Structure Elucidation of Nigricanoside A Through Enantioselective Total Synthesis

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Figure S3. Comparison of synthetic nigricanoside A dimethyl ester 2 to natural product (6.20-5.00 ppm). Spectrum of the natural product kindly provided by Prof. Raymond Andersen. * = OH peak.



Figure S4. Comparison of synthetic nigricanoside A dimethyl ester **2** to natural product (4.85-3.30 ppm). Spectrum of the natural product kindly provided by Prof. Raymond Andersen. * = OH peak.



Figure S5. Comparison of synthetic nigricanoside A dimethyl ester **2** to natural product (2.70-0.70 ppm). Spectrum of the natural product kindly provided by Prof. Raymond Andersen.

Table S1. ¹H and ¹³C NMR Data for synthetic Nigricanoside A Dimethyl Ester **2** in 25:2 C₆D₆/DMSO- d_6 QH



			<u></u>	
position	$\delta_{\rm C}$ (synthetic	$\delta_{\rm C}$ (natural product)	$\delta_{\rm H}$, mult (<i>J</i> in Hz)	$\delta_{\rm H}$, mult (<i>J</i> in Hz)
1	172 44 C	172.5	(synthetic product 2)	(natural product)
1	173.44, C	175.5	2.17	2.17
2	34.17, CH ₂	34.16	2.17	2.17
			1.62 m	1.62
3	25.37, CH ₂	25.36	1.02, m	1.62
		25.56	1.62, m	1.62
4	25.57, CH ₂		1.53. m	1.53. m
_		37.84	1.56, m	1.56, m
5	37.84, CH ₂		1.65, m	1.65
6	71.48, CH	71.46	4.25, m	4.25
7	136.29, CH	136.29	5.99, dd (15.6, 5.8)	6.00, dd (15.5, 5.5)
8	129.35, CH	129.34	6.11, dd (15.5, 6.3)	6.11, dd (15.5, 6.4)
9	73.20, CH	73.17	4.49, m	4.50, m
10	81.73, CH	81.74	3.78, m	3.78, m
	00 47 CVV	20.45	2.45, m	2.45, m
11	29.47, CH ₂	29.45	2.58, m	2.58, m
12	127.51, CH	127.52	5.68, m	5.68, m
13	131.32, CH	131.32	5.55, m	5.55, m
1.4	20.99 CH	20.97	2.11, ddd (7.3, 7.3, 7.3)	2.12, ddd (7.4, 7.4, 7.4)
14	29.88, CH ₂	29.87	2.11, ddd (7.3, 7.3, 7.3)	2.12, ddd (7.4, 7.4, 7.4)
15	23.18, CH ₂	23.16	1.40, qdd (7.4, 7.4, 7.4)	1.40, qdd (7.4, 7.4, 7.4)
15		23.10	1.40, qdd (7.4, 7.4, 7.4)	1.40, qdd (7.4, 7.4, 7.4)
16	14.13, CH ₃	14.11	0.92, t (7.4)	0.92, t (7.4)
$1-OCH_3$	51.10, CH ₃	51.10	3.42, s	3.41, s
6-OH			4.60, d (4.6)	4.55, d (4.5)
9-OH			5.10, d (4.7)	5.06, d (4.6)
1'	173.58, C	173.6		
2'	33.39, CH ₂	33.38	2.16	2.16
2			2.16	2.16
3'	25.06, CH ₂	25.05	1.62	1.62
			1.62	1.62
4'	26.99, CH ₂	26.98	2.01, ddd (7.4, 7.4, 7.4)	2.01, ddd (7.4, 7.4, 7.4)
5'	130.52, CH	130.52	5.41, m	5.41, m
6'	126.99, CH	126.99	5.59, m	5.59, m
7'	34.17, CH ₂	34.16	2.31, m	2.32, m
	, _		2.48	2.48
8'	80.84, CH	80.84	3.81	3.80
9'	134.70, CH	134.70	5.74, dd (15.7, 7.5)	5./4, dd (15.7, 7.6)
10'	131.32, CH	131.34	5.88, dd (15.7, 7.4)	5.88, dd (15.7, 7.5)
11'	83.08, CH	83.08	4.26	4.26
12'	73.83, CH	73.84	3.96	3.96
13'	30.67, CH ₂	30.66	2.53	2.53
			2.53	2.53

14'	127.51, CH	127.55	5.81, m	5.81, m
15'	131.28, CH	131.27	5.55, m	5.55, m
16'	27.86 CH	27.95	2.15	2.15
	$27.80, CH_2$	27.83	2.15	2.15
17'	20.78 CH	20.77	1.29	1.29
	29.78, CH ₂	29.11	1.38	1.38
1.01	31.85 CH	31.84	1.29	1.29
10	51.65, CH2	51.04	1.29	1.29
19'	22.96 CH ₂	22.95	1.29	1.29
19	222.90, CH2	22.95	1.29	1.29
20'	14.32, CH ₃	14.31	0.88, bt (6.8)	0.88, bt (7.0)
1'-OCH3	51.00, CH ₃	51.0	3.38, s	3.37, s
12'-OH			4.82, d (5.5)	4.79, d (5.7)
1"	105.10, CH	105.11	4.41, d (7.7)	4.41, d (7.7)
2"	71.99, CH	71.98	3.95	3.95
3"	74.51, CH	74.50	3.68, m	3.69, m
4"	69.22, CH	69.22	4.03, m	4.03, m
5"	74.51, CH	74.51	3.65, bt (5.9)	3.65, bt (6.1)
6"	68.07, CH ₂	68.06	3.72, dd (9.5, 6.0)	3.72, dd (9.6, 6.1)
		08.00	4.01, dd (9.5, 6.3)	4.01, dd (9.6, 6.1)
2"-ОН			5.29, d (3.2)	5.26, bs
3"-ОН			4.72, d (5.6)	4.68, bs
4"-OH			4.33, d (4.1)	4.30, d (3.8)
1'''	72.39, CH ₂	72.40	3.93, dd (10.3, 3.9)	3.94, dd (10.4, 4.0)
		/2.40	4.15, dd (10.5, 5.6)	4.14, dd (10.4, 5.6)
2'''	71.59, CH	71.58	4.08, m	4.09, m
3"'	64.07, CH ₂	64.07	3.88, m	3.88, m
		04.07	3.88, m	3.88, m
2'''-ОН			4.81, d (5.6)	4.79, d (5.7)
3'''-OH			4.44, bt (6.0)	4.39, m

Methods and Materials

General: Unless otherwise stated, reactions were performed under argon using freshly purified solvents, which were purified using solvent purification columns purchased from Glass Contour, Laguna Beach, CA. All Reactions were monitored by thin-layer chromatography with E. Merck silica gel 60 F₂₅₄ pre-coated plates (0.25 mm). Flash chromatography was performed with indicated solvents using silica gel (particle size 40-63 µm) purchased from Sorbent Technologies. ¹H and ¹³C NMR spectra were recorded on Varian Inova- 400 MHz, 500 MHz or 600 MHz spectrometer. Chemical shift are reported relative to internal chloroform (CDCl₃: ¹H, δ = 7.26 ppm, ¹³C, δ = 77.00 ppm), benzene (C₆D₆: ¹H, δ = 7.15 ppm, ¹³C, δ = 128.00 ppm), methanol (CD₃OD: ¹H, δ = 3.31 ppm, ¹³C, δ = 49.20 ppm) and Coupling constants are in Hz and are reported as d (doublet), t (triplet), q (quartet), and m (multiplet). Optical rotations were measured on a Rudolph Research Analytical Autopol® IV Polarimeter (50/60 Hz).Mass spectra were acquired on an Agilent Technologies 1200 series LC/MS using indicated ionization methods. Cytotoxicity measurements: HCT116 cells were plated in 96-well plates (1500, 5400, 1500 cells, respectively) in 10%RPMI + L-g+PenStrep (HCT116) or 5% RPMI + L-g media. DMSO or compound was added, at 5.5 mM to 0.85 nM in 3-fold dilutions, in duplicate. After 4 days at 37 °C, cell proliferation was measured using CellTiterGlow. IC₅₀ data was calculated using Prism 6.

Materials. Chemicals were purchased from Aldrich, Fisher or Alfa Aesar, TCI, and used without purification.



Glycidyl ether (*R*)-**6** was obtained from the reaction of commercially available (S)-glycidol (from Aldrich) with NaH (60% in mineral oil) and PMBCl in DMF following a known procedure¹.

To a stirred solution of 5-hexynoic acid tert-butyl ester 5^2 (4.4 g, 26 mmol, 1.3 equiv) in 400 mL THF at -78°C was added *n*-BuLi (9.6 mL, 24 mmol, 1.2 equiv). After stirring for 1 h at -

78 °C, BF₃·OEt₂ (2.5 mL, 20 mmol, 1.0 equiv) was added *n*-bull (9.6 mL, 24 mmol, 1.2 equiv). After stiring for 1 mat -78 °C, BF₃·OEt₂ (2.5 mL, 20 mmol, 1.0 equiv) was added slowly to the stirred solution at this temperature. The solution was stirred for 20 minutes, at which time glycidyl ether (*R*)-**6** (3.88 g in 20 mL THF, 20 mmol, 1.0 equiv) was added dropwise at -78 °C. The reaction was allowed to warm to room temperature and stirred overnight at this temperature. Then the reaction was quenched with saturated aqueous NH₄Cl, and extracted 3 times with Et₂O. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (5-25% EtOAc in hexanes) to afford the product **7** (5.39 g, 74% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.26 (d, *J* = 7.7 Hz, 2H), 6.88 (d, *J* = 7.1 Hz, 2H), 4.49 (s, 2H), 3.90 (qd, *J* = 6.4, 4.0 Hz, 1H), 3.80 (s, 3H), 3.56 (dd, *J* = 9.6, 3.9 Hz, 1H), 3.45 (dd, *J* = 9.1, 7.1 Hz, 1H), 2.43–2.35 (m, 2H), 2.30 (t, *J* = 7.4 Hz, 2H), 2.23–2.16 (m, 2H), 1.80–1.69 (m, 2H), 1.44 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.58, 159.26, 129.97, 129.38, 113.79, 81.62, 80.25, 76.37, 73.05, 72.69, 69.09, 55.25, 34.42, 28.09, 24.24, 23.86, 18.16; [α]_D²⁰ = -6.8 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₂₁H₃₀O₅Na (M+Na)⁺ 385.2, found 385.1; HRMS(ESI) calcd for C₂₁H₃₀O₅Na (M+Na)⁺ 385.1991, found 385.1982.



A stirred mixture of alcohol **7** (3.3 g, 9.1 mmol, 1.0 equiv), quinoline (32 μL, 0.27 mmol, 3 mol%), and Lindlar catalyst (~5% palladium on calcium carbonate; poisoned with lead) (0.388 g, 0.18 mmol, 2 mol %) in EtOAc (50 mL) was sparged

with N₂ for 15 minutes. H₂ gas was then bubbled through the stirred mixture for 1 h. The reaction was filtered through a plug of Celite, and purified by flash chromatography (5-25% EtOAc in hexanes) to afford the product **a** (3.2 g, 96% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.25 (d, J = 8.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 5.54–5.34 (m, 2H), 4.47 (s, 2H), 3.87–3.80 (m, 1H), 3.80 (s, 3H), 3.48 (dd, J = 9.5, 3.4 Hz, 1H), 3.33 (dd, J = 9.4, 7.4 Hz, 1H), 2.43 (s, 1H), 2.28–2.16 (m, 4H), 2.12–2.01 (m, 2H), 1.71–1.56 (m, 2H), 1.43 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.01, 159.23, 131.57, 129.99, 129.37, 125.59, 113.78, 80.05, 73.63, 73.00, 70.20, 55.23, 34.92, 31.27, 28.06, 26.56, 24.85; [α]_D²⁰ = +1.4 (c = 1.0, CHCl₃); MS(ESI) calcd for C₂₁H₃₂O₅Na (M+Na)⁺ 387.2, found 387.2; HRMS(ESI) calcd for C₂₁H₃₂O₅Na (M+Na)⁺ 387.2147, found 387.2149.

t-BuO₂C

To a stirred solution of alcohol **a** (5.95 g, 16 mmol, 1.0 equiv) in 160 mL DCM at 0 °C was added *i*-Pr₂NEt (5.7 mL, 33 mmol, 2.0 equiv). Then SEMCl (2-(Trimethylsilyl)ethoxymethyl chloride) (4.4 mL, 25 mmol, 1.5equiv) was added

slowly to the stirred solution at this temperature. The reaction was allowed to warm to room temperature and stirred overnight. Then the reaction was quenched with H₂O, and extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (5-10% EtOAc in hexanes) to afford the product **b** (7.79 g, 96% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.26–7.21 (m, 2H), 6.89–6.83 (m, 2H), 5.49–5.35 (m, 2H), 4.74 (dd, *J* = 18.3, 7.0 Hz, 2H), 4.53–4.40 (m, 2H), 3.83–3.74 (m, 1H), 3.80 (s, 3H), 3.69–3.56 (m, 2H), 3.45 (d, *J* = 5.1 Hz, 2H), 2.35–2.27 (m, 2H), 2.24–2.16 (m, 2H), 2.11–2.00 (m, 2H), 1.70–1.57 (m, 2H), 1.43 (s, 9H), 0.94–0.83 (m, 2H), -0.00 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.99, 159.08, 131.04, 130.35, 129.16, 125.96, 113.69, 93.98, 79.99, 75.59, 72.93, 71.85, 65.02, 55.23, 35.01, 29.83, 28.09, 26.69, 24.90, 18.03, -1.45; [α]_D²⁰ = +3.8 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₂₇H₅₀NO₆Si (M+NH₄)⁺ 512.3, found 512.3; HRMS(ESI) calcd for C₂₇H₄₀O₆SiNa (M+Na)⁺ 517.2961, found 517.2969.

¹ a) Dias, L. C.; Ferreira, M. A. B. *J. Org. Chem.* **2012**, *77*, 4046. b) White, J. D.; Lincoln, C. M.; Yang, J.; Martin, W. H. C.; Chan, D. B. J. Org. Chem. **2008**, *73*, 4139.

² McGinley, C. M.; Jacquot, C.; van der Donk, W. A. Bioorg. Med. Chem. Lett. 2007, 17, 4049.



DDQ (2.64 g, 11.6 mmol, 1.5 equiv) was added to a biphasic solution of PMB ether **b** (137 mg, 0.10 mmol) in 50 mL DCM and 2.5 mL phosphate buffer (pH = 7) at 0 °C. The resulting solution was stirred for 1 h at 0 °C, then warmed to room temperature

for additional 1.5 h. Then the reaction was quenched with saturated aqueous NaHCO₃ solution and extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (5-25% EtOAc in hexanes) to afford the product **c** (2.81g, 97% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.53–5.32 (m, 2H), 4.79 (d, *J* = 7.1 Hz, 1H), 4.70 (d, *J* = 7.2 Hz, 1H), 3.81–3.69 (m, 1H), 3.64–3.53 (m, 3H), 3.53–3.43 (m, 1H), 3.24 (s, 1H), 2.32–2.15 (m, 4H), 2.11–1.98 (m, 2H), 1.69–1.57 (m, 2H), 1.43 (s, 9H), 1.03–0.87 (m, 2H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.98, 131.32, 125.52, 95.07, 81.74, 80.08, 65.69, 65.28, 34.94, 29.69, 28.09, 26.66, 24.83, 18.10, -1.49; [α]_D²⁰ = -27.6 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₁₉H₃₉O₅Si (M+H)⁺ 375.3, found 375.2; HRMS(ESI) calcd for C₁₉H₃₈O₅SiNa (M+Na)⁺ 397.2386, found 397.2382.



NaHCO₃ (6.24 g, 74.2 mmol, 5.0 equiv) was added to the solution of the alcohol **c** (5.56 g, 14.8 mmol, 1.0 equiv) in 150 mL DCM at 0 °C. Dess-Martin periodinane (7.56 g, 17.8 mmol, 1.2 equiv) was added to the stirred suspension in 3 portions. After stirring overnight at this temperature, the reaction was concentrated. Then the reaction

was quenched with a solution of 20% aqueous Na₂S₂O₃/saturated aqueous NaHCO₃ (1:1), and extracted three times with EtOAc, The combined organic layer was washed with brine, and dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-10% EtOAc in hexanes) to afford the product **8** (4.95 g, 90% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 9.61 (d, *J* = 1.9 Hz, 1H), 5.55–5.33 (m, 2H), 4.74 (dd, *J* = 19.6, 7.0 Hz, 2H), 3.93 (td, *J* = 6.5, 1.8 Hz, 1H), 3.75–3.57 (m, 2H), 2.43 (t, *J* = 6.5 Hz, 2H), 2.19 (t, *J* = 7.5 Hz, 2H), 2.13–1.97 (m, 2H), 1.70–1.56 (m, 2H), 1.42 (s, 9H), 0.97–0.79 (m, 2H), 0.00 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 202.52, 172.86, 132.37, 123.77, 94.80, 81.65, 80.05, 65.76, 34.86, 28.15, 28.05, 26.62, 24.70, 17.91, -1.49; [α]_D²⁰ = +14.6 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₁₉H₃₆O₅SiNa (M+Na)⁺ 395.2, found 395.2; HRMS(ESI) calcd for C₁₉H₃₆O₅SiNa (M+Na)⁺ 395.2230, found 395.2217.



A solution of MeONa (5.4 M in MeOH, 2.6 mL, 4.0 equiv) in 70 mL THF was cooled to -78 °C. Dimethyl 1-diazo-2-oxopropylphosphonate 9^3 (2.69 g, 14.0 mmol, 4.0 equiv) in 70 mL THF was added to the above solution at -78 °C. After 15 minutes, the aldehyde (1.30 g, 3.5 mmol, 1.0 equiv) was added to the stirred solution at -78 °C.

After stirring for 0.5 h at this temperature, the reaction was quenched with saturated aqueous NH₄Cl at 0 °C, and extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-10% EtOAc in hexanes) to afford the product **10** (1.21 g, 94% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.56–5.32 (m, 2H), 4.87 (d, *J* = 7.0 Hz, 1H), 4.63 (d, *J* = 7.0 Hz, 1H), 4.30 (td, *J* = 6.5, 2.0 Hz, 1H), 3.71–3.61 (m, 1H), 3.55–3.46 (m, 1H), 2.44 (t, *J* = 5.9 Hz, 2H), 2.37 (d, *J* = 2.0 Hz, 1H), 2.17 (t, *J* = 7.5 Hz, 2H), 2.10–2.00 (m, 2H), 1.70–1.53 (m, 2H), 1.40 (s, 9H), 0.96–0.81 (m, 2H), -0.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.77, 131.79, 124.72, 92.25, 82.26, 79.85, 73.45, 65.30, 64.84, 34.83, 33.42, 28.01, 26.69, 24.75, 17.93, -1.52; [α]_D²⁰ = +87.2 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₂₀H₃₆O₄SiNa (M+Na)⁺ 391.2, found 391.2; HRMS(ESI) calcd for C₂₀H₃₆O₄SiNa (M+Na)⁺ 391.2281, found 391.2280.

The (*R*) and (*S*) Mosher's esters were synthesized from deprotecting SEM product of **10** and the (*S*) and (*R*) acid chloride, respectively (pyridine, DMAP, CH_2Cl_2 , rt, 2 h). The resulting differences in chemical shifts are consistent with (*R*) stereochemistry at C8' as shown.

³ Wijtmans, M.; de Graaf, C.; de Kloe, G.; Istyastono, E. P.; Smit, J., Lim, H.; Boonnak, R.; Nijmeijer, S.; Smits, R. A.; Jongejan, A.; Zuiderveld, O.; de Esch, I. J. P.; Leurs, R. *J. Med. Chem.* **2011**, *54*, 1693.





Glycidyl ether (S)-6 was obtained from the reaction of commercially available (R)-glycidol (from Aldrich) with NaH (60% in mineroil oil) and PMBCl in DMF following a known procedure⁴.

To a stirred solution of 1-heptyne (7.2 mL, 54.5 mmol, 2.0 equiv) in 150 mL THF at -78 °C was added *n*-BuLi (22 mL, 54.5 mmol, 2.0 equiv). After stirring for 1 h at -78

°C, BF₃·OEt₂ (5.2 mL, 40.9 mmol, 1.5 equiv) was added at this temperature. The solution was stirred for 15 minutes, at which time glycidyl ether (5.29 g in 20 mL THF, 27.3 mmol, 1.0 equiv) was added dropwise at -78 °C. The reaction was stirred at - 78 °C for 4 hours, quenched with saturated aqueous NH₄Cl, and extracted 3 times with Et₂O. The combined organic layer was washed with brine, dried with MgSO₄, filtered, and concentrated to afford the product as a yellow oil. The ¹HNMR spectrum of the crude sample was very clean and so the above alcohol was brought into the following reaction without further purification. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.18 (m, 2H), 6.91–6.79 (m, 2H), 4.48 (s, 2H), 3.94–3.83 (m, 1H), 3.79 (s, 3H), 3.55 (dd, *J* = 9.5, 3.9 Hz, 1H), 3.44 (dd, *J* = 9.5, 6.7 Hz, 1H), 2.42–2.35 (m, 2H), 2.16–2.06 (m, 2H), 1.87–1.78 (m, 2H), 1.38–1.21 (m, 4H), 0.87 (t, *J* = 7.1 Hz, 3H).

A stirred mixture of the above alcohol (3.29 g, 11.3 mmol, 1.0 equiv), quinoline (40 μ L, 0.34 mmol, 3 mol%), and Lindlar catalyst (~5% palladium on calcium carbonate; poisoned with lead) (481.6 g, 0.11 mmol, 1.0 mol %) in 120 mL EtOAc was sparged with N₂ for 15 minutes. H₂ gas was then bubbled through the stirred mixture for 1 hour. The reaction mixture was filtered through a plug of Celite and concentrated to afford the desired alkene as a yellow oil. The ¹HNMR spectrum of crude alkene was clean and therefore was used in the following reaction without further purification. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.21 (m, 2H), 6.90–6.83 (m, 2H), 5.55–5.43 (m, 1H), 5.42–5.32 (m, 1H), 4.47 (s, 2H), 3.85–3.76 (m, 1H), 3.79 (s, 3H), 3.48 (dd, *J* = 9.5, 3.2 Hz, 1H), 3.32 (dd, *J* = 9.4, 7.5 Hz, 1H), 2.29 (d, *J* = 3.5 Hz, 1H), 2.27–2.17(m, 2H), 2.08–1.94 (m, 2H), 1.37–1.16 (m, 6H), 0.87 (t, *J* = 6.8 Hz, 3H).

The alkene (5.6 g, 19.2 mmol, 1.0 equiv) was dissolved in 300 mL DCM. 4Å MS (8.4 g) and DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) (4.88 g, 21.1 mmol, 1.1 equiv) were added at 0 °C. The resulting solution was allowed to stir for 10 min at 0 °C, then warmed to room temperature and stirred for additional 2 hours. The reaction mixture was filtered, and the filtrate was washed with saturated aqueous NaHCO₃. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (3-25% EtOAc in hexanes) to afford the product **11** (3.7 g, 67% yield over three steps) as a mixture of diasteroisomers. ¹H NMR (400 MHz, CDCl₃) δ 7.47– 7.36 (m, 2H), 6.93–6.87 (m, 2H), 5.90, 5.76 (s, 1H), 5.61–5.49 (m, 1H), 5.46–5.34 (m, 1H), 4.32–4.17, 4.10–4.03 (m, 2H), 3.81, 3.80 (s, 3H), 3.77–3.71, 3.68–3.62 (m, 1H), 2.59–2.46 (m, 1H), 2.46–2.27 (m, 1H), 2.14–1.94 (m, 2H), 1.41–1.18 (m, 6H), 0.94–0.80 (m, 3H).

HO ÖPMB

d

To a stirred solution of the compound **11** (3.7 g, 12.7 mmol, 1.0 equiv) in 125 mL DCM at -78 °C was added DIBAL-H (diisobutylaluminium hydride, 1.0 M in DCM) (32 mL, 31.75 mmol, 2.5 equiv). After stirring for 0.5 hour at -78 °C, the reaction was quenched with 10% citric acid, and the heterogeneous mixture was stirred for 1 hour at room

temperature until two clear phases were present. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (3-25% EtOAc in hexanes) to afford the product **d** (2.93 g, 79% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.28 (d, *J* = 8.5 Hz, 2H), 6.89 (d, *J* = 8.5 Hz, 2H), 5.57–5.44

⁴ Nicolaou, K. C.; Li, Y.; Fylaktakidou, K. C.; Mitchell, H. J.; Wei, H.; Weyershausen, B. Angew. Chem. Int. Ed. **2001**, 40, 3849.

(m, 1H), 5.43–5.31 (m, 1H), 4.62 (d, J = 11.2 Hz, 1H), 4.47 (d, J = 11.4 Hz, 1H), 3.81 (s, 3H), 3.69–3.61 (m, 1H), 3.56–3.46 (m, 2H), 2.44–2.32 (m, 1H), 2.32–2.22 (m, 1H), 2.09–1.98 (m, 2H), 1.88 (s, 1H), 1.42–1.17 (m, 6H), 0.89 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 159.22, 132.62, 130.39, 129.34, 124.25, 113.81, 79.21, 71.14, 64.14, 55.20, 31.47, 29.17, 28.65, 27.28, 22.51, 14.01; $[\alpha]_D^{20} = +33.2$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₁₈H₂₈O₃Na (M+Na)⁺ 315.2, found 315.2; HRMS(ESI) calcd for C₁₈H₂₈O₃Na (M+Na)⁺ 315.1936, found 315.1924.



Pyridine (4.0 mL, 50.0 mmol, 5.0 equiv) was added to the solution of the alcohol **d** (2.93 g, 10.0 mmol, 1.0 equiv) in 70 mL DCM at 0 °C. Dess-Martin periodinane (5.2 g, 13.0 mmol, 1.2 equiv) was added to the stirred suspension in 2 portions. After stirring overnight at this temperature, the reaction was concentrated. Then the reaction was quenched with a solution of 20% aqueous Na₂S₂O₃/saturated aqueous NaHCO₃ (1:1), and extracted 3 times

with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-10% EtOAc in hexanes) to afford the product **12** (2.4 g, 82% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 9.62 (d, J = 2.1 Hz, 1H), 7.27 (d, J = 5.6 Hz, 2H), 6.88 (d, J = 8.6 Hz, 2H), 5.61–5.46 (m, 1H), 5.44–5.34 (m, 1H), 4.56 (q, J = 11.5 Hz, 2H), 3.80 (s, 3H), 3.76 (td, J = 6.5, 2.1 Hz, 1H), 2.46 (t, J = 6.8 Hz, 2H), 2.08–1.96 (m, 2H), 1.43–1.18 (m, 6H), 0.88 (t, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 203.40, 159.47, 133.51, 129.63, 129.30, 122.60, 113.86, 82.84, 72.20, 55.23, 31.44, 29.07, 28.32, 27.32, 22.50, 14.01; $[\alpha]_D^{-20} = -22.6$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₁₈H₂₆O₃Na (M+Na)⁺ 313.2, found 313.2; HRMS(ESI) calcd for C₁₈H₂₆O₃Na (M+Na)⁺ 313.1780, found 313.1772.



Cp₂Zr(H)Cl (1.47 g, 5.7 mmol, 1.5 equiv) was weighed and added to a flask in a glove box, suspended in 14 mL DCM and cooled to 0 °C. A solution of alkyne **10** (1.54 g, 4.2 mmol, 1.1 equiv) in 14 mL DCM was added to the stirred suspension of Cp₂Zr(H)Cl at 0 °C. Hydrozirconation was complete after 1.5

hours, after which the solution was cooled to -78 °C. At this time, a solution of Me₂Zn (2.0 M in toluene, 2.84 mL, 5.7 mmol, 2.0 equiv) was added slowly to the solution of vinyl zirconium at -78 °C. After stirring for 15 minutes at -78 °C, the reaction was allowed to warm to 0 °C. The solution was then allowed to stir for additional 15 minutes at 0 °C, after which a solution of the aldehyde **12** (1.10 g, 3.8 mmol, 1.0 equiv) in 7.0 mL toluene was added at the same temperature. The reaction was allowed to stir overnight at 0 °C. The reaction was quenched with a 10% aqueous solution of citric acid, and the heterogeneous mixture was stirred for 1 h at room temperature until two clear phases were present. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The combined organic portion was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (3-25% EtOAc in hexanes) to afford the desired alcohol (2.45 g) as a mixture of diastereoisomers.

NaHCO₃ (1.55 g, 18.5 mmol, 5.0 equiv) was added to the solution of the above alcohol (2.44 g, 3.7 mmol, 1.0 equiv) in 15 mL DCM at 0 °C. Dess-Martin periodinane (1.88 g, 4.4 mmol, 1.2 equiv) was added to the stirred suspension in 2 portions. After stirring overnight at this temperature, the reaction was concentrated. Then the reaction was quenched with a solution of 20% aqueous Na₂S₂O₃/saturated aqueous NaHCO₃ (1:1), and extracted three times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-15% EtOAc in hexanes) to afford the product **e** (2.07 g, 83% yield over two steps) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.25–7.19 (m, 2H), 6.91–6.80 (m, 3H), 6.65 (dd, *J* = 15.8, 1.1 Hz, 1H), 5.54–5.30 (m, 4H), 4.65 (d, *J* = 7.0 Hz, 1H), 4.60 (d, *J* = 7.0 Hz, 1H), 4.48 (d, *J* = 11.4 Hz, 1H), 4.34 (d, *J* = 11.4 Hz, 1H), 4.30–4.23 (m, 1H), 3.94–3.87 (m, 1H), 3.79 (s, 3H), 3.76–3.65 (m, 1H), 3.58–3.46 (m, 1H), 2.52–2.24 (m, 4H), 2.19 (t, *J* = 7.5 Hz, 2H), 2.09–2.00 (m, 2H), 2.00–1.93 (m, 2H), 1.70–1.55 (m, 2H), 1.43 (s, 9H), 1.35–1.17 (m, 6H), 0.96–0.75 (m, 5H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 200.60, 172.82, 159.30, 146.92, 133.04, 131.73, 129.52, 129.42, 124.87, 124.67, 123.28, 113.74, 92.78, 83.68, 79.99, 75.02, 71.78, 65.30, 55.20, 34.91, 32.72, 31.44, 30.37, 29.12, 28.07, 27.32, 26.73, 24.78, 22.51, 17.97, 14.02, -1.45; $[\alpha]_D^{20} = +14.6$ (*c* = 0.5, CHCl₃); MS(ESI) calcd for C₃₈H₆₂O₇SiNa (M+Na)⁺ 681.4163, found 681.4; HRMS(ESI) calcd for C₃₈H₆₂O₇SiNa (M+Na)⁺ 681.4163, found 681.4; HRMS(ESI) calcd for C₃₈H₆₂O₇SiNa (M+Na)⁺ 681.4163, found 681.4161.



Ketone e (2.07 g, 3.14 mmol, 1.0 equiv) was dissolved in 60 mL DCM and cooled to -78 °C. Super-Hydride (1.0 M in THF, 4.1 mL, 4.08 mmol, 1.3 equiv) was added slowly and the resulting solution was allowed to stir for 30 minutes at -78 °C. Then the reaction was guenched with a 10% aqueous solution

of citric acid, and the heterogeneous mixture was stirred for 1 hour at room temperature until two clear phases were present. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (3-25% EtOAc in hexanes) to afford the desired alcohol **13** (> 10:1 selectivity, 2.06 g, 97 % yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.19 (m, 2H), 6.92–6.82 (m, 2H), 5.73 (dd, *J* = 15.6, 6.0 Hz, 1H), 5.60 (ddd, *J* = 15.6, 7.4, 0.9 Hz, 1H), 5.50–5.36 (m, 4H), 4.67 (d, *J* = 6.9 Hz, 1H), 4.59 (d, *J* = 7.2 Hz, 1H), 4.57 (d, *J* = 11.2 Hz, 1H), 4.50 (d, *J* = 11.3 Hz, 1H), 4.29–4.22 (m, 1H), 4.13–4.04 (m, 1H), 3.80 (s, 3H), 3.78–3.69 (m, 1H), 3.54–3.47 (m, 1H), 3.47–3.40 (m, 1H), 2.43–2.23 (m, 4H), 2.14–2.13 (m, 3H), 2.11–1.95 (m, 4H), 1.70–1.56 (m, 2H), 1.43 (s, 9H), 1.37–1.20 (m, 6H), 0.98–0.81 (m, 5H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.02, 159.21, 132.20, 131.97, 131.59, 130.87, 130.41, 129.33, 125.86, 125.22, 113.77, 91.82, 81.82, 80.02, 75.67, 72.70, 71.79, 65.01, 55.24, 34.99, 33.44, 31.52, 29.25, 28.09, 27.71, 27.40, 26.76, 24.87, 22.57, 18.05, 14.05, -1.42; [α]_D²⁰ = +59.0 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₃₈H₆₄O₇SiNa (M+Na)⁺ 683.4, found 683.4; HRMS(ESI) calcd for C₃₈H₆₄O₇SiNa (M+Na)⁺ 683.4319, found 683.4314.

The (*R*) and (*S*) Mosher's esters were synthesized from **13** and the (*S*) and (*R*) acid chloride, respectively (pyridine, DMAP, CH_2Cl_2 , rt, 24 h). The resulting differences in chemical shifts are consistent with (*R*) stereochemistry at C11' as shown.



 O_{Et} (S)-Glycidaldehyde diethyl acetal (S)- \mathbf{A}^5 , was resolved from racemic glycidaldehyde diethyl acetal using the HKR method developed by Jacobsen⁶.

^{(S)-A} *p*-Toluenesulfonic acid (0.8 g, 1.33 mmol, 1.4 mol%) was added to a 100 mL round-bottomed flask containing a stirred solution of (*R*, *R*)-(-)-*N*,*N*'-bis(3,5-di-*tert*-butylsalicicylidene)-1,2-cyclohexanediaminocobalt (II) (0.27 g, 1.4 mmol, 1.5 mol%) in 20 mL DCM at room temperature. The reaction was allowed to stir open to air for 1 hour, after which the stir bar was removed and the solution was concentrated by rotary evaporation. The contents of the flask were placed under high vacuum for 1 hour to remove the remaining solvent. The stir bar was returned to the flask and racemic glycidaldehyde diethyl acetal (13.7 g, 93.7 mmol, 1.0 equiv) was added to the (salen)Co^{III}-OTs catalyst at room temperature. The flask was capped and stirred vigorously for 24 hours. The epoxide was transferred to a -78°C receiving flask by distillation (60°C, 10 mmHg) to afford (*S*)-**A** (5.81 g, 40.1 mmol, 43% yield, 97% ee) as a clear liquid, which was stored over 4Å molecular sieves in the freezer. The ee of (*S*)-**A** (97%) was determined by chiral GC. ¹H NMR (400 MHz, CDCl₃) δ = 4.34 (dd, *J* = 4.3, 1.5 Hz, 1H), 3.78–3.72 (m, 2H), 3.65–3.61 (m, 2H), 3.16–3.08 (m, 1H), 2.82–2.75 (m, 2H), 1.28–1.20 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 101.5, 62.9, 62.3, 51.8, 43.8, 15.2, 15.1; [α]_D²⁰ = -5.4 (*c* = 1.0, EtOH); lit. data: [α]_D²⁵ = -5.4 (*c* = 1.04, EtOH)⁷.

⁵ a) Weisblat, D. I.; Magerlein, B. J.; Myers, D. R.; Hanze, A. R.; Fairburn, E. I.; Rolfson, S. T. *J. Am. Chem. Soc.* **1953**, *75*, 5893. b) Franck, C. P. D.; Virgil H.; Soth, S.; Laurence, H. *Eur. J. Org. Chem.* **2006**, *2006*, 5526.

⁶ Nielsen, L. P. C.; Stevenson, C. P.; Blackmond, D. G.; Jacobsen, E. N. J. Am. Chem. Soc. 2004, 126, 1360.

⁷ Pederson, R. L.; Liu, K. K. C.; Rutan, J. F.; Chen, L.; Wong, C. H. J. Org. Chem. 1990, 55, 4897.



To a stirred solution of 1-pentyne (3.0 mL, 30 mmol, 2.0 equiv) in 100 mL THF at -78°C was added *n*-BuLi (12 mL, 30 mmol, 2.0 equiv). After stirring for 1 hour at -78°C, BF₃·OEt₂ (2.5 mL, 19.5 mmol, 1.3 equiv) was added at this temperature. The solution stirred for 25 minutes, at which time (*S*)-**A** (2.2 g in 15 mL THF, 15 mmol, 1.0 equiv) was added dropwise at -78°C.

The reaction was stirred at -78°C for 4 hours, quenched with saturated aqueous NH₄Cl, and extracted 3 times with Et₂O. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (6-30% EtOAc/Hexanes) to give the product **B** (2.98 g, 13.9 mmol, 93% yield) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 4.48 (d, J = 5.6, 1H), 3.80–3.75 (m, 2H), 3.72–3.65 (m, 1H), 3.66–3.58 (m, 2H), 2.56–2.48 (m, 1H), 2.46–2.38 (m, 1H), 2.32 (d, J = 4.1 Hz, 1H), 2.19–2.11 (m, 2H), 1.55–1.47 (m, 2H), 1.24 (t, J = 7.1 Hz, 3H), 1.23 (t, J = 7.1 H, 3H), 0.97 (t, J = 7.4 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 103.7, 82.2, 76.1, 70.6, 63.8, 63.5, 22.6, 22.5, 20.9, 15.4, 13.6, 13.5; $[\alpha]_D^{20} = -14$ (c = 1.19, CHCl₃).



A stirred mixture of **B** (1.5 g, 7.0 mmol, 1.0 equiv), quinoline (42 μ L, 0.35 mmol, 5 mol%), and Lindlar catalyst (0.149 g, 0.07 mmol, 1.0 mol%) in MeOH (25 mL) was sparged with N₂ for 15 minutes. H₂ gas was then bubbled through the stirred mixture for 1 hour. The reaction was filtered through a plug of Celite and concentrated to afford the product **C** (1.51 g,

quantitative yield) as a yellow oil which was used without further purification. ¹H NMR (400 MHz, CDCl₃) δ 5.64– 5.38 (m, 2H), 4.31 (d, J = 5.8 Hz, 1H), 3.87–3.68 (m, 2H), 3.68–3.49 (m, 3H), 2.46–2.32 (m, 1H), 2.32–2.19 (m, 1H), 2.15 (d, J = 3.5 Hz, 1H), 2.08–2.01 (m, 2H), 1.47–1.31 (m, 2H), 1.24 (q, J = 7.0 Hz, 6H), 0.91 (t, J = 7.3 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 132.2, 125.4, 104.6, 71.2, 63.5, 63.4, 29.9, 29.6, 22.9, 15.6, 15.5, 13.9; $[\alpha]_D^{20}$ = -6.4 (c = 1.06, CHCl₃).



To a stirred suspension of NaH (0.21 g, 5.25 mmol, 1.5 equiv) and tetrabutylammonium iodide (0.132 g, 0.35 mmol, 0.1 equiv) in 25 mL DMF at 0 °C was slowly added C (0.76 g in 5 mL DMF, 3.5 mmol, 1.0 equiv). After stirring for 1 hour at 0 °C, PMBCl (0.97 mL, 7.0 mmol, 2.0 equiv) was added at this temperature and the reaction was allowed to warm to room

temperature. The reaction was allowed to stir for 24 hours, after which it was quenched by slow addition of H₂O at 0 °C. The reaction was extracted 3 times with Et₂O, and the combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated and purified by flash chromatography (2-10% EtOAc in hexanes) to afford **D** (1.11 g, 94% yield) as a light yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.36–7.19 (m, 2H), 6.90–6.76 (m, 2H), 5.56–5.36 (m, 2H), 4.64 (d, *J* = 11.2 Hz, 1H), 4.54 (d, *J* = 11.2 Hz, 1H), 4.37 (d, *J* = 6.0 Hz, 1H), 3.76 (s, 3H), 3.76–3.66 (m, 2H), 3.66–3.57 (m, 1H), 3.57–3.48 (m, 1H), 3.46–3.37 (m, 1H), 2.46–2.33 (m, 1H), 2.33–2.22 (m, 1H), 2.10–1.91 (m, 2H), 1.44–1.29 (m, 2H), 1.29–1.14 (m, 6H), 0.89 (t, *J* = 7.4 Hz, 3H); ¹³CNMR (100 MHz, CDCl₃) δ 159.3, 131.6, 131.2, 129.6, 126.0, 113.8, 104.8, 79.8, 72.9, 64.0, 63.4, 55.3, 29.7, 28.7, 23.0, 15.7, 15.5, 14.0; [α]_D²⁰ = +13 (*c* = 1.0, CHCl₃).



To a stirred solution of **D** (0.22 g, 0.654 mmol, 1.0 equiv) in 45 mL THF at 0 °C was added a 15 mL freshly prepared solution of 10% HCl. Hydrolysis of the diethyl acetal was complete after 44 hours of stirring at 0 °C, after which the solution was poured into a stirred solution of saturated aqueous NaHCO₃ at 0 °C. The crude aldehyde **E** was extracted from the aqueous layer

by washing once with EtOAc and twice with DCM. The organic layer was pooled, dried with MgSO₄, filtered and concentrated. The crude aldehyde was unstable so it was purified quickly by flash chromatography (2.5-10% EtOAc in hexanes with 0.1% Et₃N) afforded the aldehyde **E** (0.145 g, 85% yield) as a colorless oil. This α -hydroxy aldehyde **E** is very unstable and was used directly in the following reaction without being completely characterized.

Significant decomposition occurs when stored overnight in the freezer; however, a small aliquot was removed to obtain the ¹H NMR spectrum. ¹H NMR (400MHz, CDCl₃) δ 9.62 (d, *J* = 2.1 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 2H), 6.88 (d, *J* = 8.6 Hz, 2H), 5.57–5.47 (m, 1H), 5.46–5.35 (m, 1H), 4.59 (d, *J* = 11.5 Hz, 2H), 4.53 (d, *J* = 11.5 Hz, 2H), 3.81 (s, 3H), 3.77 (dt, *J* = 6.5, 2.2 Hz, 1H), 2.49–2.42 (m, 2H), 2.04–1.95 (m, 2H), 1.42–1.30 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H).



TBSCl (0.82 g, 5.28 mmol, 1.5 eqiv) was added to a solution of **k** (1.0 g, 3.52 mmol, 1.0 equiv), imidazole (0.72 g, 10.56 mmol, 3.0 equiv), and DMAP (43 mg, 0.352 mmol, 0.1 equiv) in 20 mL DCM at 0 °C. The reaction was stirred for 30 minutes at 0 °C and 2.5 hours at room temperature. MeOH (30 mL) and K₂CO₃ (1.7 g, 12.32 mmol, 3.5 equiv) were then

added to the reaction sequentially at room temperature. After stirring overnight, the reaction was quenched with saturated aqueous NaHCO₃ and extracted 3 times with EtOAc. The organic layer was combined, washed with brine, dried with MgSO₄, filtered and concentrated. The crude mixture was filtered through a plug of SiO₂ with 10% EtOAc in hexanes to afford **F** (1.18 g, quantitative yield) which was used without further purification. ¹H NMR (400 MHz, CDCl₃) δ 4.34 (dt, *J* = 6.4, 2.1 Hz, 1H), 2.37 (d, *J* = 2.1 Hz, 1H), 2.22 (t, *J* = 7.5 Hz, 2H), 1.73–1.64 (m, 2H), 1.64–1.56 (m, 2H), 1.51–1.45 (m, 2H), 1.45 (s, 9H), 0.90 (s, 9H), 0.11 (d, *J* = 10.1 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 173.0, 85.5, 80.0, 72.3, 62.7, 38.3, 35.6, 28.2, 25.9, 24.9, 24.7, 18.3, 4.43, 4.96; $[\alpha]_D^{20} = +30.9$ (*c* = 1.1, CHCl₃).



Solid Cp₂Zr(H)Cl (0.614 g, 2.26 mmol, 1.7 equiv) was added to a stirred solution of **F** (0.652 g, 2.00 mmol, 1.5 equiv) in 7 mL DCM at 0 °C. The hydrozirconation was complete after 2 hours, at which time a solution of ZnBr₂ (2.0 M in toluene, 0.133 mL, 0.133 mmol, 0.1 equiv) was added to

the reaction mixture. After stirring for an addition 15 minutes at 0 °C, a solution of the aldehyde (\mathbf{E} , 0.35 g, 1.33 mmol, 1.0 equiv) in 2 mL DCM was added at the same temperature. The aldehyde was allowed to react overnight at 0 °C and the reaction was quenched with a 10% aqueous solution of citric acid. The organic layer was separated, and the aqueous layer was washed 3 times with DCM. The organic layer was combined, washed with brine, dried with MgSO₄, filtered and concentrated to afford the desired alcohol as a mixture of diastereomers. The crude oil was taken directly into the Dess-Martin oxidation without further purification.

The above crude alcohol was dissolved in 15 mL DCM, treated with NaHCO₃ (0.328 g, 3.9 mmol, 3.0 equiv), and cooled to 0 °C. Dess-Martin periodinane (1.14 g, 2.6 mmol, 2.0 equiv) was added to the stirred suspension in 3 portions. After 15 minutes, the reaction was removed from the ice bath and allowed to slowly warm to room temperature. The oxidation was complete after stirring for 1.5 hours at room temperature. The reaction was quenched with a solution of 20% Na₂S₂O₃/saturated aqueous NaHCO₃ (1:1), extracted 3 times with DCM. The combined layer was washed with brine, dried with MgSO₄, filtered, concentrated and purified by flash chromatography (5-8% EtOAc in hexanes) afforded of the ketone **G** (0.646 g, 84% yield over two steps) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 7.25–7.21 (m, 2H), 6.98 (dd, *J* = 15.6, 4.5 Hz, 1H), 6.88–6.84 (m, 2H), 6.66 (dd, *J* = 15.6, 1.6 Hz, 1H), 5.52–5.44 (m, 1H), 5.42–5.32 (m, 1H), 4.53 (d, *J* = 11.5 Hz, 1H), 4.34–4.29 (m, 2H), 3.92 (t, *J* = 6.6 Hz, 1H), 3.80 (s, 3H), 2.44 (t, *J* = 7.1 Hz, 2H), 2.19 (t, *J* = 7.5 Hz, 2H), 2.02–1.92 (m, 2H), 1.63–1.51 (m, 4H), 1.43 (s, 9H), 1.40–1.30 (m, 4H), 0.89 (s, 9H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.07–0.02 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 159.4, 136.28, 132.1, 130.8, 129.5, 127.9, 125.9, 114.0, 82.3, 80.2, 73.2, 72.9, 72.1, 55.5, 38.2, 35.8, 29.7, 28.4, 27.9, 26.1, 25.3, 24.9, 22.9, 18.5, 14.1, -4.03, -4.52; MS (ESI) calcd for C₃₄H₅₆O₆SiNa (M+Na)⁺ 611.9, found 611.4.



Ketone **G** (0.3 g, 0.5 mmol, 1.0 equiv) was dissolved in 10 mL DCM and cooled to -78 °C. Super Hydride (1.0 M in THF, 0.6 mL, 1.2 equiv) was added slowly and the resulting solution was allowed to stir for 20 minutes at -78 °C. Then the reaction was quenched with a 10% aqueous solution of

citric acid, allowed to warm to room temperature, and stirred until two clear layers were present The aqueous layer was washed 3 times with DCM. The organic layer was combined, washed with brine, dried with MgSO₄, filtered, concentrated and purified by flash chromatography (8-18% EtOAc in hexanes) to afford the desired alcohol **H** (19:1 selectivity, 0.244 g, 83% yield) ¹H NMR (400 MHz, CDCl₃) δ 7.26 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.76–5.59 (m, 2H), 5.53–5.35 (m, 2H), 4.58 (d, *J* = 11.3 Hz, 1H), 4.52 (d, *J* = 11.3 Hz, 1H), 4.29–4.21 (m, 1H), 4.18–4.09 (m, 1H), 3.81 (s, 3H), 3.51–3.39 (m, 1H), 2.42–2.30 (m, 1H), 2.24–2.12 (m, 4H), 2.04–1.96 (m, 2H), 1.62–1.46 (m, 4H), 1.43 (s, 9H), 1.39–1.28 (m, 4H), 0.91–0.85 (m, 12H), 0.03 (d, *J* = 8.8 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 173.4, 159.4, 136.3, 132.1, 130.8, 129.5, 127.9, 125.9, 114.0, 82.3, 80.2, 73.2, 72.9, 72.1, 55.5, 38.2, 35.8, 29.7, 28.4, 27.9, 26.1, 25.3, 24.9, 23.0, 18.5, 14.1, -4.03, -4.52; MS (ESI) calcd C₃₄H₅₈O₆SiNa (M+Na)⁺ 613.9, found 613.4.



SEMCl (0.105 mL, 0.563 mmol, 1.3 equiv) was added dropwise to a stirred solution of **H** (0.256 g, 0.433 mmol, 1.0 equiv) and *i*-Pr₂NEt (0.13 mL, 0.736 mmol, 1.7 equiv) in 2.0 mL DCM at 0 °C. The solution was allowed to slowly warm to room temperature and stir overnight. Then the

reaction was quenched with saturated aqueous NH_4Cl , The organic layer was combined, washed with brine, dried with $MgSO_4$, filtered, and concentrated to afford the crude SEM-protected alcohol. The crude compound was taken directly into the following reaction without further purification.

Phosphate buffer (pH = 7, 0.31 mL) was added to the crude SEM-protected alcohol (0.433 mmol, 1.0 equiv) in 5.5 mL DCM and the heterogeneous mixture was cooled to 0 °C. DDQ (0.151 g, 0.65 mmol, 1.5 equiv) was then added in two portions and the resulting mixture was allowed to stir overnight at 0 °C, after which the reaction was filtered through a plug of Celite, washed with saturated aqueous NaHCO₃ and extracted 3 times with DCM. The organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (5-8% EtOAc in hexanes) to afford the product **14** (0.241 g, 95% yield) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 5.73 (dd, *J* = 15.6, 5.9 Hz, 1H), 5.62–5.49 (m, 2H), 5.49–5.39 (m, 1H), 4.70–4.62 (m, 2H), 4.19–4.11 (m, 1H), 4.04 (dd, *J* = 7.7, 3.6 Hz, 1H), 3.80–3.65 (m, 2H), 3.52 (dt, *J* = 9.8, 6.6 Hz, 1H), 2.25 (d, *J* = 4.5 Hz, 1H), 2.24–2.13 (m, 6H), 2.06–1.98 (m, 2H), 1.62–1.46 (m, 5H), 1.44 (s, 9H), 1.41–1.33 (m, 3H), 0.94–0.89 (m, 3H), 0.88 (s, 9H), 0.04 (s, 3H), 0.02 (s, 12H); ¹³C NMR (100 MHz, CDCl₃) δ 173.3, 139.8, 132.7, 125.6, 124.8, 92.4, 80.2, 79.7, 73.9, 72.8, 65.7, 38.3, 35.8, 30.7, 29.9, 29.8, 28.3, 26.1, 25.3, 25.3, 25.0, 23.0, 18.4, 18.3, 14.0, -1.18, -4.10, -4.56; MS (ESI) calcd C₃₂H₆₄O₆Si₂Na (M+Na)⁺ 624.0, found 623.4.



NaH (60 % dispersion in mineral oil, 454.4 mg, 11.4 mmol, 4.0 equiv) was weighed and added to a flask in a glove box, suspended in 4 mL DMF and cooled to 0 °C. A solution of bromoacetic acid (789.2 g, 5.7 mmol, 2.0 equiv) in 4 mL THF was added dropwise to the stirred suspension of NaH at 0 °C. The

reaction was allowed to stir for 30 minutes at this temprature, and a solution of **13** (1.88 g, 2.84 mmol, 1.0 equiv) in 4 mL THF was added dropwise via cannula at 0 °C. After 30 minutes, the solution was allowed to warm to room temperature and stir overnight. Then the reaction was quenched with saturated aqueous NaH₂PO₄ at 0 °C, extracted with EtOAc, and dried with MgSO₄. The crude mixture was filtered through a plug of SiO₂ with 60% EtOAc in hexanes to afford the desired product **f** (1.86 g, 91% yield), which was used in the following reaction without further purification. ¹H NMR (400 MHz, CDCl₃) δ 7.32–7.17 (m, 2H), 6.90–6.82 (m, 2H), 5.61–5.53 (m, 2H), 5.52–5.32 (m, 4H), 4.63 (d, *J* = 6.8 Hz, 1H), 4.60 (d, *J* = 11.6 Hz, 1H), 4.59 (d, *J* = 6.8 Hz, 1H), 4.55 (d, *J* = 11.6 Hz, 1H), 9.4.18

(d, J = 17.1 Hz, 1H), 4.14–4.07 (m, 1H), 3.90 (d, J = 17.2 Hz, 1H), 3.90–3.85 (m, 1H), 3.80 (s, 3H), 3.77–3.67 (m, 1H), 3.57–3.43 (m, 2H), 2.48–2.13 (m, 6H), 2.11–1.92 (m, 4H), 1.71–1.56 (m, 2H), 1.43 (s, 9H), 1.38–1.19 (m, 6H), 0.98–0.81 (m, 5H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.11, 171.87, 159.42, 135.28, 132.48, 131.19, 129.87, 129.39, 127.89, 125.46, 125.06, 113.80, 91.98, 83.67, 80.20, 80.16, 75.38, 72.48, 66.51, 65.16, 55.21, 34.96, 33.25, 31.50, 29.19, 28.08, 27.43, 27.37, 26.77, 24.86, 22.55, 18.00, 14.04, -1.43; MS(ESI) calcd for C₄₀H₆₆O₉SiNa (M+Na)⁺ 741.4, found 741.4; HRMS(ESI) calcd for C₄₀H₆₆O₉SiNa (M+Na)⁺ 741.4374, found 741.4357.



Carboxylic acid **f** (1.86 g, 2.6 mmol, 1.0 equiv) was added to a flask and dissolved in 30 mL Et₂O. Triethylamine (578 μ L, 4.2 mmol, 1.6 equiv) was added and the stirred solution was cooled to -78 °C. Pivaloyl chloride (479 μ L, 3.9 mmol, 1.5 equiv) was then added dropwise to the reaction, which was stirred for additional 20 minutes at -78 °C and allowed to slowly warm to 0 °C. After stirring for 1 hour at this temperature, the solution was cooled once again to -78 °C.

In a separate 100 mL flask was placed (R)-(+)-4-isopropyl-2-oxazolidinone (569.3 mg, 4.4 mmol, 1.7 equiv) in 30 mL THF. The solution was cooled to -78 °C, and n-BuLi (2.5 M in hexanes, 1.66 mL, 4.2 mmol, 1.6 equiv) was added dropwise via syringe. The solution was stirred for 20 minutes, then the contents in the flask were subsequently transferred via cannula into the stirred suspension of mixed anhydride at -78 °C. After stirring for 20 minutes at -78 °C, the solution was allowed to warm to 0 °C and stir for 1 hour at this temperature. Then the reaction was guenched with saturated agueous NH_4Cl , extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentration and purified by flash chromatography (5-25% EtOAc in hexanes) to afford the desired oxazolidinone g (1.96 g, 91% yield over two steps) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.29–7.23 (m, 2H), 6.87–6.77 (m, 2H), 5.71 (dd, J = 15.7, 7.9 Hz, 1H), 5.57 (dd, J = 15.7, 7.4 Hz, 1H), 5.49-5.34 (m, 4H), 4.75-4.48 (m, 6H), 4.45-4.36 (m, 1H), 4.30 (t, J = 8.7 Hz, 1H), 4.23 (dd, J = 9.1, 3.1 Hz, 1H), 4.16–4.07 (m, 1H), 3.91 (dd, J = 7.9, 4.0 Hz, 1H), 3.78 (s, 3H), 3.77–3.67 (m, 1H), 3.66–3.57 (m, 1H), 3.53– 3.42 (m, 1H), 2.49–2.14 (m, 6H), 2.52–2.11 (m, 4H), 1.68–1.55 (m, 2H), 1.43 (s, 9H), 1.37–1.18 (m, 7H), 0.98–0.77 (m, 11H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.92, 170.06, 158.93, 153.81, 135.64, 131.96, 131.00, 130.96, 129.38, 129.34, 125.73, 125.31, 113.53, 91.83, 82.67, 80.70, 79.90, 75.48, 72.27, 67.87, 65.03, 64.15, 58.13, 55.18, 34.97, 33.39, 31.51, 29.26, 29.20, 28.07, 27.39, 26.77, 24.85, 22.55, 18.01, 17.87, 14.47, 14.04, -1.44; [α]_D²⁰ = -10.6 (c = 1.0, CHCl₃); MS(ESI) calcd for C₄₆H₇₉N₂O₁₀Si (M+NH₄)⁺ 847.5, found 847.6; HRMS(ESI) calcd for $C_{46}H_{75}NO_{10}SiNa (M+Na)^+ 852.5058$, found 852.5042.



(Z)-1-Iodohex-2-ene was prepared using a modification of a known procedure.⁸

Alkylation of the oxazolidinone **g** with (*Z*)-1-iodohex-2-ene was performed using a modification of a known procedure. ⁹ A solution of sodium bistrimethylsilylamide (0.6 M in toluene, 1.09 mL, 0.65 mmol, 0.9 equiv) was added slowly to a stirred solution

of **g** (601.0 g, 0.72 mmol, 1.0 equiv) in 12 mL THF at -78 °C. The solution was stirred at -78 °C for 40 minutes, after which (*Z*)-1-iodohex-2-ene (760.4 mg, 3.62 mmol, 5.0 equiv) was added in one portion (not dropwise). The solution was allowed to stir for an additional 2 hours at -78 °C, then the reaction was quenched with saturated aqueous NH₄Cl at this temperature. The suspension was allowed to warm to room temperature, and extracted 3 times with EtOAc. The combined layer was washed with brine, dried with MgSO₄, filtered, concentration and purified by flash chromatography (5-25% EtOAc in hexanes) to provide the desired product **15** (523.0 mg, 79%) as a colorless oil and recover the oxazolidinone **g** (55.0 mg, 9% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.23 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J*

⁸ a) Vankar, Y. D.; Rao, C. T. Tetrahedron Lett. **1985**, 26, 2717. b) Kurashina, Yusuke. K; Shigefumi, K., Biosci. Biotechnol. and Biochem. **2012**, 76, 605.

⁹ Crimmins, M. T.; Emmitte, K. A.; Katz, J. D. Org. Lett. 2000, 2, 2165.

= 8.5 Hz, 2H), 5.65 (dd, J = 15.7, 7.4 Hz, 1H), 5.51 (dd, J = 15.6, 7.6 Hz, 1H), 5.49–5.33 (m, 6H), 5.18 (dd, J = 7.6, 4.1 Hz, 1H), 4.63 (d, J = 8.8 Hz, 1H), 4.62 (d, J = 9.2, Hz, 1H), 4.54 (d, J = 6.9 Hz, 1H), 4.46 (d, J = 11.1 Hz, 1H), 4.42–4.33 (m, 1H), 4.16–4.02 (m, 3H), 3.81 (dd, J = 7.4, 3.3 Hz, 1H), 3.77 (s, 3H), 3.76–3.67 (m, 1H), 3.57–3.51 (m, 1H), 3.49–3.39 (m, 1H), 2.58–2.39 (m, 2H), 2.38–2.13 (m, 6H), 2.10–1.91 (m, 6H), 1.68–1.54 (m, 2H), 1.41 (s, 9H), 1.38–1.13 (m, 9H), 0.95–0.74 (m, 14H), -0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.97, 172.56, 158.91, 153.39, 134.91, 132.52, 131.68, 131.14, 130.89, 129.91, 129.23, 125.94, 125.86, 124.12, 113.49, 91.73, 81.97, 81.78, 79.87, 75.53, 72.64, 64.99, 63.70, 58.08, 55.21, 35.02, 33.44, 31.65, 31.56, 29.39, 29.32, 28.25, 28.08, 27.40, 26.77, 24.90, 22.63, 22.57, 18.02, 17.84, 14.71, 14.05, 13.75, -1.44; [α]_D²⁰ = -9.4 (c = 1.0, CHCl₃); MS(ESI) calcd for C₅₂H₈₅NO₁₀SiNa (M+Na)⁺ 934.5840, found 934.5834.



Compound **15** (432.0 mg, 0.47 mmol, 1.0 equiv) was dissolved in 8 mL THF, treated with anhydrous methanol (19 μ L, 0.47 mL, 1.0 equiv), and cooled to 0 °C. Lithium borohydride (2.0 M in THF, 284 μ L, 0.57 mmol, 1.0 equiv) was added dropwise to the solution at 0 °C and the reaction was allowed to stir overnight at this temperature. Then the reaction was quenched with a 10%

aqueous solution of citric acid and the heterogeneous mixture was stirred for 1 hour at room temperature until two clear phases were present. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The combined layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (6-25% EtOAc in hexanes) to afford the desired alcohol **h** (349.9 g, 94 % yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.25 (d, *J* = 8.9 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 5.67–5.50 (m, 2H), 5.48–5.21 (m, 6H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.57 (d, *J* = 6.9 Hz, 1H), 4.52 (s, 2H), 4.14–4.03 (m, 2H), 3.78 (s, 3H), 3.77–3.69 (m, 1H), 3.65–3.56 (m, 1H), 3.55–3.30 (m, 4H), 3.14–3.06 (m, 1H), 2.46–2.14 (m, 8H), 2.10–1.92 (m, 6H), 1.71–1.52 (m, 2H), 1.43 (s, 9H), 1.40–1.18 (m, 8H), 1.00–0.79 (m, 8H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.88, 159.18, 132.59, 131.91, 131.89, 131.46, 130.90, 130.05, 129.52, 125.89, 125.77, 125.12, 113.67, 91.69, 81.66, 80.89, 79.96, 79.78, 75.47, 72.01, 65.01, 64.18, 55.17, 34.96, 33.39, 31.50, 30.33, 29.34, 29.21, 28.06, 27.42, 27.35, 26.76, 24.85, 22.63, 22.55, 18.02, 14.04, 13.76, -1.44; [α]_D²⁰ = +41.6 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₄₆H₇₈O₈SiNa (M+Na)⁺ 809.5, found 809.5; HRMS(ESI) calcd for C₄₆H₇₈O₈SiNa (M+Na)⁺ 809.5364, found 809.5347.



NaHCO₃ (220.3 mg, 2.62 mmol, 5.0 equiv) was added to the solution of the alcohol **h** (412.9 mg, 0.52 mmol, 1.0 equiv) in 5 mL DCM at 0 °C. Dess-Martin periodinane (267.0 mg, 0.63 mmol, 1.2 equiv) was added to the stirred suspension in 2 portions. After stirring overnight at this temperature, the reaction was concentrated, then the reaction was quenched with a solution of 20% aqueous Na₂S₂O₃/saturated aqueous NaHCO₃ (1:1), and

extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-20% EtOAc in hexanes) to afford the product **16** (385.8 mg, 94% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 9.62 (d, *J* = 2.2 Hz, 1H), 7.27–7.20 (m, 2H), 6.88–6.81 (m, 2H), 5.62 (dd, *J* = 15.7, 7.3 Hz, 1H), 5.52 (dd, *J* = 16.0, 7.2 Hz, 1H), 5.49–5.32 (m, 6H), 4.64 (d, *J* = 6.9 Hz, 1H), 4.58 (d, *J* = 11.2 Hz, 1H), 4.56 (d, *J* = 6.8 Hz, 1H), 4.51 (d, *J* = 11.3 Hz, 1H), 4.14–4.07 (m, 1H), 3.87 (dd, *J* = 7.3, 3.8 Hz, 1H), 3.79 (s, 3H), 3.78–3.69 (m, 2H), 3.56–3.51 (m, 1H), 3.52–3.43 (m, 1H), 2.43–2.14 (m, 8H), 2.12-1.90 (m, 6H), 1.70–1.51 (m, 2H), 1.43 (s, 9H), 1.38–1.22 (m, 8H), 1.00–0.80 (m, 8H), 0.01 (s, 9H)); ¹³C NMR (100 MHz, CDCl₃) δ 203.90, 172.86, 159.04, 135.23, 132.94, 132.07, 131.02, 130.69, 129.37, 129.33, 125.73, 125.24, 123.19, 113.59, 91.79, 81.81, 81.27, 80.92, 79.95, 75.41, 72.27, 65.06, 55.19, 34.95, 33.39, 31.50, 29.38, 29.22, 28.83, 28.78, 28.07, 27.42, 26.78, 24.86, 22.56, 22.54, 18.03, 14.04, 13.75, -1.44; [α]_D²⁰ = +12.6 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₄₆H₇₆O₈SiNa (M+Na)⁺ 807.5, found 807.4; HRMS(ESI) calcd for C₄₆H₇₆O₈SiNa (M+Na)⁺ 807.5207, found 807.5197.



Following a similar procedure¹⁰, freshly distilled adipic anhydride monomer¹¹ (12.8 g, 100 mmol, 2.0 equiv) and bis(trimethylsilyl)-acetylene (8.7 g, 50 mmol, 1.0 equiv) were dissolved in 600 mL DCM and brought to 0 °C. Anhydrous AlCl₃ (20 g, 150 mmol, 3.0 equiv) was added in four portions to the stirred solution at 0 °C. The dark mixture was stirred for additional 2.5 hours at this temperature and 19 hours at room temperature.

The reaction was quenched by slowly adding 1N HCl at 0 °C and the organic layer was separated, washed with 1N HCl, H₂O, and brine. The organic layer was dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (5-50% EtOAc in hexanes) to afford the product **i** (6.91 g, 61% yield) as a viscous oil. ¹H NMR (400 MHz, CDCl₃) δ 2.59 (t, J = 7.0 Hz, 2H), 2.38 (t, J = 7.1 Hz, 2H), 1.84–1.54 (m, 4H), 0.23 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 187.17, 179.42, 101.82, 98.09, 44.74, 33.63, 23.82, 23.11, -0.81; MS(ESI) calcd for C₁₁H₁₇O₃Si (M-H)⁻ 225.1, found 225.1; HRMS(ESI) calcd for C₁₁H₁₇O₃Si (M-H)⁻ 225.0947, found 225.0949.



Trifluoroacetic anhydride (5.6 mL, 40.3 mmol, 2.2 equiv) was added slowly (over 15 minutes) to **i** (4.1 g, 18.3 mmol, 1.0 equiv) in 80 mL THF at 0 °C and the reaction solution was allowed to stir for 2.5 hours at this temperature. *t*-BuOH (5 mL) was then added slowly to the stirred solution at 0 °C and the reaction was allowed to slowly warm to room temperature. After stirring overnight at room temperature, the reaction

was quenched with H₂O, diluted with DCM, and extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (2-5% EtOAc in hexanes) to afford the product **j** (4.6 g, 89% yield) as a yellow oil. ¹H NMR (400 MHz, CDCl₃) δ 2.53 (t, *J* = 7.1 Hz, 2H), 2.18 (t, *J* = 7.0 Hz, 2H), 1.69–1.48 (m, 4H), 1.39 (s, 9H), 0.19 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 187.19, 172.50, 101.83, 97.63, 80.05, 44.77, 35.07, 27.98, 24.22, 23.12, -0.88; MS(ESI) calcd for C₁₅H₂₆O₃SiNa (M+Na)⁺ 305.2, found 305.1; HRMS(ESI) calcd for C₁₅H₂₆O₃SiNa (M+Na)⁺ 305.1549, found 305.1538.



Noyori catalyst¹² (6.0 mg, 0.01 mmol, 1 mol %) was added to a stirred solution of **j** (282.4 mg, 1.0 mmol, 1.0 equiv) in 10 mL *i*-PrOH at room temperature and the reaction was allowed to stir overnight. The solution was concentrated and purified by flash chromatography (5-20% EtOAc) to afford the product **k** (271.0 mg, 95% yield, 99% ee) as a yellow oil. The ee of **k** (99%) was determined from the benzoylated

analog I (BzCl, Et₃N, cat. DMAP, DCM) by HPLC (Chiralcel OD-H column, 1 mL/ min flow rate, 1% *i*PrOH/Hexanes; retention time of major: 7.95 min, retention time of minor: 9.18 min). ¹H NMR (400 MHz, CDCl₃) δ 4.35 (t, *J* = 6.6 Hz, 1H), 2.23 (t, *J* = 7.4 Hz, 2H), 1.87 (s, 1H), 1.74–1.67 (m, 2H), 1.67–1.57 (m, 2H), 1.52–1.45 (m, 2H), 1.44 (s, 9H), 0.16 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.04, 106.61, 89.41, 80.09, 62.63, 37.30, 35.42, 28.10, 24.66, 24.59, -0.14; $[\alpha]_D^{20} = +0.6 (c = 1.04, CHCl_3)$; MS(ESI) calcd for C₁₅H₂₈O₃SiNa (M+Na)⁺ 307.1705, found 307.1705; For the ent-**k**, $[\alpha]_D^{20} = -1.0 (c = 1.0, CHCl_3)$.



4-Methoxybenzyl-2,2,2-trichloroacetimidate¹³ (1.3 g, 4.6 mmol, 1.5 equiv) was added slowly to **k** (881.5 mg, 3.1 mmol, 1.0 equiv) in 15 mL toluene at 0 °C. Cu(OTf)₂ (112.1 mg, 0.31 mmol, 0.1 equiv) in 5 mL toluene was then added slowly to the stirred solution at 0 °C. After stirring for 2 h at this temperature, the reaction was quenched with MeOH and sat. NaHCO₃, diluted with Et₂O, and extracted 3 times with Et₂O. The

combined organic layer was washed with saturated aqueous NH₄Cl, 10% NH₄OH, H₂O and brine. The combined organic layer was dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (5-20% EtOAc in hexanes) to afford the product **m** (1.08 g, 86% yield) as a colorless oil. ¹H NMR (500 MHz, CDCl₃) δ 7.28 (d, *J* =

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8.5 Hz, 2H), 6.87 (d, J = 8.6 Hz, 2H), 4.70 (d, J = 11.4 Hz, 1H), 4.43 (d, J = 11.4 Hz, 1H), 4.03 (t, J = 6.5 Hz, 1H), 3.80 (s, 3H), 2.20 (t, J = 7.5 Hz, 2H), 1.80–1.64 (m, 2H), 1.63–1.52 (m, 2H), 1.51–1.44 (m, 2H), 1.43 (s, 9H), 0.19 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.80, 159.06, 129.90, 129.49, 113.56, 104.73, 90.37, 79.74, 69.88, 68.29, 55.02, 35.28, 35.15, 27.95, 24.63, -0.13; $[\alpha]_D^{20} = +83.8$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₂₃H₃₆O₄SiNa (M+Na)⁺ 427.2281, found 427.2267; For the ent-**m**, $[\alpha]_D^{20} = -84.6$ (c = 1.0, CHCl₃).

(R)-17 (



¹H NMR (400 MHz, CDCl₃) δ 7.29–7.22 (m, 2H), 6.88–6.82 (m, 2H), 4.70 (d, J = 11.3 Hz, 1H), 4.41 (d, J = 11.3 Hz, 1H), 4.02 (td, J = 6.5, 2.0 Hz, 1H), 3.78 (s, 3H), 2.44 (d, J = 2.0 Hz, 1H), 2.19 (t, J = 7.4 Hz, 2H), 1.81–1.64 (m, 2H), 1.61–1.51 (m, 2H), 1.51–1.43 (m, 2H), 1.41 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 172.95, 159.19, 129.81, 129.59, 113.71, 82.84,

79.96, 73.77, 70.09, 67.78, 55.20, 35.38, 35.24, 28.05, 24.71, 24.62; $[\alpha]_D{}^{20} = -81.8$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₂₀H₂₈O₄Na (M+Na)⁺ 355.2, found 355.1; HRMS(ESI) calcd for C₂₀H₂₈O₄Na (M+Na)⁺ 355.1885, found 355.1881.



Cp₂Zr(H)Cl (389.0 mg, 1.51 mmol, 2.0 equiv) was weighed and added to a flask in a glove box, suspended in 7 mL DCM and cooled to 0 °C. A solution of alkyne (*R*)-**17** (501.5 mg, 1.51 mmol, 2.0 equiv) in 7 mL DCM was added to the stirred suspension of Cp₂Zr(H)Cl at 0 °C. Hydrozirconation was complete after 1.5 hours, after which the solution was cooled to -78 °C. At this time, a solution of

Me₂Zn (2.0 M in toluene, 754 μ L, 1.51 mmol, 2.0 equiv) was added slowly to the solution of vinyl zirconium at -78 °C. After stirring for 20 minutes at -78 °C, the reaction was allowed to warm to 0 °C. The solution was then allowed to stir for additional 20 minutes at 0 °C, after which a solution of the aldehyde **16** (592.3 mg, 0.75 mmol, 1.0 equiv) in 3.5 mL toluene was added at the same temperature. The reaction was allowed to stir overnight at 0 °C. Then the reaction was quenched with 10% aqueous solution of citric acid and the heterogeneous mixture was stirred for 1 h at room temperature until two clear phases were present. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The combined organic portion was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (3-25% EtOAc in hexanes) to afford the alcohol (855.3 mg) as a mixture of diastereomers.

NaHCO₃ (192.5 mg, 2.29 mmol, 3.0 equiv) was added to the solution of the above alcohol (855.3 mg, 0.76 mmol, 1.0 equiv) in 10 mL DCM at 0 °C. Dess-Martin periodinane (356.4 mg, 0.84 mmol, 1.1 equiv) was added to the stirred suspension in 2 portions. After 0.5 hour, the reaction was allowed to slowly warm to room temperature. After 1.5 hours, the reaction was concentrated, then the reaction was quenched with a solution of 20% aqueous Na₂S₂O₃/saturated aqueous NaHCO₃ (1:1) and the aqueous layer was extracted 3 times with EtOAc, The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-20% EtOAc in hexanes) to afford the product **n** (770.3 mg, 90% yield over two steps) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.27–7.16 (m, 4H), 6.89–6.78 (m, 5H), 6.66 (dd, *J* = 15.8, 0.9 Hz, 1H), 5.64 (dd, *J* = 15.7, 8.1 Hz, 1H), 5.53–5.28 (m, 7H), 4.67–4.39 (m, 5H), 4.21 (d, *J* = 11.3 Hz, 1H), 4.14–4.06 (m, 1H),

3.97–3.91 (m, 1H), 3.90–3.82 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.75–3.64 (m, 2H), 3.55–3.49 (m, 1H), 3.49–3.41 (m, 1H), 2.48–2.10 (m, 10H), 2.11–2.01 (m, 2H), 2.00–1.84 (m, 4H), 1.66–1.56 (m, 3H), 1.55–1.46 (m, 3H), 1.42 (s, 9H), 1.41 (s, 9H), 1.37–1.17 (m, 10H), 0.97–0.75 (m, 8H), -0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 200.65, 172.90, 172.86, 159.21, 158.97, 147.76, 135.81, 132.54, 131.97, 131.04, 130.97, 130.10, 129.27, 129.23, 128.94, 125.77, 125.36, 124.58, 123.81, 113.76, 113.55, 91.82, 82.03, 81.63, 81.07, 79.97, 79.93, 77.70, 75.48, 72.48, 70.77, 65.06, 55.20, 55.19, 35.35, 35.00, 34.69, 33.46, 31.50, 30.87, 29.49, 29.43, 29.22, 28.09, 28.07, 27.41, 26.81, 24.89, 24.88, 24.76, 22.62, 22.54, 18.03, 14.03, 13.77, -1.42; $\left[\alpha\right]_{D}^{20} = +14.4$ (c = 0.25, CHCl₃); MS(ESI) calcd for C₆₆H₁₀₄O₁₂SiNa (M+Na)⁺ 1139.7195, found 1139.7; HRMS(ESI) calcd for C₆₆H₁₀₄O₁₂SiNa (M+Na)⁺ 1139.7195, found 1139.7177.

Analytical sample of 23 (anti, anti) was prepared by deprotection of 19 with DDQ in phosphate buffer (pH = 7) and DCM. Selected chemical shifts and coupling constants for the syn, syn diastereomer were determined from the TOCSY spectrum of a mixture with 23 (anti, anti). (see Figure S2)



¹H NMR (600 MHz, C₆D₆:DMSO- d_6 =25:2) δ 6.09–5.96 (m, 2H), 5.84 (dd, J = 14.8, 6.8 Hz, 1H), 5.88–5.79 (m, 1H), 5.69 (dd, J = 15.6, 7.3 Hz, 1H), 5.67–5.59 (m, 2H), 5.59–5.41 (m, 3H), 5.10 (d, J = 4.4 Hz, 1H), 4.88 (d, J = 6.2 Hz, 1H), 4.84 (d, J = 6.7 Hz, 1H), 4.65 (d, J = 6.7 Hz, 1H), 4.54–4.47 (m, 1H), 4.29–4.18 (m, 4H), 3.93–3.87 (m, 1H), 3.85 (dd, J = 17.0, 8.7 Hz, 1H), 3.69–3.63 (m, 1H), 3.53 (dd,

J = 16.7, 8.8 Hz, 1H), 2.64–2.31 (m, 6H), 2.21–2.00 (m, 10H), 1.70–1.42 (m, 10H), 1.38 (s, 9H), 1.36 (s, 9H), 1.33–1.21 (m, 6H), 0.96 (t, *J* = 8.0 Hz, 2H), 0.90 (t, *J* = 7.7 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.00 (s, 9H).



Ketone **n** (426.2 mg, 0.38 mmol, 1.0 equiv) was dissolved in 10 mL DCM and cooled to -78 °C. Super-Hydride (1.0 M in THF, 496 μ L, 0.5 mmol, 1.3 equiv) was added slowly and the resulting solution was allowed to stir for 0.5 h at -78 °C. Then the reaction was quenched with a 10% aqueous solution of citric acid and the heterogeneous mixture was stirred for 1 h at room temperature until two clear phases

were present. The organic layer was separated and the aqueous layer was extracted 3 times with DCM. The organic layer was washed with brine, dried with MgSO₄, filtered, concentrated, and purified by flash chromatography (3-25% EtOAc in hexanes) to afford the desired alcohol **19** (> 20:1 selectivity, 400.9 mg, 94 % yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.27–7.14 (m, 4H), 6.88–6.78 (m, 4H), 5.68 (dd, *J* = 15.6, 6.2 Hz, 1H), 5.63–5.49 (m, 3H), 5.46–5.28 (m, 6H), 4.62 (d, *J* = 6.9 Hz, 1H), 4.58–4.41 (m, 4H), 4.23 (d, *J* = 11.4 Hz, 1H), 4.18 (t, *J* = 4.8 Hz, 1H), 4.10 (dd, *J* = 5.1, 2.9 Hz, 1H), 4.09–4.02 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.75–3.67 (m, 2H), 3.58 (d, *J* = 6.3 Hz, 1H), 3.50–3.40 (m, 2H), 3.41–3.33 (m, 1H), 2.44–2.08 (m, 10H), 2.06–1.90 (m, 6H), 1.66–1.46 (m, 6H), 1.41 (s, 9H), 1.40 (s, 9H), 1.38–1.13 (m, 10H), 0.97–0.76 (m, 8H), -0.00 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.07, 172.86, 159.22, 158.99, 132.77, 132.75, 131.89, 131.64, 131.35, 131.23, 130.93, 130.77, 130.01, 129.58, 129.24, 125.91, 125.79, 125.77, 113.70, 113.68, 91.70, 82.64, 81.86, 81.54, 79.96, 79.86, 78.93, 75.42, 72.83, 72.11, 69.62, 65.02, 55.19, 55.17, 35.47, 35.44, 34.97, 33.42, 31.52, 29.48, 29.23, 29.20, 28.08, 27.47, 27.36, 26.78, 24.98, 24.97, 24.87, 22.65, 22.57, 18.04, 14.05, 13.79, -1.43; $\left[\alpha\right]_D^{20} = +44.8$ (*c* = 0.25, CHCl₃); MS(ESI) calcd for C₆₆H₁₀₆O₁₂SiNa (M+Na)⁺ 1141.7, found 1141.6.



NaH (60% in mineral oil, 5.2 mg, 0.13 mmol, 1.5 equiv) was weighed and added to a vial in a glove box, suspended in 1.0 mL DMF and cooled to 0 °C. A solution of the alcohol **19** (97.0 mg, 0.087 mmol, 1.0 equiv) in 1.0 mL DMF was dropwise added to the stirred suspension of NaH at 0 °C. The reaction was stirred for 0.5 hour at this temperature. Then *p*-methoxybenzyl chloride (35 μ L, 0.26

mmol, 3.0 equiv) and TBAI (tetrabutylammonium iodide, 6.4 mg, 0.017 mmol, 0.2 equiv) was added slowly to the stirred solution at 0 °C. After 10 minutes, the reaction was allowed to slowly warm to room temperature. The reaction was allowed to stir overnight at room temperature. Then the reaction was quenched with saturated aqueous NaH₂PO₄ and the aqueous layer was extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-15% EtOAc in hexanes) to afford the product o (107.9 mg, quantitative yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.25–7.17 (m, 6H), 6.88–6.76 (m, 6H), 5.75 (dd, J = 15.7, 7.9 Hz, 1H), 5.69 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.69 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.69 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.69 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.69 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.69 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, J = 14.4, 7.5 Hz, 1H), 5.54 (dd, J = 15.9, 8.5 Hz, 1H), 5.54 (dd, 1H), 5.50 (dd, J = 15.4, 7.4 Hz, 1H), 5.46–5.33 (m, 6H), 4.70–4.62 (m, 2H), 4.58–4.44 (m, 4H), 4.28 (d, J = 6.6 Hz, 1H), 4.25 (d, J = 6.6 Hz, 1H), 4.20 (dd, J = 8.2, 3.5 Hz, 1H), 4.15–4.07 (m, 1H), 3.86–3.69 (m, 3H), 3.79 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.66–3.59 (m, 1H), 3.55–3.48 (m, 1H), 3.49–3.42 (m, 1H), 2.44–2.11 (m, 10H), 2.10–2.02 (m, 2H), 2.01–1.90 (m, 4H), 1.69–1.50 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.38–1.19 (m, 10H), 0.95–0.79 (m, 8H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) & 173.03, 172.94, 159.02, 158.95, 158.86, 135.56, 134.55, 131.55, 131.30, 131.29, 131.16, 130.81, 130.71, 130.62, 130.36, 129.31, 129.25, 128.96, 126.06, 126.03, 125.93, 113.71, 113.64, 113.49, 91.70, 82.23, 82.17, 81.29, 79.96, 79.93, 78.90, 78.51, 75.62, 72.32, 70.06, 69.65, 65.01, 55.22, 55.21, 55.20, 35.61, 35.49, 35.02, 33.59, 31.54, 29.70, 29.65, 29.57, 29.30, 28.10, 27.45, 26.83, 25.13, 25.02, 24.91, 22.71, 22.59, 18.05, 14.08, 13.82, -1.40; $\left[\alpha\right]_{D}^{20} = +14.4$ (c = 0.25, CHCl₃); MS(ESI) calcd for C₇₄H₁₁₄O₁₃SiNa (M+Na)⁺ 1261.8, found 1261.5; HRMS(ESI) calcd for $C_{74}H_{114}O_{13}SiNa (M+Na)^+$ 1261.7926, found 1261.7887.



TASF (tris(dimethylamino)sulfonium difluorotrimethylsilicate, 420.8 mg, 1.53 mmol, 20.0 equiv) and 4Å MS (500 mg) were weighed, added to a flask in a glove box, and suspended in 5.0 mL HMPA (hexamethylphosphoramide) at room temperature. A solution of the SEM-ether **o** (94.7 mg, 0.076 mmol, 1.0 equiv) in 5.0 mL HMPA was added to the stirred

suspension solution. The reaction was stirred for 48 hours at 80 °C. Then the reaction was cooled to room temperature and filtered through a plug of Celite. Distilled water was added to the filtrate and the aqueous layer was extracted 3 times with EtOAc. The combined organic portion was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-25% EtOAc in hexanes) to afford the product **26** (75.1 mg, 89% yield) as a colorless oil and recover the starting material SEM-ether **o** (6.4 mg, 7% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.25–7.18 (m, 6H), 6.87–6.77 (m, 6H), 5.75 (dd, *J* = 15.7, 7.9 Hz, 1H), 5.71–5.67 (m, 2H), 5.55 (dd, *J* = 15.6, 8.0 Hz, 1H), 5.51–5.32 (m, 6H), 4.67 (d, *J* = 11.2 Hz, 1H), 4.54–4.44 (m, 3H), 4.28 (d, *J* = 11.6 Hz, 1H), 4.26 (d, *J* = 11.6 Hz, 1H), 4.21–4.14 (m, 2H), 3.79 (s, 3H), 3.85–3.70 (m, 2H), 3.77 (s, 3H), 3.76 (s, 3H), 3.66–3.59 (m, 1H), 3.57–3.51 (m, 1H), 2.37–2.13 (m, 10H), 2.12–2.03 (m, 2H), 2.02–1.88 (m, 4H), 1.71–1.51 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.38–1.17 (m, 10H), 0.86 (t, *J* = 7.2 Hz, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 173.01, 172.98, 159.01, 158.94, 158.92, 137.25, 135.49, 132.06, 131.57, 131.32, 131.21, 130.69, 130.60, 130.34, 129.33, 129.28, 128.97, 128.56, 126.08, 125.88, 125.54, 113.70, 113.62, 113.52, 82.32, 82.03, 81.39, 80.05, 79.91, 78.87, 78.57, 72.51, 71.72, 70.06, 69.64, 55.20, 55.18, 35.57, 35.46, 35.15, 34.91, 31.51, 30.18, 29.79, 29.54, 29.26, 28.07, 27.46, 26.71, 25.09, 24.90, 22.69, 22.56, 14.05, 13.80; [α]_D²⁰ = -12.4 (*c* = 0.5, CHCl₃); MS(ESI) calcd for C_{68H100}O₁₂Na (M+Na)⁺ 1131.6, found 1131.7.



NaH (60 % dispersion in mineral oil, 10.0 mg, 0.25 mmol, 3.0 equiv) was weighed and added to a flask in a glove box, suspended in 0.5 mL THF/DMF (2/1) and cooled to 0 °C. A solution of the alcohol **26** (92.2 g, 0.083 mmol, 1.0 equiv) in 0.8 mL THF/DMF (2/1) was added dropwise to the stirred suspension of NaH at 0 °C. The reaction was allowed to stir for 30 minutes at this temperature, and a solution of sugar triflate **27**¹⁴ (163.0 mg, 0.416 mmol, 5.0 equiv) in 0.2 mL THF/DMF (2/1) was added dropwise at 0 °C. After 30 minutes, the solution was allowed to warm to room temperature and stir overnight. Then the reaction was

quenched with saturated aqueous NaH₂PO₄ at 0 °C, and extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-25% EtOAc in hexanes) to afford the product galactose ether **p** (77.0 mg, 69% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 7.24–7.17 (m, 6H), 6.87–6.76 (m, 6H), 5.75 (dd, *J* = 15.8, 7.9 Hz, 1H), 5.68 (dd, *J* = 15.2, 8.4 Hz, 1H), 5.59–5.48 (m, 3H), 5.47–5.30 (m, 6H), 4.69 (d, *J* = 11.2 Hz, 1H), 4.60–4.44 (m, 4H), 4.30–4.18 (m, 5H), 3.95–3.88 (m, 1H), 3.79 (s, 3H), 3.76 (s, 3H), 3.75 (s, 3H), 3.85–3.59 (m, 5H), 3.57–3.49 (m, 1H), 3.45 (dd, *J* = 10.0, 6.5 Hz, 1H), 2.44–2.11 (m, 10H), 2.09–1.90 (m, 6H), 1.65–1.47 (m, 6H), 1.51 (s, 3H), 1.43 (s, 9H), 1.42 (s, 9H), 1.40 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H), 1.37–1.17 (m, 10H), 0.85 (t, *J* = 7.2 Hz, 3H), 0.84 (t, *J* = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.03, 172.96, 159.00, 158.93, 158.85, 135.47, 135.27, 131.53, 131.35, 131.22, 130.71, 130.63, 130.42, 129.30, 128.94, 126.25, 126.11, 125.98, 113.70, 113.64, 113.50, 108.99, 108.33, 96.27, 82.31, 82.11, 81.47, 80.60, 79.94, 79.91, 78.87, 78.43, 72.39, 70.99, 70.66, 70.59, 70.05, 69.61, 67.11, 66.38, 55.21, 55.19, 55.17, 35.59, 35.48, 35.00, 33.57, 31.48, 29.67, 29.56, 29.28, 28.09, 28.08, 27.39, 26.82, 26.09, 25.95, 25.11, 25.01, 24.92, 24.38, 22.70, 22.59, 14.06, 13.81; [α]_D²⁰ = -28.4 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₈₀H₁₁₈O₁₇Na (M+Na)⁺ 1173.8, found 1173.7.



¹H NMR (400 MHz, CDCl₃) δ 7.32 (d, J = 8.2 Hz, 2H), 6.86 (d, J = 8.1 Hz, 2H), 4.73 (dd, J = 10.4, 10.4 Hz, 2H), 4.41–4.26 (m, 2H), 4.19–4.01 (m, 3H), 3.96 (dd, J = 12.7, 8.4 Hz, 1H), 3.90–3.74 (m, 4H), 3.80 (s, 3H), 3.67 (dd, J = 10.2, 5.8 Hz, 1H), 3.38 (dd, J = 6.8, 6.8 Hz, 1H), 1.57 (s, 3H), 1.43 (s, 3H), 1.37 (s, 3H), 1.33 (s, 3H).



DDQ (29.2 mg, 0.13 mmol, 3.5 equiv) was added to a biphasic solution of PMB ether **p** (49.7 mg, 0.037 mmol) in 2 mL DCM and 200 μ L phosphate buffer (pH = 7) at 0 °C. The resulting solution was allowed to stir for 1 hour at 0 °C, then warmed to room temperature for additional 1.0 hour. Then the reaction was quenched with saturated aqueous NaHCO₃ solution and extracted 3 times with DCM. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-50% EtOAc in hexanes) to afford the

desired product triol **29** (29.5 mg, 81% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.77–5.69 (m, 2H), 5.64–5.57 (m, 2H), 5.56–5.46 (m, 2H), 5.46–5.29 (m, 5H), 4.56 (dd, J = 8.0, 2.3 Hz, 1H), 4.27 (dd, J = 5.0, 2.3 Hz, 1H), 4.22 (dd, J = 7.9, 1.8 Hz, 1H), 4.20–4.16 (m, 1H), 4.15–4.09 (m, 1H), 4.05–4.00 (m, 1H), 3.93–3.87 (m, 1H), 3.80–3.73 (m, 1H), 3.70–3.54 (m, 2H), 3.51–3.42 (m, 2H), 2.41–2.08 (m, 10H), 2.08–1.90 (m, 6H), 1.67–1.53 (m, 6H), 1.51 (s, 3H), 1.42 (s, 9H), 1.41 (s, 9H), 1.40 (s, 3H), 1.30 (s, 3H), 1.30 (s, 3H), 1.38–1.20 (m, 10H), 0.87 (t, J = 7.4 Hz, 3H); 0.86 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.12, 173.06, 135.84, 134.64, 133.20, 131.72, 130.65, 129.83, 128.88, 125.89, 125.61, 125.18, 109.05, 108.41, 96.24, 82.14, 80.84, 80.48, 80.09, 80.05, 73.50, 73.00, 72.02, 71.02, 70.57, 67.32, 66.64, 36.71, 35.38, 34.98, 33.34, 31.45, 29.48, 29.25, 28.90, 28.08, 27.35,

¹⁴ Xie, W.; Tanabe, G.; Akaki, J.; Morikawa, T.; Ninomiya, K.; Minematsu, T.; Yoshikawa, M.; Wu, X.; Muraoka, O. *Bioorg. Med. Chem.* **2011**, *19*, 2015.

26.79, 26.07, 25.93, 24.91, 24.89, 24.80, 24.36, 22.67, 22.55, 14.04, 13.81; $[\alpha]_D^{20} = -21.0$ (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₅₆H₉₄O₁₄Na (M+Na)⁺ 1013.7, found 1013.5; HRMS(ESI) calcd for C₅₆H₉₄O₁₄Na (M+Na)⁺ 1013.6541, found 1013.6521.



0.3 mL Pyridine and catalytic DMAP was added to a stirred solution of triol **29** (30.4 mg, 30.7 μ mol) in 0.4 mL DCM at 0 °C. Then 0.3 mL acetic anhydride was added dropwise to the stirred solution at 0 °C. The mixture was allowed to warm to room temperature, stirred overnight and the solvent was removed azeotropically with toluene. The crude product was quenched with saturated aqueous NaH₂PO₄, and extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by flash chromatography (5-30% EtOAc in hexanes) to afford the product tri-acetate

30 (30.2 mg, 88% yield) as a colorless oil. ¹H NMR (400 MHz, CDCl₃) δ 5.74 (dd, J = 15.7, 6.9 Hz, 1H), 5.65 (dd, J = 15.7, 6.1 Hz, 1H), 5.56 (dd, J = 15.6, 6.8 Hz, 1H), 5.2–5.37 (m, 6H), 5.36–5.21 (m, 4H), 4.94–4.84 (m, 1H), 4.57 (dd, J = 7.9, 2.1 Hz, 1H), 4.27 (dd, J = 5.0, 2.2 Hz, 1H), 4.23 (dd, J = 8.0, 1.4 Hz, 1H), 4.01 (dd, J = 7.3, 5.4 Hz, 1H), 3.94–3.87 (m, 1H), 3.79–3.70 (m, 1H), 3.60 (dd, J = 9.8, 6.4 Hz, 1H), 3.54–3.47 (m, 1H), 3.40 (dd, J = 9.8, 6.5 Hz, 1H), 2.41–2.29 (m, 3H), 2.26–2.15 (m, 5H), 2.06 (s, 3H), 2.03 (s, 3H), 2.15–1.87 (m, 8H), 2.00 (s, 3H), 1.67–1.54 (m, 6H), 1.51 (s, 3H), 1.43 (s, 9H), 1.42 (s, 9H), 1.41 (s, 3H), 1.31 (s, 3H), 1.30 (s, 3H), 1.38–1.22 (m, 10H), 0.88 (t, J = 7.2 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.90, 172.79, 170.40, 170.08, 169.78, 136.20, 133.49, 132.81, 131.83, 130.69, 129.94, 126.66, 125.85, 124.97, 124.28, 109.00, 108.35, 96.25, 80.53, 80.42, 80.01, 79.97, 77.39, 75.30, 74.82, 73.41, 70.96, 70.64, 70.57, 67.24, 66.49, 35.32, 34.96, 33.98, 33.41, 31.45, 29.51, 29.43, 29.25, 28.09, 28.07, 27.28, 26.79, 26.09, 25.95, 24.91, 24.88, 24.77, 24.61, 24.35, 22.62, 22.58, 21.22, 21.14, 14.05, 13.79; [α]_D²⁰ = -26.8 (c = 1.0, CHCl₃); MS(ESI) calcd for C₆₂H₁₀₀O₁₇Na (M+Na)⁺ 1139.7, found 1139.4; HRMS(ESI) calcd for C₆₂H₁₀₀O₁₇Na (M+Na)⁺ 1139.7195, found 1139.7209.



Trifluoroacetic acid (0.4 ml) was added to a stirred solution of tri-acetate **30** (9.0 mg, 8.05 μ mol) in 1.0 mL DCM and 0.6 mL water at room temperature. Then the resulting solution was stirred overnight and monitored by ¹H NMR. When the reaction was completed, the solvent was removed azeotropically with toluene. After drying with high vacuum, the crude product was dissolved in 1.2 mL dry toluene and 0.8 mL dry MeOH, and TMSCHN₂ (2.0 M in hexanes, 300 μ l) was added dropwise at 0 °C until the gas evolution ceased.

Then, the reaction was stirred for 30 minutes at 0 °C and quenched with acetic acid. The solvent was removed azeotropically with toluene. The residual solvent was further removed by high vacuum and the crude product was dissolved in dry 0.8 mL DCM and 0.6 mL pyridine. After cooling to 0 °C, catalytic DMAP was added to the stirred solution. Then 0.6 mL acetic anhydride was added dropwise to the solution at 0 °C. The reaction was allowed to slowly warm to room temperature. After stirring overnight at room temperature, the solvent was removed azeotropically with toluene. The crude product was quenched with saturated aqueous NaH₂PO₄, and extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by a pipette column (5-50% EtOAc in hexanes) to afford the product \mathbf{q} as a mixture of anomers (7.6 mg, 84% yield over three steps) as a colorless oil.



Hydrazine acetate (1.9 mg, 20.6 μ mol, 3.0 equiv) was added to a stirred solution of the above product (7.6 mg, 6.8 μ mol, 1.0 equiv) in 2.0 mL DMF at room temperature. After stirring for 3 h at room temperature, the reaction was quenched with saturated aqueous NaH₂PO₄, and extracted 3 times with EtOAc. The combined organic layer was washed with brine, dried with MgSO₄, concentrated, filtered, and purified by a pipette column (5-60% EtOAc in hexanes) to afford the product (5.5 mg, 75% yield) as a colorless oil.

Trichloroacetonitrile (8 µl, 80 µmol, 16.0 equiv) and catalytic DBU (1,8-diazabicyclo[5.4.0]undec-7-ene) were added to a stirred solution of the above product (5.5 mg, 5.1 µmol, 1.0 equiv) in 1.0 mL DCM at room temperature. After stirring for 3 hours at room temperature, the reaction was concentrated and purified quickly by a pipette column (5-60% EtOAc in hexanes) to afford the acetamidate **31** (3.8 mg) as a colorless oil. The sample was very unstable and so the acetamidate **31** was brought into the following reaction immediately. ¹H NMR (500 MHz, C_6D_6) δ 8.50 (s, 1H), 6.05–5.97 (m, 2H), 5.88 (dd, *J* = 10.9, 3.1 Hz, 1H), 5.79 (dd, *J* = 11.0, 3.5 Hz, 1H), 5.78–5.73 (m, 1H), 5.71–5.63 (m, 2H), 5.63–5.52 (m, 5H), 5.51–5.43 (m, 2H), 5.41–5.30 (m, 2H), 4.61 (t, *J* = 6.4 Hz, 1H), 4.23 (dd, *J* = 8.0, 5.6 Hz, 1H), 3.79–3.71 (m, 2H), 3.60–3.52 (m, 1H), 3.44–3.37 (m, 1H), 3.41 (s, 3H), 3.35 (s, 3H), 3.37–3.31 (m, 1H), 2.71–2.61 (m, 2H), 2.47–2.13 (m, 8H), 2.10–1.99 (m, 6H), 1.98 (s, 3H), 1.82 (s, 3H), 1.83 (s, 3H), 1.77 (s, 3H), 1.76 (s, 3H), 1.70–1.62 (m, 2H), 1.61 (s, 3H), 1.57–1.44 (m, 2H), 1.43–1.35 (m, 5H), 1.35–1.28 (m, 5H), 1.38–1.16 (m, 2H), 0.94 (t, *J* = 7.0 Hz, 3H), 0.93 (t, *J* = 7.0 Hz, 3H).



The acetamidate **31** (16.9 mg, 0.014 mmol, 1.0 equiv) and (*S*)-solketal **33** (17 μ l, 0.14 mmol, 10.0 equiv) were dissolved in 2.0 mL DCM, and 200 mg freshly activated 5Å MS was added to the reaction. The resulting solution was stirred for 0.5 hour at room temperature and then cooled to -78 °C. TMSOTf (1 μ l, 0.006 mmol, 0.4 equiv) was added to the reaction at -78 °C. After stirring for 2 hours at the same temperature, triethylamine (2 drops) was added to quench the reaction. Then the solvent was removed and the crude product was purified by a pipette column (5-60% EtOAc in hexanes)

to afford the product **r** as a colorless oil (11.0 mg, 72 % yield). ¹H NMR (400 MHz, C₆D₆) δ 6.03 (dd, J = 15.6, 7.1 Hz, 1H), 5.77 (dd, J = 15.8, 6.8 Hz, 1H), 5.73–5.46 (m, 11H), 5.43–5.34 (m, 1H), 5.34–5.30 (m, 1H), 5.25 (dd, J = 10.5, 3.2 Hz, 1H), 4.40 (d, J = 7.9 Hz, 1H), 4.33–4.25 (m, 1H), 4.13–4.04 (m, 1H), 3.88–3.75 (m, 4H), 3.70 (dd, J = 9.1, 6.0 Hz, 1H), 3.63–3.47 (m, 3H), 3.41 (s, 3H), 3.36 (s, 3H), 3.42–3.26 (m, 1H), 2.77–2.60 (m, 2H), 2.49–2.13 (m, 8H), 2.13–1.92 (m, 6H), 2.00 (s, 3H), 1.84 (s, 3H), 1.79 (s, 3H), 1.78 (s, 3H), 1.77 (s, 3H), 1.76 (s, 3H), 1.72–1.61 (m, 2H), 1.43 (s, 3H), 1.58–1.08 (m, 14H), 1.26 (s, 3H), 0.93 (t, J = 7.2 Hz, 3H), 0.92 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, C₆D₆) δ 173.32, 173.03, 170.06, 169.97, 169.78, 169.44, 169.41, 168.98, 136.04, 133.95, 133.18, 132.21, 131.38, 131.06, 126.00, 125.79, 125.04, 109.24, 101.83, 81.07, 80.87, 78.13, 75.23, 75.14, 74.58, 73.56, 72.39, 71.66, 69.42, 68.11, 66.95, 66.59, 51.06, 50.96, 34.22, 33.85, 33.78, 33.38, 31.86, 29.88, 29.84, 29.71, 28.88, 27.80, 27.01, 26.90, 25.39, 25.07, 24.93, 24.83, 23.07, 22.99, 21.07, 20.82, 20.78, 20.45, 20.30, 20.19, 14.30, 14.02; $[\alpha]_D^{20} = -9.0$ (c = 0.8, CHCl₃); MS (ESI) calculated for C₆₂H₉₆O₂₂Na⁺ (M+Na)⁺ 1215.6, found 1215.4.



The per-acetate **r** (11.0 mg, 0.091 mmol, 1.0 equiv) was dissolved in 2.0 mL MeOH, treated with catalytic TsOHH₂O (*p*-toluenesulfonic acid monohydrate) (0.35 mg, 1.8 µmol, 0.2 equiv), and the resulting solution was stirred overnight at room temperature. Then the reaction was concentrated and purified by a pipette column (5-60% EtOAc in hexanes) to afford the desired diol (6.5 mg). ¹H NMR (500 MHz, C₆D₆) δ 6.03 (dd, *J* = 15.6, 7.2 Hz, 1H), 5.77 (dd, *J* = 15.6, 6.7 Hz, 1H), 5.72–5.69 (m, 2H), 5.69–5.54 (m, 7H), 5.53–5.46 (m, 2H), 4.24 4.277 (m)

2H), 5.42–5.30 (m, 2H), 5.20 (dd, J = 10.5, 3.4 Hz, 1H), 4.31 (d, J = 7.9 Hz, 1H), 4.34–4.27 (m, 1H), 3.85–3.77 (m,

2H), 3.77-3.69 (m, 2H), 3.66-3.61 (m, 1H), 3.60-3.47 (m, 4H), 3.42 (s, 3H), 3.36 (s, 3H), 3.17 (dd, J = 9.4, 4.6 Hz, 1H), 2.78-2.61 (m, 2H), 2.52-2.26 (m, 4H), 2.24-2.13 (m, 4H), 2.10-2.03 (m, 6H), 2.01 (s, 3H), 1.85 (s, 3H), 1.83 (s, 3H), 1.78 (s, 3H), 1.75 (s, 3H), 1.74 (s, 3H), 1.71-1.60 (m, 2H), 1.57-1.34 (m, 8H), 1.34-1.27 (m, 4H), 1.27-1.17 (m, 2H), 0.93 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 6.8 Hz, 3H); MS (ESI) calcd for $C_{59}H_{92}O_{22}Na^+$ (M+Na)⁺ 1175.6, found 1175.4.

The diol (6.5 mg, 5.6 µmol, 1.0 equiv) was dissolved in 1.0 mL MeOH, treated with NaOMe (0.5 M in MeOH, 50 μ L), and the resulting solution was stirred overnight at room temperature. Pure nigricanoside A dimethyl ester analog 32 (4.0 mg, 48% yield over two steps) was obtained via C18 reversed-phase HPLC using a phenomenex, luna 5 μ 250 \times 10.00 mm 5 micro column, with 9:11 MeCN/H₂O as the eluent (no acid, flow rate = 2.5 mL/min, retention time: 68.0 min). The product was monitored at 194 nm wavelength. ¹H NMR (600 MHz, CD₃OD) δ 5.76 (dd, J = 15.7, 7.9 Hz, 1H), 5.71 (dd, J = 15.7, 7.8 Hz, 1H), 5.66 (dd, J = 15.7, 6.0 Hz, 1H), 5.61 (dd, J = 15.7, 6.0 Hz, 1H), 5.71 (dd, J = 15.7, 7.8 Hz, 1H), 5.66 (dd, J = 15.7, 6.0 Hz, 1H), 5.71 (dd, J = 15.7, 6.0 Hz, 1H), 5.71H), 5.51-5.34 (m, 6H), 4.22 (d, J = 7.6 Hz, 1H), 4.20 (dd, J = 5.6, 3.0 Hz, 1H), 4.08 (ddd, J = 6.3, 6.3, 6.3 Hz, 1H), 4.02 (dd, J = 6.0, 3.5 Hz, 1H), 3.87 (dd, J = 10.4, 5.2 Hz, 1H), 3.85–3.80 (m, 2H), 3.80–3.75 (m, 1H), 3.70 (dd, J = J = 9.7, 7.6 Hz, 1H), 3.62–3.52 (m, 4H), 3.47 (dd, J = 9.7, 3.4 Hz, 1H), 3.48–3.43 (m, 1H), 2.41–2.15 (m, 10H), 2.13–1.99 (m, 6H), 1.70–1.60 (m, 4H), 1.57–1.47 (m, 2H), 1.46–1.27 (m, 10H), 0.92 (t, J = 7.3 Hz, 3H); 0.91 (t, J = 7.1 Hz, 3H): ¹H NMR (600 MHz, C₆D₆:DMSO- $d_6=25:2$) δ 6.05 (dd, J=15.5, 5.6 Hz, 1H), 6.00 (dd, J=15.5, 5.6 Hz, 1H), 5.86 (dd, J = 15.6, 6.8 Hz, 1H), 5.84–5.80 (m, 1H), 5.79 (dd, J = 15.7, 6.9 Hz, 1H), 5.74–5.67 (m, 1H), 5.67– $5.61 \text{ (m, 1H)}, 5.60-5.53 \text{ (m, 2H)}, 5.47-5.40 \text{ (m, 1H)}, 4.53-4.49 \text{ (m, 1H)}, 4.42 \text{ (d, } J = 7.6 \text{ Hz, 1H)}, 4.28 \text{ (dd, } J = 6.5, 3.43 \text{ (m, 2H)}, 5.47-5.40 \text{ (m,$ 3.0 Hz, 1H), 4.25-4.21 (m, 1H), 4.14 (dd, J = 10.4, 5.6 Hz, 1H), 4.11-4.07 (m, 1H), 4.06-4.03 (m, 1H), 3.93 (dd, J = 10.4, 5.6 Hz, 1H), 4.10-4.07 (m, 1H), 4.06-4.03 (m, 1H), 3.93 (dd, J = 10.4, 5.6 Hz, 1H), 4.10-4.07 (m, 1H), 4.06-4.03 (m, 1H), 3.93 (dd, J = 10.4, 5.6 Hz, 1H), 4.10-4.07 (m, 1H), 4.06-4.03 (m, 1H), 3.93 (dd, J = 10.4, 5.6 Hz, 1H), 4.10-4.07 (m, 1H), 4.06-4.03 (m, 1H), 3.93 (dd, J = 10.4, 5.6 Hz, 1H), 4.10-4.07 (m, 1H), 4.06-4.03 (m, 1H), 3.93 (dd, J = 10.4, 5.6 Hz), 3.93 (m, 1H), 3= 9.7, 5.9 Hz, 1H), 3.92 (dd, *J* = 10.4, 5.2 Hz, 1H), 3.99–3.90 (m, 2H), 3.90–3.84 (m, 3H), 3.81 (dd, *J* = 9.7, 5.9 Hz, 1H), 3.74-3.70 (m, 2H), 3.67 (bt, J = 6.0 Hz, 1H), 3.44 (s, 3H), 3.38 (s, 3H), 2.65-2.52 (m, 3H), 2.52-2.43 (m, 2H), 2.42-2.31 (m, 1H), 2.21-2.15 (m, 6H), 2.13 (ddd, J = 7.4, 7.4, 7.4 Hz, 2H), 2.04 (ddd, J = 7.3, 7.3, 7.3 Hz, 2H), 1.72-1.51 (m, 7H), 1.47-1.37 (m, 5H), 1.33-1.26 (m, 4H), 0.93 (t, J = 7.4 Hz, 3H), 0.90 (bt, J = 6.9 Hz, 3H). ¹³C NMR (100 MHz, CD₃OD) δ 176.02, 175.93, 136.56, 135.74, 132.86, 132.50, 131.84, 130.62, 127.86, 127.58, 105.51, 84.44, 82.78, 82.03, 75.48, 75.01, 75.00, 74.34, 73.05, 72.76, 72.42, 72.40, 70.43, 68.64, 64.28, 52.27, 52.22, 38.25, 35.00, 34.73, 34.39, 32.95, 31.39, 30.83, 30.72, 30.19, 28.73, 27.97, 26.37, 26.21, 26.08, 24.10, 23.92, 14.72, 14.50; ¹³C NMR (100 MHz, C_6D_6 :DMSO- d_6 =25:2) δ 173.57, 173.50, 136.28, 134.06, 131.44, 131.27, 131.24, 130.54, 129.43, 127.03, 104.95, 83.31, 82.04, 80.62, 74.46, 74.41, 73.95, 73.01, 72.26, 71.91, 71.57, 69.45, 68.22, 63.98, 51.14, 51.00, 37.80, 34.15, 33.98, 33.43, 31.86, 30.50, 29.86, 29.79, 29.42, 27.86, 27.02, 25.56, 25.35, 25.08, 23.18, 22.97, 14.35, 14.11; $[\alpha]_D^{20} = -10.4$ (c = 0.25, CHCl₃); $[\alpha]_D^{20} = -4.8$ (c = 0.25, CH₂Cl₂); MS (ESI) calcd for C₄₇H₈₀O₁₆Na (M+Na)⁺ 923.53, found 923.4; HRMS(ESI) calcd for C₄₇H₈₀O₁₆Na (M+Na)⁺ 923.5344, found 923.5316.

Nigricanoside A dimethyl ether **2** was made analogously with compound **16** and (*S*)-**17** according to the following scheme.





¹H NMR (400 MHz, CDCl₃) δ 7.29–7.16 (m, 4H), 6.94–6.79 (m, 5H), 6.68 (d, J = 15.8 Hz, 1H), 5.66 (dd, J = 15.7, 8.2 Hz, 1H), 5.53–5.26 (m, 7H), 4.70–4.39 (m, 5H), 4.21 (d, J = 11.2 Hz, 1H), 4.16–4.07 (m, 1H), 3.99–3.92 (m, 1H), 3.92–3.85 (m, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.77–3.69 (m, 2H), 3.60–3.52 (m, 1H), 3.51–3.43 (m, 1H), 2.46–2.32 (m, 3H), 2.30–2.13 (m, 7H), 2.11–2.02 (m, 2H), 2.01–1.88 (m, 4H),

1.69–1.47 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.36–1.19 (m, 10H), 0.99–0.77 (m, 8H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 200.82, 172.92, 172.88, 159.18, 158.96, 148.00, 135.86, 132.53, 132.02, 131.05, 130.97, 130.12, 129.26, 128.92, 125.77, 125.31, 124.72, 123.80, 113.75, 113.55, 91.81, 82.07, 81.64, 80.99, 80.00, 79.94, 77.94, 75.47, 72.48, 70.78, 65.06, 55.19, 35.35, 35.00, 34.75, 33.46, 31.50, 30.93, 29.54, 29.42, 29.22, 28.09, 28.08, 27.41, 26.81, 24.89, 24.86, 24.80, 22.63, 22.55, 18.03, 14.06, 13.78, -1.42; $[\alpha]_D^{20} = -13.4$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₆₆H₁₀₄O₁₂SiNa (M+Na)⁺ 1139.7, found 1139.6; HRMS(ESI) calcd for C₆₆H₁₀₄O₁₂SiNa (M+Na)⁺, 1139.7195, found 1139.7209.



¹H NMR (500 MHz, CDCl₃) δ 7.29–7.20 (m, 4H), 6.88– 6.82 (m, 4H), 5.69 (dd, *J* = 15.6, 6.0 Hz, 1H), 5.63–5.51 (m, 3H), 5.48–5.31 (m, 6H), 4.64 (d, *J* = 7.0 Hz, 1H), 4.60– 4.50 (m, 4H), 4.25 (d, *J* = 11.4 Hz, 1H), 4.18 (d, *J* = 3.7 Hz, 1H), 4.14–4.10 (m, 1H), 4.08 (dd, *J* = 12.7, 6.4 Hz, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.77–3.68 (m, 2H), 3.51–3.42 (m, 2H), 3.41–3.35 (m, 1H), 2.44–2.09 (m, 10H), 2.08–1.91 (m,

6H), 1.70–1.49 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.38–1.20 (ddt, J = 25.6, 18.6, 9.4 Hz, 10H), 0.98–0.80 (m, 8H), 0.01 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 173.06, 172.87, 159.22, 158.95, 132.86, 132.72, 131.92, 131.60, 131.33, 131.15, 130.93, 130.84, 129.98, 129.59, 129.30, 125.90, 125.79, 125.72, 113.70, 113.64, 91.70, 82.65, 81.86, 81.50, 79.97, 79.87, 79.00, 75.40, 72.65, 72.10, 69.66, 65.03, 55.20, 55.17, 35.59, 35.49, 34.97, 33.41, 31.52, 29.50, 29.24, 29.11, 28.08, 27.43, 27.37, 26.78, 25.06, 24.98, 24.87, 22.66, 22.58, 18.03, 14.06, 13.81, -1.42; $[\alpha]_D^{20} = +10.0$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₆₆H₁₀₆O₁₂SiNa (M+Na)⁺ 1141.7, found 1141.7; HRMS(ESI) calcd for C₆₆H₁₀₆O₁₂SiNa (M+Na)⁺, 1141.7351, found 1141.7334.

The (*R*) and (*S*) Mosher's esters were synthesized from **21** and the (*S*) and (*R*) acid chloride, respectively (pyridine, DMAP, CH_2Cl_2 , rt, 24 h). The resulting differences in chemical shifts are consistent with (*R*) stereochemistry at C9 as shown.





¹H NMR (600 MHz, C₆D₆:DMSO- d_6 =25:2) δ 6.07–5.97 (m, 2H), 5.92 (dd, J = 15.6, 7.5 Hz, 1H), 5.85–5.78 (m, 1H), 5.76–5.70 (m, 1H), 5.67 (dd, J = 15.5, 7.3 Hz, 1H), 5.66– 5.60 (m, 1H), 5.58–5.42 (m, 3H), 5.18 (d, J = 4.5 Hz, 1H), 4.97 (d, J = 5.4 Hz, 1H), 4.86 (d, J = 6.8 Hz, 1H), 4.65 (d, J= 6.8 Hz, 1H), 4.42–4.37 (m, 1H), 4.33 (d, J = 4.6 Hz, 1H), 4.28–4.20 (m, 3H), 4.01–3.92 (m, 1H), 3.90–3.80 (m, 1H), 3.60–3.50 (m, 2H), 2.63–2.34 (m, 6H), 2.23–2.02 (m, 10H), 1.72–1.42 (m, 10H), 1.38 (s, 9H), 1.36 (s, 9H), 1.31–1.21 (m, 6H), 0.96 (t, *J* = 8.1 Hz, 2H), 0.91 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 6.9 Hz, 3H), 0.00 (s, 9H).

Analytical sample of 25 (anti, syn) was prepared by deprotection of t with DDQ in phosphate buffer (pH = 7) and DCM.



¹H NMR (600 MHz, C_6D_6 :DMSO- $d_6=25:2$) δ 6.05 (dd, J = 15.5, 6.5 Hz, 1H), 5.96 (dd, J = 15.6, 6.1 Hz, 1H), 5.84 (dd, J = 15.3, 6.8 Hz, 1H), 5.87–5.81 (m, 1H), 5.68 (dd, J = 15.6, 7.5 Hz, 1H), 5.65–5.58 (m, 2H), 5.58–5.41 (m, 3H), 5.18 (d, J = 4.6 Hz, 1H), 4.92 (d, J = 6.2 Hz, 1H), 4.84 (d, J = 6.8 Hz, 1H), 4.65 (d, J = 6.8 Hz, 1H), 4.49–4.44 (m, 1H), 4.34 (d, J = 4.4 Hz, 1H), 4.28–4.18 (m, 3H), 3.94–3.88 (m,

1H), 3.84 (dd, *J* = 16.9, 8.9 Hz, 1H), 3.71–3.66 (m, 1H), 3.53 (dd, *J* = 16.7, 8.9 Hz, 1H), 2.62–2.28 (m, 6H), 2.19– 1.99 (m, 10H), 1.70–1.42 (m, 10H), 1.38 (s, 9H), 1.36 (s, 9H), 1.31–1.22 (m, 6H), 0.96 (t, *J* = 8.1 Hz, 2H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.87 (t, *J* = 7.1 Hz, 3H), -0.00 (s, 9H).



¹H NMR (400 MHz, CDCl₃) δ 7.24–7.18 (m, 6H), 6.87– 6.78 (m, 6H), 5.73 (dd, J = 15.7, 8.0 Hz, 1H), 5.67 (dd, J = 15.6, 8.1 Hz, 1H), 5.54 (dd, J = 14.8, 7.0 Hz, 1H), 5.49 (dd, J = 15.6, 7.4 Hz, 1H), 5.45–5.31 (m, 6H), 4.69–4.60 (m, 2H), 4.57–4.43 (m, 4H), 4.30 (d, J = 11.5 Hz, 1H), 4.26 (d, J = 11.3 Hz, 1H), 4.15 (dd, J = 8.0, 3.7, Hz, 1H), 4.15–4.07 (m, 1H), 3.79 (s, 3H), 3.78 (s, 3H), 3.84–3.69 (m, 3H), 3.77

(s, 3H), 3.62-3.56 (m, 1H), 3.54-3.40 (m, 2H), 2.43-2.03 (m, 12H), 2.00-1.90 (m, 4H), 1.66-1.50 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.37-1.07 (m, 10H), 0.87 (t, J = 7.3 Hz, 3H), 0.86 (t, J = 6.9 Hz, 3H), 0.01 (s, 9H); 13 C NMR (100 MHz, CDCl₃) δ 173.00, 172.92, 159.03, 158.95, 158.86, 135.82, 134.50, 131.55, 131.27, 131.24, 131.22, 130.80, 130.70, 130.66, 129.93, 129.24, 129.21, 128.96, 126.04, 125.97, 125.91, 113.72, 113.65, 113.49, 91.69, 82.33, 82.05, 81.17, 79.95, 79.90, 79.15, 78.57, 75.60, 72.26, 70.07, 69.89, 65.00, 55.21, 55.18, 35.60, 35.49, 35.00, 33.57, 31.54, 30.10, 29.66, 29.58, 29.29, 28.09, 28.08, 27.44, 26.82, 25.10, 25.00, 24.90, 22.71, 22.58, 18.04, 14.07, 13.84, -1.41; $[\alpha]_D^{20} = -15.4$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₇₄H₁₁₄O₁₃SiNa (M+Na)⁺ 1261.8, found 1261.7; HRMS(ESI) calcd for C₇₄H₁₁₄O₁₃SiNa (M+Na)⁺, 1261.7926, found 1261.7942.



¹H NMR (400 MHz, CDCl₃) δ 7.25–7.19 (m, 6H), 6.87– 6.79 (m, 6H), 5.73 (dd, *J* = 15.9, 8.0 Hz, 1H), 5.73–5.66 (m, 2H), 5.55 (dd, *J* = 15.7, 7.8 Hz, 1H), 5.53–5.31 (m, 6H), 4.65 (d, *J* = 11.3 Hz, 1H), 4.58–4.46 (m, 3H), 4.31 (d, *J* = 11.6 Hz, 1H), 4.27 (d, *J* = 11.4 Hz, 1H), 4.20–4.11 (m, 2H), 3.79 (s, 3H), 3.78 (s, 3H), 3.85–3.70 (m, 2H), 3.77 (s, 3H),

3.63–3.56 (m, 1H), 3.56–3.49 (m, 1H), 2.37–2.12 (m, 10H), 2.12–2.05 (m, 2H), 2.00–1.91 (m, 4H), 1.70–1.48 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.38–1.18 (m, 10H), 0.92–0.79 (m, 6H); 13 C NMR (100 MHz, CDCl₃) δ 13 C NMR (100 MHz, CDCl₃) δ 173.00, 172.99, 159.02, 158.95, 158.92, 137.20, 135.79, 132.06, 131.58, 131.27, 131.21, 130.68, 130.63, 129.94, 129.35, 129.20, 128.98, 128.64, 126.03, 125.87, 125.55, 113.72, 113.64, 113.52, 82.41, 81.93, 81.29, 80.06, 79.92, 79.13, 78.64, 72.47, 71.72, 70.08, 69.89, 55.21, 55.19, 35.58, 35.48, 35.14, 34.92, 31.53, 30.06, 29.82, 29.57, 29.28, 28.07, 27.47, 26.72, 25.08, 24.99, 24.90, 22.71, 22.57, 14.06, 13.84; $[\alpha]_D^{-20} = -39.6$ (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₆₈H₁₀₀O₁₂Na (M+Na)⁺ 1131.7, found 1131.6; HRMS(ESI) calcd for C₆₈H₁₀₀O₁₂Na (M+Na)⁺, 1131.7112, found 1131.7108.



The compound **u** (77.7 mg, 0.07 mmol, 1.0 equiv) and 4nitrobenzoic acid (17.6 mg, 0.105 mmol, 1.5 equiv) were dissolved in 1.0 mL DCM and cooled to 0 °C DIAD (diisopropyl azodicarboxylate) (21 μ L, 0.105 mmol, 1.5 equiv) was added slowly and the resulting solution was allowed to stir for 1 h at 0 °C. Then the reaction was concentrated and purified by flash chromatography (5-25%

EtOAc in hexanes) to afford the desired ester as a colorless oil The ester was dissolved in 1.0 mL MeOH, treated with NaOMe (0.5 M in MeOH, 50 μL), and the resulting solution was stirred overnight at room temperature. Then the reaction was concentrated and purified by flash chromatography (5-20% EtOAc in hexanes) to afford the desired alcohol (56.9 mg, 73% over two steps) as a colorless oil ¹H NMR (400 MHz, CDCl₃) δ 7.25–7.18 (m, 6H), 6.90–6.77 (m, 6H), 5.73 (dd, *J* = 15.7, 8.0 Hz, 1H), 5.73–5.66 (m, 2H), 5.55 (dd, *J* = 15.8, 7.9 Hz, 1H), 5.54–5.31 (m, 6H), 4.66 (d, *J* = 11.2 Hz, 1H), 4.56–4.44 (m, 3H), 4.31 (d, *J* = 11.5 Hz, 1H), 4.27 (d, *J* = 11.4 Hz, 1H), 4.21–4.13 (m, 1H), 4.13–4.08 (m, 1H), 3.79 (s, 3H), 3.84–3.72 (m, 2H), 3.78 (s, 3H), 3.77 (s, 3H), 3.66–3.59 (m, 1H), 3.56–3.49 (m, 1H), 2.36–2.12 (m, 10H), 2.12–2.03 (m, 2H), 2.02–1.91 (m, 4H), 1.70–1.51 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H), 1.40–1.19 (m, 10H), 0.87 (t, *J* = 7.3 Hz, 3H), 0.85 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 173.02, 172.99, 159.03, 158.96, 158.92, 137.18, 135.77, 132.01, 131.57, 131.24, 130.69, 130.65, 129.97, 129.35, 129.21, 129.01, 128.57, 126.19, 125.86, 125.54, 113.72, 113.65, 113.51, 82.39, 81.86, 81.23, 80.05, 79.93, 79.14, 78.71, 72.49, 71.74, 70.09, 69.88, 55.21, 35.56, 35.48, 35.13, 34.92, 31.54, 30.02, 29.84, 29.57, 29.28, 28.08, 27.46, 26.72, 25.07, 24.99, 24.91, 22.70, 22.57, 14.06, 13.84; [α]_D²⁰ = -52.4 (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₆₈H₁₀₀O₁₂Na (M+Na)⁺ 1131.7, found 1131.7; HRMS(ESI) calcd for C₆₈H₁₀₀O₁₂Na (M+Na)⁺, 1131.7112, found 1131.7049.



¹H NMR (400 MHz, CDCl₃) δ 7.25–7.17 (m, 6H), 6.87– 6.77 (m, 6H), 5.75 (dd, J = 15.8, 8.0 Hz, 1H), 5.69 (dd, J = 15.8, 8.5 Hz, 1H), 5.58–5.47 (m, 3H), 5.45–5.30 (m, 6H), 4.66 (d, J = 11.3 Hz, 1H), 4.57–4.44 (m, 4H), 4.35–4.14 (m, 5H), 3.96–3.88 (m, 1H), 3.79 (s, 3H), 3.77 (s, 3H), 3.76 (s, 3H), 3.85–3.69 (m, 4H), 3.69–3.61 (m, 1H), 3.53–3.44 (m, 2H), 2.47–2.08 (m, 10H), 2.08–1.86 (m, 6H), 1.64–1.46 (m, 6H), 1.54 (s, 3H), 1.43 (s, 9H), 1.42 (s, 9H), 1.39 (s, 3H), 1.33 (s, 3H), 1.40–1.19 (m, 10H), 1.28 (s, 3H), 0.86 (t, J = 7.4 Hz, 3H), 0.85 (t, J = 6.9 Hz, 3H); ¹³C NMR (100 MHz,

CDCl₃) δ 172.98, 159.01, 158.93, 158.86, 135.78, 135.20, 131.47, 131.32, 131.22, 130.72, 130.66, 130.49, 129.94, 129.26, 129.20, 128.98, 126.07, 126.02, 125.99, 113.71, 113.63, 113.49, 109.02, 108.39, 96.30, 82.62, 82.16, 81.36, 80.56, 79.90, 79.89, 79.17, 78.52, 72.37, 71.17, 70.59, 70.57, 70.06, 69.87, 67.35, 67.24, 55.20, 55.17, 35.60, 35.49, 35.00, 33.55, 31.52, 30.29, 29.75, 29.59, 29.28, 28.08, 27.43, 26.80, 26.10, 25.93, 25.10, 25.00, 24.95, 24.91, 24.33, 22.71, 22.57, 14.06, 13.85; $[\alpha]_D^{20} = -61.2$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₈₀H₁₁₈O₁₇Na (M+Na)⁺ 1373.8, found 1373.8; HRMS(ESI) calcd for C₈₀H₁₁₈O₁₇Na (M+Na)⁺, 1373.8267, found 1373.8197.



¹H NMR (400 MHz, CDCl₃) δ 5.78–5.75 (m, 2H), 5.64– 5.59 (m, 2H), 5.64–5.59 (m, 1H), 5.51 (d, *J* = 4.9 Hz, 1H), 5.49–5.31 (m, 5H), 4.58 (dd, *J* = 8.0, 2.3 Hz, 1H), 4.29 (dd, *J* = 5.0, 2.3 Hz, 1H), 4.25 (dd, *J* = 7.9, 1.7 Hz, 1H), 4.22– 4.18 (m, 1H), 4.17–4.11 (m, 1H), 4.08–4.04 (m, 1H), 3.93 (t, *J* = 5.4 Hz, 1H), 3.87–3.81 (m, 1H), 3.69 (dd, *J* = 10.3, 6.2 Hz, 1H), 3.73–3.62 (m, 1H), 3.57–3.51 (m, 1H), 3.47 (dd, *J* = 10.3, 6.2 Hz, 1H), 2.45–2.10 (m, 10H), 2.09–1.92 (m, 6H), 1.67–1.48 (m, 6H), 1.54 (s, 3H), 1.44 (s, 9H), 1.43 (s, 9H), 1.41 (s, 3H), 1.33 (s, 3H), 1.32 (s, 3H), 1.39–1.24 (m, 10H), 0.89 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 6.9 Hz, 3H); ¹H NMR

(600 MHz, C_6D_6 :DMSO- d_6 =25:2) δ 6.05 (dd, J = 15.6, 6.4 Hz, 1H), 5.96 (dd, J = 15.5, 6.1 Hz, 1H), 5.82 (dd, J = 15.9, 7.1 Hz, 1H), 5.78–5.83 (m, 1H), 5.68 (dd, J = 15.8, 7.4 Hz, 1H), 5.68–5.62 (m, 1H), 5.60–5.50 (m, 3H), 5.50 (d, J = 5.0 Hz, 1H), 5.43–5.35 (m, 1H), 5.17 (d, J = 4.5 Hz, 1H), 4.84 (d, J = 6.1 Hz, 1H), 4.54 (dd, J = 7.9, 1.9 Hz, 1H), 4.49–4.43 (m, 1H), 4.36 (d, J = 4.4 Hz, 1H), 4.27–4.18 (m, 4H), 4.19–4.14 (m, 1H), 3.96 (dd, J = 10.0, 6.1 Hz, 1H), 3.92–3.80 (m, 2H), 3.74–3.69 (m, 1H), 3.67 (dd, J = 9.9, 6.3 Hz, 1H), 2.61–2.25 (m, 6H), 2.19–1.95 (m, 10H), 1.66–1.50 (m, 8H), 1.49 (s, 3H), 1.44 (s, 3H), 1.40–1.23 (m, 8H), 1.38 (s, 9H), 1.36 (s, 9H), 1.23 (s, 3H), 1.08 (s, 9H), 1.23 (s, 3H), 1.08 (s), 1.08

3H), 0.96–0.81 (m, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 173.08, 173.01, 135.86, 134.65, 133.17, 131.78, 130.75, 129.62, 128.72, 125.80, 125.57, 125.20, 109.12, 108.46, 96.29, 82.49, 81.06, 80.21, 80.02, 73.62, 73.26, 72.00, 71.12, 70.57, 70.53, 67.20, 67.17, 36.74, 35.41, 34.98, 33.45, 31.48, 29.49, 29.26, 29.21, 28.07, 27.38, 26.77, 26.07, 25.92, 24.94, 24.91, 24.88, 24.34, 22.67, 22.55, 14.05, 13.83; $[\alpha]_D^{20} = -27.0$ (*c* = 1.0, CHCl₃); MS(ESI) calcd for C₅₆H₉₄O₁₄Na (M+Na)⁺ 1013.7, found 1013.7; HRMS(ESI) calcd for C₅₆H₉₄O₁₄Na (M+Na)⁺, 1013.6541, found 1013.6533.



¹H NMR (400 MHz, CDCl₃) δ 5.76 (dd, J = 15.6, 6.9 Hz, 1H), 5.65 (dd, J = 15.6, 6.2 Hz, 1H), 5.58–5.50 (m, 3H), 5.50–5.37 (m, 4H), 5.35–5.21 (m, 4H), 4.88 (dd, J = 11.3, 6.7 Hz, 1H), 4.58 (dd, J = 8.0, 2.3 Hz, 1H), 4.29 (dd, J = 5.0, 2.3 Hz, 1H), 4.23 (dd, J = 7.9, 1.7 Hz, 1H), 4.10–4.03 (m, 1H), 3.92 (t, J = 5.1 Hz, 1H), 3.84 (d, J = 6.2 Hz, 1H), 3.67 (dd, J = 10.4, 5.5 Hz, 1H), 3.54 (d, J = 5.0 Hz, 1H), 3.44 (dd, J = 10.6, 6.6 Hz, 1H), 2.40–2.29 (m, 3H), 2.24–2.16 (m, 5H), 2.07 (s, 3H), 2.05 (s, 3H), 2.15–1.90 (m, 8H), 2.01 (s, 3H), 1.67–1.51 (m, 6H), 1.54 (s, 3H), 1.43 (s, 9H), 1.42 (s,

9H), 1.41 (s, 3H), 1.33 (s, 3H), 1.38–1.23 (m, 10H), 1.31 (s, 3H), 0.89 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 6.8 Hz, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 172.92, 172.78, 170.33, 170.05, 169.74, 135.97, 133.23, 132.73, 131.86, 130.76, 129.56, 126.27, 125.75, 125.00, 124.36, 109.06, 108.40, 96.29, 80.42, 80.16, 80.00, 79.93, 77.46, 75.49, 75.11, 73.34, 71.17, 70.56, 70.55, 67.45, 67.36, 35.31, 34.97, 34.07, 33.42, 31.47, 29.62, 29.44, 29.23, 28.08, 28.06, 27.81, 27.29, 26.80, 26.08, 25.92, 24.93, 24.87, 24.78, 24.63, 24.33, 22.64, 22.57, 21.20, 21.12, 14.04, 13.80; $[\alpha]_D^{20} = -47.6$ (c = 1.0, CHCl₃); MS(ESI) calcd for C₆₂H₁₀₀O₁₇Na (M+Na)⁺ 1139.7, found 1139.5



aa



¹H NMR (500 MHz, C_6D_6) δ 8.54 (s, 1H), 6.06 (dd, J = 15.9, 7.1 Hz, 1H), 6.02–5.97 (m, 1H), 5.87 (dd, J = 10.9, 3.1 Hz, 1H), 5.81–5.72 (m, 2H), 5.71–5.35 (m, 10H), 5.34–5.27 (m, 1H), 4.63 (t, J = 5.9 Hz, 1H), 4.34 (dd, J = 7.3, 4.7 Hz, 1H), 3.83–3.76 (m, 1H), 3.76–3.63 (m, 2H), 3.52 (dd, J = 10.0, 6.0 Hz, 1H), 3.44–3.31 (m, 1H), 3.39 (s, 3H), 3.35 (s, 3H), 2.71– 2.53 (m, 2H), 2.49–2.33 (m, 4H), 2.26–1.97 (m, 10H), 1.92 (s, 3H), 1.91 (s, 3H), 1.82 (s, 3H), 1.78 (s, 3H), 1.76 (s, 3H), 1.67–1.62 (m, 2H), 1.60 (s, 3H), 1.53–1.18 (m, 14H), 0.97 (t, J = 7.3 Hz, 3H), 0.91 (t, J = 6.8 Hz, 3H).

¹H NMR (600 MHz, C₆D₆) δ 6.06 (dd, J = 15.7, 7.1 Hz, 1H), 5.77 (dd, J = 15.7, 6.4 Hz, 1H), 5.73–5.63 (m, 5H), 5.63– 5.53 (m, 5H), 5.53–5.46 (m, 1H), 5.42–5.36 (m, 1H), 5.34– 5.30 (m, 1H), 5.27 (dd, J = 10.5, 3.4 Hz, 1H), 4.43 (d, J = 8.0 Hz, 1H), 4.35 (dd, J = 7.5, 4.7 Hz, 1H), 4.15–4.09 (m, 1H), 3.90 (dd, J = 10.4, 3.9 Hz, 1H), 3.86 (dd, J = 8.2, 5.9 Hz, 1H), 3.80 (dd, J = 7.9, 6.8 Hz, 2H), 3.72–3.66 (m, 1H), 3.65–3.61 (m, 2H), 3.58 (dd, J = 10.4, 6.5 Hz, 1H), 3.51–3.43 (m, 1H), 3.41 (s, 3H), 3.35 (s, 3H), 2.69–2.56 (m, 2H), 2.48–2.35 (m,

3H), 2.30–2.23 (m, 1H), 2.23–2.18 (m, 2H), 2.16–2.11 (m, 2H), 2.11–2.01 (m, 6H), 1.93 (s, 3H), 1.82 (s, 3H), 1.81 (s, 3H), 1.783 (s, 3H), 1.780 (s, 3H), 1.76 (s, 3H), 1.70–1.65 (m, 2H), 1.58–1.25 (m, 14H), 1.43 (s, 3H), 1.26 (s, 3H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 6.8 Hz, 3H).



¹H NMR (500 MHz, C_6D_6) δ 6.05 (dd, J = 15.6, 7.0 Hz, 1H), 5.76 (dd, J = 15.5, 5.6 Hz, 1H), 5.74–5.52 (m, 10H), 5.52– 5.43 (m, 1H), 5.42–5.36 (m, 1H), 5.35–5.29 (m, 1H), 5.26 (dd, J = 10.5, 3.4 Hz, 1H), 4.36 (d, J = 8.0 Hz, 1H), 4.37– 4.32 (m, 1H), 3.92–3.86 (m, 1H), 3.81–3.71 (m, 4H), 3.71– 3.66 (m, 1H), 3.64–3.61 (m, 1H), 3.59–3.53 (m, 2H), 3.51– 3.43 (m, 2H), 3.40 (s, 3H), 3.35 (s, 3H), 3.26 (s, 1H), 2.68– 2.59 (m, 2H), 2.54–2.44 (m, 2H), 2.34–2.27 (m, 2H), 2.22– 1.77 (s, 3H), 1.75 (s, 3H), 1.74 (s, 3H), 1.70–1.61 (m, 2H)

2.02 (m, 10H), 1.92 (s, 3H), 1.83 (s, 3H), 1.78 (s, 3H), 1.77 (s, 3H), 1.75 (s, 3H), 1.74 (s, 3H), 1.70–1.61 (m, 2H), 1.56–1.19 (m, 14H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H).



¹H NMR (600 MHz, C_6D_6 :DMSO- d_6 =25:2) & 6.11 (dd, J = 15.5, 6.3 Hz, 1H), 5.99 (dd, J = 15.6, 5.8 Hz, 1H), 5.88 (dd, J = 15.7, 7.4 Hz, 1H), 5.84–5.77 (m, 1H), 5.74 (dd, J = 15.7, 7.5 Hz, 1H), 5.71–5.65 (m, 1H), 5.62–5.57 (m, 1H), 5.58–5.51 (m, 2H), 5.45–5.38 (m, 1H), 5.29 (d, J = 3.2 Hz, 1H), 5.10 (d, J = 4.7 Hz, 1H), 4.82 (d, J = 5.5 Hz, 1H), 4.81 (d, J = 5.6 Hz, 1H), 4.72 (d, J = 5.6 Hz, 1H), 4.60 (d, J = 4.6 Hz, 1H), 4.51–4.47 (m, 1H), 4.44 (t, J = 6.0 Hz, 1H), 4.41 (d, J = 7.7

Hz, 1H), 4.33 (d, J = 4.1 Hz, 1H), 4.28–4.21 (m, 2H), 4.15 (dd, J = 10.5, 5.6 Hz, 1H), 4.11–4.06 (m, 1H), 4.05–4.02 (m, 1H), 4.01 (dd, J = 9.5, 6.3 Hz, 1H), 3.99–3.95 (m, 2H), 3.93 (dd, J = 10.3, 3.9 Hz, 1H), 3.91–3.84 (m, 2H), 3.84–3.79 (m, 1H), 3.80–3.76 (m, 1H), 3.72 (dd, J = 9.5, 6.0 Hz, 1H), 3.71–3.66 (m, 1H), 3.65 (bt, J = 5.9 Hz, 1H), 3.42 (s, 3H), 3.38 (s, 3H), 2.62–2.41 (m, 5H), 2.35–2.28 (m, 1H), 2.20–2.13 (m, 6H), 2.11 (ddd, J = 7.3, 7.3, 7.3 Hz, 2H), 2.04 (ddd, J = 7.4, 7.4, 7.4 Hz, 2H), 1.70–1.50 (m, 7H), 1.48–1.34 (m, 2H), 1.40 (qdd, J = 7.4, 7.4, 7.4 Hz, 2H), 1.32–1.23 (m, 5H), 0.92 (t, J = 7.4 Hz, 3H), 0.88 (bt, J = 6.8 Hz, 3H). ¹³C NMR (100 MHz, C₆D₆:DMSO-d₆=25:2) δ 173.58, 173.44, 136.29, 134.70, 131.32, 131.28, 130.52, 129.35, 127.51, 126.99, 105.10, 83.08, 81.73, 80.84, 74.51, 73.83, 73.20, 72.39, 71.99, 71.59, 71.48, 69.22, 68.07, 64.07, 51.10, 51.00, 37.84, 34.17, 33.39, 31.85, 30.67, 29.88, 29.78, 29.47, 27.86, 26.99, 25.57, 25.37, 25.06, 23.18, 22.96, 14.32, 14.13; [α]_D²⁰ = -22.0 (c = 0.1, CH₂Cl₂); MS (ESI) calcd for C₄₇H₈₀O₁₆Na⁺ (M+Na)⁺ 923.5, found 923.4; HRMS(ESI) calcd for C₄₇H₈₀O₁₆Na (M+Na)⁺, 923.5344, found 923.5331.

t-BuO	2c~~~ 0s	OH 7 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	$\begin{array}{c} OH \\ 10 \\ 9 \\ 8 \\ OH \\ \hline OSEM \\ OH \\ \hline OSEM \\ OH \\ \hline OH \\ \hline OH \\ \hline OSEM \\ OH \\ \hline OH \\ \hline OSEM \\ OH \\ \hline OH \\ \hline OH \\ \hline OSEM \\ OH \\ \hline OH \\ \hline OH \\ \hline OSEM \\ OH \\ \hline OH \\ $			
$23 (ahu, ahu) \qquad 22 (syn, syn) \qquad 22 (syn, syn) \qquad \qquad$						
	Natural pdt 2	23 (anti, anti)	22 $(syn, syn)^a$	25 (anti, syn)	24 (syn, anti)	
6	4.25	4.23	4.22	4.22	4.23	
7	6.00	6.00	5.91	5.96	6.01	
	dd J = 15.5, 5.5		dd J = 15.9, 6.0	dd $J = 15.6, 6.1$		
8	6.11	6.03	6.02	6.05	6.04	
	dd J = 15.5, 6.4		dd J = 14.7, 6.3	dd <i>J</i> = 15.5, 6.5		
9	4.50	4.50	4.34	4.46	4.39	
10	3.78	3.66	3.53	3.68	3.57	

^{*a*} The ¹H NMR of this compound **22** (syn, syn) was assigned by selective TOCSY experiment

Figure S6. Comparison of 4 diasteromeric triols (22-25) to nigricanoside A dimethyl ester 2



Figure S7. Comparison of 4 diasteromeric triols (22-25) to nigricanoside A dimethyl ester 2



Figure S8. Selective TOCSY experiment of the mixture (23 (anti, anti) and 22 (syn, syn))




















S43















GC Conditions: Lipodex E (Column V, Macherey-Nagel), 60°C, 19.4 min



GC chromatogram for compound (S)-A









































HPLC Conditions: Chiralcel OD-H column, 1 mL/ min flow rate, 1% i-PrOH in hexanes



HPLC Chromatogram for compound l






































gradCOSY90 NMR Spectrum of compound 32 at 600 MHz in CD₃OD







gradHMBC NMR Spectrum of compound 32 at 600 MHz in CD₃OD





gradCOSY90 NMR Spectrum of compound **32** at 600 MHz in 25:2 C₆D₆/DMSO-d₆



gradHSQC NMR Spectrum of compound **32** at 600 MHz in 25:2 C_6D_6 /DMSO- d_6



gradHMBC NMR Spectrum of compound **32** at 600 MHz in 25:2 C₆D₆/DMSO-d₆



S89





















S95



















gradCOSY60 NMR Spectrum of Nigricanoside A Dimethyl Ester 2 at 600 MHz in 25:2 C₆D₆/DMSO-d₆



gradHSQC NMR Spectrum of Nigricanoside A Dimethyl Ester 2 at 600 MHz in 25:2 C₆D₆/DMSO-d₆



gradHMBC NMR Spectrum of Nigricanoside A Dimethyl Ester 2 at 600 MHz in 25:2 C₆D₆/DMSO-d₆





S106