(E)-4-iodo-3-methylbut-3-en-1-ol (7)

To a stirred solution of zirconocene dichloride (3.86 g, 13.2 mmol, 0.22 eq.) in dichloromethane (250 mL) at rt was added trimethylaluminum (2M in toluene, 93 mL, 186 mmol, 3.1 eq.) dropwise via a dropping funnel. After stirring the resulting yellow mixture for 10 min at −25°C, water (1.7 mL, 93 mmol, 1.55 eq.) was cautiously added dropwise over 20 min. After an additional 10 min stirring, commercially available 3-butyn-1-ol (4.5 mL, 60 mmol, 1.0 eq.), pretreated with trimethylaluminum (2M in toluene, 9.3 mL, 18.6 mmol, 0.31 eq.) in anhydrous dichloromethane (50 mL) at −25°C, was added dropwise via a dropping funnel. The reaction mixture was allowed to warm to rt and the resulting yellow thick slurry was stirred for 16 h. The reaction mixture was then cooled to −25°C and a solution of iodine (22.8 g, 90 mmol, 1.5 eq.) in anhydrous tetrahydrofuran (50 mL) was added dropwise via a dropping funnel. The mixture was warmed up to 0°C and was stirred for an additional 1 h. The reaction mixture was slowly poured into a well-stirred mixture of a saturated aqueous solution of sodium potassium tartrate (500 mL) and ether (200 mL), and the resulting biphasic mixture was stirred for 18 h. The slurry was filtered through celite, the layers were separated and the aqueous layer was extracted with ether (3 × 150 mL). The combined organic layers were washed with Na₂S₂O₃ and brine, dried over anhydrous Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 1:1) to yield vinyl iodide 7 (9.21 g, 43.4 mmol, 73%) as a light yellow oil. Physical and spectral data match those previously reported.

(E)-4-iodo-3-methylbut-3-enal

To a stirred solution of alcohol 7 (2.2 g, 10.4 mmol, 1.0 eq.) in dichloromethane (40 mL) at rt was added a Dess-Martin periodinane (4.9 g, 11.5 mmol, 1.1 eq.). The solution was stirred for 2 h at same temperature. The reaction mixture was diluted with ether (200 mL) and poured into a saturated aqueous solution of NaHCO₃ (150 mL) containing solid Na₂S₂O₃ (7 g). The resulting slurry was stirred for 10 min until two clear layers separated. The aqueous layer was extracted with ether (3 × 100 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄ and concentrated in vacuo. The crude aldehyde 3 (2.1 g, 10 mmol, 96%) was obtained as a light yellow oil and was used in the next step without further purification.

R_f = 0.29 (PE/Et₂O = 5:1);
(S,E)-1-iodo-2-methylhepta-1,6-dien-4-ol (8)

Allylmagnesium bromide (1.0 M, 19 mL, 19.0 mmol) was added to a stirred solution of (−)-Ipc₂BCl (7.2 g, 22.5 mmol) in ether (100 mL) at −78°C, and the resultant mixture was warmed to rt over 1 h. The stirring was ceased, and the mother liquor was carefully transferred to another flask via a cannula such that the white precipitate remained. The resultant solution was cooled to −100°C, and a solution of aldehyde 3 (3.15 g, 15 mmol) in ether (30 mL) was added. The resultant solution was stirred at −100°C for 90 min and poured into a solution containing: phosphate pH 7 buffer (120 mL), methanol (120 mL), and 30% aqueous H₂O₂ (30 mL). The reaction mixture was then stirred at 0°C for 30 min. The aqueous layer was extracted with ether (3 × 50 mL), and the combined organic extracts were washed with saturated aqueous Na₂S₂O₃ (50 mL), brine (20 mL), then dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 4:1) to give desired product 8 as a colorless oil (2.9 g, 11.5 mmol, 77%); Physical and spectral data match those previously reported.

[α]D +10.1 (c = 1; CHCl₃);

(S,E)-1-iodo-4-methoxy-2-methylhepta-1,6-diene

Alcohol 8 (2.9 g, 11.5 mmol, 1.0 eq.) was dissolved in dry dichloromethane (30 mL). Proton sponge (3.2 g, 15 mmol, 1.3 eq.) and trimethyloxonium tetrafluoroborate (2.04 g, 13.8 mmol, 1.2 eq.) were added and the reaction mixture was stirred at 0°C for 1 h. The reaction mixture was then diluted with dichloromethane and filtered through a pad of celite. The resulting solution was washed with HCl (1 M, 20 mL), saturated sodium NaHCO₃ (10 mL), brine (10 mL) then dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 9:1) to yield desired product as a yellow oil (2.78 g, 10.45 mmol, 90%).

Rf = 0.44 (PE/Et₂O = 9:1); ¹H NMR (500 MHz, CDCl₃): δ = 5.97 (dd, J = 2.2, 1.1 Hz, 1H), 5.81 (dd, J = 17.7, 9.6 Hz, 1H), 5.11 (d, J = 3.2 Hz, 1H), 5.09 – 5.06 (m, 1H), 3.41 – 3.36 (m, 1H), 3.35 (s, 3H), 2.42 (ddd, J = 14.1, 7.1, 1.0 Hz, 1H), 2.35 (ddd, J = 14.1, 5.5, 1.1 Hz, 1H), 2.25 (dddd, J = 7.0, 5.7, 2.2, 1.2 Hz, 2H), 1.87 (t, J = 2.3 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃): δ = 145.1, 134.4, 117.6, 78.7, 77.1, 57.0, 43.6, 37.8, 24.5. [α]D −3.3 (c = 2.5; CHCl₃); HRMS (ESI): m/z calc. for C₉H₁₅IONa [M+Na]⁺: 289.0065, found 289.0094
(4R,E)-7-iodo-4-methoxy-6-methylhept-6-ene-1,2-diol (9)

To a solution of olefin 37 (2.78 mg, 10.45 mmol, 1 eq.) in tert-BuOH (100 mL) and water (100 mL) was added methan sulfon amide (1 g, 10.45 mmol, 1 eq.) and AD-mix (18.8 g, 1.8 g/mmol) in one portion at 0°C. The reaction was stirred vigorously at 0°C for 12 h. Solid sodium sulfite (2.6 g, 20.9 mmol, 2 eq.) was added to the mixture, which was allowed to warm to room temperature and after stirring for 1 h, the mixture was extracted with ethyl acetate (3 × 50 mL). The combined organic layers were washed with brine, dried over Na₂SO₄, and the solvent was removed in vacuo. The residue was transferred with ether to give a mixture of diastereomers 9 (3 g, 10 mmol, 95%) as a yellow oil. No flash chromatography was conducted.

R_f = 0.28 (EtOAc); HRMS (ESI): m/z calc. for C₉H₁₇IO₃Na [M+Na]^+: 323.0120, found 323.0115

(R,E)-3-methoxy-5-methylnona-5,8-dienal (10)

To a solution of vinyl iodide 9 (892 mg, 2.97 mmol 1 eq.) in DMF (36 mL) and benzene (36 mL) was added allyltributyltin (9.1 ml, 29.7 mmol, 10 eq.) and Pd(PPh₃)₄ (343 mg, 0.3 mmol, 0.1 eq.). The mixture was stirred for 3 h at 55°C and then cooled to room temperature. The mixture was quenched by addition of ethyl acetate (100 mL) and water (350 mL). The aqueous phase was extracted with ethyl acetate (3 × 50 mL), and the combined organic extracts were washed with brine, dried over Na₂SO₄ and concentrated in vacuo. The mixture was used for a further cleavage reaction without purification. Methanol (18 mL) and water (9 mL) were added to the resulting solution and cooled to 0°C. NaIO₄ (3.2 g, 14.9 mmol, 5 eq.) was then added and the resulting slurry was vigorously stirred for 1 h at same temperature. After completion of the reaction, the mixture was partitioned between dichloromethane (50 mL) and water (200 mL) and the organic phase was separated. The aqueous layer was extracted with dichloromethane (3 × 50 mL) and the combined organic extracts were washed with brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 10:1 to 3:1) and additional purification with (petrol ether/ether 3:1) to give aldehyde 10 (298 mg, 1.64 mmol, 55% over two steps) as a yellow oil.
$R_f = 0.28$ (PE/Et$_2$O = 3:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 9.79$ (t, $J = 2.1$ Hz, 1H), 5.83 – 5.73 (m, 1H), 5.27 – 5.22 (m, 1H), 5.04 – 4.93 (s, 3H), 3.90 – 3.83 (m, 1H), 3.36 (s, 3H), 2.76 (t, $J = 6.6$ Hz, 2H), 2.55 (ddd, $J = 3.5$, 2.5, 1.8 Hz, 1H), 2.42 (dd, $J = 13.5$, 5.4 Hz, 1H), 2.13 (dd, $J = 13.6$, 7.7 Hz, 1H), 1.65 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 201.7$, 136.9, 132.6, 125.7, 114.7, 75.3, 57.0, 48.0, 44.1, 32.5, 29.9.

(R,E)-3-methoxy-5-methylnona-5,8-dienal (13)

To a solution of (S)-3,3-dimethyl-2-((4-methylphenyl)sulfonamido)butanoic acid (467 mg, 1.64 mmol, 1 eq.) in tetrahydrofuran (33 ml) was added dropwise a BH$_3$.SMe$_2$ complex (170 µl, 1.8 mmol, 1.1 eq.) at room temperature. The solution was stirred for 30 min and the solvent was removed in vacuo. (Caution, the catalyst is very sensitive to moisture! The proper catalyst has a sponge like structure.) Nitroethane (33 mL) was added and a clear solution was cooled to $-78^\circ$C. The difluoroketene acetal (480 µL, 2.45 mmol, 1.5 eq.) was added and stirred at same temperature 10 min. A solution of the aldehyde 10 (298 mg, 1.64 mmol, 1 eq.) in nitroethane (3 ml) was then added, and the reaction mixture was stirred at $-78^\circ$C for 12 h, quenched with saturated aqueous solution of NH$_4$Cl and extracted with ether (3 × 10 mL). The combined extracts were washed with brine, dried over Na$_2$SO$_4$ and filtered. Concentration in vacuo gave a solid residue which was purified by flash chromatography (petrol ether/ether 3:1) to give 13 as yellow oil (331 mg, 1.08 mmol, 66%, d.r. 9:1).

$R_f = 0.19$ (PE/Et$_2$O = 3:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 5.84 – 5.73$ (m, 1H), 5.26 (td, $J = 7.2$, 0.9 Hz, 1H), 4.99 (dddd, $J = 17.5$, 10.1, 3.4, 1.7 Hz, 2H), 4.41 – 4.30 (m, 2H), 4.29 – 4.20 (m, 1H), 4.07 (t, $J = 2.0$ Hz, 1H), 3.64 – 3.57 (m, 1H), 3.39 (s, 3H), 2.76 (t, $J = 6.6$ Hz, 2H), 2.45 (dd, $J = 13.5$, 4.5 Hz, 1H), 2.11 (dd, $J = 13.5$, 8.0 Hz, 1H), 1.90 (dt, $J = 19.5$, 4.4 Hz, 1H), 1.76 – 1.68 (m, 1H), 1.65 (s, 3H), 1.60 (s, 1H), 1.36 (t, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 163.7$ (dd, $J = 33.1$, 30.4 Hz), 136.8, 132.1, 125.9, 114.7, 114.4 (dd, $J = 258.8$, 249.6 Hz), 80.5, 72.2 (dd, $J = 30.1$, 24.5 Hz), 63.1, 56.5, 43.7, 32.5 (d, $J = 2.6$ Hz), 32.4, 16.6, 14.1.

$^{19}$F NMR (470 MHz, CDCl$_3$) $\delta =$ Major: $-113.92$ (d, $J = 258.5$ Hz), $-125.34$ (d, $J = 258.8$ Hz); Minor: $-114.50$ (d, $J = 260.3$ Hz), $-123.26$ (d, $J = 261.9$ Hz). [$\alpha$]$_D$ $-19.7$ (c = 1; CHCl$_3$); HRMS (ESI): m/z calc. for C$_{19}$H$_{25}$F$_2$O$_4$ [M+H]$^+$: 307.1721, found 307.1723
(3R,5R,E)-2,2-difluoro-3-hydroxy-N,5-dimethoxy-N,7-dimethylundeca-7,10-dienamide (14)

A suspension of N,O-dimethylhydroxylamine hydrochloride (317 mg, 3.25 mmol, 3 eq.) in tetrahydrofuran (5.5 mL) was cooled down to 0°C before slow addition of trimethylaluminium (1.63 mL, 2M in toluene, 3.25 mmol, 3 eq.). The mixture was allowed to reach rt till a transparent solution was obtained and then cooled down to −78°C. A solution of 13 (331 mg, 1.0 8mol, 1 eq.) in tetrahydrofuran (1 mL) was added. The solution was warmed up to 0°C and kept for 1 h till a transparent solution was obtained. A saturated aqueous solution of NH₄Cl and a saturated aqueous solution of potassium tartrate were added. The mixture was stirred for 12 h. After separation of the phases and extraction of the aqueous one with ethyl acetate (3 × 5 mL), the combined organic layers were dried over Na₂SO₄ and the solvents were evaporated. The crude product was purified by flash chromatography (petroleum ether/ether 1:1) and yielded the expected product 14 as a yellow oil (335 mg, 1.04 mmol, 95%).

R_f = 0.46 (PE/EtOAc = 1:1); ¹H NMR (500 MHz, CDCl₃): δ = 5.78 (ddt, J = 16.3, 10.1, 6.2 Hz, 1H), 5.25 (td, J = 7.3, 1.2 Hz, 1H), 4.98 (dddd, J = 22.5, 10.1, 3.5, 1.6 Hz, 2H), 4.42 – 4.31 (m, 1H), 3.86 (s, broad, 1H), 3.75 (s, 3H), 3.63 – 3.56 (m, 1H), 3.37 (s, 3H), 3.29 (s, broad, 3H), 2.76 (t, J = 6.4 Hz, 2H), 2.40 (dd, J = 13.9, 5.1 Hz, 1H), 2.14 (dd, J = 13.6, 7.2 Hz, 1H), 1.88 (d, J = 14.8 Hz, 1H), 1.76 (m, 1H), 1.65 (s, 3H).

¹³C NMR (125 MHz, CDCl₃): δ = 136.9, 132.5, 125.4, 115.9 (dd, J = 275.7, 238.6 Hz), 114.6, 79.6, 71.46 (dd, J = 29.1, 24.3 Hz), 62.14, 56.5, 43.9, 32.8 (d, J = 3.8 Hz), 32.4, 16.6. ¹⁹F NMR (470 MHz, CDCl₃) δ = Major: −112.83 (d, J = 269.3 Hz), −120.99 (d, J = 268.7 Hz); δ Minor: δ −113.04 (d, J = 274.8 Hz), −120.24 (d, J = 274.3 Hz).

[a]_D −18.7 (c = 1; CHCl₃), HRMS (ESI): m/z calc. for C₁₅H₂₆F₂NO₄ [M+H]^+: 322.1830, found 322.1831
Iodoalkyne 15 (571 mg, 2 mmol, 4 eq.) in ether (2 mL) was added to a stirred solution of tert-BuLi (1.9 M, 2.1 mL, 4 mmol, 8 eq.) in ether (6 mL) at −78°C. After 15 min at this temperature, as a yellow precipitate occurred, a solution of Weinreb amide 14 (160 mg, 0.5 mmol, 1 eq.) in ether (1 mL) was added to the reaction. The reaction was stirred at same temperature for 2 h. Then a saturated aqueous solution of NH₄Cl (1 mL) was added to quench the reaction. The mixture was diluted with additional ether (5 mL) and water, the aqueous layer was removed and extracted with ether (3 × 5 mL). Combined organic layers were washed with saturated aqueous solution of NaHCO₃, brine and dried over Na₂SO₄. Solvent was removed under reduced pressure and the product was purified by flash chromatography (petroleum ether/ether 3:1) to give compound 16 (157.6 mg, 0.375 mmol, 75% yield) as a yellow oil.

R<sub>f</sub> = 0.63 (PE/EtOAc = 3:1); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.31 – 7.11 (m, 5H), 5.85 – 5.72 (m, 1H), 5.41 – 5.36 (m, 1H), 5.26 (td, J = 7.3, 1.1 Hz, 1H), 4.99 (ddq, J = 16.9, 10.1, 1.7 Hz, 2H), 4.20 (dddt, J = 17.6, 10.2, 5.4, 1.6 Hz, 1H), 4.07 (t, J = 1.9 Hz, 1H), 3.62 – 3.56 (m, 1H), 3.38 (s, 3H), 3.36 (dd, J = 7.7, 6.3 Hz, 2H), 2.89 – 2.84 (m, 2H), 2.76 (t, J = 6.5 Hz, 2H), 2.44 (dd, J = 13.5, 4.4 Hz, 1H), 2.35 (t, J = 7.5 Hz, 2H), 2.10 (dd, J = 13.5, 7.9 Hz, 1H), 1.88 (d, J = 14.9 Hz, 1H), 1.75 – 1.59 (m, 8H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 202.1 (dd, J = 31.6, 25.5 Hz), 141.5, 136.8, 134.4, 132.1, 128.5, 128.5, 125.9, 125.9, 124.0, 115.7 (dd, J = 260.7, 251.6 Hz), 114.7, 80.9, 72.2 (dd, J = 30.7, 25.0 Hz), 56.5, 43.8, 37.3, 34.3, 32.6, 32.4, 32.1, 16.6, 16.4. <sup>19</sup>F NMR (470 MHz, CDCl<sub>3</sub>) δ = Major: −113.48 (d, J = 260.3 Hz), −127.89 (d, J = 260.3 Hz); Minor: −113.53 (d, J = 267.4 Hz), −126.46 (d, J = 267.7 Hz). [α]₀<sub>D</sub> = −34.2 (c = 1; CHCl<sub>3</sub>); HRMS (ESI): m/z calc. for C<sub>25</sub>H<sub>34</sub>F<sub>2</sub>O<sub>3</sub>Na [M+Na]<sup>+</sup>: 443.2374, found 443.2370
To a solution of vinyl carboxylic acid 17 (233 mg, 0.65 mmol, 2.5 eq.) in toluene (3 ml) was added triethyl amine (150 µL, 1.07 mmol, 4 eq.) followed by 2,4,6-trichlorobenzoyl chloride (120 µL, 0.78 mmol, 3 eq.) at 0°C. After stirring for 2 h, a solution of alcohol 16 (110 mg, 0.26 mmol, 1 eq.) and DMAP (4.8 mg, 0.04 mmol, 0.15 eq.) in toluene (6 mL) was added over 1 h, leading to a yellow suspension. After stirring at 0°C for 1 h, the mixture was quenched with 5% aqueous NaHCO₃, the phases were separated, and the aqueous phase was extracted with ether (3 × 5 mL). The combined organic extracts were washed with 5% aqueous NaHCO₃ and brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography with (petrol ether/ether 20:1) to give ester 18 (160 mg, 2.1 mmol, 80%) as a yellow oil.

Rᵥ = 0.38 (PE/Et₂O = 9:1); ¹H NMR (500 MHz, CDCl₃): δ = ¹H NMR (500 MHz, CDCl₃) δ 7.31 – 7.14 (m, 5H), 6.39 (s, 1H), 5.78 (ddt, J = 16.4, 10.1, 6.2 Hz, 1H), 5.69 – 5.58 (m, 1H), 5.38 (t, J = 6.8 Hz, 1H), 5.23 (t, J = 7.1 Hz, 1H), 4.98 (ddd, J = 13.6, 11.4, 1.5 Hz, 2H), 3.78 (t, J = 6.0 Hz, 2H), 3.45 – 3.39 (m, 1H), 3.35 (d, J = 7.3 Hz, 2H), 3.26 (s, 3H), 2.89 (t, J = 5.9 Hz, 2H), 2.83 – 2.73 (m, 4H), 2.37 – 2.29 (m, 3H), 2.09 (dd, J = 13.7, 6.8 Hz, 1H), 1.92 (dt, J = 14.8, 4.2 Hz, 1H), 1.84 (dd, J = 15.4, 7.6 Hz, 1H), 1.73 (s, 3H), 1.63 (s, 3H), 0.87 (s, 9H), 0.05 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ = 199.3 (t, J = 29.0 Hz), 162.6, 141.4, 137.0, 134.1, 132.8, 128.6, 128.4, 126.0, 125.8, 125.2, 124.3, 120.1, 114.8 (dd, J = 260.2, 255.9 Hz), 114.6, 69.2 (dd, J = 28.8, 24.7 Hz), 61.3, 56.7, 51.3, 43.8, 36.2, 34.3, 32.4, 32.2, 32.1, 26.0, 18.3, 16.5, 16.4, −5.2. ¹⁹F NMR (470 MHz, CDCl₃) δ = Major: 114.36 (d, J = 273.8 Hz), −118.77 (d, J = 273.6 Hz), Minor. −114.03 (d, J = 276.3 Hz), −118.87 (d, J = 276.3 Hz). [α]D −7.4 (c = 1; CHCl₃); HRMS (ESI): m/z calc. for C₃₆H₆₃F₃O₇SiNa [M+Na]⁺: 781.2573, found 781.2576.
To a solution of vinyl iodide 18 (140 mg, 184.5 µmol, 1 eq.) in DMF (2.5 mL) and benzene (2.5 mL) was added dropwise allyltributyltin (0.55 ml, 1.85 mmol, 10 eq.) and Pd(PPh₃)₄ (21.3 mg, 18.5 µmol, 0.1 eq.) was added at the end of the addition. The mixture was stirred for 2 h at 55°C and then cooled to room temperature. The mixture was quenched by addition of ether (5 mL) and water (25 mL). The aqueous phase was extracted with ether (2 × 5 mL), and the combined organic extracts were washed with brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography with (petrol ether/ether 20:1) to give the desired compound 19 (81 mg, 120 µmol, 65%).

R_f = 0.45 (PE/Et₂O = 9:1); ¹H NMR (500 MHz, CDCl₃): δ = 7.32 – 7.11 (m, 5H), 5.85 – 5.73 (m, 2H), 5.71 (s, J = 9.8 Hz, 1H), 5.61 – 5.52 (m, 1H), 5.38 (td, J = 7.3, 1.3 Hz, 1H), 5.23 (td, J = 7.2, 1.0 Hz, 1H), 5.12 – 4.91 (m, 4H), 3.73 (t, J = 6.6 Hz, 2H), 3.41 (d, J = 6.6 Hz, 3H), 3.35 (d, J = 7.3 Hz, 2H), 3.27 (s, 3H), 2.87 – 2.72 (m, 4H), 2.39 – 2.26 (m, 5H), 2.14 – 2.07 (m, 1H), 1.92 (dt, J = 14.7, 4.5 Hz, 1H), 1.88 – 1.81 (m, 1H), 1.73 (s, 3H), 1.63 (s, 3H), 0.88 (s, 9H), 0.04 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ = 199.6 (t, J = 28.9 Hz), 164.2, 161.0, 141.4, 137.1, 134.7, 134.1, 132.9, 128.5, 128.4, 126.0, 125.1, 124.3, 116.9, 116.3, 114.9 (dd, J = 195.3, 191.3 Hz), 114.5, 76.7, 68.5 – 67.9 (m), 61.3, 56.6, 43.9, 41.2, 37.1, 36.3, 34.3, 32.4, 32.3, 32.2, 26.0, 18.4, 16.4, 16.4, 5.3. ¹⁹F NMR (470 MHz, CDCl₃) δ = Major: −113.91 (d, J = 270.6 Hz), −119.51 (d, J = 270.8 Hz), Minor: −115.36 (d, J = 267.8 Hz), −119.56 (d, J = 267.5 Hz). [α]D −9.2 (c = 5; CHCl₃); HRMS (ESI): m/z calc. for C₃₉H₅₆F₂O₅SiNa [M+Na]⁺: 695.3919, found 695.3931
(3E,6E,9E,12R,14R)-4-(2-hydroxyethyl)-12-methoxy-10-methyloxacyclotetradeca-3,6,9-trien-2-one (21)

To a degassed solution of alkene 19 (81 mg, 120 µmol, 1 eq.) in dichloromethane (120 mL, 1mL/mm) was added Fürstner catalyst (CAS 250220-36-1) (11 mg, 12 µmol, 0.1 eq.) in dichloromethane (1 mL) at room temperature. After stirring for 1 h, the same amount of catalyst was added additionally. After additional 2 h, DMSO (3 drops) was added and the resulting solution was stirred open to air for 1 h. The mixture was concentrated in vacuo and purified by flash chromatography (petrol ether/ether 20 :1) to give lactone 21 (29 mg, 47.6 µmol, 60%) as a yellow oil.

R_f = 0.38 (PE/Et2O = 9:1); ¹H NMR (500 MHz, CDCl₃): δ = 7.30 – 7.14 (m, 5H), 5.74 (d, J = 1.0 Hz, 1H), 5.43 – 5.19 (m, 4H), 3.95 (dd, J = 13.2, 8.5 Hz, 1H), 3.76 (t, J = 6.6, 1.0 Hz, 2H), 3.36 (d, J = 7.3 Hz, 2H), 3.32 – 3.25 (m, 1H), 3.24 (s, 3H), 2.85 (ddd, J = 10.0, 7.1, 3.6 Hz, 2H), 2.62 (dt, J = 13.8, 8.6 Hz, 1H), 2.53 – 2.30 (m, 6H), 2.12 (d, J = 15.9 Hz, 1H), 1.76 – 1.66 (m, 4H), 1.59 (s, 1H), 1.51 (s, 3H), 0.90 (s, 9H), 0.06 (d, J = 1.1 Hz, 6H). ¹³C NMR (125 MHz, CDCl₃): δ = 199.4 (dd, J = 31.6, 27.5 Hz), 164.6, 159.8, 141.5, 134.4, 133.2, 128.9, 128.5, 128.4, 126.4, 126.0, 125.4, 124.0, 117.1, 115.2 (dd, J = 262.6, 252.7 Hz), 74.1, 68.7 (t, J = 21.6 Hz), 61.0, 55.5, 43.4, 42.9, 35.0, 34.9, 34.3, 32.6, 32.0, 31.3, 26.0, 18.4, 16.6, 16.4, −5.2. ¹⁹F NMR (470 MHz, CDCl₃) δ: = −106.10 (d, J = 283.7 Hz), −121.09 (dd, J = 285.0, 14.7 Hz). [α]₀ +23.4 (c = 1; CHCl₃); HRMS (ESI): m/z calc. for C₃₇H₆₄F₂O₅SiNa [M+Na]⁺: 667.3606, found 667.3611

(3E,6E,9E,12R,14R)-14-((E)-1,1-difluoro-5-methyl-2-oxo-7-phenylhept-5-en-1-yl)-4-(2-hydroxyethyl)-12-methoxy-10-methyloxacyclotetradeca-3,6,9-trien-2-one (21)

To a solution of 21 (15 mg, 23 µmol) in tetrahydrofuran (0.9 mL) was added triethylamine trihydrofluoride (100 µL, 10%) at rt. The reaction mixture was stirred for 4 h at rt. The mixture was diluted with ether (1 mL), and quenched with saturated aqueous solution of NaHCO₃ (1mL). The aqueous phase was extracted with ether (3 × 1 mL), and the combined organic extracts were washed with brine, dried over
Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 1:1) to give the desired compound (11.2 mg, 21.1 µmol, 90%).

Rᵣ = 0.22 (PE/Et₂O = 1:1); ¹H NMR (500 MHz, CDCl₃): δ = 7.31 – 7.13 (m, 5H), 5.79 (d, J = 1.1 Hz, 1H), 5.47 – 5.32 (m, 3H), 5.30 – 5.19 (m, 2H), 3.97 (dd, J = 13.5, 8.5 Hz, 1H), 3.80 (t, J = 4.9 Hz, 2H), 3.38 – 3.25 (m, 4H), 3.24 (s, 3H), 2.85 (dd, J = 8.7, 4.5, 1.9 Hz, 2H), 2.64 (dt, J = 14.6, 8.4 Hz, 1H), 2.54 – 2.29 (m, 8H), 2.14 – 2.08 (m, 1H), 1.77 – 1.66 (m, 5H), 1.51 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ = 199.4 (dd, J = 32.4, 27.1 Hz), 164.5, 158.7, 141.5, 134.4, 133.4, 129.1, 128.5, 128.4, 126.2, 126.0, 125.3, 124.1, 117.9, 74.0, 68.9 (t, J = 21.8 Hz), 60.0, 55.5, 43.3, 42.9, 34.8, 34.6, 34.3, 32.7, 32.0, 31.2, 16.6, 16.4. ¹⁹F NMR (470 MHz, CDCl₃): δ: = −105.78 (d, J = 286.5 Hz), −121.13 (d, J = 286.2 Hz). [α]₀ +3.3 (c = 1.5; CHCl₃); HRMS (ESI): m/z calc. for C₃₁H₄₁F₂O₅ [M+H]⁺: 531.2922, found 531.2915

11-O-Me-14,14′-difluoro-ripostatin A (6)

A 15% DMP solution in dichloromethane (100 µL, 34.4 µmol, 1.2 eq.) was added to a solution of alcohol (15 mg, 28.2 µmol, 1 eq.) in dichloromethane (1 mL) at rt. After 2 h as the oxidation was completed, 2,3-dimethyl-2-buten (300 µL), tert-BuOH (500 µL), water (200 µL) and tetrahydrofuran (500 µL) were added. In the last step 500 µL of Pinnick solution (0.25M, 22.6 mg NaClO₂, 34.5 mg NaH₂PO₄·2H₂O in 1 mL H₂O) was added at 0°C and stirred for 30 min. The reaction was quenched by addition of ether (1 mL) and HCl (2 drops, 1 M), and the aqueous layer was washed with ethyl acetate (3 × 2 mL). The combined organic extracts were dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (DCM/MeOH 10:1) to give terminal carboxylic acid 6 (10 mg, 18.3 µmol, 65%).

Rᵣ = 0.42 (DCM/MeOH = 10:1); ¹H NMR (500 MHz, CDCl₃): δ = 7.30 – 7.13 (m, 5H), 5.88 (s, 1H), 5.47 – 5.30 (m, 3H), 5.28 – 5.22 (m, 2H), 4.01 (dd, J = 14.0, 7.4 Hz, 1H), 3.36 (d, J = 7.3 Hz, 1H), 3.32 – 3.19 (m, 7H), 2.87 – 2.81 (m, 2H), 2.67 – 2.60 (m, 1H), 2.60 – 2.45 (m, 3H), 2.43 – 2.29 (m, 4H), 2.12 (d, J = 15.8 Hz, 1H), 1.78 – 1.65 (m, 6H), 1.64 – 1.59 (m, 1H), 1.51 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ = 199.33 (dd, J = 32.1, 27.1 Hz), 174.0, 164.0, 153.2, 141.5, 134.4, 133.4, 129.5, 128.5, 128.4, 126.3, 126.0, 124.7, 124.1, 120.1, 74.0, 69.58 – 68.75 (m), 55.5, 42.9, 34.8, 34.7, 34.3, 32.6, 32.0, 31.3, 29.8, 16.5, 16.4. ¹⁹F NMR (470 MHz, CDCl₃):
δ = −105.58 (d, J = 285.9 Hz), −121.29 (d, J = 287.3 Hz). [α]D +14.4 (c = 0.5; CHCl₃);

HRMS (ESI): m/z calc. for C₃₁H₃₉F₂O₆ [M+H]^+: 545.2715, found 545.2713

(7R,9R,E)-6,6-difluoro-7-hydroxy-9-methoxy-11-methyl-1-(trimethylsilyl) pentadeca-11,14-dien-1-yn-5-one (23)

Iodoalkyne 22 (2.2 g, 8.8 mmol, 5 eq.) in ether (8 mL) was added to a stirred solution of tert-BuLi (1.9 M, 5.6 mL, 10.55 mmol, 6 eq.) in ether (8 mL) at −78°C. After 15 min at this temperature as a yellow precipitate occurred, a solution of Weinreb amide 14 (565 mg, 1.76 mmol. 1 eq.) in ether (8 mL) was added to the reaction. The reaction was stirred at −78°C for 2 h. Then a saturated aqueous solution of NH₄Cl (5 mL) was added to quench the reaction. The mixture was diluted with additional ether (5 mL) and water, the aqueous layer was removed and extracted with ether (3 × 5 mL). The combined organic layers were washed with saturated aqueous solution of NaHCO₃ and brine and dried over Na₂SO₄. The solvent was removed under reduced pressure and the product was purified by flash chromatography (petroleum ether/ether 5:1) to give compound 23 (545 mg, 1.4 mmol, 80% yield) as a colorless oil.

R_f = 0.31 (PE/Et₂O = 3:1); ¹H NMR (500 MHz, CDCl₃): δ = 5.78 (qdd, J = 10.1, 6.2, 2.3 Hz, 1H), 5.25 (td, J = 7.3, 1.0 Hz, 1H), 4.98 (dddd, J = 16.0, 10.1, 3.5, 1.7 Hz, 2H), 4.22 − 4.14 (m, 1H), 4.10 (s, 1H), 3.61 − 3.56 (m, 1H), 3.38 (s, 3H), 3.02 − 2.97 (m, 2H), 2.76 (t, J = 6.6 Hz, 2H), 2.51 (td, J = 7.6, 1.3 Hz, 2H), 2.44 (dd, J = 13.7, 4.6 Hz, 1H), 2.10 (dd, J = 13.5, 8.0 Hz, 1H), 1.87 (d, J = 14.9 Hz, 1H), 1.70 − 1.62 (m, 4H), 0.13 (s, 9H). ¹³C NMR (126 MHz, CDCl₃): δ = 13C NMR (126 MHz, CDCl₃) δ: 200.5 (dd, J = 32.0, 26.1 Hz), 136.8, 132.0, 125.9, 115.7 (dd, J = 260.3, 252.1 Hz), 114.7, 105.0, 85.4, 80.9, 72.3 (dd, J = 30.3, 25.4 Hz), 56.5, 43.8, 38.3, 32.6, 32.4, 16.6, 13.6, 0.1. ¹⁹F NMR (470 MHz, CDCl₃) δ: = −113.9 (d, J = 259.5 Hz), −127.9 (d, J = 259.9 Hz). [α]D −39.5 (c = 1; CHCl₃); HRMS (ESI): m/z calc. for C₂₀H₃₂F₄O₃SiNa [M+Na]^+:409.1986, found 409.1985
(7R,9R,E)-6,6-difluoro-9-methoxy-11-methyl-5-oxo-1-(trimethylsilyl)pentadeca-11,14-dien-1-yn-7-yl (Z)-5-((tert-butyldimethylsilyl)oxy)-3-iodopent-2-enoate (24)

To a solution of vinyl carboxylic acid 17 (1255 mg, 3.52 mmol, 2.5 eq.) in toluene (14 ml) was added triethyl amine (780 µL, 5.64 mmol, 4 eq.) followed by 2,4,6-trichlorobenzoyl chloride (660 µL, 4.23 mmol, 3 eq.) at 0°C. After stirring for 2 h, a solution of alcohol 23 (545 mg, 1.41 mmol, 1 eq.) and DMAP (26 mg, 0.21 mmol, 0.15 eq.) in toluene (28 mL) was added over 1 h, leading to a yellow suspension. After stirring at 0°C for 1 h, the mixture was quenched with 5% aqueous NaHCO₃, the phases were separated and the aqueous phase was extracted with ether (3 × 10 mL). The combined organic extracts were washed with 5% aqueous NaHCO₃ and brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 15:1) to give ester 24 (657 mg, 0.91 mmol, 64%) as a yellow oil.

\[ R_f = 0.41 \quad \text{(PE/Et}_2\text{O = 9:1)} \]

\[ ^1\text{H NMR} (500 \text{ MHz, CDCl}_3): \delta = 6.39 (s, 1H), 5.76 (ddt, J = 16.3, 10.1, 6.2 Hz, 1H), 5.63 – 5.54 (m, 1H), 5.21 (td, J = 7.2, 1.0 Hz, 1H), 4.96 (ddq, J = 22.7, 10.1, 1.6 Hz, 2H), 3.77 (t, J = 5.9 Hz, 2H), 3.43 – 3.36 (m, 1H), 3.24 (s, 3H), 2.99 – 2.83 (m, 1H), 2.74 (t, J = 6.6 Hz, 2H), 2.48 (t, J = 7.5 Hz, 2H), 2.30 (dd, J = 13.7, 5.6 Hz, 1H), 2.06 (dd, J = 13.7, 6.9 Hz, 1H), 1.90 (dt, J = 14.9, 4.3 Hz, 1H), 1.81 (dd, J = 15.3, 7.5 Hz, 1H), 1.61 (s, 3H), 0.85 (s, 9H), 0.12 (s, 9H), 0.03 (s, 6H). \]

\[ ^13\text{C NMR} (125 \text{ MHz, CDCl}_3): \delta = 197.7 (t, J = 29.6 Hz), 162.6, 136.9, 132.7, 125.7, 125.2, 120.3, 114.6, 114.6 (dd, J = 261.2, 254.4 Hz), 104.5, 85.7, 76.8, 69.1 (dd, J = 28.4, 25.2 Hz), 61.2, 56.6, 51.3, 43.7, 37.0, 32.4, 32.0, 25.9, 18.3, 16.5, 13.7, 0.1, -5.2. \]

\[ ^19\text{F NMR} (470 \text{ MHz, CDCl}_3): \delta = -114.6 (d, J = 273.9 Hz), -118.8 (d, J = 274.0 Hz). \]

\[ [\alpha]_D^2 = -7.1 \quad \text{(c = 1; CHCl}_3) \]

\[ \text{HRMS (ESI): m/z calc. for C}_{31}\text{H}_{52}\text{F}_2\text{IO}_5\text{Si}_2 \text{[M+H]+}: 725.2366 \text{ found 725.2357} \]
(7R,9R,E)-6,6-difluoro-9-methoxy-11-methyl-5-oxo-1-(trimethylsilyl)pentadeca-11,14-dien-1-yn-7-yl (E)-3-(2-((tert-butyldimethylsilyl)oxy)ethyl)hexa-2,5-dienoate (25)

To a solution of vinyl iodide 24 (657 mg, 903 µmol, 1 eq.) in DMF (11 mL) and benzene (11 mL) was added dropwise allyltributyltin (2.8 ml, 9 mmol, 10 eq.) and Pd(PPh₃)₄ (104 mg, 90 µmol, 0.1 eq.) was added at the end of the addition. The mixture was stirred for 2 h at 60°C and then cooled to room temperature. The mixture was quenched by addition of ether (30 mL) and water (110 mL). The aqueous phase was extracted with ether (2 × 10 mL), and the combined organic extracts were washed with brine, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 15:1) to give the desired compound 25 (480 mg, 752 µmol, 83%).

Rₛ = 0.47 (PE/Et₂O = 9:1); ¹H NMR (500 MHz, CDCl₃): δ = 5.83 – 5.72 (m, 2H), 5.72 (s, 1H), 5.53 (m, 1H), 5.22 (td, J = 7.2, 1.1 Hz, 1H), 5.02 (dddq, J = 27.5, 23.9, 10.1, 1.5 Hz, 4H), 3.73 (t, J = 6.5 Hz, 2H), 3.44 – 3.36 (m, 3H), 3.26 (s, 3H), 2.92 (qt, J = 19.2, 7.4 Hz, 2H), 2.75 (t, J = 6.5 Hz, 2H), 2.48 (t, J = 7.6 Hz, 2H), 2.36 (td, J = 6.5, 0.9 Hz, 2H), 2.29 (dd, J = 13.7, 5.8 Hz, 1H), 2.09 (dd, J = 13.7, 6.6 Hz, 1H), 1.92 (dt, J = 14.8, 4.5 Hz, 1H), 1.85 – 1.79 (m, 1H), 1.62 (s, 3H), 0.93 – 0.85 (m, 9H), 0.13 (s, 9H), 0.03 (s, 6H). ¹³C NMR (125 MHz, CDCl₃): δ = 197.8 (t, J = 29.5 Hz), 164.0, 161.1, 136.9, 134.4, 132.7, 125.0 116.8, 116.1, 114.8 (dd, J = 259.9, 255.3 Hz), 114.4, 104.4, 85.5, 76.5, 68.0 (dd, J = 28.7, 25.1 Hz), 61.1, 56.4, 43.7, 41.0, 37.0, 32.3, 31.9, 25.8, 18.2, 16.3, 13.5, −0.0, −5.4. ¹⁹F NMR (470 MHz, CDCl₃) δ: = −114.14 (d, J = 271.7 Hz), −119.58 (d, J = 271.4 Hz). [α]D +1.2 (c = 5; CHCl₃); HRMS (ESI): m/z calc. for C₃₄H₅₆F₂O₅Si₂Na [M+Na]⁺: 661.3532, found 661.3538

(3E,6E,9E,12R,14R)-4-(2-((tert-butyldimethylsilyl)oxy)ethyl)-14-(1,1-difluoro-2-oxo-6-(trimethylsilyl)hex-5-yn-1-yl)-12-methoxy-10-methyloxacyclotetradeca-3,6,9-trien-2-one (26)
To a degassed solution of alkene 25 (480 mg, 752 µmol, 1 eq.) in dichloromethane (750 mL, 1mL/mmol) was added Fürstner catalyst (CAS 250220-36-1) (69 mg, 75 µmol, 0.1 eq.) in dichloromethane (1 mL) at room temperature. After stirring for 1 h, the same amount of catalyst was added two additional times. After further 1 h DMSO (10 drops) was added and the resulting solution was stirred open to air for 1 h. The mixture was concentrated in vacuo and purified by flash chromatography (petrol ether/ether 15:1) to give lactone 26 (282 mg, 462 µmol, 62%) as a yellow oil.

R_f = 0.43 (PE/Et_2O = 9:1); \textsuperscript{1}H NMR (500 MHz, CDCl_3): δ = 5.74 (d, J = 1.1 Hz, 1H), 5.42 – 5.28 (m, 2H), 5.27 – 5.18 (m, 2H), 3.94 (dd, J = 13.2, 8.5 Hz, 1H), 2.67 – 2.57 (m, 1H), 2.54 – 2.45 (m, 4H), 2.42 – 2.35 (m, 3H), 2.12 (d, J = 16.1 Hz, 1H), 1.76 – 1.63 (m, 2H), 1.50 (d, J = 6.6 Hz, 3H), 0.89 (s, 9H), 0.13 (s, 9H), 0.05 (d, J = 1.6 Hz, 6H). \textsuperscript{13}C NMR (125 MHz, CDCl_3): δ = 197.8 (dd, J = 32.9, 27.9 Hz), 164.6, 159.9, 133.2, 128.9, 126.4, 125.4, 117.1, 115.0 (dd, J = 260.5, 250.0 Hz), 104.9, 85.5, 74.0, 68.7 (t, J = 21.6 Hz), 61.0, 55.5, 43.4, 42.8, 35.7, 35.0, 32.6 (d, J = 4.3 Hz), 31.3, 26.0, 18.4, 16.6, 13.5, 0.1, −5.2. \textsuperscript{19}F NMR (470 MHz, CDCl_3) δ: = −106.05 (d, J = 285.8 Hz), −121.35 (d, J = 286.1 Hz). \[^{[\alpha]}D_{+30.8\text{ (c = 1; CHCl}_3)\text{; HRMS (ESI): m/z calc. for }\text{C}_{32}\text{H}_{53}\text{F}_2\text{O}_5\text{Si}_2[\text{M+H}]^+: 611.3400, found 611.3429.}

(3E,6E,9E,12R,14R)-14-(1,1-difluoro-2-oxohex-5-yn-1-yl)-4-(2-hydroxyethyl)-12-methoxy-10-methylxacyclotetradeca-3,6,9-trien-2-one

To a solution of TBAF (218 mg, 692 µmol, 1.5 eq.) in tetrahydrofuran (10 mL) was added silyl ether 26 (282 mg, 461 µmol, 1 eq.) in tetrahydrofuran (1 mL) at 0°C. After stirring for 1 h at 0°C triethylamine trihydrofluoride (1.2 mL, 10% solution) was added at 0°C and stirred for 2 h at rt. Reaction was quenched by addition of saturated aqueous solution of NaHCO_3 (20 mL) and ether (20 mL). The aqueous phase was extracted with ether (3 × 10 mL), and the combined organic extracts were washed with brine, dried over Na_2SO_4, concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 1:1) to yield the primary alcohol (75 mg, 178 µmol, 38%).
$R_f = 0.14$ (PE/Et$_2$O = 1:1); $^1$H NMR (500 MHz, CDCl$_3$): $\delta = 5.78$ (d, $J = 1.0$ Hz, 1H), 5.43 – 5.29 (m, 2H), 5.27 – 5.17 (m, 2H), 3.95 (ddd, $J = 13.4$, 8.4 Hz, 1H), 3.79 (dd, $J = 6.4$, 1.6 Hz, 2H), 3.30 (d, $J = 8.9$ Hz, 1H), 3.25 (s, 3H), 3.04 – 2.89 (m, 2H), 2.66 – 2.58 (m, 1H), 2.52 – 2.37 (m, 7H), 2.11 (d, $J = 16.2$ Hz, 1H), 1.97 (t, $J = 2.7$ Hz, 1H), 1.75 – 1.66 (m, 3H), 1.50 (s, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta = 197.5$ (dd, $J = 32.7$, 27.8 Hz), 164.3, 158.7, 133.1, 126.9, 126.1, 125.1, 117.6, 114.8 (dd, $J = 262.5$, 252.1 Hz), 82.1, 73.8, 68.6 (t, $J = 21.5$ Hz), 69.1, 59.8, 55.3, 43.0, 42.6, 35.2, 34.4, 32.5 (d, $J = 4.2$ Hz), 31.0, 16.3, 11.9. $^{19}$F NMR (470 MHz, CDCl$_3$) $\delta$: = −105.89 (d, $J = 286.6$ Hz), −121.30 (d, $J = 286.7$ Hz).

[α]$D^+$ +57.4 (c = 1; CHCl$_3$); HRMS (ESI): m/z calc. for C$_{23}$H$_{31}$F$_2$O$_5$ [M+H]$^+$: 425.2140, found 425.2165

![Image of compound](image_url)

**2-((3E,6E,9E,12R,14R)-14-(1,1-difluoro-2-oxohex-5-yn-1-yl)-12-methoxy-10-methyl-2-oxooxacyclotetradeca-3,6,9-trien-4-yl)acetic acid (27)**

A 15% DMP solution in dichloromethane (300 µL, 106 µmol, 1.25 eq.) was added to a solution of alcohol (35 mg, 85 µmol, 1 eq.) in dichloromethane (2 mL) at 0°C. After 1h at rt as the oxidation was completed, 2,3-dimethyl-2-buten (900 µL), tert-BuOH (1700 µL), water (600 µL), tetrahydrofuran (1700 µL) were added. In the last step 500 µL of Pinnick solution (0.25M, 22.6 mg NaClO$_2$, 34.5 mg NaH$_2$PO$_4$·2H$_2$O in 1 mL H$_2$O) were added at 0°C and stirred for 30 min. The reaction was quenched by addition of ethyl acetate (5 mL), and the aqueous layer was washed with ethyl acetate (3 × 5 mL). The combined organic extracts were dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash chromatography (DCM/MeOH 30:1) to yield terminal carboxylic acid 27 (75 mg) as product inseparable from DMP byproducts. Several attempts to separate the product on HPLC lead to decomposition of product.

$R_f = 0.37$ (DCM/MeOH = 9:1); $^1$H NMR (500 MHz, MeOD): $\delta = 5.86$ (d, $J = 0.9$ Hz, 1H), 5.39 – 5.25 (m, 4H), 3.95 (ddd, $J = 12.9$, 7.8, 1.2 Hz, 1H), 3.35 (s, 1H), 3.27 (s, 3H), 3.25 (dd, $J = 15.3$, 1.2 Hz, 1H), 3.20 (dd, $J = 15.2$, 0.9 Hz, 1H), 3.05 – 2.92 (m, 2H), 2.66 (dt, $J = 13.8$, 8.3 Hz, 1H), 2.61 – 2.56 (m, 1H), 2.53 – 2.40 (m, 4H), 2.25 (t, $J = 2.7$ Hz, 1H), 2.17 – 2.11 (m, 1H), 1.72 – 1.64 (m, 2H), 1.52 (d, $J = 0.7$ Hz, 3H). $^{13}$C NMR (125 MHz, MeOD): $\delta = 199.3$ (dd, $J = 31.8$, 28.2 Hz), 173.5, 165.5, 156.9, 134.6, 130.3, 127.4, 126.3, 119.8, 116.2 (dd, $J = 261.4$, 252.4 Hz), 83.1, 75.1, 70.1, 55.8, 49.6 (m), 45.8, 43.8, 36.7, 35.6, 33.5 (d, $J = 4.0$ Hz), 32.1, 16.6, 12.6. $^{19}$F NMR (470 MHz, MeOD) $\delta$: = −108.53 (d, $J = 284.4$ Hz), −122.05 (d, $J = 284.5$ Hz). HRMS (ESI): m/z calc. for C$_{23}$H$_{28}$F$_2$O$_6$Na [M+Na]$^+$: 461.1752 found 461.1777
General procedure for Click-Chemistry

To a solution of alkine 27 (3 mg, 6.84 µmol, 1 eq.) in tert-BuOH (250 µL) and water (250 µL) was added 1 equiv (approximately 1 mg) of the corresponding azide. After the addition CuSO$_4$·5H$_2$O (1.1 mg, 6.85 µmol, 1 eq.) and sodium ascorbate (1.4 mg, 6.85 µmol, 1 eq.) were added successively. The reaction was stirred at rt for 12 h. Ethyl acetate (2 mL) was added. The reaction was quenched by addition of ethyl acetate (2 mL) and brine (2 mL). The aqueous layer was washed with ethyl acetate (3 × 1 mL). The combined organic extracts were dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash chromatography (DCM/MeOH 20:1) to yield the desired compounds.

2-((3E,6E,9E,12R,14R)-14-(1,1-difluoro-2-oxo-4-(1-phenyl-1H-1,2,3-triazol-4-yl)butyl)-12-methoxy-10-methyl-2-oxooxacyclotetradeca-3,6,9-trien-4-yl)acetic acid (28)

R$_f$ = 0.25 (DCM/MeOH = 15:1); $^1$H NMR (500 MHz, MeOD): δ = δ 7.71 (s, 1H), 7.39 – 7.32 (m, 3H), 7.31 – 7.27 (m, 2H), 5.80 (s, 1H), 5.29 (m, 4H), 3.94 (dd, $J$ = 13.1, 7.7 Hz, 1H), 3.27 – 3.18 (m, 2H), 3.17 (s, 3H), 3.15 – 3.07 (m, 2H), 2.99 (t, $J$ = 6.8 Hz, 2H), 2.69 – 2.58 (m, 2H), 2.51 – 2.43 (m, 1H), 2.40 (d, $J$ = 11.9 Hz, 1H), 2.11 (d, $J$ = 16.7 Hz, 1H), 1.66 – 1.57 (m, 3H), 1.51 (s, 3H). $^{13}$C NMR (125 MHz, MeOD): δ = 200.2 (d, $J$ = 52.2 Hz), 165.7, 158.3, 136.9, 134.6, 130.1, 130.0, 129.5, 129.1, 127.5, 126.6, 123.8, 119.1, 75.1, 69.9 (t, $J$ = 22.0 Hz), 64.4, 55.8, 54.9, 49.0, 43.8, 36.7, 35.6, 33.5, 32.1, 19.3, 16.6. $^{19}$F NMR (470 MHz, MeOD) δ: = −107.86 (d, $J$ = 290.3 Hz), −122.38 (d, $J$ = 282.9 Hz). [α]$^D$ +2.3 (c = 1.5; MeOH); HRMS (ESI): m/z calc. for C$_{29}$H$_{34}$F$_2$N$_3$O$_6$ [M+H]$^+$: 558.2416, found 558.2417
2-((3E,6E,9E,12R,14R)-14-(1-cyclohexyl-1H-1,2,3-triazol-4-yl)-1,1-difluoro-2-oxobutyl)-12-methoxy-10-methyl-2-oxooxacyclotetradeca-3,6,9-trien-4-yl)acetic acid (29)

R_f = 0.25 (DCM/MeOH = 15:1); ^1H NMR (500 MHz, MeOD): δ = 7.77 (s, 1H), 5.81 (s, 1H), 5.37 – 5.24 (m, 4H), 4.47 – 4.38 (m, 1H), 3.94 (dd, J = 12.3, 8.5 Hz, 1H), 3.25 (dd, J = 11.1, 4.9 Hz, 1H), 3.21 (s, 3H), 3.18 – 3.08 (m, 2H), 2.99 (t, J = 7.0 Hz, 2H), 2.66 (dt, J = 14.0, 8.4 Hz, 1H), 2.59 (d, J = 12.9 Hz, 1H), 2.50 – 2.45 (m, 1H), 2.43 (d, J = 12.3 Hz, 1H), 2.13 (d, J = 12.6 Hz, 3H), 1.93 – 1.89 (m, 2H), 1.82 – 1.73 (m, 4H), 1.69 – 1.59 (m, 3H), 1.55 – 1.47 (m, 6H).

^13C NMR (125 MHz, MeOD): δ = 165.6, 157.5, 134.6, 130.3, 127.4, 126.4, 119.6, 75.1, 70.0 (t, J = 21.9 Hz), 61.5, 55.8, 49.5, 43.8, 35.6, 34.5, 34.4, 33.5 (d, J = 2.8 Hz), 32.1, 30.8, 26.2, 26.2, 19.3, 16.6. ^19F NMR (470 MHz, MeOD) δ: = −108.10 (d, J = 293.1 Hz), −122.16 (d, J = 284.5 Hz).

[α]_D +2.1 (c = 1.5; MeOH); HRMS (ESI): m/z calc. for C_{29}H_{39}F_{2}N_{3}O_{6}Na [M+Na]^+: 586.2705, found 586.2722

2-((3E,6E,9E,12R,14R)-14-(1,1-difluoro-2-oxo-4-(1-(pyridin-4-ylmethyl)-1H-1,2,3-triazol-4-yl)butyl)-12-methoxy-10-methyl-2-oxooxacyclotetradeca-3,6,9-trien-4-yl)acetic acid (30)

R_f = 0.25 (DCM/MeOH = 15:1); ^1H NMR (500 MHz, MeOD): δ = 8.53 (s, 2H), 7.83 (s, 1H), 7.25 (d, J = 3.5 Hz, 2H), 5.81 (s, 1H), 5.64 (s, 2H), 5.38 – 5.24 (m, 4H), 4.44 – 4.25 (m, 1H), 3.94 (m, 1H), 3.26 – 3.10 (m, 7H), 3.03 (t, J = 7.3 Hz, 2H), 2.65 (dt, J = 14.2, 8.3 Hz, 1H), 2.62 – 2.57 (m, 1H), 2.51 – 2.44 (m, 1H), 2.41 (d, J = 12.4 Hz, 1H), 2.11 (dd, J = 16.0, 3.0 Hz, 1H), 1.67 – 1.59 (m, 2H), 1.51 (s, 3H). ^13C NMR (125 MHz, MeOD): δ = 212.9, 200.2 (t, J = 30.0 Hz), 177.4, 165.5, 157.6, 150.7, 148.0, 147.4, 134.6, 130.3, 127.4, 126.4, 124.5, 124.0, 119.5, 75.1, 74.8, 69.9 (t, J = 21.9 Hz), 55.8, 53.2, 49.5, 46.4, 43.8, 36.7, 35.6, 33.5 (d, J = 2.3 Hz), 32.1, 30.8, 19.3, 16.6. ^19F NMR (470 MHz, MeOD) δ: = −108.59 (d, J = 278.9 Hz), −121.99 (d, J = 284.5 Hz). [α]_D +2.8 (c = 0.5; CHCl_3); HRMS (ESI): m/z calc. for C_{29}H_{39}F_{2}N_{4}O_{6} [M+H]^+: 573.2525, found 573.2516
2-((3E,6E,9E,12R,14R)-14-(4-(1-benzyl-1H-1,2,3-triazol-4-yl)-1,1-difluoro-2-oxobutyl)-12-methoxy-10-methyl-2-oxooxacyclotetradeca-3,6,9-trien-4-yl)acetic acid (31)

$R_f = 0.25$ (DCM/MeOH = 15:1); $^1H$ NMR (500 MHz, MeOD): $\delta = 8.28$ (s, 1H), 7.83 – 7.77 (m, 2H), 7.58 – 7.55 (m, 2H), 7.49 – 7.46 (m, 1H), 5.81 (s, 1H), 5.40 – 5.24 (m, 4H), 3.91 (dd, $J = 13.2$, 7.9 Hz, 1H), 3.34 – 3.32 (m, 1H), 3.29 – 3.25 (m, 1H), 3.23 (s, 3H) 3.22 – 3.14 (m, 3H), 3.10 (t, $J = 7.0$ Hz, 2H), 2.65 (dt, $J = 13.9$, 8.5 Hz, 1H), 2.58 – 2.54 (m, 1H), 2.49 – 2.45 (m, 1H), 2.43 (d, $J = 12.2$ Hz, 1H), 2.13 (dd, $J = 15.9$, 2.7 Hz, 1H), 1.71 – 1.64 (m, 2H), 1.51 (s, 3H). $^{13}C$ NMR (125 MHz, MeOD): δ = 165.5, 157.1, 148.3, 138.5, 134.6, 130.9, 130.3, 130.0, 127.4, 126.4, 122.0, 121.5, 119.7, 75.2, 69.7 (t, $J = 22.4$ Hz), 55.9, 49.5, 49.0, 43.8, 36.7, 35.6, 33.5 (d, $J = 3.3$ Hz), 32.1, 19.4, 16.6. $^{19}F$ NMR (470 MHz, MeOD) δ: = −108.27 (d, $J = 281.8$ Hz), −122.02 (d, $J = 282.4$ Hz). [α]$_D$ +2.4 (c = 2; MeOH); HRMS (ESI): m/z calc. for C$_{30}$H$_{36}$F$_2$N$_3$O$_6$ [M+H]$^+$: 572.2572, found 572.2573

(2E,8R,10R,12E)-8-hydroxy-13-iodo-10-methoxy-3,12-dimethyl-1-phenyltrideca-2,12-dien-6-one (34)

To a cold solution of diol 9 (1 g, 3.33 mmol, 1 eq.) in methanol (20 mL) and water (10 mL) was added NaIO$_4$ (2.15 g, 10 mmol, 3 eq.) at 0°C. The resulting slurry was vigorously stirred for 20 min at same temperature. After completion of the reaction, the mixture was partitioned between dichloromethane (20 mL) and water (200 mL) and the layers were separated. The aqueous layer was extracted with dichloromethane (3 × 20 mL) and the combined organic extracts were washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 3:1) to yield aldehyde 34 (664 mg, 2.48 mmol, 90%) as a yellow oil.

$R_f = 0.14$ (PE/Et$_2$O = 5:1)
A 100 mL, three-necked flask containing (+)-Ipc$_2$BCl (883 mg, 2.75 mmol, 1 eq.) was placed under vacuum for 1 h to remove any traces of HCl. The flask was charged with argon and ether (5 mL) was added. The solution was cooled to −78°C and triethylamine (380 µL, 2.75 mmol, 1 eq.) was added, followed by a solution of ketone 31 (556 mg, 2.75 mmol, 1 eq.) in ether (5 mL). The reaction was stirred for 1 h at 0°C then re-cooled to −78°C. Aldehyde 33 (664 mg, from above procedure) in ether (5 mL) was added and the reaction was warmed to −20°C and stirred at this temperature for 14 h. The reaction was poured to the solution of phosphate pH 7 buffer solution (5 mL), methanol (5 mL) and NaBO$_3$ (1.7 g, 11 mmol). The reaction was stirred at 0°C for 1 h, the layers were separated and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic extracts were washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 4:1) to provide ß-hydroxyketone 34 (664 mg, 1.89 mmol, 76%, d.r. 10:1) as light yellow oil.

R$_f$ = 0.42 (DCM/EtOAc = 20:1); $^1$H NMR (500 MHz, CDCl$_3$): δ = 7.30 – 7.12 (m, 5H), 5.97 (dd, J = 2.1, 1.0 Hz, 1H), 5.34 (ddq, J = 8.6, 6.0, 1.3 Hz, 1H), 4.22 – 4.16 (m, 1H), 3.60 (d, J = 1.9 Hz, 1H), 3.59 – 3.54 (m, 1H), 3.35 (s, 3H), 3.34 (s, 1H), 2.65 – 2.28 (m, 8H), 1.87 (d, J = 1.1 Hz, 3H), 1.72 (s, 3H), 1.62 – 1.55 (m, 2H), 1.51 (ddd, J = 14.5, 4.4, 3.2 Hz, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ = 210.6, 144.5, 141.5, 134.8, 128.5, 128.4, 126.0, 123.8, 78.9, 77.7, 66.9, 56.8, 49.7, 43.5, 42.5, 40.3, 34.3, 33.3, 24.6, 16.5. [α]$_D$ = −18.3 (c = 1; CHCl$_3$): HRMS (ESI): m/z calc. for C$_{22}$H$_{31}$IO$_3$Na [M+Na]$^+$: 493.1216, found 493.1217

(1E,4R,6R,11E)-1-iodo-4-methoxy-2,11-dimethyl-8-oxo-13-phenyltrideca-1,11-dien-6-yl (Z)-5-((tert-butyldimethylsilyl)oxy)-3-iodopent-2-enolate (35)

To a solution of vinyl carboxylic acid 17 (1256 mg, 3.53 mmol, 2.5 eq.) in toluene (14 mL) was added triethylamine (720 µL, 5.64 mmol, 4 eq.) followed by 2,4,6-trichlorobenzoyl chloride (660 µL, 4.23 mmol, 3 eq.) at 0°C. After stirring for 2 h, a solution of alcohol 34 (664 mg, 1.4 mmol, 1 eq.) and DMAP (26 mg, 0.21 mmol, 0.15 eq.) in toluene (28 mL) was added over 1 h, leading to a yellow suspension. After stirring at 0°C for 3 h, the mixture was quenched with 5% aqueous NaHCO$_3$, and the phases were separated. The aqueous phase was extracted with ether (3 × 10 mL). The combined organic extracts were washed with 5% aqueous NaHCO$_3$ (20 mL) and brine, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash chromatography with (petrol ether/ether 3:1) to yield ester 35 (860 mg, 1.18 mmol, 84%) as a yellow oil.
$R_f = 0.24$ (PE/Et$_2$O = 3:1); $^1$H NMR (500 MHz, CDCl$_3$): δ = 7.30 – 7.12 (m, 5H), 6.34 (t, J = 0.9 Hz, 1H), 5.97 (d, J = 1.0 Hz, 1H), 5.46 – 5.41 (m, 1H), 5.33 (td, J = 7.2, 2.5, 1.2 Hz, 1H), 3.78 (td, J = 6.0, 1.3 Hz, 2H), 3.43 – 3.37 (m, 1H), 3.34 (d, J = 7.3 Hz, 2H), 3.27 (s, 3H), 2.90 – 2.86 (m, 2H), 2.79 (dd, J = 16.6, 6.5 Hz, 1H), 2.70 (dd, J = 16.7, 6.3 Hz, 1H), 2.55 – 2.50 (m, 2H), 2.41 (dd, J = 10.4, 6.1 Hz, 2H), 2.29 (t, J = 7.6 Hz, 2H), 1.85 (d, J = 1.0 Hz, 3H), 1.82 (dd, J = 14.5, 7.3 Hz, 1H), 1.71 (s, 4H), 1.62 (d, J = 7.3 Hz, 1H), 0.87 (s, 9H), 0.05 (s, 6H).

$^{13}$C NMR (126 MHz, CDCl$_3$) δ = 207.1, 163.6, 144.8, 141.5, 134.8, 128.6, 128.4, 126.7, 126.0, 123.8, 117.8, 77.6, 76.3, 68.4, 61.4, 56.6, 51.1, 47.0, 43.5, 42.0, 37.7, 34.3, 33.3, 26.1, 24.6, 18.4, 16.5, −5.2.

[α]$_D$ $-$4.1 (c = 1; CHCl$_3$); HRMS (ESI): m/z calc. for C$_{33}$H$_{50}$I$_2$O$_5$SiNa [M+Na]$^+$: 831.1415, found 831.1416

(2E,8R,10R,12E)-10-methoxy-3,12-dimethyl-6-oxo-1-phenylhexadeca-2,12,15-trien-8-yl (E)-3-(2-((tert-butyldimethylsilyl)oxy)ethyl)hexa-2,5-dienoate (36)

To a solution of vinyl iodide 35 (852 mg, 1.05 mmol, 1 eq.) in DMF (26 mL) and benzene (26 mL) was added dropwise allyltributyltin (6.4 ml, 21.1 mmol, 20 eq.) and Pd(PPh$_3$)$_4$ (243 mg, 0.21 mmol, 0.2 eq.) was added at the end. The mixture was stirred for 3 h at 60°C and then cooled to room temperature. The mixture was quenched by addition of ether (50 mL) and water (250 mL). The aqueous phase was extracted with ether (2 × 25 mL), and the combined organic extracts were washed with brine, dried over Na$_2$SO$_4$ and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 3:1) to yield the desired compound 36 (360 mg, 565 µmol, 54%) as a yellow oil.

$R_f = 0.30$ (PE/Et$_2$O = 3:1); $^1$H NMR (500 MHz, CDCl$_3$): δ = 7.32 – 7.11 (m, 5H), 5.84 – 5.73 (m, 2H), 5.67 (s, J = 5.2 Hz, 1H), 5.44 – 5.37 (m, 1H), 5.36 – 5.30 (m, 1H), 5.21 (td, J = 7.2, 1.2 Hz, 1H), 5.11 – 4.91 (m, 4H), 3.72 (t, J = 6.7 Hz, 2H), 3.40 (d, J = 6.7 Hz, 2H), 3.34 (d, J = 7.3 Hz, 2H), 3.28 (s, 3H), 2.77 – 2.65 (m, 4H), 2.56 – 2.51 (m, 2H), 2.36 – 2.26 (m, 5H), 2.11 (dd, J = 13.6, 6.3 Hz, 1H), 1.82 – 1.72 (m, 2H), 1.70 (s, 3H), 1.61 (d, J = 0.5 Hz, 3H), 0.88 (s, 9H), 0.03 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$): δ = 207.6, 165.3, 158.5, 141.6, 137.2, 135.1, 134.9, 133.2, 128.5, 128.4, 125.9, 124.8, 123.7, 117.6, 116.7, 114.5, 76.6, 67.7, 61.5, 56.2, 47.3, 43.9, 41.9, 41.1, 37.9, 37.0, 34.3, 33.3, 32.4, 26.0, 18.4, 16.5, 16.4, −5.2; [α]$_D$ $-$2.7 (c = 1; CHCl$_3$); HRMS (ESI): m/z calc. for C$_{39}$H$_{60}$O$_5$Si [M+H]$^+$: 637.4288, found 637.4292
(3E,6E,9E,12R,14R)-4-(2-((tert-butyldimethylsilyl)oxy)ethyl)-12-methoxy-10-methyl-14-((E)-5-methyl-2-oxo-7-phenylhept-5-en-1-yl)oxacyclotetradeca-3,6,9-trien-2-one (37)

To a degassed solution of alkene 36 (50.1 mg, 78.5 µmol, 1 eq.) in dichloromethane (80 mL, 1ml/mmol) was added Grubbs II catalyst (6.9 mg, 1.8 µmol, 0.1 eq.) in dichloromethane (1 mL) at room temperature. After stirring for 1 h the same amount of catalyst was added additionally. After additional 1 h DMSO (1 drop) was added and the resulting solution was stirred open to air for 30 min. The mixture was concentrated in vacuo and purified by flash chromatography (petrol ether/ether 3:1) to yield lactone 37 (29 mg, 47.6 µmol, 60%) as a yellow oil.

R<sub>f</sub> = 0.18 (PE/Et<sub>2</sub>O = 3:1); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.30 – 7.12 (m, 5H), 5.58 (t, J = 2.8 Hz, 1H), 5.39 – 5.31 (m, 3H), 5.27 (t, J = 7.9 Hz, 1H), 5.24 – 5.17 (m, 1H), 3.98 (dd, J = 13.0, 8.6 Hz, 1H), 3.73 (t, J = 6.6 Hz, 2H), 3.34 (d, J = 7.3 Hz, 2H), 3.30 (d, J = 3.8 Hz, 3H), 3.25 – 3.18 (m, 1H), 2.75 (ddd, J = 25.3, 17.0, 7.2 Hz, 2H), 2.64 – 2.27 (m, 11H), 2.16 (dd, J = 15.7, 3.8 Hz, 1H), 1.71 (s, 3H), 1.63 (s, 1H), 1.50 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 207.7, 165.3, 158.3, 141.6, 135.0, 133.3, 128.7, 128.5, 128.4, 126.0, 125.9, 125.7, 123.6, 117.8, 75.5, 68.1, 61.1, 55.1, 45.1, 43.4, 43.3, 41.8, 35.1, 34.9, 34.3, 33.2, 31.2, 26.0, 18.4, 16.7, 16.5, -5.2; [α]<sub>D</sub> +12.6 (c = 1; CHCl<sub>3</sub>); HRMS (ESI): m/z calc. for C<sub>37</sub>H<sub>56</sub>O<sub>5</sub>Si [M+H]<sup>+</sup>: 609.3975, found 609.3976

(3E,6E,9E,12R,14R)-4-(2-hydroxyethyl)-12-methoxy-10-methyl-14-((E)-5-methyl-2-oxo-7-phenylhept-5-en-1-yl)oxacyclotetradeca-3,6,9-trien-2-one

To a solution of silyl ether 37 (28 mg, 47.6 µmol) in dry tetrahydrofuran (4.5 mL) was added triethylamine trihydrofluoride (0.5 mL, 10%-solution) at 0°C. After stirring for 3 h at rt, the reaction mixture was put into a solution of 5% NaHCO<sub>3</sub> (5mL) and ethyl acetate (5 mL) at 0°C. The aqueous layer was washed with ethyl acetate (3 × 2 mL). The combined organic extracts were washed with brine (5 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The residue was purified by flash chromatography (petrol ether/ether 3:1) to yield lactone 38 (24 mg, 47.6 µmol, 60%) as a yellow oil.

R<sub>f</sub> = 0.18 (PE/Et<sub>2</sub>O = 3:1); <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ = 7.33 – 7.08 (m, 5H), 5.53 (t, J = 2.8 Hz, 1H), 5.39 – 5.31 (m, 3H), 5.27 (t, J = 7.9 Hz, 1H), 5.24 – 5.17 (m, 1H), 3.98 (dd, J = 13.0, 8.6 Hz, 1H), 3.73 (t, J = 6.6 Hz, 2H), 3.34 (d, J = 7.3 Hz, 2H), 3.30 (d, J = 3.8 Hz, 3H), 3.25 – 3.18 (m, 1H), 2.75 (ddd, J = 25.3, 17.0, 7.2 Hz, 2H), 2.64 – 2.27 (m, 11H), 2.16 (dd, J = 15.7, 3.8 Hz, 1H), 1.71 (s, 3H), 1.63 (s, 1H), 1.50 (s, 3H), 0.88 (s, 9H), 0.05 (s, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 207.7, 165.3, 158.3, 141.6, 135.0, 133.3, 128.7, 128.5, 128.4, 126.0, 125.9, 125.7, 123.6, 117.8, 75.5, 68.1, 61.1, 55.1, 45.1, 43.4, 43.3, 41.8, 35.1, 34.9, 34.3, 33.2, 31.2, 26.0, 18.4, 16.7, 16.5, -5.2; [α]<sub>D</sub> +12.6 (c = 1; CHCl<sub>3</sub>); HRMS (ESI): m/z calc. for C<sub>37</sub>H<sub>56</sub>O<sub>5</sub>Si [M+H]<sup>+</sup>: 609.3975, found 609.3976
chromatography (petrol ether/ether 1:1) to give primary alcohol (18 mg, 36.3 µmol, 82%) as a colorless oil.

\( R_f = 0.10 \) (PE/ET\(_2\)O = 1:1); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 7.30 - 7.14 \) (m, 5H), 5.63 (s, 1H), 5.43 – 5.32 (m, 3H), 5.27 (dd, \( J = 8.3 \), 7.4 Hz, 1H), 5.25 – 5.17 (m, 1H), 3.99 (dd, \( J = 13.2 \), 8.3 Hz, 1H), 3.77 (td, \( J = 6.4 \), 3.3 Hz, 2H), 3.35 (s, 1H), 3.33 (s, 1H), 3.31 (s, 3H), 3.26 – 3.20 (m, 1H), 2.75 (qd, \( J = 17.1 \), 7.2 Hz, 1H), 2.66 – 2.57 (m, 1H), 2.57 – 2.37 (m, 8H), 2.30 (dd, \( J = 14.8 \), 7.3 Hz, 2H), 2.15 (dt, \( J = 15.7 \), 4.2 Hz, 1H), 1.79 – 1.72 (m, 1H), 1.71 (s, 3H), 1.56 – 1.51 (m, 1H), 1.50 (s, 3H), 1.25 (s, 2H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)): \( \delta = 207.7, 165.2, 157.1, 141.6, 135.0, 133.5, 128.9, 128.5, 128.4, 125.9, 125.9, 125.6, 123.6, 118.7, 75.5, 68.2, 60.0, 55.1, 45.0, 43.3, 43.3, 41.8, 35.2, 34.5, 34.3, 33.2, 31.1, 16.6, 16.5. \([\alpha]_D^+43.4\) (c = 1; CHCl\(_3\)); HRMS (ESI): m/z calc. for C\(_{31}\)H\(_{43}\)O\(_5\) [M+H]\(^+\): 495.3110, found 495.3108

11-O-Me-ripostatin A (5)

A 15% DMP solution in dichloromethane (100 µL, 34.4 µmol, 1.8 eq.) was added to a solution of alcohol (9.5 mg, 19.2 µmol, 1 eq.) in dichloromethane (1 mL) at 0°C. After 1 h as the oxidation was completed, 2,3-dimethyl-2-buten (300 µL), tert-BuOH (500 µL), water (200 µL), tetrahydrofuran (500 µL) were added. In the last step 500 µL of Pinnick solution (0.25M, 22.6 mg NaClO\(_2\), 34.5 mg NaH\(_2\)PO\(_4\)·2H\(_2\)O in 1 mL H\(_2\)O) was added at 0°C and stirred for 30 min. The reaction was quenched by addition of ether (1 mL) and HCl (1 M, 5 dropes), and the aqueous layer was washed with ethyl acetate (3 × 2 mL). The combined organic extracts were dried over Na\(_2\)SO\(_4\) and concentrated in vacuo. The residue was purified by flash chromatography (DCM/MeOH 20:1) to give terminal carboxylic acid 5 (7.3 mg, 14.3 µmol, 75%).

\( R_f = 0.42 \) (DCM/MeOH = 10:1); \(^1\)H NMR (500 MHz, CDCl\(_3\)): \( \delta = 7.53 - 6.97 \) (m, 5H), 5.72 (s, 1H), 5.43 – 5.39 (m, 1H), 5.35 (td, \( J = 7.4 \), 1.3 Hz, 2H), 5.28 (t, \( J = 7.7 \) Hz, 1H), 5.26 – 5.20 (m, 1H), 4.04 (dd, \( J = 13.3 \), 8.6 Hz, 1H), 3.36 (s, 1H), 3.35 (s, 1H), 3.32 (s, 3H), 3.26 – 3.13 (m, 4H), 2.76 (ddd, \( J = 25.5, 17.1, 7.1 \) Hz, 3H), 2.62 (dt, \( J = 14.0 \), 8.6 Hz, 2H), 2.57 – 2.52 (m, 3H), 2.52 – 2.47 (m, 2H), 2.42 (d, \( J = 12.1 \) Hz, 1H), 2.31 (t, \( J = 7.7 \) Hz, 2H), 2.16 (dd, \( J = 15.7, 3.8 \) Hz, 1H), 1.79 - 1.73 (m, 2H), 1.72 (s, \( J = 5.1 \) Hz, 3H), 1.56 – 1.52 (m, 1H), 1.51 (s, 3H); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)): \( \delta = 207.7, 174.3, 164.7, 152.0, 141.6, 135.0, 133.4, 129.3, 128.5, 128.4, 125.9, 125.0, 123.7, 120.8, 75.5, 68.5, 55.1, 45.0, 44.3, 43.3, 41.8, 35.1, 34.6, 34.3, 33.2, 31.2, 16.6, 16.5. \([\alpha]_D^+10.6\) (c = 0.5; CHCl\(_3\)); HRMS (ESI): m/z calc. for C\(_{31}\)H\(_{45}\)O\(_5\)Na [M+Na]\(^+\): 531.2723, found 531.2706
OH
EtO
MeO,

13

1.4 1.6 1.8 2.0 2.2 2.4 2.6 2.8 3.0 3.2 3.4 3.6 3.8 4.0 4.2 4.4 4.6 4.8 5.0 5.2 5.4 5.6 5.8 6.0 6.2 6.4 6.6 6.8 7.0 7.2 7.4

f1 (ppm)
MeO

TMS

24

OTBS
The image contains a chemical structure labeled as 28, along with a corresponding NMR spectrum. The spectrum has peaks at various chemical shifts indicated by δ (ppm) values.
I
MeO
OH

34