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SYNTHESIS OF 1,2:5,6-DIANHYDRO-3,4-DIDEOXY-*erythro*- AND -D-*threo*-HEXITOL AND THEIR *E*-3-ENE DERIVATIVES*

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ABSTRACT

Starting from 1,2:5,6-di-*O*-isopropylidene-D-mannitol and -D-glucitol, respectively, D-*threo*- and *erythro*-hex-*E*-3-enitol were synthesized; these were hydrogenated to the 3,4-dideoxy compounds, which were converted into the corresponding 1,2:5,6-dianhydrides, possessing significantly different cytostatic activity. The D-*threo*- and *erythro*-*E*-3-ene diepoxides were also synthesized; they are unstable at room temperature and show no biological activity.

INTRODUCTION

The cytostatic activity of 1,2:5,6-diepoxyhexane was described by Ross[2] in 1950, but the compound investigated was a mixture of diastereomers as it had been obtained from 1,5-hexadiene by oxidation with peroxybenzoic acid[3]. The biological activity of bifunctional, biological alkylating agents depends significantly on the stereochemistry of the molecule, as was proved (among other examples) in the case of the *meso* and mixed diepoxybutane isomers[4], and the corresponding diastereomeric 1,2:5,6-dianhydrohexitols[5] and their 3,4-dimethyl ethers[6]. These facts suggested the synthesis and biological testing of the *threo*- and *erythro*-1,2:5,6-diepoxyhexane isomers, the carcinogenicity of which could differ from that of the isomeric mixture[7].

Stereochemically homogeneous 1,2:5,6-diepoxyhexane can be synthesized by starting from readily available hexitols, the 3- and 4-hydroxyl groups of which have to be eliminated; the corresponding 3,4-dideoxyhexitols can then be transformed into the desired diepoxides.

RESULTS AND DISCUSSION

For the synthesis of 1,2:5,6-diepoxy-D-*threo*-hexane (**6**), 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**1**) was used as the starting material; this was converted into 3,4-dideoxy-D-*threo*-hex-*E*-3-enitol (**2**) according to the procedure described by

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Tipson and Cohen[8]. Hydrogenation of **2** led, in unexpectedly low yield (35%), to 3,4-dideoxy-D-*threo*-hexitol* (**3**); a similar synthesis of **3** had been outlined[9], but no details were given. The optical rotation reported[9], $[\alpha]_D^{20}$ −25° (*c* 2.5, chloroform), must be erroneous, as the compound is insoluble in chloroform; it has optical rotations of $[\alpha]_D^{20}$ −24° (*c* 1, methanol), −12° (*c* 1, water). The yield from the hydrogenation could not be increased by us by applying a variety of different conditions. The structures of the side-products formed were not established, but ^{1}H-n.m.r. investigation of the acetylated reaction-mixture indicated the presence of 2,5-anhydro-3,4-dideoxy derivatives. Compound **3** was converted into the 1,6-dimesylate (**4**) of its 2,5-diacetate, and ditosylate (**5**), respectively; on treatment with sodium methoxide, both **4** and **5** gave the D-*threo*-diepoxide **6****.

For the synthesis of 1,2:5,6-diepoxy-*erythro*-hexane (**17**), 1,2:5,6-di-*O*-isopropylidene-D-glucitol (**7**) was used as the starting material. On treatment with sodium iodide–zinc in *N*,*N*-dimethylformamide according to Tipson and Cohen[8], both its dimesylate (**8**) and ditosylate[10] (**9**) afforded the *E*-3-ene derivative **10** in moderate yield***. When the isopropylidene groups of **10** were split off with aqueous acetic acid, a mixture of compounds was obtained on evaporation at room temperature, and these were separated by column chromatography. Two fractions could be crystallized, and they proved to be the unsubstituted *E*-3-enetetraol **11** and its 1,6-diacetate **12**. The other fractions were mixtures of partially acetylated derivatives, as was proved by converting them into the crystalline tetraacetate **13** which, on treatment with sodium methoxide, afforded the 3-ene-tetraol **11** in excellent yield. That means that, even under the mild conditions of evaporation under diminished pressure, partial acetylation takes place.

Hydrogenation of the double bond in **11** was performed with Pd–C as the catalyst, and the tetraol (**14**) obtained was further characterized by conversion into its tetraacetate (**15**). Partial tosylation of **14** with two equiv. of *p*-toluenesulfonyl chloride led to ditosylate **16** which, on treatment with sodium methoxide, gave the desired *erythro*-diepoxide **17**.

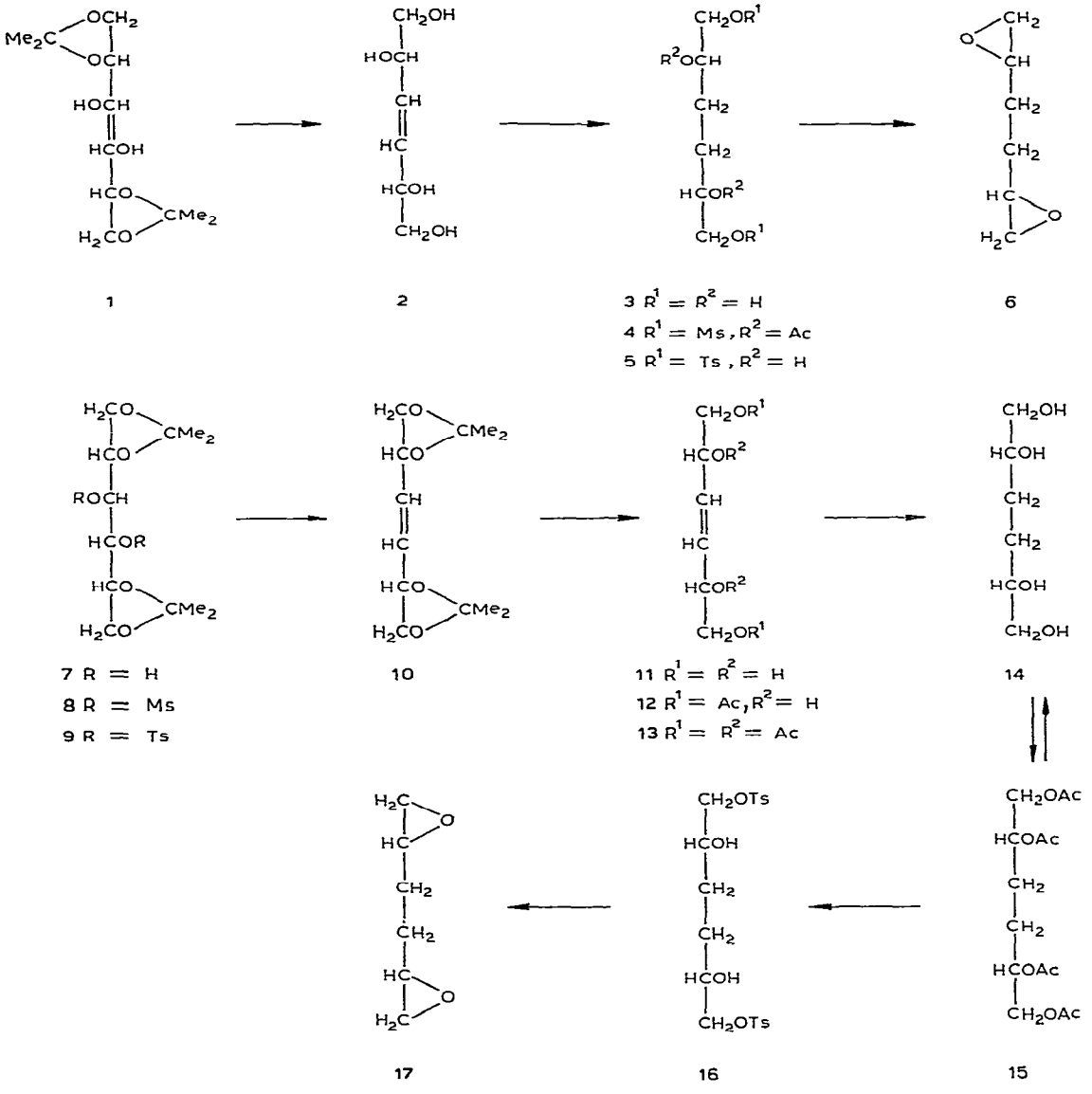
For further structure–activity studies, synthesis of the 1,2:5,6-diepoxy-3-ene diastereomers was also attempted. The D-*threo*-hex-*E*-3-enitol **2** was converted, *via* its 1,6-ditosylate **18** or 2,5-di-*O*-acetyl-1,6-di-*O*-mesyl derivative **19**, into the unsaturated diepoxide **20**, which, owing to its allyl-situated oxirane rings, proved to be unstable at room temperature and had to be stored at 0°.

The diastereomeric 1,2:5,6-dianhydro-3,4-dideoxy-*erythro*-hex-*E*-3-enitol was synthesized by converting unsaturated tetraol **11** into its crystalline 2,5-di-*O*-acetyl-1,6-di-*O*-tosyl derivative (**21**) which, on treatment with sodium methoxide, afforded

*Hexane-1,2(*S*),5(*S*),6-tetraol[9].

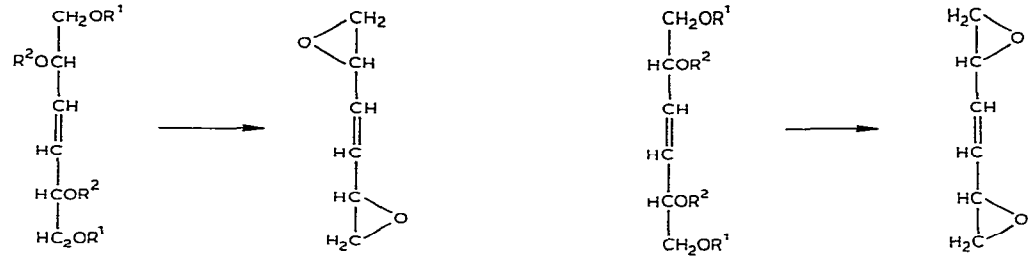
**Characteristic i.r.- and ^{1}H-n.m.r.-spectral data for compounds first described here are given in Tables I and II.

***The *E* configuration of the ethylene bond was proved by the coupling (15.5 Hz) of the olefinic protons (see Table II), estimated from the *A* part of the *AA'XX'* multiplet of the H-2,3,4,5 atoms. The rudimentary multiplet consisting of 6 lines appears as a consequence[10] of $J_{XX'} \simeq 0$.



the unsaturated diepoxide **23**. The same compound was obtained when the 1,6-diacetate **12** was mesylated, to give **22**, and **22** was then treated with sodium methoxide. In this case, inversion at C-2 and C-5 takes place, but the *erythro* configuration remains unchanged (2*S*,5*R* = 5*S*,2*R*). The unsaturated *erythro*-diepoxide **23** was even less stable than the *threo* isomer **20**, and had to be stored below −5°.

The cytostatic activity of the different epoxides was tested on virus-induced, Rauscher leukemia in mice. The saturated, *threo* compound **6** showed an inhibition of 68% at a dose of 4 × 30 mg/kg, whereas the *erythro* isomer **17** was only half as active (35%) at the same dose-level. That means that, besides the chirality of C-3



18 R^1 = Ts, R^2 = H
19 R^1 = Ms, R^2 = Ac

20

21 R^1 = Ts, R^2 = Ac
22 R^1 = Ac, R^2 = Ms

23

and C-4, that of the epoxy-bridge atoms C-2 and C-5 also plays an important role in the dependence of activity on structure of the different 1,2:5,6-dianhydro-hexitols[5,6,12].

The unsaturated diepoxides **20** and **23** were less toxic than the saturated analogs, but showed no cytostatic activity, probably because of their instability.

EXPERIMENTAL

General methods. — Melting points are uncorrected. Boiling-point pressures are given in torr*. All evaporations were performed in a rotary evaporator under diminished pressure, after the organic solution had been dried with sodium sulfate. Light petroleum refers to the fraction having b.p. 60–80°. Optical rotations were determined at *c* 1, if not stated otherwise. T.l.c. was effected on Kieselgel G with ethanol–ethyl acetate: 1:1 (*A*), 1:3 (*B*), and 1:9 (*C*), and with ethyl acetate–carbon tetrachloride: 2:1 (*D*), 1:1 (*E*), 1:3 (*F*), and 1:5 (*G*). For detection, 1:1 0.1M potassium permanganate–M sulfuric acid was used at 105°. Column chromatography was performed on Kieselgel 40 (63–200 μm). I.r. spectra of compounds in KBr pellets were recorded with a Perkin–Elmer 577 grating spectrometer, and ^{1}H-n.m.r. spectra (60 or 100 MHz) were respectively recorded at room temperature with a Jeol 60-HL and a Varian XL-100 FT spectrometer.

3,4-Dideoxy-D-threo-*hex*-E-*3-enitol* (**2**). — Pure 3,4-dideoxy-1,2:5,6-di-*O*-isopropylidene-D-*threo*-hex-*E*-3-enitol[8] (15 g) was hydrolyzed with 80% acetic acid (125 mL) for 18 h at room temperature, to give, after evaporation, and recrystallization from ethanol (20 mL)–ethyl acetate (20 mL), pure **2** (8 g, 82.2%), m.p. 72–74°, $[\alpha]_D^{20}$ −15° (*c* 2, water); lit.[8] m.p. 64–65°, $[\alpha]_D^{25}$ −13.8° (*c* 2, water); R_F 0.55 (*B*); $J_{3,4}$ 15.5 Hz.

3,4-Dideoxy-D-threo-*hexitol* (**3**). — A solution of compound **2** (9 g) in methanol (90 mL) was hydrogenated at room temperature in the presence of 10% Pd–C catalyst (1 g). After 3 h, when the theoretical amount of hydrogen had been consumed, the suspension was filtered, the filtrate evaporated, and the residue crystallized

*1 torr = 101.325/760 Pa.

from ethanol, to give pure **3** (3 g, 30%). From the mother liquor, a second crop of **3** could be obtained (0.45 g, 5%); m.p. 92–94°, $[\alpha]_D^{20}$ −24° (methanol), −12° (water); lit.[9] m.p. 84°, $[\alpha]_D^{20}$ −25° (*c* 2.5, chloroform); R_F 0.45 (*B*).

*2,5-Di-*O*-acetyl-3,4-dideoxy-1,6-di-*O*-(methylsulfonyl)-*D*-threo-hexitol* (**4**). — To a stirred solution of **3** (3 g) in dry pyridine (30 mL) was added a solution of methanesulfonyl chloride (3.9 mL) in pyridine (15 mL) during 30 min at −10°. The mixture was stirred for 30 min at 0°, and then acetic anhydride (10 mL) was added. The mixture was kept for 1 h at room temperature, and after the usual processing, and evaporation of the chloroform solution, gave **4** as a colorless syrup (7.5 g, 96%), $[\alpha]_D^{20}$ −8.6° (chloroform); R_F 0.8 (*E*).

Anal. Calc. for $C_{12}H_{22}O_{10}S_2$: S, 16.43. Found: S, 16.50.

*1,2:5,6-Dianhydro-3,4-dideoxy-*D*-threo-hexitol* (**6**). — *Method a.* To a solution of the mesylate **4** (8 g) in chloroform (100 mL) and methanol (10 mL) was added 4M methanolic sodium methoxide (10 mL); the reaction was complete in 10 min. The solution was washed with water, dried, and evaporated, and the residue distilled, to give pure diepoxide **6** (1.9 g, 79%) which solidified below 5°, $b.p._{0.01}$ 50–55°, $[\alpha]_D^{20}$ −9° (chloroform); R_F 0.40 (*F*).

Method b. To a stirred solution of the tetraol **3** (3.45 g) in pyridine (70 mL) was added a solution of *p*-toluenesulfonyl chloride (9.6 g) in pyridine (25 mL) during 45 min at 0°. Stirring was continued at room temperature; after 1.5 h, t.l.c. (*D*) revealed, besides a main spot with R_F 0.5 (corresponding to compound **5**), two minor components with R_F 0.1 and 0.85. The mixture was then treated with acetic anhydride (10 mL), kept overnight at room temperature, processed in the usual way, and the chloroform solution concentrated to 150 mL. Methanol (20 mL) and 4.3M methanolic sodium methoxide (10 mL) were added to the solution, which was processed as described in Method *a*, to yield **6** (1.8 g, 68.5%), identical with that described in *a*.

Anal. Calc. for $C_6H_{10}O_2$: C, 63.13; H, 8.83. Found: C, 63.08; H, 9.02.

*3,4-Dideoxy-1,2:5,6-di-*O*-isopropylidene-*erythro*-hex-*E*-3-enitol* (**10**). — To a solution of the dimesylate[11] **8** (42 g) or ditosylate[11] **9** (57 g) in *N,N*-dimethylformamide (380 mL) were added sodium iodide (75 g) and zinc dust (26 g). The vigorously stirred mixture was boiled under reflux for 7 h, cooled, filtered, evaporated, and the residue partitioned between chloroform and water. The basic zinc salts precipitated were dissolved by addition of 20% sodium hydroxide solution, and the organic solution was washed with water until neutral, and dried, and evaporated. The residue was extracted with hot, light petroleum, leaving undissolved ~10–15% of unchanged starting-material. Evaporation of the extract, and recrystallization of the residue from methanol–water afforded pure **10** (8.2 g, 36%), m.p. 72–73°, $[\alpha]_D^{20}$ 0° (chloroform); R_F 0.75 (*F*).

Anal. Calc. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83. Found: C, 63.02; H, 8.75.

*3,4-Dideoxy-*erythro*-hex-*E*-3-enitol* (**11**). — *Method a.* A solution of the diacetal **10** (37.7 g) in acetic acid (150 mL) and water (38 mL) was kept for 24 h at room temperature. T.l.c. then revealed complete hydrolysis; R_F 0.95→0.15 (*C*). The solution was evaporated below 20°, and water was added to, and evaporated from,

TABLE I

I.R. DATA[a] FOR COMPOUNDS **2**, **6**, **10–13**, **15**, **17**, AND **20–23**

Compound	*C=O*	*C=O*	*C=CH*	*Other bands*
2	—	1405, 1065, 1020	970	~3340 (3600–3000)[b], νOH
			870	~600 (800–350)[b], γOH
6	—	840[c], 760[c]	—	3060, epoxide-CH
10	—	1250, 1055	860	—
11	—	1120, 1065, 1030	870	~3320 (3600–3000)[b], νOH
				~690 (800–550)[b], γOH
12	1745	1255, 1235	980	~3470 and ~3400
		1120, 1040	890	(3600–3100)[b], νOH
13	1750	1260, 1235, 1225	980	—
	1740	1040, 1030	950	—
15	1735	1255, 1240, 1220	—	—
		1060, 1050		
17	—	840[c], 740[c]	—	3060, epoxide-CH
20	—	855[c], 845[c], 770[c]	980	3020, epoxide-CH
			928	
21	1750	1230	980	1600, 1360, 1190, 1180,
			835	670, 580, 560, and 530, tosyl
22	1740	1250	875	1375, 1180, 920, 555,
			810	530, and 515, mesyl
23	—	835–825[c], 775[c]	970	—
			940	

[a]In cm^{-1}. [b]Diffuse maximum, the center; the interval is given in parentheses. [c]Epoxide group.

the residue, which then solidified. Filtration with the aid of acetone gave pure tetraol **11** (18.7 g, 76.5%), m.p. 114–115°; R_F 0.15 (*C*), 0.75 (*A*). By t.l.c. could be detected in the mother liquor several components having R_F values higher than that of **11**. These partially acetylated products became preponderant when the evaporation of the hydrolyzate was conducted above 20°. For their separation, see compound **12**.

Method b. To a solution of tetraacetate **13** (8.4 g) in chloroform (25 mL) and methanol (10 mL) was added M methanolic sodium methoxide (0.1 mL), and the mixture was boiled on a steam bath for 20 min. The slurry formed was evaporated, and the residue was recrystallized from ethanol, to yield **11** (3.65 g, 95.5%), identical with that described in *a*.

Anal. Calc. for $C_6H_{12}O_4$: C, 48.63; H, 8.16. Found: C, 48.84; H, 7.93.

*1,6-Di-*O*-acetyl-3,4-dideoxy*-erythro-*hex*-E-*3-enitol* (**12**). — The diacetal **10** (28 g) was hydrolyzed with aqueous acetic acid as described for compound **11**, but the solution was evaporated at 50°. The components of the semisolid residue obtained on evaporation were separated by column chromatography, using solvent *C* for elution. The following fractions were separated: *a*, R_F 0.85 (0.5 g); *b*, R_F 0.70 (8.9 g); *c*, R_F 0.40 (0.5 g); and *d*, R_F 0.15 (9.2 g), the last being identical with **11** (50.5%).

Fraction *b* solidified; it was filtered with the aid of ethyl acetate–ether, and then

TABLE II

^{1}H-N.M.R. DATA[a] FOR COMPOUNDS **2**, **6**, **10–13**, **15**, **17**, AND **20–22**

Compound	*H-1,6 (4 H)*	*H-2,5 m (2 H)*	*H-3,4 m*[b] *(2 H)*	*Other signals*
2[c]	3.30*m*	3.95	5.65 (15.5)	4.50*t* (6) and 4.65*d* (5), OH
6[d]	2.50*dd* 2.75*dd*	2.95	1.75 (4 H)	$J_{1',2} = J_{5,6'} = 2.5$; $J_{1,1'} = J_{6,6'} \approx J_{1,2} = J_{5,6} \approx 4.5$
10	3.55*t* 4.10*t*	4.50	5.80 (15.5)	1.35 and 1.40*s*, 2 CMe_2, $J_{1,1'} = J_{6,6'} \approx J_{1,2} = J_{5,6} \approx J_{1',2} = J_{5,6'} = 7.5$
11[c]	3.30*m*	4.00	5.70 (15.5)	4.55*t* (6) and 4.75*d* (5), OH
12	4.05*m*	4.35	5.85	2.10*s*, 2 acetyl-Me
13	4.20*m*	5.60	5.80	2.05 and 2.10*s*, 2 + 2 acetyl-Me
15[d]	4.05*dd* 4.25*dd*	5.05	1.65 (4 H)	$J_{1,1'} = J_{6,6'} = 12$; $J_{1,2} = J_{5,6}$ and $J_{1,2'} = J_{5,6'}$ (6 and 4)
17	2.45*dd* 2.75*t*	2.95	1.70 (4 H)	$J_{1,1'} = J_{6,6'} \approx J_{1,2} = J_{5,6} = 5$; $J_{1',2} = J_{5,6'} = 3$
20	2.65*dd* 2.95*t*	3.35	5.70 (16)	$J_{1,1'} = J_{6,6'} \approx J_{1,2} = J_{5,6} = 4.5$; $J_{1',2} = J_{5,6'} = 3$
21	4.05*m*	5.45	5.65	2.00*s*, 2 acetyl-Me; 2.45*s*, 2 tosyl-Me
22	4.25*m*	5.30	6.00 (15)	2.10*s*, 2 acetyl-Me; 3.05*s*, 2 mesyl-Me

[a]δ scale; chloroform-*d* solution; coupling constants are given in Hz. [b]*A*, part of an *AA'XX'* multiplet (*A* = H-3,4), $J_{3,4} = J_{AA'}$ in parentheses. [c]Solvent: Me_2SO-d_6. [d]Measuring frequency, 100 MHz.

recrystallized from acetone–light petroleum, to give diacetate **12** (2.3 g, 8.5%), m.p. 90–92°.

Anal. Calc. for $C_{10}H_{16}O_6$: C, 51.72; H, 6.94. Found: C, 51.70; H, 6.89.

1,2,5,6-Tetra-O-*acetyl-3,4-dideoxy*-erythro-*hex*-E-*3-enitol* (**13**). — The unsaturated tetraol **11** (1 g) was acetylated with acetic anhydride (3.5 mL) and pyridine (5 mL), to give, after the usual processing, crude **13** (1.60 g) which was recrystallized from methanol–water (1.52 g, 71.3%); m.p. 74–75°; R_F 0.80 (*E*).

Anal. Calc. for $C_{14}H_{20}O_8$: C, 53.16; H, 6.37. Found: C, 53.02; H, 6.45.

Compound **13** was obtained when any of the aforementioned fractions *a*, *b*, *c*, or *d* was used as the starting material.

3,4-Dideoxy-erythro-*hexitol* (**14**). — A solution of **11** (3.75 g) in methanol (40 mL) was hydrogenated as described for **3**, to give, after evaporation, and recrystallization from ethanol–ethyl acetate, tetraol **14** (1.7 g, 45%), m.p. 98–100°; R_F 0.70 (*A*).

Anal. Calc. for $C_6H_{14}O_4$: C, 47.98; H, 9.39. Found: C, 47.97; H, 9.14.

1,2,5,6-Tetra-O-*acetyl-3,4-dideoxy*-erythro-*hexitol* (**15**). — The tetraol **14** (1.5 g) was acetylated with acetic anhydride (6 mL) and pyridine (10 mL), to give, after the usual processing, and recrystallization from methanol, pure **15** (2.6 g, 81.7%), m.p. 79–80°; R_F 0.75 (*E*).

Anal. Calc. for $C_{14}H_{22}O_8$: C, 52.82; H, 6.96. Found: C, 52.68; H, 6.80.

1,2:5,6-Dianhydro-3,4-dideoxy-erythro-*hexitol* (**17**). — The tetraol **14** (3 g) was *p*-toluenesulfonylated, and the chloroform solution of the crude 1,6-ditosylate **16** was treated with methanolic sodium methoxide as described for compound **6**, Method *b*. The crude diepoxide **17** was purified by distillation (1.2 g, 52.5%); $b.p._{0.01}$ 55–60°; R_F 0.50 (*G*).

Anal. Calc. for $C_6H_{10}O_2$: C, 63.13; H, 8.83. Found: C, 62.88; H, 8.56.

1,2:5,6-Dianhydro-3,4-dideoxy-D-threo-*hex*-E-*3-enitol* (**20**). — *Method a.* To a stirred solution of the unsaturated *threo*-tetraol **2** (15 g) in pyridine (100 mL) was added a solution of *p*-toluenesulfonyl chloride (41.5 g) in pyridine (100 mL) during 2 h at 0°. The mixture was stirred for 2 h at room temperature, and then processed in the usual way. The chloroform solution, containing 1,6-ditosylate **18** as the main component, R_F 0.50 (*D*), was concentrated to 500 mL. Then methanol (50 mL) and 4.3M methanolic sodium methoxide (50 mL) were added at room temperature. After 15 min, the mixture was washed with water, dried, and evaporated, and the residue chromatographed through a short column, using solvent *F* for elution. The fraction having R_F 0.75 was evaporated, and the solid residue was filtered off with the aid of ether, to give pure **20** (3.2 g, 28.6%), m.p. 76–77°, $[\alpha]_D^{20}$ +28.8° (chloroform). The compound cannot be purified by distillation as, on heating, violent decomposition occurs.

Method b. A solution of compound **2** (3 g) in pyridine (30 mL) was treated with methanesulfonyl chloride (3.4 mL) at −10°, kept for 2 h at room temperature, and treated with acetic anhydride (10 mL). After the usual processing, the chloroform solution containing the crude dimesylate **19** was treated with methanolic sodium

methoxide as described in Method *a*, to give diepoxide **20** (0.4 g, 18%), identical with that described in *a*.

Anal. Calc. for $C_6H_8O_2$: C, 64.26; H, 7.19. Found: C, 64.08; H, 6.82.

2,5-Di-O-acetyl-3,4-dideoxy-1,6-di-O-p-tolylsulfonyl-erythro-*hex*-E-*3-enitol* (**21**). — A stirred slurry of the unsaturated tetraol **11** (1.5 g) in pyridine (20 mL) was boiled for 5 min and then quickly cooled to 0°. A solution of *p*-toluenesulfonyl chloride (4.1 g) in pyridine (10 mL) was added during 30 min, and stirring was continued for 2 h at room temperature. Thereafter, acetic anhydride (4 mL) was added, the mixture was kept overnight at room temperature, and poured into water. The precipitate was filtered off, to give chromatographically pure **21** (3.7 g, 86.5%), m.p. 145–148°; R_F 0.45 (*F*). On recrystallization from acetone–ether, the m.p. decreased to 140–144°.

Anal. Calc. for $C_{24}H_{28}O_{10}S_2$: C, 53.31; H, 5.22; S, 11.86. Found: C, 53.05; H, 5.11; S, 11.92.

1,2-Di-O-acetyl-3,4-dideoxy-1,6-di-O-(methylsulfonyl)-erythro-*hex*-E-*3-enitol* (**22**). — A solution of diacetate **12** (1.15 g) in pyridine (10 mL) was treated with methanesulfonyl chloride (1.2 mL), and, after 3 h at room temperature, the mixture was poured into water. The precipitate was filtered off, washed with water, dried, and recrystallized from acetone–light petroleum, to give **22** (1.55 g, 80%), m.p. 98–100°; R_F 0.40 (*E*).

Anal. Calc. for $C_{12}H_{20}O_{10}S_2$: C, 37.10; H, 5.19; S, 16.51. Found: C, 37.22; H, 4.95; S, 16.43.

1,2:5,6-Dianhydro-3,4-dideoxy-erythro-*hex*-E-*3-enitol* (**23**). — A solution of ditosylate **21** (5.4 g) or dimesylate **22** (3.9 g) in chloroform (50 mL) and methanol (10 mL) was treated with 4.3M methanolic sodium methoxide (5 mL). After 15 min, the mixture was washed with water, dried, and evaporated. The residue was triturated with ether (15 mL), the insoluble, polymeric material was filtered off, the filtrate was concentrated to 5 mL, and light petroleum (5 mL) was added. After cooling to −5°, the crystalline diepoxide **23** was filtered off, and washed with light petroleum (0.3 g, 26.8%); m.p. 53–55°; R_F 0.70 (*F*). The compound must be stored at −5° in order to avoid decomposition.

Anal. Calc. for $C_6H_8O_2$: C, 64.26; H, 7.19. Found: C, 64.35; H, 7.02.

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REFERENCES

1 J. KUSZMANN, *Carbohydr. Res.*, 73 (1979) 93–101.
2 W. C. J. ROSS, *J. Chem. Soc.*, (1950) 2257–2272.
3 J. L. EVERETT AND G. A. R. KON, *J. Chem. Soc.*, (1950) 3131–3135.
4 J. A. HENDY, R. F. HOMER, F. L. ROSE, AND A. L. WALPOTE, *Br. J. Pharmacol.*, 6 (1951) 235–255.

5 L. A. ELSON, M. JARMAN, AND W. C. J. ROSS, *Eur. J. Cancer*, 4 (1968) 617–625.
6 J. KUSZMANN, *Carbohydr. Res.*, 71 (1979) 123–134.
7 B. L. VAN DUUREN, L. ORRIS, AND N. NELSON, *J. Natl. Cancer Inst.*, 35 (1965) 707–717.
8 R. S. TIPSON AND A. COHEN, *Carbohydr. Res.*, 1 (1965) 338–340.
9 C. C. DEANE AND T. D. INCH, *Chem. Commun.*, (1949) 813.
10 P. SOHÁR AND J. KUSZMANN, *Org. Magn. Reson.*, 3 (1971) 647–654.
11 J. KUSZMANN AND P. SOHÁR, *Carbohydr. Res.*, 74 (1979) 187–197.
12 M. J. TISDALE, L. A. ELSON, AND W. C. J. ROSS, *Eur. J. Cancer*, 9 (1973) 89–97.