Aromatic Nucleophilic Substitution Reactions of Ambident Nucleophiles. III.[1] Reactivity of the Nitrite Ion

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Received September 23, 1974

The reactivity patterns in the SNAr reactions of the ambident nitrite ion with nitrohalobenzenes depend on the solvent, the leaving group, and the position of substituents. The rate-determining step can be either the formation or decomposition of the intermediate complex, depending on the leaving group and mode of attack by the nitrite ion. The activating effect of a para relative to the same ortho substituent depends on the leaving group and on whether nitrite is attacking via its nitrogen or oxygen atom. The nitrite ion is of comparable nucleophilicity to azide ion, but is a much weaker carbon base than azide when attacking through its nitrogen atom, although it is a strong carbon base when attacking through oxygen. The reactivity patterns of nitrite ion in SNAr reactions are compared with those of other nucleophiles, such as N_3^-, SCN^-, the halides, RS^- and RO^-.

In Part II[1] we gave further evidence for a mechanism (Scheme I) first proposed by Rosenblatt, Dennis, and Goodin[2] for the reactions of nitrite ion with aromatic compounds, ArX, which are suitably activated for aromatic nucleophilic substitution. A number of rate constants were reported and used to support the mechanism. This paper takes those rate constants and some new ones and discusses reactivity patterns,[3] i.e., nucleophilicities, leaving group tendencies, solvent effects, and substituent effects in these reactions and in reactions involving related nucleophiles, such as azide, thiocyanate, and the halides.

The ambident nitrite ion[2,4] bonds to aromatic carbon via its nitrogen or its oxygen atom (N-attack or O-attack), but the end product of reaction with ArX is always the phenoxide, ArO^-, owing to the reactivity of the nitro intermediate $ArNO_2$, which can be isolated in certain reactions.[1,2]

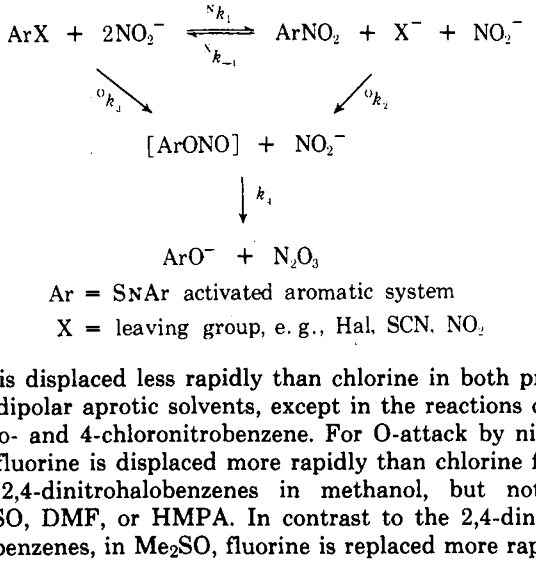
The reactions of nitrite ion have similarities to the SNAr reactions of the ambident thiocyanate ion, which were discussed in Part I.[5] Thus the compounds ArSCN and $ArNO_2$ are reactive intermediates, and SCN^- and NO_2^- are weak carbon bases. The nitrite ion has a soft[6] nitrogen atom and two harder[6] oxygen atoms, whereas SCN^- has soft sulfur and harder nitrogen. These properties cause interesting variations in leaving group tendencies,[3] in the activating effect of substituents,[3] and even in the effect of solvents on rates and mechanism, as discussed below.

Results and Discussion

Rate constants were measured and processed as described in Parts I[5] and II.[1]

Leaving Group Tendencies.[3] Table I compares the rates of reaction of three sets of fluoro-, chloro-, and iodonitro-substituted benzenes, ArX, with nitrite ion, via N-attack as log ${}^{N}k^{X}$, and O-attack as log ${}^{O}k^{X}$. Three comparisons are made, ${}^{N}k^{X}/{}^{O}k^{X}$ (the ratio of N- to O-attack), log ${}^{N}k^{F}/{}^{N}k^{Cl}$, and log ${}^{O}k^{F}/{}^{O}k^{Cl}$. The latter two comparisons show leaving group tendencies of fluorine relative to chlorine for N- and O-attack, respectively. In some cases, only upper or lower limits to these ratios have been recorded because the other rate constant was too slow to measure in competition with other reactions. However, even these ratios give useful information. All three sets of ratios show substantial changes with one or more of the variables of solvent, leaving group, or substituent. These changes are related to changes of mechanism, e.g., formation or decomposition of the SNAr intermediate as rate-determining step.[3] As shown in Table I, for N-attack by nitrite ion, fluorine is displaced less rapidly than chlorine in both protic and dipolar aprotic solvents, except in the reactions of 4-fluoro- and 4-chloronitrobenzene. For O-attack by nitrite ion, fluorine is displaced more rapidly than chlorine from the 2,4-dinitrohalobenzenes in methanol, but not in Me_2SO, DMF, or HMPA. In contrast to the 2,4-dinitrohalobenzenes, in Me_2SO, fluorine is replaced more rapidly than chlorine by O-attack of nitrite ion on both the 2- and the 4-nitrohalobenzenes in Me_2SO.

Scheme I



Ar = SNAr activated aromatic system

X = leaving group, e. g., Hal, SCN, NO_2

Variations in the relative rates of displacement of fluorine, relative to other halogens in SNAr reactions, have long been used as a probe into whether formation of the SNAr intermediate or its decomposition is rate determining.[3] If fluorine is displaced much more rapidly than other halogens, then formation of the intermediate is rate determining,but if fluorine is displaced less rapidly then its decomposition is rate determining. Hard nucleophiles which are strong carbon bases,[7] e.g., methoxide ion, displace hard fluorine much more rapidly than they displace other halogens, whereas soft nucleophiles, which are weaker carbon bases, e.g., SCN^-,[5] PhS^-,[3,8] and Br^-,[3] displace fluorine more slowly or only as fast as they displace the other halogens.

Leaving group tendencies of fluorine, chlorine, and the nitro group relative to iodine are compared in Table II. The variation is considerable, e.g., k^F/k^I decreases by more than 10,000 for reactions of the 2,4-dinitrohalobenzenes in the order of nucleophile/solvent: Pip/MeOH ≈ OMe^-/MeOH ≃ N_3^-/MeOH ≈ $\mathbf{O}NO^-$/MeOH > $SC\mathbf{N}^-$/DMF > PhS^-/MeOH > $\mathbf{O}NO^-$/DMF > $\mathbf{S}CN^-$/DMF ≈ $\mathbf{S}CN^-$/MeOH > $\mathbf{N}O_2^-$/DMF, where the atom which is bonding to carbon is boldfaced. Iodine can be replaced up to ten times *more* rapidly than fluorine, chlorine, or nitro by soft nucleophiles, but with some hard nucleophiles, iodine is replaced up to 1000 times *less* rapidly than fluorine or nitro and up to five times less rapidly than chlorine. A spectrum of leaving

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Table I
SNAr Reaction of Nitrite Ion with Halonitrobenzenes. Leaving Group Tendencies and Effect of Leaving Group and Solvent on Ratio of N-Attack to O-Attack

Substrate ArX	Solvent	Temp, °C	Log $^{N}k^{X\,a,b}$	Log $^{O}k^{X\,a,b}$	$^{N}k^{X}/^{O}k^{X}$	Log $^{N}k^{F}/^{N}k^{Cl}$	Log $^{O}k^{F}/^{O}k^{Cl}$
Ar″F	MeOH	45	<-3	-1.97	<0.1	<0.7	$>+2.4$
Ar″Cl	MeOH	45	-3.72	<-4.4	>5		
Ar″I	MeOH	45	-3.96	<-4.7	>5		
Ar″F	Me_2SO	25	<-1.5	-0.85^{c}	<1	<-1	≤-0.6
Ar″Cl	Me_2SO	25	-0.40	-0.22	0.67		
Ar″I	Me_2SO	25	-0.57^{c}		>1		
Ar″F	DMF	25	<-1	$-0.62^{c,d}$	<1	<-1	≤-1.3
Ar″Cl	DMF	25	0.48^{d}	0.65^{f}	0.67		
Ar″I	DMF	25	$0.15^{c,d}$		>1		
Ar″F	HMPA	25	<0.5	$1.0^{c,d}$	<1	<-2	≤-1.8
Ar″Cl	HMPA	25	2.66^{d}	2.84^{d}	0.67		
Ar″I	HMPA	25	$2.12^{c,d}$		>1		
o-Ar′F	Me_2SO	100	-3.98	-3.50	0.33	-0.41	$+0.24$
o-Ar′Cl	Me_2SO	100	-3.57	-3.74	1.5		
o-Ar′I	Me_2SO	100	-3.1	-4	7		
p-Ar′F	Me_2SO	100	-2.89	-3.50	4	$+0.86$	$+0.55$
p-Ar′Cl	Me_2SO	100	-3.75	-4.05	2		
p-Ar′I	Me_2SO	100	-3.3	-4.2	8		

Ar″F = 1-F-2,4$(NO_2)_2C_6H_3$, *o*-Ar′F = 1-F-2$NO_2C_6H_4$, *p*-Ar′F = 1-F-4$NO_2C_6H_4$, etc.

[a] Taken from ref 1 unless otherwise stated. [b] $^{N}k^{X}$ and $^{O}k^{X}$ are the rate constants for N- and O-attack, respectively, in l. mol^{-1} sec^{-1} with X-Hal as the leaving group. [c] Only this mode of attack could be detected. [d] This work.

group tendencies is shown by the reactions of the ambident nitrite ion (Table II), which behaves as a rather soft nucleophile and is softer when attacking through nitrogen than when attacking through oxygen.

The log $^{O}k^{F}/^{O}k^{Cl}$ value for the SNAr reaction of nitrite ion via O-attack on the 2,4-dinitrohalobenzenes is high in methanol but low in dipolar aprotic solvents (Table I). This effect has long been anticipated,[5,8] but rarely if ever observed in SNAr reactions[7,8] with other nucleophiles. It suggests that formation of the intermediate complex is rate determining in methanol but decomposition of the intermediate complex is rate determining in dipolar aprotic solvents. A reason could be that small anions, like F^-, have a much more endoenergetic free energy of transfer from methanol to the poorly solvating dipolar aprotic solvents than do anions like nitrite and especially the intermediate complex anion.[7] Thus loss of fluoride ion from a fluorine-containing complex anion requires a much higher activation energy in dipolar aprotic relative to that for the formation of the complex from NO_2^- and Ar″F than it does in methanol.

As shown in Table II, the nitrite ion is a very labile leaving group, compared to iodide ion in most SNAr reactions. As with fluorine, the lability depends on the nucleophile; e.g., NO_2 is not particularly labile when displaced by NO_2^- (O- or N-attack), but is very labile when displaced by the small azide ion.

It is believed that the strong electronegativity of the nitro group and of fluorine when bound to carbon accounts for the high reactivity of ArF and $ArNO_2$ relative to ArI in SNAr reactions for which formation of the intermediate complex is rate determining.[3] However, when the decomposition of the intermediate complex is rate determining, nitro and fluorine are much less labile, relative to iodine. Examples of both types of reaction are in Table II.

Substituent Effects.[3] The relative rates of SNAr reactions of aromatic compounds activated by a para vs. the same ortho substituent show differences which can tell us something about the mechanism of SNAr reactions.[3,9–11] There are of course steric interactions of the reaction center with ortho groups, but not with para groups in SNAr reactions. Reactivity patterns for reactions with azide ion and nitrite ion in Me_2SO are presented as para/ortho ratios for NO_2, F, and Cl as leaving groups in Table III. Para/ortho rate ratios are rates of reaction of a para isomer divided by the rate of the corresponding reaction of the ortho isomer under identical conditions.

Nitro substituents para to a leaving NO_2 or Cl are *less* effective in enhancing rate of attack by nitrite ion in Me_2SO than are ortho nitro substituents; however, when the much smaller fluorine is the leaving group, a para is *more* effective than an ortho nitro substituent (Table III). This may be related to the fact, confirmed by X-ray work, that halogens twist ortho nitro groups in halonitrobenzenes. The twisting is minor for fluorine but naturally is greater with increasing size of the halogen.[12] Thus *o*-dinitrobenzene and *o*-nitrochlorobenzene, with their bulky substituents, are likely to be more reactive species than their para isomers. Examination of models show that the twisting of the nitro group in the ortho isomers is likely to be relieved in the transition state for formation of the SNAr complex as the carbon at the reaction center becomes sp^3 hybridized.[3] The larger the leaving group, the greater the relief. Thus nitroaromatics with bulky leaving groups ortho to the nitro group react more rapidly than the corresponding para isomers, leading to low para/ortho rate ratios. This reasoning, applied to Table III, is valid for Me_2SO as solvent, but special solvent effects must be considered for reactions in some protic solvents.[10,11]

With fluorine as leaving group, the steric effect of fluorine on an ortho nitro group is small, so that para/ortho ratios close to unity are expected. The value of 12 for N-attack by nitrite ion in Me_2SO on the *o*- and *p*-nitrofluorobenzenes is anomalous in terms of a bond-forming rate-determining step. Leaving group tendencies (Table II) have suggested that this pair of reactions is likely to be one in which decomposition of the intermediate—not formation—is rate determining and the high para/ortho ratio supports this. Thus the fluorine- and nitro-containing intermediate, in which there is no steric interaction between reaction

Table II
Effect of Nucleophiles and Solvent on Leaving Group Mobility of Groups X Relative to Iodide in SNAr Reactions

Nucleophile	Solvent	Temp, °C	Substrate^{a}	Log k^{X} − log k^{I}: X = F	Cl	NO$_2$
PhS$^-$	MeOH^{e}	30	Ar″	1.3	−0.2	
PhS$^-$	MeOH^{f,g}	30	*p*-Ar′			2.1
Ar″S$^-$	MeOH^{g}	100	Ar″	0.6	−0.6	2.6
SCN^{-b}	MeOH^{g}	100	Ar″	−1.0	−0.8	
SCN^{-b}	DMF^{g}	75	Ar″	−1.1	−0.5	1.7
SCN^{-b}	DMF^{g}	75	Ar″	1.9	0.2	≤1.9
N$_3^-$	MeOH^{h,i}	25	Ar″	2.8	0.2	3.6
N$_3^-$	MeOH^{j}	100	*o*-Ar′	1.6		
N$_3^-$	MeOH^{j}	100	*p*-Ar′	1.8		
N$_3^-$	DMF^{j}	100	*p*-Ar′	2.0	−0.1	
N$_3^-$	DMF^{h}	−16	Ar″	>2	0.7	
Pip	MeOH^{k}	0	Ar″	3.5	0.6	2.9
Pip	EtOH^{l}	50	*o*-Ar′	2.7	0.1	
Pip	EtOH^{l}	50	*p*-Ar′	3.05	0.4	
Pip	Me$_2$SO^{m}	50	*p*-Ar′	3.2	0.6	
NO$_2^{-b}$	MeOH^{s}	45	Ar″	<1	0.2	~1.2^{c}
NO$_2^{-b}$	DMF^{s}	25	Ar″	<−1	~0.3	~1.4^{c,d}
NO$_2^{-b}$	Me$_2$SO^{s}	100	*o*-Ar′	−0.9	−0.5	0.5
NO$_2^{-b}$	Me$_2$SO^{s}	100	*p*-Ar′	0.4	−0.45	−0.5
ONO^{-b}	MeOH^{s}	45	Ar″	>2	0–1	>1
ONO^{-b}	DMF^{s}	25	Ar″	~0		>2^{c}
ONO^{-b}	Me$_2$SO^{s}	100	*o*-Ar′	0.5	0.3	1.3
ONO^{-b}	Me$_2$SO^{s}	100	*p*-Ar′	0.7	0.15	0.2
MeO$^-$	MeOH^{n,o}	30	Ar″	3.3	0.7	2.9
MeO$^-$	MeOH^{p}	100	*o*-Ar′	2.7	0.2	
MeO$^-$	MeOH^{q}	100	*p*-Ar′	2.6	0.4	
Br$^-$	DMF^{g,r}	73	Ar″		−1.1	
Cl$^-$	DMF^{r}	73	Ar″		−0.9	

[a] *o*-Ar′ = 2-NO$_2$C$_6$H$_4$, *p*-Ar′ = 4-NO$_2$C$_6$H$_4$, Ar″ = 2,4(NO$_2$)$_2$-C$_6$H$_3$. [b] Mode of attack for ambident nucleophiles is boldfaced to show which atom is bonding to carbon. [c] Assuming an N:O ratio similar to that for *o*-dinitrobenzene and *o*-nitroiodobenzene in Me$_2$SO. [d] Solvent is Me$_2$SO. [e] J. F. Bunnett and W. S. Merritt, *J. Am. Chem. Soc.*, 79, 5967 (1957). [f] Reference 8. [g] D. E. Giles, Ph.D. Thesis, University of Western Australia, 1970. [h] B. O. Coniglio, D. E. Giles, W. R. McDonald, and A. J. Parker, *J. Chem. Soc. B*, 152 (1966). [i] K. C. Ho, J. Miller, and K. W. Wong, *J. Chem. Soc.*, 310 (1966). [j] J. Miller and A. J. Parker, *J. Am. Chem. Soc.*, 83, 117 (1961). [k] J. F. Bunnett, E. W. Garbisch, and K. M. Pruitt, *J. Am. Chem. Soc.*, 79, 385 (1957). [l] N. B. Chapman, R. E. Parker, and P. W. Soanes, *J. Chem. Soc.*, 2109 (1954). [m] H. Suhr and H. Grube, *Ber. Bunsenges. Phys. Chem.*, 70, 544 (1966). [n] A. L. Beckwith, J. Miller, and G. D. Leahy, *J. Chem. Soc.*, 3552 (1952). [o] J. Miller and K. W. Wong, *Aust. J. Chem.*, 18, 117 (1965). [p] B. A. Bolto, J. Miller, and V. A. Williams, *J. Chem. Soc.*, 2926 (1955). [q] G. P. Briner, J. Miller, M. Liveris, and P. G. Lutz, *J. Chem. Soc.*, 1265 (1954). [r] M. Ruane, Honors Thesis, University of Western Australia, 1965. [s] This work.

Table III
Reactions of Azide and Nitrite Ion with 1-X-2-Nitro- and 1-X-4-Nitrobenzene at 100° in Me$_2$SO. Variation of Para:Ortho Rate Ratios

Nucleophile	k_p/k_o^{a}: X = NO$_2$	F	Cl
ONO^{-b}	0.1	1.0	0.5
NO$_2^{-b}$	0.14	12	0.65
N$_3^-$	0.2^{c}		0.2^{d}

[a] Rate of reaction of the para isomer divided by the rate of reaction of the ortho isomer. [b] The atom which bonds to carbon is boldfaced for ambident nucleophiles. [c] Reaction is at 40°. [d] $k_p = 3.8 \times 10^{-4}\ M^{-1}\ \mathrm{sec}^{-1}$.

center and ortho nitro group, is decomposing in the rate-determining step through a transition state, whose structure is tending toward the product, *o*-dinitrobenzene. In this product there are strong unfavorable interactions between the ortho substituent nitro group and the entering nitro group. Thus the "bond breaking reaction" of *o*-nitrofluorobenzene with nitrite ion (N-attack) is slowed relative to the reaction of the para isomer and the para/ortho ratio becomes anomalously high, when compared with SNAr reactions of fluoroaromatics in which formation of the intermediate is rate determining.

Nitrite Ion as a Nucleophile. Nucleophilic tendencies[3] of bases toward methyl iodide (SN2 reactions)[7] and toward 1-iodo-2,4-dinitrobenzene (SNAr reactions) are compared in Table IV. Two sets of nucleophilicities are given. One has chloride ion in methanol as reference nucleophile, the other has chloride in DMF. Solvent effects on nucleophilic tendencies are very substantial,[7] so comparisons can only be made within one solvent system. Table IV allows interesting comparisons of nucleophilicity for displacement of iodide from saturated and aromatic carbon, respectively.

Table IV
SNAr and SN2 Nucleophilicity (Log ^{B}k − log ^{Cl}k) of Bases B$^-$ Relative to Chloride Ion in Methanol and DMF. Leaving Group Iodine

Nucleophile B$^-$	SNAr reactions of Ar″I^{b}: MeOH	SNAr reactions of Ar″I^{b}: DMF	SN2 reactions of MeI^{c}: MeOH	SN2 reactions of MeI^{c}: DMF
PhS$^-$	11.0^{l}	9.4^{d,l}	~5^{x,y}	~4^{x,z}
Ar″S$^-$	9.3^{f,m}	3.4^{e,m}		
MeO$^-$	7.7^{n}	6.5^{d,n}	1.8^{y}	1.6^{y}
PhO$^-$	~6.8^{g,o}	8^{d,o}	1.3^{u}	0.3^{u}
p-Ar′O^{-a}	~3.9^{g,o}	1.5^{d,o}	0^{u}	−2.2^{u}
Ar″O$^-$	−0.7^{d,p}	−3.3^{e,p}	−1.7^{u}	−4.4^{u}
N$_3^-$	6.5^{q,r}	5.2^{f,q,r} 5.9^{e,f,p}	1.5^{q}	0.1^{q}
NO$_2^{-h}$	5.2^{aa}	~3.7^{f,aa}	1.2^{i}	0.4^{i,j}
ONO^{-h}	$\not>$4.4^{aa} <4^{k,s}	$\not>$2.7^{f,aa}		
SCN^{-h}	4.5^{m,q}	−0.3^{m,q}	2.5^{q}	−1.5^{q}
SCN^{-h}		−3.6^{m} −4.1^{e,p}	<1.0^{w}	<−3.0^{w}
I$^-$	2.5^{m,t}	−3.3^{m,t} −3.5^{e,p}	2.25^{i,r}	−1.7^{d,r}
Br$^-$	1.3^{r}	−1.3^{r} −2.6^{e,p}	1.3^{v}	−0.4^{v}
F$^-$	>0^{aa}	>0^{aa}		
Cl$^-$	0^{b,r}	0^{b,r}	0^{c,v}	0^{c,v}

[a] *p*-Ar′ = 4-NO$_2$C$_6$H$_4$, Ar″ = 2,4(NO$_2$)$_2$C$_6$H$_3$. [b] Log ^{Cl}k (Ar″I) = −8.86 in MeOH at 50°, E_a = 32.1 kcal/mol, $\Delta S^{\ddagger}$ = −2 eu; −2.53 in DMF at 50°, E_a = 23.7 kcal/mol, $\Delta S^{\ddagger}$ = −1 eu. [c] Log ^{Cl}k (MeI) = −7.0 in MeOH at 0°, −0.62 in DMF at 0°. [d] Estimated from $^{M}\gamma^{DMF}$ for B$^-$ and Cl$^-$ assuming $^{M}\gamma^{DMF}$ for substrate and transition state is negligible. Reference 7. [e] Reaction of Ar′ SCN. Log ^{Cl}k (Ar″SCN) ≈ log ^{Cl}k (Ar′I) (ref 5). [f] Values corrected to same temperature using E_a and $\Delta S^{\ddagger}$ quoted in footnote *b*. [g] Reaction of Ar″Cl with B$^-$ relative to reaction of Ar″I with Cl$^-$. [h] Mode of attack boldfaced for ambident nucleophiles. [i] Reaction of *n*-BuI at 25°. [j] In Me$_2$SO. [k] In CH$_3$CN–H$_2$O. [l] Footnote *e*, Table II. [m] Footnote *g*, Table II. [n] Footnote *o*, Table II. [o] G. O. Leahy, M. Liveris, J. Miller, and A. J. Parker, *Aust. J. Chem.*, 9, 382 (1956). [p] Reference 5. [q] Footnote *h*, Table II. [r] Footnote *r*, Table II. [s] Reference 2, but corrected from <1 by agreement following correspondence with Drs. Rosenblatt and Dennis. [t] F. H. Kendall and J. Miller, *J. Chem. Soc. B*, 119 (1967). [u] D. Cook, I. P. Evans, E. C. F. Ko, and A. J. Parker, *J. Chem. Soc. B*, 404 (1966). [v] A. J. Parker, *J. Chem. Soc.*, 4398 (1961). [w] No isothiocyanato compound detected. [x] Reaction of *n*-BuBr. [y] Reference 7. [z] A. J. Parker, M. Ruane, D. A. Palmer, and S. Winstein, *J. Am. Chem. Soc.*, 44, 2228 (1972). [aa] This work and ref 1.

SN2 reactions are synchronous and have a single transition state. This is "looser" than either of the transition states for formation or decomposition of the SNAr intermediate.[7] In a loose transition state, entering and/or leaving groups have only weak covalent bonding interactions with carbon. The looser the SN2 transition state, the smaller the difference in reactivity between the strongest and weakest nucleophiles,[7] the tighter the transition state, the greater the difference in nucleophilicity. Thus the very tight SNAr transition state allows a wide range of reactivity for nucleophiles. There are other differences too between SN2 and SNAr reactions, associated with the two-step formation and decomposition of the SNAr intermediate and the steric consequences of a four- (SNAr) vs. a five- (SN2) coordinate transition state.[3]

A feature of Table IV is that methoxide, phenoxide, azide, and nitrite ions are $>10^5$ times more reactive than chloride ion in SNAr reactions, but these ions are of similar reactivity to chloride ion in SN2 reactions. In the SNAr reactions, the nucleophilicity is strongly influenced by the ability of the base to form strong bonds with carbon. Nitrite ion (N-attack) has a nucleophilicity which is comparable with azide ion toward 1-iodo-2,4-dinitrobenzene.

SNAr nucleophilicities toward 1-iodo-2,4-dinitrobenzene in methanol decrease in the order $PhS^- > Ar''S^- > MeO^- > PhO^- > N_3^- > NO_2^- > SCN^- > I^- > Br^- > ONO^- > Cl^- > F^-$. As one might expect from the substantial effects of different leaving groups and solvents on reactivity, SNAr nucleophilicity toward 1-fluoro-2,4-dinitrobenzene in DMF is very different,[13] i.e., PhS^-, $PhO^- > N_3^- \gg ONO^- > Ar''S^-$, NO_2^-, $F^- > Cl^- > SCN^-$, $SCN^- > Br^- > I^-$. SN2 nucleophilic tendencies toward methyl iodide in methanol decrease in yet a different order: $PhS^- \gg SCN^- > I^- > MeO^- > PhO^-$, $N_3^- > NO_2^-$, $Br^- > SNN^-$, Cl^-.

N- vs. O-Attack. It is now apparent (see preceding discussion) why the relative rates of N-attack vs. O-attack in SNAr reactions of the ambident nitrite ion change with the solvent, the leaving group, and substituents. The following examples highlight these interesting effects, which can be explained using the principles outlined herein.

An example of the solvent effect on this ambident ion is the reaction of NO_2^- with 1-chloro-2,4-dinitrobenzene, where N-attack is more than five times faster than O-attack in methanol, but in Me_2SO O-attack is faster than N-attack (Table I).

An example of the leaving group effect on ambident NO_2^- is the reaction of the 1-halo-2,4-dinitrobenzenes with nitrite ion in methanol. Here N-attack is more than ten times *slower* than O-attack on the fluoro compound but N-attack is more than five times *faster* than O-attack for reaction with the iodo compound (Table I).

An example of the substituent effect on reactions of the ambident nitrite ion are the reactions of *o*- and *p*-fluoronitrobenzene with nitrite ion in Me_2SO at 100°. Here N-attack is three times *slower* than O-attack on the ortho isomer, but N-attack is four times *faster* than O-attack on the para isomer.

Registry No.—Ar″F, 70-34-8; Ar″Cl, 97-00-7; Ar″I, 709-49-9; *o*-Ar′F, 1493-27-2; *o*-Ar′Cl, 88-73-3; *o*-Ar′I, 609-73-4; *p*-Ar′F, 350-46-9; *p*-Ar′Cl, 100-00-5; *p*-Ar′I, 636-98-6; PhS^-, 13133-62-5; $Ar''S^-$, 56437-88-8; SCN^-, 302-04-5; N_3^-, 14343-69-2; Pip, 26330-84-7; NO_2^-, 14797-65-0; MeO^-, 3315-60-4; Br^-, 24959-67-9; Cl^-, 16887-00-6; PhO^-, 3229-70-7; *p*-$Ar'O^-$, 14609-74-6; $Ar''O^-$, 20350-26-9; I^-, 20461-54-5; F^-, 16984-48-8.

References and Notes

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The Nucleophilic Step of the Ring Opening Reactions of Cyclopropanes with Electrophiles. Mechanism and Stereochemistry. I. Reaction of 1-Phenylbicyclo[4.1.0]heptane with Mercuric Salts

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Received July 8, 1975

The regio- and stereoselectivity of the cyclopropane ring opening reactions of 1-phenylbicyclo[4.1.0]heptane (1) with mercuric salts has been investigated. The stereoselectivity of the mercuration of 1 is highly variable, ranging from a syn:anti ratio of 13.5:86.5 to one of 82.5:17.5, and it is influenced by the type of mercuric salt and by the solvent. The observed results can be accounted for by a mechanism implying transition states or intermediates with high degree of development of positive charge on the benzylic carbon, in analogy with what was found in the case of the ring opening of aryl-substituted oxiranes and oxetanes in acidic media.

The ring opening reactions of cyclopropanes with electrophiles have been the subject of many recent investigations,[1-4] and in most cases a regiospecificity in accordance with the Markovnikov rule has been observed, with some exceptions.[5,6]

As to the stereochemistry of the ring opening it has been found that the electrophilic attack can occur with either retention or inversion of configuration depending on the nature and configuration of the ring substituents, whereas the nucleophilic step is highly stereoselective with complete or