Communications

Oxygen-17 Nuclear Magnetic Resonance. 1. Alcohols

Summary: The ^{17}O chemical shifts of more than 30 simple alcohols have been measured and it is determined that a linear correlation exists between the ^{17}O chemical shifts of alcohols (ROH) and the ^{13}C chemical shifts for the methyl groups of the analogous hydrocarbons (RCH_3).

Sir: Although a survey of the ^{17}O NMR characteristics of oxygen functional groups has been available for some time,[1] relatively little work has been devoted to the influence of subtle changes in molecular structure on the ^{17}O chemical shifts of given functional units.[2] This is mainly a consequence of the experimental difficulties associated with accurate measurements of resonance signals for the ^{17}O nucleus owing to its low natural abundance (0.037%) and quadrupolar nature ($I = 5/2$). In this report we disclose our results concerning structural effects on the hydroxy group in small organic molecules.[3]

The ^{17}O chemical shift data for a number of diverse alcohols at 13.56 MHz are summarized in Table I.[4] The chemical shift values fall in the range of −40 to +70 ppm relative to external H_2O. (Positive values are deshielded relative to the reference; negative ones are shielded.) It is instructive to compare the influence of different substituents on the ^{17}O chemical shift of an OH group with their effect on the ^{13}C chemical shift of an appended CH_3 group, since there is a substantial body of empirical knowledge concerning the features which determine ^{13}C chemical shifts.[5] Strikingly, a good linear correlation exists between the ^{17}O shifts for ROH and the ^{13}C values for RCH_3[6] for a diverse set of R groups as shown in Figure 1. An equation of the form $\delta(^{17}OH) = 3.83\,[\delta(^{13}CH_3)] - 49.3$ fits the data with a standard deviation of ±2.6 ppm. This relationship may prove useful for the estimation of ^{17}O chemical shifts of alcohols from more readily available ^{13}C data.[7,8] We conclude that structural aspects important in determining the ^{13}C chemical shifts of RCH_3 are also critical for the ^{17}O chemical shifts of ROH. The OH group is, however, almost four times more sensitive to these effects.

Table I. ^{17}O Chemical Shifts for Alcohols (ROH)

R	compd	$\delta(R^{17}OH)^a$	$\delta(R^{13}CH_3)^b$
CH_3	1	−37.0	5.7
CH_3CH_2	2	5.9	15.4
$(CH_3)_2CH$	3	39.8	24.3
$(CH_3)_3C$	4	62.3	31.5
$CH_3CH_2CH_2$	5	−0.5	13.1
$(CH_3)_2CHCH_2$	6	−2.0	11.4
$(CH_3)_3CCH_2$	7	−6.8	8.5
$CH_3CH_2CH_2CH_2$	8	0.0	13.6
$(CH_3)_2CHCH_2CH_2$	9	−0.6	14.0
$(CH_3)_3CCH_2CH_2$	10	1.9	
$CH_3CH_2CH_2CH_2CH_2$	11	−0.8	13.7
$CH_3CH_2(CH_3)CH$	12	34.0	21.9
$CH_3CH_2CH_2(CH_3)CH$	13	35.3	22.4
$CH_3CH_2(CH_3)CHCH_2$	14	−7.3	11.1
$(CH_3CH_2)_2CH$	15	22.8	18.4
c-C_5H_9	16	31.1	20.2
c-C_6H_{11}	17	39.9	22.8
$CH_3CH_2(CH_3)_2C$	18	56.5	28.7
$(CH_3CH_2)_2(CH_3)C$	19	54.1	
$(CH_3CH_2)_3C$	20	43.5	
$CH_2{=}CHCH_2$	21	−1.6	12.8
$HC{\equiv}CCH_2$	22	−1.9	12.8
$HC{\equiv}C(CH_3)CH$	23	43.2	
c-$C_3H_5CH_2$	24	4.7	12.3
$CH_2{=}CHCH_2CH_2$	25	−0.8	13.8
$HC{\equiv}CCH_2CH_2$	26	3.6	12.2
$C_6H_5CH_2$	27	7.9	15.8
$HOCH_2CH_2$	28	−5.3	13.6
$(CH_3)_2NCH_2CH_2$	29	−5.6	
$ClCH_2CH_2$	30	−1.8	11.5
$CH_3SCH_2CH_2$	31	4.1	
CF_3CH_2	32	−23.6	
C_6H_5	33	69.3	
o-$CH_3C_6H_4$	34	71.3	

[a] In ppm relative to external H_2O. [b] Reference 6.

Scheme I. SCS Values for β-Methyl Substitution

	$CH_3X \rightarrow CH_3CH_2X$	$\rightarrow (CH_3)_2CHX$	$\rightarrow (CH_3)_3CX$
X = OH	43	34	22
X = CH_3	9.7	8.9	3.1

The substituent chemical shift (SCS) concept[9] is widely used in ^{13}C NMR to relate chemical shift perturbations with structural changes at various positions in a molecule. A similar treatment of ^{17}O data is also informative. In the series illustrated in Scheme I the X group experiences an increasing number of 1,3 heavy-atom interactions. For the series of substituted methanols (X = OH), these β effects (chemical shift increments per added methyl substituent) are large and deshielding, showing an attenuation in magnitude with each successive methyl substituent. This "saturation" effect is typical for β substitution in ^{13}C NMR as shown in Scheme I for the analogous series with X = CH_3. The general trends in the two series are similar, although the magnitudes of the β effects are substantially larger at an oxygen nucleus.

Substituent shifts for the introduction of γ-methyls are shown in Scheme II. In the first series successive methyl in-

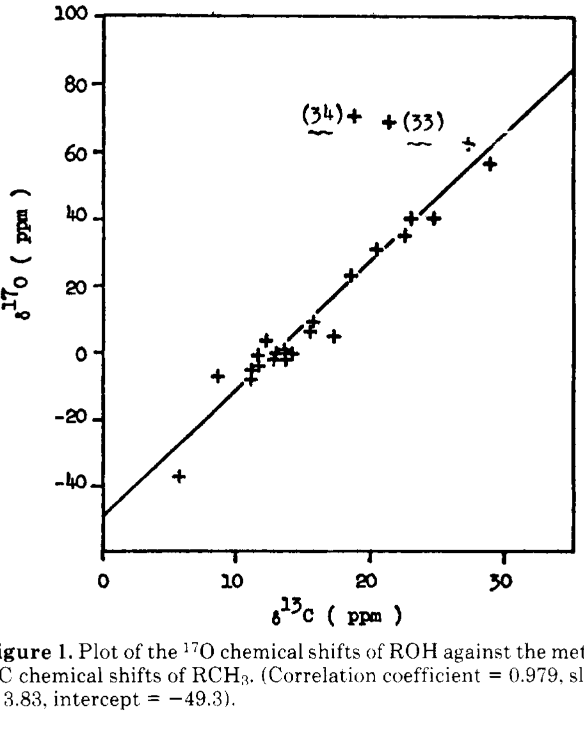

Figure 1. Plot of the ^{17}O chemical shifts of ROH against the methyl ^{13}C chemical shifts of RCH_3. (Correlation coefficient = 0.979, slope = 3.83, intercept = −49.3).

Scheme II. SCS Values for γ-Methyl Substitution

$$\begin{array}{lllll}
\multicolumn{5}{l}{CH_3CH_2X \rightarrow CH_3CH_2CH_2X \rightarrow (CH_3)_2CHCH_2X \rightarrow (CH_3)_3CCH_2X} \\
X = OH & -6 & -2 & -5 & \\
X = CH_3 & -2.3 & -1.7 & -2.8 & \\
\multicolumn{5}{l}{(CH_3)_3CX \rightarrow CH_3CH_2(CH_3)_2CX \rightarrow (CH_3CH_2)_2CH_3CX \rightarrow (CH_3CH_2)_3CX} \\
X = OH & -6 & -2 & -11 &
\end{array}$$

troduction at C_2 of ethanol causes shielding, with the first and third methyl prompting larger changes than the second methyl. This same sort of behavior is observed for the ^{13}C shifts of the terminal CH_3 in the X = CH_3 series. This is, of course, the well-known γ effect[9] in ^{13}C NMR which is traditionally rationalized in terms of 1,4-gauche interactions. The relative magnitudes of the γ steric shifts in the two series correlate qualitatively with the increase in gauche relationships of the nucleus under observation.

A second series illustrating the effect of an increasing number of γ-methyls consists of the tertiary alcohols also shown in Scheme II. The γ shifts are similar to those of the first series with the exception of an especially large SCS for the third substitution. Models suggest that interactions among the ethyl groups of triethylcarbinol should promote the population of conformers in which the OH group is subjected to gauche interactions.

An argument based on γ interactions also rationalizes the chemical shifts of cyclopentanol and cyclohexanol, which are significantly deshielded relative to an acyclic analogue such as 3-pentanol. Incorporation of the γ carbons into a five- or six-membered ring reduces gauche interactions with the OH group. Thus, cyclohexanol, which in its equatorial form is devoid of such interactions, has a similar chemical shift to isopropyl alcohol, a model without γ substituents. Some gauche interaction is present for the conformationally more flexible cyclopentanol and its chemical shift is intermediate to those of cyclohexanol and 3-pentanol.

The introduction of δ-alkyl groups does not generally appear to cause important changes in the ^{17}O chemical shifts of alcohols, although a slight deshielding trend can be deduced from the data (i.e., **5** → **8** → **9** → **10**; **12** → **13**; **5** → **11**; but see **6** → **14**).

The presence of heteroatomic substituents γ to the OH group also provokes shielding, which is usually larger than that of CH_3: CH_3, −6; OH, −11; $N(CH_3)_2$, −12; Cl, −8; and SCH_3, −2 ppm. Finally, trifluoroethanol is about 30 ppm more shielded than ethanol.

In summary, ^{17}O chemical shifts of simple alcohols show a strong resemblance to the ^{13}C behavior of a CH_3 group analogously situated, although the magnitudes of the substituent effects are generally much larger at the oxygen center. We are currently expanding our study to other functional groups.[10]

References and Notes

(1) H. A. Christ and P. Diehl, *Helv. Chim. Acta*, **44**, 865 (1961); see also B. L. Silver and Z. Luz, *Q. Rev., Chem. Soc.*, **21**, 458 (1967); P. Greenzaid, Z. Luz, and D. Samuel, *J. Am. Chem. Soc.*, **89**, 749, 756 (1967); H. A. Christ and P. Diehl, *Helv. Phys. Acta*, **36**, 170 (1963); H. Dahn, H. P. Schlunke and J. Telmer, *Helv. Chim. Acta*, **55**, 907 (1972).

(2) However, see: D. J. Sardella and J. B. Stothers, *Can. J. Chem.*, **47**, 3089 (1969); C. Delseth and J. P. Kintzinger, *Helv. Chim. Acta*, **59**, 466 (1976).

(3) W. L. Earl and W. Niederberger, *J. Magn. Reson.*, **27**, 351 (1977); J. Ruben, *J. Am. Chem. Soc.*, **91**, 5725 (1969).

(4) Spectra were obtained using a Varian XL-100-15 spectrometer equipped for Fourier transform operation. A pulse width of 22 μs with an interval of 0.11 s was employed with a spectral window of 10 000 Hz. Proton decoupling was performed concurrently. Anywhere from 10 000 to 200 000 scans were accumulated depending on the sample. An ^{17}O-enriched H_2O sample (otherwise isotopically normal) at 28 °C was used as an external reference. The spectra were generally run at 65 °C on pure, natural abundance samples from commercial sources.

(5) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972; E. Breitmaier and W. Voelter, "^{13}C NMR Spectroscopy", Verlag Chemie, Bergstr., W. Germany, 1974.

(6) D. M. Grant and E. G. Paul, *J. Am. Chem. Soc.*, **86**, 2984 (1964); H. Spiesecke and W. Schneider, *J. Chem. Phys.*, **35**, 722 (1961); D. K. Dalling and D. M. Grant, *J. Am. Chem. Soc.*, **89**, 6612 (1967).

(7) A similar relationship between the ^{15}N chemical shifts of primary amines (RNH_2) and the ^{13}C shifts of the analogous hydrocarbons (RCH_3) has been reported; R. L. Lichter and J. D. Roberts, *J. Am. Chem. Soc.*, **94**, 2495 (1972).

(8) The points for phenol (**33**) and *o*-cresol (**34**) clearly fall off the line in Figure 1 and were not included in the data treatment. This is not surprising since conjugation of a lone pair on the OH group with the aromatic ring is a capacity not present in the analogous methylbenzenes. However, the phenol–aniline point does fit a correlation of $R^{17}OH$ vs. $R^{15}NH_2$. In this comparison conjugation of a lone pair with the aromatic ring is possible in both cases.

(9) G. C. Levy, Ed., "Topics in Carbon-13 NMR Spectroscopy", Vol 1, Wiley, New York, 1974, pp 53–77; E. W. Wehrli and T. Werthlin, "Interpretation of Carbon-13 NMR Spectra", Heyden, London, 1976, pp 22–48.

(10) Support of this work by a research grant from the National Science Foundation is gratefully acknowledged. Fellowship support to Manuel A. Centeno was provided by the Universidad de Oriente, Venezuela.

Jack K. Crandall,* Manuel A. Centeno

Contribution No. 3205 from the
Department of Chemistry, Indiana University
Bloomington, Indiana 47405

Received September 12, 1978

Oxygen-17 Nuclear Magnetic Resonance. 2. Cyclohexanones

Summary: The ^{17}O chemical shifts of several substituted cyclohexanones have been measured. Substituent shifts have been derived for methyl substitution at various sites and it appears that the substituent shift for methyl substitution at the carbon adjacent to a carbonyl depends on the dihedral angle between these two groups.

Sir: In connection with a study of the ^{17}O NMR characteristics[1] of the carbonyl oxygen of aldehydes,[2,3] ketones,[2,3] esters,[4] etc., we have measured the ^{17}O chemical shifts for a number of cyclohexanones. The well-defined conformational situation for cyclohexane derivatives allows for the empirical definition of substituent effects as a function of molecular geometry. Such information should prove invaluable in the application of conformational analysis to the interpretation of ^{17}O data for acyclic carbonyl compounds.

Table I. ^{17}O and ^{13}C Carbonyl Chemical Shifts of Substituted Cyclohexanones

cyclohexanone	$\delta^{17}O$[a]	$\delta^{13}C$[b]
parent	559.9	207.4
2-methyl	548.8	209.9
3-methyl	561.8	207.0
4-methyl	560.1	207.9
2-ethyl	553.3	208.6
2-isopropyl	558.7	208.6
2-*tert*-butyl	561.9	208.5
2-*n*-propyl	552.2	209.1
3-*tert*-butyl	561.4	207.6
4-*tert*-butyl	557.4	207.2
2,2-dimethyl	554.9	211.2
3,3-dimethyl	572.3	207.1
4,4-dimethyl	561.4	207.4
cis-2,6-dimethyl	540.8	210.1
trans-2,6-dimethyl	550.8	212.4
cis-3,5-dimethyl	561.2	206.5
trans-3,5-dimethyl	571.3	207.0
cis-2-methyl-4-*tert*-butyl	549.3	208.9
3,3,5-trimethylcyclohexanone	570.0[c]	207.2
3,3,5,5-tetramethylcyclohexanone	576.5	207.2

[a] In ppm relative to external H_2O; 30% by weight in dioxane with a drop of $H_2{}^{17}O$. [b] In ppm relative to internal Me_4Si; 10% by weight in CCl_4. [c] Neat.

0022-3263/79/1944-1184$01.00/0