Supporting Information for:
**Synthesis of the Glycosphingolipid β -Galactosyl Ceramide and Analogs via
Olefin Cross Metathesis**

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General Experimental Protocols

Dry solvents (ether/THF/CH₂Cl₂/MeOH) were obtained by passing them through a column of alumina, copper oxide, and/or molecular sieves, depending on the solvent, using a commercially available solvent purification system. NMR spectra were recorded at 300 or 400 MHz for ¹H and 75 or 100 MHz for ¹³C. ¹H chemical shifts were referenced to TMS at 0 ppm or residual solvent peaks. ¹³C chemical shifts were referenced to the solvent peak, typically CDCl₃ at 77 ppm. ¹³C spectra for compounds **10a** and **10d** were acquired using a CapNMRTM probe from Magnetic Resonance Microsensors (www.protasis.com/MRM/MRM_Frame.htm, Savoy, IL). The broad resonances observed at 85 and 110 ppm are derived from the fluorocarbon FC-43 which is present in the microprobe.¹ The structure of the Grubbs Generation II catalyst used for all cross metathesis experiments is shown below.

Detailed Experimental Procedures

To a cold (0 °C) solution of **2**² (2.05 g, 5.1 mmol) and imidazole (555 mg, 5.86 mmol) in THF (50 ml) was added *tert*-butyldiphenylsilyl chloride (1.52 ml, 5.86 mmol). The reaction mixture was warmed to room temperature and stirred for 30 min. The reaction mixture was diluted with ethyl acetate (150 ml) and washed with brine. The organic layer was dried (Na₂SO₄), and the solvent was evaporated under reduced pressure. The crude product was directly used in the next step without further purification. To a solution of the silyl ether prepared above (1.8 g, 4.14 mmol) and *p*-methoxybenzyltrichloroacetimidate (2.34 g, 8.28 mmol) in toluene (50 ml) was added lanthanum triflate (1.7g, 2.89 mmol) and stirred for 1h at room temperature. The reaction

mixture was concentrated and directly purified by column chromatography (SiO₂, hexanes/ethyl acetate, 9/1) to generate 1.76 g (77% over two steps, 3.17 mmol) of **3** as an oil.

¹H NMR (300 MHz, CDCl₃): δ 1.04 (s, 3H), 2.95 (s, 3H), 3.77-3.92 (m, 4H), 3.80 (s, 3H), 4.15 (m, 1H), 4.43 (ab, 2H, J = 11.4 Hz), 4.60-4.64 (m, 1H), 5.38 (d, 1H, J = 10.2 Hz), 5.41 (d, 1H, J = 17.1 Hz), 5.73 (ddd, 1H, J = 7.5, 10.5, 17.7 Hz), 6.84 (d, 2H, J = 8.7 Hz), 7.2 (d, 2H, J = 8.7 Hz), 7.35-7.46 (m, 6H), 7.61-7.67 (m, 4H).

¹³C NMR (100 MHz, CDCl₃): δ 159.3, 135.6, 135.5, 133.3, 132.9, 132.5, 129.9, 129.8, 129.7, 129.5, 127.8, 120.6, 113.8, 84.6, 78.5, 70.5, 63.3, 55.2, 45.0, 38.6, 26.8, 19.2.

HRMS (FAB) Calcd. for C₃₀H₃₈O₆SSiNa 577.2056, Found 577.2060.

The mixture of **3** (495 mg, 0.89 mmol), *tetra*-butylammonium chloride (992 mg, 3.57l) and sodium azide (580, 8.93 mmol) in DMF (8 ml) was stirred at 90 °C for 24h. The DMF was removed, and the reaction mixture was dissolved in ether (25 ml). The mixture was filtered and solids were washed with ether (5x10 ml). The organic phase was dried (Na₂SO₄) and concentrated to give mixture of **4** and partially desilylated product. The crude reaction mixture was taken in dichloromethane (5ml) and was added Et₃N (0.25 ml, 1.78 mmol), DMAP (21mg, 0.18 mmol) followed by *tert*-butyldiphenylsilyl chloride (0.2 ml, 0.89 mmol). The reaction mixture was diluted with dichloromethane (15 ml) and washed with water (10 ml) and brine (10 ml). The organic layer was concentrated to give crude which was purified by column chromatography (SiO₂, hexanes/ethyl acetate, 20/1) to generate 300 mg (67% over two steps, 0.6 mmol) of **4**³ as oil.

A mixture of **5**³ (66 mg, 0.094 mmol) and HF/pyridine (0.66 ml, 6.6 mmol) in acetonitrile was stirred for 10h at room temperature. The reaction mixture was neutralized by careful addition of sat. sodium bicarbonate (aq.). The mixture was extracted with ethyl acetate (3 x 5 ml). The combined ethyl acetate layers were dried (Na₂SO₄) and concentrated to give crude which was

purified by column chromatography (SiO₂, ethyl acetate/hexanes, 1/5 to 1/4) to provide 38 mg (88%, 0.082 mmol) of **6** as a white solid.

¹H NMR (300 MHz, CDCl₃): δ 2.55 (dd, J = 2.2, 8.8 Hz, 1H), 3.59-3.70 (m, 2H), 3.75 (s, 3H), 4.0 (d, J = 11.1 Hz, 1H), 4.11 (m, 1H), 4.2 (t, J = 7 Hz, 1H), 4.36 (d, J = 6.9 Hz, 2H), 4.41 (ab, J = 11.1 Hz, 2H), 5.39 (d, J = 11 Hz, 1H), 5.40 (d, J = 16.5 Hz, 1H), 5.51 (d, J = 7.7 Hz, 1H), 5.84 (ddd, J = 7.1, 9.9, 17.1 Hz, 1H), 6.86 (d, J = 8.6 Hz, 2H), 7.22 (d, J = 8.3 Hz, 2H), 7.32 (td, J = 0.9, 7.4 Hz, 2H), 7.4 (t, J = 7.4 Hz, 2H), 7.59 (d, J = 7.1 Hz, 2H), 7.77 (d, J = 7.4 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 47.1, 54.8, 55.1, 61.6, 66.6, 70.7, 81.2, 113.8, 119.2, 119.8, 125.0, 126.9, 127.6, 129.4, 129.5, 135.0, 141.2, 143.8, 156.1, 159.2.

HRMS (FAB) Calcd. for C₂₈H₂₉NaNO₅ 482.1943, Found 482.1960.

To a solution of **8** (10 mg, 0.01 mmol) and heptene-1 (0.04 ml, 0.3 mmol) in toluene (0.5 ml) was added Grubbs Generation II catalyst (2.2 mg, 0.003 mmol). The reaction mixture was heated at 80 °C for 36h. The reaction mixture was concentrated and purified by column chromatography (SiO₂, ethyl acetate/hexanes, 1/10) to provide 9.7 mg (91%, 0.009 mmol) of **10a** as a white waxy solid.

¹H NMR (300 MHz, CDCl₃): δ 0.83 (t, J = 6 Hz, 3H), 1.12 (s, 9H), 1.14 (s, 9H), 1.17 (s, 9H), 1.21-1.38 (m, 6H), 1.25 (s, 9H), 1.98-2.04 (m, 2H), 3.61 (d, J = 8.8 Hz, 1H), 3.78 (s, 3H), 3.82-3.86 (m, 2H), 3.93-3.98 (m, 1H), 4.06 (dd, J = 7.1, 10.8 Hz, 1H), 4.14 (dd, J = 6.7, 10.9 Hz, 1H), 4.17-4.19 (m, 2H), 4.24-4.26 (m, 1H), 4.38 (ab, J = 11H, 2H), 4.40 (dd, J = 7.1, 9.8 Hz, 1H), 4.52 (d, J = 6.8 Hz, 1H), 4.96 (d, J = 8.3 Hz, 1H), 5.12 (dd, J = 3.2, 10.4 Hz, 1H), 5.23 (dd, J = 7.9, 10.2 Hz, 1H), 5.38 (dd, J = 6.5, 16.2 Hz, 1H), 5.145 (d, J = 2.9 Hz, 1H), 5.72 (dt, J = 6.3, 15.3 Hz, 1H), 6.86 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 10.9 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.55 (d, J = 7.7 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.76 (d, J = 7.6 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 13.9, 22.3, 27.0, 27.1, 28.7, 31.2, 32.1, 38.6, 38.7, 39.0, 47.2, 53.9, 55.1, 61.0, 66.7, 67.9, 69.0, 70.4, 70.85, 70.9, 79.3, 101.1, 113.7, 119.8, 124.9, 126.9, 127.2, 127.5, 129.2, 130.4, 136.8, 141.2, 143.9, 155.8, 159.1, 176.7, 176.8, 177.1, 177.7.

HRMS (FAB) Calcd. for $C_{59}H_{81}NaNO_{14}$ 1050.5555, found 1050.5570.

To a solution of **8** (10 mg, 0.01 mmol) and nonene-1 (0.002 ml, 0.1 mmol, diluted dichloromethane) in dichloromethane (2 ml) was added Grubbs Generation II catalyst (2.2 mg, 0.003 mmol). The reaction mixture was heated to reflux for 24h. To the reaction mixture was added nonene-1 (0.002 ml, 0.1 mmol) and it was refluxed for further 12h. The reaction mixture was concentrated and purified by column chromatography (SiO_2 , ethyl acetate/hexanes, 1/11) to provide 6 mg (76%, 0.0006 mmol) of **10b** as white waxy solid.

1H NMR (400 MHz, $CDCl_3$): δ 0.83 (t, J_{ave} = 6.6 Hz, 3H), 1.12 (s, 9H), 1.14 (s, 9H), 1.17 (s, 9H), 1.17-1.32 (m, 10H), 1.25 (s, 9H), 1.98-2.03 (m, 2H), 3.60 (d, J = 8.8 Hz, 1H), 3.77 (s, 3H), 3.82-3.88 (m, 2H), 3.94-3.98 (m, 1H), 4.06 (dd, J = 7.2, 10.8 Hz, 1H), 4.15 (dd, J = 6.7, 10.8 Hz, 1H), 4.17-4.20 (m, 2H), 4.24 (d, J = 7.6 Hz, 1H), 4.39 (ab, J = 11 Hz, 2H), 4.40 (dd, J = 6.8, 9.9 Hz, 1H), 4.51 (d, J = 7.7 Hz, 1H), 4.97 (d, J = 8.3 Hz, 1H), 5.12 (dd, J = 3, 10.4 Hz, 1H), 5.23 (dd, J = 8.1, 10 Hz, 1H), 5.36 (dd, J = 10.2, 15.6 Hz, 1H), 5.415 (d, J = 2.71, 1H), 5.72 (dt, J = 6.6, 15.5 Hz, 1H), 6.86 (d, J = 8.3 Hz, 2H), 7.24 (d, J = 9.7 Hz, 2H), 7.29 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.4 Hz, 2H), 7.545 (d, J = 7.2 Hz, 1H), 7.59 (d, J = 7.4 Hz, 1H), 7.75 (d, J = 7.5 Hz, 2H).

^{13}C NMR (100 MHz, $CDCl_3$): δ 14.1, 22.6, 27.1, 29.1, 29.16, 29.2, 31.8, 32.3, 38.8, 39.1, 47.2, 55.2, 61.0, 66.6, 66.8, 68.0, 69.0, 70.5, 70.9, 71.0, 79.4, 101.2, 113.7, 119.9, 125.1, 127.0, 127.3, 127.6, 129.3, 130.4, 137.1, 141.3, 143.9, 155.8, 159.1, 176.8, 176.9, 177.3, 177.8.

HRMS (FAB) Calcd. for $C_{61}H_{85}NaNO_{14}$ 1078.5868, found 1078.5888.

To a solution of **8** (10 mg, 0.01 mmol) and heptadecen-1 (72 mg, 0.3 mmol) in toluene (0.5 ml) was added Grubbs Generation II catalyst (2.2 mg, 0.003 mmol). The reaction mixture was heated at 80 °C for 36h. The reaction mixture was concentrated and purified by column chromatography (SiO₂, ethyl acetate/hexanes, 1/10) to provide 10.2 mg (84%, 0.009 mmol) of **9d** as a white waxy solid.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J_{ave} = 6.8 Hz, 3H), 1.12 (s, 9H), 1.14 (s, 9H), 1.17 (s, 9H), 1.19-1.32 (m, 26 H), 1.25 (s, 9H), 1.98-2.03 (m, 2H), 3.6 (d, J = 8.4 Hz, 1H), 3.78 (s, 3H), 3.82-3.88 (m, 2H), 3.96 (t, J = 6.8 Hz, 1H), 4.07 (dd, J = 7.3, 10.8 Hz, 1H), 4.15 (dd, J = 6.6, 10.8 Hz, 1H), 4.17-4.20 (m, 2H), 4.40 (dd, J = 6.8, 10 Hz, 1H), 4.23 (d, J = 7.2 Hz, 1H), 4.38 (ab, J = 11 Hz, 2H), 4.52 (d, J = 7.9 Hz, 1H), 4.97 (d, J = 8.5 Hz, 1H), 5.13 (dd, J = 3.2, 10.5 Hz, 1H), 5.23 (dd, J = 8.0, 10.2 Hz, 1H), 5.38 (dd, J = 7.8, 15.5 Hz, 1H), 5.42 (d, J = 3.0 Hz, 1H), 5.73 (dt, J = 6.7, 15.3 Hz, 1H), 6.86 (d, J = 8.5 Hz, 2H), 7.24 (d, J = 8.5 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.39 (t, J = 7.5 Hz, 2H), 7.55 (d, J = 7.4 Hz, 1H), 7.59 (d, J = 7.4 Hz, 1H), 7.76 (d, J = 7.6 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 14.1, 22.6, 27.0, 27.1, 29.2, 29.3, 29.4, 29.6, 31.9, 32.2, 38.6, 38.68, 38.7, 39.0, 47.1, 53.7, 55.1, 61.0, 66.6, 66.7, 67.9, 69.0, 70.4, 70.8, 70.9, 79.3, 101.1, 113.7, 119.9, 125.0, 126.9, 127.3, 127.6, 127.3, 129.3, 130.3, 137.0, 141.2, 143.8, 143.9, 155.8, 159.1, 176.7, 176.8, 177.2, 177.7.

HRMS (FAB) Calcd. for C₆₉H₁₀₁NaNO₁₄ 1190.7120, found 1190.7143.

A solution of **8** (11 mg, 0.011 mmol) and 20% piperidine in DMF (0.5 ml) was stirred for 5 minute. The excess of pyridine and DMF was removed by flowing N₂ through the reaction mixture for 1h to provide crude amine. The crude amine was taken up in dichloromethane (1 ml) and triethylamine (0.01 ml, 0.07 mmol), DMAP (1 mg, 0.008 mmol) and palmitoyl chloride (0.01 ml, 0.033 mmol) were added. The reaction mixture was stirred at room temperature for 1h.

The reaction mixture concentrated to give crude which was purified by column chromatography (SiO₂, ethyl acetate/hexanes, 1/10) to provide 7.1 mg (66 %, 0.007 mmol) of **11** as a waxy solid.

¹H NMR (400 MHz, CDCl₃): δ 0.88 (t, J_{ave} = 6.83 Hz, 3H), 1.12 (s, 9H), 1.16 (s, 9H), 1.17 (s, 9H), 1.22-1.32 (m, 26 H), 1.25 (s, 9H), 1.55 (m, 2H), 2.00-2.14 (m, 2H), 3.57-3.61 (m, 1H), 3.80 (s, 3H), 3.89 (t, J = 7.4 Hz, 1H), 3.94 (t, J = 7.2 Hz, 1H), 4.04 (dd, J = 7.4, 10.9 Hz, 1H), 4.13 (dd, J = 6.5, 11 Hz, 1H), 4.17-4.23 (m, 2H), 4.39 (ab, J = 11Hz, 2H), 4.505 (d, J = 7.5 Hz, 1H), 5.11 (dd, J = 3.2, 11.5 Hz, 1H), 5.19 (dd, J = 7.6, 11.5 Hz, 1H), 5.28 (d, J = 17.1 Hz, 1H), 5.29 (d, J = 10.5 Hz, 1H), 5.405 (d, J = 2.6 Hz, 1H), 5.62 (d, J = 8.5 Hz, 1H), 5.78 (ddd, J = 7.8, 11, 16.4 Hz, 1H), 6.87 (d, J = 8.6 Hz, 2H), 7.24 (d, J = 8.6 Hz, 2H).

¹³C NMR (100 MHz, CDCl₃): δ 14.1, 22.7, 25.6, 27.07, 27.1, 27.2, 29.4, 29.5, 29.66, 29.7, 31.9, 36.9, 38.7, 38.8, 39.1, 51.4, 55.3, 61.0, 66.6, 67.7, 69.2, 70.77, 70.8, 71.0, 79.7, 101.1, 113.8, 119.2, 129.3, 130.3, 135.9, 159.2, 172.5, 176.8, 176.9, 177.2, 177.8.

HRMS (FAB) Calcd. for C₅₅H₉₁NaNO₁₃ 996.6388, found 996.6370.

The mixture of **11** (6.1 mg, 0.006 mmol), pentadecene-1 (0.008 ml, 0.04 mmol) and Grubbs generation II catalyst (1.6 mg, 0.002 mmol) in dichloromethane (1 ml) were refluxed for 24h. The reaction mixture was concentrated and directly purified by column chromatography (SiO₂, hexanes/ethyl acetate, 12/1) to generate 5.1 mg (72%, 0.004 mmol) of **12** as a waxy solid.

To a cold solution (0 °C) of monoallyl diethylene glycol⁵ (484 mg, 3.3 mmol), triethylamine (1.4 ml, 9.9 mmol) and DMAP (40 mg, 0.33 mmol) in dichloromethane (10 ml) was added TBDPSCl (0.9 ml, 3.46 mmol). The reaction was stirred for 1h. The reaction mixture was diluted with dichloromethane (20 ml) and washed with water (20 ml) and brine (20 ml). The aqueous layers

were washed with dichloromethane (3x20 ml). The combined dichloromethane layer were dried (Na₂SO₄) and concentrated to give crude product. The crude reaction mixture was purified by column chromatography (SiO₂, hexanes/ethyl acetate, 5/1) to generate 1.27 g (88 %, 2.9 mmol) of **9e** as an oil.

¹H NMR (300 MHz, CDCl₃): δ 1.05 (s, 9H), 3.56-3.68 (m, 6H), 3.82 (t, J = 5.4 Hz, 2H), 4.01 (d, J = 5.7 Hz, 2H), 5.18 (dd, J = 1.1, 10.3 Hz, 1H), 5.27 (dd, J = 1.4 Hz, 17.2 Hz, 1H), 5.92 (ddd, J = 5.7, 10.9, 17.2 Hz, 1H), 7.35-7.45 (m, 6H), 7.68-7.74 (m, 4H).

¹³C NMR (75.5 MHz, CDCl₃): δ 19.1, 26.8, 63.4, 69.4, 70.7, 72.2, 72.4, 116.9, 127.5, 129.5, 133.6, 134.7, 135.5.

HRMS (FAB) Calcd. for C₂₃H₃₂O₃SiNa 407.2018, found 407.2030.

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