Dipole Moment and Conformation of Substituted Cyclohexanols

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Abstract: The dipole moments of a number of epimeric alkyl-substituted cyclohexanols have been measured in solution, and in two cases, in the gas phase. In every instance the dipole moment of the isomer with the hydroxyl group equatorial was higher than that of the isomer with the hydroxyl group axial. This result leads to the conclusion that the total dipole moment of cyclic alcohols is partially dependent upon the conformation of the hydroxyl group. Accordingly, group moment calculations should henceforth take into account the conformation of the group involved.

Dipole moments have been extremely useful to the organic chemist for the elucidation of the structure and reactivity of organic compounds.[2]

However, very little attention has been paid to the effect of the conformation of polar groups in cyclohexanes on the total moment of the molecule. Calculations based on additivity of group moments, such as a C–OH moment, rest on the assumption that the hydrocarbon portion of the molecule does not contribute significantly, if at all, to the net moment.[3] This leads to the conclusion that, for example, *cis*- and *trans*-4-*t*-butylcyclohexanol, in which the 4-*t*-butyl group remains equatorial, will have the same dipole moment. However, it is possible that a polar group, such as an hydroxyl group, can induce a small, but measurable moment in the hydrocarbon portion of the molecule, the magnitude of which will be different for axial and equatorial hydroxyl groups. Such differences, if they exist, and can be measured, could be a useful tool for distinguishing isomers not readily identified by other methods. In order to test these hypotheses, precise measurements have been made of the dipole moments of a number of *cis*- and *trans*-substituted cyclohexanols. Differences were found which indicate that the permanent and induced moments of the hydrocarbon portion of the molecule contribute significantly to the net dipole moment.

Experimental Section

Solution Measurements. The dielectric constants of the solutions were determined at 25° and 50 kc.p.s. with a capacitance–conductance bridge that has been described elsewhere.[4] The test cell consisted of three coaxial nickel cylinders in a glass jacket.[5]

The air capacitance of the cell was 25.22 ± 0.01 pf. The changes in capacitance were measured directly on a General Radio Type 722 precision variable capacitor external to the bridge proper, or through a capacitance network which allowed the capacitance to be read to 1 part in 5000 on a General Radio Type 1100 precision variable air capacitor.

The densities of the solutions were determined by pyncnometric methods.

Gas Phase Measurements. The dielectric constants were measured by a transformer bridge method in which the capacitance difference between two capacitors of identical construction, one containing the gas sample and the other evacuated, was balanced by a calibrated variable capacitor. The bridge circuit has been described elsewhere.[6]

Each cell consisted of a parallel plate structure taken from a General Radio standard 1000 pf. fixed air capacitor. This was mounted in a brass case and had a vacuum capacitance of 440.6 pf. at 110.0°. The difference between the geometric capacitances of the sample cell and reference cell was $(22.60 \pm 0.02) \times 10^{-2}$ pf. for the eight determinations.

Before a dielectric constant determination, the sample was degassed by the following method; the sample was cooled to Dry Ice temperature and the sample reservoir was evacuated to 0.02 mm., closed off, heated until the sample melted, and then allowed to cool slowly until the sample solidified. The sample was again cooled and re-evacuated. This procedure was repeated three times for each sample.

Both the capacitance cells and the null point pressure indicator were immersed in an oil bath held at 110.0 ± 0.01°. The sample reservoir was then enclosed in an oven held at 110°, and all tubing not immersed in the oil bath was heated by resistance wire. The gaseous sample in the cell was admitted to one side of a diaphragm separator and its pressure was balanced by a variable nitrogen pressure applied to the other side and measured with a di-*n*-butyl phthalate manometer read by a cathetometer. The measured pressures were typically in the range 9 to 50 mm. Determinations were made for each compound until four successive runs gave capacitance–pressure ratios which agreed to within 2%.

Materials. Benzene (Merck and Co., Inc., ACS grade) was stirred with concentrated sulfuric acid, then dried first over anhydrous sodium sulfate and next by boiling under reflux with calcium hydride for at least 48 hr. The benzene then was distilled slowly from fresh calcium hydride through a 35-cm. Widmer column equipped with a total-reflux partial-takeoff head and the middle portion of the distillate was collected. The absolute dielectric constant of the benzene was determined using the cell of Vidulich and Kay[7] and was found to be 2.274 ± 0.001, identical with reported values.

Alcohols. The monosubstituted cyclohexanols, **1**–**6** in Table I, were prepared and purified as described previously[8] and were shown to be homogeneous by v.p.c. The norborneols were also prepared as described previously,[9] and the borneols were obtained from commercial samples by purification through the acid phthalate derivatives.

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[1] Abstracted from the Ph.D. Thesis of R. H. N., Brown University, 1963. Monsanto Chemical Company Fellow, 1960–1962.

[2] G. W. Wheland, "Resonance in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1955, Chapter 5.

[3] *Cf.* C. P. Smyth, "Dielectric Behavior and Structure," McGraw-Hill Book Co., Inc., New York, N. Y., 1955, p. 252, for a discussion of some limitations of the method.

[4] R. H. Cole and P. M. Gross, Jr., *Rev. Sci. Instr.*, 20, 252 (1949).

[5] Obtained from J. C. Balsbaugh, The Massachusetts Institute of Technology.

[6] D. R. Johnston, G. J. Oudemans, and R. H. Cole, *J. Chem. Phys.*, **33**, 1310 (1960); R. M. Meighan, Ph.D. Thesis, Brown University, 1964.

[7] G. A. Vidulich and R. L. Kay, *J. Phys. Chem.*, **66**, 383 (1962).

[8] E. L. Eliel and R. S. Ro, *J. Am. Chem. Soc.*, **79**, 3992 (1957); S. Winstein and N. H. Holness, *ibid.*, 77, 5562 (1955); H. M. Ungnade, *J. Org. Chem.*, **13**, 261 (1947); D. Y. Curtin and R. J. Harder, *J. Am. Chem. Soc.*, **82**, 2359 (1960); E. L. Eliel and M. N. Rerick, *ibid.*, **82**, 1367 (1960).

[9] S. Winstein and D. S. Trifan, *ibid.*, **74**, 1145, 1147 (1952).

Table I. Values for Substituted Cyclohexanols from Solution Measurements in Benzene at 25° and 50 kc.p.s.

Compound	Conformation of Hydroxyl group	$\Delta\epsilon_{12}/W^a$		i^d	$\Delta d_{12}/W^a$		Dipole moments,[a] D.
		m	σ_m		m	σ_m	
trans-4-*t*-Butylcyclohexanol[b] **(1)**	Eq.	1.917	± 0.004	+0.020	0.0190	± 0.0022	1.725 ± 0.004
cis-4-*t*-Butylcyclohexanol[b] **(2)**	Ax.	1.757	± 0.002	+0.004	0.0211	± 0.0013	1.655 ± 0.002
trans-4-Cyclohexylcyclohexanol **(3)**	Eq.	1.674	± 0.021	+0.030	0.0610	± 0.0103	1.71 ± 0.02
cis-4-Cyclohexylcyclohexanol **(4)**	Ax.	1.618	± 0.022	−0.034	0.1075	± 0.0095	1.63 ± 0.02
trans-4-Phenylcyclohexanol **(5)**	Eq.	1.645	± 0.041	−0.015	0.1616	± 0.0082	1.55 ± 0.04
cis-4-Phenylcyclohexanol (6)	Ax.	2.210	± 0.036	−0.040	0.1405	± 0.0083	1.85 ± 0.02
cis,cis-3,5-Dimethylcyclohexanol[c] (7)	Eq.	2.669	± 0.087	−0.037	0.1388	± 0.0409	1.73 ± 0.06
cis,trans-3,5-Dimethylcyclohexanol[c] **(8)**	Ax.	1.737	± 0.065	+0.098	0.0754	± 0.0046	1.44 ± 0.03
endo-Norborneol **(9)**	...	2.718	± 0.024	−0.035	0.1135	± 0.0130	1.68 ± 0.02
exo-Norborneol **(10)**	...	2.609	± 0.028	−0.091	0.1260	± 0.0179	1.64 ± 0.02
endo-Borneol **(11)**	...	1.777	± 0.029	−0.050	0.0903	± 0.0057	1.60 ± 0.02
exo-Borneol **(12)**	...	1.702	± 0.022	−0.054	0.0783	± 0.0068	1.58 ± 0.01

[a] The slopes, m, and the standard deviations, σm, were determined by a least-squares treatment of the data. The slopes were determined from at least eight different concentrations for each compound. [b] Measurements were by Jose Sanchez. [c] We are indebted to Professor E. L. Eliel for the samples of these compounds. [d] The intercept of $\Delta\epsilon_{12}/W$ at $W = 0$.

Results

Solution Measurements. For the dilute solutions studied, both the density change, Δd, and the dielectric constant increment, $\Delta\epsilon$, were linear functions of weight per cent solute, W, within experimental error. The straight-line plots passed through zero with only small deviations, and the values of the intercept, i, on the $\Delta\epsilon/W$ axis, are given in Table I. The values of $\Delta\epsilon/W$ and of $\Delta d/W$ were therefore determined by a least-squares treatment of the data and were used to calculate the solute polarization, P_2, and the dipole moment, μ, by the relations

$$P_2 = \frac{3}{(\epsilon_1 + 2)^2}\left(\frac{M_2}{d_1}\right)\left(\frac{\Delta\epsilon_{12}}{W}\right) - \frac{(\epsilon_1 - 1)}{(\epsilon_1 + 2)}\left(\frac{M_2}{d_1}\right) \times \frac{1}{d_1}\left(\frac{\Delta d_{12}}{W}\right) + \frac{(\epsilon_1 - 1)}{(\epsilon_1 + 2)}\frac{M_2}{d_1}$$

and

$$\mu = 0.0127\sqrt{(P_2 - P_{E2})T}$$

In these equations, which are forms of the general expressions thoroughly discussed by Pohl, Hobbs, and Gross,[10] the subscripts 1 and 2 refer to solvent and solute, respectively, M is the molecular weight, d the density, and T the absolute temperature. The solute electronic polarizations, P_{E2}, were derived from the group refractions given by Smyth.[11] The values of $\Delta\epsilon/W$, $\Delta d/W$, and μ for the various alcohols are given in Table I.

Gas Phase Measurements. The slope, $\Delta C/\Delta P$, was obtained from a least-squares treatment of the data and μ was calculated from the equation

$$\mu = \sqrt{3kT\left(\frac{\Delta C}{\Delta P}\cdot\frac{RT}{4\pi N_0 C_g} - \alpha\right)}$$

where $\alpha = 3A/4\pi N_0$, and A is sum of the optical contributions to the molar polarization, equal to the sum of the bond refractivity values taken at the sodium D-line. N_0 is Avogadro's number, P is the pressure in millimeters, and C_g is the fixed capacitance of the evacuated cell. The probable error in μ was obtained from the standard deviation σ_m, in the slope m of the $\Delta C/\Delta P$ data. The data are given in Table II.

Table II. Dipole Moment Data for 4-*t*-Butylcyclohexanols in the Gas Phase at 110° and 10 kc.p.s.

Compound	Detn. no.	m, or $\Delta C/\Delta P^a$	$\sigma_m{}^b$	μ, D.
trans-4-*t*-Butylcyclohexanol	1	0.551	0.005	1.81 ± 0.02
(OH group eq.)	2	0.551	0.014	1.81 ± 0.04
	3	0.554	0.008	1.82 ± 0.02
	4	0.553	0.016	1.81 ± 0.05
cis-4-*t*-Butylcyclohexanol	1	0.522	0.011	1.71 ± 0.04
(OH group ax.)	2	0.529	0.014	1.74 ± 0.04
	3	0.530	0.010	1.74 ± 0.03
	4	0.524	0.012	1.72 ± 0.04

[a] The slope m, $\Delta C/\Delta P$, is in units of pf. × 10^{-2}/mm. and was determined from a least-squares treatment of the capacitance *vs.* pressure data. [b] The standard deviation, σm, was computed from a least-squares treatment of the data.

Discussion

From an inspection of the values given for the various pairs of axial- and equatorial-substituted cyclohexanols in Tables I and II it is evident that the dipole moment is not independent of the conformation of the hydroxyl group. The differences in μ for a given pair are beyond experimental error and may be as large as 0.3 D. Since, in all cases, the steric requirements of the alkyl substituents ensure that they will remain equatorial, this difference in μ for a pair of isomeric alcohols is indicative of a conformational effect of the hydroxyl group. There are several factors which might be responsible for the observed difference in dipole moment between these pairs of conformers; these now will be discussed, with reasons for believing they are *not* responsible for the differences.

Because of different steric environments around the axial and equatorial C–OH bonds, the degree of solvation of the isomers and the induced polarization of the solvent molecules could be different. Such solvent effects, if present, would be expected to cause a difference in the relative activities of solutions of the two isomers. In order to determine if such an effect was operating, the relative activities of solutions of *cis*- and *trans*-4-*t*-butylcyclohexanol were determined by

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(10) H. A. Pohl, M. E. Hobbs, and P. M. Gross, *Ann. N. Y. Acad. Sci.*, 40, 390 (1940).

(11) Ref. 3, p. 409.

the isopiestic method over the same concentration range as was used for the dipole moment determinations. The measurements were performed with a Mechrolab vapor pressure osmometer at 37°, using benzene as the reference solvent. The resistances, *R*, of the solutions recorded on the bridge with reference to the resistance of the pure solvent are related to the vapor pressure and to the activity. A plot of resistance *vs.* molarity for the two compounds gave superimposable straight lines. If the activities are the same, then the solvent effects on the two isomers must be the same, and the resultant effect on the dipole moments must be the same.

The fact that plots of the change in dielectric constant *vs.* concentration gave straight lines over the range studied indicates that any solvent effects present are not changing with concentration.

Perhaps the most convincing evidence that the dipole moment differences are not due to solvent effects was obtained from the gas phase measurements of a pair of conformers. *cis*- and *trans*-4-*t*-butylcyclohexanol were chosen for this determination since they had sufficient vapor pressures at 110°. The difference in dipole moments between the two isomers was in the same direction, and of the same magnitude (Table II), showing that even in the absence of solvent the two conformers had different dipole moments.

Thus all of these lines of evidence indicate that the dipole moment differences observed for the conformers are not due to solvent effects.

Also because of the different steric environment for the axial and equatorial hydroxyl groups there could be a difference in the degree of hydrogen bonding which could lead to different dipole moments. Such a difference would lead to a difference in the relative activities of the two isomers of 4-*t*-butylcyclohexanol, but as shown above, the relative activities are the same. In addition, intermolecular interactions such as hydrogen bonding should show up in deviations from linearity in $\Delta\epsilon/W_2$, which were not observed. Finally, it is extremely unlikely that there would be hydrogen bonding in the gas phase at the low pressures of the measurements, yet the measurements of *cis*- and *trans*-4-*t*-butylcyclohexanol show that the dipole moment differences are still present.

Another factor which could lead to different dipole moments for the *cis* and *trans* isomers is restricted rotation of the hydroxyl group about the C–O bond. For the *cis* isomer (OH group axial), models indicate that there is hindrance between the hydroxyl hydrogen atom and the 3- and 5-axial hydrogen atoms of the ring. This restriction would lead to a small moment for the O–H bond in a direction opposite to the hydrocarbon moment, thus reducing the net moment in the *x*-direction. (Figure 1). This in turn should lead to a slightly smaller net moment for the molecule than would be observed in the absence of restricted rotation.

However, it is also possible that restricted rotation could give rise to the opposite effect. The unshared electron pair in the p-orbital of the oxygen atom will cause van der Waals repulsion with the 3- and 5-C–H bonds, and this would cause restricted rotation in the opposite direction, with the O–H bond restrained *toward* the 3- and 5-axial hydrogen atoms, thus keeping the electron pair away from them. This would lead to a small component in the $+x$-direction which reenforces the hydrocarbon moment, and thus leads to a *higher* net moment for the axial isomer than would be observed in the absence of restricted rotation.[12]

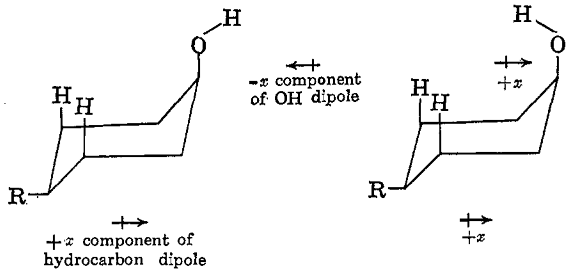

Figure 1. Restricted rotation of hydroxyl group.

In any event, there should be sufficient energy available at 110° to overcome either type of restricted rotation, but a difference in the dipole moments is still observed at this temperature, and the difference is still in the same direction as for the solution measurements. Therefore it seems unlikely that restricted rotation is a significant factor in accounting for the difference in dipole moments between axial and equatorial isomers.[13]

The only remaining explanation for the differences is that they are due to permanent and induced moments in the hydrocarbon portion of the molecules. It seems apparent that more polarizable matter is within the effective range of an axial hydroxyl group than of an equatorial one. The induced moment will oppose the field of the inducing dipole and thus lower the resultant moment of the molecule, as is observed. A remaining factor is the permanent moments of the hydrocarbon portions of the molecules. It was shown by Maryott and Birnbaum[14] that isobutane has a permanent moment of 0.132 D., and this was confirmed by Lide and Mann.[15] Using the same microwave absorption method, it was also found that propane has a moment of 0.081 D. These dipole moments were ascribed to the polarity of the carbon–carbon bonds, to a departure of the bond angles from 109° 28′, or to a combination of these factors. Small differences in the permanent moments of the hydrocarbon groups must also be involved in the total moments, therefore. In view of this evidence, then, we believe the differences for the compounds reported here are primarily due to permanent moments, induced moments, and differences in geometry.

The results obtained for the borneol and norborneol isomers are consistent with the above results. Within experimental error the dipole moments for the *exo* and *endo* isomers are the same. Since these molecules

(12) We are indebted to Professor E. C. Kooyman for calling to our attention the possibility of this type of restricted rotation.

(13) A referee has pointed out that at 110° the time-averaged population for all orientations need not be the same and hence a conformational effect of favoring or disfavoring OH toward the 3,5-hydrogens could result in the sort of difference under discussion. However, the fact that the magnitude of the difference for the *cis* and *trans* compounds at 25 and 110° is almost the same indicates that this is not an important factor. More conclusive evidence could be obtained on this point by determining the dipole moments of *cis*- and *trans*-4-*t*-butylcyclohexyl halides, where restricted rotation does not exist. Such studies are now in progress.

(14) A. A. Maryott and G. Birnbaum, *J. Chem. Phys.*, **24**, 1022 (1956).

(15) D. R. Lide and D. E. Mann, *ibid.*, **29**, 914 (1958).

are essentially spherical in shape, as opposed to the more nearly planar cyclohexanols, little or no difference would be expected. The differences between the borneols and the norborneols are due to the presence of more polarizable matter (methyl groups) in the former.

In the case of the 4-phenylcyclohexanols, the small effects described above appear to be swamped by the effect of the relatively much more polar phenyl group, which has a moment in the direction opposite to that of the equatorial hydroxyl group. This leads to a lower dipole moment for the *trans* isomer and a higher one for the *cis*.

A large difference is also observed for the two 3,5-dimethylcyclohexanols. In the *cis,trans* isomer, the two equatorial methyl groups are even closer to the axial hydroxyl group than an alkyl group in the 4-position, and thus more induced polarization, which lowers the net moment, is possible. Therefore the moment of the axial isomer is considerably lower than those for the 4-substituted axial cyclohexanols.

In summary, the dipole moment of an alicyclic alcohol is dependent upon the conformation of the hydroxyl group, upon the type of alkyl group on the ring, and upon the position on the ring of the alkyl group(s). The moment differences can be appreciable, amounting to as much as 0.3 D. for the compounds studied to date. While these differences are variously attributable, they are large enough to have considerable usefulness, and indicate that calculations based on additivity of group moments are subject to more limitations than previously realized. It is hoped that the further studies now in progress will provide additional information on the polarizability of other alkyl groups and their effect on functional groups at other positions on the cyclohexane ring.

This work also shows that alkyl groups in the four position have a small but significant polar effect, by virtue of the induced moments, on the axial hydroxyl group (and probably other functional groups) at the 1-position of the cyclohexane ring, and thus would be expected to alter the reactivity of such functional groups. This conclusion has also been reached by Kwart and Takeshita[16] on the basis of entirely different lines of evidence.

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(16) H. Kwart and T. Takeshita, *J. Am. Chem. Soc.*, **86**, 1161 (1964).

The Mechanism of the Lithium Ethoxide Induced Conversion of N-Nitroso-N-(2,2-diphenylcyclopropyl)urea to 2,2-Diphenyldiazocyclopropane[1]

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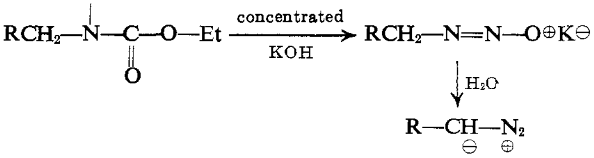
Abstract: Historically, the base-induced conversion of N-nitrosoamides, -carbamates, and -ureas to diazoalkanes has been postulated as proceeding *via* base attack on the carbonyl carbon to give a dioazotate intermediate. In the course of our investigations on the lithium ethoxide induced conversion of N-nitroso-N-(2,2-diphenylcyclopropyl)-urea to 2,2-diphenyldiazocyclopropane, we have obtained two pieces of information that *exclude* this path for our reaction. Ethyl carbamate was not formed in this reaction and lithium 2,2-diphenylcyclopropyldiazotate, the normally presumed intermediate, was synthesized and found to be totally unaffected by reaction conditions that lead to efficient conversion of the nitrosourea to the diazocyclopropane. An alternate mechanism involving attack of the base on the nitroso nitrogen is postulated. The pyrrolidine-induced decomposition of the nitrosourea also appears to proceed by this mechanism.

As early as 1902, direct evidence was presented for the course of von Pechmann's[3] hydroxide-induced conversion of nitrosocarbamates to diazoalkanes. At that time Hantzsch and Lehmann[4] actually isolated the potassium salts of methyl and benzyl diazohydroxide (I) and showed that treatment with water gave the corresponding diazoalkanes.



$$\mathrm{RCH_2{-}\overset{\displaystyle N{=}O}{N}{-}\underset{\displaystyle O}{C}{-}O{-}Et \xrightarrow[\text{KOH}]{\text{concentrated}} RCH_2{-}N{=}N{-}O^{\oplus}K^{\ominus}}$$

$$\xrightarrow{\mathrm{H_2O}} \mathrm{R{-}\underset{\ominus}{CH}{-}\underset{\oplus}{N_2}}$$

R = H, C_6H_5

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[1] Based upon dissertations submitted by D. L. Muck and T. K. Tandy, Jr., to the Faculty of the University of Florida in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Alfred P. Sloan Fellow.

[3] H. von Pechmann, *Ber.*, 27, 1888 (1894).

[4] A. Hantzch and M. Lehmann, *ibid.*, 35, 897 (1902).