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SYNTHESIS OF SOME DERIVATIVES OF PSEUDO-α-GALACTOPYRANOSE [(1,2/3,4,5)-5-HYDROXYMETHYL-1,2,3,4-CYCLOHEXANETETROL]*

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ABSTRACT

Isopropylidenation of DL-(1,2/3,4,5)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol (**1**) with 2,2-dimethoxypropane in *N,N*-dimethylformamide in the presence of toluene-*p*-sulfonic acid gave the 1,2:3,4-, 1,2:4,7-, and 2,3:4,7-di-*O*-isopropylidene derivatives. Several C-7 substituted derivatives of **1** of biological interest have been prepared by nucleophilic displacement reactions of the tosylate derived from the most readily available 1,2:3,4-di-*O*-isopropylidene derivative **3**. Condensation of **3** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide gave diastereoisomeric products, which were converted into 7-*O*-(β-D-glucopyranosyl)-pseudo-α-D- (**26A**) and -L-galactopyranose (**26B**), the structures of which were confirmed by degradation of the octa-acetate of **26A**, yielding the known pseudo-α-D-galactopyranose penta-acetate.

INTRODUCTION

Pseudo-α-D-galactopyranose (**1**) was isolated[2] as an antibacterial substance from the fermentation broth of *Streptomyces* sp. MA-4145 in 1971 and is the only known naturally occurring pseudo-sugar. We have been interested in elucidating the structure–activity relationships for this type of compound.

Synthetically useful derivatives are available easily by isopropylidenation of pseudo-sugars with 2,2-dimethoxypropane in *N,N*-dimethylformamide in the presence of toluene-*p*-sulfonic acid[3]. We now report on the isopropylidenation of DL-(1,2/3,4,5)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol (**1**) and some reactions of the 1,2:3,4-di-*O*-isopropylidene derivative **3**.

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*Pseudo-sugars, Part XVII. For Part XVI, see ref. 1.

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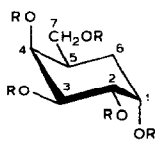
RESULTS AND DISCUSSION

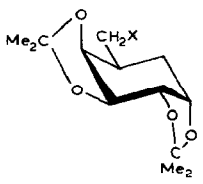
When **1** was treated with a large excess of 2,2-dimethoxypropane in *N,N*-dimethylformamide in the presence of toluene-*p*-sulfonic acid at 20–25°, t.l.c. showed the disappearance of **1** and formation of a single product within 15 min; after reaction overnight, another product was detected. Therefore, after 0.5 h, the reaction mixture was neutralised, and the product was acetylated to give, after column chromatography, the 1,2:4,7- (**10**) and 2,3:4,7-di-*O*-isopropylidene derivatives (**14**) as the crystalline acetates **11** (35%) and **15** (47%), respectively. When the amount of acid catalyst was doubled, 62% of **11** and 16% of **15** were obtained. After reaction overnight, the 1,2:3,4-di-*O*-isopropylidene derivative **3** could be isolated as the acetate[3] **4** in 62% yield. If the isopropylidenation was conducted at 70° for 1 h, tosylation of the product gave 78% of **5** (derived from **3**). The ^{1}H-n.m.r. spectra of **11** and **15** contained signals at δ 4.90 (d, *J* 3 and 8.7 Hz) and 5.52 (q, *J* 3 Hz), respectively, due to AcOC*H*, which supported the assigned structures.

Saponification of **11** and **15** gave crystalline **10** and **14**, respectively, in quantitative yields. Treatment of **10** with 2 mol of tosyl chloride in pyridine at 20–25° for 2 days gave 98% of the tosylate **12** (98%). In contrast, tosylation of **14** gave, after 10 days at 60°, only 51% of an inseparable 1:1 mixture of the tosylates **16** and **12**, the latter arising by a 2,3→1,2 migration of one isopropylidene group. However, mesylation of **10** and **14** easily gave the respective mesylates **13** and **17** in quantitative yields.

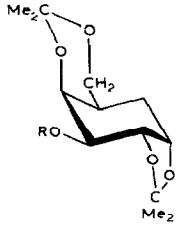
Treatment of the tosylate **5** with an excess of sodium azide in *N,N*-dimethylformamide gave the azide **6** which, after hydrogenation followed by acetylation, afforded the *N*-acetyl derivative **7** (68% from **5**). Hydrolysis of **7** with aqueous 80% acetic acid, followed by acetylation, gave the penta-*N,O*-acetyl derivative **18** (92%).



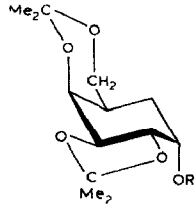
R
1 H
2 Ac



X
3 OH
4 OAc
5 OTs
6 N_3
7 NHAc
8 SAc
9 H



R
10 H
11 Ac
12 Ts
13 Ms



R
14 H
15 Ac
16 Ts
17 Ms

In the formulae schemes, for convenience, only single enantiomers corresponding to pseudo-α-D-galactopyranose are depicted

which, with methanolic sodium methoxide, gave DL-(1,2/3,4,5)-5-acetamidomethyl-1,2,3,4-cyclohexanetetrol (**21**, 87%).

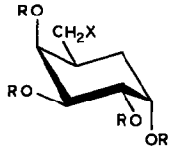
Treatment of **5** with potassium thioacetate (→**8**, 72%), followed by deprotection and acetylation, gave the crystalline penta-*O,S*-acetyl derivative **19** (74%), which was converted into the 5-mercaptomethyl derivative **22**.

Reduction of **5** with lithium aluminum hydride in boiling tetrahydrofuran gave the 5-methyl derivative **9** (92%), which was deprotected and acetylated to give the tetra-acetate **20** (77%), the ^{1}H-n.m.r. spectrum of which contained a signal at δ 0.96 (d, J 6 Hz) ascribable to Me-5. *O*-Deacetylation of **20** gave the 5-methyl derivative **23** (93%) of **1**.

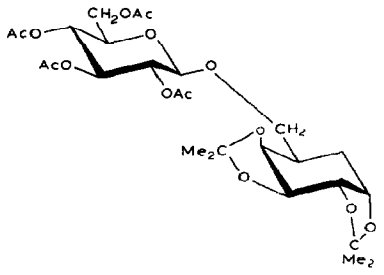
Condensation of **3** with 2,3,4,6-tetra-*O*-acetyl-α-D-glucopyranosyl bromide in boiling benzene in the presence of mercury(II) cyanide and anhydrous calcium sulfate for 21 h and column chromatography of the products gave the pseudo-disaccharide derivatives **24A** (34%), $[\alpha]_D$ −71° (chloroform), and **24B** (26%), $[\alpha]_D$ +34° (chloroform). *O*-Deisopropylidenation of **24A** and **24B** followed by acetylation gave the crystalline octa-acetate **25A**, $[\alpha]_D$ +6° (chloroform), and **25B**, $[\alpha]_D$ −44° (chloroform), respectively, in good yields, the ^{1}H-n.m.r. spectra of which contained signals at δ 4.50 (d, J 7.5 Hz) and 4.40 (d, J 7.5 Hz), respectively, ascribable to H-1 of the β-D-glucosides. The absolute structures of **25A** and **25B** were deduced on the basis of optical properties, as a dextrorotatory contribution of the cyclohexane moiety of **25A** was predicted by the fact that the penta-acetate **2** of **1** has[4] $[\alpha]_D$ +43° (chloroform). This assignment was confirmed by acetolysis of **25A**, which yielded **2** with $[\alpha]_D$ +49° (chloroform). *O*-Deacetylation of **25A** and **25B** gave syrupy 7-*O*-(β-D-glucopyranosyl)-pseudo-α-D- (**26A**) and -L-galactopyranose (**26B**), respectively.

EXPERIMENTAL

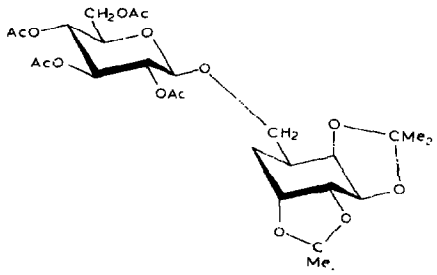
General methods. — Melting points were determined with a MEL-TEMP capillary melting-point apparatus and are uncorrected. Optical rotations were



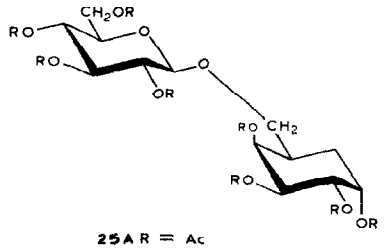
	R	X
18	Ac	NHAc
19	Ac	SAc
20	Ac	H
21	H	NHAc
22	H	SH
23	H	H



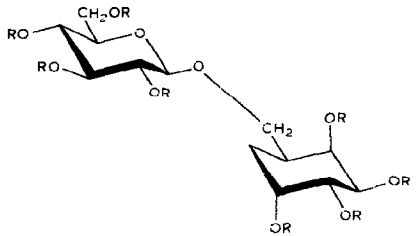
24A



24B



25A R = Ac
26A R = H



25B R = Ac
26B R = H

measured with a Jasco DIP-4 polarimeter. ^{1}H-N.m.r. spectra were recorded at 90 MHz with a Varian EM-390 spectrometer for solutions in $CDCl_3$ (internal Me_4Si). T.l.c. was performed on Wakogel B-10 (Wako Co., Osaka, Japan) with detection by charring with sulfuric acid. 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.

*(1*RS,*2*RS,*6*SR,*7*RS,*9*RS*)-7-Acetoxymethyl-4,4,11,11-tetramethyl-3,5,10,12-tetraoxatricyclo[7.3.0.0^{2,6}]dodecane* [**4**, *1,2:3,4-di-*O*-isopropylidene derivative of* DL-*(1,2/3,4,5)-5-acetoxymethyl-1,2,3,4-cyclohexanetetrol*], *(1*RS,*2*RS,*3*RS,*8*SR,*10*RS*)-2-acetoxy-5,5,12,12-tetramethyl-4,6,11,13-tetraoxatricyclo[8.3.0.0^{3,8}]tridecane* [**11**, *1,2:4,7-di-*O*-isopropylidene derivative of* DL-*(1,2/3,4,5)-3-*O*-acetyl-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol*], *and (1*RS,*2*RS,*7*SR,*9*RS,*10*RS*)-9-acetoxy-4,4,12,12-tetramethyl-3,5,11,13-tetraoxatricyclo[8.3.0.0^{2,7}]tridecane* [**15**, *2,3:4,7-di-*O*-isopropylidene derivative of* DL-*(1,2/3,4,5)-1-*O*-acetyl-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol*]. — (*a*) To a solution of DL-(1,2/3,4,5)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol[3] (**1**; 1.0 g, 5.6 mmol) in *N*,*N*-dimethylformamide (30 mL) was added 2,2-dimethoxypropane (10 mL, 81 mmol) and toluene-*p*-sulfonic acid monohydrate (40 mg, 0.21 mmol), and the mixture was stirred at ambient temperature (20–25°) for 0.5 h. Sodium hydrogencarbonate (0.9 g) was then added, the mixture was concentrated, and the residue was treated with acetic anhydride (7 mL) and pyridine (7 mL) at ambient temperature overnight. T.l.c. (1:3 ethyl

acetate–hexane) then revealed two major products (R_F 0.32 and 0.23). The mixture was concentrated, and a solution of the residue in ethyl acetate (100 mL) was washed with water, dried, and concentrated. Column chromatography (95 g of silica gel, 1:3 ethyl acetate–hexane) of the residue gave, first, **11** (0.58 g, 35%) as needles, m.p. 108–109° (from ethanol). ^{1}H-N.m.r. data: δ 4.90 (dd, 1 H, $J_{1,2}$ 8.7, $J_{2,3}$ 3 Hz, H-2), 4.44 (td, 1 H, $J_{1,10} = J_{9a,10} = 4.5$, $J_{9e,10}$ 2.3 Hz, H-10), 4.11 (dd, 1 H, $J_{7,7'}$ 11.7, $J_{7,8}$ 3 Hz, H-7), 3.52 (dd, 1 H, $J_{7',8}$ 1.5 Hz, H-7′), 2.10 (s, 3 H, OAc), 1.50, 1.41, and 1.36 (3 s, 3, 6, and 3 H, 2 CMe_2).

Anal. Calc. for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.70; H, 7.75.

Eluted second was **15** (0.68 g, 41%), obtained as needles, m.p. 89.5–92° (from ethanol). ^{1}H-N.m.r. data: δ 5.52 (q, 1 H, $J_{8a,9} = J_{8e,9} = J_{9,10} = 3$ Hz, H-9), 4.55 (t, 1 H, $J_{1,2} = J_{2,7} = 1$ Hz, H-2), 4.20 (dd, 1 H, $J_{1,10}$ 11.7 Hz, H-10), 4.09 and 3.86 (2 dd, each 1 H, $J_{6,7}$ 2.9, $J_{6,6'}$ 10.7 Hz, H-6,6′), 3.53 (dd, 1 H, H-1), 2.08 (s, 3 H, OAc), 1.49, 1.42, and 1.40 (3 s, 3, 6, and 3 H, 2 CMe_2).

Anal. Calc. for $C_{15}H_{24}O_6$: C, 59.98; H, 8.05. Found: C, 59.99; H, 7.94.

(*b*) Treatment of **1** (50 mg, 0.28 mmol) with 2,2-dimethoxypropane (0.5 mL, 4.0 mmol) in $HCONMe_2$ (1.5 mL) as described in (*a*), but in the presence of toluene-*p*-sulfonic acid monohydrate (3.5 mg, 0.02 mmol), gave **11** (52 mg, 62%) and **15** (13 mg, 16%).

(*c*) Treatment of **1** (0.30 g, 1.7 mmol) with 2,2-dimethoxypropane in $HCONMe_2$ as described in (*a*), but for 16 h, gave **4** (0.32 g, 63%), isolated as a syrup, the ^{1}H-n.m.r. spectrum of which was superimposable on that of an authentic sample[3].

(*d*) Treatment of **1** (0.30 g, 1.7 mmol) with 2,2-dimethoxypropane in $HCONMe_2$ as described in (*a*), but at 70° for 1 h, gave **4** (0.32 g, 63%), isolated as a syrup.

(1RS,2RS,3RS,8SR,10RS)-5,5,12,12-Tetramethyl-4,6,11,13-tetraoxatricyclo-[8.3.0.0^{3,8}]tridecan-2-ol [**10**, *1,2:4,7-di-O-isopropylidene derivative of* DL-*(1,2/3,4,5)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol*]. — Compound **11** (50 mg, 0.17 mmol) was treated with methanolic M sodium methoxide (0.1 mL) in methanol (2 mL) at ambient temperature for 4 h. The mixture was neutralised with carbon dioxide and concentrated. The residue was extracted with chloroform (10 mL) and the extract was passed through a short column of alumina to give **10** (43 mg, 99%) as prisms, m.p. 142–144° (from ethanol). ^{1}H-N.m.r. data: δ 4.40 (td, 1 H, $J_{9a,10} = J_{1,10} = 5.3$, $J_{9e,10}$ 3 Hz, H-10), 4.21 (t, 1 H, $J_{2,3} = J_{3,8} = 3$ Hz, H-3), 4.03 (dd, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 3.60 (dd, 1 H, H-2), 3.53 (dd, 1 H, $J_{7,7'}$ 11.3, $J_{7,8}$ 1.5 Hz, H-7), 2.41 (bs, 1 H, OH), 1.50, 1.46, and 1.38 (3 s, 3, 3, and 6 H, 2 CMe_2).

Anal. Calc. for $C_{13}H_{22}O_5$: C, 60.45; H, 8.58. Found: C, 60.52; H, 8.85.

Compound **10** (43 mg, 0.16 mmol) was treated with toluene-*p*-sulfonyl chloride (63 mg, 0.33 mmol) in pyridine (2 mL) at ambient temperature for 2 days. The mixture was then diluted with ethyl acetate (10 mL), and the solution was washed successively with saturated aqueous sodium hydrogencarbonate and water, dried, and concentrated, to give the tosylate **12** (67 mg, 98%) as needles, m.p.

139–140° (from ethanol). ^{1}H-N.m.r. data: δ 7.87 and 7.34 (2 d, each 2 H, J 9 Hz, aromatic protons), 3.54 (d, 1 H, $J_{7,7}$ 11.5 Hz, H-7), 2.46 (s, 3 H, tosyl Me), 1.38, 1.27, and 1.19 (3 s, 6, 3, and 3 H, 2 CMe_2).

Anal. Calc. for $C_{20}H_{28}O_7S$: C, 58.24; H, 6.84. Found: C, 58.35; H, 6.78.

Compound **10** (41 mg, 0.16 mmol) was treated with methanesulfonyl chloride (0.024 mL, 0.31 mmol) in pyridine (2 mL) at ambient temperature for 6 h. The mixture was processed as described in the preparation of **12**, to give the mesylate **13** (58 mg, 100%) as a syrup. ^{1}H-N.m.r. data: δ 4.59 (dd, 1 H, $J_{1,2}$ 9, $J_{2,3}$ 3 Hz, H-2), 3.54 (d, 1 H, $J_{7,7'}$ 12 Hz, H-7), 3.17 (s, 3 H, MsO), 1.52, 1.44, and 1.38 (3 s, 3, 3, and 6 H, 2 CMe_2).

Anal. Calc. for $C_{14}H_{24}O_7S$: C, 49.99; H, 7.19. Found: C, 49.92; H, 7.06.

*(1*RS*,2*RS*,7*SR*,9*RS*,10*RS*)-4,4,12,12-Tetramethyl-3,5,11,13-tetraoxatricyclo-[8.3.0.0^{3,8}]tridecan-9-ol* [**14**, *2,3:4,7-di-O-isopropylidene derivative of* DL-*(1,2/3,4,5)-5-hydroxymethyl-1,2,3,4-cyclohexanetetrol*]. — Compound **15** (50 mg, 0.17 mmol) was treated with methanolic sodium methoxide as described in the preparation of **11**, to give **14** (43 mg, 99%) as prisms, m.p. 122–125° (from ethanol). ^{1}H-N.m.r. data: δ 4.52 (bs, 1 H, H-2), 4.38 (m, 1 H, H-9), 4.19 (bd, 1 H, $J_{6,6'}$ 12, $J_{6,7}$ 3.3 Hz, H-6), 3.54 (bd, 1 H, H-6'), 2.28 (bs, 1 H, OH), 1.59, 1.45, 1.42, and 1.38 (4 s, 3, 3, 3, and 3 H, 2 CMe_2).

Anal. Calc. for $C_{13}H_{22}O_5 \cdot 0.5\ H_2O$: C, 58.41; H, 8.67. Found: C, 58.84; H, 8.30.

Compound **14** (40 mg, 0.15 mmol) was tosylated as described in the preparation of **12**, but at 60° for 10 days, to give an inseparable ~1:1 mixture (32 mg, 51%) of **12** and **16** as a syrup. ^{1}H-N.m.r. data ascribable to **16**: δ 7.84 and 7.34 (2 d, each 2 H, aromatic protons), 5.18 (q, 1 H, $J_{8a,9} = J_{8e,9} = J_{9,11}$ = 2.7 Hz, H-9), 1.49, 1.27, and 1.26 (3 s, 3, 6, and 3 H, 2 CMe_2).

Anal. Calc. for $C_{20}H_{28}O_7S$: C, 58.24; H, 6.84. Found: C, 58.38; H, 6.88.

Compound **14** (42 mg, 0.016 mmol) was mesylated as described in the preparation of **13**, to give the mesylate **17** (55 mg, 99%) as needles, m.p. 121° (dec.) (from ethanol). ^{1}H-N.m.r. data: δ 5.24 (q, 1 H, $J_{8a,9} = J_{8e,9} = J_{9,10}$ = 2.7 Hz, H-9), 4.56 (t, 1 H, $J_{1,2} = J_{2,7}$ = 2.7 Hz, H-2), 4.20 (dd, 1 H, $J_{6,7}$ 2.9, $J_{6,6'}$ 11.9 Hz, H-6), 4.09 and 3.86 (2 d, each 1 H, $J_{1,10}$ 10.4 Hz, H-1,10), 3.56 (d, 1 H, H-6'), 3.08 (s, 3 H, MsO), 1.49, 1.43, 1.40, and 1.36 (4 s, each 3 H, 2 CMe_2).

Anal. Calc. for $C_{14}H_{24}O_7S$: C, 49.99; H, 7.19. Found: C, 49.58; H, 7.01.

*(1*RS*,2*RS*,6*SR*,7*RS*,9*RS*)-4,4,11,11-Tetramethyl-7-toluene-*p*-sulfonyloxy-3,5,10,12-tetraoxatricyclo[7.3.0.0^{2,6}]dodecane* [**5**, *1,2:3,4-di-O-isopropylidene derivative of* DL-*(1,2/3,4,5)-5-toluene-p-sulfonyloxymethyl-1,2,3,4-cyclohexanetetrol*]. — Compound **1** (0.60 g, 3.4 mmol) was treated with 2,2-dimethoxypropane as described in the preparation (*d*) of **4**, to give crude **3** as a syrup, which was tosylated, as described in the preparation of **12**, to give **5** (1.1 g, 78%) as prisms, m.p. 96–98° (from ethanol). ^{1}H-N.m.r. data: δ 7.80 and 7.32 (2 d, each 2 H, J 9 Hz, aromatic protons), 4.05 (d, 1 H, $J_{13,13'}$ 7 Hz) and 3.90 (dd, 1 H, $J_{7,13}$ 6 Hz) (CH_2OTs), 2.45 (s, 3 H, tosyl Me), 1.38, 1.28, 1.25, and 1.22 (4 s, each 3 H, 2 CMe_2).

Anal. Calc. for $C_{20}H_{28}O_7S$: C, 58.21; H, 6.85; S, 7.78. Found: C, 57.90; H, 6.75; S, 7.46.

(1RS,2RS,6SR,7RS,9RS)-7-Acetamidomethyl-4,4,11,11-tetramethyl-3,5,10,-12-tetraoxatricyclo[7.3.0.0^{2,6}]dodecane [**7**, *1,2:3,4-di-O-isopropylidene derivative of* DL-*(1,2/3,4,5)-5-acetamidomethyl-1,2,3,4-cyclohexanetetrol*]. — A mixture of **5** (0.72 g, 1.8 mmol), sodium azide (0.57 g, 8.8 mmol), and $HCONMe_2$ (20 mL) was stirred at 80° for 16 h and then concentrated. The residue was extracted with ethyl acetate, and the extract was passed through a short column of alumina and concentrated to give the azide **6** (0.47 g, 93%) as a syrup. ^{1}H-N.m.r. data: δ 3.43 (dd, 1 H, $J_{7,13}$ 9, $J_{13,13'}$ 12 Hz) and 3.37 (dd, 1 H, $J_{7,13'}$ 6 Hz) (CH_2N_3), 1.44, 1.42, and 1.33 (3 s, 3, 3, and 6 H, 2 CMe_2).

Compound **6** (0.42 g, 1.5 mmol) was hydrogenated in ethyl acetate (20 mL) in the presence of Raney nickel T-4 (ref. 4) (0.5 mL) at an initial hydrogen pressure of 50 p.s.i. (Parr apparatus) for 17 h. The catalyst was removed and the filtrate was concentrated. The residue was treated with acetic anhydride (0.5 mL) in methanol (2 mL), and the product was eluted from a column of silica gel (30 g) with 15:1 chloroform–methanol, to give **7** (0.33 g, 73%) as needles, m.p. 154–155° (from ethanol). ^{1}H-N.m.r. data: δ 6.00 (m, 1 H, amide), 3.32 (t, 2 H, $J_{7,13} = J_{13,NH} = 6$ Hz, CH_2NHAc), 1.97 (s, 3 H, NAc), 1.42, 1.32, and 1.30 (3 s, 6, 3, and 3 H, 2 CMe_2).

Anal. Calc. for $C_{15}H_{25}NO_5$: C, 60.18; H, 8.42; N, 4.86. Found: C, 59.99; H, 8.21; N, 4.53.

DL-*(1,2/3,4,5)-5-Acetamidomethyl-1,2,3,4-tetra-O-acetyl-1,2,3,4-cyclohexanetetrol* (**18**). — Compound **7** (0.31 g, 1.0 mmol) was treated with aqueous 80% acetic acid (12 mL) at 80° for 1.5 h. The mixture was concentrated and the residue was acetylated in the usual way. The product was eluted from a short column of alumina with chloroform, to give **18** (0.42 g, 92%) as prisms, m.p. 151–152° (from ethanol). ^{1}H-N.m.r. data: δ 5.98 (m, 1 H, amide), 2.12, 2.10, 2.00, and 1.93 (4 s, 3, 3, 6, and 3 H, NAc and 4 OAc).

Anal. Calc. for $C_{17}H_{25}NO_9$: C, 52.71; H, 6.50; N, 3.62. Found: C, 53.03; H, 6.51; N, 3.55.

DL-*(1,2/3,4,5)-5-Acetamidomethyl-1,2,3,4-cyclohexanetetrol* (**21**). — Compound **18** (50 mg, 0.13 mmol) was treated with methanolic 0.1M sodium methoxide (2 mL) at ambient temperature for 1 h. The mixture was then passed through a short column of Amberlite IR-120B (H^+) resin and concentrated, to give **21** (25 mg, 87%) as prisms, m.p. 186–186.5° (from ethanol).

Anal. Calc. for $C_9H_{17}NO_5$: C, 49.31; H, 7.82; N, 6.39. Found: C, 49.21; H, 7.59; N, 6.99.

DL-*(1,2/3,4,5)-1,2,3,4-Tetra-O-acetyl-5-acetylthiomethyl-1,2,3,4-cyclohexanetetrol* (**19**). — A mixture of **5** (100 mg, 0.24 mmol), potassium thioacetate (60 mg, 0.48 mmol), and $HCONMe_2$ (5 mL) was stirred at 110° for 5.5 h and then concentrated. The residue was extracted with toluene, and the extract was washed with water and concentrated. The residue was purified on a column of silica gel, to give

the thioacetate **8** (55 mg, 72%) as a syrup. ^{1}H-N.m.r. data: δ 2.90 (d, 2 H, $J_{5,7}$ 6 Hz, CH_2SAc), 2.37 (s, 3 H, SAc), 1.39 and 1.30 (2 s, each 6 H, 2 CMe_2).

Compound **8** (55 mg, 0.35 mmol) was treated with aqueous 80% acetic acid (3 mL) at 80° for 18 h. The mixture was processed as described in the preparation of **18**, to give **19** (51 mg, 74%) as prisms, m.p. 121–122° (from ethanol). ^{1}H-N.m.r. data: δ 2.81 (m, 2 H, CH_2SAc), 2.13, 2.11, 2.09, and 1.98 (4 s, 3, 3, 3, and 6 H, 4 OAc and SAc).

Anal. Calc. for $C_{17}H_{24}O_9S$: C, 50.48; H, 5.98; S, 7.93. Found: C, 50.19; H, 5.91; S, 7.76.

DL-*(1,2/3,4,5)-5-Mercaptomethyl-1,2,3,4-cyclohexanetetrol* (**22**). — Compound **19** (50 mg, 0.12 mmol) was *O,S*-deacetylated, as described in the preparation of **21**, to give **22** (23 mg, 87%) as a syrup.

Anal. Calc. for $C_7H_{14}O_4S \cdot 0.5\ H_2O$: C, 41.37; H, 7.44. Found: C, 41.10; H, 7.04.

DL-*(1,2/3,4,5)-1,2,3,4-Tetra*-O-*acetyl-5-methyl-1,2,3,4-cyclohexanetetrol* (**20**). — Compound **5** (114 mg, 0.28 mmol) was treated with lithium aluminum hydride (53 mg, 1.14 mmol) in boiling tetrahydrofuran (15 mL) for 1.5 h. After treatment with ethyl acetate, the mixture was filtered, and the filtrate was concentrated to give **9** (62 mg, 92%) as a syrup. ^{1}H-N.m.r. data: δ 1.41 and 1.30 (2 s, each 6 H, 2 CMe_2), 0.96 (d, 3 H, *J* 6 Hz, Me).

Compound **9** was successively *O*-deisopropylidenated and acetylated, as described in the preparation of **21**, to give **20** (85 mg, 77%) as prisms, m.p. 134–135° (from ethanol). ^{1}H-N.m.r. data: δ 2.21, 2.10, and 1.99 (3 s, 3, 3, and 6 H, 4 OAc), 0.96 (d, 3 H, *J* 6 Hz, Me).

Anal. Calc. for $C_{15}H_{22}O_8$: C, 54.54; H, 6.71. Found: C, 54.25; H, 6.62.

DL-*(1,2/3,4,5)-5-Methyl-1,2,3,4-cyclohexanetetrol* (**23**). — Compound **20** (24 mg, 0.07 mmol) was *O*-deacetylated, to give **23** (11 mg, 93%), m.p. 153–155° (from ethanol).

Anal. Calc. for $C_7H_{14}O_4$: C, 51.84; H, 8.70. Found: C, 51.63; H, 8.33.

[*(1S)-(1,2,3/4,5)-2,3,4,5-Tetrahydroxy-1-cyclohexanemethyl*] *β*-D-*glucopyranoside octa-acetate* (**25A**) *and its diastereoisomer* (**25B**). — A mixture of **3** (235 mg, 0.91 mmol), 2,3,4,6-tetra-*O*-acetyl-*α*-D-glucopyranosyl bromide (1.36 g, 3.3 mmol), mercury(II) cyanide (0.45 g, 2.2 mmol), anhydrous calcium sulfate (0.45 g), and benzene (9 mL) was stirred at boiling temperature for 21 h. Insoluble material was removed by filtration and the filtrate was concentrated to give a syrup (2.22 g) that was fractionated roughly on a column of silica gel (85 g) with 8:1 chloroform–ethyl acetate, to give the mixture of products. Three further fractionations on a column of silica gel gave, first, the *β*-D-glucoside derivative **24B** (137 mg, 26%) as a syrup, R_F 0.45 (5:1 chloroform–ethyl acetate), $[\alpha]_D^{24}$ +34° (*c* 3, chloroform). ^{1}H-N.m.r. data: δ 2.05, 2.01, 1.98, and 1.96 (4 s, each 3 H, 4 OAc), 1.36, 1.35, and 1.29 (3 s, 3, 3, and 6 H, 2 CMe_2).

Anal. Calc. for $C_{17}H_{40}O_{14}$: C, 55.10; H, 6.85. Found: C, 55.02; H, 6.86.

Eluted second was **24A** (180 mg, 34%), isolated as a syrup, R_F 0.41 (5:1

chloroform–ethyl acetate), $[\alpha]_D^{23}$ −71° (*c* 1.5, chloroform). ^{1}H-N.m.r. data: δ 2.07, 2.04, 2.02, and 1.98 (4 s, each 3 H, 4 OAc), 1.40 and 1.32 (2 s, each 6 H, 2 CMe_2).

Anal. Found: C, 55.37; H, 7.02.

A portion (68 mg, 0.12 mmol) of **24A** was *O*-deisopropylidenated and then acetylated, as described in the preparation of **18**, to give **25A** (81 mg, 100%) as prisms, m.p. 152.5–153° (from ethanol–2-propanol), $[\alpha]_D^{26}$ +6° (*c* 1.2, chloroform). ^{1}H-N.m.r. data: δ 4.50 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.26 (dd, 1 H, $J_{5,6}$ 4.5, $J_{6,6'}$ 12 Hz) and 4.11 (dd, 1 H, $J_{5,6'}$ 3 Hz) (CH_2OAc), 3.70 and 3.38 (2 dd, each 1 H, *J* 7.5 and 9.8 Hz, CH_2O), 2.11, 2.09, 2.03, 2.00, 1.99, and 1.97 (6 s, 3, 6, 3, 3, 6, and 3 H, 8 OAc).

Anal. Calc. for $C_{29}H_{40}O_{18}$: C, 51.48; H, 5.96. Found: C, 51.35; H, 5.81.

A portion (58 mg, 0.10 mmol) of **24B** was *O*-deisopropylidenated and acetylated, as described in the preparation of **18**, to give **25B** (69 mg, 100%) as prisms, m.p. 165–166° (from ethanol–2-propanol), $[\alpha]_D^{26}$ −44° (*c* 1, chloroform). ^{1}H-N.m.r. data: δ 4.40 (d, 1 H, $J_{1,2}$ 7.5 Hz, H-1), 4.28 (dd, 1 H, $J_{5,6}$ 4.5, $J_{6,6'}$ 12 Hz) and 4.09 (dd, 1 H, $J_{5,6'}$ 3 Hz) (CH_2OAc), 2.20, 2.16, 2.14, 2.00, 1.99, and 1.94 (6 s, 6, 3, 3, 3, 6, and 3 H, 8 OAc).

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

[*(1S)-(1,2,3/4,5)-2,3,4,5-Tetrahydroxy-1-cyclohexanemethyl*] *β*-D-*glucopyranoside* (**26A**) *and its diastereoisomer* (**26B**). — Compound **25A** (72 mg, 0.12 mmol) was *O*-deacetylated with methanolic sodium methoxide in the usual way, to give **26A** (26 mg, 72%) as a syrup, $[\alpha]_D^{24}$ −6° (*c* 1, water).

Anal. Calc. for $C_{13}H_{24}O_{10}$: C, 45.88; H, 7.11. Found: C, 45.60; H, 7.32.

Compound **25B** (69 mg, 0.10 mmol) was *O*-deacetylated to give **26B** (24 mg, 70%) as a syrup, $[\alpha]_D^{24}$ −48° (*c* 1, water).

Anal. Found: C, 45.81; H, 7.19.

Acetolysis of **25A**. — Compound **25A** (50 mg, 0.07 mmol) was heated with 100:100:1 acetic acid–acetic anhydride–conc. sulfuric acid (2 mL) at 60° for 15 h. The mixture was poured into ice–water (10 mL) and extracted with ethyl acetate (10 mL). The extract was processed in the usual way, and the product was purified on a column of silica gel (3 g) with 1:2 ethyl acetate–hexane, to give a syrup (30 mg) that crystallised from ethanol, to give (1*S*)-(1,2/3,4,5)-5-acetoxymethyl-1,2,3,4-tetra-*O*-acetyl-1,2,3,4-cyclohexanetetrol (**2**; 16 mg, 55%), m.p. 141.5–142°, $[\alpha]_D^{20}$ +49° (*c* 0.7, chloroform); lit.[5] m.p. 143–144°, $[\alpha]_D^{20}$ +43.2° (*c* 1.1, chloroform).

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