ESR and ENDOR Investigations of Adrenochrome Semiquinone and Related Amino-1,2-Benzosemiquinone Radicals

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ESR-, ENDOR-Spectroscopy, Semiquinones, Adrenochrome

Dimethyl or diethylamine reacts very smoothly in ethanol solution with catechols to the corresponding aminoquinones. The paramagnetic intermediates, the semiquinones, are investigated by ESR and ENDOR spectroscopy using the spin stabilisation technique with diarylthallium cations. The spectra of these radicals show clearly the thallium and nitrogen coupling and the hydrogen hyperfine structure. For some examples the signs of the proton coupling constants are determined by TRIPLE resonance experiments. The results indicate a negative spin density in one position of the unsymmetrically substituted radical **3**. With the results obtained for the monocyclic aminosemiquinones the hyperfine structure of the adrenochrome semiquinone is analysed.

The reaction of *o*-benzosemiquinones with nucleophiles such as primary and secondary amines plays an important role in organic chemistry and biochemistry (see [1] and references cited therein). The structures of diamagnetic products, for example adrenochrome, are well established. However, little is known about the paramagnetic intermediates which are involved in the course of the reaction. Recently, ESR spectra of catecholaminosemiquinones were investigated in aqueous solution [2] as well as in organic solvents [3, 4], using the spin stabilisation technique. However, amino substituted *o*-benzosemiquinones, the parent compounds of aminochromesemiquinones, are not known, as far as we know. For this reason we studied the oxidation of catechols in the presence of dimethylamine and diethylamine in ethanol solution and investigated the paramagnetic intermediates with the spin stabilisation technique.

Methods and Materials

The ESR, ENDOR and TRIPLE spectra were recorded on a Varian E Line spectrometer equipped with a Bruker ENDOR Unit ER 810 and a Bruker Datasystem ER 140. The g-value was determined by

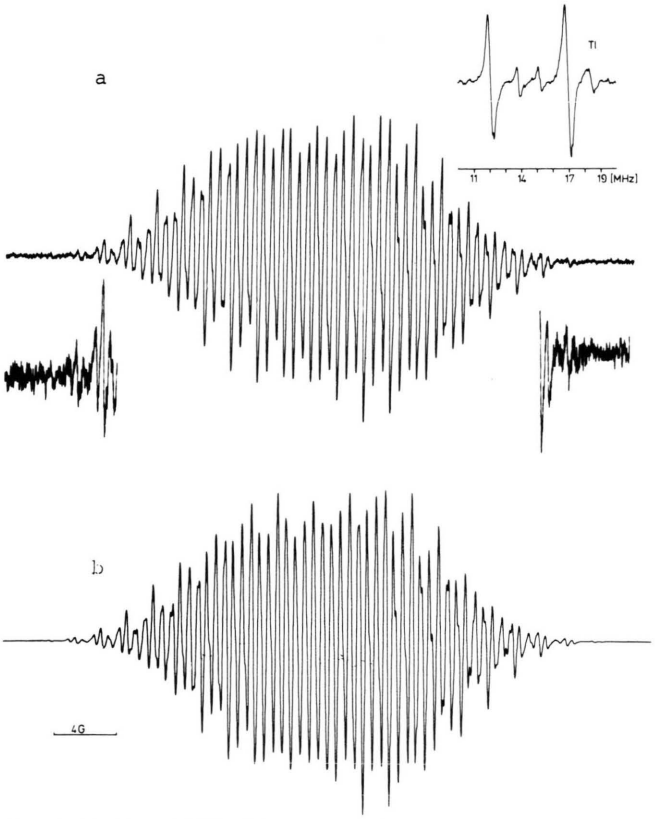

Fig. 1. ESR and ENDOR spectra of thallium complexed bis-4,5-dimethylamino-1,2-benzosemiquinone (1) in ethanol. ENDOR: MW power 50 mW; RF power 300 W; RF-modulation 70 kHz, 80 Scans. a) experimental, b) computer simulation. (The increasing intensity in the high field part is due to the decreasing line width.)

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comparison with the signal of 4-*tert*-butoxy-2,6-di-*tert*-butyl-phenoxyl (g = 2.004627) in a double resonator [5].

Adrenochrome was purchased from Sigma. The aminosemiquinones were prepared by addition of 20 mmol of the corresponding dialkylamine to a stirred solution of 1 mmol catechol in 20 ml ethanol. The oxidizing agent was air oxygen. The reaction was controlled by ESR-spectroscopy. The maximum radical concentration was observed after a reaction time of approximately 2 hours. ESR sample tubes with 2 mm i.d. containing an excess of diarylthallium-hydroxide for radical stabilization and ca. 1 ml of the reaction solution were used. After desoxygenation by carefully flushing with purified nitrogen, the radical concentration was adjusted to optimum resolution by dilution with ethanol.

Immediately after addition of the amine to the solution of the unsubstituted catechol complex, ESR signals could be observed. The intensity increased over a period of several hours. Addition of diarylthalliumhydroxide led to a stable solution containing only one paramagnetic species (s. Fig. 1).

The analysis of the extended hyperfine structure was done by ENDOR and spectra simulation. The nitrogen coupling observed indicates unambiguously the formation of amino substituted paramagnetic species. The coupling constants are given in Table I. The assignment given is in agreement with the structures of the radicals. TRIPLE resonance investigations of radical **1** show unambiguously the same sign for all proton coupling constants, whereas the thallium and the nitrogen nuclei do not show a triple effect at all. The uniform sign of the proton coupling constants may be interpreted if the following two assumptions are accepted. First: the spin density at nitrogen is positive and, therefore, the methyl groups couple, according to a hyperconjugation mechanism, positively. Second: the spin density in 3 and 6 position is negative, in contrast to the unsubstituted *o*-benzosemiquinone thallium complex [6]. That means the spin density distribution of the *o*-benzosemi-

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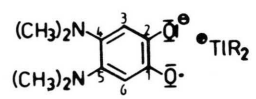

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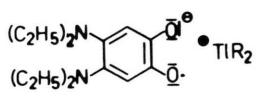

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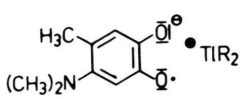

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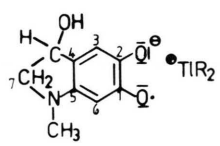

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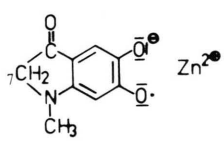

Table I. ESR and ENDOR data of aminosemiquinones in ethanol (room temperature, couplings in G).

Radical Anion	Cation	a_{Tl}	a_{H_3}	a_{H_4}[a]	a_{H_5}[a]	a_{H_6}	a_{H_7}	a_N	ΔH	g
	Mes_2Tl^+	17.25	+0.49	+1.85	+1.85	+0.49	–	2.55		2.00269
1	$(C_6H_5)_2Tl^+$	8.50	0.45	1.68	1.68	0.45	–	2.30	0.17	2.00317
	$^+NR_4$	–	0.27	1.39	1.39	0.27	–	1.94	0.12	2.00408
2	Mes_2Tl^+	13.80	0.41	1.30	1.30	0.41	–	2.14	0.33	2.00269
	$(C_6H_5)_2Tl^+$	9.4	0.55	+4.10	+2.05	0.55	–	2.55	0.2	2.00348
3	$(p\text{-Xylyl})_2Tl^+$	11.03	−0.43[b]	+4.16	+2.39	+0.61[b]	–	–		2.00342
	$^+NR_4$	–	−0.75[b]	+3.87	+1.57	+0.4[b]	–	1.99	0.1	2.00429
4	$(C_6H_5)_2Tl^+$	10.32	0.58[b]	4.77[d]	4.77	0.80[b]	2.99[d] 3.42[d]	3.88		2.00299
5 [c]	Zn^{2+}	–	–	–	5.10	–	0.91 0.91	4.44		2.0040

[a] Coupling constants of the substituents; [b] arbitrary assignment; [c] values taken from Lit. 7; [d] tentative assignment.

quinone system is changed by introduction of the amino groups analogous to the spin density redistribution observed for several alkyl substituted *o*-benzosemiquinone [6].

The 4-methyl-catechol reacts likewise very smoothly with dimethylamine forming an analogous product. The structure of 5-dimethylamino-4-methyl-*o*-benzosemiquinone (**3**) is more related to the aminochromes because the aromatic ring is linked to a sp^3 carbon as well as a nitrogen substituent. The hyperfine structure observed depends moderately on the thallium compound used for stabilizing the semiquinone radicals (Table I). If diphenylthallium is used as a counterion, the two protons in 3 and 6 position are equivalent in the ESR, as well as in the ENDOR spectra. This result is quite surprising, considering the lack of symmetry in the radical anion investigated. The assignments given in Table I are consistent with the radical structure and the computer simulation of the experimental spectrum. However, if bis-(2,5-dimethyl-phenyl)-thallium is used as counterion, the protons in 3 and 6 position appear not to be equivalent. Furthermore, TRIPLE resonance experiments lead to different signs for the 3 and 6 positions whereas the coupling constants for the methyl and the dimethylamine protons have the same sign and are therefore both positive. Thus the first assumption concerning the 4,5-bis-(dimethylamino)-semiquinone (**1**) is experimentally supported. From these results, we assume that in the diphenylthallium complex, the protons in 3 and 6 position are in fact inequivalent with respect to their signs. In support of this interpretation, TRIPLE resonance experiments do not show any intensity variations for the lines near the center by pumping other lines, neither at the high frequency, nor the low frequency side of the spectrum. ESR-spectra of monocyclic aminosemiquinones **1** and **3** may also be recorded in absence of a metalorganic counterion. However, the radicals observed under these conditions are less stable and, therefore, the spectra frequently show more HFS components than expected for one paramagnetic species.

With the results obtained for monocyclic amino substituted semiquinones, the ESR spectrum (Fig. 2) of the bicyclic adrenochrome semiquinone radical (**4**) may be analysed. The extended hyperfine structure is interpreted using the coupling constants given in Table I. These values were determined by ENDOR and used for the computer simulation. However, the

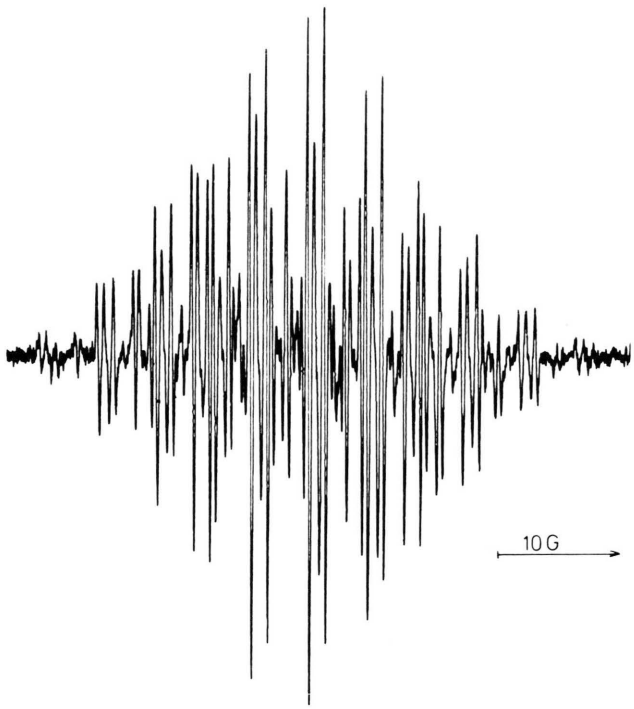

Fig. 2. ESR spectrum of thallium complexed adrenochrome-semiquinone in ethanol.

assignment of the observed coupling constants to the different positions in the molecule is complicated. By comparing the data of monocyclic aminosemiquinones with those of the adrenochrome semiquinone coupling constants, the two smallest values are due to the 3 and 6 positions. The value of 3.88 G can be unambiguously assigned to nitrogen, according to the ENDOR data of the protons and the overall width of the spectrum. The increase of up to 3.88 G may be interpreted in terms of a more coplanar conformation caused by the ring closure and, hence, an enhancement of the spin density at this atom. Consequently, an increase of the N-methyl proton coupling has been experimentally observed. A coupling of 4.7 G is assigned to the proton adjacent to the position 4 of the semiquinone ring. This value seems to be reasonable because the hyperconjugation angle has been decreased by the ring formation and, therefore, an increase of this coupling is expected. An exact comparison of monocyclic semiquinones with the adrenochrome radical cannot be done due to the lack of knowledge of the exact spin density at the 4 position in the adrenochrome semi-

quinone. If this interpretation is correct, the coupling constants of 2.99 and 3.42 G should be due to the CH_2 group of the five membered ring. The inequivalence of these two protons clearly indicates a bent structure of the heterocyclic ring, maybe envelope shaped. The results seem to be in contrast to the data recently obtained by R. C. Sealy [7] for the oxidation product (**5**) of the adrenochrome in the presence of Zn^{2+} ions. In this case the coupling constants for the 3 and 6 positions could not be detected. Apparently, the methyleneprotons in position 7 are equivalent and their coupling is very small compared to that of nitrogen and the methylprotons. Obviously, the heterocyclic ring is co-planar to the aromatic system and a participation of the carbonyl C-atom has to be considered according to the result obtained for the 4-acetyl-*o*-benzosemiquinones [8].

Acknowledgement

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