Synthesis of the Methyl α-D-Glycosides of Amicetose, Perosamine and Janose

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Kjølberg, O. and Neumann, K., 1992. Synthesis of the Methyl α-D-Glycosides of Amicetose, Perosamine and Janose. – Acta Chem. Scand. 46: 877–882.

New methods for the synthesis of tri- and di-deoxy sugars, namely methyl α-D-amicetoside, methyl α-D-perosaminoside and methyl α-D-janoside are described. The readily available methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-mannopyranoside has been used as chiral source in all three syntheses.

Deoxy sugars with several deoxy functions, and/or amino-deoxy groups occur frequently in various important natural compounds such as bacterial cell-wall polysaccharides, plant glycosides and antibiotics.[1,2] Methyl α-D-amicetoside **1** is part of axenomycin B^2 and amicitin[3] and has been synthesized from carbohydrate precursors[4a–j] and other sources.[4k,l] The family of 4-amino-4,6-dideoxy-D-hexoses, to which methyl α-D-perosaminoside **2** belongs, was discovered in antibiotics like perimycin[2] and in bacterial cell walls.[3,5a–d] Synthesis has been achieved from mannose derivatives[6a–d] and our approach shares some features with those routes. Finally, methyl α-D-janoside **3** was believed to be the carbohydrate unit of the antibiotic nyastin A_3[2,7] and has, to our knowledge, only been synthesized once from a non-carbohydrate source.[8]

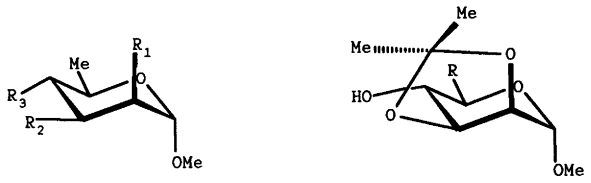
Many of these sugar derivatives show great structural diversity, and owing to their importance many of them have been synthesized by rather complicated procedures. This prompted us to investigate the possibilities of using a readily available carbohydrate derivative as a common chiral precursor in the synthesis of various deoxy sugars. A retrosynthetic analysis showed methyl 6-deoxy-2,3-*O*-isopropylidene-α-D-mannopyranoside (**6**) to be a reasonable starting material for the synthesis of **1–3** (Fig. 1).

Results and discussion

The starting material **6** could be synthesized in 60 % overall yield from methyl α-D-mannopyranoside via the 2,3-*O*-isopropylidene derivative **4** using pyridinium *p*-toluenesulfonate (PPTS)[9] as a catalyst. Following introduction of a 6-*O*-tosyl group, and reduction as described by Eis *et al.*[6b] the deoxysugar **6** was easily obtainable.

As mentioned above, methyl α-D-amicetoside **1** has already been synthesized from carbohydrate sources, but not by the route described here. Deoxygenation at C-2 and C-3 could proceed via the unsaturated sugar **11** (Fig. 2). Thus, the diol **8** was synthesized from **6** (94 % yield) by 4-*O*-benzylation and treatment of the resulting benzyl ether **7** with 90 % TFA in chloroform solution. Alternatively, the isopropylidene group could be removed by action of methanolic HCl (96 %). The Garegg–Samuelsson[10a,b] olefination, use of the Tipson–Cohen procedure,[11] via the dimesylate **9**, and elimination via the corresponding 1-dimethylamino(methylene)acetal[12] resulted in rather low yields and complex reaction mixtures. The method of choice proved to be the Barton–McCombie deoxygenation using Bu_3SnH,[13a] or better, diphenylsilane[13b] in toluene as radical chain carrier, to give the olefin **11** (86 %). The subsequent catalytic hydrogenation of **11** with 10 % Pd on carbon gave methyl α-D-amicetoside **1** (83 %). Use of **11** produced with the Bu_3SnH method resulted in incomplete hydrogenation and formation of minor impurities (detected by TLC). No isomerization at C-1 as reported for the L-enantiomer[4h] was observed (GLC). Side reactions could be avoided by stirring a solution of **11** with small amounts of the catalyst prior to hydrogenation. The trideoxy sugar **1** was characterized and converted into the dibenzyl ether **12** (86 %). The physical data were similar to those reported previously.[4b–e]

The route to methyl α-D-perosaminoside **2** required the introduction of the amino function at C-4. Former routes to **2** used nucleophilic displacement reactions of triflates,



1 R_1=R_2=H, R_3=OH
2 R_1=R_2=OH, R_3=NH_2
3 R_1=R_2=OH, R_3=H

4 R=CH_2OH
5 R=CH_2OTs
6 R=CH_3

Fig. 1. Methyl α-D-amicetoside **1**, methyl α-D-perosaminoside **2**, methyl α-D-janoside **3**, and compounds **4–6**.

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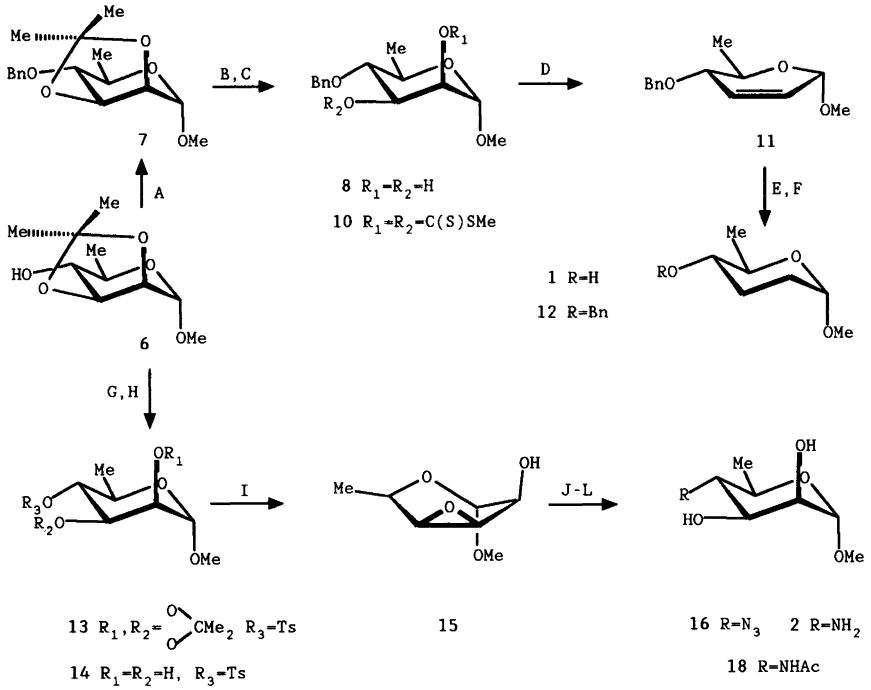

Fig. 2. Reagents: A, KOH, BnBr, DMSO; B, HCl, MeOH; C, NaH, CS_2, MeI, THF; D, diphenylsilane, AIBN, toluene; E, 10 % Pd–C, H_2, 2-propanol; F, KOH, BnBr, DMSO; G, TsCl, NEt_3, CH_2Cl_2; H, HCl, MeOH; I, NaOMe, $CHCl_3$; J, Me_3SiN_3, $Ti(OiPr)_4$, benzene; K, 10 % Pd–C, H_2, MeOH; L, Ac_2O, MeOH.

halides, or sulfonates to introduce an azide.[6b–d] We investigated the synthesis of the azide **16** via nucleophilic opening of methyl 3,4-anhydro-6-deoxy-α-D-talopyranoside (**15**). Synthesis of **15** (Fig. 2) was accomplished by 4-*O*-tosylation of **6** to give **13** (80 %), followed by removal of the isopropylidene protecting group of **13** (92 %) with methanolic HCl, and conversion of the resulting diol **14** into the epoxide **15** (70 %) using 1 M NaOMe with chloroform as the solvent. Stevens *et al.*[6a] have also used the epoxide **15** in the synthesis of perosamine derivatives. They found a marked preference for opening at C-3 when using sodium azide or ammonia as nucleophiles, which resulted in formation of *ido*-derivatives. Increasing the size of the substituent at C-2, they observed a ratio of 4:1 in favour of opening at C-4. Later, different authors have found that epoxide opening in 2,3-epoxy alcohols occurs at C-3 when using trimethylsilyl azide in the presence of $Ti(OiPr)_4$ or $Al(OiPr)_3$.[14a,b] Regioselectivity was explained by invoking coordination of the epoxy alcohol to the metal centre. When **15** was treated with Me_3SiN_3 and $Ti(OiPr)_4$ in boiling benzene we found a 3:2 ratio of products in favour of opening at C-4. Thus, the epoxy alcohol **15** seems to prefer coordination to the Ti-centre in a ^1H_O-like conformation as depicted in **15b** (Fig. 3). The azide **16** was obtained in 43 % yield. The *ido*-azide **17** (not shown), resulting from opening at C-3 (28 %), was characterized by comparison with published data. Hydrogenation of **16** with 10 % Pd on carbon yielded methyl α-D-perosaminoside **2** (79 %), which was also characterized as the acetamido derivative **18**. Physical data were in accordance with the data published elsewhere.[6c,d]

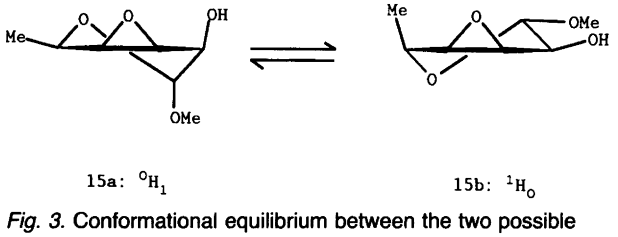

Fig. 3. Conformational equilibrium between the two possible half-chair conformations of methyl 3,4-anhydro-6-deoxy-α-D-talopyranoside (**15**).

Methyl 4,6-dideoxy-α-D-*lyxo*-hexopyranoside (methyl α-D-janoside, **3**), was synthesized from **6** (Fig. 4) by using the procedure of Barton and McCombie[15] for deoxygenation at C-4 via the xanthogenate **19**, and removal of the isopropylidene protecting group in **20** by action of 90 % TFA in chloroform solution. These three steps could be accomplished in 78 % overall yield from **6**. Since Zamojski *et al.*[8] did not characterize methyl α-D-janoside **3** completely, the dibenzyl ether **21** (82 %) was synthesized and the structure verified by comparison with published data for the L-enantiomer.[16]

Experimental

General methods. – Optical rotations were recorded with a Perkin-Elmer 241 polarimeter at 589 nm at room temperature for solutions in chloroform and the ^1H and ^{13}C NMR spectra with a Varian Gemini 200 instrument. Shifts are given in ppm for $CDCl_3$ solutions unless otherwise stated. Melting points were measured on a Bock Monoskop VS and are uncorrected. TLC was performed on Kieselgel 60 F_{254} with UV detection or/and by charring with 50 % sulfuric acid. Column chromatography was performed on silica gel 60 (230–400 mesh ASTM, Merck). The following solvent mixtures (v/v) were used for TLC and

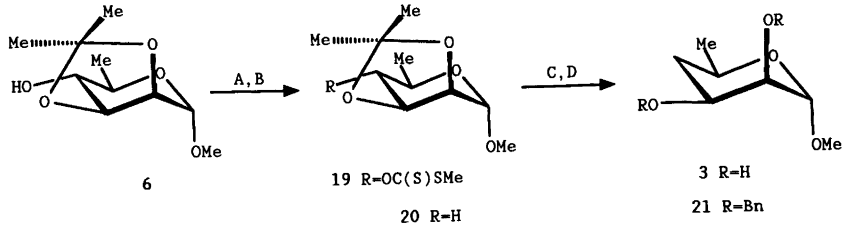

Fig. 4. Reagents: A, NaH, CS_2, MeI, THF; B, tributyltin hydride, toluene; C, 90 % TFA, $CHCl_3$; D, KOH, BnBr, DMSO.

column chromatography: A (ethyl acetate–hexane 1:1), B (dichloromethane–hexane 7:3), C (ethyl acetate), D (ethyl acetate–hexane 1:2). Organic phases were dried with magnesium sulfate and solvents were dried according to standard procedures.

Methyl 2,3-O-isopropylidene-α-D-mannopyranoside (**4**), *methyl 2,3-O-isopropylidene-6-O-tolylsulfonyl-α-D-mannopyranoside* (**5**) and *methyl 6-deoxy-2,3-O-isopropylidene-α-D-mannopyranoside* (**6**) were prepared according to standard procedures[17,18] with minor modifications.

Methyl 4-O-benzyl-6-deoxy-2,3-O-isopropylidene-α-D-mannopyranoside (**7**). To a stirred mixture of **6** (3.55 g) and KOH (3.65 g) in DMSO (50 ml) was added benzyl bromide (8.35 g) at 15 °C. Stirring was continued at room temperature for 90 min. The mixture was then cooled and MeOH (5 ml) was added to destroy the excess of reagent. After 30 min the reaction mixture was diluted with CH_2Cl_2 (50 ml) and water (50 ml) was added. The phases were separated and the organic phase was washed with water (5 × 30 ml), dried, and evaporated to yield 4.65 g (94 %) of crude syrup **7** ($R_f = 0.68$, solvent B) which was used for further reactions without purification. An analytical sample was purified by flash chromatography on silica gel (solvent B), $[\alpha]_D^{20}$ +70.9° (*c* 1.2) {Lit.[18] $[\alpha]_D$ +71.9° (*c* 1.5)}. ^{1}H NMR: δ 1.31 (d, 3 H, *J* 6.4 Hz, CH_3), 1.39 and 1.51 [2 s, 6 H, $C(CH_3)_2$], 3.23 (dd, 1 H, *J* 9.2, 6.8 Hz, H-4), 3.37 (s, 3 H, CH_3O-1), 3.60 (dd, 1 H, *J* 9.2, 6.4 Hz, H-5), 4.14 (d, 1 H, *J* 5.8 Hz, H-2), 4.28 (t, 1 H, *J* 6.8, 5.8 Hz, H-3), 4.78 (dd, 2 H, *J* 11.4 Hz, CH_2O-4), 4.87 (s, 1 H, H-1), 7.28–7.36 (m, 5 H, ArH). ^{13}C NMR: δ 19.1 (C-6), 27.4 and 29.1 [$C(CH_3)_2$], 55.7 (CH_3O-1), 65.2 (C-5), 73.7 (CH_2O-4), 76.8, 79.4 and 81.8 (C-2, C-3 and C-4), 98.6 (C-1), 109.7 [$C(CH_3)_2$], 128.0–138.7 (Ph).

Methyl 4-O-benzyl-6-deoxy-α-D-mannopyranoside (**8**). The isopropylidene group of **7** could be hydrolysed with either 90 % TFA at room temperature for 15 min to give an 82 % yield (from **6**) or as described in the following. To a solution of **7** (5.01 g) in dry MeOH (175 ml), saturated methanolic HCl (5 ml) was added dropwise and the resulting mixture was stirred at 30 °C for 4 h. The solvent was removed *in vacuo* and the resulting residue was submitted to column chromatography (solvent A). After evaporation and recrystallization from solvent D, 4.21 g (96 %) of **8** ($R_f = 0.47$, solvent A) were obtained as colourless crystals, m.p. 108–109 °C; $[\alpha]_D^{20}$ +67.6° (*c* 2.7) {Lit.[18] $[\alpha]_D$ +66.3° (*c* 5.3); Lit.[19] m.p. 108–109 °C. ^{1}H NMR: δ 1.31 (d, 3 H, *J* 6.2 Hz, CH_3), 2.94 (br s, 2 H, OH, exchangeable with D_2O), 3.33 (s, 3 H, CH_3O-1), 3.34 (m, 1 H, *J* 9.5 Hz, H-4), 3.69 (dq, 1 H, *J* 9.5, 6.2 Hz, H-5), 3.88 (m, 2 H, H-2 and H-3), 4.63 (s, 1 H, H-1), 4.74 (dd, 2 H, *J* 11.4 Hz, CH_2O-4), 7.30–7.37 (m, 5 H, ArH). ^{13}C NMR: δ 18.5 (C-6), 55.3 (CH_3O-1), 67.6 (C-5), 71.6 and 72.0 (C-2 and C-3), 75.4 (CH_2O-4), 82.1 (C-4), 100.9 (C-1), 128.4–138.8 (Ph).

Methyl 4-O-benzyl-6-deoxy-2,3-di-O-(methylthio)thiocarbonyl-α-D-mannopyranoside (**10**). To a suspension of NaH (340 mg, 60 % dispersion) in dry THF (25 ml) was added a solution of **8** (670 mg) and imidazole (5 mg) in dry THF (10 ml) at 0 °C under a nitrogen atmosphere. The mixture was allowed to reach room temperature and CS_2 (1.14 g) and, after 20 min, MeI (2.13 g) were added. After an additional 20 min the mixture was cooled to 0 °C and the excess of NaH was destroyed with acetic acid (1 ml). The solvent was removed *in vacuo*, the residue was dissolved in diethyl ether and filtered and the ether phase was washed with satd. aqueous $NaHCO_3$ (2 × 20 ml) and water (2 × 20 ml). After drying, the solvent was removed and the residue was purified by flash chromatography on silica gel with solvent B as the eluant to yield 1.04 g (93 %) of **10** as a chromatographically pure ($R_f = 0.71$, solvent B) syrup, $[\alpha]_D^{20}$ −18.4° (*c* 0.4). ^{1}H NMR: δ 1.41 (d, 3 H, *J* 6.0 Hz, CH_3), 2.55 and 2.60 (2 s, 6 H, 2 × SCH_3), 3.42 (s, 3 H, CH_3O-1), 3.75 (t, 1 H, *J* 9.6, 9.0 Hz, H-4), 3.92 (dq, 1 H, *J* 9.6, 6.0 Hz, H-5), 4.70 (dd, 2 H, *J* 11.4 Hz, CH_2O-4), 4.84 (s, 1 H, H-1), 6.29 (m, 2 H, H-2, H-3), 7.29–7.37 (m, 5 H, ArH). ^{13}C NMR: δ 18.9, 19.0 and 20.1 (2 × SCH_3 and CH_3), 55.9 (CH_3O-1), 68.3 (C-5), 75.7 (CH_2O-4), 78.3, 79.5 and 80.8 (C-2, C-3, C-4), 98.2 (C-1), 128.3–138.1 (Ph), 214.6 and 214.9 (2 × C=S).

An alternative route using two-phase-transfer catalysis with Bu_4NHSO_4 also gave **10** with the same physical data as above in 80 % yield.

Methyl 4-O-benzyl-2,3,6-trideoxy-α-D-erythro-hex-2-enopyranoside (**11**). To a solution of **10** (0.98 g) in dry toluene (35 ml) diphenylsilane (1.01 g) was added under a nitrogen atmosphere. The mixture was heated to reflux, and a solution of AIBN (1.44 g) in toluene (15 ml) was gradually added (0.5 ml each 30 min). After about 4 h, when all of the starting material **10** had reacted (TLC), the solution was allowed to cool. The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography

(CH_2Cl_2) to yield **11** (445 mg, 86 %) as a syrup ($R_f = 0.62$, CH_2Cl_2), $[\alpha]_D^{20}$ +178.5° (*c* 1.2). ^{1}H NMR: δ 1.32 (d, 3 H, *J* 6.2, CH_3), 3.43 (s, 3 H, CH_3O-1), 3.72 (ddd, 1 H, *J* 9.0, 4.8, 1.6 Hz, H-4), 3.92 (dq, 1 H, *J* 8.8, 6.2 Hz, H-5), 4.62 (dd, 2 H, *J* 11.6 Hz, CH_2O-4), 4.82 (br s, 1 H, H-1), 5.77 (ddd, 1 H, *J* 10.4, 4.8, 2.2 Hz, H-3), 6.08 (d, 1 H, *J* 10.4 Hz, H-2), 7.30–7.38 (m, 5 H, ArH). ^{13}C NMR: δ 18.5 (C-6), 55.7 (CH_3O-1), 65.8 (C-5), 70.8 (CH_2O-4), 95.5 (C-1), 126.4 and 130.6 (C-2 and C-3), 127.5, 128.0 and 138.0 (Ph).

An alternative reduction of **10** using Bu_3SnH was attempted. However, as the reaction time was longer (15 h) and the yield (62 %) lower, the method will not be described in detail.

Methyl 2,3,6-trideoxy-α-D-erythro-*hexopyranoside* (**1**). A mixture of **11** (170 mg) and 10 % Pd-on-C (50 mg) in 2-propanol (10 ml) was stirred under a hydrogen atmosphere for 24 h. The mixture was then filtered through a short silica gel column (ethyl acetate) and evaporation of the solvent gave **1** (87 mg, 83 %) as a colourless syrup ($R_f = 0.54$, solvent A), $[\alpha]_D^{20}$ +130° (*c* 1.0, H_2O) {Lit.[4e] $[\alpha]_D$ +130° (*c* 1.9, H_2O)}. ^{1}H NMR: δ 1.24 (d, 3 H, *J* 6.2 Hz, CH_3), 1.67–1.86 (m, 5 H, H-2_{ax}, H-2_{eq}, H-3_{ax}, H-3_{eq}, OH), 3.25 (m, 1 H, H-4), 3.31 (s, 3 H, CH_3O-1), 3.53 (dq, 1 H, *J* 9.0, 6.2 Hz, H-5), 4.60 (d, 1 H, *J* 1.6 Hz, H-1). ^{13}C NMR: δ 17.9 (C-6), 27.6, 29.5 (C-2 and C-3), 54.3 (CH_3O-1), 69.2 (C-5), 72.0 (C-4), 97.2 (C-1).

Methyl 4-O-benzyl-2,3,6-trideoxy-α-D-erythro-*hexopyranoside* (**12**). To a stirred mixture of **1** (87 mg), KOH (135 mg) in DMSO (4 ml) and benzyl bromide (122 mg) were added dropwise at 15 °C. The mixture was stirred for 1 h and cooled and MeOH was added to destroy the excess of reagent. After an additional 30 min CH_2Cl_2 (5 ml) and water (5 ml) were added, the phases were separated, and the CH_2Cl_2 phase was washed with water (5 × 5 ml). After drying and concentration, the syrupy residue was purified on silica gel (solvent D) to yield 122 mg (86 %) of **12**, $[\alpha]_D^{20}$ +174° (*c* 1.1) {Lit.[4h] $[\alpha]_D$ −175° (*c* 2.2) for the L-enantiomer}. ^{1}H NMR: δ 1.27 (d, 3 H, *J* 6.2 Hz, CH_3), 1.63–2.03 (2 m, 4 H, H-2_{ax}, H-2_{eq}, H-3_{ax} and H-3_{eq}), 3.08 (m, 1 H, H-4), 3.35 (s, 3 H, CH_3O-1), 3.73 (dq, 1 H, *J* 9.2, 6.2 Hz, H-5), 4.56 (dd, 2 H, *J* 11.6 Hz, CH_2O-4), 4.63 (s, 1 H, H-1), 7.30–7.36 (m, 5 H, ArH). ^{13}C NMR: δ 18.3 (C-6), 23.9 and 29.2 (C-2 and C-3), 54.3 (CH_3O-1), 67.8 (C-5), 70.6 (CH_2O-4), 78.8 (C-4), 97.3 (C-1), 127.5–138.6 (Ph).

Methyl 6-deoxy-2,3-O-*isopropylidene-4*-O-*tolylsulfonyl*-α-D-*mannopyranoside* (**13**). To a stirred mixture of **4** (2.18 g) and NEt_3 (1.31 g) in CH_2Cl_2 (30 ml) a solution of tosyl chloride (2.28 g) in CH_2Cl_2 (20 ml) was added at 0 °C over a period of 2 h. The solution was allowed to reach room temperature and stirred for 3 days. It was then diluted with CH_2Cl_2 (30 ml) and washed with satd. aqueous $NaHCO_3$ (4 × 50 ml) and water (5 × 50 ml). After drying and removal of the solvent *in vacuo*, the residue was purified by flash chromatography (solvent A) to yield **13** (2.97 g, 80 %) as a syrup ($R = 0.77$, solvent A), $[\alpha]_D$ −20.5° (*c* 1.1, MeOH) {Lit.[20] $[\alpha]_D$ −21.7° (*c* 1.0, MeOH)}. ^{1}H NMR: δ 1.23 and 1.45 [2 s, 6 H, $C(CH_3)_2$], 1.29 (d, 3 H, *J* 6.4 Hz, CH_3), 2.41 (s, 3 H, $ArCH_3$), 3.33 (s, 3 H, CH_3O-1), 3.72 (dq, 1 H, *J* 9.8, 6.4 Hz, H-5), 4.07 (m, 2 H, H-2 and H-3), 4.36 (dd, 1 H, *J* 9.8, 7.0 Hz, H-4), 4.82 (s, 1 H, H-1), 7.29 and 7.81 (2 m, 4 H, arH). ^{13}C NMR: δ 18.8 (C-6), 23.1 ($ArCH_3$), 27.5 and 28.9 [$C(CH_3)_2$], 56.1 (CH_3O-1), 64.4 (C-5), 76.5, 78.6 (C-2 and C-3), 84.2 (C-4), 98.5 (C-1), 110.2 [$C(CH_3)_2$], 128.2–144.5 (Ph).

Methyl 6-deoxy-4-O-*tolylsulfonyl*-α-D-*mannopyranoside* (**14**). A solution of **13** (2.70 g) in dry MeOH (80 ml) was treated with saturated methanolic HCl (4 ml) and stirred at 30–35 °C for 6 h. The solvent was removed and the residue was purified on silica gel (solvent A) to yield **14** (2.21 g, 92 %) as a colourless syrup ($R_f = 0.35$, solvent A), $[\alpha]_D^{20}$ +77.9° (*c* 0.75). ^{1}H NMR: δ 1.09 (d, 3 H, *J* 6.2 Hz, CH_3), 2.54 (s, 3 H, $ArCH_3$), 2.89 (br s, 2 H, 2 × OH, exchangeable with D_2O), 3.33 (s, 3 H, CH_3O-1), 3.72 (dq, 1 H, *J* 9.4, 6.2 Hz, H-5), 3.95 (m, 2 H, H-2 and H-3), 4.45 (t, 1 H, *J* 9.4 Hz, H-4), 4.87 (s, 1 H, H-1), 7.34 and 7.83 (2 m, 4 H, ArH). ^{13}C NMR: δ 17.7 (C-6), 22.2 ($PhCH_3$), 55.5 (CH_3O-1), 65.4 (C-5), 68.9 and 71.2 (C-2 and C-3), 83.8 (C-4), 100.4 (C-1), 128.5–144.9 (Ph).

Methyl 3,4-anhydro-6-deoxy-α-D-*talopyranoside* (**15**). To a solution of **14** (1.61 g) in dry chloroform (30 ml) was added methanolic NaOMe (5 ml, 1 M) over a period of 2 h, under nitrogen. After 3 h the mixture was filtered and evaporated *in vacuo*. The residue was chromatographed (solvent A) to yield a syrup which crystallized after treatment with warm hexane: 565 mg **15** (70 %); m.p. 65–66 °C; $[\alpha]_D$ +114° (*c* 1.0, H_2O) {Lit.[6a] m.p. 64–66 °C; $[\alpha]_D$ +114.37° (*c* 1.1, H_2O)}. ^{1}H NMR: δ 1.33 (d, 3 H, *J* 6.6 Hz, CH_3), 2.65 (br s, 1 H, OH, exchangeable with D_2O), 3.17 (dd, 1 H, *J* 4.0, 3.0 Hz, H-2), 3.36 (s, 3 H, CH_3O-1), 3.50 (dd, 1 H, *J* 5.0, 4.0 Hz, H-3), 3.71 (d, 1 H, *J* 5.0 Hz, H-4), 4.01 (q, 1 H, *J* 6.6 Hz, H-5), 4.40 (s, 1 H, H-1). ^{13}C NMR: δ 18.7 (C-6), 52.8, 55.8 (C-3 and C-4), 56.2 (CH_3O-1), 62.1, 64.2 (C-5 and C-2), 100.9 (C-1).

Methyl 4-azido-4,6-dideoxy-α-D-*mannopyranoside* (**16**). A solution of **15** (210 mg) and Me_3SiN_3 (450 mg) in benzene (15 ml) under nitrogen was heated to reflux. $Ti(OiPr)_4$ (555 mg) was added dropwise and heating was continued until TLC indicated that all the starting material had reacted (12 h). The mixture was cooled and evaporated *in vacuo*. The residue was treated with diethyl ether (20 ml), and stirred with 5 % sulfuric acid (10 ml) until two clear layers were observed (2 h). The phases were separated and the aqueous phase was extracted five times with diethyl ether (5 × 5 ml). The ether extracts were mixed, dried and concentrated. The residue was purified by chromatography on silica gel (solvent A). The fraction with the higher R_f-value (0.46, solvent A) proved to be methyl 3-azido-3,6-dideoxy-

α-D-idopyranoside **17** (70 mg, 28 %) with the same physical data as those published.[6a] The slower moving fraction ($R_f = 0.36$, solvent A) contained **16** (115 mg, 43 %). Melting point, specific rotation, ^1H and ^{13}C NMR data were in accordance with those published.[6c,d]

Methyl 4-amino-4,6-dideoxy-α-D-mannopyranoside (**2**). To a stirred solution of **16** (100 mg) in MeOH (5 ml) was added 10 % Pd-on-C (25 mg). Stirring was continued for 4 h under a hydrogen atmosphere. The catalyst was removed by filtration through a short silica gel column (MeOH) and the solvent was removed to afford a solid which was recrystallized from 2-propanol, to give 70 mg of **2** (79 %). Melting point, specific rotation, ^1H and ^{13}C NMR data were in accordance with those published.[6c,d]

Methyl 4-acetamido-4,6-dideoxy-α-D-mannopyranoside (**18**). To a stirred solution of **2** (88 mg) in MeOH (3 ml) was added dropwise acetic anhydride (0.5 ml) at 0 °C. Stirring was continued for 2 h at 0 °C. The solvent was removed and after codistillation of the residue with toluene, a slightly yellow syrup which crystallized when treated with diethyl ether–hexane was obtained: 90 mg (82 %) of **18**. Physical data were in accordance with those published.[6c,d]

Methyl 6-deoxy-2,3-O-isopropylidene-4-O-(methylthio)-thiocarbonyl-α-D-mannopyranoside (**19**). A solution of **6** (700 mg) in dry THF (10 ml) was cooled to 0 °C, and a solution of NaH (195 mg, 60 % suspension) and imidazole (5 mg) in dry THF (20 ml) was added under a nitrogen atmosphere. The solution was heated to room temperature and after 15 min CS_2 (720 mg) was added. After an additional 20 min MeI (800 mg) was added in one portion. When TLC indicated complete conversion of the starting material, excess NaH was destroyed by addition of acetic acid. The mixture was filtered, the solvent was evaporated *in vacuo* and the residue was treated with diethyl ether (20 ml). The ether phase was washed with satd. $NaHCO_3$ solution (1 × 10 ml) and water (2 × 20 ml) and then dried. After concentration the residue was purified on silica gel (eluant B) to yield **19** (850 mg, 86 %) as a slightly yellow syrup ($R_f = 0.62$, solvent B), $[\alpha]_D$ +39.3° (*c* 0.6) (Lit.[16] $[\alpha]_D$ −42.0° for the L-enantiomer). ^1H NMR: δ 1.23 (d, 3 H, *J* 6.6 Hz, CH_3), 1.34 and 1.59 [2 s, 6 H, $C(CH_3)_2$], 2.58 (s, 3 H, SCH_3), 3.40 (s, 3 H, CH_3O-1), 3.86 (dd, 1 H, *J* 10.0, 6.6 Hz, H-5), 4.17 (d, 1 H, *J* 5.5 Hz, H-2), 4.31 (dd, 1 H, *J* 7.6, 5.5 Hz, H-3), 4.92 (s, 1 H, H-1), 5.88 (dd, 1 H, *J* 10.0, 7.6 Hz, H-4). ^{13}C NMR: δ 17.6 (C-6), 18.8 (SCH_3), 26.8 and 28.0 [$C(CH_3)_2$], 55.4 (CH_3O-1), 64.4 (C-5), 76.1 and 76.5 (C-2 and C-3), 83.3 (C-4), 98.4 (C-1), 110.5 [$C(CH_3)_2$], 216.9 (C=S).

Methyl 4,6-dideoxy-2,3-O-isopropylidene-α-D-lyxo-hexopyranoside (**20**). To a solution of **19** (0.81 g) in dry toluene (20 ml) Bu_3SnH (1.15 g) was added under a nitrogen atmosphere. The mixture was refluxed for 6 h, cooled, concentrated *in vacuo* and purified by flash chromatography (solvent B). Evaporation of the solvent yielded 502 mg (94 %) of **20** as a syrup ($R_f = 0.32$, solvent B), $[\alpha]_D^{20}$ +41.4° (*c* 1.7) (Lit.[16] $[\alpha]_D$ −65° for the L-enantiomer). ^1H NMR: δ 1.18 (d, 2 H, *J* 6.2 Hz, CH_3), 1.30 and 1.49 [2 s, 6 H, $C(CH_3)_2$], 1.40 (m, 1 H, *J* 13.2, 10.6 Hz, H-4_{ax}), 1.82 (ddd, 1 H, *J* 13.2, 6.8, 2.2 Hz, H-4_{eq}), 3.35 (s, 3 H, CH_3O-1), 3.73 (ddd, 1 H, *J* 10.6, 6.2, 2.2, H-5), 3.88 (d, 1 H, *J* 5.6 Hz, H-2), 4.27 (ddd, 1 H, *J* 6.8, 5.6 Hz, H-3), 4.88 (s, 1 H, H-1). ^{13}C NMR: δ 21.6 (C-6), 26.7 and 28.6 [$C(CH_3)_2$], 36.6 (C-4), 55.2 (CH_3O-1), 62.4 (C-5), 71.4 and 73.2 (C-2 and C-3), 99.3 (C-1), 109.1 [$C(CH_3)_2$].

Methyl 4,6-dideoxy-α-D-lyxo-hexopyranoside (**3**). To a stirred solution of **20** (405 mg) in chloroform (10 ml) was added 90 % TFA (0.8 ml) at room temperature. After 90 min the solvent was evaporated *in vacuo* and the residue was codistilled three times with water (10 ml) and three times with toluene (10 ml). The residue was purified by flash chromatography on silica gel with ethyl acetate as the eluant. Concentratiaon of the fractions with $R_f = 0.62$ (solvent C) yielded a syrup which crystallized when treated with diethyl ether: 305 mg of **3** (94 %), m.p. 100–102 °C; $[\alpha]_D^{20}$ +81.5° (*c* 0.7) (Lit.[16] m.p. 99–100.5 °C; $[\alpha]_D$ −83° for the L-enantiomer). ^1H NMR: δ 1.21 (d, 3 H, *J* 6.4 Hz, CH_3), 1.53 (dt, 1 H, *J* 12.4, 9.6 Hz, H-4_{ax}), 1.71 (ddd, 1 H, *J* 12.4, 5.0, 2.6 Hz, H-4_{eq}), 2.78 (br s, 2 H, 2 × OH, exchangeable with D_2O), 3.36 (s, 3 H, CH_3O-1), 3.71 (br s, 1 H), 3.76–3.89 (m, 2 H), 4.70 (s, 1 H, H-1). ^{13}C NMR: δ 21.6 (C-6), 36.7 (C-4), 55.0 (CH_3O-1), 64.0 (C-5), 65.8 and 68.8 (C-2 and C-3), 101.2 (C-1).

Methyl 2,3-di-O-benzyl-4,6-dideoxy-α-D-mannopyranoside (**21**). To a stirred mixture of **3** (150 mg) and KOH (415 mg) in DMSO (10 ml) was added dropwise benzyl bromide (630 mg) at 10 °C. The mixture was stirred at room temperature for 3 h. Thereafter, MeOH (5 ml) was added to destroy the excess of reagent and after 30 min the reaction mixture was diluted with CH_2Cl_2 (10 ml) and water (10 ml). The aqueous phase was extracted with additional CH_2Cl_2 (10 ml) and the mixed CH_2Cl_2 phases werre washed five times with water (10 ml). After drying, the solvent was removed and the residue was purified by flash chromatography on silica gel (eluant B). The fractions with $R_f = 0.20$ (solvent B) were collected and concentrated to yield 261 mg **21** (82 %) as a colourless syrup, $[\alpha]_D^{20}$ +30° (*c* 3.0). ^1H NMR: δ 1.28 (d, 3 H, *J* 6.4 Hz, CH_3), 1.80 (m, 1 H, *J* 11.4 Hz, H-4_{ax}), 1.97 (t, 1 H, *J* 11.4 Hz, H-4_{eq}), 3.34 (s, 3 H, CH_3O-1), 3.70 (narrow m, 1 H), 3.85 (m, 2 H), 4.55 (s, 2 H, CH_2O), 4.79 (m, 3 H, H-1 and CH_2O), 7.29–7.45 (m, 10 H, ArH). ^{13}C NMR: δ 21.2 (C-6), 34.1 (C-4), 54.5 (CH_3O-1), 64.7 (C-5), 70.0, 72.7, 72.8 and 74.2 (C-2, C-3, and 2 × CH_2O), 100.2 (C-1), 127.2–138.7 (Ph).

Acknowledgments. This work was supported by a grant from the Royal Norwegian Council for Scientific and Industrial Research (ST.72.157.221479-Deminex 18910).

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Received November 28, 1991.