Effect of Solvation on the Menschutkin Reaction in Liquid Sulfur Dioxide[1,2]

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When the Menschutkin reaction in liquid sulfur dioxide was recently carried out,[2] it was indicated that the reaction in liquid sulfur dioxide is extremely slow compared to that in such nucleophilic dipolar solvents as dimethylformamide or dimethylsulfoxide. In the light of the facts that liquid sulfur dioxide is one of the best ionizing solvents[3] and that the product is an ion-pair (alkylammonium cation and halide anion), and judging from extensive previously-reported discussions,[4] the Menschutkin reaction should be very fast in liquid sulfur dioxide. The reasons for such a discrepancy perhaps lie both in the strong solvation of the solvent (liquid sulfur dioxide) to amines and the fact that the rate-determining step of the reaction may be the step of attack by the base on the alkyl halide.

In contrast to the cationic polymerization and the Beckmann rearrangement in liquid sulfur dioxide, which are very fast and in which unsolvated carbonium ions are favored,[2] the Menschutkin reaction is one of the reactions in which the unsolvated base (or anion) is favored. In both cases, the unsolvated or *bare* species (ion or substrate) is a predominating factor in carrying out the reactions rapidly. That a borderline case between S_N1 and S_N2 reactions has been observed by Ingold[5] in a substitution in liquid sulfur dioxide which would otherwise be an S_N1 reaction is to be understood as the result of the fact that the rate-determining ionization of alkyl halide is not followed by the fast step of the combination of alkyl carbonium ion with an anion or a base, since the base or the anion is solvated by sulfur dioxide and since the second step is also occasionally a slow step.

The organic reaction in a solution is a reaction of polymolecularity in the sense that the solvent molecule always has some interaction during the course of the reaction, as has already been pointed out by Winstein[6] and Ingold[6b]. In the present paper, the reaction of methyl iodide with *N*, *N*-dimethylaniline, pyridine, triethylamine, *N*, *N*-dimethylbenzylamine or their *o*-methyl-substituted derivatives has been undertaken in order to further elucidate the effect of the solvation of liquid sulfur dioxide on the bases as compared with that of nitrobenzene or methanol.

Experimental

Materials. — Methyl iodide was washed with a sodium thiosulfate solution, water, a sodium carbonate solution and water successively, then dried and distilled; b. p. 42.5∼43°C. *N*, *N*-Dimethyl-*o*-toluidine was synthesized from *o*-toluidine-bromohydrate and methanol at 145∼150°C,[7] and the twice-distilled product boiling at 181∼182°C was used. *N*, *N*-Dimethylaniline and triethylamine were refluxed with acetic anhydride and distilled respectively. The bases were dried over potassium hydroxide and redistilled; b. p., *N*, *N*-dimethylaniline; 189°C, and triethylamine; 89.5∼90.1°C. Pyridine was dried with potassium hydroxide and barium oxide successively and distilled; b. p. 115.5°C. *N*, *N*-Dimethylbenzylamine was dried over potassium hydroxide and distilled; b. p. 177∼177.5°C. α-Picoline and 2, 6-dimethylpyridine were purified as the following; a double salt from the base, hydrochloric acid and mercuric chloride was recrystallized three times from a dilute hydrochloric acid solution and decomposed with a sodium hydroxide solution. The product was extracted with benzene, dried with potassium hydroxide and barium oxide successively, and distilled; α-picoline; b. p. 129∼131°C, and 2, 6-dimethylpyridine; b. p. 143.0∼143.1°C. Liquid sulfur dioxide was dried with phosphorus pentoxide and distilled. Nitrobenzene and methanol were purified by known methods.

Kinetic Procedure. — The method described in a preceding paper[2] was used. A potentiometric titration was used to estimate the amount of iodide anions produced.

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[1] Substitution in Liquid Sulfur Dioxide, Part III.

[2] Part II: N. Tokura and Y. Kondo, This Bulletin, 36, 200 (1963).

[3] S. G. Smith, A. H. Fainberg and S. Winstein, *J. Am. Chem. Soc.*, **83**, 618 (1961).

[4] E. A. Moelwyn-Hughes, "Reactions in Solution," 2nd ed., Oxford Univ. Press, London (1947), p. 208; M. S. Newman, "Steric Effects in Organic Chemistry," John Wiley, New York (1956), p. 70, contributed by E. Eliel.

[5] M. L. Baird, E. D. Hughes and C. K. Ingold, *J. Chem. Soc.*, **1954**, 634.

[6] a) S. Winstein, E. Grunwald and H. W. Jones, *J. Am. Chem. Soc.*, **73**, 2700 (1951); b) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca (1953).

[7] H. Reinhardt and W. Staedel, *Ber.*, **16**, 29 (1883).

Results and Discussion

The Kinetical Order of the Reaction.—Methyl iodide was used as the alkyl halide since it is believed to be ionizable only with difficulty, since the reaction may thus be conveniently carried out by a S_N2 mechanism, and since it has the least steric hindrance to a coupling with the nitrogen atom of the amines. However, as may be seen in Table I, the kinetical order of the reaction (methyl iodide with pyridine) varied from second order to first order as the molar ratio, [base]/[halide], exceeded unity. When the base was used excessively against the halide, the reaction rate followed the first order rate law, the first order in methyl iodide, and the zero-th order in pyridine.

These phenomena are reported to be often encountered in cases wherein a one-to-one intermediate complex is formed reversibly in a reaction course.[8] In the reaction of methyl iodide and pyridine, the intermediate may be,

Pyridine⋯Me⋯I

The formation of such an intermediate is consistent with the experimental fact that the

TABLE I. THE RATE CONSTANTS OF THE REACTION BETWEEN METHYL IODIDE AND PYRIDINE IN LIQUID SULFUR DIOXIDE AT 40°C

(a) Methyl iodide: 0.399 mol./l.
Pyridine: 0.820 mol./l.

t min.	I^- $\times 10^2$ mol./l.		k_1 $\times 10^3$ min^{-1}		k_2 $\times 10^2$ l. mol^{-1} min^{-1}
10	4.25	Const.	1.13		1.45
20	8.05		1.13		1.52
30	11.45		1.16		1.65
40	14.5		1.12		1.66
50	17.3		1.13		1.75
65	20.8		1.16		1.90

(b) Methyl iodide: 0.399 mol./l.
Pyridine: 0.615 mol./l.

t min.	I^- $\times 10^2$ mol./l.		k_1 $\times 10^3$ min^{-1}		k_2 $\times 10^2$ l. mol^{-1} min^{-1}
15	4.75		8.78	Const.	1.54
30	8.95		8.20		1.56
45	12.4		7.71		1.57
60	15.4	Const.	7.55		1.64
75	18.0		7.49		1.72
90	21.0		7.31		1.81

(c) Methyl iodide: 0.399 mol./l.
Pyridine: 0.359 mol./l.

t min.	I^- $\times 10^2$ mol./l.		k_1 $\times 10^3$ min^{-1}		k_2 $\times 10^2$ l. mol^{-1} min^{-1}
20	3.50		4.85	Const.	1.50
40	6.75		4.41		1.51
60	9.47		4.16		1.58
80	11.82		3.70		1.53
100	13.76		3.50		1.59
120	15.47		3.18		1.56

TABLE II. SECOND ORDER RATE CONSTANTS OF THE REACTIONS. METHYL IODIDE WITH BASES IN LIQUID SULFUR DIOXIDE

Base	Reaction temp., °C	k, l. mol^{-1} sec^{-1}	$\Delta E^{\neq}$, kcal. mol^{-1}	A
N, *N*-Dimethylaniline[2]	30	1.72×10^{-5}	17.2	5.11×10^{7}
	40	4.77×10^{-5}		
	50	9.93×10^{-5}		
Pyridine[2]	20	3.38×10^{-5}	17.8	6.50×10^{5}
	30	9.00×10^{-5}		
	40	2.47×10^{-4}		
Triethylamine	40	5.69×10^{-5}	22.7	4.03×10^{11}
	50	1.79×10^{-4}		
	60	5.10×10^{-4}		
N, *N*-Dimethylbenzylamine	45	2.93×10^{-5}	22.6	9.91×10^{10}
	55	8.62×10^{-5}		
	65	2.41×10^{-4}		

TABLE III. A COMPARISON OF THE RELATIVE RATES IN SOLVENTS (40°C)

Base		*N*, *N*-Dimethylaniline	Pyridine	Triethylamine	*N*, *N*-Dimethylbenzylamine
K_b, 25°C*		1.15×10^{-9}	2.3×10^{-9}	7.36×10^{-4}	1.86×10^{-4}
Liq. SO_2	$k\times10^5$	4.77[2]	24.70[2]	5.69	1.64
	Relative rate	1	5.18	1.19	0.34
Nitrobenzene	$k\times10^4$	2.10[9]	9.82[10]	708[11]	Very fast
	Relative rate	1	4.68	338	
Methanol	$k\times10^5$	19.4[12]	9.29	221	579
	Relative rate	1	0.48	11.4	29.8

* Landolt-Börnstein Tabellen

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8) L. G. Cannel, *J. Am. Chem. Soc.*, **79**, 2929 (1957).
9) K. J. Laidler, *J. Chem. Soc.*, **1938**, 1786.
10) H. C. Brown and A. Cahn, *J. Am. Chem. Soc.*, **77**, 1715 (1955).
11) H. C. Brown and N. R. Eldred, ibid., **71**, 445 (1945).
12) A. G. Evans et al., *J. Chem. Soc.*, **1939**, 1345.

Table IV. The Arrhenius parameters in the Menschutkin reaction in solvents*

Solvent / Base		Liq. SO_2	Nitrobenzene	Methanol
N, N-Dimethylaniline	$\Delta E^{\neq}$	17.2	12.8$^{9)}$	15.2$^{12)}$
	$\Delta S^{\neq}$	−25.3	−36.4	−29.0
Pyridine	$\Delta E^{\neq}$	17.8	13.6$^{10)}$	18.2
	$\Delta S^{\neq}$	−20.3	−29.8	−21.0
Triethylamine	$\Delta E^{\neq}$	22.7	9.7$^{11)}$	16.4
	$\Delta S^{\neq}$	− 7.5	−34.7	−20.4
N, N-Dimethylbenzylamine	$\Delta E^{\neq}$	22.6	—	13.9
	$\Delta S^{\neq}$	−10.3	—	−26.5

* $\Delta E^{\neq}$, kcal. mol^{-1}, $\Delta S^{\neq}$, e. u.

ionizing power of the solvent has little influence on the reaction rate.²⁾ Therefore, the reaction rates were followed in the range of the molar ratio, in which the second order rate law was dominating, and in the initial stage of the reaction. A typical run with triethylamine is shown in Fig. 1.

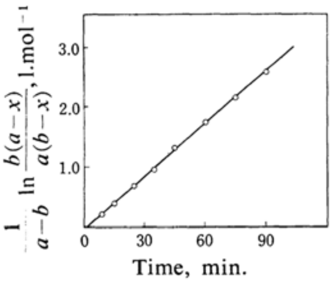

Fig. 1. A typical run in liquid sulfur dioxide. Temp. 60°C, triethylamine: 0.431 mol.l^{-1}, methyl iodide: 0.301 mol.l^{-1}

The Effect of Bases on the Reaction Velocity.—The results are indicated in Tables II and III.

In general, the rate of the Menschutkin reaction is in the order.

nitrobenzene > methanol > liquid sulfur dioxide

in liquid sulfur dioxide, however, the rate is slower than in methanol or in nitrobenzene. In nitrobenzene, the order of the relative rates of the bases is dependent upon the K_b values of the respective bases:

N, *N*-dimethylbenzylamine > triethylamine > pyridine > *N*, *N*-dimethylaniline

and in methanol, the order is:

N, *N*-dimethylbenzylamine > triethylamine > *N*, *N*-dimethylaniline > pyridine

whereas in liquid sulfur dioxide, the order is reversed:

pyridine > triethylamine > *N*, *N*-dimethylaniline > *N*, *N*-dimethylbenzylamine

Moreover, the difference in the relative rates is small (in the range of 0.34∼5.18) in liquid sulfur dioxide, whereas in nitrobenzene the relative rates are scattered throughout the 1∼338 range and in methanol, the 1∼29.8 range. Thus in liquid sulfur dioxide the rate constants are leveling, while in nitrobenzene they are differentiating. A comparison of the Arrhenius parameters is givin in Table IV.

As may be seen in Table IV, both the energy and the entropy of the activation are larger in liquid sulfur dioxide. The entropy of the activation of triethylamine is the largest (−7.5 e. u.). This is very consistent with the very small value of the dissociation constant, (0.007 in benzene¹³⁾) of the triethylamine-sulfur dioxide complex and suggests the effect of sulfur dioxide solvation on the reaction velocity. The release of the solvated sulfur dioxide may be necessary in the reaction sequences. The inverse order of the relative rates in liquid sulfur dioxide may perhaps be ascribed to the following reasons. First, in sulfur dioxide, the stronger the bases, the more will be the solvation by sulfur dioxide molecules; thus, the attacking rate may be modified according to their strength as bases. The dissociation constant of the pyridine-sulfur dioxide complex is as large as 4.0¹³⁾ (571 times that of the triethylamine-sulfur dioxide complex), while the K_b values also reflect the above relation. In methanol the hydrogen bonding may be operative, and in nitrobenzene some interaction with the bases may be considered; however, these solvents are less solvating to the bases than is liquid sulfur dioxide.

Effect of *o*-Methyl Substituents.—An intimate relation between the rate and the solvation has been further clarified by study of the ortho-substituent effect. The effect of the *o*-methyl substituent of *N*, *N*-dimethylaniline or pyridine on the reaction rate has been examined in liquid sulfur dioxide and has been compared

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13) J. A. Moede and C. Curran, *J. Am. Chem. Soc.*, **71**, 852 (1949).

TABLE V. EFFECT OF *o*-METHYL SUBSTITUENT ON THE RATE CONSTANT AND THE ARRHENIUS PARAMETER

Solvent	Base	Reaction temp., °C	k l. mol^{-1} sec^{-1}	$\Delta E^{\ne}$ kcal. mol^{-1}	A
Liquid sulfur dioxid	*N, N*-Dimethyl *o*-toluidine	40	1.65×10^{-5}	15.9	2.17×10^{6}
		50	3.62×10^{-5}		
		60	7.81×10^{-5}		
	α-Picoline	30	9.50×10^{-5}	17.4	3.39×10^{8}
		40	2.44×10^{-4}		
		50	5.63×10^{-4}		
	2, 6-Dimethyl-pyridine	30	7.95×10^{-5}	14.4	1.93×10^{6}
		40	1.72×10^{-4}		
		50	3.51×10^{-4}		
Methanol	Pyridine	40	9.29×10^{-5}	18.2	4.59×10^{8}
		50	2.26×10^{-4}		
		60	5.35×10^{-4}		
	α-Picoline	40	3.07×10^{-5}	19.2	7.66×10^{8}
		50	7.91×10^{-5}		
		60	1.95×10^{-4}		
	2, 6-Dimethyl-pyridine	55	1.25×10^{-5}	22.0	$5.3\ \times10^{9}$
		65	3.20×10^{-5}		
		75	8.60×10^{-5}		

TABLE VI. COMPARISON OF THE RATE CONSTANTS OF *o*-SUBSTITUTED BASES AT 40°C

Base \ Solvent	Liquid sulfur dioxide		Methanol	
	k	$k/k_{\rm H}$	k	$k/k_{\rm H}$
N, N-Dimethylaniline	4.77×10^{-5} 2)	1	1.19×10^{-3} a)	1
N, N-Dimethyl-*o*-toluidine	1.65×10^{-5} 2)	0.346	4.17×10^{-5} a)	0.035
Pyridine	2.47×10^{-4} 2)	1	9.29×10^{-5}	1
α-Picoline	2.44×10^{-4}	0.988	3.07×10^{-5}	0.330
2, 6-Dimethylpyridine	1.72×10^{-4}	0.696	2.34×10^{-6} b)	0.0252

a) Ref. 12
b) Calculated from the results in Table V

TABLE VII. COMPARISON OF THE ARRHENIUS PARAMETERS

Base \ Solvent		Liquid sulfur dioxide	$\Delta E^{\ne}{}_{o\text{-Me}}-\Delta E^{\ne}{}_{\rm H}$	Methanol	$\Delta E^{\ne}{}_{o\text{-Me}}-\Delta E^{\ne}{}_{\rm H}$
N, N-Dimethylaniline	$\Delta E^{\ne}$, kcal. mol^{-1}	17.2		15.2	
	$\Delta S^{\ne}$, e. u.	−25.3		−29.0	
N, N-Dimethyl-*o*-toluidine	$\Delta E^{\ne}$, kcal. mol^{-1}	15.9	−1.3	21.1	+5.9[12]
	$\Delta S^{\ne}$, e. u.	−31.6		−18.0	
Pyridine	$\Delta E^{\ne}$, kcal. mol^{-1}	17.8		18.2	
	$\Delta S^{\ne}$, e. u.	−20.3		−21.0	
α-Picoline	$\Delta E^{\ne}$, kcal. mol^{-1}	17.4	−0.4	19.2	+1.0
	$\Delta S^{\ne}$, e. u.	−21.6		−20.0	
2, 6-Dimethylpyridine	$\Delta E^{\ne}$, kcal. mol^{-1}	14.4	−3.4	22.0	+3.8
	$\Delta S^{\ne}$, e. u.	−31.9		−16.1	

with that in methanol (cf. Tables V, VI and VII).

A dramatical difference is observed in the ortho-effect between the rates in liquid sulfur dioxide and in methanol. As may be seen in Table VI, $k_{o\text{-Me}}/k_{\rm H}$ is the ratio of the rate constants of the *o*-methyl-substituted and the unsubstituted bases. In liquid sulfur dioxide, the ratios are 0.346 (*N, N*-dimethyl-*o*-toluidine), 0.988 (α-picoline) and 0.696 (2, 6-dimethylpyridine) respectively, while in methanol the ratios are greatly depressed: 0.035 (*N, N*-dimethyl-*o*-toluidine), 0.330 (α-picoline) and 0.0252 (2, 6-dimethylpyridine) respectively, a leveling effect being again prevalent in liquid sulfur dioxide.

In methanol, both the activation energy and the entropy of activation increase when the methyl group is introduced in the ortho-position. In liquid sulfur dioxide, both the parameters decrease upon the introduction of the *o*-methyl substituent, as is shown in Table VII. The above results may also be well interpreted as due to the effect of solvation by liquid sulfur dioxide. The *o*-methyl group in dimethylaniline or in the pyridine ring is expected to lower the basicity of the base, either by hydrogen bonding (chelate formation as in Fig. 2) or by partial inhibition of the resonance by the steric hindrance of the methyl group.[14] In liquid sulfur dioxide, the reduction of solvation may compensate for the basicity depression by the *o*-methyl group and thus eliminate the difference or level off the rate constants, as may be seen in Table VI. An alternative explanation is that the solvation of sulfur dioxide to the nitrogen atom of the base is competitive against the chelation or the resonance inhibition. The lack of the linear dependence of the activation energy difference on the heat of the vaporization of the base in liquid sulfur dioxide, as will be described below, seems to support both views.

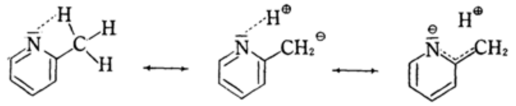

Fig. 2

The Heat of Vaporization and the Difference in the Activation Energy. — If the basicity depression of an *o*-methyl substituted base is to be ascribed to the chelation effect, the reaction rate of the Menschutkin reaction should have some linear dependence on the heat of the vaporization of the base, since it is a well-established fact[15] that the boiling point of *o*-methylaniline is lower than that of *p*-methylaniline because of the same chelation, as Fig. 2 shows. In Fig. 3, the difference, $\Delta E^{\neq}_{o\text{-Me}}-\Delta E^{\neq}_{\mathrm{H}}$, was plotted against the difference of the heat of evaporation of the *p*- and *o*-methyl derivative, $\Delta H_{\mathrm{p}}-\Delta H_{\mathrm{o}}$. In methanol, a linear plot is obtained, where ΔH_{p}, ΔH_{o}, $\Delta E^{\neq}_{o\text{-Me}}$ and $\Delta E^{\neq}_{\mathrm{H}}$ are the heat of the vaporization of the *p*-methyl derivative, that of the *o*-methyl derivative, the activation energy of *o*-methyl, and that of the unsubstituted bases respectively.

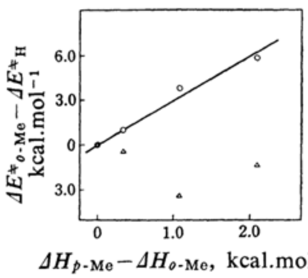

Fig. 3. Dependence of difference of activation energies on difference of heat of evaporation.
○ MeOH △ liq. SO_2

As may be seen in Fig. 3, in liquid sulfur dioxide the plots are scattered, while in methanol a linear dependence between the differences in activation energies and in heats of evaporation is observed.

TABLE VIII. THE HEAT OF VAPORIZATION OF *o*- AND *p*-METHYL-SUBSTITUTED BASES

Base	B. p. °C[a]	Heat of evaporation[a] kilojoule/mol.
N, *N*-Dimethylaniline	192.7	44.35
N, *N*-Dimethyl-*o*-toluidine	183.9	39.7
N, *N*-Dimethyl-*p*-toluidine	210.0	48.5[b]
Pyridine	115.2	35.11
α-Picoline	129.4	37.77
γ-Picoline	145.4	39.20
2,6-Dimethylpyridine	144.0	39.52
3,5-Dimethylpyridine	171.9	44.09

a) Landolt-Börnstein Tabellen
b) Calculated from the relationship between vapor pressure and temperature

The Isokinetic Relation. — Although a linear relationship has never been obtained in liquid sulfur dioxide between the activation energy and the heat of vaporization, it seems likely that a similar reaction mechanism is taking place throughout the reaction in liquid sulfur dioxide. The plots of $\Delta E^{\neq}$ against $\Delta S^{\neq}$ gave a linear isokinetic relation[16] (Fig. 4), whose slope indicates that the isokinetic temperature is 350°K. The temperature is very close to the experimental condition (30~75°C), again proving the leveling effect of liquid sulfur dioxide.

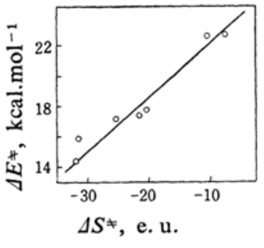

Fig. 4. Isokinetic relationship in liquid sulfur dioxide, methyl iodide with various bases.

Summary

1) The effect of the solvent solvation has been compared in the reaction between methyl

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[14] J. W. Smith, *J. Chem. Soc.*, **1961**, 31.
[15] E. Pimental and A. L. McClellan, "The Hydrogen Bond," W. H. Freeman Co., New York (1960), p. 8.
[16] J. E. Leffler, *J. Org. Chem.*, **20**, 1202 (1955).

iodide and various bases in liquid sulfur dioxide, methanol and nitrobenzene. The reaction rate in liquid sulfur dioxide is very much depressed, and the differences in the relative rates among bases are reduced in sulfur dioxide (a leveling effect) as compared to the other two solvents.

2) The order of the relative rates is reversed in liquid sulfur dioxide; pyridine > triethylamine > *N*, *N*-dimethylaniline > *N*, *N*-dimethylbenzylamine, whereas in methanol and in nitrobenzene, *N*, *N*-dimethylbenzylamine is the fastest of the bases. The reasons for this have been discussed.

3) The effect of the *o*-methyl substituent of the bases on the reaction rate has been examined. In liquid sulfur dioxide, the rate ratios $k_{o\text{-Me}}/k_{\mathrm{H}}$ are again leveling, while in methanol the ratios are differentiating. The solvation of sulfur dioxide has been considered to be the reason.

4) An isokinetic relation between $\Delta E^{\ne}$ and $\Delta S^{\ne}$ has been observed, and the isokinetic temperature calculated as 350°K; however, no linear dependence was obtained between $\Delta E^{\ne}_{o\text{-Me}} - \Delta E^{\ne}_{\mathrm{H}}$ and $\Delta H_{\mathrm{p}} - \Delta H_{\mathrm{o}}$.

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