Acta Chemica Scandinavica, 1994: 48: 228–233
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ACTA
CHEMICA SCANDINAVICA
ISSN 0904–213X

Facile Preparation of 1,6-Anhydrohexoses using Solvent Effects and a Catalytic Amount of a Lewis Acid

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Åberg, P.-M. and Ernst, B., 1994. Facile Preparation of 1,6-Anhydrohexoses using Solvent Effects and a Catalytic Amount of a Lewis Acid. – Acta Chem. Scand. 48: 228–233 © Acta Chemica Scandinavica 1994.

Refluxing solutions of monosaccharides, unprotected at the 6-position and carrying *O*-methyl, *S*-ethyl, *O*-acetyl and OH-groups at the anomeric center, in acetonitrile containing a catalytic amount of a Lewis acid (0.1–0.4 equiv.) yielded 1,6-anhydrohexopyranoses in good to high yields. Best results were obtained with methyl 2,3,4-tri-*O*-dideuteriobenzyl-α-D-glycosides (87–91%). Dideuteriobenzyl protective groups were used to facilitate NMR spectral interpretations.

Several methods for the preparation of the synthetically useful 1,6-anhydro-β-D-hexopyranoses are available. For example, pyrolysis of glycans,[1–3] treatment of phenyl 2,3,4,6-tetra-*O*-acetyl-β-D-hexopyranosides with alkali,[4,5] and intramolecular displacement of a leaving group at the primary position[6–9] have been reported.

Treatment of 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose with 2–3 equivalents of a Lewis acid gave levoglucosan triacetate in 25–95% yield.[10–12] Micheel *et al.*[13] prepared 1,6-anhydro-2,3,4-tri-*O*-benzyl-β-D-glucopyranose **5** in 76% yield by refluxing 2,3,4-tri-*O*-benzyl-D-glucopyranose with a catalytic amount of *p*-TsOH in benzene. Schmidt *et al.*[14] obtained **5** in 65% yield in a similar way by using methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside **2** and 2,2,2-trichloroethanol or 2,2,2-trifluoroethanol as a cosolvent.

1,6-Anhydrosugars have proved their usefulness in a number of applications. Benzylated 1,6-anhydro sugars have been used in the preparation of linear poly α-1(1-6′)-glycans,[15–17] and in the preparation of 2,3,4-tri-*O*-benzylthioglycosides.[18] 1,6-Anhydropyranoses have also been prepared to change the conformation and subsequently the reactivity of some sugar alcohols in glycosidation reactions.[19,20] Selective protective group manipulations on these derivatives have also been described.[21,22]

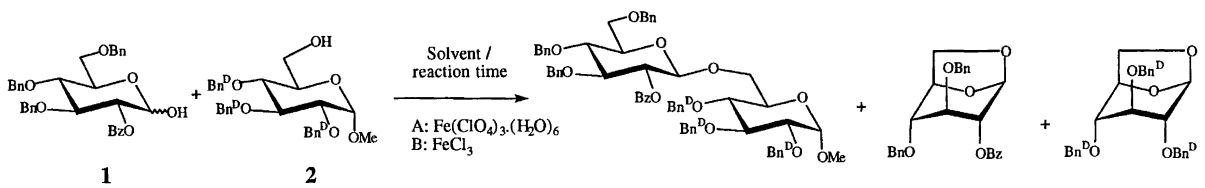
During the course of our work on catalytic glycosidation procedures, we found an efficient method for preparing tri-*O*-benzylated-1,6-anhydrohexoses with a catalytic amount of a Lewis acid in high yields. The reaction is solvent dependent, giving very good results in acetonitrile. Dideuteriobenzyl protective groups were used to facilitate NMR spectral interpretations.[23]

Results and Discussion

Glycosidation of **2** with **1** using $Fe(ClO_4)_3 \cdot (H_2O)_6$ (10 mol%) as a catalyst, in dichloromethane, gave the disaccharide **3** and 1,6-anhydrohexose **5** in approximately equal amounts, together with the 1,6-anhydrohexose **4** (Fig. 1). This reaction was also studied in dioxane and acetonitrile (Fig. 1). The only products isolated from the acetonitrile experiments were the anhydro sugars **4** and **5** in 36 and 72% yield, respectively. These results offer a useful approach to the selective formation of 1,6-anhydrohexoses.

When the hemiacetal **1** was refluxed in acetonitrile with Fe^{III} catalysis in the absence of acceptor **2** the 1,6-anhydrohexose **4** was obtained in 58% yield.[24] Similar treatment of **2** gave **5** in 87% yield. Using anhydrous $FeCl_3$, instead of the rather noxious iron perchlorate,[25] gave **5** in similar yields (90%). Using CH_2Cl_2 as the solvent gave, after 60 h, only 40% of **5** together with 40% of recovered **2**.

Further results using this method are summarized in Fig. 2. Thus, with the galacto and manno derivatives **6** and **8**, the corresponding 1,6-anhydro sugars **7** and **9** were prepared in high yields (87 and 91%, respectively). Treatment of the β-thioglycoside **10** with $Fe(ClO_4)_3 \cdot (H_2O)_6$ gave the anhydro derivative **11** (30%), whereas ca. 40% of the starting material could be recovered (as an α/β-mixture ca. 3:1). Treatment of methyl 2,3-di-*O*-deuteriobenzyl-α-D-glucopyranoside **12** with $FeCl_3$ resulted in the formation of the 1,6-anhydroglucopyranose derivative **13** and the 1,6-anhydroglucofuranose derivative **14**, each in 38% yield. Starting from ethyl 2,3-di-*O*-deuteriobenzyl-1-thio-β-D-galactopyranoside **15**, the 1,6-anhydrogalacto-



1 2 3 4 5

Entry							
1	0.2 mmol	0.2 mmol	A (0.02 mmol)	CH_2Cl_2/3h	34 %	10 %	39 %
2	0.2 mmol	0.2 mmol	A(0.02 mmol)	Dioxane/42h	–	–	ca. 40 %
3	0.2 mmol	0.2 mmol	A (0.02 mmol)	CH_3CN/25h	–	36 %	72 %
4	0.4 mmol	–	A (0.2 mmol)	CH_3CN/24h	–	58 %	
5	–	0.14 mmol	A (0.015 mmol)	CH_3CN/6h	–		87 %
6	–	0.2 mmol	B (0.062 mmol)	CH_3CN/60h	–		90 %
7	–	0.32 mmol	B (0.1 mmol)	CH_2Cl_2/41h	–		40 %[a]

[a] 40% of the starting material was recovered.

Fig. 1. The first experiments yielding 1,6-anhydro sugars.

furanose derivative **17** was obtained in 73% yield together with the 1,6-anhydrogalactopyranose derivative **16** (12%). The anhydro sugars, **13**, **14**, **16** and **17** have previously been prepared in a similar way but with almost reversed selectivity of the furanosidic and pyranosidic forms between the galacto and gluco series.[14] 1,6-Anhydro derivatives of 2-acetamido-2-deoxy sugars can also be prepared as exemplified by treatment of 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-D-mannopyranose **18** to give the anhydro derivative **19**[26] in good yield (70%). Reaction of methyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside **20** leads to the formation of the corresponding 1,4-anhydropyranose **21**[27] in 52% yield. This approach to 1,4-anhydrogalactopyranoses resulted in a higher overall yield than that of the previously described synthesis, which was based on 2,3,6-tri-*O*-benzyl-α-D-*gluco*pyranose.[27]

Acetonitrile is known to participate in glycosidation reactions to give mainly β-D-glycosides.[28,29] The effect of acetonitrile in the formation of the 1,6-anhydro sugars reported here correlates well with these findings. A proposed mechanism is shown in Fig. 3. The Lewis acid produces the glycosyloxonium ion **22**, which is stabilized by acetonitrile to give the intermediate **23**.[30] Considering the reverse anomeric effect, which has been proposed by several authors,[31] conformation **24** could be a possible second intermediate which would lead to the formation of the anhydro derivative **25**.

This simple, high yielding formation of tri-*O*-benzylated 1,6-anhydro sugars seems to be almost independent of the configuration of the starting sugar. This method offers improved yields in the preparation of several synthetically useful intermediates and can be used with a variety of protecting groups at the anomeric center (see Fig. 2). Further studies of the synthetic utility of this method are in progress.

Experimental

General methods. Concentrations were performed at diminished pressure at $<50°C$. TLC was performed on HPTLC-plates (Merck, Darmstadt, Germany), and visualized by charring with sulfuric acid. Melting points were measured on a Büchi melting point apparatus and are uncorrected. Optical rotation were measured for $CHCl_3$ solutions, at ambient temperature, using a Perkin Elmer Model 241 polarimeter. The literature values for melting points and optical rotations on dideuteriobenzyl derivatives were taken for the corresponding benzyl derivatives. ^1H NMR spectra were recorded at ambient temperature for solutions in $CDCl_3$ on Bruker AM-250 and AM-400 instruments. 500 MHz ^1H NMR spectra were recorded on a Varian Unity 500 instrument [internal standard $(CH_3)_4Si$]. ^{13}C NMR spectra were recorded on a Bruker AM-250 using $CDCl_3$ as an internal reference (77.0 ppm). MS was performed on a Finnegan MAT 90 run in FAB mode (Xe atom bombardment at 8 keV) or by chemical ionization [Cl; 150 eV; positive mode, $(M+NH_4)^+$ ions, or negative mode, $(M+Cl)^-$ and $(M-H)^-$ ions], or by a CH5 Varian Mat, run in FELD mode. Column chromatography was performed on silica gel F_{60} (0.015 – 0.040 mm Merck, Germany) and elution was with toluene–ethyl acetate or toluene–dichloromethane–ethyl acetate mixtures unless otherwise stated. Dichloromethane was distilled from P_2O_5 prior to use, tetrahydrofuran, acetonitrile, 1,4-dioxane, and pyri-

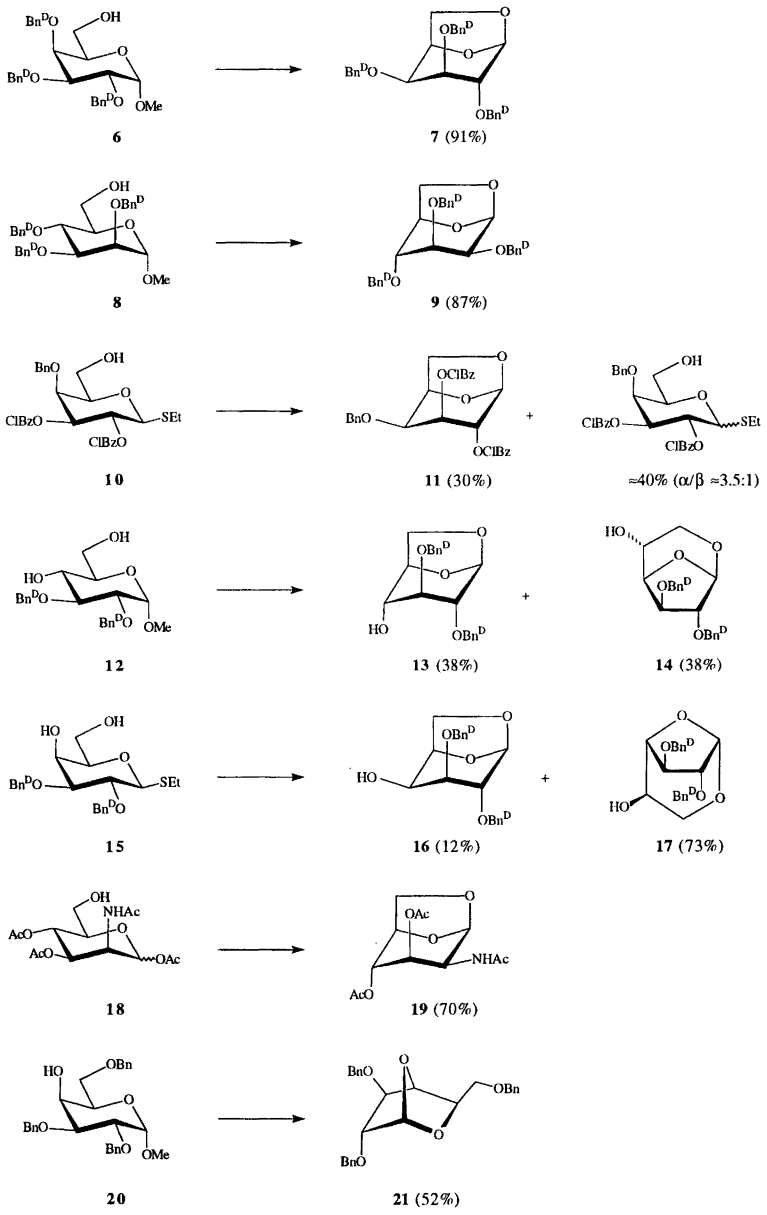


Fig. 2. Various preparations of anhydro sugars.

dine were bought *puriss*, absolute, over 4 Å molecular sieves (Fluka, Switzerland).

General procedures for the formation of 1,6-anhydrohexoses. Procedure A. The sugar derivative (ca. 100 mg, ca. 0.2 mmol) was dissolved in anhydrous acetonitrile (25 ml) and $Fe(ClO_4)_3 \cdot (H_2O)_6$ (ca. 10 mol%) was added. The reaction mixture was refluxed for the time indicated, after which TLC indicated complete conversion, or no further reaction. The reaction mixture was diluted with CH_2Cl_2 and filtered through a short pad of silica gel, to remove the catalyst. Concentration of the reaction mixture and chromatography of the residue on silica gel in the solvent system indicated, gave the products.

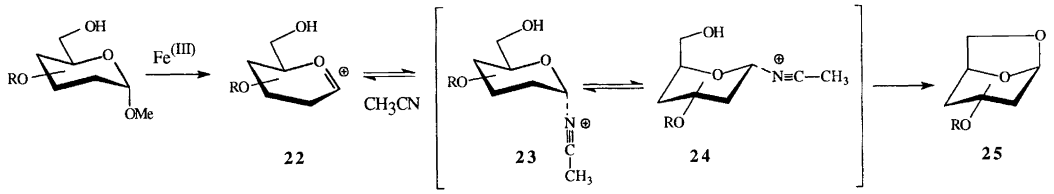


Fig. 3. Proposed mechanism for the formation of 1,6-anhydropyranoses.

Procedure B. Anhydrous $FeCl_3$ (ca. 20–30 mol%) was used as the catalyst and the work-up procedure was simplified slightly. Concentration of the reaction mixture followed by chromatography of the residue gave the products.

Methyl 2,3,4-tri-O-dideuteriobenzyl-6-O-(2-O-benzoyl-3,4,6-tri-O-benzyl-β-D-glucopyranoside)-α-D-glucopyranoside (**3**) (*Procedure A*). 2-*O*-Benzoyl-3,4,6-tri-*O*-benzyl-D-glucopyranose **1** (113 mg, 0.206 mmol), methyl 2,3,4-tri-*O*-dideuteriobenzyl-α-D-glucopyranose **2** (94 mg, 0.200 mmol), $MgSO_4$ (145 mg) and $Fe(ClO_4)_3 \cdot (H_2O)_6$ (8 mg, 0.022 mmol) were refluxed in CH_2Cl_2 (20 ml) for 3 h. Work up and chromatography (toluene–dichloromethane–ethyl acetate 7:2:1) gave **3**.

Yield: 68 mg (34%), $[\alpha]_D^{23}$ +28° (*c* 1.0); ^{1}H NMR (400 MHz): δ 3.19 (s, 3 H, OCH_3), 3.42 (dd, 1 H, $J_{2,3}$ = 9.7 Hz, H-2), 3.82 (t, 1 H, *J* = 9 Hz, H-3′), 3.86 (t, 1 H, *J* = 9.7 Hz, H-3), 4.46 (d, 1 H, $J_{1,2}$ = 3.6 Hz, H-1), 4.53 (d, 1 H, $J_{1,2}$ = 8.0 Hz, H-1′), 5.35 (dd, 1 H, $J_{2,3}$ = 9 Hz, H-2′), 7.92 (br d, 2 H, OBz). ^{13}C NMR: δ 54.9 (OCH_3), 68.0, 68.9, 73.4, 75.0 (C-6, C-6′, 3 × CH_2Ph), 69.4, 73.6, 75.4, 77.3, 78.0, 79.6, 81.8, 82.8 (C-2,3,4,5,2′,3′,4′,5′), 97.9 (C-1), 101.2 (C-1′), 127.3–132.9 (CH_{arom}), 137.7, 137.8, 138.2, 138.7 (C_{arom}), 165.0 (C = O). MS [Cl]: *m/z* 1024 $(M + NH_4)^+$ and *m/z* 1041 $(M + Cl)^-$; calc. for $C_{62}H_{58}D_6O_{12}$ 1006.48.

Compounds **4** and **5** were identified by ^{1}H NMR spectroscopy to be present in approximately 10% and 39%, respectively.

1,6-Anhydro-2-O-benzoyl-3,4-di-O-benzyl-β-D-glucopyranose (**4**). (*Procedure A*). Compound **1** (222 mg, 0.4 mmol) and $Fe(ClO_4)_3 \cdot (H_2O)_6$, (2 × 46 mg, 2 × 0.10 mmol), were refluxed in acetonitrile (40 ml) for 24 h. Work-up and chromatography (toluene–dichloromethane–ethyl acetate 5:2:1) gave **4** as an oil.

Yield: 104 mg (58%), $[\alpha]_D^{23}$ + 9.7° (*c* 0.95); ^{1}H NMR: δ 3.42 (br s, 1 H, H-4), 3.70 (quintet, 1 H, *J* = 1.6 Hz, H-3), 3.77 (dd, 1 H, $J_{5,6}$ = 5.9 Hz, $J_{6,6'}$ = 7.2 Hz, H-6), 4.14 (dd, 1 H, $J_{5,6'}$ = 1.1 Hz, H-6′), 4.48 (dd, 2 H, *J* = 12.2 Hz, CH_2Ph), 4.60 (d, 1 H, *J* = 12 Hz, CH_2Ph), 4.69 (br d,1 H, H-5), 4.83 (d, 1 H, CH_2Ph), 5.01 (br s, 1 H, H-2), 5.59 (br s, 1 H, H-1), 7.20–7.62 (m, 13 H, H_{arom}), 8.08 (br d, 2 H, H_{arom}). ^{13}C NMR: δ 65.1 (C-6), 71.2, 72.0 (CH_2Ph), 68.9, 74.4, 75.1 76.4 (C-2,3,4,5), 99.6 (C-1), 127.7–130.0 (CH_{arom}), 137.6, 137.8 (C_{arom}), 165.8 (C = O). MS [Cl]: *m/z* 481 $(M + Cl)^-$ and *m/z* 464 $(M + NH_4)^+$; calc. for $C_{27}H_{26}O_6$ 446.17.

1,6-Anhydro-2,3,4-tri-O-dideuteriobenzyl-β-D-glucopyranose (**5**) (*Procedure B*). Compound **2** (97 mg, 0.206 mmol) and $FeCl_3$ (ca. 10 mg, 0.062 mmol) were refluxed in acetonitrile (25 ml) for 2.5 days. Work-up and chromatography (toluene–ethyl acetate 3:1) gave **5** as an oil that crystallized on standing. Yield: 81 mg (90%), m.p. 85–86.5°C, $[\alpha]_D^{23}$ −27° (*c* 0.5); lit.[14] m.p 89–90°C, $[\alpha]_D^{20}$ −29.5° (*c* 1.0, $CHCl_3$). ^{1}H NMR: δ 3.33 (br s, 2 H, H-2, H-4), 3.58 (m, 1 H, H-3), 3.66 (dd, 1 H, $J_{5,6}$ = 5.8 Hz, H-6), 3.89 (dd, 1 H, $J_{5,6'}$ = 1.2 Hz, $J_{6,6'}$ = 7.2 Hz, H-6′), 4.57 (br d, 1 H, H-5), 5.45 (s, 1 H, H-1), 7.19–7.40 (m, 15 H, H_{arom}). ^{13}C NMR: δ 65.9 (C-6), 74.9, 76.5, 76.6, 77.2 (C-2,3,4,5), 101.1 (C-1), 128.3, 128.4, 128.5, 128.9, 129.0, 138.3 (C_{arom}). MS [FAB]: *m/z* 439 $(M + H)^+$; calc. for $C_{27}H_{22}D_6O_6$ 438.23.

Procedure A. Reflux of **2** (65 mg, 0.138 mmol) and $Fe(ClO_4)_3 \cdot (H_2O)_6$ (7 mg, 0.015 mmol) in acetonitrile (20 ml) for 6 h gave 53 mg **5** (87%).

Procedure B. Using CH_2Cl_2 as the solvent, reflux of **2** (150 mg, 0.319 mmol) and $FeCl_3$ (16 mg, 0.10 mmol) in 30 ml for 41 h gave 57 mg **5** (40%) and 61 mg recovered **2** (40%).

Methyl 2,3,4-tri-O-dideuteriobenzyl-α-D-galactopyranoside (**6**). Compound **6** was prepared as described for compound **8** in 50% overall yield starting from methyl α-D-galactopyranoside. Crystallization from ethyl acetate–petroleum ether gave material with m.p. 64–65°C; $[\alpha]_D^{23}$ + 3.4° (*c* 1.06); lit.[32] m.p 70°C, $[\alpha]_D$ +4° (*c* 1.38, $CHCl_3$); ^{1}H NMR: δ 1.72 (br, OH-6), 3.36 (s, 3 H, OCH_3), 3.46 (m, 1 H, H-6), 3.68 (m, 1 H, H-6′), 3.86 (br d, 1 H, H-4), 3.93 (dd, 1 H, $J_{3,4}$ = 2.8 Hz, H-3), 4.05 (dd, 1 H, $J_{2,3}$ = 9.9 Hz, H-2), 4.69 (d, 1 H, $J_{1,2}$ = 3.5 Hz, H-1), 7.25–7.44 (m, 15 H, H_{arom}). ^{13}C NMR: δ 55.3 (OCH_3), 62.3 (C-6), 70.2, 74.9, 76.3, 79.0 (C-2,3,4,5), 98.8 (C-1), 127.6–128.6 (CH_{arom}), 138.0, 138.3, 138.6 (C_{arom}). MS [Cl]: *m/z* 472 $(M + H)^+$; calc. for $C_{28}H_{26}D_6O_6$ 470.25.

1,6-Anhydro-2,3,4-tri-O-dideuteriobenzyl-β-D-galactopyranose (**7**) (*Procedure B*). Compound **6** (235 mg, 0.5 mmol), and $FeCl_3$ (14 mg, 0.086 mmol), was refluxed in acetonitrile (40 ml) for 22 h. Work-up and chromatography (toluene–dichloromethane–ethyl acetate 7:2:1) gave **7** as an oil.

Yield: 200 mg (91%), $[\alpha]_D^{23}$ −40° (*c* 1.13); lit.[33] $[\alpha]_D^{25}$ −46.1° (*c* 1.0 $CHCl_3$); ^{1}H NMR: δ 3.53 (br s, H-2), 3.63 (br t, 1 H, H-6), 3.80 (m, 1 H, H-3), 3.88 (br t, 1 H, H-4), 4.44 (br t, 1 H, H-5), 4.51 (d, 1 H, *J* = 8 Hz, H-6′), 5.36 (br s, 1 H, H-1), 7.24–7.40 (m, 15 H, H_{arom}). ^{13}C NMR: δ 64.3 (C-6), 72.7, 73.0, 74.1, 76.3 (C-2,3,4,5), 100.2 (C-1), 127.1–129.2 (CH_{arom}), 137.4, 137.8, 138.1 (C_{arom}). MS [Cl]: *m/z* 473 $(M + Cl)^-$ and *m/z* 456 $(M + NH_4)^+$; calc. for $C_{27}H_{22}D_6O_6$ 438.23.

Methyl 2,3,4-tri-O-dideuteriobenzyl-α-D-mannopyranoside (**8**). Compound **8** was prepared as the corresponding benzylated analogue[7,34] in 63% overall yield starting from methyl α-D-mannopyranoside. Purification by chromatography gave **8**, as an oil, with a purity of approximately 95%, as estimated by ^{1}H NMR spectroscopy.

$[\alpha]_D^{23}$ +36° (*c* 1.09); lit.[34] $[\alpha]_D$ +30° (*c* 0.49, $CHCl_3$); ^{1}H NMR (400 MHz): δ 2.12 (br s, 1 H, OH-6), 3.31 (s, 3 H, OCH_3), 3.61 (m, 1 H, H-5), 3.75 (m, 1 H, H-6), 3.79 (m, 1 H, H-2), 3.84 (br m, 1 H, H-6′), 3.90 (dd, 1 H, $J_{2,3}$ = 3 Hz, $J_{3,4}$ = 9.5 Hz, H-3), 3.96 (t, 1 H, $J_{4,5}$ = 9.5 Hz,

H-4), 4.70 (d, 1 H, $J_{1,2}$ = 2.0 Hz, H-1), 7.25–7.39 (m, 15 H, H_{arom}). ^{13}C NMR: δ 54.7 (OCH_3), 62.3 (C-6), 72.0, 74.5, 74.7, 80.1 (C-2,3,4,5), 99.3 (C-1), 127.6–128.3 (CH_{arom}), 138.0, 138.2, 138.3 (C_{arom}). MS [Cl]: *m/z* 505 $(M + Cl)^-$ and *m/z* 488 $(M + NH_4)^+$; calc. for $C_{28}H_{26}D_6O_6$ 470.25.

*1,6-Anhydro-2,3,4-tri-*O*-dideuteriobenzyl-β-D-mannopyranose* (**9**) (*Procedure B*). Compound **7** (210 mg, 0.446 mmol) and $FeCl_3$ (20 mg, 0.123 mmol), were refluxed in acetonitrile (40 ml) for 15 h. Work-up and chromatography (toluene–dichloromethane–ethyl acetate 4:2:1) gave **9**.

Yield: 170 mg (87%); $[\alpha]_D^{23}$ −31° (*c* 1.05); lit.[7] $[\alpha]_D$ −31.4° (*c* 0.9, $CHCl_3$); ^1H NMR: δ 3.47 (t, 1 H, $J \approx 1.9$ Hz, H-4), 3.58 (dd, 1 H, $J_{1,2}$ = 1.7 Hz, $J_{2,3}$ = 5.5 Hz, H-2), 3.72 (dd, 1 H, $J_{5,6}$ = 5.9 Hz, $J_{6,6'}$ = 7.2 Hz, H-6), 3.80 (dq, 1 H, H-3), 4.23 (dd, 1 H, $J_{5,6'}$ = 1.0 Hz, H-6′), 4.48 (m, 1 H, H-5), 5.46 (br s, 1 H, H-1), 7.21–7.43 (m, 15 H, H_{arom}). ^{13}C NMR: δ 64.9 (C-6), 74.1, 74.2, 74.3, 76.3 (C-2,3,4,5), 100.1 (C-1), 127.8–128.5 (CH_{arom}), 137.5, 137.8 (C_{arom}). MS [FAB]: *m/z* 439 $(M + H)^+$, 456 $(M + NH_4)^+$; calc. for $C_{27}H_{22}D_6O_6$ 438.23.

*Ethyl 4-*O*-benzyl-2,3-di-*O*-p-chlorobenzoyl-1-thio-β-D-galactopyranoside* (**10**). Compound **10** was prepared as described for methyl 2,3-di-*O*-benzoyl-4-*O*-benzyl-α-D-galactopyranoside.[32]

M.p. 109–110°C, $[\alpha]_D$ +116° (*c* 1.0). ^1H NMR: δ 1.26 (t, 3 H, *J* = 7.5 Hz, SCH_2CH_3), 2.77 (m, 2 H, SCH_2), 3.59 (m, 1 H, H-6), 3.76 (m, 1 H, H-5), 3.89 (m, 1 H, H-6′), 4.16 (br d, 1 H, H-4), 4.52 (d, 1 H, *J* = 11.8 Hz, CH_2Ph), 4.67 (d, 1 H, $J_{1,2}$ = 9.9 Hz, H-1), 4.74 (d, 1 H, CH_2Ph), 5.35 (dd, 1 H, $J_{2,3}$ = 10.0 Hz, $J_{3,4}$ = 3.0 Hz, H-3), 5.85 (t, 1 H, $J_{1,2} = J_{2,3}$ = 10 Hz, H-2) 7.22–7.38 (m, 9 H, H_{arom}), 7.88 (m, 4 H, H_{arom}). ^{13}C NMR: δ 14.9 (CH_3CH_2), 23.0 (SCH_2), 61.7 (C-6), 75.9 (CH_2Ph), 68.7, 73.5, 74.8, 76.5, 79.0, (C-2,3,4,5), 83.6 (C-1), 127.2–131.1 (CH_{arom}), 137.2, 139.8, 140.1 (C_{arom}), 164.6, 165.0 (C=O). MS [Cl] *m/z* 625 $(M + Cl)^-$ calc. for $C_{29}H_{28}Cl_2O_7S$ 591.51.

*1,6-Anhydro-4-*O*-benzyl-2,3-di-*O*-p-chlorobenzoyl-β-D-galactopyranose* (**11**). (*Procedure A*). Compound **10** (119 mg, 0.201 mmol) and $Fe(ClO_4)_3 \cdot 6H_2O$, (2 × 16 mg, 2 × 0.035 mmol), were refluxed in acetonitrile (20 ml) for 40 h. Work-up and chromatography (toluene–dichloromethane–ethyl acetate 7:2:1) gave **11** together with **10** as an α:β-mixture ca. 3.5:1 (ca. 40%).

Yield: 32 mg (30%), $[\alpha]_D^{23}$ +65°; ^1H NMR: δ 3.81 (dd, 1 H, H-6), 4.06 (t, 1 H, H-4), 4.51 (m, 1 H, H-6′), 4.52 (m, 1 H, CH_2Ph), 4.53 (m, 1 H, H-5), 4.71 (d, 1 H, *J* ca. 12–13 Hz, CH_2Ph), 5.11 (br s, 1 H, H-2), 5.58 (br s, 1 H, H-1), 5.71 (br d, 1 H, H-3), 7.1–7.6 (m, 9 H, H_{arom}), 8.05 (m, 4 H, OBz-H_{arom}). ^{13}C NMR: δ 64.7 (C-6), 67.8, 70.9, 71.8, 73.2 (C-2,3,4,5), 71.9 (CH_2Ph), 99.1 (C-1), 127.6–131.3 (CH_{arom}) 137.3, 139.9, 140.1 (C_{arom}), 164.1, 164.6 (2 × C=O). MS [Cl] *m/z* 527 $(M - H)^-$ and *m/z* 546 $(M + NH_4)^+$; calc. for $C_{27}H_{22}Cl_2O_7$ 528.07.

*Methyl 2,3-di-*O*-dideuteriobenzyl-α-D-glucopyranoside* (**12**). Compound **12** was prepared by dideuteriobenzylation of methyl 4,6-*O*-benzylidene-α-D-glucopyranoside followed by debenzylidenation with HCl–dioxane.

*1,6-Anhydro-2,3-di-*O*-deuteriobenzyl-β-D-glucopyranose* (**13**) *and 1,6-Anhydro-2,3-di-*O*-deuteriobenzyl-β-D-glucofuranose* (**14**). (*Procedure B*). Compound **12** (75 mg, 0.198 mmol) and $FeCl_3$, (18 mg, 0.110 mmol), were refluxed in acetonitrile (20 ml) for 16 h. Work-up and chromatography (toluene–acetone 4:1) gave **13** and **14** (crystalline material of **14** was obtained from petroleum ether–ether).

13: Yield 26 mg (38%), $[\alpha]_D^{23}$ −53° (*c* 0.92); lit.[14] $[\alpha]_D^{20}$ +54.6° (*c* 1.0 $CHCl_3$), our value is similar in magnitude, but with the opposite sign to that reported; ^1H NMR: δ 2.98 (br d, 1 H, HO-4), 3.36 (m, 1 H, H-2), 3.61 (m, 1 H, *J* = 1.6 Hz, H-3), 3.65 (br d, 1 H, H-4), 3.74 (dd, 1 H, $J_{5,6}$ = 5.8 Hz, $J_{6,6'}$ = 7.2 Hz, H-6), 4.16 (dd, 1 H, $J_{5,6'}$ = 1.0 Hz, H-6′) 4.54 (br d, 1 H, H-5), 5.44 (t, 1 H, *J* = 2.1 Hz, H-1), 7.22–7.43 (m, 10 H, H_{arom}). ^{13}C NMR: δ 64.7 (C-6), 68.6, 74.0, 76.1, 76.2, (C-2,3,4,5), 100.3 (C-1), 127.7, 127.9, 128.1, 128.5, 128.5, 137.1, 137.5 (C_{arom}). MS [Cl] *m/z* 364 $(M + NH_4)^+$; calc. for $C_{20}H_{18}D_4O_5$ 346.17.

14: Yield 26 mg (38 %), m.p. 81.5–83°C, $[\alpha]_D^{23}$ +31° (*c* 0.5); lit.[14] m.p. 84–85°C, $[\alpha]_D^{20}$ +32.2° (*c* 1.0 $CHCl_3$); ^1H NMR: δ 3.21 (d, 1 H, $J_{5,OH}$ = 11.9 Hz, HO-5), 3.65 (br d, 1 H, H-5), 3.80 (br d, 1 H, H-6), 4.20–4.26 (m, 3 H, H-2,3,6′), 4.44 (br d, 1 H, H-4), 5.18 (br s, 1 H, H-1), 7.24–7.44 (m, 10 H, H_{arom}). ^{13}C NMR: δ 67.4 (C-6), 64.8, 79.4, 83.9, 84.9 (C-2,3,4,5), 101.9 (C-1), 127.8, 128.0, 128.1, 128.2, 128.5, 128.5, 137.0 (C_{arom}). MS [Cl] *m/z* 364 $(M + NH_4)^+$ calc. for $C_{20}H_{18}D_4O_5$ 346.17.

*Ethyl 2,3-di-*O*-dideuteriobenzyl-1-thio-β-D-galactopyranoside* (**15**). Compound **15** was prepared as **12** starting from ethyl 4,6-*O*-benzylidene-1-thio-β-D-galactopyranoside.[35]

$[\alpha]_D^{23}$ −7.5° (*c* 1.07); ^1H NMR: δ 1.30 (t, 3 H, SCH_2CH_3), 2.77 (m, 2 H, SCH_2), 3.48 (m, 1 H, H-5), 3.55 (dd, 1 H, H-3), 3.68 (t, 1 H, H-2), 3.83 (m, 1 H, H-6), 3.96 (m, 1 H, H-6′), 4.06 (br d, 1 H, H-4), 4.44 (d, 1 H, $J_{1,2}$ = 9.5 Hz, H-1), 7.26–7.45 (m, 10 H, H_{arom}). ^{13}C NMR: δ 15.1 (CH_2CH_3), 24.8 (SCH_2), 62.8 (C-6), 67.5, 77.7, 77.9, 82.1 (C-2,3,4,5), 85.2 (C-1). MS [Cl] *m/z* 426 $(M + NH_4)^+$; calc. for $C_{22}H_{24}D_4O_5S$ 408.55.

*1,6-Anhydro-2,3-di-*O*-deuteriobenzyl-β-D-galactopyranose* (**16**) *and 1,6-anhydro-2,3-di-*O*-deuteriobenzyl-α-D-galactofuranose* (**17**). (*Procedure B*). Compound **15** (122 mg, 0.3 mmol) and $FeCl_3$, (2 × 14 mg, 2 × 0.086 mmol) were refluxed in acetonitrile (25 ml) for 20 h. Work-up and chromatography ($CHCl_3$–ether 5:1) gave **16** and **17**.

16: Yield 13 mg (12%), $[\alpha]_D^{23}$ −60° (*c* 0.5); lit.[14] $[\alpha]_D^{20}$ −57.6° (*c* 1.0 $CHCl_3$); ^1H NMR: δ 3.01 (d, 1 H, $J_{4,OH}$ = 9.9 Hz, OH-4), 3.56 (t, 1 H, *J* = 1.6 Hz, H-2), 3.61 (m, 1 H, H-6), 3.73 (dq, 1 H, H-3), 4.07 (m, 1 H, H-4), 4.16 (d, 1 H, $J_{6,6'}$ = 7.5 Hz, H-6′), 4.39 (br t, 1 H, H-5),

5.39 (t, 1 H, $J_{1,2}$ = 1.6 Hz, H-1), 5.71 (br d, 1 H, H-3), 7.24–7.43 (m, 10 H, H_{arom}). ^{13}C NMR: δ 63.3 (C-6), 64.6, 74.3, 74.4, 75.8, (C-2,3,4,5), 99.9 (C-1), 127.8–128.6 (CH_{arom}), 136.9, 137.2 (C_{arom}). MS [Cl] *m/z* 364 $(M + NH_4)^+$; calc. for $C_{20}H_{18}D_4O_5$ 346.17.

17: Yield 75 mg (73 %), $[\alpha]_D^{23}$ +57° (*c* 1.0); lit.[14] $[\alpha]_D^{20}$ +58° (*c* 1.0 $CHCl_3$); ^1H NMR: δ 1.96 (d, 1 H, $J_{4,OH}$ = 4.6 Hz, OH-5), 3.71 (t, 1 H, $J_{6,6'}$ = 10.5 Hz, H-6), 3.97 (ddd, 1 H, H-6′), 4.05 (m, 1 H, H-5), 4.12 (dq, 1 H, H-2), 4.15 (br d, 1 H, $J_{2,3}$ = 2.4 Hz, H-3), 4.23 (br d, 1 H, H-4), 5.33 (d, 1 H, $J_{1,2}$ = 3.7 Hz, H-1), 7.25–7.40 (m, 10 H, H_{arom}). ^{13}C NMR: δ 65.4 (C-6), 62.7, 80.9, 81.7, 85.3 (C-2,3,4,5), 96.9 (C-1), 127.9–128.4 (CH_{arom}), 137.2, 137.4 (C_{arom}). MS [Cl] *m/z* 364 $(M + NH_4)^+$; calc. for $C_{20}H_{18}D_4O_5$ 346.17.

*2-Acetamido-3,4-di-*O*-acetyl-1,6-anhydro-2-deoxy-β-*D*-mannopyranose* (**19**) (*Procedure B*). 2-Acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-D-mannopyranose[36] **18** (111 mg, 0.296 mmol) and $FeCl_3$ (13 mg, 0.080 mmol) were refluxed in acetonitrile (25 ml) for 18 h. Work-up and chromatography (*tert*-butyl methyl ether–acetone 4:1) gave **19**.

Yield: 59 mg (70%), crystalline material was obtained from $CHCl_3$–ether with m.p. 177–178°C (decomp. 140°C), $[\alpha]_D^{23}$ −94° (*c* 0.52); lit.[26] m.p. 182–183°C (sublimes at 140°C). $[\alpha]_D$ −98° (*c* 0.80, $CHCl_3$); ^1H NMR: δ 2.01 (s, 3 H, $NHCOCH_3$), 2.16, 2.17 (2 s, 6 H, $OCOCH_3$), 3.81 (dd, 1 H, $J_{5,6}$ = 5.8 Hz, $J_{6,6'}$ = 8.0 Hz H-6), 4.09 (dd, 1 H, $J_{5,6'}$ = 1.0 Hz, H-6′), 4.49 (m, 1 H, H-2), 4.62 (dm, 1 H, H-5), 4.74 (t, 1 H, *J* = 1.8Hz, H-4), 5.09 (dq, 1 H, H-3), 5.35 (br s, 1 H, H-1), 5.80 (d, 1 H, NH). ^{13}C NMR: δ 20.9 (2 × $COCH_3$), 23.2 ($NHCOCH_3$), 46.6 (C-2), 65.0 (C-6), 68.7, 70.5, 73.1 (C-3,4,5), 100.7 (C-1), 169.2, 169.6, 169.7 (C = O). MS [FELD]: *m/z* 287 $(M)^+$; calc. for $C_{12}H_{17}NO_7$ 287.10.

*1,4-Anhydro-2,3,6-tri-*O*-benzyl-β-*D*-galactopyranose* (**21**) (*Procedure B*). Methyl 2,3,6-tri-*O*-benzyl-α-D-galactopyranoside[32] **20** (165 mg, 0.355 mmol), and $FeCl_3$ (20 mg, 0.123 mmol), were refluxed in acetonitrile (40 ml) for 20 h. Work-up and chromatography (toluene–dichloromethane–ethyl acetate 5:2:1) gave **21** as an oil.

Yield: 80 mg (52%), $[\alpha]_D^{23}$ +57° (*c* 1.0); lit.[27] $[\alpha]_D^{25}$ +57.6° (*c* 1.0 $CHCl_3$); ^1H NMR (400 MHz): δ 3.35 (q, 1 H, H-6), 3.43 (q, 1 H, H-6′), 3.55 (d, 1 H, H-3), 3.82 (m, 1 H, H-5), 3.85 (br s, 1 H, H-2), 4.59 (d, 1 H, H-4), 4.46–4.62 (m, 6 H, 3 × CH_2Ph), 5.46 (d, 1 H, $J_{1,2}$ = 2.5 Hz, H-1), 7.23–7.40 (m, 10 H, H_{arom}). ^{13}C NMR: δ 69.8, 71.1, 72.3, 73.5 (C-6, 3 × CH_2Ph), 74.2, 81.3, 82.8, 87.2 (C-2,3,4,5), 98.7 (C-1), 127.8–128.5 (CH_{arom}), 137.3, 137.4, 137.8 (C_{arom}). MS [FELD]: *m/z* 433 $(M + H)^+$; calc. for $C_{27}H_{28}O_5$ 432.52.

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Received June 16, 1993.