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Note

Synthesis of some partially substituted methyl α-D- and phenyl 1-thio-α-D-mannopyranosides for the preparation of manno-oligosaccharides *

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N-Glycoproteins are very important natural compounds[1–3], and in the last two decades great efforts have been devoted to prepare the glycan chains of such materials[4]. In our research program, aimed at synthesising "high-mannose"-type glycoproteins, reactive aglycons and glycosyl donors with stable protecting groups are employed in block-synthetic approaches.

Manno-oligosaccharides may have 2,4, 2,6, and 3,6 branching points, and often contain mannobiosyl units with $1 \rightarrow 2$ linkages. However, the preparation of suitably protected mannose derivatives is rather tedious.

As the first step of our synthetic program, some partially substituted methyl α-D-mannopyranosides have been synthesised from the *exo*- and *endo*-diastereoisomers of methyl 2,3:4,6-di-*O*-benzylidene-α-D-mannopyranoside (**2** and **3**) using chemo-, stereo-, and regio-selective reductive ring-opening reactions with the $LiAlH_4$–$AlCl_3$ reagent[5,6]. Thus, the reaction of methyl α-D-mannopyranoside (**1**) with α,α-dimethoxytoluene in the presence of *p*-toluenesulfonic acid gave a 1:1 mixture of the corresponding *exo*-isomer (**2**) and *endo*-isomer (**3**) which were easily separated by simple fractional crystallisation (Scheme 1). The dibenzylidene mannopyranosides carry two acetal rings with different ring-size in the same molecule, and it has been shown earlier that the stereoselective[7] and regioselective[8] reductive ring-opening reaction of benzylidene acetals with the $LiAlH_4$–$AlCl_3$ reagent is an efficient approach for obtaining partially benzylated sugar derivatives. It has also been demonstrated[5] that the dioxolane-type acetal ring is more reactive than the dioxane-type acetal under analogous conditions.

* Dedicated to Professor Pál Nánási on the occasion of his 70th birthday.

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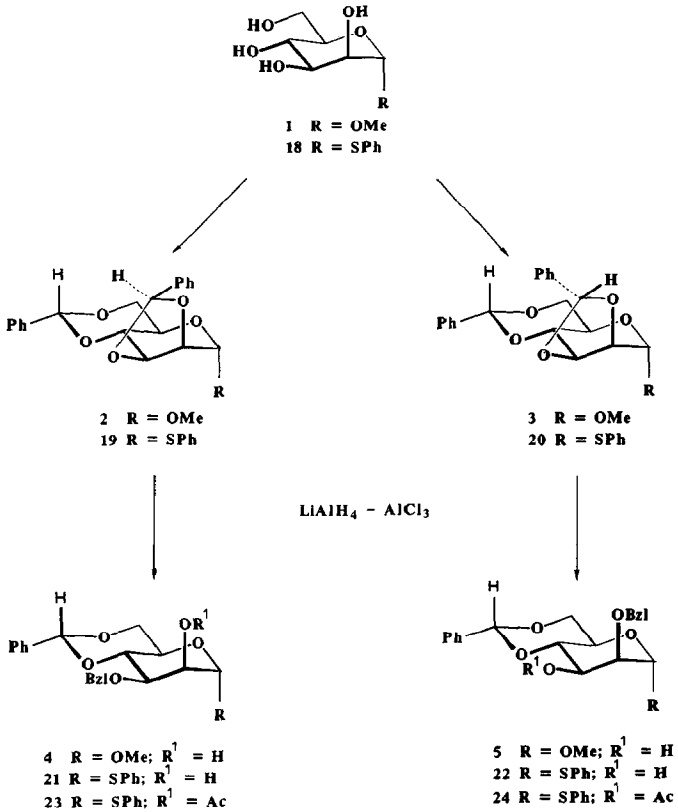
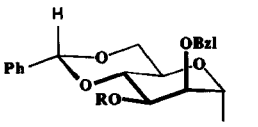


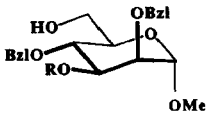
Scheme 1.

Compounds **2** and **3** were converted into methyl 3-*O*-benzyl- (**4**) and methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**5**), respectively, by stereo- and chemo-selective reactions with one equivalent of the above reagent at room temperature[5]. Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**6**) was prepared as follows: compound **2** was treated with $LiAlH_4$–$AlCl_3$ and the resulting mixture of the regioisomers **4** and **5** was benzylated. Conventional allylation of **5** gave the 3-*O*-allyl derivative (**7**).

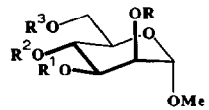
The dioxane-type benzylidene acetals can be regioselectively hydrogenolysed[8] if a bulky substituent is present at position 3. Benzyl and allyl groups are bulky enough, so the reaction of **6** and **7** with the $LiAlH_4$–$AlCl_3$ reagent yielded methyl 2,3,4-tri-*O*-benzyl-α-D-mannopyranoside (**8**) and methyl 3-*O*-allyl-2,4-di-*O*-benzyl-α-D-mannopyranoside (**9**), respectively. On the other hand, despite the bulky substituent, reductive ring-cleavage of the 3-*O*-benzyl compound **4** resulted in a 4:1 mixture of methyl 3,4-di-*O*-benzyl- (**10**) and methyl 3,6-di-*O*-benzyl-α-D-mannopyranoside (**11**). As expected, the reaction of **5** yielded a mixture (2:3) of the 2,4-dibenzyl (**12**) and 2,6-dibenzyl (**13**) ethers of **1** upon boiling with the reagent for



6 R = Bzl
7 R = All



8 R = Bzl
9 R = All



10 R = R^3 = H; R^1 = R^2 = Bzl
11 R = R^2 = H; R^1 = R^3 = Bzl
12 R = R^2 = Bzl; R^1 = R^3 = H
13 R = R^3 = Bzl; R^1 = R^2 = H
14 R = R^3 = Ac; R^1 = R^2 = Bzl
15 R = R^2 = Ac; R^1 = R^3 = Bzl
16 R = R^2 = Bzl; R^1 = R^3 = Ac
17 R = R^3 = Bzl; R^1 = R^2 = Ac

1 h. Conventional acetylation of compounds **10**, **11**, **12**, and **13** then furnished the diacetates **14**, **15**, **16**, and **17**, respectively.

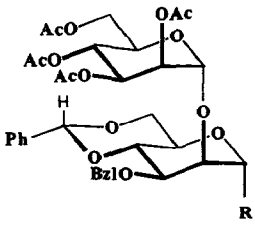
Earlier, we demonstrated that the benzylidene derivatives of phenyl 1-thioglycosides can be hydrogenolysed[9] with the $LiAlH_4$–$AlCl_3$ reagent. Thus, chemoselective ring-opening reactions of phenyl 2,3:4,6-di-*O*-benzylidene-1-thio-α-D-mannopyranosides (**19** and **20**) gave phenyl 3-*O*-benzyl-4,6-*O*-benzylidene-1-thio- (**21**) and phenyl 2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (**22**) in which the positions of the free hydroxyl groups were confirmed by means of ^1H NMR studies after conventional acetylation (**21** → **23** and **22** → **24**).

By employing compounds **4** and **21** as "aglycons", and 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide as the glycosyl donor, the (1 → 2)-linked mannobioses (**25** and **26**) have been prepared in the presence of silver triflate as promoter. Compound **25** was converted into **27** and then into **28** by standard methods. The disaccharides **26** and **28** are considered as potential mannobiosyl donors in syntheses of higher manno-oligosaccharides.

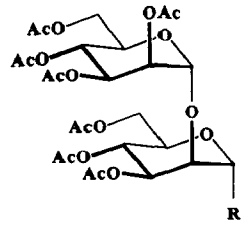
The physical data of **25** were slightly different from those reported[10], but conversion of **25** into **27** and then deacylation gave methyl 2-*O*-α-D-mannopyranosyl-α-D-mannopyranoside with consistent literature data[11].

EXPERIMENTAL

General methods.—Melting points (uncorrected) were determined on a Kofler hot-stage apparatus. Optical rotations were measured with a Perkin–Elmer 241



25 R = OMe
26 R = SPh



27 R = OMe
28 R = OAc

polarimeter. NMR spectra were recorded with a Bruker WP-200 SY spectrometer for solutions in $CDCl_3$ (internal Me_4Si). Reactions were monitored by TLC on Kieselgel $60F_{254}$ (Merck) with detection by charring with H_2SO_4. Kieselgel 60 (Chemolab, Budapest) was used for short-column chromatography.

The original procedure[5] was used for the chemo- and stereo-selective ring-opening reactions of compounds **2** and **3** (→ **4** and → **5**) with the $LiAlH_4$–$AlCl_3$ reagent.

Reductive ring-opening reactions of dioxane-type benzylidene acetals.—To a stirred solution of the starting material (1 mmol) in dry CH_2Cl_2 (8 mL) were added $LiAlH_4$ (76 mg, 2 mmol) and then $AlCl_3$ (267 mg, 2 mmol) in 8 mL of dry ether. The mixture was boiled under reflux until TLC showed that no starting material remained (0.5–8 h). After cooling, the excess of the reagent was decomposed by the addition of a few drops of EtOAc and $Al(OH)_3$ was precipitated with water. The solution was decanted, and the combined organic solutions (70 mL) were washed with water (2 × 15 mL), dried ($MgSO_4$), and concentrated. The residue was purified by means of column chromatography.

Acetylation.—To a solution of the starting material (1 mmol) in dry pyridine (3 mL) was added Ac_2O (3 mL). After standing overnight at room temperature, the mixture was evaporated in a vacuum and the residue codistilled with toluene (3 × 10 mL). The product was purified by column chromatography.

Alkylation.—To a solution of the starting material (2 mmol) in dry DMF (15 mL) was added NaH (58 mg, 2.4 mmol), and the mixture was stirred for 15 min at room temperature and cooled to 0°C. The alkyl bromide (2.4 mmol) was added, and the mixture was stirred at 0°C for 10 min and then at room temperature for 30 min. It was then cooled again, and the excess of NaH was decomposed with dry MeOH (1 mL) and water (1 mL). The solution was diluted with CH_2Cl_2 (60 mL), washed with water (2 × 15 mL), dried ($MgSO_4$), and concentrated. The product was purified by means of short-column chromatography, using gradient elution in order to remove traces of the reagent.

Methyl exo(phenyl)-*2,3 : 4,6-di*-O-*benzylidene-α*-D-*mannopyranoside* (**2**) *and methyl* endo(phenyl)-*2,3 : 4,6-di*-O-*benzylidene-α*-D-*mannopyranoside* (**3**).—A mixture of methyl α-D-mannopyranoside (**1**, 10 g), α,α-dimethoxytoluene (10 mL),

N,*N*-dimethylformamide (10 mL), and *p*-toluenesulfonic acid (100 mg) was stirred at 75°C in a vacuum. After 2 h, more DMF (100 mL), reagent (10 mL), and acid (50 mg) were added and stirring was continued for an additional 2 h. The reaction was quenched by adding satd aq $NaHCO_3$ (10 mL). After cooling, the mixture was partitioned between CH_2Cl_2 (300 mL) and water (50 mL), and the organic layer was separated, washed with water (3 × 50 mL), dried over $MgSO_4$, and concentrated. Recrystallization of the residue from a mixture of EtOH (150 mL) and acetone (120 mL) gave 6.42 g (33.7%) of **2** {mp 176–180°C; $[\alpha]_D$ −1.9° (*c* 0.76, $CHCl_3$)}. Recrystallisation yielded a sample with mp 181–182°C; $[\alpha]_D$ +0.3° (*c* 0.68, $CHCl_3$); lit.[12] mp 180–181°C; $[\alpha]_D$ −1° ($CHCl_3$).

The mother liquor was evaporated to half of its volume. After 10 min, the separated crystals were filtered off (2.52 g, 13.2%; a mixture of **2** and **3**). From the mother liquor, the *endo*-isomer (**3**) crystallised (5.44 g, 28.5%); mp 95–97°C; $[\alpha]_D$ −63° (*c* 0.64, $CHCl_3$); lit.[12] mp 97–99°C; $[\alpha]_D$ −63° ($CHCl_3$).

The filtrate was concentrated in vacuo. Column chromatography of the residue (8:2 hexane–EtOAc) yielded more **3** (2.10 g, 11%); mp 96–98°C (from hexane).

*Methyl 2,3-di-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-mannopyranoside* (**6**).—Compound **2** (741 mg, 2 mmol) was hydrogenolysed with the $LiAlH_4$–$AlCl_3$ reagent[5] to give a mixture of methyl 3-*O*-benzyl- (**4**) and methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**5**). Conventional benzylation of the crude product and then column chromatography afforded **6** (808 mg, 87.3%); syrup; $[\alpha]_D$ +30.2° (*c* 0.49, $CHCl_3$); lit.[11] $[\alpha]_D$ +29.6° ($CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.55–7.25 (m, 15 H, aromatic), 5.65 (s, 1 H, PhC*H*), 4.88–4.55 (2 q, 4 H, 2 PhCH_2), 4.68 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.26 (dd, 1 H, $J_{2,3}$ 4 Hz, H-3), 4.23 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 3.99–3.69 (m, 4 H, skeleton protons), 3.32 (s, 3 H, OMe).

*Methyl 3-*O*-allyl-2-*O*-benzyl-4,6-*O*-benzylidene-α-*D*-mannopyranoside* (**7**).—Conventional allylation of methyl 2-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**5**) and then column chromatography (99:1 → 97:3 CH_2Cl_2–EtOAc) gave **7** (795 mg, 80.6%) as a syrup; $[\alpha]_D$ +28.7° (*c* 0.63, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.55–7.25 (m, 10 H, aromatic), 5.91 (m, 1 H, –CH=), 5.62 (s, 1 H, PhC*H*), 5.22 (m, 2 H, CH_2=), 4.79 (q, 2 H, PhCH_2), 4.68 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.34–3.69 (m, 8 H, –CH_2– and skeleton protons), 3.33 (s, 3 H, OMe). Anal. Calcd for $C_{24}H_{28}O_6$ (412.47): C, 69.89; H, 6.84. Found: C, 69.91; H, 6.93%.

*Methyl 2,3,4-tri-*O*-benzyl-α-*D*-mannopyranoside* (**8**).—Hydrogenolysis with $LiAlH_4$–$AlCl_3$ of compound **6** (600 mg) and purification of the crude product by means of column chromatography yielded **8** (495 mg, 82.1%) as a syrup; $[\alpha]_D$ +29.5° (*c* 0.99, $CHCl_3$); lit.[13] $[\alpha]_D$ +30° ($CHCl_3$).

*Methyl 3-*O*-allyl-2,4-di-*O*-benzyl-α-*D*-mannopyranoside* (**9**).—Reductive ring cleavage of **7** (600 mg) and purification of the crude product gave **9** (476 mg, 78.9%) as a syrup; $[\alpha]_D$ +43.7° (*c* 0.97, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.45–7.25 (m, 10 H, aromatic), 6.05–5.84 (m, 1 H, –CH=), 5.39–5.13 (m, 2 H, CH_2=), 4.98–4.62 (m, 5 H, $J_{1,2}$ 1 Hz, 2 PhCH_2 and H-1), 4.14–3.54 (m, 8 H, skeleton protons and –CH_2–), 3.30 (s, 3 H, OMe), 2.02 (t, 1 H, OH, disappeared after

addition of D_2O). Anal. Calcd for $C_{24}H_{30}O_6$ (414.49): C, 69.55; H, 7.29; Found: C, 69.60, H, 7.24%.

Methyl 3,4-di-O-benzyl-α-D-mannopyranoside (10) and methyl 3,6-di-O-benzyl-α-D-mannopyranoside (**11**).—Compound **4** (2.0 g) was hydrogenolysed for 8 h. The products were separated by means of column chromatography using 85 : 15 → 7 : 3 CH_2Cl_2–acetone as the solvent system. Eluted first was **11** (253 mg; 12.6%); $[\alpha]_D$ +29.4° (*c* 1.1, $CHCl_3$); lit.[14] $[\alpha]_D$ +20.3°.

Eluted second was **10** (1.20 g; 59.7%); $[\alpha]_D$ +41.6° (*c* 0.74, $CHCl_3$); lit.[15] $[\alpha]_D$ +50°.

Methyl 2,4-di-O-benzyl-α-D-mannopyranoside (12) and methyl 2,6-di-O-benzyl-α-D-mannopyranoside (**13**).—Compound **5** (230 mg) was hydrogenolysed for 1 h. The products were separated by means of column chromatography. Eluted first was **12** (80 mg; 34.6%) as a syrup; $[\alpha]_D$ +23.8° (*c* 1.36, $CHCl_3$); lit.[14] $[\alpha]_D$ +23.5°.

Eluted second was **13** (120 mg; 51.9%) as a syrup; $[\alpha]_D$ −0.8° (*c* 0.60, $CHCl_3$). Anal. Calcd for $C_{21}H_{26}O_6$ (374.42): C, 67.37; H, 7.00. Found: C, 67.32; H, 7.07%.

Compound **12** was stable towards $NaIO_4$, but **13** could be oxidised, so it must be the 2,6-di-*O*-benzyl isomer.

Acetylation of the dibenzyl ethers of methyl α-D-mannopyranoside.—Conventional acetylation of compounds **10**, **11**, **12**, and **13** gave the diacetates **14**, **15**, **16**, and **17**, respectively.

(a) Methyl 2,6-di-O-acetyl-3,4-di-O-benzyl-α-D-mannopyranoside (**14**). Syrup; $[\alpha]_D$ +23.7° (*c* 0.70, $CHCl_3$); lit.[15] $[\alpha]_D$ −22.2°; ^1H NMR ($CDCl_3$): δ 7.40–7.20 (m, 10 H, aromatic), 5.37 (dd, 1 H, $J_{2,3}$ 3.4 Hz, H-2), 4.74 and 4.62 (2 q, each 2 H, 2 PhCH_2), 4.71 (d, 1 H, $J_{1,2}$ 1.8 Hz, H-1), 4.34 (m, 2 H, H-6a,6b), 3.98 (dd, 1 H, H-3), 3.81–3.73 (m, 2 H, H-4,5), 3.36 (s, 3 H, OMe), 2.16 and 2.07 (2 s, each 3 H, 2 OAc).

(b) Methyl 2,4-di-O-acetyl-3,6-di-O-benzyl-α-D-mannopyranoside (**15**). Syrup; $[\alpha]_D$ +8° (*c* 0.73, $CHCl_3$); lit.[15] $[\alpha]_D$ +7.3°; ^1H NMR ($CDCl_3$): δ 7.40–7.20 (m, 10 H, aromatic), 5.34 (dd, 1 H, $J_{2,3}$ 3.3 Hz, H-2), 5.22 (t, 1 H, $J_{3,4}$ 10 Hz, H-4), 4.73 (d, 1 H, $J_{1,2}$ 1.7 Hz, H-1), 4.55 (s, 2 H, PhCH_2), 4.52 (q, 2 H, PhCH_2), 3.87–3.81 (m, 2 H, H-3, 5), 3.56 (m, 2 H, H-6a,6b), 3.38 (s, 3 H, OMe), 2.12 and 1.90 (2 s, each 3 H, 2 OAc).

(c) Methyl 3,6-di-O-acetyl-2,4-di-O-benzyl-α-D-mannopyranoside (**16**). Amorphous foam; mp 50–60°C; $[\alpha]_D$ +12.9° (*c* 0.83, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.40–7.22 (m, 10 H, aromatic), 5.23 (d, 1 H, H-3), 4.73 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.72–4.52 (m, 4 H, 2PhCH_2), 4.41–4.23 (m, 2 H, H-6a,6b), 3.99–3.78 (m, 3 H, H-2,4,5), 3.35 (s, 3 H, OMe), 2.08 and 1.98 (2 s, each 3 H, 2 OAc). Anal. Calcd for $C_{25}H_{30}O_8$ (458.50): C, 65.49; H, 6.59; Found: C, 65.39; H, 6.63%.

(d) Methyl 3,4-di-O-acetyl-2,6-di-O-benzyl-α-D-mannopyranoside (**17**). Syrup; $[\alpha]_D$ +21.7° (*c* 0.41, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.45–7.20 (m, 10 H, aromatic), 5.39 (t, 1 H, $J_{3,4}$ 10 Hz, H-4), 5.19 (dd, 1 H, $J_{2,3}$ 3.6 Hz, H-3), 4.75 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 3.38 (s, 3 H, OMe), 2.00 and 1.92 (2 s, each 3 H, 2 OAc). Anal. Calcd for $C_{25}H_{30}O_8$ (458.50): C, 65.49 H, 6.59; Found: C, 65.38; H, 6.66%.

Phenyl exo(phenyl)-*2,3 : 4,6-di-O-benzylidene-1-thio-α-D-mannopyranoside* (**19**) *and phenyl* endo(phenyl)-*2,3 : 4,6-di-O-benzylidene-1-thio-α-D-mannopyranoside* (**20**).—The reaction of phenyl 1-thio-α-D-mannopyranoside[16] (**18**, 9.0 g) with α,α-dimethoxytoluene, as described for the preparation of **2** and **3**, yielded a 1:1 mixture of **19** and **20** which was crystallised from 1:1 EtOH–acetone (300 mL) to give **19** (6.20 g, 41.8%); mp 216–220°C; $[\alpha]_D$ +155.3° (*c* 0.90, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.60–7.28 (m, 15 H, aromatic), 6.31 (s, 1 H, PhC*H*, dioxolane), 5.87 (s, 1 H, PhC*H*, dioxane), 5.64 (s, 1 H, H-1), 4.69 (dd, 1 H, H-3), 4.41–3.73 (m 5 H, skeleton protons). Repeated recrystallisation gave a material with mp 227–230°C and $[\alpha]_D$ +153.7° (*c* 1.4, $CHCl_3$). Anal. Calcd for $C_{26}H_{24}O_5S$ (448.51): C, 69.62; H, 5.39; S, 7.15; Found: C, 69.69; H, 5.30; S, 7.12%.

The mother liquor of the first crystallisation was evaporated to half of its volume. After standing for 1 h, compound **20** crystallised from the solution; 3.32 g (22.4%); mp 140–142°C; $[\alpha]_D$ +174.4° (*c* 1.18, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.60–7.25 (m, 15 H, aromatic), 5.99 (s, 1 H, PhC*H*, dioxolane), 5.93 (s, 1 H, PhC*H*, dioxane), 5.50 (s, 1 H, H-1), 4.60–3.62 (m, 6 H, skeleton protons). Anal. Calcd for $C_{26}H_{24}O_5S$ (448.51): C, 69.62; H, 5.39; S, 7.15. Found: C, 69.68; H, 5.33; S, 7.11%.

Evaporation and column chromatography of the mother liquor yielded an additional crop of **20** (2.31 g; 15.6%); mp 139–141°C (from cyclohexane).

Phenyl 3-O-benzyl-4,6-O-benzylidene-1-thio-α-D-mannopyranoside (**21**) *and its acetate* (**23**).—To a suspension of **19** (2.24 g; 5 mmol) in 1:1 ether–CH_2Cl_2 (100 mL) was added, with stirring, a solution of $LiAlH_4$ (228 mg, 6 mmol) and $AlCl_3$ (800 mg, 6 mmol) in ether (20 mL), and stirring was continued for an additional 45 min. The excess of the reagent was decomposed with EtOAc (5 mL), and aluminium hydroxide was precipitated with water (10 mL). The organic layer was decanted, washed with water (2 × 15 mL), dried, and evaporated. The ratio of **21** and the corresponding 2-*O*-benzyl regioisomer (**22**) was 20:1 (TLC). Compound **21** was purified by means of column chromatography; 1.66 g (73.7%); mp 76–77°C (from cyclohexane); $[\alpha]_D$ +239° (*c* 0.86, $CHCl_3$). Anal. Calcd for $C_{26}H_{26}O_5S$ (450.53): C, 69.31; H, 5.82; S, 7.12. Found: C, 69.41; H, 5.90; S, 7.08%.

Conventional acetylation of **21** (200 mg) followed by column chromatography furnished phenyl 2-*O*-acetyl-3-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (**23**; 200 mg, 91.5%) as a syrup; $[\alpha]_D$ +116.9° (*c* 0.67, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.58–7.24 (m, 15 H, aromatic), 5.65 (s, 1 H, PhC*H*), 5.62 (dd, 1 H, H-2), 5.46 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.71 (s, 2 H, PhCH_2), 4.44–3.80 (m, 5 H, skeleton protons), 2.16 (s, 3 H, OAc).

Phenyl 2-O-benzyl-4,6-O-benzylidene-1-thio-α-D-mannopyranoside (**22**) *and its acetate* (**24**).—A solution of **20** (3.14 g, 7 mmol) in 1:1 ether–CH_2Cl_2 (50 mL) was treated with the $LiAlH_4$–$AlCl_3$ reagent for 25 min as described for the preparation of **21**. The ratio of **22** and **21** was 10:1 (TLC). Column chromatography of the crude product yielded **22** (1.74 g, 55.2%); mp 147–149°C (from EtOH); $[\alpha]_D$ +145° (*c* 0.80, $CHCl_3$). Anal. Calcd for $C_{26}H_{26}O_5S$ (450.53): C, 69.31; H, 5.82; S, 7.12. Found: C, 69.40; H, 5.90; S, 7.06%.

Conventional acetylation of **22** (100 mg) and subsequent column chromatography afforded phenyl 3-*O*-acetyl-2-*O*-benzyl-4,6-*O*-benzylidene-1-thio-α-D-mannopyranoside (**24**; 102 mg, 93%) as a syrup; $[\alpha]_D$ +75° (*c* 1.28, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.45–7.20 (m, 15 H, aromatic), 5.52 (s, 1 H, PhC*H*), 5.48 (d, 1 H, $J_{1,2}$ 1 Hz, H-1) 5.21 (dd, 1 H, $J_{2,3}$ 3.4, $J_{3,4}$ 10.1 Hz, H-3), 4.54 (q, 2 H, PhCH_2), 4.35–4.13 (m, 4 H, skeleton protons), 3.81 (t, 1 H, H-4), 1.98 (s, 3 H, OAc).

Methyl 3-O-benzyl-4,6-O-benzylidene-2-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**25**).—To a stirred solution of methyl 3-*O*-benzyl-4,6-*O*-benzylidene-α-D-mannopyranoside (**4**; 660 mg, 1.77 mmol), 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide (800 mg; 1.95 mmol), and 4A molecular sieves (2 g) in dry CH_2Cl_2 (30 mL) was added a solution of silver triflate (514 mg; 2 mmol) in 30 mL of dry toluene during 30 min at −40°C. Stirring was continued for an additional 1 h at −40°C, and the mixture was then neutralised by the addition of pyridine, diluted with CH_2Cl_2 (100 mL), and filtered through a Celite-pad. The filtrate was washed with aq 10% $Na_2S_2O_3$ (2 × 20 mL) and water (2 × 20 mL), dried, and evaporated. The product was purified by column chromatography to give **25** (920 mg, 73.9%); mp 142–143°C (from EtOH); $[\alpha]_D$ +41.9° (*c* 0.43, $CHCl_3$); lit.[10] mp 132–132.5°C; $[\alpha]_D$ +50.3° ($CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.55–7.25 (m, 10 H, aromatic), 5.69 (s, 1 H, PhC*H*), 5.47 (dd, 1 H, $J_{2',3'}$ 3.5 Hz, H-2'), 5.41 (dd, 1 H, $J_{3',4'}$ 10 Hz, H-3'), 5.24 (t, 1 H, $J_{4',5'}$ 10 Hz, H-4'), 5.13 (d, 1 H, $J_{1',2'}$ 1.8 Hz, H-1'), 4.73 (q, 2 H, PhCH_2), 4.70 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 4.33–3.70 (m, 9 H, skeleton protons), 3.37 (s, 3 H, OMe), 2.10, 2.09, 2.06 and 2.00 (4 s, each 3 H, 4 OAc).

Phenyl 3-O-benzyl-4,6-O-benzylidene-2-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-1-thio-α-D-mannopyranoside (**26**).—Compound **21** (400 mg) was treated with 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranosyl bromide as described for the preparation of **25**. Column chromatography (95:5 CH_2Cl_2–EtOAc) of the crude product yielded **26** (520 mg, 75%) as a glass; $[\alpha]_D$ +128.9° (*c* 0.60, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 7.55–7.25 (m, 15 H, aromatic), 5.70 (s, 1 H, PhC*H*), 5.52 (d, 1 H, $J_{1,2}$ 1 Hz, H-1), 5.47–5.16 (m, 3 H, H-2',3',4'), 5.12 (d, 1 H, $J_{1',2'}$ 1.2 Hz, H-1'), 4.77 (q, 2 H, PhCH_2), 4.40–3.86 (m, 9 H, skeleton protons), 2.11, 2.04, 2.00 and 1.89 (4 s, each 3 H, 4 OAc). Anal. Calcd for $C_{40}H_{44}O_{14}S$ (780.84): C, 61.53; H, 5.68; S, 4.11. Found: C, 61.43; H, 5.59; S, 4.10%.

Methyl 3,4,6-tri-O-acetyl-2-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranoside (**27**).—A mixture of **25** (703 mg, 1 mmol) and Pd–C (150 mg) in EtOH (100 mL) and AcOH (10 mL) was stirred overnight under an H_2 atmosphere. The catalyst was filtered off and the filtrate was concentrated in vacuo. Conventional acetylation of the residue followed by column chromatography gave **27** (640 mg, 98%) as a crystalline mass; mp 161°C (from EtOH); $[\alpha]_D$ +35.5° (*c* 0.65, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 5.47–5.20 (m, 5 H, H-3,4 and H-2',3',4'), 4.92 and 4.84 (2 d, each 1 H, $J_{1,2} = J_{1',2'}$ 1.8 Hz, H-1,1'), 4.30–3.86 (m, 7 H, skeleton protons), 3.42 (s, 3 H, OMe), 2.17 (s, 6 H, 2 OAc), 2.10, 2.08, 2.05, and 2.01 (5 s,

each 3 H, 5 OAc). Anal. Calcd for $C_{27}H_{38}O_{18}$ (650.58): C, 49.85; H, 5.89. Found: C, 49.83; H, 5.94%.

1,3,4,6-Tetra-O-acetyl-2-O-(2,3,4,6-tetra-O-acetyl-α-D-mannopyranosyl)-α-D-mannopyranose (**28**).—To a solution of **27** (300 mg) in Ac_2O (1 mL) was slowly added 4% (v/v) H_2SO_4 in Ac_2O (1 mL) at 0°C. The mixture was stirred for 3 h at 0°C, then poured into ice–water containing $NaHCO_3$, and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed with satd aq $NaHCO_3$ (15 mL) and water (3 × 20 mL), then dried and concentrated. The crystalline product (300 mg, 95.9%) was recrystallised from EtOH to give **28** (202 mg 64.6%); mp 139–140°C; $[\alpha]_D$ +38.3° (*c* 0.97, $CHCl_3$); ^1H NMR ($CDCl_3$): δ 6.25 (d, 1 H, $J_{1,2}$ 2 Hz, H-1), 5.51–5.18 (m, 5 H, H-3,4 and H-2′,3′,4′), 4.95 (d, 1 H, $J_{1',2'}$ 1.5 Hz, H-1′), 4.30–3.97 (m, 7 H, skeleton protons), 2.16 and 2.05 (2 s, each 6 h, 4 OAc), 2.15, 2.11, 2.09, and 2.02 (4 s, each 3 H, 4 OAc). Anal. Calcd for $C_{28}H_{38}O_{19}$ (678.60): C, 49.56; H, 5.64. Found: C, 49.64; H, 5.71%.

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