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ELECTRON ADDITION TO HALOGEN DERIVATIVES OF IMIDAZOLES

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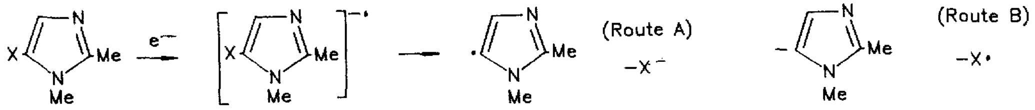
Summary: Exposure of various bromo- and iodo-imidazoles as dilute solutions in methanol or methyltetrahydrofuran at 77 K to ^{60}Co γ-rays resulted in electron addition to yield major species which were not the expected π^* radical anions but σ^* radical anions, the SOMO being primarily the C-hal σ^* orbital with little delocalisation.

"Temperature resolved" e.s.r. spectroscopic techniques have been successfully applied to the study of electron capture by 4- and 5-nitro-imidazoles.[1] In this paper we report the extension of our studies to 4- and 5-halogeno-imidazoles (*e.g.* Routes A and B).



In these studies ionizing radiation is used as a source of electrons. An excellent method of achieving electron addition, resulting in stable adducts, is to use low temperature solid solutions such that primary products are rendered stable by imobility. Ideal solvents for encouraging electron capture by solutes are methanol (usually CD_3OD for e.s.r. studies) and methyltetrahydrofuran (MeTHF). These give glassy solutions at 77 K. Electron-loss centres are stabilised as solvent radicals, but electrons are able to migrate to the solute with little competition from the solvent.[2,3]

When halogen derivatives are so treated at least four limiting reactions may occur, either consequentially or concurrently (Reactions 1-4).

$$\text{R-hal} + e^- \longrightarrow (\cdot\text{R-hal})^- \qquad (1)$$

$$\text{R-hal} + e^- \longrightarrow (\text{R}\overset{\cdot}{—}\text{hal})^- \qquad (2)$$

$$\text{R-hal} + e^- \longrightarrow \text{R}\cdot + \text{hal}^- \qquad (3)$$

$$\text{R-hal} + e^- \longrightarrow \text{R:}^- + \text{hal}\cdot \qquad (4)$$

Reaction (1) is expected if R contains unsaturated units having low-lying LUMOs (generally π^* for 'aromatic' derivatives). Reaction (2), which represents electron-capture by the R-hal σ^* orbital without bond breakage, is generally envisaged as a required intermediate process for reactions (3) and

(4). For alkyl halides there is argument about the possible stability of the σ^* radical anions, but in our view the wealth of e.s.r. evidence suggests that these species usually have no significant stability.[2,3] One of us has suggested that in systems in which the R-group is unable to flatten during the C-hal bond breaking process, there might be a greater tendency for the σ^* radical anion to be stable.[2,3] This should be augmented by the presence of electronegative substituents which will lower the σ-orbital energy on carbon, thereby making the orbital closer in energy to the p_σ-orbital on the halogen. Such R-groups are phenyl and related units[4,5] where the ring maintains strong *s-p* hybridisation.

__Results__: Our interest in radical species of imidazoles[1] led us to explore the mode of electron addition to a range of halogenoimidazoles (Table 1). In all cases the e.s.r. spectra are dominated by features characteristic of hyperfine coupling to the halogen, covering a wide field range (Figures 1 and 2).

Analysis of these spectra gives hyperfine coupling constants (^{81}Br:^{127}I) which are characteristic of σ^* species (Table 1), and we think the assignment is unequivocal. There may be concomitant formation of π^* radical anions in low yield, but no good e.s.r. evidence for this was obtained at 77 K.

On slowly increasing the temperature, for MeTHF solutions the hyperfine features for the σ^* radicals were lost close to the melting point of the solvent, with no concomitant growth of features assignable to the 4- or 5-imidazolyl radicals. For the iodo-derivatives (but not the bromo-derivatives) in CD_3OD however, a second set of hyperfine features exhibiting an increased *g*-shift were detected, on annealing. These were identical for the three iodides studied, and are tentatively assigned to iodine atoms weakly bonded to CD_3OD molecules ($I \overset{\cdot}{-} O(D)CD_3$). A second possibility for this species

Figure 1

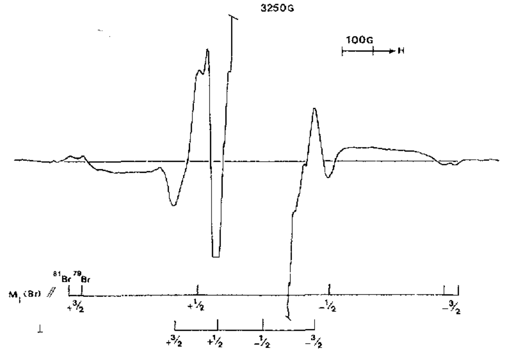
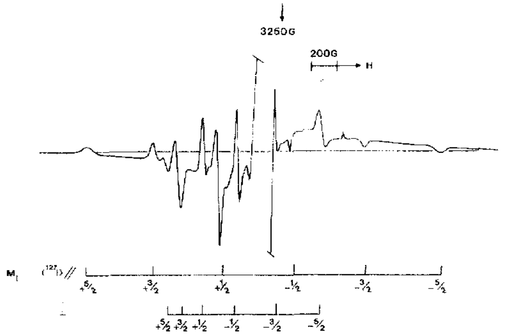
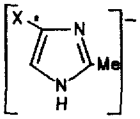
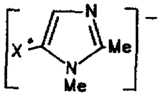
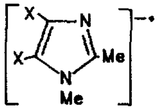
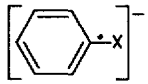


Figure 2



__Figures__. First derivative X-band e.s.r. spectra for dilute solutions of 5-bromo-1,2-dimethylimidazole in MeTHF (Figure 1) and 1,2-dimethyl-5-iodo-imidazole in MeTHF (Figure 2) after exposure to ^{60}Co γ-rays at 77 K and annealing to remove solvent signals, showing features assigned to the corresponding radical anions.

TABLE 1. Some e.s.r. parameters for σ^* C-hal radical anions.

Radical anions		X	Nucleus	Hyperfine coupling/G[a] [b]	
				$A_\parallel$	$A_\perp$
	(4-halo)	Br	$^{81}\mathrm{Br}$	487	133
		I	$^{127}\mathrm{I}$	560	260
	(5-halo)	Br	$^{81}\mathrm{Br}$	433	153
		I	$^{127}\mathrm{I}$	530	240
	(4,5-dihalo)[c]	Br	$^{81}\mathrm{Br}$	480	130
		I	$^{127}\mathrm{I}$	560	260
5-$[\mathrm{X}\overset{\cdot}{—}\mathrm{Uracil}]^-$	[d]	Br	$^{81}\mathrm{Br}$	373	143
		I	$^{127}\mathrm{I}$	505	220
	[e]	Br	$^{81}\mathrm{Br}$	503	180
		I	$^{127}\mathrm{I}$	540	230

[a] 1 G = 10^{-4}T. [b] Results for $\mathrm{CD_3OD}$ and MeTHF were similar, but the extra iodo derivatives discussed in the text only appeared using $\mathrm{CD_3OD}$.
[c] Comparison of the data strongly suggests that electron addition into the C(4)-hal site only for the dihalides. [d] Ref. 4. [e] Ref. 5.

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is the radical anion, $(\mathrm{CD_3O}\overset{\cdot}{—}\mathrm{I})^-$, formed by proton loss. Thus, for the iodides, it seems that reaction by both Route A and Route B can occur.

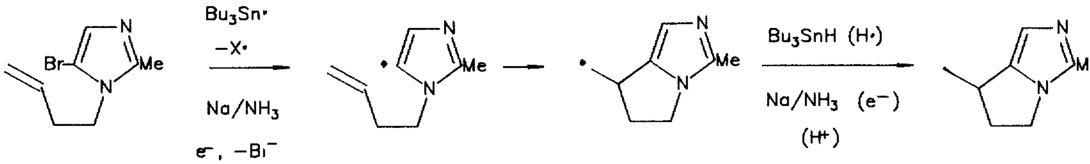
We stress that the results unequivocally establish electron addition onto the C-hal σ^* orbital, despite expectation that π-addition would occur. These are direct precursors to dissociation, but, at least for the iodo compounds, this gives solvent stabilised iodine atoms rather than/or in addition to iodide anions. The tendency for dissociation of $(\mathrm{R}\overset{\cdot}{—}\mathrm{X})^-$ to proceed to R^- and X·, rather than to R· and X^-, is favoured in the order: I > Br > Cl. Therefore it is likely that the iodo radical anions dissociate by reaction 4, but that the bromo radical anions dissociate by reaction 3. This is supported by the absence of any Br·/solvent adduct, and by liquid solution studies.[2]

It appears that the imidazole ring stabilises the C-I and C-Br σ^* radical anions in like manner to iodouracil[4] and iodopentafluorobenzene.[5] In contrast, $(\mathrm{PhI})^{-\cdot}$ exists as a π^* species under these conditions, but converts to a detectable σ* species before dissociating.[5]

Liquid solution studies provided further evidence for the intermediacy of the radical anions of 5-bromo- and 5-iodoimidazoles in reduction reactions. Reduction of 5-bromo- and 5-iodo-1,2-dimethylimidazole in Na/NH_3:t-BuOH[6] (3 equiv. Na, 5 min, NH_3 reflux) gave 1,2-dimethylimidazole (48 and 15% respectively). The radical anion of the bromoimidazole resulting from electron capture is likely to dissociate by Route A to yield the 1,2-dimethylimidazol-5-yl radical, which on further reduction yields the 1,2-dimethylimidazol-5-yl anion, whereas the 5-iodo radical anion is likely to dissociate largely by Route B to the anion.

Reduction of these halogenoimidazoles with Bu_3SnH[7] (5 equiv. Bu_3SnH, N_2, cat.AIBN, refluxing toluene) also yields 1,2-dimethylimidazole (50 and 53% respectively), but both reactions are likely to proceed *via* the intermediate imidazol-5-yl radical. The Bu_3SnH reactions provide further evidence that imidazol-5-yl radicals are feasible intermediates.

The reduction of 5-bromo-1-(buten-3-yl)-2-methyl-imidazole with Na/NH_3 or Bu_3SnH under the same conditions as above gave the cyclised product in 100 and 80% yields respectively (Equation C), thereby clearly indicating[6] the intermediacy of the imidazol-5-yl radical for both reactions with the bromo-derivative. The intramolecular trapping of the imidazol-5-yl radical in the Na/NH_3 reduction indicates that the 5-bromoimidazole radical anions dissociate with loss of bromide anion to yield the corresponding imidazol-5-yl radicals even though this dissociation was not observed in the solid matrix by e.s.r. spectroscopy.



(C)

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