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NUCLEAR MAGNETIC RESONANCE SPECTRA OF SOME 2,3-ANHYDROPYRANOSE DERIVATIVES

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ABSTRACT

Proton- and ^{13}C-n.m.r. data have been obtained for the anomeric pairs of *allo*, *manno*, and *talo* isomers of methyl 2,3-anhydro-4,6-*O*-benzylidene-D-aldohexopyranosides with the aid of 2-D homo- and hetero-correlation techniques. These data supplement and, in some instances, modify the findings of earlier studies. They concur with the general view that the 2,3-anhydropyranoside ring exists in a conformation that is possibly $^{O}H_{5}$, and also indicate that both the *trans*- and *cis*-fused 1,3-dioxane rings formed by closure of the benzylidene acetals maintain chair conformations. Isomeric differences in the ^{1}H- and ^{13}C-chemical shifts of the oxirane nuclei bear a direct relationship with respect to each other, which suggests that the electronic states at C-2 and C-3 dominate the influence of configurational change on chemical shift. It appears that the oxirane ring both affects chemical shifts and $^{1}J_{C,H}$ values of neighboring ^{13}C nuclei, and enhances the magnitude of some 3-bond, ^{13}C, ^{1}H coupling. Among additional instances of long-range coupling described are those involving H-2 and H-3 with other protons, and several 2-bond, ^{13}C, ^{1}H interactions. The presence of the oxirane ring has only a minor influence on the magnitude of coupling between H-1 and $O^{13}CH_3$, and, hence, on the anomer-dependent rotamer populations of the methoxyl groups ("exo-anomeric effect") of these glycosides. Comparative data are reported for methyl 4,6-*O*-benzylidene-α- and -β-D-galacto-, β-D-ido-, and α-D-talopyranosides.

INTRODUCTION

Oxirane derivatives are widely employed as intermediates in a variety of chemical transformations within the sugar series. A large number of these derivatives have been examined[1–9] by n.m.r. spectroscopy, mainly to determine their configurational and conformational characteristics. During a study on sulfation of methyl 4,6-*O*-benzylidene-D-glucopyranosides, some 2,3-anhydrides were found[10] among other reaction products. To facilitate their identification, we have recorded ^{1}H- and ^{13}C-n.m.r. spectra of several compounds of this type. They are methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside (**1**) and the corresponding α-D-

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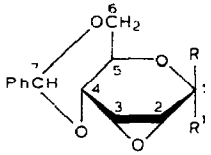
manno (**3**), α-D-*talo* (**5**), β-D-*allo* (**2**), β-D-*manno* (**4**), and β-D-*talo* (**6**) isomers. Partial spectral data for some of these, as well as related, compounds had already been reported[1–5,7]. Now, however, aided by the availability of 2-D homo- and hetero-correlation techniques, a more comprehensive n.m.r. analysis has been obtained, and is reported herein.



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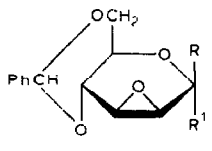

3 R = H,R' = OMe
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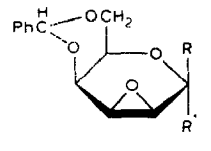


5 R = H,R' = OMe
6 R = OMe,R' = H

RESULTS AND DISCUSSION

^{1}H- and ^{13}C-chemical shifts. — In recording the ^{1}H-n.m.r. spectra, four solvents were tested, namely, chloroform-*d*, acetone-d_6, dimethyl sulfoxide-d_6, and benzene-d_6. All four were satisfactory for the acquisition of a full set of data for the *α-allo* isomer (**1**), whereas only benzene-d_6 afforded adequate separation of the ^{1}H signals of **2, 3,** and **4**. Comparing the overall results obtained for **1**, large solvent-induced shifts were found (see Experimental section and Table V), particularly for H-1 to H-4, which resonate much farther upfield in benzene-d_6 than in the other three solvents. Solvent effects on ^{13}C-chemical shifts were not expected to be large, and this was borne out by measurements on the *α-allo* isomer **1**, as well as by a comparison of our data with some literature values[5,7].

Characteristically[11], the ^{1}H- and ^{13}C-nuclei of the oxirane ring are the most strongly shielded. Although the H-2 signal always appears upfield of that of H-3 (see Table IA), the differences between their positions vary from a value of $\Delta\delta_{2,3} = 0.46$ for **4** to $\Delta\delta_{2,3} = 0.07$ for **2**. Among the ^{13}C resonances, the relative positions of C-2 and C-3 change (see Table IA), and their chemical-shift differences follow a sequence that closely parallels that of the protons, namely, from a value of $\Delta\delta_{2,3} = 3.9$ for **4** to $\Delta\delta_{2,3} = -4.1$ for **2**, as may be seen from a plot of $\Delta\delta_H$ *vs.* $\Delta\delta_C$ (see Fig. 1). According to this Figure, both the ^{1}H- and ^{13}C-chemical shifts respond to changes in configuration by being altered in the same direction. For the parent pyranosides[12–14], by contrast, a configurational inversion leading to a change in ^{13}C-chemical shift is usually accompanied by a shift in the opposite direction for the appended proton. Possibly, this distinction between an oxirane and a *vic*-diol represents differences in the balance between contributing electronic and steric influences, with the latter being more important in the diol, and the former (*e.g.*, the ring current[15]) the overriding factor for the nuclei of the oxirane ring.

The coupling of ~4 Hz (3.6–4.3 Hz) between H-2 and H-3 (see Table IA) is typical of *cis* oxiranes in the pyranose, as well as the cyclohexane[16], series. Also

TABLE I

^1H- AND ^{13}C-N.M.R. CHEMICAL-SHIFT AND COUPLING PARAMETERS FOR 2,3-ANHYDRIDES **1–6**[a]

A. Isomer	*At positions 2 and 3*						
	δ_{H-2}	$J_{2,3}$	δ_{H-3}	δ_{C-2}	$J_{C-2,H-2}$	δ_{C-3}	$J_{C-3,H-3}$
α-allo (**1**)	2.88	4.3	3.06	53.0	181.0	50.4	184.0
α-manno (**3**)	2.86	3.6	3.25	50.6	181.5	53.9	183.0
α-talo (**5**)	2.90	3.6	3.20	49.2	180.5	49.7	181.0
β-allo (**2**)	3.06	4.3	3.13	55.4	182.0	51.3	184.0
β-manno (**4**)	2.70	3.7	3.16	50.6	180.0	54.5	181.0
β-talo (**6**)[a]	3.25	3.9	3.57	50.0	180.0	51.1	183.5

B. Isomer	*At positions 1*[b] *and 4*							
	δ_{H-1}	$J_{1,2}$[c]	δ_{C-1}	$J_{C-1,H-1}$	δ_{H-4}	$J_{4,3}$[b]	δ_{C-4}	$J_{C-4,H-4}$
α-allo (**1**)	4.36	2.8 (4–6)	95.7	165.0	3.44	1.6 (0–2)	78.4	140.0
α-manno (**3**)	4.61	0.6 (0–2)	97.2	169.0	3.56	0 (0)	75.2	146.0
α-talo (**5**)	4.83	0.6 (0–2)	97.0	171.0	3.81	5.6 (4–6)	68.7	139.0
β-allo (**2**)	4.57	1.2 (0)	98.2	166.0	3.61	1.3 (0–2)	78.0	140.0
β-manno (**4**)	4.33	1.0 (0–2)	100.0	158.0	3.54	0 (0)	75.0	145.5
β-talo (**6**)	4.78	0 (0–2)	99.3	158.0	4.28	5.1 (4–6)	68.5	140.5

C. Isomer	*At positions 5 and 7*[d]						
	δ_{H-5}	$J_{5,4}$	δ_{C-5}	$J_{C-5,H-5}$	δ_{H-7}	δ_{C-7}	$J_{C-7,H-7}$
α-allo (**1**)	4.29	9.1	60.5	152.0	5.31	100.7	160.5
α-manno (**3**)	3.72	9.4	62.2	146.0	5.20	102.4	161.0
α-talo (**5**)	3.21	2.6	60.1	143.5	5.34	100.8	159.5
β-allo (**2**)	3.77	9.2	61.0	147.5	5.26	102.7	160.5
β-manno (**4**)	2.97	9.5	68.7	143.0	5.14	102.3	161.5
β-talo (**6**)	3.28	2.9	68.2	142.0	5.57	101.0	161.6

D. Isomer	*At positions 6*							
	δ_{H-6}	$\delta_{H-6'}$	$J_{5,6}$	$J_{5,6'}$	$J_{6,6'}$	δ_{C-6}	$J_{C-6,H-6}$	$J_{C-6,H-6'}$
α-allo (**1**)	4.05	3.40	5.1	10.5	−10.1	69.1	151.5	140.5
α-manno (**3**)	4.04	3.42	4.4	10.1	−10.1	69.4	149.0	139.5
α-talo (**4**)	4.05	3.73	0.8	2.8	−12.7	69.1	151.0	139.0
β-allo (**2**)	4.08	3.44	4.9	10.2	−10.2	69.2	150.5	139.0
β-manno (**4**)	4.02	3.44	4.7	10.4	−10.2	69.4	150.5	140.5
β-talo (**6**)	4.33	4.15	2.9	1.2	−12.9	69.1	151.0	140.5

[a]Solvent, C_6D_6, with the exception of the data for **6**. Due to the low solubility of the latter in C_6D_6, its ^{13}C spectrum was recorded with $CDCl_3$. However, ^1H data were obtained with both solvents. For C_6D_6, the δ values for H-1 to H-7, respectively, were 4.24, 2.73, 2.90, 3.33, 2.27, 4.06, 3.45 and 5.29 (the values of J were within ±0.3 Hz of those in $CDCl_3$). [b]Chemical shifts for the methoxy ^1H and ^{13}C of **1–6**, respectively, are (δ): 3.12, 3.16, 3.00, 3.29, 3.12, 3.42; 55.3, 56.3, 55.2, 56.3, 55.4, 56.6. [c]Values in parentheses are those (in Hz) expected according to ref. 8. [d]Benzylic.

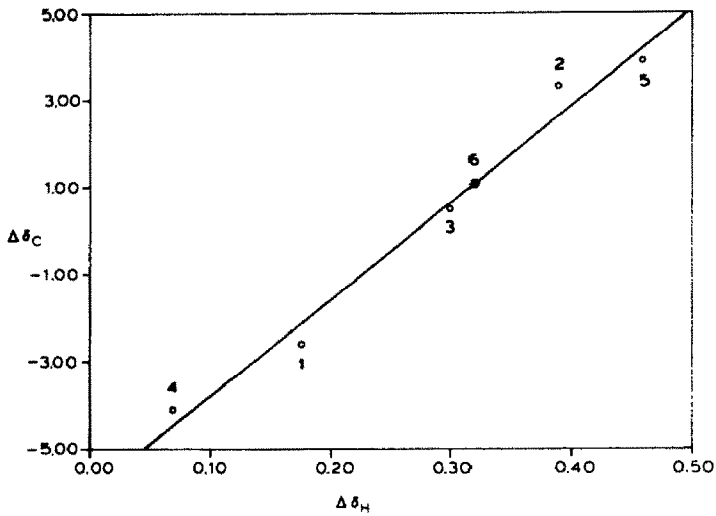
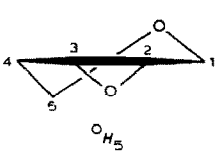


Fig. 1. A plot of the differences in chemical shift ($\Delta\delta_H$) between H-3 and H-2, and those ($\Delta\delta_C$) between C-3 and C-2, for 2,3-anhydro derivatives **1–6**, using benzene-d_6 as the solvent for all except **6**. For reasons of solubility, chloroform-*d* was used for compound **6**.

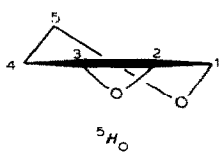
characteristic is the evidence[17] for enhanced *s* character of the oxirane carbon atoms apparent in the large $^1J_{CH}$ values of 180.0–184.0 Hz. Differences between the values of $J_{C\text{-}2,H\text{-}2}$ and $J_{C\text{-}3,H\text{-}3}$ are relatively minor, with the latter coupling being the greater by 0.5–3.5 Hz. Evidently, alterations in the configuration at the adjacent centers (C-1 and C-4) have only a small impact on these n.m.r. parameters.

Irrespective of whether the methoxyl group and the oxirane ring are *cis* or *trans*, coupling between H-1 and H-2 is 0–1 Hz for all except that of the *α-allo* isomer **1**, which is slightly larger ($J_{1,2}$ = 2.8 Hz; see Table IB). As has been proposed[1] specifically for the *α-manno* isomer (**3**), an observed $J_{1,2}$ value of ≤1 Hz is clear evidence that the conformation of the pyranose ring departs substantially from $^4C_1$. Furthermore, these very small couplings are consistent with what is expected[1–4] for the $^0H_5$ conformation on the basis, *e.g.*, of data for model epoxytetrahydropyran derivatives[8,9] (see values in parentheses, Table IB). Equally good agreement is found (see Table IB) for *vic*-coupling on the other side of the oxirane ring, *i.e.*, between H-3 and H-4. In this instance, the small $J_{3,4}$ values of 0–1.6 Hz for **1, 2, 3,** and **4** are also in accord with the order of magnitude anticipated, as are the much larger values of $J_{3,4}$ for the *α-* and *β-talo* isomers (**5** and **6**).

The markedly strong shielding exhibited by the carbon atoms of the oxirane



$^0H_5$



$^5H_0$

ring appears to have some impact on the adjacent, anomeric carbon atoms, because the latter resonate (δ 96–100; see Table IB) several p.p.m. upfield of those of the parent 4,6-*O*-benzylidene-α,β-glycosides[18] (δ 100–104). Within the group, ^{13}C-1 of the β anomers tends to have the larger chemical shift: δ 98–100 *vs.* 96–97 for the α-anomers. By analogy with glycopyranosides, this difference is consistent[12] with an axial orientation for the methoxyl group in the α-glycosides (**1, 3, 5**) and an equatorial one for the β anomers (**2, 4, 6**). Among the data for C-4 (see Table IB), it is found that chemical shifts are not affected by (remote) changes in the anomeric configuration but, rather, in the orientation of the oxirane ring or of O-4. With O-4 equatorial, the *allo* configuration is characterized by signals (δ 78) that are 3 p.p.m. downfield of those for the oppositely configured *manno* isomers (δ 75). Comparing the latter with the *talo* isomers (**5** and **6**), there is a C-4 chemical-shift difference of ~6 p.p.m., although this is consistent with the expectation that O-4 in **5** and **6** is axially oriented and hence is accompanied by stronger shielding of C-4.

Carbon atom 1 of an aldopyranose in a chair conformation exhibits[19–22] larger coupling (commonly by ~10 Hz) with an equatorial H-1 than with an axial H-1. Analogous differences [Δ^1J = 11 and 13 Hz, respectively (see Table IB)] are found for the anomeric *manno* and *talo* isomers, which suggests that the methoxyl groups of these non-chair molecules are oriented axially (α) or equatorially (β). By contrast, the *allo* anomers are atypical, in that they both give the same value of $^1J_{C\text{-}1,H\text{-}1}$. An interconversion between axial and equatorial orientations of the methoxyl group (accompanied by other charges in ring conformation) may account for this anomaly. However, another possibility is that the disposition of the oxirane ring relative to the C-1–H-1 bond influences $^1J_{CH}$, especially when examined in conjunction with coupling on the other side of the oxirane ring, *i.e.*, between C-4 and H-4. Values for the latter (see Table IB) are about 5 Hz larger for the *manno* (**3** and **4**) than for either the *allo* (**1, 2**) or *talo* (**5, 6**) isomers. Overall, then the $^1J_{CH}$ value is larger when the C-1–H-1 or C-4–H-4 bond is *cis* to the epoxy oxygen atom [in **3, 5** (C-1) or **3,4** (C-4)]. At C-4, this may reflect an enhancement in $^1J_{CH}$ in the *cis* arrangement, as already suggested by Kim *et al.*[7], or, perhaps, a diminution when *trans*. For the *β-allo* anomer (**2**), $^1J_{C\text{-}1,H\text{-}1}$ is larger than expected. However, its C-1–H-1 bond and epoxy oxygen atom are *cis*, which is the converse of that in the other two β anomers. They are *trans* in the *α-allo* isomer (**1**), for which $^1J_{C\text{-}1,H\text{-}1}$ is smaller than expected, once again the converse of the configurational arrangement in the other two α anomers. Possibly, then, these stereochemical differences contribute to the variations observed in $^1J_{C\text{-}4,H\text{-}4}$ and hence, specifically, to the seemingly anomalous values for the *allo* isomers.

There appears to be a relationship between the orientation of the oxirane ring or the anomeric methoxyl group, or both, and the chemical shift of C-5. When either, or both, is *syn* with respect to H-5 (as in **1, 2, 3,** and **5**), C-5 is far more strongly shielded than when both are *anti* (as in **4** and **6**; see Table IC). Also, direct coupling of C-5 with H-5 seems to be increased when the oxirane ring is *syn*, as shown by the comparatively large values of $^1J_{C\text{-}5,H\text{-}5}$ for the *allo* isomers (see Table IC).

TABLE II

A COMPARISON OF ^{13}C SHIELDING DIFFERENCES BETWEEN THE ANOMERS OF 2,3-ANHYDRIDES **1–6**, AND RELATED GLYCOSIDES

Compound	$\Sigma\delta_c$	Δ
Methyl 2,3-anhydro-4,6-O-benzylidene-D-glycopyranoside		
α-allo (**1**)	565.2	6.9
β-allo (**4**)	571.1	
α-manno (**3**)	566.1	10.6
β-manno (**4**)	576.7	
α-talo (**5**)	549.9	13.8
β-talo (**6**)	563.7	
Methyl 4,6-O-benzylidene-D-glycopyranoside		
α-gluco[a]	610.5	13.7
β-gluco[a]	624.2	
α-galacto[b]	606.9	12.3
β-galacto[b]	619.2	
α-altro[a]	599.4	5.5
β-altro[a]	604.9	

[a]Calculated from data in ref. 18. [b]Calculated from data in Table III.

Although the 2,3-oxirane structure obviously prevents the pyranose rings from adopting the $^4C_1$ conformation, the 1,3-dioxane rings incorporating the 4,6-*O*-benzylidene acetal do not appear to suffer distortion as well. Hence, coupling between H-4 and H-5 is always consistent[23] with the relative orientation expected for these protons. In the *trans*-fused bicyclic systems (in **1**, **2**, **3**, and **4**), an *anti* disposition of H-4 and H-5 accounts for the observed value of ~9 Hz (see Table 1C), whereas the small couplings are more typical of the *e,a* arrangement of these protons in *cis*-fused* **5** and **6**.

Also compatible with these observations are the chemical-shift and coupling parameters of the nuclei at position 6 (see Table ID). Thus, H-6′ in the *trans*-fused isomers **1**, **2**, **3**, and **4** is antiperiplanar with respect to H-5 ($J_{5,6'}$ ~10 Hz; see Table ID) and H-6 is gauche ($J_{5,6}$ ~4.5–5 Hz), whereas the H-5, H-6,6′ couplings of ≤3 Hz for *cis* isomers **5** and **6** are typical of *cis*-fused 4,6-*O*-benzylidene derivatives (see later). In addition, the couplings of H-6 and H-6′ with C-6 (see Table ID), which differ uniformly by ~10–11 Hz, are consistent with an equatorial orientation for H-6 and an axial one for H-6′ within a 1,3-dioxane chair conformation of either

*As all of the 4,6-*O*-benzylidene derivatives were initially prepared from the appropriate glycoside under acid conditions, the more stable diastereomer [(*R*) or (*S*), having an equatorial phenyl group[24]] was subsequently used in order to prepare the 2,3-anhydrides.

TABLE III

N.M.R. PARAMETERS FOR METHYL 4,6-*O*-BENZYLIDENE-D-ALDOHEXOPYRANOSIDES (**7–10**)

Isomer	*δ*										
	H-1	H-2	H-3	H-4	H-5	H-6	H-6′	H-7	OH-2	OH-3	OMe
α-galacto (**7**)	4.91	4.21	4.12	4.07	3.31	4.04	3.65	5.43	4.64	4.69	3.21
β-galacto (**8**)	4.20	3.91	3.68	3.97	2.97	4.05	3.63	5.42	5.20	4.85	3.42
β-ido (**9**)	4.94	4.02	4.36	3.95	3.65	4.17	3.63	5.29	3.53	5.62	3.45
α-talo (**10**)	4.86	3.83	4.16	3.96	3.63	4.09	3.63	5.30	4.08	4.39	3.08
	J *(Hz)*										
	1,2	*2,3*	*3,4*	*4,5*	*5,6*	*5,6′*	*6,6′*		*HO-2,2*	*HO-3,3*	
α-galacto	3.4	9.9	3.5	0.9	1.5	1.9	−12.3		6.3	6.3	
β-galacto	7.8	9.5	3.4	≤0.5	≤0.1	1.5	−12.2		4.3	6.2	
β-ido	≤0.5	2.9	2.3	≤0.5	≤0.5	1.8	−11.6		11.3	3.9	
α-talo	≤0.5	2.6	3.7	1.6	1.8	1.8	−12.7		10.5	7.7	
	δ([1]J)[b]										
	C-1	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*		*C-7*	*OMe*		
α-galacto	101.8	69.3	69.4	77.3	63.4	69.4		100.9	55.4		
	(167)	(141)	(146)	(144)	(144)	(151,139′)		(160)	(142)		
β-galacto	105.2	70.9	73.1	76.7	66.8	69.3		100.8	56.4		
	(158)	(146)	(137)	(144)	(142)	(151,139′)		(161)	(142)		
β-ido	101.0	70.3	70.3	76.3	67.1	69.9		101.5	56.4		
	(157)	(149)	(149)	(146)	(139)	(151,138′)		(160)	(142)		
α-talo	103.4	68.4	69.6	76.8	59.9	69.8		101.3	55.3		
	(169)	(149)	(152)	(145)	(144)	(152,139′)		(158)	(143)		

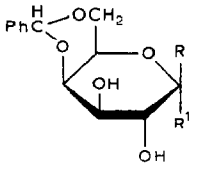
[a]Solvent, 9:1 benzene-d_6–dimethyl sulfoxide-d_6. [b]In parentheses are $J_{C,H}$ values, including, for C-6, couplings with H-6 and H-6′.

a *cis*- or *trans*-fused structure (see ref. 23, and later). Finally, data for the benzylic carbon and hydrogen atoms (C-7 and H-7; see Table IC) throughout are those expected[25] by reference to data for model compounds (see later) if, uniformly, the phenyl groups are equatorially oriented.

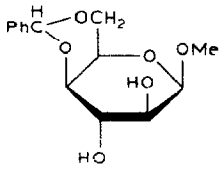
A change in the anomeric configuration of pyranoses is usually reflected[12–14,26] in chemical-shift differences for several ^{13}C nuclei. When O-1 is equatorial, the ^{13}C resonances tend to be downfield of those of the O-1-axial anomer. Hence, it is worth noting that the 2,3-anhydro derivatives (**1–6**) conform to this general pattern. As shown in Table II by the summed values of ^{13}C-chemical shifts ($\Sigma\delta$), the ^{13}C nuclei of the β anomers, averaged over the whole molecule, are the less strongly shielded. As expected, this distinction also applies for the corresponding data (see Table II) for the anomers of several methyl 4,6-*O*-benzylidene-D-aldohexopyranosides.

Methyl 4,6-O-benzylidene-D-aldohexopyranosides. — As already noted, com-

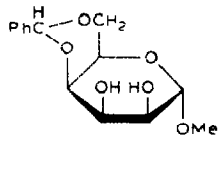
parative n.m.r. data have been obtained for nuclei of 1,3-dioxane rings formed by the attachment of benzylidene substituents to *cis*-oriented O-4 and O-6 of aldohexopyranosides. Examined for this purpose were the α- and β-D-*galacto* (**7** and **8**), β-D-*ido* (**9**), and α-D-*talo* (**10**) isomers. According to the similarities between the n.m.r. characteristics of these compounds and those of the 2,3-anhydro talosides (**5** and **6**), the 1,3-dioxane rings in all of these *cis*-fused, bicyclic structures possess the same chair conformation. That is, there are values of ~0–2 Hz throughout (see Table III) for coupling between H-5 and both H-6 and H-6', and values of ~12 Hz for $^2J_{6,6'}$. In addition, coupling of H-6 and H-6' with C-6 is consistently ~151 and ~139 Hz, respectively (see Table III), and the chemical shifts of the benzylic protons (H-7) and their couplings with C-7 are similar throughout.



7 R = H, R¹ = OMe
8 R = OMe, R¹ = H



9



10

The pyranoside rings of the bicyclic *galacto* isomers (**7** and **8**) exist in the $^4C_1$ conformation, as is evident (see Table III) from the characteristic H-1, H-2 and H-2,H-3 coupling they exhibit. Also, in each instance, the chemical shift of C-1 and the magnitude of its coupling with H-1 are those observed for the unsubstituted galactoside. The pyranose ring of the α-*talo* isomer (**10**) must have the $^4C_1$ conformation as well, because its values of $J_{3,4}$, $J_{4,5}$, and $J_{C\text{-}1,H\text{-}1}$ (see Table III) are the same as those of the α-galactoside **7**. For the β-*ido* isomer **9**, the relatively small splittings observed between H-2 and H-3 and H-3 and H-4 approximate those expected for the $^4C_1$ more readily than those of the $^1C_4$ conformation. However, there was no coupling between H-2 and H-4, as is observed[27,28] for some β-*ido* derivatives, in accord with rotatory evidence[28] that the conformation of **9** departs appreciably from $^4C_1$, possibly towards an $^0S_2$ conformation. The fact that the value of $^1J_{C\text{-}1,H\text{-}1}$ is the same as for the β-galactoside **8** suggests that the C-1–H-1 bond of **9** is also antiperiplanar with respect to one of the O-5 lone pairs, *i.e.*, that the orientation of the methoxyl group is quasi-equatorial.

It appears[29] that the anomer of **9**, methyl 4,6-*O*-benzylidene-α-D-idopyranoside, is maintained (in $CDCl_3$ solution) in the $^4C_1$ conformation by H-bonding between OH-2-*a* and O-4-*a*. Therefore, it is noteworthy that the β anomer exhibits an analogous characteristic (in benzene-d_6) in producing a comparably large OH-doublet (11.3 Hz) due to coupling between OH-2 and H-2: *i.e.*, OH-2 must be antiperiplanar with respect to H-2. Nevertheless, H-bonding with O-4 would appear to be unfavorable in the skew conformation just considered, although

O-1 may be suitably positioned[28] for H-bonding with OH-2. The data for OH-3 differ for the two anomers. In the α- (ref. 29), it probably H-bonds with axial O-1, whereas there is no equivalent possibility in the β-glycoside **9**; hence, $J_{H\text{-}3,OH\text{-}3}$ is 9.9 Hz (α) *vs.* 3.9 Hz (β). The fact that the taloside **10** also exhibits a large $J_{H\text{-}1,OH\text{-}2}$ value (10.5 Hz; see Table II) indicates the probability of strong H-bonding between OH-2 and O-4 in this bicyclic molecule.

Coupling between C-5 and H-5 in **7–10** is in the region of ~140–145 Hz, consistent with values noted earlier[22] for axial C-5–H-5 bonds. The fact that the C-4, H-4 couplings are of the same size may be a reflection of a similarity in the orientation of both sets of bonds with respect to the lone pairs of the adjacent oxygen atom. Held rigidly in the bicyclic system—O-4 of the 1,3-dioxane ring and O-5 of the pyranose ring—the lone pairs are, in each instance, both antiperiplanar and gauche with respect to the C–H bond. By contrast, there are large variations in $^1J_{C\text{-}2,H\text{-}2}$ and $^1J_{C\text{-}3,H\text{-}3}$. Presumably, these variations reflect differences in the orientation of the appended O–H group (and, hence, of the oxygen lone-pairs[19,21,22]) with respect to these C–H bonds. In only two instances, H-bonded OH-2 of **9** and **10**, is information available about this possible factor.

Long-range coupling. — Coupling across four and five bonds was observed in the ^{1}H-homocorrelation spectra of several of the 2,3-anhydro derivatives, almost all of which involved protons of the oxirane rings. However, according to molecular models, none of these splittings represent a planar-zigzag coupling pathway, and may simply reflect strain[30] in the fused-ring structures. The largest of these* is $^4J_{1,3}$ = 1.3 Hz for the *β-allo* isomer **2**. Proton-5 of its α-anomer (**1**) displays coupling both with H-3 (0.5 Hz) and H-1 (0.6 Hz), and there is coupling between H-2 and H-4 (0.5 Hz) of the *β-manno* isomer (**4**). Longer-range (^5J) splitting, involving H-3 and H-6*e*, was observed in the spectrum of **1** (0.9 Hz), **5** (0.5 Hz), and **4** (0.2 Hz).

Two- and three-bond ^{13}C–^{1}H couplings were well resolved in the gated spectra of many of the ^{13}C nuclei. However, the examples cited here are mainly limited to a relatively few in which the ^{13}C–^{1}H interactions involved were reasonably apparent.

For all of the 2,3-anhydrides, the methoxyl ^{13}C signal consisted of a quartet ($^1J_{C,H}$ ~142 Hz), each component of which was split further through coupling with H-1. It is noteworthy that these $^3J_{C,H}$ values (see Table IV) are approximately the same as those[31] of methyl α- and β-glycopyranosides. Reflecting, among the latter, the rotamer populations of the exocyclic methoxyl groups[31], the O^{13}CH$_3$,^{1}H-1 couplings are not influenced by a configurational change in OH-2 (*gluco vs. manno, etc.*; see Table IV). Consequently, the present data indicate that the closure of an oxirane ring either above or below the C-2–C-3 bond (in **1–6**) also does not substan-

*This relatively large coupling is in agreement with the possibility that an axial orientation of the methoxyl group contributes to the lowered value of $^1J_{C\text{-}1,H\text{-}1}$ for **2**, because, then, H-1 and H-3 *approach* a "W" arrangement.

TABLE IV

COUPLING BETWEEN $O^{13}CH_3$ AND H-1 IN 2,3-ANHYDRO DERIVATIVES **1–6**, AND SOME OTHER METHYL ALDOHEXOPYRANOSIDES

Compound	*Anomeric configuration*	$^3J_{C,H}$ *(Hz)*
allo **1**	α	4.0
2	β	4.8
manno **3**	α	3.8
4	β	4.8
talo **5**	α	3.8
6	β	4.6
galacto **7**	α	4.0
8	β	4.7
talo **10**	α	3.8
ido **9**	β	4.4
D-Glucopyranoside[a]	α	3.8
	β	4.5
D-Mannopyranoside[a]	α	3.3
	β	4.3

[a]From ref. 31.

tially alter the orientation of the methoxyl group which, rather, is related mainly to its anomeric configuration*.

A distinctive feature of almost all of the resolved signals is the presence of splittings of 2–3 Hz. These are smaller than the 4–6 Hz commonly observed[19,32] for $^2J_{C,H}$ values of pyranoses, although they are typical[19,26] of $^3J_{C,H}$ coupling between gauche ^{13}C and ^1H pairs of nuclei. These minor spacings contrast with the occurrence of several, relatively large splittings of 7–9 Hz. Comments on some of the latter are offered, based on comparisons of stereochemical features within the series.

In the C-2 and C-3 signals, none of these larger spacings appeared to arise from geminal coupling within the oxirane moiety. Hence, among the C-2 signals, only two instances of splittings >4 Hz were observed, *i.e.*, values of 7.5 and 7.7 Hz for the *β-manno* (**4**) and *β-talo* (**6**) isomers, respectively. By analogy with the fact[32] that methyl β-mannopyranoside exhibits $^2J_{C\text{-}2,H\text{-}1} = +7$ Hz, these distinctive couplings in the spectra of **4** and **6** are attributed to the interaction between C-2 and H-1, moderated by the quasi-antiperiplanar disposition of O-2 and H-1.

In some other instances, an increase in the *s* character of the oxirane ring-carbon atoms may account for an enhanced magnitude in splitting. For example, the C-3 signal of the *α-manno* isomer (**3**) consisted of spacings (aside from ^1J) of 8.6, 4.1, and 1.9 Hz, whereas only spacings of 3.3 and 1.5 Hz characterized its β anomer (**4**). As H-1 of **3** (but not of **4**) is antiperiplanar with respect to C-3, the value of 8.6 Hz probably represent 3-bond coupling. This contrasts with $^3J_{C,H}$

*Another characteristic of the methoxyl groups is the fact that their ^{13}C-chemical shifts are invariably δ 55.2–55.3 among the α anomers, and δ 56.3–56.6 among the β anomers (see footnote b to Table I), which is similar to the data for methyl aldopyranosides[12,18]

spacings that usually[19,26] are ≤7 Hz when sp^3-hybridized carbon atoms are involved.

Spacings of 8–9 Hz are also found in the C-4 signals of both of the *allo* and *manno* isomers, although not those of the *talo* pair. Consequently, these large splittings may arise from geminal coupling of C-4 (through C-3) with H-3, whereas they are less likely to be observed[19,32] when, as in the *talo* isomers, H-3 is antiperiplanar with respect to the C-4–O-4 bond.

cis-Fusion of the 1,3-dioxane ring to the talopyranosides may account for an analogous type of difference with respect to the *trans*-fused isomers *(allo, manno)*. That is, the C-6 signal of each of the compounds contains a spacing of 2–3 Hz, whereas only the *allo* and *manno* isomers exhibit an additional one of 5–6 Hz. If the latter arises from geminal coupling with H-5, the fact that it is not observed for the *talo* compounds may be attributed[19,32] to an antiperiplanar disposition of O-6 and H-5 in the latter.

EXPERIMENTAL

The 2,3-anhydro derivatives **1–6** were obtained[10] as secondary products of the sulfation of the appropriate methyl 4,6-*O*-benzylidene-D-aldohexopyranosides, or were prepared according to literature methods. The 4,6-*O*-benzylidene glycosides (**7–10**) were prepared by acid-catalyzed acetalation of the corresponding methyl glycopyranosides.

A Varian XL-300 n.m.r. spectrometer was used to record the ^{1}H- (300 MHz) and ^{13}C- (75 MHz) n.m.r. spectra, all at room temperature. Unless otherwise specified, the solvent was C_6D_6, and chemical shifts (δ) are referenced with respect to tetramethylsilane. As already noted, large solvent effects on ^{1}H-chemical shifts were observed; representative data are given in Table V. For ^{1}H spectra, the

TABLE V

SOLVENT EFFECT ON ^{1}H-N.M.R. SPECTRA OF METHYL 2,3-ANHYDRO-4,6-*O*-BENZYLIDENE-α-D-ALLOPYRANOSIDE

Solvent	δ							
	H-1	*H-2*	*H-3*	*H-4*	*H-5*	*H-6*	*H-6'*	*H-7*[a]
Benzene-d_6	4.36	2.88	3.08	3.44	4.29	4.05	3.40	5.31
Chloroform-d[b]	4.88	3.49	3.50	3.95	4.09	4.24	3.68	5.56
	J *(Hz)*							
	1,2	*2,3*	*3,4*	*4,5*	*5,6*	*5,6'*	*6,6'*	
Benzene-d_6	2.8	4.3	1.6	9.1	5.1	10.5	−10.1	
Chloroform-d[b]	2.5	4.4	1.0	9.0	4.9	9.9	−9.9	

[a]Benzylic ^{1}H. [b]The corresponding data obtained with acetone-d_6 or dimethyl sulfoxide-d_6 as solvent differed by ≤0.3 p.p.m. and ≤0.6 Hz.

acquisition time was 4 s and the pulse width, 35°. For ^{1}H-decoupled ^{13}C spectra, the acquisition time was 1 s and the pulse width, 18°. The gated-decoupling technique was used for the measurement of ^{13}C, ^{1}H coupling. In applying homonuclear correlated 2D spectroscopy according to the HOMCOR pulse sequence, the following parameters were used: P1 = 17 μs, 90°; PW = 17 μs, 90°; D_1 = 2.0 s. For application of heteronuclear correlated 2D spectroscopy (HETCOR pulse sequence), the parameters were: ^{13}C transmitter-PW = 17 μs, 90°; ^{1}H decoupler-PP = 42 μs, 90°; average $J_{H\text{-}C}$ = 140.0 Hz. The precisions estimated for the δ and J values, respectively, are: ^{1}H ±0.02 p.p.m. and ±0.2 Hz; ^{13}C, ±0.2 p.p.m. and ±0.5 Hz.

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