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Nuclear Magnetic Resonance Spectroscopy. The Effect of Solvent on Magnetic Nonequivalence Arising from Molecular Asymmetry^{1a}

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The chemical shift between the geminal methylene protons of 1-phenylethyl benzyl ether has been measured in a variety of solvents. An approximate correlation observed between solvent dielectric constant and the degree of the magnetic nonequivalence of the methylene protons, $\nu_A - \nu_B$, is discussed in light of similar results for structurally related compounds. It is suggested that the variation in $\nu_A - \nu_B$ with solvent may reflect changes in the conformation of the benzylic phenyl ring with respect to the methylene group.

Introduction

In a previous paper,² correlations have been developed between the degree of the magnetic nonequivalence of the protons of a methylene group close to an asymmetric center³ and the structure of the mole-

cule close to the methylene group, using 1-phenylethyl benzyl ether and related compounds as model compounds. The available evidence led to the conclusion that although a number of different structural features probably contributed to some extent to the chemical shift differences in these compounds, the most important single factor in determining the magnitude of the chemical shift between the geminal methylene protons was the conformation of the methylene group with respect to the directly bonded phenyl ring.²

The present paper presents data pertinent to an understanding of the marked solvent dependence observed for the methylene proton chemical shift difference in these ethers, and provides further support for the hypothesis that the major contribution to $\nu_A - \nu_B$ originates in the magnetic anisotropy of the phenyl ring.

Results

The chemical shift difference between the geminal methylene protons of 1-phenylethyl benzyl ether is quite solvent sensitive (Table I). In benzene, cyclohexane, carbon tetrachloride, and similar solvents, the chemical shift is approximately 10–11 c.p.s.; in dimethyl sulfoxide, acetone, and nitromethane it drops to approximately 2 c.p.s. The magnitude of the

(1) (a) Supported in part by the Office of Naval Research and the undergraduate research participation program of the National Science Foundation; (b) N.A.T.O. Fellow, 1963.

(2) G. M. Whitesides, D. Holtz, and J. D. Roberts, *J. Am. Chem. Soc.*, **86**, 2628 (1964).

(3) The term "asymmetric center" used in this paper refers to the single carbon atom in each of the compounds examined which bears four different substituents. A similar magnetic nonequivalence of stereochemically distinct geminal methylene protons has of course also been observed in both axially dissymmetric compounds [*cf.* W. L. Meyer and R. B. Meyer, *ibid.*, **85**, 2170 (1963)], and in a variety of bridged biphenyls⁴ which formally do not contain an asymmetric center.

(4) A similar suggestion has been advanced by Mislow and co-workers to account for the solvent dependence of the n.m.r. spectra of certain bridged biphenyls: K. Mislow, M. A. W. Glass, H. B. Hopps, E. Simon, and G. Wahl, Jr., *ibid.*, **86**, 1710 (1964). For another recent

examination of magnetic nonequivalence in benzylic methylene groups, see J. C. Randall, J. J. McLeskey, III, P. Smith, and M. E. Hobbs, *ibid.*, **86**, 3229 (1964).

Table I. Chemical Shift between the Methylene Protons of 1-Phenylethyl Benzyl Ether as a Function of Solvent

Solvent	$\nu_A - \nu_B^a$	Solvent dielectric constant ^b
1. <i>n</i> -Pentane	10.1 c.p.s.	1.84
2. Cyclohexane	10.1	2.05
3. Dioxane	6.9	2.21
4. Carbon tetrachloride	10.2	2.24
5. Benzene	10.9	2.28
6. Diethyl ether	9.0	4.33
7. Chloroform	8.6	5.05
8. Chlorobenzene	8.2	5.94
9. Methyl iodide	6.0	7.0
10. Aniline	7.8	7.25
11. <i>o</i> -Dichlorobenzene	7.2	7.47
12. <i>t</i> -Butyl alcohol	5.7	10.9
13. Pyridine	6.1	12.5
14. Acetic anhydride	4.6	20.5
15. Acetone	2.5	21.4
16. Cyanobenzene	3.8	25.2
17. Nitrobenzene	3.8	36.1
18. <i>N,N</i> -Dimethylformamide	2.5	36.7
19. Nitromethane	3.1	37.5 ^c
20. Dimethyl sulfoxide	2.0	48.9 ^c
21. Acetic acid	10.3	6.3
22. Ethanol	7.4	24.3
23. Formic acid	9.9	58.3

^a Tables of chemical shifts relative to tetramethylsilane and coupling constants for the aliphatic parts of this molecule will be found in the Experimental section. The uncertainty in $\nu_A - \nu_B$ varies from approximately ± 0.5 c.p.s. in low dielectric constant solvents to ± 2.0 c.p.s. in solvents of high dielectric constant. ^b "Handbook of Chemistry and Physics," 44th Ed., Chemical Rubber Publishing Co., Cleveland, Ohio, 1962. ^c H. L. Schlafer and W. Schaffnrich, *Angew. Chem.*, **72**, 618 (1960). ^d J. Hine, "Physical Organic Chemistry," 2nd Ed., McGraw-Hill Book Co., Inc., 1962, p. 39.

chemical shift in solvents of intermediate polarity falls between these two extremes.

A plot of chemical shift vs. solvent dielectric constant indicates that the degree of the magnetic nonequivalence bears an approximate inverse relation to the dielectric constant (Figure 1). However, inspection of this figure also shows that several solvents are clearly exceptions. Most important, the chemical shift between the $-\text{CH}_2-$ protons of 1-phenylethyl benzyl ether dissolved in hydrogen-bonding solvents (formic acid, acetic acid, ethanol) is larger than would be anticipated from the plot of dielectric constant vs. $\nu_A - \nu_B$. Also, the chemical shift in dioxane solution is significantly smaller than that which might have been anticipated from consideration of its dielectric constant.

Table II lists the solvent dependence of the chemical shift between the geminal benzylic protons of several compounds structurally related to 1-phenylethyl benzyl ether. These compounds appear to be separable into two classes: one (1-phenylethyl *o*-bromobenzyl ether, 1-phenylethyl *o*-chlorobenzyl ether, and 1-indyl benzyl ether) in which the two benzylic methylene protons are magnetically equivalent in all the solvents examined; and a second (the remaining compounds in Table II), which show both magnetically nonequivalent methylene protons in low dielectric constant solvents, and a solvent dependence of $\nu_A - \nu_B$ qualitatively similar to that observed for 1-phenylethyl benzyl ether. It is interesting that all the compounds in the latter group show approximately the same total variation in the difference in chemical shift between the benzylic methylene protons

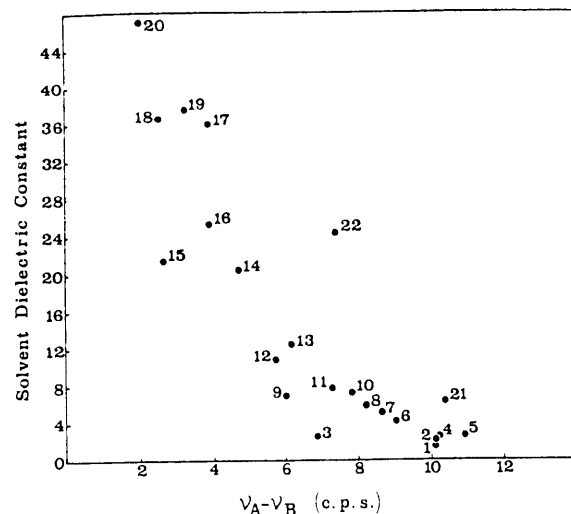
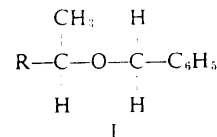


Figure 1. Plot of solvent dielectric constant vs. the chemical shift between the geminal methylene protons of 1-phenylethyl benzyl ether. Numbers refer to the solvents listed in Table I; solvent no. 23 (formic acid) is not included in this plot.

on changing from a solvent of high dielectric constant to one of low dielectric constant. Two of the compounds (1-phenyl-2-methylpropyl benzyl ether and 1-carboethoxyethyl benzyl ether) retain a large magnetic nonequivalence in the highest dielectric constant solvents examined; however, for these as for the other compounds in this class the total observed range of $\nu_A - \nu_B$ is approximately 9 c.p.s.

The solvent dependence of the spectra of ethers containing only one unsaturated group is in marked contrast to the solvent dependence of the spectra discussed above. Compounds containing a benzyl group but no unsaturated group at the asymmetric center (I, R = alkyl) give $\nu_A - \nu_B$ values which are relatively insensitive to solvent. Examples include: benzyl isobutyl ether, benzyl isopropylmethylcarbonyl ether, and benzyl *t*-butylmethylcarbonyl ether (Table III).



The small variations in chemical shift reported in Table III are probably significant. In particular, spectra taken in benzene solution have consistently the largest value for $\nu_A - \nu_B$. However, the magnitude of $\nu_A - \nu_B$ for dimethyl sulfoxide and acetone solutions indicate clearly that a large increase in solvent dielectric constant is not in general accompanied by a corresponding large decrease in the magnitude of $\nu_A - \nu_B$. Moreover, the values of $\nu_A - \nu_B$ in hydrogen bonding solvents are unexceptional.

The solvent dependence of the chemical shift in compounds containing an unsaturated group on the asymmetric center but not directly bonded to the methylene group is more complicated: 1-phenylethyl ethyl ether and 1-phenylethyl 2-methylpropyl ether both show either zero or very small nonequivalence in their $-\text{O}-\text{CH}_2-$ proton resonance in nonaromatic solvents.² In contrast, the chemical shift between the geminal methylene protons of 1-phenylethyl neopentyl ether is fairly large in some low dielectric constant

Table II. Chemical Shift (c.p.s.) between the Geminal Methylene Protons of Several Substituted Benzyl Ethers as a Function of Solvent

					<3	<3
					20.7	16.5
					17.6	16.0
					14.4	14.5
					14.4	14.4
					9.8	
					8.6	
					7.2	
					3.8	
					6.3	
					6.9	
					5.0	
					<3	
					<3	
					<3	
					<3	
					<3	
					<3	
					11.2	
					9.1	
					6.0	
					7.0	
					<3	
					10.1	
					9.1	
					7.1	
					4.3	
					<3	
					10.1	
					9.3	
					6.2	
					7.5	
					5.2	
					<3	
					10.9	
					10.2	
					6.9	
					9.0	
					8.6	
					6.1	
					2.5	
Solvent						
Benzene						
Carbon tetrachloride						
Dioxane						
Diethyl ether						
Chloroform						
Pyridine						
Acetone						

Table III. Solvent Dependence of the Magnetic Nonequivalence of the Methylene Protons for Alkylmethylcarbonyl Benzyl Ethers of Structure I^{a,b}

Solvent	R = (c.p.s.)		
	Ethyl	Iso-propyl	<i>t</i> -Butyl
Benzene	6.6	9.3	15.7
Carbon tetrachloride	5.8	8.8	14.8
Cyclohexane	5.7	8.6	...
Acetone	5.7	8.6	14.7
Dimethyl sulfoxide	4.9	8.2	15.1
Acetic acid	5.4	8.0	...
<i>t</i> -Butyl alcohol	14.9

^a Solutions were 10 ± 2% by volume in solute. The experimental error in $\nu_A - \nu_B$ is no greater than 0.5 c.p.s. ^b From ref. 2.

solvents. In the high dielectric constant solvents examined, the magnetic nonequivalence in this compound is less than 1 c.p.s. (the limit of detection). However, the manner in which this chemical shift varies with solvent is qualitatively significantly different than that observed for 1-phenylethyl benzyl ether (Table IV).

Table IV. Chemical Shift (c.p.s.) between the Methylene Protons of 1-Phenylethyl Neopentyl Ether as a Function of Solvent^a

Solvent	$\nu_A - \nu_B$	Solvent	$\nu_A - \nu_B$
Benzene	6.6	Chloroform	<1
Toluene	5.9	Carbon tetrachloride	<1
Cyclohexane	4.6	Nitrobenzene	<1
<i>n</i> -Pentane	4.5	Pyridine	<1
Bromobenzene	3.0	Formic acid	<1
Carbon disulfide	<1	Dimethyl sulfoxide	<1

^a Solutions were 10 ± 2% by volume in solute. The uncertainty in the chemical shift is estimated to be no greater than ±0.5 c.p.s.

Of particular interest among the data listed in Table IV are the small values of the magnetic nonequivalence for solutions in carbon tetrachloride and formic acid ($\nu_A - \nu_B$ is less than 1 c.p.s. for both). The values for the corresponding solutions of 1-phenylethyl benzyl ether are 10.2 and 9.9 c.p.s., respectively, both close to the maximum value observed for this ether.

Discussion

Previously reported data have indicated that, in solvents of low dielectric constant, the chemical shift between the geminal methylene protons of ethers of type I seems to depend primarily on the bulk of R, provided that R is larger than the methyl group.² In most of the compounds examined when R is an aliphatic group increasing the dielectric constant of the solvent has little effect on $\nu_A - \nu_B$; when R is an unsaturated group, $\nu_A - \nu_B$ decreases with an increase in dielectric constant. The former of these observations was previously interpreted² as evidence that neither specific solvent-solute interactions⁵ nor reaction field⁶ effects were responsible for the methylene proton nonequivalence. Although derived from observations

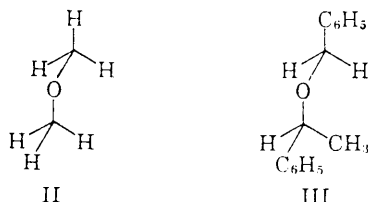
(5) For example, see S. S. Danyluk, *Can. J. Chem.*, **41**, 387 (1963); H. Suhr, *Mol. Phys.*, **6**, 153 (1963); J. V. Hatton and R. E. Richards, *ibid.*, **3**, 253 (1960); A. D. Buckingham, *Can. J. Chem.*, **38**, 300 (1960).

(6) A. D. Buckingham, T. Schaefer, and W. G. Schneider, *J. Chem. Phys.*, **32**, 1227 (1960); P. Diehl and R. Freeman, *Mol. Phys.*, **4**, 39 (1961).

for compounds in which R is an aliphatic group, this conclusion is probably also valid for those compounds in which R is an unsaturated group.

Several lines of evidence are pertinent to an understanding of the solvent dependences reported in Table I. Consideration of correlations between $\nu_A - \nu_B$ and structure suggest that conformational preference of the phenyl group directly bonded to the methylene group is responsible for the major part of the magnetic nonequivalence of the methylene protons of 1-phenylethyl benzyl ether.² Examination of the effect of substitution in the aromatic rings of the compound provides further support for this conclusion and, in addition, gives some insight into the origin of the solvent effects.

Detailed discussion of the origin of $\nu_A - \nu_B$ in the molecules examined in this study requires some reliable knowledge of the conformations of ethers. Microwave studies indicate that the most stable conformation for dimethyl ether is the one having the carbon-oxygen bond of one methyl group staggered with respect to the carbon-hydrogen bonds of the other (II).⁷ Although no structural precedents are available, it seems probable that substitution of an alkyl or aryl group for a hydrogen atom in dimethyl ether should leave unchanged the preference for conformations having the carbon-oxygen bond⁷ staggered with respect to the carbon-hydrogen or carbon-carbon bonds. Thus, one possible conformation for 1-phenylethyl benzyl ether can be represented by III.



Unfortunately, reliable structural data pertinent to the problem of rotational isomerism around a $XCH_2-C_6H_5$ bond are not available. By analogy with other sixfold potential problems,⁸ it is probably safe to assume that, for toluene itself, differences in energy between rotational conformers would be very small. Dibenzyl ether presents a more complicated problem. Although a variety of data are available which indicate that the most stable conformations of substituted propenes are those in which the substituent is eclipsed with the carbon-carbon double bond,⁹ the obvious differences between a vinyl group and a phenyl group make difficult any attempt to extend structural information concerning the former to the latter. Introduction of the methyl group into the dibenzyl ether skeleton (formally yielding 1-phenylethyl benzyl ether) thus

(7) P. H. Kasai and R. J. Myers, *J. Chem. Phys.*, **30**, 1096 (1959). Dimethyl sulfide has a similar geometry: L. Pierce and M. Hayashi, *ibid.*, **35**, 479 (1961).

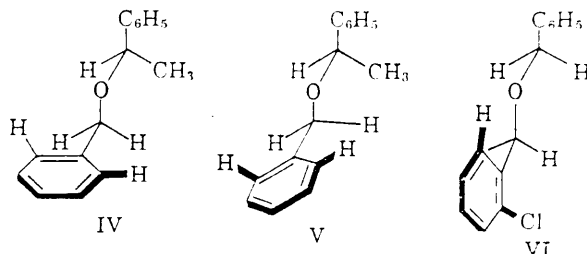
(8) For example, the barrier to rotation about the carbon-nitrogen bond of nitromethane is 6 cal./mole: E. Tannerbaum, R. J. Myers, and W. D. Gwinn, *ibid.*, **25**, 42 (1956). Similar small barriers have been determined for difluoromethylborane [R. E. Naylor and E. B. Wilson, Jr., *ibid.*, **26**, 1057 (1957)] and trimethylborane [L. S. Bartell, B. L. Carroll, and J. P. Guillory, *Tetrahedron Letters*, **13**, 705 (1964)].

(9) V. W. Laurie, *J. Chem. Phys.*, **34**, 1516 (1961); A. A. Bothner-By, C. Naar-Colin, and H. Günther, *J. Am. Chem. Soc.*, **84**, 2748 (1962). See also S. S. Butcher and E. B. Wilson, Jr., *J. Chem. Phys.*, **40**, 1671 (1964), and references therein, for a discussion of the related problem of conformation equilibria with respect to a carbonyl group.

provides a problem in conformational analysis without good precedents.

Nevertheless, several observations lend strong support to the suggestion that the magnetic nonequivalence of the methylene protons of 1-phenylethyl benzyl ether is a consequence of a preferred conformation of the phenyl group with respect to the methylene group. The first of these, discussed previously,² rests on the observation that if this phenyl group is replaced by an alkyl group the magnitude of the magnetic nonequivalence is reduced to a value close to zero. The second depends on the effect of substitution in this ring on the magnitude of $\nu_A - \nu_B$ (Table II). Substitution of a chlorine atom *para* or *meta* to the CH_2 group has only a small effect on $\nu_A - \nu_B$ in the several solvents examined. In striking contrast, substitution of one *o*-hydrogen by a chlorine or bromine atom reduces $\nu_A - \nu_B$ to some value less than the limit of detection in these experiments (approximately 3 c.p.s.). If both *o*-hydrogen atoms are substituted by chlorine atoms, $\nu_A - \nu_B$ is approximately the same as for the unsubstituted compound.

If the origin of the difference in chemical shielding of the two methylene protons lay in the asymmetric center, it is difficult to understand how substitution in the directly bonded phenyl ring would have this observed effect. In particular, although it might be possible to imagine interactions between an *o*-chlorine atom and a phenyl ring several bonds removed such that a difference in shielding of the methylene protons arising from the asymmetric center depended strongly on the presence or absence of the chlorine atom, it is difficult to explain why introduction of a second chlorine atom into the remaining *ortho* position should cancel the effect of the first. If, on the other hand, the origin of the methylene proton nonequivalence lies in conformational preference of the phenyl ring with respect to the methylene group, the substituent effects can be rationalized in a relatively straightforward and consistent manner. In the absence of an *o*-chlorine atom, the equilibrium configuration of the $CH_2-C_6H_5$ portion of the molecule might be represented by a conformation such as IV or V, in which one methylene carbon-hydrogen bond falls in the plane of the phenyl ring and the second falls out of this plane. Dipole-dipole interactions and/or steric interactions might favor conformation VI for the *ortho*-chlorinated ether, since this conformation places the carbon-oxygen bond as nearly antiparallel to the carbon-chlorine bond as possible. In this conformation, the two methylene protons would be symmetrically disposed to either side of the phenyl ring and would necessarily have the same shift.



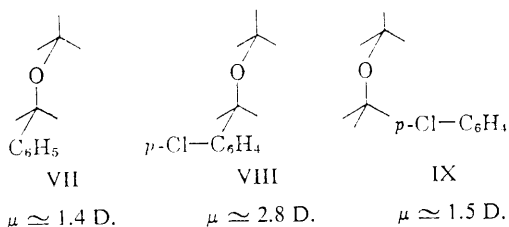
Introduction of a second *o*-chlorine should approximately cancel the effect of the first, and the favored conformation should again be that of IV or V.

Table V. Solvent Dependence of Chemical Shifts and Coupling Constants (c.p.s.) for 1-Phenylethyl Benzyl Ether

Solvent	Concn.	$\nu_A - \nu_B$	J_{AB}^b	$J_{CH_3-H}^b$	ν_A^a	ν_B^a	$\nu_C^{a,c}$	$\nu_{CH_3}^{a,b}$
Benzene	8.8	10.9	11.8	6.7	259.9 ± 0.5	248.9 ± 0.5	260.2	86.8
Chlorobenzene	9.9	8.2	11.5	6.5	261.0 ± 0.6	252.8 ± 0.6	262.0	83.7
<i>o</i> -Dichlorobenzene	9.6	7.2	11.3	6.5	260.9 ± 0.6	253.7 ± 0.6	263.6	85.0
Nitrobenzene	10.2	3.8	11.7	6.4	263.5 ± 1.0	259.7 ± 1.0	270.5	87.8
Pyridine	9.2	6.1	11.5	6.3	267.1 ± 0.6	261.0 ± 0.6	270.6	87.1
Aniline	9.4	7.8	12.1	6.4	257.2 ± 0.6	249.4 ± 0.6	257.3	81.8
Aniline	4.3	8.4	11.6	6.3	257.8 ± 0.6	249.4 ± 0.6	257.3	80.1
Cyanobenzene	10.0	3.8	10.1	6.5	262.4 ± 1.2	258.6 ± 1.2	269.4	85.9
Cyclohexane	10.2	10.1	11.5	6.3	261.5 ± 0.5	251.0 ± 0.5	261.6	
Cyclohexane	4.8	10.1	11.7	6.1	261.9 ± 0.5	251.8 ± 0.5	261.8	
<i>n</i> -Pentane	10.0	10.1	11.6	6.2	262.5 ± 0.5	252.5 ± 0.5	262.5	
<i>n</i> -Pentane	6.0	10.1	11.5	6.3	261.8 ± 0.5	251.7 ± 0.5	261.8	
Carbon tetrachloride	9.7	10.2	12.3	6.6	261.0 ± 0.5	250.8 ± 0.5	262.9	87.2
Chloroform	8.6	8.6	11.3	6.6	264.6 ± 0.6	256.0 ± 0.6	266.9	87.5
Acetone		2.5 ^d					271.2	87.6
Dimethyl sulfoxide		2.0 ^d					270.7	85.5
Nitromethane	10.3	3.1	9.3	6.5	262.1 ± 1.1	258.9 ± 1.1	269.8	85.2
Methyl iodide	10.3	6.0	11.4	7.0	261.6 ± 0.6	255.6 ± 0.6	265.9	83.2
Acetic anhydride	9.9	4.6	11.3	6.6	262.8 ± 1.0	258.2 ± 1.0	269.1	84.6
Dimethylformamide	10.1	2.5	10.2	6.5	263.3 ± 1.1	260.9 ± 1.1	272.1	85.2
Ethanol	12.5	7.4	11.4	6.5	260.5 ± 0.6	253.1 ± 0.6	264.4	83.4
<i>t</i> -Butyl alcohol	9.4	5.7	10.0	6.5	261.3 ± 0.7	255.6 ± 0.7	262.3	83.5
Diethyl ether	10.6	9.0	12.0	6.8	261.8 ± 0.5	252.8 ± 0.5	265.3	87.6
Dioxane	9.8	6.9	11.5	6.0	263.5 ± 0.6	256.7 ± 0.6	267.2	85.1
Dioxane	5.0	6.9	11.5	6.0	262.9 ± 0.6	256.0 ± 0.6	260.9	83.4
Tetrahydrofuran	8.1	6.3	11.5	6.2	263.4 ± 0.6	257.2 ± 0.6	267.6	82.7

^a Chemical shifts are measured with respect to internal tetramethylsilane. ^b The uncertainty in these values is no greater than ±0.4 c.p.s. ^c The uncertainty in ν_C is no greater than ±0.2 c.p.s. ^d These values were obtained by extrapolating the values from mixed solutions with carbon tetrachloride to zero concentration in carbon tetrachloride.

The dependence of $\nu_A - \nu_B$ on substitution in each of the two phenyl rings of 1-phenylethyl benzyl ether sheds some light on the origin of the solvent dependence of this quantity. The dipole moments of several extreme conformations for the chlorinated and unchlorinated ethers can be calculated in an approximate fashion by neglecting all bond moments except those due to C-O and C-Cl bonds (taken as 1.2 and 1.7 D., respectively),¹⁰ and measuring bond angles from Dreiding models. The values obtained for the molecular dipole moments of the *para*-chlorinated compounds are



The value for all conformations of unsubstituted 1-phenylethyl benzyl ether (VII) will be the same in this approximation.

If the principal effect of solvent variation were to change the equilibrium constant in a mixture of conformers having the phenyl groups, respectively, *trans* and *gauche* to a carbon-oxygen bond (*i.e.*, those conformations represented schematically by VIII and IX), then $\nu_A - \nu_B$ in the *para*-chlorinated ethers would be expected to respond in a different manner to changes in solvent dielectric constant than $\nu_A - \nu_B$ in 1-phenylethyl benzyl ether. This is because the change from VIII to IX involves a change in dipole moment of

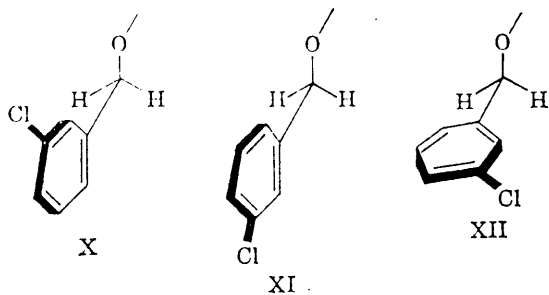
approximately 1.3 D., while the corresponding conformational change with 1-phenylethyl benzyl ether involves a much smaller change in dipole moment. In fact, although the actual values observed in each solvent for 1-phenylethyl benzyl ether, 1-*p*-chlorophenylethyl benzyl ether, and 1-phenyl *p*-chlorobenzyl ether are slightly different, the change in $\nu_A - \nu_B$ for a given change in solvent is very similar for each of these compounds. This similarity in solvent variation suggests that changes in an equilibrium involving conformations of types VIII and IX is probably not involved in determining $\nu_A - \nu_B$.

Similar arguments based on a comparison of the solvent dependence of 1-phenylethyl benzyl ether and 1-(*m*-chlorophenyl)ethyl benzyl ether suggest that major changes of conformation around the CH₂-C₆H₅ bond (illustrated schematically by structures X and XI) are also unimportant in determining $\nu_A - \nu_B$, since changes of this type should again involve dipole moment changes of significantly different magnitude in the chlorinated and unchlorinated compound. However, a smaller change (*e.g.*, XI to XII) is not precluded by the available data, since such a change would involve only a small change in dipole moment.

The data presently available do not permit an unambiguous interpretation of the mechanism by which solvent changes influence $\nu_A - \nu_B$, although they do make it seem highly probable that changes in the conformation of the benzylic phenyl group relative to the methylene protons are responsible for the observed variation in $\nu_A - \nu_B$.^{4,11,12} However, the

(11) The geminal coupling constant J_{AB} in 1-phenylethyl benzyl ether also shows an apparently significant solvent dependence (Table V); although the scatter in the experimental data is large, it seems that high values of J_{AB} are associated with low values of the solvent dielectric constant. It might be possible to rationalize this behavior in terms of changes in the relative positions of the methylene protons relative to

(10) E. Gould, "Mechanism and Structure in Organic Chemistry," Henry Holt and Co., New York, N. Y., 1959, p. 62.



observation that the magnetic nonequivalence is largely independent of solvent in those compounds containing no unsaturated groups at the asymmetric center suggests that the solvent does not *directly* influence the conformation of the phenyl group with respect to the methylene protons in 1-phenylethyl benzyl ether. A possible explanation for the solvent dependence of the spectra of the compounds reported in Table II is that the solvent may be capable of influencing the apparent "shape" of the asymmetric center by influencing the conformation of the phenyl group attached to the asymmetric center and hence the extent to which conformation IV is preferred to conformation V. If these two conformations are equally populated, or if a conformation analogous to VI is favored, then $\nu_A - \nu_B$ will of course be small. This suggestion, although tentative, finds support in the observation that 1-indyl benzyl ether, in which the configuration of the phenyl group at the asymmetric center has been fixed by incorporation into a cyclic structure, has magnetically equivalent benzylic protons in all solvents studied.

Several questions remain unanswered by this work. In particular, it is not clear whether the conformation that is primarily responsible for inducing a conformational preference of the methylene group with respect to the plane of the phenyl ring is one in which the $\text{CH}_2\text{-C}_6\text{H}_5$ bond is *trans* to the bond between the asymmetric center and the ether oxygen atom (for example, IV and V) or *gauche*. Further, it is not certain that the solvent dielectric constant is the most important factor in determining the conformation of the molecule in solution. Certain of the solvents (formic acid, acetic acid) which fall far from their expected positions in Figure 1 can be rationalized on the basis of specific solvent-solute interactions; others, particularly dioxane, are less easily rationalized.

Experimental

Spectra were taken at 60 Mc.p.s. on a Varian A-60 spectrometer at ambient temperature, using samples $10 \pm 2\%$ by volume in solute. Samples were ordinarily degassed by sweeping dry nitrogen through the solute and the solvent before mixing.

The preparations of compounds mentioned in this paper and not given below have been reported previously.²

1-*p*-Chlorophenylethyl Alcohol. In a clean, dry, 300-ml. round-bottomed, three-necked flask fitted

the plane of the directly bonded phenyl group¹²; however, several well-established examples of a solvent variation of geminal coupling constants in molecules of fixed geometry suggest that other factors may be at least of equal importance. Cf. V. S. Watts, G. S. Reddy, and J. H. Goldstein, *Mol. Spectry.*, **11**, 325 (1963); E. I. Snyder, *J. Am. Chem. Soc.*, **85**, 2624 (1963).

(12) For another possible example, see T. Takahashi, *Tetrahedron Letters*, 565 (1964).

with a stirrer equipped with a Teflon blade, dropping funnel, and condenser were placed 8.1 g. (0.33 g.-atom) of magnesium and approximately 50 ml. of anhydrous ether. A solution of 47.3 g. (0.33 mole) of methyl iodide in 25 ml. of anhydrous ether was added over a period of 30 min. The reaction mixture was heated under reflux until the reaction was complete. A mixture of 46.8 g. (0.33 mole) of *p*-chlorobenzaldehyde dissolved in approximately 50 ml. of anhydrous ether was added then over a period of 1 hr. The reaction mixture was refluxed for 30 min. and hydrolyzed with saturated aqueous ammonium chloride solution. The ether layer was separated and dried over calcium sulfate; the ether was removed. The crude alcohol so obtained was estimated to be approximately 95% pure by its n.m.r. spectrum and was used immediately without further purification. The yield was 40 g. (85%).

1-*p*-Chlorobenzylethyl Benzyl Ether. In 1-l. three-necked, round-bottomed flask fitted with a stirrer equipped with a Teflon blade, condenser, dropping funnel, and heating mantle was placed a mixture of 8.3 g. (0.19 mole based on sodium hydride) of 55% sodium hydride-mineral oil suspension with 300 ml. of anhydrous ether. To the slurry was added 30.0 g. (0.19 mole) of 1-*p*-chlorophenylethyl alcohol, dissolved in approximately 25 ml. of anhydrous ether. The mixture was heated under reflux for 3 hr. A solution of 32.4 g. (0.19 mole) of benzyl bromide in 50 ml. of anhydrous ether was then added cautiously. The mixture was refluxed for 10 hr., hydrolyzed with saturated aqueous ammonium chloride solution, and filtered. The ether layer was dried over calcium sulfate, and the ether was removed on a rotary evaporator. The clear orange liquid so obtained was distilled through a 10-cm. Podbielniak column. The yield was 10 g. (23%) of liquid ether, b.p. 135-136° (1.0 mm.). The infrared spectrum of this compound showed a carbon-chlorine stretch at 645 cm^{-1} , and the n.m.r. spectrum was consistent with the assigned structure.

Anal. Calcd. for $\text{C}_{15}\text{H}_{15}\text{OCl}$: C, 73.04; H, 6.09; Cl, 14.41. Found: C, 73.10; H, 6.01; Cl, 14.28.

1-*p*-Chlorobenzyl Alcohol. A slurry of 1.9 g. (0.05 mole) of lithium aluminum hydride and 200 ml. of anhydrous ether was placed in a 1-l. three-necked, round-bottomed flask fitted with a stirrer equipped with a Teflon blade, condenser, and dropping funnel. To this slurry was added dropwise a solution of 28.1 g. (0.2 mole) of *p*-chlorobenzaldehyde in 50 ml. of anhydrous ether. The resulting mixture was allowed to stand for 1 hr., hydrolyzed with a saturated aqueous solution of ammonium chloride, filtered, and dried over calcium sulfate. The ether was removed on a rotary evaporator, and the white crystals so obtained were recrystallized from ethanol-water. The yield was 20 g. (71%), m.p. 69-70°.

1-Phenylethyl *p*-Chlorobenzyl Ether. A mixture of 13.0 g. (0.07 mole) of *p*-chlorobenzyl alcohol, 13.0 g. (0.07 mole) of 1-phenylethyl bromide, and 15.0 g. (0.14 mole) of sodium carbonate was heated at 130-140° for 14 hr. in a 250-ml. round-bottomed flask fitted with a Teflon-covered magnetic stirring bar and a condenser. The crude product was washed five times with 25-ml. portions of water, dried over calcium sulfate, and distilled through a 10-cm. Podbielniak column. About 2 ml. of product, b.p. 79-80° (0.3-0.4

mm.), was obtained. The infrared and n.m.r. spectra of this compound were consistent with the postulated structure.

Anal. Calcd. for $C_{15}H_{15}OCl$: C, 73.04; H, 6.09; Cl, 14.41. Found: C, 72.95; H, 6.20; Cl, 14.45.

1-Bromoindane. Dry hydrogen bromide gas was bubbled through reagent grade indene in an open 250-ml. erlenmeyer flask until absorption of gas no longer took place. The n.m.r. spectrum indicated that the product was at least 95% pure (it was not purified further).

1-Indyl Benzyl Ether. A mixture of 65 g. (0.36 mole) of crude 1-bromoindane, 32 g. (0.30 mole) of benzyl alcohol, 45 g. (0.37 mole) of potassium bicarbonate, and 60 ml. of anhydrous ether was placed in a 500-ml. round-bottomed flask fitted with a Teflon-covered magnetic stirring bar and a condenser. This mixture was stirred at room temperature for 15 hr., diluted with ether and filtered; the ether was removed on a rotary evaporator. The residue (containing approximately 60% of the desired product) was used in all of the n.m.r. studies of this compound, but an analytical sample of the material was obtained by chromatography on basic alumina. The crude material (2 g.) was applied to 60 g. of alumina, and eluted with 1 l. of ligroin (b.p. 60–70°), followed by 350 ml. of 20% benzene–80% ligroin. The last 50 ml. of benzene–ligroin contained approximately 0.1 g. of product which had infrared and n.m.r. spectra consistent with the postulated structure.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.65; H, 7.14. Found: C, 85.54; H, 7.07.

1-Phenylethyl m-chlorobenzyl ether was prepared by heating a mixture of 0.3 mole of 1-phenylethanol and 0.3 mole of *m*-chlorobenzyl chloride under reflux over excess sodium carbonate for 24 hr. The resulting solution was cooled, the inorganic salts were removed by filtration, and the organic filtrate was washed once with water, twice with 2 *N* hydrochloric acid, and again with water. The organic layer was dried and distilled to yield approximately 10 g. of crude product, b.p. 110–115° (0.3 mm.). The compound was characterized by its n.m.r. spectrum; spectra were obtained

on samples containing approximately 10% of an unidentified impurity, whose resonances did not interfere with the region of interest.

1-Phenylethyl o-Chlorobenzyl Ether. Sodium 1-phenylethoxide (0.2 mole) was prepared by fractional distillation of methanol from a suspension of sodium methoxide (27 g., 0.2 mole) and 1-phenylethanol (25 g., 0.2 mole) in anhydrous benzene. *o*-Chlorobenzyl chloride (32 g., 0.2 mole) was added to the benzene suspension of the alkoxide and the mixture was heated under reflux for 24 hr. The inorganic solids were removed by filtration and the product was obtained by distillation at reduced pressure; the yield was about 15 g., b.p. 105–110° (0.1 mm.).

Anal. Calcd. for $C_{15}H_{15}ClO$: C, 73.04; H, 6.08. Found: C, 73.18; H, 6.35.

1-Phenylethyl o-Bromobenzyl Ether. Sodium 1-phenylethoxide was prepared by evaporating an ethanol solution containing sodium ethoxide (0.3 mole) and 1-phenylethanol (0.4 mole) to dryness under aspirator vacuum at 80° using a rotary evaporator. The residue was dissolved in 150 ml. of freshly distilled *N,N*-dimethylformamide, and to the resulting solution was added approximately 0.3 mole of *o*-bromobenzyl bromide (crude material prepared by bromination of *o*-bromotoluene with *N*-bromosuccinimide). The solution immediately became very hot and a white solid precipitated. The reaction mixture was allowed to cool, poured into 2 l. of water, extracted with pentane, dried, and distilled to yield approximately 30 g. of ether, b.p. 131–133° (<0.1 mm.).

Anal. Calcd. for $C_{15}H_{15}BrO$: C, 61.88; H, 5.19. Found: C, 61.87, 61.60; H, 5.20, 5.26.

1-Phenylethyl 2,6-dichlorobenzyl ether was prepared using the same procedure as that described for 1-phenylethyl *o*-chlorobenzyl ether, except that 2,6-dichlorobenzyl bromide (prepared by allylic bromination of 2,6-dichlorotoluene with *N*-bromosuccinimide) was substituted for the *o*-chlorobenzyl chloride of that preparation. The product had b.p. 130–134° (<0.1 mm.). The analysis of the material was about 1% high on carbon; however, the n.m.r. spectrum was wholly consistent with the assigned structure.