Progress Towards the Total Synthesis of Cassaine via the Transannular Diels-Alder Strategy

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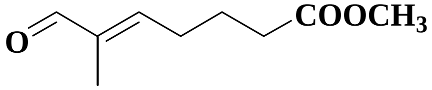
Supporting Information

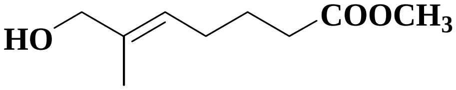
General Remarks: Reactions were performed under a nitrogen atmosphere unless otherwise specified. Tetrahydrofuran was distilled on sodium benzophenone ketyl, dichloromethane, diisopropylamine, triethylamine, NMP from calcium hydride, methanol from magnesium. Anhydrous DMF was purchased from Aldrich Chemicals co. in SureSeal bottles and used as such. All other reagents were purchased from Aldrich Chemicals co. and used with no further purification unless otherwise specified. Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and are referenced in ppm with respect to the residual signals of the solvent, using the standard abbreviations. Infrared spectra were recorded as films and are given in cm^{-1}, MS and HRMS spectra were recorded using electronic ionisation (EI).



Aldehyde 7a

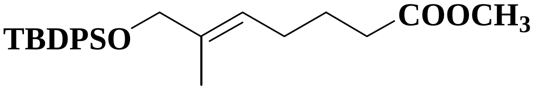
A mixture of aldehyde **7** (100 mg, 0.77 mmol) and 2-(triphenylphosphoranylidene) propionaldehyde (257 mg, 0.81 mmol) was refluxed in benzene (8 mL) over 3 h. The solution was filtered on a silica pad (hexanes / ethyl acetate 2:1) and concentrated under reduced pressure to give **7a** as a colorless oil (98 mg, 75%).

Molecular formula: $C_9H_{14}O_3$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 9.37 (1H, s, $\underline{CH}O$); 6.43 (1H, t, J=7.4 Hz, $R\underline{CH}C(CH_3)CHO$); 3.64 (3H, s, $COO\underline{CH}_3$); 2.34 (4H, m, $\underline{CH}_2CH_2\underline{CH}_2COOCH_3$); 1.82 (2H, m, $CH_2\underline{CH}_2CH_2COOCH_3$); 1.70 (3H, s, $\underline{CH}_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 195.1; 173.4; 153.0; 140.0; 51.6; 33.3; 28.2; 23.6; 9.15. IR (film, υ cm^{-1}): 2953, 1736, 1687, 1440, 1368, 1213. MS (m/e): 170 M^+. HRMS calculated: 170.0943 M^+. HRMS experimental: 170.0940 ± 0.0005.



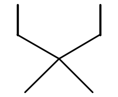
Alcohol 7b

To a solution of aldehyde **7a** (4.7 g, 27.69 mmol) in ethyl alcohol (140 mL) was added at 0 °C the sodium borohydride (1.15 g, 30.46 mmol). The mixture was stirred over 20 min and the reaction was quenched with a saturated aqueous ammonium chloride solution. The volatile solvent was evaporated and the aqueous layer was extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and the crude material was purified by a flash chromatography (hexanes / ethyl acetate 1:1) to afford the alcohol **7b** (3.69 g, 77 %) as a colorless oil.
Molecular formula: $C_9H_{16}O_3$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 5.23 (1H, t, J=7.2 Hz, $R\underline{CH}C(CH_3)CH_2OH$); 3.82 (2H, s, $\underline{CH_2}OH$); 3.52 (3H, s, $COO\underline{CH_3}$); 3.11-3.0 (1H, m, $\underline{OH}$); 2.17 (2H, t, J=7.5 Hz, $\underline{CH_2}COOCH_3$); 1.93 (2H, q, J=7.2 Hz, $\underline{CH_2}CH_2CH_2COOCH_3$); 1.55 (2H, m, $\underline{CH_2}CH_2$ $COOCH_3$); 1.49 (3H, s, $\underline{CH_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 174.2; 135.8; 124.1; 68.1; 51.3; 33.3; 27.7; 24.6; 13.4. IR (film, υ cm^{-1}): 3413, 2947, 2863, 1735, 1440, 1367, 1316, 1206, 1010. MS (m/e): 154 $(M-H_2O)^+$. HRMS calculated: 154.0994 $(M-H_2O)^+$. HRMS experimental: 154.0990 ± 0.0004.



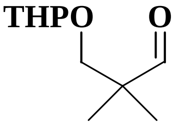
Ester 5

To a mixture of alcohol **7b** (3.69 g, 21.42 mmol) and *t*-butylchlorodiphenylsilane (6.13 mL, 23.56 mmol) in THF (110 mL) was added imidazole (2.19 g, 32.13 mmol) at 0°C. After 2 h of stirring, the reaction was quenched with aqueous ammonium chloride solution and diluted with ethyl acetate. The organic layer was washed with water, dried over magnesium sulfate and concentrated. The product was purified by flash chromatography (hexanes / ethyl acetate 9:1) to give **5** (7.18 g, 82%) as a colorless oil.
Molecular formula: $C_{25}H_{34}O_3Si_1$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.83-7.75 (4H, m $\underline{PhH}$); 7.52-7.41 (6H, m, $\underline{PhH}$); 5.51 (1H, t, J=7.3 Hz, $R\underline{CH}C(CH_3)CH_2OH$); 4.14 (2H, s, $\underline{CH_2}OTBDPS$); 3.73 (3H, s, $COO\underline{CH_3}$); 2.38 (2H, t, J=7.5 Hz, $\underline{CH_2}COOCH_3$); 2.15 (2H, q, J=7.3 Hz, $\underline{CH_2}CHC(CH_3)CH_2OTBDPS$); 1.77 (2H, quint, J=7.4 Hz, $\underline{CH_2}CH_2COOCH_3$); 1.67 (3H, s, $\underline{CH_3}$); 1.15 (9H, s, *t*-Bu). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 174.2; 135.6; 135.1; 134.9; 129.7; 127.7; 123.3; 68.9; 51.5; 33.5; 26.9; 26.7; 24.9; 19.4; 13.6. IR (film, υ cm^{-1}): 3069, 2935, 2858, 1739, 1431, 1247, 1200, 1109, 823, 703. MS (m/e): 353 $(M-C_4H_9)^+$. HRMS calculated: 353.1573 $(M-C_4H_9)^+$. HRMS experimental: 353.1568 ± 0.0010.



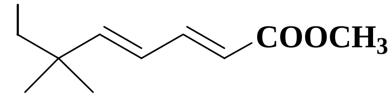
Alcohol 8d

A mixture of neopentyl glycol (2 g, 19.2 mmol), 2*H*,3*H*-dihydropyran (880 µl, 9.6 mmol) and *p*-toluenesulfonic acid (36 mg, 0.19 mmol) in THF / methylene chloride (2:1, 55 mL) was stirred at room temperature for 3 h. The solution was quenched with sodium bicarbonate and the resulting suspension was stirred for 15 min. The solid was filtered off and the solution was concentrated under vacuum. The product was purified by flash chromatography (hexanes / ethyl acetate 1:1) to give **8d** (1.55 g, 82%) as a colorless oil.
Molecular formula: $C_{10}H_{20}O_3$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 4.57 (1H, m, $\underline{CH}$(THP)), 3.90-3.80 (1H, m, $\underline{CH}_2$O (THP)); 3.63 (1H, d, J=8.6 Hz, $\underline{CH}_2$OTHP); 3.56-3.49 (1H, m, $\underline{CH}_2$OTHP); 3.49 (1H, d, J=10.7 Hz, $\underline{CH}_2$OH); 3.40 (1H, d, J=10.7 Hz, $\underline{CH}_2$OH); 3.21 (1H, d, J=18.6 Hz, $\underline{CH}_2$OTHP); 1.88-1.43 (6H, m, 3 X $\underline{CH}_2$ (THP)); 0.93 (6H, s, 2 X $\underline{CH}_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 99.4; 75.7; 62.6; 36.1; 30.5; 25.3; 21.8; 19.7. IR (film, υ cm^{-1}): 3445, 2947, 1554, 1471, 1323, 1129, 1031, 902, 812. MS (m/e): 187 (M-H)$^+$. HRMS calculated: 187.1334 (M-H)$^+$. HRMS experimental: 187.1337 ± 0.0004.



Aldehyde 8e

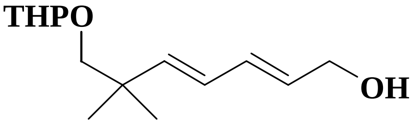
To a solution of oxalyl chloride (1.44 mL, 16.46 mmol) in methylene chloride (40 mL) at -78 °C was added DMSO (1.75 mL, 24.7 mmol) followed by a dropwise addition of alcohol **8d** (1.55g, 8.23 mmol) *via canula* The mixture was stirred for 45 min and triethylamine (4.6 mL, 32.9 mmol) was added. After 1 h of stirring at room temperature, the reaction was quenched with aqueous ammonium chloride solution and extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and concentrated under vacuum. The residue was purified by flash chromatography (hexanes / ethyl acetate 2:1 to 1:1) and the aldehyde **8e** was obtained as a colorless oil (1.44 g, 94%).
Molecular formula: $C_{10}H_{18}O_3$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 9.60 (1H, s, $\underline{CH}$O); 4.60 (1H, m, $\underline{CH}$(THP)); 3.84-3.75 (1H, m, $\underline{CH}_2$O(THP)); 3.80 (1H, d, J =9.6 Hz, $\underline{CH}_2$OTHP); 3.56-3.49 (1H, m, $\underline{CH}_2$O(THP)); 3.37 (1H, d, J =9.6 Hz, $\underline{CH}_2$OTHP); 1.59-1.48 (6H, m, 3 X $\underline{CH}_2$ (THP)); 1.13 (3H, s, $\underline{CH}_3$); 1.10 (3H, s, $\underline{CH}_3$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 205.1; 98.7; 72.2; 61.7; 46.7; 30.2; 25.3; 19.0; 18.9. IR (film, υ cm^{-1}): 3010, 2947, 2873, 2715, 1730, 1123, 1034. MS (m/e): 186 M$^+$. HRMS calculated: 186.1256 M$^+$. HRMS experimental: 186.7253 ± 0.0005.



Diene 8f

To a solution of triethyl 4-phosphonocrotonate (10.3 mL, 46.54 mmol) in ether (310 mL) was added at –10°C a solution of *n*-BuLi / hexanes [1.3 M] (32.5 mL, 42 mmol). The anion was formed over 20 min then the aldehyde **8e** (3.94 g, 21.15 mmol) was added . The mixture was stirred overnight at room temperature and the reaction was quenched with aqueous ammonium chloride solution and extracted with ether. The organic layer was dried over magnesium sulfate and concentrated under vacuum. The residue was purified by flash chromatography (hexanes / ethyl acetate 3:1) and the diene **8f** was obtained as a colorless oil (5.83 g, 98%).

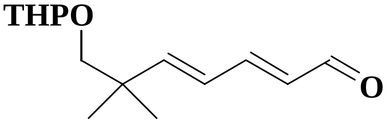
Molecular formula: $C_{16}H_{26}O_4$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.27-7.20 (1H, m, CHCHCOOEt); 6.18-6.10 (2H, m, CHCHCHCOOEt); 5.78 (1H, d, J=15.4 Hz, $C(CH_3)_2CH$); 4.53 (1H, m, CH(THP)); 4.16 (2H, q, J=7.1 Hz, CH_2CH_3); 3.80-3.72 (1H, m, CH_2O(THP)); 3.53 (1H, d, J =9.2 Hz, CH_2OTHP); 3.50-3.40 (1H, m, CH_2O(THP)); 3.07 (1H, d, J =9.2 Hz, CH_2OTHP); 1.85-1.42 (6H, m, 3 X CH_2 (THP)); 1.26 (3H, t, J=7.1 Hz, CH_2CH_3); 1.06 (3H, s, CH_3); 1.05 (3H, s, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 169.5; 151.3; 145.4; 125.3; 119.7; 98.9; 75.8; 61.8; 60.1; 38.0; 30.4; 25.4; 24.2; 19.2; 14.3. IR (film, υ cm^{-1}): 2955, 2870, 1714, 1641, 1617, 1468, 1251, 1125, 1035, 905. MS (m/e): 283 M$^+$. HRMS calculated: 283.1909 MH$^+$. HRMS experimental: 283.1904 ± 0.0008.



Alcohol 8g

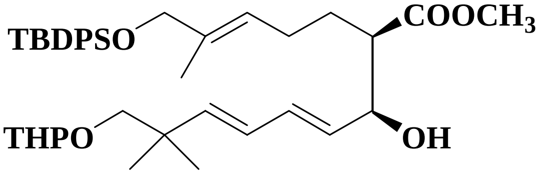
To a solution of ester **8f** (2.5 g, 8.85 mmol) in ether (60 mL) was added at 0°C the lithium aluminium hydride (336 mg, 8.85 mmol). After 1 h of stirring, the mixture was treated with water (335 µL), a aqueous solution of sodium hydroxide 15% (335 µL) and water (670 µL). The solution was stirred during 15 min and then filtered and concentrated. The product was purified by flash chromatography (hexanes / ethyl acetate 1:1) and the alcohol **8g** was obtained as a colorless oil (1.79 g, 84%).

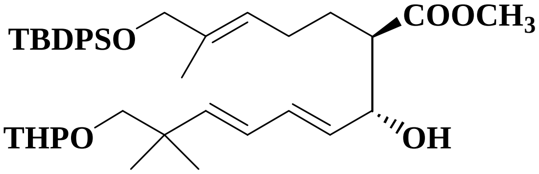
Molecular formula: $C_{14}H_{24}O_3$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 6.17 (1H, dd, J=15, 10.4 Hz, $CHCHCH_2OH$); 6.00 (1H, dd, J=14.4, 10.4 Hz, $CHCHCHCCH_2OH$); 5.70 (1H, d, J=15.0 Hz, $C(CH_3)_2CH$); 5.70 (1H, dd, J=15.0, 11.9 Hz, $CHCH_2OH$); 4.5 (1H, m, CH(THP)); 4.09 (2H, d, J=5.8 Hz, CH_2OH); 3.80-3.70 (1H, m, CH_2O(THP)); 3.47 (1H, d, J=9.1 Hz, CH_2OTHP); 3.48-3.40 (1H, m, CH_2O(THP)); 3.03 (1H, d, J=9.1 Hz, CH_2OTHP); 2.26 (1H, m, CH_2OH); 1.80-1.44 (6H, m, 3 X CH_2 (THP)); 1.02 (3H, s, CH_3); 1.01 (3H, s, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 142.3; 132.0; 130.2; 126.4; 98.9; 76.3; 63.2; 61.8; 37.3; 30.5; 25.5; 24.5; 24.5; 19.2. IR (film, υ cm^{-1}): 3387, 2952, 2869, 1469, 1379, 1201, 1121, 1034, 992. MS (m/e): 240 M$^+$. HRMS calculated: 240.1725 M$^+$. HRMS experimental: 240.1733 ± 0.0007.



Aldehyde 6

To a solution of alcohol **8g** (1.79 g, 7.45 mmol) in methylene chloride (50 mL) at room temperature was added 4-methylmorpholine *N*-oxide (1.3 g, 11.2 mmol), molecular sieves 4 Å (3.7 g) and tetrapropylammonium perruthenate (131 mg, 0.37 mmol). After 30 min of stirring, the mixture was filtered on a silica pad (hexanes / ethyl acetate 2:1) to give the aldehyde **6** (1.57 g, 89%) as a colorless oil.
Molecular formula: $C_{14}H_{22}O_3$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 9.54 (1H, d, J=7.9 Hz, $\underline{CH}O$); 7.10 (1H, ddd, J=15.3, 10.0, 2.7 Hz, $\underline{CH}CHCHO$); 6.34-6.31 (2H, m, $\underline{CH}CHCH\underline{CH}CHO$); 6.11 (1H, dd, J=15.3, 8.0 Hz, $\underline{CH}CHCHCHO$); 4.58-4.55 (1H, m, $\underline{CH}$(THP)); 3.85-3.77 (1H, m, $\underline{CH_2}$O(THP)); 3.59 (1H, d, J=9.2 Hz, $\underline{CH_2}$OTHP); 3.54-3.47 (1H, m, $\underline{CH_2}$O(THP)); 3.14 (1H, d, J=9.2 Hz, $\underline{CH_2}$OTHP); 1.85-1.50 (6H, m, 3 X $\underline{CH_2}$ (THP)); 1.13 (3H, s, $\underline{CH_3}$); 1.12 (3H, s, $\underline{CH_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 193.8; 153.8; 153.3; 130.5; 125.6; 99.0; 75.7; 62.0; 38.3; 30.4; 25.4; 24.1; 19.3. IR (film, υ cm^{-1}): 2945, 2870, 2735, 1684, 1640, 1469, 1380, 1120, 1035, 905. SM (m/e): 239 MH$^+$. HRMS calculated: 239.1647 MH$^+$. HRMS experimental: 239.1651 ± 0.0007.





Aldol adducts 9 and 10

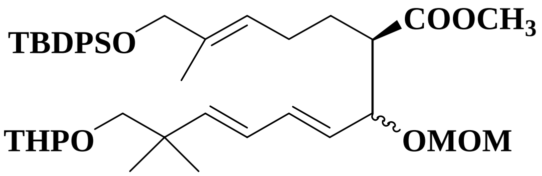
A solution of LDA 1.0 M in a mixture of heptane, THF, and ethyl benzene (853 µL, 1.28 mmol) was added dropwise at –78 °C to a stirred solution of ester **5** (525 mg, 1.28 mmol) in THF (10 mL). The anion was allowed to form during 10 min and the aldehyde **6** (277 mg, 1.16 mmol) was added at –78 °C *via canula*. After 30 min, the reaction was quenched with aqueous ammonium chloride solution. The mixture was extracted with ethyl acetate, and the organic layer was dried over magnesium sulfate. Removal of solvent gave a residue that was purified by flash chromatography (hexanes / ethyl acetate 2:1) to yield 85% of the aldol derivatives *syn* **9** (218 mg) and *anti* **10** (425 mg) as a colorless oil.

ANTI aldol **10**

Molecular formula: $C_{39}H_{56}O_6Si$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.70-7.64 (4H, m, $\underline{PhH}$); 7.48-7.34 (6H, m, $\underline{PhH}$); 6.25 (1H, dd, J=15.1, 10.2 Hz, $\underline{CH}CHCHOH$); 6.04 (1H, dd, J=15.5, 10.2 Hz, $(CH_3)_2CCH\underline{CH}$); 5.79 (1H, d, J=15.5 Hz, $C(CH_3)_2\underline{CH}$); 5.55 (1H, dd, J=15.1, 7.2 Hz, $\underline{CH}CHOH$); 5.41-5.37 (1H, m, $RCCH_3{=}\underline{CH}R$); 4.57-4.55 (1H, m, $\underline{CH}$(THP)); 4.28-4.22 (1H, m, $\underline{CH}OH$); 4.04 (2H, s, $\underline{CH_2}$OTBDPS); 3.86-3.79 (1H, m, $\underline{CH_2}$O(THP)); 3.71 (3H, s, $COO\underline{CH_3}$); 3.71 (3H, s, $COO\underline{CH_3}$); 3.56-3.48 (2H, m, $\underline{CH_2}$OTHP, $\underline{CH_2}$O(THP)); 3.08 (1H, d, J =9.1 Hz, $\underline{CH_2}$OTHP); 2.57-2.48 (2H, m, $\underline{CH}COOCH_3$, OH); 2.08-2.01 (2H, m, $\underline{CH_2}$); 1.86-1.44 (8H, m, 3 X $\underline{CH_2}$ (THP), $\underline{CH_2}$); 1.58 (3H, s, $RC\underline{CH_3}{=}CHR$); 1.06 (15H, m, $\underline{t\text{Bu}}$, 2 X $\underline{CH_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 175.5; 143.2; 135.5; 133.8; 133.2; 131.1; 129.5; 127.6; 126.2; 123.0; 99.0; 76.3; 73.6; 68.8; 61.9; 51.7; 51.2; 37.4; 30.5; 29.2; 26.9; 25.5; 25.2; 24.5; 19.3; 13.5. IR (film, υ cm^{-1}): 3442, 2953, 2858, 1735, 1430, 1379, 1261, 1112, 1064, 995, 908, 735. MS (m/e): 591 $(M-C_4H_9)^+$. HRMS calculated: 591.3142 $(M-C_4H_9)^+$. HRMS experimental: 591.3148 ± 0.0017.

SYN aldol **9**

Molecular formula: $C_{16}H_{26}O_4$. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.70-7.64 (4H, m, <u>PhH</u>); 7.45-7.35 (6H, m, <u>PhH</u>); 6.24 (1H, dd, J=14.6, 10.2 Hz, <u>CH</u>CHCHOH); 6.03 (1H, dd, J=15.5, 10.2 Hz, $(CH_3)_2$CCH<u>CH</u>); 5.77 (1H, d, J=15.5 Hz, $C(CH_3)_2$<u>CH</u>); 5.60 (1H, dd, J=15.1, 6.7 Hz, <u>CH</u>CHOH); 5.43-5.37 (1H, m, $RCCH_3$=<u>CH</u>R); 4.56-4.54 (1H, m, <u>CH</u>(THP)); 4.36-4.31 (1H, m, <u>CH</u>OH); 4.03 (2H, s, <u>CH_2</u>OTBDPS); 3.86-3.78 (1H, m, <u>CH_2</u>O(THP)); 3.70 (3H, s, COO<u>CH_3</u>); 3.54-3.45 (1H, m, <u>CH_2</u>O(THP)); 3.52 (1H, d, J=9.1 Hz, <u>CH_2</u>OTHP); 3.07 (1H, d, J=9.1 Hz, <u>CH_2</u>OTHP); 2.59 (1H, q, J=4.7 Hz, <u>CH</u>$COOCH_3$); 2.39 (1H, d, J=4.4 Hz, <u>OH</u>); 2.13-1.95 (2H, m, <u>CH_2</u>); 1.87-1.48 (8H, m, 3 X <u>CH_2</u> (THP), <u>CH_2</u>); 1.57 (3H, s, RC<u>CH_3</u>=CHR); 1.06 (15H, m, <u>*t*Bu</u>, 2 X <u>CH_3</u>). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 175.0; 143.0; 135.5; 135.0; 133.8; 132.9; 130.0; 129.5; 127.7; 126.3; 123.1; 99.0; 76.3; 73.0; 68.8; 61.9; 51.7; 50.8; 37.4; 30.5; 27.3; 26.8; 25.5; 24.5; 19.3; 13.5. IR (film, υ cm^{-1}): 3443, 2955, 2858, 1734, 1684, 1640, 1430, 1361, 1260, 1112, 1034, 907, 823, 736. MS (m/e): 591 $(M-C_4H_9)^+$. HRMS calculated: 591.3142 $(M-C_4H_9)^+$. HRMS experimental: 591.3148 ± 0.0017.



Triene 10j

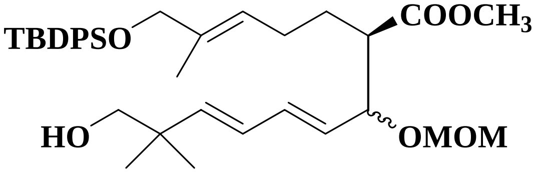
To a solution of alcohol **10** (989 mg, 1.52 mmol) and diisopropylethylamine (5.3 mL, 30.5 mmol) in methylene chloride (15 mL) was added chloromethyl methyl ether (1.74 mL, 22.9 mmol) at 0 °C. The solution was warmed at room temperature and stirred overnight. The reaction was quenched with aqueous ammonium chloride solution and extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and evaporated under reduced pressure. The product was purified by flash chromatography (hexanes / ethyl acetate 3:1) to give the protected alcohol **10j** (897 mg, 85%) as a colorless oil.

ANTI **10j**

Molecular formula: $C_{41}H_{60}O_7Si$. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.69-7.63 (4H, m, <u>PhH</u>); 7.44-7.34 (6H, m, <u>PhH</u>); 6.23 (1H, dd, J=15.1, 10.2 Hz, <u>CH</u>CHCHOMOM); 6.05 (1H, dd, J=15.5, 10.3 Hz, $(CH_3)_2$C CH<u>CH</u>); 5.82 (1H, d, J=15.5 Hz, $C(CH_3)_2$<u>CH</u>); 5.39-5.34 (1H, m, $RCCH_3$=<u>CH</u>R); 5.29 (1H, dd, J=15.2, 8.9 Hz, <u>CH</u>CHOMOM); 4.70 (1H, d, J=6.8 Hz, <u>CH_2</u>(MOM)); 4.56-4.54 (1H, m, <u>CH</u>(THP)); 4.44 (1H, d, J=6.8 Hz, <u>CH_2</u>(MOM)); 4.2 (1H, t, J=9.3 Hz, <u>CH</u>OMOM); 4.02 (2H, s, <u>CH_2</u>OTBDPS); 3.86-3.78 (1H, m, <u>CH_2</u>O(THP)); 3.73 (3H, s, COO<u>CH_3</u>); 3.56-3.43 (1H, m, <u>CH_2</u>O(THP)); 3.52 (1H, d, J =9.1 Hz, <u>CH_2</u>OTHP); 3.31 (3H, s, <u>CH_3</u>(MOM)); 3.07 (1H, d, J=9.2 Hz, <u>CH_2</u>OTHP); 2.58 (1H, td, J=10.7, 3.8 Hz, <u>CH</u>$COOCH_3$); 2.00 (2H, m, <u>CH_2</u>); 1.87-1.41 (8H, m, 3 X <u>CH_2</u> (THP), <u>CH_2</u>); 1.57 (3H, s, RC<u>CH_3</u>=CHR); 1.06 (15H, m, <u>*t*Bu</u>, 2 X <u>CH_3</u>). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 174.8;

143.8; 136.9; 135.5; 135.0; 134.0; 129.6; 127.7; 127.6; 125.9; 123.1; 99.0; 92.9; 77.8; 76.2; 68.8; 61.9; 55.5; 51.5; 50.8; 37.4; 30.5; 28.9; 26.8; 25.5; 25.2; 24.5; 24.4; 19.4; 19.3; 13.4. IR (film, υ cm^{-1}): 2951, 2858, 1738, 1430, 1377, 1112, 1033, 907, 823, 704. MS (m/e): 635 (M-C_4H_9)$^+$. HRMS calculated: 635.3404 (M-C_4H_9)$^+$. HRMS experimental: 635.3414 ± 0.0019.

SYN **9j**
Molecular formula: $C_{41}H_{60}O_7Si$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.72-7.62 (4H, m, $\underline{\mathrm{PhH}}$); 7.46-7.33 (6H, m, $\underline{\mathrm{PhH}}$); 6.17 (1H, dd, J=15.1, 10.2 Hz, $\underline{\mathrm{CH}}$CHCHOMOM); 6.03 (1H, dd, J=15.4, 10.4 Hz, $(CH_3)_2$C CH$\underline{\mathrm{CH}}$); 5.77 (1H, d, J=15.4 Hz, $C(CH_3)_2\underline{\mathrm{CH}}$); 5.49 (1H, dd, J=15.1, 8.9 Hz, $\underline{\mathrm{CH}}$CH-OMOM); 5.44-5.37 (1H, m, $RCCH_3{=}\underline{\mathrm{CH}}R$); 4.70 (1H, d, J=6.9 Hz, $\underline{\mathrm{CH}_2}$(MOM)); 4.55 (1H, m, $\underline{\mathrm{CH}}$(THP)); 4.49 (1H, d, J=6.9 Hz, $\underline{\mathrm{CH}_2}$(MOM)); 4.18 (1H, t, J=7.7 Hz, $\underline{\mathrm{CH}}$OMOM); 4.04 (2H, s, $\underline{\mathrm{CH}_2}$OTBDPS); 3.87-3.77 (1H, m, $\underline{\mathrm{CH}_2}$O(THP)); 3.65 (3H, s, $COO\underline{\mathrm{CH}_3}$); 3.55-3.44 (1H, m, $\underline{\mathrm{CH}_2}$O(THP)); 3.52 (1H, d, J =9.1 Hz, $\underline{\mathrm{CH}_2}$OTHP); 3.35 (3H, s, $\underline{\mathrm{CH}_3}$(MOM)); 3.06 (1H, d, J=9.2 Hz, $\underline{\mathrm{CH}_2}$OTHP); 2.65 (1H, q, J=7.1 Hz, $\underline{\mathrm{CH}}COOCH_3$); 2.13-1.95 (2H, m, $\underline{\mathrm{CH}_2}$); 1.85-1.44 (8H, m, 3 X $\underline{\mathrm{CH}_2}$(THP), $\underline{\mathrm{CH}_2}$); 1.58 (3H, s, $RC\underline{\mathrm{CH}_3}{=}CHR$); 1.06 (15H, m, $\underline{t\mathrm{Bu}}$, 2 X $\underline{\mathrm{CH}_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 173.9; 143.3; 135.5; 134.9; 133.8; 129.5; 127.6; 126.1; 123.3; 99.0; 93.3; 77.4; 76.2; 68.8; 61.9; 55.6; 51.5; 50.9; 37.4; 30.5; 28.4; 26.8; 25.5; 24.4; 19.3; 13.5. IR (film, υ cm^{-1}): 2953, 1738, 1430, 1361, 1112, 1034, 910, 735. MS (m/e): 635 (M-C_4H_9)$^+$. HRMS calculated: 635.3404 (M-C_4H_9)$^+$. HRMS experimental: 635.3408 ± 0.0019.



Alcohol 10k

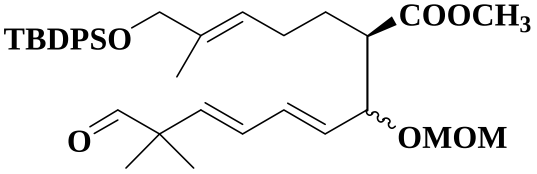
A mixture of compound **10j** (507 mg, 0.732 mmol) and piridinium *p*-toluenesulfonic acid (18 mg, 0.07 mmol) in methanol (10 mL) was refluxed over 1 h and the solution was quenched with sodium bicarbonate. The suspension was stirred over 10 min and then the solid was filtered off. The solution was concentrated and the residue was purified by flash chromatography (hexanes / ethyl acetate 3:1) to afford the alcohol **10k** (343 mg, 77%) as a colorless oil.

ANTI **10k**
Molecular formula: $C_{36}H_{52}O_6Si$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.69-7.66 (4H, m, $\underline{\mathrm{PhH}}$); 7.42-7.26 (6H, m, $\underline{\mathrm{PhH}}$); 6.25 (1H, dd, J=15.0, 10.2 Hz, $\underline{\mathrm{CH}}$CHCHOMOM); 6.07 (1H, dd, J=15.5, 10.3 Hz, $(CH_3)_2$C CH$\underline{\mathrm{CH}}$); 5.70 (1H, d, J=15.5 Hz, $C(CH_3)_2\underline{\mathrm{CH}}$); 5.39-5.35 (1H, m, $RCCH_3{=}\underline{\mathrm{CH}}R$); 5.34 (1H, dd, J=15.1, 8.9 Hz, $\underline{\mathrm{CH}}$CHOMOM); 4.69 (1H, d, J=6.8 Hz, $\underline{\mathrm{CH}_2}$(MOM)); 4.44 (1H, d, J=6.8 Hz, $\underline{\mathrm{CH}_2}$(MOM)); 4.20 (1H, t, J=9.2 Hz, $\underline{\mathrm{CH}}$OMOM); 4.03 (2H, s, $\underline{\mathrm{CH}_2}$OTBDPS); 3.73 (3H, s, $COO\underline{\mathrm{CH}_3}$); 3.35 (2H, s, CH_2OH); 3.31 (3H, s, $\underline{\mathrm{CH}_3}$(MOM)); 2.58 (1H, td, J=10.8, 3.8 Hz, $\underline{\mathrm{CH}}COOCH_3$); 2.04-1.96 (2H, m, $\underline{\mathrm{CH}_2}$); 1.67-1.41 (2H, m, $\underline{\mathrm{CH}_2}$); 1.56 (3H, s, $RC\underline{\mathrm{CH}_3}{=}CHR$); 1.52 (1H, s, $\underline{\mathrm{OH}}$); 1.05 (9H, s, $\underline{t\mathrm{Bu}}$); 1.03 (6H, 2

X $\underline{\mathrm{CH}}_3$). ^{13}C NMR (75 MHz, CDCl_3, δ ppm): 174.8; 142.6; 136.2; 135.5; 135.0; 133.8; 129.5; 128.5; 127.6; 127.5; 123.0; 92.9; 77.8; 71.5; 68.8; 55.5; 51.6; 50.8; 38.8; 28.9; 26.8; 25.2; 23.7; 23.6; 19.3; 13.4. IR (film, υ cm^{-1}): 3470, 2955, 2859, 1738, 1657, 1590, 1430, 1155, 1110, 1027. MS (m/e): 551 $(\mathrm{M-C_4H_9})^+$. HRMS calculated: 551.2829 $(\mathrm{M-C_4H_9})^+$. HRMS experimental: 551,2837 ± 0.0016.

SYN **9k**

Molecular formula: $\mathrm{C_{36}H_{52}O_6Si}$. ^{1}H NMR (300 MHz, CDCl_3, δ ppm): 7.69-7.64 (4H, m, $\underline{\mathrm{PhH}}$); 7.45-7.34 (6H, m, $\underline{\mathrm{PhH}}$); 6.24-6.02 (2H, m, $\mathrm{(CH_3)_2CCH\underline{CHCH}}$); 5.66 (1H, d, J=15.1 Hz, $\mathrm{C(CH_3)_2\underline{CH}}$); 5.55 (1H, dd, J=14.8, 8.5 Hz, $\mathrm{\underline{CH}CHOMOM}$); 5.45-5.39 (1H, m, $\mathrm{RCCH_3{=}\underline{CH}R}$); 4.69 (1H, d, J=6.8 Hz, $\mathrm{\underline{CH}_2(MOM)}$)); 4.49 (1H, d, J=6.8 Hz, $\mathrm{\underline{CH}_2(MOM)}$)); 4.19 (1H, t, J=7.8 Hz, $\mathrm{\underline{CH}OMOM}$); 4.04 (2H, s, $\mathrm{\underline{CH}_2OTBDPS}$); 3.66 (3H, s, $\mathrm{COO\underline{CH}_3}$); 3.35 (5H, s, $\mathrm{\underline{CH}_3(MOM)}$, $\mathrm{\underline{CH}_2OH}$); 2.69-2.62 (1H, m, $\mathrm{\underline{CH}COOCH_3}$); 2.13-1.95 (2H, m, $\mathrm{\underline{CH}_2}$); 1.82-1.68 (2H, m, $\mathrm{\underline{CH}_2}$); 1.58 (3H, s, $\mathrm{RC\underline{CH}_3{=}CHR}$); 1.06 (9H, s, $\underline{t\mathrm{Bu}}$); 1.03 (6H, 2 X $\mathrm{\underline{CH}_3}$). ^{13}C NMR (75 MHz, CDCl_3, δ ppm): 173.9; 142.1; 135.5; 134.9; 133.8; 129.5; 128.6; 127.8; 127.6; 123.2; 93.4; 77.2; 71.5; 68.8; 55.6; 51.5; 50.8; 38.7; 28.4; 26.8; 25.5; 23.7; 23.6; 19.3; 13.5. IR (film, υ cm^{-1}): 3502, 2956, 2859, 1737, 1429, 1110, 1032, 704. MS (m/e): 551 $(\mathrm{M-C_4H_9})^+$. HRMS calculated: 551.2829 $(\mathrm{M-C_4H_9})^+$. HRMS experimental: 551.2837 ± 0.0016.



Aldehyde 10l

To a solution of alcohol **10k** (456 mg, 0.75 mmol) in methylene chloride (10 mL) was added 4-methylmorpholine *N*-oxide (132 mg, 1.12 mmol), molecular sieves 4 Å (345 mg) followed by tetrapropylammonium perruthenate (13 mg, 0.04 mmol). The mixture was stirred during 1 h and the solution was filtered on a silica pad (hexanes / ethyl acetate 1:1) and the aldehyde **10l** was obtained as a colorless oil (408.5 mg, 90%).

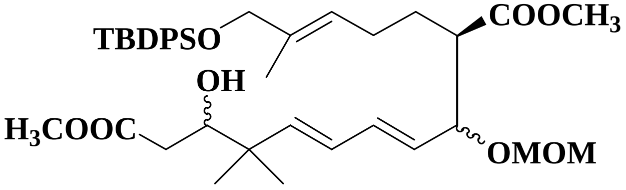
ANTI **10l**

Molecular formula: $\mathrm{C_{36}H_{50}O_6Si}$. ^{1}H NMR (300 MHz, CDCl_3, δ ppm): 9.37 (1H, s, $\mathrm{\underline{CH}O}$); 7.69-7.62 (4H, m, $\underline{\mathrm{PhH}}$); 7.44-7.33 (6H, m, $\underline{\mathrm{PhH}}$); 6.26 (1H, dd, J=15.0, 10.3 Hz, $\mathrm{\underline{CH}CHCHOMOM}$); 6.10 (1H, dd, J=15.4, 10.3 Hz, $\mathrm{(CH_3)_2CCH\underline{CH}}$); 5.68 (1H, d, J=15.4 Hz, $\mathrm{C(CH_3)_2\underline{CH}}$); 5.42 (1H, dd, J=15.1, 8.8 Hz, $\mathrm{\underline{CH}CHOMOM}$); 5.40-5.37 (1H, m, $\mathrm{RCCH_3{=}\underline{CH}R}$); 4.67 (1H, d, J=6.9 Hz, $\mathrm{\underline{CH}_2(MOM)}$)); 4.45 (1H, d, J=6.8 Hz, $\mathrm{\underline{CH}_2(MOM)}$)); 4.22 (1H, t, J=9.1 Hz, $\mathrm{\underline{CH}OMOM}$); 4.03 (2H, s, $\mathrm{\underline{CH}_2OTBDPS}$); 3.72 (3H, s, $\mathrm{COO\underline{CH}_3}$); 3.31 (3H, s, $\mathrm{\underline{CH}_3(MOM)}$)); 2.58 (1H, td, J=9.4, 3.8 Hz, $\mathrm{\underline{CH}COOCH_3}$); 2.03-1.97 (2H, m, $\mathrm{\underline{CH}_2}$); 1.68-1.39 (2H, m, $\mathrm{\underline{CH}_2}$); 1.56 (3H, s, $\mathrm{RC\underline{CH}_3{=}CHR}$); 1.20 (6H, 2 X $\mathrm{\underline{CH}_3}$); 1.06 (9H, s, $\underline{t\mathrm{Bu}}$). ^{13}C NMR (75 MHz, CDCl_3, δ ppm): 201.7; 174.6; 136.3; 135.5; 135.2; 135.0; 133.8; 130.4; 129.8; 129.6; 127.6; 123.0; 93.1; 77.6; 68.8; 55.5; 51.6; 50.7; 48.8; 28.8; 26.8; 25.2; 21.4;

19.3; 14.2; 13.4. IR (film, υ cm^{-1}): 2933, 2858, 2707, 1731, 1463, 1430, 1375, 1111, 1028, 913, 735. MS (m/e): 549 $(M-C_4H_9)^+$. HRMS calculated: 549.2672 $(M-C_4H_9)^+$. HRMS experimental: 549.2676 ± 0.0016.

SYN **9l**

Molecular formula: $C_{36}H_{50}O_6Si$. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 9.36 (1H, s, C<u>H</u>O); 7.70-7.64 (4H, m, <u>PhH</u>); 7.45-7.34 (6H, m, <u>PhH</u>); 6.25-6.06 (2H, m, $(CH_3)_2$CCH<u>CHCH</u>); 5.65 (1H, d, J=14.7 Hz, $C(CH_3)_2$<u>CH</u>); 5.61 (1H, d, J=14.7 Hz, <u>CH</u>CHOMOM); 5.44-5.40 (1H, m, $RCCH_3$=<u>CH</u>R); 4.68 (1H, d, J=6.8 Hz, <u>CH_2</u>(MOM)); 4.50 (1H, d, J=6.8 Hz, <u>CH_2</u>(MOM)); 4.21 (1H, t, J=7.8 Hz, <u>CH</u>OMOM); 4.04 (2H, s, <u>CH_2</u>OTBDPS); 3.66 (3H, s, COO<u>CH_3</u>); 3.35 (3H, s, <u>CH_3</u>(MOM)); 2.70-2.62 (1H, m, <u>CH</u>$COOCH_3$); 2.10-1.95 (2H, m, <u>CH_2</u>); 1.82-1.68 (2H, m, <u>CH_2</u>); 1.58 (3H, s, RC<u>CH_3</u>=CHR); 1.20 (6H, s, 2 X <u>CH_3</u>); 1.06 (9H, s, *t*<u>Bu</u>). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 201.8; 173.8; 135.8; 135.5; 135.0;134.0; 133.8; 130.1; 129.6; 127.2; 123.1; 93.6; 77.1; 68.8; 55.6; 51.5; 50.7; 48.8; 28.4; 26.8; 25.4; 21.4; 19.3; 13.5. IR (film, υ cm^{-1}): 2955, 2858, 2706, 1730, 1430, 1110, 1033, 704. MS (m/e): 549 $(M-C_4H_9)^+$. HRMS calculated: 549.2672 $(M-C_4H_9)^+$. HRMS experimental: 549.2676 ± 0.0016.



Ester 10m

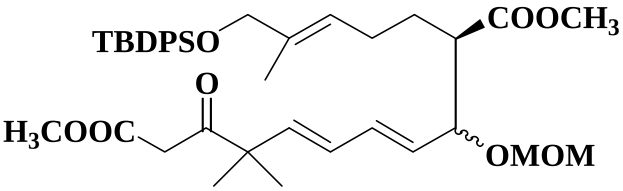
To a solution of diisopropylamine (283 µL, 2.02 mmol) in THF (14 mL) was added *n*-BuLi / hexanes [1.3 M] (1.55 mL, 2.02 mmol) at 0°C. After a stirring of 20 min, the mixture was cooled at -78 °C and methyl acetate (214 µL, 2.69 mmol) was added. The anion was formed over 10 min and the aldehyde **10l** (409 mg, 0.67 mmol) was added dropwise *via canula*. The reaction was stirred over 30 min and was quenched with aqueous ammonium chloride solution. The solution was extracted with ethyl acetate and the organic layer was dried on magnesium sulfate and concentrated under reduce pressure. The product was purified by flash chromatography (hexanes / ethyl acetate 1:1) to give a mixture of aldol products **10m** (353 mg, 77%) as a colorless oil.

ANTI **10m**

Molecular formula: $C_{39}H_{56}O_8Si$. ^1H NMR (300 MHz, $CDCl_3$, δ ppm): 7.68-7.65 (4H, m, <u>PhH</u>); 7.42-7.33 (6H, m, <u>PhH</u>); 6.24 (1H, dd, J=15.2, 10.3 Hz, <u>CH</u>CHCHOMOM); 6.05 (1H, dd, J=15.5, 10.3 Hz, $(CH_3)_2$C CH<u>CH</u>); 5.76 (1H, dd, J=9.8, 3.4 Hz, $C(CH_3)_2$<u>CH</u>); 5.39-5.34 (1H, m, $RCCH_3$=<u>CH</u>R); 5.33 (1H, dd, J=15.2, 8.9 Hz, <u>CH</u>CHOMOM); 4.68 (1H, d, J=6.8 Hz, <u>CH_2</u>(MOM)); 4.44 (1H, d, J=6.8 Hz, <u>CH_2</u>(MOM)); 4.19 (1H, t, J=9.2 Hz, <u>CH</u>OMOM); 4.03 (2H, s, <u>CH_2</u>OTBDPS); 3.79 (1H, dd, J=10.3, 2.2 Hz, <u>CH</u>OH); 3.72 (3H, s, COO<u>CH_3</u>); 3.67 (3H, s, RCH_2COO<u>CH_3</u>); 3.31 (3H, s, <u>CH_3</u>(MOM)); 2.65-2.55 (1H, m, <u>OH</u>); 2.58 (1H, td, J=10.8, 3.8 Hz, $\underline{CH}COOCH_3$); 2.48 (1H, dd, J=16.2, 2.3 Hz, $\underline{CH_2}CHOH$); 2.32 (1H, dd, J=16.2, 10.3 Hz, $\underline{CH_2}CHOH$); 2.04-1.96 (2H, m, $\underline{CH_2}$); 1.66-1.41 (2H, m, $\underline{CH_2}$); 1.56 (3H, s, $RC\underline{CH_3}=CHR$); 1.06 (6H, 2 X $\underline{CH_3}$); 1.05 (9H, s, $\underline{\textit{t}Bu}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 174.7; 173.9; 141.7; 136.2; 135.5; 135.0; 133.8; 129.5; 128.7; 127.6; 127.5; 123.0; 93.0; 77.7; 74.6; 68.8; 55.5; 51.8; 51.6; 50.8; 40.5; 36.7; 28.9; 26.8; 25.2; 23.6; 23.5; 22.8; 22.5; 19.3; 13.4. IR (film, υ cm^{-1}): 3510, 2953, 2857, 1737, 1431, 1110, 1027, 703. MS (m/e): 623 $(M\text{-}C_4H_9)^+$. HRMS calculated: 623.3040 $(M\text{-}C_4H_9)^+$. HRMS experimental: 623.3051 ± 0.0019.

SYN **9m**

Molecular formula: $C_{39}H_{56}O_8Si$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.70-7.61 (4H, m, $\underline{PhH}$), 7.45-7.32 (6H, m, $\underline{PhH}$); 6.18 (1H, dd, J=15.0, 10.2 Hz, $(CH_3)_2CCHCH\underline{CH}$); 6.05 (1H, dd, J=15.3, 10.2 Hz, $(CH_3)_2CCH\underline{CH}CH$); 5.72 (1H, d, J=15.6 Hz, $C(CH_3)_2\underline{CH}$); 5.54 (1H, dd, J=15.0, 8.5 Hz, $\underline{CH}CHOMOM$); 5.44-5.39 (1H, m, $RCCH_3=\underline{CH}R$); 4.69 (1H, d, J=6.8 Hz, $\underline{CH_2}(MOM)$); 4.49 (1H, d, J=6.8 Hz, $\underline{CH_2}(MOM)$); 4.18 (1H, t, J=7.8 Hz, $\underline{CH}OMOM$); 4.04 (2H, s, $\underline{CH_2}OTBDPS$); 3.79 (1H, d, J=10.2 Hz, $\underline{CH}OH$); 3.68 (3H, s, $COO\underline{CH_3}$); 3.66 (3H, s, $RCH_2COO\underline{CH_3}$); 3.35 (3H, s, $\underline{CH_3}(MOM)$); 2.69-2.60 (1H, m, $\underline{CH}COOCH_3$); 2.48 (1H, dt, J=16.1, 2.0 Hz, $\underline{CH_2}CHOH$); 2.31 (1H, ddd, J=16.1, 10.3, 2.4 Hz, $\underline{CH_2}CHOH$); 2.10-1.94 (2H, m, $\underline{CH_2}$); 1.82-1.66 (2H, m, $\underline{CH_2}$); 1.58 (3H, s, $RC\underline{CH_3}=CHR$); 1.25 (1H, s, $\underline{OH}$); 1.06 (9H, s, $\underline{\textit{t}Bu}$); 1.04 (6H, s, 2 X $\underline{CH_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 173.9; 141.3; 135.5; 134.9; 133.8; 129.5; 128.7; 127.7; 127.6; 123.2; 93.4; 77.2; 74.6; 68.8; 55.6; 51.8; 51.5; 50.8; 40.5; 36.8; 28.4; 26.8; 25.5; 23.6; 23.5; 22.6; 22.5; 19.3; 13.5. IR (film, υ cm^{-1}): 3518, 2955, 2858, 1741, 1433, 1111, 705. MS (m/e): 623 $(M\text{-}C_4H_9)^+$. HRMS calculated: 623.3040 $(M\text{-}C_4H_9)^+$. HRMS experimental: 623.3051 ± 0.0019.



β-ketoester 11 and 12

A mixture of alcohol **10m** (227 mg, 0.33 mmol) and Dess-Martin periodinane (211 mg, 0.5 mmol) in methylene chloride (2.5 mL) was stirred at room temperature over 3 h. The solution was diluted with a mixture of hexanes / ethyl acetate 2:1 (5mL) and then filtered on a silica pad (hexanes / ethyl acetate 1:1). The β-ketoester **12** (193.5 mg, 86%) was obtained as a colorless oil.

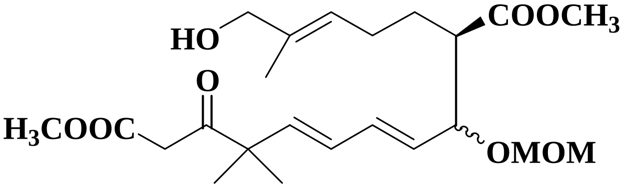
ANTI **12**

Molecular formula: $C_{39}H_{54}O_8Si$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 7.68-7.65 (4H, m, $\underline{PhH}$); 7.44-7.33 (6H, m, $\underline{PhH}$); 6.29-6.05 (2H, m, $(CH_3)_2CCH\underline{CHCH}$); 5.75 (1H, d, J=14.7 Hz, $C(CH_3)_2\underline{CH}$); 5.47-5.32 (2H, m, $\underline{CH}CHOMOM$, $RCCH_3=\underline{CH}R$); 4.67 (1H, d, J=6.8 Hz,

$\underline{CH_2}$(MOM)); 4.45 (1H, d, J=6.8 Hz, $\underline{CH_2}$(MOM)); 4.22 (1H, t, J=9.0 Hz, $\underline{CH}$OMOM); 4.03 (2H, s, $\underline{CH_2}$OTBDPS); 3.72 (3H, s, COO$\underline{CH_3}$); 3.68 (3H, s, RCH$_2$COO$\underline{CH_3}$); 3.50 (2H, s, $\underline{CH_2}$COOCH$_3$); 3.31 (3H, s, $\underline{CH_3}$(MOM)); 2.58 (1H, dt, J=9.5, 3.7 Hz, $\underline{CH}$COOCH$_3$); 2.05-1.97 (2H, m, $\underline{CH_2}$); 1.68-1.43 (2H, m, $\underline{CH_2}$); 1.56 (3H, s, RC$\underline{CH_3}$=CHR); 1.27 (6H, 2 X $\underline{CH_3}$); 1.05 (9H, s, $\underline{t\mathrm{Bu}}$). enol: 12.29 (1H, s, $\underline{OH}$); 5.06 (1H, s, R$\underline{CH}$=COHR). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm): 204.6; 174.7; 174.6; 167.8; 140.4; 137.8; 135.5; 135.1; 133.8; 130.6; 129.6; 129.4; 127.6; 127.2; 122.9; 93.1; 77.5; 68.8; 55.5; 52.2; 51.6; 50.7; 50.6; 44.5; 28.8; 26.8; 25.2; 25.0; 23.7; 23.6; 19.3; 13.4. IR (film, υ cm^{-1}): 2952, 2858, 1742, 1714, 1654, 1617, 1433, 1153, 1110, 1026. MS (m/e): 621 (M-C$_4$H$_9$)$^+$. HRMS calculated: 621.2883 (M-C$_4$H$_9$)$^+$. HRMS experimental: 621.2888 ± 0.0018.

SYN **11**

Molecular formula: C$_{39}$H$_{54}$O$_8$Si. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 7.74-7.61 (4H, m, $\underline{PhH}$); 7.46-7.31 (6H, m, $\underline{PhH}$); 6.24-6.05 (2H, m, (CH$_3$)$_2$CCH$\underline{CHCH}$); 5.80-5.53 (2H, m, C(CH$_3$)$_2$$\underline{CH}$, $\underline{CH}$CHOMOM); 5.44-5.40 (1H, m, RCCH$_3$=$\underline{CH}$R), 4.68 (1H, d, J=6.8 Hz, $\underline{CH_2}$(MOM)); 4.51 (1H, d, J=6.8 Hz, $\underline{CH_2}$(MOM)); 4.20 (1H, t, J=7.8 Hz, $\underline{CH}$OMOM); 4.04 (2H, s, $\underline{CH_2}$OTBDPS); 3.70 (3H, s, CH$_2$COO$\underline{CH_3}$); 3.66 (3H, s, RCH$_2$COO$\underline{CH_3}$); 3.50 (2H, s, $\underline{CH_2}$COOCH$_3$); 3.35 (3H, s, $\underline{CH_3}$(MOM)); 2.70-2.62 (1H, m, $\underline{CH}$COOCH$_3$); 2.10-1.94 (2H, m, $\underline{CH_2}$); 1.81-1.66 (2H, m, $\underline{CH_2}$); 1.58 (3H, s, RC$\underline{CH_3}$=CHR); 1.26 (6H, 2 X $\underline{CH_3}$); 1.06 (9H, s, $\underline{t\mathrm{Bu}}$). enol: 12.27 (1H, s, $\underline{OH}$); 5.05 (1H, s, R$\underline{CH}$=COHR). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm): 204.7; 173.8; 167.9; 140.1; 137.4; 135.5; 134.4; 133.8; 130.7; 129.6; 127.5; 123.2; 93.5; 86.8; 77.1; 68.8; 63.5; 55.7; 52.3; 51.5; 50.8; 50.7; 44.5; 30.4; 28.4; 26.8; 25.4; 25.0; 23.6; 19.3; 13.5. IR (film, υ cm^{-1}): 2934, 2858, 1744, 1714, 1432, 1151, 1029, 705. MS (m/e): 621 (M-C$_4$H$_9$)$^+$. HRMS calculated: 621.2883 (M-C$_4$H$_9$)$^+$. HRMS experimental: 621.2894 ± 0.0019.



Triene 12o

A mixture of β-ketoester **12** (223 mg, 0.33 mmol) and TBAF / THF [1.0 M] (658 μL, 0.66 mmol) was stirred overnight at room temperature. The solution was quenched with aqueous ammonium chloride solution and then extracted with ethyl acetate. The organic layer was dried over magnesium sulfate and concentrated. The product was purified by flash chromatography (hexanes / ethyl acetate 1:1) to give the alcohol **12o** (125 mg, 86%) as a colorless oil.

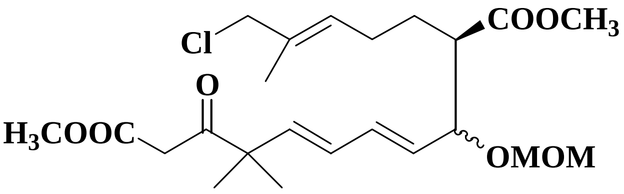
ANTI **12o**

Molecular formula: C$_{23}$H$_{36}$O$_8$. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 6.27-6.03 (2H, m, (CH$_3$)$_2$CCH$\underline{CHCH}$); 5.73 (1H, d, J=15.0 Hz, C(CH$_3$)$_2$$\underline{CH}$); 5.41 (1H, dd, J=14.7, 8.8 Hz,

$\underline{\mathrm{CH}}$CHOMOM); 5.35-5.30 (1H, m, RCCH$_3$=$\underline{\mathrm{CH}}$R); 4.64 (1H, d, J=6.9 Hz, $\underline{\mathrm{CH_2}}$(MOM)); 4.43 (1H, d, J=6.8 Hz, $\underline{\mathrm{CH_2}}$(MOM)); 4.19 (1H, t, J=9.1 Hz, $\underline{\mathrm{CH}}$OMOM); 3.96 (2H, s, $\underline{\mathrm{CH_2}}$OH); 3.71 (3H, s, COO$\underline{\mathrm{CH_3}}$); 3.70 (3H, s, RCH$_2COO\underline{\mathrm{CH_3}}$); 3.51 (2H, s, $\underline{\mathrm{CH_2}}$COOCH$_3$); 3.29 (3H, s, $\underline{\mathrm{CH_3}}$(MOM)); 2.55 (1H, dt, J=10.8, 3.8 Hz, $\underline{\mathrm{CH}}$COOCH$_3$); 2.03-1.96 (2H, m, $\underline{\mathrm{CH_2}}$); 1.61 (3H, s, RC$\underline{\mathrm{CH_3}}$=CHR); 1.68-1.33 (2H, m, $\underline{\mathrm{CH_2}}$); 1.27 (6H, 2 X $\underline{\mathrm{CH_3}}$). enol: 12.26 (1H, s, $\underline{\mathrm{OH}}$); 5.05 (1H, s, R$\underline{\mathrm{CH}}$=COHR). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm): 204.7; 174.5; 167.9; 140.5; 137.9; 135.8; 135.1; 130.5; 129.3; 127.2; 124.5; 93.2; 77.5; 68.6; 55.5; 52.3; 51.6; 50.8; 44.5; 28.6; 25.3; 23.6; 13.6. IR (film, υ cm^{-1}): 3501, 2951, 1740, 1713, 1438, 1318, 1267, 1153, 1024. MS (m/e): 408 (M-CH$_3$OH)$^+$. HRMS calculated: 408.2148 (M-CH$_3$OH)$^+$. HRMS experimental: 408.2154 ± 0.0012.

SYN **11o**

Molecular formula: $C_{23}H_{36}O_8$. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 6.20-6.00 (2H, m, (CH$_3$)$_2$CCH$\underline{\mathrm{CHCH}}$); 5.77-5.48 (2H, m, C(CH$_3$)$_2\underline{\mathrm{CH}}$, $\underline{\mathrm{CH}}$CHOMOM); 5.34 (1H, t, J=7.1 Hz, RCCH$_3$=$\underline{\mathrm{CH}}$R); 4.63 (1H, d, J=6.8 Hz, $\underline{\mathrm{CH_2}}$(MOM)); 4.47 (1H, d, J=6.8 Hz, $\underline{\mathrm{CH_2}}$(MOM)); 4.15 (1H, t, J=7.8 Hz, $\underline{\mathrm{CH}}$OMOM); 3.95 (2H, s, $\underline{\mathrm{CH_2}}$OH); 3.68 (3H, s, COO$\underline{\mathrm{CH_3}}$); 3.63 (3H, s, CHCOO$\underline{\mathrm{CH_3}}$); 3.48 (2H, s, $\underline{\mathrm{CH_2}}$COOCH$_3$); 3.32 (3H, s, $\underline{\mathrm{CH_3}}$(MOM)); 2.64-2.56 (1H, m, $\underline{\mathrm{CH}}$COOCH$_3$); 2.07-1.91 (2H, m, $\underline{\mathrm{CH_2}}$); 1.80-1.65 (2H, m, $\underline{\mathrm{CH_2}}$); 1.61 (3H, s, RC$\underline{\mathrm{CH_3}}$=CHR); 1.24 (6H, 2 X $\underline{\mathrm{CH_3}}$). enol: 12.23 (1H, s, $\underline{\mathrm{OH}}$); 5.02 (1H, s, R$\underline{\mathrm{CH}}$=COHR). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm): 204.7; 173.7; 167.9; 140.1; 137.4; 135.7; 133.8; 130.6; 129.6; 124.6; 93.6; 77.0; 68.6; 55.7; 52.3; 51.5; 50.6; 44.4; 28.2; 25.5; 25.0; 23.6; 13.6. IR (film, υ cm^{-1}): 3483, 2952, 1744, 1713, 1438, 1151, 1027. MS (m/e): 408 (M-CH$_3$OH)$^+$. HRMS calculated: 408.2148 (M-CH$_3$OH)$^+$. HRMS experimental: 408.2154 ± 0.0012.



Chloride 13 and 14

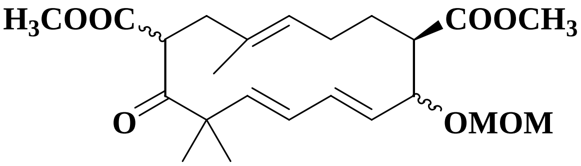
To a mixture of alcohol **12o** (27 mg, 0.04 mmol) and triphehylphosphine (16 mg, 0.06 mmol) in THF (2 mL) was added hexachloroacetone (18 μL, 0.12 mmol) at -30°C. After 30 min of stirring, the solution was quenched with aqueous ammonium chloride solution. The organic layer was extracted with ether, dried over magnesium sulfate and concentrated. The product was purified by flash chromatography (100% hexanes then hexanes / ethyl acetate 1:1) to give the chloride **14** (21 mg, 77%) as a colorless oil.

ANTI **14**

Molecular formula: $C_{23}H_{35}O_8Cl$. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 6.27-6.07 (2H, m, (CH$_3$)$_2$CCH$\underline{\mathrm{CHCH}}$); 5.75 (1H, d, J=14.9 Hz, C(CH$_3$)$_2\underline{\mathrm{CH}}$); 5.47-5.31 (2H, m, $\underline{\mathrm{CH}}$CHOMOM, RCCH$_3$=CHR); 4.65 (1H, d, J=6.8 Hz, CH$_2$(MOM)); 4.43 (1H, d, J=6.9 Hz, CH$_2$(MOM)); 4.19 (1H, t, J=8.9 Hz, CHOMOM); 3.98 (2H, s, CH$_2$Cl); 3.72 (3H, s, COOCH$_3$); 3.70 (3H, s, RCH$_2$COOCH$_3$); 3.51 (2H, s, CH$_2$COOCH$_3$); 3.29 (3H, s, CH$_3$(MOM)); 2.53 (1H, dt, J=10.8, 3.8 Hz, CHCOOCH$_3$); 2.04-1.97 (2H, m, CH$_2$); 1.69 (3H, s, RCCH$_3$=CHR); 1.69-1.32 (2H, m, CH$_2$); 1.27 (6H, 2 X CH$_3$). enol: 12.27 (1H, s, OH); 5.06 (1H, s, RCH=COHR). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm): 204.7, 174.3; 167.9; 140.6; 138.0; 135.9; 135.2; 132.7; 130.4; 129.3; 129.1; 127.1; 93.1; 93.0; 86.8; 77.4; 55.6; 52.3; 51.1; 51.7; 50.8; 50.7; 50.6; 44.5; 42.1; 28.3; 28.2; 25.8; 25.1; 25.0; 23.6; 14.1. IR (film, υ cm^{-1}): 2950, 1746, 1709, 1658, 1614, 1147, 1028. MS (m/e): 413 (M-C$_2$H$_5$O)$^+$. HRMS calculated: 413.1731 (M-C$_2$H$_5$O)$^+$. HRMS experimental: 413.1736 ± 0.0012.

SYN **13**

Molecular formula: $C_{23}H_{35}O_8Cl$. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 6.20-6.00 (2H, m, (CH$_3$)$_2$CCHCHCH); 5.69 (1H, d, J=14.4 Hz, C(CH$_3$)$_2$CH); 5.57 (1H, dd, J=14.1, 8.3 Hz, CHCHOMOM); 5.46 (1H, t, J=6.2 Hz, RCCH$_3$=CHR); 4.63 (1H, d, J=6.8 Hz, CH$_2$(MOM)); 4.47 (1H, d, J=6.8 Hz, CH$_2$(MOM)); 4.16 (1H, t, J=8.1 Hz, CHOMOM); 3.97 (2H, s, CH$_2$Cl); 3.68 (3H, s, COOCH$_3$); 3.63 (3H, s, CHCOOCH$_3$); 3.48 (2H, s, CH$_2$COOCH$_3$); 3.32 (3H, s, CH$_3$(MOM)); 2.62-2.52 (1H, m, CHCOOCH$_3$); 2.51-1.91 (2H, m, CH$_2$); 1.80-1.65 (2H, m, CH$_2$); 1.68 (3H, s, RCCH$_3$=CHR); 1.24 (6H, s, 2 X CH$_3$). enol: 12.23 (1H, s, OH); 5.02 (1H, s, RCH=COHR). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm): 204.7; 173.5; 167.9; 140.1; 137.5; 134.5; 133.8; 132.6; 129.5; 127.3; 93.6; 93.5; 86.8; 77.0; 55.7; 52.2; 51.6; 50.8; 50.6; 44.4; 27.8; 26.0; 25.0; 23.6; 14.1. IR (film, υ cm^{-1}): 2952, 1742, 1712, 1657, 1614, 1436, 1151, 1028. MS (m/e): 426 (M-CH$_4$O)$^+$. HRMS calculated: 426.1809 (M-CH$_4$O)$^+$. HRMS experimental: 426.1812 ± 0.0013.



Macrocycle 15 and 3

To a refluxed suspension of cesium carbonate (131 mg, 0.4 mmol) in acetonitrile (40 mL) was added the chloride **14** (37 mg, 0.08 mmol) with a syringe pump over 14 h. After 2 h of stirring, the solution was diluted with water (10 mL) and the volatile was evaporated. The residue was extracted with ethyl acetate and the organic layer was dried over magnesium sulfate, filtered and concentrated. The product was purified by flash chromatography (hexanes / ethyl acetate 2:1) to give macrocycle **15** as a white foam (21.5 mg, 64%).

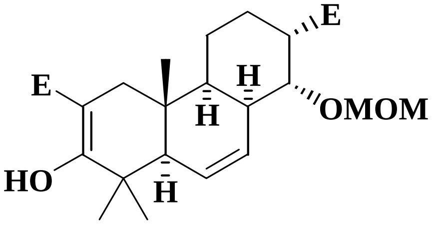
ANTI **15**

Molecular formula: $C_{23}H_{34}O_7$. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 6.39-6.14 (2H, m, (CH$_3$)$_2$CCHCHCH); 5.73-5.63 (1H, d, J=15.3 Hz, C(CH$_3$)$_2$CH); (1H, dd, J=15.3, 7.4 Hz, CHCHOMOM); 5.51-5.43 (1H, dd, J=14.8, 9.1 Hz, CHCHOMOM); (1H, d, J=15.0 Hz, C(CH$_3$)$_2$CH); 4.97-4.89 (1H, m, RCCH$_3$=CHR); 4.69 (1H, d, J=6.7 Hz, CH$_2$(MOM)); 4.67

(1H, d, J=6.7 Hz, $\underline{CH_2}$(MOM)); 4.49 (1H, d, J=6.7 Hz, $\underline{CH_2}$(MOM)); 4.48 (1H, d, J=6.7 Hz, $\underline{CH_2}$(MOM)); 4.39 (1H, t, J=9.3 Hz, $\underline{CH}$OMOM); 4.37 (1H, dd, J=10.2, 7.4 Hz, $\underline{CH}$OMOM); 3.89-3.74 (1H, m, CO-$\underline{CH}COOCH_3$); 3.72 (3H, s, $COO\underline{CH_3}$); 3.69 (3H, s, $RCH_2COO\underline{CH_3}$); 3.31 (3H, s, $\underline{CH_3}$(MOM)); 2.69-2.42 (2H, m, $\underline{CH_2}CCH_3{=}CHR$, $\underline{CH}COOCH_3$); 2.24-2.05 (2H, m, $\underline{CH_2}$, $\underline{CH_2}CCH_3{=}CHR$); 1.86-1.20 (12H, m, $RC\underline{CH_3}{=}CHR$, 2 X $\underline{CH_2}$, 2 X $\underline{CH_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 175.3; 174.7; 170.4; 170.3; 136.4; 136.3; 135.2; 133.8; 132.5; 131.4; 131.0; 130.4; 129.9; 129.4; 125.6; 94.1; 93.6; 77.8; 77.2; 75.8; 55.6; 52.6; 52.5; 52.4; 52.1; 51.8; 51.7; 51.6; 51.5; 38.8; 29.7; 28.3; 27.8; 25.9; 24.5; 23.5; 22.6; 21.7; 16.5. IR (film, υ cm^{-1}): 2933, 1738, 1709, 1436, 1160, 1033. MS (m/e): 422 M$^+$. HRMS calculated: 422.2304 M$^+$. HRMS experimental: 422.2299 ± 0.0013.

SYN **3**

Molecular formula: $C_{23}H_{34}O_7$. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 6.33 (1H, dd, J=15.4, 10.0 Hz, $(CH_3)_2CCH\underline{CH}$); 6.23-6.11 (1H, m, $C(CH_3)_2CHCH\underline{CH}$); 5.78 (1H, dd, J=15.7, 6.3 Hz, $\underline{CH}$CHOMOM); 5.53 (1H, d, J=15.4 Hz, $C(CH_3)_2\underline{CH}$); 4.94-4.90 (1H, m, $RCCH_3{=}\underline{CH}R$); 4.82 (1H, dd, J=5.95, 2.2 Hz, $\underline{CH}$OMOM); 4.66 (1H, d, J=6.8 Hz, $\underline{CH_2}$(MOM)); 4.54 (1H, d, J=6.8 Hz, $\underline{CH_2}$(MOM)); 3.96 (1H, dd, J=9.6, 1.6 Hz, $CO\underline{CH}COOCH_3$); 3.74 (3H, s, $COCHCOO\underline{CH_3}$); 3.69 (3H, s, $COO\underline{CH_3}$); 3.31 (3H, s, $\underline{CH_3}$(MOM)); 2.70 (1H, dd, J=15.3, 9.5 Hz, $\underline{CH}COOCH_3$); 2.37-2.31 (1H, m, $\underline{CH_2}$); 2.26-2.12 (2H, m, $\underline{CH_2}$); 1.95-1.71 (2H, m, CH_2); 1.49, 1.36 (3H, s, $RC(\underline{CH_3}){=}CHR$); 1.24 (6H, s, 2 X $\underline{CH_3}$). ^{13}C NMR (75 MHz, $CDCl_3$, δ ppm): 206.8; 173.5; 170.3; 135.8; 135.1; 134.5; 133.1; 131.8; 131.5; 131.3; 128.5; 124.7; 94.8; 94.6; 55.5; 52.9; 52.5; 52.1; 51.9; 51.1; 51.0; 39.1; 38.1; 26.3; 24.3; 23.9; 23.0; 22.1; 16.4. IR (film, υ cm^{-1}): 2951, 2360, 1747, 1708, 1163, 1035. MS (m/e): 422 M$^+$. HRMS calculated: 422.2304 M$^+$. HRMS experimental: 422.2308 ± 0.0013.

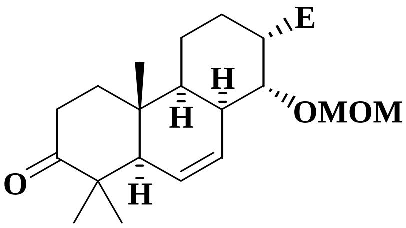


Tricycle 16 and 17

A mixture of macrocycle **3** (3.2 mg, 0.01 mmol) and triethylamine (7 μL, 0.02 mmol) in toluene (1 mL) was degazed with argon and heated in a pyrex sealed tube at 125 °C over 18 h. The solution was concentrated and the product was purified by flash chromatography (hexanes / ethyl acetate 3:1) to afford tricycle **16** (0.8 mg, 25%) and decarboxyled tricycle **17** (2.1 mg, 75%).

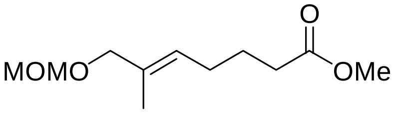
Tricycle **16**

Molecular formula: $C_{23}H_{34}O_7$. Melting point: 110-112°C. ^{1}H NMR (300 MHz, $CDCl_3$, δ ppm): 12.55 (1H, s, $\underline{OH}$); 6.04 (1H, dt, J=10.4, 3.3 Hz, $(CH_3)_2CCH\underline{CH}{=}CH$); 5.68 (1H, dt, J=10.4, 1.9 Hz, C(CH_3)$_2$CHCH=<u>CH</u>); 4.75 (1H, d, J=7.0 Hz, <u>CH</u>$_2$(MOM)); 4.62 (1H, d, J=7.0 Hz, <u>CH</u>$_2$(MOM)); 3.89 (1H, dd, J=11.8, 6.7 Hz, <u>CH</u>OMOM); 3.77 (3H, s, CHOH=CCOO<u>CH</u>$_3$); 3.70 (3H, s, COO<u>CH</u>$_3$); 3.39 (3H, s, <u>CH</u>$_3$(MOM)); 3.14 (1H, q, J=7.0 Hz, CH<u>CH</u>CHOMOM); 3.04-2.94 (1H, m, <u>CH</u>COOCH$_3$); 2.45 (1H, d, J=15.4 Hz, <u>CH</u>$_2$C(CH_3)$_2$); 2.08 (1H, m, C(CH_3)$_2$<u>CH</u>); 1.23 (3H, s, C(<u>CH</u>$_3$)$_2$); 1.14 (3H, s, C(<u>CH</u>$_3$)$_2$); 0.92 (3H, s, CH$_2$C(<u>CH</u>$_3$)R$_2$). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm) : 177.4; 174.0; 128.5; 126.1; 96.2; 94.1; 77.2; 75.3; 55.8; 51.5; 51.0; 44.1; 43.8; 38.2; 36.1; 34.3; 28.8; 24.7; 20.3; 19.1; 17.0. IR (film, υ cm^{-1}): 3442, 2932, 2857, 1735, 1654, 1472, 1253, 1112. MS (m/e): 391 (M-OCH$_3$)$^+$. HRMS calculated: 391.2120 (M-OCH$_3$)$^+$. HRMS experimental: 391.2113 ± 0.0011.



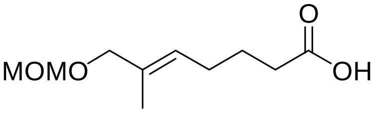
Tricycle 17

Molecular formula: $C_{23}H_{34}O_7$. ^{1}H NMR (300 MHz, CDCl$_3$, δ ppm): 6.05 (1H, dt, J=10.1, 3.2 Hz, (CH_3)$_2$CCH<u>CH</u>=CH); 5.67 (1H, dt, J=10.4, 2.3 Hz, C(CH_3)$_2$CHCH=<u>CH</u>); 4.76 (1H, d, J=7.0 Hz, <u>CH</u>$_2$(MOM)); 4.61 (1H, d, J=7.0 Hz, <u>CH</u>$_2$(MOM)); 3.89 (1H, dd, J=11.8, 6.9 Hz, <u>CH</u>OMOM); 3.70 (3H, s, COO<u>CH</u>$_3$); 3.39 (3H, s, <u>CH</u>$_3$(MOM)); 3.14 (1H, q, J=6.7 Hz, CH<u>CH</u>CHOMOM); 3.04-2.94 (1H, m, <u>CH</u>COOCH$_3$); 2.70-2.58 (1H, m, <u>CH</u>$_2$COC(CH_3)$_2$), 2.45-2.35 (1H, m, <u>CH</u>$_2$ (CO)C(CH_3)$_2$), 2.23 (1H, m, <u>CH</u>C(CH_3)$_2$); 2.03-1.40 (7H, m, 3 X <u>CH</u>$_2$, <u>CH</u>); 1.12 (3H, s, <u>CH</u>$_3$); 1.09 (3H, s, <u>CH</u>$_3$); 1.05 (3H, s, <u>CH</u>$_3$). ^{13}C NMR (75 MHz, CDCl$_3$, δ ppm) : 128.9; 126.2; 96.2; 74.6; 55.9; 53.6; 51.5; 46.9; 45.6; 43.8; 36.6; 35.9; 34.2; 26.1; 24.3; 21.5; 19.0, 18.9; 16.1. IR (film, υ cm^{-1}): 2948, 1735, 1706, 1441, 1381, 1162, 1033. MS (m/e): 364 M$^+$. HRMS calculated: 364.2250 M$^+$. HRMS experimental: 364.2243 ± 0.0011.



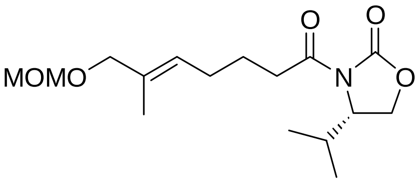
Ester 24

To a solution of allylic alcohol **7b** (4.5 g, 26.1 mmol) in dimethoxymethane (60 ml) was added lithium bromide (453 mg, 5.22 mmol) and p-toluenesulfonic acid (496 mg, 2.61 mmol). This solution was stirred 16 h at room temperature and then quenched with aqueous sodium bicarbonate (50 mL). The mixture was extracted with diethyl ether (3 x 50 mL), and the combined organic layers were washed with brine (20 mL), dried over magnesium sulfate, filtered and concentrated. The residue was purified by flash chromatography (10 % ethyl acetate in hexane) giving the protected alcohol **24** (4.8 g, 85%) as a colorless oil.
IR (film, υ cm^{-1})**:** 2944, 1739, 1145, 1048, 920; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm)**:** 5.33 (1H, t, J=7.2 Hz, C=CH), 4.52(2H, s, O–CH_2–O), 3.83(2H, s, O–CH_2–C), 3.57(3H, s, $COOCH_3$), 3.28(3H, s, O–CH_3), 2.23(2H, t, J=7.4 Hz, CH_2–CO), 2.00(2H, q, J=7.5 Hz, =CH–$\underline{CH_2}$), 1.61(2H, quint., J=7.3Hz, CH_2–$\underline{CH_2}$–CH_2), 1.56(3H, s, CH_3–C); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm) **:** 173.8, 132.7, 127.1, 95.2, 73.0, 55.1, 51.3, 33.3, 26.9, 24.5, 13.9; **MS** (EI) : 216 (M$^{+\cdot}$), 154 (M$^{+\cdot}$-CH_3OCH_2OH); **HRMS** (EI) : calcd for $C_9H_{15}O_2$ =154.0994; found = 154.0990 ± 0.0005.



Acid 24d

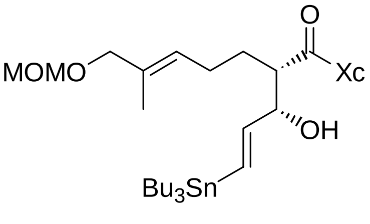
A solution of 2M potassium hydroxide (41.5 mL, 83 mmol) was added in 30 min. to a stirred solution of ester **25** (4.5 g, 20.8 mmol) in methanol (90 mL) at 0°C. This mixture was stirred one hour at 0°C and overnight at room temperature. The methanol was then evaporated, the residue was dissolved in water (60 mL) and acidified to pH 1 with sodium hydrogenosulfate. The solution was extracted with dichloromethane (3 x 50 mL), the combined organic layers were washed with brine(20 mL), dried over sodium sulfate, filtered and evaporated, affording the crude acid **24d** (4.1 g, 97%) as a colorless oil.
IR (film, υ cm^{-1})**:** 3500 to 3000, 2946, 1711, 1148, 1044; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm): 5.42 (1H, t, J= 7.2 Hz, C=CH), 4.62 (2H, s, O–CH_2–O), 3.93 (2H, s, O–CH_2–C), 3.37 (3H, s, CH_3–O), 2.36 (2H, t, J= 7.5 Hz, CH_2–CO), 2.11 (2H, q, J= 7.2 Hz, CH–$\underline{CH_2}$–CH_2), 1.72 (2H, quint., J= 7.6 Hz, CH_2–$\underline{CH_2}$–CH_2), 1.66 (3H, s, CH_3–C); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 178.4, 132.5, 127.1, 94.8, 72.8, 54.8, 33.1, 26.7, 24.2, 13.7 **MS (**EI) : 202 (M$^+$), 170 (M$^+$- CH_3OH); **HRMS** (EI) : calcd for $C_{10}H_{18}O_4$ = 202.1205; found = 202.1209 ± 0.0006



Oxazolidinone 25

To a stirred solution of acid **24d** (9.1 g, 45 mmol), in THF (180 mL), at 0^{o}C was added drpowise triethylamine (6.6 mL, 47.3 mmol). This solution was stirred 15 minutes, then cooled to –78^{o}C, and trimethylacetylchloride (5.82 mL, 47.3 mmol) was added. The mixture was stirred 1h at –78^{o}C and then warmed to rt for 15 min. In a separated flask, BuLi (30 mL, 1.5 M in hexanes, 45 mmol) was added to a solution of imide **31** (5.8 g, 45 mmol) in THF (150 mL) at –78^{o}C and then stirred 15 min. The resulting solution was added via canula to the white suspension containing the mixed anhydride at -78^{o}C. The mixture was stirred 30 min. at –78^{o}C and 1h at 0 ^{o}C. The content of the flask was then quenched with aqueous ammonium chloride and the volatiles were remove in vacuo. The resulting aqueous mixture was extracted with CH_2Cl_2 (3 X 150 mL) and the combined organic layers were then washed successively with 100 mL of 1M aqueous HCl and 100 mL of saturated aqueous sodium bicarbonate, dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. Purification by flash chromatography (20% EtOAc/ hexanes) afforded 12.5 g (88%) of **25** as a colorless oil.

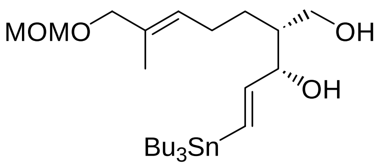
$[\alpha]^{d}_{20}$= +56^{o} (*c* 2.1, CH_2Cl_2); **IR** (film, υ cm^{-1}) 2958, 1780, 1697, 1383, 1209, 1049; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 5.44 (1H, t, J= 6.4 Hz, C=CH–CH_2), 4.61 (2H, s, O–CH_2–O), 4.44 to 4.00 (1H, m, N–CH), 4.29 to 4.18 (2H, m, O–CH_2–CH), 3.93 (2H, s, O–CH_2–C), 3.37 (3H, s, CH_3–O), 3.04 to 2.82 (2H, m, CH_2–CO–N), 2.40 to 2.32 (1H, m, $(CH_3)_2$–CH), 2.12 (2H, q, J=7.4 Hz, =CH–CH_2), 1.72 (2H, quint ., J= 7.3 Hz, CH_2– $\underline{CH_2}$–CH_2), 1.66 (3H, s, CH_3–C=), 0.91(3H, d, J=6.7 Hz, CH_3–CH), 0.86 (3H, d, J=6.64 Hz, CH_3–CH); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 172.9, 153.9, 132.6, 127.3, 95.2, 73.0, 63.2, 58.3, 55.1, 34.9, 28.3, 26.9, 24.0, 17.9, 14.6, 13.9; **MS** (EI) : 313 (M^{+}), 251 (M^{+}-CH_3OCH_2OH); **HRMS** (EI) : calcd for $C_{14}H_{21}O_3N$=251.1521, found = 251.1516±0.0007



Aldol adduct 25f

To a solution of imide **25** (4.54 g, 14.5 mmol) in CH_2Cl_2 (65 mL) at –78^{o}C was added over 15 minutes $TiCl_4$ (1.91 mL, 17.4 mmol) giving a thick suspension wich was stirred for an additionnal 15 min. N,N,N’,N’-Tetramethylethylenediamine (6.56 mL, 43.5 mmol) was

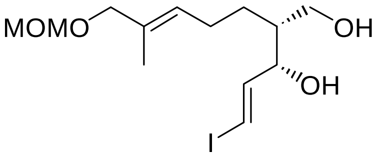
added over 5 min, then N-Methylpyrrolidinone (2.8 mL, 29 mmol) was added too and the reaction was stirred for an additionnal 20 minutes at –78°C. A solution of aldehyde **26** (5 g, 14.5 mmol) in dichloromethane (15 mL) was added via canula to the reaction mixture at –78°C and the mixture was stirred for 1 h at –78°C and then allowed to slowly warm at rt. The dark solution was quenched with NH_4Cl (aq) (6 mL), then Celite (5g) was added and the reaction mixture was stirred for 1 h at rt. The reaction mixture was filtered, concentrated and purified by flash chromatography (15% EtOAc/ hexanes) affording pure aldol condensation product **25f** (5.3 g, 55%) as a light yellow oil.
$[\alpha]^{d}_{20}$ = +21.2° (*c* 2.32, CH_2Cl_2); **IR** (film, υ cm^{-1}) 3472.5, 2956.0, 1778.7, 1696.5, 1385.0, 1202.9,1050.1, 915.0, 726.9; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 6.25 (1H, dd, J= 19.1, 1.2 Hz, Sn–$\underline{CH}$=CH), 5.99 (1H, dd, J= 19.1, 5.2 Hz, Sn–CH=$\underline{CH}$), 5.40 (1H, t, J= 7.1 Hz, C=$\underline{CH}$–CH_2), 4.60 (2H,s, O–CH_2–O), 4.51 to 4.46 (1H, m, N–CH), 4.37 to 4.34 (1H, m, CH–$\underline{CH}$(OH)–CH), 4.28 to 4.18 (2H, m, O–$\underline{CH_2}$–CH), 4.18 to 4.11 (1H, m, CH–CO), 3.90 (2H, s, O–CH_2–C=), 3.36 (3H, s, CH_3–O), 2.45 (1H, d, J= 3.4 Hz, OH), 2.40 to 2.35 (1H, m, CH–$\underline{CH}$–$(CH_3)_2$), 2.06 to 2.01 (2H, m, CH–$\underline{CH_2}$–CH_2), 1.86 to 1.81 (1H, m, CH_2–$C\underline{H_a}(H_b)$–CH), 1.68 to 1.64 (1H, m, CH_2–$C\underline{H_b}(H_a)$–CH), 1.62 (3H, s, CH_3–C), 1.53 to 1.43 (6H, m, 3 X Sn–CH_2–$\underline{CH_2}$–CH_2–CH_3), 1.36 to 1.23 (6H, m, Sn–CH_2–CH_2–$\underline{CH_2}$–CH_3), 0.97 to 0.86 (21H, m, 2 X CH–$(\underline{CH_3})_2$ and 3 X Sn–$\underline{CH_2}$–CH_2–CH_2–$\underline{CH_3}$); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm):174.9, 154.0, 146.9, 132.3, 130.1, 127.4, 95.2, 75.4, 73.0, 63.0, 58.7, 55.1, 47.6, 29.0, 28.3, 27.2, 27.1, 25.6, 17.9, 14.5, 13.9, 13.6, 9.40; **MS** (EI) : 602 (M^+-C_4H_9), 540 (M^+-$C_6H_{15}O_2$); **HRMS** (EI) : calcd for $C_{27}H_{48}O_6NSn$ = 602.2503, found = 602.2509 ± 0.0018.



Diol 25g

To a mixture of aldol product **25f** (10 g, 15.1 mmol) in THF (65 mL) at 0°C was slowly added a solution of sodium borohydride (2.3 g, 60.7 mmol) in water (20 mL). The reaction was kept 1h at 0°C, then allowed to warm to rt and stirred for 24 h. The reaction was put in ice/water bath, quenched with 1N HCl (75 mL) and extracted with ethyl acetate (3 X 75 mL). The organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography (25% EtOAc/hexanes) gave 6.25 g (78%) of pure diol **25g** as a colorless oil.
$[\alpha]^{d}_{20}$ = +9.8° (*c* 1.90, $CHCl_3$); **IR** (film, υ cm^{-1}) : 3401.5, 2912.1, 1463.7, 1151.1, 1042.3; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 6.23 (1H, d, J= 19.2 Hz, Sn–$\underline{CH}$=CH); 6.04 (1H, dd, J= 19.2, 4.9 Hz, CH=$\underline{CH}$–CH); 5.41 (1H, t, J= 7.1 Hz, C=CH–CH_2); 4.60 (2H, s, O–CH_2–O); 4.36 (1H, m, $\underline{CH}$–OH); 3.91 (2H, s, O–CH_2–C); 3.75 to 3.71 (2H, m, CH–$\underline{CH_2}$–OH); 3.36 (3H, s, CH_3–O); 2.8 to 2.5 (2H, m, 2 X OH); 2.11 to 2.04 (2H, m, CH–$\underline{CH_2}$–CH_2); 1.85 (1H, m, CH_2–$\underline{CH}$–CH_2OH); 1.65 (3H, s, CH_3–C); 1.61 to 1.54 (2H, m, CH_2–$\underline{CH_2}$–CH); 1.54 to 1.43 (6H, m, 3 X Sn–CH_2–$\underline{CH_2}$); 1.38 to 1.23 (6H, m, 3 X CH_3–$\underline{CH_2}$–CH_2); 0.97 to 0.85

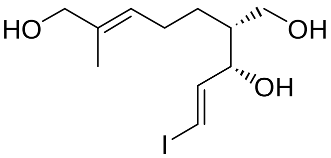
(15H, m, 3 X $\underline{CH_3}$–CH_2–CH_2–$\underline{CH_2}$–Sn); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 147.7 ,132.0, 129.3, 128.1, 95.3, 78.2, 73.3, 64.3, 55.2, 44.2, 29.1, 27.2, 25.6, 17.0, 14.0, 13.7, 9.4; **MS** (EI) : 477 (M^+- C_4H_9); **HRMS** (EI): calcd for $C_{21}H_{41}O_4Sn$ = 477.2027, found = 477.2019 ± 0.0014.



Diol 25h

Iodine (4.06 g, 16 mmol) was added, in small portion, in a periode of 15 minutes, to a solution of diol **25g** (9 g, 16.8 mmol) in CH_2Cl_2 (90 mL). The reaction was quenched with a solution of 1M of $Na_2S_2O_4$ (60 mL) and then extracted with CH_2Cl_2 (3 x 30 mL). The organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by flash chromatography (30% EtOAc/hexanes) yielded 97% (6 g) of diol **25h.**

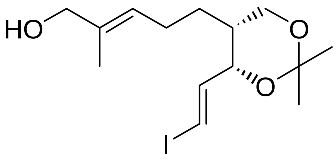
$[\alpha]^d_{20}$ = +16.6° (*c* 1.57, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 3401.1, 2919.2, 1031.7; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 6.60 (1H. dd, J= 14.4, 5.5 Hz, I–CH=$\underline{CH}$), 6.37 (1H, d, J= 14.4 Hz, I–CH=), 5.39 (1H, t, J= 7.0 Hz, C=$\underline{CH}$–CH_2), 4.61 (2H, s, O–CH_2–O), 4.33 to 4.31 (1H, m, =CH–$\underline{CH}$(OH)), 3.91 (2H,s, O–CH_2–C), 3.72 (2H, d, J= 5.8 Hz, CH–$\underline{CH_2}$OH), 3.36 (3H, s, CH_3–O), 3.1 to 2.8 (3H, s (br), 2 x OH), 2.07 (2H, quint, J= 7.4 Hz, CH–$\underline{CH_2}$–CH_2), 1.85 to 1.79 (1H, m, CH_2–$\underline{CH}$–CH_2), 1.65 (3H, s, CH_3–C), 1.29 (2H, q, J= 7.8 Hz, CH_2–$\underline{CH_2}$–CH); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 145.8, 132.4, 127.8, 95.3, 77.8, 77.4, 73.3, 64.1, 55.3, 43.8, 25.6, 25.4, 14.1; **MS** (EI) : 325 (M^+- C_2H_5O), 308 (M^+- $C_2H_6O_2$); **HRMS** (EI) : calcd for $C_{11}H_{17}O_2I$ = 308.0273, found = 308.0261 ± 0.0009.



Triol 25i

Diol **25h** (200 mg, 0.54 mmol) in isopropyl alcohol (4 mL) was heathed at 55°C for 16 h in the presence of a catalytic quantity of HCl (conc) (2 µL, 27µmol). The solution was allowed to cool to rt and then quenched by the addition of an aqueous solution of $NaHCO_3$ (8 mL). The mixture was extracted with EtOAc (5 x 10 mL), washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude product was purified by flash chromatography (75% to 100% EtOAc/hexanes) giving 130 mg (74%) of pure triol **25i** as a viscous oil.

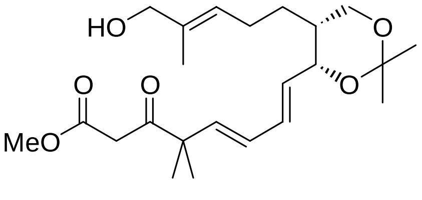
$[\alpha]^{d}_{20}$: +11.0 (*c* 1.42, CH_3OH); **IR** (film, υ cm^{-1}) : 3500 to 3200, 2933.4, 1451.8, 1028.0; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 6.60 (1H. dd, J= 14.4, 5.5 Hz, I–CH=$\underline{CH}$), 6.37 (1H, d, J= 14.4 Hz, I–CH=), 5.36 (1H, t, J= 7.0 Hz, C=$\underline{CH}$–CH_2), 4.31 (1H, m, =CH–$\underline{CH}$(OH)), 3.97 (2H, s, HO–$\underline{CH_2}$–C), 3.69 (2H, d, J= 5.8 Hz, CH–$\underline{CH_2}$OH), 2.5 to 2.3 (3H, s (br), 3 x OH), 2.06 (2H, quint, J=7.0 Hz, CH–$\underline{CH_2}$–CH_2), 1.84 to 1.78 (1H, m, CH_2–$\underline{CH}$–CH_2), 1.65 (3H, s, CH_3–C), 1.29 (2H, q, J= 7.8 Hz, CH_2–$\underline{CH_2}$–CH); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 145.8, 135.4, 125.2, 77.8, 77.1, 68.5, 63.8, 43.7, 25.7, 25.3, 13.8; **MS** (EI)**:** 309 (M^+-OH), 183 (M^+-OHI); **HRMS** (EI): calcd for $C_{11}H_{18}O_2I$ = 309.0351, found = 309.0347 ± 0.0009.



Acetonide 27

To a stirred solution of triol **25i** (385 mg, 1.18 mmol) in THF (15 mL) were added successively 2,2-Dimethoxypropane (6 mL, 48.7 mmol) and *p*-toluenesulfonic acid (11 mg, 0.05 mmol). This solution was stirred at rt for 1 h, then quenched with $NH_4Cl_{(aq)}$ (to clive the MOP formed during the protection) and stirred at rt for another hour (or until no trace of MOP protecting product by TLC). The mixture was extracted with Et_2O (5 x 15 mL), the organic layers were washed with brine, dried over $MgSO_4$ and concentrated in vacuo. Purification by flash chromatography (40% EtOAc/hexanes) gave 410 mg (95%) of pure allylic alcohol **27** as a light yellow oil.

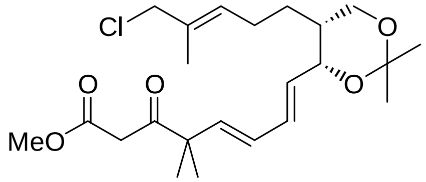
$[\alpha]^{d}_{20}$ = –16.2^{o} (*c* 1.85, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 3407.2, 2930.1, 1371.3, 1190.9, 1004.8; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 6.42 (1H, dd, J= 14.4, 4.5 Hz, I–CH=$\underline{CH}$), 6.26 (1H, dd, 14.4, 1.5 Hz, I–CH), 5.33 (1H, t, J=6.5 Hz, C=$\underline{CH}$–CH_2), 4.49 to 4.47 (1H, m, CH–$\underline{CH}$–CH), 3.99 to 3.94 (1H, m, CH_{eq} of CH–$\underline{CH_2}$–O), 3.94 (2H, s, $\underline{CH_2}$OH), 3.72 (1H, d, J= 11.9 Hz, CH_{ax} of CH–$\underline{CH_2}$–O), 2.09 to 1.94 (3H, m, CH–$\underline{CH_2}$–CH_2 + O$\underline{H}$), 1.74 to 1.64 (2H, m, CH_2–$\underline{CH_2}$–CH), 1.62 (3H, s, CH_3–C), 1.43 to 1.32 (1H, m, CH–$\underline{CH}$(CH_2)–CH_2), 1.40 (3H, s, CH_3–C–O), 1.35 (3H, s, CH_3–C–O); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 144.4, 135.2, 125.5, 98.9, 77.1, 74.3, 68.6, 62.6, 37.1, 29.5, 25.4, 24.0, 19.0, 13.8; **MS** (EI): 351 (M^+-CH_3); **HRMS** (EI) : calcd for $C_{13}H_{20}O_3I$ = 351.0457, found = 351.0451 ± 0.0010.



β-ketoester 27k

Allylic alcohol **27** (75 mg, 0.2 mmol) and stannane **23** (80 mg, 0.24 mmol) were dissolved in DMF (2 mL). The solution was degased 30 min under the vacuum of an oil pump. After that, Bis(acetonitrile)dicloropalladium (2.5 mg, 10µmol) was added, the mixture was degased in vacuuo for 5 min and then stirred for 3 h under nitrogen. The reaction mixture was quenched by the addition of aqueous NH_4Cl and extracted with Et_2O (3 x 15 mL). The organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography (40% EtOAc/hexanes) gave 69 mg (85%) of triene **27k** as a light yellow oil.

$[\alpha]^{d}_{20}$ = + 4.9^{o} (*c* 2.55, $CHCl_3$); **IR** (film, υ cm^{-1}) : 3450.4, 2991.8, 2934.4, 1745.8, 1710.8, 1616.8, 1440.1, 1273.1, 996.5, 736.5; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) :6.27 to 6.06 (2H, m, CH=CH–CH=CH), 5.74 to 5.60 (2H, m, CH=CH–CH=CH), 5.36 (1H, t, J= 6.5 Hz, C=CH–CH_2), 4.57 (1H,m, CH–CH(CH)–O), 4.00 (1H, d, J= 11.8, CH_{eq} of CH–CH_2–O), 3.95 (2H, s, HO–CH_2–C), 3.77 (1H, d, J= 11.8, CH_{ax} of CH–CH_2–O), 3.68 (3H, s, $COOOH_3$), 3.50 (2H, s, CO–CH_2–CO), 2.18 to 1.89 (2H, m, =CH–CH_2–CH_2), 1.82 to 1.70 (2H, m, CH–CH_2–CH_2–CH), 1.62 (3H, s, CH_3–C=), 1.57 to 1.47 (1H, m, CH_2–CH(CH)–CH_2), 1.44 (3H, s, CH_3–C–O), 1.39 (3H,s, CH_3–C–O), 1.24 (6H,s, 2 x CH_3–C); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 204.9, 168.0, 136.3, 134.9, 132.8, 130.2, 129.8, 125.8, 99.8, 72.2, 68.7, 62.7, 52.2, 50.7, 44.4, 37.8, 29.6, 25.4, 23.9, 23.6, 23.5, 19.1, 13.7; **MS** (EI) : 376 (M^{+}-CH_3OH), 361 (M^{+} -CH_3OH-CH_3); **HRMS** (EI): calcd for $C_{22}H_{32}O_5$ = 376.2250, found = 376.2246 ± 0.0011

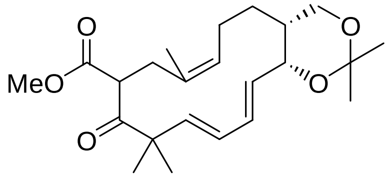


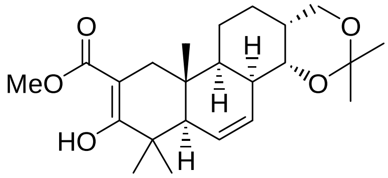
Chloride 28

To a solution of triene **27k** (80 mg, 0.2 mmol) in THF (2.5 mL) at –30^{o}C was added triphenylphosphine (77 mg, 0.29 mmol) and stirred until it was dissolved. After that, hexachloroacetone (45µL, 0.29 mmol) was added dropwise, the mixture was stirred for 10 min and then quenched with $NH_4Cl_{(aq)}$. The mixture was extracted with Et_2O (3 x 15 mL), the organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated. The yellow oil was then purified by flash chromatography (10% EtOAc/hexanes) giving 72 mg (86%) of allylic chloride **28**.

$[\alpha]^{d}_{20}$ = +10.4^{o} (*c* 6.0, $CHCl_3$); **IR** (film, υ cm^{-1}) :2291.6, 2943.8, 1750.5, 1707.5, 1653.8, 1616.1, 1439.8, 1272.0, 1197.6, 996.0, 734.3; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 6.28 to 6.08 (2H, m, CH=CH–CH=CH), 5.79 to 5.58 (2H, m, CH=CH–CH=CH), 5.49 (1H, t, J= 6.8 Hz, C=CH–CH_2), 4.59 (1H, m, CH–CH(CH)–O), 4.05 to 3.99 (1H, m, CH_{eq} of CH–CH_2–O), 3.99 (2H, s, C–CH_2–Cl), 3.76 (1H, dd, J=11.8, 1.5 Hz, CH_{ax} of CH–CH_2–O), 3.69 (3H, s, $COOCH_3$), 3.51 (2H, s, CO–CH_2–CO), 2.19 to 1.91 (2H, m, CH–CH_2–CH_2), 1.84 to 1.73 (CH–CH_2–CH_2), 1.70 (3H, s, CH_3–C=), 1.45 (3H, s, CH_3–C–O), 1.40 (3H, s, CH_3–C–O), 1.37 to 1.29 (1H, m, CH_2–CH–CH_2), 1.26 (6H, s, 2 x CH_3–C); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 204.9, 168.0, 136.4, 132.7, 131.9, 130.6, 130.1, 129.8, 98.8, 72.1, 62.7, 52.4, 52.2, 50.7, 44.4, 37.7, 29.6, 25.9, 23.6, 19.1, 14.2; **MS** (EI): 426 (M^{+}), 391 (M^{+}-Cl), 394 (M^{+}-

CH_3OH), 359 (M^+-CH_3OH-Cl); **HRMS** (EI): calcd for $C_{23}H_{35}O_5Cl$ = 426.2173, found = 426.2170 ± 0.0013.



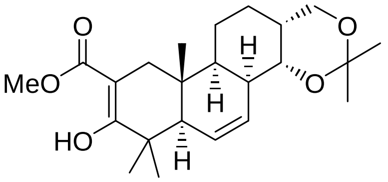


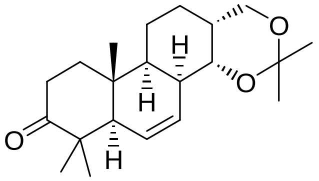
Compounds 29 and 30

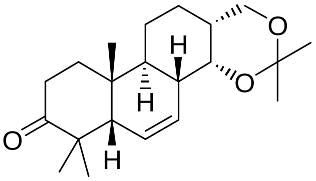
To a vigorusly stirred solution of Cs_2CO_3 (630 mg, 1.94 mmol) and NaI (290 mg, 1.94 mmol) in acetonitrile (150 mL) at reflux (oil bath at 90°C), was slowly added, with a syringe pump, in a period of 12 h, the allylic chloride **29** (110 mg, 0.26 mmol) diluted in 8 mL of acetonitrile (final concentration 1.7 x 10^{-3} M). When the addition was finished, the reaction mixture was stirred for 3 more hour at reflux, then cooled to rt and the acetonitrile was evaporated. The residue was dissolved in CH_2Cl_2 (75 mL), filtered on a small pad of Celite and evaporated. Purification by flash chromatography (10% EtOAc/hexanes) gave 7 mg of tricycle **30** (7%) and 65 mg of macocyclic triene **29** (64%) (overall yield 71%) both as a colorless oil.

Macrocycle **29 :** $[\alpha]^{d}_{20}$ = -109.8° (*c* 1.6, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 2937.7, 1751.2, 1706.8, 1379.7, 1195.9, 1160.6, 997.8; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 6.27 (1H, dd, J=15.4, 10.1 Hz, CH=$\underline{CH}$–CH=CH), 6.10 (1H, dd, J= 15.6, 10.1 Hz, CH=CH–$\underline{CH}$=CH), 5.75 (1H, dd, J= 15.8, 5.5 Hz, CH=CH–CH=$\underline{CH}$), 5.52 (1H, d, J= 15.4 Hz, $\underline{CH}$=CH–CH=CH), 5.00 (1H, t, J= 6.7, C=$\underline{CH}$–CH_2), 4.65 to 4.62 (1H, m, CH–$\underline{CH}$(OH)–CH), 4.11 (1H, dd, J= 11.4, 2.6 Hz, CH_{eq} of CH–$\underline{CH_2}$–O), 3.89 (1H, dd, J= 9.2, 2.4 Hz, OC–$\underline{CH}$(CH_2)–CO), 3.69 (3H, s, $COOCH_3$), 3.63 (1H, dd, J= 11.4, 1.5 Hz, CH_{ax} of CH–$\underline{CH_2}$–O), 2.70 (1H, dd, J= 14.5, 9.5 Hz, CH_{eq} of CH–$\underline{CH_2}$–C=), 2.35 to 2.11 (1H, m, CH_{eq} of CH–$\underline{CH_2}$–CH_2), 1.96 (1H, dd, J= 14.7, 2.2 Hz, CH_{ax} of CH–$\underline{CH_2}$–C=), 1.84 to 1.74 (1H, m, CH_{eq} of CH_2–$\underline{CH_2}$–CH), 1.71 to 1.56 (1H, m, CH_{ax} of CH–$\underline{CH_2}$–CH), 1.47 (6H, s, CH_3–C–O, CH_3–C=), 1.45 to 1.38 (1H, m, CH_{ax} of CH_2–$\underline{CH_2}$–CH), 1.40 (3H, s, CH_3–C–O), 1.35 (3H, s, CH_3–C), 1.31 to 1.25 (1H, m, CH_2–$\underline{CH}$(CH)–CH_2), 1.22 (3H, s, CH_3–C); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm): 206.6, 170.5, 135.3, 134.7, 132.3, 131.6, 129.1, 126.3, 98.5, 71.8, 64.9, 52.4, 52.0, 42.2, 40.4, 38.9, 29.7, 26.5, 24.8, 23.0, 22.2, 18.9, 16.0; **MS** (EI): 390 (M^+), 375 (M^+-CH_3), 332 (M^+-C_3H_6O); **HRMS** (EI): calcd for $C_{23}H_{34}O_5$= 390.2406, found=390.2410 ± 0.0011.

Tricycle **30** : $[\alpha]^{d}_{20}$ = +134.0° (*c* 1.0, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 2985.7, 2935.5, 1654.3, 1609.1, 1438.4, 1363.0, 1247.5, 1187.3; ^{1}**H NMR** ($CDCl_3$, 300 MHz, δ ppm) : 12.55 (1H, s, $\underline{H}$O–C(C)=C), 5.95 (1H, td, J= 10.4, 3.3 Hz, CH–$\underline{CH}$=CH–CH), 5.64 (1H, td, J= 10.4, 1.9 Hz, CH–CH=$\underline{CH}$–CH), 3.88 (1H, dd, J= 10.2, 7.7 Hz, CH–$\underline{CH}$(CH)–O), 3.75 (3H, s, $\underline{CH_3}O_2C$), 3.60 (1H, dd, J= 11.0, 6.6 Hz, CH_{eq} CH–$\underline{CH_2}$–O), 3.49 (1H, t, J=10.5 Hz, CH_{ax} CH–$\underline{CH_2}$–O) 2.34 to 2.26 (1H, m, =CH–$\underline{CH}$–CH–O), 2.28 (1H, d, J= 15.4 Hz, CH_{eq} =C(CO_2Me)–$\underline{CH_2}$–C), 2.09 (1H, dd, J= 4.9, 2.7 Hz, $\underline{CH}$–CH=CH), 2.06 to 1.93 (2H, m, CH–$\underline{CH}$(CH_2)–CH_2–O, C–$\underline{CH}$(CH)–CH_2), 1.80 (1H, d, J= 15.5 Hz, CH_{ax} =C(CO_2Me)–$\underline{CH_2}$–C), 1.85 to 1.79 (1H, m, CH_{eq} CH–$\underline{CH_2}$–CH_2), 1.5 to 1.14 (3H, m, CH_{ax} CH–$\underline{CH_2}$–CH_2, $\underline{CH_2}$–CH_2–CH), 1.36 (3H, s, $\underline{CH_3}$–C(CH_3)–O), 1.34 (3H, s, $\underline{CH_3}$–C(CH_3)–O), 1.22 (3H, s, $\underline{CH_3}$–C(CH_3)–C), 1.15 (3H, s, $\underline{CH_3}$–C(CH_3)–C), 0.77 (3H, s, CH_2–C($\underline{CH_3}$)–CH); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm) : 177.6, 173.9, 129.6, 125.5, 99.7, 94.0, 69.6, 61.8, 51.5, 51.2, 42.1, 38.3, 38.1, 35.9, 34.8, 34.1, 28.7, 26.2, 23.8, 21.6, 20.9, 20.5, 13.8; **MS** (EI) : 390 (M^+), 375 (M^+-CH_3), 332 (M^+-C_3H_6O); **HRMS** (EI): calcd for $C_{23}H_{34}O_5$ = 390.2406, found = 390.2398 ± 0.0011.







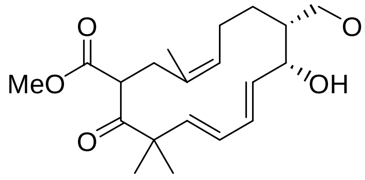
Tricycles 30, 31 and 32

Macrocycle **29** (6 mg, 15µmol) in toluene (1.5 mL) was heated at 125°C for 16 hours in a sealed tube. The solution was evaporated and the residu was purified by flash chromatography (10% EtOAc/hexanes) to give 2mg of **30**, 2mg of **31** and 1 mg of **32** (global yield of 92%)

Tricycle **31** : **IR** (film, υ cm^{-1}) : 2986.7, 2931.5, 1706.9, 1458.7, 1379.6, 1222.5; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 5.95 (1H, td, J= 10.2, 3.3 Hz, CH–$\underline{CH}$=CH–CH), 5.61 (1H, td, J= 10.2, 2.2 Hz, CH-CH=$\underline{CH}$–CH), 3.89 (1H, dd, J= 10.3, 7.8 Hz, CH–$\underline{CH}$(CH)–O), 3.60 (1H, dd, J= 10.9, 6.7 Hz, CH_{eq} CH–$\underline{CH_2}$–O), 3.50 (1H, t, J= 10.8, CH_{ax} CH–$\underline{CH_2}$–O), 2.66 (1H, ddd, J= 15.7, 12.5, 6.8 Hz, CH_{eq} O=C–$\underline{CH_2}$–CH_2), 2.40 to 2.36 (1H, m, CH_{ax} O=C–$\underline{CH_2}$–CH_2), 2.35 to 2.30 (1H, m, =CH–$\underline{CH}$–CH), 2.21 (1H, dd, J= 5.2, 2.8 Hz, $(CH_3)_2$–$\underline{CH}$–CH=), 2.08 to 1.92 (2H, m, (CH_3)C–$\underline{CH}$(CH_2)–CH, CH_2–$\underline{CH}$(CH_2)–CH), 1.86 (1H, ddd, J= 13.3, 6.8, 3.1 Hz, CH_{eq} O=C–CH_2–$\underline{CH_2}$), 1.75 (1H, tt, J= 13.1, 3.1 Hz, CH_2–$\underline{CH_2}$–CH), 1.45 (1H, td, J= 12.7, 5.8 Hz, CH_{ax} O=C–CH_2–$\underline{CH_2}$), 1.37 (3H, s, $\underline{CH_3}$–C(CH_3)–O), 1.35 (3H, s, $\underline{CH_3}$–C(CH_3)–O), 1.38 to 1.00 (3H, m, CH_{ax} CH_2–$\underline{CH_2}$–CH, $\underline{CH_2}$–CH_2–CH), 1.12 (3H, s, $\underline{CH_3}$–C(CH_3)), 1.09 (3H, s, $\underline{CH_3}$–C(CH_3)), 0.95 (3H, s, $\underline{CH_3}$–C(CH_2)–CH); ^{13}**C NMR** (75

MHz, CDCl$_3$, δ ppm) : 216.5, 130.3, 125.6, 99.7, 69.5, 61.7, 54.2, 47.1, 43.8, 38.2, 36.3, 35.6, 35.5, 34.3, 26.3, 25.6, 23.9, 21.8, 21.6, 20.9, 13.5; **MS** (EI) : 332 (M$^+$), 317 (M$^+$-CH$_3$), 274 (M$^+$-C$_3$H$_6$O); **HRMS** (EI): calcd for $C_{21}H_{32}O_3$ = 332.2351, found = 332.2343 ± 0.0010.

Tricycle **32** : **IR** (film, υ cm^{-1}) : 2930.8, 2860.7, 1708.5, 1461.0, 1377.1, 1196.7, 1085.6; **^{1}H NMR** (300 MHz, CDCl$_3$, δ ppm) : 5.63 (2H, s, CH–$\underline{\mathrm{CH}}$=$\underline{\mathrm{CH}}$–CH), 4.15 to 4.10 (2H, m, CH$_{eq}$ CH–$\underline{\mathrm{CH}_2}$–O, CH–$\underline{\mathrm{CH}}$(CH)–O); 3.52 (1H, dd, J= 11.6, 1.2 Hz, CH$_{ax}$ CH–$\underline{\mathrm{CH}_2}$–O), 2.49 (1H, ddd, J= 15.1, 8.1, 4.0 Hz, CH$_{eq}$ O=C–$\underline{\mathrm{CH}_2}$–CH$_2$), 2.33 (1H, ddd, J= 15.0, 10.6, 4.1 Hz, O=C–$\underline{\mathrm{CH}_2}$–CH$_2$), 2.09 to 1.97 (2H, m, =CH–$\underline{\mathrm{CH}}$–CH–O, CH$_2$–$\underline{\mathrm{CH}}$(CH)–CH$_2$–O), 1.93 to 1.83 (2H, m, CH$_{eq}$ O=C–CH$_2$–$\underline{\mathrm{CH}_2}$, (CH$_3$)C–$\underline{\mathrm{CH}}$–CH=), 1.72 (1H, ddd, J= 12.7, 6.7, 3.0 Hz, (CH$_3$)C–$\underline{\mathrm{CH}}$–CH$_2$), 1.71 to 1.50 (1H, m, CH$_{ax}$ O=C–CH$_2$–$\underline{\mathrm{CH}_2}$), 1.44 (3H, s, $\underline{\mathrm{CH}_3}$–C(CH$_3$)–O), 1.41 to 1.23 (2H, m, CH–CH$_2$–$\underline{\mathrm{CH}_2}$–CH), 1.30 (3H, s, $\underline{\mathrm{CH}_3}$–C(CH$_3$)–O), 1.16 to 1.00 (2H, m, CH–$\underline{\mathrm{CH}_2}$–CH$_2$–CH), 1.12 (3H, s, CH$_3$–C(CH$_3$)), 1.06 (3H, s, CH$_3$–C(CH$_3$)), 0.88 (3H,s, CH$_3$–C(CH$_2$)–CH); **^{13}C NMR** (75 MHz, CDCl$_3$, δ ppm) :217.8, 131.8, 125.5, 98.3, 70.2, 64.9, 51.9, 47.1, 42.5, 35.5, 35.3, 34.7, 34.1, 33.6, 29.6, 25.3, 25.0, 24.5, 23.5, 22.0, 18.9; **MS** (EI) : 332 (M$^+$); **HRMS** (EI) : calcd for $C_{21}H_{32}O_3$ = 332.2351, found = 332.2360 ± 0.0010.

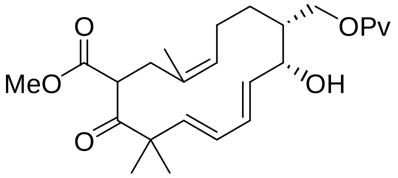


Macrocycle 29a

To a solution of macrocycle **29** (88 mg, 0.23 mmol) in THF (4 mL) at 0^{o}C, was added a solution of HCl 1N (4 mL). The mixture was stirred 1 hour at 0^{o}C, then water (5 mL) was added and the mixture was extracted 4X with EtOAc. The combined organic layers were washed with brine, dried over MgSO$_4$, filtered and evaporated. The oily residu was purified by flash chromatography (50% EtOAc/ hexanes) to afford diol **29a** in 95% yield as a viscous oil.

$[\alpha]^{d}_{20}$= -87.3^o (*c* 1.08, CH$_2$Cl$_2$); **IR** (film, υ cm^{-1}) : 3387.6, 2935.7, 1744.8, 1704.6, 1438.5, 1222.6, 1162.3; ^{1}**H NMR** (300 MHz, CDCl$_3$, δ ppm) : 6.26 (1H, dd, J=15.5, 9.8 Hz, C–CH=$\underline{\mathrm{CH}}$–CH=CH), 6.07 (1H, dd, J= 15.8, 9.9 Hz, C–CH=CH–$\underline{\mathrm{CH}}$=CH), 5.80 (1H, dd, J= 15.9, 5.2 Hz, CH=CH–CH=$\underline{\mathrm{CH}}$), 5.51 (1H, d, J= 15.5 Hz, C–$\underline{\mathrm{CH}}$=CH–CH=CH), 4.99 (1H, t, J= 7.3 Hz, C=$\underline{\mathrm{CH}}$–CH$_2$), 4.70 (1H, d, J= 5.0 Hz, =CH–$\underline{\mathrm{CH}}$(CH)–OH), 3.91 (1H, d, J= 9.3 Hz, MeO$_2$C–$\underline{\mathrm{CH}}$(C=O)–CH$_2$), 3.87 to 3.69 (2H, m, CH–$\underline{\mathrm{CH}_2}$–OH), 3.68 (3H, s, $\underline{\mathrm{CH}_3}O_2$C), 3.00 to 2.70 (2H, br s, 2 x OH), 2.71 (1H, dd, J= 15.0, 9.4 Hz, CH$_a$ CH–$\underline{\mathrm{CH}_2}$–C(CH$_3$)), 2.22 to 2.11 (1H, m, CH$_a$ =CH–$\underline{\mathrm{CH}_2}$–CH$_2$), 1.92 (1H, d, J= 15.0, CH$_b$ CH–$\underline{\mathrm{CH}_2}$–C(CH$_3$)), 1.76 to 1.68 (1H, m, CH$_b$ =CH–$\underline{\mathrm{CH}_2}$–CH$_2$), 1.57 to 1.21 (3H, m, CH$_2$–$\underline{\mathrm{CH}_2}$–$\underline{\mathrm{CH}}$–CH$_2$–OH), 1.46 (3H, s, $\underline{\mathrm{CH}_3}$–C(CH$_2$)=CH), 1.33 (3H, s, $\underline{\mathrm{CH}_3}$–C(CH$_3$)), 1.21 (3H, s, $\underline{\mathrm{CH}_3}$–C(CH$_3$)); ^{13}**C NMR** (75

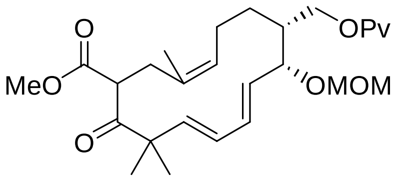
MHz, $CDCl_3$, δ ppm) : 207.2, 170.6, 138.1, 134.2, 132.5, 131.9, 128.6, 125.8, 73.2, 65.0, 52.5, 51.7, 46.9, 38.6, 25.9, 23.1, 22.6, 22.4, 15.9; **MS** (EI) : 350 (M^+); **HRMS** (EI): calcd for $C_{20}H_{30}O_5$ = 350.2093, found = 350.2100 ± 0.0010.



Macrocycle 29b

To a solution of macrocycle **29a** (50 mg, 0.14 mmol) in CH_2Cl_2 (2 mL), at 0^oC, was added 2,6-lutidine (23 mg, 0.21 mmol) and pivaloyl chloride (26 mg, 0.21 mmol). The mixture was allowed to warmed up to rt and was then stirred overnight. The reaction was quenched with $NH_4Cl_{\text{(aq)}}$ and extracted 3x with CH_2Cl_2 (10 mL). The combined oraganic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography (30% EtOAc/hexanes) gave alcohol **29b** (46 mg) in 75% yield as a colorless oil.

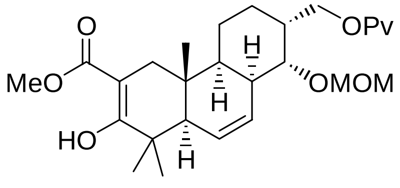
$[\alpha]^d_{20}$= -75.4^o (*c* 1.00, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 3517.9, 2965.6, 1714.5, 1162.2; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 6.27 (1H, dd, J= 15.5, 9.8 Hz, CH=$\underline{\mathrm{CH}}$–CH=CH), 6.05 (1H, dd, J= 16.0, 9.9 Hz, CH=CH–$\underline{\mathrm{CH}}$=CH), 5.80 (1H, dd, J= 15.9, 5.1 Hz, CH=CH–CH=$\underline{\mathrm{CH}}$–CH), 5.55 (1H, d, J= 15.5 Hz, C–CH=CH–CH=CH), 5.01 (1H, t, J= 6.5 Hz, C=$\underline{\mathrm{CH}}$–CH_2), 4.38 (1H, m, =CH–$\underline{\mathrm{CH}}$(CH)–OH), 4.31 (1H, dd, J= 11.2, 9.4 Hz, CH_a CH–$\underline{\mathrm{CH_2}}$–OPv), 3.98 (1H, dd, J= 11.2, 5.1 Hz, CH_b CH–$\underline{\mathrm{CH_2}}$–OPv), 3.91 (1H, dd, J= 9.4, 1.6 Hz, MeO_2C–CH(C=O)–CH_2), 3.69 (3H, s, $\underline{\mathrm{CH_3}}O_2C$), 2.73 (1H, dd, J=15.1, 9.5 Hz, CH_{eq} CH–$\underline{\mathrm{CH_2}}$–C($CH_3$)), 2.36 (1H, br s, OH), 2.23 to 2.14 (1H, m, CH_{eq} =CH–$\underline{\mathrm{CH_2}}$–$CH_2$), 1.93 (1H, d, J= 15.0 Hz, CH_{ax} CH–$\underline{\mathrm{CH_2}}$–C($CH_3$)), 1.81 to 1.70 (1H, m, CH_{ax} =CH–$\underline{\mathrm{CH_2}}$–$CH_2$), 1.69 to 1.60 (1H, m, CH_2–$\underline{\mathrm{CH}}$(CH)–CH_2–O), 1.60 to 1.00 (2H, m, CH_2–$\underline{\mathrm{CH_2}}$–CH), 1.49 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_2$)=CH), 1.35 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_3$)), 1.22 (12H, s, ($\underline{\mathrm{CH_3}}$)$_3$C–C=O, $\underline{\mathrm{CH_3}}$–C($CH_3$)); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm) : 207.0, 179.3, 170.5, 137.2, 134.5, 132.8, 131.7, 128.7, 125.6, 70.1, 65.2, 52.4, 51.9, 51.6, 45.5, 38.9, 38.5, 27.2, 26.0, 23.5, 23.1, 22.4, 15.9; **MS** (EI) : 434 (M^+); **HRMS** (EI): calcd for $C_{25}H_{38}O_6$ = 434.2668, found = 434.2672 ± 0.0013.

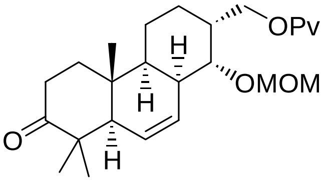


Macrocycle 33

To a stirred solution of macrocyle **29b** (20 mg, 46µmol) in CH_2Cl_2 (1 mL) at 0^{o}C, was added diisopropylethylamine (161µL, 0.92 mmol) and MOMCl (55µL, 0.69mmol). The solution was stirred overnight at rt. The reaction mixture was quenched with $NH_4Cl_{(aq)}$ and extracted 3X with Et_2O (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and then evaporated. Purification by flash chromatography (15% EtOAc/hexanes) afford 20 mg of macrocycle **33** (85%).

$[\alpha]^{d}_{20}$= -191.9^{o} (*c* =1.00, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 2950.4, 1749.0, 1724.6, 1461.5, 1159.3, 1032.6; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 6.30 (1H, dd, J= 15.6, 9.9 Hz, CH=$\underline{CH}$–CH=CH), 6.09 (1H, dd, J= 15.9, 9.7 Hz, CH=CH–$\underline{CH}$=CH), 5.80 (1H, dd, J=15.9, 5.8 Hz, CH=CH–CH=$\underline{CH}$–CH), 5.55 (1H, d, J= 15.6 Hz, C–$\underline{CH}$=CH–CH=CH), 4.99 (1H, t, J= 6.9 Hz, C=$\underline{CH}$–CH_2), 4.70 (1H, d, J=6.8 Hz, CH_a O–$\underline{CH_2}$–OCH_3), 4.54 (1H, d, J=6.8 Hz, CH_b O–$\underline{CH_2}$–O–CH_3), 4.43 (1H, d, J= 4.7 Hz, =CH–$\underline{CH}$(CH)–O–CH_2), 4.13 to 4.02 (2H, m, CH–$\underline{CH_2}$–OPv), 3.95 (1H, dd, J= 9.7, 1.4 Hz, CH_3O_2C–$\underline{CH}$(C=O)–CH_2), 3.69 (3H, s, $\underline{CH_3}O_2C$), 3.35 (3H, s, $\underline{CH_3}$–O–CH_2), 2.71 (1H, dd, J= 15.2, 5.4 Hz, CH_{eq} CH–$\underline{CH_2}$–C=), 2.19 to 2.11 (1H, m, CH_{eq} =CH–$\underline{CH_2}$–CH_2), 1.93 (1H, d, J= 15.2 Hz, CH_{ax} CH–$\underline{CH_2}$–C=), 1.86 to 1.70 (2H, m, CH_{ax} =CH–$\underline{CH_2}$–CH_2, CH_2–$\underline{CH}$(CH)–CH_2), 1.5 to 1.1 (2H, m, CH_2–$\underline{CH_2}$–CH), 1.49 (3H, s, $\underline{CH_3}$–C=), 1.35 (3H, s, $\underline{CH_3}$–C(CH_3)), 1.23 (3H, s, $\underline{CH_3}$–C(CH_3)), 1.22 (9H, s, $(\underline{CH_3})_3C$); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm) : 207.0, 178.5, 170.4, 136.1, 134.5, 132.7, 131.8, 130.3, 125.4, 94.8, 74.2, 65.1, 55.7, 52.4, 52.0, 51.4, 44.5, 38.8, 38.3, 27.2, 26.2, 24.3, 23.1, 22.4, 16.2; **MS** (EI) : 478 (M^+), 433 (M^+- C_3H_9); **HRMS** (EI) : calcd for $C_{27}H_{42}O_7$ = 478.2930, found = 478.2941 ± 0.0014.



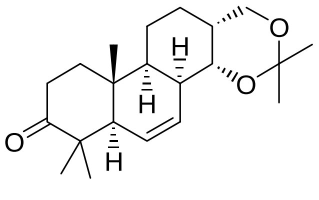


Tricycles 34 and 35

Macrocycle **33** (19 mg, 40µmol) was dissolved in toluene (1.5 mL). The solution was degased and heated 16 hours at 125^{o}C in a sealed tube. The solution was then evaporated and the residu was purified by flash chromatography (10% EtOAc/hexanes) to give 13 mg of tricycle **34** and 5 mg of tricycle **35** (global yield 100%).

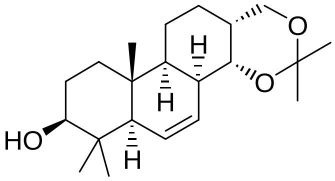
Tricycle **34** : $[\alpha]^{d}_{20}$= +94.6^{o} (*c* 1.00, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 2945.5, 1724.6, 1649.3, 1609.1, 1443.4, 1358.0, 1247.6, 1152.1, 1031.6; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 12.54 (1H, s, $\underline{HO}$–C=C), 6.00 (1H, dt, J= 10.4, 3.3 Hz, CH–$\underline{CH}$=CH–CH), 5.68 (1H, d, J= 10.2 Hz, CH–CH=$\underline{CH}$–CH), 4.76 (1H, d, J= 6.9 Hz, CH_a O–$\underline{CH_2}$–O), 4.63 (1H, d, J=6.9 Hz, O–$\underline{CH_2}$–O), 4.29 (2H, d, J= 7.1 Hz, CH–$\underline{CH_2}$–OPv), 3.88 (1H, dd, J= 11.5, 5.5 Hz, CH–$\underline{CH}$(CH)–O), 3.76 (3H, s, $\underline{CH_3}O_2C$), 3.40 (3H, s, $\underline{CH_3}$–O–CH_2), 2.49 (1H, d, J=15.4, CH_{eq} (MeO_2C)C–$\underline{CH_2}$–C), 2.45 to 2.35 (2H, m, =CH–$\underline{CH}$–CH–O, CH_2–$\underline{CH}$(CH)–CH_2–OPv), 2.05 (1H, d, 2.2 Hz, $(CH_3)_2$C–$\underline{CH}$–CH=), 1.90 to 1.59 (6H, m, CH_{ax} (MeO_2C)C–$\underline{CH_2}$–C, (CH_3)C–$\underline{CH}$–$\underline{CH_2}$–$\underline{CH_2}$–CH), 1.21 (3H, s, $\underline{CH_3}$–C(CH_3)), 1.20 (9H, s, $(\underline{CH_3})_3$C), 1.14 (3H, s, $\underline{CH_3}$–C(CH_3)), 0.95 (3H, s, $\underline{CH_3}$–C(CH_2)–CH); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm) : 178.7, 177.3, 173.9, 128.8, 126.2, 95.7, 94.2, 76.2, 62.0, 55.8, 51.6, 51.1, 44.2, 38.8, 38.2, 37.1, 36.4, 36.2, 34.6, 28.8, 27.2, 23.9, 20.2, 18.6, 17.6; **MS** (EI) : 446 (M^+-CH_3OH), 431 (M^+- C_2H_7O); **HRMS** (EI) : calcd for $C_{26}H_{38}O_6$ = 446.2668, found 446.2672±0.0013.

Tricycle **35** : $[\alpha]^{d}_{20}$= +45.2^{o} (*c* = 0.87, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 2927.4, 1726.9,1704.5, 1459.6, 1282.9, 1153.0, 1036.7; ^{1}**H NMR** (300 MHz, $CDCl_3$, δ ppm) : 6.02 (1H, dt, J= 10.3, 3.3 Hz, CH–$\underline{CH}$=CH–CH), 5.68 (1H, dt, J= 10.3, 2.2 Hz, CH–CH=$\underline{CH}$–CH), 4.76 (1H, d, J= 6.8 Hz, CH_a O–CH_2–O), 4.63 (1H, d, J= 6.8 Hz, CH_b O–$\underline{CH_2}$–O), 4.31 to 4.19 (2H, m, CH–$\underline{CH_2}$–OPv), 3.88 (1H, dd, J=11.5, 5.9 Hz, CH–$\underline{CH}$(CH)–O), 3.42 (3H, s, CH_2–O–$\underline{CH_3}$), 2.68 to 2.54 (1H, m, CH_{eq} O=C–$\underline{CH_2}$–CH_2), 2.48 to 2.38 (3H, m, =CH–$\underline{CH}$(CH)–CH–O, O–CH–$\underline{CH}$(CH_2)–CH_2–O, CH_{ax} O=C–$\underline{CH_2}$–CH_2), 2.24 (1H, dd, J= 5.2, 2.8 Hz, $(CH_3)_2$C–$\underline{CH}$–CH=), 2.05 to 1.97 (2H, m, O=C–CH_2–$\underline{CH_2}$), 1.87 (1H, dd, J= 12.3, 6.3 Hz, (CH_3)C–$\underline{CH}$(CH_2)–CH), 1.73 to 1.47 (4H, m, CH–$\underline{CH_2}$–$\underline{CH_2}$–CH), 1.97 (9H, s, $(\underline{CH_3})_3$C), 1.11 (3H, s, $\underline{CH_3}$–C(CH_3)), 1.09 (3H, s, $\underline{CH_3}$–C(CH_3)), 1.05 (3H, s, $\underline{CH_3}$–C(CH)–CH)); ^{13}**C NMR** (75 MHz, $CDCl_3$, δ ppm) : 216.8, 178.7, 129.2, 126.3, 95.7, 77.2, 75.7, 62.5, 55.9, 53.5, 46.8, 45.4, 37.1, 36.9, 36.0, 34.2, 27.2, 26.4, 23.9, 21.4, 18.7, 16.9; **MS** (CI, NH_3) : 438 (MNH_4^+), 421 (MH^+); **HRMS** (CI, NH_3) : calcd for $C_{25}H_{41}O_5$ = 421.2954, found = 421.2947 ± 0.0013.



Tricycle 31

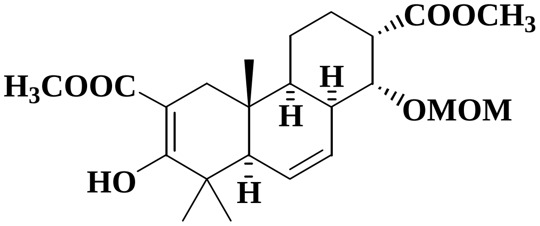
Tricycle **30** (10 mg, 25 μmol) was dissolved in 2.5 mL of a mixture of NaOH 7% in MeOH/H_2O 3/2. The mixture was heathed 2 h at 80^{o}C and then diluted with water (5 mL), extracted with 5X EtOAc (10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography (10% EtOAc/hexanes) afford 8 mg of tricycle **31** in a quantitative yield.



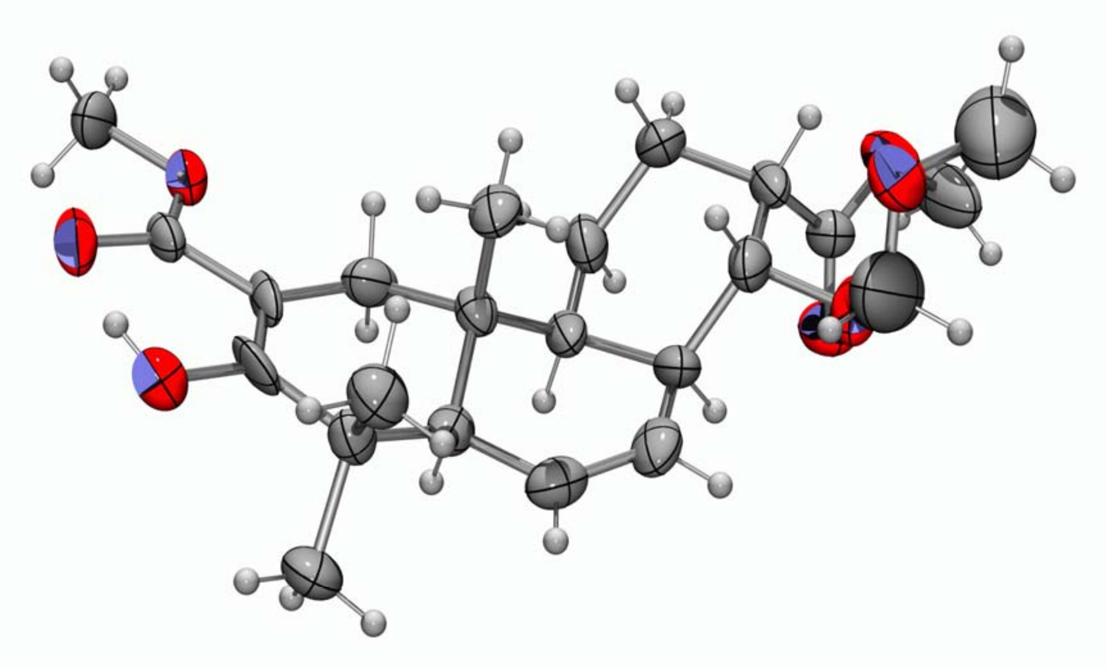
Tricycle 36

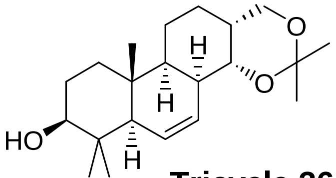
To a soluiton of tetracycle **31** (15 mg, 45 µmol) in MeOH (1 mL), at 0^{o}C, was added sodium borohydride (5 mg, 0.13 mmol). The solution was stirred 1 h at 0^{o}C and then quenched with $NH_4Cl_{(aq)}$. The mixture was extracted with 3x EtOAc (10 mL), the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and then evaporated. Purification by flash chromatography (20% EtOAc/hexanes) to give 14 mg of tetracycle **36** and less than 1 mg of the α epimer.

$[\alpha]^{d}_{20}$= +84.0^{o} (*c* = 0.73, CH_2Cl_2); **IR** (film, υ cm^{-1}) : 3447.6, 2925.4, 1458.4, 1373.1, 1222.4, 1066.8; **^{1}H NMR** (300 MHz, $CDCl_3$, δ ppm) : 5.88 (1H, td, J= 10.2, 3.2 Hz, CH–$\underline{\mathrm{CH}}$=CH–CH), 5.68 (1H, td, J= 10.2, 2.3 Hz, CH–CH=$\underline{\mathrm{CH}}$–CH), 3.83 (1H, dd, J= 10.5, 8.0 Hz, CH–$\underline{\mathrm{CH}}$(CH)–O), 3.56 (1H, dd, J= 10.88, 6.86 Hz, CH_{eq} CH–$\underline{\mathrm{CH_2}}$–O), 3.49 (1H, t, J= 10.8, CH_{ax} CH–$\underline{\mathrm{CH_2}}$–O), 3.26 (1H, dd, J= 10.9, 5.4 Hz, HO–$\underline{\mathrm{CH}}$(C)–CH_2), 2.33 to 2.25 (1H, m, =CH–$\underline{\mathrm{CH}}$–CH), 2.06 to 1.97 (1H, m, CH_2–$\underline{\mathrm{CH}}$(CH_2)–CH–O), 1.88 (1H, q, J= 9.3 Hz, (CH_3)C–$\underline{\mathrm{CH}}$(CH_2)CH), 1.75 to 1.52 (6H, m, HO–CH–$\underline{\mathrm{CH_2}}$, CH–$\underline{\mathrm{CH_2}}$–$CH_2$, $(CH_3)_2$–C–$\underline{\mathrm{CH}}$–CH=, $\underline{\mathrm{HO}}$), 1.36 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_3$)–O), 1.33 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_3$)–O), 1.30 to 1.22 (2H, m, CH–CH_2–$\underline{\mathrm{CH_2}}$), 1.19 to 1.06 (2H, m, CH–CH_2–$\underline{\mathrm{CH_2}}$–C($CH_3$)), 1.04 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_2$)–CH), 0.83 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_3$)), 0.76 (3H, s, $\underline{\mathrm{CH_3}}$–C($CH_3$)); **^{13}C NMR** (75 MHz, $CDCl_3$, δ ppm) : 129.6, 126.3, 99.7, 79.0, 69.6, 61.7, 53.9, 44.8, 38.4, 38.3, 36.2, 35.9, 34.7, 27.9, 27.3, 26.3, 24.1, 21.7, 20.9, 15.7, 13.6; **MS** (EI) : 334 (M^+), 276 (M^+-C_3H_6O); **HRMS** (EI): calcd for $C_{21}H_{34}O_3$ = 334.2508, found = 334.2513 ± 0.0010.



Tricycle 16





Tricycle 36