Acid-induced ^{13}C Nuclear Magnetic Resonance Chemical Shift Changes of Ether and Ester Carbon Atoms

Mikael Begtrup
Department of Organic Chemistry, Technical University of Denmark, DK-2800 Lyngby, Denmark

^{13}C N.m.r. chemical shifts of ethers dissolved in tetrachloromethane are displaced on addition of trifluoroacetic acid. The displacements result from independent interactions of the acid with the substrate oxygen atoms and alkyl residues. The structure-dependent and stereoselective shift changes are useful for signal assignments, structure determination, conformational analysis, assessment of the distribution of rapidly interconverting conformers of esters, and estimation of the relative basicity of ethers.

The ^{13}C n.m.r. signals of alcohols dissolved in tetrachloromethane are displaced on addition of trifluoroacetic acid. The structure-dependent shift displacements are stereoselective and caused by hydrogen bonding permitting an estimation of the relative basicity of various alcohols.[1] The previous study has now been extended to ethers and esters.

Results and Discussion

Ethers.—Addition of trifluoroacetic acid to a solution of n-butyl methyl ether in tetrachloromethane results in a displacement to low field of the two oxygen-bonded carbon signals and towards higher field of the remaining carbon signals (Figure 1, small capitals).* The magnitude of the displacements of C-2—C-4 are similar to those of butan-1-ol, while C-1 is displaced about half as much as C-1 of butan-1-ol. At low acid : ether ratios the shift displacements are linearly dependent on the acid : ether ratio. At higher ratios the lines are deflected progressively. However, neither the C-1 nor the C-4 curve converge. It is worth noting that in pure trifluoroacetic acid C-1, which is closest to the oxygen atom, is the least affected and the remote C-4 the most affected carbon atom, probably due to general solvent and concentration effects. For comparison, the trifluoroacetic acid-induced carbon shift displacements of n-octane, dissolved in tetrachloromethane, were studied. All carbon signals were displaced towards higher field (Figure 2), that from the terminal carbon atoms about twice as much as the others. (The magnitude of the displacements is virtually linearly dependent on the amount of acid.) Subtraction of the shift displacements of n-octane from those of the corresponding carbon atoms of n-butyl methyl ether yields virtually converging curves with the largest displacement for C-1 and -2 and the smallest for C-4 (Figure 1, bold face). These characteristics are those expected from specific interaction between the acid and the ether group.† The curvature of the curves corrected for acid–alkyl interaction is that expected when a weak base is progressively protonated by a strong acid. The slope (0.74 p.p.m.) of the linear part of the corrected C-1 curve, corresponding to a 1 : 1 adduct, is much smaller than expected for protonation,[3] observable (Table 1) and known to occur [4–6] in concentrated sulphuric acid. The observed extent of proton transfer in the 1 : 1 ether–trifluoracetic acid adduct is in keeping with previous conclusions with regard to hydrogen bonding between ether and trifluoroacetic acid in tetrachloromethane.[7,8]

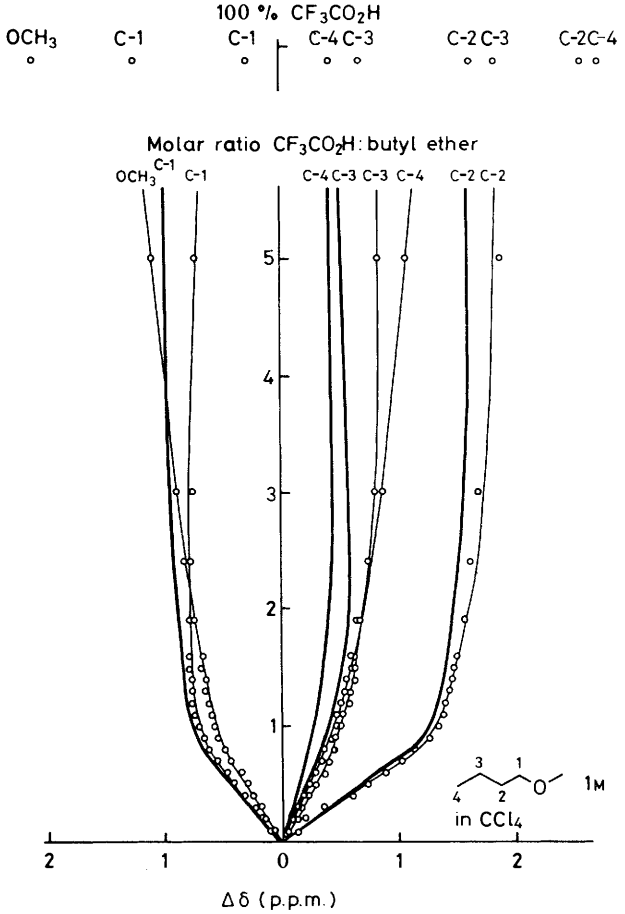

Figure 1. ^{13}C N.m.r. shift displacements of a 1M solution of 1-butyl methyl ether in CCl_4 containing CF_3CO_2H, as a function of the molar ratio acid : ether. Thin curves indicate measured shift displacements. Curves in bold present shift displacements after subtraction of those of n-octane

The extrapolated shift displacement of C-1 for a 1 : 1 adduct is slightly larger than the asymptotic limit value (Figure 1). This may result from concentration effects, to partial protonation, or to the formation of n : 1 ($n > 1$) acid–ether adduct(s).‡ As for alcohols,[1] the equilibrium constant K, characterising the extent of hydrogen bonding; is given by

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* Similar trends have been observed in diethyl and di-isopropyl ether.[2]

† Similar characteristics are obtained by subtraction of n-octane shift displacements from butan-1-ol displacements.[1]

‡ In fact, the displacements depend markedly on the concentration of 1-butyl methyl ether, but the values have not been corrected to conditions of infinite dilution since in the comparison of ethers, concentration effects become of minor significance as long as they are all studied at the same concentration.

Table 1. CF_3CO_2H- and H_2SO_4-induced ^{13}C n.m.r. shift displacements (p.p.m.) of 1M solutions of n-butyl methyl ether (relative to a 1M solution of the ether in CCl_4)

Solvent	Acid	Concentration	Carbon atom 1	2	3	4	OMe
CCl_4	CF_3CO_2H	1M	−0.66	1.26	0.50	0.41	0.53
No	CF_3CO_2H	100%	−0.28	2.57	1.82	2.70	2.14
No	H_2SO_4	98%	−10.02	1.86	1.73	4.03	−5.23

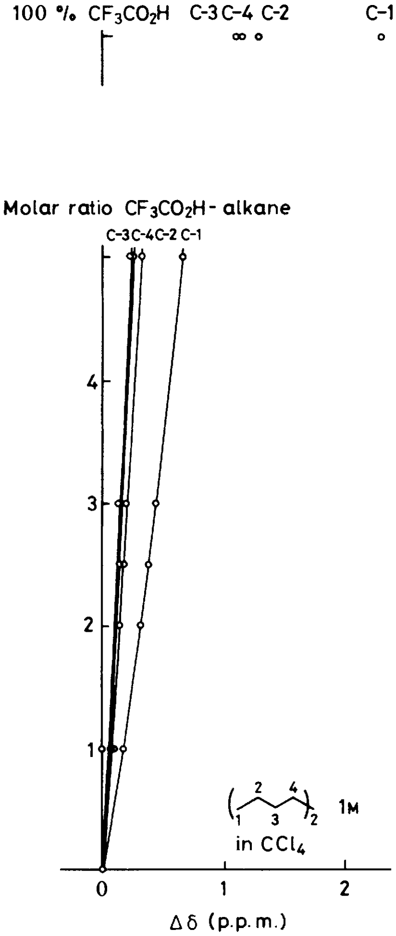

Figure 2. ^{13}C N.m.r. shift displacements of a 1M solution of n-octane in CCl_4 containing trifluoroacetic acid, as a function of the molar ratio acid : alkane

equation (1), in which $\Delta\delta_F$ is the shift displacement found in

$$K = (\Delta\delta_F/\Delta\delta_E)/[1 - (\Delta\delta_F/\Delta\delta_E)]^2 \qquad (1)$$

the 1 : 1 mixture of ether and acid and $\Delta\delta_E$ is the extrapolated shift displacement for a 1 : 1 adduct. For C-1 the latter is almost the same whether calculated on the basis of observed shift displacements, or from corrected values ($\Delta\delta_E$ −0.67 and −0.74 p.p.m., respectively). Again, identical ratios $\Delta\delta_E/\Delta\delta_F$ (1.02 and 1.01) obtain, whether calculated on the basis of observed or corrected Δδ values.

The effect of structural and stereochemical factors on the magnitude of the trifluoroacetic acid-induced carbon shift displacements is apparent from the data of Tables 2, 3, 5, and 7. In the various n-butyl ethers the shift displacements of the butyl carbon atoms are virtually invariant, with the exception of C-1 in n-butyl methyl ether (Table 2). In the linear methyl ethers the individual displacements of C-1—C-4 are almost the same (Table 3). The magnitude of the shift displacement of C-1 (low field) and C-3 (high field) is similar, while C-2 is displaced about twice as much. From C-2 the shift displacements decrease steadily towards the terminal carbon atom which exhibits a slightly larger displacement, attributable to the interaction of trifluoroacetic acid with alkyl residues. By way of illustration, the data of Table 4 reveal that trifluoroacetic acid induces much larger shift displacements of terminal alkane carbon atoms.*† The displacements of non-terminal alkane carbon atoms are small at 1 : 1 substrate : acid ratios. Therefore, $\Delta\delta_F$ and $\Delta\delta_E$ values of methoxy-substituted carbon atoms of methyl ethers are only slightly influenced by additional acid–alkyl interactions and the observed values can be used directly for calculating the *K* values.

Branched methyl ethers exhibit similar consistent carbon shift displacements (Table 5). Whereas the methoxy-carbon signal displacements vary only slightly, those of the methoxy-substituted carbon atoms increase throughout the series primary, secondary, and tertiary alkyl methyl ethers. The average increase from primary to secondary ethers amounts to 1.91 p.p.m., that from secondary to tertiary to 2.02 p.p.m. There is a linear correlation between the shift displacements of the methoxy-substituted carbon atom of ethers and the hydroxy-substituted carbon atom of alcohols {21 points [compound (2a) omitted], slope 1.15, intercept −0.35, regression constant 0.901}. No linear correlation has been found, however, between other ether and alcohol carbon shift displacements. α-Methylene carbon atoms are generally displaced more in an ether than in the corresponding alcohol. In contrast, α-methyl carbon atoms are displaced more in the alcohols, particularly in the tertiary series.[1] The increments of the shift displacements of ether carbon atoms effected by branching are summarized in Table 6. Generally, a given increment is more variable than in the alcohol series.[1] Therefore, use of the increments for prediction of the trifluoroacetic acid-induced shift displacement of the individual carbon atoms in an ether is associated with some uncertainty. Comparison of the basicities of corresponding ethers and alcohols, based on shift displacements, cannot be regarded as reliable without additional knowledge about the influence of the *O*-methyl group on the shift displacements.

The steric orientation of the methoxy group significantly influences the methoxy-substituted carbon shift displacement. Compare bornyl and isobornyl methyl ether, the conformationally rigid *cis*- and *trans*-4-t-butylcyclohexyl ethers (Table 7), and (*cf.* Table 5) the C-2 atoms of *erythro*- and *threo*-1,2-dimethylbutyl methyl ether (18a), the diastereotopic C-4 atoms of 1,2-dimethylpropyl methyl ether (15a), and the di-

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* The alkane carbon shift displacements in Table 4 follow the same trends as those observed when the solvent is changed from cyclohexane to halogenomethanes.[9]

† This feature can be utilized for determining of the number of terminal carbon atoms in alkanes and hence the extent of branching.

Table 2. ^{13}C N.m.r. shift displacements (p.p.m.) observed on addition of 1 mol equiv. of CF_3CO_2H to 1M solutions of n-butyl alkyl ethers in CCl_4

Ether	Carbon atom 1	2	3	4	1′	2′	3′	4′
n-Butyl methyl ether [a]	−0.66	1.26	0.50	0.41	0.54			
n-Butyl ethyl ether [b]	−0.37	1.24	0.57	0.41	−0.51	1.12		
n-Butyl n-propyl ether [b]	−0.42	1.22	0.52	0.46	−0.24	1.05	0.77	
Di-n-butyl ether [c]	−0.35	1.21	0.55	0.42	−0.35	1.21	0.55	0.42

[a] Assignments according to D. E. Dorman, D. Bauer, and J. D. Roberts, *J. Org. Chem.*, 1975, **40**, 3729. [b] *Cf.* ref. 2. [c] Assignments according to C. Delseth and J.-P. Kintzinger, *Helv. Chim. Acta*, 1978, **61**, 1327.

Table 3. ^{13}C N.m.r. shift displacements (p.p.m.) observed on addition of 1 mol equiv. of CF_3CO_2H to 1M solutions of unbranched methyl ethers in CCl_4

Ether	Carbon atom 1	2	3	4	5	6	7	8	9	OCH_3
n-Propyl methyl ether [a]	−0.56	1.24	0.88							0.56
n-Butyl methyl ether [a]	−0.66	1.26	0.50	0.41						0.53
n-Pentyl methyl ether [b]	−0.64	1.21	0.69	0.29	0.49					0.56
n-Hexyl methyl ether [c]	−0.59	1.08	0.53	0.31	0.21	0.27				0.48
n-Heptyl methyl ether [c]	−0.62	1.14	0.55	0.29	0.24	0.18	0.25			0.52
n-Octyl methyl ether [c]	−0.65	1.16	0.59	0.32	0.26	0.17	0.15	0.24		0.51
n-Nonyl methyl ether [c]	−0.68	1.25	0.65	0.35	0.31	0.13	0.16	0.12	0.19	0.54

[a] Assignments according to D. E. Dorman, D. Bauer, and J. D. Roberts, *J. Org. Chem.*, 1975, **40**, 3729. [b] Assignments according to C. Konna and H. Hikino, *Tetrahedron*, 1976, **32**, 325. [c] Assignments according to the present study (see Experimental section).

Table 4. ^{13}C N.m.r. shift displacements (p.p.m.) observed on addition of 1 mol equiv. of CF_3CO_2H to 1M solutions of alkanes in CCl_4 [a]

Alkane	Carbon atom 1	2	3	4	5	6
n-Hexane	0.23	0.04	0.10			
n-Heptane	0.17	0.07	0.08	0.06		
n-Octane	0.17	0.08	0	0.07		
n-Decane	0.15	0.06	0.05	0.05	0.03	
n-Dodecane	0.17	0.07	0.05	0.06	0.06	0.06
2,3-Dimethylbutane	0.16	0.05				
2,2,3,3-Tetramethylbutane	0.14	0.10			Me	
3-Methylpentane	0.18	0.08	0.02		0.19	
Methylcyclohexane	0.06	0.05	0.05	0.05	0.15	

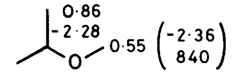
[a] Assignments according to D. M. Grant and E. G. Paul, *J. Am. Chem. Soc.*, 1964, **86**, 2984.

astereotopic C-5 atoms of 1,3-dimethylbutyl methyl ether (21a). In contrast, the shift displacements of the diastereotopic C-1 atoms of 1,1,2-trimethylbutyl methyl ether (19a) are almost identical. Significant differences can be a useful aid in distinguishing between stereoisomers.

γ-Substitution hardly affects the shift displacement of the methoxy-substituted carbon atom. Therefore, 1-ethylpropyl methyl ether can be regarded as a conformationally mobile analogue of cyclohexyl methyl ether. Accordingly, the shift displacement of its methoxy-substituted carbon atom almost equals the mean value of those of *cis*- and *trans*-4-t-butylcyclohexyl methyl ether (Tables 5 and 7). The shift displacement of the methoxy-substituted carbon atom of cyclohexyl methyl ether when compared with those of *cis*- and *trans*-4-t-butylcyclohexyl methyl ether indicates the presence of 17% of the *trans*-conformer. This does not agree well with a reported conformational energy of 2.51 kJ mol^{-1} under similar conditions.[10,11] Therefore, shift displacements of alkoxy-substituted carbon atoms do not seem applicable by assessing the distribution between rapidly interconverting conformers with different oriented alkoxy-groups.

K Values calculated from equation (1) by using observed shift displacements of the methoxy-substituted carbon atoms are presented in Table 5. No values are given for the compounds (17a), (18a) (*threo*-isomer), (22a), and (23a) since in these cases $\Delta\delta_F$ exceeds $\Delta\delta_E$. This may be due to general solvent effects. In contrast to the alcohol series[1] no simple correlation between *K* values and structural features of the ethers was found. However, it should be pointed out that large *K* values, obtained when the $\Delta\delta_E/\Delta\delta_F$ ratio is close to unity, and hence very sensitive to variations, require great accuracy in the measurements. Hydrogen-bonding ability may run parallel with proton-transfer basicity within closely related compounds having similar bonding sites.[12,13] If so, the *K* values are a measure of the relative basicity of ethers. On this basis, an equatorial methoxy-group is more basic than an axial one. The relative basicities arising from the *K* values do not agree with the decreasing basicity $Bu^tOMe > Pr^iOMe > Bu^nOMe > Pr^nOMe > EtOMe > Me_2O$ found in aqueous solution.[14,15] However, conflicting results have been reported and the order $Me_2O > EtOMe \sim Pr^iOMe$ has also been advocated.[7] Unfortunately, the *K* values cannot be checked

Table 5. ^{13}C N.m.r. shift displacements (p.p.m.) of a 1M solution of alkyl methyl ether and CF_3CO_2H in CCl_4,[a] extrapolated shift displacements of oxygen-substituted carbon atoms in a 1 : 1 ether–CF_3CO_2H adduct[b] (top position in parentheses), and *K* values[c] in l mol^{-1} (lower position in parentheses)



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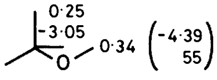

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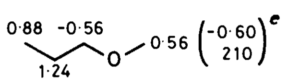

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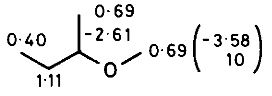

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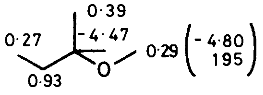

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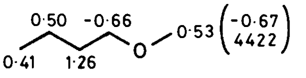

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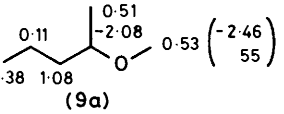

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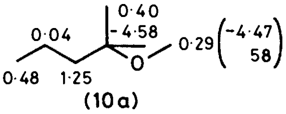

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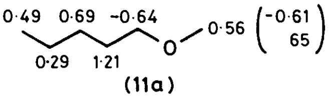

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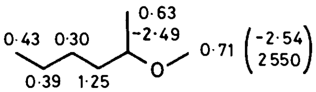

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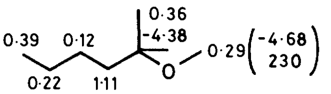

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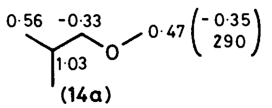

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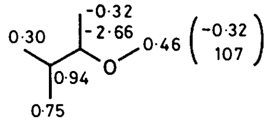

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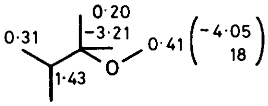

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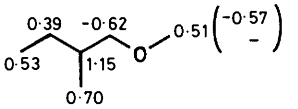

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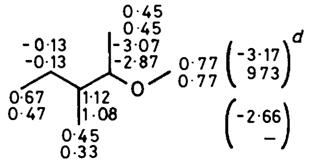

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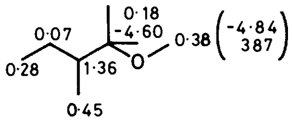

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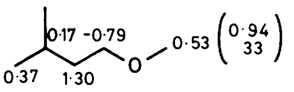

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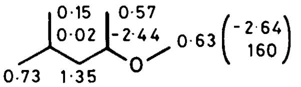

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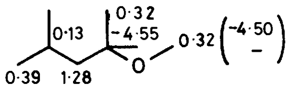

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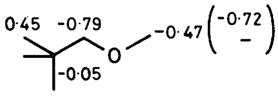

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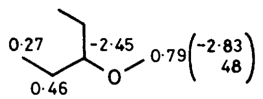

(26a)

[a] The ^{13}C n.m.r. spectra were assigned following D. E. Dorman, D. Bauer, and J. D. Roberts, *J. Org. Chem.*, 1975, **40**, 3729, ref. 3 [n-pentyl methyl ether and (11a)], and C. Delseth and J.-P. Kintzinger, *Helv. Chim. Acta*, 1978, **61**, 1327 [(14) and (20)] except (7a), (10a), (12a), (13a), (15a)—(19a), (21a), (22a), and (26a), all assigned as described in Experimental section. [b] Obtained from a least-squares calculation using shift displacements observed on stepwise addition of 0.05 mol equiv. of CF_3CO_2H to a 1M solution of ether in CCl_4. Accuracy better than ±0.02. [c] Calculated as described in the text. [d] The *erythro-* (upper figures and parentheses) and the *threo-* isomers were investigated in *ca.* 1 : 1 mixture. This may give rise to slightly erratic shift displacements. [e] The solvent was $CDCl_3$.

against reported gas-phase data since these are limited to a few low-molecular weight species, for which the basicity decreased in the order $Pr^i_2O > Pr^iOEt > Et_2O > EtOMe > Me_2O$.[16,17]

Previous results indicate that dimethyl and diethyl ether are stronger bases than the corresponding alcohols in the gas phase[16] while the opposite obtains for aqueous solutions.[6,18] The present *K* values of methyl ethers are larger than those of the corresponding alcohols.* Exceptions are n-pentyl and 1-methylpropyl methyl ether. It should be noted that whereas

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* The figures stated as *K* values in Table 3, ref. 1 are in fact the $\Delta\delta_E/\Delta\delta_F$ ratios. From these the *K* values can be calculated using equation (1) in the present paper.

Table 6. The effect of branching on trifluoroacetic acid-induced alkyl methyl ether carbon shift displacements. Mean values in p.p.m. extracted from Table 5. If values are scattered more than 0.3 p.p.m. the interval is given

Alkyl methyl ether	Position of branch	Carbon atom C-OMe	C-α	C-β	C-γ	α-CH_3
Primary	C-OMe	−2.45 to −1.4	−0.1	−0.5 to 0.2	0.05	
	C-α	−0.2	−0.15	−0.1	0.1	
	C-β					
Secondary	C-OMe	−2.5 to −0.6	−0.6 to 0.5	−0.2 to 0.2	−0.4 to 0.15	−0.3 to 0.5
	C-α	−1.0 to −0.05	−0.05	−0.15	0.2	−1.0
	C-β	−0.35	0.25	−0.1	−0.25 to 0.35	0.05
Tertiary	C-α	0 to 1.25	0.1 to 0.5	0	−0.2	−0.2
	C-β	0.05	0.05	0.05	−0.15	0

Table 7. ^{13}C N.m.r. shift displacements (p.p.m.) of a 1 M solution of cyclic ether and CF_3CO_2H in CCl_4, extrapolated shift displacements of a 1 : 1 ether–CF_3CO_2H adduct [a] (in parentheses), conformer distribution, and *K* values [b]

Ether	Carbon atom 1	2	3	4	5	6
Bornyl methyl ether [c]		−2.52 (−2.98)	0.23	0.48	0.16	0.29
Isobornyl methyl ether [c]		−1.67 (−1.55)	0.50	0.25	0.39	−0.16
Cyclohexyl methyl ether [d]	−2.56 (−2.86)	0.70	−0.23	0.51		
cis-4-t-Butylcyclohexyl methyl ether [e]	−2.70 (−2.56)	0.84	0.36	0.50	0.18	0.41
trans-4-t-Butylcyclohexyl methyl ether [e]	−1.87 (−2.03)	0.78	0.23	0.47	0.00	0.24

Ether	Carbon atom 7	8	9	10	OMe	*K*/l mol^{-1}	Percentage of conformer with axial hydroxy-group (previous determinations in parentheses)
Bornyl methyl ether [c]					−0.15	29.4	
Isobornyl methyl ether [c]	0.08	0.40	0.23	0.13	0.10		
Cyclohexyl methyl ether [d]					0.49	81.3	17 (47) [f]
cis-4-t-Butylcyclohexyl methyl ether [e]					0.57		
trans-4-t-Butylcyclohexyl methyl ether [e]					0.44	148	

[a] Footnote *b*, Table 5. [b] Calculated as described in the text. [c] ^{13}C N.m.r. signals assigned as described in Experimental section. [d] T. Pehk and E. Lippmaa, *Org. Magn. Reson.*, 1971, **3**, 679. [e] H. J. Schneider and V. Hoppen, *J. Org. Chem.*, 1978, **43**, 3866. [f] Ref. 10.

the C–O shift displacements of ethers and alcohols are linearly related the *K* values are not.

Conclusions.—The magnitude of the trifluoroacetic acid-induced ^{13}C n.m.r. shift displacements of ether carbon atoms makes it possible to distinguish between primary, secondary, and tertiary ethers and to obtain some information on the structure using increments characteristic of the position of branching. The shift displacements are stereoselective and permit distinction between *endo* and *exo* or between axial and equatorial alkoxy-groups but not estimation of the composition of rapidly interconverting mixtures of conformers. The C–O shift displacements of alcohols and their methyl ethers are linearly related. The ratio between shift displacements of other alcohol and ether carbon atoms depends on their position and is different in primary, secondary, or tertiary species. Association constants calculated on the basis of the shift displacements of ethers are a sensitive measure of structural and steric influence upon their relative hydrogen-bonding acceptance, and hence, conceivably, of their relative basicity. The methyl ethers, with few exceptions, display larger association constants than the corresponding alcohols in tetrachloromethane solution.

Esters.—Addition of trifluoroacetic acid to a solution of butyl acetate in tetrachloromethane effects low-field shift displacements of C-1 and C=O and high-field displacements of the C-2—C-4 signals (Figure 3). The acetyl methyl carbon atom is only slightly influenced. The displacement of C-1 is *ca.* 40% larger than that of butan-1-ol.[1] C-3, C-4, and particularly C-2 are displaced less than the same carbon atoms of butan-1-ol. The shift displacements depend linearly on the acid : ester ratio at low ratios. The lines are deflected progressively at higher ratios. The shift displacements can be corrected by subtraction of the shift displacements of the corresponding carbon atoms of n-octane. This yields converging curves and displacements which decrease from C-1 to C-4. These are the features expected if the displacements reflect progressive hydrogen bonding between ester and acid.[19] True protonation seems insignificant since the extrapolated displacements of the oxygen-substituted and the carbonyl carbon atoms (Table 11) for a 1 : 1 acid–ester adduct are con-

Table 8. CF_3CO_2H- and H_2SO_4-induced ^{13}C n.m.r. shift displacements (p.p.m.) of 1M solutions of n-butyl acetate (relative to a 1M solution of the ester in CCl_4)

			Carbon atom					
Solvent	Acid	Concentration	1	2	3	4	C=O	OMe
CCl_4	CF_3CO_2H	1M	−1.95	0.47	0.24	0.31	−5.17	0.05
No	CF_3CO_2H	100%	−2.61	1.63	1.49	2.52	−7.94	1.97
No	H_2SO_4	98%	−8.03	0.53	0.37	−1.11		−1.88

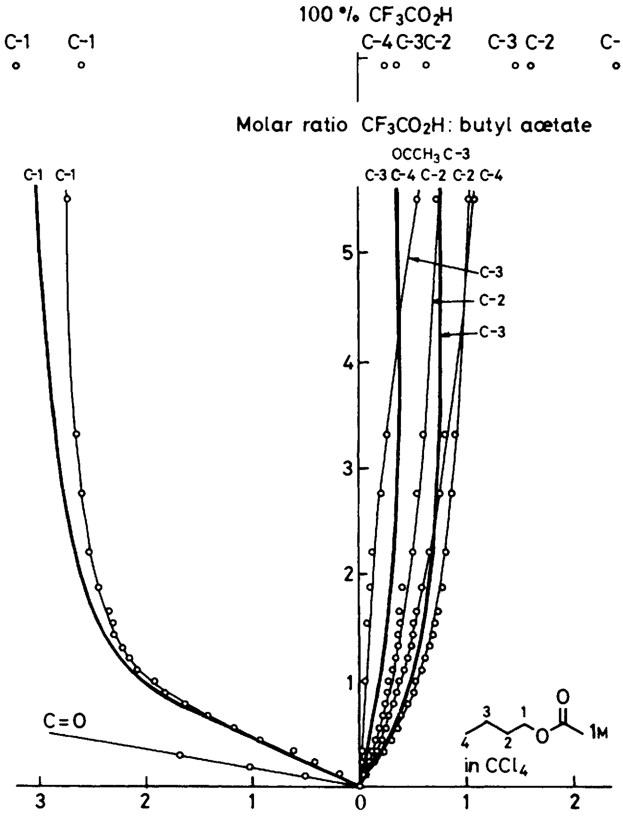
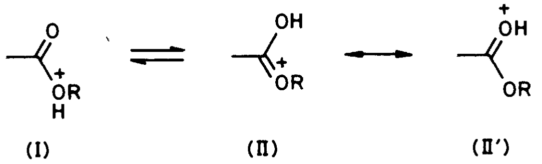


Figure 3. ^{13}C N.m.r. shift displacements of a 1M solution of n-butyl acetate in CCl_4 containing CF_3CO_2H, as a function of the molar ratio acid : ester. Thin curves represent measured shift displacements. Bold curves indicate shift displacements after subtraction of those of n-octane



Scheme.

siderably smaller than those expected from protonation [20] and those observed in concentrated sulphuric acid (Table 8) where extensive protonation occurs.[15]

Even if using shift displacements corrected with n-octane shift displacements the extrapolated value for a 1 : 1 acid–ester adduct is exceeded by the asymptotic limit values (Figure 3). This may be due to concentration effects, to protonation, to formation of *n* : 1 acid–ester adduct(s), or to the presence of two basic sites. The displacements calculated on the basis of observed and corrected C-1 shift displacements are similar (1.03 and 1.02, respectively). Therefore, it seems acceptable to use uncorrected shift displacement values for the calculation of *K* values.

Tables 9—11 and 13 present the effect of structural and stereochemical factors on the magnitude of trifluoroacetic acid-induced carbon shift displacements of esters. The nature of the acyl group does not influence the shift displacement of C-1—C-4 in n-butyl esters (Table 9). However, the shift displacement of the carbonyl carbon atom is smaller in the formate and slightly larger in the acetate than in the higher butyl esters. In linear acetates the displacements of the oxygen-substituted and the carbonyl carbon atom are almost invariant. Only the displacements of C-1 of methyl acetate and C=O of ethyl acetate are slightly decreased. The magnitude of the shift displacements decreases regularly from C-2 to the terminal carbon atom, the latter exhibiting a larger displacement. This may be due to contributions from the specific influence of trifluoroacetic acid on the shift of the methyl carbon atoms in the alkyl moieties.

Branched-alkyl acetates also exhibit nicely consistent carbon shift displacements (Table 11). Those of the carbonyl carbon atoms generally increase slightly in the primary, secondary, and tertiary series, as do the displacements of the oxygen-substituted carbon atoms. Here the average increase from primary to secondary acetates amounts to 0.93 p.p.m., that from secondary to tertiary acetates to 0.82 p.p.m. (the corresponding values for alcohols are 1.49 and 1.54 p.p.m.[1]). The displacements of C=O and C-1 exhibit only minor variations in primary acetates. This indicates that the displacement of these carbon signals is little affected by branching at C-α or more remote carbon atoms. The same obtains for C=O and C-2 of secondary and tertiary acetates. The ratio between the shift displacement of the carbonyl and the oxygen-bonded carbon atom is almost invariant (2.75) in primary esters. So it is in secondary and tertiary esters, yet with smaller ratios (1.85 and 1.55, respectively). Protonation of esters preferentially takes place at the carbonyl oxygen atom both in the gas phase [16,17] and in anhydrous acids.[21,22] The decreasing C=O : C–O shift displacement ratio in the primary, secondary, and tertiary acetates suggest that hydrogen-bonding to the single-bonded oxygen atom becomes of increasing importance with respect to bonding to the carbonyl oxygen atom in the order primary, secondary, and tertiary esters. However, the decreasing C=O : C–O shift displacement ratio may also be due to increasing delocalization of positive charge to the alkoxy-carbon atom in a carbonyl-oxygen-protonated species by way of the resonance structure (II) (Scheme). Increasing delocalization, in its turn, can be explained by the increasing electron-releasing effect in primary, secondary, and tertiary alkyl groups. There is a linear correlation between the shift displacement of the oxygen-substituted carbon atoms in corresponding ester and alcohol alkyl groups (21 points, slope 0.56, intercept 1.39, regression constant 0.975). Again, this

Table 9. ^{13}C N.m.r. shift displacements (p.p.m.) observed on addition of 1 mol equiv. of CF_3CO_2H to a 1M solution of a n-butyl ester in CCl_4

	Carbon atom								
n-Butyl ester	1	2	3	4	C=O	1′	2′	3′	4′
n-Butyl formate [a]	−1.86	0.37	0.22	0.28	−3.83				
n-Butyl acetate [a]	−1.95	0.47	0.24	0.31	−5.17	0.05			
n-Butyl propionate [b]	−1.94	0.50	0.25	0.33	−4.81	−0.48	0.30		
n-Butyl butyrate [c]	−1.95	0.49	0.23	0.31	−4.84	−0.38	−0.03	0.39	
n-Butyl valerate [d]	−1.98	0.48	0.23	0.34	−4.86	−0.45	0.06	0.18	0.34

[a] Assignments according to D. E. Dorman, D. Bauer, and J. D. Roberts, *J. Org. Chem.*, 1975, **40**, 3729. [b] Assignments according to A. B. Terentov and V. I. Dostalova, *Org. Magn. Reson.*, 1977, **9**, 301, with interchange of the C-1′ and C-2 signals. [c] Assignments according to Sadtler Standard Carbon-13 N.M.R. Spectra. [d] Assignments described in Experimental section.

Table 10. ^{13}C N.m.r. shift displacements (p.p.m.) observed on addition of 1 mol equiv. of CF_3CO_2H to a 1M solution of an unbranched acetate in CCl_4

	Carbon atom											
Acetate	1	2	3	4	5	6	7	8	9	10	C=O	Me
Methyl acetate [a]	−1.43										−5.40	−0.02
Ethyl acetate [a]	−1.91	0.55									−4.92	−0.02
n-Propyl acetate [b]	−1.90	0.39	0.39								−5.21	−0.03
n-Butyl acetate [b]	−1.95	0.47	0.24	0.31							−5.17	0.05
n-Pentyl acetate [c]	−1.91	0.49	0.32	0.24	0.33						−5.28	0.01
n-Hexyl acetate [d]	−2.00	0.45	0.26	0.21	0.16	0.25					−5.34	−0.05
n-Heptyl acetate [e]	−2.02	0.46	0.26	0.19	0.16	0.14	0.23				−5.30	−0.06
n-Octyl acetate [c]	−1.96	0.45	0.27	0.19	0.19	0.15	0.13	0.21			−5.28	−0.03
n-Nonyl acetate [c]	−2.15	0.48	0.28	0.19	0.16	0.10	0.09	0.08	0.20		−5.67	−0.06
n-Decyl acetate [c]	−1.97	0.45	0.26	0.11	0.14	0.14	0.11	0.08	0.09	0.19	−5.26	−0.03

[a] Assignments according to ref. 20. [b] Assignments according to D. E. Dorman, D. Bauer, and J. D. Roberts, *J. Org. Chem.*, 1975, **40**, 3729. [c] Assignments described in Experimental section. [d] Assignments according to Sadtler Standard Carbon-13 N.M.R. Spectra. [e] As *d* but assignment of C-2 and -3 has been interchanged.

may be explained either by partial protonation at the singly bonded ester oxygen atom, proportional to that of the alcohols, or by stabilization of (II) to an extent governed by the inductive effect of the alkyl group.

The effect of branching on the shift displacement of individual carbon atoms is summarized in Table 12. The increments are small and rather constant. Therefore, prediction of the trifluoroacetic acid-induced shift displacements of the individual carbon atoms of the alkyl part of any ester, not excessive crowded, is possible along the lines described in ref. 1.

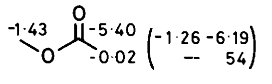
The steric orientation of the acyloxy-group influences the shift displacement of the oxygen-substituted carbon atom much more than structural changes, as appears from a comparison between *cis*- and *trans*-4-t-butylcyclohexyl acetate (Table 13). This difference can be a valuable aid in distinguishing between axial and equatorial acyloxy-groups in cyclohexanes. In contrast, bornyl and isobornyl acetate exhibit similar shift displacements of their oxygen-substituted carbon atoms. This also holds for *erythro*- and *threo*-1,2-dimethylbutyl acetate (18b) (Table 11). However, in the latter cases it is possible to distinguish between the isomers on the basis of the carbonyl carbon shift displacements. The diastereotopic C-5 atoms of 1,3-dimethylbutyl acetate (21b) exhibit significantly different shift displacements, but not so for the diastereotopic C-4 atoms of 1,2-dimethylpropyl acetate (15b).

γ-Substitution of alkyl acetates affects the shift displacement of the oxygen-substituted carbon atoms so little that 1-ethylpropyl acetate can be regarded as a conformationally mobile analogue of cyclohexyl acetate. Accordingly, the shift displacements of C-3 and C=O of 1-ethylpropyl acetate almost equal the mean values of those of *cis*- and *trans*-4-t-butylcyclohexyl acetate. Comparison of the shift displacement of the oxygen-substituted carbon atom of cyclohexyl acetate with those of *cis*- and *trans*-4-t-butylcyclohexyl acetate, representing the individual conformers of cyclohexyl acetate, suggests the presence of 73% of the equatorial conformer (Table 13). This agrees nicely with reported conformational energies of 2.5—3.0 kJ mol^{-1} [10,11,23] under similar conditions. A similar analysis based on C=O shift displacements breaks down since the C=O displacement of cyclohexyl acetate (beyond *trans*) exceeds those of *cis*- and *trans*-4-t-butylcyclohexyl acetate. This demonstrates that the shift displacements of the oxygen-substituted atoms can be useful when assessing the distribution between rapidly interconverting conformers with differently oriented acyloxy-groups.

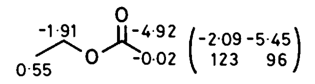
The influence of structural factors on the *K* values of esters calculated from equation (1) using observed shift displacements of the oxygen-substituted carbon atom is not as clear-cut as in the alcohol series [1] (Table 11). A tendency exists that secondary esters exhibit lower *K* values than their primary and tertiary analogues. In the primary esters α- or β-branching normally gives rise to a decrease of the *K* value, yet with (14b) as an exception. No other generalizations seem justifiable. No correlation between *K* values and the magnitude of shift displacements has been found.

K Values calculated using shift displacements of the carbonyl carbon atoms show no clear-cut trends in the series primary, secondary, and tertiary esters. In all types, α- or β-branching leads to a decrease in the *K* value, again with (14b) as an exception. In some compounds the *K* values calculated from C–O and C=O shift displacements are similar. This suggests that only one of the ester oxygen atoms is involved in hydrogen-bond formation or that both oxygen atoms are in-

Table 11. ^{13}C N.m.r. shift displacements (p.p.m.) of a 1M solution of alkyl acetate and CF_3CO_2H in CCl_4,[a] extrapolated displacements of oxygen-substituted and carbonyl carbon shift displacements in a 1 : 1 ester–CF_3CO_2H adduct[b] (in parentheses above left and right), and *K* values[c] in l mol^{-1} (in parentheses below[d])



(1b)



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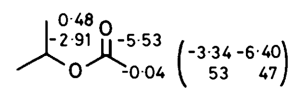

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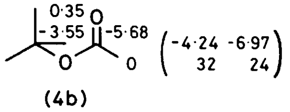

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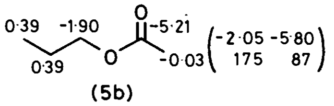

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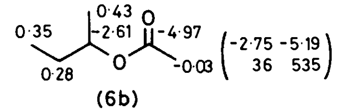
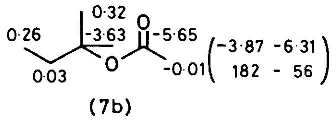
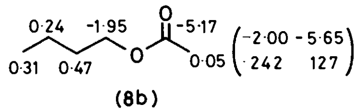


(6b)



(7b)



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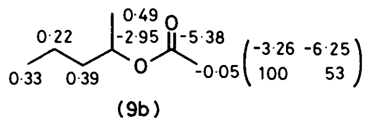
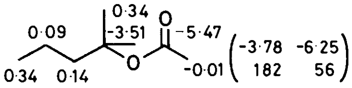
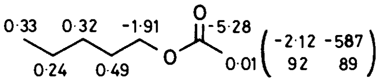


(9b)



(10b)



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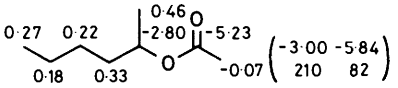

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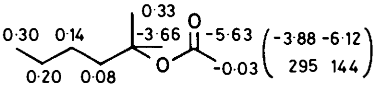

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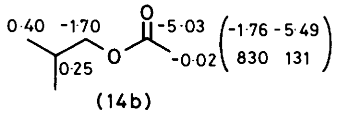

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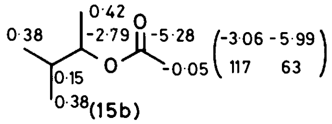

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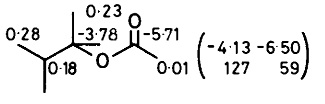

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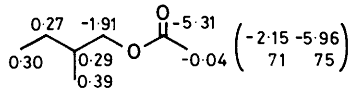

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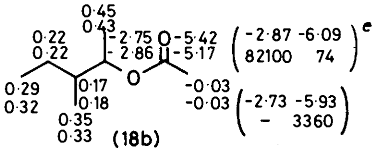

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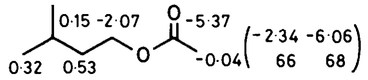
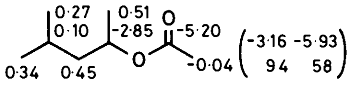
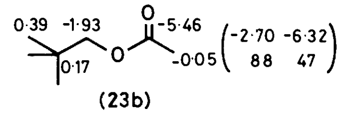


(20b)



(21b)



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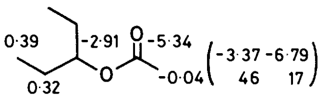

(26b)

[a] The ^{13}C n.m.r. spectra were assigned following ref. 20, Sadtler Standard Carbon-13 Spectra (14b), and D. E. Dorman, D. Bauer, and J. D. Roberts, *J. Org. Chem.*, 1975, **40**, 3729 (n-butyl acetate), except (7b), (9b), (10b)—(13b), (15b)—(18b), (20b), (21b), (23b), and (26b), which were assigned as described in the Experimental section. [b] Obtained as described in Table 5, footnote *b*. [c] Calculated as described in the text. [d] Values based on oxygen-substituted carbon shift displacements at left. Values based on carbonyl carbon shift displacements at right. [e] As Table 5, footnote *d*.

volved to the same extent. The two *K* values are significantly different in compounds (6a), (14a), (18a) (*erythro*-isomer), and (23a). This may be caused by hydrogen-bond participation of the ester oxygen atoms to different extents, but may also be attributable to general solvent effects. Despite the fact that no convincing correlation between structure and *K* values has been found the latter may well be a sensitive measure for the extent of association. This is demonstrated by the fact that the *K* value based on C–O shift displacements of 1-ethylpropyl acetate, a model of conformationally mobile cyclohexyl acetate, falls between those of the rigid *cis*- and *trans*-4-t-butylcyclohexyl acetates (Tables 11 and 13). So does the *K* value of cyclohexyl acetate, being close to that of *trans*-4-t-butylcyclohexyl acetate in accord with the known distribution of conformers in cyclohexyl acetate.[10,11,23]

With respect to *K* values based on C=O shift displacements that of cyclohexyl acetate exceeds those of *cis*- and *trans*-4-t-butylcyclohexyl acetate (beyond that of *trans*). Thus, C=O shift displacements again do not form a basis for assessment of the distribution of rapidly interconverting conformers.

The *K* values reflecting hydrogen-bond acceptance may also reflect relative basicities of those acetates where the two hydro-

Table 12. The effect of branching on trifluoroacetic acid-induced alkyl acetate carbon shift displacements. Mean values in p.p.m. extracted from Table 11. If values are scattered by more than 0.3 p.p.m. the interval is given

Alkyl acetate	Position of branch	Carbon atom					
		C-OAc	C-α	C-β	C-γ	C=O	α-CH_3
Primary	C-OAc	−1.1 to −0.7	−0.1	0	0	−0.6 to 0.25	
	C-α	−0.25 to 0.2	−0.15	0	0.1	−0.2 to 0.45	
	C-β	−0.1	0.05	−0.1	0	0.2	
Secondary	C-OAc	−1.0 to −0.55	−0.15	−0.1	0	0.1 to −0.7	−0.15
	C-α	−0.2 to 0.2	−0.2	0.15	0	−0.2 to 0.2	−0.05
	C-β	0.1	0.05	−0.1	0	0.2	0
Tertiary	C-α	−0.15	0.15	0		−0.05	−0.1

Table 13. ^{13}C N.m.r. shift displacements (p.p.m.) of 1M solutions of cyclic alkyl acetates and CF_3CO_2H in CCl_4, extrapolated shift displacements of 1 : 1 ester–CF_3CO_2H adducts[a] (in parentheses), conformer distribution, and K values[b]

Ester	Carbon atom						
	1	2	3	4	5	6	7
Bornyl acetate[c]	−0.06	−2.70 (−3.02)	0.34	0.15	0.25	0.21	0.02
Isobornyl acetate[c]	−0.09	−2.62 (−3.03)	0.25	0.08	0.25	0.23	−0.01
Cyclohexyl acetate[d]	−2.60 (−2.99)	0.38	0.31	0.36			
cis-4-t-Butylcyclohexyl acetate[e]	−3.12 (−4.34)	0.31	0.21	0.26	0.15	0.25	
trans-4-t-Butylcyclohexyl acetate[e]	−2.41 (−2.77)	0.37	0.26	0.24	0.16	0.25	

Ester	Carbon atom						Percentage of conformer with axial methoxy-carbonyl group[f] (previous determinations[g] in parentheses)
	8	9	10	C=O	OMe	K^f/l mol^{-1}	
Bornyl acetate[c]	0.31	0.27	0.28	−5.29 (−6.06)	−0.02	79.6 54.1	
Isobornyl acetate[c]	0.25	0.23	0.22	−5.11 (−6.04)	−0.06	47.2 35.7	
Cyclohexyl acetate[d]				−5.98 (−6.40)	−0.04	51.1 217	73 (73)
cis-4-t-Butylcyclohexyl acetate[e]				−5.41 (−6.20)	−0.04	9.1 53.7	
trans-4-t-Butylcyclohexyl acetate[e]				−5.59 (−6.05)	0.00	51.5 160	

[a] Footnote *b*, Table 5. [b] Calculated as described in the text. [c] F. Bohlmann, R. Zeisberg, and E. Klein, *Org. Magn. Reson.*, 1975, **7**, 426. [d] T. Pehk and E. Lippmaa, *Org. Magn. Reson.*, 1971, **3**, 679. [e] H. J. Reich, M. Jautelat, M. T. Messe, F. J. Weigert, and J. D. Roberts, *J. Am. Chem. Soc.*, 1969, **91**, 7445. [f] Calculated on basis of C–O shift displacements (upper figures) and C=O shift displacements (lower figures). [g] Ref. 10.

gen-bond acceptor sites are involved in association to the same extent. As discussed above, this holds for acetates where K values based on C=O and C–O shift displacements are similar. When significantly dissimilar, a change in the proportion of the association of the two oxygen atoms may be suspected (see above). In thise case estimation of basicity may be more uncertain. In such cases, assuming predominant carbonyl oxygen protonation, their relative basicities are best estimated by comparison of K values calculated on the basis of C=O shift displacements. Provided that the K values reflect basicity it can be seen from the K values of *cis*- and *trans*-4-t-butylcyclohexyl acetate that an equatorial acetoxy-group is more basic than an axial. The K values also reveal that the acetoxy-group of bornyl acetate is more basic than that of isobornyl acetate. No correlation between the K values of acetates and the corresponding alcohols or methyl ethers has been found.

Conclusions.—A linear correlation exists between the trifluoroacetic acid-induced ^{13}C n.m.r. shift displacements of the alkoxy-carbon atoms of acetates and the corresponding alcohols. For the remaining carbon atoms the ratio between shift displacements of alcohols and their acetates depends on the position of the carbon atom and exhibits minor variations in primary, secondary, or tertiary compounds. The magnitude of the trifluoroacetic acid-induced shift displacements of ester carbon atoms makes it possible to distinguish between primary, secondary, and tertiary esters. Further structural information is obtainable on this basis but the increments characteristic of the position of additional branching of the alkoxy-group are small. The shift displacements are stereoselective and permit distinction between axial and equatorial acyloxy-groups as well as estimation of the composition of rapidly interconverting mixtures of conformers. For esters in which association constants, calculated on the basis of C=O and C–O shift displacements, are similar the *K* values seem to provide information about the relative basicity and its dependence of structural and steric factors. Estimation of the relative basicity of esters which possess two significantly different *K* values is more uncertain.

Experimental

n-Butyl and t-butyl methyl ether are commercially available (Fluka). The remaining methyl ethers, except the higher straight-chain ones (see below), were all prepared in good yield by treatment of alcoholates (sodium salts of primary and secondary, potassium salts of tertiary alcohols) with methyl iodide (0.5 h at 20 °C, then 1 h reflux) followed by distillation and redistillation from sodium. In all cases but n-butyl, n-pentyl, n-hexyl, n-propyl, and isopropyl alcohol, sodium alcoholates were obtained by reflux (2 h) of the alcohols with sodium hydride (1.2 equiv., freed from mineral oil and dried) in dry ether (low-boiling products) or tetrahydrofuran (four volumes). Potassium alcoholates were prepared similarly using potassium hydride and tetrahydrofuran.[24] In the case of n-butyl, n-pentyl, n-hexyl, n-propyl, and isopropyl alcohol only 0.5 equiv. sodium hydride was used. No solvent was used for the propanols. Ether was used in all other cases. The reflux time was 4 h. Ethyl and n-propyl n-butyl ether were prepared similarly. In the latter case unchanged alcohol in the crude product was benzoylated (PhCOCl, Et_3N, aqueous work-up, extraction with hexane) whereupon the pure ether was isolated by distillation. n-Heptyl, n-octyl, and n-nonyl methyl ether were prepared by alkylation of chloromethyl methyl ether with alkylmagnesium bromide.[25] All reactions were run under nitrogen and all alcohols were distilled from barium oxide prior to use. The procedures described above were found the best among several investigated.[26–31] 2,2,3,3-Tetramethylbutane was prepared as described in ref. 32. Other alkanes were commercially available.

The non-commercially available esters [(6b), (7b), (9b), (10b), (12b), (13b), (15b)—(18b), (20b), (21b), (23b), (26b), heptyl to decyl acetate, n-butyl propionate, butyrate, and valerate] were obtained analogously to the ethers by reflux (1 h) of the alcoholates with acyl chloride. The procedure gave unsatisfactorily low yields of (19b) and (22b). The esters were purified by repeated distillation. n-Butyl formate was prepared as described previously.[33] Bornyl acetate and *cis*- and *trans*-4-t-butylcyclohexyl acetate were obtained by heating (145 °C, 2 h) the alcohol with acetic anhydride (1.2 equiv.) followed by distillation. Isobornyl acetate was prepared from camphene.[34]

^{13}C N.m.r. spectra were obtained as described in ref. 1 with 10 s repetition time. The accuracy in concentration of substrates and acid was better than 2%. The spectra of n-hexyl to n-nonyl methyl ether, of (7a), (10a), (12a), (13a), (15a)—(19a), (21a), (22a), (26a), of bornyl and isobornyl methyl ether, n-butyl valerate, n-pentyl, n-octyl, n-nonyl, and n-decyl acetate, of (7b), (9b)—(13b), (15b)—(18b), (20b), (21b), (23b), and (26b), seem not to have been reported previously. The spectra of these compounds were assigned from coupled spectra through the multiplicity of the one-bond coupling constants. When informative, two-bond coupling constants were also employed. The signals of the higher homologues were assigned by comparison with lower analogues and with the corresponding alcohols. In the case of (6a) and n-butyl propionate previous assignments were found to be in error. ^{13}C N.m.r. chemical shifts of the methyl ethers and the alkyl acetates are given in Supplementary Publication No. SUP 23697 (5 pp.).*

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