Electron Spin Resonance Studies of Electron Capture Processes. Part 7.[1] σ^* (3-Electron Covalent Bond) Radical Anions of Halogenoimidazoles

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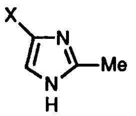
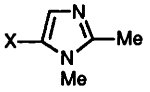
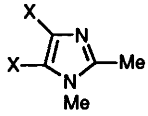
Exposure of dilute solutions of 4-bromo- and 4-iodo-2-methylimidazole, 5-bromo- and 5-iodo-1,2-dimethylimidazole, and 4,5-dibromo- and 4,5-di-iodo-1,2-dimethylimidazole [(**1**)–(**6**)] in methanol (CD_3OD) or methyltetrahydrofuran (MeTHF) to ^{60}Co γ-rays at 77 K resulted in electron addition to yield not the expected π^* radical anions but σ^* radicals anions. In these radical anions the SOMO is primarily the C–Hal σ^* molecular orbital with little delocalisation into the imidazole ring, *i.e.* a 3-electron σ bond. On slowly increasing the temperature of the MeTHF solutions of the bromoimidazoles the hyperfine features for the σ^* radical anions were lost but with no clear concommitant growth of features assignable to 4- or 5-imidazolyl radicals. However, for the iodoimidazoles (**2**), (**4**), and (**6**) in CD_3OD a new species was observed on annealing. The same species was observed for all three iodo compounds and is assigned to iodine atoms weakly bonded to CD_3OD molecules $[\mathrm{I}\dot{-}\mathrm{O(D)CD_3}]$. The results are discussed in the light of the σ^* and/or π^* species obtained from electron capture by other aromatic halides and other substituted imidazoles.

Until relatively recently it has been supposed that organic compounds containing carbon-halogen (Cl, Br, I) bonds undergo direct dissociative electron-capture to give carbon-centred radicals and halide anions. However, under certain conditions it has been possible to isolate and study species containing three σ-electrons.[2] A key factor in the quest for such species has been the selection of compounds having approximately sp^2 hybridised carbon orbitals in cyclic systems for which major changes in orbital energy on dissociation are prevented.[3] Examples of such σ^* species are $(\mathrm{Ph}\dot{-}\mathrm{I})^-$,[5] $[\mathrm{C_6F_5}\dot{-}\mathrm{Hal}]^-$,[5] and various halogenouracil radical anions.[6] In a preliminary communication we have suggested that such radicals can also be isolated in solid matrices at low temperatures from various halogenoimidazoles.[7] The results from ESR spectroscopy are very similar to those for other such σ^* species in this class.


(**1**) X = Br
(**2**) X = I


(**3**) X = Br
(**4**) X = I


(**5**) X = Br
(**6**) X = I

The importance of σ^* $(\sigma_1^2\sigma_2^1)$ radicals as major intermediates has only recently been clearly recognised,[8] although they have been known for many years. Probably the first examples of this class of radicals are the V_K centres, such as $[\mathrm{Cl{-}Cl}]^-$, formed in alkali halide crystals.[9] They can be formed either by electron addition into the pertinent σ orbital, or by electron loss followed by bonding, as in the case of $[\mathrm{Cl}\dot{-}\mathrm{Cl}]^-$ [equations (1) and (2)]. In general, 'dimerisation' as in equation (3) is favoured over equation (2), except that first-row dimers, other than $[\mathrm{F}\dot{-}\mathrm{F}]^-$, are remarkably rare.[10] (We illustrate these reactions with neutral precursors; obviously anionic precursors, such as Cl^- can undergo the set of reactions). In the present study, besides forming σ^* species by electron addition, we have formed them by the sequence of reactions (1) and (2). Both types of radical fall into the $[\mathrm{A}\dot{-}\mathrm{B}]^-$ (σ^*) class, one atom contributing to the σ^* orbital being a first-row species.

$$\mathrm{A}\!: \longrightarrow \mathrm{A}^{+\bullet} + e^- \qquad (1)$$

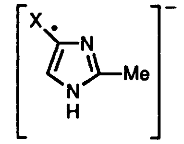
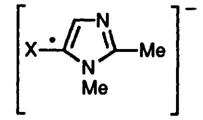
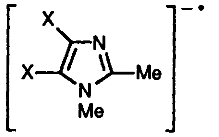
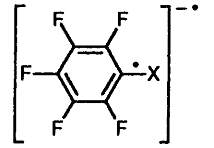
$$\mathrm{A}^{+\bullet} + \mathrm{B}\!: \longrightarrow [\mathrm{A}\dot{-}\mathrm{B}]^+ \qquad (2)$$

$$\mathrm{A}^{+\bullet} + \mathrm{A}\!: \longrightarrow [\mathrm{A}\dot{-}\mathrm{A}]^+ \qquad (3)$$

We have successfully used 'temperature resolved' ESR spectroscopy to study neutral radical and radical anion intermediates in various reactions proceeding by single electron transfer. The application of these techniques to $S_{RN}1$ (substitution, radical-nucleophilic, unimolecular) reactions has proved especially useful and has provided evidence for the structure and reactivity of various reactive intermediates which could not easily be obtained by other methods. We have applied the ESR techniques to the $S_{RN}1$ reactions of 2-substituted-2-nitropropanes,[11] *p*-nitrobenzyl- and *p*-nitrocumyl-derivatives,[12] α-substituted 2-methyl-2-nitrofurans,[13] and α-substituted 1,2-dimethyl-5-nitroimidazoles.[1] We have also used the technique to provide evidence[1] for the structures of the radical anions of 2- and 5-nitroimidazoles which are putative intermediates in the antimicrobial activity of these compounds. The extension of these latter studies[1] to the 4- and 5-halogenoimidazoles [(**1**)–(**6**)] is reported in this paper.

We are also interested in using ESR spectroscopy to study the intermediates proposed in the liquid solution studies of the reactions involving the reduction of halogenoimidazoles.[7,14] ESR spectroscopy of matrix-isolated radical anions and neutral radicals at low temperature[2] has provided evidence for these unstable species. Ionizing radiation from a ^{60}Co γ-ray source is used as the source of electrons, and achieves electron addition to suitable substrates. The resulting stable adducts are rendered immobile in solid matrices, thereby often allowing observation of first-formed species, and, for strongly coupled nuclei, anisotropic coupling constants are obtained which lead to good estimates of spin density. The disadvantage is that the lines may be broad and smaller hyperfine splittings are often not resolved. By using solvents such as CD_3OD and MeTHF,

Table. ESR parameters for σ*radical anions.

Radical anion	Solvent	Nucleus (X)	Hyperfine coupling/G[a]			Orbital populations (%)	
			$A_{\parallel}$	$A_{\perp}$	A_{iso}[b]	a_s^2	a_p^2
	MeTHF	^{81}Br	487	133	251	3	48
		^{127}I	560	260	360	5	44
4-halogeno	CD_3OD	^{81}Br	425	110	215	2.5	42.5
	MeTHF	^{81}Br	433	153	246	3	38
		^{127}I	520	240	333	4.5	41
5-halogeno	CD_3OD	^{81}Br	356	100	185	2.2	34
	MeTHF	^{81}Br	485	130	248	3	48
		^{127}I	560	260	360	5	44
4,5-dihalogeno[c]	CD_3OD	^{81}Br	356	100	185	2.2	34
5-[X∸Uracil]$^-$ [d]	MeTHF	^{81}Br	373	143	220	2.5	31
		^{127}I	505	220	315	4.5	42
[e] 	MeTHF	^{81}Br	503	180	288	3.5	44
		^{127}I	540	230	333	4.5	46
[Ph∸I]$^-$ [f]	MeTHF	^{127}I	540	230	333	4.5	45.6

[a] 1 G = 10^{-4} T. [b] Using $A^0(^{81}Br)$ = 8 341 G, $2B^0$ = 493 G, $A^0(^{127}I)$ = 7 294, $2B^0$ = 453 G. [c] Comparison of the data strongly suggests that the electron adds into the C-4 halogen site for the dihalides. [d] Ref. 6. [e] Ref. 5. [f] Ref. 4.

it has been established[2] that the major reaction exhibited by dilute solutes is electron addition. This 'temperature resolved' technique is fully described in the literature.[2]

Results and Discussion

Identities of Radicals.—We have focused our attention on the radicals characterised by large hyperfine couplings to bromine or iodine nuclei (Table and Figures 1, 2, and 3). These have been generated in cold MeTHF and CD_3OD matrices under conditions that very strongly favour addition. With both matrices, in the absence of any electron-attracting molecules, the electrons are weakly trapped in solvent vacancies to give e_t^- units having intense blue (MeTHF) or violet (MeOH) colours. These colourations were completely suppressed in the imidazole solutions showing that electron capture is an important process here.

The ESR results show unambiguously that one expected reaction *i.e.* dissociative electron capture, does not occur at 77 K, and that, for the anions formed, there is an extremely large hyperfine coupling to bromide or iodine in all cases. This rules out the π* radical anions, leaving σ* radical anions as the only reasonable species. These are, in all cases (Table) the major products. It is possible that the π* species are also formed, since their ESR spectra could be concealed by signals from solvent radicals. However, inspection shows that they cannot be major products.

The σ* radical anions are thought to have 3-electron σ-bonds as indicated in Figure 4(*a*). From the halogen hyperfine coupling constants we have estimated very approximate s- and p-orbital spin densities in the usual way.[15] The results show that, as expected, there is only a small s-orbital contribution, the σ* bond comprising primarily the p_z halogen orbitals.

Comparisons between 4- *and* 5-*Bromo Derivatives.*—The spin density on bromine is clearly higher for the 4-bromo derivative (Table). This could imply that dissociation towards bromide anion formation is less developed for the 4-bromo derivative, or that the carbon orbital is deeper (closer to the bromine level) for the 4-bromo rather than the 5-bromo derivative. It is not obvious to us why this should be the case, and we favour the former explanation [Figure 4(*b*)].

Changing solvent from MeTHF to CD_3OD has almost no effect on the 4-bromo derivative, but there is a clear fall in hyperfine coupling to bromine for the 5-bromo derivative. The latter result suggests that solvation of the bromine by CD_3OD has increased the incipient Br^- character. Absence of any solvent effect for the 4-bromo derivative accords with the suggestion that Br^- character is less developed in this case.

The bromine hyperfine coupling for the 4,5-dibromo derivative is far closer to the 4-bromo rather than the 5-bromo derivative. This suggests that the unpaired electron is strongly localised in the C_4–Br σ* orbital. Electron-transfer between

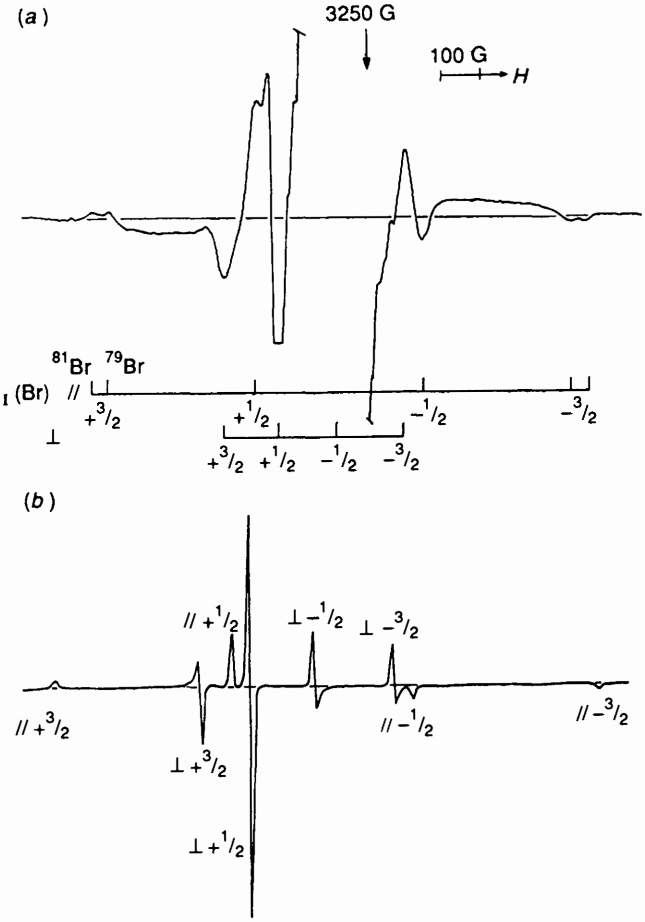


Figure 1. (*a*) First-derivative X-band ESR spectrum of a dilute solution of 5-bromo-1,2-dimethylimidazole in MeTHF after exposure to ^{60}Co γ-rays and annealing to remove some solvent signals. Spectrum shows features assigned to the corresponding σ* radical anion. Central features due to solvent radicals are not shown. (*b*) Computer reconstruction using the tabulated data: only the ^{81}Br spectrum is given, and the features are narrow so that the form of the spectrum is explained. Inclusion of the ^{79}Br and selective line broading gives a good fit.

the two adjacent σ* orbitals might have been expected. If this were rapid on the ESR time-scale, the data would lie between those for the 4- and 5-bromo derivatives, and have hyperfine features for two bromine nuclei, which is not the case. If such transfer were slow, two species would have been detected. In fact, only one centre is clearly defined. Thus it seems that the C_4–Br site is the most stable.

A 1:1 mixture of 4- and 5-bromo-1,2-dimethylimidazole gave signals for only the radical anion of the 4-bromoimidazole, again indicating that the C_4–Br bond has a stronger electron affinity than the C_5–Br bond and that electron-transfer from the 5-bromo- to the 4-bromo-imidazole must be favoured.

The 4- *and* 5-*Iodo Derivatives.*—Again, the spin density on the iodine for the electron-adducts in MeTHF is greater for the 4-halogeno derivative in accordance with the concept that the 5-iodo derivative has moved further along the reaction co-ordinate than the 4-iodo derivative. Also, the di-iodo derivative gave a species having resolved hyperfine coupling to only one iodine nucleus, the data being much closer to those for the 4-iodo than those for the 5-iodo compound. Thus the results for bromine and iodine are consistent. In CD_3OD a reaction discussed below interfered with our studies of the parent radical anions.

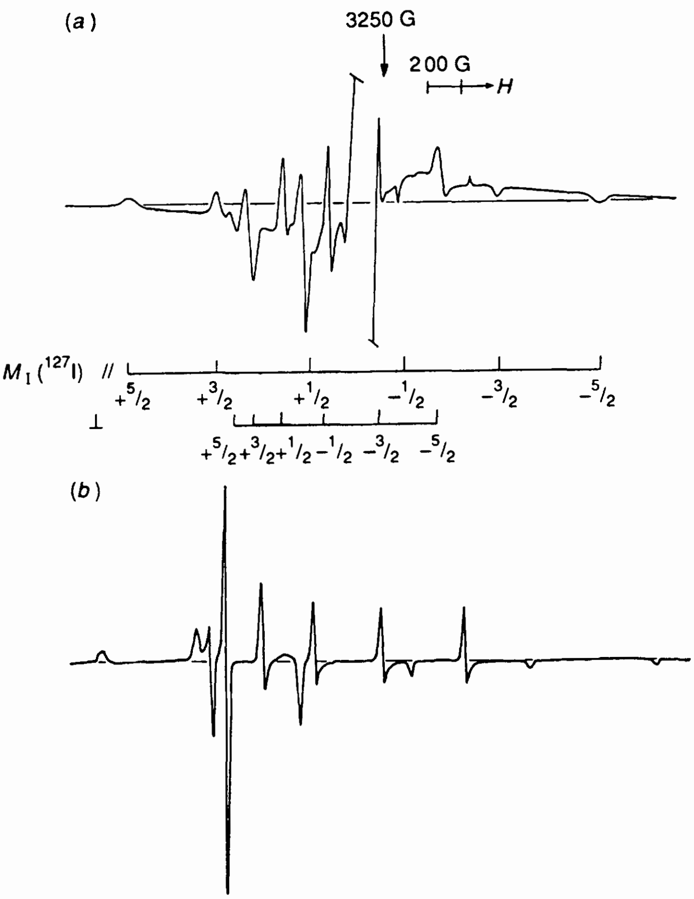


Figure 2. (*a*) First-derivative X-band ESR spectrum of a dilute solution of 1,2-dimethyl-5-iodoimidazole in MeTHF after exposure to ^{60}Co γ-rays and annealing to remove solvent signals, showing features assigned to the corresponding σ* radical anion. Central features are due to solvent radicals. (*b*) Computer reconstruction using narrow features to illustrate the form of the spectrum. A reasonable fit is obtained when these features are selectively broadened.

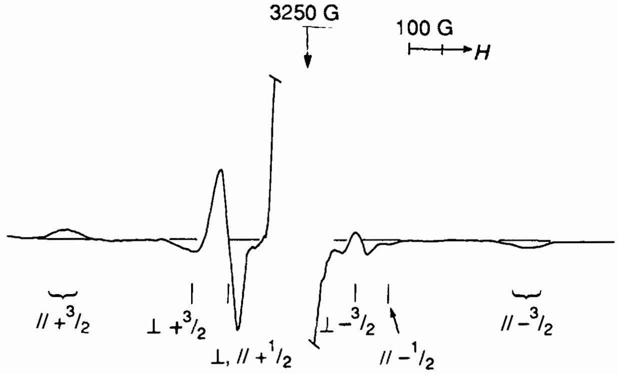


Figure 3. First-derivative X-band ESR spectrum for a dilute solution of 4-bromo-2-methylimidazole in CD_3OD after exposure to ^{60}Co γ-rays and annealing to remove solvent signals, showing features assigned to the corresponding σ* radical anions.

Reactions of the σ* *Radical Anions.*—Using a MeTHF matrix, the species having the large hyperfine coupling constants decayed on annealing above *ca.* 120 K and broad unresolved singlets were revealed at *ca.* $g = 2$ after loss of solvent radicals. These are probably the imidazol-4-yl and -5-yl centres formed by loss of halide ions (*e.g.* Scheme), but the

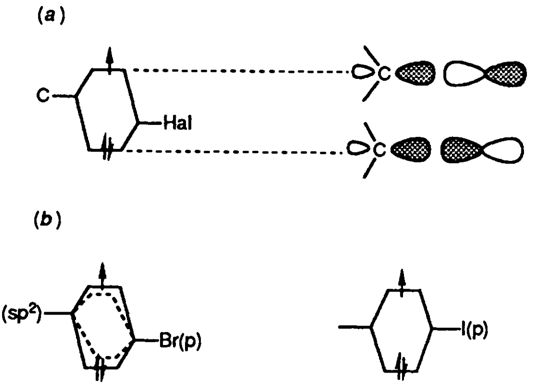
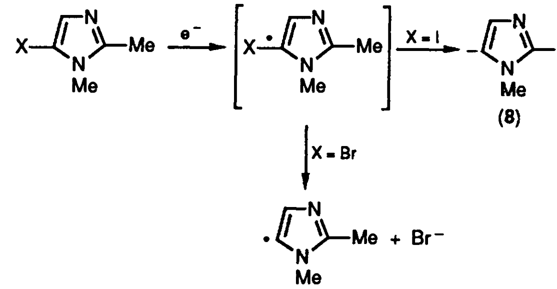


Figure 4. (*a*) Qualitative energy level diagram for σ* radical anions with three-electron bonds. (*b*) Qualitative energy level diagram for bromo and iodo radical anions. The dashed line indicates the effect of increasing the C–Br bond length (see text).



(8)

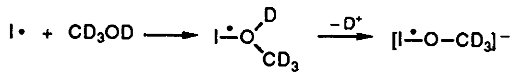
(7)

Scheme. Formation of the radical anions of 5-halogeno-1,2-dimethylimidazoles and their dissociation processes.

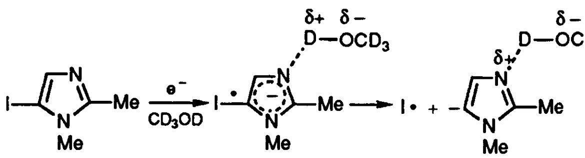
absence of resolved structure makes this identification tentative. The products from the dibromo and di-iodo anions had considerably broader spectra, but still no resolved structure. The imidazol-4-yl radical would be expected to give a nitrogen coupling of *ca.* 30 G by comparison with the 2-pyridyl radical.[16] The imidazol-4-yl radical is predicted to be more stable than the -5-yl radical because of overlap of the σ orbital of the radical with the sp^2 lone pair of electrons on N-3.

Similar results were obtained for the bromine derivatives in CD_3OD on annealing. However, for the iodo derivative a novel iodine centre was obtained, which was identical for all three compounds. Results with other iodine containing compounds[17] strongly suggest that this spectrum is due to iodine atoms weakly bonded to solvent molecules $[\mathrm{I}\dot{-}\mathrm{O(H)Me}]$ or possibly $[\mathrm{I}\dot{-}\mathrm{OMe}]^-$ [*e.g.* equation (4)]. This suggests that whilst the bromo derivatives in CD_3OD dissociate to give imidazolyl radicals [*e.g.* (**7**)] plus bromide ions, the iodo derivatives give imidazolyl anions [*e.g.* (**8**)] (see Scheme). These anions are expected to be rapidly protonated by solvent after dissociation. Since these reactions did not occur in MeTHF, strong anion solvation is invoked to explain the results. The interpretation of these 'iodine-atom' spectra will be presented elsewhere.[17]

We have previously invoked such solvation of partially formed halide ions to explain the greater dissociation often found for solutions in methanol matrices.[18] In the present case we suggest that such incipient solvation is stronger on the imidazole side of these radical anions. The most likely centre for solvation is the di-bonded nitrogen. Strong hydrogen bonding at this nitrogen [*e.g.* (**9**)] could tip the scales to favour iodine formation [equation (5)], provided the balance of spin densities is fairly evenly disposed between carbon and iodine, as indeed the results suggest.



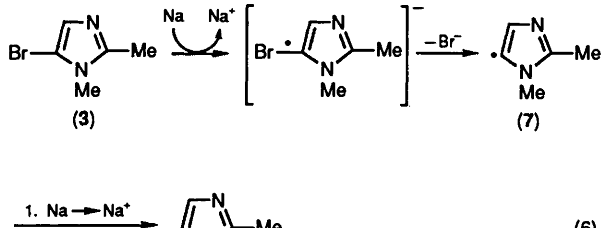
$$\mathrm{I}\bullet + \mathrm{CD_3OD} \longrightarrow \mathrm{I}\dot{-}\mathrm{O}{<}^{\mathrm{D}}_{\mathrm{CD_3}} \xrightarrow{-\mathrm{D}^+} [\mathrm{I}\dot{-}\mathrm{O{-}CD_3}]^- \qquad (4)$$



(4) (9) (5)

Attempted Nitrite Addition to Imidazol-5-yl Radicals.—We have previously used nitrite ions to trap intermediate radicals in solid matrices.[19] In these studies 2-nitroprop-2-yl radicals, resulting from the dissociation of the radical anions of 2-bromo-2-nitropropane, were trapped with added nitrite to yield the radical anions of 2,2-dinitropropane. Because the imidazolyl radicals could not clearly be identified, we attempted to use the same method in the hope that nitrite ions would add to the intermediate imidazol-5-yl radicals to give the clearly identifiable radical anions of 1,2-dimethyl-5-nitroimidazole.[1] When the bromoimidazole (**3**) was irradiated in the presence of added nitrite ions a large number of signals were obtained in the ESR spectrum. Unfortunately possible signals for the expected radical anion were masked by signals of radiation products from nitrite itself.

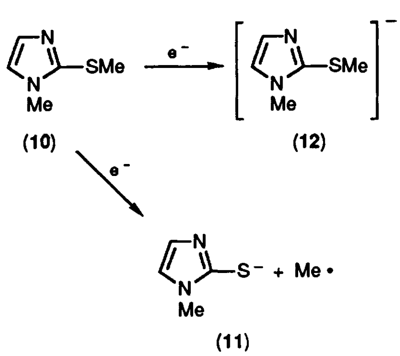
Correlation with Liquid Solution Studies.—One of the important uses[1,2,7,11–14] of 'temperature resolved' ESR spectroscopy is the provision of information regarding the structure of reactive intermediates which cannot be obtained by other methods. The radical anions of 5-bromo- and 5-iodo-1,2-dimethylimidazole and 1,2-dimethylimidazol-5-yl radicals have been proposed as reactive intermediates in the reduction reactions of 5-halogenoimidazoles.[7,14] For example, the reduction of 5-bromo-1,2-dimethylimidazole in sodium–liquid ammonia–t-butyl alcohol was shown to proceed *via* electron addition to form a radical anion which dissociated to the imidazol-5-yl radical and finally by further reduction to yield 1,2-dimethylimidazole [equation (6)].[7,14] The intermediacy of the imidazol-5-yl radical was proved by intramolecular trapping with an *N*-butenyl group in the reduction of 5-bromo-1-(but-3-en-1-yl)-2-methylimidazole.[7,14] Therefore, the use of ESR spectroscopy provides evidence for the intermediacy of the proposed halogenoimidazole radical anions and probable evidence for the dissociation to imidazolyl radicals.



(3) (7) (6)

Unfortunately the cyclisation method could not be used on the iodo-analogue to indicate whether the intermediate radical anion dissociates to the imidazolyl radical (**7**) or anion (**8**) (as indicated by the results from ESR spectroscopy). The different route of dissociation for iodo- and bromo-imidazoles is not unexpected because the tendency for dissociation of (R–Hal)$^-$ to proceed to R$^-$ and X$^\cdot$ rather than to R$^\cdot$ and X$^-$ is in the order: I > Br > Cl.[5]

Radical Anions of Other Substituted Imidazoles.—The radical anions of 2-, 4-, and 5-nitroimidazoles have been extensively studied[1] and are remarkably stable. The radical anions of 4- and 5-nitroimidazoles have similar SOMOs with *ca.* 46% of the spin density localised on the nitrogen atom of the nitro group and *ca.* 20% on the adjacent C-4 or C-5 carbons, whereas the radical anions of 2-nitroimidazoles have *ca.* 34% on the nitrogen of the nitro group. We also studied the radical anions of 1-methyl-2-thiomethylimidazole (**10**) at low temperature. The ESR spectrum showed that (**10**) underwent dissociative electron capture to yield methyl radicals and thiolate (**11**) [equation (7)]. This behaviour is typical of aliphatic thioethers. The spectrum also showed an 11 G doublet with low *g* indicating low spin density on sulphur. The best interpretation is that the radical anion (**12**) has a π* SOMO with very high density on C-4 or C-5 but not both. Therefore, in contrast to the halogenoimidazoles there is no clear evidence for a (C∸SMe)$^-$ σ* radical anion.



(7)

Studies on the radical anions of nitrosoimidazoles are underway.

Experimental

ESR Studies.—Degassed samples were irradiated as dilute solutions (*ca.* 1% v/v) in methanol (CD_3OD was used to avoid overlap with solvent features) or MeTHF. They were frozen as small beads in liquid nitrogen and irradiated at 77 K in a Vickrad ^{60}Co γ-ray source to doses of up to 1 Mrad. ESR spectra were measured on a Varian E109 spectrometer. Samples were annealed to selected temperatures or until significant changes occurred in the ESR spectra, and recooled to 77 K for study.

Materials.—4(5)-Bromo-2-methylimidazole[20] and 4(5)-iodo-2-methylimidazole[21] were prepared by sodium sulphite reduction of the corresponding 4,5-dihalogeno-2-methylimidazoles. 4,5-Dibromo-2-methylimidazole[22] and 4,5-di-iodo-2-methylimidazole[20] were prepared by bromination and iodination respectively of 2-methylimidazole. 4,5-Dibromo- and 4,5-di-iodo-1,2-dimethylimidazole[23,24] were prepared by methylation of the respective 4,5-dihalogeno-2-methylimidazoles with dimethyl sulphate in ethanolic NaOH. 5-Bromo-1,2-dimethylimidazole and 1,2-dimethyl-5-iodoimidazole were prepared by methylation of the respective 4(5)-halogeno-2-methylimidazoles with methyl *p*-toluenesulphonate at 140 °C.[14] 1-Methyl-2-(methylthio)imidazole was prepared by methylation of 2-mercapto-1-methylimidazole with methyl iodide.[25]

Acknowledgements

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