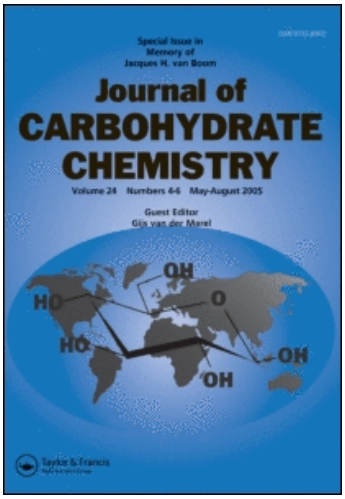


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# A Convenient Route to Functionalized Branched-Chain Sugars Via a Tosyl-Epoxide Derivative

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# A CONVENIENT ROUTE TO FUNCTIONALIZED BRANCHED-CHAIN SUGARS VIA A TOSYL-EPOXIDE DERIVATIVE

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## ABSTRACT

Starting from methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside-3-ulose **1** and proceeding through its corresponding tosyl-epoxide derivative **2**, various branched-chain sugars (**3-8**) were prepared by nucleophilic and reductive ring openings. The presence of the sulfonylated oxirane group was found to be compatible with chemical transformations of the benzylidene acetal group (**9-11**), allowing facile access to the 6-deoxyhexoses (**12-13**).

## INTRODUCTION

The natural occurence of branched-chain amino-sugars in various antibiotics has stimulated extensive research for their synthesis.[1] In connection with our interest in this area,[2] we reported some years ago the synthesis of branched-chain α-azido-*C*-formyl sugars based on regiospecific ring-opening of α,β-epoxy-sulfone precursors.[3] Recent reports from Sato et al.[4,5] described a similar reaction with a useful spiro-chloroepoxy derivative and its application in the total synthesis of an optically active tetrodotoxin key

intermediate. In consideration of the potential utility of this approach in the creation of a quaternary centre, extension of this methodology to some representative nucleophiles was undertaken; the chemical reactivity of the sulfonylated epoxy group was also examined through the classical deprotecting reactions of the 4,6-*O*-benzylidene system.

The α,β-epoxy-sulfones have been prepared by two principal routes, namely by nucleophilic epoxidation of α,β-unsaturated sulfones[6,7] and by a Darzens type condensation of carbonyl compounds with α-halosulfones.[8-11] Their chemistry was investigated through thermal and acidic rearrangement studies[11,13] and some nucleophilic ring-opening reactions leading to α-substituted ketones and aldehydes were reported by Durst[11,12] and Watt.[14,15] In most of the examples on the ring-opening of α,β-epoxy-sulfones, the observed regioselectivity on the β carbon was rationalized by the known retarding effect of the sulfonyl group on the α carbon in an intermolecular $S_N2$ reaction.[16] However, some examples of exclusive[14] or partial[17] nucleophilic attack on the α carbon were also reported. The reasons for this alternate mechanism are not clear.



## RESULTS and DISCUSSION

The model α,β-epoxy-sulfone **2** utilized in this study, was stereoselectively prepared by a Darzens type condensation of chloromethyl-*p*-tolyl sulfone[9] with the readily available methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*erythro*-hexopyranosid-3-ulose **1**. A minor experimental modification of the Tavares procedure[9] afforded the desired epoxy-sulfone derivative **2** on a multigram scale in good yield (75%). The stereochemistry at the quaternary centre was previously deduced on the basis of $^{13}C$ NMR spectroscopy.[3]

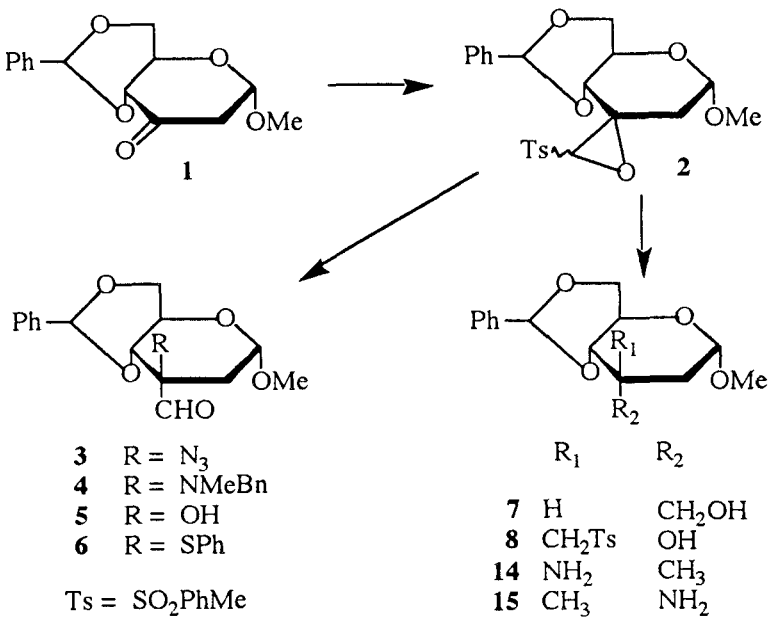
Convenient access to a precursor of highly functionalized branched-chain amino-sugars was initially effected using sodium azide in hot dimethylformamide. Regioselective attack of azide ion on the carbon β to the sulfonyl group of **2** furnished the α-azido-*C*-formyl derivative **3** in 75% yield. The same mode of ring-opening was observed with an aminolysis reaction. Thus, in the presence of benzylmethylamine, **2** was cleaved to the expected disubstituted α-amino aldehyde **4** in 87% yield with complete regioselectivity. For formation of a branched-chain of the type HO-C-CHO, various attempts with a powerful nucleophilic hydroxide ion, generated according to the Gassman's procedure,[19] were unsuccessful. However, transformation of **2** into the α-hydroxyaldehyde derivative **5** was easily achieved by simple addition of water to a suspension of sodium iodide in DMF at 80 °C. This convenient, good-yield overall conversion (67%) of the ulose **1** to the important hydroxyaldehyde structure **5** may constitute an alternative to the sequence reported by Dyong et al.[18]

While the model compound **2** reacted readily with sodium thiophenolate in excess under mild conditions (absolute ethanol at ca. 50 °C) to give the unstable α-phenylthio-aldehyde **6** (60%), direct access to the hydroxymethyl derivative **7** by reaction of sodium borohydride on **2** was not effective even after several attempts. However, on reductive cleavage of **2** by lithium triethylborohydride, the dideoxy compound **7** was obtained as the main product in 60% yield; the minor compound, isolated in 30% yield, proved to be the tertiary alcohol **8** as a result of a hydride attack at the carbon α to the sulfonyl group. This β-hydroxysulfone structure **8** was on the other hand the sole reaction product (90%) isolated from the reduction of **2** with lithium aluminium hydride in ether. The exclusive attack on the α carbon was again observed when **2** was subjected to catalytic hydrogenation over Raney nickel (88%) (Scheme 1).

All the compounds of the oxirane opening gave interpretable infrared and NMR spectra that were consistent with the postulated structures. For the establishment of the configuration at the quaternary centre, $^{13}C$ NMR proved to be very useful.[3,20] Carbon signal assignments for **3**,**4**,**5**,**6**, and **8** are recorded in Table 1 together with those of epimeric model compounds **14** and **15**. The chemical shifts of C-5 in the spectrum of the α-substituted aldehyde derivatives **3-6**, when compared to the chemical shift of C-5 of compound **14** (*arabino* configuration), indicate that these compounds have an axially disposed carbon-carbon linkage at C-3. The relative shielding of C-5 (59.6 ppm) in the spectrum of the tertiary alcohol **8** is comparable to that of the *ribo* model compound **15**. It was previously rationalized as the result of a greater steric compression experienced by C-5 when the axial H-5 interacts 1,3-diaxially with a C3-heteroatom bond. For the dideoxy compound **7**, axial orientation of the hydroxymethyl group was easily deduced from the coupling constant of the axial H-4 and the equatorial H-3 ($J_{4a,3e}$ 5.3 Hz).

From the preceding results, the ring opening of the α,β-epoxysulfone glycoside **2** by heteroatom nucleophiles ($^-N_3$, NHMeBn, $^-OH$, $^-SPh$) occurred with complete regioselectivity at the β carbon, affording important α-substituted aldehyde structures (**3-6**). In the presence of chemical or catalytic reducing agents, a marked contrast was observed with the opposite regioselectivity, resulting from exclusive attack at the methine carbon. The generated β-hydroxysulfone **8** constitutes an interesting example of a rare nucleophilic sugar derivative.[21] The reasons for this difference in regioselectivity of the sulfonylated oxirane ring opening are not clear; especially as in the reduction with lithium triethylborohydride, both the two carbons Cα and Cβ were involved .

In regard to the known acid-sensitive and thermolabile character of the epoxy-sulfone group[11,13] associated with the simultaneous presence of acetals in the model methyl 4,6-*O*-benzylidene-2-deoxy-3,3'-epoxy-3'(*p*-tolylsulfonyl)-α-D-*ribo*-pyranoside **2**, chemical reactivity of the sulfonylated oxirane was briefly examined through classical debenzylidenation reactions on **2** (Scheme 2).



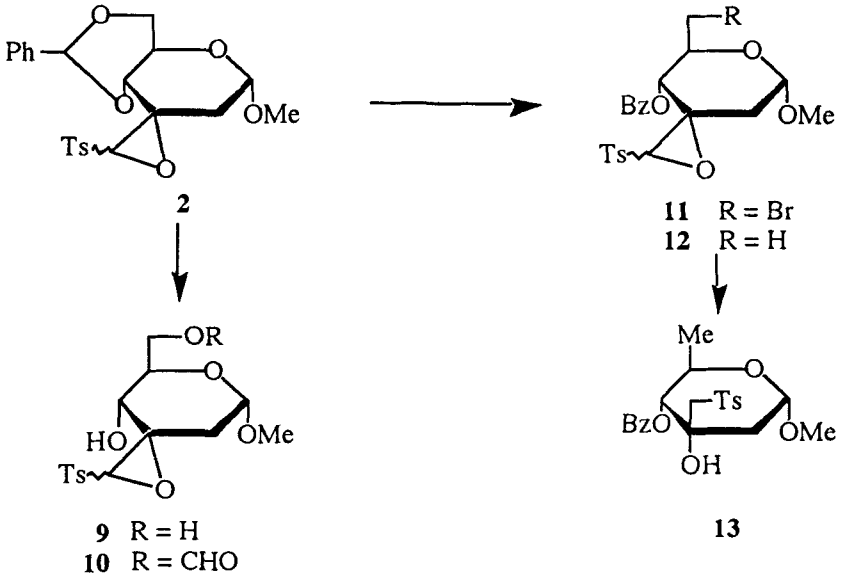

**Scheme 1**



**Table 1. $^{13}C$ Chemical shifts** (δ values)[a]

| Carbon | (3) | (4) | (5) | (6) | (8) | (14) | (15) |
|---|---|---|---|---|---|---|---|
| C-1 | 97.5 | 97.9 | 98.4 | 97.9 | 98.7 | 98.9 | 99.0 |
| C-2 | 38.4 | 36.1 | 40.1 | 36.5 | 38.8 | 43.4 | 41.6 |
| C-3 | 66.7 | 65.0 | 76.0 | 56.9 | 70.2 | 49.9 | 49.2 |
| C-4 | 83.0 | 82.4 | 83.5 | 82.2 | 80.7 | 86.6 | 84.1 |
| C-5 | 61.0 | 60.8 | 61.7 | 62.0 | 59.6 | 61.2 | 59.4 |
| C-6 | 69.6 | 69.8 | 69.6 | 69.5 | 69.1 | 69.5 | 69.3 |
| C-7 | 102.3 | 102.0 | 102.3 | 102.4 | 102.0 | 101.9 | 101.7 |
| OMe | 55.3 | 55.0 | 55.1 | 55.1 | 55.0 | 55.0 | 55.1 |
| CHO | 196.5 | 199.9 | 201.5 | 191.1 | --- | --- | --- |

a. Chemical shifts for remaining signals are given in the Experimental section.




**Scheme 2**



When compound **2** in methanol was treated with 5% aqueous perchloric acid at room temperature, only cleavage of the benzylidene acetal occurred, giving rise to the diol **9** in excellent yield (92%). When concentrated formic acid in dichloromethane was used, a partial protected 6-formyloxy derivative **10** was obtained (82%); in the two cases, the epoxy-sulfone group was unaffected.

On the other hand, in order to enter into the 2,6 dideoxyhexose series through the 6-bromo derivative, the Hanessian reaction[22] was performed on **2**. Treatment of **2** with *N*-bromosuccinimide in refluxing carbon tetrachloride in the presence of barium carbonate led to the expected 6-bromo 6-deoxy derivative **11** in 92% yield. The reaction was clean and no complication by possible competing bromination at the oxirane carbon was detected. On catalytic hydrogenation over 10% Pd/C, partial selective removal of bromine atom could be achieved (to the extent of 75% conversion) giving the 6-deoxy derivative **12** (80%). On extensive hydrogenolysis of **11** (15 h), cleavage of the spiro-epoxide occurred, leading to the β-hydroxysulfone derivative **13** (72%). The foregoing results indicate that the presence of a sulfonyl-epoxy ring is compatible with classical conversion of benzylidenated sugars into the corresponding 6-deoxy derivatives.

In conclusion, the examples shown in this study briefly illustrate the potential scope of a simple, two-step procedure for the elaboration of a quaternary centre in carbohydrate

field. This is based on the stereoselective formation of an α,β-epoxysulfone as the source of a masked formyl group. Upon nucleophilic epoxy ring opening, a second substituent is introduced regioselectively with inversion of configuration and concomitant liberation of the aldehyde function. The method described here may allow facile access to a wide variety of highly functionalized branched-chain sugars with predictable configuration at the newly created quaternary centre.

## EXPERIMENTAL

**General procedures**. Melting points were determined with a Büchi apparatus and are uncorrected. Optical rotations were recorded at room temperature on chloroform solutions with a Perkin-Elmer 241 polarimeter using a 1dm cell. Infrared (IR) spectra were measured directly on a NaCl plate (film) or in KBr disks with a Beckman Acculab-4 spectrometer. $^1$H NMR spectra were recorded in chloroform-d-solution (internal $Me_4Si$) at 90 MHz (Varian EM 390) and 300.13 MHz (Bruker AM300). $^{13}$C NMR spectra were measured in chloroform-d-solution at 50.3 MHz with a Bruker WP-200 spectrometer. Mass-spectral data were obtained from a JEOL JMS DX300 in FAB (+) mode without matrice substraction (NBA). Microanalyses were performed by the Service Central de Microanalyse du CNRS. Chromatography was done on Merck silica gel (230-400 mesh) and precoated Merck silica gel plates (60 F-254) were used for TLC. Standard work-up involved extracting the products with an organic solvent, washing with water, drying over $Na_2SO_4$ and removing the solvent at reduced pressure.

**Methyl 4,6-*O*-Benzylidene-2-deoxy-3,3'-epoxy-3'(*p*-tolylsulfonyl)-α-D-*ribo*-hexopyranoside (2)**. To a solution of chloromethyl *p*-tolylsulfone (2.05 g, 10 mmol) and ulose **1** (2.64g, 10 mmol)[23] in a mixture of tetrahydrofuran (75 mL) and *t*-butyl alcohol (2 mL) at 5 °C was added potassium *t*-butoxide (1.12 g, 10 mmol) in portions. At the end of the addition, the reaction mixture was stirred for 3 h at room temperature, diluted with diethyl ether (250 mL) and filtered on a celite cake. The solvents were evaporated and the residue chromatographed on a column of silica gel (ethyl acetate-petroleum ether 1:3) to give the pure α,β-epoxy sulfone **2** as a foam (3.24 g, 75%); $[\alpha]_D$ +18° (*c* 1.0); IR (film): 1590, 1320, 1150, 900, 810 cm$^{-1}$; $^1$H NMR. δ: 7.8 and 7.25(m, 9H, 2Ph), 5.49(s, 1H, H-7), 4.89(d, 1H, $J_{1,2a}$ 4Hz, H-1), 4.29(dd, 1H, $J_{gem}$ 10.4Hz, $J_{6e,5}$ 5Hz, H-6e), 4.15(m, 1H, H-5), 4.13(s, 1H, H-3'), 3.94(d, 1H, $J_{4,5}$ 9.6Hz, H-4), 3.74(t, 1H, $J_{6a,5}$ 10.4Hz, H-6a), 3.43(s, 3H, OMe), 2.94(d, 1H, $J_{gem}$15.3Hz, H-2e), 2.55(dd, 1H, H-2a), 2.42(s, 3H, MePh); $^{13}$C NMR. δ: 102.3(C-7), 98.1(C-1), 75.3(C-4), 69.9(C-6), 66.6(C-3'), 63.5(C-3), 61.6(C-5), 55.4(OMe),

33.1(C-2), 21.8(Me-Ph), 145.7, 136.9, 135.7, 130.1, 129.4, 128.6, 126.5, (aromatic carbons). MS (*m/z*) : 433(M+H)$^+$, 139, 105.

Anal. Calcd for $C_{22}H_{24}O_7S$: C, 61.11; H, 5.55. Found: C, 60.87; H, 5.50.

**Methyl 3-Azido-4,6-*O*-benzylidene-2,3-dideoxy-3-*C*-formyl-α-D-*arabino*-hexopyranoside (3).** A mixture of the α,β-epoxy-sulfone **2** (3 g, 7 mmol) and sodium azide (1.5 g, 23 mmol) in dry dimethylformamide (30 mL) was stirred at 80 °C for 4 h. The solvent was removed under reduced pressure, and after usual work-up with dichloromethane (200 mL) a rapid filtration on a column of silica gel (ethyl acetate-petroleum ether 1:4) gave pure azido aldehyde **3** (1.73 g, 78 %); mp 148-149 °C; $[\alpha]_D$ +66° (*c* 0.8); IR (KBr): 2100, 1740 cm$^{-1}$; $^1$H NMR. δ: 10.1(s, 1H, CHO), 7.4-7.25(m, 5H, Ph), 5.62(s, 1H, H-7), 4.81(dd, 1H, $J_{1,2e}$ 1Hz, $J_{1,2a}$ 3.7Hz, H-1), 4.37(dd, 1H, $J_{gem}$ 10Hz, $J_{6e,5}$ 4.8Hz, H-6e), 4.23 (dt, 1H, $J_{5,4}$ 10Hz, $J_{5,6e}$ 4.8Hz, H-5), 3.93(d, 1H, $J_{4,5}$ 10Hz, H-4), 3.79(t, 1H, $J_{6a,5} = J_{gem}$ 10Hz, H-6a), 3.38(s, 3H, OMe), 2.23(dd, 1H, $J_{gem}$ 14Hz, H-2e), 1.98(dd, 1H, H-2a); $^{13}$C NMR. δ: 196.5 (CO) 102.3(C-7), 97.5(C-1), 83.0(C-4), 69.6 (C-6), 66.7(C-3), 61.0(C-5), 55.3(OMe), 38.4(C-2), 136.7, 129.3, 128.4, 126.1, (aromatic carbons). MS (*m/z*) : 320(M+H)$^+$, 105, 91.

Anal. Calcd for $C_{15}H_{17}N_3O_5$: C, 56.42; H, 5.33. Found : C, 56.12; H 5.23.

**Methyl 4,6-*O*-Benzylidene-3-benzylmethylamino-2,3-dideoxy-3-*C*-formyl-α-D-*arabino*-hexopyranoside (4).** A solution of **2** (150 mg, 0.35 mmol) in dry DMSO (0.7 mL) containing an excess of *N*-benzylmethylamine (0.45 mL, 3.5 mmol) was stirred under $N_2$ atmosphere at 85-90 °C for 60 h. The reaction mixture was diluted with ethyl acetate (50 mL) and after standard work-up, chromatography of the residue (hexane-ethyl acetate 95:5) gave the pure benzylmethylaminoaldehyde **4** as an oil (120 mg, 87%); $[\alpha]_D$ -22° (*c* 1.3); IR (film): 1720, 1600 cm$^{-1}$; $^1$H NMR. δ: 10.0(s, 1H, CHO), 7.4-7.2(m, 10H, 2Ph), 5.56(s, 1H, H-7), 4.81(dd, 1H, $J_{1,2e}$ 1Hz, $J_{1,2a}$ 4Hz, H-1), 4.34(dd, 1H, $J_{6e,5}$ 4.4Hz, $J_{gem}$ 10Hz, H-6e), 4.14(dt, 1H, $J_{5,6a} = J_{5,4}$ 10Hz, H-5), 4.09(d, 1H, H-4), 3.97 and 3.65(2d, 2H, $J_{gem}$ 14.2Hz, $CH_2$-Ph), 3.77(t, 1H, $J_{6a,5} = J_{gem}$ 10Hz, H-6a), 3.34(s, 3H, OMe), 2.40(dd, 1H, $J_{gem}$ 14Hz, H-2e), 2.34(s, 3H, NMe), 1.96(dd, 1H, H-2a); $^{13}$C NMR. δ: 199.9(CHO), 102.0(C-7), 97.9(C-1), 82.4(C-4), 69.8(C-6), 65.0(C-3), 60.8(C-5), 56.5($CH_2$Ph), 55.0(OMe), 36.1(C-2), 35.2(NMe), 140.1, 137.2, 129.1, 128.3, 128.2, 126.9, 126.1, (aromatic carbons).
MS (*m/z*) : 398 (M+H)$^+$,105, 91.

Anal. Calcd for $C_{23}H_{27}NO_5$: C, 69.52; H, 6.80. Found : C, 69.37; H, 6.79.

**Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*C*-formyl-α-D-*arabino*-hexopyranoside (5).** To a solution of **2** (350 mg, 0.8 mmol) in a mixture of DMF-water (10:0.5 mL) was added sodium iodide (0.7 g, 4.7 mmol). After stirring at 85 °C for 15 h,

the solvent was evaporated, the residue after standard work-up was purified over silica gel (dichloromethane-petroleum ether 4:1) to give the hydroxyaldehyde derivative **5** as an oil (210 mg, 91%); $[\alpha]_D$ +64° (*c* 0.7); IR (film): 3450, 1710 $cm^{-1}$; $^1H$ NMR δ: 10.1 (s, 1H, CHO), 7.4-7.2(m, 5H, Ph), 5.52(s, 1H, H-7), 4.91(dd, 1H, $J_{1,2e}$ 1Hz, $J_{1,2a}$ 3.7Hz, H-1), 4.34(dd, 1H, $J_{6e,5}$ 4.9Hz, $J_{gem}$ 10Hz, H-6e), 4.24(dt, 1H, $J_{5,4} = J_{5,6a}$ 10Hz, H-5), 3.87(d, 1H, H-4), 3.77(t, 1H, $J_{gem}$ 10Hz, H-6a), 3.42(s, 3H, OMe), 2.15(dd, 1H, $J_{gem}$ 14.4Hz, H-2a), 2.0(dd, 1H, H-2e), 4.0-4.1(broad s, 1H, OH);. $^{13}C$ NMR δ: 201.5(CHO), 102.3(C-7), 98.4(C-1), 83.5(C-4), 76(C-3), 69.6(C-6), 61.7(C-5), 55.1(OMe), 40.1(C-2), 136.1, 129.2, 128.2, 126.2, (aromatic carbons).

MS (*m/z*) : 295 $(M+H)^+$, 105, 91.

Anal. Calcd for $C_{15}H_{18}O_6$: C, 61.22; H, 6.12. Found: C, 61.06; H, 6.30.

**Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-formyl-3-phenylthio-α-D-*arabino*-hexopyranoside** (**6**). To a solution of **2** (108 mg, 0.25 mmol) in dry ethanol (5 mL) under $N_2$ atmosphere, was added excess sodium thiophenolate (160 mg, 1.2 mmol) and the reaction mixture was stirred at 50 °C for 4 h. The residue after evaporation of ethanol was extracted with dichloromethane (25 mL). Usual work-up and chromatography (dichloromethane-petroleum ether 4:1) afforded the pure thiophenyl derivative **6** (58 mg, 60%); mp 102-103 °C; $[\alpha]_D$ -80° (*c* 0.6); IR (KBr): 1710 $cm^{-1}$; $^1H$ NMR δ: 9.85(s, 1H, CHO), 7.5-7.2(m, 10H, 2Ph), 5.54(s, 1H, H-7), 4.67(dd, 1H, $J_{1,2e}$ 1Hz, $J_{1,2a}$ 3.9Hz, H-1), 4.28(dd, 1H, $J_{6e,5}$ 4Hz, $J_{gem}$ 10Hz, H-6e), 3.9(m, 2H, H-4, H-5), 3.71(t, 1H, $J_{6a,5}$ 10Hz, H-6a), 3.24(s, 3H, OMe), 2.27(dd, 1H, $J_{gem}$ 14Hz, H-2e), 1.99(dd, 1H, H-2a); $^{13}C$ NMR δ: 191.1(CHO), 102.4(C-7), 97.9(C-1), 82.2(C-4), 69.5(C-6), 62.0(C-5), 56.9(C-3), 55.1(OMe), 36.5(C-2), 137.0, 130.1, 129.3, 129.0, 128.4, 126.3, (aromatic carbons). MS (*m/z*): 387$(M+H)^+$, 105, 91.

Anal. Calcd for $C_{21}H_{22}O_5S$ : C, 65.28; H, 5.70.Found : C, 64.87; H, 5.59.

**Methyl 4,6-*O*-Benzylidene-2-deoxy-3-*C*-(*p*-tolylsulfonylmethyl)-α-D-*ribo*-hexopyranoside** (**8**). a. *Reduction with LAH.* A solution of **2** (90 mg, 0.2 mmol) in dry ether (20 mL) was treated at 5 °C with lithium aluminium hydride (15 mg, 0.4 mmol). After 1 h at room temperature, the usual work-up with ethyl acetate (20 mL) gave the tertiary alcohol **8** as white crystals (82 mg, 90 %). Recrystallization from dichloromethane-hexane furnished the analytical sample: mp 210-212 °C ; $[\alpha]_D$ +59° (*c* 1.0); IR (KBr): 3450, 1600 $cm^{-1}$; $^1H$ NMR δ: 7.8-7.25 (m, 9H, 2Ph), 5.44(s, 1H, H-7), 4.86(d, 1H, $J_{1,2a}$ 3.8Hz, H-1), 4.29(dd, 1H, $J_{6e,5}$ 5Hz, $J_{gem}$ 10Hz, H-6e), 4.10(dt, 1H, $J_{5,4} = J_{5,6a}$ 10Hz, H-5), 3.93(s, 1H, OH), 3.77(d, 1H, H-4),3.74 (t, 1H, $J_{gem}$ 10Hz, H-6a), 3.47(q, 2H, $J_{gem}$ 14Hz, $CH_2Ts$), 3.39(s, 3H, OMe), 2.57(dd, 1H, $J_{gem}$ 14.8Hz, H-2a), 2.46 (d, 1H, H-2e), 2.38(s, 3H, MePh); $^{13}C$ NMR δ : 102.0(C-7), 98.7(C-1), 80.7(C-4), 70.2(C-3), 69.1(C-6), 60.9(C-3'), 59.6(C-5), 55.5(OMe),

38.8(C-2), 21.6(MePh), 144.7, 138.2, 137.3, 129.9, 129.1, 128.2, 127.9, 126.3, (aromatic carbons). MS (*m/z*): 435($(M+H)^+$, 155 ($ArSO_2^+$), 139($ArSO^+$), 105.

Anal. Calcd for $C_{22}H_{26}O_7S$: C, 60.83; H, 5.99. Found: C, 60.45; H, 6.38.

b. *Hydrogenolysis of 2 with Raney-nickel.* A solution of compound **2** (120 mg, 0.27 mmol) in methanol ( 5 mL) containing potassium hydroxide (25 mg) was hydrogenated in the presence of Raney nickel (ca. 1 g) for 4 h at room temperature. Work-up procedure and a rapid filtration on silica gel gave the pure β-hydroxysulfonyl derivative **8** (103 mg, 88%).

**Methyl 4,6-*O*-Benzylidene-2,3-dideoxy-3-*C*-hydroxymethyl-α-D-*ribo*-hexopyranoside** (**7**). The α,β-epoxy-sulfone **2** (200 mg, 0.46 mmol) was treated with an excess of lithium triethylborohydride in THF (2 mL of 1M solution). After stirring at 60 °C for 30 minutes, customary work-up and chromatography on silica gel (dichloromethane-ether 98:2) gave first the pure tertiary alcohol **8** (59 mg, 30 %) and next the major hydroxymethyl derivative **7** as an oil (79 mg, 60 %); $[\alpha]_D$ +140° (*c* 0.5) ; IR (film): 3500 $cm^{-1}$; $^1H$ NMR δ:7.4-7.2 (m, 5H, Ph), 5.52(s, 1H, H-7), 4.62 (d, 1H, $J_{1,2a}$ 4Hz, H-1), 4.26(dd, 1H, $J_{6e,5}$ 5Hz, $J_{gem}$ 10Hz, H-6e), 4.24(dd, 1H, $J_{3'a,3}$ 8.5Hz, $J_{gem}$ 12Hz, H-3'a), 4.09 (dt, 1H, $J_{5,4} = J_{5,6a}$ 10Hz, H-5), 3.91(dd, 1H, $J_{4,3}$ 5.3Hz, H-4), 3.70 (t, 1H, H-6a), 3.68 (d, 1H, $J_{gem}$ 12Hz, H-3'b), 3.33(s, 3H, OMe), 2.45(m, 2H, H-3 and OH), 2.01(m, 1H, H-2a), 1.88(d, 1H, $J_{gem}$ 14Hz, H-2e) ; $^{13}C$ NMR δ: 102.4(C-7), 97.8(C-1), 80.6(C-4), 69.8(C-6), 63.5(C-3'), 59.5(C-5), 54.9(OMe), 36.7(C-3), 32.0(C-2), 137.4, 129.2, 128.4, 126.1, (aromatic carbons).

Anal. Calcd for $C_{15}H_{20}O_5$: C,64.28; H, 7.14. Found : C, 64.09; H, 7.20.

**Methyl 2-Deoxy-3,3'-epoxy-3'(*p*-tolylsulfonyl)-α-D-*ribo*-hexopyranoside** (**9**). The α,β-epoxy-sulfone glycoside **2** (160 mg, 0.38 mmol) in methanol (7 mL) was debenzylidenated with 5% aqueous perchloric acid (0.5 mL). The reaction was complete after 15 h at room temperature. After neutralization of the reaction mixture ($PbCO_3$), filtration and evaporation of solvent, the residue was purified on silica gel (dichloromethane-methanol 95:5) giving **9** as an oil (128 mg, 92%); $[\alpha]_D$ +3° (*c* 0.6); IR (film): 3450, 1590, 1320, 1150 $cm^{-1}$; $^1H$ NMR δ: 7.8-7.3(2d, 4H, Ph), 4.87(d, 1H, $J_{1,2a}$ 4Hz,H-1),4.16(s, 1H, H-3'), 3.91(d, 1H, $J_{4,5}$ 10Hz, H-4), 3.83 and 3.79 (2dd, 2H, $J_{6,5} = J_{6',5}$ 3.7Hz,$J_{gem}$ 12Hz, H-6,6'), 3.71(dt, 1H, H-5), 3.38(s, 3H, OMe), 2.90(d, 1H, $J_{gem}$ 15.2Hz,H-2e), 2.44(s, 3H, MePh), 2.42(dd, 1H, H-2a), 1.91(bs, 2H, OH).

Anal. Calcd for $C_{15}H_{20}O_7S$: C, 52.32; H, 5.81. Found: C, 51.42; H, 5.51.

**Methyl 2-Deoxy-3,3'-epoxy-3'(*p*-tolylsulfonyl)-6-*O*-formyl-α-D-*ribo*-hexopyranoside** (**10**). A solution of **2** (310 mg, 0.7 mmol) in dichloromethane (15 mL) containing concentrated formic acid (97%, 0.3 mL) was strirred at room temperature for

8 h. After usual work-up with dichloromethane, the residue was chromatographed on a column of silica gel to give **10** as an oil (220 mg, 82%); $[\alpha]_D$ +3° (*c* 1.0); IR (film): 3500, 1715, 1590, 970cm$^{-1}$; $^1$H NMR δ: 8.11(s, 1H, CHO), 7.8 and 7.3(2d, 4H, Ph), 4.88(d, 1H, $J_{1,2a}$ 4Hz, H-1), 4.45(dd, 1H, $J_{6a,5}$ 2Hz, $J_{gem}$ 12Hz, H-6a), 4.39(dd, 1H, $J_{6b,5}$ 4.5Hz, H-6b), 4.17(s, 1H, H-3'), 3.90(ddd, 1H, $J_{5,4}$ 10Hz, H-5), 3.83(d, 1H, H-4) 3.39(s, 3H, OMe),2.90(dd, 1H, $J_{2e,1}$ 1Hz, $J_{gem}$ 15.4Hz, H-2e), 2.45(dd, 1H, H-2a), 2.43(s, 3H, MePh), 1.90(s, 1H, OH).

Anal. Calcd for $C_{16}H_{20}O_8S$ : C, 51.61; H, 5.37. Found: C, 51.38; H, 5.21.

**Methyl 4-*O*-Benzoyl-6-bromo-2,6-dideoxy-3,3'-epoxy-3'(*p*-tolylsulfonyl)-α-D-*ribo*-hexopyranoside (11).** A mixture of the benzylidene acetal **2** (430 mg, 1 mmol) barium carbonate (0.6 g) and *N*-bromosuccinimide (210 mg, 1.1 mmol) in carbon tetrachloride (20 mL) was refluxed with magnetic stirring for 2 h. The reaction mixture was filtered and the solid residue washed with dichloromethane (20 mL). After usual work-up and chromatography (ether-petroleum-ether 1:1) the pure bromo derivative **11** was obtained as a foam (470 mg, 92%); $[\alpha]_D$ +25° (*c* 0.6); IR (film): 1720, 1590, 1330, 1150, 910, 810 cm$^{-1}$; $^1$H NMR (90MHz) δ: 8.0-7.2 (m, 9H, 2Ph), 5.36 (d, 1H, $J_{4,5}$ 9.5Hz, H-4), 4.97(dd, 1H, $J_{1,2e}$ 1Hz, $J_{1,2a}$ 4Hz, H-1), 4.3(m, 1H, H-5), 3.75(s, 1H, H-3'), 3.5(s, 3H, OMe), 3.4(m, 2H, H-6,6'), 2.96 (dd, 1H, $J_{gem}$ 14Hz, H-2e), 2.50 (dd, 1H, H-2a), 2.40 (s, 3H, MePh).

Anal. Calcd for $C_{22}H_{23}BrO_7S$ : C, 51.76; H, 4.50. Found: C, 51.47; H, 4.29.

**Methyl 4-*O*-Benzoyl-2,6-dideoxy-3,3'-epoxy-3'(p-tolylsulfonyl)-α-D-*ribo*-hexopyranoside (12).** A solution of the bromo derivative **11** (262 mg, 0.5 mmol) in methanol (10 mL) containing barium carbonate (0.2 g) was hydrogenated over 10% Pd/C (0.2 g) at room temperature. After 2 h, TLC (dichloromethane-hexane 4:1) showed the formation of a major product (Rf 0.35) and a trace of slow moving compound (Rf 0.15) together with some starting material (Rf 0.5). The partial hydrogenation was stopped at this point, the catalyst filtered and the solvent evaporated. Column chromatography (dichloromethane-hexane 4:1) of organic materials gave, besides the starting compound **11** (65 mg, 25%), the pure major product **12** as an oil (130 mg, 79% from the consumed bromo derivative); $[\alpha]_D$ +22° (*c* 0.5); IR (film): 1725, 1590, 1330, 1150, 910, 810 cm$^{-1}$; $^1$H NMR δ: 8.0-7.2(m, 9H, 2Ph), 5.21(d, 1H, $J_{4,5}$ 10Hz, H-4), 4.90(dd, 1H, $J_{1,2e}$ 1Hz, $J_{1,2a}$ 4Hz, H-1), 4.25(m, 1H, H-5), 3.76 (s, 1H, H-3'), 3.45 (s, 3H, OMe), 2.96(dd, 1H, $J_{gem}$ 14Hz, H-2e), 2.51(dd, 1H, H-2a), 2.4(s, 3H, MePh), 1.21(d, 3H, $J_{6,5}$ 6Hz, Me-6).

Anal. Calcd for $C_{22}H_{24}O_7S$ : C, 61.11; H, 5.55. Found: C, 60.92; H, 5.42. The minor product **13** was obtained as white crystals (9 mg, 5 %): mp 157-159 °C.

**Methyl 4-*O*-Benzoyl-2,6-dideoxy-3-*C*-(*p*-tolylsulfonylmethyl)-α-D-*ribo*-hexopyranoside (13).** In another experiment, hydrogenation of **11** (65 mg, 0.12 mmol) in methanol (5 mL) and barium carbonate (50 mg) was continued to complete disappearance of the starting material (4 h). At this point, TLC showed the presence of two products **12** and **13** in the approximative ratio of 1:1. Hydrogenation was prolonged for a total of 15 h; after this period **13** was the sole product detected on TLC. It was isolated as white crystals (40 mg, 72%); mp 157-159 °C ; $[\alpha]_D$ +80° (*c* 0.9); IR (KBr): 3480, 1710, 1590, 1310, 1150 $cm^{-1}$; $^1H$ NMR δ: 8.0-7.25 (m, 9H, 2Ph), 4.89(d, 1H, $J_{1,2a}$ 3.8Hz, H-1), 4.88(d, 1H, $J_{4,5}$ 9.5HZ, H-4), 4.22 (s, 1H, OH), 4.17(m, 1H, H-5), 3.41(s, 3H, OMe), 3.38 and 3.13(2d, 2H, $J_{gem}$ 14.5Hz, $CH_2Ts$), 2.90(d, 1H, $J_{gem}$ 14.8Hz, H-2e), 2.40(s, 3H, MePh), 2.24(dd, 1H, H-2a), 1.19(d, 3H, $J_{6,5}$ 6.3Hz, Me-6).

Anal. Calcd for $C_{22}H_{26}O_7S$ : C, 60.83; H, 5.99. Found: C, 60.56; H, 5.72.

## REFERENCES


1. J. Yoshimura, *Adv. Carbohydr. Chem. Biochem.*, **42**, 69 (1984).
2. R. J. Alves, S. Castillon, A. Dessinges, P. Herczegh, J. C. Lopez, G. Lukacs, A. Olesker and T. Ton-That, *J. Org. Chem.*, **53**, 4616 (1988).
3. T. Ton-That, M. De Los. A. Laborde, A. Olesker and G. Lukacs, *J. Chem. Soc. Chem. Commun.*, 1581 (1988).
4. K. I. Sato, Y. Kajihara, Y. Nakamura and J. Yoshimura, *Chem. Lett.*, 1559 (1991).
5. K. I. Sato, K. Suzuki, M. Ueda, M. Katayama and Y. Kajihara, *Chem. Lett.*, 1469 (1991).
6. B. Zwanenburg and J. Ter.Wiel, *Tetrahedron Lett.*, **12**, 935 (1970).
7. R. Curci and F. DiFuria, *Tetrahedron Lett.*, **47**, 4085 (1974).
8. F. Bohlmann and G. Haffer, *Chem. Ber.*, **102**, 4017 (1969).
9. P. F. Vogt and D. F. Tavares, *Can. J. Chem.*, **47**, 2875 (1969).
10. A. Jonczyk, K. Banko and M. Makosza, *J. Org. Chem.*, **40**, 266 (1975).
11. T. Durst, K. C. Tin, F. De Reinach-Hirtzbach, J. M. Decesare and M. D. Ryan, *Can. J. Chem.*, **57**, 258 (1979).
12. F. De Reinach-Hirzbach and T. Durst, *Tetrahedron Lett.*, **41**, 3677 (1976).
13. D. F. Tavares, R.E. Estep and S.M. Blezard, *Tetrahedron Lett.*, **27**, 2373 (1970).
14. M. Adamzyk, E. K. Dolence, D.S. Watt, M. R. Christy, J. H. Reibenspies and O. P. Anderson, *J. Org. Chem.*, **49**, 1378 (1984).
15. A. D. Barone, D. L. Snitman and D. S. Watt, *J. Org. Chem.*, **43**, 2066 (1978).
16. F. G. Bordwell and W. T. Brannen, *J. Am. Chem. Soc.*, **86**, 4645 (1964).
17. E. C. Taylor, C. A. Maryanoff and J. S. Skotnicki, *J. Org. Chem.*, **45**, 2512 (1980).
18. I. Dyong, J. Weigand and W. Meyer, *Tetrahedron Lett.*, **22**, 2969 (1981).
19. P. G. Gassman, P. K. G. Hodgson and R. J. Balchunis, *J. Am. Chem. Soc.*, **98**, 1275 (1976).
20. T. Ton-That, F. Winternitz, A. Lagrange, A. Olesker and G. Lukacs, *J. Chem. Soc. Chem. Commun.*, 153 (1979).
21. K. S. Kim, J. K. Sohng, S.B. Ha, C. S. Cheong, D. I. Jung and C. S. Hahn, *Tetrahedron Lett.*, **29**, 2847 (1988).
22. S. Hanessian, *Carbohydr. Res.*, **2**, 86 (1966).
23. D. Horton and W. Weckerle, *Carbohydr. Res.*, **44**, 227 (1975).