Radical-Nucleophilic Substitution ($S_{RN}1$) Reactions. Part 6.[1] *N*-Anions of Diazoles in $S_{RN}1$ and Oxidative Additions

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The anions of imidazole, benzimidazole, 5(6)-nitrobenzimidazole, and 5(and 6)-nitro-1*H*-and -2*H*-indazoles have been shown to undergo oxidative addition to the anion of 2-nitropropane (using potassium ferricyanide and sodium persulphate), and $S_{RN}1$ reactions with $Me_2C(X)NO_2$ (X = Cl, Br, and NO_2) to yield the corresponding 1-(1-methyl-1-nitroethyl) derivatives. The anions of 5(6)-nitrobenzimidazole and 5(6)-nitro-1*H*- and -2*H*-indazoles underwent reaction with *p*-nitrobenzyl chloride by a $S_{RN}1$ and/or S_N2 mechanism to yield the corresponding 1-(*p*-nitrobenzyl) derivatives. The ambident anions of 5- and 6-nitrobenzimidazole, 5-nitro-1*H*- and -2*H*-indazoles, and 6-nitro-1*H*- and -2*H*-indazoles gave *ca.* 50:50 mixtures of the *N*-1 alkylation products resulting from respective pairs of ambident anions. The 1-(1-methyl-1-nitroethyl) derivatives of benzimidazole and 5- and 6-nitro-1*H*-indazole underwent further substitution of the aliphatic nitro group with the respective diazole to yield 2,2-di(benzimidazol-1-yl)-, 2,2-di[5(and 6)-nitro-1*H*-indazol-1-yl]-propanes.

Substitutions proceeding by the $S_{RN}1$ mechanism (substitution, radical-nucleophilic, unimolecular) are now well known. The $S_{RN}1$ reactions of α-substituted nitroalkanes $[R_2C(X)NO_2]$[2] and, more generally, compounds in which $S_{RN}1$ substitution takes place at sp^3 carbon,[3] have been recently reviewed. α-Substituted nitroalkanes are also prepared by oxidative addition of anions to nitronate anions.[2,3] Both mechanistic sequences proceed with α-nitroalkyl radicals ($R_2\dot{C}NO_2$) and the radical anions of α-substituted nitroalkanes, $[R_2C(X)NO_2]^{-\bullet}$, as reactive intermediates.

Early studies had indicated that nitrogen-centred nucleophiles did not readily undergo $S_{RN}1$ substitutions or oxidative addition reactions.[2,3] A limited number of examples have been reported in the literature. For example, azide anions react with $R_2C(X)NO_2$ in $S_{RN}1$ substitutions and undergo oxidative addition to nitronate anions ($R_2C{=}NO_2^-$).[4] Nitrite anions and tertiary amines undergo $S_{RN}1$ reactions with *p*-nitrobenzyl derivatives[5] and nitrite undergoes oxidative addition to nitronate anions.[6] Our initial studies showed that the anions of 2- and 4(5)-nitroimidazoles[1,7] undergo $S_{RN}1$ reactions with $R_2C(X)NO_2$ and *p*-nitrobenzyl chloride, and oxidative additions to $R_2C{=}NO_2^-$. These results indicated that the use of *N*-centred anions in reactions proceeding by single electron transfer (s.e.t.) and *via* radical and radical anion intermediates, could be extended. The mechanisms for these $S_{RN}1$ and oxidative addition reactions are shown in Schemes 1 and 2 respectively [$>N^-$ = anions of 4(5)-nitroimidazoles].

$$>NH + B: \longrightarrow >N^- + B^+H \quad (1)$$

$$>N^- + RX \xrightarrow[h\nu]{\text{s.e.t.}} >N^\bullet + (RX)^{-\bullet} \quad (2)$$

$$(RX)^{-\bullet} \longrightarrow R^\bullet + X^- \quad (3)$$

$$R^\bullet + >N^- \longrightarrow (>N{-}R)^{-\bullet} \quad (4)$$

$$(>N{-}R)^{-\bullet} + RX \xrightarrow{\text{s.e.t.}} >N{-}R + (RX)^{-\bullet} \quad (5)$$

Summary

$$>N^- + RX \longrightarrow >N{-}R + X^- \quad (6)$$

Scheme 1. $S_{RN}1$ mechanism for the reactions between diazole anions and halogeno nitro substrates

$$Me_2C{=}NO_2^- + Fe^{III} \longrightarrow Me_2\dot{C}{-}NO_2 + Fe^{II} \quad (7)$$

$$Me_2\dot{C}NO_2 + >N^- \longrightarrow [>N{-}C(NO_2)Me_2]^{-\bullet} \quad (8)$$

$$[>N{-}C(NO_2)Me_2]^{-\bullet} + Fe^{III} \longrightarrow >N{-}C(NO_2)Me_2 + Fe^{II} \quad (9)$$

Summary:

$$>N^- + Me_2C{=}NO_2^- + 2Fe^{III} \longrightarrow >N{-}C(NO_2)Me_2 + 2Fe^{II} \quad (10)$$

Scheme 2. Oxidative addition of nitronate anions to the *N*-anions of diazoles

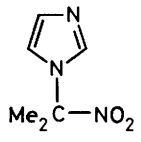
We therefore sought to investigate whether anions of diazoles other than nitroimidazoles would participate in $S_{RN}1$ and oxidative addition reactions. We also wished to compare the new *N*-alkylated compounds with 2- and 5-nitroimidazoles for activity against anaerobic micro-organisms. 5-Nitroimidazoles are the main antibiotics used medicinally against anaerobic bacterial and protozoal infections.[8] The biological results will be reported elsewhere.

This paper reports the extension of our studies to other nitrodiazole anions [5(6)-nitrobenzimidazole and 5- and 6-nitro-1*H*-indazoles] and to diazole anions not containing a nitro group (benzimidazole and imidazole). Since these investigations were carried out, Beugelmans and co-workers have reported[9] the $S_{RN}1$ reactions between various substrates [$R_2C(X)NO_2$ and *p*-nitrobenzyl chloride] and several non-nitro diazole anions (imidazole, benzimidazole, 1,2,4-triazole, and pyrazole).

Results and Discussion

Oxidative Additions of Diazole Anions to $Me_2C{=}NO_2^-$.—The *N*-anions of imidazole, benzimidazole, 5-nitrobenzimidazole, and 5- and 6-nitro-1*H*- and -2*H*-indazoles all readily underwent oxidative addition to $Me_2C{=}NO_2^-$ using potassium ferricyanide [$K_3Fe(CN)_6$] in catalytic amounts and 2 equiv. of sodium persulphate to re-oxidise and recycle Fe^{II} to Fe^{III}. The probable mechanism for these oxidative additions is shown in Scheme 2 ($>N^-$ = diazole anions).

Imidazole and benzimidazole have *N*-ambient anions but the products arising from the ambident anions are identical. Imidazole yielded only the expected $Me_2C(NO_2)$ derivative (**1**). However, the reactions with benzimidazole yielded the expected

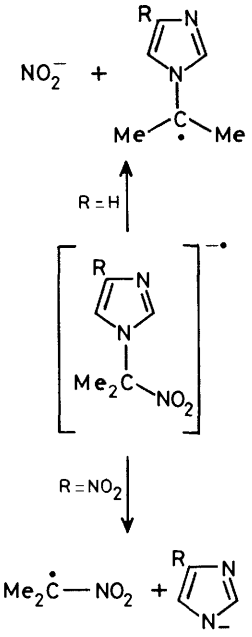


(1)

product (3) but also yielded a further product (5) in low yield. The formation of the 'disubstitution' product (5) raises interesting mechanistic questions. The two most likely mechanisms are shown in Scheme 3 and are dependent on whether the intermediate radical anion, $(3)^{-\bullet}$, undergoes loss of an electron to Fe^{III} or dissociation with loss of nitrite anion. The former process would yield the mono substituted product (3) whereas the latter process would yield the intermediate radical (4), which could then undergo addition of a further benzimidazole anion to yield a second intermediate radical anion, $(5)^{-\bullet}$. Oxidation of this radical anion with Fe^{III} would give the 'disubstitution' product.

We posed this question in our earlier work [1] with 1-(1-methyl-1-nitroethyl)-4-nitroimidazole. The radical anion of this nitroimidazole could possibly dissociate with loss of nitrite or with loss of the nitroimidazole anion (Scheme 4). The former dissociation was not observed in $S_{RN}1$ or oxidative addition reactions. We suggested that the nitroimidazole anion is the favoured nucleofuge from the radical anion. Studies using low temperature e.s.r. spectroscopy [10] supported this conclusion because only $Me_2\dot{C}NO_2$ radicals were observed on dissociation of the radical anion. The e.s.r. spectrum [10] of the radical anion showed that the unpaired electron was localised in the imidazole nitro group with no overlap into the aliphatic nitro group. Dissociation by loss of nitrite would, therefore, require s.e.t. from the imidazole nitro group to the aliphatic nitro group.

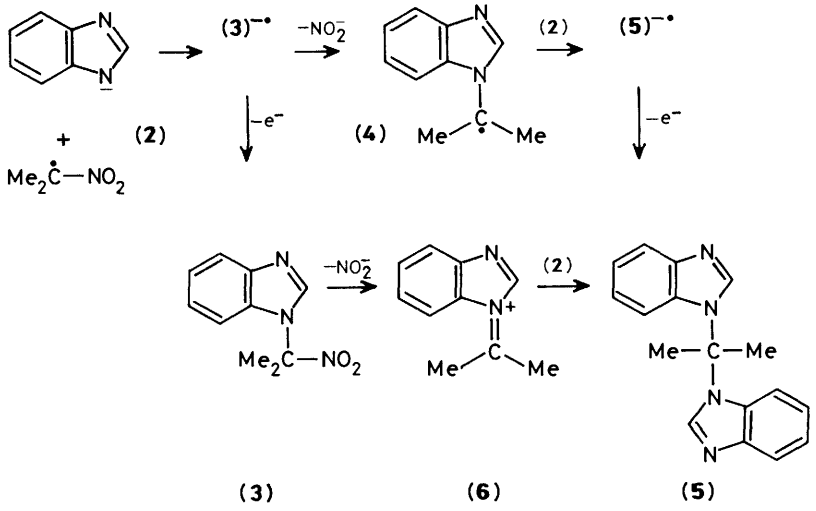
However, when the imidazole nitro group is absent, $S_{RN}1$ reactions *via* loss of nitrite take place slowly.[11] We propose that this different behaviour is explained by different nucleofugicities from the intermediate radical anions, *i.e.* 4-nitroimidazole anion > NO_2^- > imidazole anion. The unpaired electron in the radical anion of 1-(1-methyl-1-nitroethyl)-imidazole almost certainly resides in the π^* molecular orbital of the nitro group and thereby favours loss of NO_2^- (Scheme 4). The benzimidazole radical anion, $(3)^{-\bullet}$, could behave in a similar manner. It is therefore surprising that the 'disubstitution' analogue of the imidazole (1) was not also observed. This



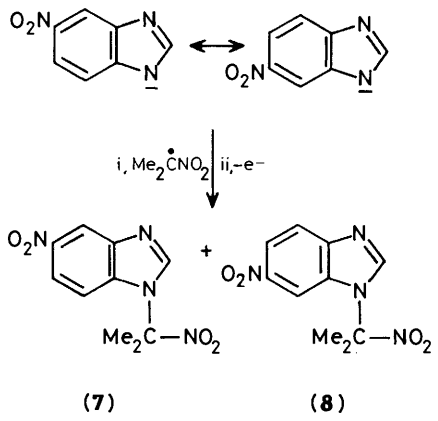
Scheme 4.

difference in behaviour between the imidazole and benzimidazole reactions can be explained by the benzimidazole radical (4) retaining aromatic stability in the benzene ring but the imidazole analogue losing aromatic stability by overlap of the *N*(1) lone pair of electrons into the carbon radical centre. Therefore, loss of NO_2^- from the benzimidazole radical anion is faster than from the imidazole radical anion and allows a small amount of competition with s.e.t. to Fe^{II} in the benzimidazole case but not for the imidazole analogue.

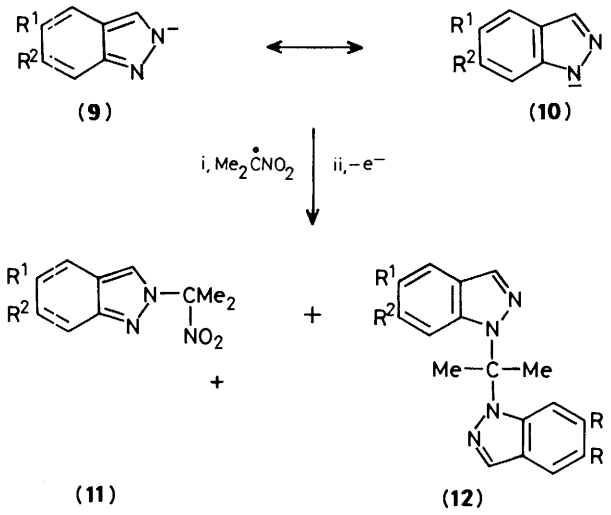
The second possible mechanism for the formation of the disubstitution product (5) is loss of nitrite from the benzimidazole (3) to yield a stabilised cation (6) which undergoes nucleophilic attack by a second benzimidazole molecule. The lack of disubstitution for the imidazole reaction by this mechanism can also be explained by loss of aromatic stability in the intermediate cation, or in the intermediate radical in the radical-anion mechanism. S_N1 Type substitutions proceeding *via* loss of nitrite have been reported [2,12] in several instances when the intermediate cation is stabilised and a suitable Lewis



Scheme 3.



Scheme 5.



(9), (10), (11), (12), a, $R^1 = NO_2$, $R^2 = H$; b, $R^1 = H$, $R^2 = NO_2$

Scheme 6.

acid is used. Loss of nitrite to yield a cation stabilised by a nitrogen atom in a flavin analogue has also been reported.[13] This mechanism is unlikely to explain our results because the reactions were carried out in base, unless the substitution takes place during work-up. Attempts to convert benzimidazole and 1-(1-methyl-1-nitroethyl)benzimidazole to the 'disubstitution' product (**5**), by either 'S_N1' or '$S_{RN}1$' conditions, failed. Similarly, attempts at acid catalysed condensation of acetone with benzimidazole to yield (**5**) failed. The only experimental support for loss of nitrite to yield the intermediate cation (**6**) was the acid catalysed hydrolysis of (**3**) to acetone and benzimidazole.

The oxidative addition of the anion of 5(6)-nitrobenzimidazole, an ambident anion, to $Me_2C{=}NO_2^-$ gave both the expected products, (**7**) and (**8**) (Scheme 5). No products resulting from loss of nitrite were observed. An intermediate cation, analogous to (**6**), would be destabilised by the nitro group thereby making this process less favourable as compared to the benzimidazole oxidative addition reaction. Similarly, the intermediate-radical anions, $(7)^{-\bullet}$ and $(8)^{-\bullet}$, would be predicted to dissociate with loss of diazole anion rather than nitrite as observed for the nitroimidazole analogues. Therefore, the lack of disubstitution can be explained by either mechanism.

The anions of 5- and 6-nitroimidazoles also underwent oxidative addition (Scheme 6). The 2*H*-indazole ambident anions (**9a**) and (**9b**) gave the expected 1-methyl-1-nitroethyl products (**11a**) and (**11b**), whereas the indazole anions (**10a**) and (**10b**) gave 'disubstitution' products (**12a**) and (**12b**). This difference in reactivity can also be explained by retention of aromatic stability for an intermediate radical [analogous to (**4**)] or cation [analogous to (**6**)] in the indazole route, thereby favouring 'disubstitution' *via* loss of nitrite anions. The reason for the more favourable loss of nitrite in the nitroindazole cases as compared to benzimidazole, 5(6)-nitrobenzimidazole, and imidazole is not clear, but the adjacent nitrogen in indazoles may be important in stabilising the intermediate radical or cation. However, if the same argument as expounded in Scheme 4 for imidazoles is used, then a S_N1 mechanism appears more likely than the radical anion dissociation for the formation of the 'disubstitution' products for the nitroindazoles. The isoindazole product (**11b**) could not be separated and fully characterised but the ^1H and ^{13}C n.m.r. spectra of the mixture of (**11b**) and (**12b**) support this assignment.

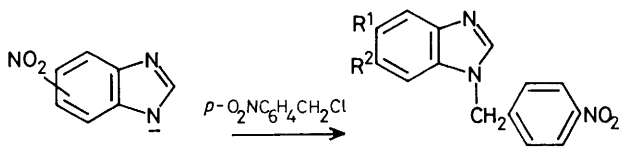
The by-product, 2,3-dimethyl-2,3-dinitrobutane arises from competitive addition, by $Me_2C{=}NO_2^-$ and diazole anions, to $Me_2\dot{C}NO_2$ as shown in equation (11). Similarly, in those reactions producing nitrite anions from 'disubstitution', 2,2-dinitropropane was observed as a by-product [equation (12)].

$$Me_2\dot{C}NO_2 + Me_2C{=}NO_2^- \longrightarrow [Me_2C(NO_2)C(NO_2)Me_2]^{-\bullet} \xrightarrow{-e^-} Me_2C(NO_2)C(NO_2)Me_2 \quad (11)$$

$$Me_2\dot{C}NO_2 + NO_2^- \longrightarrow [Me_2C(NO_2)_2]^{-\bullet} \xrightarrow{-e^-} Me_2C(NO_2)_2 \quad (12)$$

$S_{RN}1$ Reactions between Diazole Anions and $Me_2C(X)NO_2$.— The $S_{RN}1$ substitutions between the diazole anions and $Me_2C(X)NO_2$ (X = Cl, Br, and NO_2), using similar conditions to those for nitroimidazole anions, gave poor yields in slow reactions (Table 1). The nitrodiazoles gave better yields than imidazole and benzimidazole suggesting that lack of *N*-anion formation in the latter is important. The anions of imidazole and benzimidazole are also more nucleophilic and therefore, some abstraction of Br^+ and NO_2^+ from $Me_2C(Br)NO_2$ and $Me_2C(NO_2)_2$ respectively takes place. The resulting $Me_2C{=}NO_2^-$ anions then undergo $S_{RN}1$ reaction with $Me_2C(X)NO_2$ to yield 2,3-dimethyl-2,3-dinitrobutane.

Mechanistic studies were not carried out, but the $S_{RN}1$ mechanism [Scheme 1, >N = diazole and RX = $Me_2C(X)NO_2$] is most probable, as shown for the analogous nitroimidazole anions.[1,7] Strong red colours in the reactions indicate charge-



(**13**) $R^1 = NO_2$, $R^2 = H$ (29%)
(**14**) $R^1 = H$, $R^2 = NO_2$ (30%)

Scheme 7.

Table 1. $S_{RN}1$ reactions between diazole anions and $Me_2C(X)NO_2$

Diazole	$Me_2C(X)NO_2$	Conditions	% Yields: Products	Unchanged diazole	Unchanged $Me_2C(X)NO_2$	$Me_2C(NO_2)C(NO_2)Me_2$
Imidazole	$Me_2C(Cl)NO_2$	DMSO, 96 h	2 (**1**)	25	7	
		HMPA, 48 h	3	22	5	
	$Me_2C(Br)NO_2$	DMSO, 48 h	8	24	9	2
	$MeC(NO_2)_2$	HMPA, 24 h	8	25	12	8
Benzimidazole	$Me_2C(Cl)NO_2$	DMSO, 72 h	5 (**3**); 1 (**5**)	28	5	
	$Me_2C(Br)NO_2$	DMSO, 68 h	6 1	15	3	24
	$Me_2C(NO_2)_2$	DMSO, 48 h	5 1	29	5	36
5(6)-Nitrobenzimidazole	$Me_2C(Cl)NO_2$	DMSO, 48 h	17 (**7**); 12 (**8**)	16	9	
5-Nitroindazole	$Me_2C(Cl)NO_2$	DMSO, 72 h	20 (**11a**); 12 (**12a**)	22	2	
6-Nitroindazole	$Me_2C(Cl)NO_2$	DMSO, 48 h	12 (**12a**); 7 (**12b**)	18	5	

Table 2. A comparison of ambident anion reactivity of nitrodiazole anions

Diazole	Alkylating substrate	Alkylating species	Ratio of *N*-alkyl isomers (%)[a]: 5-NO_2-benzimidazole	6-NO_2-benzimidazole
5(6)-Nitrobenzimidazole	Me_2SO_4[b]	$Me^{\delta+}$(electrophile)	(**7**) 53—61	(**8**) 39—47
	$Me_2C(X)NO_2$	$Me_2\dot{C}NO_2$	58	42
	$Me_2C{=}NO_2^-$	$Me_2\dot{C}NO_2$	52	48
	p-$NO_2C_6H_4CH_2Cl$	*p*-$NO_2C_6H_4\dot{C}H_2$ and/or *p*-$NO_2C_6H_4CH_2^{\delta+}$	(**13**) 55	(**14**) 45
			5-NO_2-1*H*-indazole	5-NO_2-2*H*-indazole
5-Nitro-1*H*(2*H*)-indazole	Me_2SO_4[c]	$Me^{\delta+}$(electrophile)	(**12a**) 47[d]	(**11a**) 53
	$Me_2C(X)NO_2$	$MeCNO_2$	40[d]	60
	$Me_2C{=}NO_2^-$	$MeCNO_2$	43[d]	57
	p-$NO_2C_6H_4CH_2Cl$	*p*-$NO_2C_6H_4\dot{C}H_2$ and/or *p*-$NO_2C_6H_4CH_2^{\delta+}$	(**16a**) 45	(**15a**) 55
			6-NO_2-1*H*-indazole	6-NO_2-2*H*-indazole
6-Nitro-1*H*(2*H*)indazole	Me_2SO_4[d]	$Me^{\delta+}$(electrophile)	(**12b**) 50[d]	(**11b**) 50
	$Me_2C(X)NO_2$	$Me_2\dot{C}NO_2$	43[d]	57
	$Me_2C{=}NO_2^-$	$Me_2\dot{C}NO_2$	44[d]	56
	p-$NO_2C_6H_4CH_2Cl$	*p*-$NO_2C_6H_4\dot{C}H_2$ and/or *p*-$NO_2C_6H_4CH_2^{\delta+}$	(**16b**) 46	(**15b**) 54
			4-NO_2-imidazole[f]	5-NO_2-imidazole[f]
4(5)-Nitroimidazole	Me_2SO_4[e]	$Me^{\delta+}$(electrophile)	90	10
	$Me_2C(X)NO_2$[g]	$Me_2\dot{C}NO_2$	100	0
	$Me_2C{=}NO_2^-$[g]	$Me_2\dot{C}NO_2$	100	0
	p-$NO_2C_6H_4CH_2Cl$[g]	*p*-$NO_2C_6H_4CH_2\cdot$	>95	<5

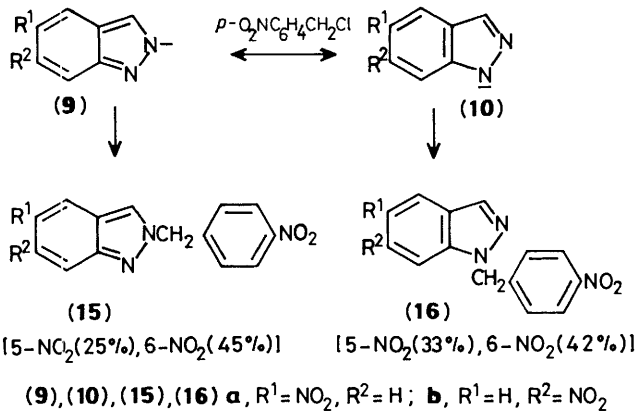
[a] The ratios of the two alkylation products were calculated using ^1H n.m.r. analysis of crude reaction products. [b] Ref. 15. [c] Ref. 16. [d] Calculated from the disubstitution' product. [e] Ref. 14. [f] 4- and 5-Nitroisomers of the respective *N*-alkylated imidazoles. [g] Refs. 1 and 7.

transfer complexes between diazole anions and $Me_2C(X)NO_2$.[1,2] Beugelmans and co-workers[9] have also carried out mechanistic studies to prove the $S_{RN}1$ mechanism for the reaction between imidazole and 5-bromo-5-nitro-2-phenyl-1,3-dioxane. The use of a mild base (potassium carbonate) and acetonitrile as solvent in their reactions[9] gave considerably better yields than our system (sodium hydroxide in dimethyl sulphoxide). The ratio of products from the different ambident anions was very similar (see Table 2) to that of the oxidative addition reactions because the same key step is involved in both mechanisms, *i.e.* addition of diazole anion to $Me_2\dot{C}NO_2$ [equations (4) and (8)].

Substitution Reactions between Diazole Anions and p-*Nitrobenzyl Chloride.*—The nitrodiazole anions were treated with *p*-nitrobenzyl chloride and gave the expected substitution products in good yields. The yields were considerably higher than observed for the reactions with $Me_2C(X)NO_2$. The anions of imidazole and benzimidazole gave intractable products.

The reaction between 6-nitro-1*H*-indazole and *p*-nitrobenzyl chloride was carried out in the presence of radical traps (di-t-butyl nitroxide and oxygen) and a strong electron acceptor (oxygen), and in the absence of light. Although decreases in the yields of the substitution products (**15b**) and (**16b**) and a slight increase in the yields of unaltered *p*-nitrobenzyl chloride were observed, the results are not clear-cut enough to indicate the radical-chain $S_{RN}1$ mechanism. Therefore, it must be concluded that both $S_{RN}1$ and S_N2 mechanisms are operating. Results supporting the $S_{RN}1$ mechanism for the reactions between *p*-nitrobenzyl chloride and other diazole anions [4(5)-nitroimidazole[1,7] and imidazole[9]] have been reported.

Reactivity of Nitrodiazole Ambident Anions.—We reported[1,7] in our previous paper that the regioselectivity exhibited in



Scheme 8.

alkylations by 4(5)-nitroimidazole anions towards the strongly electrophilic radicals, $Me_2\dot{C}NO_2$ and p-NO_2-C_6H_4-CH_2·, was similar to that shown towards the electrophile, dimethyl sulphate (Me_2SO_4).[14] This was explained by kinetic control of the addition of the nitroimidazole anions, *i.e.* the 5-nitro ambident anion being less nucleophilic than the 4-nitro anion because of the proximity of the 5-NO_2 group to the N(1)-anion, and therefore reacting more slowly (see Table 2).

The relative percentages of isomers resulting from each pair of ambident anions was measured using ^{1}H n.m.r. spectroscopy (error *ca.* ±5%). Within experimental error, all three pairs of ambident anions, 5- and 6-nitrobenzimidazole, 5-nitro-1*H*- and -2*H*-indazole and 6-nitro-1*H*-and -2*H*-indazole, gave a *ca.* 50:50 ratio of products (Table 2). Ridd and co-workers[15] and Palmer and co-workers[16] have also reported that *ca.* 50:50 ratios of isomers result from methylation of 5(6)-nitrobenzimidazole and 5- and 6-nitro-1*H*-indazole respectively with the electrophile, Me_2SO_4 (Table 2). Therefore, the regioselectivity of these nitrodiazole anions in reactions with electrophiles and electrophilic radicals is again similar, as observed for 4(5)-nitroimidazoles. These authors[15,16] suggest that strongly electronegative groups in the carbocyclic ring probably exert a minimal influence on the regioselectivity of alkylation with electrophiles, and the same argument probably also applies to alkylation *via* electrophilic radicals.

Identification of Products.—All compounds had satisfactory analytical data, and i.r. and mass spectra. The structures of the various isomers and 'disubstitution' products were assigned on the basis of their ^{1}H and ^{13}C n.m.r. spectra. The n.m.r. spectroscopy of these isomers (5- and 6-nitrobenzimidazoles, 5-and 6-nitro-1*H*- and -2*H*-indazoles) have been extensively studied[16,17] and therefore our data is presented as a supplementary publication [supp. no. 56756 (5pp.)]*. The only noticeable difference was the *ca.* 1.0 p.p.m. upfield shift of 7-H in the ^{1}H n.m.r. spectrum of 2,2-di(benzimidazole-1-yl)propane (**5**) due to the effect of the ring current of the 'other' aromatic ring. A similar 1.2 p.p.m. upfield shift was observed for the analogous nitroindazoles, (**12a**) and (**12b**).

Experimental

General.—M.p.s. were recorded on a Kofler block and are uncorrected. I.r. spectra were measured as Nujol mulls on a Pye Unicam PU 516 spectrometer. ^{1}H N.m.r. spectra were determined at 90 MHz on a Perkin-Elmer R32 spectrometer or at 60 MHz on a Varian EM 360A spectrometer using $SiMe_4$ as an internal standard. All reaction product mixtures were analysed using ^{1}H n.m.r. spectroscopy with a known amount of an added internal standard (*p*-dinitrobenzene or *p*-dimethoxybenzene). ^{13}C N.m.r. spectra were carried out on a Bruker WP-80 spectrometer and mass spectra on a Kratos MS80 instrument. The ^{1}H and ^{13}C n.m.r. spectroscopic data are contained in a supplementary appendix.

Materials.—DMF and DMSO were distilled at low pressure from calcium hydride and stored over molecular sieves. 2-Bromo-2-nitropropane,[18] 2-chloro-2-nitropropane,[18] 2,2-dinitropropane,[6] 2,3-dimethyl-2,3-dinitropropane,[18] and the anion of 2-nitropropane[18] were prepared by literature procedures. Benzimidazole, imidazole, indazole, 5(6)-nitrobenzimidazole, and *p*-nitrobenzyl chloride were purchased commercially and 5-and 6-nitroindazoles were a gift from Fisons PLC (Pharmaceutical Division), Loughborough.

1-(1-*Methyl*-1-*nitroethyl*)*imidazole* (**1**): *General Procedure for Oxidative Additions.*—Imidazole (1.0 g, 14.7 mmol) was dissolved in a solution of sodium hydroxide (1.5 mol equiv.) in water (10 ml) and stirred under oxygen-free nitrogen at 0 °C. Dichloromethane (30 ml) was added to form a two-phase reaction mixture. The anion of 2-nitropropane (2.45 g, 22.1 mmol, 1.5 equiv.) was added to the solution followed by a solution of $K_3Fe(CN)_6$ (0.97 g, 2.94 mmol, 0.2 equiv.) in water (10 ml), and then immediately followed by solid sodium persulphate (7.00 g, 29.5 mmol). The mixture was stirred for 2 h, after which the CH_2Cl_2 and aqueous layers were separated, and the aqueous fraction washed with CH_2Cl_2. The CH_2Cl_2 extracts were washed with water, dried, and evaporated to dryness to yield a crude product. N.m.r. analysis of the mixture showed the imidazole (**1**) (43%) and 2,3-dimethyl-2,3-dinitropropane (16%). Chromatography on neutral alumina with CH_2Cl_2–ethyl acetate (EtOAc) (1:4) followed by recrystallisation from light petroleum (b.p. 40—60 °C) gave pale yellow crystals of 1-(1-*methyl*-1-*nitroethyl*)*imidazole* (**1**) (0.67 g, 28%), m.p. 57—58 °C (Found: C, 46.1; H, 6.0; N, 27.5. $C_6H_9N_3O_2$ requires C, 46.45; H, 5.85; N, 27.0%); $\nu_{max.}$ 3 120, 1 550, and 1 340 cm^{-1}; δ_H($CDCl_3$) 2.26 (6 H, s, Me_2), 7.10 (2 H, br s, 4-H and 5-H), and 7.73 (1 H, s, 2-H) [Found: M^+, 155.0695 (1.5%) $C_6H_9N_3O_2$ requires M, 155.0699]; m/z 109 (100), 82 (30), 68 (10), and 55 (21).

Oxidative Additions of Diazole Anions to the Anion of 2-Nitropropane.—The following compounds were prepared using the general procedure for oxidative addition. Analyses of product mixtures were carried out using n.m.r. spectroscopy. Unchanged diazole was isolated by acidification of the aqueous fraction and extraction with $CHCl_3$. (*a*) 1-(1-*Methyl*-1-*nitroethyl*)*benzimidazole* (**3**). Benzimidazole (1.0 g, 8.47 mmol) was treated with sodium hydroxide (0.51 g, 1.5 equiv.), $K_3Fe(CN)_6$ (0.2 equiv.), sodium persulphate (2 equiv.), and $Me_2C{=}NO_2^-$ (1.5 equiv.) for 75 min to yield a crude mixture. Chromatography using neutral alumina with CH_2Cl_2–chloroform (1:1) as eluant gave two pure products: (i) 1-(1-*methyl*-1-*nitroethyl*)*benzimidazole* (**3**) (0.84 g, 48%), m.p. 69—70 °C (Found: C, 58.3; H, 5.1; N, 20.3. $C_{10}H_{10}N_3O_2$ requires C, 58.55; H, 5.4; N, 20.5%); $\nu_{max.}$ 3 130, 1 605, 1 560, and 1 500 (ArH) and 1 550 and 1 340 cm^{-1} (NO_2) [Found: M^+ 205.0851 (0.02%) $C_{10}H_{11}N_3O_2$ requires 205.0855]; m/z 159 (14), 118 (100), 117 (12), 91 (28), 90 (17), and 64 (19).

(ii) 2,2-*Di*(*benzimidazol*-1-*yl*)*propane* (**5**) (0.14 g, 6%), m.p. 215—216 °C (Found: C, 73.8; H, 5.8; N, 20.15. $C_{17}H_{16}N_4$ requires C, 73.9; H, 5.79; N, 20.3%; $\nu_{max.}$ 3 160—3 060, 1 600, 1 560, and 1 500 cm^{-1} [Found: M^+, 276.1374 (1.5%). $C_{17}H_{16}N_4$ requires 276.1375]; m/z 158 (77), 118 (100), and 90 (23).

Analysis of the residues using n.m.r. spectroscopy indicated:

* For details of the Supplementary publications scheme see 'Instructions for Authors (1989),' *J. Chem. Soc., Perkin Trans. 1*, 1989, Issue 1.

unaltered benzimidazole (19%), 2,2-dinitropropane (5%), and 2,3-dimethyl-2,3-dinitrobutane (14%).

The reaction was repeated under different conditions (only 1.0 equiv. of $Me_2C{=}NO_2^-$; 0, 5, and 60 min reaction times; 2.0 equiv. of $K_3Fe(CN)_6$ with no persulphate) but the yields of products were not improved. Shorter reaction times gave larger amounts of unchanged benzimidazole.

(*b*) 1-(1-*Methyl*-1-*nitroethyl*)-5-(*and* 6)-*nitrobenzimidazoles* (**7**) *and* (**8**). 5(6)-Nitrobenzimidazole (1.0 g) was treated with $Me_2C{=}NO_2^-$, $K_3Fe(CN)_6$, and sodium persulphate for 75 min to yield a crude mixture which was separated using prep. t.l.c. on alumina plates with CH_2Cl_2–light petroleum (b.p. 40—60 °C) (1:1) as eluant to yield two products: (i) The faster running compound was recrystallised from $CHCl_3$–light petroleum (b.p. 40—60 °C) to yield 1-(1-*methyl*-1-*nitroethyl*)-5-*nitrobenzimidazole* (**7**) (0.52 g, 34%), m.p. 211—212 °C (Found: C, 47.85; H, 4.0; N, 22.2. $C_{10}H_{10}N_4O_4$ requires C, 48.0; H, 4.0; N, 22.4%); $\nu_{max.}$ 3 160—3 100, 1 610, 1 520, 1 310 and 1 310 (ArH), and 1 550 and 1 340 cm^{-1} (NO_2) [Found: M^+, 250.0702 (0.7%). $C_{10}H_{10}N_4O_4$ requires 250.0701]; *m/z* 204 (100), 163 (52), 158 (75), 157 (20), 133 (17), 118 (13), 117 (46), and 90 (55).

(ii) The slower running compound was recrystallised from $CHCl_3$–light petroleum (b.p. 40—60 °C) to yield 1-(1-*methyl*-1-*nitroethyl*)-6-*nitrobenzimidazole* (**8**) (0.35 g, 23%), m.p. 129—130 °C (Found: C, 48.1; H, 4.0; N, 22.2. $C_{10}H_{10}N_4O_4$ requires C, 48.0; H, 4.0; N, 22.4%). Analyses indicated unaltered 5(6)-nitrobenzimidazole (29%) and 2,3-dimethyl-2,3-dinitropropane (11%).

(*c*) 1-(1-*Methyl*-1-*nitroethyl*)-5-*nitro*-2H-*indazole* (**11a**) *and* 2,2-*di*(5-*nitro*-1H-*indazol*-1-*yl*)*propane* (**12a**). 5-Nitro-1*H*-indazole was treated with $Me_2C{=}NO_2^-$, $K_3Fe(CN)_6$, and sodium persulphate for 75 min using the general procedure except that 4.0 equiv. of NaOH were used. The resulting crude mixture was subjected to prep. t.l.c. using alumina plates with CH_2Cl_2–light petroleum (b.p. 40—60 °C) as eluant to yield two products: (i) recrystallisation of the faster running component gave 1-(1-*methyl*-1-*nitroethyl*)-5-*nitro*-2H-*indazole* (**11a**) as colourless crystals (0.64 g, 42%), m.p. 135—136 °C (Found: C, 48.0; H, 3.9; N, 22.0. $C_{10}H_{10}N_4O_4$ requires C, 48.0; H, 4.0; N, 22.4%), $\nu_{max.}$ 3 160—3 100, 1 610 (aromatic), 1 550 and 1 340 (aliphatic NO_2), 1 570, and 1 350 (aromatic NO_2) [Found: M^+, 250.0702 (3%). $C_{10}H_{10}N_4O_4$ requires *M*, 250.0701]; *m/z* 204 (100), 158 (47), 118 (54), and 90 (36).

(ii) Recrystallisation of the slower running fraction gave yellow crystals of 2,2-*di*(5-*nitro*-1H-*indazol*-1-*yl*)*propane* (**12a**) (0.27 g, 32%), m.p. 159—161 °C (Found: C, 55.5; H, 3.85; N, 22.65. $C_{17}H_{14}N_6O_4$ requires C, 55.75; H, 3.85; N, 22.95%); *m/z* 366 (0.7%), 204 (100), 163 (9), 158 (11), and 118 (8). Analyses using n.m.r. spectroscopy indicated unchanged 5-nitro-1*H*-indazole (16%), 2,2-dinitropropane (2%), and 2,3-dimethyl-2,3-dinitropropane (9%). Repeat reactions using a shorter reaction time (60 min) or 1.5 equiv. of NaOH gave similar yields.

(*d*) 2,2-*Di*(6-*nitro*-1H-*indazol*-1-*yl*)*propane* (**12b**). 6-Nitroindazole was treated for 75 min to yield a crude mixture. The two main products had almost identical R_F values on various chromatographic media and with various solvents. Repeated prep. t.l.c. using alumina plates with CH_2Cl_2–light petroleum (b.p. 40—60 °C) as eluant gave the 'dimeric' product. Recrystallisation from $CHCl_3$–light petroleum (b.p. 40—60 °C) gave yellow crystals of the title compound (**12b**) (0.65 g, 29%), m.p. 210—213 °C (Found: C, 55.25; H, 4.2; N, 22.95. $C_{17}H_{14}N_6O_4$ requires C, 55.75; H, 4.17; N, 23.0%); *m/z* 366 (M^+, 1%) and 204 ($M^+ - 162$, 100).

A second fraction from the t.l.c. gave a mixture of the latter compound (**12b**) and a major compound which was assigned to 1-(1-methyl-1-nitroethyl)-6-nitro-2*H*-indazole on the basis of the ^1H and ^{13}C n.m.r. spectra. Further purification proved unsuccessful. Analysis using ^1H n.m.r. spectroscopy on the reaction crude showed unchanged 6-nitro-1*H*-indazole (18%), 2,2-dinitropropane (4%), and 2,3-dimethyl-2,3-dinitrobutane (10%).

Reaction between Benzimidazole and 1-(1-*Methyl*-1-*nitroethyl*)*benzimidazole* (**3**).—(*a*) The anion of benzimidazole (0.58 g) and 1-(1-methyl-1-nitroethyl)benzimidazole (1 equiv.) were stirred in CH_2Cl_2–$CHCl_3$ (4:1) for 2 h under an atmosphere of nitrogen and with normal irradiation. The unchanged starting materials were recovered on work-up and no 2,2-di-(benzimidazol-1-yl)propane could be detected.

(*b*) The reaction was repeated for 4 h using MeOH–water (3:2) as the solvent and five drops of conc. hydrochloric acid were added as a catalyst. The reaction mixture was extracted with $CHCl_3$, and the $CHCl_3$ layer treated with 2,4-dinitrophenylhydrazine. Crystals of acetone were filtered off, recrystallised, and characterised (42%).

(*c*) The above reaction was repeated except that five drops of 2M aqueous Na_2CO_3 solution were added in place of hydrochloric acid. The starting materials were recovered and no acetone resulted.

(*d*) The reaction was repeated using dry CH_2Cl_2 as solvent and tin(IV) chloride (2 mol equiv.) was added. After the mixture had been stirred for 26 h it was worked up to yield unchanged 1-(1-methyl-1-nitroethyl)benzimidazole (**3**) (58%). No 2,2-di-(benzimidazol-1-yl)propane could be detected.

Attempted Preparation of 2,2-*Di*(*benzimidazol*-1-*yl*)*propane from Benzimidazole and Acetone*.—Benzimidazole (2.0 g), acetone (20 ml), and a catalytic amount of toluene-*p*-sulphonic acid were dissolved in benzene (100 ml) and heated under reflux with a Dean-Stark water separator for 48 h. Unchanged benzimidazole (95%) was recovered and no 2,2-di(benzimidazole-1-yl)propane was detected.

$S_{RN}1$ Reactions between Diazole Anions and 2-*Substituted* 2-*Nitropropanes: General Procedure for $S_{RN}1$ Reactions*.—The diazole (1.0 g) was dissolved in dry DMSO or HMPA (50 ml) and deoxygenated with dry oxygen-free nitrogen for 30 min under anhydrous conditions. Potassium t-butoxide (1.5 equiv.) suspended in dry DMSO was added to the solution and the mixture stirred for a further 30 min. 2-Bromo-2-nitropropane, 2-chloro-2-nitropropane, or 2,2-dinitropropane (1.5 equiv.) was added. The solution, which rapidly turned red, was irradiated with fluorescent lamps [2 × 150 W, mercury blended tungsten universal mounted (MBTU) emitting light maximally at 430 nm] from a distance of 10 cm for the determined time. The reaction was worked up when the red colour faded to orange. Water (50 ml) was added and the mixture extracted with CH_2Cl_2. The CH_2Cl_2 extracts were washed with water (7 × 50 ml), dried, and evaporated to dryness. The crude mixtures were analysed using t.l.c. and ^1H n.m.r. spectroscopy. The results are presented in Table 1. The aqueous layer was acidified and the precipitated unchanged diazole starting material was filtered off and dried.

Substitutions between Diazole Anions and p-*Nitrobenzyl Chloride*.—The following compounds were prepared using the general procedure for $S_{RN}1$ reactions. (*a*) 1-(p-*Nitrobenzyl*)-5-(*and* 6)-*nitrobenzimidazoles* (**13**) and (**14**). The reaction time was 22 h. The resulting crude mixture was separated into two products using column chromatography on neutral alumina with $CHCl_3$–light petroleum (b.p. 40—60 °C) (1 : 2) as eluant. (i) The faster running fraction was recrystallised from EtOAc–light petroleum (b.p. 40—60 °C) to yield 1-(p-*nitrobenzyl*)-5-*nitrobenzimidazole* (**13**) (0.53 g, 29%), m.p. 196—198 °C (Found: C, 55.95; H, 3.3; N, 18.6. $C_{14}H_{10}N_4O_4$ requires C, 56.35; H, 3.4; N, 18.8%) [Found: M^+ 298.0709 (100%). $C_{14}H_{10}N_4O_4$ requires

298.0702]; *m/z* 163 (14), 136 (63), 117 (11), and 90 (32). (ii) The slower running fraction was recrystallised from EtOAc–light petroleum (b.p. 40—60 °C) to yield 1-(p-*nitrobenzyl*)-6-*nitrobenzimidazole* (**14**) (0.55 g, 30%), m.p. 187—188 °C (Found: C, 56.1; H, 3.3; N, 18.5. $C_{14}H_{10}N_4O_4$ requires C, 56.35; H, 3.4; N, 18.8%) [Found: M^+, 298.0695 (100%). $C_{14}H_{10}N_4O_4$ requires 298.0702]; *m/z* 136 (56), and 90 (36). Analysis showed unchanged diazole (4%) and unchanged *p*-nitrobenzyl chloride (2%).

(*b*) 1-(p-*Nitrobenzyl*)-5-*nitro*-1H- *and* -2H-*indazoles* (**16a**) *and* (**15a**). The reaction time was 20 h. Column chromatography of the crude product on neutral alumina with $CHCl_3$–light petroleum (b.p. 40—60 °C) as eluant gave: (i) 1-(p-*nitrobenzyl*)-5-*nitro*-1H-*indazole* (**16a**) (0.60 g, 33%), m.p. 159—161 °C [EtOAc–light petroleum (60—80 °C)] (Found: C, 56.5; H, 3.2; N, 19.0. $C_{14}H_{10}N_4O_4$ requires C, 56.35; H, 3.4; N, 18.8%) [Found: M^+, 298.0677 (100%). $C_{14}H_{10}N_4O_4$ requires *M*, 298.0702]; *m/z* 136 (35) and 90 (20).

(ii) 1-(p-*Nitrobenzyl*)-5-*nitro*-2H-*indazole* (**15a**) (0.45 g, 25%), m.p. 179—180 °C [EtOAc–light petroleum (b.p. 60—80 °C)] (Found: C, 55.8; H, 3.2; N, 18.7. $C_{14}H_{10}N_4O_4$ requires C, 56.35; H, 3.4; N, 18.8%); [Found: M^+, 298.0694 (100%). $C_{14}H_{10}N_4O_4$ requires *M*, 298.0702]; *m/z* 136 (30), 106 (23), and 90 (23).

Analysis showed unchanged 5-nitro-1*H*-indazole (8%) and unchanged *p*-nitrobenzyl chloride (2%).

(*c*) 1-(p-*Nitrobenzyl*)-6-*nitro*-1H- *and* -2H-*indazoles* (**16b**) *and* (**15b**). The reaction time was 22 h. The reaction product mixture was separated into two compounds using column chromatography on alumina with $CHCl_3$–light petroleum (b.p. 40—60 °C) as eluant. (i) 1-(p-*Nitrobenzyl*)-6-*nitro*-1H-*indazole* (**16b**) (colourless crystals from $CHCl_3$–hexane) (0.77 g, 42%), m.p. 184—185 °C (Found: C, 56.3; H, 3.2; N, 19.0. $C_{14}H_{10}N_4O_4$ requires C, 56.35; H, 3.4; N, 18.8%); $\nu_{max.}$ 3 030, 3 040, 1 610, and 1 600 (aromatic), 1 520, 1 360, and 1 320 cm^{-1} (NO_2) [Found: M^+, 298.0702 (100%). $C_{14}H_{10}N_4O_4$ requires *M*, 298.0702]; *m/z* 251 (14), 136 (65), 106 (56), 90 (61), and 89 (75).

(ii) 1-(p-*Nitrobenzyl*)-6-*nitro*-2H-*indazole* (**15b**) (yellow needles from $CHCl_3$–hexane) (0.82 g, 45%), m.p. 217—219 °C (Found: C, 56.5; H, 3.2; N, 18.8. $C_{14}H_{10}N_4O_4$ requires C, 56.35; H, 3.4; N, 18.8%); $\nu_{max.}$ 3 040, 1 610 (aromatic), 1 520, 1 380, and 1 340 cm^{-1} (NO_2); [Found: M^+, 298.0713 (100%). $C_{14}H_{10}N_4O_4$ requires *M*, 298.0702]; *m/z* 251 (17), 136 (18), 106 (21), 90 (18), and 89 (25).

The reaction was repeated for 30 min and the product analysed by ^1H n.m.r. spectroscopy: it contained the 6-nitro-1*H*-indazole (**16b**) (25%), the 6-nitro-2*H*-indazole (**15b**) (33%), and *p*-nitrobenzyl chloride (< 1%).

(i) The reaction was repeated under the same conditions except that 40 mol% of di-t-butyl nitroxide was added prior to its illumination. The yields were (**16b**) (14%), (**15b**) (33%), and *p*-nitrobenzyl chloride (5%),

(ii) The reaction was carried out with exclusion of light which was effected by wrapping the flask in aluminium foil. The yields were: (**16b**) (12%), (**15b**) (25%), and *p*-nitrobenzyl chloride (10%).

(iii) The reaction was repeated with the exclusion of light under an atmosphere of oxygen instead of nitrogen. The yields were (**16b**) (8%), (**15b**) (21%), and *p*-nitrobenzyl chloride (8%).

(*d*) *Reactions between* p-*nitrobenzyl chloride and imidazole, and benzimidazole.* The reactions gave impure products which could not be purified.

Acknowledgements

We thank Mr. Tony Manners of Fisons (Pharmaceutical Division) Loughborough for assistance with n.m.r. spectroscopy, Fisons (Pharmaceutical Division) Loughborough for a gift of the nitroindazoles, Mr. M. Harris for the measurement of ^{13}C n.m.r. spectra, and Mr. J. Greenfield for the measurement of mass spectra.

We also thank Lorenzayo Ltd., Lagos, for financial assistance (A. T. O. M. A.).

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Received 24*th November* 1988; *Paper* 8/04653K