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ASSIGNMENT OF RING SIZE IN ISOPROPYLIDENE ACETALS BY ^{13}C N.M.R.

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Summary: Cyclic isopropylidene acetals containing 5,6 and 7-membered rings can be distinguished by measurement of the ^{13}C chemical shifts of the acetal carbon and the methyl groups.

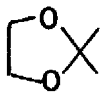
Cyclic isopropylidene acetals are widely used for the protection of diol functions, particularly in carbohydrate chemistry.[1-4] Polyols capable of reacting with more than one equivalent of acetone can form 5,6 or 7-membered rings. Structure determination of these acetals using partial acidic hydrolysis may be difficult because of the possibility of rearrangements. In the 1960s Foster and his coworkers[5] used ^{1}H n.m.r. spectroscopy for the study of 5-membered rings and in 1975 Stoddart[6] reported small differences in the ^{13}C chemical shifts of the acetal carbon of methylene acetals containing 5,6 and 7-membered rings. Recently, Rogers and his coworkers[7] have reported substantial differences in the ^{13}C chemical shifts of the acetal carbon in the acetals (1), (5), and (13) (see Table 1). While the present work was in progress less marked correlations were reported by Grindley[8] for cyclic benzylidene acetals.

Following Rogers' paper we examined the ^{13}C n.m.r. spectra of several carbohydrate isopropylidene acetals of unambiguous structure (Table 1). The overall trends and conclusions of Table 1 are summarised in Table 2. We confirm Rogers' results for the ^{13}C shifts of the acetal carbon (Table 2) and we noticed in addition that the acetal carbon of a 5-membered ring acetal fused to a second 5-membered (furanose) ring is further deshielded. The effect is shown in compounds (6) and (7) and in several examples already published by Moffatt,[9] Szarek[10] and their colleagues. A 5-membered acetal fused to a pyranose ring does not show this effect.[11-13]

We have also noted correlations for the isopropylidene methyl groups which have clear diagnostic value. This has been observed by Garegg and Lindberg[14] in their work on acetals of pyruvic acid and derived compounds, but not for isopropylidene acetals. In a 6-membered ring the ^{13}C chemical shifts of the methyl groups are separated by about 10 p.p.m.

This large difference presumably reflects the difference in environment of equatorial and axial methyl groups in a chair conformation and we agree with Garegg and Lindberg[14] that the higher field signal is due to the axial group which is more crowded. For 5-membered acetals the methyl signals are only slightly separated, probably due to the conformational mobility of the system and to the fact that the methyl groups are pseudoequatorial and pseudoaxial. In the 7-membered acetal (14) the isopropylidene methyl signals were coincident. This is a monocyclic system with considerable conformational freedom not present in bicyclic systems, examples of which are described in the following Communication.[15]

The acetals (6) and (7) make an interesting comparison. In the low field region of the spectrum both show the presence of a 5- and 6-membered acetal ring, although the signal for (7) is downfield of the normal range. At high field (6) shows the presence of methyl groups corresponding to both 5- and 6-membered rings, but in the spectrum of (7) there is only one signal, of increased intensity, due to the methyl groups of the 6-membered ring. Mills[2] has pointed out that in the 6-deoxy-6-nitro compound (8) both chair forms of the 1,3-dioxan ring have unfavourable interactions and it appears that (7) exists in a skew conformation where the methyl groups have similar environments.



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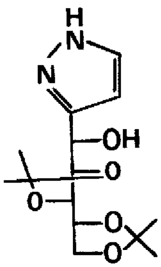

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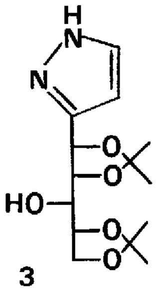

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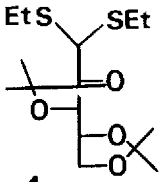

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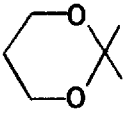

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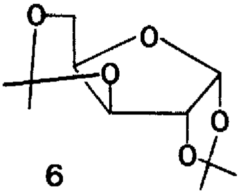

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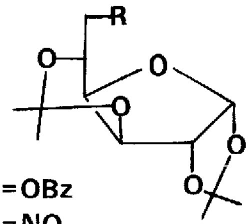
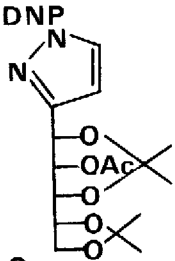


7 R=OBz

8 R=NO_2



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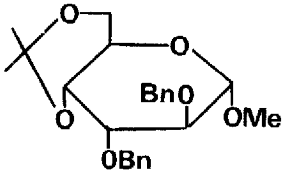

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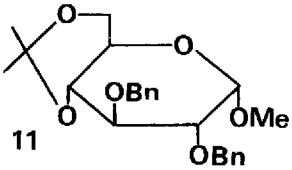

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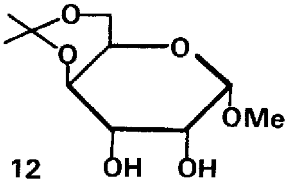
DNP=2,4-Dinitrophenyl Bn= Benzyl



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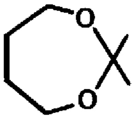

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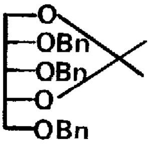

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Table 1. ^{13}C Chemical Shifts (20 MHz, $CDCl_3$)[a] for Isopropylidene Acetals.

Compound	Acetal Carbon		Methyl Groups		Acetal ring size
1	108.50[7]		c		5
2[b]	109.71 109.37		26.98 26.91 25.92 25.46		5,5
3[b]	109.03 108.93		26.22(x2) 25.23 24.95		5,5
4[16]	109.56 109.07		25.77 25.24 24.96 24.55		5,5
5		97.70[7]	c		6
6[17]	111.30	97.16	26.49 25.91	28.60 18.44	5,6
7[18]	112.08	100.89	27.01 26.37	23.74 (x2)	5,6
9[b]	109.56	99.54	26.24 25.15	29.04 19.26	5,6
10[b]		99.20		29.10 18.87	6
11[b]		99.09		29.02 18.97	6
12[19]		98.33		29.14 18.26	6
13	100.90[7]		c		7
14[b]	100.78		24.66		7

[a] Chemical shifts in p.p.m. downfield from Me_4Si. [b] Full analytical and spectroscopic data have been obtained for these compounds. [c] Not measured.[7]

Table 2. ^{13}C Chemical Shift Correlations for Isopropylidene Acetals.

Ring Size	Acetal Carbon	Methyl Carbons	Δδ Methyl Carbons
5	108.5-111.4[9-13] (Monocyclic or fused to pyranose ring) 111.4-115.7[9,10] (Fused to furanose ring)	23.7-27.8	0.0-2.4[9-13]
6	97.1-99.5	18.2-19.3 and 28.6-29.2	9.8-10.9
7	100.7,100.9	See ref. 15	See ref. 15

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