

The Electron Spin Resonance Spectra of Semiquinones obtained from Some Heterocyclic Quinones

John D. R. Clay and David Murphy*

Royal Holloway and Bedford Colleges, The Bourne Laboratory, Egham, Surrey TW20 0EX

Radical anions of heterocyclic quinones and related compounds were generated in a static system in alkaline media. The unpaired electron distribution in several of the radicals could not be satisfactorily verified by simplified SCF calculations. It is shown that, using a smooth variation of splitting pattern with substitution in radicals related to phenoxyl, quite convincing assignments of the splitting patterns can be made based on comparison with related species.

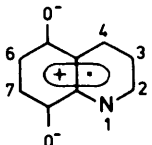
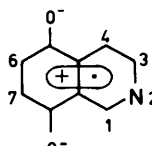
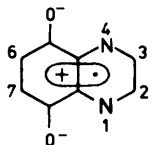
Many imidazo-¹, quinoline-² and quinoxaline-quinones³ have been investigated for anti-malarial and antibiotic activity following the postulation by Schönhöfer^{2,4} that the *in vivo* action of 6-methoxy-8-aminoquinolines upon the erythrocytic forms of malarial plasmodia is due to quinonoid products into which these drugs are converted by the host organism. Owing to the ease of formation of semiquinone radicals from both 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 benzo- and naphthosemiquinones have been studied in this way^{5,6} and the techniques established extended to radicals related to pyridines,⁷ coumarins,⁸

tropolones,^{9,10} and to fungal metabolites such as fumigatin.¹¹ Very few benzosemiquinones with fused heterocyclic rings have been studied by e.s.r. spectroscopy, and it was the aim of the present investigation to extend these studies to a range of radicals of this type, and to any products formed by further oxidation or degradation of the parent structures.

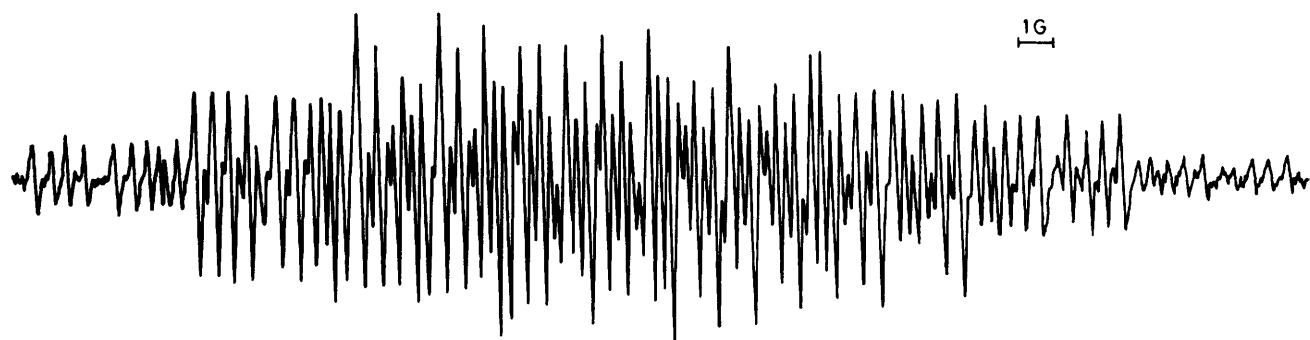
Results and Discussion

Radicals were generated by autoxidation of the corresponding dihydric phenols in aqueous sodium hydroxide solution.^{6,12}

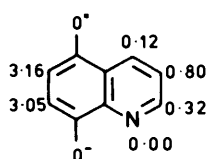
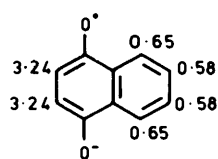
Table. E.s.r. parameters ($a/10^{-4}T$) for heterocyclic semiquinones (calculated values in parentheses)^a

| | | Coupling constants (± 0.05) | | | | | |
|---|-------|-----------------------------------|-------------|-------------|-------------|-------------|-------------------------|
| (i) substituents in | | | | | | | |
|  | | a_N | a_2 | a_3 | a_4 | a_6 | a_7 |
| (A) | | 0.00(1.06) | 0.32(-0.56) | 0.80(1.13) | 0.12(-0.24) | 3.16(4.19) | 3.05(2.59) |
| (D) | 6 - 0 | 0.15 | 1.95 | 0.15 | 1.00 | | 0.20 |
| | 7 - 0 | 0.75(1.56) | 0.25(-0.78) | 2.25(2.07) | 0.50(-0.76) | 0.25(-0.32) | |
| (ii) substituents in | | | | | | | |
|  | | a_1 | a_N | a_3 | a_4 | a_6 | a_7 |
| (B) | | 0.00(-0.21) | 0.37(0.56) | 1.14(2.57) | 0.37(1.53) | 2.55(2.50) | 3.25(4.08) ^b |
| (E) | 7 - 0 | 0.28(0.19) | 0.75(0.28) | 2.70(3.85) | 0.28(0.08) | 0.28(-1.19) | |
| (iii) substituents in | | | | | | | |
|  | | a_{1N} | a_2 | a_3 | a_{4N} | a_6 | a_7 |
| (C) | | 0.18(0.26) | 0.54(-0.24) | 0.54(-0.24) | 0.18(0.26) | 2.90(3.39) | 2.90(3.39) ^c |
| (F) | 6 - 0 | 0.60(-0.49) | 2.30(1.53) | 0.20(-0.83) | 0.80(1.35) | | 0.20(-0.41) |

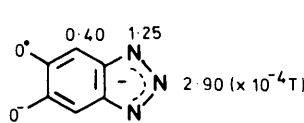
^a Parameters from ref. 16: $-O^-$; h_0 1.6, k_{CO} 1.3, $-N$; h_N 1.3, k_{CN} 1.00. ^b The result reported by M. K. V. Nair, K. S. V. Santhanam, and B. Venkataraman, *J. Magn. Reson.*, 1973, 9, 229 evidently contains a misprint. ^c There is the expected close agreement between this result and that reported by Nair *et al.* for the 2,3-dimethyl compound.



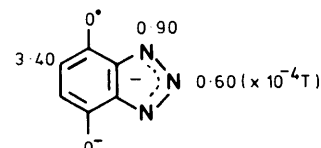
E.s.r. spectrum from adrenochrome (N)



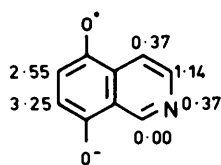
(A)



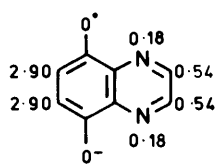
(G)



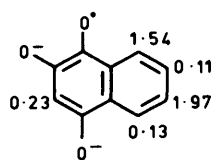
(H)



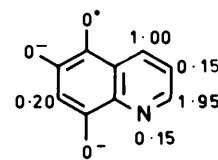
(B)



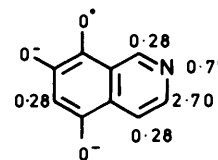
(C)



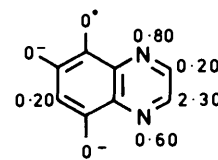
(D)



(D)



(E)



(F)

Using this well established procedure it is usually possible to make quite convincing assignments of the splitting patterns based on comparison with related species.

Quinoline-, Isoquinoline- and Quinoxaline-5,8-semiquinones.—Here the assignments have been made on the basis of comparison with equivalent naphthosemiquinones and with the aid of McLachlan SCF calculations.¹³ This method of assignment has also helped to define the position in which oxygen ($-O^-$) is substituted in the secondary radicals (Scheme 1). As was the case with 2,3-dihydroxynaphthalene,⁶ 6,7-dihydroxy-quinoline and -quinoxaline were not autoxidised to give semiquinone radicals.

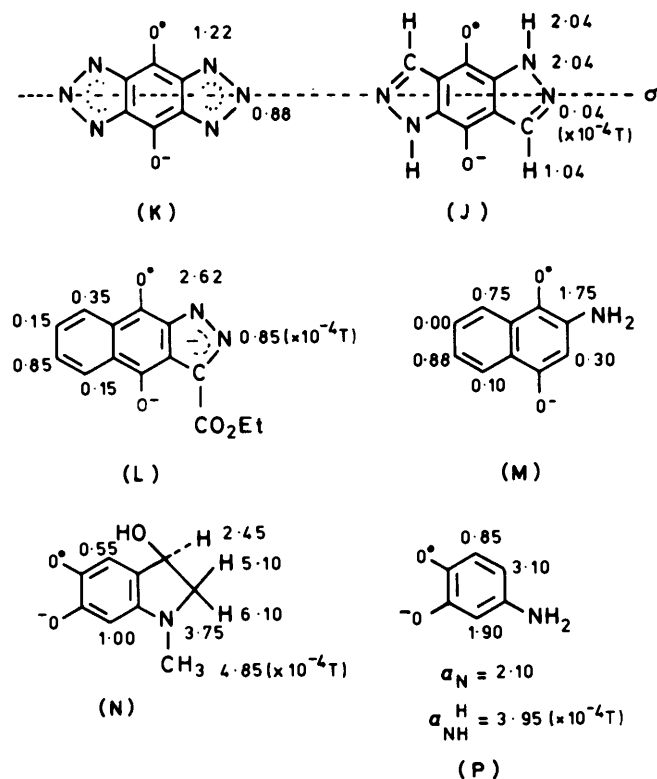
Triazolosemiquinones.—The assignment of coupling constants in radical (G) is unambiguous due to its symmetry. The spectrum of 2,3-triazolo-1,4-benzosemiquinone (H) is the same as that obtained previously,¹⁶ except that the present spectrum (obtained in water) lacked the considerable line broadening effect at high field due to the slow tumbling of the radical in DMF solution.^{16,17}

Benzo[1,2-c:4,5-c']dipyrazole-4,8-(1H,5H)-semiquinone (J).—The spectrum from radical (J) is made up of splittings from two pairs of equivalent protons of 2.04 and $1.04 \times 10^{-4}T$, respectively, and two pairs of equivalent nitrogen atoms of 2.04 and $0.40 \times 10^{-4}T$, respectively. The assignment of these coupling constants is not obvious, and has been made on the basis of comparison with related systems. A general feature of 1,4-semiquinones is that the unpaired electron occupies an orbital which is antisymmetrical with respect to the symmetry plane, σ , bisecting the C(2)–C(3) and C(5)–C(6) bonds, so that atoms in the nodal plane exhibit small splittings. Although radical (J) does not itself have a symmetry plane it is very similar to the symmetrical bistriazolosemiquinone (K),¹⁶ so the nitrogen splittings are assigned as in the Table. The assignment of the two pairs of protons is less easy, but previous studies¹⁸ have shown that for radicals in which a proton is attached to a heterocyclic nitrogen atom, the relationship $a^N \approx a_{NH}$ applies, so that the protons are assigned as shown.

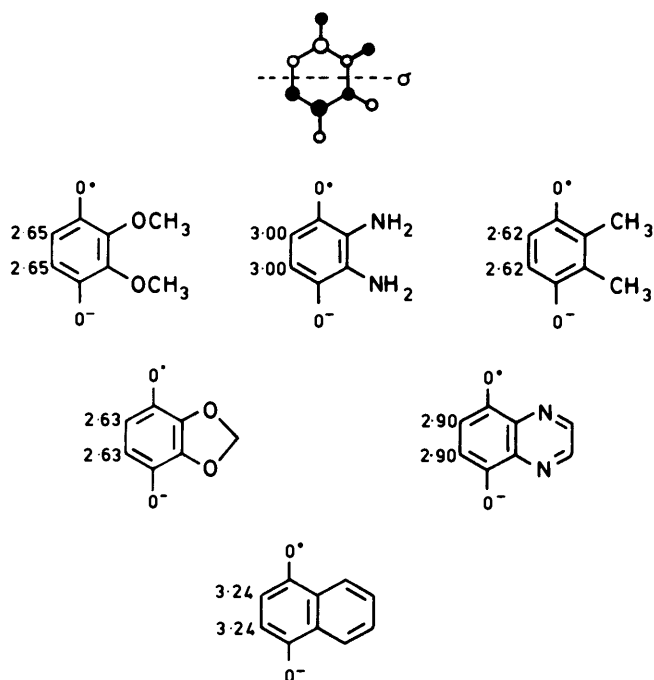
Scheme 1. Assignment of coupling constants ($a/10^{-4}T$) in heterocyclic semiquinones by comparison with corresponding naphthosemiquinones⁶

Well resolved spectra were generally observed (Figure) and the parameters obtained are given in the Table.

Assignment of Coupling Constants.—As in the case of the methoxybenzosemiquinones¹¹ the McLachlan semi-empirical SCF procedure,¹³ which has proved highly satisfactory elsewhere,^{14,15} failed to give acceptable predictions of the splittings for several of the radicals in the Table. However, previous work has shown that in radicals related to phenoxyl, there exists a smooth variation of splitting pattern with substitution.^{11,14}



3-Ethoxycarbonylnaphthindazole-4,9-semiquinone (L)—The assignment of the two nitrogen splittings has been made as for radical (J). Comparison may also be drawn with 2-amino-1,4-naphthosemiquinone¹⁶ (M) and it is upon this basis that the assignments of the ring protons have been made.



Scheme 2. Coefficients of the odd-electron orbital in 2,3-disubstituted 1,4-benzosemiquinones, and some representative examples of observed splittings^{6,11,19}

Adrenochrome.—The spectrum of the semiquinone from adrenochrome (N) analysed as five non-equivalent protons with splittings 0.55, 1.00, 2.45, 5.10, and $6.10 \times 10^4 T$ a nitrogen atom, $a_N 3.75 \times 10^{-4} T$ and three equivalent protons, $a_H 4.85 \times 10^4 T$. The two small splittings have been assigned by comparison with 4-amino-1,2-benzosemiquinone¹⁹ (P). The two large splittings are assigned to the two diastereoisomeric CH_2 protons, which are favourably positioned for maximum hyperconjugation with the nitrogen p^* orbital; the ratio of these two splittings is comparable to that previously reported²⁰ for a pair of diastereoisomeric protons adjacent to nitrogen. The remainder of the assignment is unambiguous.

Conclusions.—The results given in this paper confirm an earlier observation²¹ that in heterocyclic semiquinones the ring containing nitrogen atoms has very little effect on the spin density, which remains mainly on the semiquinone part. An investigation of the molecular orbitals in these compounds helps to illustrate why, in general, the splitting patterns are similar. In 1,2,3,4-substituted systems the unpaired electron is in an antisymmetrical orbital the calculated coefficients of which are illustrated diagrammatically²² in Scheme 2. Clearly very little change occurs to the small spin densities at C(5) and C(6) whether the 2,3-substituents are oxygen, nitrogen, or even carbon.

Experimental

E.s.r. Spectra.—Spectra of semiquinones were obtained in a static system⁵ following autoxidation⁶ of the dihydroxy compounds in aqueous alkaline solution, pH 8–12. Secondary radicals were sometimes observed following the decay of the primary radicals.⁶ Quinone precursors were reduced, using alkaline dithionite, immediately prior to the autoxidation; autoxidation of the quinones did not result in the generation of semiquinone radicals as has been observed with carbocyclic systems.¹²

Materials.—Quinolinequinone,²³ isoquinolinequinone,²³ 5,8-dihydroxyquinoxaline,²⁴ ethoxycarbonylnaphthindazole-4,9-quinone,²⁵ and benzo[1,2-c:4,5-c']dipyrazole-4,8-(1*H*,5*H*)-quinone²⁶ were prepared as in the cited literature. 2,3-Triazolo-1,4-benzoquinone and 4,5-triazolo-1,2-benzoquinone were not isolated; the spectra were obtained from solutions of the corresponding 2,3-diamino-1,4-dihydroxy- and 4,5-diamino-1,2-dihydroxy-benzene¹⁹ after treatment with nitrous acid. Adrenochrome was a commercial material, used without further purification. All the compounds had physical constants which agreed well with those of the literature.

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