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ESR, ENDOR and TRIPLE Resonance Studies on Radical Reactions of 1,4-Benzoquinone and 1,4-Hydroquinone in Alkaline Methanol and Liquid Ammonia

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The relative signs and absolute values of the hyperfine coupling constants of different methoxy-1,4-benzoquinones were measured by ESR, ENDOR and TRIPLE resonance spectroscopy. Reactions of 1,4-benzoquinone and 1,4-hydroquinone with methanol took place in alkaline methanol, giving rise to methoxy-substituted 1,4-benzoquinones. The same substitution reaction occurred in a mixture of ammonia and methanol. The reactions depended on temperature and the alkali concentration. Coupling constants were assigned by the modified additivity relationship method. An extremely small line width of 0.014 G was measured in the ESR spectrum of deuterated 2,5-dimethoxy-1,4-benzoquinone.

KEY WORDS EPR ESR ENDOR TRIPLE RESONANCE INDO Additivity relationship Liquid phase 1,4-Benzoquinone 1,4-Hydroquinone Methoxybenzoquinone Dimethoxybenzoquinone Trimethoxybenzoquinone Radical reaction

INTRODUCTION

Methoxy-substituted 1,4-benzoquinones are of interest as model compounds of biologically important quinones. In alcoholic solutions they undergo chemical reactions in which radical stages appear as products. The same radicals are formed from 1,4-benzoquinone and 1,4-hydroquinone. These radicals appear as secondary and further radical stages, causing considerable difficulties in the assigning and interpreting of hyperfine coupling constants. Substituted 1,4-benzoquinone has been widely studied,[1–12] but its reactions with solvent are less well understood.[13–22] ENDOR spectroscopy was previously used to analyse and to determine the hyperfine coupling constants of methoxy-substituted 1,4-benzoquinones in solution.[23–26] To the best of our knowledge, TRIPLE resonance spectroscopy has not been carried out previously, and the relative signs of the hyperfine coupling constants are not known. Combined ESR–ENDOR–TRIPLE spectroscopy provides valuable information about the reaction products, which is difficult to obtain by other methods.

In solutions ranging from slightly to saturated alkaline, 1,4-benzoquinone forms substitution products in the radical state which are relatively stable from the freezing point of the solvent to room temperature. Some of these substitution products are biologically interesting catalysts and some are decomposition products of lignins. Related compounds are known to have a potent cytotoxic action.[27] The substitution reactions proceed to different levels of substitution depending on the temperature and the alkali concentration.

RESULTS AND DISCUSSION

1,4-Benzoquinone forms three types of anion radicals when dissolved in alkaline methanol: benzoquinone radical anion and mono- and di-substituted methoxy radical anions. As the alkali concentration increases, the rate of the methoxy-substitution reaction increases slightly and the level of substitution increases; below an alkali concentration of 0.001 M, the methoxylation reaction stops completely. The critical temperature at which the methoxylation starts or stops is about 238 K.

Scheme 1 presents a comprehensive view of the reactions studied in this work. 2-Methoxy-1,4-benzoquinone anion radical was obtained separately from 1,4-benzoquinone, 1,4-hydroquinone and 2-methoxy-1,4-hydroquinone (1) in KOH and methanol and (2) in a mixture of methanol and liquid ammonia. In addition, it was obtained from 2-methoxy-1,4-hydroquinone (3) in pure liquid ammonia and (4) in liquid ammonia to which sodium metal was added.

1,4-Benzoquinone anion radical

The anion radical of benzoquinone ($BQ^{-\cdot}$) measured in alkaline methanol shows slight anisotropy in the ESR spectra at low temperatures, as demonstrated earlier by Carrington and Smith.[28] The hyperfine coupling of -2.37 G is in accord with the literature. In accordance with general practice, we assume a negative sign for ring

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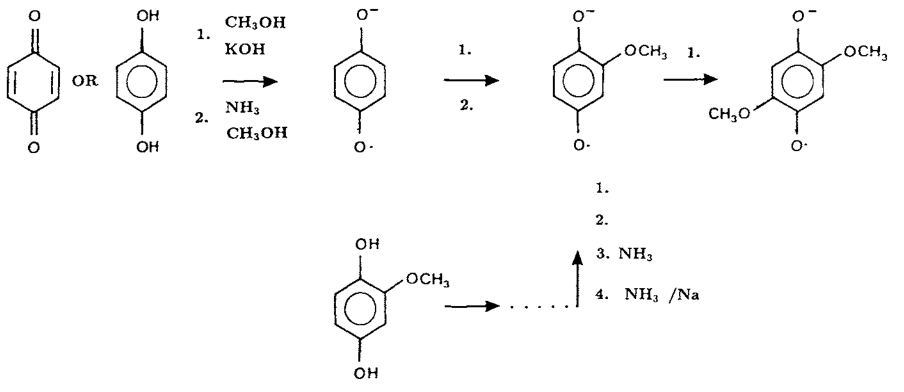


Scheme 1.

protons. All hyperfine coupling constants obtained in this work are shown in Table 1. The *g*-value measured was 2.004644.

2-Methoxy-1,4-benzoquinone anion radical

The experimental and simulated ESR spectra of the anion radical of 2-methoxy-1,4-benzoquinone are shown in Fig. 1. The ENDOR spectrum in Fig. 2 was measured in a mixture of methanol and potassium hydroxide and that in Fig. 3 in liquid ammonia and methanol. The ENDOR spectrum in Fig. 3 is different from that in Fig. 2 because the HFC constant at position 3 of the 2-MeOBQ anion radical has increased from 0.59 to 1.01 G, whereas the HFC constant of the methoxy protons has decreased from 0.8 to 0.65 G. The differences can also be seen in the SPECIAL TRIPLE spectra. The multiplicities are further confirmed by ESR simulations. The GENERAL TRIPLE spectra show opposite signs for the HFC constants of the methoxy and ring protons. The values for the ammonia spectrum are given in parentheses.

2,5-Dimethoxy-1,4-benzoquinone anion radical

2-Methoxy-1,4-benzoquinone ($2\text{-MeOBQ}^{-\bullet}$) anion radical reacts further to form the 2,5-dimethoxy-1,4-benzoquinone ($2,5\text{-DiMeOBQ}^{-\bullet}$) radical anion (method 1), which gives a highly resolved ESR spectrum. The spectrum has been published previously.[15,17] The

Table 1. Experimental hyperfine coupling constants for the methoxylation products of 1,4-benzoquinone in alkaline methanol and (in parentheses) in methanolic liquid ammonia, in gauss, and the theoretical values calculated by McLachlan, INDO and additivity relationship methods[a]

Radical	Unpaired orbital	Position	Calculated McLachlan	INDO	Additivity relationship[a]	Experimental MeOH (or NH_3)
1,4-Benzoquinone	5	2	−2.4	−1.7	−2.37	−2.37
2-Methoxy-	7	2 (methoxy)	+0.5	+0.3		+0.8 (+0.65)
1,4-benzoquinone		3	−0.5	−0.95	−0.60	−0.59 (−1.01)
		5	−2.1	−1.9	−3.64	−3.64 (−3.83)
		6	−3.4	−1.56	−2.05	−2.04 (−2.02)
2,3-Dimethoxy-	9	2 (methoxy)	+1.4	−0.14		
1,4-benzoquinone		5	−3.2	−2.09	−3.32	
2,5-Dimethoxy-	9	2 (methoxy)	+1.8	+0.15		+1.01
1,4-benzoquinone						+0.97[b]
		3	−0.8	−0.5	−0.28	−0.28
						−0.49[b]
Deuterated	9	2 (methoxy)				+0.151[c]
2,5-dimethoxy-		3				−0.036[c]
1,4-benzoquinone						
2,6-Dimethoxy-	9	2 (methoxy)	+2.7	−0.08		
1,4-benzoquinone		3	−1.8	−1.26	−1.87	
2,3,5-Trimethoxy-		2 (methoxy)		−0.07		
1,4-benzoquinone		3 (methoxy)		−0.18		
		5 (methoxy)		−0.01		
		6		−0.89	−1.55	

[a] Couplings in methanol were used in the additivity relationship method, Ref. 34.
[b] At high alkaline concentration.
[c] Deuterium hyperfine coupling.

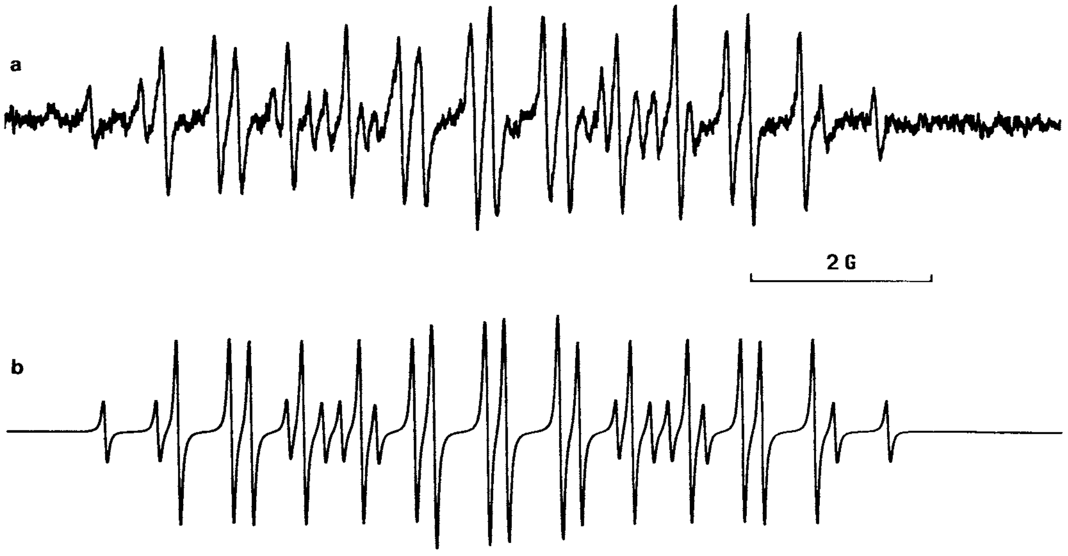


Figure 1. (a) Experimental and (b) simulated ESR spectra of 2-methoxy-1,4-benzoquinone (2-MeOBQ$^{-\bullet}$) anion radical in methanol at 233 K.

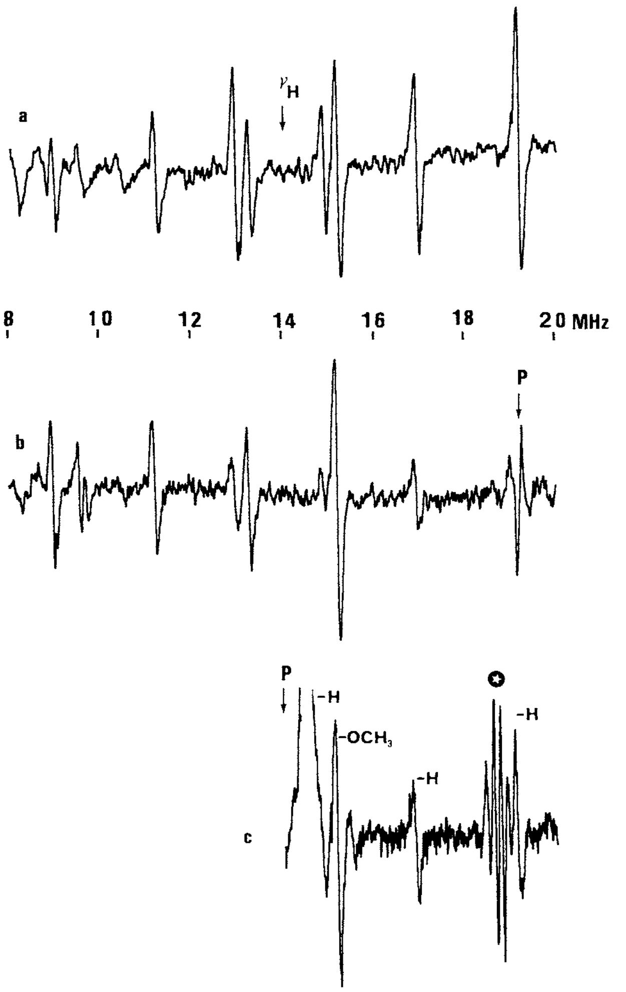


Figure 2. (a) ENDOR, (b) GENERAL TRIPLE and (c) SPECIAL TRIPLE spectra of the 2-methoxy-1,4-benzoquinone (2-MeOBQ$^{-\bullet}$) anion radical prepared from 1,4-benzoquinone in a mixture of methanol and potassium hydroxide at 253 K (method 1). The smallest proton hyperfine coupling constant cannot be seen in the SPECIAL TRIPLE spectrum owing to the pumping frequency (shown by P). Additional peaks in the SPECIAL TRIPLE spectrum marked with asterisks are due to the reflection on 50 Ω load.

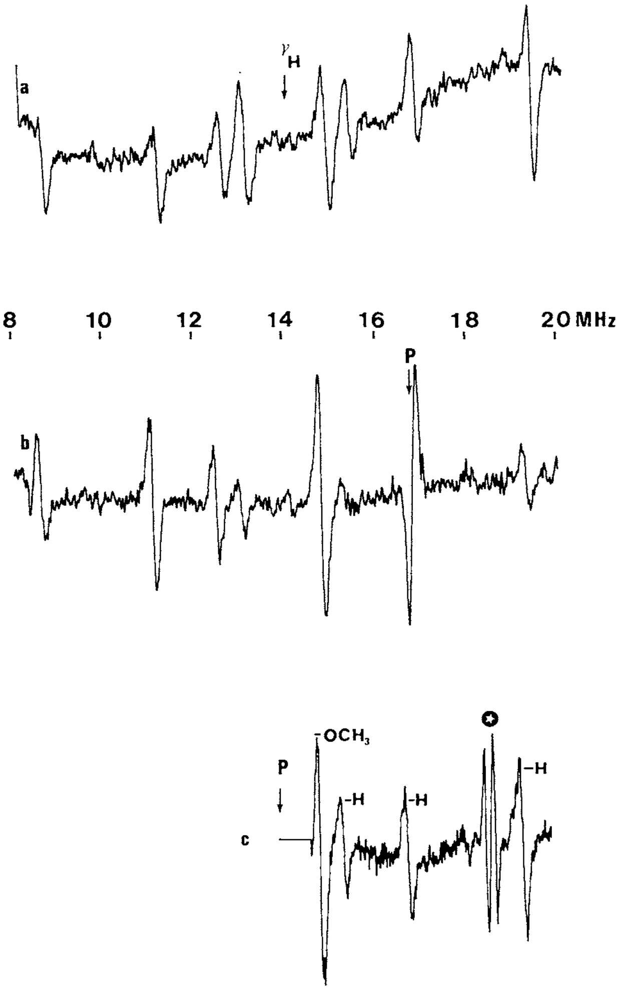


Figure 3. (a) ENDOR, (b) GENERAL TRIPLE and (c) SPECIAL TRIPLE spectra of 2-methoxy-1,4-benzoquinone (2-MeOBQ$^{-\bullet}$) anion radical prepared from 2-methoxy-1,4-hydroquinone in a mixture of ammonia and methanol (method 2) at 198 K. The pumping frequency is shown by P. Additional peaks marked with asterisks are due to the reflection on 50 Ω load.

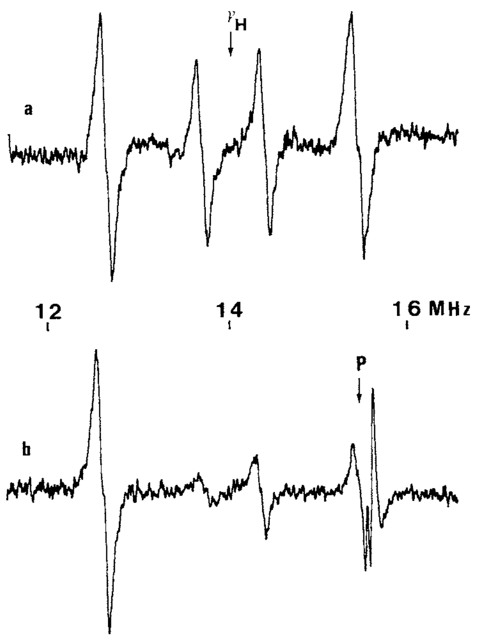


Figure 4. (a) ENDOR and (b) GENERAL TRIPLE spectra of 2,5-dimethoxy-1,4-benzoquinone (2,5-DiMeOBQ$^{-\cdot}$) anion radical at 273 K. The pumping frequency is shown by P.

g-value measured from the ESR spectrum is 2.004577 (at 263 K). The ENDOR spectrum shows two hyperfine couplings: -0.28 G (ring protons) and $+1.01$ G (methoxy protons). The relative signs were determined to be opposite by TRIPLE resonance spectroscopy, as shown in Fig. 4; the sign of the ring protons is again assumed to be negative.

High alkali concentration (3.89 M) favours the reaction to the disubstituted compound. When hydroquinone is used as starting material the reaction proceeds very quickly to 2,5-dimethoxy-1,4-benzoquinone anion radical, and the monomethoxy compound is not detected at all. The alkali concentration influences the hyperfine couplings: the coupling of the methoxy protons is smaller (down to $+0.97$ G) and the coupling of the ring protons larger (up to -0.49 G) at high concentrations.

The ENDOR spectrum of 2,5-dimethoxy-1,4-benzoquinone exhibits two line pairs, except at 250 K where each line pair appears as a doublet. The mean values of the split line pairs (Fig. 5) are identical with the values of the non-split line pairs in spectra recorded at other temperatures (Fig. 4). The splitting at 250 K might be due to the weak bonding between quinodic oxygen and either hydrogen or alkali metal cation, which causes unsymmetric perturbation in the molecule. The unsymmetric stabilization is temporary and the symmetric situation returns when the temperature is decreased further. Alternatively, the unsymmetric stage might be a transient stage, where one oxygen is perturbed. When the second quinodic oxygen is similarly perturbed, the symmetric situation returns.

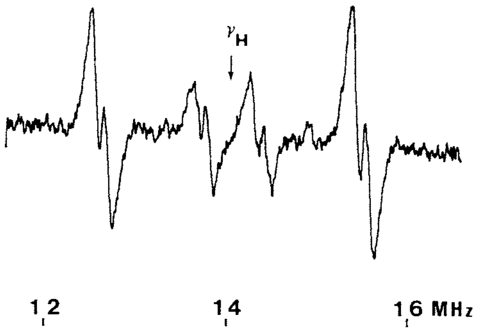


Figure 5. ENDOR spectrum of 2,5-dimethoxy-1,4-benzoquinone (2,5-DiMeOBQ$^{-\cdot}$) anion radical at 250 K. The hyperfine couplings obtained for partially resolved absorptions are 0.27, 0.33, 0.97 and 1.07 G.

2,3,5-Trimethoxy-1,4-benzoquinone anion radical

2,3,5-Trimethoxy-1,4-benzoquinone anion radical was not detected, which means that the reaction does not proceed further in this system. The hyperfine coupling constant for the doublet of the ring proton is -1.55 G, calculated by the additivity relationship (Table 1).

2,5-Dimethoxy-1,4-benzoquinone-d_8 anion radical

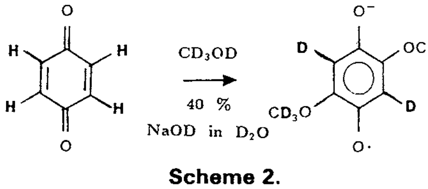
Reaction of BQ with 40% NaOD–D_2O in CD_3OD solution (Scheme 2) gives the anion radical 2,5-dimethoxy-1,4-benzoquinone-d_8 (2,5-DiMeOBQ-$d_8^{-\cdot}$). Figure 6 shows the ESR spectrum and Fig. 7 the ENDOR and the GENERAL TRIPLE spectra of 2,5-DiMeBQ-$d_8^{-\cdot}$. Analysis of the ESR, ENDOR and simulated spectra shows that the ring protons are also deuterated. The deuteromethoxy deuterons have an HFC constant of $+0.151$ G and the ring deuterons a value of -0.036 G. Transformation to proton values ($g_H/g_D = 0.156$) gives $+0.95$ and -0.23 G, respectively, which are close to the values obtained for 2,5-DiMeOBQ$^{-\cdot}$.

A line width of 0.014 G in the ESR spectrum was achieved by using a modulation frequency of 1.5625 kHz and modulation amplitude of 0.01 G. This is an extremely small line width in solution ESR spectroscopy.

The deuteration of the ring protons is explained by the rapid exchange of ring protons with the solvent D_2O deuterons. The rate-determining step in deuteration reactions is the breaking of a C—H bond. As is well known, the zero-point energy of the C—D bond is reduced, because the deuterium atom is heavier than the hydrogen atom. From the differerence in zero-point energy it can be predicted[29] that at room temperature the C—H cleavage would be about seven times faster than C—D cleavage.

Theoretical calculations

Molecular orbital theory can be applied at several levels: for instance, the INDO method[30] and the



Scheme 2.

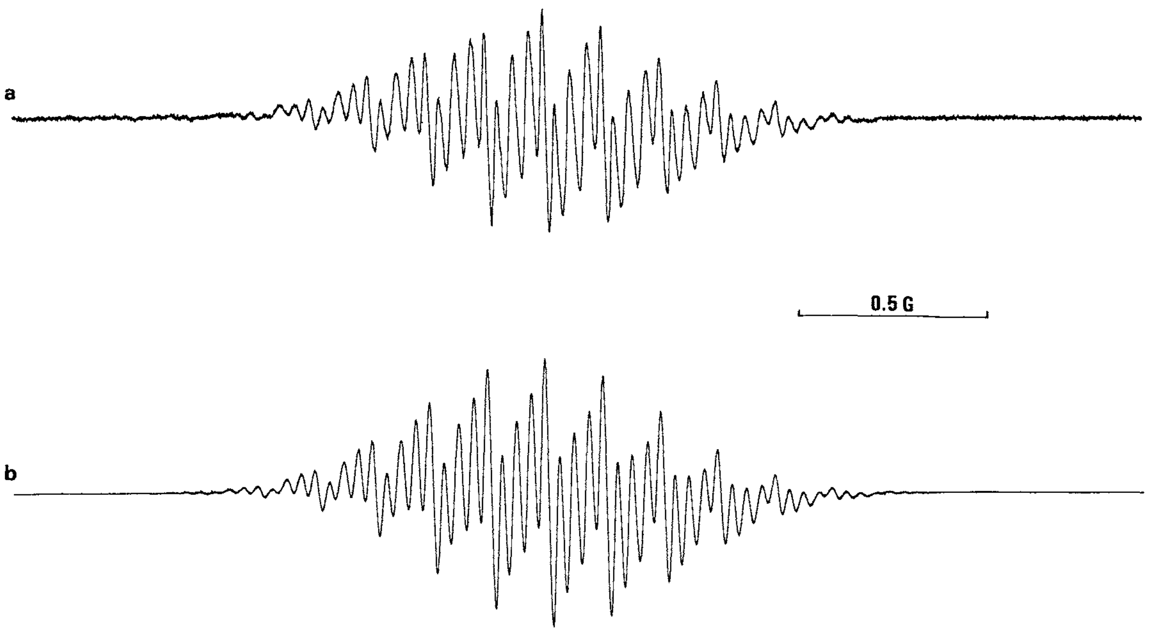


Figure 6. (a) Experimental and (b) simulated ESR spectra of totally deuterated 2,5-dimethoxy-1,4-benzoquinone-d_8 (2,5-DiMeOBQ-$d_8^{-\cdot}$) anion radical at 278 K.

method described by McLachlan[31–33] are suitable for molecules such as ours. Table 1 shows the results of the calculations by two methods.

Bakker *et al.*[34] have very effectively used the additivity relationship method for assigning the hyperfine coupling constants of organic radicals. In this work, we applied a program recently developed in our laboratory for the calculation of the additivity relationship.[35] The method is suitable for methoxy-substituted benzoquinones because a large number of hyperfine coupling constants are available for these molecules. The additivity parameters for all vacant positions are $a_1 = -2.37$, $a_2 = +1.77$, $a_3 = -1.27$ and $a_4 = +0.32$ G. All the possible methoxy substitutions of 1,4-benzoquinone can be calculated with these values and Table 1 shows the results.

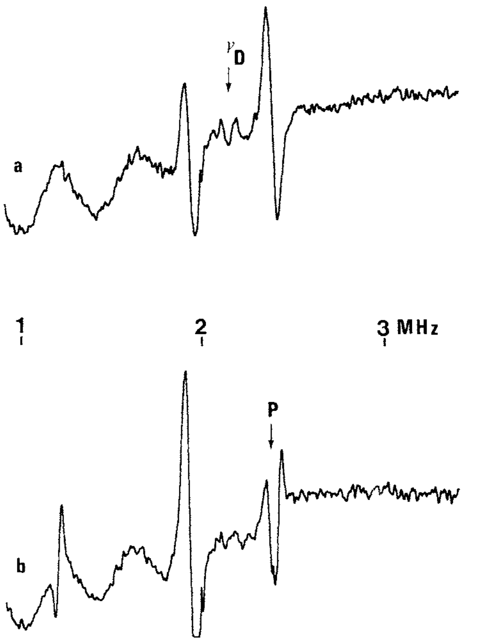


Figure 7. (a) Deuterium ENDOR and (b) GENERAL TRIPLE spectra of 2,5-dimethoxy-1,4-benzoquinone-d_8 (2,5-DiMeOBQ-$d_8^{-\cdot}$) anion radical at 203 K.

The additivity relationship calculations are seen to give a more reliable assignment for the ring protons than the molecular orbital methods. Both the additivity and INDO methods give a qualitative order for couplings. Methoxy couplings cannot be determined by the additivity method.

Standard bond lengths and bond angles[36] were used in the calculations carried out with the INDO and McLachlan methods.

In McLachlan's method we used the parameters $k(\text{C—C}_{sp^3}) = 0.9$, $k(\text{C}_{sp^3}{\equiv}\text{H}_3) = 2.5$, $h(\text{C}_{sp^3}) = -0.1$ and $h(\text{H}_3) = -0.5$, as given by Wilson,[37] and the parameters $k(\text{C—O}) = 1.22$, $k(\text{C}_{sp^3}\text{—O}) = 0.75$, $k(\text{C}_{sp^3}{\equiv}\text{H}_3) = 2.5$, $h(\text{O}) = 1.5$, $h(\text{C}_{sp^3}) = -0.1$ and $h(\text{H}_3) = -0.5$ for the methoxy group as given by Sullivan[38] in the hyperconjugation model. The parameters $h(\text{=O}) = 1.5$ and $k(\text{C=O}) = 1.5$ were selected for the quinone oxygen.

Many values have been used for McConnell[39,40] Q-values; of these, we chose McLachlan's value of -24.2 G when using sp^2 carbon spin density. Many complicated equations have been presented for the calculation of methyl and methoxy proton couplings. We used instead a method allowing direct calculation of couplings of methyl or methoxy groups from sp^3 carbon spin density. The McConnell type relationship $a_\text{H} = Q\rho(\text{CH}_3)$ was also used for the methoxy group. The $Q(\text{C}_{sp^3}{\equiv}\text{H}_3)$ value was assumed to be $Q \times (|Q|Q/1G) = -586$ G. The $\rho(\text{CH}_3)$ was the σ-spin density at the sp^3 carbon. Agreement can be improved by changing the $Q(\text{C}_{sp^3}{\equiv}\text{H}_3)$ parameter from methyl to methoxy in this way. However, the change of the *h* and *k* parameters provides still better agreement, and some standard values should be kept. The spin state is problematic. Here we assume that the unpaired electron occupies a similar symmetry state as in 1,4-benzoquinone, the orbital number 5. The orbital numbers are shown in Table 1, where the experimental values in methanol are compared with the theoretical results.

The experimentally measured relative signs of the coupling constants can be used in the additivity calculations and as a means of evaluating the semiempirical methods. Knowing the signs and absolute values of hyperfine coupling constants is also important in finding the right state for the unpaired electron. A general conclusion from the theoretical calculations, as from the experimental measurements, is that the sign of the ring protons is opposite to that of the methoxy protons.

CONCLUSION

Methoxylation of 1,4-BQ and 1,4-HQ in alkaline methanol gives monomethoxy and dimethoxy compounds in the radical state. Hyperfine coupling constants are most easily assigned by the additivity relationship method, assuming a fixed hyperfine coupling for the methoxy protons. The rate and degree of methoxylation of 1,4-benzoquinone depend on temperature, the alkali concentration and the amount of free oxygen in the sample. The rate of the radical reaction can be decelerated markedly by cooling the high-vacuum sample. Owing to the fast speed of the reactions it was not possible to measure ENDOR spectra of the reaction intermediates under a normal atmosphere. The most stable radical under the conditions studied was the 2.5-dimethoxybenzoquinone anion radical.

The line width of the deuterated 2,5-diMeOBQ-d_8 anion radical is proof of a completely isotropic ESR spectrum. No sign of deuterium quadrupolar line broadening was detected as the unresolved pattern was due to overmodulation.

In conclusion, ENDOR and TRIPLE resonance spectroscopy are effective methods for the analysis of radical mixtures of this type. Presumably the same kind of method could be applied to more complicated systems.

EXPERIMENTAL

ESR spectra were recorded on a Varian E-9 spectrometer equipped with a TR 5211 microwave counter and a Varian E 500 gaussmeter and interfaced with an Apple II microcomputer, and on a Bruker ESP 380 spectrometer equipped with a PB 1010 pulse bridge with CW option. ENDOR and TRIPLE resonance spectra were recorded on a Bruker ER 200 D-SRC spectrometer, with a laboratory-built ENDOR coil and a Varian field frequency lock. g-Values were measured using a microcomputerized ESR system.[41] The accuracy of this system is ± 0.0000005.

Samples were prepared by three methods: under normal atmosphere, under a nitrogen atmosphere and by a high-vacuum technique. Starting materials were 1,4-benzoquinone (BQ), Aldrich (puriss., 99%); 1,4-hydroquinone (HQ), Merck (photopur.); 2-methoxyhydroquinone (2-MeOHQ), Fluka (p.a., 95%); NH_3, Merck (99.99%) and methanol, J. T. Baker (99.5%), distilled over magnesia. Ammonia was condensed from gas to liquid and frozen under a nitrogen atmosphere before preparing high-vacuum samples. High-performance liquid chromatography (HPLC) was used to identify the products.

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