Rate measurements were accomplished by the usual techniques.[6,17] The titrating solutions were for acetolyses, 0.050 N sodium acetate in acetic acid and, for ethanolyses and methanolyses, 0.04 1 N sodium methoxide in anhydrous methanol. The indicators used were bromophenol blue and bromothymol blue, respectively.

Solvents.—Absolute ethanol was prepared according to the method of Fieser.[18] Absolute methanol was prepared by distillation from magnesium turnings. Aqueous ethanol (80% by volume) was prepared volumetrically from absolute ethanol and distilled water. Acetic acid solvent was prepared from 985 ml. glacial acetic acid (Du Pont, 99.7% min.) and 15 ml. acetic anhydride.

Treatment of Kinetic Data.—The thermodynamic activation functions were obtained by IBM 1620 computer regression analysis. Solvent ionizing strength sensitivity, a, and the Hammett ρ-value also were obtained by IBM 1620 computer regression analysis.[19]

Product Studies. A. Acetolysis.—Cyclopropylcarbinyl p-toluenesulfonate (IIIb, 885 mg.) was solvolyzed in 25 ml. of acetic acid (*cf.* above for solvent composition) containing potassium acetate (500 mg.) at 30° for 20 half-lives in one run and at 60° for 10 days in a second run. The material was added to ice-water (200 ml.) and extracted with three 60-ml. portions of ether. The ether extract was washed with saturated sodium bicarbonate followed by water, dried over sodium sulfate, and most of the ether removed by distillation. Injection of a sample of this solution into a vapor fractometer (sucrose acetate isobutyrate, 125°) gave in addition to a solvent peak one small peak (A, 5.8-min. retention time) and two large, sharp peaks (B, 7.1-min. retention time, and C, 8.0-min. retention time). A sample of authentic cyclopropylcarbinyl acetate[20] in ether gave a chromatogram with a retention time identical with peak C and, similarly, a sample of authentic cyclobutyl acetate[20] in ether gave a chromatogram with a retention time identical with peak B.

B. Ethanolysis.—Cyclopropylcarbinyl p-toluenesulfonate (IIIb, 1.2 g.) was solvolyzed in 50 ml. of absolute ethanol at 30° for 20 half-lives. The material was added to ice-water (200 ml.) and extracted with three 40-ml. portions of ether, dried over sodium sulfate, and most of the solvent removed by distillation. Injection of a sample of this solution into a vapor fractometer (Apiezon grease, 100°) gave, almost immediately, a strong peak corresponding to volatile solvent. The only other peak was a strong, sharp peak with a retention time of 4.9 min.

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[17] Aliquot samples were removed from a single container for titrations rather than individual ampoules. This modification reduced the "pre-run" solvolysis and shortened the sampling time for each individual titration.

[18] L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., Rev., D. C. Heath and Co., Boston, Mass., 1957, p. 285.

[19] These analyses were performed through the courtesy of the Louisiana Polytechnic Institute Computer Center, Ruston, La.

[20] J. D. Roberts and V. C. Chambers, *J. Am. Chem. Soc.*, **73**, 5034 (1951).

The Conformations of Cyclic Compounds in Solution. I. Shikimic Acid

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The conformation of shikimic acid has been determined in solution and is shown to be essentially a half-chair conformation.

The importance of shikimic acid (I) as an intermediate in the conversion of carbohydrates to aromatic compounds in nature is well-known.[2] In view of this it is surprising that no attempt has been made previously to measure the precise conformation of this compound in solution. N.m.r. spectroscopy has been used to determine the precise conformations of several important cyclic biochemicals[3,4] in solution and this method has now been used to determine the conformation of shikimic acid.

Experimental

The compound used was a commercial sample from the Aldrich Chemical Co. and was used without further purification, m.p. 84.0–184.5°, $[\alpha]_D$ $-175°$ (c 2, water). The spectrum (Fig. 1) was measured in deuterium oxide solution with a Varian 4302 B spectrometer and a Varian V 3521 integrator for base-line stabilization. Calibration was by the usual side-band technique and, in the absence of any generally accepted n.m.r. internal standard for aqueous solutions, acetonitrile[5] (7.98 τ) was used.

The assignment of the spectrum was straightforward. The signal at lowest field could be assigned with certainty to the olefinic proton (H-2) and the multiplets at highest field must have been due to the C-6 methylene protons. Allocation of the remaining multiplets then followed, and the first-order coupling constants and chemical shifts are shown in Table I. An explicit analysis of this spectrum would involve the solution of a six-spin system which would be tedious and in fact unnecessary. It seemed improbable that second-order effects would be significant and to check this a series of partial analyses were made. The spectrum was subdivided into five sections (H-5, H-6e, H-6a), (H-3, H-4, H-5), (H-2, H-3, H-4), (H-4, H-5, H-6a), (H-4, H-5, H-6e) and each of these was analyzed[6] separately. The values thus obtained are shown in Table I together with the first-order values, and it can be seen that both sets are in close agreement. In addition to the vicinal coupling constants, long-range couplings were observed between the C-6 protons and the C-2 and C-3 protons. In view of the opposite relative signs of these couplings,[7] the values shown in Table I are probably the averaged values.

TABLE I

SPECTRAL DATA FOR SHIKIMIC ACID

Chemical shifts (τ-values)[a]

	H-2	H-3	H-4	H-5	H-6e	H-6a
First order	3.12	5.59	6.31	6.00	7.23	7.86
From analysis	3.12	5.59	6.24	5.82	7.19	7.89

Coupling constants (c.p.s.)

	$J_{2,3}$	$J_{2,6}$	$J_{3,4}$	$J_{3,6}$	$J_{4,5a}$	$J_{5,6a}$	$J_{5,6e}$	$J_{6a,6e}$
First order	4.0	1.8	3.9	1.5	8.4	6.2	5.0	18.5
From analysis	4.0	1.8[b]	3.8	1.5[b]	8.4	5.9	4.8	18.5

[a] Since spectra were measured in deuterium oxide solution, no signals were observed from –OH or –CO_2H. [b] Uncorrected values.

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[1] University of Ottawa Postdoctoral Fellow, 1962–1963; Department of Chemistry, University of British Columbia, Vancouver 8, B. C.

[2] "Biochemists Handbook," C. Long, Ed., E. and F. N. Spon Ltd., London, 1961, p. 594.

[3] C. D. Jardetsky, *J. Am. Chem. Soc.*, **83**, 2919 (1961), and previous references.

[4] R. U. Lemieux, *Can. J. Chem.*, **39**, 116 (1961).

[5] R. A. Y. Jones, A. R. Katritzky, J. N. Murrel, and N. Sheppard, *J. Chem. Soc.*, 2576 (1962).

[6] The author is indebted to Miss O. Boshko of the Ottawa University Computing Centre for computing these analyses on an IBM 650 computer.

[7] D. D. Elleman and S. L. Manatt, *J. Chem. Phys.*, **36**, 2346 (1962).

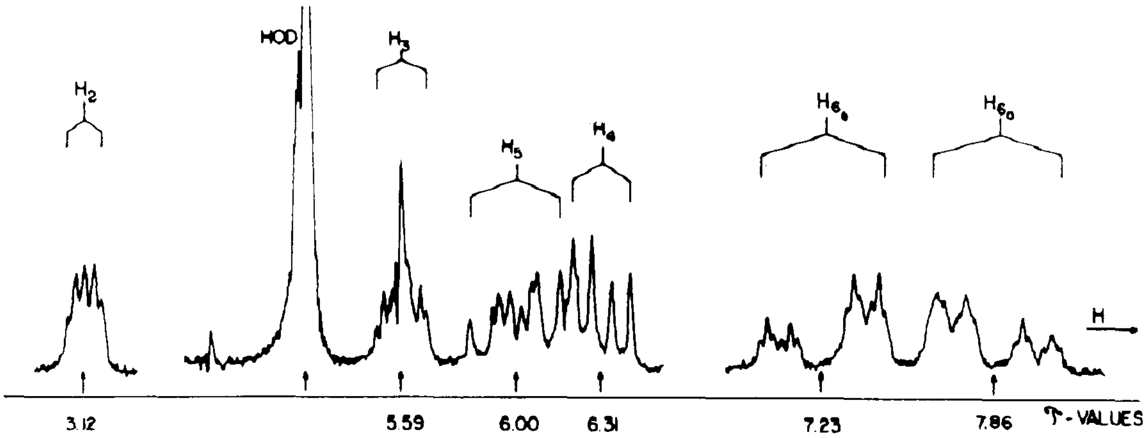

Fig. 1.—Nuclear magnetic resonance spectrum of shikimic acid in deuterium oxide, measured at 60 Mc./sec.

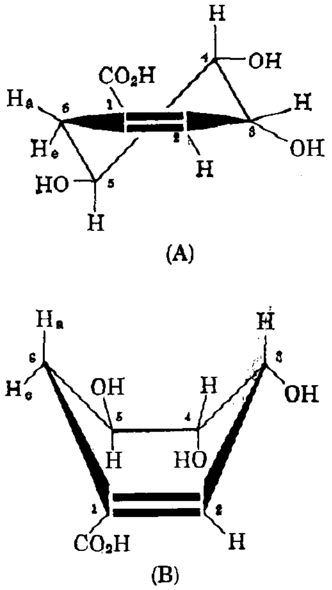

Fig. 2.—Conformations of shikimic acid: (A) the half-chair conformation; (B) the boat conformation.

Discussion and Results

The geometry of a cyclohexene ring is essentially defined by the double bond with its two sp^2-hybridized carbon atoms. These force the four adjacent carbon atoms of the double bond to be coplanar which prevents the ring from adopting the chair conformation commonly assumed by cyclohexanes. To accommodate this coplanarity the cyclohexene ring can adopt either a "boat" conformation or a "half-chair" conformation. Beckett, Freeman, and Pitzer[8] have calculated that for cyclohexene itself the half-chair conformation is energetically more favored than the boat form by 2.7 kcal./mole. However it was not known whether a similar energy difference would apply in the case of a substituted cyclohexene.

It is known that many cyclic systems, such as cyclohexane, undergo rapid conformational inversion at room temperature, and in such cases the observed conformation is "time-averaged" and represents a statistical average of all the conformational species participating in the inversion cycle. However, if the cyclohexane ring bears substituents which are arranged such that one conformational species is more favored energetically than any other, then the observed conformation of the ring will approximate to that of the favored species. Similar considerations can be applied to substituted cyclohexenes. In the case of shikimic acid, four "extreme" conformations are possible, two half-chair forms and two boat forms. The two most energetically favored of these are shown in Fig. 2. In the following discussion it is assumed that the shape of shikimic acid can be considered in terms of these two basic conformations and that conformational inversion can occur between the two. The most energetically favored species will contribute most to the observed time-averaged conformation. Contributions of the other less favored species to the observed conformation are likely to be small. The approximate dihedral angles for the theoretical half-chair and boat conformations were measured with Barton[9] models and the values obtained are shown in Table II. Although such measurements make no allowance for angular strain, the agreement between these values and those calculated by Corey and Sneen[10] is quite good, and they serve to indicate the relative magnitudes of the dihedral angles.

TABLE II

DIHEDRAL ANGLES FOR SHIKIMIC ACID[a]

(Deg.)

	H-2, H-3	H-3, H-4	H-4, H-5	H-5, H-6a	H-5, H-6e
Half-chair	43	50	180	170	50
Boat	115	60	120	180	60

[a] Using Barton Models.

The experimental dihedral angles were obtained from the coupling constants by the Karplus[11] equation. Since this relationship can only be applied to hydrogens attached to carbon atoms which are approximately sp^3-hybridized no estimate could be made of the angle between H-2 and H-3. Since there is at present some uncertainty[12] as to the precise values of the J_0-parameters, the values originally suggested by Karplus ($J_0 = 8.5$ for $0° \leq \phi \leq 90°$ and $J_0 = 9.5$ for $90° \leq \phi \leq 180°$)

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[8] C. W. Beckett, N. K. Freeman, and K. S. Pitzer, *J. Am. Chem. Soc.*, **70**, 4227 (1948).

[9] D. H. R. Barton, *Chem. Ind.* (London), 1136 (1956).

[10] E. J. Corey and R. A. Sneen, *J. Am. Chem. Soc.*, **77**, 2505 (1955).

[11] M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959). The Karplus equation has the form $J = J_0 \cos^2 \phi - 0.28$ where J is the coupling constant between two hydrogens attached to adjacent carbon atoms and separated by a dihedral angle ϕ. J_0 is a parameter of the particular system.

[12] K. L. Williamson [*J. Am. Chem. Soc.*, **85**, 516 (1963)] has shown that there is a definite relationship between the J_0 parameters of a system and the electronegativity of its substituents.

and those subsequently adopted[13] for carbohydrates ($J_0 = 9.3$ for $0° \leq \phi \leq 90°$ and $J_0 = 10.4$ for $90° \leq \phi \leq 180°$) were used. The two sets of angles thus obtained are shown in Table III. It is clear that the modified parameters only make significant changes for larger dihedral angles.

TABLE III

EXPERIMENTAL DIHEDRAL ANGLES FOR SHIKIMIC ACID (Deg.)

Parameters	3, 4	4, 5	5, 6a	5, 6e
Unmodified[a]	46	163	144	39
Modified[b]	48	156	141	42

[a] See ref. 11. [b] See ref. 13.

Comparison of the experimental and theoretical dihedral angles shows immediately that shikimic acid adopts a conformation which approximates most closely to the half-chair form (A) shown in Fig. 2. In terms of a "time-averaged" conformation this means that the half-chair species makes the major contribution and is hence more favored energetically than the boat form. Alternatively the difference between the calculated and experimental angles can be rationalized on a "static" basis, if it is assumed that the angle between H-4 and H-5 is *genuinely* less than 180°, which is reasonable. Then rotation about the C-3, C-4 and C-4, C-5 bonds could decrease the H-4, H-5 angle. This also would decrease the H-3, H-4, and H-5, H-6a angles which is again in accord with the experimental finding. On this basis it seems that the conformation of shikimic acid is essentially the half-chair conformation (A) shown in Fig. 2, with some deformation towards the boat conformation (B).

This work represents the first complete p.m.r. analysis of a substituted cyclohexene.[14] It also indicates that fairly accurate conformational deductions can be made from first-order coupling constants *providing* that sufficient care is taken. Although the *experimental* errors in the dihedral angles are only *ca.* ±1° due to the errors in the coupling constants, a *systematic* error of much greater magnitude is introduced by the uncertainty of the Karplus parameters. Clearly the method is generally applicable to cyclic molecules as long as suitably modified J_0 values are used.

Acknowledgment.—The author is indebted to Dr. F. A. L. Anet for the facilities used and wishes to thank the National Research Council for financial support.

(13) R. J. Abraham, L. D. Hall, L. Hough and K. A. McLauchlan, *J. Chem. Soc.*, 3699 (1962).

(14) Since the completion of this work, E. W. Garbisch [*J. Org. Chem.*, **27**, 4249 (1962)] has published data which he considers indicative that 6-substituted 1-phenylcyclohexenes also adopt a half-chair conformation, but his investigation did not yield any complete analyses.

The Function of Base in the Catalytic Dehalogenation of Aliphatic Halides. Reduction of Dichloromethylmethylcyclohexanones in the Presence of Potassium Hydroxide and Triethylamine

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In order to elucidate the function of base in the catalytic dehalogenation of aliphatic halides, the effect of two bases of widely different character, potassium hydroxide and triethylamine, on the hydrogenolysis of 2-dichloromethyl-2-methylcyclohexanone and 4-dichloromethyl-4-methylcyclohexanone was investigated. With the 2-substituted dichloro ketone the only difference was in the time required for reduction. This difference was shown not to be due to poisoning of the catalyst and was ascribed to a basic dissimilarity in mechanism. In the case of the 4-substituted dichloro ketone, dehalogenation proceeded smoothly in the presence of hydroxide ion but led to substantial amounts of 4-dichloromethyl-4-methylcyclohexanol in the presence of triethylamine. This facile reduction of the carbonyl group of the dichloro ketone, as well as the inertness of the chlorine atoms of the dichloro alcohol to hydrogenolysis under the dehalogenation conditions, are explained in terms of intermolecular interactions, probably on the catalyst surface, involving the chlorine atoms, the oxygen function, and the amine. Possible functions of the amine in this interaction, and of bases in dehalogenations in general, are considered.

Catalytic hydrogenolysis is a useful method for the removal of halogen atoms from organic compounds under relatively mild conditions.[1] In acidic or neutral solutions aryl halides are reduced while alkyl halides are not, except certain ones activated by adjacent unsaturation.[2] In basic solutions, however, aliphatic halides are so readily and completely dehalogenated that the reaction has been used as an analytical method for the determination of halogen.[3] A similar activation of aryl halides occurs if the molecule contains a basic nitrogen atom.[2] This marked effect of base on catalytic dehalogenation often influences the selective reduction of other functional groups in the presence of halogen atoms[4-6] and is, therefore, of interest to the synthetic organic chemist.

Originally,[3] base was used in catalytic dehalogenations to prevent disintegration of the palladium-on-calcium carbonate catalyst by the halogen acid formed in the reaction. A similar reason for the necessity of base has been suggested for other catalysts,[7] including nickel[6,8] and palladium on charcoal,[9] but without supporting evidence.

(1) W. Theilheimer, "Synthetic Methods of Organic Chemistry," Vol. I–XV, Interscience Publishers, Inc., New York, N. Y., 1947–1962, lists over eighty applications of this reaction.

(2) R. Baltzly and A. Phillips, *J. Am. Chem. Soc.*, **68**, 261 (1946).

(3) M. Busch and H. Stove, *Ber.*, **49**, 1063 (1916).

(4) M. Freifelder, W. Martin, G. Stone, and E. Coffin, *J. Org. Chem.*, **26**, 383 (1961).

(5) R. Adams and R. Miller, *J. Am. Chem. Soc.*, **58**, 787 (1936).

(6) W. Whitmore and A. Revukas, *ibid.*, **62**, 1692 (1940).

(7) K. Rosenmund and F. Zetzsche, *Ber.*, **51**, 578 (1918).

(8) C. Kelber, *ibid.*, **50**, 305 (1917).

(9) M. Mladenovic, *Bull. soc. chim. roy. Yougoslav.*, **4**, 187 (1933).