NUCLEAR MAGNETIC RESONANCE STUDIES OF SOLVENT EFFECT ON THE MOLECULAR STRUCTURE OF SOME ARYL AND ALKYL ETHERS

Thesis by

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ABSTRACT

The nuclear magnetic resonance spectra of several substituted benzyl ethers containing a center of asymmetry reveals that in certain solvents the methylene protons of the ether are magnetically nonequivalent. Further investigation shows that the magnitude of this effect is related to the dielectric constant of the solvent.

From this information a structure for the molecule in solution is postulated, and the observed magnetic nonequivalence of the protons is explained on the basis of steric and electronic effects.

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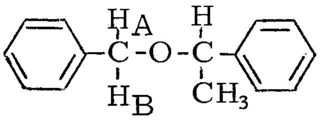
INTRODUCTION

The protons of a methylene group separated from a center of molecular asymmetry by an oxygen atom are, in some cases, magnetically nonequivalent and display AB-type nuclear magnetic resonance (n. m. r.) spectra (1). The magnitude of the magnetic nonequivalence of the methylene protons of 1-phenylethyl benzyl ether (I) is markedly dependent on the medium in which the ether is



I

dissolved (2). This dependence is remarkable in that the difference in chemical shift between H_A and H_B ($\nu_A - \nu_B$) seems to be inversely proportional to the dielectric constant of the solvent (Table 1, Fig. 7). It was felt that a study of the solvent dependence of I and of structurally similar ethers (II, III, IV.....X) might suggest the answers to two important questions: first, why are these protons (H_A and H_B) magnetically nonequivalent; second, why does the value of $\nu_A - \nu_B$ change with the dielectric constant of the solvent?

Before discussing these results and their significance, it would be useful to outline the possible causes of the magnetic nonequivalence of these protons. First, consider an isolated molecule of ether I in the gas phase. Similar reasoning can be used for ethers II - X. There are nine energetically favorable configurations of this compound (Fig. 1-1 - 1-9). The magnetic nonequivalence of the methylene protons may be a result of any combination of these structures.

In any structure there are several possible effects that can give rise to an AB-type of spectra. The first of these, for the purpose of this discussion, is the effect of the "ring currents" associated with a benzene ring. The benzene molecule, in the free state, or when σ bonded to another molecule, has six π electrons distributed above and below its ring. These electrons circulate rapidly (3) under the influence of an applied magnetic field H_0, their angular frequency being $\frac{eH_0}{2Mc}$ where e is the charge of an electron, M is the mass of an electron and c is the speed of light. This circulation is equivalent to a current $J = \frac{3e^2H_0}{2\pi Mc}$. The direction of the current is such that it gives rise to an induced field opposed to the primary field. The field due to the ring current is shown schematically in Fig. 2. A simplification of the ring-current effect can be made by replacing the ring current J by a magnetic dipole $J\pi a^2/c$ (where a is the radius of the ring) positioned at the center of the ring and perpendicular to it (4). Using this approximation, Pople finds that at a point at a distance r from the center of the ring, the secondary magnetic field due to the ring current is $\frac{3e^2H_0a^2}{2Mc^2r}$.

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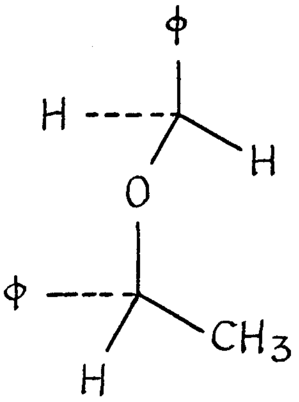

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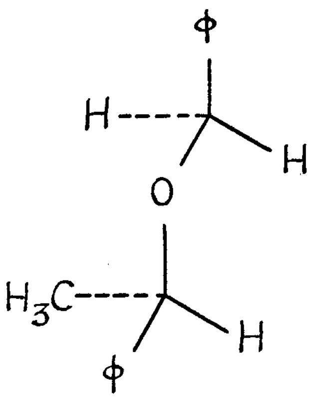

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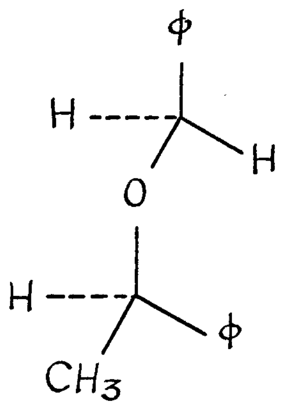

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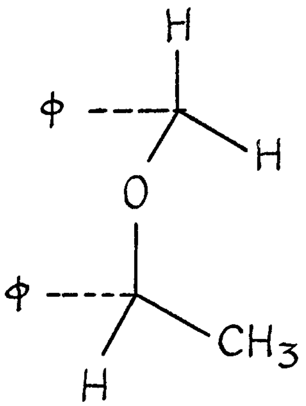

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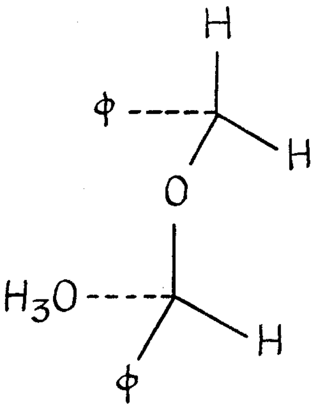

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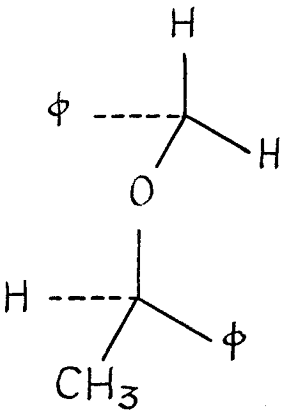

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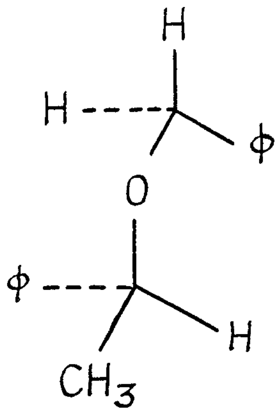

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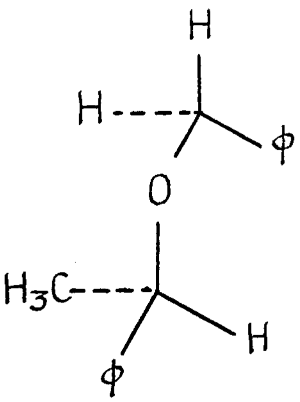

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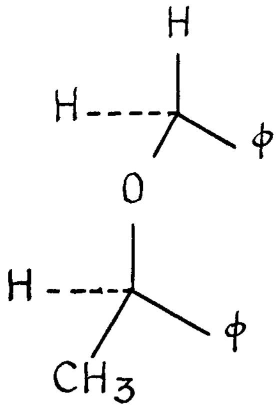


Fig. 1. Possible Configurations of Ether I

Therefore for two protons to be magnetically equivalent in the presence of a benzene molecule they must lie on the same or equal lines of magnetic force as shown in Fig. 2. Both of the benzene rings on I have the same sort of magnetic field associated with them; however, the benzene ring bound directly to the methylene carbon probably will have the larger effect due to its proximity to H_A and H_B.

The second possible cause of magnetic nonequivalence between the methylene protons is the screening contribution of the two unshared pairs of electrons on the oxygen. If each of these pairs is regarded as a dipole, the only ways in which H_A and H_B can experience equal shielding from these electrons would be for these protons to be eclipsed by or opposed to the two unshared pairs (Figs. 3 and 4). Examination of models shows that these are sterically unfavorable configurations and probably not dominant forms.

A third possible contributing factor to nonequivalence of the methylene protons is what Pople terms the "neighboring group anisotropy" effect (5). This important factor in compounds without aromatic rings arises from electron movement in the σ bonds. Under the influence of an external magnetic field the electrons will give rise to a secondary magnetic field, the magnitude of which varies with the nature of the bond (6). These secondary magnetic fields may increase or decrease the shielding of neighboring protons.

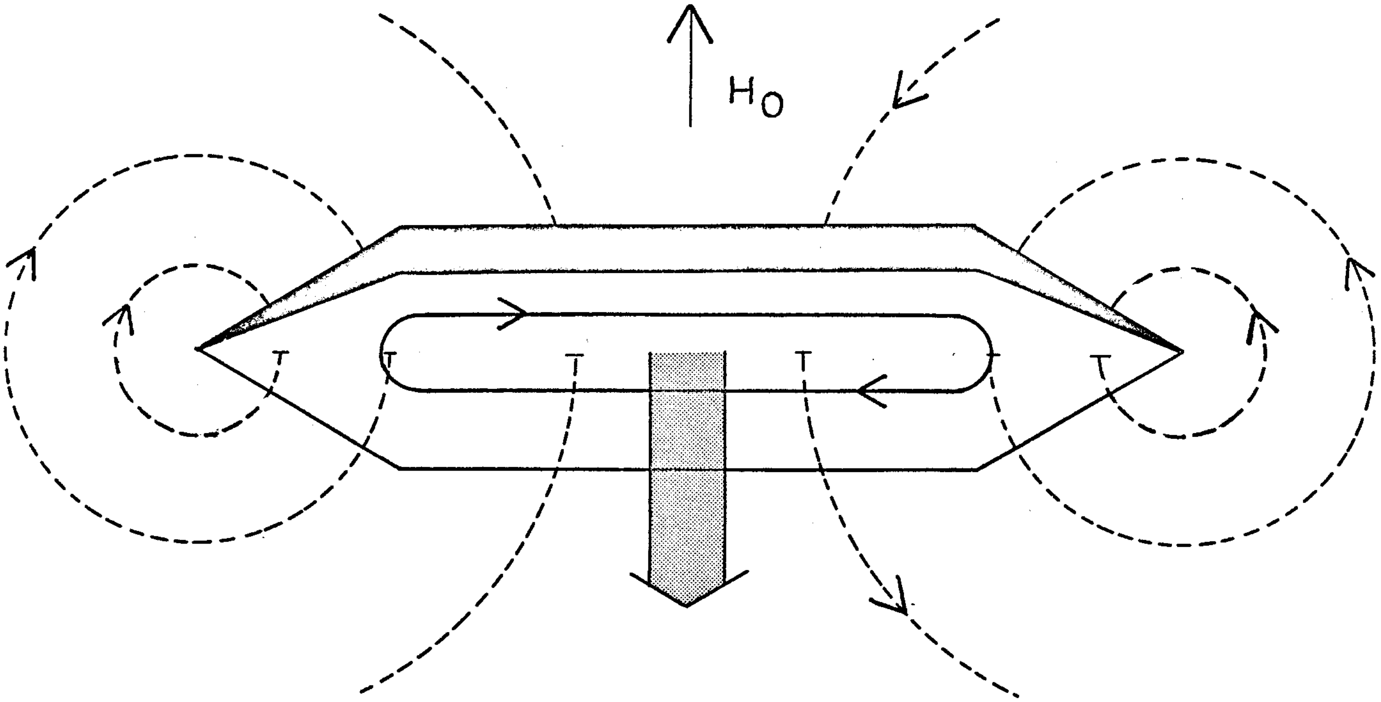


Fig. 2. Lines of Magnetic Force Induced in Benzene by External Field H_0.

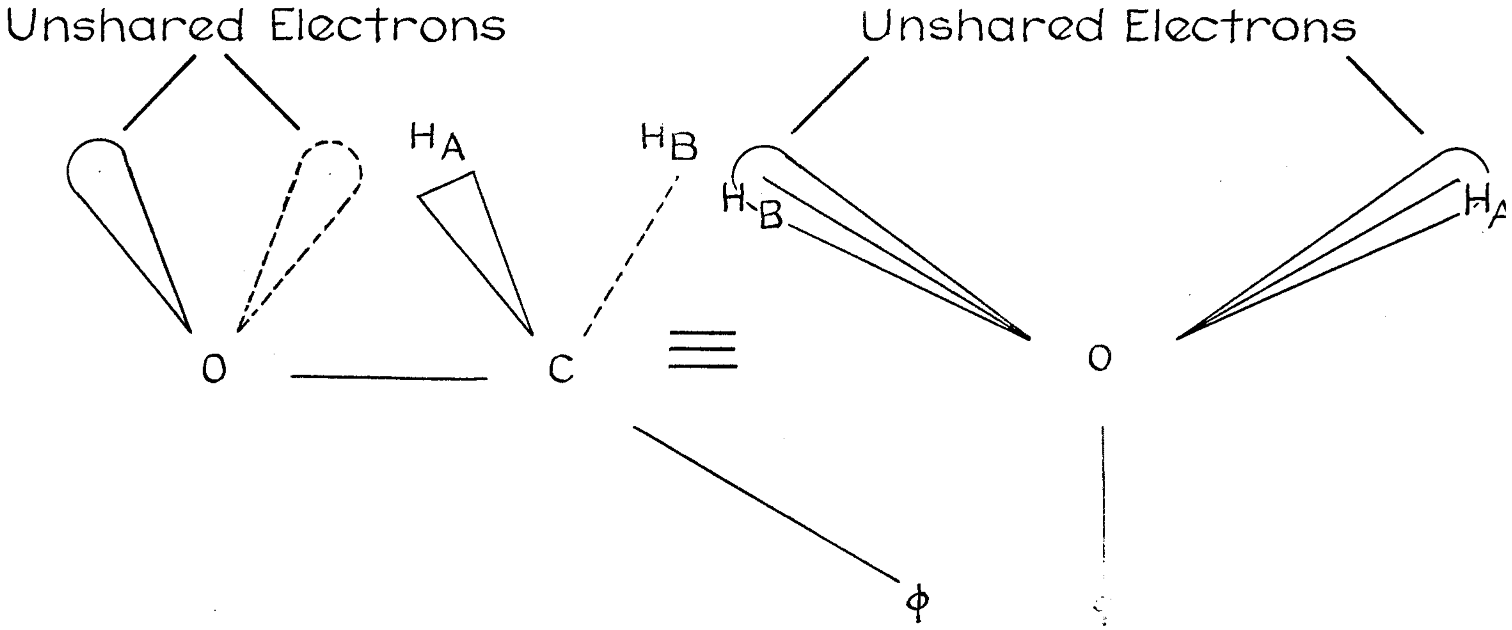


Fig. 3. Unshared Pairs of Electrons on Oxygen of I

Eclipsed by H_A and H_B

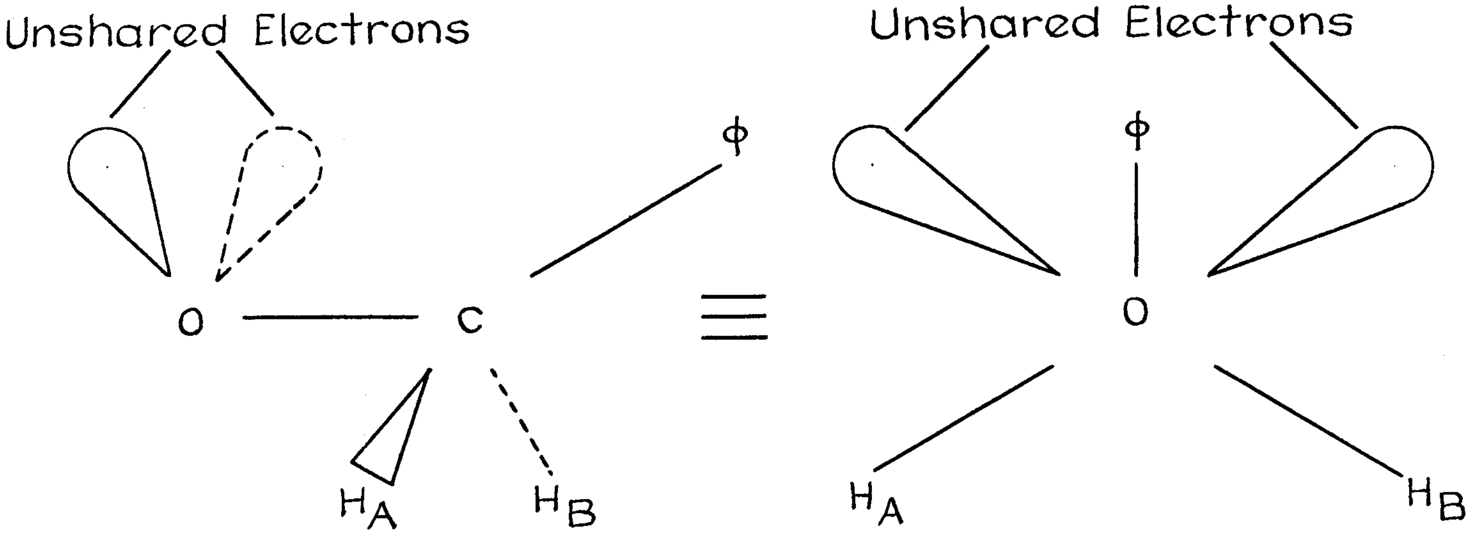


Fig. 4. Unshared Pairs of Electrons on Oxygen of I Opposed to H_A and H_B

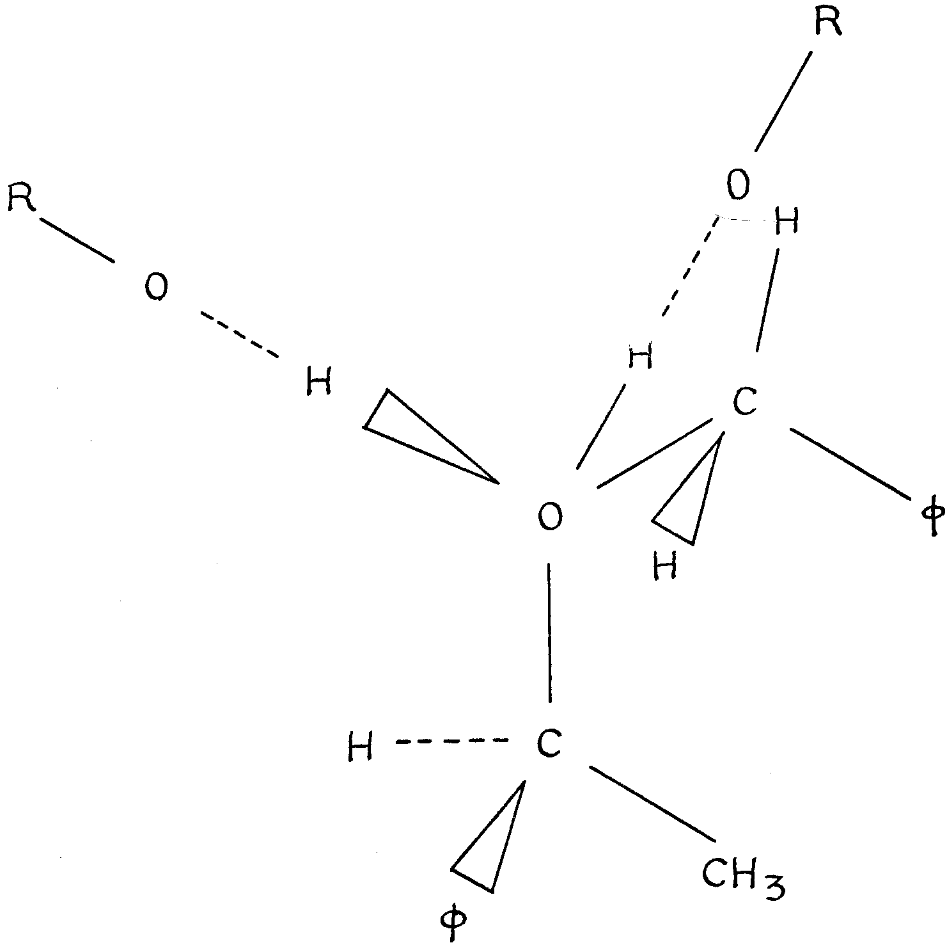


Fig. 5. Hydrogen Bonding in Ether I

The ethers described here all contain an asymmetric center, and it is possible that each of the C-X ($X = H$, CH_3, etc.) bonds may give rise to a different magnetic field. Consequently, the methylene protons may experience different degrees of shielding from these secondary magnetic fields, and become magnetically nonequivalent.

The carbon-oxygen bond on the far side of an oxygen from the methylene group is also magnetically anisotropic due to the circulation of electrons in the bond. If this bond is oriented so that one of the methylene protons is closer to it than the other, there is a possibility that the secondary magnetic field due to the bond might change the shielding of the proton.

All of these causes for the magnetic nonequivalence of the methylene protons of an isolated gas molecule hold only if there is one or more preferred configuration for the molecule, in which case these effects can be brought to bear against the methylene protons. If there are no preferred conformations and there is rapid exchange between the conformations, the effects are expected to average to zero, giving only an A_2 spectrum for the molecule.

When the asymmetric molecule is placed in a solvent, several new factors become important. The net chemical shift of a proton in a solvent can be expressed as the sum of several factors (7).

$$\sigma = \text{the shift of the molecule} =$$

$$\sigma_G + \sigma_B + \sigma_A + \sigma_W + \sigma_E + \sigma_C + \sigma_H + \sigma_S$$

where σ_G is the shift of an isolated gas molecule, σ_B is the shift due to the bulk diamagnetic susceptibility of the solvent, σ_A is the shift due to the solvent magnetic anisotropy, σ_W is the shift due to van der Waals interactions between the solute and the solvent and other electronic effects such as hydrogen bonding, σ_E is the shift due to the "reaction field" of the solvent, σ_C is the shift due to the formation of complexes between solute and solvent, σ_H is the shift due to steric hinderance to rotation or change of configuration imposed by the presence of solvent molecules around the solute, and σ_S is the shift due to self-solvation.

Each of these factors will now be discussed with reference to the ethers being examined.

Factors bearing on σ_G have been explained earlier and will not be discussed further here.

The bulk diamagnetic susceptibility of the solvent is an isotropic property of the solvent, and should influence each proton equally (8).

Each individual solvent molecule possesses its own anisotropic magnetic field due to the electronic currents in it. Since it is probable that the solvent molecules do not always arrange themselves symmetrically around a complex solute, it is likely that certain parts of the solute might be screened differently than others and that the methylene protons might be magnetically nonequivalent.

If the solvent molecules arrange themselves symmetrically around the solute, no effect will be observed.

In a solvent containing an acidic hydrogen atom (acids, alcohols, etc.), there is a distinct possibility of hydrogen bonding to the oxygen of the ether linkage (Fig. 5). There is also the remote possibility of hydrogen bonding to the benzene rings, but this effect will be neglected. The association of the solvent molecules with the solute greatly alters the magnetic environment of the methylene protons, and may also change the configuration of the molecule. The increased (or decreased) shielding caused by the presence of the hydrogen-bonded solvent molecules could cause the magnetic non-equivalence of the methylene protons. Since there are two pairs of non-bonding electrons on the oxygen, there will be a maximum of two hydrogen bonds attached to each oxygen. Therefore for H_A and H_B to be magnetically equivalent they must be oriented as in Fig. 3 and 4. These conformations do not appear to be energetically favorable.

Also under this heading come interactions of the electron clouds of the solute and solvent which might tend to produce changes in the orientation of the solvent molecules around the solute. These changes in orientation might result in the magnetic nonequivalence of the methylene protons through a combination of all the effects discussed in this section.

It has been shown (9, 10) that for a polar solute and a solvent of dielectric constant ϵ the solute dipole polarizes the surrounding medium, setting up an electrostatic "reaction field" E, at the solute. The component of this field along the axis of a C-H bond will change the shielding of the proton, by shifting the electrons along the bond. The magnitude of E is given by $E = \frac{\mu}{r^3} \frac{n^2 + 2}{3} \frac{\epsilon - 1}{\epsilon + 1/2\, n^2}$ where n is the refractive index of the solute, r is the distance between the molecules or parts of molecules responsible for the field, and μ is the dipole moment of the solute. Hence, a solvent of low dielectric constant such as carbon tetrachloride would be expected to have a small reaction field, and a solvent of relatively high dielectric constant such as acetone, a large reaction field.

Several studies have been reported (11, 12) of the effect of complex formation between solute and solvent molecules on proton chemical shifts. Complexing might change the electronic structure of portions of the solute molecule, affect the configurational preferences of the solute by steric interaction, and change the conformational populations of the molecule. Most of the reported types of solvent - solute complexes are of the nature of specific dipole-induced interactions (Fig. 6). This type of interaction may be important in aromatic solvents and aliphatic solvents possessing high dipole moments.

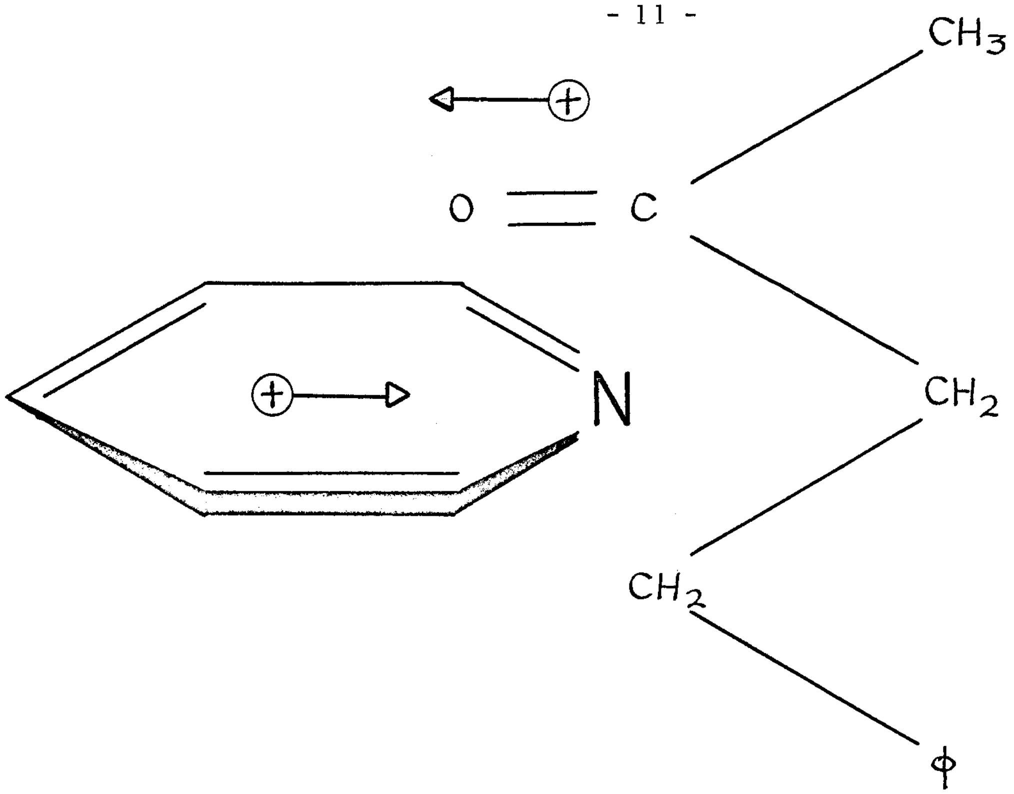


Fig. 6. Dipole Induced Solvent - Solute Complex

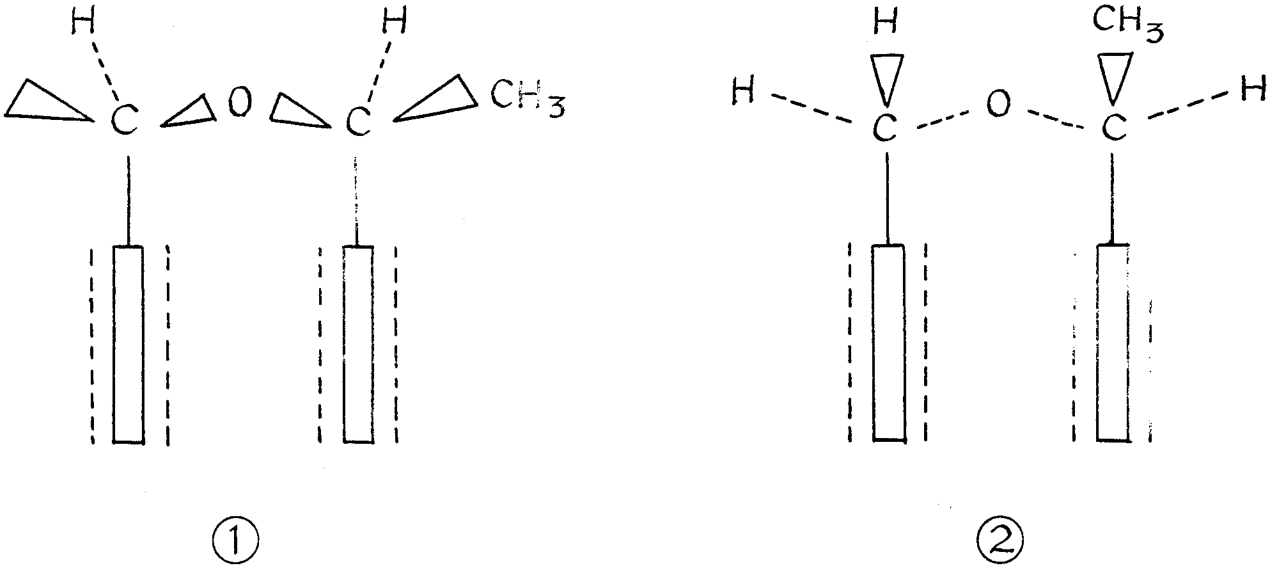


Fig. 9. Dominant Contributing Configuration of 1-Phenylethyl Benzyl Ether in the Closed Form

It is obvious that if the solvent and solute interact sufficiently to create a physical barrier to rotation or other configurational change, the n. m. r. spectrum of the solute is expected to be changed. It is very difficult to evaluate the magnitude of this effect on a theoretical basis because of the difficulties in determining if the solvent will interfere with each solute molecule in the same way.

The final term in the expression is that for self-solvation. This is not a distinct effect in itself. This term is probably not of major importance in the dilute solutions studied, and will be neglected.

The possible causes for the observed AB spectra having been pointed out, an attempt will now be made to relate these causes to the observed data.

RESULTS AND DISCUSSION

Examination of the data in Tables 1 - 11, and graphical evaluation of these data (Fig. 7-8), reveals that the ethers which have been examined can be divided into two classes. The first class (Fig. 7) exhibits a solvent effect, i.e., an increase in $\nu_A - \nu_B$ with a decrease in the dielectric constant of the solvent. The second class (Fig. 8) does not show any appreciable solvent effect. There are strong similarities between the compounds in each class as can be seen from the chart below.

Class I

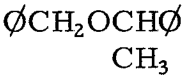
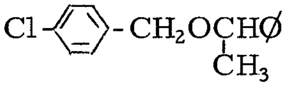
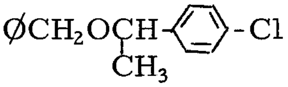
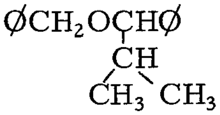
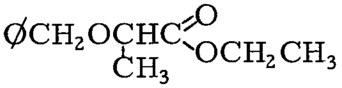
Compound No.	Structure
I	 $\phi CH_2O\underset{CH_3}{CH}\phi$
II	
III	
IV	 $\phi CH_2O\underset{\underset{CH_3\quad CH_3}{CH}}{CH}\phi$
V	 $\phi CH_2O\underset{CH_3}{CH}C\begin{smallmatrix}\nearrow O\\ \searrow OCH_2CH_3\end{smallmatrix}$ (13)

Fig. 7. Plot of $\nu_A - \nu_B$ vs. Dielectric Constant ϵ

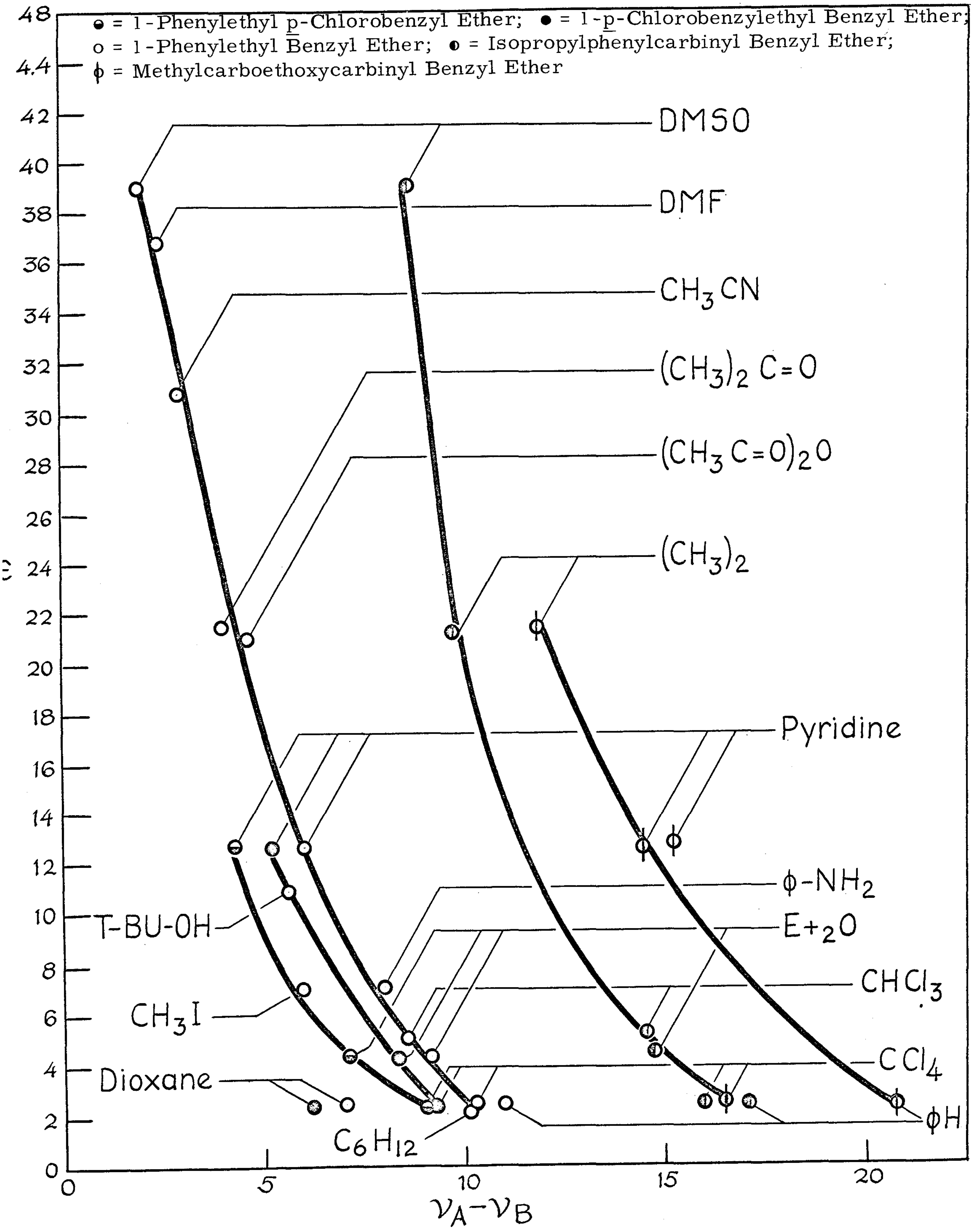
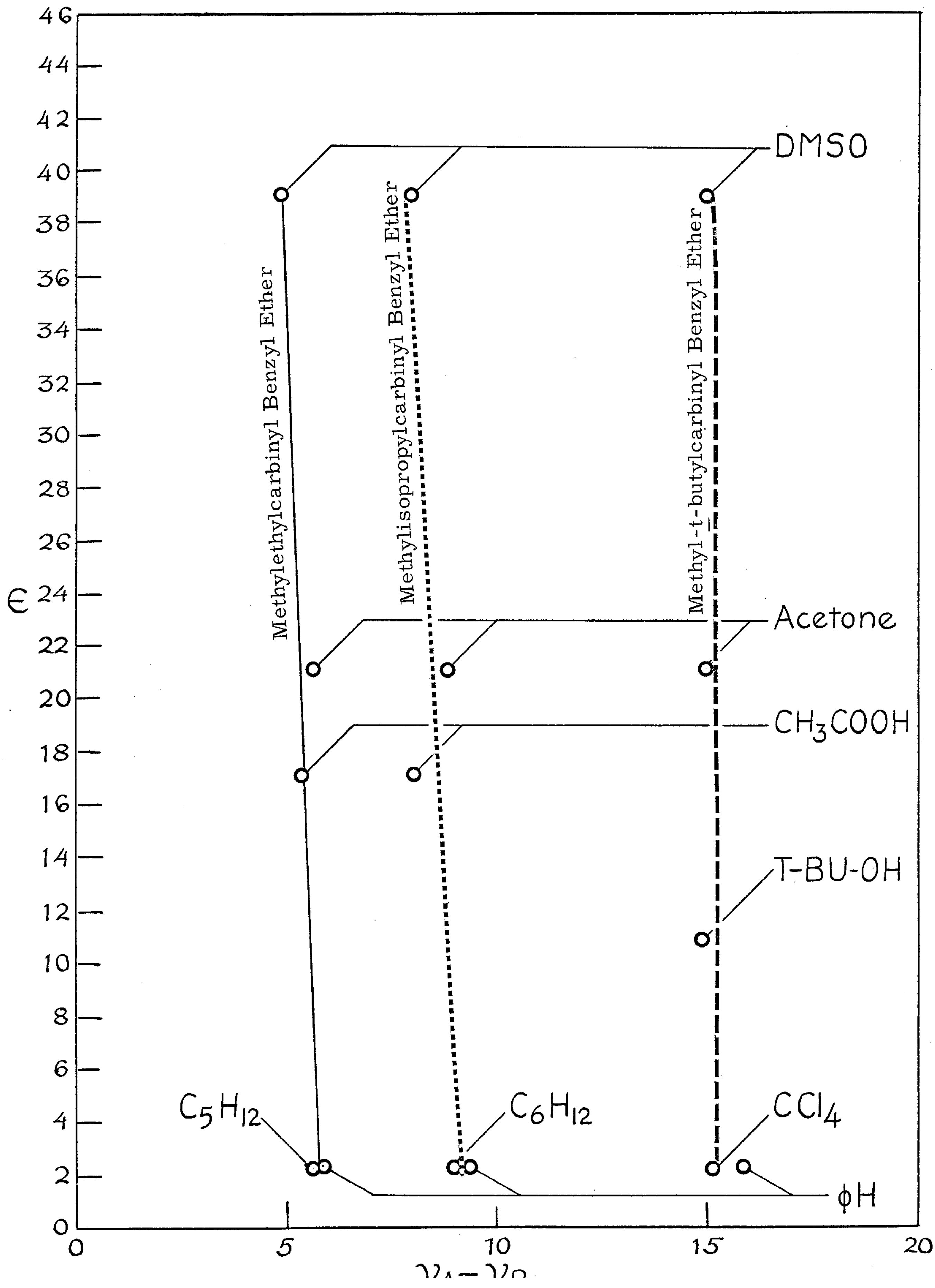
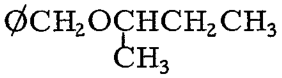
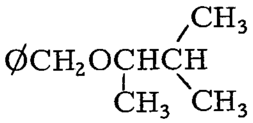
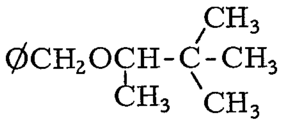
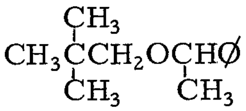
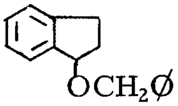


Fig. 8. Plot of $\nu_A - \nu_B$ vs. Dielectric Constant ϵ



Class II

Compound No.	Structure
VI	 $\phi CH_2O\underset{CH_3}{CH}CH_2CH_3$
VII	 $\phi CH_2O\underset{CH_3}{CH}\overset{CH_3}{\underset{CH_3}{CH}}$
VIII	 $\phi CH_2O\underset{CH_3}{CH}-\overset{CH_3}{\underset{CH_3}{C}}-CH_3$
IX	 $CH_3\overset{CH_3}{\underset{CH_3}{C}}CH_2O\underset{CH_3}{CH}\phi$
X	

All of the compounds in Class I have an unsaturated moiety bonded both to the asymmetric center and to the methylene group. All of the compounds in Class II have only one center of unsaturation except X which has an indene nucleus in place of the aliphatic group.

A second generalization becomes evident from the compounds in Class II: an increase in size of the aliphatic group attached to the asymmetric center results in an increase in the magnitude of $\nu_A - \nu_B$.

Two more facts that are obvious from these data are: first, only compounds of the type $-CH_2\phi$ are AB, and therefore the phenyl adjacent to the methylene protons is responsible for most of the magnetic nonequivalence of these protons; second, only compounds with two centers of unsaturation exhibit a solvent dependence. Therefore the two centers of unsaturation may have some connection with the dependence of $\nu_A - \nu_B$ on the dielectric constant of the solvent.

As pointed out above, the main reason for the magnetic nonequivalence of the methylene protons is the ring currents in the benzene ring attached to the methylene group, and the resultant anisotropic magnetic field. Examination of various models of ether I reveals that in most of its configurations (Fig. 1-1, 1-3, 1-4, and 1-6 through 1-9) the benzene ring adjacent to the methylene protons cannot rotate freely around its bond. In these configurations, one of the methylene protons is approximately in the place of the benzene ring, while the other proton is about 1 Å above the plane of the ring. In this configuration there will be considerable difference at each proton in the magnetic field due to the benzene ring current. The literature (14, 15) reports changes in chemical shift for a benzene molecule attached to a methylene group of magnitudes large enough to account for the magnetic nonequivalence of the methylene protons observed here.

Although the benzene ring cannot rotate freely, it can at least twist to some extent around the carbon-carbon bond. Such motion might equalize the shielding arising from the ring currents at the methylene protons, if it were not for the presence of the methyl group on the asymmetric center. This group causes one of the configurations to be slightly more favorable from a steric standpoint, the result being the magnetic nonequivalence of the protons.

It has been shown (16) that a net attractive force exists between two molecules in solution. This force is related to the dipole moment and polarizability of the molecules, and molecules of high dipole moment tend to form the stronger bonds. This force is generally explained on the basis of a dipole-induced interaction.

The recent literature (17) has revived the idea of a solvent possessing an "internal pressure," which is an effect of the attractive forces between the solvent molecules. It has been shown (18) that this internal pressure is related to the dielectric constant of the solvent.

The two effects mentioned previously account for the observed dependence of $\nu_A - \nu_B$ on the dielectric constant of the solvent in this way; in solution there exists a structure similar to that shown in Fig. 1-6, in which the two benzene rings are in parallel planes (Fig. 9-1, 9-2), and lie next to each other. This structure exists in two forms, one with H_A in the plane of the ring attached to the methylene group (Fig. 9-1), and the other with H_B in this position (Fig. 9-2). If the populations of these states are equal, A_2 spectra would be expected. However the methyl group attached to the asymmetric center provides a degree of steric hindrance to free interchange between these two forms. Fig. 9-2 shows the proximity of the methyl group to the methylene protons.

As one spreads the benzene rings apart (Fig. 10-1, 10-2), the methyl group is forced even closer to the methylene proton (Fig. 10-2), and the energy difference between the two states becomes greater. This over-all configuration would give rise to a greater degree of nonequivalence than the one mentioned earlier. It is proposed, therefore, that this species is present in solution, and is the cause of the AB spectra observed for ethers I, II, III and IV (ether V will be discussed later). The apparent dependence of $\nu_A - \nu_B$ on the dielectric constant of the solvent is due to the shifts in position of the two benzene rings relative to each other. In solvents of high dielectric constant, the benzene rings are relatively close together, causing rapid interchange between the two conformers, giving rise to little difference in chemical shift between the methylene protons. In solvents of low dielectric constant, the rings are relatively far apart, giving rise to a large difference in chemical shift between these two protons.

The presence of this type of configuration (Fig. 9, 10) in solution is best explained in this way. First, this is the most compact form of the molecule, and it would require less energy to solvate it in this configuration than in any other, because the energy of solvation is a function of the internal pressure of the solvent and

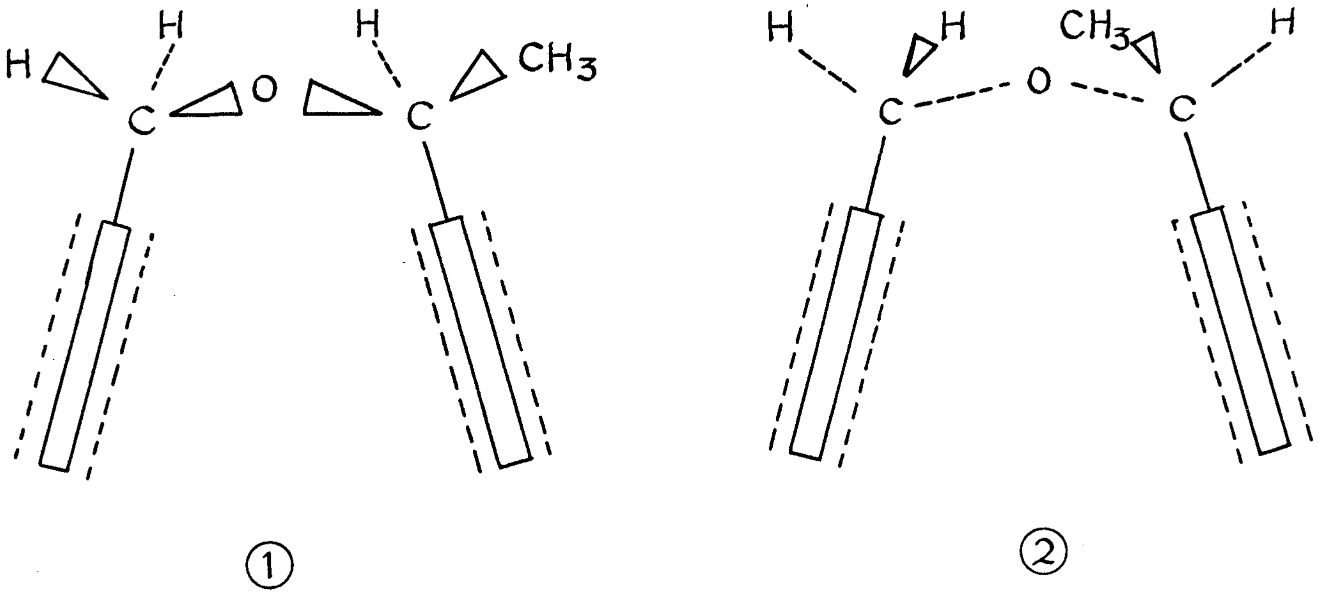


Fig. 10. Dominant Contributing Configuration of 1-Phenylethyl Benzyl Ether in the Open Form

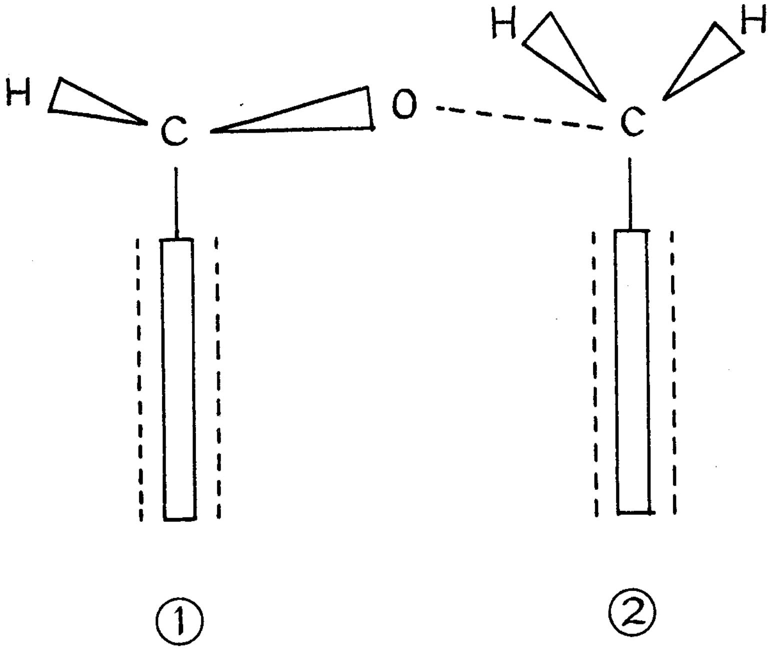


Fig. 11. Compact Configuration of 1-Indyl Benzyl Ether

the volume of the solute (19). It has been shown that the internal pressure of organic liquids is related to the dielectric constant and dipole moment of the liquids (20). In fact, as the dielectric constant of the solvent increases, the internal pressure of the solvent increases, thereby forcing the solute molecules into a more compact configuration. This continues until the internal pressure of the solvent is balanced by the intramolecular forces in the solute. It has been shown that forcing the ether molecule into a more compact configuration decreases the magnetic nonequivalence of the methylene protons.

The second possible cause of the solvent effect is a solvent molecule associating with one of the benzene rings of the solute, by a dipole-induced dipole interaction of the type discussed previously. In this case, a solvent molecule "attaches" itself to each of the benzene rings, and the induced dipoles in each ring orient themselves so that there is a net attractive force between the rings. Since the magnitude of the dipole induced in the rings is related to the dipole moment of the solvent, one would expect stronger attractive forces between the benzene rings in solvents of high dipole moment and dielectric constant. Strong attractive forces between the rings will cause them to be drawn closer together and, as has been shown previously, the closer to one another the benzene rings are, the smaller the difference in chemical shifts between H_A and

H_B will be.

The abnormally high values obtained when acetic acid, formic acid, and ethanol were used as solvents for Class I ethers, are attributed to hydrogen bonding involving the unshared pairs of the ether oxygens. With bulky solvent molecules attached to these electrons, it is very difficult for the ether to undergo transitions from one conformer to another, and the ether is forced, more than one would expect from the dielectric constant of the solvent, into the configuration of Fig. 9-1. This gives rise to an abnormally high value for $\nu_A - \nu_B$.

The substitution of an isopropyl group for a methyl group on the asymmetric center of I only serves to make the configuration shown in Fig. 9-2 more energetically unfavorable, causing the value for $\nu_A - \nu_B$ to be substantially higher than that obtained for I in the same solvent.

Methylcarboethoxycarbinyl benzyl ether (V) displays a solvent-dependent AB-type of spectra for the same reasons as ethers I - IV, but here the bulky, non-planar carboethoxy group cannot get as close to the plane of the benzene ring as another benzene nucleus. Hence the observed splitting for H_A and H_B for this compound is much larger than it is for compounds I - III.

As previously pointed out, the prime contributing factor to the magnetic nonequivalence of the methylene protons is the ring currents surrounding the benzene nucleus attached to the methylene carbon atom. This explains why ether IX shows no AB type of spectra in most cases.

Compounds VI, VII and VIII all have aliphatic groups attached to the asymmetric center in place of one of the benzene nuclei. None of these ethers shows an appreciable change of $\nu_A - \nu_B$ with the dielectric constant of the solvent (Fig. 8, Tables 6 - 8). Examination of models of ether VI shows that in some configurations the benzene ring is free to rotate around its bond, while in others it cannot. In those configurations in which the benzene ring cannot rotate freely, one of the methylene protons is shielded more than the other because the methyl group on the asymmetric center acts as a barrier to equal twisting of the benzene ring relative to the methylene protons. As the size of the group attached to the asymmetric center increases, the magnitude of $\nu_A - \nu_B$ also increases. This effect is due to the increasing size of the aliphatic group causing an increase in occurrence of those configurations in which the benzene ring is not free to rotate. This results in a larger nonequivalence between H_A and H_B.

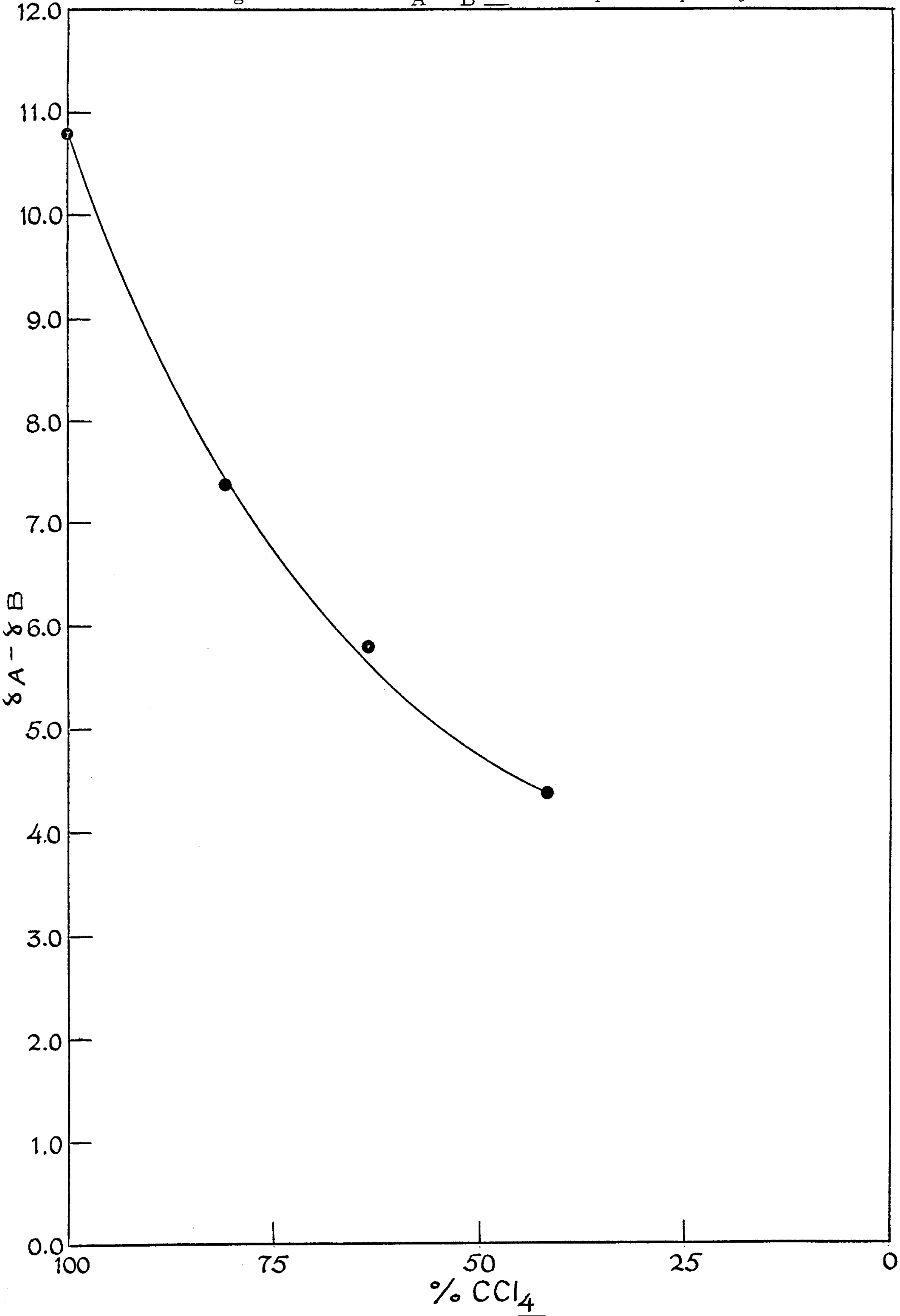
A solvent effect is not observed in this case because the aliphatic groups are not sufficiently polarizable to give an induced dipole large enough to change configurational preferences to a noticeable extent.

In 1-indyl benzyl ether (X) the asymmetric center is fixed in a single configuration. Even if the molecule is in a configuration in which the benzene rings are in parallel planes as in Fig. 9, there is only one position in which the methylene protons can be (Fig. 11). In this configuration these protons are practically equivalent. In all of this ether's other possible configurations, the benzene ring adjacent to the methylene protons is free to rotate, and no magnetic nonequivalence can result from its presence.

For all of these ethers, benzene seems to give a slightly larger value for $\nu_A - \nu_B$ than would be predicted from its dielectric constant. This is a result of the effect termed in the introduction "solvent magnetic anisotropy," and the ring currents in the solvent are causing an enhancement of the "normal" solvent effect.

When a molecule of I is placed in a mixture of two solvents of different dielectric constants, it will find itself in an environment of one solvent or the other. The number of solute molecules in an environment of a given solvent will be proportional to the concentration of that solvent. Therefore what one observes in the n. m. r. spectrum of such a solution is a statistical average of all the chemical shifts in the solution. The preceding statement indicates a straight-line dependence of $\nu_A - \nu_B$ on the per cent of a given solvent. In practice (Fig. 12) there is some slope to the curve which may be due to the effects of self-solvation and the presence of an

Fig. 12. Plot of $\nu_A - \nu_B$ vs. % CCl_4 in $CCl_4 - CH_3CN$ Mixture



internal standard (tetramethylsilane).

TABLE 1

Solvent Dependence of $\nu_A - \nu_B$ for 1-Phenylethyl Benzyl Ether (2)

Solvent	ϵ	$\nu_A - \nu_B$
CCl_4	2.2	10.2
$CHCl_3$	5.0	8.6
$(CH_3)_2CO$	21.4	4.0
$(CH_3)_2SO$	39	2.0
CH_3CN	38.8	2.8
CH_3I	7.0	6.0
Ac_2O	20.5	4.6
$CH_3\overset{O}{\overset{\parallel}{C}}N(CH_3)_2$	36.7	2.5
EtOH	24.3	7.4
<u>t</u>-BuOH	10.9	5.7
Et_2O	4.3	9.0
Dioxane	2.2	6.9
C_6H_6	2.2	10.9
Pyridine	12.5	6.1
$C_6H_6N_2H_2$	7.2	7.8 and 8.4
C_6H_{12}	2.0	10.1

TABLE 2

Solvent Dependence of $\nu_A - \nu_B$ for 1-Phenylethyl p-Chlorobenzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	0
$(CH_3)_2CO$	21.4	0
Pyridine	12.5	4.3
Et_2O	4.3	7.1
CCl_4	2.2	9.1
C_6H_6	2.2	10.3

TABLE 3

Solvent Dependence of $\nu_A - \nu_B$ for 1-p-Chlorobenzylethyl Benzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
$(CH_3)_2CO$	21.4	0
Pyridine	12.5	5.2
Et_2O	4.3	7.5
Dioxane	2.2	6.2
C_6H_6	2.2	10.1
CCl_4	2.2	9.3

TABLE 4

Solvent Dependence of $\nu_A - \nu_B$ for Isopropylphenylcarbinyl Benzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	8.7
$(CH_3)_2CO$	21.4	9.8
Pyridine	12.5	14.4
$HCCl_3$	5.0	14.5
Et_2O	4.3	14.7
C_6H_6	2.2	17.6
CCl_4	2.2	16.0

TABLE 5

Solvent Dependence of $\nu_A - \nu_B$ for Methylcarboethoxycarbinyl Benzyl Ether (12)

Solvent	ϵ	$\nu_A - \nu_B$
$(CH_3)_2CO$	21.4	11.8
Pyridine	12.5	15.2
CCl_4	2.2	16.5
C_6H_6	2.2	20.7

TABLE 6

Solvent Dependence of $\nu_A - \nu_B$ for Methylethylcarbinyl Benzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	4.9
$(CH_3)_2CO$	21.4	5.7
CH_3COOH	17	5.4
CCl_4	2.2	5.8
C_6H_{12}	2.0	5.7

TABLE 7

Solvent Dependence of $\nu_A - \nu_B$ for Methylisopropylcarbinyl Benzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	8.2
$(CH_3)_2CO$	21.4	8.8
CH_3COOH	17	8.2
CCl_4	2.2	9.3
C_6H_{12}	2.0	8.9

TABLE 8

Solvent Dependence of $\nu_A - \nu_B$ for Methyl-t-butylcarbinyl Benzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	15.1
$(CH_3)_2CO$	21.4	15.0
t-BuOH	10.9	14.9
CCl_4	2.2	15.1
C_6H_6	2.2	15.9

TABLE 9

Solvent Dependence of $\nu_A - \nu_B$ for Methylphenylcarbinyl Neopentyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	0
$C_6H_5NO_2$	36	0
HCOOH	58	0
Pyridine	12.5	0
$HCCl_3$	5.0	0
CS_2	0	0
C_6H_6	2.2	6.6
CCl_4	2.2	0
C_6H_{12}	2.0	4.6
C_5H_{12}	1.8	4.5

TABLE 10

Solvent Dependence of $\nu_A - \nu_B$ for 1-Indyl Benzyl Ether

Solvent	ϵ	$\nu_A - \nu_B$
CH_3SOCH_3	39	0
$(CH_3)_2CO$	21.4	0
CH_3COOH	17	0
Pyridine	12.5	0
Et_2O	4.3	0
C_6H_6	2.2	0
CCl_4	2.2	0
C_5H_{12}	1.8	0

TABLE 11

Solvent Dependence of Shift of Protons of α-Phenylethyl Benzyl Ether in CCl_4 - CH_3CN Mixtures

% CCl_4	ν_A	ν_B	ν_C
100.0	264.1	253.3	264.5
81.2	263.4	256.0	267.1
63.7	262.9	257.1	268.7
41.7	263.0	259.0	270.8
22.4	0	0	271.8
0.0	0	0	270.8

EXPERIMENTAL

1-Phenylethyl Benzyl Ether. - A mixture of 216 g. (2.0 moles) of benzyl alcohol, 410 g. (2.0 moles) of 1-phenylethyl bromide and 130 g. (1.25 moles) of sodium carbonate was heated with stirring on a steam bath for 5 hours. Inorganic salts were removed from the resulting orange oil by washing five times with 50-ml. portions of water. The organic layer was separated, dried over calcium sulfate, and distilled through a 10-cm. Podbielniak column. The clear liquid obtained was allowed to stand over powdered calcium chloride for 24 hours and then filtered. The yield was 211 g. (51%) of product of b.p. 90-94° (1.5 mm.). The n.m.r. spectrum of this compound (as compared to a previous spectrum of the pure material obtained by George Whitesides) showed it to be at least 99% pure.

Methylethylcarbinyl Benzyl Ether, Methylisopropylcarbinyl Benzyl Ether, Methyl-t-butylcarbinyl Benzyl Ether, Methylphenylcarbinyl Neopentyl Ether and Methylcarboethoxycarbinyl Benzyl Ether - were prepared in these laboratories by George Whitesides.

1-p-Chlorophenylethyl Alcohol. - In a clean, dry 300-ml. round-bottomed three-necked flask fitted with a stirrer equipped with a Teflon blade, dropping funnel and condenser were placed 8.1 g. (0.33 mole) 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 refluxed until hydrogen evolution was complete (approximately 15 min.). A mixture of 46.8 g. (0.33 mole) of p-chlorobenzaldehyde dissolved in approximately 50 ml. of anhydrous ether was added over a period of an hour. The reaction mixture was refluxed for 30 min. and then hydrolyzed with saturated aqueous ammonium chloride solution. The ether layer was separated and dried over calcium sulfate, and 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 a 1-l. three-necked, round-bottomed flask fitted with a stirrer equipped with a Teflon blade, condenser, dropping funnel and heating mantle was placed 8.3 g. (0.19 mole based on sodium hydride) of 55% sodium hydride - mineral oil in 300 ml. of anhydrous ether. To this slurry was added 30.0 g. (0.19 mole) of the 1-p-chlorophenylethyl alcohol prepared previously, dissolved in approximately 25 ml. of anhydrous ether. The mixture was refluxed for 3 hours. A solution of 32.4 g. (0.19 mole) of benzyl bromide in 50 ml. of anhydrous ether was then added cautiously. This mixture was refluxed for 10 hours, 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 clear liquid, 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 $C_{15}H_{13}OCl$: C, 73.04; H, 6.09; Cl, 14.41. Found: C, 73.10; H, 6.01; Cl, 14.28.

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 a solution of 28.1 g. (0.2 mole) of p-chlorobenzaldehyde in 50 ml. of anhydrous ether was added dropwise. The resulting mixture was allowed to stand for an hour, 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° (literature (21) gives m.p. 70.5°).

1-Phenylethyl p-Chlorobenzyl Ether. - A mixture of 13.0 g. (0.07 mole) of 1-phenylethyl bromide, 10.0 g. (0.07 mole) of p-chlorobenzyl alcohol and 15.0 g. (0.14 mole) of sodium carbonate was heated at 130-140° for 14 hours in a 250-ml. round-bottomed flask fitted with a magnetic stirrer 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.

Isopropylphenylcarbinyl Benzyl Ether - was prepared in these laboratories by David Holtz.

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 (as compared with a spectrum previously obtained by George Whitesides).

1-Indyl Benzyl Ether. - A mixture of 65 g. (0.36 mole) of 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 magnetic stirrer and a condenser. This mixture was stirred at room temperature for 15 hours, filtered, and the ether removed on a rotary evaporator. This crude material (containing about 60% of 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 liter of 60-70° ligroin, followed by 350 ml. of 20% benzene - 80% 60-70° ligroin. The last 50 ml. of benzene - ligroin contained approximately 0. 1 g. of product. The infrared and n. m. r. spectra of this compound were consistent with the postulated structure. A small amount of this material was flash-distilled under vacuum to obtain the analytical sample.

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

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