pound **8** is comparable in analgesic activity to the corresponding 5-methyl homolog.[2,16]

Acknowledgment. We are indebted to Mrs. Ann Wright and to Dr. Henry Fales, both of the National Institutes of Health, for the nmr and mass spectral data, respectively.

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(16) E. L. May and J. G. Murphy, *J. Org. Chem.*, **20**, 257 (1955).
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Ring Inversion in 1-Methylenecyclohexane

Sir:

The study of the conformations of six-membered rings of sp^3-hydridized atoms has been an active area of research in the past few years.[1] Of the many physical and chemical techniques that can be applied to these conformational problems, nuclear magnetic resonance spectroscopy is especially useful in that nmr spectra can often be made to yield the rates of conformational interconversions. It is therefore possible to deduce the energetics of these processes and thereby gain additional information about the nonbonded interactions rampant in the molecule. A number of experiments with deuterated and fluorinated cyclohexanes have shown that the rate of chair–chair interconversion in this molecule is 7.1×10^{-2} sec^{-1} at $-105°$.[1f] The activation parameters $\Delta F^{\ddagger}$, $\Delta H^{\ddagger}$, and $\Delta S^{\ddagger}$ are about 10.2 kcal/mole, 10.8 kcal/mole, and 3 eu, respectively, for this motion.[1d,f,2]

A report has also described an nmr study of the conformational properties of cyclohexene, a carbocycle with four tetrahedral and two trigonal (sp^2) carbon atoms.[3] The free-energy barrier to ring inversion of cyclohexene is about 5 kcal/mole, much less than the barrier in cyclohexane.

There has been considerable interest in the conformational behavior of cyclohexyl systems with a single trigonal carbon atom. This system would correspond to the ring skeleton of cyclohexanone[4,5] as well as to the basic geometry expected of the cyclohexyl carbonium ion.[6,7] The chair form of this ring is presumably the most stable and one would anticipate a chair–chair interconversion in this system analogous to that found in cyclohexane.[8] The rates of interconversion of six-membered rings with one trigonal carbon have not, to our knowledge, been determined, and we report here preliminary proton magnetic resonance experiments with 1-methylenecyclohexane which permit an estimate of this rate.

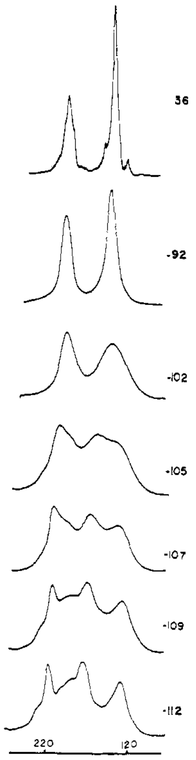
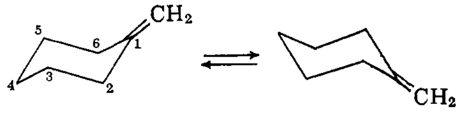


Figure 1. The alkyl portion of the pmr spectrum of methylenecyclohexane at 100 MHz. The peak positions, in hertz, are relative to internal TMS.

The pmr spectrum of methylenecyclohexane at ambient temperature consists of three signals: (a) a barely resolved triplet of lines (apparent J = 0.9 Hz, relative area 2) centered at 4.49 ppm, (b) a broad triplet (apparent J = 4.7 Hz, relative area 4) centered at 2.06 ppm, and (c) an ill-defined multiplet (relative area 6) centered at 1.52 ppm downfield from internal tetramethylsilane. These signals can comfortably be assigned to the vinyl protons, the 2- and 6-methylene groups, and the 3-, 4-, and 5-methylene groups, respectively. As the temperature of the sample is progressively lowered, the methylene portion of the spectrum broadens and finally, at temperatures below $-100°$ evolves into at least four broad signals centered at 2.16, 1.96, 1.74, and 1.29 ppm (Figure 1). Experiments at both 60 and 100 MHz confirm that the separations between these four envelopes correspond to chemical shifts.[9] The width of the peaks must be due to extensive spin–spin coupling since both the vinyl and the reference signals remain sharp at all temperatures.



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(1) For reviews see (a) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y. 1965; (b) H. Feltkamp and N. C. Franklin, *Angew. Chem. Intern. Ed. Engl.*, **4**, 774 (1965); (c) M. Hanack, "Conformation Theory," Academic Press Inc., New York, N. Y., 1965. Some more recent work includes (d) S. L. Spassov, D. L. Griffith, E. S. Glazer, K. Nararajan, and J. D. Roberts, *J. Am. Chem. Soc.*, **89**, 88 (1967); (e) J. B. Lambert and R. G. Keske, *ibid.*, **88**, 620 (1966); (f) F. A. L. Anet and A. J. R. Bourn, *ibid.*, **89**, 760 (1967).

(2) F. A. Bovey, F. P. Hood, E. W. Anderson, and R. L. Kornegay, *J. Chem. Phys.*, **41**, 2041 (1964).

(3) F. A. L. Anet and M. A. Haq, *J. Am. Chem. Soc.*, **87**, 3147 (1965).

(4) Reference 1a, p 112.

(5) B. Rickborn, *J. Am. Chem. Soc.*, **84**, 2414 (1962).

(6) S. Winstein and N. J. Holness, *ibid*, **77**, 5562 (1955).

(7) H. Kwart and T. Takeshita, *ibid.*, **86**, 1161 (1964).

(8) W. Moffit, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *ibid.*, **83**, 4013 (1961).

(9) Spectra were recorded with Varian Associates HA-100 and JEOL C-60H spectrometers using a 10% sample of methylenecyclohexane (Aldrich) in Freon-11. Temperatures were determined with a Digitec Model 560 digital thermometer and are believed to be accurate to a least 1°.

It is believed that these spectral changes are due to a slowing of the ring-inversion process for the following reasons. The resonances for the 3-, 4-, and 5-methylene groups develop into two resonances separated by 0.45 ppm. One may compare this value to 0.48 ppm found for the chemical shift difference between axial and equatorial protons in cyclohexane.[2] The upfield resonance of this set, at 1.29 ppm, is assigned to three axial protons and is somewhat broader than the one at lower field. Qualitatively, the same variation in line widths is found in cyclohexane. Similarly, the 2,6-methylene signal unfolds into two peaks separated by ~0.27 ppm, a value close to 0.24 ppm found for the chemical shift difference between axial and equatorial protons in the methylene groups adjacent to the double bond in cyclohexene.[3] Again, the upfield (axial) resonance is considerably broader than the downfield (equatorial) peak. The vinyl portion of the spectrum undergoes no change beyond slight viscosity broadening over the entire temperature range investigated. That the vinyl protons remain magnetically equivalent even when the conformational rate process is slow tends to rule out the presence of appreciable amounts of certain twist-boat and twist-chair conformations that, *a priori*, have nonequivalent methylene environments.

The signals at 1.74 and 1.29 ppm coalesce at ~ −105°, and it is estimated that the rate of the interconversion is 2×10^2 sec^{-1} at this temperature, a rate that corresponds to $\Delta F^\ddagger = 7.7$ kcal/mole.[10] It thus appears that replacement of a single sp^3 carbon atom in cyclohexane with an sp^2 carbon results in a lower barrier to chair–chair interconversion, probably because the number of repulsive H–H nonbonded interactions are reduced. A more accurate assessment of the nature of the conformations of methylenecyclohexane and the energetics of their interconversion will have to await the results of studies with certain deuterated analogs of this molecule.

Acknowledgment. We are indebted to Professors C. B. Anderson and B. Rickborn for helpful discussions. This work was supported by Grant 868-G1 from the Petroleum Research Fund of the American Chemical Society and, in part, by Grant GM-14692 from the National Institutes of Health.

[10] Estimated from the formula $k = 2^{1/2}\pi\Delta\nu$; *cf.* E. F. Caldin, "Fast Reactions in Solution," John Wiley and Sons, Inc., New York, N. Y., 1964, p 237.

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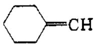
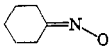
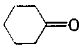
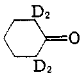
The Barrier to the Inversion of Six-Membered Rings Containing an sp^2-Hybridized Carbon

Sir:

Although the barriers to the ring inversion of cyclohexane and cyclohexene derivatives have been studied by variable-temperature nmr, no barrier for a six-membered ring containing only one sp^2-hybridized carbon atom has been reported. (From epr studies a barrier to the ring inversion of the cyclohexyl radical was estimated to be 4.9 ± 0.5 kcal/mole;[1] however, the exact hybridization of this species is uncertain.) Previous investigations of cyclohexanone have shown that at −140° the conformers appear to be rapidly interconverting on the nmr time scale.[2]

Changes have now been observed in the nmr spectra of cyclohexanone, tetradeuteriocyclohexanone, methylenecyclohexane, and O-methylcyclohexanone oxime at low temperatures. From these changes barriers to the interconversion of these compounds have been calculated (Table I).

Table I. Barriers for Chair–Twist Interconversions of Six-Membered Ring Compounds Containing a Trigonal Carbon Atom

Compound	$\Delta F^\ddagger$, kcal/mole	*T*, °C
	7.7 ± 0.5	−115
	5.6 ± 0.5	−152
	<5.1^a	−170
	<5.2^a	−168

^{a} From the data, barriers of 4.9 kcal/mole were calculated, but because of viscosity effects only upper limits could be obtained with confidence.

Clear transitions were observed in the variable-temperature nmr spectra of methylenecyclohexane and O-methylcyclohexanone oxime. For methylenecyclohexane (Figure 1) the two broad peaks of the ring protons, which are observed at room temperature, upon cooling below −109° change into a very complicated set of peaks. Because of the complexity of the spectrum, only maximum and minimum barriers to the interconversion were obtained. (All of the barriers were calculated assuming an intermediate occurs which has a 0.5 probability of becoming product. The reported barriers are to the formation of this intermediate.) From the low-temperature spectrum it is seen that the maximum peak separations lie between 10 and 40 Hz. At −109° (Figure 1b) no separation for any signal is observed; however, assuming the separation is already half complete for a signal whose final maximum separation is 10 Hz, a maximum $\Delta F^\ddagger$ of 8.2 kcal/mole can be calculated. Similarly at −119° (Figure 1c) the peaks appear almost completely separated, but assuming that a signal whose maximum separation is 40 Hz is only half-separated at this temperature, a minimum $\Delta F^\ddagger$ of 7.2 kcal/mole is obtained. Thus at −114°, $\Delta F^\ddagger = 7.7 \pm 0.5$ kcal/mole assuming an intermediate occurs having a 0.5 probability of becoming product.

Similarly, the barrier for the interconversion of O-methylcyclohexanone oxime was determined to be 5.6 ± 0.5 kcal/mole at −152°.

For cyclohexanone (20% by volume in vinyl chloride) and tetradeuteriocyclohexanone (20% by volume in a mixture of vinyl chloride and trifluorochloroethylene),

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(1) S. Ogawa and R. W. Fessenden, *J. Chem. Phys.*, **41**, 994 (1964).

(2) J. E. Anderson, D. D. MacNicol, and B. D. Batts, unpublished results as quoted by J. E Anderson, *Quart. Rev.* (London), **19**, 426 (1965).