Supporting information

Iron(III) Chloride-Catalyzed Activation of Glycosyl Chlorides

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General Experimental

Column chromatography was performed on silica gel 60 (70-230 mesh), reactions were monitored by TLC on Kieselgel 60 F254. The compounds were detected by examination under UV light and by charring with 10% sulfuric acid in methanol. Solvents were removed under reduced pressure at <40 °C. CH₂Cl₂ and ClCH₂CH₂Cl (1,2-DCE) were distilled from CaH₂ directly prior to application. Anhydrous DMF was used as it is. Molecular sieves (4 Å), used for reactions, were crushed and activated in vacuo at 390 °C during 8 h in the first instance and then for 2-3 h at 390 °C directly prior to application. Optical rotations were measured at ‘Jasco P-2000’ polarimeter. ¹H NMR spectra were recorded in CDCl₃ at 300 or 600 MHz.
Synthesis of Glycosyl Chloride Donors

2,3,4,6-Tetra-O-benzyl-α-D-glucopyranosyl chloride (1). A solution of oxalyl chloride (621.1 mg, 4.89 mmol) in dichloromethane (2.0 mL) was added dropwise to a stirring solution of 2,3,4,5-tetra-O-benzyl-D-glucopyranose (881.8 mg, 1.63 mmol) in dichloromethane (6.0 mL) and DMF (2.0 mL) and the resulting mixture was stirred under argon for 30 min at 0 °C. The external cooling was then removed and the reaction mixture was allowed to slowly warm to rt and stirred for additional 1 h at rt. After that, the resulting mixture was concentrated in vacuo. The residue was dissolved in a mixture of ethyl acetate and hexane (10 mL, 1/1, v/v) and passed through a pad of silica gel (10 g). The pad of silica gel was washed with a mixture of ethyl acetate and hexane (100 mL, 1/1, v/v) and the combined eluate was concentrated in vacuo to afford the title compound as a clear oil in 98% yield (899.1 mg, 1.59 mmol). Analytical data for 1 was essentially the same as reported previously.

2,3,4,6-Tetra-O-benzyl-α-D-galactopyranosyl chloride (10). Thionyl chloride (302.8 mg, 2.54 mmol) was added dropwise to a stirring solution of 2,3,4,5-tetra-O-benzyl-D-galactopyranose (458.7 mg, 0.848 mmol) in 1,2-dichloroethane (5.0 mL) and DMF (0.1 mL) and the resulting mixture was stirred under argon for 1 h at 0 °C. The reaction mixture was concentrated in vacuo, the residue was dissolved in a mixture of ethyl acetate and hexane (5 mL, 1/1, v/v) and passed through a pad of silica gel (5 g). The pad of silica gel was washed with a mixture of ethyl acetate and hexane (75 mL, 1/1, v/v) and the combined eluate was concentrated in vacuo to afford the title compound as a clear oil in 95% yield (451.0 mg, 0.81 mmol). Analytical data for 10 was essentially the same as reported previously.

2,3,4,6-Tetra-O-benzyl-α-D-mannopyranosyl chloride (15). A solution of oxalyl chloride (322.6 mg, 2.54 mmol) in dichloromethane (6.5 mL) was added dropwise to a stirring solution of 2,3,4,5-tetra-O-benzyl-D-mannopyranose (458.1 mg, 0.847 mmol) in 1,2-dichloroethane (5.0 mL) and DMF (0.1 mL) and the resulting mixture was stirred under argon for 30 min at 0 °C. The external cooling was then removed and the reaction mixture was allowed to slowly warm to rt and stirred for additional 1 h at rt. After that, the resulting mixture was concentrated in vacuo. The residue was dissolved in a mixture of ethyl acetate and hexane (5 mL, 1/1, v/v) and passed through a pad of silica gel (5 g). The pad of silica gel was washed with a mixture of ethyl acetate and hexane (100 mL, 1/1, v/v) and the combined eluate was concentrated in vacuo to afford the title compound as a clear oil in 95% yield (452 mg, 0.81 mmol). Analytical data for 15 was essentially the same as reported previously.

2,3,4,6-Tetra-O-benzoyl-β-D-glucopyranosyl chloride (20). Thionyl chloride (106.85 mg, 0.898 mmol) was added dropwise to a stirring solution of 2,3,4,5-tetra-O-benzoyl-D-glucopyranose (242.8 mg, 0.45 mmol) in 1,2-dichloroethane (5.0 mL) and DMF (0.1 mL) and the resulting mixture was stirred under argon for 1 h at 0 °C. The reaction mixture was then concentrated in vacuo. The residue was dissolved in a mixture of ethyl acetate and hexane (5 mL, 1/1, v/v) and passed through a pad of silica gel (3.5 g). The pad of silica gel was washed with a
mixture of ethyl acetate and hexane (50 mL, 1/1, v/v) and the combined eluate was concentrated \textit{in vacuo} to afford the title compound as a white foam in 98% yield (276.8 mg, 0.44 mmol). Analytical data for 20 was essentially the same as reported previously.\textsuperscript{3}

**Synthesis of Disaccharides**

**General procedure for glycosidation of glycosyl chlorides in the presence of FeCl$_3$.** A mixture of glycosyl chloride donor (0.05 mmol), glycosyl acceptor (0.025 mmol) and molecular sieves (4 Å, 60 mg) in dichloromethane (1.0 mL) was stirred under argon for 1 h at rt. The mixture was then cooled to 0 °C, FeCl$_3$ (0.01 mmol) was added, and the reaction mixture was stirred for the time specified in Table 1 of the article. If the reaction was incomplete after 3 h at 0 °C, the external cooling was removed, the reaction mixture was allowed to slowly warm to rt, and stirred for additional 13 h at rt. After that, the solid was filtered off through a pad of Celite and rinsed successively with dichloromethane. The combined filtrate (~30 mL) was washed with sat. aq. NaHCO$_3$ (10 mL) and water (2 x 10 mL). The organic phase was separated, dried over magnesium sulfate, filtered, and concentrated \textit{in vacuo}. The residue was purified by column chromatography on silica gel (ethyl acetate/toluene gradient elution). If necessary, further purification was accomplished by size-exclusion column chromatography on Sephadex LH20 (methanol/dichloromethane, 1/1, v/v, isocratic elution). Anomeric ratios were determined by comparison of integral intensities of their respective signals in the $^1$H NMR spectra of anomeric mixtures.

- **Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-α/β-D-glucopyranosyl)-α-D-glucopyranoside (3).** The title compound was obtained from donor 1 and acceptor 2 under the general glycosylation method as a colorless foam in 67% yield (α/β = 1.1/1). Analytical data for 3 was in accordance with that previously reported.\textsuperscript{5}

- **Methyl 2,4,6-tri-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-α/β-D-glucopyranosyl)-α-D-glucopyranoside (5).** The title compound was obtained from donor 1 and acceptor 4 under the general glycosylation method as an oil in 47% yield of 5 (α/β = 1.2/1). Analytical data for 5 was in accordance with previously reported values.\textsuperscript{6}

- **Methyl 2,4,6-tri-O-benzyl-3-O-(2,3,4,6-tetra-O-benzyl-α/β-D-glucopyranosyl)-α-D-glucopyranoside (7).** The title compound was obtained from donor 1 and acceptor 6 under the general glycosylation method as an oil in 60% yield of 7(α/β = 1.5/1). Analytical data for 7 was in accordance with previously reported values.\textsuperscript{7}
Methyl 3,4,6-tri-O-benzyl-2-O-(2,3,4,6-tetra-O-benzyl-α/β-D-glucopyranosyl)-α-D-glucopyranoside (9). The title compound was obtained from donor 1 and acceptor 8 under the general glycosylation method as a colorless foam in 80% yield of 9 (α/β = 1.0/1). Analytical data for 9 was in accordance with previously reported values.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-α/β-D-galactopyranosyl)-α-D-glucopyranoside (11). The title compound was obtained from donor 10 and acceptor 2 under the general glycosylation method as an oil in 88% yield of 11 (α/β = 1/1.4). Analytical data for 11 was in accordance with previously reported values.

Methyl 2,3,6-tri-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-α/β-D-galactopyranosyl)-α-D-glucopyranoside (12). The title compound was obtained from donor 10 and acceptor 4 under the general glycosylation method as an oil in 57% yield of 12 (α/β = 1.6/1). Analytical data for 12 was in accordance with previously reported values.

Methyl 2,4,6-tri-O-benzyl-3-O-(2,3,4,6-tetra-O-benzyl-α/β-D-galactopyranosyl)-α-D-glucopyranoside (13). The title compound was obtained from donor 10 and acceptor 6 under the general glycosylation method as an oil in 80% yield of 13 (α/β = 1.3/1). Analytical data for 13 was in accordance with previously reported values.

Methyl 3,4,6-tri-O-benzyl-2-O-(2,3,4,6-tetra-O-benzyl-α/β-D-galactopyranosyl)-α-D-glucopyranoside (14). The title compound was obtained from donor 10 and acceptor 8 under the general glycosylation method as an oil in 90% yield of 14 (α/β = 1/2.7). Analytical data for 14 was in accordance with previously reported values.

Methyl 2,3,4-tri-O-benzyl-6-O-(2,3,4,6-tetra-O-benzyl-α/β-D-mannopyranosyl)-α-D-glucopyranoside (16). The title compound was obtained from donor 15 and acceptor 5 under the general glycosylation method as an oil in 80% yield of 16 (α/β = 4.5/1). Analytical data for 16 was in accordance with previously reported values.
Methyl 2,3,6-tri-O-benzyl-4-O-(2,3,4,6-tetra-O-benzyl-α-D-mannopyranosyl)-α-D-glucopyranoside (17). The title compound was obtained from donor 15 and acceptor 6 under the general glycosylation method as an oil in 66% yield of 17. Analytical data for 17 was in accordance with previously reported values.14

Methyl 2,4,6-tri-O-benzyl-3-O-(2,3,4,6-tetra-O-benzyl-α-D-mannopyranosyl)-α-D-glucopyranoside (18). The title compound was obtained from donor 15 and acceptor under the general glycosylation method as an oil in 56% yield of 18. Analytical data for 18 was in accordance with previously reported values.15

Methyl 3,4,6-tri-O-benzyl-2-O-(2,3,4,6-tetra-O-benzyl-α/β-D-mannopyranosyl)-α-D-glucopyranoside (19). The title compound was obtained from donor 15 and acceptor 8 under the general glycosylation method as an oil in 95% yield of 19 (α/β = 2.6/1). Analytical data for 19 was in accordance with previously reported values.8

Methyl 6-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,3,4-tri-O-benzyl-α-D-glucopyranoside (21). The title compound was obtained from donor 20 and acceptor 5 under the general glycosylation method as an oil in 98% yield of 21. Analytical data for 21 was in accordance with previously reported values.16

Methyl 4-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,3,6-tri-O-benzyl-α-D-glucopyranoside (22). The title compound was obtained from donor 20 and acceptor 6 under the general glycosylation method as an oil in 80% yield of 22. Analytical data for 22 was in accordance with previously reported values.16

Methyl 3-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-2,4,6-tri-O-benzyl-α-D-glucopyranoside (23). The title compound was obtained from donor 20 and acceptor 7 under the general glycosylation method as an oil in 52% yield of 23. Analytical data for 23 was in accordance with previously reported values.4
Methyl 2-O-(2,3,4,6-tetra-O-benzoyl-β-D-glucopyranosyl)-3,4,6-tri-O-benzyl-α-D-glucopyranoside (24).
The title compound was obtained from donor 20 and acceptor 8 under the general glycosylation method as an oil in 73% yield of 24. Analytical data for 24 was in accordance with previously reported values.\(^\text{17}\)

References

NMR Spectra of known glycosyl chlorides
NMR Spectra of known disaccharides