

865. *Solvation of Ions. Part III.*¹ *The S_N2 Reactivity of Some Group VI Anions, Pyridine, and Alkyl Halides in Dipolar Aprotic Solvents.*

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Nucleophilic tendencies of some Group VI anions decrease in the series $\text{SeCN}^- > \text{SCN}^-$ and $\text{PhS}^- > \text{PhO}^-$ in both protic and dipolar aprotic solvents. The rate of a typical S_N2 reaction between dipolar molecules is not appreciably influenced by the change from protic to dipolar aprotic solvent. The solvent influence on rates of S_N2 reactions of alkyl halides does not vary as the alkyl group is changed in a homologous series.

In Part II¹ it was shown that nucleophilic tendencies of anions are different in dipolar aprotic and in protic solvents, the former solvents appearing to "level" these tendencies. Towards alkyl halides in acetone there is the series $\text{Br}^- > \text{Cl}^-$, I^- with small differences, whereas in methanol or water the order is $\text{I}^- > \text{Br}^- > \text{Cl}^-$ and the differences are large. The relative tendencies towards methyl iodide of thiocyanate, azide, and chloride ions were markedly affected by the change from methanol to dimethylformamide.¹ We have now extended this work to some halogen-like anions, whose nucleophilic atom (*i.e.*, the atom forming a new bond with carbon) was a Group VI element, in two types of bimolecular nucleophilic replacement, namely, thiocyanate and selenocyanate ions with methyl iodide, and thiophenoxide and phenoxide ions with *p*-iodonitrobenzene, all in both methanol and dimethylformamide.

The kinetic results, summarized in Table 1, lead to the following conclusions: In both methanol and dimethylformamide, potassium selenocyanate reacts faster than potassium thiocyanate with methyl iodide, and sodium thiophenoxide faster than sodium phenoxide with *p*-iodonitrobenzene. The nucleophilic tendencies of SeCN^- and SCN^- , and of PhS^-

¹ Part II, Parker, *J.*, 1961, 1328.

TABLE I.

Reactions of Group VI nucleophiles in protic and in dipolar aprotic solvents. Rate constants (k_2 ; l. mole⁻¹ sec.⁻¹) at 0°. Equimolar proportions of reactants initially at 0.03—0.04M.

	10 ⁴ k_2 in MeOH	10 ⁴ k_2 in H·CO·NMe ₂	$\frac{k_2(\text{H}\cdot\text{CO}\cdot\text{NMe}_2)}{k_2(\text{MeOH})}$
MeI + NCS ⁻	0.20 ^a	117	585
MeI + NCSe ⁻	4.0	916	229
<i>p</i> -NO ₂ ·C ₆ H ₄ I + PhS ⁻	0.034 ^b	820	2.4 × 10 ⁴
<i>p</i> -NO ₂ ·C ₆ H ₄ I + PhO ⁻	0.004 ^b	0.066 ^b	1.7 × 10 ⁵

^a Ref. 1. ^b Extrapolated from rates at higher temperatures (Table 4).

and PhO⁻ are levelled slightly by the change from protic to dipolar aprotic solvent, as might be expected.¹ Thiophenoxide ion is much more susceptible than thiocyanate ion to solvent change, suggesting that, in methanol, hydrogen bonding contributes more to the solvation of the former.¹

Now that it has been established that the nucleophilic tendencies of similarly constituted Group VI nucleophiles are in the same order in both classes of solvent, it is reasonable to attribute part of their nucleophilic tendencies to the nucleophile itself, rather than to differential solvation of the nucleophile.

Nucleophilic tendencies generally increase, within a group of the Periodic Table, with the atomic number of the atom forming the new bond to carbon.² This leads to the nucleophilic tendencies SeCN⁻ > SCN⁻ > OCN⁻ and PhSe⁻ > PhS⁻ > PhO⁻. The nucleophilic tendency of RM⁻, where *M* is a Group VI atom and *R* is a group satisfying the valency requirements of *M*, will be reduced by any contribution made by the second resonance structure of the pair R-M⁻ ↔ -R=M. Conjugative electron withdrawal by *R* favours the latter structure, leading to the nucleophilic tendencies PhS⁻ > NCS⁻ (ref. 3) and PhO⁻ > *p*-NO₂·C₆H₄·O⁻ > 2,4-(NO₂)₂C₆H₃·O⁻ (ref. 4). Conjugative electron release from *M* to the same *R* group favours structure -R=M and decreases in the series^{3,5} RO⁻ > RS⁻ > RSe⁻, leading to the nucleophilic tendencies NCSe⁻ > NCS⁻ > NCO⁻ and PhSe⁻ > PhS⁻ > PhO⁻. It is relevant that OCN⁻ forms isocyanates,⁶ SCN⁻ usually forms thiocyanates,⁶ and SeCN⁻ always forms selenocyanates⁷ in S_N2 reactions with alkyl halides.

Thus both factors, the ability of M⁻ to form a bond with carbon and the interaction between *R* and M⁻, lead to the same nucleophilic tendencies in a series RM⁻. Nucleophilic tendencies of Group VII anions do not increase with increasing atomic number in media where hydrogen-bonding solvation forces are absent,¹ and this might suggest that interactions between *R* and M⁻ largely account for the nucleophilic tendencies of Group VI anions in dimethylformamide.

Many investigations of S_N2 reactions between dipolar molecules in a variety of solvents have been reported.^{8,9} The rates suggest that this class of reaction is not greatly affected by the change from a protic to a dipolar aprotic solvent, provided that the dielectric constant and ionic strength of the medium are standardized. Some anomalies exist, however,¹⁰ so the rates of the reaction between pyridine and butyl bromide in dimethylformamide, in methanol, and in aqueous methanol have been measured under

² Hine, "Physical Organic Chemistry," McGraw-Hill, New York, 1956.

³ Parker, "Sulfur Nucleophiles in S_NAr Reactions," in "Organic Sulfur Compounds," Pergamon, London, 1961.

⁴ Leahy, Liveris, Miller, and Parker, *Austral. J. Chem.*, 1956, **9**, 382.

⁵ Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, New York, 1953.

⁶ Sidgwick, "Organic Chemistry of Nitrogen," Oxford Univ. Press, Oxford, 1937.

⁷ Houben-Weyl, "Methoden der Organischen Chemie," Vol. IX, G. Thieme, Stuttgart, 1955.

⁸ Hinshelwood and his co-workers, *J.*, 1938, 858, 1786, and earlier papers; Popvici and Pop, *Compt. rend.*, 1957, **245**, 846.

⁹ Coleman and Fuoss, *J. Amer. Chem. Soc.*, 1955, **77**, 5472; Kronick and Fuoss, *ibid.*, p. 6114; Fuoss and Hirsch, *ibid.*, p. 6115.

¹⁰ Palit, *J. Org. Chem.*, 1947, **12**, 752.

standard conditions. The results can be compared with those obtained by Fuoss and his co-workers⁹ who used other solvents (cf. Table 2). It is clear that the rate of reaction

TABLE 2.

Reactions of pyridine with butyl bromide in protic and in dipolar aprotic solvents of similar dielectric constant, at the same ionic strength. Rate constants (k_2 ; 1. mole⁻¹ sec.⁻¹) at 50°. [Pyridine]₀ = 0.2M; [butyl bromide]₀ = 0.1M.

Solvent	ϵ	$10^6 k_2$	Solvent	ϵ	$10^6 k_2$
Sulpholan ^b	42.0	61 ^a	MeOH	33	18
4 : 1 v/v MeOH-H ₂ O	42	21	Dimethylsulpholan ^c	29.5	21 ^a
H·CO·NMe ₂	37	30	2-Methyl-1,3-dioxolan	65.1	37 ^a

^a Ref. 9. ^b Tetrahydrothiophen 1,1-dioxide. Tetrahydro-2,4-dimethylthiophen 1,1-dioxide.

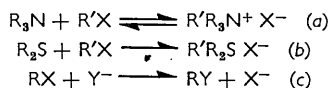
TABLE 3.

Effect of different alkyl groups on solvent influence on the rate of Finkelstein substitutions. Rate constants (k_2) are in 1. mole⁻¹ sec.⁻¹. Equimolar proportions of reactants, initially 0.02—0.04M.

	$10^4 k_2$ in MeOH	$10^4 k_2$ in H·CO·NMe ₂	$\frac{k_2(\text{H}\cdot\text{CO}\cdot\text{NMe}_2)}{k_2(\text{MeOH})}$
MeI + LiCl at 0°	0.0011 ^a	1300	1.2×10^6
EtI + LiCl at 0°	0.00043	630	1.5×10^6
Pr ⁿ I + LiCl at 0°	0.00028	480	1.7×10^6
	$10^4 k_2$ in MeOH	$10^4 k_2$ in acetone	$\frac{k_2(\text{acetone})}{k_2(\text{MeOH})}$
MeBr + LiCl at 25°	0.046 ^c	5950 ^b	1.3×10^5
Pr ⁿ Br + LiCl at 25°	0.00049	64 ^b	1.3×10^5

^a Ref. 1. Ingold, *Quart. Rev.*, 1957, **11**, 1. ^c Moelwyn-Hughes, *Trans. Faraday Soc.*, 1939, **35**, 368.

of pyridine with butyl bromide is not appreciably influenced by the solvent provided that the dielectric constant and salt effect are standardised. This confirms the view that the dipolar aprotic-protic solvent effect observed for S_N2 reactions¹ applies only when at least one of the reactants is an anion. For this reason, equilibria (a) and (b) (R's are alkyl) will lie much further to the left in dipolar aprotic than in protic solvents of the same dielectric constant:



To establish whether the effect of solvent on the rate of reaction (c) depended on the nature of R, the rates of reaction of methyl, ethyl, and propyl iodide with lithium chloride in methanol and in dimethylformamide, and of propyl bromide with lithium chloride in methanol were measured under standard conditions. Table 3 shows that variation of the alkyl group R does not influence the solvent effect in these cases. S_N2 reactions of propyl halides are as susceptible to the change from protic to dipolar aprotic solvent as the corresponding reactions of the same methyl halides.

EXPERIMENTAL

Materials.—Solvents, substrates, lithium chloride, pyridine, and potassium thiocyanate were purified by methods already described.^{1,9,11} Dimethylformamide was purified in the usual way,¹¹ then passed through a molecular sieve. Its purity was confirmed by gas chromatography. Rates in this grade of solvent were identical with those obtained in earlier work.¹ Potassium selenocyanate of reagent grade, dried *in vacuo*, was made into stock solutions in dimethylformamide and in methanol, which were stable under the conditions used. These stock solutions were tested potentiometrically¹ for other anions which give insoluble silver salts and were standardised against silver nitrate before use. The pH of aqueous solutions was 5—6.

Sodium thiophenoxide and sodium phenoxide were obtained from thiophenol and phenol,

¹¹ Miller and Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 117.

respectively, by treatment with an equivalent amount of sodium hydroxide solution. They were crystallised from a little water, then twice from acetone-ether, and were dried under a vacuum.

Kinetics.—All reactions followed second-order kinetics for at least 70% reaction. The procedure for study of reactions of alkyl halides with halide ions has been described.¹ The reactions of selenocyanate ions with methyl iodide were followed in the same way. Control measurements showed that iodide and selenocyanate ions could be estimated separately in their mixtures by potentiometric titration with silver nitrate, in the presence of barium nitrate, by use of a silver wire and calomel electrode. Total halogenoid content and pH remained constant throughout. New results are in Table 4.

TABLE 4.

Rate constants (k_2 ; l. mole⁻¹ sec.⁻¹) for reactions in methanol and dimethylformamide.

	10 ⁴ k_2 in MeOH	10 ⁴ k_2 in H·CO·NMe ₂
MeI + KSCN	—	117 [0°]
MeI + KSeCN	4·0 [0·0°]; 91·3 [25·0°]	916 [0°]
EtI + LiCl	0·035 [35·8°]; 0·47 [59·8°]	63 [0°]
Pr ⁿ I + LiCl	0·024 [35·8°]; 0·31 [59·8°]	48 [0°]
Pr ⁿ Br + LiCl	9·2 [100·0°]; 84·5 [123·1°]	—
<i>p</i> -NO ₂ ·C ₆ H ₄ I + PhONa	0·145 [100·0°]; 1·18 [123·1°]	6·7 [35·8°]; 100 [59·8°]
<i>p</i> -NO ₂ ·C ₆ H ₄ I + PhSNa	8·80 [50·0°]; 12·6 [55·0°]	823 [0°]
	55·5 [69·9°]; 504 [100·0°]	

Reactions of pyridine with butyl bromide were followed by stopping reaction of samples with dilute nitric acid and titrating the bromide ion. Methanol, dimethylformamide, and 4 : 1 v/v methanol-water (of dielectric constant equivalent to that of sulfolan⁹) were used as solvents. New results are in Table 2.

Reactions of sodium thiophenoxide and sodium phenoxide with *p*-iodonitrobenzene in methanol were carried out in the presence of a ten-fold excess of thiophenol and phenol, respectively, to prevent methanolysis and subsequent attack by methoxide ion.⁴ The dry sodium salts were used without their conjugate acids in dimethylformamide, because phenol and thiophenol are strong hydrogen-donors and would reduce the rate of reaction. Reactions were carried out under nitrogen, in solutions flushed out with nitrogen, as a precaution against oxidation of thiophenoxide or iodide. Reaction of samples of thiophenoxide reactions were stopped in hydrochloric acid and unconsumed hydrochloric acid was estimated (pH meter to detect the end point). Iodide ion could not be estimated in the presence of thiophenol. Reactions of phenoxide ion were followed by estimating both unconsumed phenoxide and iodide ion; the total remained constant throughout reaction. Rates are in Table 4.

Reaction Products.—The alkyl halide-halogen (etc.) exchanges were replacements, since total halogen was constant and no acid was formed. Each anion was identified by the characteristic potential at the end point of a silver ion titration. No cyanide ion was detected during the reaction of methyl iodide with potassium selenocyanate, and the characteristically evil-smelling methyl selenocyanate,⁷ b. p. 155°, was isolated in 80% yield from reaction in both solvents. The crude product, freed from selenocyanate ion, gave hydrogen cyanide with concentrated hydrochloric acid, confirming the expectation that selenocyanate and not isoselenocyanate was the major product.⁷

p-Iodonitrobenzene gave *p*-nitrophenyl phenyl sulphide, m. p. 55°, with sodium thiophenoxide, and *p*-nitrophenyl phenyl ether, m. p. 60°, with sodium phenoxide, in both methanol and dimethylformamide. Mixtures of sodium thiophenoxide with *p*-iodonitrobenzene in dimethylformamide became momentarily blue, then deep green, and finally red at the completion of reaction. The green colour may be that of the complex $\begin{matrix} \text{O} \\ \diagup \\ \text{N}^+ = \text{C}_6\text{H}_4 \\ \diagdown \\ \text{O} \end{matrix} \begin{matrix} \text{I} \\ \diagup \\ \text{SPh} \end{matrix}$ in dimethylformamide.¹¹

Butyl bromide was not hydrolysed by 4 : 1 methanol-water or methanol under the conditions of its reaction with pyridine. 1-Butylpyridinium bromide is the product of this reaction.⁹

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