

## The Electron Spin Resonance Spectra of Semiquinones obtained from Some Naturally Occurring Methoxybenzoquinones

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Radical anions of methoxyquinones and related compounds were generated in a static system in alkaline media. The unpaired electron distribution in these radicals could not be satisfactorily verified by simplified SCF calculations. It is shown that a simple relationship exists between splittings in the semiquinones and corresponding splittings in the closely related alkyl aryl ether radical cations. This relationship correlates very closely with the excess charge effect which has been examined quantitatively for aromatic hydrocarbon radical ions, indicating that the same effect is operative in the oxygenated radicals, in which the splittings of the cations are *ca.* 20% greater than corresponding splittings in the anions. These correlations, together with observed smooth variations of splitting patterns with substitution have permitted unambiguous assignment of the coupling constants of radicals such as the fumigatin anion or the 1,2-methylenedioxy-naphthalene cation, without recourse to new computation.

ABOUT 90 benzoquinones have been obtained from natural sources,<sup>1</sup> most of them distributed among *ca.* 20 families of flowering plants and of fungi. Due to the ease of formation of semiquinone radicals from both the quinones and the corresponding reduced forms, e.s.r. spectroscopy has become an important tool for the characterisation of these compounds. A wide range of *o*-, *m*-, and *p*-semiquinones has been studied in this way,<sup>2,3</sup> and the techniques established have been extended to radicals related to pyridines,<sup>4</sup> naphthalenes,<sup>5</sup> coumarins,<sup>6,7</sup> and tropolones.<sup>8,9</sup> However, the formation of semiquinone radicals is only the first step in the autoxidation of a dihydric phenol or, indirectly, of quinones in alkaline media,<sup>10</sup> and e.s.r. has been usefully employed in the study of products formed by further oxidation, dimerisation, and degradation of the parent structures. It was the aim of the present investigation to extend e.s.r. studies of this type to the important group of fungal metabolites such as fumigatin (2-hydroxy-3-methoxy-6-methyl-*p*-benzoquinone) and the antibiotic aurantiogliocladin (2,3-dimethoxy-5,6-dimethyl-*p*-benzoquinone) and to other quinones related to the tetrahydroxybenzenes.

### RESULTS

Radicals were generated by autoxidation of the corresponding dihydric phenols in aqueous sodium hydroxide solution.<sup>5,10</sup> Well resolved e.s.r. spectra were generally observed (Figure 1), and the parameters obtained are given in the Table.

*Assignment of Coupling Constants.*—Simple graphical procedures<sup>11,12</sup> have been developed, which can be used to assign definite patterns of unpaired electron distribution to the various modes of oxygen substitution. As these spin distributions are not perturbed significantly by other substituents, it has sometimes been feasible for e.s.r. parameters to be used analytically.<sup>7,13</sup> The patterns obtained in this way are then verified by calculations based on simple MO theory.<sup>11,14,15</sup> The assignment of the many small splittings given in the Table, especially those due to methoxy-groups, presents an interesting and severe test of these graphical methods.

In some cases there is a smooth variation of the splitting pattern with substitution, as in radicals (A)—(C), where the

trends of the coupling constants are clearly shown. It is unfortunate that in other instances in which there is serious ambiguity, the McLachlan semiempirical SCF procedure, which has proved highly satisfactory elsewhere,<sup>14,15</sup> fails to predict many splittings with acceptable accuracy.

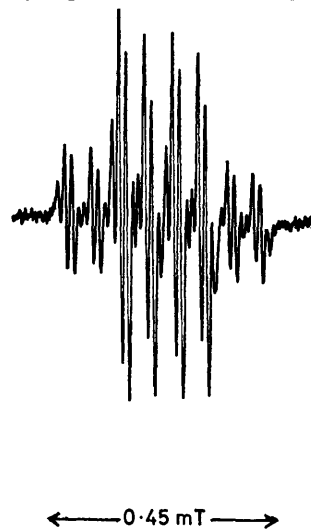
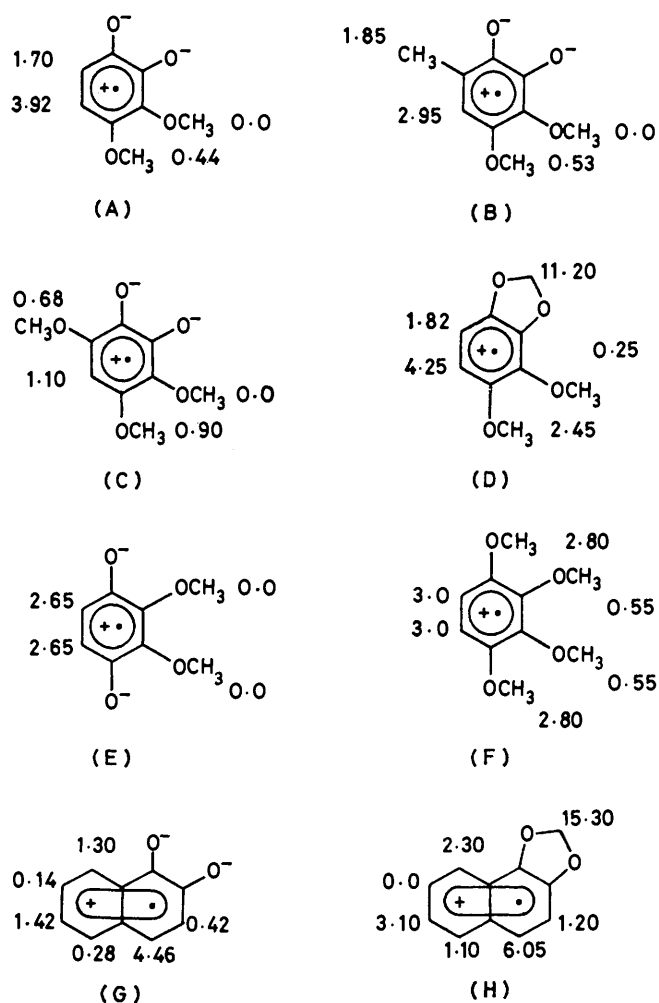


FIGURE 1 E.s.r. spectrum of 3,4,5-trimethoxy-*o*-benzosemiquinone

Many values are reproduced only by using different parameters for each radical, a process which is virtually meaningless for diagnostic purposes.

A simple relationship between corresponding splittings in phenoxy radicals and phenol radical cations has been used to assign coupling constants in ambiguous cases,<sup>12</sup> and it can be seen that corresponding splittings in semiquinones and ether radical cations<sup>15,16</sup> are similarly related [(A) and (D), (E) and (F)]. This similarity has been reported previously,<sup>16</sup> and is a clear indication of virtually identical spin distributions in the corresponding anions and cations. It follows then, since it has been demonstrated that the splittings in the ether radical cations can be successfully predicted using SCF theory,<sup>15</sup> that this method provides a convincing assignment of many of the splittings in the Table. Alternatively, where the spin distribution of a semiquinone is well established, assignments in the corresponding cation can be made with reasonable certainty. An interesting and slightly more complex example is provided by radicals (G) and (H). Here the splittings for



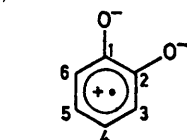
the radical cation from 1,2-methylenedioxy-naphthalene,<sup>17</sup> a potent synergist for carbamate insecticides, are assigned by comparison with 1,2-naphthosemi-quinone.<sup>5</sup> Radical (H) is the first species of this type in the naphthalene series which has been examined by e.s.r. spectroscopy.

*Excess Charge Effects.*—It is important to note that the relationship discussed in the previous section is strictly only applicable to the *ratios* of the splittings in the various radicals, [e.g. in radical (A),  $a_5/a_6 = 2.30$ ; in radical (D),  $a_5/a_6 = 2.33$ ]. In each case, the *magnitude* of the splittings of the cations exceeds that of the anions by *ca.* 20%. In the case of the aromatic hydrocarbon radical ions, this effect has been examined quantitatively,<sup>18,19</sup> and a reasonable explanation of the experimental observations has been provided in terms of the total charge on the radicals. Qualitatively, the effect is due to the 'contraction' of the carbon  $2p_z$  orbitals in the positively charged ions.<sup>20</sup> If the spin distribution in corresponding pairs of semiquinones and ether radical cations is indeed nearly identical,<sup>16</sup> a similar effect could account for the difference in the magnitudes of the splittings in these species.

Figure 2 shows a plot of the splittings of semiquinones from derivatives of 1,2-, 1,4-, 1,2,3-, 1,2,4-, 1,2,3,4-, 1,2,4,5-, and 1,2,3,4,5-polyhydroxybenzenes against corresponding values for the related ether radical cations.<sup>15,16</sup> All suitably related pairs of anion and cation radicals for which e.s.r. spectra have been observed in this and in earlier work<sup>11,15,16</sup> are given in Figure 2. For comparison, values for a number of aromatic radical ions<sup>18</sup> have been included. Within experimental error a straight line relationship is obtained embracing both sets of data. This plot is good evidence that the effect in the oxygenated radicals is identical to that in the hydrocarbons, and that the same explanation for it probably applies to all of the radicals. The agreement is particularly encouraging due to the assumptions made in grouping together apparently different classes of radical in this way.

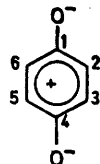
TABLE 1

E.s.r. parameters ( $a/10^{-4}$  T) for semiquinones from derivatives of tetra- and penta-hydroxybenzenes  
(i) Substituents in



	$a_3$	$a_4$	$a_5$	$a_6$
(A) 3,4-(OCH <sub>3</sub> ) <sub>2</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.44	3.92	1.70
(B) 3,4-(OCH <sub>3</sub> ) <sub>2</sub> , 6-CH <sub>3</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.53	2.95	$a_{\text{CH}_3}$ 1.85
3,6-(OCH <sub>3</sub> ) <sub>2</sub> , 4-CH <sub>3</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{CH}_3}$ 5.61	1.70	$a_{\text{OCH}_3}$ 0.61
4,5-(OCH <sub>3</sub> ) <sub>2</sub>	0.32	$a_{\text{OCH}_3}$ 1.10	$a_{\text{OCH}_3}$ 1.10	0.32
4,5-(OCH <sub>2</sub> O)	0.33	$a_{\text{CH}_2}$ 4.22	$a_{\text{CH}_2}$ 4.22	0.33
3,4,5-(OCH <sub>3</sub> ) <sub>3</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.10	$a_{\text{OCH}_3}$ 1.20	0.60
(C) 3,4,6-(OCH <sub>3</sub> ) <sub>3</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.90	1.10	$a_{\text{OCH}_3}$ 0.68
3,5-(OCH <sub>3</sub> ) <sub>2</sub>	$a_{\text{OCH}_3}$ 0.75	1.70	$a_{\text{OCH}_3}$ 1.00	0.95

(ii) Substituents in



	$a_2$	$a_3$	$a_5$	$a_6$
(E) 2,3-(OCH <sub>3</sub> ) <sub>2</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.0	2.65	2.65
2,3-(OCH <sub>2</sub> O)	$a_{\text{CH}_2}$ 0.18	$a_{\text{CH}_2}$ 0.18	2.63	2.63
2,3-(OCH <sub>3</sub> ) <sub>2</sub> , 5-CH <sub>3</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.0	$a_{\text{CH}_3}$ 2.45	1.98
2,3-(OCH <sub>3</sub> ) <sub>2</sub> , 5,6-(CH <sub>3</sub> ) <sub>2</sub>	$a_{\text{OCH}_3}$ 0.0	$a_{\text{OCH}_3}$ 0.0	$a_{\text{CH}_3}$ 2.15	$a_{\text{CH}_3}$ 2.15
(J) 2-O <sup>-</sup> , 3-OCH <sub>3</sub> , 6-CH <sub>3</sub>	4.0	$a_{\text{OCH}_3}$ 0.0	4.0	$a_{\text{CH}_3}$ 1.18
2,6-(OCH <sub>3</sub> ) <sub>2</sub>	$a_{\text{OCH}_3}$ 0.81	1.45	1.45	$a_{\text{OCH}_3}$ 0.81

The existence of this systematic relationship greatly strengthens the validity of this approach to the assignment of splitting patterns in both semiquinones and the corresponding radical cations. The method permits the

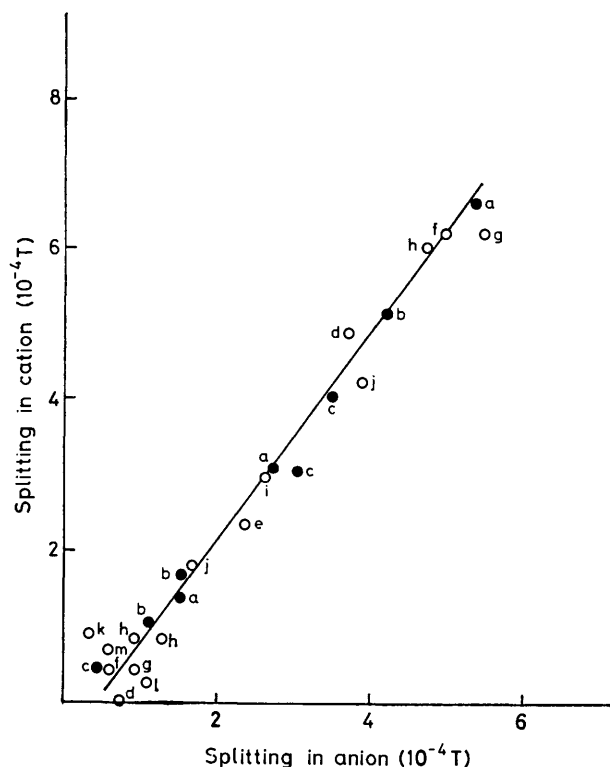
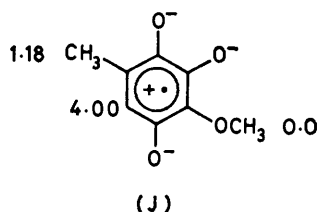


FIGURE 2 Graphical relationship between corresponding coupling constants in radical cations and radical anions. ●, Aromatic hydrocarbon radical ions (from ref. 18); a, anthracene; b, tetracene; c, perylene. ○, semiquinones and related radical cations (from this work and from refs. 11, 15, and 16). Substituents: d, 1,2-(OCH<sub>3</sub>)<sub>2</sub>, 1,2-(O<sup>-</sup>)<sub>2</sub>; e, 1,4-(OCH<sub>3</sub>)<sub>2</sub>, 1,4-(O<sup>-</sup>)<sub>2</sub>; f, 1,2-(OCH<sub>2</sub>O)-4-OCH<sub>3</sub>, 1,2,4-(O<sup>-</sup>)<sub>3</sub>; g, 1,2,3-(OCH<sub>3</sub>)<sub>3</sub>, 1,2,3-(O<sup>-</sup>)<sub>3</sub>; h, 1,2-(OCH<sub>2</sub>O)-3-OCH<sub>3</sub>, 1,2-(O<sup>-</sup>)<sub>2</sub>-3-OCH<sub>3</sub>; i, 1,2,3,4-(OCH<sub>3</sub>)<sub>4</sub>, 1,4-(O<sup>-</sup>)<sub>2</sub>-2,3-(OCH<sub>3</sub>)<sub>2</sub>; j, 1,2-(OCH<sub>2</sub>O)-3,4-(OCH<sub>3</sub>)<sub>2</sub>, 1,2-(O<sup>-</sup>)<sub>2</sub>-3,4-(OCH<sub>3</sub>)<sub>2</sub>; k, 1,2,4,5-(OCH<sub>3</sub>)<sub>4</sub>, 1,2-(O<sup>-</sup>)<sub>2</sub>-4,5-(OCH<sub>3</sub>)<sub>2</sub>; l, 1,2-(OCH<sub>2</sub>O)-3,4,6-(OCH<sub>3</sub>)<sub>3</sub>, 1,2-(O<sup>-</sup>)<sub>2</sub>-3,4,6-(OCH<sub>3</sub>)<sub>3</sub>; m, 1,2-(OCH<sub>2</sub>O)-3,4,5-(OCH<sub>3</sub>)<sub>3</sub>, 1,2-(O<sup>-</sup>)<sub>2</sub>-3,4,5-(OCH<sub>3</sub>)<sub>3</sub>. (All splittings due to aromatic C-H protons are included)

splitting pattern in anions such as that from fumigatin (J) or the 4-O-methyl ether (C) to be written down, using only data from related radical cations<sup>15</sup> which have been previously confirmed by computation.



#### EXPERIMENTAL

*E.s.r. Spectra.*—Spectra of semiquinone anions were obtained in a static system<sup>2</sup> following autoxidation<sup>5</sup> of dihydric phenols in aqueous alkaline solution (pH 8–12). Where the dihydroxy-compounds were very susceptible to aerial oxidation, the corresponding quinones were reduced

using alkaline dithionite immediately prior to the autoxidation; autoxidation of the quinones in aqueous alkali did not result in generation of semiquinone radicals as has been observed with less highly substituted substrates.<sup>10</sup> Spectra from 3,4-dimethoxy-1,2-methylenedioxybenzene<sup>21</sup> and 1,2-methylenedioxy-naphthalene<sup>17</sup> were obtained by oxidation of the ethers ( $10^{-2}$  mol dm<sup>-3</sup>) in H<sub>2</sub>SO<sub>4</sub>·4H<sub>2</sub>O using  $10^{-2}$  mol dm<sup>-3</sup> cerium(IV) sulphate in H<sub>2</sub>SO<sub>4</sub>·4H<sub>2</sub>O in a flow system as described previously.<sup>16</sup> Unresolved second-order effects were manifested in the broadening of the centre lines in the spectra of the methylenedioxy-compounds.

*Materials.*—1,2-Dihydroxy-3,4-dimethoxybenzene,<sup>21</sup> 1,2-dihydroxy-3,4-dimethoxy-6-methylbenzene,<sup>22</sup> 1,2-dihydroxy-3,4,5-trimethoxybenzene,<sup>23</sup> 1,2-dihydroxy-3,4,6-trimethoxybenzene,<sup>23</sup> 1,2-dihydroxy-4,5-methylenedioxybenzene,<sup>24</sup> 1,4-dihydroxy-2,3-dimethoxybenzene,<sup>25</sup> 1,4-dihydroxy-2,3-methylenedioxybenzene and 1,2,4-trihydroxy-3-methoxy-6-methylbenzene<sup>22</sup> were prepared as in the cited literature. 1,2-Dihydroxy-3,6-dimethoxy-4-methylbenzene was obtained by hydrazine hydrate-potassium hydroxide reduction of the corresponding aldehyde.<sup>25</sup> 1,2-Dihydroxy-3,5-dimethoxybenzene was prepared by alkaline hydrogen peroxide oxidation of commercial 2'-hydroxy-4',6'-dimethoxyacetophenone. 1,2-Dihydroxy-4,5-dimethoxybenzene and 1,4-dihydroxy-2,3-dimethoxy-5,6-dimethylbenzene were obtained by alkaline sodium dithionite reduction of the corresponding commercial quinones. The other precursors were commercial materials. All compounds used were purified by the usual methods, and had physical constants which agreed well with those of the literature.

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