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O-17 NMR SPECTRA OF RING COMPOUNDS. CORRELATION OF ^{17}O AND ^{13}C METHYL SUBSTITUTION PARAMETERS

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Summary: The ^{17}O NMR spectra of 22 1,3-dioxanes, four oxanes, four 4-heterooxanes, four tetrahydrofurans and four 1,3-dioxolanes have been recorded and methyl substitution parameters determined for the 1,3-dioxanes. The parameters, including γ_a, correlate linearly with corresponding ^{13}C parameters for methyloxanes.

NMR investigation of the ^{17}O nucleus has been discouraged by its low natural abundance (0.037%). Its large quadrupole moment (I = 5/2) leads to substantial line broadening but also to very short relaxation times which permit acquisition periods as short as 25 msec. Line broadening is somewhat offset, as far as resolution is concerned, by sizeable chemical shifts.

A limited number of ^{17}O NMR studies are on record, some concerned with isotopically enriched compounds. Early pioneering survey studies[1] were followed by investigations of N-O containing species[2] and of carbonyl compounds[3,4], ethers[5] and alcohols[6]. In the latter three cases[3,5,6], a linear correlation of ^{17}O with ^{13}C shifts was found.

The present investigation is concerned with cyclic oxygen compounds, primarily 1,3-dioxanes (Table 1) but also related ring compounds [tetrahydropyrans, 1,4-dioxane, morpholines, 1,4-oxathiane, tetrahydrofurans and 1,3-dioxolanes (Table 2)]. The spectra were recorded on a Varian XL-100 spectrometer equipped with an 18-mm Nicolet probe at 13.56 MHz in FT mode employing an external ^{19}F lock. Samples (natural ^{17}O abundance) were neat, in stationary 18-mm (OD) tubes. Shifts were measured without proton decoupling[7] and are referred to external $H_2{}^{17}O$ as standard[8]. Usually 10,000 scans were accumulated.

The accuracy of the chemical shifts is only ± 1.0 ppm for the following reasons: a) The peaks were quite broad (width at half-height ca. 3 ppm) and frequently somewhat jagged[9]. b) The 18-mm probe could not be temperature controlled. A few experiments with thermostatted 10-mm tubes (requiring many more scans and corresponding larger blocks of instrument time) revealed surprisingly large temperature effects on ^{17}O shifts; for example, the shifts for 2,2,4-trimethyl-1,3-dioxane (anancomeric) are 45.5 and 76.5 ppm at 24°C but 52.4 and 80.0 ppm at 90°C. Small fluctuations around the mean of 24°C may have occurred in some runs. c) Reproducibility of shifts was not better than 1 ppm being least good in the case of the more highly substituted dioxanes.

Table 1

1,3-Dioxanes

Substituent	none	2-Me	4-Me	5-Me
Shift[a], expt.	35.3	52.5	32.6, 61.7	35.5
calc'd	b	52.3	31.9, 61.6	35.6

Substituent	2,2-di-Me	4,4-di-Me	5,5-di-Me	*cis*-4,6-di-Me
Shift, expt.	51.8	30.9, 69.3	31.1	58.0
cal'd	50.9	31.3, 69.9	31.3	58.3

Substituent	*trans*-4,6-di-Me	*cis*-2,4-di-Me	2,5,5-tri-Me	2,2,4-tri-Me	*trans*-2,4-di-Me[c]
Shift, expt.	52.4	48.8, 78.3	47.7	45.5, 76.5	47.4, 63.6
cal'd	51.6	49.0, 78.7	48.3	47.5, 77.2	48.3, 64.7

Substituent	*r*-2,*trans*-4,*trans*-6-tri-Me	2,2,5,5-tetra-Me	*r*-2,*cis*-4,*cis*-6-tri-Me
Shift, expt.	63.3	47.7	76.4
cal'd	b	46.9	75.4

Substituent	2-*i*-Pr	2-Et	2-*t*-Bu	*cis*-5-Me-2-*i*-Pr	*trans*-5-Me-2-*i*-Pr	2,2,4,4,6-penta-Me
Shift, expt.	46.2	48.8	42.5	34.9	46.7	73.6, 82.8
cal'd	46.3	b	b	34.9	46.6	73.2, 82.2

Table 2

Other Ring Compounds

Compound	THP[d]	2-MeTHP	3-MeTHP	4-MeTHP	Morph[e]	2,6-di-Me-morph	1,4-Oxathiane
Shift[a]	8.8	33.6	10.3	7.7	2.6	49.4	5.9

Compound	THF[f]	2-Me-THF	3-Me-THF	2,5-di-Me-THF[g]	1,3-diox[h]	2-Me-1,3-diox	4-Me-1,3-diox
Shift	16.2	43.9	15.5	66.7, 74.5	34.8	56.0	61.9, 36.9

Compound	2,2-di-Me-1,3-diox	1,4-dioxane
Shift	64.2	-1.7

[a] in ppm downfield from $H_2{}^{17}O$. [b] No independent calculation possible. [c] Assumed to be 88.4% in the 2(e),4(a) conformation. [d] Tetrahydropyran. [e] Morpholine. [f] Tetrahydrofuran. [g] 1:1 *cis* and *trans*. [h] 1,3-Dioxolane.

The observed shifts for the 1,3-dioxanes (samples available from previous work[10] or prepared according to previously described methods[11]) are reported in Table 1; those for the other compounds investigated are in Table 2. Additive substitution parameters[11,12] for methyl substituents in the 1,3-dioxane system were computed by an analysis-of-variance program and are reported in Table 3. The shifts calculated using these substitution parameters are indicated in Table 1. Agreement of calculated with experimental values is good, indicating that additivity of substitution parameters is as satisfactory for ^{17}O as it is for ^{13}C.

In those cases (total of 16) where comparison with structurally analogous oxanes is possible, the ^{17}O shifts of the methyl-substituted dioxanes are proportional to the ^{13}C shifts in corresponding methyloxanes[12] with a slope of 2.6 and a root mean square (rms) of residuals of 1.8. (A bad fit results for 2,2-dimethyl- and 2,2,4-trimethyl-1,3-dioxane which have[10] highly crowded axial methyl groups; when these compounds are omitted in the correlation, the rms of residuals becomes 1.1.) Correspondingly, the methyl substitution parameters (except 2-gem) for

Table 3

Methyl Parameters in 1,3-Dioxane[a]

Parameter	$\beta_e(2)$[b]	$\beta_e(4)$	$\gamma_e(5)$	$\delta_e(6)$	$\beta_a(2)$	$\beta_a(4)$	$\gamma_a(5)$
Value	17.1	26.4	0.3	-3.4	5.0	12.2	-11.4

Parameter	$\delta_a(6)$	i-$Pr_e(2)$	2-gem	4-gem	5-gem	6-gem
Value	-2.6	11.0	-6.5	-3.9	7.1	11.9

[a] Computed as $\delta = 35.3 + \Sigma p$ where the p's are the appropriate β, γ, δ and gem parameters for each compound. [b] Figure in parenthesis indicates origin of parameters.

Other Methyl Parameters[a]

Compound, parameter	THP:	β_e	γ_e	δ_e	THF:	β_a	γ_e	1,3-Dioxolane:	$\beta_e(2)$	$\beta_e(4)$
Value		24.8	1.5	-1.1		27.7	-0.7		21.2	27.1

[a] Single values, calculated by difference between methyl-substituted and parent compounds.

^{17}O are proportional to those for ^{13}C with a scale factor of ca. 2.5; this is true for the γ_a parameter even though in the case of ^{17}O there is very little steric compression[10]. Thus, as in other investigations[13], it appears that the γ_a effect may not have its origin in compression. The β_e effect of C(4) is 26.4 ppm and β-effects in 2-methyltetrahydropyrans and 2-methyltetrahydrofurans as well as 4-methyl-1,3-dioxolane are similar (24.8 - 27.7 ppm). However, when the substituted carbon is between two oxygens, the deshielding effect is markedly diminished: β_e in 2-methyl-1,3-dioxane is 17.1 ppm and in 2-methyl-1,3-dioxolane 21.2 ppm. A similar effect is seen in ^{13}C parameters: the β_e effect at C(3) in tetrahydropyran of 8.6 ppm is reduced to 7.3 ppm in 4-methyl-1,3-dioxane and the effect of 9.0 ppm in cyclohexane is reduced to 7.2 ppm in 2-methyltetrahydropyran. A similar diminuition (from 12.2 ppm for axial 4-Me to 5.0 ppm for axial 2-Me) is found for the β-effects of axial methyl groups on ^{17}O shifts.

Surprisingly, the scale-up factor for gauche (correponding to γ_a) effects for ^{17}O over ^{13}C is not seen in the series 2-ethyl-1,3-dioxane, 2-isopropyl-1,3-dioxane, 2-t-butyl-1,3-dioxane (Table 1), the upfield increment of ca. 3 ppm per methyl group being similar to the 2.5 ppm increment found in the $^{13}C(2)$ shift in the series of ethylcyclohexane, isopropylcyclohexane, t-butylcyclohexane.

In summary, ^{17}O shifts of oxygen-containing six-membered saturated heterocycles can be used conveniently in conformational and configurational assignments being similar in this respect to ^{13}C shifts.

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References and Footnotes

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7. Proton irradiation had little or no effect on the spectra; there was no evidence either of palpable decoupling or of an NOE effect.
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