

262. *Aryloxy-radicals. Part IV.¹ Electron Spin Resonance Spectra of Some ortho-Monobenzosemiquinones and Secondary Radicals Derived Therefrom.*

By T. J. STONE and WILLIAM A. WATERS.

The electron spin resonance spectra of several *o*-benzosemiquinones have been obtained by the oxidation of substituted catechols both in dimethylformamide solution, using a static method, and in water, using a flow apparatus. Secondary radicals have also been obtained from some catechols in aqueous solution; these have been characterised and shown probably to arise from attack by the hydroxyl anion on *o*-quinone molecules. The position of attack has been shown to be different for 4-alkyl- and for 4-carbonyl-substituted catechols; the former giving semiquinones derived from 5-alkyl-1,2,4-trihydroxy-benzenes, the latter semiquinones from 4-substituted-1,2,3-trihydroxybenzenes. This difference of reactivity is discussed.

ALTHOUGH the electron spin resonance (e.s.r.) spectra of many *para*-semiquinones have been published,² and several *meta*-semiquinones have recently been characterised,¹ there

¹ Part III, *J.*, 1964, 4302.

² *E.g.*, Ingram, "Free Radicals as studied by E.S.R.," Butterworths, London, 1958.

have been few reports on the e.s.r. investigation of *ortho*-monobenzosemiquinones. The spectrum of the semiquinone from catechol itself is well known,³ but the only reported⁴ e.s.r. spectra of radicals from substituted catechols are those from 4-phenyl-, 4-*t*-butyl-, and 3-phenyl-catechol. Only in the latter was hyperfine splitting observed from interaction of the unpaired electron with all the ring protons.

It has been found that when the usual conditions for producing *p*-semiquinones, *i.e.*, aerial oxidation of the quinol in alkaline ethanolic solution, are applied to the oxidation of catechols, complex asymmetric e.s.r. spectra result, on account of the superposition of the primary spectra of the *o*-semiquinone and those of one or more secondary radicals. Secondary radical production in alcoholic solution has already been reported⁵ for *p*-semiquinones, and has been shown to be due in some cases to alkoxy-attack on the benzene ring.

We have found two systems which allow the spectra of many, but by no means all, of the simple *o*-semiquinones investigated to be recorded: (i) aerial oxidation in alkaline dimethylformamide-water (9:1), using the static method of observing spectra, and (ii) oxidation in aqueous alkali by potassium ferricyanide or by air, using in most cases a flow apparatus. In aqueous alkali solution the spectra of several secondary radicals were also observed; the characterisation of these radicals is described below.

EXPERIMENTAL

E.s.r. spectra were obtained with a Varian V4500 spectrometer with a 6 in. magnet and 100 kc./sec. modulation, using both flow and static methods. The flow apparatus was the one previously described,⁶ except that as the lifetimes of the *o*-semiquinones were somewhat longer than those of the phenoxy-radicals, better spectra were obtained by using a flow apparatus with a larger space (*ca.* 2 ml.) between the mixing point and the flat portion of the sample cell. The catechols (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- and tri-hydroxy-compound (5 mg.) with air in a 4 ml. test tube with either (i) dimethylformamide (DMF) (2 ml.) containing 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 stabilise it.

The production of secondary radicals occurred in some cases (*i.e.*, 3,4-dihydroxybenzaldehyde) to the exclusion of the primary radicals; occasionally (*i.e.*, 4-isopropylcatechol) the spectrum of the primary radical decayed into that of the secondary radical whilst the solution was in the spectrometer; and in other cases (*i.e.*, 4-methylcatechol) considerable shaking was necessary to produce a secondary radical solution.

Materials.—3,4-Dihydroxyacetophenone, m. p. 118° (lit.,⁷ 119°), was prepared from catechol by a Friedel-Crafts reaction.⁷ 4,5-Dibromocatechol, m. p. 119° (lit.,⁸ 119–121°), was prepared by bromination of catechol.⁸ 1,2,4-Trihydroxybenzene, m. p. 140° (lit.,⁹ 140.5°), was prepared by deacetylating⁹ 1,2,4-triacetoxybenzene, m. p. 96° (lit.,¹⁰ 96°), which was obtained from *p*-benzoquinone by a Thiele acetylation.¹⁰ 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, it being assumed that the acetyl groups would be hydrolysed off by the alkaline medium of the subsequent oxidation.

³ Adams, Blois, and Sands, *J. Chem. Phys.*, 1958, **28**, 774.

⁴ Hoskins, *J. Chem. Phys.*, 1955, **23**, 1975.

⁵ Anderson, Frank, and Gutowsky, *J. Chem. Phys.*, 1950, **32**, 196; Reitz, Hollahan, Dravnieks, and Wertz, *ibid.*, 1961, **34**, 1457.

⁶ Stone and Waters, *J.*, 1964, 213.

⁷ Howton, Mead, and Clark, *J. Amer. Chem. Soc.*, 1955, **77**, 2896.

⁸ Kohn, *J. Amer. Chem. Soc.*, 1951, **73**, 480.

⁹ Thiele and Winter, *Annalen*, 1900, **311**, 341.

¹⁰ Vliet, *Org. Synth.*, Coll. Vol., I, 317.

1,2,4-Triacetoxy-5-methylbenzene, m. p. 109° (lit.,¹¹ 110—113°), was prepared from *p*-toluquinone by a Thiele acetylation.¹¹ 2,3,4-Trihydroxybenzaldehyde, m. p. 161—162° (lit.,¹² 161—162°), was prepared from pyrogallol by a modified Gatterman reaction.¹² 1,2,3-Triacetoxy-5-methylbenzene, m. p. 100—101° (lit.,¹³ 101.5—102.5°), was prepared by the method of Goodwin and Witkop¹³ from 2,2-diacetoxy-4-methylcyclohexadien-1-one, m. p. 129° (lit.,¹⁴ 128—134°), which was obtained by the oxidation of *p*-cresol with lead tetra-acetate.¹⁴

RESULTS AND DISCUSSION

The ortho-Semiquinones.—On aerial oxidation of substituted catechols in dimethylformamide (DMF) containing 10% by volume of water, the e.s.r. spectra obtained by the normal static method could, in many cases, be analysed clearly for the simple *ortho*-semi-

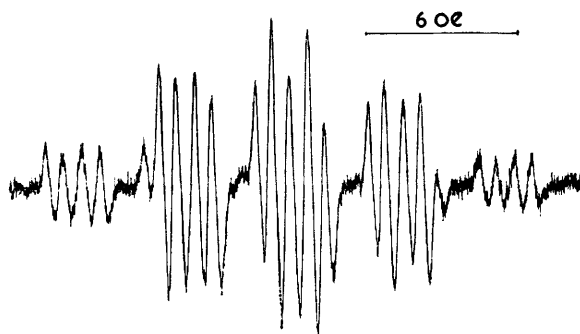


FIG. 1. E.s.r. spectrum of 4-methyl-*o*-semiquinone in DMF-water (9:1).

quinone. With only one exception, where clear symmetrical spectra were obtained, hyperfine splitting due to the interaction of the free electron with all available ring protons and α -protons of alkyl groups, was observed. A typical example, the spectrum of the semiquinone from 4-methylcatechol, is shown in Fig. 1.

With water alone as the solvent some catechols on oxidation gave spectra which have been identified as being due to secondary radicals (see below). For these catechols, and for others from which poor spectra were obtained by the static method, satisfactory e.s.r. spectra were obtained by oxidation with alkaline potassium ferricyanide in a flow apparatus. In several such cases the spectra showed hyperfine splitting from one less proton than would be expected from the corresponding simple semiquinone radical. For example, Fig. 2 shows the spectrum obtained by oxidation of 4-methylcatechol in the flow apparatus. By comparison of 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.

That the spectra obtained by the flow method were in fact probably those of the simple semiquinone has been shown indirectly in the following way. (i) The spectrum obtained by aerial oxidation of 4-methylcatechol on immediate observation by the static method was clearly a superposition of both primary and secondary radicals. However the general form of Fig. 2 was discernible, but with each line split into a doublet of small separation 0.25 Oersted. It has previously^{1,6} proved difficult, using the flow apparatus, to observe splittings of less than *ca.* 0.3 Oe. (ii) By oxidising 4-methylcatechol under the same conditions as used in the flow experiment but waiting about 10 min. before recording the e.s.r. spectrum, a signal was obtained which was that of the secondary radical alone; this, as is shown below, is the semiquinone of 1,2,4-trihydroxy-5-methylbenzene. Thus the radical observed using the flow method can be regarded as the simple primary *o*-semiquinone.

¹¹ Woodward, Sondheimer, Taub, Heusler, and McLamore, *J. Amer. Chem. Soc.*, 1952, **74**, 4223.

¹² Adams and Levine, *J. Amer. Chem. Soc.*, 1923, **45**, 2377.

¹³ Goodwin and Witkop, *J. Amer. Chem. Soc.*, 1957, **79**, 179.

¹⁴ Wessely and Sinwell, *Monatsh.*, 1950, **81**, 1055.

The coupling constants of the *o*-semiquinones in both solvents are given in Table I. 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. Because of the unsymmetrical nature of the radicals

TABLE I.
Coupling constants of ortho-semiquinones.

Parent catechol	Coupling constants (Oersted) *								F/S †
	In DMF-water				In water				
	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) ‡	1.0	5.1	4.0	F
4-CH ₂ CO ₂ H	0.6	1.15	3.0	4.1	(0.25) ‡	0.9	3.0	3.9	F
4-Pr ^l §									
4-Bu ^t §									
4-CO ₂ H	0.9	1.4	—	3.3	0.7	1.3	—	3.3	F, S
4-COR § ¶									
3-Me	0.8	0.8	2.9	3.7	0.7	?	3.0	4.25	F
3-Pr ^l	0.7	0.7	2.7	3.95	0.7	?	2.95	4.5	F
3,6-Pr ₂	0.45	0.45	3.2	—	?	?	3.4	3.4	F
3-CO ₂ H §									
3-Bu ^t -5-Me	—	?	3.0	4.35	—	0.3	2.65	5.4	S
3-Bu ^t -5-OMe	—	0.6	3.2	1.1 **	—	0.8	3.1	1.1 **	F
3,5-(SO ₃ Na) ₂	—	1.8	3.9	—	—	1.9 ₅	3.6	—	S
4,5-Br ₂	1.4	1.4	—	—	0.5	0.5	—	—	S

* Coupling constants not definitely assigned between positions 3 and 6 for 4-substituted radicals, and between positions 4 and 5 for 3-substituted radicals; a_1 represents either ring or α -proton coupling constants. † Oxidation carried out by (F) flow method, or (S) static method. ‡ See text. § Unanalysable spectra obtained. ¶ R = H, Me, or Et. ** Methoxy-proton splitting.

investigated, it is difficult to make even qualitative observations as to the effect of substituents on the coupling constants at the unsubstituted positions.

It can be seen that the solvent has a considerable effect on the values of the coupling constants. Solvent effects have been previously noted for some *p*-semiquinones,¹⁵ and variations in coupling constants of from 1 to 44% have been observed. Fraenkel and his colleagues¹⁶ have discussed these effects theoretically on the basis that changes in proton splittings result directly from the formation of localised complexes between the solvent and a polar substituent in the radical. A solvent such as water probably interacts primarily by hydrogen bonding to the oxygen atoms of the semiquinones. It is evident that with the *o*-semiquinones the solvent causes little change in the total spin density at the ring positions, but only a redistribution. In general the values of the coupling constants at positions 4 and 5 are increased, and those at position 3 and 6 are decreased, when the solvent is changed from DMF to water.

For several substituted catechols it has, so far, proved impossible to obtain reasonable spectra of their simple semiquinones. Thus, though 4-methyl-, 3-isopropyl- and 3,5-diisopropylcatechol give simple *o*-semiquinone spectra, no reasonable spectra could be obtained from 4-isopropyl- or 4-*t*-butyl-catechol. From these compounds the former 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 Hoskins⁴). On oxidation in DMF, or in water in the flow apparatus, the catechols with substituents -COR (R = H or Alkyl) in the 4-position gave no clearly analysable spectra.

The Secondary Radicals.—(a) *4-Alkylcatechols.* 4-Methylcatechol, on shaking with aqueous alkali for several minutes, gave an e.s.r. spectrum (Fig. 3) different from that produced by rapid oxidation (Fig. 2). Fig. 3 clearly corresponds to a large quartet (5.1 Oe) of small triplets (0.65 Oe), which indicates interaction with three equivalent

¹⁵ Stone and Maki, *J. Chem. Phys.*, 1962, **36**, 1944.

¹⁶ Gendel, Freed, and Fraenkel, *J. Chem. Phys.*, 1962, **37**, 2832.

protons. As the original catechol contains a methyl group it is reasonable to suppose that this 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 can be inferred that one ring proton has been lost in the production of the secondary radical. Further, since the reaction is carried out in aqueous 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 (I)—(III).

The e.s.r. spectrum of unsubstituted pyrogallol semiquinone has been previously recorded³ and has coupling constants of 5.41 and 0.96 Oe, interaction with the two ring protons adjacent to the hydroxy-groups giving rise to the smaller coupling constants. Taking account of these values, 4-methylpyrogallol (I) 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.

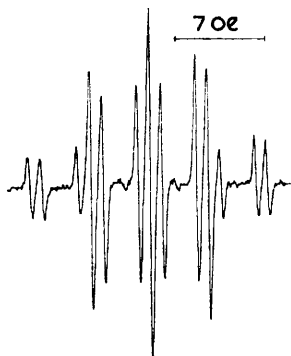


FIG. 2. E.s.r. spectrum of 4-methyl-*o*-semiquinone in water.

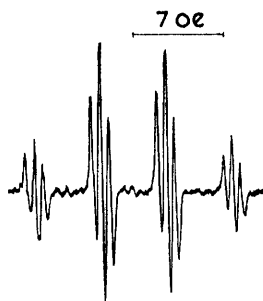


FIG. 3. E.s.r. spectrum of the secondary radical from 4-methylcatechol in water.

Of the two remaining possibilities, *i.e.*, the radicals from 1,2,4-trihydroxy-5-methylbenzene (II) or 5-methylpyrogallol (III), the latter would seem 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 to give a small triplet. Accordingly both compounds (II) and (III) were oxidised in aqueous alkaline solution and the e.s.r. spectra of the resulting radicals recorded.

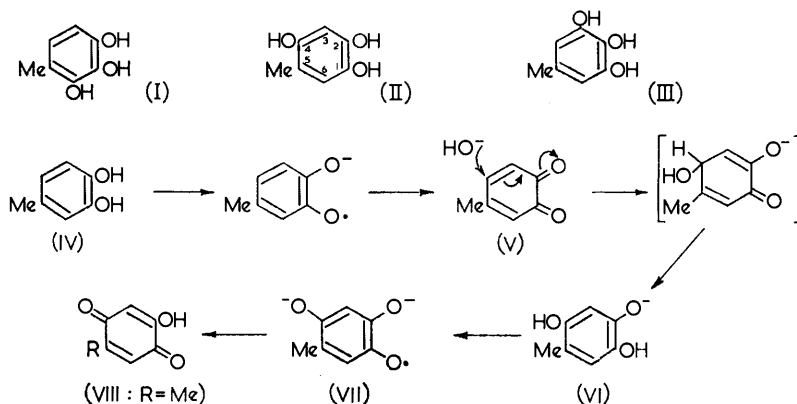
It was found that the spectrum of the radical from 1,2,4-trihydroxy-5-methylbenzene (II) corresponded exactly to that of the secondary radical from 4-methylcatechol, both spectra being superimposable; a mixture of the two compounds on oxidation gave the same single spectrum. The spectrum from 5-methylpyrogallol (III), 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 (II).

Pospišil and Ettl¹⁷ have also isolated a small quantity of the quinone (VIII; R = Me) corresponding to 1,2,4-trihydroxy-5-methylbenzene (II) on oxidation of 4-methylcatechol in aqueous alkaline solution. Consequently the following reaction scheme for the formation of the semiquinone (VII) may be postulated. 4-Methylcatechol (IV) is oxidised in the normal way to the quinone (V), which is then attacked by hydroxyl ions to form the trihydroxy-compound (VI). The further oxidation (VI) \rightarrow (VII) \rightarrow (VIII; R = Me) is analogous to the oxidation of the catechol, *i.e.*, (IV) \rightarrow (V), but it results this time, however, in a *p*-quinone.

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

¹⁷ Pospišil and Ettl, *Coll. Czech. Chem. Comm.*, 1959, **24**, 341.

doublet of triplets. A different, but unanalysable, spectrum was obtained immediately after mixing but this very rapidly changed to the final secondary radical spectrum. By analogy with the result above the doublet splitting would correspond to the α -proton of



the isopropyl group, and the triplet again to the fortuitous equivalence of the ring protons at positions 3 and 6.

Both results are consistent with the spectrum of the semiquinone from the unsubstituted 1,2,4-trihydroxybenzene. The coupling constants obtained show that the protons at positions 3 and 6 are no longer equivalent. The coupling constants quoted above, together with those obtained by oxidation of the two trihydroxy-compounds in DMF-water, are given in Table 2. It may be noticed that in the latter solvent the proton at positions 3 and 6 in the 5-methyl compound are now also no longer equivalent.

TABLE 2.
Coupling constants of secondary radicals.

Catechol substituent or trihydroxy-compound	Solvent	Coupling constants (Oe) *		
		a_3	a_5	a_6
1,2,4-Trihydroxybenzene	H ₂ O	1.3	4.8	0.60
	DMF-H ₂ O	1.7	3.7	0.69
4-Me	H ₂ O	0.65	5.1	0.65
1,2,4-Trihydroxy-5-methylbenzene	H ₂ O	0.64	5.1	0.64
	DMF-H ₂ O	0.80	5.2	0.50
4-Pr ¹	H ₂ O	0.70	2.8	0.70
4-CHO	H ₂ O	—	0.80	4.4
2,3,4-Trihydroxybenzaldehyde	H ₂ O	—	0.80	4.4
4-COMe	H ₂ O	—	0.80	4.8
2,3,4-Trihydroxyacetophenone	H ₂ O	—	0.82	4.8
4-COEt	H ₂ O	—	0.80	4.8
4,6-(SO ₃ Na) ₂	H ₂ O	—	—	4.6
4,5-Br ₂	H ₂ O	—	0.70	—

* For numbering see diagrams in text; in the case of non-equivalent values for a_3 and a_6 a definite assignment has not been made.

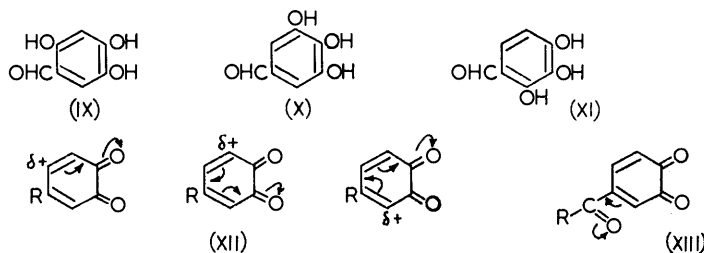
It would be expected, from the evidence of Pospíšil and Ettl¹⁸ who have obtained 2-hydroxy-5-t-octyl-1,4-benzoquinone (VIII; R = t-octyl), from the oxidation of 4-t-octylcatechol, that 4-t-butylcatechol should give a secondary radical analogous to those obtained from 4-methyl- and 4-isopropylcatechol described above, but no conclusive evidence could be found in the e.s.r. spectrum for a radical of this type.

(b) 4-Carbonyl-substituted catechols. The oxidation in aqueous solution of 3,4-dihydroxybenzoic acid gave a radical which was clearly the *o*-semiquinone. This radical decayed slowly and was in fact the most stable *o*-semiquinone investigated. No evidence

¹⁸ Pospíšil and Ettl, *Coll. Czech. Chem. Comm.*, 1959, **24**, 729.

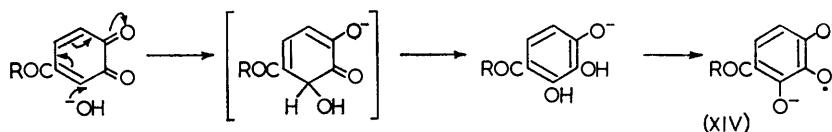
for the formation of a secondary radical was found. However, on oxidation in aqueous solution, 3,4-dihydroxybenzaldehyde, 3,4-dihydroxyacetophenone, and 3,4-dihydroxypropiofenone gave in each case a spectrum consisting of a doublet of doublets. The average values of the coupling constants were *ca.* 4.6 and 0.8 Oe.

Now if the secondary radicals are of the same form as those discussed for the 4-alkylcatechol, 3,4-dihydroxybenzaldehyde should give the semiquinones from 5-formyl-1,2,4-trihydroxybenzene (IX). 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 the radical from (IX), since it has been shown that in alkyl-substituted radicals



these protons both give coupling constants of the order of 0.8 Oe. If it is assumed that hydroxyl attack again occurs, there are two possibilities for the structure of the secondary radical, *i.e.*, the radicals from the two pyrogallols (X) and (XI). The radical derived from (X) can be excluded 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 (XI) is most likely; on oxidation the latter compound gave an e.s.r. spectrum exactly similar to that of the secondary radical from 3,4-dihydroxybenzaldehyde. Similar results, which are summarised in Table 2, were obtained with the two ketones.

It is possible to explain the difference in reactivity between 4-methyl- and 4-formylcatechol in the following way: the electron withdrawing effect of the two quinone oxygen atoms in a 4-substituted *o*-quinone create positive centres, susceptible to nucleophilic attack, at all ring positions (*i.e.*, XII). However with 4-carbonyl substituents there is the additional electron-withdrawing effect of the carbonyl group, which reinforces the positive centre at position 3, but *not* at position 5 (*i.e.*, XIII). Thus for carbonyl-substituted catechols attack by hydroxyl anions would be more likely at position 3. The formation of the secondary radical (XIV) can therefore be depicted as follows:



The observation 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 whereas a carbonyl group is an electron withdrawing substituent.

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THE DYSON PERRINS LABORATORY, OXFORD UNIVERSITY.

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