remained constant with time; only the distribution changed. Concentrations were calculated by multiplying the normalized intensity for each species by the initial concentration of NBD-acid present. Allowance was made for the two NBD species present in each anhydride molecule.

The dilutor/injector was programmed to initiate the reaction by mixing suitable aliquots of pure solvent and solutions of DCC and NBD-acid. In all cases DCC concentration was maintained in 10-fold excess. The dilutor/injector automatically sampled the reaction mixture at appropriate intervals and injected these samples onto the column. Reactions took place in a 2-mL screw top vial sealed with a septum and were quenched upon injection by dilution and separation on the column. No hydrolysis or other reaction of the products occurs while on the column. Mixtures were stirred during reaction with a small stir bar. Temperatures were controlled to within ±1 °C of 30 °C.

Chemicals. NBD-acid was prepared by reacting *N*-methyl-6-aminohexanoic acid and 4-chloro-7-nitrobenz-2-oxa-1,3-diazole (NBD-Cl) as previously described.[45]

The NBD-acid analogue *N*-(nitrobenz-2-oxa-1,3-diazol-4-yl)-5-pentylamine (NBD-amine) was prepared by the direct reaction of NBD-Cl and pentylamine in methanol.[46] The resulting solution was washed with acidic and basic buffers and then extracted with ethyl acetate to isolate NBD-amine.

The rearranged *N*-acylurea product was isolated by column chromatography. The *N*-acylurea eluted from silica gel with a 75/25 mixture of methylene chloride and ethyl acetate. Identity of this product was confirmed by ^1H and ^{13}C NMR and high resolution mass spectroscopy.

The anhydride product was not isolated. However, in the presence of a catalyst and 1-undecanol (esterification conditions), one observes quantitative conversion of the presumed anhydride to the ester product. This product was isolated by column chromatography (previous conditions) and identified by ^1H and ^{13}C NMR and high resolution mass spectroscopy. This confirms the identity of the carboxylic acid anhydride.

Solvents methylene chloride, tetrahydrofuran and nitrobenzene (Baker), nitropropane (Kodak), and acetone and acetonitrile (BDH) were distilled or vacuum distilled and stored over molecular sieves in sealed vessels.

DCC and pentylamine were purchased from Kodak. NBD-Cl was purchased from Sigma.

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Conformations of Acyclic Sugar Derivatives. 8. Partially Acetylated Alditols[1]

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Received July 20, 1988

From the previously published (ref 8) NMR data for partially acetylated alditols, their conformations in chloroform solution have been deduced and were shown to be determined mainly by hydrogen bonding between the free hydroxyl groups.

There has been much interest lately in the solution conformations of alditols and their peracetylated derivatives. Extensive studies by Horton,[2] Angyal,[1,3] Lewis,[4] and their co-workers have shown that the preponderant conformation of polyhydroxyalkyl chains is the one in which the chain is extended and planar, except when the configuration of alternate carbon centers is the same (when expressed as D or L), in which case it is bent ("sickle" shaped[5]) to avoid an 1,3-parallel interaction between two oxygen atoms. The same conformations were found to occur in the crystals of alditols.[6] With very few exceptions, the alditol acetates in solution also assume the same conformations. Several heptitols present a problem because they cannot assume any conformation free of 1,3-parallel interactions;[7] their conformations have also been studied in detail.[1,3a,4d]

One could hardly justify the suggestion that the conformations of partially acetylated heptitols should also be studied. Fortuitously, however, the data required for such a study have become available through a completely different research project. Moore et al.[8] have studied the complexation of alditols with borate ion; these complexes were acetylated and subsequently the borate was removed, producing acetylated alditols with two free hydroxyl groups. ^1H NMR data for some 60 fully or partially acetylated alditols were published by Moore et al.;[8] these data show that some of the partially acetylated alditols assume conformations different from those of the fully acetylated ones. This appeared to be of interest, and, with Professor Moore's concurrence, we have now analyzed the conformations of all of these compounds.

The configurations of the alditols discussed here are shown in Figure 1. It is not possible to reproduce all of Moore's data. The reader who wants to follow our argu-

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0022-3263/89/1954-1927$01.50/0

Table I. NMR Data[a] for Acetylated Heptitols in $CDCl_3$

compd	coupling constants, Hz 2,3	3,4	4,5	5,6	CH,OH[b]	δ, ppm OH[b]
meso-glycero-gulo-heptitol heptaacetate (**22**)	5.6	5.1	5.1	5.6		
1,2,5,6,7-pentaacetate (**22a**)	8.2	1.6	3.6	6.3	8.2 (4), 7.3 (3)	2.90 (4), 2.94 (3)
1,2,4,6,7-pentaacetate (**22b**)	9.1	1.9	1.9	9.1	4.1 (3), 4.1 (5)	4.01 (3), 4.01 (5)
1,3,4,6,7-pentaacetate (**22c**)	8.3	4.1	1.9	9.4	8.0 (5), 5.1 (2)	2.91 (5), 3.40 (2)
1,2,3,4,7-pentaacetate (**22d**)	8.2	1.7	4.4	7.3	7.8 (5), 5.7 (6)	2.61 (5), 3.20 (6)
D-*glycero*-D-*manno*-heptitol heptaacetate (**23**)	8.8	2.4	8.6	3.3		
1,2,5,6,7-pentaacetate (**23a**)	8.9	1.0	8.7	2.7	7.8 (3), 8.2 (4)	3.17 (3), 3.22 (4)
1,2,4,6,7-pentaacetate (**23b**)	9.7	1.7	5.4	6.7	6.4 (3), 7.3 (5)	3.57 (3), 3.55 (5)
1,2,3,5,7-pentaacetate (**23c**)	7.5	1.6	8.9	5.0	6.7 (4), 4.6 (6)	3.46 (4), 2.92 (6)
1,3,5,6,7-pentaacetate (**23d**)	7.2	1.7	9.7	2.6	4.1 (2), 7.8 (4)	3.10 (2), 3.02 (4)

[a] From ref 8, **23** renumbered to accord with the revised configuration. [b] Number in parentheses refers to carbon position for OH group.

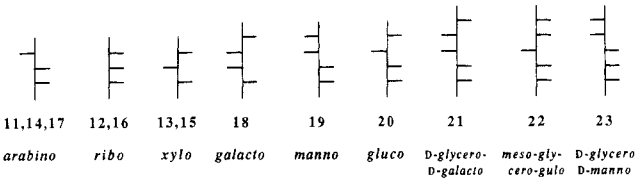

Figure 1. Configurations of the alditols discussed in this paper.

ments closely will therefore need to look at Table II of ref 8; to facilitate this, we have used Moore's formula numbers for the compounds discussed here. We have, however, reproduced the NMR data for two heptitols and their derivatives because these provide examples of all the conformational variants (Table I). They will be discussed in detail, and then the conclusions will be extended to the other compounds.

Two Heptitols. The heptaacetate of *meso-glycero-gulo*-heptitol (**22**) is, as shown by the coupling constants, predominantly in the ${}_2G^-,{}_3G^-$ form[9] and the ${}_4G^+,{}_5G^+$ form (Figure 2); these two forms are enantiomers and therefore occur in equal amounts.[3a] This means that, in order to avoid the O-3//O-5 interaction, only half of each molecule is planar and the other half has two gauche C/C interactions. These are the conformations also found in the crystal of the free heptitol;[11] here, also, the enantiomers occur in equal proportions. The couplings observed between all of the methine hydrogen atoms are the average of the anti coupling (ca. 9.5 Hz) and the gauche coupling (ca. 2 Hz).[12] The planar form (*P*), well represented in the

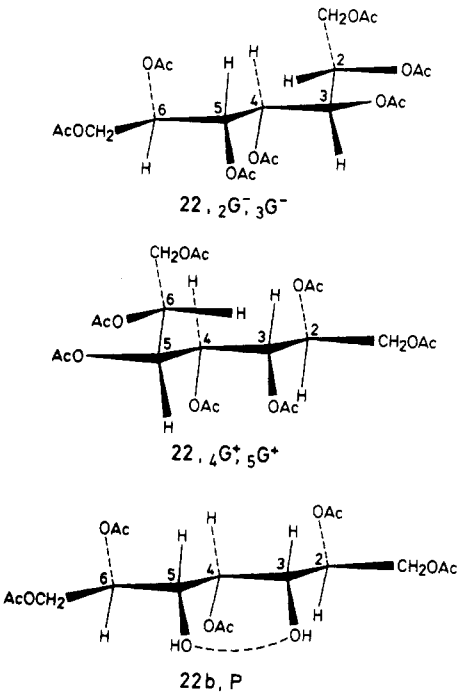

Figure 2. The principal conformations of *meso-glycero-gulo*-heptitol acetates.

equilibrium of the free heptitol,[3a] seems to occur in only a small proportion in the heptaacetate.[14]

The 1,2,4,6,7-pentaacetate (**22b**), on the other hand, is nearly completely in the planar form (Figure 2) as shown by the coupling constants: the O-2–O-6 segment is anti-gauche-gauche-anti. The relative configuration of the free hydroxyl groups is 1,3-erythro. Since the O-3//O-5 interaction does not, in this instance, force the molecule into a sickle form, it must be ineffective, owing to a hydrogen bond between the two free hydroxyl groups on C-3 and C-5. There are indications of the existence of this hydrogen bond in the value of $J_{CH,OH}$. Usually, the hydrogen atom of the OH group is mostly antiperiplanar to that on the carbon atom, and J is ca. 8 Hz.[8] The low value of 4 Hz indicates a much smaller dihedral angle; this would be the case if the hydrogen atom were located between O-3 and O-5. The δ value of the hydroxylic hydrogen atoms (4.0 ppm), higher than usual, also indicates the presence of a hydrogen bond: the signal of hydroxylic hydrogen atoms is usually at lower field if they are involved in hydrogen bonding.[16]

(9) That is, the conformation derived from the planar form by a 120° clockwise rotation of the remote carbon atom around the C-2–C-3 bond, and around the C-3–C-4 bond. For a definition of this terminology, see ref 10. The meso compounds have been numbered in such a way that the highest numbered asymmetric carbon atom has the D configuration. (This proviso was not applied in the preceding papers of the series, hence the present designations sometimes differ from earlier ones.) For racemic compounds, the designation applies to the D enantiomer.

(10) Horton, D.; Wander, J. D. *J. Org. Chem.* **1974**, *39*, 1859.

(11) Nimgirawath, K.; James, V. J.; Mills, J. A. *J. Chem. Soc., Perkin Trans. 2* **1976**, 349.

(12) We used only these two values for the vicinal H–H coupling constants. Lewis and co-workers[4] used three values (0.5, 2.3, and 4.0 Hz) for the gauche coupling, depending on the relative positions of the oxygen atoms, values derived by Haasnoot et al.[13] from a modified Karplus equation. Although these values are useful for the more rigid cyclic compounds, they do not seem to be valid for the alditols; in particular, a J value as low as 0.5 Hz has not been found in the spectra of any alditol acetate. These coupling constants can be, and have been,[4] used to calculate numerical values for the conformational equilibria of alditols, but this procedure is not justified, for two reasons.[14] The calculations assume that the bonds are fully staggered, that is, that the torsion angles are 60° and 180°. In fact, there are considerable deviations from these values, as shown by crystal structure determinations[1,6] and MNDO calculations.[15] Further, the contribution to the equilibrium of two or three conformers can readily be calculated; but there may be other conformers present in small proportions, and their presence may considerably alter the coupling constants. The NMR spectra provide insufficient data to allow the inclusion of these minor forms into the calculations.[14] Hence we refrain from giving figures for the proportion of conformers and use only approximate terms for them (predominant, about one-third, etc.).

(13) Haasnoot, C. A. G.; De Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783.

(14) Le Fur, R. Thèse Docteur ès-Sciences, Grenoble, 1987; p 225.

(15) Bell, C. F.; Beauchamp, R. D.; Short, E. L. *Carbohydr. Res.* **1989**, *185*, 39.

(16) Emsley, J. *Chem. Soc. Rev.* **1980**, *9*, 91.

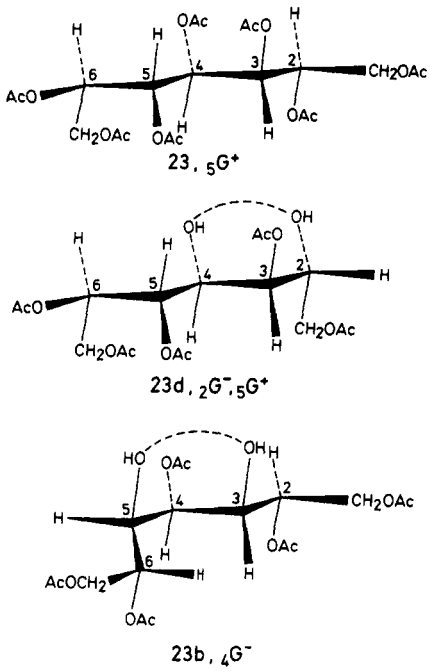

Figure 3. The principal conformations of D-*glycero*-D-*manno*-heptitol acetates.

The 1,2,3,4,7-pentaacetate (**22d**) is an example of a 1,2-*erythro*-diol. In solution it is a conformational mixture of the planar (*P*) and the $_4G^+,_5G^+$ forms, the former predominating. There is very little of the $_2G^-,_3G^-$ form present: the large value of $J_{2,3}$ and the small value of $J_{3,4}$ show that the C-1–C-4 segment of the molecule is essentially planar. Again, one has to invoke a hydrogen bond between the free hydroxyl groups: in the $_4G^+,_5G^+$ form, O-5 and O-6 are gauche and a hydrogen bond can form between them; in the $_2G^-,_3G^-$ form, they are anti, and a hydrogen bond is not possible. The large proportion of the planar form is surprising; possibly this means that a hydrogen bond is also present between OH-5 and O-3 (although the latter carries an acetyl group).

In the 1,2,5,6,7-pentaacetate (**22a**), a hydrogen bond can exist between the free hydroxyl groups in the *P*, the $_2G^-,_3G^-$, and the $_4G^+,_5G^+$ forms. In solution, the diol consists of a conformational mixture of at least three forms of which the planar one is predominant; its exact composition cannot be deduced from the coupling constants. The $_4G^+,_5G^+$ form is probably present, but not the $_2G^-,_3G^-$ form.

The 1,3,4,6,7-pentaacetate (**22c**) is a 1,4-diol. There are at least two conformers present of which one is the planar form; the other appears to be the $_3G^-$ form in which a hydrogen bond is possible between O-2 and O-5. The low value of $J_{CH,OH}$ and the low-field position of the signal for OH-2 suggest that there is, indeed, a hydrogen bond present.

The heptaacetate of D-*glycero*-D-*manno*-heptitol (**23**) assumes mainly the $_5G^+$ form[3a] (Figure 3). The same conformation is the major form of the 1,2,5,6,7-pentaacetate (**23a**), a 1,2-*threo*-diol; a hydrogen bond is possible in this conformation between O-3 and O-4 and is probably present. In the 1,2,3,5,7-pentaacetate (**23c**), a 1,3-*erythro*-diol, a hydrogen bond is possible between O-4 and O-6, which would cause the molecule to become planar. Indeed, the value of $J_{5,6}$ indicates that about one-third of the compound is in the planar form. The 1,3,5,6,7-pentaacetate (**23d**) is an example of a 1,3-*threo*-diol. The value of $J_{2,3}$ (7.2 Hz) indicates that in equilibrium there occurs a small proportion of a conformer in which the carbon chain is gauche at C-2–C-3; this must be the $_2G^-,_5G^+$ form, which allows the formation of a hydrogen bond between O-2 and O-4. Introduction of the gauche interaction is, of course, unfavorable, and the hydrogen bond is not strong enough to fully compensate for it; hence there is only a small proportion of the $_2G^-,_5G^+$ form present. The 1,2,4,6,7-pentaacetate (**23b**) is also of the 1,3-*threo*-diol type but here the $_4G^-$ form, which enables the formation of a hydrogen bond between O-3 and O-5, involves not only the creation of a gauche interaction (at C-4–C-5) but also the removal of a gauche interaction from C-5–C-6. Hence this conformation is favorable, and more than half of the molecules assume it. In these last three cases $J_{CH,OH}$ and/or δ_{OH} values support the assumption of intramolecular hydrogen bonds.

It is clear from this analysis that in many cases a hydrogen bond between the two free hydroxyl groups affects the conformational equilibrium. The hydrogen bond in 1,3-diols is not a strong one because it is far from linear. It does not occur in aqueous solution and it is rare in crystal structures of polyhydroxy compounds.[17] In these rare cases the O–H–O angle is 129–147° and the O–O distance is 2.62–2.83 Å. The hydrogen bond between vicinal hydroxyl groups is even weaker because the O–H–O angle would be less then 120°. To our knowledge, there is only one instance of it having been found[18] in a carbohydrate crystal structure [that of 1-deoxy-1-ethylthio-1-(5-fluorouracil-1-yl)-D-arabinose aldehydrol] but the position of the hydrogen atom was not determined. Nevertheless, in chloroform solution, in the absence of any intermolecular hydrogen bonds, it seems to occur in some cases. The hydrogen bond in a 1,4-diol can be quite strong but it requires a conformation which is not favorable; the only instance of its occurrence in a crystal structure involves a primary hydroxyl group, between O-2 and O-5 of D-ribose (*p*-bromophenyl)hydrazone.[19]

General Conclusions

Having discussed two heptitols, we can now extend our considerations to all of Moore's compounds. We shall discuss them according to the nature of their diol groupings.

(i) 1,3-*erythro*-Diols. Alditols having such an arrangement, and their peracetates, will be in a sickle form to avoid the 1,3-parallel interaction (O//O). However, when these two hydroxyl groups are free, a hydrogen bond between them will reduce this interaction and the alditol will assume, at least partially, the planar form.

The extent to which the planar conformation is assumed will depend on conformational features. When there is a double-sickle form, that is, two gauche C/C interactions, the hydrogen bond will cause nearly complete conversion into the *P* form, as seen in 1,2,4,6,7-*meso*-*glycero*-*gulo*-heptitol (**22b**). When the sickle has only one gauche interaction, the energy gained by the hydrogen bond is insufficient to convert it completely into the planar form. If the diol is part of a xylo sequence, about two-thirds is changed into the *P* form, e.g., 1,3,5-tri-*O*-acetylxylitol (**13a**), 1,3,5,6-tetra-*O*-acetyl-D-glucitol (**20b**), and 1,4,6-tri-*O*-acetyl-2-deoxy-D-*xylo*-hexitol (**15c**) (see Figure 4). For reasons that are not obvious, the hydrogen bond causes conversion of only about one-fifth to a planar form when it is part of a ribo arrangement, e.g., 1,3,5-tri-*O*-acetylribitol (**12b**), 1,4,6-tri-*O*-acetyl-2-deoxy-*ribo*-hexitol (**16a**), and 1,2,3,5,7-penta-*O*-acetyl-D-*glycero*-D-*manno*-heptitol (**23c**).

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(18) Ducruix, A.; Pascard, C. *Acta Crystallogr.* **1977**, *B33*, 2505.
(19) Bjåmer, K.; Furberg, S.; Petersen, C. S. *Acta Chem. Scand.* **1964**, *18*, 587.

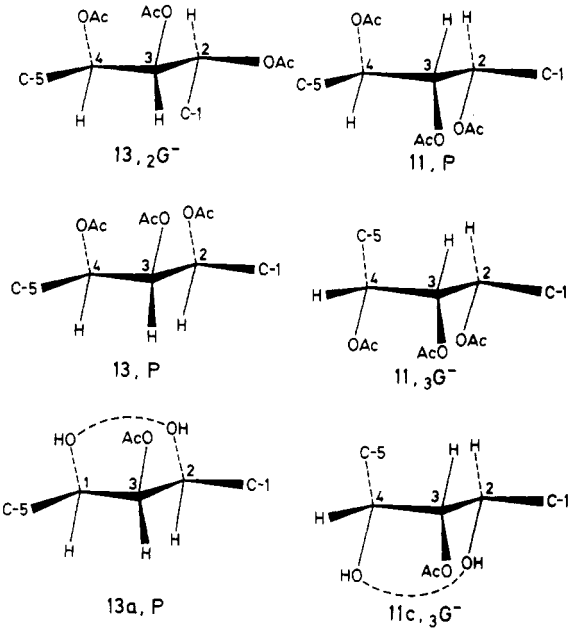


Figure 4. Conformations in $CDCl_3$ of the acetates of xylitol (**13**) (for the pentaacetate, $_2G^-$, favorable, *P*, unfavorable; for the 1,3,5-triacetate, *P*, major form) and arabinitol (**11**) (for the pentaacetate, *P*, favorable, $_3G^-$, very unfavorable; for the 1,3,5-triacetate, $_3G^-$, minor form).

In all these cases at least one of the $J_{CH,OH}$ values is between 4.1 and 5.1 Hz and the chemical shift of the hydroxylic hydrogen atom is at 2.9–4.0 ppm.

(ii) 1,3-*threo*-Diols. An alditol containing this grouping will normally be planar; a hydrogen bond could only be formed in the partially acetylated alditol after it changes into a sickle form to bring the two free hydroxyl groups into a 1,3-parallel arrangement. One of the hydroxyl groups is threo to the interjacent acetoxyl group and the other one is erythro, and rotation can occur in two ways; between the erythro group, it changes the coupling constant from ca. 9.5 to ca. 2 Hz, but rotation between threo groups causes no change in the coupling constant and is therefore not detectable in this way. The former change yields an arrangement of two hydroxyl groups in 1,3-parallel arrangement with the interjacent acetoxyl group gauche to them both; as pointed out above for xylo type 1,3-*erythro*-diols, this is the more favored arrangement, and therefore the "undetectable" sickle form may only make a minor contribution to the equilibrium.

Since rotation into the conformation capable of hydrogen bonding causes the appearance of a gauche arrangement, it will be less favored than in the 1,3-*erythro* cases; the hydrogen-bonded form will not be preponderant (see Figure 4). Thus, NMR spectra show that, besides the planar form, about a third is in the $_3G^-$ form in 1,3,5-tri-*O*-acetyl-D-arabinitol (**11c**), in the $_3G^-$ form in 1,4,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hexitol[20] (**14c**), in the $_4G^-$ form in 1,4,6-tri-*O*-actyl-2-deoxy-D-*arabino*-hexitol (**17c**), in the $_2G^-$ form in 1,3,5,6-tetra-*O*-acetyl-D-mannitol (**19d**), in the $_5G^-$ form in 1,2,3,5,7-penta-*O*-acetyl-D-*glycero*-D-*galacto*-heptitol (**21d**), and in the $_2G^-$,$_5G^+$ form of 1,3,5,6,7-penta-*O*-acetyl-D-*glycero*-D-*manno*-heptitol (**23d**). There are possibly smaller amounts of the "undetectable" $_2G^-$ form of **11c**, the $_3G^-$ form for **17c**, and the $_3G^-$,$_5G^+$ form for **23d**; however, the $_3G^-$ form of **19d** and the $_4G^-$ form of **21d** are unfavorable, owing to additional 1,3-parallel interactions, and would not be present in substantial amounts. The ("detectable") $_3G^+$ form of 1,3,5,6-tetra-*O*-acetylgalactitol (**18b**) and 1,3,5,6,7-penta-*O*-acetyl-D-*glycero*-D-*galacto*-heptitol (**21e**) are unfavorable, and the coupling constants are found to be the same as those of the peracetylated alditols; the "undetectable" $_2G^+$ forms may, however, be present. In the case of 1,2,4,6,7-penta-*O*-acetyl-D-*glycero*-D-*galacto*-heptitol (**21c**), both forms that could have hydrogen bonds, $_3G^-$ and $_4G^-$, are unfavorable; there is no more than 10% of the former present, and none of the latter.

The previously discussed 1,2,4,6,7-penta-*O*-acetyl-D-*glycero*-D-*manno*-heptitol (**23b**) presents a special case. Change of the usual $_5G^+$ form into the hydrogen-bonded $_4G^-$ form involves the formation of a gauche arrangement but also the removal of a gauche arrangement and is therefore more favorable: more than half of the heptitol is in the $_4G^-$ form at equilibrium.

In all these cases, a $J_{CH,OH}$ of <6 Hz or a δ_{OH} value of >3.0 ppm, or both, indicate the presence of a hydrogen bond.

The behavior of the 1,3-diols is analogous to that of the pentane-2,4-diols,[21] which can be regarded as model compounds. The meso (erythro) isomer is bent in water and in DMSO but planar in carbon tetrachloride; its diacetate is bent in benzene and in carbon tetrachloride. The racemic (threo) isomer is preponderantly in the planar form in hydrogen-bonding solvents but about half of it is sickle in nonpolar solvents, owing to formation of an intramolecular hydrogen bond.

(iii) 1,2-*threo*-Diols. The hydrogen bond between adjacent hydroxyl groups is expected to be weaker than that in 1,3-diols, owing to the small (<120°) O–H–O angle. In most instances this hydrogen bond has little effect on the conformational equilibrium; it only shows up when it affects the proportion of two forms of otherwise equal energy.

Most of Moore's examples of 1,2-*threo*-diols have an arabino arrangement of OH–OH–OAc and are therefore planar (or, at least, the arabino segment is planar), as are also their acetates. There being no difference in conformation, there is no indication whether a hydrogen bond is present or not; the $J_{CH,OH}$ and δ_{OH} values do not, in the 1,2-diols, show any regularity that could disclose the presence of a hydrogen bond. However, the coupling between the two hydrogen atoms of the 1,2-diol is unusually small (1.0–1.7 Hz); this is probably due to the hydrogen bonding bringing the two oxygen atoms closer to each other, thereby reducing the dihedral angle between them and increasing it between the hydrogen atoms. These small couplings therefore indicate the presence of a hydrogen bond. Examples are 1,4,5-tri-*O*-acetyl-D-arabinitol (**11a**), 1,3,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hexitol (**14a**), 1,5,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexitol (**17a**), 1,4,5,6-tetra-*O*-acetylgalactitol (**18a**), 1,2,5,6-tetra-*O*-acetyl-D-mannitol (**19a**), 1,4,5,6,7-penta-*O*-acetyl-D-*glycero*-D-*galacto*-heptitol (**21b**), and 1,2,5,6,7-penta-*O*-acetyl-D-*glycero*-D-*manno*-heptitol (**23a**).

When the OH–OH–OAc arrangement is xylo, there are two possible sickle forms, and a hydrogen bond may exist between the hydroxyl groups in both of them, and also in the *P* form. The coupling between the hydrogen atoms geminal to the hydroxyl groups is smaller than the one between the adjacent threo pair, indicating the presence of a hydrogen bond. Thus, for 1,4,5-tri-*O*-acetylxylitol (**13b**) $J_{2,3} < J_{3,4}$ and for 1,3,6-tri-*O*-acetyl-2-deoxy-D-*xylo*-

(20) Curiously, the pentaacetate (**14**) also contains quite a lot of the sickle form.

(21) (a) Doskočilová, D.; Štokr, J.; Votavová, E.; Schneider, B.; Lím, D. *J. Polym. Sci., Part C* **1967**, 2225. (b) Fukuroi, T.; Fujiwara, Y.; Fujiwara, S.; Fujii, K. *Anal. Chem.* **1968**, *40*, 879.

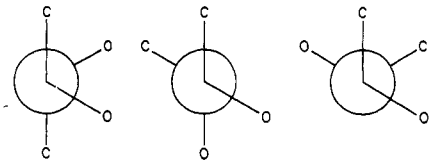
hexitol (**15b**) $J_{4,5} < J_{3,4}$. Both contain a considerable proportion of the planar form.

The hexaacetate (**20**) of D-glucitol assumes the $_2G^-$ form (ca. 60%), the $_3G^+$,$_4G^+$ form (ca. 40%), and very little of the planar form. The 2,3-diol (**20c**) and the 3,4-diol (**20a**) both have a much higher proportion (over 40%) of the planar form; $J_{2,3}$ is much smaller for the 2,3-diol and $J_{3,4}$ for the 3,4-diol than for the hexaacetate, suggesting the possible existence of hydrogen bonds between the hydroxyl groups.

(iv) 1,2-*erythro*-Diols. With one exception, the examples of this structural type all have the diol segment in the planar conformation when fully acetylated. Formation of a hydrogen bond in the diol would require a change into the sickle form. This does not happen; the diols are preponderantly in the planar form, the hydrogen bond not supplying sufficient energy for this change. Examples are 1,4,5-tri-*O*-acetylribitol (**12a**), 1,5,6-tri-*O*-acetyl-2-deoxy-D-*lyxo*-hexitol (**14b**), and 1,3,6-tri-*O*-acetyl-2-deoxy-D-*arabino*-hexitol (**17b**). The only exception is 1,2,3,4,7-penta-*O*-acetyl-*meso*-*glycero*-*gulo*-heptitol (**22d**), which has already been discussed; the heptaacetate assumes two sickle forms, of which the one capable of hydrogen-bond formation is favored by the diol.

(v) 1,4-Diols. There are only two examples of this type in the Moore collection. 1,3,4,6-Tetra-*O*-acetyl-D-mannitol (**19b**) is planar like the hexaacetate; there can be no hydrogen bond. For 1,3,4,6,7-penta-*O*-acetyl-*meso*-*glycero*-*gulo*-heptitol (**22c**), however, the $J_{3,4}$ value of 4.1 Hz suggests that some of the $_3G^-$ form is present, which would allow the formation of a hydrogen bond between O-2 and O-5.

The presence of two free hydroxyl groups therefore affects the conformation of partially acetylated alditols, by formation of an intramolecular hydrogen bond, in the following (decreasing) order: 1,3-*erythro*-diol, 1,3-*threo*-diol, 1,2-*threo*-diol, and 1,2-*erythro*-diol. The proportion of the hydrogen-bonded conformation, however, will depend on the configuration and conformation of the rest of the molecule, particularly on the number and nature of gauche interactions in the carbon chain. It appears that conformation A is more favorable for hydrogen-bond formation than conformation B. As already postulated by Mills,[7] conformation C is avoided by the molecules whenever possible.



Moore[8] noted that the coupling constants for vicinal methine protons generally become larger for anti (erythro) 1,2-protons and smaller for syn (threo) 1,2-protons when partially acetylated alditols were compared with fully acetylated alditols. The present paper explains this observation as being the consequence of the formation of hydrogen bonds in the partially acetylated alditols.

Synthesis of 3,4-Disubstituted 3,4-Dihydro-2-pyrones via 2-(Silyloxy)pyrylium Salts: Regioselective Introduction of Substituents into 2-Pyrones

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Received June 7, 1988

Silylation of 4,6-dimethyl- and 6-methyl-2-pyrone with *tert*-butyldimethylsilyl triflate affords the corresponding 2-(silyloxy)pyrylium triflates **2** quantitatively. Lithium diorganocuprates add regioselectively at position 4 of triflates **2** to give 4-substituted 2-(silyloxy)-4*H*-pyrans **4**. Compounds **4** react with electrophiles at position 3 to give 3-bromo- (**8**), 3-(silyloxy)- (**9**), 3-methylene- (**15**), and 3-(1-hydroxybutyl)-3,4-dihydro-2-pyrones (**16**).

Introduction

2-Pyrones and their dihydro derivatives play an important role in organic synthesis and occur in several types of natural products.[1] Most reported syntheses of 2-pyrones involve ring closure of a 5-keto acid derivative as the final step,[1] which imposes limitations on the substituents that can be attached to the 2-pyrone ring, especially at position 3. The direct addition of nucleophiles into 2-pyrones has had only limited success because of complex reactivities of 2-pyrones toward nucleophiles. For example, Grignard reagents attack position 2 or 4 of 2-pyrones, and the resulting adducts react further with the Grignard reagent to afford several products.[2] Ireland and coworkers have reported regioselective γ-addition of a Grignard reagent to 3-(methoxycarbonyl)-2-pyrone; the resulting adduct was used for the synthesis of lasalocid A.[3] The regioselective addition was attributed to stabilization of the carbanion generated at position 3 by the methoxycarbonyl group. Michael addition of pyrones with organocopper reagents is sluggish,[3] and our attempt to react 4,6-dimethyl-2-pyrone (**1a**) with lithium dibutylcuprate failed.

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