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## Note

# A convenient preparation of 3-deoxy-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-β-L-*threo*-pentofuranose

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3-Deoxy-1,2-*O*-isopropylidene-5-*O*-*p*-tolylsulfonyl-β-L-*threo*-pentofuranose (**7**) was required as a precursor for the bulk synthesis of 4′,5′-unsaturated nucleosides[1]. A previous preparation[2] of **7** followed a rather lengthy and somewhat low-yielding pathway. Two of the reactions cause some problems. The formation of an alkene, 3-deoxy-1,2:5,6-di-*O*-isopropylidene-α-D-*erythro*-hex-3-enofuranose, proceeds in only moderate yields, and later on, the selective acid hydrolysis of a 5,6-isopropylidene group to form 3-deoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hexofuranose affords only low to moderate yields thereof. Moreover, this route requires the shortening of the carbon chain by one carbon atom in order to complete the synthesis of the pentofuranose derivative. The commercial availability of moderately priced 1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-α-D-xylofuranose appeared to offer a practicable, shorter route to **7**.

1,2-*O*-Isopropylidene-5-*O*-(methoxycarbonyl)-α-D-xylofuranose (**1**) was treated with triflic anhydride, to yield crystalline 1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-3-*O*-triflyl-α-D-xylofuranose (**2**). For the elimination reaction, 1,8-diazabicyclo[5.4.0]undec-5-ene in ethyl ether[3] was utilized, and 3-deoxy-1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-α-D-*glycero*-pent-3-enofuranose (**3**) was obtained. This compound had previously been prepared by treatment of 1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-α-D-*erythro*-pentofuranos-3-ulose 3-(*p*-tolylsulfonylhydrazone) (**4**) with sodium acetate in hot *N*,*N*-dimethylformamide[4]. Although the spectral data matched the reported data quite well, a sample of **4** was used in order to prepare **3** by the reported method[4]. The i.r. and n.m.r. spectra of the two oils were identical. Catalytic hydrogenation of **3** gave an oil that appeared to be mainly 3-deoxy-1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-β-L-*threo*-pentofuranose (**5**). Base-catalyzed methanolysis afforded crude 3-deoxy-1,2-*O*-isopropylidene-β-L-*threo*-pentofuranose (**6**) as an oil that was tosylated directly, to afford the desired product **7**.

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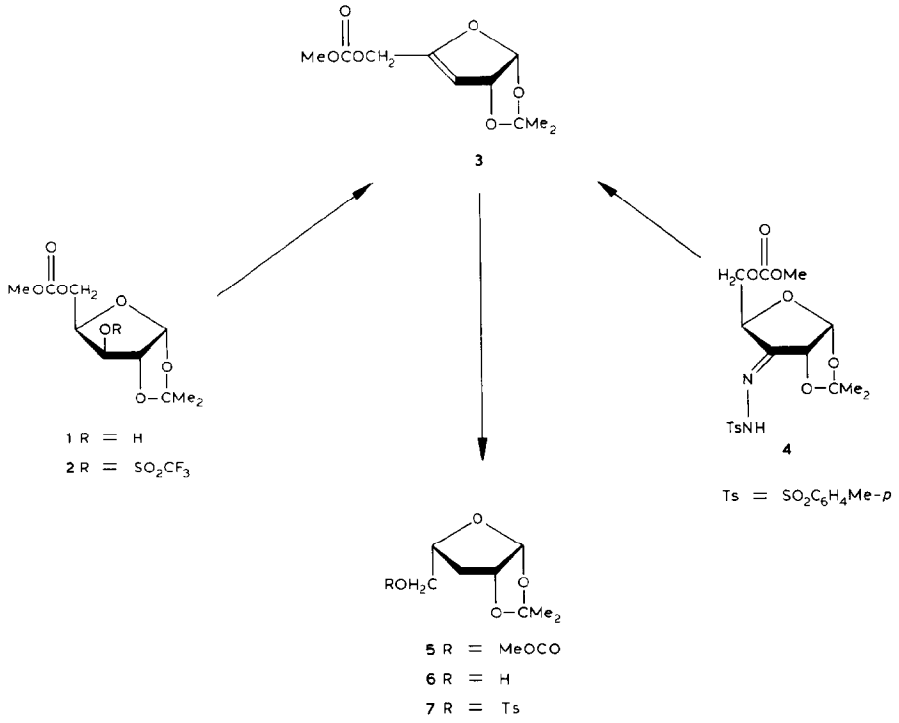


## EXPERIMENTAL

*General methods.* — Melting points were determined with a Kofler micro hot-stage and are corrected values. I.r. spectra were recorded with a Perkin–Elmer Model 21 spectrophotometer, and optical rotations were measured with a Perkin–Elmer Model 141 polarimeter. T.l.c. was performed on 0.25-mm thick layers of silica gel GF-254 (type 60, E. Merck, Darmstadt). Column chromatography was conducted on silica gel, 40–140 mesh (Baker No. 3404). Evaporations were performed in a rotary evaporator under diminished pressure, with a bath temperature of 35–40°. Moist organic solutions were dried with anhydrous magnesium sulfate. The starting material, 1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-α-D-xylofuranose (1), was purchased from Pfanstiehl Laboratories, Inc., Waukegan, Illinois. Elementary analyses were performed by Spang Microanalytical Laboratory, Eagle Harbor, Michigan. $^1$H-N.m.r. spectra were recorded with a Varian T-60A spectrometer. All samples were dissolved in chloroform-*d*, with tetramethylsilane as the internal reference-standard.

*1,2-O-Isopropylidene-5-O-(methoxycarbonyl)-3-O-triflyl-α-D-xylofuranose* (**2**). — The triflation of **1** was based upon the procedure of Flechtner[3]. Triflic anhydride (1 mL) was mixed with dichloromethane (20 mL) in a 50-mL, three-necked flask fitted with a thermometer and a dropping funnel containing dry pyridine (1

mL) in dichloromethane (10 mL). The flask was chilled to −15° with a Dry Ice–ethanol bath. The solution in the funnel was added dropwise, the temperature of the contents of the flask being kept below −10°. Following this, a solution of **1** (1 g) in dichloromethane (10 mL) was slowly added dropwise, while the temperature was kept between −10° and −15°. After all of the **1** had been added, the mixture was stirred for 30 min at the identical temperature, and then poured into a mixture of ice and water (100 mL) containing sodium hydrogencarbonate. This mixture was stirred for 15 min, and the organic layer was separated, successively washed with saturated sodium hydrogencarbonate (100 mL) and water (100 mL), dried, and evaporated. The residual, pale-yellow oil was coevaporated three times with toluene in order to remove traces of pyridine, whereupon the oil crystallized (1.47 g, 96% yield). This crude product was recrystallized from hexane, giving feathery, white needles (1.079 g). A second crop (0.142 g) was obtained from the mother liquor; total yield, 1 221 g (80%). This derivative, when in pure, crystalline form, is markedly stable compared to many other triflate derivatives of monosaccharides, and it may be stored for fairly long periods of time. Some crystals kept on a watch-glass under ambient conditions in the laboratory survived several months before showing signs of deterioration; m.p. 76.5–77.5°. When recrystallized from hexane, it had m.p. 78.5–79°, $[\alpha]_D^{26}$ −20.6° (*c* 1.55, chloroform); $\nu_{max}^{KBr}$ 1752 (carbonyl), 1382, 1370 (*gem*-dimethyl), 1358 (sulfonate), 1160, 1134, 1100, 1083, 1066, and 1037 $cm^{-1}$ (sulfonate and C–O, C–O–C); $^1$H-n.m.r.: $\delta$ 6.03 (d, 1 H, *J* 3 Hz, H-1), 5.28 (d, 1 H, H-3), 4.80 (d, 1 H, *J* 3 Hz, H-2), 4.67–4.55 (m, 1 H, H-4), 4.48–4.25 (m, 2 H, H-5a,5b), 3.82 (s, 3 H, $CH_3OC{=}O$), and 1.52 and 1.35 (both s, 3 H each, *gem*-diMe).

*Anal.* Calc. for $C_{11}H_{15}F_3O_9S$: C, 34.74; H, 3.98; S, 8.43. Found: C, 34.81; H, 3.93; S, 8.54.

In a larger preparation, **1** (10 g) was converted into **2** (14.8 g), and the crude, crystalline product was used in the next step without recrystallization.

*3-Deoxy-1,2-O-isopropylidene-5-O-(methoxycarbonyl)-α-*D-glycero-*pent-3-enofuranose* (**3**). — The entire sample (14.8 g) of **2** from the foregoing preparation was dissolved in ethyl ether (350 mL) and 1,8-diazabicyclo[5.4.0]undec-5-ene (15.3 g) was added. The mixture was stirred at room temperature, and after stirring for ~2 h, an insoluble oil began to settle out. The mixture was stirred for a total of 20 h, and then transferred to a separatory funnel with the aid of ether (70 mL) and water (200 mL). The water layer was removed, and the ether layer was successively washed with 3% aqueous hydrochloric acid solution (2 × 200 mL), water (200 mL), saturated sodium hydrogencarbonate solution (200 mL), and water (200 mL), dried, and evaporated, to afford 7.74 g (84% yield) of a pale-yellow oil; $[\alpha]_D^{26}$ −2.1° (*c* 1.76, chloroform). The i.r. and n.m.r. spectra were identical with those of a sample of **3** obtained by reaction of 1,2-*O*-isopropylidene-5-*O*-(methoxycarbonyl)-α-D-*erythro*-pentofuranos-3-ulose 3-(*p*-tolylsulfonylhydrazone) (**4**) with sodium acetate in hot *N,N*-dimethylformamide[4]; $^1$H-n.m.r.: $\delta$ 6.11 (d, 1 H, H-1), 5.40–5.22 (m, 2 H, H-3,2), 4.68 (s, 2 H, H-5a,5b), 3.80 (s, 3 H, $CH_3OC{=}O$), 1.62 (s, 6 H, *gem*-

diMe); $\nu_{max}^{film}$ 1743 (carbonyl), 1666 (C=C), 1376, 1368 (*gem*-dimethyl), 1153, 1084, and 1043 $cm^{-1}$ (C–O, C–O–C).

*3-Deoxy-1,2-O-isopropylidene-5-O-p-tolylsulfonyl-β-*L-threo-*pentofuranose* (**7**). — The unsaturated derivative **3** (7.7 g) was dissolved in ethanol (200 mL), and hydrogenated at 240 kPa for 24 h in the presence of 5% palladium-on-barium sulfate catalyst (2 g). The mixture was filtered by suction through a pad of Celite-545, and the reaction bottle and pad were washed with ethanol. The filtrate and washings were combined and evaporated, the residue was mixed with dichloromethane (75 mL), the suspension filtered, and the filtrate evaporated, to give clear, colorless oily **5** (5.83 g, 75%), which contained no unreacted **3**, but did have two minor contaminants, as shown by t.l.c. using chloroform (neat), and 9:1 chloroform–methanol. The i.r. spectrum showed that the double bond had disappeared; $\nu_{max}^{film}$ 1744 (carbonyl) and 1370 $cm^{-1}$ (*gem*-dimethyl); $^1$H-n.m.r.: $\delta$ 5.83 (d, H-1), 5.07–4.63 (m, H-2), 4.57–4.13 (complex m, H-4,5a,5b), 3.78 (s, $CH_3C{=}O$), 2.20 (m, H-3a,3b), and 1.57 and 1.33 (both s, *gem*-diMe).

A solution of oil **5** (5.7 g) in 0.05M methanolic sodium methoxide (100 mL) was stirred for 2 h at room temperature, made neutral with Amberlite CG-120 ($H^+$) ion-exchange resin, the resin filtered off, and washed with methanol, and the filtrate and washings were combined and evaporated. The light-brown residue was dissolved in the minimal volume of chloroform, and the solution was chromatographed on a column (30 × 3.8 cm) of silica gel, eluted with 1:19 methanol–chloroform. The first 530 mL of eluate was discarded. The next 200 mL contained the product **6**, and was evaporated; yield of crude **6**, 4.23 g (100%). T.l.c. (9:1 chloroform–methanol) showed two minor spots. The entire product was dissolved in dry pyridine (35 mL), the solution was chilled in an ice-bath, and *p*-toluenesulfonyl chloride (5.1 g) was added. The mixture was stirred in the ice-bath for 0.5 h, and then for 20 h at room temperature. It was rechilled, water (4 mL) was added dropwise, and the mixture was stirred for 1 h at room temperature, poured into cold water, stirred for a few min, and then extracted with chloroform (3 × 50 mL). The extracts were combined, successively washed with sodium hydrogencarbonate (150 mL) and water (200 mL), dried, and evaporated, to give a dark-orange oil that was chromatographed on a column (26 × 3.8 cm) of silica gel using 1:19 methanol–chloroform as the eluant. The fractions containing **7** (detected by t.l.c.) were evaporated, and the product crystallized from ethanol; yield, 2.11 g; m.p. 76.5–77.5°. The m.p. with a sample obtained earlier[1] by another route gave no lowering in m.p., and the i.r. spectra were identical.

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