figs. 6 and 7) both confirm the assignments made above. Alkaline oxidation of the 2-methyl compound gives a spectrum consisting of a triplet of doublets, each line being split further into 4 lines of coupling constant 1.0 Oe, corresponding to interaction with 3 methyl protons at the position with the smallest coupling constant. Similarly 5-methylresorcinol shows a splitting due to the methyl protons of the same order as that of the proton assigned to position 5 in the unsubstituted compound. The 4-alkylresorcinols fit into the proposed scheme, with the α-protons giving rise to large coupling constants (i.e. Fig. 8).



9 Oe

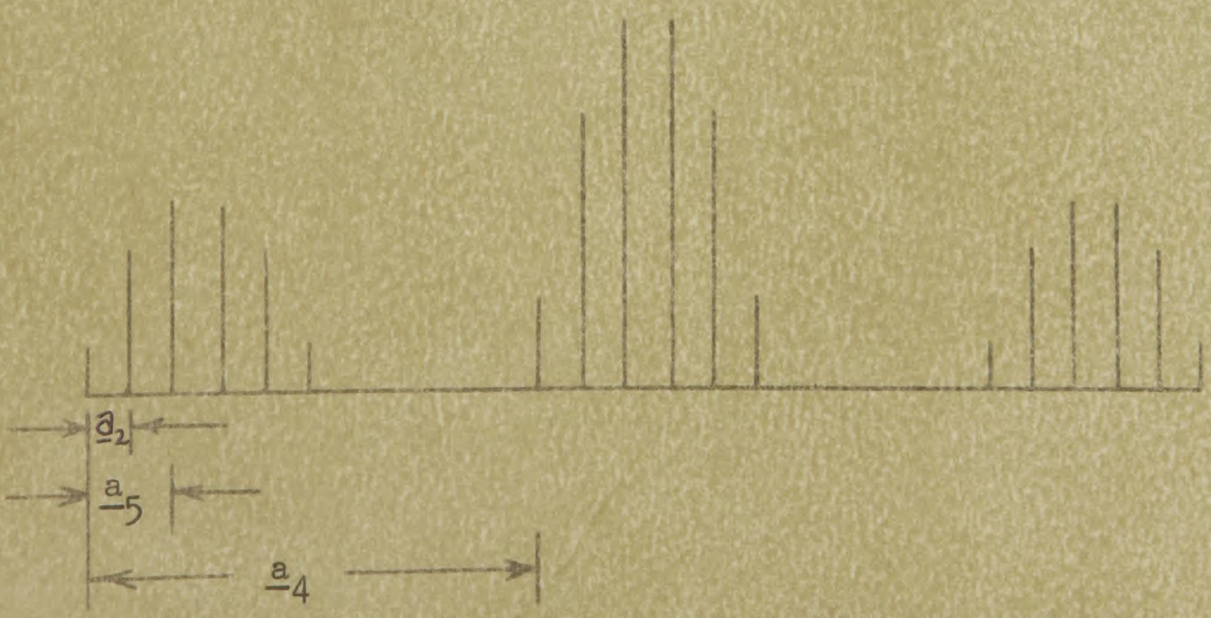


FIG. 3.6. Alkaline oxidation of 2-methylresorcinol

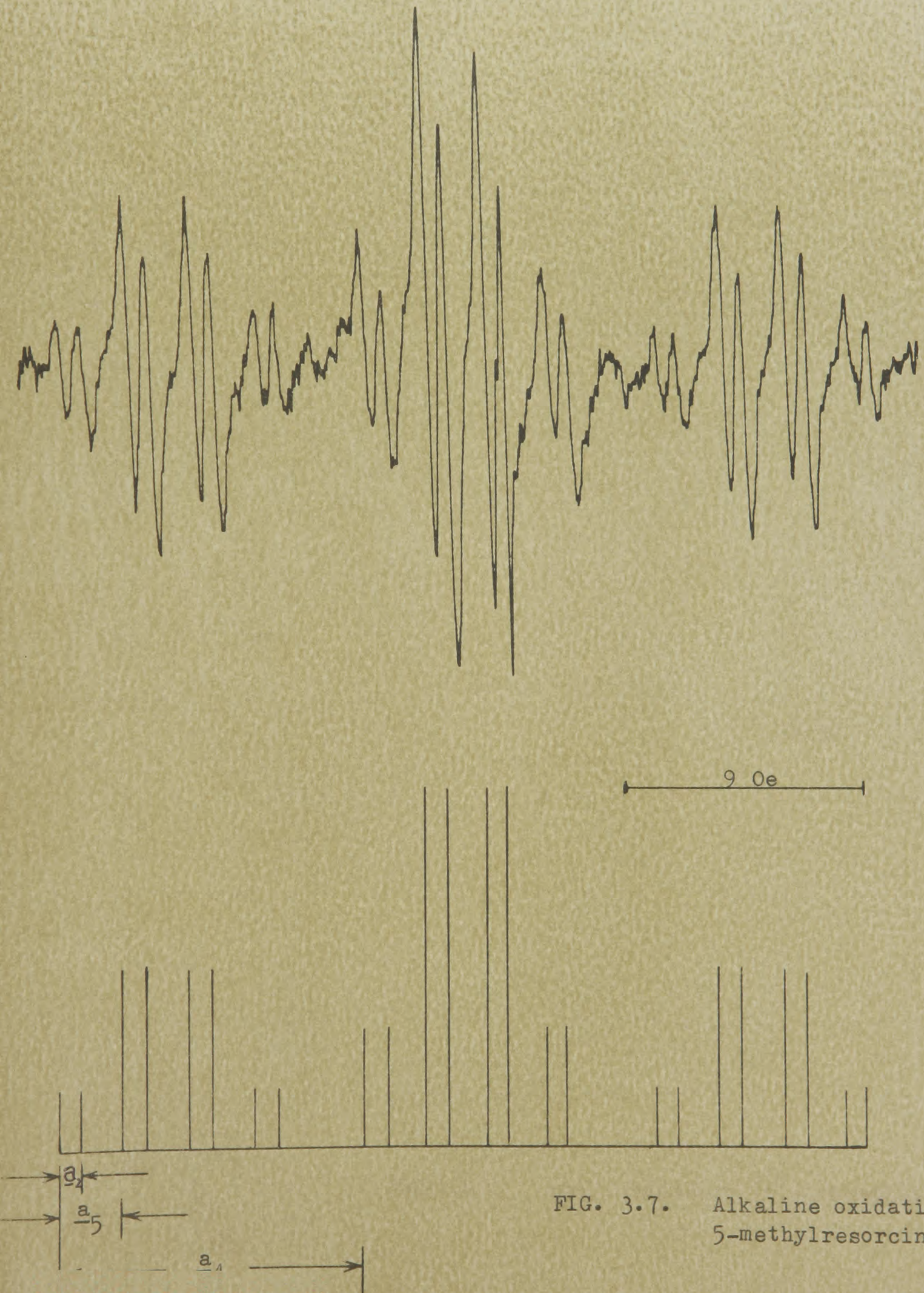


FIG. 3.7. Alkaline oxidation of 5-methylresorcinol

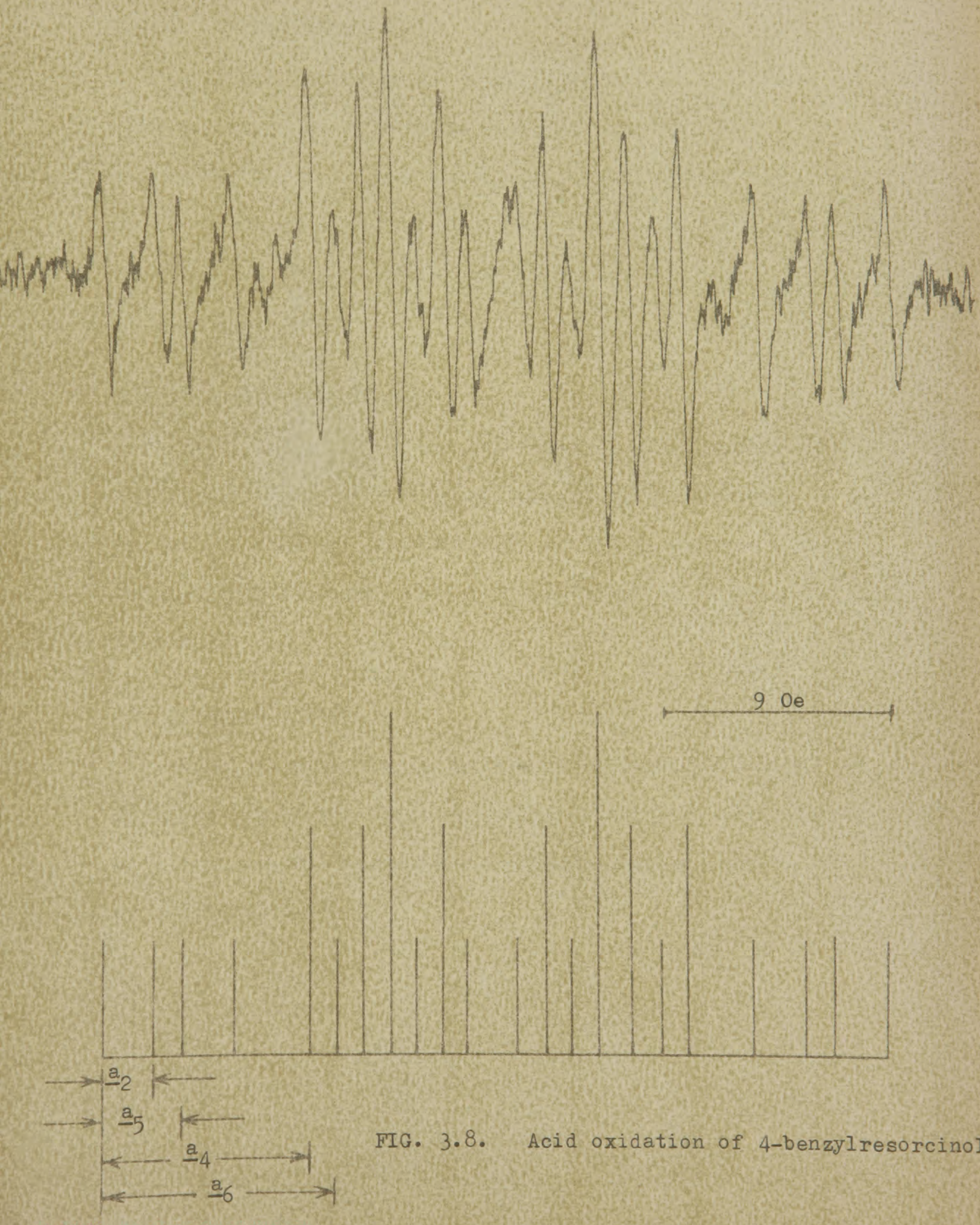


FIG. 3.8. Acid oxidation of 4-benzylresorcinol

3.3.4. 4-CHLORORESORCINOL

Alkaline oxidation of 4-chlororesorcinol produced a spectrum with the expected splittings from the ring protons but in addition giving further splitting which could only be reasonably interpreted on the basis of a 1:1:1:1 splitting of 2.0 Oe from the chlorine atom ($I=\frac{3}{2}$). Only a small badly-resolved spectrum was obtained by acid oxidation.

3.3.5. 2-NITRORESORCINOL

The spectrum obtained from alkaline oxidation of 2-nitroresorcinol showed only a broad triplet of doublets and no splitting due to the nitrogen atom could be detected, whereas a small, incompletely resolved, nitrogen splitting was observed on acid oxidation.

3.3.6. PHLOROGLUCINOL

Alkaline oxidation of phloroglucinol gave a 1:3:3:1 quartet spectrum due to the three equivalent protons at positions 2, 4 and 6. A strong but asymmetric and unanalysable spectrum was obtained by acid oxidation.

3.3.7. OTHER SUBSTITUTED RESORCINOLS

Several mono-substituted resorcinols gave only poor spectra on oxidation. Examples of such compounds investigated are 4-phenylazo-, 4-bromo- and 4-aminoresorcinols. None of the di- or tri-substituted resorcinols produced reasonable spectra i.e. 2,4-dinitro-, 4,6-dibromo-, 4,6-diiodo- and 2,4,6-tribromo-resorcinol. In all cases the spectra obtained were scarcely discernable above the noise level.

3.4. DISCUSSION

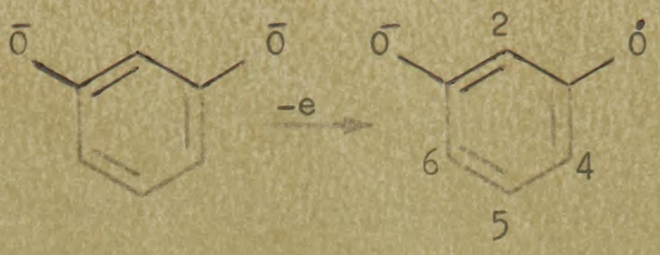
The primary oxidation products, by the loss of one electron, of the dianions of both quinols and catechols are the para- and ortho-semiquinones respectively. Similarly it is to be expected that the primary oxidation product of the dianion of resorcinol produces the meta-semiquinone (I).

The usual method for obtaining the e.s.r. spectra of most para-semiquinones, and of ortho-semiquinone itself, involves shaking the parent dihydric compound in air in alkaline ethanolic solution, filling the e.s.r. sample tube and observing the spectrum in the usual way. For most catechols this technique must be modified as secondary radicals are quickly produced (see Part 5), and for resorcinols spectra are obtained[51] which appear to be impossible to analyse for a meta-semiquinone such as (I). For example, Adams and colleagues[51] report an 11 line spectrum from the oxidation of resorcinol itself and give the value (0.23 n) Oe for the only coupling constant, where n is an integer $\geqslant 1$ due to lack of line assignment for the spectrum.

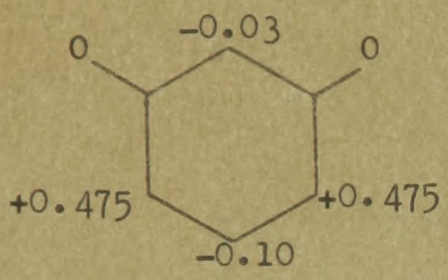
On oxidising resorcinol in the flow apparatus it is reasonable to assume that the e.s.r. spectra observed is that due to the primary oxidation product, which in this case must be meta-benzo-

semiquinone. The spectrum obtained clearly fits that expected from a species such as (I), with protons at positions 4 and 6 being equivalent, and two non-equivalent protons at positions 2 and 5. The coupling constants of these latter protons have been unambiguously assigned using the carboxy acids as described in the Experimental section.

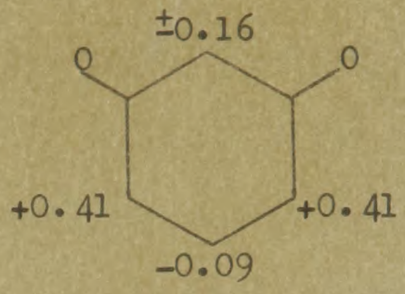
The values of the spin densities, calculated as in Part 2 above, at the carbon atoms of the benzene nucleus of the unsubstituted meta-semiquinone are, temporarily ignoring signs: $\rho_4 = \rho_6 = 0.475$, $\rho_2 = 0.03$, $\rho_5 = 0.10$. It will be seen that even if there is no spin density associated with the oxygen atoms, the sum of the above spin densities is greater than unity. Clearly either the spin density at position 5, or at both positions 5 and 2, must be negative (assuming that $|Q| \leqslant 25$ Oe; the value 23.7 has been used in the above calculations). An absolute assignment is not possible at present, although if, as seems likely, the molecule may be described as a state which has a node through C_2 and C_5, simple theory would predict zero spin density at both these atoms. It is well known[7b] that negative spin densities are more likely to occur where a simple Hückel treatment yields zero spin densities and if this is the case the spin density distribution in meta-semiquinone is as shown in (II).



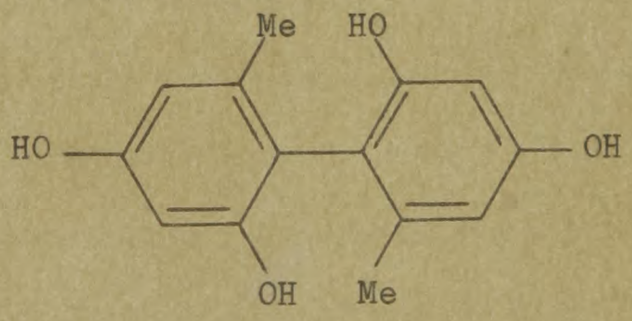
(I)



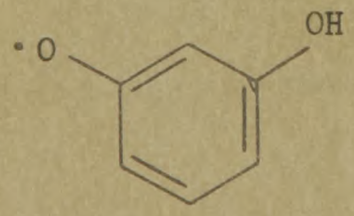
(II) Spin densities in radical from alkaline oxidation



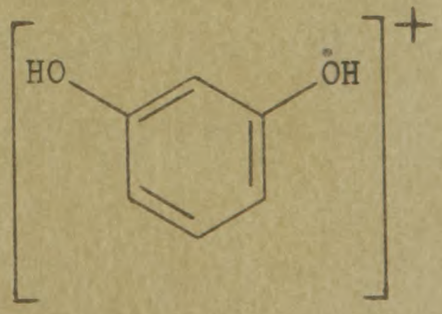
(III) Spin densities in radical from acid oxidation



(IV)



(V)



(VI)

It can be seen that a very large proportion of the spin density is associated with carbon atoms 4 and 6, and only some 18% with both oxygen atoms and the carbon atoms to which they are attached. These values are quite different from those obtaining in both o- and p-semiquinones, which have approximately 65% and 60% of the spin density associated with the two oxygen atoms.

The spin densities of the two methyl-substituted meta-semiquinones are shown in Table 3. Although the presence of a methyl group causes small changes in individual spin densities the total spin density at the ring carbon atoms remains constant. Other substituents, such as carboxy and nitro groups, cause changes in individual coupling constants but these are too small to warrant any quantitative discussion.

Considering the very high spin density at the 4- and 6-positions it is to be expected that further oxidation products of resorcinol and its mono-substituted compounds would occur by the dimerization of the primary radicals at one of these two positions to form a biphenyl compound. The dimer (IV) has been obtained[27(a)] as a minor product from the oxidation of orcinol (5-methylresorcinol), although further coupling occurs to produce a mixture of polymers. It appears that the basic unit in these polymers is a biphenyl unit,

TABLE 3.3.

Spin densities for radicals from resorcinols

Radical from	Method of Oxidation[a]	Spin densities[b]			
		ρ_2	ρ_4	ρ_5	$(\rho_2 + 2\rho_4 + \rho_5)$
Resorcinol	A	-0.03	0.475	-0.10	0.82
	B	-0.16	0.41	-0.095	0.565
	B	0.16	0.41	-0.095	0.885
2-Methylresorcinol	A	-0.04	0.46	-0.09	0.79
	B	-0.195	0.375	-0.08	0.475
	B	0.195	0.375	-0.08	0.865
5-Methylresorcinol	A	-0.035	0.47	-0.09	0.815
	B	-0.17	0.40	-0.075	0.555
	B	0.17	0.40	-0.075	0.895

[a] oxidation in (A) alkaline solution, (B) acid solution

[b] calculated using $Q_{C-H} = -23.7$ Oe, $Q_{C-CH_3} = 27.2$ Oe

indicating that the primary reaction is a dimerization at position 4 (or 6).

The form of the radical produced by the oxidation of resorcinol in acid solution is less obvious than that of the radicals from the alkaline oxidation discussed above. The spectra from the acid oxidation indicate that the same number of interacting protons are involved, and it is therefore likely that these nuclei correspond to the four ring protons. Since the anion (I) would not exist in acid solution, two possibilities for the structure of the radical observed seem most likely. First, the singly protonated form (V) i.e. a hydroxyphenoxy radical, in which either the hydroxyl proton splitting is too small to be observed (a splitting of less than ca. 0.3 Oe would probably not be observed using the flow technique), or rapid exchange of this proton occurs with the solvent. Second, and a more symmetrical radical, is the doubly protonated semiquinone cation (VI). Such cations have been observed[56] in the p-semiquinones but appreciable (ca. 2 Oe) splittings have been found for the hydroxyl protons. However, as mentioned above, the spin density associated with the oxygen atom in p-semiquinones is very much larger than in the m-semiquinones, and thus the splitting from the two hydroxyl protons in (VI) might again be too small to be observed.

If indeed the species being observed are similar to (V) analogies may be drawn with the phenoxy radicals regarding the signs of the spin densities at the ring positions. In the phenoxy radicals positions ortho- and meta to the phenoxy oxygen are associated with positive and negative spin densities respectively. In a radical such as (V), C_2 and C_5 are ortho and meta respectively to the phenoxy oxygen and thus a positive spin density at C_2 might be expected. A radical such as (VI) is more similar to the one from alkaline oxidation and similar signs for the spin densities would be expected. Table 3, and, for the unsubstituted radical, diagram (III) give values for the spin densities at the ring positions in the radicals produced by acid oxidation. Values are included for both negative and positive spin densities at C_2, and it will be noticed that the sum of the spin densities at the ring positions is more nearly constant when a positive spin density at C_2 is assumed.

PART 4

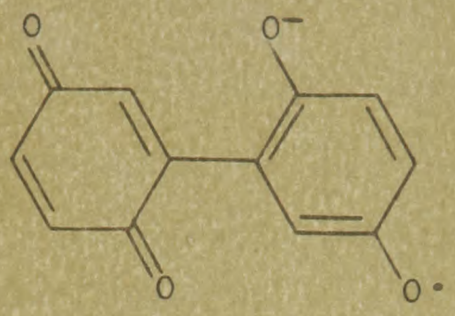
THE PRODUCTION OF SECONDARY RADICALS FROM CATECHOL AND SOME 2-*o*-HYDROXYPHENYL-1,4-BENZOQUINONES.

4.1. INTRODUCTION

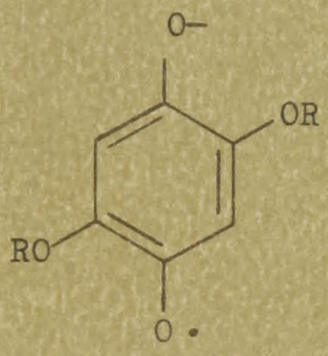
The production of secondary radicals from the oxidation of hydroquinone or the reduction of p-benzoquinone has been previously observed.[23,57] It has been shown that radical (I) is formed in aqueous alkaline solution, and radical (II; R=Me or Et) in alkaline methanol or ethanol.

This Part describes the formation and characterisation of secondary radicals produced from the oxidation of catechol (III) and the reduction of 2-o-hydroxyphenyl-1,4-benzoquinones (i.e. IV) in dimethylformamide (DMF) solutions. This work was an indirect result of two other investigations: the former arising from a study of o-semiquinones in general (Part 5) and the latter arising from an unrelated (and unsuccessful) e.s.r. study of some oxidation products of alkoxy-phenols obtained by Hewgill.[58]

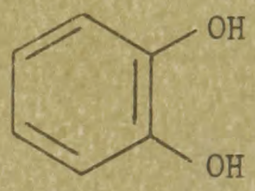
In both cases the normal stationary method of observing radicals in the e.s.r. spectrometer was used, and the main interest lay in the spectra of the secondary radicals, which were either produced instead of those expected from the primary radical or superimposed on them. In some cases the spectrum of a secondary radical appeared only some 15-30 min. after the initial spectrum had been obtained,



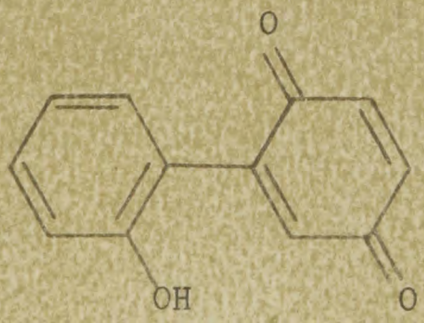
(I)



(II)



(III)



(IV)

indicating that important information may easily be lost unless initial spectra are run several times. From the observations described below suggestions have been made as to the reaction mechanisms resulting in the production of the secondary radicals.

4.2. EXPERIMENTAL

NOTE: The author wishes to emphasise that this work was carried out in collaboration with F.R. Hewgill while the latter was on short study leave from the University of Western Australia. The labour involved was roughly allocated so that Hewgill carried out most of the preparative work and the present author the e.s.r. work.

Reduction of quinones

Samples (5 mg.) of the quinones were vigorously shaken in a stoppered 4 ml. test tube with DMF (2 ml.) containing 10% v/v of water in the presence of an excess of solid sodium dithionite and a little sodium hydroxide, until a deeply coloured solution resulted. The solution was then poured into the sample cell and its e.s.r. spectrum was recorded at regular intervals.

Oxidation of catechol and quinols

These were carried out in a similar manner to the reductions, omitting the sodium dithionite.

Materials

As mentioned above preparative work was carried out mainly by Hewgill, details of which may be found in his joint paper[59] with the

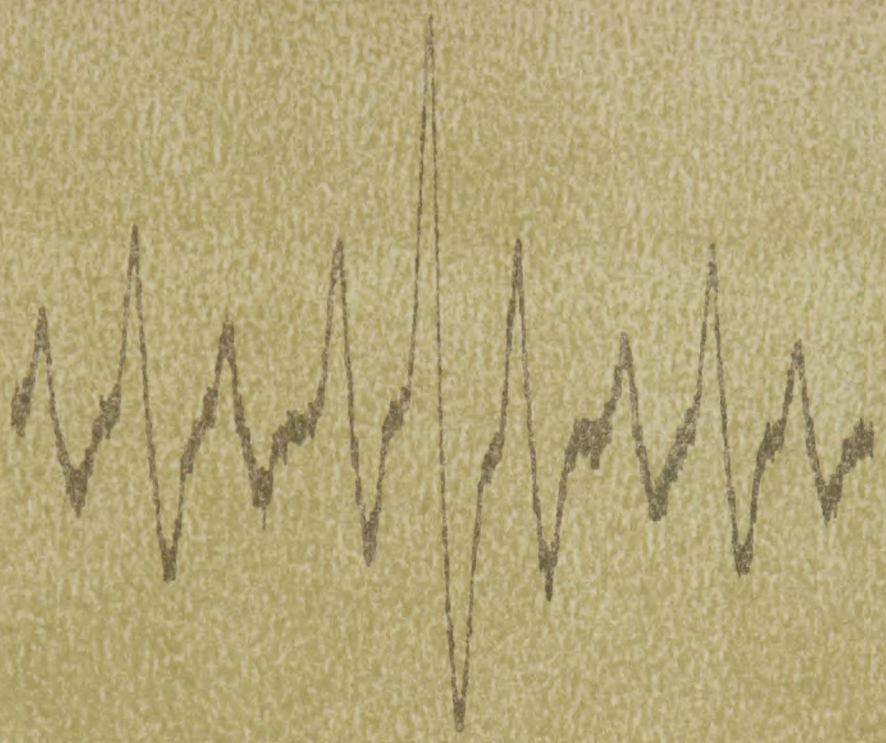
present author. This describes the preparation of dibenzo-[1,4]-dioxin-2,3-quinone (IX) by iodate oxidation of catechol, the aerial oxidation of catechol and detection by thin-layer chromatography of (IX) among the reaction products, and the preparation of 2-o-hydroxyphenyl-1,4-benzoquinone (IV) and of dibenzofuran-1,4-quinone (XIII-e). 2-(2-Hydroxy-5-methoxy-4-t-butylphenyl)-5-t-butyl-1,4-benzoquinone (XIV) was the sample previously described[58] by Hewgill. He has subsequently supplied samples of 2,5,6'-trihydroxy-3'-methoxy-3,5'-di-t-butylbiphenyl (XVI) and 8-methoxy-2,6-di-t-butyldibenzofuran-1,4-quinone (XVII-e).

4.3. RESULTS AND DISCUSSION

4.3.1. CATECHOL

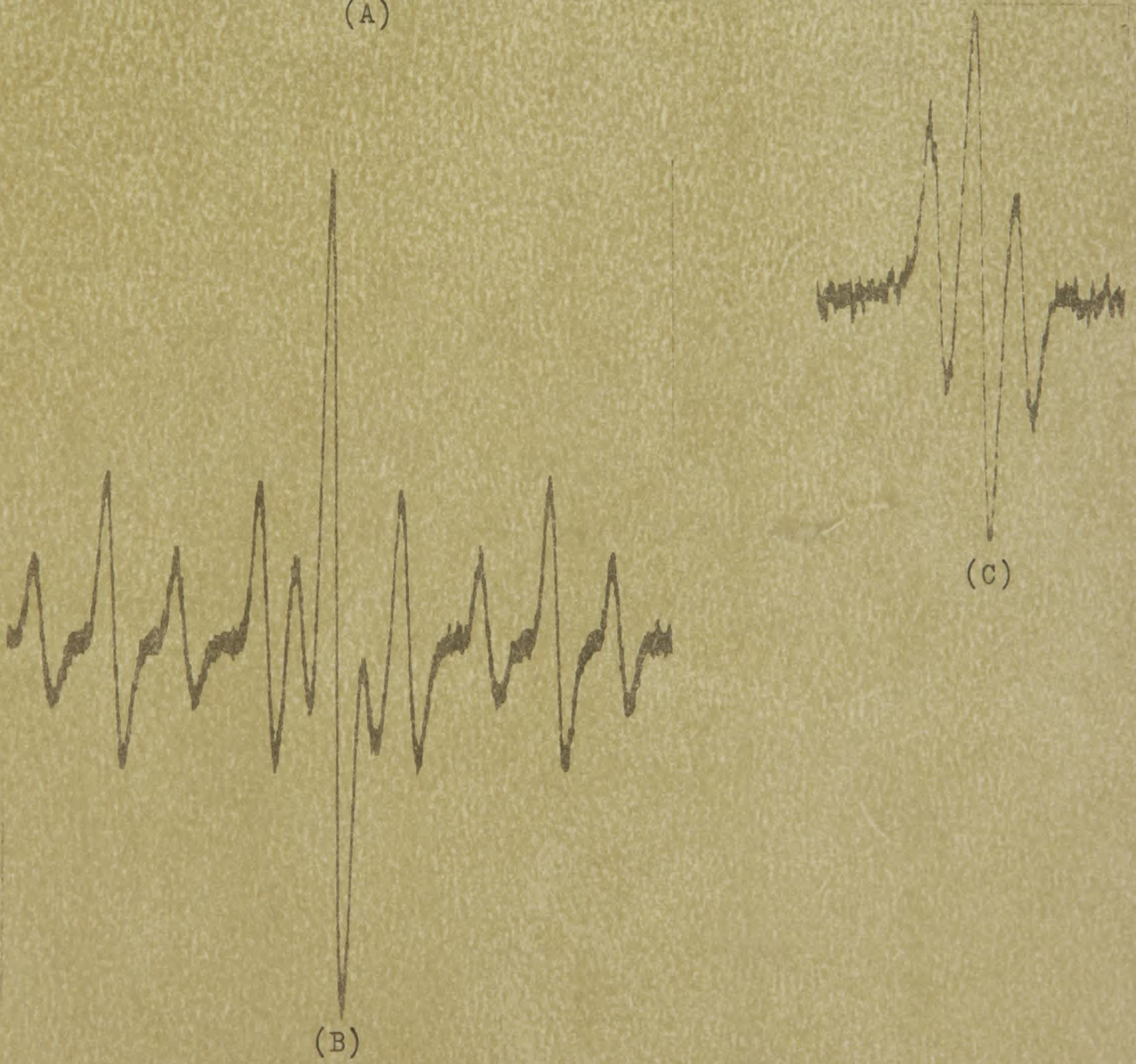
A solution of catechol in alkaline ethanol gives the e.s.r. spectrum of o-benzosemiquinone (V) first reported by Hoskins[60] who obtained coupling constants $a_{H(3,6)} = 1.0$, $a_{H(4,5)} = 4.0$ Oe. The coupling constants obtained in this work are 0.95 and 3.65 Oe, respectively, which are similar to those obtained by Adams and his colleagues[51] in later work. In DMF the coupling constants are 1.16 and 3.55 Oe, respectively (Fig. 1a). Solvent effects of this type have been previously observed by Stone and Maki[61] for p-semiquinones.

While recording the spectrum of o-benzosemiquinone in alkaline DMF the gradual appearance of a triplet superimposed on the centre of the original spectrum (Fig. 1b) was observed. This triplet, which decayed with time much less rapidly than did the triplet of triplets characteristic of o-benzosemiquinone, had a coupling constant of 0.64 Oe. A 1:2:1 triplet e.s.r. spectrum corresponds to a radical having only two equivalent protons which can interact appreciably with the free electron. Of the known oxidation products of catechol it seemed likely that only dibenzo-[1,4]-dioxin-2,3-quinone (IX) could yield a radical (VIII) of this type.



4 Oe

(A)



(C)

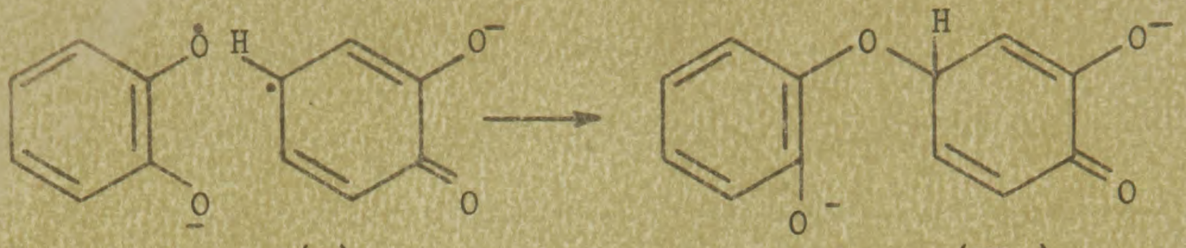
(B)

FIG. 4.1. E.s.r. spectra of (A) o-benzosemiquinone alone, (B) o-benzosemiquinone showing appearance of secondary radical, and (C) semiquinone (VIII).

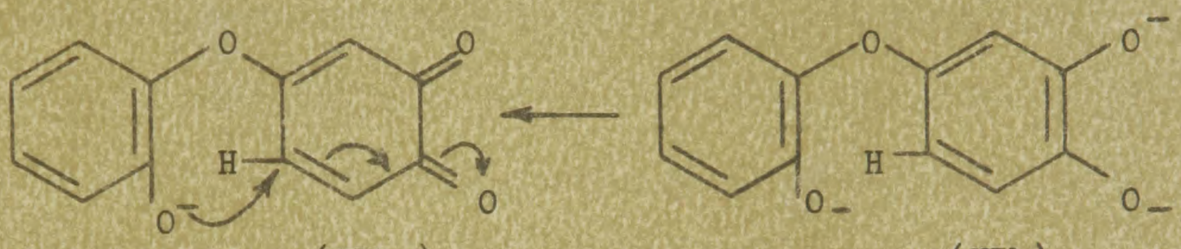
Accordingly the quinone (IX) was synthesised; reduction of this by alkaline dithionite in DMF gave the triplet e.s.r. spectrum of Fig. 1c, with coupling constant 0.65 Oe, identical, within experimental error, with that of the central triplet of Fig. 1b. The course of oxidation of catechol by air may possibly thus be represented by the annexed reaction scheme. Further evidence has been obtained by isolating a small amount of the quinone (IX) on aerial oxidation of an alkaline solution of catechol in DMF.

It is suggested that the dimer (VIa) from the initial radical (V) oxidises very rapidly to the quinone (VIIa), as there is no sign of even the transient appearance of the e.s.r. spectrum of radical (X). Ring closure of the quinone (VIIa) is a typical heterolytic reaction of a phenol with a quinone, but oxidation of (VIIb) must be a one-electron oxidation since the e.s.r. spectrum of (VIII) has been definitely characterised.

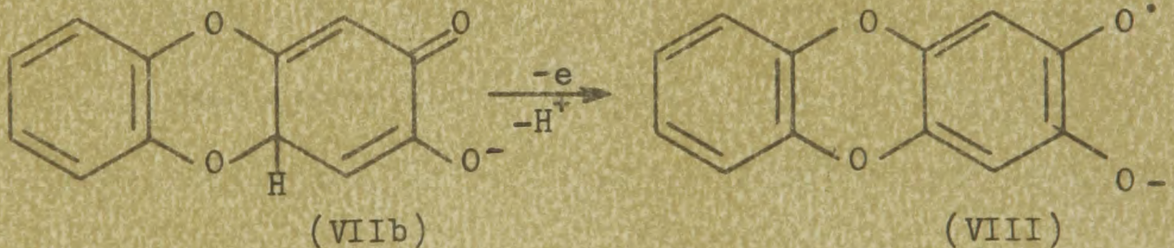
A reaction analogous to the one discussed above is the formation of the diaminophenazine (XI) as an oxidation product of ortho-phenylene-diamine.[62]



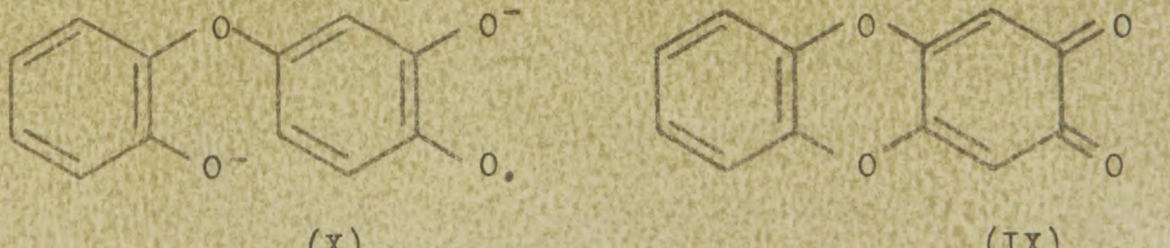
(V) (VIa)



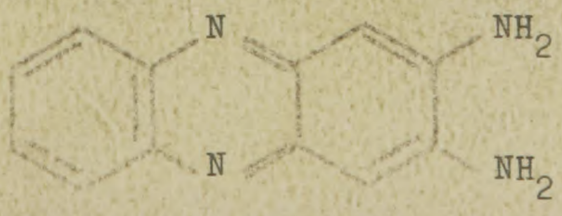
(VIIa) (VIb)



(VIIb) (VIII)



(X) (IX)

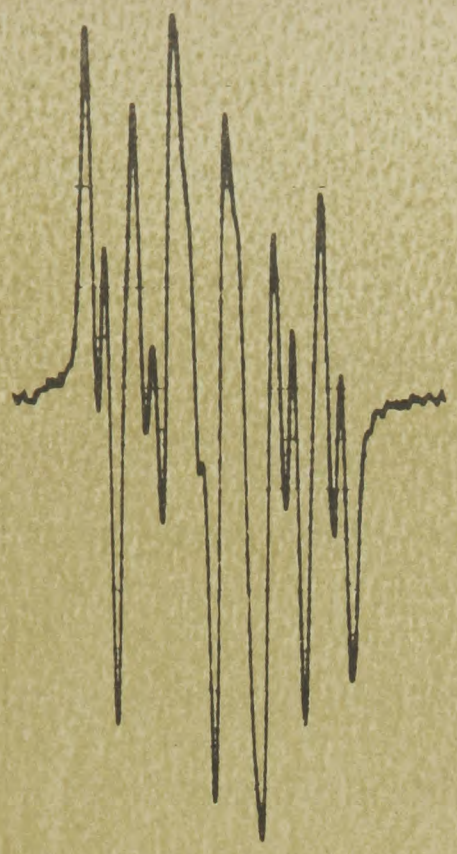


(XI)

4.3.2. 2-o-HYDROXYPHENYL-1,4-BENZOQUINONES

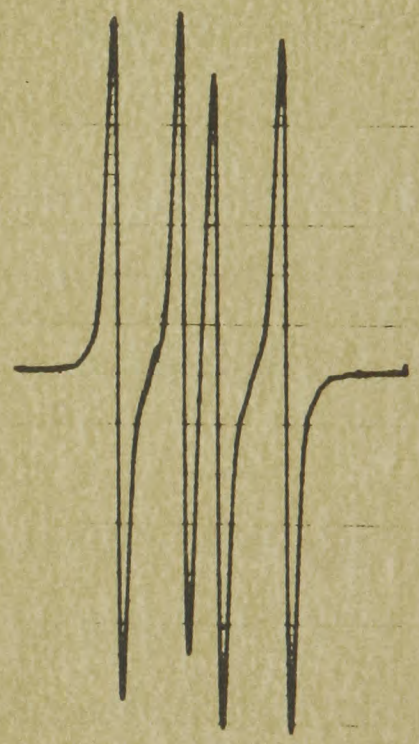
The reduction of 2-o-hydroxyphenyl-1,4-benzoquinones also involves the production of spectra other than those expected from the simple benzosemiquinone. The first evidence for this was the observation of a doublet splitting of 2.64 Oe in a radical formed by dithionite reduction of 2-(2-hydroxy-5-methoxy-4-t-butylphenyl)-5-t-butyl-1,4-benzoquinone (XIV), for the semiquinone of (XIV), which has two non-identical protons on the semiquinone ring, should have an hfs of a doublet of doublets. Moreover, the simple doublet spectrum was observed, with practically undiminished intensity, for samples which had been kept for more than 24 hours. Since this doublet spectrum might correspond to that of a radical formed by reduction ofadibenzofuranquinone, the course of reduction of 2-o-hydroxyphenyl-1,4-benzoquinone (IV) by alkaline dithionite was investigated by e.s.r.

In anhydrous DMF reduction of the quinone (IV) gave a triplet of doublets, corresponding to two equivalent protons with coupling constant 3.20 Oe, and one other proton with coupling constant 1.60 Oe, which is consistent with the predicted e.s.r. spectrum of the semiquinone (XII). However in aqueous DMF, although the initial spectrum (Fig. 2a) was too unsymmetrical for analysis, after about 15 min. the spectrum had changed to a doublet of



7 Oe

(A)



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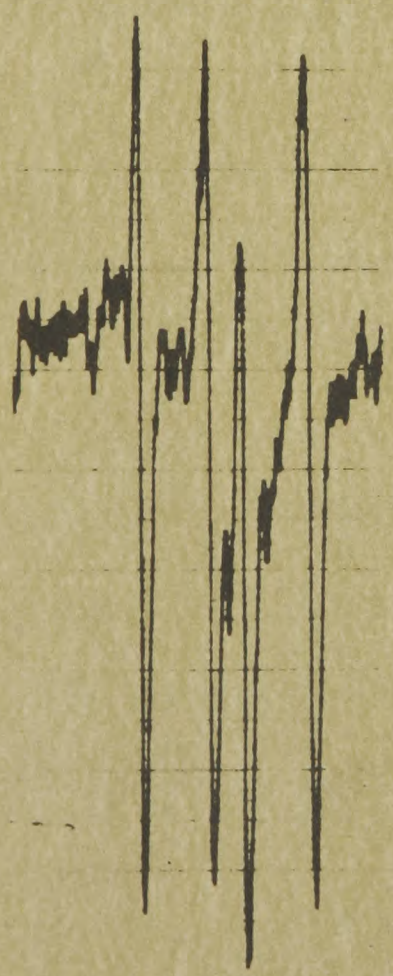


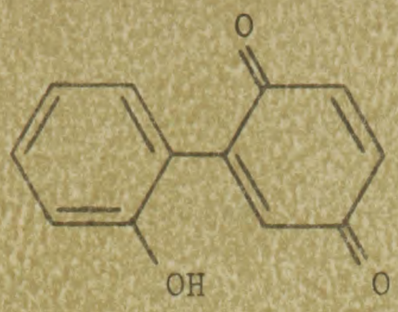
(B)

FIG. 4.2. E.s.r. spectra of (A) initial radical from (IV), (B) radical from (IV) after 15 min., and (C) semiquinone (XIII).

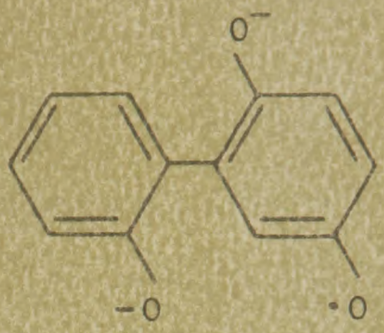
doublets (Fig. 2b) corresponding to two non-equivalent protons with coupling constants of 3.41 amd 2.25 Oe. Such a spectrum might correspond to dibenzofuran-1,4-semiquinone (XIII). Accordingly dibenzofuran-1,4-quinone was prepared; on reduction it gave the e.s.r. spectrum shown in Fig. 2c with identical coupling constants.

Similar secondary radicals were also shown to be formed on oxidation of the corresponding quinols. For example, 2,5,6'-trihydroxy-3'-methoxy-3,5'-di-t-butylbiphenyl (XVI) on aerial oxidation in aqueous DMF gives a doublet spectrum, coupling constant 1.75 Oe, identical with that from the reduction of 8-methyoxy-2,6-di-t-butyldibenzofuran-1,4-quinone (i.e. quinone corresponding to XVII).

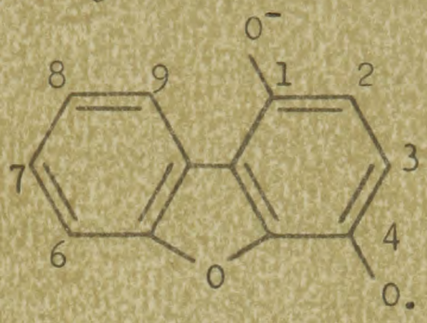
It can be seen that in both the t-butyl-substituted dibenzofuransemiquinones the coupling constant of the proton at the unsubstituted position adjacent to the t-butyl group has been reduced by ca 22% in each case from the corresponding value in the unsubstituted dibenzofuransemiquinone. For example, the 2-proton in radicals (XIII) and (XV) have coupling constants 3.41 and 2.61 Oe (23% decrease) and the 3-proton in radicals (XIII) and (XVII) have coupling constants 2.25 and 1.75 Oe (22% decrease).



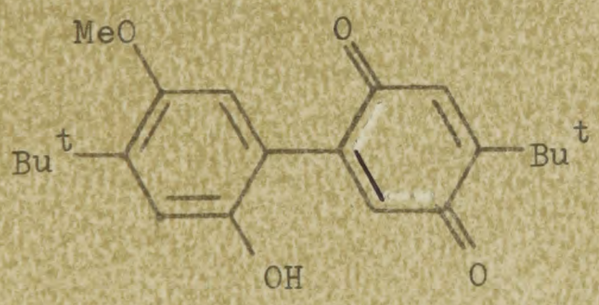
(IV)



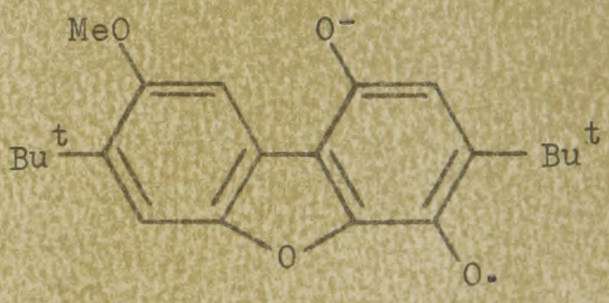
(XII)



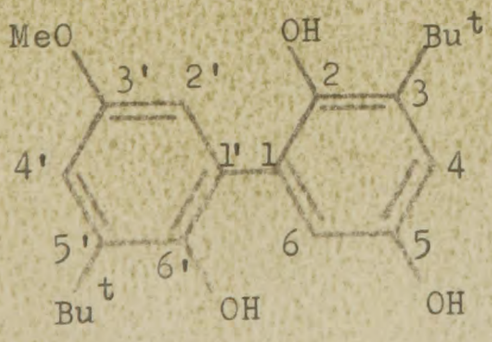
(XIII)



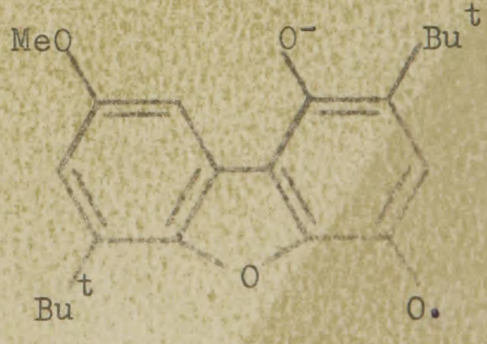
(XIV)



(XV)



(XVI)



(XVII)

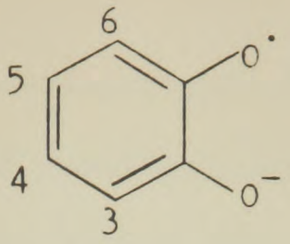
Since the dibenzofuran ring closure seems to require the presence of aqueous alkali a probable mechanism for the formation of compound (XIII) is nucleophilic attack of the hydroxyl group of compound (IV) on the adjacent free ortho-position in the p-quinonoid ring; this would lead heterolytically to the hydroquinone of radical (XIII). This step is similar to the steps (VIIa) → (VIIb) → (VIII) in the catechol oxidation discussed above. The production of a doublet spectrum even in anhydrous DMF from compounds (XIV) and (XVI), and the failure to observe the spectra of the simple semiquinones corresponding to (XII), can perhaps be attributed to the activating effect of the p-methoxy-group on the heterolytic ring closure.

PART 5: OXIDATION OF SUBSTITUTED CATECHOLS

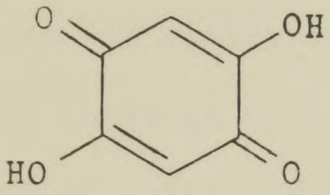
5.1 INTRODUCTION

The formation of ortho-benzosemiquinone (I) as the primary oxidation product of catechol is well known and has been discussed in the previous Part. There has apparently been no comprehensive study of the further oxidation products of substituted catechols, although a few individual catechols have been investigated. Pospíšil[63-7] has found that aerial oxidation of catechol and some 4-alkylcatechols in aqueous alkaline solution leads to the introduction of further hydroxyl groups. For example, catechol[63,64] itself forms 2,5-dihydroxy-1,4-benzoquinone (II). The reaction products from the oxidation of 4-methylcatechol[65,67] differ depending on the solvent and oxidant; alkaline aqueous methanol gives only unstable, probably quinoid, compounds and polymers, alkaline hydrogen peroxide gave (II), and from aerial oxidation in aqueous alkali the unstable 2-hydroxy-5-methyl-1,4-benzoquinone (III; R=Me) was detected. An analogous reaction was obtained[66] with 4-t-octylcatechol when 2-hydroxy-5-t-octyl-1,4-benzoquinone (III; R=t-octyl) was isolated.

Dimeric products have also been obtained from the oxidation of substituted catechols. The production of the dibenzodioxin-o-quinone has been discussed previously and other examples are



(I)



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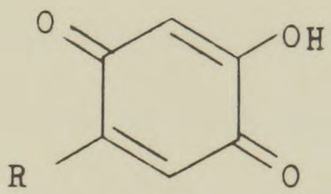

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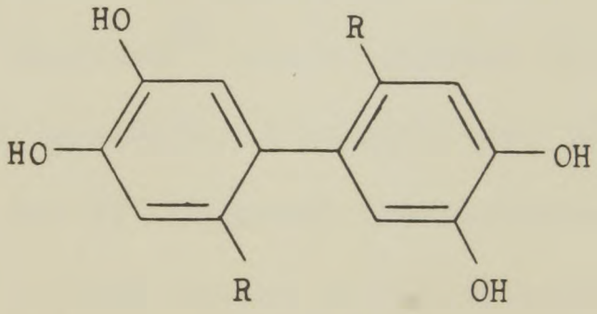

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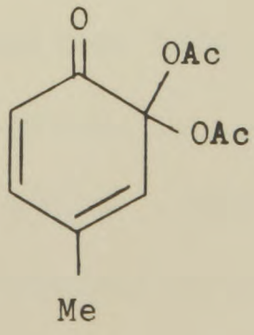


(V)

the production of the tetrahydroxybiphenyl compound, (IV; R=OMe), by alkaline oxidation of 4-methoxycatechol[68], and the tetraacetoxy derivative of (IV; R=Me) formed from 4-methylcatechol by oxidation with ferric acetate.[69]

It can be safely said that in almost all the oxidation reactions investigated no single product is formed exclusively, and in many cases very low yields of the isolated crystalline compounds were obtained, together with varying amounts of dark humic substances. A similar situation was found to occur in the present investigation. In many cases e.s.r. spectra were obtained which were clearly due to the presence of more than one radical; in others the spectrum of the primary radical quickly changed to that of a secondary radical.

The only reported[60] e.s.r. spectra of radicals from catechols are those from 4-phenyl-, 4-t-butyl- and 3-phenyl-catechol. Only in the latter was hfs observed from interaction with all the ring protons. As a large number of substituted p-benzosemiquinones have been investigated by e.s.r. an attempt was made to obtain spectra of the corresponding o-semiquinones. This turned out to be a more difficult proposition than expected. The usual condition for obtaining the p-semiquinone is aerial oxidation of the quinol in alkaline alcoholic solution. The oxidation of catechols under these conditions mostly produced an abundance of mostly very complex

and unanalysable spectra. Two systems were, however, found which gave simple semiquinone spectra from many, but by no means all, of the catechols investigated: (i) aerial oxidation in dimethylformamide/water (9:1) and (ii) oxidation in aqueous alkali by potassium ferricyanide or air, using in some cases the flow apparatus and in others the normal static system.

In addition to the simple o-semiquinone spectra several cases occurred in which the spectra of secondary radicals were observed. The characterisation of these secondary radicals has been achieved in most cases and is described below.

5.2. EXPERIMENTAL

E.s.r. spectra were obtained using both the flow and static methods. As the lifetimes of the semiquinones were somewhat longer than those of the phenoxy radicals better spectra were obtained by using a flow system with a larger space between the mixing point and the flat portion of the sample cell. The catechols (ca 10^{-3}M) in water were oxidised with potassium ferricyanide (10^{-3}M) in aqueous sodium hydroxide (10^{-1}M).

The static method involved shaking the di- or tri-hydroxy compound (5 mg.) with air in a 4 ml. test tube with either (i) dimethylformamide (DMF) (2 ml.) containing ca 10% v/v of water in the presence of a little sodium hydroxide, or (ii) an aqueous solution of sodium hydroxide. In many cases when the catechols were oxidised in this way the resulting solution underwent several consecutive colour changes as the shaking was continued. Trial and error was used to determine which colour corresponded to the required radical; if a particular colour disappeared too rapidly it was found that the pouring of the solution into a further 2 ml. of DMF helped to stabilize it.

The production of secondary radicals occurred in some cases (i.e. 3,4-dihydroxybenzaldehyde) to the complete exclusion of the

primary radicals; in others (i.e. 4-i-propylcatechol) the spectrum of the primary radical decayed into that of the secondary radical whilst the solution was in the spectrometer; and in others (i.e. 4-methylcatechol) considerable shaking was necessary to produce a secondary radical solution.

Materials used

All compounds except those described below were commercially available products or had been previously prepared in this laboratory. All were recrystallised before use. It was found that 1,2,4-trihydroxybenzene and 1,2,4-triacetoxybenzene on oxidation under the same conditions both gave exactly the same spectrum. Consequently when other trihydroxy compounds were required the synthesis was carried out only as far as the triacetoxy stage.

3,4-Dihydroxyacetophenone was prepared from catechol by a Friedel-Crafts reaction with acetyl chloride and aluminium chloride by the method of Howton[70] using ten times his quantities. The product was recrystallised from benzene; m.p. 118° (lit. 119°), yield 5 g. (52%).

4,5-Dibromocatechol was prepared by bromination of catechol (11 g.) in acetic acid according to Kohn.[71] The product was recrystallised from benzene; m.p. 119° (lit. 119-121°), yield 12 g. (45%).

1,2,4-Triacetoxybenzene was prepared from p-benzoquinone by a Thiele acetylation with acetic anhydride and sulphuric acid by the method of Vliet[72] using $\frac{1}{20}$ of his quantities. The product was recrystallised from ethanol; m.p. 96° (lit. 96°), yield 6 g. (85%).

1,2,4-Trihydroxybenzene was prepared by deacetylating the previous compound (12 g.) as described by Thiele and Winter.[73] The product was recrystallised from ether; m.p. 140° (lit. 140.5°), yield 9.7 g. (90%).

1,2,4-Triacetoxy-4-methylbenzene was prepared from p-toluquinone by a Thiele reaction as described by Woodward[74], using $\frac{1}{20}$ quantities. The product was recrystallised from ethanol; m.p. 109° (lit. 110-3°), yield 10 g. (40%).

2,3,4-Trihydroxybenzaldehyde was prepared from pyrogallol by the modified Gatterman reaction of Adams and Levine[75] using zinc cyanide and hydrogen chloride. The product was recrystallised from water; m.p. 159° (lit. 161-2°), yield 9.7 g. (41%).

2,3,4-Trihydroxybenzoic acid was prepared by the reaction of pyrogallol and potassium bicarbonate as described by Weygand[76], using $\frac{1}{10}$ quantities. The product was recrystallised from water; m.p. 206° (lit. 207-8°), yield 7.5 g. (56%).

1,2,3-Triacetoxy-5-methylbenzene. p-Cresol was oxidised with lead tetraacetate in glacial acetic acid, according to the method of Wessily[77], to yield 6.5 g. (29%) of 2,2-diacetoxy-4-methylcyclohexadiene-1-one (V), m.p. 129° (lit. 128-34°). This latter was rearranged under the influence of acetic anhydride and sulphuric acid as described by Goodwin and Witkop[78] and yielded the acetylated methylpyrogallol. The product was recrystallised from aqueous methanol; m.p. 100-1° (lit. 101.5-2.5°), yield 1.4 g. (89%).

5.3. RESULTS AND DISCUSSION

The initial object of the work discussed in the present Part was to obtain spectra of the simple ortho-semiquinones by oxidation of substituted catechols. Aerial oxidation in alkaline ethanol mainly produced radicals giving very complex e.s.r. spectra, which, by their asymmetry and the fact that some of the lines decayed at different rates from others, indicated that two or more radicals were present. Radicals which might be present are the simple semiquinone, secondary radicals such as those discussed below, and radicals produced by ethoxy substitution, evidence for the latter reaction having been obtained for some p-semiquinones (see Part 4).

It was found that aerial oxidation of several catechols in DMF in the presence of a little aqueous alkali produced radicals whose e.s.r. spectra could readily be interpreted on the basis of the formation of the o-semiquinone. Similarly, oxidation in aqueous alkaline ferricyanide, or aqueous alkali alone, produced spectra which very probably correspond to the semiquinone. In some cases secondary radicals were formed using this method and it was necessary to use the flow apparatus to obtain reasonable spectra.

Secondary radicasl were formed from several of the catechols

investigated and the emphasis of the work tended to shift from the production and e.s.r. spectra of the simple o-semiquinones to the investigation of the nature of the secondary radicals formed.

The catechols investigated include a representative (and readily available) selection of 3-, 4- and di-substituted compounds. The results of the oxidation of these catechols by the methods mentioned above may be conveniently summed-up as shown in Table 1. Entries given as small letters indicate that spectra were obtained but that it has not been possible to analyse them. These gaps are rather numerous and in many cases it is difficult to offer explanations for the absence of the expected spectra. The results are discussed more fully below from two aspects: one being the production of the simple semiquinones, the other the production and characterisation of the secondary radicals.

5.3.1. THE ortho-SEMIQUINONES.

The coupling constants obtained from the spectra of the simple o-semiquinones both in DMF/water and water alone are given in Table 2. The spectra of the radicals in the former solvent, with one exception, showed hfs due to all the ring or α-alkyl protons. An example of a spectrum obtained in DMF/water is

TABLE 5.1.

Summary of the e.s.r. spectra obtained from oxidation of catechols

Catechol	Method of oxidation		
	Air, NaOH, DMF/H_2O, static	$Fe(CN)_6^{3-}$ or air, H_2O, NaOH flow (F) or static (S)	Air, NaOH H_2O static
4-Me	SQ	SQ(F)	THB
4-CH_2CO_2H	SQ	SQ(F)	s
4-Pr^i	s	SQ(F)	THB
4-Bu^t	s	s	s
4-CHO	s	s	Py
4-COEt	Py	s	Py
4-COMe	Py	s	Py
4-CO_2H	SQ	SQ(F,S)	SQ
3-Me	SQ	SQ(F)	s
3-Pr^i	SQ	SQ(F)	s
3,6-Pr^i_2	SQ	SQ(F)	s
3-CO_2H	s	SQ(F,S)	s
4-Me-6-Bu^t	SQ	SQ(S)	s
4,6-$(SO_3Na)_2$	SQ	SQ(S)	Py
4-OMe-6-Bu^t	SQ	SQ(F)	s
4-OMe-5-Bu^t	s	SQ(F)	s
4,5-Br_2	SQ	SQ(S)	Py

SQ simple ortho-semiquinone

THB 1,2,4-trihydroxybenzene semiquinone

Py pyrogallol semiquinone

s spectrum obtained but unanalysable

TABLE 5.2.

Coupling constants of ortho-semiquinones

Catechol	Coupling constants (Oe)[a,b]							
	DMF/H_2O				H_2O			
	a_3	a_6	a_4	a_5	a_3	a_6	a_4	a_5
4-Me	0.7	1.4	4.4	3.7	(0.25)[c]	1.0	5.1	4.0
4-CH_2CO_2H	0.6	1.1_5	3.0	4.1	(0.25)[c]	0.9	3.0	3.9
4-CO_2H	0.9	1.4	-	3.3	0.7	1.3	-	3.3
3-Me	0.8	0.8	2.9	3.7	0.7	?	3.0	4.2_5
3-Pr^i	0.7	0.7	2.7	3.9_5	0.7	?	2.9_5	4.5
(3-Ph	-	0.7[d]	2.8[d]	3.5[d])				
3,6-Pr^i_2	0.45	0.45	3.2	3.2	?	?	3.4	3.4
3-Bu^t-5-Me	-	?	3.0	4.3_5	-	0.3	2.6_5	5.4
3-Bu^t-5-OMe	-	0.6	3.2	1.1[e]	-	0.8	3.1	1.1[e]
3,5-$(SO_3Na)_2$	-	1.8	3.9	-	-	1.9_5	3.6	-
4,5-Br_2	1.4	1.4	-	-	0.5	0.5	-	-

[a] coupling constants not definitely assigned between positions 3 and 6 for 4-substitued radicals, and between positions 4 and 5 for 3-substituted radicals.

[b] a_i represents either ring or α-proton coupling constants.

[c] see text

[d] taken from ref. 60 for comparison.

[e] methoxy proton splitting.

shown in Fig. 1. for 4-methyl-o-semiquinone. In the 4-substituted radicals the 3- and 6- positions are non-equivalent, similarly the 4- and 5-positions differ in the 3-substituted radicals: a definite assignment between these positions has not been made.

Using water alone as the solvent it was found that in several cases the radicals gave spectra showing hfs from one less proton than would be expected for the o-semiquinone. For example, Fig. 2 shows the spectrum obtained by oxidation of 4-methylcatechol in the flow apparatus. Comparing this spectrum with that of Fig. 1 it can be seen that each line of Fig. 2 should be split into a further small doublet. Repeated attempts were made to increase the resolution of the spectra by decreasing the concentration of radicals, decreasing the microwave power etc., but by using the flow method no indication of the extra doublet could be found.

That the spectra obtained were in fact probably those of the simple semiquinone was shown indirectly by two pieces of evidence. The spectrum obtained by aerial oxidation of 4-methylcatechol on immediate observation in the spectrometer by the normal static method produced a spectrum which was clearly a superposition of both the primary and secondary radical spectra. However the general form of the spectrum shown in Fig. 2 was discernable, with, however, each line split into a small doublet of 0.25 Oe. Further

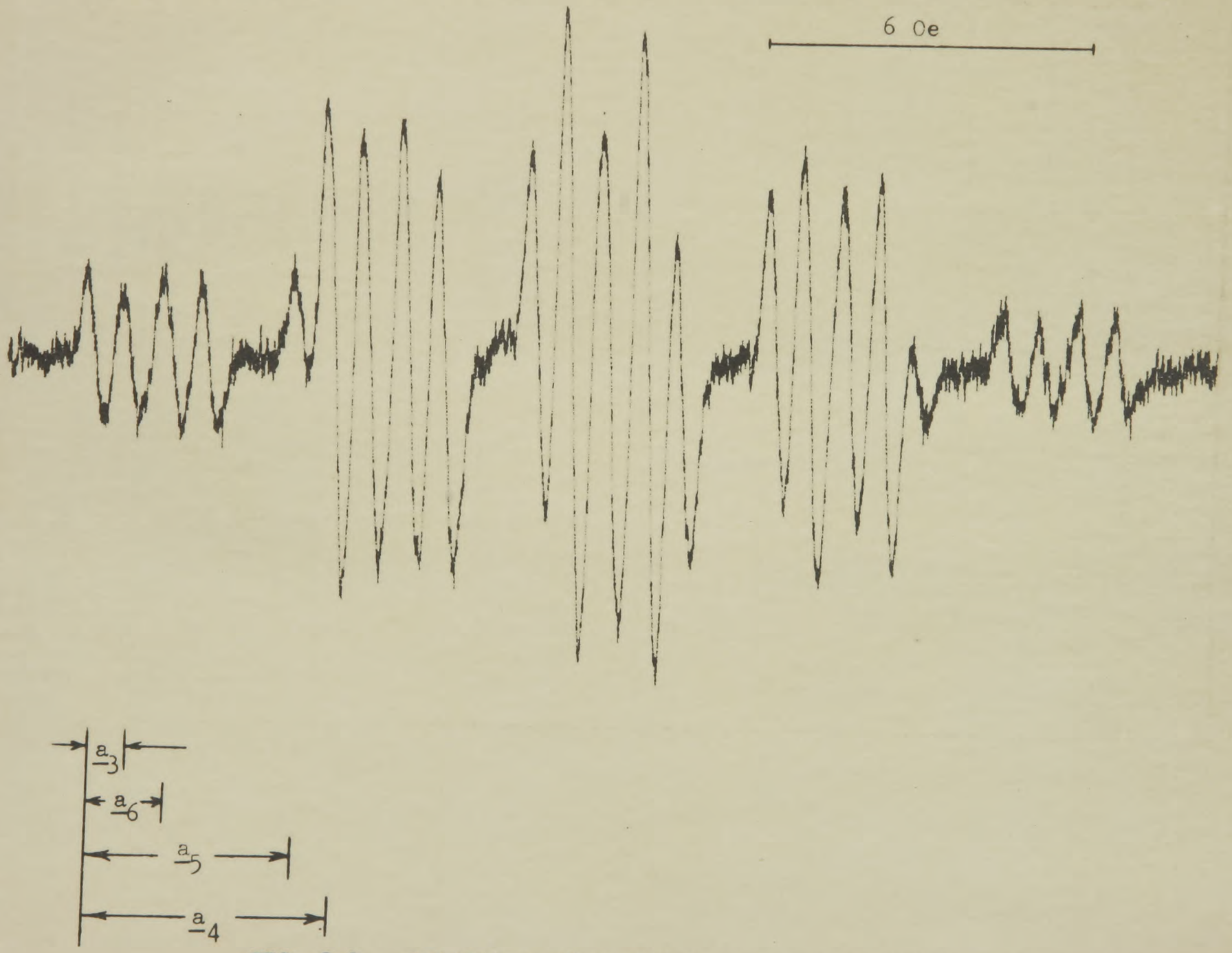


FIG. 5.1. Oxidation of 4-methyl catechol in DMF/water

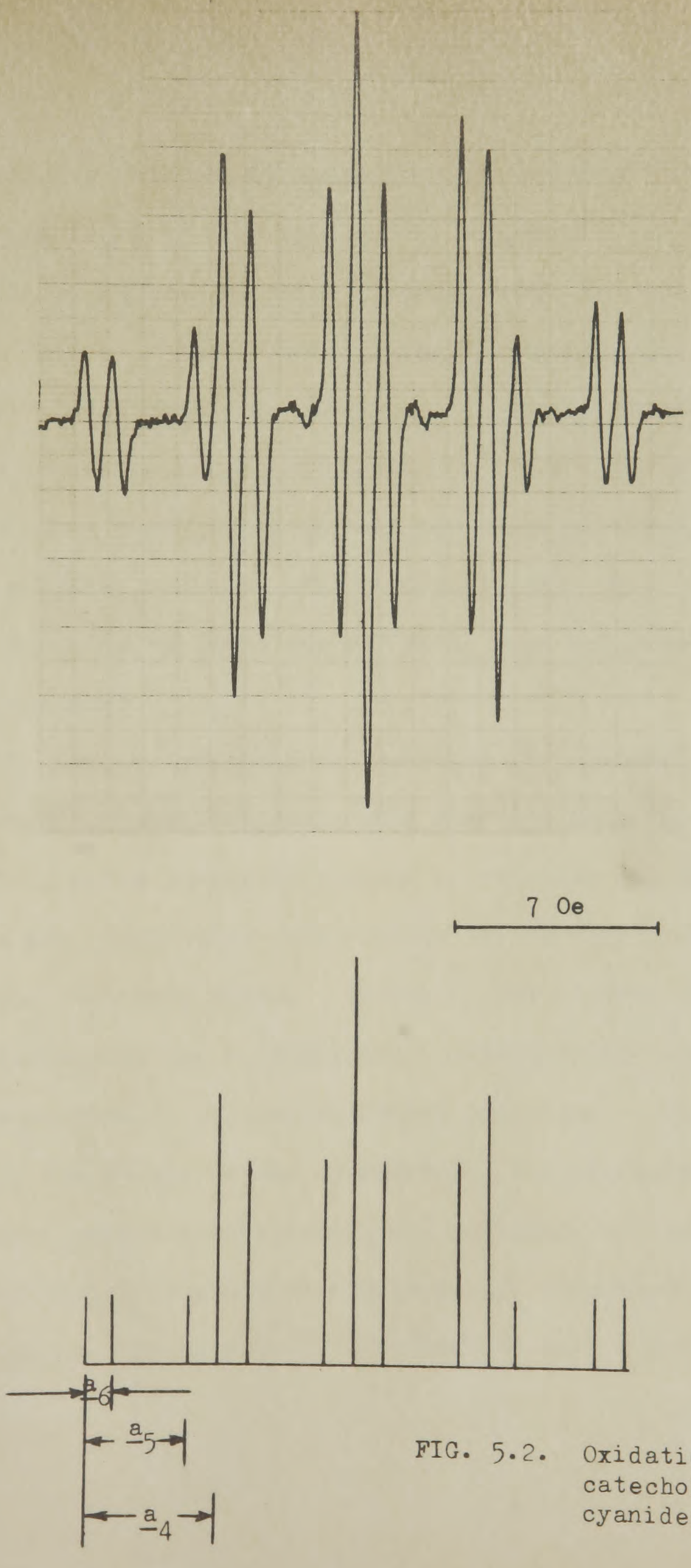


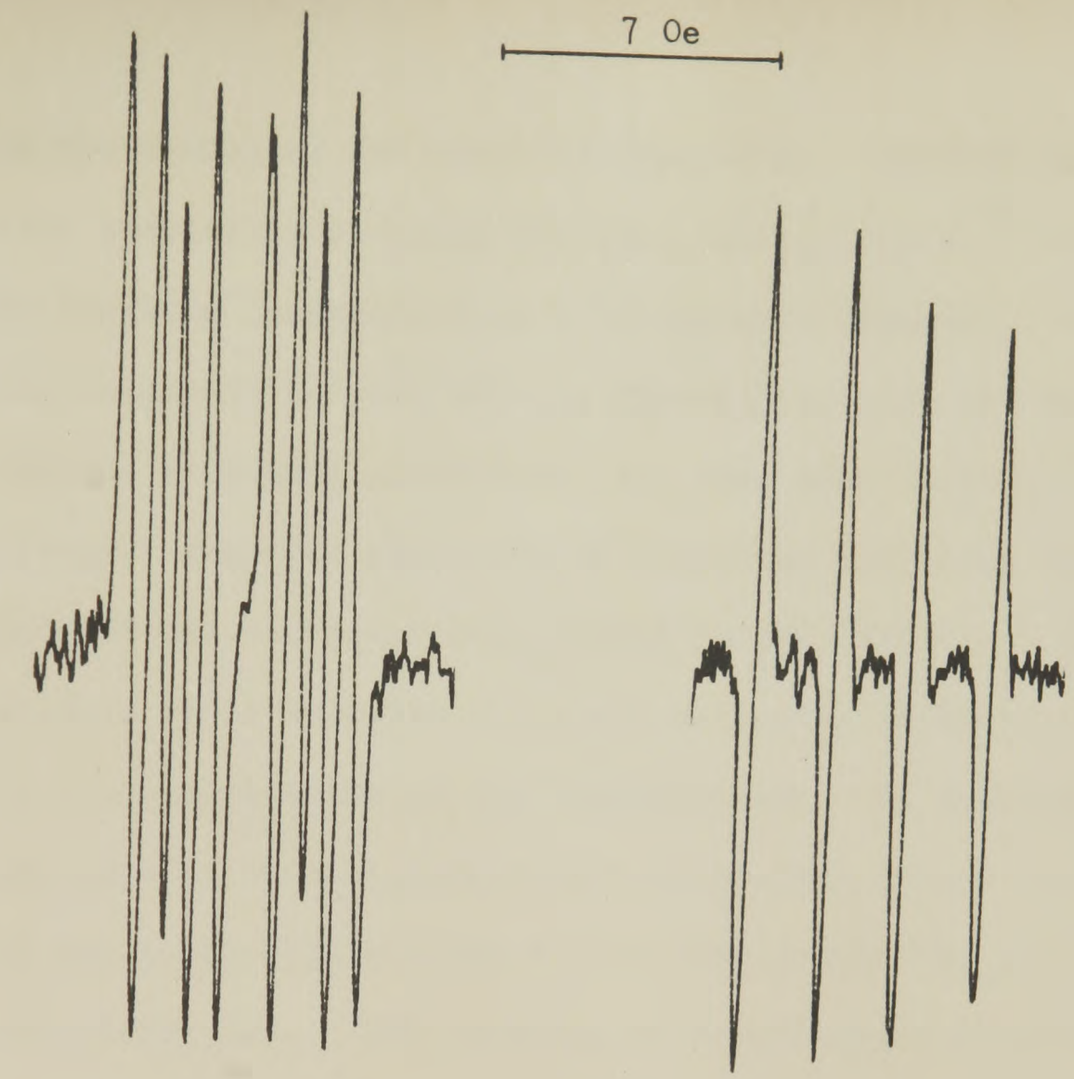
FIG. 5.2. Oxidation of 4-methylcatechol with ferricyanide in water

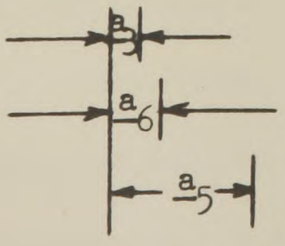
evidence was obtained by oxidising 4-methylcatechol under the same conditions as used in the flow experiment but allowing the reaction to proceed for some 10 min. before the e.s.r. spectrum was recorded. This procedure gave the spectrum of the secondary radical alone, which, as shown below, has been characterised as the semiquinone of 1,2,4-trihydroxy-5-methylbenzene. As it is difficult to formulate a radical intermediate between the latter and 4-methyl-1,2-semiquinone it seems likely that the radical observed using the flow method was in fact the simple primary o-semiquinone.

The spectra obtained by oxidation of 3,4-dihydroxybenzoic acid and catechol-3,5-disulphonic acid disodium salt, in which hfs due to the expected number of protons is obtained are shown in Fig. 3.

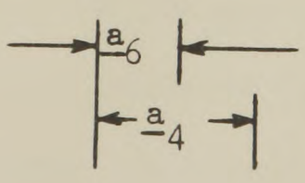
A few qualitative observations may be made from the table of coupling constants above. First, it can be seen that the presence of substituents has a considerable effect on the coupling constants of the protons at the unsubstituted positions. However, since most of the molecules are unsymmetric, and ambiguous coupling constants have not been definitely assigned, a clear pattern of the changes in coupling constants is not discernable.

Second, the solvent is also seen to have a considerable effect





(A)



(B)

FIG. 5.3. Oxidation of (A) 3,4-dihydroxybenzoic acid, and (B) catechol-3,5-disulphonic acid in water

on the values of the coupling constants. Solvent effects have been previously observed for the p-semiquinones,[61] where variations in coupling constants from 1 to 44% were observed. Fraenkel[79] has discussed solvent effects theoretically on the basis that changes in proton splittings (and thus spin densities) result directly from the formation of localised complexes between the solvent and the polar substituent in the radical. A solvent such as water probably interacts primarily by hydrogen bonding to the oxygen atoms of the semiquinones. It appears that in the case of the o-semiquinones the solvent causes little change in the total spin density at the ring positions, but only a redistribution. For example, in 4-methyl-o-semiquinone the total spin density at positions 3-6 has the same value of 0.41 in both solvents; the corresponding value for 3-methyl-o-semiquinone is 0.34. In general it would appear that the values of the coupling constants at positions 4 and 5 are increased and those at positions 3 and 6 decreased when the solvent is changed from DMF to water.

The third and last observation concerns those catechols which gave no simple semiquinone spectra. Although 4-methyl-, 3-i-propyl- and 3,6-di-i-propyl-catechol all gave simple o-semiquinone spectra, no reasonable spectra from 4-i-propyl- or 4-t-butyl-

catechol could be obtained. The former compound appeared to give only the spectrum of a secondary radical, the latter only a broad doublet containing much poorly resolved fine structure (similar to the spectrum published by Hoskins[60]). The catechols with substituents -COR (R=H, Alkyl) in the 4-position on oxidation in the flow apparatus gave no clearly analysable spectra, and on oxidation in DMF gave only what appeared to be secondary radicals.

5.3.2. THE SECONDARY RADICALS

(a) 4-Alkylcatechols. 4-Methylcatechol, on shaking with aqueous alkali for several minutes gave an e.s.r. spectrum (Fig. 4A) different from that produced by rapid oxidation (Fig. 2). The former spectrum clearly corresponds to a large quartet (5.1 Oe) of small triplets (0.65 Oe), which indicates interaction with three equivalent protons and a smaller interaction with two other equivalent protons. As the original catechol contains a methyl group it is reasonable to suppose that this group gives rise to the large quartet splitting. As, also, the catechol contains three ring protons and since the spectrum of the secondary radical indicates interaction with only two, it seems likely that one ring proton has been lost in the production of the secondary radical. Further, since the reaction is carried out in aqueous



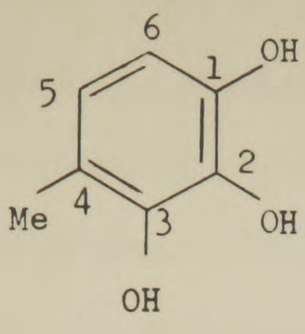
FIG. 5.4.(A)
Secondary radical from oxidation of 4-methylcatechol in water

FIG. 5.4.(B)
Semiquinone radical from 5-methyl-pyrogallol

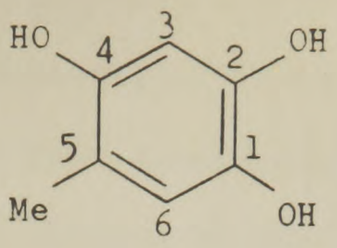
alkaline solution, attack by the hydroxyl anion on the ring, to lead ultimately to a radical derived from a trihydroxybenzene system, is a possibility. The three possible trihydroxybenzenes are shown (VI) - (VIII).

The e.s.r. spectrum of the unsubstituted pyrogallol semiquinone has been recorded[51] and coupling constants of 5.41 and 0.96 Oe were obtained; interaction with the two ring protons adjacent to the hydroxy groups giving rise to the smaller coupling constant. Taking account of these values, 4-methylpyrogallol (VI) may be eliminated as this would give a radical whose e.s.r. spectrum would be expected to consist of a large doublet of *ca.* 5.5 Oe, further split into a small quintet or small quartet of doublets all of *ca.* 1 Oe. Of the two remaining possibilities, *i.e.* the radicals from 1,2,4-trihydroxy-5-methylbenzene (VII) or 5-methylpyrogallol (VIII), the latter seems the most likely on symmetry grounds. It contains a methyl group which would be expected to give a large quartet splitting, and two equivalent protons giving a small triplet. Both compounds (VII) and (VIII) were synthesised, oxidised in aqueous alkaline solution and the e.s.r. spectra of the resulting radicals recorded.

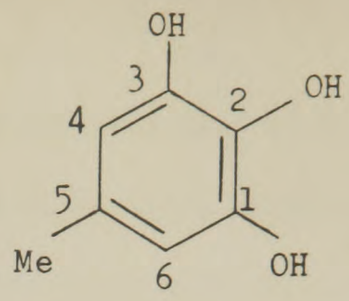
It was found that the spectrum of the radical from 1,2,4-



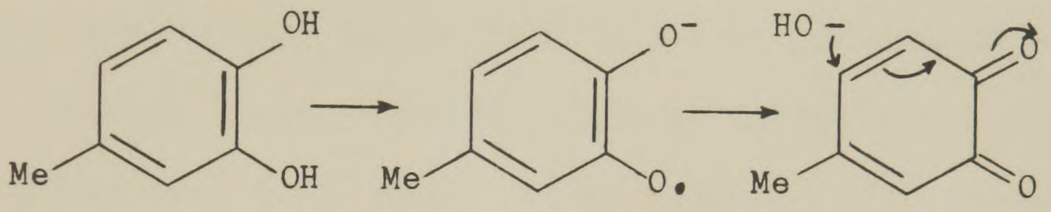
(VI)



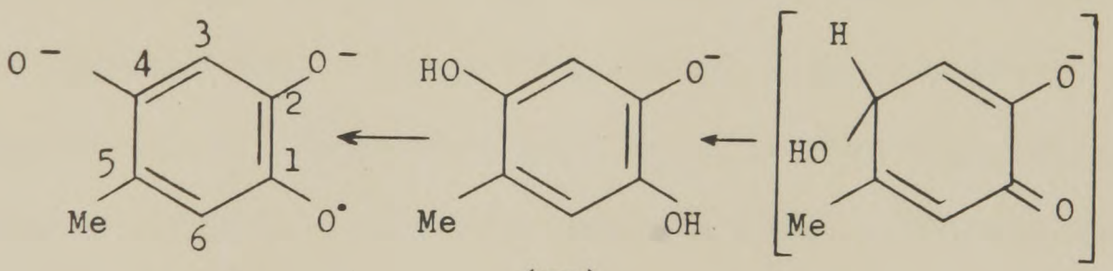
(VII)



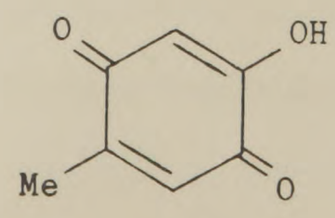
(VIII)



(IX) (X)



(XII) (XI)



(III; R=Me)

trihydroxy-5-methylbenzene (VII) corresponded exactly to that of the secondary radical from 4-methylcatechol, both spectra being superimposable, and a mixture of the two compounds on oxidation giving the same single spectrum. The spectrum of the radical from 5-methylpyrogallol, shown in Fig. 4B, gave the expected spectrum, (quartet 6.2 Oe and triplet 0.8 Oe), the quartet splitting being clearly much larger than that from the radical from (VIII). As mentioned above, Pospíšil has also detected a small quantity of the quinone (III, R=Me) corresponding to 1,2,4-trihydroxy-5-methylbenzene (VII) on oxidation of 4-methylcatechol in aqueous alkaline solution.

A reaction scheme for the formation of the semiquinone (XII) may be postulated involving nucleophilic attack on the o-quinone by hydroxyl ion. The methylcatechol (IX) is oxidised in the normal way to the quinone (X), which is then attacked by hydroxyl ions to form the trihydroxy compound (XI). The further oxidation (XI) → (XII) → (III, R=Me) is analogous to the oxidation of the catechol *i.e.* (IX) → (X), but it is interesting that the oxidation yields a para-quinone in preference to an ortho-quinone.

The secondary radical from the oxidation of 4-i-propylcatechol in water appears to be also derived from the corresponding 1,2,4-trihydroxybenzene. The e.s.r. spectrum is a doublet of triplets

(Fig. 5). A different, but unanalysable spectrum, was obtained immediately after mixing but this very rapidly changed to that of Fig. 5. By analogy with the result above the doublet splitting would correspond to the α-proton of the i-propyl group, and the triplet to the again fortuitous equivalence of the ring protons at positions 3 and 6.

Both results are consistent with the semiquinone from the unsubstituted 1,2,4-trihydroxybenzene, which was synthesised and oxidised in a similar way. The spectrum of this radical (Fig. 6) shows that the splitting due to the proton at positions 3 and 6 are no longer equivalent. The coupling constants quoted above, together with those obtained by oxidation of the two synthesised trihydroxy compounds in DMF are given in Table 3 below. It will be noticed that in the latter solvent the protons at positions 3 and 6 in the 5-methyl compound are now also no longer equivalent.

It would be expected, from the evidence of Pospíšil who has obtained 2-hydroxy-5-t-octyl-1,4-benzoquinone (III; R=t-octyl) from the oxidation of 4-t-octylcatechol, that 4-t-butylcatechol should give a secondary radical analogous to those obtained from the 4-methyl- and 4-i-propyl-catechols described above. In fact no evidence could be found in the e.s.r. spectrum for a radical of this type.

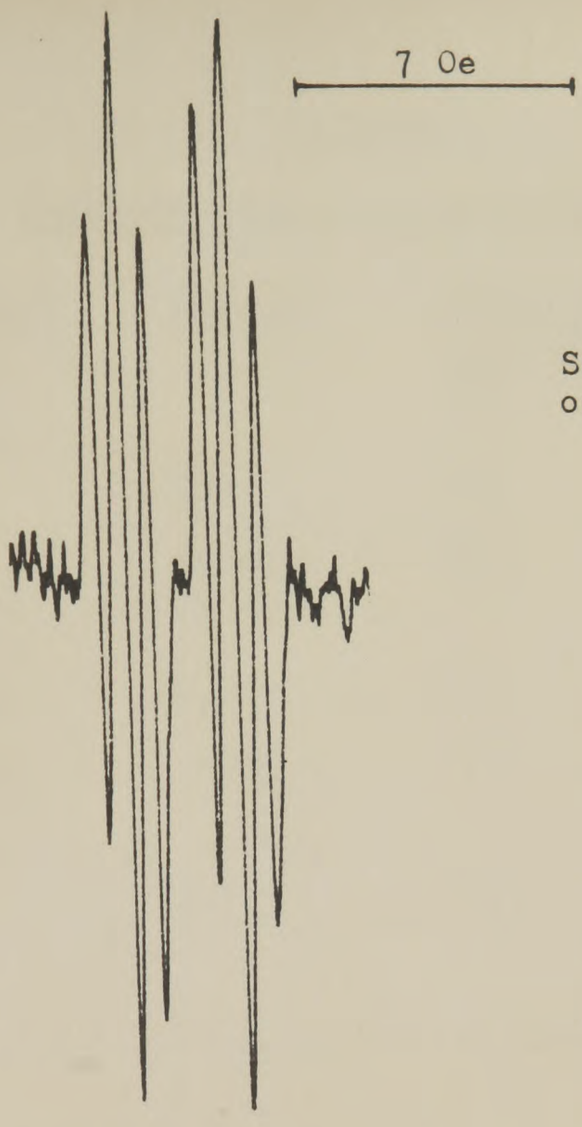


FIG. 5.5.

Secondary radical from oxidation of 4-i-propylcatechol in water

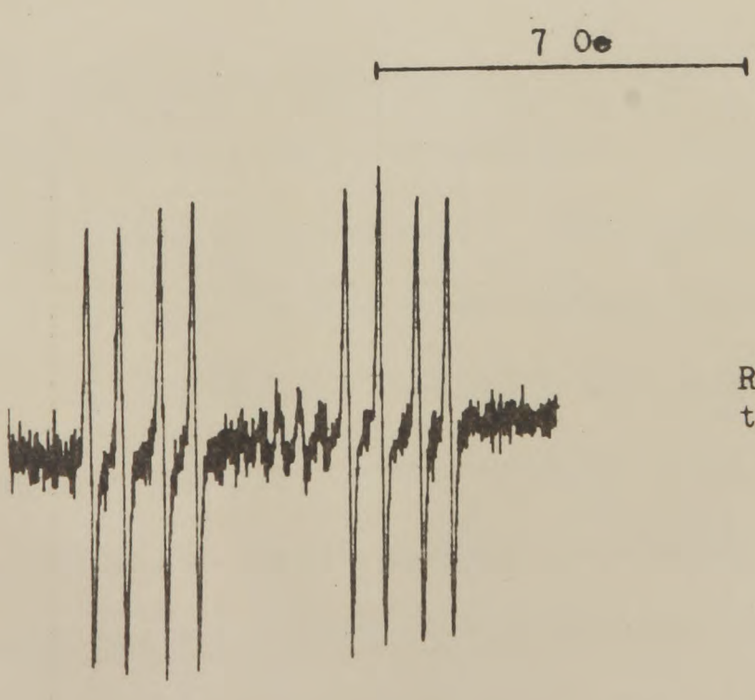


FIG. 5.6.

Radical from oxidation of 1,2,4-trihydroxybenzene

TABLE 5.3.

Radicals from 1,2,4-trihydroxybenzenes

Substituent	Solvent	Coupling constants (Oe)*		
		a_4	a_3	a_6
None	H_2O	4.8	1.3	0.6
	DMF/H_2O	~~5.4~~ 3.7	~~0.8~~ 1.7	~~0.5~~ 0.7
4-Me	H_2O	5.1	0.65	0.65
	DMF/H_2O	5.2	0.8	0.5
4-Pr^i	H_2O	2.8	0.7	0.7

* in the case of non-equivalent values for a_3 and a_6 a definite assignment has not been made.

(b) 4-Carbonyl-substituted catechols. The oxidation in aqueous solution of 3,4-dihydroxybenzoic acid gives a radical which is clearly the o-semiquinone. This radical decays slowly and is in fact the most stable o-semiquinone investigated in this work. No evidence for the formation of a secondary radical could be found. However, on oxidation in aqueous solution, 3,4-dihydroxybenzaldehyde, -acetophenone and -propiophenone give, first, spectra which are not clearly analysable for the simple o-semiquinone,

and then in each case a spectrum consisting of a doublet of doublets (Fig. 7). The average values of the coupling constants are approximately 4.6 and 0.8 Oe. Now if the secondary radicals are of the same form as those discussed for the 4-alkylcatechols, 3,4-dihydroxybenzaldehyde (XIII), for example, should give the semiquinone (XIV) derived from 5-aldehydo-1,2,4-trihydroxybenzene. So, unless there has been a drastic rearrangement of spin density, the coupling constants of 4.6 and 0.8 Oe. cannot correspond to the protons at positions 3 and 6 of radical (XIV), since it has been shown that these protons both give coupling constants of the order of 0.8 Oe in the alkyl-substituted radicals.

If it is assumed that hydroxyl attack again occurs, there are two possibilities for the structure of the secondary radical, i.e. the radical derived from the two pyrogallols (XV) and (XVI). That it cannot be the radical derived from (XV) can be clearly seen on symmetry grounds: the two ring protons would be equivalent and have a coupling constant of ca. 1 Oe. Thus the radical from 2,3,4-trihydroxybenzaldehyde (XVI) is most likely, and consequently this latter compound was synthesised and gave on oxidation an e.s.r. spectrum exactly similar to that of the secondary radical obtained. Similar results, which are summarised in Table 4, were obtained with the two ketones.

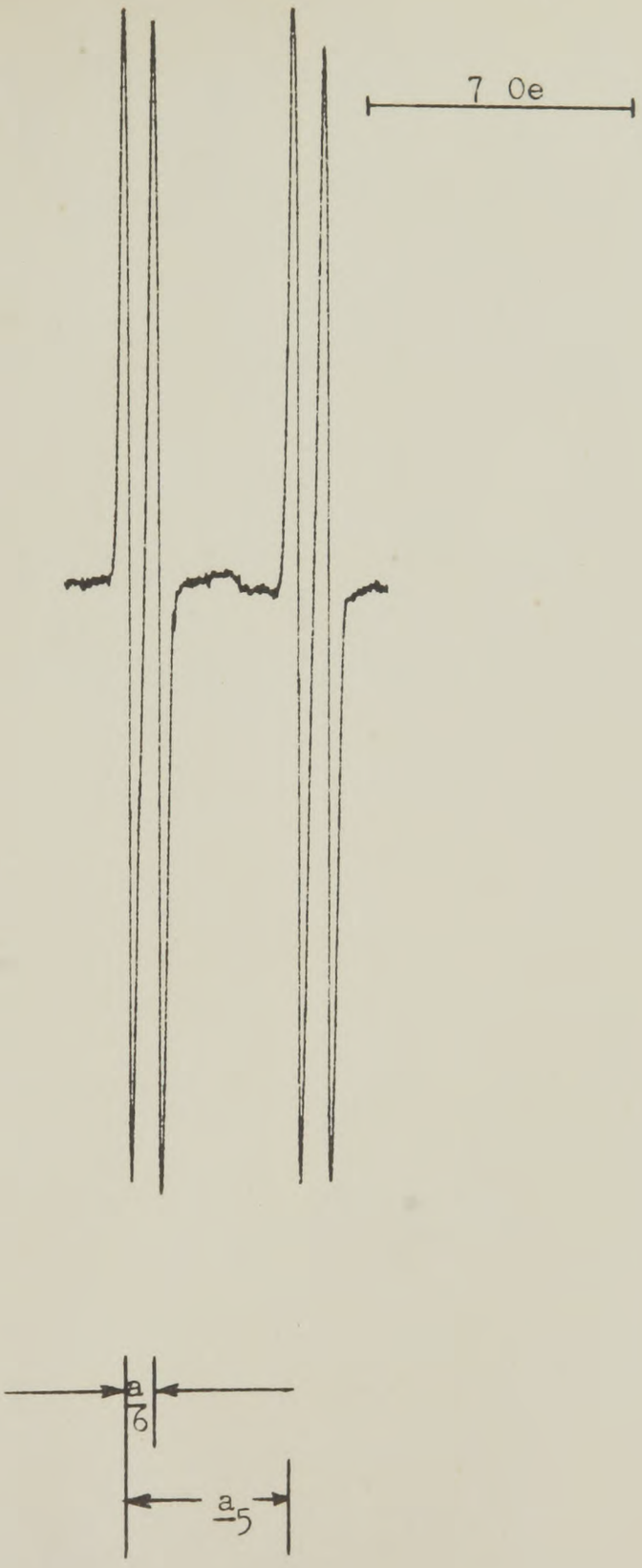
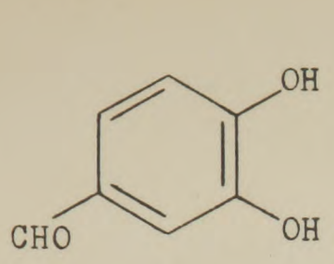
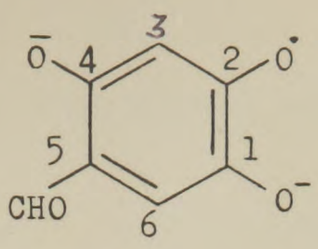


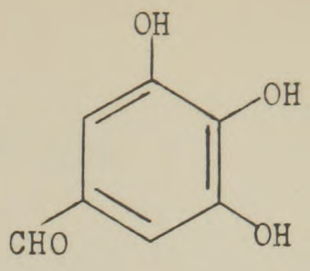
FIG. 5.7. Secondary radical from oxidation of 3,4-dihydroxybenzaldehyde in water



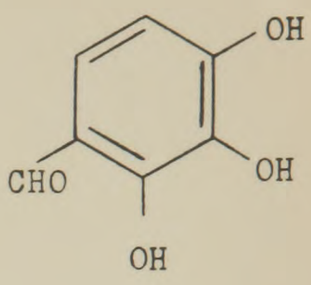
(XIII)



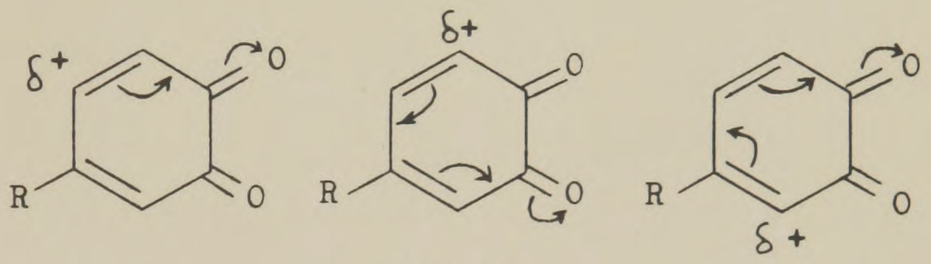
(XIV)



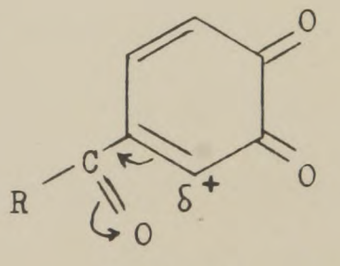
(XV)



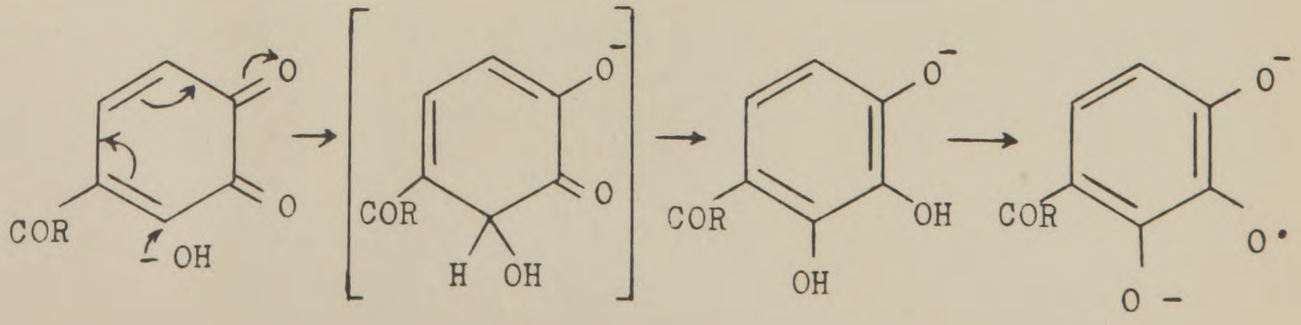
(XVI)



(XVII)



(XVIII)



(XIX)

TABLE 5.4.

Radicals from pyrogallols

Pyrogallol	Coupling constants (Oe)	
	a_5	a_6
unsubstituted	5.4	0.96
4-CHO	4.4	0.80
4-COMe	4.8	0.80
4-COEt	4.8	0.80
4-CO_2H	4.8	0.75
4,6-$(SO_3Na)_2$	4.6	-
4,5-Br_2	-	0.70

It is possible to explain this difference of reactivity between 4-methyl- and 4-aldehydo-catechols in the following way: the electron withdrawing effect of the two quinone oxygen atoms in a 4-substituted ortho-quinone create positive centres, susceptible to nucleophilic attack, at all ring positions, i.e. (XVII). However, with 4-carbonyl substituents there is the additional electron-withdrawing effect of the carbonyl group which creates a positive centre at position 3, but not at position 5, i.e. (XVIII). A combination of the two effects would thus suggest

that attack by the hydroxyl anion occurs at position 3. The formation of the secondary radical is therefore probably as shown in the reaction scheme (XIX). That 3,4-dihydroxybenzoic acid does not behave in a similar manner may partly be explained by the fact that in alkaline solution the $-COO^-$ substituent is electron donating in contrast to the electron withdrawing effect of, say, the -CHO group.

Two disubstituted catechols have also been shown to give secondary radicals which are consistent with the production of the pyrogallol semiquinones. Catechol-3,5-disulphonic acid gave a large doublet of 4.6 Oe corresponding to interaction with the proton at position 5; 4,6-dibromocatechol a small doublet of 0.7 Oe corresponding to the proton at position 6.

REFERENCES

1. Ingram, 'Free Radicals as studied by e.s.r', Butterworths, London, 1958, Chapter 1.
2. McConnell, J.Chem.Phys., 1956, 24, 632.
3. (a) McConnell, ibid., 1956, 24, 764; (b) Bersohn, ibid., p.1066; (c) Weissman, ibid., 1956, 25, 890; (d) Jarrett, ibid., p.1289.
4. (a) McConnell and Chesnut, ibid., 1958, 28, 107; (b) McConnell, ibid., p.1188; (c) Brovetto and Feroni, Nuovo Cim., 1957, 5, 142.
5. Weissman, Townsend, Paul and Pake, J.Chem.Phys., 1953, 21, 2227.
6. Karplus and Fraenkel, ibid., 1961, 35, 1312.
7. (a) Coulson, 'Valence', Oxford University Press, Oxford, 1961; (b) Streitwieser, 'Molecular Orbital Theory for Organic Chemists', Wiley and Sons, Inc., New York, 1961.
8. (a) Weissman, Tuttle and De Boer, J.Phys.Chem., 1957, 61, 28; (b) De Boer and Weissman, J.Amer.Chem.Soc., 1958, 80, 4549.
9. (a) Carrington, Dravnicks and Symons, J., 1959, 947; (b) Weissman, De Boer and Conradi, J.Chem.Phys., 1957, 26, 963.
10. Sogo, Wakazaki and Calvin, ibid., 1957, 26, 1343.
11. McConnell and Dearman, ibid., 1958, 28, 51.
12. Carrington, Quart.Rev., 1963, 17, 67.
13. Lefebvre, J.Chem.Phys., 1961, 34, 2035.

14. Morozova, Russ.Chem.Rev., 1962, 575.

15. Bolton, Carrington and McLachlan, Mol.Phys., 1962, 5, 32.

16. Mulliken, Ricke and Brown, J.Amer.Chem.Soc., 1941, 63, 41; Coulson and Crawford, J., 1953, 2082.

17. McLachlan, Mol.Phys., 1958, 1, 233.

18. Fessenden and Schuler, J.Chem.Phys., 1960, 33, 936.

19. Forman, Murrel and Orgel, ibid., 1959, 31, 1129.

20. (a) Lockhard and Jones in 'N.M.R. and E.P.R. Spectroscopy', Pergamon Press, London, 1960, p. 65; (b) Varian Assoc. Instruction Manual No. 87-100-074; (c) Stone, Part II Thesis, Oxford, 1962.

21. Ref. 1, p. 78.

22. Maki and Geske, J.Amer.Chem.Soc., 1961, 83, 1852.

23. Venkataraman and Fraenkel, ibid., 1955, 77, 2707.

24. Piette, Yamazaki and Mason in 'Free Radicals in Biological Systems', Ed. Blois et al., Academic Press, New York, 1961, p. 195.

25. Dixon and Norman, J., 1963, 3119.

26. Kolker and Waters, J., 1964, 1136.

27. (a) Musso, Angew.Chem., 1963, 75, 965; (b) Barton and Cohen in 'Festschrift für Arthur Stoll', Birkhäuser, Basel, 1957, p. 117.

28. Moore and Waters, J., 1954, 243.

29. Cosgrove and Waters, J., 1951, 388.

30. Müller et al., (a) Part I, Ber, 1954, 87, 922; (b) Part X, Ber., 1958, 91, 2682; (c) Part XXIV, Ann., 1962, 657, 5.

31. Cook et al., (a) Part I, J.Org.Chem., 1953, 18, 261; (b) Part X, ibid., 1960, 25, 1429.

32. Cook, Kuhn and Fianu, J.Amer.Chem.Soc., 1956, 78, 2002; Müller and Ley, Ber., 1955, 88, 601.

33. Coppinger, Tetrahedron, 1962, 18, 61.

34. Becconsall, Scott and Clough, Proc.Chem.Soc., 1959, 308; Trans. Faraday Soc., 1960, 56, 469.

35. Pannell, Chem. and Ind., 1962, 1797.

36. Porter and Land in 'Preprints of papers read at the Fifth International Symposium on Free Radicals, 1961, Uppsala', Almqvist and Wiksell, Stockholm, 1961, paper B4-1.

37. Vogel, 'Textbook of Practical Organic Chemistry', Longmans, London, Third Edition, 1960, p. 680.

38. Moffett and Seay, J.Med.Pharm.Chem., 1960, 2., 201.

39. Southwick, Foltz and McIntyre, J.Amer.Chem.Soc., 1953, 75, 5877.

40. Müller, Ricker, Mayer and Scheffler, Ann., 1961, 645, 36.

41. Ayscough, Sargent and Wilson, J., 1963, 5418.

42. Atherton, Land and Porter, Trans.Faraday Soc., 1963, 59, 818.

43. Schug, Brown and Karplus, J.Chem.Phys., 1962, 37, 330.

44. Symons, Adv.Phys.Org.Chem., 1963, 1., 283.

45. Mulcahy and Williams, Nature, 1963, 199, 761.

46. Atherton and Harding, ibid., 1963, 198, 987.

47. Anderson, Frank and Gutowsky, J.Chem.Phys., 1960, 32, 196.

48. Rieger and Fraenkel, ibid., 1962, 37, 2811.

49. Eaton, Josey, Phillips and Benson, Mol.Phys., 1962, 5, 407; Eaton, Josey, Benson, Phillips and Cairns, J.Amer.Chem.Soc., 1962, 84, 4100.

50. Matsunaga and McDowell, Canad.J.Chem., 1960, 38, 1158.

51. Adams, Blois and Sands, J.Chem.Phys., 1958, 28, 774.

52. Ref. 1, p. 151.

53. Kohn and Löff, Monatsh., 1924, 45, 589.

54. Nicolet and Sampey, J.Amer.Chem.Soc., 1927, 49, 1796.

55. Davis and Hill, ibid., 1929, 51, 493.

56. Land and Porter, Proc.Chem.Soc., 1960, 84; Bolton and Carrington, ibid., 1961, 385.

57. (a) Ref. 47; (b) Reitz, Hollahan, Dravnicks and Wertz, ibid., 1961, 34, 1457.

58. Hewgill, J., 1962, 4987.

59. Hewgill, Stone and Waters, J., 1964, 408.

60. Hoskins, J.Chem.Phys., 1955, 23, 1975.

61. Stone and Maki, ibid., 1962, 36, 1944.

62. Waters, 'Mechanisms of Oxidation of Organic Compounds', Methuen, London, 1964, p. 149.

63. Ettel, Pospíšil and Bauer, Coll.Czech.Chem.Comm., 1957, 22, 1621.

64. Ettel and Pospíšil, ibid., 1957, 22, 1624.

65. Pospíšil and Ettel, ibid., 1959, 24, 341.

66. Pospíšil and Ettel, ibid., 1959, 24, 729.

67. Pospíšil, Kožařství, 1959, 9, 266; Chem.Abs., 1960, 54, 12042.

68. Horner and Weber, Ber., 1963, 96, 1568.

69. Burton and Hopkins, J., 1952, 2445.

70. Howton, Mead and Clark, J.Amer.Chem.Soc., 1955, 77, 2896.

71. Kohn, ibid., 1951, 73, 480.

72. Vliet, Org.Synth.Coll.Vol., 1, 317.

73. Thiele and Winter, Ann., 1900, 311, 341.

74. Woodward, Sondheimer, Taub, Heusler and McLamore, J.Amer.Chem. Soc., 1952, 74, 4223.

75. Adams and Levine, ibid., 1923, 45, 2377.

76. Weygand, Weber and Maekawâ, Ber., 1957, 90, 1879.

77. Wessely and Sinwell, Monatsh., 1950, 81, 1055.

78. Goodwin and Pitkop, J.Amer.Chem.Soc., 1957, 79, 179.

79. Gendel, Freed and Fraenkel, J.Chem.Phys., 1962, 37, 2832.

ABSTRACT

This work is concerned with the investigation by electron spin resonance (e.s.r.) of organic free radicals in solution. All the radicals investigated contained oxygen functional groups and were all produced by one-electron oxidation or reduction. The thesis is presented in five Parts, Part 1 being an introductory Part in which the basic principles of e.s.r. are discussed and the apparatus described. A flow apparatus, which is able to detect transient free radicals with lifetimes of ca. 10^{-2} sec., is described; this apparatus has been used to detect many of the radicals investigated in this work.

Part 2 describes the oxidation of monohydric phenols, ArOH, by a one-electron oxidising agent, ceric sulphate, to produce phenoxy radicals, ArO$^{\bullet}$. The e.s.r. spectrum of the unsubstituted phenoxy radical itself, PhO$^{\bullet}$, has been recorded, together with the spectra of some 50 other substituted phenoxy radicals. In a large majority of cases the spectra have been analysed successfully and coupling constants, arising from interaction of the free electron with both the ring protons and the α-protons of alkyl-substituents, have been obtained. It was found that the total spin density associated with the ring carbon atoms C_2-C_6 is

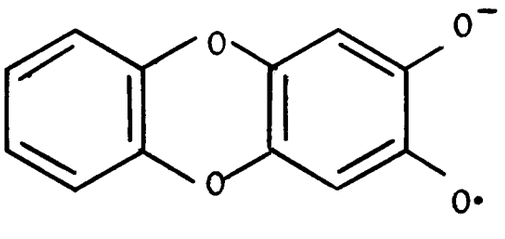
ca. 0.80, thus indicating that ca. 20% of the spin density is associated with the phenoxy oxygen atom and the carbon atom to which it is attached.

Qualitative trends in the coupling constants of the ring protons were observed and discussed; for example, it was found that the algebraic sum of the ortho and meta coupling constants was approximately constant with different substituents at the para position. This would suggest that the only effect of the para substituents is to cause a redistribution of the spin density between the ortho and meta positions.

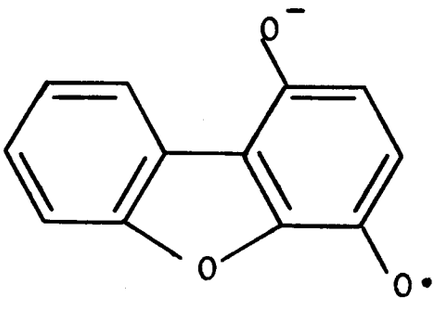
Part 3 describes the oxidation, both with potassium ferricyanide in alkaline solution and with ceric sulphate in acid solution, of resorcinol and substituted resorcinols, using the flow apparatus in each case. Different spectra were obtained from the oxidation of the same resorcinol under the different conditions. The spectra obtained by alkaline oxidation have been characterised as the meta-semiquinones, i.e. m-$^{-}O \cdot C_6H_4 \cdot O^{\cdot}$; this being the first time such radicals have been described. Coupling constants have been unambiguously assigned by obtaining the spectra of m-semiquinones substituted with a carboxyl group at each ring position in turn.

It was found that only ca. 18% of the total spin density can be associated with both oxygen atoms. This situation is quite different from that obtaining in ortho- or para-semiquinones, where some 60% of the spin density is associated with the oxygen atoms. Suggestions have also been made as to the radical species present in acid solution; a singly or doubly protonated radical, i.e. $[\cdot O \cdot C_6H_4 \cdot OH]$ or $[HO \cdot C_6H_4 \cdot OH]^+$ respectively, being most likely.

Part 4 describes examples of the production of secondary radicals from catechol and some 2-(o-hydroxyphenyl)-1,4-benzoquinones in alkaline dimethylformamide/water solutions. The e.s.r. spectrum of the o-semiquinone from catechol was found to quickly change to one which contained a superimposed spectrum due to a secondary radical. This radical was shown to be dibenzo-[1,4]-dioxin-2,3-semiquinone (i).



(i)



(ii)

Secondary radicals were also observed on reduction of some 2-(o-hydroxyphenyl)-1,4-benzoquinones, or oxidation of the corresponding quinol, under the same conditions as used for the

oxidation of catechol. In this case the secondary radicals were shown to be dibenzofuran-1,4-semiquinones, i.e. (ii). Possible mechanisms for the production of these radicals have been suggested.

Part 5 deals with the e.s.r. investigation of the radicals produced by the oxidation of simple substituted catechols. Two methods, i.e. aerial oxidation in alkaline dimethylformamide/water and oxidation with alkaline ferricyanide in water, were found, which in many cases permitted the spectra of the simple ortho-semiquinones to be recorded. In several cases secondary radicals were formed in aqueous solution, and the characterisation of these has been described.

It was found that the secondary radicals were probably formed by nucleophilic hydroxyl anion attack on the o-quinone to produce a trihydroxybenzene system. 4-Methylcatechol was shown to give the radical from 1,2,4-trihydroxy-5-methylbenzene, whilst 3,4-dihydroxybenzaldehyde, for example, gave the pyrogallol semiquinone from 2,3,4-trihydroxybenzaldehyde. Possible reaction mechanisms have been discussed and an explanation offered for the difference in reactivity between the two substituted catechols.