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Note

Synthesis of pseudo-sugar derivatives from 5*exo*, 6*exo*-dihydroxy-*endo*- and -*exo*-7-oxabicyclo[2.2.1]heptane-2-carboxylic acids*

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We have developed synthetic routes[2] to pseudo-sugars and their derivatives by using *endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid[3–6] (**1**), the Diels–Alder adduct of furan and acrylic acid, as the common starting material. In these syntheses, cleavage of the 1,4-anhydro ring is a crucial step in the generation of cyclohexane compounds having desired functional groups with appropriate stereochemistry, and the products need to be stable under the reaction conditions. In fact, when a fully acetylated pseudo-sugar derivative with an all-*trans* configuration is formed, it is obtained selectively in high yield, because neither aromatisation nor epimerisation *via* an intermediate cyclic acetoxonium ion occurs under acidic conditions.

We now report on the acetolysis and bromination of some derivatives of 5*exo*,6*exo*-dihydroxy-*endo*- and -*exo*-7-oxabicyclo[2.2.1]heptane-2-carboxylic acid, which are expected to afford otherwise inaccessible pseudo-sugar derivatives.

Oxidation of methyl *endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylate[4,5] (**2**) derived from the acid **1**[6] with potassium permanganate and magnesium sulfate in ethanol, followed by acetylation, gave the *cis*-diacetate **3** in 53% yield. Reduction of **3** with lithium aluminium hydride in tetrahydrofuran, followed by acetylation, gave the triacetate **4** in 65% yield. The ^{1}H-n.m.r. spectra of **3** and **4** supported the structures assigned.

Treatment of **3** with 30% hydrobromic acid–acetic acid in a sealed tube for 24 h at 100° produced a 52% yield of a single bromide, which was identical with an authentic sample of **5** (ref. 7). Mechanistically, **5** was deduced to be formed through an intramolecular rear-side attack of the carboxyl function in the intermediate cyclic

* Pseudo-sugars, Part XXII. For Part XXI, see ref. 1.
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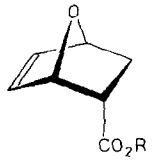
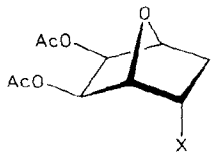
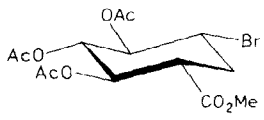


1 R = H
2 R = Me



3 X = CO_2Me
4 X = CH_2OAc



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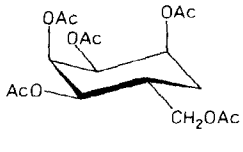

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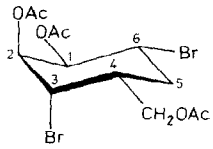

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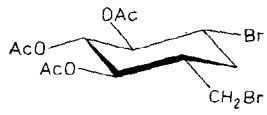

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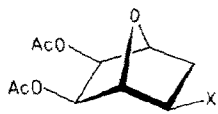
acetoxonium ion after cleavage of the 1,4-anhydro ring with a bromide ion at C-4.

Acetolysis of **3** with acetic acid–acetic anhydride–conc. sulfuric acid (14:8:1) at 90° afforded a complex mixture of products, involving appreciable aromatisation. However, similar treatment of **4** afforded a 98% yield of a single pseudo-sugar penta-acetate **6**, which was identical with the pseudo-α-*allo* isomer[8]. The anhydro ring is opened at C-1 and/or C-4, and the intermediates then isomerise through a cyclic acetoxonium ion to the most stable isomer **6** under the reaction conditions[9]. The formation of **6** can also be explained by assuming an acid-catalysed *cis*-cleavage of the anhydro ring.

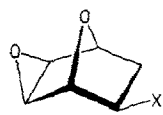
Bromination of **4** gave an inseparable 4:1 mixture of the dibromides **7** and **8** in 66% yield. The 400-MHz ^{1}H-n.m.r. spectrum indicated the major product **7** to be DL-(1,2/3,4,6)-4-acetoxymethyl-1,2-di-*O*-acetyl-3,6-dibromo-1,2-cyclohexanediol. Thus, it contained coupled signals at δ 5.64 (dd, *J* 3.2, 11 Hz), 5.49 (t, *J* 3.2 Hz), 4.31 (bq, *J* 3 Hz), and 4.19 (ddd, *J* 4.8, 11, 12.8 Hz), ascribable to H-1,2,3, and 6, respectively, supporting the structure assigned. The formation of **7** and **8** involved initial cleavage of the anhydro ring of **4** by attack of bromide ion at C-4, and the resulting monobromide was attacked through an activated form (cyclic acetoxonium ion) by a bromide ion[10] at C-1 (→**7**) or intramolecularly by the 2-CH_2OAc at C-2. The latter intermediate was then displaced at C-7 with bromide ion (→**8**). The 7-OAc of **7** may be further replaced by a bromide atom when excess of HBr is present.

The *exo*-acid **9**[3–5] was easily accessible by fractional crystallisation of the precipitates obtained from a long-standing mixture of products of the Diels–Alder reaction of furan with acrylic acid, after removal of the *endo*-acid **1**. Compound **9** was esterified to give the methyl ester **10**[6], which was oxidised with potassium permanganate and then acetylated to give the diacetate **12** in 34% total yield. The

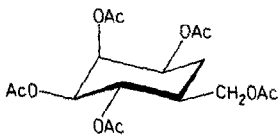
9 X = CO_2H
10 X = CO_2Me
11 X = CH_2OAc



12 X = CO_2Me
13 X = CH_2OAc



14 X = CO_2H
15 X = CO_2Me
16 X = CH_2OAc



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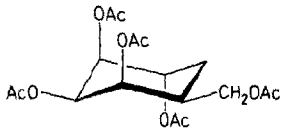

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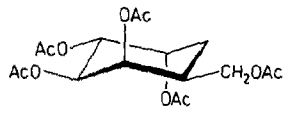

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triacetate **13** was prepared in 42% total yield from **9** by reduction with lithium aluminium hydride, followed by acetylation.

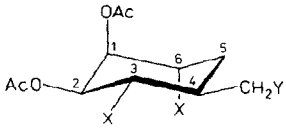
Compounds **9** and **10** were further converted into the *cis*-diepoxides **14**[3] and **15**, respectively, by treatment with peroxy acid. Compound **15** was convertible into the acetate **16**.

Acetolysis or bromination of **12**, **14**, **15**, and **16** under the usual conditions gave complex mixtures of products, accompanied by appreciable aromatisation.

Acetolysis of the triacetate **13** proceeded cleanly to give, after chromatography, three pseudo-hexopyranose penta-acetates with the *β-manno*[11] (**17**, 11%), *α-talo*[12] (**18**, 33%), and *α-galacto* configuration[13] (**19**, 22%). They were identified with authentic samples by comparison of ^{1}H-n.m.r. spectra. Compounds **17** and **18** are formed by opening of the anhydro ring, and the latter is epimerised at C-2 to give **19** *via* the intermediate 1,2-cyclic acetoxonium ion[9]. Similar results were observed by McCasland *et al.*[13].

Brominaton of **13** gave one di- (**20**, 12%) and one tri-bromide (**21**, 66%). Compound **21** was convertible into **20** in good yield by treatment with sodium acetate in *N*,*N*-dimethylformamide at 60°. The ^{1}H-n.m.r. spectrum of **20** contained coupled signals at δ 5.72 (dd, J 3, 10.5 Hz), 5.42 (t, J 3 Hz), and 4.14 (t, J 10.5 Hz, due to H-2, H-1, and H-3, respectively, which were consistent with the structure assigned. The anhydro ring of **13** is first attacked by a bromide ion at C-1 and/or C-4, and then the second bromine atom is introduced at the remote carbon atom[10].

On treatment with sodium azide in boiling aqueous 90% 2-methoxyethanol for 1.5 h, **20** afforded an 87% yield of a single azide **22**, the ^{1}H-n.m.r. spectrum of which was very similar to that of **20**, indicative of retention of configuration. The



	X	Y
20	Br	OAc
21	Br	Br
22	N_3	OAc
23	NHAc	OAc

reaction proceeded by a neighbouring-group participation of acetoxyl groups, followed by a diaxial opening of the intermediate with azide ion. Hydrogenation of **22** in methanol containing acetic anhydride in the presence of Raney nickel[14] gave the di-*N*-acetyl derivative **23** in 81% yield. Therefore, starting form **20**, it may be possible to prepare pseudo-sugar derivatives with the *α-manno* configuration by use of different nucleophiles.

EXPERIMENTAL

General methods. — Melting points were determined with a MEL-TEMP capillary melting-point apparatus and are uncorrected. Unless otherwise noted, ^{1}H-n.m.r. spectra were recorded for solutions in $CDCl_3$ (internal Me_4Si) with a Varian EM-390 (90 MHz) instrument. The spectrum at 400 MHz was recorded with a Jeol GX-400 (400 MHz) instrument. T.l.c. was performed on Silca Gel 60 F_{254} (Merck) with detection by charring with sulfuric acid. Column chromatography was conducted on Wakogel C-300 (300 Mesh, Wako Co., Osaka). Organic solutions were dried over anhydrous Na_2SO_4 and concentrated at $<50°$ under diminished pressure.

*Methyl (±)-*endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylate* (**2**). — A mixture of (±)-*endo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid (**1**; 5.0 g, 36 mmol), methanol (250 mL), and acetyl chloride (2.5 mL) was stirred for 3 h at room temperature, then neutralised with sodium hydrogencarbonate, and concentrated. The residue was extracted with chloroform (50 mL) and the extract concentrated to give **2** (5.1 g, 93%) as a syrup. The ^{1}H-n.m.r. spectrum was superimposable on that of an authentic sample.

*Methyl (±)-5*exo*,6*exo*-diacetoxy-*endo*-7-oxabicyclo[2.2.1]heptane-2-carboxylate* (**3**). — To a solution of the ester **2** (0.83 g, 5.4 mmol) in ethanol (12 mL) was added dropwise a solution of potassium permanganate (0.83 g) and anhydrous magnesium sulfate (0.67 g) in water (15 mL), and the mixture was stirred for 3 h at 0°. An aqueous solution of sodium hydrogensulfate (1.2 g) and 2M sulfuric acid (2.4 mL) was then added and the mixture was stirred until it became colorless. The

solution was concentrated and the residue was treated with acetic anhydride (5 mL) and pyridine (5 mL) overnight at room temperature. The mixture was concentrated and the residue was extracted with ethyl acetate (20 mL). The extract was washed with M hydrocloric acid, aqueous sodium hydrogencarbonate, and aqueous sodium chloride, dried, and concentrated. The residue was crystallised from ethanol to give **3** (780 mg, 53%) as prisms, m.p. 111–111.5°. ^{1}H-N.m.r. data: δ 5.20–4.30 (m, 4 H, H-1,4,5,6), 3.79 (s, 3 H, Me), 2.07 (s, 6 H, 2 OAc).

Anal. Calc. for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92. Found: C, 52.83; H, 5.79.

*(±)-2*exo,*3*exo-*Diacetoxy-5*endo-*acetoxymethyl-7-oxabicyclo[2.2.1]heptane* (**4**). — Compound **3** (0.20 g, 0.74 mmol) was treated with lithium aluminium hydride (0.09 g, 2.4 mmol) in tetrahydrofuran (3.5 mL) for 6 h at room temperature. To the mixture was added water (2 mL), aqueous 15% sodium hydroxide (1 mL), and acetone–water (1:1, 20 mL) in turn, and it was then filtered through Celite and concentrated to dryness. The residue was acetylated in the usual way. The product was crystallised from ethanol to give **4** (0.14 g, 65%) as prisms, m.p. 71–72°. ^{1}H-N.m.r. data: δ 5.17 (d, 1 H, $J_{2,3}$ 10 Hz, H-3), 4.85 (d, H-2), 4.44 (m, 2 H, C*H*$_2$OAc), 4.3–3.9 (m, 2 H, H-1,4), 2.11 (s, 9 H, 3 OAc), 2.75–1.70 (m, 2 H, H-5,6*exo*), 1.16 (dd, 1 H, $J_{6,6}$ 13, $J_{5,6endo}$ 6 Hz, H-6*endo*).

Anal. Calc. for $C_{13}H_{18}O_7$: C, 54.54; H, 6.34. Found: C, 54.70; H, 6.24.

Methyl DL-*(1,3,5/2,4)-2,3,4-triacetoxy-5-bromocyclohexane-1-carboxylate* (**5**). — A mixture of **3** (0.25 g, 0.92 mmol) and 30% hydrogen bromide–acetic acid (3.5 mL) was heated in a sealed tube for 24 h at 100°, and then poured into ice–water (10 mL). After heating for 3 h at 100°, the mixture was concentrated to dryness, and the residue was treated with boiling methanol (20 mL) and acetyl chloride (0.5 mL) for 3 h. The mixture was then neutralised with sodium hydrogencarbonate and concentrated. The residue was extracted with chloroform and the product was acetylated in the usual way to give **5** (0.38 g, 52%) as needles, m.p. 153–153.5° (from ethanol); lit.[7] m.p. 153–154°; compound **5** was identical with an authentic sample[7].

DL-*(1,2,3,4/5)-5-Acetoxymethyl-1,2,3,4-tetra*-O-*acetyl-1,2,3,4-cyclohexanetetrol* (**6**). — A mixture of **4** (100 mg, 0.35 mmol), acetic acid (3.1 mL), acetic anhydride (1.7 mL), and conc. sulfuric acid (0.22 mL) was heated in a sealed tube for 45 h at 90°. The mixture was poured into ice–water (15 mL) and extracted with chloroform (15 mL). The extract was washed with saturated aqueous sodium hydrogencarbonate and water, and dried. Evaporation of the solvent gave a syrup, which was eluted from a column of silica gel with 2-butanone–toluene (1:5), to give **6** (133 mg, 98%) as prisms, m.p. 122–123° (from ethanol); lit.[8] m.p. 120–121°; which was identical to an authentic sample[8].

DL-*(1,2/3,4,6)-4-Acetoxymethyl-1,2-di*-O-*acetyl-3,6-dibromo*-1,2-*cyclohexanediol* (**7**) *and* DL-*(1,3/2,4,6)-1,2,3-tri*-O-*acetyl-4-bromo-6-bromomethyl-1,2,3-cyclohexanetriol* (**8**). — A mixture of **4** (100 mg, 0.35 mmol), 30% hydrogen bromide–acetic acid (1.5 mL), and acetic acid (1.0 mL) was heated in a sealed tube for 24 h at 80°. The mixture was poured into ice–water (15 mL) and extracted with ethyl acetate (15 mL). The extract was processed similarly and the product was eluted

from a column of silica gel with acetone–hexane (1:20) to give a 3:1 mixture (100 mg 66%) of **7** and **8** as inseparable needles, m.p. 124–125° (from ethanol). ^{1}H-N.m.r. data (400 MHz) for **7**: δ 5.64 (dd, 1 H, $J_{1,2}$ 3.2, $J_{1,6}$ 11 Hz, H-1), 5.49 (t, 1 H, $J_{2,3}$ 3.2 Hz, H-2), 4.31 (bq, $J_{3,4} = J_{3,5} = 3$ Hz, H-3), 4.19 (ddd, 1 H, $J_{5a,6}$ 12.8, $J_{5e,6}$ 4.8 Hz, H-6), 4.12 and 4.00 (2 dd, each 1 H, $J_{4,7}$ 7.5, $J_{7,7}$ 11.7 Hz, CH_2OAc), 2.14, 2.08, and 2.07 (3 s, each 3 H, 3 OAc).

Anal. Calc. for $C_{13}H_{18}Br_2O_6$: C, 36.30; H, 4.22. Found: C, 36.36; H, 4.18.

*(±)-*exo*-7-Oxabicyclo[2.2.1]hept-5-ene-2-carboxylic acid* (**9**). — Compound **9** (10%) was obtained as needles by recrystallisation of the product precipitated from the mother liquor of the *endo*-acid **1** after having been stored for a long time; m.p. 78–81° (from ethyl acetate–hexane). ^{1}H-N.m.r. data: δ 5.45 (2 H, bs, H-5,6), 5.25 (s, 1 H, $J_{1,2endo} = J_{1,6} = \sim 0$ Hz, H-1), 5.19 (d, 1 H, $J_{3exo,4}$ 4, $J_{4,5} \sim 0$ Hz, H-4), 2.45 (dd, 1 H, $J_{2,3endo}$ 8, $J_{2,3exo}$ 4 Hz, H-2*endo*), 2.20 (td, 1 H, $J_{2endo,3exo} = J_{3exo,4} = 4$, $J_{3,3}$ 12 Hz, H-3*exo*), 1.56 (dd, 1 H, $J_{2endo,3endo}$ 8 Hz, H-3*endo*).

Anal. Calc. for $C_7H_8O_3$: C, 59.97; H, 5.75. Found: C, 59.99; H, 5.73.

*Methyl (±)-*exo*-7-oxabicyclo[2.2.1]hept-5-ene-2-carboxylate* (**10**). — The acid **9** (2.0 g, 14.2 mmol) was esterified as in the preparation of **2**. The product was purified by chromatography on a column of silica gel with 2-butanone–toluene (1:10), to give **10** (2.1 g, 96%) as a syrup. The ^{1}H-n.m.r. spectrum was superimposable on that of an authentic sample[5].

*(±)-2*exo*-Acetoxymethyl-7-oxabicyclo[2.2.1]hept-5-ene* (**11**). — A mixture of the acid **9** (10.0 g, 71 mmol) and lithium aluminium hydride (5.4 g, 142 mmol) in tetrahydrofuran (100 mL) was stirred for 3 h, at room temperature, and then processed as in the preparation of **4**. The product was eluted form a column of silica gel with chloroform–ethanol (10:1) to give **11** (9.5 g, 82%) as a syrup. ^{1}H-N.m.r. data: δ 6.34 (s, 2 H, H-5,6), 4.95 (d, 1 H, $J_{3exo,4}$ 4.2 Hz, H-4), 4.80 (s, 1 H, H-1), (dd, 1 H, $J_{2,8}$ 6.3, $J_{8,8}$ 10.5 Hz, H-8), 3.93 (dd, 1 H, $J_{2,8'}$ 9.6 Hz, H-8′), 2.07 (s, 3 H, OAc), 1.95–1.20 (m, 3 H, H-2,3*endo*,3*exo*).

Anal. Calc. for $C_9H_{12}O_3$: C, 64.27; H, 7.19. Found: C, 64.33; H, 7.29.

*Methyl (±)-*5exo,6exo*-diacetoxy-*exo*-7-oxabicyclo[2.2.1]heptane-2-carboxylate* (**12**). — A solution of the ester **10** (0.72 g, 4.7 mmol) in ethanol (10 mL) was treated with a solution of potassium permanganate (0.72 g) and anhydrous magnesium sulfate (0.54 g) in water (15 mL) for 1 h at 0°. The mixture was processed as in the preparation of **3**, and the product was acetylated in the usual way to give **12** (0.92 g) as a syrup, which was crystallised from ethanol to give crystals (0.44 g, 35%), m.p. 70–71°. ^{1}H-N.m.r. data: δ 5.05–4.40 (m, 4 H, H-1,4,5,6), 3.76 (s, 3 H, Me), and 2.02 (s, 6 H, 2 OAc).

Anal. Calc. for $C_{12}H_{16}O_7$: C, 52.94; H, 5.92. Found: C, 53.23; H, 5.86.

*(±)-2*exo,3exo*-Diacetoxy-5*exo*-acetoxymethyl-7-oxabicyclo[2.2.1]heptane* (**13**). — To a solution of the acetate **11** (11.6 g, 69 mmol) in ethanol (150 mL) was added a solution of potassium permanganate (11 g, 69 mmol) and magnesium sulfate (8.3 g, 69 mmol) in water (220 mL) at 0–5°. The mixture was stirred for 2 h, and then processed in the usual manner, and the product was acetylated and

crystallised from ethanol to give **13** (10.1 g, 51%) as prisms, m.p. 98–99°. ^{1}H-N.m.r. data: δ 4.90 (s, 2 H, H-2,3), 4.50 (d, 1 H, $J_{1,6exo}$ 5.3 Hz, H-1), 4.35 (s, 1 H, H-4), 4.01 (dd, 1 H, $J_{5,8}$ 6.8, $J_{8,8}$ 10.5 Hz) and 3.81 (dd, $J_{5,8'}$ 8.9 Hz) (CH_2OAc), 2.04 (s, 9 H, 3 OAc), 1.67 (dd, 1 H, $J_{5,6endo}$ 8.3, $J_{6,6}$ 12 Hz, H-6*endo*), 1.27 (dt, 1 H, H-6*exo*).

Anal. Calc. for $C_{13}H_{18}O_7$: C, 54.54; H, 6.34. Found: C, 54.62; H, 6.33.

*(±)-*exo*-3,8-Dioxatricyclo[3.2.1.0^{2,4}]octane-6*exo*-carboxylic acid* (**14**). — The acid **9** (2.0 g, 14 mmol) was treated with aqueous 90% formic acid (30 mL) and aqueous 35% hydrogen peroxide (9 mL) for 2 h at 60°. The mixture was concentrated and the residue was crystallised from ethanol to give **14** (2.0 g, 89%) as prisms, m.p. 127–128°; lit.[3] m.p. 131–132°. ^{1}H-N.m.r. data: δ 4.70 (s, 1 H, H-5), 4.48 (d, 1 H, $J_{1,7exo}$ 4.5 Hz, H-1), 3.42 (s, 2 H, H-2,3), 2.67 (dd, 1 H, $J_{6,7endo}$ 9, $J_{6,7exo}$ 4.5 Hz, H-6), 2.10 (dt, 1 H, $J_{7,7}$ 12 Hz, H-7*exo*), and 1.76 (dd, 1 H, H-7*endo*).

Anal. Calc. for $C_7H_8O_4$: C, 53.85; H, 5.16. Found: C, 53.45; H, 5.17.

*Methyl (±)-*exo*-3,8-dioxatricyclo[3.2.1.0^{2,4}]octane-6*exo*-carboxylate* (**15**). — A mixture of the ester **10** (2.12 g, 13.8 mmol), *m*-chloroperbenzoic acid (5.38 g, ~40 mmol), and dichloromethane (60 mL) was stirred for 2 h at room temperature, and then concentrated. The residue was extracted with ethyl acetate (250 mL), and the extract was washed successively with aqueous 10% sodium thiosulfate, aqueous sodium hydrogencarbonate, and aqueous sodium chloride, dried, and then concentrated. The product was eluted from a column of silica gel with ethyl acetate–hexane (1:3) to give **15** (1.94 g, 83%) as a syrup. ^{1}H-N.m.r. data: δ 4.75 (s, 1 H, H-5), 4.55 (d, 1 H, $J_{1,7}$ 4.5 Hz, H-1), 3.72 (s, 3 H, ester), 3.32 (s, 2 H, H-2,4), 2.40 (dd, 1 H, $J_{6,7}$ 4.5, $J_{6,7'}$ 9 Hz, H-6), 2.20 (dt, 1 H, $J_{7,7}$ 12 Hz H-7), 1.72 (dd, 1 H, H-7′).

Anal. Calc. for $C_8H_{10}O_4$: C, 56.47; H, 5.92. Found: C, 56.61; H, 5.80.

*(±)-*6exo*-Acetoxymethyl-*exo*-3,8-dioxatricyclo[3.2.1.0^{2,4}]octane* (**16**). — The ester **15** (97 mg, 0.57 mmol) was treated with lithium aluminium hydride (23 mg, 0.61 mmol) in tetrahydrofuran (3 mL) for 1 h at room temperature. The mixture was processed as in the preparation of **3** and the product was acetylated in the usual way, to give **16** (67 mg, 64%) as a syrup. ^{1}H-N.m.r. data: δ 4.47 (d, 1 H, $J_{1,7}$ 4.5 Hz, H-1), 4.34 (s, 1 H, H-5), 4.28–3.60 (m, 2 H, CH_2OAc), 3.26 (s, 2 H, H-2,4), 2.04 (s, 3 H, OAc), 1.66 (dd, 1 H, $J_{6,7}$ 7.2, $J_{7,7}$ 12 Hz, H-7), 1.31 (dt, 1 H, $J_{1,7'}$ 4.5 Hz, H-7′).

Anal. Calc. for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.58; H, 6.54.

DL-*(1,2,3,5/4)-*(**17**), DL-*(1/2,3,4,5)-*(**18**), and DL-*(1,2/3,4,5)-5-Acetoxymethyl-1,2,3,4-tri-*O*-acetyl-1,2,3,4-cyclohexanetetrol* (**19**). — A mixture of **12** (200 mg, 0.70 mmol), acetic acid (4.2 mL), acetic anhydride (2.4 mL), and conc. sulfuric acid (0.24 mL) was heated in a sealed tube for 60 h at 100°, and then poured into ice-water. The solution was processed as in the preparation of **6** and the products were eluted from a column of silica gel (30 g) with 2-butanone–toluene (1:30) to give three fractions, which were crystallised from ethanol to give **19** (60 mg, 22%) as prisms, m.p. 142–143° (lit.[13] m.p. 147–148°), **17** (30 mg, 11%) as prisms, m.p. 125–125.5° (lit.[11] m.p. 123–125°), and **18** (90 mg, 33%) as prisms, m.p. 110.5–112° (lit.[12] m.p. 111–112°). The ^{1}H-n.m.r. spectra of **17**, **18** and **19** were identical to those of

the respective authentic samples[11-13].

DL-*(1,2,4/3,6)-4-Acetoxymethyl-1,2-di-O-acetyl-3,6-dibromo*-1,2-*cyclohexanediol* (**20**) *and 3,6-dibromo-4-bromomethylcyclohexane* (**21**). — A mixture of **13** (2.0 g, 7.0 mmol) and 20% hydrogen bromide in acetic acid (18 mL) was heated in a sealed tube for 36 h at 80°. The mixture was processed as in the preparation of 7 and the products were eluted from a column of silica gel with 2-butanone–toluene (1:17) to give, first, **21** (2.1 g, 66%) as prisms, m.p. 118–119° (from ethanol). ^{1}H-N.m.r. data: δ 5.71 (dd, 1 H, $J_{1,2}$ 3, $J_{2,3}$ 10.5 Hz, H-2), 5.32 (t, 1 H, $J_{1,6}$ 3 Hz, H-1), 4.29 (m, H-6), 4.20 (t, 1 H, $J_{3,4}$ 10.5 Hz, H-3), 3.96 (dd, 1 H, $J_{4,7}$ 3, $J_{7,7}$ 11.3 Hz) and 3.58 (dd, 1 H, $J_{4,7'}$ 3 Hz) (CH_2Br), 2.12 and 2.05 (2 s, each 3 H, 2 OAc).

Anal. Calc. for $C_{11}H_{15}Br_3O_4$: C, 29.30; H, 3.35. Found: C, 29.50; H, 3.32.

Eluted second was **20** (0.36 g, 12%), isolated as prisms, m.p. 92–93°. ^{1}H-N.m.r. data: δ 5.72 (dd, 1 H, $J_{1,2}$ 3, $J_{2,3}$ 10.5 Hz, H-2), 5.42 (t, 1 H, $J_{1,6}$ 3 Hz, H-1), 4.35 (m, 1 H, H-6), 4.38 (d, 2 H, $J_{4,7}$ 3 Hz, CH_2OAc), 4.14 (t, 1 H, $J_{3,4}$ 10.5 Hz, H-3), 2.16, 2.13, and 2.08 (3 s, each 3 H, 3 OAc).

Anal. Calc. for $C_{13}H_{18}Br_2O_6$: C, 36.30; H, 4.22. Found: C, 36.44; H, 4.17.

Treatment of **21** (47 mg, 0.10 mmol) with anhydrous sodium acetate (17 mg, 0.21 mmol) in *N,N*-dimethylformamide (1.5 mL) for 20 h at 60° gave **20** (40 mg, 90%) as prisms (from methanol), identical to the above compound in all respects.

DL-*(1,2,4/3,6)-4-Acetoxymethyl-1,2-di-O-acetyl-3,6-diazido-1,2-cyclohexanediol* (**22**). — A mixture of the dibromide **20** (70 mg, 0.16 mmol) and sodium azide (33 mg, 0.51 mmol) in aqueous 90% 2-methoxyethanol was boiled under reflux for 1.5 h and then concentrated. The residue was extracted with ethyl acetate and the usual work-up gave the product, which was eluted from a column of silica gel with ethyl acetate–hexane (1:5.5) to give **22** (43 mg, 87%) as needles, m.p. 60–60.5° (from ethanol). ^{1}H-N.m.r. data: δ 5.30 (t, 1 H, $J_{1,2} = J_{1,6} = 3$ Hz, H-1), 5.13 (dd, 1 H, $J_{2,3}$ 10.5 Hz, H-2), 4.37 (d, 2 H, $J_{4,7}$ 3 Hz, CH_2OAc), 3.90 (bq, 1 H, J 3 Hz, H-6), 3.59 (t, 1 H, $J_{3,4}$ 10.5 Hz, H-3), 2.13, 2.10, and 2.07 (3 s, each 3 H, 3 OAc).

Anal. Calc. for $C_{13}H_{18}N_6O_6$: C, 44.07; H, 5.12; N, 23.72. Found: C, 43.99; H, 5.08; N, 23.75.

DL-*(1,4/2,3,5)-1,4-Diacetamido-5-acetoxymethyl-2,3-di-O-acetyl*-2,3-*cyclohexanediol* (**23**). — A solution of **22** (130 mg, 0.37 mmol) in methanol (2 mL) and acetic anhydride (1 mL) was hydrogenated in the presence of Raney nickel at an initial hydrogen pressure of 3.4 kg/cm^2 (Parr apparatus) overnight at room temperature. The product was eluted from a column of silica gel with ethanol–toluene (1:5) to give **22** (115 mg, 81%) as an amorphous solid. ^{1}H-N.m.r. data: δ 7.54 and 6.73 (2 bd, each 1 H, J 9 Hz, 2 N*H*Ac), 5.30 (t, 1 H, $J_{1,2} = J_{2,3} = 3$ Hz, H-2), 5.20 (dd, 1 H, $J_{3,4}$ 10.5 Hz, H-3), 4.25–4.00 (m, 2 H, H-1,4), 4.10 (d, 2 H, $J_{4,7}$ 3 Hz, CH_2OAc), 2.14, 2.06, 1.98, 1.97, and 1.94 (5 s, each 3 H, 2 NHAc and 3 OAc).

Anal. Calc. for $C_{17}H_{26}N_2O_8 \cdot H_2O$: C, 50.48; H, 6.48; N, 6.93. Found: C, 50.58; H, 6.36; N, 6.76.

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