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Reactivity of Halogenated Aromatic Radical Anions. Electron Spin Resonance Evidence for the Dimerization of the 6-Halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-semidiones

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The reactions of the 6-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones (6-X-BTD; X = F, Cl, Br, I) with potassium or sodium *tert*-butoxide in Me_2SO, with KOH in DMF or with *t*-BuONa in DME in the presence of crown ether afforded radicals whose ESR spectra indicate that the radical anions of the starting products dimerize. It is suggested that the observed dimeric radicals form through an initial coupling between the oxygen atom at position 3 and the carbon atom at position 6, followed by elimination of halide ions and reduction. The dimerization process is suppressed in *t*-BuOH or in DME where the halogenated semidiones are present as chelated complexes with the metal cations.

The frequently reported way in which halogenated aromatic radical anions evolve is the unimolecular fragmentation of the carbon–halogen bond to give an aryl radical and the halide ions. Several electrochemical and ESR studies on relatively long-lived radical anions such as halogenonitrobenzenes,[1] halogenobenzonitriles,[2] halogenobenzophenones,[3] (chlorostiryl)pyridines,[4] and halogenofluorenones[5] have clearly established that the identity of the halogen, as well as its position in the aromatic substrate, have a marked influence on the rate of this process. As expected on the basis of the C–X bond energies, the order of the halogen mobility is F < Cl < Br < I; moreover, the loss of the halide ion is faster for the isomer having the halogen linked to the carbon atom with higher spin density.

In a previous ESR investigation[6] concerning the reactions of 5-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones with several nucleophiles in Me_2SO, we found that 5-halogenobenzothiophenesemidiones are particularly stable radical anions; nevertheless, all but the fluoro derivative suffer a slow fragmentation in the expected direction. Extending our study to the corresponding 6-isomers (I) we noted a quite different chemical behavior which forms the subject of the present paper.

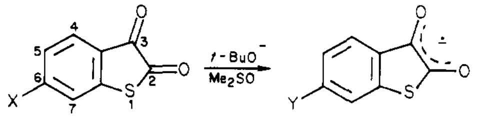
Results

When the 6-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones (6-X-BTD; X = F, Cl, Br, I; I) were treated with an excess of *t*-BuOK in Me_2SO at room temperature and the resulting solutions immediately examined by ESR spectroscopy, the spectra reported in Figure 1 were observed. Only three spectra are reported since the chloro and bromo derivatives gave almost identical resonances. In addition to a main hyperfine pattern which, according to earlier studies,[6,7] can be easily assigned to the interaction with the proton at C-4, C-5, and C-7 of the benzothiophenesemidione system, each spectrum exhibits an individual minor hyperfine structure revealing interaction of the unpaired electron with some nuclei of spin $^1/_2$. Spectrum a from 6-F-BTD shows a doublet of triplets (1:2:1), spectrum b from 6-Cl-BTD or 6-Br-BTD shows only the triplet (1:2:1), and spectrum c from 6-I-BTD shows only a quartet (1:3:3:1). The hyperfine splitting constants measured from these spectra are collected in Table I. These resonances, unlike those observed under similar conditions from 5-X-BTD,[6] cannot be attributed to the radical anions of the starting materials or to the reduction product (BTD), but they clearly indicate that new 6-substituted benzothiophenesemidiones II are formed (Scheme I). Similar results were obtained by using *t*-BuONa in Me_2SO.

Table I. Hyperfine Splitting Constants (Gauss) of the Radicals Obtained from 6-X-BTD with *t*-BuOK in Me_2SO

X	a_4	a_5	a_7	a_{ext}
F	2.45	0.67	0.80	0.09 (t), 0.24 (d)
Cl	2.45	0.67	0.82	0.09 (t)
Br	2.47	0.68	0.82	0.09 (t)
I	2.45	0.67	0.82	0.09 (q)

Scheme I



I II

The spectral features are not sufficient for an immediate elucidation of the structure of the groups Y, and we

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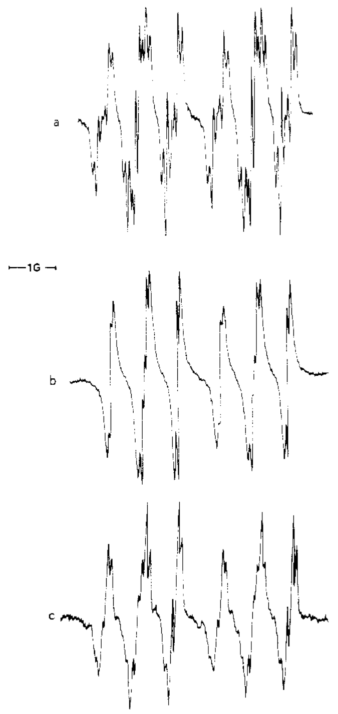


Figure 1. ESR spectra of the radicals obtained from (a) 6-F-BTD, (b) 6-Cl-BTD, and (c) 6-I-BTD by treatment with t-BuOK in Me_2SO.

Table II. Hyperfine Splitting Constants[a] (Gauss) of the Radicals Obtained from 6-X-BTD with t-BuOK or t-BuONa in t-BuOH

X	counterion	a_4	a_5	a_6	a_7	$a_{\text{counterion}}$
F	K^+	2.60	0.81	6.66[b]	0.87	
	Na^+	2.60	0.85	6.65[b]	0.85	0.17
Cl	K^+	2.58	0.85	0.15[c]	0.95	
Br	K^+	2.61	0.90		0.90	
I	K^+	2.61	0.91		0.91	

[a] Measured at 70 °C. [b] Splitting from one fluorine atom. [c] Splitting from one chlorine atom.

therefore carried out experiments under different experimental conditions.

The reactions of compounds I with KOH in DMF afforded results similar to those observed with t-BuOK in Me_2SO; ESR spectra identical with those reported in Figure 1 could be recorded, the minor differences being due to poorer resolution. This result indicates that the groups Y do not derive from the solvent or from the reducing agent.

On the contrary, when the 6-halogenobenzothiophendiones I were treated with t-BuOK in t-BuOH, spectra were recorded that, on the basis of the arguments reported below, can be assigned to the radical anions of the starting materials, present in solution as contact ion pairs with the potassium cation. The relative coupling constants, listed in Table II, were measured from spectra recorded at 70 °C in order to minimize the broadening due to the quadrupolar relaxation of the halogen atoms. Also reported in Table II are the spectral parameters of the paramagnetic species detected by reducing the 6-F-BTD with sodium *tert*-butoxide in t-BuOH. The additional quartet (0.17 G), consistent with the interaction with a sodium nucleus, is compelling evidence for the formation of a tight ion pair between the halogenated semidione and the metal cation. The coupling constants with the three protons and the fluorine atom are practically identical with those obsd. when the 6-F-BTD is treated with t-BuOK. It can therefore be assumed that in t-BuOH the halogenated semidiones are present as ion pairs also with the potassium cation, even if the coupling with the metal is not detected. This, however, is not surprising. In fact, in a parallel study[7] we have found that, in the series of chelated complexes of the unsubstituted benzothiophenesemidiones with alkali metals in DME, the potassium counterion does not give detectable coupling constants as noted for similar complexes of o-semiquinones.[8]

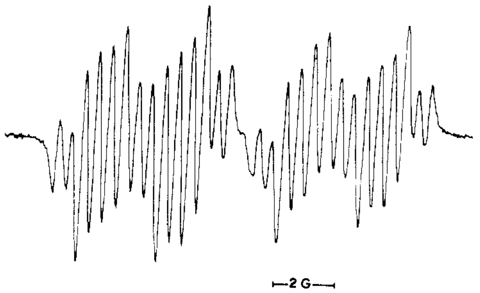
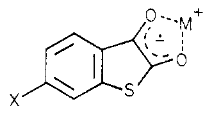


Figure 2. ESR spectrum of the radical obtained from the 6-F-BTD by treatment with t-BuONa in DME.

A final interesting experiment was carried out in DME. When 6-F-BTD was treated with t-BuONa, the spectrum reported in Figure 2 was recorded. This is clearly the spectrum of the ion pair between the 6-fluorobenzothiophenesemidione and the sodium cation. The following coupling constants were measured: $a_4 = 2.50$, $a_{5,7} = 0.82$, $a_F = 6.37$, $a_{Na} = 0.4$ G. If this experiment is affected in the presence of 18-crown-6, a spectrum is obsd. which is identical with that reported in Figure 1a obtained with t-BuOK or t-BuONa in Me_2SO.

Discussion

The results described in the previous section demonstrate that the reduction of the 6-halogenobenzothiophendiones I takes a different course as a function of the experimental conditions employed. Whenever a scarcely polar solvent is employed (t-BuOH or DME), the only paramagnetic species observed is the ion pair III which does not suffer any chemical transformation.



III

If, however, Me_2SO or DMF is used as the solvent or crown ether is added to the DME, III is not observed, and the spectra of the radicals II are obtained. The fact that the same radicals II are obtained in different solvents and with different reducing agents suggests that the groups Y derive from the substrates I. A reaction sequence which can satisfactorily rationalize this chemical behavior and explain the observed extra splittings of the spectra in Figure 1 is sketched in Scheme II.

Two radical anions (IV), presumably formed from I in Me_2SO or in DMF (even if they could not be detected), can be suggested to give a fast carbon–oxygen coupling to form, V. This dianion can now easily rearomatize by expelling the halide ion to afford the 6-substituted benzothiophendione VI which is finally reduced to the observed radical II. The suggested dimerization of the radical anion

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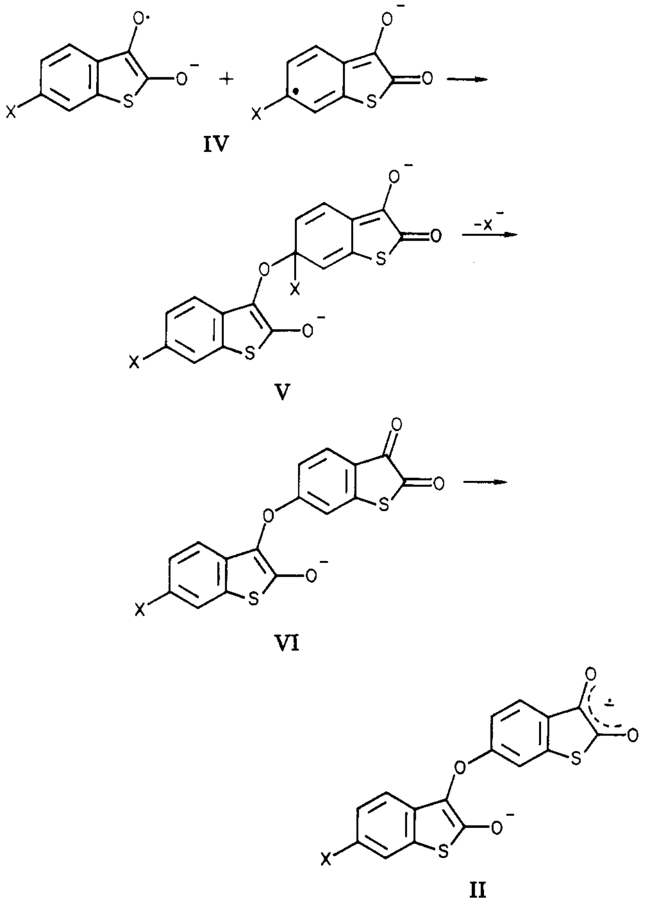
Scheme II



IV is not an uncommon process. An example of the coupling of halogenated radical anions as a reaction pathway alternative to the more frequently encountered fragmentation of the carbon–halogen bond has been reported for the electrochemical formation of 4,4′-dicyanobiphenyl from *p*-fluorobenzonitrile.[9] The peculiar behavior of the *p*-fluoro- in respect to the other *p*-halogenobenzonitrile radical anions has been attributed to its particular stability. In our case it can reasonably be suggested that such a dimerization process can occur with all the halogeno derivatives in view of the particular intrinsic stability of the benzothiophenesemidione system.

A radical coupling reaction would be favored by high spin densities at the interacting centers. While the hyperfine splitting constants of the proton at position 6 in the unsubstituted benzothiophenesemidione[6] and of the fluorine atom in the ion pair of the 6-F-BTD$^{-\cdot}$ testify for the high spin density at the carbon-6, analogous experimental evaluations of the spin densities at the two oxygen atoms are not available. For this purpose we calculated the spin-density distribution for the benzothiophenesemidione using a McLachlan perturbative modification[10] of the HMO method. As shown in Table III, these results are in excellent agreement with the experimental values.[6] High spin densities are predicted for both the oxygen atoms, the value for the oxygen at C-3 (0.237) being higher than that at C-2 (0.138). On this basis we chose the first oxygen as the most likely center for the coupling process, even though the other possibility cannot completely be ruled out.

Table III. Calculated and Experimental Spin Densities for Benzo[*b*]thiophene-2,3-semidione

position	$\rho_{\text{calcd}}{}^a$	$\rho_{\text{exptl}}{}^b$
oxygen (C-2)	0.138	
oxygen (C-3)	0.237	
4	0.086	0.097
5	−0.027	(−)0.028
6	0.116	0.113
7	−0.039	(−)0.033

[a] $h_S = 1.00$, $k_{CS} = 0.86$, $h_O = 1.20$, $k_{C=O} = 1.56$.
[b] Calculated from a_H taken from ref 6 by using $Q_{CH}{}^H = -25$ G.

The proposed structures II for the observed radicals in Me$_2$SO, DMF, and DME in the presence of crown ether can explain the ESR spectra of Figure 1. The observed extra splittings can be attributed to the benzothiophene moiety linked at the position 6. In the case of 6-F-BTD (Figure 1a) the triplet (0.09 G) and the doublet (0.24 G) can be assigned to the interaction with two of the three protons and with the fluorine atom, respectively. The triplet (0.09 G) of Figure 1b can similarly be assigned to the same two protons. In this case the couplings with the chlorine and the bromine atoms are not detectable; it is, in fact, well documented[11] that the coupling constants given by these latter halogens are considerably smaller than that given by fluorine. As far as the spectrum of Figure 1c is concerned, the presence of a quartet (0.09 G) suggests that, for the iodo derivative, the halogen atom of the group Y has been replaced by hydrogen. However, from the available results it cannot be predicted at which stage this process can occur. Further confidence in the internal consistency of these assignments comes from the comparison of a_F in Figure 1a and the corresponding proton coupling constant in Figure 1c; the value of 2.7 for the a_F/a_H ratio is close to that generally observed.[11] Finally, the smallness of the coupling constants, their accidental equivalance, and the fact that only three of the four atoms linked to the benzene ring of the group Y couple with the unpaired electron should be related to the presence in II of the bridging oxygen which precludes extensive delocalization of the unpaired electron into the substituent Y.

A chemical indirect support to the proposed mechanism for the formation of radicals II comes from the fact that whenever experimental conditions are employed in which the radical anions are present in solution as ion pairs III no reaction occurs. In this case, in fact, the strong interaction of the metal cation with the two oxygen atoms obviously inhibits the dimerization process, which, as indicated in Scheme II, occurs with the free ions IV. A striking difference in behavior is thus observed between IV and the radical anions of the isomeric 5-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones;[6] in fact, while these latter radicals evolve by fragmentation of the carbon–halogen bond (with the exception of the fluoro derivative which remains unchanged), radicals IV dimerize.

In the case of 5-halogenobenzothiophenesemidiones a dimerization similar to that reported in Scheme II is unlikely; in fact, the spin density at the C-5 is very low, and moreover, the resulting dimeric intermediate cannot be stabilized by delocalization of the negative charge onto the oxygen atoms. On the contrary, the high spin density observed at the C-6 of radicals IV can in principle favor both the processes; the results described in this paper indicate that the dimerization is a much faster reaction

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than the fragmentation of the carbon–halogen bonds.

Experimental Section

The four 6-halogeno-2*H*,3*H*-benzo[*b*]thiophene-2,3-diones were prepared by cyclization of the appropriate 3-halogenophenylthioacetic acid[12,13] according to the general procedure described by Werner et al.[14] and by subsequent oxidation of the 6-halogeno-3-hydroxybenzo[*b*]thiophene[14,15] by the method of El Shanta et al.:[16] 6-F, mp 108–111 °C (from methanol); 6-Cl, mp 134–135 °C (from methanol); 6-Br, mp 169–170 °C (from methanol); 6-I, mp 197–198 °C (from benzene). Satisfactory elemental analyses were obtained. Carbonyl adsorptions were recorded at 1725 cm^{-1} (CS_2). Solid potassium *tert*-butoxide and hydroxide were commercial materials while sodium *tert*-butoxide was prepared by a standard method. Reagent grade solvents were utilized without further purification with the exception of dimethyl sulfoxide which was distilled under reduced pressure from calcium hydride and stored over molecular sieves.

Radical anions, detected with a Varian E-109 spectrometer, were simply generated in capillary glass tubes by adding the solvent to the solid reagents. Degassing of the solutions resulted neither in any improvement of the quality of the ESR spectra nor in any change of the observed reactivity.

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Registry No. I (X = F), 73655-11-5; I (X = Cl), 50789-28-1; I (X = Br), 73655-14-8; I (X = I), 73655-16-0; I (X = H), 493-57-2; II (X = F) K^+, 75750-94-6; II (Y = F) Na^+, 75716-07-3; II (Y = Cl) K^+, 75716-08-4; II (Y = Br) K^+, 75716-09-5; II (Y = I) K^+, 75716-10-8.

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Gas-Phase Synthesis of Nitriles

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n-Octanenitrile is obtained in 87% yield from the copper-catalyzed, gas-phase reaction of 1-octanol with ammonia at 325 °C and 1 atm. Similar high yields of alkyl or aryl nitriles are obtained from the reaction of ammonia with primary alcohols, aldehydes, primary amines, secondary amines, and esters. The effect of reaction variables is examined: highest yields of nitriles are obtained when the reaction is carried out at ca. 300 °C and at ammonia to substrate ratios of greater than 10:1. The 15% Cu/Al_2O_3 case was examined most extensively, but vanadium, iron, and nickel also show selectivity to nitriles while manganese and antimony give only very small amounts of these products.

A number of methods have been developed for the synthesis of organic nitriles. Although it is often possible to convert a specific functional group into a nitrile group, no convenient, general method of synthesis has been reported.

Approaches to nitrile synthesis may be divided into two distinct groups. The first generally involves the use of cyanide as a nucleophile and results in the formation of an organic nitrile containing one more carbon atom than the starting material. Several modifications in this methodology have appeared recently. The reaction of potassium cyanide with alkyl halides is facilitated by the use of crown ether in acetonitrile solvent[1] or by the use of hexamethylphosphoramide solvent with or without added crown ether.[2] The reaction of *n*-alkyl bromides with sodium cyanide impregnated onto alumina allows the small-scale synthesis of aliphatic nitriles in hydrocarbon solvent,[3] and aryl nitriles are formed from the reaction of aryl halides with sodium cyanide in the presence of catalytic amounts of nickel phosphine[4] or palladium phosphine[5] complexes.

An alternative approach involves the conversion of an organic compound into a nitrile containing the same total number of carbon atoms. One example involves the conversion of aliphatic primary alcohols to nitriles over a fused iron catalyst[6] (eq 1). Nitriles have also been obtained from

$$n\text{-}C_4H_9OH + NH_3 \xrightarrow[320\ ^\circ C,\ 1\ atm]{\text{“Fe”}} \underset{85\%}{n\text{-}C_3H_7C{\equiv}N} \qquad (1)$$

the ammoxidation of aldehydes, ketones,[7] and benzylic or allylic methyl groups,[8] but these reactions require severe conditions (usually >400 °C). Aryl nitriles are obtained from the reaction of aryl aldehydes with ammonia and an excess of nickel peroxide.[9] Methods have also appeared for the conversion of amides to nitriles,[10] the dehydration of aldoximes,[11,12] the synthesis of nitriles from nitro compounds,[13] and the synthesis of nitriles via the reaction of sulfimide with aldehydes.[14]

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