Regioselective Monotosylation of Non-protected and Partially Protected Glycosides by the Dibutyltin Oxide Method[1)]

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Tosylation of non-protected glycopyranosides with *p*-toluenesulfonyl chloride in the presence of 4-dimethylaminopyridine, after activiation of the glycosides by dibutyltin oxide, gave mono-*O*-tosylates in good yield. The regioselectivity in this tosylation was different from that in the corresponding benzoylation for some glycosides. The reason for this difference is discussed based on an equilibrium of the tin intermediates and kinetic attack of the tosyl chloride on the intermediates. Thus, by application of this tosylation method to non-protected and partially protected glycosides, various glycoside mono-*O*-tosylates were synthesized regioselectively.

Keywords glycoside; regioselective mono-*O*-tosylation; dibutyltin oxide method; tin intermediate

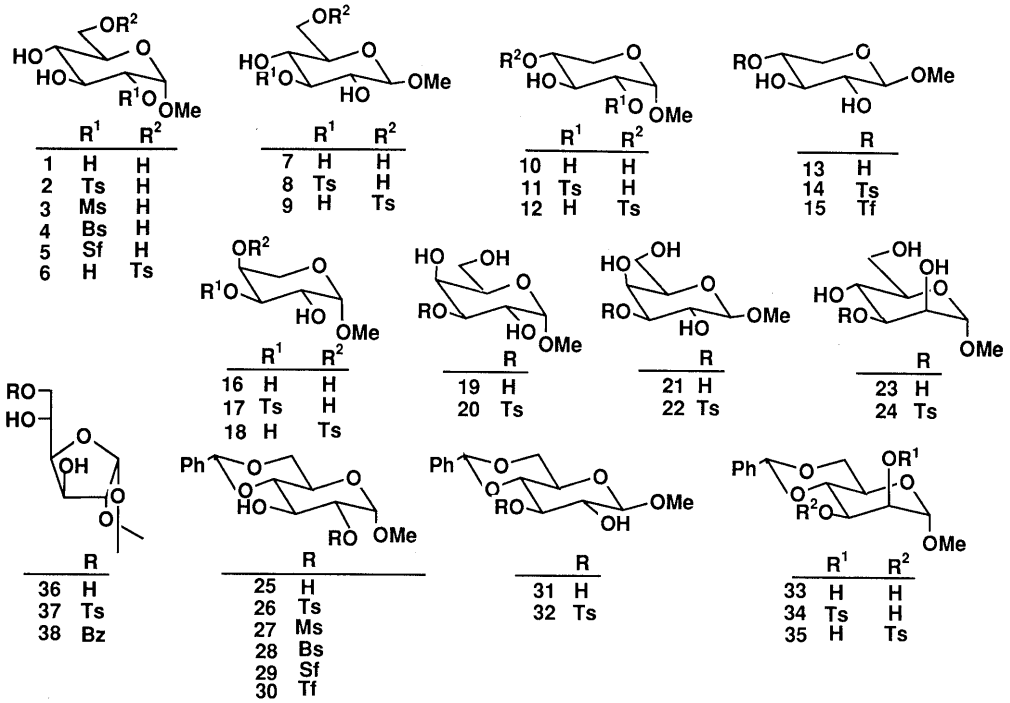
The tosyl group is useful in the field of carbohydrate chemistry as a protecting group,[3)] and for preparation of an epoxide on a glycoside ring, which can be employed as a synthetic intermediate of high reactivity.[4)] However, preparation of a particular mono-*O*-tosylate of glycosides often requires multisteps, *i.e.*, a protection–deprotection procedure, and this fact has limited the utilization of mono-*O*-tosylates in carbohydrate chemistry.

The success of regioselective monoacylation[5)] of non-protected glycosides through activation of a particular hydroxyl group by stannylation with dibutyltin oxide suggests that regioselective mono-*O*-sulfonation could also be achieved by a similar method. However, acylation (benzoylation) and sulfonation (tosylation) of a stannylene intermediate derived from a glycoside sometimes give different results.[6)] This paper described the results of mono-*O*-tosylation of various non-protected and partially protected glycosides, in comparison with previously reported regioselective mono-benzoylations.[5)]

Results and Discussion

The results of tosylation of various glycopyranosides with *p*-toluenesulfonyl chloride (TsCl) after treatment of the glycoside with dibutyltin oxide in boiling methanol are listed in Table I. It should be noted that tosylation is slower than benzoylation (which is usually completed within a few hours in the absence of a basic catalyst),[5)] and usually requires a basic catalyst such as 4-dimethylaminopyridine (DMAP) and overnight reaction to ensure completion. The yield and ratio were determined by chromatographic isolation of each product. Structure determinations are done mainly by carbon-13-nuclear magnetic resonance (^{13}C-NMR) spectral analysis: for example, in the 2-*O*-tosylate **2**, the C-2 signal is shifted downfield by 8.0 ppm and the C-1 and C-3 signals are shifted upfield by 3.2 and 3.7 ppm, respectively, compared to those of the original glycoside **1**.

Non-protected Glycopyranosides Tosylation of Me β-D-Glc[7)] (**7**) and Me β-D-Xyl (**13**) gave the 6-*O*-tosyl and 4-*O*-tosyl derivatives, **9** and **14**, in excellent yields, as in



Ms = methanesulfonyl, Ts = *p*-toluenesulfonyl, Bs = benzenesulfonyl, Sf = *p*-toluenesulfinyl, Tf = trifluoromethanesulfonyl, Bz = benzoyl

Chart 1

TABLE I. Regioselectivity in Monotosylation and Monobenzoylation of Non-protected Glycopyranosides by the Dibutyltin Oxide Method

Substrate	Tosylation					Benzoylation[a]				
	Yield (%)	Composition (%)				Yield (%)	Composition (%)			
	Mono	2-*O*	3-*O*	4-*O*	6-*O*	Mono	2-*O*	3-*O*	4-*O*	6-*O*
Me α-D-Glc (**1**)	50	56	—	—	44	76	100	—	—	—
Me β-D-Glc (**7**)	92	—	—	—	100	86	—	—	—	100
Me α-D-Gal (**19**)	62	—	100	—	—	68	26	51	—	23
Me β-D-Gal (**21**)	78	—	100	—	—	53	—	100	—	—
Me α-D-Man (**23**)	65	—	100	—	—	65	—	100	—	—
Me α-D-Xyl (**10**)	84	38	—	62		82	64	—	36	
Me β-D-Xyl (**13**)	100	—	—	100		78	—	—	100	
Me β-L-Ara (**16**)	94	—	44	56		80	10	61	39	

a) Ref. 5.

TABLE II. ^{13}C-NMR Data for Mono-*O*-sulfonyl Glycopyranosides

Compd.	Hexopyranosides									Pentopyranosides (in Chloroform-*d*)						
	2[a]	**3**[a]	**4**[a]	**5**[a]	**6**[a]	**8**[a]	**20**[b]	**22**[b]	**24**[b]	**11**	**12**	**14**	**15**	**17**	**18**	[c]
C-1	98.1	98.7	98.0	99.6	101.3	105.5	102.2	106.3	103.2	97.3	99.0	103.5	103.4	100.1	99.6	98.0
	(−3.2)	(−2.6)	(−3.3)	(−1.7)	(0)	(0)	(+0.5)	(+2.4)	(+1.2)	(−0.1)	(+0.7)	(−0.3)	(−0.4)	(+0.1)	(−0.4)	(−2.0)
C-2	81.7	81.6	81.9	79.8	73.3	72.6	68.0	70.5	71.2	79.5	72.2	72.7	72.8	68.6	69.5	78.6
	(+8.0)	(+7.9)	(+8.2)	(+6.1)	(−0.4)	(−2.4)	(−2.5)	(−0.3)	(−0.5)	(+8.3)	(+1.0)	(0)	(+0.1)	(−0.5)	(+0.4)	(+9.5)
C-3	71.6	71.9	71.6	72.5	75.0	89.6	83.4	85.6	84.7	71.5	71.5	72.7	72.3	81.1	68.5	67.3
	(−3.7)	(−3.4)	(−3.7)	(−2.8)	(−0.3)	(+11)	(+11.8)	(+12.7)	(+13.6)	(−1.7)	(−1.7)	(−3.0)	(−3.4)	(+12)	(−0.6)	(−1.8)
C-4	71.7	71.7	71.7	71.8	71.2	68.6	70.2	69.6	66.3	70.1	78.0	75.7	83.0	66.8	78.9	69.8
	(−0.3)	(−0.3)	(−0.3)	(−0.2)	(−0.8)	(−2.9)	(−0.7)	(+0.8)	(−1.6)	(+0.7)	(+8.6)	(+6.4)	(+14)	(−1.6)	(+10.5)	(+1.4)
C-5	73.9	73.8	73.9	74.0	70.8	77.9	72.6	76.6	75.4	60.8	58.8	62.3	61.9	62.0	60.7	62.0
	(−0.1)	(−0.2)	(−0.1)	(0)	(−3.2)	(+1.3)	(+0.1)	(+1.4)	(+1.7)	(+0.1)	(−1.9)	(−2.4)	(−2.8)	(−0.6)	(−1.9)	(−0.6)
C-6	62.1	62.0	62.1	62.4	71.2	61.8	62.9	62.8	63.3							
	(−0.7)	(−0.8)	(−0.7)	(−0.4)	(+8.4)	(−0.8)	(+0.3)	(+1.7)	(+1.2)							

Parenthetical values indicate shift values from the original glycosides. *a*) In pyridine-d_5. *b*) In methanol-d_4. *c*) Me β-L-Ara 2-*O*-tosylate, prepared by a classical method for comparison.

the case of benzoylation. Trifluoromethanesulfonation (triflation: Tf) of Me β-D-Xyl (**13**) gave the 4-*O*-Tf derivative **15** as well, though in low yield due to the instability of the product.

Me α-D-Gal (**19**), Me β-D-Gal (**21**), and Me α-D-Man (**23**) produced only the 3-*O*-tosyl derivatives, **20**, **22**, and **24**, as the mono-*O*-tosylates,[8] respectively, in accordance with the mechanism proposed for benzoylation: *i.e.*, the formation of a cyclic tin intermediate involving *cis*-vicinal hydroxyls with enhancement of the reactivity of the equatorial hydroxyl group.[5] In these compounds tosylation would have proceeded through the *C1* conformations.

In contrast to the above substrates, Me β-L-Ara (**16**) produced a mixture of the 3-*O* and 4-*O*-tosylates, **17** and **18**, with a slight preference for the latter: the result is different from that of benzoylation and also from benzylation[9] by the dibutyltin oxide method, where the ratio of the 3-*O*-alkyl to 4-*O*-alkyl derivatives is 85 : 15. The present result can be explained by a greater contribution of the *1C* conformer (B) in tosylation. The initially formed *C1* conformer (A) would equilibrate, in a slow tosylation reaction, with the *1C* conformer (B), in which the equatorial 4-*O*-*Sn* bond is the most reactive to a bulky electrophile.

Tosylation of Me α-D-Xyl (**10**) gave a mixture of the 2-*O* and 4-*O*-tosylate, **11** and **12**: the ratio of these compounds, however, is the reverse of that in the case of benzoylation. This result can again be explained by a significant contribution of the *1C* conformer (D), where the 4-*O*–*Sn* bond is the most reactive to a bulky electrophile for steric reasons.

The difference of regioselectivity between benzoylation and tosylation of Me α-D-Glc (**1**) requires a different explanation. The initially formed tin intermediate (E) (benzoylation proceeds through this species)[5] will equilibrate with many species such as E–H in the slow tosylation condition, in which the 6-*O*–*Sn* bond of G and H is the most reactive for steric reasons. Thus, a contribution of G or H, at least partially, would increase the formation of the 6-*O*-tosyl derivative **6**.

From the above results, we conclude that benzoylation (a fast reaction) reflects the relative stability and abundance of the tin intermediates as suggested already,[5] while in tosylation (a slow reaction) the tin intermediate comes into equilibrium with several species, so the contribution of the kinetically most favored species increases the proportion of the product formed through that intermediate, even if it exists in only a small amount.

Partially Protected Glycosides Tosylation of Me 4,6-*O*-benzylidene-α-D-Glc (**25**) by the above method gave the 2-*O*-tosyl derivative **26** in high yield. Methanesulfonation, triflation, benzensulfonation, and *p*-toluenesulfination gave

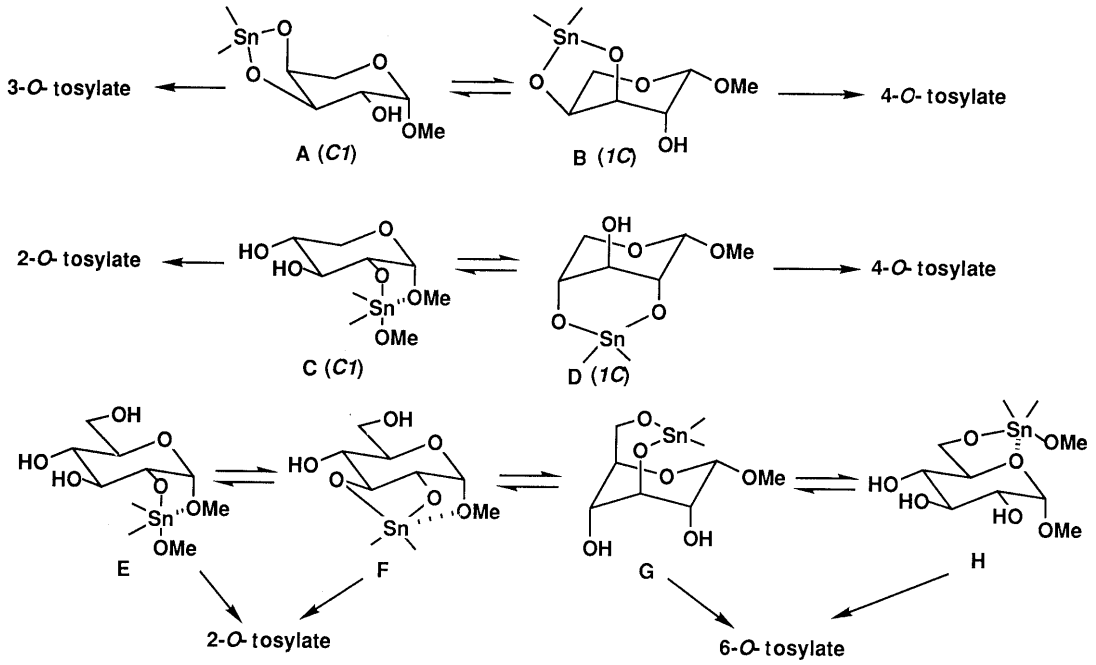


Chart 2

TABLE III. ^{13}C-NMR Data for Partially Protected Glycoside *O*-Sulfonates and *O*-Sulfinate (in Chloroform-*d*)

Compd.	26	27	28	30	29	32	34	35	37
C-1	98.0	98.6	98.1	97.6	99.4	104.3	99.6	101.7	105.9
	(−2.0)	(−1.4)	(−1.9)	(−2.4)	(−0.6)	(+0.5)	(−1.8)	(+0.3)	(0)
C-2	79.4	79.3	79.6	84.1	78.4	73.9	78.6	70.5	86.2
	(+6.6)	(+6.5)	(+6.8)	(+11)	(+5.6)	(−0.9)	(+8.2)	(+0.1)	(−0.2)
C-3	68.6	68.7	68.3	68.1	68.6	82.0	66.8	78.7	74.5
	(−2.7)	(−2.6)	(−3.0)	(−3.2)	(−2.7)	(+9.4)	(−0.8)	(+11.1)	(−0.8)
C-4	80.8	81.4	81.0	81.0	81.0	78.0	78.5	75.5	81.5
	(−0.2)	(+0.4)	(0)	(0)	(0)	(−2.0)	(+0.2)	(−2.8)	(+0.1)
C-5	61.9	61.2	61.9	62.0	62.4	66.1	63.4	63.7	67.0
	(−0.5)	(−1.2)	(−0.5)	(−0.4)	(−0.4)	(+0.4)	(+0.7)	(+1.0)	(−3.6)
C-6	68.1	68.8	69.0	68.6	68.8	68.7	68.6	68.6	74.7
	(−0.8)	(−0.1)	(−0.1)	(−0.3)	(−0.1)	(+0.8)	(+0.6)	(+0.6)	(+11)

Parenthetical value indicate shift values from the original glycosides.

the corresponding sulfonates and sulfinate, **27**—**30**, as well. These products were smoothly hydrolyzed with 50% acetic acid, except for the triflate **30**, to the corresponding Me α-D-Glc 2-*O*-sulfonates or sulfinates **3**—**5** in excellent yields. The *O*-triflate, however, could not be isolated because of its instability.

Me 4,6-*O*-benzylidene-β-D-Glc (**31**) gave, with high regioselectivity, the 3-*O*-tosylate **32**, which was hydrolyzed with 50% acetic acid to Me β-D-Glc 3-*O*-tosylate (**8**) in an excellent yield.

Tosylation of Me 4,6-*O*-benzylidene-α-D-Man (**33**) under the same conditions gave the 3-*O*-tosylate **35** as a single product in high yield. However, when this tosylation was performed without any base catalyst, the product was accompanied with the 2-*O*-tosylate **34**, though the total conversion yield was low. It has been suggested that the dibutylstannylene intermediate derived from **33** is dimeric in non-coordinating solvents such as benzene (in this case, the 2-*O*–*Sn* bond is the most reactive, because it is in an apical orientation), while in coordinating solvents such as dioxane, or in the presence of a base it is possibly monomeric (an equatorial 3-*O*–*Sn* bond is esterified).[10] The present result suggests that, even in coordinating solvent such as dioxane, the cyclic stannylene derivative is not completely monomeric. Complete monomerization of the stannylene intermediate may only be achieved by addition of a powerful coordinating ligand such as DMAP.

Tosylation and benzoylation of 1,2-*O*-isopropylidene-α-D-glucofuranose (**36**) gave the same regioselectivity, where the 6-*O*-tosylate **37** and benzoate **38** were produced in 98% and 75% yields, respectively. Comparisons of the yields with those of direct tosylation and benzoylation (51% and 41%, respectively) clearly indicate that the dibutyltin oxide method is superior to direct tosylation or acylation even for the primary hydroxyl group.

Experimental

Unless otherwise stated, infrared spectra (IR) were taken as KBr disks (data are given in cm^{-1}) and NMR spectra with tetramethylsilane as an internal standard (chemical shifts are given in δ values). Data for the aromatic group and any other protecting group are omitted. For mass spectra (MS) and high-resolution MS (HRMS), major peaks are indicated in *m/z* (%). For other items, see Experimental in ref. 1. Identities were confirmed by mixed melting-point determination (for crystalline compounds), and also by comparisons of thin layer chromatographic (TLC) behavior and ^{1}H-NMR and IR spectra.

Tosylation of Glycosides by the Dibutyltin Oxide Method (General Procedure) A mixture of glycoside (0.3—1 g) and Bu_2SnO (1.0 mol eq) in dry MeOH (10—30 ml) was heated under reflux for 3—10 h. After evaporation of the solvent, the residue was dried, dissolved (or suspended) in dioxane (25—50 ml) and tosylated with TsCl (1.1 mol eq) and DMAP (0.1—0.2 mol eq) for 3—20 h at room temperature with periodic monitoring of the progress of the reaction by TLC. Amounts of materials and reaction times with TsCl are given for each individual experiment. For processing, the mixture was concentrated under reduced pressure below 30 °C and the residue was chromatographed on a silica gel column for separation. Benzene and $CHCl_3$ elution removed tin compounds and the EtOAc eluate gave a mono-*O*-tosylate, which was further purified by medium-pressure liquid chromatography, if necessary. The results for non-protected glycopyranosides are summarized in Table I.

Tosylation of Me α-D-Glc (1) Reaction of **1** (0.3 g) for 11 h gave the 2-*O*-tosylate **2** (142 mg. 28%) and the 6-*O*-tosylate **6**, mp 118—120 °C[11] (116 mg, 22%).

Methyl 2-*O*-Tosyl-α-D-glucopyranoside (**2**): Colorless needles from EtOAc–ether, mp 140—142 °C. IR: 3435, 1366, 1171. ^{1}H-NMR

(pyridine-d_5): 5.11 (1H, d, J=3.8 Hz, H-1), 4.80 (1H, dd, J=3.8, 10 Hz, H-2), 4.6—4.0 (5H, H-3, 4, 5, 6), 3.29 (3H, s, OMe). MS: 317 (M^+ −OMe, 1.6), 161 (100). *Anal.* Calcd for $C_{14}H_{20}O_8S$: C, 48.27; H, 5.79. Found: C, 48.22; H, 5.85.

Tosylation of Me β-D-Glc (7) Reaction of **7** (0.5 g) for 12 h gave the 6-*O*-tosylate **9**, gum,[11] (778 mg, 92%).

Tosylation of Me α-D-Xyl (10) Reaction of **10** (1.0 g) for 16 h gave the 2-*O*-tosylate **11** (625 mg, 32%) and 4-*O*-tosylate **12** (1.01 g, 52%).

Methyl 2-*O*-Tosyl-α-D-xylopyranoside (**11**): Colorless needles from EtOAc–hexane, mp 140—141 °C. IR: 3520, 1355, 1170. ^{1}H-NMR: 4.58 (1H, d, J=3.7 Hz, H-1), 4.28 (1H, dd, J=3.7, 9.8 Hz, H-2), 4.0—3.5 (4H, H-3, 4, 5), 3.27 (3H, s, OMe). MS: 287 (M^+ −OMe, 0.5), 103 (100). *Anal.* Calcd for $C_{13}H_{18}O_7S$: C, 49.05; H, 5.70. Found: C, 49.19; H, 5.77.

Methyl 4-*O*-Tosyl-α-D-xylopyranoside (**12**): Colorless solid. IR ($CHCl_3$): 3560, 1366, 1174. ^{1}H-NMR: 4.67 (1H, d, J=4.5 Hz, H-1), 4.30 (1H, m, H-4), 3.9—3.4 (4H, H-2,3,5), 3.38 (3H, s, OMe). MS: 319 (M^+ − 1, 0.8), 287 (M^+ −OMe, 4), 155 (100). HRMS: Calcd for $C_{13}H_{17}O_7S$ (M^+ − 1); $C_{12}H_{15}O_6S$ (M^+ −OMe): 319.0849; 287.0588. Found: 319.0839; 287.0605.

Tosylation of Me β-D-Xyl (13) Reaction of **13** (2.0 g) for 2 h gave the 4-*O*-tosylate **14** (3.87 g, 100%).

Methyl 4-*O*-Tosyl-β-D-xylopyranoside (**14**): Colorless needles from EtOAc–hexane, mp 135—136 °C. IR: 3530, 1327, 1170. ^{1}H-NMR: 4.64 (1H, d, J=8.0 Hz, H-1), 4.4—3.8 (5H, H-2,3,4,5), 3.50, (3H, s, OMe). MS: 287 (M^+ −OMe, 1.7), 155 (100). *Anal.* Calcd for $C_{13}H_{18}O_7S$: C, 49.05; H, 5.70. Found: C, 49.15; H, 5.70.

Tosylation of Me β-L-Ara (16) Reaction of **16** (0.5 g) for 16 h gave the 3-*O*-tosylate **17** (396 mg, 41%) and the 4-*O*-tosylate **18** (515 mg, 53%).

Methyl 3-*O*-Tosyl-β-L-arabinopyranoside (**17**): Colorless prisms from EtOAc–hexane, mp 69—72 °C. IR: 3535, 1361, 1175. ^{1}H-NMR: 4.78 (1H, d, J=3.7 Hz, H-1), 4.66 (1H, dd, J=3.4, 9.8 Hz, H-3), 4.16 (1H, m, H-4), 4.00 (1H, dd, J=3.7, 9.8 Hz, H-2), 3.8—3.7 (2H, H-5), 3.41 (3H, s, OMe). MS: 287 (M^+ −OMe, 1.8), 86 (100). *Anal.* Calcd for $C_{13}H_{18}O_7S \cdot H_2O$: C, 46.43; H, 5.99. Found: C, 46.77; H, 6.05.

Methyl 4-*O*-Tosyl-β-L-arabinopyranoside (**18**): Colorless needles from ether–hexane, mp 152—153 °C. IR: 3460, 1368, 1173. ^{1}H-NMR: 4.82 (1H, m, H-4), 4.77 (1H, d, J=3.7 Hz, H-1), 3.88 (1H, dd, J=3.7, 9.8 Hz, H-2), 3.8—3.7 (3H, H-3,5), 3.40 (3H, s, OMe). MS: 287 (M^+ −OMe, 0.4), 155 (100). *Anal.* Calcd for $C_{13}H_{18}O_7S$: C, 49.05; H, 5.70. Found: C, 48.97; H, 5.76.

Sulfonation and Sulfination of Me 4,6-*O*-Benzylidene-α-D-Glc (25) Compound **25** (1 g) was stannylated with Bu_2SnO as described above. The dried tin intermediate was dissolved in dioxane and treated with an appropriate sulfonyl or sulfinyl chloride (1.1 mol eq) and DMAP (0.1—0.2 mol eq) under reflux for 2—4 h, then concentrated to dryness. Chromatography of the residue with benzene and $CHCl_3$ removed tin compounds. Further elution of the column with $CHCl_3$–EtOAc and EtOAc gave the *O*-sulfonate or sulfinate. The following compounds were prepared.

The 2-*O*-Tosylate **26**: Yield 99%. Colorless needles from ether–hexane, mp 158—161 °C (lit. mp 151—153 °C).[12]

The 2-*O*-Methanesulfonate **27**: Yield 93%. Colorless needles from benzene, mp 138—140 °C. IR: 3465, 1329, 1171. ^{1}H-NMR: 4.91 (1H, d, J=3.9 Hz, H-1), 4.47 (1H, dd, J=3.9, 9.2 Hz, H-2), 4.4—3.5 (5H, H-3,4,5,6), 3.44 (3H, s, OMe), 3.11 (3H, s, Ms). MS: 360 (M^+, 20), 107 (100). *Anal.* Calcd for $C_{15}H_{20}O_8S$: C, 50.00; H, 5.60. Found: C, 49.86; H, 5.77.

The 2-*O*-Benzenesulfonate **28**: Yield 100%. Colorless needles from EtOAc–hexane, mp 157—160 °C. IR: 3460, 1361, 1184. ^{1}H-NMR: 4.83 (1H, d, J=3.7 Hz, H-1), 4.40 (1H, dd, J=3.7, 9.3 Hz, H-2), 4.3–3.4 (5H, H-3,4,5,6), 3.33 (3H, s, OMe). MS: 422 (M^+, 0.5), 107 (100). *Anal.* Calcd for $C_{20}H_{22}O_8S$: C, 56.86; H, 5.25. Found: C, 56.50; H, 5.25.

The 2-*O*-Triflate **30**: Yield 90%. Colorless needles from benzene–hexane, mp 110—111 °C. IR: 3485, 1414, 1145. ^{1}H-NMR: 4.95 (1H, d, J=3.9 Hz, H-1), 4.62 (1H, dd, J=3.9, 9.3 Hz, H-2), 4.4—3.6 (5H, H-3,4,5,6), 3.46 (3H, s, OMe). MS: 414 (M^+, 94), 87 (100).

The 2-*O*-*p*-Toluenesulfinate **29**: Yield 100%. Colorless prisms from EtOAc–hexane, mp 164.5—165.5 °C. IR: 3420, 1129. ^{1}H-NMR (400 MHz): 4.95 (1H, d, J=2.8 Hz, H-1), 4.27 (1H, dd, J=4.9, 10.4 Hz, H-6), 4.13—4.11 (2H, H-2,3), 3.85 (1H, dt, J=4.9, 10.4 Hz, H-5), 3.71 (1H, br t, J=10.4 Hz, H-6), 3.48 (1H, m, H-4), 3.45 (3H, s, OMe). MS: 420 (M^+, 0.3), 389 (M^+ −OMe, 0.7), 107 (100). *Anal.* Calcd for $C_{21}H_{24}O_7S \cdot 1/2H_2O$: C, 58.73; H, 5.87. Found: C, 58.49; H, 5.68.

Deprotection of the Benzylidene Derivatives The above benzylidene derivatives were heated in 50% AcOH under reflux for 1 h, then the solvent was evaporated off. Chromatography of the residue gave the deprotected compounds in yields of 85—100%, except for the 2-*O*-triflate.

Methyl 2-*O*-Tosyl-α-D-glucopyranoside (**2**): Yield 100%. Data, see above.

Methyl 2-*O*-Methanesulfonyl-α-D-glucopyranoside (**3**): Yield 100%. Colorless prisms from EtOAc, mp 120—121 °C. IR: 3440, 1364, 1171. ^{1}H-NMR (pyridine-d_5): 5.26 (1H, d, J=4.0 Hz, H-1), 4.86 (1H, dd, J=4.0, 9.0 Hz, H-2), 4.6—4.0 (5H, H-3,4,5,6), 3.40 (3H, s, OMe), 3.37 (3H, s, Ms). MS: 241 (M^+ −OMe, 0.6), 87 (100). *Anal.* Calcd for $C_8H_{16}O_8S$: C, 35.29; H, 5.92. Found: C, 35.19; H, 5.98.

Methyl 2-*O*-Benzenesulfonyl-α-D-glucopyranoside (**4**): Yield 100%. Colorless needles from EtOAc, mp 201—203 °C. IR: 3530, 1356, 1175. ^{1}H-NMR (pyridine-d_5): 5.09 (1H, d, J=3.7 Hz, H-1), 4.80 (1H, dd, J=3.7, 9.4 Hz, H-2), 4.6—4.0 (5H, H-3,4,5,6), 3.36 (3H, s, OMe). MS: 303 (M^+ −OMe, 0.3), 73 (100). *Anal.* Calcd for $C_{13}H_{18}O_8S$: C, 46.70; H, 5.43. Found: C, 46.56; H, 5.48.

Methyl 2-*O*-*p*-Toluenesulfinyl-α-D-glucopyranoside (**5**): Yield 85%. Colorless prisms from acetone–ether, mp 134—137 °C. IR: 3445, 1149. ^{1}H-NMR (400 MHz, pyridine-d_5): 5.43 (1H, br s, H-1), 4.65—4.55 (2H, H-2,3), 4.45 (1H, br d, J=11.9 Hz, H-6), 4.29 (1H, dd, J=4.9, 11.9 Hz, H-6), 4.22—4.13 (2H, H-4,5), 3.46 (3H, s, OMe). MS: 333 (M^+ + 1, 0.3), 139 (100). *Anal.* Calcd for $C_{14}H_{20}O_7S \cdot 1/2H_2O$: C, 49.26; H, 6.20. Found: C, 49.49; H, 6.16.

Tosylation of Me 4,6-*O*-Benzylidene-β-D-Glc (31) Compound **31** (800 mg) was tosylated and worked up as described for the sulfonation of **25** to give the 3-*O*-tosylate **32** (949 mg, 77%), as colorless prisms from benzene–hexane, mp 166—167 °C. IR: 3380. 1367, 1173. ^{1}H-NMR: 5.42 (1H, t, J=9.0 Hz, H-3), 4.71 (1H, d, J=7.2 Hz, H-1), 4.4 (1H, m, H-6), 4.1—3.6 (4H, H-2,4,5,6). MS: 436 (M^+, 7), 107 (100). *Anal.* Calcd for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.54. Found: C, 57.85; H, 5.57.

Methyl 3-*O*-Tosyl-β-D-glucopyranoside (8) Compound **32** (200 mg) was deprotected as described above to give **8** (142 mg, 89%), as a gum, from the EtOAc eluate. IR ($CHCl_3$): 3585, 1355, 1171. ^{1}H-NMR (400 MHz, pyridine-d_5): 5.50 (1H, t, J=9.5 Hz, H-3), 4.68 (1H, d, J=7.6 Hz, H-1), 4.44 (1H, dd, J=2.1, 12.2 Hz, H-6), 4.37—4.32 (2H, H-4,6), 3.95 (1H, dd, J=7.6, 9.5 Hz, H-2), 3.85 (1H, ddd, J=2.1, 2.4, 9.4 Hz, H-5), 3.55 (3H, s, OMe). MS: 349 (M^+ + 1, 0.4), 317 (M^+ −OMe, 5), 144 (100).

Tosylation of Me 4,6-*O*-Benzylidene-α-D-Man (33) (1) The stannylene derivative of **33** (100 mg), prepared as described above, was tosylated in dioxane (20 ml) with TsCl (1.0 mol eq) and DMAP (0.4 mol eq) to give the 3-*O*-tosylate **35** (150 mg, 97%).

(2) Tosylation of the stannylene derivative of **33** (100 mg) in dioxane with TsCl (1.0 mol eq) (without DMAP) for 12 h gave a mixture of the 2-*O*-tosylate **34** and 3-*O*-tosylate **35** (75 mg, 49%, **34**/**35** ratio was 1:4 on the basis of the NMR spectrum).

The 2-*O*-Tosylate **34**: Colorless prisms from ether, mp 82—84 °C. ^{1}H-NMR: 4.82 (1H, d, J=1.5 Hz, H-1), 4.75 (1H, dd, J=1.5, 3.4 Hz, H-2), 4.3—4.1 (2H), 3.9—3.7 (3H) (H-3,4,5,6), 3.37 (3H, s, OMe). MS: 436 (M^+, 12), 105 (100). *Anal.* Calcd for $C_{21}H_{24}O_8S$: C, 57.79; H, 5.54. Found: C, 57.51; H, 5.66.

The 3-*O*-Tosylate **35**: Colorless needless from CH_2Cl_2–hexane, mp 151—154 °C. IR: 3425, 1353, 1169. ^{1}H-NMR: 4.77 (1H, d, J=1.2 Hz, H-1), 4.77 (1H, dd, J=3.4, 9.5 Hz, H-3), 4.32 (1H, dd, J=1.2, 3.4 Hz, H-2), 4.21 (1H, m, H-5), 4.08 (1H, t, J=9.5 Hz, H-4), 3.8—3.7 (1H, m, H-6), 3.37 (3H, s, OMe). MS: 436 (M^+, 41), 155 (100). *Anal.* Calcd for $C_{21}H_{24}O_8S$: C, 57.79, H, 5.54. Found: C, 57.58; H, 5.58.

Tosylation of 1,2-*O*-Isopropylidene-α-D-glucofuranose (36) (1) The Bu_2SnO Method: Compound **36** (220 mg) was stannylated according to the general procedure and the resulting tin intermediate in dioxane (15 ml) was tosylated with TsCl (229 mg, 1.2 mol eq) (without using DMAP) for 10 min at room temperature. Chromatography of the product gave the 6-*O*-tosylate **37** (366 mg, 98%) as colorless prisms from ether–hexane, mp 103—105 °C. IR: 3530, 1330, 1170. ^{1}H-NMR: 6.14 (1H, d, J=3.5 Hz, H-1), 5.0—4.4 (6H, H-2,3,4,5,6), 2.21 (3H, s, $ArCH_3$), 1.32, 1.52 (each 3H, s, CMe_2). *Anal.* Calcd for $C_{16}H_{22}O_8S$: C, 51.33; H, 5.92. Found: C, 51.41; H, 5.95.

(2) Direct Tosylation: A mixture of **36** (220 mg) and TsCl (229 mg, 1.2 mol eq) in pyridine (2 ml) was stirred for 30 min at room temperature, then weakly acidified with 0.5 N HCl and extracted with EtOAc. Chromatography of the product gave the 6-*O*-tosylate **37** (190 mg, 51%).

Benzoylation of 1,2-*O*-Isopropylidene-α-D-glucofuranose (36) (1) The Bu_2SnO Method: Compound **36** (220 mg) was stannylated and benzoylated with benzoyl chloride (169 mg, 1.2 mol eq) as in the case of tosylation, for 10 min at room temperature. Chromatography of the product gave the 6-*O*-benzoate **38** (244 mg, 75%), as colorless needles from EtOAc, mp 188—191 °C. IR: 3480, 1685. ^{1}H-NMR: 6.30 (1H, d, J=4.0 Hz, H-1), 5.3—4.7 (6H, H-2,3,4,5,6), 1.39, 1.60 (each 3H, s, CMe_2). *Anal.* Calcd for

$C_{16}H_{20}O_7$: C, 59.25; H, 6.22. Found: C, 59.01; H, 6.23.

(2) Direct Benzoylation: Compound **36** (110 mg) in pyridine (2 ml) was benzoylated with benzoyl chloride (1.2 mol eq) for 1.5 h at room temperature to give the 6-*O*-benzoate **38** (80 mg, 49%).

References and Notes

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3) The *O*-tosyl group is not susceptible to migration, and it can be readily and selectively removed by irradiation with 254 nm light without causing other structural changes [R. W. Binkley, *Adv. Carbohydr. Chem. Biochem.*, **38**, 105 (1981)].
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7) Abbreviations: Me = methyl, Ara = arabinopyranoside, Gal = galactopyranoside, Glc = glucopyranoside, Man = mannopyranoside, Xyl = xylopyranoside.
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