B/C-*trans*-10-Bromo-4a-(2-dimethylaminoethyl)-6-methoxy-1,2,3,4,4a,10a-hexahydro-10*H*-9-phenanthrone Hydrobromide (24). Ketone **17** was converted to the hydrobromide (mp 236–238° from MeOH–Me_2CO). As described in the bromination of **6** HBr, the hydrobromide (152 mg) and Br_2 (77 mg) yielded, after addition of ether to the reaction mixture and cooling, 145 mg of **24:** mp 188–190°; ir (Nujol) 2400–2700 (N^+H), 1680 cm^{-1} (C=O); NMR (DMSO-d_6) δ 3.33 (s, 6, $>N^+Me_2$), 3.88 (s, 3, OMe), 5.28 (d, J = 12.0 Hz, 1, C-10 H), 6.87 (d, $J_{5,7}$ = 2.5 Hz, 1, C-5 H), 7.03 (q, $J_{7,5}$ = 2.5, $J_{7,8}$ = 8.5 Hz, 1, C-7 H), 7.92 (d, $J_{8,7}$ = 8.5 Hz, 1, C-8 H).

Anal. Calcd for $C_{19}H_{26}BrNO_2{\cdot}HBr$: C, 49.48; H, 5.90; N, 3.04. Found: C, 49.77; H, 5.80; N, 2.95.

3-Methoxy-10-oxo-*N*-methylisomorphinan Methobromide (25). The bromo ketone hydrobromide **24** (58 mg) was converted to the free base (40 mg). It solidified on standing. Recrystallization from MeOH–Me_2CO gave **25** as colorless prisms: mp 234–235°; ir (Nujol) 1675 cm^{-1} (C=O); NMR (CD_3OD) δ 3.04 (s, 3, N^+Me), 3.48 (s, 3, N^+Me), 3.90 (s, 3, OMe), 3.95 (d, J = 6.0 Hz, 1, C-9 H), 6.98–7.10 (m, 2, C-2 and C-4 H), 8.02 (d, J = 9.0 Hz, 1, C-1 H).

Anal. Calcd for $C_{19}H_{26}BrNO_2$: C, 60.00; H, 6.81; N, 3.68. Found: C, 60.01; H, 6.99; N, 3.61.

Acknowledgment. The author wishes to express his deep appreciation to Dr. E. L. May, Chief of this Section, for his interest and encouragement.

Registry No.—**2**, 53661-21-5; **3**, 55156-34-8; **4**, 55156-35-9; **4** HCl, 55156-36-0; **4′**, 55156-37-1; **4′** HCl, 55156-38-2; **5**, 55156-39-3; **6**, 55156-40-6; **6** HCl, 55156-41-7; **6** HBr, 55156-42-8; **7**, 55156-43-9; **7** picrate, 55156-44-0; **9**, 55156-45-1; **10**, 55156-46-2; **10** picrate, 55177-18-9; **11**, 55156-47-3; **12**, 55156-48-4; **12** HCl, 55177-19-0; **13a**, 55156-49-5; **13b** HBr, 55156-50-8; **15**, 50282-12-7; **16b**, 55156-51-9; **16b** oxalate, 55156-52-0; **17**, 55156-53-1; **17** HCl, 55156-54-2; **17** HBr, 55156-55-3; **18**, 55156-56-4; **19**, 55177-20-3; **19** picrate, 55220-80-9; **20**, 55156-47-3; **21a**, 55177-21-4; **21a** picrate, 55220-81-0; **21b** HBr, 55177-22-5; **22**, 55156-57-5; **23** HBr, 55156-58-6; **24**, 55156-59-7; **24** HBr, 55156-60-0; **25**, 55177-47-4.

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(1) Assistant Professor, Toyama Technical College, Hongo 13, Toyama, Japan. This research was performed while the author was a "guest worker" at NIH.

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Aromatic Nucleophilic Substitution Reactions of Ambident Nucleophiles. II.[1a] Reactions of Nitrite Ion with Nitrohalobenzenes

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Nitrophenols are the eventual products of the aromatic nucleophilic substitution reactions of the ambident nitrite ion with suitably substituted nitrobenzenes. This is the case no matter whether the nitrogen or the oxygen of the nitrite ion is the original site for bonding to aromatic carbon. However, the intermediacy of di- or trinitroaromatics, i.e., the first products of N-attack, has been demonstrated by labeling the substituted nitrobenzenes with deuterium, or with a methyl group, or by using $^{15}NO_2^-$ as the nucleophile. N-Attack is faster than O-attack when Cl, Br, or I is displaced from the nitrohalobenzenes by nitrite ion but O-attack is faster when fluorine is displaced. Reactions are about 10^5 faster in dipolar aprotic solvents than in methanol and the rate of O-attack is enhanced more than N-attack on transfer from methanol to dipolar aprotic solvents. The principles discussed here enable one to optimize the conditions for a maximum yield of the initial product of N-attack and for a minimum yield of nitrophenols. If the substrate has a substituent ortho to the site of nucleophilic attack, the proportion of nitrophenol to dinitrobenzene is very high throughout the reaction.

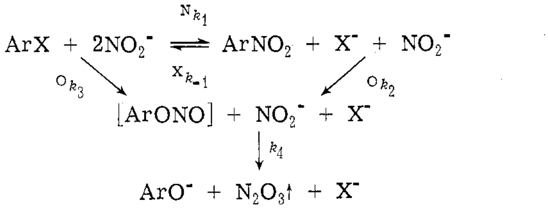
Aromatic nucleophilic substitution (SNAr) reactions of aryl halides (ArX) with nitrite ion have the potential for preparing nitroaromatic compounds in which the nitro group is in a specifically predetermined position. This position might be inaccessible by electrophilic nitration procedures.[1c] However, SNAr reactions of nitrite ion with many aryl halides give phenols rather than nitroaromatics as the major or only product. This paper investigates such reactions in an attempt to optimize conditions for a maximum yield of nitroaromatics.

The SNAr reactions of nitrite ion have been studied in methanol, DMF, DMSO, and HMPT. This choice of solvents allows a wide range of substrate (ArX) reactivity to be covered, including ArX as the weakly activated ortho and para nitrohalobenzenes, as well as the 2,4-dinitrohalobenzenes.

Nucleophilic substitution by nitrite ion at a *saturated* carbon atom gives both nitro compounds (RNO_2) and nitrite esters RONO.[2,3] Kornblum has noted that bonding by oxygen to saturated carbon (O-attack) is pronounced when the transition state has a well-developed positive charge on the carbon atom (loose SN2 or SN1 reactions) and bonding by nitrogen to carbon (N-attack) is pronounced in tight SN2 transition states where the carbon is softer and carries little if any positive charge.[2] Pearson's hard and soft acids and bases principle is relevant;[4] the harder oxygen atom of NO_2^- prefers to bond to hard positively charged carbon in the loose transition state, the softer nitrogen of NO_2^- prefers to bond to softer carbon in the tighter transition state.

The situation for nucleophilic substitution of ArX by nitrite ion at an *aromatic* (sp^2) carbon atom requires different considerations. Aromatic nitrite esters ArONO are very unstable under SNAr conditions. The nitro group in $ArNO_2$ is an extremely labile leaving group in the presence of nucleophiles. Thus SNAr reactions of nitrite ion are often complicated by reactions in which the entering nitrite ion is displaced from the initial product by the leaving group, by other nucleophiles, or by another nitrite ion. The pathways for the reactions of nitrite ion with aromatics are set out in Scheme I. They are similar to those proposed by Rosen-

Scheme I



In presence of air	$2N_2O_3 + O_2 \longrightarrow 4NO_2$
In presence of H_2O	$N_2O_3 + H_2O \longrightarrow 2HNO_2$
In presence of triethylamine	$HNO_2 + Et_3N \longrightarrow Et_3NH^+ + NO_2^-$
In presence of F^- in an aprotic solvent	$HNO_2 + F^- \longrightarrow HF + NO_2^-$

blatt, Dennis, and Goodin[5] from work with 2,4-dinitrohalobenzenes in aqueous acetonitrile.

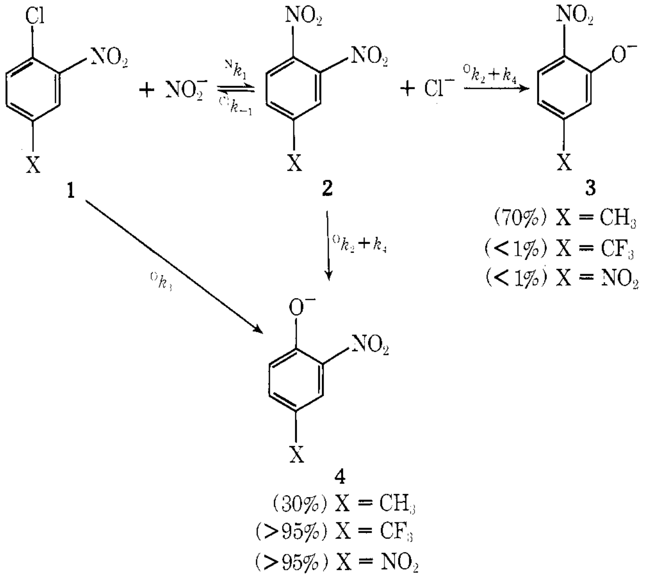
As shown in Scheme I and by this work, nitrite ion produces phenoxides from ArX in three ways: (1) by consecutive O-attack of $ArNO_2$ following N-attack of ArX, i.e., $^{N}k_1$, $^{O}k_2$, k_4; (2) by direct O-attack of ArX, i.e., $^{O}k_3$, k_4; (3) by reversal of N-attack followed by O-attack of ArX, i.e., $^{N}k_1$, $^{X}k_{-1}$, $^{O}k_3$, k_4.

It is useful to identify the pathways shown in Scheme I and to measure the values of the various rate constants. This is because we are interested in the effects of different leaving groups X, of different substituents in Ar, and in the effects of solvents on the nucleophilicities of NO_2^-. We are also interested in the leaving group tendencies of NO_2 from $ArNO_2$ in reactions $^{O}k_2$ and $^{X}k_{-1}$. Evidence which adds strong support for Scheme I follows.

Results and Discussion

Kinetics and Stoichiometry. The kinetics of the reaction of 1-chloro-2,4-dinitrobenzene (Ar″Cl) with sodium nitrite in DMSO at 25° and in methanol at 45° show that the rate of production of 2,4-dinitrophenoxide is first order in nitrite ion and in Ar″Cl. However, 2 mol of nitrite ion were consumed per mole of 2,4-dinitrophenoxide produced as required by Scheme I. In methanol, no 2,4-dinitroanisole was detected (i.e., <1%), which excludes methanolysis of a 1,2,4-trinitrobenzene intermediate and, by analogy, excludes hydrolysis as a pathway to Ar″OH in DMSO–water mixtures. 1,2,4-Trinitrobenzene (Ar″NO_2) reacted much faster than Ar″Cl with NO_2^- ($^{O}k_2 > {}^{N}k_1$ or $^{O}k_3$) to give a quantitative yield of 2,4-dinitrophenoxide in both methanol and DMSO. Only 1 mol of nitrite was consumed per mole of 2,4-dinitrophenoxide produced (Scheme I). In dry DMSO a brown gas was evolved from the reaction of nitrite ion with Ar″Cl. Scheme I caters for some further reactions of the N_2O_3 produced by reaction of ArONO with nitrite ion. In wetted DMSO, no gas was evolved, but the solution increased in acidity owing to the formation of nitrous acid as the reaction proceeded. The stoichiometry of Scheme I in moist DMSO was 2 mol of nitrite per mole of Ar″Cl for its complete conversion to phenoxide. However, this stoichiometry in moist DMSO was reduced to less than 1 mol of nitrite per mole of Ar″Cl by adding the base triethylamine. The reaction of 1-fluoro-2,4-dinitrobenzene (Ar″F) with nitrite ion in slightly moist DMSO, unlike the same reaction of Ar″Cl, had a stoichiometry of less than 1 mol of nitrite per mole of Ar″F. One explanation for the difference between Ar″Cl and Ar″F is that HNO_2, formed by the reaction of N_2O_3 with water, is not a nucleophile under the reaction conditions, but in the presence of strongly basic triethylamine or fluoride ion in moist DMSO, nitrite ion is regenerated from the weak nitrous acid and is available for further reaction with Ar″X. However, chloride ion, unlike fluoride, is too weak a base in moist DMSO to regenerate nitrite ion from weak nitrous acid. These observations are consistent with Scheme I.

Scheme II



3: (70%) X = CH_3; (<1%) X = CF_3; (<1%) X = NO_2

4: (30%) X = CH_3; (>95%) X = CF_3; (>95%) X = NO_2

Like Russell,[6] we detected no radicals (ESR) and believe that the decomposition of the very unstable nitrite esters (k_4 in Scheme I) is a heterolytic reaction involving nucleophilic attack by NO_2^- on the nitrogen of ArONO to displace ArO^- and form N_2O_3.

N-Attack vs. O-Attack. As noted, phenols could be formed by the consecutive reactions $^{N}k_1$, $^{O}k_2$ then k_4, by the concurrent reaction $^{O}k_3$ then k_4, or by reversal of reaction $^{N}k_1$ (i.e., $^{X}k_{-1}$) then $^{O}k_3$ and k_4 in Scheme I. The following evidence suggests that all three pathways are used in different situations.

As shown in Table IV, during the reaction of NO_2^- with 2,4-dinitrochlorobenzene (Ar″Cl) in DMSO, the rate of production of 2,4-dinitrophenoxide ion (Ar″O^-) lagged behind the rate of chloride ion production, i.e., [Ar″O^-]/[Cl^-] was 0.85 during the first half-life of chloride ion production. Thus a small steady-state concentration of an organic product, other than Ar″O^-, presumably 1,2,4-trinitrobenzene (Ar″NO_2), must be present in the early stages of reaction. At the completion of reaction, the concentration of Ar″O^- equaled that of chloride ion, so that the assumed 1,2,4-trinitrobenzene is a true intermediate in the formation of 2,4-dinitrophenoxide, as shown in Scheme I. As noted, a separate experiment showed that Ar″NO_2 rapidly gave Ar″O^- with NO_2^- in DMSO.

Scheme II records and explains the products of some reaction of 4-chloro-3-nitro substituted aromatics with nitrite ion in DMSO. A very weakly deactivating methyl group is used to detect the intermediacy of 3,4-dinitrotoluene (**2**, X = CH_3). As shown in Scheme II (X = CH_3), the product was a mixture of 3-hydroxy-4-nitrotoluene with rather less 4-hydroxy-3-nitrotoluene. Thus, 3,4-dinitrotoluene, which is the product of reaction $^{N}k_1$ in Scheme II (X = CH_3), is an intermediate and N-attack $^{N}k_1$ is faster than O-attack $^{O}k_3$. If $^{O}k_3$ were the sole route to phenoxides, then the reaction would give only **4** (X = CH_3), as was obtained when **1** (X = CH_3) was hydroxydechlorinated with sodium hydroxide in 75% DMSO–water. Further confirmation was obtained when 3,4-dinitrotoluene was treated with sodium nitrite in DMSO. This very rapidly produced a similar distribution of **3** (X = CH_3) and **4** (X = CH_3) as in the

Table I
Isotopic Analysis of Some SNAr Reactions of $Na^{15}NO_2$[a] in HMPT at 100°

Substrate[b]	Product	$M:M + 1$	$^{N}k_1/^{O}k_3$[c]
p-$Ar'NO_2$	p-$Ar'OH$	100:20	2
o-$Ar'NO_2$	o-$Ar'OH$	100:16	3/2
p-$Ar'F$	p-$Ar'OH$	100:26	4

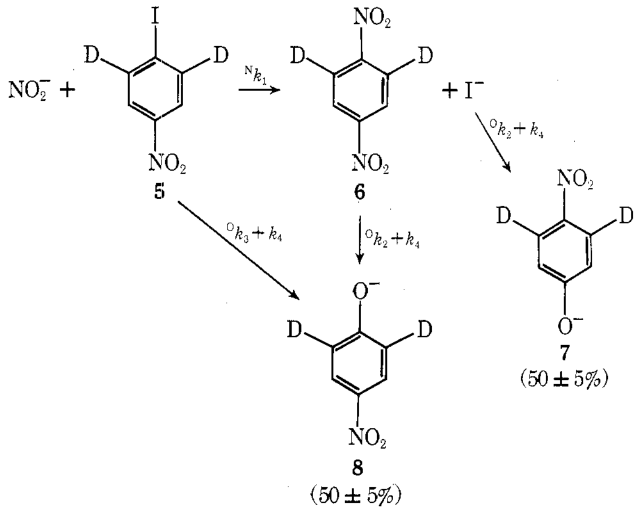
[a] $Na^{15}NO_2$ contained 33% ^{15}N and was present in at least 40-fold excess. [b] p-Ar′ is $4\text{-}NO_2C_6H_4$ and o-Ar′ is $2\text{-}NO_2C_6N_4$. [c] Calculated as described in the text.

reaction of NO_2^- with 4-chloro-3-nitrotoluene. The preponderence of phenoxide **3** over **4** ($X = CH_3$) from reaction of **2** ($X = CH_3$) is a result of the small deactivating electron-donating effect of methyl when para to a SNAr reaction center; thus the 3-nitro group is displaced more readily than 4-nitro. Similar differences in lability of the two nitro groups have been observed in reaction of **2** ($X = CH_3$) with other nucleophiles.[7]

As shown in Scheme II and Table I, when X is CF_3 or NO_2 rather than CH_3, the sole product is **4**, i.e., the presence of strongly SNAr activating CF_3 and NO_2 groups (X) leads to only one product, $4\text{-}OH\text{-}3\text{-}NO_2C_6H_3X$. With these compounds, there is thus no way of telling whether the pathway is via the intermediate **2** and $^{N}k_1$ or directly from **1** and $^{O}k_3$, because both **1** and **2** give the same product.

The results of some deuterium-labeling experiments are explained and presented in Scheme III. Compound **5** was

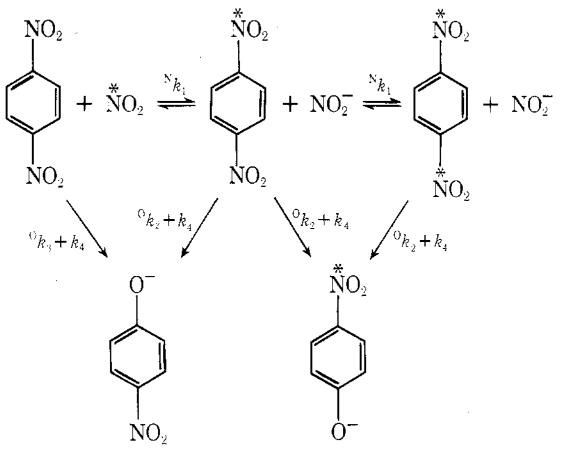
Scheme III



prepared with >95% isotopic purity. Its NMR spectrum showed only a singlet at 7.96 ppm. After reaction of **5** with $NaNO_2$ in DMSO, the phenolic products were isolated and in acetone showed two singlets of approximately similar intensity at 7.68 and 6.53 ppm. This is as expected for an equimolar mixture of compounds **7** and **8**. There can be little direct O-attack by NO_2^- on **5**, because reaction $^{O}k_3 + k_4$ of compound **5** in Scheme III would give only phenol **8** and no **7**; the intermediate **6**, however, gives roughly equal amounts of **7** and **8** as found for reaction of **5** with nitrite ion.

The results of some experiments with ^{15}N-labeled sodium nitrite are in Table I and are explained by Scheme IV. p-Dinitrobenzene was treated with excess $NaNO_2$ (assaying 33% ^{15}N) in hexamethylphosphoramide at 100°. The product was 4-nitrophenol and this was analyzed for ^{14}N, ^{15}N proportions by mass spectrometry. The corrected

Scheme IV



$M:M + 1$ ratio was 100:20. Sole O-attack ($^{O}k_3 + k_4$ in Scheme IV) would give $M:M + 1$ as 100:0, sole N-attack ($^{N}k_1$) would give 100:50, and equal proportions of N- to O-attack would give 100:12.5 in the 4-nitrophenol. The observed $M:M + 1$ of 100:20 means that N-attack of 4-dinitrobenzene by nitrite ion in HMPT is twice as fast as O-attack. Other $^{N}k_1:^{O}k_3$ ratios in Table I were calculated by similar reasoning.

A detailed kinetic analysis of the rate of ^{15}N incorporation into the phenolic product and of the rate of phenoxide production for reaction of nitrite ion in DMSO at 100° with various substrates was then carried out. Analysis was by mass spectrometry. For reaction with p-dinitrobenzene, the rate constant for ^{15}N incorporation was $6.4 \times 10^{-4}\ M^{-1}\ sec^{-1}$, that for phenoxide production was $2.7 \times 10^{-4}\ M^{-1}\ sec^{-1}$. Table I shows values of $^{N}k_1:^{O}k_3$, i.e., relative rates of initial N-attack and O-attack, by nitrite ion on various substrates. The results in Table I confirm that direct O-attack ($^{O}k_3$ in Scheme I) is usually slower than direct N-attack ($^{N}k_1$). However, some direct O-attack is usually observed; i.e., both the concurrent as well as the consecutive route to phenols are utilized in the SNAr reactions of nitrite ion.

Reactions of Mononitro-Substituted Benzenes. The concentrations of aryl substrate and nitro intermediate from reaction of mononitro-substituted benzenes with nitrite ion in DMSO were analyzed by GLC and concentrations of phenoxide were estimated spectrophotometrically at various stages of reaction. Results are in Table II, together with rate constants for these reactions. A comparison of the proportion of phenoxide product, $Ar'O^-$, to nitro compound, $Ar'NO_2$, over the first 10% of reaction gives, as shown in Table II, the ratio of N-attack to O-attack ($^{N}k_1$:$^{O}k_3$). This is because in Scheme I a negligible amount of phenoxide ($Ar'O^-$) is produced from the aryl substrate ($Ar'X$) via aryl nitro compound ($Ar'NO_2$), i.e., via $^{N}k_1$, $^{O}k_2$, k_4 during the first 10% of reaction. As we show later, the rates $^{N}k_1[Ar'X]$ are $\gg$ $^{O}k_2[Ar'NO_2]$ up to 10% reaction, when $[Ar'NO_2]$ is small. Thus phenoxide produced in the first 10% reaction is almost entirely from direct O-attack on $Ar'X$ (i.e., by $^{O}k_3$ in Scheme I).

The maximum possible yield of nitro intermediate from the consecutive reactions $^{N}k_1$, $^{O}k_2$, k_4 and the stage of consumption of $Ar'X$ at which $[Ar'NO_2]$ is a maximum are topics of interest and are shown in Table II. The greatest yield of $Ar'NO_2$ occurs in the absence of bulky substituents ortho to the reaction center, i.e., from the 4-nitro-substituted benzenes. As shown in Table II, the ratio $^{N}k_1:^{O}k_3$ for N- and O-attack on o-$Ar'X$ increases according to the leaving group in the series of $X = F < NO_2 \approx Cl < I$. There is a similar tendency for attack on p-$Ar'X$, but there is more

Table II
Reaction of Ortho- and Para-Mononitro-Substituted Benzenes Ar′X with $NaNO_2$ in DMSO at 100°

Substrate[a] Ar′X	Registry no.	$10^4 k$, l. mol^{-1} sec^{-1}	$^{N}k_1 : ^{O}k_3$ [b,h]	100 $[ArNO_2]/[ArX]_0$ [g]	100 $([Ar'X]_0 - [Ar'X])/[Ar'X]_0$ max[i]
o-Ar′F	1493-27-2	4.2[d]	1:3	4	30
o-Ar′NO_2	528-29-0	46[d]	3:2[e]		
o-Ar′Cl	88-73-3	4.5[c,d]	3:2	5	25
o-Ar′I	609-73-4	~9[d]	7:1	15	30
p-Ar′F	350-46-9	16.2[f]	4:1	40	70
p-Ar′NO_2	100-25-4	2.7[d]	2:1[e]		
p-Ar′Cl	100-00-5	2.7[c]	2:1	25	50
p-Ar′I	636-98-6	~6[d]	8:1	25	60

[a] o-Ar′ is 2-$NO_2C_6H_4$; p-Ar′ is 4-$NO_2C_6H_4$. [b] The error in GLC analysis is estimated at ±10% and $[Ar'X]_t$, $[Ar'NO_2]_t$, and $[Ar'NO_2]_{max}$ were measured by GLC. [c] This is the rate constant for production of Cl^-. [d] This is the rate constant for production of $Ar'O^-$ measured spectrophotometrically. [e] From mass spectral analyses as discussed for data in Table I. [f] This is the rate constant for consumption of NO_2^-. [g] This represents the maximum percent yield of Ar′NO_2 which can ever be obtained under these reaction conditions. As reaction proceeds the concentration of Ar′NO_2 decreases (see text). [h] I. e., $[Ar'NO_2]_t : [Ar'O^-]_t$ (see text) where t is a time in the first 10% of consumption of Ar′X′ at which the concentrations of $Ar'O^-$ and Ar′NO_2 were determined. [i] This represents the percentage of consumption of Ar′X at which the yield of Ar′NO_2 is a maximum from these consecutive reactions.

N-attack on p-nitrofluorobenzene than on 4-nitrochlorobenzene.

While considering reactivity patterns, it is noteworthy in Table II that fluorine is displaced more slowly than iodine from the ortho nitrohalobenzenes and only slightly more rapidly than iodine from the para nitrohalobenzenes by nitrite ion in DMSO. In SNAr reactions with many nucleophiles (e.g., OMe^- in MeOH[8], N_3^- in DMF[9]), fluorine is displaced very much more rapidly than iodine from Ar′Hal. These reactivity differences have important mechanistic implications, which will be discussed in a later paper.

Reactions of 2,4-Dinitrohalobenzenes. The reactions of the 2,4-dinitrohalobenzenes with nitrite ion and other nucleophiles were studied in a variety of solvents. The reactions were measured under pseudo-first-order conditions, with excess (10^{-2} M) of nucleophile, and the rate of production of 2,4-dinitrophenoxide ion, as measured spectrophotometrically at 360 nm, is recorded as a second-order rate constant in Table III.

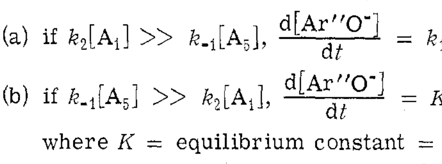
Table III
Rates of Production of 2,4-Dinitrophenoxide Ion from 1-X,2,4-Dinitrobenzene (Ar″X)[e] in Various Solvents at 25°

Nucleophile	X in Ar″X[g]	DMSO	DMF	HMPT	MeOH[f]
NO_2^-	NO_2	8	96		3.8×10^{-3}
NO_2^-	F	0.14	0.24	11	10.8×10^{-3}
NO_2^-	Cl	1.05	7.5	1150	0.19×10^{-3} [b]
NO_2^-	SCN	~1.5	9.2		3×10^{-3} [c]
NO_2^-	I	0.27[a]	1.4	132	0.11×10^{-3}
F^-	NO_2	16			
Cl^-	NO_2	0.05			
I^-	NO_2	~0.001[d]			

[a] E_a = 16.3 kcal/mol, $\Delta S^{\ddagger}$ = −8 eu. [b] E_a = 17.9 kcal/mol, $\Delta S^{\ddagger}$ = −25 eu. [c] Reference 12. [d] Reaction is subject to interference from the production of iodine. [e] Rates are recorded as second-order rate constants (M^{-1} sec^{-1}) for production of 2,4-dinitrophenoxide ion. [f] At 45°. [g] Registry no. are, respectively, 121-14-2, 70-34-8, 97-00-7, 1594-56-5, 709-49-9.

The kinetic expressions for the reaction steps of Scheme I in terms of the rate of production of $Ar''O^-$ are shown in Scheme V.[10] Some account must be taken of the relative basicity of halide and nitrite ions toward carbon. In methanol as solvent, the reverse reaction $^{X}k_{-1}$ is not significant, because in methanol nitrite ion is a much stronger base toward aromatic carbon than the halide ions. However, in dipolar aprotic solvents, chloride and fluoride ions are stronger bases than NO_2^- toward aromatic carbon. Thus tetramethylammonium chloride, bromide, and fluoride readily produced 2,4-dinitrophenoxide when treated with 1,2,4-trinitrobenzene (Ar″NO_2) in DMSO, presumably by the reactions $^{X}k_{-1}$, $^{O}k_3$ and $^{O}k_2$, then k_4. However, there is no phenoxide produced by halide ions in methanol as solvent.

Scheme V
Kinetics Expressions for the Reaction of NO_2^- with 2,4-Dinitrohalobenzenes (cf. Scheme I) in Terms of the Rate of Production of 2,4-Dinitrophenoxide Ion



$$\underset{[A_2]}{Ar''Hal} + \underset{[A_1]}{NO_2^-} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{[A_3]}{Ar''NO_2} + \underset{[A_5]}{Hal^-}$$

$$\underset{[A_1]}{NO_2^-} + \underset{[A_3]}{Ar''NO_2} \xrightarrow{k_2} \underset{[A_4]}{Ar''O^-} + N_2O_3$$

Case 1 Assume $[A_2]$ is the initial reactant, $\frac{d[A_3]}{dt} = 0$

$$\text{then } \frac{d[Ar''O^-]}{dt} = \frac{k_2k_1[A_1][A_1][A_2]}{k_{-1}[A_5] + k_2[A_1]}$$

$$\text{(a) if } k_2[A_1] >> k_{-1}[A_5],\ \frac{d[Ar''O^-]}{dt} = k_1[A_1][A_2]$$

$$\text{(b) if } k_{-1}[A_5] >> k_2[A_1],\ \frac{d[Ar''O^-]}{dt} = Kk_2[A_1]$$

where K = equilibrium constant = k_1/k_{-1}

Case 2 Assume $[A_3]$ is the initial reactant, $\frac{d[A_1]}{dt} = 0$

$$\text{then } \frac{d[Ar''O^-]}{dt} = \frac{k_{-1}k_2[A_3][A_3][A_5]}{k_1[A_2] + k_2[A_3]}$$

$$\text{if } k_2[A_3] >> k_1[A_2] \frac{d[Ar''O^-]}{dt} = k_{-1}[A_3][A_5]$$

From Table III it can be seen that the rate of production of $Ar''O^-$ from Ar″F is *faster* than the rate of production of $Ar''O^-$ from Ar″NO_2 by nitrite ion in methanol. Thus the consecutive sequence $^{N}k_1$, $^{O}k_2$ then k_4 of Scheme I for production of $Ar''O^-$ via N-attack and the intermediate Ar″NO_2 must play a minor role in the overall production of $Ar''O^-$ from Ar″F. The observed rate in Table III must be largely for direct O-attack on Ar″F, i.e., via route $^{O}k_3$ of Scheme I and $^{O}k_3$ is greater than $^{O}k_2$. A GLC analysis of the products of reaction of Ar″F with nitrite ion in metha-

Table IV
Product Analyses of the Reaction of Ar″Cl and Ar″SCN with Nitrite Ion in DMSO

% reaction of Ar″SCN[a]	8	15	20	24	30
	$[Ar''O^-]/[SCN^-]$				
Observed	0.21	0.30	0.45	0.52	0.62
Calculated[b]	0.18	0.28	0.44	0.50	0.56

% reaction of Ar″Cl[c]	19	26	30	43
	$[Ar''O^-]/[Cl^-]$			
Observed	0.86	0.78	0.90	0.89
Calculated[b]	0.46	0.59	0.62	0.76
Calculated[d]	0.81	0.86	0.87	0.91
Calculated[e]	0.72	0.79	0.81	0.87

[a] At 0.4° Ar″SCN = 0.025 M, NO_2^- = 0.025 N, $^{O}k_2 = 4.5\ M^{-1}\ sec^{-1}$, $^{N}k_1 = 0.91\ M^{-1}\ sec^{-1}$. [b] Assuming $^{O}k_3$ negligible relative to $^{N}k_1$. [c] At −19° Ar″Cl = 0.014 M, NO_2^- = 0.041 M, $^{O}k_2 = 0.52\ M^{-1}\ sec^{-1}$, $^{N}k_1 = 0.082\ M^{-1}\ sec^{-1}$. [d] Computed for a $^{N}k_1$:$^{O}k_3$ rate ratio of 1:2. [e] Computed for a $^{N}k_1$:$^{O}k_3$ ratio of 1:1.

nol during the early stages of reaction confirmed this interpretation. No more than 1% of $Ar''NO_2$ (as a percentage of products) could be detected at any stage of reaction. If a consecutive $^{N}k_1$, $^{O}k_2$ sequence was significant with $^{N}k_1 \geq {}^{O}k_2$, then at least 30% $Ar''NO_2$ would be detected under the reaction conditions. In contrast, a GLC analysis of the reaction of NO_2^- with Ar″Cl in methanol detected a maximum of 5 ± 1% $Ar''NO_2$. A maximum of 4.2% of $Ar''NO_2$ was expected by calculation from the concentrations of Ar″Cl and NO_2^-, the overall rate for production of $Ar''O^-$ and from $^{O}k_2$ (Table III). Such a calculation assumes that $^{O}k_3$ is negligible for reaction of Ar″Cl with NO_2^- and the correspondence between observed and calculated maximum concentration of $Ar''NO_2$ confirms that in contrast to the reaction with Ar″F, $^{O}k_3$ is negligible for reaction of NO_2^- with Ar″Cl.

Thus for reaction of Ar″F with NO_2^- in methanol, direct O-attack on Ar″F by step $^{O}k_3$ is favored by at least 10:1 over direct N-attack by step $^{N}k_1$. The corresponding reactions of Ar″Cl in methanol proceed mainly by N-attack via $^{N}k_1$. The reasons for the change in the mode of attack by nitrite ion with change of leaving group will be discussed in a later paper. Similar rate relationships and conclusions were reached by Rosenblatt, Dennis, and Goodin[5] using aqueous acetonitrile as a solvent; however, it should be noted their rate constants have been calculated by a different method from us. Rosenblatt and Dennis now agree[11] that the rate constants for O-attack by NO_2^- in aqueous acetonitrile at 25° on Ar″Cl and Ar″Br are 2.5×10^{-5} and $2.2 \times 10^{-5}\ M^{-1}\ min^{-1}$, respectively. The N:O ratio ($^{N}k_1$:$^{O}k_3$) of nitrite attack on Ar″Cl in aqueous acetonitrile is therefore about 70:1 and not 18,000:1 as implied from their stated rate constants. The rates of production of $Ar''O^-$ in DMSO as solvent (Table III) introduce new considerations. The rate of production of 2,4-dinitrophenoxide from 1,2,4-trinitrobenzene by halide ions in DMSO (Table III) follows the kinetic expression[10] corresponding to case 2 in Scheme V where $k_2[A_3] \gg k_1[A_2]$.

Table III shows that the displacement of nitrite ion by halide, $^{X}k_{-1}$ of Scheme I, is not kinetically significant for reaction of nitrite ion with Ar″Cl or Ar″I in DMSO (X = Cl^- or I^-). For reaction of Ar″F with nitrite ion in DMSO, displacement of nitrite ion by the strongly nucleophilic fluoride ion in DMSO ($^{F}k_{-1}$) must be considered when evaluating the kinetics of $Ar''O^-$ production. The step $^{F}k_{-1}$ would be kinetically significant if the consecutive route to $Ar''O^-$ involving N-attack ($^{N}k_1$, $^{O}k_2$ then k_4, Scheme I) were being utilized. However, two observations suggest that $^{F}k_{-1}$ and hence $^{N}k_1$ is not kinetically significant in the production of $Ar''O^-$ from the reaction of Ar″F with NO_2^- in DMSO and that preequilibrium does not occur.

(1) Thorium nitrate, which completely suppresses the normally fast reaction of KF with $Ar''NO_2$ ($^{F}k_{-1}$) in DMSO, has no effect on the rate of $Ar''O^-$ production from Ar″F and NO_2^- in DMSO.

(2) For a range of nitrite ion concentrations, the overall rate of $Ar''O^-$ production from Ar″F with NO_2^- in DMSO follows a simple second-order rate law. There was no rate acceleration during the initial stages of the reaction to indicate any significant formation of $Ar''NO_2$. If $^{F}k_{-1}$ were kinetically significant, then from case I, Scheme V, we would expect a more complex rate law to be followed for nitrite ion concentrations where $^{F}k_{-1}[F^-] \approx k_2[NO_2^-]$).

These observations confirm that in DMSO, just as in methanol, $^{O}k_3$ is much faster than $^{N}k_1$ for reaction of Ar″F with NO_2^-.

The extent of O-attack ($^{O}k_3$) to N-attack ($^{N}k_1$) in the $^{N}k_1$ reaction of nitrite ion with Ar″SCN[12] and Ar″Cl in DMSO was readily determined by comparing the rate of thiocyanate or chloride ion production with the rate of phenoxide ion production (Table IV). From the rate constants for the consecutive reactions, assuming complete N-attack ($^{N}k_1$ and $^{O}k_2$ then k_4) and no $^{O}k_3$, the concentrations of $Ar''O^-$ and Cl^- or SCN^- can be computed at any part in the reaction. Deviations of the observed concentrations from the concentrations computed on the above assumption thus reflect the extent of competitive O-attack, $^{O}k_3$. In Table IV, the computed and observed amounts of $Ar''O^-$, Cl^-, or SCN^- are compared.

It can be seen in Table IV that Ar″Cl gives a much higher $[Ar''O^-]$:$[Cl^-]$ ratio than the $[Ar''O^-]$:$[SCN^-]$ ratio from Ar″SCN at any stage of reaction. The calculated values show that >5% of Ar″SCN and about 60% of Ar″Cl ($^{N}k_1$:$^{O}k_3 \approx$ 1:1.5) reacts via direct O-attack, $^{O}k_3$, of the nitrite ion in DMSO. Ar″SCN thus reacts unusually slowly in step $^{O}k_3$ relative to Ar″Cl and Ar″F. This may be due to a preference for a "soft" nucleophilic attack by the soft nitrogen "end" of NO_2^- when attacking Ar″SCN.

The substantial proportion of direct O-attack by nitrite ion on Ar″Cl in DMSO ($^{O}k_3/^{N}k_1 \approx 1.5$) contrasts to the much smaller proportion of direct O-attack on this substrate in methanol and aqueous acetonitrile ($^{O}k_3$:$^{N}k_1 \approx 0.014$) but correlates with that found for *o*-nitrochlorobenzene in DMSO (Table II). Apparently there is a significant solvent effect, whereby protic solvents "deactivate" the oxygen more than the nitrogen of NO_2^-.

To summarize, the nitrite ion attacks 2,4-dinitrohalobenzenes both via N- and O-attack in methanol and in DMSO or DMF. However, there is a significant solvent effect favoring O-attack in the dipolar aprotic solvents and the proportions of N- to O-attack depend on the leaving group.

Experimental Section

Melting points were determined using a Kofler micro hot stage and were uncorrected. NMR spectra were recorded on a Varian Associates A-60 spectrometer. Carbon tetrachloride was the solvent. All chemical shifts are quoted on the τ scale relative to an internal standard, tetramethylsilane. The percentage of ^{15}N in nitrogenous samples was determined by mass spectroscopy using an Associated Electronic Industries Model MS3 spectrometer by courtesy of Dr. C. A. Parker, Department of Soil Science, Institute of Agriculture, University of Western Australia. Isotopic measurements on the phenolic products were made using a MS9 spectrophotometer. Uv and visible spectroscopic measurements were made using a Gilford Model 240 spectrophotometer.

The 4-nitrohalobenzenes, the 2,4-dinitrohalobenzenes, *o*- and *p*-dinitrobenzene, 2-nitrochlorobenzene, 4-chloro-3-nitrobenzotrifluoromethane, and 4-chloro-3-nitrotoluene were commercial products and were purified by recrystallization or fractional distillation. Melting points correspond to within 1° of literature values,[13] and, where applicable, analysis of the group displaced by excess base in 80% DMSO–methanol at 100° was quantitative.

1,2,4-Trinitrobenzene was donated by Dr. D. E. Giles.

2-Fluoronitrobenzene, bp 90–95° (9 mm) [lit.[13] bp 86–87° (11 mm)], was prepared by halide exchange of 2-chloronitrobenzene with potassium fluoride in DMSO.[14] A Beilstein flame test confirmed the absence of chlorine in the product.

3,4-Dinitrotoluene, mp 61° (ethanol) (lit.[13] mp 61°), was prepared by stepwise oxidation of 4-amino-3-nitrotoluene using Caro's acid and hot fuming nitric acid. 4-Amino-3-nitrotoluene was obtained by nitration of *p*-methylacetanilide followed by hydrolysis.

4-Hydroxy-3-nitrotoluene, mp 30–33° (ethanol–water) (lit.[13] mp 36.5°), was prepared by the hydroxydechlorination of 4-chloro-3-nitrotoluene at 100° in 70% DMSO–water.

[2,4,6-$^{2}H_{3}$]-Iodobenzene. [N,N,N,2,4,6-$^{2}H_{6}$]-aniline hydrochloride was prepared by heating aniline hydrochloride with deuterium oxide for 24 hr at 100°, removing the water, and repeating the procedure twice.[15] The NMR spectrum consisted of one peak (τ 2.60) (2 H, referred to internal standard of methylene chloride). Diazotization and decomposition of the diazonium salt with potassium iodide gave [2,4,6-$^{2}H_{3}$]-iodobenzene. The NMR spectrum consisted of one peak (τ 3.00) (2 H).

[4,6-$^{2}H_{2}$]-2-Nitro- and [2,6-$^{2}H_{2}$]-4-nitroiodobenzene[16] were prepared as a mixture from the nitration of [2,4,6-$^{2}H_{3}$]-iodobenzene with a solution of potassium nitrate (10 g) in [$^{2}H_{2}$]-sulfuric acid at 25° for 24 hr. Fractional crystallization (pentane) of the product gave [2,6-$^{2}H_{2}$]-4-nitroiodobenzene, mp 171–172° (lit.[13] $^{1}H_{4}$ mp 172°). The NMR spectrum consisted of one peak (τ 2.04) (2 H). Steam distillation of the product mixture gave [4,6-$^{2}H_{2}$]-2-nitroiodobenzene, mp 53–54° (lit.[13] $^{1}H_{4}$ mp 54°). The NMR spectrum consisted of two broad doublets [τ 2.64, 3.10 (2 H) with $J_{\text{meta}} = 5$ Hz].

Analytical grade sodium nitrite was dried by heating to 120° for 2 hr and stored in a desiccator. Spectrophotometric analysis[17] showed this material to be 99.5% sodium nitrite.

Nitrous anhydride was prepared by the oxidation of arsenious oxide with dilute nitric acid[18] (sp gr 1.3). Condensation of the equimolar gaseous mixture of nitric oxide and nitrogen dioxide in a Dry Ice–acetone trap gave liquid nitrous anhydride (N_2O_3).

General Reaction Conditions. Sodium nitrite (3.5 g, 0.05 mol) was added to a stirred solution of the aromatic compound (0.02 mol) in DMSO (50 ml). The mixture was allowed to react, diluted with water (200 ml), and extracted with ether to get neutral products. The aqueous layer was acidified (1 *M* HCl) and extracted with ether. The ether extract was dried (Na_2SO_4) and evaporated to dryness to get acidic products.

For reactions yielding 2-nitrophenol and 4-nitrophenol, excess 2-chloroaniline was added to prevent further nitrosation of the phenol. Spectroscopic measurements of rate data were carried out directly in a 1-cm cell using a Gilford Model 240 spectrophotometer. Measurement was at the absorption maximum of the phenoxide ion. At least a 20-fold excess of NO_2^- was used with aromatic substrates at 10^{-4}–10^{-5} *M* to give pseudo-first-order rate constants.

GC Analysis. *o*-and *p*-nitrofluoro-, nitrochloro-, and dinitrobenzene were separated on a 6 ft × 0.25 in. packed column coated with APL in the temperature range 140–180°. 4-Nitroiodobenzene and *p*-dinitrobenzene were separated on a 6 ft × 0.25 in. packed column coated with Carbowax 20M at a temperature of 190°. Peak areas were measured by planimetry. The extent of reaction was determined from the reaction time and decrease in the area of the substrate peak.

Registry No.—3,4-Dinitrotoluene, 610-39-9; 4-amino-3-nitrotoluene, 89-62-3; 4-hydroxy-3-nitrotoluene, 119-33-5; 4-chloro-3-nitrotoluene, 89-60-1; [2,4,6-$^{2}H_{3}$]-iodobenzene, 13122-40-2; [N,N,N,2,4,6-$^{2}H_{6}$]-aniline hydrochloride, 55223-35-3; [4,6-$^{2}H_{2}$]-2-nitroiodobenzene, 55223-36-4; [2,6-$^{2}H_{2}$]-4-nitroiodobenzene, 55223-37-5.

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Reaction of 2-Carboalkoxymethylenecyclopropanes with Phenyl Azide[1a]

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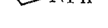
The reaction of phenyl azide with several 2-carboalkoxymethylenecyclopropanes has been examined. 2,3-Dicarbomethoxymethylenecyclopropane (**1a**) gives 1-phenyl-4-(1,2-dicarbomethoxyethyl)-1,2,3-triazole (**2a**). Similarly, esters **1b** and **1c** yield triazoles **2b** and **2c**, respectively. The ^{13}C spectra of triazoles **2a–c** are given. The formation of these triazoles is rationalized in terms of a rearrangement of an intermediate triazoline adduct.

We have recently reported on the synthesis of the novel 1-azaspiropentane structure.[2,3] This highly strained heterocyclic system was formed by photochemical expulsion of molecular nitrogen from the appropriate triazoline precursor, which was itself obtained from the thermal cycloaddition of phenyl azide to the corresponding methylenecyclopropane (see eq 1). In the present paper we relate our unsuccessful attempts to apply this synthetic scheme to methylenecyclopropanes bearing alkoxycarbonyl substituents on the cyclopropyl ring. In this instance, 1,2,3-triazoles isomeric with the desired triazolines are produced in the initial reaction of the synthetic sequence.



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