A Suzuki-Miyaura Coupling Mediated Deprotection as Key to the Synthesis of A Fully Lipidated Malarial GPI Disaccharide

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General Information. All chemicals used were reagent grade and used as supplied except where noted. All reactions were performed in oven-dried glassware under an inert atmosphere (nitrogen or argon) unless noted otherwise. Reagent grade dichloromethane (CH_2Cl_2), tetrahydrofuran (THF), diethyl ether (Et_2O) and toluene (PhMe) were passed through activated neutral alumina column prior to use.[1] Reagent grade N,N-dimethylformamide (DMF) and methanol (MeOH) were dried over activated molecular sieves prior to use. Pyridine, triethylamine and acetonitrile were distilled over CaH_2 prior to use. Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} plates (0.25mm). Compounds were visualized by UV irradiation or dipping the plate in a cerium sulfate-ammonium molybdate solution. Flash column chromatography (FC) was carried out using forced flow of the indicated solvent on Fluka Kieselgel 60 (230-400 mesh)

^{1}H, ^{13}C and ^{31}P NMR spectra were recorded on a Varian Mercury 300 (300 MHz), Varian Gemini 300 (300 MHz), Bruker DRX400 (400 MHz), Bruker DRX500 (500 MHz), or a Bruker AV600 (600 MHz) spectrometer in $CDCl_3$ with chemical shifts referenced to internal standards $CDCl_3$ (7.26 ppm ^{1}H, 77.0 ppm ^{13}C), ^{31}P spectra are reported in δ value relative to H_3PO_4 (0.0 ppm) as an external reference. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; brs, broad singlet for ^{1}H NMR data. High-resolution mass spectral (HRMS) analyses were performed by the MS-service at the Laboratorium für Organische Chemie at ETH Zürich. ESI-MS and MALDI-MS were run on an IonSpec Ultra instrument. In case of MALDI-MS, 2,5-dihydroxybenzoic acid (DHB) served as the matrix. IR spectra were recorded on a Perkin-Elmer 1600 FTIR spectrometer. Optical rotations were measured using a Perkin-Elmer 241 polarimeter.

General Procedure for *para*-Bromobenzylation of Alcohols: The alcohol (0.5 mmol) was dissolved in DMF (10 mL) in an oven-dried flask. The reaction solution was then cooled to 0 ºC. Under a flow of nitrogen gas, sodium hydride (0.6 mmol, 60% in mineral oil) was added in one portion, followed by the addition of *p*-bromobenzylbromide (0.6 mmol). The resulting mixture was then warmed to room temperature gradually. After complete consumption of starting alcohol as assessed by TLC, the reaction was quenched by the addition of MeOH. The mixture was then poured into water (20 mL) and the aqueous layer was extracted with Et_2O four times. The combined organic layers were then washed with additional water, brine and dried over Na_2SO_4. Rotary evaporation gave a crude residue, which was subsequently purified by flash silica column chromatography to furnish the PBB-protected compound.

6-*O*-(4-Bromobenzyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (3a): General procedure using 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (1.56 g, 6 mmol), NaH (288 mg, 7.2 mmol, 60% in mineral oil) and 4-bromobenzyl bromide (1.80 g, 7.2 mmol) gave **3a** (2.47 g, 96% yield) as a colorless syrup. Analytical data are in accordance with the literature.[2]

***tert*-Butyldimethylsilyl 2-azido-3,6-di-*O*-benzyl-3-*O*-(4-bromobenzyl)-2-deoxy-α-D-glucopyranoside (3b):** General procedure using *tert*-butyldimethylsilyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (1.49 g, 3 mmol), NaH (144 mg, 3.6 mmol, 60% in mineral oil) and 4-bromobenzyl bromide (0.91 g, 3.6 mmol) gave **3b** (1.86 g, 93% yield) as a colorless syrup. R_f 0.53 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.} = -24.9$ (c = 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.12 (s, 3H), 0.13 (s, 3H), 0.91 (s, 9H), 3.27-3.36 (m, 3H), 3.52-3.65 (m, 3H), 4.44-4.51 (m, 3H), 4.56 (d, *J* = 12.2 Hz, 1H), 4.67 (d, *J* = 11.0 Hz, 1H), 4.68 (d, *J* = 11.5 Hz, 1H), 4.84 (d, *J* = 11.0 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 7.14-7.31 (m, 10H), 7.35 (d, *J* = 8.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ -5.18, -4.23, 18.0, 25.6, 68.7, 68.8, 73.5, 74.0, 75.0, 75.4, 77.7, 82.9, 97.2, 121.6, 127.6, 127.7, 127.8, 127.9, 128.3, 128.4, 129.4, 131.5, 137.1, 138.07, 138.09; IR (film): 3064, 2928, 2109, 1594, 1488, 1454, 1389, 1360, 1256, 1069, 1011, 840 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{33}H_{42}BrN_3O_5Si$ $[M+Na]^+$, 690.1969; Found, 690.1960

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(4-bromobenzyl)-α-D-glucopyranoside (3c): General procedure using methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (1.39 g, 3 mmol), NaH (144 mg, 3.6 mmol, 60% in mineral oil) and 4-bromobenzyl bromide (0.91 g, 3.6 mmol) gave **3c** (1.82 g, 96% yield) as a colorless syrup. R_f 0.35 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.} = +26.7$ (c = 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.37 (s, 3H), 3.53-3.76 (m, 5H), 3.98 (t, *J* = 9.3 Hz, 1H), 4.40 (d, *J* = 12.3 Hz, 1H), 4.46 (d, *J* = 10.8 Hz, 1H), 4.52 (d, *J* = 12.3 Hz, 1H), 4.62 (d, *J* = 3.6 Hz, 1H), 4.66 (d, *J* = 12.1 Hz, 1H), 4.80 (d, *J* = 12.1 Hz, 1H), 4.81 (d, *J* = 10.5 Hz, 1H), 4.85 (d, *J* = 10.5 Hz, 1H), 4.98 (d, *J* = 10.8 Hz, 1H), 7.12-7.19 (m, 4H), 7.27-7.41 (m, 13H), 7.42 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.2, 68.6, 69.9, 72.6, 73.3, 75.0, 75.7, 76.6, 77.6, 79.7, 82.0, 98.1, 121.4, 127.5, 127.6, 127.76, 127.8, 128.0, 128.2, 128.3, 129.3, 131.3, 136.8, 137.9, 138.0, 138.5; IR (film): 3062, 3029, 2907, 1735, 1488, 1380, 1160, 1070, 738 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{35}H_{37}BrO_6$ $[M+Na]^+$, 655.1666; Found, 655.1662

Allyl 2-azido-3,6-di-*O*-benzyl-3-*O*-(4-bromobenzyl)-2-deoxy-β-D-glucopyranoside (3d): General procedure using allyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (1.28 g, 3 mmol), NaH (144 mg, 3.6 mmol, 60% in mineral oil) and 4-bromobenzyl bromide (0.91 g, 3.6 mmol) gave **3d** (1.68 g, 94% yield) as a colorless syrup. R_f 0.20 (hexanes/ethyl acetate = 10 : 1); $[\alpha]_D^{r.t.}$ = -39.1 (c = 1.3, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 3.37-3.49 (m, 3H), 3.57-3.72 (m, 3H), 4.15 (ddt, *J* = 13.2, 5.7, 1.5 Hz, 1H), 4.32 (d, *J* = 7.2 Hz, 1H), 3.90-4.48 (m, 3H), 4.52 (d, *J* = 12.3 Hz, 1H), 4.63 (d, *J* = 12.3 Hz, 1H), 4.72 (d, *J* = 11.1 Hz, 1H), 4.73 (d, *J* = 10.8 Hz, 1H), 4.90 (d, *J* = 10.8 Hz, 1H), 5.23 (ddd, *J* = 10.8, 2.8, 1.5 Hz, 1H), 5.35 (ddd, *J* = 17.1, 2.8, 1.5 Hz, 1H), 5.89-6.03 (m, 1H), 6.98 (d, *J* = 8.4 Hz, 2H), 7.27-7.33 (m, 10H), 7.39 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 66.2, 68.3, 70.2, 73.4, 74.0, 74.8, 75.4, 77.6, 83.1, 100.9, 117.6, 121.6, 127.6, 127.7, 127.8, 127.9, 128.3, 128.4, 129.3, 131.4, 133.4, 136.9, 137.8; IR (film): 3026, 2861, 2103, 1451, 1354, 1267, 1067, 1010, 800 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{30}H_{32}BrN_3O_5$ $[M+Na]^+$, 616.1418; Found, 616.1396.

1,5-Anhydro-6-*O*-(4-bromobenzyl)-2-deoxy-3,4-di-*O*-pivaloyl-D-arabinohex-1-enitol (3e): General procedure using 1,5-anhydro-2-deoxy-3,4-di-*O*-pivaloyl-D-arabinohex-1-enitol (1.89 g, 6 mmol), NaH (288 mg, 7.2 mmol, 60% in mineral oil) and 4-bromobenzyl bromide (1.82 g, 7.2 mmol) gave **3e** (2.81 g, 97% yield) as a colorless syrup. R_f 0.68 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = -11.7 (c = 2.2, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.20 (s, 18H), 3.76 (dd, *J* = 6.9, 4.8 Hz, 1H), 4.18-4.23 (m, 1H), 4.31 (dd, *J* = 11.7, 3.3 Hz, 1H), 4.37 (dd, *J* = 11.7, 5.7 Hz, 1H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.71 (d, *J* = 11.7 Hz, 1H), 4.79 (dd, *J* = 6.0, 3.0 Hz, 1H), 5.36 (t, *J* = 4.2 Hz, 1H), 6.42 (d, *J* = 6.0 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.0, 27.1, 38.7, 38.8, 61.8, 68.7, 72.3, 73.4, 74.8, 98.7, 121.9, 129.2, 131.6, 136.5, 145.5, 177.8, 178.0; IR (film): 2972, 1731, 1648, 1479, 1281, 1148 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{23}H_{31}BrO_6$ $[M+Na]^+$, 505.1198; Found, 505.1201.

General Procedure for the Ligandless Suzuki-Miyaura Coupling and the Sequential Deprotection of *p*-(3,4-Dimethoxyphenyl)benzyl ethers: To an oven dried Schlenk flask was added *p*-bromobenzyl ether (0.2 mmol), 3,4-dimethoxyphenyl boronic acid (0.24 mmol), tetrabutylammonium bromide (TBABr) (0.02 mmol), potassium phosphate (K_3PO_4) (0.6 mmol) and ethanol (1 mL). The resulting mixture was subjected to the freeze-pump-thaw cycle for three times to exclude air. $Pd(OAc)_2$ (0.01 mmol) was then added under a flow of argon. The reaction mixture was then stirred at room temperature for 2-3 h. After the TLC indication of complete consumption of *p*-bromobenzyl ether, EtOAc was added and the organic layer was washed with saturated aqueous $NaHCO_3$ solution. The aqueous layer was back-extracted with EtOAc three times. The combined organic layer was washed with water and brine and dried over Na_2SO_4. Rotary evaporation gave a crude residue, which was subsequently purified by flash silica column chromatography to furnish the pure product (**4a**-**4e**). Subsequently, *p*-(3,4-dimethoxyphenyl)benzyl ether (0.1 mmol) was dissolved in CH_2Cl_2 (2 mL) and water (0.2 mL) in a round-bottom flask. To this mixture was added DDQ (0.3 mmol) at room temperature. The deprotection proceeded to completion within 3 h and the reaction mixture was diluted with CH_2Cl_2 and washed with freshly prepared aqueous solution of sodium ascorbate to remove excess DDQ. The aqueous solution was then back-extracted with CH_2Cl_2 three times. The combined organic layers were additionally washed with saturated aqueous $NaHCO_3$ solution, brine and dried over Na_2SO_4. Rotary evaporation gave a crude residue, which was subsequently purified by flash silica column chromatography to furnish the deprotected alcohol (**5a**-**5e**).

6-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (4a) and 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranoside (5a): General procedure using **3a** (42.9 mg, 0.1 mmol), 3,4-dimethoxyphenyl boronic acid (21.8 mg, 0.12 mmol), TBABr (3.2 mg, 10 μmol), K_3PO_4 (63.5 mg, 0.3 mmol) and $Pd(OAc)_2$ (1.1 mg, 5 μmol) afforded **4a** (44.7 mg) in 92% yield as a white foam. R_f 0.32 (hexanes/ethyl acetate = 4 : 1, twice); $[\alpha]_D^{r.t.}$ = -61.1 (c = 1.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 3H), 1.34 (s, 3H), 1.45 (s, 3H), 1.54 (s, 3H), 3.65 (dd, *J* = 10.1, 6.8 Hz, 1H), 3.72 (dd, *J* = 10.1, 6.8 Hz, 1H), 3.92 (s, 3H), 3.95 (s, 3H), 4.02 (td, *J* = 6.2, 1.5 Hz, 1H), 4.29 (dd, *J* = 8.0, 1.8 Hz, 1H), 4.32 (dd, *J* = 5.1, 1.8 Hz, 1H), 4.58 (d, *J* = 12.3 Hz, 1H), 4.60 (dd, *J* = 8.0, 2.1 Hz, 1H), 4.66 (d, *J* = 12.3 Hz, 1H), 5.55 (d, *J* = 2.1 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.09-7.15 (m, 2H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.52 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 24.4, 24.9, 26.0, 26.1, 55.91, 55.96, 66.9, 68.8, 70.5, 70.6, 71.2, 73.0, 96.4, 108.5, 109.2, 110.4, 111.4, 119.3, 126.8, 128.2, 134.0, 136.9, 140.3, 148.6, 149.1; IR (film): 3021, 2985, 2841, 1600, 1502, 1379, 1251, 1005, 892, 800 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{27}H_{34}O_8$ $[M+Na]^+$, 509.2146; Found, 509.2144.

Compound **4a** (34 mg, 70 μmol) was then subjected to the standard deprotection procedure using DDQ (47.6 mg, 0.21 mmol) to give **5a** (15.5 mg) in 85% yield. Analytical data are in accordance with the literature.[3]

***tert*-Butyldimethylsilyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-α-D-glucopyranoside (4b) and *tert*-butyldimethylsilyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-α-D-glucopyranoside (5b):** General procedure using **3b** (43 mg, 64 μmol), 3,4-dimethoxyphenyl boronic acid (14.0 mg, 77 μmol), TBABr (2.1 mg, 6.4 μmol), K_3PO_4 (27.2 mg, 0.19 mmol) and $Pd(OAc)_2$ (0.7 mg, 3.2 μmol) afforded **4b** (42.3 mg) in 89% yield as a white foam. R_f 0.43 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = -39.1 (c = 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.19 (s, 3H), 0.20 (s, 3H), 0.97 (s, 9H), 3.34-3.46 (m, 3H), 3.64-3.72 (m, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 4.52-4.65 (m, 4H), 4.80-4.93 (m, 3H), 6.95 (d, *J* = 8.4 Hz, 2H), 7.09-7.16 (m, 2H), 7.25-7.42 (m, 10H), 7.49 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ -5.07, -4.09, 18.1, 25.7, 55.9, 56.0, 68.7, 73.4, 74.6, 75.0, 75.4, 77.6, 82.9, 97.1, 110.3, 111.4, 119.2, 126.7, 127.4, 127.5, 127.7, 127.9, 128.22, 128.26, 128.3, 133.7, 136.4, 137.98, 138.00, 140.5, 148.5, 149.0; IR (film): 3032, 2930, 2109, 1589, 1503, 1464, 1252, 1064, 909 cm^{-1}. HRMS-MALDI (*m/z*): Calcd for $C_{41}H_{51}N_3O_8Si$ [M+Na]$^+$, 748.3389; Found, 748.3400.

Compound **4b** (36.3, 50 μmol) was then subjected to the standard deprotection procedure using DDQ (34.1 mg, 0.15 mmol) to give **5b** (21.5 mg) in 86% yield. Analytical data are in accordance with the literature.[4]

Methyl 2,3,4-tri-*O*-benzyl-6-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-α-D-glucopyranoside (4c) and methyl 2,3,4-tri-*O*-benzyl-α-D-glucopyranoside (5c): General procedure using **3c** (67.2 mg, 0.1 mmol), 3,4-dimethoxyphenyl boronic acid (21.8 mg, 0.12 mmol), TBABr (3.2 mg, 10 μmol), K_3PO_4 (63.5 mg, 0.3 mmol) and Pd(OAc)$_2$ (1.1 mg, 5 μmol) afforded **4c** (63.5 mg) in 93% yield as a white foam. R$_f$ 0.48 (hexanes/ethyl acetate = 2 : 1); $[\alpha]_D^{r.t.}$ = +24.6 (c = 1.7, CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.40 (s, 3H), 3.58 (dd, *J* = 9.6, 6.3 Hz, 1H), 3.65-3.78 (m, 4H), 3.93 (s, 6H), 3.99 (t, *J* = 6.3 Hz, 1H), 4.47 (d, *J* = 10.5 Hz, 1H), 4.50 (d, *J* = 12.0 Hz, 1H), 4.64-4.70 (m, 3H), 4.81 (d, *J* = 12.0 Hz, 1H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.84 (d, *J* = 10.5 Hz, 1H), 4.99 (d, *J* = 10.8 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.05-7.14 (m, 4H), 7.22-7.40 (m, 15H), 7.51 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, CDCl$_3$) δ 55.2, 55.89, 55.96, 68.3, 70.0, 73.2, 73.4, 75.0, 75.7, 77.6, 79.7, 82.1, 98.1, 110.2, 111.3, 119.2, 126.7, 127.4, 127.5, 127.70, 127.75, 127.8, 128.0, 128.20, 128.24, 128.29, 128.3, 133.6, 136.3, 138.0, 138.1, 138.6, 140.4, 148.4, 148.9; IR (film): 3086, 2913, 1600, 1503, 1456, 1210, 1031, 991 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{43}H_{46}O_8$ [M+Na]$^+$, 713.3085; Found, 713.3080.

Compound **4c** (34.5 mg, 50 μmol) was then subjected to the standard deprotection procedure using DDQ (34.1 mg, 0.15 mmol) to give **5c** (19.7 mg) in 85% yield. Analytical data are in accordance with the literature.[5]

Allyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-3-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-β-D-glucopyranoside (4d) and allyl 2-azido-3,6-di-*O*-benzyl-2-deoxy-β-D-glucopyranoside (5d): General procedure using **3d** (59.3 mg, 0.1 mmol), 3,4-dimethoxyphenyl boronic acid (21.8 mg, 0.12 mmol), TBABr (3.2 mg, 10 μmol), K_3PO_4 (63.5 mg, 0.3 mmol) and Pd(OAc)$_2$ (1.1 mg, 5 μmol) afforded **4d** (40.4 mg) in 63% yield as a colorless syrup. R$_f$ 0.50 (hexanes/ethyl acetate = 2 : 1); $[\alpha]_D^{r.t.}$ = -52.7 (c = 1.6, CHCl$_3$); ^{1}H NMR (300 MHz, CDCl$_3$) δ 3.41-3.52 (m, 3H), 3.64-3.78 (m, 3H), 3.94 (s, 3H), 3.96 (s, 3H), 4.16 (ddt, *J* = 14.7, 6.3, 1.8 Hz, 1H), 4.34 (d, *J* = 7.8 Hz, 1H), 4.43 (ddt, *J* = 14.7, 6.3, 1.8 Hz, 1H), 4.56 (d, *J* = 12.1 Hz, 1H), 4.59 (d, *J* = 10.5 Hz, 1H), 4.65 (d, *J* = 12.1 Hz, 1H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.85 (d, *J* = 10.5 Hz, 1H), 4.92 (d, *J* = 10.8 Hz, 1H), 5.24 (ddd, *J* = 10.5, 2.8, 1.5 Hz, 1H), 5.36 (ddd, *J* = 17.1, 2.8, 1.5 Hz, 1H), 5.92-6.02 (m, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 7.09-7.41 (m, 14H), 7.49 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.98, 56.0, 66.3, 68.6, 70.3, 73.5, 74.7, 75.0, 75.6, 77.7, 83.2, 100.9, 110.3, 111.4, 117.6, 119.3, 126.8, 127.6, 127.7, 127.8, 127.9, 128.3, 128.4, 133.4, 133.7, 136.3, 137.8, 137.9, 140.5, 148.5, 149.0; IR (film): 3086, 2913, 1600, 1503, 1456, 1210, 1031, 991 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{38}H_{41}N_3O_7$ $[M+Na]^+$, 674.2837; Found, 674.2845.

Compound **4d** (25.6 mg, 40 μmol) was then subjected to the standard deprotection procedure using DDQ (27.2mg, 0.12 mmol) to give **5d** (15.0 mg) in 88% yield as colorless oil. R_f 0.26 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = -41.7 (c = 0.9, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.67 (d, *J* = 2.1 Hz, 1H), 3.26 (dd, *J* = 9.9, 8.7 Hz, 1H), 3.38-3.46 (m, 2H), 3.64 (td, *J* = 9.0, 2.4 Hz, 1H), 3.73 (d, *J* = 4.8 Hz, 1H), 4.14 (ddt, *J* = 12.6, 6.3, 1.5 Hz, 1H), 4.34 (d, *J* = 8.1 Hz, 1H), 4.40 (ddt, *J* = 12.6, 6.3, 1.5 Hz, 1H), 4.56 (d, *J* = 12.0 Hz, 1H), 4.62 (d, *J* = 12.0 Hz, 1H), 4.78 (d, *J* = 11.1 Hz, 1H), 4.92 (d, *J* = 11.1 Hz, 1H), 5.23 (ddd, *J* = 10.5, 2.8, 1.2 Hz, 1H), 5.35 (ddd, *J* = 17.4, 2.8, 1.2 Hz, 1H), 5.89-6.02 (m, 1H), 7.28-7.43 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 65.7, 70.2, 70.3, 72.0, 73.7, 73.9, 75.1, 82.5, 100.9, 117.7, 127.6, 127.7, 127.9, 128.0, 128.3, 128.5, 133.3, 137.5, 137.9; IR (film): 3467, 3015, 2923, 2871, 2102, 1451, 1359, 1266, 1071 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{23}H_{27}N_3O_5$ $[M+Na]^+$, 448.1843; Found, 448.1848.

1,5-Anhydro-2-deoxy-6-*O*-(4-(3,4-dimethoxyphenyl)benzyl)-3,4-di-*O*-pivaloyl-D-arabinohex-1-enitol (4e) and 1,5-anhydro-2-deoxy-3,4-di-*O*-pivaloyl-D-arabinohex-1-enitol (5e): General procedure using **3e** (48.2 mg, 0.1 mmol), 3,4-dimethoxyphenyl boronic acid (21.8 mg, 0.12 mmol), TBABr (3.2 mg, 10 μmol), K_3PO_4 (63.5 mg, 0.3 mmol) and $Pd(OAc)_2$ (1.1 mg, 5 μmol) afforded **4e** (47.5 mg) in 90% yield as a colorless syrup. R_f 0.48 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = -4.54 (c = 1.8, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.21 (s, 9H), 1.23 (s, 9H), 3.83 (dd, *J* = 7.2, 5.1 Hz, 1H), 3.92 (s, 3H), 3.95 (s, 3H), 4.20-4.26 (m, 1H), 4.35 (dd, *J* = 12.0, 3.6 Hz, 1H), 4.41 (d, *J* = 12.0, 5.4 Hz, 1H), 4.65 (d, *J* = 11.4 Hz, 1H), 4.79-4.82 (m, 2H), 5.41 (t, *J* = 4.5 Hz, 1H), 6.44 (d, *J* = 6.0 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.08-7.15 (m, 2H), 7.36 (d, *J* = 8.1 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.2, 27.3, 38.8, 38.9, 55.9, 56.0, 62.0, 69.2, 73.0, 73.2, 74.9, 98.8, 110.3, 111.4, 119.2, 126.8, 128.1, 133.6, 135.8, 140.7, 145.3, 148.5, 149.0, 177.7, 177.9; IR (film): 3021, 2972, 1724, 1654, 1505, 1248, 1145, 1028 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{31}H_{40}O_8$ $[M+Na]^+$, 563.2615; Found, 563.2615.

Compound **4e** (26.5 mg, 50 μmol) was then subjected to the standard deprotection procedure using DDQ (34.1 mg, 0.15 mmol) to give **5e** (13.0 mg) in 83% yield as colorless oil. R_f 0.23 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = -66.8 (c = 4.6, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.12 (s, 9H), 1.15 (s, 9H), 2.64 (brs, 1H), 3.61 (dd, *J* = 12.8, 4.8 Hz, 1H), 3.72 (dd, *J* = 12.8, 2.4 Hz, 1H), 3.94-4.00 (m, 1H), 4.71 (dd, *J* = 6.0, 2.4 Hz, 1H), 5.17 (dd, *J* = 9.3, 7.0 Hz, 1H), 5.42 (d, *J* = 7.0 Hz, 1H), 6.43 (d, *J* = 6.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.9, 38.6, 38.7, 60.5, 67.3, 68.3, 76.6, 99.2, 145.6, 177.8, 177.9; IR (film): 3527, 2972, 2887, 1733, 1656, 1488, 1397, 1280, 1163, 1032 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{16}H_{26}O_6$ $[M+Na]^+$, 337.1622; Found, 337.1618.

Preparation of *p*-(3,4-Dimethoxyphenyl)benzyl Bromide and Selective Deprotection of *p*-(3,4-Dimethoxyphenyl)benzyl Ether in the Presence of *p*-Methoxybenzyl Ether:

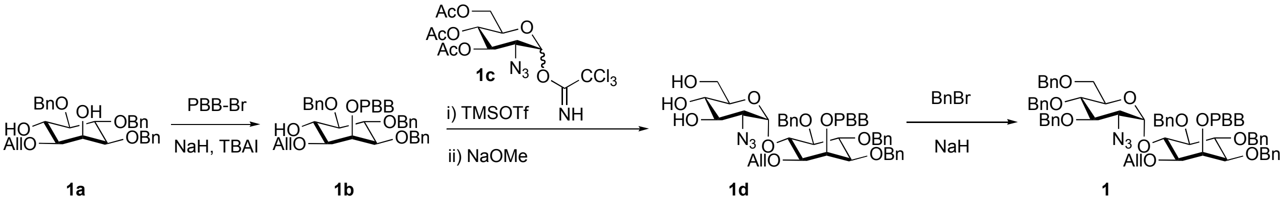
4-(3,4-Dimethoxyphenyl)benzyl Bromide (6): 4-Bromobenzyl alcohol (935 mg, 5 mmol) and 3,4-dimethoxyphenyl boronic acid (912 mg, 6 mmol) were cross-coupled using the general procedure to afford 4-(3,4-dimethoxyphenyl)benzyl alcohol (1.16 g) in 95% isolated yield. Then 4-(3,4-dimethoxyphenyl)benzyl alcohol (732 mg, 3 mmol) was dissolved in THF (10 mL). The mixture was cooled to 0 ºC and phosphorus tribromide (322 μL, 3 mmol) was added dropwise. Temperature was gradually elevated to room temperature and the reaction completed in 2 h. Excess solvent was evaporated and the residue was subjected to flash silica column chromatography to afford **6** (836 mg) in 91% yield as white solid. R_f 0.40 (hexanes/ethyl acetate = 4 : 1); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.93 (s, 3H), 3.95 (s, 3H), 4.55 (s, 2H), 6.95 (d, *J* = 8.1 Hz, 1H), 7.09-7.16 (m, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.54 (d, *J* = 8.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.5, 55.9, 110.3, 111.4, 119.4, 127.2, 129.5, 133.4, 136.3, 141.2, 148.8, 149.2; IR (KBr): 3048, 2986, 1604, 1382, 1209, 1011 cm^{-1}. HRMS-ESI (*m*/*z*): Calcd for $C_{15}H_{15}BrO_2$ $[M+Na]^+$, 306.0250; Found, 306.0247.

1,5-Anhydro-3-*O*-benzyl-6-*O*-(3,4-dimethoxyphenyl)benzyl-2-deoxy-4-*O*-(4-methoxybenzyl)-D-arabinohex-1-enitol (8):
1,5-Anhydro-3-*O*-benzyl-2-deoxy-4-*O*-(4-methoxybenzyl)-D-arabinohex-1-enitol (**7**) [6] (107 mg, 0.3 mmol) and 4-(3,4-dimethoxyphenyl)benzyl bromide (**6**) (111 mg, 0.36 mmol) were dissolved in DMF (4 mL). The mixture was cooled to 0 ºC and NaH (18 mg, 0.45 mmol, 60% in mineral oil) was added under a flow of nitrogen. The temperature was gradually elevated to room temperature and the reaction completed within 4 h. Methanol was added to remove excess NaH and the reaction mixture was diluted with water (10 mL). The aqueous phase was extracted with Et_2O (10 mL x 4). The combined organic layers were further washed with water and dried over Na_2SO_4. Evaporation led to the crude product, which was further purified by flash silica column chromatography to afford **8** (162 mg) in 93% yield as white foam. R_f 0.52 (hexanes/ethyl acetate = 2 : 1); $[\alpha]_D^{r.t.} = +14.9$ (c = 2.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.75 (s, 3H), 3.75-3.95 (m, 3H), 3.93 (s, 3H), 3.96 (s, 3H), 4.04-4.06 (m, 1H), 4.21-4.23 (m, 1H), 4.56-4.68 (m, 5H), 4.78 (d, *J* = 10.8 Hz, 1H), 4.89 (dd, *J* = 6.3,

2.4 Hz, 1H), 6.44 (d, *J* = 6.3 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 6.95 (d, *J* = 8.4 Hz, 1H), 7.10-7.18 (m, 4H), 7.28-7.42 (m, 7H), 7.55 (d, *J* = 8.1 Hz, 2H), ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.1, 55.8, 55.9, 68.4, 70.4, 73.2, 73.4, 74.0, 75.8, 76.8, 99.9, 110.3, 111.4, 113.7, 119.3, 126.8, 127.6, 127.7, 128.29, 128.3, 129.5, 130.2, 133.8, 136.5, 138.3, 140.4, 144.6, 148.6, 149.1; IR (film): 3023, 2935, 1646, 1503, 1221, 1028 cm^{-1}. HRMS-MALDI (*m/z*): Calcd for $C_{36}H_{38}O_7$ $[M+Na]^+$, 605.2510; Found, 605.2500.

1,5-Anhydro-3-*O*-benzyl-6-*O*-(3,4-dimethoxyphenyl)benzyl-2-deoxy)-D-arabinohex-1-enitol (9): Compound **8** (58 mg, 0.1 mmol) was dissolved in dry CH_3CN (1 mL). And $ZrCl_4$ (4.7 mg, 20 μmol) was added under nitrogen. The reaction mixture was then stirred at room temperature for 1 h and diluted with EtOAc. The organic layer was successively washed with saturated aqueous $NaHCO_3$ solution, brine and dried over Na_2SO_4. Rotary evaporation yielded the crude residue, which was purified by flash silica column chromatography to furnish **9** (37.9 mg) in 82% yield as colorless syrup. R_f 0.23 (hexanes/ethyl acetate = 2 : 1); $[\alpha]_D^{r.t.} = +11.2$ (c = 1.3, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.96 (s, 1H), 3.81-3.99 (m, 4H), 3.93 (s, 3H), 3.95 (s, 3H), 4.26 (m, 1H), 4.59 (d, *J* = 11.4 Hz, 1H), 4.69 (d, *J* = 11.4 Hz, 1H), 4.76 (d, *J* = 11.4 Hz, 1H), 4.90 (d, *J* = 11.4 Hz, 1H), 4.91 (dd, *J* = 6.0, 3.3 Hz, 1H), 6.41 (dd, *J* = 6.3, 1.2 Hz, 1H), 6.94 (d, *J* = 8.4 Hz, 1H), 7.08-7.15 (m, 2H), 7.26-7.39 (m, 6H), 7.53 (d, *J* = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 55.9, 56.0, 68.8, 70.6, 73.4, 74.5, 75.5, 102.7, 110.4, 111.4, 119.4, 126.9, 127.7, 127.8, 128.4, 133.8, 136.5, 136.7, 137.7, 140.7, 144.6, 148.6, 149.1; IR (film): 3528, 3023, 2935, 1646, 1503, 1221, 1028 cm^{-1}. HRMS-MALDI (*m/z*): Calcd for $C_{28}H_{30}O_6$ $[M+Na]^+$, 485.1942; Found, 485.1960.

Preparation of Disaccharide 1:



1-*O*-Allyl-3,4,5-tri-*O*-benzyl-2-*O*-(4-bromobenzyl)-D-*myo*-inositol (1b): Inositol **1a** [5,7] (1.34 g, 2.7 mmol) and TBAI (1.0 g, 2.7 mmol) were dissolved in DMF (60 mL). This solution was cooled to 0 ºC, and NaH (60% in mineral oil, 0.48 g, 10.3 mmol) was added in one portion. After 30 min stirring at 0 ºC, the reaction mixture was cooled to –20 ºC using an ice/aceton bath. Then, *p*-bromobenzyl bromide (700 mg, 2.8 mmol) in DMF (5 mL) was added dropwise. The reaction was stirred while the reaction warmed to ambient temperature. The reaction was quenched with water, and extracted by Et_2O (50 mL x 4). The combined organic layer was further washed with water, brine, and dried over Na_2SO_4. Rotary evaporation led to the crude residue, which was further purified by flash silica column chromatography. The appropriate fractions were collected and concentrated to give **1b** (1.44g, 81%) as white solid. R$_f$ 0.31 (hexanes/ethyl acetate = 4 : 1, eluted twice); $[\alpha]_D^{r.t.} = -10.8$ (c = 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (s, 1H), 3.16 (dd, *J* = 9.9, 2.1 Hz, 1H), 3.44 (m, 2H), 4.04-4.17 (m, 5H), 4.67 (d, *J* = 12.1 Hz, 1H), 4.77 (d, *J* = 11.6 Hz, 1H), 4.82 (dd, *J* = 12.3, 3.5 Hz, 1H), 4.88-4.99 (m, 4H), 5.24 (dd, *J* = 10.4, 1.1 Hz, 1H), 5.32 (dd, *J* = 17.2, 1.3 Hz, 1H), 5.93 (m, 1H), 7.29-7.47 (m, 19H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 71.7, 73.2, 73.5, 73.8, 74.4, 75.9, 76.3, 80.2, 81.5, 81.8, 83.8, 117.9, 121.6, 128.0, 128.1, 128.2, 128.3, 128.5, 128.8, 128.9, 129.8, 131.7, 134.8, 138.3, 138.7, 139.1, 139.2; IR (film): 3477, 3056, 2882, 1497, 1451, 1359, 1118, 1062 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{37}H_{39}BrO_6$ $[M+Na]^+$, 681.1821; Found, 681.1840.

(2-Azido-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-(4-bromobenzyl)-D-*myo*-inositol (1d): Glucosamine trichloroimidate **1c** [4,8] (211 mg, 0.44 mmol) and inositol **1b** (200 mg, 0.32 mmol) were co-evaporated with toluene (2 mL) three times and subsequently dried under high vacuum for 2 h, then dissolved in CH_2Cl_2 (5 mL) and cooled to 0 ºC. Freshly-made TMSOTf solution in CH_2Cl_2 (0.125 M, 253 μL, 32 μmol) was added. After 20 min, the reaction was quenched with Et_3N. The solvent was evaporated *in vacuo*. The residue was dissolved in MeOH (6 mL) and NaOMe (0.5 M in MeOH, 0.6 mL, 0.3 mmol) was added at room temperature. After further stirring for 2 h, the solution was neutralized with acidic DOWEX resin to pH6. The organic layer was collected by filtrating off the resin, and was evaporated to give the crude product. Subsequent purification by flash silica column chromatography afforded a diastereomeric mixture of **1d** (233 mg, 95%, α:β ≈ 9:1) as white foam, and further purification using preparative MPLC gave exclusively α-linked **1d** (165 mg, 67%). R$_f$ 0.25 (hexanes/ethyl acetate = 1 : 1, eluted twice); $[\alpha]_D^{r.t.} = +39.4$ (c = 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.18 (t, *J* = 6.9 Hz, 1H), 1.49 (s, 1H), 1.97 (d, *J* = 3.8 Hz, 1H), 2.80 (d, *J* = 4.4 Hz, 1H), 2.98 (dd, *J* = 10.4, 3.7 Hz, 1H), 3.21-3.36 (m, 7H), 3.65-4.07 (m, 7H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.56 (d, *J* = 11.3 Hz, 1H), 4.61 (d, *J* = 11.7 Hz, 1H), 4.70 (s, 2H), 4.74 (d, *J* = 10.6 Hz, 1H), 4.89 (d, *J* = 10.6 Hz, 1H), 5.02 (d, *J* = 11.3 Hz, 1H), 5.11 (dd, *J* = 13.0, 1.3 Hz, 1H), 5.18 (dd, *J* = 17.2, 1.3 Hz, 1H), 5.52 (d, *J* = 3.7 Hz, 1H), 5.80-5.90 (m, 1H), 7.15-7.35 (m, 19H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 61.7, 63.3, 70.6, 71.3, 71.5, 71.9, 73.4, 73.6, 73.7, 75.9, 76.0, 76.2, 81.2, 81.7, 82.0, 82.4, 98.2, 117.8, 121.8, 127.9, 128.0, 128.2, 128.4, 128.8, 128.9, 129.9, 131.8, 134.6, 138.2, 138.5, 138.9; IR (film): 3404, 3008, 2880, 2108, 1454, 1352, 1129, 1033, 1027 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{43}H_{48}BrN_3O_{10}$ $[M+Na]^+$, 868.2421; Found, 868.2412.

(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-(4-bromobenzyl)-D-*myo*-inositol (1): Disaccharide **1d** (70 mg, 80 μmol) and tetrabutylammonium iodide (TBAI) (29 mg, 80 μmol) were dissolved in DMF (3 mL). The solution was cooled to 0 ºC, and NaH (60% in mineral oil, 20.9 mg, 0.48 mmol) was added in one portion. After 20 min, BnBr (48 μL, 0.4 mmol) was added. The reaction mixture was allowed to warm to ambient temperature over 5 h, and then quenched with water. Extraction with Et_2O (10 mL x 3) and further evaporation of the combined organic layer afforded the crude product. It was further purified by flash silica column chromatography to give pure **1** (73 mg, 86%) as white foam. R_f 0.50 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = +51.7 (c = 0.81, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.06 (dd, *J* = 10.8, 1.8 Hz, 1H), 3.14 (dd, *J* = 10.8, 1.8 Hz, 1H), 3.23 (dd, *J* = 10.5, 3.9 Hz, 1H), 3.30 (dd, *J* = 10.0, 2.5 Hz, 1H), 3.33 (dd, *J* = 10.0, 2.5 Hz, 1H), 3.35 (t, *J* = 9.6 Hz, 1H), 3.65 (dd, *J* = 10.5, 9.0 Hz, 1H), 3.87 (dd, *J* = 10.5, 9.0 Hz, 1H), 3.90-3.98 (m, 4H), 4.04 (t, *J* = 9.5 Hz, 1H), 4.15 (t, *J* = 9.5 Hz, 1H), 4.17 (d, *J* = 12.5 Hz, 1H), 4.32 (d, *J* = 11.0 Hz, 1H), 4.46 (d, *J* = 12.0 Hz, 1H), 4.53 (d, *J* = 10.5 Hz, 1H), 4.58-4.66 (m, 3H), 4.70 (s, 2H), 4.75 (d, *J* = 10.5 Hz, 1H), 4.81 (s, 2H), 4.90 (d, *J* = 11.0 Hz, 1H), 4.95 (d, *J* = 11.0 Hz, 1H), 5.13 (ddd, *J* = 10.5, 3.5, 1.5 Hz, 1H), 5.21 (ddd, *J* = 17.1, 3.5, 1.5 Hz, 1H), 5.65 (d, *J* = 4.0 Hz, 1H), 5.84-5.93 (m, 1H), 6.97-7.00 (m, 4H), 7.06-7.10 (m, 1H), 7.15-7.31 (m, 27H), 7.35-7.38 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 63.5, 67.7, 70.1, 71.0, 73.0, 73.36, 73.4, 75.2, 75.3, 75.6, 75.7, 78.3, 80.2, 80.8, 81.3, 81.9, 82.0, 97.7, 117.0, 121.3, 127.52, 127.5,, 127.57, 127.64, 127.66, 127.74, 127.78, 128.02, 128.03, 128.13, 128.16, 128.2, 128.3, 128.4, 128.5, 131.3, 134.2, 137.9, 138.0, 138.12, 138.15, 138.52, 138.57; IR (film): 3056, 3015, 2861, 2102, 1497, 1451, 1359, 1128, 1056 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{64}H_{66}BrN_3O_{10}$ $[M+Na]^+$, 1138.3824; Found, 1138.3800.

Synthesis of the Fully Lipidated Malarial Disaccharide

(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-D-*myo*-inositol (10): Disaccharide **1** (68 mg, 60.7 μmol) was cross-coupled with 3,4-dimethoxyphenylboronic acid using the standard procedure to furnish DMPBn-protected disaccharide. The DMPBn-protected disaccharide was then dissolved in a mixture of CH_2Cl_2 (2.8 mL) and water (0.2 mL). DDQ (41 mg, 0.18 mmol) was added in one portion at room temperature. The reaction mixture was stirred further for 2 h, and worked up by dilution with CH_2Cl_2 and washing the organic phase with freshly prepared aqueous solution of sodium ascorbate. The organic layer was further washed with saturated aqueous $NaHCO_3$ solution and water, and dried over Na_2SO_4. Evaporation led to the crude product, which was purified by flash silica column chromatography to give pure **10** (45 mg, 79%) as colorless syrup. R_f 0.41 (hexanes/ethyl acetate = 2 : 1); $[\alpha]_D^{r.t.}$ = +46.4 (c = 0.15, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.43 (s, 1H), 3.15 (dd, *J* = 11.4, 2.4 Hz, 1H), 3.24 (dd, *J* = 11.4, 2.4 Hz, 1H), 3.32 (dd, *J* = 10.2, 3.9 Hz, 1H), 3.37-3.46 (m, 3H), 3.72 (t, *J* = 9.7 Hz, 1H), 3.95 (t, *J* = 9.7 Hz, 1H), 4.03-4.28 (m, 7H), 4.41 (d, *J* = 11.1 Hz, 1H), 4.53 (d, *J* = 12.0 Hz, 1H), 4.67

(d, *J* = 10.5 Hz, 1H), 4.73 (d, *J* = 12.0 Hz, 1H), 4.74 (s, 2H), 4.84 (d, *J* = 10.5 Hz, 1H), 4.89 (s, 2H), 4.97 (d, *J* = 11.1 Hz, 1H), 5.00 (d, *J* = 10.5 Hz, 1H), 5.22 (dd, *J* = 10.5, 1.8 Hz, 1H), 5.31 (dd, *J* = 17.1, 1.7 Hz, 1H), 5.68 (d, *J* = 3.6 Hz, 1H), 5.92-6.06 (m, 1H), 7.05-7.07 (m, 3H), 7.22-7.36 (m, 27H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 63.4, 66.4, 67.6, 70.1, 71.0, 72.7, 73.3, 74.6, 74.8, 75.2, 75.7, 75.8, 78.2, 79.6, 80.1, 80.8, 81.1, 81.4, 97.5, 117.8, 127.3, 127.4, 127.5, 127.6, 127.7, 127.8, 127.90, 127.95, 127.98, 128.0, 128.1, 128.2, 128.3, 128.4, 128.5, 134.0, 137.8, 137.92, 137.98, 138.0, 138.4, 138.5; IR (film): 3467, 3015, 2861, 2092, 1497, 1451, 1359, 1128, 1066 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{57}H_{61}N_3O_{10}$ $[M+Na]^+$, 970.4249; Found, 970.4238.

(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-3,4,5-tri-*O*-benzyl-2-*O*-hexadecanoyl-D-*myo*-inositol (11): Disaccharide **10** (45 mg, 48 μmol) was dissolved in CH_2Cl_2 (2 mL). Palmitic acid (17.3 mg, 67 μmol), DCC solution in CH_2Cl_2 (1 M, 67 μL, 67 μmol) and DMAP (8.2 mg, 67 μmol) were added to the reaction mixture in sequential order. The solution was stirred overnight at room temperature. Then, the solvent was evaporated *in vacuo* and the residue was subjected directly to flash silica column chromatography to afford pure (2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-hexadecanoyl-D-*myo*-inositol (50 mg, 87%) as colorless syrup. R$_f$ 0.45 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = +50.9 (c = 1.7, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, *J* = 6.6 Hz, 1H), 1.27 (m, 24H), 1.59-1.67 (m, 2H), 2.42 (t, *J* = 7.2 Hz, 1H), 3.18 (dd, *J* = 11.1, 1.8 Hz, 1H), 3.23 (dd, *J* = 11.1, 1.8 Hz, 1H), 3.30 (dd, *J* = 10.2, 3.6 Hz, 1H), 3.46 (t, *J* = 9.6 Hz, 1H), 3.52 (dd, *J* = 9.4, 1.8 Hz, 1H), 3.74 (t, *J* = 9.6 Hz, 1H), 3.89-4.05 (m, 4H), 4.08-4.26 (m, 2H), 4.40 (d, *J* = 10.8 Hz, 1H), 4.53 (d, *J* = 10. Hz, 1H), 4.54 (d, *J* = 12.0 Hz, 1H), 4.66 (d, *J* = 10.5 Hz, 1H), 4.75 (d, *J* = 10.8 Hz, 1H), 4.81 (d, *J* = 10.8 Hz, 1H), 4.90 (s, 2H), 4.97 (d, *J* = 10.8 Hz, 1H), 5.05 (d, *J* = 10.5 Hz, 1H), 5.19 (dd, *J* = 10.5, 1.5 Hz, 1H), 5.28 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.69 (d, *J* = 3.6 Hz, 1H), 5.83 (t, *J* = 2.4 Hz, 1H), 5.91-6.02 (m, 1H), 7.05-7.10 (m, 3H), 7.26-7.39 (m, 27H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 22.8, 25.3, 29.1, 29.4, 29.6, 29.8, 32.0, 34.4, 63.4, 65.5, 67.6, 70.1, 70.7, 73.3, 74.7, 75.2, 75.5, 75.8, 76.0, 78.1, 78.3, 79.1, 80.1, 80.7, 81.7, 97.7, 117.4, 127.3, 127.5, 127.70, 127.74, 127.78, 127.9, 128.1, 128.2, 128.23, 128.29, 133.9, 137.4, 137.9, 138.3, 173.0; IR (film): 3025, 2919, 2855, 2102, 1738, 1638, 1357, 1086 cm^{-1}. HRMS-MALDI (*m*/*z*): Calcd for $C_{73}H_{91}N_3O_{11}$ $[M+Na]^+$, 1208.6546; Found, 1208.656.

(2-Azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-1-*O*-allyl-3,4,5-tri-*O*-benzyl-2-*O*-hexadecanoyl-D-*myo*-inositol (45 mg, 38 μmol), $PdCl_2$ (67.3 mg, 0.38 mmol) and NaOAc (62.2 mg, 0.76 mmol) were dissolved in a mixture of acetic acid and water (19:1, 2.5 mL) at room temperature.. The reaction mixture was stirred for additional 4 h and carefully quenched by the addition of saturated aqueous $NaHCO_3$ solution and solid Na_2CO_3. The aqueous layer was extracted with CH_2Cl_2 for three times and the combined organic layer was further washed with saturated $NaHCO_3$ solution and brine. Evaporation *in vacuo* gave the crude product, which was purified by flash silica column chromatography to recover small amount of the starting inositol (6.2 mg, 14%), and pure **11** (30 mg, 69 %) as colorless syrup, R_f 0.21 (hexanes/ethyl acetate = 4 : 1); $[\alpha]_D^{r.t.}$ = +40.2 (c = 1.0, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (t, *J* = 7.0 Hz, 1H), 1.23-1.36 (m, 24H), 1.63-1.69 (m, 2H), 2.41 (t, *J* = 7.5 Hz, 1H), 2.97 (dd, *J* = 11.1, 1.8 Hz, 1H), 3.23 (dd, *J* = 11.1, 1.8 Hz, 1H), 3.39 (t, *J* = 9.4 Hz, 1H), 3.53-3.57 (m, 2H), 3.71-3.75 (m, 3H), 3.83-3.94 (m, 4H), 4.11 (d, *J* = 12.0 Hz, 1H), 4.42 (t, *J* = 10.9 Hz, 1H), 4.49 (d, *J* = 11.0 Hz, 1H), 4.62 (d, *J* = 11.0 Hz, 1H), 4.71 (d, *J* = 12.0 Hz, 1H), 4.72 (t, *J* = 10.9 Hz, 1H), 4.83 (d, *J* = 10.8 Hz, 1H), 4.89 (d, *J* = 10.8 Hz, 1H), 4.90 (d, *J* = 10.9 Hz, 1H), 5.06 (d, *J* = 10.9 Hz, 1H), 5.26 (d, *J* = 3.6 Hz, 1H), 5.74 (t, *J* = 2.6 Hz, 1H), 7.07-7.10 (m, 2H), 7.16-7.37 (m, 28H); ^{13}C NMR (125MHz, $CDCl_3$) δ 14.2, 22.7, 25.3, 29.1, 29.3, 29.4, 29.5, 29.6, 29.70, 29.72, 31.9, 34.5, 64.4, 67.4, 68.9, 71.3, 72.1, 73.4, 74.8, 75.4, 75.6, 75.9, 78.1, 78.5, 80.8, 81.0, 81.8, 82.1, 99.3, 127.46, 127.47, 127.65, 127.68, 127.7, 127.8, 127.9, 128.01, 128.03, 128.07, 128.27, 128.30, 128.31, 128.33, 128.34, 128.37, 128.5, 137.6, 137.76, 137.77, 138.1, 138.3, 138.5, 173.4; IR (film): 3447, 3029, 2925, 2831, 2108, 1739, 1454,1369, 1264, 1126, 1056 cm^{-1}. HRMS-ESI (*m/z*): Calcd for $C_{70}H_{87}N_3O_{11}$ $[M+Na]^+$,1168.6233; Found, 1168.6240.

Triethylammonium(2-azido-3,4,6-tri-*O*-benzyl-2-deoxy-α-D-glucopyranosyl)-(1→6)-3,4,5-tri-*O*-benzyl-2-*O*-hexadecanoyl-1-*O*-(1,2-di-*O*-octadecanoyl-*sn*-glyceryl-phosphonato)-D-*myo*-inositol (13): Disaccharide **11** (30 mg, 26.2 μmol) and H-phosphonate **12** [9] (103 mg, 0.131 mmol) were co-evaporated three times with pyridine (2 mL) and dried under high vacuum overnight. The mixture was then dissolved in pyridine (1 mL) at room temperature and pivaloyl chloride (32.2 μL, 0.262 mmol) was added. This reaction mixture was stirred for 4 h, and iodine (66.5 mg, 0.262 mmol) in a mixture of pyridine and water (19:1, 0.6 mL) was added. After 1 h stirring, the reaction was quenched by diluting with CH_2Cl_2 first and washing with aqueous $Na_2S_2O_3$ solution to remove excess iodine. The aqueous layer was back extracted with CH_2Cl_2 (5 mL x 3), and the combined organic layer was washed with triethyl ammonium borate buffer (pH = 7, 10 mL x 2) and dried over Na_2SO_4. Concentration *in vacuo* gave a crude residue, that was then purified by flash silica column chromatography to afford **13** (36 mg, 90%) as white foam. R_f 0.46 (chloroform/methanol = 20 : 1 with 1% Et_3N); $[\alpha]_D^{r.t.}$ = +37.7 (c = 2.0, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 0.87-0.89 (m, 9H), 1.13-1.26 (m, 89H), 1.53-1.60 (m, 6H), 2.27-2.37 (m, 6H), 2.72-2.80 (m, 6H), 3.20 (dd, *J* = 10.6, 3.6 Hz, 1H), 3.46-3.82 (m, 8H), 3.90-4.06 (m, 3H), 4.16-4.26 (m, 3H), 4.58 (d, *J* = 12.0 Hz, 1H), 4.67-4.90 (m, 7H), 5.30 (m, 1H), 5.88 (d, *J* = 3.6 Hz, 1H), 6.07 (t, *J* = 2.1 Hz, 1H), 6.96-7.36 (m, 30H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.2, 14.1, 22.7, 24.8, 24.9, 25.3, 29.1, 29.2, 29.3, 29.4, 29.5, 29.6, 29.7, 31.9, 34.1, 34.3, 45.9, 63.0, 63.1, 63.6, 63.7, 68.2, 69.3, 70.1, 70.5, 70.7, 71.9, 73.2, 73.6, 73.7, 74.8, 75.1, 75.6, 76.4, 77.2, 78.4, 79.1, 79.7, 81.2, 81.7, 96.6, 127.40, 127.45, 127.70, 127.76, 127.79, 128.0, 128.1, 128.2, 128.32, 128.35, 137.9, 138.0, 138.1, 138.2, 138.5, 138.6, 172.6, 173.1, 173.5; IR (film): 3025, 2923, 2852, 2107, 1738, 1457, 1362, 1215, 1062 cm^{-1}. ^{31}P NMR (121 MHz, CDCl$_3$) δ -0.70; HRMS-MALDI (*m*/*z*): Calcd for $C_{109}H_{161}N_3O_{18}P$ [M+2Na]$^+$, 1877.1303; Found, 1877.126.

(2-Amino-2-deoxy-α-D-glucopyranosyl)-(1→6)-2-*O*-hexadecanoyl-1-*O*-(1,2-di-*O*-octadecanoyl-*sn*-glyceryl-phosphonato)-D-*myo*-inositol (14): To phosphorylated disaccharide **13** (10 mg, 5.5 μmol) and 20% Pd(OH)$_2$/C (20 mg, 28.5 μmol) was added a mixture of CHCl$_3$, MeOH and water (3:3:1, 1.5 mL). The reaction flask was evacuated by careful control of pressure, and back-charged with hydrogen gas. This cycle was repeated 3 times, and the mixture was stirred vigorously at room temperature for 24 h. The reaction mixture was then passed through a short column of Celite and the collected filtrate was evaporated to dryness to afford **14** (6.9 mg, quant.) as white solid. ^{31}P NMR (121 MHz, CDCl$_3$:CD$_3$OD:D$_2$O = 3:3:1) δ 2.19; HRMS-MALDI (*m*/*z*): Calcd for $C_{67}H_{127}NO_{18}P$,1264.8796; Found, 1264.837. Due to the great tendency of **14** to form micelles in the corresponding NMR solvent, ^{1}H and ^{13}C NMR spectra obtained possessed broad signals and were not easily assignable. However, the lack of aromatic proton in ^{1}H NMR firmly indicated that the global deprotection was complete.

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