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Note

Cyclitol epoxides. Synthesis of methylsulfonyl derivatives of inositol oxiranes

RAÚL A. CADENAS, GUILLERMO J. AGUILAR, AND MARÍA E. GELPI

Departamento de Química, Facultad de Agronomía, Universidad de Buenos Aires, 1417 Av. San Martín 4453, Buenos Aires (Argentina)

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The epoxy- and diepoxy-cyclitols are valuable intermediates in synthesis, and appear to have interesting potentialities as bio-active substances, as is shown by the many oxirane compounds involved in the chemistry of natural products[1] and of synthetic carbohydrates, including cyclitols[2]. In both aspects, the mesyl derivatives of carbohydrates also evidence similar importance[3]. The literature reports a few mesyl epoxy-inositols[4–6], which were employed in the synthesis of deoxy[5,6] and nitrogenated[7] derivatives. We describe here the synthesis of some mesylated inositol oxiranes, with the intention of testing their biological actions. Their use as reactive species in coupling reactions with nitrogenated heterocycles had been briefly exemplified[8], and is here extensively investigated.

Previously reported[9] was the synthesis of 1,4,5,6-tetra-*O*-(methylsulfonyl)-*myo*-inositol (**1**) which we now employ as the starting compound. The reaction of the tetrasulfonate **1** (see Scheme 1) with sodium methoxide in methanol afforded 2,3-anhydro-1,5,6-tri-*O*-(methylsulfonyl)-*epi*-inositol (**2**). The use of this compound in further epoxidation reactions would imply the previous formation of a *trans*-vicinal mesyloxy–hydroxyl grouping, which would be achieved by favored hydrolysis of **2** to give a *myo*-inositol derivative. However, hydrolysis of **2** gave, stereoselectively, the *muco* derivative, which exclusively presents a *cis*-vicinal relationship of those groups. On the other hand, attempts at epoxidation of two *trans*-vicinal mesyloxy groups required drastic conditions, and did not give a simple pattern of reaction.

On the assumption that esterification of the free hydroxyl group could change the stereochemistry of hydrolytic opening, compound **2** was benzoylated, taking into account the usual resistance of the benzoyl group to moderate hydrolysis by acid*. Benzoic anhydride gave the corresponding benzoylated epoxide (**4**) in 71%

*Small-scale hydrolysis experiments with acetate **3** in 80% acetic acid did not give satisfactory results.

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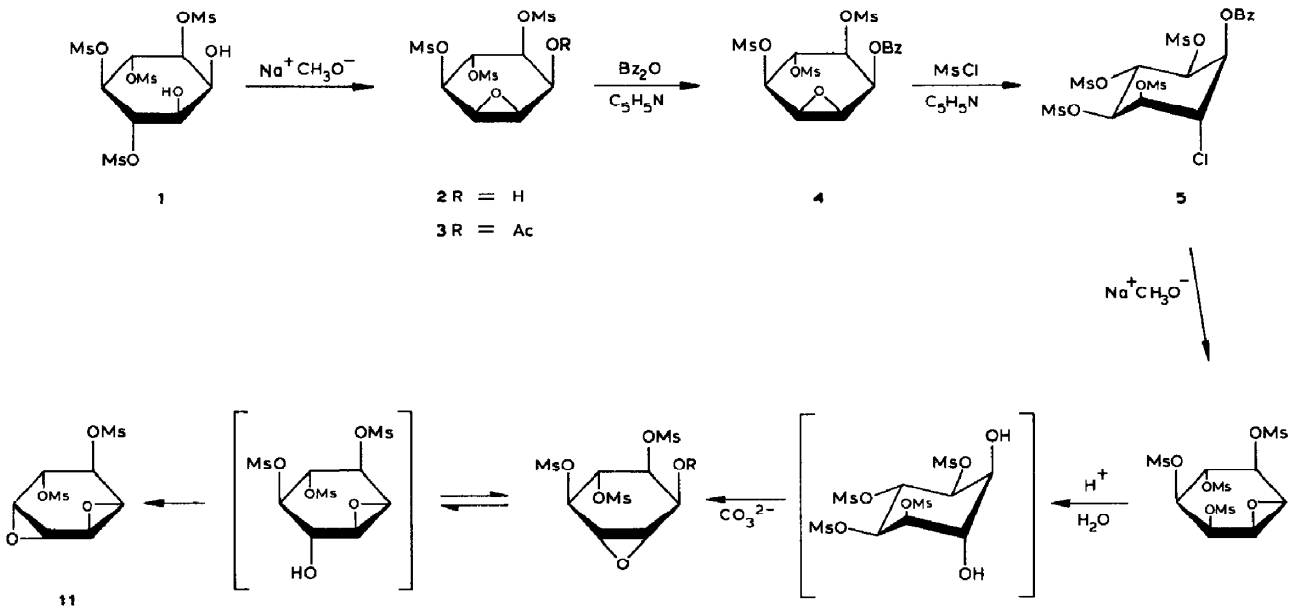


Scheme 1

All of the compounds shown here are racemic, and the formulas depict one enantiomer of the corresponding racemate.

yield, but the oxirane ring was extremely resistant to hydrolysis, which was only achieved after the benzoyl group had been split off, to give again the *muco*-inositol derivative.

The reaction of benzoate **4** with mesyl chloride gave, through a chloromesylation reaction, 1-*O*-benzoyl-6-chloro-6-deoxy-2,3,4,5-tetra-*O*-(methylsulfonyl)-*muco*-inositol (**5**) in 95% yield. The stereochemistry of opening of the oxirane ring was obvious from the subsequent formation of 2,3-anhydro-1,4,5,6-tetra-*O*-(methylsulfonyl)-*epi*-inositol (**6**) by refluxing **5** with sodium methoxide in methanol.

The conformation depicted for compound **5**, with three mesyloxy groups in equatorial orientation, is proposed on the assumption of its being the more stable one, and, although the ^{1}H-n.m.r. spectrum could not be fully interpreted, some of its features support that view. Only two protons are amenable to first-order analysis; one of them, at the lowest field (δ 5.71) can be ascribed to H-6 The coupling constants ($J_{1,6} = J_{5,6} = 4$ Hz) are consistent with its symmetrical relationship to the two vicinal, *gauche* protons; the other proton, attributable to H-1 (or H-5), appeared as a quartet at δ 4.93 ($J_{1,2}$ 2, $J_{1,6}$ 4 Hz). The easy epoxidation of C-1–C-6 in **5** supports the *trans*-diaxial arrangement of their substituents.

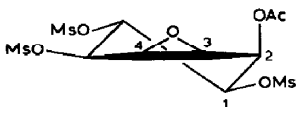
Epoxide **6** was very resistant to acid hydrolysis and gave, as the final product, a new epoxide, namely, 1,2-anhydro-3,4,5-tri-*O*-(methylsulfonyl)-*chiro*-inositol (**8**). This finding can be rationalized through the intermediacy of 1,2,3,4-tetra-*O*-(methylsulfonyl)-*muco*-inositol (**7**), which in the presence of dissolved traces of the barium carbonate employed to neutralize the sulfuric acid solution gave, on evaporation to dryness, the epoxide **8**. The relatively mild, alkaline conditions would not suffice to provoke an isomerization to **10**; compound **8** was thus obtained pure by crystallization and, in turn, its acetate (**9**) was prepared.

Finally, by refluxing this epoxide for 14 h with sodium methoxide in methanol, 1,2:5,6-dianhydro-3,4-di-*O*-(methylsulfonyl)-*neo*-inositol (**11**) was obtained, whose structure is postulated on the basis of a rational mechanism through the intermediate **10**, and the symmetrical pattern of its ^{1}H-n.m.r. spectrum. Its parent compound, *i.e.*, 1,2:5,6-dianhydro-*neo*-inositol had previously been obtained, in low yield, from *chiro*-inositol[10].

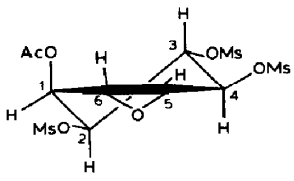
The ^{1}H-n.m.r. spectra of the oxiranes **3** *and* **9**. — Only the spectra of the epoxide acetates **3** and **9** showed a clear pattern of signals, which supported the structures proposed for the parent compounds **2** and **8**, respectively.

The assignment of the ring-proton signals of **3** was made by first-order analysis and double-resonance techniques. The oxirane protons resonated at δ 3.86 (H-3) and 4.14 (H-4), each as a pair of doublets, with $J_{3,4}$ 4 Hz and, respectively, $J_{2,3}$ 4.5 and $J_{4,5}$ 2 Hz. The definite coupling with the vicinal protons indicated their *cis*-relationship with them, as otherwise, an almost zero value for the coupling constants would be expected[11]. Irradiation of H-3 changed a downfield, H-2 triplet (δ 6.07, $J_{2,3}$ 4.5, $J_{1,2}$ 4.5) to a doublet. On the other hand, by irradiation of H-4, the H-5 pair of doublets (δ 5.84, $J_{5,6}$ 8, $J_{4,5}$ 2 Hz) collapsed to a doublet, $J_{5,6}$ 8 Hz. Finally, the H-1 and H-6 signals appeared superimposed as a multiplet, at δ 5.50.

According to these data, and on the basis of steric considerations, the favored conformation for compound **3** would be that depicted in **3a**. This formula shows the equatorial (or *quasi*-equatorial) orientation of the mesyl groups, and is also consistent with the observed coupling constants; in particular, the value of 8 Hz for $J_{5,6}$ suggests a significant contribution of this conformation to the equilibrium. The spectrum of the benzoate **4** was very similar to that of **3**, but the oxirane protons appeared superimposed, as a multiplet at δ 3.92.



3a



9a

In the ^{1}H-n.m.r. spectrum of 1-*O*-acetyl-5,6-anhydro-2,3,4-tri-*O*-(methylsulfonyl)-*chiro*-inositol (**9**), the oxirane-ring protons appeared as doublets at δ 3.63 and 3.86, both with $J_{5,6}$ 3.8 Hz. The former, in the spectrum of a solution in pyridine-d_5, appeared partially superimposed on one mesyl group, but, in solution in acetone-d_6, both protons appeared superimposed as a doublet. This lack of detectable coupling with the vicinal protons indicated the *trans* arrangement[11] of the oxirane ring with the vicinal substituents. However, by irradiation of the doublet at δ 3.63, a sharpening of the signal at the lowest field (δ 6.40) could be observed, which, on this basis, would be assignable to H-1 ($J_{1,2}$ 3 Hz). When this proton, in turn, was irradiated, a pair of doublets (δ 5.30), attributable to H-2, collapsed to a doublet ($J_{2,3}$ 10 Hz).

The irradiation of the other oxirane proton, at δ 3.86, provoked a sharpening in a peak at δ 5.48, which was assigned to H-4 ($J_{3,4}$ 8 Hz). Finally, H-3 would correspond to a distorted triplet at δ 5.68. The values of the observed coupling-constants, and conformational considerations, supported the conformation depicted in **9a**. The spectrum of **9** did not indicate a mixture with the acetate of the *myo*-inositol isomer **10**, whose pattern of coupling constants should have been different.

Comparing the chemical shifts of the oxirane protons in the *epi*-inositol epoxide **3** (δ 3.92 and 4.15) with that of the *chiro* isomer (δ 3.86 and 3.60), a deshielding effect is apparent in the former. This effect has been previously observed in such spectra of carbohydrate epoxides[12], and was attributed to *trans*-vicinal oxygen atoms.

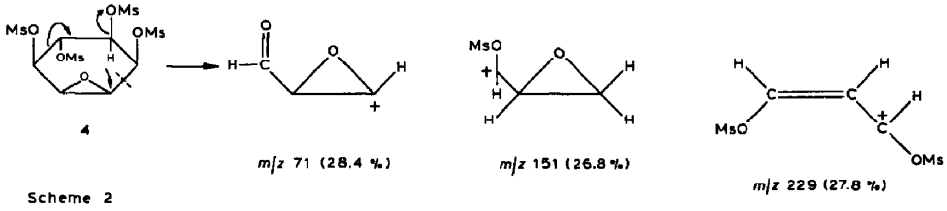
The spectrum of the diepoxide **11** reflects its symmetrical structure, as the four oxirane-protons appear as a slightly distorted quartet (δ 3.82), the two mesyl groups as a singlet (δ 3.50), and the two remaining ring protons, also as a singlet (δ 5.57).

On the reasonable assumption that the benzoic (**4**) and methanesulfonic (**6**)

esters of epoxide **2** would have the same favored conformation as that depicted in **3a** for the acetate, the regioselective opening of these esters by chloromesylation and hydrolysis, respectively, could be rationalized on the basis of a favored, diaxial opening by attack of the nucleophile at C-3, rather than at C-4. This would imply a transition state resembling the more-stable conformation for the product.

Mass spectra of compounds **4** *and* **6**. — The mass spectra of the 4-*O*-mesyl- (**4**) and 4-*O*-benzoyl (**6**) derivatives of 2,3-anhydro-1,5,6-tri-*O*-(methylsulfonyl)-*epi*-inositol were recorded comparatively, in order to ascertain the mode of epoxide fragmentation. For both compounds, an identical, simple scheme was observed that was characterized by (*a*) relatively high-intensity peaks originating in the favored rupture of the ring into three-carbon fragments, and (*b*) the stability of the oxirane ring.

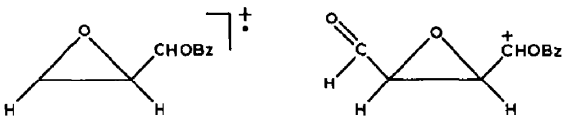
Compound **6** did not show the molecular ion (*m/z* 474), and gave a series of peaks expected from elimination of methanesulfonic acid, and ruptures of mesyl substituents ($CH_3SO_2^+$ as the base peak). The fragmentation of the inositol ring gave high-intensity peaks at *m/z* 151, 229, and 71, which, among other isomeric possibilities, can be represented as shown in Scheme 2.



Scheme 2

A hypothesis for the formation of peaks *m/z* 151 and 229 would imply, respectively, the transfer[13] of a proton to a three-carbon portion containing the oxirane ring, or double-bond formation with rupture (or transference) of a mesyloxy group, as depicted in Scheme 2. These two peaks would be the mesylated alternatives for the very important peak at *m/z* 73, found in the mass spectra of several inositols[14].

On the other hand, compound **4** (M^+ 500, 2.2%) showed the same peaks as **6**, but in much lower intensity, which was a general feature of the spectrum. Thus, peaks at *m/z* 71, 151, and 229 appeared as 3.3, 1.6, and 1.3% of the base peak ($C_6H_5CO^+$). The benzoyl peak would appear involved in peaks at *m/z* 176 and 205.



m/z 176 (0.72 %) *m/z* 205 (1.7 %)

EXPERIMENTAL

General procedures. — Melting points (Kofler hot-stage) are uncorrected. T.l.c. was conducted on Silica Gel G (Merck) plates (0.25-mm layer-thickness) with solvent (*A*), 9:1 (v/v) benzene–abs. ethanol. The spots were detected with (*1*) iodine vapor and (*2*) sodium iodide–1-butanol for epoxides[15]. ^{1}H-N.m.r. spectra were recorded at 20–25°, at 100 MHz, with a Varian XL-100 spectrometer, with tetramethylsilane as the internal reference standard. Mass spectra were recorded with a Varian-Math 7 spectrometer commanded by a Varian Math data-system 166 computer at an ionizing potential of 70 eV; the temperature of the direct-insertion probe was 240°.

*2,3-Anhydro-1,5,6-tri-*O*-(methylsulfonyl)-*epi*-inositol* (**2**). — 1,4,5,6-Tetra-*O*-(methylsulfonyl)-*myo*-inositol[9] (**1**; 4.4 g, 11.1 mmol) was dissolved in boiling methanol (600 mL) and a 3.5% solution of sodium methoxide in methanol was added in three portions (3 × 5 mL) at 10-min intervals. The solution was refluxed for 15 min after the last addition, cooled, and kept overnight in a refrigerator. A first crop (2.72 g) of **2** was filtered off, and, by concentration of the filtrate to a small volume, and cooling, a second crop (250 mg) was obtained (total yield 2.97 g; 90.7%). Recrystallized from water, it had m.p. 207–208°; t.l.c. R_F 0.22 (solvent *A*, reagents *1* and *2*); ν_{max}^{Nujol} 3530 (HO), 1195 (C–S), 1270, 900, and 840 cm^{-1} (oxirane ring).

Anal. Calc. for $C_9H_{16}O_{11}S_3$: C, 27.27; H, 4.04; S, 24.24. Found: C, 27.46; H, 4.21; S, 24.65.

*2-*O*-Acetyl-3,4-anhydro-1,5,6-tri-*O*-(methylsulfonyl)-*epi*-inositol* (**3**). — A solution of compound **2** (200 mg) in 1:1 pyridine–acetic anhydride (3 mL) was kept for 24 h at room temperature. Evaporation, and drying in a vacuum desiccator afforded **3** (180 mg), which, recrystallized from chloroform, had m.p. 168–169°; t.l.c. R_F 0.42 (solvent *A*, reagents *1* and *2*); ν_{max}^{Nujol} 1775 (CO), 1200 (C–S), 1260, 930, and 850 cm^{-1} (oxirane ring); n.m.r. data (C_5D_5N): δ 2.01 (s, 3 H, acetyl group), 3.46 (s, 3 H, CH_3SO_2), 3.50 (s, 3 H, CH_3SO_2), 3.54 (s, 3 H, CH_3SO_2), 3.86 (dd, H-3, $J_{3,4}$ 4, $J_{2,3}$ 4.5 Hz), 4.14 (dd, H-4, $J_{4,5}$ 2 Hz), 5.50 (m, H-1,6), 5.84 (dd, H-5, $J_{5,6}$ 8 Hz), and 6.07 (t, H-2, $J_{1,2}$ 4.5 Hz).

Anal. Calc. for $C_{11}H_{18}O_{12}S_3$: C, 30.14; H, 4.11; S, 21.91. Found: C, 30.48; H, 4.31; S, 21.73.

*2,3-Anhydro-4-*O*-benzoyl-1,5,6-tri-*O*-(methylsulfonyl)-*epi*-inositol* (**4**). — Compound **2** (3.0 g, 7.5 mmol) was suspended in pyridine (24 mL) and to the hot suspension was added benzoic anhydride (6 g); heating was continued until complete dissolution of the solid occurred, and the solution was cooled, and kept for 4 days at room temperature. Then, it was poured into ice–water and the white precipitate obtained was repeatedly washed with water by decantation, filtered, and dried (2.7 g, 71.2% yield). Recrystallization from chloroform (125 mL) gave **4**, m.p. 185–186°; t.l.c. R_F 0.50 (solvent *A*, reagents *1* and *2*); ν_{max}^{Nujol} 1740 (CO), 1190 (C–S), 1290, 917, and 830 cm^{-1} (oxirane ring); n.m.r. data (acetone-d_6): δ 3.27,

3.30, 3.37 (9 H, 3 CH_3SO_2), 3.92 (m, H-2,3), 5.14 (m, H-6,1), 5.48 (dd, H-5, $J_{4,5}$ 2, $J_{5,6}$ 8 Hz), 5.88 (t, H-4, $J_{3,4} = J_{4,5} = 4$ Hz), and 7.50–8.20 (m, 5 H, benzoyl group); *m/z* (intensity, as % of base peak, and then assignments): 500 (2.2, M^+), 405 (6.0, $M^+ - CH_3SO_3$), 325 [6.2, $(SO_3CH_3)_3C_3H_3 + H^+$], 229 (1.3, see text), 205 (1.7, see text), 175 [6.6, $(CH_3SO_2)_2OH$], 151 (1.6, see text), 105 (100, C_6H_5CO), 97 (6.3, $CH_3SO_3H_2$), 79 (12.2, CH_3SO_2), 77 (26.8, C_6H_5), and 71 (3.3, see text).

Anal. Calc. for $C_{16}H_{20}O_{12}S_3$: C, 38.40; H, 4.00; S, 19.20. Found: C, 38.32; H, 4.22; S, 19.10.

The starting epoxide can be quantitatively reobtained from this benzoate by reaction with sodium methoxide in methanol for a few hours at room temperature.

*1-O-Benzoyl-6-chloro-6-deoxy-2,3,4,5-tetra-*O*-(methylsulfonyl)-*muco*-inositol* (**5**). — To a solution of compound **4** (250 mg, 0.5 mmol) in pyridine (1 mL) was added methanesulfonyl chloride (0.3 mL, 3.9 mmol). The solution was kept for 6 days at room temperature, and was then poured into ice–water; the syrup obtained was macerated with water until there was formed a white precipitate of **5**, which was filtered off, and dried (292 mg, 95.2% yield). Recrystallized from ethanol, it had m.p. 223–224°; t.l.c., R_F 0.64 (solvent *A*, reagent *1*); n.m.r. data (Me_2SO-d_6): δ 3.30 (s, 9 H, CH_3SO_2), 3.45 (s, 3 H, CH_3SO_2), 4.93 (dd, H-1, $J_{1,6}$ 4, $J_{1,2}$ 2 Hz), 5.10–5.60 (m, 4 H, H-2–5), 5.71 (t, H-6, $J_{5,6}$ 4 Hz), and 7.46–8.14 (m, C_6H_5CO).

Anal. Calc. for $C_{17}H_{23}ClO_{14}S_4$: C, 33.20; H, 3.74; S, 20.83; Cl, 5.78. Found: C, 32.92; H, 3.78; S, 20.91; Cl, 6.10.

*2,3-Anhydro-1,4,5,6-tetra-*O*-(methylsulfonyl)-*epi*-inositol* (**6**). — To a solution of compound **5** (5 g) in methanol (1.2 L) was added a 3.5% solution of sodium methoxide in methanol to pH ~8. The solution was kept for 24 h at room temperature and then for 1 h in a refrigerator. A first crop of **6** (2.30 g) was filtered off, and, by evaporation of the filtrate to a small volume, a second crop was obtained (0.49; total yield of **6**, 72%); recrystallization from methanol gave **6**, m.p. 193–194°; t.l.c., R_F 0.30 (solvent *A*, reagent *2*); *m/z* (intensity, as % of base peak, and then assignment): 378 (1.1, $M^+ - CH_3SO_3H$), 282 (3.5, $M^+ - 2\ CH_3SO_3H$), 229 (27.8, see text); 203 (30.2, $M^+ - 2\ CH_3SO_3H - CH_3SO_2$), 175 [40.9, $(CH_3SO)_2OH$], 151 (26.8, see text), 97 (41.5, $CH_3SO_3H_2$), 79 (100, CH_3SO_2), and 71 (28.4, see text).

Anal. Calc. for $C_{10}H_{18}O_{13}S_4$: C, 25.32; H, 3.80; S, 27.00. Found: C, 25.37; H, 3.89; S, 26.78.

*1,2-Anhydro-3,4,5-tri-*O*-(methylsulfonyl)-*chiro*-inositol* (**8**). — Compound **6** (2 g) was refluxed with 2M sulfuric acid (350 mL) during 6 h. The unreacted material (280 mg) was filtered off, and, on standing, a second crop (754 mg) of starting material was deposited and filtered off. The acid filtrate was made neutral ($BaCO_3$), the suspension filtered, and the filtrate evaporated to dryness. The dried residue was repeatedly extracted with boiling acetone, and the extracts were combined, and evaporated to dryness, to give a syrup that, on maceration with ethanol, afforded crystals (405 mg, 50.2% yield) of **8**, m.p. 165–167°; t.l.c., R_F 0.26 (solvent *A*, reagent *2*). This compound is revealed with reagent *2* more slowly than compound **6**; ν_{max}^{Nujol} 3525 (HO), 1193 (C–S), 1260, 917, and 837 cm^{-1} (oxirane ring).

Anal. Calc. for $C_9H_{16}O_{11}S_3$: C, 27.27; H, 4.04; S, 24.24. Found: C, 27.30; H, 4.04; S, 24.00.

1-O-Acetyl-5,6-anhydro-2,3,4-tri-O-(methylsulfonyl)-chiro-*inositol* (**9**). — Compound **8** (40 mg) was dissolved in 1:1 acetic anhydride–pyridine, the solution kept for 24 h at room temperature, and then evaporated. The crystals obtained, recrystallized from ethanol, gave **9**, m.p. 141–143°; t.l.c., R_F 0.51 (solvent *A*, reagent *2*); ν_{max}^{Nujol} 1760 (CO), 1192 (C–S), 1260, 917, and 836 cm^{-1} (oxirane ring); n.m.r. data (C_5H_5N-d_5): δ 2.01 (s, 3 H, CH_3CO), 3.52 (s, 3 H, CH_3SO_2), 3.55 (s, 3 H, CH_3SO_2), 3.58 (s, 3 H, CH_3SO_2), 3.63 (d, H-6), 3.86 (d, H-5, $J_{5,6}$ 3.8 Hz), 5.30 (dd, H-2, $J_{1,2}$ 3, $J_{2,3}$ 10 Hz), 5.48 (d, H-4, $J_{3,4}$ 8, $J_{4,5}$ 0 Hz), 5.68 (t, H-3), and 6.40 (H-1, $J_{1,2}$ 3 Hz).

Anal. Calc. for $C_{11}H_{18}O_{12}S_3$: C, 30.14; H, 4.11; S, 21.91. Found: C, 30.44; H, 4.35; S, 22.03.

1,2:5,6-Dianhydro-3,4-di-O-(methylsulfonyl)-neo-*inositol* (**11**). — To a solution of compound **8** (150 mg, 0.38 mmol) in boiling methanol (15 mL) was added methanolic sodium methoxide, to pH ~8, and the solution was refluxed for 14 h. The epoxidation was monitored by t.l.c. (solvent *A*, reagents *1* and *2*). The solution was cooled, made neutral with Dowex 50 (H^+) resin, the suspension filtered, and the filtrate decolorized, and kept in a refrigerator for 24 h. A first crop (41 mg of **11**) was filtered off, and, by concentration of the methanol solution, a second crop (22 mg) was obtained. The mother liquors showed, in t.l.c., three spots, corresponding to the diepoxide (**11**), the starting material (**8**), and a slow-moving compound (R_F 0.15, solvent *A*), which were not further separated. The total yield of **11** was 55.5%, m.p. 164°; t.l.c., R_F 0.43 (solvent *A*, reagents *1* and *2*); n.m.r. data (C_5D_5N): δ 3.50 (s, 6 H, CH_3SO_2), 3.82 (4 H, oxirane-ring protons), and 5.57 (s, 2 H, H-3,4).

Anal. Calc. for $C_8H_{12}S_2O_8$: C, 32.00; H, 4.00; S, 21.33. Found: C, 31.84; H, 4.32; S, 21.19.

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REFERENCES

1 S. M. KUPCHAN, R. J. HEMINGWAY, P. COGGON, A. T. MCPHAIL, AND G. A. SIM, *J. Am. Chem. Soc.*, 90 (1968) 2982–2983; S. M. KUPCHAN, R. J. HEMINGWAY, AND R. M. SMITH, *J. Org. Chem.*, 34 (1969) 3898–3902; S. TAKAHASHI, *Phytochemistry*, 8 (1969) 321–322; *Chem. Pharm. Bull.*, 18 (1970) 199–202; D. B. BORDERS, P. SHU, AND J. E. LANCASTER, *J. Am. Chem. Soc.*, 94 (1972) 2540–2541.

2 M. JARMAN AND W. C. ROSS, *Chem. Ind. (London)*, (1967) 1789; J. KUSZMANN AND L. VARGHA, *Carbohydr. Res.*, 16 (1971) 261–271; L. VARGHA AND J. KUSZMANN, *ibid.*, 8 (1968) 157–163; S.

OGAWA AND T. SUAMI, Jpn. Kokai 75 36,442 (1975); *Chem. Abstr.*, 83 (1975) 97,851c; S. OGAWA AND T. SUAMI, Jpn. Kokai 74 92,042 (1974); *Chem. Abstr.*, 82 (1974) 98,341c; R. JUNG, D. BEERMAN, H. P. GLATT, AND F. OESCH, *Mutat. Res.*, 81 (1981) 11–19.

3 R. S. TIPSON, *Adv. Carbohydr. Chem.*, 8 (1953) 107–215; A. HADDOW, G. M. TIMMIS, AND S. S. BROWN, *Nature*, 182 (1958) 1164–1165; L. VARGHA AND J. KUSZMANN, *Naturwissenschaften*, 46 (1959) 84; J. KUSZMANN, *Carbohydr. Res.*, 71 (1979) 123–124.

4 T. SUAMI, S. OGAWA, K. OHASHI, AND S. OKI, *Bull. Chem. Soc. Jpn.*, 45 (1972) 3660–3667.

5 T. SUAMI, S. OGAWA, AND Y. FUNAKI, *Bull. Chem. Soc. Jpn.*, 48 (1975) 1545–1548.

6 H. PRINZBACH AND H. W. SCHNEIDER, *Tetrahedron Lett.*, (1975) 3073–3076.

7 T. SUAMI, S. OGAWA, S. OKI, AND H. KUNITOMO, *Bull. Chem. Soc. Jpn.*, 47 (1974) 1737–1743.

8 R. A. CADENAS, J. MOSETTIG, AND M. E. GELPI, *Abstr. Int. Carbohydr. Symp., 12th, Utrecht, The Netherlands*, (1984) 33.

9 M. C. P. DE FREIRE AND R. A. CADENAS, *Carbohydr. Res.*, 63 (1978) 157–164.

10 S. OGAWA, S. OKI, AND T. SUAMI, *Bull. Chem. Soc. Jpn.*, 52 (1979) 1095–1101.

11 D. H. BUSS, L. HOUGH, L. D. HALL, AND J. F. MANVILLE, *Tetrahedron*, 21 (1965) 69–74.

12 R. J. FERRIER AND N. PRASAD, *J. Chem. Soc.*, (1969) 575–580.

13 A. BUCHS AND E. CHAROLLAIS, *Helv. Chim. Acta*, 56 (1973) 207–215.

14 A. BUCHS, E. CHAROLLAIS, AND T. POSTERNAK, *Helv. Chim. Acta*, 51 (1968) 695–707.

15 J. G. BUCHANAN AND J. C. P. SCHWARTZ, *J. Chem. Soc.*, (1962) 4770–4777.