Table II. Reaction Mechanism of the λ-Process

Mechanism	$[\partial(1/T_2')/\partial\tau]$ for $\lambda = 0$[a]	$(1/T_2' - 1/T_2)$, sec.$^{-1}$ at 5° Calcd., eq. 13[b,c]	$(1/T_2' - 1/T_2)$, sec.$^{-1}$ at 5° Obsd.[c]
1	$-[(\delta_2' + \delta_3')(\delta_1' + \delta_4')/2 + \delta_2'\delta_3'/K]$	3.51 ± 0.66	3.18 ± 0.50
2	$-[(\delta_2' + \delta_3')(\delta_1' + \delta_4')/2 + \delta_1'\delta_4'/K]$	5.78 ± 0.83	3.18 ± 0.50
3	$[(\delta_4' - \delta_1') + (\delta_3' - \delta_2')/K]^2K/16$	4.31 ± 0.69	3.18 ± 0.50

[a] δ_i' is the chemical shift of the i th n.m.r. line, in radians/sec., relative to the average chemical shift, δ_0, of all β-C(CH$_3$)$_2$ protons. That is, $\delta_i' = \delta_i - \delta_0$, where $\delta_0 = [K(\delta_1 + \delta_4) + (\delta_2 + \delta_3)]/2(1 + K)$. The values of δ_1' and δ_2' are negative, those of δ_3' and δ_4' are positive. [b] $\lambda[\partial(1/T_2')/\partial\lambda] = 3.30$; $\tau[\partial(1/T_2')/\partial(\tau)] = 0.21$ (1), 2.48 (2), 1.01 (3). [c] Error estimates correspond to two standard deviations.

Appendix

In this section we wish to give some useful p.m.r. spectral relationships for proton exchange between two chemical shifts. These relationships are special solutions of a more general equation given by Gutowsky and Saika.[22] The mathematics is straightforward, and only the final results will be reported.

Let the chemical shifts that are involved in the exchange be δ_A and δ_B, and let the corresponding proton fractions be p_A and p_B ($p_B = 1 - p_A$). Let the *average* chemical shift of the A–B proton system be δ_0, where $\delta_0 = p_A\delta_A + p_B\delta_B$. Let τ be the relaxation time for exchange, that is, $\tau^{-1} = \tau_A^{-1} + \tau_B^{-1}$.

When τ is very large, there are two p.m.r. lines with maxima at δ_A and δ_B, respectively. As τ decreases, these maxima move closer together, and eventually the lines merge. While the two resonances are still quite apart, the positions of the maxima, d_A and d_B, are given by eq. 16, provided that $1/T_2 << |\delta_A - \delta_B|$. After the resonances are coalesced, and if

$$d_A - \delta_0 = (\delta_A - \delta_0)\left[1 - \frac{1}{1 + (\delta_B - \delta_A)^2\tau^2}\right] \quad (16a)$$

$$d_A - d_B = (\delta_A - \delta_B)\left[1 - \frac{1}{1 + (\delta_B - \delta_A)^2\tau^2}\right] \quad (16b)$$

$\tau^{-1} >$ *ca.* $|2\delta_A - 2\delta_B|$, the position, d_0, of the maximum of the combined line is given by eq. 17. If

$$d_0 - \delta_0 = p_Ap_B(p_B - p_A)(\delta_B - \delta_A)^3\tau^2 \quad (17)$$

$d_A > p_B$, then it follows from eq. 17 that $(d_0 - \delta_0)$ and $(\delta_A - \delta_0)$ have the same algebraic sign.

Under the conditions where eq. 17 applies, the line half-width, $1/T_2'$, is given by eq. 18.

$$\frac{1}{T_2'} = \frac{1}{T_2} + p_Ap_B(\delta_A - \delta_B)^2\tau \times [1 + (p_Ap_B - [p_B - p_A]^2)(\delta_A - \delta_B)^2\tau^2] \quad (18)$$

---

(22) H. S. Gutowsky and A. Saika, *J. Chem. Phys.*, **21**, 1688 (1953), eq. 17.

Ring Inversion in Cyclohexene[1]

F. A. L. Anet[2] and M. Z. Haq

Contribution from the Department of Chemistry, University of Ottawa, Ottawa, Ontario, and No. 1799 from the Department of Chemistry, University of California, Los Angeles, California. *Received March 15, 1965*

The proton n.m.r. spectrum of cyclohexene-cis-3,3,4,-5,6,6-d_6 has been measured in bromotrifluoromethane solution at various temperatures down to −170°. The band of H-4 and H-5 broadens at about −150° and separates into two bands at −164°. The rate constant for ring inversion at −164° is 45 sec.$^{-1}$ and the nature of the inversion process is discussed. The chemical shift difference between axial and equatorial protons in cyclohexene is estimated to be 24 ± 2 c.p.s.

Introduction

In recent years the rates of ring inversion in saturated, six-membered rings have been extensively studied by nuclear magnetic resonance (n.m.r.) spectroscopy. The compounds investigated include cyclohexane,[3] substituted cyclohexanes,[4] and derivatives of piperidine,[5] piperazine,[6] 1,2-dioxane,[7] and 1,2-dithiane.[7] All these compounds exist in chair conformations and the rates of inversion are such that the n.m.r. measure-

---

(1) Supported by the National Research Council of Canada and by the National Science Foundation (Grant No. GP 3780).

(2) Department of Chemistry, University of California, Los Angeles, Calif. 90024.

(3) (a) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Am. Chem. Soc.*, **82**, 1256 (1960); **84**, 386 (1962); (b) R. K. Harris and N. Sheppard, *Proc. Chem. Soc.*, 419 (1961); (c) W. B. Moniz and J. A. Dixon, *J. Am. Chem. Soc.*, **83**, 1671 (1961); (d) S. Meiboom, paper presented at the Symposium on High Resolution Nuclear Magnetic Resonance, Boulder, Colo., July 1962; (e) F. A. L. Anet, M. Ahmad, and L. D. Hall, *Proc. Chem. Soc.*, 145 (1964); (f) F. A. Bovey, F. P. Hood, III, E. W. Anderson, and R. L. Kornegay, *ibid.*, 146 (1964); *J. Chem. Phys.*, **41**, 2041 (1964).

(4) G. V. D. Tiers, *Proc. Chem. Soc.*, 389 (1960); L. W. Reeves and K. O. Stromme, *Trans. Faraday Soc.*, **57**, 390 (1961); *Can. J. Chem.*, **38**, 1241 (1960); *J. Chem. Phys.*, **34**, 1711 (1961); S. Brownstein, *Can. J. Chem.*, **40**, 870 (1962); J. D. Roberts, *Angew. Chem.*, **75**, 20 (1963); N. Muller and W. C. Tosch, *J. Chem. Phys.*, **37**, 1167 (1962); N. O. Brace, *J. Am. Chem. Soc.*, **86**, 665 (1964); W. C. Neikam and B. P. Dailey, *J. Chem. Phys.*, **38**, 445 (1963).

(5) L. W. Reeves and E. J. Wells, *Discussions Faraday Soc.*, **34**, 177 (1962).

(6) L. W. Reeves and K. O. Stromme, *J. Chem. Phys.*, **34**, 1711 (1961).

(7) G. Claeson, G. H. Androes, and M. Calvin, *J. Am. Chem. Soc.*, **82**, 4428 (1960); **83**, 4357 (1961); A. Lüttringhaus, S. Kabuss, W. Maier, and H. Friebolin, *Z. Naturforsch.*, **16b**, 761 (1961).

ments have been made in the range of −80° to room temperature.

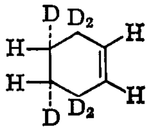
Calculations,[8] of a more or less empirical character, of the energy barrier to inversion in cyclohexane have been carried out. The results, which are in good agreement with experiment, also serve to define the transition states and the presence of boat intermediates.

The introduction of an endocyclic double bond in a six-membered ring results in a change of conformation from a chair to a half-chair,[9] at least in a carbocyclic compound.[10] Ring inversion can take place in the half-chair, but there is no report in the literature of any determination of the rate of this process.[11] It would be expected that the rate of ring inversion would be much larger for the half-chair than for the chair conformation and might even be too large for determination by n.m.r.

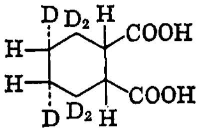
In fact, as will be shown in this paper, the rate constant for ring inversion in cyclohexene is very large indeed and is close to the upper limit that can be studied (at least directly) by that method. In practice, this means that measurements have to be made at very low temperatures, where the experimental difficulties are considerable. Furthermore, as the temperature is lowered, T_1 becomes rather short, even in the most mobile solvents. The lines observed are therefore rather broad; *e.g.*, at −150° the line width of tetramethylsilane is several cycles per second instead of the few tenths of a cycle per second found at room temperature.

The 60-Mc./sec. proton spectrum of cyclohexene as measured[12] at room temperature is clearly consistent with rapid inversion. Apart from the olefinic protons at τ 4.41 there are two bands of equal intensities at 8.04 and 8.35 which can[12] be assigned to the allylic and homoallylic protons, respectively. Because of complicated spin–spin coupling, the bands of the methylene protons are very complex multiplets.

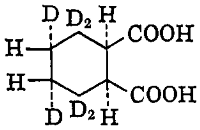
If averaging effects resulting from inversion were not present, separate signals would be observed for the axial and equatorial homoallylic protons. The allylic protons would also be of two types, namely quasi-axial and quasi-equatorial. It is obvious that the spectrum of the methylene protons would be even more complex under these conditions than it is at room temperature. For these reasons we have synthesized cyclohexene-*cis*-3,3,4,5,6,6-d_6 (I) and have studied its n.m.r. spectrum at various temperatures. The choice of this compound was a compromise between spectral simplicity[3e,f] and ease of synthesis. Compound I was obtained by the reaction[13] of lead tetraacetate on a mixture of dicarboxylic acids[14] II and III, and was purified by gas chromatography.



I



II



III

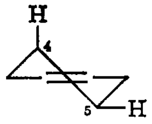
Results

The n.m.r. spectrum of I at about −50° in bromotrifluoromethane consisted of two bands (τ 4.40 and 8.42) of equal intensities, as expected. The bands were broad because of proton–deuteron coupling; they became much sharper when the proton spectrum was observed with simultaneous strong irradiation at the deuteron resonance frequency. All the low temperature spectra of I were taken under the latter conditions, *i.e.*, with the protons decoupled from the deuterons.

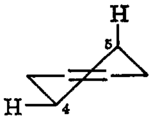
The band at τ 8.42 broadened appreciably at temperatures below about −150°. At −164°, the band became a doublet whose separation gradually increased and was 19.8 c.p.s. at −170° (Figure 1). The mean chemical shift at −170° was τ 8.39. The line width at half-height of the internal tetramethylsilane reference was 6 c.p.s. at −170°.

Discussion

The two half-chair conformations[9] of I are Ia and Ib, where only the protons on C-4 and C-5 are shown.



Ia



Ib

In Ia H-4 is axial while H-5 is equatorial, and *vice versa* in Ib.

The coupling constants between H-4 and H-5 in either Ia or Ib should be small, probably in the range of 2 to 4 c.p.s., in analogy[15] with other *gauche* vicinal coupling constants. The chemical shift between H-4 and H-5 is difficult to predict. In cyclohexane the axial–equatorial shift is[3e,f] 28.7 c.p.s. (at 60 Mc./sec.). If a similar chemical shift exists in Ia and Ib, the spectrum of H-4 and H-5, in the absence of ring inversion, will be approximately of the AX type. Since the inherent line widths at the significant temperatures are greater than 4 c.p.s., the splitting which results from the coupling of H-4 with H-5 is not expected to be resolved. Under these conditions the spectrum is essentially a doublet, whose separation is the H-4–H-5 chemical shift.

The fact that the spectrum of H-4 and H-5 in I consists of two bands below −164° shows that the rate of ring inversion at these temperatures is sufficiently low that the spectrum is no longer the average of Ia and Ib. At −170° the separation of the two bands is 19.8 c.p.s. but has not yet reached a constant value. The true chemical shift between H-4 and H-5 is estimated to be 24 ± 2 c.p.s.

The rate constant (k, in units of sec.$^{-1}$) for the ring inversion Ia $\rightleftarrows$ Ib can be calculated at the coalescence temperature from the expression[16] $k = \pi\nu/\sqrt{2}$, where ν

---

[8] J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961).

[9] W. Klyne, "Progress in Stereochemistry," Vol. 1, Butterworths and Co. (Publishers) Ltd., London, 1954, p. 81.

[10] A. McL. Mathieson, *Tetrahedron Letters*, **No. 2**, 81 (1963).

[11] The half-chair conformation of cyclohexene exists in *dl* forms. Ring inversion results in a change of configuration and thus provides a mechanism for racemization. An unsuccessful attempt to resolve cyclohexene-*cis*-4,5-dicarboxylic acid was interpreted in terms of rapid ring inversion by J. Boeseken and W. J. F. de Rijck van der Gracht, *Rec. trav. chim.*, **56**, 1203 (1937). For conformational analysis of various cyclohexene derivatives under conditions of rapid ring inversion, see E. W. Garbisch, *J. Org. Chem.*, **27**, 4249 (1962).

[12] K. B. Wiberg and B. J. Nist, *J. Am. Chem. Soc.*, **83**, 1226 (1961).

[13] C. A. Grob and A. Weiss, *Helv. Chim. Acta*, **43**, 1390 (1960); E. E. van Tamelen and S. P. Pappas, *J. Am. Chem. Soc.*, **85**, 3297 (1963); E. J. Corey and J. Casanova, Jr., *ibid.*, **85**, 165 (1963).

[14] F. A. L. Anet and M. Z. Haq, to be published.

[15] N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry," Holden-Day, Inc., San Francisco, Calif., 1964, p. 49.

[16] H. S. Gutowsky and C. H. Holm, *J. Chem. Phys.*, **25**, 1228

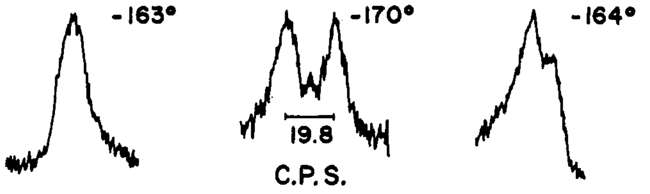


Figure 1. Bands of H-4 and H-5 in cyclohexene-*cis*-3,3,4,5,6,6-d_6 in bromotrifluoromethane solution at low temperatures.

is the chemical shift (in c.p.s.). This expression is actually valid only when the spectrum consists of two sharp lines of equal intensities when $k << \nu$, and one sharp line when $k >> \nu$, conditions which are not well satisfied in the present instance. The value of k (53 sec.$^{-1}$) so calculated is actually quite close to the value (45 sec.$^{-1}$) obtained by taking into account a finite line width according to the method[16] of Gutowsky and Holm. In both cases, the free energy of activation (ΔF^*), calculated with a transmission coefficient of one, is 5.3 kcal./mole.

The effect of deuterium substitution on the rate of ring inversion of the half-chair is expected[3e] to be negligible compared to likely errors in the present measurements. In the remaining discussion we will therefore discuss the data with respect to (undeuterated) cyclohexene.

The spectra of I are hardly suitable for obtaining k with any accuracy over a reasonable range of temperatures. It is therefore not possible[17] to obtain the energy of activation of ΔH^* or ΔS^*. In a simple process such as ring inversion, which is taking place in an inert solvent, the contributions to ΔS^* from changes in vibrational and rotational frequencies and in solute–solvent interactions on going from the initial state to the transition state should be very small.[18] The contribution of symmetry to ΔS^* can be calculated[19] easily if the geometry of the transition state is known.

Two transition states can be envisaged for the ring inversion of cyclohexene. One possibility is a structure with a planar carbon skeleton, but because this has a large number of eclipsed CH bonds as well as large angle distortions, it is undoubtedly much higher in energy than a structure (AB in Figure 2) with only five carbon atoms in one plane. This latter structure leads to the boat form (B) of cyclohexene. From specific heat measurements on cyclohexene, it has been deduced[20] that the boat form is 2.7 kcal./mole less stable than the half-chair. The boat is thus an intermediate in the ring inversion of the half-chair (Figure 2).

The symmetry number[19] of the half-chair is 2, and that of the transition state discussed above is 1. Both forms exist in pairs of nonsuperposable mirror images. This effect contributes $+R \ln 2$ to ΔS^*. In terms of the structures in Figure 2, there are two ways that A can go to the transition state, namely A → AB and A → AB′ (note that AB and AB′ are superposable, although the out-of-plane carbon atom in AB is different from that in AB′).

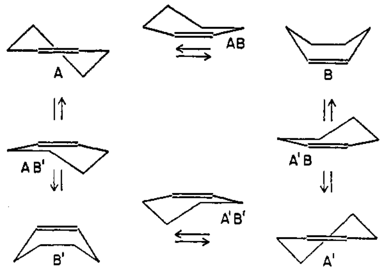


Figure 2. Interrelationship of various forms of cyclohexene: A and A′ (half-chairs); B and B′ (boats); AB, A′B, A′B′, AB′ (transition states). Only the carbon skeletons are shown.

Because the boat form is a necessary intermediate in the ring inversion, a molecule starting at A and passing over transition state AB to the boat form B on its way to A′ has an equal probability of coming back to A as of going to A′. Thus k for the half-chair to boat process is twice that for the full inversion of the half-chair. Such an effect is equivalent to a contribution of $-R \ln 2$ to ΔS^*. The two effects therefore cancel. This can be clearly seen from Figure 3. The rate of A′ → B′ is the same as that of A′ → A (note that the two ends of the graph should really be joined).

Thus, ΔF^* for the process A → B is 5.3 kcal./mole, and for this process $\Delta S^* = 0$ from symmetry contributions. Therefore, ΔH^* is 35. kcal./mole, as shown in Figure 3. An identical statement is that ΔF^* for the half-chair to boat process (*e.g.*, A → B *and* B′ in Figure 2) is 5.2 kcal./mole; now $\Delta S^* = +R \ln 2$ from symmetry effects, so that ΔH^* has the same value as previously calculated. The various kinetic parameters for the half-chair to boat and for the complete inversion processes are given in Table I.

Table I. Kinetic Parameters for Conformational Changes in Cyclohexene

Process	k, sec.$^{-1}$	ΔF^* kcal./mole	ΔH^*, kcal./mole	ΔS^*, e.u.
Half-chair to boat	90	5.2^a	5.3^b	+1.3^c
Inversion of half-chair	45	5.3^a	5.3^b	0^c

^{a} At −164°. ^{b} Calculated from $\Delta H^* = \Delta F^* + T\Delta^*$. ^{c} Calculated from theoretical considerations.

If the values given in Table I for ΔH^* and ΔS^* are accepted, it can be calculated that the average lifetime at 25° of a cyclohexene molecule before inversion is of the order of 10^{-9} sec. By comparison, the corresponding lifetime of a cyclohexane molecule at 25° is[21] 4×10^{-4} sec.

(1956); J. A. Pople, W. G. Schneider, and J. H. Bernstein, "High-resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, p. 218.

(17) See A. Allerhand and H. S. Gutowsky, *J. Chem. Phys.*, **41**, 2115 (1964), for the errors which can occur in obtaining ΔS^* and ΔH^* from n.m.r. spectra.

(18) J. E. Leffler and E. Grunwald, "Rates and Equilibria of Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1963, p. 118.

(19) J. G. Aston in "Determination of Organic Structures by Physical Methods," E. A. Braude and F. C. Nachod, Ed., Academic Press Inc., New York, N. Y., 1955, p. 525.

(20) C. W. Beckett, N. K. Freeman, and K. S. Pitzer, *J. Am. Chem. Soc.*, **70**, 4227 (1948). On the basis of eclipsing effects these authors calculated that the half-chair was more stable than the boat by 2.2 kcal./mole. Since they concluded that the experimental value was in good agreement with this, the error in their thermodynamic result is probably not greater than ±0.5 kcal./mole.

(21) This value comes from spin-echo n.m.r. studies on cyclohexane and cyclohexane-d_{11} by A. Allerhand, F. Chen, and H. S. Gutowsky (private communication of H. S. G. to F. A. L. A.) and is probably more reliable than the data of ref. 3. The value of ΔH^* given by us (ref. 3e) for ring inversion of cyclohexane-d_{11} is too large by at least 1 kcal./mole because of an arithmetical error in the calculations of the rate constants by the slow exchange approximation. The original rate constants were too small by a factor of two.

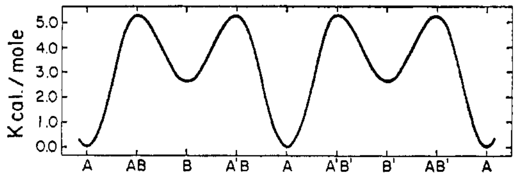


Figure 3. Diagrammatic representation of the energies of the various forms of cyclohexene shown in Figure 2.

This picture of ring inversion in cyclohexene is similar in many ways to that of the ring inversion in cyclohexane.[8] It differs in some respects, however, because the boat form of cyclohexene is fairly rigid and cannot undergo easy pseudo-rotation as can the boat form of cyclohexane. As shown in Figures 2 and 3, inversion of the boat form of cyclohexene (*e.g.*, B → B′) takes place *via* the half-chair form as an intermediate. It is interesting that the boat form appears to be more stable than the half-chair form in six-membered lactones and amides. Mathieson[10] has ascribed this difference from the carbocyclic analog to short bond lengths around the heteroatoms in lactones and amides.

The spectrum of I at −170° gives no evidence for an equilibrium mixture of boat and half-chair forms, where substantial amounts of both forms are present. This does not rule out such a possibility, because the spectrum is also consistent with any proportion of the two forms, provided that the axial–equatorial chemical shifts are roughly the same in the boat as in the half-chair. Previous results, of course, strongly favor the half-chair as the stable state for cyclohexene, and the proportion of the boat form which is present at −170° according to the thermodynamic work[20] is far too small to be observed by n.m.r.

Finally, the assignment of the axial and equatorial protons to the high- (τ 8.59) and low-field (τ 8.19) bands, respectively, rather than *vice versa* is not required by any of the present evidence. However, the magnetic anisotropy[22] of the double bond is not expected to reverse the normal shift of axial and equatorial protons, as found in cyclohexane derivatives, and data[23] on various simple cyclohexene derivatives obtained in this laboratory support this contention.

Experimental

Cyclohexene-cis-3,3,4,5,6,6-d_6. A mixture of the dicarboxylic acids[14] II and III (1.0 g.), lead tetraacetate (3.0 g.), and pyridine (12 ml.) was heated to 50–60° while a stream of nitrogen was passed through the solution. The gas stream was passed through a receiver cooled in a Dry Ice–acetone bath. About 3 to 4 ml. of a pyridine solution of the deuterated cyclohexene was thus collected. The product was treated with excess dilute hydrochloric acid and extracted with 1 ml. of methylene chloride. The methylene chloride extract was dried over anhydrous sodium sulfate and its volume was reduced to about one-third by distillation. The concentrated extract was injected, in small portions, in a gas chromatograph. A column of diisodecyl phthalate at 97° was used and the peak corresponding to cyclohexene was collected in a receiver cooled in liquid nitrogen. Experiments with undeuterated substrate showed that the product thus obtained was identical with cyclohexene as shown by infrared and n.m.r. spectroscopy, and that the yield was about 20%. The deuterated product which collected in the receiver was transferred to an n.m.r. tube on a vacuum line. Bromotrifluoromethane was then condensed in the tube, which was cooled in Dry Ice. After tetramethylsilane had been added, the solution was stirred with a small glass rod. The loosely stoppered tube was then quickly transferred to the previously cooled probe of the spectrometer.

N.m.r. Spectra. The spectra were obtained on a Varian HR60 (60 Mc./sec.) spectrometer equipped with a low temperature system of a type previously described.[24] Rather large flow rates of cold nitrogen were required to obtain a temperature of −170°. An NMR Specialties SD60 decoupler was used for double irradiation at the deuteron resonance frequency.

[22] L. M. Jackman, "Applications of NMR in Organic Chemistry," Pergamon Press, Inc., New York, N. Y., 1959, Chapter 7; W. A. Ayer, C. E. McDonald, and J. B. Stothers, *Can. J. Chem.*, **41**, 1113 (1963).

[23] Unpublished results of F. A. L. Anet, M. Ahmad, and A. J. R. Bourn.

[24] F. A. L. Anet, *J. Am. Chem. Soc.*, **86**, 458 (1954).