

學位申請論文

井上久幸

主論文 1

新制

理

3 39 函

THE REACTION OF NITRILE WITH  $\alpha$ -HYDROGENS AT HIGH PRESSURE II  
PRESSURE EFFECTS ON THE IMINOETHER FORMATION AND DEUTERIUM-  
HYDROGEN EXCHANGE REACTION OF PHENYLACETONITRILE IN  
METHANOL

By HISAYUKI INOUE

*Reprinted from* The Review of Physical Chemistry of Japan

Vol. 48, No. 2 *Published* February 10, 1978

## THE REACTION OF NITRILE WITH $\alpha$ -HYDROGENS AT HIGH PRESSURE II PRESSURE EFFECTS ON THE IMINOETHER FORMATION AND DEUTERIUM- HYDROGEN EXCHANGE REACTION OF PHENYLACETONITRILE IN METHANOL

BY HISAYUKI INOUE

The rates of the nucleophilic attack of methoxide ion to phenylacetonitrile in methanol were studied at high pressure. The attack resulted in two different types of reactions, one being the elimination of  $\alpha$ -hydrogens while the other the base-catalyzed methanol addition to  $C\equiv N$  triple bond. Positive ( $+24\text{cm}^3\text{mol}^{-1}$  at 303.2K) and negative ( $-13.1\text{cm}^3\text{mol}^{-1}$  at 313.2K) activation volume changes were observed for the deuterium elimination and the nucleophilic attack of methoxide ion to  $C\equiv N$  triple bond, respectively. An expression which permits the distinction between the electrostatic volume change and the covalent volume change has been derived from a perturbed molecular-orbital theory combined with the Owen-Brinkley formula. Validity of the expression has been tested for various types of high-pressure reactions including those here studied.

### Introduction

For the understanding of chemical dynamics in solution the interaction of solute with surroundings has to be unavoidably taken into account. The features of this interaction are informed by the knowledge of the effects of the surrounding conditions, such as solvent polarity, temperature and/or pressure on the thermodynamic activation parameter. In particular, the activation volume change which can be estimated from the pressure effect is well known to reflect the reaction coordinate from the viewpoint of the geometry change as well as the solvation change. However, such a macroscopic parameter often fails to account for relative reactivities of a molecule at different reaction sites; for example, the difference in reactivity of *meta*- and *para*- positions could not be explained successfully by considering only a single parameter. The molecular-orbital treatment has, on the other hand, succeeded in interpreting this kind of reactivity semiquantitatively, though the theoretically-derived reactivity indices do not incorporate the effect of the medium. In this paper the author has tried to derive a formula, which is generally applicable to the variation in reaction rate constants with pressure. Klopman's perturbation theory<sup>1)</sup> has been used, in which the charge density and the charge transfer between reacting sites are considered together with the solvation of charged atoms. The derived formula has been applied to several reactions which were studied by other researchers. The

---

(Received August 29, 1978)

1) G.Klopman, *J. Am. Chem. Soc.*, **90**, 223 (1968)

nucleophilic reaction of methoxide ion to phenylacetonitrile, which involves the elimination of an  $\alpha$ -hydrogen and the methoxide addition to the  $C\equiv N$  triple bond, has also been tested.

### Experimental and Dielectric Constant at High Pressure

Phenylacetonitrile was distilled twice at reduced pressure of nitrogen atmosphere. Methyl phenylacetiminoether was prepared by the neutralization of methyl phenylacetiminoether hydrochloride which was synthesized according to Pinner's method<sup>2)</sup> at 263K in order to prevent the "Pinner Cleavage." The mixture was extracted with carbon tetrachloride, and the extract was distilled twice at reduced pressure of nitrogen atmosphere. Phenylacetonitrile- $d_2$  was prepared by the base-catalyzed hydrogen-deuterium exchange in methanol- $d_4$ . Methanol and triethylamine were purified in the same way as reported before<sup>3)</sup>. The concentration of methoxide ion was determined by measuring the electrical conductivity, the way of which has an advantage to be able to correct the influence of carbon dioxide<sup>3)</sup>. The elimination reaction could be easily quenched by blowing the carbon dioxide into the reaction mixture. At atmospheric pressure, the amine-catalyzed iminoether formation is too late to lead to serious errors during the evaporation of the solvent. The high-pressure generating systems and the reaction cell were reported elsewhere<sup>4)</sup>. The yield of each product was determined from the NMR peak areas corresponding to the methylene protons.

The dielectric constants of pure liquids at high pressure were calculated by means of the Owen-Brinkley expression:<sup>5)</sup>  $1 - D^{(1)}/D^{(P)} = A \ln(B+P)/(B+1)$ , where  $D^{(1)}$  and  $D^{(P)}$  are the dielectric constant at 1 and  $P$  kg  $cm^{-2}$ , respectively, and  $A$  and  $B$  are empirical constants<sup>6)</sup>.

## Results and Discussion

### Iminoether formation

Although phenylacetonitrile remained unreacted in methanol at pressure up to 7000 kg/ $cm^2$  and 343K for 7h, the addition of triethylamine produced methyl phenylacetiminoether. It has been reported that in the presence of alkoxide ion nitriles convert partially to iminoether even at atmospheric pressure<sup>7)</sup>. Thus the apparent amine-catalysis in methanol at high pressure is considered to be due to the promoted production of methoxide ion by proton transfer. The reaction scheme is represented as follows:

---

\*1atm = 1.033 kg  $cm^{-2}$  =  $1.013 \times 10^5$  pa, 1cal = 4.184J

2) A. Pinner, "Die Imidoäther und ihre Derivate," Oppenheim, Berlin (1892)

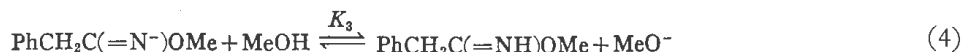
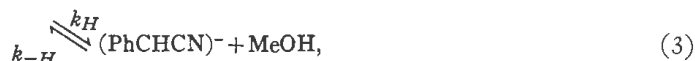
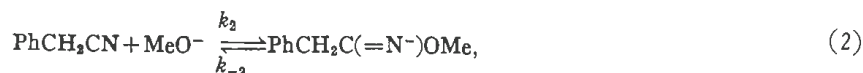
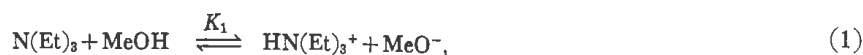
3) H. Inoue, K. Hara, and J. Osugi, *This Journal*, **48**, 44 (1978)

4) H. Inoue, K. Hara, and J. Osugi, *This Journal*, **46**, 64 (1976)

5) B.B. Owen and S.R. Brinkley, *Phys. Rev.*, **64**, 32 (1943)

6) K.R. Srinivasan and R.L. Kay, *J. Solution Chem.*, **4**, 299 (1975);

H. Hartmann, A. Neumann, and G. Rinck, *Z. Phys. Chem., Neue Folge* **44**, 204, 218 (1965); L.G. Schornack and C.A. Eckert, *J. Phys. Chem.*, **74**, 3014 (1970); E. Schadow and R. Steiner, *Z. Phys. Chem., Neue Folge* **66**, 105 (1969)



The ionic dissociation constants of triethylamine in methanol at high pressure were estimated by extrapolating the values which were determined from the measurements of electrical conductivities<sup>3)</sup>.

Time dependence of the formation of methyl phenylacetiminoether is shown in Figs. 1 and 2. The base-catalyzed hydrogen exchange (3) was confirmed by using  $\text{MeOH-}d_1$  as the solvent. For some nitriles such a base-catalyzed  $\alpha$ -proton transfer in methanol has also been reported<sup>8)</sup>. The proton

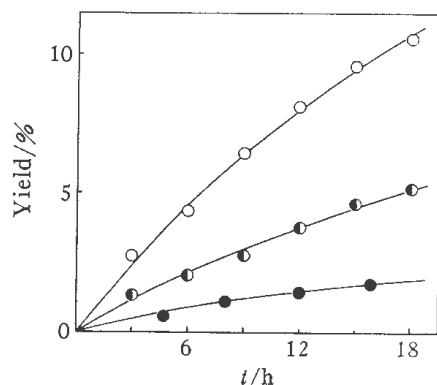


Fig. 1 Time dependence of the yield of  $\text{PhCH}_2\text{C(=NH)OMe}$  in  $\text{MeOH}$  at 323.2K

$[\text{PhCH}_2\text{CN}]_0 = 0.05 \text{ mol/kg}$ ,

$[\text{N(Et)}_3] = 0.25 \text{ mol/kg}$

●: 1000  $\text{kg/cm}^2$ , ◐: 2000  $\text{kg/cm}^2$ ,

○: 3000  $\text{kg/cm}^2$

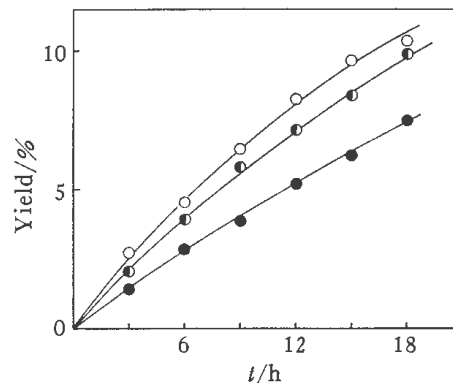


Fig. 2 Time dependence of the yield of  $\text{PhCH}_2\text{C(=NH)OMe}$  in  $\text{MeOH}$  at 3000  $\text{kg/cm}^2$

$[\text{PhCH}_2\text{CN}]_0 = 0.05 \text{ mol/kg}$ ,

$[\text{N(Et)}_3] = 0.25 \text{ mol/kg}$

●: 313.2K, ◐: 318.2K, ○: 323.2K

transfer(3) is fast as compared with the iminoether formation(2), the relaxation time being several minutes under our experimental condition. Therefore, step(3) can be regarded to be in equilibrium during the course of the iminoether formation, maintaining the relationship  $[\text{PhCH}_2\text{CN}] \gg [(\text{PhCHCN})^-]$ <sup>9, 10)</sup>.

By applying the steady-state assumption to  $\text{PhCH}_2\text{C(=N}^-\text{)OMe}$ , the iminoether formation can be expressed as a function of time:

7) F.G. Schaefer and G.A. Peters, *J. Org. Chem.*, **26**, 412 (1961)

8) For example, N.-Å. Bergman and I. Källson, *Acta Chem. Scand.*, **A30**, 421 (1976); *ibid.*, **A30**, 411 (1976); R. Stewart, J.P. O'Donnell, D.J. Cram, and B. Rickborn, *Tetrahedron* **18**, 917 (1962); D.J. Cram, C.A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 3688 (1961)

9) J.R. Jones, "Progress in Physical Organic Chemistry," Wiley, **9**, 241 (1972)

10) It has been reported that *p*-nitrophenylacetonitrile gave pink solution,  $\lambda_{\text{max}} = 530 \text{ nm}$  and  $\epsilon = 2.87 \times 10^4$ , in  $\text{MeO}^-$ - $\text{MeOH}$ . See, for example, R.A. More O'Ferrall and J.H. Ridd, *J. Chem. Soc.*, **1963**, 5030. The absorbance of  $(\text{PhCHCN})^-$  was not observed from 290 to 800 nm within experimental error.

$$\ln \frac{X_e}{X_e - X} = (k_2' + k_{-2}')t, \quad (5)$$

where  $k_2' = k_2[\text{MeO}^-]$  and  $k_{-2}' = k_{-2}K_3^{-1}[\text{MeO}^-]$  are the pseudo-first order rate constants,  $X$  the molar concentration of iminoether at time  $t$ , and  $X_e$  its equilibrium value. In order to obtain the value of  $X_e$ , the mixture of the components whose concentration was approximately estimated from the intercept of the Guggenheim plot was kept at each pressure for a sufficiently long time. The exact equilibrium concentrations determined are listed in Table 1. Plots of  $\ln[X_e/(X_e - X)]$  against  $t$  gave a satisfactory straight line at each pressure. Table 2 shows the values of the ionic dissociation constants of triethylamine and the rate constants of iminoether formation.

Table 1 Equilibrium conversion (%)\* of  $\text{PhCH}_2\text{CN}$  to  $\text{PhCH}_2\text{C}(=\text{NH})\text{OMe}^{**}$

| $P/\text{kg cm}^{-2}$ | $T/\text{K}$ |       |       |
|-----------------------|--------------|-------|-------|
|                       | 323.2        | 318.2 | 313.2 |
| 1                     | 5.2          | 5.2   | 5.5   |
| 1000                  | 8.3          | 8.6   | 9.5   |
| 2000                  | 13.7         | 14.2  | 15.0  |
| 3000                  | 18.8         | 22.4  | 23.2  |

\* Theoretical yield based on  $\text{PhCH}_2\text{CN}$

\*\* Reaction time, 72–96h

Table 2 The values of  $K_1$ ,  $k_2$ , and  $k_{-2}K_3^{-1}$  at high pressures

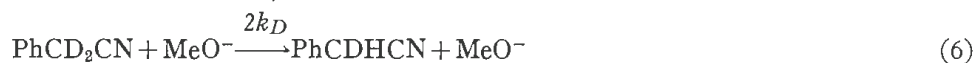
| $P/\text{kg cm}^{-2}$ | $T/\text{K}$        |                     |                                |                   |                   |                              |                   |                   |                              |
|-----------------------|---------------------|---------------------|--------------------------------|-------------------|-------------------|------------------------------|-------------------|-------------------|------------------------------|
|                       | 323.2               |                     |                                | 318.2             |                   |                              | 313.2             |                   |                              |
|                       | $K_1 \times 10^6^*$ | $k_2 \times 10^3^*$ | $k_{-2}K_3^{-1} \times 10^3^*$ | $K_1 \times 10^6$ | $k_2 \times 10^3$ | $k_{-2}K_3^{-1} \times 10^3$ | $K_1 \times 10^6$ | $k_2 \times 10^3$ | $k_{-2}K_3^{-1} \times 10^3$ |
| 1                     | 0.26                | 0.43                | 7.9                            | 0.23              | 0.32              | 5.8                          | 0.21              | 0.24              | 4.1                          |
| 1000                  | 1.4                 | 0.67                | 7.3                            | 1.3               | 0.51              | 5.4                          | 1.3               | 0.36              | 3.4                          |
| 2000                  | 5.2                 | 1.0                 | 6.3                            | 5.0               | 0.78              | 4.7                          | 5.0               | 0.55              | 3.1                          |
| 3000                  | 16                  | 1.4                 | 5.5                            | 16                | 1.2               | 4.2                          | 17                | 0.78              | 2.6                          |

\*  $K_1/\text{mol kg}^{-1}$ ,  $k_2/\text{kg mol}^{-1}\text{s}^{-1}$

### Deuterium-Hydrogen Exchange

The pressure effect on the nucleophilic attack to  $\alpha$ -hydrogens was estimated for phenylacetone-trile- $d_2$  in methanol, because the reaction of phenylacetone-trile in  $\text{MeO}^-$ - $\text{MeOH}$ - $d_1$  was too fast to be followed at high pressure. The rate equations of the deuterium-hydrogen exchange are derived from

the simplified reaction scheme;



Since the deuterium-hydrogen exchange is very fast in comparison with the iminoether formation, the term of iminoether formation can be neglected. Hence, we can write

$$-\frac{d[\text{PhCD}_2\text{CN}]}{dt} = 2k_D[\text{PhCD}_2\text{CN}][\text{MeO}^-] = 2k_D'[\text{PhCD}_2\text{CN}] \quad (8)$$

$$\begin{aligned} \frac{d[\text{PhCDHCN}]}{dt} &= 2k_D[\text{PhCD}_2\text{CN}][\text{MeO}^-] - k_D[\text{PhCDHCN}][\text{MeO}^-] \\ &= 2k_D'[\text{PhCD}_2\text{CN}] - k_D'[\text{PhCDHCN}] \end{aligned} \quad (9)$$

$$\frac{d[\text{PhCH}_2\text{CN}]}{dt} = k_D[\text{PhCDHCN}][\text{MeO}^-] = k_D'[\text{PhCDHCN}] \quad (10)$$

From Eqs. (8), (9), and (10), we obtain upon integration the following equation:

$$\frac{2[\text{PhCH}_2\text{CN}] + [\text{PhCDHCN}]}{2a} - 1 = \left( \frac{2[\text{PhCH}_2\text{CN}]_0 + [\text{PhCDHCN}]_0}{2a} - 1 \right) \times \exp(-k_D't), \quad (11)$$

where  $a = [\text{PhCD}_2\text{CN}]_0 + [\text{PhCDHCN}]_0 + [\text{PhCH}_2\text{CN}]_0$ , the subscript 0 refers to the initial concentration, and  $(2[\text{PhCH}_2\text{CN}] + [\text{PhCDHCN}])/2a$  is the quantity measured from the NMR spectral intensity. Plots of  $\ln[1 - (2[\text{PhCH}_2\text{CN}] + [\text{PhCDHCN}])/2a]$  against  $t$  seem to give a straight line, and the rates of the deuterium-hydrogen exchange was found to decrease with pressure, as is shown in Fig. 3 and Table 3.

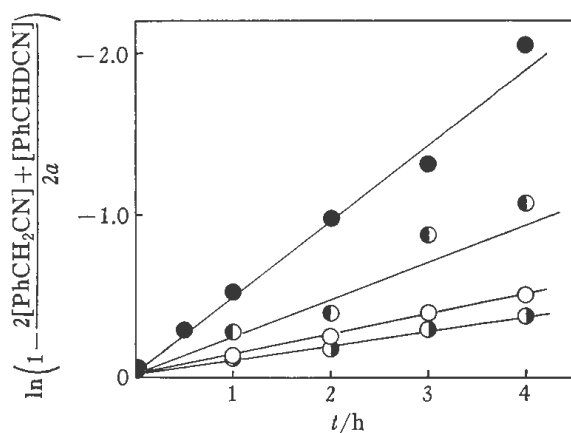


Fig. 3 Deuterium-hydrogen exchange of  $\text{PhCD}_2\text{CN}$  in  $\text{MeO}-\text{MeOH}$  at 303.2 K

$[\text{PhCD}_2\text{CN}] \cong 0.07 \text{ mol/kg}$ ,  
 $[\text{MeOK}] = 0.31 \times 10^{-4} \text{ mol/kg}$   
 ●: 1 atm, ◐: 1000  $\text{kg/cm}^2$ ,  
 ○: 2000  $\text{kg/cm}^2$ , ●: 3000  $\text{kg/cm}^2$

Table 3 Rate constants of deuterium-hydrogen exchange at 303.2 K

| $P/\text{kg cm}^{-2}$ | $k_D/\text{kg mol}^{-1}\text{s}^{-1}$ |
|-----------------------|---------------------------------------|
| 1                     | 4.0                                   |
| 1000                  | 2.0                                   |
| 2000                  | 1.2                                   |
| 3000                  | 0.9                                   |

### Pressure dependence of the rate constants based on the perturbation theory

The molecular orbital theory has proved useful in explaining the relative reactivities of various reaction sites of organic compounds. The perturbation method has been especially successful, though its application is limited only to an early stage of the reaction. The energy contributions to the interaction energy can be divided into several terms including Coulomb ( $E_Q$ ), exchange-repulsion ( $E_K$ ), induction ( $E_I$ ), and charge-transfer ( $E_{CT}$ ) energies<sup>11</sup>.

Klopman has introduced a simple perturbation theory taking account of only the Coulombic and electron-transfer effects in sophisticated solvent<sup>1,12</sup>. The interaction energy was roughly estimated from the solvation energy change produced by the partial electron transfer, neglecting the overlap integrals between the interacting orbitals, and the energy change due to the non-reactive sites:

$$\Delta G \sim q_r q_s F / D + \sum_m^{occ} \sum_n^{un} 2(C_r^m C_s^n \beta)^2 / (E_m^* - E_n^*), \quad (12)$$

where  $q_r$  is the initial net charge of atom  $r$ ,  $F$  a Coulombic intensity factor for the interaction between  $r$  and  $s$ ,  $D$  a polarity parameter of the solvent,  $E_m^*$  and  $E_n^*$  the energies of the respective molecular orbitals  $m$  and  $n$  of molecules  $R$  and  $S$  under interaction in the medium. The second term of the right-hand side can be approximated by considering only the frontier orbitals<sup>13</sup>:

$$\Delta G \sim q_r q_s F / D + 2(C_r^{HOMO} C_s^{LUMO} \beta)^2 / (E_{HOMO}^* - E_{LUMO}^*) \quad (13)$$

where *HOMO* and *LUMO* represent the highest occupied and the lowest unoccupied molecular orbitals, respectively. Since the first term of the right-hand side of Eq. (13) expresses a rather long range energy where electron transfer does not occur,  $D$  is approximately considered to be a macroscopic dielectric constant of the medium. On the other hand, the solvent parameter involved in  $E_m^*$  and  $E_n^*$  should be a function of a local dielectric constant because the second term represents the energy due to the partial charge transfer in the vicinity of the sophisticated solvent molecules.

Assuming that only  $D$  and  $E^*$  are pressure dependent, we can derive from Eq. (13) the following relationship:

$$\begin{aligned} \Delta G^{(P)} - \Delta G^{(1)} = & q_r q_s F (1/D^{(P)} - 1/D^{(1)}) + 2(C_r^{HOMO} C_s^{LUMO} \beta)^2 \times \\ & [1/(E_{HOMO}^{*(P)} - E_{LUMO}^{*(P)}) - 1/(E_{HOMO}^{*(1)} - E_{LUMO}^{*(1)})]. \end{aligned} \quad (14)$$

The first term of the right-hand side is analogous to that of Born's solvation theory if  $q_r$  and  $q_s$  are the integral charge and  $F$  is the function of reciprocal of distance. Following Nakahara's derivation in the case of the ionization equilibrium, it can be expressed as follows<sup>14</sup>:

$$q_r q_s F (1/D^{(P)} - 1/D^{(1)}) = \Delta V_{elect}^{(1)} (B+1) \ln(B+P) / (B+1), \quad (15)$$

where  $\Delta V_{elect}^{(1)}$  refers to the electrostatic volume change at 1 atm and  $B$  is an empirical parameter in the Owen-Brinkley expression. The difference of energy levels can be expanded as a power series

- 
- 11) J.N. Murrell, M. Randić, and D.R. Williams, *Proc. Roy. Soc., Ser. A* **284**, 566 (1965); T. Fueno, S. Nagase, K. Tatsumi, and K. Yamaguchi, *Theor. Chim. Acta*, **26**, 43 (1972); K. Fukui and H. Fujimoto, *Bull. Chem. Soc. Jpn.*, **41**, 1989 (1968)
  - 12) G. Klopman, *Chem. Phys. Letters*, **1**, 200 (1967); G. Klopman and R.F. Hudson, *Theor. Chim. Acta*, **8**, 165 (1967)
  - 13) K. Fukui, T. Yonezawa, and H. Shingu, *J. Chem. Phys.*, **20**, 722 (1952); **22**, 1433 (1954)
  - 14) M. Nakahara, *This Journal* **44**, 57 (1974)

of pressure,

$$E^*_{HOMO}^{(P)} - E^*_{LUMO}^{(P)} = E^*_{HOMO}^{(1)} - E^*_{LUMO}^{(1)} + (\partial(E^*_{HOMO} - E^*_{LUMO})/\partial P)_{P=1,T}(P-1) + \dots \quad (16)$$

Equation(16) could well be truncated by the term of the first order in  $(P-1)$  if the operational pressure is low, and/or if the function of the local dielectric constant of the solvated molecules has a very small pressure dependence.\*)

From Eqs. (14), (15), and (16), we obtain

$$\Delta G^{(P)} - \Delta G^{(1)} = \Delta V_{elect}^{(1)}(B+1)\ln[(B+P)/(B+1)] + \Delta V_{cov}^{(1)}(P-1), \quad (17)$$

where  $\Delta V_{cov}^{(1)}$  is the volume change at 1 atm for the structural change due to the formation of covalent bond and the desolvation change due to the partial electron transfer. It can be expressed as

$$\Delta V_{cov}^{(1)} \cong - \left[ \frac{\sqrt{2}(C_r^{HOMO} C_s^{LUMO} \beta)}{E^*_{HOMO}^{(1)} - E^*_{LUMO}^{(1)}} \right]^2 \left( \frac{\partial(E^*_{HOMO} - E^*_{LUMO})}{\partial P} \right)_{P=1,T} \quad (18)$$

If Eq. (17) can be expanded and applied to the transition states as such, the pressure dependence of the rate constant may be expressed as follows:

$$-RT \ln(k^{(P)}/k^{(1)}) = \Delta V_{elect}^{\ddagger(1)}(B+1)\ln[(B+P)/(B+1)] + \Delta V_{cov}^{\ddagger(1)}(P-1). \quad (19)$$

Thus the pressure dependence of the rate constant can be predicted qualitatively from the knowledges on the electronic properties of the isolated reactant molecules. When the difference between  $E^*_{HOMO}$  and  $E^*_{LUMO}$  is large, the pressure dependence of  $\ln(k^{(P)}/k^{(1)})$  should show a curvature such as calculated from the Owen-Brinkley expression. On the other hand, when the frontier orbitals lie close, the contribution of the second term becomes appreciable. A formula starting from the Tait equation has never interpreted the linearity of the plot of  $\ln(k^{(P)}/k^{(1)})$  against pressure, while such a tendency has been found so often for the reactions of neutral or weakly polarized species.

Several points may be raised against the present theoretical treatment; a) molecular structure deformations with the progress of reaction were precluded, b) overlap integrals were neglected between the interacting orbitals, c) the solvation model is extremely crude, d) the value of  $\Delta V_{elect}^{\ddagger(1)}$  and  $\Delta V_{cov}^{\ddagger(1)}$  cannot be calculated directly from the molecular orbitals of isolated reactants, and so on. In spite of these deficiencies, we believe that Eq. (19) can shed light on the physical meaning of the pressure dependence of rate constants.

From the viewpoint of practical use, the validity of Eq. (19) has been confirmed by using the experimental results of various types of reactions. Plots of the experimental values<sup>15-18)</sup> for  $[-RT/(P-1)] \ln(k^{(P)}/k^{(1)})$  against  $[(B+1)/(P-1)] \ln[(B+P)/(B+1)]$  lie well on straight lines as shown in Fig. 4. The slope and intercept of the linearity are  $\Delta V_{elect}^{\ddagger(1)}$  and  $\Delta V_{cov}^{\ddagger(1)}$ , respectively. It should be noted that these activation volumes at 1 atm can be correctly estimated even when the data are available

\*)  $E_m^* = IP_m - q_s(C_r^m)^2 F/\epsilon - a^2[IP_m - EA_m + (C_r^m)^2(C_s^n)^2 F(2/\epsilon - 1)] - \frac{\sum_r \chi_r (C_r^m)^2 [q_r + 2b^2 \chi_r (C_r^m)^2]}{R_r} (1 - 1/\epsilon)$   
 $E_n^* = IP_n - [q_r + 2(C_r^m)^2](C_s^n)^2 F/\epsilon - b^2[IP_n - EA_n + (C_r^m)^2(C_s^n)^2 F(2/\epsilon - 1)] - \frac{\sum_s \chi_s (C_s^n)^2 [q_s - 2b^2 \chi_s (C_s^n)^2]}{R_s} (1 - 1/\epsilon)$

Here,  $\epsilon$  is the solvent parameter, and other various symbols have the same meanings as in lit. 1).

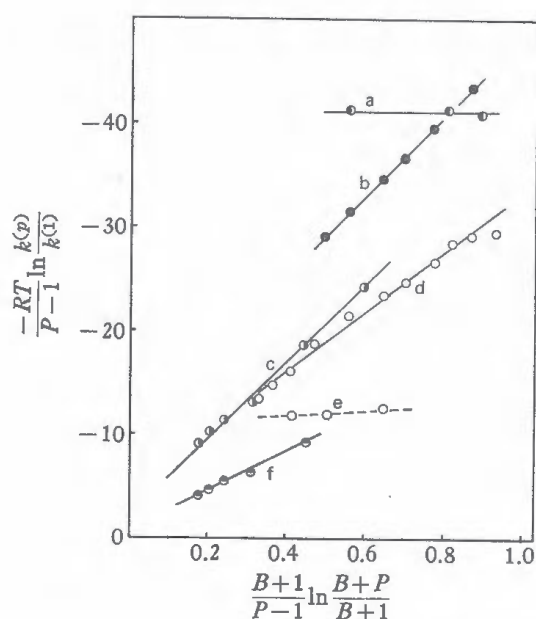


Fig. 4 Pressure dependence of the rate constants of various reactions

- a)  $n\text{-BuOCH=CH}_2 + \text{TCNE}$  in benzene<sup>15)</sup>
- b)  $n\text{-BuOCH=CH}_2 + \text{TCNE}$  in acetone<sup>15)</sup>
- c)  $\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2 + \text{CH}_3\text{I}$  in methanol<sup>16)</sup>
- d) cyclopentadiene + dimethyl acetylenedicarboxylate in ethyl acetate<sup>17)</sup>
- e)  $\text{PhCH}_2\text{CN} + \text{MeO}^-$  in methanol
- f)  $\text{CH}_3\text{Br} + \text{MeO}^-$  in methanol<sup>18)</sup>

only at high pressure. After all, the pressure dependence of the rate constant has been expressed adequately by dividing the activation volume into two terms,  $\Delta V_{\text{elect}}^{\ddagger(1)}$  and  $\Delta V_{\text{cov}}^{\ddagger(1)}$ , whose physical grounds could be clarified on a simple molecular-orbital interaction model. Starting from Born's solvation model, a similar expression was derived for the pressure dependence of the ionization constant<sup>3,14)</sup>. It has been reported that both the electrostrictive volume change and other volume changes (crystal volume, void volume, etc.) play important roles in the pressure effect on the ionization in methanol.

#### Activation volumes of iminoether formation and deuterium elimination

Activation volumes have been evaluated by applying Eq. (19) to the reactions of phenylacetonitrile in methanol. The results are summarized in Table 4. The covalent volume change plays an

Table 4 Activation volumes of iminoether formation and deuterium-hydrogen exchange at 1 atm

| $T/\text{K}$ | $B/\text{kg cm}^{-2}$ | $\Delta V_{\text{cov}}^{\ddagger(2)*}$ | $\Delta V_{\text{elect}}^{\ddagger(2)*}$ | $\Delta V_{\text{cov}}^{\ddagger(-2)} + \Delta V_{\text{cov}}^{\ddagger(-3)}$ | $\Delta V_{\text{elect}}^{\ddagger(-2)} + \Delta V_{\text{elect}}^{\ddagger(-3)}$ | $\Delta V_{\text{cov}}^{\ddagger(\text{D})}$ | $\Delta V_{\text{elect}}^{\ddagger(\text{D})}$ |
|--------------|-----------------------|----------------------------------------|------------------------------------------|-------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|----------------------------------------------|------------------------------------------------|
| 323.2        | 750                   | -10.1                                  | -3.0                                     | +4.1                                                                          | -2.2                                                                              |                                              |                                                |
| 318.2        | 780                   | -10.9                                  | -2.4                                     | +3.6                                                                          | -2.0                                                                              |                                              |                                                |
| 313.2        | 817                   | -10.2                                  | -1.0                                     | +4.1                                                                          | 0                                                                                 |                                              |                                                |
| 303.2        | 853                   |                                        |                                          |                                                                               |                                                                                   | $\sim +4$                                    | $\sim +20$                                     |

\*  $\Delta V/\text{cm}^3 \text{ mol}^{-1}$

important role in the case of the nucleophilic attack ( $k_2$ ) to the  $\text{C}\equiv\text{N}$  triple bond as expected. Both

15) F.K. Fleischmann and H. Kelm, *Tetrahedron Lett.*, **39**, 3773 (1973)

16) S.D. Hamann and D.R. Teplitzky, *Disc. Faraday Soc.*, **22**, 114 (1956)

17) R.A. Grieger and C.A. Eckert, *J. Am. Chem. Soc.*, **92**, 7149 (1970)

18) H.G. David and S.D. Hamann, *Trans. Faraday Soc.*, **50**, 1188 (1954)

$\Delta V_{elect}^{\ddagger(1)}$  and  $\Delta V_{cov}^{\ddagger(1)}$  for step (2) are negative, and the magnitude of  $\Delta V_{elect}^{\ddagger(1)}$  seems to indicate the fairly localized transition states. For the reverse process ( $k_{-2}K_3^{-1}$ ) of iminoether formation, the covalent term is found to be positive, while the electrostatic term, negative. Since  $k_{-2}$  represents the rate constant for the bond cleavage of ion, both  $\Delta V_{cov}^{\ddagger(1)}(-2)$  and  $\Delta V_{elect}^{\ddagger(1)}(-2)$  would be positive. If  $\text{PhCH}_2\text{C}(=\text{N}^-)\text{OMe}$  is assumed to have the most negative electrostrictive volume among those species in the course of the iminoether formation, the negative  $\Delta V_{elect}^{\ddagger(1)}(-2) + \Delta V_{elect}^{\ddagger(1)}(-3)$  can be understood; that is, the negative  $\Delta V_{elect}^{\ddagger(1)}(-2) + \Delta V_{elect}^{\ddagger(1)}(-3)$  comes mainly from the negative  $\Delta V_{elect}^{\ddagger(1)}(-3)$  term. Judging from the relative correlation of activation volumes, the transition state would be product-like, and the penetration of the van der Waals volumes between two reactants contribute largely to the volume contraction at the transition state for the iminoether formation.

Both  $\Delta V_{cov}^{\ddagger(1)}(\text{D})$  and  $\Delta V_{elect}^{\ddagger(1)}(\text{D})$  were positive for the deuterium-hydrogen exchange reaction. Since the large positive value of  $\Delta V_{elect}^{\ddagger(1)}(\text{D})$  reflects an extensive delocalization of the minus charge, the transition state of the deuterium-hydrogen exchange reaction is considered to be like a carbanion in which the  $\alpha$ -carbon is nearly in the  $\text{sp}^2$  structure. As  $\Delta V_{cov}^{\ddagger(1)}$  in Eq. (19) involves not only the structural volume change of reactants but also the desolvation term produced by the electron transfer, it is dangerous to explain  $\Delta V_{cov}^{\ddagger(1)}$  only in terms of the structural volume change. A small  $\Delta V_{cov}^{\ddagger(1)}(\text{D})$  value seems to indicate that a small amount of penetration of the van der Waals volume competes with the void volume change. The arguments delineated above can be represented diagrammatically by the volume profile as shown in Fig. 5. The enthalpy and entropy of activation

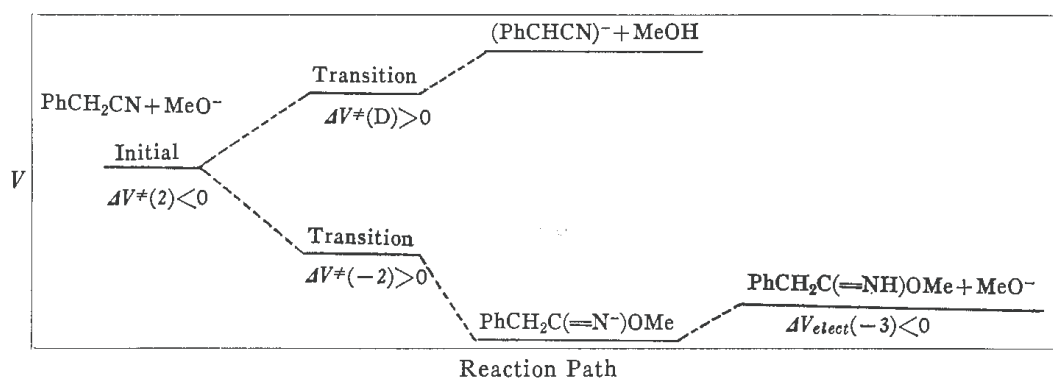


Fig. 5 Volume profile of the nucleophilic attack of methoxide ion to phenylacetonitrile

for the iminoether formation were determined to be  $\Delta H^{\ddagger} \sim 12 \text{ kcal/mol}$  and  $\Delta S^{\ddagger} \sim -5 \text{ e.u.}$  The activation free energy of the deuterium elimination reaction was not determined, but it would be small compared with the value of  $\Delta G_2^{\ddagger}$ .

### Acknowledgements

The author wishes to thank Prof. J. Osugi for his helpful suggestions, and is indebted to Dr. M. Sasaki, Dr.M. Ueno, and Dr. K. Hara for their advices during this work.

*Laboratory of Physical Chemistry  
Department of Chemistry  
Faculty of Science  
Kyoto University  
Kyoto 606  
Japan*

THE REACTION OF NITRILE WITH  $\alpha$ -HYDROGENS AT HIGH PRESSURE III  
PRESSURE EFFECTS ON THE RATES OF THE IMINOETHER FORMATION  
AND PROTON/DEUTERON TRANSFER REACTIONS OF SUBSTITUTED  
PHENYLACETONITRILES IN METHANOL

By HISAYUKI INOUE

*Reprinted from* The Review of Physical Chemistry of Japan

Vol. 49, No. 2 *Published* February 20, 1980

THE REACTION OF NITRILE WITH  $\alpha$ -HYDROGENS AT HIGH PRESSURE III  
PRESSURE EFFECTS ON THE RATES OF THE IMINOETHER FORMATION  
AND PROTON/DEUTERON TRANSFER REACTIONS OF SUBSTITUTED  
PHENYLACETONITRILES IN METHANOL

BY HISAYUKI INOUE

The rates of the addition of methoxide ion to the CN bond and the proton/deuteron transfer reactions between methoxide ion and substituted phenylacetonitriles ( $\text{XC}_6\text{H}_4\text{CY}_1\text{Y}_2\text{CN}$ :  $\text{X}=\text{CH}_3\text{O}$ ,  $\text{CH}_3$ ,  $\text{Cl}$ ,  $\text{Y}_1=\text{H}$ ,  $\text{D}$ ,  $\text{Y}_2=\text{H}$ ,  $\text{D}$ ;  $\text{X}=\text{H}$ ,  $\text{Y}_1=\text{CH}_3$ ,  $\text{Y}_2=\text{H}, \text{D}$ ) have been determined at high pressures. The rate constant at each pressure is fitted to the previously derived formula which permits the distinction between the structural volume change and the electrostatic volume change. The activation volume varies with the substituent from  $-(9.5 \pm 2.5)$  to  $-(13.7 \pm 1.8)$   $\text{cm}^3/\text{mol}$  for the iminoether formation, and from  $+(18.2 \pm 2.9)$  to  $+(7.7 \pm 2.7)$   $\text{cm}^3/\text{mol}$  for the deuteron transfer. The activation volume of the proton transfer reaction coincides with the value of the deuteron transfer reaction within experimental error.

In the iminoether formation, the activation volume is more contributed from the structural term which does not vary so much with the substituent than the electrostatic one. And volume profile for that reaction suggests a product-like transition state. On the other hand, in the deuteron transfer reaction, the electrostatic term which varies considerably with the substituents, contributes to the activation volume much more than the covalent one.

It is also suggested from the fractionation theory that the solvation number does not change remarkably with pressure.

### Introduction

The substituent effect often causes the variation of the activation volume change as much as about  $\pm 6$   $\text{cm}^3/\text{mol}$ . For example, the activation volume difference changes from  $-5.2$  to  $+6.6$   $\text{cm}^3/\text{mol}$  in the nitration of the substituted benzene<sup>1)</sup>. If the steric term is not involved in the activation volume of a series of reactions, it would be possible to know the substituent effect on the geometrical structure and the interaction with the solvent of the transition state from each of the structural and electrostatic term of the activation volume. It is fascinating to try to discuss the activation volume profile of a series of reactions from the viewpoint of a theory, such as "Hammond postulate" and so on<sup>2-4)</sup>.

---

(Received August 31, 1979)

- 1) T. Asano and W. J. le Noble, *Chem. Rev.*, **78**, 407 (1978)
- 2) G. S. Hammond, *J. Am. Chem. Soc.*, **77**, 334 (1955)
- 3) C. G. Swain and E. R. Thornton, *ibid.*, **84**, 817 (1962)
- 4) E. R. Thornton, *ibid.*, **89**, 2915 (1967)

It seems important to know how the activation volume reflects the energy of the interacting molecules. A formula which permits the distinction between the structural volume change and the electrostatic volume change has been derived<sup>5)</sup> from Klopman's perturbed molecular orbital theory<sup>6)</sup>. The usefulness of the expression has been confirmed by the experimental results of various types of reactions<sup>5)</sup>. The expression also explains qualitatively the feature of the change of the rate constant with pressure by taking into account the difference of the energy levels under interaction in the medium, though several defects are contained.

At high pressure nitriles undergo several types of reactions in the presence of base: dimer or trimer formation, iminoether formation and proton transfer reactions. Cairns *et al.*<sup>7)</sup> have reported that some nitriles readily trimerize to the corresponding *sym*-triazine under the influence of methanol or weak bases at pressures of 7000–8500 atm\*. Bieniek and Korte<sup>8)</sup> also have reported that the reaction of some heterocyclic nitriles which are reported to hardly trimerize gives the *sym*-triazine at high pressures. Kurabayashi and his co-workers<sup>9)</sup> have elucidated in the mechanistic study that in alcoholic solvents *sym*-triazine may be produced by the cyclotrimerization of the iminoether which is formed by the alcoholysis of nitriles. Further, Jarre *et al.*<sup>10)</sup> have reported the *sym*-triazine formation in sulfolane at high pressures, and presupposed the "zwitterionic" reaction mechanism. Although several investigations have been done as described above, there are only a few studies about the volume change. Kurabayashi *et al.*<sup>9)</sup> and the author<sup>5)</sup> have determined the volume change of the iminoether formation in methanol.

Bengelsdorf<sup>11,12)</sup> has studied the reaction of nitriles in the neat at very high pressures (35–50 kbar) and high temperatures (623–774 K). Aromatic nitriles trimerize rather readily to the corresponding *sym*-triazine, and aliphatic nitriles with  $\alpha$ -hydrogens, on the other hand, do not trimerize but polymerize. He has suggested that aliphatic nitriles polymerize by the Thorpe-type reaction mechanism which involves the proton transfer reaction. From the study on the dimerization and trimerization of malononitrile which has active  $\alpha$ -hydrogens in methanol at high pressure<sup>13)</sup>, we have disclosed that *sym*-triazine is not formed, and the autocatalytic formation of the dimer is one of the Thorpe-type reactions. However, the nitriles having  $\alpha$ -hydrogens do not usually react via the Thorpe-type mechanism in  $\text{CH}_3\text{O}^-$ - $\text{CH}_3\text{OH}$  even though a proton is abstracted by a methoxide ion.<sup>5,14)</sup>

The proton transfer reactions of some nitriles have been studied in methanol at the ordinary

---

\*  $1 \text{ kg/cm}^2 = 0.9807 \text{ bar} = 0.9678 \text{ atm} = 0.9807 \times 10^5 \text{ Pa}$

5) H. Inoue, *This Journal*, **48**, 105 (1978)

6) G. Klopman, *J. Am. Chem. Soc.*, **90**, 223 (1968)

7) T. L. Cairns, A. W. Larcher, and B. C. McKusick, *ibid.*, **74**, 5633 (1952)

8) D. Bieniek and F. Korte, *Naturwissenschaften*, **59**, 529 (1972)

9) M. Kurabayashi, K. Yanagiya, and M. Yasumoto, *Bull. Chem. Soc. Jpn.*, **44**, 3413 (1971); *ibid.*, **46**, 2804 (1973)

10) W. Jarre, D. Bieniek, and F. Korte, *Tetrahedron*, **31**, 619 (1975)

11) I. S. Bengelsdorf, *J. Am. Chem. Soc.*, **80**, 1422 (1958)

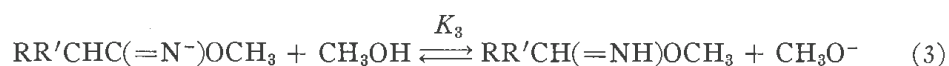
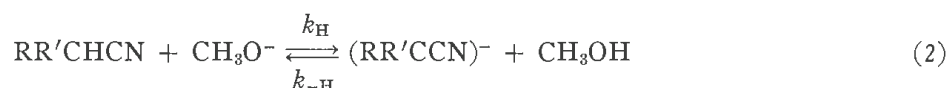
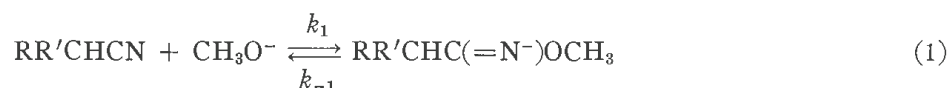
12) I. S. Bengelsdorf, *J. Org. Chem.*, **28**, 1369 (1963)

13) H. Inoue, K. Hara, and J. Osugi, *This Journal*, **46**, 64 (1976)

14) Y. Tanaka and S. Sato, *Kogyokagaku Zasshi*, **72**, 2023 (1969); D. Wöhrle, *Makromol. Chem.*, **160**, 83 (1972)

pressure<sup>15-23</sup>). But from the viewpoint of the pressure effect, only several investigations have been carried out. By means of a laser temperature-jump apparatus, Hubbard *et al.*<sup>24</sup>) have determined the volumes of activation of the fast proton transfer reaction between 4-nitrophenylnitromethane and 1,1', 3,3'-tetramethylguanidine in five aprotic solvents. They have reported that an electrostatic consideration is not adequate to explain the results. Isaacs *et al.*<sup>25</sup>) have reported that the primary isotope effect of the reaction between leuco crystal violet and chloranil in acetonitrile smoothly decreases from 11.2 at 1 atm to 7.5 at 2 kbar. They have suggested that the decrease of the primary isotope effect would be attributed to the diminution of the tunnelling contribution. Hamann and Linton have examined the effects of pressure on the rates of deuteration of formate and acetate ions in D<sub>2</sub>O, and have discussed the reaction mechanism<sup>26</sup>). Palmer and Kelm have determined the activation volumes for hydrogen transfer reactions in toluene between 2,2-diphenyl-1-picrylhydrazyl (DPPH) and a series of substituted phenols<sup>27</sup>). They have reported that the activation volume can be entirely attributed to the intrinsic volume change. Brower *et al.* have reported the deuteron transfer reaction of phenylacetonitrile-*d*<sub>2</sub> in CH<sub>3</sub>CO<sub>2</sub><sup>-</sup>-CH<sub>3</sub>OH at high pressure<sup>28</sup>). The author has determined the activation volume of the reaction between phenylacetonitrile-*d*<sub>2</sub> and methoxide ion, and reported the importance of the charge delocalization effect<sup>5</sup>).

After all, the nucleophilic attack of methoxide ion in methanol to nitriles having  $\alpha$ -hydrogens resulted in two different types of reactions, one being the iminoether formation and the other the proton transfer reaction.



The present paper attempts to elucidate how the substituent influences on each term of the activation volume with respect to the reactions of nitriles having  $\alpha$ -hydrogens in CH<sub>3</sub>O<sup>-</sup>-CH<sub>3</sub>OH solution.

15) D. J. Cram, C. A. Kingsbury, and B. Rickborn, *J. Am. Chem. Soc.*, **83**, 3688 (1961)

16) R. Stewart, J. P. O' Donnell, D. J. Cram, and B. Rickborn, *Tetrahedron*, **18**, 917 (1962)

17) L. Melander and N.-Å. Bergman, *Acta Chem. Scand.*, **A25**, 2264 (1971)

18) N.-Å. Bergman and L. Melander, *ibid.*, **A28**, 747 (1974)

19) N.-Å. Bergman and I. Kallsson, *ibid.*, **A30**, 411 (1976)

20) N.-Å. Bergman and I. Kallsson, *ibid.*, **A30**, 421 (1976)

21) E. F. Caldin and E. Harbron, *J. Chem. Soc.*, **1962**, 2314

22) E. F. Caldin and G. Tomalin, *Trans. Faraday Soc.*, **64**, 2814 (1968)

23) E. F. Caldin, M. Kasparian, and G. Tomalin, *ibid.*, **64**, 2823 (1968)

24) C. D. Hubbard, C. J. Wilson, and E. F. Caldin, *J. Am. Chem. Soc.*, **98**, 1870 (1976)

25) N. S. Isaacs, K. Javai, and E. Rannala, *Nature*, **268**, 372 (1977)

26) S. D. Hamann and M. Linton, *Aust. J. Chem.*, **30**, 1883 (1977)

27) D. A. Palmer and H. Kelm, *ibid.*, **30**, 1229 (1977)

28) K. R. Brower and D. Hughes, *J. Am. Chem. Soc.*, **100**, 7591 (1978)

## Experimental

### Materials

*p*-Chlorophenylacetonitrile, (Nakarai Chemicals Ltd.,) was recrystallized twice from 95% ethanol. *p*-Methylphenylacetonitrile, *p*-methoxyphenylacetonitrile, and 2-phenylpropionitrile (Merck) were distilled twice under nitrogen at reduced pressure. ( $\pm$ )-2-Phenylpropionic acid was prepared by the oxidation of ( $\pm$ )-2-phenylpropionitrile<sup>19</sup>. (+)-2-Phenylpropionic acid (lit.  $[\alpha]_D^{25} = +75.5^\circ$  in ethanol<sup>19</sup>) and (–)-2-phenylpropionic acid (lit.  $[\alpha]_D^{25} = -76.5^\circ$  in ethanol<sup>19</sup>) were separated by the method of Petterson *et al.*<sup>29</sup>) (+)-2-Phenylpropionitrile ( $[\alpha]_D^{25} = +14.2^\circ$  in methanol, lit.  $[\alpha]_D^{25} = +13.7^\circ$  in 50% alcohol<sup>30</sup>), and  $[\alpha]_{436}^{25} = +39.7^\circ$  in methanol<sup>19</sup>) and (–)-2-phenylpropionitrile ( $[\alpha]_D^{25} = -14.3^\circ$  in methanol, lit.  $[\alpha]_{436}^{25} = -43.4^\circ$  in methanol<sup>19</sup>) were synthesized from the corresponding acid by the method of Levene *et al.*<sup>30</sup>) No residual activity could be detected after the racemization of (+)-2-phenylpropionitrile and (–)-2-phenylpropionitrile in  $\text{CH}_3\text{O}^- - \text{CH}_3\text{OH}$  solution. After the distillation from silver nitrate and sodium methoxide, methanol was dried at least for 10 h by refluxing 3 dm<sup>3</sup> batches over 10 g of aluminum powder and 2 g of mercuric chloride. Methanol, as the solvent, was used just after one more distillation under nitrogen gas. Triethylamine was purified by the way described in the literature<sup>31</sup>).

### Procedure

The concentration of methoxide ion was determined by measuring the electrical conductivity at 298.2 K. This way has an advantage to be able to correct the presence of the carbon dioxide<sup>32</sup>).

The reaction where potassium methoxide was used as a catalyst was quenched meticulously with methanolic HCl solution. The yield of the iminoether formation and the deuterium content for the deuterium-hydrogen exchange reaction were determined by integrating several sweeps of the NMR spectrum under the appropriate conditions. The composition of a sample, after quenching and standing for a long time, was reproducible within  $\pm 2.0\%$ .

It has been reported that the racemization rate of 2-phenylpropionitrile is as same as the hydrogen-deuterium exchange rate<sup>19</sup>). The racemization rate of the optically active 2-phenylpropionitrile at high pressure was determined, after quenching, by JASCO DIP-4 polarimeter which has an accuracy of  $\pm 0.002^\circ$  in the full scale of  $\pm 2^\circ$ .

The high pressure generating systems, the reaction cell, and the other general experimental technique were described previously<sup>5, 13</sup>).

## Results and Discussion

### Rates of the Iminoether Formation

29) K. Petterson, *Ark. Kemi*, **10**, 283 (1956)

30) P. A. Levene and L. A. Mikeska, and K. Passoth, *J. Biol. Chem.*, **88**, 27 (1930)

31) W. S. Muney and J. F. Coetzee, *J. Phys. Chem.*, **66**, 89 (1962)

32) H. Inoue, K. Hara, and J. Osugi, *This Journal*, **48**, 44 (1978)

The rate constant is determined from the rate equation (4) which includes the pseudo-first order rate constant and equilibrium value of the iminoether,

$$\ln \frac{X_e}{X_e - X} = (k'_1 + k'_{-1})t, \quad (4)$$

where  $k'_1 = k_1[\text{CH}_3\text{O}^-]$  and  $k'_{-1} = k_{-1}K_3^{-1}[\text{CH}_3\text{O}^-]$  are the pseudo-first order rate constants,  $X$  the molar concentration of the iminoether at time  $t$ , and  $X_e$  its equilibrium value. Table 1 shows the equilibrium conversion of the iminoether, which was determined by the method as reported before<sup>5)</sup>. For the methyl  $p$ -chlorophenylacetiminoether formation was found no considerable change of the rate constant despite the change of the catalyst as shown in Table 2. The rate constant decreases by

Table 1 Equilibrium conversion (%) of nitrile to iminoether at 313.2 K<sup>a)</sup>

| $P/\text{kg cm}^{-2}$ | $p\text{-ClC}_6\text{H}_4\text{CH}_2\text{CN}$ | $\text{C}_6\text{H}_5\text{CH}_2\text{CN}$ | $p\text{-CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{CN}$ | $p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}_2\text{CN}$ | $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CN}$ |
|-----------------------|------------------------------------------------|--------------------------------------------|---------------------------------------------------------|----------------------------------------------------------|-------------------------------------------------------|
| 1                     | 11.2                                           | 5.5                                        | 6.6                                                     | 6.4                                                      | 3.4                                                   |
| 500                   | 14.0                                           |                                            | 8.6                                                     | 8.3                                                      | 4.2                                                   |
| 1000                  | 17.1                                           | 9.5                                        | 10.4                                                    | 10.2                                                     | 5.8                                                   |
| 1500                  | 21.0                                           |                                            | 13.1                                                    | 12.7                                                     | 7.5                                                   |
| 2000                  | 24.6                                           | 15.0                                       | 15.8                                                    | 15.2                                                     | 10.3                                                  |
| 3000                  | 34.4                                           | 23.2                                       | 21.9                                                    | 21.2                                                     | 16.5                                                  |

a) Reaction time, 32–48 h

Table 2 Rate constant of the methyl  $p$ -chlorophenylacetiminoether formation in  $\text{N}(\text{Et})_3\text{—CH}_3\text{OH}$  and in  $\text{CH}_3\text{OK—CH}_3\text{OH}$  at 313.2 K

| $P/\text{kg cm}^{-2}$ | $k_1 \times 10^3 / \text{kg mol}^{-1} \text{ s}^{-1}$ |                        | $k_{-1}K_3^{-1} \times 10^3 / \text{kg mol}^{-1} \text{ s}^{-1}$ |                        |
|-----------------------|-------------------------------------------------------|------------------------|------------------------------------------------------------------|------------------------|
|                       | $\text{N}(\text{Et})_3$ <sup>a)</sup>                 | $\text{CH}_3\text{OK}$ | $\text{N}(\text{Et})_3$ <sup>a)</sup>                            | $\text{CH}_3\text{OK}$ |
| 1                     | $0.700 \pm 0.041$                                     | $0.674 \pm 0.015$      | $5.55 \pm 0.34$                                                  | $5.35 \pm 0.12$        |
| 1500                  | $1.17 \pm 0.04$                                       | $1.17 \pm 0.04$        | $4.40 \pm 0.15$                                                  | $4.38 \pm 0.15$        |
| 3000                  | $1.84 \pm 0.03$                                       | $1.69 \pm 0.02$        | $3.52 \pm 0.05$                                                  | $3.23 \pm 0.03$        |

a) The dissociation constant of  $\text{N}(\text{Et})_3$  at high pressure has been already reported.<sup>32)</sup>

Table 3-1 Pressure dependence of  $k_1$  and  $k_{-1}K_3^{-1}$  at 313.2 K

| $P/\text{kg cm}^{-2}$ | $p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}_2\text{CN}$    |                                                                        | $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CN}$       |                                                                        |
|-----------------------|-------------------------------------------------------------|------------------------------------------------------------------------|-------------------------------------------------------------|------------------------------------------------------------------------|
|                       | $\frac{k_1 \times 10^3}{\text{kg mol}^{-1} \text{ s}^{-1}}$ | $\frac{k_{-1}K_3^{-1} \times 10^3}{\text{kg mol}^{-1} \text{ s}^{-1}}$ | $\frac{k_1 \times 10^3}{\text{kg mol}^{-1} \text{ s}^{-1}}$ | $\frac{k_{-1}K_3^{-1} \times 10^3}{\text{kg mol}^{-1} \text{ s}^{-1}}$ |
| 1                     | $0.098 \pm 0.006$                                           | $1.43 \pm 0.07$                                                        | $0.068 \pm 0.006$                                           | $1.93 \pm 0.11$                                                        |
| 500                   | $0.127 \pm 0.006$                                           | $1.40 \pm 0.06$                                                        | $0.084 \pm 0.005$                                           | $1.81 \pm 0.07$                                                        |
| 1000                  | $0.155 \pm 0.011$                                           | $1.36 \pm 0.08$                                                        | $0.110 \pm 0.006$                                           | $1.79 \pm 0.07$                                                        |
| 1500                  | $0.191 \pm 0.021$                                           | $1.31 \pm 0.14$                                                        | $0.140 \pm 0.009$                                           | $1.73 \pm 0.09$                                                        |
| 2000                  | $0.240 \pm 0.011$                                           | $1.34 \pm 0.05$                                                        | $0.177 \pm 0.006$                                           | $1.55 \pm 0.04$                                                        |
| 3000                  | $0.360 \pm 0.010$                                           | $1.34 \pm 0.03$                                                        | $0.272 \pm 0.012$                                           | $1.38 \pm 0.05$                                                        |

| $P/\text{kg cm}^{-2}$ | $p\text{-ClC}_6\text{H}_4\text{CH}_2\text{CN}$             |                                                                       | $\text{C}_6\text{H}_5\text{CH}_2\text{CN}^{\text{a)}$      |                                                                       | $p\text{-CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{CN}$    |                                                                       |
|-----------------------|------------------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------|-----------------------------------------------------------------------|------------------------------------------------------------|-----------------------------------------------------------------------|
|                       | $\frac{k_1 \times 10^3}{\text{kg mol}^{-1} \text{s}^{-1}}$ | $\frac{k_{-1}K_3^{-1} \times 10^3}{\text{kg mol}^{-1} \text{s}^{-1}}$ | $\frac{k_1 \times 10^3}{\text{kg mol}^{-1} \text{s}^{-1}}$ | $\frac{k_{-1}K_3^{-1} \times 10^3}{\text{kg mol}^{-1} \text{s}^{-1}}$ | $\frac{k_1 \times 10^3}{\text{kg mol}^{-1} \text{s}^{-1}}$ | $\frac{k_{-1}K_3^{-1} \times 10^3}{\text{kg mol}^{-1} \text{s}^{-1}}$ |
| 1                     | $0.700 \pm 0.041$                                          | $5.55 \pm 0.34$                                                       | 0.24                                                       | 4.1                                                                   | $0.110 \pm 0.006$                                          | $1.55 \pm 0.07$                                                       |
| 500                   | $0.992 \pm 0.040$                                          | $5.10 \pm 0.21$                                                       |                                                            |                                                                       | $0.140 \pm 0.008$                                          | $1.52 \pm 0.07$                                                       |
| 1000                  | $1.00 \pm 0.03$                                            | $4.80 \pm 0.11$                                                       | 0.36                                                       | 3.4                                                                   | $0.175 \pm 0.006$                                          | $1.50 \pm 0.04$                                                       |
| 1500                  | $1.17 \pm 0.04$                                            | $4.40 \pm 0.15$                                                       |                                                            |                                                                       | $0.220 \pm 0.015$                                          | $1.46 \pm 0.10$                                                       |
| 2000                  | $1.39 \pm 0.05$                                            | $4.20 \pm 0.09$                                                       | 0.55                                                       | 3.1                                                                   | $0.270 \pm 0.011$                                          | $1.44 \pm 0.05$                                                       |
| 3000                  | $1.84 \pm 0.03$                                            | $3.52 \pm 0.05$                                                       | 0.78                                                       | 2.6                                                                   | $0.381 \pm 0.015$                                          | $1.37 \pm 0.05$                                                       |

a) ref. 5

the electron-donating substituent as shown in Table 3-1.

### Rates of the Proton/Deuteron Transfer

The rate constant of the deuteron transfer reaction for nitriles having two equivalent reactive positions was approximately determined from Eq (5)<sup>5)</sup> by neglecting the secondary isotope effect.

$$1 - \frac{2[\text{RCH}_2\text{CN}] + [\text{RCHDCN}]}{2a} = \left(1 - \frac{2[\text{RCH}_2\text{CN}]_0 + [\text{RCHDCN}]_0}{2a}\right) \exp(-k'_D t), \quad (5)$$

where  $k'_D = k_D[\text{CH}_3\text{O}^-]$ ,  $a = [\text{RCH}_2\text{CN}]_0 + [\text{RCHDCN}]_0 + [\text{RCD}_2\text{CN}]_0$ , the subscript 0 refers to the initial concentration, and  $(2[\text{RCH}_2\text{CN}] + [\text{RCHDCN}])/2a$  is measured from the integrated NMR

Table 3-2 Numerical values of  $k/\text{kg mol}^{-1}\text{s}^{-1}$  of the proton/deuteron transfer reaction in  $\text{CH}_3\text{OH}$  or  $\text{CH}_3\text{OD}$  at 303.2 K

| $P/\text{kg cm}^{-2}$ | $p\text{-ClC}_6\text{H}_4\text{CD}_2\text{CN}^{\text{a)}$ | $\text{C}_6\text{H}_5\text{CD}_2\text{CN}^{\text{b)}$ | $p\text{-CH}_3\text{C}_6\text{H}_4\text{CD}_2\text{CN}^{\text{a)}$ | $p\text{-CH}_3\text{OC}_6\text{H}_4\text{CD}_2\text{CN}^{\text{a)}$ | $\text{C}_6\text{H}_5\text{CD}(\text{CH}_3)\text{CN}^{\text{a)}$ |
|-----------------------|-----------------------------------------------------------|-------------------------------------------------------|--------------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------------------|
| 1                     | $6.5 \pm 0.3$                                             | 4.0                                                   | $0.850 \pm 0.061$                                                  | $0.150 \pm 0.010$                                                   | $0.129 \pm 0.006$                                                |
| 500                   | $4.9 \pm 0.4$                                             |                                                       | $0.649 \pm 0.055$                                                  | $0.113 \pm 0.012$                                                   | $0.110 \pm 0.007$                                                |
| 1000                  | $3.9 \pm 0.1$                                             | 2.0                                                   | $0.536 \pm 0.047$                                                  | $0.104 \pm 0.009$                                                   | $0.103 \pm 0.008$                                                |
| 1500                  | $3.2 \pm 0.3$                                             |                                                       | $0.475 \pm 0.047$                                                  | $0.0900 \pm 0.0061$                                                 | $0.0945 \pm 0.0019$                                              |
| 2000                  | $2.7 \pm 0.1$                                             | 1.2                                                   | $0.423 \pm 0.030$                                                  | $0.0857 \pm 0.0062$                                                 | $0.0913 \pm 0.0062$                                              |
| 3000                  | $2.4 \pm 0.2$                                             | 0.9                                                   | $0.366 \pm 0.034$                                                  | $0.0701 \pm 0.0022$                                                 | $0.0833 \pm 0.0039$                                              |

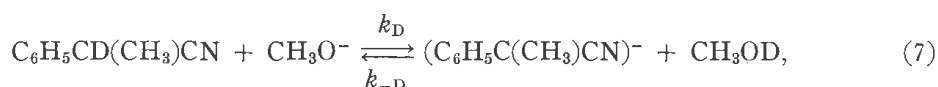
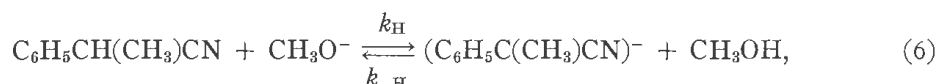
| $P/\text{kg cm}^{-2}$ | $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CN}^{\text{a)}$ | $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CN}^{\text{c)}$ |
|-----------------------|------------------------------------------------------------------|------------------------------------------------------------------|
| 1                     | $0.285 \pm 0.011$                                                | $0.548 \pm 0.028$                                                |
| 500                   | $0.253 \pm 0.009$                                                | $0.483 \pm 0.010$                                                |
| 1000                  | $0.244 \pm 0.016$                                                | $0.447 \pm 0.034$                                                |
| 1500                  |                                                                  |                                                                  |
| 2000                  | $0.210 \pm 0.027$                                                | $0.406 \pm 0.018$                                                |
| 3000                  | $0.191 \pm 0.008$                                                | $0.351 \pm 0.008$                                                |

a) in  $\text{CH}_3\text{OH}$  b) ref. 5 c) in  $\text{CH}_3\text{OD}$

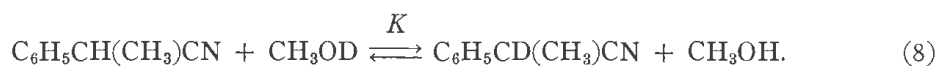
intensity. The substituent effect on the rate constant shows the similar tendency to the iminoether formation; the rate constant decreases by increasing the electron-donating power of a substituent as shown in Table 3-2.

### Primary Isotope Effect in Proton Transfer Reaction of 2-Phenylpropionitrile

In order to know the primary isotope effect on the reverse reaction ( $k_{-H}/k_{-D}$ ), the equilibrium isotope effect was, at first, determined by taking into account the following reactions,



where  $K_H = k_H/k_{-H}$ ,  $K_D = k_D/k_{-D}$ , and  $k_{-H}/k_{-D} = (k_H/k_D) \cdot (K_D/K_H) = (k_H/k_D)/K$ . The equilibrium constant  $K$  of the exchange reaction is represented as,



The exchange equilibrium constant can be determined in the mixture of  $\text{CH}_3\text{OH}$ – $\text{CH}_3\text{OD}$  by using the potassium methoxide as a catalyst. Figure 1 shows the equilibrium constant against the fraction of the mixture composed of  $\text{CH}_3\text{OH}$  and  $\text{CH}_3\text{OD}$  at 1 atm and 303.2 K. The equilibrium constant  $K$  does not change so much with pressure in mixtures of different  $\text{CH}_3\text{OH}$ – $\text{CH}_3\text{OD}$  composition as shown in Fig. 2. So the value of  $K$  in pure  $\text{CH}_3\text{OH}$ , which is estimated to be around 1.8 by extrapolating to  $[\text{CH}_3\text{OD}] \rightarrow 0$  in Fig. 1, is also expected to be almost independent of pressure. Since the primary isotope effect  $k_H/k_D$  is  $2.21 \pm 0.13$  as calculated from the values on Table 3-2,  $k_{-H}/k_{-D}$  would lie around 1.2.

Many models have been proposed in order to explain the value of the primary isotope effect. There exist two main theoretical approaches to the study of the transition state of the proton

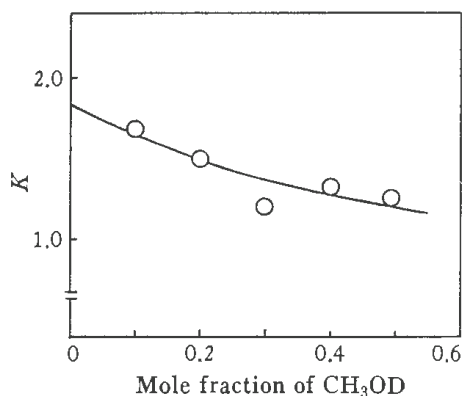


Fig. 1 Equilibrium constant for D-H exchange between  $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CN}$  and  $\text{CH}_3\text{OD}$  in different mixture of  $\text{CH}_3\text{OH}$ – $\text{CH}_3\text{OD}$  at 1 atm and 303.2 K.

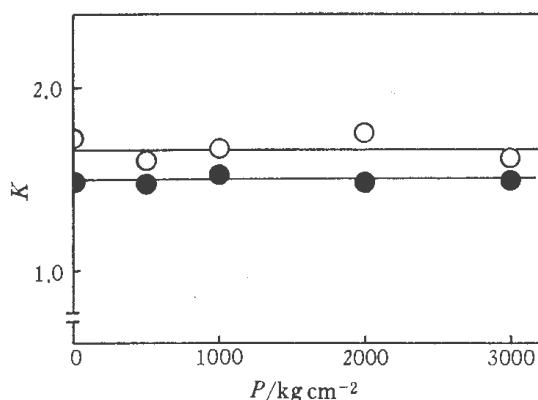


Fig. 2 Pressure dependence of  $K$  at 303.2 K.

○: 11.6 mol% of  $\text{CH}_3\text{OD}$ ,  
●: 19.9 mol% of  $\text{CH}_3\text{OD}$ .

transfer: the simple three center model,  $X\cdots H\cdots Y$ <sup>33~35</sup>), and the correction of the tunneling effect<sup>36</sup>). Judging from the primary isotope effect on both forward and reverse reactions, it seems to be probable that the tunneling effect scarcely contributes to this proton transfer. The variation of the primary isotope effect has been reported in relation to the symmetry of the transition state<sup>37</sup>). The more symmetrical the transition state is, the larger is the primary isotope effect. Many of the theoretical treatments are based on Eq. (9) which represents the change in the potential energy ( $\Delta\Psi$ ) for small displacement ( $\Delta r$ ) along the molecular axis.

$$2\Delta\Psi = k_{XH}\Delta r_{XH}^2 + k_{YH}\Delta r_{YH}^2 + 2k_{XHYH}\Delta r_{XH}\Delta r_{YH}, \quad (9)$$

where  $\Delta$  represents the departure of each quantity from its equilibrium value, and  $k_{IJ}$  is the force constant for the I-J binding. Albery has given a general formula which includes all possible values of the force constant<sup>35</sup>). This consideration is helpful to predict the geometry of the transition state. The "small" isotope effect as found in the present reaction suggests that the transition state is far from the geometric symmetry, so that the transition state may lie on either reactant-side or product-side on a reaction coordinate.

#### Activation Volumes of the Iminoether Formation

Activation volume of each nitrile for the formation of the iminoether was determined from the least-square fit to Eq. (10) as shown in Fig. 3,

$$-\frac{RT}{P-1} \ln \frac{k(P)}{k(1)} = \Delta V_e^\ddagger \frac{B+1}{P-1} \ln \frac{B+P}{B+1} + \Delta V_e^\ddagger, \quad (10)$$

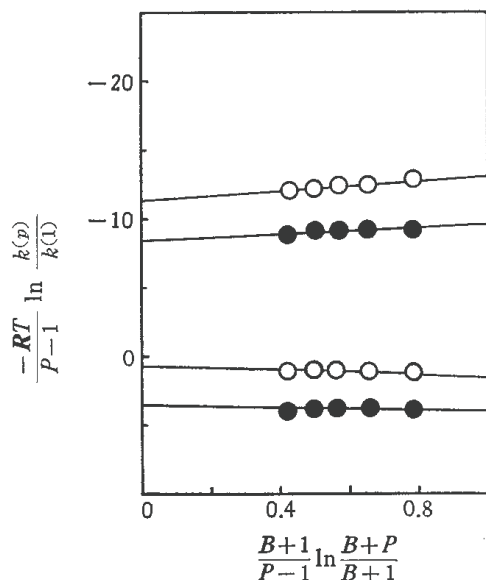


Fig. 3 Pressure dependence of  $k_1$  and  $k_{-1}K_3^{-1}$  at 313.2 K.

○:  $p\text{-CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{CN}$ ,  
●:  $p\text{-ClC}_6\text{H}_4\text{CH}_2\text{CN}$ .

33) F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961)

34) R. P. Bell, *Trans. Faraday Soc.*, **57**, 961 (1961)

35) W. J. Albery, *ibid.*, **63**, 200 (1967)

36) R. P. Bell, W. H. Sachs, and R. L. Tranter, *ibid.*, **67**, 1995 (1971)

37) See for example, S. B. Hanna, C. Jermini, H. Loewenschuss, and H. Zollinger, *J. Am. Chem. Soc.*, **96**, 7222 (1974), and references cited therein.

Table 4 Activation volumes of the iminoether formation at 1 atm and 303.2 K

| Nitrile                                                                     | $\frac{\Delta V_e^*(1)}{\text{cm}^3\text{mol}^{-1}}$ | $\frac{\Delta V_e^*(1)}{\text{cm}^3\text{mol}^{-1}}$ | $\frac{\Delta V^*(1)}{\text{cm}^3\text{mol}^{-1}}$ | $\frac{\Delta V_e^*(-1) - \Delta V_e(3)}{\text{cm}^3\text{mol}^{-1}}$ | $\frac{\Delta V_e^*(-1) - \Delta V_e(3)}{\text{cm}^3\text{mol}^{-1}}$ | $\frac{\Delta V^*(-1) - \Delta V(3)}{\text{cm}^3\text{mol}^{-1}}$ |
|-----------------------------------------------------------------------------|------------------------------------------------------|------------------------------------------------------|----------------------------------------------------|-----------------------------------------------------------------------|-----------------------------------------------------------------------|-------------------------------------------------------------------|
| <i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CN                | -8.3 ± 1.1                                           | -1.2 ± 1.5                                           | -9.5                                               | +3.3 ± 1.0                                                            | +1.3 ± 1.5                                                            | +4.6                                                              |
| C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CN <sup>a)</sup>              | -10.2                                                | -1.0                                                 | -11.2                                              | +4.1                                                                  | ~0                                                                    | +4.1                                                              |
| <i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CN  | -10.9 ± 1.1                                          | -1.8 ± 1.5                                           | -12.7                                              | +0.5 ± 0.9                                                            | +1.3 ± 1.3                                                            | +1.8                                                              |
| <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CH <sub>2</sub> CN | -10.4 ± 1.0                                          | -2.7 ± 1.7                                           | -13.1                                              | +0.2 ± 1.0                                                            | +1.6 ± 1.6                                                            | +1.8                                                              |
| C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CN                        | -11.5 ± 1.0                                          | -2.2 ± 1.8                                           | -13.7                                              | +2.3 ± 1.0                                                            | +0.6 ± 1.4                                                            | +2.9                                                              |

a) ref. 5

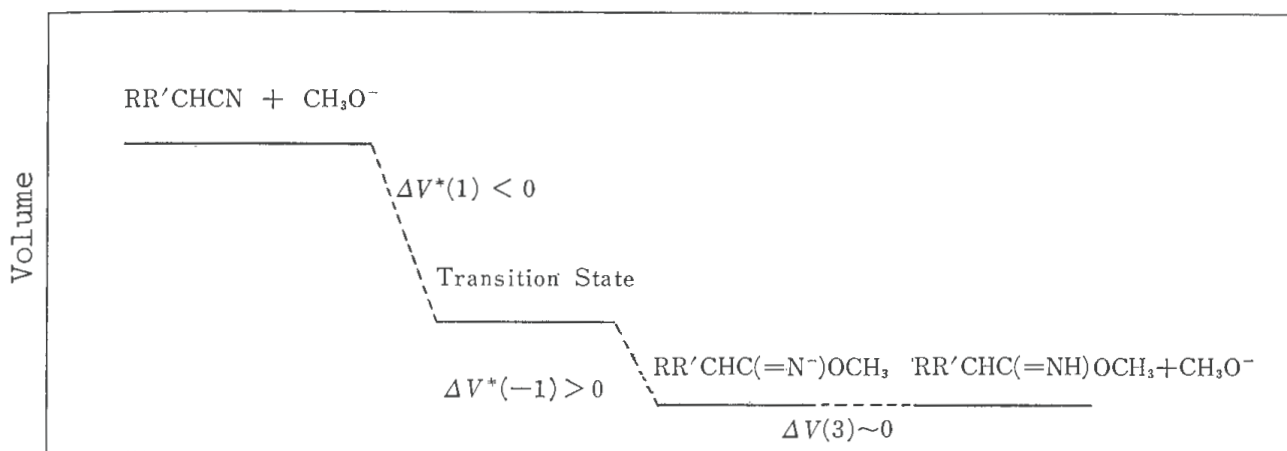


Fig. 4 Volume profile of the iminoether formation.

where  $\Delta V_e^*$  and  $\Delta V_e^\ddagger$  refer to the electrostatic volume change and the structural volume change at 1 atm respectively, and  $B$  is the empirical parameter in the Owen-Brinkley expression<sup>38)</sup> for the pressure effect on the dielectric constant. The activation volumes are listed in Table 4. We could not experimentally define the value of  $\Delta V^*(-1)$  and  $\Delta V(3)$ , but  $\Delta V^*(-1)$  is expected to be positive because the reverse reaction of step (1) is of a bond breakage. The volume change of equilibrium (3),  $\Delta V(3)$  is expected to be around zero, since this step includes no change of the charge and number of molecule. So, the quantities of composite term  $\Delta V^*(-1) - \Delta V(3)$  shown in Table 4 are explained, and we can draw a volume profile as shown in Fig. 4.

The quantity of  $\Delta V_e^\ddagger(1)/\Delta V_e(1)$  indicates a degree of the geometric symmetry of the transition state of step (1). The value of  $\Delta V_e(1)$  can not be experimentally determined, but calculated as  $\Delta V_e(1) = \Delta V_e^\ddagger(1) - \Delta V_e^\ddagger(-1)$ , if  $\Delta V_e^\ddagger(-1)$  is estimated by other data. In Table 4 the term  $\Delta V_e^\ddagger(-1) - \Delta V_e(3)$  is given, and the quantity of  $\Delta V_e(3)$  is assumed to be much smaller than  $\Delta V_e^\ddagger(-1)$  for the above mentioned reason. So, using the experimentally determined terms,  $\Delta V_e(1)$  is approximated as,

$$\Delta V_e(1) \simeq \Delta V_e^\ddagger(1) - \{\Delta V_e^\ddagger(-1) - \Delta V_e(3)\}, \quad (11)$$

and the value of  $\Delta V_e^\ddagger(1)/\Delta V_e(1)$  can be easily calculated\*; for *p*-ClC<sub>6</sub>H<sub>4</sub>CH<sub>2</sub>CN: 0.67, C<sub>6</sub>H<sub>5</sub>CH<sub>2</sub>CN:

\* The mean value of  $\Delta V_e(1)$  (-12.4 cm<sup>3</sup>/mol) was used.38) B. B. Owen and S. R. Brinkley, *Phys. Rev.*, **64**, 32 (1943)

0.82,  $p\text{-CH}_3\text{C}_6\text{H}_4\text{CH}_2\text{CN}$ : 0.88,  $p\text{-CH}_3\text{OC}_6\text{H}_4\text{CH}_2\text{CN}$ : 0.84,  $\text{C}_6\text{H}_5\text{CH}(\text{CH}_3)\text{CN}$ : 0.93. The error of  $\Delta V_e^\ddagger(1)/\Delta V_e(1)$  is of the order of  $\pm 0.1$ . It seems that the donation of  $\pi$  electron into the aromatic ring enhances the  $\Delta V_e^\ddagger(1)/\Delta V_e(1)$ , which means that the transition state becomes more product-like, though more conclusive discussions have to be evaded at present.

The value of  $\Delta V_e(1) + \Delta V_e(3) (=V_e^\ddagger(1) - \{\Delta V_e^\ddagger(-1) - \Delta V_e(3)\})$  is slightly negative, even though both iminoether and nitrile are the neutral molecules. An iminoether has the functional groups of  $-\text{OCH}_3$  and  $=\text{NH}$  which make it easy to form the hydrogen-bonding with solvents. Usually hydrogen-bonded species show larger volume contraction than those of similar but non-hydrogen-bonded ones<sup>39)</sup>. For example, it has been reported that the formation of a hydrogen bond in  $\text{O}-\text{H}\cdots\text{O}$  is accompanied with a volume contraction about  $3.8 \text{ cm}^3/\text{mol}$ <sup>40)</sup>. The negative value of  $\Delta V_e(1) + \Delta V_e(3)$  may be mainly attributed to the formation of the hydrogen-bonding between iminoether and methanol molecules.

#### Activation Volumes of the Proton/Deuteron Transfer Reaction

The rate constants of proton/deuteron transfer reactions depend on pressures as described by the similar formula to Eq. (10). The fitness is shown in Fig. 5 and the activation volumes,  $\Delta V_e^\ddagger$  and  $\Delta V_e^\ddagger$  are obtained (Table 5). It has been known that most of the proton or hydrogen transfer from carbon acids accompanies the negative activation volume<sup>24~28)</sup>, and it comes mainly from the structural contribution that is the contraction of the van der Waals distance. However, the results obtained here are in quite contrast to the hitherto reported ones. The proton/deuteron transfer reactions exhibit positive activation volumes. The fact that each  $\Delta V_e^\ddagger(\text{D})$  or  $\Delta V_e^\ddagger(\text{H})$  is larger than the corresponding  $\Delta V_e^\ddagger$  suggests that there exists a large charge delocalization effect at the transition state. This is also supported by the study of Bergman *et al.*<sup>17,19)</sup> who have measured the rate

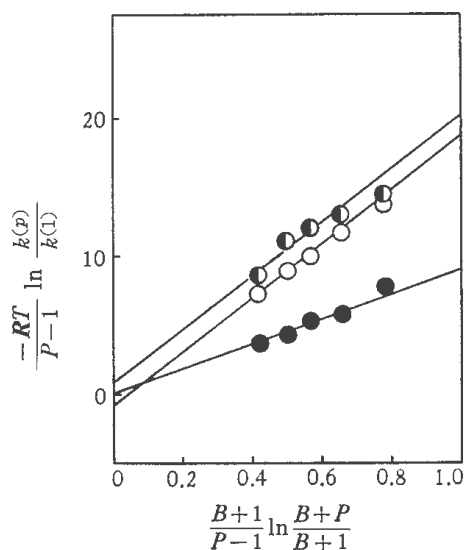


Fig. 5 Pressure dependence of  $k_D$  in  $\text{CH}_3\text{OH}$  at 303.2 K.

- :  $p\text{-ClC}_6\text{H}_4\text{CD}_2\text{CN}$ ,
- :  $p\text{-CH}_3\text{C}_6\text{H}_4\text{CD}_2\text{CN}$ ,
- :  $\text{C}_6\text{H}_5\text{CD}(\text{CH}_3)\text{CN}$ .

39) K. E. Weale, "Chemical Reactions at High Pressures," E. and F. N. Spon Limited, London (1967), Chap. 5.

40) S. D. Hamann, "Physico-Chemical Effects of Pressure," Butterworth, London (1957), Chap. 8.

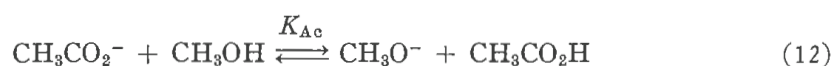
Table 5 Activation volumes of the proton/deuteron transfer reactions at 1 atm and 303.2 K

| Nitrile                                                                     | Solvent                          | $\Delta V_c^*/\text{cm}^3\text{mol}^{-1}$ | $\Delta V_e^*/\text{cm}^3\text{mol}^{-1}$ | $\Delta V^*/\text{cm}^3\text{mol}^{-1}$ |
|-----------------------------------------------------------------------------|----------------------------------|-------------------------------------------|-------------------------------------------|-----------------------------------------|
| <i>p</i> -ClC <sub>6</sub> H <sub>4</sub> CD <sub>2</sub> CN                | CH <sub>3</sub> OH               | $+0.9 \pm 1.2$                            | $+18.9 \pm 1.7$                           | $+19.8$                                 |
| C <sub>6</sub> H <sub>5</sub> CD <sub>2</sub> CN <sup>a)</sup>              | CH <sub>3</sub> OH               | $+4$                                      | $+20$                                     | $+24$                                   |
| <i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> CD <sub>2</sub> CN  | CH <sub>3</sub> OH               | $-0.7 \pm 1.6$                            | $+18.6 \pm 2.2$                           | $+17.9$                                 |
| <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> CD <sub>2</sub> CN | CH <sub>3</sub> OH               | $+0.9 \pm 1.0$                            | $+13.0 \pm 1.7$                           | $+13.9$                                 |
| C <sub>6</sub> H <sub>5</sub> CD(CH <sub>3</sub> )CN                        | CH <sub>3</sub> OH               | $0.0 \pm 0.8$                             | $+8.9 \pm 1.3$                            | $+8.9$                                  |
| C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CN                        | CH <sub>3</sub> OH               | $+0.3 \pm 1.4$                            | $+6.7 \pm 1.9$                            | $+7.0$                                  |
| C <sub>6</sub> H <sub>5</sub> CH(CH <sub>3</sub> )CN                        | CD <sub>3</sub> OD <sup>b)</sup> | $+0.1 \pm 1.1$                            | $+7.9 \pm 1.6$                            | $+8.0$                                  |

a) ref. 5    b) The value of *B* is assumed to be same as that of CH<sub>3</sub>OH.

constants of the racemization of 2-phenylpropionitrile and 2-methyl-3-phenylpropionitrile with sodium methoxide as a base in methanol. They reported that the rate constant increased about a factor of  $10^7$  by leaving out a methylene group between phenyl and cyano group. The enhancement would be attributed entirely to the difference of the stability between two transition states; 2-methyl-3-phenylpropionitrile has little possibility of delocalizing the negative charge into the phenyl group at the transition state and product.

Although Brower *et al.*<sup>28)</sup> have reported the activation volume is  $-4 \text{ cm}^3/\text{mol}$  for the deuteron transfer reaction between phenylacetone-*d*<sub>2</sub> and acetate ion in methanol, their treatment seems too rough to infer the transition state of an elementary process. In that case it is necessary, at least, to consider the influence of the ion-pair formation between acetate ion and potassium ion<sup>41)</sup> and the equilibrium (12).



As the dissociation constant of acetic acid in methanol<sup>42)</sup> and the autoprotolysis constant of methanol<sup>43)</sup> at 1 atm and 298.2 K have been reported, the equilibrium constant of Eq. (12) can be calculated as  $8.4 \times 10^{-8} \text{ mol/dm}^3$ . In their experimental condition the acetate ion concentration is so high that the existence of the methoxide ion ( $\sim 10^{-4} \text{ mol/dm}^3$ ) can not be neglected.

As mentioned above  $\Delta V_e^*$  is qualitatively understood by the electrostatic solvation model, though Hubbard *et al.*<sup>24)</sup> have reported the inadequacy of the simple solvation model for the reaction between 4-nitrophenylnitromethane and 1, 1', 3, 3'-tetramethylguanidine in aprotic solvents.

On the other hand,  $\Delta V_c^*$  obtained in the present study is around zero, or sometimes positive. These facts would indicate that the distance between the  $\alpha$ -carbon and the oxygen of the methoxide at the transition state does not so much contract, and it is kept around the van der Waals distance.

41) See for example, K. T. Leffek and A. Suzzka, *Can. J. Chem.*, **53**, 1537 (1975), N.-Å. Bergman and I. Kallsson, *Acta Chem. Scand.*, **A31**, 887 (1977), and so on.

42) T. Shedlovsky and R. L. Kay, *J. Phys. Chem.*, **60**, 151 (1956)

43) S. Bruckenstein and I. M. Kolthoff, "Treatise on Analytical Chemistry," Interscience, New York (1959), Vol. 1, Part I, p. 475 ff.

It has been reported that the contraction of the van der Waals volume for the linear triatomic proton transfer model based on the crude energy calculation is about  $-(6\sim 10)$  cm<sup>3</sup>/mol<sup>44)</sup>. In other experiments the structural change of the proton or hydrogen transfer reaction is often considered to be  $-(13\sim 15)$  cm<sup>3</sup>/mol. For example, Palmer and Kelm have reported the volume of activation between DPPH and 2, 4, 6-trisubstituted phenols in toluene is about  $-13.3$  cm<sup>3</sup>/mol<sup>27)</sup>. This value, however, should unavoidably include the volume term coming from the steric hindrance.

Although we believe that in most cases  $\Delta V_e^\ddagger$  mainly represents the structural change, the difficulty may arise in order to interpret the meaning of  $\Delta V_e^\ddagger$  further in detail. It has been reported that the geometric contribution to the partial molar volume of an ion includes the intrinsic volume of an ion and the void space around the ion<sup>45)</sup>. The void space has been considered to be one of the quantity which reflects the geometry of the coordination shell. It may be necessary to consider this void volume change in the interpretation of  $\Delta V_e^\ddagger$ .

Kelm and his co-workers<sup>27)</sup> have reported the independence of  $\Delta V^\ddagger$  from the substituent in a radical reaction. Zhulin *et al.*<sup>46)</sup> have reported the substituent effect on the activation volume of the reaction between *p*- or *m*-substituted toluene and N-bromosuccinimide at 343 K in CH<sub>2</sub>Cl<sub>2</sub>. The difference of the activation volume largely depends on the substituent. Its maximum difference is 8.9 cm<sup>3</sup>/mol. As the reaction should proceed via radical mechanism, the change of  $\Delta V^\ddagger$  would be mainly attributed to the geometric change at the transition state.

However, no study of the substituent effect on high-pressure kinetics on the proton transfer reactions appears so far. As seen in Table 5, the introduction of an electron-donating substituent decreases the magnitude of the activation volume. Furthermore, the electrostatic term  $\Delta V_e^\ddagger$  is predominantly influenced. But at present the substituent effect on  $\Delta V_e^\ddagger$  can not be satisfactorily explained. Difficulty arises in the estimation of the partial molar volume of the resulting carbanion. Each carbanion may have a considerably different partial molar volume by the different effects on the charge distribution due to the substituent. For example,  $\alpha$ -carbon of the resulting anion of 2-phenylpropionitrile would not be thoroughly in *sp*<sup>2</sup> state judging from the steric hindrance between methyl group and *ortho*-hydrogen atom of the phenyl ring.

On the problem of the difference of the pressure effect between proton and deuteron transfer, there appeared no appreciable change on either  $\Delta V_e^\ddagger$  or  $\Delta V_e^\ddagger$  as seen in Table 5 and the difference of the activation volume for the reverse reaction ( $k_{-H}$ ). In some systems, it is expected that there may appear the distinct difference. For example, if the reaction rate of the proton transfer is so fast that it is competed with the dielectric relaxation time, the degree of "non-equilibrium solvation"<sup>47)</sup> would be greater in proton transfer than deuteron transfer, which would result in the different electrostrictive volume change. That "non-equilibrium solvation" effect may be more distinct when the curvature

44) S. D. Hamann, "High Pressure Physics and Chemistry," ed by R. S. Bradley, Academic Press, London & New York (1963), Vol. 2, Chap. 8.

45) F. J. Millero, *J. Phys. Chem.*, **73**, 2417 (1969); *Chem. Rev.*, **71**, 147 (1971); F. Kawaizumi and R. Zana, *J. Phys. Chem.*, **78**, 1099 (1974)

46) V. M. Zhulin, M. Ya. Botnikov, and I. Kh. Milyavskaya, *Bull. Acad. Sci. USSR, Div. Chem. Sci. (English Transl.)*, **24**, 424 (1975)

47) R. P. Bell, *Disc. Faraday Soc.*, **39**, 16 (1966)

of the Brønsted plot<sup>48)</sup> or the change of electrostrictive volume in the proton transfer reaction of a series of carbon acids is taken into account.

### Deuterium Solvent Isotope Effect on Proton-Transfer Reaction

The ratio of the rate constant in deuterium substituted solvent to that in non-deuterated one is given by Eq. (13) according to the fractionation theory<sup>49)</sup>,

$$\frac{k_n}{k_0} = \frac{(1 - n + n\phi^\ddagger)^p}{(1 - n + n\phi_{\text{CH}_3\text{O}^-})^m}, \quad (13)$$

where  $n$  is the fraction of deuterium,  $\phi^\ddagger$  and  $\phi_{\text{CH}_3\text{O}^-}$  are the fractionation factors for the transition state and the methoxide ion, respectively, and  $m$  and  $p$  denote the number of methanol molecules solvating to the methoxide ion and the transition state, respectively. In Eq. (13) it is assumed that  $m$  and  $p$  do not change with  $n$ . From the limiting isotope effect for isotopically pure solvents,

$$\frac{k_1}{k_0} = \frac{(\phi^\ddagger)^p}{(\phi_{\text{CH}_3\text{O}^-})^m}. \quad (14)$$

Gold and Grist have determined the value of  $\phi_{\text{CH}_3\text{O}^-}$  as 0.74 by the NMR method<sup>50)</sup>. The fact of  $\phi < 1$  means that a proton is stronger as hydrogen bond donor than a deuteron. And usually the maximum value of  $\phi^\ddagger$  is considered to be unity. The maximum value of  $k_1/k_0$  can be determined from Eq. (14). When  $m=3$  the maximum value is 2.5, 1.8 for  $m=2$ , and 1.4 for  $m=1$ . Since the experimental value for  $k_1/k_0$  observed in this investigation is  $1.92 \pm 0.12$  as calculated for 2-phenylpropionitrile (Table 3-2), the case of  $m \leq 2$  seems to be improbable. Other considerations of the solvent isotope effect on proton transfer and methanolysis in methanol<sup>51)</sup> suggested  $m=3$  as the most probable number of solvent molecule within the first solvation sphere. The difference of the partial molar volume of the methoxide ion in methanol and methanol- $d_1$  would be expected so small that the fractionation factor  $\phi_{\text{CH}_3\text{O}^-}$  may be reasonably assumed to be little dependent on pressure.

The physical meaning of  $m$  and  $p$  seems to correspond to the solvation number derived from the electrical conductivity measurement. It is known that the solvation number derived from the electrical conductivity measurement usually shows the smallest number among those by other methods, which is considered to be the number of the first solvation sphere<sup>52)</sup>. Nakahara *et al.*<sup>53)</sup> have reported that the solvation number for potassium and chloride ion in aqueous solution does not change so widely with pressure within experimental error.

Under the assumption that both  $\phi_{\text{CH}_3\text{O}^-}$  and  $m$  do not change with pressure, the value of  $\phi^\ddagger$  is calculated when  $\phi_{\text{CH}_3\text{O}^-}=0.74$  and  $m=3$  (Table 6). The result implies that the equilibrium abundance of deuterium at the transition state is greater than that of the methoxide ion. At a fixed value

48) See for example, D. J. Hupe and D. Wu, *J. Am. Chem. Soc.*, **99**, 7653 (1977) and references cited therein.

49) A. J. Kresge, *Pure Appl. Chem.*, **8**, 243 (1964)

50) V. Gold and S. Grist, *J. Chem. Soc., (B)* **1971**, 1665

51) V. Gold and S. Grist, *ibid.*, (B) **1971**, 2282 and references cited therein.

52) J. O' M. Bockris, *Quart. Rev.*, **3**, 173 (1949); R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," Butterworth, London (1965), Chap. 3.

53) M. Nakahara, K. Shimizu, and J. Osugi, *This Journal*, **42**, 12 (1972)

Table 6 Transition state fractionation factor for  $m=3$  and  $\phi_{\text{CH}_3\text{O}^-}=0.74$ 

| $P/\text{kg cm}^{-2}$ | $p=1$                              | $p=2$                              | $p=3$                              |
|-----------------------|------------------------------------|------------------------------------|------------------------------------|
| 1                     | $0.78 \pm 0.05(0.831)^{\text{a)}}$ | $0.88 \pm 0.03(0.911)^{\text{a)}}$ | $0.92 \pm 0.02(0.940)^{\text{a)}}$ |
| 500                   | $0.77 \pm 0.04$                    | $0.88 \pm 0.02$                    | $0.92 \pm 0.01$                    |
| 1000                  | $0.74 \pm 0.07$                    | $0.86 \pm 0.04$                    | $0.91 \pm 0.02$                    |
| 2000                  | $0.78 \pm 0.10$                    | $0.88 \pm 0.06$                    | $0.92 \pm 0.04$                    |
| 3000                  | $0.75 \pm 0.06$                    | $0.86 \pm 0.04$                    | $0.91 \pm 0.02$                    |

a) ref. 20

of  $p$  the value of  $\phi^\ddagger$  does not change so much with pressure. Although some problems remain unsolved, it may be concluded that the solvation number of the transition state would not change remarkably with pressure.

#### Acknowledgment

The author is grateful to Professor J. Osugi for his helpful suggestions and discussions during the course of this work, and indebted to Dr. M. Sasaki for his many valuable comments. He also wishes to thank Dr. K. Hara for his continued interest and encouragement.

*Laboratory of Physical Chemistry  
Department of Chemistry  
Faculty of Science  
Kyoto University  
Kyoto 606, Japan*