Supporting Information for:

Revealing the Pharmacophore of Ipomoeassin F through Molecular Editing

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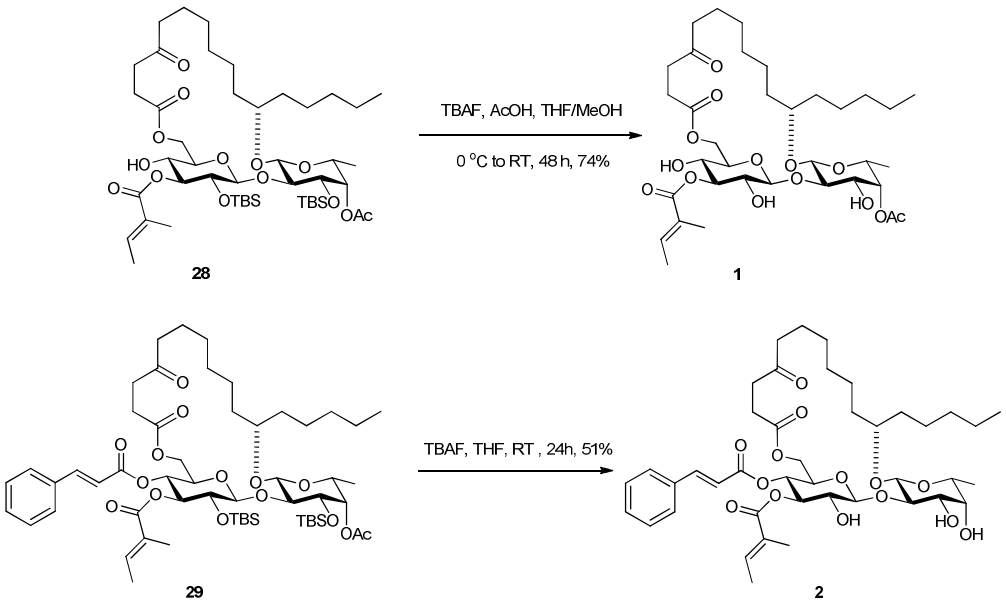
General Methods

Reactions were carried out in oven-dried glassware. All reagents were purchased from commercial sources and were used without further purification unless noted. Unless stated otherwise, all reactions were carried out under a nitrogen atmosphere and monitored by thin layer chromatography (TLC) using Silica Gel GF_{254} plates (Agela) with detection by charring with 5% (v/v) H_2SO_4 in EtOH or by visualizing in UV light (254 nm). Column chromatography was performed on silica gel (230–450 mesh, Sorbent). The ratio between silica gel and crude product ranged from 100 to 50:1 (w/w). NMR data were collected on a Bruker 400 MHz NMR spectrometer and a Bruker 400 MHz system. ^{1}H NMR spectra were obtained in deuteriochloroform ($CDCl_3$) with chloroform ($CHCl_3$, δ = 7.27 for ^{1}H) as an internal reference. ^{13}C NMR spectra were proton decoupled and were in $CDCl_3$ with $CHCl_3$ (δ = 77.0 for ^{13}C) as an internal reference. Chemical shifts are reported in ppm (δ). Data are presented in the form: chemical shift (multiplicity, coupling constants, and integration). ^{1}H data are reported as though they were first order. The errors between the coupling constants for two coupled protons were less than 0.5 Hz, and the average number was reported. Proton assignments, when made, were done so with the aid of COSY NMR spectra. For some compounds, HSQC and HMBC NMR were also applied to assign the proton signals. Optical rotations were measured on a Autopol III Automatic Polarimeter at 25 ± 1 ^{o}C for solutions in a 1.0 dm cell. High resolution mass spectrum (HRMS) and were acquired in the ESI mode.

Chemistry: Synthetic Procedures and Analytical Data



Scheme 1. Syntheses of analogues **1** and **2** of ipomoeassin F

During the synthesis of ipomoeassin F, TBS-cleavage of the intermediate **28**[1] with TBAF smoothly afforded the analogue **1** (Scheme 1). In addition, the acetyl group in **29**[1] was simultaneously removed together with the two TBS groups to deliver another analogue **2** when exposed to an excess of TBAF at elevated temperature for extended reaction time (Scheme 1).

Analogue 1

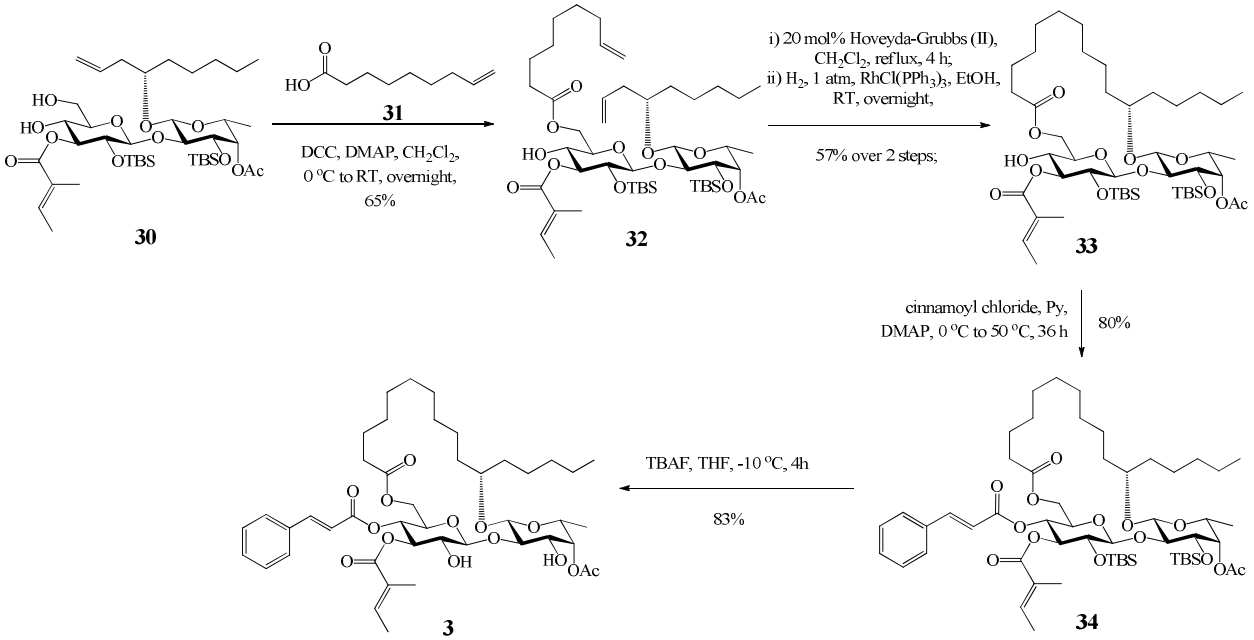
To a solution of **28**[1] (43.0 mg, 0.0463 mmol) in THF (3 mL) and MeOH (1 mL) was added AcOH (529 μL, 9.25 mmol) and TBAF (1M solution in THF, 4.63 mL, 4.63 mmol) at 0 °C. The reaction was allowed to warm to ambient temperature and stirred for 48 h. At this point, TLC (silica, 2:1 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with Et_2O (30 mL), washed with 1M HCl (15 mL), saturated aqueous $NaHCO_3$ (15 mL), brine (15 mL). The aqueous layer was extracted with Et_2O (30 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 2:1) gave compound **1** (24.0 mg, 74%) as a colorless syrup. $[\alpha]_D^{25}$ –34.6° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.10 – 6.92 (m, 1H, Me-C*H*-C(Me)-C=O), 5.15 – 5.10 (m, 1H, H-4-Fuc*p*), 4.90 (t, *J* = 9.2 Hz, 1H, H-3-Glu*p*), 4.76 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6-Glu*p*), 4.53 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 4.38 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.15 (dd, *J* = 12.4, 2.0 Hz, 1H, H-6-Glu*p*), 3.89 (dd, *J* = 9.6, 3.6 Hz, 1H, H-3-Fuc*p*), 3.71 – 3.59 (m, 3H, H-2-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.57 – 3.47 (m, 2H, H-2-Glu*p*, H-4-Glu*p*), 3.47 – 3.40 (m, 1H, H-5-Glu*p*), 3.00 – 2.57 (m, 7H), 2.50 – 2.36 (m, 2H), 2.17 (s, 3H, CH_3-C=O), 1.90 – 1.79 (m, 6H, C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.65 – 1.61 (m, 2H), 1.59 – 1.45 (m, 4H), 1.43 – 1.21 (m, 12H), 1.17 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.88 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.06, 173.66, 171.72, 169.72, 139.47, 127.87, 105.90, 100.28, 82.92, 79.48, 75.16, 74.03, 72.65, 72.39, 68.71, 67.69, 62.89, 42.05, 37.23, 34.30, 33.15, 31.85, 29.65, 29.50, 29.32, 28.77, 28.35, 24.79, 24.44, 22.62, 20.88, 16.30, 14.52, 14.06, 12.05. HRMS for $C_{35}H_{56}NaO_{14}$ $(M+Na)^+$ 723.3568. Found: 723.3561.

Analogue 2

To a solution of **29**[1] (20 mg, 0.019 mmol) in THF (2 mL) was added TBAF (1M solution in THF, 0.38 mL, 0.38 mmol, 20 equiv) at rt. The reaction mixture was stirred at the same temperature for 24 hours at which point TLC (silica, 1:1 EtOAc–hexanes) showed it was complete. The reaction mixture was diluted with Et_2O (40 mL), washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL). The aqueous layer was extracted with Et_2O (40 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:1) gave compound **2** (8.0 mg, 51%) as a white solid. $[\alpha]_D^{25}$ –[2]59.6° (*c* 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.54 – 7.48

(m, 2H, 2 × Ar*H*), 7.43 – 7.35 (m, 3H, 2 × Ar*H*), 6.94 – 6.86 (m, 1H, Me-C*H*-C(Me)-C=O), 6.35 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.33 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 5.14 (t, *J* = 9.6 Hz, 1H, H-3-Glu*p*), 4.60 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 4.56 (br, 1H, O*H*), 4.46 (dd, *J* = 12.4, 3.6 Hz, 1H, H-6-Glu*p*), 4.38 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.26 – 4.24 (m, 1H, O*H*), 4.18 (dd, *J* = 12.4, 2.0 Hz, 1H, H-6-Glu*p*), 3.81 – 3.69 (m, 4H, H-2-Glu*p*, H-5-Glu*p*, H-3-Fuc*p*, H-4-Fuc*p*), 3.68 – 3.55 (m, 3H, H-2-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.86 – 2.70 (m, 2H), 2.69 – 2.53 (m, 2H), 2.53 – 2.37 (m, 3H), 1.81 – 1.71 (m, 6H), 1.71 – 1.64 (m, 2H), 1.57 – 1.42 (m, 4H), 1.39 – 1.19 (m, 15H, H-6-Fuc*p*), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.96, 171.91, 168.94, 165.41, 146.18, 139.90, 133.98, 130.65, 128.90(2), 128.26(2), 127.54, 116.67, 105.47, 99.82, 82.66, 79.24, 75.98, 73.64, 73.49, 72.82, 71.47, 69.96, 67.33, 61.58, 41.90, 37.63, 34.26, 33.18, 31.89, 29.04, 29.01, 28.17, 24.66, 24.48, 23.33, 22.63, 16.29, 14.60, 14.11, 11.95.

Analogue **3** was obtained from **30**[1] in analogy to the synthesis of ipomoeassin F, using 8-nonenoic acid **31** instead of 4-oxo-8-nonenoic acid to form the diene precursor **32** (Scheme 2), which was then subjected to the RCM conditions followed by hydrogenation to give **33**. The transformation of **33** to the desired analogue **3** did not run into any problems.



Scheme 2. Synthesis of analogue **3** of ipomoeassin F

Compound 32

DCC (49 mg, 0.24 mmol) was added in one portion to a 0ºC CH_2Cl_2 (10 mL) solution of **30** (172 mg, 0.21 mmol), 8-nonenoic acid **31** (37 mg, 0.24 mmol) and 4-dimethylaminopyridine (2.6 mg, 0.021 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point,

TLC (silica, 1:4 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (10 mL) and hexanes (5 mL), irred for 20 minutes then filtered thru a pad of celite using ether (10 mL) as the eluent and the filtrate concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:9 → 1:8) gave diene **32** (130 mg, 65%) as a colorless syrup. $[\alpha]_D^{25}$ +17.3° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 – 6.88 (m, 1H, Me-C*H*-C(Me)-C=O), 6.20 – 6.06 (m, 1H, CH_2=C*H*-CH_2-), 5.86 – 5.74 (m, 1H, CH_2=C*H*-CH_2-), 5.14 – 4.88 (m, 7H, 2 × CH_2=CH-CH_2-, H-1-Glu*p*, H-3-Glu*p*, H-4-Fuc*p*), 4.41 – 4.29 (m, 3H, 2 × H-6-Glu*p*, H-1-Fuc*p*), 4.08 (dd, *J* = 9.2, 8.0 Hz, 1H, H-2-Fuc*p*), 3.89 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3-Fuc*p*), 3.68 – 3.60 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.56 (dd, *J* = 8.8, 7.6 Hz, 1H, H-2-Glu*p*), 3.52 – 3.39 (m, 2H, H-4-Glu*p*, H-5-Glu*p*), 2.92 (d, *J* = 4.8 Hz, 1H, O*H*), 2.35 – 2.30 (m, 4H), 2.13 (s, 3H, CH_3-C=O), 2.09 – 2.00 (m, 2H), 1.90 – 1.79 (m, 6H, CH_3-CH-C(CH_3)-C=O), 1.70 – 1.60 (m, 3H), 1.58 – 1.45 (m, 1H), 1.43 – 1.22 (m, 12H), 1.15 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.93 – 0.84 (m, 12H), 0.80 (s, 9H), 0.15 (s, 3H, CH_3-Si), 0.11 (s, 6H, CH_3-Si), 0.02 (s, 3H, CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.01, 170.83, 168.97, 138.87, 138.55, 136.08, 128.16, 116.13, 114.25, 100.83, 99.87, 80.72, 78.70, 74.13, 73.87(2), 73.71, 73.36, 70.12, 68.86, 62.99, 38.53, 34.39, 34.02, 33.64, 31.86, 28.97, 28.66(2), 25.78(6), 24.69, 24.52, 22.57, 20.98, 18.03, 17.58, 16.63, 14.41, 14.02, 12.01, –3.15, –4.00, –4.32, –5.35.

Compound 33

To a solution of diene **32** (88.0 mg, 0.0935 mmol) in CH_2Cl_2 (40 mL) was added Hoveyda-Grubbs catalyst 2nd generation (5.9 mg, 9.3 μmol) in one portion at room temperature. The reaction mixture was refluxed for 4 h. At this point, TLC (silica, 1:6 EtOAc–hexanes) showed the reaction was complete. The reaction was cooled to ambient temperature and then concentrated. Flash chromatography (silica, EtOAc–hexanes, 1:4 → 1:2) gave recovered starting material **32** (8.0 mg) along with desired cycloalkene isomer (55.3 mg, 65 %, 71% BORSM) as a colorless syrup which was not fully characterized. The obtained isomer was subjected to hydrogenation in next step and the product was fully characterized. To a solution of the cycloalkene isomer (49 mg, 0.054 mmol) in EtOH (1 mL) was added Wilkinson's catalyst (10 mg, 0.011 mmol) in one portion at room temperature. The reaction was then stirred under an atmosphere of hydrogen (1 atm) overnight. At this point, TLC (silica, 1:4 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was filtered through a pad of Celite using EtOAc (2 mL) as the eluent and the resulting filtrate concentrated. Flash chromatography (silica, EtOAc–hexanes, 1:10 → 1:8) gave **33** (39 mg, 80%, 57% over two steps) as a colorless syrup. $[\alpha]_D^{25}$ +0.87° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.95 – 6.84 (m, 1H, Me-C*H*-C(Me)-C=O), 5.05 – 4.97 (m, 3H, H-1-Glu*p*, H-3-Glu*p*, H-4-Fuc*p*), 4.80 – 4.68 (m, 1H, H-6-Glu*p*), 4.33 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.20 – 4.10 (m, 2H, H-6-Glu*p*, H-2-Fuc*p*), 3.90 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3-Fuc*p*), 3.68 –

3.61 (m, 1H, H-5-Fuc*p*), 3.58 – 3.49 (m, 2H, H-2-Glu*p*, -CH_2-C*H*-CH_2-), 3.48 – 3.35 (m, 2H, H-4-Glu*p*, H-5-Glu*p*), 3.32 (d, *J* = 3.6 Hz, 1H, O*H*), 2.51 – 2.31 (m, 2H), 2.12 (s, 3H, CH_3-C=O), 1.84 – 1.79 (m, 6H, C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.79 – 1.60 (m, 3H), 1.58 – 1.23 (m, 21H), 1.14 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.94 – 0.84 (m, 12H), 0.82 (s, 9H), 0.16 (s, 3H, C*H*$_3$-Si), 0.12 (s, 3H, C*H*$_3$-Si), 0.11 (s, 3H, C*H*$_3$-Si), 0.03 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.43, 170.92, 168.19, 138.05, 128.43, 101.81, 100.34, 82.55, 78.02, 77.31, 74.79, 74.41, 73.97, 73.60, 69.41, 68.78, 62.98, 35.02, 34.16, 33.89, 32.07, 28.86, 27.55, 27.21, 26.80, 26.69, 25.82(6), 25.33, 24.64, 24.12, 22.60, 21.00, 18.07, 17.60, 16.73, 14.41, 14.06, 12.00, –3.20, –3.92, –4.18, –5.10.

Compound 34

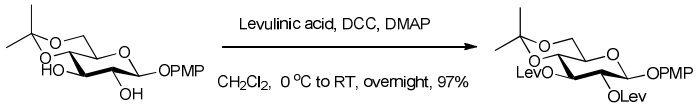
To a cold (0 ^{o}C) solution of compound **33** (35 mg, 0.038 mmol) and DMAP (9.3 mg, 0.076 mmol) in pyridine (2 mL) was added cinnamoyl chloride (25 mg, 0.15 mmol). The reaction mixture was heated to 50 ^{o}C and stirred for a further 36 h, at the end of which time TLC (silica, 1:4 EtOAc–hexanes) indicated that the reaction was complete. The reaction was quenched with MeOH (20 µL) and diluted with CH_2Cl_2 (20 mL), washed with 1 M HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and dried (Na_2SO_4). The solvent was evaporated under vacuum and the residue was purified by column chromatography (silica, EtOAc–hexanes, 1:8) to afford compound **34** (32 mg, 80%) as a colorless syrup. $[\alpha]_D^{25}$ –30.0° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.53 – 7.47 (m, 2H, 2 × Ar*H*), 7.43 – 7.35 (m, 3H, 3 × Ar*H*), 6.85 – 6.77 (m, 1H, Me-C*H*-C(Me)-C=O), 6.32 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.32 – 5.16 (m, 2H, H-3-Glu*p*, H-4-Glu*p*), 5.11 (d, *J* = 7.6 Hz, 1H, H-1-Glu*p*), 5.03 – 4.97 (m, 1H, H-4-Fuc*p*), 4.50 –4.40 (br, 1H, H-1-Fuc*p*), 4.35 (dd, *J* = 12.4, 3.6 Hz, 1H, H-6-Glu*p*), 4.19 – 4.05 (m, 2H, H-6-Glu*p*, H-2-Fuc*p*), 3.95 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3-Fuc*p*), 3.72 – 3.58 (m, 4H, H-2-Glu*p*, H-5-Glu*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.39 – 2.30 (m, 2H), 2.13 (s, 3H, CH_3-C=O), 1.79 – 1.72 (m, 6H, C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.71 – 1.62 (m, 4H), 1.50 – 1.22 (m, 18H), 1.15 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.97 – 0.85 (m, 12H), 0.81 (s, 9H), 0.20 (s, 3H, C*H*$_3$-Si), 0.13 (s, 3H, C*H*$_3$-Si), 0.12 (s, 3H, C*H*$_3$-Si), 0.01 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.59, 170.94, 167.00, 165.31, 145.72, 138.00, 134.16, 130.43, 128.82(2), 128.20(2), 128.17, 116.95, 100.27(2), 75.55, 74.51, 74.03, 73.59(2), 71.69, 69.20, 68.87, 62.28, 34.73, 34.11, 32.06, 29.69, 28.50, 27.28, 27.21, 27.02, 26.60, 25.85(3), 25.75(3), 25.26, 24.78, 24.63, 23.95, 22.63, 21.03, 18.06, 17.69, 16.68, 14.42, 14.10, 11.97, –3.44, –3.89, –4.26, –5.17.

Analogue 3

To a solution of **34** (31 mg, 0.030 mmol) in THF (2 mL) was added TBAF (1M solution in THF, 0.15 mL, 0.15 mmol, 5 equiv) at –10 ^{o}C. The reaction mixture was stirred at the same temperature for 4 hours at which point TLC (silica, 1:1 EtOAc–hexanes) showed it was complete. The reaction mixture

was diluted with Et_2O (20 mL), washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL). The aqueous layer was extracted with Et_2O (20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 2:3) gave compound **3** (20 mg, 83%) as a white foam. $[\alpha]_D^{25}$ – 49.4° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.51 – 7.49 (m, 2H, 2 × Ar*H*), 7.43 – 7.33 (m, 3H, 3 × Ar*H*), 6.94 – 6.84 (m, 1H, Me-C*H*-C(Me)-C=O), 6.34 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.38 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 5.20 – 5.13 (m, 2H, H-3-Glu*p*, H-4-Fuc*p*), 4.64 (d, *J* = 7.6 Hz, 1H, H-1-Glu*p*), 4.60 (d, *J* = 1.6 Hz, 1H, O*H*), 4.47 (dd, *J* = 12.4, 3.2 Hz, 1H, H-6-Glu*p*), 4.41 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.11 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6-Glu*p*), 4.00 – 3.97 (m, 1H, O*H*), 3.93 – 3.85 (m, 1H, H-3-Fuc*p*), 3.81 –3.62 (m, 5H, H-2-Glu*p*, H-5-Glu*p*, H-2-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.51 – 2.42 (m, 1H), 2.38 – 2.28 (m, 1H), 2.19 (s, 3H, CH_3-C=O), 1.80 – 1.71 (m, 6H, C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.72 – 1.65 (m, 2H), 1.60 – 1.47 (m, 4H), 1.41 – 1.22 (m, 18H), 1.19 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.90 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.76, 171.73, 168.89, 165.29, 146.17, 139.87, 133.97, 130.64, 128.89(2), 128.25(2), 127.53, 116.62, 105.75, 100.28, 82.81, 80.07, 75.95, 73.73, 72.60, 72.56, 72.54, 68.89, 67.44, 61.63, 34.10, 33.54, 33.27, 31.92, 28.58, 27.13, 27.02, 26.55, 26.41, 24.42, 24.30, 24.19, 22.65, 20.95, 16.36, 14.59, 14.10, 11.96. HRMS for $C_{44}H_{64}NaO_{14}$ $(M+Na)^+$ 839.4194. Found: 839.4182.

***p*-Methoxyphenyl 2,3-di-*O*-levulinoyl-4,6-*O*-isopropylidene-β-D-glucopyranoside (6)**

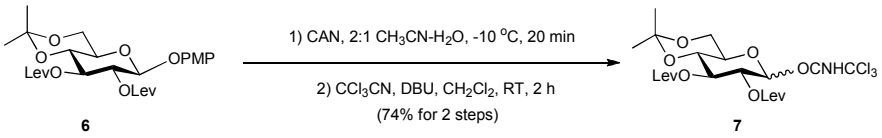


5 **6**

DCC (4.74 g, 23.0 mmol) was added in one portion to a 0ºC CH_2Cl_2 (1 mL) solution of **5**[2] (2.50 g, 7.66 mmol), levulinic acid (2.67 g, 23.0 mmol) and 4-dimethylaminopyridine (0.19 g, 1.53 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 2:1 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (30 mL) and hexanes (15 mL), stirred for 20 minutes then filtered thru a pad of Celite using ether (20 mL) as the eluent and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:4) gave **6** (3.90 g, 97%) as a colorless syrup. $[\alpha]_D^{25}$ –21.1° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.01 – 6.90 (m, 2H, 2 × Ar*H*), 6.86 – 6.76 (m, 2H, 2 × Ar*H*), 5.27 – 5.13 (m, 2H, H-2, H-3), 5.00 – 4.90 (m, 1H, H-1), 3.98 (dd, *J* = 10.8, 5.2 Hz, 1H, H-6), 3.88 – 3.70 (m, 5H, H-4, H-6, -OC*H*$_3$), 3.50 – 3.35 (m, 1H, H-5), 2.89 – 2.69 (m, 4H, CH_3-CO(C*H*$_2$)$_2$CO), 2.69 – 2.52 (m, 4H, CH_3-CO(C*H*$_2$)$_2$CO), 2.18 (s, 3H, C*H*$_3$-CO(CH_2)$_2$CO), 2.16 (s, 3H, C*H*$_3$-CO(CH_2)$_2$CO), 1.48 (s, 3H, (C*H*$_3$)$_2$C), 1.38 (s, 3H, (C*H*$_3$)$_2$C). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.35, 206.23, 171.89,

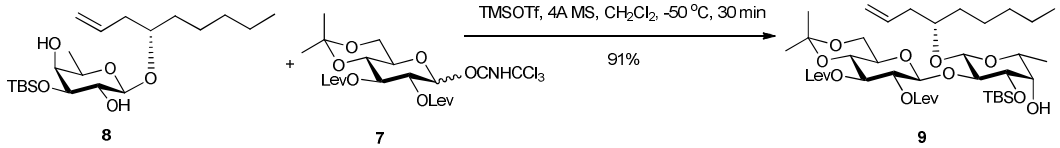
171.42, 155.69, 150.97, 118.73(2), 114.51(2), 100.98, 99.80, 71.99, 71.93, 71.08, 67.48, 61.92, 55.58, 37.75, 37.69, 29.76, 29.73, 28.85, 27.89, 27.76, 18.84.

2,3-di-*O*-Levulinoyl-4,6-*O*-isopropylidene-D-glucopyranosyl trichloroacetimidate (7)



To a solution of compound **6** (1.20 g, 2.30 mmol) in acetonitrile (20 mL) and water (5 mL) was added a solution of ceric ammonium nitrate (CAN) (2.52 g, 4.59 mmol) in water (5 mL) in 5 min at –10 ^{o}C. The mixture was stirred for 15 min at the same temperature, at the end of which time TLC (silica, 2:1 EtOAc–hexanes) indicated that the reaction was complete. The reaction was quenched with saturated aqueous $NaHCO_3$ and extracted with EtOAc (80 mL × 2). The combined organic phase was dried over Na_2SO_4 and concentrated. The obtained residue was purified by column chromatography (silica, EtOAc–hexanes, 2:1) to afford the desired hemiacetal. To a solution of the obtained hemiacetal in CH_2Cl_2 (20 mL) was added trichloroacetonitrile (0.92 mL, 9.19 mmol), and 1,8-diazabicyclo[5.4.0]undecene (DBU) (0.03 mL, 0.23 mmol). The mixture was stirred for 2 hours at room temperature and then was concentrated. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:1) to afford the glucosyl donor **7** (0.95 g, 74% over 2 steps) as a yellowish syrup. $[\alpha]_D^{25}$ +52.0° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.71, 8.64 (2s, 1H, OCN*H*CCl_3), 6.44 (d, *J* = 4.0 Hz, 1H, H-1), 5.49 (t, *J* = 9.6 Hz, 1H, H-3), 5.13 (dd, *J* = 10.0, 4.0 Hz, 1H, H-2), 3.97 – 3.88 (m, 2H, H-5, H-6), 3.85 – 3.70 (m, 2H, H-4, H-6), 2.88 – 2.46 (m, 8H, 2 × CH_3-CO(C*H*$_2$)$_2$CO), 2.18 (s, 3H, C*H*$_3$-CO(CH$_2$)$_2$CO), 2.16, 2.15 (2s, 3H, C*H*$_3$-CO(CH$_2$)$_2$CO), 1.49, 1.48 (2s, 3H, (C*H*$_3$)$_2$C), 1.40, 1.39 (2s, 3H, (C*H*$_3$)$_2$C). ^{13}C NMR (101 MHz, $CDCl_3$) δ 206.36, 206.21, 171.81, 171.73, 160.95, 99.98, 93.61, 90.71, 71.33, 70.31, 69.16, 66.09, 61.94, 37.78, 37.57, 29.77, 29.70, 28.79, 27.86, 27.59, 18.90.

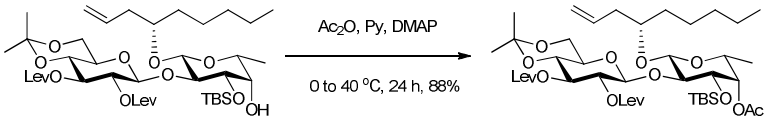
1-Nonen-4*S*-yl 2,3-di-*O*-levulinoyl-4,6-*O*-isopropylidene-β-D-glucopyranosyl-(1→2)-3-*O*-*tert*-butyldimethylsilyl-β-D-fucopyranoside (9)



A mixture of acceptor **8**[1] (0.810 g, 2.01 mmol), donor **7** (1.30 g, 2.31 mmol), and 4 Å molecular sieves (2 g) in anhydrous, redistilled CH_2Cl_2 (80 mL) was stirred under an N_2 atmosphere for 30 min and then cooled to –50 ^{o}C. TMSOTf (36 μL, 0.20 mmol) was added to the mixture. Then the reaction mixture was stirred for 30 min, at the end of which time TLC (silica, 1:2 EtOAc–hexanes) showed it was complete. Then the reaction mixture was quenched with Et_3N (30 μL) and filtrated. The filtrate was

evaporated *in vacuo* to give a residue, which was purified by silica gel column chromatography (silica, EtOAc–hexanes, 1:3 → 1:2) to give compound **9** (1.46 g, 91%) as a colorless syrup. $[\alpha]_D^{25}$ –27.3° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 – 5.87 (m, 1H, CH_2=C*H*-CH_2-), 5.13 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 5.11 – 5.01 (m, 3H, C*H*$_2$=CH-CH_2-, H-3-Glu*p*), 4.88 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2-Glu*p*), 4.29 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 3.95 (dd, *J* = 10.8, 5.2 Hz, 1H, H-6-Glu*p*), 3.84 – 3.62 (m, 5H, H-4-Glu*p*, H-6-Glu*p*, H-2-Fuc*p*, H-3-Fuc*p*, H-4-Fuc*p*), 3.55 – 3.47 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.31– 3.24 (m, 1H, H-5-Glu*p*), 2.85 – 2.50 (m, 9H, O*H*-4-Fuc*p*, 2 × $CH_3C(O)CH_2CH_2C$=O), 2.35 – 2.23 (m, 2H), 2.17 (2s, 6H, 2 × C*H*$_3$C(O)CH_2CH_2C=O), 1.57 – 1.48 (m, 2H), 1.46 (s, 3H, (C*H*$_3$)$_2$C), 1.41 – 1.21 (m, 12H, (C*H*$_3$)$_2$C, H-6-Fuc*p*), 0.92 (s, 9H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.17 (s, 3H, C*H*$_3$-Si), 0.12 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.37, 206.26, 171.96, 171.23, 135.24, 116.47, 101.05, 99.65, 99.49, 79.07, 75.86, 75.45, 73.78, 72.63, 72.52, 71.32, 69.59, 67.35, 62.10, 38.27, 37.72, 37.63, 34.28, 31.82, 29.79, 29.77, 28.87, 27.88, 27.80, 25.93(3), 24.54, 22.58, 18.84, 18.03, 16.34, 14.07, –4.25, –4.62.

1-Nonen-4*S*-yl 2,3-di-*O*-levulinoyl-4,6-*O*-isopropylidene-β-D-glucopyranosyl-(1→2)-4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-β-D-fucopyranoside (10)

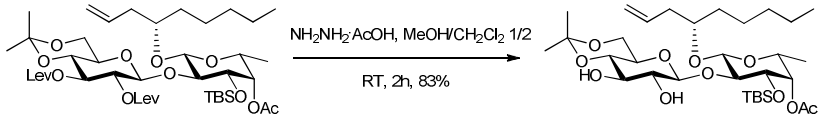


9 **10**

To a cold (0 °C) solution of compound **9** (1.46 g, 1.82 mmol) and DMAP (111 mg, 0.911 mmol) in pyridine (10 mL) was added acetic anhydride (3 mL). The reaction mixture was heated to 40 °C and stirred for a further 24 h, at the end of which time TLC (silica, 1:2 EtOAc–hexanes) indicated that the reaction was complete. The mixture was concentrated under diminished pressure and then co-evaporated with toluene (2 × 20 mL) gave the crude product. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:3 → 1:2) to afford compound **10** (1.36 g, 88%) as a colorless syrup. $[\alpha]_D^{25}$ –19.1° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.05 – 5.94 (m, 1H, CH_2=C*H*-CH_2-), 5.13 – 5.04 (m, 4H, C*H*$_2$=CH-CH_2-, H-1-Glu*p*, H-3-Glu*p*), 5.00 (m, 1H, H-4-Fuc*p*), 4.90 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2-Glu*p*), 4.29 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 3.98 (dd, *J* = 10.8, 5.2 Hz, 1H, H-6-Glu*p*), 3.88 (dd, *J* = 9.6, 8.0 Hz, 1H, H-2-Fuc*p*), 3.83 – 3.74 (m, 2H, H-6-Glu*p*, H-3-Fuc*p*), 3.68 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 3.65 – 3.57 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.32 – 3.25 (m, 1H, H-5-Glu*p*), 2.86 – 2.53 (m, 8H, 2 × $CH_3C(O)CH_2CH_2C$=O), 2.35 – 2.28 (m, 2H), 2.17 (2s, 6H, 2 × C*H*$_3$C(O)CH_2CH_2C=O), 2.13 (s, 3H, C*H*$_3$-C=O), 1.60 – 1.48 (m, 2H), 1.47 (s, 3H, (C*H*$_3$)$_2$C), 1.41 – 1.21 (m, 9H, (C*H*$_3$)$_2$C), 1.12 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.95 – 0.84 (m, 12H), 0.14 (s, 3H, C*H*$_3$-Si), 0.10 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.39, 206.18, 171.92, 171.35, 170.75, 135.37,

116.35, 101.44, 99.67, 99.38, 80.35, 75.22, 73.42(3), 72.39, 71.51, 68.81, 67.36, 62.16, 38.33, 37.71(2), 34.19, 31.79, 29.77, 29.76, 28.86, 27.85(2), 25.81(3), 24.54, 22.58, 20.88, 18.82, 17.74, 16.46, 14.02, –4.47(2).

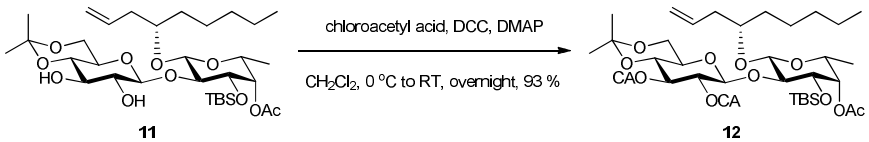
1-Nonen-4*S*-yl 4,6-*O*-isopropylidene-β-D-glucopyranosyl-(1→2)-4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-β-D-fucopyranoside (11)



10 **11**

Hydrazine acetate (1.19 g, 12.9 mmol) was added to a solution of compound **10** (1.36 g, 1.61 mmol) in 2:1 CH_2Cl_2/MeOH (18 mL) at room temperature. The reaction mixture was stirred for 2h, at which point TLC (silica, 1:2 EtOAc–hexanes) showed the reaction was complete. Then it was quenched with saturated aqueous $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (60 mL × 2). The combined organic extracts were dried over Na_2SO_4. Evaporation and purification by column chromatography (silica, EtOAc–hexanes, 1:4 → 1:3) to afford compound **11** (0.87 g, 83%) as a white foam. $[\alpha]_D^{25}$ –16.9° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.93 – 5.76 (m, 1H, CH_2=C*H*-CH_2-), 5.14 – 4.93 (m, 3H, CH_2=CH-CH_2-, H-4-Fuc*p*), 4.62 (d, *J* = 7.6 Hz, 1H, H-1-Glu*p*), 4.40 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 3.86 – 3.77 (m, 4H, 2 × H-6-Glu*p*, H-2-Fuc*p*, H-3-Fuc*p*), 3.73 – 3.57 (m, 5H, H-3-Glu*p*, H-4-Glu*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-, O*H*), 3.48 – 3.38 (m, 1H, H-2-Glu*p*), 3.35 – 3.28 (m, 1H, H-5-Glu*p*), 2.57 (d, *J* = 1.6 Hz, 1H, O*H*), 2.37 – 2.25 (m, 2H), 2.13 (d, *J* = 3.5 Hz, 3H), 1.57 – 1.49 (m, 5H, (CH_3)$_2$C), 1.46 (s, 3H, (CH_3)$_2$C), 1.40 – 1.20 (m, 6H), 1.15 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.93 – 0.85 (m, 12H), 0.18 (s, 3H, CH_3-Si), 0.16 (s, 3H, CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.68, 134.51, 116.94, 104.43, 101.34, 99.76, 79.27, 79.23, 76.61, 73.16, 72.90, 72.61, 72.58, 68.72, 68.20, 62.08, 38.09, 33.94, 31.75, 28.98, 25.84(3), 24.29, 22.55, 20.79, 18.98, 17.81, 16.42, 14.02, –4.41, –4.68.

1-Nonen-4*S*-yl 2,3-di-*O*-chloroacetyl-4,6-*O*-isopropylidene-β-D-glucopyranosyl-(1→2)-4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-β-D-fucopyranoside (12)

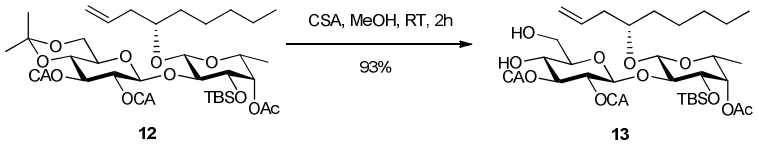


11 **12**

DCC (434 mg, 2.10 mmol) was added in one portion to a 0ºC CH_2Cl_2 (5 mL) solution of **11** (340 mg, 0.53 mmol), chloroacetyl acid (237 mg, 2.10 mmol) and 4-dimethylaminopyridine (64 mg, 0.53 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 1:6 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (10 mL) and hexanes (5 mL), stirred for 20 minutes then filtered thru a pad of celite using ether

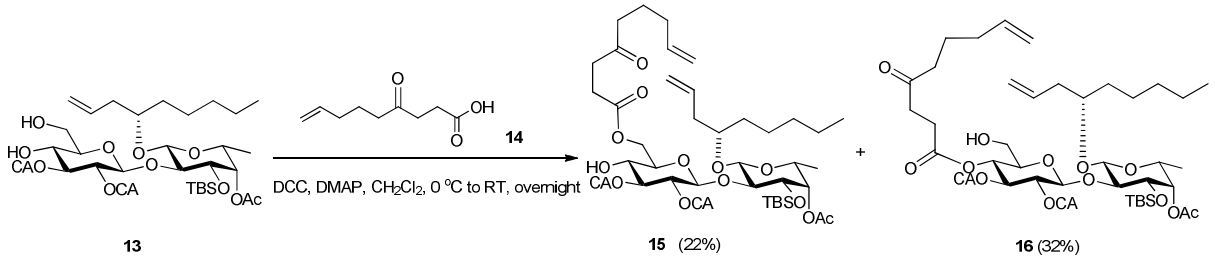
(10 mL) as the eluent and the filtrate concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:12 → 1:10) gave **12** (392 mg, 93 %) as a white foam. $[\alpha]_D^{25}$ –28.0° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.98 – 5.89 (m, 1H, CH_2=C*H*-CH_2-), 5.16 – 5.06 (m, 4H, CH_2=CH-CH_2-, H-1-Glu*p*, H-3-Glu*p*), 5.03 – 5.00 (m, 1H, H-4-Fuc*p*), 4.93 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2-Glu*p*), 4.32 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.11 – 3.97 (m, 5H, 2 × Cl-CH_2-C=O, H-6-Glu*p*), 3.90 – 3.71 (m, 4H, H-4-Glu*p*, H-6-Glu*p*, H-2-Fuc*p*, H-3-Fuc*p*), 3.68 – 3.57 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.35 – 3.28 (m, 1H, H-5-Glu*p*), 2.34 – 2.30 (m, 2H), 2.13 (s, 3H, CH_3-C=O), 1.59 – 1.50 (m, 2H), 1.48 (s, 3H, (CH_3)$_2$C), 1.39 (s, 3H, (CH_3)$_2$C), 1.36 – 1.26 (m, 6H), 1.13 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.92 – 0.83 (m, 12H), 0.11 (s, 3H, CH_3-Si), 0.10 (s, 3H, CH_3-Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.56, 166.90, 166.18, 134.8 116.69, 101.29, 99.87, 99.25, 79.92, 76.02, 75.46, 74.14, 73.40, 73.12, 71.00, 68.89, 67.45, 61.96, 40.61, 40.55, 38.26, 34.19, 31.75, 28.78, 25.84(3), 24.51, 22.56, 20.80, 18.83, 17.86, 16.36, 14.01, –4.45, –4.60.

1-Nonen-4*S*-yl 2,3-di-*O*-chloroacetyl-β-D-glucopyranosyl-(1→2)-4-*O*-acetyl-3-*O*-*tert*-butyldimethylsilyl-β-D-fucopyranoside (13)



CSA (26.1 mg, 0.113 mmol) was added in one portion to a solution of **12** (450 mg, 0.563 mmol) in MeOH (5 mL) at room temperature. The reaction mixture was stirred for 2 hours at which point TLC (silica, 1:2 EtOAc–hexanes) showed it was complete. The solvent was removed and the residue was purified by column chromatography (silica, EtOAc–hexanes, 1:2) gave compound **13** (396 mg, 93 %) as a colorless syrup. $[\alpha]_D^{25}$ –20.3° (*c* 1 $CHCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.99 – 5.88 (m, 1H, CH_2=C*H*-CH_2-), 5.13 – 4.97 (m, 5H, CH_2=CH-CH_2-, H-1-Glu*p*, H-3-Glu*p*, H-4-Fuc*p*), 4.94 – 4.89 (m, 1H, H-2-Glu*p*), 4.29 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.12 – 3.98 (m, 4H, 2 × Cl-CH_2-C=O), 3.96 – 3.90 (m, 1H, H-6-Glu*p*), 3.90 – 3.78 (m, 3H, H-4-Glu*p*, H-6-Glu*p*, H-2-Fuc*p*), 3.75 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3-Fuc*p*), 3.66 – 3.57 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.42 – 3.38 (m, 1H, H-5-Glu*p*), 3.19 – 3.08 (m, 1H, O*H*), 2.53 – 2.47 (m, 1H, O*H*), 2.30 (m, 2H), 2.14 (s, 3H, CH_3-C=O), 1.63 – 1.47 (m, 2H), 1.42 – 1.20 (m, 6H), 1.12 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.93 – 0.82 (m, 12H), 0.10 (2s, 6H, 2 × CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.73, 167.55, 166.18, 134.83, 116.97, 101.30, 98.40, 80.59, 77.20, 75.15, 75.02, 74.03, 73.40, 73.25, 68.96, 68.60, 61.47, 40.60, 40.58, 38.31, 34.30, 31.70, 25.74(3), 24.68, 22.55, 20.89, 17.73, 16.39, 14.01, –4.42, –4.62.

Diene 15



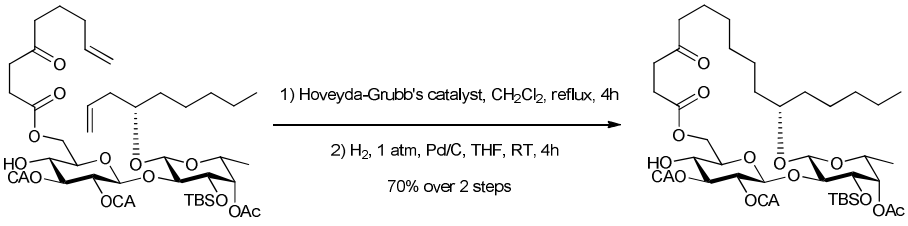
DCC (117 mg, 0.565 mmol) was added in one portion to a 0ºC CH_2Cl_2 (20 mL) solution of **13** (390 mg, 0.513 mmol), 4-oxo-8-nonenoic acid **14**[3] (96 mg, 0.565 mmol) and 4-dimethylaminopyridine (6.3 mg, 0.0513 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 1:2 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (20 mL) and hexanes (10 mL), stirred for 20 minutes then filtered thru a pad of celite using ether (10 mL) as the eluent and the filtrate concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:5 → 1:2) gave diene **15** (102 mg, 22%) as a colorless syrup and **16** (152 mg, 32%) as a white foam.

Compound **15**: $[\alpha]_D^{25}$ –32.2° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.01 – 5.95 (m, 1H, CH_2=C*H*-CH_2-), 5.82 – 5.71 (m, 1H, CH_2=C*H*-CH_2-), 5.14 – 4.96 (m, 7H, 2 × C*H*$_2$=CH-CH_2-, H-1-Glu*p*, H-3-Glu*p*, H-4-Fuc*p*), 4.93 (dd, *J* = 9.6, 8.0 Hz, 1H, H-2-Glu*p*), 4.71 (dd, *J* = 12.4, 3.2 Hz, 1H, H-6-Glu*p*), 4.32 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.22 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6-Glu*p*), 4.13 – 4.01 (m, 4H, 2 × Cl-C*H*$_2$-C=O), 3.89 (dd, *J* = 9.2, 7.6 Hz, 1H, H-2-Fuc*p*), 3.80 – 3.70 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.51 – 3.46 (m, 1H, H-5-Glu*p*), 3.31 (d, *J* = 4.8 Hz, 1H, O*H*-4-Glu*p*), 2.86 – 2.51 (m, 4H), 2.49 – 2.44 (m, 2H), 2.34 – 2.31 (m, 2H), 2.14 (s, 3H, C*H*$_3$-C=O), 2.09 – 2.03 (m, 2H), 1.74 – 1.62 (m, 2H), 1.60 – 1.47 (m, 2H), 1.40 – 1.21 (m, 6H), 1.13 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.93 – 0.83 (m, 12H), 0.11 (s, 3H, C*H*$_3$-Si), 0.10 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.32, 173.88, 170.65, 167.34, 166.16, 137.76, 135.31, 116.69, 115.39, 101.43, 98.82, 80.45, 76.46, 75.71, 74.46, 74.24, 73.45, 73.32, 68.96, 68.02, 62.59, 41.70, 40.64(2), 38.42, 37.20, 34.27, 32.95, 31.83, 27.79, 25.86(3), 24.58, 22.67, 22.59, 20.89, 17.85, 16.47, 14.05, –4.45, –4.50.

Compound **16**: $[\alpha]_D^{25}$ –4.9° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 – 5.88 (m, 1H, CH_2=C*H*-CH_2-), 5.82 – 5.69 (m, 1H, CH_2=C*H*-CH_2-), 5.26 (t, *J* = 9.6 Hz, 1H, H-3-Glu*p*), 5.17 – 5.07 (m, 4H, C*H*$_2$=CH-CH_2-, H-1-Glu*p*, H-4-Glu*p*), 5.05 – 4.94 (m, 4H, C*H*$_2$=CH-CH_2-, H-2-Glu*p*, H-4-Fuc*p*), 4.32 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.25 – 4.01 (m, 4H, 2 × Cl-C*H*$_2$-C=O), 3.85 (dd, *J* = 9.6, 7.6 Hz, 1H, H-2-Fuc*p*), 3.83 – 3.74 (m, 2H, H-6-Glu*p*, H-3-Fuc*p*), 3.67 – 3.51 (m, 4H, H-5-Glu*p*, H-6-Glu*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.83 – 2.60 (m, 2H), 2.55 – 2.39 (m, 5H), 2.34 – 2.30 (m, 2H), 2.14 (s, 3H, C*H*$_3$-C=O), 2.08 – 2.00 (m, 2H), 1.71 – 1.65 (m, 2H), 1.59 – 1.47 (m, 2H), 1.40 – 1.21 (m, 6H), 1.13 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.91 – 0.84 (m, 12H), 0.11 (s, 3H, C*H*$_3$-Si), 0.10 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.63, 171.85, 170.67, 167.29, 166.00, 137.76, 134.78, 117.10, 115.36,

101.06, 98.61, 80.17, 75.80, 74.22, 73.99, 73.85, 73.30, 73.28, 68.90, 68.44, 61.26, 41.53, 40.69, 40.58, 38.32, 36.91, 34.31, 32.96, 31.75, 27.69, 25.80(3), 24.68, 22.65, 22.58, 20.93, 17.80, 16.44, 14.04, –4.40, –4.55.

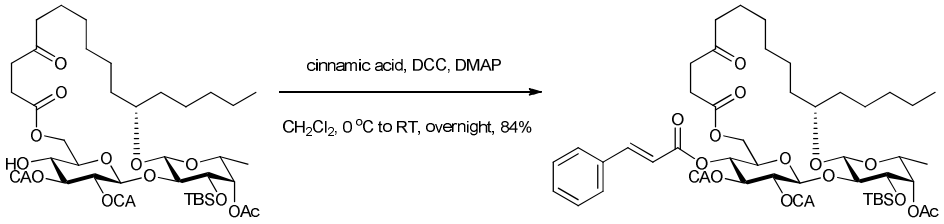
Compound 17



15 **17**

To a solution of diene **15** (95.0 mg, 0.104 mmol) in CH_2Cl_2 (50 mL) was added Hoveyda-Grubbs catalyst 2nd generation (13.0 mg, 0.0208 mmol) in one portion at room temperature. The reaction mixture was refluxed for 4 h. At this point, TLC (silica, 1:2 EtOAc–hexanes) showed the reaction was complete. The reaction was cooled to ambient temperature and then concentrated. Flash chromatography (silica, EtOAc–hexanes, 1:2 → 1:1) gave the desired cycloalkene isomer (81.0 mg, 88%) as a colorless syrup. The obtained isomer was subjected to hydrogenation in next step and the product was fully characterized. To a solution of the cycloalkene isomer (81.0 mg, 0.052 mmol) in THF (2 mL) was added 10% Pd/C (10 mg) in one portion at room temperature. The reaction was then stirred under an atmosphere of hydrogen for 4 hours at the same temperature. At this point, TLC (silica, 1:2 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was filtered thru a pad of celite using EtOAc (5 mL) as the eluent and the resulting filtrate concentrated. Flash chromatography (silica, EtOAc–hexanes, 1:2 → 1:1) gave **17** (65 mg, 70% over 2 steps) as a colorless syrup. $[\alpha]_D^{25}$ –3.1° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.12 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 5.09 (t, *J* = 9.2 Hz, 1H, H-3-Glu*p*), 5.02 – 4.95 (m, 2H, H-6-Glu*p*, H-4-Fuc*p*), 4.90 (dd, *J* = 9.6, 8.0 Hz, 1H, H-2-Glu*p*), 4.22 (d, *J* = 8.0 Hz, 1H, H-1-Fuc*p*), 4.15 – 3.95 (m, 6H, H-6-Glu*p*, H-2-Fuc*p*, 2 × Cl-C*H*$_2$-C=O), 3.80 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3-Fuc*p*), 3.66 – 3.56 (m, 2H, H-4-Glu*p*, H-5-Fuc*p*), 3.52 – 3.39 (m, 3H, H-5-Glu*p*, O*H*-4-Glu*p*, -CH_2-C*H*-CH_2-), 3.01 – 2.89 (m, 1H), 2.75 – 2.56 (m, 3H), 2.55 – 2.45 (m, 1H), 2.38 – 2.27 (m, 1H), 2.10 (s, 3H, C*H*$_3$-C=O), 1.84 – 1.57 (m, 4H), 1.55 – 1.20 (m, 14H), 1.12 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.91 – 0.84 (m, 12H), 0.13 (s, 3H, C*H*$_3$-Si), 0.12 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 211.80, 172.60, 170.67, 167.08, 166.25, 102.12, 98.76, 82.83, 76.32, 74.40, 74.25, 74.07, 74.04, 73.46, 68.89, 67.58, 62.53, 42.55, 40.72, 40.67, 37.16, 34.93, 34.07, 32.00, 29.27, 29.02, 28.97, 25.81(3), 24.88, 24.72, 24.25, 22.60, 20.87, 17.67, 16.56, 14.04, –4.19, –4.62.

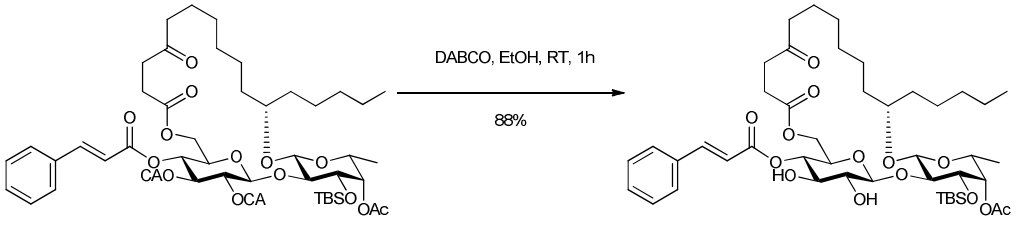
Compound 18



17 18

DCC (22.0 mg, 0.107 mmol) was added in one portion to a 0ºC CH_2Cl_2 (2 mL) solution of **17** (63.0 mg, 0.071 mmol), 8-nonenoic acid (15.8 mg, 0.107 mmol) and 4-dimethylaminopyridine (0.9 mg, 0.007 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 1:2 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (2 mL) and hexanes (1 mL), stirred for 20 minutes then filtered thru a pad of Celite using ether (5 mL) as the eluent and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:6 → 1:3) gave **18** (62.0 mg, 84%) as a colorless syrup. $[\alpha]_D^{25}$ –28.6° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.55 – 7.49 (m, 2H, 2 × Ar*H*), 7.43 – 7.35 (m, 3H, 3 × Ar*H*), 6.38 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.34 – 5.21 (m, 3H, H-1-Glu*p*, H-3-Glu*p*, H-4-Glu*p*), 5.07 – 4.96 (m, 2H, H-2-Glu*p*, H-4-Fuc*p*), 4.44 – 4.37 (m, 2H, H-6-Glu*p*, H-1-Fuc*p*), 4.16 (dd, *J* = 12.4, 4.0 Hz, 1H, H-6-Glu*p*), 4.14 – 3.96 (m, 4H, 2 × Cl-CH_2-C=O), 3.95 – 3.83 (m, 2H, H-2-Fuc*p*, H-3-Fuc*p*), 3.77 – 3.70 (m, 1H, H-5-Glu*p*), 3.68 – 3.59 (m, 2H, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.86 – 2.64 (m, 2H), 2.63 – 2.39 (m, 4H), 2.13 (s, 3H, CH_3-C=O), 1.75 – 1.22 (m, 18H), 1.13 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.94 – 0.84 (m, 12H), 0.15 (s, 3H, CH_3-Si), 0.13 (s, 3H, CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.67, 171.66, 170.63, 167.02, 165.98, 165.27, 146.91, 133.81, 130.82, 128.92(2), 128.34(2), 116.10, 100.70, 98.67, 80.60, 76.18, 74.75, 74.26, 73.62, 73.46, 71.64, 68.94, 68.56, 62.39, 41.82, 40.52, 40.40, 37.09, 34.33, 32.83, 31.95, 28.70, 28.48, 27.92, 25.92(3), 24.51, 24.39, 23.59, 22.61, 20.84, 17.99, 16.45, 14.07, –4.37, –4.51.

Compound 19

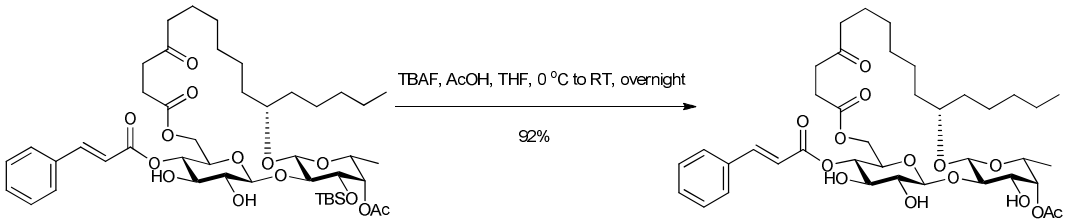


18 19

DABCO (121 mg, 1.08mmol) was added in one portion to a solution of **18** (55 mg, 0.054 mmol) in EtOH (2 mL) at room temperature. The reaction mixture was stirred for 1 hour at which point TLC (silica, 1:2 EtOAc–hexanes) showed it was complete. The reaction mixture was diluted with CH_2Cl_2 (20 mL), washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL). The aqueous layer was extracted with CH_2Cl_2 (20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated

under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:3 → 1:2) gave compound **19** (41.1 mg, 88%) as a colorless syrup. $[\alpha]_D^{25}$ –13.8° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.57 – 7.52 (m, 2H, 2 × Ar*H*), 7.43 – 7.36 (m, 3H, 3 × Ar*H*), 6.51 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.14 – 5.08 (m, 2H, H-4-Fuc*p*, H-4-Glu*p*), 4.59 (d, *J* = 7.6 Hz, 1H, H-1-Glu*p*), 4.40 (d, *J* = 7.2 Hz, 1H, H-1-Fuc*p*), 4.33 (dd, *J* = 12.0, 2.8 Hz, 1H, H-6-Glu*p*), 4.18 (dd, *J* = 12.0, 5.2 Hz, 1H, H-6-Glu*p*), 4.02 (d, *J* = 2.0 Hz, 1H, O*H*-2-Glu*p*), 3.92 (dd, *J* = 10.0, 7.6 Hz, 1H, H-2-Fuc*p*), 3.85 (dd, *J* = 9.6, 3.2 Hz, 1H, H-3-Fuc*p*), 3.78 (td, *J* = 9.6, 2.4 Hz, 1H, H-3-Glu*p*), 3.71 – 3.61 (m, 3H, H-5-Fuc*p*, H-5-Glu*p*, -CH_2-C*H*-CH_2-), 3.48 – 3.41 (m, 1H, H-2-Glu*p*), 2.71 – 2.61 (m, 2H), 2.61 – 2.53 (m, 3H, O*H*-3-Glu*p*), 2.51 – 2.40 (m, 2H), 2.14 (s, 3H, CH_3-C=O), 1.70 – 1.62 (m, 2H), 1.59 – 1.43 (m, 4H), 1.40 – 1.20 (m, 12H), 1.15 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.95 – 0.86 (m, 12H), 0.22 (s, 3H, CH_3-Si), 0.19 (s, 3H, CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.22, 171.60, 170.70, 166.20, 146.08, 134.15, 130.54, 128.92(2), 128.19(2), 117.17, 104.02, 101.24, 80.28, 78.92, 76.05, 73.48, 73.07, 72.77, 72.16, 71.54, 68.81, 63.31, 42.01, 37.31, 34.11, 33.28, 31.95, 29.46, 29.08, 28.45, 25.89(3), 25.10, 24.36, 23.61, 22.64, 20.83, 17.90, 16.49, 14.08, –4.32, –4.66.

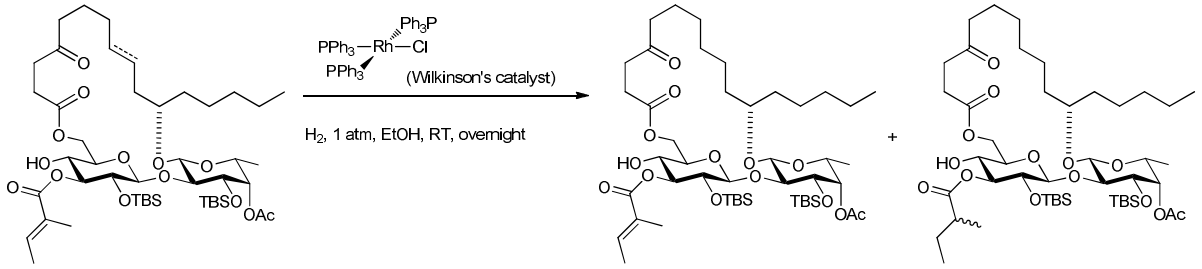
Analogue 4



To a solution of **19** (16.0 mg, 0.0185 mmol) in THF (2 mL) was added AcOH (106 μL, 1.85 mmol) and TBAF (1M solution in THF, 927 μL, 0.927 mmol) at 0 °C. The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, EtOAc) showed the reaction was complete. The reaction mixture was concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 5:1 → EtOAc) gave compound **4** (12.8 mg, 92%) as a colorless syrup. $[\alpha]_D^{25}$ –22.9° (*c* 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.55 – 7.51 (m, 2H, 2 × Ar*H*), 7.42 – 7.36 (m, 3H, 3 × Ar*H*), 6.46 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.15 (m, 1H, H-4-Fuc*p*), 5.04 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 4.53 (m, 2H, H-1-Glu*p*, O*H*), 4.48 – 4.39 (m, 2H, H-6-Glu*p*, H-1-Fuc*p*), 4.25 (br, 1H, O*H*), 4.16 (dd, *J* = 12.0, 2.0 Hz, 1H, H-6-Glu*p*), 3.92 (m, 1H, H-5-Fuc*p*), 3.76 (dd, *J* = 9.2, 3.6 Hz, 1H, H-3-Fuc*p*), 3.74 – 3.63 (m, 4H, H-2-Fuc*p*, H-3-Glu*p*, H-5-Glu*p*, -CH_2-C*H*-CH_2-), 3.58 (d, *J* = 8.4 Hz, 1H, H-2-Glu*p*), 3.27 (d, *J* = 4.0 Hz, 1H, O*H*), 2.85 – 2.67 (m, 2H), 2.66 – 2.52 (m, 2H), 2.51–2.39 (m, 2H), 2.18 (s, 3H, CH_3-C=O), 1.70 – 1.59 (m, 2H), 1.57 – 1.46 (m, 4H), 1.42 – 1.21 (m, 12H), 1.18 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.89 (t, *J* = 6.8 Hz,

3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.09, 171.82, 171.76, 166.64, 146.42, 134.07, 130.62, 128.89(2), 128.29(2), 116.91, 104.56, 100.03, 81.73, 79.70, 75.00, 74.92, 72.80, 72.64, 72.42, 70.29, 68.82, 62.10, 41.86, 37.60, 34.34, 32.91, 31.89, 29.02(2), 28.21, 24.59, 24.22, 23.44, 22.64, 20.99, 16.28, 14.09. HRMS for $C_{39}H_{56}NaO_{14}$ $(M+Na)^+$ 771.3562. Found: 771.3557.

Hydrogenation Byproduct 35



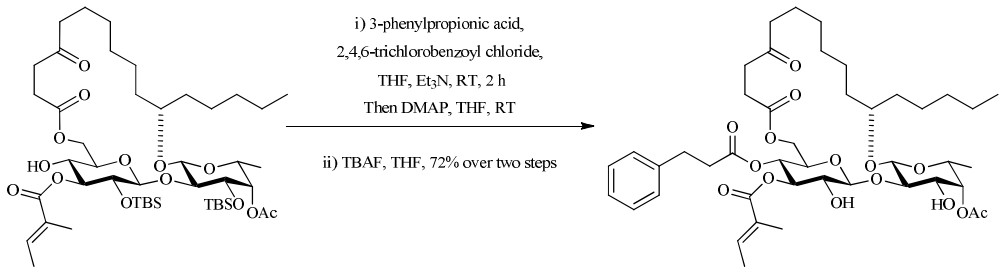
36 **28** (79%) **35** (10%)

During the total synthesis of ipomoeassin F, hydrogenation of intermediate **36**[1] over Wilkinson's catalyst gave agylcone alkene-reduced compound **28** as the major product (79%). We also isolated the tiglate alkene-reduced products **35** (10%) from the reaction mixture.

To a solution of **36** (715 mg, 0.771 mmol) in EtOH (4 mL) was added Wilkinson's catalyst (143 mg, 0.154 mmol) in one portion at room temperature. The reaction was then stirred under an atmosphere of hydrogen (1 atm) overnight. At this point, TLC (silica, 1:2 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was filtered thru a pad of celite using EtOAc (5 mL) as the eluent and the resulting filtrate concentrated. Flash chromatography (silica, EtOAc–hexanes, 1:5 → 1:3) gave **28**[1] (565 mg, 79%) as a colorless syrup and tiglate alkene-reduced product **35** (72.0 mg, 10%) as a colorless syrup.

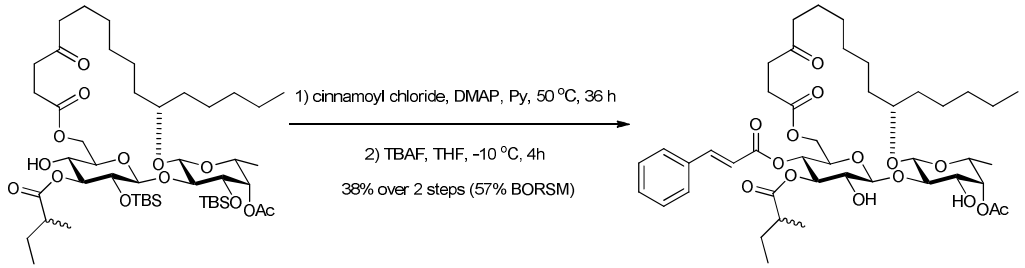
Compound **35**: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.04 – 4.86 (m, 3H, H-1-Glu*p*, H-3-Glu*p*, H-4-Fuc*p*), 4.74 (m, 1H, H-6-Glu*p*), 4.38 (br, 1H, H-1-Fuc*p*), 4.11 – 3.99 (m, 2H, H-6-Glu*p*, H-2-Fuc*p*), 3.97 – 3.89 (m, 1H, H-3-Fuc*p*), 3.72 – 3.65 (m, 1H, H-5-Fuc*p*), 3.57 (br, 1H, H-5-Glu*p*), 3.48 – 3.32 (m, 3H, H-2-Glu*p*, H-4-Glu*p*, -CH_2-C*H*-CH_2-), 3.18 (d, *J* = 4.8 Hz, 1H, O*H*), 2.99 – 2.79 (m, 1H), 2.74 – 2.54 (m, 3H), 2.52 – 2.26 (m, 3H), 2.10 (s, 3H, CH_3-C=O), 1.83 – 1.21 (m, 22H), 1.17 – 1.10 (m, 4H), 1.03 – 0.80 (m, 24H), 0.15 (s, 3H, C*H*$_3$-Si), 0.11 (s, 3H, C*H*$_3$-Si), 0.11 (s, 3H, C*H*$_3$-Si), 0.06 (s, 3H, C*H*$_3$-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.48, 210.26, 177.01, 172.38, 172.36, 170.92, 101.11, 100.25, 81.72, 78.03, 77.94, 74.48, 73.88, 73.82(2), 73.67, 69.38, 68.72, 63.41, 42.02, 41.97, 41.23, 40.71, 37.08, 34.87, 33.48, 32.03, 29.13, 29.09, 28.68, 27.28, 25.92(2), 25.88, 25.80(3), 25.32, 25.24, 24.51, 23.52, 22.61, 20.98, 18.12, 17.61, 17.11, 16.69, 15.32, 14.06, 11.69, 11.22, –3.23, –3.29, –3.96, –3.97, –4.26, –4.82, –4.88.

Compound 20



To a solution of 3-phenylpropionic acid (11.8 mg, 0.079 mmol) in THF (3 mL) was added Et_3N (27 μL, 0.197 mmol) and 2,4,6-trichlorobenzoyl chloride (25 μL, 0.157 mmol). The resulting mixture was stirred for 2 hours before a solution of compound **28** (36 mg, 0.039 mmol) and DMAP (12 mg, 0.10 mmol) in THF (3 mL) was introduced. The mixture was stirred for 12 h, at the end of which time TLC (silica, 1:3 EtOAc–hexanes) indicated that the reaction was complete. The reaction was quenched with water (1 mL) and diluted with EtOAc (30 mL), washed with brine (20 mL). The organic layer was dried over Na_2SO_4. Evaporation and purification by column chromatography (silica, EtOAc–hexanes, 1:6) to afford an ester (37.4 mg, 90%) as a colorless syrup. To a solution of the obtained ester (32 mg, 0.030 mmol) in THF (2 mL) was added TBAF (1M solution in THF, 0.18 mL, 0.18 mmol, 6 equiv) at –10 ^oC. The reaction mixture was stirred at the same temperature for 4 hours at which point TLC (silica, 1:1 EtOAc–hexanes) showed it was complete. The reaction mixture was diluted with Et_2O (20 mL), washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL). The aqueous layer was extracted with Et_2O (20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:1) gave compound **20** (20.1 mg, 80%, 72% over two steps) as a white foam. $[\alpha]_D^{25}$ –38.3° (*c* 1 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 – 7.22 (m, 2H, 2 × Ar*H*), 7.21 – 7.12 (m, 3H, 3 × Ar*H*), 6.93 – 6.85 (m, 1H, Me-C*H*-C(Me)-C=O), 5.17 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 5.14 – 5.12 (m, 1H, H-4-Fuc*p*), 5.04 (t, *J* = 9.6 Hz, 1H, H-3-Glu*p*), 4.58 – 4.47 (m, 3H, H-1-Glu*p*, O*H*, H-6-Glu*p*), 4.39 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.00 (dd, *J* = 12.4, 1.6 Hz, 1H, H-6-Glu*p*), 3.93 – 3.86 (m, 2H, O*H*, H-5-Glu*p*), 3.72 – 3.57 (m, 5H, H-2-Glu*p*, H-2-Fuc*p*, H-3-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.90 – 2.36 (m, 10H), 2.17 (s, 3H, CH_3-C=O), 1.82 – 1.73 (m, 6H, C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.73 – 1.62 (m, 2H), 1.55 – 1.44 (m, 4H), 1.41 – 1.20 (m, 12H), 1.18 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 210.00, 171.83, 171.65, 171.52, 168.64, 140.06, 139.81, 128.45(2), 128.07(2), 127.54, 126.24, 105.92, 100.14, 83.11, 79.62, 75.82, 74.01, 72.72, 72.63, 72.50, 68.76, 67.00, 61.21, 41.84, 37.60, 35.29, 34.39, 33.14, 31.88, 30.48, 29.21, 28.96, 28.34, 24.79, 24.50, 23.63, 22.64, 20.91, 16.31, 14.62, 14.09, 11.96.

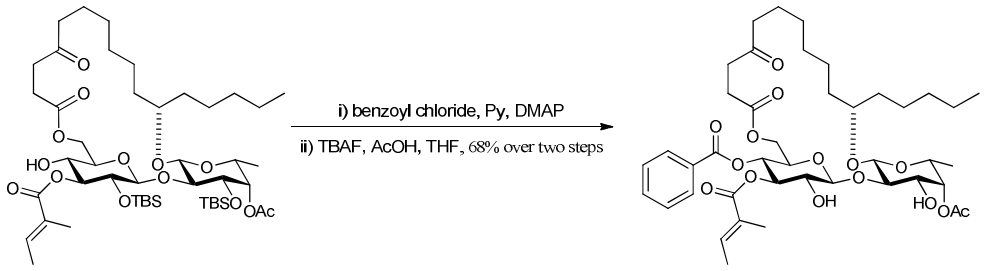
Analogue 21



To a cold (0 °C) solution of compound **35** (60 mg, 0.064 mmol) and DMAP (16 mg, 0.13 mmol) in pyridine (2 mL) was added cinnamoyl chloride (43 mg, 0.26 mmol). The reaction mixture was heated to 50 °C and stirred for a 24 h, at the end of which time TLC (silica, 1:4 EtOAc–hexanes) showed starting material remaining. More cinnamoyl chloride (22 mg, 0.13 mmol) was added. After stirring for another 24 hours at 50 °C, TLC (silica, 1:4 EtOAc–hexanes) showed there was still some starting material remaining. The reaction was quenched with MeOH (50 μL) and diluted with CH_2Cl_2 (20 mL), washed with 1 M HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and dried (Na_2SO_4). The solvent was evaporated under vacuum and the residue was purified by column chromatography (silica, EtOAc–hexanes, 1:6 → 1:3) gave recovered starting material **35** (19.7 mg) along with desired cinnamic ester (39.2 mg, 57 %, 86% BORSM) as a colorless syrup. To a solution of the obtained cinnamic ester (37 mg, 0.035 mmol) in THF (2 mL) was added TBAF (1M solution in THF, 0.21 mL, 0.21 mmol, 6 equiv) at –10 °C. The reaction mixture was stirred at the same temperature for 5 hours at which point TLC (silica, 1:1 EtOAc–hexanes) showed it was complete. The reaction mixture was diluted with Et_2O (20 mL), washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL). The aqueous layer was extracted with Et_2O (20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:1) gave compound **21** (19 mg, 66 %, 38% over two steps) as a colorless film. $[\alpha]_D^{25}$ –38.1° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.53 – 7.47 (m, 2H, 2 × Ar*H*), 7.42 – 7.30 (m, 3H, 3 × Ar*H*), 6.41 – 6.32 (m, 1H, Ph-CH=C*H*-), 5.29 – 5.15 (m, 2H, H-4-Glu*p*, H-3-Glu*p*), 5.16 – 5.11 (m, 1H, H-4-Fuc*p*), 4.59 (d, *J* = 7.6 Hz, 1H, H-1-Glu*p*), 4.47 – 4.38 (m, 2H, H-6-Glu*p*, H-1-Fuc*p*), 4.35 – 4.26 (m, 1H, O*H*), 4.15 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6-Glu*p*), 3.93 (dd, *J* = 9.6, 3.6 Hz, 1H, H-3-Fuc*p*), 3.79 – 3.60 (m, 6H, O*H*, H-2-Glu*p*, H-5-Glu*p*, H-2-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.80 – 2.33 (m, 7H), 2.19 (s, 3H, CH_3-C=O), 1.66 – 1.20 (m, 20H), 1.19 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 1.13 – 1.02 (2d, *J* = 6.8, 7.2 Hz, 3H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.87 – 0.77 (2t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.00, 177.07, 172.01, 171.75, 165.43, 165.41, 146.32, 133.98, 130.64, 128.90, 128.24, 116.68, 116.62, 105.44, 100.03, 82.17, 79.56, 74.53, 73.63, 73.48, 72.82, 72.68, 72.48, 68.79, 67.71, 67.62, 61.82, 41.86, 41.17, 37.59, 34.27, 32.93, 31.89, 29.08, 29.05,

28.27, 26.52, 24.52, 23.38, 22.64, 20.94, 16.62, 16.39, 16.32, 14.09, 11.57, 11.48. HRMS for $C_{44}H_{64}NaO_{15}$ $(M+Na)^+$ 855.4143. Found: 855.4141.

Analogue 22

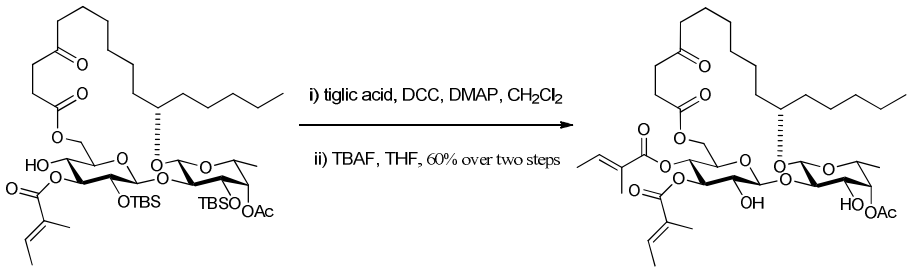


28 22

To a cold (0 °C) solution of compound **28** (35 mg, 0.038 mmol) and DMAP (9.3 mg, 0.076 mmol) in pyridine (2 mL) was added benzoyl chloride (18 μg, 0.15 mmol). The reaction mixture was heated to 40 °C and stirred for a further 72 h, at the end of which time TLC (silica, 1:3 EtOAc–hexanes) indicated that the reaction was complete. The reaction was quenched with MeOH (20 μL) and diluted with CH_2Cl_2 (20 mL), washed with 1 M HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and dried (Na_2SO_4). The solvent was evaporated under vacuum and the residue was purified by column chromatography (silica, EtOAc–hexanes, 1:6) to afford the desired ester (36 mg, 83%) as a colorless syrup. To a solution of the obtained ester (30 mg, 0.029 mmol) in THF (1.5 mL) was added AcOH (166 μL, 2.9 mmol) and TBAF (1M solution in THF, 1.45 mL, 1.45 mmol) at 0 °C. The reaction was allowed to warm to ambient temperature and stirred for 1 week. At this point, TLC (silica, 1:1 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with Et_2O (30 mL), washed with 1M HCl (15 mL), saturated aqueous $NaHCO_3$ (15 mL), brine (15 mL). The aqueous layer was extracted with Et_2O (30 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:1) gave analogue **22** (19.3 mg, 82%, 68% over two steps) as a colorless syrup. $[\alpha]_D^{25}$ –47.1° (*c* 1 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.89 (m, 2H, 2 × Ar*H*), 7.60 – 7.52 (m, 1H, Ar*H*), 7.46 – 7.38 (m, 2H, 2 × Ar*H*), 6.91 – 6.79 (m, 1H, Me-C*H*-C(Me)-C=O), 5.42 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 5.25 (t, *J* = 9.6 Hz, 1H, H-3-Glu*p*), 5.16 – 5.12 (m, 1H, H-4-Fuc*p*), 4.66 (d, *J* = 7.6 Hz, 1H, H-1-Glu*p*), 4.59 (br, 1H, O*H*), 4.47 – 4.38 (m, 2H, H-1-Fuc*p*, H-6-Glu*p*), 4.19 (dd, *J* = 12.4, 2.8 Hz, 1H, H-6-Glu*p*), 3.97 – 3.87 (m, 2H, O*H*, H-3-Fuc*p*), 3.86 – 3.80 (m, 1H, H-5-Glu*p*), 3.76 – 3.61 (m, 4H, H-2-Glu*p*, H-2-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.75 – 2.40 (m, 6H), 2.19 (s, 3H, CH_3-C=O), 1.72 – 1.67 (m, 6H, CH_3-CH-C(CH_3)-C=O), 1.67 – 1.60 (m, 2H), 1.58 – 1.45 (m, 4H), 1.40 – 1.22 (m, 12H), 1.19 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 209.99, 171.86, 171.65, 168.68, 165.27, 139.71, 133.41, 129.70(2), 129.11, 128.46(2), 127.47, 105.61, 100.23, 82.60, 79.84, 75.60,

73.93, 72.73, 72.56, 72.47, 68.80, 68.22, 61.98, 41.84, 37.52, 34.30, 33.09, 31.92, 29.12, 28.95, 28.30, 24.66, 24.50, 23.45, 22.65, 20.95, 16.35, 14.52, 14.10, 11.90.

Analogue 23

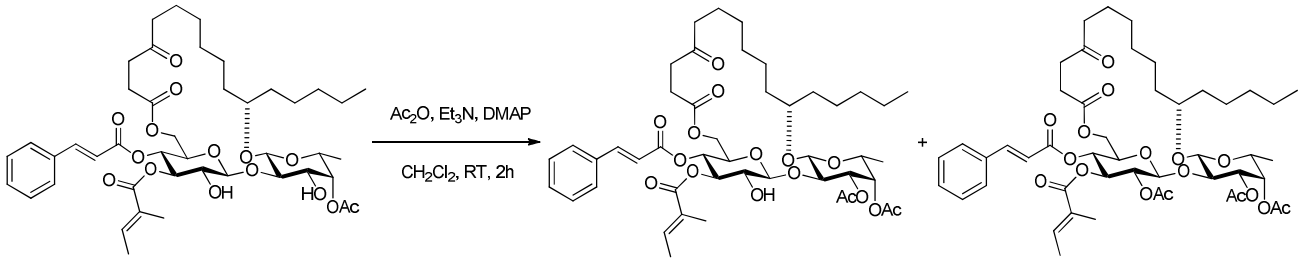


28 23

DCC (15.0 mg, 0.073 mmol) was added in one portion to a 0ºC CH_2Cl_2 (1 mL) solution of **28** (45.0 mg, 0.048 mmol), tiglic acid (7.3 mg, 0.073 mmol) and 4-dimethylaminopyridine (0.6 mg, 0.005 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 1:3 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (2 mL) and hexanes (1 mL), stirred for 20 minutes then filtered thru a pad of Celite using ether (3 mL) as the eluent and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:5 → 1:3) gave the desired ester (43.0 mg, 88%) as a colorless syrup. To a solution of the obtained ester (34 mg, 0.034 mmol) in THF (3 mL) was added TBAF (1M solution in THF, 168 μL, 0.168 mmol, 5 equiv) at –10 ^oC. The reaction mixture was stirred at the same temperature for 5 hours at which point TLC (silica, 1:1 EtOAc–hexanes) showed it was complete. The reaction mixture was diluted with Et_2O (20 mL), washed with 1M HCl (10 mL), saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL). The aqueous layer was extracted with Et_2O (20 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexane, 1:3 → 1:1) gave recovered starting material **28** (8.0 mg) along with analogue **23** (18 mg, 68 %, 60% over two steps) as a colorless syrup. $[\alpha]_D^{25}$ –43.0° (*c* 1 $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 6.95 – 6.81 (m, 1H, Me-C*H*-C(Me)-C=O), 6.81 – 6.70 (m, 1H, Me-C*H*-C(Me)-C=O), 5.24 (t, *J* = 9.6 Hz, 1H, H-4-Glu*p*), 5.16 – 5.13 (m, 1H, H-4-Fuc*p*), 5.09 (t, *J* = 9.6 Hz, 1H, H-3-Glu*p*), 4.60 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 4.54 – 4.50 (m, 1H, O*H*), 4.44 (dd, *J* = 12.4, 3.6 Hz, 1H, H-6-Glu*p*), 4.40 (d, *J* = 8.0 Hz, 1H, H-1-Fuc*p*), 4.09 (dd, *J* = 12.4, 2.0 Hz, 1H, H-6-Glu*p*), 3.96 – 3.87 (m, 2H, O*H*, H-3-Fucp), 3.76 – 3.59 (m, 5H, H-2-Glu*p*, H-5-Glu*p*, H-2-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.87 – 2.37 (m, 6H), 2.18 (s, 3H, CH_3-C=O), 1.83 – 1.72 (m, 12H, 2 × C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.72 – 1.62 (m, 2H), 1.58 – 1.44 (m, 4H), 1.41 – 1.20 (m, 12H), 1.18 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.89 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.03, 171.76, 171.69, 168.78, 166.49, 139.61, 138.62, 127.70, 127.57, 105.66, 100.15, 82.71, 79.69, 75.91, 73.85, 72.71, 72.67, 72.44, 68.81, 67.24, 61.68, 41.81, 37.62, 34.36, 33.06, 31.88, 29.08, 29.00, 28.27,

24.59, 24.51, 23.47, 22.63, 20.92, 16.31, 14.55, 14.44, 14.08, 12.02, 11.93. HRMS for $C_{40}H_{62}NaO_{15}$ $(M+Na)^+$ 805.3986. Found: 805.3969.

Analogue 24 and 25



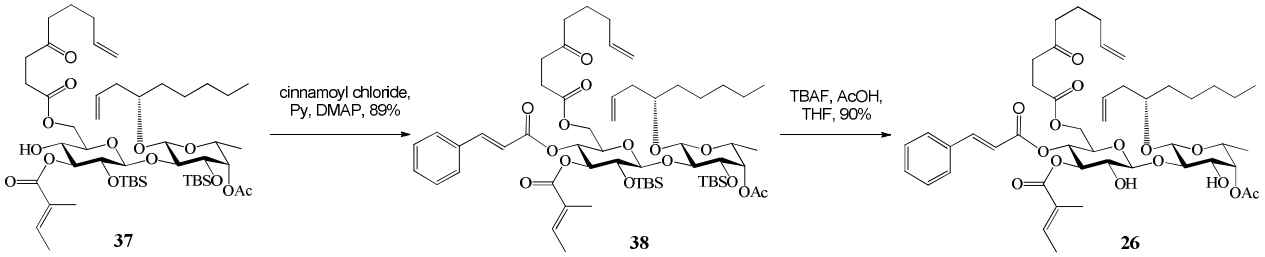
Acetic anhydride (3.4 μL, 0.097 mmol) was added in one portion to a solution of Ipomoeassin **F**[1] (20.0 mg, 0.0241 mmol) in CH_2Cl_2 (1 mL) containing trimethylamine (10 μL, 0.072 mmol) and DMAP (0.6 mg, 0.005 mmol). The reaction was stirred at room temperature for 2 h. At this point, TLC (silica, 1:1 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1: 5→1:3) gave analogue **24** (8.9 mg, colorless syrup, 42%) and analogue **25** (9.6 mg, colorless syrup, 44%).

24: $[\alpha]_D^{25}$ –63.6° (*c* 0.3 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$). δ 7.62 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.52 – 7.48 (m, 2H, 2 × Ar*H*), 7.40 – 7.35 (m, 3H, 3 × Ar*H*), 6.90 – 6.84 (m, 1H, Me-C*H*-C(Me)-C=O), 6.33 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 5.30 – 5.19 (m, 3H, H-3-Glu*p*, H-4-Glu*p*, H-4-Fuc*p*), 5.06 (dd, *J* = 10.4, 3.6 Hz, 1H, H-3-Fuc*p*), 4.60 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 4.51 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.38 (dd, *J* = 12.4, 3.6 Hz, 1H, H-6-Glu*p*), 4.19 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6-Glu*p*), 3.89 (dd, *J* = 10.4, 7.6 Hz, 1H, H-2-Fuc*p*), 3.80 – 3.73 (m, 2H, H-5-Glu*p*, H-5-Fuc*p*), 3.72 – 3.64 (m, 1H, -CH_2-C*H*-CH_2-), 3.64 – 3.54 (m, 1H, H-2-Glu*p*), 2.97 (d, *J* = 2.0 Hz, 1H, O*H*), 2.86 – 2.39 (m, 6H), 2.16 (s, 3H, CH_3-C=O), 2.06 (s, 3H, CH_3-C=O), 1.80 – 1.72 (m, 6H, CH_3-CH-C(CH_3)-C=O), 1.70 – 1.60 (m, 2H), 1.56 – 1.20 (m, 16H), 1.17 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.90 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.03, 171.72, 170.71, 169.93, 167.75, 165.44, 146.11, 138.84, 134.00, 130.60, 128.87(2), 128.25(2), 127.77, 116.67, 104.51, 100.15, 79.67, 77.62, 74.37, 73.23, 73.15, 72.45, 70.70, 68.65, 67.95, 61.93, 41.86, 37.54, 34.39, 32.83, 31.90, 28.99, 28.92, 28.09, 24.62, 24.40, 23.59, 22.65, 20.89, 20.78, 16.10, 14.51, 14.10, 12.05. HRMS (ESI) *m*/*z* calcd for $C_{46}H_{64}NaO_{16}$ $[M+Na]^+$ 895.4092, found: 895.4086.

25: $[\alpha]_D^{25}$ –80.3° (*c* 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$). δ 7.62 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.55 – 7.46 (m, 2H, 2 × Ar*H*), 7.43 – 7.33 (m, 3H, 3 × Ar*H*), 6.83 – 6.76 (m, 1H, Me-C*H*-C(Me)-C=O), 6.33 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-),5.35 – 5.24 (m, 2H, H-3-Glu*p*, H-4-Glu*p*), 5.21 – 5.18 (m, 1H, H-4-Fuc*p*), 5.07 – 4.98 (m, 1H, H-2-Glu*p*), 4.94 (dd, *J* = 10.0, 3.2 Hz, 1H, H-3-Fuc*p*), 4.89 (d, *J* = 8.0 Hz, 1H, H-1-Glu*p*), 4.48 (dd, *J* = 12.4, 3.6 Hz, 1H, H-6-Glu*p*), 4.43 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*),

4.13 (dd, *J* = 12.4, 2.4 Hz, 1H, H-6-Glu*p*), 3.86 (dd, *J* = 10.0, 7.6 Hz, 1H, H-2-Fuc*p*), 3.82 – 3.77 (m, 1H, H-5-Glu*p*), 3.77 – 3.70 (m, 1H, H-5-Fuc*p*), 3.67 – 3.55 (m, 1H, -CH_2-C*H*-CH_2-), 2.97 – 2.86 (m, 1H), 2.80 – 2.69 (m, 1H), 2.66 – 2.50 (m, 2H), 2.48 – 2.37 (m, 1H), 2.16 (s, 3H, CH_3-C=O), 2.09 (s, 3H, CH_3-C=O), 1.98 (s, 3H, CH_3-C=O), 1.76 – 1.65 (m, 8H), 1.58 – 1.23 (m, 16H), 1.17 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.91 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 210.03, 171.61, 170.60, 170.17, 169.45, 167.16, 165.20, 146.20, 139.14, 133.98, 130.63, 128.88(2), 128.25(2), 127.42, 116.53, 101.06, 100.97, 81.05, 75.97, 73.72, 72.97, 72.31, 71.99, 70.76, 68.58, 68.11, 62.10, 41.84, 37.53, 34.46, 33.25, 31.96, 28.91, 28.80, 28.06, 24.63, 24.18, 23.87, 22.65, 20.85, 20.75, 20.53, 16.13, 14.54, 14.10, 11.95. HRMS (ESI) *m*/*z* calcd for $C_{48}H_{66}NaO_{17}$ $[M+Na]^+$ 937.4198, found: 937.4196.

Analogue 26



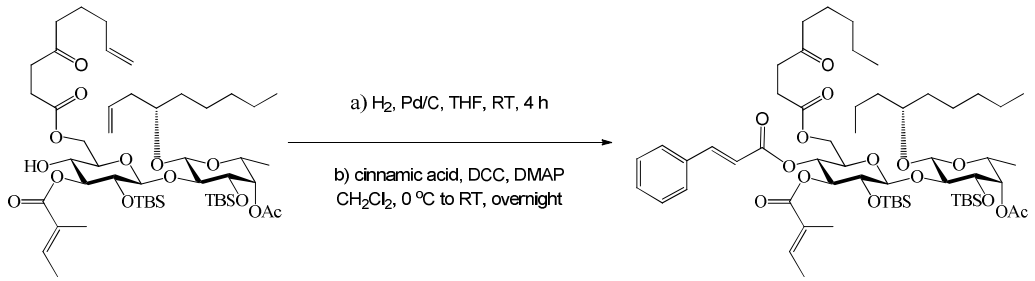
To a cold (0 °C) solution of compound **37**[1] (76 mg, 0.080 mmol) and DMAP (19 mg, 0.16 mmol) in pyridine (4 mL) was added cinnamoyl chloride (53 mg, 0.32 mmol). The reaction mixture was heated to 30 °C and stirred for a further 24 h, at the end of which time TLC (silica, 1:3 EtOAc–hexanes) indicated that the reaction was complete. The reaction was quenched with MeOH (20 μL) and diluted with CH_2Cl_2 (30 mL), washed with 1 M HCl (20 mL), sat. aq. $NaHCO_3$ (20 mL), and dried (Na_2SO_4). The solvent was evaporated under vacuum and the residue was purified by column chromatography (silica, EtOAc–hexanes, 1:6) to afford ester **38** (77 mg, 89%) as a colorless syrup. To a solution of **38** (66 mg, 0.061 mmol) in THF (5 mL) was added AcOH (348 μL, 6.08 mmol) and TBAF (1M solution in THF, 3.04 mL, 3.04 mmol) at 0 °C. The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 1:1 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with Et_2O (10 mL), washed with 1M HCl (5 mL), saturated $NaHCO_3$ (5 mL), brine (5 mL). The aqueous layer was extracted with Et_2O (10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:2 → 1:1) gave analogue **26** (47 mg, 90%) as a white foam.

38: $[\alpha]_D^{25}$ –21.2° (*c* 0.5 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.53 – 7.45 (m, 2H, 2 × Ar*H*), 7.41 – 7.33 (m, 3H, 3 × Ar*H*), 6.83 – 6.75 (m, 1H, Me-C*H*-C(Me)-C=O), 6.31 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 6.20 – 6.09 (m, 1H, CH_2=C*H*-CH_2-), 5.80 – 5.67 (m, 1H, CH_2=C*H*-CH_2-), 5.27 (dd, *J* = 9.2 Hz, 1H, H-3-Glu*p*), 5.18 – 5.05 (m, 3H, H-4-Glu*p*, CH_2=CH-CH_2-),

5.04 – 4.90 (m, 4H, H-1-Glu*p*, H-4-Fuc*p*, CH_2=CH-CH_2-), 4.39 (d, *J* = 8.0 Hz, 1H, H-1-Fuc*p*), 4.27 – 4.14 (m, 2H, 2 × H-6-Glu*p*), 4.10 – 4.03 (m, 1H, H-2-Fuc*p*), 3.91 (dd, *J* = 9.2, 4.0 Hz, 1H, H-3-Fuc*p*), 3.75 – 3.58 (m, 4H, H-2-Glu*p*, H-5-Glu*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.73 – 2.65 (m, 2H), 2.61 – 2.55 (m, 2H), 2.43 (t, *J* = 7.2 Hz, 2H), 2.37 – 2.30 (m, 2H), 2.13 (s, 3H, CH_3-C=O), 2.08 – 1.99 (m, 2H), 1.75 – 1.50 (m, 10H), 1.40 – 1.22 (m, 6H), 1.14 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.93 – 0.85 (m, 12H), 0.79 (s, 9H), 0.18 (s, 3H, CH_3-Si), 0.11 (s, 3H, CH_3-Si), 0.10 (s, 3H, CH_3-Si), -0.00 (s, 3H, CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.33, 172.40, 170.84, 166.92, 165.48, 146.00, 137.97, 137.85, 135.84, 134.08, 130.45, 128.79(2), 128.19(2), 128.10, 116.76, 116.48, 115.16, 100.68, 100.00, 80.60, 74.85, 74.24, 74.11, 74.05, 73.37, 71.49, 69.43, 68.84, 62.86, 41.72, 38.48, 37.01, 34.36, 32.97, 31.85, 27.68, 25.79(3), 25.73(3), 24.51, 22.64, 22.56, 20.97, 18.01, 17.61, 16.61, 14.33, 14.01, 11.92, -3.36, -3.98, -4.34, -5.34.

26: $[\alpha]_D^{25}$ –36.0° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.55 – 7.44 (m, 2H, 2 × Ar*H*), 7.43 – 7.36 (m, 3H, 3 × Ar*H*), 6.93 – 6.82 (m, 1H, Me-C*H*-C(Me)-C=O), 6.35 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.94 – 5.82 (m, 1H, CH_2=C*H*-CH_2-), 5.81 – 5.68 (m, 1H, CH_2=C*H*-CH_2-), 5.31 – 5.22 (m, 2H, H-3-Glu*p*, H-4-Glu*p*), 5.21 – 5.16 (m, 1H, H-4-Fuc*p*), 5.12 – 4.92 (m, 4H, 2 × CH_2=CH-CH_2-), 4.72 (d, *J* = 8.4 Hz, 1H, H-1-Glu*p*), 4.46 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.25 (dd, *J* = 12.4, 2.8 Hz, 1H, H-6-Glu*p*), 4.19 (dd, *J* = 12.4, 5.2 Hz, 1H, H-6-Glu*p*), 3.90 – 3.84 (m, 1H, H-5-Glu*p*), 3.83 – 3.67 (m, 5H, H-2-Glu*p*, H-2-Fuc*p*, H-3-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.75 – 2.66 (m, 2H), 2.64 – 2.57 (m, 2H), 2.45 (t, *J* = 7.4 Hz, 2H), 2.38 – 2.27 (m, 2H), 2.21 (s, 3H, CH_3-C=O), 2.07 – 2.02 (m, 2H), 1.79 – 1.72 (m, 6H), 1.71 – 1.64 (m, 2H), 1.58 – 1.50 (m, 2H), 1.44 – 1.22 (m, 6H), 1.19 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.52, 172.46, 171.31, 167.99, 165.43, 146.42, 139.08, 137.91, 134.29, 133.92, 130.65, 128.87(2), 128.24(2), 127.66, 117.47, 116.45, 115.16, 103.04, 99.65, 78.62, 78.41, 74.39, 72.56, 72.15, 71.79, 71.40, 69.14, 68.09, 62.38, 41.74, 37.99, 36.94, 34.17, 32.98, 31.66, 27.69, 24.61, 22.66, 22.51, 20.90, 16.22, 14.46, 14.02, 11.96. HRMS for $C_{46}H_{64}N_aO_{15}$ $(M+Na)^+$ 879.4143. Found: 879.4138.

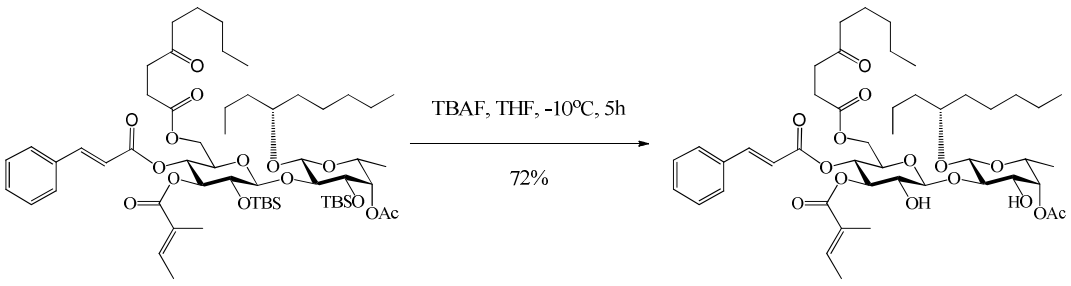
Compound 39



37 **39** (73% over two steps)

To a solution of compound **37** (40 mg, 0.042 mmol) in THF (2 mL) was added 10% Pd/C (10 mg) in one portion at room temperature. The reaction was then stirred under an atmosphere of hydrogen for 4 h at the same temperature. At this point, TLC (silica, 1:4 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was filtered through a pad of Celite using EtOAc (5 mL) as the eluent and the resulting filtrate concentrated to give a colorless syrup. Then DCC (15.1 mg, 0.073 mmol) was added in one portion to a 0ºC CH_2Cl_2 (2 mL) solution of the syrup, cinnamic acid (10.8 mg, 0.073 mmol) and 4-dimethylaminopyridine (0.5 mg, 0.003 mmol). The reaction was allowed to warm to ambient temperature and stirred overnight. At this point, TLC (silica, 1:6 EtOAc–hexanes) showed the reaction was complete. The reaction mixture was diluted with ether (2 mL) and hexanes (1 mL), stirred for 20 minutes then filtered through a pad of Celite using ether (2 mL) as the eluent and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:10 → 1:6) gave compound **39** (33.1 mg, 73% over two steps) as a colorless syrup. $[\alpha]_D^{25}$ –25.0° (*c* 1 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.53 – 7.46 (m, 2H, 2 × Ar*H*), 7.43 – 7.33 (m, 3H, 3 × Ar*H*), 6.85 – 6.75 (m, 1H, Me-C*H*-C(Me)-C=O), 6.32 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.27 (t, *J* = 9.6 Hz, 1H, H-3-Glu*p*), 5.09 – 4.97 (m, 3H, H-1-Glu*p*, H-4-Glu*p*, H-4-Fuc*p*), 4.39 (d, *J* = 7.6 Hz, 1H, H-1-Fuc*p*), 4.24 – 4.15 (m, 2H, H-6-Glu*p*), 4.09 – 4.01 (m, 1H, H-2-Fuc*p*), 3.92 (dd, *J* = 8.0, 4.0 Hz, 1H, H-3-Fuc*p*), 3.72 – 3.66 (m, 1H, H-5-Glu*p*), 3.65 – 3.53 (m, 3H, H-2-Glu*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 2.71 (t, *J* = 6.8 Hz, 2H), 2.65 – 2.51 (m, 2H), 2.42 (t, *J* = 7.2 Hz, 2H), 2.13 (s, 3H, CH_3-C=O), 1.78 – 1.69 (m, 6H, CH_3-CH-C(CH_3)-C=O), 1.68 – 1.20 (m, 18H), 1.14 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.94 – 0.83 (m, 15H), 0.81 (s, 9H), 0.19 (s, 3H, CH_3-Si), 0.12 (s, 3H, CH_3-Si), 0.11 (s, 3H, CH_3-Si), 0.02 (s, 3H, CH_3-Si). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.75, 172.48, 170.95, 166.96, 165.57, 146.05, 138.03, 134.14, 130.49, 128.84(2), 128.24(2), 128.14, 116.82, 100.88, 100.05, 80.98, 74.91, 74.44, 74.24, 74.12, 73.48, 71.56, 69.66, 68.74, 63.13, 42.70, 36.96, 36.25, 34.65, 32.03, 31.34, 27.69, 25.85(3), 25.78(3), 24.68, 23.43, 22.64, 22.41, 21.04, 18.47, 18.07, 17.67, 16.70, 14.54, 14.38, 14.09, 13.89, 11.98, -3.35, -3.90, -4.27, -5.25.

Analogue 27



39 **27**

To a solution of **39** (17.2 mg, 0.016 mmol) in THF (2 mL) was added TBAF (1M solution in THF, 79 µL, 79 µmol, 5 equiv) at –10 °C. The reaction mixture was stirred at the same temperature for 5 h at which point TLC (silica, 1:2 EtOAc–hexanes) showed it was complete. The reaction mixture was diluted with Et_2O (10 mL), washed with 1M HCl (5 mL), saturated $NaHCO_3$ (5 mL), brine (5 mL). The aqueous layer was extracted with Et_2O (10 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography (silica, EtOAc–hexanes, 1:2) gave analogue **27** (9.8 mg, 72%) as a colorless syrup. $[\alpha]_D^{25}$ –32.4° (*c* 0.4 $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 16.0 Hz, 1H, Ph-C*H*=C-), 7.56 – 7.46 (m, 2H, 2 × Ar*H*), 7.44 – 7.33 (m, 3H, 3 × Ar*H*), 6.92 – 6.83 (m, 1H, Me-C*H*-C(Me)-C=O), 6.35 (d, *J* = 16.0 Hz, 1H, Ph-CH=C*H*-), 5.32 – 5.18 (m, 3H, H-3-Glu*p*, H-4-Glu*p*, H-4-Fuc*p*), 4.73 (d, *J* = 8.4 Hz, 1H, H-1-Glu*p*), 4.41 (d, *J* = 7.2 Hz, 1H, H-1-Fuc*p*), 4.29 (d, *J* = 2.4 Hz, 1H, O*H*), 4.25 (dd, *J* = 12.4, 2.8 Hz, 1H, H-6-Glu*p*), 4.19 (dd, *J* = 12.0, 5.2 Hz, 1H, H-6-Glu*p*), 3.91 – 3.82 (m, 1H, H-5-Glu*p*), 3.82 – 3.67 (m, 5H, H-2-Glu*p*, H-2-Fuc*p*, H-3-Fuc*p*, H-5-Fuc*p*, -CH_2-C*H*-CH_2-), 3.66 (d, *J* = 1.6 Hz, 1H, O*H*), 2.77 – 2.66 (m, 2H), 2.64 – 2.55 (m, 2H), 2.43 (t, *J* = 7.6 Hz, 2H), 2.12 (s, 3H, C*H*$_3$-C=O), 1.80 – 1.70 (m, 6H, C*H*$_3$-CH-C(C*H*$_3$)-C=O), 1.57 – 1.22 (m, 18H), 1.20 (d, *J* = 6.4 Hz, 3H, H-6-Fuc*p*), 0.98 – 0.81 (m, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 208.92, 172.53, 171.28, 167.94, 165.49, 146.50, 139.02, 133.96, 130.69, 128.91(2), 128.29(2), 127.73, 116.47, 102.51, 99.63, 79.12, 74.24, 72.69, 72.09, 71.75, 70.64, 69.23, 68.22, 62.40, 42.68, 36.88, 35.69, 34.41, 31.79, 31.35, 29.69, 27.72, 24.68, 23.43, 22.57, 22.42, 20.96, 18.28, 16.25, 14.49, 14.26, 14.08, 13.90, 12.00. HRMS (ESI) *m*/*z* calcd for $C_{46}H_{72}NO_{15}$ $[M+NH_4]^+$ 878.4902, found: 878.4895.

Biology.

MTT Cytotoxicity Assay

Counting of viable cells was performed before each experiment. The compounds were dissolved in DMSO (dimethyl sulfoxide) to make drug stocks. The stock solutions were diluted with a DMEM or RPMI medium (according to the cell type) to make fresh working solutions at varying concentrations right before each test. Experiments were done in triplicate. First, 100 µL of cell suspension at the density of 50,000 cells/mL was seeded in a 96-well plate (5,000 cells/well), which was incubated at 37 ºC in 5% CO_2 for 24 hours. Subsequently, the cells were treated with a compound at various concentrations in the total volume of 200 µL/well for 72 hours. After 72 hours, the media were discarded and 200 µL of fresh medium containing 10% of MTT stock solution (5 mg/mL) was added to each well. The plate was then incubated at 37 ºC in 5% CO_2 for another 3 hours. Next, 180 µL of the medium was discarded from each well. The formed formazan crystals were dissolved with 180 µL of

DMSO. An absorbance of formazan was detected by a microplate reader (BioTek Synergy H1) at 570 nm with 650 nm as the reference wavelength. The percentage of viability compared to the negative control (DMSO-treated cells) was determined. The GraphPad Prism 6 software was used to make a plot of % viability versus sample concentration and to calculate the concentration at which a compound exhibited 50% cytotoxicity (IC_{50}).

Alamar Blue Cytotoxicity Assay

Counting of viable cells was performed before each experiment. The compounds were dissolved in DMSO (dimethyl sulfoxide) to make drug stocks. The stock solutions were diluted with a DMEM or RPMI medium (according to the cell type) to make fresh working solutions at varying concentrations right before each test. Experiments were done in triplicate. First, 100 μL of cell suspension at the density of 50,000 cells/mL was seeded in a 96-well plate (5,000 cells/well), which was incubated at 37 ºC in 5% CO_2 for 24 hours. Subsequently, the cells were treated with a compound at various concentrations in the total volume of 200 μL/well for 72 hours. After 72 hours, the media were discarded and 200 μL of fresh medium containing 10% of AlamarBlue (resazurin) stock solution (3 mg/27.15mL) was added to each well. The plate was then incubated at 37 ºC in 5% CO_2 for another 3 hours. An fluorescence of metabolic resorufin was detected by a microplate reader (BioTek Synergy H1) at excitation 570 nm with emission 650 nm as the reference wavelength. The percentage of viability compared to the negative control (DMSO-treated cells) was determined. The GraphPad Prism 6 software was used to make a plot of % viability versus sample concentration and to calculate the concentration at which a compound exhibited 50% cytotoxicity (IC_{50}).

Synthesized compound activity assay

Cytotoxicity of synthesized compounds was tested on breast cancer cell line MCF-7 and MDA-MB-231. Among the systematic toxicity assay, analogues **1, 4, 20, 22** and **23** were detected by Alamar Blue Cytotoxicity Assay on the both breast cancer cell line; analogues **2, 3, 21, 24, 25, 26** and **27**, on the other hand, were tested by Alamar Blue Cytotoxicity Assay on MDA-MB-231 cell line, but MTT Cytotoxicity Assay on MCF-7 cell line. Besides breast cancer cell line, analogues **2, 3, 24, 26** and **27,** were also further explored on HeLa cell line, U-937 cell line, Jurkat-T cell line, MCF-10A cell line and 3T3 cell line by Alamar Blue Cytotoxicity Assay.

IC50 curves for Ipomoeassin F, analogue 3 and 27

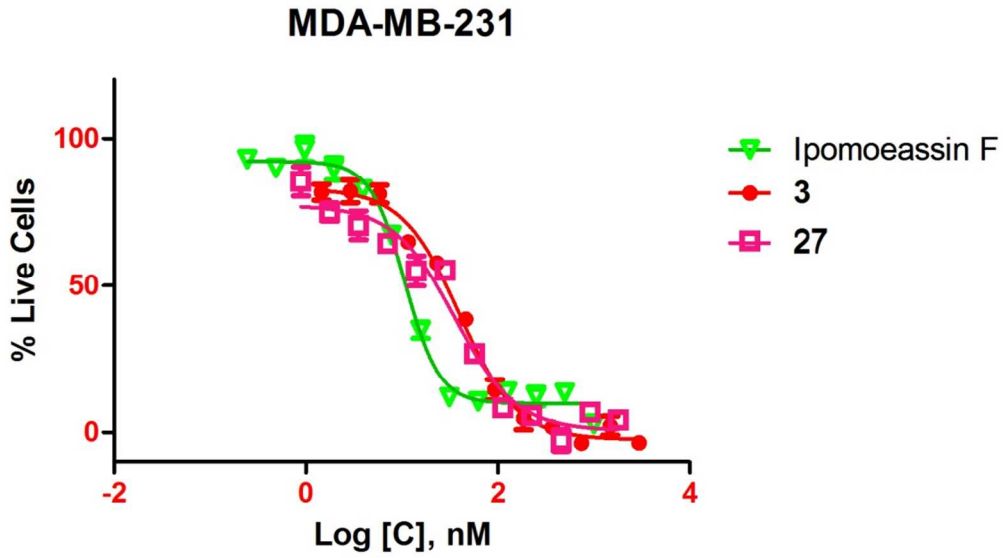


Figure S1. IC_{50} curves on MDA-MB-231 cell line.

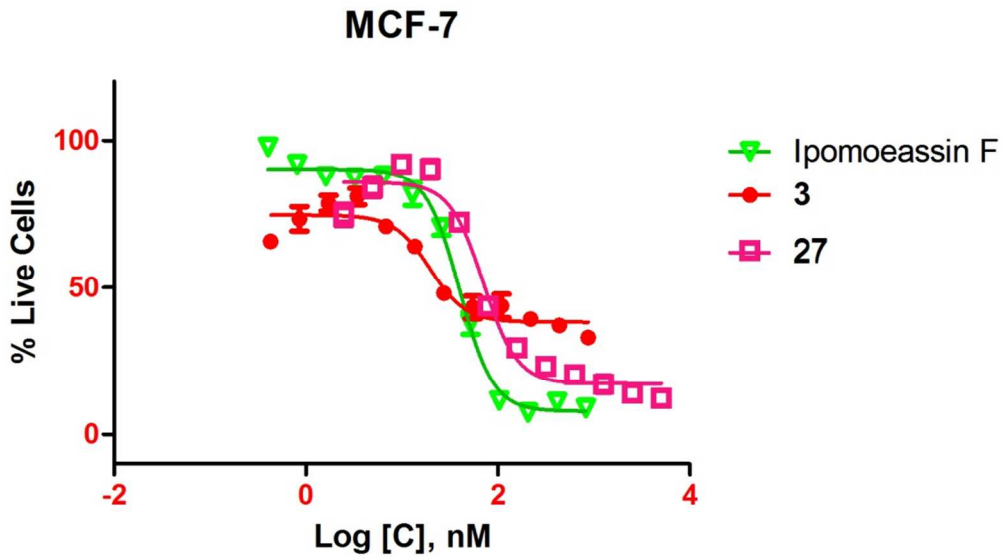


Figure S2. IC_{50} curves on MCF-7 cell line.

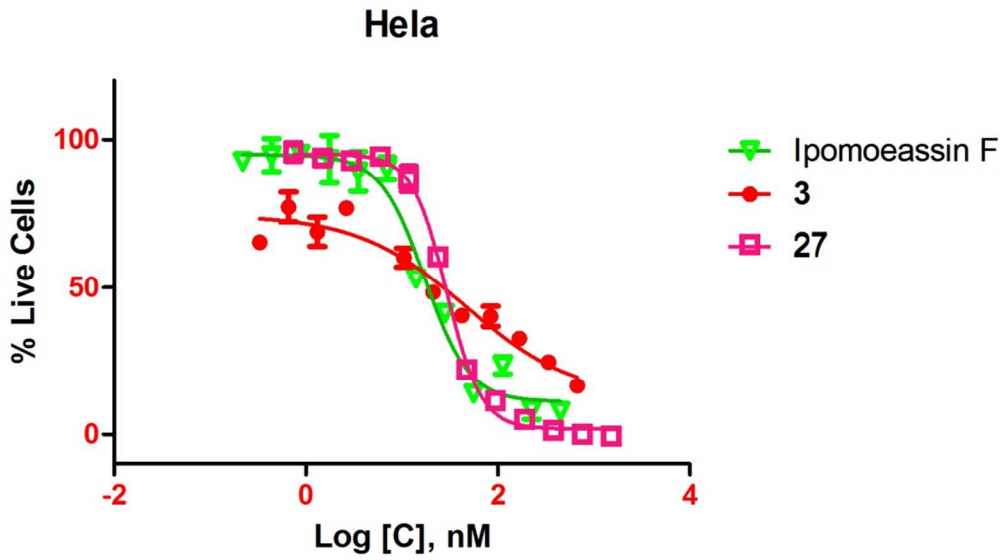


Figure S3. IC_{50} curves on Hela cell line.

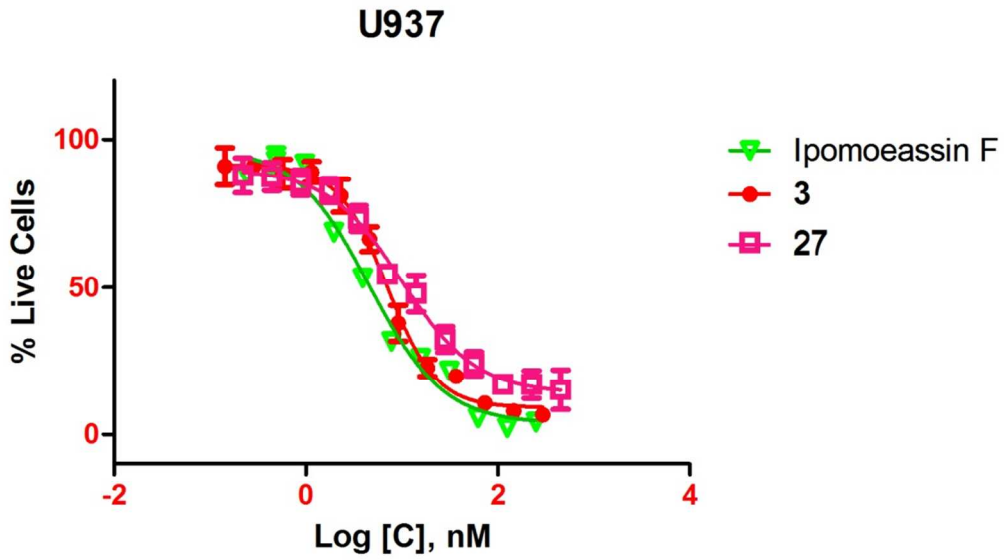


Figure S4. IC_{50} curves on U937 cell line.

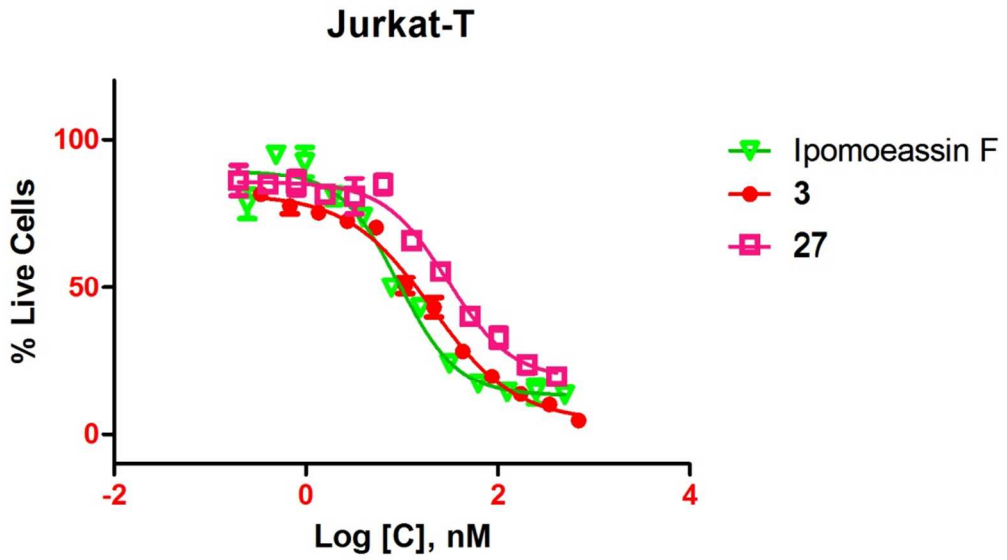


Figure S5. IC_{50} curves on Jurkat-T cell line.

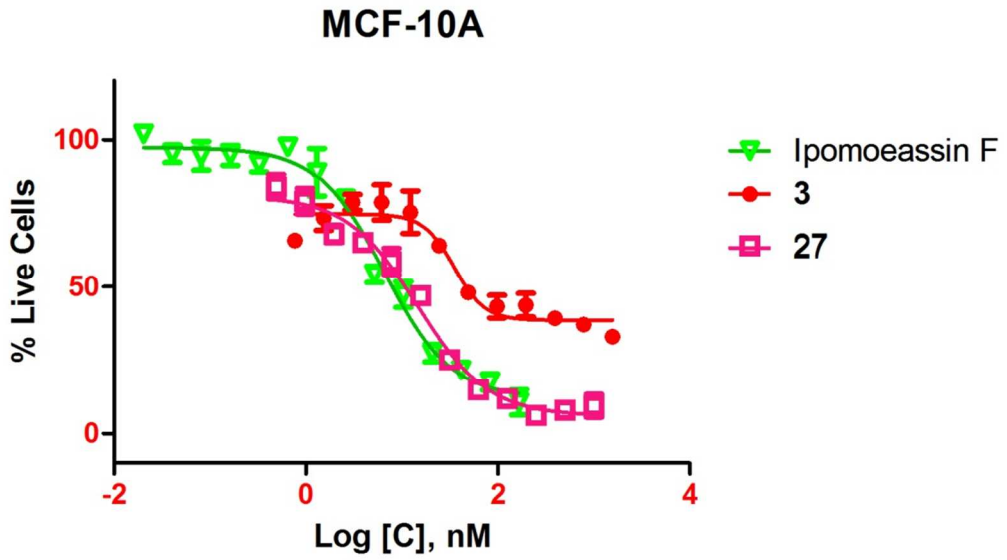


Figure S6. IC_{50} curves on MCF-10A cell line.

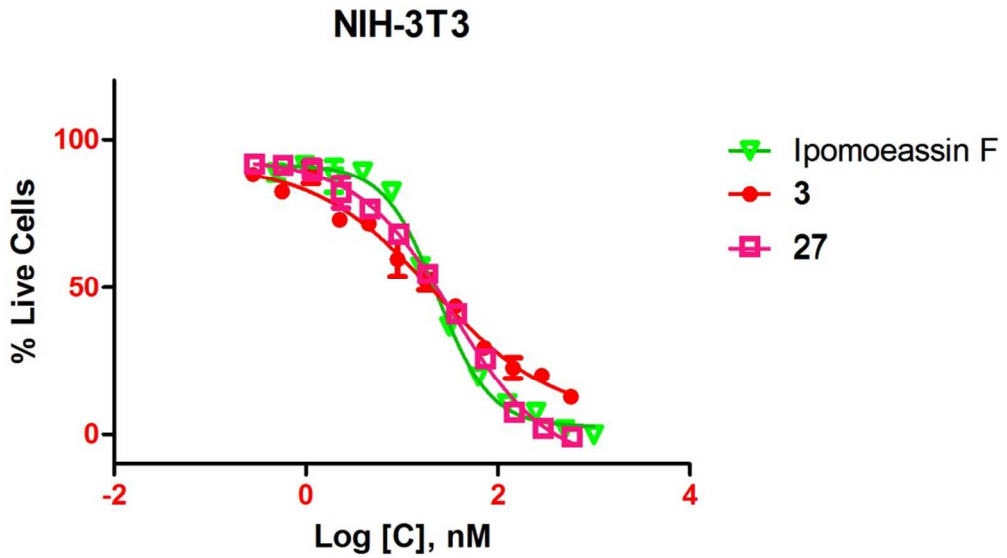


Figure S7. IC_{50} curves on NIH-3T3 cell line.

Table S1. Selectivity index (SI) of ipomoeassin F, its analogue **26** and Taxol over MCF-10A cells[a].

	MDA-MB-231	MCF7	HeLa	U937	Jurkat
Ipomoeassin F	0.83	0.12	0.33	1	0.89
26	2.55	1.22	1.73	5.51	0.62
Taxol	8.04	3.73	25.6	15.2	14.6

[a] The data were obtained from at least two independent experiments, and the standard errors are within 20%.

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