Nucleofugicity in the Aromatic Nucleophilic Substitution Reaction of Picryl Derivatives with Nitrite Ion in Acetonitrile

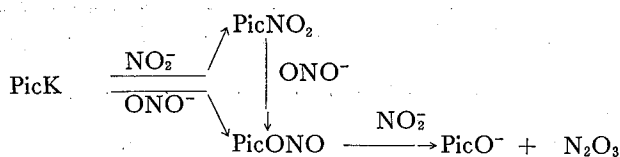Jun-ichi HAYAMI,*[†] Masaki ASAHI,[††]

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In the course of the study to examine the nucleophilicities and the nucleofugicities of the anionic nucleophiles in acetonitrile, a very rapid reacion of nitrite ion with 2, 4, 6-trinitrohalobenzenes (picryl halides) was observed. In this reaction, 2, 4, 6-trinitrophenoxide (picrate) ion was produced quantitatively. In an inert atmosphere, when the concentration of the reactants is high enough, the reaction is accompanied with the vivid evolution of dinitrogen trioxide.

Stoichiometry and the composition of the products in this reaction show that a reaction course first proposed by Rosenblatt, Dennis, and Goodin is operative in the reaction of nitrite with the activated S_NAr substrate like 2, 4, 6-trinitrohalobenzenes (picryl halides PicX) (Scheme 1)[1].

$$\text{PicK} \quad \frac{\text{NO}_2^-}{\text{ONO}^-} \quad \begin{array}{c} \text{PicNO}_2 \\ \downarrow \text{ONO}^- \\ \text{PicONO} \end{array} \quad \xrightarrow{\text{NO}_2^-} \text{PicO}^- + \text{N}_2\text{O}_3$$

(Scheme 1)

Production of picrate ion was so rapid that no means was available to estimate the individual contribution of the oxygen-attack and the nitrogen-attack by the ambident nitrite separately. However, the overall reactivity of these reactions has an important implication to the other fast S_NAr reactions and thus the present system serves as a model to study fast reactions in dipolar aprotic solvents.

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In the present study, the effect of the leaving group upon this fast reaction was examined by making use of the stopped-flow kinetic measurements. The rate of the reaction was measured under pseudo-first-order conditions, with excess of tetraethyl-ammonium nitrite, and the rate of production of picrate ion, as measured spectrophoto-metrically at 375 nm, is shown as second-order rate constants inTables I and II[2].

Table I. Pseudo-first-order Rate Constant of the Production of PicO⁻ from the Reaction of PicCl and Et₄ NNO₂ in Acetonitrile at 50°C

$[NO_2^-]$ $\times 10^4 1$ mol^{-1}	1.60	3.19	6.39	9.58
$k_\varphi \times s$	2.44	4.85	9.33	14.04

$$k_\varphi = 1.446 \times 10^4 [NO_2^-] + 1.600 \times 10^{-1} (s^{-1}) \quad (r = 0.9999)$$

Table II. Second-order Rate Constant of the Production of PicO⁻ in the Reaction of PicX and Et₄NNO₂ in Acetonitrile

a) X=F			
Temp. $\times 1/°C$	6.5	15.0	25.0
$k_2 \times 10^{-3}$mol s l^{-1}	7.32	10.4	14.7

b) X=Cl						
Temp. $\times 1/°C$	6.5	13.9	25.0	37.0	43.0	50.0
$k_2 \times 10^{-3}$mol s l^{-1}	3.06	3.99	6.20	10.6₂	12.5₈	14.4₆

c) X=Br			
Temp. $\times 1/°C$	15.0	25.0	35.0
$k_2 \times 10^{-3}$mol s l^{-1}	4.09	5.82	8.29

d) X=I			
Temp. $\times 1/°C$	15.0	25.0	35.0
$k_2 \times 10^{-3}$mol s l^{-1}	1.56	2.73	4.11

As the reaction strongly suggests the intervention of 1, 2, 3, 5-tetranitrobenzene (PicNO₂), the reaction of nitrite ion with PicNO₂ was also undetraken.

The rate of production of picrate ion from PicNO₂ was very high and to get the reliable data the averaging of the multiple runs was necessary. Pseudo-first-order rate constant increased proportionally with the increase of $[NO_2^-]$ and showed no sign of levelling off at the very fast rate of more than 800 s^{-1}. The second-order rate constant was calculated by the linear regresison analysis of $k_\phi - [NO_2^-]$ plot and the reaction was

found to be one of the fastest S_NAr reactions reported[3]. The results are summarized in Table III.

Table III. Pseudo-first-order Rate Constant and Second-order Rate Constant of the Production of $PicO^{-1}$ in the Reaction of $PicNO_2$ and $Et_4 NNO_2$ in Acetonitrile

	a) at 33.9 °C				
$\times \begin{array}{c}[NO_2^-]\\10^4\ 1\ mol^{-1}\end{array}$	1.858	4.647	9.294		
$\times \begin{array}{c}k_\varphi\\10^{-2}\ s\end{array}$	1.03$_4$	2.93	7.36		
	$k_2 = 8.54 \times 10^5\ 1\ mol^{-1}\ s^{-1}$				
	b) at 15.9 °C				
$\times \begin{array}{c}[NO_2^-]\\10^2\ 1\ mol^{-1}\end{array}$	3.279	4.057	8.114	10.13	20.27
$\times \begin{array}{c}k_\varphi\\10^{-2}\ s\end{array}$	1.07$_6$	1.33$_1$	3.08	3.83	8.12
	$k_2 = 4.16 \times 10^5\ 1\ mol^{-1}\ s^{-1}$				
	c) at 6.5 °C				
$\times \begin{array}{c}[NO_2^-]\\10^4\ 1\ mol^{-1}\end{array}$	3.279	6.057	8.392	10.71	
$\times \begin{array}{c}k_\varphi\\10^{-2}\ s\end{array}$	0.735	1.46$_4$	2.15	2.75	
	$k_2 = 2.73 \times 10^5\ 1\ mol^{-1}\ s^{-1}$				

Data in Table III with that in Table II reveals that under the pseudo-first-order condition, the disappearace of this intermediate $PicNO_2$ is fast enough not to affect the kinetic course of the reaction of picryl halides ($k_\phi^{PicNO_2} = 3—18 \times 10^2\ s^{-1}$ and $k_\phi^{PicF} = 7.35—44.1\ s^-$ for $[NO_3^-] = 5—30 \times 10^{-4}$ M at 25°C). In fact no "lag" or "burst" kinetics was followed in the course of the reaction of picryl halides with nitrite ion.

In any events, these findings definitely show that none of the O- or N-attack by nitrite ion on any of the picryl halide is faster than the O-attack on $PicNO_2$.

The other intermediate postulated in the Rosenblatt mechanism is 2, 4, 6-trinitrophenyl nitrite[1], which should exhibit a very high reactivity against nitrite ion. Accordingly, no trial was made of the kinetic study of this nitrite ester.

Table IV. Leaving Group Tendencies in the Reaction of PicX and $Et_4 NNO_2$ in Acetonitrile at 25°C

X	NO$_2$	F	Cl	Br	I
Relative Rate	98	2.4	1.00[*]	0.94	0.44

*) $k_2^{Cl} = 6.20 \times 10^3\ 1\ mol^{-1} s^{-1}$

Table V. Arrhenius Parameters of the Over-all Rate of the Production of PicO$^-$ in the Reaction of PicX and Et$_4$NNO$_2$ in Acetonitrile. (at 25.0 °C)

X	NO$_2$	F	Cl	Br	I
ΔH^* $\times$ mol kcal^{-1}	6.5	5.7	6.1	5.6	8.0
ΔS^* $\times$ K mol cal^{-1}	-10.3	-20	-20	-22	-16

Leaving group tendencies in these S_NAr reactions of picryl derivatives are shown in Table IV. Parker reported that nitro group is a more labile leaving group than fluorine in the reaction of 1-x-2, 4-dinitrobenzenes and is less labile than fluorine in the reaction of 1-x-4-nitrobenzenes[1]. He also reported fluorine is more labile, in the reaction of mononitrohalobenzenes, than chlorine and that the reverse was true in the reaction of dinitrohalobenzenes.

In the present work, leaving group tendencies are NO$_2$>F>Cl>Br>I. However, the reactivities of all the picryl halide are quite close. This reflects upon the activation parameters of the S_NAr reactions with nitrite ion. Data are shown in Tavle V.

Activation enthalpies found are fairly small and are quite similar all through the picryl derivatives studied. This latter finding can be an outcome of the balance of the competing O- and N-attack in the course of the rate determining attack by the ambient nitrite ion. The effect of a preferred hard to hard interaction in the O-attack on PicF can be equaled by the effect of a preferred soft to soft interaction in the N-attack on PicI[4]. The similar situation should be the case in PicCl and in PicBr.

Small activation enthalpies such as found can easily be attenuated by the change of solvent through a solute-solute interaction or a solute-solvent interaction. Especially, an activation enthalpy for the reaction of PicNO$_2$ is worthy to note. Read and Parker reported that the S_NAr reactions of aromatic amines with picryl derivatives showed a very small activation enthalpy[5], although these amines reacted much more sluggishly than nitrite ion.

Recently, one of the present authors reported an example of the nucleofugicity scale of halogen anion and of other anionic nucleophiles in the Finkelstein reaction of benzyl derivatives where the bond breaking of the carbon-leaving group is the major rate discriminating facter of the reaction[6]. Nucleofugicity differences between the halide ions are signiflcant and are of the "normal" order, I>Br>Cl>F.

In a separate paper, the present authors proved the operation of a base catalysis in the reaction of picryl derivatives with aromatic amines in cyclohexane[7]. In this example of the S_NAr reaction where the expulsion of the leaving group is definitely rate-determining[8], the leaving group tendency was "normal" for an S_NAr reaction. Thus the leaving group tendency alone gives no clue of the nature of these reactions.

In some instances of the S_NAr reactions, a Meisenheimer adduct, which is often identifled as 1, 3-adduct, accumulates in the reaction at the rate much higher than that of the production of the final substitution product[9,10]. (Scheme 2)

However, in no case studied with PicNO$_2$, PicF, and PicCl was observed the accu-

1,1-Meisenheimer Adduct

1,3-Meisenheimer Adduct

Quite Often $k_{1,3} \gg k_{1,1}$

(Scheme 2)
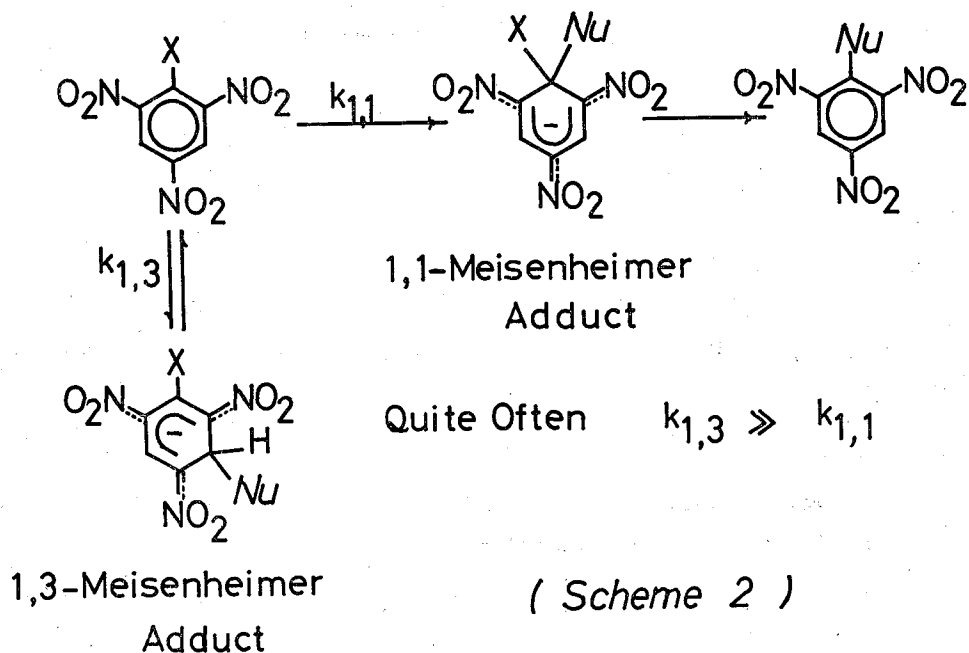
mulation of colored species absorbing between 450—550 nm.   The absence of a very rapid rate process that precedes the production of the final product is rather unexpected for the reaction of extremely activated S_NAr substrate.

Sasaki proved the parasitic intervention of an 1, 3-Meisenheimer adduct in the reaction of PicCl with SO_3^{-}[10].   However, alkali metal sulfite is insoluble in anhydrous CH_3CN and, in this solvent, tetraethylammonium sulfite decomposes quite readily not to allow a kinetic application of this nucleophile.

The absence of a 1, 3-Meisenheimer adduct is not without examples.   In the S_NAr reaction of picryl derivatives with aromatic amine, the production of a substituted diphenylamine is not accompanied with the prior formation of such kinetically favored adduct[5,7].   It is quite possible that a soft nucleophile may not undertake this kinetically favored parasitic addition reaction.   Instead it may readily undergo an ipso attack to the potential nucleofugic group.

Studies on the amine nucleophile is in progress to study the effect of solute-solute interaction in the S_NAr reaction.   These should be the subject of forthcoming papers.

EXPERIMENTAL

Materials

Commercial PicCl was repeatedly recrystallized from ethanol and finally from anhydrous ether to give mp 83 °C.   PicF, PicBr, and PicI were prepared by the standard method. PicF mp 122—123 °C[11]; PicBr mp 122.5—123.5 °C[12]; PicI mp 169—170°C[13]. 1, 2, 3, 5-Tetranitrobenzene (PicNO$_2$) was prepared from trinitrophenylhydroxylamine by the oxidation with fuming nitric acid.[14]   Purification was achieved by recrystallization from dry chloroform by cooling from room temperature to -40 °C. mp 127 °C.

Tetraethylammonium nitrite was prepared by the double decomposition of silver nitrite and tetraethylammonium bromide in acetonitrile or of potassium nitrite and tetraethylammonium perchlorate in dry methanol. The product was repeatedly recrystallized from dry acetonitrile, diethyl ether was added when necessary.

Solvent acetonitrile was puified by repeated distillation from phosphorus pentoxide and from dry potassium carbonate.

Apparatus and procedure

Kinetic measurement were performed by use of a Union Giken RA-1300 Stopped-Flow Rapid-Scan spectrophotometer. For extremely rapid reactions, was utilized a Union Giken RA-1100 Stopped-Flow Spectrophotometer equipped with a nitrogen-gas-driven end-stop mixer. A Union Gike-RA-450 Microprocessor was used to perform an averaging of the multiple runs of reactions. Thermostatted water-ethanol mixture was circulated around the observation-cell compartment and the reservoirs, and the temperature was regulated within $\pm 0.05°C$ or better.

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(2) In a separate experiment where PicNO$_2$ was treated with a large excess of tetraethylammonium chloride in acetonitrile, the rate of the production of PicO$^-$ was quite low, the second-order-rate constant being about $1.0 \times 10^{-2} M^{-1}s^{-1}$. Accordingly, the observed pseudo-first-order rate constant in the reaction of picryl halides and nitrite ion should not be affected by the following reverse reaction with halide ion which is produced in the forward reactions ($[Hal] < 10^{-4}M^{-1}$ or $k_2^{Hal}[Hal] < 10^{-6}s^{-1}$), and the contribution of such a reverse reaction on the overall rate can be ignored.

$$PicNO_2 + Cl^- \xrightarrow{k_2^{Cl}} PicCl + NO_2^-$$

(or $PicNO_2 + Hal^- \xrightarrow{k_2^{Hal}} PicHal + NO_2^-$)

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