Supporting Information

A Sequential Three-Component One-Pot Synthesis of a Common Tetrasaccharide Block Related to the Lipopolysaccharide of the *Escherichia Coli O9*, *Klebsiella pneumonia O3* and *Hafnia alvei PCM 1223*

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Experimental Section

General Procedure

All reactions were performed in flamed-dried flasks fitted with rubber septa under a positive pressure of argon, unless otherwise stated. Dichloromethane was refluxed with P₂O₅ and distilled before use. Diethyl ether (Merck, India) and acetonitrile (Merck, India) were distilled over P₂O₅, and stored over 4Å molecular sieves before use. Trimethylsilyl trifluoromethanesulfonate was purchased from Aldrich and used without further purification. Triethylamine was purchased from Merck (India) and distilled over potassium hydroxide before use. N-(p-methylthiophenyl)-ε-caprolactam (A) was synthesized. Traces of water in the donor and acceptor glycosides were removed by co-evaporation with toluene. Molecular sieves (4Å) were flame dried before use. Flash column chromatography was performed employing Silica Gel 60 Sorbent (40-63 μm, 230-400 mesh). Thin-layer chromatography (analytical and preparative) was performed using Merck silica gel plates (60-F₂₅₄) to monitor the reactions and visualized under UV (254 nm) and/or by charring with 5% ethanolic solution of sulfuric acid. ¹H and ¹³C NMR spectra were recorded on a Bruker DPX-300 (300 MHz), or a Bruker Avance DRX-500 (500 MHz) spectrometer at ambient temperature using CDCl₃ and D₂O as solvents, and assigned using 2D-methods (COSY, HSQC and HMBC). Chemical shifts were expressed in parts per million (δ scale). Optical rotations were measured using Jasco P-1020 digital polarimeter. High Resolution Mass Spectra (HRMS) were measured in a QTOF I (quadrupole-hexapole-TOF) mass spectrometer with an orthogonal Z-spray-electrospray interface on Micro (YA-263) mass spectrometer (Manchester, UK).
Preparation of \( N-(p\text{-methylphenylthio})-\varepsilon\text{-caprolactam} \) (A) A solution of freshly prepared \( p\text{-toluenesulfonyl chloride} \)\(^1\) (5.0 g, 31.6 mmol), in \( \text{CCl}_4 \) (20 mL) was added drop wise with stirring, at \( 0-5 \) °C and under anhydrous conditions, to a solution of caprolactam (6.85 g, 31.6 mmol) and \( \text{Et}_3\text{N} \) (5.3 mL, \( 38 \) mmol) in \( \text{CCl}_4 \) (30 mL). The reaction mixture was stirred at ambient temperature for 3 h, and then filtered to remove the precipitate. The precipitate was washed with \( \text{CCl}_4 \) (2 x 10 mL). The combined filtrate and washings was washed with water. The organic phase was dried over anhydrous \( \text{Na}_2\text{SO}_4 \), and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel (eluent: hexane/EtOAc, 15:1) to give \( N-(p\text{-methylphenylthio})-\varepsilon\text{-caprolactam} \) as white solid (6.56 g, 88%). Crystallization from hexane-EtOAc afforded white needle shaped crystal; m.p. 70-72 °C; \(^1\text{H NMR} \) (400 MHz, CDCl\(_3\)): \( \delta \) 7.28-7.26 (m, 2H, ArH), 7.13-7.11 (m, 2H, ArH), 3.86-3.83 (m, 2H), 2.70-2.67 (m, 2H), 2.31 (s, 3H), 1.72-1.65 (m, 6H); \(^1\text{C NMR} \) (100 MHz, CDCl\(_3\)): \( \delta \) 178.1 (C=O), 137.9, 134.4, 130.0, 128.4, 58.3, 37.3, 29.8, 29.2, 23.5, 21.3; HRMS (ESI-TOF) calcd for \( \text{C}_{13}\text{H}_{17}\text{NOSNa} \) [M + Na]\(^+\) 258.0929, found 258.0926.

**Methyl 2-O-acetyl-3,4,6-tri-O-benzyl-\( \alpha \text{-D-mannopyranosyl-(1→2)} \)-3,4,6-tri-O-benzyl-\( \alpha \text{-D-mannopyranoside} \) (7).** A solution of 3 (200.0 mg, 0.373 mmol), 6 (157.2 mg, 0.339 mmol), \( N-(p\text{-methylphenylthio})-\varepsilon\text{-caprolactam} \) (97.0 mg, 0.411 mmol) and flame activated 4Å MS were stirred in dry CH\(_2\text{Cl}_2 \) (8 ml) for 30 min at room temperature. The reaction mixture was then cooled to 0 °C, stirred for 5 min followed by injection of TMSOTf (81 \( \mu\text{L}, 0.448 \) mmol). The reaction mixture was warmed gradually to room temperature over 30 min. The reaction was quenched with Et\(_3\text{N} \) (0.7 mL). The reaction mixture after dilution with CH\(_2\text{Cl}_2 \) (10 mL) was filtered through Celite bed, and the bed was

washed with CH$_2$Cl$_2$ (3 x 10 mL). The combined filtrate and washings was concentrated under reduced pressure. The crude residue was directly purified by silica gel flash column chromatography (hexane/EtOAc, 6:1) to afford 10$^2$ (293.3 mg, 92%) as a white foam. R$_f$ 0.31 (25% EtOAc in hexane); $[\alpha]^{24}_D$ +20.8 (c 1.0, CHCl$_3$); Lit.$^2$ $[\alpha]_D$ +19.0 (c 1.8, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.35-7.15 (m, 30H, ArH), 5.55 (br s, 1H), 5.09 (br s, 1H), 4.87 (d, 1H, $J$ = 2.7 Hz), 4.84 (d, 1H, $J$ = 2.7 Hz), 4.78 (br s, 1H), 4.69-4.65 (m, 5H), 4.57 (d, 1H, $J$ = 2.5 Hz), 4.54-4.39 (m, 4H), 4.01 (br s, 1H), 3.97 (d, 1H, $J$ = 3.1 Hz), 3.94-3.92 (m, 1H), 3.88-3.69 (m, 8H), 3.26 (s, 3H, OCH$_3$).

**Methyl 3,4,6-tri-O-benzyl-$\alpha$-D-mannopyranosyl-(1$\rightarrow$2)-3,4,6-tri-O-benzyl-$\alpha$-D-mannopyranoside (5).** To a stirred solution of 7 (210.2 mg, 0.224 mmol) in dry MeOH (9.5 mL), was added 1M methanolic NaOMe (0.5 mL) solution, and the reaction mixture was stirred for 5 h at room temperature. The reaction mixture was then neutralized with Amberlite-120 (H$^+$) and filtered. The resin was washed with MeOH, and the combined filtrates were concentrated under reduced pressure. The residue was purified by flash column chromatography (elute: hexane/EtOAc, 5:1) to give the title product as glassy syrup (198.8 mg, 99%); $[\alpha]^{24}_D$ +25.3 (c 1.0, CHCl$_3$), Lit.$^2$ $[\alpha]_D$ +26.8 (c 1.7, CHCl$_3$); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ 7.35-7.17 (m, 30H, ArH), 5.15 (br s, 1H), 4.86-4.80 (m, 3H), 4.72-4.66 (m, 3H), 4.61 (s, 1H), 4.58-4.53 (m, 5H), 4.49 (d, 1H, $J$ = 4.2 Hz), 4.13 (br s, 1H), 4.04 (br s, 1H), 3.95-3.77 (m, 6H), 3.73-3.70 (m, 4H), 3.24 (s, 3H, OCH$_3$).

**Methyl $\alpha$-D-mannopyranosyl-(1$\rightarrow$3)-$\alpha$-D-mannopyranosyl-(1$\rightarrow$2)-$\alpha$-D-mannopyranosyl-(1$\rightarrow$2)-$\alpha$-D-mannopyranoside (1).**

A solution of 2 (81.2 mg, 0.0489 mmol) in 0.05M NaOMe in dry MeOH (10 mL) was stirred for 5 h at room temperature. The reaction mixture was then neutralized with Amberlite-120 (H⁺) and filtered. The resin was washed with MeOH, and the combined filtrates were concentrated under reduced pressure. A mixture of the residue, 10% Pd-C (100 mg) in MeOH (5 mL), EtOAc (2 mL), and AcOH (0.5 mL) was stirred under H₂ atmosphere for 24 h. The catalyst was then removed by filtration through Celite bed. The bed was then washed with MeOH (5 x 5 mL). The combined filtrate and washings was concentrated. The residue was subject to C-18 reverse phase column chromatography (H₂O) to provide 1 (29.3 mg, 88 %) as white solid after lyophilization. \([\alpha]^{26}_D +49.2 \ (c \ 0.40, \ H_2O)\); ¹H NMR (500 MHz, D₂O): δ 5.19 (d, 1H, \(J = 1.5 \text{ Hz, H-1'}\)), 5.04 (d, 1H, \(J = 1.5 \text{ Hz, H-1''}\)), 4.92 (d, 1H, \(J = 1.5 \text{ Hz, H-1}\)), 4.88 (d, 1H, \(J = 1.5 \text{ Hz, H-1''}\)), 4.12 (dd, 1H, \(J = 2.0, 3.5 \text{ Hz, H-2}\)), 4.00 (dd, 1H, \(J = 1.5, 3.0 \text{ Hz, H-2'}\)), 3.96 (dd, 1H, \(J = 2.0, 3.5 \text{ Hz, H-2''}\)), 3.85 (dd, 1H, \(J = 3.0, 5.5 \text{ Hz, H-2''}\)), 3.83-3.74 (m, 8H), 3.70-3.61 (m, 8H), 3.60-3.50 (m, 4H), 3.30 (s, 3H, OCH₃); ¹³C NMR (125 MHz, D₂O): δ 102.2 (C-1), 102.1 (C-1''), 100.6 (C-1'), 99.3 (C-1''), 78.7, 78.5, 77.9, 73.32, 73.28, 72.5, 70.3, 70.2, 70.02, 69.95, 69.6, 67.1, 66.93, 66.86, 66.2, 61.13, 61.07, 60.9, 54.8; ); HRMS (ESI-TOF) calcd for C₂₅H₄₄O₂₁Na \([M + Na]^+\) 703.2273, found 703.2274.
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\text{Time} 11.49
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