THE REACTION OF NITRILE WITH α-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 (XC_6H_4 CY_1Y_2 CN: $X=CH_3O$, CH_3, Cl, $Y_1=H$, D, $Y_2=H$, D; $X=H$, $Y_1=CH_3$, $Y_2=H,D$) 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 $-(9.5\pm2.5)$ to $-(13.7\pm1.8)$ cm³/mol for the iminoether formation, and from $+(18.2\pm2.9)$ to $+(7.7\pm2.7)$ cm³/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 ±6 cm³/mol. For example, the activation volume difference changes from -5.2 to $+6.6$ cm³/mol in the nitration of the substituted benzene[1]. 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[2~4].

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[5] from Klopman's perturbed molecular orbital theory[6]. The usefulness of the expression has been confirmed by the experimental results of various types of reactions[5]. 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.[7] 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[8] 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[9] 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.[10] 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.[9] and the author[5] have determined the volume change of the iminoether formation in methanol.

Bengelsdorf[11,12] 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 α-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 α-hydrogens in methanol at high pressure[13], 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 α-hydrogens do not usually react via the Thorpe-type mechanism in CH_3O^-–CH_3OH even though a proton is abstracted by a methoxide ion.[5,14]

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

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* $1 kg/cm^2 = 0.9807$ bar $= 0.9678$ atm $= 0.9807 \times 10^5$ 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)

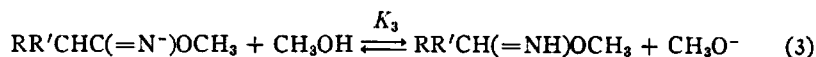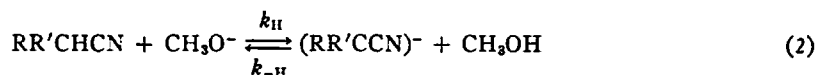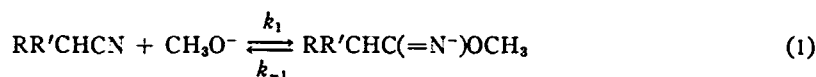11) I. S. Bengelsdorf, *J. Am. Chem. Soc.*, **80**, 1422 (1958)

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[15-23]. 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.[24] 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.[25] 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_2O, and have discussed the reaction mechanism[26]. Palmer and Kelm have determined the activation velumes for hydrogen transfer reactions in toluene between 2,2-diphenyl-1-picrylhydrazyl (DPPH) and a series of substituted phenols[27]. 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_2 in $CH_3CO_2^- - CH_3OH$ at high pressure[28]. The author has determined the activation volume of the reaction between phenylacetonitrile-d_2 and methoxide ion, and reported the importance of the charge delocalization effect[5].

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

$$RR'CHCN + CH_3O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} RR'CHC(=N^-)OCH_3 \qquad (1)$$

$$RR'CHCN + CH_3O^- \underset{k_{-II}}{\overset{k_{II}}{\rightleftharpoons}} (RR'CCN)^- + CH_3OH \qquad (2)$$

$$RR'CHC(=N^-)OCH_3 + CH_3OH \overset{K_3}{\rightleftharpoons} RR'CH(=NH)OCH_3 + CH_3O^- \qquad (3)$$

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 α-hydrogens in $CH_3O^- - CH_3OH$ 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. Javaid, 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)

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Experimental

Materials

p-Chlorophenylacetonitrile, (Nakarai Chemicals Ltd.,) was recrystallized twice from 95% etha-nol. *p*-Methylphenylacetonitrile, *p*-methoxyphenylacetonitrile, and 2-phenylopionitrile (Merck) were distilled twice under nitrogen at reduced pressure. (±)-2-Phenylpropionic acid was prepared by the oxidation of (±)-2-phenylproionitrile[19]. (+)-2-Phenylpropionic acid (lit. $[\alpha]_D^{25} = +75.5°$ in ethanol[19]) and (−)-2-phenylpropionic acid (lit. $[\alpha]_D^{25} = -76.5°$ in ethanol[19]) were separated by the method of Petterson *et al.*[29] (+)-2-Phenylpropionitrile ($[\alpha]_D^{25} = +14.2°$ in methanol, lit. $[\alpha]_D^{25} = +13.7°$ in 50% alcohol[30], and $[\alpha]_{436}^{25} = +39.7°$ in methanol[19]) and (−)-2-phenylpropionitrile ($[\alpha]_D^{25} = -14.3°$ in methanol, lit. $[\alpha]_{436}^{25} = -43.4°$ in methanol[19]) were synthesized from the corresponding acid by the method of Levene *et al.*[30] No residual activity could be detected after the racemization of (+)-2-phenylpropionitrile and (−)-2-phenylpropionitrile in $CH_3O^- - CH_3OH$ solution. After the distillation from silver nitrate and sodium methoxide, methanol was dried at least for 10 h by reflux-ing 3 dm³ batches over 10 g of aluminum powder and 2 g of merculic 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[31].

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[32].

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 ±2.0%.

It has been reported that the racemization rate of 2-phenylpropionitrile is as same as the hydrogen-deuterium exchange rate[19]. The racemization rate of the optically active 2-phenylpropio-nitrile at high pressure was determined, after quenching, by JASCO DIP-4 polarimeter which has an accuracy of ±0.002° in the full scale of ±2°.

The high pressure generating systems, the reaction cell, and the other general experimental tech-nique were described previously[5,13].

Results and Discussion

Rates of the Iminoether Formation

29) K. Pettersson, *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,

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

where $k'_1 = k_1[CH_3O^-]$ and $k'_{-1} = k_{-1}K_3^{-1}[CH_3O^-]$ 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[5]. 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[n]

$P/kg\ cm^{-2}$	$p-ClC_6H_4CH_2CN$	$C_6H_5CH_2CN$	$p-CH_3C_6H_4CH_2CN$	$p-CH_3OC_6H_4CH_2CN$	$C_6H_5CH(CH_3)CN$
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 $N(Et)_3$—CH_3OH and in CH_3OK—CH_3OH at 313.2 K

$P/kg\ cm^{-2}$	$k_1 \times 10^3$ / kg mol^{-1} s^{-1}		$k_{-1}K_3^{-1} \times 10^3$ / kg mol^{-1} s^{-1}	
	$N(Et)_3$ [a]	CH_3OK	$N(Et)_3$ [a]	CH_3OK
1	0.700±0.041	0.674±0.015	5.55±0.34	5.35±0.12
1500	1.17 ±0.04	1.17 ±0.04	4.40±0.15	4.38±0.15
3000	1.84 ±0.03	1.69 ±0.02	3.52±0.05	3.23±0.03

a) The dissociation constant of $N(Et)_3$ at high pressure has been already reported.[32]

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

$P/kg\ cm^{-2}$	$p-CH_3OC_6H_4CH_2CN$		$C_6H_5CH(CH_3)CN$	
	$\dfrac{k_1 \times 10^3}{kg\ mol^{-1}\ s^{-1}}$	$\dfrac{k_{-1}K_3^{-1} \times 10^3}{kg\ mol^{-1}\ s^{-1}}$	$\dfrac{k_1 \times 10^3}{kg\ mol^{-1}\ s^{-1}}$	$\dfrac{k_{-1}K_3^{-1} \times 10^3}{kg\ mol^{-1}\ s^{-1}}$
1	0.098±0.006	1.43±0.07	0.068±0.006	1.93±0.11
500	0.127±0.006	1.40±0.06	0.084±0.005	1.81±0.07
1000	0.155±0.011	1.36±0.08	0.110±0.006	1.79±0.07
1500	0.191±0.021	1.31±0.14	0.140±0.009	1.73±0.09
2000	0.240±0.011	1.34±0.05	0.177±0.006	1.55±0.04
3000	0.360±0.010	1.34±0.03	0.272±0.012	1.38±0.05

$P/\text{kg cm}^{-2}$	$p-ClC_6H_4CH_2CN$		$C_6H_5CH_2CN$ [a]		$p-CH_3C_6H_4CH_2CN$	
	$\dfrac{k_1 \times 10^3}{\text{kg mol}^{-1}\,\text{s}^{-1}}$	$\dfrac{k_{-1}K_s^{-1} \times 10^3}{\text{kg mol}^{-1}\,\text{s}^{-1}}$	$\dfrac{k_1 \times 10^3}{\text{kg mol}^{-1}\,\text{s}^{-1}}$	$\dfrac{k_{-1}K_s^{-1} \times 10^3}{\text{kg mol}^{-1}\,\text{s}^{-1}}$	$\dfrac{k_1 \times 10^3}{\text{kg mol}^{-1}\,\text{s}^{-1}}$	$\dfrac{k_{-1}K_s^{-1} \times 10^3}{\text{kg mol}^{-1}\,\text{s}^{-1}}$
1	0.700±0.041	5.55±0.34	0.24	4.1	0.110±0.006	1.55±0.07
500	0.992±0.040	5.10±0.21			0.140±0.008	1.52±0.07
1000	1.00 ±0.03	4.80±0.11	0.36	3.4	0.175±0.006	1.50±0.04
1500	1.17 ±0.04	4.40±0.15			0.220±0.015	1.46±0.10
2000	1.39 ±0.05	4.20±0.09	0.55	3.1	0.270±0.011	1.44±0.05
3000	1.84 ±0.03	3.52±0.05	0.78	2.6	0.381±0.015	1.37±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)[5] by neglecting the secondary isotope effect.

$$1-\frac{2[RCH_2CN]+[RCHDCN]}{2a}=\left(1-\frac{2[RCH_2CN]_0+[RCHDCN]_0}{2a}\right)\exp\left(-k'_Dt\right), \quad (5)$$

where $k'_D=k_D[CH_3O^-]$, $a=[RCH_2CN]_0+[RCHDCN]_0+[RCD_2CN]_0$, the subscript 0 refers to the initial concentration, and $(2[RCH_2CN]+[RCHDCN])/2a$ is measured from the integrated NMR

Table 3-2   Numerical values of $k/\text{kg mol}^{-1}\text{s}^{-1}$ of the proton/deuteron tranfer reaction in CH_3OH or CH_3OD at 303.2 K

$P/\text{kg cm}^{-2}$	$p-ClC_6H_4CD_2CN$ [a]	$C_6H_5CD_2CN$ [b]	$p-CH_3C_6H_4CD_2CN$ [a]	$p-CH_3OC_6H_4CD_2CN$ [a]	$C_6H_5CD(CH_3)CN$ [a]
1	6.5±0.3	4.0	0.850±0.061	0.150 ±0.010	0.129 ±0.006
500	4.9±0.4		0.649±0.055	0.113 ±0.012	0.110 ±0.007
1000	3.9±0.1	2.0	0.536±0.047	0.104 ±0.009	0.103 ±0.008
1500	3.2±0.3		0.475±0.047	0.0900±0.0061	0.0945±0.0019
2000	2.7±0.1	1.2	0.423±0.030	0.0857±0.0062	0.0913±0.0062
3000	2.4±0.2	0.9	0.366±0.034	0.0701±0.0022	0.0833±0.0039

$P/\text{kg cm}^{-2}$	$C_6H_5CH(CH_3)CN$ [a]	$C_6H_5CH(CH_3)CN$ [c]
1	0.285±0.011	0.548±0.028
500	0.253±0.009	0.483±0.010
1000	0.244±0.016	0.447±0.034
1500		
2000	0.210±0.027	0.406±0.018
3000	0.191±0.008	0.351±0.008

a) in CH_3OH b) ref. 5   c) in CH_3OD

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,

$$C_6H_5CH(CH_3)CN + CH_3O^- \underset{k_{-H}}{\overset{k_H}{\rightleftharpoons}} (C_6H_5C(CH_3)CN)^- + CH_3OH, \qquad (6)$$

$$C_6H_5CD(CH_3)CN + CH_3O^- \underset{k_{-D}}{\overset{k_D}{\rightleftharpoons}} (C_6H_5C(CH_3)CN)^- + CH_3OD, \qquad (7)$$
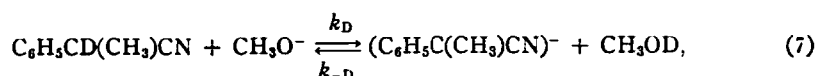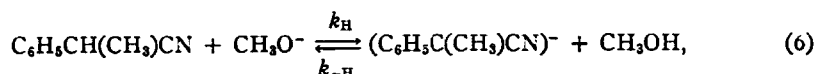
where $K_H = k_H/k_{-H}$, $K_D = k_D/k_{-D}$, and $k_{-H}/k_{-D} = (k_H/k_D)\cdot(K_D/K_H) = (k_H/k_D)/K$. The equilibrium constant K of the exchange reaction is represented as,

$$C_6H_5CH(CH_3)CN + CH_3OD \overset{K}{\rightleftharpoons} C_6H_5CD(CH_3)CN + CH_3OH. \qquad (8)$$
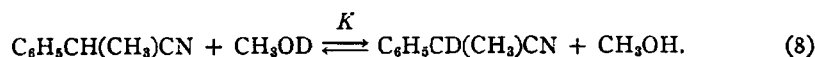
The exchange equilibrium constant can be determined in the mixture of CH_3OH-CH_3OD by using the potassium methoxide as a catalyst. Figure 1 shows the equilibrium constant against the fraction of the mixture composed of CH_3OH and CH_3OD at 1 atm and 303.2 K. The equilibrium constant K does not change so much with pressure in mixtures of different CH_3OH-CH_3OD composition as shown in Fig. 2. So the value of K in pure CH_3OH, which is estimated to be around 1.8 by extrapolating to [CH_3OD]→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±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 exsist two main theoretical approaches to the study of the transition state of the proton
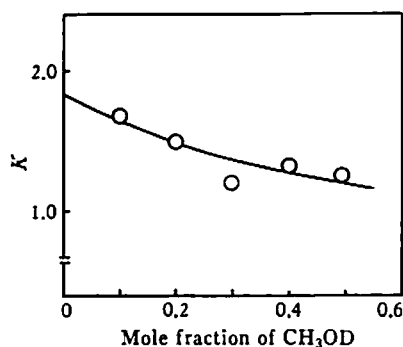

Fig. 1 Equilibrium constant for D–H exchange between $C_6H_5CH(CH_3)CN$ and CH_3OD in different mixture of CH_3OH-CH_3OD at 1 atm and 303.2 K.

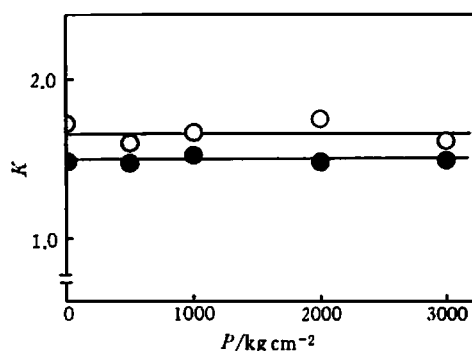Fig. 2 Pressure dependence of K at 303. 2K.
○: 11.6 mol% of CH_3OD,
●: 19.9 mol% of CH_3OD.

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transfer: the simple three center model, $X \cdots H \cdots Y$[33~35], and the correction of the tunneling effect[36]. 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 repotred in relation to the symmetry of the transition state[37]. 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 (Δr) along the molecular axis.

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

where Δ represents the departure of cach 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[35]. 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,

$$-\frac{RT}{P-1}\ln\frac{k^{(P)}}{k^{(1)}} = \Delta V_e^{*}\cdot\frac{B+1}{P-1}\ln\frac{B+P}{B+1} + \Delta V_c^{*} , \qquad (10)$$
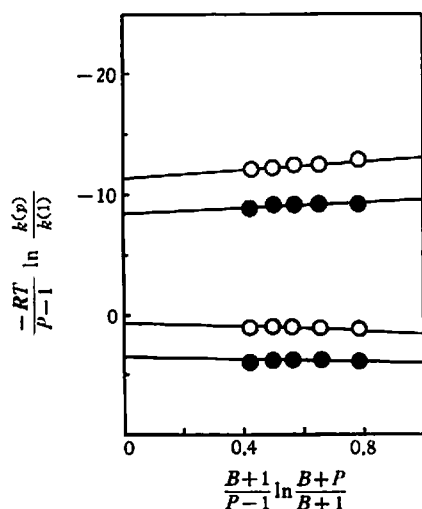

Fig. 3 Pressure dependence of k_1 and $k_{-1}K_3^{-1}$ at 313.2 K.
○: p-CH$_3$C$_6$H$_4$CH$_2$CN,
●: p-ClC$_6$H$_4$CH$_2$CN.

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.

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

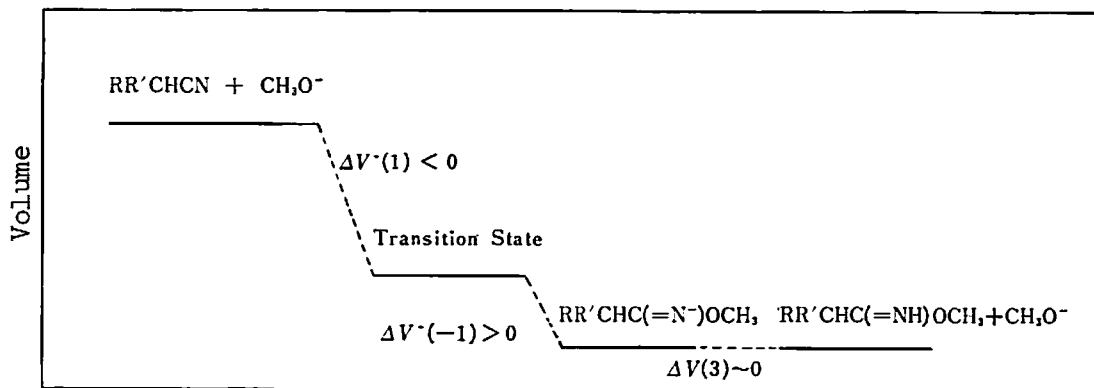| Nitrile	$\dfrac{\Delta V_c^*(1)}{cm^3mol^{-1}}$	$\dfrac{\Delta V_e^*(1)}{cm^3mol^{-1}}$	$\dfrac{\Delta V^*(1)}{cm^3mol^{-1}}$	$\dfrac{\Delta V_c^*(-1)-\Delta V_c(3)}{cm^3mol^{-1}}$	$\dfrac{\Delta V_e^*(-1)-\Delta V_e(3)}{cm^3mol^{-1}}$	$\dfrac{\Delta V^*(-1)-\Delta V(3)}{cm^3mol^{-1}}$
$p-ClC_6H_4CH_2CN$	-8.3 ± 1.1	-1.2 ± 1.5	-9.5	$+3.3\pm1.0$	$+1.3\pm1.5$	$+4.6$
$C_6H_5CH_2CN$ [a]	-10.2	-1.0	-11.2	$+4.1$	~0	$+4.1$
$p-CH_3C_6H_4CH_2CN$	-10.9 ± 1.1	-1.8 ± 1.5	-12.7	$+0.5\pm0.9$	$+1.3\pm1.3$	$+1.8$
$p-CH_3OC_6H_4CH_2CN$	-10.4 ± 1.0	-2.7 ± 1.7	-13.1	$+0.2\pm1.0$	$+1.6\pm1.6$	$+1.8$
$C_6H_5CH(CH_3)CN$	-11.5 ± 1.0	-2.2 ± 1.8	-13.7	$+2.3\pm1.0$	$+0.6\pm1.4$	$+2.9$

a) ref. 5

Fig. 4   Volume profile of the iminoether formation.

where ΔV_e^* and ΔV_c^* 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[38] 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 $\Delta V_e^*(1)/\Delta V_c(1)$ indicates a degree of the geometric symmetry of the transition state of step (1). The value of $\Delta V_c(1)$ can not be experimentally determined, but calculated as $\Delta V_c(1)=\Delta V_c^*(1)-\Delta V_c^*(-1)$, if $\Delta V_c^*(-1)$ is estimated by other data. In Table 4 the term $\Delta V_c^*(-1)-\Delta V_c(3)$ is given, and the quantity of $\Delta V_c(3)$ is assumed to be much smaller than $\Delta V_c^*(-1)$ for the above mentioned reason. So, using the experimentally determined terms, $\Delta V_c(1)$ is approximated as,

$$\Delta V_c(1)\simeq\Delta V_c^*(1)-\{\Delta V_c^*(-1)-\Delta V_c(3)\}, \tag{11}$$

and the value of $\Delta V_c^*(1)/\Delta V_c(1)$ can be easily calculated*; for p-ClC$_6$H$_4$CH$_2$CN: 0.67, C$_6$H$_5$CH$_2$CN:

* The mean value of ΔV_c (1) (-12.4 cm³/mol) was used.
38) B. B. Owen and S. R. Brinkley, *Phys. Rev.*, **64**, 32 (1943)

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

The value of $\Delta V_e(1)+\Delta V_e(3)(=V_e{}^{*}(1)-\{\Delta V_e{}^{*}(-1)-\Delta V_e(3)\})$ is slightly negative. even though both iminoether and nitrile are the neutral molecules. An iminoether has the functional groups of $-$OCH$_3$ and $=$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[39]. For example, it has been reported that the formation of a hydrogen bond in O–H···O is accompanied with a volume contraction about 3.8 cm^3/mol[40]. 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, $\Delta V_e{}^{*}$ and $\Delta V_c{}^{*}$ are obtained (Table 5). It has been known that most of the proton or hydrogen transfer from carbon acids accompanies the negative activation volume[24~28], 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 $\Delta V_e{}^{*}$(D) or $\Delta V_e{}^{*}$(H) is larger than the corresponding $\Delta V_c{}^{*}$ suggests that there exists a large charge delocalization effect at the transition state. This is also supported by the study of Bergman $et\ al.$[17,19] who have measured the rate
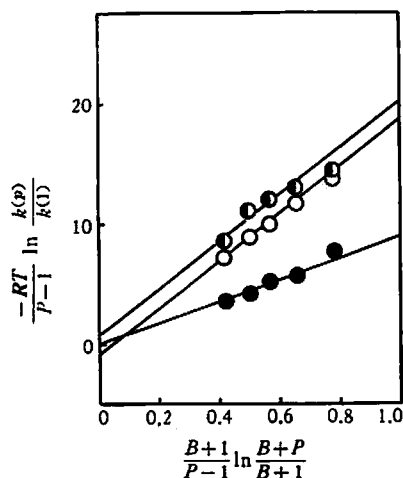

Fig. 5 Pressure dependence of k_D in CH$_3$OH at 303.2 K.
  ◐: p-ClC$_6$H$_4$CD$_2$CN,
  ○: p-CH$_3$C$_6$H$_4$CD$_2$CN,
  ●: C$_6$H$_5$CD(CH$_3$)CN.

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	$\Delta V_c^{\div}/cm^3mol^{-1}$	$\Delta V_c^{\div}/cm^3mol^{-1}$	$\Delta V^{\div}/cm^3mol^{-1}$
$p-ClC_6H_4CD_2CN$	CH_3OH	$+0.9\pm1.2$	$+18.9\pm1.7$	$+19.8$
$C_6H_5CD_2CN$ [a]	CH_3OH	$+4$	$+20$	$+24$
$p-CH_3C_6H_4CD_2CN$	CH_3OH	-0.7 ± 1.6	$+18.6\pm2.2$	$+17.9$
$p-CH_3OC_6H_4CD_2CN$	CH_3OH	$+0.9\pm1.0$	$+13.0\pm1.7$	$+13.9$
$C_6H_5CD(CH_3)CN$	CH_3OH	0.0 ± 0.8	$+8.9\pm1.3$	$+8.9$
$C_6H_5CH(CH_3)CN$	CH_3OH	$+0.3\pm1.4$	$+6.7\pm1.9$	$+7.0$
$C_6H_5CH(CH_3)CN$	CD_3OD [b]	$+0.1\pm1.1$	$+7.9\pm1.6$	$+8.0$

a) ref. 5   b) The value of B is assumed to be same as that of CH_3OH.

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.[28] have reported the activation volume is $-4 cm^3/mol$ for the deuteron transfer reaction between phenylacetonitrile-d_2 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[41] and the equilibrium (12).

$$CH_3CO_2^- + CH_3OH \overset{K_{Ac}}{\rightleftharpoons} CH_3O^- + CH_3CO_2H \qquad (12)$$
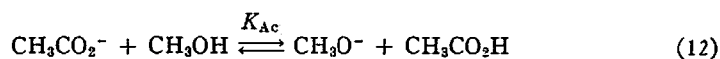
As the dissociation constant of acetic acid in methanol[42] and the autoprotolysis constant of methanol[43] at 1 atm and 298.2 K have been reported, the equilibrium constant of Eq. (12) can be calculated as 8.4×10^{-8} mol/dm³. In their experimental condition the acetate ion concentration is so high that the exsistence of the methoxide ion ($\sim10^{-4}$ mol/dm³) can not be neglected.

As mentioned above $\Delta V_e^{\div}$ is qualitatively understood by the electrostatic solvation model, though Hubbard et al.[24] 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, $\Delta V_c^{\div}$ obtained in the present study is around zero, or sometimes positive. These facts would indicate that the distance between the α-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. Suszka, *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 $-(6\sim10)$ cm^3/mol[44]. In other experiments the structural change of the proton or hydrogen transfer reaction is often considered to be $-(13\sim15)$ cm^3/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^3/mol[27]. This value, however, should unavoidably include the volume term coming from the steric hindrance.

Although we believe that in most cases $\Delta V_c^{\neq}$ mainly represents the structural change, the difficulty may arise in order to interpret the meaning of $\Delta V_c^{\neq}$ 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[45]. 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 $\Delta V_c^{\neq}$.

Kelm and his co-workers[27] have reported the independence of $\Delta V^{\neq}$ from the substituent in a radical reaction. Zhulin et al.[46] 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$_2$Cl$_2$. The difference of the activation volume largely depends on the substituent. Its maximum difference is 8.9 cm^3/mol. As the reaction should proceed via radical mechanism, the change of $\Delta V^{\neq}$ 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 $\Delta V_e^{\neq}$ is predominantly influenced. But at present the substituent effect on $\Delta V_e^{\neq}$ 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, α-carbon of the resulting anion of 2-phenylpropionitrile would not be thoroughly in sp^2 state judging from the steric hindrance between methyl group and ortho-hydrogen atom of the phenyl ring.

On the problem of the differece of the pressure effect between proton and deuteron transfer, there appeared no appreciable change on either $\Delta V_c^{\neq}$ or $\Delta V_e^{\neq}$ 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"[47] 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[48] 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[49],

$$\frac{k_n}{k_0} = \frac{(1-n+n\phi^{\neq})^p}{(1-n+n\phi_{CH_3O^-})^m},\tag{13}$$

where n is the fraction of deuterium, $\phi^{\neq}$ and $\phi_{CH_3O^-}$ 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,

$$\frac{k_1}{k_0} = \frac{(\phi^{\neq})^p}{(\phi_{CH_3O^-})^m}.\tag{14}$$

Gold and Grist have determined the value of $\phi_{CH_3O^-}$ as 0.74 by the NMR method[50]. The fact of $\phi < 1$ means that a proton is stronger as hydrogen bond donor than a deuteron. And usually the maximum value of $\phi^{\neq}$ 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 ± 0.12 as calculated for 2-phenyl-propionitrile (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[51] 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 $\phi_{CH_3O^-}$ 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[52]. Nakahara et al.[53] 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 $\phi_{CH_3O^-}$ and m do not change with pressure, the value of $\phi^{\neq}$ is calculated when $\phi_{CH_3O^-}=0.74$ 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)

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Table 6   Transition state fractionation factor for $m=3$ and $\phi_{CH_3O^-}=0.74$

$P/\mathrm{kg\ cm^{-2}}$	$p=1$	$p=2$	$p=3$
1	$0.78\pm0.05(0.831)$ [a]	$0.88\pm0.03(0.911)$ [a]	$0.92\pm0.02(0.940)$ [a]
500	0.77 ± 0.04	0.88 ± 0.02	0.92 ± 0.01
1000	0.74 ± 0.07	0.86 ± 0.04	0.91 ± 0.02
2000	0.78 ± 0.10	0.88 ± 0.06	0.92 ± 0.04
3000	0.75 ± 0.06	0.86 ± 0.04	0.91 ± 0.02

a) ref. 20

of p the value of $\phi^{\ast}$ does not change so much with pressure. Although some problems remain un-solved, it may be concluded that the solvation number of the transition state would not change re-markably with pressure.

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