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Kinetic Studies of Bimolecular Nucleophilic Substitution. VIII.[*1] The Effect of Hydroxylic Solvents on the Nucleophilicity of Aliphatic Amines in the Menschutkin Reaction

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The rate of the reactions of methyl iodide with various aliphatic amines, *i. e.*, methyl-, ethyl-, *n*-butyl-, ethanol- and benzyl-amines, have been measured in methanol solvent and compared with the previous results obtained in benzene solvent. Ethylamine, diethylamine, and triethylamine react slower in methanol than in benzene. In a similar fashion, butylamine, dibutylamine, tributylamine, methylamine and dimethylamine are less reactive in methanol than in benzene. These unusual results, *i. e.*, the lower S_N2 reactivity of amines in the more ionizing protic solvent, are attributed to the retardation by the higher activation energy in methanol solvent at the expense of the acceleration by higher values of the entropy of activation. The increase of the activation energy is ascribed to specific solvation, *e. g.*, hydrogen bonding of methanol toward amines. Benzylamines and ethanolamines, which are comparatively less solvated by methanol exhibit the usual reactivity sequence toward methyl iodide, *i. e.*, the higher S_N2 reactivity in the more polar solvent.

Since Menschutkin[1a] found that ethyl iodide reacts with triethylamine more rapidly in more polar solvents, subsequent investigators[1b-11] seem to have clearly established the same general conclusion for a number of Menschutkin reactions. The general solvent theory[2] also predicts the higher rate in the more ionizing media. However, as pointed out by Bunton,[3b] when comparison is made between ethanol and benzene, the theory is less satisfactory. Namely, although the reaction of methyl iodide toward pyridine[3a] is as predicted faster in ethanol than in benzene, the activation energy is higher in ethanol than in benzene. This higher value of the activation energy in a hydroxylic solvent has been ascribed to the hydrogen bonding between ethanol and the nucleophilic amine.[3]

If the retardation by the higher activation energy, caused by the stronger solvation or hydrogen bonding toward amines, outweighs the acceleration by the entropy of activation, it is anticipated, contrary to the general prediction of the solvent theory,[2] that the rate of the Menschutkin reaction would become lower in the more polar protic solvent. In this paper we will report on the examples of such unusual rate sequence observed in the case of Menschutkin reactions of methyl iodide with various primary, secondary and tertiary aliphatic amines in methanol solvent.

Results and Discussion

A series of the Menschutkin reactions of methyl iodide was carried out in methanol and in *n*-butanol, and the results were compared with the previous observations in water[4] and in benzene.[5] As an amine with hydrogen bonding interaction toward hydroxylic solvent, various primary, secondary and tertiary aliphatic amines, *i. e.*, methylamines, ethylamines, *n*-butylamines, ethanolamines and benzylamines, were chosen along with ammonia as a standard compound. The reaction was followed by measuring the rate of formation of iodide ion by Volhard method, and the rate data were interpreted by a standard second-order rate equation. The rate constants so obtained for

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[*1] Part VII: K. Okamoto, S. Fukui, I. Nitta and H. Shingu, This Bulletin, **40**, 2350 (1967).

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2) a) E. D. Hughes and C. K. Ingold, *ibid.*, **1935**, 255; b) S. Glasstone, K. J. Laidler and H. Eyring, "The Theory of Rate Processes," McGraw-Hill Book Co., New York (1941), Chap. 8.

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5) K. Okamoto, S. Fukui, I. Nitta and H. Shingu, *ibid.*, **40**, 2350 (1967).

Table 1. Rate constants and activation parameters of the reactions of 0.10 M methyl iodide with methylamines and ammonia in various solvents at 30.0°C a)

Solvent		NH_3	$MeNH_2$	Me_2NH	Me_3N
H_2O b)	10^4k_2	1.75	39.0	162	451
	E_A	23.5	21.8	21.0	20.6
	$\Delta S^{\neq}$	+0.2	+0.4	+0.6	+1.2
MeOH	10^4k_2	0.693	4.78	43.0	96.2
C_6H_6 c)	10^4k_2	0.261	7.28	48.7	88.9
	E_A	—	9.10	7.31	7.0
	$\Delta S^{\neq}$	—	−43.8	−47.0	−46.9

a) k_2 (sec^{-1} M^{-1}); E_A (kcal/mol); $\Delta S^{\neq}$ 30° (e. u.). Initial concentrations of amines and ammonia were 0.10 M. b) Ref. 4. c) Ref. 5.

Table 2. Rate constants and activation parameters of the reactions of 0.10 M methyl iodide with ethylamines, *n*-butylamines, ethanolamines and ammonia in methanol and benzene at 30.0°C a)

Solvent		NH_3	$EtNH_2$	Et_2NH	Et_3N
MeOH	10^5k_2	6.93	51.3	113	865
	E_A	20.8	18.8	16.8	14.9
	$\Delta S^{\neq}$	−10.9	−13.5	−18.5	−25.4
C_6H_6 b)	10^5k_2	2.61	56.2	278	1850
	E_A	—	12.8	10.7	9.1
	$\Delta S^{\neq}$	—	−33.2	−36.9	−42.9
			n-$BuNH_2$	(*n*-Bu)$_2$NH	(*n*-Bu)$_3$N
MeOH	10^5k_2		33.5	113	65.8
	E_A		17.5	15.5	16.3
	$\Delta S^{\neq}$		−18.9	−23.2	−21.3
C_6H_6 b)	10^5k_2		55.3	149	68.7
			$HOCH_2CH_2NH_2$	$(HOCH_2CH_2)_2NH$	$(HOCH_2CH_2)_3N$
MeOH	10^5k_2		45.0	60.0	4.37
	E_A		16.4	16.3	16.7
	$\Delta S^{\neq}$		−21.8	−21.6	−25.5
C_6H_6 b)	10^5k_2		37.5	38.3	1.29 c)
	E_A		11.2	11.4	13.1
	$\Delta S^{\neq}$		−39.4	−38.8	−39.8

a) k_2 (sec^{-1} M^{-1}); E_A (kcal/mol); $\Delta S^{\neq}$ 30° (e. u.). Initial concentrations of ethylamines and *n*-butylamines were 0.10 M. Initial concentrations of ethanolamines were 0.01—0.02 M.

b) Ref. 5.

c) Extrapolated from the data at 50, 60 and 70°C.

Table 3. Rate constants and activation parameters of the reactions of 0.10 M methyl iodide with 0.10 M benzylamines and ammonia in *n*-butanol and benzene at 30.0°C a)

Solvent		NH_3	$C_6H_5CH_2NH_2$	$(C_6H_5CH_2)_2NH$	$(C_6H_5CH_2)_3N$
n-BuOH	10^5k_2	—	33.7	48.0	0.07 c)
	E_A	—	12.2	13.2	17.1
	$\Delta S^{\neq}$	—	−36.4	−32.3	−32.3
C_6H_6 b)	10^5k_2	2.61	22.4	5.96	2.09×10^{-3} d)
	E_A	—	12.5	14.3	19.7
	$\Delta S^{\neq}$	—	−35.8	−32.7	−30.9

a) k_2 (sec^{-1} M^{-1}); E_A (kcal/mol); $\Delta S^{\neq}_{30°}$ (e. u.).

b) Ref. 5.

c) Extrapolated form the data at 40, 50 and 60°C.

d) Extrapolated from the data at 110 and 130°C.

TABLE 4. RATE CONSTANTS OF THE REACTIONS OF 0.10 M METHYL IODIDE WITH VARIOUS ALIPHATIC AMINES AND AMMONIA[a)]

R	Temp., °C	RNH_2	R_2NH	R_3N
H	20.0	6.93×10^{-5}		
	30.0	2.15×10^{-4}		
	40.0	5.87×10^{-5}		
Et	20.0	—	4.73×10^{-4}	3.70×10^{-4}
	30.0	5.13×10^{-4}	1.13×10^{-3}	8.65×10^{-4}
	40.0	1.39×10^{-3}	2.98×10^{-3}	1.88×10^{-3}
	50.0	3.53×10^{-3}		
n-Bu	10.0	—	1.83×10^{-4}	—
	20.0	—	4.72×10^{-4}	—
	30.0	3.35×10^{-4}	1.13×10^{-3}	6.58×10^{-4}
	40.0	8.37×10^{-4}	—	1.56×10^{-3}
	50.0	2.00×10^{-3}	—	3.50×10^{-3}
$HOCH_2CH_2$[b)]	20.0	1.80×10^{-4}	2.38×10^{-4}	—
	30.0	4.50×10^{-4}	6.00×10^{-4}	4.37×10^{-5}
	40.0	1.09×10^{-3}	1.42×10^{-3}	1.06×10^{-4}
	50.0	—	—	2.42×10^{-4}
$C_6H_5CH_2$[c)]	20.0	1.70×10^{-4}	2.13×10^{-4}	—
	30.0	3.37×10^{-4}	4.80×10^{-4}	—
	40.0	6.43×10^{-4}	9.12×10^{-4}	1.82×10^{-6}
	50.0	—	—	4.27×10^{-6}
	60.0	—	—	9.50×10^{-6}

a) k_2 (sec^{-1} M^{-1}); E_A (kcal/mol); $\Delta S^{\ddagger}_{30°}$ (e. u.). Initial concentrations of amines were 0.10 M except when otherwise noted. The solvent was methanol except when noted otherwise.

b) The initial concentrations of ethanolamines were 0.01—0.02 M.

c) The solvent was *n*-butanol.

secondary and primary amines were plotted against the percentage of completion and extrapolated to zero of the reaction time; as previously reported,[4)] this approximation was successful in the S_N2 reactions of methyl iodide with methylamines in aqueous solutions.

The values of rate constants for the reactions with methylamines in water, methanol and benzene are listed in Table 1, for ethylamines, *n*-butylamines and ethanolamines in methanol and benzene in Table 2, and for benzylamines in *n*-butanol and benzene in Table 3, together with activation paramters.

Inspection of Table 1 shows that the rates of three methylamines and ammonia are higher in water than in methanol and benzene. This is consistent with the prediction of the general solvent theory[2)] for the Menschutkin reaction. However, both methylamine and dimethylamine are more reactive in benzene than in methanol. Furthermore, as is shown in Table 2, the rates of three ethylamines and three *n*-butylamines are also higher in benzene than in methanol. These unusual results, which are contrary to the prediction for the Menschutkin reaction,[2)] are ascribed to the preponderance of the retarding effect of the higher activation energy at the expense of the accelerating effect by the more positive values of the entropy of activation in methanol solvent. The higher values of the activation energy in methanol solvent and in water solvent are most probably interpreted as a reflection of the strong hydrogen bonding[6)] between methanol and the amines.

It is of interest to note that the values of the activation energy for three benzylamines are almost as much in *n*-butanol as in benzene, and accordingly the usual rate sequence, *i. e.*, *n*-butanol > benzene, is observed for each of these amines. This is illustrated in Table 3.

As is shown in the usual rate sequence, *i. e.*, methanol>benzene, listed in Table 2, the values of the activation energy for three ethanolamines are not enough higher in methanol to surpass the accelerating effect of the enetropy of activation. This is probably ascribed to diminution of intermolecular hydrogen bonding interaction between methanol and these amines, since intramolecular hydrogen bonding of ethanolamines or association of the monomeric amines would interrupt the interaction of these amines toward methanol.

In Fig. 1 the rate constants for various amines, measured in methanol solvent at 30.0°C, are compared with each other by plotting the logarithms of the rate constants against the number of the

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6) G. Briegleb, *Z. Elektrochem.*, **53**, 350 (1949).

substituents attached to nitrogen atom. A similar tendency to that observed in benzene solvent (see Fig. 1 in previous paper⁵⁾ of this series) is found, indicating the preponderance of the steric retardation by the di- and tri-substitution on nitrogen atom, especially in the case of tri-*n*-butylamine, diethanolamine and triethanolamine. As compared with ammonia, these primary amines exhibit relatively lower nucleophilicity in methanol than in benzene solvent.⁵⁾ This diminution of the nucleophilicity in methanol solvent may be attributed to the relatively stronger solvation between methanol and these aimes.

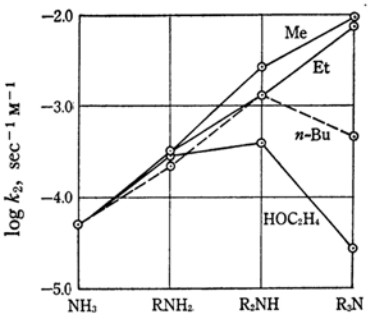

Fig. 1. Rate constants of the reactions of methyl iodide with various aliphatic amines and ammonia in methanol solvent at 30.0°C.

TABLE 5. KINETICS OF THE REACTION OF METHYL IODIDE WITH METHYLAMINE IN METHANOL SOLVENT AT 30.02±0.02°C

$(\text{MeI})_0 = 0.1025$ M; $(\text{Methylamine})_0 = 0.102$ M

Time min	0.0524 N KSCN/2.00 cc$^{b)}$	Completion %	$10^3\,k_2$ sec^{-1}M^{-1}
	(1.981)	0.00	—
0.00$^{e)}$	1.900	2.03	4.78$^{a)}$
2.00	1.870	2.82	6.49
5.25	1.800	4.57	8.40
7.00	1.760	5.36	8.90
10.00	1.677	7.71	10.16
12.00	1.615	9.29	10.98
14.00	1.575	10.30	10.86
16.00	1.525	11.56	11.14
∞$^{d)}$	(0.020)$^{c)}$		

a) Extrapolated from the k_2 values plotted against the percentage of completion.
b) 1.000 cc of 0.1031 N $AgNO_3$ was added before the titration at 0°C.
c) 2.000 cc of 0.1031 N $AgNO_3$ was added before the titration at 0°C.
d) Three hours at 110°C.
e) The time when the first ampoule was removed for the interruption of the reaction.

TABLE 6. KINETICS OF THE REACTION OF METHYL IODIDE WITH DIMETHYLAMINE IN METHANOL SOLVENT AT 30.02±0.02°C

Time min	0.0504 N KSCN/2.00 cc$^{b)}$	Completion %	10^3k_2 sec^{-1}M^{-1}
0.00	1.971	0.00	4.30$^{a)}$
2.00	1.780	4.86	4.30
3.00	1.675	7.50	4.57
4.00	1.575	10.1	4.72
5.00	1.488	12.3	4.72
6.00	1.400	14.5	4.66
7.00	1.310	16.8	4.77
8.00	1.210	19.3	5.05
9.00	1.132	21.3	5.08
10.00	1.051	23.4	5.14
∞$^{d)}$	(0.011)$^{c)}$		

a) Extrapolated from the k_2 values plotted against the percentage of completion.
b) 1.000 cc of 0.0991 N $AgNO_3$ was added before the titration at 0°C.
c) 2.000 cc of 0.0991 N $AgNO_3$ was added before the titration at 0°C.
d) Two hours at 110°C.

Experimental

Materials. Methanol, bp 65.0°C, was fractionated after reluxing over magnesium. *n*-Butanol, bp 117.0°C, was purified by fractional distillation. Methyl iodide, diethylamine, triethylamine, *n*-butylamine, di-*n*-butylamine, tri-*n*-butylamine, ethanolamine, diethanolamine, triethanolamine, benzylamine, dibenzylamine, and tribenzylamine were purified by the methods described in Part VII.⁵⁾ The methanol solutions of ammonia, methylamine, dimethylamine, trimethylammine and ethylamine were prepared by leading the respective gaseous amine into methanol. The gaseous amines were prepared by the method described in Part VII.⁵⁾

Kinetic Measurements. The kinetic runs were carried out in a manner similar to that previously reported.⁵⁾ The rate data were interpreted as described in text. The results are summarized in Tables 1—4. The kinetic data for the representative runs for methylamine and dimethylamine are illustrated in Tables 5 and 6, respectively.