Supporting Information

Improved Synthesis for Modular Ascarosides Uncovers Biological Activity

Ying K. Zhang†, Marco A. Sanchez-Ayala†, Paul W. Sternberg‡, Jagan Srinivasan§, and Frank C. Schroeder†*

†Boyce Thompson Institute and Department of Chemistry and Chemical Biology, Cornell University, Ithaca, New York 14853, United States;
‡Howard Hughes Medical Institute and Division of Biology, California Institute of Technology, Pasadena, California 91125, United States;
§Department of Biology and Biotechnology, Worcester Polytechnic Institute, Worcester, Massachusetts 01609, United States

*Corresponding Author: fs31@cornell.edu

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1. Experimental

1.1 General procedures

Unless otherwise stated, all oxygen and moisture-sensitive reactions were carried out under argon atmosphere in flame-dried glassware. Solutions and solvents sensitive to moisture and oxygen were transferred via standard syringe and cannula techniques. All commercial reagents were purchased as reagent grade and, unless otherwise stated, used without any further purification. Tetrahydrofuran, dichloromethane, and dimethylformamide were dried over 4Å molecular sieves prior to use; N,N-diisopropylethylamine was distilled from calcium hydride under argon. Thin-layer chromatography (TLC) was performed using J. T. Baker Silica Gel IB2-F. Flash chromatography was performed using Teledyne Isco CombiFlash systems and Teledyne Isco RediSep Rf silica columns. Nuclear Magnetic Resonance (NMR) spectra were recorded on Varian INOVA 600 (600 MHz) or Varian INOVA 400 (400 MHz) spectrometers in Cornell University’s NMR facility. $^1$H NMR chemical shifts are reported in ppm (δ) relative to residual solvent peaks (7.26 ppm for CDCl$_3$, 3.31 ppm for CD$_3$OD). NMR-spectroscopic data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constants (Hz), and integration. $^{13}$C NMR chemical shifts are reported in ppm (δ) relative to CHCl$_3$ (δ 77.2) in CDCl$_3$, CH$_3$OH (δ 49.0) in CD$_3$OD.
1.2 Synthesis of key intermediate 13

(3R,4R,6S,7S,7aR)-2,2,6-trimethyltetrahydro-4H-[1,3]dioxolo[4,5-c]pyran-7-ol (7).

To a solution of 6 (4.0 g, 22.4 mmol) in dry N,N-dimethylformamide (40 mL), 2,2-dimethoxypropane (13.8 mL, 0.11 mol) and p-toluenesulfonic acid (427 mg, 2.24 mmol) were added, and the mixture was allowed to stir at room temperature. After 5 hours, the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-60% ethyl acetate in hexane afforded 7 (4.82 g, 22.1 mmol, 98.6%) as a clear oil.

\[ ^1H \text{ NMR (600 MHz, chloroform-}d\text{): } \delta \text{ (ppm) } 4.83 \text{ (br s, 1H), 4.12-4.08 (m, 1H), 4.05 (dd, } J = 7.2, 6.2 \text{ Hz, 1H), 3.62 (dq, } J = 9.4, 6.4 \text{ Hz, 1H), 3.37 (s, 3H), 3.38 (dd, } J = 9.4, 7.2 \text{ Hz, 1H), 1.51 (s, 3H), 1.34 (s, 3H), 1.29 (d, } J = 6.4 \text{ Hz, 3H).} \]

\[ ^{13}C \text{ NMR (151 MHz, chloroform-}d\text{): } \delta \text{ (ppm) } 109.6, 98.3, 78.6, 75.9, 74.6, 65.9, 55.1, 28.1, 26.3, 17.6. \]

HRMS (ESI) m/z calcd for C_{10}H_{18}O_{5} [M+Na]^+ 241.10464, found 241.10466, Δ ppm 0.063.

(2R,3R,4S,5R,6S)-5-((tert-butyldiphenylsilyl)oxy)-2-methoxy-6-methyl-tetrahydro-2H-pyran-3,4-diol (8).

To a stirred solution of 7 (4.82 g, 22.1 mmol) in dry N,N-dimethylformamide (40 mL) at 0 °C, tert-butyldiphenylchlorosilane (28.7 mL, 0.11 mol) and imidazole (4.5 g, 66.3 mmol) were added. After stirring overnight at room temperature, the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-35% ethyl acetate in hexanes afforded 8 (9.08g, 98.6%) as a clear oil.

\[ ^1H \text{ NMR (600 MHz, chloroform-}d\text{): } \delta \text{ (ppm) } 7.77-7.73 \text{ (m, 2H), 7.71-7.67 (m, 2H), 7.47-7.38 (m, 6H), 4.58 (br s, 1H), 3.81 (dd, } J = 8.8, 3.5 \text{ Hz, 1H), 3.78 (dd, } J = 3.5, 1.6 \text{ Hz, 1H), 3.74 (dq, } J = 9.2, 6.3 \text{ Hz, 1H), 3.56-3.51 (m, 1H), 3.37 (s, 3H), 1.26 (d, } J = 6.3 \text{ Hz, 3H), 1.07 (s, 9H).} \]

\[ ^{13}C \text{ NMR (151 MHz, chloroform-}d\text{): } \delta \text{ (ppm) } 136.3, 135.6, 134.6, 132.9, 130.13, 130.05, 128.08, 127.98, 100.3, 76.1, 72.0, 71.2, 68.1, 55.1, 27.3, 19.8, 18.3. \]

HRMS (ESI) m/z calcd for C_{23}H_{32}O_{5}Si [M+Na]^+ 439.19112, found 439.19089, Δ ppm -0.528.
(3aR,4R,6S,7S,7aR)-7-((tert-butyldiphenylsilyl)oxy)-4-methoxy-6-methyltetrahydro-4H-[1,3,2]dioxathiole[4,5-c]pyran 2-oxide (9).

To a solution of 8 (9.08 g, 21.8 mmol) in ethyl acetate (100 mL), pyridine (3.52 mL, 43.6 mmol) was added with stirring. After 1 min, the reaction was cooled to 0 °C with ice bath. Thionyl chloride (2.38 mL, 32.7 mmol) was added and the reaction turned cloudy instantly. After stirring for 30 min, the reaction was diluted with ethyl acetate, washed with water, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexane afforded a mixture of 9 and the corresponding β-anomer (9.98 g, 99%) in a ratio of about 6.25:1 as a clear oil.

α-anomer, 9 (major): ¹H NMR (600 MHz, chloroform-d): δ (ppm) 7.73-7.65 (m, 4H), 7.44-7.34 (m, 6H), 4.91 (dd, J = 7.6, 5.5 Hz, 1H), 4.90 (br s, 1H), 4.73 (dd, J = 5.5 Hz, 0.7 Hz, 1H), 3.75 (dq, J = 9.7 Hz, 6.3 Hz, 1H), 3.37 (s, 3H), 3.14 (dd, J = 9.7 Hz, 7.6 Hz, 1H), 1.12 (d, J = 6.3 Hz, 3H), 1.06 (s, 9H). ¹³C NMR (151 MHz, chloroform-d): δ (ppm) 136.2, 136.1, 133.0, 132.3, 130.0, 129.9, 127.7, 127.6, 96.3, 84.7, 76.3, 76.0, 65.8, 55.2, 27.1, 19.7, 17.9. β-anomer (minor): ¹H NMR (600 MHz, chloroform-d): δ (ppm) 7.73-7.65 (m, 4H), 7.42-7.34 (m, 6H), 4.92 (br s, 1H), 4.73 (dd, J = 7.7, 6.2 Hz, 1H), 4.37 (dd, J = 6.2, 0.8 Hz, 1H), 3.69 (dq, J = 9.6, 6.2 Hz, 1H), 3.35 (s, 3H), 1.07 (s, 9H), 0.98 (d, J = 6.2 Hz, 3H). ¹³C NMR (151 MHz, chloroform-d): δ (ppm) 136.4, 136.1, 133.2, 132.4, 129.9, 129.8, 127.6, 127.5, 96.8, 83.5, 81.8, 76.0, 66.5, 55.1, 27.1, 19.8, 17.8. HRMS (ESI) m/z calcd for C₂₃H₃₀O₆SSi [M+Na]⁺ 485.14246, found 485.14279, Δ ppm 0.686.

(3aR,4R,6S,7S,7aR)-7-((tert-butyldiphenylsilyl)oxy)-4-methoxy-6-methyltetrahydro-4H-[1,3,2]dioxathiole[4,5-c]pyran 2,2-dioxide (10).

To a vigorously stirred solution of 9 (9.98 g, 21.6 mmol) in dichloromethane (80 mL), acetonitrile (80 mL) and water (70 mL), ruthenium (III) chloride hydrate (223 mg, 1.1 mmol) in 10 mL water was added followed by the addition of sodium periodate (23 g, 0.11 mol). After stirring for 30 min, the reaction was diluted with water and extracted with two 50-mL portions of dichloromethane. The combined organic extracts were dried over Na₂SO₄ and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexane afforded 10 (9.92 g, 96%) as a clear oil.
**1H NMR (600 MHz, chloroform-d):** δ (ppm) 7.71-7.65 (m, 4H), 7.46-7.36 (m, 6H), 4.97 (dd, J = 7.5, 5.4 Hz, 1H), 4.89 (dd, J = 5.4, 0.8Hz, 1H), 4.84 (br s, 1H), 3.81 (dd, J = 7.5 Hz, 1H), 3.73 (dq, J = 9.7, 6.2 Hz, 1H), 3.36 (s, 3H), 1.05 (s, 9H), 1.02 (d, J = 6.2 Hz, 3H).

**13C NMR (151 MHz, chloroform-d):** δ (ppm) 136.3, 136.1, 132.6, 131.6, 130.3, 130.0, 127.9, 127.8, 95.2, 86.2, 79.5, 73.8, 65.7, 55.3, 27.1, 19.8, 17.7.

**HRMS (ESI) m/z** calcd for C\textsubscript{23}H\textsubscript{30}O\textsubscript{7}SSi [M+Na]\textsuperscript{+} 501.13737, found 501.13785, Δ ppm 0.955.

(2R,3R,5R,6S)-5-((tert-butyldiphenylsilyl)oxy)-2-methoxy-6-methyl-tetrahydro-2H-pyran-3-ol (11).

A solution of 10 (9.92 g, 20.7 mmol) in tetrahydrofuran (70 mL) was stirred and heated to 55 °C. To this mixture, tetrabutylammonium borohydride (10.7 g, 41.4 mmol) was added and the reaction was allowed to stir overnight. After 18 h, the reaction was cooled to 0 °C and quenched with acetone. Concentrated sulfuric acid (5 mL) was added and the mixture was stirred for 1 h before methanol (5 mL) was added. After an additional 30 min of stirring, the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded 11 (6.4 g, 77%) as clear oil.

**1H NMR (600 MHz, chloroform-d):** δ (ppm) 7.72-7.64 (m, 4H), 7.46-7.34 (m, 6H), 4.38 (br s, 1H), 3.75 (dq, J = 8.9, 6.3 Hz, 1H), 3.69-3.67 (m, 1H), 3.64 (ddd, J = 10.7, 9.1, 4.7 Hz, 1H), 3.38 (s, 3H), 1.85 (ddd, J = 13.5, 10.7, 3.1 Hz, 1H), 1.78 (ddd, J = 13.5, 4.7, 3.5 Hz, 1H), 1.19 (d, J = 6.3 Hz, 3H), 1.06 (s, 9H).

**13C NMR (151 MHz, chloroform-d):** δ (ppm) 136.1, 134.5, 133.7, 130.0, 129.8, 127.8, 127.7, 100.3, 69.9, 69.8, 68.7, 55.0, 35.8, 27.2, 19.5, 18.4. **HRMS (ESI) m/z** calcd for C\textsubscript{23}H\textsubscript{32}O\textsubscript{4}Si [M+Na]\textsuperscript{+} 423.19621, found 423.19665, Δ ppm 1.046.

(2R,3R,5R,6S)-5-((tert-butyldiphenylsilyl)oxy)-2-methoxy-6-methyl-tetrahydro-2H-pyran-3-yl benzoate (13).

To a solution of 11 (0.9 g, 2.2 mmol) in pyridine (40 mL), benzoyl chloride (0.76 mL, 6.6 mmol) was added slowly at 0 °C. After 3 hours, the reaction
was diluted with water, extracted with hexanes, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-15% ethyl acetate in hexanes afforded 13 (1.04 g, 94%) as a white powder.

¹H NMR (600 MHz, chloroform-d): δ (ppm) 7.75-7.71 (m, 2H), 7.69-7.63 (m, 4H), 7.57-7.53 (m, 1H), 7.41-7.35 (m, 3H), 7.35-7.27 (m, 5H), 4.94-4.92 (m, 1H), 4.54 (br s, 1H), 3.84 (dq, J = 9.2, 6.3 Hz, 1H), 3.65 (ddd, J = 11.2, 9.2, 4.4 Hz, 1H), 3.40 (s, 3H), 2.03 (ddd, J = 13.7, 11.2, 3.1 Hz, 1H), 1.89-1.84 (m, 1H), 1.29 (d, J = 6.3 Hz, 1H), 1.05 (s, 9H). ¹³C NMR (151 MHz, chloroform-d): δ (ppm) 165.4, 136.1, 136.0, 134.2, 133.3, 133.1, 130.0, 129.89, 129.87, 129.8, 128.3, 127.8, 127.6, 97.3, 71.1, 70.3, 69.6, 54.9, 33.4, 27.2, 19.5, 18.6. HRMS (ESI) m/z calcd for C₃₀H₃₆O₅Si [M+Na]⁺ 527.22242, found 527.22326, Δ ppm 1.590.

1.3 Synthesis of icas#9

To a solution of 13 (0.9 g, 1.8 mmol) in dichloromethane (20 mL) cooled to -78 °C in a dry ice/acetone bath, boron tribromide solution (1 M in dichloromethane, 1.5 mL, 1.5 mmol) was added dropwise under argon. After 5 min, the reaction was quenched with sat. NaHCO₃, extracted with ethyl acetate, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded SI-1, containing 24% of the β-anomer (440 mg, 50%, 98% BRSM) as a white powder.

¹H NMR for major anomer (400 MHz, chloroform-d): δ (ppm) 7.82-7.52 (m, 7H), 7.43-7.27 (m, 8H), 5.07 (br s, 1H), 4.99-4.96 (m, 1H), 4.10 (dq, J = 9.2, 6.2 Hz, 1H), 3.66 (ddd, J = 11.4, 9.2, 4.4 Hz, 1H), 2.12 (ddd, J = 13.8, 11.4, 3.0 Hz, 1H), 1.88 (dt, J = 13.8, 3.8 Hz, 1H), 1.27 (d, J = 6.2 Hz, 3H), 1.05 (s, 9H). ¹³C NMR for major anomer (100 MHz, chloroform-d): δ (ppm) 165.5, 136.1, 136.0, 134.2, 133.3, 133.2, 130.0, 129.9, 128.3, 127.8, 127.7, 91.0, 71.5, 70.3, 69.8, 32.7, 27.2, 19.5, 18.6. HRMS (ESI) m/z calcd for C₂₉H₃₄O₅Si [M+Na]⁺ 513.20677, found 513.20740, Δ ppm 1.224.

To a stirred solution of SI-1 (45 mg, 0.09 mmol) in dry dichloromethane (2 mL), trichloroacetonitrile (18.4 μL, 0.18 mmol) and 1,8-diazabicycloundec-7-ene (1.4 μL, 9 μmol) were added at room temperature. After 90 min, the reaction was concentrated in vacuo to evaporate most solvent. Flash column chromatography on silica using a gradient of 15-25% ethyl acetate in hexanes afforded 17 (49.6 mg, 85%) as a clear oil. A stirred solution of 17 and (R)-(-)-5-hexen-2-ol (13.4 μL, 0.11 mmol) was cooled to 0 °C in an ice bath, trimethylsilyl trifluoromethanesulfonate (3.3 μL, 18 μmol) was added, and the solution was allowed to warm to room temperature. After an hour, the reaction was quenched with sat. NaHCO₃, extracted with dichloromethane, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-15% ethyl acetate in hexanes afforded 19 (40.6 mg, 77%) as a clear oil.

¹H NMR (600 MHz, chloroform-d): δ (ppm) 7.75-7.72 (m, 2H), 7.70-7.64 (m, 4H), 7.57-7.53 (m, 1H), 7.41-7.27 (m, 8H), 5.89 (ddt, J = 16.7, 10.1, 6.3 Hz, 1H), 5.12-5.07 (m, 1H), 5.04-5.00 (m, 1H), 4.90-4.87 (m, 1H), 4.75 (br s, 1H), 3.90 (dq, J = 9.3, 6.2 Hz, 1H), 3.85-3.78 (m, 1H), 3.67 (ddd, J =11.3, 9.4, 4.3 Hz, 1H), 2.29-2.14 (m, 2H), 2.04 (ddd, J = 13.6, 11.3, 3.0 Hz, 1H), 1.88 (dt, J = 13.6, 3.6 Hz, 1H), 1.62-1.55 (m, 2H), 1.26 (d, J = 6.2 Hz, 3H), 1.14 (d, J = 6.2 Hz, 3H), 1.06 (s, 9H). ¹³C NMR (151 MHz, chloroform-d): δ (ppm) 165.6, 138.7, 136.1, 136.0, 134.3, 133.5, 133.1, 130.1, 129.90, 129.87, 129.8, 128.3, 127.8, 127.7, 114.9, 93.6, 72.1, 71.8, 70.5, 70.1, 36.6, 33.5, 30.2, 27.2, 19.5, 19.3, 18.6. HRMS (ESI) m/z calcd for C₃₅H₆₄O₅Si [M+Na]⁺ 595.28502, found 595.28575, Δ ppm 1.223.


To a solution of 19 (40.6 mg, 0.071 mmol) in dichloromethane (1 mL), acetonitrile (1 mL) and H₂O (0.5 mL), ruthenium(III) chloride hydrate
(1.5 mg, 7 μmol) in H$_2$O (0.5 mL) was added while stirring vigorously. After 5 min, sodium periodate (75 mg, 0.35 mmol) was added and the resulting mixture was stirred for 90 min at room temperature. The reaction was diluted with H$_2$O, extracted with dichloromethane, dried over Na$_2$SO$_4$, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-50% ethyl acetate in hexanes afforded 24 (41.5 mg, 99%) as a clear oil.

$^1$H NMR (600 MHz, chloroform-d): δ (ppm) 7.75-7.71 (m, 2H), 7.70-7.64 (m, 4H), 7.57-7.53 (m, 1H), 7.40-7.27 (m, 8H), 4.89-4.86 (m, 1H), 4.75 (br s, 1H), 3.89-3.82 (m, 2H), 3.66 (ddd, $J$ = 11.2, 9.2, 4.2 Hz, 1H), 2.61-2.50 (m, 2H), 2.01 (ddd, $J$ = 13.9, 11.1, 2.9 Hz, 1H), 1.92-1.86 (m, 3H), 1.26 (d, $J$ = 6.3 Hz, 3H), 1.17 (d, $J$ = 6.2 Hz, 3H), 1.06 (s, 9H).

$^{13}$C NMR (151 MHz, chloroform-d): δ (ppm) 178.0, 165.5, 136.1, 136.0, 134.3, 133.4, 133.2, 130.7, 130.0, 129.91, 129.88, 129.81, 128.36, 127.8, 127.7, 93.6, 71.9, 71.2, 70.35, 70.31, 33.4, 32.0, 30.3, 27.2, 19.5, 19.1, 18.5. HRMS (ESI) m/z calcd for C$_{34}$H$_{42}$O$_7$Si [M-H]$^-$ 589.26270, found 589.26329, Δ ppm 0.996.


To a solution of 24 (277 mg, 0.5 mmol) in 1,4-dioxane (15 mL), lithium hydroxide monohydrate (79 mg, 1.9 mmol) in H$_2$O (2 mL) was added and the resulting mixture was stirred at 60 °C for 3 hours. Glacial acetic acid (1 mL) was added, and the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-40% ethyl acetate in hexanes afforded SI-2 (218 mg, 90%) as a clear oil.

$^1$H NMR (600 MHz, chloroform-d): δ (ppm) 7.71-7.64 (m, 4H), 7.45-7.35 (m, 6H), 4.59 (br s, 1H), 3.87-3.81 (m, 1H), 3.75 (dq, $J$ = 8.8, 6.2 Hz, 1H), 3.68-3.62 (m, 3H), 2.58-2.47 (m, 2H), 1.89-1.81 (m, 3H), 1.78 (dt, $J$ = 13.2, 4.2 Hz, 1H), 1.16 (d, $J$ = 6.2 Hz, 3H), 1.13 (d, $J$ = 6.0 Hz, 3H), 1.05 (s, 9H). HRMS (ESI) m/z calcd for C$_{27}$H$_{38}$O$_6$Si [M-H]$^-$ 485.23649, found 485.23707, Δ ppm 1.198.

To a stirred solution of SI-2 (218 mg, 0.45 mmol) in dry N,N-dimethylformamide (7 mL) under argon, benzyl bromide (0.32 mL, 2.7 mmol) and sodium hydride (64.5 mg, 2.7 mmol) were added. After stirring overnight, the reaction was carefully quenched by drop-wise addition of sat. NaHCO₃, extracted with ethyl acetate, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexane afforded SI-3 (187 mg, 63%) as a clear oil.

¹H NMR (600 MHz, chloroform-d): δ (ppm) 7.73-7.68 (m, 5H), 7.45-7.30 (m, 10H), 7.26-7.20 (m, 3H), 7.08-7.05 (m, 2H), 5.17 (d, J = 12.4 Hz, 1H), 5.13 (d, J = 12.4 Hz, 1H), 4.64 (br s, 1H), 4.15 (d, J = 12.3 Hz, 1H), 4.05 (d, J = 12.3 Hz, 1H), 3.85-3.69 (m, 3H), 3.30-3.27 (m, 1H), 2.58-2.41 (m, 2H), 1.91-1.78 (m, 3H), 1.66 (ddd, J = 13.5, 10.6, 2.9 Hz, 1H), 1.24 (d, J = 6.3 Hz, 3H), 1.07 (d, J = 6.1 Hz, 3H), 1.05 (s, 9H). ¹³C NMR (151 MHz, chloroform-d): δ (ppm) 173.6, 136.2, 136.11, 136.06, 135.63, 135.56, 134.8, 133.9, 129.9, 129.7, 128.8, 128.4, 129.38, 128.3, 127.9, 127.7, 127.6, 127.5, 94.6, 75.6, 70.5, 70.2, 70.3, 70.1, 66.4, 32.4, 30.8, 29.6, 27.2, 19.6, 18.9, 18.5. HRMS (ESI) m/z calcld for C₄₁H₅₀O₆Si [M+Na]⁺ 689.32689, found 689.32780, Δ ppm 1.325.


To a solution of SI-3 (152 mg, 0.23 mmol) in tetrahydrofuran (6 mL), tetrabutylammonium fluoride solution (1 M in THF, 1.14 mL, 1.14 mmol) was added. After stirring overnight, the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-50% ethyl acetate in hexanes afforded 27 (79.6 mg, 81%) as a clear oil.

¹H NMR (600 MHz, chloroform-d): δ (ppm) 7.38-7.27 (m, 10H), 5.13 (d, J = 12.4 Hz, 1H), 5.10 (d, J = 12.4 Hz, 1H), 4.78 (br s, 1H), 4.59 (d, J = 12.4 Hz, 1H), 4.56 (d, J = 12.2 Hz, 1H), 3.86-3.80 (m, 1H), 3.62 (ddd, J = 11.1, 9.3, 4.4 Hz, 1H), 3.56 (dq, J = 9.1, 6.1 Hz, 1H), 3.51-
3.49 (m, 1H), 2.52-2.41 (m, 2H), 2.13 (dt, J = 13.4, 3.8 Hz, 1H), 1.89-1.79 (m, 2H), 1.68 (ddd, J = 13.4, 11.1, 3.1 Hz, 1H), 1.25 (d, J = 6.1 Hz, 3H), 1.09 (d, J = 6.1 Hz, 3H). \( ^{13} \text{C NMR (151 MHz, chloroform-} \text{d):} \) δ (ppm) 173.7, 138.4, 136.1, 128.7, 128.6, 128.44, 128.43, 127.87, 127.82, 114.7, 93.9, 75.9, 71.3, 70.06, 68.5, 66.4, 32.9, 32.3, 30.9, 18.8, 17.9. \( \text{HRMS (ESI) m/z} \) calcd for \( \text{C}_{25} \text{H}_{32} \text{O}_{6} [\text{M+Na}^{+}] \) 451.20911, found 451.20959, Δ ppm 1.064.

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\text{(2S,3R,5R,6R)-5-(benzyloxy)-6-(((R)-5-(benzyloxy)-5-oxopent-2-yl)oxy)-2-methyltetrahydro-2H-pyran-3-yl 1H-indole-3-carboxylate (SI-4).}
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Indole-3-carboxylic acid (16 mg, 0.1 mmol) was dissolved in dry dichloromethane (1 mL) with a drop of dimethylformamide and the solution was cooled to 0 °C in an ice bath. Oxalyl chloride (17 μL, 0.2 mmol) was added slowly, and the resulting solution was stirred for 20 min at room temperature. The reaction mixture was concentrated to dryness in vacuo, and the residue was redissolved in dry dichloromethane (1 mL). The resulting solution was added dropwise to a stirred solution containing 27 (21 mg, 0.05 mmol) and \( \text{N,N-diisopropylethylamine (34 μL, 0.2 mmol)} \) in dry dichloromethane (1 mL) at 0 °C in an ice bath. After 20 min, the reaction was quenched with sat. NaHCO\(_3\), extracted with dichloromethane, dried over Na\(_2\)SO\(_4\), and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-35% ethyl acetate in hexanes afforded SI-4 (16 mg, 56%) as a clear oil.

\( ^{1} \text{H NMR (600 MHz, chloroform-d):} \) δ (ppm) 8.72 (br s, 1H), 8.18-8.15 (m, 1H), 7.89-7.87 (m, 1H), 7.44-7.26 (m, 13H), 5.15-5.12 (m, 3H), 4.85 (br s, 1H), 4.75 (d, J = 12.1 Hz, 1H), 4.58 (d, J = 12.1 Hz, 1H), 3.99 (dq, J = 9.3, 6.3 Hz, 1H), 3.92-3.86 (m, 1H), 3.58-3.56 (m, 1H), 2.61-2.50 (m, 2H), 2.14 (dt, J = 13.1, 3.4 Hz, 1H), 1.95-1.85 (m, 2H), 1.69 (ddd, J = 13.1, 11.1, 3.1 Hz, 1H), 1.25 (d, J = 6.1 Hz, 3H), 1.13 (d, J = 6.1 Hz, 3H). \( \text{HRMS (ESI) m/z} \) calcd for \( \text{C}_{34} \text{H}_{37} \text{NO}_{7} [\text{M+Na}^{+}] \) 594.24622, found 594.24665, Δ ppm 0.718.

\[
\text{(R)-4-(((2R,3R,5R,6S)-5-(((1H-indole-3-carbonyl)oxy)-3-hydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)pentanoic acid (icas#9).}
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To a suspension of palladium on activated carbon (10 wt%, 16 mg, 15 μmol) in methanol (2 mL), SI-4 (8.8 mg, 15.4 μmol) in methanol (3 mL)
was added under argon. After 5 min, argon was purged by flushing hydrogen through the reaction flask. The resulting mixture was stirred for 90 min at room temperature, and hydrogen was purged by flushing argon. After removing the catalyst particles from the solution by filtration, the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-15% methanol in dichloromethane afforded icas#9 (4.7 mg, 78%) as clear oil. Spectroscopic data were identical to those reported previously [1].

1.4 Synthesis of dasc#1

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To a stirred solution of 1 (220 mg, 0.62 mmol) in dry dichloromethane (10 mL), trichloroacetonitrile (0.12 mL, 1.2 mmol) and 1,8-diazabicycloundec-7-ene (5 μL, 33 μmol) were added at room temperature. After 90 min, the reaction was concentrated in vacuo to evaporate most solvent. Flash column chromatography on silica using a gradient of 15-25% ethyl acetate in hexanes afforded SI-6 (200 mg, 66%) as a clear oil.

A solution of SI-6 and 21 (84 mg, 0.66 mmol) in dry dichloromethane (10 mL) was cooled in an ice bath, trimethylsilyl trifluoromethanesulfonate (22 μL, 0.12 mmol) was added, and the solution was allowed to warm to room temperature. After an hour, the reaction was quenched with sat. NaHCO₃, extracted with dichloromethane, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded SI-5 (165 mg, 52%) as clear oil.

\(^1^H\) NMR (600 MHz, chloroform-\textit{d}): δ (ppm) 8.13-8.09 (m, 2H), 8.07-8.03 (m, 2H), 7.61-7.55 (m, 2H), 7.50-7.43 (m, 4H), 5.18 (ddd, \(J = 11.3, 9.9, 4.7\) Hz, 1H), 5.15-5.12 (m, 1H), 4.95 (br s, 1H), 4.16-4.07 (m, 3H), 3.88-3.82 (m, 1H), 2.41 (dt, \(J = 13.5, 3.9\) Hz, 1H), 2.35 (t, \(J = 7.5\) Hz, 2H), 2.20 (ddd, \(J = 13.5, 11.5, 3.2\) Hz, 1H), 1.74 -1.63 (m, 3H), 1.57-1.39 (m, 3H), 1.28 (d, \(J = 6.3\) Hz, 3H), 1.25 (t, \(J = 7.1\) Hz, 3H), 1.19 (d, \(J = 6.1\) Hz, 3H). \(^1^3^C\) NMR (151 MHz,
chloroform-d): δ (ppm) 173.8, 166.0, 165.9, 133.42, 133.36, 130.1, 129.8, 128.6, 94.0, 72.6, 71.4, 70.8, 67.2, 60.4, 37.0, 29.9, 25.5, 25.2, 19.3, 18.1 [2].

\[
\text{SI-7}
\]

\[\text{(R)}-6-(((2R,3R,5R,6S)-3,5-dihydroxy-6-methyltetrahydro-2H-pyran-2-yl)oxy)heptanoic acid (SI-7, ascr#1).}\]

To a solution of SI-5 (165 mg, 0.32 mmol) in 1,4-dioxane (10 mL), lithium hydroxide monohydrate (108 mg, 2.6 mmol) in H₂O (2 mL) was added, and the resulting mixture was stirred at 60 °C for 2.5 hours. Glacial acetic acid (1 mL) was added, and the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-10% methanol in dichloromethane afforded SI-7 (88 mg, 99%) as a clear oil. Spectroscopic data were identical to those reported previously [3].

\[
\text{SI-8}
\]

\[\text{Benzyl (R)}-6-(((2R,3R,5R,6S)-3,5-bis(benzyloxy)-6-methyltetrahydro-2H-pyran-2-yl)oxy)heptanoate (SI-8).}\]

To a stirred solution of SI-7 (88 mg, 0.32 mmol) in dry N,N-dimethylformamide (4 mL), benzyl bromide (0.4 mL, 3.2 mmol) and sodium hydride (77 mg, 3.2 mmol) were added. After stirring overnight, the reaction was quenched with sat. NaHCO₃, extracted with ethyl acetate, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-10% ethyl acetate in hexanes afforded SI-8 (107 mg, 61%) as a clear oil.

\[\text{1H NMR (600 MHz, chloroform-d): } \delta (\text{ppm}) 7.39-7.26 (m, 15H), 5.10 (s, 2H), 4.76 (br s, 1H), 4.58 -4.51 (m, 3H), 4.46 (d, J = 11.6 Hz, 1H), 3.80-3.71 (m, 3H), 3.55-3.51 (m, 1H), 3.44 (ddd, J = 11.0, 9.4, 4.3 Hz, 1H), 2.35 (t, J = 7.5 Hz, 2H), 2.21 (dt, J = 13.4, 3.8 Hz, 1H), 1.72 (ddd, J = 13.4, 11.0, 3.0 Hz, 1H), 1.69-1.60 (m, 2H), 1.56-1.31 (m, 4H), 1.27 (t, J = 6.3 Hz, 3H), 1.05 (d, J = 6.1 Hz, 3H).\]

\[\text{13C NMR (151 MHz, chloroform-d): } \delta (\text{ppm}) 173.6, 138.7, 138.6, 136.3, 128.7, 128.6, 128.33, 128.31, 128.0, 127.9, 127.8, 94.4, 76.0, 75.7, 71.5, 71.3, 68.6, 66.3, 37.0, 34.4, 29.7, 25.4, 25.1, 19.0, 18.3.\]

\[\text{HRMS (ESI) m/z calcd for C}_{34}\text{H}_{42}\text{O}_{6} [\text{M+Na}]^{+} 569.28736, \text{ found 569.28816, } \Delta \text{ ppm 1.405.}\]
To a solution of SI-8 (107 mg, 0.2 mmol) in 1,4-dioxane (10 mL), lithium hydroxide monohydrate (24 mg, 0.6 mmol) in H₂O (0.5 mL) was added, and the resulting mixture was stirred at 60 °C for 12 hours. Glacial acetic acid (1 mL) was added, and the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-40% ethyl acetate in hexane afforded 29 (75 mg, 82%) as a clear oil.

**1H NMR (600 MHz, chloroform-d):** δ (ppm) 7.37-7.27 (m, 10H), 4.80 (br s, 1H), 4.59 (d, J = 11.5 Hz, 1H), 4.58 (d, J = 12.4 Hz, 1H), 4.55 (d, J = 12.4 Hz, 1H), 4.49 (d, J = 11.5 Hz, 1H), 3.82-3.74 (m, 2H), 3.56-3.54 (m, 1H), 3.47 (ddd, J = 11.1, 9.6, 4.3 Hz, 1H), 2.35 (t, J = 7.4 Hz, 2H), 2.23 (dt, J = 13.3, 3.8 Hz, 1H), 1.75 (ddd, J = 13.3, 11.1, 2.9 Hz, 1H), 1.69-1.35 (m, 6H), 1.30 (d, J = 6.2 Hz, 3H), 1.08 (d, J = 6.1 Hz, 3H). **13C NMR (151 MHz, chloroform-d):** δ (ppm) 179.6, 138.6, 138.5, 128.5, 128.0, 127.83, 127.80, 94.3, 76.0, 75.7, 71.4, 71.3, 71.0, 68.6, 36.9, 34.1, 29.7, 25.3, 24.8, 19.0, 18.2. **HRMS (ESI) m/z** calcd for C₁₇H₃₆O₆ [M-H]⁻ 455.24391, found 455.24452, Δ ppm 1.335.

To a stirred solution of SI-1 (206 mg, 0.42 mmol) in dry dichloromethane (10 mL), trichloroacetonitrile (84 μL, 0.84 mmol) and 1,8-diazabicycloundec-7-ene (10 μL, 67 μmol) were added at room temperature. After 90 min, the reaction was concentrated in vacuo to evaporate most solvent. Flash column chromatography on silica using a gradient of 15-20% ethyl acetate in hexanes afforded 17 (266 mg, 100%) as a clear oil. A solution of 17 and 21 (87 mg, 0.5 mmol) in dry dichloromethane (10 mL) was cooled to 0 °C in an ice bath, trimethylsilyl trifluoromethanesulfonate (15 μL, 84 μmol) was added, and the solution was allowed to warm to room temperature. After an hour, the
reaction was quenched with sat. NaHCO₃, extracted with dichloromethane, dried over Na₂SO₄, and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded 23 (263 mg, 97%) as a clear oil.

**¹H NMR (600 MHz, chloroform-d):** δ (ppm) 7.74 - 7.71 (m, 2H), 7.69 - 7.64 (m, 4H), 7.57 - 7.53 (m, 1H), 7.40 - 7.27 (m, 8H), 4.88 - 4.86 (m, 1H), 4.74 (br s, 1H), 4.15 (q, J = 7.1 Hz, 2H), 3.87 (dq, J = 9.3, 6.2 Hz, 1H), 3.81 - 3.75 (m, 1H), 3.66 (ddd, J = 11.3, 9.2, 4.3 Hz, 1H), 2.36 (t, J = 7.5 Hz, 2H), 2.02 (ddd, J = 13.9, 11.3, 3.0 Hz, 1H), 1.87 (dt, J = 13.9, 3.8 Hz, 1H), 1.73 - 1.61 (m, 3H), 1.55 - 1.39 (m, 3H), 1.27 (t, J = 7.1 Hz, 3H), 1.26 (d, J = 6.2 Hz, 1H), 1.13 (d, J = 6.1 Hz, 3H), 1.06 (s, 9H).

**¹³C NMR (151 MHz, chloroform-d):** δ (ppm) 173.9, 165.5, 136.1, 136.0, 134.3, 133.4, 133.1, 130.1, 129.89, 129.86, 129.8, 128.3, 127.8, 127.7, 93.7, 72.2, 72.0, 70.5, 70.1, 60.6, 37.0, 34.5, 33.5, 27.2, 25.5, 25.2, 19.5, 19.3, 18.5. HRMS (ESI) m/z calcd for C₃₈H₅₀O₇Si [M+Na]⁺ 669.32180, found 669.32280, Δ ppm 1.492.

To a solution of 23 (263 mg, 0.4 mmol) in 1,4-dioxane (20 mL), lithium hydroxide monohydrate (100 mg, 2.4 mmol) in H₂O (2 mL) was added and the resulting mixture was stirred at 60 °C for 12 hours. Glacial acetic acid (2 mL) was added, and the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 20-50% ethyl acetate in hexanes afforded SI-9 (190 mg, 92%) as clear oil.

**¹H NMR (400 MHz, methanol-d₄):** δ (ppm) 7.73 - 7.64 (m, 4H), 7.47 - 7.36 (m, 6H), 4.56 (br s, 1H), 3.87 - 3.71 (m, 3H), 3.58 - 3.54 (m, 1H), 2.34 (t, J = 7.5 Hz, 2H), 1.83 - 1.77 (m, 2H), 1.71 - 1.40 (m, 6H), 1.11 (d, J = 5.9 Hz, 3H), 1.10 (d, J = 5.8 Hz, 3H), 1.05 (s, 9H). **¹³C NMR (100 MHz, methanol-d₄):** δ (ppm) 177.5, 137.09, 137.05, 135.0, 130.9, 130.8, 128.7, 128.6, 97.4, 72.2, 71.7, 71.3, 71.2, 69.7, 39.1, 39.0, 38.0, 36.9, 35.0, 27.5, 26.5, 26.0, 20.9, 20.1, 19.3, 18.7. HRMS (ESI) m/z calcd for C₂⁹H₄₂O₆Si [M-H]⁻ 513.26779, found 513.26821, Δ ppm 0.821.
Benzyl (R)-6-(((2R,3R,5R,6S)-3-(benzyloxy)-5-((tert-
butyldiphenylsilyloxy)-6-methyltetrahydro-2H-pyran-2-
yloxy)heptanoate (SI-10).

To a stirred solution of SI-9 (190 mg, 0.37 mmol) in dry N,N-dimethylformamide (10 mL),
benzyl bromide (0.35 mL, 2.95 mmol) and sodium hydride (71 mg, 2.95 mmol) were added.
After stirring overnight at room temperature, the reaction was quenched with sat. NaHCO₃,
extracted with ethyl acetate, dried over Na₂SO₄, and concentrated *in vacuo*. Flash column
chromatography on silica using a gradient of 0-10% ethyl acetate in hexane afforded SI-10 (194
mg, 75%) as clear oil.

**^1H NMR (600 MHz, chloroform-d):** δ (ppm) 7.74-7.68 (m, 4H), 7.44-7.12 (m, 14H), 7.09-
7.05 (m, 2H), 5.13 (s, 2H), 4.64 (br s, 1H), 4.15 (d, J = 12.5 Hz, 1H), 4.06 (d, J = 12.5 Hz, 1H), 3.80-
3.72 (m, 3H), 3.31-3.27 (m, 1H), 2.40 (t, J = 7.5 Hz, 2H), 1.83 (dt, J = 13.5 Hz, 3H), 1.74-1.35
(m, 7H), 1.25 (d, J = 6.1 Hz, 3H), 1.05 (s, 9H), 1.04 (d, J = 6.0 Hz, 3H).

**^13C NMR (151 MHz, chloroform-d):** δ (ppm) 173.6, 138.4, 136.3, 136.11, 136.05, 135.0, 134.8, 133.9, 129.9, 129.8,
129.7, 128.7, 128.4, 128.3, 127.9, 127.8, 127.7, 127.6, 127.5, 94.7, 75.7, 71.1, 70.4, 70.3, 70.1,
66.3, 37.0, 34.5, 32.5, 27.2, 26.7, 25.5, 25.1, 19.6, 19.1, 18.5. **HRMS (ESI) m/z** calcd for
C₄₃H₅₄O₆Si [M+Na]^+ 717.35819, found 717.35896, Δ ppm 1.078.

Benzyl (R)-6-(((2R,3R,5R,6S)-3-(benzyloxy)-5-hydroxy-6-
methyltetrahydro-2H-pyran-2-yl)oxy)heptanoate (26).

To a stirred solution of SI-10 (160 mg, 0.23 mmol) in tetrahydrofuran (3 mL), tetrabutylammonium fluoride solution (1M in THF, 1.4 mL, 1.4 mmol) was added. After stirring overnight, the reaction was concentrated *in vacuo*. Flash column
chromatography on silica using a gradient of 0-40% ethyl acetate in hexanes afforded 26 (76 mg, 72%) as
a clear oil.

**^1H NMR (400 MHz, chloroform-d):** δ (ppm) 7.40-7.26 (m, 10H), 5.11 (s, 2H), 4.79 (br s, 1H),
4.60 (d, J = 12.3 Hz, 1H), 4.57 (d, J = 12.3 Hz, 1H), 3.82-3.74 (m, 1H), 3.67-3.58 (m, 2H), 3.53-
3.50 (m, 1H), 2.37 (t, J = 7.4 Hz, 2H), 2.15 (dt, J = 13.5, 3.6 Hz, 1H), 1.77-1.34 (m, 6H), 1.27 (d, J = 5.5 Hz, 3H), 1.06 (d, J = 6.0 Hz, 3H).

**^13C NMR (151 MHz, chloroform-d):** δ (ppm) 173.8,
Benzy1 (R)-6-(((2R,3R,5R,6S)-3-(benzylOxy)-5-(((R)-6-
(((2R,3R,5R,6S)-3,5-bis(benzylOxy)-6-methyltetrahydro-2H-
pyran-2-yl)Oxy)heptanoyl)Oxy)-6-methyltetrahydro-2H-pyran-2-
yl)Oxy)heptanoate (SI-11).

To a stirred solution of 29 (17.4 mg, 0.038 mmol) in dry
dichloromethane (2 mL), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride
(EDC-HCl) (10.9 mg, 0.06 mmol) and 4-dimethylaminopyridine (7.0 mg, 0.06 mmol) were
added at room temperature. The resulting mixture was stirred for 30 min, and 26 (8.7 mg, 0.019
mmol) in dry dichloromethane (2 mL) was added. After 2 hours, the reaction was washed with
sat. NaHCO$_3$, extracted with ethyl acetate, dried over Na$_2$SO$_4$, and concentrated in vacuo. Flash
column chromatography on silica using a gradient of 0-30% ethyl acetate in hexanes afforded SI-
11 (10.5 mg, 62%) as a clear oil.

$^1$H NMR (400 MHz, chloroform-d): $\delta$ (ppm) 7.38-7.27 (m, 20H), 5.11 (s, 2H), 4.84 (ddd, $J$
= 11.0, 9.6, 4.5 Hz, 1H), 4.78 (br s, 1H), 4.77 (br s, 1H), 4.67 (d, $J$ = 12.1 Hz, 1H), 4.57 (d, $J$
= 12.1 Hz, 2H), 4.53 (d, $J$ = 12.1 Hz, 2H), 4.46 (d, $J$ = 12.1 Hz, 1H), 3.84-3.70 (m, 4H), 3.55 -
3.51 (m, 1H), 3.51-3.48 (m, 1H), 3.44 (ddd, $J$ = 10.9, 9.4, 4.2 Hz, 1H), 2.37 (t, $J$ = 7.5 Hz, 2H),
2.31-2.18 (m, 4H), 1.76-1.30 (m, 12H), 1.28 (d, $J$ = 6.2 Hz, 3H), 1.15 (d, $J$ = 6.2 Hz, 3H), 1.061
(d, $J$ = 6.1 Hz, 3H), 1.058 (d, $J$ = 6.0 Hz, 3H). HRMS (ESI) m/z calcd for C$_{54}$H$_{70}$O$_{11}$ [M+Na]$^+$
917.48103, found 917.48202, $\Delta$ ppm 1.075.

(R)-6-(((2R,3R,5R,6S)-5-(((R)-6-(((2R,3R,5R,6S)-3,5-dihydroxy-6-
methyltetrahydro-2H-pyran-2-yl)Oxy)heptanoyl)Oxy)-3-hydroxy-
6-methyltetrahydro-2H-pyran-2-yl)Oxy)heptanoic acid (dasc#1).
To a suspension of palladium on activated carbon (10 wt%, 11 mg, 1 μmol) in methanol (2 mL), SI-11 (10.5 mg, 12 μmol) in methanol (1 mL) was added under argon. After 5 min, argon was purged by flushing hydrogen through the reaction flask. The resulting mixture was stirred for 2 hours at room temperature. Subsequently, hydrogen was purged by flushing argon. After removing the catalyst particles from the solution by filtration, the filtrate was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-20% methanol in dichloromethane afforded dasc#1 (5.4 mg, 91%) as a clear oil.

1H NMR (600 MHz, methanol-d4): δ (ppm) 4.86 (ddd, J = 11.3, 9.6, 4.7 Hz, 1H), 4.64 (br s, 1H), 3.84 (dq, J = 9.6, 6.3 Hz, 1H), 3.82-3.76 (m, 2H), 3.73-3.70 (m, 2H), 3.61 (dq, J = 9.5, 6.3 Hz, 1H), 3.52 (ddd, J = 11.4, 9.5, 4.5 Hz, 1H), 2.34 (t, J = 7.4 Hz, 2H), 2.30 (t, J = 7.4 Hz, 2H), 2.04 (dt, J = 13.0, 4.0 Hz, 1H), 1.95 (dt, J = 13.2, 3.9 Hz, 1H), 1.83 (ddd, J = 13.0, 11.3, 3.1 Hz, 1H), 1.76 (ddd, J = 13.1, 11.4, 3.1 Hz, 1H), 1.69-1.37 (m, 12H), 1.22 (d, J = 6.3 Hz, 3H), 1.138 (d, J = 6.3 Hz, 3H), 1.135 (d, J = 6.0 Hz, 3H), 1.12 (d, J = 6.0 Hz, 3H).

13C NMR (151 MHz, methanol-d4): δ (ppm) 177.1, 174.6, 97.8, 97.6, 72.8, 72.3, 71.4, 71.3, 70.1, 69.6, 68.44, 68.40, 38.09, 38.07, 36.1, 35.3, 35.2, 33.1, 26.5, 26.4, 26.2, 26.1, 19.39, 19.37, 18.24, 18.19.

1.5 Synthesis of mbas#3


To a stirred solution of SI-1 (132 mg, 0.28 mmol) in dry dichloromethane (4 mL), trichloroacetonitrile (56 μL, 0.56 mmol) and 1,8-diazabicycloundecene (5 μL, 33 μmol) were added at room temperature. After 90 min, the reaction was concentrated in vacuo to evaporate most solvent. Flash column chromatography on silica using a gradient of 15-20% ethyl acetate in hexanes afforded 17 (176.7 mg, 99%) as clear oil. A stirred solution of 17 and 20 (67.5 mg, 0.34 mmol) in dry dichloromethane (4 mL) was cooled to 0 °C in an ice bath, trimethylsilyl trifluoromethanesulfonate (10 μL, 56 μmol) was added, and the solution was allowed to warm to room temperature. After one hour, the reaction was quenched with sat. NaHCO3, extracted with dichloromethane, dried over Na2SO4, and concentrated in
Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded 22 (185.4 mg, 98%) as a clear oil.

$^1$H NMR (600 MHz, chloroform-d): $\delta$ (ppm) 7.75-7.71 (m, 2H), 7.69-7.64 (m, 4H), 7.57-7.53 (m, 1H), 7.40-7.27 (m, 8H), 7.00 (dt, $J = 15.5$, 7.0 Hz, 1H), 5.85 (dt, $J = 15.5$, 1.5 Hz, 1H), 4.88-4.86 (m, 1H), 4.74 (br s, 1H), 4.19 (q, $J = 7.1$ Hz, 2H), 3.87 (dq, $J = 9.2$, 6.2 Hz, 1H), 3.81-3.75 (m, 1H), 3.66 (ddd, $J = 11.3$, 9.2, 4.3 Hz, 1H), 2.26 (dq, $J = 7.0$, 1.5 Hz, 2H), 2.03 (ddd, $J = 13.9$, 11.3, 3.0 Hz, 1H), 1.87 (dt, $J = 13.9$, 3.7 Hz, 1H), 1.67-1.38 (m, 6H), 1.29 (t, $J = 7.1$ Hz, 3H), 1.26 (d, $J = 6.2$ Hz, 1H), 1.13 (d, $J = 6.1$ Hz, 3H), 1.06 (s, 9H).

$^{13}$C NMR (151 MHz, chloroform-d): $\delta$ (ppm) 166.9, 165.5, 149.3, 136.1, 136.0, 134.3, 133.4, 133.1, 130.1, 130.1, 129.9, 129.8, 128.3, 127.8, 127.7, 121.6, 93.7, 72.3, 72.0, 70.5, 70.0, 60.3, 37.1, 33.5, 32.4, 28.2, 27.2, 25.6, 19.5, 19.1, 18.6. HRMS (ESI) m/z calcd for C$_{40}$H$_{52}$O$_7$Si [M+Na]$^+$ 695.33745, found 695.33826, $\Delta$ ppm 1.163.


To a solution of 22 (171 mg, 0.25 mmol) in 1,4-dioxane (10 mL), lithium hydroxide monohydrate (64 mg, 1.5 mmol) in H$_2$O (2 mL) was added, and the resulting mixture was stirred at 60 °C for 12 hours. Glacial acetic acid (2 mL) was added, and the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 20-50% ethyl acetate in hexanes afforded SI-12 (118.6 mg, 88%) as a clear oil.

$^1$H NMR (600 MHz, chloroform-d): $\delta$ (ppm) 7.70-7.64 (m, 4H), 7.45-7.34 (m, 6H), 7.10 (dt, $J = 15.7$, 7.0 Hz, 1H), 5.85 (dt, $J = 15.7$, 1.4 Hz), 4.59 (br s, 1H), 3.80-3.73 (m, 2H), 3.68-3.61 (m, 2H), 2.28 (dq, $J = 7.0$, 1.4 Hz, 2H), 1.84 (ddd, $J = 13.4$, 10.9, 2.9 Hz, 1H), 1.78 (dt, $J = 13.4$, 4.2Hz, 1H), 1.65-1.38 (m, 6H), 1.16 (d, $J = 6.3$ Hz, 3H), 1.10 (d, $J = 6.3$ Hz, 3H), 1.05 (s, 9H).
13C NMR (151 MHz, chloroform-\textit{d}): \( \delta \) (ppm) 170.7, 151.5, 136.1, 134.6, 133.8, 129.9, 129.8, 127.8, 127.6, 121.0, 96.3, 71.6, 70.2, 70.0, 69.3, 50.8, 37.1, 35.8, 32.5, 28.1, 27.2, 25.5, 19.5, 19.1, 18.3. HRMS (ESI) \textit{m/z} calcd for C\textsubscript{31}H\textsubscript{44}O\textsubscript{6}Si [M-H]\textsuperscript{−} 539.28344, found 539.28407, \( \Delta \) ppm 1.170.


To a stirred solution of SI-12 (40 mg, 74 \( \mu \)mol) in dry dichloromethane (2 mL), 4-methoxybenzyl-2,2,2-trichloroacetimidate (184 \( \mu \)L, 0.888 mol) was added and the resulting mixture was cooled to 0 °C.

One drop of boron trifluoride diethyl etherate was added to the reaction, which was slowly warmed to room temperature and stirred overnight. The reaction was quenched with sat. NaHCO\textsubscript{3}, extracted with dichloromethane, dried over Na\textsubscript{2}SO\textsubscript{4}, and concentrated \textit{in vacuo}. Flash column chromatography on silica using a gradient of 0-20% ethyl acetate in hexanes afforded SI-13 together with reagent not separated from product (67.1 mg) as a clear oil.

The obtained product was dissolved in tetrahydrofuran (2 mL), and tetrabutylammonium fluoride solution (1M in THF, 0.34 mL, 0.34 mmol) was added. After stirring 72 hours*, the reaction was concentrated \textit{in vacuo}. Flash column chromatography on silica using a gradient of 0-50% ethyl acetate in hexanes afforded 25 (10.1 mg, 43.4% BRSM over 2 steps) as a clear oil.

\textbf{1H NMR (600 MHz, methanol-\textit{d}4):} \( \delta \) (ppm) 7.31-7.25 (m, 4H), 6.98 (dt, \( J = 15.5, 7.1 \) Hz, 1H), 6.91-6.88 (m, 4H), 5.86 (dt, \( J = 15.5, 1.4 \) Hz, 1H), 5.08 (s, 2H), 4.69 (br s, 1H), 4.52 (d, \( J = 11.7 \) Hz, 1H), 4.47 (d, \( J = 11.7 \) Hz, 1H), 3.782 (s, 3H), 3.778 (s, 3H), 3.77-3.72 (m, 1H), 3.60 (dq, \( J = 9.4, 6.3 \) Hz, 1H), 3.50-3.48 (m, 1H), 3.46 (ddd, \( J = 11.4, 9.4, 4.5 \) Hz, 1H), 2.23 (dt, \( J = 6.7, 1.4 \) Hz, 2H), 2.06 (dt, \( J = 13.2, 3.7 \) Hz, 1H), 1.56-1.35 (m, 6H), 1.19 (d, \( J = 6.3 \) Hz, 3H), 1.05 (d, \( J = 6.1 \) Hz, 3H). \textbf{13C NMR (151 MHz, methanol-\textit{d}4):} \( \delta \) (ppm) 168.1, 161.2, 160.9, 153.2, 151.2, 131.6, 131.1, 130.6, 129.6, 122.2, 114.9, 114.8, 95.5, 77.0, 72.5, 71.9, 71.2, 68.6, 66.9, 55.7, 38.0, 33.5, 33.1, 29.0, 27.0, 26.4, 19.4, 18.1. \textbf{HRMS (ESI) \textit{m/z} calcd for C\textsubscript{31}H\textsubscript{42}O\textsubscript{8} [M+Na]\textsuperscript{+} 565.27719, found 565.27778, \( \Delta \) ppm 1.045.

*Note: Subsequent trials proved that reaction time could be significantly reduced by heating up to 45°C.
4-methoxybenzyl \((R,E)-8-(((2R,3R,5R,6S)-3-(4-

To a stirred solution of 25 (4.0 mg, 7.4 μmol) in dry dichloromethane (100 μL), tiglic acid (2.95 mg, 29.5 μmol), \(N,N'\)-dicyclohexylcarbodiimide (6.09 mg, 29.5 μmol), and 4-dimethylaminopyridine (2 mg, 3 μmol) were added at room temperature. After stirring overnight, the reaction was diluted with dichloromethane, quenched with sat. NaHCO\(_3\), extracted with dichloromethane, dried over Na\(_2\)SO\(_4\), and concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-30% ethyl acetate in hexanes afforded SI-14 (3.5 mg, 76%) as a clear oil.

\(^1\)H NMR (600 MHz, chloroform-\(d\)): δ (ppm) 7.32-7.27 (m, 4H), 6.99 (dt, \(J = 15.7, 6.9\) Hz, 1H), 6.91-6.81 (m, 5H), 5.84 (dt, \(J = 15.7, 1.5\) Hz, 1H), 5.10 (s, 2H), 4.87 (ddd, \(J = 11.1, 9.7, 4.4\) Hz, 1H), 4.76 (br s, 1H), 4.63 (d, \(J = 11.8\) Hz, 1H), 4.47 (d, \(J = 11.8\) Hz, 1H), 3.85 (dq, \(J = 9.7, 6.3\) Hz, 1H), 3.81 (s, 3H), 3.79 (s, 3H), 3.79-3.73 (m, 1H), 2.31 (dt, \(J = 13.3, 3.8\) Hz, 1H), 2.20 (dq, \(J = 7.2, 1.5\) Hz, 2H), 1.83 (s, 3H), 1.79 (d, \(J = 7.1\) Hz, 3H), 1.73 (ddd, \(J = 13.3, 11.8, 2.9\) Hz, 1H), 1.60-1.35 (m, 6H), 1.17 (d, \(J = 6.3\) Hz, 3H), 1.07 (d, \(J = 6.1\) Hz, 3H). HRMS (ESI) m/z calcd for C\(_{36}\)H\(_{48}\)O\(_9\) [M+Na]\(^+\) 647.31905, found 647.31943, Δ ppm 0.581.


To a stirred solution of SI-14 (3.5 mg, 5.6 μmol) in dry dichloromethane (1 mL), trifluoroacetic acid (50 μL) was added at room temperature. After stirring 30 min, the reaction was concentrated in vacuo. Flash column chromatography on silica using a gradient of 0-100% ethyl acetate in hexanes afforded mbas#3 (1.7 mg, 79%) as a clear oil. Spectroscopic data were identical to those reported previously [4].
2. References


3. NMR spectra
*This is a mixture of 27 and SI-4
Baseline corrected by Whittaker Smoother method