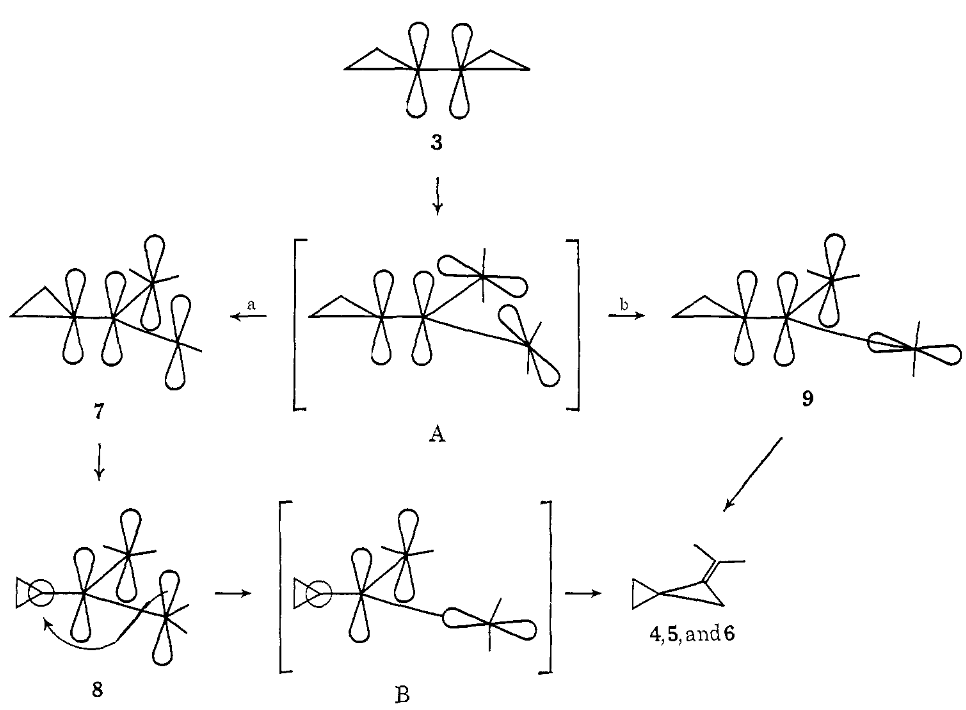
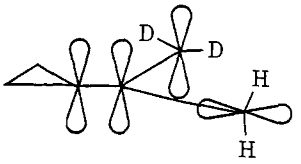
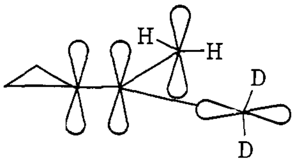
Scheme II

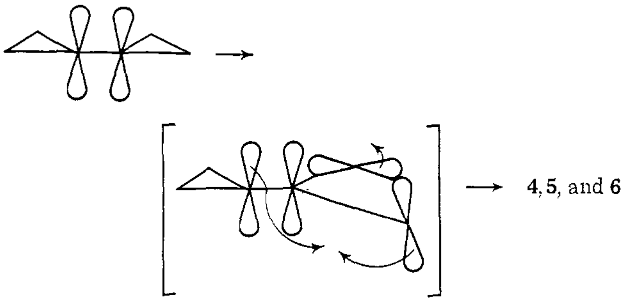


fect can be rationalized for path b if one considers that intermediate **9a** will be lower in energy than **9b**.[13]


9a


9b

In considering a concerted mechanism, the "pivot" type of transition state (transition state C) can rationalize the data if one assumes that the pivot methylene is the loosest CH_2 group in the transition state.



C

While a complete distinguishing of the mechanism is not possible in this case, significant insight is gained into the mechanistic process, insight which will undoubtedly be magnified as more analogy becomes available relating to secondary deuterium isotope effects in sigmatropic processes. In these and in our earlier results we want to emphasize that the isotope effect data may be interpreted using a simple, rule of thumb, "steric" interpretation of secondary isotope effects and that useful mechanistic conclusions can be deduced without rigorous theoretical analysis.

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[13] This is likely because of the greater steric requirement of CH_2 *vs.* CD_2 and, as described earlier, because of the differences between a planar and an orthogonal allylic CH_2 group in the twisting vibration.

Ring Inversion in Cyclohexanone

Sir:

We wish to report the first experimental determination of the free-energy barrier ($\Delta G^{\ddagger}$) for ring inversion in cyclohexanone.[1] For reasons discussed below, we

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[1] The claim by Jensen and Beck[2] that the "most probable" $\Delta G^{\ddagger}$ for ring inversion in cyclohexanone is 4.9 ± 0.3 kcal/mol was based on the observation that the proton nmr lines of this ketone (or its 2,2,6,6-d_4 derivative) are broader than the tetramethylsilane line at −168 to −172°. This extra broadening was attributed to the rate constant for ring inversion being in an intermediate region between the slow and fast exchange limits. However, there are large and *different* contributions to the line widths at low temperatures as a result of dipole–dipole relaxation, and thus no valid deduction about $\Delta G^{\ddagger}$ can be made from these experiments. Furthermore, the "confident" conclusion[2] that $\Delta G^{\ddagger}$ has a maximum value of 5.1 kcal/mol (5.2 kcal/mol for the tetradeuterio derivative) depends on the absence of near-coincidences in chemical shifts between the axial and equatorial protons on a CH_2 group. Such near-coincidences are found in 1,4-dioxane[3] and cannot be eliminated with real confidence for cyclohexanone. The barrier to ring inversion in 4,4-difluorocyclohexanone has been stated to be ≤ 2.3 kcal/mol because of the absence of broadening of the fluorine resonance at −183°.[4] Although near-coincidences in chemical shifts are less likely for fluorines than for protons,[5] such a possibility cannot be completely ruled out. The only well-established barriers for ring inversion in six-membered ketones are for 2,2,5,5-tetramethylcyclohexanone ($\Delta G^{\ddagger}$ = 8.1 kcal/mol)[6] and 2,2,5,5-tetramethyl-3-methylenecyclohexanone ($\Delta G^{\ddagger}$ = 5.9 kcal/mol),[7] where substituent effects are undoubtedly quite large.

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[3] F. A. L. Anet and J. Sandström, *Chem. Commun.*, 1558 (1971); F. R. Jensen and R. A. Neese, *J. Amer. Chem. Soc.*, **93,** 6329 (1971).

[4] R. E. Lack, C. Ganter, and J. D. Roberts, *ibid.*, **90,** 7001 (1968).

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[6] M. Bernard and M. St. Jacques, *Chem. Commun.*, 1097 (1970).

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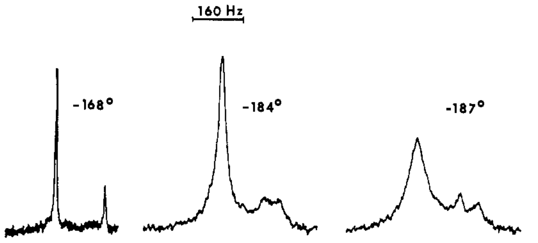
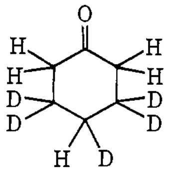


Figure 1. 251-MHz ^{1}H nmr spectra of cyclohexanone-*3,3,4,5,5-d*$_5$ in a 5:1 mixture of $CHClF_2$ and $CHCl_2F$ at various temperatures.

prepared and studied the nmr spectrum of cyclohexanone-*3,3,4,5,5-d*$_5$ (I). Exchange of 4-hydroxycyclohexanone with D_2O-Na_2CO_3 gave the 2,2,6,6-tetradeuterio derivative[8] which was converted into its *p*-toluenesulfonylhydrazone.[9] Treatment of the latter compound with $LiAlD_4$ in tetrahydrofuran followed by decomposition with water[9] gave cyclohexanol-*3,3,4,5,5-d*$_5$, which on chromic acid oxidation[10] gave I, isolated by vpc.



I

The 251-MHz proton nmr spectrum of I, obtained with the deuterons decoupled, is shown at several temperatures in Figure 1. From room temperature down to about −170° the spectrum consists of two lines (intensity ratio ≃4:1) which can be assigned to the four α protons and the single γ proton, respectively. The line of the γ proton broadens greatly below −180° and splits into a doublet below −184°.[11] The α-proton line merely broadens continuously as the temperature is lowered below −180°, but does not separate into two lines down to −190°. The much greater broadening of the α-proton line as compared to the γ-proton lines at temperatures below −185° is ascribed to faster intramolecular dipole–dipole relaxation in the CH_2 group as compared to the CHD group.[12] Thus, the advantage of deuteration in the present situation is not merely a simplification of the spectrum because of the reduction of the number of chemical shifts and the removal of strong *J* coupling effects, but includes an important reduction in the inherent line widths. The chemical-shift difference between an axial and equatorial γ proton in I is 0.24 ppm, and is thus considerably smaller than the 0.47-ppm chemical-shift difference in cyclohexane.[13]

From the nmr data on I the rate constant for ring inversion at −183° is calculated to be 130 sec^{-1}. The boat or twist-boat being assumed as an intermediate, the $\Delta G^{\ne}$ at −183° for the chair–boat process is calculated to be 4.0 ± 0.1 kcal/mol ($\Delta G^{\ne}$ at −183° for the chair–chair process is 4.1 kcal/mol). These kinetic parameters are expected to be valid for cyclohexanone itself since isotope effects should be very small.[14]

Strain-energy calculations give a value of 3.9 kcal/mol for the barrier to ring inversion in cyclohexanone,[15] in excellent agreement with the present experimental results. The barrier in cyclohexanone is substantially lower than the barriers in cyclohexanone oxime methyl ether[2] ($\Delta G^{\ne}$ = 5.6 ± 0.5 kcal/mol), methylenecyclohexane[2,16] ($\Delta G^{\ne}$ = 8.4 ± 0.1 kcal/mol), and cyclohexane[13,14] ($\Delta G^{\ne}$ = 10.2 kcal/mol) mainly because of differences in the torsional barriers about sp^3–sp^3 and various kinds of sp^3–sp^2 C–C bonds.[2,15]

Acknowledgment. This work was supported by the National Science Foundation.

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Detection of a Crown Family Conformation in Cyclooctane by Proton and Carbon-13 Nuclear Magnetic Resonance

Sir:

Cyclooctane and its simple derivatives appear to exist predominantly in boat–chair conformations, as shown by X-ray diffraction[1] and nmr[2] studies. The introduction of certain substituents or heteroatoms, however, can make a crown family[2f,3] conformation

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