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Supporting Information

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Total Synthesis of Phoslactomycin B (Phospholine) and the Biosynthetic Deamino Precursor

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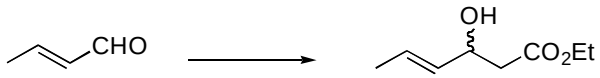
General

The ^{1}H NMR (300 MHz, 500 MHz) and ^{13}C NMR (75 MHz) spectra were measured in $CDCl_3$ or CD_3OD. The following solvents were distilled before use: THF (from Na/benzophenone), Et_2O (from Na/benzophenone), and CH_2Cl_2 (from CaH_2). Silica gel for chromatography was purchased from Merck (silica gel 60).

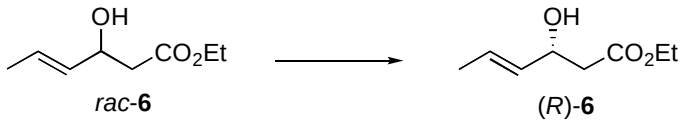
Ethyl (*E*)-3-Hydroxy-4-hexenoate (*rac*-6)



rac-**6**

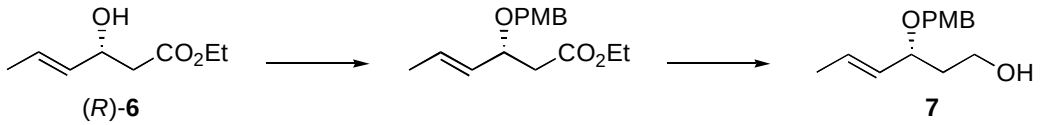
To an ice-cold solution of *i*Pr_2NH (24.4 mL, 174.1 mmol) in THF (70 mL) was added *n*BuLi (66.5 mL, 2.24 M in hexane, 149 mmol) dropwise. After 10 min at 0 °C, the solution was cooled to –78 °C, and EtOAc (14.6 mL, 149 mmol) was added dropwise. The solution was stirred at –78 °C for additional 40 min, and crotonaldehyde (10.0 mL, 124.1 mmol) dissolved in THF (10 mL) was added slowly. After 1 h at –78 °C, the solution was poured into an ice-cold mixture of saturated NH_4Cl and EtOAc. The resulting mixture was stirred vigorously for a few minutes, and the layers were separated. The aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a yellow residue, which was distilled under reduced pressure to furnish *rac*-**6** (18.9 g, 96%): Bp. 88–92 °C (3 Torr); IR (neat) 3442, 1735, 1175, 1029 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.27 (t, *J* = 7 Hz, 3 H), 1. 70 (ddd, *J* = 7, 2, 1 Hz, 3 H), 2.45–2.60 (m, 2 H), 2.88 (br s, 1 H), 4.18 (q, *J* = 7 Hz, 2 H), 4.48 (m, 1 H), 5.51 (ddq, *J* = 15, 7, 2 Hz, 1 H), 5.74 (ddq, *J* = 15, 2, 6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.0 (–), 17.4 (–), 41.7 (+), 60.4 (+), 68.7 (–), 126.9 (–), 132.0 (–), 172.0 (+).

Ethyl (3*R*,4*E*)-3-Hydroxy-4-hexenoate ((*R*)-6)



To a mixture of 4A molecular sieves (9.48 g) and Ti(O-*i*Pr)$_4$ (23.2 mL, 78.9 mmol) in CH_2Cl_2 (140 mL) was added L-(+)-DIPT (19.8 mL, 94.7 mmol) dropwise at –20 °C. The mixture was stirred at –20 °C for 30 min, and a solution of *rac*-**6** (50.0 g, 316.1 mmol) in CH_2Cl_2 (20 mL) was injected. The mixture was stirred for additional 30 min at –20 °C, and then cooled to –40 °C. A solution of *t*BuOOH in CH_2Cl_2 (43.6 mL, 7.26 M, 317 mmol) was added dropwise. The reaction was carried out at –20 °C for 30 h, and quenched by addition of Me_2S (23.2 mL, 315.9 mmol). After 30 min at –20 °C, 10% tartaric acid (40 mL), NaF (16.6 g, 395 mmol), and Celite (15 g) were added. The resulting mixture was stirred at room temperature for 30 min and filtered through a pad of Celite with Et_2O. The filtrate was concentrated to afford a residue, which was purified by distillation under reduced pressure to furnish (*R*)-**6** (22.0 g, 44%): $[\alpha]^{25}_D$ +20 (*c* 0.208, $CHCl_3$). Enantiomeric excess of (*R*)-**6** was > 97% by HPLC analysis of the derived benzoate using a chiral column (Daicel, Chiralcel OD-H) with hexane/*i*-propanol as solvent.

(3*R*,4*E*)-3-(4-Methoxybenzyloxy)-4-hexen-1-ol (7)

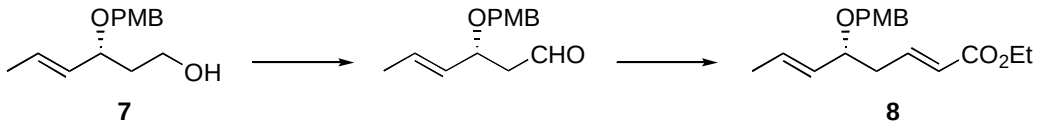


A solution of (*R*)-**6** (13.3 g, 84.1 mmol), 4-methoxybenzyl 2,2,2-trichloroacetimidate (47.5 g, 168.1 mmol), and (+)-10-camphorsulfonic acid (586 mg, 2.52 mmol) in CH_2Cl_2 (90 mL) was stirred at room temperature for 10 h, and concentrated to afford a residual oil, which was diluted with hexane. The mixture was filtered through Celite with hexane. The filtrate was concentrated to obtain a residue, which was flashed through short chromatography on silica gel (hexane/EtOAc) to afford the corresponding PMB ether, which was used for the next reaction without further purification: $[\alpha]^{29}_D$ = +28 (*c* 0.179, $CHCl_3$); IR (neat) 1735, 1513, 1248, 1037 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (t, *J* = 7 Hz, 3 H), 1.73 (dd, *J* = 6, 2 Hz, 3 H), 2.44 (dd, *J* = 15, 6 Hz, 1 H), 2.63 (dd, *J* = 15, 8 Hz, 1 H), 3.78 (s, 3 H), 4.10 (dq, *J* = 2, 7 Hz, 2 H), 4.14–4.24 (m, 1 H), 4.29 (d, *J* = 11 Hz, 1 H), 4.49 (d, *J* = 11 Hz, 1 H), 5.38 (ddq, *J*

= 15, 7, 2 Hz, 1 H), 5.68 (dq, *J* = 15, 6 Hz, 1 H), 6.85 (d, *J* = 9 Hz, 2 H), 7.23 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.2 (–), 17.7 (–), 41.5 (+), 55.2 (–), 60.3 (+), 69.7 (+), 76.4 (–), 113.7 (–), 129.3 (–), 129.6 (–), 130.4 (–), 130.6 (+), 159.1 (+), 171.0 (+).

To an ice-cold solution of the above compound in THF (100 mL) was added $LiAlH_4$ (2.23 g, 58.8 mmol) portionwise at 0 °C. The mixture was stirred at room temperature for 1 h, and excess hydride was quenched at 0 °C by addition of H_2O (10.6 mL, 590 mmol). After being stirred at 0 °C, the solution was poured into a mixture of 3 N HCl (98 mL, 294 mmol) and EtOAc at 0 °C. The resulting mixture was stirred for a few minutes. The organic phase was separated and the aqueous phase was extracted with EtOAc twice. The combined organic phases were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish alcohol **7** (17.3 g, 87% from (*R*)-**6**): $[\alpha]^{29}_D$ = +56 (*c* 0.181, $CHCl_3$); IR (neat) 3421, 1613, 1514, 1249, 1037 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.62–1.91 (m, 2 H), 1.74 (dd, *J* = 6, 2 Hz, 3 H), 2.69 (br s, 1 H), 3.64–3.77 (m, 2 H), 3.78 (s, 3 H), 3.93 (dt, *J* = 4, 8 Hz, 1 H), 4.26 (d, *J* = 11 Hz, 1 H), 4.52 (d, *J* = 11 Hz, 1 H), 5.41 (ddq, *J* = 15, 8, 2 Hz, 1 H), 5.67 (dq, *J* = 15, 6 Hz, 1 H), 6.86 (d, *J* = 9 Hz, 2 H), 7.23 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 38.0, 55.2, 60.7, 69.5, 79.3, 113.8, 129.1, 129.4, 130.5, 131.3, 159.1.

Ethyl (2*E*,5*R*,6*E*)-5-(4-Methoxybenzyloxy)-2,6-octadienoate (8)



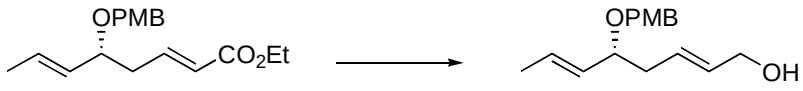
7 **8**

To a solution of $(COCl)_2$ (6.49 mL, 74.1 mmol) in CH_2Cl_2 (180 mL) was added DMSO (13.2 mL, 186 mmol) at –78 °C. After being stirred 15 min at –78 °C, alcohol **7** (14.6 g, 61.8 mmol) in CH_2Cl_2 (20 mL) was added dropwise. The solution was stirred between –78 °C and –40 °C for 30 min, and then Et_3N (34.4 mL, 246.8 mmol) was added. After 1 h at –40 °C, the solution was poured into an ice-cold mixture of saturated $NaHCO_3$ and CH_2Cl_2. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 twice. The combined extracts were dried over $MgSO_4$ and concentrated to afford the corresponding aldehyde, which was used for the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.76 (dd, *J* = 6, 2 Hz, 3 H), 2.50 (ddd, *J* = 16, 5, 2 Hz, 1 H), 2.69 (ddd, *J* = 16, 8, 3 Hz, 1 H), 3.80 (s, 3 H), 4.25 (dt, *J* = 5, 8 Hz, 1 H), 4.30 (d, *J* = 11 Hz, 1 H), 4.52 (d, *J* = 11 Hz, 1 H),

5.41 (ddq, *J* = 15, 8, 2 Hz, 1 H), 5.75 (ddq, *J* = 15, 1, 6 Hz, 1 H), 6.87 (d, *J* = 8 Hz, 2 H), 7.22 (d, *J* = 8 Hz, 2 H), 9.72 (dd, *J* = 3, 2 Hz, 1 H).

To a mixture of LiCl (3.67 g, 86.6 mmol) and DBU (12.5 mL, 83.6 mmol) in MeCN (85 mL) was added $(EtO)_2P(O)CH_2CO_2Et$ (16.1 mL, 80.4 mmol) at 0 °C. After 30 min at 0 °C, the above aldehyde dissolved in MeCN (15 mL) was added dropwise. The mixture was stirred at 0 °C for 10 min and then at room temperature for additional 1 h, and diluted with saturated $NaHCO_3$ and EtOAc. The organic phase was separated, and the aqueous phase was extracted with EtOAc twice. The combined extracts were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish ester **8** (15.7 g, 83% for 2 steps): $[\alpha]^{28}_D$ = +31 (*c* 0.119, $CHCl_3$); IR (neat) 1718, 1513, 1248, 1038 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.28 (t, *J* = 7 Hz, 3 H), 1.74 (dd, *J* = 6, 2 Hz, 3 H), 2.33–2.56 (m, 2 H), 3.78–3.82 (m, 1 H), 3.79 (s, 3 H), 4.18 (q, *J* = 7 Hz, 2 H), 4.27 (d, *J* = 11 Hz, 1 H), 4.50 (d, *J* = 11 Hz, 1 H), 5.37 (ddq, *J* = 16, 5, 2 Hz, 1 H), 5.67 (dq, *J* = 15, 6 Hz, 1 H), 5.84 (dt, *J* = 16, 2 Hz, 1 H), 6.86 (d, *J* = 8 Hz, 2 H), 6.93 (dt, *J* = 16, 7 Hz, 1 H), 7.23 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.3, 17.7, 38.7, 55.3, 60.2, 69.4, 78.2, 113.8, 123.2, 129.3, 129.8, 130.6, 131.0, 145.3, 159.1, 166.5.

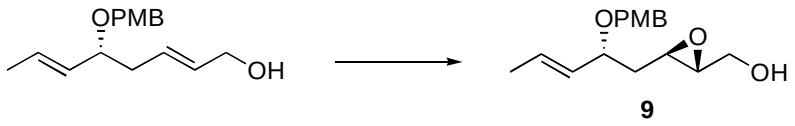
(2*E*,5*R*,6*E*)-5-(4-Methoxybenzyloxy)-2,6-octadien-1-ol



8

To a solution of ester **8** (15.0 g, 49.3 mmol) in THF (40 mL) was added DIBAL-H (115 mL, 0.94 M in hexane, 108 mmol) dropwise at –78 °C. After being stirred between –78 °C and –60 °C for 1 h, 3 N HCl (180 mL, 540 mmol) was added to the solution dropwise at 0 °C. The resulting mixture was extracted with EtOAc twice. The combined organic phases were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding alcohol (12.4 g, 96%): $[\alpha]^{28}_D$ = +36 (*c* 0.109, $CHCl_3$); IR (neat) 3409, 1513, 1248, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.74 (dd, *J* = 6, 1 Hz, 3 H), 1.60–1.85 (m, 1 H), 2.18–2.45 (m, 2 H), 3.72 (q, *J* = 8 Hz, 1 H), 3.79 (s, 3 H), 4.05 (d, *J* = 2 Hz, 2 H), 4.26 (d, *J* = 11 Hz, 1 H), 4.50 (d, *J* = 11 Hz, 1 H), 5.37 (ddq, *J* = 15, 8, 1 Hz, 1 H), 5.54–5.74 (m, 3 H), 6.86 (d, *J* = 9 Hz, 2 H), 7.24 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8, 38.6, 55.3, 63.6, 69.3, 79.2, 113.7, 129.0, 129.1, 129.3, 130.9, 131.3, 131.5, 159.0.

(2*R*,3*R*,5*R*,6*E*)-2,3-Epoxy-5-(4-methoxybenzyloxy)-6-octen-1-ol (9)



9

To a mixture of 4A molecular sieves (2.88 g) and Ti(O-*i*Pr)$_4$ (4.24 mL, 14.4 mmol) in CH_2Cl_2 (35 mL) was added D-(–)-DIPT (3.62 mL, 17.3 mmol) dropwise at –20 °C. The mixture was stirred at –20 °C for 20 min, and a solution of the above alcohol (12.6 g, 48.0 mmol) in CH_2Cl_2 (5 mL) was added slowly. The mixture was stirred at –20 °C for additional 30 min and then cooled to –40 °C. A solution of *t*BuOOH in CH_2Cl_2 (10.9 mL, 6.64 M, 72.4 mmol) was added dropwise. The reaction was carried out at –20 °C for 10 h, and quenched by addition of Me_2S (5.29 mL, 72.0 mmol). After 30 min at –20 °C, 10% tartaric acid (7 mL) and NaF (6.05 g, 144 mmol) were added. The resulting mixture was stirred at room temperature for 1 h and filtered through a pad of Celite with CH_2Cl_2. To a filtrate was added 3 N NaOH (28.8 mL, 86.4 mmol) and the resulting mixture was stirred at room temperature for 20 min. The organic phase was separated and the aqueous phase was extracted with EtOAc. The combined organic phases were dried over $MgSO_4$ and concentrated to afford a residue which was purified by chromatography on silica gel (hexane/EtOAc) to afford the epoxy alcohol **9** (12.4 g, 93%): $[\alpha]^{28}_D$ = +55 (*c* 0.117, $CHCl_3$); IR (neat) 3438, 1513, 1248, 1036 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.60 (dd, *J* = 6, 5 Hz, 1 H), 1.67 (ddd, *J* = 15, 7, 5 Hz, 1 H), 1.75 (dd, *J* = 7, 2 Hz, 3 H), 1.88 (ddd, *J* = 15, 9, 5 Hz, 1 H), 2.94 (dt, *J* = 7, 3 Hz, 1 H), 3.11 (ddd, *J* = 7, 5, 3 Hz, 1 H), 3.61 (ddd, *J* = 12, 7, 5 Hz, 1 H), 3.80 (s, 3 H), 3.89 (ddd, *J* = 12, 6, 3 Hz, 1 H), 3.93 (dt, *J* = 5, 9 Hz, 1 H), 4.28 (d, *J* = 12 Hz, 1 H), 4.52 (d, *J* = 12 Hz, 1 H), 5.40 (ddq, *J* = 15, 9, 2 Hz, 1 H), 5.71 (dq, *J* = 15, 7 Hz, 1 H), 6.87 (d, *J* = 9 Hz, 2 H), 7.24 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.8, 38.6, 53.4, 55.3, 58.9, 61.9, 69.7, 77.2, 113.8, 129.2, 129.3, 130.8, 131.4, 159.1.

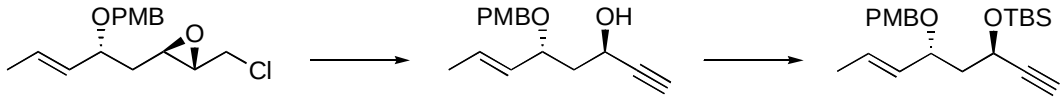
(2*S*,3*R*,5*R*,6*E*)-1-Chloro-2,3-epoxy-5-(4-methoxybenzyloxy)-6-octene

9

A mixture of the epoxy alcohol **9** (15.6 g, 56.1 mmol), PPh_3 (17.6 g, 67.1 mmol), and $NaHCO_3$ (1.06 g, 12.6 mmol) in CCl_4 (120 mL) was refluxed for 3 h and most of the

volatile material was removed by evaporation. The residue was diluted with hexane, and the resulting mixture was filtered through a pad of Celite. The filtrate was concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding chloride (14.7 g, 88%): $[\alpha]^{28}_{D}$ = +50 (*c* 0.226, $CHCl_3$); IR (neat) 1738, 1514, 1248, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.66 (ddd, *J* = 14, 6, 4 Hz, 1 H), 1.75 (dd, *J* = 6, 1 Hz, 3 H), 1.88 (ddd, *J* = 14, 9, 5 Hz, 1 H), 2.97–3.09 (m, 2 H), 3.53 (d, *J* = 5 Hz, 2 H), 3.80 (s, 3 H), 3.92 (dt, *J* = 4, 8 Hz, 1 H), 4.28 (d, *J* = 11 Hz, 1 H), 4.47 (d, *J* = 11 Hz, 1 H), 5.40 (ddq, *J* = 15, 8, 1 Hz, 1 H), 5.71 (dq, *J* = 15, 6 Hz, 1 H), 6.87 (d, *J* = 8 Hz, 2 H), 7.24 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 17.7, 38.5, 44.8, 55.3, 56.4, 57.6, 69.7, 77.1, 113.8, 129.3, 129.4, 130.7, 131.2, 159.2.

(3*R*,5*R*,6*E*)-3-(*tert*-Butyldimethylsiloxy)-5-(4-methoxybenzyloxy)-6-octen-1-yne (10)



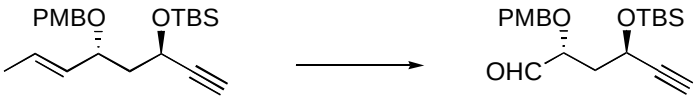
10

To a solution of the above chloride (8.0 g, 27.0 mmol) in THF (40 mL) was added *n*BuLi (31.2 mL, 2.72 M in hexane, 84.9 mmol) dropwise at –78 °C. The solution was stirred at –78 °C for 20 min and poured into a mixture of saturated NH_4Cl and EtOAc. After being stirred for a few minutes, the organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to obtain the corresponding propargyl alcohol, which was used for the next reaction without further purification: $[\alpha]^{28}_{D}$ = +68 (*c* 0.111, $CHCl_3$); IR (neat) 3425, 3292, 1514, 1249, 1037 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.76 (dd, *J* = 7, 2 Hz, 3 H), 1.82 (ddd, *J* = 14, 6, 4 Hz, 1 H), 2.04 (ddd, *J* = 14, 10, 4 Hz, 1 H), 2.43 (d, *J* = 2 Hz, 1 H), 3.68 (dd, *J* = 8, 1 Hz, 1 H), 3.80 (s, 3 H), 4.24–4.35 (m, 1 H), 4.30 (d, *J* = 11 Hz, 1 H), 4.52 (d, *J* = 11 Hz, 1 H), 4.52–4.61 (m, 1 H), 5.42 (ddq, *J* = 15, 8, 2 Hz, 1 H), 5.75 (dq, *J* = 15, 7 Hz, 1 H), 6.87 (d, *J* = 8 Hz, 2 H), 7.26 (d, *J* = 8 Hz, 2 H); ^{13}NMR (75 MHz, $CDCl_3$) δ 17.6, 42.0, 55.1, 60.0, 69.7, 72.6, 77.6, 84.7, 113.7, 129.4, 129.5, 130.1, 130.5, 159.1.

A solution of the above alcohol, TBSCl (4.88 g, 32.4 mmol), and imidazole (3.67 g, 53.9 mmol) in DMF (50 mL) was stirred at room temperature for 1 h and diluted with saturated $NaHCO_3$ and hexane at 0 °C. After being stirred for a few minutes, the layers were separated, and the aqueous layer was extracted with hexane twice. The

combined organic layers were dried over $MgSO_4$ and concentrated to obtain an oil, which was purified by chromatography on silica gel (hexane/EtOAc) to afford TBS ether **10** (9.22 g, 91% for 2 steps): $[\alpha]^{28}_D$ = +40 (*c* 0.174, $CHCl_3$); IR (neat) 3303, 1514, 1250, 1087 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 3 H), 0.14 (s, 3 H), 0.90 (s, 9 H), 1.74 (dd, *J* = 7, 2 Hz, 3 H), 1.85 (ddd, *J* = 14, 9, 4 Hz, 1 H), 1.97 (ddd, *J* = 14, 9, 4 Hz, 1 H), 2.35 (d, *J* = 2 Hz, 1 H), 3.78 (s, 3 H), 3.93 (dt, *J* = 4, 9 Hz, 1 H), 4.19 (d, *J* = 11 Hz, 1 H), 4.48 (d, *J* = 11 Hz, 1 H), 4.57 (ddd, *J* = 9, 4, 2 Hz, 1 H), 5.38 (ddq, *J* = 15, 9, 2 Hz, 1 H), 5.70 (dq, *J* = 15, 7 Hz, 1 H), 6.86 (d, *J* = 9 Hz, 2 H), 7.24 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –5.00, –4.33, 17.7, 18.2, 25.9, 45.3, 55.2, 59.2, 69.6, 72.1, 76.2, 85.9, 113.8, 128.9, 129.3, 131.0, 131.7, 159.1.

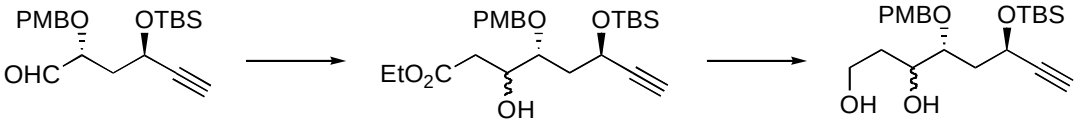
(2*R*,4*R*)-4-(*tert*-Butyldimethylsiloxy)-2-(4-methoxybenzyloxy)-5-hexynal



10

A stream of O_3 in O_2 was gently bubbled into a solution of **10** (12.1 g, 32.3 mmol) and 2,6-lutidine (5.64 mL, 48.4 mmol) in MeOH (70 mL) at –78 °C for 2 h. Excess O_3 remaining in the solution was purged by bubbling argon at –78 °C, and then Me_2S (7.12 mL, 97.0 mmol) was added. After being stirred at room temperature for 1 h, the solution was concentrated to leave a residue, which was flashed through short chromatography on silica gel (hexane/EtOAc) to furnish the corresponding aldehyde, which was used for the next reaction without further purification: ^1H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3 H), 0.17 (s, 3 H), 0.91 (s, 9 H), 1.95 (ddd, *J* = 14, 9, 4 Hz, 1 H), 2.08 (ddd, *J* = 14, 9, 4 Hz, 1 H), 2.41 (d, *J* = 2 Hz, 1 H), 3.80 (s, 3 H), 4.02 (ddd, *J* = 9, 4, 2 Hz, 1 H), 4.47 (d, *J* = 11 Hz, 1 H), 4.58 (d, *J* = 11 Hz, 1 H), 4.61 (ddd, *J* = 9, 4, 2 Hz, 1 H), 6.88 (d, *J* = 9 Hz, 2 H), 7.28 (d, *J* = 9 Hz, 2 H), 9.63 (d, *J* = 2 Hz, 1 H).

(4*R*,6*R*)-6-(*tert*-Butyldimethylsiloxy)-4-(4-methoxybenzyloxy)-7-octyne-1,3-diol (11)



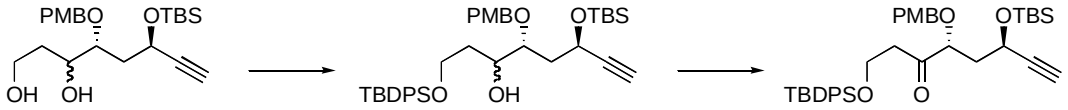
11

To an ice-cold solution of *i*Pr_2NH (11.3 mL, 80.6 mmol) in THF (50 mL) was added *n*BuLi (30.0 mL, 2.26 M in hexane, 67.8 mmol) dropwise. After 10 min at 0 °C, the solution was cooled to –78 °C, and EtOAc (6.64 mL, 67.8 mmol) was added dropwise.

The solution was stirred at –78 °C for additional 1 h, and the above aldehyde dissolved in THF (10 mL) was added slowly. The solution was stirred at –78 °C for 30 min and poured into an ice-cold mixture of saturated NH_4Cl and EtOAc. After being stirred for a few minutes, the layers were separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a hydroxyl ester, which was used for the next reaction without further purification.

To an ice-cold solution of the above ester in THF (60 mL) was added $LiAlH_4$ (1.84 g, 48.5 mmol) portionwise. The mixture was stirred at 0 °C for 30 min, and excess hydride was quenched at 0 °C by addition of H_2O (4.36 mL, 242 mmol) dropwise. After addition of NaF (10.2 g, 243 mmol), the resulting mixture was stirred at 0 °C for 30 min, and filtered through a pad of Celite with EtOAc. The filtrate was concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford alcohol **11** (8.42 g, 64% from compound **10**).

(4*R*,6*R*)-6-(*tert*-Butyldimethylsiloxy)-1-(*tert*-butyldiphenylsiloxy)-4-(4-methoxybenzyloxy)-7-octyn-3-one (12)

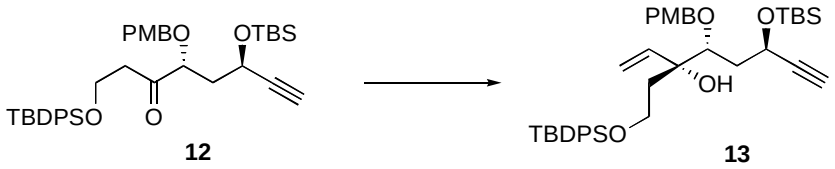


A solution of alcohol **11** (5.35 g, 13.2 mmol), TBDPSCl (4.06 mL, 15.8 mmol), and imidazole (1.79 g, 26.3 mmol) in DMF (35 mL) was stirred at room temperature for 1 h and diluted with saturated $NaHCO_3$ and Et_2O at 0 °C. After being stirred vigorously for a few minutes, the layers were separated, and the aqueous layer was extracted with Et_2O twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford an oil, which was purified by short chromatography on silica gel (hexane/EtOAc) to furnish the corresponding TBDPS ether, which was used for the next reaction without further purification.

To a solution of $(COCl)_2$ (1.50 mL, 17.1 mmol) in CH_2Cl_2 (55 mL) was added DMSO (2.80 mL, 39.4 mmol) at –78 °C. After 5 min at –78 °C, the above compound in CH_2Cl_2 (5 mL) was added dropwise. The solution was stirred between –70 °C and –50 °C for 30 min, and then Et_3N (9.17 mL, 65.8 mmol) was added. After being stirred for additional 30 min, the mixture was diluted with saturated $NaHCO_3$. The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 twice.

The combined extracts were dried over $MgSO_4$ and evaporated to afford a residue, which was semi-purified by short chromatography on silica gel (hexane/EtOAc) to furnish ketone **12**, which was used for the next reaction without further purification: $[\alpha]^{28}_D$ = +15 (*c* 0.08, $CHCl_3$); IR (neat) 3441, 1718, 1251, 1113 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 0.11 (s, 3 H), 0.17 (s, 3 H), 0.92 (s, 9 H), 1.02 (s, 9 H), 1.88–2.13 (m, 2 H), 2.37 (d, *J* = 3 Hz, 1 H), 2.62–2.80 (m, 2 H), 3.80 (s, 3 H), 3.95 (t, *J* = 6 Hz, 2 H), 4.10 (dd, *J* = 10, 3 Hz, 1 H), 4.31 (d, *J* = 11 Hz, 1 H), 4.50 (d, *J* = 11 Hz, 1 H), 4.60 (dt, *J* = 10, 3 Hz, 1 H), 6.86 (d, *J* = 8.5 Hz, 2 H), 7.25 (d, *J* = 8.5 Hz, 2 H), 7.34–7.46 (m, 6 H), 7.66 (d, *J* = 7 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –5.0, –4.3, 18.2, 19.2, 25.9, 26.9, 40.6, 40.8, 55.3, 58.8, 59.3, 72.2, 72.9, 81.3, 85.0, 113.9, 127.8, 129.7, 129.8, 133.4, 133.5, 134.9, 135.63, 135.64, 159.5, 210.5.

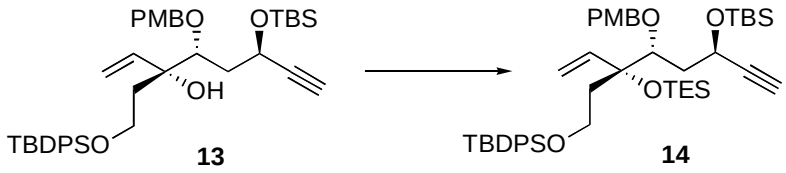
(3*R*,4*R*,6*R*)-6-(*tert*-Butyldimethylsiloxy)-1-(*tert*-butyldiphenylsiloxy)-3-ethenyl-4-(4-methoxybenzyloxy)-7-octyn-3-ol (13)



To a solution of ketone **12** obtained above in THF (50 mL) was added CH_2=CHMgBr (29.2 mL, 0.90 M in THF, 26.3 mmol) dropwise at –78 °C over 10 min. After being stirred at –78 °C for 1 h, the reaction mixture was poured into a mixture of saturated NH_4Cl and EtOAc with vigorous stirring. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish alcohol **13** (7.68 g, 87% from diol **11**): $[\alpha]^{28}_D$ = +16 (*c* 0.09, $CHCl_3$); IR (neat) 3474, 3294, 1249, 1113 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 3 H), 0.18 (s, 3 H), 0.92 (s, 9 H), 1.04 (s, 9 H), 1.71–1.85 (m, 2 H), 1.98–2.14 (m, 2 H), 2.41 (d, *J* = 2 Hz, 1 H), 3.59 (dd, *J* = 8, 4 Hz, 1 H), 3.78 (s, 3 H), 3.70–3.92 (m, 2 H), 4.27 (s, 1 H), 4.56–4.70 (m, 3 H), 5.29 (dd, *J* = 11, 2 Hz, 1 H), 5.54 (dd, *J* = 17, 2 Hz, 1 H), 5.90 (dd, *J* = 17, 11 Hz, 1 H), 6.83 (d, *J* = 9 Hz, 2 H), 7.24 (d, *J* = 9 Hz, 2 H), 7.33–7.49 (m, 6 H), 7.62–7.72 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7, –4.0, 18.3, 19.0, 26.0, 26.8, 37.2, 40.2, 55.3, 60.6, 62.0, 72.7, 73.4, 79.2, 81.3, 86.1, 113.8, 115.6, 127.8, 127.9, 129.2, 129.9, 131.2, 132.7, 132.8, 135.6, 140.3, 159.1.

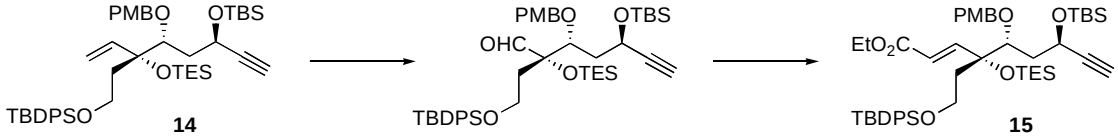
(3*R*,4*R*,6*R*)-6-(*tert*-Butyldimethylsiloxy)-1-(*tert*-butyldiphenylsiloxy)-3-ethenyl-4-

(4-methoxybenzyloxy)-3-(triethylsiloxy)-7-octyne (14)



To an ice-cold solution of alcohol **13** (5.58 g, 10.2 mmol) and 2,6-lutidine (2.37 mL, 20.4 mmol) in CH_2Cl_2 (20 mL) was added TESOTf (2.53 mL, 11.2 mmol) dropwise. The solution was stirred for 30 min at 0 °C and diluted with saturated $NaHCO_3$. The phases were separated, and the aqueous phase was extracted with CH_2Cl_2 twice. The combined organic phases were dried over $MgSO_4$ and concentrated to obtain an oil, which was purified by chromatography on silica gel (EtOAc/hexane) to furnish TES ether **14** (6.13 g, 91%): $[\alpha]^{28}_D$ = +15 (*c* 0.12, $CHCl_3$); IR (neat) 3311, 1249, 1112 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 3 H), 0.21 (s, 3 H), 0.59 (q, *J* = 8 Hz, 6 H), 0.84–1.03 (m, 18 H), 1.08 (s, 9 H), 1.58–1.67 (m, 2 H), 1.97 (dd, *J* = 14, 12 Hz, 1 H), 2.13 (t, *J* = 8 Hz, 1 H), 2.40 (d, *J* = 2 Hz, 1 H), 3.56 (d, *J* = 10 Hz, 1 H), 3.77–4.04 (m, 2 H), 3.82 (s, 3 H), 4.45–4.64 (m, 2 H), 4.71 (d, *J* = 11 Hz, 2 H), 5.13 (d, *J* = 11 Hz, 1 H), 5.21 (d, *J* = 18 Hz, 1 H), 5.84 (dd, *J* = 18, 11 Hz, 1 H), 6.85 (d, *J* = 8.5 Hz, 2 H), 7.19 (d, *J* = 8.5 Hz, 2 H), 7.32–7.48 (m, 6 H), 7.69 (d, *J* = 8 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7, –3.8, 6.9, 7.3, 18.2, 19.2, 26.0, 27.0, 39.1, 40.7, 55.3, 59.8, 60.7, 72.7, 74.5, 79.9, 81.7, 86.1, 113.8, 115.2, 127.7, 128.9, 129.2, 129.6, 131.4, 134.2, 135.7, 140.9, 159.0.

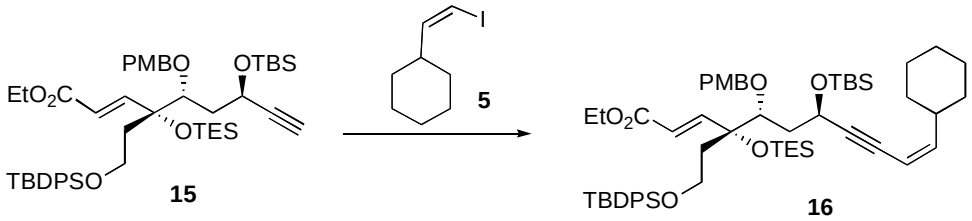
Ethyl (4*R*,5*R*,7*R*,*E*)-7-(*tert*-Butyldimethylsilyloxy)-4-(2-(*tert*-butyldiphenylsilyl-oxy)ethyl)-5-(4-methoxybenzyloxy)-4-(triethylsilyloxy)non-2-en-8-ynoate (15)



A stream of O_3 in O_2 was gently bubbled into a solution of olefin **14** (13.5 g, 17.2 mmol) and 2,6-lutidine (4.0 mL, 34.3 mmol) in MeOH/*i*PrOH (1 : 1, 100 mL) at –78 °C for 5 h. Excess O_3 remaining in the solution was purged by bubbling argon at –78 °C. Me_2S (3.8 mL, 51.74 mmol) was added at –78 °C and the cooling bath was removed. After being stirred at room temperature for 1 h, the solution was concentrated to leave a residue, which was flashed through short chromatography on silica gel (hexane/EtOAc) to furnish the corresponding aldehyde, which was used for the next reaction without further purification.

NaH (1.37 g, 60% in mineral oil, 34.3 mmol) was washed with dry hexane three times before THF (80 mL) was added. To this suspension was added $(EtO)_2P(O)CH_2CO_2Et$ (7.21 mL, 36.0 mmol) dropwise at 0 °C. After 20 min, the above aldehyde in THF (20 mL) was added dropwise. The resulting solution was warmed to room temperature, stirred overnight, and poured into a mixture of saturated NH_4Cl with vigorous stirring. The phases were separated, and the aqueous phase was extracted with hexane twice. The combined organic phases were dried over $MgSO_4$ and concentrated to obtain an oil, which was purified by chromatography on silica gel (EtOAc/hexane) to afford the corresponding ester **15** (7.14 g, 48% from **14**): $[\alpha]^{28}_D$ = +23 (*c* 0.053, $CHCl_3$); IR (neat) 3303, 1740, 1249, 1092 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3 H), 0.17 (s, 3 H), 0.57 (q, *J* = 8 Hz, 6 H), 0.80–0.95 (m, 9 H), 0.91 (s, 9 H), 1.03 (s, 9 H), 1.27 (t, *J* = 7 Hz, 3 H), 1.45–1.70 (m, 2 H), 1.85–2.30 (m, 2 H), 2.38 (d, *J* = 2 Hz, 1 H), 3.58 (dd, *J* = 10, 2 Hz, 1 H), 3.72–3.88 (m, 2 H), 3.81 (s, 3 H), 4.16 (q, *J* = 7 Hz, 2 H), 4.45–4.54 (m, 1 H), 4.49 (d, *J* = 11 Hz, 1 H), 4.59 (d, *J* = 11 Hz, 1 H), 5.93 (d, *J* = 16 Hz, 1 H), 6.84 (d, *J* = 8 Hz, 2 H), 6.93 (d, *J* = 16 Hz, 1 H), 7.18 (d, *J* = 8 Hz, 2 H), 7.28–7.45 (m, 6 H), 7.57–7.69 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.6, –3.9, 6.8, 7.2, 14.3, 18.2, 19.2, 25.9, 26.0, 26.9, 40.2, 40.5, 55.3, 59.7, 60.0, 60.4, 73.0, 74.7, 79.7, 81.5, 85.8, 113.8, 121.1, 127.7, 128.9, 129.6, 130.7, 133.9, 135.6, 150.4, 159.2, 166.4.

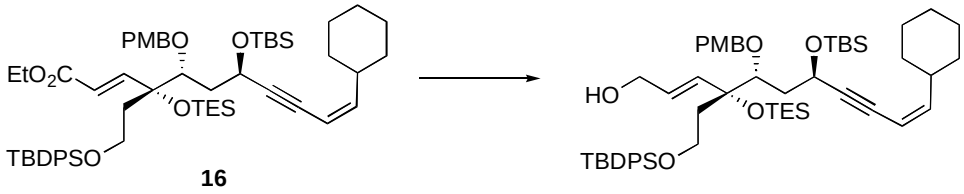
Ethyl (2*E*,4*R*,5*R*,7*R*,10*Z*)-7-(*tert*-Butyldimethylsilyloxy)-4-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-11-cyclohexyl-5-(4-methoxybenzyloxy)-4-(triethylsilyloxy)undeca-2,10-dien-8-ynoate (16)



To a solution of acetylene **15** (7.14 g, 8.31 mmol) and vinyl iodide **5** (2.35 g, 9.95 mmol) in benzene (40 mL) were added *t*$BuNH_2$ (8.68 mL, 83.1 mmol), $Pd(PPh_3)_4$ (0.481 g, 0.416 mmol), and CuI (0.238 g, 1.25 mmol) sequentially. The mixture was stirred at room temperature under dark overnight and diluted with saturated NH_4Cl and hexane. The organic layer was separated, and the aqueous layer was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated

to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish enyne **16** (7.0 g, 87%): $[\alpha]^{28}_{D}$ = +14 (*c* 0.06, $CHCl_3$); IR (neat) 1740, 1247, 1099, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 3 H), 0.17 (s, 3 H), 0.57 (q, *J* = 8 Hz, 6 H), 0.90–2.30 (m, 23 H), 0.91 (s, 9 H), 1.02 (s, 9 H), 1.26 (t, *J* = 7 Hz, 3 H), 2.46–2.66 (m, 1 H), 3.61 (d, *J* = 9 Hz, 1 H), 3.68–3.90 (m, 2 H), 3.80 (s, 3 H), 4.15 (q, *J* = 7 Hz, 2 H), 4.45–4.72 (m, 3 H), 5.32 (d, *J* = 10 Hz, 1 H), 5.70 (t, *J* = 10 Hz, 1 H), 5.93 (d, *J* = 16 Hz, 1 H), 6.84 (d, *J* = 8 Hz, 2 H), 6.94 (d, *J* = 16 Hz, 1 H), 7.19 (d, *J* = 8 Hz, 2 H), 7.29–7.44 (m, 6 H), 7.59–7.67 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.6 (–), –3.8 (–), 6.8 (+), 7.2 (–), 14.2 (–), 18.2 (+), 19.1 (+), 25.7 (+), 25.9 (–), 26.0 (–), 26.8 (–), 32.3 (+), 32.4 (+), 39.3 (–), 40.3 (+), 40.7 (+), 55.1 (–), 60.0 (+), 60.2 (+), 60.4 (–), 74.6 (+), 79.7 (+), 81.6 (–), 81.8 (+), 94.7 (+), 106.6 (–), 113.7 (–), 120.9 (–), 127.6 (–), 128.9 (–), 129.6 (–), 130.7 (+), 133.8 (+), 133.9 (+), 135.5 (–), 149.6 (–), 150.4 (–), 159.2 (+), 166.2 (+).

(2*E*,4*R*,5*R*,7*R*,10*Z*)-7-(*tert*-Butyldimethylsilyloxy)-4-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-11-cyclohexyl-5-(4-methoxybenzyloxy)-4-(triethylsilyloxy)undeca-2,10-dien-8-yn-1-ol

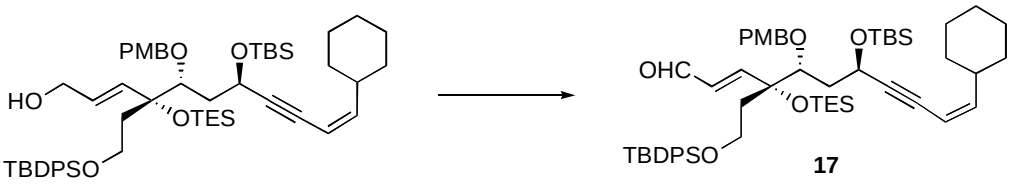


16

To a solution of ester **16** (4.32 g, 4.46 mmol) in THF (30 mL) was added DIBAL-H (11.9 mL, 0.94 M in hexane, 11.2 mmol) dropwise at –70 °C. After being stirred at –70 °C to –60 °C for 30 min, the reaction was quenched with H_2O (1.0 mL, 56 mmol) and NaF (2.34g, 56 mmol) at 0 °C with vigorous stirring. After 30 min of additional stirring, the resulting suspension was filtered through a pad of Celite with EtOAc. The filtrate was concentrated to afford a residue which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding alcohol (4.01 g, 97%): $[\alpha]^{28}_{D}$ = –2 (*c* 0.08, $CHCl_3$); IR (neat) 3458, 1740, 1248, 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 3 H), 0.17 (s, 3 H), 0.55 (q, *J* = 8 Hz, 6 H), 0.80–2.15 (m, 23 H), 0.91 (s, 9 H), 1.03 (s, 9 H), 2.48–2.68 (m, 1 H), 3.55 (d, *J* = 8 Hz, 1 H), 3.76–3.90 (m, 2 H), 3.80 (s, 3 H), 4.05 (t, *J* = 5 Hz, 2 H), 4.46 (d, *J* = 11 Hz, 1 H), 4.62 (d, *J* = 11 Hz, 1 H), 4.58–4.71 (m, 1 H), 5.33 (d, *J* = 11 Hz, 1 H), 5.58–5.85 (m, 3 H), 6.82 (d, *J* = 8 Hz, 2 H), 7.16 (d, *J* = 8 Hz, 2 H), 7.30–7.45 (m, 6 H), 7.64 (d, *J* = 8 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (–), –3.8 (–), 6.9 (+), 7.2 (–), 18.2 (+), 19.2 (+), 25.7 (+), 26.0 (–), 27.0 (–), 32.4 (+), 39.3 (–), 39.8 (+), 40.8 (+), 55.2 (–),

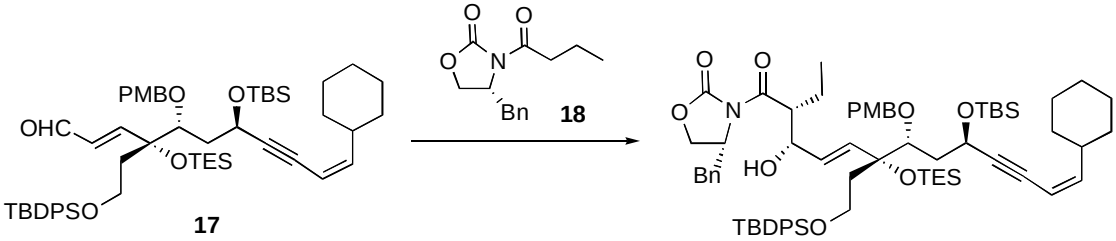
60.6 (+), 63.2 (+), 74.5 (+), 79.1 (+), 81.6 (+), 81.9 (–), 94.9 (+), 106.6 (–), 113.7 (–), 127.6 (–), 129.0 (–), 129.5 (–), 131.2 (+), 133.9 (–), 134.08 (+), 134.12 (+), 135.6 (–), 149.5 (–), 159.0 (+).

(2*E*,4*R*,5*R*,7*R*,10*Z*)-7-(*tert*-Butyldimethylsilyloxy)-4-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-11-cyclohexyl-5-(4-methoxybenzyloxy)-4-(triethylsilyloxy)undeca-2,10-dien-8-ynal (17)



To an ice-cold solution of the above alcohol (6.30 g, 6.81 mmol) in CH_2Cl_2 (40 mL) were added Et_3N (9.49 mL, 68.1 mmol) and DMSO (14.4 mL, 204.1 mmol). After 5 min at 0 °C, SO_3·Py (3.25 g, 20.4 mmol) was added portionwise. After being stirred at room temperature for 30 min, the resulting solution was diluted with saturated $NaHCO_3$ and hexane. The organic layer was separated, and the aqueous layer was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford aldehyde **17** (6.10 g, 97%): $[\alpha]^{29}_D$ = +33 (*c* 0.12, $CHCl_3$); IR (neat) 1740, 1703, 1248, 1092 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.16 (s, 3 H), 0.19 (s, 3 H), 0.48–0.68 (m, 6 H), 0.76–2.10 (m, 22 H), 0.93 (s, 9 H), 1.02 (s, 9 H), 2.23–2.65 (m, 2 H), 3.53–3.90 (m, 3 H), 3.81 (s, 3 H), 4.43–4.47 (m, 3 H), 5.27–5.39 (m, 1 H), 5.65–5.79 (m, 1 H), 6.22 (dd, *J* = 16, 8 Hz, 1 H), 6.79 (d, *J* = 16 Hz, 1 H), 6.88 (d, *J* = 9 Hz, 2 H), 7.22 (d, *J* = 9 Hz, 2 H), 7.26–7.46 (m, 6 H), 7.50–7.70 (m, 6 H), 9.44 (d, *J* = 8 Hz, 1 H).

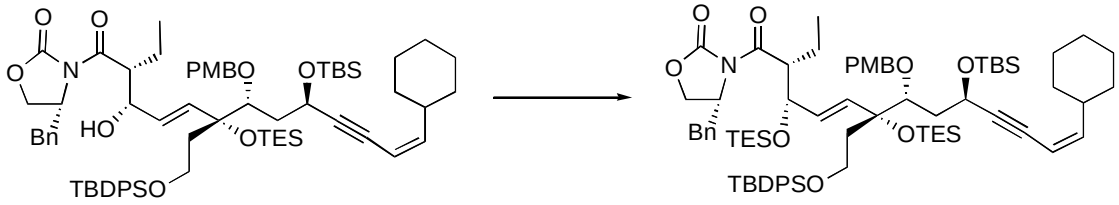
(*R*)-4-Benzyl-3-[(2*R*,3*S*,4*E*,6*R*,7*R*,9*R*,12*Z*)-9-(*tert*-butyldimethylsilyloxy)-6-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-13-cyclohexyl-2-ethyl-3-hydroxy-7-(4-methoxybenzyloxy)-6-(triethylsilyloxy)trideca-4,12-dien-10-ynoyl]oxazolidin-2-one



To an ice-cold solution of (*R*)-*N*-butyryl-4-benzyl-2-oxazolidinone (**18**) (2.53 g, 10.2

mmol) in CH_2Cl_2 (40 mL) were added Bu_2BOTf (9.91 mL, 1.0 M in CH_2Cl_2, 9.91 mmol) and $(i\text{Pr})_2\text{NEt}$ (2.53 mL, 14.5 mmol) sequentially. After being stirred at 0 °C for 30 min, the solution was cooled to –78 °C and aldehyde **17** (6.10 g, 6.61 mmol) in CH_2Cl_2 (10 mL) was added dropwise over 10 min. The mixture was stirred for 10 min at –78 °C and at room temperature for another 3.5 h. The resulting solution was diluted with saturated NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by flash chromatography on silica gel (hexane/EtOAc) to furnish an aldol adduct, which was used for the next reaction without further purification: $[\alpha]^{29}_D = -10$ (*c* 0.04, $CHCl_3$); IR (neat) 3490, 1793, 1740, 1245, 1115 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.10 (s, 3 H), 0.13 (s, 3 H), 0.54 (q, *J* = 8 Hz, 6 H), 0.75–2.24 (m, 28 H), 0.88 (s, 9 H), 1.01 (s, 9 H), 2.53 (q, *J* = 10 Hz, 1 H), 2.67 (dd, *J* = 13, 10 Hz, 1 H), 3.27 (dd, *J* = 14, 3 Hz, 1 H), 3.52 (d, *J* = 9 Hz, 1 H), 3.77 (s, 3 H), 3.72–4.18 (m, 5 H), 4.28–4.72 (m, 5 H), 5.16 (d, *J* = 11 Hz, 1 H), 5.54–5.78 (m, 3 H), 6.86 (d, *J* = 9 Hz, 2 H), 7.14 (d, *J* = 9 Hz, 2 H), 7.14–7.42 (m, 11 H), 7.62 (d, *J* = 6 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (–), –3.8 (–), 6.8 (+), 7.2 (–), 11.8 (–), 18.2 (+), 19.2 (+), 20.5 (+), 25.6 (+), 26.0 (–), 26.9 (–), 32.4 (+), 38.0 (+), 39.2 (–), 39.9 (+), 40.6 (+), 49.3 (–), 55.3 (–), 55.5 (–), 60.6 (–), 60.7 (+), 65.9 (+), 72.4 (–), 74.4 (+), 79.3 (+), 81.5 (+), 81.7 (–), 94.9 (+), 106.5 (–), 113.7 (–), 127.4 (–), 127.6 (–), 128.86 (–), 128.98 (–), 129.4 (–), 129.5 (–), 129.8 (–), 131.2 (+), 134.1 (+), 134.2 (+), 134.9 (–), 135.3 (+), 135.6 (–), 149.4 (–), 153.4 (+), 159.0 (+), 175.0 (+).

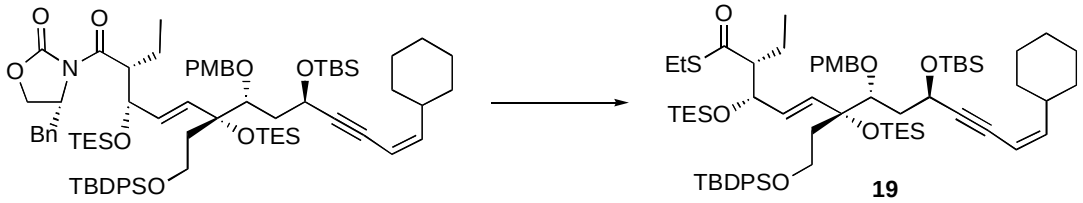
(*R*)-4-Benzyl-3-[(2*R*,3*S*,4*E*,6*R*,7*R*,9*R*,12*Z*)-9-(*tert*-butyldimethylsilyloxy)-6-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-13-cyclohexyl-2-ethyl-7-(4-methoxybenzyl-oxy)-3,6-bis(triethylsilyloxy)trideca-4,12-dien-10-ynoyl]oxazolidin-2-one



To an ice-cold solution of the above alcohol in CH_2Cl_2 (5 mL) and pyridine (7.96 mL, 99 mmol) was added TESCl (2.21 mL, 13.2 mmol) dropwise. After 30 min at 0 °C, the resulting solution was diluted with saturated $NaHCO_3$ and hexane. The organic layer was separated, and the aqueous layer was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the

corresponding TES ether (8.10 g, 95% from aldehyde **17**): $[\alpha]^{28}_{D}$ = –6 (*c* 0.13, $CHCl_3$); IR (neat) 1801, 1744, 1246, 1078 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.09 (s, 3 H), 0.12 (s, 3 H), 0.45 (q, *J* = 8 Hz, 6 H), 0.55 (q, *J* = 8 Hz, 6 H), 0.82–2.22 (m, 37 H), 0.87 (s, 9 H), 1.00 (s, 9 H), 2.43–2.61 (m, 1 H), 2.67 (dd, *J* = 13, 10 Hz, 1 H), 3.24 (d, *J* = 11 Hz, 1 H), 3.49 (d, *J* = 8 Hz, 1 H), 3.77 (s, 3 H), 3.72–4.15 (m, 5 H), 4.29–4.66 (m, 5 H), 5.18 (d, *J* = 11 Hz, 1 H), 5.52–5.74 (m, 3 H), 6.80 (d, *J* = 9 Hz, 2 H), 7.14 (d, *J* = 9 Hz, 2 H), 7.10–7.40 (m, 11 H), 7.62 (d, *J* = 6 Hz, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (–), –3.8 (–), 4.9 (+), 6.88 (+), 6.93 (–), 7.3 (–), 11.8 (–), 18.2 (+), 19.2 (+), 20.8 (+), 25.7 (+), 26.0 (–), 26.9 (–), 32.4 (+), 38.0 (+), 39.2 (–), 40.6 (+), 41.1 (+), 51.3 (–), 55.3 (–), 55.8 (–), 60.7 (+), 65.8 (+), 74.0 (–), 74.2 (+), 79.3 (+), 81.5 (+), 81.9 (–), 94.9 (+), 106.6 (–), 113.6 (–), 127.3 (–), 127.6 (–), 128.7 (–), 128.9 (–), 129.5 (–), 131.3 (+), 131.4 (–), 133.8 (–), 134.2 (+), 135.6 (–), 135.6 (–), 149.3 (–), 153.2 (+), 158.9 (+), 173.6 (+).

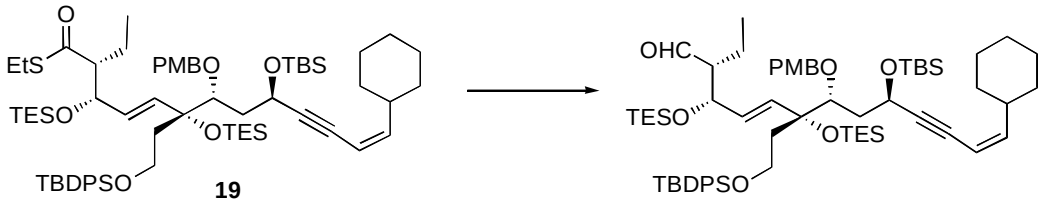
Ethyl (2*R*,3*S*,4*E*,6*R*,7*R*,9*R*,12*Z*)-9-(*tert*-Butyldimethylsilyloxy)-6-[2-(*tert*-butyl-diphenylsilyloxy)ethyl]-13-cyclohexyl-2-ethyl-7-(4-methoxybenzyloxy)-3,6-bis(triethylsilyloxy)trideca-4,12-dien-10-ynethioate (19)



To an ice-cold solution of the above TES ether (8.10 g, 6.30 mmol) in THF (20 mL) was added EtSLi, which had been prepared by addition of *n*BuLi (6.95 mL, 2.72 M in hexane, 18.9 mmol) to EtSH (2.36 mL, 31.5 mmol) in THF (20 mL) at 0 °C. The suspension was stirred at 0 °C for 1.5 h, and diluted with saturated NH_4Cl. The organic phase was separated, and the aqueous phase was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish thioester **19** (6.80 g, 90%): $[\alpha]^{28}_{D}$ = –5 (*c* 0.08, $CHCl_3$); IR (neat) 1743, 1245, 1086 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3 H), 0.16 (s, 3 H), 0.48 (q, *J* = 8 Hz, 6 H), 0.56 (q, *J* = 8 Hz, 6 H), 0.78–2.26 (m, 40 H), 0.91 (s, 9 H), 1.03 (s, 9 H), 2.40 (ddd, *J* = 10, 6, 4 Hz, 1 H), 2.51–2.63 (m, 1 H), 2.64–2.95 (m, 2 H), 3.51 (d, *J* = 8 Hz, 1 H), 3.80 (s, 3 H), 3.74–3.88 (m, 2 H), 4.31 (t, *J* = 5 Hz, 1 H), 4.35–4.69 (m, 3 H), 5.31 (dd, *J* = 11, 2 Hz, 1 H), 5.52–5.73 (m, 3 H), 6.83 (d, *J* = 8 Hz, 2 H), 7.17 (d, *J* = 8 Hz, 2 H), 7.28–7.42 (m, 6 H), 7.58–7.70 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.6 (–), –3.8 (–), 5.0 (+), 6.9 (+), 7.0 (–), 7.3 (–), 12.1 (–), 14.7 (–), 18.2 (+), 19.2 (+), 21.3

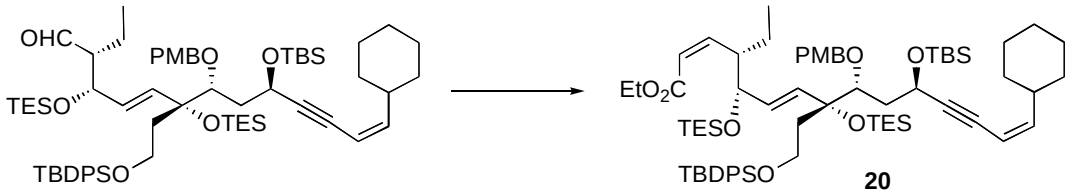
(+), 23.2 (+), 25.7 (+), 26.0 (–), 26.9 (–), 32.5 (+), 39.3 (–), 40.5 (+), 41.1 (+), 55.3 (–), 60.6 (–), 60.7 (+), 63.6 (–), 74.1 (–), 74.3 (+), 79.4 (+), 81.6 (+), 82.1 (–), 95.0 (+), 106.7 (–), 113.7 (–), 127.6 (–), 128.8 (–), 129.5 (–), 131.3 (+), 131.4 (–), 133.0 (–), 134.22 (+), 134.24 (+), 135.6 (–), 149.0 (–), 159.0 (+), 200.6 (+).

(2*R*,3*S*,4*E*,6*R*,7*R*,9*R*,12*Z*)-9-(*tert*-Butyldimethylsilyloxy)-6-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-13-cyclohexyl-2-ethyl-7-(4-methoxybenzyloxy)-3,6-bis(triethylsilyloxy)trideca-4,12-dien-10-ynal



To a solution of thioester **19** (2.77 g, 2.37 mmol) in toluene (20 mL) was added DIBAL-H (3.27 mL, 0.94 M in hexane, 3.07 mmol) dropwise at –78 °C. After being stirred at –78 °C for 30 min, EtOAc (a few drops) was added and the solution was warmed to 0 °C. Then, H_2O (0.24 mL, 13 mmol) and NaF (550 mg, 13 mmol) were added. The resulting mixture was stirred vigorously for 30 min and filtered through a pad of Celite with EtOAc. The filtrate was concentrated to afford the corresponding aldehyde, which was used for the next reaction without further purification: ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.12 (s, 3 H), 0.16 (s, 3 H), 0.47 (q, *J* = 8 Hz, 6 H), 0.56 (q, *J* = 8 Hz, 6 H), 0.78–2.28 (m, 38 H), 0.88 (s, 9 H), 1.04 (s, 9 H), 2.48–2.66 (m, 1 H), 3.53 (d, *J* = 8 Hz, 1 H), 3.80 (s, 3 H), 3.70–3.92 (m, 2 H), 4.38–4.70 (m, 4 H), 5.26–5.38 (m, 1 H), 5.55–5.74 (m, 3 H), 6.83 (d, *J* = 9 Hz, 2 H), 7.17 (d, *J* = 9 Hz, 2 H), 7.28–7.44 (m, 6 H), 7.58–7.70 (m, 4 H), 9.62 (d, *J* = 2 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (–), –3.8 (–), 4.9 (+), 6.85 (–), 6.92 (+), 7.3 (–), 12.3 (–), 17.5 (+), 18.2 (+), 19.2 (+), 25.7 (+), 25.9 (–), 26.0 (–), 26.9 (–), 32.4 (+), 39.3 (–), 40.7 (+), 40.8 (+), 55.3 (–), 60.5 (–), 60.6 (–), 60.7 (+), 72.7 (–), 74.4 (+), 79.4 (+), 81.6 (+), 81.9 (–), 94.9 (+), 106.6 (–), 113.7 (–), 127.6 (–), 128.9 (–), 129.6 (–), 130.6 (–), 131.2 (+), 133.4 (–), 134.1 (+), 135.6 (–), 149.4 (–), 159.0 (+), 205.0 (–).

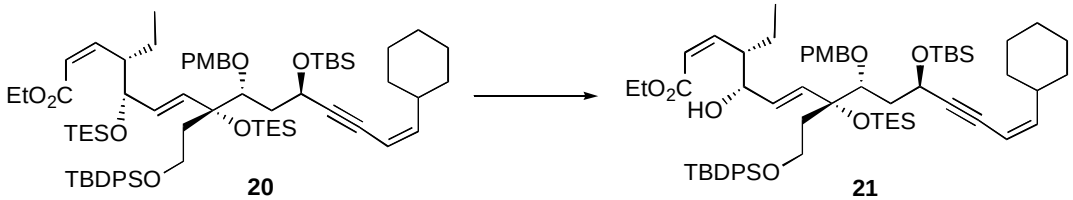
Ethyl (2*Z*,4*S*,5*S*,6*E*,8*R*,9*R*,11*R*,14*Z*)-11-(*tert*-Butyldimethylsilyloxy)-8-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-15-cyclohexyl-4-ethyl-9-(4-methoxybenzyloxy)-5,8-bis(triethylsilyloxy)pentadeca-2,6,14-trien-12-ynoate (20)



20

To a solution of $(PhO)_2P(O)CH_2CO_2Et$ (1.37 g, 4.27 mmol) in THF (20 mL) was added Bu_4NOH (4.15 mL, 1.0 M in MeOH, 4.15 mmol). After 20 min, a solution of the above aldehyde in THF (5 mL) was added dropwise at –78 °C. The solution was immersed into another cooling bath of –18 °C, and stirred for another 6 h at –18 °C. The resulting solution was diluted with saturated NH_4Cl and hexane. The organic phase was separated, dried over $MgSO_4$, and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding *cis*-α,β-unsaturated ester **20** (2.40 g, 86% from thioester **19**): $[\alpha]^{28}_D$ = +33 (*c* 0.12, $CHCl_3$); IR (neat) 1743, 1248, 1083 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 3 H), 0.17 (s, 3 H), 0.48 (q, *J* = 8 Hz, 6 H), 0.57 (q, *J* = 8 Hz, 6 H), 0.70–2.25 (m, 41 H), 0.91 (s, 9 H), 1.04 (s, 9 H), 2.46–2.67 (m, 1 H), 3.81 (s, 3 H), 3.35–3.95 (m, 4 H), 4.06–4.24 (m, 3 H), 4.42–4.70 (m, 3 H), 5.33 (dd, *J* = 11, 2 Hz, 1 H), 5.54–5.82 (m, 4 H), 5.98 (dd, *J* = 14, 11 Hz, 1 H), 6.83 (d, *J* = 8 Hz, 2 H), 7.17 (d, *J* = 8 Hz, 2 H), 7.28–7.43 (m, 6 H), 7.60–7.70 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (–), –3.8 (–), 5.0 (+), 6.5 (+), 6.9 (–), 7.0 (+), 7.3 (–), 11.9 (–), 14.3 (–), 18.2 (+), 19.2 (+), 22.5 (+), 25.7 (+), 26.0 (–), 27.0 (–), 32.4 (+), 39.3 (–), 40.5 (+), 40.9 (+), 46.8 (–), 55.3 (–), 59.7 (+), 60.6 (–), 60.9 (+), 74.4 (+), 75.5 (–), 79.5 (+), 81.5 (+), 82.1 (–), 95.1 (+), 106.7 (–), 113.7 (–), 120.9 (–), 127.6 (–), 128.8 (–), 129.5 (–), 131.4 (+), 131.6 (–), 132.9 (–), 134.2 (+), 135.6 (–), 149.2 (–), 151.6 (–), 159.0 (+), 166.3 (+).

Ethyl (2*Z*,4*S*,5*S*,6*E*,8*R*,9*R*,11*R*,14*Z*)-11-(*tert*-Butyldimethylsilyloxy)-8-[2-(*tert*-butyldiphenylsilyloxy)ethyl]-15-cyclohexyl-4-ethyl-5-hydroxy-9-(4-methoxybenzyloxy)-8-(triethylsilyloxy)pentadeca-2,6,14-trien-12-ynoate (21)

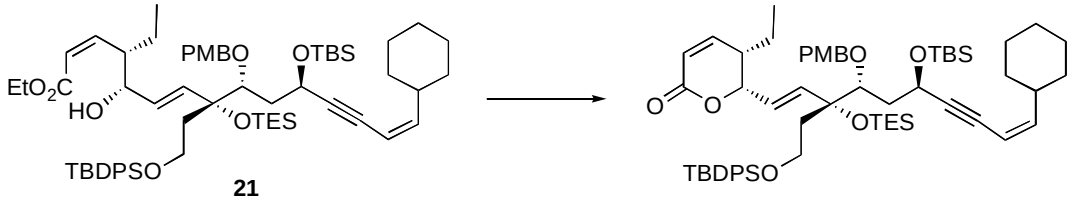


20 **21**

To a solution of TES ether **20** (4.86 g, 4.12 mmol) in THF (10 mL) and MeOH (30 mL) was added PPTS (31 mg, 0.12 mmol). The solution was stirred at ambient temperature overnight, and diluted with saturated $NaHCO_3$ and EtOAc. The organic phase was separated, and the aqueous phase was extracted with EtOAc twice. The

combined organic layers were dried over $MgSO_4$ and concentrated to afford an oil, which was purified by chromatography on silica gel (hexane/EtOAc) to isolate alcohol **21** (3.78 g, 86%): $[\alpha]^{28}_D$ = +41 (*c* 0.21, $CHCl_3$); IR (neat) 3466, 1719, 1262, 1084 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.03 (s, 3 H), 0.07 (s, 3 H), 0.46 (q, *J* = 8 Hz, 6 H), 0.62–2.15 (m, 32 H), 0.81 (s, 9 H), 0.94 (s, 9 H), 2.38–2.58 (m, 1 H), 3.24–3.48 (m, 1 H), 3.44 (d, *J* = 8 Hz, 1 H), 3.70 (s, 3 H), 3.60–3.90 (m, 2 H), 3.99–4.15 (m, 3 H), 4.37 (d, *J* = 11 Hz, 1 H), 4.50 (d, *J* = 11 Hz, 1 H), 4.46–4.60 (m, 1 H), 5.24 (dd, *J* = 11, 2 Hz, 1 H), 5.45–5.80 (m, 5 H), 6.73 (d, *J* = 8 Hz, 2 H), 7.07 (d, *J* = 8 Hz, 2 H), 7.20–7.35 (m, 6 H), 7.50–7.60 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.8 (–), –3.9 (–), 6.8 (+), 7.1 (–), 11.9 (–), 14.1 (–), 18.1 (+), 19.1(+), 24.1 (+), 25.6 (+), 25.9 (–), 26.8 (+), 26.9 (–), 32.3 (+), 39.2 (–), 39.8 (+), 40.9 (+), 46.2 (–), 55.0 (–), 60.1 (+), 60.5 (–), 60.7 (+), 74.3 (+), 74.8 (–), 79.4 (+), 81.5 (+), 81.6 (–), 94.9 (+), 106.6 (–), 113.6 (–), 122.1 (–), 127.5 (–), 128.8 (–), 129.4 (–), 131.2 (+), 133.9 (–), 134.0 (+), 135.5 (–), 149.2 (–), 150.7 (–), 159.0 (+), 167.2 (+).

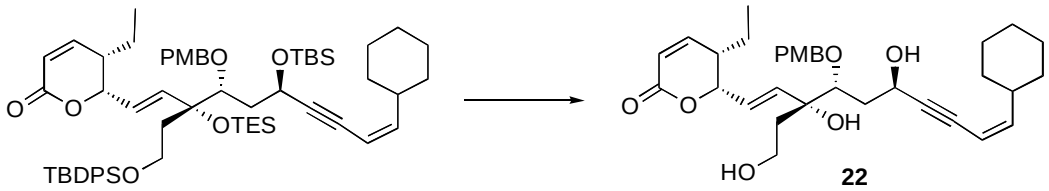
(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,9*Z*)-6-(*tert*-Butyldimethylsilyloxy)-3-(2-(*tert*-butyldiphenylsilyloxy)ethyl)-10-cyclohexyl-4-(4-methoxybenzyloxy)-3-(triethylsilyloxy)deca-1,9-dien-7-ynyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one



To a solution of alcohol **21** (3.78 g, 3.54 mmol) in benzene (30 mL) was added Ti(O-*i*Pr)$_4$ (0.21 mL, 0.71 mmol). After being stirred at 80 °C for 20 min, the mixture was cooled to room temperature and a few drops of H_2O was added to quench Ti(O-*i*Pr)$_4$. The resulting suspension was filtered through a pad of Celite with EtOAc. The filtrate was concentrated to give a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding lactone (3.40 g, 94%): $[\alpha]^{28}_D$ = +44 (*c* 0.096, $CHCl_3$); IR (neat) 1740, 1246, 1099, 1047 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.14 (s, 3 H), 0.17 (s, 3 H), 0.58 (q, *J* = 8 Hz, 6 H), 0.87–2.38 (m, 29 H), 0.92 (s, 9 H), 1.04 (s, 9 H), 2.50–2.66 (m, 1 H), 3.56 (d, *J* = 8 Hz, 1 H), 3.80 (s, 3 H), 3.70–3.94 (m, 2 H), 4.45–4.70 (m, 3 H), 4.89 (t, *J* = 5 Hz, 1 H), 5.33 (dd, *J* = 11, 2 Hz, 1 H), 5.61–5.88 (m, 3 H), 5.98 (d, *J* = 10 Hz, 1 H), 6.85 (dd, *J* = 10, 5 Hz, 1 H), 6.85 (d, *J* = 8 Hz, 2 H), 7.18 (d, *J* = 8 Hz, 2 H), 7.30–7.45 (m, 6 H), 7.60–7.69 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ –4.7 (–), –3.9 (–), 6.8 (+), 7.2 (–), 11.0 (–), 18.1 (+), 19.1 (+), 21.5 (+), 25.6 (+), 25.9 (–), 26.8 (–), 32.3 (+), 39.2 (–), 39.7 (–), 40.4 (+),

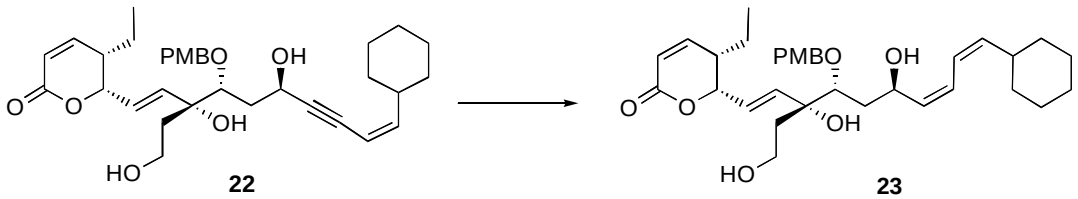
40.8 (+), 55.1 (–), 60.5 (+), 74.4 (+), 79.4 (+), 80.1 (–), 81.57 (+), 81.62 (–), 94.8 (+), 106.6 (–), 113.7 (–), 120.8 (–), 124.7 (–), 127.6 (–), 128.9 (–), 129.5 (–), 130.9 (+), 133.9 (+), 135.5 (–), 136.0 (–), 149.4 (–) ,149.5 (–), 159.1 (+), 163.7 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,9*Z*)-10-Cyclohexyl-3,6-dihydroxy-3-(2-hydroxyethyl)-4-(4-methoxybenzyloxy)deca-1,9-dien-7-ynyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one



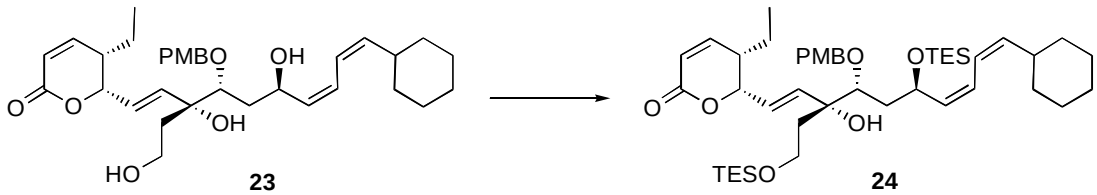
To an ice-cold solution of the above lactone (3.10 g, 3.04 mmol) was added Bu_4NF (12.2 mL, 1.0 M in THF, 12.2 mmol) dropwise. The solution was stirred at 0 °C for 20 min, warmed to ambient temperature over 30 min, and diluted with saturated NH_4Cl and EtOAc. The organic phase was separated, and the aqueous was extracted EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding triol **22** (1.48 g, 88%): $[\alpha]^{28}_D$ = +66 (*c* 0.03, $CHCl_3$); IR (neat) 3425, 1734, 1248, 1050 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, *J* = 7 Hz, 3 H), 1.00–2.16 (m, 16 H), 2.46–2.66 (m, 2 H), 2.93 (br s, 1 H), 3.47 (br s, 1 H), 3.60–3.95 (m, 3 H), 3.80 (s, 3 H), 4.47 (br s, 1 H), 4.59 (d, *J* = 11 Hz, 1 H), 4.68 (d, *J* = 11 Hz, 1 H), 4.55–4.75 (m, 1 H), 5.06 (br s, 1 H), 5.38 (d, *J* = 11 Hz, 1 H), 5.75 (dd, *J* = 11, 9 Hz, 1 H), 5.95–6.03 (m, 2 H), 6.05 (dd, *J* = 10, 2 Hz, 1 H), 6.88 (d, *J* = 9 Hz, 2 H), 6.96 (dd, *J* = 10, 5 Hz, 1 H), 7.26 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.0 (–), 21.5 (+), 25.5 (+), 25.9 (+), 32.2 (+), 37.3 (+), 38.5 (+), 39.1 (–), 39.3 (–), 55.2 (–), 59.7 (+), 60.7 (–), 73.6 (+), 78.7 (+), 80.5 (–), 81.3 (+), 82.5 (–), 93.9 (+), 106.4 (–), 113.8 (–), 120.6 (–), 125.6, (–) 129.5 (–), 130.1 (+), 136.2 (–), 149.7 (–), 150.3 (–), 159.3 (+), 164.4 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-3,6-dihydroxy-3-(2-hydroxyethyl)-4-(4-methoxybenzyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (23)



To a suspension of Zn powder (24.1 g, 369 mmol) in EtOH (50 mL) was added dibromoethane (1.35 mL, 15.7 mmol) at 80 °C. When the release of gas ceased, an additional dibromoethane (1.40 mL, 16.2 mmol) was added dropwise. After being stirred at 80 °C for 15 min, the suspension was cooled to 50 °C and a solution of LiBr (8.27 g, 95.2 mmol) and CuBr (5.52 g, 38.5 mmol) in THF (35 mL) was added dropwise with vigorous stirring. A solution of triol **22** (1.33 g, 2.41 mmol) in EtOH (5 mL) was added to the mixture. The vial was washed with EtOH (5 mL) which was added to the mixture. This operation was repeated with THF (5 mL). The resulting suspension was heated to 80 °C for 2 h and cooled to room temperature. The resulting suspension was filtered through a pad of Celite with EtOAc. The filtrate was concentrated and diluted with saturated NH_4Cl and EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish diene **23** as the sole product (1.10 g, 83%): $[\alpha]^{28}_D$ = +53 (*c* 0.0076, $CHCl_3$); IR (neat) 3389, 1717, 1249, 1058 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7 Hz, 3 H), 0.90–2.0 (m, 17 H), 2.34–2.56 (m, 2 H), 2.98 (br s, 2 H), 3.58 (t, *J* = 6 Hz, 1 H), 3.70–3.90 (m, 2 H), 3.81 (s, 3 H), 4.50 (d, *J* = 11 Hz, 1 H), 4.61 (d, *J* = 11 Hz, 1 H), 4.60–4.75 (m, 1 H), 5.06 (t, *J* = 4 Hz, 1 H), 5.30–5.46 (m, 2 H), 5.95–6.05 (m, 2 H), 6.04 (dd *J* = 11, 1 Hz, 1 H), 6.08 (t, *J* = 11 Hz, 1 H), 6.29 (t, *J* = 11 Hz, 1 H), 6.88 (d, *J* = 9 Hz, 2 H), 6.95 (dd, *J* = 11, 5 Hz, 1 H), 7.24 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.0 (–), 21.3 (+), 25.5 (+), 25.7 (+), 32.8 (+), 36.1 (–), 37.8 (+), 38.1 (+), 39.2 (–), 55.0, (–) 59.3 (+), 65.3 (–), 72.8 (+), 78.2 (+), 80.4 (–), 82.4 (–), 113.5 (–), 120.3 (–), 121.0 (–), 123.8 (–), 125.2 (–), 129.2 (–), 130.2 (+), 133.5 (–), 136.0 (–), 139.7 (–), 150.2 (–), 159.0 (+), 164.2 (+).

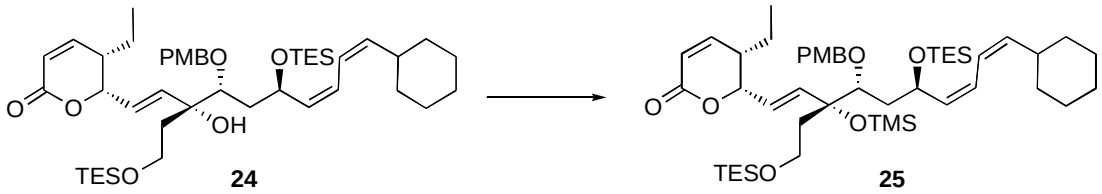
(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-3-hydroxy-4-(4-methoxybenzyl-oxy)-6-(triethylsilyloxy)-3-(2-(triethylsilyloxy)ethyl)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (24)



To an ice-cold solution of triol **23** (910 mg, 1.64 mmol) and pyridine (3.95 mL, 49.2 mmol) in CH_2Cl_2 (2 mL) was added TESCl (1.10 mL, 6.57 mmol) dropwise. After 30 min at 0 °C, the resulting solution was diluted with saturated $NaHCO_3$ and Et_2O.

The organic layer was separated, and the aqueous layer was extracted with Et_2O twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish **24** (1.10 g, 85%): $[\alpha]^{28}_D$ = +39 (*c* 0.11, $CHCl_3$); IR (neat) 3445, 1733, 1247, 1084 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.48–0.66 (m, 12 H), 0.84–2.02 (m, 37 H), 2.32–2.52 (m, 2 H), 3.48 (dd, *J* = 7, 4 Hz, 1 H), 3.68–3.88 (m, 2 H), 3.81 (s, 3 H), 4.44–4.64 (m, 2 H), 4.50 (s, 1 H), 4.75–4.88 (m, 1 H), 5.02 (t, *J* = 5 Hz, 1 H), 5.26–5.44 (m, 2 H), 5.95–6.08 (m, 3 H), 6.07 (t, *J* = 11 Hz, 1 H), 6.21 (t, *J* = 11 Hz, 1 H), 6.87 (d, *J* = 9 Hz, 2 H), 6.89 (dd, *J* = 11, 5 Hz, 1 H), 7.24 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 4.0 (+), 5.0 (+), 6.5 (–), 6.7 (–), 10.8 (–), 21.5 (+), 25.7 (+), 25.8 (+), 32.99 (+), 33.05 (+), 36.2 (–), 37.7 (+), 39.3 (–), 39.6 (–), 55.0 (–), 60.3 (+), 66.1 (–), 73.0 (+), 78.3 (+), 80.5 (–), 81.6 (–), 113.5 (–), 120.7 (–), 121.3 (–), 123.0 (–), 125.0 (–), 128.8 (–), 131.0 (+), 134.4 (–), 137.1 (–), 139.4 (–), 149.6 (–), 158.9 (+), 163.7 (+).

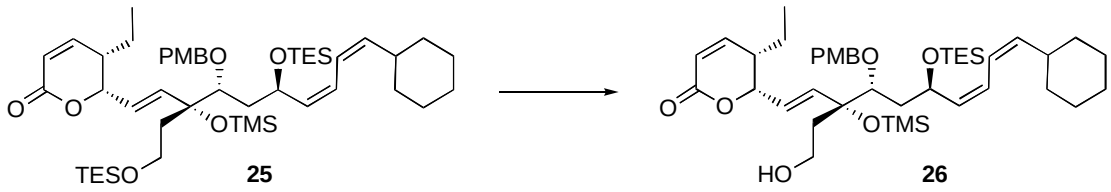
(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-4-(4-methoxybenzyloxy)-6-(triethylsilyloxy)-3-(2-(triethylsilyloxy)ethyl)-3-(trimethylsilyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (25)



To an ice-cold solution of **24** (1.10 g, 1.40 mmol) and 2,6-lutidine (4.91 mL, 42.2 mmol) in CH_2Cl_2 (2 mL) was added TMSOTf (1.00 mL, 5.67 mmol) dropwise. After 20 min at 0 °C, the resulting solution was diluted with saturated $NaHCO_3$ and Et_2O. The organic layer was separated, and the aqueous layer was extracted with Et_2O twice. The combined organic layers were dried over $MgSO_4$ and concentrated to give a residue, which was purified by short chromatography on silica gel (hexane/EtOAc) to furnish TMS ether **25**, which was used for the next reaction without further purification: $[\alpha]^{28}_D$ = +42 (*c* 0.12, $CHCl_3$); IR (neat) 1734, 1250, 1084 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.18 (s, 9 H), 0.48–0.63 (m, 12 H), 0.90–2.45 (m, 39 H), 3.55–3.90 (m, 3 H), 3.80 (s, 3 H), 4.58 (d, *J* = 11 Hz, 1 H), 4.67 (d, *J* = 11 Hz, 1 H), 4.79 (t, *J* = 9 Hz, 1 H), 4.95 (br s, 1 H), 5.18–5.42 (m, 2 H), 5.70 (dd, *J* = 16, 6 Hz, 1 H), 5.82–6.22 (m, 4 H), 6.82–6.95 (m, 3 H), 7.20–7.30 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.5 (–), 4.4 (+), 5.3 (+), 6.8 (–), 7.0 (–), 11.0 (–), 21.5 (+), 25.8 (+), 26.0 (+), 33.1 (+), 33.2 (+), 36.4 (–), 39.8 (–), 40.1 (+), 40.2 (+), 55.2 (–), 59.1 (+), 65.9 (–),

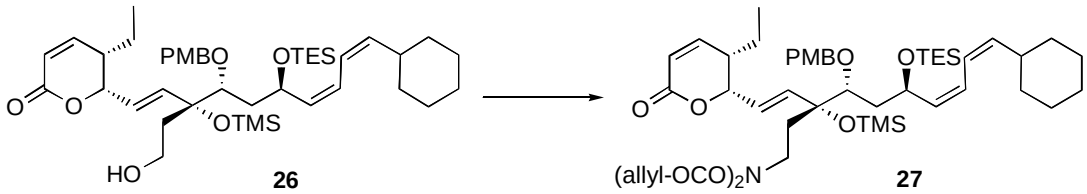
74.3 (+), 80.0 (+), 80.5 (–), 81.9 (–), 113.7 (–), 120.8 (–), 121.2 (–), 122.8 (–), 124.6 (–), 128.7 (–), 131.3 (+), 134.9 (–), 136.4 (–), 139.7 (–), 149.8 (–), 159.0 (+), 164.0 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-3-(2-hydroxyethyl)-4-(4-methoxybenzyloxy)-6-(triethylsilyloxy)-3-(trimethylsilyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (26)



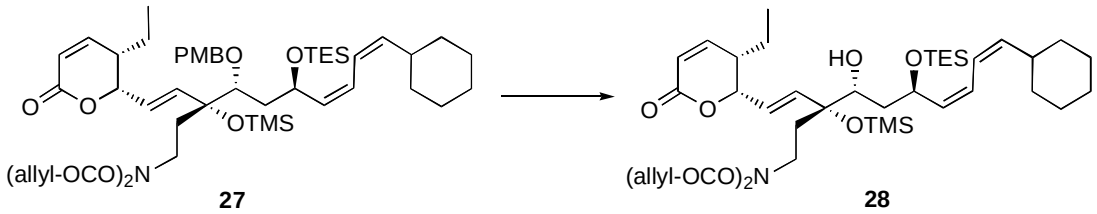
To an ice-cold solution of the silyl ether **25** in MeOH/THF (30 mL, 1 : 1) was added PPTS (35 mg, 0.14 mmol). After being stirred at 0 °C for 4 h, the mixture was diluted with $NaHCO_3$ and EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish alcohol **26** [558 mg, 86% for 2 steps, based on recovered silyl ether **25** (450 mg, 38% recovery)]: $[\alpha]^{28}_{D}$ = +53 (*c* 0.022, $CHCl_3$); IR (neat) 3447, 1729, 1250, 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.18 (s, 9 H), 0.56 (q, *J* = 8 Hz, 6 H), 0.84–1.80 (m, 17 H), 0.94 (t, *J* = 8 Hz, 9 H), 1.98 (t, *J* = 5 Hz, 2 H), 2.28–2.52 (m, 2 H), 3.0 (br s, 1 H), 3.55–4.00 (m, 3 H), 3.82 (s, 3 H), 4.60 (d, *J* = 11 Hz, 1 H), 4.78 (t, *J* = 8 Hz, 1 H), 4.86 (d, *J* = 11 Hz, 1 H), 4.98 (t, *J* = 5 Hz, 1 H), 5.32 (t, *J* = 10 Hz, 2 H), 5.75 (dd, *J* = 16, 6 Hz, 1 H), 5.90–6.10 (m, 3 H), 6.17 (t, *J* = 11 Hz, 1 H), 6.89 (d, *J* = 9 Hz, 2 H), 6.94 (dd, *J* = 10, 6 Hz, 1 H), 7.28 (d, *J* = 9 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.4 (–), 5.1 (+), 6.8 (–), 10.8 (–), 21.4 (+), 25.6 (+), 25.8 (+), 32.9 (+), 33.0 (+), 36.2 (–), 38.8 (+), 39.4 (–), 40.2 (+), 55.0 (–), 58.0 (+), 65.6 (–), 74.7 (+), 80.0 (–), 80.1 (+), 82.1 (–), 113.6 (–), 120.6 (–), 120.9 (–), 122.8 (–), 124.9 (–), 128.8 (–), 130.7 (+), 134.3 (–), 137.5 (–), 139.6 (–), 149.6 (–), 159.0 (+), 163.5 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-3-(2-(Bis(allyloxycarbonyl)amino)ethyl)-10-cyclohexyl-4-(4-methoxybenzyloxy)-6-(triethylsilyloxy)-3-(trimethylsilyloxy)-deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (27)



To a solution of PPh_3 (277 mg, 1.06 mmol) and DIAD (0.594 mL, 1.90 M in toluene, 1.13 mmol) in toluene (3 mL) were added (allyl-OCO)$_2$NH (0.197 g, 0.98 mmol) and a solution of alcohol **26** (558 mg, 0.75 mmol) in toluene (5 mL) at –78 °C. The resulting suspension was warmed to 0 °C over 10 min and cooled to –78 °C again. A solution of PPh_3 (197 mg, 0.75 mmol) and DIAD (0.436 mL, 1.90 M in toluene, 0.83 mmol) in toluene (1 mL) was again added at –78 °C. The solution was warmed to 0 °C over 30 min, and diluted with saturated $NaHCO_3$ and hexane. The organic layer was separated, and the aqueous layer was extracted with hexane twice. The combined organic layers were dried over $MgSO_4$ and concentrated to obtain a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish amide **27** (501 mg, 73%): $[\alpha]^{28}_D$ = +26 (*c* 0.10, $CHCl_3$); IR (neat) 1734, 1249, 1099 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.04 (s, 9 H), 0.39 (q, *J* = 8 Hz, 6 H), 0.66–1.62 (m, 26 H), 1.76–1.94 (m, 2 H), 2.08–2.30 (m, 2 H), 3.45–3.75 (m, 3 H), 3.63 (s, 3 H), 4.35–4.60 (m, 6 H), 4.63 (t, *J* = 8 Hz, 1 H), 4.80 (t, *J* = 6 Hz, 1 H), 5.05 (d, *J* = 11 Hz, 2 H), 5.18 (dd, *J* = 17, 1 Hz, 2 H), 5.00–5.24 (m, 2 H), 5.60 (dd, *J* = 16, 6 Hz, 1 H), 5.65–5.90 (m, 5 H), 6.00 (t, *J* = 11 Hz, 1 H), 6.69 (d, *J* = 8 Hz, 2 H), 6.73 (dd, *J* = 10, 5 Hz, 1 H), 7.06 (d, *J* = 8 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.5 (–), 5.4 (+), 7.0 (–), 11.1 (–), 21.5 (+), 21.7 (–), 22.0 (–), 25.8 (+), 26.0 (+), 33.1 (+), 33.2 (+), 35.6 (+), 36.4 (–), 39.8 (–), 40.2 (+), 43.2 (+), 55.3 (–), 65.7 (–), 67.4 (+), 74.6 (+), 80.1 (+), 80.6 (–), 81.9 (–), 113.7 (–), 119.0 (+), 120.8 (–), 121.2 (–), 122.9 (–), 125.5 (–), 128.9 (–), 131.2 (+), 131.6 (–), 134.7 (–), 136.0 (–), 139.8 (–), 149.9 (–), 153.2 (+), 159.1 (+), 164.0 (+).

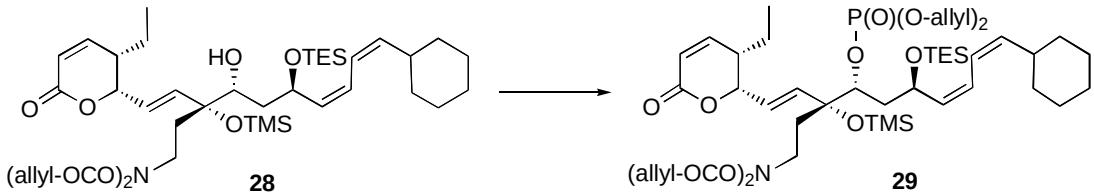
(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-3-(2-(Bis(allyloxycarbonyl)amino)ethyl)-10-cyclohexyl-4-hydroxy-6-(triethylsilyloxy)-3-(trimethylsilyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (28)



To an ice-cold mixture of PMB ether **27** (450 mg, 0.495 mmol) in CH_2Cl_2/H_2O (19 : 1,

6 mL) was added DDQ (169 mg, 0.74 mmol) in one portion. The mixture was stirred at 0 °C for 30 min, and diluted with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish alcohol **28** (346 mg, 85%): $[\alpha]^{28}_D$ = +30 (*c* 0.04, $CHCl_3$); IR (neat) 3498, 1734, 1106 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.15 (s, 9 H), 0.58 (q, *J* = 8 Hz, 6 H), 0.93 (t, *J* = 8 Hz, 9 H), 0.82–1.80 (m, 17 H), 1.88–2.10 (m, 2 H), 2.34–2.50 (m, 2 H), 3.30 (d, *J* = 2 Hz, 1 H), 3.67–3.92 (m, 3 H), 4.70 (d, *J* = 6 Hz, 4 H), 4.87–4.97 (m, 1 H), 5.00–5.06 (m, 1 H), 5.22–5.55 (m, 1 H), 5.26 (d, *J* = 11 Hz, 2 H), 5.39 (dd, *J* = 17, 2 Hz, 2 H), 5.48 (t, *J* = 10 Hz, 1 H), 5.81 (dd, *J* = 12, 5 Hz, 1 H), 5.88–6.12 (m, 5 H), 6.23 (t, *J* = 11 Hz, 1 H), 6.96 (dd, *J* = 10, 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.5 (–), 4.8 (+), 6.8 (–), 11.1 (–), 21.6 (+), 25.8 (+), 26.0 (+), 33.09 (+), 33.14 (+), 34.6 (+), 36.4 (–), 38.5 (+), 39.6 (–), 43.0 (+), 67.0 (–), 67.5 (–), 73.7 (–), 79.4 (+), 80.4 (–), 119.0 (+), 120.9 (–), 123.1 (–), 125.8 (–), 131.6 (–), 133.6 (–), 135.6 (–), 140.1 (–), 149.9 (–), 153.2 (+), 164.0 (+).

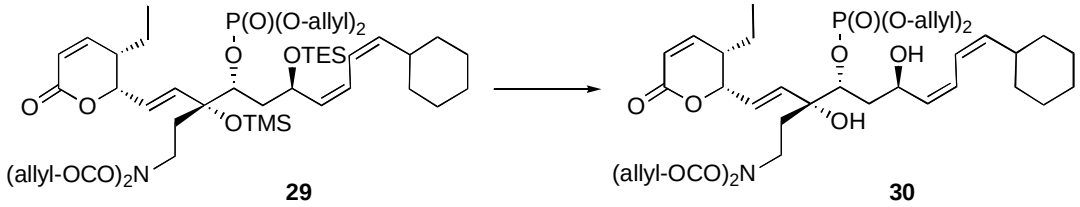
(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-3-(2-(Bis(allyloxycarbonyl)amino)ethyl)-10-cyclohexyl-4-(diallylphosphate)-6-(triethylsilyloxy)-3-(trimethylsilyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (29)



To an ice-cold solution of alcohol **28** (318 mg, 0.388 mmol) in CH_2Cl_2 (5 mL) were added 1*H*-tetrazole (54 mg, 0.77 mmol) and diallyl diisopropylphosphoramidite (133 mg, 0.542 mmol). After being stirred at room temperature for 30 min, the mixture was cooled to 0 °C and H_2O_2 (0.17 mL, 35%, 1.94 mmol) was added. The solution was stirred for 2 h and diluted with $NaHCO_3$ and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish phosphate **29** (311 mg, 85%): $[\alpha]^{28}_D$ = +41 (*c* 0.12, $CHCl_3$); IR (neat) 1734, 1252, 1019 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.23 (s, 9 H), 0.60 (q, *J* = 8 Hz, 6 H), 0.93 (t, *J* = 8 Hz, 9 H), 0.82–2.20 (m, 19 H), 2.32–2.50 (m, 2 H), 3.60–3.93 (m, 2 H), 4.45–4.75 (m, 9 H), 4.84–5.08 (m, 2 H), 5.18–5.45 (m, 10 H), 5.80–6.30 (m, 9 H), 6.96 (dd, *J* = 10, 6 Hz, 1

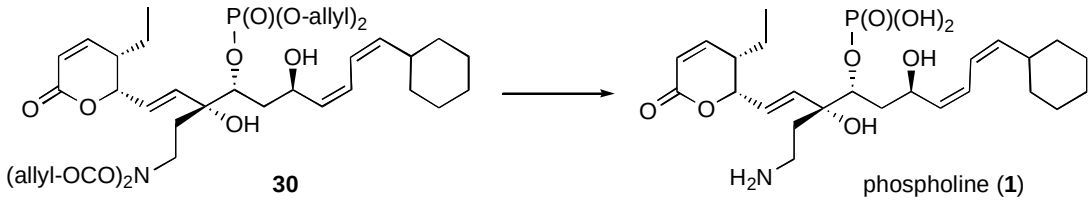
H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.4 (–), 5.1 (+), 7.0 (–), 11.1 (–), 21.6 (+), 22.0 (–), 25.8 (+), 26.0 (+), 33.1 (+), 33.2 (+), 36.4 (–), 39.7 (–), 43.0 (+), 64.9 (–), 67.5 (+), 68.07 (+), 68.14 (+), 78.6 (+), 78.7 (+), 80.2 (–), 81.2 (–), 81.3 (–), 118.1 (+), 118.2 (+), 119.0 (+), 120.9 (–), 121.3 (–), 123.1 (–), 126.8 (–), 131.6 (–), 132.51 (–), 132.58 (–), 132.61 (–), 132.68 (–), 134.0 (–), 139.8 (–), 149.9 (–), 153.1 (+), 163.9 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-3-(2-(Bis(allyloxycarbonyl)amino)ethyl)-10-cyclohexyl-4-(diallylphosphate)-3,6-dihydroxydeca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (30)



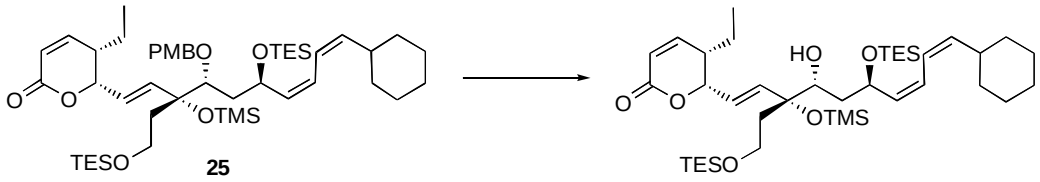
To an ice-cold solution of **29** (275 mg, 0.29 mmol) in CH_2Cl_2/THF/MeOH (11 mL, 5 : 5 : 1) was added AcCl (0.012 mL, 0.17 mmol) in MeOH (0.10 mL) dropwise. After being stirred at 0 °C for 2.5 h, the solution was diluted with $NaHCO_3$ and EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to obtain a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford diol **30** (210 mg, 95%): $[\alpha]^{28}_D$ = +57 (*c* 0.018, $CHCl_3$); IR (neat) 3423, 1726, 1248, 1025 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.94 (t, *J* = 8 Hz, 3 H), 1.00–2.06 (m, 16 H), 2.36–2.54 (m, 2 H), 3.52 (br s, 1 H), 3.65 (s, 1 H), 3.60–3.95 (m, 2 H), 4.43–4.85 (m, 10 H), 5.03 (t, *J* = 4 Hz, 1 H), 5.22–5.49 (m, 10 H), 5.80–6.15 (m, 8 H), 6.30 (t, *J* = 11 Hz, 1 H), 6.96 (dd, *J* = 10, 6 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 10.9 (–), 21.5 (+), 25.7 (+), 25.8 (+), 33.0 (+), 34.5 (+), 36.4 (–), 38.6 (+), 39.1 (–), 42.2 (+), 63.2 (–), 67.5 (+), 68.6 (+), 68.7 (+), 68.8 (+), 75.29 (+), 75.35 (+), 79.7 (–), 82.5 (–), 118.7 (+), 118.8 (+), 120.8 (–), 121.0 (–), 124.1 (–), 127.0 (–), 131.4 (–), 132.0 (–), 132.1 (–), 132.2 (–), 132.6 (–), 133.0 (–), 141.1 (–), 149.9 (–), 153.2 (+), 163.8 (+).

Phospholine (1)



To an ice-cold solution of diol **30** (35 mg, 0.046 mmol) in CH_2Cl_2 (0.6 mL) were added H_2O (0.042 mL, 2.33 mmol), $PdCl_2(PPh_3)_2$ (1.6 mg, 0.0023 mmol), and Bu_3SnH (0.062 mL, 0.23 mmol). After being stirred at 0 °C for 1.5 h, the solution was diluted with H_2O and hexane. The solutions were removed to leave white solids, which were purified by preparative TLC (silica gel plates, MeOH/H_2O = 8 : 1) to yield phospholine (**1)** as white solids (21 mg, 88%): $[\alpha]^{28}_D$ = +80 (*c* 0.03, MeOH); IR (neat) 3370, 1132, 1028 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 0.96 (t, *J* = 7 Hz, 3 H), 1.01–1.81 (m, 17 H), 2.22–2.33 (m, 1 H), 2.41–2.62 (m, 2 H), 3.01 (t, *J* = 7 Hz, 2 H), 3.62–3.66 (m, 1 H), 4.22 (dt, *J* = 10, 4 Hz, 1 H), 5.04 (t, *J* = 4 Hz, 1 H), 5.09 (t, *J* = 5 Hz, 1 H), 5.29 (t, *J* = 10 Hz, 1 H), 5.41 (t, *J* = 10 Hz, 1 H), 5.86 (d, *J* = 16 Hz, 1 H), 6.01 (d, *J* = 10 Hz, 1 H), 6.13 (dd, *J* = 16, 8 Hz, 1 H), 6.24 (t, *J* = 8 Hz, 2 H), 7.09 (dd, *J* = 10, 6 Hz, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 11.0 (–), 22.7 (+), 26.9 (+), 27.1 (+), 34.3 (+), 34.4 (+), 37.6 (–), 40.5 (–), 40.6 (+), 64.4 (–), 77.6 (–), 78.7 (+), 82.3 (–), 121.0 (–), 123.1 (–), 124.3 (–), 127.1 (–), 134.7 (–), 138.6 (–), 139.9 (–), 152.8 (–), 166.5 (+).

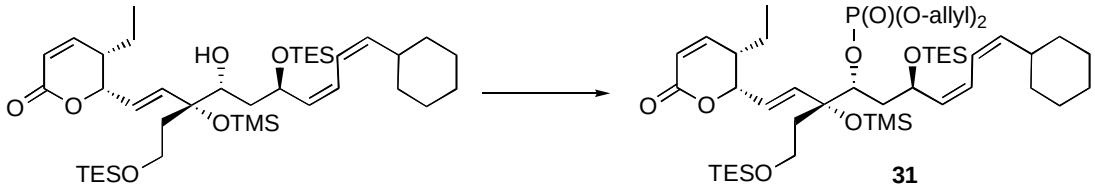
(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-4-hydroxy-6-(triethylsilyloxy)-3-(2-(triethylsilyloxy)ethyl)-3-(trimethylsilyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one



To an ice-cold mixture of PMB ether **25** (280 mg, 0.327 mmol) in CH_2Cl_2/H_2O (19 : 1, 5 mL) was added DDQ (89 mg, 0.39 mmol) in one portion. The mixture was stirred at 0 °C for 30 min, and diluted with saturated $NaHCO_3$. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish the corresponding alcohol (172 mg, 87%): $[\alpha]^{28}_D$ = +44 (*c* 0.063, $CHCl_3$); IR (neat) 3474, 1733, 1251, 1082 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.13 (s, 9 H), 0.57 (q, *J* = 8 Hz, 6 H), 0.61 (q, *J* = 8 Hz, 6 H), 0.80–1.80 (m, 36 H), 1.86–2.06 (m, 2 H), 2.33–2.50 (m, 2 H), 3.60–3.85 (m, 3 H), 4.88 (t, *J* = 9 Hz, 1 H), 4.99 (dd, *J* = 6, 5 Hz, 1 H), 5.38 (t, *J* = 10 Hz, 1 H), 5.45 (t, *J* = 10 Hz, 1 H), 5.76 (dd, *J* = 16, 6 Hz, 1 H), 5.99 (d, *J* = 16 Hz, 1 H), 6.04 (d, *J* = 10 Hz, 1 H), 6.08 (t, *J* = 12 Hz, 1 H), 6.18 (t, *J* = 12 Hz, 1 H), 6.91 (dd, *J* = 10, 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.6 (–), 4.3 (+), 4.9 (+), 6.8 (–), 6.9

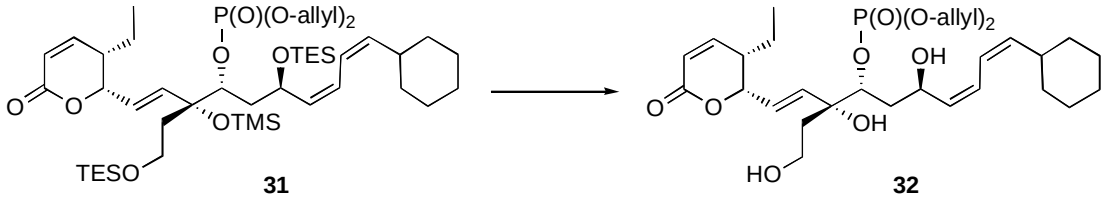
(–), 11.1 (–), 21.6 (+), 25.9 (+), 26.0 (+), 33.16 (+), 33.20 (+), 36.4 (–), 39.6 (+), 39.7 (–), 40.9 (+), 58.8 (+), 66.3 (–), 72.7 (–), 79.7 (+), 80.8 (–), 120.9 (–), 121.3 (–), 122.5 (–), 124.4 (–), 134.7 (–), 137.3 (–), 139.5 (–), 149.8 (–), 164.1 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-4-(diallylphosphate)-6-(triethylsilyloxy)-3-(2-(triethylsilyloxy)ethyl)-3-(trimethylsilyloxy)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (31)



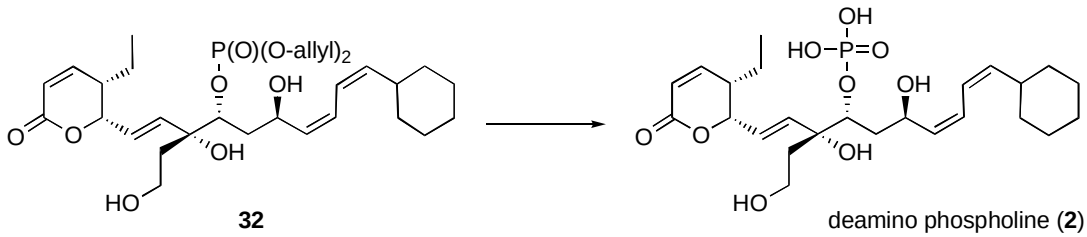
To an ice-cold solution of the above alcohol (131 mg, 0.217 mmol) in CH_2Cl_2 (3 mL) were added 1*H*-tetrazole (30 mg, 0.43 mmol) and diallyl diisopropylphosphoramidite (75 mg, 0.31 mmol). After being stirred at room temperature for 30 min, the mixture was cooled to 0 °C and H_2O_2 (0.15 mL, 35%, 0.84 mmol) was added. The solution was stirred for 2 h and diluted with $NaHCO_3$ and CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to afford a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to furnish phosphate **31** (121 mg, 73%): $[\alpha]^{28}_D$ = +6 (*c* 0.022, $CHCl_3$); IR (neat) 3447, 1733, 1252, 1083, 1022 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.19 (s, 9 H), 0.57 (q, *J* = 8 Hz, 6 H), 0.60 (q, *J* = 8 Hz, 6 H), 0.80–1.94 (m, 35 H), 2.06 (t, *J* = 8 Hz, 2 H), 2.32–2.52 (m, 2 H), 3.55–3.90 (m, 2 H), 4.44–4.64 (m, 5 H), 4.93 (t, *J* = 9 Hz, 1 H), 5.00 (t, *J* = 5 Hz, 1 H), 5.17–5.44 (m, 6 H), 5.75 (dd, *J* = 14, 6 Hz, 1 H), 5.82–6.25 (m, 4 H), 5.88 (d, *J* = 14 Hz, 1 H), 6.04 (d, *J* = 10 Hz, 1 H), 6.95 (dd, *J* = 10, 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 2.6 (–), 4.5 (+), 5.3 (+), 6.9 (–), 7.1 (–), 11.2 (–), 21.7 (+), 25.9 (+), 26.1 (+), 33.2 (+), 33.3 (+), 36.5 (–), 39.5 (+), 39.7 (–), 58.7 (+), 65.0 (–), 66.1 (+), 66.2 (+), 68.0 (+), 68.1 (+), 68.2 (+), 78.25 (+), 78.33 (+), 80.2 (–), 117.97 (+), 118.07 (+), 118.5 (+), 120.8 (–), 121.3 (–), 123.0 (–), 125.7 (–), 132.1 (–), 132.4 (–), 132.5 (–), 132.6 (–), 134.45 (–), 134.50 (–), 139.6 (–), 149.7 (–), 163.7 (+).

(5*S*,6*S*)-6-[(1*E*,3*R*,4*R*,6*R*,7*Z*,9*Z*)-10-Cyclohexyl-4-(diallylphosphate)-3,6-dihydroxy-3-(2-(hydroxy)ethyl)deca-1,7,9-trienyl]-5-ethyl-5,6-dihydro-2*H*-pyran-2-one (32)



To an ice-cold solution of phosphate **31** (95 mg, 0.12 mmol) in CH_2Cl_2/THF/MeOH (4.4 mL, 5 : 5 : 1) was added AcCl (0.0053 mL, 0.075 mmol) in MeOH (0.20 mL). After being stirred at 0 °C for 20 min, the solution was diluted with $NaHCO_3$ and EtOAc. The organic layer was separated, and the aqueous layer was extracted with EtOAc twice. The combined organic layers were dried over $MgSO_4$ and concentrated to obtain a residue, which was purified by chromatography on silica gel (hexane/EtOAc) to afford triol **32** (68 mg, 92%): $[\alpha]^{28}_D$ = –15 (*c* 0.014, $CHCl_3$); IR (neat) 3392, 1718, 1251, 1025 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.96 (t, *J* = 8 Hz, 3 H), 0.90–2.20 (m, 19 H), 2.35–2.55 (m, 2 H), 3.88–3.96 (m, 2 H), 4.50–4.73 (m, 5 H), 4.81 (t, *J* = 8 Hz, 1 H), 5.02–5.16 (m, 1 H), 5.23–5.53 (m, 6 H), 5.85–6.18 (m, 6 H), 6.30 (t, *J* = 12 Hz, 1 H), 6.97 (dd, *J* = 10, 5 Hz, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.0 (–), 21.6 (+), 25.8 (+), 26.0 (+), 33.1 (+), 36.5 (–), 37.2 (+), 38.6 (+), 39.2 (–), 59.5 (+), 63.5 (–), 68.7 (+), 77.3 (+), 77.4 (+), 80.0 (+), 81.6 (–), 118.8 (+), 120.8 (–), 121.2 (–), 124.2 (–), 126.7 (–), 132.06 (–), 132.13 (–), 132.16 (–), 132.22 (–), 132.8 (–), 133.8 (–), 140.2 (–), 150.2 (–), 164.2 (+).

Deamino Phospholine (2)



To an ice-cold solution of triol **32** (21 mg, 0.035 mmol) in CH_2Cl_2 (0.4 mL) were added H_2O (0.019 mL, 1.06 mmol), $PdCl_2(PPh_3)_2$ (1.3 mg, 0.0018 mmol), and Bu_3SnH (0.024 mL, 0.089 mmol) sequentially. After being stirred at 0 °C for 1 h, the resulting solution was diluted with H_2O and hexane. The solutions were removed to leave white solids, which were purified by chromatography on silica gel (EtOAc/MeOH from 100 : 0 to 1 : 2) to afford deamino phospholine **2** (14 mg, 77%): $[\alpha]^{22}_D$ = +75 (*c* 0.075, MeOH); IR (neat) 3361, 1718, 1108 cm^{-1}; ^1H NMR (500 MHz, CD_3OD) δ 0.94 (t, *J* = 7.5 Hz, 3 H), 1.02–1.98 (m), 2.08–2.22 (m, 1 H), 2.40–2.62 (m, 2 H), 3.60–3.83 (m, 2 H), 4.25 (t, *J* = 11 Hz, 1 H), 5.01 (dd, *J* = 6, 4 Hz, 1 H), 5.31 (t, *J* = 9 Hz, 1 H),

5.41 (t, *J* = 9 Hz, 1 H), 5.80–6.07 (m, 3 H), 6.24 (d, *J* = 10 Hz, 2 H), 7.08 (dd, *J* = 10, 5 Hz, 1 H); ^{13}C NMR (75 MHz, CD_3OD) δ 11.3 (–), 22.7 (+), 26.9 (+), 27.1 (+), 34.3 (+), 37.6 (–), 38.6 (+), 40.4 (+), 40.6 (–), 59.8 (+), 64.5 (–), 78.3 (+), 78.8 (–), 82.4 (–), 121.0 (–), 123.0 (–), 124.4 (–), 126.4 (–), 134.5 (–), 138.1 (–), 140.0 (–), 152.8 (–), 166.6 (+).