Preparation of Some 2-Bromo-2-deoxy-D-hexopyranoses

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Dedicated to Professor K. A. Jensen on his 70th birthday

The zinc bromide catalyzed reaction of tetra-O-acetyl-α-D-glucopyranosyl bromide (1a) with acetyl bromide gives tri-O-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (2a). A similar treatment of tri-O-acetyl-1,6-deoxy-α-L-glucopyranosyl bromide (4a) yields di-O-acetyl-2-bromo-2,6-dIDEOXY-α-L-glucopyranosyl bromide (7a). An analogous reaction takes place with the corresponding benzoylated pyranosyl bromides. The 2-bromo-2-deoxy bromides form 2-bromo-1,2-dideoxy-hex-1-enopyranoses on treatment with triethylamine.

In previous work it was shown that reaction of tri-O-acetyl-D-xylopyranosyl bromide with acetyl bromide and zinc bromide led to the formation of di-O-acetyl-2-bromo-2-deoxy-D-xylopyranosyl bromide in moderate yield. A better yield was obtained when the corresponding benzoylated bromide was treated with benzoyl bromide. Other acetylated or benzoylated pentopyranosyl bromides did not give bromo-deoxy-pentoses by this treatment.
The reaction of some acetylated and benzoylated hexopyranosyl bromides with acetyl bromide and zinc bromide has now been studied. When tetra-O-acetyl-α-D-glucopyranosyl bromide (1a) was treated with anhydrous zinc bromide and acetyl bromide it was converted into tri-O-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (2a). After ca. 20 h at room temperature the reaction mixture no longer contained 1a. When the mixture was worked up 2a could be crystallized in ca. 30 % yield. An NMR spectrum showed that the material in the mother liquor contained rather large amounts of 2a and the α-1-acetate (3); besides, some of the unsaturated compound (5a) was present. Treatment with hydrogen bromide converted the 1-acetate (3) into the bromide (2a) and after this treatment additional amounts of 2a could be obtained. Treatment of the mother liquor from this product with silver benzoate yielded ca. 10 % of the known β-1-benzoate (6). The 1-acetate (3) is probably formed by zinc bromide catalyzed reaction of 2a with acetic anhydride; the latter arising from the acetic acid cleaved off from 1a.

It was found necessary to use a rather large amount of zinc bromide to catalyse the reaction of 1a with acetyl bromide. With smaller amounts of zinc bromide the reaction was slower and coloured by-products were formed. No reaction took place when 1a was treated with acetyl bromide in the presence of boron trifluoride or aluminium tribromide.

The dibromo compound (2a) has been previously obtained, together with isomers, by addition of bromine to tri-O-acetyl-1,2-dideoxy-D-arabino-hex-1-enopyranose. The reaction described above gave 2a as the only detectable bromo-deoxy bromide.

A similar treatment of tri-O-acetyl-6-deoxy-α-L-glucopyranosyl bromide (4a) gave the 2-bromo-2-deoxy bromide (7a) in ca. 50 % yield. The benzoylated bromides, 1b and 4b, also reacted with acetyl bromide and zinc bromide to give the corresponding 2-bromo-compounds 2b and 8b, respectively, in yields comparable to those obtained with the acetates.

Attempts to prepare bromo-deoxy compounds from acetylated galacto- or manno-pyranosyl bromides were unsuccessful. In the pentose series it was also found that only xylopyranosyl bromide gives a bromo-deoxy bromide. Thus, only pyranosyl bromides with the substituents at C2, C3, and C4 trans-oriented react with acetyl bromide and zinc bromide.

The mechanism for the formation of 2 from 1, or 7 from 4, is probably the same as that proposed for the reaction of tri-O-acetyl-D-xylopyranosyl bromide with acetyl bromide-zinc bromide, and for the reaction of pentosyl bromides with dibromomethyl methyl ether. The latter reagent is not, however, suited for the preparation of bromo-deoxy-hexoses.

The bromides 2a and 2b, as well as 7a and 7b, eliminated hydrogen bromide readily when treated with triethylamine to give the 1,2-unsaturated products 5a and 5b and 8a and 8b, respectively. The latter compounds rearrange to 2,3-unsaturated bromides with acetyl bromide. This will be described in a forthcoming paper.

EXPERIMENTAL

Melting points are uncorrected. Preparative TLC was performed on 1 mm layers of silica gel (Merck PF6). 1H NMR spectra were measured on Varian HA-100 or on Bruker HX-90E instruments in deuteriochloroform solution using tetramethylsilane as internal reference. Optical rotations were measured in chloroform solution on a Perkin Elmer 141 instrument. Tri-O-acetyl-2-bromo-2-deoxy-α-D-glucopyranosyl bromide (2a). A mixture of tetra-O-acetyl-α-D-glucopyranosyl bromide (1a) (10.0 g), anhydrous zinc bromide (20 g), and acetyl bromide (25 ml) was stirred at room temperature for 20 h. A 1H NMR spectrum of a sample then showed that the major component present was 2a; besides, signals corresponding to smaller amounts of the α-1-acetate (3) and of the unsaturated compound (5a) were seen. The starting material (1a) was no longer present. The mixture was diluted with dichloromethane (100 ml) and poured on ice. The organic phase was washed three times with 4 N hydrochloric acid and once with aqueous NaHCO3, dried, filtered through carbon, and evaporated. The syrupy residue was crystallized from ether-pentane to give 3.0 g (28.5 %) of 2a, m. p. 85 °C.

To the material in the mother liquor was added 15 ml of a 30 % solution of hydrogen bromide in glacial acetic acid and the mixture was kept for 1 h at room temperature. Dichloromethane was then added and the solution was washed with water and aqueous NaHCO3, dried and evaporated. The residue was crystallized from ether-pentane to give an additional 2.8 g of 2a, bringing the total yield to 55 %. The product was sufficiently pure for most purposes, but could be recrystallized from ether-pentane, or from cyclohexane.

The material in the mother liquor contained some 2a as seen from an NMR spectrum. It was dissolved in acetonitrile and stirred with silver benzoate for 3 h. Filtration through carbon and evaporation gave a yellow syrup which was dissolved in dichloromethane and washed with aqueous NaHCO3. The solvent was evaporated and the residue was crystallized from ether-pentane to give 800 mg (12 %) of tri-O-acetyl-1-O-benzoyl-2-bromo-2-deoxy-β-D-glucopyranosyl (6), m.p. 150—153 °C. Recrystallization from ether-pentane gave the pure product, m.p. 157—168 °C, [α]D20 10.5° (c 2.8) (reported 8 m.p. 161—162 °C, [α]D20 15.3°). 1H NMR: δ 6.08 (H1), 4.09 (H2), 5.44 (H3), 5.09 (H4), 3.53 (H5), 4.37 (H6), 4.10 (H6'). J12 = 9.0 Hz, J12 = 8.1 Hz, J12 = 9.1 Hz, J12 = 1.5 Hz, J12 = 4.5 Hz, J12 = 5.6. J12 = 12.5.

Di-O-acetyl-2-bromo-2,6-dideoxy-a-L-glucopyranosyl bromide (7a). A mixture of tri-O-acetyl-6-deoxy-α-L-glucopyranosyl bromide 7 (2.0 g), acetyl bromide (20 mL) and anhydrous zinc bromide (4 g) was stirred at room temperature for 3 h. Work up as described above gave 1.9 g of a product which was crystallized from ether-pentane to give 1.1 g (61%) of 7a, m.p. 126—128 °C. Recrystallization from ether-pentane gave the pure product, m.p. 130—132 °C, [α]D20 —355° (c 1.4). Anal. C13H31BrO4; C, H, Br. 1H NMR: δ 6.44 (H1), 4.13 (H2), 5.56 (H3), 4.89 (H4), 4.33 (H5), 1.26 (H6). J12 = 3.7 Hz, J12 = 10.8, J12 = 9.2, J12 = 9.9, J12 = 6.1.

Tri-O-benzoyl-2-bromo-2,6-dideoxy-a-L-glucopyranosyl bromide (2b). A mixture of tetra-O-benzoyl-a-D-glucopyranosyl bromide (IB) (5.0 g), acetyl bromide (35 mL), and zinc bromide (10 g) was stirred at room temperature for 15—20 h. Work up as described above and crystallization from ether-pentane gave 3.12 g (66%) of 2b, m.p. 151—155 °C. Recrystallization from the same solvent gave 2.35 g (50%) of pure product, m.p. 165—167 °C, [α]D20 141° (c 3.8). Anal. C13H31BrO4; C, H. 1H NMR: δ 6.82 (H1), 4.45 (H2), 6.18 (H3), 5.96 (H4), 4.82 (H5), 4.71 (H6), 4.49 (H6'). J12 = 3.5 Hz, J12 = 10.5, J12 = 9.3, J12 = 10.0, J12 = 2.5, J12 = 5, J12 = 12.5.

Di-O-benzoyl-2-bromo-2,6-dideoxy-a-L-glucopyranosyl bromide (7b). Tri-O-benzoyl-6-deoxy-a-L-glucopyranosyl bromide 7 (IB) (1.0 g), acetyl bromide (6 mL) and zinc bromide (2 g) were stirred at 5 °C for 18 h. Work up as described above gave 1 g of product which was crystallized from ether-pentane to give 483 mg (52%) of 7b, m.p. 90—94 °C. Recrystallization from ether-pentane gave the pure product, m.p. 91—92 °C, [α]D20 —125° (c 4.1). Anal. C13H31BrO4; C, H. 1H NMR: δ 6.60 (H1), 4.38 (H2), 6.07 (H3), 5.33 (H4), 4.58 (H5), 1.40 (H6); J12 = 5.6 Hz, J12 = 10.9, J12 = 9.5, J12 = 9.5, J12 = 6.1.

Tri-O-acetyl-2-bromo-1,2-dideoxy-D-arabinopyranose 5a. A solution of 2a (1.0 g) and diethylamine (2.0 mL) in dichloromethane (4 mL) was kept at 0 °C for 30 min. It was then diluted with dichloromethane, washed with 4 N hydrochloric acid and with aqueous NaHCO3, dried and evaporated. The residue was a syrup (802 mg, 99%) which was pure as seen from TLC and 1H NMR. A sample was purified by preparative TLC (ether-pentane 1:1), [α]D20 19.1° (c 2.9). Anal. C13H31BrO4; C, H. 1H NMR: δ 6.83 (H1), 5.57 (H3), 5.27 (H4), 4.1—4.6 (H5—H6); J12 = 1 Hz, J12 = 4.8 Hz, J12 = 4.8 Hz. Crude 5a has been prepared in the same way by Hurd and Jenkins.

Tri-O-benzoyl-2-bromo-1,2-dideoxy-D-arabinohex-1-enopyranose (5b) was prepared as described above from 500 mg of 2b. The crude product (423 mg) was purified by preparative TLC, using 3 elutions with ether-pentane (1:2), to give 376 mg (87%) of pure 5b as a syrup, [α]D20 —92.7° (c 1.1). Anal. C13H31BrO4; C, H. 1H NMR: δ 6.98 (H1), 6.02 (H3), 5.85 (H4), 5.4—4.5 (H5—H6); J12 = 4.0 Hz, J12 = 4.0 Hz.

Di-O-acetyl-2-bromo-1,2,5-trideoxy-L-arabinohex-1-enopyranose (8a) was prepared analogously from 706 mg of 7a. The crude product (457 mg) was purified by preparative TLC (ether-pentane 1:1) to give 350 mg (63%) of 8a as a syrup, [α]D20 18.9° (c 3.8). Anal. C13H31BrO4; C, H. 1H NMR: δ 6.77 (H1), 5.50 (H3), 5.02 (H4), 4.27 (H5), 1.33 (H6); J12 = 0.8 Hz, J12 = 4.8, J12 = 6.3, J12 = 6.8.

Di-O-benzoyl-2-bromo-1,2,5-trideoxy-L-arabinohex-1-enopyranose (8b) was also prepared in the same way from 1.0 g of 7b. The crude product crystallized from ether to give 309 mg (47%) of 8b, m.p. 106—108 °C. Recrystallization from ether gave the pure product, m.p. 109—110 °C, [α]D20 19.3° (c 3.4). Anal. C13H31BrO4; C, H. 1H NMR: δ 6.89 (H1), 6.00 (H3), 5.51 (H4), 4.53 (H5), 1.51 (H6); J12 = 1 Hz, J12 = 0.8 Hz, J12 = 1, J12 = 5.6, J12 = 6.8.

Microanalyses were performed by Novo Microanalytical Laboratory.

REFERENCES


Received April 18, 1977.