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Gas-Phase NMR Spectroscopy of Cyclohexane: Environmental Effects on Conformational Isomerism[1]

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Although gas-phase NMR studies can provide kinetic information similar to that obtained for condensed-phase samples without solvent perturbations,[2] conformational studies using dynamic NMR (DNMR) spectroscopy as a kinetic probe have almost exclusively addressed processes occurring in the liquid phase.[3] In this communication, we report gas-phase unimolecular ring inversion rates for cyclohexane that are ca. 2–3 times slower and activation parameters that are slightly higher than those obtained in liquid phase studies. $\Delta G^{\ddagger}_{298}$ for conversion of the chair conformation of cyclohexane to the transition state is 10.4 (2) kcal mol^{-1} in the gas phase and 10.1 kcal mol^{-1} in CS_2 solutions.[4] These results demonstrate that even in the absence of strong electrostatic interactions, kinetic parameters of molecules undergoing conformational exchange can be phase dependent. In this nonpolar system, the observed kinetic differences between gas- and liquid-phase samples are compatible with expected internal-pressure effects arising from packing forces in the liquid.[5] Higher gas-phase activation parameters are consistent with a process proceeding via a transition state that is smaller than the equilibrium chair conformation.[6]

All our NMR measurements were made with a Nicolet 200-WB spectrometer using a 12-mm ^{1}H probe. Typically, 300–500 transients were collected for each sample at each temperature, stored in 8K of memory and zero-filled to 16K prior to Fourier transformation, yielding spectra with signal/noise ratios of $\sim$50/1. Temperature equilibration and calibration and sample preparation techniques have been described previously.[2] Aldrich gold label (99+%) cyclohexane and Matheson instrument grade (99.99% min) SF_6 were used in this study. Rates were obtained for all gas-phase spectra above coalescence by using the program DNMR3-IT2[7] using a simple AB-spin model.[8] Details of this analysis will be described elsewhere.[9]

Ring-inversion rates of gaseous cyclohexane are pressure dependent. Figure 1 displays exchange-broadened NMR spectra at 248 K for samples containing 1 torr of cyclohexane and amounts of SF_6 ranging from 6 to 2500 torr. Associated rates range from 22 (5) s^{-1} for the sample containing 6 torr of SF_6 to ca. 600 s^{-1} for the samples containing 1000 torr or more of SF_6. Additional spectra were obtained over a pressure range of 6–2150 torr SF_6 at 253, 263, and 273 K in order to delineate the bimolecular and unimolecular kinetic regions. The low sample volatility of cyclohexane (1 torr at 228 K) necessitated addition of at least 1000 torr of an efficient collision partner such as SF_6 in order to obtain unimolecular (pressure independent) interconversion rates. Spectra were obtained for 1500- and 2500-torr samples[10] between 235 and 270 K in 3-K increments to determine infinite-pressure unimolecular activation parameters. Spectra of a 100-torr sample were obtained between 245 and 290 K in 3-K increments to determine the bimolecular activation energy. Associated rates appear in the Arrhenius plot shown in Figure 2 for 2500- and 100-torr samples. Results obtained previously for a 1% solution of cyclohexane–CS_2 are shown for comparison.[11] Corresponding rates obtained for a 1500-torr sample are similar to those obtained for the 2500-torr sample within our experimental uncertainty.

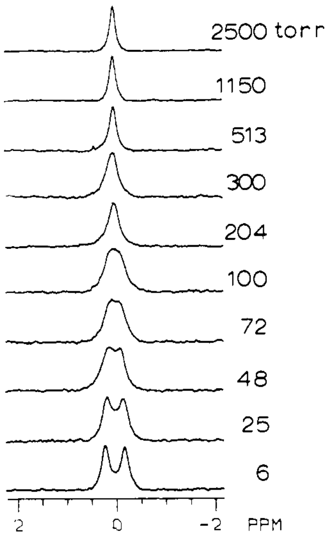

Figure 1. Gas-phase ^{1}H NMR spectra at 248 K. Samples contained 1 torr of cyclohexane and from 6 to 2500 torr of SF_6.

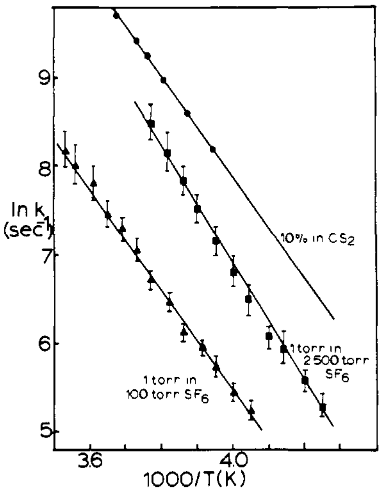

Figure 2. Chair $\rightleftharpoons$ chair isomerization rates of cyclohexane for a 1% solution in CS_2[11] (●), a 1-torr sample of cyclohexane and 2500 torr SF_6 (■), and a 1-torr sample of cyclohexane and 100 torr SF_6 (▲).

The unimolecular activation parameters are as follows: E_∞, 12.5 (5) kcal/mol; $\Delta H^{\ddagger}$, 12.1 (5) kcal/mol; $\Delta G^{\ddagger}$, 10.4 (2) kcal/mol; $\Delta S^{\ddagger}$, 5.7 (5) eu. For the 100-torr sample, the bimolecular activation energy is 11.2 (5) kcal/mol. The $E_\infty - E_{b_1}$ activation-energy difference, 1.3 kcal/mol, and the $\Delta S^{\ddagger}$ value are both consistent with a transition state of greater entropy than the chair conformer. For a process that follows RRKM kinetics, an $E_\infty - E_0$ difference equal to kT indicates that the partition function of the transition state is equivalent to that of the reactant.[12] The gas-phase activation parameters may be compared to the lower values obtained previously for cyclohexane solutions. The most recent solution studies of cyclohexane ring inversion are those of Anet and Bourne,[13] Höfner, Leski, and Binsch,[14] and Poupko and

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Luz.[15] They report activation parameters of 10.2, 10.1, and 10.15 kca/mol for $\Delta G^{\ddagger}_{298}$, 10.9, 11.5, and 10.3 kcal/mol for $\Delta H^{\ddagger}$, and 2.8, 4.6, and 0.5 eu for $\Delta S^{\ddagger}$, respectively.

The observed phase dependence is compatible with a negative activation volume. The partial derivative of $\Delta G^{\ddagger}$, the free energy of activation, with respect to pressure, equals the activation volume, $\Delta H^{\ddagger}$, for the process. The internal pressure of an ideal gas is zero, and of liquid CS_2 at 298 K, it is 3714 atm.[16] Using these values and a $\Delta(\Delta G^{\ddagger})$ of 370 cal, a $\Delta V^{\ddagger}$ value of ~−4 cm^3/mol is obtained. Recently, variable-pressure and -temperature NMR studies of cyclohexane in several solvents have revealed that interconversion rates increase with increasing pressure. The pressure dependence observed over a pressure range 1-5000 bar yields activation volumes, $\Delta H^{\ddagger}$'s, ranging from −5.0 cm^3/mol for an acetone solution to −1.5 cm^3/mol for a $C_6D_{11}CD_3$ solution.[17] These results are qualitatively consistent with the slower gas-phase inversion rates reported in the present study.

Registry No. Cyclohexane, 110-82-7; sulfur hexafluoride, 2551-62-4.

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Hydroalumination of 1-(Trimethylsilyl)-1,3-diynes. Syntheses of Stereodefined Enynes and Dienes

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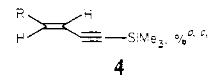
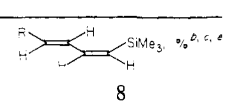
The conjugated enyne moiety is incorporated in a number of natural products.[1] Also, it can be readily converted in a stereospecific manner into the corresponding diene system.[2] Thus, it is not surprising that considerable effort has been expended in seeking stereoselective methods for syntheses of conjugated enynes.[3]

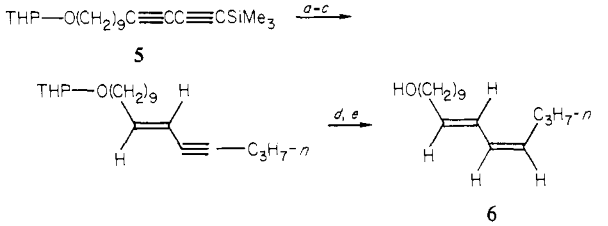
We have previously shown that symmetrically substituted 1,3-diynes react with lithium diisobutylmethylaluminum hydride in diglyme solvent to produce, after hydrolysis of the intermediate (*Z*)-enynylalanates, the corresponding *trans*-enynes.[4] Unfortunately, this *trans*-enyne synthesis cannot be employed for the preparation of unsymmetrical enynes since the reducing agent does not discriminate in its addition between the triple bonds of unsymmetrically alkyl-substituted conjugated diynes.[4] Hence, we have searched for a readily accessible 1,3-diyne system in which the triple bonds exhibit appreciably different reactivities toward nucleophilic and electrophilic reducing agents and contain a functionality capable of being elaborated into various derivatives. We now report that 1-(trimethylsilyl)-1,3-diynes **1**[5] fulfill this requirement.

Table I. Yields of 1-(Trimethylsilyl)-3-en-1-ynes **4** and 1-(Trimethylsilyl)-1,3-dienes 8

$RC{\equiv}C{-}C{\equiv}CSiMe_3$ **1**	 %^{a,c,e} **4**	 %^{b,c,e} 8
a, R = n-C_6H_{13}	95 (99)	97 (99)
b, R = Cy	93 (98)	96 (98)
c, R = t-Bu	90 (95)	91 (95)
d, R = Me_3Si	91 (96)^d	93 (96)^f

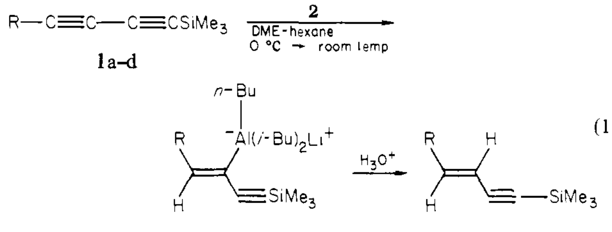
^{a} Derived from hydroalumination of **1** with Li[AlH(i-Bu)$_2$-n-Bu] followed by protonolysis. ^{b} Derived from hydroalumination of **4** with i-Bu_2AlH followed by protonolysis. ^{c} Isolated yields (Kugelrohr distillations). Isomeric purities are in parentheses. ^{d} The reaction was carried out at 25 °C for 18 h. ^{e} The IR, ^{1}H NMR, and mass spectral data of the compounds were consistent with the assigned structures. ^{f} Reference 16.

Scheme I



^{a} Li[AlH(i-Bu)$_2$-n-Bu]/DME-hexane/25 °C/1 h; 3 N HCl. ^{b} KF·2H_2O/DMF/25 °C.[7] ^{c} n-BuLi/hexane-diglyme/−78 → 25 °C; n-C_3H_7Br/25 → 80 °C/18 h.[9] ^{d} Disiamylborane/THF/0 °C/3 h; AcOH/60 °C/5 h, H_2O_2–NaOH/30 → 50 °C.[10] ^{e} CH_3OH–3 N HCl (trace).

Addition of 1-(trimethylsilyl)-1,3-decadiyne (**1a**) to lithium diisobutyl-n-butylaluminum hydride (**2**, Li[AlH(i-Bu)$_2$-n-Bu]) furnished, as evidenced by ^{1}H NMR analysis, the enynylalanate **3a** (eq 1). The regioselective formation of **3** points to a strong electron-withdrawing effect of the (trimethylsilyl)ethynyl moiety upon the alkyl-substituted triple bond, thus making it more susceptible to attack by the nucleophilic reducing agent **2**. This activating effect of the (trimethylsilyl)ethynyl group is further evidenced by the observation that treatment of an equimolar mixture of **1a** and 4,6-decadiyne with **2** (1 equiv) resulted in the nearly exclusive hydroalumination of the silyldiyne **1a**. The *Z* stereochemistry of the enynylalanate **3a** follows from its conversion to 1-(trimethylsilyl)-*trans*-3-decen-1-yne (**4a**) upon protonolysis. As shown in Table I, trans hydroalumination of 1-(trimethylsilyl)-1,3-diynes **1** followed by protonolysis represents a high-yield method for synthesis of a variety of 1-(trimethylsilyl)-*trans*-3-en-1-ynes **4**.[6]



(1)

a, R = n-hexyl; **b**, R = cyclohexyl;
c, R = *tert*-butyl; **d**, R = trimethylsilyl

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