

## Synthesis of 3,6-Di-*O*-( $\alpha$ -D-mannopyranosyl)-D-mannose

JAN ARNARP and JÖRGEN LÖNNGREN

Department of Organic Chemistry, Arrhenius Laboratory, University of Stockholm, S-106 91 Stockholm, Sweden

All oligosaccharide chains that are *N*-glycosidically linked to L-asparagine in glycoproteins seem to contain the structural element 1, which may be substituted in different ways.<sup>1</sup> These oligosaccharide chains are assumed to carry several biological functions.<sup>1</sup> The synthesis of oligosaccharides which are part of these structures is therefore of some interest. The recent report<sup>2</sup> by Ogawa and coworkers on the synthesis of methyl 3,6-di-*O*-( $\alpha$ -D-mannopyranosyl)- $\alpha$ -D-mannopyranoside prompts us to report the synthesis of the corresponding free trisaccharide.

Benzyl 3,6-di-*O*-allyl- $\alpha$ -D-mannopyranoside (2) was prepared from benzyl  $\alpha$ -D-mannopyranoside *via* a tributylstannylated intermediate essentially as devised for the corresponding methyl glycoside.<sup>3</sup>

Compound 2 was then subjected to benzylation and the allyl groups were removed<sup>4,5</sup> to give crystalline benzyl 2,4-di-*O*-benzyl- $\alpha$ -D-mannopyranoside (3).

3,4,6-Tri-*O*-benzyl-1,2-*O*-methylorthoacetyl- $\beta$ -D-mannose<sup>6,7</sup> (4) was treated with hydrogen chloride<sup>7</sup> in diethyl ether to give crude 2-*O*-acetyl-3,4,6-tri-*O*-benzyl- $\alpha$ -D-mannosyl chloride (5) which was used in the subsequent condensation reaction without purification.

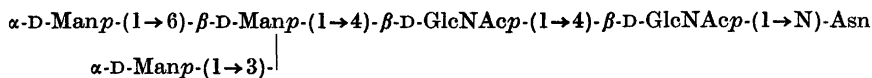
The aglycone (3) and 5 were condensed in toluene-nitromethane using a mixture of mercury(II) bromide-mercury(II) cyanide as promoter. This modification of the Koenigs-Knorr reaction has recently been shown to give high yields of  $\alpha$ -D-mannosides.<sup>7</sup> The condensation product (6) was enriched by chromatography on silica gel and deacetylated. The reaction mixture was purified by chromatography on silica gel to give benzyl 3,6-di-*O*-(3,4,6-tri-*O*-benzyl- $\alpha$ -D-mannopyranosyl)-2,4-di-*O*-benzyl- $\alpha$ -D-mannopyranoside (7) as a homogeneous syrup in 49% yield from 3. <sup>13</sup>C NMR spectroscopy of 7 showed, *inter alia*, three signals corresponding to anomeric carbons. Removal of benzyl groups by catalytic hydrogenation yielded the title compound (8). <sup>13</sup>C NMR spectroscopy of 8 showed, *inter alia*, two signals corresponding to anomeric carbons of glycosidically linked sugar residues. The

values of the coupling constants [<sup>1</sup>*J* (C1, H1) 171 Hz and 170 Hz] show that the D-mannopyranosyl groups are  $\alpha$ -linked<sup>8</sup> as is further indicated by the high optical rotation ( $[\alpha]_{589} + 59^\circ$ ) of 8. The methylated alditol of 8 gave a single peak on GC and showed the expected mass spectrum.<sup>9</sup>

**Experimental.** Concentrations were performed under reduced pressure and for column chromatography, Merck silica gel was used. NMR spectra were recorded using a JEOL FX-100 instrument. <sup>1</sup>H NMR data were in accordance with the proposed structures for all compounds. All non-crystalline compounds gave single spots on TLC.

**Benzyl 3,6-di-*O*-allyl- $\alpha$ -D-mannopyranoside (2).** A solution of benzyl  $\alpha$ -D-mannopyranoside<sup>10</sup> (2.7 g) and bis(tributylstannyl) oxide (7.6 ml) in toluene (300 ml) was refluxed for 4 h with continuous removal of water. After evaporation of the toluene, allyl bromide (50 ml) was added and the mixture was kept under nitrogen for 7 days at 80°C. Compound 2 was isolated as a syrup [2.0 g, 57%,  $[\alpha]_{589}^{22} + 56^\circ$  (c 0.6, chloroform)] after chromatography on silica gel using ethyl acetate-light petroleum (3:1) as irrigant.

**Benzyl 2,4-di-*O*-benzyl- $\alpha$ -D-mannopyranoside (3).** 2 (1.6 g) was dissolved in methyl sulfoxide (40 ml), sodium methylsulfinylmethanide in methyl sulfoxide (1.5 M, 20 ml) was added and the mixture was kept under nitrogen at room temperature overnight. Benzyl bromide (5 ml) was added dropwise and the mixture was left at room temperature for another 4 h. After work-up, the material was dissolved in ethanol-benzene-water (8:3:1, 240 ml), tris(triphenylphosphine) rhodium(I) chloride (120 mg) and diazabicyclo[2.2.2]octane (700 mg) were added and the mixture refluxed overnight and concentrated. The residue was dissolved in acetone-water (10:1, 66 ml), mercury(II) oxide (1.2 g) was added, followed by a solution of mercury(II) chloride (1.2 g) in acetone-water (10:1, 11 ml). The mixture was stirred at room temperature overnight, the solvent was evaporated and the residue dissolved in chloroform. The chloroform phase was washed with aqueous potassium iodide and water and then evaporated to dryness. Chromatography on silica gel using toluene-ethyl acetate (3:1) as irrigant followed by crystallization from ethanol-water gave pure 3 (1.4 g, 68%). M.p. 85–86°C,  $[\alpha]_{589}^{22} + 51^\circ$  (c 0.2, chloroform). (Anal. C<sub>27</sub>H<sub>30</sub>O<sub>8</sub>; C, H.) Methylation of a sample of 3 followed by catalytic hydrogenation over palladium on charcoal gave 3,6-di-*O*-methyl-D-mannose identified by GLC-MS of its alditol acetate.<sup>11</sup>



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2-*O*-Acetyl-3,4,6-*tri-O*-benzyl- $\alpha$ -D-mannosyl chloride (5). 4<sup>6,7</sup> (3.3 g) was dissolved in diethyl ether (40 ml) saturated with hydrogen chloride and stirred for 2 h at room temperature. The crude product obtained after evaporation was used in the following step.

Benzyl 3,6-*di-O*-(3,4,6-*tri-O*-benzyl- $\alpha$ -D-mannopyranosyl)-2,4-*di-O*-benzyl- $\alpha$ -D-mannopyranoside (7). 3 (1.12 g), mercury(II) bromide (1.5 g) and mercury(II) cyanide (1.5 g) were dissolved in toluene-nitromethane (1:1, 300 ml) and 5 (from 3.3 g 4) was added. The mixture was stirred for 48 h at room temperature when further portions of 5 (from 2.0 g 4) and mercury(II) cyanide (0.5 g) were added. The stirring was continued for 24 h when chloroform (500 ml) was added. The chloroform phase was washed with solutions of saturated sodium hydrogen carbonate and potassium iodide and finally with water and evaporated to dryness. The products were fractionated on silica gel using toluene-ethyl acetate (3:1) as irrigant to give crude 6 (2.84 g) as a syrup. Crude 6 (166 mg) was dissolved in methanol (50 ml) and a piece of sodium (~20 mg) was added. The mixture was left at room temperature overnight, neutralized with Dowex 50 (H<sup>+</sup>) and evaporated to dryness. Compound 7 was isolated as a syrup [93 mg, 49 % from 3,  $[\alpha]_{D}^{25} + 58^\circ$  (c 0.2, chloroform)] after chromatography on silica gel using toluene-ethyl acetate (2:1) as irrigant. <sup>13</sup>C NMR (CDCl<sub>3</sub>, ref. internal TMS):  $\delta$  101.6, 99.8 and 96.3 (anomeric carbons).

3,6-*Di-O*-( $\alpha$ -D-mannopyranosyl)-D-mannose (8). 7 (88 mg) was dissolved in methanol (55 ml) and hydrogenated at 400 kPa over 10 % palladium on charcoal (100 mg). After work-up, 8 was obtained as a syrup [35 mg, 100 %,  $[\alpha]_{D}^{25} + 59^\circ$  (c 0.3, water)]. <sup>13</sup>C NMR (D<sub>2</sub>O, ref. external TMS):  $\delta$  103.7 and 100.8 [<sup>1</sup>J (Cl, Hl) = 171 Hz and 170 Hz, Cl of  $\alpha$ -D-mannosyl groups], 95.5 [<sup>1</sup>J (Cl, Hl) = 170 Hz, Cl of  $\alpha$ -D-mannose residue], 95.0 [<sup>1</sup>J (Cl, Hl) = 161 Hz, Cl of  $\beta$ -D-mannose residue]. A sample (~5 mg) of 8 was reduced with sodium borohydride and methylated.<sup>11</sup> The methylated alditol showed  $T = 0.96$  relative to permethylated celotriitol on a 3 % OV-1 column at 250 °C and the MS (70 eV) showed, *inter alia*, the following peaks (% rel. int. in brackets and some assignments<sup>9</sup> in square brackets): 88(100), 101(78), 187(42)[aA<sub>2</sub>], 219(16)[aA<sub>1</sub>], 293(1).

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## Preparation of *N*-Sulfonylformamides

SVEND TREPPENDAHL and  
PALLE JAKOBSEN

Medicinsk-Kemisk Institut, University of  
Copenhagen, Rådmandsgade 71,  
DK-2200 Copenhagen N, Denmark

In connection with our investigations of *N*-sulfonylformamidines<sup>1</sup> and *N'*-sulfonylformamidrazones<sup>2</sup> we became interested in the *N*-alkyl- and *N*-aryl-*N*-sulfonylformamides as model compounds in the spectroscopic investigation and as reference compounds for the degradation products. A literature search showed that only the *N*-unsubstituted-*N*-sulfonylformamides had previously been synthesized. As the method described for their preparation<sup>3</sup> did not work for preparation of *N*-substituted-*N*-sulfonylformamides it was necessary to develop new methods. We here report the preparation of *N*-