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Electronic Supplementary Information

Total syntheses of all tri-oxygenated 16-phytoprostane classes via a common precursor constructed by oxidative cyclization and alkyl-alkyl coupling reactions as the key steps

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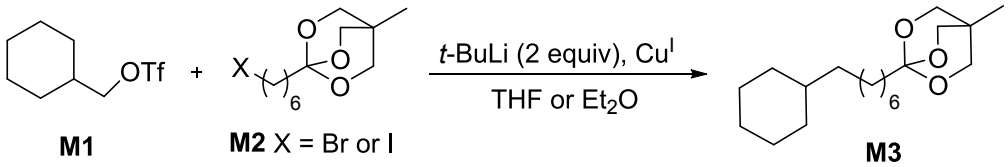
Contents:

Model study for the copper-catalyzed alkyl-alkyl cross-coupling reaction for the attachment of the α-chain to the ring

A copper(I)-catalyzed alkyl-alkyl coupling was envisaged to connect the α-chain precursor with the ring system of PhytoPs. The challenge consisted of choosing an appropriate methyl ester surrogate and suitable coupling conditions. Initially, a series of a model reactions was performed with cyclohexylmethyl triflate (**M1**) and ω-halo orthoesters **M2** with the 4-methyl-2,6,7-trioxabicyclo[2.2.2]octane (OBO) group and monitoring by GC-MS. Using halogen-lithium exchange to activate **M2** and subsequent coupling with **M1** in varying ratios in the presence of superstoichiometric amounts of CuI or CuBr•SMe_2 in THF or DME was not efficient (Table S1, entries 1-7). Switching the solvent to diethyl ether and using catalytic amounts of CuBr•SMe_2 led to a low yield of sensitive orthoester **M3** (entry 8), which could, however, not be further improved (entries 9, 10). The bromide of **M2** reacted similarly as the iodide (entry 9 vs 11), therefore the approach using orthoesters **M2** was abandoned.

Table S1. Cu(I)-mediated cross-coupling of **M1** and **M2**.



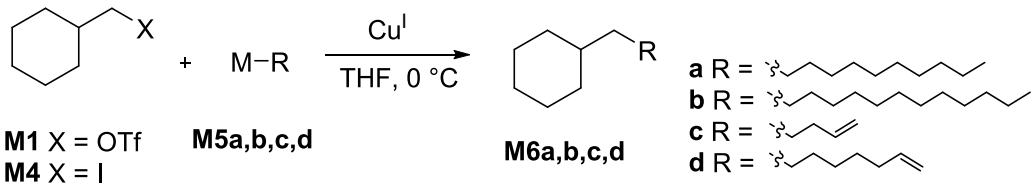
M1 **M2** X = Br or I **M3**

Entry	**M1** : **M2**	X	Cu source (equiv.)[a]	Solvent	**M3** (%)[b]
1	1 : 1.1	I	CuI (3)	THF	-
2	1 : 1	I	CuI (3)	THF	-
3	1 : 1	I	CuBr•SMe_2 (1)	THF	-
4	1 : 1	I	CuBr•SMe_2 (2)	THF	-
5	1 : 2	I	CuBr•SMe_2 (2)	DME	-
6	1 : 1	I	CuBr•SMe_2 (2)	THF	-
7	1 : 2	I	CuBr•SMe_2 (1)	THF	-
8	1 : 1.1	I	CuBr•SMe_2 (0.2)	Et_2O	30
9	1 : 1.2	I	CuBr•SMe_2 (0.5)	Et_2O, THF	-
10	1 : 1.1	I	LiCl, $CuCl_2$ (0.1)	Et_2O, THF	5
11	1 : 1.1	Br	LiCl, $CuCl_2$ (0.1)	Et_2O, THF	30

[a] Equiv. based on **M1.** [b] Determinated by gas chromatography.

The application of organometallic reagents with alkyl or alkenyl units, which could be subsequently transformed to an ester, was a more promising strategy (Table S2). Cross-coupling of **M1** with decyllithium generated by halogen-lithium exchange did not proceed in the presence of stoichiometric amounts of Cu(I) (Table S2, entry 1), but gave a moderate yield of coupling product **M6a** in the presence of catalytic amounts of Cu(I) (entry 2). The use of Grignard reagents proved to be more successful. All tested linear alkyl or ω-alkenyl Grignard reagents **M5b-d** coupled with **M1** using CuBr•SMe_2 or in situ generated Li_2CuCl_4 as the catalysts affording products **M6b-d** in good isolated yields (entries 3,4,6,7). Catalytic Cu(I) was more efficient than stoichiometric amounts (entry 6 vs. 5). Iodide **M4** was similarly active as the triflate **M1** in the coupling reaction (entry 4 vs. 3). However, attempts to generate Grignard reagents from **M2** (cf. Table 1) were not successful.

Table S2. Cu-mediated or catalyzed cross-coupling of triflates **M1** or iodide **M4** with organometallic agents **M5**.



Entry	**M1, M4**	**M5** M	**M1(M4)**:**M5**	Cu(I) (equiv.)[a]	Solvent	**M6** (%)[b]
1	**M1**	**a** Li	1 : 2	CuBr•SMe_2 (1.1)	Et_2O	0
2	**M1**	**a** Li	1 : 1.1	CuBr•SMe_2 (0.3)	Et_2O	46
3	**M1**	**b** MgBr	1 : 1.1	CuBr•SMe_2 (0.2)	THF	73
4	**M4**	**b** MgBr	1 : 1.1	LiCl, $CuCl_2$ (0.1)	THF	85
5	**M1**	**c** MgBr	1 : 2	CuBr•SMe_2 (1.1)	THF	55
6	**M1**	**c** MgBr	1 : 2	CuBr•SMe_2 (0.2)	THF	81
7	**M1**	**d** MgBr	1 : 2	CuBr•SMe_2 (0.4)	THF	90

[a] Equiv. based on **M1** and **M4** respectively. [b] Isolated yield, calculated to **M1** and **M4** respectively.

Copper(I)-catalyzed coupling of cylohexylmethyl triflate with alkyllithium compounds:
t-BuLi (1.7M in pentane) was added dropwise to a solution of halide **M2** or decyl bromide in dry Et_2O at –78 °C. The mixture was stirred for 30 min, warmed to r.t. and stirred for 10 min. The copper(I) catalyst was added after cooling to –40 °C followed by dropwise addition of triflate **M1** in dry Et_2O. The reaction was stirred until complete as monitored by TLC (approx.

3 h) and subsequently quenched with saturated NH_4Cl solution. The layers were separated and the aqueous was extracted with Et_2O. The combined organic fractions were washed with brine and dried over $MgSO_4$. The solvent was evaporated and the crude material was purified by column chromatography (silica gel, pentane).

Model reaction with Grignard reagents M5b-d (General procedure):
A solution of alkyl or alkenyl magnesium bromide **M5b-d** in THF was cooled to 0 °C and the copper(I) catalyst was added. A solution of triflate **M1** or iodide **M4** in dry THF was added dropwise. The reaction was stirred at 0 °C until complete as monitored by TLC (approx. 3 h) and subsequently quenched with saturated NH_4Cl solution. The layers were separated and the aqueous was extracted with Et_2O. The combined organic fractions were washed with brine and dried over $MgSO_4$. The solvent was evaporated and the crude material was purified by column chromatography (silica gel, pentane).

Undecylcyclohexane (M6a):[1] HRMS (+EI) *m/z*: ($C_{17}H_{34}$) calc.: 238.2661, found: 238.2663. - ^{1}H NMR (400 MHz): δ = 0.77-0.97 (m, 2H, cyclohexane 2,6-CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3), 1.09-1.34 (m, 24H, cyclohexane 3,4,5-CH_2, 1-CH, undecyl CH_2), 1.58-1.75 (m, 5H, cyclohexane 2,3,4,5,6-CH_2). - ^{13}C NMR (100 MHz): δ = 14.3 (q, CH_3), 22.9 (t, CH_2), 26.6 (t, 2C, cyclohexane 3,5-CH_2), 27.0 (t, cyclohexane 4-CH_2), 27.1 (t, CH_2), 29.5 (t, CH_2), 29.83 (t, CH_2), 29.86 (t, CH_2), 29.87 (t, CH_2), 29.90 (t, CH_2), 30.2 (t, CH_2), 32.1 (t, CH_2), 33.6 (t, 2C, cyclohexane 2,6-CH_2), 37.7 (t, CH_2), 37.9 (d, CH).

Tridecylcyclohexane (M6b):[2] HRMS (+EI) *m/z*: ($C_{19}H_{38}$) calc.: 266.2974, found: 266.2978. - ^{1}H NMR (400 MHz): δ = 0.77-0.96 (m, 2H, cyclohexane 2,6-CH_2), 0.88 (t, *J* = 6.8 Hz, 3H, CH_3), 1.08-1.35 (m, 28H, cyclohexane 3,4,5-CH_2, 1-CH, tridecyl CH_2), 1.58-1.75 (m, 5H, cyclohexane 2,3,4,5,6-CH_2). - ^{13}C NMR (100 MHz): δ = 14.3 (q, CH_3), 22.9 (t, CH_2), 26.7 (t, 2C, cyclohexane 3,5-CH_2), 27.0 (t, cyclohexane 4-CH_2), 27.1 (t, CH_2), 29.6 (t, CH_2), 29.86 (t, CH_2), 29.90 (t, 4C, CH_2), 29.93 (t, CH_2), 30.2 (t, CH_2), 32.1 (t, CH_2), 33.7 (t, 2C, cyclohexane 2,6-CH_2), 37.8 (t, CH_2), 37.9 (d, CH).

Pent-4-en-1-ylcyclohexane (M6c):[3] HRMS (+EI) *m/z*: ($C_{11}H_{20}$) calc.: 152.1565, found: 152.1566. - ^{1}H NMR (400 MHz): δ = 0.82-0.96 (m, 2H, cyclohexane 2,6-CH_2), 1.09-1.29 (m, 6H, cyclohexane 3,4,5-CH_2, 1-CH, C*H*$_2$(CH_2)$_2$CH=CH_2), 1.36-1.45 (m, 2H, C*H*$_2$$CH_2$CH=$CH_2$), 1.60-1.76 (m, 5H, cyclohexane 2,3,4,5,6-CH_2), 2.04 (qt, *J* = 7.1, 1.5 Hz,

2H, C*H*$_2$CH=CH$_2$), 4.95 (dquint, *J* = 10.2, 1.3 Hz, 1H, C*H*$_2$=CH), 5.01 (dq, *J* = 17.0, 1.7 Hz, 1H, C*H*$_2$=CH), 5.84 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$). - ^{13}C NMR (100 MHz): δ = 26.6 (t, 2C, cyclohexane 3,5-CH$_2$), 27.0 (t, cyclohexane 4-CH$_2$), 30.3 (t, *C*H$_2$CH$_2$CH=CH$_2$), 33.6 (t, 2C, cyclohexane 2,6-CH$_2$), 34.3 (t, *C*H$_2$CH=CH$_2$), 37.2 (t, *C*H$_2$(CH$_2$)$_2$CH=CH$_2$), 37.8 (d, CH), 114.2 (t, *C*H$_2$=CH), 139.4 (d, *C*H=CH$_2$).

Oct-7-en-1-ylcyclohexane (M6d): MS (+EI) *m/z*, (%): 194 (33) $[M]^{\cdot+}$, 166 (15) $[M-C_2H_4]^{\cdot+}$, 152 (10) $[M-C_3H_6]^{\cdot+}$, 138 (10) $[M-C_4H_8]^{\cdot+}$, 124 (8) $[M-C_5H_{10}]^{\cdot+}$, 109 (31) $[M-C_6H_{13}]^{+}$, 96 (100) $[M-C_7H_{14}]^{\cdot+}$, 83 (53) $[M-C_8H_{15}]^{+}$, 82 (40) $[M-C_8H_{16}]^{\cdot+}$, 81 (55) $[M-C_8H_{17}]^{+}$, 69 (9) $[M-C_9H_{17}]^{+}$, 68 (6) $[M-C_9H_{18}]^{\cdot+}$, 67 (27) $[M-C_9H_{19}]^{+}$, 55 (37) $[M-C_9H_{19}]^{+}$. - HRMS (+EI) *m/z*: (C$_{14}$H$_{26}$) calc.: 194.2035, found: 194.2037. - ^{1}H NMR (400 MHz): δ = 0.79-0.85 (m, 2H, cyclohexane 2,6-CH$_2$), 1.09-1.29 (m, 14H, cyclohexane 3,4,5-CH$_2$, 1-CH, (C*H*$_2$)$_5$CH$_2$CH=CH$_2$), 1.55-1.75 (m, 5H, cyclohexane 2,3,4,5,6-CH$_2$), 2.04 (tdt, *J* = 8.0, 6.7, 1.4 Hz, 2H, C*H*$_2$CH=CH$_2$), 4.93 (ddt, *J* = 10.2, 2.2, 1.2 Hz, 1H, C*H*$_2$=CH), 4.99 (dq, *J* = 17.0, 1.7 Hz, 1H, C*H*$_2$=CH), 5.81 (ddt, *J* = 16.9, 10.2, 6.7 Hz, 1H, C*H*=CH$_2$). - ^{13}C NMR (100 MHz): δ = 26.6 (t, 2C, cyclohexane 3,5-CH$_2$), 26.9 (t, CH$_2$), 27.0 (t, cyclohexane 4-CH$_2$), 29.1 (t, *C*H$_2$), 29.4 (t, *C*H$_2$), 30.0 (t, *C*H$_2$), 33.6 (t, 2C, cyclohexane 2,6-CH$_2$), 34.0 (t, *C*H$_2$CH=CH$_2$), 37.7 (t, *C*H$_2$(CH$_2$)$_5$CH=CH$_2$), 37.8 (d, CH), 114.2 (t, *C*H$_2$=CH), 139.4 (d, *C*H=CH$_2$).

1 a) M. Feldhues, H. J. Schäfer, *Tetrahedron*, 1985, **41**, 4195–4212; b) *Spectral Database for Organic Compounds (SDBS)*; SDBS No.: 961; RN 54105-66-7; http://sdbs.db.aist.go.jp/ (accessed March 20, 2017).

2 *Spectral Database for Organic Compounds (SDBS)*; SDBS No.: 628; RN 6006-33-3; http://sdbs.db.aist.go.jp/ (accessed March 20, 2017).

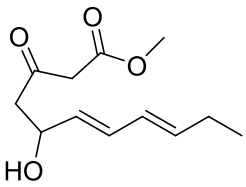
3 D. Takeuchi, *J. Am. Chem. Soc.*, 2011, **133**, 11106–11109.

General experimental techniques

All reactions were conducted in flame-dried glassware under an atmosphere of dry argon or nitrogen. THF, DME, DCM, MeOH and ferrocenium hexafluorophosphate were dried following standard methods under a nitrogen or argon atmosphere. TLC plates (Fluka or Macherey-Nagel, silica gel on TLC-PET foils with fluorescent indicator 254 nm) were used for monitoring reactions. Flash column chromatographic separations were performed at silica gel 60 (Merck or Acros, 230-400 mesh). IR spectra were taken on a Bruker ALPHA spectrometer as neat samples using an ATR device. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker AV III 600 HD, AV III 500 HD or AV III 400 HD spectrometers equipped with cryo-probes or a Bruker AV III 400 spectrometer equipped with inverse broad-band probe at 600, 500 or 400 MHz for ^{1}H NMR, and 151, 126 or 100 MHz for ^{13}C NMR, respectively. ^{1}H NMR chemical shifts are provided in ppm vs. TMS as the internal standard; ^{13}C NMR spectra are referenced against the residual solvent peak. The connectivity was determined by ^{1}H-^{1}H COSY experiments. Stereochemical assignments are based on NOE-Diff and NOESY experiments. ^{13}C NMR spectral assignments were obtained from APT, HSQC and HMBC experiments. GC/MS(EI) measurements were performed on an Agilent 5975C MSD coupled to a 7890N gas chromatograph or an Agilent 5975B MSD coupled to a 6890N gas chromatograph. ESI mass spectra were obtained on a Thermo Fisher Scientific LCQ Fleet spectrometer, sample concentration approx. 1 µg/mL. HRMS spectra were measured on a Waters Q-Tof micro spectrometer, resolution: 100000.

Experimental procedures and analytical data

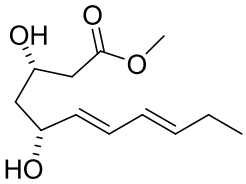
Methyl (6*E*,8*E*)-5-hydroxy-3-oxoundeca-6,8-dienoate (11):



Methyl acetoacetate (**10**) (50 mmol, 5.4 mL) was added dropwise to a suspension of NaH (65 mmol, 2.6 g, 60% suspension in mineral oil) in dry THF (100 mL) at 0 °C under a nitrogen atmosphere. After foaming stopped, stirring was continued at the same temperature for 30 min. Dry HMPA (60 mmol, 10.5 mL) was added and the mixture was cooled to –78 °C. *n*-BuLi (60 mmol, 27 mL, 1.6 M in hexanes) was added dropwise over a 30 min period. The reaction mixture was warmed to –65 °C and stirred at this temperature for 30 min. It was cooled back to –78 °C and *trans*,*trans*-2,4-heptadienal (**9**) (50 mmol, 6.25 mL) was added dropwise. The color of the turbid mixture changed during the addition from brown to maroon, with the last drop it changed to pink and slowly turned to orange-red. The mixture was slowly warmed to –60 °C and quenched after 100 min by a few drops 99% AcOH followed by 10% aqueous AcOH solution (50 mL). The reaction mixture was diluted with Et_2O (50 mL) and warmed to r.t. The layers were separated and the aqueous was extracted with EtOAc (4×50 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution and brine, dried over $MgSO_4$ and evaporated. The crude material was purified by flash chromatography (silica gel 200 g, hexane/EtOAc, gradient 10:1 to 1:1). Yield 11.0 g (97%) as a yellow oil. - R_f (hexane/EtOAc 2.5:1) = 0.3. - IR (film): ν = 3437, 2964, 2935, 2879, 1736, 1715, 1438, 1406, 1323, 1209, 1153, 1065, 975, 864. - MS (+ESI) *m/z*, (%): 491 (63) $[2M+K]^+$, 283 (100) $[M+K+H_2O]^+$, 265 (50) $[M+K]^+$, 249 (18) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{12}H_{18}O_4Na$) calc.: 249.1097, found: 249.1098. - ^{1}H NMR (400 MHz): δ = 0.94 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 2.04 (dq, *J* = 6.4, 7.5 Hz, 2H, C*H*$_2$CH$_3$), 2.68 (dd, *J* = 4.6, 17.0 Hz, 1H, CH*H*CHOH), 2.74 (dd, *J* = 7.7, 17.0 Hz, 1H, CH*H*CHOH), 2.82 (br s, 1H, O*H*), 3.45 (s, 2H, COC*H*$_2$CO), 3.68 (s, 3H, OC*H*$_3$), 4.56 (ddd, *J* = 4.6, 6.3, 7.5 Hz, 1H, C*H*OH), 5.51 (dd, *J* = 6.4, 15.3 Hz, 1H, CH=C*H*CHOH), 5.70 (dt, *J* = 6.5, 15.1 Hz, 1H, =C*H*CH$_2$CH$_3$), 5.94 (dd, *J* = 10.5, 15.1 Hz, 1H, C*H*=CHCH$_2$), 5.55 (dd, *J* = 10.4, 15.3 Hz, 1H, C*H*=CHCHOH). - ^{13}C NMR (100 MHz): δ = 13.5 (q, *C*H$_3$CH$_2$), 25.7 (t, *C*H$_2$CH$_3$), 49.8 (t, HOCH*C*H$_2$CO), 49.9 (t, CO*C*H$_2$CO), 52.5 (q, O*C*H$_3$), 68.3 (d, *C*HOH), 128.3 (d, *C*H=CHCH$_2$), 131.0 (d,

CH=*C*HCHOH), 131.5 (d, *C*H=CHCHOH), 137.8 (d, CH=*C*HCH$_2$), 167.5 (s, *C*OOCH$_3$), 202.6 (s, CH$_2$*C*OCH$_2$).

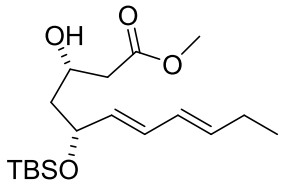
Methyl (3*S,5*R**,6*E*,8*E*)-3,5-dihydroxyundeca-6,8-dienoate (12):**



Diethyl(methoxy)borane (55 mmol, 55 mL, 1.0 M in THF) was added dropwise over 30 min to a solution of (6*E*,8*E*)-methyl 5-hydroxy-3-oxoundeca-6,8-dienoate (**11**) (36.6 mmol, 8.3 g) in dry THF (250 mL) and MeOH (60 mL) at –78 °C. The mixture was stirred for 1 h and $NaBH_4$ (55 mmol, 2.1 g) was added in approx. 50 mg portions at –95 °C. A gas evolution was observed and the reaction mixture became turbid and pale yellow. The reaction mixture was stirred at –78 °C for 120 min, quenched with AcOH (30 mL), diluted with Et_2O (150 mL) and warmed to r.t. Saturated $NaHCO_3$ solution (150 mL) was added slowly and the mixture was stirred for 5 min. The layers were separated and the aqueous was extracted with Et_2O (3×100 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution, water and brine, dried over $MgSO_4$ and the solvents were evaporated. Water (60 mL), THF (180 mL) and NaOAc (83 mmol, 6 g) were added to the residue. The mixture was cooled to 0 °C, H_2O_2 (30%, 50 mL) was added slowly and stirring was continued for 1 h. A saturated Na_2SO_3 solution (100 mL) was added followed by Et_2O (100 mL) and stirring was continued at r.t. for 10 min. The layers were separated and the aqueous was extracted with Et_2O (3×100 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$ and evaporated. The crude material was purified by flash chromatography (silica gel 120 g, hexane/ethyl acetate, gradient 5:1 to 1:1). Yield 7.2 g (86%) as a colorless oil. - R_f (hexane/EtOAc 2.5:1) = 0.2. - IR (film): ν = 3511, 2956, 2930, 2856, 1738, 1460, 1438, 1362, 1253, 1199, 1170, 1070, 989, 836, 776, 669. - MS (+ESI) *m/z*, (%): 479 (29) $[2M+Na]^+$, 267 (33) $[M+K]^+$, 251 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{12}H_{20}O_4Na$) calc.: 251.1254, found: 251.1254. - ^{1}H NMR (400 MHz): δ = 0.96 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.58 (dt, *J* = 3.4, 14.3 Hz, 1H, HOCHCH*H*CHOH), 1.67 (dt, *J* = 9.4, 14.3 Hz, 1H, HOCHCH*H*CHOH), 2.05 (dq, *J* = 6.4, 7.5 Hz, 2H, C*H*$_2$CH$_3$), 2.42 (dd, *J* = 4.7, 16.1 Hz, 1H, CH*H*COOCH$_3$), 2.48 (dd, *J* = 7.5, 16.1 Hz, 1H, CH*H*COOCH$_3$), 3.27 (br s, 1H, O*H*), 3.66 (s, 3H, OC*H*$_3$), 3.84 (br s, 1H, O*H*), 4.15-4.28 (m, 1H, CH$_2$C*H*OHCH$_2$), 4.32-4.43 (m, 1H, HOC*H*CH=), 5.52 (dd, *J* = 6.7, 15.2 Hz, 1H, CH=C*H*CHOH), 5.70 (dt, *J* = 6.5, 15.1 Hz, 1H, CH=C*H*CH$_2$), 5.94 (dd, *J* =

10.4, 15.1 Hz, 1H, C*H*=CHCH$_2$), 6.18 (dd, *J* = 10.4, 15.2 Hz, 1H, C*H*=CHCHOH). - ^{13}C NMR (100 MHz): δ = 13.6 (q, *C*H$_3$CH$_2$), 25.8 (t, *C*H$_2$CH$_3$), 41.7 (t, CHOH*C*H$_2$CO), 42.9 (t, HOCHC*H*$_2$CHOH), 52.0 (q, O*C*H$_3$), 68.4 (d, CH$_2$*C*HOHCH$_2$), 72.7 (d, HO*C*HCH=CH), 128.5 (d, *C*H=CHCH$_2$), 131.2 (d, *C*H=CHCHOH), 132.6 (d, CH=*C*HCHOH), 137.6 (d, CH=*C*HCH$_2$), 172.8 (s, *C*OOCH$_3$).

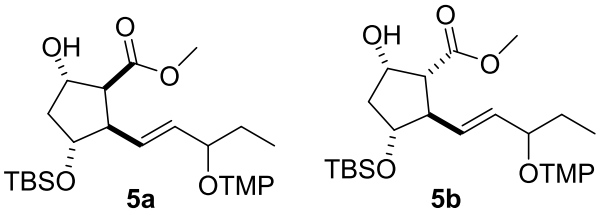
Methyl (3S*,5*R,6*E*,8*E*)-5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxyundeca-6,8-dienoate (8):**



2,6-Lutidine (22.4 mmol, 2.6 mL) was added to a solution of diol **12** (7.5 mmol, 1.70 g) in dry DCM (70 mL). The mixture was cooled to –78 °C and TBSOTf (7.8 mmol, 1.8 mL) was added dropwise. The reaction mixture was stirred at –78 °C for 3 h. The reaction was quenched with saturated NaHSO$_4$ solution (60 mL), diluted with EtOAc (50 mL) and warmed to r.t. The layers were separated and the aqueous was extracted with Et$_2$O (2x50 mL) and EtOAc (50 mL). The combined organic layers were washed with water, saturated NaHCO$_3$ solution, water and brine, dried over MgSO$_4$ and evaporated. The crude material was purified by flash chromatography (silica gel 100 g, hexane/ethyl acetate 10:1, gradient to 1:1). Yield 1.93 g (82%) as a yellow oil. - R$_f$ (hexane/EtOAc 2.5:1) = 0.25. - IR (film): ν = 3397, 2962, 2932, 2874, 1732, 1437, 1293, 1261, 1200, 1166, 1066, 988, 844, 774. - MS (+ESI) *m/z*, (%): 707 (22) [2M+Na]$^+$, 365 (100) [M+Na]$^+$. - HRMS (+ESI) *m/z*: (C$_{18}$H$_{34}$O$_4$NaSi) calc.: 365.2119, found: 365.2119. - ^{1}H NMR (400 MHz): δ = 0.03 (s, 3H, SiC*H*$_3$), 0.07 (s, 3H, SiC*H*$_3$), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.98 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.59 (ddd, *J* = 3.0, 5.3, 14.0 Hz, 1H, CH*H*CHOSi), 1.73 (ddd, *J* = 7.5, 9.4, 14.0 Hz, 1H, CH*H*CHOSi), 2.07 (dq, *J* = 6.6, 7.5 Hz, 2H, C*H*$_2$CH$_3$), 2.41 (dd, *J* = 5.3, 16.0 Hz, 1H, CH*H*COOCH$_3$), 2.46 (dd, *J* = 7.5, 16.1 Hz, 1H, CH*H*COOCH$_3$), 3.50 (d, *J* = 2.6 Hz, 1H, O*H*), 3.67 (s, 3H, OC*H*$_3$), 4.15 (dddddd, *J* = 1.5, 2.7, 3.0, 5.3, 7.7, 9.4 Hz, 1H, C*H*OH), 4.37 (ddt, *J* = 1.5, 5.3, 7.6 Hz, 1H, C*H*OSi), 5.47 (dd, *J* = 7.4, 15.1 Hz, 1H, =C*H*CHOSi), 5.69 (dt, *J* = 6.5, 14.9 Hz, 1H, =C*H*CH$_2$), 5.96 (dd, *J* = 10.4, 15.1 Hz, 1H, C*H*=CHCH$_2$), 6.08 (dd, *J* = 10.4, 15.2 Hz, 1H, C*H*=CHCHOSi). - ^{13}C NMR (100 MHz): δ = –4.6 (q, Si*C*H$_3$), –3.7 (q, Si*C*H$_3$), 13.6 (q, CH$_2$*C*H$_3$), 18.3 (s, Si*C*(CH$_3$)$_3$), 25.8 (t, *C*H$_2$CH$_3$), 26.1 (q, SiC(*C*H$_3$)$_3$), 41.9 (t, *C*H$_2$COOCH$_3$), 44.4 (t, *C*H$_2$CHOSi), 51.9 (q, O*C*H$_3$), 67.1 (d, *C*HOH), 73.6 (d, *C*HOSi), 128.5 (d,

*C*H=CHCH$_2$), 131.0 (d, *C*H=CHCHOSi), 133.3 (d, CH=*C*HCHOSi), 137.3 (d, CH=*C*HCH$_2$), 172.8 (s, *C*OOCH$_3$).

Methyl (1*S,2*S**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-1-hydroxy-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)cyclopentane-2-carboxylate (5a), methyl (1*S**,2*R**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-1-hydroxy-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)cyclopentane-2-carboxylate (5b):**

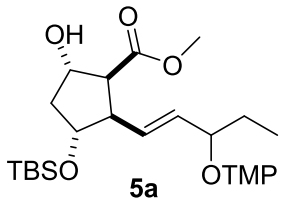


***Method A**:* Anhydrous LiCl (6 mmol, 260 mg) was flame dried under reduced pressure. After cooling to r.t., dry DME (20 mL) was added. The mixture was cooled to –78 °C and *i*Pr$_2$NH (2.7 mmol, 380 μL) and BuLi (2.6 mmol, 1.78 mL, 1.6 M in hexane) were subsequently added. The resulting mixture was stirred for 30 min. Dienoate **8** (1 mmol, 340 mg) dissolved in dry DME (2 mL) was added dropwise. The mixture was warmed to –55 °C during 40 min. After cooling to –78 °C, HMPA (12 mmol, 2.1 mL) was added dropwise followed by TEMPO (1.2 mmol, 200 mg) mixed with FeCp$_2$PF$_6$ (20 mg). Subsequently FeCp$_2$PF$_6$ (overall 1.7 mmol, 570 mg) was added in portions (ca 50 mg each) until the color remained dark blue. The reaction mixture was slowly warmed to –35 °C and quenched by a few drops of water after an hour. The mixture was diluted with Et$_2$O (ca 20 mL) and filtered through a plug of silica gel with Et$_2$O (2×20 mL). The solvent was evaporated and the inhomogeneous residue was preadsorbed at silica gel (1 g) and purified by column chromatography (silica gel 30 g, hexane/EtOAc 10:1, gradient to 1:1). Yield 318 mg (64%) as an inseparable 2:1 mixture of **5a**/**5b** as a colorless oil.

***Method B**: t*-BuMgCl in THF (0.75 mmol, 375 μL, 2.0 M in Et$_2$O) was added to a solution of dienoate **8** (0.5 mmol, 170 mg) in dry THF (5 mL) at –78 °C. The mixture was stirred at –78 to –60 °C for 40 min. A solution of LDA, freshly prepared from *i*Pr$_2$NH (1.3 mmol, 190 μL) and BuLi (1.3 mmol, 840 μL, 1.6 M in hexane) in dry THF (1.3 mL) was added dropwise at –78 °C. The resulting mixture was stirred between –78 and –50 °C for 1 h. Dry THF (10 mL) and HMPA (3 mmol, 520 μL) were added at –78 °C followed by TEMPO (0.6 mmol, 100 mg) mixed with FeCp$_2$PF$_6$ (0.3 mmol, 100 mg). After 5 min, more FeCp$_2$PF$_6$ (1.0 mmol, 320 mg) was added in portions (ca 50 mg each) until the color remained dark blue. The reaction

was quenched by a few drops of water after 40 min. The mixture was diluted with Et_2O (20 mL) and filtered through a plug of silica gel. The solvent was evaporated, the inhomogeneous residue was preadsorbed at silica gel (1 g) and purified by column chromatography (silica gel 30 g, hexane/EtOAc 10:1, gradient to 1:1). Yield 118 mg (47%) as 1:5 inseparable mixture of **5a**/**5b** as a colorless oil.

R_f (hexane/EtOAc 5:1) = 0.3. - IR (film): ν = 3490, 2928, 2856, 1734, 1463, 1437, 1375, 1360, 1255, 1207, 1172, 1131, 1079, 1004, 971, 861, 836, 809, 776, 712, 668. - MS (+ESI) *m/z*, (%): 498 (100) $[M+H]^+$, 364 (5) $[M–OTMP+Na]^+$, 158 (17) $[TMPOH+H]^+$. - HRMS (+ESI) *m/z*: ($C_{27}H_{52}O_5NSi$) calc.: 498.3609, found: 498.3607.

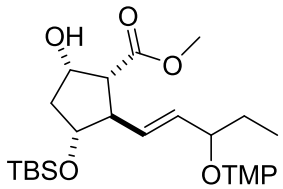


5a

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.11 (s, 3H, SiC*H*$_3$), 0.14 (s, 3H, SiC*H*$_3$), 0.79 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 0.87 (s, 9H, SiC(C*H*$_3$)$_3$), 0.99-1.19 (m, 12H, NC(C*H*$_3$)$_2$), 1.38-1.50 (m, 7H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CH$_3$), 1.66-1.80 (m, 2H, CH*H*CHOSi, CH*H*CH$_3$), 2.31-2.42 (m, 1H, CH*H*CHOSi), 2.50 (d, *J* = 7.8 Hz, 1H, O*H*), 2.99-3.10 (m, 1H, C*H*COOCH$_3$), 3.19-3.29 (m, 1H, *C*HCHOSi), 3.66 (s, 3H, OC*H*$_3$), 3.84-3.94 (m, 1H, C*H*OTMP), 4.03-4.09 (m, 1H, C*H*OSi), 4.48-4.57 (m, 1H, C*H*OH), 5.17 (dd, *J* = 9.1, 15.5 Hz, 1H, C*H*=CHCHOTMP), 5.50 (dd, *J* = 7.9, 15.5 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.8 (q, Si*C*H$_3$), –4.6 (q, Si*C*H$_3$), 9.9 (q, *C*H$_3$CH$_2$), 17.4 (t, NCCH$_2$*C*H$_2$), 18.1 (s, Si*C*(CH$_3$)$_3$), 20.4 (q, NC(*C*H$_3$)$_2$), 20.5 (q, NC(*C*H$_3$)$_2$), 25.90 (q, SiC(*C*H$_3$)$_3$), 27.3 (t, *C*H$_2$CH$_3$), 34.0 (q, NC(*C*H$_3$)$_2$), 35.5 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 42.7 (t, *C*H$_2$CHOSi), 51.8 (q, OCH$_3$), 53.8 (d, *C*HCHOSi), 56.3 (d, *C*HCOOCH$_3$), 59.4 (s, N*C*(CH$_3$)$_2$), 60.2 (s, N*C*(CH$_3$)$_2$), 74.1 (d, *C*HOH), 78.6 (d, *C*HOSi), 85.7 (d, *C*HOTMP), 128.8 (d, *C*H=CHCHOTMP), 135.8 (d, CH=*C*HCHOTMP), 172.4 (s, *C*OOCH$_3$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.04 (s, 3H, SiC*H*$_3$), 0.06 (s, 3H, SiC*H*$_3$), 0.77 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 0.88 (s, 9H, SiC(C*H*$_3$)$_3$), 0.99-1.16 (m, 12H, NC(C*H*$_3$)$_2$), 1.38-1.50 (m, 7H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CH$_3$), 1.66-1.80 (m, 2H, CH*H*CHOSi, CH*H*CH$_3$), 2.31-2.42 (m, 1H, CH*H*CHOSi), 2.54 (d, *J* = 8.3 Hz, 1H, O*H*), 2.99-3.10 (m, 1H, C*H*COOCH$_3$), 3.19-3.29 (m, 1H, *C*HCHOSi), 3.61 (s, 3H, OC*H*$_3$), 3.84-3.94 (m, 1H, C*H*OTMP), 4.10-4.15 (m, 1H, C*H*OSi), 4.54-4.61 (m, 1H, C*H*OH), 5.05 (dd, *J* = 9.9, 15.3 Hz, 1H,

C*H*=CHCHOTMP), 5.46 (dd, *J* = 7.9, 15.4 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.8 (q, Si*C*H$_3$), –4.7 (q, Si*C*H$_3$), 9.8 (q, *C*H$_3$CH$_2$), 17.4 (t, NCCH$_2$*C*H$_2$), 18.1 (s, Si*C*(CH$_3$)$_3$), 20.4 (q, NC(*C*H$_3$)$_2$), 20.5 (q, NC(*C*H$_3$)$_2$), 25.93 (q, SiC(*C*H$_3$)$_3$), 27.6 (t, *C*H$_2$CH$_3$), 34.0 (q, NC(*C*H$_3$)$_2$), 35.5 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 42.5 (t, *C*H$_2$CHOSi), 51.6 (q, O*C*H$_3$), 54.6 (d, *C*HCHOSi), 56.8 (d, *C*HCOOCH$_3$), 59.4 (s, N*C*(CH$_3$)$_2$), 60.2 (s, N*C*(CH$_3$)$_2$), 74.2 (d, *C*HOH), 78.5 (d, *C*HOSi), 86.0 (d, *C*HOTMP), 127.8 (d, *C*H=CHCHOTMP), 136.6 (d, CH=*C*HCHOTMP), 173.4 (s, *C*OOCH$_3$).



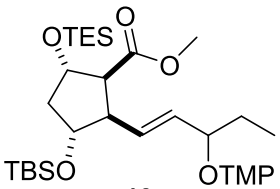
5b

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.06 (s, 3H, SiC*H*$_3$), 0.08 (s, 3H, SiC*H*$_3$), 0.82 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 0.881 (s, 9H, SiC(C*H*$_3$)$_3$), 1.03 (s, 6H, NC(C*H*$_3$)$_2$), 1.09 (s, 3H, NC(C*H*$_3$)$_2$), 1.12 (s, 3H, NC(C*H*$_3$)$_2$), 1.29-1.58 (m, 7H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CH$_3$), 1.65-1.78 (m, 1H, CH*H*CH$_3$), 1.86-2.01 (m, 2H, C*H*$_2$CHOSi), 2.71 (dd, *J* = 5.3, 8.2 Hz, 1H, C*H*COOCH$_3$), 3.25 (dt, *J* = 4.7, 8.0 Hz, 1H, C*H*CH=CH), 3.31 (d, *J* = 9.7 Hz, 1H, O*H*), 3.71 (s, 3H, OC*H*$_3$), 3.93 (td, *J* = 4.5, 8.2 Hz, 1H, C*H*OTMP), 4.04-4.10 (m, 1H, C*H*OSi), 4.41-4.49 (m, 1H, C*H*OH), 5.30 (dd, *J* = 8.3, 15.5 Hz, 1H, C*H*=CHCHOTMP), 5.44 (dd, *J* = 8.5, 15.8 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.8 (q, Si*C*H$_3$), –4.6 (q, Si*C*H$_3$), 10.0 (q, *C*H$_3$CH$_2$), 17.40 (t, NCCH$_2$*C*H$_2$), 18.0 (s, Si*C*(CH$_3$)$_3$), 20.4 (q, NC(*C*H$_3$)$_2$), 20.5 (q, NC(*C*H$_3$)$_2$), 25.88 (q, SiC(*C*H$_3$)$_3$), 27.5 (t, *C*H$_2$CH$_3$), 34.1 (q, NC(*C*H$_3$)$_2$), 35.4 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 43.2 (t, *C*H$_2$CHOSi), 51.9 (q, O*C*H$_3$), 52.1 (d, *C*HCHOSi), 56.7 (d, *C*HCOOCH$_3$), 59.3 (s, N*C*(CH$_3$)$_2$), 60.2 (s, N*C*(CH$_3$)$_2$), 75.3 (d, *C*HOH), 79.7 (d, *C*HOSi), 86.3 (d, *C*HOTMP), 131.5 (d, *C*H=CHCHOTMP), 134.0 (d, CH=*C*HCHOTMP), 172.35 (s, *C*OOCH$_3$).

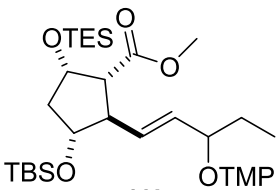
Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.08 (s, 3H, SiC*H*$_3$), 0.10 (s, 3H, SiC*H*$_3$), 0.77 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 0.884 (s, 9H, SiC(C*H*$_3$)$_3$), 1.03 (s, 6H, NC(C*H*$_3$)$_2$), 1.09 (s, 3H, NC(C*H*$_3$)$_2$), 1.12 (s, 3H, NC(C*H*$_3$)$_2$), 1.29-1.58 (m, 7H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CH$_3$), 1.65-1.78 (m, 1H, CH*H*CH$_3$), 1.86-2.01 (m, 2H, C*H*$_2$CHOSi), 2.67 (dd, *J* = 5.2, 8.1 Hz, C*H*COOCH$_3$), 3.25 (dt, *J* = 4.7, 8.0 Hz, 1H, C*H*CH=CH), 3.40 (d, *J* = 9.8 Hz, 1H, O*H*), 3.71 (s, 3H, OC*H*$_3$), 3.91 (td, *J* = 4.2, 8.4 Hz, 1H, C*H*OTMP), 4.10-4.15 (m, 1H, C*H*OSi), 4.41-4.49 (m, 1H, C*H*OH), 5.32 (dd, *J* = 8.4, 15.8 Hz, 1H, C*H*=CHCHOTMP), 5.46 (dd, *J* = 8.3,

15.4 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.8 (q, Si*C*H$_3$), –4.5 (q, Si*C*H$_3$), 10.0 (q, *C*H$_3$CH$_2$), 17.42 (t, NCCH$_2$*C*H$_2$), 18.0 (s, Si*C*(CH$_3$)$_3$), 20.4 (q, NC(*C*H$_3$)$_2$), 20.5 (q, NC(*C*H$_3$)$_2$), 25.90 (q, SiC(*C*H$_3$)$_3$), 27.4 (t, *C*H$_2$CH$_3$), 34.1 (q, NC(*C*H$_3$)$_2$), 35.4 (q, NC(*C*H$_3$)$_2$), 40.3 (t, NC*C*H$_2$), 43.1 (t, *C*H$_2$CHOSi), 51.9 (q, O*C*H$_3$), 52.1 (d, *C*HCHOSi), 56.7 (d, *C*HCOOCH$_3$), 59.3 (s, N*C*(CH$_3$)$_2$), 60.2 (s, N*C*(CH$_3$)$_2$), 75.1 (d, *C*HOH), 79.4 (d, *C*HOSi), 86.2 (d, *C*HOTMP), 131.4 (d, *C*H=CHCHOTMP), 133.6 (d, CH=*C*HCHOTMP), 172.44 (s, *C*OOCH$_3$).

Methyl (1*S,2*S**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane-2-carboxylate (13a),**
methyl (1*S,2*R**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane-2-carboxylate (13b) :**



13a

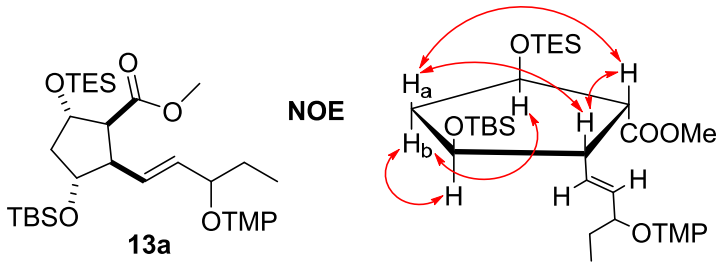


13b

***Method A2** (**5a** reacts faster)*: TESCl (5.8 mmol, 0.98 mL) was added dropwise to a solution of **5a**/**5b** (1.7:1, 9.1 mmol, 4.54 g) and imidazole (11.6 mmol, 790 mg) in dry DCM (120 mL) at –60 °C. The reaction was stopped by adding saturated NH_4Cl solution (100 mL) after 90 min. The layers were separated and the aqueous was extracted with Et_2O (3×100 mL). The combined organic layers were washed with water and brine, dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 80 g, hexane/EtOAc 80:1). Yield 3.37 g (95%) as a partially separable 6.2:1 mixture of **13a**/**13b** as a colorless oil.

***Method B2** (unselective)*: TESOTf (3.1 mmol, 700 μL) was added dropwise to a solution of **5a**/**5b** (1:2, 3.0 mmol, 1.48 g) and 2,6-lutidine (6.2 mmol, 720 μL) in dry DCM (40 mL) at –78 °C. The reaction was stopped by addition of water (2 mL) after 90 min, and the mixture was washed with saturated $KHSO_4$ solution and brine, dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 100 g, hexane/EtOAc

80:1). Yield 1.67 g (92%) as a partially separable 1:2 mixture of **13a**/**13b** as a colorless oil. The 16-C epimers of **13b** are also partially separable.

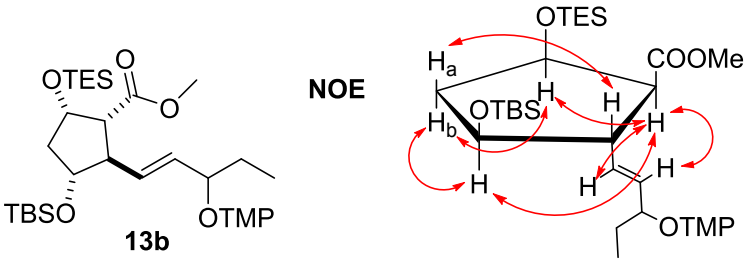


R_f (hexane/EtOAc 5:1) = 0.8. - IR (film): ν = 2963, 2938, 2885, 2856, 1741, 1467, 1440, 1380, 1365, 1259, 1285, 1187, 1166, 1129, 1096, 1009, 975, 890, 839, 778, 748, 672. - MS (+ESI) *m/z*, (%): 612 (100) $[M+H]^+$. - HRMS (+ESI) *m/z*: ($C_{33}H_{66}O_5NSi_2$) calc.: 612.4474, found: 612.4473.

Major C16 epimer: ^{1}H NMR (400 MHz): δ = –0.05 (s, 3H, SiC*H*$_3$), –0.03 (s, 3H, SiC*H*$_3$), 0.56 (q, *J* = 7.8 Hz, 6H, SiC*H*$_2$), 0.86 (t, *J* = 7.6 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.88 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.03 (br s, 3H, NC(C*H*$_3$)$_2$), 1.04 (br s, 3H, NC(C*H*$_3$)$_2$), 1.06 (br s, 3H, NC(C*H*$_3$)$_2$), 1.10 (br s, 3H, NC(C*H*$_3$)$_2$), 1.31-1.43 (m, 6H, NCC*H*$_2$C*H*$_2$C*H*$_2$), 1.57-1.67 (m, 1H, CH*H*CHOTMP), 1.69-1.79 (m, 2H, CH*H*CHOTMP, CH*H*CHOTBS), 2.34-2.46 (m, 1H, CH*H*CHOTBS), 2.85-2.94 (m, 1H, C*H*CHOTBS), 3.07 (dd, *J* = 5.5, 9.2 Hz, 1H, C*H*COOCH$_3$), 3.68 (s, 3H, OC*H*$_3$), 3.92-4.11 (m, 2H, C*H*OTBS, C*H*OTMP), 4.48 (dt, *J* = 5.5, 7.3 Hz, 1H, C*H*OTES), 5.15-5.29 (m, 1H, C*H*=CHCHOTMP), 5.45-5.55 (m, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.54 (q, SiCH$_3$), –4.3 (q, SiCH$_3$), 4.78 (t, SiCH$_2$), 6.8 (q, SiCH$_2$CH$_3$), 10.0 (q, CH$_3$CH$_2$CHOTMP), 17.5 (t, NCCH$_2$CH$_2$), 18.1 (s, SiC(CH$_3$)$_3$), 20.4 (q, NC(CH$_3$)$_2$), 20.6 (q, NC(CH$_3$)$_2$), 25.96 (q, SiC(CH$_3$)$_3$), 27.4 (t, CH$_2$CHOTMP), 34.2 (q, NC(CH$_3$)$_2$), 35.1 (q, NC(CH$_3$)$_2$), 40.4 (t, NCCH$_2$), 44.5 (t, CH$_2$CHOTBS), 51.6 (q, OCH$_3$), 53.2 (d, CHCHOTBS), 56.2 (d, CHCOOCH$_3$), 59.4 (s, NC(CH$_3$)$_2$), 60.1 (s, NC(CH$_3$)$_2$), 72.75 (d, CHOTES), 76.3 (d, CHOTBS), 85.8 (d, CHOTMP), 128.8 (d, CH=CHCHOTMP), 135.9 (d, CH=CHCHOTMP), 174.2 (s, COOCH$_3$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = –0.05 (s, 3H, SiC*H*$_3$), –0.03 (s, 3H, SiC*H*$_3$), 0.53 (q, *J* = 7.8 Hz, 6H, SiC*H*$_2$), 0.81 (t, *J* = 7.6 Hz, 3H, CH$_2$C*H*$_3$), 0.90 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.03 (br s, 3H, NC(C*H*$_3$)$_2$), 1.04 (br s, 3H, NC(C*H*$_3$)$_2$), 1.06 (br s, 3H, NC(C*H*$_3$)$_2$), 1.10 (br s, 3H, NC(C*H*$_3$)$_2$), 1.31-1.43 (m, 6H, NCC*H*$_2$C*H*$_2$C*H*$_2$), 1.57-1.67

(m, 1H, CH*H*CHOTMP), 1.69-1.79 (m, 2H, CH*H*CHOTMP, CH*H*CHOTBS), 2.34-2.46 (m, 1H, CH*H*CHOTBS), 2.85-2.94 (m, 1H, C*H*CHOTBS), 3.15 (dd, *J* = 6.3, 8.6 Hz, 1H, C*H*COOCH$_3$), 3.63 (s, 3H, OC*H*$_3$), 3.92-4.11 (m, 2H, C*H*OTBS, C*H*OTMP), 4.54 (dt, *J* = 6.1, 7.7 Hz, 1H, C*H*OTES), 5.15-5.29 (m, 1H, C*H*=CHCHOTMP), 5.45-5.55 (m, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.51 (q, SiCH$_3$), –4.3 (q, SiCH$_3$), 4.80 (t, SiCH$_2$), 6.8 (q, SiCH$_2$CH$_3$), 9.9 (q, CH$_3$CH$_2$CHOTMP), 17.5 (t, NCCH$_2$CH$_2$), 18.2 (s, SiC(CH$_3$)$_3$), 20.4 (q, NC(CH$_3$)$_2$), 20.6 (q, NC(CH$_3$)$_2$), 26.02 (q, SiC(CH$_3$)$_3$), 27.5 (t, CH$_2$CHOTMP), 34.3 (q, NC(CH$_3$)$_2$), 35.3 (q, NC(CH$_3$)$_2$), 40.5 (t, NCCH$_2$), 44.4 (t, CH$_2$CHOTBS), 51.5 (q, OCH$_3$), 53.9 (d, CHCHOTBS), 56.6 (d, CHCOOCH$_3$), 59.4 (s, NC(CH$_3$)$_2$), 60.1 (s, NC(CH$_3$)$_2$), 72.79 (d, CHOTES), 76.6 (d, CHOTBS), 86.0 (d, CHOTMP), 128.6 (d, CH=CHCHOTMP), 136.1 (d, CH=CHCHOTMP), 173.9 (s, COOCH$_3$).



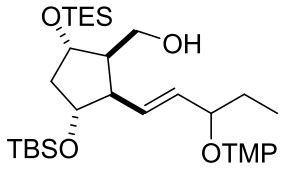
R$_f$ (hexane/EtOAc 5:1) = 0.8. - IR (film): ν = 2962, 2941, 2887, 1740, 1466, 1440, 1380, 1256, 1212, 1128, 1090, 1010, 973, 921, 889, 838, 777, 741, 672. - MS (+ESI) *m/z*, (%): 612 (100) [M+H]$^+$, 158 (3) [TMPOH+H]$^+$. - HRMS (+ESI) *m/z*: (C$_{33}$H$_{66}$O$_5$NSi$_2$) calc.: 612.4474, found: 612.4474.

Less polar C16 epimer: ^{1}H NMR (400 MHz): δ = 0.015 (s, 3H, SiC*H*$_3$), 0.022 (s, 3H, SiC*H*$_3$), 0.54 (q, *J* = 7.9 Hz, 6H, SiC*H*$_2$), 0.76 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.91 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.02 (br s, 6H, NC(C*H*$_3$)$_2$), 1.06 (br s, 3H, NC(C*H*$_3$)$_2$), 1.11 (br s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.32 (m, 1H, NCCH$_2$CH*H*), 1.33-1.42 (m, 5H, NCC*H*$_2$CH*H*C*H*$_2$), 1.42-1.51 (m, 1H, CH*H*CHOTMP), 1.65-1.80 (m, 2H, CH*H*CHOTMP, CH*H*CHOTBS), 2.28 (ddd, *J* = 6.4, 7.7, 11.7 Hz, 1H, CH*H*CHOTBS), 2.60 (dd, *J* = 6.7, 11.8 Hz, C*H*COOCH$_3$), 3.12 (ddd, *J* = 5.5, 8.6, 11.9 Hz, 1H, C*H*CHOTBS), 3.61 (s, 3H, OC*H*$_3$), 3.76 (dt, *J* = 7.7, 8.6 Hz, 1H, C*H*OTBS), 3.95 (ddd, *J* = 4.5, 7.0, 8.5 Hz, 1H, C*H*OTMP), 4.35 (td, *J* = 4.6, 6.5 Hz, 1H, C*H*OTES), 5.35-5.53 (m, 2H, C*H*=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.4 (q, SiC*H*$_3$), –4.29 (q, SiC*H*$_3$), 4.84 (t, SiC*H*$_2$), 6.9 (q, SiCH$_2$C*H*$_3$), 10.1 (q, C*H*$_3$CH$_2$CHOTMP), 17.5 (t, NCCH$_2$C*H*$_2$), 18.2 (s, SiC(CH$_3$)$_3$), 20.43 (q, NC(C*H*$_3$)$_2$), 20.58 (q, NC(C*H*$_3$)$_2$), 26.0 (q, SiC(C*H*$_3$)$_3$), 27.4 (t, C*H*$_2$CHOTMP), 34.3 (q, NC(C*H*$_3$)$_2$), 35.1 (q,

NC(CH_3)$_2$), 40.3 (t, NCCH_2), 45.2 (t, CH_2CHOTBS), 50.0 (d, CHCHOTBS), 51.4 (q, OCH_3), 54.2 (d, CHCOOCH$_3$), 59.4 (s, NC(CH$_3$)$_2$), 60.0 (s, NC(CH$_3$)$_2$), 70.96 (d, CHOTES), 76.3 (d, CHOTBS), 86.3 (d, CHOTMP), 131.1 (d, CH=CHCHOTMP), 133.6 (d, CH=CHCHOTMP), 171.4 (s, COOCH$_3$).

More polar C16 epimer: ^{1}H NMR (400 MHz): δ = 0.04 (s, 6H, SiCH_3), 0.56 (q, *J* = 7.9 Hz, 6H, SiCH_2), 0.85 (t, *J* = 7.5 Hz, 3H, CH_3CH$_2$CHOTMP), 0.89 (s, 9H, SiC(CH_3)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$CH_3), 1.02 (br s, 3H, NC(CH_3)$_2$), 1.05 (br s, 3H, NC(CH_3)$_2$), 1.12 (br s, 3H, NC(CH_3)$_2$), 1.16 (br s, 3H, NC(CH_3)$_2$), 1.25-1.35 (m, 1H, NCCH$_2$CHH), 1.33-1.42 (m, 4H, NCCH_2CH$_2$CH_2), 1.42-1.51 (m, 2H, CHHCHOTMP, NCCH$_2$CHH), 1.65-1.80 (m, 2H, CHHCHOTMP, CHHCHOTBS), 2.30 (ddd, *J* = 6.4, 7.5, 13.5 Hz, 1H, CHHCHOTBS), 2.69 (dd, *J* = 7.1, 11.4 Hz, CHCOOCH$_3$), 3.14 (ddd, *J* = 6.8, 8.5, 11.4 Hz, 1H, CHCHOTBS), 3.66 (s, 3H, OCH_3), 3.77 (dt, *J* = 7.8, 8.6 Hz, 1H, CHOTBS), 3.97 (td, *J* = 4.6, 7.9 Hz, 1H, CHOTMP), 4.39 (td, *J* = 6.5, 11.9 Hz, 1H, CHOTES), 5.35-5.53 (m, 2H, CH=CHCHOTMP). - ^{13}C NMR (100 MHz): δ = –4.5 (q, SiCH$_3$), –4.26 (q, SiCH$_3$), 4.83 (t, SiCH$_2$), 6.9 (q, SiCH$_2$$CH_3$), 10.0 (q, CH$_3CH_2$CHOTMP), 17.4 (t, NCCH$_2$$CH_2$), 18.1 (s, Si$C$(CH$_3$)$_3$), 20.37 (q, NC($CH_3$)$_2$), 20.55 (q, NC($CH_3$)$_2$), 25.9 (q, SiC($CH_3$)$_3$), 27.6 (t, CH$_2$CHOTMP), 34.2 (q, NC(CH$_3$)$_2$), 35.5 (q, NC(CH$_3$)$_2$), 40.4 (t, NCCH$_2$), 45.0 (t, CH$_2$CHOTBS), 50.5 (d, CHCHOTBS), 51.5 (q, OCH$_3$), 54.0 (d, CHCOOCH$_3$), 59.1 (s, NC(CH$_3$)$_2$), 60.1 (s, NC(CH$_3$)$_2$), 70.98 (d, CHOTES), 76.1 (d, CHOTBS), 86.5 (d, CHOTMP), 131.5 (d, CH=CHCHOTMP), 134.1 (d, CH=CHCHOTMP), 171.5 (s, COOCH$_3$).

(1*S,2*R**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(hydroxymethyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane (14):**



Dibal-H (3.70 mmol, 3.7 mL, 1 M in DCM) was added dropwise to a solution of ester **13a** (1.24 mmol, 760 mg) in dry DCM (25 mL) at –78 °C. The reaction was stirred at –78 °C for 60 min and subsequently quenched by a few drops of MeOH. The mixture was diluted with Et_2O, filtered through a plug of sand and celite and dried over $MgSO_4$. The solvent was evaporated and the crude material was purified by column chromatography (silica gel 40 g, hexane/EtOAc 40:1 gradient to 10:1, with 0.5 vol% of Et_3N). Yield 694 mg (96%) as a

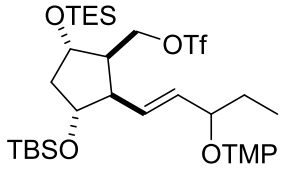
colorless oil. - R_f (hexane/EtOAc 5:1) = 0.6. - IR (film): ν = 3417, 2964, 2935, 2864, 1467, 1380, 1257, 1187, 1075, 1009, 976, 838, 778, 745, 671. - MS (+ESI) *m/z*, (%): 584 (52) $[M+H]^+$, 470 (100) $[M–HOTES+H_2O+H]^+$. - HRMS (+ESI) *m/z*: ($C_{32}H_{66}O_4NSi_2$) calc.: 584.4525, found: 584.4524.

Major C16 epimer: ^{1}H NMR (400 MHz): δ = –0.03 (s, 3H, SiC*H*$_3$), –0.01 (s, 3H, SiC*H*$_3$), 0.56 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.85 (s, 9H, SiC(C*H*$_3$)$_3$), 0.89 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.93 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.037 (s, 3H, NC(C*H*$_3$)$_2$), 1.05 (s, 3H, NC(C*H*$_3$)$_2$), 1.12 (s, 3H, NC(C*H*$_3$)$_2$), 1.142 (s, 3H, NC(C*H*$_3$)$_2$), 1.30-1.70 (m, 9H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CHOTBS, C*H*$_2$CHOTMP), 2.24 (td, *J* = 6.4, 12.9 Hz, 1H, CH*H*CHOTBS), 2.33-2.42 (m, 1H, C*H*CHOTES), 2.66 (dt, *J* = 5.1, 10.1 Hz, 1H, C*H*CHOTBS), 2.99 (br s, 1H, O*H*), 3.68 (d, *J* = 6.2 Hz, 2H, C*H*$_2$OH), 3.78 (ddd, 1H, *J* = 5.1, 6.3, 7.4 Hz, 1H, C*H*OTBS), 3.87 (dt, *J* = 6.9, 8.4 Hz, 1H, C*H*OTES), 4.10 (dt, *J* = 6.2, 9.3 Hz, 1H, C*H*OTMP), 5.40 (dd, *J* = 10.1, 15.2 Hz, 1H, C*H*=CHCHOTMP), 5.51-5.60 (m, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.4 (q, Si*C*H$_3$), 5.03 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 10.2 (q, *C*H$_3$CH$_2$CHOTMP), 17.4 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.8 (q, NC(*C*H$_3$)$_2$), 20.9 (q, NC(*C*H$_3$)$_2$), 25.96 (q, SiC(*C*H$_3$)$_3$), 27.7 (t, *C*H$_2$CHOTMP), 34.4 (q, NC(*C*H$_3$)$_2$), 34.5 (q, NC(*C*H$_3$)$_2$), 39.3 (t, NC*C*H$_2$), 39.8 (t, NC*C*H$_2$), 44.6 (t, *C*H$_2$CHOTBS), 52.1 (d, *C*HCHOTES), 53.4 (d, *C*HCHOTBS), 59.6 (s, N*C*(CH$_3$)$_2$), 61.2 (s, N*C*(CH$_3$)$_2$), 62.1 (t, *C*H$_2$OH), 72.7 (d, *C*HOTES), 76.1 (d, *C*HOTBS), 85.6 (d, *C*HOTMP), 133.6 (d, *C*H=CHCHOTMP), 135.4 (d, CH=*C*HCHOTMP).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.02 (s, 6H, SiC*H*$_3$), 0.57 (q, *J* = 7.9 Hz, 6H, SiC*H*$_2$), 0.83 (s, 9H, SiC(C*H*$_3$)$_3$), 0.89 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.93 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.042 (s, 3H, NC(C*H*$_3$)$_2$), 1.07 (s, 3H, NC(C*H*$_3$)$_2$), 1.10 (s, 3H, NC(C*H*$_3$)$_2$), 1.137 (s, 3H, NC(C*H*$_3$)$_2$), 1.25-1.65 (m, 9H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CHOTBS, C*H*$_2$CHOTMP), 2.28-2.44 (m, 2H, CH*H*CHOTBS, C*H*CHOTES), 2.56 (br t, *J* = 6.3 Hz, 1H, O*H*), 2.72 (td, *J* = 5.9, 9.2 Hz, 1H, C*H*CHOTBS), 3.55-3.62 (m, 1H, CH*H*OH), 3.64-3.70 (m, 1H, CH*H*OH), 3.97-4.12 (m, 3H, C*H*OTBS, C*H*OTES, C*H*OTMP), 5.43-5.58 (m, 2H, C*H*=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.1 (q, Si*C*H$_3$), 5.01 (t, Si*C*H$_2$), 6.9 (q, SiCH$_2$*C*H$_3$), 10.2 (q, *C*H$_3$CH$_2$CHOTMP), 17.5 (t, NCCH$_2$*C*H$_2$), 18.1 (s, Si*C*(CH$_3$)$_3$), 20.7 (q, NC(*C*H$_3$)$_2$), 20.8 (q, NC(*C*H$_3$)$_2$), 25.99 (q, SiC(*C*H$_3$)$_3$), 27.7 (t, *C*H$_2$CHOTMP), 34.4 (q, NC(*C*H$_3$)$_2$), 39.7 (t, NC*C*H$_2$), 40.0 (t, NC*C*H$_2$), 44.9 (t, *C*H$_2$CHOTBS), 50.8 (d, *C*HCHOTES), 51.9 (d, *C*HCHOTBS), 59.7 (s, N*C*(CH$_3$)$_2$), 61.1 (s, N*C*(CH$_3$)$_2$), 63.1 (t,

*C*H$_2$OH), 73.9 (d, *C*HOTES), 74.5 (d, *C*HOTBS), 86.3 (d, *C*HOTMP), 131.2 (d, *C*H=CHCHOTMP), 133.5 (d, CH=*C*HCHOTMP).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)-2-(((trifluoromethanesulfonyl)oxy)methyl)cyclopentane (15):**



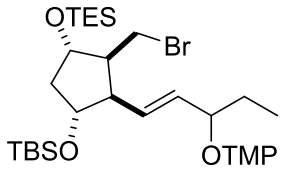
Alcohol **14** (0.68 mmol, 398 mg) was dissolved in dry DCM (13 mL) and 2,6-lutidine (0.80 mmol, 0.09 mL) was added after cooling to –78 °C. A solution of triflic anhydride (0.75 mmol, 0.75 mL, 1 M in DCM) was added dropwise. The reaction was stirred for 60 min and warmed to –60 °C. The mixture was poured into pentane (150 mL) and filtered through a plug of sand and celite. The solvent was evaporated and the crude material was purified by column chromatography (silica gel 10 g, hexane/EtOAc 50:1 gradient to 30:1, with 0.5 vol% of Et_3N). Yield 477 mg (98%) as a colorless oil. - R_f (hexane/EtOAc 20:1) = 0.8. - IR (film): ν = 2966, 2942, 2888, 1469, 1421, 1381, 1250, 1212, 1151, 1124, 1068, 1009, 977, 939, 838, 779, 747. - MS (+ESI) *m/z*, (%): 716 (100) $[M+H]^+$, 584 (20) $[M–HOTES+H]^+$, 567 (24) $[M–OTf+H]^+$, 452 (10) $[M–HOTES–HOTBS+H]^+$. - HRMS (+ESI) *m/z*: ($C_{33}H_{65}O_6NF_3SSi_2$) calc.: 716.4018, found: 716.4018.

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.01 (s, 3H, SiC*H*$_3$), 0.02 (s, 3H, SiC*H*$_3$), 0.58 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.852 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.87 (s, 9H, SiC(C*H*$_3$)$_3$), 0.96 (t, *J* = 8.1 Hz, 9H, SiCH$_2$C*H*$_3$), 1.08 (br s, 6H, NC(C*H*$_3$)$_2$), 1.13 (br s, 3H, NC(C*H*$_3$)$_2$), 1.17 (br s, 3H, NC(C*H*$_3$)$_2$), 1.27-1.59 (m, 7H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CHOTMP), 1.60-1.69 (m, 1H, CH*H*CHOTBS), 1.70-79 (m, 1H, CH*H*CHOTMP), 2.39 (ddd, *J* = 6.5, 7.8, 14.0 Hz, 1H, CH*H*CHOTBS), 2.59 (dq, *J* = 6.5, 8.2 Hz, 1H, C*H*CHOTES), 2.74-2.83 (m, 1H, C*H*CHOTBS), 3.94 (dt, *J* = 4.9, 6.4 Hz, 1H, C*H*OTBS), 4.01-4.10 (m, 2H, C*H*OTES, C*H*OTMP), 4.61 (d, *J* = 6.3 Hz, 2H, C*H*$_2$OTf), 5.19 (ddd, *J* = 0.7, 9.4, 15.3 Hz, 1H, C*H*=CHCHOTMP), 5.55 (ddd, *J* = 0.9, 8.4, 15.5 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.6 (q, Si*C*H$_3$), 4.9 (t, Si*C*H$_2$), 6.9 (q, SiCH$_2$*C*H$_3$), 10.0 (q, *C*H$_3$CH$_2$CHOTMP), 17.4 (t, NCCH$_2$*C*H$_2$), 18.1 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 25.9 (q, SiC(*C*H$_3$)$_3$), 27.4 (t, *C*H$_2$CHOTMP), 34.3 (q, NC(*C*H$_3$)$_2$), 35.0 (q, NC(*C*H$_3$)$_2$), 40.4 (t,

NC*C*H$_2$), 44.5 (t, *C*H$_2$CHOTBS), 49.7 (d, *C*HCHOTES), 51.7 (d, *C*HCHOTBS), 59.4 (s, N*C*(CH$_3$)$_2$), 61.3 (s, N*C*(CH$_3$)$_2$), 72.5 (d, *C*HOTES), 75.8 (d, *C*HOTBS), 77.3 (t, *C*H$_2$OTf), 85.8 (d, *C*HOTMP), 118.8 (q, J_{CF} = 320 Hz, *C*F$_3$), 127.8 (d, *C*H=CHCHOTMP), 137.3 (d, CH=*C*HCHOTMP).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.04 (s, 3H, SiC*H*$_3$), 0.05 (s, 3H, SiC*H*$_3$), 0.57 (q, *J* = 8.1 Hz, 6H, SiC*H*$_2$), 0.854 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.88 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.08 (br s, 6H, NC(C*H*$_3$)$_2$), 1.13 (br s, 3H, NC(C*H*$_3$)$_2$), 1.17 (br s, 3H, NC(C*H*$_3$)$_2$), 1.27-1.59 (m, 7H, NCC*H*$_2$C*H*$_2$C*H*$_2$, CH*H*CHOTMP), 1.60-1.69 (m, 1H, CH*H*CHOTBS), 1.70-1.79 (m, 1H, CH*H*CHOTMP), 2.44 (ddd, *J* = 6.3, 8.0, 14.1 Hz, 1H, CH*H*CHOTBS), 2.68 (dq, *J* = 7.9, 5.4 Hz, 1H, C*H*CHOTES), 2.74-2.83 (m, 1H, C*H*CHOTBS), 4.01-4.10 (m, 3H, C*H*OTBS, C*H*OTES, C*H*OTMP), 4.45-4.57 (m, 2H, C*H*$_2$OTf), 5.12 (ddd, *J* = 0.7, 9.5, 15.4 Hz, 1H, C*H*=CHCHOTMP), 5.56 (ddd, *J* = 0.9, 8.3, 15.5 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.5 (q, Si*C*H$_3$), 4.9 (t, Si*C*H$_2$), 6.9 (q, SiCH$_2$*C*H$_3$), 9.9 (q, *C*H$_3$CH$_2$CHOTMP), 17.5 (t, NCCH$_2$*C*H$_2$), 18.3 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 26.0 (q, SiC(*C*H$_3$)$_3$), 27.5 (t, *C*H$_2$CHOTMP), 34.3 (q, NC(*C*H$_3$)$_2$), 35.0 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.4 (t, *C*H$_2$CHOTBS), 49.5 (d, *C*HCHOTES), 52.1 (d, *C*HCHOTBS), 59.4 (s, N*C*(CH$_3$)$_2$), 61.3 (s, N*C*(CH$_3$)$_2$), 72.6 (d, *C*HOTES), 75.7 (d, *C*HOTBS), 77.3 (t, *C*H$_2$OTf), 86.0 (d, *C*HOTMP), 118.8 (q, J_{CF} = 320 Hz, *C*F$_3$), 126.9 (d, *C*H=CHCHOTMP), 137.5 (d, CH=*C*HCHOTMP).

(1*S,2*S**,3*R**,4*R**)-2-(Bromomethyl)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane (18):**



A solution of hept-6-en-1-ylmagnesium bromide (**16a**) (0.45 mmol, 1.5 mL, 0.3 M in THF) was cooled to 0 °C and copper(I) bromide-dimethyl sulfide complex (0.04 mmol, 9 mg) was added. A solution of triflate **15** (0.22 mmol, 160 mg) in dry THF (1 mL) was added dropwise by canula, which was flushed with dry THF (1 mL). The reaction was stirred at 0 °C for 2.5 h and subsequently quenched with saturated NH_4Cl solution (5 mL). The layers were separated and the aqueous was extracted with Et_2O (2×5 mL). The combined organic fractions were washed with brine (20 mL) and dried over $MgSO_4$. The solvent was evaporated and the crude

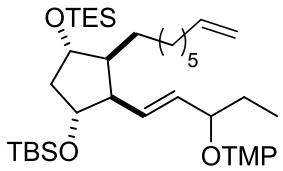
material was partially purified by column chromatography (silica gel 20 g, hexane/EtOAc 60:1 gradient to 30:1, with 0.5 vol% of Et_3N), since the alkyl-alkyl coupling product **17** was not separable from bromide **18**. Yield 110 mg (77%) as a pale yellow oil. - R_f (hexane/EtOAc 20:1) = 0.6. - IR (film): ν = 2964, 2939, 2886, 1467, 1379, 1364, 1255, 1187, 1115, 1069, 1008, 972, 882, 836, 777, 728, 672. - MS (+ESI) *m/z*, (%): 648/646 (100/97) $[M+H]^+$, 566 (8) $[M–HBr+H]^+$, 514/512 (16/15) $[M–TEMPO+Na]^+$, 158 (12) $[TMPOH+H]^+$. - HRMS (+ESI) *m/z*: ($C_{32}H_{65}O_3N^{79}BrSi_2$) calc.: 646.3681, found: 646.3684; ($C_{32}H_{65}O_3N^{81}BrSi_2$) calc.: 648.3660, found: 646.3664.

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.02 (s, 6H, SiC*H*$_3$), 0.59 (q, *J* = 7.9 Hz, 6H, SiC*H*$_2$), 0.85 (t, *J* = 7.6 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.87 (s, 9H, SiC(C*H*$_3$)$_3$), 0.953 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.06 (s, 6H, NC(C*H*$_3$)$_2$), 1.10 (s, 3H, NC(C*H*$_3$)$_2$), 1.16 (s, 3H, NC(C*H*$_3$)$_2$), 1.28-1.36 (m, 1H, NCCH$_2$CH*H*), 1.38-1.49 (m, 4H, NCC*H*$_2$), 1.45-1.55 (m, 1H, CH*H*CHOTMP), 1.50-1.59 (m, 1H, NCCH$_2$CH*H*), 1.63 (ddd, *J* = 5.0, 6.4, 13.2 Hz, 1H, CH*H*CHOTBS), 1.67-1.77 (m, 1H, CH*H*CHOTMP), 2.42 (td, *J* = 7.0, 13.2 Hz, 1H, CH*H*CHOTBS), 2.61 (dtd, *J* = 5.0, 7.5, 15.0 Hz, 1H, C*H*CHOTES), 2.73-2.82 (m, 1H, C*H*CHOTBS), 3.43-3.56 (m, 2H, C*H*$_2$Br), 3.92-4.06 (m, 3H, C*H*OTBS, C*H*OTES, C*H*OTMP), 5.28 (dd, *J* = 9.3, 15.5 Hz, 1H, C*H*=CHCHOTMP), 5.53 (dd, *J* = 8.5, 15.6 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.50 (q, Si*C*H$_3$), –4.48 (q, Si*C*H$_3$), 5.0 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 10.1 (q, *C*H$_3$CH$_2$CHOTMP), 17.50 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 25.99 (q, SiC(*C*H$_3$)$_3$), 27.61 (t, *C*H$_2$CHOTMP), 33.6 (t, *C*H$_2$Br), 34.4 (q, NC(*C*H$_3$)$_2$), 35.0 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 45.0 (t, *C*H$_2$CHOTBS), 52.3 (d, *C*HCHOTES), 52.6 (d, *C*HCHOTBS), 59.3 (s, N*C*(CH$_3$)$_2$), 60.3 (s, N*C*(CH$_3$)$_2$), 74.7 (d, *C*HOTES), 75.3 (d, *C*HOTBS), 86.3 (d, *C*HOTMP), 129.0 (d, *C*H=CHCHOTMP), 136.1 (d, CH=*C*HCHOTMP).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.03 (s, 3H, SiC*H*$_3$), 0.04 (s, 3H, SiC*H*$_3$), 0.58 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.85 (t, *J* = 7.6 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.88 (s, 9H, SiC(C*H*$_3$)$_3$), 0.948 (t, *J* = 7.8 Hz, 9H, SiCH$_2$C*H*$_3$), 1.06 (s, 6H, NC(C*H*$_3$)$_2$), 1.10 (s, 3H, NC(C*H*$_3$)$_2$), 1.16 (s, 3H, NC(C*H*$_3$)$_2$), 1.28-1.36 (m, 1H, NCCH$_2$CH*H*), 1.38-1.49 (m, 4H, NCC*H*$_2$), 1.48-1.59 (m, 2H, CH*H*CHOTMP, NCCH$_2$CH*H*), 1.59-1.69 (m, 1H, CH*H*CHOTBS), 1.70-1.80 (m, 1H, CH*H*CHOTMP), 2.46 (ddd, *J* = 6.7, 8.1, 13.8 Hz, 1H, CH*H*CHOTBS), 2.60-2.68 (m, 1H, C*H*CHOTES), 2.73-2.82 (m, 1H, C*H*CHOTBS), 3.43-3.56 (m, 2H, C*H*$_2$Br), 3.87 (dt, *J* = 6.0, 8.1 Hz, 1H, C*H*OTES), 3.95-4.06 (m, 2H, C*H*OTBS, C*H*OTMP), 5.14 (dd, *J* = 9.6, 15.4 Hz, 1H, C*H*=CHCHOTMP), 5.56 (dd, *J* = 8.6, 15.3 Hz,

1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.54 (q, Si*C*H$_3$), –4.43 (q, Si*C*H$_3$), 5.0 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 10.0 (q, *C*H$_3$CH$_2$CHOTMP), 17.47 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 26.02 (q, SiC(*C*H$_3$)$_3$), 27.64 (t, *C*H$_2$CHOTMP), 33.3 (t, *C*H$_2$Br), 34.2 (q, NC(*C*H$_3$)$_2$), 35.2 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 45.2 (t, *C*H$_2$CHOTBS), 52.2 (d, *C*HCHOTES), 53.1 (d, *C*HCHOTBS), 59.3 (s, N*C*(CH$_3$)$_2$), 60.3 (s, N*C*(CH$_3$)$_2$), 75.0 (d, *C*HOTES), 75.1 (d, *C*HOTBS), 86.5 (d, *C*HOTMP), 127.4 (d, *C*H=CHCHOTMP), 136.7 (d, CH=*C*HCHOTMP).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(oct-7-en-1-yl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane (17):**



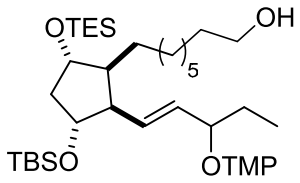
Anhydrous LiCl (2.41 mmol, 102 mg) was flame-dried under reduced pressure in a Schlenk flask. THF (5 mL) and hept-6-en-1-ylmagnesium chloride (**16b**) (1.2 mmol, 1.5 mL, 0.8 M in THF) were added at r.t. under an argon atmosphere. The mixture was cooled to –78 °C and copper(I) bromide-dimethyl sulfide complex (0.18 mmol, 37 mg) was added. A solution of triflate **15** (0.46 mmol, 330 mg) in dry THF (5 mL) was added dropwise by canula, which was flushed with THF (5 mL). The reaction mixture was stirred and slowly warmed to –50 °C. The reaction was quenched with saturated NH_4Cl solution (10 mL) after 3 h. The layers were separated and the aqueous was extracted with Et_2O (2×10 mL). The combined organic fractions were washed with saturated NH_4Cl solution (2×30 mL), brine (30 mL) and dried over $MgSO_4$. The solvent was evaporated and the crude material was purified by column chromatography (silica gel 40 g, hexane/EtOAc/Et_3N 100:1:1). Yield 217 mg (71%) as a colorless oil. - R_f (hexane/EtOAc 20:1) = 0.6. - IR (film): ν = 2964, 2935, 2885, 2864, 1463, 1422, 1379, 1365, 1257, 1115, 1067, 1008, 974, 912, 837, 777, 744, 727, 672. - MS (+ESI) *m/z*, (%): 664 (100) $[M+H]^+$, 530 (10) $[M–OTMP+Na]^+$, 158 (7) $[TMPOH+H]^+$. - HRMS (+ESI) *m/z*: ($C_{39}H_{78}O_3NSi_2$) calc.: 664.5515, found: 664.5514.

Major C16 epimer : ^{1}H NMR (400 MHz): δ = 0.00 (s, 3H, SiC*H*$_3$), 0.01 (s, 3H, SiC*H*$_3$), 0.57 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.83 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.06 (s, 3H, NC(C*H*$_3$)$_2$), 1.10 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.26-1.37 (m, 11H, C*H*$_2$, NCCH$_2$CH*H*), 1.39-1.49 (m,

5H, NCCH_2CH$_2$CH_2, CHHCHOTMP), 1.50-1.60 (m, 2H, CHHCHOTBS, NCCH$_2$CHH), 1.68-1.78 (m, 1H, CHHCHOTMP), 1.99-2.08 (m, 3H, CHCHOTES, CH_2CH=CH$_2$), 2.34 (dt, J = 7.3, 14.8 Hz, 1H, CHHCHOTBS), 2.52-2.61 (m, 1H, CHCHOTBS), 3.78 (dq, J = 1.3, 7.3 Hz, 1H, CHOTES), 3.89 (dt, J = 3.8, 7.2 Hz, 1H, CHOTBS), 3.93-4.00 (m, 1H, CHOTMP), 4.92 (ddt, J = 1.2, 2.3, 10.2 Hz, 1H, CH=CHH), 4.99 (ddt, J = 1.6, 2.3, 17.1 Hz, 1H, CH=CHH), 5.24 (dd, J = 9.2, 15.5 Hz, 1H, CH=CHCHOTMP), 5.40 (ddd, J = 0.7, 8.3, 15.5 Hz, 1H, CH=CHCHOTMP), 5.808 (tdd, J = 6.6, 10.1, 16.9 Hz, 1H, CH=CH$_2$). - ^{13}C NMR (100 MHz): δ = –4.48 (q, SiCH$_3$), –4.45 (q, SiCH$_3$), 5.1 (t, SiCH$_2$), 7.0 (q, SiCH$_2$$CH_3$), 10.1 (q, CH$_3CH_2$CHOTMP), 17.51 (t, NCCH$_2$$CH_2$), 18.2 (s, Si$C$(CH$_3$)$_3$), 20.5 (q, NC$CH_3$), 20.6 (q, NC$CH_3$), 26.03 (q, SiC($CH_3$)$_3$), 27.70 (t, CH$_2$CHOTMP), 28.4 (t, CH$_2$), 28.7 (t, CH$_2$), 29.2 (t, CH$_2$), 29.34 (t, CH$_2$), 30.1 (t, CH$_2$), 33.98 (t, CH$_2$CH=CH$_2$), 34.3 (q, NC(CH$_3$)$_2$), 35.2 (q, NC(CH$_3$)$_2$), 40.4 (t, NCCH$_2$), 44.7 (t, CH$_2$CHOTBS), 49.2 (d, CHCHOTES), 52.8 (d, CHCHOTBS), 59.4 (s, NC(CH$_3$)$_2$), 60.1 (s, NC(CH$_3$)$_2$), 76.4 (d, CHOTBS), 76.6 (d, CHOTES), 86.5 (d, CHOTMP), 114.2 (t, CH=CH$_2$), 130.5 (d, CH=CHCHOTMP), 134.2 (d, CH=CHCHOTMP), 139.4 (d, CH=CH$_2$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.02 (s, 6H, SiCH_3), 0.58 (q, J = 8.0 Hz, 6H, SiCH_2), 0.82 (t, J = 7.5 Hz, 3H, CH_3CH$_2$CHOTMP), 0.87 (s, 9H, SiC(CH_3)$_3$), 0.95 (t, J = 7.9 Hz, 9H, SiCH$_2$CH_3), 1.06 (s, 3H, NC(CH_3)$_2$), 1.10 (s, 6H, NC(CH_3)$_2$), 1.15 (s, 3H, NC(CH_3)$_2$), 1.26-1.37 (m, 11H, CH_2, NCCH$_2$CHH), 1.39-1.49 (m, 5H, NCCH_2CH$_2$CH_2, CHHCHOTMP), 1.50-1.60 (m, 2H, CHHCHOTBS, NCCH$_2$CHH), 1.68-1.78 (m, 1H, CHHCHOTMP), 1.99-2.08 (m, 3H, CHCHOTES, CH_2CH=CH$_2$), 2.38 (dt, J = 7.3, 13.9 Hz, 1H, CHHCHOTBS), 2.52-2.61 (m, 1H, CHCHOTBS), 3.74-3.80 (m, 1H, CHOTES), 3.92-4.01 (m, 2H, CHOTMP, CHOTBS), 4.92 (ddt, J = 1.2, 2.3, 10.2 Hz, 1H, CH=CHH), 4.99 (ddt, J = 1.6, 2.3, 17.1 Hz, 1H, CH=CHH), 5.13 (dd, J = 9.9, 15.4 Hz, 1H, CH=CHCHOTMP), 5.40 (dd, J = 8.0, 15.4 Hz, 1H, CH=CHCHOTMP), 5.806 (tdd, J = 6.7, 10.1, 16.9 Hz, 1H, CH=CH$_2$). - ^{13}C NMR (100 MHz): δ = –4.49 (q, SiCH$_3$), –4.39 (q, SiCH$_3$), 5.1 (t, SiCH$_2$), 7.0 (q, SiCH$_2$$CH_3$), 9.9 (q, CH$_3CH_2$CHOTMP), 17.48 (t, NCCH$_2$$CH_2$), 18.2 (s, Si$C$(CH$_3$)$_3$), 20.5 (q, NC($CH_3$)$_2$), 20.6 (q, NC($CH_3$)$_2$), 26.05 (q, SiC($CH_3$)$_3$), 27.72 (q, CH$_2$CHOTMP), 28.0 (t, CH$_2$), 28.8 (t, CH$_2$), 29.1 (t, CH$_2$), 29.28 (t, CH$_2$), 30.0 (t, CH$_2$), 33.96 (t, CH$_2$CH=CH$_2$), 34.2 (q, NC(CH$_3$)$_2$), 35.5 (q, NC(CH$_3$)$_2$), 40.4 (t, NCCH$_2$), 44.7 (t, CH$_2$CHOTBS), 49.0 (d, CHCHOTES), 53.5 (d, CHCHOTBS), 59.3 (s, NC(CH$_3$)$_2$), 60.1 (s, NC(CH$_3$)$_2$), 76.1 (d, CHOTBS), 76.8 (d, CHOTES), 86.7 (d, CHOTMP), 114.2 (t, CH=CH$_2$), 129.6 (d, CH=CHCHOTMP), 134.7 (d, CH=CHCHOTMP), 139.4 (d, CH=CH$_2$).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-hydroxyoctyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane (19):**



Method A3: 9-BBN solution (0.80 mmol, 1.6 mL, 0.5 M in THF) was added to olefin **17** (0.20 mmol, 130 mg) and the reaction mixture was stirred under an argon atmosphere at r.t. for 20 h. A 10% NaOH solution (2.5 mL) and 30% H_2O_2 solution (2.5 mL) were subsequently added. The mixture was stirred for another hour, neutralized with saturated NH_4Cl solution (20 mL) and extracted with Et_2O (3×10 mL). The combined organic layers were washed with 10% $Na_2S_2O_3$ solution, dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 15 g, hexane/EtOAc 40:1 gradient to 1:1, with 0.5 vol% of Et_3N). Yield 131 mg (98%) as a colorless oil.

Method B3 *(microwave)*: A solution of olefin **17** (0.18 mmol, 122 mg) in THF (0.5 mL) in a microwave reactor tube was degassed by three freeze-pump-thaw cycles and filled with argon. A 9-BBN solution (0.25 mmol, 0.5 mL, 0.5 M in THF) was added and the reaction mixture was heated in a microwave reactor at 85 °C for 45 min. A 10% NaOH solution (0.8 mL) and 30% H_2O_2 solution (0.8 mL) were subsequently added and the mixture was stirred at r.t. for 30 min, neutralized with saturated NH_4Cl solution (20 mL) and extracted with Et_2O (3×10 mL). The combined organic layers were washed with 10% $Na_2S_2O_3$ solution, dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 15 g, hexane/EtOAc 40:1 gradient to 1:1, with 0.5 vol% of Et_3N). Yield 125 mg (99%) as a colorless oil.

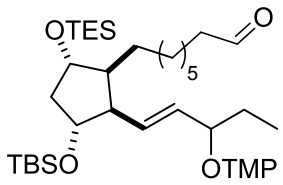
R_f (hexane/EtOAc 5:1) = 0.3. - IR (film): ν = 3600-3200, 2965, 2934, 2883, 2863, 1463, 1380, 1365, 1261, 1068, 1018, 975, 838, 802, 779, 745, 725, 692. - MS (+ESI) *m/z*, (%): 704 (10) $[M+Na]^+$, 682 (100) $[M+H]^+$, 548 (7) $[M–OTMP+Na]^+$, 158 (16) $[TMPOH+H]^+$. - HRMS (+ESI) *m/z*: ($C_{39}H_{80}O_4NSi_2$) calc.: 682.5620, found: 682.5621.

Major C16 epimer : ^{1}H NMR (400 MHz): δ = 0.00 (s, 3H, SiC*H*$_3$), 0.01 (s, 3H, SiC*H*$_3$), 0.57 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.83 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.06 (s, 3H, NC(C*H*$_3$)$_2$), 1.09 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.33 (m, 13H, C*H*$_2$, NCCH$_2$CH*H*), 1.37-1.44 (m,

5H, NCC*H*$_2$CH$_2$C*H*$_2$, CH*H*CHOTMP), 1.50-1.63 (m, 5H, C*H*$_2$CH$_2$O*H*, CH*H*CHOTBS, NCCH$_2$CH*H*), 1.67-1.78 (m, 1H, CH*H*CHOTMP), 2.00-2.10 (m, 1H, C*H*CHOTES), 2.33 (dt, *J* = 7.4, 13.8 Hz, 1H, C*H*$_2$CHOTBS), 2.53-2.62 (m, 1H, C*H*CHOTBS), 3.63 (t, *J* = 6.7 Hz, 2H, C*H*$_2$OH), 3.78 (dt, *J* = 6.0, 7.6 Hz, 1H, C*H*OTES), 3.81 (dt, *J* = 3.8, 7.2 Hz, 1H, C*H*OTBS), 3.96 (dt, *J* = 4.5, 8.6 Hz, 1H, C*H*OTMP), 5.24 (dd, *J* = 9.2, 15.5 Hz, 1H, C*H*=CHCHOTMP), 5.39 (ddd, *J* = 0.7, 8.3, 15.5 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.51 (q, Si*C*H$_3$), –4.47 (q, Si*C*H$_3$), 5.1 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 10.1 (q, *C*H$_3$CH$_2$CHOTMP), 17.51 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.4 (q, NC*C*H$_3$), 20.5 (q, NC*C*H$_3$), 25.89 (t, *C*H$_2$CH$_2$CH$_2$OH), 26.03 (q, SiC(*C*H$_3$)$_3$), 27.69 (t, *C*H$_2$CHOTMP), 28.4 (t, *C*H$_2$), 28.7 (t, *C*H$_2$), 29.64 (t, *C*H$_2$), 29.8 (t, *C*H$_2$), 30.13 (t, *C*H$_2$), 33.0 (t, *C*H$_2$CH$_2$OH), 34.3 (q, NC(*C*H$_3$)$_2$), 35.2 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.7 (t, *C*H$_2$CHOTBS), 49.2 (d, *C*HCHOTES), 52.8 (d, *C*HCHOTBS), 59.3 (s, N*C*(CH$_3$)$_2$), 60.1 (s, N*C*(CH$_3$)$_2$), 63.3 (t, *C*H$_2$OH), 76.4 (d, *C*HOTBS), 76.5 (d, *C*HOTES), 86.5 (d, *C*HOTMP), 130.4 (d, *C*H=CHCHOTMP), 134.2 (d, CH=*C*HCHOTMP).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.02 (s, 6H, SiC*H*$_3$), 0.58 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.82 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.06 (s, 3H, NC(C*H*$_3$)$_2$), 1.09 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.33 (m, 13H, C*H*$_2$, NCCH$_2$CH*H*), 1.37-1.44 (m, 5H, NCC*H*$_2$CH$_2$C*H*$_2$, CH*H*CHOTMP), 1.50-1.63 (m, 5H, C*H*$_2$CH$_2$O*H*, CH*H*CHOTBS, NCCH$_2$CH*H*), 1.67-1.78 (m, 1H, CH*H*CHOTMP), 2.00-2.10 (m, 1H, C*H*CHOTES), 2.38 (ddd, *J* = 6.6, 8.1, 14.5 Hz, 1H, CH*H*CHOTBS), 2.53-2.62 (m, 1H, C*H*CHOTBS), 3.63 (t, *J* = 6.7 Hz, 2H, C*H*$_2$OH), 3.74-3.80 (m, 1H, C*H*OTES), 3.93-4.00 (m, 2H, C*H*OTMP, C*H*OTBS), 5.12 (dd, *J* = 10.0, 15.3 Hz, 1H, C*H*=CHCHOTMP), 5.40 (dd, *J* = 8.4, 15.4 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.50 (q, Si*C*H$_3$), –4.39 (q, Si*C*H$_3$), 5.1 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 9.9 (q, *C*H$_3$CH$_2$CHOTMP), 17.47 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 20.6 (q, NC(*C*H$_3$)$_2$), 25.87 (t, *C*H$_2$CH$_2$CH$_2$OH), 26.05 (q, SiC(*C*H$_3$)$_3$), 27.72 (t, *C*H$_2$CHOTMP), 28.0 (t, *C*H$_2$), 28.8 (t, *C*H$_2$), 29.60 (t, *C*H$_2$), 29.7 (t, *C*H$_2$), 30.06 (t, *C*H$_2$), 33.0 (t, *C*H$_2$CH$_2$OH), 34.3 (q, NC(*C*H$_3$)$_2$), 35.5 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.7 (t, *C*H$_2$CHOTBS), 49.0 (d, *C*HCHOTES), 53.5 (d, *C*HCHOTBS), 59.3 (s, N*C*(CH$_3$)$_2$), 60.1 (s, N*C*(CH$_3$)$_2$), 63.3 (t, *C*H$_2$OH), 76.1 (d, *C*HOTBS), 76.8 (d, *C*HOTES), 86.7 (d, *C*HOTMP), 129.5 (d, *C*H=CHCHOTMP), 134.7 (d, CH=*C*HCHOTMP).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-oxooctyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane (20):**



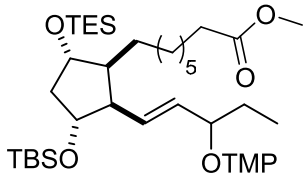
Alcohol **19** (0.13 mmol, 90 mg), 4-methylmorpholine *N*-oxide (0.20 mmol, 24 mg), tetrapropylammonium perruthenate (26 μmol, 9 mg) and molecular sieves (4 Å, 90 mg) were stirred in DCM (6 mL) at r.t. under an argon atmosphere for 60 min. The suspension was filtered through a plug of celite and sand and the solvent was evaporated. The crude material was purified by column chromatography (silica gel 2 g, hexane/EtOAc 20:1 with 0.5 vol% of Et_3N). Yield 84 mg (93%) as a colorless oil. - R_f (hexane/EtOAc 10:1) = 0.6. - IR (film): ν = 2936, 2885, 2866, 1735, 1467, 1417, 1379, 1364, 1256, 1212, 1186, 1105, 1067, 1008, 974, 837, 777, 744, 727, 672. - MS (+ESI) *m/z*, (%): 734 (14) $[M+MeOH+Na]^+$, 712 (100) $[M+MeOH+H]^+$, 680 (46) $[M+H]^+$, 578 (10) $[M+MeOH–OTMP+Na]^+$, 546 (7) $[M–OTMP+Na]^+$, 158 (5) $[TMPOH+H]^+$. - HRMS (+ESI) *m/z*: ($C_{39}H_{78}O_4NSi_2$) calc.: 680.5464, found: 680.5467.

Major C16 epimer : ^{1}H NMR (400 MHz): δ = 0.00 (s, 3H, SiC*H*$_3$), 0.01 (s, 3H, SiC*H*$_3$), 0.57 (q, *J* = 8.0 Hz, 6H, SiC*H*$_2$), 0.83 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.05 (s, 3H, NC(C*H*$_3$)$_2$), 1.09 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.33 (m, 11H, C*H*$_2$, NCCH$_2$CH*H*), 1.37-1.44 (m, 5H, NCC*H*$_2$CH$_2$C*H*$_2$, CH*H*CHOTMP), 1.47-1.66 (m, 2H, NCCH$_2$CH*H*, CH*H*CHOTBS), 1.61-1.68 (m, 2H, C*H*$_2$CH$_2$CHO), 1.68-1.79 (m, 1H, CH*H*CHOTMP), 2.00-2.10 (m, 1H, C*H*CHOTES), 2.29-2.39 (m, 1H, CH*H*CHOTBS), 2.40 (dt, *J* = 1.9, 7.5 Hz, 2H, C*H*$_2$CHO), 2.51-2.60 (m, 1H, C*H*CHOTBS), 3.74-3.80 (m, 1H, C*H*OTES), 3.89 (dt, 1H, *J* = 3.8, 7.1 Hz, 1H, C*H*OTBS), 3.92-4.00 (m, 1H, C*H*OTMP), 5.23 (dd, *J* = 9.2, 15.5 Hz, 1H, C*H*=CHCHOTMP), 5.39 (ddd, *J* = 0.7, 8.4, 15.5 Hz, 1H, CH=C*H*CHOTMP), 9.76 (t, *J* = 1.9 Hz, 1H, C*H*O). - ^{13}C NMR (100 MHz): δ = –4.49 (q, Si*C*H$_3$), –4.46 (q, Si*C*H$_3$), 5.06 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 10.1 (q, *C*H$_3$CH$_2$CHOTMP), 17.50 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.4 (q, NC*C*H$_3$), 20.6 (q, NC*C*H$_3$), 22.26 (t, *C*H$_2$CH$_2$CHO), 26.03 (q, SiC(*C*H$_3$)$_3$), 27.68 (t, *C*H$_2$CHOTMP), 28.4 (t, *C*H$_2$), 28.7 (t, *C*H$_2$), 29.4 (t, *C*H$_2$), 29.55 (t, *C*H$_2$), 30.0 (t, *C*H$_2$), 34.2 (q, NC(*C*H$_3$)$_2$), 35.2 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.1 (t,

CH_2CHO), 44.7 (t, *C*H_2CHOTBS), 49.2 (d, *C*HCHOTES), 52.8 (d, *C*HCHOTBS), 59.3 (s, N*C*$(CH_3)_2$), 60.1 (s, N*C*$(CH_3)_2$), 76.4 (d, *C*HOTBS), 76.5 (d, *C*HOTES), 86.5 (d, *C*HOTMP), 130.4 (d, *C*H=CHCHOTMP), 134.3 (d, CH=*C*HCHOTMP), 203.1 (d, *C*HO).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.02 (s, 6H, SiC*H*$_3$), 0.58 (q, *J* = 7.9 Hz, 6H, SiC*H*$_2$), 0.82 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.87 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.05 (s, 3H, NC(C*H*$_3$)$_2$), 1.09 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.33 (m, 11H, C*H*$_2$, NCCH$_2$CH*H*), 1.37-1.44 (m, 5H, NCC*H*$_2$CH$_2$C*H*$_2$, CH*H*CHOTMP), 1.47-1.66 (m, 2H, NCCH$_2$CH*H*, CH*H*CHOTBS), 1.61-1.68 (m, 2H, C*H*$_2$CH$_2$CHO), 1.68-1.79 (m, 1H, C*H*$_2$CHOTMP), 2.00-2.10 (m, 1H, C*H*CHOTES), 2.29-2.39 (m, 1H, C*H*$_2$CHOTBS), 2.41 (dt, *J* = 1.9, 7.5 Hz, 2H, C*H*$_2$CHO), 3.74-3.80 (m, 1H, C*H*OTES), 3.92-4.00 (m, 2H, C*H*OTMP, C*H*OTBS), 5.12 (dd, *J* = 9.9, 15.4 Hz, 1H, C*H*=CHCHOTMP), 5.40 (ddd, *J* = 0.8, 8.4, 15.3 Hz, 1H, CH=C*H*CHOTMP), 9.76 (t, *J* = 1.9 Hz, 1H, C*H*O). - ^{13}C NMR (100 MHz): δ = –4.50 (q, Si*C*H$_3$), –4.40 (q, Si*C*H$_3$), 5.04 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 9.9 (q, *C*H$_3$CH$_2$CHOTMP), 17.47 (t, NCCH$_2$*C*H$_2$), 18.2 (s, Si*C*$(CH_3)_3$), 20.4 (q, NC(*C*H$_3$)$_2$), 20.6 (q, NC(*C*H$_3$)$_2$), 22.23 (t, *C*H$_2$CH$_2$CHO), 26.06 (q, SiC(*C*H$_3$)$_3$), 27.72 (t, *C*H$_2$CHOTMP), 27.9 (t, *C*H$_2$), 28.8 (t, *C*H$_2$), 29.3 (t, *C*H$_2$), 29.49 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 34.3 (q, NC(*C*H$_3$)$_2$), 35.5 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.1 (t, *C*H$_2$CHO), 44.7 (t, *C*H$_2$CHOTBS), 49.0 (d, *C*HCHOTES), 53.5 (d, *C*HCHOTBS), 59.3 (s, N*C*$(CH_3)_2$), 60.1 (s, N*C*$(CH_3)_2$), 76.1 (d, *C*HOTBS), 76.8 (d, *C*HOTES), 86.6 (d, *C*HOTMP), 129.5 (d, *C*H=CHCHOTMP), 134.8 (d, CH=*C*HCHOTMP), 203.1 (d, *C*HO).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane (4):**



Aldehyde **20** (0.20 mmol, 135 mg) was dissolved in *t*-BuOH (7.5 mL). 2-Methyl-2-butene (4 mmol, 0.42 mL) was added after cooling to 0 °C followed by a solution of $NaClO_2$ (2 mmol, 230 mg) and $Na_2HPO_4 \cdot H_2O$ (2 mmol, 275 mg) in water (7.5 mL). The cooling bath was removed and the reaction mixture was stirred at r.t. for 70 min. The mixture was extracted with DCM (3×15 mL) and the combined organic layers were dried over $MgSO_4$ and

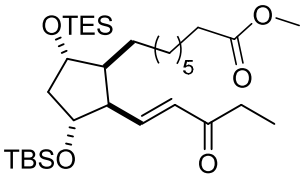
evaporated. The crude acid was not further purified. The evaporation residue was diluted by a 1:4 MeOH/benzene mixture (7.5 mL) and (trimethylsilyl)diazomethane solution (0.30 mmol, 0.15 mL, 2M in Et_2O) was added dropwise at r.t. The mixture was stirred for an hour and solid NH_4Cl was added. The mixture was filtered and the solvents were evaporated. The crude material was purified by column chromatography (silica gel 15 g, hexane/EtOAc 20:1 with 0.5 vol% of Et_3N). Yield 131 mg (93%, 2 steps) as a colorless oil. - R_f (hexane/EtOAc 10:1) = 0.6. - IR (film): ν = 2965, 2936, 2885, 2863, 1749, 1466, 1440, 1380, 1364, 1258, 1174, 1136, 1120, 1102, 1066, 1008, 975, 837, 777, 746, 726, 670. - MS (+ESI) *m/z*, (%): 732 (19) $[M+Na]^+$, 710 (100) $[M+H]^+$. - HRMS (+ESI) *m/z*: ($C_{40}H_{80}O_5NSi_2$) calc.: 710.5570, found: 710.5570.

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.00 (s, 3H, SiC*H*$_3$), 0.01 (s, 3H, SiC*H*$_3$), 0.58 (q, *J* = 7.9 Hz, 6H, SiC*H*$_2$), 0.83 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.05 (s, 3H, NC(C*H*$_3$)$_2$), 1.09 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.33 (m, 10H, C*H*$_2$), 1.37-1.44 (m, 6H, NCC*H*$_2$CH*H*C*H*$_2$, CH*H*CHOTMP), 1.47-1.66 (m, 4H, NCCH$_2$CH*H*, CH*H*CHOTBS, C*H*$_2$CH$_2$COOCH$_3$), 1.68-1.78 (m, 1H, CH*H*CHOTMP), 2.00-2.10 (m, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.6 Hz, 2H, C*H*$_2$COOCH$_3$), 2.33-2.44 (m, 1H, CH*H*CHOTBS), 2.51-2.60 (m, 1H, C*H*CHOTBS), 3.66 (s, 3H, OC*H*$_3$), 3.74-3.80 (m, 1H, C*H*OTES), 3.89 (dt, *J* = 3.8, 7.2 Hz, 1H, C*H*OTBS), 3.92-4.00 (m, 1H, C*H*OTMP), 5.19 (dd, *J* = 9.2, 15.5 Hz, 1H, C*H*=CHCHOTMP), 5.39 (ddd, *J* = 0.7, 8.4, 15.4 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.49 (q, Si*C*H$_3$), –4.36 (q, Si*C*H$_3$), 5.1 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 10.1 (q, *C*H$_3$CH$_2$CHOTMP), 17.50 (t, NCCH$_2$*C*H$_2$), 18.21 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 20.6 (q, NC(*C*H$_3$)$_2$), 25.14 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.03 (q, SiC(*C*H$_3$)$_3$), 27.69 (t, *C*H$_2$CHOTMP), 28.4 (t, *C*H$_2$), 28.7 (t, *C*H$_2$), 29.40 (t, *C*H$_2$), 29.5 (t, *C*H$_2$), 30.04 (t, *C*H$_2$), 34.29 (t, *C*H$_2$COOCH$_3$), 35.1 (q, NC(*C*H$_3$)$_2$), 35.5 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.7 (t, *C*H$_2$CHOTBS), 49.2 (d, *C*HCHOTES), 51.6 (q, O*C*H$_3$) 52.8 (d, *C*HCHOTBS), 59.3 (s, N*C*(CH$_3$)$_2$), 60.1 (s, N*C*(CH$_3$)$_2$), 76.4 (d, *C*HOTBS), 76.5 (d, *C*HOTES), 86.5 (d, *C*HOTMP), 130.5 (d, *C*H=CHCHOTMP), 134.2 (d, CH=*C*HCHOTMP), 174.5 (s, *C*OOCH$_3$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.02 (s, 6H, SiC*H*$_3$), 0.58 (q, *J* = 7.9 Hz, 6H, SiC*H*$_2$), 0.82 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOTMP), 0.87 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, SiCH$_2$C*H*$_3$), 1.05 (s, 3H, NC(C*H*$_3$)$_2$), 1.09 (s, 6H, NC(C*H*$_3$)$_2$), 1.15 (s, 3H, NC(C*H*$_3$)$_2$), 1.22-1.33 (m, 10H, C*H*$_2$), 1.37-1.44 (m, 6H, NCC*H*$_2$CH*H*C*H*$_2$, CH*H*CHOTMP), 1.47-1.66 (m, 4H, NCCH$_2$CH*H*, CH*H*CHOTBS, C*H*$_2$CH$_2$COOCH$_3$), 1.68-1.78 (m, 1H,

CH*H*CHOTMP), 2.00-2.10 (m, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.6 Hz, 2H, C*H*$_2$COOCH$_3$), 2.33-2.44 (m, 1H, CH*H*CHOTBS), 2.51-2.60 (m, 1H, C*H*CHOTBS), 3.66 (s, 3H, OC*H*$_3$), 3.74-3.80 (m, 1H, C*H*OTES), 3.90-4.00 (m, 2H, C*H*OTMP, C*H*OTBS), 5.12 (dd, *J* = 9.9, 15.3 Hz, 1H, C*H*=CHCHOTMP), 5.40 (ddd, *J* = 0.8, 8.4, 15.4 Hz, 1H, CH=C*H*CHOTMP). - ^{13}C NMR (100 MHz): δ = –4.50 (q, Si*C*H$_3$), –4.39 (q, Si*C*H$_3$), 5.1 (t, Si*C*H$_2$), 7.0 (q, SiCH$_2$*C*H$_3$), 9.9 (q, *C*H$_3$CH$_2$CHOTMP), 17.47 (t, NCCH$_2$*C*H$_2$), 18.20 (s, Si*C*(CH$_3$)$_3$), 20.5 (q, NC(*C*H$_3$)$_2$), 20.6 (q, NC(*C*H$_3$)$_2$), 25.12 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.05 (q, SiC(*C*H$_3$)$_3$), 27.72 (t, *C*H$_2$CHOTMP), 28.0 (t, *C*H$_2$), 28.8 (t, *C*H$_2$), 29.3 (t, *C*H$_2$), 29.41 (t, *C*H$_2$), 29.96 (t, *C*H$_2$), 34.27 (t, *C*H$_2$COOCH$_3$), 35.1 (q, NC(*C*H$_3$)$_2$), 35.5 (q, NC(*C*H$_3$)$_2$), 40.4 (t, NC*C*H$_2$), 44.7 (t, *C*H$_2$CHOTBS), 49.0 (d, *C*HCHOTES), 51.6 (q, O*C*H$_3$), 53.5 (d, *C*HCHOTBS), 59.3 (s, N*C*(CH$_3$)$_2$), 60.1 (s, N*C*(CH$_3$)$_2$), 76.1 (d, *C*HOTBS), 76.8 (d, *C*HOTES), 86.6 (d, *C*HOTMP), 129.5 (d, *C*H=CHCHOTMP), 134.8 (d, CH=*C*HCHOTMP), 174.5 (s, *C*OOCH$_3$).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-pent-1-en-3-on-1-yl)-1-((triethylsilyl)oxy)cyclopentane (21):**

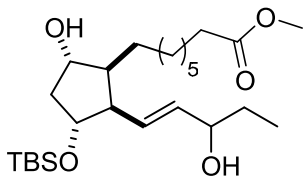


*m*CPBA (0.41 mmol, 70 mg) was added to a solution of ester **4** (0.23 mmol, 166 mg) in dry DCM (15 mL) at 0 °C under an argon atmosphere. The reaction mixture was stirred for 8 min and saturated Na$_2$SO$_3$ solution (10 mL) was added. This mixture was extracted with DCM (2×20 mL). The combined organic layers were dried over MgSO$_4$ and evaporated. The crude material was purified by column chromatography (silica gel 10 g, hexane/EtOAc 30:1 with 0.5 vol% of Et$_3$N). Yield 129 mg (99%) as a colorless oil. - R$_f$ (hexane/EtOAc 10:1) = 0.5. - IR (film): ν = 2966, 2937, 2886, 2864, 1747, 1706, 1683, 1633, 1466, 1440, 1419, 1384, 1365, 1258, 1199, 1173, 1121, 1071, 1009, 982, 869, 838, 779, 749, 762, 670. - MS (+ESI) *m/z*, (%): 1159 (68) [2M+Na]$^+$, 591 (100) [M+Na]$^+$, 569 (60) [M+H]$^+$. - HRMS (+ESI) *m/z*: (C$_{31}$H$_{61}$O$_5$Si$_2$) calc.: 569.4052, found: 569.4054.

^{1}H NMR (400 MHz): δ = –0.01 (s, 3H, SiC*H*$_3$), 0.01 (s, 3H, SiC*H*$_3$), 0.58 (q, *J* = 7.9 Hz, 6H, C*H*$_2$Si), 0.86 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, C*H*$_3$CH$_2$Si), 1.11 (t, *J* = 7.3 Hz, 3H, C*H*$_3$CH$_2$CO), 1.22-1.33 (m, 10H, C*H*$_2$), 1.55-1.64 (m, 3H, CH*H*CHOTES, C*H*$_2$CH$_2$COOCH$_3$), 2.09 (quint, *J* = 7.0 Hz, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.6 Hz, 2H,

CH_2COOCH_3), 2.37 (dt, *J* = 7.1, 14.1 Hz, 1H, CH*H*CHOTES), 2.55 (q, *J* = 7.3 Hz, 2H, CH_2CO), 2.77 (ddd, *J* = 5.1, 7.2, 9.9 Hz, 1H, C*H*CHOTBS), 3.66 (s, 3H, OCH_3), 3.84 (q, *J* = 6.5 Hz, 1H, C*H*OTES), 3.94 (dt, *J* = 5.1, 7.2 Hz, 1H, C*H*OTBS), 6.15 (dd, *J* = 0.9, 15.7 Hz, 1H, CH=C*H*CO), 6.64 (dd, *J* = 10.0, 15.7 Hz, 1H, C*H*=CHCO). - ^{13}C NMR (100 MHz): δ = –4.5 (q, *C*H_3Si), –4.4 (q, *C*H_3Si), 5.0 (t, *C*H_2Si), 7.0 (q, *C*H_3CH_2Si), 8.3 (q, *C*H_3CH_2), 18.2 (s, Si*C*(CH_3)$_3$), 25.0 (t, *C*H_2CH_2COOCH_3), 25.9 (q, SiC(*C*H_3)$_3$), 28.8 (t, *C*H_2), 29.17 (t, *C*H_2), 29.22 (t, *C*H_2), 29.7 (t, *C*H_2), 29.8 (t, *C*H_2), 34.1 (t, *C*H_2CO), 34.2 (t, *C*H_2COOCH_3), 44.7 (t, *C*H_2CHOTES), 50.1 (d, *C*HCHOTES), 51.6 (q, O*C*H_3), 53.1 (d, *C*HCHOTBS), 75.5 (d, *C*HOTBS), 76.0 (d, *C*HOTES), 131.0 (d, CH=*C*HCO), 145.6 (d, *C*H=CHCO), 174.4 (s, *C*OOCH_3), 200.7 (s, *C*OCH_2CH_3).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-(hydroxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentan-1-ol (22):**



Method 1 (F$_{1t}$-PhytoP synthesis): Crude ketone **21** (max. 0.03 mmol, 16 mg) was dissolved in dry MeOH (1 mL) under an argon atmosphere. Dry $CeCl_3$ (0.03 mmol, 8 mg) was added and the mixture was stirred at r.t., for 10 min, cooled to –60 °C and $NaBH_4$ (cca 0.01 mmol, 0.4 mg) was added. The reaction was warmed to –10 °C during 30 min and stirred at this temperature for 30 min. The reaction was quenched by a few drops of water. The reaction mixture was extracted with Et_2O (3×2 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was not further purified. Crude yield 15 mg as a colorless oil.

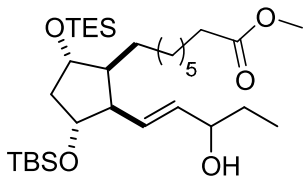
Method 2 (D$_{1t}$-PhytoP synhesis): Alcohol **23** (0.04 mmol, 23 mg) was dissolved in THF (0.5 mL), water (0.1 mL) and acetic acid (8.3 mmol, 0.5 mL) were added and the mixture was stirred at r.t. for 15 min. Solid K_2CO_3 (7.25 mmol, 1 g) was added and the mixture was diluted with water (5 mL) and extracted with Et_2O (4×5 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was not further purified. Yield 18 mg (98%) as a colorless oil.

R_f (hexane/EtOAc 2:1) = 0.3. - IR (film): ν = 3454, 2938, 2865, 1745, 1464, 1366, 1257, 1203, 1176, 1114, 1069, 1010, 975, 839, 779. - MS (+ESI) *m/z*, (%): 935 (4) $[2M+Na]^+$, 479 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{25}H_{48}O_5NaSi$) calc.: 479.3163, found: 479.3163.

Major C16 epimer: ^{1}H NMR (600 MHz): δ = 0.046 (s, 3H, SiC*H*$_3$), 0.049 (s, 3H, SiC*H*$_3$), 0.879 (s, 9H, SiC(C*H*$_3$)$_3$), 0.90 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.25-1.35 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.42 (br s, 1H, O*H*), 1.48-1.58 (m, 2H, C*H*$_2$CH$_3$), 1.57-1.66 (m, 3H, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CHOTBS), 1.94 (s, 1H, O*H*), 2.08-2.14 (m, 1H, C*H*CH$_2$CH$_2$), 2.25 (ddd, *J* = 5.3, 7.3, 14.2 Hz, 1H, CH*H*CHOTBS), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.71 (ddd, *J* = 2.6, 7.5, 9.9 Hz, 1H, C*H*CH=CH), 3.66 (s, 3H, OC*H*$_3$), 3.83-3.88 (m, 1H, HOC*H*CHCH$_2$), 3.95 (dt, *J* = 2.6, 5.4 Hz, 1H, C*H*OTBS), 4.00 (dt, *J* = 6.1, 6.9 Hz, 1H, HOC*H*CH=CH), 5.34 (ddd, *J* = 1.1, 10.0, 15.3 Hz, 1H, C*H*=CHCHOH), 5.52 (ddd, *J* = 0.7, 6.4, 15.3 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (150 MHz): δ = –4.61 (q, Si*C*H$_3$), –4.54 (q, Si*C*H$_3$), 9.79 (q, *C*H$_3$CH$_2$), 18.1 (s, Si*C*(CH$_3$)$_3$), 25.04 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.4 (t, *C*H$_2$), 29.21 (t, *C*H$_2$), 29.28 (t, *C*H$_2$), 29.6 (t, *C*H$_2$), 29.77 (t, *C*H$_2$), 30.39 (t, *C*H$_2$CH$_3$), 34.2 (t, *C*H$_2$COOCH$_3$), 43.30 (t, *C*H$_2$CHOTBS), 50.93 (d, *C*HCH$_2$CH$_2$), 51.6 (q, O*C*H$_3$), 54.3 (d, *C*HCH=CH), 74.1 (d, HO*C*HCH=CH), 77.96 (d, HO*C*HCHCH$_2$), 78.4 (d, *C*HOTBS), 129.4 (d, *C*H=CHCHOH), 135.36 (d, CH=*C*HCHOH), 174.5 (s, *C*OOCH$_3$).

Minor C16 epimer: ^{1}H NMR (600 MHz): δ = 0.051 (s, 3H, SiC*H*$_3$), 0.056 (s, 3H, SiC*H*$_3$), 0.881 (s, 9H, SiC(C*H*$_3$)$_3$), 0.91 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.25-1.35 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.42 (br s, 1H, O*H*), 1.48-1.58 (m, 2H, C*H*$_2$CH$_3$), 1.57-1.66 (m, 3H, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CHOTBS), 1.94 (s, 1H, O*H*), 2.08-2.14 (m, 1H, C*H*CH$_2$CH$_2$), 2.26 (ddd, *J* = 5.2, 7.6, 14.3 Hz, 1H, CH*H*CHOTBS), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.70 (ddd, *J* = 2.8, 7.5, 10.2 Hz, 1H, C*H*CH=CH), 3.66 (s, 3H, OC*H*$_3$), 3.83-3.88 (m, 1H, HOC*H*CHCH$_2$), 3.95 (dt, *J* = 2.6, 5.4 Hz, 1H, C*H*OTBS), 3.96-3.99 (m, 1H, HOC*H*CH=CH), 5.30 (ddd, *J* = 1.1, 10.2, 15.3 Hz, 1H, C*H*=CHCHOH), 5.50 (ddd, *J* = 0.6, 6.9, 15.3 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (150 MHz): δ = –4.59 (q, Si*C*H$_3$), –4.50 (q, Si*C*H$_3$), 9.83 (q, *C*H$_3$CH$_2$), 18.1 (s, Si*C*(CH$_3$)$_3$), 25.06 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.4 (t, *C*H$_2$), 29.24 (t, *C*H$_2$), 29.30 (t, *C*H$_2$), 29.80 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 30.42 (t, *C*H$_2$CH$_3$), 34.2 (t, *C*H$_2$COOCH$_3$), 43.29 (t, *C*H$_2$CHOTBS), 50.96 (d, *C*HCH$_2$CH$_2$), 51.6 (q, COO*C*H$_3$), 54.5 (d, *C*HCH=CH), 74.5 (d, HO*C*HCH=CH), 78.02 (d, HO*C*HCHCH$_2$), 78.3 (d, *C*HOTBS), 129.9 (d, *C*H=CHCHOH), 135.38 (d, CH=*C*HCHOH), 174.5 (s, *C*OOCH$_3$).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-(hydroxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)-1-((triethylsilyl)oxy)cyclopentane (23):**

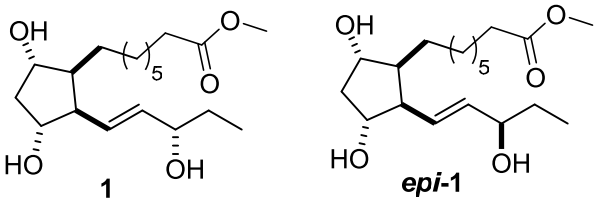


Ketone **21** (0.08 mmol, 45 mg) was dissolved in dry MeOH (5 mL) under an argon atmosphere. Dry $CeCl_3$ (0.01 mmol, 25 mg) was added and the mixture was stirred for 20 min. The reaction mixture was cooled to –78 °C and $NaBH_4$ (0.08 mmol, 3 mg) was added in three portions at 30 min intervals. The reaction was stirred at the same temperature for 2 h and subsequently quenched with a few drops of acetone followed by addition of phosphate buffer (2 mL). The reaction mixture was extracted with DCM (4×5 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 3 g, hexane/EtOAc 20:1 with 0.5 vol% of Et_3N). Yield 43 mg (94%) as colorless oil. - R_f (hexane/EtOAc 5:1) = 0.6. - IR (film): ν = 3600-3200, 2965, 2937, 2886, 2864, 1749, 1466, 1441, 1419, 1382, 1365, 1257, 1202, 1175, 1120, 1103, 1008, 974, 838, 778, 747, 726, 670. - MS (+ESI) *m/z*, (%): 593 (100) $[M+Na]^+$, 233 (25) [M–OTES–OTBS–OH–COOMe+H]$^+$. - HRMS (+ESI) *m/z*: ($C_{31}H_{62}O_5NaSi_2$) calc.: 593.4028, found: 593.4027.

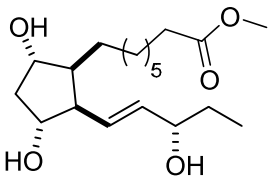
Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.01 (s, 6H, SiC*H*$_3$), 0.57 (q, *J* = 7.9 Hz, 6H, C*H*$_2$Si), 0.861 (s, 9H, SiC(C*H*$_3$)$_3$), 0.91 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$CHOH), 0.95 (t, *J* = 7.9 Hz, 9H, C*H*$_3$CH$_2$Si), 1.22-1.34 (m, 10H, C*H*$_2$), 1.44 (br s, 1H, O*H*), 1.47-1.66 (m, 5H, C*H*$_2$CHOH, CH*H*CHOTES, C*H*$_2$CH$_2$COOCH$_3$), 1.98-2.06 (m, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.30-2.38 (m, 1H, CH*H*CHOTES), 2.54-2.61 (m, 1H, C*H*CHOTBS), 3.66 (s, 3H, COOC*H*$_3$), 3.77 (q, *J* = 7.2 Hz, 1H, C*H*OTES), 3.83-3.89 (m, 1H, C*H*OTBS), 3.95-4.04 (m, 1H, C*H*OH), 5.34-5.53 (m, 2H, C*H*=C*H*CHOH). - ^{13}C NMR (100 MHz): δ = –4.43 (q, *C*H$_3$Si), 5.0 (t, *C*H$_2$Si), 7.0 (q, *C*H$_3$CH$_2$Si), 9.8 (q, *C*H$_3$CH$_2$CHOH), 18.2 (s, Si*C*(CH$_3$)$_3$), 25.06 (t, *C*H$_2$), 26.0 (q, SiC(*C*H$_3$)$_3$), 27.9 (t, *C*H$_2$), 28.7 (t, *C*H$_2$), 29.24 (t, *C*H$_2$), 29.30 (t, *C*H$_2$), 29.86 (t, *C*H$_2$), 30.4 (t, *C*H$_2$CHOH), 34.2 (t, *C*H$_2$COOCH$_3$), 44.7 (t, CH$_2$CHOTES), 49.33 (d, *C*HCHOTES), 51.6 (q, O*C*H$_3$), 52.8 (d, *C*HCHOTBS), 74.3 (d, *C*HOH), 76.24 (d, *C*HOTES or *C*HOTBS), 76.26 (d, *C*HOTES or *C*HOTBS), 130.1 (d, *C*H=CHCHOH), 134.87 (d, CH=*C*HCHOH), 174.50 (s, *C*OOCH$_3$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.01 (s, 6H, SiC*H*$_3$), 0.57 (q, *J* = 7.9 Hz, 6H, C*H*$_2$Si), 0.864 (s, 9H, SiC(C*H*$_3$)$_3$), 0.90 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$CHOH), 0.95 (t, *J* = 7.9 Hz, 9H, C*H*$_3$CH$_2$Si), 1.22-1.34 (m, 10H, C*H*$_2$), 1.40 (br s, 1H, O*H*), 1.47-1.66 (m, 5H, C*H*$_2$CHOH, CH*H*CHOTES, C*H*$_2$CH$_2$COOCH$_3$), 1.98-2.06 (m, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.30-2.38 (m, 1H, CH*H*CHOTES), 2.54-2.61 (m, 1H, C*H*CHOTBS), 3.66 (s, 3H, OC*H*$_3$), 3.76 (q, *J* = 7.2 Hz, 1H, C*H*OTES), 3.83-389 (m, 1H, C*H*OTBS), 3.95-4.04 (m, 1H, C*H*OH), 5.34-5.53 (m, 2H, C*H*=C*H*CHOH). - ^{13}C NMR (100 MHz): δ = –4.40 (q, *C*H$_3$Si), –4.37 (q, *C*H$_3$Si), 5.0 (t, *C*H$_2$Si), 7.0 (q, *C*H$_3$CH$_2$Si), 9.9 (q, *C*H$_3$CH$_2$CHOH), 18.2 (s, Si*C*(CH$_3$)$_3$), 25.07 (t, *C*H$_2$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.0 (t, *C*H$_2$), 28.6 (t, *C*H$_2$), 29.27 (t, *C*H$_2$), 29.33 (t, *C*H$_2$), 29.87 (t, *C*H$_2$), 30.4 (t, *C*H$_2$CHOH), 34.2 (t, *C*H$_2$COOCH$_3$), 44.6 (t, *C*H$_2$CHOTES), 49.28 (d, *C*HCHOTES), 51.6 (q, COO*C*H$_3$), 52.9 (d, *C*HCHOTBS), 74.6 (d, *C*HOH), 76.28 (d, *C*HOTES or *C*HOTBS), 76.33 (d, *C*HOTES or *C*HOTBS), 130.4 (d, *C*H=CHCHOH), 134.91 (d, CH=*C*HCHOH), 174.47 (s, *C*OOCH$_3$).

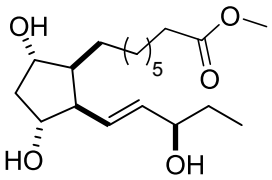
16-F$_{1t}$-Phytoprostane methyl ester (1) and 16-*epi*-16-F$_{1t}$-phytoprostane methyl ester (*epi*-1):



Crude diol **22** (max. 0.03 mmol, 14 mg) was dissolved in dry THF (1.5 mL) in a flame-dried Schlenk flask under an argon atmosphere. The solution was cooled to 0 °C and TBAF (0.04 mmol, 40 μL, 1 M in THF) was added. The reaction was stirred at the same temperature for 4 h, warmed to r.t. and stirred for another hour. The reaction was quenched with saturated NH_4Cl solution (2 mL), diluted with Et_2O and the layers were separated. The aqueous layer was extracted with Et_2O (3×2 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 2 g, EtOAc). Yield 9 mg (89%, 2 steps from **21**) of a separable 1:1.2 **1**/***epi*-1** mixture as a colorless oil.



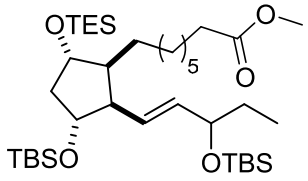
16-F$_{1t}$-Phytoprostane methyl ester **1**: R_f (EtOAc/acetone 1:1) = 0.2. - IR (film): ν = 3352, 2934, 2863, 1743, 1675, 1464, 1442, 1344, 1264, 1259, 1203, 1175, 1068, 1015, 972, 804, 727. - MS (+ESI): *m/z*, 381 (9) $[M+K]^+$, 365 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{34}O_5Na$) calc.: 365.2299, found: 365.2299. - ^{1}H NMR (600 MHz): δ = 0.91 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.27-1.36 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.52-1.70 (m, 6H, O*H*, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$, HOCHCH*H*CHOH), 1.75 (s, 1H, O*H*), 1.86 (s, 1H, O*H*), 2.10 (dtd, *J* = 7.5, 6.5, 5.4 Hz, 1H, C*H*CH$_2$CH$_2$), 2.32 (t, *J* = 7.6 Hz, 2H, C*H*$_2$COOCH$_3$), 2.41 (dtd, *J* = 1.2, 6.6, 14.8 Hz, 1H, HOCHCH*H*CHOH), 2.76 (dddd, *J* = 1.2, 3.6, 7.3, 9.8 Hz, 1H, C*H*CH=CH), 3.69 (s, 3H, OC*H*$_3$), 3.96 (dt, *J* = 3.6, 6.6 Hz, 1H, HOC*H*CHCH$_2$), 4.00 (dt, *J* = 6.4, 6.7 Hz, 1H, HOC*H*CH=CH), 4.03 (td, *J* = 3.5, 6.6 Hz, 1H, HOC*H*CHCH=CH), 5.39 (ddd, *J* = 1.0, 9.8, 15.3 Hz, 1H, C*H*=CHCHOH), 5.56 (ddd, *J* = 1.8, 6.8, 15.6 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (151 MHz): δ = 9.84 (q, *C*H$_3$CH$_2$), 25.02 (t, *C*H$_2$CH$_2$COOCH$_3$), 28.25 (t, *C*H$_2$), 29.18 (t, *C*H$_2$), 29.26 (t, *C*H$_2$), 29.37 (t, *C*H$_2$), 29.69 (t, *C*H$_2$), 30.41 (t, *C*H$_2$CH$_3$), 34.2 (t, *C*H$_2$COOCH$_3$), 42.88 (t, HOCH*C*H$_2$CHOH), 50.70 (d, *C*HCH$_2$CH$_2$), 51.62 (q, OC*H*$_3$), 54.0 (d, *C*HCH=CH), 74.5 (d, HO*C*HCH=CH), 77.09 (d, HO*C*HCHCH=CH), 77.3 (d, HO*C*HCHCH$_2$), 129.5 (d, *C*H=CHCHOH), 135.8 (d, CH=*C*HCHOH), 174.5 (s, *C*OOCH$_3$).



16-epi-16-F$_{1t}$-Phytoprostane methyl ester ***epi*-1:** R_f (EtOAc/acetone 1:1) = 0.3. - IR (film): ν = 3370, 2935, 2864, 1743, 1464, 1441, 1366, 1259, 1248, 1204, 1176, 1072, 1015, 976, 801, 729. - MS (+ESI): *m/z*, 365 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{34}O_5Na$) calc.: 365.2299, found: 365.2299. - ^{1}H NMR (600 MHz): δ = 0.91 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.23-1.35 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.49-1.57 (m, 6H, O*H*, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$, HOCHCH*H*CHOH), 1.74 (s, 1H, O*H*), 1.80 (s, 1H, O*H*), 2.10 (quint, *J* = 6.9 Hz, 1H, C*H*CH$_2$CH$_2$), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.41 (ddd, *J* = 6.7, 7.2, 14.0 Hz, 1H, HOCHCH*H*CHOH), 2.77 (ddd, *J* = 3.6, 7.0, 9.6 Hz, 1H, C*H*CH=CH), 3.67 (s, 3H, OC*H*$_3$),

3.95-3.99 (m, 1H, HOC*H*CHCH$_2$), 4.00-4.04 (m, 2H, HOC*H*CHCH=CHC*H*OH), 5.42 (ddd, *J* = 1.1, 9.5, 15.4 Hz, 1H, C*H*=CHCHOH), 5.58 (ddd, *J* = 0.8, 6.4, 15.4 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (151 MHz): δ = 9.84 (q, *C*H$_3$CH$_2$), 25.00 (t, *C*H$_2$CH$_2$COOCH$_3$), 28.26 (t, *C*H$_2$), 29.15 (t, *C*H$_2$), 29.23 (t, *C*H$_2$), 29.30 (t, *C*H$_2$), 29.67 (t, *C*H$_2$), 30.39 (t, *C*H$_2$CH$_3$), 34.2 (t, *C*H$_2$COOCH$_3$), 42.89 (t, CHOH*C*H$_2$CHOH), 50.67 (d, *C*HCH$_2$CH$_2$), 51.63 (q, O*C*H$_3$), 53.9 (d, *C*HCH=CH), 74.1 (d, HO*C*HCH=CH), 77.10 (d, HO*C*HCHCH=CH), 77.2 (d, HO*C*HCHCH$_2$), 128.9 (d, *C*H=CHCHOH), 135.7 (d, CH=*C*HCHOH), 174.5 (s, *C*OOCH$_3$).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)-1-((triethylsilyl)oxy)cyclopentane (24):**



Alcohol **23** (0.08 mmol, 42 mg) was dissolved in dry DCM (2 mL) under an argon atmosphere, 2,6-lutidine (0.50 mmol, 75 µL) was added and the reaction mixture was cooled to –78 °C. TBSOTf (0.16 mmol, 38 µL) was added dropwise. The reaction was stirred at the same temperature for 40 min and quenched with saturated KHSO$_4$ solution (4 mL). The layers were separated and the aqueous extracted with DCM (4×5 mL). The combined organic layers were dried over MgSO$_4$ and evaporated. The crude material was purified by column chromatography (silica gel 3 g, hexane/EtOAc 70:1 gradient to 30:1 with 0.5 vol% of Et$_3$N). Yield 48 mg (95%) as a colorless oil. - R$_f$ (hexane/EtOAc 5:1) = 0.9. - IR (film): ν = 2967, 2937, 2864, 1748, 1469, 1366, 1255, 1173, 1119, 1066, 1010, 974, 836, 777, 743, 725, 672. - MS (+ESI) *m/z*, (%): 707 (100) [M+Na]$^+$, 553 (30) [M–HOTES+H]$^+$. - HRMS (+ESI) *m/z*: (C$_{37}$H$_{76}$O$_5$NaSi$_3$) calc.: 707.4893, found: 707.4889.

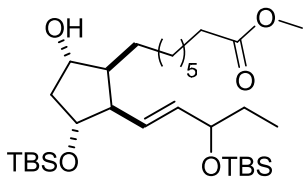
*NMR signals o*f Si-*CH*$_3$: ^{1}H NMR (400 MHz): δ = 0.003, 0.010, 0.014, 0.02, 0.04 *could not be assigned to the individual C16 epimers.*

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.57 (q, *J* = 7.9 Hz, 6H, C*H*$_2$Si), 0.84 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$OTBS), 0.859 (s, 9H, SiC(C*H*$_3$)$_3$), 0.889 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, C*H*$_3$CH$_2$Si), 1.20-1.32 (m, 10H, C*H*$_2$), 1.40-1.53 (m, 3H, CH$_3$C*H*$_2$CHOTBS,

CH*H*CHOTES), 1.56-1.65 (m, 2H, C*H*$_2$CH$_2$COOCH$_3$), 1.98-2.09 (m, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.30-2.39 (m, 1H, CH*H*CHOTES), 2.48-2.57 (m, 1H, C*H*CH=CH), 3.66 (s, 3H, OC*H*$_3$), 3.75 (td, *J* = 6.5, 13.0 Hz, 1H, C*H*OTES), 3.84 (td, *J* = 3.0, 6.5 Hz, 1H, TBSOC*H*CH$_2$CHOTES), 3.98 (td, *J* = 6.0, 7.1 Hz, 1H, TBSOC*H*CH$_2$CH$_3$), 5.30 (ddd, *J* = 1.1, 9.7, 15.3 Hz, 1H, C*H*=CHCHOTBS), 5.42 (ddd, *J* = 0.6, 6.1, 15.3 Hz, 1H, CH=C*H*CHOTBS). - ^{13}C NMR (100 MHz): δ = –4.60 (q, *C*H$_3$Si), –4.49 (q, *C*H$_3$Si), –4.44 (q, *C*H$_3$Si), –4.24 (q, *C*H$_3$Si), 5.04 (t, *C*H$_2$Si), 7.0 (q, *C*H$_3$CH$_2$Si), 9.79 (q, *C*H$_3$CH$_2$CHOTBS), 18.2 (s, Si*C*(CH$_3$)$_3$), 18.4 (s, Si*C*(CH$_3$)$_3$), 25.13 (t, *C*H$_2$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.2 (t, *C*H$_2$), 28.8 (t, *C*H$_2$), 29.36 (t, *C*H$_2$), 29.44 (t, *C*H$_2$), 30.0 (t, *C*H$_2$), 31.47 (t, CH$_3$*C*H$_2$CHOTBS), 34.3 (t, *C*H$_2$COOCH$_3$), 44.69 (t, *C*H$_2$CHOTES), 49.1 (d, *C*HCHOTES), 51.6 (q, O*C*H$_3$), 52.7 (d, *C*HCH=CH), 74.6 (d, TBSO*C*HCH=CH), 76.3 (d, TBSO*C*HCH$_2$CHOTES), 76.5 (d, *C*HOTES), 128.3 (d, *C*H=CHCHOTBS), 135.35 (d, CH=*C*HCHOTBS), 174.5 (s, *C*OOCH$_3$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.57 (q, *J* = 7.9 Hz, 6H, C*H*$_2$Si), 0.84 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$OTBS), 0.862 (s, 9H, SiC(C*H*$_3$)$_3$), 0.892 (s, 9H, SiC(C*H*$_3$)$_3$), 0.95 (t, *J* = 7.9 Hz, 9H, C*H*$_3$CH$_2$Si), 1.20-1.32 (m, 10H, C*H*$_2$), 1.40-1.53 (m, 3H, CH$_3$C*H*$_2$CHOTBS, CH*H*CHOTES), 1.56-1.65 (m, 2H, C*H*$_2$CH$_2$COOCH$_3$), 1.98-2.09 (m, 1H, C*H*CHOTES), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.30-2.39 (m, 1H, CH*H*CHOTES), 2.48-2.57 (m, 1H, C*H*CH=CH), 3.66 (s, 3H, OC*H*$_3$), 3.75 (td, *J* = 6.5, 13.0 Hz, 1H, C*H*OTES), 3.88 (td, *J* = 3.0, 6.5 Hz, 1H, TBSOC*H*CH$_2$CHOTES), 3.98 (td, *J* = 6.0, 7.1 Hz, 1H, TBSOC*H*CH$_2$CH$_3$), 5.25 (ddd, *J* = 1.1, 10.0, 15.3 Hz, 1H, C*H*=CHCHOTBS), 5.43 (ddd, *J* = 0.7, 6.0, 15.3 Hz, 1H, CH=C*H*CHOTBS). - ^{13}C NMR (100 MHz): δ = –4.56 (q, *C*H$_3$Si), –4.51 (q, *C*H$_3$Si), –4.42 (q, *C*H$_3$Si), –4.21 (q, *C*H$_3$Si), 5.03 (t, *C*H$_2$Si), 7.0 (q, *C*H$_3$CH$_2$Si), 9.78 (q, *C*H$_3$CH$_2$CHOTBS), 18.2 (s, Si*C*(CH$_3$)$_3$), 18.4 (s, Si*C*(CH$_3$)$_3$), 25.12 (t, *C*H$_2$), 26.0 (q, SiC(*C*H$_3$)$_3$), 27.9 (t, *C*H$_2$), 28.7 (t, *C*H$_2$), 29.34 (t, *C*H$_2$), 29.40 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 31.53 (t, CH$_3$*C*H$_2$CHOTBS), 34.3 (t, *C*H$_2$COOCH$_3$), 44.72 (t, *C*H$_2$CHOTES), 49.0 (d, *C*HCHOTES), 51.6 (q, O*C*H$_3$), 53.0 (d, *C*HCH=CH), 74.7 (d, TBSO*C*HCH=CH), 76.5 (d, TBSO*C*HCH$_2$CHOTES), 76.6 (d, *C*HOTES), 127.9 (d, *C*H=CHCHOTBS), 135.38 (d, CH=*C*HCHOTBS), 174.5 (s, *C*OOCH$_3$).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentan-1-ol (25):**



Ester **24** (0.03 mmol, 19 mg) was dissolved in THF (0.5 mL), water (0.5 mL) and acetic acid (25 mmol, 1.5 mL) were added and the mixture was stirred at 45 °C for 20 min. Solid K_2CO_3 (14.5 mmol, 2 g) was added after cooling to r.t. The mixture was diluted with water (10 mL) and extracted with DCM (3×10 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was not further purified. Yield 15 mg (94%) as a colorless oil. - R_f (hexane/EtOAc 5:1) = 0.5. - IR (film): ν = 3452, 2968, 2937, 2864, 1746, 1470, 1441, 1366, 1256, 1200, 1173, 1118, 1074, 1010, 975, 867, 838, 777, 726, 673. - MS (+ESI) *m/z*, (%): 593 (100) $[M+Na]^+$, 439 (8) $[M–HOTBS+H]^+$, 307 (5) $[M–2HOTBS+H]^+$. - HRMS (+ESI) *m/z*: ($C_{31}H_{62}O_5N4Si_2$) calc.: 593.4028, found: 593.4028.

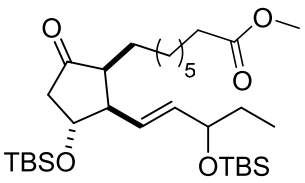
*NMR signals o*f Si-*C*H_3: ^{1}H NMR (400 MHz): δ = 0.008, 0.013, 0.034, 0.036, 0.040, 0.045, 0.047, 0.053. - ^{13}C NMR (100 MHz): δ = –4.69, –4.66, –4.62, –4.57 (2C), –4.52, –4.24, –4.17 *could not be assigned to the individual C16 epimers.*

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.83 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 0.88 (s, 18H, SiC(C*H*$_3$)$_3$), 1.20-1.35 (m, 9H, C*H*$_2$), 1.40-1.67 (m, 6H, C*H*$_2$CH$_3$, CH*H*CHOH, C*H*$_2$), 2.00 (s, 1H, O*H*), 2.07-2.15 (m, 1H, C*H*CHOH), 2.18-2.26 (m, 1H, CH*H*CHOH), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.64-2.71 (m, 1H, C*H*CH=CH), 3.66 (s, 3H, OC*H*$_3$), 3.81-3.88 (m, 1H, TBSOC*H*CH$_2$CHOH), 3.90-3.95 (m, 1H, C*H*OH), 3.94-3.99 (m, 1H, TBSOC*H*CH$_2$CH$_3$), 5.23 (ddd, *J* = 1.0, 10.0, 15.3 Hz, 1H, C*H*=CHCHOTBS), 5.45 (ddd, *J* = 0.7, 6.2, 15.3 Hz, 1H, CH=C*H*CHOTBS). - ^{13}C NMR (100 MHz): δ = 9.77 (q, *C*H$_3$CH$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 18.4 (s, Si*C*(CH$_3$)$_3$), 25.10 (t, *C*H$_2$), 26.02 (q, SiC(*C*H$_3$)$_3$), 28.6 (t, *C*H$_2$), 29.30 (t, *C*H$_2$), 29.38 (t, *C*H$_2$), 29.87 (t, 2C, *C*H$_2$), 31.4 (t, *C*H$_2$CH$_3$), 34.3 (t, *C*H$_2$COOCH$_3$), 43.24 (t, *C*H$_2$CHOH), 51.01 (d, *C*HCHOH), 51.6 (q, O*C*H$_3$), 54.4 (d, *C*HCH=CH), 74.6 (d, *C*HOH), 78.1 (d, TBSO*C*HCH$_2$CHOH), 78.8 (d, TBSO*C*HCH=CH), 127.8 (d, *C*H=CHCHOTBS), 135.9 (d, CH=*C*HCHOTBS), 174.5 (s, *C*OOCH$_3$).

Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.84 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 0.88 (s, 18H, SiC(C*H*$_3$)$_3$), 1.20-1.35 (m, 9H, C*H*$_2$), 1.40-1.67 (m, 6H, C*H*$_2$CH$_3$, CH*H*CHOH, C*H*$_2$), 2.00 (s,

1H, O*H*), 2.07-2.15 (m, 1H, C*H*CHOH), 2.18-2.26 (m, 1H, CH*H*CHOH), 2.29 (t, *J* = 7.5 Hz, 2H, CH_2COOCH$_3$), 2.64-2.71 (m, 1H, C*H*CH=CH), 3.66 (s, 3H, OCH_3), 3.81-3.88 (m, 1H, TBSOC*H*CH$_2$CHOH), 3.90-3.95 (m, 1H, C*H*OH), 3.94-3.99 (m, 1H, TBSOC*H*CH$_2$CH$_3$), 5.17 (ddd, *J* = 1.0, 10.2, 15.3 Hz, 1H, C*H*=CHCHOTBS), 5.44 (ddd, *J* = 0.7, 6.4, 15.3 Hz, 1H, CH=C*H*CHOTBS). - ^{13}C NMR (100 MHz): δ = 9.78 (q, *C*H$_3$CH$_2$), 18.2 (s, Si*C*(CH$_3$)$_3$), 18.4 (s, Si*C*(CH$_3$)$_3$), 25.09 (t, *C*H$_2$), 25.99 (q, SiC(*C*H$_3$)$_3$), 28.4 (t, *C*H$_2$), 29.29 (t, *C*H$_2$), 29.35 (t, *C*H$_2$), 29.87 (t, *C*H$_2$), 29.91 (t, *C*H$_2$), 31.5 (t, *C*H$_2$CH$_3$), 34.3 (t, *C*H$_2$COOCH$_3$), 43.17 (t, *C*H$_2$CHOH), 51.02 (d, *C*HCHOH), 51.6 (q, OCH$_3$), 54.6 (d, *C*HCH=CH), 74.8 (d, *C*HOH), 78.4 (d, TBSO*C*HCH$_2$CHOH), 78.7 (d, TBSO*C*HCH=CH), 127.7 (d, *C*H=CHCHOTBS), 136.1 (d, CH=*C*HCHOTBS), 174.5 (s, *C*OOCH$_3$).

(2*S,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentanone (26):**



Alcohol **25** (0.05 mmol, 28 mg), 4-methylmorpholine-N-oxide (0.10 mmol, 11 mg), tetrapropylammonium perruthenate (0.01 mmol, 4 mg) and molecular sieves (4 Å, 50 mg) were stirred in DCM (1 mL) at r.t. under an argon atmosphere for 60 min. The suspension was diluted with DCM (2 mL), filtered through a plug of celite, silica gel and sand and evaporated. The crude material was not further purified. Yield 25 mg (90%) as a colorless oil. - R_f (hexane/EtOAc 5:1) = 0.9. - IR (film): ν = 2968, 2938, 2865, 1748, 1470, 1441, 1367, 1258, 1171, 1065, 1011, 975, 912, 838, 779, 726, 674. - MS (+ESI) *m/z*, (%): 591 (100) $[M+Na]^+$, 437 (9) $[M–HOTBS+H]^+$. - HRMS (+ESI) *m/z*: ($C_{31}H_{60}O_5NaSi_2$) calc.: 591.3872, found: 591.3870.

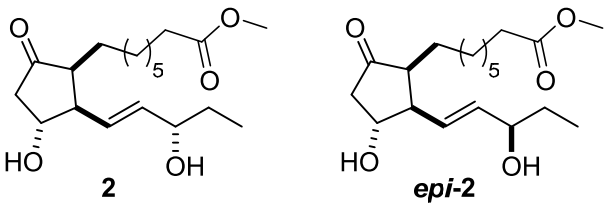
NMR signals of Si-*CH*$_3$ ^{1}H NMR (400 MHz): δ = –0.01, 0.01, 0.03, 0.06, 0.08. - ^{13}C NMR (100 MHz): δ = –4.7, –4.6, –4.5, –4.3, –4.2 *could not be assigned to the individual C16-epimers.*

Major C16 epimer: ^{1}H NMR (400 MHz): δ = 0.825 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 0.88 (s, 18H, SiC(C*H*$_3$)$_3$), 1.12-1.42 (m, 9H, C*H*$_2$), 1.42-1.52 (m, 2H, C*H*$_2$CH$_3$), 1.57-1.64 (m, 2H, C*H*$_2$), 1.65-1.74 (m, 1H, C*H*$_2$), 2.22-2.26 (m, 1H, CH*H*CO), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.35-2.44 (m, 1H, CH*H*CO), 2.58-2.65 (m, 1H, C*H*CO), 2.91 (ddd, *J* = 1.8,

7.5, 10.1 Hz, 1H, C*H*CH=CH), 3.66 (s, 3H, OCH_3), 3.93-4.01 (m, 1H, TBSOC*H*CH_2CH_3), 4.13-4.18 (m, 1H, TBSOC*H*CH_2CO), 5.18 (ddd, *J* = 1.3, 10.1, 15.5 Hz, 1H, C*H*=CHCHOTBS), 5.60 (ddd, *J* = 0.7, 6.8, 15.6 Hz, 1H, CH=C*H*CHOTBS). - ^{13}C NMR (100 MHz): δ = 9.6 (q, *C*H_3CH_2), 18.17 (s, Si*C*$(CH_3)_3$), 18.39 (s, Si*C*$(CH_3)_3$), 25.10 (t, *C*H_2), 25.15 (t, *C*H_2), 25.90 (q, SiC(*C*$H_3)_3$), 25.98 (q, SiC(*C*$H_3)_3$), 27.6 (t, *C*H_2), 29.27 (t, *C*H_2), 29.31 (t, *C*H_2), 29.32 (t, *C*H_2), 31.28 (t, *C*H_2CH_3), 34.2 (t, *C*H_2COOCH_3), 45.7 (t, *C*H_2CO), 50.1 (d, *C*HCO), 51.6 (q, O*C*H_3), 52.1 (d, *C*HCH=CH), 73.4 (d, TBSO*C*HCH_2CO), 74.1 (d, TBSO*C*HCH=CH), 126.0 (d, *C*H=CHCHOTBS), 137.4 (d, CH=*C*HCHOTBS), 174.4 (s, *C*$OOCH_3$), 218.77 (s, *C*OCH).

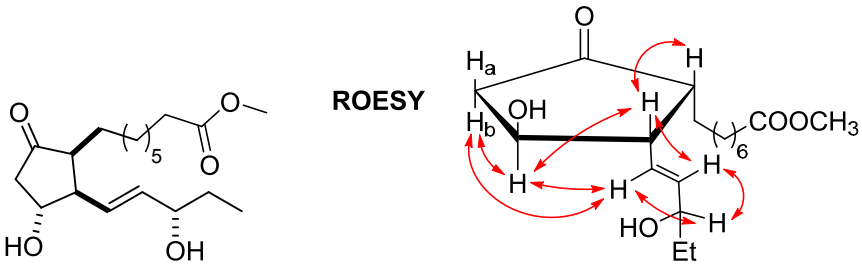
Minor C16 epimer: ^{1}H NMR (400 MHz): δ = 0.830 (t, *J* = 7.4 Hz, 3H, C*H*$_3CH_2$), 0.88 (s, 18H, SiC(C*H*$_3)_3$), 1.12-1.42 (m, 9H, C*H*$_2$), 1.42-1.52 (m, 2H, C*H*$_2CH_3$), 1.57-1.64 (m, 2H, C*H*$_2$), 1.65-1.74 (m, 1H, C*H*$_2$), 2.18-2.23 (m, 1H, CH*H*CO), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2COOCH_3$), 2.35-2.44 (m, 1H, CH*H*CO), 2.58-2.65 (m, 1H, C*H*CO), 2.91 (ddd, *J* = 1.8, 7.5, 10.1 Hz, 1H, C*H*CH=CH), 3.66 (s, 3H, OC*H*$_3$), 3.93-4.01 (m, 1H, TBSOC*H*CH_2CH_3), 4.19-4.24 (m, 1H, TBSOC*H*CH_2CO), 5.07 (ddd, *J* = 1.2, 10.2, 15.3 Hz, 1H, C*H*=CHCHOTBS), 5.59 (ddd, *J* = 0.8, 6.5, 15.2 Hz, 1H, CH=C*H*CHOTBS). - ^{13}C NMR (100 MHz): δ = 9.7 (q, *C*H_3CH_2), 18.18 (s, Si*C*$(CH_3)_3$), 18.38 (s, Si*C*$(CH_3)_3$), 25.07 (t, *C*H_2), 25.13 (t, *C*H_2), 25.91 (q, SiC(*C*$H_3)_3$), 26.00 (q, SiC(*C*$H_3)_3$), 27.4 (t, *C*H_2), 29.56 (t, *C*H_2), 29.58 (t, *C*H_2), 29.9 (t, *C*H_2), 31.32 (t, *C*H_2CH_3), 34.2 (t, *C*H_2COOCH_3), 45.6 (t, *C*H_2CO), 50.0 (d, *C*HCO), 51.6 (q, O*C*H_3), 52.2 (d, *C*HCH=CH), 73.1 (d, TBSO*C*HCH_2CO), 74.7 (d, TBSO*C*HCH=CH), 126.1 (d, *C*H=CHCHOTBS), 137.7 (d, CH=*C*HCHOTBS), 174.4 (s, *C*$OOCH_3$), 218.79 (s, *C*OCH).

16-E_1-Phytoprostane methyl ester (2) and 16-*epi*-16-E_1-phytoprostane methyl ester (*epi*-2):

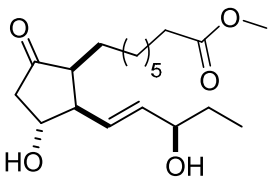


Ketone **26** (0.04 mmol, 25 mg) was dissolved in dry THF (2 mL). The solution was cooled to 0 °C and 70% HF solution in pyridine (10 μL, 0.38 mmol) was added. The mixture was warmed to r.t. and stirred for 21 h. The reaction was quenched with saturated Na_2CO_3 solution (3 mL) and the layers were separated. The aqueous was extracted with DCM (3×5 mL). The

combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (Florisil 3 g, EtOAc). Yield 13 mg (86%) as a 1:1.2 **2**/***epi*-2** mixture. The individual C16 epimers were subsequently separated by multiple flash column chromatography (silica gel 0.5 g, EtOAc).



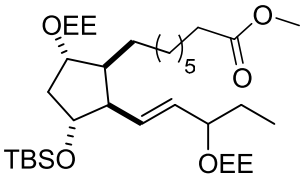
16-E$_1$-Phytoprostane methyl ester **2**: R_f (EtOAc) = 0.2. - IR (film): ν = 3429, 2935, 2864, 1741, 1465, 1443, 1371, 1326, 1252, 1204, 1173, 1127, 1092, 1007, 975, 881, 725. - MS (+ESI) *m/z*, (%): 703 (4) $[2M+Na]^+$, 379 (8) $[M+K]^+$, 363 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{32}O_5Na$) calc.: 363.2142, found: 365.2143. - ^{1}H NMR (500 MHz): δ = 0.90 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.15-1.39 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.47-1.71 (m, 5H, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$, *H*OCHCH=CH), 1.75 (d, *J* = 2.1 Hz, 1H, *H*OCHCH$_2$CO), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.32 (dq, *J* = 1.7, 19.2 Hz, 1H, CH*H*CO), 2.53 (dd, 1H, *J* = 5.7, 19.2 Hz, CH*H*CO), 2.65 (dddd, 1H, *J* = 1.6, 5.2, 7.8, 9.3 Hz, C*H*CO), 2.98 (tdd, *J* = 1.7, 7.8, 10.0 Hz, 1H, C*H*CH=CHCHOH), 3.66 (s, 3H, OC*H*$_3$), 4.00 (dq, *J* = 3.5, 6.6 Hz, 1H, C*H*OHCH=CH), 4.36 (tdd, *J* = 1.7, 2.1, 5.7 Hz, 1H, C*H*OHCH$_2$CO), 5.26 (ddd, *J* = 1.1, 10.1, 15.3 Hz, 1H, C*H*=CHCHOH), 5.67 (ddd, *J* = 0.6, 6.8, 15.3 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (126 MHz): δ = 9.62 (q, *C*H$_3$CH$_2$), 24.87 (t, *C*H$_2$), 25.11 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.20 (t, *C*H$_2$), 29.01 (t, 2C, *C*H$_2$), 29.27 (t, *C*H$_2$), 30.26 (t, *C*H$_2$CH$_3$), 34.1 (t, *C*H$_2$COOCH$_3$), 44.8 (t, CO*C*H$_2$CHOH), 50.0 (d, *C*HCO), 51.5 (q, O*C*H$_3$), 51.7 (d, *C*HCH=CH), 72.2 (d, HO*C*HCH$_2$CO), 74.1 (d, HO*C*HCH$_2$CH$_3$), 127.2 (d, *C*H=CHCHOH), 137.00 (d, CH=*C*HCHOH), 174.3 (s, *C*OOCH$_3$), 217.3 (s, *C*OCH).



16-epi-16-E$_1$-Phytoprostane methyl ester ***epi*-2**: R_f (EtOAc) = 0.3. - IR (film): ν = 3424, 2933, 2863, 1739, 1465, 1444, 1357, 1327, 1250, 1204, 1172, 1127, 1091, 1006, 975, 881, 725. - MS (+ESI) *m/z*, (%): 703 (8) $[2M+Na]^+$, 379 (5) $[M+K]^+$, 363 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{32}O_5Na$) calc.: 363.2142, found: 365.2143. - ^{1}H NMR (500 MHz): δ = 0.91

(t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.15-1.39 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.47-1.71 (m, 5H, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$, OH), 1.75 (br s, 1H, OH), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.31 (dq, *J* = 1.8, 19.2 Hz, 1H, CH*H*CO), 2.53 (dd, *J* = 5.8, 19.2 Hz, 1H, CH*H*CO), 2.65 (dddd, *J* = 1.8, 5.5, 7.2, 9.0 Hz, 1H, C*H*CO), 2.98 (tdd, *J* = 1.8, 7.2, 9.8 Hz, 1H, C*H*CH=CHCHOH), 3.66 (s, 3H, OC*H*$_3$), 4.03 (dq, *J* = 1.1, 6.3 Hz, 1H, HOC*H*CH=CH), 4.34 (td, *J* = 1.8, 5.8 Hz, 1H, C*H*OHCH$_2$CO), 5.31 (ddd, *J* = 1.1, 9.8, 15.4 Hz, 1H, C*H*=CHCHOH), 5.69 (ddd, *J* = 0.6, 6.1, 15.4 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (126 MHz): δ = 9.56 (q, *C*H$_3$CH$_2$), 24.83 (t, *C*H$_2$), 25.08 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.22 (t, *C*H$_2$), 28.95 (t, *C*H$_2$), 28.97 (t, *C*H$_2$), 29.24 (t, *C*H$_2$), 30.20 (t, *C*H$_2$CH$_3$), 34.0 (t, *C*H$_2$COOCH$_3$), 44.9 (t, CO*C*H$_2$CHOH), 50.1 (d, *C*HCO), 51.5 (q, O*C*H$_3$), 51.6 (d, *C*HCH=CH), 72.3 (d, HO*C*HCH$_2$CO), 73.5 (d, HO*C*HCH$_2$CH$_3$), 126.5 (d, *C*H=CHCHOH), 137.02 (d, CH=*C*HCHOH), 174.4 (s, *C*OOCH$_3$), 217.2 (s, *C*OCH).

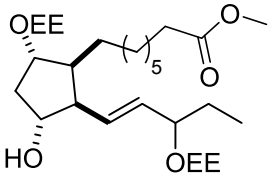
(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-1-(1-ethoxyethoxy)-3-((*E*)-3-(1-ethoxyethoxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentane (27a):**



Diol **22** (0.12 mmol, 53 mg) and a catalytic amount of pyridinium *p*-toluenesulfonate (0.01 mmol, 3 mg) were dissolved in dry DCM (2 mL) under an argon atmosphere. Ethyl vinyl ether (10.46 mmol, 1 mL) was added and the mixture was stirred at r.t. for two hours. The reaction mixture was poured into saturated NaHCO$_3$ solution (10 mL), the layers were separated and the aqueous was extracted with DCM (3×3 mL). The combined organic layers were dried over MgSO$_4$ and evaporated. The crude material was purified by flash chromatography (silica gel 1 g, hexane/EtOAc 20:1). Yield 58 mg (83%) as an inseparable mixture of C16 epimers and ethoxyethoxy (C-1) diastereoisomers as a colorless oil. - R$_f$ (hexane/EtOAc 5:1) = 0.6. - IR (film): ν = 2938, 2865, 1747, 1466, 1445, 1381, 1344, 1257, 1175, 1129, 1097, 1061, 1034, 979, 939, 862, 839, 778. - MS (+ESI) *m/z*, (%): 623 (100) [M+Na]$^+$, 549 (36) [M-Et$_2$O+Na]$^+$. - HRMS (+ESI) *m/z*: (C$_{33}$H$_{64}$O$_7$NaSi) calc.: 623.4314, found: 623.4314. - ^{1}H NMR (400 MHz): δ = 0.006/0.009/0.013 (s, 6H, SiC*H*$_3$), 0.83-0.90 (m, 12H, SiC(C*H*$_3$)$_3$, C*H*$_3$CH$_2$CHOEE), 1.13-1.22 (m, 6H, OCH$_2$C*H*$_3$), 1.22-1.35 (m, 16H, OCHC*H*$_3$, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.42-1.66 (m, 5H, CHC*H*$_2$CH$_3$, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CHOTBS), 2.07-2.20 (m, 1H, C*H*CHOTBS), 2.29 (t, *J* = 7.6 Hz, 2H, C*H*$_2$COOCH$_3$),

2.32-2.44 (m, 1H, CH*H*CHOTBS), 2.53-2.62 (m, 1H, C*H*CH=CH), 3.35-3.90 (m, 6H, EEOC*H*CHCH$_2$, EEOC*H*CH=CH, OC*H*$_2$CH$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.85-3.95 (m, 1H, C*H*OTBS), 4.64-4.72 (m, 2H, OC*H*O), 5.24-5.49 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = –4.52/–4.50/–4.48/–4.46 (q, Si*C*H$_3$), 9.79/9.82/10.13/10.17 (q, *C*H$_3$CH$_2$CH), 15.39/15.41/15.47/15.65/15.66/15.81 (q, OCH$_2$*C*H$_3$), 18.2 (s, Si*C*(CH$_3$)$_3$), 20.58/20.60/20.69/20.72 (q, OCH*C*H$_3$), 25.1 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.0 (t, *C*H$_2$), 28.86/28.89/28.9 (t, *C*H$_2$CH$_3$), 29.00/29.02 (t, *C*H$_2$), 29.31/29.34 (t, *C*H$_2$), 29.40/29.42/29.45/29.46/29.47/29.49 (t, *C*H$_2$), 29.85/29.92/30.00/30.01 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 41.2/41.3/41.4/42.38/42.41/42.5 (t, *C*H$_2$CHOTBS), 47.03/47.05/47.14/47.17/47.19/47.27 (d, *C*HCH$_2$CH$_2$), 51.6 (q, OC*H*$_3$), 52.94/52.99/53.03/53.13/53.17/53.27 (d, *C*HCH=CH), 59.09/59.10/59.14/59.16 and 59.65/59.70/59.74 and 60.28/60.32 and 61.38/61.39/61.43/61.46 (t, OC*H*$_2$CH$_3$), 76.42/76.47/76.51/76.55/76.57 (d, *C*HOTBS), 77.95/77.99/78.19/78.24 (d, EEO*C*HCHCH$_2$), 78.57/78.59/78.62/78.64 (d, EEO*C*HCH=CH), 80.14/80.18/80.22/80.29 (d, EEO*C*HCHCH$_2$), 96.8/96.9 and 98.39/98.40/98.43 and 98.53 and 99.77/99.83/99.86 (q, O*C*HO), 130.34/130.38/130.59/130.60 and 131.84/131.85/131.99/132.01 (d, *C*H=CHCHOEE), 133.08/133.11 and 133.69/133.84 (d, CH=*C*HCHOEE), 174.4 (s, *C*OOCH$_3$).

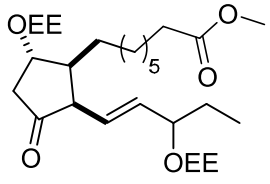
(1*R,2*R**,3*S**,4*S**)-4-(1-Ethoxyethoxy)-2-((*E*)-3-(1-ethoxyethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentan-1-ol (28a):**



Silyl ether **27a** (0.04 mmol, 24 mg) was dissolved in dry THF (1.5 mL) in a flame dried Schlenk flask under an argon atmosphere. The solution was cooled to 0 °C and TBAF (0.4 mmol, 400 µL, 1 M in THF) was added dropwise. The reaction was stirred at the same temperature for 30 min, warmed to r.t. and stirred for an hour. Another portion of TBAF (0.4 mmol, 400 µL, 1 M in THF) was added and the reaction was quenched after 30 min with saturated NH$_4$Cl solution (5 mL), diluted with Et$_2$O (5 mL) and the layers were separated. The aqueous was extracted with Et$_2$O (3×5 mL). The combined organic layers were dried over MgSO$_4$ and evaporated. The crude material was purified by column chromatography (silica gel 1 g, hexane/EtOAc 5:1 gradient to 2:1). Yield 17 mg (87%) as an inseparable mixture of C16 epimers and ethoxyethoxy (C-1) diastereoisomers as a colorless oil. - R$_f$ (hexane/EtOAc

2:1) = 0.3. - IR (film): ν = 3469, 2985, 2937, 2865, 1745, 1445, 1381, 1342, 1253, 1175, 1129, 1095, 1059, 1033, 977, 937, 882, 845, 750. - MS (+ESI) *m/z*, (%): 509 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{27}H_{50}O_7Na$) calc.: 509.3449, found: 509.3449. - ^{1}H NMR (400 MHz): δ = 0.856/0.863/0.880/0.884 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOEE), 1.15-1.25 (m, 6H, OCH$_2$C*H*$_3$), 1.24-1.35 (m, 16H, OCHC*H*$_3$, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.44-1.55 (m, 1H, CHC*H*HCH$_3$), 1.57-1.75 (m, 4H, CHC*H*HCH$_3$, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CHOH), 1.75-2.05 (br s, 1H, O*H*), 2.10-2.20 (m, 1H, C*H*CHOEE), 2.28 (t, *J* = 7.6 Hz, 2H, C*H*$_2$COOCH$_3$), 2.31-2.45 (m, 1H, CH*H*CHOH), 2.67-2.75 (m, 1H, C*H*CH=CH), 3.34-3.73 (m, 4H, OC*H*$_2$CH$_3$), 3.65 (s, 3H, OC*H*$_3$), 3.74-3.91 (m, 2H, EEOC*H*CHCH$_2$, EEOC*H*CH=CH), 3.92-4.00 (m, 1H, C*H*OH), 4.65-4.73 (m, 2H, OC*H*O), 5.30-5.54 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = 9.76/9.83/10.08/10.17 (q, *C*H$_3$CH$_2$CH), 15.40/15.44/15.59/15.63 (q, 2C, OCH$_2$*C*H$_3$), 20.50/20.55/20.62/20.65/20.67/20.69 (q, 2C, OCH*C*H$_3$), 25.1 (t, *C*H$_2$CH$_2$COOCH$_3$), 28.18/28.26/28.27/28.31/28.33 (t, *C*H$_2$), 28.72/28.74/28.75/28.86/28.94 (t, *C*H$_2$CHOEECH=CH), 29.12/29.15/29.22/29.26/29.28 (t, 2C, *C*H$_2$), 29.37/29.40/29.41/29.43 (t, *C*H$_2$), 29.80/29.86/29.88 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 40.05/40.10/40.14/41.23/41.29/41.33 (t, *C*H$_2$CHOTBS), 47.71/47.81/47.87/47.92 (d, *C*HCH$_2$CH$_2$), 51.6 (q, OC*H*$_3$), 53.29/53.35/53.40/53.46 (d, *C*HCH=CH), 59.13 and 59.84 and 60.34/60.38/60.41 and 60.59/60.62/61.2 (t, OC*H*$_2$CH$_3$), 76.69/76.72/76.76/76.79/76.94/76.99 (d, *C*HOH), 78.02/78.06/78.15/78.17 and 78.46/78.85 and 79.24/79.32/79.36 and 80.26/80.39/80.41 (d, 2C, *C*HOEE), 96.86/96.87 and 98.50/98.83 and 98.59/98.67 and 99.55/99.58/99.65 (d, 2C, O*C*HO), 129.90/129.92/130.03/130.06 and 131.29/131.33/131.35 (d, *C*H=CHCHOEE), 133.55/133.57/133.62/133.64 and 134.13/134.15/134.43/134.44 (d, CH=*C*HCHOEE), 174.38/174.39 (s, *C*OOCH$_3$).

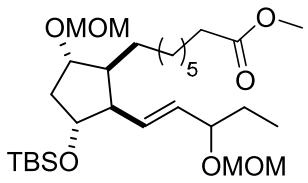
(2*R,3*S**,4*S**)-4-(1-Ethoxyethoxy)-2-((*E*)-3-(1-ethoxyethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentanone (29a):**



Alcohol **28a** (0.03 mmol, 16 mg), Dess-Martin periodinane (0.05 mmol, 21 mg) and $NaHCO_3$ (0.07 mmol, 6 mg) were stirred in dry DCM (2 mL) under an argon atmosphere at 0 °C to r.t. The reaction was stopped by 10% $Na_2S_2O_3$ solution (5 mL) after 3 h. The layers were separated and the aqueous was extracted with DCM (3×2 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated. The crude

material was not further purified. Yield 15 mg (94%) as an inseparable mixture of C16 epimers and ethoxyethoxy (C-1) diastereoisomers as a colorless oil. - R_f (hexane/EtOAc 2:1) = 0.8. - IR (film): ν = 2984, 2937, 2865, 1747, 1445, 1382, 1343, 1242, 1175, 1130, 1095, 1060, 1032, 980, 954, 937, 883, 750. - MS (+ESI) *m/z*, (%): 539 (69) $[M+MeOH+Na]^+$, 525 (37) $[M+H_2O+Na]^+$, 507 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{27}H_{48}O_7Na$) calc.: 507.3292, found: 507.3292. - ^{1}H NMR (400 MHz): δ = 0.87/0.88/0.89/0.90 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$CHOEE), 1.15-1.22 (m, 6H, OCH$_2$C*H*$_3$), 1.23-1.33 (m, 16H, OCHC*H*$_3$, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.45-1.55 (m, 1H, CHC*H*HCH$_3$), 1.56-1.69 (m, 3H, CHCH*H*CH$_3$, C*H*$_2$CH$_2$COOCH$_3$), 2.21-2.37 (m, 2H, C*H*CHOEE, CH*H*COCH), 2.29 (t, *J* = 7.6 Hz, 2H, C*H*$_2$COOCH$_3$), 2.48-2.62 (m, 1H, CH*H*COCH), 3.24-3.32 (m, 1H, C*H*CH=CH), 3.36-3.72 (m, 4H, OC*H*$_2$CH$_3$), 3.66 (s, 3H, OC*H*$_3$), 3.74-3.85/3.89-3.97 (m, 1H, EEOC*H*CH=CH), 4.11-4.17/4.20-4.25 (m, 1H, EEOC*H*CH$_2$CO), 4.65-4.79 (m, 2H, OC*H*O), 5.39-5.64 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = 9.73/9.75/9.77 and 10.06/10.08 (q, *C*H$_3$CH$_2$CH), 15.38/15.41/15.45/15.60/15.62 (q, 2C, OCH$_2$*C*H$_3$), 20.48/20.54/20.59/20.67/20.73 (q, 2C, OCH*C*H$_3$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.71/27.73/27.78/27.81/27.84 (t, *C*H$_2$), 28.08/28.13/28.2 (t, *C*H$_2$), 28.62/28.64/28.71/28.75/28.78/28.85 (t, *C*H$_2$CH$_3$), 29.23/29.25/29.29/29.35 (t, 2C, *C*H$_2$), 29.71/29.75/29.78 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 42.97/43.01/43.04/43.1 and 44.01/44.03/44.1/44.2 (t, *C*H$_2$CO), 47.24/47.27/47.32/47.58/47.65/47.72 (d, *C*HCH$_2$CH$_2$), 51.6 (q, O*C*H$_3$), 54.38/54.39/54.42/54.43/54.59/54.64 (d, *C*HCH=CH), 59.27/59.29/59.68/ 60.2/60.5/61.33/61.36/61.6 (t, 2C, O*C*H$_2$CH$_3$), 73.77/73.80/73.82/74.89/74.91/75.00/75.03 (d, EEO*C*HCH$_2$CO), 77.9/78.0/78.07/78.13/78.31/78.33 (d, EEO*C*HCH=CH), 97.14/97.15/97.22 and 98.68/98.70 and 98.78/98.82/98.83 and 99.54/99.57/99.64 (d, 2C, O*C*HO), 123.99/124.04/124.33 and 125.27/125.65 (d, *C*H=CHCHOEE), 136.50/136.53 and 137.10/137.13/137.15 (d, CH=*C*HCHOEE), 174.34/174.35 (s, *C*OOCH$_3$), 215.14/215.17/215.21/215.24/215.29/215.35/215.43 (s, *C*O).

(1*S,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-1-(1-methoxymethoxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-3-(1-methoxymethoxy)pent-1-en-1-yl)cyclopentane (27b):**



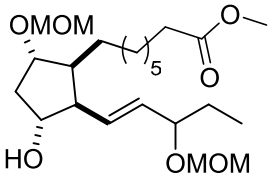
Bromomethyl methyl ether (0.60 mmol, 40 μL) was added to solution of diol **22** (0.15 mmol, 68 mg) and *N*,*N*-diisopropylethylamine (0.86 mmol, 150 μL) in dry DCM (2 mL) at r.t. under an argon atmosphere. The reaction was stirred at the same temperature for 20 h and stopped with saturated NH_4Cl solution (5 mL). The layers were separated and the aqueous was extracted with DCM (3×5 mL). The combined organic layers were dried over $MgSO_4$ and evaporated. The crude material was purified by column chromatography (silica gel 6 g, hexane/EtOAc 30:1 with 0.5 vol% of Et_3N). Yield 40 mg (49%) as an inseparable mixture of C16 epimers as a colorless oil. R_f (hexane/EtOAc 5:1) = 0.7. - IR (film): ν = 2938, 2865, 1747, 1653, 1468, 1443, 1368, 1257, 1217, 1156, 1102, 1038, 921, 839, 779. - MS (+ESI) *m/z*, (%): 567 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{29}H_{56}O_7SiNa$) calc.: 567.3688, found: 567.3687.

Major epimer: ^{1}H NMR (400 MHz): δ = 0.013 (s, 3H, SiC*H*$_3$), 0.015 (s, 3H, SiC*H*$_3$), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.92 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.20-1.34 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.46-1.57 (m, 1H, CH*H*CH$_3$), 1.55-1.71 (m, 4H, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CH$_3$, CH*H*CHOTBS), 2.15 (dtd, *J* = 8.0, 7.3, 5.3 Hz, 1H, C*H*CH$_2$CH$_2$), 2.29 (t, *J* = 7.4 Hz, 2H, C*H*$_2$COOCH$_3$), 2.39 (dt, *J* = 15.0, 7.3 Hz, 1H, CH*H*CHOTBS), 2.60 (td, *J* = 8.0, 3.7 Hz, 1H, C*H*CHOTBS), 3.359 (s, 3H, CH$_2$OC*H*$_3$), 3.363 (s, 3H, CH$_2$OC*H*$_3$), 3.66 (s, 3H, COOC*H*$_3$), 3.73 (td, *J* = 7.5, 5.3 Hz, 1H, MOMOC*H*CHCH$_2$), 3.83-3.95 (m, 2H, MOMOC*H*CH=CH, C*H*OTBS), 4.48-4.50 (m, 1H, OC*H*$_2$O), 4.58-4.73 (m, 3H, OC*H*$_2$O), 5.27-5.40 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = –4.52 (q, CH$_3$Si), –4.51 (q, CH$_3$Si), 10.11 (q, *C*H$_3$CH$_2$), 18.19 (s, Si*C*(CH$_3$)$_3$), 25.1 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.1 (t, *C*H$_2$), 28.7 (t, *C*H$_2$CH$_3$), 28.99 (t, *C*H$_2$), 29.3 (t, *C*H$_2$), 29.4 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 41.3 (t, *C*H$_2$CHOTBS), 47.0 (d, *C*HCH$_2$CH$_2$), 51.6 (q, COO*C*H$_3$), 53.26 (d, *C*HCH=CH), 55.43 (q, CH$_2$O*C*H$_3$), 55.5 (q, CH$_2$O*C*H$_3$), 76.4 (d, *C*HOTBS), 78.0 (d, MOMO*C*HCH=CH), 81.0 (d, MOMOC*H*CHCH$_2$), 93.4 (t, OCH$_2$O), 95.8

(t, O*C*H$_2$O), 132.36 (d, *C*H=CHCHOMOM), 132.43 (d, CH=*C*HCHOMOM), 174.4 (s, *C*OOCH$_3$).

Minor epimer: ^{1}H NMR (400 MHz): δ = 0.019 (s, 6H, SiC*H*$_3$), 0.89 (s, 9H, SiC(C*H*$_3$)$_3$), 0.91 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.20-1.34 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.46-1.57 (m, 1H, CH*H*CH$_3$), 1.55-1.71 (m, 4H, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CH$_3$, CH*H*CHOTBS), 2.15 (dtd, *J* = 8.0, 7.3, 5.3 Hz, 1H, C*H*CH$_2$CH$_2$), 2.29 (t, *J* = 7.4 Hz, 2H, C*H*$_2$COOCH$_3$), 2.41 (dt, *J* = 14.0, 7.0 Hz, 1H, CH*H*CHOTBS), 2.60 (td, *J* = 8.0, 3.7 Hz, 1H, C*H*CH=CH), 3.359 (s, 3H, CH$_2$OC*H*$_3$), 3.363 (s, 3H, CH$_2$OC*H*$_3$), 3.66 (s, 3H, COOC*H*$_3$), 3.72 (td, *J* = 7.5, 5.3 Hz, 1H, MOMOC*H*CHCH$_2$), 3.83-3.95 (m, 2H, MOMOC*H*CH=CH, C*H*OTBS), 4.48-4.50 (m, 1H, OCH$_2$O), 4.58-4.73 (m, 3H, OCH$_2$O), 5.27-5.40 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = –4.46 (q, CH$_3$Si), 10.09 (q, *C*H$_3$CH$_2$), 18.18 (s, Si*C*(CH$_3$)$_3$), 25.1 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.0 (q, SiC(*C*H$_3$)$_3$), 28.0 (t, *C*H$_2$), 28.8 (t, *C*H$_2$CH$_3$), 28.96 (t, *C*H$_2$), 29.3 (t, *C*H$_2$), 29.4 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 41.3 (t, *C*H$_2$CHOTBS), 47.1 (d, *C*HCH$_2$CH$_2$), 51.6 (q, COO*C*H$_3$), 53.30 (d, *C*HCH=CH), 55.42 (q, CH$_2$O*C*H$_3$), 55.5 (q, CH$_2$O*C*H$_3$), 76.5 (d, *C*HOTBS), 78.2 (d, MOMO*C*HCH=CH), 81.1 (d, MOMOC*H*CHCH$_2$), 93.5 (t, O*C*H$_2$O), 95.9 (t, O*C*H$_2$O), 132.2 (d, *C*H=CHCHOMOM), 132.5 (d, CH=*C*HCHOMOM), 174.4 (s, *C*OOCH$_3$).

(1*R,2*R**,3*S**,4*S**)-4-(1-Methoxymethoxy)-2-((*E*)-3-(1-methoxymethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentan-1-ol (28b):**

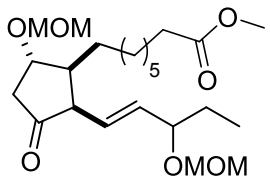


Silyl ether **27b** (0.07 mmol, 38 mg) was dissolved in dry THF (2 mL) under an argon atmosphere. The solution was cooled to 0 °C and TBAF (0.1 mmol, 100 μL, 1 M in THF) was added. The reaction mixture was stirred at the same temperature for 60 min and warmed to r.t. over 30 min. Another four portions of TBAF (0.4 mmol, 4×100 μL, 1 M in THF) were added in 30 min intervals. The reaction was quenched after 120 min with saturated NH$_4$Cl solution (10 mL). The mixture was diluted with Et$_2$O (5 mL) and the layers were separated. The aqueous was extracted with Et$_2$O (3×15 mL). The combined organic layers were dried over MgSO$_4$ and evaporated. The crude material was purified by column chromatography (silica

gel 1 g, hexane/EtOAc 10:1 with 0.5 vol% of Et_3N). Yield 17 mg (69%) as an inseparable mixture of C16 epimers as a colorless oil. - R_f (hexane/EtOAc 2:1) = 0.2. - IR (film): ν = 3472 (br), 2938, 2865, 1745, 1663, 1463, 1463, 1368, 1252, 1209, 1156, 1105, 1039, 994, 922. - MS (+ESI) *m/z*, (%): 453 (100) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{23}H_{42}O_7Na$) calc.: 453.2823, found: 453.2823.

Major epimer: ^{1}H NMR (400 MHz): δ = 0.91 (t, *J* = 7.3 Hz, 3H, C*H*$_3$CH$_2$), 1.20-1.33 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.51 (dqd, *J* = 13.9, 7.3, 6.5 Hz, 1H, CH*H*CH$_3$), 1.57-1.90 (m, 5H, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CHO*H*, CH*H*CH$_3$), 2.14-2.23 (m, 1H, C*H*CH$_2$CH$_2$), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.39 (dt, *J* = 15.0, 7.1 Hz, 1H, CH*H*CHOH), 2.68-2.78 (m, 1H, C*H*CHOH), 3.363 (s, 3H, CH$_2$OC*H*$_3$), 3.366 (s, 3H, CH$_2$OC*H*$_3$), 3.66 (s, 3H, COOC*H*$_3$), 3.80-3.91 (m, 2H, C*H*OMOM), 3.98-4.01 (m, 1H, C*H*OH), 4.48-4.79 (m, 4H, OCH$_2$O), 5.36-5.44 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = 10.0 (q, *C*H$_3$CH$_2$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 28.06 (t, *C*H$_2$), 28.5 (t, *C*H$_2$CH$_3$), 29.16 (t, 2C, *C*H$_2$), 29.24 (t, *C*H$_2$), 29.7 (t, *C*H$_2$), 34.1 (t, *C*H$_2$COOCH$_3$), 40.1 (t, *C*H$_2$CHOH), 47.4 (d, *C*HCH$_2$CH$_2$), 51.5 (q, COO*C*H$_3$), 53.45 (d, *C*HCH=CH), 55.35 (q, CH$_2$O*C*H$_3$), 55.5 (q, CH$_2$O*C*H$_3$), 76.6 (d, *C*HOH), 78.0 (d, MOMO*C*HCH=CH), 81.2 (d, MOMOC*H*CH$_2$CHOH), 93.4 (t, OCH$_2$O), 95.5 (t, OCH$_2$O), 131.58 (d, *C*H=CHCHOMOM), 133.3 (d, CH=*C*HCHOMOM), 174.3 (s, *C*OOCH$_3$).
Minor epimer: ^{1}H NMR (400 MHz): δ = 0.91 (t, *J* = 7.3 Hz, 3H, C*H*$_3$CH$_2$), 1.20-1.33 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.46-1.56 (m, 1H, CH*H*CH$_3$), 1.57-1.90 (m, 5H, C*H*$_2$CH$_2$COOCH$_3$, CH*H*CH$_3$, CH*H*CHO*H*), 2.14-2.23 (m, 1H, C*H*CH$_2$CH$_2$), 2.29 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.41 (dt, *J* = 14.0, 7.2 Hz, 1H, CH*H*CHOH), 2.68-2.78 (m, 1H, C*H*CHOH), 3.358 (s, 3H, CH$_2$OC*H*$_3$), 3.365 (s, 3H, CH$_2$OC*H*$_3$), 3.66 (s, 3H, COOC*H*$_3$), 3.80-3.91 (m, 2H, C*H*OMOM), 3.98-4.01 (m, 1H, C*H*OH), 4.48-4.79 (m, 4H, OCH$_2$O), 5.36-5.44 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = 9.9 (q, *C*H$_3$CH$_2$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 28.05 (t, *C*H$_2$), 28.5 (t, *C*H$_2$CH$_3$), 29.16 (t, 2C, *C*H$_2$), 29.25 (t, *C*H$_2$), 29.7 (t, *C*H$_2$), 34.1 (t, *C*H$_2$COOCH$_3$), 40.0 (t, *C*H$_2$CHOH), 47.4 (d, *C*HCH$_2$CH$_2$), 51.5 (q, COO*C*H$_3$), 53.52 (d, *C*HCH=CH), 55.32 (q, CH$_2$O*C*H$_3$), 55.5 (q, CH$_2$O*C*H$_3$), 76.5 (d, *C*HOH), 79.0 (d, MOMO*C*HCH=CH), 81.1 (d, MOMOC*H*CH$_2$CHOH), 93.8 (t, OCH$_2$O), 95.4 (t, OCH$_2$O), 131.61 (d, *C*H=CHCHOMOM), 132.8 (d, CH=*C*HCHOMOM), 174.3 (s, *C*OOCH$_3$).

(2*R,3*S**,4*S**)-4-(1-Methoxymethoxy)-2-((*E*)-3-(1-methoxymethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentanone (29b):**



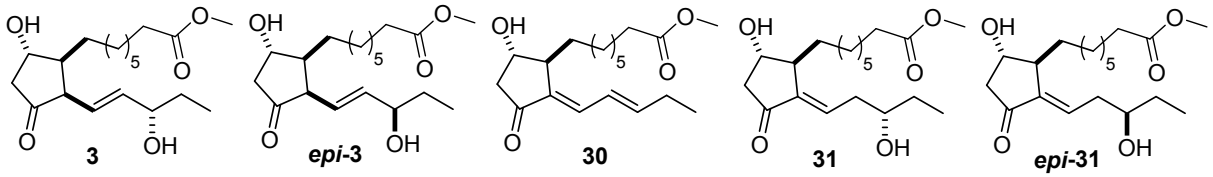
Alcohol **28b** (0.02 mmol, 10 mg), Dess-Martin periodinane (0.03 mmol, 13 mg) and $NaHCO_3$ (0.05 mmol, 4 mg) were stirred in dry DCM (1.5 mL) under an argon atmosphere at 0 to 10 °C for 2 h. The reaction was stopped by 10% $Na_2S_2O_3$ solution (5 mL) and diluted with DCM (2 mL). The layers were separated and aqueous was extracted with DCM (3×3 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution, dried over $MgSO_4$ and evaporated. The crude material was not further purified. Yield 10 mg (97%) as an inseparable mixture of C16 epimers as a colorless oil. - R_f (hexane/EtOAc 2:1) = 0.7. - IR (film): ν = 2936, 2864, 1745, 1664, 1464, 1443, 1368, 1264, 1208, 1154, 1100, 1033, 995, 921, 803. - MS (+ESI) *m/z*, (%): 467 (100) $[M+K]^+$, 451 (42) $[M+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{23}H_{40}O_7Na$) calc.: 451.2666, found: 451.2667.

Major epimer: ^{1}H NMR (400 MHz): δ = 0.923 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.20-1.39 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.50-1.67 (m, 4H, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$), 2.25-2.37 (m, 2H, CH*H*COCH, C*H*CH$_2$CH$_2$), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.584 (dd, *J* = 19.2, 6.5 Hz, 1H, CH*H*COCH), 3.28 (t, *J* = 7.1 Hz, 1H, COC*H*CH=CH), 3.36 (s, 3H, CH$_2$OC*H*$_3$), 3.38 (s, 3H, CH$_2$OC*H*$_3$), 3.66 (s, 3H, COOC*H*$_3$), 3.923 (q, *J* = 6.5 Hz, 1H, MOMOC*H*CH=CH), 4.13-4.19 (m, 1H, MOMOC*H*CH$_2$CO), 4.42 (dd, *J* = 6.7, 1.5 Hz, 1H, OCH$_2$O), 4.62-4.73 (m, 3H, OCH$_2$O), 5.42-5.50 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = 10.0 (q, *C*H$_3$CH$_2$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.63 (t, *C*H$_2$), 28.0 (t, *C*H$_2$), 28.4 (t, *C*H$_2$CH$_3$), 29.16 (t, *C*H$_2$), 29.22 (t, *C*H$_2$), 29.6 (t, *C*H$_2$), 34.1 (t, *C*H$_2$COOCH$_3$), 43.13 (t, *C*H$_2$CO), 47.1 (d, *C*HCH$_2$CH$_2$), 51.6 (q, COO*C*H$_3$), 54.6 (d, *C*HCH=CH), 55.4 (q, CH$_2$O*C*H$_3$), 76.07 (d, MOMO*C*HCH$_2$CO), 77.9 (d, MOMO*C*HCH=CH), 93.7 (t, OCH$_2$O), 95.6 (t, OCH$_2$O), 125.5 (d, *C*H=CHCHOMOM), 135.8 (d, CH=*C*HCHOMOM), 174.3 (s, *C*OOCH$_3$), 214.8 or 215.0 (s, *C*O).

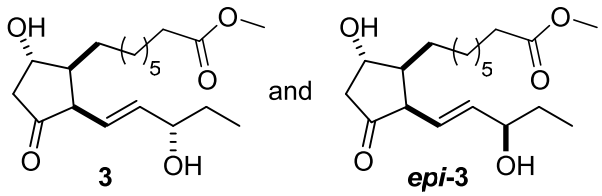
Minor epimer: ^{1}H NMR (400 MHz): δ = 0.917 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.20-1.39 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.50-1.67 (m, 4H, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$), 2.25-2.37 (m, 2H, CH*H*COCH, C*H*CH$_2$CH$_2$), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.579 (dd, *J* =

19.2, 6.5 Hz, 1H, CH*H*COCH), 3.28 (t, *J* = 7.1 Hz, 1H, COC*H*CH=CH), 3.36 (s, 3H, CH_2OCH_3), 3.38 (s, 3H, CH_2OCH_3), 3.66 (s, 3H, $COOCH_3$), 3.918 (q, *J* = 6.5 Hz, 1H, MOMOC*H*CH=CH), 4.13-4.19 (m, 1H, MOMOC*H*CH_2CO), 4.42 (dd, *J* = 6.7, 1.5 Hz, 1H, OCH_2O), 4.62-4.73 (m, 3H, OCH_2O), 5.42-5.50 (m, 2H, C*H*=C*H*). - ^{13}C NMR (100 MHz): δ = 9.9 (q, CH_3CH_2), 25.0 (t, $CH_2CH_2COOCH_3$), 27.63 (t, CH_2), 28.0 (t, CH_2), 28.5 (t, CH_2CH_3), 29.16 (t, CH_2), 29.21 (t, CH_2), 29.6 (t, CH_2), 34.1 (t, CH_2COOCH_3), 43.09 (t, CH_2CO), 47.1 (d, $CHCH_2CH_2$), 51.6 (q, $COOCH_3$), 54.5 (d, *C*HCH=CH), 55.6 (q, CH_2OCH_3), 76.14 (d, MOMO*C*HCH_2CO), 77.7 (d, MOMO*C*HCH=CH), 93.6 (t, OCH_2O), 95.6 (t, OCH_2O), 125.9 (d, *C*H=CHCHOMOM), 135.7 (d, CH=*C*HCHOMOM), 174.3 (s, *C*$OOCH_3$), 214.8 or 215.0 (s, *C*O).

16-D_{1t}-Phytoprostane methyl ester (3), 16-*epi*-16-D_{1t}-phytoprostane methyl ester (*epi*-3), 16-deoxy-$\Delta^{13,15}$-16-D_{1t}-phytoprostane methyl ester (30), Δ^{13}-16-D_{1t}-phytoprostane methyl ester (31), 16-*epi*-Δ^{13}-16-D_{1t}-phytoprostane methyl ester (*epi*-31)



Ketone **29b** (0.03 mmol, 15 mg) was dissolved in dry DCM (0.1 mL) and a solution of pyridinium *p*-toluenesulfonate (0.01 mmol, 1 mg) in dry MeOH (1 mL) was added at room temperature under an argon atmosphere. The reaction mixture was stirred for 3 h and quenched by addition of a few crystals solid $NaHCO_3$, filtered through a short plug of celite and evaporated. The crude material, which according to ^{1}H NMR spectroscopy consisted of a 2:1 mixture of **3** and **30**, but did not contain **31**, was purified by multiple column chromatography (celite 0.5 g /silica gel 0.2 g, DCM/Et_2O gradient 2:1 to 1:2). Yield 5 mg (47%) as inseparable 3:1 mixture of **3** and **31** and 3 mg (30%) of **30** as colorless oils. Thus, the 3:1 ratio of **3** to **31** determined by ^{1}H NMR spectroscopy results from isomerization at silica gel.



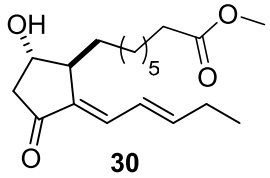
IR and mass spectra were measured on a 3:1 mixture of **3** and **31**. The NMR data were extracted from the spectra of inseparable mixtures of C16 epimers of **3** with **31** and ***epi*-31** in various ratios (3:1, 2:1, 1:15, 1:30).

R_f (hexane/EtOAc 1:2) = 0.3. - IR (film): ν = 3415 (br), 2933, 2862, 1743, 1657, 1466, 1442, 1338, 1264, 1202, 1107, 1023, 863, 829. - MS (+ESI) *m/z*, (%): 409 (100) $[M-H_2O+2MeOH+Na]^+$, 363 (36) $[M+Na]^+$, 345 (30) $[M-H_2O+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{32}O_5Na$) calc.: 363.2142, found: 363.2142.

Major epimer ***epi*-3**: ^{1}H NMR (500 MHz): δ = 0.92 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.23-1.35 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.43-1.69 (m, 5H, C*H*HCH$_3$, C*H*$_2$CH$_2$COOCH$_3$, O*H*), 1.93-2.06 (m, 2H, C*H*CH$_2$CH$_2$, C*H*HCH$_3$), 2.26-2.36 (m, 1H, CH*H*COCH), 2.31 (t, *J* = 7.4 Hz, 2H, C*H*$_2$COOCH$_3$), 2.56 (ddd, *J* = 10.8, 7.3, 1.2 Hz, 1H, COC*H*CH=CH), 2.76 (ddd, *J* = 18.6, 7.1, 1.2 Hz, 1H, CH*H*COCH), 3.67 (s, 3H, OC*H*$_3$), 4.04 (q, *J* = 6.4 Hz, 1H, HOC*H*CH=CH), 4.15 (q, *J* = 7.4 Hz, 1H, HOC*H*CH$_2$CO), 5.52 (dd, *J* = 15.5, 7.3 Hz, 1H, C*H*=CHCHOH), 5.59 (dd, *J* = 15.5, 6.4 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (126 MHz): δ = 9.84 (q, *C*H$_3$CH$_2$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.0 (t, *C*H$_2$CH$_3$), 29.12 (t, *C*H$_2$), 29.52 (t, *C*H$_2$), 29.74 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 29.99 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 47.0 (t, *C*H$_2$CO), 50.5 (d, *C*HCH$_2$CH$_2$), 51.7 (q, O*C*H$_3$), 58.48 (d, *C*HCH=CH), 72.96 (d, HO*C*HCH$_2$CO), 74.1 (d, HO*C*HCH=CH), 126.9 (d, *C*H=CHCHOH), 137.8 (d, CH=*C*HCHOH), 174.5 (s, *C*OOCH$_3$), 214.7 (s, *C*O).

Minor epimer **3**: ^{1}H NMR (500 MHz): δ = 0.94 (t, *J* = 7.5 Hz, 3H, C*H*$_3$CH$_2$), 1.23-1.35 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.43-1.69 (m, 5H, C*H*HCH$_3$, C*H*$_2$CH$_2$COOCH$_3$, O*H*), 1.93-2.06 (m, 2H, C*H*CH$_2$CH$_2$, C*H*HCH$_3$), 2.26-2.36 (m, 1H, CH*H*COCH), 2.31 (t, *J* = 7.4 Hz, 2H, C*H*$_2$COOCH$_3$), 2.56 (ddd, *J* = 10.8, 7.3, 1.2 Hz, 1H, COC*H*CH=CH), 2.75 (ddd, *J* = 18.6, 7.1, 1.2 Hz, 1H, CH*H*COCH), 3.67 (s, 3H, OC*H*$_3$), 4.07 (q, *J* = 5.9 Hz, 1H, HOC*H*CH=CH), 4.15 (q, *J* = 7.4 Hz, 1H, HOC*H*CH$_2$CO), 5.53 (dd, *J* = 15.5, 7.3 Hz, 1H, C*H*=CHCHOH), 5.60 (dd, *J* = 15.5, 5.8 Hz, 1H, CH=C*H*CHOH). - ^{13}C NMR (126 MHz): δ = 9.83 (q, *C*H$_3$CH$_2$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.1 (t, *C*H$_2$CH$_3$), 29.08 (t, *C*H$_2$), 29.48 (t, *C*H$_2$), 29.72 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 30.02 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 47.0 (t, *C*H$_2$CO), 50.6 (d, *C*HCH$_2$CH$_2$), 51.7 (q,

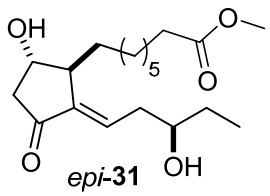
O*C*H$_3$), 58.47 (d, *C*HCH=CH), 73.03 (d, HO*C*HCH$_2$CO), 73.9 (d, HO*C*HCH=CH), 126.5 (d, *C*H=CHCHOH), 137.6 (d, CH=*C*HCHOH), 174.5 (s, *C*OOCH$_3$), 214.7 (s, *C*O).



30

R_f (hexane/EtOAc 1:1) = 0.5. - IR (film): ν = 3452 (br), 2934, 2863, 1741, 1635, 1613, 1465, 1442, 1376, 1248, 1196, 1134, 1099, 1060, 978, 886, 862, 728. - MS (+ESI) *m/z*, (%): 361 (45) $[M+K]^+$, 345 (100) $[M+Na]^+$, 327 (73) $[M-H_2O+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{30}O_4Na$) calc.: 345.2036, found: 345.2037. - ^{1}H NMR (400 MHz): δ = 1.07 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.25-1.40 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.57-1.64 (m, 2H, C*H*$_2$CH$_2$COOCH$_3$), 2.24 (qd, *J* = 7.5, 6.3 Hz, 2H, C*H*$_2$CH$_3$), 2.30 (t, *J* = 7.5 Hz, 2H, C*H*$_2$COOCH$_3$), 2.33 (ddd, *J* = 18.6, 1.5, 0.7 Hz, CH*H*CO), 2.66 (dd, *J* = 18.6, 5.1 Hz, 1H, CH*H*CO), 2.96 (td, *J* = 7.1, 1.5 Hz, 1H, C*H*CH$_2$CH$_2$), 3.63-3.72 (m, 1H, OH), 3.67 (s, 3H, OC*H*$_3$), 4.34 (dd, *J* = 5.1, 0.7 Hz, 1H, C*H*OH), 6.16 (ddt, *J* = 15.0, 11.3, 1.3 Hz, 1H, C*H*=CHCH$_2$), 6.29 (dt, *J* = 15.0, 6.3 Hz, 1H, CH=C*H*CH$_2$), 7.05 (dd, *J* = 11.2, 1.7 Hz, 1H, C*H*=C). - ^{13}C NMR (100 MHz): δ = 13.8 (q, *C*H$_3$CH$_2$), 25.0 (t, *C*H$_2$CH$_2$COOCH$_3$), 26.7 (t, *C*H$_2$CH$_3$), 29.2 (t, *C*H$_2$), 29.3 (t, *C*H$_2$), 29.6 (t, *C*H$_2$), 29.9 (t, *C*H$_2$), 33.6 (t, *C*H$_2$), 34.2 (t, *C*H$_2$COOCH$_3$), 46.1 (t, *C*H$_2$CO), 49.3 (d, *C*HCH$_2$CH$_2$), 51.6 (q, O*C*H$_3$), 71.8 (d, *C*HOH), 125.5 (d, *C*H=CHCH$_2$), 134.7 (d, *C*H=C), 137.3 (s, *C*=CH), 148.7 (d, CH$_2$*C*H=CH), 174.4 (s, *C*OOCH$_3$), 205.6 (s, *C*O).

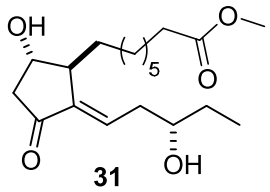
A mixture of **3** and **31** (5 mg, 0.015 mmol) was stirred with silica gel (0.5 g) in $CDCl_3$ (2 mL) at r.t. for 3 days, filtered, extracted with acetone-d_6 and evaporated. The formed epimers of **31** and ***epi*-31** were partially separated by multiple column chromatography (silica gel 0.5 g, $CDCl_3$/acetone-d_6 gradient 5:1 to 1:1) to obtain 1.5 mg of each epimer and 2 mg of an unseparated mixture.



epi-**31**

Less polar epimer: R_f (hexane/EtOAc 1:1) = 0.3. - IR (film): ν = 3446 (br), 2937, 2865, 1727, 1653, 1466, 1443, 1264, 1185, 1102, 1025, 805. - MS (+ESI) *m/z*, (%): 703 (12) $[2M+Na]^+$,

363 (100) $[M+Na]^+$, 345 (35) $[M-H_2O+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{32}O_5Na$) calc.: 363.2142, found: 363.2144. - ^{1}H NMR (500 MHz): δ = 0.97 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.26-1.40 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.49 (ddq, *J* = 14.0, 7.5, 7.4 Hz, 1H, C*H*HCH$_3$), 1.54-1.64 (m, 3H, C*H*$_2$CH$_2$COOCH$_3$, C*H*HCH$_3$), 2.30-2.41 (m, 3H, CH*H*COC=CHC*H*$_2$), 2.31 (t, *J* = 7.4 Hz, 2H, C*H*$_2$COOCH$_3$), 2.64 (dd, *J* = 18.6, 5.0 Hz, 1H, CH*H*COC), 2.88 (t, *J* = 6.9 Hz, 1H, C*H*C=CH), 3.60-3.73 (m, 2H, OH), 3.67 (s, 3H, OC*H*$_3$), 3.73 (dddd, *J* = 7.5, 6.8, 5.4, 5.0 Hz, 1H, HOC*H*CH$_2$CH$_3$), 4.35 (d, *J* = 4.9 Hz, 1H, HOC*H*CH$_2$CO), 6.74 (ddd, *J* = 8.6, 7.0, 1.9 Hz, 1H, C=C*H*). - ^{13}C NMR (126 MHz): δ = 10.1 (q, *C*H$_3$CH$_2$), 24.96 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.61 (t, *C*H$_2$), 29.09 (t, *C*H$_2$), 29.20 (t, *C*H$_2$), 29.5 (t, *C*H$_2$), 30.0 (t, *C*H$_2$CH$_3$), 33.14 (t, *C*H$_2$), 34.15 (t, *C*H$_2$COOCH$_3$), 37.0 (t, *C*H$_2$CH=C), 45.9 (t, *C*H$_2$CO), 48.9 (d, *C*HCH$_2$CH$_2$), 51.67 (q, O*C*H$_3$), 71.4 (d, HO*C*HCH$_2$CO), 72.53 (d, HO*C*HCH$_2$CH$_3$), 134.3 (d, *C*H=C), 142.2 (s, *C*=CH), 174.5 (s, *C*OOCH$_3$), 204.3 (s, *C*O).

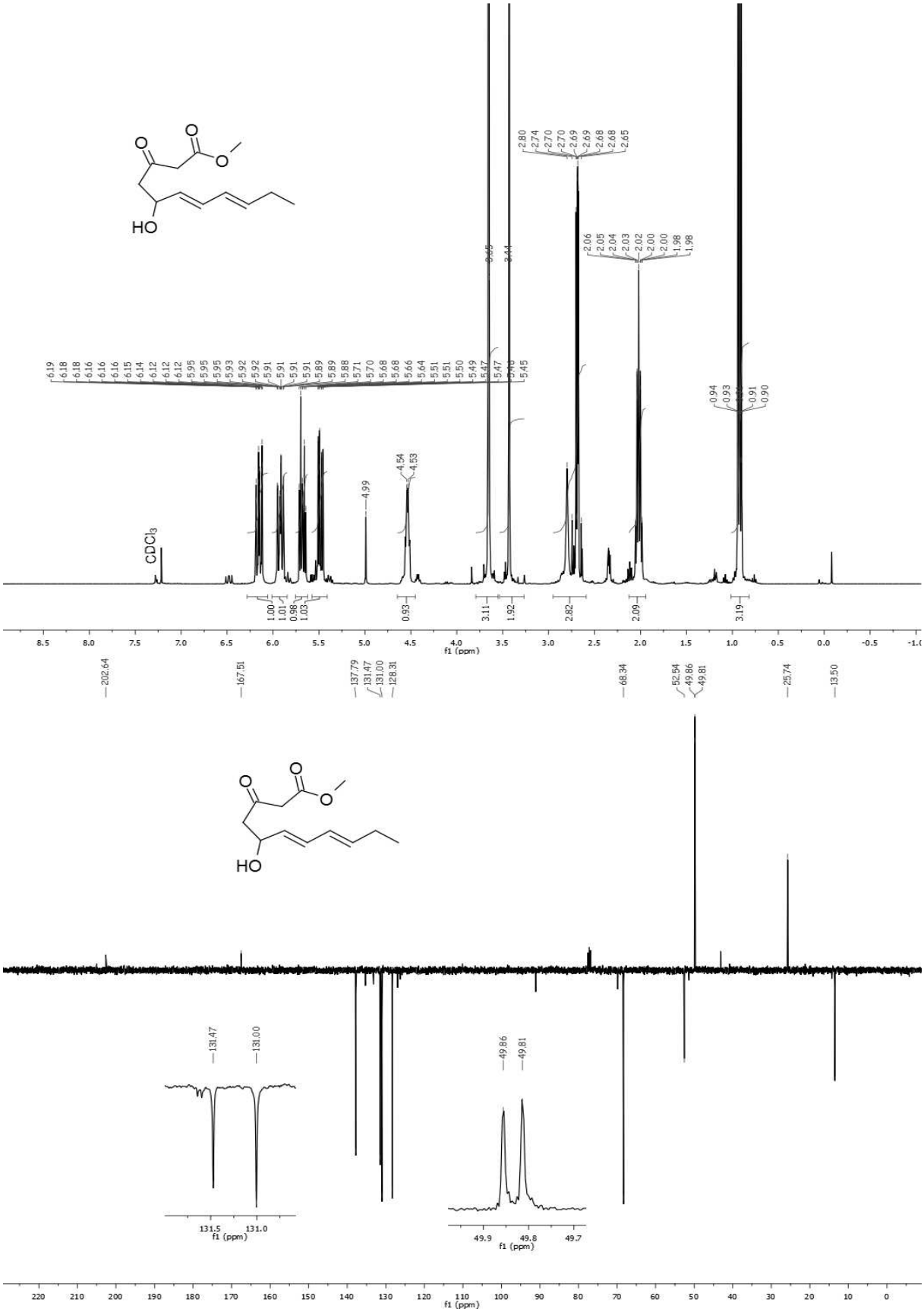


31

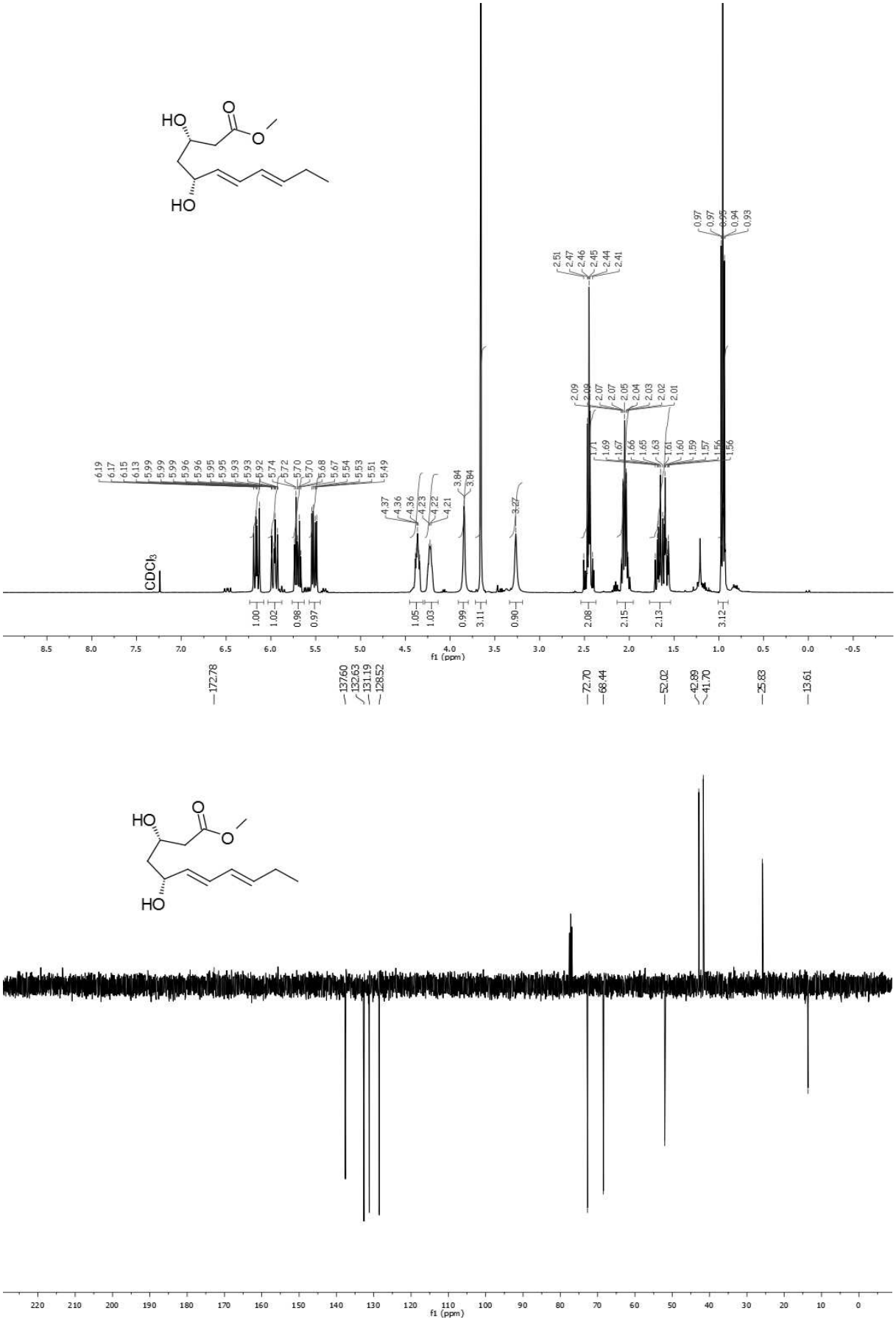
More polar epimer: R_f (hexane/EtOAc 1:1) = 0.2. - IR (film): ν = 3424 (br), 2937, 2865, 1730, 1652, 1466, 1445, 1264, 1240, 1186, 1104, 1025, 803. - MS (+ESI) *m/z*, (%): 703 (4) $[2M+Na]^+$, 363 (100) $[M+Na]^+$, 345 (7) $[M-H_2O+Na]^+$. - HRMS (+ESI) *m/z*: ($C_{19}H_{32}O_5Na$) calc.: 363.2142, found: 363.2142. - ^{1}H NMR (500 MHz): δ = 0.98 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$), 1.23-1.39 (m, 10H, (C*H*$_2$)$_5$CH$_2$CH$_2$COOCH$_3$), 1.51-1.64 (m, 4H, C*H*$_2$CH$_2$COOCH$_3$, C*H*$_2$CH$_3$), 1.78-1.99 (br s, 1H, *H*OCHCH$_2$CH$_3$), 2.26-2.39 (m, 3H, CH*H*COC=CHC*H*$_2$), 2.30 (t, *J* = 7.4 Hz, 2H, C*H*$_2$COOCH$_3$), 2.63 (dd, *J* = 18.7, 5.0 Hz, 1H, CH*H*COC), 2.93 (t, *J* = 6.5 Hz, 1H, C*H*C=CH), 3.60-3.73 (m, 2H, HOC*H*CH$_2$CH$_3$, *H*OCHCH$_2$CO), 3.67 (s, 3H, OC*H*$_3$), 4.34 (d, *J* = 5.0 Hz, 1H, HOC*H*CH$_2$CO), 6.69 (ddd, *J* = 8.7, 6.6, 1.5 Hz, 1H, C=C*H*). - ^{13}C NMR (126 MHz): δ = 10.2 (q, *C*H$_3$CH$_2$), 24.97 (t, *C*H$_2$CH$_2$COOCH$_3$), 27.60 (t, *C*H$_2$), 29.13 (t, *C*H$_2$), 29.23 (t, *C*H$_2$), 29.6 (t, *C*H$_2$), 30.3 (t, *C*H$_2$CH$_3$), 33.08 (t, *C*H$_2$), 34.16 (t, *C*H$_2$COOCH$_3$), 37.2 (t, *C*H$_2$CH=C), 45.7 (t, *C*H$_2$CO), 48.8 (d, *C*HCH$_2$CH$_2$), 51.66 (q, O*C*H$_3$), 71.5 (d, HO*C*HCH$_2$CO), 72.45 (d, HO*C*HCH$_2$CH$_3$), 134.4 (d, *C*H=C), 142.7 (s, *C*=CH), 174.1 (s, *C*OOCH$_3$), 204.9 (s, *C*O).

Copies of ^{1}H and ^{13}C NMR spectra

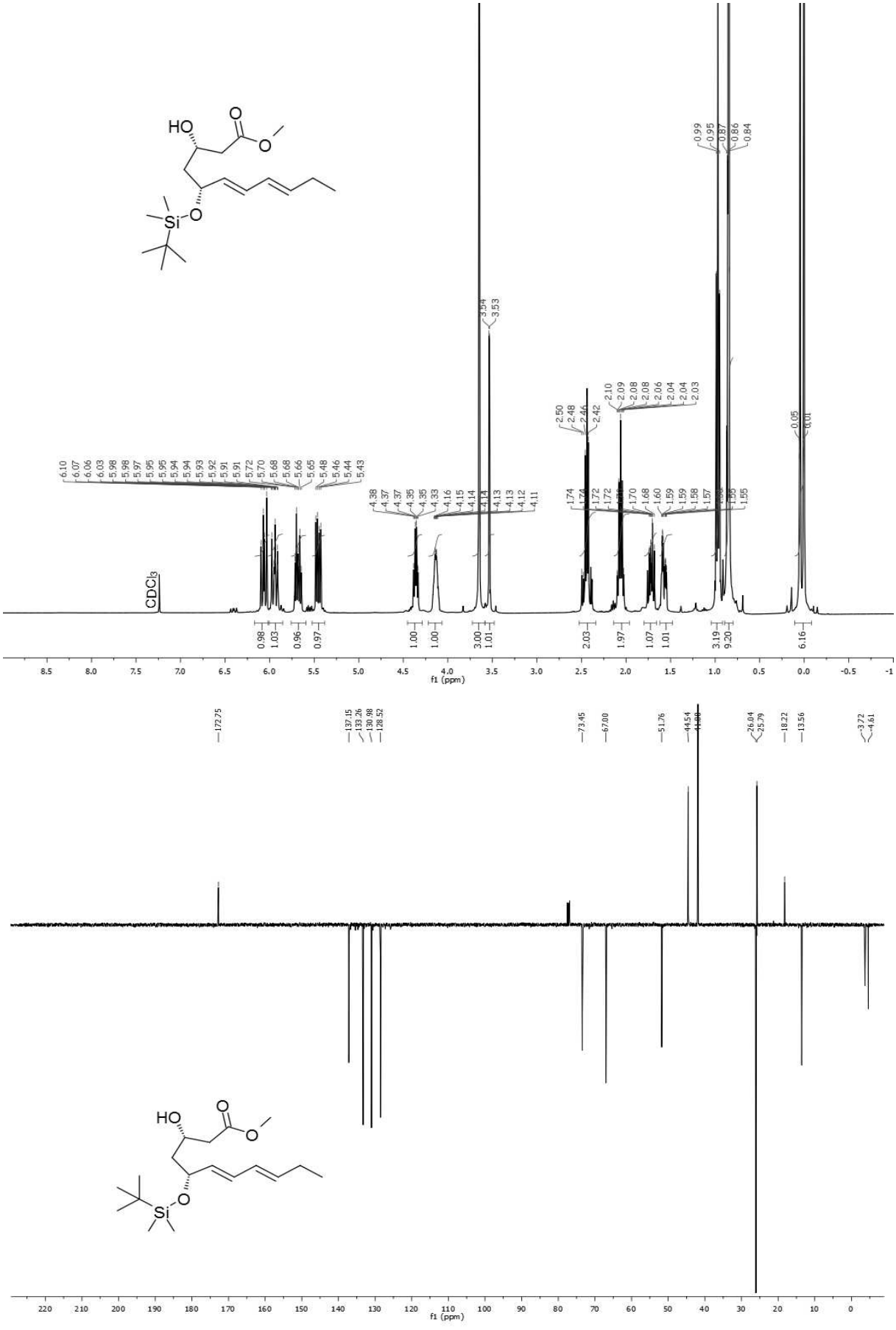
Methyl (6*E*,8*E*)-5-hydroxy-3-oxoundeca-6,8-dienoate **11**



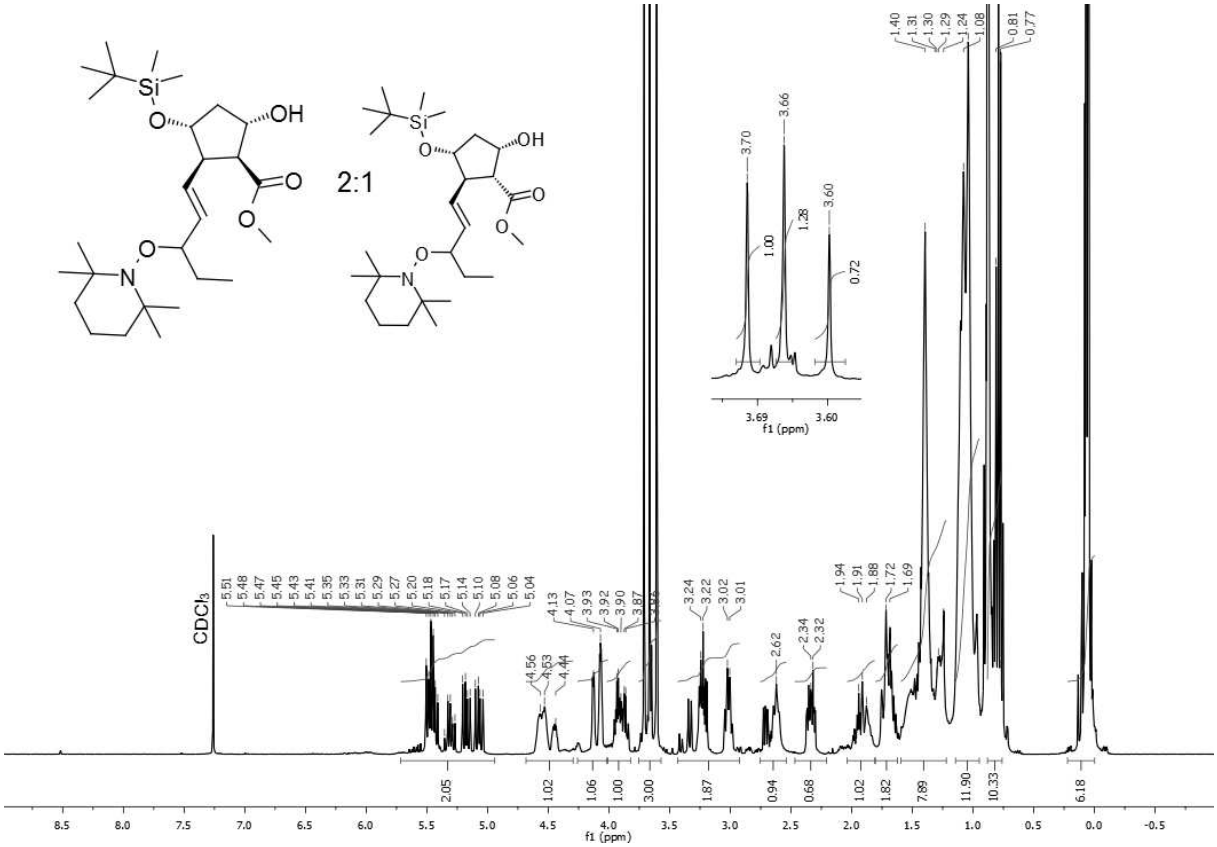
Methyl (3*S**,5*R**,6*E*,8*E*)-3,5-dihydroxyundeca-6,8-dienoate **12**

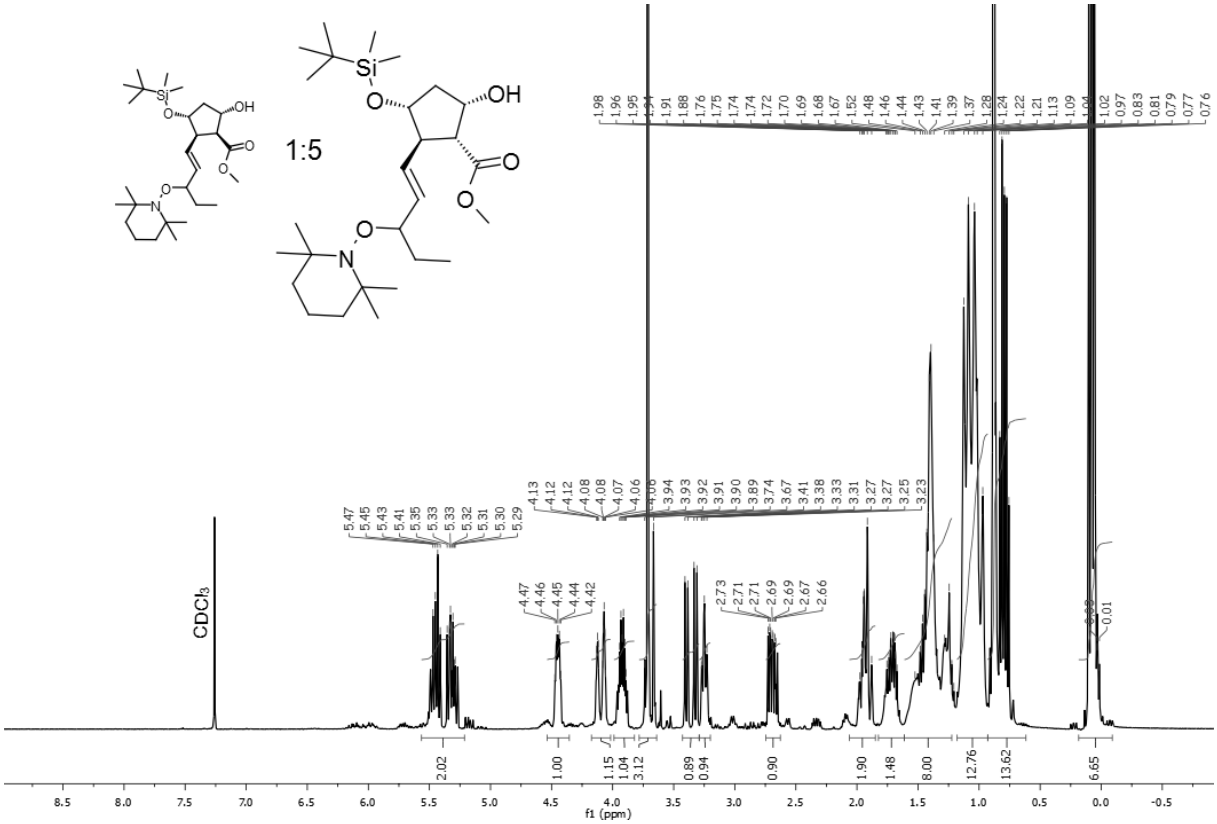


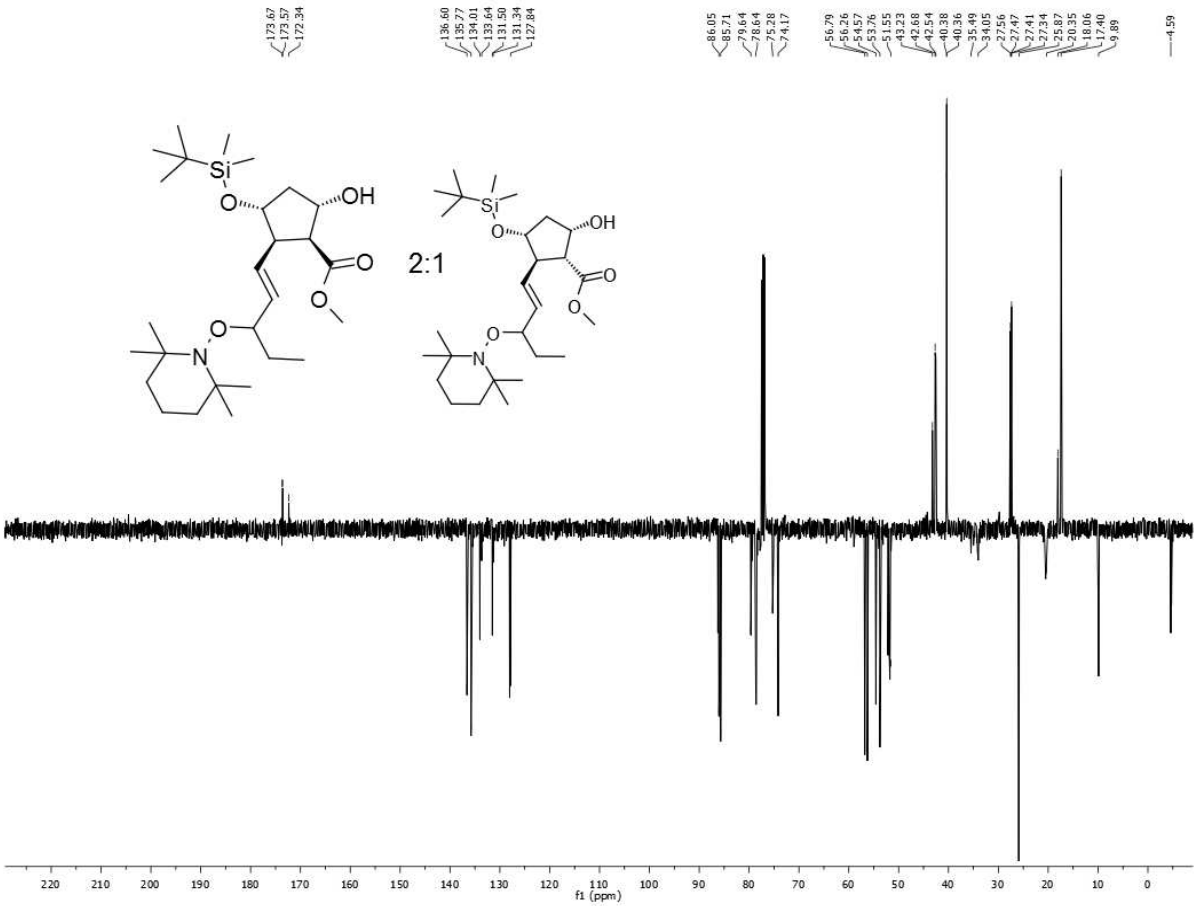
Methyl (3*S**,5*R**,6*E*,8*E*)-5-((*tert*-butyldimethylsilyl)oxy)-3-hydroxyundeca-6,8-dienoate **8**

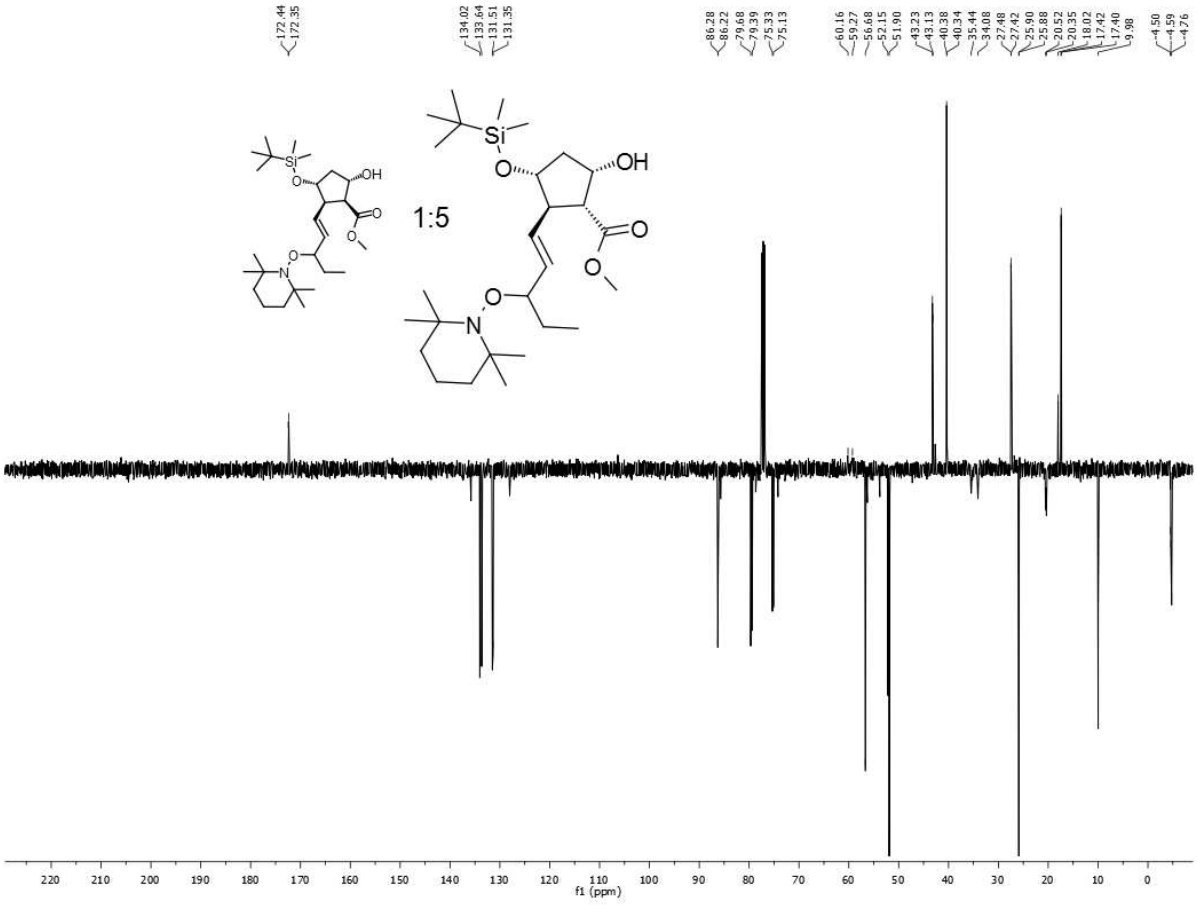


Methyl (1*S**,2*S**,3*R**,4*R**)- and (1*S**,2*R**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-1-(hydroxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)cyclopentane-2-carboxylates **5a** and **5b**

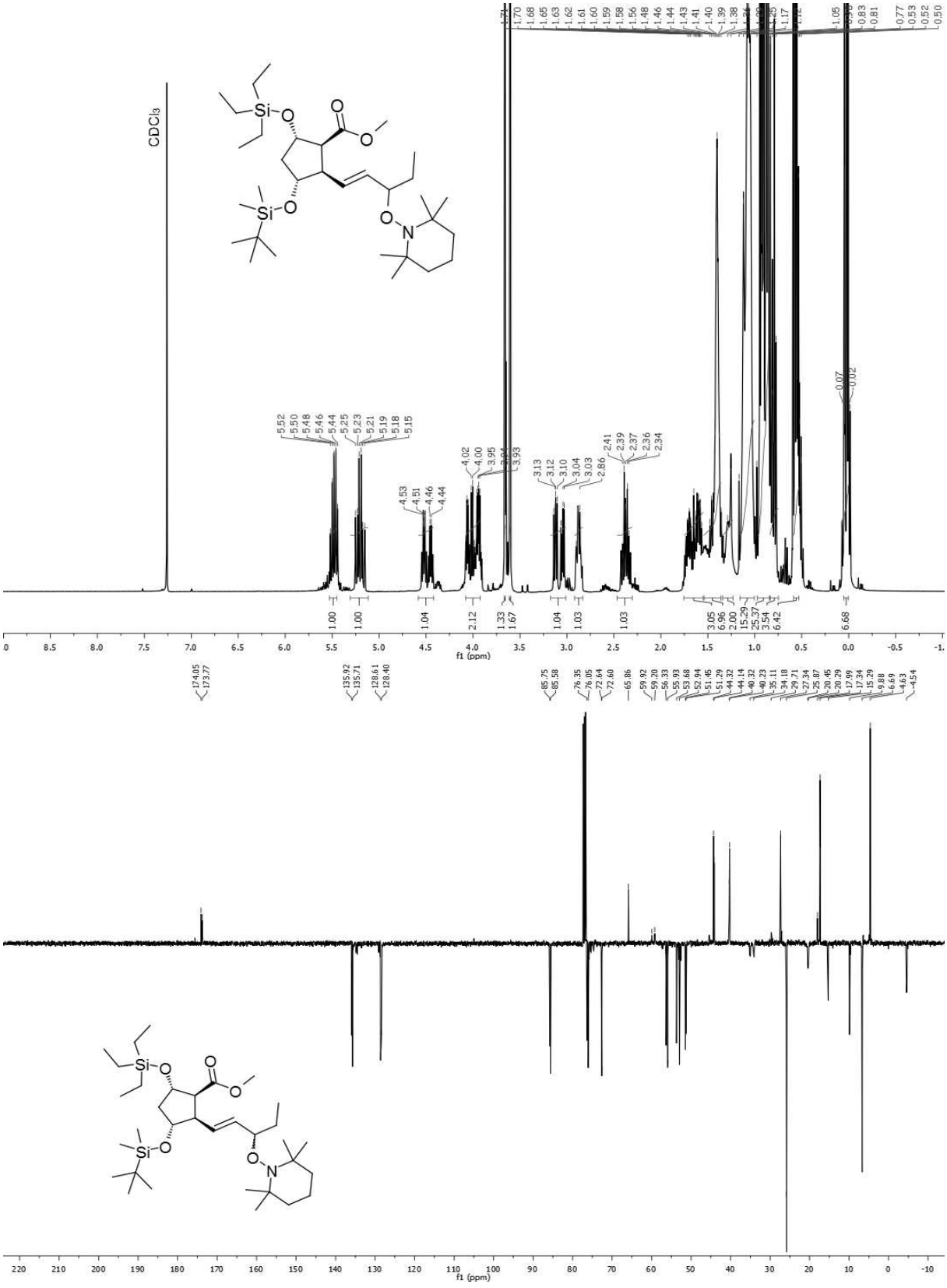




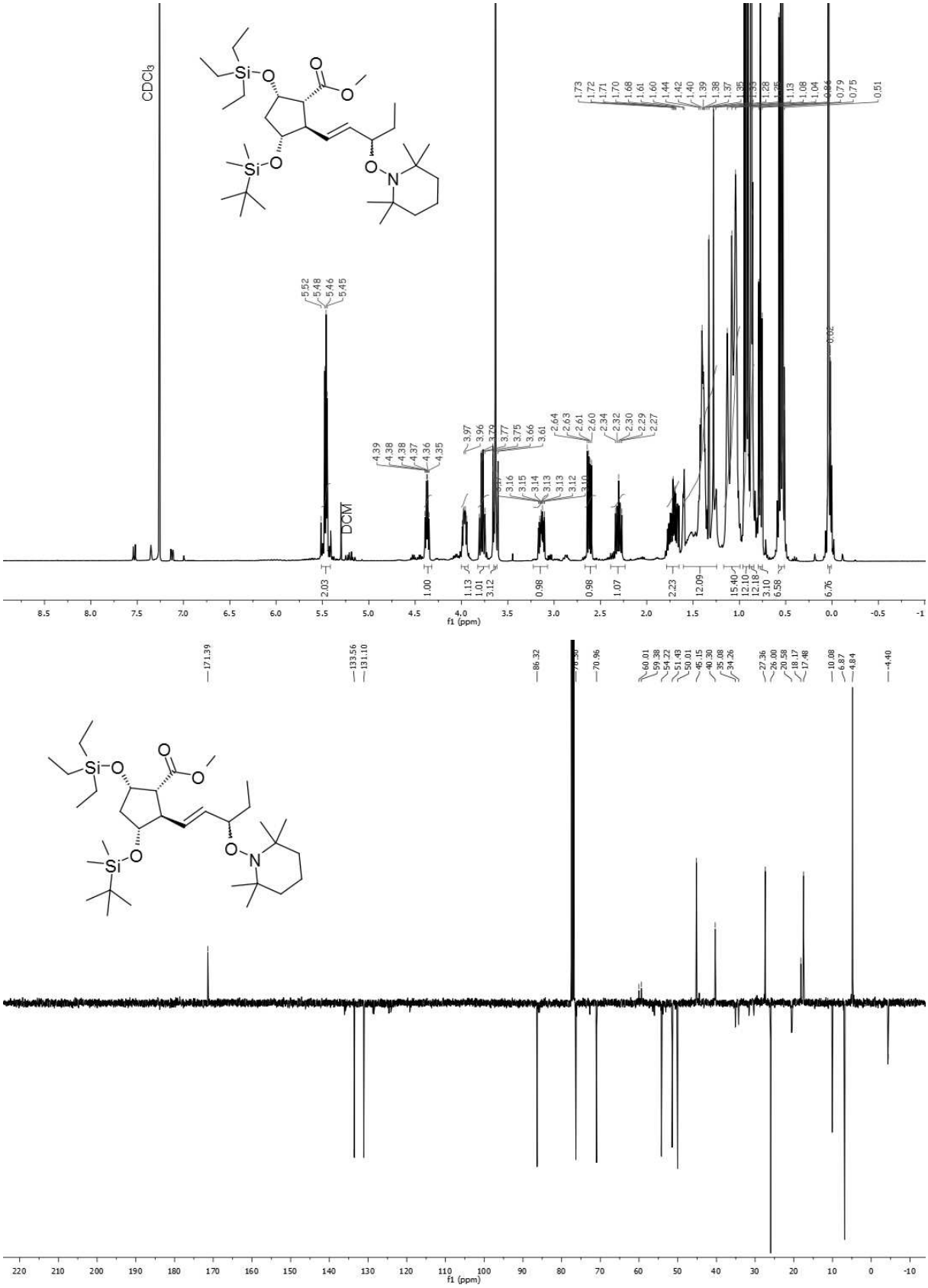

173.67
173.57
172.34
136.60
135.77
134.01
133.64
131.50
131.34
127.84
86.05
85.71
79.64
78.64
75.28
74.17
56.79
56.26
54.57
53.76
51.55
43.23
42.68
42.54
40.38
40.36
35.49
34.05
27.56
27.47
27.41
27.34
25.87
20.35
18.06
17.40
9.89
-4.59
2:1
f1 (ppm)


172.44
172.35
134.02
133.64
131.51
131.35
86.28
86.22
79.68
79.39
75.33
75.13
60.16
59.27
56.68
52.15
51.90
43.23
43.13
40.38
40.34
35.44
34.08
27.48
27.42
25.90
25.88
20.52
20.35
18.02
17.42
17.40
9.98
-4.50
-4.59
-4.76
1:5
f1 (ppm)

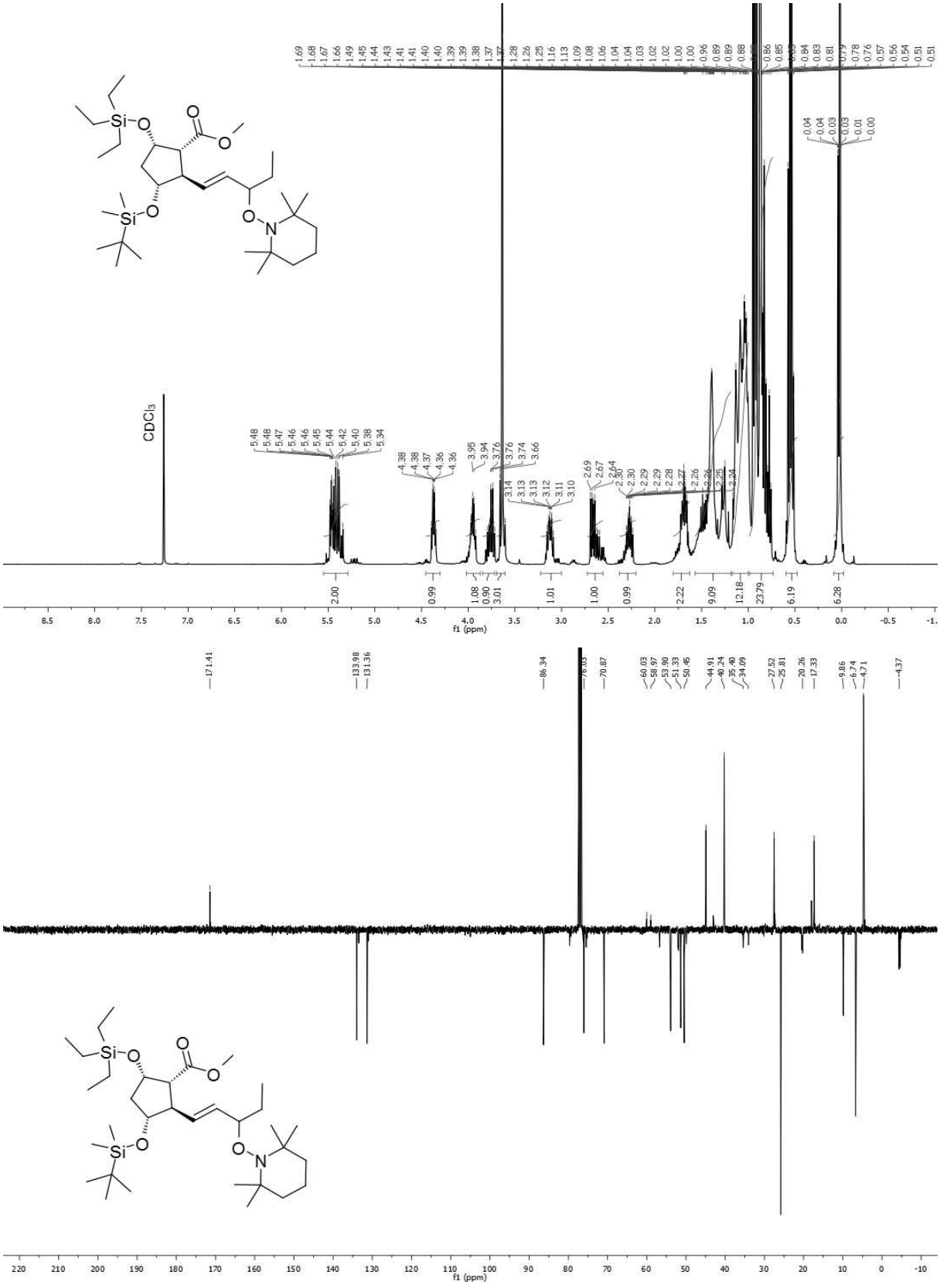
Methyl (1*S**,2*S**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane-2-carboxylate **13a**



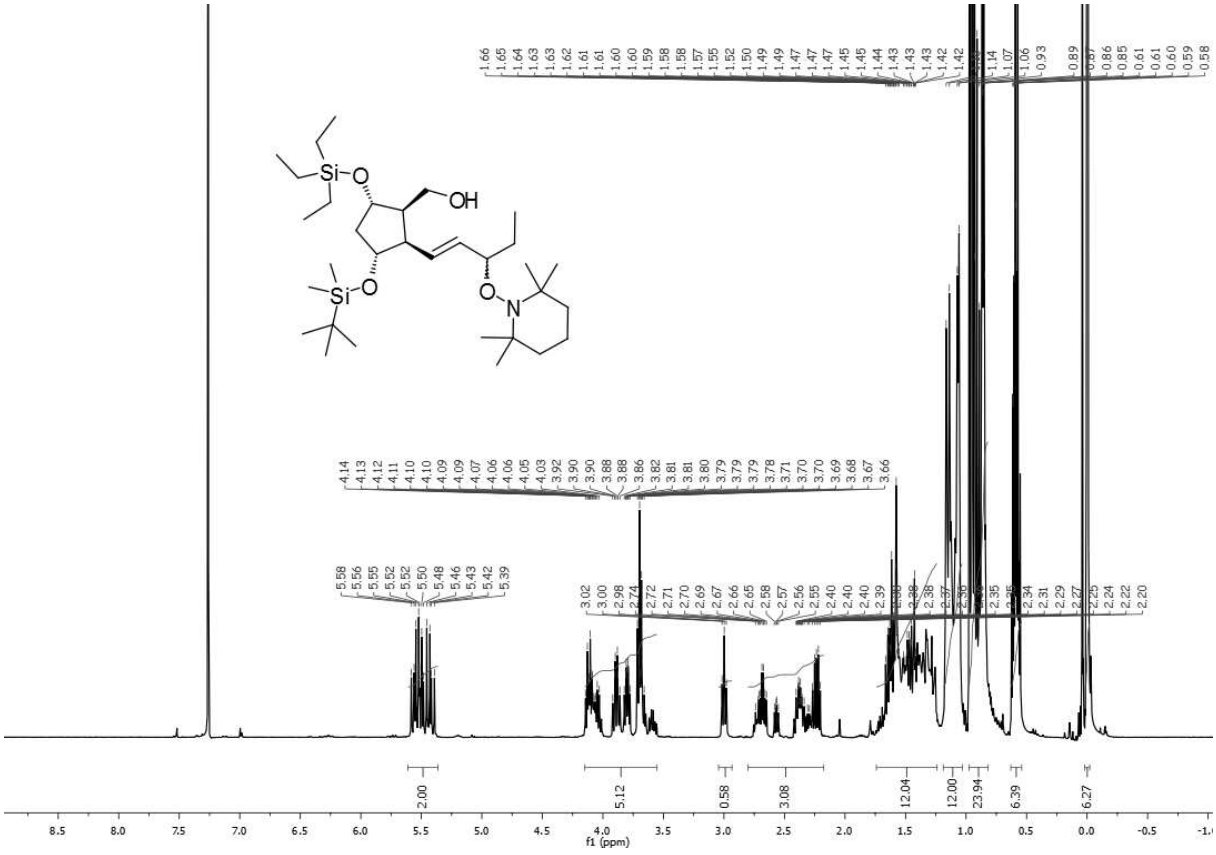
Methyl (1*S**,2*R**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane-2-carboxylate **13b** *(less polar C16 epimer)*

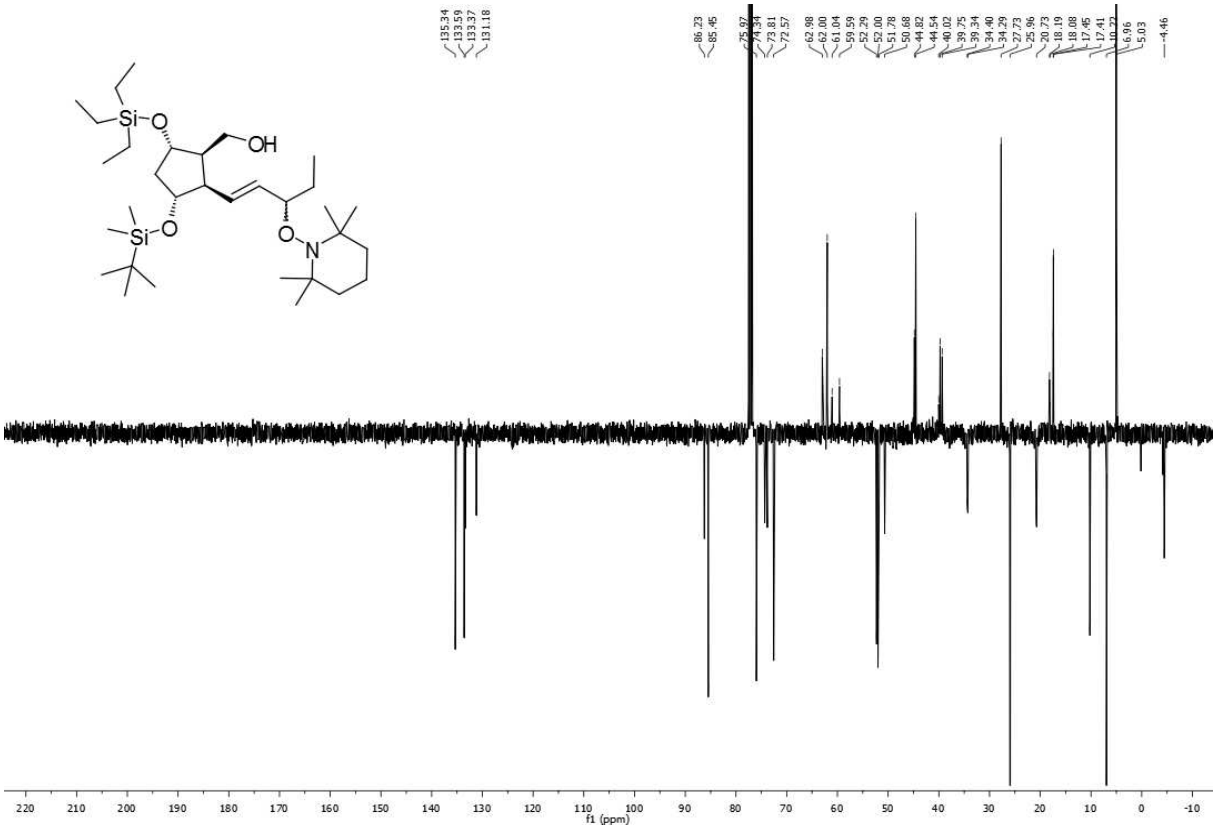


Methyl (1*S**,2*R**,3*R**,4*R**)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane-2-carboxylate **13b** *(more polar C16 epimer)*

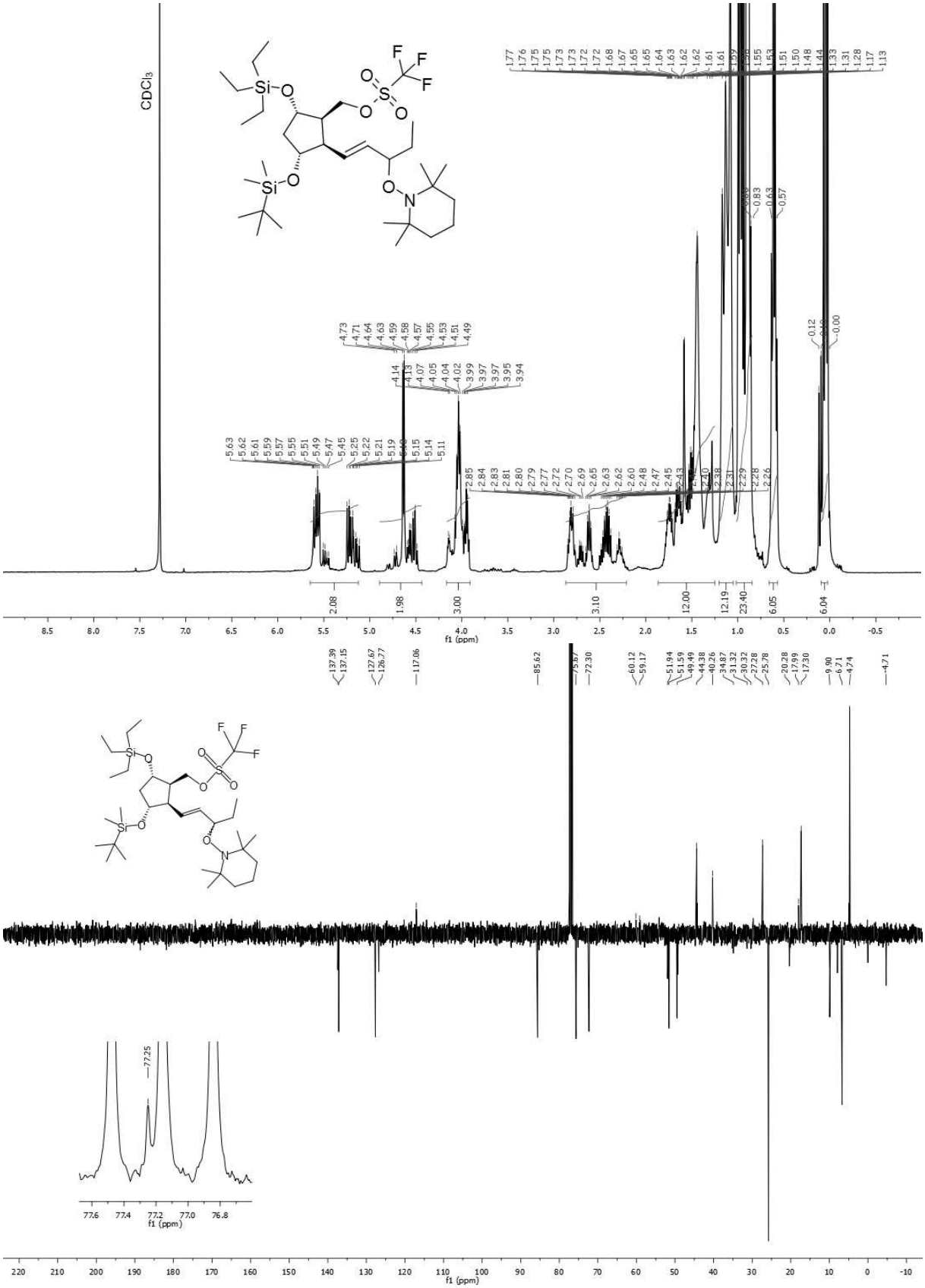


(1*S**,2*R**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(hydroxomethyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane **14**

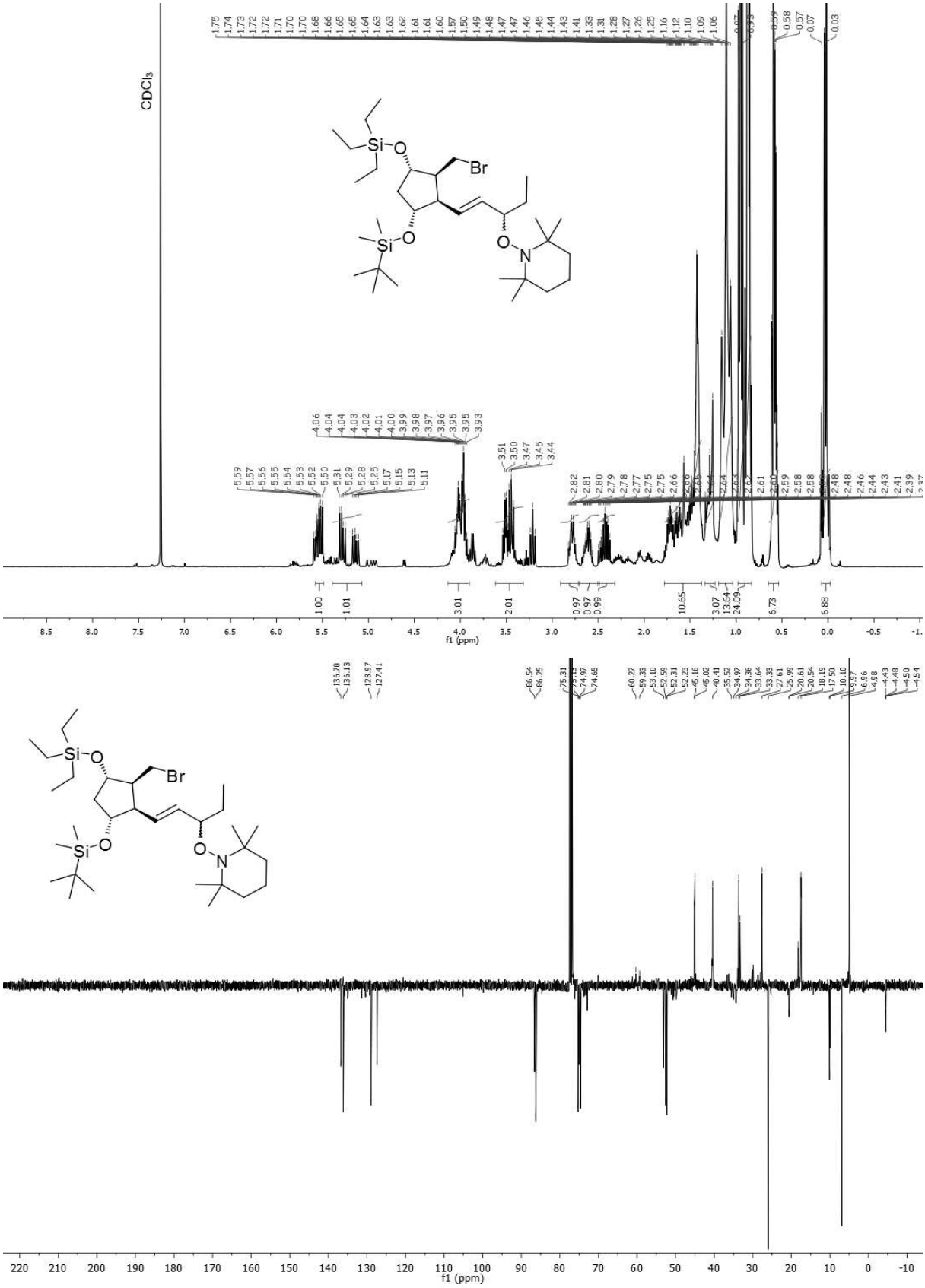




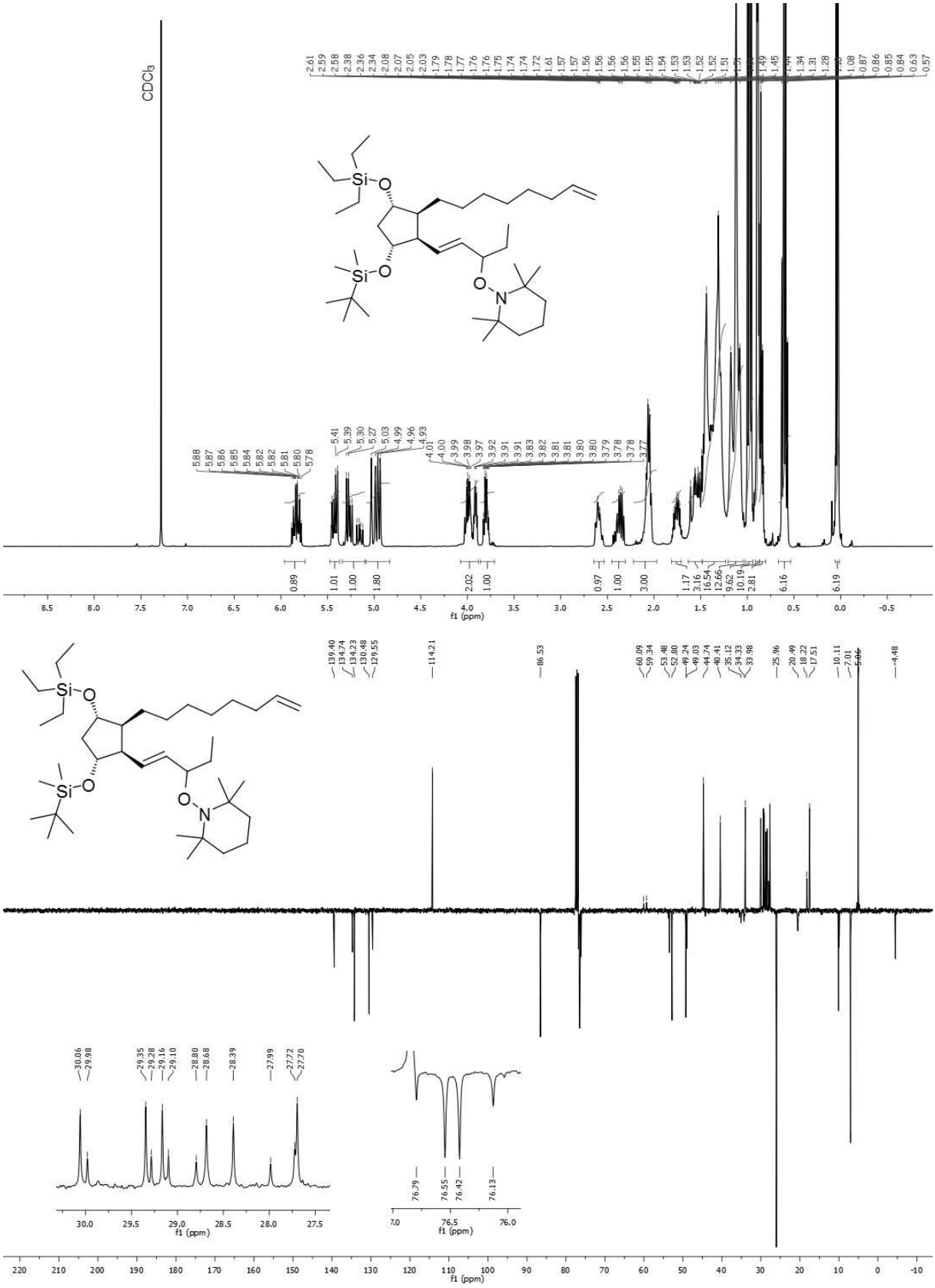
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-(((triethylsilyl)oxy))-2-(((trifluoromethanesulfonyl)oxy)methyl)-cyclopentane **15**



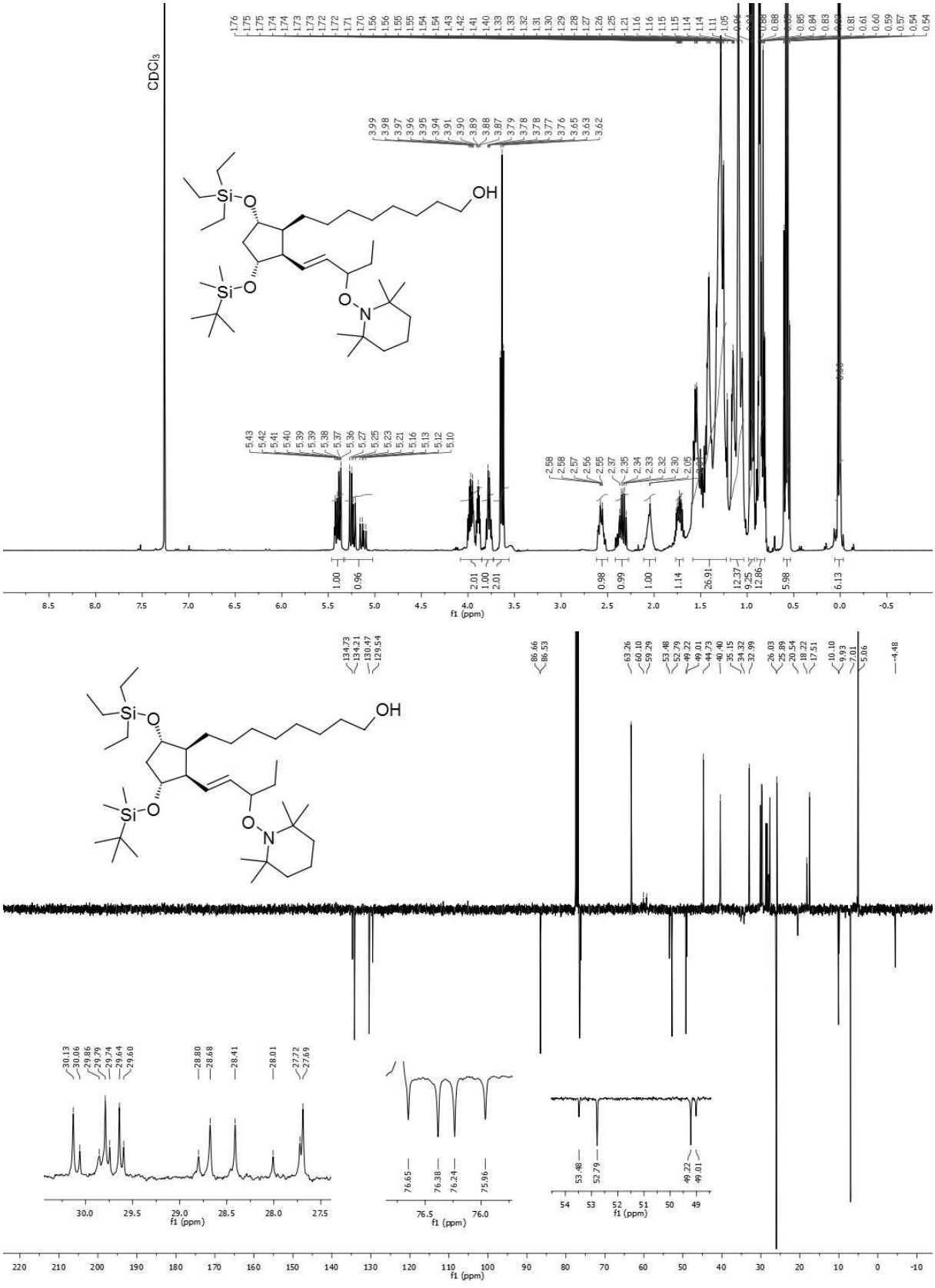
(1*S**,2*S**,3*R**,4*R**)-2-(Bromomethyl)-4-((*tert*-butyldimethylsilyl)oxy)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-(((triethylsilyl)oxy))cyclopentane **18** *(contaminated by* **17**, *inseparable by column chromatography)*



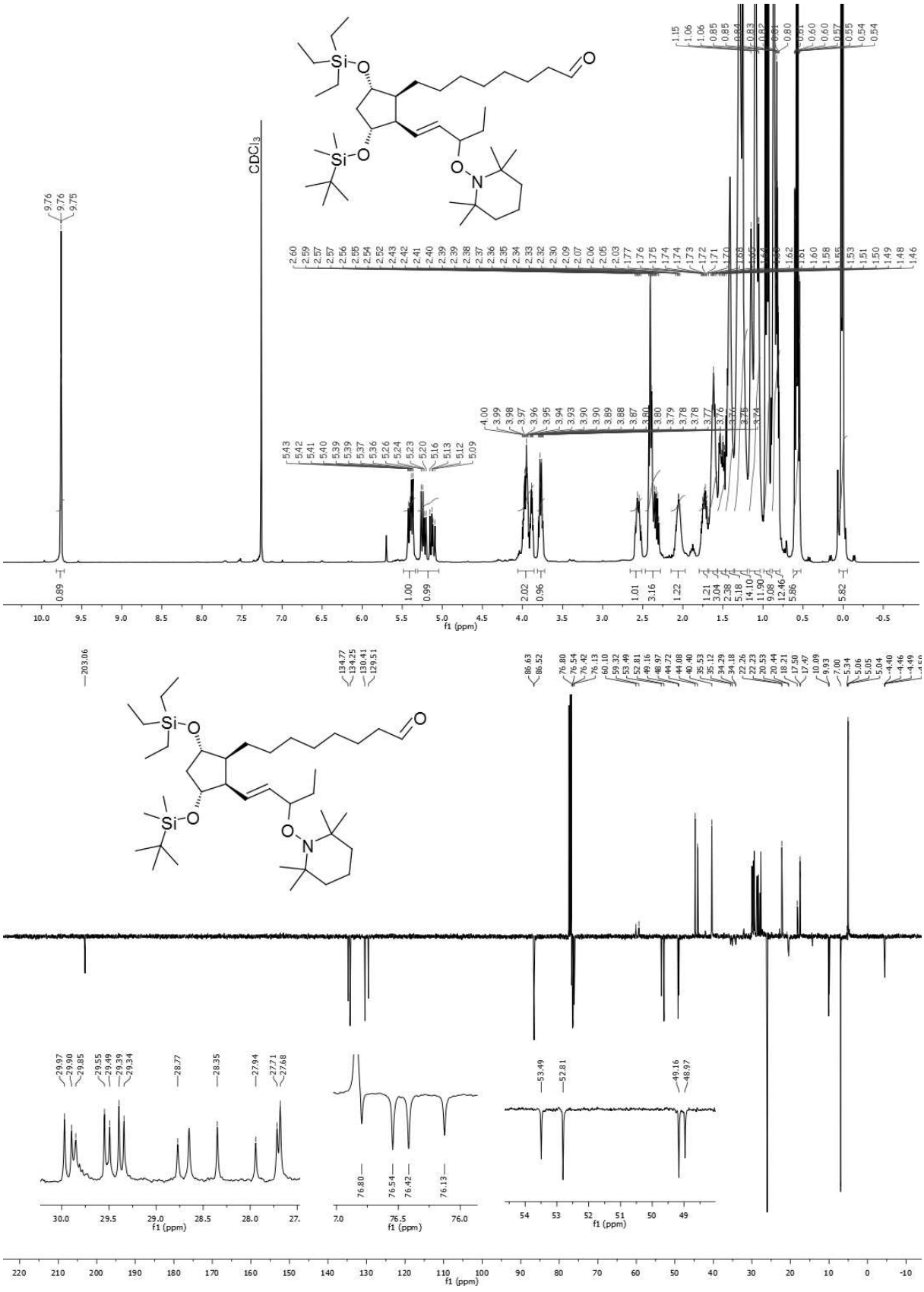
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(oct-7-en-1-yl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-(((triethylsilyl)oxy))cyclopentane **17**



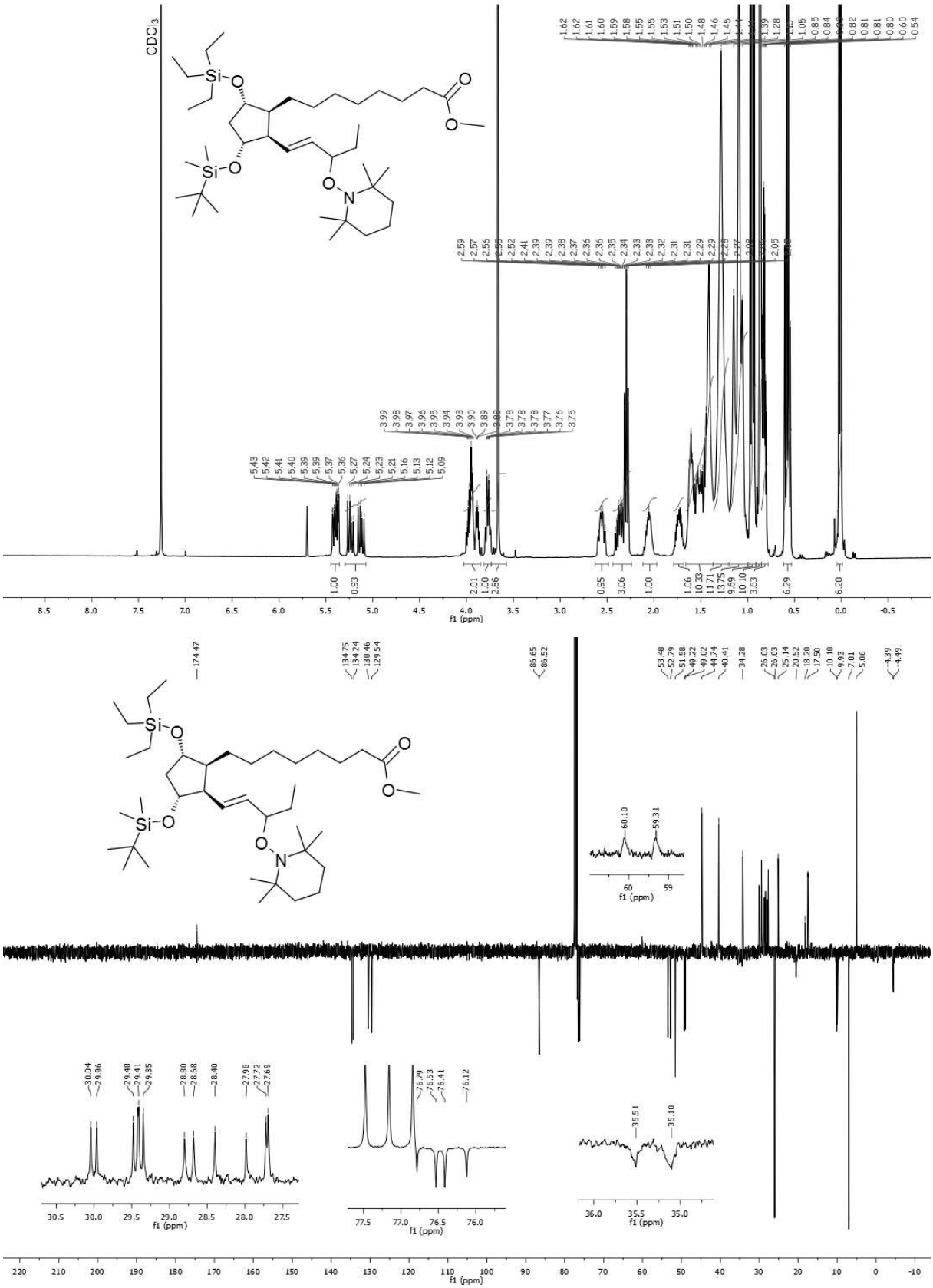
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-hydroxyoctyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane **19**



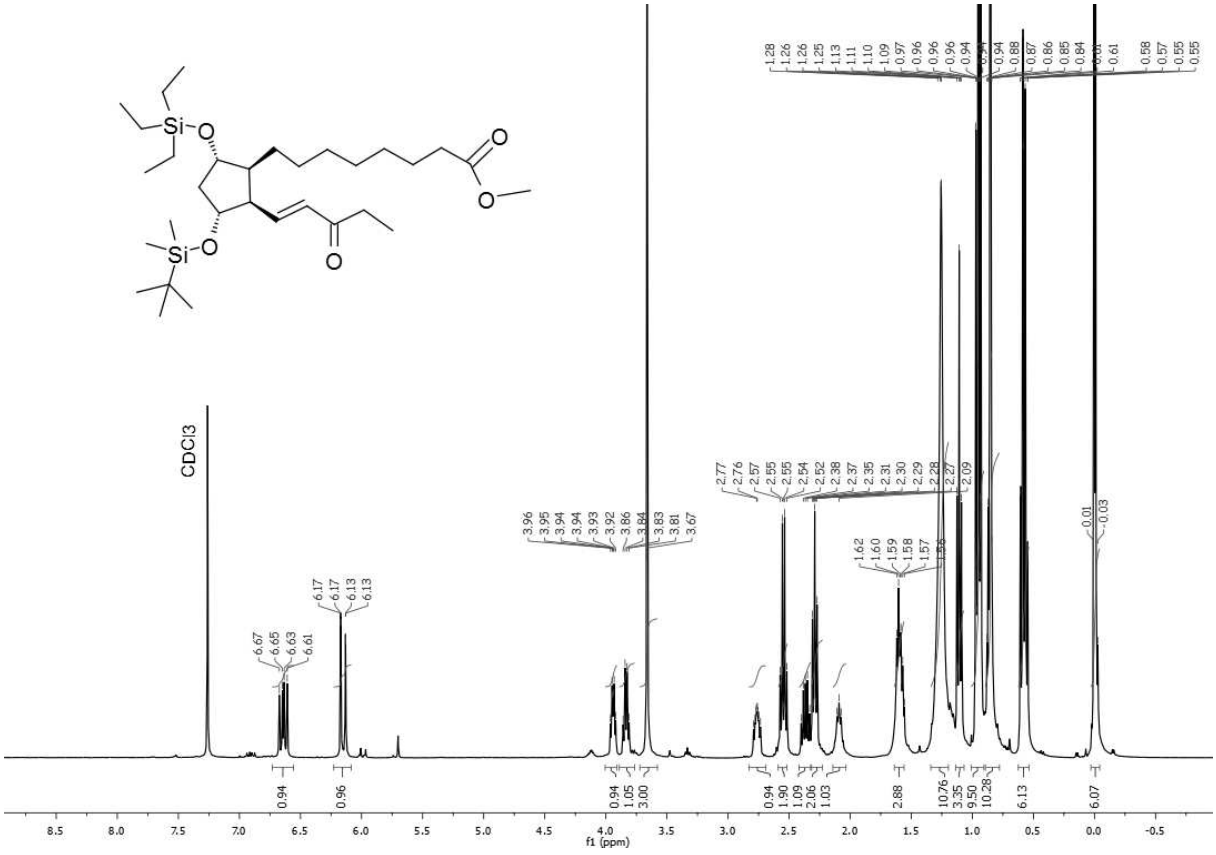
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-oxooctyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane **20**

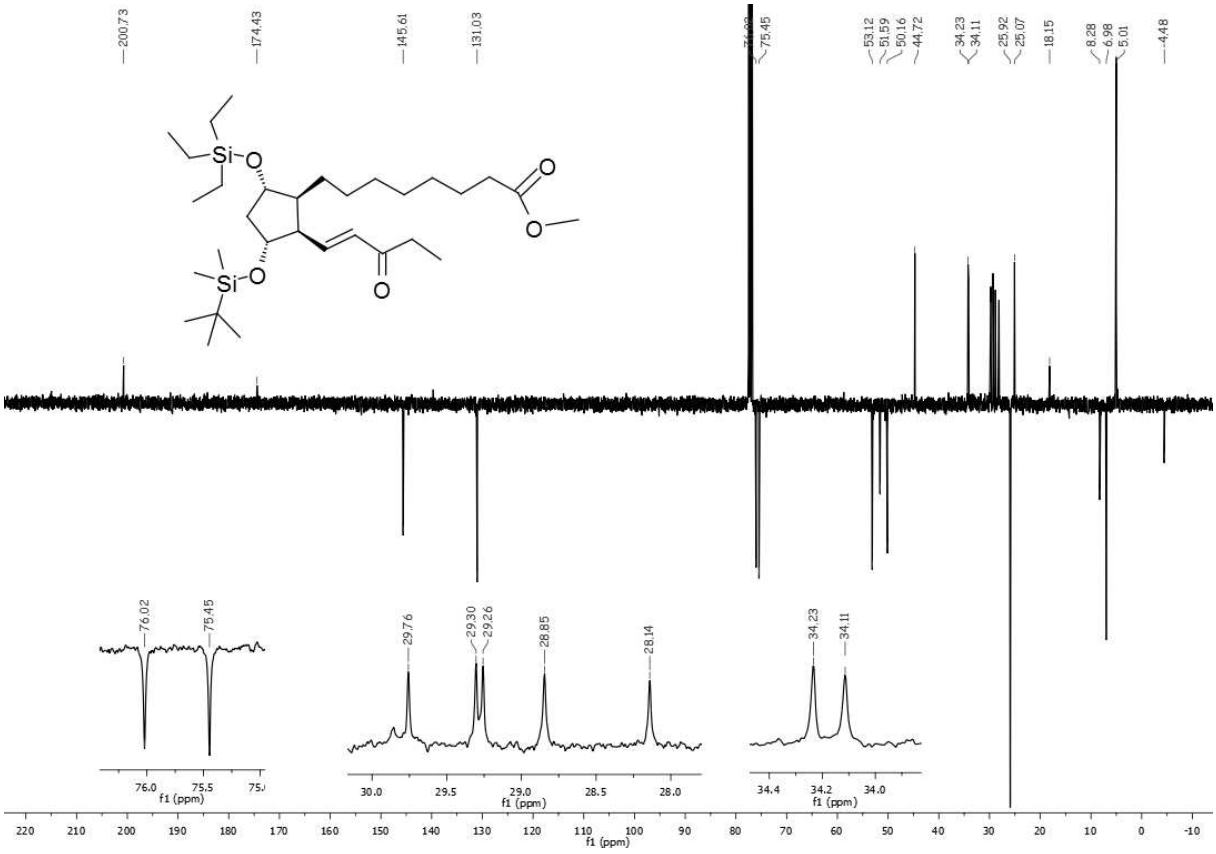


(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-3-((2,2,6,6-tetramethylpiperidin-1-yl)oxy)-pent-1-en-1-yl)-1-((triethylsilyl)oxy)cyclopentane **4**

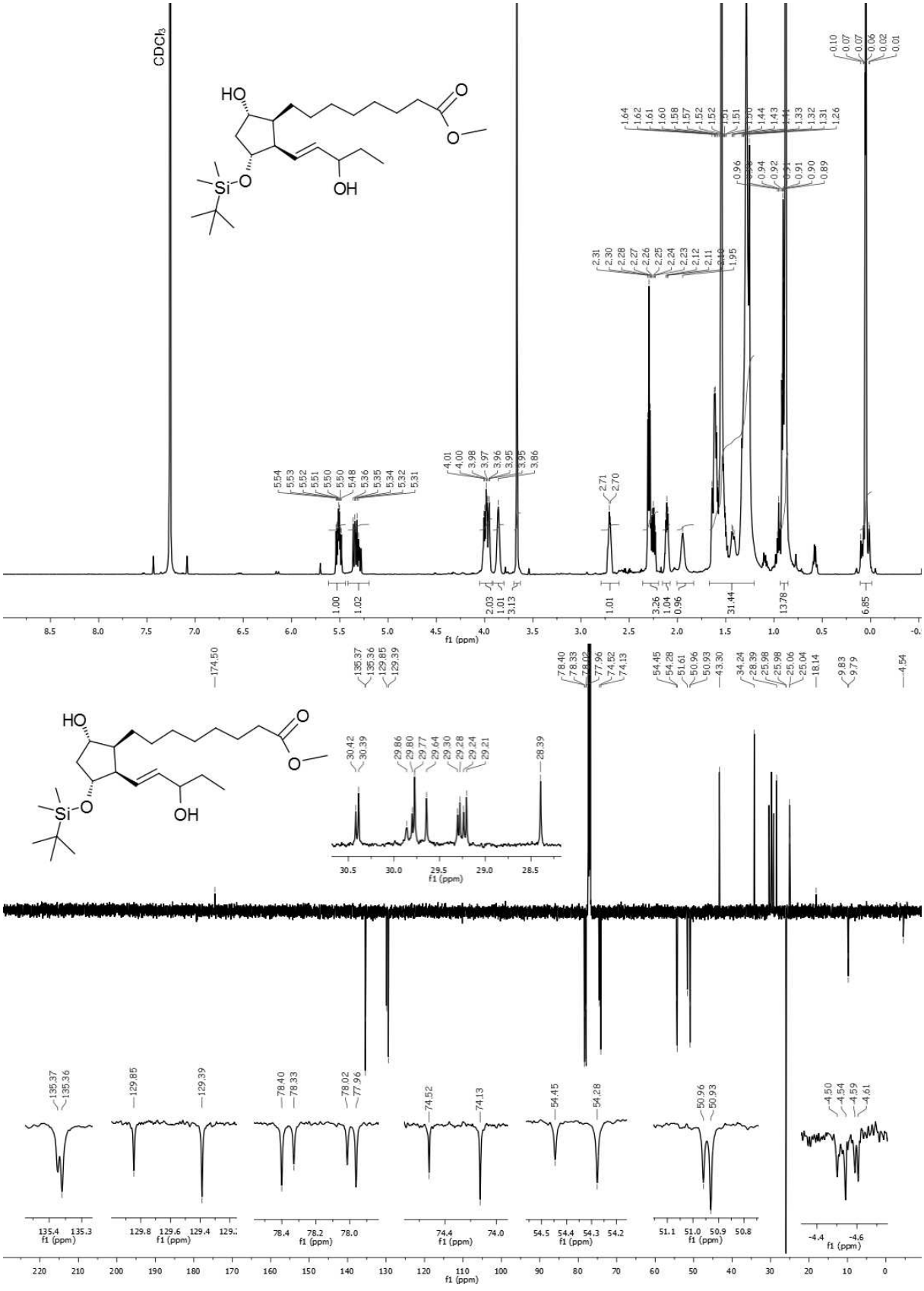


(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-pent-1-en-3-on-1-yl)-1-((triethylsilyl)oxy)cyclopentane **21**

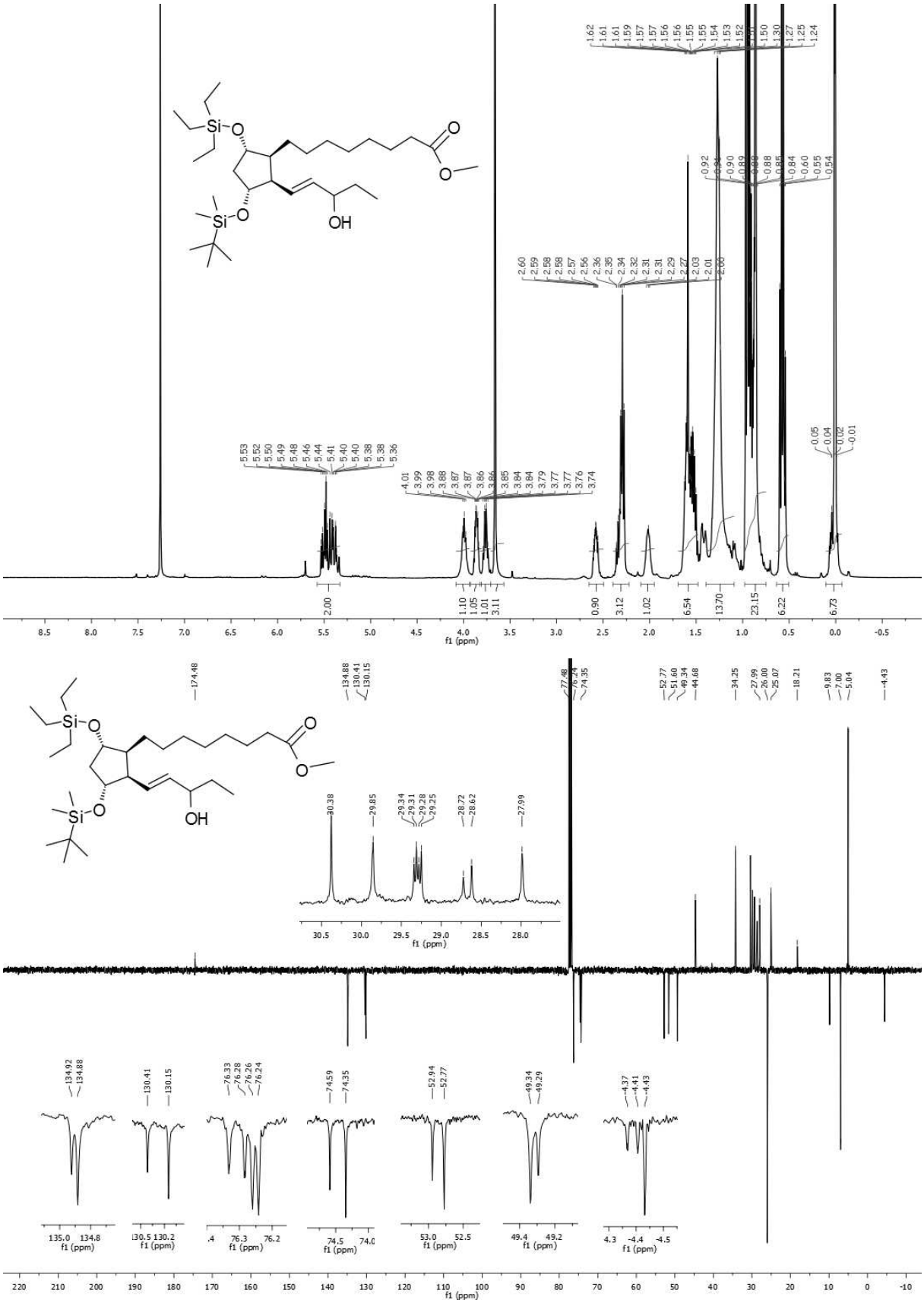




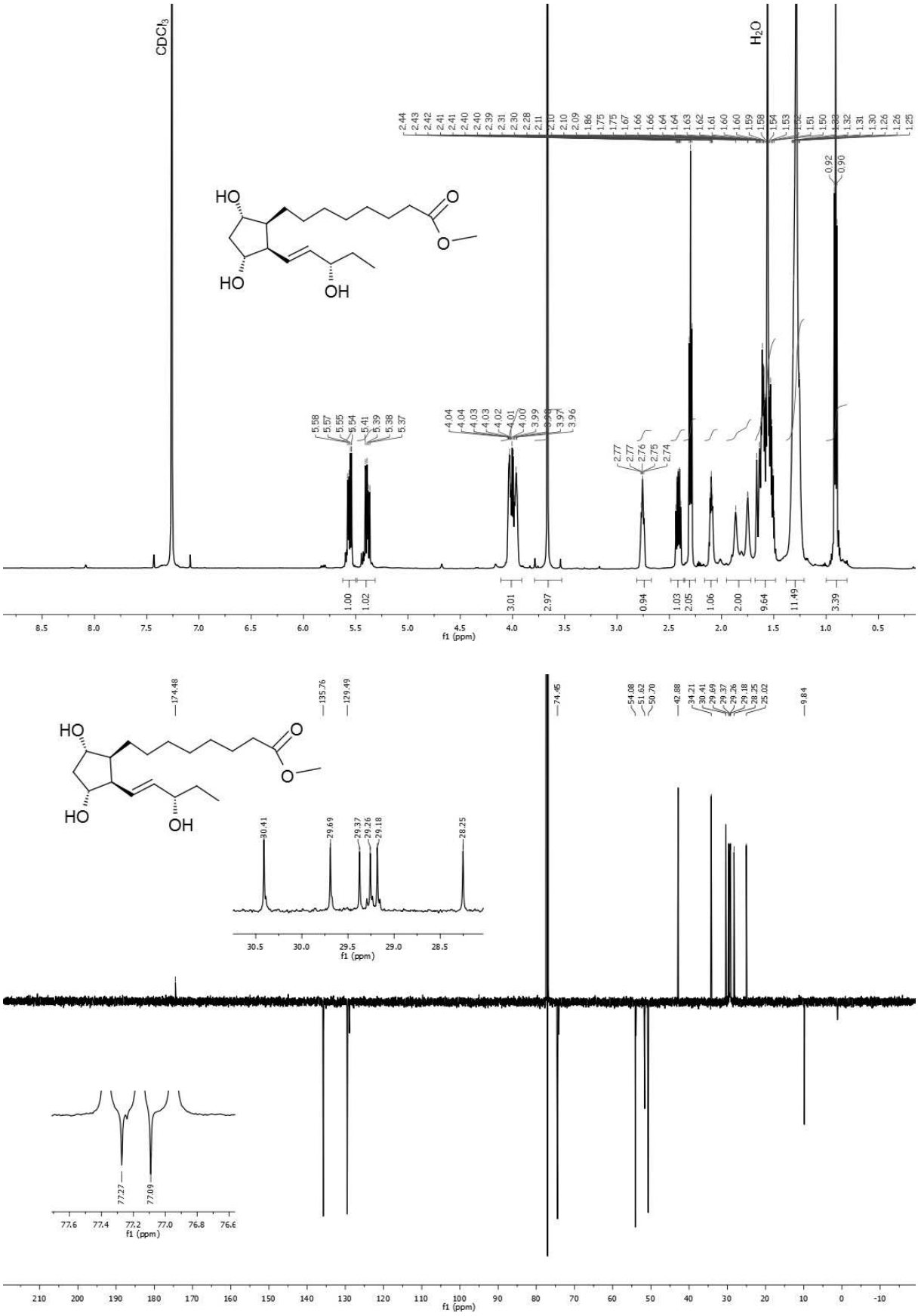
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-(hydroxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentan-1-ol **22**



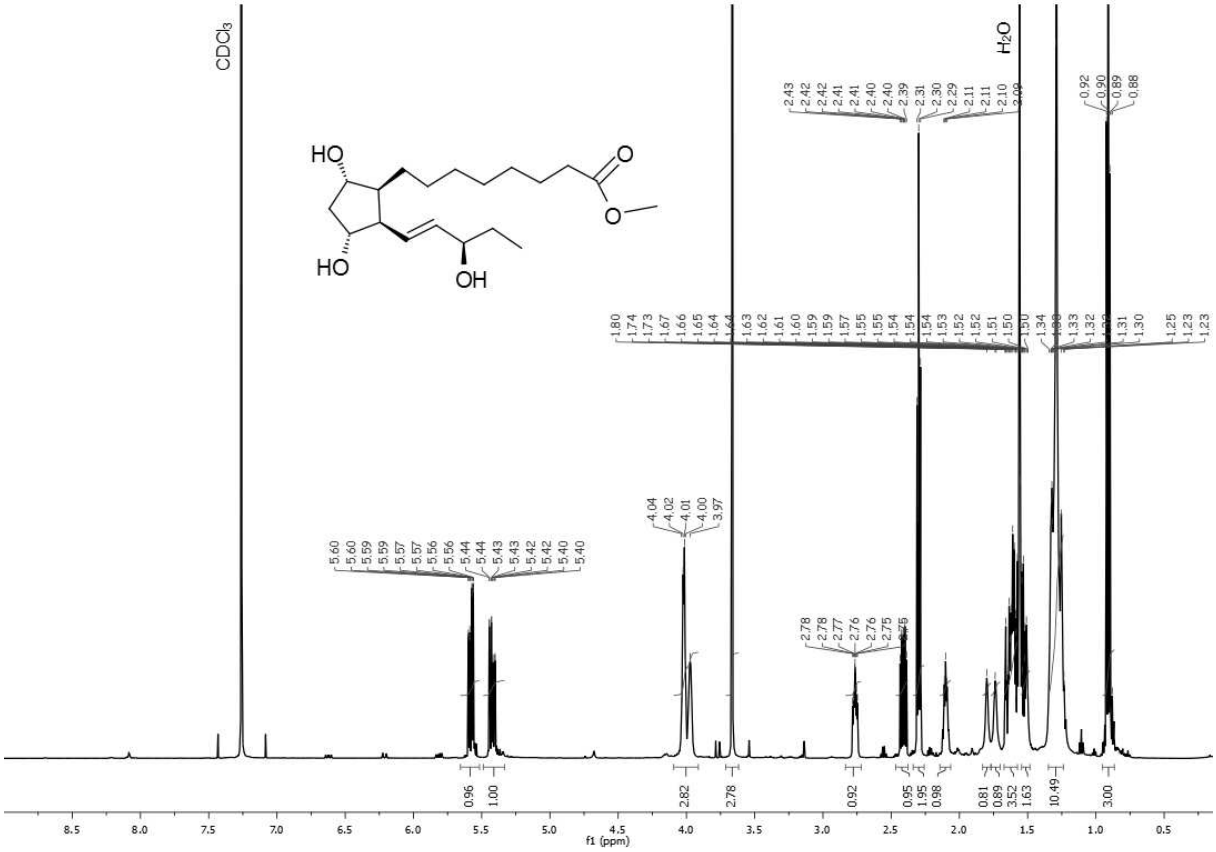
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-(hydroxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)-1-((triethylsilyl)oxy)cyclopentane **23**

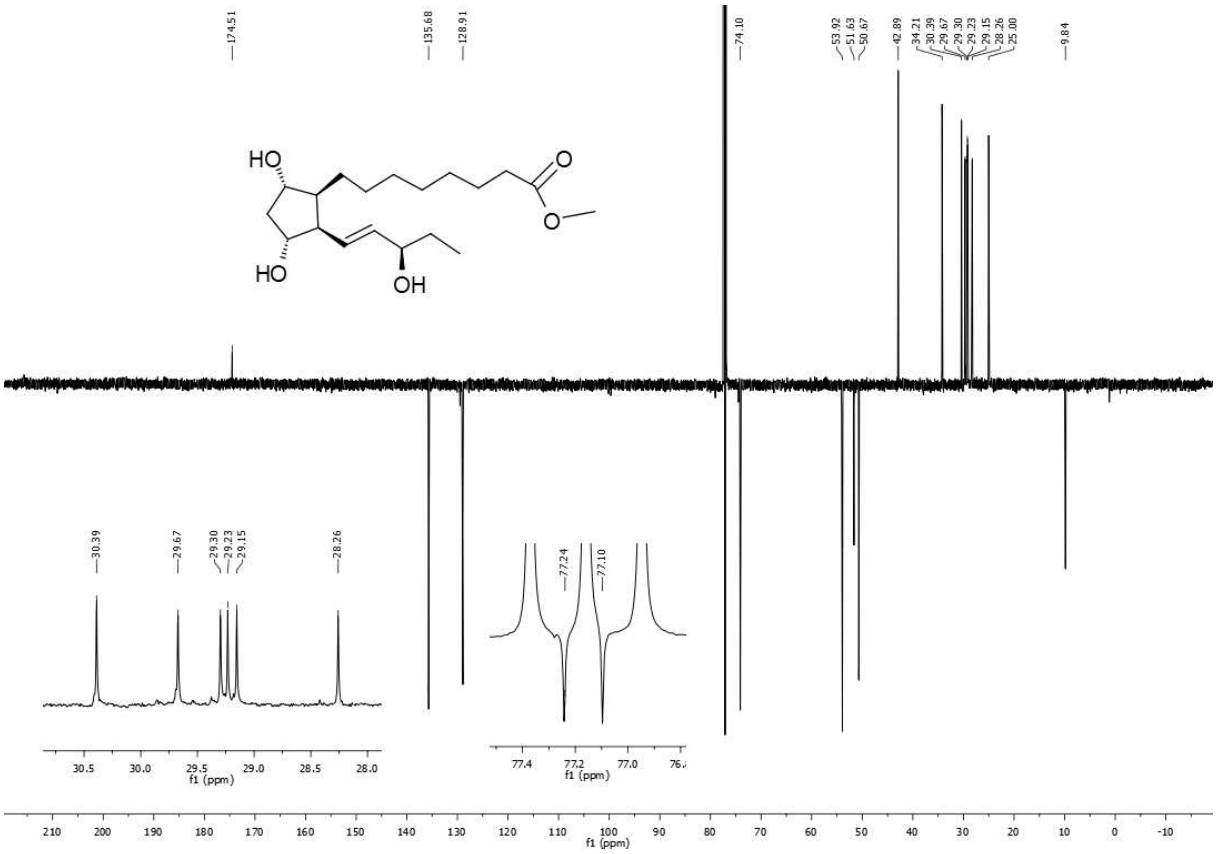


16-F_{1t}-Phytoprostane methyl ester **1**

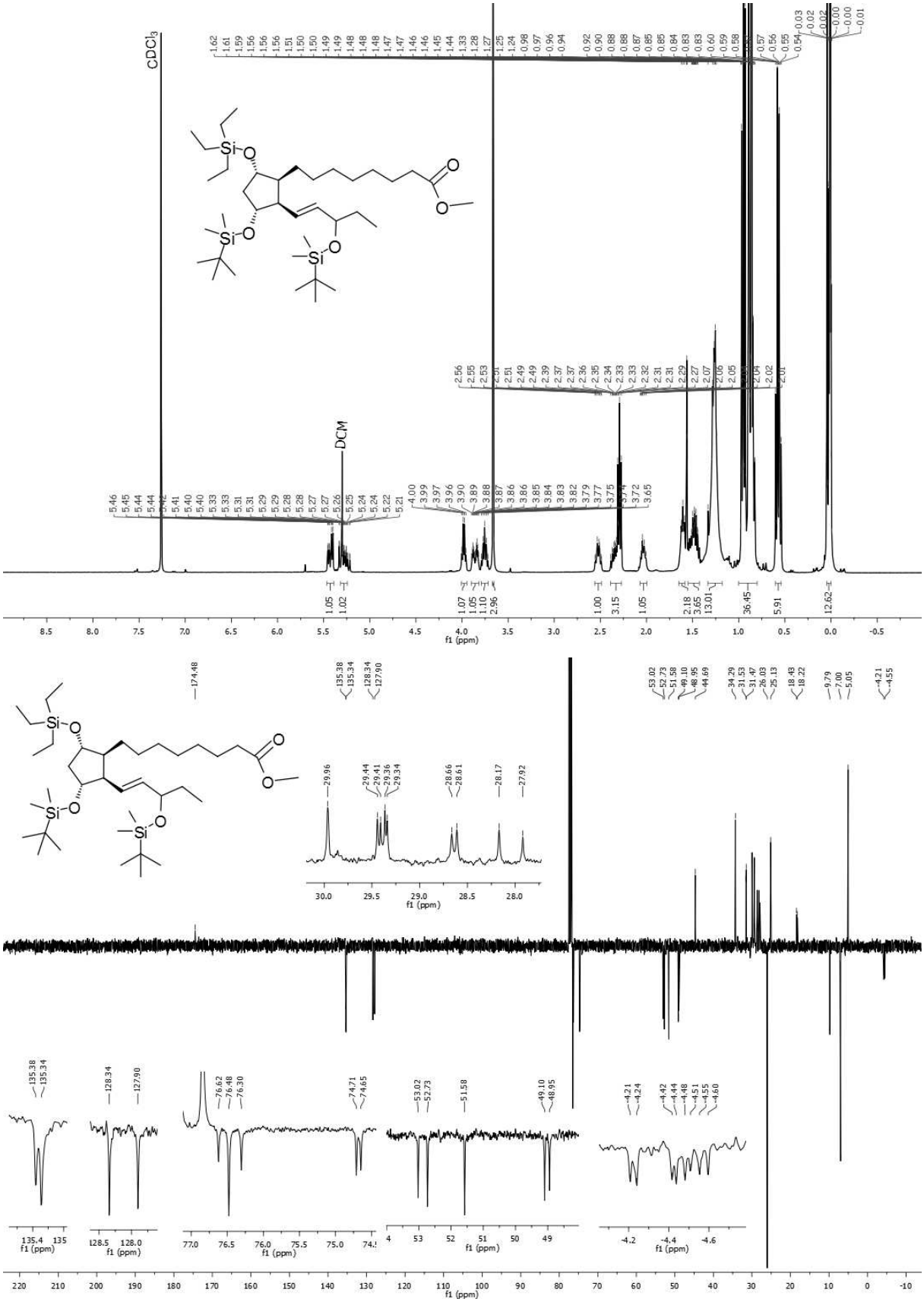


16-epi-16-F_{1t}-Phytoprostane methyl ester ***epi*-1**

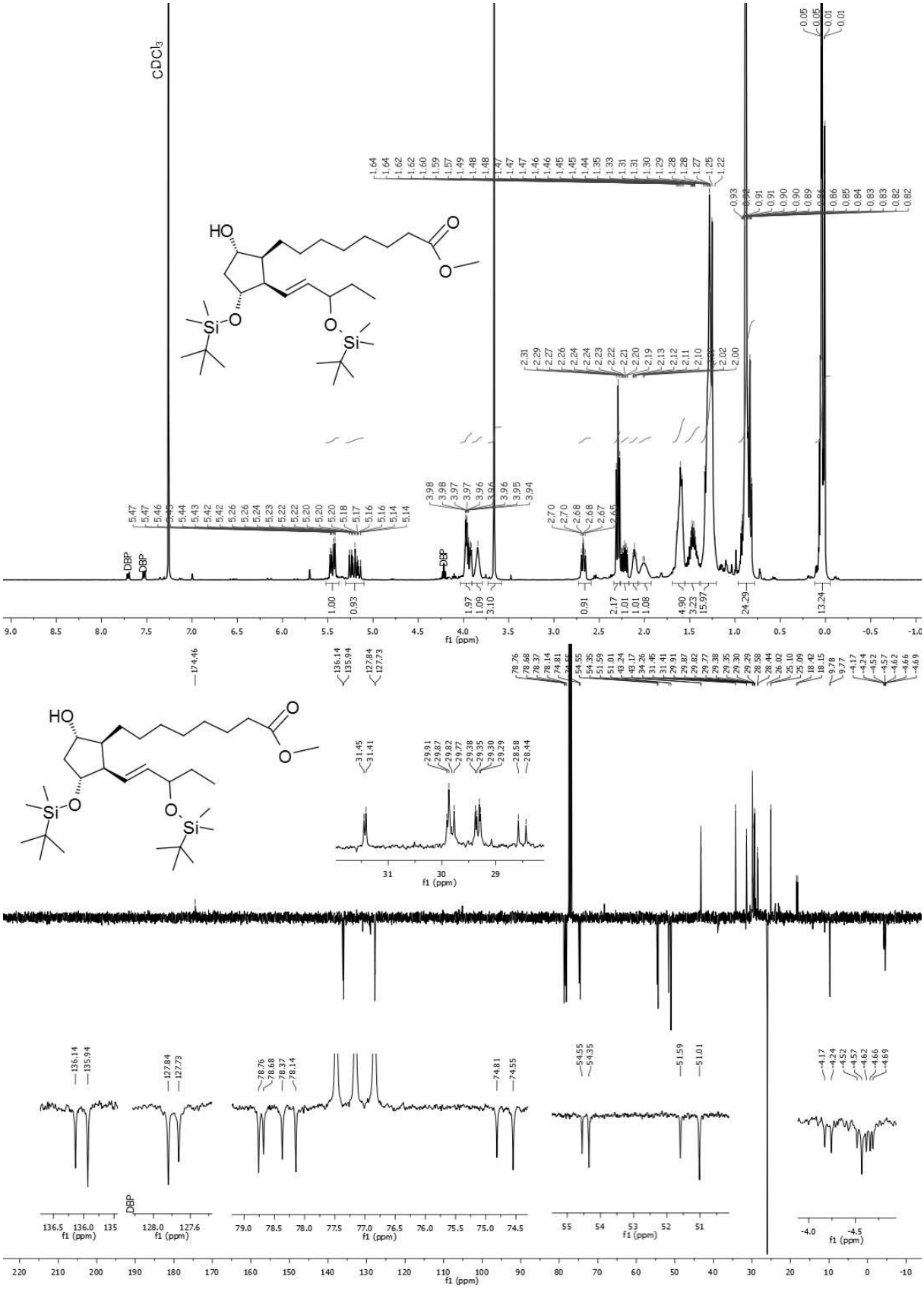




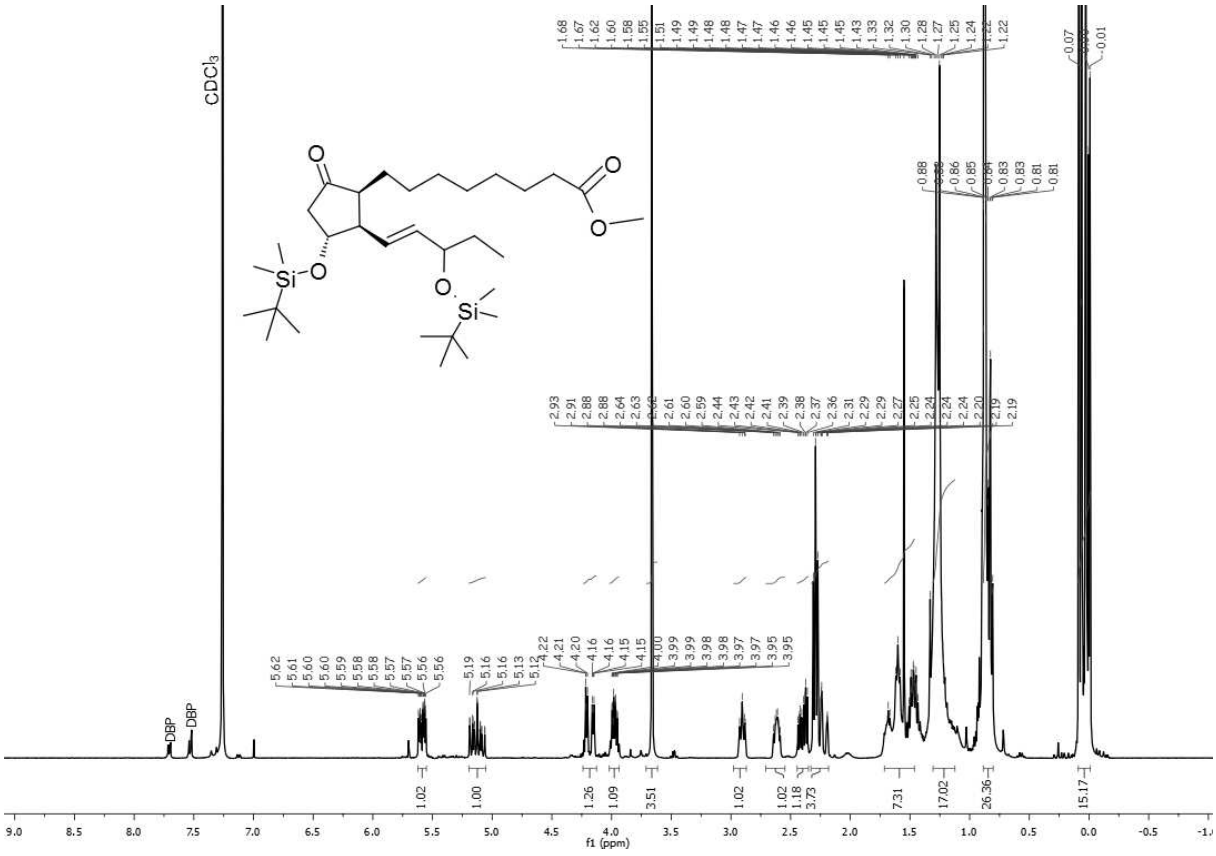
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((*tert*-butyldimethylsilyl)oxy)-pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)-1-((triethylsilyl)oxy)cyclopentane **24**

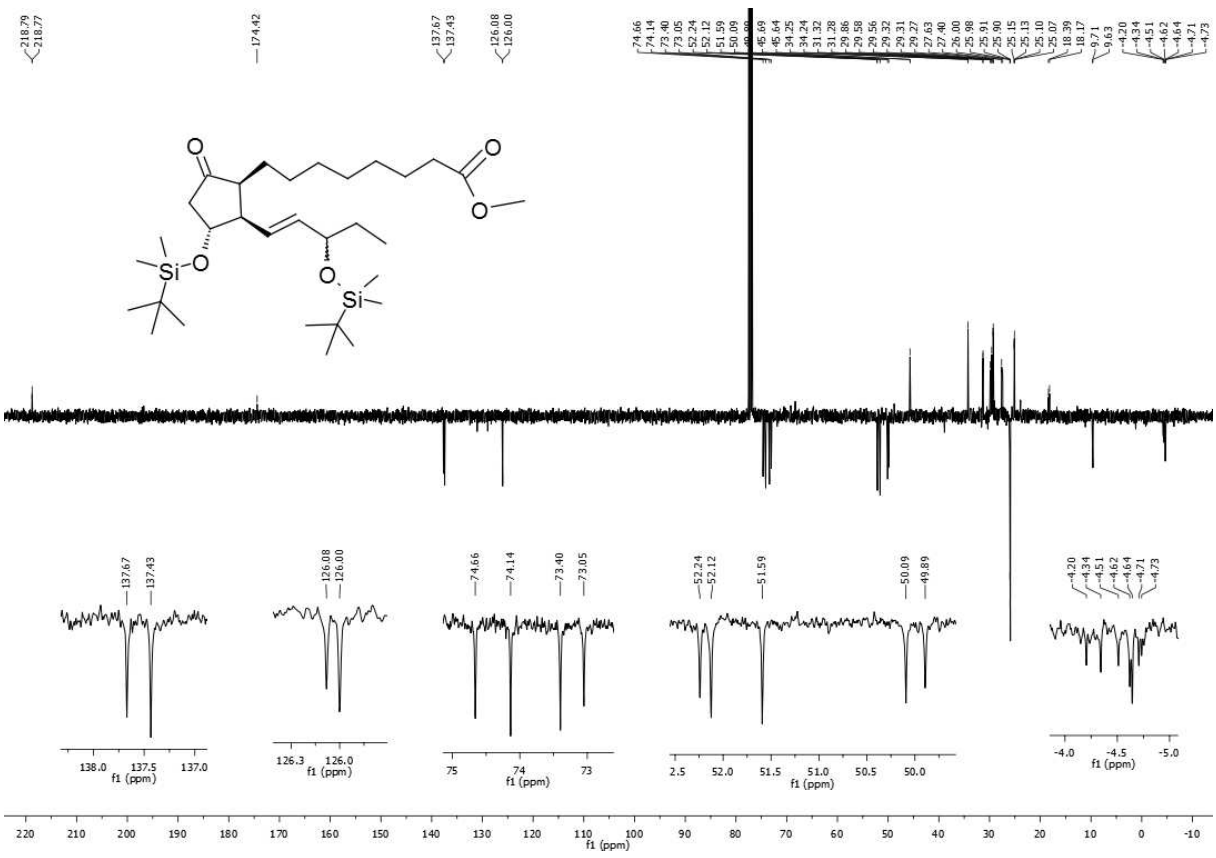


(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((*tert*-butyldimethylsilyl)-oxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentan-1-ol **25** *(crude, DBP = dibutyl phthalate)*

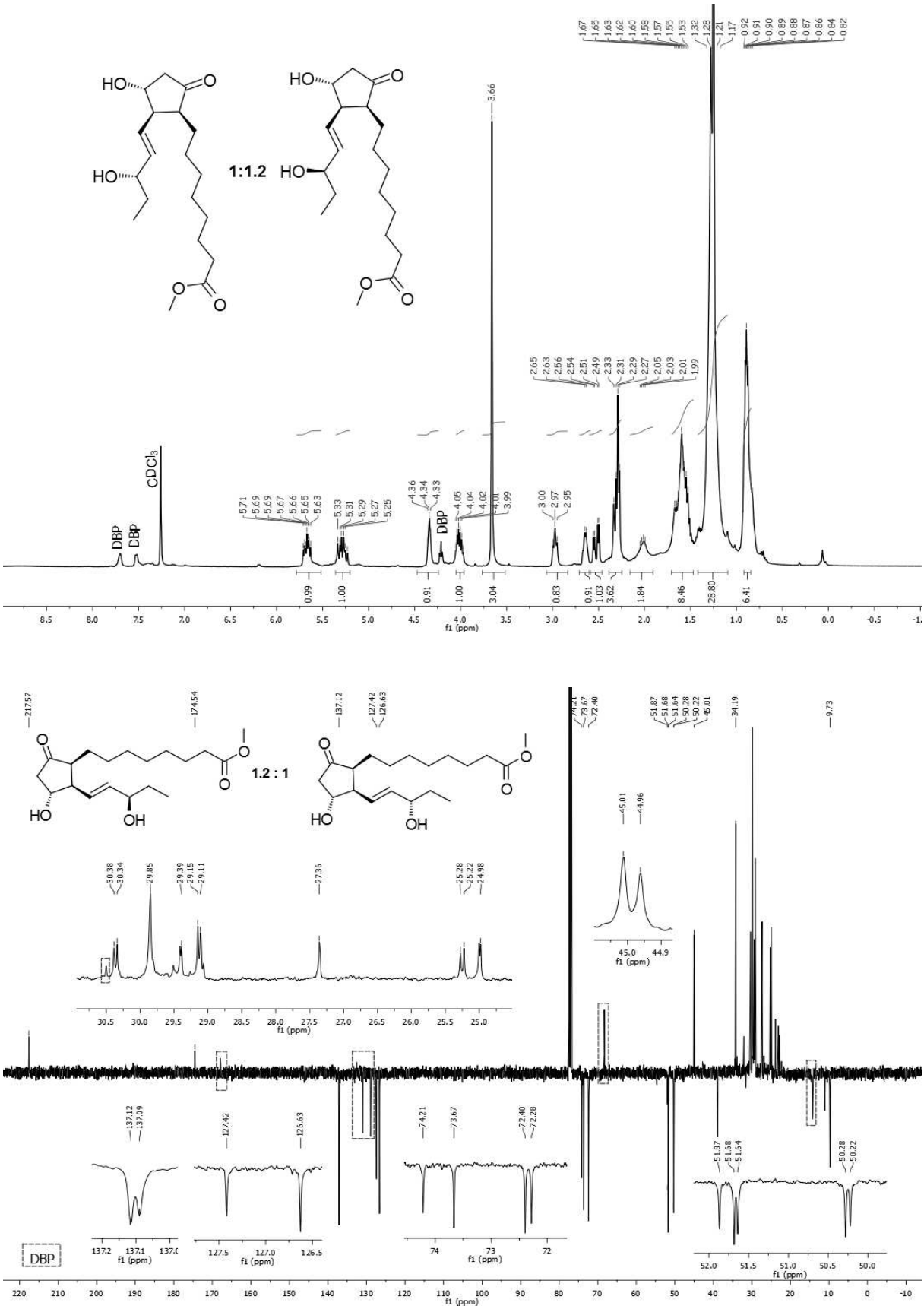


(2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-3-((*E*)-3-((*tert*-butyldimethylsilyl)oxy)pent-1-en-1-yl)-2-(8-methoxy-8-oxooctyl)cyclopentanone **26** *(crude)*

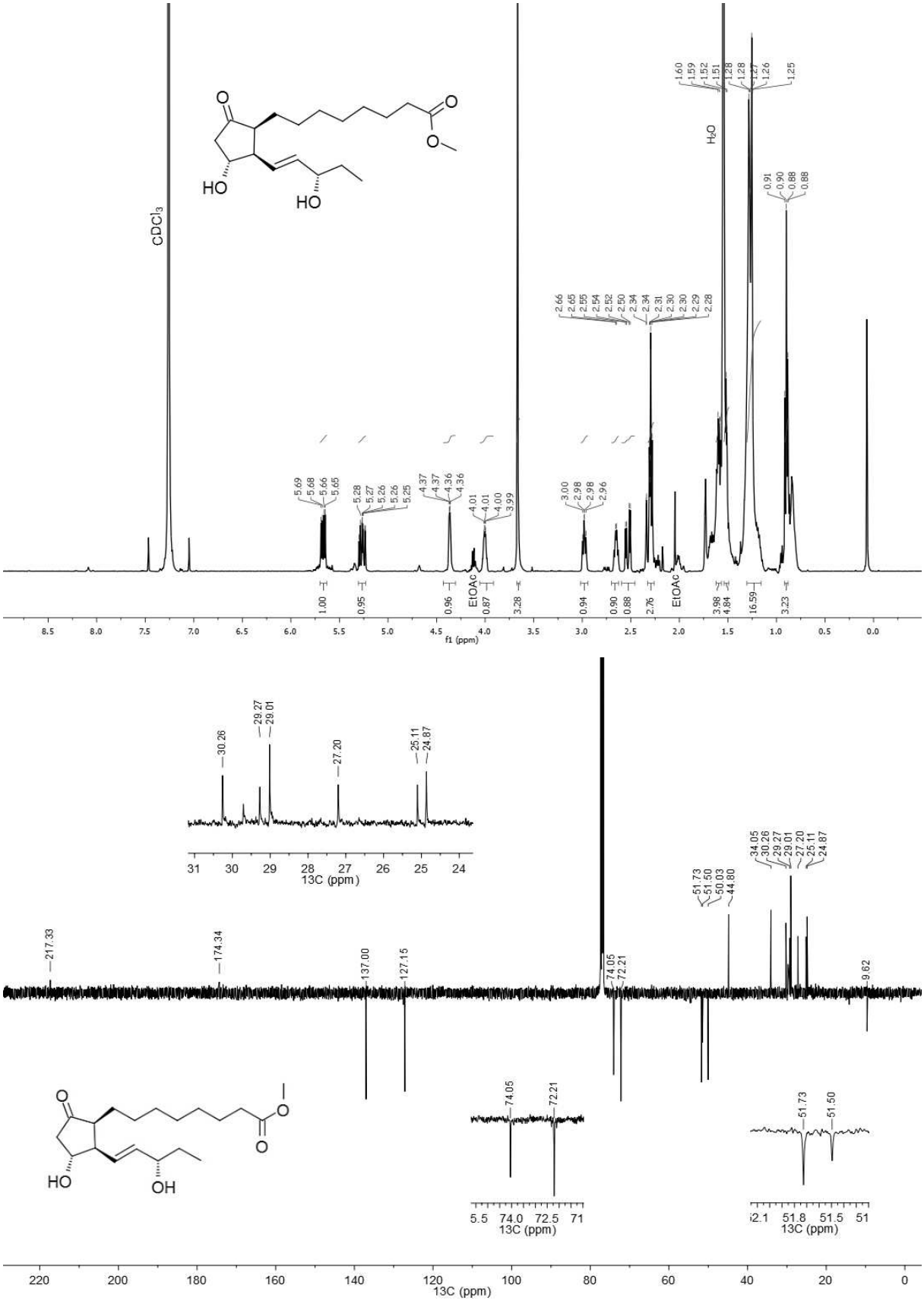




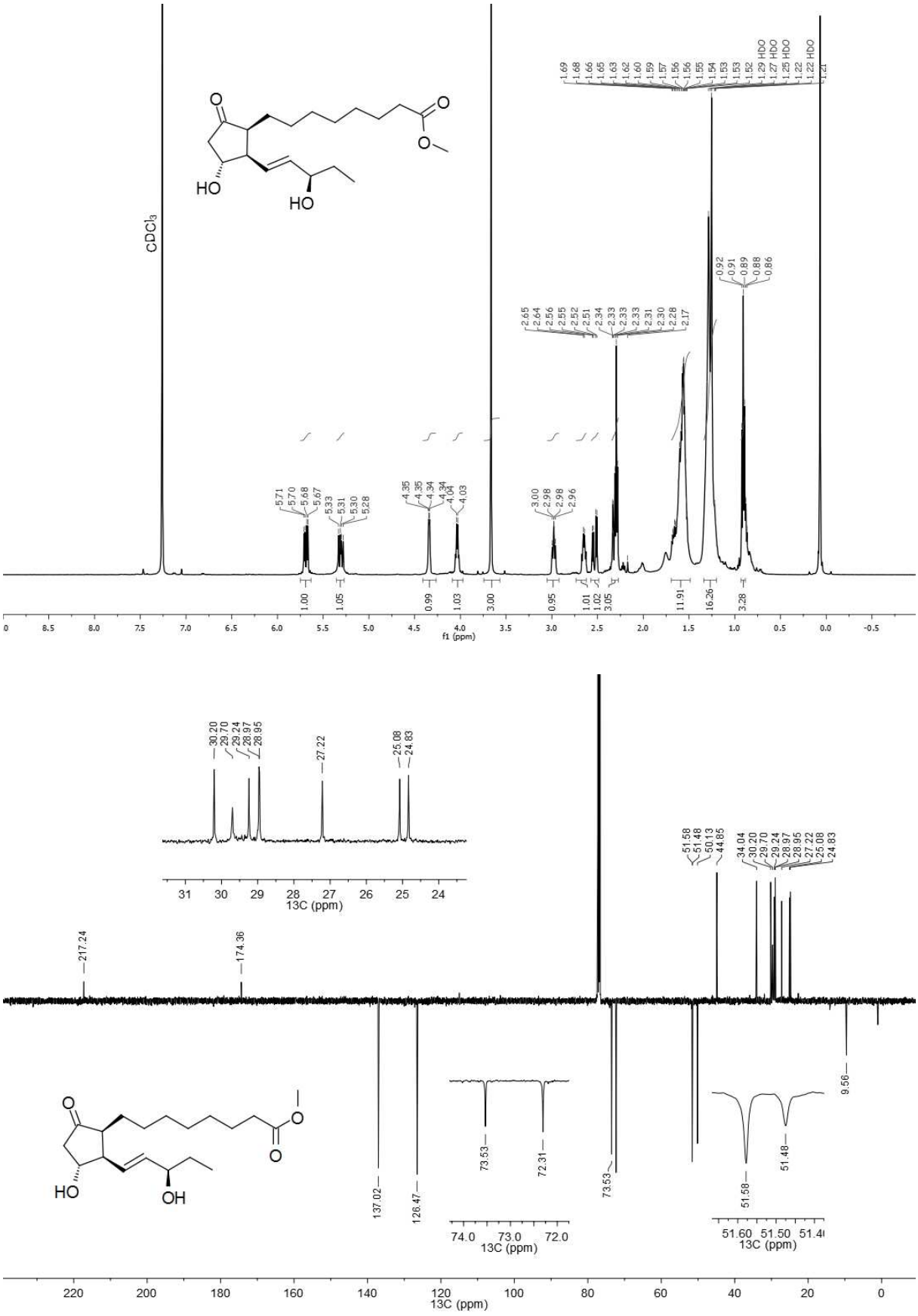
16-E_{1t}-Phytoprostane methyl ester **2** and *16-epi*-16-E_{1t}-phytoprostane methyl ester ***epi*-2** *(crude, traces of DBP)*



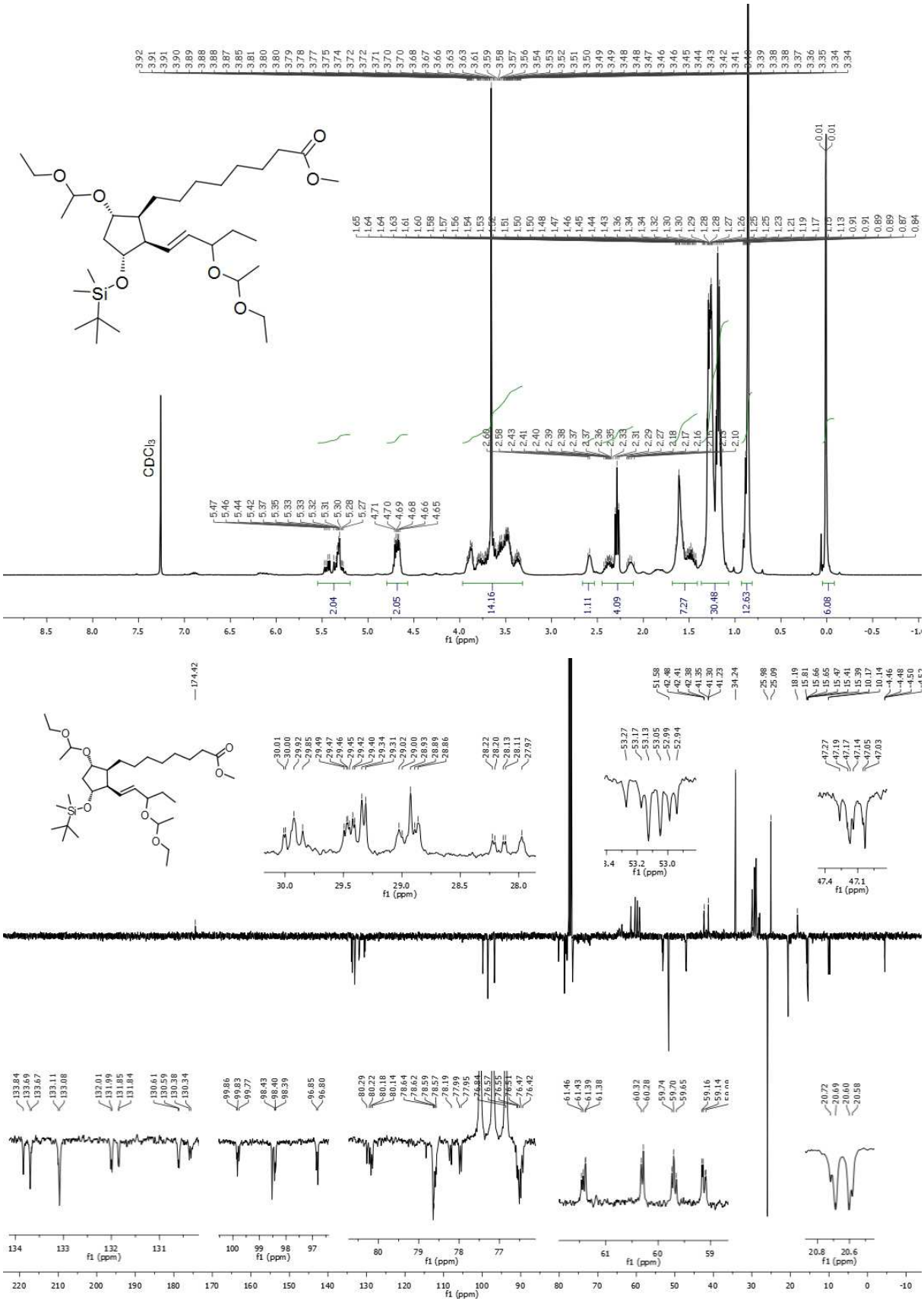
16-E_1-Phytoprostane methyl ester **2**



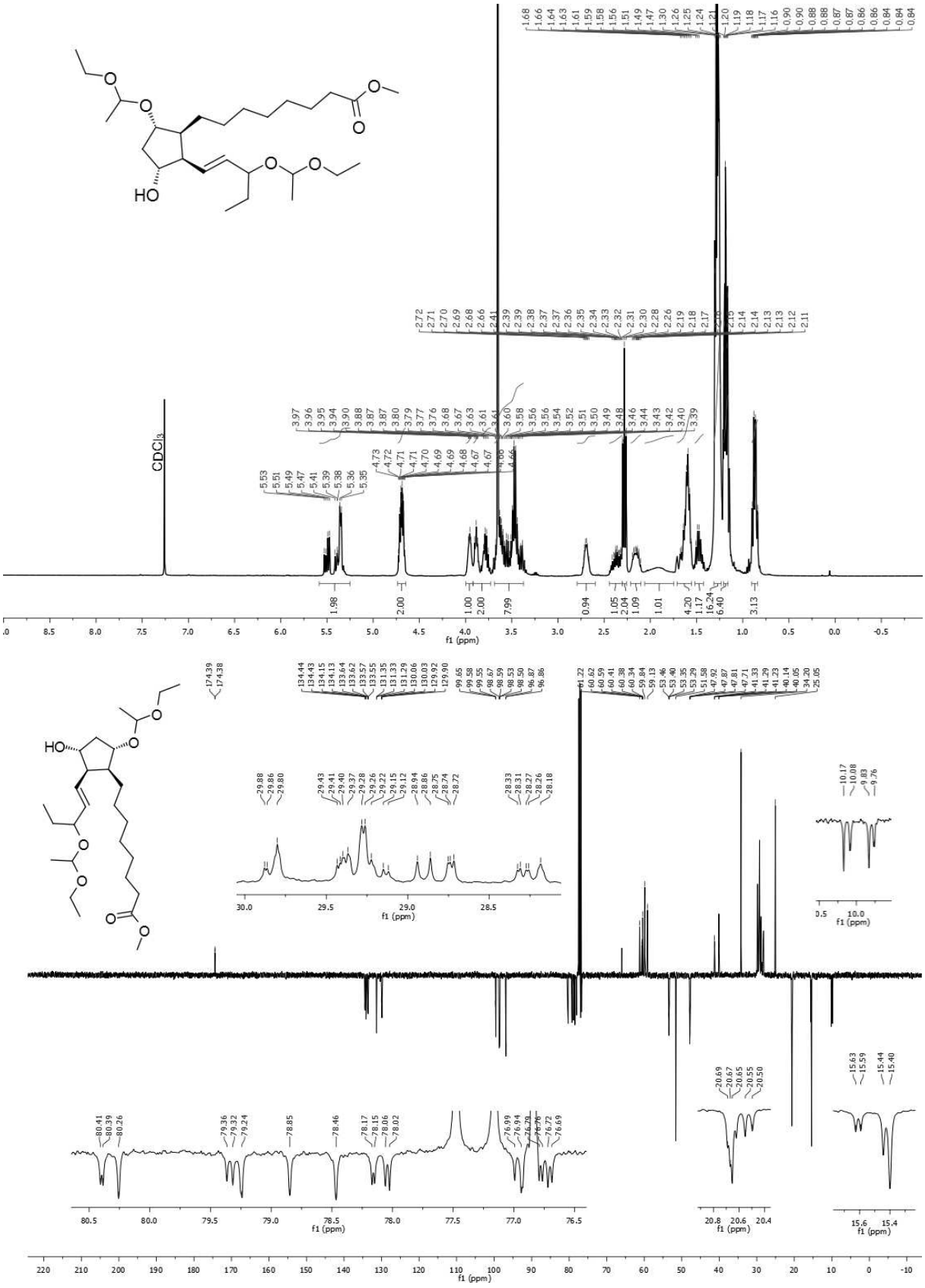
16-epi-16-E_1-Phytoprostane methyl ester ***epi*-2**



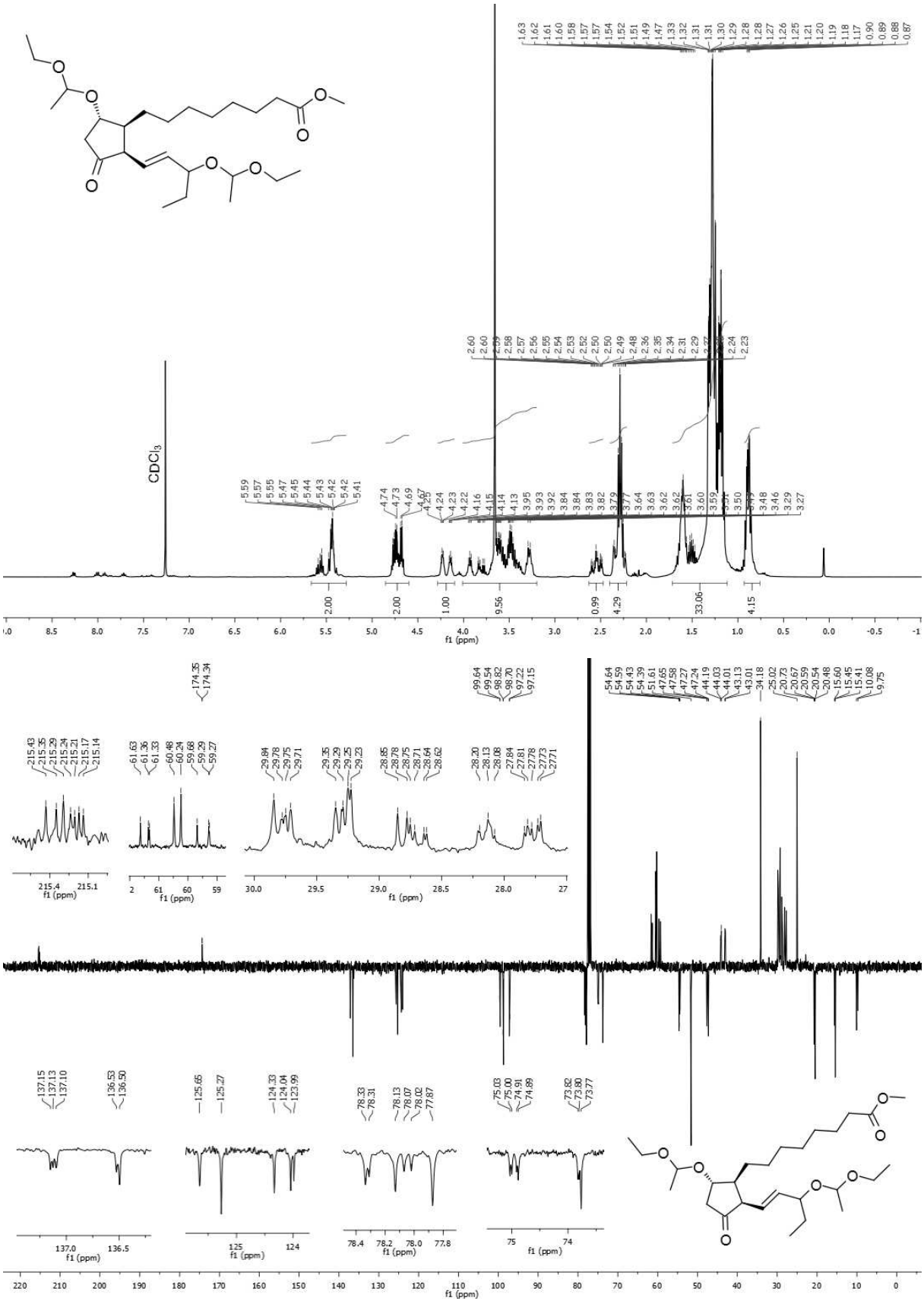
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-1-(1-ethoxyethoxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-3-(1-ethoxyethoxy)pent-1-en-1-yl)cyclopentane **27a**



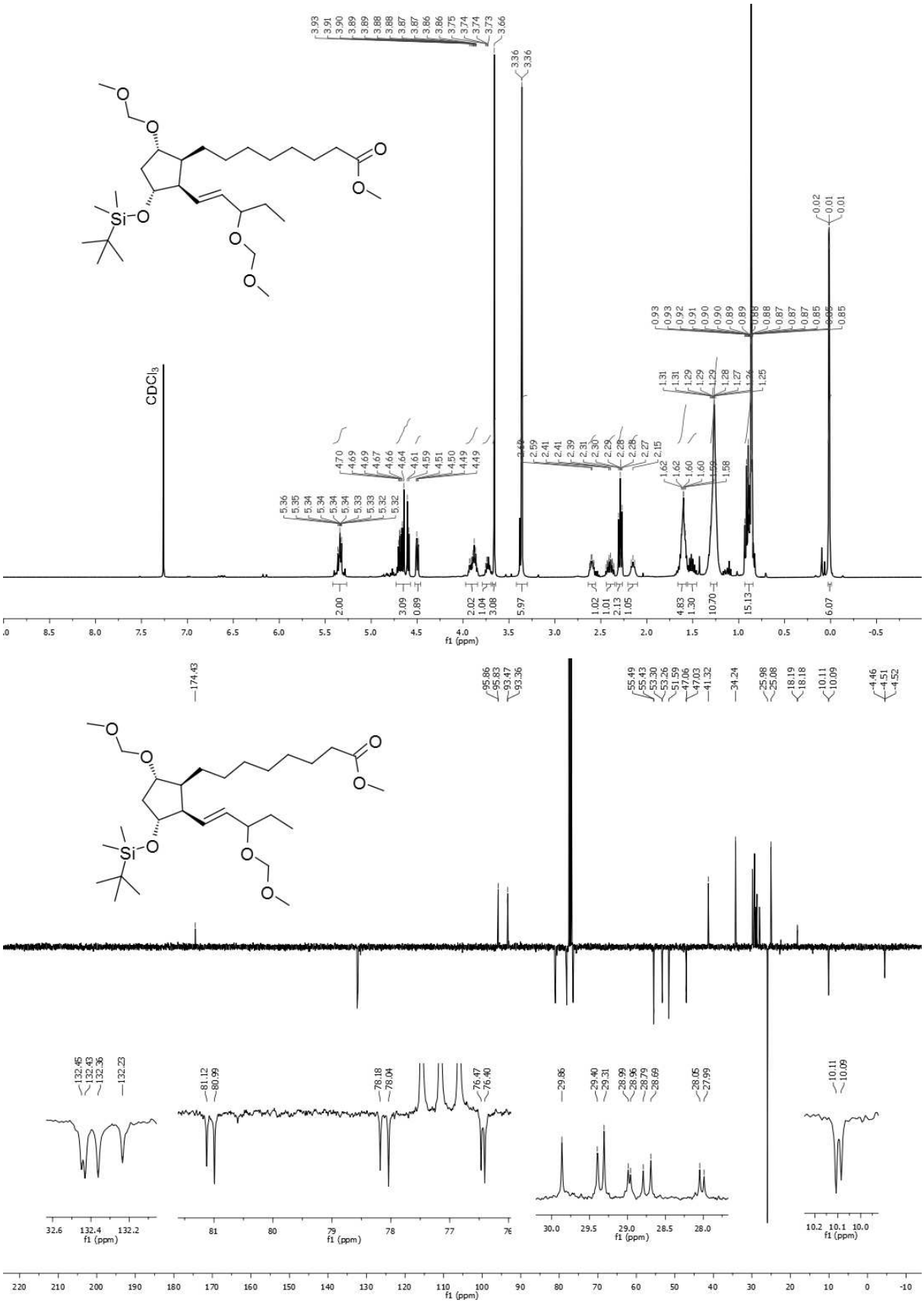
(1*R**,2*R**,3*S**,4*S**)-4-(1-Ethoxyethoxy)-2-((*E*)-3-(1-ethoxyethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentan-1-ol **28a**



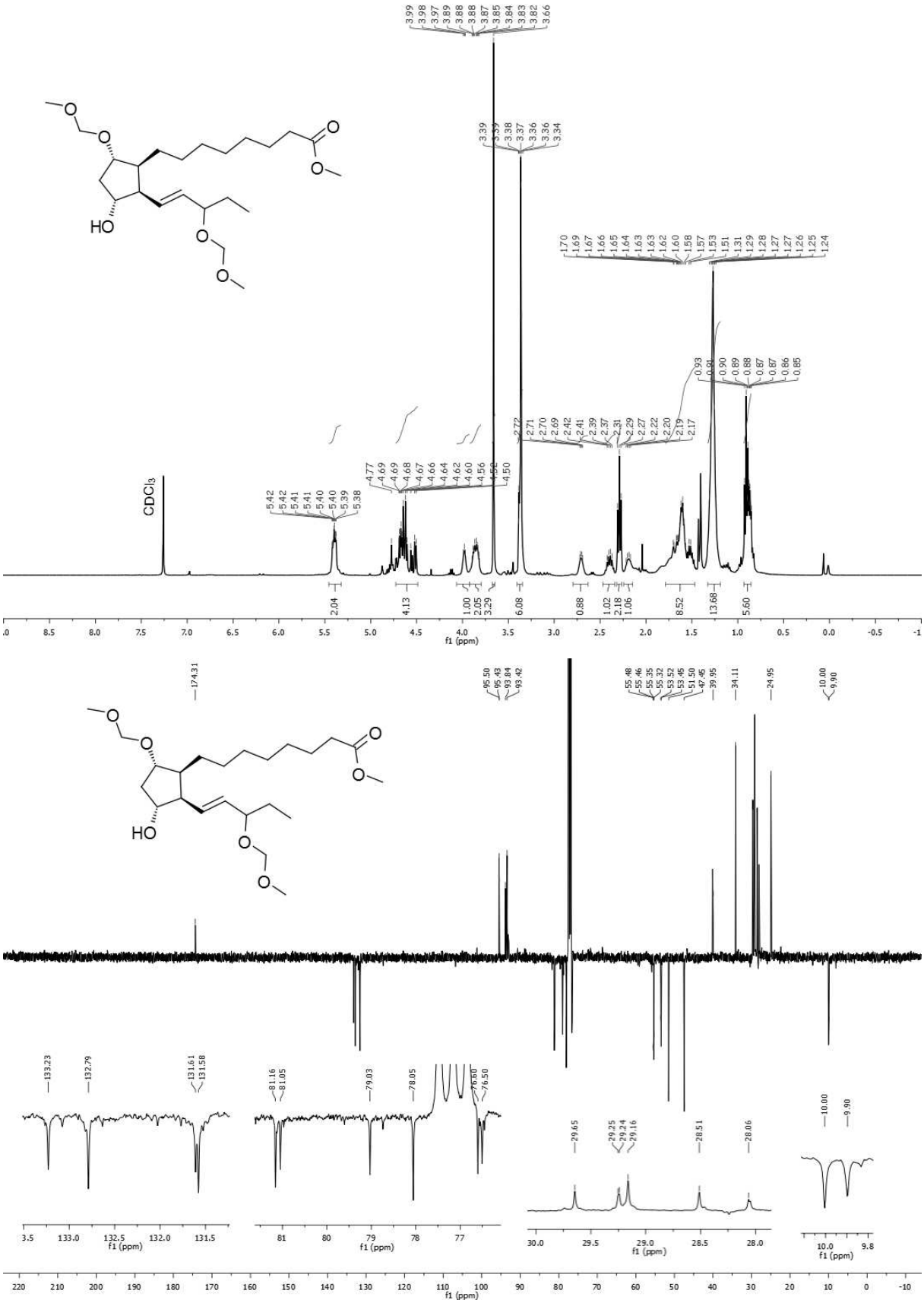
(2*R**,3*S**,4*S**)-4-(1-Ethoxyethoxy)-2-((*E*)-3-(1-ethoxyethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentanone **29a** *(crude)*



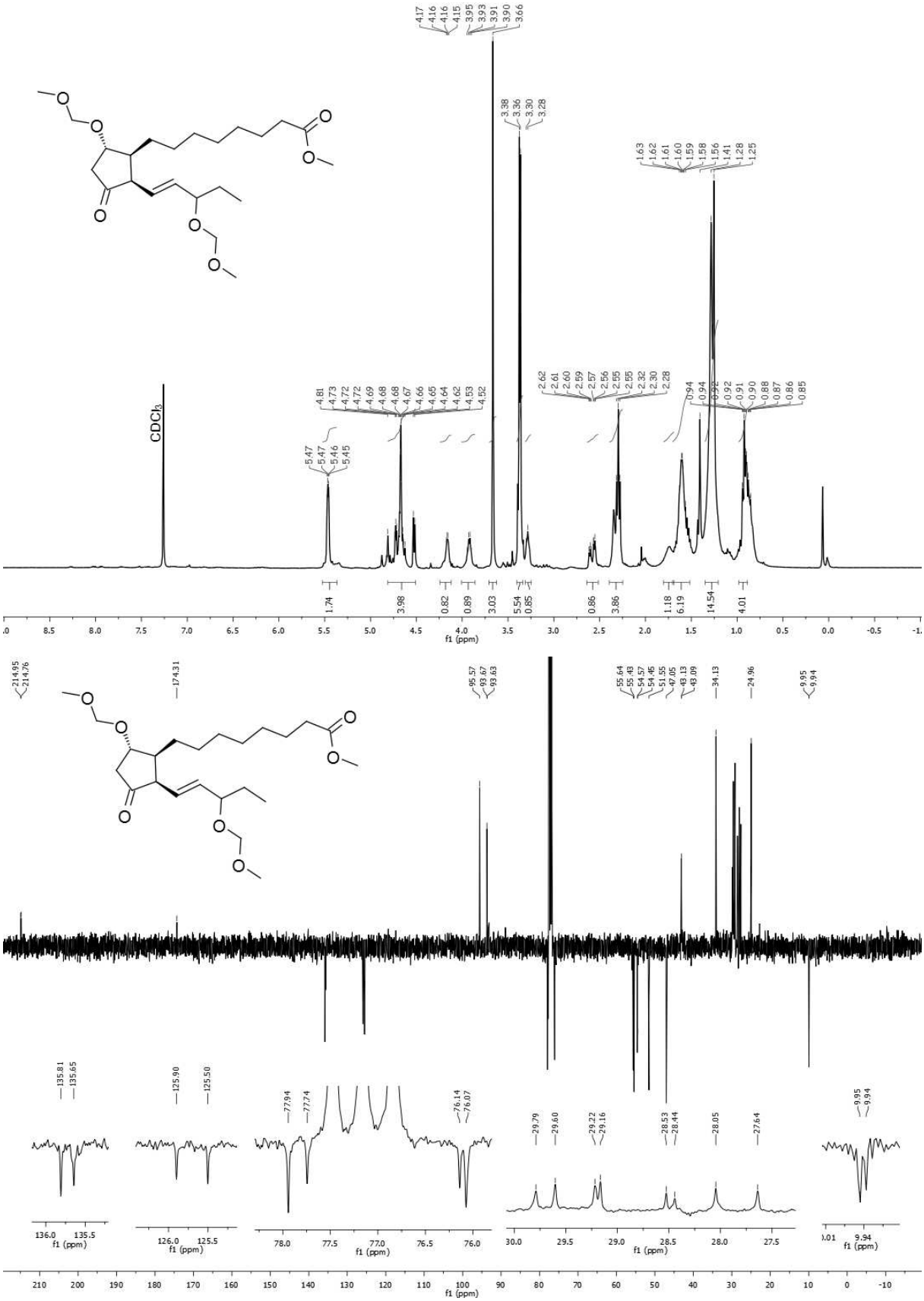
(1*S**,2*S**,3*R**,4*R**)-4-((*tert*-Butyldimethylsilyl)oxy)-1-(1-methoxymethoxy)-2-(8-methoxy-8-oxooctyl)-3-((*E*)-3-(1-methoxymethoxy)pent-1-en-1-yl)cyclopentane **27b**



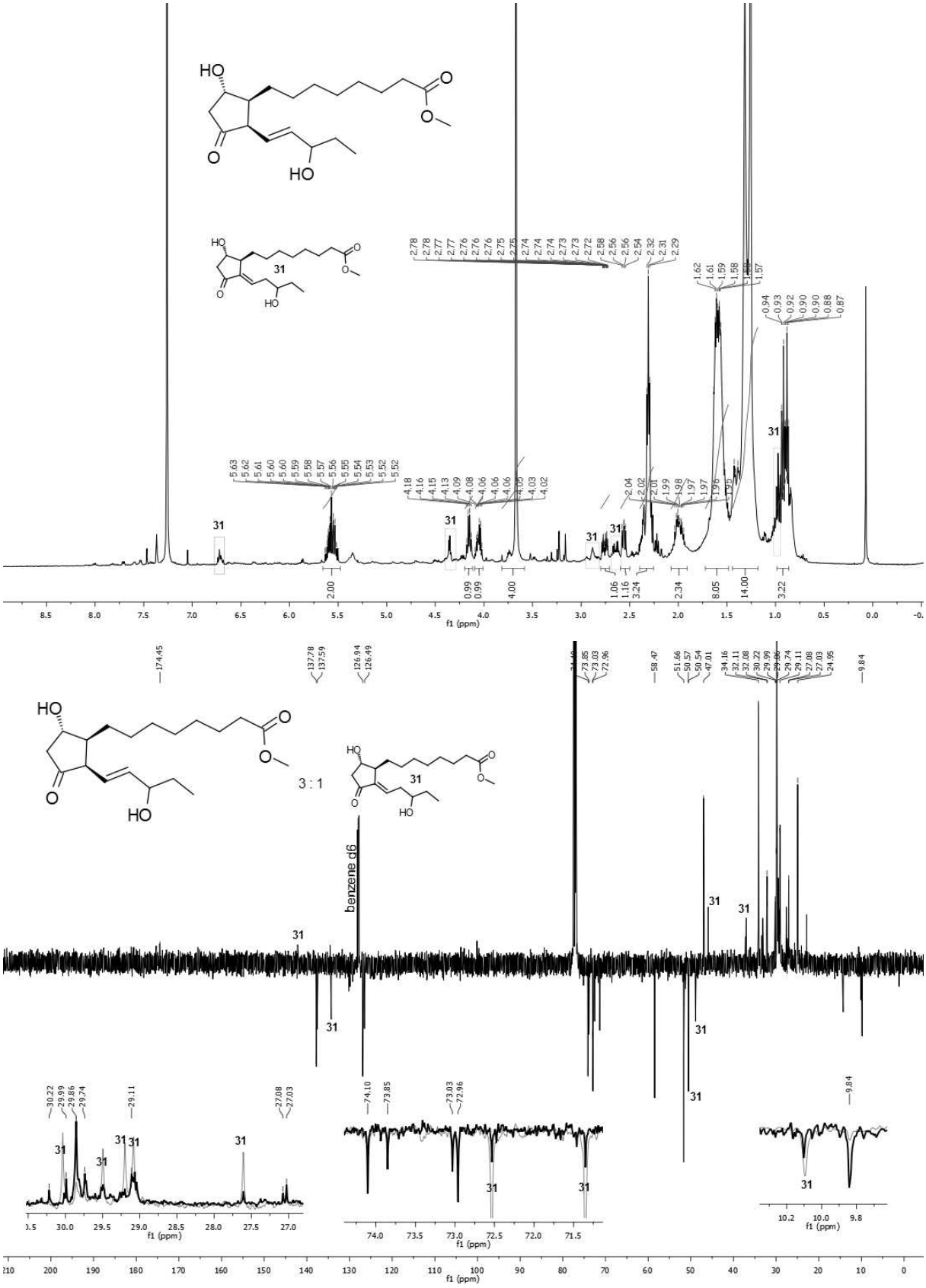
(1*R**,2*R**,3*S**,4*S**)-4-(1-Methoxymethoxy)-2-((*E*)-3-(1-methoxymethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentan-1-ol **28b**



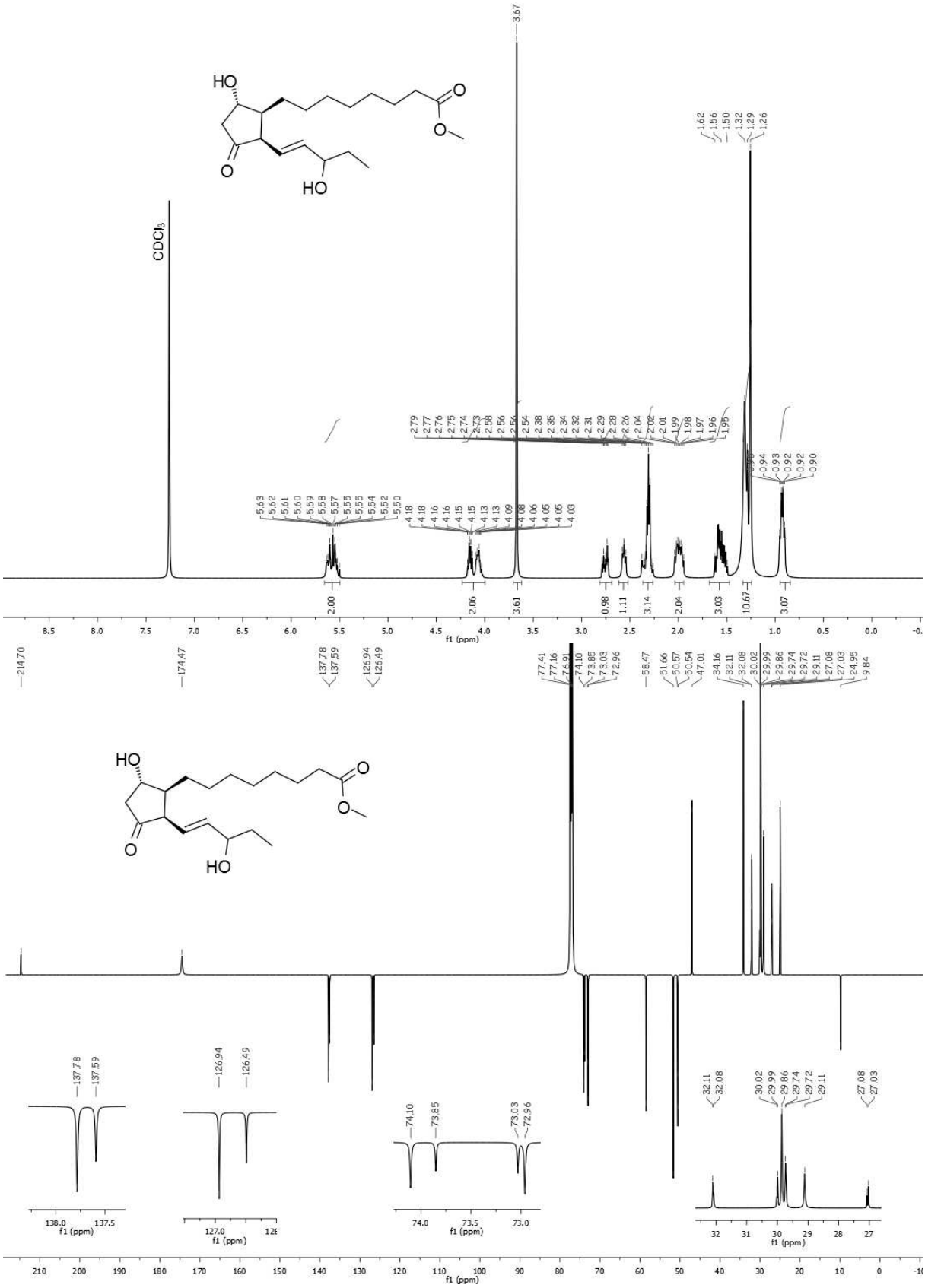
(2*R**,3*S**,4*S**)-4-(1-Methoxymethoxy)-2-((*E*)-3-(1-methoxymethoxy)pent-1-en-1-yl)-3-(8-methoxy-8-oxooctyl)cyclopentanone **29b** *(crude)*



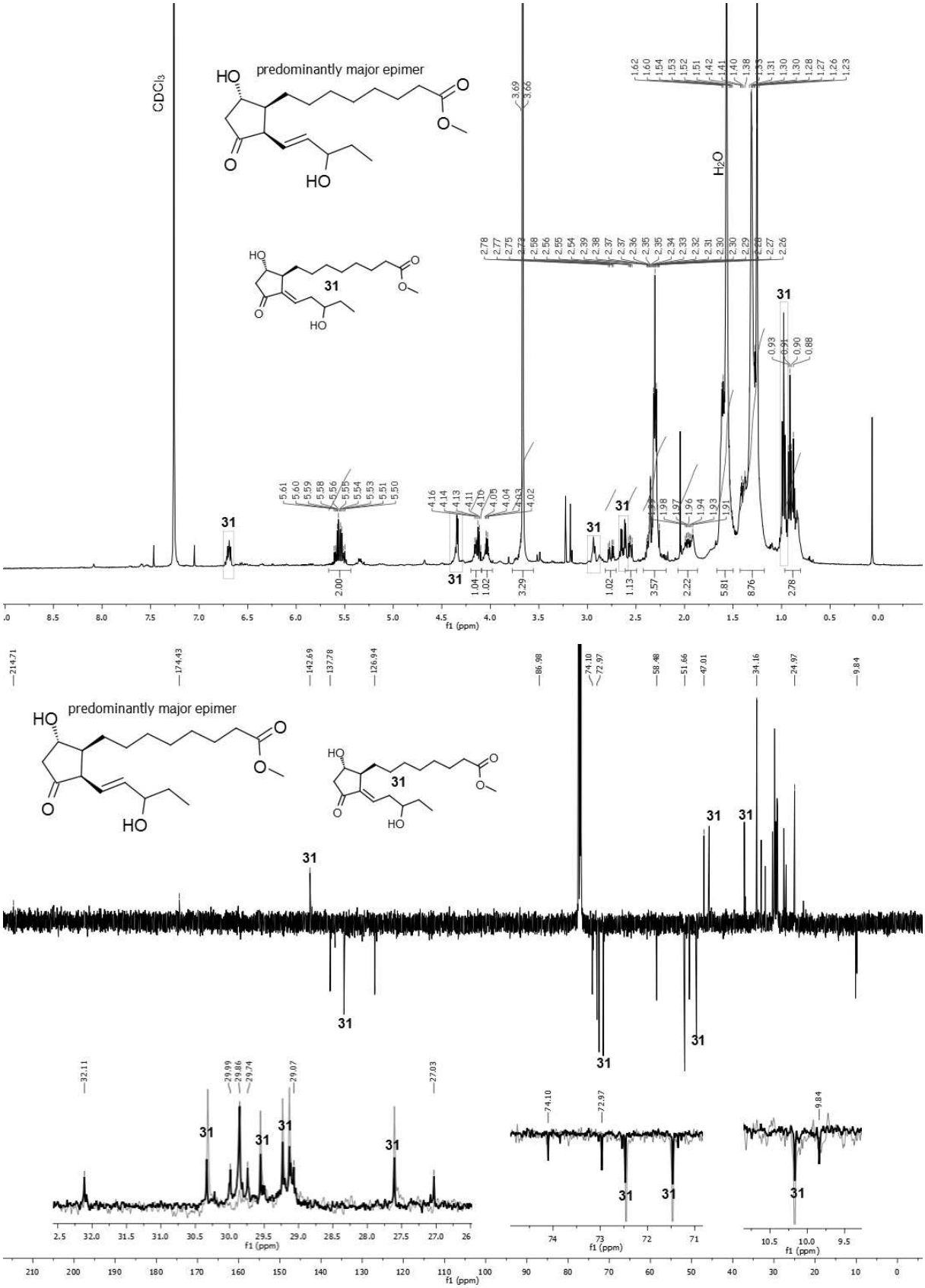
16-D_{1t}-Phytoprostane methyl ester **3,** 16-*epi*-16-D_{1t}-phytoprostane methyl ester ***epi*-3**, Δ^{13}-16-D_{1t}-phytoprostane methyl ester **31**, 16-*epi*-Δ^{13}-16-D_{1t}-phytoprostane methyl ester ***epi*-31**



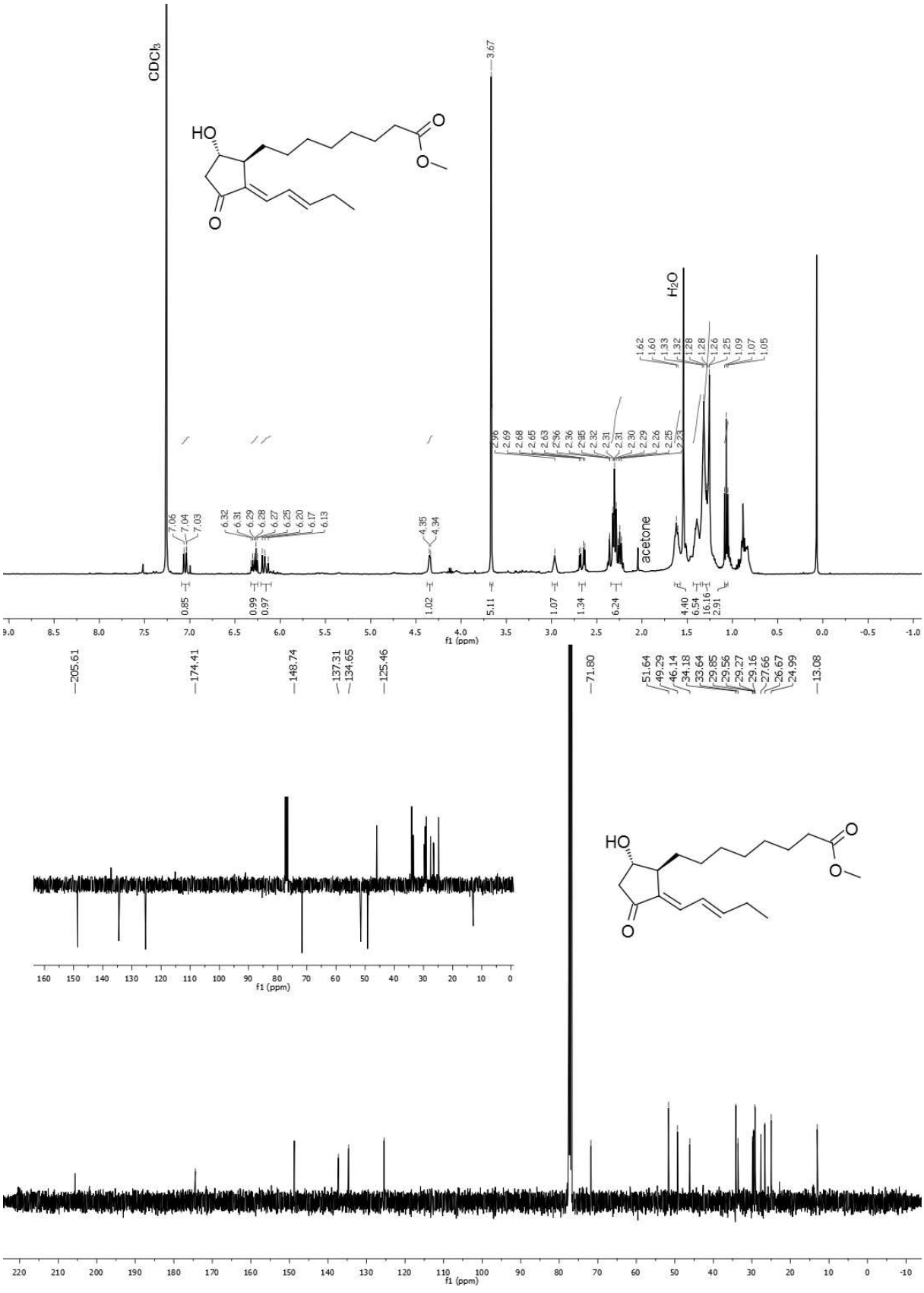
16-D_{1t}-Phytoprostane methyl ester **3** and 16-*epi*-16-D_{1t}-phytoprostane methyl ester ***epi*-3** (*Extracted spectra from the above mixture with **31**)*



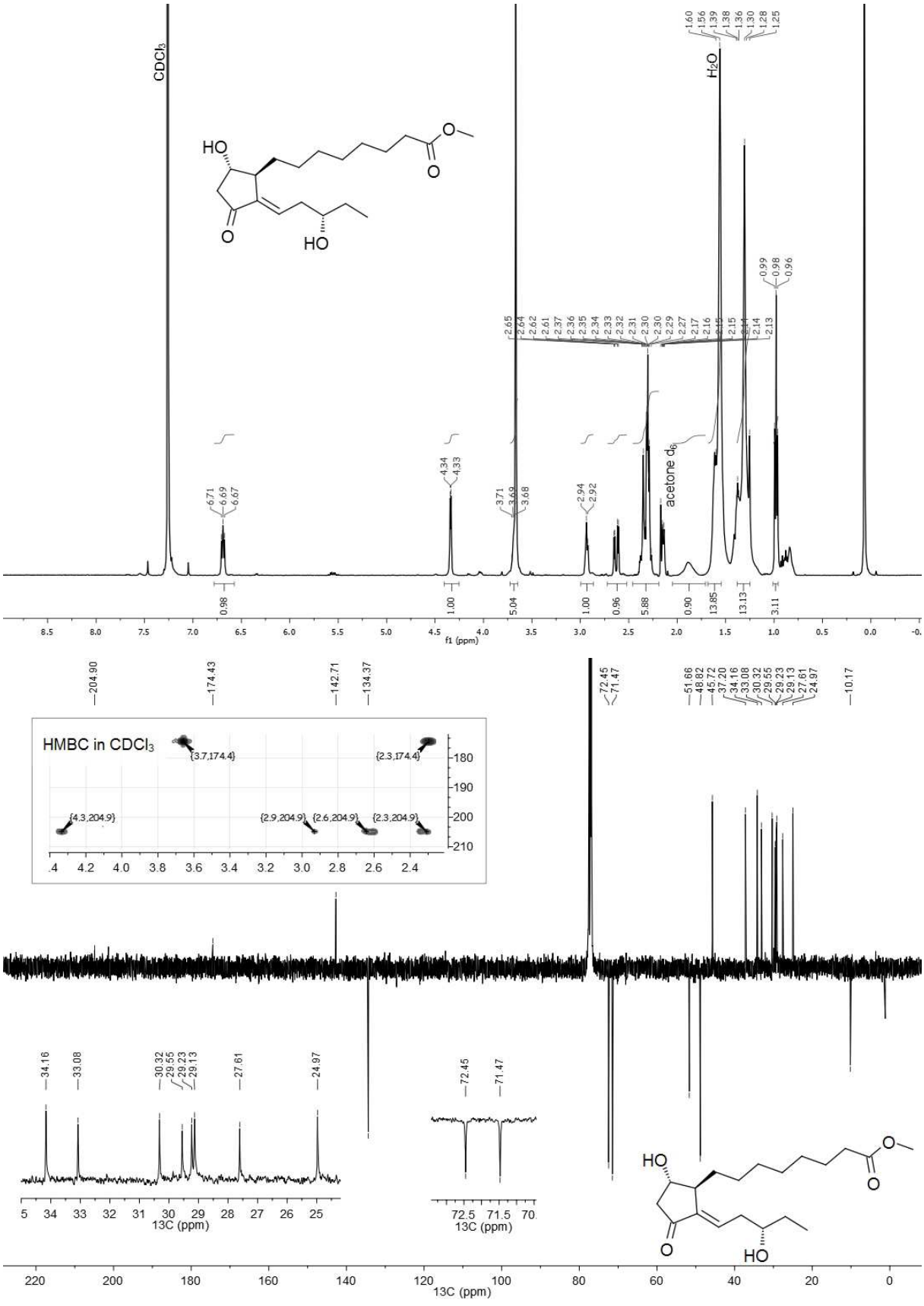
16-*epi*-16-D_{1t}-Phytoprostane methyl ester ***epi*-3**, 16-D_{1t}-phytoprostane methyl ester **3**, Δ^{13}-16-D_{1t}-phytoprostane methyl ester **31**, 16-*epi*-Δ^{13}-16-D_{1t}-phytoprostane methyl ester ***epi*-31**



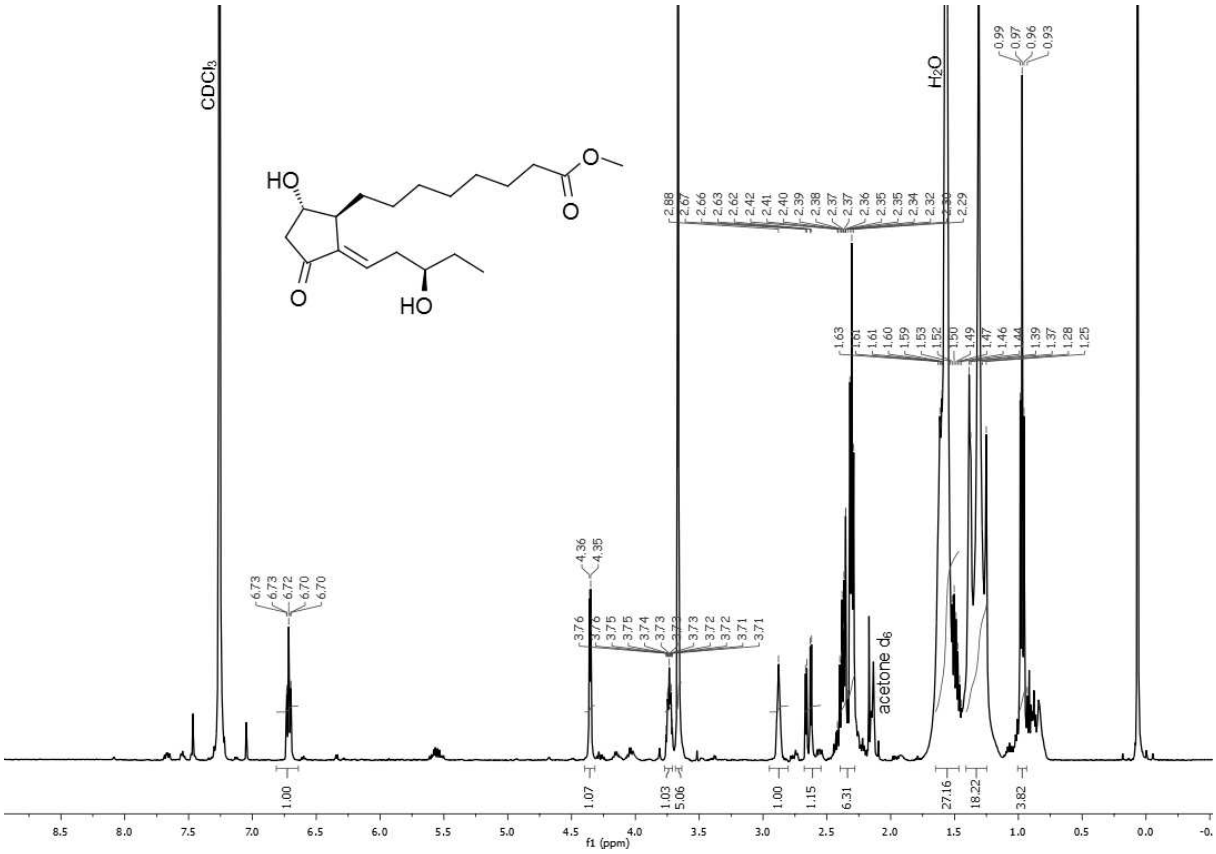
16-Deoxy-$\Delta^{13,15}$-16-D_{1t}-phytoprostane methyl ester **30**

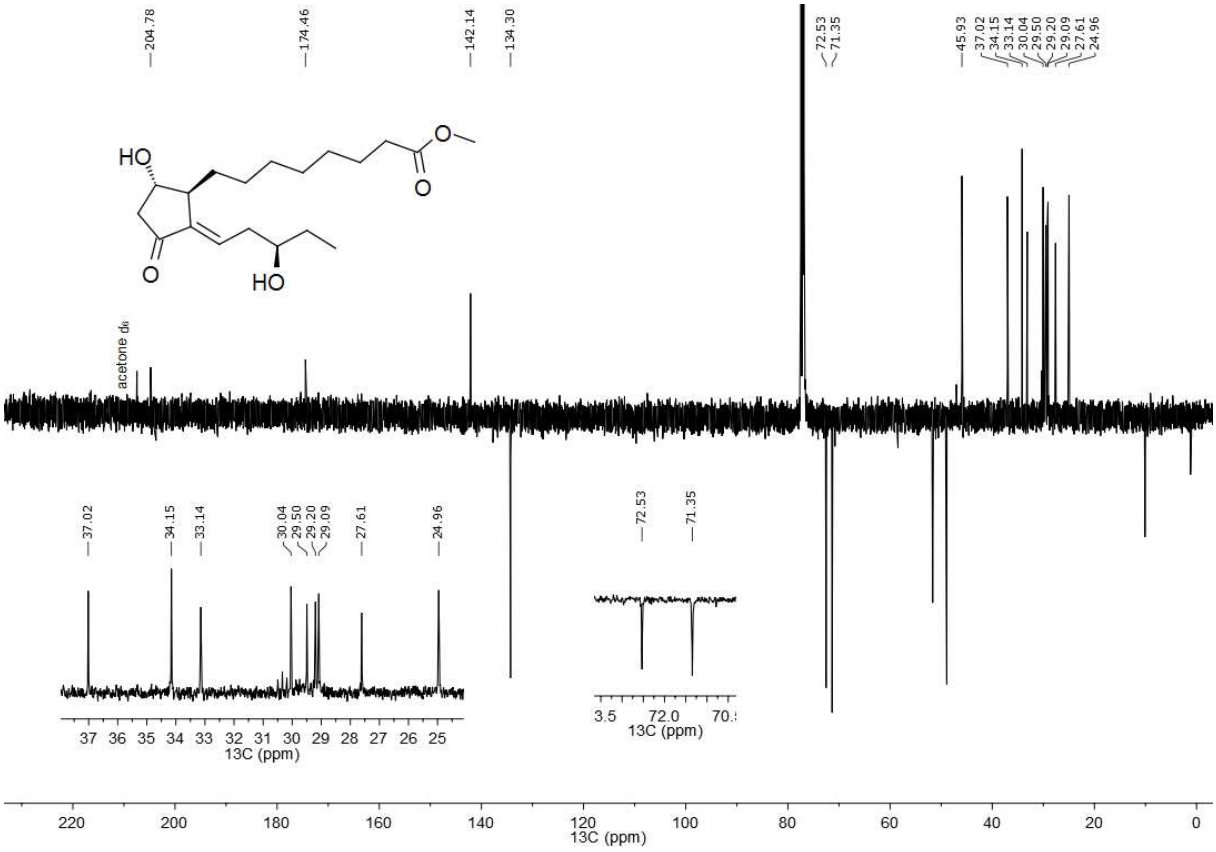


Δ^{13}-16-D_{1t}-Phytoprostane methyl ester **31**



16-*epi*-Δ^{13}-16-D_{1t}-Phytoprostane methyl ester ***epi*-31**





Comparison of ^{13}C NMR shifts of **3/*epi*-3** with **29b/*epi*-29b** and **31/*epi*-31**