Mono-, Di-, and Tri-C-Deuteration of 1,5-Anhydro-D-glucitol

Masuo FUNABASHI* and Toshimori HASEGAWA
Chemistry Department, College of Arts and Sciences, Chiba University, Yayoi-cho, Chiba 260
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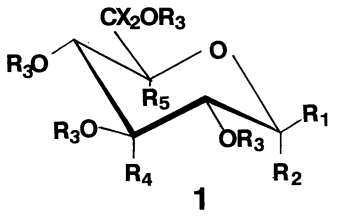
Deuterium was effectively introduced into the title sugar (**1a**) at C-1, C-3, C-5, and C-6 to afford 1,5-anhydro-D-[1-$^2H_1$], -[3-^2H], -[5-^2H], -[1-$^2H_2$], -[6-$^2H_2$], and -[5,6-$^2H_3$]glucitols respectively as primary targets for a basic study of the unknown metabolism of **1a**, which had been suggested to be a candidate of metabolic indexes for insulin-dependent diabetes mellitus.

1,5-Anhydro-D-glucitol (polygalitol: **1a**) which had been known as a component of some plants such as *polygala amara,*[1] *polygala vulgaris,*[2] and *polygala tenuifolia*[3] has been first identified in human cerebrospinal fluid from diabetic uremic patients by pitkänen,[4] and confirmed later by Smith et al.[5]

Yoshioka and his co-workers,[6] on the other hand, have also confirmed the presence of a considerable amount of the sugar alcohol (average: 2.5 mg dl^{-1}) in human plasma from healthy persons of various ages and they observed a gradual recovery of **1a** in the plasma of diabetic patients receiving insulin regularly during several months, in contrast with the fact that the content of **1a** in the plasma from diabetic patients receiving no insulin remained negligibly small.

Though both physiological and metabolic meaning of this minor sugar is still uncertain, some studies concerning feeding suppression in rats,[7] transport inhibition in hamster[8] or inhibitory effects to enzymes such as hexokinase[9] and α-glucosidase[10] have been reported so far.

These phenomena prompted us to prepare both hot and cold labeled derivatives of **1a** in order to elucidate the unknown metabolism of the sugar alcohol.



1

a) $R_1=R_2=R_3=R_4=R_5=X=H$
b) $R_1=OCOCH_3$, $R_2=D$, $R_3=COCH_3$, $R_4=R_5=X=H$
c) $R_1=D$, $R_2=OH$, $R_3=Bn$, $R_4=R_5=X=H$
d) $R_1=H$, $R_2=D$, $R_3=Bn$, $R_4=R_5=X=H$
e) $R_1=H$, $R_2=D$, $R_3=COCH_3$, $R_4=R_5=X=H$
f) $R_1=R_2=R_5=X=H$, $R_4=D$, $R_3=COCH_3$
g) $R_1=R_2=R_4=X=H$, $R_3=COCH_3$, $R_5=D$
h) $R_1=R_2=D$, $R_3=Bn$, $R_4=R_5=X=H$
i) $R_1=R_2=D$, $R_3=COCH_3$, $R_4=R_5=X=H$
j) $R_1=R_3=R_4=R_5=X=H$, $R_2=D$
k) $R_1=R_2=R_3=R_5=X=H$, $R_4=D$
l) $R_1=R_2=R_3=R_4=X=H$, $R_5=D$
m) $R_1=R_2=D$, $R_3=R_4=R_5=X=H$
n) $R_1=R_2=R_3=R_4=R_5=H$, $X=D$
o) $R_1=R_2=R_4=R_5=H$, $R_3=COCH_3$, $X=D$
p) $R_1=R_2=R_4=H$, $R_3=COCH_3$, $R_5=X=D$
q) $R_1=R_2=R_3=R_4=H$, $R_5=X=D$

In a previous communication,[11a] we briefly reported a synthesis of 1,5-anhydro-D-[1-$^2H_1$]glucitol (**1j**) and 1,5-anhydro-D-[1-$^2H_2$]glucitol (**1m**) as preliminary targets.

The present paper comprehensively describes mono-, di-, and tri-C-deuteration of **1a** in detail.

Results and Discussion

For the synthesis of **1a**, there are several useful methods such as direct reduction of 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide with lithium aluminum hydride,[12] palladium on carbon[13] or tributylstannane,[14] and reductive desulfurization[15] of phenyl 2,3,4,6-tetra-*O*-acetyl-1-thio-β-D-glucopyranoside with Raney-nickel.

From the standpoint of stereospecificity and work-up, the direct reduction of protected glucosyl halides with lithium aluminum hydride (LAH) or lithium aluminum deuteride (LAD) is our main choice and the respective syntheses are described as follows.

(1) Mono-C-deuteration

(a) (1*R*)-1,5-Anhydro-D-[1-$^2H_1$]glucitol (1j). Two different routes were achieved for the synthesis of **1j**. First, we chose, as a starting material, 1,2,3,4,6-penta-*O*-acetyl-β-D-[1-^{2}H]glucopyranose[11] (**1b**) obtained in two steps from D-gluco-1,5-lactone. The pentaacetate (**1b**) was then converted into 2,3,4,6-tetra-*O*-acetyl-α-D-[1-^{2}H]glucopyranosyl bromide, which was directly treated with excess amount of LAH to afford the desired product (**1j**) having 1*R* configuration. ^{1}H NMR of the acetate (**1e**) showed the disappearence of H_1 axial proton at δ=3.00 and the presence of H_1 equatorial proton at δ=4.15 having $J_{1,2}$=5.6 Hz. ^{13}C NMR of **1e** also revealed the signal of C_1 at δ=66.86 was missing.

Comparison of mass spectra of **1e** with that of the peracetate of **1a** clearly demonstrated the shift of one mass unit in several peaks [97 to 98, 170 to 171, 212 to 213, 273 to 274, and 333 (M^++1) to 334 (M^++1)].

Secondly, we chose 2,3,4,6-tetra-*O*-benzyl-α-D-[1-^{2}H]glucopyranosyl chloride easily obtained by treating 2,3,4,6-tetra-*O*-benzyl-α-D-[1-^{2}H]glucopyranose (**1c**) with methanesulfonyl chloride, and the resulting glucosyl chloride was reduced with an equimolar amount of LAH in dry ether to yield a syrupy (1*R*)-2,3,4,6-tetra-*O*-

benzyl-1,5-anhydro-D-[1-$^2H_1$]glucitol (**1d**) in a 58% yield. The benzyl groups of **1d** were then removed conventionally in the presence of Pd/C (10%) in acetic acid to afford the compound **1j** described above.

The second route requires multi-step reactions, and was less satisfactory as for a scale-up of preparation.

(b) 1,5-Anhydro-D-[3-^{2}H]glucitol (1k). 1,2,3,4,6-Penta-*O*-acetyl-β-D-[3-^{2}H]glucopyranose was first prepared by the reported method[16] in four steps from 1,2;5,6-di-*O*-isopropylidene-α-D-[3-^{2}H]allofuranose,[17] and next converted to the corresponding glucopyranosyl bromide, which was successively reduced with LAH in the same manner described above to give the desired compound **1k** in a total yield of 7% from D-glucose. ^{13}C NMR spectrum of the tetraacetate (**1f**) disclosed complete disappearence of C-2 signal observed at δ=73.79 in the corresponding light compound. Mass spectrum of **1f** also indicated the presence of m/z 334 (M^++1).

(c) 1,5-Anhydro-D-[5-^{2}H]glucitol (1l). 1,2,3,4,6-Penta-*O*-acetyl-β-D-[5-^{2}H]glucopyranose prepared stepwise by the known method[18] from 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-trityl-α-D-xylofurano-5-ulose, was first transformed into the corresponding bromide, which was then similarly treated with LAH to afford the compound (**1l**) in an overall yield of 35% from the 5-ulose. ^{13}C NMR spectrum of the tetraacetate (**1g**) showed the absence of C-5 signal at δ=76.47, and the mass spectrum also indicated the presence of m/z 334 (M^++1) peak.

(2) Di-C-deuteration

(a) 1,5-Anhydro-D-[1-$^2H_2$]glucitol (1m). Direct reduction of 2,3,4,6-tetra-*O*-benzyl-α-D-[1-^{2}H]glucopyranosyl chloride described in the case of **1c** was effected with LAD in dry ether to afford the corrresponding 2,3,4,6-tetra-*O*-benzyl-1,5-anhydro-D-[1-$^1H_2$]glucitol (**1h**) in 63% yield. Removal of benzyl groups in **1h** by means of hydrogenolysis in the presence of Pd/C (10%) gave **1m** as crystals, which was then converted to 2,3,4,6-tetra-*O*-acetyl-1,5-anhydro-D-[1-$^2H_2$]glucitol (**1i**). Double introduction of deuterium into C-1 of was unambiguously confirmed by ^{1}H NMR spectrum of **1i**, in which both H_1 axial proton at δ=3.30 and H_1 equatorial proton at δ=4.15 completely disappeared. ^{13}C NMR spectrum of **1i** disclosed the absence of C-1 signal at δ=66.86, coinciding with the result of ^{1}H NMR.

The presence of m/z 335 (M^++1) peak in the mass spectrum of **1i** clearly indicates two mass unit increase in comparison with that of the light compound.

An alternative route to **1m** was similarly achieved by reducing 2,3,4,6-tetra-*O*-acetyl-α-D-[1-^{1}H]glucopyranosyl bromide with LAD in dry ether. In terms of economy of LAD, which was excessively required in the latter case, the former seems to be better, but the latter is superior from the standpoint of short reaction steps and convenience.

(b) 1,5-Anhydro-D-[6-$^2H_2$]glucitol (1n). 1,2,3,4,6-Penta-*O*-acetyl-β-D-[6-$^2H_2$]glucopyranose,[18] prepared in three steps [(i) reduction with LAD, (ii) hydrolysis with 80% acetic acid, and (iii) acetylation with acetic anhydride/sodium acetate] from 1,2-*O*-isopropylidene-α-D-glucofuranurono-6,3-lactone, was brominated and successively reduced with LAH to afford the desired product (**1n**) in a total yield of 32%. ^{1}H and ^{13}C NMR spectra of the acetate (**1o**) showed the disappearence of H-6 multiplet at δ=4.17 and C-6 signal at δ=62.22 respectively. The octet of H-5 signal at δ=3.59 was definitely changed to doublet ($J_{4,5}$=9.9 Hz). The presence of m/z 335 (M^++1) peak in the mass spectrum of **1o** also supported the double deuteration of **1a**.

(3) Tri-C-deuteration

1,5-Anhydro-D-[5,6-$^2H_3$]glucitol (1q). 1,2-*O*-isopropylidene-α-D-[5,6-$^2H_3$]glucofuranose, obtained by stereoselective reduction[19] of 1,2-*O*-isopropylidene-α-D-xylohexofuranurono-6,3-lactone with sodium borodeuteride, was similarly converted to 2,3,4,6-tetra-*O*-acetyl-α-D-[5,6-$^2H_3$]glucopyranosyl bromide, and the bromide was immediately reduced with LAH to afford the desired compound (**1q**) in a total yield of 19% from the starting lactone. ^{13}C NMR spectrum of the peracetate (**1p**) disclosed both signals at δ=62.22 (C-6) and 76.47 (C-5) were completely disappeared, and the presence of m/z 336 (M^++1) peak in the mass spectrum of **1p** also supported the triple deuteration.

Experimental

Melting points were determined on a YAZAWA micro hotstage and were uncorrected. Solvents were evaporated off in vacuo below 40 °C. Optical rotations were measured with a JASCO DIP-140 digital polarimeter. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL GX-100 spectrometer in $CDCl_3$ using TMS as internal standard. Mass spectra measured with a Hitachi M-60 mass spectrometer connected with Hitachi data processing system M-003. TLC were carried out on Merck plates (silica gel 60, 0.25 mm). Column chromatography was performed on Wakogel C-200 or C-300.

1,2,3,4,6-Penta-*O*-acetyl-β-D-[1-^{2}H]glucopyranose (1b): To a cooled solution (0 °C) of D-glucono-1,5-lactone (10 g, 0.56 mmol) in a buffer solution (130 ml) of sodium acetate–acetic acid (pH 5.7) was gradually added sodium borodeuteride (Merck 98%, 1 g, 24 mmol) for 10 min and keeping pH at below 6.0 (dropwise addition of acetic acid). The reaction solution was then treated with IR-120 (H^+) and the resin was filtered off. The filtrate was concentrated in vacuo with aid of methanol and ethanol repeatedly. The resulting amorphous residue was dried, and acetylated with acetic anhydride (100 ml) and sodium acetate (5 g). The reaction mixture was then poured into ice-water, and the precipitate was filtered, and recrystallized from ethanol, giving 9.9 g (45%). mp 131—132 °C (lit,[20] 132 °C). ^{1}H NMR: no peak due to H-1 at δ=5.73. Anal. ($C_{16}H_{22}O_{11}$) C, H.

2,3,4,6-Tetra-*O*-benzyl-α-D-[1-^{2}H]glucopyranose (1c): A solution of 2,3,4,6-tetra-*O*-benzyl-D-glucono-1,5-lactone[21] (540 mg, 1 mmol) in dry ether (40 ml) and boron trifluoride

etherate (7.5 ml) was gradually added to a suspension of lithium aluminum deuteride (Merck 98%; 490 mg, 12 mmol) in dry ether (40 ml) under ice-cooling. The reaction mixture was then heated to reflux for 2 h and cooled. Dilute hydrochloric acid (2 M, 5 ml) was carefully added to the mixture, and the precipitate was filtered off. The filtrate was washed with aqueous $NaHCO_3$ and brine. The ethereal layer was dried ($MgSO_4$), concentrated to a crystalline mass, which was recrystallized from ethanol giving 0.49 g (90%); mp 150—151 °C, $[\alpha]_D^{12}$ +14.0° (*c* 1.0, $CHCl_3$); MS (70 eV) *m/z* (rel intensity) 432 (M^+−109; 0.60), 253 (14), 181(19), 92 (100), 79 (12), 65 (13). Anal. ($C_{34}H_{36}O_6$) C, H.

(1*R*)-2,3,4,6-Tetra-*O*-benzyl-1,5-anhydro-D-[1-$^2H_1$]glucitol (1d): To a solution of **1c** (2.2 g, 4.2 mmol) in CH_2Cl_2 (20 ml) was added *s*-collidine (2 g, 16.5 mmol) and methanesulfonyl chloride (0.96 g, 8.4 mmol), and the reaction mixture was kept overnight at room temperature (16 °C). The solution was successively treated with 1 M HCl, aqueous $NaHCO_3$, and water. The organic layer was dried ($CaCl_2$), and concentrated to a syrup, which was directly treated with lithium aluminum hydride (0.5 g, 13 mmol) in dry ether (50 ml). Excess of LAH was then decomposed with ethyl acetate and water, and the precipitate was filtered off. The ethereal layer was concentrated to a pale yellow syrup, which was chromatographed on a silica gel (C-200) with benzene–ethyl acetate (10/1). Evaporation of the eluates gave a pure syrup (1.23 g, 58%), having $[\alpha]_D^{14}$ +7.5° (*c* 0.42, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=7.2—7.4 (20H, aromatic), 4.46—5.00 (8H, m, CH_2Ph), 4.04 (1H, H-1, d, $J_{1,2}$=4.6 Hz), 3.37 (1H, m, H-5). No peak due to H-1 axial (δ=3.21). Anal. ($C_{34}H_{36}O_5$) C, H.

(1*R*)-1,5-Anhydro-D-[1-^2H]glucitol (1j): (a) 2,3,4,6-tetra-*O*-acetyl-α-D-[1-^2H]glucopyranosyl bromide (1.8 g), prepared by reacting **1b** (2.1 g) with 10 ml of a chilled solution of 25% HBr in acetic acid, was dissolved in dry ether (20 ml). This ethereal solution was gradually added to a stirred suspension of lithium aluminum hydride (1 g) in dry ether (30 ml) with keeping gentle reflux. Excess hydride was then decomposed with ethyl acetate and water. The precipitate was filtered and washed twice with water. The aqueous layer was then deionized with IR-120 (H^+) and IR-45 (OH^-), and concentrated in vacuo in the presence of benzene and ethanol to a thick syrup, which gradually solidified. Recrystallization from methanol gave crystals (0.42 g, 58%); mp 143—144 °C, $[\alpha]_D^{9}$ +43.2° (*c* 0.74, H_2O) [lit,[12] nondeuterated: Mp 142—143 °C, $[\alpha]_D$ +42.3° (*c* 0.84, H_2O)]. Anal. ($C_6H_{12}O_5$) C, H.

(b) A mixture of **1d** (1.57 g) and palladium on carbon (10%, 1.5 g) in acetic acid (25 ml) was shaken at room temperature with hydrogen until absorption ceased. The catalyst was filtered and washed with water. The combined and washings were concentrated in vacuo to a syrup, which was dried in the presence of ethanol and benzene azeotropically. The solidified mass was recrystallized from methanol to give 0.25 g (52%) of crystals; mp 142—143 °C, $[\alpha]_D^{12}$ +43.0° (*c* 0.5, H_2O).

(1*R*)-2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-[1-$^2H_1$]glucitol (1e): A solution of **1j** (0.50 g) dissolved in acetic anhydride (6 ml) and pyridine (6 ml) was kept overnight at room temperature, and poured into ice-water containing $NaHCO_3$.

The resulting mixture was then extracted with $CHCl_3$ (30 ml), and the $CHCl_3$ layer was washed with aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and concentrated to a syrupy residue, which was chromatographed on a silica gel (Wako gel C-300) with benzene–ethyl acetate (5/1) to give a crystalline mass; mp 71—72 °C, $[\alpha]_D^{12}$ +42.0° (*c* 0.87, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=2.028 (9H, s, $COCH_3$), 2.034 (3H, s, $COCH_3$), 3.60 (1H, m, H-5), 4.14 (1H, dd, H-6, $J_{5,6}$=2.3, $J_{6,6}$=12.2 Hz), 4.15 (1H, d, H-1 equatorial, $J_{1,2}$=5.6 Hz), 4.19 (1H, dd, H-6′ *J*=4.6 Hz), 5.01 (1H, dd, H-2, $J_{2,3}$=9.5 Hz), 5.03 (1H, t, H-4, $J_{3,4}$=$J_{4,5}$=9.5 Hz), 5.20 (1H, t, H-3). Anal. ($C_{14}H_{20}O_9$) C, H.

1,5-Anhydro-D-[3-^2H]glucitol (1k): 1,2,3,4,6-Penta-*O*-acetyl-β-D-[3-^2H]glucopyranose (1.5 g), obtained by acetylation of D-[3-^2H]glucopyranose[16] with acetic anhydride–sodium acetate, was treated with 10 ml of 25% solution of HBr in acetic acid, and the resulting bromide was reduced with lithium aluminum hydride (0.80 g) as menthioned above. After the same work-up, the compound **1k** was obtained as crystals (0.32 g); mp 142—143 °C, $[\alpha]_D^{12}$ +42.5° (*c* 0.65, H_2O).

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-[3-^2H]glucitol (1f): The compound **1k** (0.21 g) was acetylated in the same manner as **1j** and chromatographed on silica gel to give a solid mass (0.26 g); mp 71—73 °C, $[\alpha]_D^{12}$ +42.0° (*c* 0.52, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ=20.59—20.71 ($\underline{C}H_3$×4), 62.24 (t, C-6), 66.85 (t, C-1), 68.39 (d, C-4), 68.91 (d, C-2), 76.47 (d, C-5), 169.49—170.62 ($\underline{C}O$×4).

1,5-Anhydro-D-[5-^2H]glucitol (1l): 1,2,3,4,6-Penta-*O*-acetyl-β-D-[5-^2H]glucopyranose (1.2 g), prepared from D-[5-^2H]-glucopyranose,[19] was treated with 25% solution (10 ml) of HBr in acetic acid, and the resulting bromide was reduced with lithium aluminum hydride (0.6 g) to give crystals after the same work-up; yield 0.24 g, mp 142—143 °C, $[\alpha]_D^{12}$ +42.7° (*c* 0.51, H_2O).

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-[5-^2H]glucitol (1g): The compound (0.20 g) was acetylated and chromatographed in the same conditions as **1e** to give a crystalline mass (0.24 g); mp 72—73 °C (ether–petroleum ether), $[\alpha]_D^{13}$ +42.5° (*c* 0.50, $CHCl_3$); ^1H NMR δ=2.028 (9H, s, $COCH_3$), 2.034 (3H, s, $COCH_3$), 3.30 (1H, t, H-1 axial, $J_{1,2}$=$J_{1,1}$=10.6 Hz), 4.13 (1H, d, H-6, $J_{2,6'}$=12.2 Hz), 4.14 (1H, dd, H-1 equatorial, $J_{1,2}$=5.6 Hz), 4.20 (1H, d, H-6′), 5.01 (1H, m, H-2), 5.03 (1H, d, H-4, $J_{3,4}$=9.5 Hz), 5.20 (1H, t, H-3, $J_{2,3}$=$J_{3,4}$).

2,3,4,6-Tetra-*O*-benzyl-1,5-anhydro-D-[1-$^2H_2$]glucitol (1h): 2,3,4,6-Tetra-*O*-benzyl-α-D-[1-^2H]glucopyranosyl chloride (2.0 g), described in the preparation of **1d**, was reduced with lithium aluminum deuteride (0.6 g) in dry ether. The excess of LAD was then decomposed in the same manner as **1c** to give a crude syrup, which was chromatographed on silica gel (Wako gel C-300). Evaporation of the corresponding fractions gave a clear syrup (1.18 g, 63%); $[\alpha]_D^{15}$ +7.0 (*c* 0.50, $CHCl_3$); ^1H NMR ($CDCl_3$) δ=3.38 (1H, m, H-5), 3.55—3.67 (5H, m, H-2, H-3, H-4, H-6 and H-6′), 4.47—4.99 (8H, m, $\underline{C}H_2Ph$), 7.2—7.4 (20H, aromatics).

1,5-Anhydro-D-[1-$^2H_2$]glucitol (1m): (a) Hydrogenolysis of **1h** (2.1 g) was carried out in the same manner as described in **1d** to give a crystalline residue (0.40 g, 60%), which was recrystallized from methanol; mp 143—144 °C, $[\alpha]_D^{13}$ +43.0° (c 1.0, H_2O).

(b) Lithium aluminum deuteride reduction of 2,3,4,6-tetra-*O*-acetyl-α-D-[1-^2H]glucopyranosyl bromide (2.1 g, see experiment **1j**) gave the compound **1m** (0.48 g, 57%).

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-[1-$^2H_2$]glucitol (1i): Acetylation of **1m** (0.30 g) followed by chromatography and recrystallization described in the preparation of **1e** gave a crystalline compound **1i** (0.45 g) having mp 72—73 °C and $[\alpha]_D^{13}$ +43.0° (*c* 0.50, $CHCl_3$); ^{13}C NMR δ=20.59—20.71 ($\underline{C}H_3CO$), 62.22 (t, C-6), 68.47 (d, C-4), 68.99 (d, C-2), 73.74 (d, C-3), 76.47 (d, C-5), 169.5—170.6 ($\underline{C}OCH_3$).

1,5-Anhydro-D-[6-$^2H_2$]glucitol (1n): 1,2,3,4,6-Penta-*O*-acetyl-

β-D-[6-$^2H_2$]glucopyranose[18] (1.0 g) was converted to the corresponding bromide (see experiment **1j**), which was then reduced with LAH (0.30 g) to give crystals (0.72 g); mp 142—143 °C, $[\alpha]_D^{13}$ +42.8° (*c* 1.0, H_2O).

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-[6-$^2H_2$]glucitol (1o): The compound **1n** (0.20 g) was acetylated and chromatographed in the same conditions as **1e** to give a clear syrup (0.26 g), which gradually crystallized; mp 71—73 °C, $[\alpha]_D^{13}$ +42.0° (*c* 0.52, $CHCl_3$); ^{13}C NMR δ=20.60—20.71 ($\underline{C}H_3CO$), 66.88 (t, C-1), 68.47 (d, C-4), 68.98 (d, C-2), 73.74 (d, C-3), 76.38 (d, C-5), 169.5—170.6 ($\underline{C}O\times4$). Anal. ($C_{16}H_{20}O_9$) C, H.

2,3,4,6-Tetra-*O*-acetyl-1,5-anhydro-D-[5,6-$^2H_2$]glucitol (1p): 1,2,3,4,6-Penta-*O*-acetyl-β-D-[5,6-$^2H_3$]glucopyranose[19] (1.56 g) was treated with 30% HBr solution (1.0 ml) in acetic acid, and the resulting bromide was reduced with LAH in the same manner as **1j** to give a syrupy residue, which was then acetylated with acetic anhydride (10 ml)/pyridine (10 ml), and chromatographed on silica gel with benzene–ethyl acetate (5/1). Evaporation of the eluates afforded a clear syrup (1.08 g), which gradually crystallized; mp 72—73 °C, $[\alpha]_D^{13}$ +42.5° (*c* 0.65, $CHCl_3$); ^{13}C NMR ($CDCl_3$) δ=20.59, 20.67 ($\underline{C}H_3CO$), 66.86 (t, C-1), 68.44 (d, C-4), 68.99 (d, C-2), 73.74 (d, C-3), 169.5—170.6 ($\underline{C}O\times4$). Anal. ($C_{14}H_{20}O_9$) C, H.

1,5-Anhydro-D-[5,6-$^2H_3$]glucitol (1q): The tetraacetate **1p** (1.00 g) was deacetylated with sodium methoxide in methanol and deionized with IR-120 (H^+). The aqueous methanol solution was then concentrated in vacuo to a syrupy residue (0.42 g), which was treated with methanol to give crystals (0.26 g); mp 142—143 °C, $[\alpha]_D^{13}$ +43.0° (*c* 0.53, H_2O). Anal. ($C_6H_{12}O_5$) C, H.

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