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Note

Partial tosylation of 1,5-anhydroxylitol

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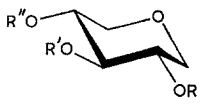
In a previous paper[1], we reported partial tosylation of 1,5-anhydro-D-glucitol and investigated the influence of the aglycon on the relative reactivity of the hydroxyl groups. As an extension of this study, this communication describes the partial tosylation of 1,5-anhydroxylitol (**1**).

Partial tosylation of **1** with 2 molar equivalents of tosyl chloride in pyridine at 0° gave the 2,3,4-trisulfonate **2** (24.8%), the 2,4-disulfonate **3** (69.1%), the 2,3-disulfonate **4** (3.3%), and the 2-sulfonate **5** (2.8%) as detected by t.l.c. Chromatographic separation of the mixture afforded two crystalline products (**2** and **3**) and two syrupy compounds (**4** and **5**).



	R	R′	R″
1	H	H	H
2	Ts	Ts	Ts
3	Ts	H	Ts
4	Ts	Ts	H
5	Ts	H	H
6	Ts	Ac	Ts
7	Ts	Ts	Ac
8	Ts	Ac	Ac

The position of the sulfonate group in **3** was assigned from the n.m.r. spectrum. The quartet at δ 3.18 was assigned to the superposed H-1a and H-5a resonances by analogy with the n.m.r. parameters described for compound **2**, showing that the diester **3** was symmetrically substituted. Similarly, the lowest-field ring-proton resonance was assigned to the H-2 and H-4 protons and appeared at δ 4.33 as a sextet, suggesting that these protons must be geminal to deshielding sulfonyloxy groups. This was further proved from the n.m.r. spectrum of the acetate **6**. The H-3 triplet

resonance appeared to low field of all other ring-proton resonances, because of the known tendency[2,3] of acyloxy groups to deshield strongly those methine protons attached to the same carbon atoms. The sulfonate **4** was converted into the acetate **7** to substantiate its structure. The n.m.r. spectrum of **7** showed the presence of two tosyloxy groups and one acetoxy group. The lack of symmetry of this compound was clearly evident from the slightly separated resonances for H-1a and H-5a, and H-1e and H-5e. The structure of the monosulfonate **5** was also confirmed by acetylation to give the diacetate **8**. The n.m.r. spectrum of **8** showed dissymmetry of this compound by the slightly separated resonances for H-1a and H-5a, and H-1e and H-5e. The triplet for the ring-proton resonance at lowest field (δ 5.14) was assigned to H-3, which is deshielded by the geminal acetoxy group.

The isolation of **3** as the major product in dimolar tosylation of **1** shows that the order of the relative reactivity of the hydroxyl groups is 2-OH (4-OH) > 3-OH. It is noteworthy that **4** was isolated in extremely low yield and the 3-sulfonate could not be detected. This observation is interpreted in terms of gauche interactions. The 3-OH group in **5** has gauche interactions with a tosyloxy group and a hydroxyl group, whereas the 4-OH group is adjacent to a hydrogen atom and a hydroxyl group. Thus the 4-OH group is tosylated faster than the 3-OH group, giving **3** exclusively. This finding is in accord with a possible prediction[1] that, if intramolecular hydrogen-bonding is not present, stereochemical factors are more important than electronic effects to account for the difference in the relative reactivities of the secondary hydroxyl groups.

EXPERIMENTAL

General methods. — Melting points were determined with a Yanagimoto micro hot-stage apparatus and are uncorrected. N.m.r. spectra were recorded with a Hitachi R-24 60 MHz instrument for solutions in chloroform-*d* with tetramethylsilane as the internal reference. Quantitative analysis of the products from partial tosylation was performed by thin-layer chromatography on a quartz rod sintered with silica gel H (Merck) and glass powder (1:2), with 9:1 toluene–acetone, and spots were detected by using an Iatoron chromatoscanner TH-10 equipped with a hydrogen flame-ionization detector. Percentages are expressed on a relative molar basis.

Dimolar tosylation of 1,5-anhydroxylitol (**1**). — *p*-Toluenesulfonyl chloride (1.775 g, 2.2 molar equiv.) was added to a solution of compound[4] **1** (500 mg) in distilled pyridine (20 mL) at 0°. After 24 h at 0°, the mixture was stirred for 48 h at 5°, and then extracted with chloroform. The extract was washed with dilute sulfuric acid, saturated sodium hydrogencarbonate, and water, and dried over sodium sulfate. The chloroform solution was used for t.l.c. analysis.

The residual syrup after evaporation of the solvent was resolved on a column of silica gel. Elution with 9:1 benzene–ethyl acetate gave 1,5-anhydro-2,3,4-tri-*O*-tosylxylitol (**2**) (446 mg, 18%) which was crystallized from benzene, m.p. 102–105°, R_F 0.58; n.m.r.: δ 4.72 (t, 1 H, $J_{2,3} = J_{3,4} = 6$ Hz, H-3), 4.28 (sextet, 2 H, $J_{1a,2} =$

$J_{4,5a}$ = 6, $J_{1e,2}$ = $J_{4,5e}$ = 3 Hz, H-2, H-4), 3.88 (q, 2 H, $J_{1a,1e}$ = $J_{5a,5e}$ = 12 Hz, H-1e, H-5e), 3.45 (q, 2 H, H-1a, H-5a), and 2.43 (s, 9 H, $C_6H_4CH_3$).

Anal. Calc. for $C_{26}H_{28}O_{10}S_3$: C, 52.33; H, 4.74; S, 16.12. Found: C, 52.11; H, 4.95; S, 15.86.

Benzene–ethyl acetate (4:1) eluted 1,5-anhydro-2,4-di-*O*-tosylxylitol (**3**, 888 mg, 48%), which crystallized from 2-propanol–petroleum ether, m.p. 132–133°, R_F 0.49; n.m.r.: δ 4.33 (sextet, 2 H, $J_{1a,2}$ = $J_{4,5a}$ = 10, $J_{1e,2}$ = $J_{4,5e}$ = 5 Hz, H-2, H-4), 3.87 (q, 2 H, $J_{1a,1e}$ = $J_{5a,5e}$ = 11 Hz, H-1e, H-5e), 3.83 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 8 Hz, H-3), 3.18 (q, 2 H, H-1a, H-5a), 3.00 (s, 1 H, OH exchanges in D_2O), and 2.40 (s, 6 H, $C_6H_4CH_3$).

Anal. Calc. for $C_{19}H_{22}O_8S_2$: C, 51.56; H, 5.02; S, 14.49. Found: C, 51.77; H, 4.91; S, 14.32.

Further elution with benzene–ethyl acetate mixtures (2:1, 1:1) yielded two syrupy fractions; 1,5-anhydro-2,3-di-*O*-tosyl-DL-xylitol (**4**, 92 mg, 5%), R_F 0.36 and 1,5-anhydro-2-*O*-tosyl-DL-xylitol (**5**, 51 mg, 4%).

3-O-Acetyl-1,5-anhydro-2,4-di-O-tosylxylitol (**6**). — Conventional acetylation of a solution of **3** (100 mg) in pyridine (1 mL) with acetic anhydride (1 mL) gave a syrup which on crystallization from chloroform–ethanol yielded the title compound (94 mg, 80%), m.p. 155–156°; n.m.r.: δ 5.13 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 8 Hz, H-3), 4.59 (sextet, 2 H, $J_{1a,2}$ = $J_{4,5a}$ = 12, $J_{1e,2}$ = $J_{4,5e}$ = 6 Hz, H-2, H-4), 4.02 (q, 2 H, $J_{1a,1e}$ = $J_{5a,5e}$ = 12 Hz, H-1e, H-5e), 3.25 (t, 2 H, H-1a, H-5a), 2.45 (s, 6 H, $C_6H_4CH_3$), and 1.62 (s, 3 H, $COCH_3$).

Anal. Calc. for $C_{21}H_{24}O_9S_2$: C, 52.05; H, 5.00; S, 13.23. Found: C, 51.79; H, 5.14; S, 12.93.

4-O-Acetyl-1,5-anhydro-2,3-di-O-tosyl-DL-xylitol (**7**). — Acetylation of **4** (92 mg) with acetic anhydride (1 mL) in pyridine (1 mL) gave the title compound (91 mg, 90%), m.p. 129–131°; n.m.r.: δ 2.7–3.0 (m, 2 H, H-3, H-4), 4.43 (m, 1 H, H-2), 3.93 (q, 1 H, $J_{4,5e}$ 3, $J_{5a,5e}$ 12 Hz, H-5e), 3.85 (q, 1 H, $J_{1e,2}$ 3, $J_{1a,1e}$ 12 Hz, H-1e), 3.45 (q, 1 H, $J_{4,5a}$ 5 Hz, H-5a), 3.32 (q, 1 H, $J_{1a,2}$ 5 Hz, H-1a), 2.45 (s, 6 H, $C_6H_4CH_3$), and 1.95 (s, 3 H, $COCH_3$).

Anal. Calc. for $C_{21}H_{24}O_9S_2$: C, 52.05; H, 5.00; S, 13.23. Found: C, 51.78; H, 5.29; S, 13.38.

3,4-Di-O-acetyl-1,5-anhydro-2-O-tosyl-DL-xylitol (**8**). — Compound **5** (51 mg) was treated with acetic anhydride (0.5 mL) in pyridine (1 mL) to afford the title compound (58 mg, 88%), m.p. 153–155°; n.m.r.: δ 5.14 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9 Hz, H-3), 2.4–3.0 (m, 2 H, H-2, H-4), 4.17 (q, 1 H, $J_{4,5e}$ 6, $J_{5a,5e}$ = 12 Hz, H-1e), 4.00 (q, 1 H, $J_{1e,2}$ 6, $J_{1a,1e}$ 12 Hz, H-5e), 3.35 (q, 1 H, $J_{4,5a}$ 9 Hz, H-1a), 3.22 (q, 1 H, $J_{1a,2}$ 9 Hz, H-5a), 2.45 (s, 3 H, $C_6H_4CH_3$), 2.02 and 1.85 (2s, 6 H, $COCH_3$).

Anal. Calc. for $C_{16}H_{20}O_8S$: C, 51.60; H, 5.42; S, 8.61. Found: C, 51.60; H, 5.55; S, 8.63.

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