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KINETIC STUDY OF NUCLEOPHILIC SUBSTITUTION REACTION ON NITROGEN ATOM

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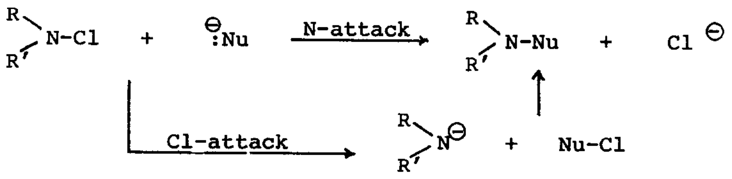
Although the nucleophilic substitution on sp^3 carbon atom has been studied extensively in the past three decades and well understood, those on hetero atoms of the second-row of the periodic table have been investigated very little. Therefore, no systematic generalization can be made on the nature of the nucleophilic displacements on any of these hetero atoms except that on oxygen atom1), even which has drown very little attention as compared to that on sp^3 carbon atom. Only recently, the nucleophilic displacement on boron atom has been reported2). As to the nucleophilic displacement reaction on the trivalent nitrogen atom no systematic investigation has been made available, although a few reactions which appear to be the nucleophilic displacement on trivalent nitrogen atom have been reported in the literatures3,4,5), however, these reactions require critical examination before they are classified as S_N2 type reaction on the nitrogen atom.

Earlier Corbett et al.4) and McCoy5) have studied the hydrolysis of chloramine, however, there remains a possibility that the nucleophiles could attack chlorine atom instead of nitrogen atom in this reaction as shown below.

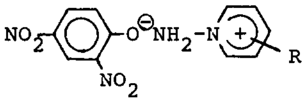


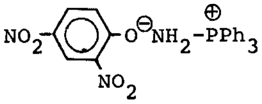
Moreover, chloramine itself is too unstable to be subjected to the kinetic experiment. Therefore, the reaction is not suitable for examining the nature of the S_N2 type displacement on the nitrogen atom.

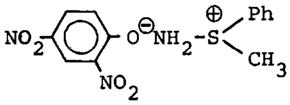
The reactions between O-(2,4-dinitrophenyl)-hydroxylamine(I) with nucleophiles, first reported by Sheradsky6), appear to be the most promising.

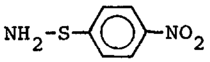
Moreover, we have fortunately been able to obtain the hydroxylamine in crystalline form, m.p. 113°C.

Therefore, we have chosen O-(2,4-dinitrophenyl)-hydroxylamine as a suitable substrate and dealt it with various nucleophiles such as pyridine derivatives, triphenylphosphine, methyl phenyl sulfide, sodium p-nitrothiophenolate and p-tolylmercaptan. Except for p-tolylmercaptan these reactions gave readily isolable products, respectively, as shown below.

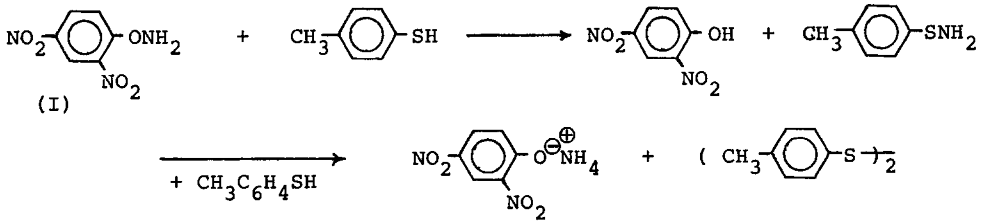








In the case of p-tolylmercaptan the nucleophilic displacement takes place initially at nitrogen and is immediately decomposed as shown below.



These products thus obtaind indicate undoubtedly that the nucleophilic displacement did take place only at the nitrogen atom. In all these reactions with various nucleophiles, kinetic measurements can be carried out conveniently by following the UV absorption spectrum of 2,4-dinitrophenolate ion (λ_{max} 370nm ε 11000).

The kinetic data indicate the rate to be of second order, namely, first order with respect to both substrate and the nucleophile. The activation energy and entropy for the reaction of the substrate with pyridine were calculated to be 16.6 kcal/mol, -20.1 eu., respectively, suggesting that the reaction proceeds via the S_N2 path on the nitrogen atom. Relative reactivities of a few representative nucleophiles are listed in Table I.

Table I. Rate constants for S_N2 reactions on nitrogen and carbon atom.

Compound	Nucleophile				
	pyridine	α-picoline	2,6-lutidine	$PhSCH_3$	Ph_3P
(I)	0.38a) (1)c)	0.43 (1.1)	0.11 (0.3)	2.71 (8)	23.1 (60)
CH_3Id)	2.2b) (1)c)	0.65 (0.3)	0.042 (0.02)	5.87 (3)	129 (58)

a) $k_{obsd} \times 10^3\ M^{-1}sec^{-1}$. b) $k_{obsd} \times 10^5\ M^{-1}sec^{-1}$.

c) parentheses denote the relative rate.

d) ref. 7).

Inspection of the data in Table I indicates that unlike in the S_N2 reaction on the sp^3 carbon atom, the rate of α-picoline is somewhat higher than that of pyridine and even lutidine bearing two methyl groups on both side of nucleophile center has the rate constant not much smaller than that with pyridine. These observations clearly show that the S_N2 reaction on the nitrogen atom is not very sensitive to the steric effect of nucleophiles as compared to that on the sp^3 carbon atom presumably because the lone pair of nitrogen atom on the substrate is much more vulnerable to distortion8) than the sigma bonded carbon atom at the transition state. Hence the reaction would be controlled more by the basicity of the pyridine bases.

The rate of triphenylphosphine is about 60 times as large as that of pyridine while the rate of methyl phenyl sulfide is 8 times higher than that of pyridine. This trend is in keeping with that of the S_N2 reactions at the sp^3 carbon atom, i.e., 58 and 3, respectively, implying that the reactivity order, in other words, 'azaphilicities', of common nucleophiles lie in somewhat similar order with that of the nucleophilicities toward sp^3 carbon atom.

Further works are in progress on our laboratries.

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