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Supporting Information

Oxygenated Metabolites of *n*-3 Polyunsaturated Fatty Acids as Potential Oxidative Stress Biomarkers: Total Synthesis of 8-F_{3t}-IsoP, 10-F_{4t}-NeuroP and [D_4]-10-F_{4t}-NeuroP

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((1R,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)methanol : 5

To a solution of the lactone **4** (2 g, 5 mmol, 1.0 eq) in CH_2Cl_2 (100 mL) at -78°C, was added dropwise the solution of Dibal-H (1.2 M in toluene, 6.2 mL, 7.5 mmol, 1.5 eq). After 30 min at -78°C, 100 mL of a solution of 1M Rochelle salt were added. The mixture was stirred during 3 hours. The layers were separated and the aqueous one was extracted with 3 x 50 mL of CH_2Cl_2. The combined organic layers were extracted with 2 x 50 mL of brine and dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The lactol was obtained as colourless oil and directly used in the next step without further purification.

To a suspension of the (n-propyl) triphenyl-phosphonium bromide (6.42 g, 16.6 mmol, 3.2 eq) in THF (70 mL), at 0 °C, was added dropwise ^tBuOK (1 M in THF, 15.6 mL, 15.6 mmol, 3 eq). After 30 min at 0 °C, the mixture was canulated into the lactol solution (5 mmol, 1.0 eq) in THF (25 mL) at 0°C. The reaction was stirred 30 min. Then, 100 mL of brine were added. The layers were separated and the aqueous one extracted with 3 x 100 mL of Et_2O. The combined organic layers were washed with 2 x 50 mL of brine and dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was purified under silica gel chromatography (97.5/2.5 to 90/10: Pentane/ Et_2O) and the compound **5** was obtained as an oil (2.01 g, 94%, 2 steps). R_f = 0.6 (8/2: Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -+5 (c= 5, $CHCl_3$); IR (neat) : ν= 3432 cm^{-1} (OH) ; ^1H NMR (300 MHz, $CDCl_3$): δ= 5.44-5.27 (m, 4H); 4.02 (q, $^3J(H,H)$ = 7.2 Hz, 1H); 3.82-3.77 (m, 1H); 3.73-3.60 (m, 2H); 2.34-2.25 (m, 2H); 2.07-1.91 (m, 5H); 1.71 (ls, 1H, OH); 1.51 (dt, $^3J(H,H)$ = 13.4, 5.8 Hz, 1H); 0.95 (t, $^3J(H,H)$ = 7.5 Hz, 1H); 8.86 (s, 18H); 0.03 (s, 6H); 0.00 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 132.6 (CH); 127.7 (CH); 75.6 (CHOH); 75.0 (CHOH); 62.6 (CH_2OH); 50.1 (CH); 48.2 (CH); 44.4 (CH_2); 25.7 (CH_2); 25.6 (CH_3); 20.6 (CH_2); 17.9 (Cquat); 17.8 (Cquat); 14.0 (CH_3); -4.3 (CH_3); -4.5 (CH_3); -4.8 (CH_3); -4.9 (CH_3); HRMS (ESI^+) calculated for $C_{23}H_{49}O_3Si_2$ $[M+H]^+$ 429.3220, found 429.3234.

(E)-3-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-1-(trimethylsilyl)prop-2-en-1-one : 6

To a solution of the alcohol **5** (2 g, 4.66 mmol, 1.0 eq) in CH_2Cl_2 (50 mL), was added dropwise the Dess-Martin periodinane (15% w/w in CH_2Cl_2, 14.9 mL, 6.9 mmol, 1.5 eq). After 0.5 hour at room temperature, 150 mL of a solution of $NaHCO_3/Na_2S_2O_3$ (1/1: v/v; 10%) were added. The layers were stirred 2 hours and separated. The aqueous phase was extracted with 3 x 100 mL of Et_2O. The combined organic layers were extracted with 2 x 50 mL of brine and dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The aldehyde was obtained as colorless oil and directly used in the next step without further purification.

To a solution of diisopropylamine (496 µl, 3.53 mmol, 2.4 eq) in THF (5 mL) at 0°C was added a solution of BuLi (2.5 M in Hexane, 1.23 mL, 3.085 mmol, 2.1 eq). The mixture was stirred for 30 min, treated with a solution of [(trimethylsilyl)acetyl]trimethylsilane (608 mg, 3.23 mmol, 1.2 eq) in THF (10 mL) and re-stirred 30 min. The mixture was treated at -78°C with a solution of aldehyde (626 mg, 1.46 mmol, 1 eq) in THF (10 mL). The resulting mixture was stirred 30 min at – 78°C. A saturated solution of NH_4Cl (25 mL) were added, and the layers were separated. The aqueous layer was extracted with 3 x 25 mL of Et_2O. The combined organic layers were washed with 25 mL of brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was purified under silica gel chromatography (9/1: Cyclohexane/ Et_2O) and **6** (655 mg, 85%, 2 steps) was obtained as a colorless oil. R_f = 0.66 (9.5/.5: Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 6.58 (dd, ^{3}J(H,H) = 9.6, 15.9 Hz, 1H); 6.28 (d, ^{3}J(H,H) = 15.9 Hz, 1H); 5.42-5.20 (m, 2H); 3.99 (q, ^{3}J(H,H) = 6.6 Hz 1H), 3.85 (q, ^{3}J(H,H) = 6.3 Hz, 1H); 2.83 (q, ^{3}J(H,H) = 5.7 Hz, 1H); 2.35 (dt, ^{3}J(H,H) = 13.9, 6.9 Hz, 1H); 2.16 (quint, ^{3}J(H,H) = 6.2 Hz, 1H); 2.10-1.79 (m, 4H); 1.58 (m, 1H); 0.91 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.86 (s, 9H); 0.83 (s, 9H); 0.23 (s, 9H); 0.02 (s, 6H); -0.01 (s, 3H); -003 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 146.4 (CH); 137.1 (CH); 132.8 (CH); 126.9 (CH); 75.5 (CHOH); 75.4 (CHOH); 53.0 (CH); 50.9 (CH); 44.3 (CH_2); 26.2 (CH_2); 25.7 (CH_3); 20.6 (CH_2); 17.9 (Cquat); 14.0 (CH_3); -2.2 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3); -9.0 (Cquat).

(E)-methyl 10-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-8-hydroxy-8-(trimethylsilyl)dec-9-en-5-ynoate : 7

A solution of (7-methoxy-7-oxohept-2-ynyl)zinc(II) bromide, was prepared from zinc dust (572 mg, 8.74 mmol, 7 eq), 1,2 dibromoethane (75µl, 0.87 mmol, 0.7 eq) and methyl 7-bromohept-5-ynoate (1.37 g, 6.25 mmol, 5 eq) in THF (20 mL) at 0°C. The mixture was stirred 2 hours and added to a solution of **6** (655 mg, 1.25 mmol, 1 eq) in THF (13 mL). The mixture was heated around 30°C for 30 min. 50 mL of a saturated solution of NH_4Cl were added, and the layers were separated. The aqueous layer was extracted with 3 x 50 mL of Et_2O. The combined organic layers were washed with 2 x 50 mL of brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was purified under silica gel chromatography (98/2 to 95/5: pentane/Et_2O) and **7** (602 mg, 73%) was obtained. R_f = 0.25 (9.5/.5: Cyclohexane/AcOEt); IR (neat) : ν= 3503 cm^{-1} (OH), 1741 cm^{-1} (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.43 (dd, ^{3}J(H,H) = 11.9, 15.4, 1H); 5.37-5.21 (m, 3H); 3.92-3.78 (m, 2H); 3.65-3.64 (m, 3H); 2.65-2.63 (m, 1H); 2.53-2.30 (m, 5H); 2.21-1.97 (m, 6H); 1.89-1.70 (m, 4H); 1.55-1.48 (m, 1H); 0.92 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.86 (s, 9H), 0.84 (s, 9H); 0.02-0.00 (m, 21H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 173.8 (Cquat); 136.1 (CH); 135.9 (CH); 131.9 (CH); 131.6 (CH); 127.8 (CH); 127.7

(CH); 126.0 (CH); 82.9 (Cquat); 82.7 (Cquat); 76.7 (Cquat); 76.2 (CHOH); 75.9 (CHOH); 68.8 (CHOH); 68.7 (CHOH); 53.1 (CH); 52.8 (CH); 51.4 (CH); 50.2 (CH); 44.3 (CH_2); 44.2 (CH_2); 32.9 (CH_2); 28.8 (CH_2); 28.7 (CH_2); 25.9 (CH_2); 25.8 (CH_2); 25.7 (CH_3); 24.1 (CH_2); 24.0 (CH_2); 20.6 (CH_2); 20.5 (CH_2); 18.2 (Cquat); 17.9 (Cquat); 14.2 (CH_3); 14.1 (CH_3); -4.0 (CH_3); -4,1(CH_3); -4.4 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.8 (CH_3).

(E)-3-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl) cyclopentyl) acrylaldehyde : 9

To a solution of the alcohol **5** (2 g, 4.66 mmol, 1 eq) in CH_2Cl_2 (50 mL), was added dropwise the Dess-Martin periodinane (15% w/w in CH_2Cl_2, 14.9 mL, 6.90 mmol, 1.5 eq). After 0.5 hour at room temperature, 150 mL of a solution of $NaHCO_3/Na_2S_2O_3$ (1/1: v/v; 10%) were added. The layers were stirred 2 hours and separated. The aqueous phase was extracted with 3 x 100 mL of Et_2O. The combined organic layers were extracted with 2 x 50 mL of brine and dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The aldehyde was obtained as colorless oil and directly used in the next step without further purification.

To a solution of the aldehyde in THF (50 mL) was added methyl(triphenylphosphoranylidene)-acetate (3.25 g, 9.32 mmole, 2 eq) at room temperature. The mixture was stirred 2 days. Celite ® was added and the solvents were removed under reduced pressure. The crude of the reaction was purified under silica gel chromatography (97.5/2.5: Pentane/Et_2O) and the ester (1.74 g, 75%) was obtained. R_f = 0.6 (8/2: Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -5.4 (c= 5, $CHCl_3$) ; IR (neat) : ν= 1721cm^{-1} (C=O) 1651 cm^{-1}, (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 6.76 (dd, ^{3}J(H,H) =10.0, 15.5 Hz, 1H); 5.82 (dd, ^{3}J(H,H) = 0.9, 15.5 Hz, 1H); 5.38-5.21 (m, 2H); 4.17 (dq, ^{3}J(H,H) = 1.0, 7.1 Hz, 2H); 3.99-3.95 (m, 1H); 3.84 (q, ^{3}J(H,H) =6.0 Hz, 1H); 2.79-2.74 (m, 1H); 2.35 (dt, ^{3}J(H,H) = 6.9, 13.8 Hz, 1H); 2.20-1.83 (m, 5H); 1.57-1.53 (m, 1H); 1.26 (t, ^{3}J(H,H) = 7.1 Hz, 3H); 0.92 (t, ^{3}J(H,H) = 7.4 Hz, 3H); 0.87 (s, 9H); 0.84 (s, 9H); 0.01 (s, 6H); -0.01 (s, 3H); -0.02 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 166.3 (Cquat); 147.5 (CH); 132.5 (CH); 127.1 (CH); 122.8 (CH); 75.6 (CHOH); 75.2 (CHOH); 60.0 (CH_2OH); 52.6 (CH); 50.5 (CH); 44.2 (CH_2); 26.2 (CH_2); 25.7 (CH_3); 20.6 (CH_2); 17.8 (Cquat); 14.2 (CH_3); 14.0 (CH_3); -4.5 (CH_3); -4.7 (CH_3); -4.8 (CH_3);); HRMS (ESI$^+$) calculated for $C_{27}H_{53}O_4Si_2$ $[M+H]^+$ 497.3482, found 497.3459.

To a solution of the ester (1.7 g, 3.5 mmol, 1 eq) in CH_2Cl_2 (35 mL) at -78°C, was added dropwise the solution of Dibal-H (1 M in heptane, 7.7 mL, 7.7 mmol, 2.2 eq). After 30 min at -78°C, 60 mL of a solution of 1M Rochelle salt were added. The mixture was stirred during 3

hours. The layers were separated and the aqueous one was extracted with 3 x 50 mL of Et_2O. The combined organic layers were washed with 3 x 25 mL of brine and dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The allylic alcohol (1.69 g) with solvent's traces was directly used in the next step without further purification. R_f= 0.35 (3/1 : Cyclohexane/AcOEt); IR (neat) : ν= 3342cm^{-1} (OH); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.67 (dt, ^{3}J(H,H) = 5.6, 15.3 Hz, 1H); 5.49 (dd, ^{3}J(H,H) = 9.5, 15.3 Hz, 1H); 5.38-5.25 (m, 2H); 4.09 (d, ^{3}J(H,H) = 5.6 Hz, 2H); 3.89 (dt, ^{3}J(H,H) = 4.8, 7.0 Hz, 1H); 3.79 (q, ^{3}J(H,H) = 5.7 Hz, 1H); 2.68-2.61 (m, 1H); 2.30 (dt, ^{3}J(H,H) = 7.2 Hz, ^{2}J(H,H) = 13.7 Hz, 1H); 2.11-1.88 (m, 5H); 1.52 (dt, ^{3}J(H,H) = 5.3 Hz, ^{2}J(H,H) = = 13.7 Hz, 1H); 0.93 (t, ^{3}J(H,H) = 7.2 Hz, 3H); 0.86 (s, 9H); 0.84 s, 9H); 0.00 (s, 6H); -0.01 (s, 3H); -0.02 (s, 3H);); ^{13}C NMR (75 MHz, $CDCl_3$): δ=132.0 (CH); 131.2 (CH); 130.9 (CH); 127.7 (CH); 76.0 (CHOH); 75.7 (CHOH); 63.5 (CH_2OH); 52.4 (CH); 50.1 (CH); 44.1 (CH_2); 26.1 (CH_2); 25.7 (CH_3); 20.6 (CH_2); 17.9 (Cquat); 17.8 (Cquat); 14.1 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.8 (CH_3); HRMS (ESI$^+$) calculated for $C_{25}H_{51}O_3Si_2$ $[M+H]^+$ 455.3377, found 455.3378.

To a solution of the allylic alcohol ("3.5 mmol") in CH_2Cl_2 (35 mL), was added dropwise the Dess-Martin periodinane (15% w/w in CH_2Cl_2, 11.4 mL, 5.25 mmol, 1.5 eq). After 0.5 hour at room temperature, 100 mL of a solution of $NaHCO_3$/$Na_2S_2O_3$ (1/1: v/v; 10%) were added. The layers were stirred 2 hours and separated. The aqueous phase was extracted with 3 x 100 mL of Et_2O. The combined organic layers were extracted with 2 x 50 mL of brine and dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The aldehyde **9** (1.42 g, 92%), was directly used in the next step without further purification. R_f= 0.45 (9/1 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= +4.5 (c= 2, $CHCl_3$) ; IR (neat) : ν= 1693 cm^{-1} (C=O), 1634 cm^{-1} (C=C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 9.49 (d, ^{3}J(H,H) = 7.8 Hz, 1H); 6.69 (dd, ^{3}J(H,H) = 9.3, 15.6 Hz, 1H); 6.13 (dd, ^{3}J(H,H) = 7.8, 15.6 Hz, 1H); 5.40-5.20 (m, 2H); 4.04 (dt, ^{3}J(H,H) = 5.5, 7.2 Hz, 1H); 3.86 (q, ^{3}J(H,H) = 6.8 Hz, 1H); 3.00-2.93 (m, 1H), 2.37 (dt, ^{3}J(H,H) = 7.1 Hz, ^{2}J(H,H) = 13.8 Hz, 1H); 2.23-2.15 (m, 1H); 2.05-1.87 (m, 4H); 1.60 (dt, ^{3}J(H,H) = 5.3 Hz, ^{2}J(H,H) = 13.8 Hz, 1H); 0.93 (t, ^{3}J(H,H) =5.6 Hz, 3H); 0.86 (s, 9H); 0.83 (s, 9H); 0.02 (s, 6H); 0.00 (s, 3H); -0.04 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ=193.4 (CHO); 157.1 (CH); 134.2 (CH); 132.8 (CH); 126.8 (CH); 75.4 (CHOH); 75.1 (CHOH); 52.9 (CH); 50.8 (CH); 44.2 (CH_2); 26.2 (CH_2); 25.7 (CH_3); 25.6 (CH_3); 20.6 (CH_2); 17.8 (Cquat); 14.1 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3); HRMS (ESI$^+$) calculated for $C_{25}H_{49}O_3Si_2$ $[M+H]^+$ 453.3220, found 453.3226.

(E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hex-1-en-5-yn-3-ol 10 :

To a solution of the aldehyde **9** (1.2 g, 2.6 mmol, 1 eq), in Et_2O (20 mL), was added a freshly prepared solution of propargyl magnesium bromide (0.5 M in Et_2O, 10.5 mL, 5.25 mmol, 2 eq) at 0°C. After 3 hours at the same temperature, HCl (0.1 M, 50 mL) was added and the mixture was stirred 1 hour. The layers were separated. The crude of the reaction was purified by flash chromatography (98/2 to 96/4 Pentane/Et_2O) and the propargyl alcohol **10** was obtained as an oil (1.38 g, 80%). R_f = 0.54 (8/2 : Cyclohexane/AcOEt); IR (neat) : ν= 3420 cm^{-1} (OH), 3314 cm^{-1} (C≡C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.62-5.52(m, 2H); 5.39-5.24 (m, 2H); 4.19-4.27 (m, 1H); 3.79 (q, ^{3}J(H,H) = 6.7 Hz, 1H); 2.68-2.61 (m, 1H); 2.44-2.39 (m, 2H); 2.31 (dtd, ^{3}J(H,H) = 1.3, 7.2 Hz, ^{2}J(H,H) = 13.9 Hz, 1H); 2.09-1.82 (m, 7H); 1.56-1.40 (m, 1H); 0.93 (dt, ^{3}J(H,H) = 1.0, 7.4 Hz, 3H); 0.90 (s, 9H); 0.84 (s, 9H); 0.00 (s, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 132.7 (CH); 132.0 (2xCH); 131.2 (CH); 131.0 (CH); 127.7 (CH); 80.3 (Cquat); 75.9 (2xCHOH); 75.7 (CHOH); 75.6 (CHOH); 70.7 (≡CH); 70.5 (CHOH); 52.3 (CH); 52.2 (CH); 50.2 (CH); 44.2 (CH_2); 27.6 (CH_2); 26.0 (CH_2); 25.7 (CH_3); 20.6 (CH_2); 17.9 (Cquat); 17.8 (Cquat); 14.1 (CH_3); -4.5 (CH_3); -4.6 (2 x CH_3); -4.8 (CH_3); HRMS (ESI^+) calculated for $C_{28}H_{53}O_3Si_2$ $[M+H]^+$ 493.3533, found 493.3532.

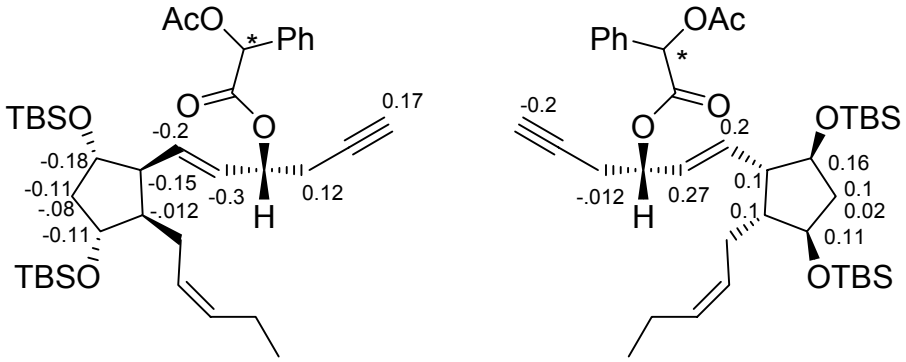
(S)-((E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hex-1-en-5-yn-3-yloxy)(phenyl)methyl acetate : 11

To a solution of alcohol **10** (1.33 g, 2.8 mmol, 1 eq) in CH_2Cl_2 (56 mL), at room temperature, were added (S)-acetyl phenyl acetic acid (1.09 g, 5.6 mmol, 2 eq), EDCI (1.1g, 5.6 mmol, 2 eq) and DMAP (137 mg, 1.1 mmol, 0.4 eq). After 1.5 hour, a saturated solution of NaCl (80 mL) was added. The layers were separated and the aqueous one was extracted with 3 x 80 mL of Et_2O. The combined organic layers were washed with 2 x 40 mL of brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude was purified under silica gel chromatography (97.5/2.5: Pentane/Et_2O). the two epimers (S)-**11a** (752 mg, 40%) and (R)-**11b** (904 mg, 48%) were separated.

11b R_f = 0.44 (8/1 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= +21.5 (c= 2, $CHCl_3$); IR (neat) : ν= 3314 (C≡C); 1748 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.48-7.45 (m, 2H); 7.36-7.34 (m, 3H); 5.90 (s, 1H); 5.63-5.47 (m, 2H); 5.37-5.25 (m, 3H); 3.92-3.86 (m, 1H); 3.82-3.78 (m, 1H); 2.65-2.61 (m, 1H); 2.38-2.36 (m, 2H); 2.31 (dt, ^{3}J(H,H) = 6.9 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 2.16 (s, 3H); 2.04-1.93 (m, 4H); 1.88-1.75 (m, 2H); 1.51 (dt, ^{3}J(H,H) = 5.2 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.86 (s, 9H); 0.84 (s, 9H); 0.01 (s, 6H); -0.01 (s, 6H); ^{13}C NMR (75 MHz,

$CDCl_3$): δ= 170.0 (Cquat); 167.8 (Cquat); 134.1 (CH); 133.7 (Cquat); 132.1 (CH); 129.1 (CH); 128.6 (CH); 127.7 (CH); 127.5 (CH); 127.4 (CH); 78.7 (C≡); 76.5 (CHOH); 75.7 (CHOH); 75.5 (CHOH); 74.5 (CHOH); 73.1 (CHOH); 70.4 (CH≡); 52.4 (CH); 50.3 (CH); 44.1 (CH); 25.9 (CH_2); 25.8 (CH_3); 24.5 (CH_2); 20.6 (CH_2 + CH_3); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3).

11a R_f = 0.34 (8/2 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= +16 (c= 2, $CHCl_3$); IR (neat) : ν= 3314 (C≡C); 1748 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.45-7.43 (m, 2H); 7.36-7.33 (m, 3H); 5.92 (s, 1H); 5.44-5.25 (m, 4H); 5.22-5.14 (m, 1H); 3.72-3.66 (m, 2H); 2.54-2.48 (m, 3H); 2.24-2.15 (m, 4H); 2.01-1.87 (m, 5H); 1.68-1.63 (m, 1H); 1.45 (dt, ^{3}J(H,H) = 5.4 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.85 (s, 9H); 0.81 (s, 9H); 0.01 (s, 3H); 0.00 (s, 3H); -0.05 (s, 3H); -0.07 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 170.2 (Cquat); 167.7 (Cquat); 133.9 (CH); 132.7 (Cquat); 129.1 (CH); 128.7 (CH); 127.7 (2 x CH); 127.6 (CH); 127.4 (CH); 78.9 (C≡); 75.7 (CHOH); 75.5 (CHOH); 74.4 (CHOH); 73.1 (CHOH); 70.7 (CH≡); 52.3 (CH); 50.4 (CH); 44.1 (CH); 25.9 (CH_2); 25.7 (CH_3); 24.7 (CH_2); 20.6 (CH_2); 20.5 (CH_3); 17.9 (2 x Cquat); 14.2 (CH_3); -4.4 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3).



11a **11b**

Determination of the absolute configuration and Δδ values for the (S) and (R)-MTPA ester derivatives of **11a** and **11b** ($\Delta d = \delta_S - \delta_R$).

((1R,3S,4S,5R)-4-((S,E)-3-(tert-butyldimethylsilyloxy)hex-1-en-5-ynyl)-5-((Z)-pent-2-enyl)cyclopentane-1,3-diyl)bis(oxy)bis(tert-butyldimethylsilane): 13a.

To a solution of **11a** (752 mg, 1.12 mmol, 1 eq), in MeOH (25 mL), was added K_2CO_3 (466 mg, 3.37 mmol, 3 eq). After 1 hour, 100 mL of brine was added. The aqueous layer was extracted with 3 x 100 mL of a mixture of pentane/Et_2O (v/v:1/1). The combined organic layers were washed with 2 x 50 mL of brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was used directly.

To a solution of the allylic alcohol (1.12 mmol, 1 eq) in CH_2Cl_2 (10 mL), were successively added TBSCl (210 mg, 1.40 mmol, 1.25 eq), imidazole (190 mg, 2.8 mmol, 2.5 eq) at 0°C. After 1 night, 50 mL of a saturated solution of $NaHCO_3$ was added. The mixture was then extracted with 3 x 50 mL of Et_2O. The organic layer was washed with 2 x 30 mL of a saturated solution of $NaHCO_3$ and 30 mL of brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was purified by silica gel chromatography (99/1: Pentane/Et_2O) and the silylated ether **13a** was obtained as a colourless oil (537 mg, 79%). R_f = 0.70 (9/1 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -1.2 (c= 5, $CHCl_3$); IR (neat) : ν= 3316 (C≡C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.52-5.43 (m, 2H); 5.35-5.31 (m, 2H); 4.21 (q, ^{3}J(H,H) = 4.9 Hz, 1H); 3.91 (dt, ^{3}J(H,H) = 4.2, 7.0 Hz, 1H); 3.79 (q, ^{3}J(H,H) = 7.1 Hz, 1H); 2.65-5.68 (m, 1H); 2.40-2.24 (m, 3H); 2.09-1.88 (m, 6H); 1.55-1.47 (m, 1H); 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.88 (s, 9H); 0.87 (s, 9H); 0.85 (s, 9H); 0.06 (s, 3H); 0.03 (s, 3H), 0.00 (m, 6H); -0.01 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 133.6 (CH); 131.9 (CH); 129.6 (CH); 127.8 (CH); 81.4 (Cquat); 75.92 (CHOH); 75.88 (CHOH); 72.0 (CHOH); 69.7 (CH≡); 52.0 (CH); 50.0 (CH); 44.5 (CH_2); 28.6 (CH_2); 26.0 (CH2); 25.8 (CH_3); 20.6 (CH_2); 18.1 (Cquat); 17.9 (Cquat); 14.1 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.8 (CH_3); HRMS (ESI^+) calculated for $C_{34}H_{67}O_3Si_3$ $[M+H]^+$ 607.4398, found 607.4392

((1R,3S,4S,5R)-4-((R,E)-3-(tert-butyldimethylsilyloxy)hex-1-en-5-ynyl)-5-((Z)-pent-2-enyl)cyclopentane-1,3-diyl)bis(oxy)bis(tert-butyldimethylsilane): 13b.

In the same way, the silylated ether **13b** was obtained as colourless oil (672 mg, 81%). R_f = 0.70 (9/1 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -24.8 (c= 5, $CHCl_3$); IR (neat) : ν= 3315 (C≡C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.45 (dd, ^{3}J(H,H) = 7.7, 16.9 Hz, 1H); 5.36 (dd, ^{3}J(H,H) = 5.2, 16.9 Hz); 5.33-5.22 (m, 2H); 4.22 (q, ^{3}J(H,H) = 5.9 Hz, 1H); 3.92 (dt, ^{3}J(H,H) = 3.9, 6.7 Hz, 1H); 3.78 (q, ^{3}J(H,H) = 6.6 Hz, 1H); 2.63-2.56 (m, 1H); 2.54-2.22 (m, 3H); 2.11-1.86 (m, 6H); 1.56-1.48 (m, 1H); 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.87 (s, 9H); 0.86 (s, 9H); 0.85 (s, 9H); 0.07 (s, 3H); 0.04 (s, 3H); 0.01—0.01 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 133.7 (CH); 131.9 (CH); 129.1 (CH); 127.8 (CH); 81.3 (Cquat); 75.94 (CHOH); 75.91 (CHOH); 71.8 (CHOH); 69.8 (CH≡); 52.3 (CH); 50.1 (CH); 44.2 (CH_2); 28.7 (CH_2); 26.0 (CH2); 25.8 (CH_3); 20.6 (CH_2); 18.1 (Cquat); 17.9 (Cquat); 14.1 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3); HRMS (ESI^+) calculated for $C_{34}H_{67}O_3Si_3$ $[M+H]^+$ 607.4398, found 607.4396.

For the determination of the configuration of allylic alcohol, **11a**, after saponification, was treated with (R)-acetyl phenyl acetic acid. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.47-7.45 (m, 2H); 7.35-7.34

(m, 3H); 5.90 (s, 1H); 5.65-5.49 (m, 2H); 5.37-5.24 (m, 3H); 3.89-3.86 (m, 1H); 3.82-3.77 (m, 1H); 2.67-2.61 (m, 1H); 2.39-2.37 (m, 2H); 2.30 (dt, ^{3}J(H,H) = 6.9 Hz, ^{2}J(H,H) = 13.5 Hz, 1H); 2.16 (s, 3H); 2.04-1.96 (m, 4H); 1.88-1.76 (m, 2H); 1.51 (m, , 1H); 0.94 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.87 (s, 9H); 0.84 (s, 9H); 0.01 (s, 6H); -0.02 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 170.0 (Cquat); 167.8 (Cquat); 134.5 (CH); 133.7 (Cquat); 132.1 (CH); 129.0 (CH); 128.6 (CH); 127.7 (CH); 127.5 (CH); 127.4 (CH); 78.7 (C≡); 76.5 (CHOH); 75.7 (CHOH); 75.5 (CHOH); 74.5 (CHOH); 73.1 (CHOH); 70.4 (CH≡); 52.4 (CH); 50.4 (CH); 44.2 (CH); 25.9 (CH_2); 25.8 (CH_3); 24.5 (CH_2); 20.6 (CH_2 + CH_3); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); -4.5 (CH_3); -4.6 (2 x CH_3); -4.8 (CH_3).

For the same reason and the same way, **11b**, after saponification, was treated with (R)-acetyl phenyl acetic acid. ^{1}H NMR (300 MHz, $CDCl_3$): δ= 7.46-7.43 (m, 2H); 7.36-7.33 (m, 3H); 5.92 (s, 1H); 5.42-5.18 (m, 5H); 3.75-3.65 (m, 2H); 2.54-2.48 (m, 3H); 2.24-2.17 (m, 4H); 1.99-1.86 (m, 5H); 1.74-1.61 (m, 1H); 1.45 (dt, ^{3}J(H,H) = 5.4 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.85 (s, 9H); 0.81 (s, 9H); 0.00 (s, 6H); -0.06 (s, 3H); -0.09 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 170.2 (Cquat); 167.7 (Cquat); 133.6 (CH); 132.0 (Cquat); 129.1 (CH); 128.7 (CH); 127.6 (2 x CH); 127.4 (CH); 78.9 (C≡); 75.7 (CHOH); 75.5 (CHOH); 74.4 (CHOH); 73.3 (CHOH); 70.8 (CH≡); 52.3 (CH); 50.4 (CH); 44.1 (CH); 25.9 (CH_2); 25.7 (CH_3); 24.8 (CH_2); 20.6 (CH_2); 20.5 (CH_3); 17.8 (2 x Cquat); 14.2 (CH_3); -4.4 (CH_3); -4.6 (2 x CH_3); -4.8 (CH_3).

Methyl 6-bromohex-4-ynoate: 15.

To a solution of the 4-pentynol (10 g, 119 mmol, 1 eq) and *p*-toluene sulfonic acid (565 mg, 2.9 mmol, 0.025 eq) in CH_2Cl_2 (120 mL), 2,4 dihydropyran (12.35 mL, 243 mmol, 1.2 eq) diluted in CH_2Cl_2 (20 mL) were added dropwise at room temperature. The mixture was stirred all the night and 150 mL of saturated solution of $NaHCO_3$ was added. The mixture was stirred 15 min and the layers were separated. The aqueous one was extracted with 2 x 200 mL of Et_2O. The combined organic layers were washed with 100 mL of saturated solution of $NaHCO_3$ and 2 x100 mL of brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was purified under silica gel chromatography (95/5: Pentane/Et_2O) and the protected alcohol (18.9 g, 95%) was obtained. R_f = 0.5 (8/2 : Cyclohexane/AcOEt^{1}H NMR (300 MHz, $CDCl_3$): δ= 4.54 (lt, ^{3}J(H,H) = 3.5 Hz, 1H); 3.84-3.73 (m, 2H); 3.48-3.38 (m, 2H); 2.24 (dt, ^{3}J(H,H) = 4.2, 11.2 Hz, 2H); 1.88 (t, ^{3}J(H,H) = 2.7 Hz, 1H); 1.78 (quint, ^{3}J(H,H) = 5.1 Hz, 2H); 1.71-1.73 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 98.6 (CH(O-)$_2$); 83.8 (C≡); 68.3 (HC≡); 65.4 (CH_2O); 62.0 (CH_2O); 30.5 (CH_2); 28.6 (CH_2); 25.4 (CH_2); 19.4 (CH_2); 15.2 (CH_2).

At room temperature, a commercial solution of methyl magnesium bromide (3M in Et_2O, 42 mL, 127 mmol, 2.0 eq) was added dropwise in a solution of alkyne (10.7 g, 63.6 mmol, 1 eq) in anhydrous THF (60 mL). The solution was refluxed 1.5 hour. The solution was cooled (0°C) and *p*-formaldehyde (2.86 g, 95 mmol, 1.5 eq). The reaction was refluxed two hours and *p*-formaldehyde (2.4 g, 80 mmol, 1.5 eq) more was added. After refluxing overnight, the solution was cooled at 0°C, and Et_2O (200 mL), saturated solution of $NaHCO_3$ (100 mL) were added dropwise. Celite® (50 mL) was added and the mixture was filtered. The solid was washed with Et_2O (4 x 100 mL). The layers were separated. The aqueous one was extracted with 2 x 100 mL of Et_2O. The combined organic layers were washed with 2 x 100 mL of brine and 50 mL of saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude of the reaction was purified under silica gel chromatography (8/2 to 1/1: Pentane/Et_2O) and the alcohol (9.65 g, 79%) was obtained. R_f = 0.5 (5/5 : Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 4.55 (t, ^{3}J(H,H) = 3.4 Hz, 1H); 4.17 (dt, ^{3}J(H,H) = 2.1, 5.9 Hz, 2H); 3.82-3.73 (m, 2H); 3.48-3.39 (m, 2H); 2.46 (t, ^{3}J(H,H) = 5.8 Hz, 1H); 2.8 (tt, ^{3}J(H,H) = 5.8, 7.2 Hz, 2H); 1.74 (quint, ^{3}J(H,H) =6.8 Hz, 2H); 1.67-1.45 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 98.7 (CH(O-)2); 85.4 (C≡); 78.8 (C≡); 65.8 (CH_2O); 62.1 (CH_2O); 51.0 (CH_2O); 30.5 (CH_2); 28.6 (CH_2); 25.3 (CH_2); 19.4 (CH_2); 15.6 (CH_2).

To a solution of the propargyl alcohol (7.5 g, 39 mmol, 1 eq), triphenylphosphine (17.2 g, 58.5 mmol, 1.5 eq), triethylamine (0.54 mL, 3.9 mmol, 0.1 eq) in CH_2Br_2 (35 mL), at -10°C, was added a solution of CBr4 (19.4 g, 58.5 mmol, 1.5 eq) in CH_2Br_2 (35 mL). The mixture was stirred 3 hours at room temperature. The mixture was then quenched with 100 mL of a 10% solution of $Na_2S_2O_3$ and 100 mL of a saturated solution of $NaHCO_3$. The layers separated. The aqueous one was extracted with 3 x 250 mL of CH_2Cl_2 and the combined organic layers were extracted with $Na_2S_2O_3$ (20 mL), brine (20 mL) and dried over $MgSO_4$, filtered and the solvents were removed. The crude was diluted in a mixture of Pentane/Et_2O 4/1 (250 mL) and filtered. After evaporation, the crude of the reaction was purified under silica gel chromatography (100/0 to 80/20 pentane/Et_2O) and compound (4.2 g, 41%) was obtained. R_f = 0.7 (5/5 : Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 4.56 (t, ^{3}J(H,H) = 2.8 Hz, 1H); 3.88 (t, ^{3}J(H,H) = 2.3 Hz, 2H); 3.82-3.75 (m, 2H); 3.49-3.41 (m, 2H); 2.36-2.30 (m, 2H); 1.76 (quint, ^{3}J(H,H) = 6.5 Hz, 2H); 1.68-1.46 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 98.7 (CH(O-)$_2$); 87.4 (C≡); 75.5 (C≡); 65.7 (CH_2O); 62.1 (CH_2O); 30.6 (CH_2); 28.5 (CH_2); 25.4 (CH_2); 19.4 (CH_2); 15.8 (CH_2); 15.5 (CH_2O).

To the solution of protected alcohol (4.2 g, 16 mmol, 1 eq) in acetone (320 mL) was added dropwise at 0°C, a Jones' solution (2.17 M, 37 mL, 80 mmol, 5.0 eq). The solution was stirred 3

hours at 0°C and 2 hours at room temperature. Isopropanol (45 mL) was slowly added. The mixture was filtered over Celite and rinsed with pentane/Et_2O 1/1 (3 x 500 mL). The organic layer was washed with 4 x 250 mL of acidified brine, dried over $MgSO_4$, filtered and the solvents removed under reduced pressure. The crude was diluted in anhydrous MeOH (65 mL) and $BF_3.Et_2O$ (510 µl, 4 mmol, 0.25 eq) was added. The solution was refluxed 1H and 250 mL of a saturated solution of $NaHCO_3$ was added. The mixture was extracted with 3 x 250 mL of pentane/Et_2O 1/1. The organic layers were washed with 3 x 100 mL of brine, dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified under silica gel chromatography (95/5: Pentane/ Et_2O) and **15** (2.65 g, 80%) was obtained. R_f = 0.5 (8/2 : Cyclohexane/AcOEt); IR (neat) : ν= 1733 (C=O); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 3.85 (t, ^{3}J(H,H) = 2.1 Hz, 2H); 3.65 (s, 3H); 2.56-2.49 (m, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 172.0 (Cquat); 85.7 (Cquat); 76.0 (Cquat); 51.7 (CH_3); 32.9 (CH_2); 15.0 (CH_2); 14.8 (CH_2); HRMS (ESI^+) calculated for $C_7H_{10}O_{2Br}$ $[M+H]^+$ 204.9864, found 204.9866.

(S,E)-methyl 12-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-10-(tert-butyldimethylsilyloxy)dodeca-11-en-4,7-diynoate: 16a.

At room temperature, to a solution of **13a** (75 mg, 0.12 mmol, 1 eq) and **15** (44 mg, 0.21 mmol, 1.75 eq) in DMF (4 mL) were added successively $CsCO_3$ (120 mg, 0.28 mmol, 3 eq), NaI (55 mg, 0.38 mmol, 3eq), CuI (58 mg, 0.31 mmol, 2.5 eq). The reaction was stirred 2 days. A solution of NH_4Cl 10% (25 mL) and NH_4OH (0.5 mL) were added. The mixture was extracted with 3 x 25 mL of Et_2O. The organic layers were washed with 2 x 25 mL of brine, dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified under silica gel (30nm, spherical) with pentane/Et_2O (98/3 in presence of BHT) and **13a** was obtained (46 mg, 56%) in presence of allene. R_f = 0.4 (8/2 : Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.55-5.45 (m, 2H); 5.36-5.27 (m, 2H); 4.18 (q, ^{3}J(H,H) = 5.9 Hz, 1H); 3.88 (dt, ^{3}J(H,H) = 4.3, 6.9 Hz, 1H); 3.79 (q, ^{3}J(H,H) = 6.9 Hz, 1H); 3.67 (s, 3H); 3.06 (t, ^{3}J(H,H) = 2 Hz, 2H); 2.64-2.53 (m, 1H); 2.52-2.42 (m, 4H); 2.38-2.21 (m, 3H); 2.10-1.86 (m, 5H); 1.50 (dt, ^{3}J(H,H) = 5.0 Hz, ^{2}J(H,H) = 13.7 Hz, 1H), 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.88 (s, 9H); 0.86 (s, 9H); 0.84 (s, 9H); 0.07 (s, 3H); 0.03 (s, 3H); 0.01- -0.01 (12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 173.0 (Cquat); 1.33.0 (CH); 132.0 (CH); 129.1 (CH); 127.8 (CH); 78.3 (Cquat); 77.7 (Cquat); 76.0 (CHO-); 75.9 (CHO-); 75.6 (Cquat); 75.5 (Cquat); 72.1 (CHO-); 52.1 (CH); 51.6 (OCH_3); 50.0 (CH); 44.2 (CH_2); 33.3 (CH_2); 30.3 (CH_2); 28.9 (CH_2); 26.0 (CH_2); 25.8 (CH_3); 20.6 (CH_2); 18.1 (Cquat); 17.9 (Cquat); 14.6 (CH_3); 9.7 (CH_2); -4.5 (CH_3); -4.6 (CH_3); -4.8 (CH_2).

(R,E)-methyl 12-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-10-(tert-butyldimethylsilyloxy)dodeca-11-en-4,7-diynoate: 16b.

In the same way, the silylated ether **16b** (71 mg, 79%) was obtained with allene too. R_f = 0.4 (8/2 : Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.54-5.26 (m, 4H); 4.19 (q, ^{3}J(H,H) = 5.7 Hz, 1H); 3.91-3.88 (m, 1H); 3.77 (q, ^{3}J(H,H) = 6.6 Hz, 1H); 3.67 (s, 3H); 3.07-3.02 (m, 2H); 2.78-2.44 (m, 5H); 2.39-2.19 (m, 3H); 2.11-1.85 (m, 5H); 1.51 (dt, ^{3}J(H,H) = 5.4 Hz, ^{2}J(H,H) = 13.6 Hz, 1H), 0.93 (t, ^{3}J(H,H) = 7.4 Hz, 3H); 0.88 (s, 9H); 0.87 (s, 9H); 0.85 (s, 9H); 0.07 (s, 3H); 0.04 (s, 3H); 0.01- -0.01 (12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 173.0 (Cquat); 134.1(CH); 132.0 (CH); 128.8 (CH); 127.8 (CH); 78.3 (Cquat); 77.7 (Cquat); 75.9 (2 x CHO-); 75.7 (Cquat); 75.6 (Cquat); 72.0 (CHO-); 52.3 (CH); 51.6 (OCH_3); 50.1 (CH); 44.2 (CH_2); 33.3 (CH_2); 30.2 (CH_2); 29.0 (CH_2); 26.0 (CH_2); 25.7 (CH_3); 20.6 (CH_2); 18.1 (Cquat); 17.9 (Cquat); 14.6 (CH_3); 9.6 (CH_2); -4.4 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_2).

(S,4Z,7Z,11E)-methyl 12-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-10-(tert-butyldimethylsilyloxy)dodeca-4,7,11-trienoate: 17a.

To a suspension of $Ni(OAc)_2.4H_2O$ (9.6 mg, 0.04 mmol, 0.33 eq), in ethanol with 0.01% BHT (3 mL) was added under H_2 atmosphere, $NaBH_4$, in ethanol (0.5 M, 139 µL, 0.07 mmol, 0.6 eq). After 10 minutes was added under the black suspension, the ethylenediamine in solution in ethanol, (0.5 M, 348 µL, 0.17 mmol, 1.5 eq). After 10 minutes, skipped diyne 16**a** (85 mg, 0.12 mmol, 1.0 eq) in ethanol with 0.01% BHT (4 mL) was added. Before and after each addition, three cycles vacuum/H_2 were realized. The reaction was then stirred during 4 hours under H_2 atmosphere (GC control). The mixture was then quenched with 20 mL of a saturated solution of NH_4Cl and stirred 30 min. The layers were extracted with 3 x 25 mL of Pentane/Et_2O 1/1. The combined organic layers were washed with water (10 mL), brine (2 x 10 mL) and dried over $MgSO_4$, filtered and the solvents were removed. Compound **17a** with allene, overreduction by-products and some solvents traces (98 mg) was obtained and used directly. R_f = 0.4 (9/1 : Cyclohexane/AcOEt).

(R,4Z,7Z,11E)-methyl 12-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-10-(tert-butyldimethylsilyloxy)dodeca-4,7,11-trienoate: 17b.

In the same way and the same quantities, the tetraene **17b.** was obtained (87 mg) with allene, overreduction by-products some solvents traces.

10-F_{4t}-NeuroP: 1a.

At room temperature, a solution of HCl (0.5 M in MeOH, 2.32 mL, 1.16 mmol, 10 eq) was added to the crude of **17a** (0.12 mmol, 1 eq) in MeOH/THF (10mL/16mL). The mixture was stirred 2 hours and $NaHCO_3$ solid was added. After 15 min, Celite® was added and the crude was filtered on Silica gel pad with AcOEt. The deprotected crude was directly used.

The solution of crude (0.116 mmol) in THF (5.8 mL) was stirred 2 hours with LiOH (0.5 M in H_2O, 5.8 mL, 2.4 mmol, 25 eq). The base was neutralized with a solution of $NaHSO_4$ (1M in H_2O, 2.4 mL, 2.4 mmol, 25 eq) and NaCl solid was added. The mixture was stirred 2 hours more. The crude was extracted with 3 x 20 mL of AcOEt. The organic layers were washed with 2 x 10 mL of brine, dried over $MgSO_4$, filtered and the solvents removed. The crude was purified by flash chromatography (98/2 AcOEt/HCO_2H). To eliminated overreduction products and allene, the mixture was purified by semipreparative HPLC (250x8 mm C18 column, 2.5 mL.min^{-1}, (ACN/MeOH 95/5 with 0.1% HCO_2H)/H2O with 0.1% HCO_2H : 35/65, λ = 205 nm), a total of (21.4 mg, 48%) of 10-F_{4t}-NeuroP **1a** was collected.

Tr = 27.5 min (250x4 mm C18 Nucleodur, 0.4 mL.min^{-1} , (ACN/MeOH 95/5 with 0.1% HCO_2H)/H_2O with 0.1% HCO_2H : 35/65, λ = 205 nm);); $[\alpha]_D^{20}$= -6 (c= 1, MeOH) ;^{1}H NMR (300 MHz, MeOD): δ= 5.60-5.57 (m, 2H); 5.47-5.41 (m, 6H); 4.1 (q, ^{3}J(H,H) = 5 Hz, 1H); 4.0 (dt, ^{3}J(H,H) = 2.3, 7.0 Hz, 1H); 3.91-3.87 (m, 1H); 2.87 (t, ^{3}J(H,H) = 4.5 Hz, 2H); 2.76-2.69 (m, 1H); 2.50 (dt, ^{3}J(H,H) = 7.1 Hz, ^{2}J(H,H) = 14.2 Hz, 1H); 2.44-2.29 (m, 6H); 2.16-2.04 (m, 5H); 1.56 (dt, ^{3}J(H,H) = 4.9 Hz, ^{2}J(H,H) = 14.2 Hz, 1H); 0.99 (t, ^{3}J(H,H) = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, MeOD): δ= 177.2 (Cquat); 133.0 (CH); 130.3 (CH); 127.7 (CH); 127.2 (CH); 127.1 (CH); 126.3 (CH); 125.8 (CH); 123.9 (CH); 73.2 (2xHCOH); 70.2 (HCOH); 50.5 (CH); 48.5(CH); 40.7 (CH_2); 33.4 (CH_2); 24.2 (2xCH_2); 23.8 (CH_2); 21.1 (CH_2); 18.7 (CH_2); 11.7 (CH_3);); HRMS (ESI$^+$) calculated for $C_{22}H_{34}O_5Na$ $[M+Na]^+$ 401.2304, found 401.2308..

10-epi-10-F_{4t}-NeuroP: 1b.

In the same way and with **17b** (87 mg), 10-epi-10-F_{4t}-NeuroP **1b** was obtained (35 mg; 79%). Tr = 30.1 min (250x4 mm C18 Nucleodur, 0.4 mL.min$^-$, (ACN/MeOH 95/5 with 0.1% HCO_2H)/H_2O with 0.1% HCO_2H : 35/65, λ = 205 nm);); $[\alpha]_D^{20}$= -8 (c= 1, MeOH); ^{1}H NMR (300 MHz, MeOD): δ= 5.66-5.49 (m, 2H); 5.46-5.36 (m, 6H); 4.09 (q, ^{3}J(H,H) = 6.0 Hz, 1H); 4.02-3.97 (m, 1H); 3.93-3.87 (m, 1H); 2.91-2.80 (m, 2H); 2.78-2.68 (m, 1H); 2.51 (quint, ^{3}J(H,H) = 7.1 Hz; 1H); 2.45-2.24 (m, 6H); 2.17-2.02 (m, 5H); 1.56 (dt, ^{3}J(H,H) = 5.1 Hz; ^{2}J(H,H) = 14.1 Hz; 0.99 (t, ^{3}J(H,H) = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, MeOD): δ= 177.2 (Cquat); 133.2(CH); 130.2 (CH); 127.8 (2xCH); 127.1 (CH); 126.3 (CH); 125.8 (CH); 123.8 (CH); 73.4 (HCOH); 73.3 (HCOH); 70.6 (HCOH); 50.8 (CH); 48.5(CH); 40.6 (CH_2); 33.4 (CH_2); 24.3 (2xCH_2); 23.8

(CH_2); 21.1 (CH_2); 18.7 (CH_2); 11.6 (CH_3); HRMS (ESI^+) calculated for $C_{22}H_{34}O_5Na$ $[M+Na]^+$ 401.2303, found 401.2304.

4,5,7,8 d_4-(S,4Z,7Z,11E)-methyl 12-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-10-(tert-butyldimethylsilyloxy)dodeca-4,7,11-trienoate: 18a.

To a suspension of $Ni(OAc)_2.4H_2O$ (9.6 mg, 0.04 mmol, 0.33 eq), in ethanol with 0.01% BHT (3 mL) was added under D_2 atmosphere, $NaBH_4$, in ethanol (0.5 M, 139 µL, 0.07 mmole, 0.6 eq). After 10 minutes was added under the black suspension, the ethylenediamine in solution in ethanol, (0.5 M, 348 µL, 0.17 mmol, 1.5 eq). After 10 minutes, skipped diyne 16**a** (85 mg, 0.12 mmol, 1.0 eq) in ethanol with 0.01% BHT (4 mL) was added. Before and after each addition, three cycles vacuum/D_2 were realized. The reaction was then stirred during 4 hours under D_2 atmosphere (GC control). The mixture was then quenched with 20 mL of a saturated solution of NH_4Cl and stirred 30 min. The layers were extracted with 3 x 25 mL of Pentane/Et_2O 1/1. The combined organic layers were washed with water (10 mL), brine (2 x 10 mL) and dried over $MgSO_4$, filtered and the solvents were removed. Compound **18a** with allene, overreduction by-products and some solvents traces (77 mg) was obtained and used directly. R_f = 0.4 (9/1 : Cyclohexane/AcOEt).

4,5,7,8 d_4-(R,4Z,7Z,11E)-methyl 12-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)-10-(tert-butyldimethylsilyloxy)dodeca-4,7,11-trienoate: 18b.

In the same way and the same quantities, the tetraene **18b.** was obtained (104 mg) with allene, overreduction by-products some solvents traces.

4,5,7,8 d_4-10-F_{4t}-NeuroP: 2a.

At room temperature, a solution of HCl (0.5 M in MeOH, 2.32 mL, 1.16 mmol, 10 eq) was added to the crude of **17a** (0.13 mmol, 1 eq) in MeOH/THF (10 mL/16 mL). The mixture was stirred 2 hours and $NaHCO_3$ solid was added. After 15 min, Celite® was added and the crude was filtered on Silica gel pad with AcOEt. The deprotected crude was directly used.

The solution of crude (0.12 mmol) in THF (5.8 mL) was stirred 2 hours with LiOH (0.5 M in H_2O, 5.8 mL, 2.4 mmol, 25 eq). The base was neutralized with a solution of $NaHSO_4$ (1 M in H_2O, 2.4 mL, 2.4 mmol, 25 eq) and NaCl solid was added and the mixture was stirred 2 hours more. The crude was extracted with 3 x 20 mL of AcOEt. The organic layers were washed with 2 x 10 mL of brine, dried over $MgSO_4$, filtered and the solvents removed. The crude was purified by flash chromatography (98/2 AcOEt/HCO_2H). To eliminated overreduction products and allene, the crude was purified by semipreparative HPLC (250x8 mm C18 column, 2.5 $mL.min^{-1}$,

(ACN/MeOH 95/5 with 0.1% HCO_2H)/H2O with 0.1% HCO_2H : 35/65, λ = 205 nm), a total of (22.3 mg, 50%) of 4,5,7,8 d_4-10-F_{4t}-NeuroP **2a** was collected. Tr = 27.0 min (250x4 mm C18 Nucleodur, 0.4 $mL.min^{-1}$, (ACN/MeOH 95/5 with 0.1% HCO_2H)/H2O with 0.1% HCO_2H : 35/65, λ = 205 nm);); ^1H NMR (300 MHz, MeOD): δ= 5.66-5.52 (m, 2H); 5.47-5.37 (m, 2H); 4.10 (q, $^3J(H,H)$ = 5 Hz, 1H); 4.03-3.98 (m, 1H); 3.94-3.85 (m, 1H); 2.86 (sl, 2H); 2.78-2.67 (m, 1H); 2.50 (dt, $^3J(H,H)$ = 7.5 Hz, $^2J(H,H)$ = 14.2 Hz, 1H); 2.42-2.28 (m, 6H); 2.14-2.04 (m, 5H); 1.56 (dt, $^3J(H,H)$ = 4.8 Hz, $^2J(H,H)$ = 14.2 Hz, 1H); 0.99 (t, $^3J(H,H)$ = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, MeOD): δ= 177.4 (Cquat); 133.0 (CH); 130.3 (CH); 127.1 (CH); 125.9 (CH); 73.2 (2xHCOH); 70.2 (HCOH); 50.5 (CH); 48.5(CH); 40.7 (CH_2); 33.3 (CH_2); 24.2 (2xCH_2); 23.5 (CH_2); 20.9 (CH_2); 18.7 (CH_2); 11.7 (CH_3);); HRMS (ESI^+) calculated for $C_{22}H_{30}D_4O_5Na$ $[M+Na]^+$ 405.2555, found 405.2553.

4,5,7,8 d_4-10-epi-10-F_{4t}-NeuroP: 2b.

In the same way and with **2b.** (87 mg), 4,5,7,8 d_4-10-epi-10-F_{4t}-NeuroP **2b** was obtained (31 mg; 70%). tr = 29.7 min (250x4 mm C18 Nucleodur, 0.4 $mL.min^-$, (ACN/MeOH 95/5 with 0.1% HCO_2H)/H2O with 0.1% HCO_2H : 35/65, λ = 205 nm);); ^1H NMR (300 MHz, MeOD): δ= 5.63-5.49 (m, 2H); 5.46-5.34 (m, 6H); 4.09 (q, $^3J(H,H)$ = 6.1 Hz, 1H); 4.02-3.96 (m, 1H); 3.92-3.87 (m, 1H); 2.86 (sl, 2H); 2.76-2.67 (m, 1H); 2.51 (dt, $^3J(H,H)$ = 7.2 Hz; $^2J(H,H)$ = 14.2 Hz; 1H); 2.43-2.26 (m, 6H); 2.17-2.03 (m, 5H); 1.56 (dt, $^3J(H,H)$ = 5.1Hz; $^2J(H,H)$ = 14.2 Hz; 0.99 (t, $^3J(H,H)$ = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, MeOD): δ= 177.3 (Cquat); 133.2(CH); 130.2 (CH); 127.8 (CH); 125.8 (CH); 73.4 (HCOH); 73.3 (HCOH); 70.6 (HCOH); 50.8 (CH); 48.5(CH); 40.6 (CH_2); 33.3 (CH_2); 24.3 (2xCH_2); 23.5 (CH_2); 20.9 (CH_2); 18.7 (CH_2); 11.7 (CH_3);); HRMS (ESI^+) calculated for $C_{22}H_{30}D_4O_5Na$ $[M+Na]^+$ 405.2555, found 405.2557.

(E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hept-1-en-5-yn-3-ol: 20 ; (E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hepta-1,4,5-trien-3-ol 19.

To a solution of the aldehyde **9** (1.1 g, 2.45 mmol, 1 eq), in Et_2O (10 mL), was added a freshly prepared solution of but-2-ynyl magnesium bromide (0.5 M in Et_2O, 9.8 mL, 4.9 mmol, 2 eq) at 0°C. After 40 min at the same temperature, HCl (0.1 M, 100 mL) was added and the mixture was stirred 15 min. The layers were separated. The aqueous layer was extracted with Et_2O (3 x 50 mL). The organic layers were washed with a saturated solution of $NaHCO_3$ (50 mL) and brine (2 x 50 mL), dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography (98/2 to 95/5 Pentane/Et_2O) and the propargyl alcohol **19** (161

mg, 13%) and allenic alcool **20** (550 mg, 44%) were obtained. **20 :**R_f= 0.41 (9/1 : Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.53-5.49 (m, 2H); 5.34-5.28 (m, 2H); 4.80-4.75 (m, 2H); 4.44 (sl, 1H); 3.95-3.89 (m, 1H); 3.79 (q, ^{3}J(H,H) = 6.6 Hz, 1H); 2.69-2.60 (m, 1H); 2.31 (dt, ^{3}J(H,H) = 6.8 Hz, ^{2}J(H,H) = 13.7 Hz, 1H); 2.06-1.90 (m, 5H); 1.76-1.73 (m, 1H); 1.66 (t, ^{3}J(H,H) = 3.0 Hz, 3H); 1.51 (dt, ^{3}J(H,H) = 4.4 Hz, ^{2}J(H,H) = 13.7 Hz, 1H); 0.92 (dt, ^{3}J(H,H) = 1.6, 7.5 Hz, 3H); 0.84 (s, 9H); 0.83 (s, 9H); 0.00- -0.02 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 132.3 (CH); 132.2 (CH); 132.1 (CH); 131.1 (CH); 131.0 (CH); 127.7 (CH); 77.4 (CH); 76.5 (CH); 76.0 (HCO-); 75.8 (HCO-); 75.7 (HCO-); 73.3 (HCO-); 73.1 (HCO-); 52.4 (CH); 52.2 (CH); 50.3 (CH); 50.2 (CH); 44.2 (CH_2); 26.1 (CH_2); 26.0 (CH_2); 25.7 (CH_3); 25.7 (CH_2); 20.6 (CH_2); 17.9 (Cquat); 17.8 (Cquat); 14.6 (CH_3); 14.5 (CH_3); 14.1 (CH_3); -4.4 (CH_3); -4.6 (CH_3); -4.8 (CH); **19:** R_f = 0.38 (9/1 : Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.56-5.50 (m, 2H); 5.34-5.28 (m, 2H); 4.18-4.13 (m, 1H); 3.92-3.86 (m, 1H); 3.78 (q, 6.0 Hz, 1H); 2.66-2.60 (m, 1H); 2.37-2.26 (m, 3H); 2.05-1.88 (m, 6H); 1.76 (t, ^{3}J(H,H) = 2.5 Hz, 3H); 1.50 (dt, ^{3}J(H,H) = 5.1 Hz; ^{2}J(H,H) = 13.5 Hz, 1H); 0.92 (dt, ^{3}J(H,H) = 1.2, 7.5 Hz, 3H); 0.85 (s, 9H); 0.84 (s, 9H); 0.02- -0.02 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 133.2 (CH); 132.0 (CH); 131.9 (CH); 130.7 (CH); 130.6 (CH); 127.8 (CH); 78.4 (Cquat); 78.3 (Cquat); 75.7 (HCO-); 75.7 (HCO-); 75.6 (CHO-); 74.9 (Cquat); 74.8 (Cquat); 70.8 ((HCO-); 70.7 (HCO-); 52.3 (CH); 52.2 (CH); 50.2(CH); 44.2 (CH_2); 28.0 (CH_2); 26.0 (CH_2); 25.7 (CH_3); 20.6 (CH_2); 17.9 (Cquat); 17.8 (Cquat); 14.1 (CH_3); 3.4 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.8 (CH_3).

((1R,3S,4S,5R)-4-((S,E)-3-(1-ethoxyethoxy)hept-1-en-5-ynyl)-5-((Z)-pent-2-enyl)cyclopentane-1,3-diyl)bis(oxy)bis(tert-butyldimethylsilane) 21a:

At room temperature, pyridinium *p*-toluene sulfonate (14 mg, 0.05 mmol, 0.015 eq) was added to **12a** (550 mg, 1.12 mmol, 1 eq) in a mixture of ethylvinyl ether/CH_2Cl_2 1/1 (10 mL). The reaction was stirred 5 hours, $NaHCO_3$ powder (100 mg) was added, and the solution was stirred 10 min more. CH_2Cl_2 (25 mL) and saturated $NaHCO_3$ solution (25 mL) were added. The layers were separated. The aqueous one was extracted with CH_2Cl_2 (2 x 25 mL). The organic layers were washed with brine (2 x 25 mL), dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography pre-treated by Et_3N (95/5 Pentane/Et_2O) to obtain protected alkyne (487 mg, 77%). R_f = 0.53 (9/1 : Cyclohexane/AcOEt); IR (neat) : ν= 3313 cm^{-1} (C≡C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.56-5.50 (m, 2H); 5.41-5.56 (m, 2H); 4.77 (q, ^{3}J(H,H) = 4 Hz, 0.5 H); 4.71 (q, ^{3}J(H,H) = 0.5 H); 4.15 (q, ^{3}J(H,H) = 5.8 Hz, 0.5 H); 4.11-4.07 (m, 0.5H); 3.95-3.90 (m, 1H); 3.81-3.77 (m, 1H); 3.72-3.36 (m, 2H); 2.79-2.63 (m, 1H); 2.52-2.34 (m, 2H); 2.31 (dt, ^{3}J(H,H) = 5.3 Hz, ^{2}J(H,H) = 10.5 Hz, 1H); 2.08-1.88 (m, 6H); 1.54-1.49 (m, 1H);

1.30 (d, $^{3}J(H,H)$ = 4.0 Hz, 1.5H); 1.27 (d, $^{3}J(H,H)$ = 4.0 Hz, 1.5H); 1.20-1.14 (m, 3H); 0.94 (t, $^{3}J(H,H)$ = 5.6 Hz, 3H); 0.86 (s, 9H); 0.85 (s, 9H); 0.01-0.00 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 133.5 (CH); 132.2 (CH); 132.1 (CH), 131.8 (CH); 131.7 (CH); 130.8 (CH); 127.7 (CH); 127.6 (CH), 98.8 ($HC(O-)_2$); 97.1 ($HC(O-)_2$); 81.0 (C≡); 80.9 (C≡); 75.9 (HCO-); 75.8 (HCO-); 75.7 (HCO-); 75.0 (HCO-); 74.4 (HCO-); 70.0 (HC≡); 69.8 (HC≡); 61.1(H_2CO-) ; 59.1 (H_2CO-); 52.3 (CH); 52.2 (CH); 50.2 (CH); 50.1 (CH); 44.3(CH_2); 26.2 (CH_2); 26.1 (CH_2); 25.8 (CH_3); 20.6 (CH_2); 20.4 (CH_2); 20.2 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 15.4 (CH_3); 15.2 (CH_3); 14.2 (CH_3); -4.4 (CH_3); -4.5 (CH_3); 4.6 (CH_3); -4.7 (CH_3).

At-78°C, LDA was prepared with diisopopyl amine (212 µl, 1.5 mmol, 2.3 eq) and BuLi (1.6 M in hexane, 900 µl, 1.44 mmol, 2.2 eq) in THF (15 mL). After 15 min, LDA was added to a solution of alkyne (370 mg, 0.65 mmol, 1 eq) in THF (15 mL) at -78°C. The mixture was stirred 1 hour at the same temperature and DMPU (160 µl, 1.3 mmol, 2 eq) and MeI (61 µl, 0.98 mmol, 1.5 eq) was added. The reaction was stirred overnight. Brine (25 mL) with Na_2CO_3 solution (2.5 mL) was added. The mixture was extracted with Et_2O (3 x 20 mL). The organic one were washed with brine (2 x 10 mL), dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography pre-treated by Et_3N (95/5 Pentane/Et_2O) to obtain **21a** (269 mg, 71%). R_f = 0.5 (9/1 : Cyclohexane/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 5.52-5.47 (m, 2H); 5.40-5.30 (m, 2H); 4.78-4.75 (m, 0.5H); 4.72-4.70 (m, 0.5H); 4.17-4.01 (m, 1H); 3.95-3.89 (m, 1H); 3.81-3.76 (m, 1H); 3.72-3.65 (m, 0.5H); 3.62-3.52 (m, 1H); 3.43-3.67 (m, 0.5H); 2.69-2.63 (m, 1H); 2.53-2.29 (m, 4H); 2.09-1.85 (m, 5H); 1.74-1.73 (m, 3H); 1.53-1.47 (m, 1H); 1.31-1.14 (m, 6H); 0.94 t, $^{3}J(H,H)$ = 7.5 Hz, 3H); 0.86 (s, 9H); 0.85 (s, 9H); 0.01 (s, 6H); 0.00 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 133.5 (CH); 132.2 (CH); 132.1 (CH); 131.8 (CH); 131.7 (CH); 130.9 (CH); 127.8 (CH); 127.7 (CH); 98.9 ($HC(O-)_2$); 97.1 ($HC(O-)_2$); 81.0 (C≡); 80.9 (C≡); 76.0 (HCO-); 75.9 (HCO-); 75.8 (HCO-); 75.7 (C≡); 75.6 (C≡); 70.0 (HCO-); 69.8 (HCO-); 59.1 (H_2CO-); 59.0 (H_2CO-); 52.3 (CH); 52.2 (CH); 50.2 (CH); 50.1 (CH); 44.3 (CH_2); 26.5 (CH_2); 26.4 (CH_2); 26.6 (CH_2); 25.8 (CH_3); 20.6 (CH_2); 20.5 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 15.4 (CH_3); 15.2 (CH_3); 14.2 (CH_3); 14.0 (CH_3); 3.5 (CH_3); -4.4 (CH_3); -4.5 (CH_3).

((1R,3S,4S,5R)-4-((R,E)-3-(1-ethoxyethoxy)hept-1-en-5-ynyl)-5-((Z)-pent-2-enyl)cyclopentane-1,3-diyl)bis(oxy)bis(tert-butyldimethylsilane) 21b :

In the same way, with the other diastereoisomer **12b** (665 mg, 1.35 mmol, 1 eq), the protected alkyne was obtained (672 mg, 88%). R_f = 0.53 (9/1 : Cyclohexane/AcOEt); IR (neat) : ν= 3313 cm^{-1} (C≡C); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 5.56-5.47 (m, 2H); 5.45-5.27 (m, 2H); 4.80-4.70 (m,1H); 4.18-4.08 (m, 1H); 3.96-3.90 (m, 1H); 3.81-3.75 (m, 1H); 3.73-3.32 (m, 2H); 2.68-2.62

(m, 1H); 2.52-2.29 (m, 3H); 2.10-1.85 (m, 6H); 1.56-1.49 (m, 1H); 1.31-1.26 (m, 3H); 1.31-1.26 (m, 3H); 1.21-1.15 (m, 4H); 0.93 (t, ^{3}J(H,H) = 5.6 Hz, 3H); 0.86 (s, 9H); 0.85 (s, 9H); 0.01-0.00 (m, 12 H); ^{13}C NMR (75 MHz, $CDCl_3$): δ= 133.3 (CH); 132.1 (CH); 132.0 (CH), 131.8 (CH); 131.5 (CH); 131.0 (CH); 127.8 (CH); 127.7 (CH), 98.8 (HC(O-)$_2$); 97.1 (HC(O-)$_2$); 80.9 (C≡); 80.8 (C≡); 76.0 (HCO-); 75.9 (HCO-); 75.8 (HCO-); 75.7 (HCO-); 75.0 (HCO-); 74.2 (HCO-); 70.0 (HC≡); 69.8 (HC≡); 61.2(H_2CO-); 59.0 (H_2CO-); 52.5 (CH); 50.2 (CH); 50.3 (CH); 44.3(CH_2); 26.2 (CH_2); 26.0 (CH_2); 25.8 (CH_3); 20.6 (CH_2); 20.5 (CH_2); 20.2 (CH_2); 18.0 (Cquat); 15.4 (CH_3); 15.2 (CH_3); 14.2 (CH_3); -4.4 (CH_3); -4.5 (CH_3).

In the same way, the other diastereoisomer (660 mg, 1.17 mmol, 1 eq), **21b** was obtained (481 mg, 87%). R_f = 0.5 (9/1 : Cyclohexane/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 5.54-5.41 (m, 2H); 5.38-5.31 (m, 2H); 4.76-4.71 (m, 1H); 4.11-4.01 (m, 1H); 3.96-3.88 (m, 1H); 3.80-3.76 (m, 1H); 3.71-3.28 (m, 2H); 2.67-2.59 (m, 1H); 2.52-2.26 (m, 4H); 2.10-1.85 (m, 5H); 1.72 (sl, 3H); 1.54-1.49 (m, 1H); 1.30-1.15 (m, 6H); 0.93 t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.86 (s, 9H); 0.84 (s, 9H); 0.01- -0.01(m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$): δ= 132.9 (CH); 132.3 (CH); 132.1 (CH); 131.6 (CH); 131.1 (CH); 127.8 (CH); 127.7 (CH); 98.8 (HC(O-)$_2$); 97.1 (HC(O-)$_2$); 77.2 (C≡); 77.0 (C≡); 76.1 (HCO-); 76.0 (HCO-); 75.9 (HCO-); 75.8 (C≡); 75.7 (C≡); 75.6 (HCO-); 75.0 (HCO-); 61.1 (H_2CO-); 58.9 (H_2CO-); 52.6 (CH); 52.5 (CH); 50.4 (CH); 44.4 (CH_2); 44.3 (CH_2); 26.6 (CH_2); 26.5 (CH_2); 26.1 (CH_2); 26.0 (CH_2); 25.8 (CH_3); 20.6 (CH_2); 20.5 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 15.4 (CH_3); 15.2 (CH_3); 14.2 (CH_3); 13.9 (CH_3); 3.5 (CH_3); -4.4 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.8 (CH_3).

(S,E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hept-1-en-5-yn-3-ol 19a :

At room temperature, **21a** (232 mg, 0.4 mmol, 1 eq), and pyridinium *p*-toluene sulfonate (50 mg, 0.2 mmol, 0.5 eq) in a solution of propanol/CH_2Cl_2 6/1 (26 mL) were stirred 4 hours. $NaHCO_3$ powder was added, the solvent were removed and the crude was purified by flash chromatography (95/5 to 90/10 Pentane/Et_2O) to obtain **19a** (145 mg, 71%). R_f = 0.26 (9/1 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -16.5 (c= 10, $CHCl_3$) ; IR (neat) : ν= 3360 cm^{-1} (OH); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 5.62-5.52 (m, 2H); 5.42-5.29 (m, 2H); 4.23-4.18 (m, 1H); 3.92 (dt, ^{3}J(H,H) = 5.0, 7.1 Hz, 1H); 3.95-3.80 (m, 1H); 3.70-3.65 (m, 1H); 2.47-2.30 (m, 3H); 2.12-1.91 (m, 6H); 1.80 (t, ^{4}J(H,H) = 2.5 Hz, 3H); 1.54 (dt, ^{3}J(H,H) = 5.3 Hz, ^{2}J(H,H) = 13.7 Hz, 1H); 0.96 (t, ^{3}J(H,H) = 7.6 Hz, 3H); 0.89 (s, 9H); 0.87 (s, 9H); 0.04-0.02 (m, 12H); NMR (100 MHz, $CDCl_3$): δ= 133.2 (CH); 132.1 (CH); 130.8 (CH); 127.8 (CH); 78.5 (C≡); 76.0 (HCO-); 75.7 (C≡); 74.8 (HCO-); 70.8 (HCO-); 52.2 (CH); 50.3 (CH); 44.3 (CH_2); 28.1 (CH_2); 26.1 (CH_2);

25.8 (CH_3); 20.7 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); 3.5 (CH_3); -4.4 (CH_3); -4.6 (CH_3); -4.8 (CH_3); HRMS (ESI^+) calculated for $C_{29}H_{55}O_3Si_2$ $[M+H]^+$ 507.3690, found 507.3684.

(R,E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hept-1-en-5-yn-3-ol 19b :

In the same way, with **21b** (480 mg, 0.83 mmol, 1 eq), deprotected alcohol **19b** was obtain (241 mg, 57%). R_f = 0.26 (9/1 : Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -6.9 (c= 10, $CHCl_3$); IR (neat) : ν= 3360 cm^{-1} (OH); ^1H NMR (400 MHz, $CDCl_3$): δ= 5.61-5.49 (m, 2H); 5.39-5.30 (m, 2H); 4.20 (q, $^3J(H,H)$ = 5.8 Hz; 1H); 3.94 (dt, $^3J(H,H)$ = 4.7, 7.0 Hz, 1H); 3.84-3.79 (m, 1H); 3.68-3.63 (m, 1H); 2.45-2.30 (m, 3H); 2.11-1.88 (m, 6H); 1.80 (t, $^4J(H,H)$ = 2.5 Hz, 3H); 1.54 (dt, $^3J(H,H)$ = 5.2 Hz, $^2J(H,H)$ = 13.7 Hz, 1H); 0.96 (t, $^3J(H,H)$ = 7.5 Hz, 3H); 0.88 (s, 9H); 0.87 (s, 9H); 0.04-0.02 (m, 12H); NMR (100 MHz, $CDCl_3$): δ= 133.2 (CH); 132.1 (CH); 130.7 (CH); 127.8 (CH); 78.4 (C≡); 76.0 (HCO-); 75.8 (C≡); 74.9 (HCO-); 70.9 (HCO-); 52.4 (CH); 50.3 (CH); 44.2 (CH_2); 28.1 (CH_2); 26.1 (CH_2); 25.8 (CH_3); 20.6 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); 3.5 (CH_3); -4.4 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3); HRMS (ESI^+) calculated for $C_{29}H_{55}O_3Si_2$ $[M+H]^+$ 507.3690, found 507.3685.

4-hydroxybutyl hept-5-ynoate : 23.

At-78°C, LDA was prepared with diisopopylamine (8.65 mL, 61.5 mmol, 2.3 eq) and BuLi (1.6 M in hexane, 36.7 mL, 58.8 mmol, 2.2 eq) in THF (250 mL). After 15 min, LDA was added to a solution of 5-hexynoïc acid (3 g, 26.7 mmol, 1 eq) at -78°C. The mixture was stirred 1 hour at the same temperature and DMPU (6.47 mL, 53.5 mmol, 2 eq) and MeI (2.5 mL, 40.1 mmol, 1.5 eq) was added. The reaction was stirred overnight. A solution of HCl 1M (150 mL) was added and saturated with NaCl powder. The mixture was extracted with Et_2O (3 x 200 mL). The organic one were washed with brine (2 x 150 mL), dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography (69/29/2 Pentane/Et_2O/HCO_2H) to obtain hept-5-ynoic acid (3.27 g, 97%). R_f = 0.45 (1/1 : Cyclohexane/AcOEt); ^1H NMR (300 MHz, $CDCl_3$): δ= 10.6 (ls, 1H); 2.46 (t, $^3J(H,H)$ = 7.4 Hz, 2H); 2.27-2.15 (m, 2H); 1.86-1.73 (m, 5H); NMR (75 MHz, $CDCl_3$): δ= 179.6 (C=O); 77.6 (C≡); 76.3 (C≡); 32.7 (CH_2); 23.8 (CH_2); 18.0 (CH_2); 3.3 (CH_3).

Hept-5-ynoic acid (3g, 23.7 mmol, 1 eq), 1,4 butan-diol (10.5 mL, 119 mmol, 5 eq) and p-toluenesulfonyl acid (113 mg, 0.6 mmol, 0.025 eq) in heptane (250 mL) were refluxed 1 hour with Dean-Stark apparatus. The reaction was cooled and brine (200 mL) was added. The layers were separated. The aqueous one was extracted with 3 x 200 mL of Et_2O. The organic layers were washed with brine (3 x 100 mL), dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography (8/2 to 4/6 Pentane/Et_2O) to obtain **23**

(4.3 g, 91%). R_f = 0.27 (1/1: Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 4.07 (t, ^{3}J(H,H) = 6.3 Hz, 2H); 3.63 (t, ^{3}J(H,H) = 6.3 Hz, 2H); 2.38 (t, ^{3}J(H,H) = 7.4 Hz, 2H); 2.11-2.18 (m, 2H); 1.77-1.59 (m, 10H); NMR (75 MHz, $CDCl_3$): δ= 173.3 (C=O); 77.8 (C≡); 76.3 (C≡); 64.1 (H_2CO-); 62.2 (H_2CO-); 33.1 (CH_2); 29.0 (CH_2); 25.0 (CH_2); 24.1 (CH_2); 18.1 (CH_2); 3.3 (CH_3).

4-(hept-5-ynoyloxy)butanoic acid: 22.

At -60°C, DMSO (3.84 mL, 54.2 mmol, 2.5 eq) was added to a solution of oxalyl chloride (2.35 mL, 27.1 mmol, 1.25 eq) in CH_2Cl_2 (150 mL). The reaction was stirred 10 min and **23** (4.3 g, 21.7 mmol, 1eq) diluted in CH_2Cl_2 (45 mL) was added. After 10 min more, Et_3N (16.6 mL, 119.3 mmol, 5.5 eq) was added. The reaction mixture was allowed to reach 0°C. Brine (100 mL) and water (100 mL) were added. The layers were separated. The aqueous one was extracted with 3 x 200 mL of CH_2Cl_2. The organic layers were washed with brine (3 x 100 mL), dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography (9/1 to 7/3 Pentane/Et_2O) to obtain 4-oxobutyl hept-5-ynoate (4.19 g, 98%). R_f = 0.24 (3/1: Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 9.72 (ls, 1H); 4.04 (t, ^{3}J(H,H) =, 6.3 Hz, 2H); 2.47 (t, ^{3}J(H,H) = 7.2 Hz, 2H); 2.34 (t, ^{3}J(H,H) = 7.4 Hz, 2H); 2.09-2.16 (m, 2H); 1.90 (quint, ^{3}J(H,H) = 7.0 Hz, 2H); 1.73-1.68 (m, 5H); NMR (75 MHz, $CDCl_3$): δ= 200.9 (C=O); 173.0 (C=O); 77.7 (C≡); 76.3 (C≡); 63.1 (H_2CO-); 40.3 (CH_2); 32.9 (CH_2); 24.0 (CH_2); 21.3 (CH_2); 18.1 (CH_2); 3.3 (CH_3).

At room temperature, Sodium Chlorite (2.11 g, 23.3 mmol, 1.1 eq) was added by portion to a solution of aldehyde (4.19 g, 21.3 mmol, 1 eq), 2 methyl butene (3.48 mL, 32.9 mmol, 1.5 eq), KH_2PO_4 (450 mg, 3.29 mmol, 0.15 eq) in a mixture of H_2O/^{t}BuOH 1/4 (40 mL). The mixture was stirred 1 hour and was acidified to pH = 1 with a solution of HCl 1M. The solution was extracted with 3 x 100 mL of CH_2Cl_2. The organic layer was washed with 2 x 100 mL of brine, dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography (3/1 to 1/1 Pentane/Et_2O) to obtain **22** (3.6 g, 78 %). R_f = 0.3 (1/1: Cyclohexane/AcOEt); ^{1}H NMR (300 MHz, $CDCl_3$): δ= 4.09 (t, ^{3}J(H,H) = 6.3 Hz, 2H); 2.44-2.36 (m, 4H); 2.17-2.11 (m, 2H); 1.94 (quint, ^{3}J(H,H) = 6.7 Hz, 2H); 1.78-1.69 (m, 5H); NMR (75 MHz, $CDCl_3$): δ= 178.8 (C=O); 173.2 (C=O); 77.7 (C≡); 76.4 (C≡); 63.1 (H_2CO-); 32.9 (CH_2); 30.4 (CH_2); 24.0 (CH_2); 23.7 (CH_2); 18.1 (CH_2); 3.3 (CH_3).

4-((S,E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hept-1-en-5-yn-3-yloxy)-4-oxobutyl hept-5-ynoate: 24a .

At room temperature, alcohol **19a** (145 mg, 0.28 mmol, 1 eq), acid **22** (121 mg, 0.57 mmol, 2 eq), EDCI (109 mg, 0.57 mmol, 2 eq), DMAP (14 mg, 0.114 mmol, 0.4 eq) in CH_2Cl_2 (10 mL) were

stirred overnight. Brine (10 mL) and water (5 mL) were added. The reaction mixture was extracted with 3 x 20 mL of Et_2O. The organic layers were washed with 3 x 10 mL of brine, dried over $MgSO_4$, filtered and the solvents removed. The crude of the reaction was purified by flash chromatography (97/3 Pentane/Et_2O) to obtain **24a** (191 mg, 95 %). R_f= 0.34 (9/1: Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -17.6 (c= 10, $CHCl_3$); IR (neat) : ν= 1737 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 5.63 (dd, ^{3}J(H,H) = 9.2, 15.4 Hz, 1H); 5.54 (dd, ^{3}J(H,H) = 6.9, 15.4 Hz, 1H); 5.39-5.30 (m, 3H); 4.11 (t, ^{3}J(H,H) = 6.4 Hz, 2H); 3.95-3.89 (m, 1H); 3.81 (q, ^{3}J(H,H) = 5.8 Hz, 1H); 2.70-2.64 (m, 1H); 2.46-2.17 (m, 7H); 2.21-2.17 (m, 2H); 2.08-1.85 (m, 8H); 1.83-1.75 (m, 7H); 1.54 (dt, ^{3}J(H,H) = 5.3 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.95 (t, ^{3}J(H,H) = 7.5 Hz, 3H), 0.88 (s, 9H); 0.86 (s, 9H); 0.03-0.01 (m, 12H); NMR (100 MHz, $CDCl_3$): δ= 173.2 (C=O); 171.8 (C=O); 134.1 (CH); 132.2 (CH); 128.8 ; (CH) 127.7 (CH); 77.9 (C≡); 77.8 (C≡); 76.4 (C≡); 75.8 (C≡); 75.6 (HCO-); 74.2 (HCO-); 73.0 (HCO-); 63.3 (H_2CO-); 52.2 (CH); 50.4 (CH); 44.3 (CH_2); 33.1 (CH_2); 31.0 (CH_2); 26.0 (CH_2); 25.8 (CH_3); 25.1 (CH_2); 24.2 (CH_2); 24.1 (CH_2); 20.6 (CH_2); 18.2 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); 3.5 (CH_3); 3.4 (CH_3); -4.4 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); HRMS (ESI^+) calculated for $C_{40}H_{69}O_6Si_2$ $[M+H]^+$ 701.4633, found 701.4632.

4-((R,E)-1-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyloxy)-2-((Z)-pent-2-enyl)cyclopentyl)hept-1-en-5-yn-3-yloxy)-4-oxobutyl hept-5-ynoate: 24a .

In the same way and with **19b.** (166 mg), **24b** was obtained (174 mg; 76%). R_f= 0.34 (9/1: Cyclohexane/AcOEt); $[\alpha]_D^{20}$= +3.0 (c= 10, $CHCl_3$); IR (neat) : ν= 1739 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 5.58 (dd, ^{3}J(H,H) = 9.4, 15.3 Hz, 1H); 5.48 (dd, ^{3}J(H,H) = 7.1, 15.3 Hz, 1H); 5.35-5.25 (m, 3H); 4.09 (t, ^{3}J(H,H) = 6.4 Hz, 2H); 3.91-3.86 (m, 1H); 3.76 (q, ^{3}J(H,H) = 6.4 Hz, 1H); 2.66-2.60 (m, 1H); 2.44-2.22 (m, 7H); 2.19-2.14 (m, 2H); 2.02-1.82 (m, 8H); 1.80-1.71 (m, 7H); 1.51 (dt, ^{3}J(H,H) = 5.2 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.93 (t, ^{3}J(H,H) = 7.5 Hz, 3H), 0.85 (s, 9H); 0.83 (s, 9H); 0.00 (s, 6H); -0.02 (s, 3H); -0.03 (s, 3H); NMR (100 MHz, $CDCl_3$): δ= 173.2 (C=O); 171.7 (C=O); 134.1 (CH); 132.2 (CH); 128.9 (CH); 127.7 (CH); 77.9 (2 x C≡); 76.4 (C≡); 75.8 (C≡); 75.6 (HCO-); 74.2 (HCO-); 73.1 (HCO-); 63.3 (H_2CO-); 52.4 (CH); 50.5 (CH); 44.3 (CH_2); 33.1 (CH_2); 31.0 (CH_2); 26.0 (CH_2); 25.8 (CH_3); 25.6 (CH_2); 24.2 (CH_2); 24.1 (CH_2); 20.6 (CH_2); 18.2 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); 3.4 (2 x CH_3); -4.4 (CH_3); -4.6 (CH_3); -4.7 (CH_3); -4.8 (CH_3). HRMS (ESI^+) calculated for $C_{40}H_{69}O_6Si_2$ $[M+H]^+$ 701.4633, found 701.4630.

(S,E)-10-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyl)-2-((Z)-pent-2-enyl)cyclopentyl)-8-(4-hydroxybutanoyloxy)dec-9-en-5-ynoate: 26a.

$MnCl_2$ was dried under vacuum at 150°C overnight, 5 Å molecular sieves powder was dried under vacuum at 400 °C during 30 min. **24**Fehler! Verweisquelle konnte nicht gefunden werden.**a** was dried by azeotropic evaporation with toluene.

Catalyst **25**Fehler! Verweisquelle konnte nicht gefunden werden. (50 mg, 0.04 mmol, 15% mol), $MnCl_2$ (10.3 mg, 0.08 mmol, 30% mol) and molecular sieves powder (5 Å, 1 g) in toluene (5 mL) were heated at 80°C during 30 min. **24**Fehler! Verweisquelle konnte nicht gefunden werden.**a** (191 mg, 0.27 mmol, 1 eq) in toluene (10 mL) was added and the resulting reaction mixture heated 6 hours at 80°C and stirred overnight at room temperature. For work up, the molecular sieves were filtered off through a short pad of silica, the filtrate was evaporated and the residue purified by flash chromatography (97/3 to 90/10, pentane/Et_2O) to obtain Fehler! Verweisquelle konnte nicht gefunden werden.a colorless syrup **26a** (126 mg, 69 % with traces of silanol impurities). R_f = 0.21 (9/1: cyclohexane/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.64 (dd, ^{3}J(H,H) = 9.5, 14.8 Hz, 1H); 5.49-5.28 (m, 4H); 4.19-4.07 (m, 2H); 3.91-3.87 (m, 1H); 3.83-3.78 (m, 1H); 2.68-2.57 (m, 2H); 2.47-2.24 (m, 9H); 2.06-1.81 (m, 7H); 1.74-1.65 (m, 1H); 1.53 (dt, ^{3}J(H,H) = 5.5 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.96 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.88 (s, 9H); 0.86 (s, 9H); 0.03 (s, 6H); 0.01 (s, 3H); 0.00 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.3 (C=O); 172.2 (C=O); 134.3 (CH); 132.2 (CH); 129.2 ; (CH) 127.7 (CH); 79.8 (C≡); 78.0 (C≡); 75.8 (HCO-); 75.5 (HCO-); 73.3 (HCO-); 63.9 (H_2CO-); 52.2 (CH); 50.6 (CH); 44.2 (CH_2); 31.9 (CH_2); 31.6 (CH_2); 26.0 (CH_2); 25.8 (CH_3); 25.1 (CH_2); 23.3 (CH_2); 22.1 (CH_2); 20.6 (CH_2); 18.0 (CH_2); 17.9 (Cquat); 17.6 (Cquat); 14.2 (CH_3); -4.4 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); HRMS (ESI$^+$) calculated for $C_{36}H_{63}O_6Si_2$ $[M+H]^+$ 647.4163, found 647.4154.

(R,E)-10-((1S,2R,3R,5S)-3,5-bis(tert-butyldimethylsilyl)-2-((Z)-pent-2-enyl)cyclopentyl)-8-(4-hydroxybutanoyloxy)dec-9-en-5-ynoate: 26b.

Prepared analogously from **24**Fehler! Verweisquelle konnte nicht gefunden werden.**b** (174 mg); product **26**Fehler! Verweisquelle konnte nicht gefunden werden.**b** was obtained as a colorless syrup (110 mg; 66%). R_f = 0.21 (9/1: cyclohexane/AcOEt); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.61 (dd, ^{3}J(H,H) = 9.6, 14.5 Hz, 1H); 5.47-5.25 (m, 4H); 4.19-4.06 (m, 2H); 3.92-3.87 (m, 1H); 3.80-3.76 (m, 1H); 2.62-2.55 (m, 2H); 2.44-2.18 (m, 9H); 2.05-1.80 (m, 7H); 1.74-1.65 (m, 1H); 1.52 (dt, ^{3}J(H,H) = 5.5 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.95 (t, ^{3}J(H,H) = 7.5 Hz, 3H); 0.87 (s, 9H); 0.85 (s, 9H); 0.02 (s, 6H); 0.00 (s, 3H); -0.01 (s, 3H); NMR (100 MHz, $CDCl_3$): δ = 173.3 (C=O); 172.2 (C=O); 134.0 (CH); 132.3 (CH); 129.3 (CH); 127.6 (CH); 79.8 (C≡); 78.0 (C≡); 75.7 (HCO-); 75.5 (HCO-); 73.2 (HCO-); 63.8 (H_2CO-); 52.3 (CH); 50.5 (CH); 44.2 (CH_2); 32.0 (CH_2); 31.7 (CH_2); 26.1 (CH_2); 25.8 (CH_3); 25.2 (CH_2); 23.3 (CH_2); 22.2 (CH_2); 20.7 (CH_2); 18.0

(CH_2); 17.9 (2 x Cquat); 14.2 (CH_3); -4.4 (CH_3); -4.6 (2 x CH_3); -4.7 (CH_3); HRMS (ESI^+) calculated for $C_{36}H_{63}O_6Si_2$ $[M+H]^+$ 647.4163, found 647.4146.

8-F_{3t}-IsoP: 3a.

To a suspension of $Ni(OAc)_2.4H_2O$ (23.5 mg, 0.09 mmol, 0.5 eq), in ethanol with 0.01% BHT (5 mL) was added under H_2 atmosphere, $NaBH_4$, in ethanol (0.5 M, 339 µL, 0.17 mmol, 0.9 eq). After 10 minutes was added under the black suspension, the ethylenediamine in solution in ethanol, (0.5 M, 1.7 mL, 0.85 mmol, 4.5 eq). After 10 minutes, **26a** (126 mg, 0.19 mmol, 1.0 eq) in ethanol with 0.01% BHT (10 mL) was added. Before and after each addition, three cycles vacuum/H_2 were realized. The reaction was then stirred during 48 hours under H_2 atmosphere (GC control). The mixture was then quenched with 20 mL of a saturated solution of NH_4Cl and stirred 30 min. The layers were extracted with 3 x 20 mL of Et_2O. The combined organic layers were washed with brine (3 x 10 mL) and dried over $MgSO_4$, filtered and the solvents were removed. The crude of the reaction was purified by flash chromatography (97/3 Pentane/Et_2O) to obtain ethylenic compound (88.3 mg, 70 %). R_f = 0.29 (9/1: Cyclohexane/AcOEt); $[\alpha]_D^{20}$= -50.5 (c= 10, $CHCl_3$); ν= 1737 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): δ= 5.58-5.56 (m, 2H); 5.45-5.27 (m, 5H); 4.20 (dt, $^3J(H,H)$ = 4.4; $^2J(H,H)$ = 11 Hz, 1H); 4.03 (dt, $^3J(H,H)$ = 3.6; $^2J(H,H)$ = 11 Hz; 1H); 3.93-3.89 (m, 1H); 3.81 (q, $^3J(H,H)$ = 5.6 Hz; 1H); 2.69-2.65 (m, 1H); 2.54 (ddd, $^3J(H,H)$ = 4.4, 11.3, 15.6 Hz, 1H); 2.48-2.25 (m, 6H); 2.12-1.88 (m, 9H); 1.79 (quint, $^3J(H,H)$ = 5.6 Hz, 1H); 1.54 (dt, $^3J(H,H)$ = 5.5 Hz, $^2J(H,H)$ = 13.7 Hz, 1H); 0.96 (t, $^3J(H,H)$ = 7.6 Hz, 3H); 0.88 (s, 9H); 0.86 (s, 9H); 0.03 (s, 6H); 0.02 (s, 3H); 0.01 (s, 3H); NMR (100 MHz, $CDCl_3$): δ= 173.7 (C=O); 172.0 (C=O); 132.8 (CH); 132.2 (CH); 131.8 (CH); 129.6 ; (CH) 127.7 (CH); 124.8 (CH); 75.9 (HCO-); 75.5 (HCO-); 73.7 (HCO-); 62.1 (H_2CO-); 52.4 (CH); 50.5 (CH); 44.2 (CH_2); 33.7 (CH_2); 32.8 (CH_2); 30.3 (CH_2); 26.4 (CH_2); 26.1 (CH_2); 25.8 (CH_3); 24.9 (CH_2); 23.3 (CH_2); 20.6 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 14.2 (CH_3); -4.4 (CH_3); -4.5 (CH_3); -4.6 (CH_3); -4.7 (CH_3); HRMS (ESI^+) calculated for $C_{36}H_{65}O_6Si_2$ $[M+H]^+$ 649.4320, found 649.4333.

At room temperature, a HCl solution (0.5 M in MeOH, 2.46 mL, 1.23 mmol, 10 eq) was added to a solution of protected compound (83 mg, 0.12 mmol, 1 eq) in THF/MeOH (17 mL/9 mL). The reaction was stirred 2 hours and $NaHCO_3$ powder was added. After 5 min of agitation, celite® was added and the solvent were evaporated. The crude of the reaction was purified by flash chromatography (95/5 to 90/10 Pentane/Et_2O) to obtain free hydroxyl compound (44 mg, 84 %). R_f = 0.3 (AcOEt); $[\alpha]_D^{20}$= -51.9 (c= 10, $CHCl_3$); ν= 3389 (OH); 1732 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): δ= 5.61 (dd, $^3J(H,H)$ = 6.4 Hz, $^2J(H,H)$ = 16 Hz, 1H); 5.53 (dd, $^3J(H,H)$ = 8.8 Hz, $^2J(H,H)$ = 16 Hz, 1H); 5.45-5.31 (m, 5H); 4.19 (dt, $^3J(H,H)$ = 3.6; $^2J(H,H)$ = 11.2 Hz, 1H); 4.07-3.95 (m, 3H); 2.81-2.76 (m, 1H); 2.54 (ddd, $^3J(H,H)$ = 4.5, 11.1, 15.5 Hz, 1H); 2.46-2.37 (m,

4H); 3.31-2.24 (m, 2H); 2.21-2.16 (m, 1H); 2.12-1.90 (m, 8H); 1.78 (quint, ^{3}J(H,H) = 6.7 Hz, 2H); 1.66 (dt, ^{3}J(H,H) = 3.6 Hz, ^{2}J(H,H) = 14.4 Hz, 1H); 0.96 (t, ^{3}J(H,H) = 7.5 Hz, 3H); NMR (100 MHz, $CDCl_3$): δ= 173.7 (C=O); 172.2 (C=O); 133.1 (CH); 132.0 (CH); 131.2 (CH); 130.5 ; (CH) 127.2 (CH); 124.6 (CH); 76.4 (HCOH); 76.2 (HCOH); 73.6 (HCO-); 62.2 (H_2CO-); 53.6 (CH); 50.9 (CH); 42.3 (CH_2); 33.6 (CH_2); 32.8 (CH_2); 30.4 (CH_2); 26.9 (CH_2); 26.4 (CH_2); 24.7 (CH_3); 23.4 (CH_2); 20.7 (CH_2); 14.2 (CH_3); HRMS (ESI^+) calculated for $C_{24}H_{37}O_6$ $[M+H]^+$ 421.2590, found 421.2588.

At room temperature, a solution of LiOH (0.5 M, 5 mL, 2.5 mmol, 25 eq) was added to a solution of lactone (44 mg, 0.1 mmol, 1 eq) in THF (5 mL). The reaction was stirred 4 hours and was acidified with a solution of $NaHSO_4$ (1M) until pH = 2. The mixture was extracted with 3 x 20 mL of AcOEt. The combined organic layers were washed with brine (2 x 10 mL) and dried over $MgSO_4$, filtered and the solvents were removed. The crude of the reaction was purified by flash chromatography (100/0 to 98/2 AcOEt/HCO_2H) to obtain **3a** (34.8 mg, 94 %). R_f = 0.27 (AcOEt/HCO_2H 95/5); $[\alpha]_D^{20}$= -8.0 (c= 5, MeOH); ^{1}H NMR (300 MHz, MeOD): δ= 5.59-5.57 (m, 2H); 5.51-5.45 (m, 2H); 5.43-5.40 (m, 2H); 4.09 (q, ^{3}J(H,H) = 6.4 Hz, 1H); 4.03-3.97 (m, 1H); 3.91-3.87 (m, 1H); 2.74-2.69 (m, 1H); 2.50 (dt, ^{3}J(H,H) = 7.4 Hz, ^{2}J(H,H) = 14.2 Hz, 1H); 2.35-2.29 (m, 4H); 2.17-2.06 (m, 7H); 1.69 (quint, ^{3}J(H,H) = 7.3 Hz, 1H); 1.56 (dt, ^{3}J(H,H) = 4.9 Hz, ^{2}J(H,H) = 14.2 Hz, 1H); 0.99 (t, ^{3}J(H,H) = 7.5 Hz, 3H); NMR (75 MHz, MeOD): δ= 175.0 (C=O); 133.0 (CH); 130.3 (CH); 128.7 (CH); 127.2 (CH); 125.8 (CH); 124.5 (CH); 73.2 (2 x HCOH); 70.3 (HCOH); 50.5 (CH); 48.5 (CH); 40.6 (CH_2); 33.4 (CH_2); 31.7 (CH_2); 24.7 (CH_3); 24.2 (CH_2); 23.1 (CH_2); 18.7 (CH_2); 11.7 (CH_3); HRMS (ESI^+) calculated for $C_{20}H_{32}O_5$ $[M+Na]^+$ 375.2147, found 375.2150.

8-*epi*-8-F_{3t}-IsoP: 3b.

In the same way and with **26b.** (110 mg), ethylenic compound was obtained (58.4 mg; 53%). R_f = 0.29 (9/1: Cyclohexane/AcOEt);); $[\alpha]_D^{20}$= -50.5 (c= 10, $CHCl_3$); ν= 1737 cm^{-1} (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): δ= 5.55-5.54 (m, 2H); 5.44-5.24 (m, 5H); 4.20 (dt, ^{3}J(H,H) = 4.3; ^{2}J(H,H) = 11 Hz, 1H); 4.00 (dt, ^{3}J(H,H) = 3.6; ^{2}J(H,H) = 11 Hz; 1H); 3.92-3.89 (m, 1H); 3.79 (q, ^{3}J(H,H) = 6.7 Hz; 1H); 2.68-2.68 (m, 1H); 2.53 (ddd, ^{3}J(H,H) = 4.3, 11.1, 15.6 Hz, 1H); 2.44-2.26 (m, 6H); 2.10-1.84 (m, 9H); 1.78 (quint, ^{3}J(H,H) = 5.7 Hz, 1H); 1.53 (dt, ^{3}J(H,H) = 5.6 Hz, ^{2}J(H,H) = 13.6 Hz, 1H); 0.95 (t, ^{3}J(H,H) = 7.6 Hz, 3H); 0.88 (s, 9H); 0.86 (s, 9H); 0.02 (s, 6H); 0.00 (s, 3H); -0.01 (s, 3H); NMR (100 MHz, $CDCl_3$): δ= 173.6 (C=O); 171.9 (C=O); 132.6 (CH); 132.2 (CH); 131.7 (CH); 129.7 (CH); 127.7 (CH); 125.0 (CH); 75.9 (HCO-); 75.7 (HCO-); 73.6 (HCO-); 62.1 (H_2CO-); 52.4 (CH); 50.5 (CH); 44.3 (CH_2); 33.6 (CH_2); 32.9 (CH_2); 30.4 (CH_2); 26.4 (CH_2); 26.2 (CH_2); 25.8 (CH_3); 24.8 (CH_2); 23.4 (CH_2); 20.7 (CH_2); 18.0 (Cquat); 17.9 (Cquat); 14.2

(CH_3); -4.4 (CH_3); -4.6 (2 x CH_3); -4.7 (CH_3); HRMS (ESI^+) calculated for $C_{36}H_{65}O_6Si_2$ $[M+H]^+$ 649.4320, found 649.4332.

The ethylenic compound was desilylated to obtain free hydroxyl compound (25.1 mg, 71%). R_f = 0.3 (AcOEt); $[\alpha]_D^{20}$= +62.8 (c= 10, $CHCl_3$); ν= 3393 (OH); 1730 cm^{-1} (C=O); ^1H NMR (400 MHz, $CDCl_3$): δ= 5.61 (dd, $^3J(H,H)$ = 6.3 Hz, $^2J(H,H)$ = 15.4 Hz, 1H); 5.53 (dd, $^3J(H,H)$ = 8.9 Hz, $^2J(H,H)$ = 15.4 Hz, 1H); 5.45-5.32 (m, 5H); 4.20 (dt, $^3J(H,H)$ = 3.3; $^2J(H,H)$ = 11.2 Hz, 1H); 4.05-3.97 (m, 3H); 2.81-2.78 (m, 1H); 2.54 (ddd, $^3J(H,H)$ = 4.5, 11.2, 15.6 Hz, 1H); 2.46-2.38 (m, 4H); 3.32-2.24 (m, 2H); 2.21-2.16 (m, 1H); 2.12-1.91 (m, 8H); 1.78 (quint, $^3J(H,H)$ = 6.6 Hz, 2H); 1.66 (dt, $^3J(H,H)$ = 3.3 Hz, $^2J(H,H)$ = 14.5 Hz, 1H); 0.96 (t, $^3J(H,H)$ = 7.5 Hz, 3H); NMR (100 MHz, $CDCl_3$): δ= 173.6 (C=O); 172.1 (C=O); 133.1 (CH); 132.0 (CH); 131.3 (CH); 130.4 (CH); 127.2 (CH); 124.6 (CH); 76.5 (HCOH); 76.3 (HCOH); 73.4 (HCO-); 62.1 (H_2CO-); 53.6 (CH); 50.9 (CH); 42.4 (CH_2); 33.6 (CH_2); 32.6 (CH_2); 30.4 (CH_2); 26.9 (CH_2); 26.4 (CH_2); 24.8 (CH_3); 23.4 (CH_2); 20.7 (CH_2); 14.3 (CH_3); HRMS (ESI^+) calculated for $C_{24}H_{37}O_6$ $[M+H]^+$ 421.2590, found 421.2588.

The last compound was saponified to obtain **3b** (19 mg, 90 %). R_f = 0.27 (AcOEt/HCO_2H 95/5); $[\alpha]_D^{20}$= -24.0 (c= 5, MeOH); ^1H NMR (300 MHz, MeOD): δ= 5.57-5.54 (m, 2H); 5.51-5.44 (m, 2H); 5.42-5.39 (m, 2H); 4.07 (q, $^3J(H,H)$ = 5.8 Hz, 1H); 4.02-3.96 (m, 1H); 3.92-3.87 (m, 1H); 2.73-2.68 (m, 1H); 2.50 (dt, $^3J(H,H)$ = 7.4 Hz, $^2J(H,H)$ = 14.2 Hz, 1H); 2.38-2.27 (m, 4H); 2.17-2.05 (m, 7H); 1.69 (quint, $^3J(H,H)$ = 7.2 Hz, 1H); 1.56 (dt, $^3J(H,H)$ = 5.0 Hz, $^2J(H,H)$ = 14.2 Hz, 1H); 0.99 (t, $^3J(H,H)$ = 7.5 Hz, 3H); NMR (75 MHz, MeOD): δ= 175.0 (C=O); 133.2 (CH); 130.2 (CH); 128.9 (CH); 127.7 (CH); 125.8 (CH); 124.3 (CH); 73.4 (HCOH); 73.3 (HCOH); 70.6 (HCOH); 50.8 (CH); 48.5 (CH); 40.6 (CH_2); 33.4 (CH_2); 32.3 (CH_2); 25.0 (CH_3); 24.3 (CH_2); 23.3 (CH_2); 18.7 (CH_2); 11.7 (CH_3); HRMS (ESI^+) calculated for $C_{20}H_{32}O_5$ $[M+Na]^+$ 375.2147, found 375.2169.