Formal Synthesis of a 3-Deoxy-D-manno-Octulosonic acid (KDO) and 3-Deoxy-D-arabino-2-Heptulosonic acid (DAH)

Tapan Kumar Pradhan, Kwok Kong Tony Mong*

Applied Chemistry Department,
National Chiao Tung University (Taiwan),
1001 Ta Hsueh Road, Hsinchu,
Taiwan, R.O.C

Contents:
1. General experimental methods................................................................. S2
2. Synthesis and spectroscopic data for compounds 2a-6a..........................S3-S6
3. Synthesis and spectroscopic data for compounds 2b-6b..........................S6-S9
4. Synthesis for compounds 7.................................................................S9
5. Synthesis and spectroscopic data for compounds 7a, 9, 10, 11, 13, and 14.....S9-S13
6. NMR spectra for compounds 2a-6a, 2b-6b, 7, 7a, 9, 10, 11, 13, 14........S14-S30
Section A: Experimental section

Reagent-grade chemicals were purchased from commercial vendors and used without purification. Dichloromethane (CH$_2$Cl$_2$) was dried by Asian-wong solvent system (AWS-1000). Progress of reactions was monitored by thin layer chromatography on silica gel 60 F-254 plate and visualized under UV illumination and/or by staining with acidic ceric ammonium molybdate or p-anisaldehyde. Silica gel (Geduran Si-60, 0.063-0.200 mm) for chromatography was obtained from Merck. $^1$H- and 13C-NMR spectrum was recorded with 400 and 100 MHz in Varian console as specified. The coupling constants (Hz) were calculated from chemical shifts of $^1$H NMR spectra.
Preparation of 5-\textit{O-}[(\textit{t}-Butyl)dimethylsilyl]-3,4:6,7-di-\textit{O}-isopropylidene-\textit{D}-\textit{erythro}-\textit{D}-manno-1-heptene(2a):

![Chemical structure](image)

Imidazole (4.7 g, 69.4 mmol) and TBSCl (7.8 g, 52.0 mmol) were added sequentially to a solution of the Wittig compound\textsuperscript{1} (8.89 g, 34.72 mmol) in dry DMF (102 mL) at 0 °C under N\textsubscript{2} atmosphere. After being stirred for 10 h at RT the reaction mixture was quenched with saturated NH\textsubscript{4}Cl solution (20 mL) and extracted with EtOAc (200 mL). The organic extracts were washed with water (5 × 50 mL), brine (30 mL), dried over (Na\textsubscript{2}SO\textsubscript{4}) and filtered. After concentration in vacuum, it was subjected to chromatography purification (5-10% EtOAc in petroleum ether) to provide compound 2a (87%) \([\alpha]_{D}^{33} = +65.72 (c = 1.23\text{ in CHCl}_{3});\) \(^1\)H NMR (400 MHz, CDCl\textsubscript{3}): \(\delta = 5.81 (m, 1H), 5.26 (d, J = 17.1\text{ Hz, 1H}), 5.21 (d, J = 10.4\text{ Hz, 1H}), 4.42 (t, J = 6.1\text{ Hz, 1H}), 4.08\text{-}3.77 (m, 5H), 1.46 (s, 3H, CH\textsubscript{3}), 1.35 (s, 3H, CH\textsubscript{3}), 1.31 (s, 3H, CH\textsubscript{3}), 1.28 (s, 3H, CH\textsubscript{3}), 0.86 (s, 9H, \textit{t}-Bu-Si), 0.08 (s, 3H, Me-Si), 0.06 (s, 3H, Me-Si); \(^{13}\)C NMR (100 MHz, CDCl\textsubscript{3}): \(\delta = 134.7, 118.5, 108.9, 108.0, 79.8, 78.7, 76.3, 71.2, 65.9, 28.0, 26.2, 25.8, 25.5, 25.3, 18.4, -4.1, -4.5.\)

Preparation of 5-\textit{O-}[(\textit{t}-Butyl)dimethylsilyl]-2-deoxy-3,4:6,7-di-\textit{O}-isopropylidene-\textit{D}-\textit{erythro}-\textit{D}-manno-1-heptanol(3a):

![Chemical structure](image)

To a solution of above compound 2a (4.37 g, 14.16 mmol) in dry THF (42 mL), 9-BBN (84 mL, 42.4 mmol) was added at 0 °C under N\textsubscript{2} atmosphere and the mixture was stirred for 4 h. After consumption of the starting material the reaction was quenched with 4% NaOH solution (112 mL) followed by 35% H\textsubscript{2}O\textsubscript{2} (112 mL) at 0 °C and the mixture was
stirred for 4-5 h. The organic layer was extracted with EtOAc (2 × 200 mL). The organic extracts were washed with water (5 × 50 mL), brine (40 mL), dried over (Na₂SO₄) and filtered. After concentration in vacuum, it was subjected to chromatography purification (35% EtOAc in petroleum ether) to provide compound 3a (75%). [α]_{D}^{33} = +62.45 (c = 1.27 in CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 4.28 (m, 2H), 4.03 (m, 1H), 3.95-3.67 (m, 6H), 2.63 (bs, 1H, OH), 1.81-1.60 (m, 2H), 1.44 (s, 3H, CH₃), 1.34 (s, 3H, CH₃), 1.28 (s, 6H, 2CH₃), 0.84 (s, 9H, tBu-Si), 0.07 (s, 3H, Me-Si), 0.06 (s, 3H, Me-Si); ¹³C NMR (100 MHz, CDCl₃): δ = 109.3, 107.6, 80.0, 77.0, 76.7, 71.7, 67.3, 60.8, 32.6, 28.3, 26.1, 25.9, 25.8, 25.1, 18.4, - 3.9, - 4.6.

Preparation of 6-O-[(t-Butyl)dimethylsilyl]-1,2,3-trideoxy-4,5:7,8-di-O-isopropylidene-D-erythro-D-manno-1-yno-octitol (4a):

To a solution of oxaly chloride (1.52 mL, 17.7 mmol) in dry CH₂Cl₂ (50 mL) at −78 °C, DMSO (2.7 mL, 37.9 mmol) was added dropwise with stirring under nitrogen atmosphere. After 15 min, compound 3a (3.00 g, 11.8 mmol) in dry CH₂Cl₂ (20 mL) was added to the reaction mixture. After 0.5 h of stirring at −78 °C, Et₃N (8.17 mL, 59 mmol) was added and stirred for another 0.5 h at −78 °C and then for 0.5 h at 0 °C. The reaction mixture was then quenched with saturated NH₄Cl solution (40 mL) and extracted with EtOAc (2 × 300 mL). The combined organic extracts were washed with water (50 mL), brine (50 mL), dried over (Na₂SO₄) and concentrated in vacuo. The aldehyde, thus obtained, was used in the next step without further characterization.

CBr₄ (7.84 g, 23.6 mmol) was added to a solution of Ph₃P (24.73 g, 94.4 mmol) in dry CH₂Cl₂ (30 mL) at 0 °C. To the resulting orange-red solution, aldehyde (obtained from in
previous step) in CH₂Cl₂ (30 mL) was added and after stirring for 1 h, the reaction mixture was poured into the petroleum ether (250 mL). The solvent was decanted from the sticky precipitate and the residue was dissolved again in CH₂Cl₂ (50 mL). The solution was again poured into petroleum ether (150 mL) and solvent was again decanted from the sticky precipitate. This procedure was repeated twice more. The precipitate was then discarded. The solvent fractions were combined and concentrated to give vinyl dibromide intermediate.

To a solution of dibromide intermediate in dry THF (33 mL) at −78 °C, EtMgBr (1 M in THF, 35 mL) was added slowly with stirring under nitrogen atmosphere. After slow warming to 0 °C, the reaction mixture was quenched with saturated NH₄Cl solution (1 mL) and extracted with EtOAc (200 mL). The organic extracts were washed with water (10 mL), brine (10 mL), dried (Na₂SO₄), filtered and concentrated for column chromatography (Elution: 5% EtOAc in petroleum ether) to give compound 4a (65%) as a syrupy liquid. Rₚ = 0.6 (10% EtOAc in petroleum ether). [α]D = +81.25 (c = 2.63 in CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 4.19 (q, J = 4.4 Hz, 1H), 4.05 (t, J = 7.7 Hz, 1H), 3.95-3.84 (m, 2H), 3.86-3.70 (m, 2H), 2.51 (d, J = 16.0 Hz, 1H), 2.31 (dd, J = 16.0, 9.3 Hz, 1H), 1.95 (s, 1H, alkyne-CH), 1.45 (s, 3H, CH₃), 1.35 (s, 3H, CH₃), 1.28 (s, 3H, CH₃), 1.27 (s, 3H, CH₃), 0.82 (s, 9H, tBu-Si), 0.06 (s, 3H, Me-Si), 0.05 (s, 3H, Me-Si); ¹³C NMR (100 MHz, CDCl₃): δ = 109.4, 107.7, 81.3, 80.1, 77.0, 75.5, 71.9, 69.4, 67.8, 28.0, 26.0, 25.8, 25.6, 24.9, 21.6, 18.2, -3.8, -4.7.

Preparation of 6-O-[(t-Butyl)dimethylsilyl]-1-bromo-1,2,3-trideoxy-4,5:7,8-di-O-isopropylidene-D-erythro-D-manno-1-yno-octitol(5a):
Compound 4a (2.43 g, 9.83 mmol) was taken in dry acetone (27) and the mixture was cooled to 0 °C. NBS (2.07 g, 12.2 mmol) followed by silver nitrate (434 mg, 2.45 mmol) were added to this solution and allowed the reaction mixture stirred at RT for 30 min. After completion of the reaction, the reaction mixture was filtered through sintered glass funnel and after concentration, the crude was directly taken for Column chromatography (5% EtOAc in petroleum ether) to give compound 5a (95%) as a syrupy liquid. $R_f = 0.5$ (10% EtOAc in petroleum ether). $[\alpha]_{D}^{33} = +77.36$ (c = 0.948 in CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$ 4.19 (q, $J = 4.4$ Hz, 1H), 4.08 (t, $J = 7.0$ Hz, 1H), 3.99-3.88 (m, 2H), 3.86-3.76 (m, 2H), 2.57 (dd, $J = 17.0$, 3.8 Hz, 1H), 2.41 (dd, $J = 17.0$, 8.0 Hz, 1H), 1.48 (s, 3H, CH$_3$), 1.38 (s, 3H, CH$_3$), 1.31 (s, 3H, CH$_3$), 0.85 (s, 9H, $^t$Bu-Si), 0.10 (s, 3H, Me-Si), 0.09 (s, 3H, Me-Si); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 109.5, 107.9, 80.2, 77.2, 77.1, 75.3, 71.9, 67.9, 39.2, 27.9, 26.2, 25.9, 25.6, 25.1, 23.0, 18.4, - 3.7, - 4.6.

**Preparation of methyl (6-$O$-[(t-Butyl)dimethylsilyl]-4,5:7,8-di-$O$-isopropylidene-3-deoxy-D-erythro-D-manno-2-keto) octate (6a):**

To a solution of bromo compound 5a (245 mg, 0.74 mmol) in (1:1) methanol/H$_2$O (30 mL) mixture, MgSO$_4$ (180 mg, 1.49 mmol) followed by NaHCO$_3$ (31 mg, 0.374 mmol) were added at RT. Methanol (55 mL) was added portion wise and the mixture was allowed to stir for 30 min at RT. The reaction mixture was cooled to 0 °C then KMnO$_4$ (236 mg, 1.49 mmol) was added and stirred for 4 h. After completion of the reaction the mixture was filtered and the filtrate was extracted with EtOAc (2 × 100 mL). The combined organic extracts were washed with water (3 × 20 mL), brine (40 mL), dried over (Na$_2$SO$_4$) and concentrated for Column chromatography (30% EtOAc in petroleum ether) to give compound 6a (80%) as a syrupy liquid. $R_f = 0.5$ (40% EtOAc in petroleum ether). $^1$H NMR (400 MHz, CDCl$_3$): $\delta =$
4.74 (ddd, $J = 10.4$, 4.7, 3.3 Hz, 1H), 4.13 (dd, $J = 8.0$, 6.4 Hz, 1H), 4.05-3.97 (m, 2H), 3.94 (dd, $J = 13.8$, 7.3 Hz, 1H), 3.86 (s, 3H, O-Me), 3.79 (t, $J = 8.0$ Hz, 1H), 3.70 (m, 1H), 3.11 (dd, $J = 15.0$, 3.2 Hz, 1H), 3.02 (dd, $J = 15.0$, 10.8 Hz, 1H), 1.41 (s, 3H, CH$_3$), 1.36 (s, 3H, CH$_3$), 1.32 (s, 3H, CH$_3$), 1.29 (s, 3H, CH$_3$), 0.86 (s, 9H, tBu-Si), 0.11 (s, 3H, Me-Si), 0.10 (s, 3H, Me-Si); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 192.1, 161.3, 109.8, 108.3, 80.6, 76.9, 73.3, 72.6, 68.5, 52.9, 42.0, 28.1, 26.1, 25.9, 25.8, 25.0, 18.3, -3.7, -4.6.

Preparation of 5-benzyloxy-3,4:6,7-di-O-isopropylidene-D-erythro-D-manno-1-heptene (2b):

![Chemical Structure](image)

Alkene precursor$^1$ (2 g, 7.81 mmol) was taken in dry THF (21 mL) and cooled to 0 \degree C. NaH (625 mg, 15.6 mmol) was added portion wise to that reaction mixture and stirred for 10 min. BnBr (1.42 mL, 11.71 mmol) followed by TBAI (288 mg, 0.781 mmol) were added respectively and the reaction was allowed to stir for 6 h at RT. After consumption of the starting material the reaction mixture was quenched with saturated NH$_4$Cl solution (5 mL) and extracted with EtOAc (100 mL). The organic extract was washed with water (10 mL), brine (10 mL), dried over (Na$_2$SO$_4$), filtered and concentrated for column chromatography purification (10% EtOAc in petroleum ether) to give compound 2b (93%) as a syrupy liquid. $R_f = 0.2$ (10% EtOAc in petroleum ether). $[\alpha]^{14}_{D} = -10.25$ (c = 1.18 in CHCl$_3$; $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 7.34-7.26 (m, 5H), 5.99 (ddd, $J = 17.2$, 10.3, 7.6 Hz, 1H), 5.35 (td, $J = 1.2$, 17.2 Hz, 1H), 5.26 (td, $J = 1.0$, 10.3 Hz, 1H), 4.87 (d, $J = 11.5$ Hz, 1H, benzyl-H), 4.70 (d, $J = 11.5$ Hz, 1H, benzyl-H), 4.64 (dd, $J = 7.5$, 6.4 Hz, 1H), 4.24-4.15 (m, 2H), 4.10-3.98 (m, 2H), 3.73 (t, $J = 4.1$ Hz, 1H), 1.52 (s, 3H, CH$_3$), 1.40 (s, 3H, CH$_3$), 1.38 (s, 3H, CH$_3$), 1.35 (s, 3H, CH$_3$); $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 138.6, 134.4, 128.1, 127.2, 127.1, 118.9, 109.0, 108.3, 79.5, 79.1, 77.6, 77.3, 73.7, 65.7, 26.9, 26.2, 25.6, 25.1.

S7
Preparation of 5-benzyloxy-2-deoxy-3,4:6,7-di-O-isopropylidene-D-erythro-D-manno-1-heptanol(3b):

To a solution of above compound 2b (1.5 g, 3.52 mmol) in dry THF (15 mL), 9-BBN (21 mL, 10.56 mmol) was added at 0 °C under N₂ atmosphere and the mixture was stirred for 4.5 h. After consumption of the starting material the reaction was quenched with 4% NaOH solution (24 mL) followed by 35% H₂O₂ (24 mL) at 0 °C and the mixture was stirred for 6 h. The organic layer was extracted with EtOAc (300 mL). The organic extract was washed with water (5 × 10 mL), brine (20 mL), dried over (Na₂SO₄) and filtered. After concentration in vacuum, it was subjected to chromatography purification (30% EtOAc in petroleum ether) to provide compound 3b in 70% yield. [α]⁺³³_D = +34.37 (c = 0.746 in CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 7.44-7.21 (m, 5H), 4.84 (d, J = 11.6 Hz, 1H, benzyl-H), 4.76 (d, J = 11.6 Hz, 1H, benzyl-H), 4.34 (ddd, J = 10.1, 5.8, 2.9 Hz, 1H), 4.21-4.03 (m, 3H), 3.93 (m, 1H), 3.87-3.74 (m, 2H), 3.72 (t, J = 4.9 Hz, 1H), 2.32 (bs, 1H, OH), 1.91 (m, 1H), 1.78 (m, 1H), 1.49 (s, 3H, CH₃), 1.38 (s, 3H, CH₃), 1.35 (s, 3H, CH₃), 1.33 (s, 3H, CH₃); ¹³C NMR (100 MHz, CDCl₃): δ = 138.4, 128.2, 127.4, 127.4, 108.6, 108.6, 79.4, 77.5, 77.4, 76.5, 73.8, 66.4, 61.0, 32.1, 27.2, 26.2, 25.9, 25.0.

Preparation of 6-benzyloxy-1,2,3-trideoxy-4,5:7,8-di-O-isopropylidene-D-erythro-D-manno-1-yno-octitol(4b):
The compound 4b was prepared following the same procedure as used for 4a. \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.48-7.20\) (m, 5H), 4.92 (d, \(J = 11.6\) Hz, 1H, benzyl-H), 4.76 (d, \(J = 11.6\) Hz, 1H, benzyl-H), 4.36 (dd, \(J = 13.9, 6.8\) Hz, 1H), 4.25-4.14 (m, 2H), 4.10 (dd, \(J = 8.4, 6.4\) Hz, 1H), 3.97 (m, 1H), 3.92 (t, \(J = 4.4\) Hz, 1H), 2.67-2.54 (m, 2H), 2.04 (t, \(J = 2.7\) Hz, 1H, alkyne-CH), 1.51 (s, 3H, CH\(_3\)), 1.42 (s, 3H, CH\(_3\)), 1.36 (s, 3H, CH\(_3\)), 1.34 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 138.4, 128.2, 127.4, 127.3, 108.8, 108.4, 80.5, 78.9, 77.7, 77.1, 76.8, 75.4, 73.6, 70.2, 66.3, 26.9, 26.2, 25.7, 24.9, 20.3.

Preparation of 6-benzyloxy-1-bromo-1,2,3-trideoxy-4,5:7,8-di-O-isopropylidene-D-erythro-D-manno-1-yno-octitol (5b):

![Structure of 5b]

This compound was prepared following the same procedure as was used for 5a \([\alpha]^{30}_D = -7.45\) (c = 0.909 in CHCl\(_3\)); \(^1\)H NMR (400 MHz, CDCl\(_3\)): \(\delta = 7.42-7.22\) (m, 5H), 4.90 (d, \(J = 11.6\) Hz, 1H, benzyl-H), 4.76 (d, \(J = 11.6\) Hz, 1H, benzyl-H), 4.33 (dd, \(J = 12.6, 6.1\) Hz, 1H), 4.21 (dd, \(J = 5.7, 5.0\) Hz, 1H), 4.17 (m, 1H), 4.09 (m, 1H), 3.94 (dd, \(J = 8.2, 7.5\) Hz, 1H), 3.87 (t, \(J = 4.8\) Hz, 1H), 2.64 (dd, \(J = 16.6, 6.6\) Hz, 1H), 2.60 (dd, \(J = 16.6, 6.8\) Hz, 1H), 1.51 (s, 3H, CH\(_3\)), 1.42 (s, 3H, CH\(_3\)), 1.36 (s, 3H, CH\(_3\)), 1.35 (s, 3H, CH\(_3\)); \(^{13}\)C NMR (100 MHz, CDCl\(_3\)): \(\delta = 138.4, 128.3, 127.4, 127.4, 108.8, 108.6, 79.0, 77.6, 77.3, 76.5, 75.3, 73.8, 66.5, 40.0, 26.9, 26.2, 25.7, 24.9, 21.7.

Preparation of methyl (6-benzyloxy-4,5:7,8-di-O-isopropylidene-3-deoxy-D-erythro-D-manno-2-keto) octate(6b):
This was prepared following the same procedure as was used for 6a. $[\alpha]^3_D = +33.60$

(c = 0.316 in CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta = 7.40-7.22$ (m, 5H), 4.88-4.69 (m, 2H), 4.25 (t, $J = 5.7$ Hz, 1H), 4.19-4.04 (m, 2H), 3.88 (m, 1H), 3.82 (s, 3H), 3.60 (t, $J = 5.6$ Hz, 1H), 3.24 (dd, $J = 16.7$, 8.6 Hz, 1H), 3.16 (dd, $J = 16.7$, 5.0 Hz, 1H), 1.47 (s, 3H, CH$_3$), 1.38 (s, 3H, CH$_3$), 1.34 (s, 3H, CH$_3$), 1.32 (s, 3H, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta =$ 191.9, 161.0, 138.1, 128.4, 128.3, 128.2, 127.7, 127.6, 109.0, 108.8, 79.5, 77.5, 77.3, 73.7, 72.9, 66.9, 52.9, 41.1, 27.4, 26.2, 25.8, 24.8.

**Preparation of Methyl 4,5,7,8-di-O-isopropylidene-3-deoxy-2-hydroxyl-D-manno-octopyranos-2-ulosonate (7):**

To a stirred solution of compound 6b (200 mg, 0.47 mmol) in EtOAc: petroleum ether (1:1) (2 mL each), Pd/C was added and the mixture was stirred under the H$_2$ balloon for 10 h. After completion of the reaction, the mixture was filtered over celite and after concentration, the crude mixture was purified by Column chromatography (35% EtOAc in petroleum ether eluant) to give compound 7 (96%) as a white solid. $R_f = 0.3$ (40% EtOAc in petroleum ether).

**Preparation of Methyl 2–O-acetyl-4,5,7,8-di-O-isopropylidene-3-deoxy-D-manno-octopyranos-2-ulosonate (7a):**
To a stirred solution of compound 7 (50 mg, 0.15 mmol) in dry CH$_2$Cl$_2$ (2 mL), pyridine (0.024 mL, 0.3 mmol) was added at 0 °C. After 10 min, acetic anhydride (0.021 mL, 0.225 mmol) followed by DMAP (2 mg, 0.015 mmol) were added and the mixture was stirred for 2 h at RT. After completion of the acylation, it was quenched with NaHCO$_3$ (1 mL) and the product extracted with EtOAc (30 mL). The organic extract was washed with water (5 mL), brine (5 mL), dried over (Na$_2$SO$_4$), filtered and concentrated for chromatography purification (20-30% EtOAc in petroleum ether) to furnish pure compound 7a (87%) $\left[\alpha\right]^{34}_D = +60.68$ (c = 0.116 in CHCl$_3$); $^1$H NMR (400 MHz, CDCl$_3$): $\delta$ = 4.45 (m, 1H), 4.44-4.31 (m, 2H), 4.10 (dd, $J$ = 9.0, 6.2 Hz, 1H), 3.85 (dd, $J$ = 9.0, 3.4 Hz, 1H), 3.77 (s, 3H), 3.59 (dd, $J$ = 8.5, 1.3 Hz, 1H), 2.71 (dd, $J$ = 15.6, 3.5 Hz, 1H, C-3$_{ax}$), 2.08 (t, $J$ = 2.8 Hz, 1H), 2.06 (s, 3H, COCH$_3$), 1.47 (s, 3H, CH$_3$), 1.42 (s, 3H, CH$_3$), 1.35 (s, 3H, CH$_3$), 1.32 (s, 3H, CH$_3$). $^{13}$C NMR (100 MHz, CDCl$_3$): $\delta$ = 169.1, 169.1, 109.7, 109.5, 96.7 (C-2), 73.2, 73.1, 71.2, 69.3, 67.1, 52.9, 32.1, 27.1, 25.2, 25.0, 24.6, 21.0.

Preparation of 1,3,4-Tris-benzyloxy-D-arabino-hex-5-en-2-ol (9):

To a stirred solution of methyltriphenylphosphoniumbromide (4.71 g, 13.8 mmol) in dry THF (50 mL), $n$-butyl-lithium (8.31 mL, 1.6 M solution in hexane, 13.2 mmol) was added at -78 °C and the resulting solution was stirred for 30 min at ambient temperature. The compound 8 (1.18 g, 2.77 mmol) was dissolved in THF (10 mL) and added to the above mixture via syringe in one portion. Finally the reaction mixture was stirred for 30 min at RT.
and quenched with saturated NH₄Cl solution (5 mL) and extracted with EtOAc (100 mL). The organic extract was washed with water (10 mL), brine (10 mL), dried over (Na₂SO₄), filtered and concentrated for column chromatography purification (10% EtOAc in petroleum ether) to give compound 9 (80%) as a syrupy liquid. Rᶠ = 0.5 (20% EtOAc in petroleum ether). This compound was previously synthesized by many groups²,³. The analytical data was in good agreement with the literature. ¹H NMR (400 MHz, CDCl₃): δ = 7.43 (m, 15H), 6.01 (ddd, J = 17.4, 10.7, 7.7 Hz, 1H), 5.37 (d, J = 10.8 Hz, 1H), 5.36 (d, J = 17.5 Hz, 1H), 4.68 (d, J = 11.6 Hz, 2H), 4.60 (d, J = 11.1 Hz, 1H), 4.55 (s, 2H), 4.40 (d, J = 11.6 Hz, 1H), 4.13 (q, J = 3.8 Hz, 1H), 4.06 (m, 1H), 3.73-3.61 (m, 3H), 2.91 (d, J = 4.3 Hz, 1H); ¹³C NMR (100 MHz, CDCl₃): δ = 138.1, 138.0, 137.8, 135.0, 128.3, 128.2, 128.2, 127.9, 127.9, 127.7, 127.5, 118.8, 80.5, 80.0, 74.0, 73.2, 70.8, 70.5, 70.2.

**Preparation of 2-O-[(t-Butyl)-dimethylsilyl]-1,3,4-tris-benzyloxy-D-arabino-6-hexanol (10):**

Compound 9 (1.0 g, 2.34 mmol) was taken in dry CH₂Cl₂ (6 mL) and cooled to 0 °C. 2, 6-lutidine (0.54 mL, 4.68 mmol) was added to the reaction mixture at the same temperature and stirred for 10 min. TBS-OTf (0.80 mL, 3.51 mmol) was added to above reaction mixture and allowed to stir for 10-15 min at RT. After completion of the starting material the reaction mixture was quenched with saturated NH₄Cl solution (5 mL) and extracted with EtOAc (50 mL). The organic extract was washed with water (5 mL), brine (5 mL), dried over (Na₂SO₄), filtered and concentrated for column chromatography purification (10% EtOAc in petroleum ether) to give silyl compound (85%) as a syrupy liquid. This was taken to the next step without any analytical characterization.
To the above silyl compound (995 mg, 1.83 mmol), in dry THF (10 mL), 9-BBN (11 mL, 5.50 mmol) was added at 0 °C under N₂ atmosphere and the mixture was stirred for 5 h. After consumption of the starting material the reaction was quenched with 4% NaOH solution (40 mL) followed by 35% H₂O₂ (40 mL) at 0 °C and the mixture was stirred for 4-5 h. The organic layer was extracted with EtOAc (2 × 100 mL). The organic extracts were washed with water (5 × 10 mL), brine (20 mL), dried over (Na₂SO₄) and filtered. After concentration in vacuum, it was subjected to chromatography purification (25% EtOAc in petroleum ether) to provide compound 10 (92%). [α]³³_D = +3.66 (c = 1.52 in CHCl₃); H NMR (400 MHz, CDCl₃): δ = 7.45-7.23 (m, 15H), 4.91 (d, J = 11.3 Hz, 1H), 4.80 (d, J = 11.3 Hz, 1H), 4.74 (d, J = 11.3 Hz, 1H), 4.59 (d, J = 11.2 Hz, 1H), 4.55 (dd, J = 14.6, 12.0 Hz, 2H), 4.15 (ddd, J = 7.6, 5.0, 2.8 Hz, 1H), 3.91-3.80 (m, 2H), 3.75 (dd, J = 6.7, 2.7 Hz, 1H), 3.74-3.69 (m, 2H), 3.63 (dd, J = 9.8, 5.8 Hz, 1H), 2.19 (bs, 1H, OH), 1.92 (m, 1H), 1.82 (m, 1H), 0.96 (s, 9H, Bu-Si), 0.15 (s, 6H, 2 Me-Si); C NMR (100 MHz, CDCl₃): δ = 138.8, 138.3, 138.1, 128.3, 128.1, 128.1, 127.9, 127.7, 127.6, 127.5, 127.4, 127.3, 84.9, 78.4, 74.5, 73.5, 73.2, 72.8, 71.8, 60.2, 34.1, 25.8, 18.0, -4.5, -4.8.

Preparation of 2-O-[(t-Butyl)dimethylsilyl]-1,3,4-tris-benzyloxy-5,6,7-trIDEOXY-D-arabino-6-yno-heptitol(11):

![Structure](image)

This compound was prepared following the same procedure as was used for 4a. H NMR (400 MHz, CDCl₃): δ = 7.47-7.31 (m, 5H), 4.91 (d, J = 11.4 Hz, 1H), 4.85-4.73 (m, 2H), 4.70 (d, J = 11.4 Hz, 1H), 4.58 (s, 2H), 4.22 (td, J = 5.5, 4.1 Hz, 1H), 3.96 (dd, J = 5.2, 3.8 Hz, 1H), 3.93-3.87 (m, 2H), 3.68 (dd, J = 9.8, 5.5 Hz, 1H), 2.69 (dd, J = 17.0, 6.0, 2.8 Hz, 1H), 2.62 (ddd, J = 17.0, 5.3, 2.6 Hz, 1H), 2.10 (t, J = 2.6 Hz, 1H), 1.02 (s, 9H), 0.19 (s, 6H); C NMR (100 MHz, CDCl₃): δ = 138.8, 138.4, 138.2, 128.3, 128.2, 128.2, 128.1,
128.0, 127.9, 127.8, 127.8, 127.6, 127.5, 127.4, 127.4, 127.3, 82.9, 81.1, 77.9, 75.0, 73.9, 72.9, 72.6, 71.8, 70.3, 25.8, 21.0, 18.0, -4.4, -4.7.

Preparation of methyl (2-O-[(t-Butyl)dimethylsilyl]-1,3,4-tris-benzyloxy-5-deoxy-D-arabino-6-keto) heptate (13):

![Chemical structure of compound 13]

Compound 13 was prepared from 12 following the same procedure as used for 6a. $^1$H NMR (400 MHz, CDCl$_3$): δ = 7.41-7.19 (m, 15H), 4.75 (d, $J = 11.6$ Hz, 1H), 4.61 (dd, $J = 12.9$, 11.2 Hz, 2H), 4.55 (d, $J = 11.0$ Hz, 1H), 4.49 (s, 2H), 4.25 (ddd, $J = 8.0$, 5.4, 4.5 Hz, 1H), 4.13 (ddd, $J = 5.4$, 4.5, 3.4 Hz, 1H), 3.78 (dd, $J = 9.8$, 4.6 Hz, 1H), 3.76 (s, 3H), 3.71 (dd, $J = 5.4$, 3.4 Hz, 1H), 3.25 (dd, $J = 17.0$, 8.0 Hz, 1H), 3.12 (dd, $J = 17.0$, 4.4 Hz, 1H), 0.91 (s, 9H), 0.91 (s, 3H), 0.90 (s, 3H); $^{13}$C NMR (100 MHz, CDCl$_3$): δ = 192.4, 161.0, 138.4, 138.2, 138.1, 128.4, 128.2, 127.9, 127.6, 127.5, 127.5, 127.5, 81.9, 75.5, 73.8, 73.3, 73.2, 73.0, 72.0, 52.7, 41.7, 25.8, 18.1, -4.5, -4.7.

Preparation of Methyl 4,5,7-tribenzyloxy-3-deoxy-2-hydroxyl-D-arabino-heptopyranos-2-ulosonate (14):

![Chemical structure of compound 14]

To a stirred solution of compound 13 (342 mg, 0.56 mmol) in (2:3) CH$_2$Cl$_2$:MeOH (11 mL), 6% HCl(aq) (few drops) was added at 0 °C and the mixture was allowed to stirred for 30 min at the same temperature. After completion of the reaction, the reaction was quenched with saturated NaHCO$_3$ (5 mL) and the product was extracted with EtOAc (2 × 50 mL). The
combined organic extracts were washed with water (10 mL), brine (5 mL), dried over (Na$_2$SO$_4$), filtered and concentrated for Column chromatography (30% EtOAc in petroleum ether) to give compound 14 (90%) as a syrupy liquid. $R_f = 0.4$ (20% EtOAc in petroleum ether).
$^1$H NMR spectrum of compound 2a (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 2a (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 3a (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 3a (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 4a (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 4a (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 5a (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 5a (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 6a (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 6a (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 2b (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 2b (100 MHz, CDCl$_3$)
\(^1\)H NMR spectrum of compound 3b (400 MHz, CDCl\(_3\))

\(^{13}\)C NMR spectrum of compound 3b (100 MHz, CDCl\(_3\))
$^1$H NMR spectrum of compound 4b (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 4b (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 5b (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 5b (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 6b (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 6b (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 7 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 7 (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 7a (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 7a (100 MHz, CDCl$_3$)
1H NMR spectrum of compound 9 (400 MHz, CDCl₃)

13C NMR spectrum of compound 9 (100 MHz, CDCl₃)
$^1$H NMR spectrum of compound 10 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 10 (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound 11 (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound 11 (100 MHz, CDCl$_3$)
$^1$H NMR spectrum of compound **13** (400 MHz, CDCl$_3$)

$^{13}$C NMR spectrum of compound **13** (100 MHz, CDCl$_3$)
\(^1\)H NMR spectrum of compound 14 (400 MHz, CDCl\(_3\))

\(^{13}\)C NMR spectrum of compound 14 (100 MHz, CDCl\(_3\))
References:

