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DERIVATIVES OF 2,3-ANHYDRO-DL-THREITOL, 2,3-ANHYDROERYTHRITOL, 2,3:4,5-DIANHYDROGALACTITOL, AND 2,3:4,5-DIANHYDROALLITOL*†

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ABSTRACT

α,ω-Disubstituted derivatives of 2,3-anhydro-DL-threitol (**2**), 2,3-anhydroerythritol (**4**), 2,3:4,5-dianhydrogalactitol (**8**), and 2,3:4,5-dianhydroallitol (**12**) have been synthesised by epoxidation of the appropriate alkenes and dienes. Benzyloxycarbonyl groups were used for protecting the primary hydroxyl groups during epoxidation.

INTRODUCTION

2,3:4,5-Dianhydro-1,6-di-*O*-methanesulphonyl-L-iditol[1] is a new, tetrafunctional, biological alkylating agent that inhibits the growth of a broad spectrum of experimentally induced tumours in animals[2]. In investigating structure–activity relationships, analogues of this compound have been synthesized[3] and assayed[4], and we now report on other analogues differing in configuration and in the length of the carbon chain.

Of the 2,3:4,5-dianhydrohexitols, only the D-*ido*[5], L-*ido*[1,6], and *galacto*[7] derivatives, in which the two oxirane rings are *threo*, have been described; the corresponding *erythro* compounds were unknown hitherto.

For acyclic compounds, *erythro*-oxiranes cannot be formed *via* alkaline treatment of appropriate, partially substituted alditols, but can be obtained *via* epoxidation of alkenes. Epoxidation is a stereospecific reaction[8]; *erythro*-oxiranes are obtained from *cis*-alkenes, whereas *trans*-alkenes yield *threo*-oxiranes. This reaction has been used in the synthesis of sugar derivatives containing only one oxirane ring[9]. We have applied this reaction in the synthesis of derivatives of 2,3:4,5-dianhydrogalactitol and 2,3:4,5-dianhydroallitol. To investigate the effect of variation of chain length, 2,3-anhydro-1,4-di-*O*-methanesulphonyl-DL-threitol and the erythritol analogue were synthesized.

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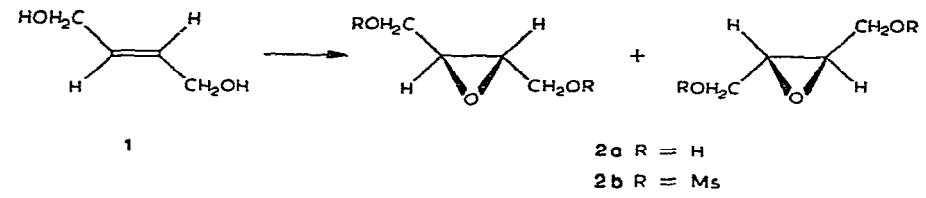
RESULTS AND DISCUSSION

Epoxidation of *trans*-but-2-ene-1,4-diol[10] (**1**) in chloroform with perbenzoic acid gave 2,3-anhydro-DL-threitol[11] (**2a**) in excellent yield, and similar treatment of the *cis*-isomer[12] **3** afforded 2,3-anhydroerythritol[13] (**4a**). Each anhydro compound could be converted smoothly into the 1,4-di-*O*-mesyl derivative (**2b** and **4b**).



1

2a R = H
2b R = Ms

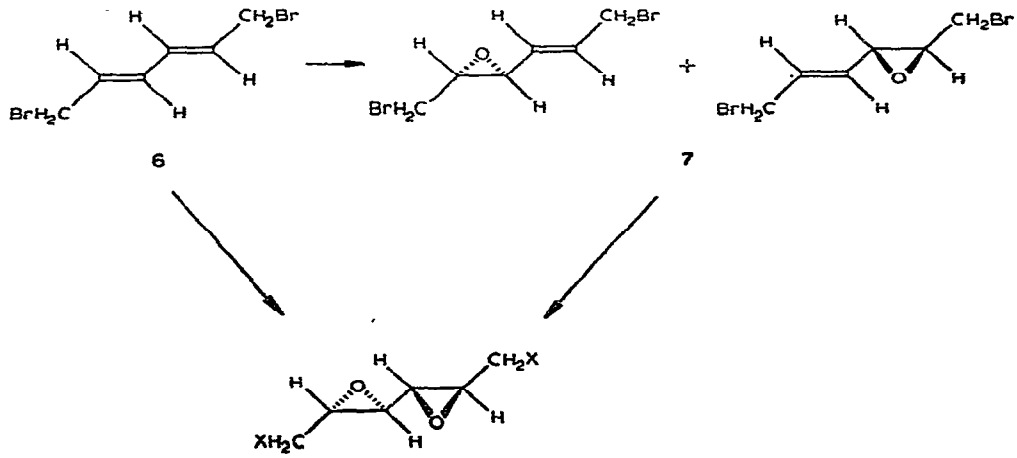
3

4a R = H
4b R = Ms

When epoxidation of *trans,trans*-hexa-2,4-diene-1,6-diol[14] was attempted under similar conditions, or with 3-chloroperoxybenzoic acid, no dianhydro compound was obtained. Likewise, attempted reactions with dichloromethane or tetrahydrofuran as solvents and in the presence of inorganic bases (sodium carbonate, disodium hydrogen phosphate) were also unsuccessful.

In order to avoid interference by the primary hydroxyl groups, the corresponding 1,6-dibromo derivative was investigated. The readily obtained[15] hexa-1,5-diene-3,4-diol (**5**) was converted into the known[16] 1,6-dibromo-*trans,trans*-hexa-2,4-diene (**6**), which, on epoxidation with an excess of 3-chloroperoxybenzoic acid, gave 2,3:4,5-dianhydro-1,6-dibromo-1,6-dideoxygalactitol (**8a**, 15%), which was identical with the product obtained from 3,5-di-*O*-acetyl-1,6-dibromo-1,6-dideoxy-2,4-di-*O*-mesyl-D-mannitol[7]. Theoretically, epoxidation of **6** could also lead to 2,3:4,5-dianhydro-1,6-dibromo-1,6-dideoxy-DL-iditol, but **8a** was the only dianhydride detected (t.l.c.). Treatment of **8a** with silver methanesulphonate in acetonitrile afforded the 1,6-dimesylate **8b**. When **6** was treated with only 1.2 mol. of peroxy acid, a racemic mixture of the monoanhydro compounds **7** was obtained.

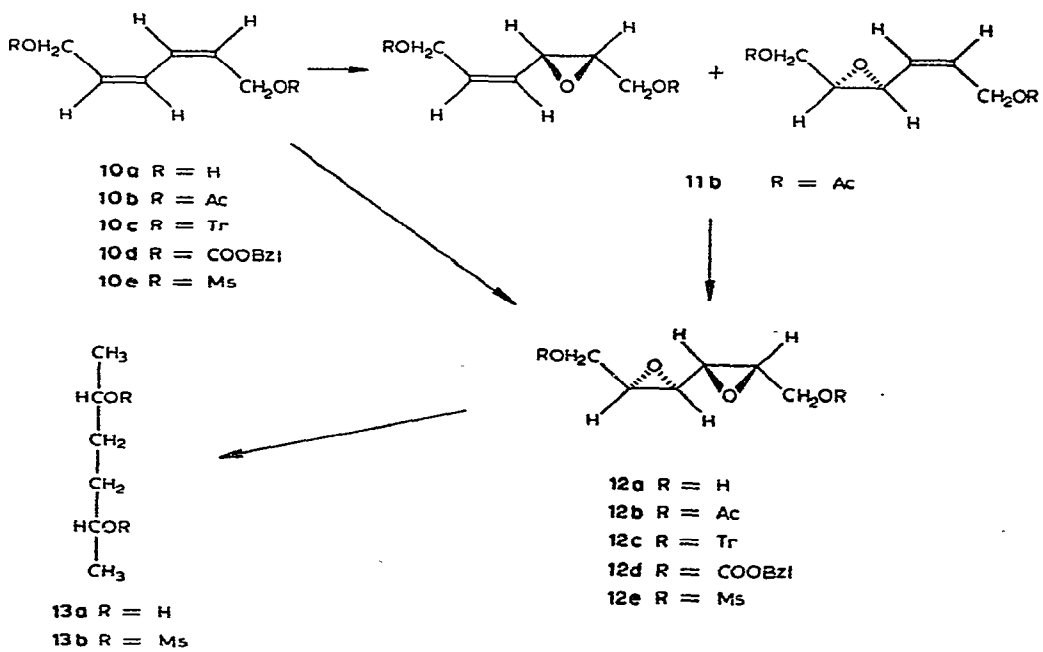
The synthesis of 2,3:4,5-dianhydroallitol (**12a**) was attempted by epoxidation of *cis,cis*-hexa-2,4-diene-1,6-diol (**10a**), which was obtained in 30% yield from the corresponding diyne[17] (**9**) by partial hydrogenation in the presence of Lindlar catalyst. As compound **10a** was almost insoluble in chlorinated solvents, epoxidation was carried out with 3-chloroperoxybenzoic acid in tetrahydrofuran in the presence of



6 7

8a X = Br
8b X = OMs

sodium carbonate. The reaction gave only 2% of **12a**, and a route similar to that used to obtain the galactitol isomer **8a** was therefore investigated. However, when **10a** was treated with hydrogen bromide or phosphorus tribromide, isomerisation occurred and the *trans,trans* dibromide **6** was obtained. Although the diacetate **10b** and the dityrityl compound **10c** could be converted into the corresponding dianhydro



10a R = H
10b R = Ac
10c R = Tr
10d R = COOBzl
10e R = Ms

11b R = Ac

12a R = H
12b R = Ac
12c R = Tr
12d R = COOBzl
12e R = Ms

13a R = H
13b R = Ms

derivatives **12b** and **12c**, respectively, the protecting groups could not be removed selectively by sodium methoxide or hydrogenolysis. Epoxidation of **10b** with 1.4 mol. of peroxy acid gave a racemic mixture (**11b**) of the monoanhydro compound.

As the benzyl group could not be introduced into **10a**, the 1,6-di-*O*-benzyloxycarbonyl derivative **10d** was investigated. Epoxidation of **10d** in chloroform at 20°, maintaining a relatively high concentration of 3-chloroperoxybenzoic acid (the decomposition of which was suppressed by the addition of magnesium sulphate), gave the dianhydro compound **12d** (16.4%). The protecting groups were removed by hydrogenolysis (palladium-on-charcoal) in the presence of silver carbonate. Compound **12a** was converted into a diacetate (**12b**), dityityl ether (**12c**), and dimesylate (**12e**).

The dimesylate **12e** was also synthesized by a second route. The 1,6-dimesylate **10e**, derived from **10a**, decomposed violently at room temperature but could be recrystallized from propan-2-ol, and its solution in tetrahydrofuran was stable at −5°. Epoxidation of **10e** yielded **12e**.

Reduction of **12e** with an excess of lithium aluminium hydride gave (g.l.c. of the product mixture) a 2,5-diol as the major component, together with some 2,4-diol and a trace of the 3,4-diol. A fourth product, probably the 1,5-diol, was also detected, which could have been formed *via* an epoxide migration. Mesylation of the 2,5-diol **13a**, which was isolated by preparative g.l.c., gave a product (**13b**) that was identical with the dimesylate of *erythro*-hexane-2,5-diol[18]. Thus, **12e**, and therefore other compounds in the series **12**, must have the *allo* configuration.

Since, on epoxidation of dienes, the formation of the second oxirane ring is a much slower process than that of the first one, the intermediate monoanhydrides **7** and **11** could be prepared in relatively high yield when 1.2 mol. of peroxy acid was used. It is advisable to use a solvent in which the unsaturated compound, but not the dianhydride, is readily soluble. The dianhydride compound formed will then precipitate from the reaction mixture, and acid-catalysed decomposition will be minimized. The use of inorganic bases (sodium carbonate, disodium hydrogen phosphate, magnesium oxide) to neutralise the strong acid formed results in catalytic decomposition of the peroxy acid. As the solubility of peroxy acids is much higher in chlorinated solvents than that of the corresponding acids, it is advisable to use a saturated solution of the peroxy acid and to maintain saturation during the reaction.

2,3:4,5-Dianhydro-1,6-di-*O*-methanesulphonylgalactitol (**8b**) exhibited a strong cytostatic effect on the Ehrlich ascites sarcoma, whereas the allitol derivative **12e** was less effective. The cytostatic activity of the anhydrotetritol derivatives **2b** and **4b** was less pronounced than that of 1,4-dimethanesulphonyloxybutane[19] (Myleran).

EXPERIMENTAL

General methods. — Melting points are uncorrected. T.l.c. was performed on Kieselgel G with *A*, ethyl acetate–water (20:1); *B*, ether–hexane (9:1); *C*, hexane–ether–1-butanol (12:7:1); and *D*, ethyl acetate–chloroform (3:2). Detection was

effected with 0.1M potassium permanganate–M sulphuric acid (1:1). 4-*p*-Nitrobenzylpyridine–2M sodium hydroxide was used for epoxides. I.r. spectra were recorded on a Perkin–Elmer 457 spectrometer and n.m.r. spectra (60 MHz) on a Varian A-60D spectrometer with Me_4Si as the internal standard. G.l.c. was performed on a Gasofract 400C gas chromatograph.

Evaporation of solvents was carried out with a rotary evaporator under diminished pressure, after drying the organic solutions over magnesium sulphate.

2,3-Anhydro-DL-*threitol*[11] (**2a**). — A solution of *trans*-but-2-ene-1,4-diol[10] (**1**, 35.2 g) in chloroform (100 ml) was added at −10° to stirred 1.8M peroxybenzoic acid in chloroform (370 ml) during 30 min. Stirring was continued at 10° for 1 h, the slurry was then filtered, and the crystalline material was washed with chloroform (50 ml) and ether (50 ml). A solution of the resulting, crude oxirane (90%, m.p. 60–64°) in *p*-dioxane was stirred with powdered, dry potassium carbonate (30 g) for 10 min, then filtered, and concentrated, and the residue was recrystallized from acetone–ether to give **2a** (31.2 g, 75%), m.p. 66–67°; lit.[11] m.p. 73.5–74.5°.

2,3-Anhydro-1,4-di-O-*methanesulphonyl*-DL-*threitol* (**2b**). — To a solution of **2a** (10.4 g) in acetone (60 ml), a solution of mesyl chloride (19.6 ml) in pyridine (32 ml) and dry tetrahydrofuran (30 ml) was added at −30° during 30 min. The mixture was stirred for 30 min at −30° and then for 1 h at 0°. After cooling to −30°, water (20 ml) was added, and the product was conventionally extracted with chloroform and recrystallized from methanol to give **2b** (17.7 g, 68%), m.p. 105–106°; ν_{max}^{KBr} 1345, 1170, 940, 850, 530, 525 (mesyl), and 892 cm^{-1} (*threo*-oxirane). N.m.r. data (Me_2SO-d_6): δ 4.25 and 4.60 (2 dd, $J_{1,1'} = J_{4,4'} = 12$, $J_{1,2} = J_{3,4} = 6$, $J_{1',2} = J_{3,4'} = 2.5$ Hz, H-1,4), 3.25–3.58 (m, H-2,3), and 3.20 (s, 2 Me).

Anal. Calc. for $C_6H_{12}O_7S_2$: C, 27.64; H, 4.65; S, 24.65. Found: C, 27.71; H, 4.50; S, 24.55.

2,3-Anhydroerythritol[13] (**4a**). — *cis*-But-2-ene-1,4-diol[12] (**3**), when distilled and crystallized from methanol (1.5 vol.) at −70° overnight, had m.p. 9–11°, n_D^{25} 1.473. Treatment of **3** with perbenzoic acid, as described for **2a** and with recrystallization of the crude product (34.1 g, 82%) from ethyl acetate, afforded **4a** (28.5 g, 68.2%), m.p. 59–60°; lit.[13] m.p. 57.5–58.5°.

2,3-Anhydro-1,4-di-O-*methanesulphonylerythritol* (**4b**). — Mesylation of **4a**, as described for **2a**, gave **4b** (16.5 g, 63.5%), m.p. 53–54° (from methanol); ν_{max}^{KBr} 1350, 1180–1165, 980–970, 835, 530, 520 (mesyl), and 855 cm^{-1} (*erythro*-oxirane). N.m.r. data (Me_2SO-d_6): δ 4.30 and 4.65 (2 dd, $J_{1,1'} = J_{4,4'} = 12$, $J_{1,2} = J_{3,4} = 7$, $J_{1',2} = J_{3,4'} = 3.5$ Hz, H-1,4), 3.33–3.65 (m, H-2,3), and 3.25 (s, 2 Me).

Anal. Calc. for $C_6H_{12}O_7S_2$: C, 27.64; H, 4.65; S, 24.65. Found: C, 27.94; H, 4.94; S, 24.57.

1,6-Dibromo-trans,trans-*hexa-2,4-diene* (**6**). — A solution of hexa-1,5-diene-3,4-diol[15] (114.14 g) and copper(I) chloride (10 g) in 48% aqueous hydrogen bromide (840 ml) was kept at 50° for 15 min. The precipitate was collected, washed with water, and recrystallised from hexane (2.5 l) to give **6** (150.5 g, 63%), m.p. 86–87°, R_F 0.85 (solvent *C*); lit.[16] m.p. 88°.

Compound **6** was also obtained when *trans,trans*-hexa-2,4-diene-1,6-diol[14] was used as starting material.

*1,6-Dibromo-2,3-*DL-threo-*epoxy*-trans-*hex-4-ene* (**7**). — A solution of **6** (12 g) in chloroform (60 ml) was treated at 30–35° with 3-chloroperoxybenzoic acid (83.5%, 12.4 g) for 1 h and then poured into a cooled slurry of powdered, dry potassium carbonate (55 g) in acetone (200 ml). The slurry was stirred for 10 min, then filtered, and concentrated, and a solution of the residue in chloroform (100 ml) was filtered and concentrated. The residual oil was crystallised from ether (50 ml) and hexane (50 ml) at −50°. The product was twice recrystallized from methanol at −50° to give **7** (5.58 g, 43.6%), m.p. 50–52°, R_F 0.65 (solvent *C*); ν_{max}^{KBr} 960 (*trans*-olefin) and 860 cm^{-1} (*threo*-oxirane). N.m.r. data (CCl_4): δ 2.90–3.75 (m, H-1,1',2,3), 5.58 (dd, $J_{3,4}$ 6.5 Hz, H-4), 6.15 [dt, $J_{4,5}$ 15 Hz (characteristic of *trans*-olefins), H-5], and 3.95 (d, $J_{5,6}$ 7 Hz, H-6).

Anal. Calc. for $C_6H_8Br_2O$: C, 28.20; H, 3.16; Br, 62.40. Found: C, 28.16; H, 3.30; Br, 62.42.

2,3:4,5-Dianhydro-1,6-dibromo-1,6-dideoxygalactitol (**8a**). — To 0.77M 3-chloroperoxybenzoic acid in chloroform (780 ml), **6** (47.8 g) was added and the temperature of the reaction mixture was kept at 25°. After 2 h, the mixture was kept at room temperature in the dark for 4 days, and then worked-up as described for **7**. The product was recrystallized from methanol to give **8a** (8.8 g, 14.9%), m.p. 131–132° alone and in admixture with authentic material[7].

*2,3:4,5-Dianhydro-1,6-di-*O-*methanesulphonylgalactitol* (**8b**). — A solution of **8a** (4.08 g) in acetonitrile (75 ml) was boiled in the presence of silver methanesulphonate (9 g) for 6 h, then filtered, and concentrated. The residue was filtered with ethanol, and washed with water, ethanol, and ether, and the crude product (4.1 g, 90%) was recrystallized from acetone to yield **8b** (2.82 g, 62.5%), m.p. 129–129.5°, R_F 0.0 (solvent *C*); ν_{max}^{KBr} 1365–1350, 1175, 980–950, 545–530, 520, 470 (mesyl), and 900 cm^{-1} (*threo*-oxirane). N.m.r. data (Me_2SO-d_6): δ 4.14 and 4.59 (2 dd, $J_{1,1'} = J_{6,6'} = 12$, $J_{1,2} = J_{5,6} = 7$, $J_{1',2} = J_{5,6'} = 3$ Hz, H-1,6), 3.15–3.50 (m, H-2,3,4,5), and 3.25 (s, 2 Me).

Anal. Calc. for $C_8H_{14}O_8S_2$: C, 31.78; H, 4.66; S, 21.21. Found: C, 31.81; H, 4.77; S, 21.18.

cis,cis-*Hexa-2,4-diene-1,6-diol* (**10a**). — A solution of hexa-2,4-diyne-1,6-diol[17] (110.1 g) in methanol (500 ml) was filtered with charcoal. After the addition of quinoline (10 ml), methanol (500 ml), and Lindlar catalyst (50 g), the solution was hydrogenated at −5° until 2.1 mol. of hydrogen had been consumed (3–4 h). The mixture was filtered and concentrated, and benzene (200 ml) was evaporated from the residue, which was then thrice recrystallized from ethyl acetate (500 ml) at −60° to give **10a** (35.5 g, 31.1%), m.p. 62–63°, R_F 0.48 (Solvent *A*), λ_{max} 232 nm (ε 22,950); ν_{max}^{KBr} 3600–3000 (OH), 1010 [C–O(H)], 705 (CH, *cis*-olefin), and 640 cm^{-1} (OH). N.m.r. data (Me_2SO-d_6): δ 4.15 (t, $J_{1,OH} = J_{6,OH} = J_{1,2} = J_{5,6} = 6$ Hz, H-1,6), 5.33–5.85 (m, H-2,5), 6.10–6.40 [m, $J_{2,3} = J_{4,5} = 10$ Hz (characteristic of *cis*-olefins), H-3,4], and 4.67 (t, 2 OH).

Anal. Calc. for $C_6H_{10}O_2$: C, 63.17; H, 8.79. Found: C, 63.19; H, 8.76.

On storage at room temperature, polymerization occurred, but a solution of **10a** in ethyl acetate can be stored at −10° in the presence of 0.1% of hydroquinone and one drop of pyridine for months without decomposition.

Conventional treatment of **10a** with acetic anhydride in pyridine afforded a syrupy diacetate **10b** (82%) which crystallized on cooling; m.p. 10–12°.

Anal. Calc. for $C_{10}H_{14}O_4$: C, 60.78; H, 6.94. Found: C, 60.85; H, 7.03.

The dityrityl derivative **10c**, prepared conventionally by using pyridine and trityl chloride, had m.p. 185–186° (from *p*-dioxane–methanol).

Anal. Calc. for $C_{44}H_{38}O_2$: C, 88.25; H, 6.40. Found: C, 88.11; H, 6.75.

1,6-Dibenzyloxycarbonyloxy-cis,cis-*hexa-2,4-diene* (**10d**). — A solution of **10a** (57.1 g) in pyridine (400 ml) and chloroform (400 ml) was treated at ~ −30° with a solution of benzyloxycarbonyl chloride (225 ml) in dry chloroform (550 ml) for 1 h. The mixture was kept at −20° for 1 h and subsequently at −5° overnight, then poured into water, and extracted with chloroform (2 × 250 ml). The chloroform solution was adjusted to pH 5 with 20% sulphuric acid in the presence of ice, and then washed with water and concentrated. The residue was recrystallized first from methanol and then ether to give **10d** (123.6 g, 64.5%), m.p. 47.5–48.5°, R_F 0.80 (solvent *A*); ν_{max}^{KBr} 1745 (C=O), 1260 (C–O ester), 710 and 700 cm^{-1} (CH, *cis*-olefin). N.m.r. data ($CDCl_3$): δ 4.85 (d, $J_{1,2} = J_{5,6} = 6$ Hz, H-1,6), 5.45–6.10 (m, H-2,5), 6.45–6.65 (m, $J_{2,3} = J_{4,5} = 10$ Hz, H-3,4), 5.20 (s, 2 benzyl CH_2), and 7.40 (s, 2 Ph).

Anal. Calc. for $C_{22}H_{22}O_6$: C, 69.14; H, 5.81. Found: C, 69.06; H, 5.78.

1,6-Dimethanesulphonyloxy-cis,cis-*hexa-2,4-diene* (**10e**). — To a solution of **10a** (11.4 g) in tetrahydrofuran (80 ml) and benzene (40 ml), triethylamine (28 ml) and powdered potassium hydroxide (25 g) were added. The slurry was treated at −10° with mesyl chloride (15.6 ml) and stirring was continued at 10° for 1 h. The filtered mixture was concentrated and propan-2-ol (100 ml) was added to the residue. The product was collected, and recrystallized from tetrahydrofuran–propan-2-ol to yield **12e** (11.2 g, 41.5%), m.p. 64–67° (dec.). At room temperature, the compound decomposed violently within a few hours, but its solution in tetrahydrofuran could be stored at −5° for months.

Anal. Calc. for $C_8H_{14}O_6S_2$: S, 23.72. Found: S, 23.65.

1,6-Diacetoxy-2,3-DL-erythro-*epoxy*-cis-*hex-4-ene* (**11b**). — A solution of **10b** (13.9 g) in M 3-chloroperoxybenzoic acid (100 ml) in chloroform was made up at −25° and then kept at −10° for 10 h. The mixture was poured into a cold solution of potassium carbonate (20 g) in water (150 ml), the chloroform was separated, and the aqueous phase was twice extracted with chloroform. The combined extracts were washed with water, dried, and concentrated. The residue was crystallized from ether (100 ml) at −40° and then from methanol at −50°, to yield **11b** (6.5 g, 41%), m.p. 47–48°, R_F 0.60 (solvent *B*); ν_{max}^{KBr} 1735 (C=O), 1240 and 1035 (C–O ester), 780 (CH, *cis*-olefin), and 845 cm^{-1} (*erythro*-oxirane). N.m.r. data ($CDCl_3$): δ 4.08 and 4.30 [2 dd, $J_{1,1'}$ 12, $\frac{1}{2}(J_{1,2} + J_{1',2})$ 6 Hz, H-1], 3.40 (2 d, H-2), 3.80 (2 d, $J_{2,3}$ 4.5, $J_{3,4}$ 6 Hz, H-3), 5.54

(dd, H-4), 5.92 [dt, $J_{4,5}$ 11.5 (*cis*-olefin), $J_{5,6}$ 6 Hz, H-5], 4.80 (d, H-6), 2.05 and 2.10 (2 s, 2 Me).

Anal. Calc. for $C_{10}H_{14}O_5$: C, 56.10; H, 6.58. Found: C, 56.05; H, 6.62.

2,3:4,5-Dianhydroallitol (**12a**). — (*a*) To a solution of **10a** (3.42 g) in tetrahydrofuran (40 ml), powdered sodium carbonate (10 g) was added. 3-Chloroperoxybenzoic acid (20 g) was added in four parts to the stirred slurry during 8 h, keeping the temperature at 15–20°. After addition of the third portion of peroxy acid, powdered sodium carbonate (10 g) was added. The reaction mixture was stirred for 8 h at room temperature and then poured into a stirred slurry of powdered, dry potassium carbonate (50 g) in acetone (200 ml). The filtered solution was concentrated and the residue was treated first with ether and then with ethyl acetate to give, after recrystallization from ethyl acetate, **12a** (82 mg, 1.9%), m.p. 140–141°, R_F 0.10 (solvent *D*); ν_{max}^{KBr} 3290 and 3200 (OH), 1040 and 1015 [C–O(H)], and 875 cm^{-1} (*erythro*-oxirane). N.m.r. data (Me_2SO-d_6): δ 3.57 and 3.87 (2 dd, $J_{1,1'} = J_{6,6'} = 12$, $J_{1,2} = J_{5,6} = 6$, $J_{1',2} = J_{5,6'} = 4$ Hz, H-1,6), 3.00–3.30 (m, H-2,3,4,5), and 5.00 (t, $J_{1,OH} = J_{6,OH} =$ 6 Hz, 2 OH).

Anal. Calc. for $C_6H_{10}O_4$: C, 49.35; H, 6.91. Found: 49.40; H, 6.95.

(*b*) A solution of **12d** (41.45 g) in tetrahydrofuran (400 ml) and dry methanol (400 ml) was hydrogenated over palladium-on-carbon (4 g) and silver carbonate (10 g) at room temperature for 1 h. The mixture was filtered and the insoluble material was extracted with hot *p*-dioxane (400 ml). The combined filtrates and washings were concentrated and the residue was recrystallized from ethyl acetate to give **12a** (9.86 g, 67.5%), which was identical with the product from (*a*).

1,6-Di-O-*acetyl-2,3:4,5-dianhydroallitol* (**12b**). — The diene **10b** (6.95 g) was treated with peroxy acid, as described for the epoxidation of **10d**. The crude product was treated with ether (50 ml) at −70° for 15 min, then collected, washed with ether and methanol, and recrystallized from propan-2-ol to give **12b** (1.22 g, 15.1%), m.p. 88.5–89°, R_F 0.45 (solvent *B*); ν_{max}^{KBr} 1735 (C=O), 1260 and 1050 (C–O ester), and 870 cm^{-1} (*erythro*-oxirane). N.m.r. data ($CDCl_3$): δ 4.19 and 4.44 (2 dd, $J_{1,1'} = J_{6,6'} = 12.5$, $J_{1,2} = J_{5,6} = 6$, $J_{1',2} = J_{5,6'} = 4$ Hz, H-1,6), 1.80–2.10 (m, H-2,3,4,5), and 2.10 (s, 2 Me).

Anal. Calc. for $C_{10}H_{14}O_6$: C, 52.21; H, 6.12. Found: C, 52.30; H, 6.28.

Compound **12b** (22.2%) was obtained when **11b** was used as starting material. Conventional acetylation of **12a** with pyridine–acetic anhydride afforded **12b** (91%).

2,3:4,5-Dianhydro-1,6-di-O-*tritylallitol* (**12c**). — Epoxidation of **10c**, as described for **10d**, afforded, after recrystallization from methanol and then from chloroform–methanol, **12c** (26%), m.p. 194–196°.

Anal. Calc. for $C_{44}H_{38}O_4$: C, 83.78; H, 6.07. Found: C, 83.75; H, 6.12.

Compound **12c** was also obtained by tritylation of **12a**.

2,3:4,5-Dianhydro-1,6-di-O-*benzyloxycarbonylallitol* (**12d**). — To a solution of **10d** (65.0 g) in chloroform (200 ml), dry magnesium sulphate (20 g) was added followed, during 10 h, by 3-chloroperoxybenzoic acid (94% purity, 95.3 g) in four parts. The temperature of the reaction mixture was kept at 20–22°. After 48 h, the

mixture was poured into a stirred and cooled slurry of powdered potassium carbonate (440 g) in acetone (1500 ml). Stirring was continued for 15 min, the slurry was filtered, the filtrate was concentrated, and the residue was treated with methanol. The crude product was twice recrystallized from ether at −40° to give **12d** (11.5 g, 16.3%), m.p. 74–74.5°, R_F 0.50 (solvent *C*); ν_{max}^{KBr} 1740 (C=O), 1280 (C–O), and 875 cm^{-1} (*erythro*-oxirane). N.m.r. data: ($CDCl_3$): δ 4.30 and 4.49 (2 dd, $J_{1,1'} = J_{6,6'} = 12.5$, $J_{1,2} = J_{5,6} = 6$, $J_{1',2} = J_{5,6'} = 4$ Hz, H-1,6), 3.00–3.50 (m, H-2,3,4,5), 5.20 (s, 2 benzyl CH_2), and 7.40 (s, 2 Ph).

Anal. Calc. for $C_{22}H_{22}O_8$: C, 63.85; H, 5.31. Found: C, 63.97; H, 5.61.

2,3:4,5-Dianhydro-1,6-di-O-methanesulphonylallitol (**12e**). — (*a*) Conventional mesylation of **12a** (14.62 g) gave **12e** (27.2 g, 93%), m.p. 132.5–133.5° (from acetone), R_F 0.55 (solvent *A*); ν_{max}^{KBr} 1345–1330, 1170, 975, 955, 550, 520, 455 (mesyl), and 885 cm^{-1} (*erythro*-oxirane). N.m.r. data (Me_2SO-d_6): δ 4.37 and 4.85 (2 dd, $J_{1,1'} = J_{6,6'} = 12$, $J_{1,2} = J_{5,6} = 7$, $J_{1',2} = J_{5,6'} = 3$ Hz, H-1,6), 3.15–3.70 (m, H-2,3,4,5), and 3.30 (s, 2 Me).

Anal. Calc. for $C_8H_{14}O_8S_2$: C, 31.78; H, 4.66; S, 21.21. Found: C, 31.80; H, 4.79; S, 21.17.

erythro-*Hexane-2,5-diol* (**13a**). — A mixture of **12e** (12.08 g), dry tetrahydrofuran (800 ml), and lithium aluminium hydride (20 g) was boiled under reflux for 16 h. The excess of hydride was decomposed by the addition of ethanol (100 ml) and water (50 ml). The resulting slurry was filtered, and the insoluble material was washed first with hot tetrahydrofuran (2 × 200 ml) and then with hot ethanol (3 × 200 ml). The combined filtrates and washings were concentrated and a solution of the residue in tetrahydrofuran (100 ml) was filtered and concentrated. The residue was distilled at 132–134°/15 mTorr. G.l.c. of the product (3.6 g, 76%) revealed hexane-2,5-diol (67.1%), hexane-2,4-diol (6.9%), hexane-3,4-diol (0.82%), and, probably, hexane-1,5-diol (22.4%). The 2,5-diol **13a**, which was separated by preparative g.l.c. on a steel column (300 × 0.4 cm) containing 15% of Carbowax 20M on AW-DMCS Chromosorb W (80–100 mesh) at 150°, had R_F 0.32 (solvent *A*).

Anal. Calc. for $C_6H_{14}O_2$: C, 61.50; H, 11.95. Found: C, 61.28; H, 12.07.

erythro-*2,5-Dimethanesulphonyloxyhexane* (**13b**). — Conventional treatment of **13a** (0.118 g) with mesyl chloride in pyridine gave **13b** (0.25 g, 77%), m.p. 96–98° (from methanol) alone and in admixture with authentic material[18].

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