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Note

Lanthanide-shift-reagent study of some deoxyhexopyranosides

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^{1}H-N.m.r. and ^{13}C-n.m.r. spectroscopy have contributed significantly to knowledge of the structure and conformation of the 4,6-*O*-benzylidene-D-aldohexopyranosides and their derivatives, including some deoxy sugars[1–4]. A quantitative investigation of the n.m.r. line shifts (^{1}H) induced by Eu(fod)$_3$ in the spectra of the 4,6-*O*-benzylidene derivatives of methyl 3-deoxy[5] (**1**), 3-deoxy-2-*O*-*p*-tolylsulfonyl[5] (**2**), and 2-deoxy[6] (**3**) -α-D-*ribo*-hexopyranosides, and of the methyl 2-deoxy-α-D-*arabino*[7,2] (**4**) and 3-deoxy-β-D-*ribo*[8] (**5**) isomers have now been carried out. The ^{13}C-n.m.r. spectra of these systems were completely assigned by selective ^{1}H-spin-decoupling and off-resonance experiments.

The observed shift data for **1, 2,** and **4** were in good agreement with those calculated for the $^4C_1$ conformation of the pyranoid ring, using a single-site model[9] (Tables I and II), and co-ordination of MeO-1 does not take place. In these compounds, the staggered position away from Eu was chosen for MeO-1. It was not

TABLE I

OBSERVED RELATIVE SHIFT-GRADIENTS[a] *FOR* **1–5**

Proton	**1**	**2**	*Proton*	**3**	**4**	*Proton*	**5**
H-1	15.07	0.55	H-1	11.20	2.26	H-1	15.07
H-2	15.63	1.03	H-2*a*	10.30	8.85	H-2	16.13
H-3*a*	13.12	0.48	H-2*e*	16.52	6.33	H-3*a*	7.42
H-3*e*	10.86	0.48	H-3	14.30	13.54	H-3*e*	6.17
H-4	[b]	0.21	H-4	8.47	9.96	H-4	[b]
H-5	[b]	0.25	H-5	12.50	5.52	H-5	4.63
H-6*a*	3.15	0.10	H-6*a*	4.80	3.04	H-6*a*	2.41
H-6*e*	3.06	0.11	H-6*e*	3.40	2.30	H-6*e*	2.58
H-7	2.32	0.11	H-7	3.97	4.14	H-7	1.60
MeO	5.93	0.21	MeO	6.60	1.04	MeO	6.79
HO	33.30		HO	28.70	[b]	HO	24.47

[a]P.p.m. per mol of Eu(fod)$_3$ per mol of substrate. [b]Obscured.

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TABLE II

CALCULATED RELATIVE SHIFT-GRADIENTS FOR *model* A FOR **1**, **2**, AND **4**, AND FOR *model* D FOR **3**

Proton	**1**	**2**	*Proton*	**3**	**4**	
H-1	14.99	0.54	H-1	10.95	2.41	
H-2	15.68	1.03	H-2*a*	10.70	9.23	
H-3*a*	13.16	0.48	H-2*e*	16.80	6.37	
H-3*e*	10.63	0.48	H-3	13.90	13.28	
H-4		0.24	H-4	8.73	10.10	
H-5		0.25	H-5	12.35	4.96	
H-6*a*	3.27	0.10	H-6*a*	4.94	2.86	
H-6*e*	2.82	0.10	H-6*e*	3.43	2.12	
H-7	2.81	0.10	H-7	3.85	4.14	
Eu···O-2	3.37	3.50	Eu···O-1(Å)	2.34	Eu···O-3(Å)	2.84
R	2.23%	2.34%	Eu···O-3(Å)	2.48	R	2.60%
			R	2.55%		

possible to fit shift data for the 2-deoxy-α-D- (**3**) and 3-deoxy-β-D-*ribo*-hexopyranosides (**5**) to the simple single-site model. Furthermore, the somewhat larger shifts observed for the resonance of MeO-1 in **3** and **5** relative to **1** suggest some degree of co-ordination of the MeO group. The position chosen for MeO-1 in **3** was again as in **1**, **2**, and **4** (which is the only position possible if chelation takes place). When the shift data for **3** were fitted to the $^4C_1$ conformation, using the chelation model D[10], the reasonable fit described in Table II resulted.

The fit obtained for **5**, using monodentate co-ordination by O-1 and O-2 (when in this example chelation is not possible and not observed) is quite good (Table III). It is surprising perhaps that this implies equal binding constants for O-1 and O-2. However, many other models including weighted averaging of computed shifts were used without success. Therefore, it appears that, in this instance, OMe and OH co-ordination are competitive. An example of reduced reactivity at O-2

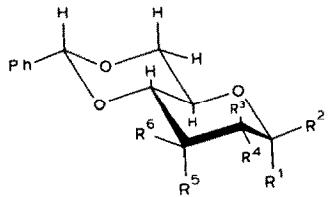
TABLE III

CALCULATED RELATIVE SHIFT-GRADIENTS FOR **5**

Proton	*Eu···O-1*	*Eu···O-2*	*Average*
H-1	17.09	13.45	15.27
H-2	10.93	21.31	16.12
H-3*a*	2.31	13.53	7.92
H-3*e*	0.19	12.69	6.44
H-5	4.76	4.48	4.62
H-6*a*	3.01	1.55	2.78
H-6*e*	3.29	1.69	2.49
H-7	1.53	2.23	1.88
Eu–O (Å)	3.10	3.39	
R			2.75%

TABLE IV

^{13}C-N.M.R. CHEMICAL SHIFT DATA (P.P.M. DOWNFIELD FROM Me_4Si)



Compound	*Hexose configuration*	*R¹*	*R²*	*R³*	*R⁴*	*R⁵*	*R⁶*	*C-1*	*C-2*	*C-3*	*C-4*	*C-5*	*C-6*	*C-7*	*MeO*
1	3-deoxy-*α-ribo*	MeO	H	H	OH	H	H	99.2	67.6	33.8	76.3	64.0	69.4	101.8	55.3
2	3-deoxy-*α-ribo*	MeO	H	H	OTs	H	H	96.9	74.7	30.2	76.0	63.5	69.1	101.8	55.3
3	2-deoxy-*α-ribo*	MeO	H	H	H	OH	H	98.6	35.5	65.0	79.7	58.2	69.4	102.1	55.5
4	2-deoxy-*α-arabino*	MeO	H	H	H	H	OH	99.1	37.3	65.9	83.9	62.5	69.1	102.1	54.9
5	3-deoxy-*β-ribo*	H	MeO	H	OH	H	H	106.4	69.2	35.1	76.2	69.1	70.6	101.8	57.4

(regioselectivity seems to be better for α- than for β-D-glycosides) is provided by tosylation[4,12]. The position chosen for Eu co-ordination was along the line defined by the mid-points of the lines joining C-1,C-2 and O-1,O-2 with Eu–O distances of 3.0Å. The orientation of the HO-2 and MeO-1 bonds were such that the bisectors of the C–O–R angles were in the plane of O-1, O-2, and Eu.

^{13}C-N.m.r. chemical shift data for the deoxyhexopyranosides are presented in Table IV. Selective ^{1}H-spin-decoupling allowed complete assignment of signals. For example, the ^{13}C-n.m.r. spectrum of the 2-deoxy-α-D-*ribo*-hexopyranoside (**3**) contained four signals at lowest field due to the six aromatic carbons [137.3 (quaternary), 129.1 (*para*), 128.3 and 126.3 p.p.m. (*ortho* and *meta*)] with little or no change in the positions of these signals throughout the series. Selective irradiation at the position of the H-7 signal confirmed that the signal at 102.1 was due to C-7. The signal at 98.6 was assigned to C-1 following selective irradiation at the position of the H-1 signal. Likewise, the signals at 35.5, 65.0, 79.7, and 58.2 were assigned to C-2, C-3, C-4, and C-5, respectively. Finally, examination of the off-resonance spectrum showed that the signal at 55.5 p.p.m. was due to the methoxyl carbon, and the signal at 69.4 p.p.m. was assigned to C-6.

Comparison of the ^{13}C-n.m.r. data for **1** and the *p*-tolylsulfonyl derivative **2** showed that the sulfonylation caused an upfield shift of 2.3 p.p.m. ($\Delta\delta$ for C-1 in **2** compared to **1**) → 3.6 p.p.m. ($\Delta\delta$ for C-3 in **2** compared to **1**) in the resonances for the β-carbon atoms, and strong deshielding of 7.1 p.p.m. ($\Delta\delta$ for C-2 in **2** compared to **1**) for the α-carbon. Comparison of the ^{13}C-data (Table IV) for the C-3 epimeric pairs **3** and **4** shows that the greatest difference in their relative chemical shift values occurs for the C-4 and C-5 resonances, which are shifted markedly upfield in **3** (4.2 p.p.m. for C-4 and 4.3 p.p.m. for C-5). As expected, comparison of the data for the anomeric pairs, the 3-deoxy α- and β-D-*ribo*-hexopyranosides **1** and **5**, shows that C-5, which is β to C-1, is strongly shielded (5.1 p.p.m.) on changing from the β to the α anomer; C-4, which is γ to C-1, is virtually unaffected.

The additional data now provided should contribute to future n.m.r. assignments for related carbohydrate structures that are in the $^{4}C_{1}$ conformation[4,11].

EXPERIMENTAL

The deoxy compounds **1-5** were prepared as described[2,5,8]. N.m.r. spectra were recorded at 24° with a Jeol GX-270 spectrometer for solutions in $CDCl_3$ (internal Me_4Si). Shift reagent was added until the molar ratio of reagent to substrate was 0.35, and spectra were recorded after each addition. Good straight-line plots of induced shift *vs.* molar ratio of shift reagent to substrate were obtained for all the compounds studied. Calculations were made by the grid-search procedure[9,10].

Compound **1** prepared[5] from methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-α-D-glucopyranoside, had m.p. 186–187°, $[\alpha]_D$ +124° (*c* 1, chloroform); lit.[5] m.p. 186–187°, $[\alpha]_D$ +127° (chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.50–7.35

(m, 5 H, Ph), 5.52 (s, for PhC*H*), 4.68 (d, $J_{1,2}$ 3.7 Hz, H-1), 4.28 (q, $J_{6a,6e}$ 10, $J_{5,6e}$ 4.5 Hz, H-6*e*), 3.47 (s, 3 H, OMe), 2.30 (m, H-3*e*), 2.40 (d, $J_{2,OH}$ 11.3 Hz, HO-2), 1.93–1.84 (q, $J_{3a,3e}$ 11.3 Hz, H-3*a*). The overlapping four-proton envelope (δ 3.8–3.5) was due to H-2,4,5,6*a*. During the shift study, partial resolution of these resonances gave a triplet due to H-6*a*; however, the resonances of H-4 and H-5 were shifted equally throughout the study and were not resolved. The resonance of H-2 was shifted quite rapidly and remained as a broad singlet throughout the shift study.

Compound **2**, prepared by treatment of **1** with *p*-toluenesulfonyl chloride in pyridine[5], had m.p. 122–124°, $[\alpha]_D$ +54° (*c* 1, chloroform); lit.[5] m.p. 123–124°, $[\alpha]_D$ +57° (chloroform). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.83 (d, 2 H, $J_{AA'}$, 8.5 Hz, Ts ring AA'), 7.44–7.26 (m, 7 H, Ph and Ts ring BB'), 5.47 (s, for Ph*H*), 4.66 (d, $J_{1,2}$ 3.5 Hz, H-1), 4.55 (m, H-2), 4.22 (q, $J_{6a,6e}$ 9.5, $J_{5,6e}$ 4 Hz, H-6*e*), 3.50 (m, H-4), 3.37 (s, 3 H, OMe), and 2.45 (s, 3 H, Ts-Me), and 2.21–2.10 (m, 2 H, H-3*a*,3*e*). The overlapping two-proton envelope (δ 3.8–3.6) was due to H-5,6*a*. During the shift study, these resonances were resolved to give a triplet due to H-6*a* ($J_{5,6a}$ 10 Hz) and a multiplet due to H-5. Complete assignment was possible by spin-decoupling of the normal and shifted spectra.

Compound **3**, prepared from methyl 2,3-anhydro-4,6-*O*-benzylidene-α-D-allopyranoside by treatment with lithium aluminium hydride in ether, had m.p. 129–131°, $[\alpha]_D$ +149° (*c* 1.1, chloroform); lit.[6] m.p. 127–129°, $[\alpha]_D$ +156° (chloroform). The ^{1}H-n.m.r. data were essentially in accord with those reported[4]. Additional data: δ 3.61 (dd, $J_{3,4}$ 2.8, $J_{4,5}$ 9.3 Hz, H-4), 3.80 (t, $J_{5,6a}$ 9.7, $J_{6a,6e}$ 10.1 Hz, H-6*a*), 4.40–4.20 (H-3,5,6*e*). During the shift study, these protons separated to give a q ($J_{5,6e}$ 4.9 Hz, H-6*e*), a bm (H-3), and a m (H-5).

Compound **4**, obtained by conventional reaction of methyl 2-deoxy-α-D-*arabino*-hexopyranoside with benzaldehyde and anhydrous copper sulphate, had m.p. 138–140°, $[\alpha]_D$ +77.5° (*c* 1, chloroform); lit.[7] m.p. 137–139°, $[\alpha]_D$ +77° (ethanol). ^{1}H-N.m.r. data ($CDCl_3$): δ 7.50–7.36 (m, 5 H, Ph), 5.56 (s, PhC*H*), 4.80 (d, $J_{1,2}$ 3.5 Hz, H-1), 4.23 (q, $J_{5,6e}$ 3.4, $J_{6a,6e}$ 9.8 Hz, H-6*e*), 4.20 (m, H-3), 3.42 (t, $J_{3,4} = J_{4,5}$ = 9.0 Hz, H-4), 3.34 (s, 3 H, OMe), 2.50 (d, $J_{3,OH}$ 2.6 Hz, HO-3), 2.20 (dd, $J_{2a,2e}$ 13 Hz, H-2*e*), 1.80 (m, H-2*a*), and 3.80–3.70 (H-5,6*a*). During the shift study, these protons gave a t ($J_{5,6a}$ 10 Hz, H-6*a*) and a m (H-5).

Compound **5**, prepared by reduction of methyl 4,6-*O*-benzylidene-2,3-di-*O*-*p*-tolylsulfonyl-β-D-glucopyranoside in tetrahydrofuran with lithium aluminium hydride, had m.p. 166–167°, $[\alpha]_D$ −62° (*c* 2.5, chloroform); lit.[8] m.p. 165°, $[\alpha]_D$ −60° (chloroform). The ^{1}H-n.m.r. data agreed with those published[4]. In addition, during the shift study, the overlapping six-proton envelope at δ 3.60–3.44 (OMe and H-2,4,5) was resolved to give a s (OMe) and 2 m (H-2 and H-5); the resonance of H-4 was not resolved. The two-proton envelope at δ 2.48–2.44 was assigned to H-2,3*e*. During the shift study, these resonances separated to give a bs (HO-2) and a m (H-3*e*). These assignments were made by spin-decoupling of the normal and shifted spectra.

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