

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OHIO STATE UNIVERSITY, COLUMBUS 10, OHIO]

Conformational Analysis. I. The Conformational Preference of the Ethynyl Group

BY ROBERT J. OUELLETTE

RECEIVED FEBRUARY 29, 1964

The conformational preference of the ethynyl group in cyclohexane has been determined indirectly from the conformation of 1-ethynylcyclohexanol. The hydroxyl proton experiences a chemical shift which is a function of the degree of hydrogen bonding and its conformation. Dilution studies have been carried out to determine the chemical shift of the monomeric hydroxyl proton in 1-ethynyl-*trans*-4-*t*-butylcyclohexanol and 1-ethynyl-*cis*-4-*t*-butylcyclohexanol. The hydroxyl proton in the axial position occurs at higher field than the hydroxyl proton in the equatorial position. The conformational preference of the ethynyl group in 1-ethynylcyclohexanol is smaller than that of the hydroxyl group by 0.60 kcal./mole. Using the value of 0.78 kcal./mole for the hydroxyl group, the "A-value" for the ethynyl group is 0.18 kcal./mole.

Introduction

In recent years, the determination of the conformational preference of substituents in the cyclohexane system has been greatly aided by use of nuclear magnetic resonance spectroscopy. This method depends on the difference in magnetic environment of the axial and equatorial proton in cyclohexyl compounds. The axial proton appears at higher field except in the case of α -haloketones.¹ The n.m.r. method has been used to determine the conformational preference of several groups.^{2,3} There are inherent limitations to this method. The 1-proton must experience a chemical shift of sufficient magnitude to place it in an uncomplicated part of the spectrum. The 1-proton is invariably split into a broad multiplet by adjacent hydrogens thus making the selection of a value for the chemical shift uncertain. This uncertainty can be removed by spin decoupling or by selective deuteration.³

These problems can be eliminated to a large extent by use and examination of the hydroxyl proton in 1-substituted cyclohexanols. The n.m.r. signal of the hydroxyl proton is unsplit except in highly purified samples.⁴ The preparation of the necessary reference compounds is straightforward from 4-*t*-butylcyclohexanone. Furthermore, the isomeric 1-substituted *cis*- and *trans*-4-*t*-butylcyclohexanols⁵ are invariably separable by column chromatography.^{6,7}



There are two possible disadvantages to the proposed scheme of utilizing 1-substituted cyclohexanols. The chemical shift of the hydroxyl proton is a function of concentration.⁸ This problem can be circumvented by dilution studies which are easily carried out. The hydroxyl proton might appear at a point identical with some other proton in the compound. In this study this effect has been encountered and there is little

difficulty in locating the hydroxyl proton as it shifts with changes in concentration.

Results

The hydroxyl proton of 1-ethynyl-*cis*-4-*t*-butylcyclohexanol (III) is at higher field than the hydroxyl proton of 1-ethynyl-*trans*-4-*t*-butylcyclohexanol (IV). The chemical shift of both hydroxyl protons would be expected to be concentration dependent and this was expressed by Huitric in his examination of these compounds.⁹ However, in quoting the positions of the hydroxyl protons, the concentrations of the compounds were not given.

If it is assumed that the degree of hydrogen bonding as a function of concentration is independent of stereochemistry, then the conformational preference of the ethynyl group in 1-ethynylcyclohexanol (V) could be readily obtained by determining the chemical shift of the hydroxyl proton at a given concentration and comparing it to the chemical shifts of the corresponding proton in compound III and IV at the same concentration. However, one would not expect the degree of

TABLE I

Cyclohexanol	Mole fraction	Chemical shift ^{a,b}
1-Ethynyl-	0.00101	88.5
	.00266	90.4
	.00398	92.0
	.00623	94.1
	.00806	95.8
	.01001	97.8
	.01285	101.2
	.01575	104.2
1-Ethynyl- <i>trans</i> -4- <i>t</i> -butyl-	.02128	110.0
	.00155	95.8
	.00280	97.1
	.00425	98.8
	.00636	101.0
	.00791	103.0
	.00924	104.6
	.01183	107.4
1-Ethynyl- <i>cis</i> -4- <i>t</i> -butyl-	.00070	70.1
	.00193	70.5
	.00360	72.1
	.00430	73.0
	.00602	73.5
	.00791	75.0
	.01033	77.1
	.01342	79.0
	.01705	81.4

^a Cycles/sec. downfield from tetramethylsilane as internal standard (0.001 mole fraction) in carbon tetrachloride. ^b At 41°.

(9) A. C. Huitric, W. S. Staupoulos, and B. J. Nist, *J. Org. Chem.*, **28**, 1539 (1963).

(1) A. Nickon, M. A. Castle, R. Harada, C. E. Berkoff, and R. O. Williams, *J. Am. Chem. Soc.*, **85**, 2185 (1963).

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

(3) A. H. Lewin and S. Winstein, *J. Am. Chem. Soc.*, **84**, 2464 (1962).

(4) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, pp. 26-27.

(5) The *cis* and *trans* prefix refers to the hydroxyl and the *t*-butyl groups.

(6) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955).

(7) E. W. Garbisch, Jr., and D. B. Patterson, *ibid.*, **85**, 3228 (1963).

(8) J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp. 410-415.

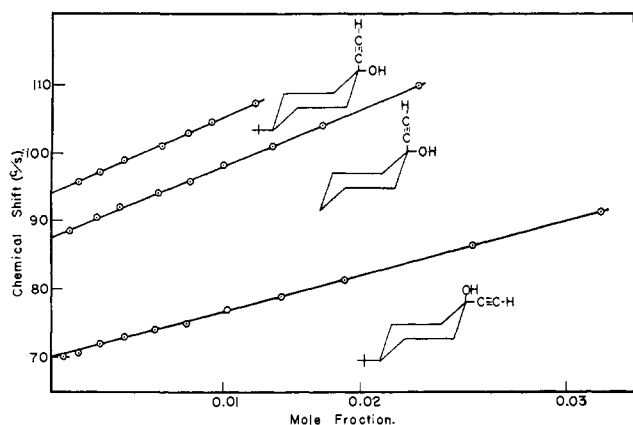


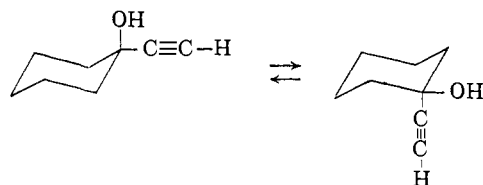
Fig. 1.—Chemical shift dependence of hydroxyl proton with concentration at 41°

hydrogen bonding to be independent of stereochemistry. The axial hydroxyl proton might reasonably be expected to be bonded to a lesser extent than the equatorial hydroxyl proton.

It is necessary to determine the chemical shift of the hydroxyl protons in compounds III, IV, and V as a function of concentration. By extrapolating to infinite dilution the chemical shifts of the individual monomeric alcohols can be determined. Table I gives the data for all compounds. The chemical shifts are expressed in c./sec. downfield from tetramethylsilane as an internal standard. The concentrations are expressed in mole fractions. Figure 1 shows the dependence of the chemical shift as a function of mole fraction for the three compounds investigated.

The data were extrapolated to infinite dilution to determine the chemical shift of the monomeric alcohols. The chemical shifts of the hydroxyl protons in 1-ethynyl-*cis*-4-*t*-butylcyclohexanol, 1-ethynyl-*trans*-4-*t*-butylcyclohexanol, and 1-ethynylcyclohexanol are 70.1, 94.0, and 87.4 c./sec., respectively. Each chemical shift is estimated to be accurate to ± 0.2 c./sec.

Considering the following transformation, the equilibrium constant can be obtained from the chemical shifts reported above. The equilibrium constant is 2.6 ± 0.1 . The free energy change at 41° is -0.60 kcal./mole. Using -0.78 kcal./mole as the change in



free energy for the hydroxy group transformation,³ the "A-value" of the ethynyl group is 0.18 kcal./mole.

Discussion of Results

The use of the chemical shift of the hydroxy proton as a means of determining the conformational preference of substituents in flexible systems appears to be fea-

sible and can serve as a complimentary method to those currently being used. The conformational preference of the ethynyl group has been readily obtained from available compounds, whereas utilizing the 1-ethynyl-4-*t*-butylcyclohexanes would involve synthesis and separation of two hydrocarbons. The ease with which the corresponding 1-ethynyl-4-*t*-butylcyclohexanols can be obtained pure by column chromatography serves as an example of the utility of having an additional method to analyze the conformational preference of substituents in the cyclohexane system.

The cyano group¹⁰ is the only case of a linear group containing more than one atom which has been examined. The value of 0.18 kcal./mole for the ethynyl group is remarkably close to the value of 0.15 kcal./mole for the cyano group. Although as a first approximation the ethynyl and cyano group would be expected to be of similar steric size, an argument could be made for the ethynyl group being larger than the cyano group. The electron distribution in the cyano group is polarized toward the nitrogen atom and this might decrease the effective bulk of the electron cloud at the carbon atom. Jensen¹⁰ points out that such effects may indeed be important in determining the conformational preference of substituents. If there is any effect of the polarization of the cyano group on its effective size, the magnitude is extremely small. The cyano and ethynyl groups are of equal steric size within the combined experimental errors associated with the individual measurements.

Experimental

Carbon tetrachloride was distilled at atmospheric pressure into a dry system under nitrogen. The center fraction boiling at 76.5° was collected and stored under nitrogen. Tetramethylsilane was added to the solvent to produce a solution that was 0.001 mole fraction in the internal standard.

The compounds employed possessed the correct reported physical properties¹¹ and the n.m.r. spectra agreed with those published by Huitric⁹ except for the position of the hydroxyl proton.

All glassware was dried and placed in a vacuum desiccator. All manipulations were carried out under a nitrogen atmosphere to eliminate the uptake of atmospheric moisture.

Solutions were prepared in 2- and 5-ml. volumetric flasks. The weight of the compound and solvent was determined by difference.

The n.m.r. spectra were obtained on a Varian A-60 instrument and the chemical shifts of the hydroxyl protons were determined relative to the internal tetramethylsilane standard. The chemical shifts were determined to 0.2 c./sec. The position of the *t*-butyl group and ethynyl hydrogens served as an additional internal reference. Each compound was run under the same conditions of sweep rate and tube rotation in matched n.m.r. tubes.¹² The spectrum was repeated several times to determine the reproducibility of the instrument. The temperature of the instrument was maintained at 41°.

Acknowledgment.—The author wishes to acknowledge the donation of authentic samples of the compounds used in the study from Professor M. S. Newman.

(10) F. R. Jensen and B. Rickborn, *ibid.*, **27**, 4606 (1962).

(11) G. F. Hennicot and F. X. O'Shea, *J. Am. Chem. Soc.*, **80**, 614 (1958).

(12) "Precision" N.M.R. tubes, N.M.R. Specialties, New Kensington, Penna.