The Conformation of Aliphatic Ethers

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The observation that the unique conformation of 1,5,9,13-tetraoxacyclohexadecane [1] and the stable crystal conformation of poly(trimethylene oxide) [2] are such that in each $-O-CH_2CH_2-CH_2-O-$ unit both CO-bonds are *anti* and both CC-bonds *gauche* of the same sign $(ag \pm g \pm a)$ suggests that the 1,4-CH$\cdots$O interaction may be attractive, whereas the the 1,4-CH$\cdots$CH interaction must be even more repulsive than in hydrocarbons. [3]

It was of interest to verify this in simpler molecules and to check whether the relatively acidic character of the α-CH is a necessary condition for such an attractive interaction. We have therefore examined a series of dialkyl ethers and dimethoxypropanes where such interactions are possible between ether oxygen and either a non-acidic γ-hydrogen or an acidic α-hydrogen (Table 1). It was expected that any interaction would be reflected in an abnormal averaged chemical shift of the protons involved, in a relatively

small vicinal α,β coupling constant, and in a relatively low dipole moment of the 1,3-dimethoxypropanes.

Chemical shift. The measured chemical shift values are shown in Table 1. For the methyl groups in propyl- and isobutyl ethers no significant chemical shift change due to interaction with or closeness to ether oxygen is noticeable, if the more distant methyl group in the butyl ether is taken as the reference. Of course, any interaction would be weak and averaged over three (or six) protons, so at most one can only conclude that such interaction is not demonstrated in the chemical shift.

In dimethoxypropane the α-methylene groups, which are those that would be involved in the interaction, appear about 0.10 ppm lower than α-methylene in the mono-ethers. This is a significantly larger effect than the 0.02 ppm that would be expected [4] merely by introducing an ether function in the γ-position.

For 1,3-dimethoxy-2,2-dimethylpropane no conclusion can be drawn, since the relatively large upfield shift of the α-methylene groups, due to the branching at the β-carbon, [5] dominates the picture. Similar upfield shifts are observed for methyl isobutyl ether (Table 1) and for methyl neopentyl ether. [5]

Table 1. NMR spectral data for simple ethers.

Solvent	Chemical shifts (δ)				Observed $J_{H\alpha H\beta}$ 58 °C	35 °C	-58 °C[a]	Expected $J_{H\alpha H\beta}$ Pure conformers			Statistical average
	$O(CH_2-CH_2-CH_3)_2$							a	g		
CCl$_4$	3.27	1.55	0.90		6.15	6.25	6.5	7.5	5.75		6.33
CDCl$_3$	3.35	1.57	0.92		6.50	6.62	7.0				
	$CH_3-O-CH_2-CH_2-CH_3$										
CCl$_4$	3.25	3.25	1.53	0.90	6.38	6.38	6.5	»	»		»
CDCl$_3$	3.32	3.32	1.57	0.90	6.50	6.62	6.75				
	$CH_3-O-CH_2-(CH_2)_2-CH_3$										
CCl$_4$	3.23	3.28	1.4	0.91		6.3		»	»		»
	$CH_3-O-CH_2-CH(CH_3)_2$							$a(g)$	$g(g)$		
CCl$_4$	3.23	3.03	1.75	0.87	6.25	6.45	6.5	7.5	4.0		6.33
CDCl$_3$	3.31	3.13	1.84	0.91	6.5	6.5	6.7				
	$(CH_3-O-CH_2-)_2CH_2$							aa	ag	gg	
CCl$_4$	3.25	3.35	1.73		6.2	6.2	6.12	7.5	6.63	5.75	6.5
CDCl$_3$	3.31	3.43	1.85		6.45	6.38	6.25				
	$(CH_3-O-CH_2-)_2C(CH_3)_2$										
CCl$_4$	3.25	3.03	0.83								
CDCl$_3$	3.31	3.13	0.88								

[a] -30 °C for CCl$_4$.

Vicinal coupling constants. Since the α-methylene protons give rise to a simple triplet* (or doublet) in a region well separated from the other resonances, except the single line of the methoxy group, the average α,β-vicinal coupling constant can be observed directly. For each conformer as well as for any mixture of conformers, an averaged coupling constant can be estimated, provided reliable values of *gauche* and *anti* H − H coupling constants are known. These have been shown [6],[7] to depend additively on substituent electronegativities. Thus for "freely rotating" systems, with three identical conformers, the averaged vicinal coupling constant (representing *anti* and *gauche* couplings in the ratio of 1:2) has the values 8, 7.26, and 7 Hz for CH_3CH_3, $CH_3CH_2CH_3$, and CH_3CH_2OR, respectively.[6] Assuming additivity, we therefore expect the averaged α,β-coupling constant for $CH_3CH_2CH_2OR$ to be 6.26 Hz. From studies with rigid systems, such as *t*-butylcyclohexanols [8] and substituted 1,3-dioxans,[9] the best values for the corresponding individual coupling constants are $J_{anti} = 11$ Hz and $J_{gauche} = 4$ Hz, which gives 6.33 Hz as the average value for equally populated conformers, in excellent agreement with the value derived above. For the unbranched aliphatic mono-ethers, the calculated α,β-vicinal coupling constant is then 7.5 Hz if only the *anti*-conformer is populated, and 5.75 Hz for averaging between only two enantiomeric *gauche*-conformers. For methyl isobutyl ether the "double *gauche*" conformer, if it were populated exclusively, should have $J = 4$ Hz and the two "*gauche-anti*" conformers alone an averaged $J = 7.5$, but again the average value for equally populated conformers is 6.33 Hz. For each of four pure conformers of 1,3-dimethoxypropane (Fig. 1) the vicinal coupling constant can also be simply calculated (7.5, 6.63, 5.75, and 5.75 for aa, $ag\pm$, $g\pm g\pm$, and $g\pm g\mp$) but since the $g\pm g\mp$ conformer is sterically forbidden, we get the average value 6.5 Hz for a statistical 1:4:2 population of the other three conformers, taking symmetry number and chirality into account.[10]

Before comparing these calculated values, summarized in Table 1, with the experimentally observed coupling constants, the expected influence of solvent and temperature on conformer population must be considered. Hydrogen bonding of chloroform to ethers has been demonstrated,[11] and this could influence the values of the coupling constants by altering the electronega-

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* Such a "deceptivelty simple" AA'XX' spectrum (Abraham, R. J. *The Analysis of High Resolution NMR Spectra*, Elsevier 1971) is a perfect triplet only when the *anti* and *gauche* conformers are equally populated, but even when a sligt broadening of the middle line betrays some enthalpy difference, the average vicinal coupling constant can still be extracted (= half the separation of the two outer lines).
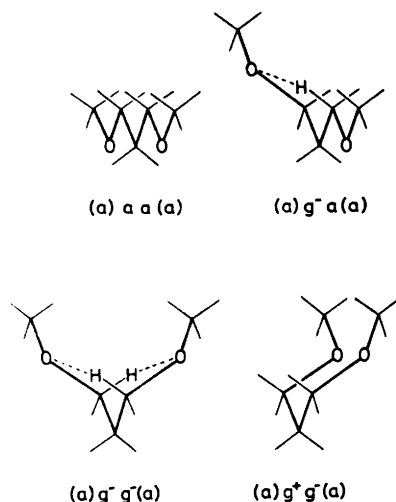

(a) a a (a)   (a) g⁻ a (a)

(a) g⁻ g⁻ (a)   (a) g⁺ g⁻ (a)

Fig. 1. Conformers of 1,3-dimethoxypropane.

tivity of ether oxygen and/or the conformer populations. Since diethyl ether has the same coupling constant in $CDCl_3$ and CCl_4, any observed increase of the α,β-vicinal coupling constant in going from CCl_4 can be simply taken as the result of a decreased *gauche* conformer population.

When the observed coupling constant is close to the value expected for the statistical population of equi-enthalpic conformers, the direction of change observed on cooling may still reveal whether *gauche* or *anti* is enthalpy-preferred. All spectra were therefore recorded also at temperatures higher and lower than the usual probe temperature (Table 1).

Conclusions. For the normal unbranched monoethers, the numerical values of the averaged α,β-vicinal coupling constants show that there can be no important enthalpy difference between *gauche* and *anti* in CCl_4 solution, but the clear decrease observed as equal population is approached at higher temperature suggests that *anti* is slightly preferred. In $CDCl_3$ solution, the interaction of $CDCl_3$ with ether oxygen clearly favours the *anti*-conformers, as shown both by the numerical values and the temperature variation of the coupling constant. One can therefore conclude that the 1,4-*gauche* CH···O interaction is not attractive, but slightly repulsive when CH has no acidic character.

For the branched methyl isobutyl ether the same conclusions can be drawn.

1,3-Dimethoxypropane on the other hand has a significantly low coupling constant in CCl_4 solution and must consist at room temperature of roughly equal quantities of the ag and $g\pm g\pm$ forms. Since the ag form is statistically favoured, this means that the $g\pm g\pm$ conformer is lowest in enthalpy. The temperature variation of the

coupling constant supports this conclusion. In CDCl$_3$ solution the situation is qualitatively similar, but the preference for *gauche* is much less pronounced. We thus conclude that the 1,4-*gauche* CH$\cdots$O interaction is attractive, and competitive with the chloroform-ether interaction, when CH is made sufficiently acidic by the adjacent ether oxygen. Also the chemical shift data led to this conclusion. The dipole moment measured in benzene solution is 1.57 D (and 1.35 D for 1,3-dimethoxy-2,2-dimethylpropane) and this is significantly lower than calculated for randomly oriented ether groups (1.3 D $\times$ $\sqrt{2} = 1.8$ D) or for the *aa*-conformer (2.6 D), and so supports a general *gauche* preference. The even lower dipole moment of the 2,2-dimethyl derivative shows that there is no competition for the ether oxygen from the non-acidic methyl protons.

Experimental. Dipropyl ether was bought from Fluka and was used without purification. The methyl alkyl ethers were prepared [12] by gently heating the corresponding alcohol with dimethyl sulfate and distilling until the vapour temperature reached 100 °C. The distillate was passed through an alumina column and redistilled from sodium metal. Methyl propyl ether, b.p. $39 - 40$ °C; methyl butyl ether, b.p. $70 - 71$ °C; methyl isobutyl ether, b.p. $59 - 60$ °C.

1,3-Dimethoxy-2,2-dimethylpropane was prepared [13] from neopentyl glycol by reaction with sodium hydride and methyl iodide in dry tetrahydrofuran and the product purified on an alumina column.

Dimethoxypropane [14] was prepared by the action of dimethyl sulfate on the dry disodium salt of trimethylene glycol (from sodium methoxide and trimethylene glycol in methanol). The distillate was twice redistilled from solid sodium hydroxide, passed through an alumina column and finally distilled from sodium hydride; b.p. $106 - 107$ °C.

No impurity signals were apparent in the NMR spectra of the ethers so prepared.

The NMR spectra were recorded on a Varian HA 100 instrument for solutions containing about 7 % of the ether and TMS as internal reference. The dipole moments were determined as described previously.[15]

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The Use of Tetrabutylammonium Azide in the Curtius Rearrangement

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The conversion of a carboxylic acid chloride to the corresponding azide is traditionally carried out with sodium azide.[1] The insolubility of the latter in common organic media makes it desirable to use a water-containing solvent mixture, *e.g.*, with aromatic acid chlorides. With lower aliphatic acid chlorides, their sensitivity to hydrolysis precludes the use of protic solvents, and heterogeneous conditions have to be accepted, leading to irreproducible results.

The use of hydrazoic acid and pyridine is described in a recent communication.[2] Acyl azides can thus be prepared under mild and homogeneous conditions. The same is the case when tetramethylguanidinium azide is used.[3] However, the latter two methods require the