[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY]

Conformational Analysis of Disubstituted Cyclohexanes by Proton Resonance Spectroscopy

S. BROWNSTEIN[1] AND R. MILLER

Received April 27, 1959

It is shown that the stereochemistry of a disubstituted cyclohexane may be determined from its proton resonance spectrum provided that the positions of the substituents on the ring are known.

Proton magnetic resonance spectroscopy has been found useful in studying conformations of polysubstituted six-membered ring compounds.[2-4] In many cases it has been shown that rapid conformational interconversion of the ring causes averaging of the magnetic environment of the ring protons so that only a single resonance peak is observed. This happens when there are two types of ring protons which exchange identity when the ring goes from one chair conformation to the other. As the effect of a substituent upon a distant ring proton depends primarily upon the bulk of the substituent and the geometry of the compound, it was thought that in disubstituted cyclohexanes the spectra of the methylene ring protons should not depend appreciably upon the substituent but only upon the stereochemistry of the compounds provided the substituents are not too bulky.

EXPERIMENTAL

The proton resonance spectra were obtained in a manner described previously using a Varian Associates nuclear magnetic resonance spectrometer at a frequency of 40 mc. per second.[5] The side band modulation[6] was generated by a Heathkit Square Wave Generator, Model SQ1. After the frequency was adjusted for superposition of a side-band from the solvent at various positions on the spectra the pulses from the square wave generator were counted on an Instrument Development Laboratories Model 161 Scaling Unit. The modulating frequency could be adjusted to within 1 c.p.s. and its value determined within 0.1 c.p.s. It was assumed that the sweep of the magnetic field was linear between the locations determined by sideband modulation. Peak widths were measured at half the peak height. In those cases where overlap occurred between the methyl and methylene peaks the methylene peak was extended symmetrically for the determination of its half width. Although positions are quoted to 0.1 c.p.s., instrumental irregularities and the discrete width of the sideband signals make it unlikely that the accuracy is better than 0.3 c.p.s. These effects however are small compared with the differences between the various spectra.

cis and trans 3-Methylcyclohexanol and trans 4-methylcyclohexanol were obtained from Professor E. L. Eliel[7] and their purity confirmed by infrared spectroscopy. *trans*-2-Methylcyclohexanol was prepared according to the literature.[7] *cis*-2-Methylcyclohexanol and *cis*-4-methylcyclohexanol were separated by fractional distillation with a spinning-band column from the Eastman 2-, and 4-methylcyclohexanol. The infrared spectra corresponded to those of the pure isomers.

cis-1,2-Diacetoxycyclohexane was prepared by a reported method.[8] *cis*- and *trans*-1,2-Cyclohexanediol and the trans acetate and benzoate were obtained from the stockrooms of Cornell University. The spectra of all samples were obtained in methylene chloride solution, except the diols which were dissolved in water. The data on the dimethylcyclohexanes had been reported previously.[9]

RESULTS

It was found that the width of the resonance absorption peak due to the ring protons was always considerably greater in the isomer which would have the diequatorial conformation than in the one with an axial-equatorial conformation. These observations are listed in Table I and representative spectra are shown in Fig. 1.

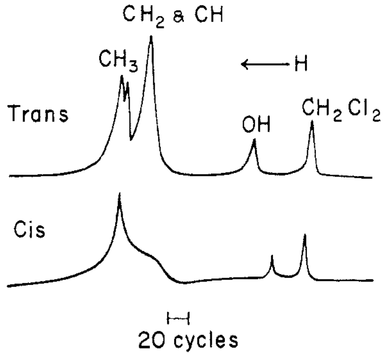

Fig. 1. 3-Methylcyclohexanol in CH_2Cl_2 solution

Although the proton attached to a ring carbon atom bearing a substituent is normally shifted relative to those on an unsubstituted ring carbon atom, this was not observed for the methyl cyclohexanols, nor for most of the dimethylcyclohexanes. The

---

(1) Present address: Division of Applied Chemistry, National Research Council, Ottawa, Canada.

(2) R. U. Lemieux, R. K. Kullnig, H. J. Bernstein, and W. G. Schneider, *J. Am. Chem. Soc.*, **79**, 1005 (1957); **80**, 6098 (1958).

(3) R. U. Lemieux, R. K. Kullnig, and R. Y. Moir, *J. Am. Chem. Soc.*, **80**, 2237 (1958).

(4) S. Brownstein, *J. Am. Chem. Soc.*, **81**, 1606 (1959).

(5) S. Brownstein, *J. Am. Chem. Soc.*, **80**, 2300 (1958).

(6) J. T. Arnold and M. E. Packard, *J. Chem. Phys.*, **19**, 1608 (1951).

(7) E. L. Eliel and C. A. Lukach, *J. Am. Chem. Soc.*, **79**, 5986 (1957).

(8) F. V. Brutcher and G. Evans, *J. Org. Chem.*, **23**, 618 (1958).

(9) N. F. Chamberlain, *Anal. Chem.*, **31**, 56 (1959).

TABLE I

RING PROTON PEAK WIDTHS

Compound	Conformation	Peak Width, Cycles/Sec.
Methylcyclohexanols		
cis-1,2	a, e	8.4
trans-1,2	e, e	22.0
cis-1,3	e, e	37.8
trans-1,3	a, e	12.5
cis-1,4	a, e	14.3
trans-1,4	e, e	38.4
Dimethylcyclohexanes		
cis-1,2	a, e	4.8
trans-1,2	e, e	14.1
cis-1,3	e, e	12.8
trans-1,3	a, e	8.6
cis-1,4	a, e	4.8
trans-1,4	e, e	19.2
Cyclohexanediols		
cis-1,2	a, e	7.1
trans-1,2	e, e	20.2
Cyclohexanediacetates		
cis-1,2	a, e	10.3
trans-1,2	e, e	35.0
Cyclohexanedibenzoates		
trans-1,2	e, e	16.0

effect of conformation on the chemical shift of the methyl group in the methylcyclohexanols is shown in Table II.

TABLE II

CHEMICAL SHIFT OF METHYL PROTONS

Methylcyclohexanol	Conformation	$\delta_{\text{int.}}^{\mathrm{CH_2Cl_2}}$[a]
cis-1,2	a, e	4.33
trans-1,2	e, e	4.10
cis-1,3	e, e	4.33
trans-1,3	a, e	4.60
cis-1,4-	a, e	4.55
trans-1,4	e, e	4.43

[a] The separation is in parts per million of the applied field from the protons of the solvent, CH_2Cl_2. This notation is fully explained in *Chem. Revs.*, **59,** 463 (1959).

DISCUSSION

It has been shown that spin-spin coupling is greater between two protons that are axial than between axial-equatorial protons, which is in turn greater than for two equatorial protons (I). This results in a broad spin-spin multiplet for ring protons which are restrained in an axial position.[10] A compound in which both substituents must be either equatorial or axial will exist primarily in the diequatorial conformation. This restrains to axial positions the protons which are on the same carbon atoms as the substituents, and consequently there is considerable spin coupling between these and the other ring protons. If the resolution is not sufficient to observe the individual lines of the multiplets, a comparatively broad envelope is observed due to the proton resonance of the ring hydrogens.

In a compound where one substituent is axial and the other is equatorial there will be rapid interconversion between the two possible conformations and their populations will be similar provided that the size of the substituents is not too different. This will result in the protons attached to the substituent bearing carbon atoms having an equatorial position about half the time. There will be smaller spin coupling constants with the other ring protons and the envelope of resonance absorption due to the ring protons will be narrower. Therefore, if the position of the substituents on the cyclohexane ring is known, one can determine from the proton resonance spectrum of a compound whether the substituents are cis or trans.

The chemical shift of the methyl protons in the methylcyclohexanols should be the weighted average of the shift for a purely axial methyl group and a purely equatorial one since there is rapid conversion between the two possible conformations. A greater contribution from the axial positions would be expected when one substituent is axial and the other equatorial rather than when both substituents must be either axial or equatorial. It is found that the methyl protons occur at higher field in the axialequatorial isomer than the diequatorial isomer for the various methylcyclohexanols.

Acknowledgment. This work was supported in part by a research grant No. A-2172 from the National Institute of Arthritis and Metabolic Diseases, Public Health Service.

ITHACA, N. Y.

---

(10) E. L. Eliel, *Chem. and Ind.* (*London*), 568 (1959).