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A Synthesis of Methyl 3-*O*-(β-D-Mannopyranosyl)-α-D-mannopyranoside from Sulfonate Intermediates

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Methyl 3-*O*-(β-D-mannopyranosyl)-α-D-mannopyranoside was synthesized by the reaction of 3,4,6-tri-*O*-benzyl-2-*O*-benzylsulfonyl-1-*O*-tresyl-D-mannopyranose with methyl 2,4,6-tri-*O*-benzyl- and 2,4,6-tri-*O*-(*p*-bromobenzyl)-α-D-mannopyranoside, followed by deprotection. The corresponding 1-*O*-(*p*-tolylsulfonyl) derivative gave better yield and stereoselectivity in the reaction with methanol, but was not sufficiently reactive to couple with a hindered secondary alcohol. The 2-*O*-benzylsulfonyl group is comparable in β-directing effect to 2-*O*-methylsulfonyl group, but its stereoselectivity is dependent on the structure of the reactant alcohol. It can be selectively removed by the reaction with sodium amide in *N*,*N*-dimethylformamide.

Stereoselectivity in syntheses of 1,2-*trans* and 1,2-*cis*-mannopyranosyl glycosides and oligosaccharides depends greatly on the protecting group at *O*-2 of the reactive mannosyl derivative and on its leaving group on *C*-1. In our previous paper[1] we investigated conditions for the formation of the 1,2-*trans* α-D-mannopyranosyl linkage using ester functions on *O*-2 and sulfonate leaving groups on *C*-1. β-D-Mannopyranosides are also of great interest because of their presence as structural elements in glycoproteins and the *O*-antigenic lipopolysaccharides,[2—8] and a number of methods have been proposed for their synthesis. Gorin and Perlin[9] first used 4,6-di-*O*-acetyl-2,3-*O*-carbonyl-α-D-mannopyranosyl bromide for the synthesis of β-D-mannopyranosides and it has since been used successfully for those of primary alcohols, while the stereoselectivity was uncertain[10—13] in cases of secondary alcohols. Garegg's method, using 2,3:4,6-di-*O*-cyclohexylidene-α-D-mannopyranosyl chloride and silver carbonate[14,15] or silver imidazole and mercury(II) chloride,[16] also gives better yields and stereoselectivity with primary alcohols. A widely used complex reaction sequence involves β-glucosidation, hydrolysis of a 2-*O*-acyl group, oxidation, and reduction.[17—21] 1,1-Dimannosides of various anomeric forms have been prepared with trifluoromethanesulfonyl (triflic) anhydride and 2,3,4,6-tetra-*O*-benzyl-D-mannose.[22] Silver silicate was successfully used by Paulsen and Lockhoff[23] as catalyst for the coupling of 6-*O*-acetyl-2,3,4-tri-*O*-benzyl-α-D-mannopyranosyl bromide to the equatorial 4-OH of a 1,6-anhydrogalactopyranose derivative to form the (1→4) β-linked disaccharide. β-D-Mannopyranosides have also been prepared by *O*-alkylation by Srivastava and Schuerch[24] and an interesting synthesis of β-D-mannopyranosides and -furanosides was recently reported by Schmidt, Reichrath and Morering,[25] in which 1-*O*-metallated derivatives are treated with alkyl triflates. The stereoselectivity is controlled by means of solvent and temperature. These methods are also presumably most useful for primary mannopyranosides. We have used a strongly electron-withdrawing, non-participating substituent on *O*-2 and a strongly electronegative leaving group at *C*-1 to control the stereoselectivity and yield of 1,2-*cis*-β-D-mannopyranosides and -β-L-rhamnopyranosides.[26—30] High β-selectivity has been observed in the formation of primary mannopyranosides, but results in the secondary positions of sugar derivatives were less satisfactory.[26,28,30]

The methylsulfonyl (mesyl) group has been used as a non-participating electron-withdrawing group on *O*-2, which can be removed selectively be reductive cleavage.[31] Herein we report the use of the benzylsulfonyl group as a substituent on *O*-2 and describe glycosidation results and the selective removal of the benzylsulfonyl group from the resultant glycosides and disaccharides.

Results and Discussion

3,4,6-Tri-*O*-benzyl-2-*O*-benzylsulfonyl-α-D-mannopyranosyl chloride (**2**) was prepared in 72% yield in one step by treating 3,4,6-tri-*O*-benzyl-D-mannose (**1**) in dichloromethane with excess benzylsulfonyl chloride in the presence of 2,6-lutidine. 3,4,6-Tri-*O*-benzyl-2-*O*-benzylsulfonyl-β-D-mannopyranose (**3**) was also separated as a by-product. The structure of both **2** and **3** was confirmed by ^{1}H and ^{13}C NMR spectroscopy. The methylene carbon of benzylsulfonyl group was found to have a characteristic signal in ^{13}C NMR, which resonate at δ 57.8 and 57.9 for **2** and **3**, respectively. The presence of the sulfonate function at *O*-2 caused a downfield shift of *H*-2 and it appeared as either a triplet in **2** or broad doublet in **3**. The β-configuration of **3** was confirmed by ^{13}C NMR and by its negative optical rotation. The chloride **2** was also obtained in 90% yield, when an ethereal solution of **3** was saturated with hydrogen chloride at 0 °C and worked up conventionally. The 1-*O*-(2,2,2-

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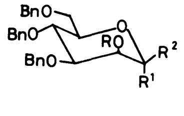
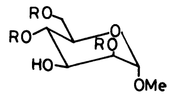
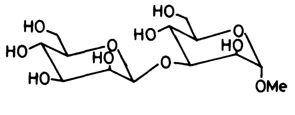
trifluoroethylsulfonyl) (tresyl) derivative of **3** was prepared by the condensation of **2** and silver tresylate as described before[1] and was then coupled with absolute methanol to give methyl 3,4,6-tri-*O*-benzyl-2-*O*-benzylsulfonyl-α,β-D-mannopyranosides (**4**,**5**) in 57% yield with an α:β ratio of 2:3. When, instead of tresylate as leaving group, *p*-toluenesulfonate (tosylate) was used for the same coupling reaction, the stereoselectivity and the yield were improved with a 74% overall yield and α:β ratio of 18:82. Optical rotational values and ^{1}H and ^{13}C NMR spectra (see Experimental) confirmed the anomeric configuration of the anomers separated. When the 1-tosylate was prepared from **2** and treated with methyl 2,4,6-tri-*O*-(*p*-bromobenzyl)-α-D-mannopyranoside (**8**),[32] no reaction occurred and starting materials were recovered. However, the corresponding 1-tresytlate derived from **2** in the same reaction gave methyl 3-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-benzylsulfonyl-α,β-D-mannopyranosyl)-2,4,6-tri-*O*-(*p*-bromobenzyl)-α-D-mannopyranosides (α:**10**, β:**14**) in 49% yield and in α:β ratio of 1:2. The structures of both **10** and **14** were confirmed by ^{1}H and ^{13}C NMR spectroscopy and optical rotation. The H-1′ proton of **10** and **14** appeared at δ 5.1—4.97 and 4.2—4.1, respectively. Anomeric carbons *C*-1′ in **10** and **14** resonated at δ 98.3 and 99.8, while the anomeric carbon *C*-1 of **14** resonated at δ 96.6. The *C*-5′ of β-isomer **14** was also observed in downfield as expected at δ 76.2.



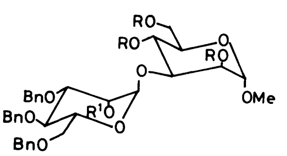
1 R=H, R^1, R_2=H, OH
2 R=O_2SBn, R^1=Cl, R^2=H
3 R=O_2SBn, R^1=H, R^2=OH
4 R=O_2SBn, R^1=OCH_3, R^2=H
5 R=O_2SBn, R^1=H, R^2=OCH_3
6 R=H, R^1=OCH_3, R^2=H
7 R=H, R^1=H, R^2=OCH_3

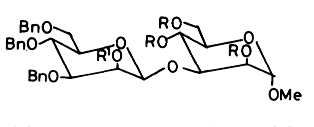


8 R=BnBr-*p*
9 R=Bn



18





10 R=BnBr-*p*, R^1=O_2SBn
11 R=Bn, R^1=O_2SBn
12 R=BnBr-*p*, R^1=H
13 R=Bn, R^1=H

14 R=BnBr-*p*, R^1=O_2SBn
15 R=Bn, R^1=O_2SBn
16 R=BnBr-*p*, R^1=H
17 R=Bn, R^1=H

An analogous reaction was carried out on the 1-*O*-tresyl derivative from **2** with methyl 2,4,6-tri-*O*-benzyl-α-D-mannopyranoside (**9**).[33] The disaccharide methyl 2,4,6-tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl-α,β-D-mannopyranosyl) α-D-mannopyranosides (α:**11**, β:**15**) were obtained in an improved yield (70%) but poorer β-selectivity (α:β of 61:39). As in the case of compounds **10** and **14**, the β-anomeric carbon resonates in upfield (δ=97.2) than α-anomeric carbon (δ=99.6), and C-5′ of **15** was found as expected at δ=76.2.

There is a surprising difference in stereoselectivity of the reactions of the 1-*O*-tresyl derivative from **2** with **8** and **9**. These results may reflect differences in reaction conditions rather than reactivity differences between **8** and **9**. In the reaction with **8**, the formation of tresylate was allowed to proceed for 6 h before the addition of **8**. In reaction with **9**, **2** and silver tresylate were allowed to react for only 1 h and silver halide precipitation was far from complete, when **9** was added. In the first case, therefore, there was a much better chance for an S_N2-like mechanism or shielded S_N1 mechanism to control stereoselectivity predominantly. In the second case, the cation generated directly by reaction of **2** with silver ion may be less shielded and steric control was less effective.

There is also an interesting difference between reaction of the tosylate and tresylate derived from **2** with alcohols. The tosylate gave better β-selectivity than the tresylate on reaction with methanol, but was insufficiently reactive to form product with relatively hindered secondary alcoholic functions, at least at ambient temperatures.

In summary, the benzylsulfonyl group is comparable to mesyl as a β-directing group in mannoside syntheses. In both cases stereoselectivity also depends on the nature of the alcoholic function reacting, and is usually better with primary alcohols. For separation of anomeric products, the benzylsulfonate group was preferable as the substituent.

A second objective of this research is to achieve a selective deblocking of the 2-*O*-benzylsulfonyl group. Sulfonate substituents have been removed in many cases by reductive cleavage[34—39] and this method has been applied to the cleavage of 2-*O*-mesyl groups.[37] Alternatively aryl *p*-toluenesulfonates have been hydrolyzed by bases.[40—42] The mechanism involves nucleophilic attack on sulfur by amine or hydroxide, causing sulfur–oxygen bond fission.[40,43,44] This mechanism apparently requires a good leaving group on sulfur. Mesyl chloride[45] and aryl benzylsulfonates are more readily hydrolyzed or aminolyzed, and these reactions proceed by a stepwise elimination-addition mechanism with the formation of a sulfene intermediate in the rate-determining step which is rapidly scavenged by amine or base.[46,47]

$$\mathrm{ArCH_2\text{-}SO_2\text{-}O\text{-}Ar' + Et_3N \rightleftharpoons Et_3\overset{+}{N}H + Ar\overset{-}{C}H\text{-}SO_2\text{-}O\text{-}Ar'}$$

$$\mathrm{Ar'O^- + ArCH{=}SO_2 \xrightarrow{^-OH} ArCH_2\text{-}SO_3^-}$$

The latter approach was tried in the present instance.

Various amines under a variety of conditions failed to remove the benzylsulfonyl group, presumably because the sugar anion is a poor leaving group, and a stronger base is required to remove benzylic proton and to form the sulfene intermediate. However, the stronger base, sodium amide, in *N,N*-dimethylformamide at room temperature readily removed the substituent without the formation of by-product from **4**, **5**, **10**, **11**, **14**, and **15**. Yields of product ranged from 65 to 95% with the higher recoveries due to purer reagents and improved work-up procedures. ^{1}H and ^{13}C NMR and optical rotations of **6** and **7** agreed with those in the literature.27,31,48,49) ^{13}C NMR of **12**, **13**, **16**, and **17** showed an upfield shift of *C*-2 and elimination of the benzylsulfonyl methylene carbons.

Methyl 3-*O*-(β-D-mannopyranosyl)-α-D-mannopyranoside (**18**) was obtained in quantitative yield by catalytic hydrogenation of **17**, while **16** gave **18** together with some decomposition products. A comparison of the ^{13}C NMR spectrum of **18** and **17** showed that the peak positions of *C*-2, *C*-3′, *C*-6, and *C*-6′ moved 6 to 7 ppm upfield on debenzylation as expected. The same was apparently true of *C*-4 and *C*-4′, although in **17** these positions could not be clearly distinguished from the six benzylic methylene carbons. Also as expected, *C*-1, *C*-1′, *C*-2′, and *C*-5′ moved downfield from δ 2.3 to 4.6, while the position of *C*-5 in **17** was also uncertain. A comparison of the ^{13}C NMR of **18** with those of methyl α- and β-D-mannopyranoside50) confirmed these assignments and the specific rotation of **18**, $[\alpha]_D^{23}$+5.76°, was consistent with a β-linkage in comparison with the rotation of the corresponding α-linked disaccharide.51)

Experimental

Generals. ^{1}H NMR spectra were determined with a Varian EM 360 MHz spectrometer for solution in chloroform-*d* with tetramethylsilane. ^{13}C NMR, optical rotations, melting point, TLC, high pressure liquid chromatography (LC) and coupling reactions were done as described previously.1,29) *N,N*-Dimethylformamide (DMF) was distilled on the high vacuum rack and dried over Molecular Sieve. Silver 2,2,2-trifluroethanesulfonate was prepared as described.1)

3,4,6-Tri-*O*-benzyl-2-*O*-benzylsulfonyl-α-D-mannopyranosyl Chloride (2). To a stirred solution of 3,4,6-tri-*O*-benzyl-D-mannopyranose (**1**) (1 g, 2.2 mmol) in dichloromethane (10 ml) and dry 2,6-lutidine (0.614 g, 5.7 mmol) was added benzylsulfonyl chloride (1.058 g, 5.5 mmol), and the reaction mixture was stirred overnight, and concentrated. The resulting residue was extracted with ether. The extract was washed with 1 M† hydrochloric acid, sodium hydrogencarbonate and water, dried, and concentrated. The resulting syrup was separated on LC using ethyl acetate–hexane (1:2) to give **2** (1 g) as syrup in 72.5% yield; $[\alpha]_D^{22}$ +31.3° (*c* 1.04, chloroform); ^{1}H NMR δ=7.1—7.35 (t, 20H, aromatic), 5.84—5.9 (d, 1H, H-1), 5.0—5.13 (t, 1H, H-2), 4.26—4.96 (m, 8H, 3×CH_2Ph and O_2SCH_2Ph), 3.53—4.2 (m, 5H, H-3,4,5,6, and 6′); ^{13}C NMR δ=90.2 (C-1), 77.9 (C-3), 76.4, 75.5, 74.8, 73.6, and 73.1 (C-2,4,5, and 3×CH_2Ph), 68.2 (C-6), 57.8 (O_2SCH_2Ph). 3,4,6-Tri-*O*-benzyl-2-*O*-benzylsulfonyl-β-D-mannopyranose (**3**) was also separated as syrup in 23% yield (0.3 g); $[\alpha]_D^{23}$−14.7° (*c* 1.06, chloroform), ^{1}H NMR δ=7.45 (20H, aromatic), 5.1—5.19 (d, 1H, H-2), 4.25—4.93 (m, 9H, H-1, 3×CH_2Ph and O_2SCH_2Ph), 4.1—3.4 (5H, H-3,4,5,6, and 6′), 2.59 (s, 1H, exchange with D_2O, OH); ^{13}C NMR δ=86.1 (C-1), 80.5 (C-3), 79.8 (C-5), 79.2 (C-4), 75.4, 73.7, 73.5, and 72.9 (C-2 and 3×CH_2Ph), 68.7 (C-6), 57.9 (O_2SCH_2Ph).

Compound **2** was also obtained from **3** in 90% yield. A solution of **3** (0.2 g, 0.33 mmol) in dry ether (10 ml) saturated with hydrogen chloride at 0 °C was left overnight with stirring at room temperature, swept by bubbling nitrogen to remove hydrogen chloride, washed with sodium hydrogencarbonate and water, dried, and concentrated. Separation of the product by LC using ethyl acetate–hexane (1:2) gave **2** (185 mg).

Found: C, 65.18; H, 5.80; Cl, 5.71; S, 5.09%. Calcd for $C_{34}H_{35}ClO_7S$: C, 65.52; H, 5.66; Cl, 5.68; S, 5.14%.

Methyl 3,4,6-Tri-*O*-benzyl-2-*O*-benzylsulfonyl-α,β-D-mannopyranosides (4,5). The chloride **2** (366 mg, 0.588 mmol), silver tresylate (159 mg, 0.588 mmol) and absolute methanol (25 mg, 0.78 mmol) were left separately under vacuum on a high vacuum rack for 3 h at room temperature. Acetonitrile (2 ml) was then distilled onto **2** and the resulting solution was left to react with silver tresylate for 1 h in the dark. The reaction mixture was then mixed with absolute methanol and kept for 70 h at room temperature in the dark. The reaction mixture was diluted with dichloromethane, filtered, washed with sodium thiosulfate, sodium hydrogencarbonate and water, dried, and concentrated. After separation of syrupy product by LC using ethyl acetate–hexane (1:3), compound **4** was obtained in 23% (64 mg) yield and **5** in 34% (94 mg) yield. The chloride **2** was recovered in 23% yield (85 mg).

Compounds **4** and **5** were also obtained in 14 and 61% yield, when **2** (468 mg, 751 mmol), silver *p*-toluenesulfonate (210 mg, 751 mmol), and absolute methanol (36 mg, 1.125 mmol) were treated as described above. Compound **4**: $[\alpha]_D^{23}$ +6.9° (*c* 1.1, chloroform); ^{1}H NMR δ=7.38—7.0 (d, 20 H, aromatic), 5.0—4.78 (t adjacent to d, 2H, H-2 and 1), 4.75—4.2 (m, 8H, 3×CH_2Ph, O_2SCH_2Ph) and 3.93—3.45 (5H, H-3,4,5,6, and 6′), 3.3 (s, 3H, OMe); ^{13}C NMR δ=99.0 (C-1), 78.1 (C-3), 76.3 (C-4), 75.3 (C-2), 71.98 (C-5), 69.1 (C-6), 57.7 (O_2SCH_2Ph), 55.2 (OMe). Compound **5**: $[\alpha]_D^{25}$−37.5° (*c* 0.98, chloroform); ^{1}H NMR δ=7.5—7.0 (d, 20H, aromatic), 5.2—5.06 (d, 1H, H-2), 4.95—4.25 (m, 9H, H-1, 3×CH_2Ph and O_2SCH_2Ph), 3.75—3.56 (m, 5H, H-3,4,5,6, and 6′), 3.5 (s, 3H, OMe); ^{13}C NMR δ=99.6 (C-1), 79.8 (C-3), 77.2 (C-5), 76.0 (C-4), 74.4 (C-2), 69.3 (C-6), 57.1 (O_2SCH_2Ph), 56.9 (OMe). The overall yield for this coupling was 74.6% (0.308 g) and the ratio of α:β was 18:82.

Found: C, 67.43; H, 6.02; S, 4.90%. Calcd for $C_{35}H_{38}SO_8$: C, 67.94; H, 6.12; S, 5.18%.

Methyl 3,4,6-Tri-*O*-benzyl-α-D-mannopyranoside (6). A solution of **4** (50 mg, 0.08 mmol) in DMF (5 ml) was treated with sodium amide (30 mg, 0.08 mmol) at room temperature overnight with stirring under anhydrous conditions. Methanol (2 ml) was then added and the

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† 1 M=1 mol dm^{-3}.

reaction mixture was neutralized with acetic acid. The reaction mixture was evaportated on the high vacuum rack without heating. The resulting residue was extracted with ether, and the extract was washed with sodium hydrogencarbonate and water, dried, and concentrated. After separation of the residue on LC using ethyl acetate–hexane (2:3), **6** was obtained in 65% (24 mg) yield as a syrup; $[\alpha]_D^{23}$ +57.2° (*c* 0.5, chloroform), ^{1}H and ^{13}C NMR agree with those in the literature.31,48,49)

Methyl 3,4,6-Tri-*O*-benzyl-β-D-mannopyranoside (7). A solution of **5** (0.1 g, 0.161 mmol) in DMF (5 ml) was treated with sodium amide (6.5 mg, 0.166 mmol) as described for **6**. Separation of the product by LC using ethyl acetate–hexane (1:1) gave **7** in 67% (50 mg) yield. $[\alpha]_D^{23}-13.1°$ (*c* 0.94, chloroform); lit,27,31) $[\alpha]_D^{20}-10.2°$ (*c* 0.45, chloroform), $[\alpha]_D^{20}-8.77°$ (*c* 1.0, chloroform).

Methyl 3-*O*-(3,4,6-Tri-*O*-benzyl-2-*O*-benzylsulfonyl-α,β-D-mannopyranosyl)-2,4,6-tri-*O*-(*p*-bromobenzyl)-α-D-mannopyranoside (10,14). Compound **8**32) (526 mg, 0.75 mmol), **2** (467 mg, 0.75 mmol), and silver tresylate (302 mg, 1.12 mmol) were left under vacuum for 5 h on the high vacuum rack. Acetonitrile was distilled onto **2**, and the resulting solution was left to react with silver tresylate for 6 h in the dark with stirring. The formed 1-*O*-tresyl derivative was then treated with **8** for 40 h in the dark. The reaction mixture was processed as described for **4** and **5** to give **10**, in 17% (160 mg) yield as a syrup. $[\alpha]_D^{23}+6.9°$ (*c* 1, chloroform), ^{1}H NMR δ=7.4—6.8 (m, 32H, aromatic), 5.1—4.97 (d, 1H, H-1′), 4.95—4.8 (t, 1H, H-2′), 4.73—4.1 (m, 15H, H-1, $3\times CH_2C_6H_4Br$-*p*, $3\times CH_2Ph$, and O_2SCH_2Ph), 4.0—3.35 (m, 11H, H-2,3,3′,4,4′,5,5′,6, and 6′), 3.2 (s, 3H, OMe); ^{13}C NMR δ=99.8 (C-1′), 98.3 (C-1), 79.4 (C-3′), 77.7 (C-2 and 3), 76.4 (C-4), 69.2 and 69.5 (C-6 and 6′), 57.6 (O_2SCH_2Ph), 54.9 (OMe), 75.2, 74.8, 74.5, 74.2, 73.7, 72.7, and 71.9 (C-2′,4′,5,5′, $3\times CH_2Ph$, and $3\times CH_2C_6H_4Br$-*p*).

The β-disaccharide (**14**) was separated as a syrup in 32% (0.31 g) yield, which crystallized from ether; mp 113 °C; $[\alpha]_D^{22}$ −12.8° (*c* 0.86, chloroform); ^{1}H NMR δ =7.5—6.75 (m, 32H, aromatic), 5.13—5.03 (d, 1H, H-2′), 4.93 (s, 1H, H-1), 4.85—4.25 (m, 14H, $3\times CH_2Ph$, $3\times CH_2C_6H_4Br$-*p*, and O_2SCH_2Ph), 4.2—4.1 (bd, 1H, H-1′), 3.4—4.06 (m, 11H, H-2,3,3′,4,4′,5,5′,6, and 6′), 3.3 (s, 3H, OMe); ^{13}C NMR δ=99.1 (C-1), 96.6 (C-1′), 80.5 (C-3′), 78.1 and 77.6 (C-3 and 2), 76.2 (C-5′), 75.5 and 75.4 (C-4 and 4′), 74.3, 73.7, 73.2, 72.8, 72.7, 71.9, and 71.6 (C-2′,5, $3\times CH_2Ph$, and $3\times CH_2C_6H_4Br$-*p*), 69.5 and 69.2 (C-6 and 6′), 57.8 (O_2SCH_2Ph), 54.9 (OMe).

Found for **9**: C, 57.36; H, 5.02; S, 2.83; for **10**: C, 57.95; H, 4.79; S, 2.38%. Calcd for $C_{62}H_{63}O_{13}SBr_3$: C, 57.81; H, 4.93; S, 2.48%.

Methyl 3-*O*-(3,4,6-Tri-*O*-benzyl-α-D-mannopyranosyl)-2,4,6-tri-*O*-*p*-bromobenzyl-α-D-mannopyranoside (12). A well stirred solution of **10** (80 mg, 0.0621 mmol) and sodium amide (12 mg, 0.31 mmol) in DMF (5 ml) was processed as described for **6** to give **12** (50 mg) as a syrup in 70% yield. $[\alpha]_D^{24}+19.5°$ (*c* 0.8, chloroform); ^{1}H NMR δ=7.45—6.85 (m, 27H, aromatic), 5.06 (s, 1H, H-1′), 4.86 (s, 1H, H-1), 4.75—4.21 (m, 12H, $3\times CH_2Ph$, and $3\times CH_2C_6H_4Br$-*p*), 4.1—3.5 (m, 12H, H-2,2′,3,3′,4,4′,5,5′,6 and 6′), 3.23 (s, 3H, OMe); ^{13}C NMR δ=101.6 (C-1′), 98.7 (C-1), 80.2 (C-3′), 78.9, and 77.9 (C-3 and 2), 75.3, 75.1, 74.7, 74.2, 73.7, 72.8, 72.2, 71.9, and 71.6 (C-5,5′,4,4′, $3\times CH_2Ph$, and $3\times CH_2C_6H_4Br$-*p*), 69.7 and 69.3 (C-6 and 6′), 68.8 (C-2′), 55.0 (OMe).

Found: C, 59.15; H, 4.56%. Calcd for $C_{55}H_{57}O_{11}Br_3$: C, 59.24; H, 5.06%.

Methyl 3-*O*-(3,4,6-Tri-*O*-benzyl-β-D-mannopyranosyl)-2,4,6-tri-*O*-(*p*-bromobenzyl)-α-D-mannopyranoside (16). A solution of **14** (0.1 g, 0.078 mmol) and sodium amide (15 mg, 0.387 mmol) in freshly distilled DMF (5 ml) was processed as described for **6** to give **16** (83 mg) in 95% yield as a syrup. $[\alpha]_D^{22}+11.6°$ (*c* 1, chloroform); ^{1}H NMR δ=7.45—6.86 (m, 27H, aromatic), 4.93—4.8 (s, 1H, H-1), 4.76—4.2 (m, 14H, H-1′,5′, $3\times CH_2Ph$, and $3\times CH_2C_6H_4Br$-*p*), 4.0—3.4 (m, 11H, H-2,2′,3,3′,4,4′,5,6, and 6′), 3.23 (s, 3H, OMe), 2.5—2.26 (bs, 1H, OH); ^{13}C NMR δ=98.9 (C-1), 97.6 (C-1′), 81.8 (C-3′), 76.7, 75.9, 75.4, 75.2, 74.3, 73.7, 72.8, 71.9, and 71.7 (C-5,5′,4,4′,3,2, $3\times CH_2Ph$, and $3\times CH_2C_6H_4Br$-*p*), 69.5 (C-6 and 6′), 68.8 (C-2′), 54.9 (OMe).

Found: C, 57.78; H, 4.96%. Calcd for $C_{55}H_{57}O_{11}Br_3$: C, 58.24; H, 5.06%.

Methyl 2,4,6-Tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl-2-*O*-benzylsulfonyl-α,β-D-mannopyranosyl)-α-D-mannopyranoside (11,15). Compound **9**33) (405 mg, 0.874 mmol), silver tresylate (320 mg, 1.18 mmol), and **2** (0.7 g, 1.124 mmol) were left for 3 h on the high vacuum rack. Acetonitrile (3 ml) was distilled onto **2**, and the resulting solution was mixed with silver tresylate. The reaction mixture was left for 30—60 min with stirring in the dark, mixed with **9**, and then processed as described for **4** and **5** to give **11** (394 mg) in 43% yield as a syrup. $[\alpha]_D^{24}$ +9.8° (*c* 1.04, chloroform); ^{1}H NMR δ=7.36—7.37 (d, 35H, aromatic), 5.23—5.13 (d, 1H, H-1′), 5.13—5.15 (bs, 1H, H-2′), 4.92 (s, 1H, H-1), 4.8—4.17 (m, 14H, $6\times CH_2Ph$ and O_2SCH_2Ph), 4.13—3.5 (m, 11H, H-2,3,3′,4,4′,5,5′,6, and 6′), 3.25 (s, 3H, OMe): ^{13}C NMR δ=99.6 (C-1′), 98.4 (C-1), 79.1 (C-3′), 77.8 and 77.6 (C-2 and 3), 76.7, 74.9, 74.4, 73.5, 72.8, 72.7, 72.3, 72.2, and 72.0 (C-5,5′,4,4′,2′, and $6\times CH_2Ph$), 69.3 and 68.9 (C-6 and 6′), 57.6 (O_2SCH_2Ph), 54.8 (OMe). The compound **15** was separated in 28% yield (252 mg) as a syrup. $[\alpha]_D^{24}-17.2°$ (*c* 0.83, chloroform); ^{1}H NMR δ=7.5—7.7 (m, 35H, aromatic), 5.18—5.06 (d, 1H, H-2′), ca. 5.4 (bm, 18H, H-1,1′, $6\times CH_2Ph$, O_2SCH_2Ph and 2H of sugar protons), 4.0—3.46 (bm, 9H, rest of the sugar protons), 3.36 (s, 3H, OMe); ^{13}C NMR δ=99.3 (C-1), 97.2 (C-1′), 80.2 (C-3′), 77.8 (C-3), 77.4 (C-2), 76.2 (C-5′), 75.5, 75.3, 74.9, 74.3, 73.7, and 73.4 (C-5 and $6\times CH_2Ph$), 72.5 (C-4′), 72.2 (C-4), 71.5 (C-2′), 69.7, 69.3 (C-6 and 6′), 57.8 (O_2SCH_2Ph), 54.9 (OMe).

Found for **11**: C, 70.25; H, 6.25; S, 3.13, and for **15**: C, 70.00; H, 6.05; S, 2.86%. Calcd for $C_{62}H_{66}SO_{13}$: C, 70.83; H, 6.32; S, 3.05%.

Methyl 2,4,6-Tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl-α-D-mannopyranosyl)-α-D-mannopyranoside (13). Compound **11** (129 mg, 0.127 mmol) in freshly distilled DMF (5 ml) was left to react with pure sodium amide (24 mg, 0.613 mmol) for 48 h as described for **6** to give **13** (90 mg) in 82% yield. $[\alpha]_D^{22}+25.2°$ (*c* 0.85, chloroform,); ^{1}H NMR δ=7.4—7.05 (m, 30H, aromatic), 5.18 (s, 1H, H-1′), 4.9 (s, 1H, H-1), 4.83—4.43 (m, 12H, $6\times CH_2Ph$), 4.4—3.5 (bm, 12H, H-2,2′,3,3′,4,4′,5,5′,6, and 6′), 3.3 (s, 3H, OMe), 2.65—2.93 (bs, 1H, OH); ^{13}C NMR δ=101.5 (C-1′), 98.8 (C-1), 80.2 (C-3′), 78.7 (C-2), 77.8 (C-3), 75.5, 75.01, 74.7, 73.6, 72.4, 72.2, 72.1 (C-5,5′,4,4′ and $6\times CH_2Ph$), 69.6 and 69.4 (C-6 and 6′), 68.9 (C-2′), 54.9 (OMe).

Found: C, 73.05; H, 6.83%. Calcd for $C_{55}H_{60}O_{11}$: C, 73.63; H, 6,74%.

Methyl 2,4,6-Tri-*O*-benzyl-3-*O*-(3,4,6-tri-*O*-benzyl-β-D-mannopyranosyl)-α-D-mannopyranoside (17). Pure sodium amide (24 mg, 0.623 mmol) was left to react with compound **15** (132 mg, 0.125 mmol) in freshly distilled DMF (5 ml) for 48 h as described for **6** to give **17** (0.1 g) as a syrup in 90% yield. $[\alpha]_D^{22}$+16.6° (*c* 0.72, chloroform); ^{1}H NMR δ=7.37—7.17 (m, 30H, aromatic), 4.92—4.90 (d, 1H, H-1), 4.87—4.43 (m, 12H, 6×CH_2Ph), 4.35—4.21 (d, 1H, H-1′), 4.39 (s, 1H, one of sugar protons), 3.9—3.69 (m, 11H, rest of sugar protons), 3.31 (s, 3H, OMe), 2.65—2.50 (bs, 1H, OH). ^{13}C NMR δ=98.9 (C-1), 97.2 (C-1′), 81.6 (C-3′), 76.3 and 76.0 (C-2 and 3), 75.3 (C-5′), 74.6, 73.7, 73.5, 72.5, 71.9, 71.7, 71.4 (C-5,4,4′, and 6×CH_2Ph), 69.6, and 69.4 (C-6 and 6′), 68.6 (C-2′), 54.9 (OMe).

Found: C, 73.74; H, 7.14%. Calcd for $C_{55}H_{60}O_{11}$: C, 73.63; H, 6.74%.

Methyl 3-*O*-(β-D-Mannopyranosyl)-α-D-mannopyranoside (18). A suspension of **17** (84 mg) and palladium over carbon (0.04 g), in methanol (15 ml) and water (5 ml) was hydrogenated for 48 h at room temperature with stirring. After filtration and freeze drying, **18** was obtained in quantitative yield. $[\alpha]_D^{23}$+5.8° (*c* 0.59, water), ^{13}C NMR δ=103.03 (C-1), 99.5 (C-1′), 79.8 (C-3), 78.7 (C-5′), 75.2 (C-5); 74.7 (C-3′), 73.2 (C-2′), 69.4 (C-2), 69.1 (C-4′), 67.5 (C-4), 63.3 (C-6 and 6′), 57.1 (OMe). The same compound was obtained from **16** in 30% yield by the same procedure.

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