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the enzymatic reaction, may be offered. (i) Though the N^5-oxide of the cofactor binds well to the active site of *p*-hydroxybenzoate hydroxylase, it does not transfer oxygen to substrate.[26] (ii) Monooxygenase-bound 4a-FlHOOH, in the absence of substrate, decomposes quantitatively by elimination of H_2O_2 with the formation of enzyme-bound oxidized flavin so that there is no evidence for the proposed intramolecular formation of a flavin oxaziridine.

Acknowledgment. This study was supported by grants from the National Institutes of Health and the National Science Foundation.

Registry No. 1, 128-39-2; **1**$^-$·K$^+$, 24676-69-5; **2**, 719-22-2; **3**, 24457-07-6; **4**, 128-38-1; **5**, 2455-14-3; **4a**-FlEtOOH, 59587-26-7; **4a**-FlEtOO$^-$, 74976-70-8.

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High-Pressure NMR Study of Dynamical Effects on Conformational Isomerization of Cyclohexane

D. L. Hasha, T. Eguchi,† and J. Jonas*

Contribution from the Department of Chemistry, School of Chemical Sciences and Materials Research Laboratory, University of Illinois, Urbana, Illinois 61801.

Received September 14, 1981

Abstract: The effect of temperature and pressure on the conformational inversion of cyclohexane in solution has been investigated with use of ^{1}H FT NMR spectroscopy. The solvents used in this study are methylcyclohexane-d_{14}, carbon disulfide, and acetone-d_6. It is found that the activation parameters as obtained from the temperature dependence of the rate constant are independent of solvent. However, the coalescence temperature in the methylcyclohexane-d_{14} solvent is 1.5 °C higher than in the other two solvents. It is observed that the ring inversion in cyclohexane is accelerated when pressure is increased, and this pressure dependence of the rate constant is nonlinear. In the lower viscosity solvents, acetone-d_6 and carbon disulfide, the rate constant shows a larger pressure dependence than in the more viscous methylcyclohexane-d_{14} solvent. The experimental data are interpreted with use of results of the stochastic models for isomerization reactions. In these models it is proposed that there are dynamical effects on isomerization because the reaction coordinate is coupled to the surrounding medium. We find that the observed activation volume is strongly pressure and solvent dependent as is the collisional contribution to the activation volume. Since the collision frequency reflecting the coupling of the reaction coordinate to the solvent mediums is proportional to solvent viscosity, the observed activation volume and the transmission coefficient κ correlate well with the solvent viscosity. In addition, the experimental data indicate a non-monotonic transition between the inertial (weak coupling) and diffusive (strong coupling) regimes of isomerization reactions. Our results represent the first experimental proof of the predictions of stochastic models for isomerization reactions in condensed phases.

I. Introduction

A large number of studies employing different NMR techniques have been devoted to the investigation of the temperature dependence of ring inversion of cyclohexane. This is not surprising since the cyclohexane moiety is of primary importance in the theory of conformational analysis. What is surprising, however, is that all these studies used a single solvent, carbon disulfide. Recently a limited pressure study (up to 2 kbar) of cyclohexane in a complex mixture of solvents has been performed by Lüdemann and co-workers.[1]

Our understanding of the ring-inversion process in cyclohexane is based upon these variable-temperature measurements and the results of force-field calculations. These calculations[2-12] have shown that the lowest energy path for ring inversion proceeds via a half-chair transition state with the twist–boat and its slightly higher energy pseudorotation partner the boat as intermediates. The barrier for isomerization, which is equal to the energy difference between the half-chair transition state and chair forms, depends on the parameters chosen for the calculation. The calculated value for the barrier height varies from 9.5 to 12.7 kcal/mol and is in good agreement with experiment. In order to describe the relatively complex potential energy surface of cyclohexane two degrees of freedom are necessary.[7,10,12] Since this potential corresponds to isolated molecules, direct comparison with experiment is not strictly correct and quantitative agreement should not be expected. Recently, it has been shown that even in the absence of electrostatic contributions the packing of solvent molecules can dramatically alter the gas-phase potential.[13-15] This would result in a possible dependence of the barrier height ($\Delta H^\ddagger$) on the local structure of the solvent.

The application of stochastic models to isomerization reactions as proposed by Skinner and Wolynes[16] and Montgomery, Chan-

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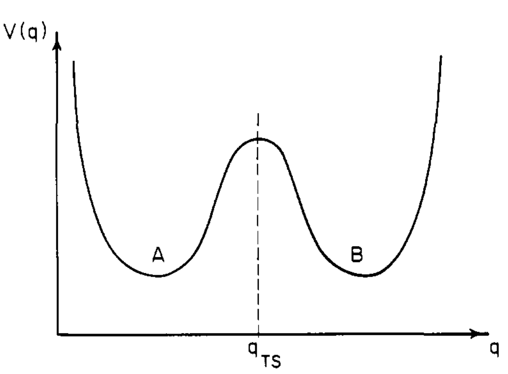

Figure 1. A one-dimensional bistable model potential. The transition state is at q_{TS}. States A and B are equal in energy.

dler, and Berne[17] has revealed an additional solvent effect. According to these models the reaction coordinate is coupled to the solvent, enabling the system to gain sufficient energy to cross the barrier, lose energy, and become trapped into the product well. In the absence of electrostatic interactions this coupling is produced by collisions between the solvent and solute molecules. In contrast to classical transition-state theory[18-20] for isomerization reactions the stochastic models[16,17] propose a dependence of the transmission coefficient κ upon the so-called "collision frequency", which reflects the actual coupling of the reaction coordinate to the surrounding medium. The stochastic models predict a large collisional contribution to the activation volume which is expected to be pressure dependent. The theoretical results of the stochastic models provided the main motivation for our experiments. First, we wanted to investigate the effects of temperature and pressure on the isomerization rate of cyclohexane in several solvents. Second, we attempted to provide the first experimental proof of the predictions of stochastic models for isomerization reactions.

II. Unimolecular Reactions in Condensed Phases: Transition-State Theory and Stochastic Models

In order to understand the significance of our experimental results, one has to mention the main features of the stochastic models for isomerization dynamics. To discuss the results of these models, we begin by considering the simple one-dimensional bistable potential $V(q)$ shown in Figure 1. The two states A and B are separated by a transition state located atop the barrier ($q = q_{TS}$). The height of the barrier is large compared to k_BT. According to transition-state theory (TST) the rate constant, k_{TST}, is given by the one-way flux across the barrier

$$k_{TST} = \tfrac{1}{2}\langle|\dot{q}|\rangle' S(q_{TS}) \qquad (1)$$

where $S(q_{TS})$ is the probability distribution of finding the system atop the barrier and the primed brackets, $\langle\,\rangle'$, indicate the equilibrium average with the reaction coordinate restricted to the transition state. Since the probability distribution is dependent on the solvated potential,[13,14,21] TST takes into account the static solvent effect.

The conventional expression for the TST rate constant is[18-20]

$$k_{TST} = \kappa\,\frac{k_BT}{h}\exp\left(\frac{-\Delta G^{\ddagger}}{RT}\right)\frac{\Pi f_R}{f^{\ddagger}} \qquad (2)$$

where f_R and $f^{\ddagger}$ are the activity coefficients of the reactants and the transition state, κ is the transmission coefficient, $\Delta G^{\ddagger}$ is the Gibbs free energy of activation, and the other symbols have their usual meaning. The standard states of the reactants and the transition state are defined so that in solution their activity coefficients are unity at infinite dilution. For sufficiently dilute solutions $\Pi f_R/f^{\ddagger}$ is safely assumed to be unity and independent of temperature and pressure. The transmission coefficient is also taken to be unity and independent of the thermodynamic state. With these assumptions, which form the basis of traditional transition-state theory, eq 2 becomes

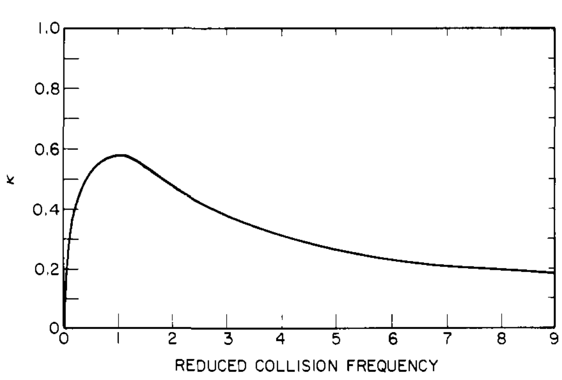

Figure 2. The dependence of the transmission coefficient κ on collision frequency. The maximum value of κ occurs at a reduced collision frequency of 1.

$$k_{TST} = \frac{k_BT}{h}\exp\left(\frac{-\Delta G^{\ddagger}}{RT}\right) \qquad (3)$$

This expression is equivalent to the one-way flux across the barrier given by eq 1.

The stochastic models reintroduce the transmission coefficient as

$$k(\Delta t) = \kappa k_{TST} \qquad (4)$$

where $k(\Delta t)$ is the observed (calculated) isomerization rate. The details of the calculation of $k(\Delta t)$ can be found in the original references.[16,17,22-24] The transmission coefficient is found to be a strong nonmonotonic function of the coupling strength between the reaction coordinate and the surrounding medium. For our specific experiments the coupling strength is given by the collision frequency, α. A generalized plot of κ vs. the reduced collision frequency, α_R, is shown in Figure 2. The exact shape of the curve and the maximum value of κ are dependent on the potential and method of calculation, but it is clear that TST is never a good approximation to the actual rate. In the κ vs. α_R dependence one can distinguish two different limits. At low collision frequencies (weak coupling, low damping, or inertial regime) activation due to collision is rate limiting. This activation process is proportional to α,[16,17] and κ is found to be a linear function of α in this regime. When α is low the reaction coordinate may oscillate back and forth between states A and B before suffering a collision and being trapped in either state A or B. Since TST neglects these recrossings, it overestimates the actual rate. As α increases, the probability of the system being trapped before it reverses its direction becomes larger which results in an increased rate. At high collision frequencies (strong coupling, high damping, or diffusive regime), particles which have crossed but not yet cleared the barrier may suffer collisions and recross the barrier. Therefore, TST will overestimate the actual rate in this regime also. The reaction in this limit is said to be diffusion controlled and the rate is inversely proportional to α.[25] Between these two regimes there is a non-monotonic transition. The reduced collision frequency is defined such that this transition occurs at $\alpha_R = 1$. Even in this intermediate region TST is not an accurate description of the rate.

The dynamical variable κ leads to collisional contributions to the activation parameters. The activation energy, $\Delta E^{\ddagger} = \Delta H^{\ddagger}$

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+ RT, and the activation volume are defined by

$$RT^2\left(\frac{\partial \ln [k(\Delta t)]}{\partial T}\right)_P = \Delta E^\ddagger_{\mathrm{TST}} + \Delta E^\ddagger_{\mathrm{COLL}} = \Delta E^\ddagger_{\mathrm{OBS}} \quad (5)$$

$$-RT\left(\frac{\partial \ln [k(\Delta t)]}{\partial P}\right)_T = \Delta V^\ddagger_{\mathrm{TST}} + \Delta V^\ddagger_{\mathrm{COLL}} = \Delta V^\ddagger_{\mathrm{OBS}} \quad (6)$$

respectively, with

$$RT^2\left(\frac{\partial \ln k_{\mathrm{TST}}}{\partial T}\right)_P = \Delta E^\ddagger_{\mathrm{TST}};\quad -RT\left(\frac{\partial \ln k_{\mathrm{TST}}}{\partial P}\right)_T = \Delta V^\ddagger_{\mathrm{TST}} \quad (7)$$

and the collisional contributions are given by

$$RT^2\left(\frac{\partial \ln \kappa}{\partial T}\right)_P = \Delta E^\ddagger_{\mathrm{COLL}};\quad -RT\left(\frac{\partial \ln \kappa}{\partial P}\right)_T = \Delta V^\ddagger_{\mathrm{COLL}} \quad (8)$$

Montgomery, Chandler, and Berne[17] estimated the collisional and TST contributions to $\Delta E^\ddagger_{\mathrm{OBS}}$ and $\Delta V^\ddagger_{\mathrm{OBS}}$ for their stochastic model of the trans-gauche isomerization of *n*-butane dissolved in liquid CCl_4. They found $\Delta E^\ddagger_{\mathrm{COLL}}$ to be small compared to $\Delta E^\ddagger_{\mathrm{TST}}$ which is approximately equal to the barrier height. However, for the volume of activation they found $\Delta V^\ddagger_{\mathrm{COLL}}$ of an order of magnitude larger at 1 bar and room temperature than $\Delta V^\ddagger_{\mathrm{TST}}$. They predicted the pressure dependence of κ and $\Delta V^\ddagger_{\mathrm{COLL}}$. Therefore, the traditional TST approximation overlooks important features of reaction dynamics in condensed phases.

The barrier height, $\Delta H^\ddagger_{\mathrm{TST}} = \Delta E^\ddagger_{\mathrm{TST}} - RT$, for conformational isomerization of cyclohexane is approximately four times larger than the barrier height for *n*-butane. If we make the reasonable assumption that $\Delta E^\ddagger_{\mathrm{COLL}}$ is similar in magnitude to the *n*-butane system, then for our experiments $\Delta E^\ddagger_{\mathrm{COLL}}$ can be neglected, since $\Delta E^\ddagger_{\mathrm{COLL}}$ would then be much smaller than $\Delta E^\ddagger_{\mathrm{TST}}$. Therefore, the temperature dependence of the rate constant would yield the barrier height and give information about the static solvent effect. The observation of a strongly pressure dependent $\Delta V^\ddagger_{\mathrm{COLL}}$ would indicate dynamical effects caused by the coupling between the reaction coordinate and the surrounding medium.

III. Experimental Section

Photex grade cyclohexane and carbon disulfide were obtained from J. T. Baker Chemical Co. The deuterated solvents, acetone-d_6 and methylcyclohexane-d_{14}, were obtained from Stohler Isotope Chemicals. The 5 mol % cyclohexane solutions were degassed by using the freeze–pump–thaw method.

The high-resolution, high-pressure probe has recently been described elsewhere.[26] An improvement in signal to noise ratio over the original design was accomplished by inserting a 2.8 pF capacitor in the high-pressure vessel between the coil and ground. This modification allowed us to tune the probe, using the tapped-parallel tuned circuit.[27] The resulting signal-to-noise ratio observed for 5 mol % cyclohexane solutions was 60:1. The NMR probe allows measurements in the pressure range of 1–5000 bar and the temperature range of 200 to –70 °C.

The temperature was measured by copper–constantan thermocouples inside the high-pressure vessel near the sample cell. The temperature gradient across the sample was less than 0.1 °C at these temperatures. During the pressure runs the temperature was held constant to within 0.1 °C. To avoid systematic errors, we staggered the pressure cycles. Data were taken at 1-kbar intervals up to the maximum pressure, and the intermediate pressure points were taken during the decompression run.

^{1}H FT NMR spectra were obtained on a spectrometer system similar to the system which has been described earlier.[28-30] The superconducting magnet (180 MHz for protons) made by Oxford Instruments, Inc. equipped with superconducting and room-temperature shim coils allowed us to obtain NMR spectra with line widths of 1 Hz at 180 MHz for 6-mm samples. The shear viscosity of solvents was measured under the same experimental conditions with a rolling ball viscometer.

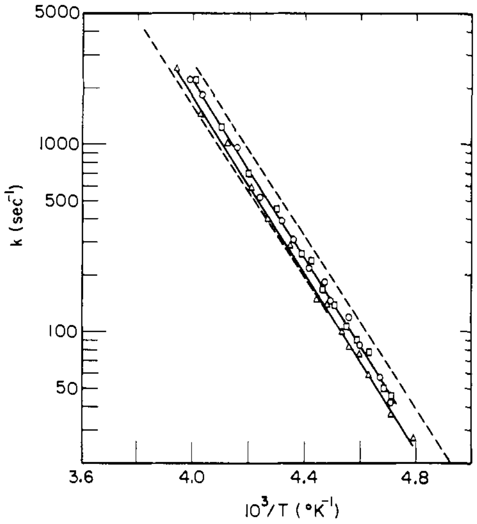

Figure 3. The temperature dependence of the chair-to-chair isomerization rate in cyclohexane. Solvents: methylcyclohexane-d_{14} (△), carbon disulfide (□); and acetone-d_6 (○). The results of earlier line shape analysis (- - -) are also shown. The upper line is $C_6D_{11}H$ (ref 43) while the lower line is C_6H_{12} (ref 35).

IV. Results and Discussion

A. Variable-Temperature Measurements at Atmospheric Pressure. Cyclohexane is a very complex twelve-spin system (A_6B_6 at best), and below coalescence the spectrum is not well described by a coupled or uncoupled AB system. However, in the fast exchange limit the spectrum is not affected by the spin–spin coupling, provided this coupling is weak.[31] Analysis of the spectra as an uncoupled AB system is therefore appropriate above the coalescence temperature. Below coalescence the line widths are anomalously broad due to unresolved coupling. An approximate rate constant can be obtained by increasing the value used for the line width in the absence of exchange. Extrapolation of the fast exchange data in the CS_2 solvent to 212 K yields a rate constant, $k = 1/2\tau$, of 46 s^{-1}. Using this rate and the corresponding spectrum, we obtained an effective line width in the absence of exchange, $\Delta\nu_0 = 20$ Hz. This effective broadening is used to analyze all the spectra below coalescence.

The rate constants for chair-to-chair isomerization as a function of temperature are shown in Figure 3. In $C_6D_{11}CD_3$ the rate constant is consistently lower than in CS_2 and acetone-d_6. The coalescence temperature is different in $C_6D_{11}CD_3$, 223.5 K as opposed to 222 K in the other two solvents. This difference is reproducible. Also shown in Figure 3 are line-shape data for C_6H_{12} and $C_6D_{11}H$.

One can show, using straightforward procedures, that the phenomenological rate constant, $k = {}^1/_2k_1$, where k_1 is the rate of formation of the intermediate is unaffected by the equilibrium between the chair and intermediate forms. Thus, the observed rate can be described by a single-step rate constant. Using the TST formulation, we can calculate the activation parameters. The values obtained, $\Delta G^\ddagger = 10.7$ kcal/mol, $\Delta H^\ddagger = 10.0 \pm 0.3$ kcal/mol, and $\Delta S^\ddagger = 2.7 \pm 1$ eu, are in good agreement with the reported literature values.[32-44] The important finding is the

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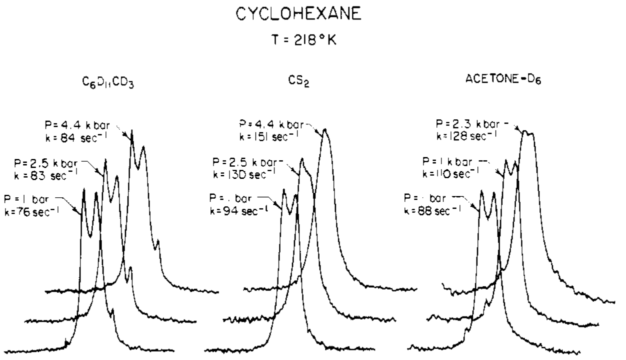

Figure 4. Experimental ^{1}H NMR spectra of cyclohexane illustrating the effect of solvent and pressure on ring inversion at 218 K.

independence of the activation parameters upon solvent (evident from Figure 3). The longest temperature interval yields the most accurate values.[43] Since our measurements span a narrow range of temperatures, the resulting $\Delta H^{\ddagger}$ is smaller than the best experimental value, 10.7 kcal/mol.[44] Measurements conducted over a wider range of temperature would eliminate this difference, but the observation that $\Delta H^{\ddagger}$ is independent of solvent would remain unaltered. One should point out that there is good agreement in the literature on the value of $\Delta G^{\ddagger}$ but the reported $\Delta H^{\ddagger}$ varies from 9.1 to 11.5 kcal/mol and, consequently, $\Delta S^{\ddagger}$ varies from −7.2 to 3.2 eu. This variation is due to experimental inaccuracies, mainly reflecting the temperature interval investigated.

As mentioned previously the collisional contribution to $\Delta H^{\neq}$ is small and can be neglected. Thus, the barrier height for isomerization is independent of solvent. Since during the isomerization process no bonds are broken or charge distributions created or destroyed, preferential solvation of the transition state relative to the chair form is due entirely to the packing of solvent molecules, i.e., the solvent cage. Therefore, we conclude that differences in the local structure of the solvents are not large enough to produce noticeable differences in the barrier heights. The absolute value of the rate, on the other hand, is very sensitive to the actual potential[21] and thus to differences in the molecular packing of solvent. This is a possible explanation for the observation that the rate constant in $C_6D_{11}CD_3$ is lower than those in the other solvents. Alternatively, differences in the transmission coefficient caused by differences in the dynamic structure of the solvents may be responsible. There is no reason to prefer one interpretation over the other, and it is equally possible that both static and dynamic solvent effects contribute to the difference in the rate simultaneously.

B. High-Pressure Measurements. The effect of pressure on the ^{1}H FT NMR spectra at 218 K is shown in Figure 4. In agreement with Lüdemann and co-workers[1] we observe an acceleration of the isomerization rate as pressure is increased. The rate constants for the isomerization process as a function of pressure near the coalescence temperature are shown graphically in Figure 5. It is clear that the isomerization rate exhibits a stronger pressure dependence in acetone-d_6 and carbon disulfide than in methylcyclohexane-d_{14}. The experimental data are fit to a cubic equation of the form

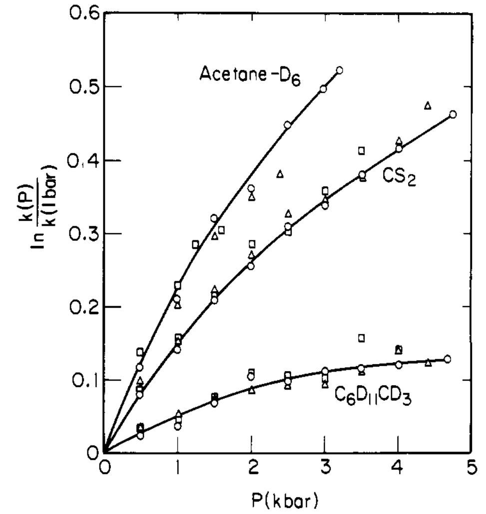

Figure 5. The pressure dependence of the chair-to-chair isomerization rate in cyclohexane: 225 K (○); 218 K (△); 213 K (□). The solid lines represent the best fit to the data at 225 K.

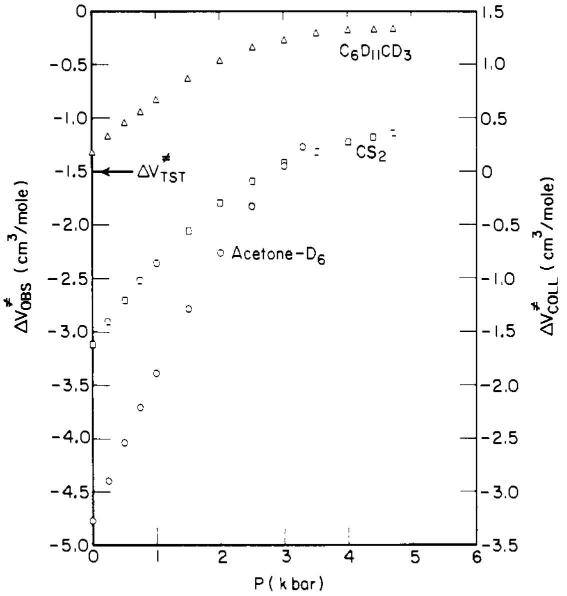

Figure 6. Pressure effects on the activation volumes for chair–chair isomerization of cyclohexane at 225 K in solvents: acetone-d_6 (○); carbon disulfide (□); and methylcyclohexane-d_{14} (△). The left-hand scale refers to $\Delta V^{\neq}{}_{\text{OBS}}$, the observed activation volume, and $\Delta V^{\neq}{}_{\text{TST}}$, the transition-state-theory activation volume. The right-hand scale refers to $\Delta V^{\neq}{}_{\text{COLL}}$, the collisional contribution to the activation volume (for details, see the text).

$$\ln\,[k(P)] = A_0 + A_1P + A_2P^2 + A_3P^3 \tag{9}$$

where P is the pressure in bar and the A_n's are adjustable parameters. The quadratic function ($A_3 = 0$) widely used in the literature[45-47] does not give a good representation of our data over the entire pressure range. It must be noted that there is no physical justification for the use of eq 9.

Differentiation of eq 9 with respect to pressure yields the observed volume of activation

$$\Delta V^{\neq}{}_{\text{OBS}} = -RT(A_1 + 2A_2P + 3A_3P^2) \tag{10}$$

where $\Delta V^{\neq}{}_{\text{OBS}}$ is in cm^3/mol. In Figure 6 the observed volumes

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Table I. Activation Volumes for Conformational Isomerization of Cyclohexane

solution	temp, K	P_{MAX}, bar	$\Delta V^{\ddagger}$,[a] cm^3/mol	$\Delta V^{0\ddagger}{}_{\text{OBS}}$,[b] cm^3/mol	$V^{0\ddagger}{}_{\text{COLL}}$,[c] cm^3/mol
40% CYH, 30% Me_4Si 15% CD_2Cl_2, 15% $C_6D_{11}CD_3$[d]	217	2000	−1.9 ± 0.5		
5% CYH, $C_6D_{11}CD_3$	225	4700	−0.5 ± 0.2	−1.3	0.2
	218	4400	−0.5 ± 0.2	−1.0	0.5
	213	4000	−0.6 ± 0.2	−1.0	0.5
5% CYH, CS_2	225	4700	−1.8 ± 0.3	−3.1	−1.6
	218	4400	−1.9 ± 0.3	−3.4	−1.9
	213	3500	−2.1 ± 0.3	−3.2	−1.7
5% CYH, acetone-d_6	225	3250	−3.0 ± 0.5	−4.8	−3.3
	218	2350	−2.9 ± 0.5	−4.0	−2.5
	213	1600	−3.3 ± 0.5	−4.9	−3.4

[a] Linear least-squares fit of data which assumes the volume of activation to be independent of pressure. [b] Obtained from the initial slopes of the data in Figure 5. [c] $\Delta V^{0\ddagger}{}_{\text{COLL}} = \Delta V^{0\ddagger}{}_{\text{OBS}} - \Delta V^{\ddagger}{}_{\text{TST}}$; $\Delta V_{\text{TST}} = -1.5$ cm^3/mol. See text. [d] Solution composition in percent by volume, ref 1.

of activation are plotted as a function of pressure at 225 K. Although the values of $\Delta V^{\ddagger}{}_{\text{OBS}}$ are extremely sensitive to the fit of the cubic equation to the experimental data, it is clear that $\Delta V^{\ddagger}{}_{\text{OBS}}$ is a nonlinear function of pressure. This is not unusual since there are many examples of the nonlinear behavior of $\Delta V^{\ddagger}{}_{\text{OBS}}$ in the literature.[45,47,48] The observed volume of activation is a stronger function of pressure in acetone-d_6 than in the other two solvents.

Also shown in Figure 6 are $\Delta V^{\ddagger}{}_{\text{TST}}$ and $\Delta V^{\ddagger}{}_{\text{COLL}}$. $\Delta V^{\ddagger}{}_{\text{TST}}$ is considered to be the sum of two contributions:[18] (a) an intrinsic part resulting from nuclear displacements within the ring during the formation of the transition state and (b) a solvation term due to the change in volume associated with differing interactions between the solvent and the cyclohexane molecules during the activation process. It is usually assumed that this solvent effect is negligibly small for nonpolar reactions.[49] Although it is well known that the addition of nonpolar solute produces solvent–solute interactions and also changes in solvent–solvent interactions,[49] it is doubtful that these interactions are greatly altered during the activation process. This assertion is supported by our observation that the barrier height for isomerization of cyclohexane is independent of solvent. Therefore, $\Delta V^{\ddagger}{}_{\text{TST}}$ is strictly the volume difference between the transition state and the chair conformer. This volume difference is independent of pressure, and we may conclude that $\Delta V^{\ddagger}{}_{\text{COLL}}$ is responsible for the pressure dependence of $\Delta V^{\ddagger}{}_{\text{OBS}}$.

The half-chair transition state has a structure similar to cyclohexene. $\Delta V^{\ddagger}{}_{\text{TST}}$ can be estimated by the molar volume difference between cyclohexene and cyclohexane, −6.7 cm^3/mol (293 K).[50] Since cyclohexene substantially underestimates the molar volume of the transition state, we can compensate for the loss of volume due to the loss of two protons and a shortened double bond in cyclohexene by adding the molar volume difference between ethane and ethene, 4.2 cm^3/mol (115 K).[50] The molar volume differences were determined at common temperatures near the freezing point. The double bond in cyclohexene also constricts the ring; therefore the resulting value of $\Delta V^{\ddagger}{}_{\text{TST}} = -2.5$ cm^3/mol is a lower limit and a better estimate would be $\Delta V^{\ddagger}{}_{\text{TST}} = -1.5$ cm^3/mol. This compares favorably with the estimate $\Delta V^{\ddagger}{}_{\text{TST}} = -1.0$ cm^3/mol given by Le Noble.[51] Using our estimate we find $\Delta V^{\ddagger}{}_{\text{COLL}}$ changes sign in acetone-d_6 and carbon disulfide solvents. Choosing an alternative value of $\Delta V^{\ddagger}{}_{\text{TST}}$ would merely shift the $\Delta V^{\ddagger}{}_{\text{COLL}}$ scale up or down.

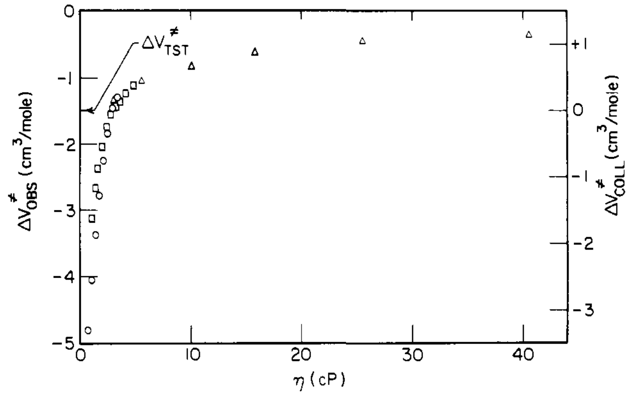

Figure 7. Activation volumes $\Delta V^{\ddagger}{}_{\text{OBS}}$ and $\Delta V^{\ddagger}{}_{\text{COLL}}$ as a function of viscosity of solvent: acetone-d_6 (○); carbon disulfide (□); methylcyclohexane-d_{14} (△).

The values of the observed and collisional activation volumes at zero pressure ($\Delta V^{0\ddagger}{}_{\text{OBS}}$ and $\Delta V^{0\ddagger}{}_{\text{COLL}}$) and $\Delta V^{\ddagger}$, which is obtained from a linear least-squares fit of the experimental data assuming pressure independence, are given in Table I. $\Delta V^{0\ddagger}{}_{\text{OBS}}$ and $\Delta V^{0\ddagger}{}_{\text{COLL}}$ are clearly solvent dependent as is the pressure-independent $\Delta V^{\ddagger}$. Since our experiments cover a narrow temperature range, the volumes of activation are expected to be independent of temperature. The observed variation is caused by two factors: (a) the approximate method by which the rate constant is determined below the coalescence temperature and (b) the sensitivity of the empirical fit to the experimental data. One has to be aware of the fact that the collision frequency α is really the frequency of collisions which couple to the reaction degree of freedom, rather than the actual collision frequency.

For cyclohexane, one expects that the collision frequency α is related to the shear viscosity of the medium.

For a direct comparison of $\Delta V^{\ddagger}{}_{\text{OBS}}$ in the different solvents the collision frequency, which is related to the friction coefficient of the medium, ζ, and the molecular mass, m, of the solute by

$$\alpha = \zeta/m \tag{11}$$

must be known. An estimate for ζ can be obtained by applying Stoke's law

$$\zeta = C\pi\eta(\sigma/2) \tag{12}$$

where η is the shear viscosity of the solvent, σ is the hard-core diameter of the cyclohexane molecule, and $\sigma \simeq 5.5$ Å.[52-54] The parameter C is equal to 4 in the slipping boundary limit, whereas it is 6 for the sticking boundary limit. Recent work in the area of molecular hydrodynamics[55,56] and molecular dynamics[57] as well

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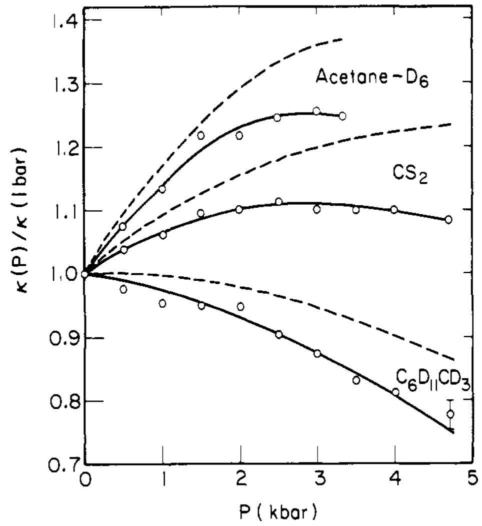

Figure 8. Reduced transmission coefficient as a function of pressure and solvent at 225 K. The circles are values calculated from experimental rate constants, using $\Delta V^{\ddagger}_{TST} = -1.5$ cm^3/mol. The lines represent values obtained from $\Delta V^{\ddagger}_{OBS}$ in Figure 6 with $\Delta V^{\ddagger}_{TST} = -1.5$ cm^3/mol (—) and $\Delta V^{\ddagger}_{TST} = -1.0$ cm^3/mol (- - -).

as experiment[58] show that on the molecular level the slip rather than stick boundary conditions apply. Therefore the collision frequency is given by

$$\alpha = \frac{2\pi}{m}\eta\sigma \tag{13}$$

As already mentioned, the shear viscosities of the solvents have been measured under the same experimental conditions and the observed volume of activation for isomerization is shown as a function of shear viscosity in Figure 7. Considering the errors inherent in the calculation of $\Delta V^{\ddagger}_{OBS}$, it correlates extremely well with the shear viscosity of the solvents. The collisional contribution to $\Delta V^{\ddagger}_{OBS}$ changes sign at approximately $\eta = 2.5$ cP. Thus the experimental data lie in the intermediate region between the inertial and diffusive regimes. If the value of $\Delta V^{\ddagger}_{TST}$ proposed by Le Noble[51] is used ($\Delta V^{\ddagger}_{TST} = -1.0$ cm^3/mol), the position of the transition between the two limits is shifted to higher shear viscosity, i.e., higher α. However, the data still fall in the intermediate region, and even in the unlikely event that our estimate of $\Delta V^{\ddagger}_{TST}$ is off by ±1 cm^3/mol this observation would not be affected.

The transmission coefficient can be obtained by substituting eq 8 into eq 6 and integrating. The result is

$$\frac{\kappa(P)}{\kappa_0} = \frac{k(P)}{k_0}\exp\left(\frac{P\Delta V^{\ddagger}_{TST}}{RT}\right) \tag{14}$$

where κ_0 and k_0 are the transmission coefficient and observed rate constant at 1 bar. Since κ and k_{TST} cannot be determined independently, we must consider the ratio κ/κ_0. The pressure dependence of this ratio at 225 K is shown in Figure 8. In acetone-d_6 κ increases by 30% of its initial value at 2.5 kbar where it levels off. κ reaches a maximum in carbon disulfide, near 2.5 kbar, where it takes a value of 10% larger than at 1 bar. It then decreases slightly. In methylcyclohexane-d_{14} κ decreases to approximately 80% its initial value at the highest pressure. In order to illustrate that the pressure dependence of κ is strongly influenced by the value chosen for $\Delta V^{\ddagger}_{TST}$, we have also determined $\kappa(P)/\kappa_0$ using $\Delta V^{\ddagger}_{TST} = -1.0$ cm^3/mol (see Figure 8). As expected the maximum value of κ is shifted to higher pressures resulting in larger values of $\kappa(P)/\kappa_0$ at every pressure.

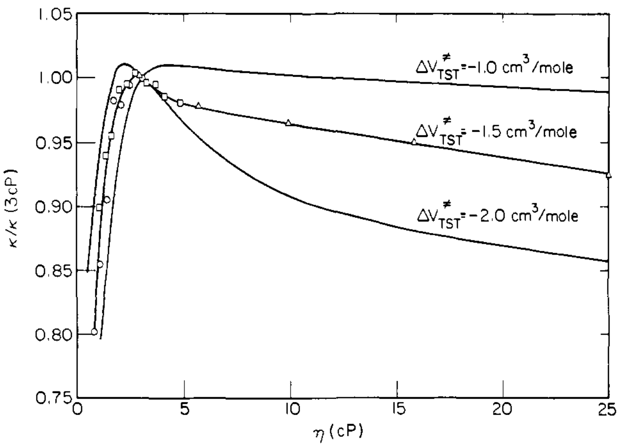

Figure 9. Relationship between reduced transmission coefficient and solvent viscosity for different values of $\Delta V^{\ddagger}_{TST}$ at 225 K. Solvents: acetone-d_6 (○); carbon disulfide (□); methylcyclohexane-d_{14} (△).

The strong correlation between κ and solvent viscosity is shown in Figure 9. In this figure we plot the ratio κ/κ(3 cP) as a function of η for different values of $\Delta V^{\ddagger}_{TST}$. We emphasize that in Figure 9 all three full lines are experimental $\kappa(P)/\kappa_0$ vs. η plots for different values of $\Delta V^{\ddagger}_{TST}$ as obtained from eq 14. We have drawn the actual experimental points only for the case $\Delta V^{\ddagger}_{TST} = -1.5$ cm^3/mol. With use of our estimate of $\Delta V^{\ddagger}_{TST}$, κ is found to decrease only slightly from its maximum value as the shear viscosity increases from 2.5 to ~25 cP. Over this same range of collision frequencies, i.e., $1 \leq \alpha_R \leq 10$, the theoretical curve shown in Figure 2 falls off more rapidly. Since the one-dimensional bistable potential used in the stochastic models is a poor description of the cyclohexane system, comparison between these two curves may not be justified. It is not known how intermediates and higher order potentials would affect the dependence of κ on the collision frequency. However, one might imagine that the reaction coordinate would become trapped in the intermediate well along the pseudorotation axis and many of the subsequent collisions would not contribute to the forward or reverse isomerization reaction. This would cause the onset of the diffusive regime to occur at lower collisional frequencies than in the simple one-dimensional models. Thus, the presence of intermediate and the multidimensional potential cannot explain our observation. Skinner and Wolynes[22] have recently shown that in the limit m(solvent) ≫ m(solute), the stochastic models do produce curves similar in shape to our experimental curves. Although we do not satisfy this condition it is important to note that κ is dependent not only on α but also on the nature of the collision. The relative size, shape, and mass of the molecules influences the nature of the collisions. With these differences it is surprising that κ correlates with α as well as it does.

In section II we assumed that the collisional contribution to the activation energy is small compared to $\Delta E^{\ddagger}_{TST}$. In order to check this assumption we use the results of the preceding section. Since κ depends on the thermodynamic state through its dependence on the shear viscosity, we may rewrite eq 8 as

$$\Delta E^{\ddagger}_{COLL} = RT^2\frac{\mathrm{d}\ln\kappa}{\mathrm{d}\eta}\left(\frac{\partial\eta}{\partial T}\right)_P \tag{15}$$

By combining our calculated results for d ln κ/dη corresponding to $\Delta V^{\ddagger}_{TST} = -1.5$ cm^3/mol with the temperature dependence of η for $C_6D_{11}CD_3$, we have estimated $\Delta E^{\ddagger}_{COLL}$ in this solvent. We find that over the temperature interval studied the magnitude of $\Delta E^{\ddagger}_{COLL}$ is never larger than 0.3 kcal/mol, which is small compared to $\Delta E^{\ddagger}_{TST} \approx 11$ kcal/mol. $\Delta E^{\ddagger}_{COLL}$ is temperature dependent, changing from −0.28 kcal/mol at 250 K to 0.12 kcal/mol at 210 K. Since this deviation in $\Delta E^{\ddagger}_{COLL}$ is approximately equal to our experimental uncertainty in $\Delta E^{\ddagger}_{OBS}$, we are unable to detect $\Delta E^{\ddagger}_{COLL}$. Therefore, our assumption that the collisional contribution is negligible compared to the TST value is justified. Although the estimated values of $\Delta E^{\ddagger}_{COLL}$ are dependent on

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$\Delta V^{\ddagger}_{\mathrm{TST}}$ and solvent, the assumption remains valid.

V. Summary

We observe that ring inversion in cyclohexane is accelerated as pressure is applied. This pressure dependence which is nonlinear is more pronounced in acetone-d_6 and carbon disulfide than in the more viscous methylcyclohexane-d_{14} solvent. The experimental data are interpreted in terms of the stochastic model of isomerization reactions. The observed activation volume is strongly pressure and solvent dependent as is the collisional contribution to the activation volume. $\Delta V^{\ddagger}_{\mathrm{OBS}}$ and the transmission coefficient correlate extremely well with the solvent viscosity, which is proportional to the collision frequency. Thus we conclude that the reaction coordinate is coupled via collisions to the surrounding medium. To the best of our knowledge these results represent the first experimental proof of the predictions of stochastic models[16,17] for isomerization reactions in condensed phases.

The main result is our observation of a large collisional contribution to the activation volume, $\Delta V^{\ddagger}_{\mathrm{COLL}}$, which is strongly pressure dependent. The experimental data also indicate nonmonotonic transition between the inertial and diffusive regimes of isomerization reactions.

Acknowledgment. We express our thanks to Drs. D. Chandler and Peter Wolynes for helpful discussions. This research was supported partly by the National Science Foundation under grant No. NSF CHE79-12-8011420 and by the Department of Energy under contract No. DE-AC02-76ER01198 55. Detailed tables of experimental data are available on request from the corresponding auther (J.J.).

Registry No. Cyclohexane, 110-82-7.

Relative Bond Dissociation Energies for Two-Ligand Complexes of Cu^+ with Organic Molecules in the Gas Phase

Roger W. Jones and Ralph H. Staley*[1]

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139. *Received June 15, 1981*

Abstract: Relative two-ligand dissociation enthalpies, $\delta D(Cu^+–2L)$, for Cu^+ with 43 organic molecules are determined. A pulsed-laser volatilization/ionization source is used to generate Cu^+ which reacts with EtCl and/or other molecules to give $Cu(ligand)_2^+$ species. Equilibrium constants are measured for the ligand-exchange reactions which occur when pairs of ligand molecules are present. Free energies for two-ligand exchange are obtained from the equilibrium constant for the reaction $Cu(A)_2^+ + 2B \rightleftarrows Cu(B)_2^+ + 2A$. The free-energy differences are added to give a scale of relative free energies for ligand exchange. These are converted to enthalpies to give the $\delta D(Cu^+–2L)$ scale with the assumption that entropy changes are small and can be neglected except for symmetry corrections which are made in appropriate cases. Dependence of $\delta D(Cu^+–2L)$ on functional group and substituent effects is analyzed. The results for Cu^+ are compared to available results for other reference acids: H^+, Al^+, Mn^+, Li^+, and $CpNi^+$. These comparisons show that Cu^+ is a softer acid than the other reference acids. This is apparent from the relative preference of Cu^+ for mercaptans and HCN compared to alcohols and other oxygen bases.

Relative gas-phase ligand binding energies, $D(M^+–L)$, for Al^+ and Mn^+ have recently been obtained by use of ion cyclotron resonance (ICR) spectroscopy with a pulsed-laser volatilization/ionization source of atomic-metal cations.[2,3] Such binding energies are useful in evaluating the energetics of reaction processes and in developing models for understanding molecular interactions. Recent work in our laboratory has also shown that complexes of Cu^+ with two ligands can be readily produced and do not react further with a variety of organic molecules except by ligand-exchange reactions.[4,5] Determination of relative binding energies of organic molecules in two-ligand complexes of Cu^+ is therefore possible. These two-ligand binding energies should reveal bonding effects due to the presence of a second ligand when compared to the one-ligand binding energies that have been previously obtained. Also, Cu^+ is a classic example of a soft acid,[6] and thus should show a preference for soft bases such as nitriles and sulfur bases. Data obtained in gas-phase ligand binding energy studies can provide a quantitative measure for hard and soft acid–base concepts unencumbered by solvation and other complicating effects. In the present paper we report determinations of relative binding energies of 43 organic molecules in two-ligand complexes with Cu^+. The results are compared to available gas-phase basicity scales for other reference acids: H^+, Li^+, Al^+, Mn^+, and $CpNi^+$ ($Cp \equiv \eta^5\text{-}C_5H_5$).

Experimental Section

Experiments were carried out with ICR instrumentation and techniques which have been previously described.[2-5,7,8] The output of a pulsed YAG laser is focused onto a copper wire target at the end of the ICR cell to produce atomic-copper cations. The mass spectrum for this source with no added gases shows 69% ^{63}Cu and 31% ^{65}Cu in their natural ratio. No Cu^{2+} or Cu_2^+ are observed. HCN was obtained by mixing NaCN and H_2SO_4 under vacuum. Chemicals were from commercial sources and were degassed by repeated freeze–pump–thaw cycles before use. Gas mixtures were prepared in the cell and partial pressures measured by difference as has been previously described.[2] Accuracy of pressure ratios is limited to about ±30% because the ion gauge is not individually calibrated for each gas.

Results

Ethyl chloride was used as a reagent for prepartion of the two-ligand complex $Cu(EtCl)_2^+$ which is formed in a rapid biomolecular reaction sequence as has been previously described.[4] Other molecules studied as ligands in this work readily displace EtCl to give $Cu(ligand)_2^+$ complexes. With many of the more

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(1) Address correspondence to this author at the Central Research Department, Experimental Station, DuPont Company, E356, Wilmington, DE 19898.

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