

Influence of Pressure on Primary Kinetic Isotope Effects of the Proton-Transfer Reaction between 4-Nitrophenyl-nitromethane and 1, 1', 3, 3'-Tetramethylguanidine in Toluene and Dichloromethane

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Influence of pressure on the primary kinetic isotope effects of the fast proton-transfer reaction between title compounds, which showed a significant tunneling contribution, was studied in toluene and dichloromethane at 25°C up to 1000 bar by means of a high-pressure stopped-flow method. In dichloromethane there is no appreciable difference in the volume of activation between the proton- and deuterium-transfer reaction; $\Delta V^\ddagger(\text{H}) = -15.3 \pm 1.5$, $\Delta V^\ddagger(\text{D}) = -14.6 \pm 1.7$ cm³mol⁻¹, and there is no pressure effect on the kinetic isotope rate ratio $k^{\text{H}}/k^{\text{D}}$ ($=10.7 \pm 0.2$) up to 1000 bar. On the other hand, $\Delta V^\ddagger$ in toluene is isotope-dependent; $\Delta V^\ddagger(\text{H}) = -18.8 \pm 1.9$, $\Delta V^\ddagger(\text{D}) = -24.2 \pm 3.0$ cm³mol⁻¹, and $k^{\text{H}}/k^{\text{D}}$ decreases from 11.9 at 1 bar to 9.3 at 1000 bar. The results are discussed in comparison with those of other proton/deuterium-transfer reaction.

KEY WORDS: Tunneling/ Volume of activation/ High-pressure stopped-flow/

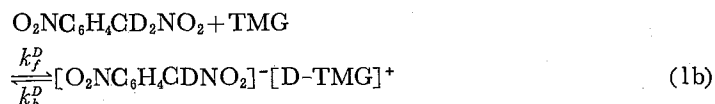
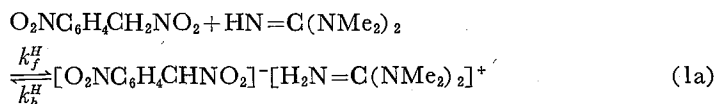
INTRODUCTION

Recently the primary kinetic isotope effect of the proton-transfer reaction has been extensively studied from the theoretical and phenomenological viewpoints.^{1,2)} Many models have been proposed in order to explain the numerical values of the primary kinetic isotope effect.³⁻⁵⁾ Westheimer³⁾ has predicted that the kinetic isotope rate ratio $k^{\text{H}}/k^{\text{D}}$ should be maximum in the symmetrical transition state if tunneling is not taken into account. Many investigators⁶⁾ have presented discussions along these lines. However, the explanation of such a maximum only by Westheimer's treatment has been questioned;⁷⁾ there is another theoretical treatment based on the tunneling correction.⁸⁾ About the relation between the ratio $k^{\text{H}}/k^{\text{D}}$ and the solvent characters in the proton-transfer reaction between 4-nitrophenylnitromethane (4NPNM) and 1, 1', 3, 3'-tetramethylguanidine (TMG), Caldin and Mateo⁹⁾ have found very interesting results that the variation of $k^{\text{H}}/k^{\text{D}}$ with solvents at 298K was between 10 and 50; the higher the dielectric constant the smaller is the rate ratio. And in the proton-transfer reaction between 2, 4, 6-trinitrotoluene (TNT) and TMG the dependences of $k^{\text{H}}/k^{\text{D}}$ on the dielectric constant and on the steric effect of solvent were studied;^{10,11)} the rate ratio for this reaction was less dependent on both factors than for the 4NPNM+TMG system. However, the dependence of $k^{\text{H}}/k^{\text{D}}$ on the solvent characters has ever received less attention except in the above instances.

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There are only a few reports concerning the ratio k^H/k^D of the proton-transfer reaction in solution at high pressure although the informations obtained by pressure effect are recognized to be invaluable. Palmer and Kelm¹²⁾ have determined the volumes of activation for hydrogen transfer reaction in toluene between 2, 2-diphenyl-1-picrylhydrazyl (DPPH) and a series of substituted phenols. Brower *et al.*¹³⁾ have reported the deuterium-transfer reaction of phenylacetonitrile- d_2 in MeCO_2^- - CH_3OH at high pressure. Inoue¹⁴⁾ has investigated intensively the volume profile of the proton/deuteron-transfer reactions of various phenylacetonitriles in MeO^- - CH_3OH and has postulated a method to divide the structural and electrostrictive volume terms by means of a generalized perturbation theory. But all of these authors concluded that no significant pressure influence on the kinetic isotope effects was found. While these systems have shown normal and quite small isotope effects, Isaacs *et al.*¹⁵⁾ have found that the kinetic isotope rate ratio of the slow hydride-transfer reaction larger than the normal value, which was believed to be to the tunneling contribution, is appreciably pressure dependent. But, to our knowledge no paper has appeared on the pressure effects upon the rate ratio k^H/k^D in proton-transfer reactions which are too fast to be followed by the usual high pressure technique.

In this paper we deal with the proton/deuteron transfer reaction between 4NPNM and TMG [Eqs. (1a) and (1b)] in toluene (less polar solvent) and in dichloromethane (more polar solvent) investigated by means of a high-pressure stopped-flow method to discuss pressure influence on the primary kinetic isotope effect.



EXPERIMENTAL

Materials. 4-Nitrophenylnitromethane (4NPNM) was synthesized from 4-nitrobenzyl bromide and silver nitrite;¹⁶⁾ colorless needle, mp. 90, 5–91°C (lit. 91°C). Deuteration of methylene group of 4NPNM was done in the purified dioxane in a glove box under a nitrogen atmosphere in the dark;⁹⁾ to the solution of 15 ml of *ca.* 50 mM 4NPNM, was added 2 ml of dilute solution (*ca.* 0.1 M) of NaOD in D_2O . After standing overnight at 10–15°C, this mixture was neutralized with a few drops of DCl in D_2O and the solvent evaporated off in vacuum. These procedures were repeated more than four times, and the solid 4NPNM- d_2 was recrystallized from toluene; mp. 89–90°C. The degree of deuteration was ascertained to be more than 98% by means of a NMR spectrum.

1, 1', 3, 3'-Tetramethylguanidine (TMG, Nakarai Chemicals Co. Ltd.) was dried over potassium hydroxide and then distilled under a nitrogen atmosphere; bp. 161°C (lit. 161°C).

Toluene (spectrograde reagent, Merck) and dichloromethane (spectrograde reagent,

Nakarai Chemicals Co. Ltd.), as solvent, were used without further purification.

Apparatus and Procedure. Absorption spectra were determined by a Shimadzu UV-200S spectrophotometer. Kinetic measurements at 1 bar (1 bar = 10^5 Pa) were carried out by a Union Giken RA-401 stopped-flow apparatus. At high pressure, the reaction rates were followed by means of a high-pressure stopped-flow apparatus; the details were published elsewhere.¹⁷⁾ This apparatus is enough for reactions from several milliseconds to a few minutes. In all measurements the temperature was kept at $25.0 \pm 0.5^\circ\text{C}$ by circulating thermostatted fluid.

The following weighed-in concentrations at 1 bar were used: 4NPNM- d_2 , 20–50 μM ; TMG, 1–15 mM in dichloromethane and 2–30 mM in toluene. The rate of the deuterium-transfer reaction was determined by monitoring the change of the absorption at 440 nm with time; the increase of the absorbance obeyed first-order kinetics when the base (TMG) existed in large excess over 4NPNM- d_2 . The observed rate constant k_{obs} was determined by the Guggenheim plot.

RESULTS

The reaction mixtures in toluene and dichloromethane show a broad absorption with

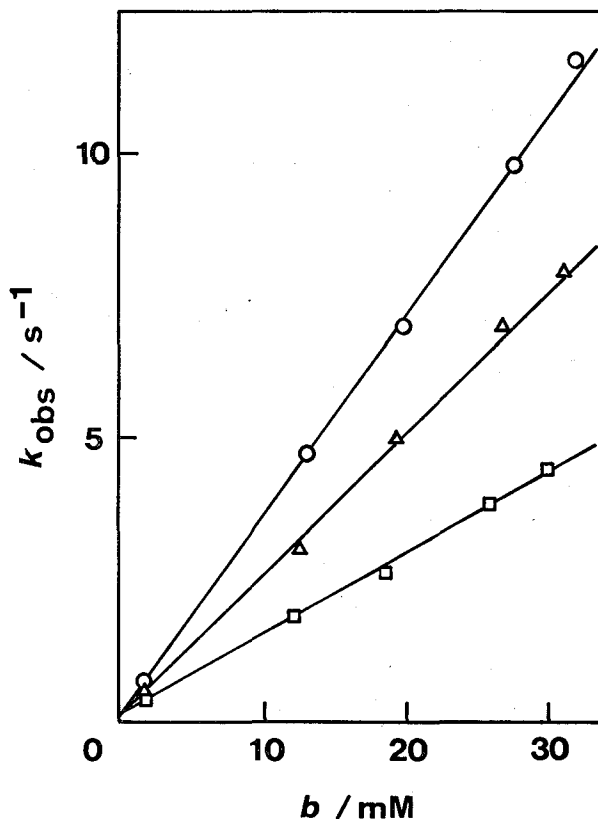


Fig. 1. Dependence of k_{obs} on TMG concentration in toluene at 25°C : $\square$, 1 bar; $\triangle$, 500 bar; $\circ$, 1000 bar.

a maximum at around 440 nm due to an ion pair, while each reactant is transparent in the visible region. The spectra of the proton- and deuterium-transferred ion pairs are almost identical.

The plot of k_{obs} against TMG concentration (b) gave a straight line at each pressure (Figs. 1 and 2), in agreement with Eq. (2).

$$k_{obs} = k_f^D b + k_b^D \quad (2)$$

In this equation, k_f^D and k_b^D are the forward and backward rate constants of the deuterium-transfer reaction. Since molar concentration unit is convenient to compare the rate constants at various conditions, we corrected the weighed-in concentration at 1 bar for the compression of each solvent to know b of molar unit at high pressure. In the plots of Figs. 1 and 2, compression was taken into account on the basis of data of Mopsik¹⁸⁾ for toluene and of Newitt *et al.*¹⁹⁾ for dichloromethane. Thus the values of k_f^D and k_b^D were determined from the dependence of k_{obs} on TMG concentration by a least-squares method. Rogn ²⁰⁾ reported that the kinetic behavior of the deuterium-transfer reaction between 4NPNM- d_2 and TMG in toluene did not obey the simple mechanism of (1b) but the complicated one including some consecutive steps concerned with 4NPNM- d_2 ,

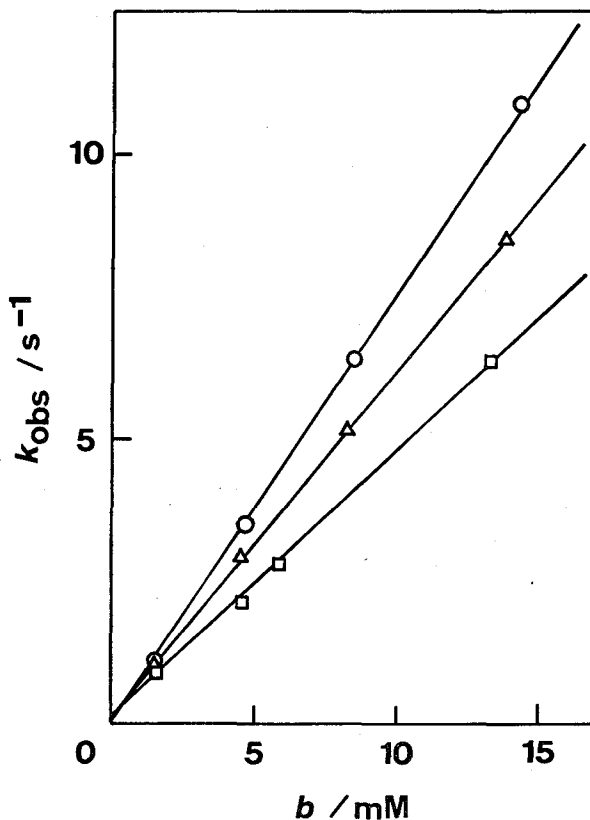
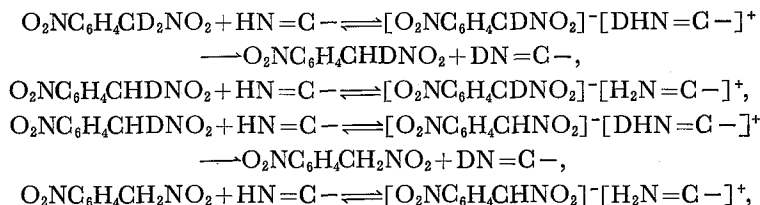


Fig. 2. Dependence of k_{obs} on TMG concentration in dichloromethane at 25°C: $\square$, 1 bar; $\triangle$, 500 bar; $\circ$, 1000 bar.

undeuterated 4NPNM and TMG:



so k_{obs} was not first-order with regard to TMG concentration. However, in our experiment the stopped-flow traces at each pressure obeyed a single exponential curve very well and a plot of k_{obs} against TMG concentration gave a straight line (Figs. 1 and 2). So the scrambling of the isotopic exchange of 4NPNM described above is considered to contribute minor importance to the observed reaction rate under the present experimental condition, and for the present we analyzed the rate data of this deuteron transfer reaction by the simple reaction mechanism (1b). Caldin and Mateo found no significant difference in k_f^D between TMG and TMG- d_1 as base, which also suggested that the isotopic scrambling was not reflected on the observed reaction rate. However it may be desirable to investigate the reaction rate using TMG- d_1 even at high pressure. The values of k_f^D are given in Table I with the values of k_f^H which were previously determined for the proton-transfer reaction,²¹⁾ but the values of k_b^D are too small to be reliable and are not recorded.

Table I. Rate Constants, k_f^H and k_f^D at 25°C

p/bar	$10^{-3}k_f^H/\text{M}^{-1}\text{s}^{-1}$		$10^{-2}k_f^D/\text{M}^{-1}\text{s}^{-1}$	
	toluene	dichloromethane	toluene	dichloromethane
1	1.72±0.03 (2.29±0.01 ^a) (1.74 ^b)	4.97±0.04	1.44±0.04 (0.58 ^a) (2.31 ^c)	4.67±0.07
250	1.94±0.02	5.62±0.04	1.93±0.04	5.37±0.07
500	2.46±0.02	6.68±0.04	2.50±0.05	6.11±0.04
750	2.77±0.01	7.38±0.06	2.94±0.04	6.94±0.04
1000	3.30±0.02	8.31±0.05	3.56±0.05	7.64±0.04

a) Ref. 9. b) Ref. 26 at 30°C. c) Ref. 20.

The volume of activation $\Delta V_f^\ddagger$ for the forward reaction was determined by

$$\left(\frac{\partial \ln k_f}{\partial p}\right)_T = -\frac{\Delta V_f^\ddagger}{RT} + \Delta n^\ddagger \kappa, \quad (3)$$

where, κ is the compressibility of the solvent, $\Delta n^\ddagger$ the difference of the number of molecules between the initial and the transition state, T the absolute temperature, and R the gas constant. In the present reaction, the value of $\Delta n^\ddagger$ is -1 for the forward reaction. The values of κ at 25°C were calculated from the literatures.^{18,19)} The plots of $\ln k_f^H$ and $\ln k_f^D$ against pressure were almost linear for both solvents (Figs. 3 and 4). The values of $\Delta V_f^\ddagger(\text{D})$ for the deuteron-transfer reaction are given in Table II together

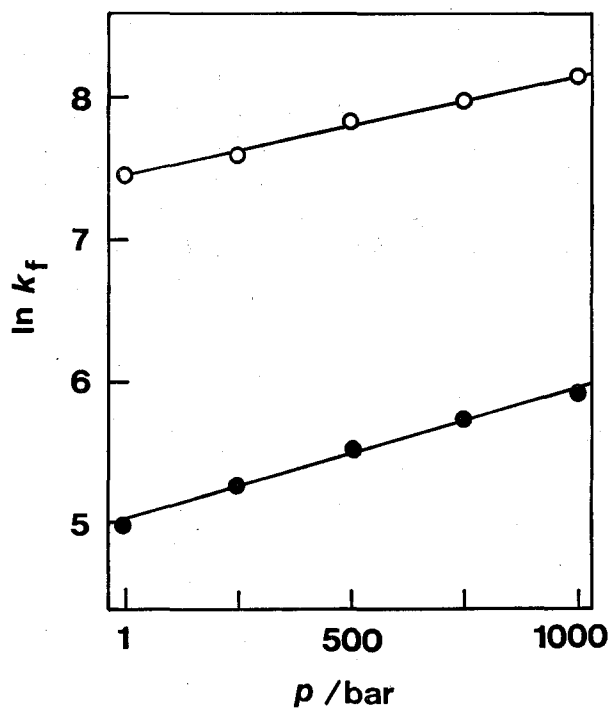


Fig. 3. Pressure dependence of $\ln k_f^H$ and $\ln k_f^D$ in toluene: ○, $\ln k_f^H$; ●, $\ln k_f^D$.

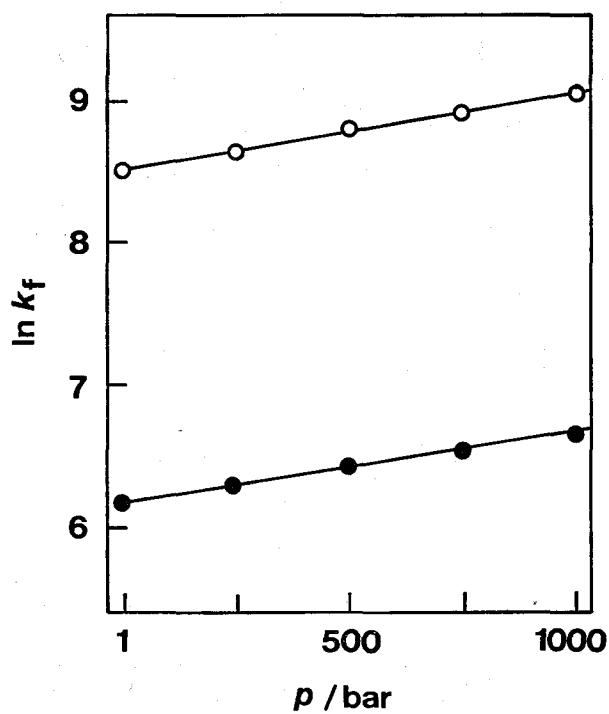


Fig. 4. Pressure dependence of $\ln k_f^H$ and $\ln k_f^D$ in dichloromethane: ○, $\ln k_f^H$; ●, $\ln k_f^D$.

Influence of Pressure on Primary Kinetic Isotope Effects

Table II. k_f^H/k_f^D and Volumes of Activation in Toluene and Dichloromethane

p/bar	k_f^H/k_f^D					$\Delta V_f^\ddagger(\text{H})$	$\Delta V_f^\ddagger(\text{D})$
	1	250	500	750	1000	$\text{cm}^3\text{mol}^{-1}$	$\text{cm}^3\text{mol}^{-1}$
toluene	11.9	10.1	9.8	9.4	9.3	-18.8 ± 1.9	-24.3 ± 3.0
dichloromethane	10.6	10.5	10.9	10.6	10.9	-15.3 ± 1.5	-14.6 ± 1.7

with the values of $\Delta V_f^\ddagger(\text{H})$ for the proton-transfer reaction,²¹⁾ and the kinetic isotope rate ratio k_f^H/k_f^D are shown in the same table.

DISCUSSION

Reaction Rate at Atmospheric Pressure. The rate constants at 1 bar in dichloromethane agree well with those of Caldin and Mateo,⁹⁾ but in toluene disagree with those of either Caldin and Mateo⁹⁾ or Rogne.²⁰⁾ In the present results the uncertainty of the rate constants is within a few percent, and the value of k_f^D lies between Caldin and Mateos' and Rogne's, while the reason of disagreement is incomprehensible. The rate constant of the forward reaction k_f^D for dichloromethane is larger than that for toluene. These kinetics are in accord with the view that this reaction involves the formation of a polar transition state since it is, in general, more stabilized in the higher polarity of solvent. The ratio k_f^H/k_f^D at 25°C is 10.6 in dichloromethane and 11.9 in toluene. These values are larger than those expected only by the loss of zero-point energy of the C-H stretching vibration in the transition state. And so the large kinetic isotope effects are attributable to the tunneling of a proton.^{1,2,22)}

Our value of k_f^H/k_f^D in dichloromethane (dielectric constant: $\epsilon=8.6$) is almost equal to Caldin's,⁹⁾ but that in toluene ($\epsilon=2.4$) is much smaller than theirs, $k_f^H/k_f^D=45$. The present value in toluene is very similar to that by Rogne *et al.*, who experimentally confirmed the value of 11 in the reaction of deuterated TMG²⁰⁾ and pentamethylguanidine²³⁾ as base. In the results by Caldin *et al.*,⁹⁾ there appeared a sharp difference in the degree of tunneling effect between the more polar solvent ($\epsilon>6$) and the less polar one ($\epsilon<6$). Their extensive and intensive consideration on the extraordinary dependence of k_f^H/k_f^D on the dielectric constant on the medium seem to be persuasive as far as their results are concerned. In the solvent of high polarity the solvent molecules are coupled with the moving proton and hence its effective mass is greater than unity (1.17–1.27 a. m. u.), while in the less polar solvent the absence of such a coupling results in the small effective mass of unity: the increase of the effective mass in the polar solvent is associated with the reduction of the amount of tunneling contribution and so of the rate ratio. However, in the reaction of TMG with 2, 4, 6-trinitrotoluene (TNT), Pruszyński *et al.*,¹⁰⁾ found a reverse tendency that k_f^H/k_f^D was 20.4 in acetonitrile ($\epsilon=35$) and 13.7 in benzonitrile ($\epsilon=25$). Leffek *et al.*¹¹⁾ focused their attention to the steric effect of solvent molecules around the reaction center in the same system, but they did not recognize appreciable influence of the bulkiness of the solvent molecule. Thus the problem seems to remain uncertain what character of the medium plays an important role in the variation of the large kinetic isotope effect on a proton-transfer reaction.

Pressure Effect on Reaction Rates. The volume of activation $\Delta V^\ddagger$ of chemical reaction in solution is recognized to give very important information about the reaction mechanism and the role of the solvent during activation.²⁴⁾ $\Delta V^\ddagger$ mainly consists of structural change ($\Delta V_{str}^\ddagger$) and solvation change ($\Delta V_{solv}^\ddagger$) on going from the initial to the transition state.²⁵⁾ In the case of the bond-forming process, $\Delta V_{str}^\ddagger$ would be negative. When electronic charge is generated during activation, $\Delta V_{solv}^\ddagger$ will also be negative. The proton/deuteron-transfer reaction between 4NPNM and TMG conforms to the above case; in fact, our data result in the negative values of the volume of activation.

In dichloromethane there was no appreciable difference in $\Delta V_{str}^\ddagger$ between the proton- and the deuteron-transfer reaction; $\Delta V_{str}^\ddagger(\text{H}) = -15.3 \pm 1.5$, $\Delta V_{str}^\ddagger(\text{D}) = -14.6 \pm 1.7$ cm³ mol⁻¹ and there is no pressure effect on the ratio $k_H^\ddagger/k_D^\ddagger$ up to 1000 bar. As for $\Delta V_{str}^\ddagger$ in toluene, it is isotope dependent; $\Delta V_{str}^\ddagger(\text{H}) = -18.8 \pm 1.9$, $\Delta V_{str}^\ddagger(\text{D}) = -24.6 \pm 3.0$ cm³ mol⁻¹, and $k_H^\ddagger/k_D^\ddagger$ diminishes from 11.9 at 1 bar to 9.3 at 1000 bar.

At high pressure, Isaacs *et al.*¹⁵⁾ investigated the slow proton-transfer reaction between diphenyldiazomethane and benzoic [²H] acid which has normal kinetic isotope effect, and the hydride-transfer reaction between [²H] leuco-crystal violet and chloranil which had a significant tunneling contribution. While the former reaction showed k^H/k^D ($\approx 4.5-4.7$) was almost invariant with pressure, the rate ratio of the latter one decreased from 11 at 1 bar to 8 at 2 kbar. From these results they thought that the increased effective mass of the hydrogen under pressure diminished the extent of tunneling. Their consideration is based on the concept that zero-point energies and vibrational frequencies would not be significantly affected by moderate pressures and normal kinetic isotope effects would be independent of pressure while kinetic isotope effects deriving in part from tunneling would be pressure dependent. In our case, in spite of the occurrence of tunneling in both solvents, the kinetic rate ratio in toluene is appreciably pressure-dependent but that in dichloromethane is almost pressure-independent.

In many proton-transfer reaction which show quantum mechanical tunneling effect, it has often been said that the translational motion occurs within considerably hindered cage-like space due to the exclusion of solvent molecules from the vicinity of the reactive site. Consideration along this direction will lead to the explanation that the more bulky solvent may bring about the higher degree of tunneling and more rapid decrease of $k_H^\ddagger/k_D^\ddagger$ by pressure, since pressure is to force the solvent molecules into the vicinity of the reaction site. Our results seem apparently to lie on this concept, however such an explanation must be consistent with the expectation that $\Delta V_{str}^\ddagger(\text{H})$ at 1 bar should be almost contributed the structural term, $\Delta V_{str}^\ddagger$. Unfortunately it is not exact in our case as reported previously,²¹⁾ although Caldin *et al.*²⁶⁾ suggested that $\Delta V_{str}^\ddagger(\text{H})$ was invariable (about 15 cm³ mol⁻¹) in less polar solvent ($\epsilon=2-6$).

Our results that the forward reaction proceeds faster and $\Delta V_{str}^\ddagger$ is less negative in the more polar solvent, will be qualitatively explained by the electrostatic solvation model of an ionogenic reaction: similar tendency is found in many Menschutkin reactions.²⁷⁾ Hence it seems probable that even in the solvent of low polarity such as toluene solvation in the proximity of reaction center, more or less, takes place. Further studies of the rate and its kinetic isotope effect in many solvents and other systems at high pressure will more clearly reveal the connection of the amount of tunneling with solvent proper-

ties.

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