^{1}H Nuclear Magnetic Resonance Spectra and Conformations of Some Secondary Deoxyalditols in Deuterium Oxide

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Shifts and coupling constants obtained by computer simulation of the ^{1}H NMR spectra of nine C_4 to C_6 unbranched chain polyols, containing one or more deoxy groups, have been used to derive conformational data which support and extend previous results on acyclic polyols.

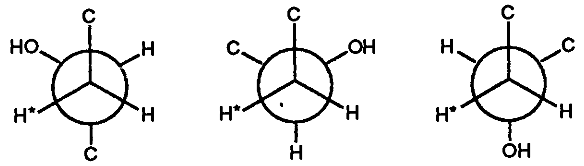
The preferred aqueous solution conformations of alditols have been studied by ^{1}H[1–5] and ^{13}C[6,7] NMR spectroscopy. Conformations of some primary deoxy polyols have also been reported[8] but secondary deoxy polyols have received little attention.[9] This study looks at conformations of polyols with an in-chain methylene group, in order to see how the loss of an oxygen atom from a secondary alcohol group of an alditol affects the conformation of the chain.

Results and Discussion

Assignment of Spectra.—Proton chemical shifts (Table 1) and proton–proton coupling constants (Table 2) were derived in the usual way except that for polyols with a hydroxymethyl group next to a methylene group, the hydroxymethyl protons were identified but could not be assigned. Also, the ethylene fragment of compounds (**6**) and (**7**) proved too complex to analyse.

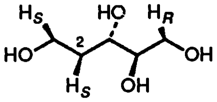
Conformational Data.—In addition to the ^3J values derived from a Karplus-type equation[10] and used for determining the conformations of alditols and primary deoxyalditols,[8] the ^3J values (Hz) in the Figure were also needed for the secondary deoxyalditols. Previous work by us on the conformation of polyols quoted quantitative figures for the amounts of the different conformers present. In view of valid criticism[11] made against this, the chain conformer distributions (Table 3) are generally given to the nearest 5%. However, except where stated in Table 3, the values were derived without using the fact that the sum of the conformers for each polyol should add up to 100 (±5). The fact that they do except for compound (**4**) is taken as some evidence that they are reliable.

(*a*) $\geqslant CCH_2$-C*H*OH-C*H*OH-CH$_2$OH and
(*b*) $\geqslant CCH_2$-C*H*OH-C*H*OH-CHOHC$\leqslant$ as for MeC*H*OH-C*H*OH-CHOHC$\leqslant$ fragment[8] but for (*a*) T_t = 3.9 and for (*b*), $T_g = E_p$ = 9.25 and T_t = 4.0
(*c*) HOC*H*$_2$-C*H*OH-CH$_2$C$\leqslant$ as for HOC*H*$_2$-C*H*OH- CHOHC$\leqslant$ fragment.[1]
(*d*)

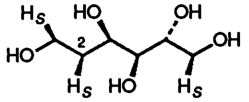


$^3J_{H,H}$	2.2	3.9	11.5
$^3J_{H,H^*}$	11.5	1.9	4.1

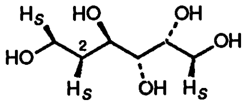
Figure. ^3J Values (Hz) for carbon chain fragments containing or adjacent to a methylene group.



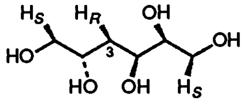
(**1**)



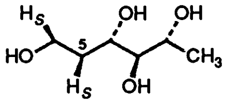
(**2**)



(**3**)



(**4**)



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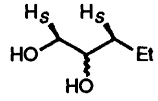
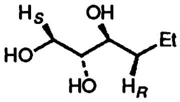
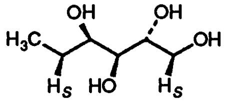


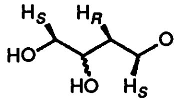
(**6**)



(**7**)



(**8**)



(**9**)

Since a secondary monodeoxy compound is related to two alditols, and Table 3 shows that conformations of the corresponding alditols are also present in a deoxy compound, the conformational purity of secondary deoxy compounds is necessarily low. In addition 2-deoxy-D-*lyxo*-hexitol (**3**) has the $_3G^+$, $_4G^+$ form (for nomenclature, see ref. 6) and 2-deoxy-D-*erythro*-pentitol (**1**) has the $_2G^+$, $_3G^+$ form. The most interesting aspect of the results is that in a C_a–CH_2–C_b–C_c–C_d fragment, though a planar chain would be favoured [except in 1,5-dideoxy-L-*ribo*-hexitol, which has a 1,3-parallel oxygen–oxygen (*i.e.*, O//O) interaction], the chain is significantly *gauche* about the CH_2–C_b or the C_b–C_c bond, provided that this does not give rise to an O//O or C//O interaction, *e.g.*, L-*erythro*-hexane-1,2,3-triol (**7**) has 50% of the $_2G^+$ and or $_2G^-$ forms. Since the polyols can accommodate a C/C (*gauche*, *i.e.*, H//C) interaction, this implies that in the acyclic series, such interactions cannot be too high. Thus, we have further evidence[4] that interactions in acyclic chains are less than those shown by substituents on six-membered rings. Similarly, in ^{13}C NMR spectroscopy,[12] *gauche* or 1,3-parallel interactions give smaller shielding parameters in acyclic chains than on six-membered rings.

Considering some of the results in detail, in (**3**) the greater amount (25%) of the doubly twisted chain form over that (15%) of the singly twisted chain seems incorrect; (**2**) is a similar molecule and it gives the expected result of the $_2G^-$ form

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Table 1. Proton chemical shifts [a] (δ) in D_2O.

Compound	H-1	H-2	H-3	H-4	H-5	H-6
2-Deoxy-D-*erythro*-pentitol (**1**)	3.80 *R** 3.76 *S*	1.69 *R* 1.89 *S*	3.78	3.65_5	3.62 *R* 3.78_5 *S*	
2-Deoxy-D-*arabino*-hexitol (**2**)	3.73 *R** 3.74 *S*	1.74 *R* 1.84 *S*	4.00	3.42	3.74	3.64 *R* 3.83 *S*
2-Deoxy-D-*lyxo*-hexitol (**3**)	3.75 *R** 3.79 *S*	1.97 *R* 1.66 *S*	3.79	3.46	3.91	3.64 *R* 3.66 *S*
3-Deoxy-L-*xylo*-hexitol (**4**)	3.49 *R* 3.60 *S*	3.90	1.64 *R* 1.52 *S*	3.85	3.58	3.70 *R* 3.60 *S*
1,5-Dideoxy-L-*ribo*-hexitol (**5**)	1.22	3.96	3.50	3.79	1.68 *R* 1.96 *S*	3.81 *R** 3.76 *S*
(±)-Pentane-1,2-diol (**6**)	3.45 *R* 3.56 *S*	3.69	*ca.* 1.4 *R* *ca.* 1.4 *S*	*ca.* 1.4 *R* *ca.* 1.4 *S*	0.90	
L-*erythro*-Hexane-1,2,3-triol (**7**)	3.55 *R* 3.73_5 *S*	3.57	3.60	*ca.* 1.4 *R* *ca.* 1.4 *S*	*ca.* 1.4 *R* *ca.* 1.4 *S*	0.89
1,2-Dideoxy-D-*arabino*-hexitol (**8**)	0.96	1.57 *R** 1.60 *S*	3.75	3.49	3.76	3.66 *R* 3.84 *S*
(±)-Butane-1,2,4-triol (**9**)	3.45_5 *R* 3.57 *S*	3.79	1.70 *R* 1.61 *S*	3.69 *R** 3.68 *S*		

[a] Compounds (**1**), (**2**), (**4**), and (**9**) referenced to external tetramethylsilane, the remainder to external sodium 3-(trimethylsilyl)propionate. * The *R* and *S* protons may be interchanged.

Table 2. Proton–proton coupling constants (Hz) of deoxy compounds in D_2O.

Compound	$J_{1R,1S}$	$J_{1R,2}$	$J_{1S,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6}$	Other *J*
(**1**)	−10.9	5.0 2*R* 7.2 2*S*	6.3 2*R* 8.1 2*S*	2*R* 10.1 2*S* 2.8	5.8	7.5 5*R* 3.4 5*S*		2*R*,2*S* −14.4 5*R*,5*S* −11.8
(**2**)	−11.1	7.6 2*R* 5.8 2*S*	$7.0_5$2*R* 5.8 2*S*	2*R* 4.2_5 2*S* 9.5	2.0	8.5	6.5 6*R* 3.0 6*S*	2*R*,2*S* -14.3_5 6*R*,6*S* -11.7_5
(**3**)	−10.8	8.0 2*R* 5.8_5 2*S*	7.3 2*R* 5.0_5 2*S*	2*R* 2.6_5 2*S* 10.4	7.3	2.7_5	7.5 6*R* 4.7_5 6*S*	2*R*,2*S* −14.5 6*R*,6*S* −11.5
(**4**)	-11.7_5	6.8	3.9	2.8_5 3*R* 10.13 *S*	3*R* 10.7 3*S* 2.6	4.0	4.6_5 6*R* 7.1_5 6*S*	3*R*,3*S* −14.6 6*R*,6*S* -11.7_5
(**5**)				5.5	6.5	10.2_5 5*R* 2.5_5 5*S*	5*R* 5.0 6*R* 5*S* 7.4 6*R* 5*R* 6.4_5 6*S* 5*S* 2.5_5 6*S*	1,2 6.4 5*R*,5*S* -14.3_5 6*R*,6*S* −10.9
(**6**)	−11.7	6.8_5	3.8_5	4.0, 8.0	?	6.7_5		
(**7**)	-11.8_5	7.3_5	3.3	5.4_5	9.1_5 4*R* 3.0 4*S*	?	7.2	
(**8**)				2*R* 5.9 2*S* 7.9	2.3	8.1_5	6.5 6*R* 3.0_5 6*S*	1,2 7.5 2*R*,2*S* -13.7_5 6*R*,6*S* -11.8_5
(**9**)	-11.6_5	6.8	3.9	4.1 3*R* 8.8 3*S*	3*R* 7.0 4*R* 3*S* 6.0 4*R* 3*R* 7.5 4*S* 3*S* 6.0 4*S*			3*R*, 3*S* −14.3 4*R*, 4*S* −11.2

If protons labelled *R* and *S* are interchanged as indicated in Table 1, corresponding changes are required in this Table. ? = not able to be determined.

favoured over the $_3G^+$, $_4G^+$ form. The only compound examined where the deoxy group is flanked on each side by a hydroxymethylene group, is (**4**). Unfortunately, two pairs of equations used to derive the conformer ratios were nearly degenerate, so that the amounts present could only be expressed within limits. In considering the series glucitol,[8] (**2**) ('2-deoxyglucitol'), and (**8**) ('1,2-dideoxyglucitol'), the amounts of the planar chain, $_2G^-$, and $_3G^+$, $_4G^+$ forms are 22:61:13, 60:25:15, and 40:40:20, respectively. Absence of the O-2 atom in (**2**) allows the planar chain form to be the major form. In (**8**) the increased $_2G^-$ form relative to that in (**2**) is because there is less steric hindrance to a methyl group than to a hydroxymethyl group.

Rotamer populations of the hydroxymethyl group reflect the conformation of the chain near the group, and galactitol (O_e, O_g, and O_t 53:16:31) and mannitol (54:46:0) can be taken as examples of a planar *lyxo*- and *arabino*-configuration.[1] For (**2**) and (**8**) the planar chain and $_2G^-$ forms (total 80–85%) are both *arabino*-type, and the $_3G^+$, $_4G^+$ forms, which favour the O_e rotamer will result in an *arabino*-type ratio with an enhanced O_e component, as observed (Table 3). In (**3**) the planar and $_2G^+$ forms yield a *lyxo*-type ratio, while the $_3G^+$, $_4G^+$ form approximates to an *arabino*-type situation if the C-3–C-4 bond and O-4 are interchanged. The calculated ratio is thus 53:21:26, in fair agreement with that observed. It seems that the rotamer ratios derived from alditols cannot be used for compounds in which the hydroxymethyl and a deoxy group are only separated by one or two hydroxymethylene(s), *i.e.*, (**6**), (**9**), and C-1 of (**4**); and (**1**), (**7**), and C-6 of (**4**). The former case and propane-1,2-diol give a ratio of *ca.* 55:33:12. Concerning the rotamers of a hydroxymethyl group next to a methylene group, it was mentioned earlier that we could not assign which hydroxymethyl proton was which. A more important difficulty was that although ${}^3J$ values for the 12 couplings (4 protons, 3 rotamers)

Table 3. Conformer distributions[a] (%) in the deoxyalditols.

Compound	CH_2OH group				
		O_e	O_g	O_t	
(1)	C-5	65	30	5	P40, $_2G^-$ 10, $_3G^+$ and/or $_3G^-$ 45, $_2G^+$, $_3G^+$ 5[b]
(2)	C-6	57	43	0	P 60, $_2G^-$ 25, $_3G^+$, $_4G^+$ 15
(3)	C-6	58	20	22	P 60, $_2G^+$ 15, $_3G^+$, $_4G^+$ 25
(4)	C-1	55	33	12	$_2G^+$, $_3G^+$ 5, and assuming $_4G^- \geqslant {}_4G^+$,
	C-6	55	24	21	P 30–50, $_4G^-$ 30–40, $_4G^+$ 0–30
(5)		57	42	1	P 0, $_2G^+$ 42, $_3G^-$ 42, $_2G^+$, $_4G^-$15
(6)		56	33	11	C-1 to C-4 portion;[b] P 60, $_2G^+$ 20, $_2G^-$20
(7)		64	32	4	C-1 to C-5 portion; [b] P 25, $_2G^+$ and/or $_2G^-$ 50, $_3G^-$ 20, $_2G^+$, $_3G^+$ 5
(8)		57	42	1	P 40, $_2G^-$ 40, $_3G^+$, $_4G^+$ 20
(9)	C-1	55	33	12	P 70, $_2G^+$ 15, $_2G^-$ 15[b]

[a] For nomenclature, see ref. 6. [b] Sum of conformers = 100 used to derive figures.

could be calculated[10] or were available[13,14] and agreed well, equations using these values were internally inconsistent. The reason for this is unclear.

The separation (Δ, ppm) of the shifts of the protons of a hydroxymethyl group is another probe for the chain conformation near the hydroxymethyl group.[1] The separation of *lyxo*- and *arabino*-configurations is *ca.* 0.0025 and 0.200, respectively. The *arabino*-type separation of **(2)** and **(8)** is slightly reduced by the $_3G^+$, $_4G^+$ forms (*cf.* 1-deoxyglucitol,[8] Δ 0.186 with 14% of $_3G^+$, $_4G^+$), while **(3)** should have a mainly *lyxo*-type arrangement, with the $_3G^+$, $_4G^+$ form increasing the separation. The diol situation in **(6)**, **(9)** and C-1 of **(4)** is characterised by Δ *ca.* 0.1125.

Comparing the shifts of the protons of secondary monodeoxy compounds with those of the corresponding alditols shows that the deoxy protons are shielded by 1.91–2.26 ppm, the proton(s) on C-ω-1 vary between a shielding of 0.12 to a deshielding of 0.21, proton(s) on C-ω-2 are shielded by 0.01–0.41, and protons further removed than this are shielded by up to 0.11 ppm. The wide ranges of these figures are a reflection that the change alditol ⟶ secondary deoxyalditol can produce considerable conformational changes. These shift differences are therefore of limited value for spectral analysis, a situation which contrasts the change alditol ⟶ primary deoxyalditol, where the conformational changes are more limited. The large shift difference (0.41 ppm) between H-5 of galactitol and H-5 of **(4)** arises because in galactitol H-5 is antiparallel to O-4 and parallel to O-3, both deshielding influences. In **(4)** the planar form has H-5 parallel to H_S-3, the $_4G^-$ form has H-5 parallel to H_R-3 and *gauche* to O-4, and the $_4G^+$ form has H-5 extending the chain and *gauche* to O-4, all three situations being shielding ones.[15] Similar reasoning applies to the large shift difference (0.37 ppm) between mannitol H-4 and **(2)** H-4. Such explanations can also be applied to those compounds in which methylene deoxy protons show significant shift differences.

Since the conformational purity of secondary deoxy polyols (Table 3) is low, energy differences between the conformers are usually small, and conformational energy calculations for acyclic systems based on group interaction energies derived from 6-membered ring systems, are not refined enough accurately to predict conformer populations, though qualitatively such interactions correctly give the main chain conformer(s). The main chain conformers can be deduced without considering the conformations of the hydroxy bonds about their C–O bonds, and without a knowledge of the important role of water in stabilising the chain conformers.

Experimental

Spectra were recorded[8] and computed[1] as previously cited. Gaussian resolution enhancement give line widths of 0.5–1.0 Hz at half height. Shifts and coupling constants were typically fitted to within 0.15 Hz error.

Materials.—Compounds **(6)** and **(9)** were commercial products. Sodium borohydride reduction of the commercial aldoses and work-up[16] yielded compounds **(1)** [syrup (lit.,[17] syrup; lit.,[18] m.p. 55–57 °C), pure by GLC of its tetra(trimethylsilyl ether)], **(2)** [m.p. 106–107 °C (lit.,[19] 105–106 °C)], **(3)** [m.p. 110–110.5 °C (lit.,[20] 112–113 °C)], and **(5)** [m.p. 86–89 °C (lit.,[21] 88 °C)]. Compound **(4)**[22] had m.p. 93–94 °C. The syntheses of compounds **(7)** {m.p. 81–83 °C, $[\alpha]_D^{20}$ − 8.9° (*c* 2.2 in H_2O) (lit.,[23] 82 °C, [α] − 4.5° for a hexane-1,2,3-triol of assumed L-*erythro*-configuration)} and **(8)** {m.p. 120–122 °C, $[\alpha]_D^{19}$ + 4.7° (*c* 3.9 in H_2O) (lit.,[24] 121–122.5 °C, [α] + 6.8°)} will be reported elsewhere.

Acknowledgements

The 400 MHz ^1H NMR spectra were obtained from the University of London Intercollegiate Research Service (ULIRS) WH-400 NMR spectrometer at Queen Mary College.

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Paper 9/03863I
Received 11*th September* 1989
Accepted 5*th February* 1990