2,3,4-Triamino-2,3,4-trideoxy-derivatives of 6-Deoxy-L-glucose and L-Rhamnose

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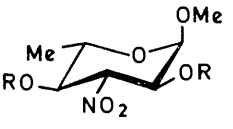
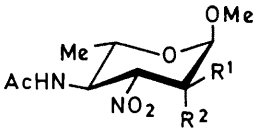
Summary Methyl 2,3,4-triacetamido-2,3,4,6-tetradeoxy-α-L-hexosides of *gluco-* and *manno*-configuration are obtained from methyl 2,4-di-*O*-acetyl-3-deoxy-3-nitro-α-L-rhamnoside in three steps, involving as the crucial stage a diamination with ammonia, the course of which is strongly dependent on the conditions used.

CONSIDERABLE interest has recently been shown in the smooth diamination of cyclic nitro-$\beta\beta'$-diacetoxy-compounds on treatment with ammonia. When followed by hydrogenation this procedure provides a general synthetic approach to inosatriamines,[1,2] triaminosugars,[1,3] and triaminosugar nucleosides.[4] The results presented below on the reaction of methyl 2,4-di-*O*-acetyl-3,6-dideoxy-3-nitro-α-L-hexopyranosides (**2**), (**6**), and (**7**) with ammonia demonstrate that the steric course of the diamination is in fact strongly dependent on the conditions used and to some extent on the stereochemistry of the acetoxy-functions in the starting material.

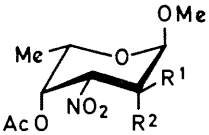
When the nitro-diacetate (**2**), m.p. 109—110°, $[\alpha]_D$ −154° (*c* 1·0, $CHCl_3$), readily obtained from methyl 3-deoxy-3-nitro-α-L-rhamnopyranoside (**1**)[5] by acid-catalysed acetylation, is treated with ammonia in dioxan (1·5 h, 25°), the acetoxy-functions vicinal to the nitro-group are replaced by amino-groups *via* an elimination–addition mechanism.[6] Subsequent *N*-acetylation with acetic anhydride in methanol affords, in addition to a trace of another compound,† an approximately 3 : 2 mixture of methyl 2,4-diacetamido-2,3,4,6-tetradeoxy-3-nitro-α-L-glucopyranoside (**3**) and the corresponding *manno*-isomer (**4**). The *gluco*-compound (**3**), $[\alpha]_D$ −113° (*c* 0·5, MeOH), m.p. 309° (decomp.) crystallizes on standing (49%) and is removed by filtration. The rhamnoside (**4**), m.p. 241—242°, $[\alpha]_D$ −80° (*c* 1, MeOH) is isolated from the filtrate in 21% yield by chromatography over Kieselgel (chloroform–methanol 10 : 1). In an analogous reaction sequence using liquid ammonia for the amination of (**2**) (1 h, −50°), the ratio of the *gluco-* and *manno*-isomers is reversed to 2 : 3. The use of protic solvents in the amination step again changes the product distribution; aqueous ammonia (3 h, 25°) or aqueous ammonia–tetrahydrofuran[7] afford the C-2 epimers in equal amounts, whereas ammonia in methanol yields a 3 : 1 mixture of (**3**) and (**4**). Any further products can only be detected in trace amounts.† However, on subjecting a mixture of (**6**) and (**7**)—obtained as a syrup by acetylation of the *galacto-* and *talo*-fractions from the nitromethane cyclization mixture[5]—to amination with methanolic ammonia and subsequent *N*-acetylation, apart from (**3**) and (**4**) a third product, methyl 4-acetamido-3,4,6-trideoxy-3-nitro-α-L-glucopyranoside (**5**), m.p. 201—203°, $[\alpha]_D$ −159° (*c* 0·5, MeOH) can be isolated in yields of 4—5%. Since (**5**) is not encountered in aminations of (**2**) under identical conditions, its formation from (**6**)–(**7**) must be due to different steric arrangements of the acetoxy-groups. It seems probable that (**5**) arises primarily from the *galacto*-isomer (**6**), in which a diaxial 3,4-elimination of acetic acid—and thus amination—should be considerably enhanced over elimination of the equatorial 2-acetoxy-group, allowing de-*O*-acetylation at C-2 to become a competitive reaction.



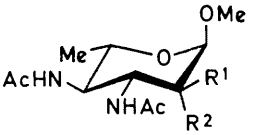
(1) R = H
(2) R = Ac



(3) R^1 = NHAc, R^2 = H
(4) R^1 = H, R^2 = NHAc
(5) R^1 = OH, R^2 = H



(6) R^1 = OAc, R^2 = H
(7) R^1 = H, R^2 = OAc



(8) R^1 = NHAc, R^2 = H
(9) R^1 = H, R^2 = NHAc

The nitro-groups in (**3**) and (**4**) can readily be hydrogenated over palladium–charcoal in an acidic medium, to afford, after subsequent *N*-acetylation, methyl 2,3,4-triacetamido-2,3,4,6-tetradeoxy-α-L-glucopyranoside (**8**), $[\alpha]_D$ −124° (*c* 0·5, HOAc), m.p. >320°, and the rhamnoside (**9**), m.p. 248–250°, $[\alpha]_D$ −98° (*c* 0·5, MeOH) in yields over 85%.

The configurations assigned were deduced from 100 MHz n.m.r. spectra. In $(CD_3)_2SO$, compounds (**2**), (**3**), and (**5**) exhibited 10—11 Hz triplets for the nitromethine proton (3-H) at τ 5·08, 5·13, and 5·25 respectively, clearly indicating the equatorial orientation of the substituents at C-2 to C-4. The *manno*-derivative (**4**) exhibits a quartet at τ 4·93 with $J_{2,3}$ 4 and $J_{3,4}$ 11 Hz, which together with the 2 Hz doublet for the anomeric proton at τ 5·47 proves the acetamido-group at C-2 to be axial. The assignments were sustained by double resonance and are additionally supported by the chemical shift of the acetyl resonances of (**8**) and (**9**), which are in accord with the "acetyl resonance rule".[8]

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† T.l.c. on Kieselgel Merck F 254 with chloroform–methanol (10 : 1).

[1] F. W. Lichtenthaler, P. Voss, and N. Majer, *Angew. Chem. Internat. Edn.*, 1969, **8**, 211.
[2] F. W. Lichtenthaler and P. Voss, *Tetrahedron Letters*, 1969, 2297.
[3] T. Nakagawa, Y. Sato, T. Takamoto, N. Majer, and F. W. Lichtenthaler, *Bull. Chem. Soc. Japan*, 1970, **43**, in the press.
[4] F. W. Lichtenthaler, G. Trummlitz, and H. Zinke, *Tetrahedron Letters*, 1969, 1213.
[5] K. Čapek, J. Šteffková, and J. Jarý, *Coll. Czech. Chem. Comm.*, 1966, **31**, 1854; H. H. Baer and K. Čapek, *Canad. J. Chem.*, 1969, **47**, 99.
[6] *Cf.* T. Nakagawa, T. Sakakibara, and F. W. Lichtenthaler, *Bull. Chem. Soc. Japan*, 1970, **43**, in the press.
[7] Under conditions used for monoaminations by H. H. Baer and F. Rajabalee, *Carbohydrate Res.*, 1970, **12**, 241.
[8] F. W. Lichtenthaler and P. Emig, *Carbohydrate Res.*, 1968, **7**, 121; F. W. Lichtenthaler, G. Bambach, and P. Emig, *Chem. Ber.*, 1969, **102**, 994.