Tosylation Reaction of D-Glucuronolactone

Hiroshi Itoh* and Kiyohiko Tajima
The Noguchi Institute, 1-8-1 Kaga, Itabashi-ku, Tokyo 173
(Received September 13, 1982)

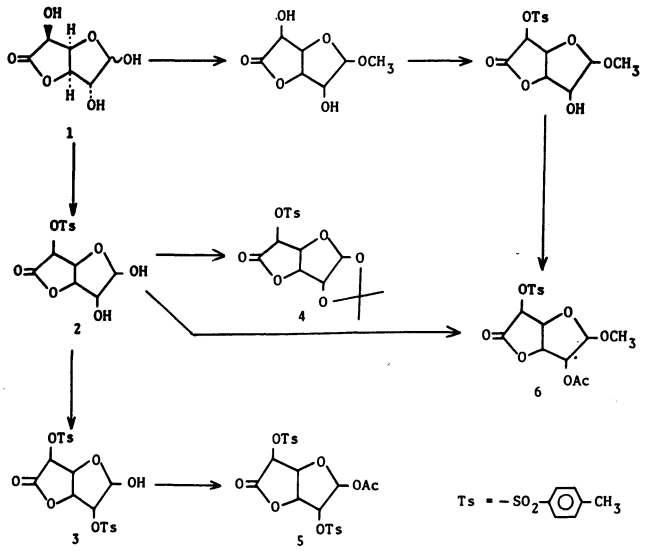
Synopsis. The tosylation reaction of D-glucuronolactone with tosyl chloride in pyridine gave directly 5-*O*-tosyl-D-glucuronolactone and 2,5-di-*O*-tosyl-D-glucuronolactone.

The selective acylation for hydroxyl groups in carbohydrate is important in the synthesis of carbohydrate derivatives. The formation of the quarternary pyridinium salts or chlorination at anomeric carbon take place in the tosylation of carbohydrates having a free glycosidic hydroxyl group with tosyl chloride in pyridine.[1] For example, 2,3,6-tri-*O*-methyl-4-*O*-tosyl-D-glucose or 6-*O*-tosyl-D-glucose was not directly obtained from 2,3,6-tri-*O*-methyl-D-glucose or D-glucose, respectively.[2,3] In continuing the studies about reactions of D-glucuronolactone (**1**), however, 5-*O*-tosyl-D-glucuronolactone (**2**) or 2,5-di-*O*-tosyl-D-glucuronolactone (**3**) was obtained by the direct tosylation of **1** in pyridine with tosyl chloride.

At first, equimolar tosyl chloride was used to afford **2** in 49% yield with a trace of **3**. Compound **2** was also tosylated under the same conditions to give **3** in 39% yield. And then tosylation of **1** with bimolar tosyl chloride gave **2** and **3** in 30 and 31% yields, respectively. The structure of **2** was confirmed by elemental analysis, IR, and ^{1}H-NMR spectra, and by converting it into the isopropylidene derivative, 1,2-*O*-isopropylidene-5-*O*-tosyl-D-glucuronolactone (**4**).[4] The structure of **3** was confirmed by elemental analysis, IR, and ^{1}H-NMR spectra, and by converting it into the acetate, 1-*O*-acetyl-2,5-di-*O*-tosyl-D-glucuronolactone (**5**). The chemical shifts of the ^{1}H-NMR spectra for compounds **1**, **2**, and **3** are listed in the Table. These show the characteristic deshielding effect of the sulfonyl group, the signals of H-2 or H-5 being shifted to lower field. And compound **2** was further methylated and acetylated to give methyl 2-*O*-acetyl-5-*O*-tosyl-D-glucurosiduronolactone (**6**). Compound **6** was also synthesized from methyl D-glucurosiduronolactone by tosylation with equimolar tosyl chloride followed by acetylation. These results indicate a selectivity of the hydroxyl groups in **1** towards tosylation. The order of reactivity HO-5> HO-2 agree well with the result that the degree of hydrogen bonding of HO-5 is higher than that of HO-2.[5]

Table 1. Chemical shifts of ^{1}H-NMR (DMSO-d_6) for compounds **1**, **2**, and **3**

Compound	H-1	H-2	H-3	H-4	H-5 (δ)
1	5.17	3.77	← 4.20—4.90 →		
2	5.23	4.03	← 4.50—4.90 →		5.55
3	5.31	4.67	← 4.60—5.06 →		5.56



Experimental

Melting points are uncorrected. The infrared spectra and ^{1}H-NMR spectra were recorded on a JASCO A-102 spectrometer and a JNM-PMX 60 spectrometer, respectively, under standard conditions.

5-O-Tosyl-D-glucuronolactone (2). To a solution of D-glucuronolactone (**1**) (1.8 g) in pyridine (10 ml) was added dropwise a solution of tosyl chloride (1.9 g) in pyridine (10 ml) within 15 min at 0 °C. The mixture was stirred for 16 h at room temperature, after which time pyridine was evaporated under reduced pressure. The residue was extracted with ethyl acetate–5% HCl solution and the ethyl acetate solution was washed with $NaHCO_3$ aq and water. After evaporation of ethyl acetate, the residue was recrystallized from acetone–petroleum ether to give **2** (1.6 g, 49%) as white needles: mp 183—184 °C. ^{1}H-NMR (DMSO-d_6) δ=2.43 (3H, s), 4.03 (1H, s), 4.50—4.90 (2H, m), 5.23 (1H, d, J=3.6 Hz), 5.46—5.80 (2H, m), 6.75 (1H, d, J=3.6 Hz), 7.68 (4H, m). IR (KBr) 3500, 3420, 1780, 1580, 1175 cm^{-1}. Found: C, 47.20; H, 4.09; S, 9.73%. Calcd for $C_{13}H_{14}O_8S$: C, 47.27; H, 4.27; S, 9.71%.

2,5-Di-O-tosyl-D-glucuronolactone (3). Compound **3** was prepared for 64 h in a similar manner to that described above, using 1.8 g of **1** and 3.8 g of tosyl chloride. After evaporation of ethyl acetate, the residue was extracted with benzene. The insoluble material was **2** (1.0 g, 30%). The soluble material was **3**; it was recrystallized from benzene–petroleum ether twice (1.4 g, 31%) and was further recrystallized from acetone–petroleum ether to give **3** as white curdy crystals having a constant mp of 173—175 °C. ^{1}H-NMR (DMSO-d_6) δ=2.43 (6H, s), 4.60—5.06 (3H, s), 5.31 (1H, d, J=3.2 Hz), 5.56 (1H, d, J=6.4 Hz), 7.37—8.06 (9H, m). IR (KBr) 3460, 1800, 1580 cm^{-1}. Found: C, 49.47; H, 4.07; S, 13.21%. Calcd for $C_{20}H_{20}O_{10}S_2$: C, 49.58; H, 4.16; S, 13.24%.

1,2-O-Isopropylidene-5-O-tosyl-D-glucuronolactone (4). The solution of **2** (0.48 g) in acetone (5 ml) and trifluoroacetic acid (0.5 ml) was refluxed for 20 h. After evaporation of the excess reagent under reduced pressure, the residue was recrystallized from benzene–petroleum ether to give **4** (0.48 g, 90%): mp 187—188 °C (lit,[4] 189—194 °C).

1-O-Acetyl-2,5-di-O-tosyl-D-glucuronolactone (5). Compound **3** was acetylated with acetic anhydride–trifluoroacetic acid (55 °C, 15 h). The obtained **5** was a mixture of α and β

anomers (1 : 4.7).

Methyl 2-O-acetyl-5-O-tosyl-D-glucurosiduronolactone (6). Compound **2** was methylated with methanol–Dowex 50WX2 (R. T. 2 h) and acetylated with acetic anhydride–pyridine (R. T. 2 h) and **6** was recrystallized from acetone–petroleum ether; white needles: mp 121—122.5 °C. ^{1}H-NMR ($CDCl_3$) δ=2.11 (3H, s), 2.48 (3H, s), 3.33 (3H, s), 4.86—5.33 (5H, m), 7.66 (4H, m). IR (KBr) 2920, 1800, 1750, 1590 cm^{-1}.

References

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