Radical-nucleophilic Substitution ($S_{RN}1$) Reactions. Part 5.[1] Anions of Nitroimidazoles in $S_{RN}1$ and Oxidative Addition Reactions

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The anions of 2- and 4(5)-nitroimidazole, and 2-methyl-4(5)-nitroimidazole, have been shown to undergo $S_{RN}1$ reactions with a range of halogeno-nitroalkanes (which include *p*-nitrobenzyl chloride, 2-bromo- and 2-chloro-2-nitropropane, 2,2-dinitropropane, 5-bromo-5-nitro-1,3-dioxane, and 2-(bromo- and chloromethyl)-1-methyl-5-nitroimidazole to yield the corresponding *N*(1)-(nitroalkyl) derivatives. The anions of 2-methyl-4(5)-nitro- and 4(5)-nitro-imidazole, but not the anion of 2-nitroimidazole, underwent oxidative addition to the anion of 2-nitropropane (using potassium ferricyanide and sodium persulphate as oxidants) to yield the corresponding *N*(1)-(1-methyl-1-nitroethyl) derivatives. The anions of 2-methyl-4-nitro- and 4-nitro-imidazole have also been shown to act as nucleofuges in the $S_{RN}1$ reactions between their 1-(1-methyl-1-nitroethyl)-derivatives [$Me_2C(NO_2)$-X] and anions (which include $Me_2CNO_2^-$ and $PhSO_2^-$). Steric constraints, kinetic control, and the nature of the intermediate radical anions in the above reactions are discussed.

The $S_{RN}1$ mechanism is now well established and many of the reaction parameters are clearly understood. Several different types of substrates have been shown to undergo $S_{RN}1$ reactions. These substrates include substituted arenes (ArX)[2] and heterocycles, aliphatic α-substituted nitro-alkanes [$R_2C(X)NO_2$],[3] and *o*- and *p*-nitrobenzyl derivatives (*o*, *p*-$NO_2C_6H_4CH_2X$).[3] The generalised $S_{RN}1$ mechanism is shown in Scheme 1. The range of nucleofuges (X^-) which are suitable for $S_{RN}1$ reactions are similar for all three groups of substrates and include Br^-, I^-, Cl^-, ^-SCN, N_3^-, NO_2^-, ^-SR, $^-S(O)R$, $^-SO_2R$, NR_3, and $^-OP(O)(OR)_2$.

$$RX + e^-(Nu^-) \xrightarrow[h\nu]{s.e.t.} (RX)^{-\bullet} + (Nu^\bullet) \quad \text{(Initiation)} \quad (1)$$

$$(RX)^{-\bullet} \longrightarrow R^\bullet + X^- \quad (2)$$

$$R^\bullet + Nu^- \longrightarrow (RNu)^{-\bullet} \quad \text{(Propagation)} \quad (3)$$

$$(RNu)^{-\bullet} + RX \xrightarrow{s.e.t.} RNu + (RX)^{-\bullet} \quad (4)$$

$$\text{Summary: } RX + Nu^- \longrightarrow RNu + X^- \quad (5)$$

Scheme 1.

The nature of the nucleophiles (Nu^-) which participate in $S_{RN}1$ reactions differs between the aromatic substrates and the aliphatic nitro and *p*-nitrobenzyl substrates. Some nucleophiles undergo reaction [2,3] in both groups [*e.g.* RS^-, $(RO)_2PO^-$] but most nucleophiles will only undergo reaction with ArX, or with nitrohalogeno substrates, *e.g.* nitronate anions ($R_2CNO_2^-$) readily react with nitrohalogeno substrates but do not react with ArX substrates.[2,3] On the other hand, some nucleophiles will only react with both substrates under biased conditions, *e.g.* malonate anions undergo reaction with nitrohalogeno substrates but will only react with aryl substrates when strong electron-withdrawing groups are present on ArX.[2,3]

Two groups of nucleophiles are largely absent from reactions with both aromatic and nitrohalogeno derivatives; these are *N*- and *O*-centred anions. A few examples of $S_{RN}1$ reactions of *N*-centred anions are known and include the reactions between: amide ($^-NH_2$) and ArX;[2] *p*-nitrocumyl chloride, nitrite anions, and quinuclidine;[3] and azide and α-substituted nitroalkanes.[1,4] An explanation has been proposed [5] for the lack of reactivity of *O*-anions; *i.e.* the reaction between *O*-anions and the intermediate radicals yields radical anions which contain the unpaired electrons in C–O σ* SOMO's, which are of very high energy, thus acting as a barrier to reaction. A similar argument can be applied to the reactions of *N*-centred anions which would have intermediate radical anions containing high energy C–N σ* SOMO's.

This paper describes our studies of the application of the $S_{RN}1$ mechanism, and the related oxidative addition reactions of nitronates, to the *N*-alkylation of nitroimidazoles. The central step in these reactions is the addition of the *N*-anions, obtained by deprotonation of the nitroimidazoles, to radical intermediates. The studies were based on the prediction that these *N*-anions, because of their aromatic nature, may yield intermediate radical anions which were of sufficiently low energy to allow reaction to proceed, unlike previous observations of the lack of reaction of *N*-centred anions in $S_{RN}1$ reactions.

Our initial studies, which were aimed at the synthesis of novel nitroimidazole compounds, have been reported in a preliminary communication.[6] Nitroimidazoles are of particular pharmaceutical interest because 2- and 5-nitroimidazoles are the main antibiotics used against anaerobic microbial infections.[7]

Results and Discussion

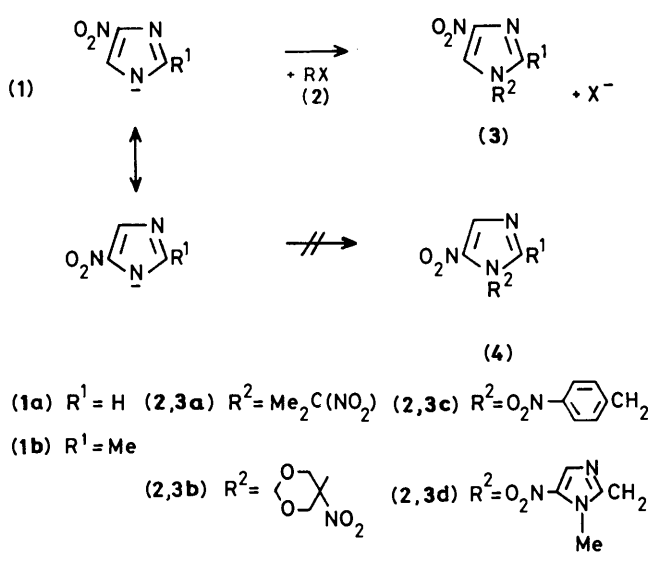
$S_{RN}1$ *Reactions of Nitroimidazole Anions.*—The anions of 4(5)-nitroimidazole and 2-methyl-4(5)-nitroimidazole were treated with a variety of potential $S_{RN}1$ substrates under conditions conducive to $S_{RN}1$ reactions (nitrogen, light catalysis) (Scheme 2), to yield the analogous 1-*alkyl*-4-*nitroimidazoles* (**3**) and not 1-*alkyl*-5-*nitroimidazoles* (**4**). The results are tabulated in Table 1.

The 2-substituted 2-nitropropanes (**2a**; X = Br or NO_2) reacted slowly with both anions (**1a**) and (**2a**) to yield the corresponding 1-(1-methyl-1-nitroethyl)-4-nitroimidazoles (**3a**). The rates of the $S_{RN}1$ reactions were slower than normally observed for $S_{RN}1$ reactions of these compounds. We suggest that the slow rate is due to steric hindrance (see later) of the addition of the anion to the intermediate radical ($Me_2\dot{C}NO_2$) [equation (8)]. This reasoning, however, does not explain why the chloro compound [$Me_2C(Cl)NO_2$] reacted considerably slower than, and gave lower yields of product than, the bromo- or dinitro-analogues because this step is independent of the nature of the nucleofuge.[8] Similarly, a possible explanation for the slow rate of reaction of $Me_2C(Cl)NO_2$ is that the intermediate

Table 1. $S_{RN}1$ reactions between 4(5)-nitroimidazoles anions (**1**) and substrates (R^2X)

Nitroimidazole anion (**1**)	R^2X (**2**)	Conditions[a]	% Yield[b] 1-Alkyl-4-nitroimidazole (**3**)	Unchanged R^2X	Unchanged Nitroimidazole[c]
(**1a**)	$Me_2C(Br)NO_2$	44 h; 8 h; 4 h	92 (59); 68; 48 (31)	0; 0; 29	0; 0; 12
		6 h; 6 h, O_2	41; 0, 0	25; 3, 28	0; 40, 27
		6 h, *p*-dinitrobenzene (5 mol%)	49, 52	20, 8	3, 0
		6 h, di-t-butyl nitroxide (10 mol%)	3	3	62
		6 h, dark	28, 28	58, 23	0, 0
	$Me_2C(Cl)NO_2$	30 h	11 (6)	50	
	p-$NO_2C_6H_4CH_2Cl$	8 h; 5 h; 2 h	100 (75); 60; 55	0; 0; 0	0; 0; 0
		2 h, O_2; 2 h, dark	1; 30	0; 16	48; 0
		2 h, *p*-dinitrobenzene (10 mol%)	35	0	0
		2 h, di-t-butyl nitroxide (10, 25 mol%)	38; 3	10; 11	4; 57
	(**2b**; X = Br)	27 h	81 (42)	0	
	PhI[d]	24 h	0	58	1
(**1b**)	$Me_2C(Br)NO_2$	72 h; 8 h	41 (37); 31 (20)	0; 0	0; 12
		DMF, 8 h	6	0	56
	$Me_2C(Cl)NO_2$	96 h; 25 h; 4 h	12 (5); 9; 6	0; 0; 0	6; 14; 26
	$Me_2C(NO_2)_2$	48 h	80 (37)	0	0
	p-$NO_2C_6H_4CH_2Cl$	22 h	100 (73)	0	
	(**2d**; X = Br)	24 h[e]; 16 h[e]	50 (35); 41 (27)	0; 0	0; 0
	(**2d**; X = Cl)	28 h[e]	28 (19)	0	0
	$BrCH_2NO_2$	36 h	0	0	45

[a] All reactions were carried out in DMSO under nitrogen with fluorescent lamps (2 × 150 W) with nitroimidazole (1 equiv.), Bu^{t}OK (1.5 equiv.), and R^2X (1.5 equiv.) unless otherwise stated. [b] % Yields are based on nitroimidazole and were calculated by n.m.r. spectroscopy using an internal standard; yields of pure isolated material are in parentheses. [c] % Nitroimidazole recovered by filtration after pouring the reaction into water (a large amount remains in solution). [d] Also carried out using light at 250 nm with similar results. [e] NaH used in place of Bu^{t}OK.

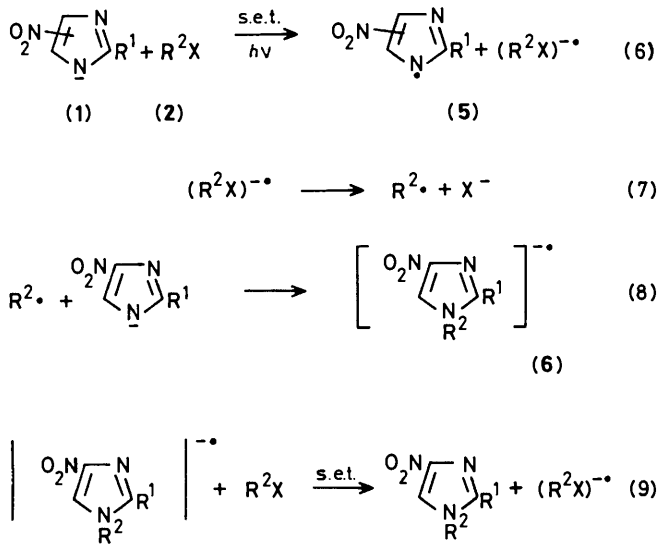


Scheme 2.

radical anion, $Me_2C(Cl)\dot{N}O_2^-$ [equation (7) with $R^2 = Me_2C(NO_2)$ and X = Cl] dissociates more slowly than the bromo- and dinitro-analogues. However, this can only be part of the explanation because its rate of dissociation is similar to that of the dinitro-analogue, $[Me_2C(NO_2)_2]^{-\bullet}$, as observed by e.s.r. spectroscopy.[9] The related bromonitro analogue, 5-bromo-5-nitro-1,3-dioxane (**2b**; X = Br), which is a commercially used antimicrobial agent,[10] reacted similarly in 81% yield.

Reactions between the anions (**1a**) and (**1b**) and *p*-nitrobenzyl chloride (**2c**; X = Cl) and 2-(chloromethyl)-1-methyl-5-nitroimidazole (**2d**; X = Cl and Br) gave high yields of the corresponding 1-alkyl-4-nitroimidazoles (**3c**) and (**3d**). An attempt at aromatic $S_{RN}1$ substitution using iodobenzene failed. The reaction between imidazole and iodobenzene has also been reported to be unsuccessful.[2b] Similarly, reaction with bromonitromethane failed, possibly due to immediate deprotonation[11] of $BrCH_2NO_2$ by the nitroimidazole anion.

Proof for the $S_{RN}1$ mechanism for these reactions was obtained by using the normal criteria for establishing the mechanism[2,3,12] for two representative reactions (see Table 1). The use of radical scavengers (O_2 and di-t-butyl nitroxide) gave strong inhibition of the chain reaction, but the use of the strong electron acceptor, *p*-dinitrobenzene, gave little inhibition. It has been pointed out[12] that if one of the intermediate radical anions has a similar reduction potential to that of *p*-dinitrobenzene then inhibition will be poor; *i.e.* the radical anion (**6**), which is an intermediate in the chain reaction (Scheme 3) may not readily undergo s.e.t. (single electron transfer) to *p*-dinitrobenzene. Reactions carried out in the absence of light showed lower yields indicating a level of light catalysis. Strong red colours were observed in all the reactions which faded on completion. Light catalysis by visible light is dependent on some intermediate which absorbs in the visible region. Neither of the starting materials absorb in the visible region and, therefore, we suggest, although with no evidence but on reported precedence,[1,2,12] that these colours are caused by charge-transfer complexes between nitroimidazole anions (**1**) and substrates (**2**) prior to light-catalysed s.e.t. We propose that all these data provide good evidence for assigning the $S_{RN}1$ to these reactions as fully illustrated by Scheme 3.

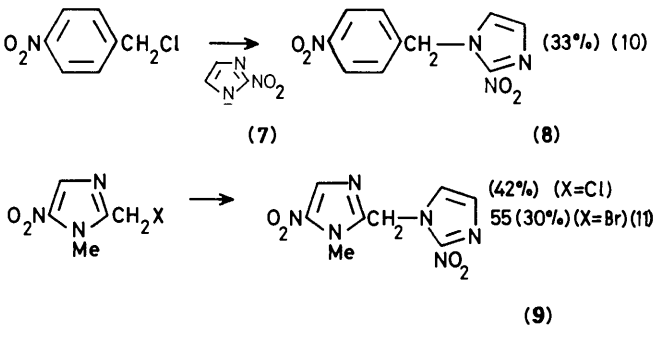


Scheme 3.

4(5)-Nitroimidazole anions are ambident and are able to react *via* the *N*–centres to yield 4- or 5-nitroimidazole products, which is one of the major problems[13] of nitroimidazole chemistry. In these $S_{RN}1$ reactions the anions (**1a**) or (**1b**) can react with the intermediate radicals ($R^{2\bullet}$) [equation (8)] to yield either 1-alkyl-4-nitroimidazole radical anions (**6**) or the analogous 5-nitroimidazole radical anions. In most of the reactions the 4-isomer is exclusively formed. Detailed searching for traces of any 5-isomer in two reactions showed an absence of the 5-isomer in the reaction between $Me_2C(Br)NO_2$ and the anion (**1a**) and traces of the 5-isomer were observed by ^1H and ^{13}C n.m.r. spectroscopy in the reaction between the anion (**1a**) and *p*-nitrobenzyl chloride; the 5-isomer could not be isolated in our hands. The position of the nitro group in all the products was determined by n.m.r. spectroscopy.[14] ^{13}C N.m.r. spectroscopy is especially clear-cut: the ^{13}C n.m.r. signal for C-4 in the 5-nitro isomers is in the range 131—134 p.p.m., whereas the signal for C-5 in the 4-nitro isomers is in the range 119—123 p.p.m.

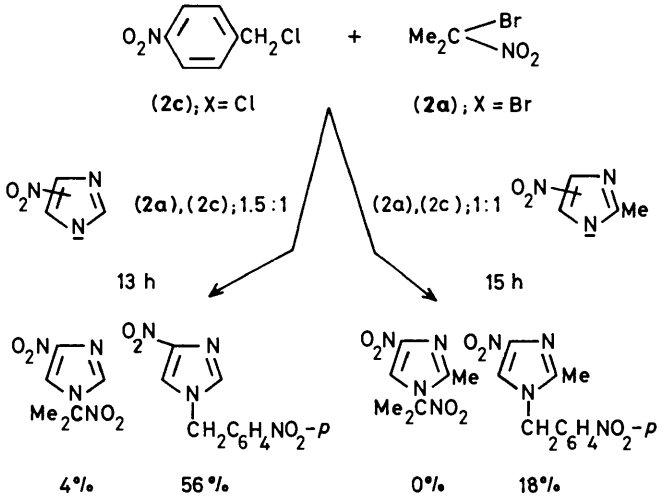
The regioselectivity observed in the $S_{RN}1$ reactions is also found in the reactions between the anion (**1a**) and dimethyl sulphate.[15] In this reaction the regioselectivity (ratio of the 4-nitro to the 5-nitro products was *ca.* 8:1) was explained by the greater nucleophilicity of the 4-nitroimidazole anion, which is the result of the nitro group being further away from the reacting *N*-anion, thereby causing higher electron density on the *N*-anion than in the 5-nitro isomers.[15] We propose that the same logic applies to radical reactions, *i.e.* kinetic control of the nucleophilic attack by the nitroimidazole anions (**1a**) and (**1b**) on the intermediate radicals [equation (8)] to yield 4-nitroimidazole radical anions (**6**). In $S_{RN}1$ reactions involving ambident anions, exclusive formation of products *via* the most nucleophilic centre is usually observed.[16] These results provide further confirmatory evidence that the addition of ambident anions to radicals is under kinetic control.[17]

The anion of 2-nitroimidazole, (**7**), also underwent $S_{RN}1$ reactions with the 'benzylic' substrates (**2c**; X = Cl) and (**2d**; X = Cl) to give the expected products, (**8**) and (**9**), in reasonable yield [equations (10) and (11)], but did not undergo reaction with $Me_2C(X)NO_2$ (X = Br, Cl, or NO_2) even under forcing conditions. In the reactions of $Me_2C(X)NO_2$ (X = Br or NO_2), 2,3-dimethyl-2,3-dinitrobutane was also isolated, resulting from abstraction of the α-substituent to yield the anion of 2-nitropropane ($Me_2CNO_2^-$) and subsequent reaction[3] of this anion with $Me_2C(X)NO_2$ by the $S_{RN}1$ mechanism.



Steric Effects in the $S_{RN}1$ *Reactions of Nitroimidazole Anions.*—Several of the above reactions appear to be affected by steric hindrance even though $S_{RN}1$ reactions are not easily influenced by steric factors.[17b,18] Norris and co-workers[18] have, however, shown that there is a level of steric hindrance at which addition of the nucleophile to the intermediate radical is blocked. In our reactions, steric hindrance is indicated by (i) the preference for 4-nitro over 5-nitro products, (ii) the faster rates of reaction between the less hindered nitroimidazole anions (**1a**) relative to the more hindered anions (**1b**) and the sterically crowded nitropropanes, [$Me_2C(X)NO_2$], (iii) the lack of reactivity of 2-nitroimidazole anions with $Me_2C(X)NO_2$, and (iv) the faster rates of reaction for all imidazole anions with *p*-nitrobenzyl chloride as compared with $Me_2C(X)NO_2$. We suggest, therefore that substituents in the α-positions of the imidazole anions (2-NO_2, 5-NO_2, and 2-Me) cause steric hindrance in the addition of these anions to radicals, especially to more bulky radicals (*i.e.* $Me_2\dot{C}NO_2$ as compared with *p*-$NO_2C_6H_4\dot{C}H_2$). Therefore the preferential formation of 4-nitro isomers relative to 5-nitro isomers is caused by electronic and steric factors.

In order to confirm these proposals competitive reactions were carried out. It has been assumed[9] that the slowest step in the $S_{RN}1$ chain is the dissociation of the radical anion [equation (2)]. Therefore, reactions proceeding by radical anions which dissociate faster would be predicted to read faster. Studies of the dissociation of radical anions at low temperature using e.s.r. spectroscopy have shown that the radical anions of $Me_2C(Br)NO_2$[9] dissociate considerably faster than the radical anions of *p*-nitrobenzyl chloride,[19] but the reverse order of reactivity is apparently observed with nitroimidazole reactions. Therefore, both imidazole anions (**1a**) and (**1b**) were treated with a mixture of $Me_2C(Br)NO_2$ and *p*-$NO_2C_6H_4CH_2Cl$ under similar conditions (see Scheme 4). Products from *p*-

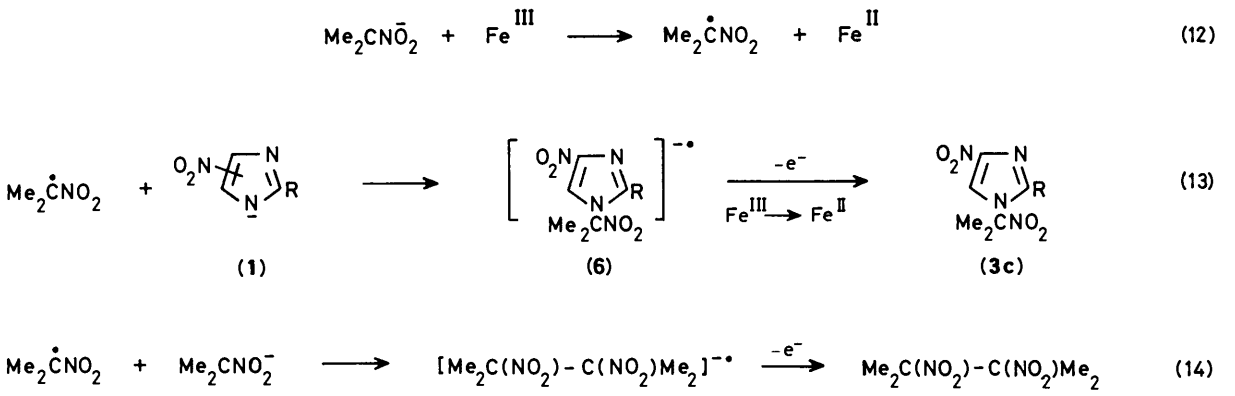


Scheme 4. Competitive reactions between (**2a**; X = Cl) and (**2c**; X = Cl)

Table 2. Oxidative addition of nitroimidazole anions (**1a**), (**1b**), and (**7**) to $Me_2CNO_2^-$

Nitroimidazole	Reaction time (min)[b]	$K_3Fe(CN)$ (Equiv.)	% Yield[a] 1-[$Me_2C(NO_2)$]-nitroimidazole	% Yield[a] 2,3-dimethyl-2,3-dinitrobutane	% Yield[a] Unchanged nitroimidazole
4(5)-Nitroimidazole	60	1.5	21 (**3a**; R′ = H)	9	16
	5	1.5	8	0	2
	60	0.2[c]	34	20	
2-Methyl-4(5)-nitroimidazole	5	1.5	(14) (**3a**; R′ = Me)	(13)	
	30	1.5	(13)	(15)	
	60	1.5	(12)	(20)	
	30	1.75	16, 17	14, 14,	19, 9
	10	2.0	9, 12	2, —	24, —
	10	0.2[c]	31	13	
2-Nitroimidazole	75	0.2[c]	0	18	100

[a] % Yield based on starting nitroimidazole; yields analysed by ^1H n.m.r. are in parentheses. [b] All reactions were carried out in CH_2Cl_2–H_2O under nitrogen with $Me_2CNO_2^-$ (1.5 equiv.) and NaOH (2.5 equiv.). [c] Plus $Na_2S_2O_8$ (2 equiv.).



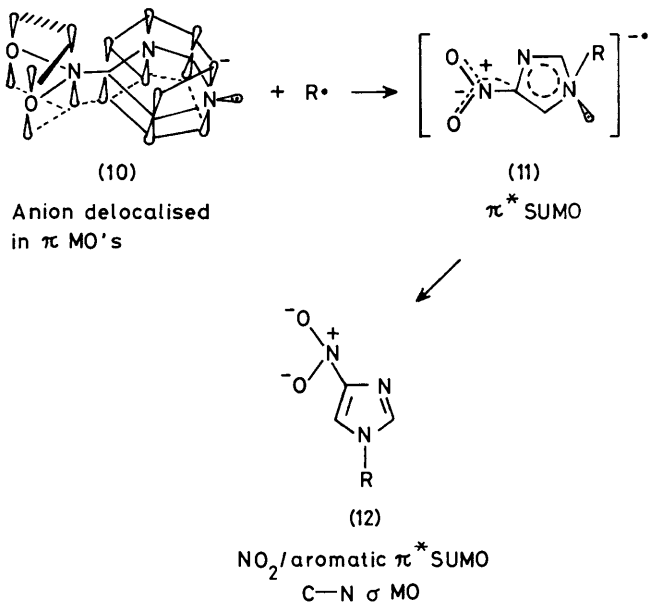
Scheme 5. Oxidative addition of 4(5)-nitroimidazole anions to $Me_2CNO_2^-$

$NO_2C_6H_4CH_2Cl$ were preferentially formed over products from $Me_2C(Br)NO_2$ with both anions and lower yields (lower rates) were observed for the more hindered anion (**1b**) providing confirmatory evidence for steric hindrance. Caution must, however, be practised in chain reactions in which the initiating reactions [equation (6)] may influence observed results.

Oxidative Addition of Nitroimidazole Anions to $Me_2CNO_2^-$.—The oxidative addition of anions to $Me_2CNO_2^-$ to yield 2-substituted 2-nitropropanes has been developed in recent years.[1,16,20,21] Originally potassium ferricyanide was used as the oxidant but recent improvements[21] using only a catalytic amount of ferricyanide, and persulphate to regenerate ferricyanide from ferrocyanide, have proved more successful. The method was used successfully to add the 4(5)-nitroimidazole anions (**1a**) and (**1b**) to $Me_2CNO_2^-$ (see Scheme 5 and Table 2). Addition of the anion of 2-nitroimidazole to $Me_2CNO_2^-$ was unsuccessful and only 2,3-dimethyl-2,3-dinitrobutane was isolated. The key step in the oxidation is the addition of the imidazole anion to $Me_2\dot{C}NO_2$ [equation (13)], *i.e.* the same as step 3 [equation (8)] in the $S_{RN}1$ reactions. Therefore, it was not surprising that the 4-nitro isomer (**3a**) was exclusively formed for both anions (**1a**) and (**1b**), and that no product was formed in the reaction with 2-nitroimidazole. These observations provide further evidence for our proposals for steric and electronic control of the addition of nitroimidazole anions to radicals.

Experimentally, the best yields of 1-alkyl-4-nitroimidazoles (**3a**) were obtained when 2 equivalents of sodium persulphate and only catalytic amounts of $K_3Fe(CN)_6$ were used. Initial studies using only $K_3Fe(CN)_6$ gave poor yields and longer reaction times only resulted in the production of more of the 2,3-dimethyl-2,3-dinitrobutane by-product. This by-product results from the addition of the $Me_2CNO_2^-$ anion to the intermediate $Me_2\dot{C}NO_2$ radical in competition with the nitroimidazole anion [see equation (10)]. Traces of 2,2-dinitropropane were also obtained in all the reactions. This by-product probably arises from the addition of nitrite anions to the $Me_2\dot{C}NO_2$ radicals. The origin of nitrite anions is not known.

Mechanism of Reaction between Nitroimidazole Anions and Radicals.—In the introduction we proposed that the lack of reaction between *N*-centred anions of amines and radicals in $S_{RN}1$ reactions is because of the high energy of the C–N σ* SOMO in which the unpaired electron of the resultant radical anions reside. In order to explain why nitroimidazole anions are able to react, and sp^3 hybridised *N*-nucleophiles do not react, we propose the following: the electrons in the imidazole anion are symmetrically delocalised in the π-molecular orbitals of the ring[22] [compound (**10**), Scheme 6] and, therefore, when the anion reacts with a radical the initially formed radical anion has the unpaired electron in a π* MO of relatively low energy [compound (**11**), Scheme 6], and not in a C–N σ* MO, thereby allowing the reaction to take place. The nitro group will further lower the energy of the SOMO by conjugation. The initially formed radical anion almost certainly undergoes smooth reorganization of molecular orbitals to form a radical anion [compound (**12**), Scheme 6] of lower energy consisting of the unpaired electron in an NO_2/aromatic, π* SOMO and a C–N σ



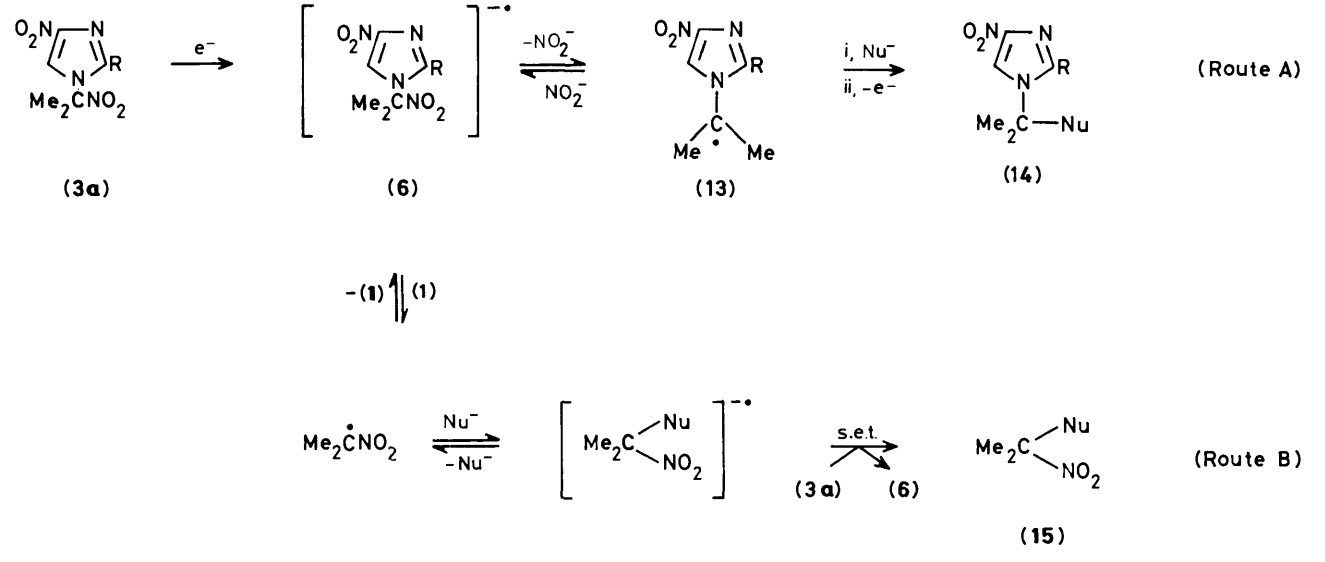
Scheme 6.

molecular orbital. Thus, the 'lone pair' of electrons in the anion (**10**) which were in a sp^2 orbital undergo smooth reorganisation into the p orbitals (and part of the aromatic system) of the product radical anion (**12**). In the case of aromatic $S_{RN}1$ substitution of aryl halides with amines, a similar argument could be construed, *i.e.* the unpaired electron of the radical anion could be in a π* MO resulting from the combination of reactant MO's (the phenyl radical σ orbital and the amine p orbitals). We suggest that the energy of this π* orbital is probably of much higher energy than the delocalised π* SOMO in the imidazole case, thereby discouraging reaction. A determination of the structure of these radical anions using e.s.r. spectroscopy at low temperature is underway, the results of which will be published in due course.

Reaction between Anions and 2-Halogenomethyl-1-methyl-5-nitroimidazoles (**2d**).—The reactions between nitro anions and 2-(chloromethyl)-1-methyl-5-nitroimidazole have been reported[23] to proceed by the $S_{RN}1$ mechanism. Our work has provided several further examples of $S_{RN}1$ reactions between these 2-halogenomethylnitroimidazoles and anions [*i.e.* 2-methyl-4(5)-nitroimidazole (see Table 1) and 2-nitroimidazole, equation (11)]. Although inhibition studies of these reactions were not carried out, we suggest that the mechanism is unlikely to differ from that observed for the reaction between the same anions and *p*-nitrobenzyl chloride. 2-(Halomethyl)-5-nitroimidazoles therefore appear to show similar $S_{RN}1$ reactivity to that of the analogous *p*-nitrobenzyl and *p*-nitrocumyl halides, 2-(halogenomethyl)-5-nitrofurans,[24] and α-substituted 2-(propan-2-yl)-5-nitrothiophenes.[25]

$S_{RN}1$ *Reactivity of 1-(1-Methyl-1-nitroethyl)-4-nitro-imidazoles* (**3a**).—2-Substituted 2-nitropropanes [$Me_2C(X)NO_2$] react with nucleophiles by the $S_{RN}1$ mechanism with loss of either the α-substituent (X) or nitrite anion, *i.e.* the intermediate radical anion, $[Me_2C(X)NO_2]^{-\cdot}$ is able to dissociate to either $Me_2\dot{C}NO_2$ and X^-, or $Me_2\dot{C}X$ and NO_2^-.[1,3] The former route is observed for X = halogen, SCN, SR, S(O)R, SO_2R, and NO_2 and the latter route for X = COR, CO_2R, R, N_3, NO_2, and *p*-$NO_2C_6H_4$; *i.e.* the direction of dissociation is largely determined by relative nucleofugicity.[1,3,9] This behaviour therefore poses a question regarding the $S_{RN}1$ reactions between 2-halogeno-2-nitropropanes and 4(5)-nitroimidazole anions; *i.e.* why does the product of the reaction (**3a**) not react further as shown in Scheme 7 by Route A to yield a disubstituted product (**14**; Nu = 4-nitroimidazole). We propose that this question is answered by the better nucleofugicity of 4(5)-nitroimidazole anions as compared with nitrite anions, *i.e.* that further $S_{RN}1$ reactions between the products (**3a**) and the 4(5)-nitroimidazole anions (**1**) do not yield new products because the nucleofuge = nucleophile as illustrated by Route B in Scheme 7.

In order to test this hypothesis, and to test the $S_{RN}1$ reactivity of 1-(1-methyl-1-nitroethyl)-4-nitroimidazoles, several reactions were carried out. The results are shown in Table 3. As expected, reaction between the nitroimidazole (**3a**; R = H) and the nitroimidazole anion (**1a**) only gave unaltered starting materials. However, reaction between both of the nitroimidazoles (**3a**; R = H) and (**3a**; R = Me) and $Me_2CNO_2^-$ gave the expected $S_{RN}1$ product 2,3-dimethyl-2,3-dinitrobutane in reasonable



Scheme 7. Possible $S_{RN}1$ reactions of 1-(1-methyl-1-nitroethyl)-4-nitroimidazoles

Table 3. Reaction between 1-(1-methyl-1-nitroethyl)-4-nitroimidazoles (**3a**) and nucleophiles

1-(1-Methyl-1-nitroethyl)-4-nitroimidazole (**3a**)	Nucleophile	Conditions	% Yield[a] Product (**15**)	Unchanged (**3a**)	Unchanged nucleophile[b]
(**3a**; R = H)	(**1a**)	DMSO, 24 h		(**3a**; R = H); 57, 61	(17), (26)
	$Me_2CNO_2^-$[c]	DMF, 31 h	[**15**; R = $Me_2C(NO_2)$] (30), (35)	(28), (45)	
		DMF, 31 h DTBN[d] (50 mol%)	6	81	
		DMF, 31 h *p*-DNB[e] (40 mol%)	16	40	
		DMF, 4.5 h; 11 h	4; 10	64; 32	
(**3a**; R = Me)	(**1a**)	DMSO, 14 h	(**3a**; R = H) 47	26	
	$Me_2CNO_2^-$	DMF, 4.5 h; 5 h	[**15**; R = $Me_2C(NO_2)$] (54); (51)	0; (18)	
		DMF, DTBN[d] (50 mol%) 4.5 h; 5 h	12; 7	12; 49	
		DMF, 4.5 h, O_2, dark	13	89	
		DMF, 4.5 h, *p*-DNB[e] (40 mol%)	16	81	
	$PhSO_2^-$	DMSO, 24 h	0	(86)	(88)

[a] % Yields were calculated by ^1H n.m.r. spectroscopy using an internal standard. Isolated yields are shown in parentheses. [b] Isolated as the conjugate acid. [c] 3 Equiv. [d] DTBN = di-t-butyl nitroxide. [e] *p*-DNB = *p*-dinitrobenzene.

yields. The formation of the product was inhibited in both cases by addition of radical traps (di-t-butyl nitroxide and O_2) and strong electron acceptors (*p*-dinitrobenzene and O_2) thereby indicating the $S_{RN}1$ mechanism.

The nitroimidazole (**3a**; R = Me) was treated with the anion of 4(5)-nitroimidazole on the basis that the 2-methyl-4(5)-nitroimidazole (**1b**) would act as a better nucleofuge than 4(5)-nitroimidazole (**1a**) in this potentially reversible reaction (Scheme 7 with Nu = **1a**) due to steric effects (see earlier section). This predicted steric effect was observed with 47% (Table 3) of the $S_{RN}1$ product (**3a**; R = H) being formed, and only 26% of the unaltered starting material (**3a**; R = Me).

As the final confirmation of our nucleofugicity proposal, the nitroimidazole (**3a**; R = Me) was treated with sodium benzenesulphinate. No reaction would be expected because the loss of phenylsulphinate from the intermediate radical anion $[Me_2C(SO_2Ph)NO_2]^{-\bullet}$ would be much faster than loss of the nitroimidazole anion (**1b**) from the intermediate radical anion (**6**; R = Me). No reaction was observed and starting materials were recovered. Our results show that nitroimidazole anions are able to act as nucleofuges as well as nucleophiles in the $S_{RN}1$ reactions of 2-substituted 2-nitropropanes and that nitroimidazoles are better nucleofuges (Route B, Scheme 7) than nitrite anions (Route A, Scheme 7) from intermediate radical anions (**6**).

Experimental

General.—DMF and DMSO were distilled at low pressure from calcium hydride and stored over molecular sieves. M.p.s were recorded on a Kofler block and are uncorrected. I.r. spectra were determined as Nujol mulls on a Pye Unicam PU 516 spectrometer. ^1H N.m.r. spectra were determined at 90 MHz on a Perkin-Elmer R32 spectrometer or at 60 MHz on a Varian EM 360A instrument using $SiMe_4$ as an internal standard. N.m.r. analyses of reaction mixtures were carried out using a known amount of an internal standard (*p*-dinitrobenzene). ^{13}C N.m.r. spectra were carried out on a Bruker WP-80 spectrometer. Mass spectra were carried out on Kratos MS 80 instrument.

Materials.—2-Bromo-2-nitropropane,[26] 2-chloro-2-nitropropane,[26] 2,2-dinitropropane,[20] 2,3-dimethyl-2,3-dinitrobutane,[26] 2-nitroimidazole,[27] 4(5)-nitroimidazole,[28] and the sodium salt of 2-nitropropane[29] were prepared by literature procedures. We thank the Boots Co. p.l.c. for a generous gift of 5-bromo-5-nitro-1,3-dioxane. 2-Methyl-4(5)-nitroimidazole, *p*-nitrobenzyl chloride, bromonitromethane, iodobenzene, imidazole, and sodium benzenesulphinate were purchased commercially.

(a) 2-*Chloromethyl*-1-*methyl*-5-*nitromidazole* (**2d**; X = Cl). 4-Nitroimidazole was methylated as reported in the literature.[28] The crude mixture of 4- and 5-nitro isomers was subjected to column chromatography on neutral alumina with dichloromethane (CH_2Cl_2) as eluant. The crude 1-methyl-5-nitroimidazole was recrystallised from diethyl ether (Et_2O) to yield pale yellow crystals or pure material (41%), m.p. 56—58 °C (lit.,[28] 55 °C). The 1-methyl-5-nitroimidazole was hydroxymethylated[30] as reported using paraformaldehyde in dimethyl sulphoxide (DMSO). The DMSO solution was evaporated to dryness and chromatography on neutral alumina with chloroform ($CHCl_3$) as eluant yielded the starting imidazole (9%), followed by 2-hydroxymethyl-1-methyl-5-nitroimidazole, which was recrystallised from toluene to yield pale yellow crystals of pure product (80%), m.p. 115—116 °C (lit.,[30] 112—114 °C). The hydroxymethyl compound was converted[31] into 2-chloromethyl-1-methyl-5-nitroimidazole (**2d**; X = Cl) using thionyl chloride (72%), m.p. 43.5—44 °C (no lit. m.p.); $\nu_{max.}$(Nujol) 3 200, 3 028, 1 560, and 1 310 cm^{-1}; $\delta_H(CDCl_3)$ 4.0 (3 H, s, Me), 4.8 (2 H, s, CH_2), and 8.00 (1 H, s 4-H) (Found: M^+, 177.012 and 175.048. $C_5H_6ClN_3O_2$ requires *M*, 177.0119 and 175.0148); *m/z* 140 (100), 129 (9), and 94 (11).

(b) 2-*Bromomethyl*-1-*methyl*-5-*nitroimidazole* (**2d**; X = Br). 2-Hydroxymethyl-1-methyl-5-nitroimidazole was treated with thionyl bromide[31] to yield an orange solid which was basified and extracted with chloroform ($CHCl_3$) to yield impure crystals. Recrystallisation from Et_2O gave colourless crystals of the bromide (**2d**; X = Br) (76%), m.p. 75—77 °C (no lit. m.p.); $\nu_{max.}$(Nujol) 3 100, 3 030, 1 530, and 1 370 cm^-; $\delta_H(CDCl_3)$ 3.96 (3 H, s, NMe), 4.46 (2 H, s, CH_2), and 7.88 (1 H, s, 4-H); [Found: M^+, 220.963 and 218.964 (5%). $C_5H_6BrN_3O_2$ requires *M*, 220.9624 and 218.9643]; *m/z* 140 (100) and 94 (31).

1-(p-*Nitrobenzyl*)-4-*nitroimidazole* (**3c**; R^1 = H): *General Procedure for* $S_{RN}1$ *Reactions*.—Potassium t-butoxide (2.97 g, 26.5 mmol) was suspended in dry DMSO (10 ml) and added to a solution of 4(5)-nitroimidazole (2.0 g, 17.6 mmol) in dry DMSO (50 ml) under nitrogen and under anhydrous conditions. The mixture was stirred under nitrogen for 30 min to allow complete deoxygenation. *p*-Nitrobenzyl chloride (4.55 g, 26.5 mmol) in DMSO (10 ml) was added to the solution which rapidly turned red in colour. The reaction mixture was then irradiated with 2 × 150 W fluorescent discharge lamps [mercury blended tungsten universal mounted (MBTU) lamps emitting light maximally at 430 nm] from a distance of 10 cm. After 8 h the red colour changed to light orange and the reaction was terminated by adding water (50 ml). The aqueous solution was extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with water (7 × 50 ml) to remove DMSO, dried, and evaporated to dryness to yield pure 1-(p-*nitrobenzyl*)-4-*nitroimidazole* (**3c**; R^1 = H) (100%). The pure crystals were further recrystallised from ethyl acetate–light petroleum (b.p. 40—60 °C) (1:1) (3.3 g, 75%), m.p. 138.139 °C (Found: C, 48.8; H, 3.3; N, 22.6. $C_{12}H_8N_4O_4$ requires C, 48.39, H, 3.25; N, 22.58%); $\delta_H(CDCl_3)$ 5.73 (2 H, s, CH_2), 8.00 (1 H, d, 2-H), 8.33 (1 H, d, 5-H), and 7.78—8.40 (4 H, ABq, phenyl H); δ_C 49.59 (t, CH_2), 113.28, (d, 2-C), 119.46 (d, 5-C), 123.12 (d, phenyl-2-C), 128.04 (d, phenyl-3-C), 141.93 (s, 4-C), and 147.13 (s, phenyl-4-*C*NO_2); (Found: M^+, 248.0547. $C_{12}H_8N_4O_4$ requires *M*, 248.0545); *m/z* 202 (1), 136 (100), 113 (7), 89 (36), 48 (48), and 65 (14).

General Procedure for Light Catalysis and Inhibitions Studies of $S_{RN}1$ *Reactions*.—The general procedure was followed except as outlined in each method detailed below. (*a*) Inhibition studies with *p*-dinitrobenzene or di-t-butyl nitroxide were carried out by adding the required amount of *p*-dinitrobenzene or di-t-butyl nitroxide to the reaction mixture immediately prior to the alkyl halide (**2**). (*b*) Inhibition studies with oxygen were carried out by replacing nitrogen gas by oxygen gas. (*c*) The studies on the effect of light catalysis were carried out by exclusion of light from the reaction which was effected by wrapping the flask in aluminium foil. The results of these respective studies are shown in Tables 1 and 3.

$S_{RN}1$ *Reactions between Nitroimidazole Anions* (**1**) *and Substrates* (**2**).—The following compounds were prepared using the general procedure for $S_{RN}1$ reactions. (a) 1-(1-*Methyl*-1-*nitroethyl*)-4-*nitroimidazole* (**3d**; R^1 = H). The anion of 4(5)-nitroimidazole (**1a**) (2.0 g, 17.6 mmol) was treated with 2-bromo-2-nitropropane (4.46 g, 26.5 mmol) to yield the pure (by t.l.c. and ^1H n.m.r. spectroscopy) nitroimidazole (**3a**) (3.27 g, 92%). Recrystallisation from ethyl acetate–light petroleum (40—60 °C) (1:1) gave analytically pure 1-(1-*methyl*-1-*nitroethyl*)-4-*nitroimidazole* (**3a**; R^1 = H) (2.09 g, 59%), m.p. 163—165 °C (Found: C, 36.1; H, 4.0; N, 28.0. $C_6H_8N_4O_4$ requires C, 36.0; H, 4.0; N, 28.0%); $\delta_H([^2H_6]$acetone) 2.50 (6 H, s, Me), 8.40 (1 H, d, 2-H), and 8.75 (1 H, d, 5-H); $\delta_C([^2H_6]$acetone) 26.13 (q, Me), 97.15 (s, CMe_2), 120.28 (d, 5-C), 137.17 (d, 2-C), and 149.47 (s, 4-C); [Found: M^+, 200.0545 (0.25%). $C_6H_8N_4O_4$ requires 200.0545]; *m/z* 154 (100), 96 (32), and 69 (99).

Repeat reactions for various reaction times and inhibition and light catalysis studies are shown in Table 1. The reaction between the anion (**1a**) and 2-chloro-2-nitropropane is also shown in Table 1.

(b) 5-(4-*Nitroimidazol*-1-*yl*)-5-*nitro*-1,3-*dioxane* (**3b**; R^1 = H). 4(5)-nitroimidazole (2.0 g, 17.6 mmol) was treated with the dioxane (**2b**; X = Br) (5.0 g, 23.6 mmol) to yield a crude mixture (3.5 g). Chromatography on neutral alumina with CH_2Cl_2 as the eluant, followed by recrystallisation from ethanol, gave crystals of the pure *imidazole* (**3b**; R^1 = H) (1.8 g, 42%), m.p. 147—148 °C (Found: C, 34.5; H, 3.3; N, 22.8. $C_7H_8N_4O_6$ requires C, 34.4; H, 3.3; N, 22.95%); $\delta_H([^2H_6]$acetone) 5.10 (6 H, m, CH_2), 8.5 (1 H, d, 2-H), and 9.10 (1 H, d, 5-H); $\delta_C([^2H_6]$acetone) 68.08 (t, OCH_2C), 93.34 (t, OCH_2O), 90.08 (s, quat. C-NO_2), 119.96 (d, 5-C), and 136.86 (d, 2-C); [Found: M^+, 244.039 (9%). $C_7H_8N_4O_6$ requires 244.0443]; *m/z* 198 (55), 168 (100), 152 (34), 123 (51), 96 (21), 81 (10), and 67 (10).

(c) 2-*Methyl*-1-(1-*methyl*-1-*nitroethyl*)-4-*nitroimidazole* (**3a**; R^1 = Me). 2-Methyl-4(5)-nitroimidazole (2.0 g, 15.7 mmol) was treated with 2,2-dinitropropane (3.16 g, 23.6 mmol) to yield a crude mixture (2.7 g). Chromatography on neutral alumina with CH_2Cl_2–$CHCl_3$ (2:1) as the eluant, followed by recrystallisation from ethyl acetate, yielded colourless crystals of the *nitroimidazole* (**3a**; R^1 = Me) (1.25 g, 37%), m.p. 147—149 °C (Found: C, 39.3; H, 4.7; N, 25.9. $C_7H_{10}N_4O_4$ requires C, 39.25; H, 4.71; N, 26.15%); $\lambda_{max.}$ 290 nm ($\varepsilon = 6 \times 10^5$); $\nu_{max.}$ 3 160, 3 100, 1 560, and 1 350 cm^{-1}; $\delta_H([^2H_6]$acetone) 2.32 (6 H, s, Me_2), 2.45 (3 H, s, 2-Me), and 8.50 (1 H, s, 5-H); $\delta_C([^2H_6]$acetone) 15.71 (q, 2-Me), 25.53 (q, Me_2), 97.74 (s, quat. *C*NO_2), 121.50 (d, 5-C), and 145.23 (s, 4-C) [Found: M^+, 214.0703 (2%). $C_7H_{10}N_4O_4$ requires 214.0702]; *m/z* 168 (15), 126 (15), 96 (100), and 69 (15).

(d) 2-*Methyl*-1-(p-*nitrobenzyl*)-4-*nitroimidazole* (**3c**; R^1 = Me). The anion (**1b**) (2.00 g, 15.7 mmol) was treated with *p*-nitrobenzyl chloride (4.03 g, 23.6 mmol) to yield crude product (5.00 g). Chromatography on neutral alumina with CH_2Cl_2–$CHCl_3$ (2:1) as eluting solvent, followed by recrystallisation from EtOAc, gave yellow crystals of the *nitroimidazole* (**3c**; R^1 = Me) (3.01 g, 73%), m.p. 181—183 °C (Found: C, 50.8; H, 3.9; N, 21.4. $C_{11}H_{10}N_4O_4$ requires C, 50.4; H, 3.8; N, 21.4%); δ_H 2.35 (3 H, s, Me), 5.50 (2 H, s, CH_2), 7.04—8.10 (4 H, ABq, phenyl-H), and 8.20 (1 H, s, 5-H); $\delta_C(CDCl_3)$ 13.18 (q, 2-Me), 50.63 (t, CH_2), 122.36 (d, 5-C), 125.14 (d, phenyl-2-C), 129.46 (d, phenyl-3-C), 144.0 (s, 4-COR 2-C), 148.58 (s, phenyl-4-*C*NO_2) [Found: M^+, 262.0700 (100%), $C_{11}H_{10}N_4O_6$ requires 262.0702]; *m/z* 216 (1), 155 (25), 136 (89), 120 (14), 106 (54), 89 (85), 78 (48), and 63 (9).

(e) 2-*Methyl*-1-[(1-*methyl*-5-*nitroimidazol*-2-*yl*)-*methyl*]-4-*nitroimidazole* (**3d**; R^1 = Me). 2-Methyl-4(5)-nitroimidazole (250 mg, 1.97 mmol) was treated with the 5-nitroimidazole (**2d**; X = Br) (250 mg, 1.14 mmol) to yield crude product (262 mg). Purification using alumina prep. t.l.c. with EtOAc–CH_2Cl_2 (9:1) as the eluant, followed by recyrstallisation from EtOAc gave crystals of the *nitroimidazole* (**3d**; R^1 = Me) (183 mg, 35%), m.p. 208—209 °C (Found: C, 40.4; H, 3.65; N, 31.6. $C_9H_{10}N_6O_4$ requires C, 40.6; H, 3.79; N, 31.57%); $\delta_H(CDCl_3)$ 2.40 (3 H, s, 2-Me), 4.06 (3 H, s, N-Me), 5.72 (2 H, s, CH_2), 8.18 (1 H, s, 5-H), and 8.48 (1 H, s, 4′-H).

The reaction was repeated using the 5-nitroimidazole (**2d**; X = Cl) in place of the 5-nitroimidazole (**3d**; X = Br). The results are reported in Table 1.

(f) 1-(p-*Nitrobenzyl*)-2-*nitroimidazole* (**8**). 2-Nitroimidazole (250 mg, 2.21 mmol) was treated with *p*-nitrobenzyl chloride (379 mg, 2.21 mmol) to yield crude product (365 mg). Purification using silica gel prep. t.l.c. with $CHCl_3$ as eluting solvent, followed by recrystallisation from EtOAc–light petroleum (b.p. 40—60 °C) (1:1), gave colourless crystals of the 2-*nitroimidazole* (**8**) (181 mg, 33%), m.p. 134—135 °C (Found: C, 48.6; H, 3.4; N, 22.1. $C_{10}H_8N_4O_4$ requires C, 48.4; H, 3.25; N, 22.55%); δ_H 6.01 (2 H, s, CH_2), 7.35 (1 H, br s, 4-H), 7.81 (1 H, br s, 5-H), and 7.60—8.91 (4 H, ABq, phenyl-H); $\delta_C([^2H_6]$acetone) 57.12 (t, CH_2), 127.57 (d, 4-C), 128.17 (d, 5-C), 128.39 (d, phenyl-3-C), and 143.53 (s, 2-CNO_2 or phenyl-4-CNO_2) (no other signals were observed) [Found: M^+, 248.0548 (1%), $C_{10}H_8N_4O_4$ requires 248.0545]; *m/z* 136 (25), 90 (21), 97 (100), 78 (40), and 63 (9).

(g) 1-[(1-*Methyl*-4-*nitroimidazol*-2-*yl*)-*methyl*]-2-*nitroimidazole* (**9**). 2-Nitroimidazole (250 mg, 2.21 mmol) was treated

with the 5-nitroimidazole (**2d**; X = Cl) (388 mg, 2.21 mmol) to yield a crude mixture. Chromatography using silica gel prep. t.l.c. with EtOAc–CH_2Cl_2 (9:1) as eluant gave pure product. Recrystallisation from acetone–light petroleum (b.p. 60—80 °C) gave colourless crystals of the nitroimidazole (**9**) (234 mg, 42%), m.p. 168—169 °C (Found: C, 38.3; H, 3.2; N, 33.6. $C_8H_8N_6O_4$ requires C, 38.1; H, 3.2; N, 33.3%); δ_H([$^2H_6$]acetone) 4.10 (3 H, s, NMe), 6.00 (2 H, s, CH_2), 7.18 (1 H, br s, 4-H), 7.48 (1 H, s, 4′-H), and 7.82 (1 H, s, 5-H); *m/z* 206 ($M^+ - NO_2$, 100%), 160 (24), 140 (13), 94 (17), 80 (10), and 67 (11).

The reaction was repeated using the 5-nitroimidazole (**2d**; X = Br) in place of the 5-nitroimidazole (**2d**; X = Cl) and the results are reported in the text.

Competitive $S_{RN}1$ *Reactions.*—4(5)-Nitroimidazole (1.00 g, 8.85 mmol) and sodium hydride (318 mg, 13.3 mmol) were stirred in dry DMSO (25 ml) under nitrogen until both reagents had reacted and dissolved. *p*-Nitrobenzyl chloride (1.52 g, 8.85 mmol) and 2-bromo-2-nitropropane (2.23 g, 13.3 mmol, 1.5 mol equiv.) were added simultaneously to the reaction mixture. The reaction was then irradiated with 2 × 150 W fluorescent lamps for 13 h. The work-up was as described in the general procedure for $S_{RN}1$ reactions. The crude product mixture was analysed by ^1H n.m.r. spectroscopy using *p*-dimethoxybenzene as an internal standard.

The reaction was repeated with 2-methyl-4(5)-nitroimidazole (8.85 mmol), replacing the 4(5)-nitroimidazole, and equimolar amounts (8.85 mmol) of *p*-nitrobenzyl chloride and 2-bromo-2-nitropropane. The results of both reactions are shown in Scheme 4.

Oxidative Addition of Nitroimidazole Anions to the Anions of 2-Nitropropane.—(a) *Preparation of* 1-(1-*methyl*-1-*nitroethyl*)-4-*nitroimidazole* (**3a**; R^1 = H). 4(5)-Nitroimidazole (1.00 g, 8.85 mmol) was added to a solution of sodium hydroxide (0.90 g, 22.5 mmol, 2.5 equiv.) in water (10 ml) and stirred under nitrogen at 0 °C until the nitroimidazole dissolved. CH_2Cl_2 (30 ml) Was added to form a two-phase reaction mixture. The anion of 2-nitropropane (1.47 g, 13.28 mmol, 1.5 equiv.) was added to the solution followed by a solution of potassium ferricyanide (330 mg, 1.77 mmol, 0.2 equiv.) in water (10 ml), and then immediately followed by solid sodium persulphate (2.10 g, 8.85 mmol, 2 equiv.). The mixture was stirred for 1 h, the CH_2Cl_2 and water layers were separated, and the aqueous fraction was further extracted with CH_2Cl_2. The CH_2Cl_2 extracts were combined, washed with water, dried, and evaporated to dryness to yield a crude product (1.11 g). Prep. t.l.c. on alumina with EtOAc–Et_2O (4:1) as eluant gave the nitroimidazole (**3a**; R^1 = H) (0.60 g, 34%) and 2,3-dimethyl-2,3-dinitrobutane [312 mg, 20% based on the 4(5)-nitroimidaozle]. The products were characterised by comparison of ^1H n.m.r. spectra and m.p.s with authentic material.

The reaction was repeated several times under differing conditions; the results are reported in Table 2.

(b) 2-*Methyl*-1-(1-*methyl*-1-*nitroethyl*)-4-*nitroimidazole* (**3a**; R^1 = Me). The reactions were carried out and worked up as reported above in the general procedure except that 2-methyl-4(5)-nitroimidazole replaced 4(5)-nitroimidazole. The results are tabulated in Table 2. Oxidative addition of the anion of 2-nitroimidazole to the anion of 2-nitropropane, carried out as outlined in the general procedure, was unsuccessful.

$S_{RN}1$ *Reactions between* 1-(1-*Methyl*-1-*nitroethyl*)-4-*nitroimidazoles* (**3a**) *and Nucleophiles.*—The reactions were carried out as detailed in the general procedures for $S_{RN}1$ reactions and the general procedure for light catalysis and inhibition studies of $S_{RN}1$ reactions. The results are reported in Table 3.

(a) *Reaction between the* 4-*nitroimidazole* (**3a**; R^1 = H), *and the anion of* 2-*nitropropane.* The nitroimidazole, (**3a**; R^1 = H) (200 mg, 1 mmol) and $Me_2CNO_2^-$ (334 mg, 3 mmol) were allowed to react to yield a crude pure unaltered 1-(1-methyl-1-nitroethyl)-4-nitroimidazole (56 mg, 28%). The CH_2Cl_2 solution was evaporated to dryness to yield pure 2,3-dimethyl-2,3-dinitropropane (53 mg, 30%). Both compounds were characterised by comparison with authentic material by ^1H n.m.r. spectroscopy and m.p.s. Inhibition studies are reported in Table 3.

(b) *Reaction between the* 4-*nitroimidazole* (**3a**; R^1 = Me) *and the anion of* 2-*nitropropane.* The reaction was carried out as above on the same scale and using the same method of purification of products. The results of two reactions (4.5 and 5 h) and inhibition and light catalysis studies are reported in Table 3.

(c) *Reaction between the nitroimidazole* (**3a**; R^1 = H) *and* 4(5)-*nitroimidazole.* The crude product was purified using alumina prep. t.l.c. with CH_2Cl_2–$CHCl_3$ (1:1) as the eluant to yield pure unaltered nitroimidaozle (**3a**; R^1 = Me), and nitroimidazole (**3a**; R^1 = H). Both were characterised by comparison of t.l.c. R_Fs, n.m.r. spectra, and m.p.s with authentic materials.

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