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Solvent Effects under High Pressures. IV.[1] A Procedure for the Estimation of Solvation in the Transition State

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The rate constants and activation parameters were measured for the reaction of pyridine with benzyl bromide in various solvents. The rate constants were better correlated to the activation volumes than to the activation entropies. The linear free-energy relationships were observed in the plots of the log k values of some Menschutkin reactions *vs.* the log k values of the present reaction in various solvents. Corresponding to their good correlations between the values of log k and of their pressure derivatives for the present reaction, the values of $(z \cdot \Delta P)$, which are the slopes of the plots of $\Delta V_0^{\neq}$ *vs.* KV^0, increased with the increase in the slopes of the above linear free-energy relationships. The activation volumes in various solvents are linearly correlated to their pressure derivatives. An equation which predicts the relationship has been derived. Using this equation, the solvation number in the activated complex and the average pressure within its cosphere have been estimated to be *ca.* 4 and 910 (kg. cm^{-2}) respectively. Based on these results, discussions have been given on the solvation in the transition state for the present reaction.

In the works of this series,[1,2] the Menschutkin reaction of triethylamine with ethyl iodide has been chosen as the standard system in order to investigate the mechanisms of the solute-solvent interaction in the transition state. As the work continued, we needed a system sensitive to the change in the medium. As an example of such a system, the reaction of pyridine with benzyl bromide was chosen.

On the other hand, this system has long been referred to as the standard example of conforming to the Kirkwood theory.[3,4] However, contributions from the specific interaction between a solute and solvents have been suggested to play a significant role in the solvent effect in typical Menschutkin reactions.[5–7]

Therefore, the detailed analysis of the present system will throw some light on the origin of these interactions.

In this paper, the activation parameters of the reaction will be analyzed by empirical procedures, and then we will discuss the pressure dependence of

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[1] Part III; Y. Kondo and N. Tokura, This Bulletin, **42**, 1660 (1969).

[2] Y. Kondo, M. Uchida, and N. Tokura, *ibid.*, **41**, 992 (1968).

[3] S. Glasstone *et al.*, "The Theory of Rate Processes," McGraw-Hill Book Company, New York (1941).

[4] K. B. Wiberg, "Physical Organic Chemistry," John Wiley & Sons, New York (1964).

[5] H. Hartmann and A. P. Schmidt, *Z. Phys. Chem.*, (Frankfurt), **62**, 312 (1968).

[6] H. Hartmann and A. P. Schmidt, *ibid.*, **66**, 183 (1969).

[7] Y. Kondo and N. Tokura, This Bulletin, **40**, 1433 (1967).

the activation volumes.

Experimental

Materials. Pyridine, a special-grade reagent, was refluxed over potassium hydroxide for a few days and then distilled. The middle fraction was stored over barium oxide and redistilled before use. Benzyl bromide, another special-grade reagent, was dried over anhydrous potassium carbonate and distilled twice under reduced pressure. The other solvents were commercial reagent-grade reagents and were purified by procedures described elsewhere.[8-11]

Kinetic Procedure. Separate solutions of pyridine and the bromide in a solvent were prepared by weight (usually the concentrations of the reagents were *ca.* 0.01—0.05 M in the reaction mixture). The solutions were mixed in polyethylene ampoules. These ampoules were sealed quickly, shaken vigorously, and immersed into a glass test tube containing mercury which was maintained at the reaction temperature. The test tube was then immersed into the oil of the pressure vessel in a thermostat bath. After a given period, the reaction mixture was partitioned between light petroleum and water. The aqueous layer was potentiometrically titrated with a silver nitrate solution.

Usually reactions were carried out at six fixed pressures (1, 300, 600, 900, 1,200, and 1,500 kg cm^{-2}) and at four fixed temperatures (20.0, 30.0, 40.0, and 50.0°C).

The Rate Law in Alcohols. In methanol and 2-propanol, a spontaneous solvolysis has been observed for the bromide. Therefore, the total rate law can be written as follows:

$$\frac{dx}{dt} = k_2(a-x)(b-x) + k_1(a-x) \qquad (1)$$

where a, b, x stand for the initial mole fractions of benzyl bromide and of pyridine, and the mole fraction of the bromide ion at the time, t; respectively.

The second-order rate constants (k_2) for the Menschutkin reaction were calculated by means of Eq. (1) after the corrections of the first-order solvolysis rate (k_1), which was measured independently under the same reaction conditions.

Results

All the reaction rates followed second-order kinetics except in alcohols, where both the first order- and second order-rate constants were calculated by the procedure mentioned above. All the second order-rate constants, k_x, are expressed in a mole fraction unit (sec^{-1}), which is related to the rate constants in a molar unit, k_M ($l\cdot$mol$^{-1}\cdot$sec^{-1}), by the equation: $k_x = k_M V_s^{-1}$, where V_s stands for the molar volume of the solvent (in l) at the reaction temperature. For most of the reaction conditions, the measurements were repeated more than twice. The rate constants thus obtained under hydrostatic pressures were first scrutinized by the procedure developed by the present authors,[2] and then the pressure-dependence parameters were calculated by the least-squares method based on the following equations:

$$\ln k = A + BP + CP^2 \qquad (2)$$

$$\Delta V_0^{\neq} = -\boldsymbol{R}TB \qquad (3)$$

$$(\partial \Delta V^{\neq}/\partial P)_0 = -2\boldsymbol{R}TC \qquad (4)$$

The least-squares calculations were also performed for the temperature-dependence parameters on the basis of the following equations:

$$\ln (k_x/T) = A'/T + B' \qquad (5)$$

$$\Delta H^{\neq} = -\boldsymbol{R}A' \qquad (6)$$

$$\Delta S^{\neq} = \boldsymbol{R}(B' - \ln \boldsymbol{k}_b/h) \qquad (7)$$

where $\boldsymbol{k}_b$ and h stand for the Boltzmann and the Plank constants.

These calculations were done using a NEAC 2200—500 computer. The results thus obtained are collected in Table 1.

The estimated errors are as follows: k_x; ±1.7%, $\Delta V_0^{\neq}$; ±1.3 (cm$^3\cdot$mol^{-1}), $(\partial \Delta V^{\neq}/\partial P)_0$; ±0.002 (cm$^5\cdot$mol$^{-1}\cdot$kg^{-1}), $\Delta H^{\neq}$; ±0.2 (kcal$\cdot$mol^{-1}), $\Delta S^{\neq}$;

Table 1. Rate constants and activation parameters (30°C)

No.	Solvents	$k_x \times 10^5$	$-\Delta V_0^{\neq}$	$(\partial \Delta V^{\neq}/\partial P)_0$	$\Delta H^{\neq}$	$\Delta S^{\neq}$
1	Toluene	4.85	39.1	0.0154	13.4	34.2
2	Benzene	10.996	35.3	0.0193	—	—
3	Chlorobenzene	50.0	29.1	0.0077	12.1	33.9
4	Bromobenzene	60.4	24.9	0.0031	—	—
5	Nitrobenzene	601.	23.7	0.0120	11.8	29.9
6	Acetone	297.	34.9	0.0115	11.7	31.4
7	Tetrahydrofuran	28.8	32.3	0.0118	12.4	33.7
8	Dichloroethane	129.	25.4	0.0000	—	—
9	2-Propanol	147.	20.4	0.0057	—	—
10	Methanol	629.	27.2	0.0134	16.5	14.3
11	Acetonitrile	2140.	29.2	0.0105	11.4	28.8
12	Cyclohexanone	177.	—	—	12.2	31.1
	Solvolysis of Benzyl Bromide					
	Methanol	0.337	22.8	0.0064	20.3	16.8
	2-Propanol	0.0275	19.4	0.0064	—	—

Dimensions, k_x; (sec^{-1}), $-\Delta V_0^{\neq}$; (cm$^3\cdot$mol^{-1}), $(\partial \Delta V^{\neq}/\partial P)_0$; (cm$^5\cdot$mol$^{-1}\cdot$kg^{-1}), $\Delta H^{\neq}$; (kcal$\cdot$mol^{-1}), $\Delta S^{\neq}$; (e. u.)

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8) Y. Kondo, T. Matsui and N. Tokura, This Bulletin, **42**, 1037 (1969).

9) T. Matsui and N. Tokura, *ibid.*, **44**, 756 (1971).

10) J. F. Coetzee, G. P. Cunningham, D. K. McGuire, and G. R. Padmanabhan, *Anal. Chem.*, **34**, 1139 (1962).

11) "Technique of Organic Chemistry, VII. Organic Solvents," ed. by A. Weissberger, Interscience, New York (1955).

±0.4 (e. u.).

Discussion

Empirical Analysis of Activation Parameters. Figure 1 shows the relation between these parameters and the solvent characteristics.

An interesting feature of the plot is that the activation volumes are fairly well correlated to the rate constants, except for a few solvents, the molar volumes of which are fairly smaller than those of the correlative solvents; *i.e.*, for the former solvents they are *ca.* 40—75 m*l*·mol^{-1}, and for the latter, 100—110 m*l*·mol^{-1}. However, the sign of the slope suggests, if we use the theory of the absolute reaction rates[3] as a base, that the reaction systems are under a negative pressure. This unreasonable conclusion indicates that the solvent characteristics manifest themselves on the rate constant through the form of an enthalpy and of an entropy, but not directly in the form of a volume.

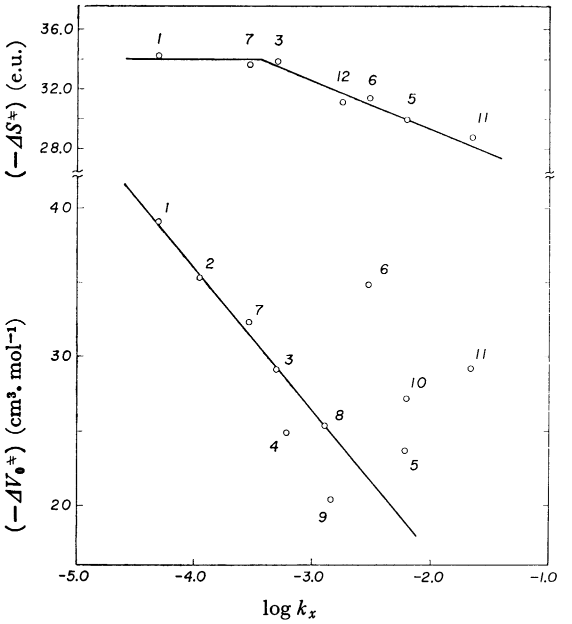

Fig. 1. Plots of activation parameters *vs.* rate constants for the reaction of pyridine and benzyl bromide at 30°C. The numbers refer to the Table 1.

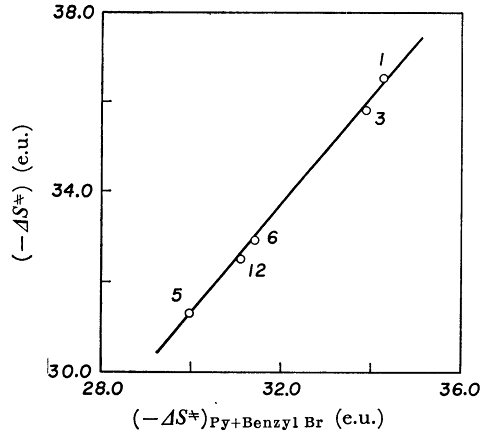

Fig. 2. The activation entropies of the two types of the Menschutkin reactions.
ordinate; the reaction of ω-bromoacetophenone with α-picoline[14]
abscissa; the present system
The numbers refer to the Table 1.

As far as the activation entropy is concerned, there seem to be two series of solvents, each grouped around a line; it follows that there exist two negative isokinetic temperatures with regard to the solvent variations. The accuracy of our measurements may be discerned by the nearly complete correlation with a slope greater than unity (Fig. 2). As will be described in the next discussion, the activation volumes of the present reaction show the largest sensitivity to environmental changes. Therefore, the above observation on the activation entropies is in contrast to the behavior of the activation volumes.

Up till now, as for the Menschutkin reaction four systems have been reported in connection with the systematic studies of the solvent effects on their reaction rates under high pressure.[2,12–15] These results are plotted against those of the present system in Fig. 3. It should be noted that over a fairly wide range of rate constants there are very good correlations among them.

The slope of the plot serves as a measure of the sensitivity of the relevant system to the environmental change.

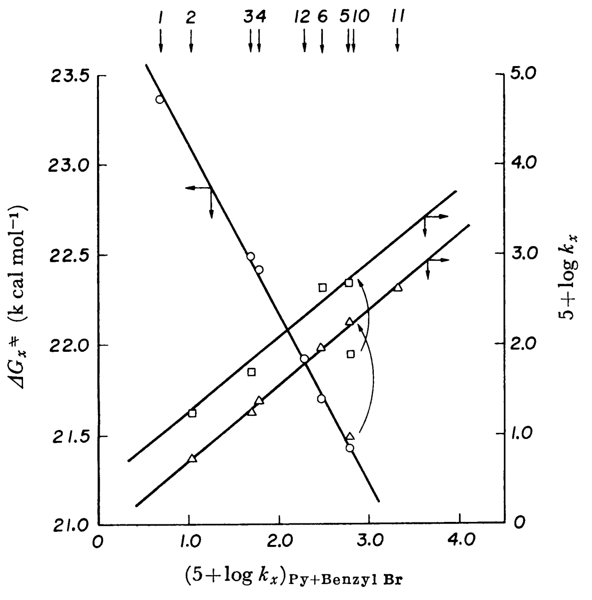

Fig. 3. The linear free energy relationships for the Menschutkin reactions in various solvents.
ordinate, ○; ω-Bromoacetophenone+α-Picoline[14]
△; MeI+Pyridine[13]
□; EtI+Et$_3$N by the present authors
abscissa; the present system
The numbers refer to the Table 1.

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[12] M. G. Gonikberg and B. S. EL'yanov, *Dokl. Akad. Nauk SSSR*, **138**, 1103 (1961).

[13] H. Hartmann, H. Kelm, and G. Rink, *Z. Phys. Chem.*, (Frankfurt), **44**, 335 (1965).

[14] H. Heydtmann, A. P. Schmidt, and H. Hartmann, *Ber. Bunsenges. Phys. Chem.*, **70**, 444 (1966).

[15] H. Hartmann, H. D. Brauer, H. Kelm, and G. Rink, *Z. Phys. Chem.*, (Frankfurt), **61**, 53 (1968).

TABLE 2. COMPARISONS OF TWO TYPES OF SLOPES

	$\Delta\log k/(\Delta\log k)_{\text{Benzyl Br+Py}}$	$(z\cdot\Delta P)[\text{kg}\cdot\text{cm}^{-2}]$
Benzyl bromide + Pyridine	1.0	3.45×10^3
Ethyl iodide + Triethylamine	0.84	2.6×10^3
Methyl iodide + Pyridine	0.82	2.6×10^3
ω-Bromoacetophenone + α-Picoline	0.68	1.9×10^3

In our previous papers, the activation volume has been reported to have a linear relation with the product of the compressibility and the molar volume of the solvent, KV^0. According to our model, the slope of the plot should give the value of $(z\cdot\Delta P)$, which is supposed to act as a measure of sensitivity to the solvent variation, as may partly be inferred from the observations in Fig. 1. These two types of slopes, *i.e.*, the slopes of the plots of Figs. 3 and 4, are collected in Table 2 (the listed values of $(z\cdot\Delta P)$ indicate the least-squared values as calculated by means of Eq. (12)).

Based on the values of Table 2, it would be possible to classify the systems into three groups—(pyridine+benzyl bromide), (Et_3N+EtI and pyridine+MeI), and (α-picoline+ω-bromoacetophenone). The sensitivity difference between the first two groups may be ascribed to the nature of the benzyl bromide, since the C–Br bond of the bromide is expected to be more labile than that of the aliphatic halides, and, as a result, all the reacting systems, *i.e.*, both the reactants and the activated complex, will be more sensitive to the environmental change. On the contrary, the difference between the last two groups may be understood by taking into account the steric hindrance due to both α-methyl and carbonyl groups to solvation at the cationic center.

Another interesting feature shown by Fig. 3 is that the rate constants in methanol show a marked deviation from the correlating lines. This deviation should be ascribed to the extra acceleration of the pyridine-benzyl bromide system by methanol compared to that of the aliphatic alkyl iodide systems, as can partly be anticipated from the fact that the benzyl bromide solvolyses fairly easily in methanol compared to the other halides shown in Table 2.

In another respect, this effect may be responsible for the discrepancy pointed out by Heydtmann and Buttner[16] that, for benzyl bromide, the rate constants in ethanol-benzene mixtures satisfy the Kirkwood relationship, whereas for the reaction of methyl iodide with pyridine in the same mixture, they do not.

Glew and Moelwyn-Hughes studied the base-catalyzed and uncatalyzed hydrolyses of methyl halides in water and found that the activation energies for the latter process are greater by *ca.* 3.5 (kcal·mol⁻¹) than those of the former.[17,18] The situation is quite similar to the present case. However, the absolute magnitudes of the activation parameters are not particularly helpful in leading to a conclusion as to the type of mechanism.

A linear relation between $\Delta S^{\ne}$ and $\Delta V^{\ne}$ has been observed by Laidler *et al.* for miscellaneous reactions in aqueous solvent,[19,20] and has been supposed to be evidence for the electrostriction theory. For the present case and the other quaternization reactions, no simple relations between the two quantities could be observed. This fact is not unexpected from the figures described above.

As can partly be inferred from the above discussion, these facts suggest that the major factors which give rise to perturbations on the activation entropy are not necessarily the same as those influencing the activation volumes, especially for the Menschutkin reaction.

Activation Volumes and Its Pressure Dependence. In a previous publication,[2] an equation which is helpful for correlating the activation volume with the solvent characteristics has been developed. In discussing the pressure dependence of the activation volumes, a slight modification is necessary.

Based on a concept similar to that used in the previous publication,[2] the total volume, V_t, of a solution composed of N moles of the pure solvents and n moles of the solute at a certain pressure, P, would be given by:

$$V_t = (N-nz)V_p{}^0 + nV_s + nzV' \tag{8}$$

where $V_p{}^0$, V_s, V', and z are the molar volumes of a pure solvent, of a pure solute and of a solvated solvent, and the solvation number of the solute, respectively.

In this case, the partial molar volume of the solute, $V_s{}^0$, is given by:

$$\bar{V}_s{}^0 = (\partial V_t/\partial n)_N = V_s + z(V'-V_p{}^0) \tag{9}$$

As for the Menschutkin reaction, it has been suggested that the polarity of the activated complex is considerably larger than those of the reactants,[3,14] and that the change in the activation volume by solvents is mainly controlled by the interaction between the activated complex and solvent molecules.[14]

On the basis of these facts, the activation volume at an external pressure P, $\Delta V_p{}^{\ne}$, would be given by this equation, applying Eq. (9) only to an activated complex:[1]

$$\begin{aligned}\Delta V_p{}^{\ne} &= (\bar{V}_{\ne}{}^0-(\bar{V}_a{}^0+\bar{V}_b{}^0))\\ &= (V_{\ne}-(\bar{V}_a{}^0+\bar{V}_b{}^0)) + z(V'-V_p{}^0)\end{aligned} \tag{10}$$

Using the definition of the compressibility of the solvent, the activation volume at zero external pressure, $\Delta V_0{}^{\ne}$, is expressed as follows:

$$K = -\frac{1}{V}(\partial V/\partial P)_{\mathrm{T}} \tag{11}$$

$$\Delta V_0{}^{\ne} = (V^{\ne}-(\bar{V}_a{}^0+\bar{V}_b{}^0)) - (z\cdot\Delta P)KV^0 \tag{12}$$

where V^0 and ΔP stand for the molar volume of a pure solvent and the difference between the average pressure in the cosphere of the activated complex and

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[16] H. Heydtmann and D. Buttner, *ibid.*, **63**, 39 (1969).

[17] E. A. Moelwyn-Hughes, *Proc. Roy. Soc. Ser. A*, **164**, 295 (1938).

[18] D. N. Glew and E. A. Moelwyn-Hughes, *ibid.*, **211**, 254 (1952).

[19] D. Chen and K. J. Laidler, *Trans. Faraday Soc.*, **54**, 1026 (1958).

[20] K. J. Laidler and R. Martin, *Int. J. Chem. Kinet.*, **1**, 113 (1969).

the atmosphere.

As for the pressure dependence of $\Delta V^{\ddagger}$, by the differentiation of Eq. (10) with respect to a pressure:

$$(\partial \Delta V^{\ddagger}/\partial P) = (\partial/\partial P)\{V_{\ddagger} - (\bar{V}_a{}^0 + \bar{V}_b{}^0) + zV'\} - z(\partial V_p{}^0/\partial P) \qquad (13)$$

Since, for the discussions of the solvent dependence of the activation volume and its pressure derivative, the first term of Eq. (13) would be taken as a constant, the pressure derivative of the activation volume at zero external pressure, $(\partial \Delta V^{\ddagger}/\partial P)_0$, is given by:

$$(\partial \Delta V^{\ddagger}/\partial P)_0 = \text{const.} + zKV^0 \qquad (14)$$

By the cancellation of the KV^0 term from Eqs. (12) and (14):

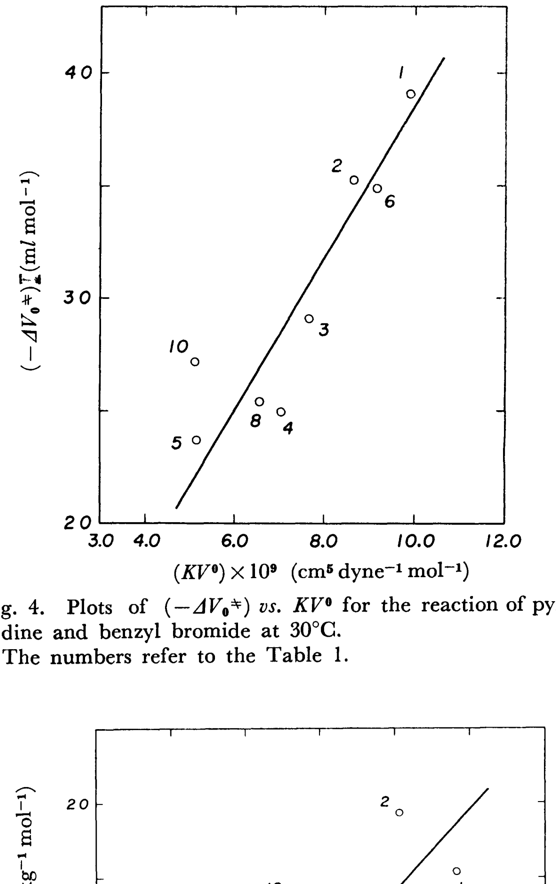

Fig. 4. Plots of $(-\Delta V_0{}^{\ddagger})$ *vs.* KV^0 for the reaction of pyridine and benzyl bromide at 30°C.
The numbers refer to the Table 1.

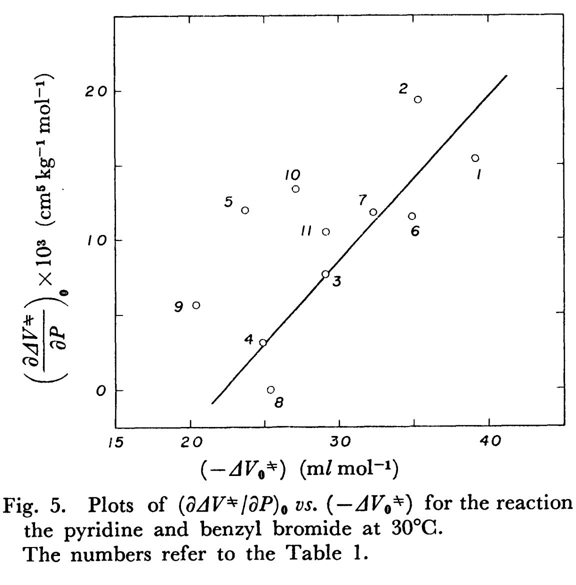

Fig. 5. Plots of $(\partial \Delta V^{\ddagger}/\partial P)_0$ *vs.* $(-\Delta V_0{}^{\ddagger})$ for the reaction of the pyridine and benzyl bromide at 30°C.
The numbers refer to the Table 1.

$$(\partial \Delta V^{\ddagger}/\partial P)_0 = \text{const.} + (1/\Delta P)(-\Delta V_0{}^{\ddagger}) \qquad (15)$$

Two types of plots, *i.e.*, Eqs. (12) and (15), are shown in Figs. 4 and 5. In Fig. 5, the regression line is drawn with the exception of three solvents-*i.e.*, nitrobenzene methanol, and 2-propanol, which show larger deviations than would be expected from the experimental errors.

From these slopes, the solvation number of the activated complex is estimated to be *ca.* 4 (*i.e.*, $(z\cdot\Delta P)/\Delta P = (3.8\times10^3)/(9.1\times10^2) \doteqdot 4$), and the average pressure within the cosphere of the activated complex, to be 9.1×10^2 (kg·cm^{-2}).

Although it is difficult to estimate the uncertainties to be associated with those values, at least three factors should be taken into account in doing so.

First, the fundamental ideas on the reaction systems are based on the discrete model, which might give only a qualitative description of the reaction system. Further, the linear assumptions used in deriving these equations would be the second factor restricting the conclusions reached. Finally, for evaluating the solvation number in the transition state, it is necessary to calculate the second derivatives of the rate constant with respect to the pressure.

Linear relations have been found between ΔV^0 and $(\partial \Delta V^0/\partial P)$ for the dissociation of weak acids in water.[21,22] These slopes correspond to *ca.* 4.7×10^3 (kg·cm^{-2}). Similar values have been estimated for the ionization in water by a different procedure.[23]

According to our model, these values indicate the effective pressures in the vicinity of the ion. A comparison of the two slopes is quite interesting, leading to the view that the charge development in the transition state of the Menschutkin reaction is about one-fifth of the ionization reaction.

As has been described above, the reference works were carried out in aqueous solvents,[19–23] while the present works were done in non-aqueous solvents. Many recent works have clearly shown the marked differences in solvent characteristics between aqueous and non-aqueous solvents. Some uncertainties might be introduced into the above conclusion as a result of having avoided the factor in our model.[24]

Although qualitative, the above estimation of the charge development in the transition state is not unexpected, for the transition state has been suggested to be not so highly ionic as quaternary ammonium halides.[25] The incomplete charge development in the transition state might be responsible for the lack of linear relationships between $\Delta S^{\ddagger}$ and $\Delta V_0{}^{\ddagger}$ for the present reaction.

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[21] D. A. Lown, H. R. Thirsh, and Lord Wynne-Jones, *Trans. Faraday Soc.*, **64**, 2073 (1968).

[22] D. A. Lown, H. R. Thirsh, and Lord Wynne-Jones, *ibid.*, **66**, 51 (1970).

[23] L. G. Hepler, *J. Phys. Chem.*, **69**, 965 (1965).

[24] The authors wish to express their gratitude to the referee for his helpful discussions.

[25] K. E. Weale, "Chemical Reactions at High Pressures," E. & F. N. Spon., London (1967).