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Note

A conformational study of some benzyl β-D-xylopyranoside derivatives

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Considerable work[1] has been done on the interpretation of ^{1}H-n m r data for acetylated sugar derivatives, including the tetra-*O*-acetylxylosides Some 3-deoxy-3-fluoro-D-glycopyranosyl fluoride acetates have been studied by Hall *et al* [2 3], and it was concluded, mainly on the basis of F–H couplings, that 2,4-di-*O*-acetyl-3-deoxy-3-fluoro-β-D-xylopyranosyl fluoride occurs almost exclusively in the *1C*(D) conformation We now report on the conformational features of some benzyl β-D-xylopyranosides on the basis of ^{1}H-n m r. parameters (Tables I and II)

TABLE I

CHEMICAL SHIFTS δ (P P M) FOR SOME BENZYL β-D-XYLOPYRANOSIDES

Compound	*Solvent*	*Benzyl-CH₂*		*H-1*	*H-2*	*H-3*eq	*H-3*ax	*H-4*	*H-5*eq	*H-5*ax
1	D_2O	4 88	4 71	4 48	3 30	—	3 42	3 63	3 96	3 31
2	D_2O	4 83	4 65	4 55	3 58	2 24	1 60	3 85	3 97	3 40
3[a]	Acetone-d_6	4 84	4 61	4 39	3 49	—	4 23	3 78	3 91	3 25

[a] δ HO-2 and HO-4 are 4 75 and 4 69, respectively.

The $J_{4,5ax}$ value of 10 8 Hz in the spectrum of benzyl β-D-xylopyranoside (**1**) points to a *C1*(D) conformation For similar acetates, Durette and Horton found[4 5] a value of 11 1 Hz as the upper limit for $J_{4,5ax}$ Since the electronegativities of OH[6] (E = 3 43) and OAc[7] (E = 3.70) are very similar, we can expect[8] nearly the same limit value for this coupling constant

The *C1*(D) conformation of **1** is further substantiated by the values for $J_{1,2}$ of 7.8 Hz, which is almost identical to that for aldohexoses and aldopentoses (including

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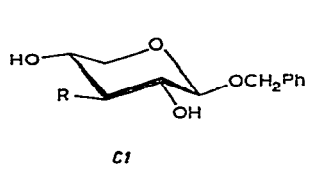
TABLE II

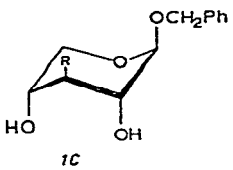
COUPLING CONSTANTS (J VALUES, Hz) FOR BENZYL β-D-XYLOPYRANOSIDES[a]

Compound	*Solvent*	$J_{1,2}$	$J_{2,3eq}$	$J_{2,3ax}$	$J_{3eq,4}$	$J_{3eq,3ax}$	$J_{3ax,4}$	$J_{4,5eq}$	$J_{4,5ax}$	$J_{5eq,5ax}$
1	D_2O	7 8	—	9 1	—	—	9.0	5 4	10 8	−11.6
2[b]	D_2O	5.8	4 4	8 6	4 4	−13 0	8 6	3 8	7 2	−11 4
3[c,d]	Acetone d_6	7 6	—	8 4	—	—	8 4	5 6	10.1	−11 3

[a]As obtained from first-order and/or subspectral graphical analysis, which at 300 MHz is a very good approximation, as follows from the shift values in Table I. [b]$J_{3eq,5eq}$ is ±1.6 Hz. The major (60%) *C1* form (see text) is taken as the conformation for the definition of *eq* and *ax* positions. [c]$J_{2,HO-2}$ is 4 6 Hz and $J_{4,HO-4}$ is 5 0 Hz [d] $^{19}F-^{1}H$ coupling constants (Hz) for 3 $J_{2,F}$ +13 4, $J_{3,F}$ −52 4, $J_{F,4}$ +13 5, $J_{F,5eq}$ −5 7, $J_{F,5ax}$ −1 0 Hz.



C1



1C

1 R = OH
2 R = H
3 R = F

β-D-xylose[9]) in that form, and for $J_{2,3}$ and $J_{3,4}$, which are very similar to those for β-D-glucopyranose and methyl β-D-glucopyranoside[10]. Further, a value of -11.6 Hz for $J_{5ax,5eq}$ is typical for a methylene ring-moiety, somewhat lowered[11] in absolute value because of the presence of an adjacent *eq*-OH group. Thus, a value of 5.4 Hz can be predicted as typical for a *cis* H-4*ax*/H-5*eq* relationship in *C1*(D) conformations.

Benzyl 3-deoxy-β-D-*erythro*-pentopyranoside (**2**) has lower $J_{4,5eq}$, $J_{4,5ax}$, and $J_{1,2}$ values than for **1**. This indicates the presence of a considerable amount of the *1C* form, which has the benzyl group axial and is presumably favoured by the anomeric effect[12]. From an interpolation of the lowered values between the typical limit values ($J_{4ax,5ax}$ 11.1, $J_{4eq,5eq}$ 1.5, $J_{4ax,5eq}$ 5.4 Hz) for *C1* and *1C* forms, we conclude that ~40% of the *1C* conformation is present in D_2O solution. From the computed population of the *1C* form, a typical value of 1.4 Hz for $J_{1eq,2eq}$ was calculated, although a value of 1.7 Hz has been observed for α-D-mannopyranose[9]. Considering the geminal coupling of H-3,3', a time-average value can be expected, in the *C1* form, two OR groups bisect the ring-hydrogens, resulting in a less-negative geminal coupling than in the corresponding *1C* form[10]. A time-averaged, long-range ^4J coupling constant of 1.6 Hz has been observed in the spectrum of **2** (Table II), attributable to a W-path in each conformation[13]. These results are predictable from calculations based on interaction energies[14].

Hall *et al.*[2] have shown that, whereas for 3-deoxy-3-fluoro-D-glucopyranosyl fluoride tetra-acetate both the α and β forms occur in the *C1*(D) conformation, the corresponding β-D-xylopyranosyl fluoride prefers exclusively the *1C*(D) conformation. The spectral data for benzyl 3-deoxy-3-fluoro-β-D-xylopyranoside (**3**) indicate mainly the *C1* conformation, which follows from the close similarity between the coupling constants of **1** and **3**. The slightly lower values for $J_{2,3}$ and $J_{3,4}$ may be rationalised[8] by the more pronounced electronegativity of F as compared with OH. Also, the $J_{H,F}$ values are almost equal to those observed in 3-deoxy-3-fluoro-2,4-di-*O*-methyl-β-D-glucopyranosyl fluoride[2] and are compatible only with the *C1* form. Thus, the anomeric effect is more important in the fluoride than in the benzyl glycoside[14].

In acetone-d_6, the signals for the HO protons in **3** occur as sharp, separated doublets with slightly different vicinal couplings (Tables I and II). On the addition of trifluoroacetic acid, the doublets collapse to a singlet. Therefore, in the original spectrum, the exchange mechanism is slowed down by possible hydrogen-bond formation with fluorine.

EXPERIMENTAL

All melting points (Mettler FP2 microscope) are uncorrected Optical rotations were determined with a Perkin–Elmer Model 141 polarimeter ^{1}H-N m r spectra were obtained with a Varian HR 300 instrument at 18° on 10% solutions, with Me_4Si and sodium 2,2,3,3-tetradeuterio-3-(trimethylsilyl)propionate (for D_2O) as the internal standard I r. spectra were obtained with a Perkin–Elmer grating spectrophotometer, and u v spectra with a Beckman DBGT instrument T l c was performed on Silica gel G (Merck), using *A*, benzene–ethyl acetate (3 1) for acetates, and *B*, acetic acid–water–ethyl acetate (1 1 3) for glycosides Detection was effected with sulphuric acid in ethanol

*Benzyl β-*D*-xylopyranoside* (**1**) — Using a modified Koenigs–Knorr synthesis[15] with mercuric benzylate and 2,3,4-tri-*O*-acetyl-α-D-xylopyranosyl bromide, followed by deacetylation with sodium methoxide in methanol, **1** (60%) was obtained with m p 112–113°, $[\alpha]_D^{22}$ −69° (*c* 1, methanol), λ_{max} 254 nm

Anal Calc for $C_{12}H_{16}O_5$. C, 60 0, H, 6 7 Found C, 59 8, H, 6 8

*Benzyl 3-deoxy-β-*D-erythro-*pentopyranoside* (**2**) — To a suspension of lithium aluminium hydride (1 2 g) in dry ether (30 ml), a solution of benzyl 4-*O*-acetyl-2,3-anhydro-β-D-ribopyranoside[16] (2 g) in 100 ml of ether was added with stirring After 2 h at room temperature, a few ml of water were added carefully, to decompose excess of reductant, and then chloroform (50 ml) was added The filtered mixture was washed with water, dried, and concentrated *in vacuo* to afford **2** as a yellow syrup (95%) which showed one spot on t l c (R_F 0 85, solvent *B*), $[\alpha]_D^{20}$ −121° (*c* 1, methanol) The 2,4-diacetate also failed to crystallize

*Benzyl 3-deoxy-3-fluoro-β-*D-*xylopyranoside* (**3**) — A mixture of benzyl 4-*O*-acetyl-2,3-anhydro-β-D-ribopyranoside (2 g), KHF_2 (2 g), and NaF (2 g) in dry ethylene glycol[17] (40 ml) was refluxed for 2 h and then poured into saturated, aqueous sodium hydrogen carbonate (100 ml) After extraction with dichloromethane and concentration of the extract, the product crystallized from ether–acetone and was recrystallized from methanol to give **3** (18%), m p 163–165°, $[\alpha]_D^{20}$ −73° (*c* 1, methanol)

Anal Calc for $C_{12}H_{15}FO_4$ C, 59 5, H, 6 2 Found C, 59 1, H, 6 4

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