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Note

Synthesis and reactions of 5-chloro-5-deoxy-L-idose derivatives

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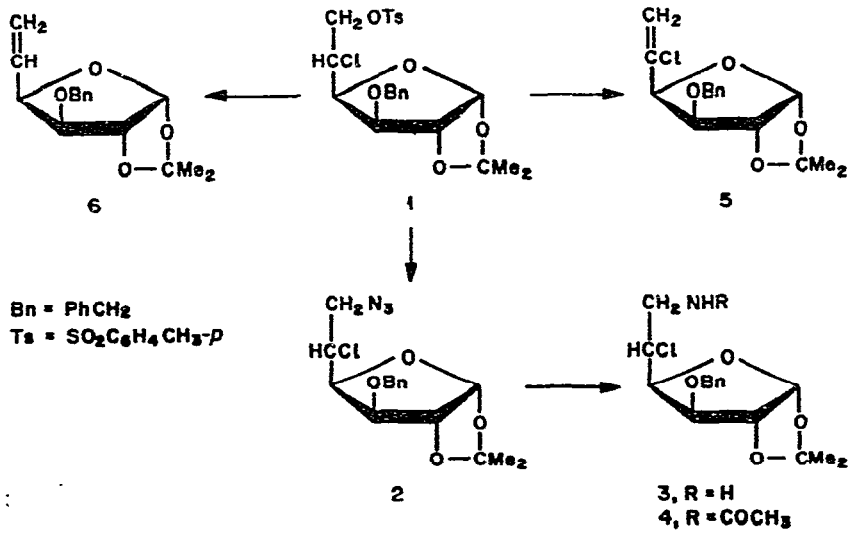
The preparation of chlorodeoxy sugars by the reaction of sulfuryl chloride with carbohydrates containing free hydroxyl groups has been reported[1]. These reactions involve the formation of the chlorosulfuric ester, followed by SN2 displacement by chloride ion[2,3]. Thus, treatment of 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-glucofuranose[4] with sulfuryl chloride[5] afforded 3-*O*-benzyl-5-chloro-5-deoxy-1,2-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-β-L-idofuranose (**1**).

Treatment of **1** with sodium azide in *N*,*N*-dimethylformamide (DMF) for 0.5 h at 100° yielded 6-azido-3-*O*-benzyl-5-chloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**2**). Controlled catalytic hydrogenolysis of **2** in methanol in the presence of palladium–charcoal afforded only 6-amino-3-*O*-benzyl-5-chloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**3**). *N*-Acetylation with acetic anhydride in



methanol gave the crystalline *N*-acetyl derivative, 6-acetamido-3-*O*-benzyl-5-chloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**4**).

Treatment of **1** with sodium methoxide in methanol at 40° afforded a product (**5**) which, in t.l.c., moved faster than the starting material. P.m.r. and i.r. spectra of **5** indicated the absence of hydroxyl and tolylsulfonyl groups. The structure of **5** was established as 3-*O*-benzyl-5-chloro-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-*xylo*-hex-5-enofuranose by analyses of its p.m.r. and mass spectra.

The reaction of **1** with sodium iodide in acetone gave 3-*O*-benzyl-5,6-dideoxy-1,2-*O*-isopropylidene-α-D-xylofuranose (**6**), identical with an authentic sample[6,7].

EXPERIMENTAL

General. — Melting points were determined with a Kofler hot-stage apparatus, and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer 237 spectrophotometer. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. P.m.r. spectra were recorded with a Varian HA-100 instrument for solutions in chloroform-*d*, with tetramethylsilane as the internal standard. Mass spectra were determined with an A.E.I. MS-9 spectrometer, using the direct-insertion technique and an ionizing voltage of 70 eV. Column chromatography was conducted on Silica Gel 60 (70–230 mesh; Merck). T.l.c. was performed on plates precoated with a 250-μm layer of Silica Gel 60 F-254 (Merck) in the following solvent systems (v/v): (*A*) 2:1 petroleum ether–ethyl acetate, (*B*) 4:1 petroleum ether– ethyl acetate, (*C*) 1:1 petroleum ether–ethyl acetate, and (*D*) 4:1 ethyl acetate–methanol. The term "petroleum ether" refers to the fraction of b.p. 100–120°.

3-O-Benzyl-5-chloro-5-deoxy-1,2-O-isopropylidene-6-O-p-tolylsulfonyl-β-L-idofuranose (**1**). — To a solution, cooled in a Dry Ice–acetone bath, of 3-*O*-benzyl-1,2-*O*-isopropylidene-6-*O*-*p*-tolylsulfonyl-α-D-glucofuranose[4] (25 g) in dry pyridine (120 ml) and chloroform (200 ml) was added, dropwise with stirring, freshly distilled sulfuryl chloride (60 ml) during 2 h. The mixture was stirred for a further 2 h at −70°, and for 16 h at room temperature; it was then poured into iced, M sulfuric acid (500 ml), and the solution was extracted four times with chloroform. The extracts were combined, washed successively with saturated sodium hydrogen carbonate solution and water, dried (sodium sulfate), and evaporated to a syrup (25 g). The product was purified by column chromatography (solvent *B*), and was obtained as a solid. Recrystallization from petroleum ether–ethyl acetate gave **1** as colorless needles (23 g, 89%), m.p. 101°, $[\alpha]_D^{20}$ −30° (*c* 2.3, chloroform); R_F 0.44 (solvent *A*); $\nu_{max}^{CHCl_3}$ 1383 and 1375 cm^{-1} (CMe_2), no absorption attributable to OH; mass spectrum: *m/e* 467 ($M^+ - CH_3$); p.m.r. data: τ 2.30 and 2.72 (2-proton doublets, tosyl-C_6H_4), 2.70 (*m*, 5 protons, benzyl-C_6H_5), 4.12 (*d*, 1 proton, $J_{1,2}$ 3.8 Hz, H-1), 5.3–5.8 (*m*, 8 protons, H-2,3,4,5,6,6′, benzyl-CH_2), 6.00 (*d*, 1 proton, H-3), 7.59 (*s*, 3 protons, tosyl-CH_3), and 8.53 and 8.71 (3-proton singlets, CMe_2).

Anal. Calc. for $C_{23}H_{27}ClO_7S$: C, 57.2; H, 5.6; Cl, 7.3; S, 6.6. Found: C, 57.3; H, 5.5; Cl, 7.5; S, 6.5.

6-Azido-3-O-benzyl-5-chloro-5,6-dideoxy-1,2-O-isopropylidene-β-L-idofuranose (**2**). — To a solution of compound **1** (5.0 g) in dry DMF (10 ml) was added sodium azide (1.0 g). The mixture was stirred for 0.5 h at 100°, chloroform was added, the suspension was filtered, and the filtrate was evaporated to a syrup which was dissolved in chloroform, washed with water, dried (sodium sulfate), and evaporated to afford the product (**2**) as a syrup (3.6 g, 98%); R_F 0.54 (solvent *A*), $[\alpha]_D^{20}$ −67° (*c* 2.7, chloroform); ν_{max}^{film} 2100 (N_3), and 1383 and 1374 cm^{-1} (CMe_2), no absorption attributable to OH; mass spectrum: *m/e* 338 ($M^+ - CH_3$); p.m.r. data: τ 2.68 (*m*, 5 protons, C_6H_5), 4.06 (d, 1 proton, $J_{1,2}$ 3.8 Hz, H-1), 5.2–5.8 (*m*, 5 protons, H-2,4,5, benzyl-CH_2), 6.03 (*d*, 1 proton, H-3), 6.57 (*m*, 2 protons, H-6,6′), and 8.50 and 8.68 (3-proton singlets, CMe_2).

Anal. Calc. for $C_{16}H_{20}ClN_3O_4$: C, 54.3; H, 5.7; Cl, 10.0; N, 11.9. Found: C, 54.0; H, 5.5; Cl, 10.1; N, 11.6.

6-Acetamido-3-O-benzyl-5-chloro-5,6-dideoxy-1,2-O-isopropylidene-β-L-idofuranose (**4**). — To a solution of compound **2** (1.2 g) in methanol (20 ml) was added palladium-on-charcoal (10%, 300 mg), and the mixture was shaken for 2 h under hydrogen (1 atm.). T.l.c. (solvent *C*) then showed that one major product had formed. The mixture was filtered, and the filtrate was evaporated to a syrup. A solution of the syrup in chloroform was extracted with M sulfuric acid. The aqueous extract was made alkaline with M sodium hydroxide, and extracted with chloroform. The extract was washed with water, dried (sodium sulfate), and evaporated to give 6-amino-3-*O*-benzyl-5-chloro-5,6-dideoxy-1,2-*O*-isopropylidene-β-L-idofuranose (**3**) as a syrup (868 mg, 78%); R_F 0.71 (solvent *D*); ν_{max}^{film} 3380, 3310 (NH_2), and 1382 and 1372 cm^{-1} (CMe_2); mass spectrum: *m/e* 312 ($M^+ - CH_3$).

Compound **3** was further characterized as its *N*-acetyl derivative. To a solution of **3** in methanol was added acetic anhydride, and the mixture was kept for 0.5 h at room temperature. Pyridine was added, and the solvents were removed under diminished pressure. The residue was partitioned between chloroform and M sulfuric acid; the chloroform layer was successively washed with saturated sodium hydrogen carbonate solution and water, dried (sodium sulfate), and evaporated to a syrup which crystallized on standing. Recrystallization from petroleum ether–ethyl acetate afforded compound **4** as colorless needles, m.p. 160°, $[\alpha]_D^{20}$ −12° (*c* 2.1, chloroform); R_F 0.86 (solvent *D*); ν_{max}^{KBr} 3330 (NH), 1648 (Amide I), 1540 (Amide II), and 1383 and 1374 cm^{-1} (CMe_2); mass spectrum; *m/e* 354 ($M^+ - CH_3$); p.m.r. data: τ 2.68 (*s*, 5 protons, C_6H_5), 3.93 (*t*, 1 proton, D_2O exchangeable, NH), 4.07 (*d*, 1 proton, $J_{1,2}$ 3.9 Hz, H-1), 5.3–6.4 (*m*, 8 protons, H-2,3,4,5,6,6′, benzyl-CH_2), 8.02 (*s*, 3 protons, NAc), and 8.53 and 8.70 (3-proton singlets, CMe_2).

Anal. Calc. for $C_{18}H_{24}ClNO_5$: C, 58.5; H, 6.5; Cl, 9.6; N, 3.8. Found: C, 58.6; H, 6.5; Cl, 9.5; N, 3.6.

3-O-Benzyl-5-chloro-5,6-dideoxy-1,2-O-isopropylidene-α-D-xylo-hex-5-enofuranose (**5**). — To a solution of compound **1** (6.0 g) in methanol (200 ml) was added 0.5M sodium methoxide (400 ml), and the solution was stirred for 48 h at 40°. The mixture was made neutral with solid carbon dioxide, and filtered, and the filtrate was

evaporated. The residue was partitioned between chloroform and water, and the aqueous solution was extracted three times with chloroform. The extracts were combined, washed with water, dried (sodium sulfate), and evaporated to a syrup (3.3 g). The crude product was applied to a column of silica gel, and eluted with solvent *B*, yielding **5** as a colorless syrup (2.7 g, 70%), R_F 0.64 (solvent *A*), $[\alpha]_D^{20}$ −24° (*c* 2.7, chloroform); ν_{max}^{film} 1385 and 1375 cm^{-1} (CMe_2), no absorption attributable to OH; mass spectrum: *m/e* 295 ($M^+ - CH_3$); p.m.r. data: τ 2.67 (*m*, 5 protons, C_6H_5), 4.03 (*d*, 1 proton, $J_{1,2}$ 3.7 Hz, H-1), 4.30 (*t*, 1 proton, $J_{4,6}$ 1.6 Hz, $J_{6,6'}$ 1.6 Hz, H-6), 4.56 (*t*, 1 proton, $J_{4,6'}$ 1.6 Hz, H-6'), 5.29 (*m*, 1 proton, $J_{3,4}$ 3.0 Hz, H-4), 5.37 (*s*, 2 protons, benzyl-CH_2), 5.43 (*d*, 1 proton, $J_{2,3}$ ~0 Hz, H-2), 5.87 (*d*, 1 proton, H-3), and 8.49 and 8.67 (3-proton singlets, CMe_2).

Anal. Calc. for $C_{16}H_{19}ClO_4$: C, 61.8; H, 6.2; Cl, 11.4. Found: C, 61.6; H, 6.0; Cl, 11.2.

3-O-Benzyl-5,6-dideoxy-1,2-O-isopropylidene-α-D-xylo-hex-5-enofuranose (**6**). — To a solution of compound **1** (0.5 g) in acetone (50 ml) was added sodium iodide (0.5 g). The mixture was boiled for 20 h under reflux, evaporated, and the residue partitioned between chloroform and water. The chloroform extract was successively washed with sodium thiosulfate solution and water, dried (sodium sulfate), and evaporated, to afford **6** (refs. 6 and 7) as a syrup (240 mg, 84%), R_F 0.60 (solvent *A*), $[\alpha]_D^{20}$ −57° (*c* 3.5, chloroform); ν_{max}^{film} 1385 and 1375 cm^{-1} (CMe_2), no absorption attributable to OH; mass spectrum: *m/e* 261 ($M^+ - CH_3$); p.m.r. data: 2.72 (*m*, 5 protons, C_6H_5), 3.99 (*m*, 1 proton, $J_{4,5}$ 7.0 Hz, $J_{5,6}$ 16 Hz, $J_{5,6'}$ 10.5 Hz, H-5), 4.07 (*d*, 1 proton, $J_{1,2}$ 3.8 Hz, H-1), 4.62 (*q*, 1 proton, $J_{6,6'}$ 1.5 Hz, H-6), 4.74 (*q*, 1 proton, H-6'), 5.40 (*m*, 2 protons, H-2,4), 5.42 (*s*, 2 protons, benzyl-CH_2), 6.14 (*d*, 1 proton, $J_{3,4}$ 3.2 Hz, H-3), and 8.52 and 8.70 (3-proton singlets, CMe_2).

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