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Radical anions of nitrobenzothiazoles: EPR study of conjugative properties of benzothiazolyl systems

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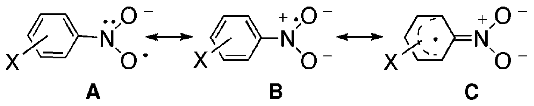
Dedicated to Professor Paolo E. Todesco on the occasion of his 70th birthday

Abstract—The electrochemical reduction in DMSO of the five isomers of nitrobenzothiazole (NBTZ) gave quite persistent radical anions that could be easily characterised by EPR spectroscopy. By contrast, the chemical reduction in alkaline solution, that is by *t*-BuOK in DMSO or by glucose and MeOK in MeOH, presented some problems with 6- and 4-NBTZ, and in the case of 2-NBTZ did not provide any detectable paramagnetic species. The internal consistency of coupling constants of the nitrobenzothiazole radical anions is in good agreement with the conjugative properties of the various benzothiazolyl systems and allows rectifying a recent EPR characterisation of 6-NBTZ radical anion.

Nitroaromatic radical anions have most of the spin density (65%, as estimated in the case of nitrobenzene)[1] localised on the nitro group. Correspondingly their EPR spectra are characterised by a nitrogen hyperfine coupling constant,[2] a_N, which generally is significantly larger than the coupling constant of any magnetic nucleus[3] belonging to the aryl system of the same radical anion.[4] As shown by the a_N values reported in the first study of the substituent effects on the EPR spectra of *para* substituted nitrobenzene radical anions,[5] the nitrogen coupling constant decreases with electron-withdrawing groups and increases with electron-donating groups. For example, for nitrobenzene, *p*-nitrobenzonitrile and *p*-methoxynitrobenzene in acetonitrile a_N is 10.32, 7.15, and 11.57 G, respectively. On a quantitative basis, Janzen[6] obtained a satisfactory Hammett correlation between a_N and σ^- constants. Accordingly, he described the substituent effect on a_N as due principally to a polar effect on the electron distribution within the nitro group with very little effect on the spin distribution in the aromatic system. In terms of resonance structures this means that the polar effect of a substituent, X, would influence the relative contribution of structures **A** and **B**, more than the contribution of structure **C**. An electron-withdrawing substituent, for example, is expected to decrease a_N simply because it stabilises structure **A** (possibly, when in *para* position, by direct conjugation with the nitrogen) compared to **B**, thus causing a shift of spin density from the nitrogen to the oxygen atoms.



A similar explanation would hold when heteroaromatic systems are compared to aromatic systems. As a relevant example it is worth mentioning the a_N values reported for the radical anions of 2-nitrothiazole[7] and nitrobenzene[8] in DMSO: 8.05 and 9.87 G, respectively. The lower value for the heterocyclic system is, in fact, very consistent with the polar effect of the thiazolyl ring that is controlled principally by the electron-withdrawing effect of the aza group.

Recently, paramagnetic species derived from 6-nitro-6′-piperidyl-2,2′-bisbenzothiazole and 6-nitrobenzothiazole in DMSO were characterised by EPR as the radical anions of the parent heterocyclic compounds, and the coupling constants assigned to the nitro group were 6.87 and 0.86 G, respectively.[9] The latter, however, is in principle too low for the nitro function of any nitroaromatic radical anion that is not bearing a second nitro group at a conjugate position, as for example the

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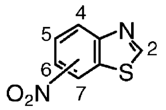
p-dinitrobenzene radical anion, which still has a larger a_N (1.53 G).[8] Moreover, comparison with the former radical anion or with that of 2-nitrothiazole[7] suggests as appropriate for 6-nitrobenzothiazole a value of a_N larger than that of either radical anion, that is 6.87 or 8.05 G, respectively. Such a prediction stems from considering that the 6′-piperidyl-2,2′-bisbenzothiazol-6-yl and the thiazol-2-yl compared to benzothiazol-6-yl would exert a stronger electron-withdrawing effect on the nitro group of related radical anions.



NBTZ

I report herein an EPR study of the radical anions obtained by means of different reductive methods from all of nitrobenzothiazole (NBTZ) isomers.[10] Treatment of each NBTZ with excess *t*-BuOK in DMSO developed a deep red-violet colouration immediately after mixing of the reagents.[12] Reproducible and readable EPR spectra were recorded, however, only in the case of 5-, 6-, and 7-NBTZ. In contrast, a fairly complicated spectrum denoting more than one paramagnetic species was immediately seen in the case of 4-NBTZ, whereas no paramagnetic resonance was detected from 2-NBTZ. Both kinds of problems, namely complexity of the spectrum or no paramagnetic resonance detected, were occasionally met also for 6-NBTZ, depending on the excess of *t*-BuOK. Because of the obvious presence of nucleophilic species in the reducing conditions (*t*-BuOK/DMSO) used, the problems with attaining persistent, 2-, 4-, and 6-$\text{NBTZ}^{\cdot-}$ might be a consequence of the known susceptibility of the parent nitrobenzothiazoles to nucleophilic attack at C-2.[13a–c] In the case of 2-NBTZ, for example, an expected rapid displacement of the nitro group,[13b] whose presence is essential for the substrate to undergo a one electron reduction, should account for the inability to detect any paramagnetic species. A ring opening of the thiazole moiety, akin to that already ascertained in the reaction of methoxide ion with 6-NBTZ in DMSO,[13c] might prevent observing single paramagnetic species in the case of 6-, and 4-NBTZ.

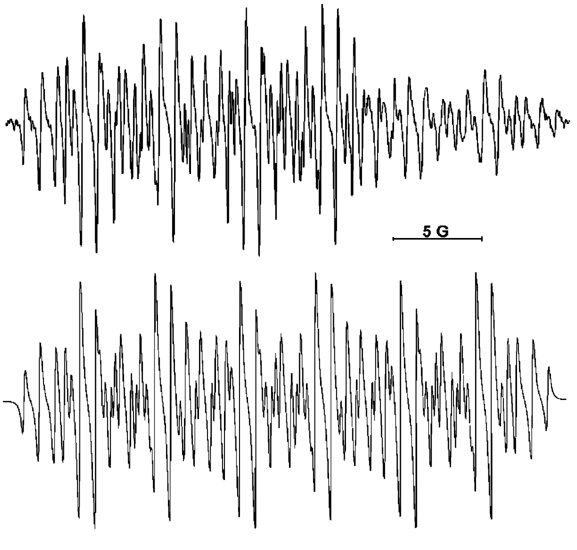


Figure 1. Experimental (above) and simulated (below) spectra of 6-$\text{NBTZ}^{\cdot-}$ obtained by reduction with *t*-BuOK in DMSO.

The electrochemical reduction of nitrobenzothiazoles in DMSO (10^{-3} M) with tetraethylammonium perchlorate (0.1 M) as supporting electrolyte, avoiding the presence of nucleophiles, proved to be of more general applicability. The electrolysed solution of each NBTZ, including 2- and 4-NBTZ, displayed a well-resolved EPR spectrum. For 5-, 6-, and 7-NBTZ this was very similar to that obtained by chemical reduction with *t*-BuOK. The spectrum of 6-$\text{NBTZ}^{\cdot-}$ is reported as an example in Figure 1. All the spectra recorded in DMSO were satisfactorily simulated on the basis of the coupling constants reported in Table 1.

Proton assignments to the various positions of nitrobenzothiazoles were based on calculations of electron spin distribution by the McLachlan's[14] procedure. The agreement between the experimental and calculated coupling constants was very satisfactory for all $\text{NBTZ}^{\cdot-}$, except for a_N (NO_2) of 2-$\text{NBTZ}^{\cdot-}$. For the sake of comparison with the previous characterisation of 6-$\text{NBTZ}^{\cdot-}$,[9] I report the calculated coupling constants for this radical anion only: a_N $(NO_2) = 9.11$, $a_4 = 0.83$, $a_5 = 1.83$, $a_7 = 4.97$, $a_2 = 2.40$ G.

Generation of $\text{NBTZ}^{\cdot-}$ was accomplished, with the only exception of the 2-isomer, also in MeOH following the Ayscough's[15] method, that is by treatment[16] of the par-

Table 1. Hyperfine coupling constants (in G) of the nitrobenzothiazole radical anions obtained in DMSO by (**a**) chemical reduction with *t*-BuOK, (**b**) electrochemical reduction

Nitrobenzothiazole	Generation method	a_N (NO_2)	a_4	a_5	a_6	a_7	a_2	a_N (N=C)
2-NBTZ	**b**	6.65	1.63	0.42	1.34	0.42		3.34
4-NBTZ	**b**	7.65		4.05	1.18	4.79	2.07	0.75
5-NBTZ	**a**	9.71	4.39		2.41	0.95	0.24	0.31
	b	9.61	4.38		2.40	0.92	0.26	0.31
6-NBTZ	**a**	9.15	0.90	2.32		4.30	2.32	0.90
	b	8.75	0.90	2.30		4.28	2.37	0.90
7-NBTZ	**a**	8.82	4.76	1.24	4.46		<ΔHpp	0.25
	b	8.75	4.78	1.23	4.47		<ΔHpp	0.25

Table 2. Hyperfine coupling constants (in G) of the nitrobenzothiazole radical anions obtained in MeOH by reduction with MeOK and glucose

Nitrobenzothiazole	a_N (NO_2)	a_4	a_5	a_6	a_7	a_2	a_N (N=C)
4-NBTZ	11.64		4.27	1.28	4.27	1.49	0.60
5-NBTZ	13.00	4.22		2.50	1.05	0.17	0.30
6-NBTZ	12.50	1.10	2.70		4.27	1.85	0.70
7-NBTZ	11.83	4.40	1.27	4.44		0.15	0.27

ent nitrocompound with MeOK and glucose. Failure in obtaining 2-NBTZ$^{\cdot-}$ was at variance with the reported case of a 2-nitrothiazole derivative,[17] but should agree with a faster nucleophilic denitration on the benzocondensated heterocyclic compound.[13b] In spite of the use of a base, the chemical reduction in MeOH was deemed potentially compatible with 6-NBTZ and 4-NBTZ, because the competitive ring opening reaction should significantly slow down in this solvent, as indicated by previous kinetic studies on the ring opening of 6-NBTZ with MeO$^-$ in DMSO-MeOH.[18] The coupling constants drawn out from the spectra recorded in MeOH were confirmed by satisfactory simulations, and are reported in Table 2. The general agreement with the spectral data of Table 1 clearly indicates that the same paramagnetic species were obtained in MeOH as in DMSO. The larger values of a_N (NO_2) measured in MeOH, however, reflect the normal solvent effect of protic solvents on the nitrogen coupling constant of a nitroaromatic radical anion.[19]

The values of a_N (NO_2) from electrochemical generated radical anions (Table 1, method **b**) allow a comparative discussion on the electron-withdrawing effect of all the benzothiazolyl systems in stabilising canonical structures akin **A** as far as the electron distribution on the nitro group is concerned. The lowest value of the series belongs to 2-NBTZ$^{\cdot-}$. This accounts for the greatest electron withdrawal of the benzothiazol-2-yl fragment due to its ability to delocalise the charge from the $NO_2^{\cdot-}$ fragment directly onto the aza nitrogen. The finding that this a_N (NO_2) is also smaller than the corresponding coupling constant of the 2-nitrothiazole[7] radical anion is telling of the important contribution given by the fused benzene ring to the π-delocalising power of benzothiazol-2-yl group. An analogous effect of the benzocondensation was invoked to explain the above mentioned enhancement of reactivity of 2-nitrobenzothiazole with respect to 2-nitrothiazole in nucleophilic denitration reactions.[13b] According to a_N (NO_2) values of the corresponding radical anions, the order of increasing delocalising ability for the other benzothiazolyl systems should be as follows: benzothiazol-5-yl < benzothiazol-6-yl, benzothiazol-7-yl < benzothiazol-4-yl. This order agrees with the increasing number of resonance structures one can draw for each heteroaryl system, taking into account only the most contributing ones, namely: (a) those leaving the aromaticity of the thiazole moiety intact; (b) those where the charge is directly delocalised onto the heterocyclic N=C function. Such a number is one for benzothiazol-5-yl[1(*a*)], two for benzothiazol-6-yl[1(*a*)+1(*b*)] and benzothiazol-7-yl[2(*a*)], and three for benzothiazol-4-yl[2(*a*)+1(*b*)].

In conclusion, the results presented confirm that the paradigm about the localisation of an unpaired electron on the nitro group in radical anions of nitroaromatic compounds holds also for nitrobenzothiazoles. Thus, any apparent violation of this paradigm, such as the previous EPR characterisation of 6-NBTZ$^{\cdot-}$,[9] should in principle cast doubt on the identity of the observed paramagnetic species.

Acknowledgements

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