CONFORMATIONAL STUDIES ON PYRANOID SUGAR DERIVATIVES BY N.M.R. SPECTROSCOPY. THE CONFORMATIONAL EQUILIBRIA OF SOME ALKYL TRI-*O*-ACETYL- AND TRI-*O*-BENZOYL-β-D-RIBOPYRANOSIDES IN SOLUTION*†

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ABSTRACT

The conformational populations of tribenzoylated β-D-ribopyranosides (**1–4**) having as aglycons the methyl, ethyl, isopropyl, and *tert*-butyl groups, respectively, together with the corresponding triacetates (**5–8**), were studied in acetone-d_6 by the n.m.r. spectroscopic method of averaging of spin coupling to determine the conformational effect of varying the aglycon in an otherwise fixed structure. The benzoylated methyl and ethyl glycosides (**1** and **2**) adopt the *1C*(D) conformation to the extent of about 80%, whereas the acetylated analogs (**5** and **6**) have only about 60% of the *1C*(D) form. In each series, the *tert*-butyl glycosides favor the *1C*(D) form to a lesser extent, about 75% for the benzoate **4**, and 55% for the acetate **8**. The results are interpreted in terms of steric and polar effects. The isopropyl methyl groups in **3** and **7**, and the ethyl methylene groups in **2** and **6** are magnetically nonequivalent as a result of their dissymmetric environment and not as a consequence of hindered rotation.

INTRODUCTION

A number of investigations dealing with the conformational analysis of 2-alkoxytetrahydropyrans[3–10], 2-methoxy-1,3-dioxanes[11], and 2-alkoxy-1,4-dioxanes[12] have been reported. The aim of these studies was the delineation of the relative roles played by electrostatic and steric interactions in determining conformational and configurational populations for the mobile, heterocyclic ring-systems.

From their studies on the conformational equilibria of various 2-alkoxytetrahydropyrans, Pierson and Runquist[6] concluded that the steric influence of a group R had little or no effect on the free-energy difference between the two chair conformers. A satisfactory correlation between the free-energy differences for the equilibria and

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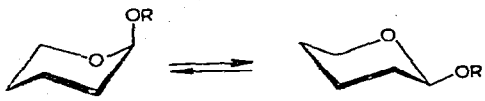
the Taft polar constants of the R groups was observed. Consequently, the shift in the position of the conformational equilibrium, observed upon changing the R group,



toward that chair conformation having the alkoxy substituent axial, was attributed to an increase in the magnitude of the anomeric effect with an increase in the polarity of the substituent. However, since the coupling constants measured to determine the conformational populations were estimated to be accurate only to ± 0.5 Hz, the equilibrium constants thereby calculated were not very accurate.

The influence of steric factors was, in fact, considered as an alternative interpretation for similar observations made by Eliel and Giza[7] on the configurational equilibria of 2-alkoxy- and 2-alkylthio-6-methyltetrahydropyrans. The proportion of the *cis* form present at equilibrium increased in the series R = methyl, ethyl, isopropyl, and *tert*-butyl. This observation indicated a decrease, in the same direction, of the magnitude of the anomeric effect for the alkoxy substituent. However, the trend observed could also be explained by an increase in the conformational free-energy of the R group, as the equilibrium constant for the derivative having the dimethylethinylcarbinyl group was rationalizable only in terms of such a steric argument.

de Hoog *et al.*[8] obtained similar results from their investigations of the conformations of 2-alkoxytetrahydropyrans. The observed decrease in the equilibrium proportion of that chair conformation having the alkoxy substituent axial, with increasing size of the R group, was ascribed to steric factors. Differences in the magnitude of the anomeric effect were not considered in their interpretation of the results. Supporting evidence for this view is provided by data on the corresponding alkylthio derivatives[13].

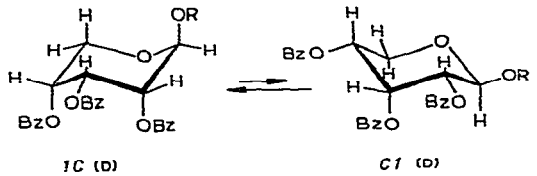
As part of a general program concerned with the study of conformations of pyranoid sugar derivatives, we have been interested in evaluating the influence of the aglycon in determining conformational tendencies of multisubstituted tetrahydropyran ring-systems. The present work reports experimental findings from n.m.r. spectroscopy on the effect of varying the nature of the alkoxy substituent at C-1 on the conformational populations of several peracylated alkyl β-D-ribopyranosides.

MATERIALS AND METHODS

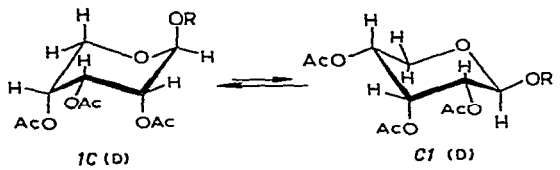
Methyl, ethyl, isopropyl, and *tert*-butyl tri-*O*-benzoyl-β-D-ribopyranosides (**1–4**) were prepared from tri-*O*-benzoyl-β-D-ribopyranosyl bromide and the appropriate alcohols. The known methyl and ethyl derivatives were obtained crystalline. The isopropyl derivative was also obtained crystalline, and the *tert*-butyl analog was isolated as an amorphous glass; the last two are reported for the first time.

The corresponding alkyl tri-*O*-acetyl-β-D-ribopyranosides (**5–8**) were prepared from **1–4** by Zemplén deacylation followed by acetylation. All four compounds were

obtained as distilled syrups. The ethyl, isopropyl, and *tert*-butyl tri-*O*-acetyl-β-D-ribopyranosides are reported for the first time. Methyl tri-*O*-acetyl-β-D-ribopyranoside had been previously prepared, but the physical constants for the pure compound have not hitherto been reported.



1 R = Me
2 R = Et
3 R = Me_2CH
4 R = Me_3C



5 R = Me
6 R = Et
7 R = Me_2CH
8 R = Me_3C

The structures of the eight peracylated alkyl β-D-ribopyranosides were confirmed by elemental analysis, optical rotations, and i.r. and n.m.r. spectroscopy.

The n.m.r. spectra were measured at 100 MHz with 20% (w/v) solutions of the freshly prepared compounds in acetone-d_6 containing 5% of tetramethylsilane. The chemical shifts recorded, given on the τ scale, were obtained by analysis of the spectra on a first-order basis, and are considered accurate to ±0.005 p.p.m. The time-averaged $J_{4,5}$ and $J_{4,5'}$ spin-couplings employed in the calculation of conformational populations were obtained by ABX analysis[14] of spectra measured at 100-Hz sweep-width. All other coupling-constants recorded were obtained on a first-order basis as direct peak-spacings from spectra measured at a sweep width of 100 Hz. The values reported are considered accurate to ±0.1 Hz.

For each of the peracylated alkyl β-D-ribopyranosides (**1–4**, **5–8**) in acetone-d_6 at 33°, the n.m.r. spectral method of averaging of spin coupling[15] was used to determine the proportions of the *1C*(D) and *C1*(D) conformers, and hence the equilibrium constant *K* and free energy ΔG° values for the *1C*(D) ⇄ *C1*(D) equilibria, by procedures previously detailed[16]. Analysis of the signals of H-4 and the two protons at C-5, as ABX spin-systems, gave $J_{4,5}$ and $J_{4,5'}$ values for **1–4** and **5–8** that are weighted time-averages for the two chair conformers in rapid equilibrium. Conformational populations at 33° were determined from the observed coupling of H-4 with the *trans*-disposed proton at C-5, taken in conjunction with values for $J_{4e,5e}$ and $J_{4a,5a}$ that had been obtained from the following model compounds. Methyl tri-*O*-benzoyl-α-D-xylopyranoside in acetone-d_6 gives a $J_{4,5a}$ value (11.1 Hz)[17] that was taken as the limiting

magnitude of $J_{4a,5a}$ for each alkyl tri-*O*-benzoyl-β-D-ribopyranoside. As the observed spin-couplings for this α-*xylo* derivative remained unchanged as the temperature was lowered[2], it was concluded that this model compound is overwhelmingly (>95%) in the *Cl*(D) conformation at 33°. Similarly, the $J_{4,5a}$ value (11.1 Hz)[17] for methyl tri-*O*-acetyl-α-D-xylopyranoside in acetone-d_6 was used as the magnitude of $J_{4a,5a}$ for each alkyl tri-*O*-acetyl-β-D-ribopyranoside. For each alkyl tri-*O*-benzoyl- and tri-*O*-acetyl-β-D-ribopyranoside, the magnitude of $J_{4e,5e}$ was taken as 1.5 Hz; this value is the limit at low temperature of the smaller of the $J_{4,5}$ values for methyl tri-*O*-benzoyl-β-D-arabinopyranoside and methyl tri-*O*-acetyl-β-D-arabinopyranoside in[17] acetone-d_6. From the conformational populations determined from the spin-coupling data, the equilibrium constants and values for free-energy differences given in Tables I and II were calculated. The limits of accuracy for the calculations were determined from the uncertainty of ±0.1 Hz in the experimental values of the time-averaged couplings, in conjunction with a conservative estimate (±0.5 Hz) of the extent to which the "model" coupling-values actually differ from the true couplings for the separate conformers of each compound.

TABLE I

CONFORMATIONAL EQUILIBRIA OF THE ALKYL TRI-*O*-BENZOYL-β-D-RIBOPYRANOSIDES IN ACETONE-d_6 AT 33°

Compound	*Aglycon*	*Equilibrium data*			$\Delta G^0_{33°}$, *kcal.mole*$^{-1}$ *for* 1C(D)⇄C1(D)
		% C1	% 1C	K = C1/1C	
1	OMe	20	80	0.25	+0.86 ±0.37
2	OEt	19	81	0.23	+0.90 ±0.38
3	$OCHMe_2$	22	78	0.28	+0.78 ±0.35
4	$OCMe_3$	26	74	0.35	+0.64 ±0.33

TABLE II

CONFORMATIONAL EQUILIBRIA OF THE ALKYL TRI-*O*-ACETYL-β-D-RIBOPYRANOSIDES IN ACETONE-d_6 AT 33°

Compound	*Aglycon*	*Equilibrium data*			$\Delta G^0_{33°}$, *kcal. mole*$^{-1}$ *for* 1C(D)⇄C1(D)
		% C1	% 1C	K = C1/1C	
5	OMe	39	61	0.63	+0.29 ±0.29
6	OEt	39	61	0.63	+0.29 ±0.29
7	$OCHMe_2$	38	62	0.60	+0.31 ±0.29
8	$OCMe_3$	46	54	0.85	+0.10 ±0.28

Spectral data for the eight compounds (**1–4**, **5–8**) are given in Tables III–VI. The partial, 100-MHz, n.m.r. spectra of compounds **1**, **2**, **3**, and **8** in acetone-d_6 are given in Figs. 1–4, respectively.

TABLE III

FIRST-ORDER CHEMICAL SHIFTS[a] OF THE ALKYL TRI-*O*-BENZOYL-β-D-RIBOPYRANOSIDES IN ACETONE-d_6 AT 33°

Compound	*Aglycon*	*Chemical shifts*[b], τ							*Benzoyl*
		H-1	*H-2*	*H-3*	*H-4*	[c]*H-5*	[c]*H-5′*	*OR*	
1	OMe	4.92d	4.50sp	4.16t	4.36m	5.66q	5.89q	6.50s	1.94–2.76
2	OEt	4.79d	4.50sp	4.13t	4.35m	5.64q	5.90q	CH_2- 6.24m CH_3- 8.73t	1.96–2.77
3	$OCHMe_2$	4.68d	4.55sp	4.11t	4.36m	5.60q	5.90q	$(CH_3)_2$- 8.71, 8.78q, CH- 5.96q	1.95–2.76
4	$OCMe_3$	4.51d	4.65sx	4.08t	4.38m	5.54q	5.92q	8.67s	1.97–2.76

[a]Data taken from spectra measured at 100 MHz. [b]Observed multiplicities: d, doublet; m, complex multiplet; q, quartet; s, singlet; sp, septet; sx, sextet; t, triplet. [c]The proton on C-5 giving the higher-field signal is designated H-5′.

TABLE IV

FIRST-ORDER CHEMICAL SHIFTS[a] OF THE ALKYL TRI-*O*-ACETYL-β-D-RIBOPYRANOSIDES IN ACETONE-d_6 AT 33°

Compound	*Aglycon*	*Chemical shifts*[b], τ							*Acetyl methyl*
		H-1	*H-2*	*H-3*	*H-4*	[c]*H-5*	[c]*H-5′*	*OR*	
5	OMe	5.31d	5.09sx	4.67t	4.94m	6.03q	6.28q	6.63s	7.98[d], 8.03
6	OEt	5.20d	5.10sx	4.65t	4.93m	6.00q	6.28q	CH_2- 6.39m CH_3- 8.81t	7.97, 7.98, 8.03
7	$OCHMe_2$	5.09d	5.16sp	4.65t	4.94m	5.98q	6.28q	$(CH_3)_2$- 8.81, 8.87t, CH- 6.05q	7.97, 7.99, 8.03
8	$OCMe_3$	4.96d	5.25sp	4.61t	4.97m	5.97q	6.29q	8.77s	7.99, 8.00, 8.01

[a]Data taken from spectra measured at 100 MHz. [b]Observed multiplicities: d, doublet; m, complex multiplet; q, quartet; s, singlet; sp, septet; sx, sextet; t, triplet. [c]The proton on C-5 giving the higher-field signal is designated H-5′. [d]6-Proton singlet.

RESULTS AND DISCUSSION

Conformational equilibrium near room temperature. — Methyl and ethyl 2,3,4-tri-*O*-benzoyl-β-D-ribopyranosides (**1** and **2**) in acetone-d_6 at 33° both have about 80% of the *1C*(D) form in equilibrium with the *C1*(D) form (see Table I). For the isopropyl derivative **3**, there is somewhat less of the *1C*(D) form, and this trend is continued in the *tert*-butyl derivative **4**, which has only about 75% of the *1C*(D) form. With the corresponding acetates (see Table II), the methyl (**5**), ethyl (**6**), and isopropyl (**7**) derivatives all have about 60% of the *1C*(D) form, decreasing to about 55% for the *tert*-butyl derivative (**8**).

TABLE V

COUPLING CONSTANTS OF METHINE AND METHYLENE PROTONS FOR THE ALKYL TRI-*O*-BENZOYL-β-D-RIBOPYRANOSIDES IN ACETONE-d_6 AT 33°

Compound	*Aglycon*	*Coupling constants*[a], *Hz*						
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$[b,c]	$J_{4,5'}$[b,c]	$J_{5,5'}$	$J_{2,4}$
1	OMe	2.8	3.8	3.7	2.4	3.4	−12.9	0.8
2	OEt[d]	2.8	3.8	3.6	2.2	3.3	−12.9	0.8
3	$OCHMe_2$[e]	3.0	3.8	3.7	2.5	3.6	−12.9	0.8
4	$OCMe_3$	3.5	3.7	3.6	2.7	4.0	−12.6	0.7

[a]Data taken from spectra measured at 100 MHz at a sweep width of 100 Hz. [b]Coupling constants calculated by ABX analysis. [c]The proton on C-5 giving the higher-field signal is designated H-5′. [d]$J_{CH_2CH_3}$ = 7.1, 6.9 Hz (measured at 500-Hz sweep-width). [e]$J_{CH(CH_3)_2}$ = 6.1, 6.0 Hz (measured at 500-Hz sweep-width).

TABLE VI

COUPLING CONSTANTS OF METHINE AND METHYLENE PROTONS FOR THE ALKYL TRI-*O*-ACETYL-β-D-RIBOPYRANOSIDES IN ACETONE-d_6 AT 33°

Compound	*Aglycon*	*Coupling constants*[a], *Hz*						
		$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$[b,c]	$J_{4,5'}$[b,c]	$J_{5,5'}$	$J_{2,4}$
5	OMe	4.0	3.6	3.4	3.0	5.2	−12.5	0.8
6	OEt[d]	4.0	3.4	3.3	3.0	5.2	−12.3	0.7
7	$OCHMe_2$[e]	4.5	3.3	3.2	3.2	5.1	−12.3	0.8
8	$OCMe_3$	4.5	3.3	3.3	3.3	5.9	−12.2	0.7

[a]Data taken from spectra measured at 100 MHz at a sweep width of 100 Hz. [b]Coupling constants calculated by ABX analysis. [c]The proton on C-5 giving the higher-field signal is designated H-5′. [d]$J_{CH_2CH_3}$ = 7.1, 6.9 Hz (measured at 500-Hz sweep-width). [e]$J_{CH(CH_3)_2}$ = 6.4, 5.5 Hz (measured at 500-Hz sweep-width).

In contrast to the 2-alkoxytetrahydropyrans, where only the magnitude of the anomeric effect and the conformational free-energy of the alkoxy substituent need to be considered to explain changes in conformational populations upon changing the R group, at least one other factor must be taken into account when dealing with the peracylated alkyl D-aldopyranosides having the C-1 and C-2 substituents *trans*. This factor is the vicinal, gauche interaction (between the acyloxy group at C-2 and the alkoxy substituent at C-1) that is present in one of the chair conformers. In the *β-ribo* series under study, such an interaction is found in the *C1*(D) conformation but is absent in the alternative *1C*(D) conformation, where the substituents at C-1 and C-2 are antiparallel.

Although the magnitude of the anomeric effect of the alkoxy substituent can be expected to decrease slightly through the series methyl, ethyl, isopropyl, and *tert*-butyl because of a decrease in the polarity of the substituent[6], the present results can be rationalized on steric grounds alone.

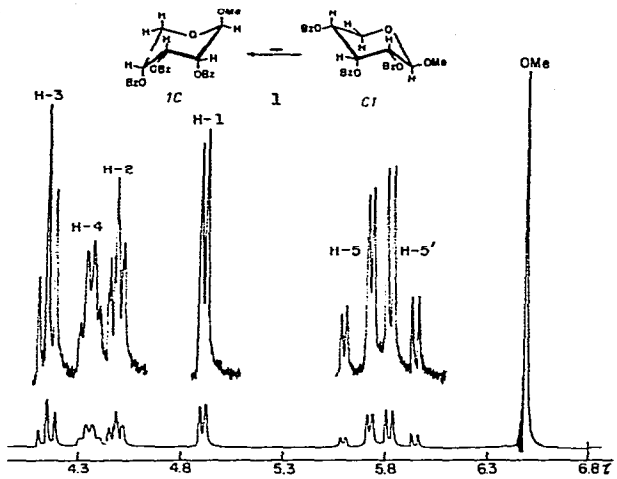


Fig. 1. Partial n.m.r. spectrum of methyl tri-*O*-benzoyl-β-D-ribopyranoside (1) at 100 MHz in acetone-d_6.

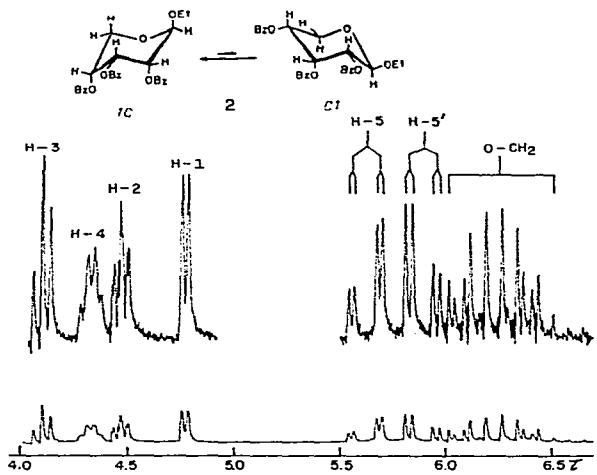


Fig. 2. Partial n.m.r. spectrum of ethyl tri-*O*-benzoyl-β-D-ribopyranoside (2) at 100 MHz in acetone-d_6.

The conformational free-energies of the alkoxy group should increase only very slightly through the series methyl, ethyl, and isopropyl, because the group attached to O-1 can be rotated to orientations where it causes no extra interference with the ring-system[18]. Any small increase in the "A-values" may be ascribed mainly to a decrease in the entropy (ΔS) term. On the other hand, the conformational free-energy of the *tert*-butoxy group can be expected to be appreciably larger, because it is no longer possible to avoid some steric repulsions if rotation occurs about the C-1–O-1 bond. The lack of reliable "A-values" for these four alkoxy groups precludes a more quantitative discussion; it would be worth while to measure these values for the alkoxycyclohexanes by the precise, low-temperature method of Jensen and co-workers[19].

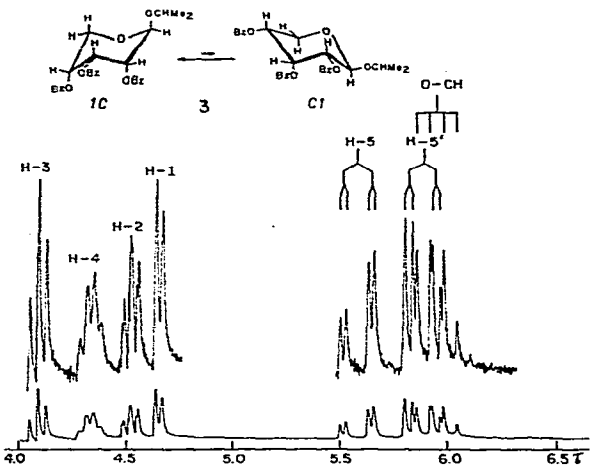


Fig. 3. Partial n.m.r. spectrum of isopropyl tri-*O*-benzoyl-β-D-ribopyranoside (3) at 100 MHz in acetone-d_6.

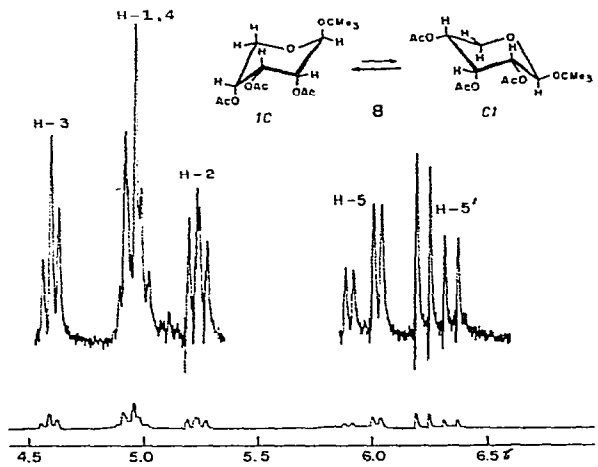


Fig. 4. Partial n.m.r. spectrum of *tert*-butyl tri-*O*-acetyl-β-D-ribopyranoside (8) at 100 MHz in acetone-d_6.

From the foregoing considerations, it might be concluded that an increase in the steric influence of the R group would cause an increase in the equilibrium proportion of that chair conformer having the alkoxy substituent equatorial. However, the 1,2-gauche interaction, which would tend to shift the equilibrium position in the opposite direction, should also increase with the steric influence of the R group, and might possibly counterbalance the first effect. In the alkyl tri-*O*-benzoyl-β-D-ribopyranosides, the effects appear to be balanced in the methyl and ethyl derivatives, but the tendency toward the equatorial orientation of the OR group becomes more pronounced with the isopropyl and *tert*-butyl derivatives, indicating that axial, steric destabilization becomes more significant with the latter groups.

Similar effects are observed with the alkyl tri-*O*-acetyl-β-D-ribopyranosides; there is little net difference for the methyl, ethyl, and isopropyl derivatives, but, with the *tert*-butyl derivative, the axial, steric destabilization evidently outweighs the 1,2-gauche interaction, and the form having the OR group equatorial is more favored than for the first three examples.

These results show that the size of the aglycon does influence the ring-conformation adopted, and this steric effect can be observed experimentally when a suitable system having a substantial proportion of the minor chair conformer is present. A suggestion to the contrary[20] may not be valid, because the examples chosen (alkyl 2-deoxy-α-D-*arabino*-hexopyranosides) can all be expected to favor one chair conformation strongly.

It may thus be concluded that, in evaluating the effect of changing the aglycon on conformational populations in alkyl aldopentopyranosides, not only axial, steric destabilization but also gauche interactions between vicinal substituents should be taken into account.

The four alkyl tri-*O*-benzoyl-β-D-ribopyranosides (**1**–**4**) all have at equilibrium a greater proportion of that chair conformer having the anomeric substituent axial [the *1C*(D) conformation] than do the corresponding triacetates (**5**–**8**). A similar observation has been made for the tri-*O*-benzoyl- and tri-*O*-acetyl-D-aldopentopyranosyl halides[2], and it was attributed to an enhancement in the magnitude of the axial-directing influence of the aglycon by the more electronegative benzoyloxy substituents at the other three ring-positions.

Observations on chemical shifts. — The ring protons of the four alkyl tri-*O*-benzoyl-β-D-ribopyranosides resonate at lower field than the corresponding protons in the triacetates. Although the differences in conformational populations for the two series may make some contribution to the observed changes in field position for corresponding protons, the greater deshielding effect of the benzoyloxy groups relative to the acetoxy groups is probably the major factor responsible for the observed downfield shifts, because a similar trend was observed for the conformationally homogeneous tri-*O*-acetyl- and tri-*O*-benzoyl-α-D-xylopyranosyl chlorides[2].

In each of the two series of compounds was also detected a progressive, downfield shift of the H-1 signal through the series methyl, ethyl, isopropyl, and *tert*-butyl. A similar trend may be seen in the data reported by Pierson and Runquist[6] on the alkoxytetrahydropyrans. These observations cannot be explained by a shift in the conformational equilibria or a decrease in the electronegativity of the alkoxy group in the same direction, because the reverse trend would be anticipated. Evidently, the magnetic anisotropy of the C-1–O-1 bond and/or intramolecular, dispersion effects[21] increase with the electron-donating ability of the R group and lead to greater deshielding of the adjacent proton*.

Magnetic nonequivalence of isopropyl methyl and ethyl methylene protons. — The isopropyl methyl protons of compounds **3** and **7** and the ethyl methylene protons of

*For a review of the diamagnetic anisotropy of single bonds, see Ref. 22.

compounds **2** and **6** were observed to be magnetically nonequivalent. Thus, the n.m.r. spectrum of **7** in acetone-d_6 showed a high-field triplet for the isopropyl methyl protons, and not the doublet expected had the methyl groups been equivalent. The difference in the chemical shift between the two methyl groups was 6 Hz, and each methyl group was spin-coupled differently to the isopropyl methine proton ($J = 5.5$, 6.4 Hz). Similar nonequivalence in an isopropyl glycoside was recorded in a previous report from this laboratory[23]. The n.m.r. spectra of **2** and **6** showed a complex multiplet for the ethyl methylene protons, instead of the simple quartet that would have resulted had the two protons been equivalent.

The presence of the asymmetric center at C-1 provides a condition of dissymmetry sufficient for the nonequivalence observed, but the asymmetric effect might possibly be enhanced by restricted rotation, with steric preference for certain rotamer states[24]. High-temperature n.m.r. measurements were performed on **2** and **3** in methyl sulfoxide-d_6 in order to determine whether restricted rotation was involved. Had restricted rotation been a contributory factor in the nonequivalence of the protons, an increase in the temperature would have caused some merging of the signals. However, as the temperature was raised over the range 25–150°, the difference in chemical shift remained unchanged and the signals became even sharper (not tending toward coalescence), confirming that the observed nonequivalence was due solely to the nearby asymmetric center. In light of these results, the suggestion that the nonequivalence of the ethyl methylene protons in ethyl 4,5-di-*O*-acetyl-1,3-*O*-isopropylidene-α-L-sorbopyranoside[25] and in 2-ethoxytetrahydropyran[12] is due to restricted rotation about the C-1–OR bond should be reconsidered.

Low-temperature studies. — Studies at 100 MHz of methyl and *tert*-butyl tri-*O*-acetyl-β-D-ribopyranoside (**5** and **8**) in acetone-d_6 have shown the effect of "conformational freeze-out" at low temperature (~ −85°). However, because of extensive overlap of signals of the separate conformers in the 100-MHz spectra, assignment of individual peaks is difficult. Studies at higher field-strengths can be expected to yield accurate values for the equilibrium constants at low temperatures, and for the rates of conformational interconversion.

EXPERIMENTAL

General. — Evaporations were performed below 50° under diminished pressure. Melting points are uncorrected. Specific rotations were determined in a 1-dm, narrow-bore polarimeter tube. Microanalyses were made by W. N. Rond. T.l.c. was performed with 0.25-mm layers of Silica Gel G (E. Merck, Darmstadt, Germany), activated at 120°, as the adsorbent, and sulfuric acid as the indicator. Column chromatography was conducted with Silica Gel (7734, Merck) as the adsorbent, with 1 g of mixture to be separated per 30 g of adsorbent, and the compounds were eluted with the solvents specified.

N.m.r. spectra. — Spectra were recorded at 100 MHz with a Varian HA-100 n.m.r. spectrometer under the general conditions specified in Ref. 2.

Preparation of the alkyl 2,3,4-tri-O-benzoyl-β-D-ribopyranosides. — *Methyl tri-O-benzoyl-β-D-ribopyranoside* (**1**). Tri-*O*-benzoyl-β-D-ribopyranosyl bromide[26] (2.4 g, 4.6 mmoles) was refluxed in abs. methanol (25 ml) for several min. The solution was then refrigerated overnight, and the resultant, crystalline **1** was recrystallized from ether–pentane; yield 1.9 g (87%); m.p. 109–110°, $[\alpha]_D^{20}$ −69.8° (*c* 1.1, chloroform) [lit.[27] m.p. 109–110° $[\alpha]_D$ −69.5° (*c* 0.82, chloroform)].

Ethyl tri-O-benzoyl-β-D-ribopyranoside (**2**). Prepared in the same manner as **1**, by using tri-*O*-benzoyl-β-D-ribopyranosyl bromide (2.0 g, 3.8 mmoles) in abs. ethanol (29 ml), the ethyl analog **2** (yield 1.5 g, 78%) had m.p. 131–132°, $[\alpha]_D^{19}$ −83.1° (*c* 1.27, chloroform) [lit.[27] m.p. 132–133°; $[\alpha]_D$ −83.9° (*c* 0.900, chloroform)].

Isopropyl tri-O-benzoyl-β-D-ribopyranoside (**3**). The procedure used for **2**, with use of isopropyl alcohol, gave **3** as white needles; yield 1.4 g (71%); m.p. 78–79°, $[\alpha]_D^{20}$ −90.0° (*c* 1.09, chloroform); R_F 0.47 (9:1 benzene–ether); λ_{max}^{KBr} 5.80 (C=O), 6.91, 7.62, 7.74, 7.92, 8.49, 9.45, 9.75, 10.52, and 14.08 μm (aryl).

Anal. Calc. for $C_{29}H_{28}O_8$: C, 69.04; H, 5.59. Found: C, 68.81; H, 5.89.

tert-*Butyl tri-O-benzoyl-β-D-ribopyranoside* (**4**). Tri-*O*-benzoyl-β-D-ribopyranosyl bromide (2.0 g, 3.8 mmoles) was refluxed for 24 h in *tert*-butyl alcohol (48 ml). The mixture was then cooled, and evaporated to a thick syrup which was dissolved in the minimal volume of benzene and the solution passed through a column of silica gel. Ether–benzene (1:9) was used as the eluant to separate the main product from a slower-moving component that was not characterized. The faster-moving component (**4**) was obtained as an amorphous glass; yield 1.1 g (56%); $[\alpha]_D^{21}$ −66.5° (*c* 1.13, chloroform); R_F 0.48 (9:1 benzene–ether); λ_{max}^{KBr} 5.79 (C=O), 6.92, 7.61, 7.94, 8.50, 8.90, 9.37, 9.77, 10.51, and 14.10 μm (aryl).

Anal. Calc. for $C_{30}H_{30}O_8$: C, 69.49; H, 5.83. Found: C, 69.47; H, 6.06.

Preparation of alkyl 2,3,4-tri-O-acetyl-β-D-ribopyranosides. — *Methyl β-D-ribopyranoside.* A solution of methyl tri-*O*-benzoyl-β-D-ribopyranoside (**1**, 1.0 g, 2.1 mmoles) in dry methanol (50 ml) was treated with a catalytic amount of sodium, and the solution was kept for 14 h at room temperature. A few drops of water were then added, and carbon dioxide gas was bubbled through for 15 min. The solution was then concentrated to a syrup. Addition of ethyl acetate precipitated out the inorganic salts. After filtration of the mixture through a Celite pad, the filtrate was concentrated to a syrup, which was crystallized from anhydrous ether to give the title glycoside, yield 0.25 g (73%); m.p. 82–83° (lit.[28] m.p. 83°).

Methyl tri-O-acetyl-β-D-ribopyranoside (**5**). Methyl β-D-ribopyranoside (1.0 g, 6.1 mmoles) was dissolved in dry pyridine (2.5 ml) with cooling in an ice-bath and treated with acetic anhydride (2.0 ml, 20 mmoles). The resulting solution was kept overnight at 0° and then evaporated. Toluene and finally carbon tetrachloride were added to and evaporated from the residue. Distillation of the residue under high vacuum gave **5** as a thick, colorless syrup; yield 1.3 g (76%); $[\alpha]_D^{20}$ −88.1° (*c* 0.99 chloroform), R_F 0.63 (3:1 dichloromethane–ether); λ_{max}^{film} 3.41 (C–H), 5.71 (C=O), 6.98, 7.29, 7.88, 8.20, 8.82, 9.15, 10.20, 11.15, 12.03, and 12.68 μm.

Anal. Calc. for $C_{12}H_{18}O_8$: C, 49.65; H, 6.25. Found: C, 49.78; H, 6.29.

Ethyl tri-O-acetyl-β-D-ribopyranoside (**6**). Ethyl tri-*O*-benzoyl-β-D-ribopyranoside (**2**, 0.29 g, 0.60 mmole) was saponified, and the product acetylated by the procedure used for preparing compound **5**. Distillation of the residue under high vacuum gave **6** as a thick, colorless syrup; yield 0.13 g (73% based on **2**); $[\alpha]_D^{20}$ −92.1° (*c* 1.40, chloroform); R_F 0.65 (3:1 dichloromethane–ether); λ_{max}^{film} 3.40 (C–H), 5.72 (C=O), 7.30, 7.97, 8.18, 8.81, 10.22, 11.09, 11.40, and 12.05 μm.

Anal. Calc. for $C_{13}H_{20}O_8$: C, 51.31; H, 6.62. Found: C, 51.29; H, 6.76.

Isopropyl tri-O-acetyl-β-D-ribopyranoside (**7**). Isopropyl tri-*O*-benzoyl-β-D-ribopyranoside (**3**, 0.36 g, 0.72 mmole) was saponified, and the product acetylated as for **5** and **6**. Distillation of the residue under high vacuum gave **7** as a thick, colorless syrup; yield 0.19 g (81% based on **3**); $[\alpha]_D^{23}$ −99.0° (*c* 0.98, chloroform); R_F 0.73 (3:1 dichloromethane–ether); λ_{max}^{film} 3.37 (C–H), 5.72 (C=O), 7.03, 7.33, 8.07, 8.84, 9.37, 9.77, 10.22, 10.61, 11.17, 12.00, and 12.70 μm.

Anal. Calc. for $C_{14}H_{22}O_8$: C, 52.83; H, 6.97. Found: C, 52.81; H, 6.99.

tert-*Butyl tri-O-acetyl-β-D-ribopyranoside* (**8**). *tert*-Butyl tri-*O*-benzoyl-β-D-ribopyranoside (**4**, 0.27 g, 0.54 mmole) was saponified, and the product acetylated as for **5** and **6**. Distillation of the residue under high vacuum gave **8** as a thick, colorless syrup; yield 0.13 g (75% based on **4**); $[\alpha]_D^{21}$ −63.4° (*c* 1.22, chloroform); R_F 0.76 (3:1 dichloromethane–ether); λ_{max}^{film} 3.41 (C–H), 5.74 (C=O), 7.35, 8.07, 8.90, 9.40, 9.80, 10.25, 11.12, and 11.41 μm.

Anal. Calc. for $C_{15}H_{24}O_8$: C, 54.21; H, 7.28. Found: C, 54.26; H, 7.17.

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