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Supporting Information

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Confirmation of the stereostructure of (+)-cytostatin by fluorous mixture synthesis of four candidate stereoisomers

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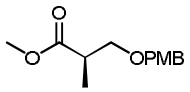
EXPERIMENTAL

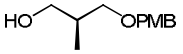
General: All reactions were run under argon unless otherwise noted. Toluene, THF, dichloromethane, and diethyl ether were purified by filtration through a column of activated alumina under a nitrogen atmosphere. Other reagents were used as they were received from Aldrich. 4 Å Molecular sieves were flame-dried for at least 1 h before use. ^{1}H and ^{13}C NMR spectra were recorded on Bruker Avance DPX 300 (300 MHz), Avance DRX 500 (500 MHz) and Avance 600 (600 MHz) spectrometers. Chemical shifts were reported in ppm. In reporting spectral data, the following abbreviations were used: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Coupling constants were measured in Hertz (Hz). Infrared spectra were taken on a Mattson Genesis Series FTIR using thin film deposition on NaCl plates unless otherwise noted. Peaks are reported in wavenumbers (cm^{-1}). Low resolution mass spectra were obtained on a Fision Autospec. High resolution mass spectra were obtained on a VG Autospec double focusing instrument. Optical rotations are measured on a Perkin-Elmer 241 polarimeter at the Na D-line (λ= 589 nm) using a 1 dm cell. HPLC analyses were conducted by using Waters 600 controller and Waters 2487 dual λ absorbance detector. Thin layer chromatography (TLC) was performed on silica gel 60 F_{254} glass backed plates with a layer thickness of 0.25 mm manufactured by E.Merck. TLC visualization was performed by illumination with a 254 nm UV lamp or by staining with phosphomolybdic acid in ethanol and subsequent heating. Flash chromatography was performed on silica gel (230–400 mesh ASTM) purchased from Sorbtech or Bodman.

(*R*)-Methyl 3-(4-methoxybenzyloxy)-2-methylpropanoate.



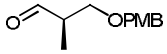
(*R*)-Roche ester (0.94 mL, 8.5 mmol) was dissolved in dichloromethane/cyclohexane (1:2, 12 mL) cooled to 0 °C where PMB-trichloroimidate (2.9 g, 11 mmol) followed by PPTS (108 mg, 0.43 mmol) were added. The clear mixture was left stirred at 0 °C for 1 h. Then the white mixture was warmed up to room temperature for 16 h. The solvent was evaporated; the white residue obtained was filtered through a short pad of silica (ethyl acetate and hexane, 1:4, 100 mL) affording a crude mixture (3.16 g), which was immediately used in the next step: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34 (dd, *J* = 9, 10.5 Hz, 2H), 6.97 (dd, *J* = 6, 12 Hz, 2H), 4.54 (s, 2H), 3.89 (s, 3H), 3.77 (s, 3H), 3.71 (dd, *J* = 6, 9 Hz, 1H), 3.40 (dd, *J* = 6, 9 Hz, 1H), 2.70 (m, 1H), 1.25 (s, *J* = 6 Hz, 3H).

(*S*)-3-(4-Methoxybenzyloxy)-2-methylpropan-1-ol.



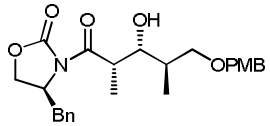
To a suspension of $LiAlH_4$ (365 mg, 9.35 mmol) in THF (15 mL) at 0 °C was added a solution of (*R*)-methyl 3-(4-methoxybenzyloxy)-2-methylpropanoate (2.03 g, 8.5 mmol) in THF (15 mL). The reaction mixture was stirred at 0 °C for 1 h, warmed up to room temperature and stirred for another 2 h. The mixture was successively quenched dropwise at 0 °C with water (0.35 mL), 15% NaOH (0.35 mL) and water (1.05 mL), respectively. $MgSO_4$ (160 mg) was added, filtered, rinsed with ether and the solvent was removed *in vacuo*. The purification by flash chromatography (ethyl acetate and hexane, 1:3 to 3:7) provided the product (1.08 g, 5.1 mmol, 60% over two steps): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41 (d, *J* = 7.5 Hz, 2H), 7.03 (d, *J* = 6 Hz, 2H), 4.60 (s, 2H), 3.96 (s, 3H), 3.80-3.68 (m, 3H), 3.54 (t, *J* = 8.4 Hz, 1H), 2.74 (dd, *J* = 6, 9 Hz, 1H), 2.23 (m, 1H), 1.02 (d, *J* = 7.5 Hz, 3H).

(*R*)-3-(4-Methoxybenzyloxy)-2-methylpropanal.



(*S*)-3-(4-Methoxybenzyloxy)-2-methylpropan-1-ol (1.074 g, 5.1 mmol) was dissolved in dichloromethane, cooled to 0 °C where TEMPO (7.98 mg, 51 μmol), 2.75 N KBr (3.89 mL, 10.71 mmol), 1.6 N $KHCO_3$ (35 mL, 56.1 mmol) were added, followed by dropwise addition of bleach (Chlorox 6.15% w/v, 8.26 mL, 6.834 mmol). The orange mixture became yellow after 5 min, stirred for 45 min at 0 °C. The mixture was quenched with saturated sodium thiosulfate, extracted with dichloromethane (3 x 10 mL). Organic layers were combined, dried over $MgSO_4$, filtered and solvent evaporated. The crude aldehyde was immediately used in the next: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.87 (s, 1H), 7.40 (d, *J* = 7.5 Hz, 2H), 7.02 (d, *J* = 6.63 Hz, 2H), 4.59 (s, 2H), 3.96 (s, 3H), 3.76 (m, 2H), 2.80 (m, 1H), 1.28 (d, *J* = 6 Hz, 3H).

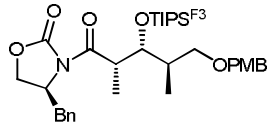
(*S*)-3-((2*S*,3*R*,4*R*)-5-(4-Methoxybenzyloxy)-3-hydroxy-2,4-dimethylpentanoyl)-4-benzyloxazolidin-2-one ((*S*,*S*,*R*,*R*)-8).



(*S*)-4-Benzyl-3-propionyloxazolidin-2-one (3.76 g, 16.15 mmol) was dissolved in dichloromethane (50 mL), cooled to 0 °C where 1 N Bu_2BOTf (19.38 mL, 19.38 mmol) was added dropwise followed by Et_3N (2.97 mL, 21.32 mmol) keeping the internal temperature below 3 °C. The yellow mixture was stirred at 0 °C for 40 min, then cooled to -78 °C where crude (*R*)-3-(4-methoxybenzyloxy)-2-methylpropanal (3.86 g, 18.57 mmol) in dichloromethane (10 mL) was added dropwise over 30 min. The reaction was left stirred at -78 °C for 1.5 h, after which it was slowly warmed up to -50 °C for 30 min and stirred for 45 min at this temperature. The mixture was warmed up to 0 °C and stirred for another 1.5 h. The reaction mixture was then cautiously quenched dropwise with pH7 buffer and MeOH (1:3, 15.6 mL), followed by 30% H_2O_2 and MeOH (1:2, 46.65 mL) maintaining the internal temperature between 0-5 °C. The cloudy mixture was left stirred at 0 °C for 1 h and then warmed up to

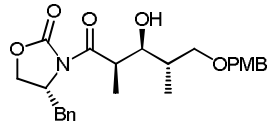
room temperature. The volatile material was removed *in vacuo*. The residue obtained was extracted with dichloromethane (3 x 20 mL), organic layers were combined, washed with brine, dried over $MgSO_4$, filtered and solvent evaporated. The purification by flash chromatography (ethyl acetate and hexane, 3:17 to 1:1) provided the product (5.31 g, 12 mmol, 75%) as a clear oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.19 (m, 7H), 6.85 (d, J = 9 Hz, 2H), 4.65 (m, 1H), 4.44 (s, 2H), 4.17 (m, 2H), 3.97 (m, 1H), 3.86 (m, 1H), 3.79 (s, 3H), 3.56 (m, 2H), 3.31 (dd, J = 3, 13.2 Hz, 1H), 2.76 (dd, J = 9.8, 13.3 Hz, 1H), 1.96 (m, 1H), 1.26 (d, J = 6.7 Hz, 3H), 0.93 (d, J = 6.9 Hz, 3H).

(*S*)-3-((2*S*,3*R*,4*R*)-5-(4-Methoxybenzyloxy)-3-((3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diisopropylsilyloxy)-2,4-dimethylpentanoyl)-4-benzyloxazolidin-2-one (9r).



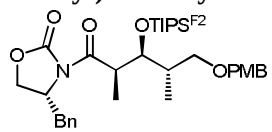
To neat TIPS^{F3}-H (14.3 g, 25.4 mmol) at 0 °C was added dropwise triflic acid (2.29 mL, 20.3 mmol). The yellow mixture was left stirred at room temperature for 16 h, and then added dropwise to a solution of alcohol **8** (5.6 g, 12.7 mmol) and 2,6-lutidine (3.25 mL, 27.94 mmol) in dichloromethane (30 mL) at 0 °C. The yellow reaction mixture was then left stirred at 0 °C for 4 h, after which it was quenched with saturated NH_4Cl, extracted with dichloromethane (3 x 40 mL). Organic layers were collected, combined, dried over $MgSO_4$, filtered and solvent evaporated. The product was purified by flash chromatography (ethyl acetate and hexane, 1:19 to 3:7) affording an oil (11.7 g, 11.7 mmol, 92%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (m, 7H), 6.82 (d, J = 9 Hz, 2H), 4.50 (m, 1H), 4.46 (s, 2H), 4.27 (dd, J = 4, 6.3 Hz, 1H), 4.03 (m, 2H), 3.87 (s, 3H), 3.85 (m, 1H), 3.45 (dd, J = 6.3, 9.1 Hz, 1H), 3.21 (m, 2H), 2,70 (dd, J = 9.7, 13.3 Hz, 1H), 2.24-2.00 (m, 5H), 1.25 (d, J = 8 Hz, 3H), 1.07 (s, 12H), 1.00 (d, J = 7 Hz, 3H), 0.89 (dd, J = 6.5, 11.2 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9, 159.1, 152.8, 135.4, 130.6, 129.4, 129.0 (2C), 127.3 (2C), 113.7 (2C), 105-120 (8C), 75.1, 72.6, 71.7, 65.8, 55.4, 55.2, 40.6, 39.7, 37.8, 27.7, 25.6, 18.0, 17.8 (2C), 17.2 (2C), 14.2, 13.6, 13.2 (2C), 1.3.

(*R*)-3-((2*R*,3*S*,4*S*)-5-(4-Methoxybenzyloxy)-3-hydroxy-2,4-dimethylpentanoyl)-4-benzyloxazolidin-2-one ((*R*,*R*,*S*,*S*)-8).



Following the procedure for (*S*,*S*,*R*,*R*)-**8**, (*S*)-3-(4-methoxybenzyloxy)-2-methylpropanal (4.21 g, 20.22 mmol) was reacted with (*R*)-4-Benzyl-3-propionyloxazolidin-2-one (3.78 g, 16.2 mmol), 1 M Bu_2BOTf (19.47 mL, 19.47 mmol), and Et_3N (2.98 mL, 21.38 mmol). The purification by flash column chromatography (ethyl acetate and hexane, 3:17 to 1:1) gave a yellow oil (4.39 g, 9.9 mmol, 65%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39-7.30 (m, 7H), 6.94 (d, J = 9 Hz, 2H), 4.69 (m, 1H), 4.67 (s, 2H), 4.16 (m, 2H), 3.83 (m, 2H), 3.82 (s, 3H), 3.57 (m, 2H), 3.35 (dd, J = 3, 13.2 Hz, 1H), 2.77 (dd, J = 9.8, 13.3 Hz, 2H), 2.05 (m, 1H), 1.22 (d, J = 6.7 Hz, 3H), 0.94 (d, J = 6.9 Hz, 3H).

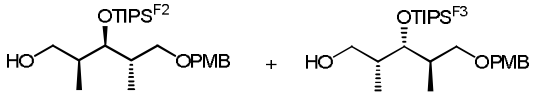
(*R*)-3-((2*R*,3*S*,4*S*)-5-(4-Methoxybenzyloxy)-3-(diisopropyl(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyloxy)-2,4-dimethylpentanoyl)-4-benzyloxazolidin-2-one (9s).



Following the procedure for **9r**, the alcohol (*R*,*R*,*S*,*S*)-**8** (0.71 g, 1.6 mmol) was reacted with TIPS^{F2}-H (1.48 g, 3.2 mmol), triflic acid (0.29 mL, 2.6 mmol), and 2,6-lutidine (0.32 mL, 2.79 mmol). The purification by flash column chromatography (ethyl acetate and hexane, 1:19 to 3:7) gave a clear oil (1 g, 1.16 mmol, 72%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36-7.17(m, 7H), 6.83 (d, J = 8.6 Hz, 2H), 4.45 (m, 1H), 4.35 (s, 2H), 4.27 (dd, J = 4.0, 6.3 Hz,

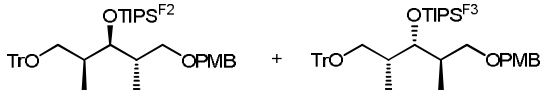
1H), 3.97 (m, 2H), 3.85 (m, 4H), 3.42 (dd, *J* = 6.2, 9.0 Hz, 1H), 3.20 (m, 2H), 2.69 (dd, *J* = 9.7, 13.3 Hz, 1H), 2.12 (m, 5H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.07 (s, 12H), 1.01 (d, *J* = 7.1 Hz, 3H), 0.89 (q, *J* = 6.5 Hz, 2H).

(2*S*,3*R*,4*S*)-5-(4-Methoxybenzyloxy)-3-(diisopropyl(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyloxy)-2,4-dimethylpentan-1-ol and (2*R*,3*S*,4*R*)-5-(4-methoxybenzyloxy)-3-((3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diisopropylsilyloxy)-2,4-dimethylpentan-1-ol (M-10).



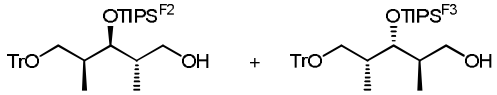
A mixture of **9s** (7.7 g, 8.6 mmol) and **9r** (8.6 g, 8.6 mmol) was dissolved in THF and MeOH (10:1, 22.0 mL), cooled to 0 °C where 2 M $LiBH_4$ (25.6 mL, 51.28 mmol) was added dropwise. The mixture was warmed up to room temperature and stirred for 3 h. The mixture was quenched with saturated NaK tartrate solution at 0 °C, extracted with ethyl acetate (4 x 50 mL). Organic layers were collected, combined, dried over sodium sulphate, filtered and solvent removed *in vacuo*. The product (10.2 g, 13.1 mmol) was isolated as a colorless oil after flash chromatography in 77% yield (ethyl acetate and hexane, 1:9): ^{1}H NMR (300 MHz, $CDCl_3$**)** δ 7.23 (d, *J* = 8.6 Hz, 4H), 6.88 (d, *J* = 8.6 Hz, 4H), 4.42 (q, *J* = 11.6 Hz, 4H), 3.96 (dd, *J* = 3, 5.3 Hz, 2H), 3.81 (s, 6H), 3.53 (d, *J* = 6 Hz, 4H), 3.48 (q, *J* = 3 Hz, 2H), 3.3 (q, *J* = 6.3 Hz, 2H), 2.17 (m, 4H), 2.04 (t, *J* = 4.5 Hz, 2H), 1.83 (m, 6H), 1.04 (s, 24H), 0.95 (d, *J* = 7 Hz, 6H), 0.88 (d, *J* = 7 Hz, 6H), 0.88 (m, 4H).

((2*S*,3*S*,4*S*)-5-(4-Methoxybenzyloxy)-2,4-dimethyl-1-(trityloxy)pentan-3-yloxy)diisopropyl(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silane and ((2*R*,3*R*,4*R*)-5-(4-methoxybenzyloxy)-2,4-dimethyl-1-(trityloxy)pentan-3-yloxy)(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diisopropylsilane (M-11).



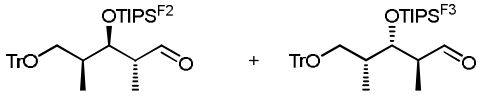
To a solution of **M-10** (1.26 g, 1.61 mmol) in dichloromethane (25 mL) at 0 °C were added successively Et_3N (0.34 mL, 2.42 mmol) and DMAP (20 mg, 0.16 mmol), followed by tritylchloride (0.90 g, 3.22 mmol). The cloudy yellow mixture was left stirred at room temperature for 76 h. The reaction mixture was quenched with water (30 mL), extracted with dichloromethane (3 x 20 mL). Organic layers were collected, combined, washed with brine, dried over sodium sulphate, filtered and the solvent was removed *in vacuo*. The product was isolated as a colorless oil (1.41 g, 1.4 mmol) in 86% yield after flash chromatography (ethyl acetate and hexane, 1:19): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, *J* = 1.6, 8.4 Hz, 4H), 7.33-7.18 (m, 30H), 6.84 (d, *J* = 8.7 Hz, 4H), 4.38 (s, 4H), 3.94 (dd, *J* = 1.9, 6.1 Hz, 2H), 3.79 (s, 6H), 3.39 (dd, *J* = 5.1, 8.9 Hz, 2H), 3.23 (dd, *J* = 6.9, 15.7 Hz, 2H), 2.95 (m, 4H), 2.11-1.89 (m, 12H), 0.97 (d, *J* = 6.9 Hz, 6H), 0.98-0.68 (m, 34H).

(2*S*,3*S*,4*S*)-3-(Diisopropyl(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyloxy)-2,4-dimethyl-5-(trityloxy)pentan-1-ol and (2*R*,3*R*,4*R*)-3-((3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-diisopropylsilyloxy)-2,4-dimethyl-5-(trityloxy)pentan-1-ol (M-12).



To a solution of **M-11** (5.1 g, 5 mmol) in dichloromethane and pH7 buffer (10:1, 100 mL) at 0 °C was added in one portion DDQ (1.7 g, 7.5 mmol). The green mixture was stirred for 1 h at 0 °C. Then it was quenched with saturated $NaHCO_3$ (150 mL), extracted with dichloromethane (3 x 100 mL). The organic layers were collected, combined, dried over sodium sulphate, filtered and solvent removed *in vacuo*. The product was purified by flash chromatography (ethyl acetate and hexane, 1:9) affording a yellow oil (3.4 g, 3.77 mmol) in 75% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (m, 30H), 4.07 (dd, *J* = 2.5, 5.5 Hz, 2H), 3.65 (m, 4H), 3.13 (m, 4H), 2.10 (m, 6H), 1.89 (m, 2H), 1.17-0.78 (m, 40H).

(2*R*,3*R*,4*S*)-3-(Diisopropyl(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyloxy)-2,4-dimethyl-5-(trityloxy)pentanal and (2*S*,3*S*,4*R*)-3-((3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)-diisopropylsilyloxy)-2,4-dimethyl-5-(trityloxy)pentanal (M-6).

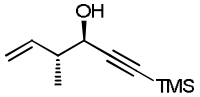


A mixture of **M-12** (7.48 g, 8.3 mmol) was dissolved in dichloromethane (215 mL), cooled to 0 °C where DMP (5.30 g, 12.45 mmol) was added in one portion. The cloudy mixture was left stirred at 0 °C for 2 h. Then the mixture was poured into a solution of saturated $NaHCO_3$ and $Na_2S_2O_3$ (1:1). The organic layers were collected, combined, dried over sodium sulfate, filtered and solvent removed *in vacuo*. The product was purified by flash chromatography (ethyl acetate and hexane 1: 9) affording a colorless oil (6.3 g, 6.99 mmol) in 84% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.67 (d, J = 2.2 Hz, 1H), 9.57 (s, 1H), 7.42-7.19 (m, 30H), 4.51 (dd, J = 2.9, 5.3 Hz, 1H), 4.22 (dd, J = 3.1, 5.8 Hz, 1H), 3.03 (m, 4H), 2.56 (m, 1H), 2.28 (m, 1H), 2.04 (m, 5H), 1.07 (d, J = 7.1 Hz, 6H), 0.89 (m, 34H).

3-(Trimethylsilyl)propiolaldehyde.

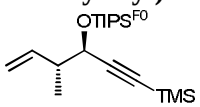
To a solution of trimethylsilylacetylene (3 g, 30.5 mmol) in Et_2O (10 mL) at -40 °C was added dropwise 2.5 N *n*-BuLi (11.09 mL, 27.7 mmol) followed by the addition of anhydrous DMF (4.27 mL, 55.4 mmol) in one portion. The clear reaction mixture was allowed to warmed up to room temperature and stirred for 30 min. The yellow solution was then poured into a biphasic mixture of 10% KH_2PO_4 and ether (100 mL) at 0 °C. The mixture was stirred vigorously, and layers were partitioned. The aqueous layer was extracted with ether (3 x 25 mL). The organic layers were collected, combined, dried over $MgSO_4$, filtered and solvent removed *in vacuo* (bath < 20 °C). Vacuum distillation (bp: 21 °C) provided a clear solution of the desired product (3 g, 24 mmol) in 79%, which was stored in the fridge over 4Å MS for a short period: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.16 (s, 1H), 0.19 (s, 9H).

(3*R*,4*R*)-4-Methyl-1-(trimethylsilyl)hex-5-en-1-yn-3-ol ((*R*,*R*)-13).



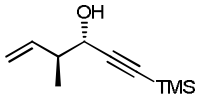
To a suspension of *t*-BuOK (5.10 g, 42.9 mmol) in THF (277 mL) was bubbled through a syringe *trans*-butene (26.0 mL, 277.0 mmol), followed by the addition of 1.6 M *n*-BuLi (26.8 mL, 42.9 mmol, 1.6 M in n-hexane) at -78 °C. The resulting yellow solution was warmed up to -45 °C and stirred for 30 min, then cooled back to -78 °C where (+)-methoxydiisopinocampheylborane (13.6 g, 42.9 mmol) in THF (69.4 mL) was added. The light yellow mixture was stirred for 40 min, then BF_3•OEt_2 (5.4 mL, 42.94 mmol) was added dropwise over 30 min, followed by addition of 3-(trimethylsilyl)propiolaldehyde (2.7 g, 21.4 mmol). The cloudy mixture was stirred for 6 h at -78 °C. After this time, the mixture was carefully quenched dropwise with MeOH (14mL) at -78 °C and warmed up to room temperature and the solvent was removed *in vacuo*. The white residue obtained was dissolved in THF and H_2O (2:1, 210 mL), the solution was cooled to 0 °C where sodium perborate (21.50 g, 0.14 mmol) was added portionwise. The white mixture was stirred for 14 h at room temperature. Ethyl acetate and H_2O (1:1, 300mL) was added, the mixture was extracted with ethyl acetate (2 x 200 mL). The organic layers were collected, combined, washed with water (300 mL), brine (300 mL), dried over magnesium sulfate, filtered and solvent removed *in vacuo*. The product was purified by flash chromatography (ethyl acetate and hexane 1:9) affording a colorless oil in 69% yield (2.8 g, 14.84 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.18 (d, J = 3.6 Hz, 1H), 5.14 (s, 1H), 4.19 (t, J = 5.5 Hz, 1H), 2.47 (q, J = 6.7, 13.4 Hz, 1H), 1.87 (d, J = 5.4 Hz, 1H), 1.14 (d, J = 6.8 Hz, 3H), 0.17 (s, 9H).

(3*R*,4*R*)-3-Methyl-4-(triisopropylsilyloxy)-6-(trimethylsilyl)hex-1-en-5-yne (14s).



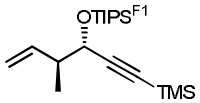
To a solution of alcohol (*R*,*R*)-**13** (0.93 g, 5.1 mmol) in dichloromethane (10 mL) and 2,6-lutidine (1.06 mL, 9.16 mmol) at 0 °C was added dropwise TIPSOTf (2.06 mL, 7.63 mmol). The clear mixture was stirred at 0 °C for 10 min then warmed up to room temperature and stirred for 1 h. The mixture was then quenched with water, extracted with dichloromethane (3 x 20 mL). The organic layers were collected, combined, dried over sodium sulfate, filtered and solvent removed *in vacuo*. The product was purified by flash chromatography (hexane, 100%) affording a colorless oil in 80% yield (1.37 g, 4 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.84 (ddd, J = 7.6, 10.3, 17.3 Hz, 1H), 5.05 (m, 2H), 4.35 (d, J = 5.2 Hz, 1H), 2.41 (m, 1H), 1.30-0.80 (m, 24 H), 0.15 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 140.2, 115.0, 106.0, 89.6, 67.4, 45.1, 18.1, 14.6, 12.3, -0.2.

(3*S*,4*S*)-4-Methyl-1-(trimethylsilyl)hex-5-en-1-yn-3-ol ((*S*,*S*)-13).



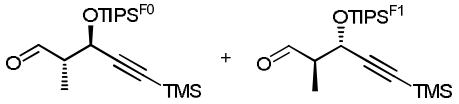
Following the procedure for (*R*,*R*)-**13**, 3-(trimethylsilyl)propiolaldehyde (1.7 g, 13.6 mmol) was reacted with *t*-BuOK (3.1 g, 27.2 mmol), 2.5 N *n*-BuLi (10.88 mL, 27.2 mmol), *trans*-butene (12.65 mL, 0.136 mol), (-)-methoxydiisopinocampheylborane (8.6 g, 27.2 mmol), and BF_3•OEt_2 (3.42 mL, 27.2 mmol). Purification by chromatography (ethyl acetate and hexane, 1:9) afforded a colorless oil in 81% yield (1.45 g, 7.97 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.81 (m, 1H), 5.18 (d, J = 3.6 Hz, 1H), 5.14 (s, 1H), 4.19 (t, J = 5.5 Hz, 1H), 2.47 (q, J = 6.7, 13.4 Hz, 1H), 1.87 (d, J = 5.4 Hz, 1H), 1.14 (d, J = 6.8 Hz, 3H), 0.17 (s, 9H).

(3*S*,4*S*)-4-(Diisopropyl(3,3,4,4,5,5,6,6,6-nonafluorohexyl)silyloxy)-3-methyl-6-(trimethylsilyl)hex-1-en-5-yne (14r).



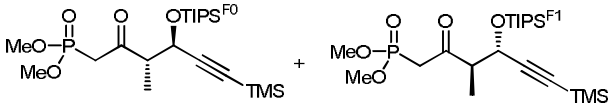
Following the procedure for **14s**, alcohol (*S*,*S*)-**13** (0.89 g, 7.95 mmol) was reacted with TIPS^{F1}-H (5.84 g, 16.1 mmol), triflic acid (1.5 mL, 13.3 mmol), and 2,6-lutidine (3.72 mL, 32.2 mmol). The product was purified by flash chromatography (100% hexane) affording a colorless oil (3.41 g, 7.25 mmol, 91%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.80 (ddd, J = 7.6, 10.3, 17.3 Hz, 1H), 5.06 (m, 2H), 4.31 (d, J = 5.6 Hz, 1H), 2.39 (q, J = 6.6, 13.3 Hz, 1H), 2.19 (m, 4H), 1.26-0.90 (m, 17 H), 0.15 (s, 9H).

(2*S*,3*R*)-2-Methyl-3-(triisopropylsilyloxy)-5-(trimethylsilyl)pent-4-ynal and (2*R*,3*S*)-3-(diisopropyl(3,3,4,4,5,5,6,6,6-nonafluorohexyl)silyloxy)-2-methyl-5-(trimethylsilyl)pent-4-ynal (M-15).



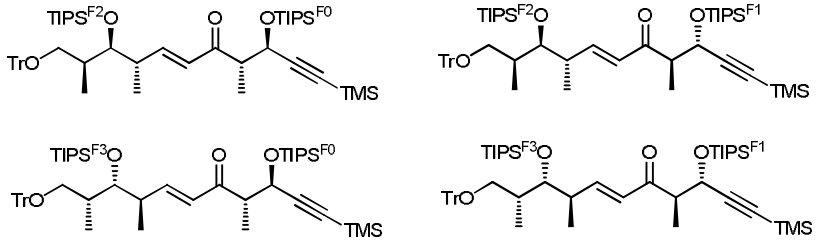
To a solution of a mixture of **14s** (0.66 g, 1.94 mmol) and **14r** (1.05 g, 1.94 mmol) in acetone and H_2O (8:1, 38 mL) at 0 °C was added osmium tetroxide (19.6 mg, 0.077 mmol). After 10 min, NMO (0.54 g, 4.61 mmol) was added. The brown mixture was stirred for 16 h at room temperature. After this time, periodic acid (1.77 g, 7.76 mmol) was added at 0 °C. The brown mixture was stirred for 30 min at 0 °C, then 1h at room temperature. The orange mixture was quenched with saturated sodium thiosulfate solution, extracted with ethyl acetate (3 x 50 mL). The organic layers were collected, combined, dried over sodium sulfate and solvent removed *in vacuo*. The product was purified by flash chromatography (ethyl acetate and hexane, 0:1 to 1:19) affording an orange oil in 90% yield (1.54 g, 3.5 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.86 (d, J = 9 Hz, 2H), 4.70 (m, 2H), 2.63 (m, 2H), 2.19-2.13 (m, 2H), 1.19-1.05 (m, 43H), 0.16 (s, 18H).

Dimethyl (3*S*,4*R*)-3-methyl-2-oxo-4-(triisopropylsilyloxy)-6-(trimethylsilyl)hex-5-ynylphosphonate and dimethyl (3*R*,4*S*)-4-(diisopropyl(3,3,4,4,5,5,6,6,6-nonafluorohexyl)silyloxy)-3-methyl-2-oxo-6-(trimethylsilyl)hex-5-ynylphosphonate (M-7).



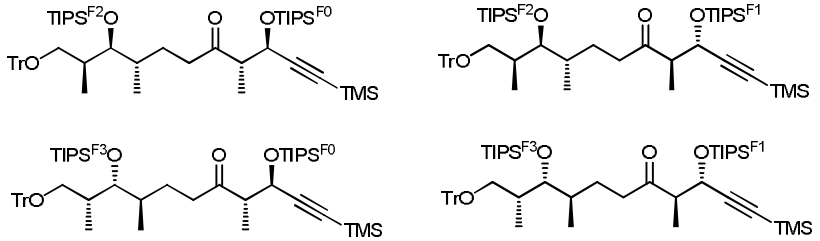
To a solution of dimethylmethylphosphonate (0.257 mL, 2.3 mmol) in THF (19 mL) at -78 °C was added dropwise 2.5 M *n*-BuLi (0.83 mL, 2.07 mmol). After 30 min, a mixture of aldehyde **M-15** (1.18 g, 2.67 mmol) in THF (5 mL) was added dropwise to the white mixture and stirred for 25 min at -78 °C. The reaction was then quenched with saturated NH_4Cl (8 mL) and warmed up to room temperature. The mixture was extracted with ethyl acetate (20 mL) and dichloromethane (3 x 20 mL). The organic layers were collected, combined, dried over sodium sulfate filtered and solvent removed *in vacuo*. The crude orange oil was dissolved in dichloromethane (40 mL), cooled to 0 °C where DMP (1.13 g, 2.67 mmol) was added in one portion, the mixture was stirred for 30 min at 0 °C and 30 min at room temperature. The mixture was quenched at 0 °C with a solution of saturated $NaHCO_3$ and $Na_2S_2O_4$ (1:1, 40 mL), extracted with dichloromethane (3 x 40 mL). The organic layers were collected, combined, washed with brine, dried over sodium sulfate, filtered and solvent evaporated. The product was purified by flash chromatography (ethyl acetate and hexane, 1:1) affording a yellow oil in 82% yield (0.96 g, 1.7 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.55 (d, J = 8.2 Hz, 2H), 3.78 (dd, J = 4.6, 11.2 Hz, 12 H), 3.43 (m, 2H), 3.10 (m, 4H), 2.10 (m, 2H), 1.18-1.00 (m, 43H), 0.15 (s, 18H).

M-5.



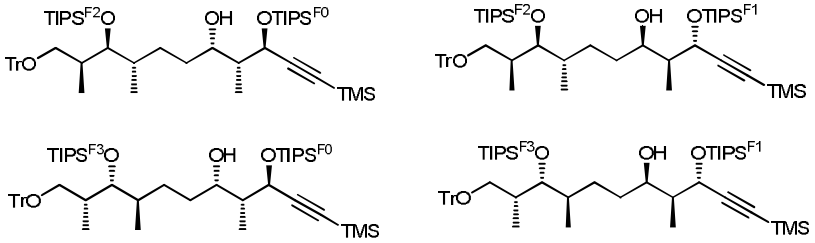
A mixture of phosphonates **M-7** (4.16 g, 7.37 mmol) was dissolved in THF (110 mL), cooled to 0 °C where activated $Ba(OH)_2$ (1.25 g, 7.3 mmol) was added. The mixture was warmed up to room temperature and stirred for 1 h. A mixture of aldehydes **M-6** (6.27 g, 6.98 mmol) in THF and H_2O (40:1, 184 mL) was added dropwise at 0 °C. The mixture was warmed up to room temperature and stirred for 16 h. The yellow mixture was quenched with saturated $NaHCO_3$ (100 mL), extracted with ethyl acetate (3 x 100 mL). The organic layers were collected, combined, dried over Na_2SO_4, filtered and solvent removed *in vacuo*. The product was purified by flash chromatography (2.5 %, ethyl acetate and hexane) yielding a yellow oil in 80% (7.45 g, 5.6 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.13 (m, 60H), 6.80 (m, 4H), 5.98 (m, 4H), 4.58 (m, 4H), 3.90-3.86 (m, 4H), 2.90 (m, 12H), 2.36 (m, 4H), 1.99-1.86 (m, 20H), 0.98-0.54 (m, 176H), 0.08 (s, 36H).

Reduction of M-5.



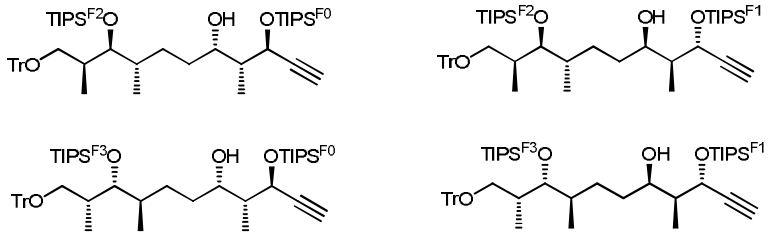
To a solution of **M-5** (0.98 g, 0.73 mmol) in degassed toluene (21 mL) and degassed water (79 µL, 4.38 mmol) was added quickly the Stryker reagent (red powder) (0.86 g, 0.44 mmol). The red mixture was stirred at room temperature for 72 h. The mixture was diluted with hexanes and the solvent was evaporated *in vacuo*. The product was purified by flash chromatography (2.5 %, Et_2O and hexane) affording a colorless oil (0.69 g, 0.52 mmol) in 71% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37-7.12 (m, 60H), 4.57 (m, 4H), 3.73 (m, 4H), 2.88 (m, 8H), 2.71 (m, 4H), 1.89 (m, 12H), 1.60 (m, 6H), 1.39 (m, 11H), 1.16 (m, 7H), 0.97-0.77 (m, 176H), 0.06 (s, 36H).

M-16.



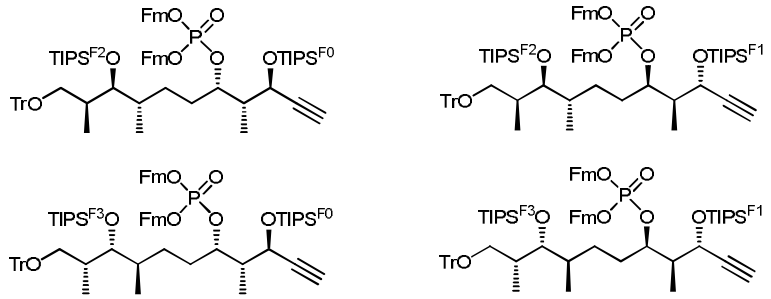
To a solution of the ketones (0.411 g, 0.32 mmol) in THF (3 mL) at 0 °C was added dropwise 1M LiAl(O*t*-Bu)$_3$H (0.97 mL, 0.97 mmol). The yellow mixture was warmed up to room temperature and left stirred for 5.5h. The mixture was quenched at 0 °C with saturated NH_4Cl (5 mL), extracted with ethyl acetate (3 x 5 mL). Organic layers were collected, combined, dried over sodium sulfate and the solvent was evaporated. The product was purified by flash chromatography (2.5% to 5%, Et_2O and hexane) affording a colorless oil in 88% yield (0.37 g, 0.28 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 7.44 Hz, 24H), 7.31-7.19 (m, 36H), 4.56-4.48 (m, 4H), 4.12 (m, 4H), 3.79 (m, 4H), 3.16-2.96 (m, 13H), 2.45 (m, 3H), 2.01 (m, 16H), 1.55-1.44 (m, 16H), 1.21-0.68 (176H), 0.15 (s, 36H).

M-17.



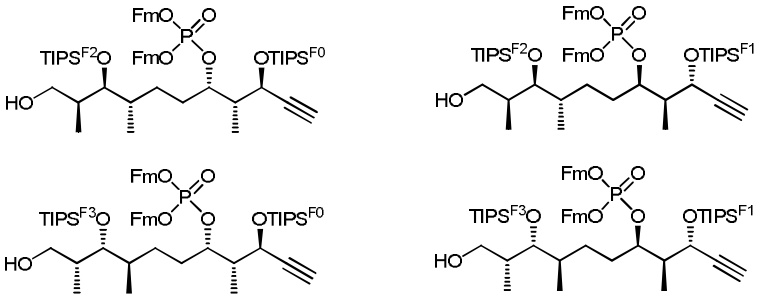
To a solution of **M-16** (2.12 g, 1.63 mmol) in THF and MeOH (2:3, 50 mL) at 0 °C was added KOH (0.38 g, 6.83 mmol). Light yellow mixture was left stirred at 0 °C. After 3.5 h, the mixture was diluted with water (50 mL), extracted with ethyl acetate (3 x 50 mL). The organic layers were combined, dried over sodium sulfate, filtered and solvent evaporated. The product was purified by flash chromatography (2.5%, Et_2O and hexane) affording a colorless oil in 85% yield (1.76 g, 1.4 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42 (d, J = 7.21 Hz, 24H), 7.31-7.19 (m, 36H), 4.58 (m, 3H), 4.51 (m, 1H), 4.24 (m, 3H), 4.05 (m, 1H), 3.85-3.80 (m, 4H), 2.97 (m, 12H), 2.45 (m, 4H), 2.02 (m, 16H), 1.62-1.44 (m, 20H), 1.27-0.60 (m, 176H).

M-18.



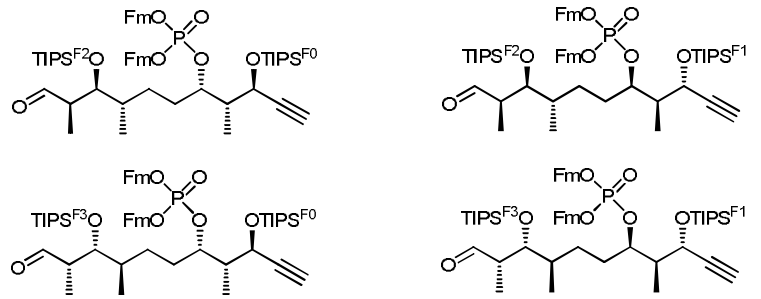
To a solution of **M-17** (50.5 mg, 0.04 mmol) in acetonitrile (0.7 mL) at 0 °C was added tetrazole (0.24 mL, 0.11 mmol) followed by phosphoramidite (66.5 mg, 0.13 mmol) in dichloromethane (0.5 mL). The cloudy mixture was warmed up to room temperature and stirred for 4.5 h. The reaction mixture was quenched at 0 °C with 0.1 M solution of iodine in pyridine/THF/H_2O (2:7:1, 1.2 mL). The orange solution was warmed up to room temperature and stirred for 5 min, after which it was poured into a solution of saturated $Na_2S_2O_4$ and $NaHCO_3$ (1:1, 6 mL). The organic layers were separated, extracted with ethyl acetate (3 x 1 mL), combined, dried over sodium sulfate, filtered and solvent evaporated. The product was purified by flash chromatography (2.5% to 25%, ethyl acetate and hexane) yielding a colorless oil in 81% yield (55.5 mg, 0.032 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (m, 64H), 7.53-7.19 (m, 60H), 4.49 (m, 4H), 4.44 (m, 4H), 4.24-4.09 (m, 24H), 3.74 (m, 4H), 2.92-2.85 (m, 8H), 2.37-2.33 (m, 4H), 2.06-1.98 (m, 20H), 1.59-1.46 (m, 16H), 1.15-0.68 (m, 176H).

Detritylation of M-18.



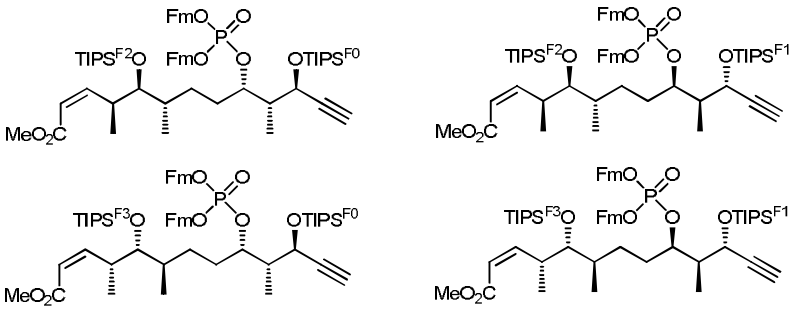
To a solution of **M-18** (1.96 g, 1.15 mmol) in dichloromethane (75 mL) and MeOH (40 mL) was added CSA (0.45 g, 1.94 mmol) at 0 °C. The mixture was stirred at 0 °C for 15 min then warmed up to room temperature. After 3.5 h, the reaction mixture was poured into saturated $NaHCO_3$, extracted with dichloromethane (3 x 50 mL). The organic layers were collected, combined, washed with brine, dried over sodium sulfate, filtered and solvent removed *in vacuo*. The product was purified by flash chromatography (ethyl acetate and hexane, 1:4) affording a light yellow oil in 78% yield (1.34 g, 0.91 mmol): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.76-7.18 (m, 64H), 4.41-4.36 (m, 8H), 4.27-4.09 (m, 28H), 4.02-3.98 (m, 4H), 3.44-3.32 (m, 8H), 2.38 (d, J = 2.4 Hz, 2H), 2.37 (d, J = 1.8 Hz, 2H), 2.21-2.04 (m, 16H), 1.94-1.58 (m, 10H), 1.07-0.77 (s, 176H).

M-19.



To a solution of the above alcohols (1.19 g, 0.81 mmol) in dichloromethane (22 mL) at 0 °C was successively added $NaHCO_3$ (782 mg, 9.31 mmol) and DMP (515 mg, 1.22 mmol). After stirring for 1.5 h at 0 °C and 15 min at room temperature, the white mixture was poured into a solution of saturated $NaHCO_3$ and $Na_2S_2O_3$ (1:1, 50 mL), extracted with dichloromethane (3 x 30 mL). The organic layers were collected, combined, dried over sodium sulfate, filtered and solvent evaporated. The crude residue was purified by flash chromatography (ethyl acetate and hexane, 1:4) affording a colorless oil in 93% yield (1.1 g, 0.75 mmol), which was used immediately for the next reaction.

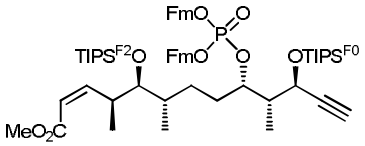
M-20.



To a mixture of 18-crown-6 (0.80 g, 2.96 mmol) in THF (37 mL) and bis(2,2,2-trifluoroethyl) (methoxycarbonylmethyl)phosphonate (0.31 mL, 1.48 mmol) at -78 °C was added dropwise 0.5 M KHMDS (2.22 mL, 1.11 mmol). The mixture was stirred at -78 °C for 30 min, then warmed up to -42 °C over 25 min and stirred for 1 h at this temperature. The mixture was then cooled back to -78 °C where **M-19** (1.04 g, 0.74 mmol) in THF

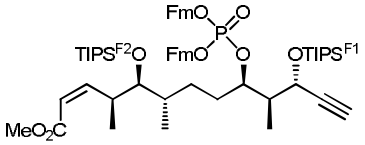
(12 mL) was added dropwise. The clear mixture was stirred at –78 °C for 5h. Then the solution was quenched at -78 °C with saturated NH_4Cl and warmed up to room temperature. It was then extracted with ethyl acetate (3 x 40 mL). The organic layers were collected, combined, dried over sodium sulfate, filtered and solvent removed evaporated. The product was purified by flash chromatography (ethyl acetate and hexane, 1:4) affording light yellow oil (1.06 g, 0.7 mmol) in 95% yield, which was demixed by fluorous HPLC (FluoroFlash PFC8 FTI preparative column, MeOH in H_2O (0 to100% over 10 min)) affording the four desired compounds.
20ss: 199.4 mg (R_t = 3.27 min, FTI2 analytical column)
20rs: 304.3 mg (R_t = 4.72 min)
20sr: 163 mg (R_t = 5.24 min)
20rr: 22.6 mg (R_t = 10.12 min)
20rr-1Fm: 21.3 mg (21.73 min)
Impurities: 140 mg

(4*S*,5*S*,6*S*,9*S*,10*S*,11*R*,*Z*)-Methyl 9-(bis((9H-fluoren-9-yl)methoxy)phosphoryloxy)-5-(diisopropyl-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyloxy)-4,6,10-trimethyl-11-(triisopropylsilyloxy)tridec-2-en-12-ynoate (20ss).



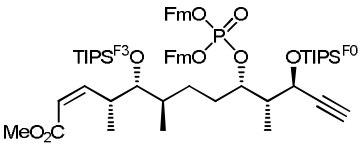
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.74-7.21 (m, 16H), 6.05 (dd, *J* = 11.5, 11.0 Hz, 1H), 5.68 (d, *J* = 11.5 Hz, 1H), 4.53 (m, 1H), 4.47 (dd, *J* = 6.0, 2.0 Hz, 1H), 4.22 (m, 4H), 4.12 (m, 2H), 3.78-3.73 (m, 2H), 3.64 (s, 3H), 3.58 (m, 1H), 2.35 (d, *J* = 2.0 Hz, 1H), 2.13 (m, 4H), 1.98 (m, 1H), 1.60-1.46 (m, 5H), 1.07-0.91 (m, 44H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.2, 153.7, 143.3, 143.2, 143.1, 141.3, 127.8, 127.0, 125.2, 125.10, 125.07, 120.0, 119.9, 117.8, 80.7 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 80.1, 77.2, 74.3, 69.1 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 68.0, 63.7, 51.0, 47.9 (d, *J* (^{13}C,^{31}P) 7.5 Hz), 43.5 (d, *J* (^{13}C,^{31}P) 5.8 Hz), 39.8, 35.6, 31.2, 28.1, 25.6, 25.5, 18.07, 18.06, 17.90, 17.89, 17.80, 17.7, 15.8, 15.7, 15.5, 13.2, 13.1, 12.4, 9.9, 1.2; LRMS (API, M + H) 1365.4; HRMS (ESI) calcd. for ($C_{68}H_{87}F_{13}O_8PSi_2$) 1365.5470, found 1365.5499.

(4*S*,5*S*,6*S*,9*R*,10*R*,11*S*,*Z*)-Methyl 9-(bis((9H-fluoren-9-yl)methoxy)phosphoryloxy)-11-(diisopropyl-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)silyloxy)-5-(diisopropyl(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooctyl)silyloxy)-4,6,10-trimethyltridec-2-en-12-ynoate (20sr).



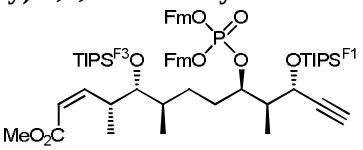
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76-7.20 (m, 16H), 6.10 (dd, *J* = 12.0, 11.5 Hz, 1H), 5.71 (d, *J* = 12.0 Hz, 1H), 4.60-4.55 (m, 1H), 4.48 (dd, *J* = 6.0, 2.0 Hz, 1H), 4.29-4.23 (m, 4H), 4.17-4.07 (m, 2H), 3.83-3.71 (m, 2H), 3.66 (s, 3H), 3.59-3.54 (m, 1H), 2.41 (d, *J* = 2.0 Hz, 1H), 2.22-2.07 (m, 8H), 1.96-1.85 (m, 1H), 1.77-1.63 (m, 2H), 1.60-1.50 (m, 2H), 1.15-0.88 (m, 37H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.3, 153.6, 143.2, 143.1, 143.09, 143.07, 141.2, 127.6, 127.0, 125.2, 125.1, 125.0, 120.0, 119.9, 118.1, 80.3, 79.6 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 77.2, 74.8, 69.1 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 69.0 (d, *J* (^{13}C,^{31}P) 5.0 Hz), 68.0, 63.9, 51.0, 48.0 47.9, 43.3 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 38.3, 35.8, 30.8, 27.3, 25.7, 25.6, 25.5, 25.4, 25.3, 25.2, 18.0, 17.91, 17.86, 17.78, 17.76, 17.71, 17.65, 17.62, 17.60, 17.50, 17.45, 17.41, 17.29, 15.9, 15.8, 13.2, 13.11, 13.05, 12.59, 1258, 1246, 12.4, 9.6, 1.3, 0.7; LRMS (API, M + H) 1569.3; HRMS (ESI) calcd. for ($C_{71}H_{84}F_{22}O_8PSi_2$) 1569.5091, found 1569.5067.

(4*R*,5*R*,6*R*,9*S*,10*S*,11*R*,*Z*)-Methyl 9-(bis((9H-fluoren-9-yl)methoxy)phosphoryloxy)-5-((3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diisopropylsilyloxy)-4,6,10-trimethyl-11-(triisopropylsilyloxy)tridec-2-en-12-ynoate (20rs).



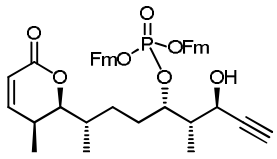
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 8, 15.5 Hz, 4H), 7.54 (t, *J* = 6.5 Hz, 2H), 7.48 (dd, *J* = 2.5, 7.5 Hz, 2H), 7.39 (t, *J* = 8 Hz, 2H), 7.33 (t, *J* = 6.5 Hz, 2H), 7.23 (dd, *J* = 7, 14 Hz, 4H), 6.04 (t, *J* = 6 Hz, 1H), 5.68 (d, *J* = 11.5 Hz, 1H), 4.53 (q, *J* = 6 Hz, 1H), 4.49 (dd, *J* = 2, 6 Hz, 1H), 4.22 (m, 4H), 4.11 (t, *J* = 6 Hz, 2H), 3.75 (m, 1H), 3.64 (s, 3H), 3.57 (m, 1H), 2.35 (d, *J* = 2 Hz, 1H), 2.10 (m, 3H), 1.93 (bs, 3H), 1.72 (m, 2H), 1.52 (m, 2H), 1.07-0.99 (m, 44H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.3, 153.6, 143.3, 143.2, 143.1, 143.1, 141.3, 127.8, 127.0, 125.2, 125.1, 119.9, 119.9, 118.0, 83.6, 80.3 (*J* (^{13}C,^{31}P) 7.5 Hz), 74.2, 69.1 (dd, *J* (^{13}C,^{31}P) 6.3, 13.8 Hz), 63.8, 51.0, 47.9 (d, *J* (^{13}C,^{31}P) 7.5 Hz), 43.4 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 39.2, 35.7, 30.9, 27.5, 25.5, 25.3, 18.0, 17.9, 17.8, 17.8, 17.616.0, 15.9, 15.6, 13.2, 13.1, 12.4, 12.2, 12.1, 9.8, 1.2; LRMS (API, M + H) 1465.3; HRMS (ESI) calcd. for ($C_{70}H_{87}F_{17}O_8PSi_2$) 1465.5377, found 1465.5406.

(4*R*,5*R*,6*R*,9*R*,10*R*,11*S*,*Z*)-Methyl 9-(bis((9H-fluoren-9-yl)methoxy)phosphoryloxy)-11-(diisopropyl-(3,3,4,4,5,5,6,6,6-nonafluorohexyl)silyloxy)-5-((3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodecyl)diisopropylsilyloxy)-4,6,10-trimethyltridec-2-en-12-ynoate (20rr).



^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (ddd, *J* = 3.5, 7.5, 15.5 Hz, 4H), 7.53 (t, *J* = 8.0 Hz, 2H), 7.49 (dd, *J* = 7.5, 17.0 Hz, 2H), 7.38 (dt, *J* = 3.5, 7.5 Hz, 2H), 7.33 (dt, *J* = 3.0, 7.5 Hz, 2H), 7.25 (m, 4H), 6.05 (t, *J* = 11 Hz, 1H), 5.69 (d, *J* = 11.5 Hz, 1H), 4.51 (m, 1H), 4.43 (dd, *J* = 2.0, 7.0 Hz, 1H), 4.21 (m, 4H), 4.10 (q, *J* = 7.0 Hz, 2H), 3.74 (m, 1H), 3.64 (s, 3H), 3.59 (t, *J* = 4.5 Hz, 1H), 2.39 (d, *J* = 2.0 Hz, 1H), 2.11 (m, 5H), 1.92 (m, 1H), 1.81 (m, 1H), 1.69 (m, 3H), 1.47 (m, 4H), 1.27 (m, 3H), 1.14-0.97 (m, 35 H), 0.91 (d, *J* = 4.0 Hz, 3H), 0.89-0.84 (m, 6H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 166.3, 153.7, 143.2, 143.1, 143.1, 141.3, 127.8, 127.0, 125.1, 125.0, 125.0, 119.9, 119.9, 118.3, 117.9, 83.1, 80.1, 80.0, 80.0, 74.9, 69.1, 63.9, 50.9, 47.9 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 43.6, 39.7, 35.6, 31.2, 25.7, 25.5, 25.4, 25.2, 28.3, 17.8, 17.8, 17.7, 17.6, 17.6, 17.5, 17.4, 15.7, 15.6, 13.2, 13.1, 12.6, 12.6, 9.7, 1.24, 0.66; $[\alpha]_D^{25}$ = –13 (*c* 2.21, $CHCl_3$); LRMS (API, M + H) 1669.5; HRMS (ESI) calcd. for ($C_{73}H_{84}F_{26}O_8PSi_2$) 1669.4904, found 1669.5027.

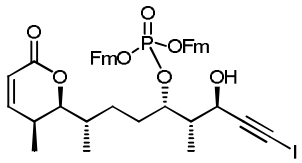
Bis((9H-fluoren-9-yl)methyl) (3*R*,4*S*,5*S*,8*S*)-3-hydroxy-4-methyl-8-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate (21ss).



The silyl ether **20ss** (53.1 mg, 0.039 mmol) was dissolved in THF (1.32 mL), cooled to 0 °C where HF•pyr (0.61 mL) was added dropwise. The white mixture was stirred at room temperature for 24 h. The mixture was carefully quenched at 0 °C with saturated $NaHCO_3$ (10 mL), extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were washed with brine (30 mL), collected, dried over anhydrous sodium sulfate, filtered, and the solvent was removed *in vacuo*. The residue was purified by flash chromatography (ethyl acetate and hexane, 3:2) to give the product (16.4 mg, 0.023 mmol) in 59% yield as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75-7.23 (m, 16H), 6.97 (dd, *J* = 9.5, 6.5 Hz, 1H), 5.95 (d, *J* = 9.5 Hz, 1H), 4.72-4.70 (m, 1H), 4.38-4.35 (m, 1H), 4.28-4.10 (m, 6H), 3.86 (dd, *J* = 10.4, 2.8 Hz, 1H), 2.44-2.39 (m, 1H), 2.45 (d, *J* = 2.1 Hz, 1H), 1.85-1.71 (m, 4H), 1.52-1.50 (m, 1H), 1.17-1.07 (m, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.71 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.5, 151.7, 143.3, 143.0, 142.9, 141.4, 141.4, 141.4, 128.0, 128.0, 127.9, 127.2, 127.2, 127.1, 125.1, 125.120.1, 120.0, 120.0, 84.2, 83.6, 78.6 (d, J (^{13}C, ^{31}P) 6.3 Hz), 73.0, 69.4 (d, J (^{13}C, ^{31}P) 6.3 Hz), 69.4 (d, J (^{13}C, ^{31}P) 6.3 Hz), 63.7, 60.4, 47.9 (d, J (^{13}C, ^{31}P) 7.5 Hz), 47.8 (d, J (^{13}C, ^{31}P) 7.5 Hz), 43.8

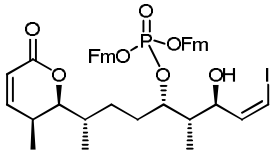
(d, J (13C, 31P) 3.8 Hz), 33.9, 30.7, 30.3, 28.5, 21.1, 14.7, 14.2, 10.8, 9.1; $[\alpha]_D^{25}$ = +43 (*c* 1.18, $CHCl_3$); FT-IR (thin film, KBr disk, ν cm^{-1}) 3294.0, 2976.1, 2931.9, 2864.0, 1716.4, 1450.5, 1377.5, 1273.4, 1249.2, 989.3, 915.6, 826.8, 758.1, 740.9; LRMS (API, M + Na) 739.2; HRMS (ESI) calcd. for ($C_{44}H_{45}O_7NaP$) 739.2801, found 739.2817.

Bis((9H-fluoren-9-yl)methyl) (3*R*,4*S*,5*S*,8*S*)-3-hydroxy-1-iodo-4-methyl-8-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate.



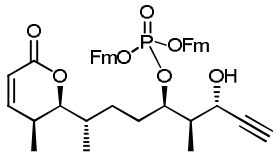
A solution of $AgNO_3$ (1.1 mg, 6.6 μmol) in DMF (30.6 μL) was added to a solution of the alkyne **21ss** (28.1 mg, 0.04 mmol) and *N*-iodosuccinimide (13.5 mg, 0.06 mmol) in DMF (0.44 mL) at 0 °C. The mixture was stirred at room temperature for 1.5 h. The reaction mixture was quenched by addition of saturated $Na_2S_2O_3$ (5 mL), extracted with ethyl acetate (3 x 5 mL). The organic layers were collected, washed with brine (30 mL), the dried and concentrated. The residue was purified by flash chromatography (ethyl acetate and hexane, 3:2) to give a colorless oil (31.8 mg, 0.04 mmol) in 97% yield: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75-7.19 (m, 16H), 6.96 (dd, *J* = 9.5, 6.5 Hz, 1H), 5.94 (d, *J* = 9.6 Hz, 1H), 4.69-4.63 (m, 1H), 4.40-4.32 (m, 1H), 4.27-4.10 (m, 6H), 3.86 (dd, *J* = 10.3, 2.6 Hz, 1H), 2.43-2.38 (m, 1H), 1.85-1.68 (m, 4H), 1.52-1.46 (m, 1H), 1.12-1.08 (m, 1H), 0.99 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 6.9 Hz, 3H), 0.79 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.5, 162.6, 151.7, 143.2, 143.0, 142.9, 142.9, 141.4, 141.4, 141.3, 128.0, 127.9, 127.9, 127.2, 127.2, 125.1, 125.0, 120.1, 120.0, 120.0, 94.8, 83.6, 78.5 (d, J (13C, 31P) 6.3 Hz), 69.4, 69.4, 69.3, 65.1, 48.0 (d, J (^{13}C, ^{31}P) 8.8 Hz) 47.8 (d, J (^{13}C, ^{31}P) 8.8 Hz), 43.9 (d, J (^{13}C, ^{31}P) 3.8 Hz), 36.5, 33.8, 31.5, 30.6 (d, J (13C, 31P) 3.8 Hz), 30.3, 29.6, 28.5, 14.7, 10.8, 9.2, 1.2; $[\alpha]_D^{25}$ = +38 (*c* 1.19, $CHCl_3$); FT-IR (thin film, KBr disk, ν cm^{-1}) 2922.3, 1718.3, 1449.9, 1377.7, 1254.1, 1105.3, 989.4, 914.3, 824.9, 757.6, 740.9; LRMS (API, M + Na) 865.0; HRMS (ESI) calcd. for ($C_{44}H_{44}O_7NaPI$) 865.1767, found 865.1799.

Bis((9H-fluoren-9-yl)methyl) (3*R*,4*S*,5*S*,8*S*,*Z*)-3-hydroxy-1-iodo-4-methyl-8-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-en-5-yl phosphate (3ss).



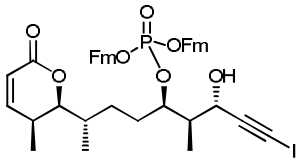
A solution of acetic acid (3.2 μL, 0.053 mmol) in 2-propanol (44 μL) was added dropwise over a period of 1 h to a mixture of iodoalkyne (11.9 mg, 0.014 mmol) and potassium azodicarboxylate (5.5 mg, 0.030 mmol) in 2-propanol (100 μL) and 1,4-dioxane (15 μL) and the mixture was stirred for 16 h at room temperature. The reaction mixture was quenched with pH7 buffer (5 mL) at 0 °C and extracted with ethyl acetate (3 x 5 mL). The combined organics layers were washed with brine (15 mL), then dried with sodium sulfate and concentrated. The residue was purified by flash chromatography (ethyl acetate and hexane, 3:2) to give *Z*-iodoalkene (6.8 mg, 0.008 mmol) in 58% yield as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78-7.20 (m, 16H), 6.97 (dd, *J* = 9.6, 6.5 Hz, 1H), 6.40 (d, *J* = 7.6 Hz, 1H), 6.17 (t, *J* = 7.6 Hz, 1H), 5.95 (d, *J* = 9.6 Hz, 1H), 4.80 (m, 1H), 4.45-4.40 (m, 1H), 4.36-4.12 (m, 6H), 3.87 (dd, *J* = 10.3, 2.8 Hz, 1H), 2.49-2.39 (m, 1H), 1.85-1.64 (m, 4H), 1.59-1.47 (m, 1H), 1.19-1.13 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.81 (d, *J* = 7.0 Hz, 3H), 0.78 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (151.1 MHz, $CDCl_3$) δ 164.5, 151.8, 143.2, 143.0, 142.9, 141.9, 141.4, 141.3, 128.9, 128.8, 127.2, 125.4, 125.2, 125.1, 120.07, 120.04, 120.01, 119.98, 119.96, 84.4, 84.0, 78.7 (d, *J* (^{13}C,^{31}P) 6.0 Hz), 74.2, 69.8 (d, *J* (^{13}C,^{31}P) 6.0 Hz), 69.6 (d, *J* (^{13}C,^{31}P) 6.0 Hz), 47.93 (d, *J* (^{13}C,^{31}P) 3.0 Hz), 47.88 (d, *J* (^{13}C,^{31}P) 3.0 Hz), 42.6 (d, *J* (^{13}C,^{31}P) 3.0 Hz), 33.9, 30.6, 30.3, 28.7, 14.6, 10.7, 8.2; $[\alpha]_D^{25}$ = +25 (*c* 0.76, $CHCl_3$).

Bis((9H-fluoren-9-yl)methyl) (3*S*,4*R*,5*R*,8*S*)-3-hydroxy-4-methyl-8-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate (21sr).



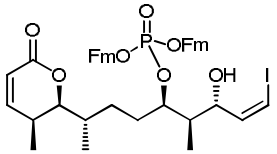
Following the procedure for **21ss**, **20sr** (60.2 mg, 0.038 mmol) was reacted with HF•pyr (0.6 mL). The purification by flash chromatography (ethyl acetate and hexane, 3:2) gave the product (18.6 mg, 0.026 mmol) in 68% yield as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78-7.25 (m, 16H), 6.97 (dd, J = 9.4, 6.6 Hz, 1H), 5.97 (d, J = 9.4 Hz, 1H), 4.62 (m, 1H), 4.44 (m, 1H), 4.22 (m, 1H), 4.33-4.11 (m, 6H), 3.90 (dd, J = 10.4, 2.5 Hz, 1H), 2.43 (m, 1H), 1.81-1.72 (m, 4H), 1.57-1.52 (m, 1H), 1.07 (m, 1H), 1.03 (d, J = 7.0 Hz, 3H), 0.89 (d, J = 6.8 Hz, 3H), 0.81 (d, J = 6.7 Hz, 3H); ^{13}C NMR (151.1 MHz, $CDCl_3$) δ 164.3, 151.5, 143.1, 142.95, 142.93, 142.89, 141.5, 141.34, 141.30, 127.90, 127.89, 127.80, 127.3, 127.2, 127.1, 127.07, 125.1, 125.0, 124.9, 120.1, 120.01, 120.00, 84.3, 83.7, 83.3, 78.0 (d, J (^{13}C,^{31}P) 5.9 Hz), 72.8, 69.4 (d, J (^{13}C,^{31}P) 6.3 Hz), 69.1 (d, J (^{13}C,^{31}P) 5.6 Hz), 63.5, 47.9 (d, J (^{13}C,^{31}P) 8.0 Hz), 47.8 (d, J (^{13}C,^{31}P) 8.0 Hz), 43.1 (d, J (^{13}C,^{31}P) 3.2 Hz), 33.5, 30.3, 29.80, 29.79, 29.7, 27.8, 14.4, 10.8, 8.8; $[\alpha]_D^{25}$ = +30 (*c* 1.97, $CHCl_3$); LRMS (API, M + Na) 739.2.

Bis((9H-fluoren-9-yl)methyl) (3*S*,4*R*,5*R*,8*S*)-3-hydroxy-1-iodo-4-methyl-8-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate.



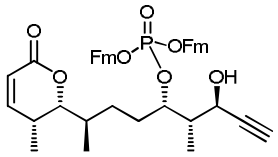
Following the procedure for iodination of **21ss**, the alkyne **21sr** (19.1 mg, 0.027 mmol) was reacted with $AgNO_3$ (0.7 mg, 0.004 mmol) and *N*-iodosuccinimide (8.3 mg, 0.040 mmol). The purification by flash chromatography (ethyl acetate and hexane, 3:2) gave the product (14.7 mg, 0.017 mmol) as a colorless oil in 63% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79-7.28 (m, 16H), 6.97 (dd, J = 9.5, 6.5 Hz, 1H), 5.97 (d, J = 9.5 Hz, 1H), 4.56 (m, 1H), 4.42 (m, 1H), 4.32-4.08 (m, 6H), 3.89 (dd, J = 10.3, 2.8 Hz, 1H), 2.43 (m, 1H), 1.75 (m, 4H), 1.52 (m, 1H), 1.00 (m, 1H), 1.03 (d, J = 7.0 Hz, 3H), 0.86 (d, J = 6.5 Hz, 3H), 0.80 (d, J = 7.0 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.4, 151.7, 143.0, 142.9, 142.8, 141.5, 141.34, 141.32, 141.30, 127.93, 127.88, 127.81, 127.3, 127.2, 127.12, 127.08, 125.05, 125.01, 124.9, 120.09, 120.05, 120.02, 120.00, 94.8, 83.3, 77.9 (d, J (^{13}C,^{31}P) 6.3 Hz), 69.4 (d, J (^{13}C,^{31}P) 6.3 Hz), 69.1 (d, J (^{13}C,^{31}P) 6.3 Hz), 65.1, 47.9 (d, J (^{13}C,^{31}P) 7.5 Hz), 47.8 (d, J (^{13}C,^{31}P) 7.5 Hz), 43.3 (d, J (^{13}C,^{31}P) 3.8 Hz), 33.5, 30.3, 29.8, 29.75, 29.68, 29.6, 27.8, 14.4, 10.8, 8.8, 0.9; $[\alpha]_D^{25}$ = +23 (*c* 1.71, $CHCl_3$); LRMS (API, M + Na) 865.0.

Bis((9H-fluoren-9-yl)methyl) (3*S*,4*R*,5*R*,8*S*,*Z*)-3-hydroxy-1-iodo-4-methyl-8-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-en-5-yl phosphate (3sr).



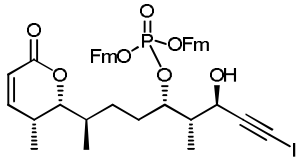
Following the procedure for **3ss**, the iodoalkyne (11.9 mg, 0.014 mmol) was reacted with acetic acid (3.7 μL, 0.062 mmol), potassium azodicarboxylate (6.4 mg, 0.030 mmol). The purification by flash chromatography (ethyl acetate and hexane, 3: 2) gave *Z*-iodoalkene (8.1 mg, 0.010 mmol) in 71% yield as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75-7.29 (m, 16H), 6.39 (d, J = 7.5 Hz, 1H), 6.16 (t, J = 8.0 Hz, 1H), 4.74 (m, 1H), 4.40 (m, 1H), 4.29 (m, 2H), 4.18 (m, 4H), 3.80 (m, 1H), 2.50 (m, 1H), 1.85-1.64 (m, 4H), 1.59-1.47 (m, 1H), 1.19-1.13 (m, 1H), 0.95 (d, J = 6.5 Hz, 3H), 0.81 (d, J = 7.0 Hz, 3H), 0.75 (d, J = 6.5 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.5, 151.7, 143.2, 143.0, 143.0, 141.9, 141.5, 141.4, 141.3, 127.9, 127.9, 127.9, 127.8, 127.2, 127.2, 127.1, 127.1, 125.4, 125.3, 125.2, 125.1, 120.1, 120.0, 84.4, 83.2, 78.2 (d, J (^{13}C,^{31}P) 6.3 Hz), 74.0, 69.9 (d, J (^{13}C,^{31}P) 6.3 Hz), 69.5 (d, J (^{13}C,^{31}P) 6.3 Hz), 48.0, 48.0, 41.9, 33.5, 30.3, 29.7, 29.6, 27.9, 14.4, 14.2, 10.8, 7.9, 0.9; $[\alpha]_D^{25}$ = +18 (*c* 0.63, $CHCl_3$).

Bis((9H-fluoren-9-yl)methyl) (3*R*,4*S*,5*S*,8*R*)-3-hydroxy-4-methyl-8-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate (21rs).



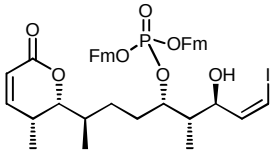
Following the procedure for **21ss**, **20rs** (38.8 mg, 0.026 mmol) was reacted with HF•pyr (0.41 mL). The purification by flash chromatography (ethyl acetate and hexane, 3:2) gave the product (16 mg, 0.022 mmol) in 86% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 1H), 7.74 (q, *J* = 10 Hz, 3H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.47 (m, 3H), 7.38 (q, *J* = 7 Hz, 2H), 7.31 (m, 4H), 7.25 (m, 2H), 6.97 (dd, *J* = 6.5, 9.5 Hz, 1H), 5.96 (d, *J* = 9.5 Hz, 1H), 4.60 (q, *J* = 8.5 Hz, 1H), 4.43 (m, 1H), 4.34 (m, 1H), 4.28 (m, 1H), 4.20 – 4.10 (m, 4H), 3.88 (dd, *J* = 3, 10.5 Hz, 1H), 2.42 (m, 1H), 1.82-1.71 (m, 4H), 1.58-1.50 (m, 1H), 1.03 (d, *J* = 7.5 Hz, 3H), 0.88 (d, *J* = 7 Hz, 3H), 0.79 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.5, 151.8, 143.1, 143.0, 142.9, 141.5, 141.4, 141.3, 128.0 (d, *J* (^{13}C, ^{31}P) 5.0 Hz), 127.9, 127.3, 127.2, 127.1 (d, J (^{13}C, ^{31}P) 3.8 Hz), 125.1, 125.1, 124.9, 120.1, 120.1, 120.0, 84.3, 83.3, 78.0 (d, *J* (^{13}C, ^{31}P) 6.3 Hz), 72.9, 69.5 (d, *J* (^{13}C, ^{31}P) 6.3 Hz), 69.1 (d, *J* (^{13}C, ^{31}P) 5.03 Hz), 63.5, 48.0 (d, *J* (^{13}C, ^{31}P) 8.8 Hz), 47.8 (d, *J* (^{13}C, ^{31}P) 7.5 Hz), 43.1 (d, *J* (^{13}C, ^{31}P) 3.8 Hz), 33.6, 30.3, 29.8 (d, *J* (^{13}C, ^{31}P) 3.8 Hz), 29.7, 27.8, 14.5, 10.9, 8.8; $[\alpha]_D^{25}$ = –42 (*c* 1.76, $CHCl_3$); LRMS (API, M + Na) 739.2.

Bis((9H-fluoren-9-yl)methyl) (3*R*,4*S*,5*S*,8*R*)-3-hydroxy-1-iodo-4-methyl-8-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate.



Following the procedure for iodination of **21ss**, the alkyne **21rs** (16 mg, 0.024 mmol) was reacted with $AgNO_3$ (0.7 mg, 0.004 mmol) and *N*-iodosuccinimide (8.3 mg, 0.040 mmol). The purification by flash chromatography (ethyl acetate and hexane, 3:2) gave the product (17.8 mg, 0.020 mmol) as a colorless oil in 83% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 1H), 7.71 (q, *J* = 7 Hz, 3H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.48 (t, *J* = 8.5, 2H), 7.43 (m, 3H), 7.31 (m, 4H), 7.26 (m, 3H), 6.96 (dd, *J* = 9.5, 6.5 Hz, 1H), 5.96 (d, *J* = 9.5 Hz, 1H), 4.56 (q, *J* = 7.5 Hz, 1H), 4.42 (q, *J* = 5.5 Hz, 1H), 4.3 (m, 2H), 4.2-4.02 (m, 5H), 3.89 (dd, *J* = 2.5, 10 Hz, 1H), 2.42 (m, 1H), 1.81-1.65 (m, 4H), 1.59-1.45 (m, 2H), 1.26 (m, 1H), 1.02 (d, *J* = 7 Hz, 3H), 0.84 (d, *J* = 6.5 Hz, 3H), 0.80 (d, *J* = 7 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 177.3, 164.5, 151.7, 143.1, 142.9, 141.5, 141.3, 128.0, 127.9, 127.3, 127.2, 127.1,125.1, 124.9, 120.1, 120.0, 94.9, 83.3, 78.0 (d, *J* (^{13}C, ^{31}P) 6.3 Hz), 69.4, 69.1, 65.1, 48.0 (d, *J* (^{13}C, ^{31}P) 8.8 Hz), 47.8 (d, *J* (^{13}C, ^{31}P) 8.8 Hz), 43.3, 33.6, 30.3, 29.6, 27.8, , 14.5, 10.8, 8.9, 1.0; $[\alpha]_D^{25}$ = –28 (*c* 1.56, $CHCl_3$); LRMS (API, M + Na) 865.0; HRMS (ESI) calcd. for ($C_{44}H_{44}O_7NaPI$) 865.1767, found 865.1849.

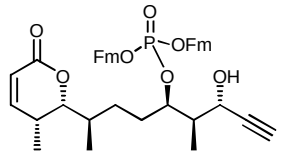
Bis((9H-fluoren-9-yl)methyl) (3*R*,4*S*,5*S*,8*R*,*Z*)-3-hydroxy-1-iodo-4-methyl-8-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-en-5-yl phosphate (3rs).



Following the procedure for **3ss**, the iodoalkyne (18.4 mg, 0.022 mmol) was reacted with acetic acid (5 μL, 0.087 mmol), potassium azodicarboxylate (8.5 mg, 0.044 mmol). The purification by flash chromatography (ethyl acetate and hexane, 3:2) gave *Z*-iodoalkene (8.7 mg, 0.010 mmol) in 49% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.5 Hz, 1H), 7.70 (q, *J* = 7.0 Hz, 4H), 7.63 (d, *J* = 7.5 Hz, 1H), 7.56-7.50(m, 4H), 7.43-7.22 (m, 11H), 6.96 (dd, *J* = 6.5, 9.5 Hz, 1H), 6.38 (d, *J* = 7.5 Hz, 1H), 6.16 (t, *J* = 8.0 Hz, 1H), 5.95 (d, *J* =

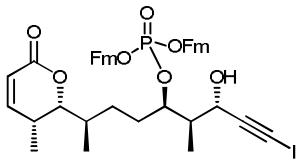
9.5 Hz, 1H), 4.73 (q, *J* = 7.2 Hz, 1H), 4.44-4.36 (m, 3H), 4.32-4.29 (m, 4H), 4.18-4.06 (m, 5H), 3.90 (dd, *J* = 3.0, 10.5 Hz, 1H), 2.44-2.41 (m, 1H), 1.80 (m, 3H), 1.63 (m, 2H), 1.09 (m, 1H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 7.0 Hz, 3H), 0.78 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (151.1 MHz, $CDCl_3$) δ 164.5, 151.6, 143.2, 143.1, 143.0, 141.9, 141.4, 127.9, 127.9, 127.2, 127.2, 125.4, 125.3, 125.1, 120.1, 120.1, 120.0, 84.4, 83.2, 78.2 (d, *J* (^{13}C,^{31}P) 6.0 Hz), 74.1, 69.9 (d, *J* (^{13}C,^{31}P) 6.0 Hz), 69.5 (d, *J* (^{13}C,^{31}P) 6.0 Hz), 48.0 (d, *J* (^{13}C,^{31}P) 9.1 Hz), 42.0 (d, *J* (^{13}C,^{31}P) 3.0 Hz), 33.5, 29.6, 29.4, 27.9, 14.5, 10.8, 7.9; $[\alpha]_D^{25}$ = –23 (*c* 0.7, $CHCl_3$); FT-IR (thin film, KBr disk, ν cm^{-1}) 2920.7, 1714.6, 1450.1, 1250.5, 1183.3, 989.5, 758.2, 740.8; LRMS (API, M + Na) 739.2.

Bis((9H-fluoren-9-yl)methyl) (3*S*,4*R*,5*R*,8*R*)-3-hydroxy-4-methyl-8-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate (21rr).



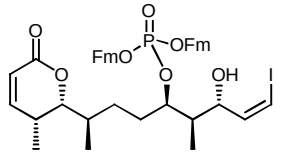
Following the procedure for **21ss**, **20rr** (22.4 mg, 0.013 mmol) was reacted with HF•pyr (0.2 mL). The purification by flash chromatography (ethyl acetate and hexane, 2:3) gave the product (8.2 mg, 0.011 mmol) in 88% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 7.5 Hz, 1H), 7.74 (q, *J* = 10 Hz, 3H), 7.58 (d, *J* = 7.4 Hz, 1H), 7.47 (m, 3H), 7.37 (q, *J* = 7.1 Hz, 2H), 7.30 (m, 4H), 7.25 (m, 2H), 6.96 (dd, *J* = 6.4, 9.5 Hz, 1H), 5.95 (d, *J* = 9.4 Hz, 1H), 4.61 (q, *J* = 8.4 Hz, 1H), 4.43 (m, 1H), 4.34 (m, 1H), 4.28 (m, 1H), 4.21-4.11 (m, 4H), 3.87 (dd, *J* = 3.1, 10.2 Hz, 1H), 2.42 (m, 1H), 1.83-1.70 (m, 4H), 1.59-1.49 (m, 1H), 1.03 (d, *J* = 7.4 Hz, 3H), 0.87 (d, *J* = 7.0 Hz, 3H), 0.79 (d, *J* = 6.5 Hz, 3H); $[\alpha]_D^{25}$ = –44 (*c* 0.82, $CHCl_3$); LRMS (API, M + Na) 739.2; HRMS (ESI) calcd. for ($C_{44}H_{45}O_7NaP$) 739.2801, found 739.2858.

Bis((9H-fluoren-9-yl)methyl) (3*S*,4*R*,5*R*,8*R*)-3-hydroxy-1-iodo-4-methyl-8-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-yn-5-yl phosphate.



Following the procedure for iodination of **21ss**, the alkyne **21rr** (9.1 mg, 0.013 mmol) was reacted with $AgNO_3$ (0.7 mg, 0.004 mmol) and *N*-iodosuccinimide (7 mg, 0.030 mmol). The purification by flash chromatography (ethyl acetate and hexane, 3:2) gave the product (7.9 mg, 0.009 mmol) as a colorless oil in 72% yield: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75-7.69 (m, 5H), 7.56-7.23 (m, 11H), 6.98 (dd, *J* = 5.5, 11.5 Hz, 1H), 5.94 (d, *J* = 11.4 Hz, 1H), 4.64 (m, 1H), 4.33 (m, 1H), 4.26-4.14 (m, 5H), 4.13-4.02 (m, 1H), 3.86 (dd, *J* = 3, 10.5 Hz, 1H), 2.41 (m, 1H), 1.75 (m, 4H), 1.49 (m, 1H), 1.1 (m, 1H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.90 (d, *J* = 7.0 Hz, 3H), 0.78 (d, *J* = 6.5 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.5, 151.6, 143.2, 142.9, 142.8, 141.4, 127.9, 127.9, 127.2, 127.1, 125.1, 120.09, 120.0, 94.8, 83.6, 78.5 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 69.4 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 65.2, 47.8 (d, *J* (^{13}C,^{31}P) 7.5 Hz), 47.8 (d, *J* (^{13}C,^{31}P) 7.5 Hz), 44 (d, *J* (^{13}C,^{31}P) 3.8 Hz), 33.8, 30.3, 28.5, 14.7, 10.8, 9.1, 0.9; $[\alpha]_D^{25}$ = –41 (*c* 0.79, $CHCl_3$); LRMS (API, M + Na) 865.0; HRMS (ESI) calcd. for ($C_{44}H_{44}O_7NaPI$) 865.1767, found 865.1791.

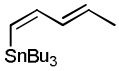
Bis((9H-fluoren-9-yl)methyl) (3*S*,4*R*,5*R*,8*R*,*Z*)-3-hydroxy-1-iodo-4-methyl-8-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)non-1-en-5-yl phosphate (3rr).



Following the procedure for **3ss**, the iodoalkyne (7.2 mg, 0.008 mmol) was reacted with acetic acid (2 μL, 0.035 mmol), potassium azodicarboxylate (3.1 mg, 0.020 mmol). The purification by flash chromatography (ethyl acetate and hexane, 3: 2) gave *Z*-iodoalkene (4.8 mg, 0.006 mmol) in 71% yield as a colorless oil: ^{1}H NMR (600

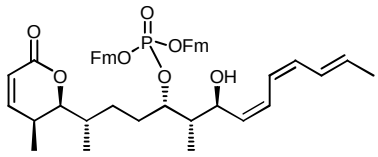
MHz, $CDCl_3$) δ 7.72 (m, 5H), 7.60 (d, *J* = 7.8 Hz, 1H), 7.52 (m, 4H), 7.41-7.24 (m, 12H), 6.96 (dd, *J* = 6.6, 9.6 Hz, 1H), 6.40 (d, *J* = 7.2 Hz, 1H), 6.17 (t, *J* = 7.8 Hz, 1H), 5.95 (d, *J* = 7.2 Hz, 1H), 4.74 (m, 1H), 4.40 (m, 1H), 4.79 (q, *J* = 6.6 Hz, 1H), 4.44 (m, 1H), 4.33 (m, 4H), 4.27 (m, 2H), 4.20-4.11 (m, 5H), 3.87 (dd, *J* = 3.0, 10.2 Hz, 1H), 2.43 (m, 1H), 1.75-1.68 (m, 3H), 1.55-1.50 (m, 2H), 1.18-1.12 (m, 2H), 1.00 (d, *J* = 7.2 Hz, 3H), 0.9 (m, 1H), 0.81 (d, *J* = 6.6 Hz, 3H), 0.78 (d, *J* = 6.6 Hz, 3H); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 164.6, 151.7, 143.3, 143.0, 143.0, 141.9, 141.4, 141.4, 127.9, 127.2, 125.4, 125.3, 120.1, 84.5, 83.7, 78.7 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 74.1, 69.8 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 69.6 (d, *J* (^{13}C,^{31}P) 6.3 Hz), 48.0, 48.0, 42.6, 34.0, 30.7, 30.3, 29.7, 29.6, 28.6, 14.7, 14.2, 10.8, 8.2; $[\alpha]_D^{25}$ = –27 (*c* 0.45, $CHCl_3$).

Tributyl((1*Z*,3*E*)-penta-1,3-dienyl)stannane (4).



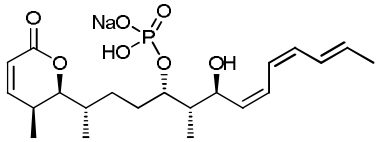
To a suspension of Schwartz reagent (Cp_2ZrH•HCl) (101 mg, 0.39 mmol) in THF (1 mL) at 0 °C was added dropwise (*E*)-tributyl(pent-3-en-1-ynyl)stannane (47 mg, 0.14 mmol) in THF (0.6 mL), the mixture was stirred for 5 min at 0 °C then the yellow suspension was warmed up to room temperature and stirred for 45 min. The dark orange mixture was cooled back to 0 °C where pentane (5.6 mL) was added, and then left stirred for 40 min at room temperature. The reaction mixture was filtered through a short pad of silica (7 cm high), eluted with pentane and ethyl ether (30:1, 30 mL), the filtrate was concentrated *in vacuo*. The crude oil was used immediately in the following step because of its instability: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.04 (dd, *J* = 10.5, 12.5 Hz, 1H), 6.02 (m, 1H), 5.90 (d, *J* = 12.5 Hz, 1H), 5.74 (m, 1H), 1.80 (d, *J* = 6.7 Hz, 3H), 1.60-1.43 (m 6H), 1.41-1.20 (m, 10H), 1.02-0.80 (m, 20H).

Bis((9*H*-fluoren-9-yl)methyl) (2*S*,5*S*,6*S*,7*S*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)tetradeca-8,10,12-trien-5-yl phosphate.



To a solution of the iodide **3ss** (4.5 mg, 5.33 µmol) and the dienylstannane **4** (6.9 mg, 19.29 µmol) in degassed THF and DMF (7%, 0.19 mL) at room temperature was added $Pd_2(dba)_3$•$CHCl_3$. (1.5 mg, 1.45 µmol). The mixture was stirred for 24 h in the dark, and concentrated *in vacuo*. To the resulting residue was added 2-propanol/hexane (1:4, 2 mL). The mixture was stirred for 15 min and filtered off through PTFE membrane syringe filter, which was rinsed with 2-propanol/hexane (1:4, 0.2 mL x 4). The filtrate was concentrated *in vacuo* and the residue was purified by normal-phase preparative HPLC (Chiral cel OD column with 2-propanol/hexane, 1:9) to give the triene (2.0 mg, 2.55 µmol) in 48% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.69 (m, 4H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.54 (t, *J* = 7.0 Hz, 2H), 7.49 (d, *J* = 7.6 Hz, 1H), 7.43-7.20 (m, 8H), 6.96 (dd, *J* = 6.5, 9.6 Hz, 1H), 6.55 (t, *J* = 11.6 Hz, 1H), 6.51 (dd, *J* = 12.1, 13.6 Hz, 1H), 5.98 (d, *J* = 9.6 Hz, 1H), 5.94 (t, *J* = 11.6 Hz, 1H), 5.83 (t, *J* = 11.1 Hz, 1H), 5.77 (dt, *J* = 6.9, 8.0 Hz, 1H), 5.38 (t, *J* = 10.3 Hz, 1H), 4.82 (m, 1H), 4.37-4.11 (m, 7H), 3.89 (dd, *J* = 2.9, 10.3 Hz, 1H), 3.79 (d, *J* = 4.6 Hz, 1H), 2.42 (m, 1H), 2.01 (m, 1H), 1.85 (m, 1H), 1.82 (d, *J* = 6.8 Hz, 3H), 1.76-1.52 (m, 3H), 1.14 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.81 (d, *J* = 6.7 Hz, 3H), 0.73 (d, *J* = 6.9 Hz, 3H); $[\alpha]_D^{25}$ = +45 (*c* 0.15, $CHCl_3$); FT-IR (thin film, NaCl, ν cm^{-1}) =3390.7, 2964.7, 2928.0, 1720.2, 1450.5, 1255.0, 1017.5; HRMS (ESI) calcd. for ($C_{49}H_{53}O_7NaP$) 807.3427, found 807.3735.

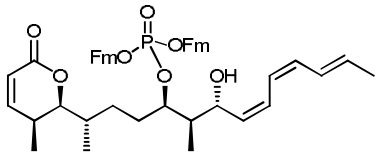
Sodium (2*S*,5*S*,6*S*,7*S*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)tetradeca-8,10,12-trien-5-yl hydrogenphosphate (1ss).



To a solution of the triene (1.6 mg, 2.04 µmol) in acetonitrile (0.4 mL) at 0 °C was added triethylamine (0.1 mL). The mixture was warmed to room temperature and stirred for 24 h in the dark. Toluene (2 mL) was added and the

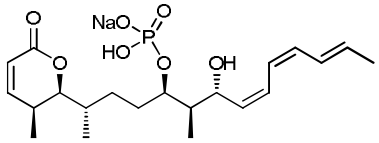
mixture was concentrated *in vacuo*. The residue was dissolved in water (5 mL) and rinsed with diethyl ether (2 mL) until no uv-active compounds are seen. The aqueous layer was concentrated *in vacuo* at 25 °C. The residue was dissolved in MeOH/water (1:1) and passed through the column of Dowex, which was washed successively with sat. $NaHCO_3$, water, and MeOH/water (1:1) before use. The collected mixture was concentrated *in vacuo* at 25 °C to give **1ss** (0.9 mg, 2.04 μmol) in 100% yield as a powder: ^{1}H NMR (500 MHz, CD_3OD) δ7.15 (dd, *J* = 6.6, 9.6 Hz, 1H), 6.57 (t, *J* = 11.8 Hz, 2H), 6.28 (t, *J* = 11.4 Hz, 1H), 5.97 (t, *J* = 11.0 Hz, 1H), 5.92 (d, *J* = 9.6 Hz, 1H), 5.75 (dq, *J* = 7.1, 14.5 Hz, 1H), 5.41 (t, *J* = 10.4 Hz, 1H), 4.61 (t, *J* = 9.6 Hz, 1H), 4.48 (m, 1H), 4.10 (dd, *J* = 2.7, 10.0 Hz, 1H), 2.58 (dt, *J* = 2.7, 6.7 Hz, 1H), 2.07 (m, 1H), 1.81 (m, 1H), 1.80 (d, *J* = 7.0 Hz, 3H), 1.78 (m, 1H), 1.55-1.46 (m, 2H), 1.21 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.78 (d, *J* = 6.8 Hz, 3H); $[\alpha]_D^{25}$ = +45 (*c* 0.08, CD_3OD); HRMS (ESI) calcd. for ($C_{21}H_{33}NaO_7P$) 451.1862, found 451.1881.

Bis((9*H*-fluoren-9-yl)methyl) (2*S*,5*R*,6*R*,7*R*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)tetradeca-8,10,12-trien-5-yl phosphate.



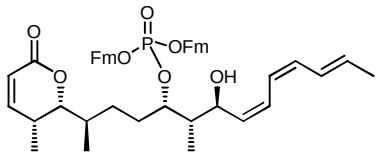
Following the procedure for the synthesis of triene from **3ss**, the iodide **3sr** (6.0 mg, 7.10 μmol) was reacted with $Pd_2(dba)_3$•$CHCl_3$. (2.0 mg, 1.93 μmol) and the dienylstannane **4** (9.2 mg, 25.87 μmol). The purification by normal-phase preparative HPLC (Chiral cel OD column with 2-propanol/hexane, 1:9) gave the triene (2.1 mg, 2.68 μmol) in 38% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ7.77-7.70 (m, 4H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 6.6 Hz, 2H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.41-7.22 (m, 8H), 6.98 (dd, *J* = 6.5, 9.6 Hz, 1H), 6.56 (t, *J* = 11.5 Hz, 1H), 6.47 (t, *J* = 12.0 Hz, 1H), 5.97 (d, *J* = 9.7 Hz, 1H), 5.92 (t, *J* = 11.5 Hz, 1H), 5.84 (t, *J* = 11.0 Hz, 1H), 5.75 (dt, *J* = 6.9, 7.9 Hz, 1H), 5.39 (t, *J* = 10.2 Hz, 1H), 4.76 (q, *J* = 7.8 Hz, 1H), 4.41 (dt, *J* = 6.0, 9.9 Hz, 1H), 4.33-4.12 (m, 6H), 3.92 (dd, *J* = 2.9, 10.4 Hz, 1H), 3.82 (d, *J* = 4.7 Hz, 1H), 2.43 (dt, *J* = 2.9, 6.7 Hz, 1H), 2.02 (m, 1H), 1.85 (m, 1H), 1.82 (d, *J* = 6.7 Hz, 3H), 1.77 (m, 1H), 1.74-1.51 (m, 2H), 1.08 (m, 1H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.69 (d, *J* = 6.9 Hz, 3H); $[\alpha]_D^{25}$ = +28 (*c* 0.21, $CHCl_3$); FT-IR (thin film, NaCl, ν cm^{-1}) =3367.4, 2926.3, 1717.8, 1450.5, 1253.1, 1018.1; HRMS (ESI) calcd. for ($C_{49}H_{53}O_7NaP$) 807.3427, found 807.4073.

Sodium (2*S*,5*R*,6*R*,7*R*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*S*,3*S*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)tetradeca-8,10,12-trien-5-yl hydrogenphosphate (1sr).



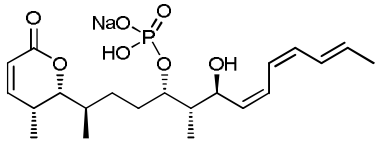
Following the procedure for **1ss**, the triene (2.1 mg, 2.67 μmol) was reacted with triethylamine (0.3 mL). The work-up and ion-exchange procedure used for **1ss** gave **1sr** (1.2 mg, 2.67 μmol) in 100% yield as a powder: ^{1}H NMR (500 MHz, CD_3OD) δ7.15 (dd, *J* = 6.6, 9.6 Hz, 1H), 6.57 (t, *J* = 11.8 Hz, 1H), 6.56 (t, *J* = 11.6 Hz, 1H), 6.28 (t, *J* = 11.1 Hz, 1H), 5.96 (t, *J* = 11.5 Hz, 1H), 5.92 (d, *J* = 9.6 Hz, 1H), 5.75 (dq, *J* = 7.0, 14.7 Hz, 1H), 5.41 (t, *J* = 10.3 Hz, 1H), 4.62 (t, *J* = 9.6 Hz, 1H), 4.50 (m, 1H), 4.09 (dd, *J* = 2.9, 10.3 Hz, 1H), 2.58 (dt, *J* = 2.9, 6.8 Hz, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.80 (d, *J* = 7.0 Hz, 3H), 1.78 (m, 1H), 1.65 (m, 1H), 1.50 (m, 1H), 1.17 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H); $[\alpha]_D^{25}$ = +29 (*c* 0.09, CD_3OD); HRMS (ESI) calcd. for ($C_{21}H_{33}NaO_7P$) 451.1862, found 451.1878.

Bis((9*H*-fluoren-9-yl)methyl) (2*R*,5*S*,6*S*,7*S*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)tetradeca-8,10,12-trien-5-yl phosphate.



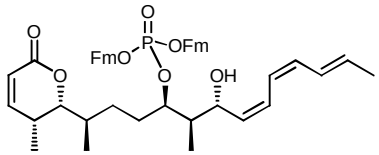
Following the procedure for the synthesis of triene from **3ss**, the iodide **3rs** (4.0 mg, 4.73 μmol) was reacted with $Pd_2(dba)_3$•$CHCl_3$. (1.3 mg, 1.25 μmol) and the dienylstannane **4** (7.4 mg, 20.73 μmol). The purification by normal-phase preparative HPLC (Chiral cel OD column with 2-propanol/hexane, 1:9) gave the triene (2.5 mg, 3.19 μmol) in 66% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.69 (m, 4H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.44-7.22 (m, 8H), 6.98 (dd, *J* = 6.6, 9.5 Hz, 1H), 6.54 (t, *J* = 11.4 Hz, 1H), 6.50 (dd, *J* = 12.5, 13.4 Hz, 1H), 5.97 (d, *J* = 9.7 Hz, 1H), 5.92 (t, *J* = 11.5 Hz, 1H), 5.82 (t, *J* = 11.0 Hz, 1H), 5.76 (dt, *J* = 7.1, 7.7 Hz, 1H), 5.37 (t, *J* = 10.0 Hz, 1H), 4.78 (q, *J* = 7.5 Hz, 1H), 4.46-4.09 (m, 7H), 3.92 (dd, *J* = 2.5, 10.3 Hz, 1H), 3.79 (d, *J* = 9.3 Hz, 1H), 2.43 (m, 1H), 2.01 (m, 1H), 1.84 (m, 1H), 1.82 (d, *J* = 6.6 Hz, 3H), 1.78 (m, 1H), 1.60 (m, 1H), 1.55 (m, 1H), 1.08 (m, 1H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.69 (d, *J* = 6.9 Hz, 3H); $[\alpha]_D^{25}$ = –13 (*c* 0.15, $CHCl_3$); FT-IR (thin film, NaCl, ν cm^{-1}) = 3368.2, 2928.3, 1717.4, 1450.7, 1253.3, 1018.7; HRMS (ESI) calcd. for ($C_{49}H_{53}O_7NaP$) 807.3427, found 807.3552.

Sodium (2*R*,5*S*,6*S*,7*S*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)tetradeca-8,10,12-trien-5-yl hydrogenphosphate (1rs).



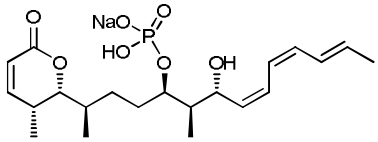
Following the procedure for **1ss**, the triene (2.7 mg, 3.44 μmol) was reacted with triethylamine (0.3 mL). The work-up and ion-exchange procedure used for **1ss** gave **1rs** (1.5 mg, 3.33 μmol) in 97% yield as a powder: ^{1}H NMR (300 MHz, CD_3OD) δ 7.15 (dd, *J* = 6.5, 9.6 Hz, 1H), 6.59 (t, *J* = 11.4 Hz, 1H), 6.55 (t, *J* = 11.3 Hz, 1H), 6.30 (t, *J* = 11.2 Hz, 1H), 5.95 (t, *J* = 10.8 Hz, 1H), 5.93 (d, *J* = 9.6 Hz, 1H), 5.75 (dq, *J* = 7.1, 14.8 Hz, 1H), 5.42 (t, *J* = 10.2 Hz, 1H), 4.63 (t, *J* = 9.3 Hz, 1H), 4.48 (m, 1H), 4.10 (dd, *J* = 2.9, 10.4 Hz, 1H), 2.57 (dt, *J* = 2.7, 6.8 Hz, 1H), 1.91 (m, 1H), 1.82 (m, 1H), 1.80 (d, *J* = 6.8 Hz, 3H), 1.78 (m, 1H), 1.65 (m, 1H), 1.49 (m, 1H), 1.13 (m, 1H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.98 (d, *J* = 6.9 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H); $[\alpha]_D^{25}$ = –9 (*c* 0.13, CD_3OD); HRMS (ESI) calcd. for ($C_{21}H_{33}NaO_7P$) 451.1862, found 451.1850.

Bis((9*H*-fluoren-9-yl)methyl) (2*R*,5*R*,6*R*,7*R*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2*H*-pyran-2-yl)tetradeca-8,10,12-trien-5-yl phosphate.



Following the procedure for the synthesis of triene from **3ss**, the iodide **3rr** (5.1 mg, 6.03 μmol) was reacted with $Pd_2(dba)_3$•$CHCl_3$. (1.7 mg, 1.64 μmol) and the dienylstannane **4** (7.8 mg, 21.87 μmol). The purification by normal-phase preparative HPLC (Chiral cel OD column with 2-propanol/hexane, 1:9) gave the triene (1.2 mg, 1.53 μmol) in 25% yield as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78-7.69 (m, 4H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.8 Hz, 2H), 7.49 (d, *J* = 7.4 Hz, 1H), 7.44-7.22 (m, 8H), 6.98 (dd, *J* = 6.6, 9.5 Hz, 1H), 6.54 (t, *J* = 11.4 Hz, 1H), 6.50 (dd, *J* = 12.5, 13.4 Hz, 1H), 5.97 (d, *J* = 9.7 Hz, 1H), 5.92 (t, *J* = 11.5 Hz, 1H), 5.82 (t, *J* = 11.0 Hz, 1H), 5.76 (dt, *J* = 7.1, 7.7 Hz, 1H), 5.37 (t, *J* = 10.0 Hz, 1H), 4.78 (q, *J* = 7.5 Hz, 1H), 4.46-4.09 (m, 7H), 3.92 (dd, *J* = 2.5, 10.3 Hz, 1H), 3.79 (d, *J* = 9.3 Hz, 1H), 2.43 (m, 1H), 2.01 (m, 1H), 1.84 (m, 1H), 1.82 (d, *J* = 6.6 Hz, 3H), 1.78 (m, 1H), 1.60 (m, 1H), 1.55 (m, 1H), 1.08 (m, 1H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.82 (d, *J* = 6.9 Hz, 3H), 0.69 (d, *J* = 6.9 Hz, 3H); $[\alpha]_D^{25}$ = –44 (*c* 0.08, $CHCl_3$); FT-IR (thin film, NaCl, ν cm^{-1}) = 3367.3, 2926.1, 1717.7, 1451.3, 1020.8; HRMS (ESI) calcd. for ($C_{49}H_{53}O_7NaP$) 807.3427, found 807.3604.

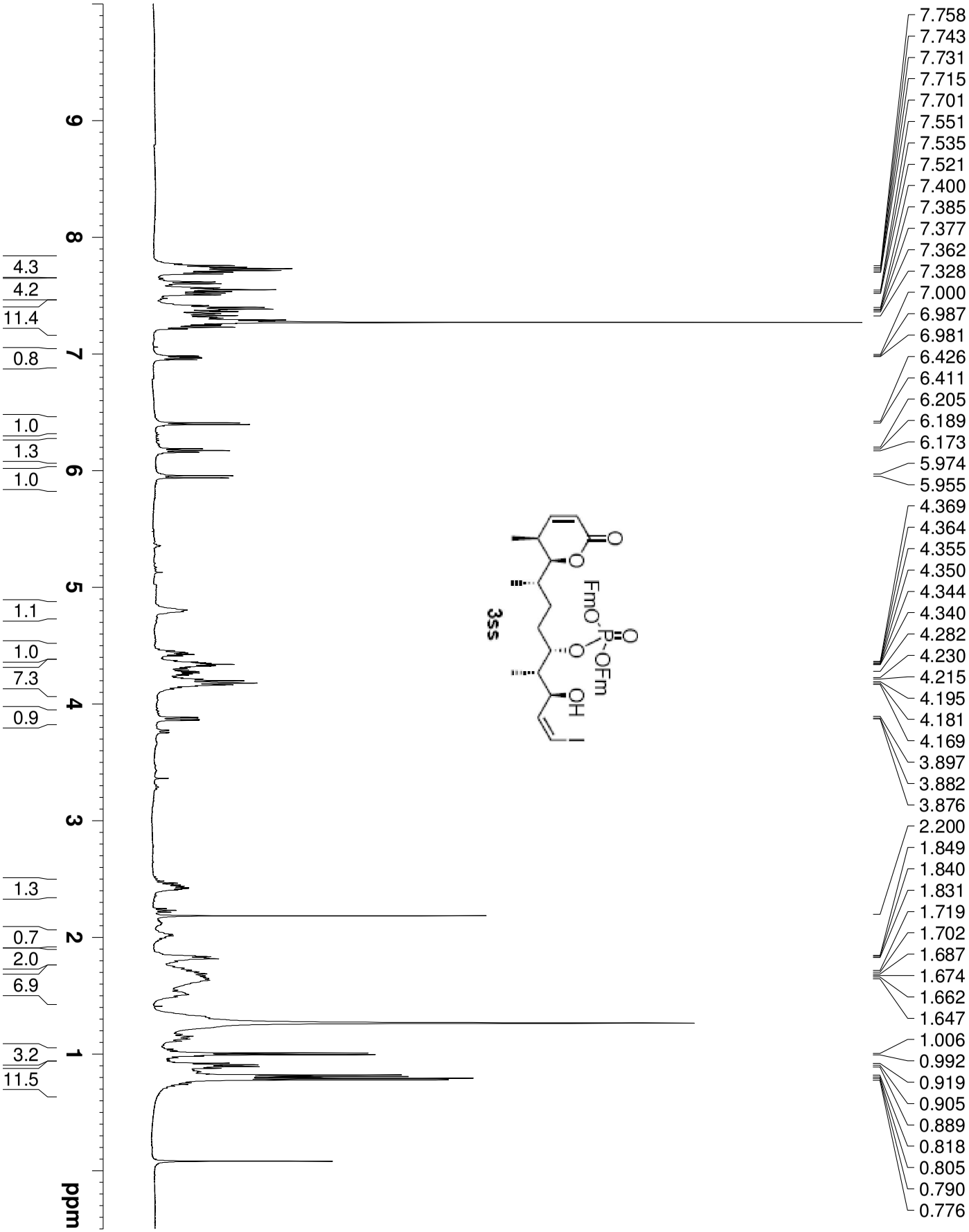
Sodium (2*R*,5*R*,6*R*,7*R*,8*Z*,10*Z*,12*E*)-7-hydroxy-6-methyl-2-((2*R*,3*R*)-3-methyl-6-oxo-3,6-dihydro-2H-pyran-2-yl)tetradeca-8,10,12-trien-5-yl hydrogenphosphate (1rr).



Following the procedure for **1ss**, the triene (1.0 mg, 1.27 µmol) was reacted with triethylamine (0.2 mL). The work-up and ion-exchange procedure used for **1ss** gave **1rr** (0.6 mg) in 100% yield as a powder: ^{1}H NMR (300 MHz, CD_3OD) δ7.15 (dd, *J* = 6.6, 9.6 Hz, 1H), 6.57 (t, *J* = 11.8 Hz, 1H), 6.56 (t, *J* = 11.6 Hz, 1H), 6.28 (t, *J* = 11.1 Hz, 1H), 5.96 (t, *J* = 11.5 Hz, 1H), 5.92 (d, *J* = 9.6 Hz, 1H), 5.75 (dq, *J* = 7.0, 14.7 Hz, 1H), 5.41 (t, *J* = 10.3 Hz, 1H), 4.62 (t, *J* = 9.6 Hz, 1H), 4.50 (m, 1H), 4.09 (dd, *J* = 2.9, 10.3 Hz, 1H), 2.58 (dt, *J* = 2.9, 6.8 Hz, 1H), 1.92 (m, 1H), 1.82 (m, 1H), 1.80 (d, *J* = 7.0 Hz, 3H), 1.78 (m, 1H), 1.65 (m, 1H), 1.50 (m, 1H), 1.17 (m, 1H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 6.8 Hz, 3H), 0.76 (d, *J* = 6.9 Hz, 3H); $[\alpha]_D^{25}$ = –28 (*c* 0.05, CD_3OD); HRMS (ESI) calcd. for ($C_{21}H_{33}NaO_7P$) 451.1862, found 451.1848.

Table 1. ^{1}H NMR comparison for natural cytostatin, **1ss**, and **1sr**.
δ ppm (multiplicity, *J*, Hz)

Position	Natural sample (500 MHz)	**1ss** (500 MHz)	**1sr** (500 MHz)
1	-	-	-
2	5.92 (d 9.5)	5.92 (d 9.6)	5.92 (d 9.6)
3	7.15 (dd 6.5, 9.5)	7.15 (dd 6.6, 9.6)	7.15 (dd 6.6, 9.6)
4	2.58 (dt,2.7, 6.9)	2.58 (dt, 2.7, 6.7)	2.58 (dt, 2.9, 6.8)
5	4.10 (dd 3.1, 10.3)	4.10 (dd 2.7, 10.0)	4.09 (dd 2.9, 10.3)
6	1.78 (m)	1.78 (m)	1.78 (m)
7	1.22, 1.80 (m)	1.21, 1.80 (m)	1.17, 1.82 (m)
8	1.51, 2.04 (m)	1.51, 2.07 (m)	1.65, 1.92 (m)
9	4.49 (m)	4.48 (m)	4.50 (m)
10	1.52 (m)	1.51 (m)	1.50 (m)
11	4.61 (t 9.6)	4.61 (t 9.6)	4.62 (t 9.6)
12	5.41 (t 11.0)	5.41 (t 10.4)	5.41 (t 10.3)
13	6.57 (t, 12.0)	6.57 (t, 11.8)	6.56 (t, 11.6)
14	6.28 (t 11.5)	6.28 (t, 11.4)	6.28 (t, 11.1)
15	5.97 (t 11.0)	5.97 (t 11.0)	5.96 (t 11.5)
16	6.57 (t, 12.0)	6.57 (t, 11.8)	6.57 (t, 11.8)
17	5.76 (dq 7.0, 14.5)	5.75 (dq 7.1, 14.5)	5.75 (dq 7.0, 14.7)
18	1.80 (d 6.7)	1.80 (d 7.0)	1.80 (d 7.0)
18	1.00 (d 7.0)	1.00 (d 7.0)	1.00 (d 7.0)
20	0.97 (d 6.7)	0.97 (d 6.7)	0.97 (d 6.8)
21	0.80 (d 6.7)	0.78 (d 6.8)	0.76 (d 6.9)


7.758
7.743
7.731
7.715
7.701
7.551
7.535
7.521
7.400
7.385
7.377
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7.000
6.987
6.981
6.426
6.411
6.205
6.189
6.173
5.974
5.955
4.369
4.364
4.355
4.350
4.344
4.340
4.282
4.230
4.215
4.195
4.181
4.169
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3.882
3.876
2.200
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1.840
1.831
1.719
1.702
1.687
1.674
1.662
1.647
1.006
0.992
0.919
0.905
0.889
0.818
0.805
0.790
0.776
4.3
4.2
11.4
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1.0
1.3
1.0
1.1
1.0
7.3
0.9
1.3
0.7
2.0
6.9
3.2
11.5
ppm
3ss

6.990
6.977
6.971
6.958
6.397
6.382
6.175
6.159
6.143
5.969
5.950
4.726
4.434
4.427
4.422
4.415
4.402
4.393
4.387
4.381
4.380
4.331
4.320
4.317
4.311
4.306
4.297
4.291
4.287
4.277
4.208
4.196
4.187
4.170
4.151
3.923
3.917
3.902
3.897
2.778
2.430
1.798
1.792
1.787
1.780
1.770
1.765
1.685
1.670
1.657
1.651
1.642
1.637
1.616
1.600
1.584
1.568
FmO
OFm
OH
I
3sr
9
8
7
6
5
4
3
2
1
ppm
5.5
1.3
4.5
14.2
1.2
1.0
0.2
1.3
1.0
1.1
0.3
2.6
3.0
4.8
1.1
0.3
2.1
1.7
0.6
0.7
3.8
3.9
3.6
3.4
1.0
1.3
5.6
3.7

6.989
6.976
6.970
6.957
6.398
6.382
6.176
6.160
6.144
5.968
5.949
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4.725
4.436
4.428
4.423
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4.403
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4.393
4.387
4.380
4.368
4.332
4.321
4.311
4.307
4.301
4.298
4.292
4.288
4.278
4.209
4.196
4.188
4.172
4.152
4.138
4.123
4.109
3.922
3.917
3.902
3.896
2.768
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2.429
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1.671
1.656
1.652
1.641
1.638
1.616
1.600
1.584
1.568

FmO
OFm
OH
I

3rs

9
8
7
6
5
4
3
2
1
ppm
4.6
1.2
3.7
10.4
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0.1
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0.9
1.0
2.4
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4.6
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1.4
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1.0
3.0
2.0
2.9
3.7
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1.1
3.9
3.3

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6.172
6.156
5.957
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4.326
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4.318
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4.304
4.290
4.276
4.265
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4.199
4.178
4.164
4.151
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3.880
3.865
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2.424
2.419
1.839
1.832
1.823
1.818
1.814
1.735
1.717
1.703
1.687
1.670
1.657
1.629
1.597
1.546
1.528
1.516
1.507
FmO
OFm
OH
I
3rr
9
8
7
6
5
4
3
2
1
ppm
4.7
1.3
3.4
12.7
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1.0
1.1
0.9
1.0
1.3
2.7
1.4
3.5
1.0
1.4
0.7
2.5
2.9
6.8
3.6
2.9
8.2

7.752
7.741
7.739
7.737
7.724
7.716
7.707
7.700
7.589
7.574
7.557
7.544
7.529
7.487
7.476
7.473
7.411
7.396
7.382
7.350
7.337
7.324
7.310
7.295
7.293
7.290
7.288
7.243
7.240
7.228
7.226
6.979
5.957
5.937
4.338
4.333
4.325
4.313
4.288
4.284
4.276
4.270
4.263
4.257
4.250
4.176
4.163
4.151
1.829
1.815
1.152
1.006
0.992
0.818
0.804
0.734
0.720
FmO
OFm
OH
Triene from 3ss
9
8
7
6
5
4
3
2
1
ppm
6.5
4.5
1.9
32.0
1.9
2.0
2.2
1.2
1.1
1.2
1.4
3.2
4.1
3.5
1.5
1.2
1.0
1.3
5.7
4.6
5.2
4.1

7.769
7.753
7.744
7.729
7.724
7.717
7.709
7.623
7.609
7.608
7.553
7.540
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7.397
7.396
7.383
7.349
7.343
7.333
7.327
7.312
7.310
7.298
7.295
7.253
7.250
7.238
7.236
6.972
6.966
6.953
5.970
5.969
5.950
4.333
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4.313
4.231
4.219
4.207
4.191
4.138
3.818
1.821
1.808
1.037
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0.829
0.816
0.693
0.679
FmO
OFm
OH
Triene from 3sr
9
8
7
6
5
4
3
2
1
ppm
6.2
1.3
2.9
1.8
3.0
20.6
1.4
2.0
2.2
1.0
1.1
1.1
1.3
1.4
2.9
4.2
2.0
1.5
0.9
1.7
3.7
4.1
5.0
2.9

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7.744
7.729
7.725
7.716
7.709
7.623
7.609
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7.540
7.527
7.488
7.474
7.425
7.411
7.397
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7.364
7.349
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7.327
7.312
7.297
7.252
7.237
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5.951
5.923
5.823
4.332
4.325
4.314
4.303
4.244
4.237
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4.225
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0.816
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0.679
FmO
OFm
OH
Triene from 3rs
9
8
7
6
5
4
3
2
1
ppm
6.3
1.5
3.0
1.5
3.4
19.0
0.9
2.3
2.0
1.1
1.4
1.1
1.4
1.5
2.9
4.9
1.7
1.0
1.5
1.4
1.4
1.1
1.1
0.9
4.7
3.7
2.5
5.9
4.2

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7.707
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2.415
2.401
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1.815
1.006
0.992
0.818
0.804
0.734
0.720
FmO
OFm
OH
Triene from 3rr
28
9
8
7
6
5
4
3
2
1
ppm
5.4
4.1
1.6
2.8
3.1
22.3
1.3
1.5
1.9
0.9
1.0
1.0
1.2
6.5
3.1
1.4
1.1
0.5
1.3
5.1
4.3
4.7
3.6

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7.133
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6.574
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0.854
0.841
0.791
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NaO
HO
P
O
OH
1ss
9
8
7
6
5
4
3
2
1
ppm
1.0
2.2
1.0
2.0
1.2
1.0
1.4
1.6
1.1
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0.3
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0.6
1.2
0.5
1.7
2.5
6.9
2.9
5.0

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2.574
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1.792
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0.863
0.849
0.766
0.752
NaO
HO
P
O
O
O
O
OH
1sr
9
8
7
6
5
4
3
2
1
ppm
1.5
2.3
0.8
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0.9
1.1
1.1
1.5
1.7
5.2
4.8
4.0
2.0
2.9

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6.301
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5.934
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NaO
HO
P
O
O
O
O
OH
1rs
9
8
7
6
5
4
3
2
1
ppm
1.0
3.0
1.2
2.1
1.3
1.0
2.4
2.6
1.2
4.5
1.6
10.6
12.7
5.4
6.9

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6.608
6.569
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4.132
4.106
4.098
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2.595
2.582
2.573
2.560
2.549
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1.812
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1.017
0.994
0.972
0.783
0.761
NaO
HO
P
O
O
O
O
OH
1rr
9
8
7
6
5
4
3
2
1
ppm
1.2
1.8
0.7
1.9
0.9
1.0
1.1
1.4
1.3
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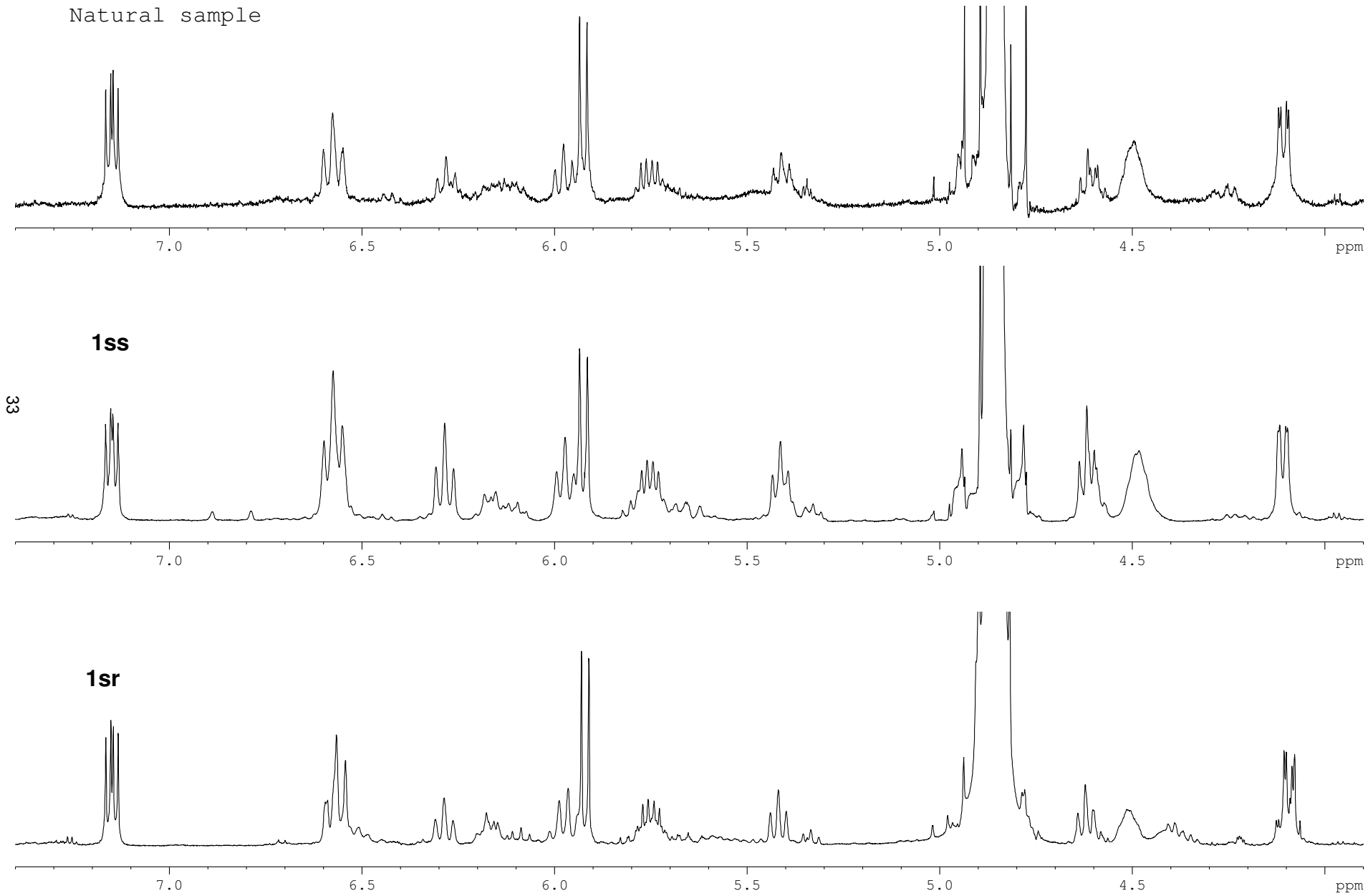
3.1
8.1
10.7
4.4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6.0
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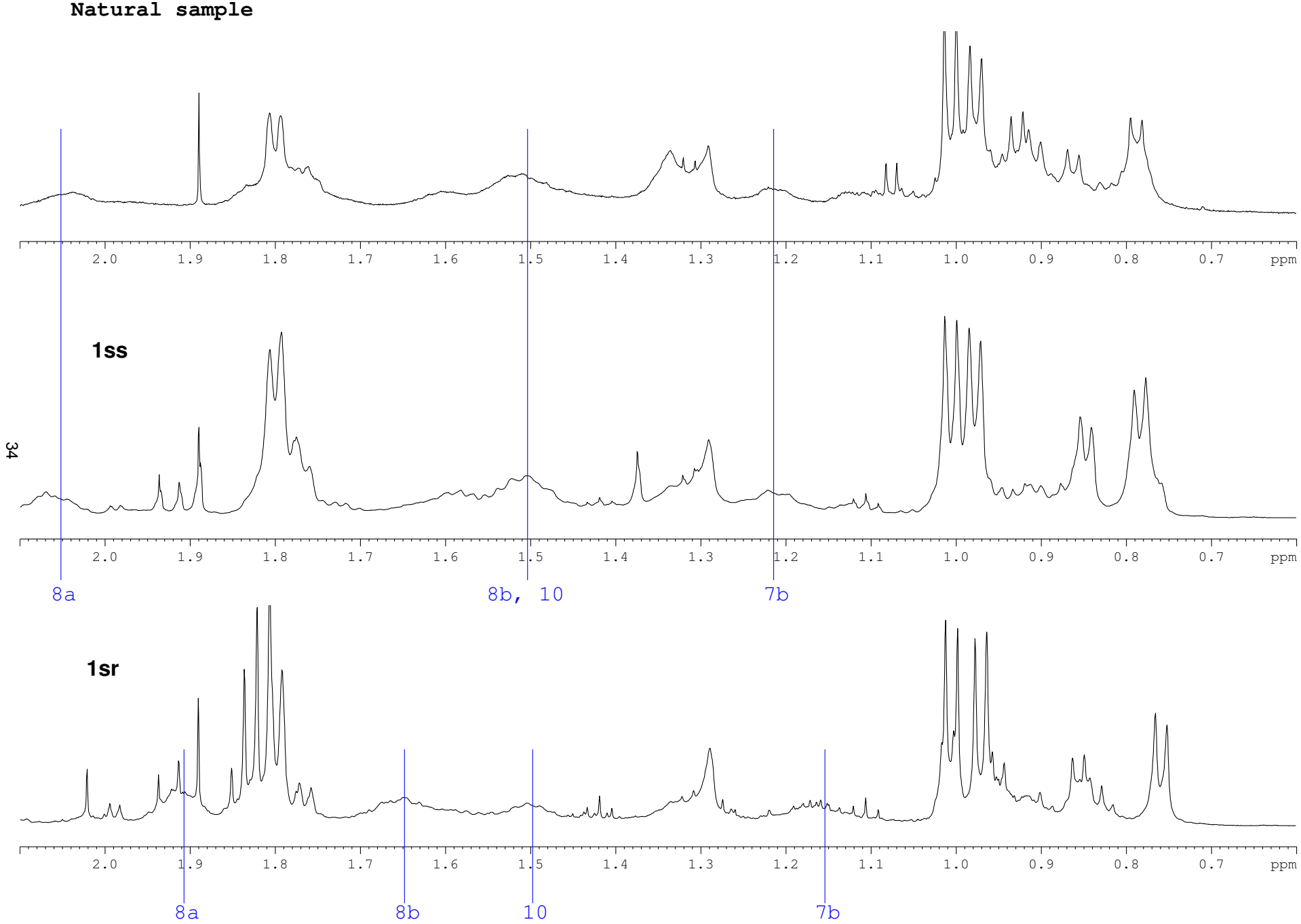
5.0
4.5
ppm
1ss
33
7.0
6.5
6.0
5.5
5.0
4.5
ppm
1sr
7.0
6.5
6.0
5.5
5.0
4.5
ppm


Natural sample
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1.8
1.7
1.6
1.5
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
ppm
1ss
34
8a
8b, 10
7b
1sr
8a
8b
10
7b