Note

Nucleophilic replacement reactions of sulphonates Part VIII[1] Methyl 2-benzamido-2-deoxy-6-*O*-tosyl-α-D-glucopyranoside, and its conversion into 6-deoxy and other derivatives

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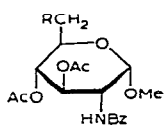
Selective tosylation of methyl 2-benzamido-2-deoxy-α-D-glucopyranoside in pyridine at room temperature affords[1] a mixture of the 6-sulphonate and the 3,6- and 4,6-disulphonates. Conditions have now to be sought for an improved yield of the 6-sulphonate which could be an important intermediate in the synthesis of 2-amino-2,6-dideoxy-D-glucose (D-chinovosamine) derivatives, previously isolated from bacterial polysaccharides[2] and synthesised by the amino nitrile method from 5-deoxy-L-arabinose[3] and also from a 6-sulphonate derivative by iodide displacement and subsequent reduction[4] The conversion of the 6-sulphonate into other 6-substituted derivatives and into unsaturated, exocyclic vinyl ethers has also been investigated in view of their potential importance as synthetic and biological intermediates in medicinal chemistry



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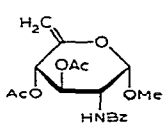
3 R = N_3
4 R = H



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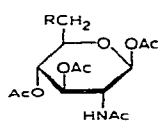
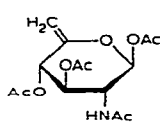


6 R = OTs
7 R = I
9 R = H



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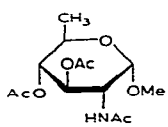

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Treatment of methyl 2-benzamido-2-deoxy-α-D-glucopyranoside[5] with toluene-*p*-sulphonyl chloride in pyridine at −10° afforded a syrupy product which, on acetylation, gave crystalline methyl 3,4-di-*O*-acetyl-2-benzamido-2-deoxy-6-*O*-tosyl-α-D-glucopyranoside (**1**) in 39% overall yield The 6-sulphonate **1** underwent nucleophilic displacement with sodium iodide in butanone to give the 6-deoxy-6-iodo compound **2** Similarly, with sodium azide in a mixture of butanone and *N*,*N*-dimethylformamide,

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1 gave the 6-azido-6-deoxy derivative **3**, a precursor of 2,6-diamino-2,6-dideoxy-D-glucose derivatives[6]

Reductive dehalogenation of the 6-iodo derivative **2**, either by shaking with Raney nickel in the presence of triethylamine in an atmosphere of hydrogen, or by refluxing with excess of Raney nickel in ethanol, gave the corresponding 6-deoxy compound **4**.

Elimination of hydrogen iodide from the 6-iodo derivative **2** and from 2-acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-6-iodo-β-D-glucopyranose[4], by treatment with silver fluoride in pyridine[7], afforded the exocyclic vinyl ethers methyl 3,4-di-*O*-acetyl-2-benzamido-2,6-dideoxy-α-D-*xylo*-hex-5-enopyranoside (**5**) and 2-acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-β-D-*xylo*-hex-5-enopyranose (**8**) Hydrogenation of the 5-ene **8**, using platinum oxide as catalyst, afforded exclusively 2-acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-β-D-glucopyranose[4] (**9**) The absence of the L-*ido* isomer showed that hydrogenation had occurred exclusively by axial attack at C-5, as observed in similar cases[8]

The structure of the 2,6-dideoxy-2-benzamido derivative **4** was confirmed by relating it to the known[4] 2-acetamido derivative **9** Saponification of **4**, followed by acetylation, gave methyl 2-acetamido-3,4-di-*O*-acetyl-2,6-dideoxy-α-D-glucopyranoside (**10**) Treatment of 2-acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-β-D-glucopyranose (**9**) with cation-exchange resin (H^+ form) in boiling, dry methanol, with subsequent reacetylation, gave the methyl α-D-glucoside **10**, which was identical with that obtained by the preceding route

EXPERIMENTAL

The general experimental data are as described previously[11]

Methyl 3,4,6-*tri*-O-*acetyl*-2-*benzamido*-2-*deoxy*-α-D-*glucopyranoside* — Methyl 2-benzamido-2-deoxy-α-D-glucopyranoside[5] (1 5 g) in pyridine (30 ml) was treated with acetic anhydride (5 ml) at room temperature for 24 h After addition of a little water, the solution was concentrated, and a solution of the syrupy residue in chloroform was washed successively with 2M hydrochloric acid, water, aqeuous sodium hydrogen carbonate, and water The pyridine-free chloroform solution was dried (Na_2SO_4) and concentrated to a syrup which gave the tri-acetate (1 6 g, 74%), m p 109–110° (from ethanol), $[\alpha]_D$ +122 8° (*c* 1 25, methylene chloride) (Found C, 57 0, H, 6 0, N, 3 3 $C_{20}H_{25}NO_9$ calc C, 56 6, H, 6 0, N, 3 4%)

Methyl 3,4-di-O-*acetyl*-2-*benzamido*-2-*deoxy*-6-O-*tosyl*-α-D-*glucopyranoside* (**1**) — To a cooled (−10°) solution of methyl 2-benzamido-2-deoxy-α-D-glucopyranoside[5] (7 g) in pyridine (150 ml), a solution of toluene-*p*-sulphonyl chloride (8 2 g) in pyridine (20 ml) was added dropwise during 0 5 h The reaction mixture was then stored at −5° for 24 h A little ice–water was added to decompose the excess of toluene-*p*-sulphonyl chloride, and after storage for 1 h at room temperature, the solution was concentrated A solution of the syrupy residue in chloroform was washed successively with 2M hydrochloric acid, water, aqueous sodium hydrogen carbonate, and water,

dried (Na_2SO_4), and concentrated The resulting, dry syrup was actylated in pyridine (50 ml), using acetic anhydride (4 ml) at room temperature for 24 h The reaction mixture was poured on to ice–water and extracted with chloroform, the extract was concentrated, and the residue was taken up again in chloroform The traces of pyridine were removed as described previously to give (from ethanol) the 6-sulphonate **1** (7 g, 39%), m p 129–131°, $[\alpha]_D$ +115 6° (*c* 1 43, chloroform) Found C, 55 6, H, 5 4, N, 2 6, S, 6 0 $C_{25}H_{29}NO_{10}S$ calc C, 56 1, H, 5 4, N, 2 6; S, 5 9%)

N m r data τ 5 3 (*d*, 1 proton, $J_{1,2}$ 3 5 Hz, H-1), 5 6 (1 proton, $J_{2,3}$ 9 3 Hz, H-2), 4 72 (*t*, 1 proton, $J_{3\,4}$ 9 3 Hz, H-3), 5 06 (*q*, 1 proton, $J_{4\,5}$ 8 2 Hz, H-4), 5 94 (*m*, 2 protons, H-6, H-6'), 3 7 (*d*, 1 proton, $J_{NH\,CH}$ 9 3 Hz, H–N), 6 69 (*s*, 3 protons, OMe), 7 56 (*s*, 3 protons, Me–Ph), 8 02 and 8 07 (*s*, 6 protons, 2Ac)

Methyl 3,4-di-O-acetyl-6-azido-2-benzamido-2,6-dideoxy-α-D-glucopyranoside (**3**) — A solution of the 6-sulphonate **1** (1 g) in butanone–*N*,*N*-dimethylformamide (50 ml, 10 1) containing sodium azide (500 mg) was heated at 105° for 40 h T l c (ether–light petroleum, 3 2) indicated a fast-moving product The sodium toluene-*p*-sulphonate was filtered off, the filtrate was concentrated to dryness, and the traces of *N*,*N*-dimethylformamide were removed by storing at 30° *in vacuo* A solution of the residue in chloroform was washed with water, dried (Na_2SO_4), and concentrated to a syrup, which gave the 6-azide **3** (700 mg, 89%), m p 101–102° (from ether–light petroleum), $[\alpha]_D$ +124 6° (*c* 1 93, chloroform) (Found C, 53 4, H, 5 4, N, 13 6 $C_{18}H_{22}N_4O_7$ calc C, 53 2, H, 5 4, N, 13 8%)

N m r data τ 5 22 (*d*, 1 proton, $J_{1\,2}$ 3 7 Hz, H-1), 4 72 (*t*, 1 proton, $J_{3\,4}$ 9 7 Hz, H-3), 5 02 (*t*, 1 proton, $J_{4\,5}$ 9 7 Hz, H-4), 6 15 (*sx*, 1 proton, $J_{5\,6}$ 4 9 Hz, H-5), 3 7 (*d*, 1 proton, $J_{NH\,CH}$ 9 7 Hz, H–N), 6 62 (*s*, 3 protons, OMe), 7 98 and 8 07 (*s*, 6 protons, 2 Ac)

Methyl 3,4-di-O-acetyl-2-benzamido-2,6-dideoxy-6-iodo-α-D-glucopyranoside (**2**). — A solution of the 6-sulphonate **1** (2 g) in butanone (50 ml) containing sodium iodide (1 5 g) was refluxed for 24 h Precipitated sodium toluene-*p*-sulphonate was filtered off, and the filtrate concentrated to dryness The residue was partitioned between water and chloroform, and the organic layer was washed with aqueous sodium thiosulphate and water, dried (Na_2SO_4), and concentrated to give the 6-iodo derivative **2** (1 8 g, 95%), m p 144–145° (from ethanol–light petroleum), $[\alpha]_D$ +101 5° (*c* 2 0, chloroform) (Found C, 44 0, H, 4 5, I, 26 0, N, 3 1 $C_{18}H_{22}INO_7$ calc C, 44 0, H, 4 5, I, 25 9, N, 2 85%)

N m r data τ 5 11 (*d*, 1 proton, $J_{1\,2}$ 3 2 Hz, H-1), 5 46 (*sx*, 1 proton, $J_{2\,3}$ 9 7 Hz, H-2), 4 98 (*t*, 1 proton, $J_{3,4}$ 9 7 Hz, H-3), 6 7 (2 protons, H-6 and H-6'), 3 59 (*d*, 1 proton, $J_{NH\,CH}$ 9 7, H–N), 6 5 (*s*, 3 protons, OMe), 7 9 and 8 0 (2*s*, 6 protons, 2 Ac)

Methyl 3,4-di-O-acetyl-2-benzamido-2,6-dideoxy-α-D-glucopyranoside (**4**) — (*a*) A solution of **2** (1 g) in ethyl acetate (10 ml) containing triethylamine (0 11 ml) was hydrogenated in the presence of Raney nickel at room temperature and normal pressure T l c (ether–light petroleum 1 1) revealed that the reaction was complete after 24 h The catalyst was filtered off and the filtrate concentrated to dryness A solution of the residue in chloroform was washed successively with 2M hydrochloric

acid, water, aqueous sodium hydrogen carbonate, and water, dried (Na_2SO_4), and concentrated The syrupy residue gave **4** (550 mg, 73%), m p 123–124° (from ether–light petroleum), $[\alpha]_D$ +146 6° (*c* 3 54, methylene chloride) (Found C, 59 4, H, 6 4, N, 4 0 $C_{18}H_{23}NO_7$ calc C, 59 2, H, 6 3, N, 3 8%)

N m r data τ 5 23 (*d*, 1 proton, $J_{1,2}$ 3 3 Hz, H-1), 5 61 (*sx*, 1 proton, $J_{2,3}$ 9 5 Hz, H-2), 4 67 (*t*, 1 proton, $J_{3,4}$ 9 5 Hz, H-3), 4 08 (*t*, 1 proton, $J_{4,5}$ 9 5 Hz, H-4), 6 17 (*o*, 1 proton, $J_{5,6}$ 6 3, H-5), 3 57 (*d*, 1 proton, $J_{NH,CH}$ 9 5 Hz, H–N), 6 61 (*s*, 3 protons, OMe), 8 79 (*d*, 3 protons, $J_{5,6}$ 6 3 Hz, Me-5), 7 93 and 8 01 (*s*, 6 protons, 2 Ac)

(*b*) A solution of the 6-iodo derivative **2** (500 mg) in ethanol (50 ml) was refluxed with freshly prepared Raney nickel (*ca* 3 g) for 5 h The catalyst was filtered off and the filtrate concentrated to dryness The residue was partitioned between water and chloroform The organic layer was dried (Na_2SO_4) and concentrated, and the residue was crystallised from ether–light petroleum to give **4** (250 mg, 73%)

*Methyl 3,4-di-O-acetyl-2-benzamido-2,6-dideoxy-α-*D-xylo-*hex-5-enopyranoside* (**5**) — A mixture of the 6-iodide **2** (2 g) and anhydrous silver fluoride (2 g) in pyridine (15 ml) was shaken at room temperature for 20 h The reaction mixture was then diluted with ether and the supernatant layer decanted The inorganic residue was extracted with ether, and the combined extracts were filtered through "Hyflo", diatomaceous earth The filtrate was concentrated by co-distillation with toluene, and the traces of pyridine were removed by storing overnight at 30° *in vacuo* A solution of the residue in ether was decolourised by passage through a small column of silica gel and then concentrated to afford the 5-ene **5** (600 mg, 42%), m p 118–119° (from ether–light petroleum), $[\alpha]_D$ +118° (*c* 1 65, chloroform) (Found C, 60 2, H, 6 1, N, 3 9 $C_{18}H_{21}NO_7$ calc C, 59 5, H, 5 8, N, 3 9%)

N m r data τ 5 14 (*d*, 1 proton, $J_{1,2}$ 3 1 Hz, H-1), 4 73 (*t*, 1 proton, $J_{3,4}$ 9 5 Hz, H-3), 4 45 (*d*, 1 proton, $J_{4,5}$ 9 5 Hz, H-4), τ 3 6 (*d*, 1 proton, $J_{NH,CH}$ 9 5 Hz, H–N), 6 6 (*s*, 3 protons, OMe), 7 88 and 8 03 (*s*, 6 protons, 2 Ac)

*2-Acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-β-*D-xylo-*hex-5-enopyranose* (**8**) — A solution of 2-acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-6-iodo-β-D-glucopyranoside[4] (2 g) in pyridine was shaken with anhydrous silver fluoride (2 g) at room temperature The reaction was worked up as described previously to give **8** (1 g, 70%), m p 197–198° (from ethanol), $[\alpha]_D$ −37° (*c* 1 0, chloroform) (Found C, 50 9, H, 5 7, N, 4 35 $C_{14}H_{19}NO_8$ calc C, 51 1, H, 5 8; N, 4 25%)

N m r data τ 4 1 (*d* 1, proton, $J_{1,2}$ 5 5 Hz, H-1), 5 58 (*o*, 1 proton, $J_{2,3}$ 7 2 Hz, H-2), 4 93 (*t*, 1 proton, $J_{3,4}$ 7 2 Hz, H-3), 4 44 (*d*, 1 proton, $J_{4,5}$ 7 2 Hz, H-4), 3 62 (*d*, 1 proton, $J_{NH,CH}$ 9 3 Hz, H–N), 7 84, 7 88, 7 91, and 8 01 (*s*, 12 protons, 4 Ac) H-4 showed allylic long-range coupling[10,11]

*2-Acetamido-1,3,4-tri-*O*-acetyl-2,6-dideoxy-β-*D-glucopyranose* (**9**) — A solution of the 5-ene **8** (1 g) in ether (70 ml) was hydrogenated in the presence of Adams' platinum oxide catalyst at room temperature and normal pressure T l c (chloroform–acetone, 4 1) indicated that the reaction was complete after 20 h. The catalyst was filtered off and the filtrate concentrated to give the 2,6-dideoxy derivative **9** (600 mg,

60%), m p 213–214° (from ether–light petroleum), $[\alpha]_D$ +14.5° (*c* 1.0, chloroform), lit[4] m p 209–210°, $[\alpha]_D$ +17 5° (*c* 1 0, chloroform)

N m r data, τ 4 26 (*d*, 1 proton, $J_{1,2}$ 8 7 Hz, H-1), 5 69 (*q*, 1 proton, $J_{2\,3}$ 9 6 Hz, H-2), 4 76 (*t*, 1 proton, $J_{3\,4}$ 9 6 Hz, H-3), 5 1 (*t*, 1 proton, $J_{4,5}$ 9 6 Hz, H-4), 3 67 (*d*, 1 proton, $J_{NH\,CH}$ 9 7, H–N), 8 23 (*d*, 3 protons, *J* 6 4 Hz, Me-5), 7 86, 7 9, 8 01, and 8 04 (*s*, 12 protons, 4 Ac)

*Methyl 2-acetamido-3,4-*O*-acetyl-2,6-dideoxy-α-*D*-glucopyranoside* (**10**) — (*a*) A solution of the 2-benzamido derivative **4** (500 mg) in M sodium hydroxide (50 ml) was heated at 115° for 19 h The cooled solution was then extracted with chloroform continuously for 20 h, and the extract was washed with water, dried (Na_2SO_4), and concentrated The dry syrup was acetylated in the usual way with pyridine–acetic anhydride, at room temperature for 24 h, to give the 2-acetamido derivative **10** (148 mg, 39%), m p. 150–151° (from ether–light petroleum), $[\alpha]_D$ +111 1° (*c* 1 07, chloroform) (Found C, 51 6, H, 6 6, N, 4 7 $C_{13}H_{21}NO_7$ calc · C, 51 5, H, 6 9, N, 4 6%)

N m r data τ 5 36 (*d*, 1 proton, $J_{1\,2}$ 3 4 Hz, H-1), 5 74 (*sx*, 1 proton, $J_{2\,3}$ 9.4 Hz, H-2), 4 83 (*t*, 1 proton, $J_{3,4}$ 9 4 Hz, H-3), 5 19 (*t*, 1 proton, $J_{4,5}$ 9 4 Hz, H-4), 4.14 (*d*, 1 proton, $J_{NH\,CH}$, 9 4 Hz, H–N), 6 62 (*s*, 3 protons, OMe), 8 82 (*d*, 3 protons, $J_{5,6}$ 6 1 Hz, Me-5), 8 0, 8 01, and 8 05, (*s*, 9 protons, 3 Ac)

(*b*) A solution of the 1,3,4-triacetate **9** (1 2 g) in dry methanol containing Amberlite IR-120 (H^+) resin (10 g) was refluxed for 48 h The resin was filtered off, and the filtrate was concentrated and dried overnight at 30° *in vacuo* The residue in pyridine (20 ml) was then treated with acetic anhydride (6 ml) at room temperature for 24 h The reaction was worked up as described previously to give a syrup which, on crystallisation from ether–light petroleum afforded **10** (800 mg, 73%), m p and mixed m p 150–151°, $[\alpha]_D$ +112° (*c* 1 4, methylene chloride) The n m r. spectrum was identical with that of the product from (*a*)

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