Nucleophilic Substitution on Trivalent Nitrogen Atom.[1] Menschutkin Type Reaction of *O*-2,4-Dinitrophenylhydroxylamine with Uncharged Nucleophiles

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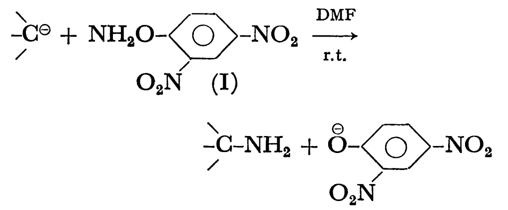
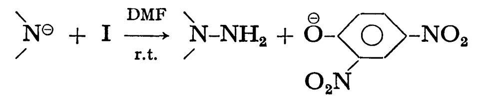
Kinetic investigation carried out on the reaction between *O*-2,4-dinitrophenylhydroxylamine and neutral nucleophiles revealed that the reaction is a typical S_N2 reaction on the trivalent nitrogen atom. Moreover, the order of reactivities of common nucleophiles was found to be somewhat similar to that of the nucleophilicities toward sp^3 carbon atom. However, unlike the S_N2 reaction on sp^3 carbon atom, the S_N2 reaction on the trivalent nitrogen atom found to be not very sensitive to the steric effect of substituted pyridine.

Nitrogen and carbon are adjacent elements in the periodic table and, as such, share certain common chemical properties, such as the ability to form trigonal and tetrahedral bonding skeletons, the octet electronic environment, *etc.* While the nucleophilic substitutions on carbon atom have been studied systematically in the past three decades, those on nitrogen atom have been investigated very little except for a few fragmental examples.[2,3] Those studied were chloramine[2] and hydroxylamine-*O*-sulfonic acid[3] which are too unstable to be subjected to the kinetic experiments, reacting only under the limited conditions, *e.g.*, in liq. ammonia solution.

Recently, Sheradsky[4] first observed the following reactions shown in Eqs. (1) and (2).


(1)


(2)

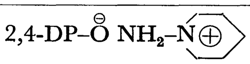
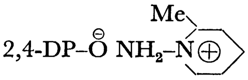
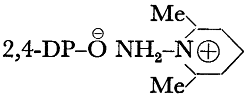
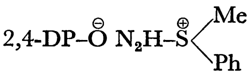
These reactions appear to be the most suitable for examining the nature of the S_N2 reaction on the nitrogen atom if the starting compound (I) can be made in pure form. Fortunately, the hydroxylamine (I) was able to be made in crystalline form, mp 113 °C.

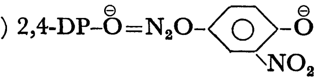
We have therefore undertaken a kinetic study of Menschutkin type reactions with *O*-2,4-dinitrophenylhydroxylamine (I). Pyridine derivatives, aryl alkyl sulfide and triphenylphosphine were chosen as representative uncharged nucleophiles.

Results and Discussion

All these nucleophiles react smoothly with the hydroxylamine (I) in dioxane at room temperature and gave the readily isolable products, which are summarized in Table 1. The structures of the reaction products were determined on the basis of the spectral data and elemental analyses, details of which are given in the experimental section. These results indicate undoubtedly that the nucleophilic displacement takes place only at the nitrogen atom.

Table 1. Reaction products of the hydroxylamine (I) with some nucleophiles

Nucleophile	Product[a)]		Mp °C	Yield (%)
Pyridine		(Ia)	158—159	95
2-Picoline		(Ib)	160—161	90
2,6-Lutidine		(Ic)	143—144	80
PhSCH$_3$		(Id)	106—107	85
Ph$_3$P	$2,4\text{-DP-}\overset{\ominus}{O}\ N_2H\text{-}\overset{\oplus}{P}Ph_3$	(Ie)	140—141	95

a) 

Kinetic measurements were carried out by following the UV spectra of 2,4-dinitrophenolate ion formed during the reaction.

Figure 1 shows the plot of pseudo-first-order rate

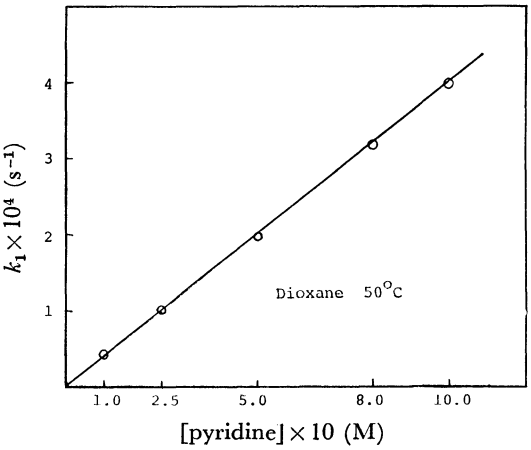


Fig. 1. Plot of pseud-first-order rate constant *vs.* pyridine concentration.

TABLE 2. THERMODYNAMIC DATA FOR THE REACTION OF THE HYDROXYLAMINE (I) WITH PYRIDINE IN DIOXANE

Temp. (°C)	$k_2(M^{-1}s^{-1}) \times 10^4$	
35	1.20	$E_a = 15.5$ kcal/mol
40	1.87	
45	2.90	$\Delta S^{\ddagger}_{40} = -28.1$ e.u.
50	3.83	$\Delta H^{\ddagger}_{40} = 14.9$ kcal/mol

constants against the initial concentration of pyridine in large excess, *e.g.*, from 10 to 100 times, over that of the hydroxylamine (I). Dioxane was employed as the solvent while temperature was set at 50 °C. From the slope of the line the second order nature of the reaction is apparent with $k_2 = 3.83 \times 10^{-4}$ $M^{-1} s^{-1}$. The observed second-order rate constants are listed in Table 2 along with the calculated activation parameters. Obviously, these values also suggest the reaction to proceed *via* the S_N2 path at the nitrogen atom. The values of the activation parameters are quite similar to and only somewhat smaller than that of Menschutkin reaction ($E_a = 13.6$ kcal/mol, $\Delta S^{\ddagger} = -33.1$ e.u., $\Delta H^{\ddagger} = 13.0$ kcal/mol)[5] of methyl iodide and the same base.

TABLE 3. SOLVENT EFFECTS FOR THE REACTION OF THE HYDROXYLAMINE(I) WITH PYRIDINE AT 40 °C

Solvent	D.C.	$k_2 \times 10^4$ $(M^{-1}s^{-1})$
Dioxane	2.21	1.87
$CHCl_3$	4.81	3.30
Acetone	20.5	6.68
CH_3CN	37.5	7.32
DMF	36.7	14.01
CH_3OH	32.6	2.09
C_2H_5OH	24.3	2.52
H_2O–Dioxane (25%v/v)		5.00
H_2O–Dioxane (50%v/v)		7.16
H_2O–Dioxane (75%v/v)		7.66

Table 3 shows solvent effect for the reaction of the hydroxylamine(I) with pyridine at 40 °C. All these values indicate the same tendency as that of the Menschutkin reaction.[6] As the polarity of the solvent and the solvation of the leaving group, *i.e.*, 2,4-dinitrophenolate ion, increases with increasing water content, the reaction rate also increases.

Relative reactivites of a few representative nucleophiles are listed in Table 4.

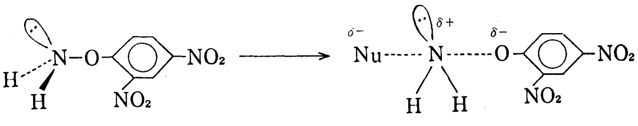
Inspection of the data in Table 4 indicates that the reactivity order of these common nucleophiles lie in somewhat similar order with those of the nucleophilicities toward sp^3 carbon atom.[7] However, unlike in the S_N2 reaction on sp^3 carbon atom, the rate of 2-picoline is somewhat higher than that of pyridine. Even for 2,6-lutidine bearing two methyl groups on both side of the nucleophilic center, the rate constant is not much smaller than pyridine. These observations clearly show that the S_N2 reaction on the trivalent nitrogen atom is not very sensitive to the steric effect of methyl substitution as compared to that on the sp^3 carbon atom.

TABLE 4. RELATIVE RATIOS OF S_N2 REACTIONS ON NITROGEN AND CARBON ATOMS

Compound	Nucleophiles				
	Pyridine	2-Picoline	2,6-Lutidine	$PhSCH_3$	Ph_3P
I	1[a]	1.1	0.3	8	60
CH_3I[c]	1[b]	0.3	0.02	3	58

a) $3.38 \times 10^{-4} M^{-1}s^{-1}$ at 50 °C. b) $2.20 \times 10^{-5} M^{-1}s^{-1}$ at 25 °C. c) Reference 7.

As the lone pair of the trivalent nitrogen atom of the substrate (I) is considered to bear a substantial s-character,[8] it is much more vulnerable to distortion than the C–H sigma bond at the transition state as shown below.



sp^2 transition state

The lone pair would not be solvated much in an aprotic solvent, but in a protic solvent it would be solvated markedly due to the hydrogen bonding.[9]

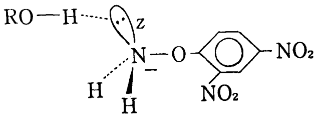


TABLE 5. STERIC EFFECT OF PYRIDINE DERIVATIVES IN VARIOUS SOLVENTS AT 40 °C

Solvent	Pyridine[a]	2-Picoline	2,6-Lutidine
Dioxane	1	1.10	0.29
CH_3CN	1	0.98	0.24
CH_3OH	1	0.79	0.19
H_2O–Dioxane (25%v/v)	1	0.89	0.20
H_2O–Dioxane (75%v/v)	1	0.77	0.19

a) The each value of k_2 are shown in Table 3.

Table 5 shows the magnitude of the steric effect of these substituted pyridines in both aprotic and protic solvents. On account of the hydrogen bonding as shown below, the steric effect increases by changing the solvent from aprotic to protic solvent. Since these nucleophiles are also solvated in protic solvents the reaction becomes more sensitive to the steric effect in protic solvent, and the order of reactivities approaches to that on the sp^3 carbon atom.

Experimental

Pyridine derivatives were purified according to the Coetzee and Padmanabhan's method.[10] Other nucleophiles were purified by distillation or by recrystallization of the commercial products. *O*-2,4-Dinitrophenylhydroxylamine(I) was prepared by the reaction of ethyl *O*-2,4-dinitrophenyl-acetohydroxamate with 70% perchloric acid in dioxane,[11] mp 113 °C (lt,[12] 112 °C). Found: C, 36.10; H, 2.64; N, 21.04%. Calcd for $C_6H_5N_3O_5$: C, 36.17; H, 2.54; N, 21.19%.

An equimolar mixture of the hydroxylamine(I) and nucleophile dissolved in dioxane was allowed to stand at room temperature for a few hours. After evapolation of solvent the residual crystals were washed with hot benzene and recrystallized from ethanol or chloroform. The products were identified by elemental analysis and by comparing the NMR and IR spectra with those of the hydroxylamine(I) and nucleophilies.

TABLE 6. ELEMENTAL ANALYSIS DATA

Compound	Calcd (%)			Found (%)		
	C	H	N	C	H	N
Ia	47.49	3.62	20.14	47.41	3.61	20.30
Ib	49.32	4.14	19.17	49.46	4.05	19.50
Ic	50.98	4.61	18.29	50.90	4.60	18.31
Id	48.29	4.05	13.00	48.21	3.97	13.40
Ie	62.47	4.37	9.11	62.14	4.35	8.45

Kinetic Measurement. All kinetic runs were followed by pipetting 1 ml aliquots from 20 ml glass-stopped flask into 50 ml of ice water or ethanol a portion of which was subjected to measurement of the absorption spectra of 2,4-dinitrophenolate ion (λ_{max} 360 nm, ε 11000) by UV spectrometer. All the rate constants were determined from the pseudo-first-rate equation as follows.

$k=(2.303/bt)\log(a_\infty-a_0)/(a_\infty-a_t)$

a_∞: the final intensity of produced phenolate ion.

a_0: the initial intensity of produced phenolate ion.

a_t: the intensity of produced phenolate ion after t.

b: the initial concentration of nucleophile.

A typical run is shown in Table 7. (50 °C).

TABLE 7.

Time (min)	a_t	$\log(a_\infty-a_0)/(a_\infty-a_t)$	$k_1(s^{-1})\times 10^4$
0	0.35		
3	0.51	0.0290	3.72
6	0.66	0.0577	3.70
9	0.82	0.0909	3.87
12	0.96	0.1219	3.89
18	1.21	0.1840	3.90
24	1.40	0.2377	3.83
30	1.59	0.2993	3.83
	2.86		

Hydroxylamine(I) $=1\times 10^{-2}$M. Mean of k_1s.; 3.83 $\pm 0.06\times 10^{-4}$ M^{-1} s^{-1}. Pyridine(b) = 1 M.

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