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Note

Synthesis of a carba-sugar analog of trehalosamine, [(1*S*)-(1,2,4/3,5)-2-amino-3,4-dihydroxy-5-hydroxymethyl-1-cyclohexyl] α-D-glucopyranoside, and a revised synthesis of its β anomer*

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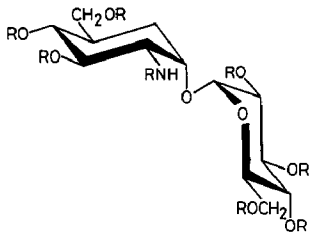
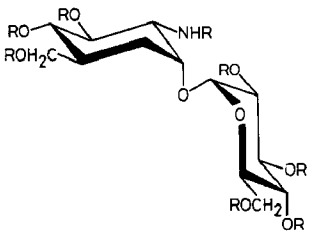
In connection with the previous paper[1], the title pseudodisaccharide **1A**, one of the carba-sugar analogs of the antibiotic trehalosamine, and related compounds have been synthesized, and their antimicrobial and hydrolase-inhibitory activities examined.

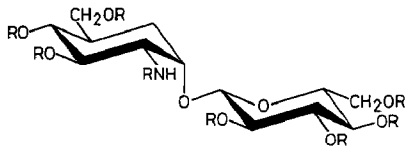
The synthesis of the α-D-glucosides **1A,B** was performed by condensation of the newly prepared 3,4,7-tri-*O*-benzyl-2-deoxy-2-*p*-toluenesulfonamido-5a-carba-α-DL-glucopyranose (**7**) with 1,6-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-β-D-glucopyranose[2] (**13**) in the presence of trimethylsilyl trifluoromethanesulfonate.



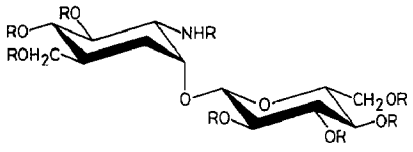
1A R = H
2A R = Ac



1B R = H
2B R = Ac



3A R = H
4A R = Ac



3B R = H
4B R = Ac

* Synthesis of Pseudo-trehalosamine and Related Pseudo-disaccharides, Part IV. For Part III, see ref. 1.
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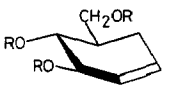
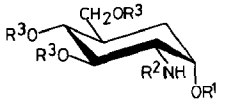
Likewise, the β-glucosides (**3A,B**) were also synthesized using 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose as the glycosyl donor, which led to a revision of the structure of the β anomer previously synthesized and incorrectly assigned by one of the authors.

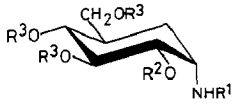
First, the aglycon **7** was prepared by the following sequence. The tribenzyl ether **6** prepared from DL-(1,3/2)-3-hydroxymethyl-5-cyclohexene-1,2-diol (**5**) was subjected to oxyamination under Sharpless conditions[3]. The reaction proceeded *via* preferential rear-side attack of the reagent to give, after column chromatography, a 2:3 mixture of the positional isomers **7** (21%) and **10** (33%), the structures of which were characterized by the ^{1}H-n.m.r. spectra of their acetates **8** and **11**, and further confirmed by converting them into the known penta-*N,O*-acetyl derivatives **9** (ref. 4) and **12** (ref. 5), respectively. Interestingly, similar reaction of the corresponding 3-bromomethyl-1,2-diacetoxy compound[6] gave almost exclusively the 2-*p*-toluenesulfonamide[7].



5 R = H
6 R = Bn



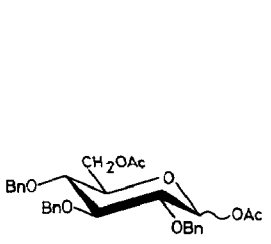
	R^1	R^2	R^3
7	H	Ts	Bn
8	Ac	Ts	Bn
9	Ac	Ac	Ac



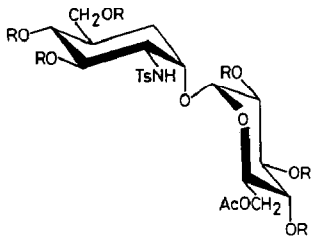
	R^1	R^2	R^3
10	Ts	H	Bn
11	Ts	Ac	Bn
12	Ac	Ac	Ac

Condensation of **7** with **13** in dichloromethane in the presence of trimethylsilyl trifluoromethanesulfonate and molecular sieves for 2.5 h at room temperature produced, after fractionation by column chromatography, the α-glucosides **14A**, $[\alpha]_D$ +47°($CHCl_3$), and **14B**, $[\alpha]_D$ +5°($CHCl_3$), in 39 and 40% yields, respectively, along with a mixture of the β anomers (~7%). *O*-Debenzylation of **14A** and **14B** by hydrogenolysis with Pd–C in ethanol containing acetic acid, followed by conventional acetylation, gave the respective heptaacetates **15A** and **15B**, which were reduced with sodium in liquid ammonia followed by acetylation to give the octa-*N,O*-acetyl derivatives **2A**, $[\alpha]_D$ +110° ($CHCl_3$), and **2B**, $[\alpha]_D$ +28° ($CHCl_3$), in 57 and 56% yields, respectively. The structures of **2A** and **2B** were confirmed by their ^{1}H-n.m.r. spectra, which showed doublets at δ 5.16 (J 3.7 Hz) and 5.30 (J 4 Hz), respectively, attributable to the signals for the α-anomeric protons. The difference of the optical rotations is large enough for assignment of the absolute configurations. Hydrazinolysis of **2A** and **2B** afforded the free pseudo-disaccharides **1A** and **1B**, which were directly used for biological assay.

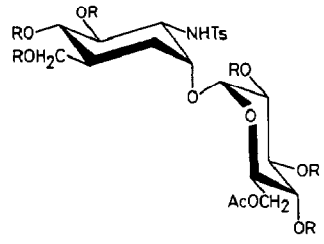
In the first paper[8] of this series of studies, a synthesis of the protected pseudo-disaccharide composed of "pseudo-2-amino-2-deoxy-α-D-glucopyranose" and D-glucopyranose bonded by a β-glucosidic linkage was described. However, we have subsequently found that, under standard Koenigs–Knorr reaction conditions, glycosidation of DL-(1,2,4/3,5)-3,4-di-*O*-acetyl-5-bromomethyl-2-*p*-toluenesulfonamido-1,3,4-cyclohexanetriol[7] with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide did



13



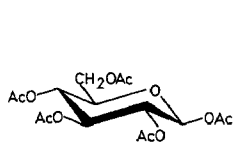
14A R = Bn
15A R = Ac



14B R = Bn
15B R = Ac

not occur and instead a stable ortho ester was formed. Therefore, a synthesis of the β-glucoside was reinvestigated, using **7**.

Condensation of **7** with 1,2,3,4,6-penta-*O*-acetyl-β-D-glucopyranose (**16**) was conducted as in the preparation of **14A,B** to give in 66% yield a mixture of the β-glucosides **17A** and **17B**, which were successively *O*-debenzylated and acetylated to afford, after chromatography, the respective heptaacetates **18A**, $[\alpha]_D$ +50° ($CHCl_3$), and **18B**, $[\alpha]_D$ −59° ($CHCl_3$), in 14 and 19% isolated yields based on **7** consumed. Similarly, they were *N*-detosylated and acetylated to give the octa-*N*,*O*-acetyl derivatives **4A**, $[\alpha]_D$ +26° ($CHCl_3$), and **4B**, $[\alpha]_D$ −61° ($CHCl_3$), whose ^{1}H-n.m.r. spectra revealed anomeric-proton signals at δ 4.55 (*J* 7.7 Hz) and 4.49 (*J* 7.8 Hz), respectively, indicative of the β-glucosides. The absolute configurations were deduced on the basis of the difference of optical rotations. A preliminary experiment[9] for the preparation of **18A**, $[\alpha]_D$ +52° ($CHCl_3$), from optically active **7**, $[\alpha]_D$ +26° ($CHCl_3$), also supported these assignments.



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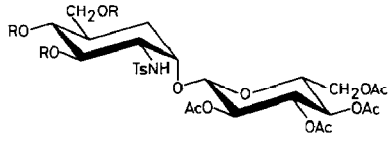
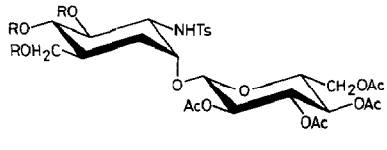


17A R = Bn
18A R = Ac



17B R = Bn
18B R = Ac

As the ^{1}H-n.m.r. data and optical rotations of **18A** and **18B** were clearly different from those of the respective compounds $[\alpha]_D$ +43° ($CHCl_3$) and $[\alpha]_D$ −34° ($CHCl_3$), which were previously assigned as the β-glucosides[8], the previous compounds are evidently the ortho esters; their ^{1}H-n.m.r. spectra showed the anomeric-proton signals[10] at δ 5.64–5.74 (*J* 5.3–6 Hz).

The free pseudo-disaccharides **3A** and **3B** were obtained by hydrazinolysis of **4A** and **4B**, and subjected to biological tests.

Bioassay. — Pseudo-disaccharides **1A**, **1B**, **3A**, and **3B** showed no antibacterial activity against *Staphylococcus aureus* FDA 209P, *Bacillus subtilis* PCI 219, *Escherichia coli* K-12, and *Mycobacterium smegmatis* ATCC 607.

No inhibitory activity against baker's yeast trehalase was detected for any of them

at the concentration of 10^{-3} M. In contrast, the other diastereoisomer, [(1*S*)-(1,2,4/3,5)-2,3,4-trihydroxy-5-hydroxymethyl-1-cyclohexyl] 2-amino-2-deoxy-α-D-glucopyranoside[1] showed an inhibition of 23% at 10^{-3} M.

EXPERIMENTAL

General methods. — Melting points were determined with a Mel-Temp capillary melting-point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-4 polarimeter. ^{1}H-N.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Jeol JNM FX-90A (90 MHz) or a Jeol GSX-270 f.t. (270 MHz) instrument. T.l.c. was performed on Silica Gel 60 GF (Merck) with detection by charring with H_2SO_4. Column chromatography was conducted on Wakogel C-300 (300 mesh). Organic solutions were dried over anhydrous Na_2SO_4 and concentrated at $< 50°$ under diminished pressure.

DL-*(1,3/2)-3-Hydroxymethyl-5-cyclohexene-1,2-diol* (**5**). — (*a*) A mixture of DL-(1,3/2)-1,2-di-*O*-acetyl-3-bromomethyl-5-cyclohexene-1,2-diol[6] (3.0 g, 10.3 mmol), anhydrous NaOAc (3.38 g, 41.2 mmol), and aq. 20% *N*,*N*-dimethylformamide (20 mL) was stirred for 4 h at 100°, and then evaporated to dryness. The residue was digested with EtOAc (100 mL) and the organic layer was washed with water, dried, and evaporated to give the triacetate. The crude compound was treated with methanolic M NaOMe (1 mL) in MeOH (8 mL) for 2 h at room temperature. The mixture was made neutral with Amberlite IR 120-B (H^+) resin and evaporated to give **5** (1.08 g, 73%) as prisms, m.p. 113–114° (from EtOAc).

Anal. Calc. for $C_7H_{12}O_3$: C, 58.32; H, 8.39. Found: C, 58.53; H, 8.10.

(*b*) To a solution of DL-(1,3/2)-2,3-diacetoxy-4-cyclohexene-1-carboxylic acid[11] (5.53 g, 22.8 mmol) in tetrahydrofuran (100 mL) was added dropwise a solution of $LiAlH_4$ (5.2 g, 137 mmol) in tetrahydrofuran (30 mL), and the mixture was stirred for 1.5 h at room temperature. The excess of reagent was decomposed by addition of water (6 mL), aq. 15% NaOH (6 mL), and water (15 mL), and the product was then digested with 1:1 acetone–water (50 mL). The mixture was filtered through a Celite bed and the filtrate was evaporated. The residue was acetylated with Ac_2O (100 mL) and pyridine (100 mL) for 2 h at room temperature, and the mixture was processed conventionally to give the triacetate (6.9 g). This compound was similarly *O*-deacetylated to give **5** (2.89 g, 86%).

DL-*(1,3/2)-1,2-Di-O-benzyl-3-benzyloxymethyl-5-cyclohexene-1,2-diol* (**6**). — Compound **5** (1.0 g, 6.9 mmol) was treated with 60% NaH (2.33 g, 58 mmol) in *N*,*N*-dimethylformamide (100 mL) for 30 min at 0°, and $PhCH_2Br$ (6.4 mL, 52 mmol) was added to the mixture, which was then stirred for 3 h at room temperature. After dropwise addition of EtOH (50 mL) at 0°, the mixture was evaporated and the residue was eluted from a column of silica gel with 1:30 EtOAc–hexane to give **6** (2.4 g, 83%) as a syrup; ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.42–7.13 (m, 15 H, 3 CH_2Ph), 5.80–5.65 (m, 2 H, H-5,6), 4.89 and 4.61 (2 d, each 1 H, *J* 11 Hz), 4.68 and 4.48 (2 s, each 2 H) (3CH_2Ph), 4.15 (dd, 1 H, *J* 3 and 7 Hz, H-7), 3.83–3.45 (m, 3 H, H-1,2,7′), and 2.36–1.96 (m, 3 H, H-3,4,4′).

Anal. Calc. for $C_{28}H_{30}O_3$: C, 81.13; H, 7.29. Found: C, 81.44; H, 7.20.

DL-*(1,2,4/3,5)-3,4-Di*-O-*benzyl-5-benzyloxymethyl-2*-p-*toluenesulfonamido-1,3,4-cyclohexanetriol* (**7**) and DL-*(1,3,4/2,6)-1,2-di*-O-*benzyl-6-benzyloxymethyl-4*-p-*toluenesulfonamido-1,2,3-cyclohexanetriol* (**10**). — To a stirred solution of **6** (3.01 g, 7.3 mmol) in $CHCl_3$ (30 mL) were added in turn chloramine T trihydrate (3.4 g, 12 mmol), 0.05M OsO_4–*tert*-butanol (1.9 mL, 0.095 mmol), triethylbenzylammonium chloride (90 mg, 0.4 mmol), and water (30 mL), and the mixture was agitated vigorously for 20 h at 60°. Then $NaHSO_3$ (2 g) was added and the mixture was boiled under reflux for 5 h. The organic layer was separated, washed successively with aq. 1% NaOH and water, dried, and evaporated. The residue was crystallized from EtOH to give **7** (0.90 g, 21%) as thin needles, m.p. 153–154°. The mother liquor was evaporated and the residue chromatographed on a column of silica gel (90 g) with 1:3 EtOAc–hexane to give **10** (1.42 g, 33%), m.p. 112–113° (from EtOH), and **7** (0.13 g, total 24%); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): for **7**, δ 7.64 (d, 2 H, *J* 9 Hz, MeC_6H_4), 7.46–7.07 (m, 17 H, 3 CH_2Ph and MeC_6H_4), 4.90–4.74 (m, 2 H, NH and H-1), 4.66 and 4.60 (2 d, each 2 H, *J* 10 Hz), and 4.39 (s, 2 H) (3 CH_2Ph), 2.40 (s, 3 H, Me); for **10**, δ 7.72 (d, 2 H, *J* 9 Hz, MeC_6H_4), 7.34–7.13 (m, 17 H, 3 CH_2Ph and MeC_6H_4), 4.99–4.38 (m, 6 H, H-2, NH and CH_2Ph), 4.37 (s, 2 H, CH_2Ph), and 2.38 (s, 3 H, Ts).

Anal. Calc. for $C_{35}H_{39}NO_6S$: C, 69.86; H, 6.53; N, 2.33. Found: **7**, C, 69.70; H, 6.42; N, 2.23; **10**, C, 69.75; H, 6.51; N, 2.22.

DL-*(1,2,4/3,5)-1*-O-*Acetyl-3,4-di*-O-*benzyl-5-benzyloxymethyl-2*-p-*toluenesulfonamido-1,3,4-cyclohexanetriol* (**8**). — Compound **7** (11 mg, 0.018 mmol) was treated with Ac_2O and pyridine overnight at room temperature. The product was crystallized from EtOH to give **8** (8.5 mg, 73%); m.p. 137–138°; ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 7.66 (d, 2 H, *J* 8.1 Hz, MeC_6H_4), 7.35–7.12 (m, 17 H, 3 CH_2Ph and MeC_6H_4), 4.98–4.92 (m, 2 H, NH and H-1), 4.72 and 4.49 (2 d, each 1 H, *J* 11 Hz), and, 4.68 and 4.40 (2 s, each 2 H) (3 CH_2Ph), 2.37 (s, 3 H, Ts), and 2.00 (s, 3 H, OAc).

Anal. Calc. for $C_{37}H_{41}NO_7S$: C, 69.03; H, 6.42; N, 2.18. Found: C, 68.86; H, 6.32; N, 2.29.

DL-*(1,3,4/2,6)-3*-O-*Acetyl-1,2-di*-O-*benzyl-6-benzyloxymethyl-4*-p-*toluenesulfonamido-1,2,3-cyclohexanetriol* (**11**). — Compound **10** (20 mg, 0.033 mmol) was acetylated as just described to give **11** (15 mg, 69%), m.p. 123–124° (from EtOH); ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 7.72 (d, 2 H, *J* 8.4 Hz, MeC_6H_4), 7.36–7.17 (m, 17 H, 3 CH_2Ph and MeC_6H_4), 4.80–4.74 (m, 2 H, NH and H-3), 4.77, 4.76, 4.63, and 4.49 (4 d, each 1 H, *J* 11 Hz), and 4.38 (s, 2 H) (3 CH_2Ph), 2.39 (s, 3 H, Ts), and 1.76 (s, 3 H, OAc).

Anal. Calc. for $C_{37}H_{41}NO_7S$: C, 69.03; H, 6.42; N, 2.18. Found: C, 68.77; H, 6.70; N, 2.05.

DL-*(1,2,4/3,5)-2-Acetamido-1,3,4-tri*-O-*acetyl-5-acetoxymethyl-1,3,4-cyclohexanetriol* (**9**). — To stirred liquid ammonia (~20 mL) containing sodium (~530 mg) was added dropwise a solution of **7** (149 mg, 0.25 mmol) in tetrahydrofuran (6 mL) at −78°, and the mixture was stirred for 7 h at the same temperature. After addition of NH_4Cl, the mixture was allowed to evaporate spontaneously and further concentrated to dryness. The residue was acetylated conventionally and the product was eluted from a

column of silica gel with 30:1 $CHCl_3$–MeOH to give **9** (57 mg, 59%), m.p. 134–135° (from EtOH) (lit.[4] m.p. 134–136°); identical with an authentic sample[4] by ^{1}H-n.m.r. spectroscopy; ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 5.69 (d, 1 H, *J* 9 Hz, NH), 5.20 (q, 1 H, *J* 3 Hz, H-1), 5.16 (t, 1 H, m, *J* 11 Hz, H-3), 5.10 (t, 1 H, *J* 11 Hz, H-4), 4.27 (ddd, 1 H, *J* 3, 9, and 11 Hz, H-2), 4.13 (dd, 1 H, *J* 4 and 11 Hz, H-7), 3.87 (dd, 1 H, *J* 3 and 11 Hz, H-7'), 2.16, 2.06, 2.045, 2.04, and 1.93 (5 s, each 3 H, 5 Ac).

Anal. Calc. for $C_{17}H_{25}NO_9$: C, 52.64; H, 6.44; N, 3.67. Found: C, 52.71; H, 6.50; N, 3.62.

DL-*(1,3,4/2,6)-4-Acetamido-1,2,3-tri*-O-*acetyl-6-acetoxymethyl-1,2,3-cyclohexanetriol* (**12**). — Compound **10** (142 mg, 0.34 mmol) was reduced and acetylated as just described to give **12** (46 mg, 50%), m.p. 199–201° (lit.[5] 199–199.5°), identical with an authentic sample[5] by ^{1}H-n.m.r. spectroscopy.

*[(1S)-(1,2,4/3,5)-3,4-Dibenzyloxy-5-benzyloxymethyl-2-*p-*toluenesulfonamido-1-cyclohexyl] 6-*O-*acetyl-2,3,4-tri*-O-*benzyl-α*-D-*glucopyranoside* (**14A**) *and its (1R) diastereoisomer* (**14B**). — To a mixture of **7** (0.60 g, 1.0 mmol), 1,6-di-*O*-acetyl-2,3,4-tri-*O*-benzyl-β-D-glucopyranose (**13**, 1.07 g, 2.0 mmol), powdered molecular sieves 4A (0.6 g), and CH_2Cl_2 (40 mL) was added trimethylsilyl trifluoromethanesulfonate (0.46 mL, 2.34 mmol), and the suspension was stirred for 2.5 h at room temperature. The mixture was filtered, and the filtrate was diluted with CH_2Cl_2 (50 mL) and washed successively with saturated aq. $NaHCO_3$ and water, dried, and evaporated. Column chromatography of the residue on silica gel (60 g) with 1:5 EtOAc–hexane gave **14A** (418 mg, 39%) and **14B** (149 mg, 14%) both as hygroscopic syrups, and a mixture (390 mg) of **14B** and the β anomers. The mixture was rechromatographed to give **14B** (278 mg, total 40%) and a diastereoisomeric mixture (74 mg, 7%) of the β anomers.

Compound **14A**, $[\alpha]_D^{23}$ +47° (*c* 1.3, $CHCl_3$); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.67 (d, 2 H, *J* 9 Hz, MeC_6H_4), 7.37–7.03 (m,17 H, 3 CH_2Ph and MeC_6H_4), 2.32 (s, 3 H, Ts), and 2.00 (s, 3 H, OAc).

Compound **14B**, $[\alpha]_D^{24}$ +5° (*c* 1.4, $CHCl_3$); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.45 (d, 2 H, *J* 9 Hz, MeC_6H_4), 7.33–7.12 (m, 17 H, 3 CH_2Ph and MeC_6H_4), 6.96 (d, 1 H, *J* 9 Hz, NH), 2.25 (s, 3 H, Ts), and 1.94 (s, 3 H, OAc).

Anal. Calc. for $C_{64}H_{69}NO_{12}S{\cdot}0.5H_2O$: C, 70.83; H, 6.50; N, 1.29. Found: for **14A**, C, 70.72; H, 6.60; N, 1.42; for **14B**, C, 71.12; H, 6.31; N, 1.36.

*[(1S)-(1,2,4/3,5)-3,4-Dihydroxy-5-hydroxymethyl-2-*p-*toluenesulfonamido-1-cyclohexyl] α*-D-*glucopyranoside heptaacetate* (**15A**) *and its (1R) diastereoisomer* (**15B**). — A solution of **14A** (353 mg, 0.33 mmol) in EtOH (22 mL) containing AcOH (0.5 mL) was hydrogenated in the presence of 10% Pd on C (350 mg) in Parr apparatus (an initial hydrogen pressure of 3.4 kg/cm^2) for 43 h at room temperature. The mixture was filtered and the filtrate evaporated, and the residue was acetylated. Column chromatography of the product on silica gel with 3:1 $CHCl_3$–EtOAc gave **15A** (140 mg, 54%) as a syrup, $[\alpha]_D^{23}$ +114° (*c* 1.2, $CHCl_3$); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.69 and 7.28 (2 d, each 2 H, *J* 9 Hz, MeC_6H_4), 5.53 (d, 1 H, *J* 11 Hz, NH), 5.49 (t, 1 H, *J* 10 Hz, H-3), 4.88 (dd, 1 H, *J* 4 and 10 Hz, H-2), 3.48 (ddd, 1 H, *J* 3, 9, and 11 Hz, H-2'), 2.42 (s, 3 H, Ts), 2.10, 2.08, 2.06, 2.04, 2.01, and 1.59 (6 s, 3, 3, 3, 6, 3, and 3 H, 7 OAc).

Anal. Calc. for $C_{34}H_{45}NO_{18}S$: C, 51.84; H, 5.76; N, 1.78. Found: C, 51.68; H, 5.72; N, 1.58.

Compound **14B** (342 mg, 0.32 mmol) was similarly *O*-debenzylated and then acetylated to give, after chromatography, **15B** (145 mg, 58%) as a syrup, $[\alpha]_D^{18}$ +3.8° (*c* 0.8, $CHCl_3$); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.66 and 7.27 (2 d, each 2 H, *J* 9 Hz, MeC_6H_4), 3.40 (dt, 1 H, *J* 3, 10, and 10 Hz, H-2'), 2.40 (s, 3 H, Me), 2.18, 2.04, 2.00, 1.96, and 1.58 (5 s, 3, 3, 6, 6, and 3 H, 7 OAc).

Anal. Found: C, 51.51; H, 5.71; N, 1.68.

[(1S)-(1,2,4/3,5)-2-Acetamido-3,4-dihydroxy-5-hydroxymethyl-1-cyclohexyl] α-D-*glucopyranoside heptaacetate* (**2A**) *and its (1R) diastereoisomer* (**2B**). — Compound **15A** (140 mg, 0.18 mmol) was *N*-detosylated with Na in liquid NH_3 and then acetylated as in the preparation of **9**. Column chromatography of the product on silica gel with 1:10 EtOH–PhMe gave crude **2A** (59 mg), which was again chromatographed to give 29 mg (28%) as needles, m.p. 127–128° (from EtOH), $[\alpha]_D^{23}$ +110° (*c* 1.1, $CHCl_3$); ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 6.43 (d, 1 H, *J* 8.8 Hz, NH), 5.51 (dd, 1 H, *J* 10 and 10.3 Hz, H-3), 5.16 (d, 1 H, *J* 3.7 Hz, H-1), 5.16 (t, 1 H, *J* 10 Hz, H-4), 5.07 and 5.00 (2 t, each 1 H, *J* 10 Hz, H-3',4'), 4.88 (dd, 1 H, *J* 3.7 and 10.3 Hz, H-2), 2.09, 2.07, 2.05, 2.045, 2.04, and 1.97 (6 s, 3, 9, 3, 3, 3, and 3 H, NAc and 7 OAc).

Anal. Calc. for $C_{29}H_{41}NO_{17}\cdot 0.5H_2O$: C, 50.87; H, 6.18; N, 2.05. Found: C, 50.43; H, 5.84; N, 2.19.

Compound **15B** (126 mg, 0.16 mmol) was similarly converted into **2B** (56 mg, 52%), m.p. 143–144° (from EtOH); $[\alpha]_D^{22}$ +28° (*c* 0.8, $CHCl_3$); ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 6.00 (d, 1 H, *J* 8.1 Hz, NH), 5.44 (t, 1 H, *J* 10 Hz, H-3),5.30 (d, 1 H, *J* 4 Hz, H-1), 5.11–5.01 (m, 3 H, H-4,3',4'), 4.82 (dd, 1 H, *J* 4 and 10 Hz, H-2), 2.19, 2.08, 2.07, 2.068, 2.063, 2.05, 2.03, and 1.94 (8 s, each 3 H, NAc and 7 OAc).

Anal. Found: C, 51.13; H, 5.99; N, 2.04.

[(1S)-(1,2,4/3,5)-2-Amino-3,4-dihydroxy-5-hydroxymethyl-1-cyclohexyl] α-D-*glucopyranoside* (**1A**) *and its (1R) diastereoisomer* (**1B**). — Compound **2A** (16 mg, 0.024 mmol) was treated with hydrazine hydrate (0.5 mL) for 1.5 h at 70°. The mixture was concentrated and the product was eluted from a column of Dowex 50W-X2 (H^+) resin (2.31 mL) with MeOH and then from a column of Amberlite IRA-400 (OH^-) resin with MeOH to give **1A** (8.3 mg, 100%) as an amorphous solid; $[\alpha]_D^{24}$ +123° (*c* 0.4, MeOH).

Similarly, compound **2B** (13 mg, 0.020 mmol) was converted into **1B** (7.2 mg, quantitative), $[\alpha]_D^{28}$ −2.2° (*c* 0.4, MeOH).

Compounds **1A** and **1B** are very hygroscopic and did not give satisfactory elemental analyses.

*[(1S)-(1,2,4/3,5)-3,4-Dibenzyloxy-5-benzyloxymethyl-2-*p-*toluenesulfonamido-1-cyclohexyl] 2,3,4,6-tetra-*O-*acetyl-β-*D-*glucopyranoside* (**17A**) *and its (1R) diastereoisomer* (**17B**). — A mixture of **7** (0.80 g, 1.3 mmol), 1,2,3,4,6-penta-*O*-acetyl-D-glucopyranose (**16**, 1.04 g, 2.7 mmol), molecular sieves 4A (0.8 g), and trimethylsilyl trifluoromethanesulfonate (0.62 mL, 3.2 mmol) in CH_2Cl_2 (30 mL) was processed as in the preparation of **14A,B** to give, after chromatography, an inseparable syrupy mixture (0.82 g) of **17A,B** and **8**, which was used directly in the following reaction.

*[(1S)-(1,2,4/3,5)-3,4-Diacetoxy-5-acetoxymethyl-2-*p*-toluenesulfonamido-1-cyclohexyl] 2,3,4,6-tetra-*O*-acetyl-β-*D*-glucopyranoside* (**18A**) *and its (1R) diasteroisomer* (**18B**). — The mixture (0.82 g) of **17A,B** and **8** was *O*-debenzylated and then acetylated as in the preparation of **15A,B**. Repeated column chromatography of the products (0.71 g) on silica gel with 2:1 $CHCl_3$–EtOAc and fractional crystallization from EtOH gave **18A** (142 mg, 21% based on **7** consumed) and **18B** (109 mg, 16%), both as prisms.

Compound **18A**, m.p. 194–195° (from EtOH), $[\alpha]_D^{25}$ +50° (*c* 1.6, $CHCl_3$); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.70 and 7.29 (2 d, each 2 H, *J* 9 Hz, MeC_6H_4), 2.42 (s, 3 H, Ts), 2.19, 2.09, 2.04, 2.02, 1.98, and 1.54 (6 s, 3, 3, 6, 3, 3, and 3 H, 7 OAc).

Anal. Calc. for $C_{34}H_{45}NO_{18}S$: C,51.84; H, 5.76; N, 1.78. Found: C, 51.27; H, 5.51; N, 1.88.

Compound **18B**, m.p. 233–234° (from EtOH), $[\alpha]_D^{25}$ −59° (*c* 0.6, $CHCl_3$); ^{1}H-n.m.r. (90 MHz, $CDCl_3$): δ 7.72 and 7.28 (2 d, each 2 H, *J* 9 Hz, MeC_6H_4), 5.71 (d, 1 H, *J* 10 Hz, NH), 3.39 (dt, 1 H, *J* 3, 10, and 10 Hz, H-2′), 2.41 (s, 3 H, Ts), 2.10, 2.04, 1.98, and 1.51 (4 s, 3, 12, 3, and 3 H, 7 OAc).

Anal. Found: C, 51.83; H, 5.67; N, 1.73.

*[(1S)-(1,2,4/3,5)-2-Acetamido-3,4-dihydroxy-5-hydroxymethyl-1-cyclohexyl] β-*D*-glucopyranoside heptaacetate* (**4A**) *and its (1R) diastereoisomer* (**4B**). — Compound **18A** (97 mg, 0.12 mmol) was reduced and acetylated as in the preparation of **2A**, and the product was eluted from a column of silica gel (4 g) with 1:9 acetone–$CHCl_3$ to give **4A** (38 mg, 46%) as a syrup, $[\alpha]_D^{28}$ +26° (*c* 0.7, $CHCl_3$); ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 5.94 (d, 1 H, *J* 8.8 Hz, NH), 5.25–4.98 (m, 5 H, H-2,3,4,3′,4′), 4.55 (d, 1 H, *J* 7.7 Hz, H-1), 4.17 (d, 2 H, *J* 4 Hz, H-6,6′), 4.14 (dd, 1 H, *J* 4 and 12 Hz, CH_2OAc), 4.18–4.08 (m, 1 H, H-2′), 4.05 (q, 1 H, *J* 1.5 Hz, H-1′), 3.88 (dd, 1 H, *J* 3 and 12 Hz, H-7′), 3.68 (dt, 1 H, *J* 4, 4, and 9.9 Hz, H-5), 2.14, 2.10, 2.05, 2.04, 2.03, 2.01, and 1.96 (7 s, 3, 3, 3, 3, 6, 3, and 3 H, NAc and 7 OAc).

Anal. Calc. for $C_{29}H_{41}NO_{17}$: C, 51.55; H, 6.12; N, 2.07. Found: C, 51.31; H, 6.15; N, 2.11.

Compound **18B** (62 mg, 0.08 mmol) was similarly converted into **4B** (21 mg, 40%); syrup, $[\alpha]_D^{28}$ −61° (*c* 1, $CHCl_3$); ^{1}H-n.m.r. (270 MHz, $CDCl_3$): δ 6.12 (d, 1 H, *J* 9 Hz, NH), 5.22, 5.10, 5.06, and 5.02 (4 t, each 1 H, *J* 9.5 Hz, H-3,4,3′,4′), 5.01 (dd, 1 H, *J* 7.8 and 9 Hz, H-2), 4.49 (d, 1 H, *J* 7.8 Hz, H-1), 4.27 (dd, 1 H, *J* 4.4 and 12 Hz, H-6), 4.16 (ddd, 1 H, *J* 2, 9, and 9.5 Hz, H-2′), 4.10 (dd, 1 H, *J* 2.2 and 12 Hz, H-6), 4.09 (dd, 1 H, *J* 5 and 11.4 Hz, H-7), 4.03 (q, 1 H, *J* 2 Hz, H-1′), 3.86 (dd, 1 H, *J* 3.3 and 11.4 Hz, H-7′), 3.69 (ddd, 1 H, *J* 2.2, 4.4, and 9.5 Hz, H-5), 2.11, 2.06, 2.05, 2.04, 2.035, 2.00, and 1.93 (7 s, 3, 3, 3, 3, 6, 3, and 3 H, NAc and 7 OAc).

Anal. Found: C, 51.47; H, 5.99; N, 2.23.

*[(1S)-(1,2,4/3,5)-2-Amino-3,4-dihydroxy-5-hydroxymethyl-1-cyclohexyl] β-*D*-glucopyranoside* (**3A**) *and its (1R) diastereoisomer* (**3B**). — Compound **4A** (14 mg, 0.02 mmol) was treated with hydrazine as in the preparation of **1A** to give **3A** (6.3 mg, 90%), as an amorphous powder, $[\alpha]_D^{25}$ +32° (*c* 0.3, MeOH).

Similarly, **4B** (22 mg, 0.03 mmol) was converted into **3B** (11 mg, 100%), as an amorphous powder, $[\alpha]_D^{25}$ −77° (*c* 0.5, MeOH).

Compounds **4A** and **4B** are very hygroscopic and did not give satisfactory elemental analyses.

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REFERENCES

1 S. Ogawa and Y. Shibata, *Carbohydr. Res.*, 176 (1988) 309–315.
2 G. Zemplen, Z. Csuros, and S. J. Angyal, *Ber.*, 70 (1937) 1848–1856; S. A. Holick, S. -H. L. Chiu, and L. Anderson, *Carbohydr. Res.*, 50 (1976) 215–225.
3 K. B. Sharpless, D. W. Patrick, L. K. Truesdale, and S. A. Biller, *J. Am. Chem. Soc.*, 97 (1975) 2305–2307.
4 S. Ogawa, N. Sasaki, T. Nose, Y. Yato, T. Takagaki, and T. Suami, Abstr. *Eur. Symp. Carbohydr., Third*, Grenoble, France, 1985, No. B4-11 P, p. 181.
5 T. Suami, S. Ogawa, K.Nakamoto, and I. Kasahara, *Carbohydr. Res.*, 58 (1977) 240–244.
6 S. Ogawa, T. Toyokuni, M. Ara, M. Suetsugu, and T. Suami, *Chem. Lett.*, (1980) 379–382; *Bull. Chem. Soc. Jpn.*, 56 (1983) 1710–1714.
7 S. Ogawa, T. Toyokuni, T. Kondoh, Y. Hattori, S. Iwasaki, M. Suetsugu, and T. Suami, *Bull. Chem.Soc. Jpn.*, 54 (1981) 2739–2746.
8 S. Ogawa, T. Toyokuni, Y. Hattori, T. Nose, and T. Suami, *Carbohydr. Res.*, 146 (1986) 167–173.
9 S. Ogawa and K. Nishi, unpublished results.
10 S. Ogawa, T. Nose, T. Ogawa, T. Toyokuni, Y. Iwasawa, and T. Suami, *J. Chem. Soc., Perkin Trans. 1*, (1985) 2369–2374.
11 S. Ogawa, Y. Yato, K. Nakamura, M. Takata, and T. Takagaki, *Carbohydr. Res.*, 148 (1986) 249–255.