

Supporting Information

Synthesis of the C50 Diastereomers of the C33-C51 Fragment of Stambomycin D

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1. General Experimental

Reagents, solvents and reaction conditions

All reactions were performed in dry glassware under a nitrogen atmosphere unless otherwise stated. Solvents and commercially available reagents were dried and purified before use where appropriate using standard procedures. Tetrahydrofuran (THF), dichloromethane, dimethylformamide (DMF), dioxane, toluene and triethylamine were obtained anhydrous from solvent dispenser units having been passed through an activated alumina column under nitrogen. Dry methanol and dimethylsulfoxide (DMSO) were obtained commercially and used directly without further purification. Brine refers to a saturated aqueous solution of NaCl.

Chromatography methods

Reactions were monitored by thin layer chromatography using Merck DC Kieselgel 60 F₂₅₄ 0.2 mm precoated plates. Visualisation was carried out under UV light ($\lambda = 254$ nm) or stains such as vanillin, phosphomolybdic acid (PMA) and potassium permanganate (KMnO₄). Flash column chromatography was performed on Macherey-Nagel Kieselgel 60 Å (230-400 mesh particle size) as static phase and under increased pressure. High performance liquid chromatography (HPLC) was performed on an Agilent 1200 series under UV-vis detection. The analytical chiral column used was a CHIRALPAK-IC column (250 mm x 4.6 mm, 5µm, Daicel Corporation) and the analytical as well as semi-preparative reverse phase column used was an Eclipse XDB-C18 column (150 mm x 4.6 mm, 5µm, Agilent Technologies).

Instrumental analytical methods

Optical rotations were recorded on a Perkin-Elmer 241 or 341 polarimeter with a 1 dm path length cell (using the sodium D line, 589 nm). Specific rotations ($[\alpha]_D^{25}$) are given in deg dm²g⁻¹. Concentration (c) is reported in g/100 mL.

Infrared spectra were recorded on a Bruker Tensor 27 Fourier FT-IR spectrometer, and the samples were prepared as a thin film on a diamond/ZnSe PIKE Miracle ATR module. Absorption maxima (ν_{\max}) are quoted in wavenumbers (cm⁻¹).

NMR spectra were recorded on a Bruker AVIII HD 400 (operating at 400 MHz for ¹H and 101 MHz

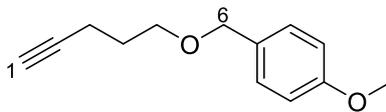
for ^{13}C acquisitions), a Bruker AVIII HD 500 (500 MHz for ^1H acquisitions and 126 MHz for ^{13}C acquisitions), or a Bruker AVIII HD 600 (600 MHz for ^1H and 151 MHz for ^{13}C acquisitions). The analysis of the NMR spectra was carried out with MestReNova®. Chemical shifts δ are given in parts per million (ppm) to the nearest 0.01 ppm for ^1H and 0.1 ppm for ^{13}C spectra, with the solvent resonance as internal standard: chloroform- d_1 : 7.26 (^1H NMR) and 77.16 (^{13}C NMR), methanol- d_4 : 3.31, 4.87 (^1H NMR) and 49.00 (^{13}C NMR). Coupling constants J are reported to the nearest 0.1 Hz. Multiplicities are reported as follows: s = singlet, br s = broad singlet, d = doublet, dd = doublet of doublets etc., t = triplet, q = quartet, sept = septet, m = multiplet. Assignments of compounds were based on two-dimensional NMR (COSY, HSQC, HMBC).

High resolution mass spectra (HRMS) were recorded under ESI conditions on a Bruker MicroTOF (resolution = 5000 FWHM) using tetraoctylammonium bromide as a lock-mass in both positive and negative ion mode. Values are calculated to 4 decimal places from the molecular formula. The parent ion $[\text{M}]^+$, $[\text{M}+\text{H}]^+$ or $[\text{M}+\text{Na}]^+$ are quoted.

Liquid chromatography–mass spectrometry (LC-MS) was performed on a Xevo G2-XS QToF equipped with a high resolution, high stability quadrupole analyzer (MS1), plus pre-filters and a high performance oaToF mass analyzer (MS2) with a mass range up to m/z 100,000 and a resolving power of $>40,000$ FWHM. The ionization mode used is ESI+ mode and the TOF mass range is m/z 20 to 100000.

2. Characterization of compounds

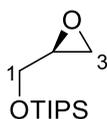
1-Methoxy-4-((pent-4-yn-1-yloxy)methyl)benzene (6)



To a suspension of sodium hydride (2.72 g, 60% dispersion in mineral oil, 68.0 mmol, 1.1 equiv.) in THF (88 mL) at 0 °C was added 4-pentyn-1-ol (5.20 g, 61.8 mmol, 1.0 equiv.). After stirring at room temperature for 30 min, the mixture was cooled to 0 °C, then 4-methoxybenzyl chloride (9.2 mL, 68.0 mmol, 1.1 equiv.) and tetrabutylammonium iodide (1.14 g, 3.09 mmol, 0.05 equiv.) were added. The resulting mixture was gradually warmed to room temperature and stirred overnight. The reaction was cooled to 0 °C, quenched with water (50 mL) and extracted with Et₂O (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (2% Et₂O/pentane to 10% Et₂O/pentane) to obtain alkyne **6** (10.5 g, 51.4 mmol, 83%) as a colourless oil.

R_f 0.45 (10% Et₂O/pentane); **IR** (thin film, ν_{\max} / cm⁻¹) 3294, 2955, 2861, 1613, 1513, 1246, 1173, 1101, 1035, 819, 640; **¹H NMR** (400 MHz, CDCl₃); δ 7.26 (2H, d, J = 8.8 Hz, ArH), 6.88(2H, d, J = 8.7 Hz, ArH), 4.44 (2H, s, H6), 3.81 (3H, s, OCH₃), 3.55 (2H, t, J = 6.2 Hz, H5), 2.31 (2H, td, J = 7.1, 2.7 Hz, H3), 1.94 (1H, t, J = 2.6 Hz, H1), 1.83-1.75 (2H, tt, J = 7.1, 6.1 Hz, H4); **¹³C NMR** (101MHz, CDCl₃) δ 159.3, 130.7, 129.4, 113.9, 84.2, 72.7, 68.6, 68.5, 55.4, 28.8, 15.5; **HRMS** (ESI⁺) calc. for C₁₃H₁₆O₂Na [M+Na]⁺ 227.1053, found 227.1044.

(S)-Triisopropyl(oxiran-2-ylmethoxy)silane (5)

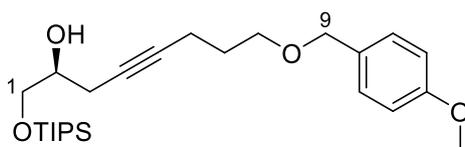


(*R*)-glycidol (3.00 g, 40.5 mmol, 1.0 equiv.) was added to a stirred mixture of triisopropylsilyl chloride (11.3 mL, 52.7 mmol, 1.3 equiv.) and imidazole (4.41 g, 64.8 mmol, 1.6 equiv.) in anhydrous DMF (24 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 30 min, during which time a white precipitate formed, then it was allowed to warm to room temperature. After stirring at room temperature for 2 h, the reaction was quenched with water (100 mL). The mixture was stirred for an

additional 20 min and then extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (5% Et₂O/pentane to 10% Et₂O/pentane) to afford epoxide **5** as a colourless oil (7.01 g, 30.4 mmol, 75%).

R_f 0.65 (10% Et₂O/pentane); **[α]_D²⁵** -2.0 (*c* = 0.91, CHCl₃); **IR** (thin film, *v*_{max} / cm⁻¹) 2980, 2867, 1463, 1384, 1253, 1161, 1137, 1099, 882, 681; **¹H NMR** (400 MHz, CDCl₃); δ 3.91 (1H, dd, *J* = 11.6, 3.3 Hz, H1), 3.75 (1H, dd, *J* = 11.6, 4.7 Hz, H1), 3.11 (1H, tt, *J* = 4.4, 3.0 Hz, H2), 2.77 (1H, dd, *J* = 5.2, 4.0 Hz, H3), 2.67 (1H, dd, *J* = 5.2, 2.7 Hz, H3), 1.15-1.03 (21H, m, TIPS); **¹³C NMR** (101MHz, CDCl₃) δ 64.1, 52.7, 44.6, 18.1, 12.1; **HRMS** (ESI⁺) calc. for C₁₂H₂₇O₂Si [M+H]⁺ 253.1594, found 253.1595.

(S)-8-((4-Methoxybenzyl)oxy)-1-((triisopropylsilyl)oxy)oct-4-yn-2-ol (7)

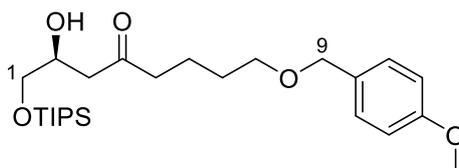


To a solution of PMB alkyne (6.41 g, 31.4 mmol, 1.3 equiv.) in THF (63 mL) at -78 °C under argon, was added *n*-butyl lithium (11.6 mL, 2.5 M in hexane, 29.0 mmol, 1.2 equiv.) dropwise. The reaction mixture was stirred at -78 °C for 1 h, then warmed gradually to 0 °C. After stirring at 0 °C for 1 h, the reaction mixture was recooled to -78 °C and a solution of epoxide **5** (5.56 g, 24.1 mmol, 1.0 equiv.) in THF (48 mL) was added, followed by boron trifluoride diethyl etherate (3.0 mL, 24.1 mmol, 1.0 equiv.). The resulting mixture was warmed to -70 °C. After stirring at -70 °C for 3 h, the reaction was quenched with sat. aq. NH₄Cl solution (50 mL) then warmed to room temperature and extracted with Et₂O (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10% Et₂O/pentane to 20% Et₂O/pentane) to afford alkynyl alcohol **7** (8.5 g, 19.6 mmol, 81%) as a colourless oil.

R_f 0.40 (20% Et₂O/pentane); **[α]_D²⁵** +10.0 (*c* = 0.69, CHCl₃); **IR** (thin film, *v*_{max} / cm⁻¹) 3460, 2942, 2865, 1613, 1513, 1463, 1366, 1247, 1102, 1038, 883, 663; **¹H NMR** (400 MHz, CDCl₃) δ 7.27

(2H, d, $J = 8.6$ Hz, ArH), 6.88 (2H, d, $J = 8.6$ Hz, ArH), 4.43 (2H, s, H9), 3.80 (3H, s, OCH₃), 3.78-3.72 (2H, m, H1), 3.71-3.67 (1H, m, H2), 3.52 (2H, t, $J = 6.2$ Hz, H8), 2.40 (2H, dq, $J = 6.8, 2.4$ Hz, H3), 2.28 (2H, tt, $J = 7.1, 2.4$ Hz, H7), 1.81-1.71 (2H, m, H6), 1.15-1.04 (21H, m, TIPS); ¹³C NMR (101 MHz, CDCl₃) 159.3, 130.7, 129.3, 113.9, 82.0, 76.3, 72.7, 70.8, 68.8, 66.1, 55.4, 29.3, 23.6, 18.1, 15.8, 12.1; HRMS (ESI⁺) calc. for C₂₅H₄₂O₄NaSi [M+Na]⁺ 457.2745, found 457.2744.

(S)-2-hydroxy-8-((4-methoxybenzyl)oxy)-1-((triisopropylsilyl)oxy)octan-4-one (8)

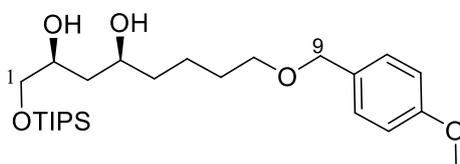


Alkynyl alcohol **7** (8.50 g, 19.6 mmol, 1.0 equiv.) was dissolved in 1,1,3,3-tetramethyldisilazane (25 mL) and the resulting mixture was heated to 100 °C. After stirring at 100 °C for 16 h, the reaction mixture was cooled to room temperature and the volatiles were removed by rotavap. The residue was dried under high vacuum for 2 h, then dissolved in THF (40 mL). Platinum(0)-1,3-divinyl-1,1,3,3-tetramethyldisiloxane complex in xylene (1.2 mL, 2% Pt in xylene) was added, and the resulting mixture was stirred at room temperature overnight, producing a cyclic siloxane. EDTA disodium salt dihydrate (100 mg) was added to sequester platinum ions. After filtration of the EDTA salt, the mixture was concentrated and the resulting residue was dissolved in THF/MeOH (1:1, 100 mL), followed by addition of solid KHCO₃ (5.49 g, 54.8 mmol, 3.0 equiv.) and KF (3.18 g, 54.8 mmol, 3.0 equiv.). Aqueous hydrogen peroxide (62 g, 30% w/w in water, 548 mmol, 30.0 equiv.) was added dropwise to the mixture dropwise at room temperature, and the mixture was stirred for 6 h. The reaction was then cooled to 0 °C and precooled sat. aq. Na₂SO₃ solution (100 mL) was added slowly. After gas and heat evolution ceased, the reaction was warmed to room temperature and stirred for 30 min. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 200 mL). The combined organic layers were washed with brine (200 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc/pentane to 20% EtOAc/pentane) to afford β -hydroxyketone **8** (5.31 g, 11.7 mmol, 60%) as a colourless oil.

R_f 0.40 (20% EtOAc /pentane); **[α]_D²⁵** -4.2 ($c = 0.38$, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 3461, 2942,

2865, 1712, 1613, 1513, 1247, 1098, 1037, 883, 683; **¹H NMR** (500 MHz, CDCl₃) δ 7.25 (2H, d, *J* = 8.7 Hz, ArH), 6.87 (2H, d, *J* = 8.7 Hz, ArH), 4.42 (2H, s, H₉), 4.14-4.07 (1H, m, H₂), 3.80 (3H, s, OCH₃), 3.68 (1H, dd, *J* = 9.7, 5.1 Hz, H₁), 3.61 (1H, dd, *J* = 9.8, 6.1 Hz, H_{1'}), 3.44 (2H, t, *J* = 6.2 Hz, H₈), 2.92 (1H, d, *J* = 4.2 Hz, OH), 2.60 (2H, d, *J* = 6.1 Hz, H₃), 2.48 (2H, t, *J* = 7.1 Hz, H₅), 1.70-1.57 (4H, m, H₆, H₇), 1.14-1.00 (21H, m, TIPS); **¹³C NMR** (126 MHz, CDCl₃) δ 210.7, 159.3, 130.8, 129.4, 113.9, 72.7, 69.8, 68.6, 66.7, 55.4, 45.7, 43.6, 29.3, 20.5, 18.1, 12.0; **HRMS** (ESI⁺) calc. for C₂₅H₄₄O₅NaSi [M+Na]⁺ 475.2850, found 475.2847.

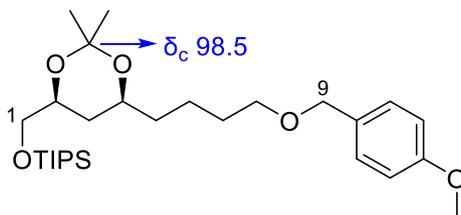
(2*R*, 4*R*)-8-((4-methoxybenzyl)oxy)-1-((triisopropylsilyl)oxy)octane-2,4-diol (9)



To a solution of β -hydroxyketone **8** (3.34 g, 7.38 mmol, 1.0 equiv.) in THF (30 mL) at -70 °C was added anhydrous methanol (7.4 mL), followed by slow addition of diethylmethoxyborane (8.9 mL, 1.0 M in THF, 8.85 mmol, 1.2 equiv.). The resulting mixture was stirred at -70 °C for 2 h and then sodium borohydride (0.59 g, 15.5 mmol, 2.1 equiv.) was added portionwise. After stirring at -70 °C for 5 h, the reaction was quenched with water (20 mL) and extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue thus obtained was azeotroped with methanol (x 2) until the TLC showed hydrolysis of the boronate was complete. The residue was concentrated under reduced pressure and purified by flash chromatography (10% EtOAc/pentane to 30% EtOAc/pentane) to obtain diol **9** (2.68 g, 5.89 mmol, 80%) as a colourless oil.

R_f 0.35 (20% EtOAc/pentane); [α]_D²⁵ +5.0 (*c* = 0.54, CHCl₃); **IR** (thin film, ν_{\max} /cm⁻¹) 3396, 2941, 2865, 1613, 1513, 1462, 1247, 1097, 1037, 883, 806, 683; **¹H NMR** (400 MHz, CDCl₃) δ 7.25 (2H, d, *J* = 8.6 Hz, ArH), 6.87 (2H, d, *J* = 8.7 Hz, ArH), 4.43 (2H, s, H₉), 3.95-3.84 (2H, m, H₂ and H₄), 3.80 (3H, s, OMe), 3.66 (1H, dd, *J* = 9.8, 3.9 Hz, H₁), 3.52 (1H, dd, *J* = 9.7, 7.3 Hz, H_{1'}), 3.45 (2H, t, *J* = 6.5 Hz, H₈), 1.68-1.38 (8H, m, H₃, H₅, H₆ and H₇), 1.19-1.00 (21H, m, TIPS); **¹³C NMR** (101 MHz, CDCl₃) δ 159.3, 130.9, 129.4, 113.9, 73.2, 72.7, 72.0, 70.2, 67.6, 55.4, 39.1, 37.7, 29.9, 22.3, 18.1, 12.0; **HRMS** (ESI⁺) calc. for C₂₅H₄₆O₅NaSi [M+Na]⁺ 477.3007, found 477.3006.

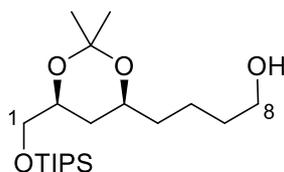
Triisopropyl(((4*S*,6*S*)-6-(4-((4-methoxybenzyl)oxy)butyl)-2,2-dimethyl-1,3-dioxan-4-yl)methoxy)silane (10**)**



To a solution of diol **9** (2.68 g, 5.89 mmol, 1.0 equiv.) in CH₂Cl₂ (23 mL) and 2,2-dimethoxypropane (23 mL) was added pyridinium *p*-toluenesulfonate (0.15 g, 0.589 mmol, 0.1 equiv.). After stirring at room temperature for 15 h, the mixture was quenched with sat. aq. NaHCO₃ solution (20 mL) and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc/pentane) to obtain acetonide **10** (2.47g, 5.01 mmol, 85%) as a colorless oil.

R_f 0.50 (10% EtOAc/pentane); [α]_D²⁵ -2.1 (*c* = 0.42, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 2941, 2865, 1613, 1513, 1463, 1379, 1248, 1111, 1039, 882, 820, 683; **¹H NMR** (400 MHz, CDCl₃) δ 7.26 (2H, d, *J* = 8.6 Hz, ArH), 6.87 (2H, d, *J* = 8.6 Hz, ArH), 4.43 (2H, s, H₉), 3.95-3.88 (1H, m, H₄), 3.86-3.81 (1H, m, H₂), 3.80 (3H, s, OCH₃), 3.75 (1H, dd, *J* = 9.7, 5.0 Hz, H₁), 3.52 (1H, dd, *J* = 9.7, 6.7 Hz, H_{1'}), 3.44 (2H, t, *J* = 6.6 Hz, H₈), 1.70-1.56 (4H, m, H₃ and H₇), 1.55-1.39 (4H, m, H₅, H₆), 1.43 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.16-0.99 (21H, m, TIPS); **¹³C NMR** (101 MHz, CDCl₃) δ 159.3, 130.9, 129.4, 113.9, 98.5, 72.7, 70.2, 70.2, 69.0, 67.5, 55.4, 36.5, 34.4, 30.3, 29.9, 21.8, 20.0, 18.1, 12.1; **HRMS** (ESI⁺) calc. for C₂₈H₅₀O₅NaSi [M+Na]⁺ 517.3320, found 517.3318.

4-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)butan-1-ol (S1**)**

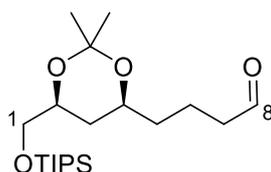


To a stirred solution of the ether **10** (2.47 g, 5.01 mmol, 1.0 equiv.) in CH₂Cl₂ (50 mL) and pH 7 phosphate buffer solution (3.8 mL) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (2.26 g, 10.0 mmol, 2.0 equiv.) After stirring vigorously at room temperature for 1 h, the reaction mixture

was quenched with sat. aq. NaHCO₃ solution (50 mL), diluted with CH₂Cl₂ (100 mL) and filtered through a Büchner funnel to remove solids. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc/pentane to 20% EtOAc/pentane) to afford alcohol **S1** (1.41 g, 3.77 mmol, 75%) as a colorless oil.

R_f 0.45 (30% EtOAc/pentane); [α]_D²⁵ -5.4 (*c* = 0.55, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 3378, 2941, 2866, 1463, 1380, 1220, 1113, 882, 682; **¹H NMR** (400 MHz, CDCl₃) δ 3.93 (1H, dddd, *J* = 11.8, 6.9, 5.1, 2.6 Hz, H4), 3.84 (1H, *J* = 11.5, 7.0, 4.5, 2.4 Hz, H2), 3.76 (1H, dd, *J* = 9.7, 5.1 Hz, H1), 3.65 (2H, q, *J* = 6.0 Hz, H8), 3.52 (1H, dd, *J* = 9.7, 6.7 Hz, H1'), 1.67 (1H, dt, *J* = 13.0, 2.6 Hz, H3), 1.63-1.45 (7H, m, H3, H5, H6 and H7), 1.44 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.18-1.00 (21H, m, TIPS); **¹³C NMR** (101 MHz, CDCl₃) δ 98.6, 70.2, 69.0, 67.4, 63.0, 36.4, 34.4, 32.8, 30.3, 21.4, 20.0, 18.1, 12.1; **HRMS** (ESI⁺) calc. for C₂₀H₄₂O₄NaSi [M+Na]⁺ 397.2745, found 397.2746.

4-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)butanal (**11**)

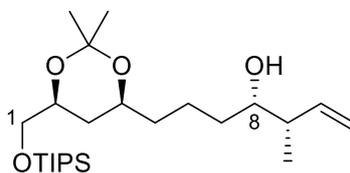


To a solution of alcohol **S1** (1.41 g, 3.77 mmol, 1.0 equiv.) in CH₂Cl₂ (40.0 mL) was added solid sodium bicarbonate (3.17 g, 37.7 mmol, 10.0 equiv.), followed by Dess-Martin periodinane (2.39 g, 5.66 mmol, 1.5 equiv.). After stirring at room temperature for 1 h, the reaction mixture was quenched with sat. aq. NaHCO₃ solution (20 mL) and dropwise addition of sat. aq. Na₂S₂O₃ solution (20 mL) at 0 °C. The resulting mixture was extracted with CH₂Cl₂ (3 x 50 mL) and the combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (10% EtOAc/pentane) to obtain aldehyde **11** (1.29 g, 3.46 mmol, 92%) as a colourless oil.

R_f 0.50 (10% EtOAc/pentane); [α]_D²⁵ -13.0 (*c* = 0.49, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 2958, 2865, 1734, 1462, 1379, 1239, 1165, 882, 683; **¹H NMR** (400 MHz, CDCl₃) δ 9.77 (1H, s, H8), 3.93 (1H,

dddd, $J = 11.6, 6.7, 5.0, 2.6$ Hz, H4), 3.85 (1H, dddd, $J = 11.8, 7.3, 4.9, 2.5$ Hz, H2), 3.76 (1H, dd, $J = 9.7, 5.1$ Hz, H1), 3.52 (1H, dd, $J = 9.7, 6.7$ Hz, H1'), 2.46 (2H, td, $J = 7.4, 1.7$ Hz, H7), 1.88-1.55 (4H, m, H3 and H6), 1.50 (2H, dtd, $J = 9.5, 6.7, 5.3$ Hz, H5), 1.44 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.19-1.01 (21H, m, TIPS); ^{13}C NMR (101 MHz, CDCl_3) δ 202.7, 98.6, 70.1, 68.7, 67.4, 43.9, 36.0, 34.4, 30.2, 20.0, 18.1, 18.0, 12.1; HRMS (ESI⁺) calc. for $\text{C}_{20}\text{H}_{40}\text{O}_4\text{NaSi}$ $[\text{M}+\text{Na}]^+$ 395.2588, found 395.2583.

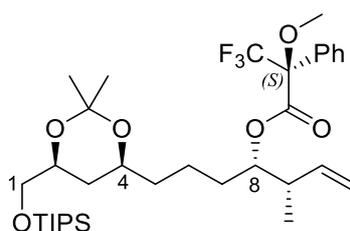
(3*S*,4*S*)-7-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-3-methylhept-1-en-4-ol (14)



To a solution of (*S,S*)-**13** (1.10 g, 3.81 mmol, 1.1 equiv.) in CH_2Cl_2 (10 mL) at 0 °C was added 1,8-diazabicyclo[5.4.0]undec-7-ene (1.7 mL, 11.4 mmol, 3.3 equiv.), followed by slow addition of *cis*-crotyl trichlorosilane **12** (0.8 mL, 4.15 mmol, 1.2 equiv.). The ice/water bath was removed. After stirring at room temperature for 1 h, the mixture was recooled to 0 °C and a solution of aldehyde **11** (1.29 g, 3.46 mmol, 1.0 equiv.) in CH_2Cl_2 (1.4 mL) was added dropwise. After stirring at 0 °C for 1 h, the mixture was concentrated under reduced pressure and diethyl ether (10 mL) was added. The resulting mixture was stirred vigorously for 30 min to ensure complete precipitation of the DBU·HCl salts. The reaction mixture was filtered through a Büchner funnel to remove solid and subsequently, tetrabutylammonium fluoride solution (3.5 mL, 1.0 M in THF, 3.46 mmol, 1.0 equiv.) was added to the filtrate. After stirring at room temperature for 30 min, the reaction mixture was quenched with 1 M HCl (5 mL, aq.). The layers were separated and the aqueous layer was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with brine (50 mL), filtered and concentrated under reduced pressure. The residue was purified by flash chromatography (5% EtOAc/pentane to 15% EtOAc/pentane) to obtain alcohol **14** (0.91 g, 2.12 mmol, 61%, 12:1 *dr*) as a colourless oil. (The procedure for the synthesis of known compounds (*S,S*)-**13**, **12** and recovery of (*S,S*)-**12** was described in our previous work).¹

R_f 0.50 (15% EtOAc/pentane); $[\alpha]_D^{25}$ -22.1 (*c* = 0.50, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 3421, 2943, 2866, 1463, 1381, 1116, 996, 881, 683; **¹H NMR** (400 MHz, CDCl₃) δ 5.83-5.74 (1H, m, H10), 5.08 (1H, dt, *J* = 7.3, 1.6 Hz, H11), 5.06 (1H, s, H11), 3.93 (1H, dddd, *J* = 11.7, 7.3, 5.1, 2.5 Hz, H4), 3.83 (1H, ddd, *J* = 11.3, 5.9, 3.2 Hz, H2), 3.75 (1H, dd, *J* = 9.7, 5.0 Hz, H1), 3.54-3.47 (2H, m, H1' and H8), 2.30-2.23 (1H, m, H9), 1.69-1.65 (1H, m, H3), 1.57-1.40 (7H, m, H3, H5, H6, H7), 1.43 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.17-1.04 (21H, m, TIPS), 1.02 (3H, d, *J* = 6.9 Hz, C9-Me); **¹³C NMR** (101 MHz, CDCl₃) δ 141.2, 115.4, 98.5, 74.7, 70.2, 69.1, 67.4, 43.6, 36.5, 34.5, 33.9, 30.2, 21.9, 20.0, 18.1, 14.3, 12.1; **HRMS** (ESI⁺) calc. for C₂₄H₄₈O₄NaSi [M+Na]⁺ 451.3214, found 451.3216.

(3*S*,4*S*)-7-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-3-methylhept-1-en-4-yl (*S*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (14-*S*-ester)

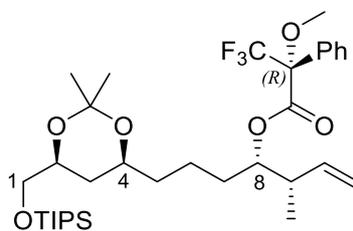


To a solution of alcohol **15** (13.4 mg, 0.0313 mmol, 1.0 equiv.) in CH₂Cl₂ (0.5 mL) was added anhydrous pyridine (15.7 μ L, 0.194 mmol, 6.2 equiv.), followed by dropwise addition of (*R*)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride (22.2 μ L, 0.119 mmol, 3.8 equiv.) at room temperature. After stirring at ambient temperature for 3 h, the reaction was quenched with water (1 mL), extracted with CH₂Cl₂ (3 x 1 mL). The combined organic layers were washed with brine (1 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane) to afford **14-*S*-ester** (15.2 mg, 0.0236 mmol, 76%).

R_f 0.50 (5% EtOAc/pentane); $[\alpha]_D^{25}$ -44.2 (*c* = 3.6, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 2948, 2867, 1745, 1453, 1381, 1272, 1171, 1120, 994, 965, 882, 764, 717, 698; **¹H NMR** (500 MHz, CDCl₃, ¹⁹F decoupled) δ 7.56 (2H, dd, *J* = 6.7, 2.9 Hz, ArH), 7.41-7.36 (3H, m, ArH), 5.76 (ddd, 1H, *J* = 16.9, 10.8, 7.1, H10), 5.08-5.07 (1H, m, H8), 5.07-5.03 (2H, m, H11), 3.91 (1H, dddd, *J* = 11.6, 7.3, 5.0,

2.5 Hz, H4), 3.76-3.69 (2H, m, H1 and H2), 3.54 (3H, s, OCH₃), 3.51 (1H, dd, $J = 9.7, 6.7$ Hz, H1'), 2.53 (1H, dtd, $J = 8.4, 6.8, 1.4$ Hz, H9), 1.65-1.52 (4H, m, H3 and H7), 1.50-1.45 (1H, m, H5), 1.42 (3H, s, acetonide), 1.35 (3H, s, acetonide), 1.32-1.27 (3H, m, H5' and H6), 1.10-1.04 (21H, m, TIPS), 1.02 (3H, d, $J = 6.9$ Hz, C9-Me). ¹³C NMR (126 MHz, CDCl₃) δ 166.5, 139.4, 132.4, 129.7, 128.4, 127.7, 123.2 (q, $J = 289$ Hz), 115.9, 98.5, 84.2 (q, $J = 28$ Hz), 80.4, 70.2, 68.6, 67.4, 55.6, 40.7, 36.3, 34.3, 30.9 30.2, 20.8, 19.9, 18.1, 14.9, 12.1; ¹⁹F NMR (470 Hz, CDCl₃) δ -71.1; HRMS (ESI⁺) calc. for C₃₄H₅₅F₃O₆Si [M+Na]⁺ 667.3612, found 667.3608.

(3*S*,4*S*)-7-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-3-methylhept-1-en-4-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (14-*R*-ester)



To a solution of alcohol **9** (6.1 mg, 0.0142 mmol, 1.0 equiv.) in CH₂Cl₂ (0.15 mL) was added anhydrous pyridine (7.1 μ L, 0.0882 mmol, 6.2 equiv.) and (*S*)-(+)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride (10.1 μ L, 0.0541 mmol, 3.8 equiv.) at room temperature. The resulting mixture was stirred at ambient temperature for 3 h. The reaction was quenched with water (1 mL) and extracted with CH₂Cl₂ (3 x 1 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane) to afford **14-*R*-ester** (7.8 mg, 0.0121 mmol, 85%).

R_f 0.50 (4% EtOAc/pentane); [α]_D²⁵ -2.4 ($c = 1.2$, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 2943, 2866, 1745, 1462, 1380, 1259, 1169, 1122, 995, 919, 882, 767, 719, 683; **¹H NMR** (500 MHz, CDCl₃, ¹⁹F decoupled) δ 7.56 (2H, dd, $J = 6.8, 3.0$ Hz, ArH), 7.41-7.36 (3H, m, ArH), 5.64 (ddd, 1H, $J = 17.5, 10.5, 7.3$, H10), 5.04 (1H, dt, $J = 7.3, 5.3$ Hz, H8), 5.01-4.94 (2H, m, H11), 3.91 (1H, dddd, $J = 11.6, 7.3, 5.0, 2.6$ Hz, H4), 3.81-3.74 (2H, m, H1 and H2), 3.55 (3H, s, OCH₃), 3.51 (1H, dd, $J = 9.7, 6.8$ Hz, H1'), 2.47 (1H, td, $J = 7.1, 5.7$ Hz, H9), 1.64-1.60 (4H, m, H3 and H7), 1.52-1.48 (1H, m, H5), 1.42 (3H, s, acetonide), 1.40-1.37 (3H, m, H5' and H6), 1.35 (3H, s, acetonide), 1.10-1.04 (21H, m, TIPS), 0.95 (3H, d, $J = 6.9$ Hz, C9-Me). ¹³C NMR (126 MHz, CDCl₃) δ 166.4, 139.2, 132.5, 129.7,

128.5, 127.6, 123.6 (q, $J=289$ Hz), 115.8, 98.5, 84.6 (q, $J=28$ Hz), 80.3, 70.1, 68.6, 67.4, 55.6, 40.6, 36.4, 34.4, 31.1, 30.2, 21.0, 19.9, 18.1, 14.9, 12.1; ^{19}F NMR (470 Hz, CDCl_3) δ -71.2; HRMS (ESI $^+$) calc. for $\text{C}_{34}\text{H}_{55}\text{F}_3\text{O}_6\text{Si}$ $[\text{M}+\text{Na}]^+$ 667.3612, found 667.3611.

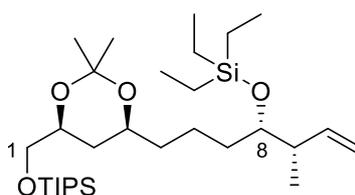
Comparison of ^1H NMR data of two Mosher ester derivatives is shown below:

Proton position	14-S-ester (ppm)	14-R-ester (ppm)	$\Delta\delta_{\text{SR}}$
H1 and H2	3.74	3.76	-0.02
H3 and H7	1.59	1.62	-0.03
H5	1.47	1.50	-0.03
H5' and H6	1.29	1.38	+0.09
H9	2.53	2.47	+0.06
H9-Me	1.02	0.95	+0.07
H10	5.76	5.64	+0.12
H11	5.05	4.98	+0.07

Negative values obtained for alkene portion and positive values obtained for acetone portion.

Analysis of all the values reveals the C8 centre is of *S* configuration.

(((3*S*,4*S*)-7-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-3-methylhept-1-en-4-yl)oxy)triethylsilane (S2)

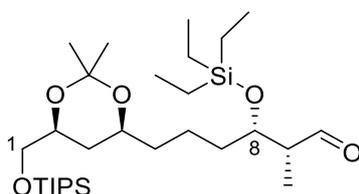


To a solution of alcohol **14** (0.91g, 2.12 mmol, 1.0 equiv.) in CH_2Cl_2 (4.3 mL) at -78 °C was added anhydrous 2,6-lutidine (0.37 mL, 3.18 mmol, 1.5 equiv.) followed by slow addition of triethylsilyl trifluoromethanesulfonate (0.49 mL 2.33 mmol, 1.1 equiv.). The resulting mixture was stirred at -78 °C for 30 min, then the reaction was gradually warmed to 0 °C and stirred for a further 30 min. The reaction mixture was quenched with water (5 mL), diluted with CH_2Cl_2 (5 mL) and brought back to room temperature. The layers were separated and the aqueous layer was extracted with CH_2Cl_2 (3 x 10 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4 , filtered

and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% Et₂O/pentane) to obtain TES ether **S2** (1.05 g, 2.00 mmol, 94%) as a colourless oil.

R_f 0.50 (5% Et₂O/pentane); [α]_D²⁵ -16.9 (*c* = 0.47 CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 2954, 2870, 1711, 1512, 1461, 1379, 1248, 1115, 1007, 882, 741, 682; **¹H NMR** (400 MHz, CDCl₃) δ 5.84 (1H, ddd, *J* = 17.6, 10.7, 7.1 Hz, H10), 5.01 (1H, dt, *J* = 8.4, 1.7 Hz, H11), 4.97 (1H, s, H11'), 3.93 (1H, dddd, *J* = 11.6, 7.3, 5.0, 2.5 Hz, H4), 3.85-3.80 (1H, m, H2), 3.76 (1H, dd, *J* = 9.6, 5.0 Hz, H1), 3.56-3.47 (2H, m, H1' and H8), 2.28 (1H, qd, *J* = 7.1, 5.4 Hz, H9), 1.68 (1H, dt, *J* = 12.9, 2.5 Hz, H3), 1.58-1.37 (7H, m, H3', H5, H6, H7), 1.43 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.16-1.04 (21H, m, TIPS), 0.98 (3H, d, *J* = 2.5 Hz, C9-Me), 0.95 (9H, t, *J* = 8.0 Hz, TES) 0.60 (6H, q, *J* = 8.1 Hz, TES); **¹³C NMR** (101 MHz, CDCl₃) δ 141.6, 114.1, 98.5, 76.2, 70.2, 69.0, 67.4, 43.3, 36.9, 34.6, 34.0, 30.2, 21.1, 20.0, 18.1, 15.3, 12.1, 7.2, 5.4; **HRMS** (ESI⁺) calc. for C₃₀H₆₂O₄NaSi₂ [M+Na]⁺ 565.4079, found 565.4080.

(2*R*,3*S*)-6-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-2-methyl-3-((triethylsilyl)oxy)hexanal (3**)**

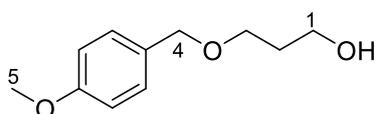


To a solution of TES ether **S2** (1.05 g, 2.00 mmol, 1.0 equiv.) in dioxane/water (20 mL, 3:1) was added 2,6-lutidine (0.47 mL, 4.00 mmol, 2.0 equiv.), osmium tetroxide (0.24 mL, 4% w/w in water, 0.0387 mmol, 0.02 equiv.), and sodium periodate (2.14 g, 10.0 mmol, 5.0 equiv.). The resulting mixture was stirred at room temperature overnight. The reaction was diluted with water (50 mL) and CH₂Cl₂ (50 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% Et₂O/pentane) to afford aldehyde **3** (0.93 g, 1.71 mmol, 85%) as a colourless oil.

R_f 0.50 (10% Et₂O/pentane); [α]_D²⁵ -31.2 (*c* = 0.55 CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 2943, 2867, 1727, 1462, 1379, 1112, 1011, 882, 742; **¹H NMR** (400 MHz, CDCl₃) δ 9.77 (1H, s, H10), 4.11 (1H,

td, $J = 6.4, 3.6$ Hz, H8), 3.93 (1H, dddd, $J = 11.6, 7.2, 5.0, 2.5$ Hz, H4), 3.82 (1H, dddd, $J = 11.5, 7.2, 4.5, 2.4$ Hz, H2), 3.76 (1H, dd, $J = 9.7, 5.0$ Hz, H1), 3.52 (1H, dd, $J = 9.7, 6.8$ Hz, H1), 2.44 (1H, qd, $J = 6.9, 3.4$ Hz, H9), 1.66 (1H, dt, $J = 12.8, 2.5$ Hz, H3), 1.57-1.45 (4H, m, H3, H7 and H5), 1.43 (3H, s, acetonide) 1.43-1.36 (3H, m, H5' and H6), 1.37 (3H, s, acetonide), 1.15-1.02 (24H, m, H9-Me and TIPS), 0.94 (9H, t, $J = 7.9$ Hz, TES), 0.59 (6H, q, $J = 7.7$ Hz, TES); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 205.5, 98.5, 72.4, 70.2, 68.8, 67.4, 51.5, 36.6, 34.7, 34.5, 30.2, 21.6, 20.0, 18.1, 12.1, 7.9, 7.0, 5.3; **HRMS** (ESI⁺) calc. for $\text{C}_{29}\text{H}_{60}\text{O}_5\text{NaSi}_2$ $[\text{M}+\text{Na}]^+$ 567.3871, found 567.3871.

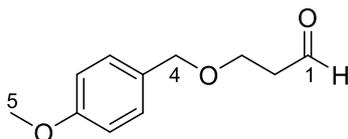
3-((4-Methoxybenzyl)oxy)propan-1-ol (S3)



To a solution of propane-1,3-diol (5.48 g, 72.0 mmol, 2.0 equiv.) in DMSO (25 mL) at 0 °C was added potassium hydroxide (4.04 g, 72.0 mmol, 2.0 equiv.) portionwise. The resulting mixture was stirred until the solution turned clear again and then 4-methoxy benzyl chloride (4.9 mL, 36.0 mmol, 1.0 equiv.) was added dropwise. The reaction was warmed to room temperature, stirred for 4 h, then recooled to 0 °C and quenched with water (100 mL). After warming to room temperature, diethyl ether (20 mL) was added and the aqueous phase was extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (20% EtOAc/pentane to 40% EtOAc/pentane) to afford alcohol **17** (5.33 g, 27.2 mmol, 75%) as a colourless oil.

R_f 0.50 (50% EtOAc/pentane); **IR** (thin film, ν_{max} / cm^{-1}) 3387, 2936, 2864, 1612, 1512, 1245, 1032, 818; $^1\text{H NMR}$ (400 MHz, CDCl_3) 7.25 (2H, d, $J = 6.7$ Hz, ArH), 6.88 (2H, d, $J = 6.7$ Hz, ArH), 4.45 (2H, s, H4), 3.81 (3H, s, H5), 3.77 (2H, t, $J = 6.1$ Hz, H3), 3.64 (2H, t, $J = 5.8$ Hz, H1), 1.88-1.83 (2H, m, H2); $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 159.4, 130.3, 129.4, 114.0, 73.1, 69.4, 62.2, 55.4, 32.2. **HRMS** (ESI⁺) calculated for $\text{C}_{11}\text{H}_{16}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$: 219.0992, found: 219.0993.

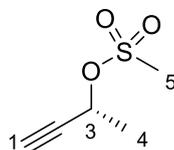
3-((4-Methoxybenzyl)oxy)propanal (**15**)



To a solution of alcohol **S3** (2.50 g, 12.7 mmol, 1.0 equiv.) in CH₂Cl₂ (84.9 mL), was added sodium bicarbonate (10.7 g, 12.7 mmol, 10.0 equiv.), followed by Dess-Martin periodinane (8.10 g, 19.1 mmol, 1.5 equiv.). After stirring at room temperature for 2 h, the reaction was cooled to 0 °C and quenched with sat. aq. NaHCO₃ solution (20 mL) and sat. aq. Na₂S₂O₃ solution (20 mL). The resulting mixture was warmed to room temperature and stirred until the layers turned clear. The aqueous layer was extracted with CH₂Cl₂ (3 x 100 mL) and the combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure to afford aldehyde **15** (2.15 g, 11.1 mmol, 87%) as a yellow oil, which was used directly in the next step without further purification.

Data for purified sample: **R_f** 0.50 (30% EtOAc/pentane); **IR** (thin film, ν_{\max} / cm⁻¹) 2860, 2731, 1723, 1613, 1513, 1247, 1092, 1033, 820; **¹H NMR** (400 MHz, CDCl₃) δ 9.79 (1H, t, J = 1.8 Hz, H1), 7.25 (2H, d, J = 8.6 Hz, ArH), 6.88 (2H, d, J = 8.6 Hz, ArH), 4.46 (2H, s, H4), 3.81 (3H, s, H5), 3.79 (2H, t, J = 6.1 Hz, H3), 2.69 (2H, t, J = 6.1, 1.8 Hz, H2); **¹³C NMR** (101 MHz, CDCl₃) δ 201.3, 159.5, 130.1, 129.5, 114.0, 73.1, 63.7, 55.4, 44.0. **HRMS** (ESI⁺) calc. for C₁₁H₁₄O₃Na [M+Na]⁺ 217.0835, found 217.0837.

(*S*)-But-3-yn-2-yl methanesulfonate (**16**)

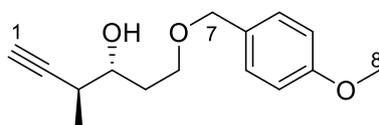


To a solution of (*R*)-(+)-3-butyn-2-ol (1.10 g, 15.7 mmol, 1.0 equiv.) in CH₂Cl₂ (105 mL) at -78 °C, was added triethylamine (4.4 mL, 31.4 mmol, 2.0 equiv.) followed by dropwise addition of methanesulfonyl chloride (1.8 mL, 23.5 mmol, 1.5 equiv.). The resulting mixture was stirred at -78 °C for 1 h, then quenched by addition of sat. aq. NaHCO₃ solution (50 mL) and allowed to warm to room temperature. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 100 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered

and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (20% EtOAc/pentane) to afford mesylate **16** (2.18 g, 14.7 mmol, 94%) as a yellow oil.

R_f 0.40 (20% EtOAc/pentane); **IR** (thin film, ν_{\max} / cm^{-1}) 3283, 2941, 2124, 1354, 1173, 1089, 1016, 973, 905, 851; **¹H NMR** (400 MHz, CDCl_3) δ 5.29 (1H, dq, $J = 6.7, 2.1$ Hz, H3), 3.12 (3H, s, H5), 2.70 (1H, d, $J = 2.2$ Hz, H1), 1.66 (3H, d, $J = 6.7$ Hz, H4); **¹³C NMR** (101MHz, CDCl_3) δ 80.3, 76.4, 67.6, 39.3, 22.6; **HRMS** (ESI⁺) calc. for $\text{C}_5\text{H}_8\text{O}_3\text{NaS}$ $[\text{M}+\text{Na}]^+$ 171.0086, found 171.0087.

(3*R*,4*S*)-1-((4-Methoxybenzyl)oxy)-4-methylhex-5-yn-3-ol (17)

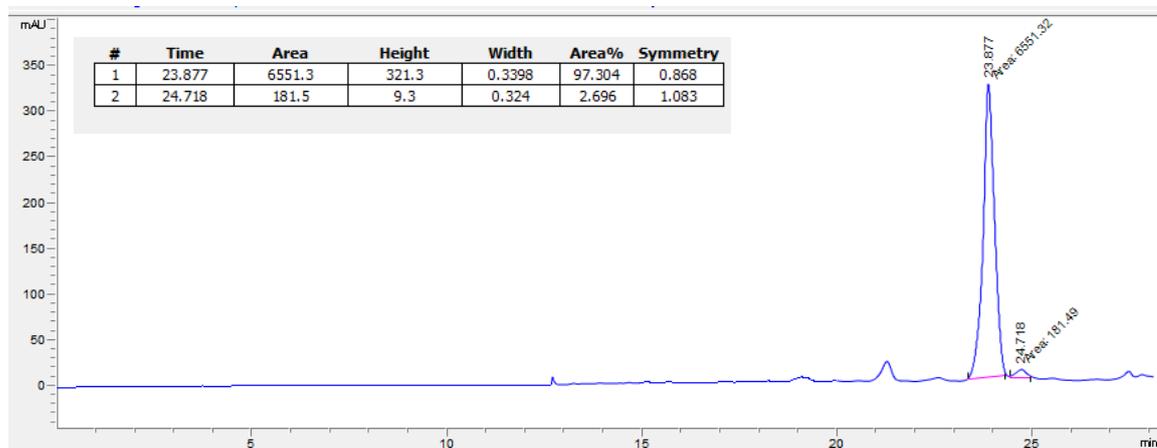
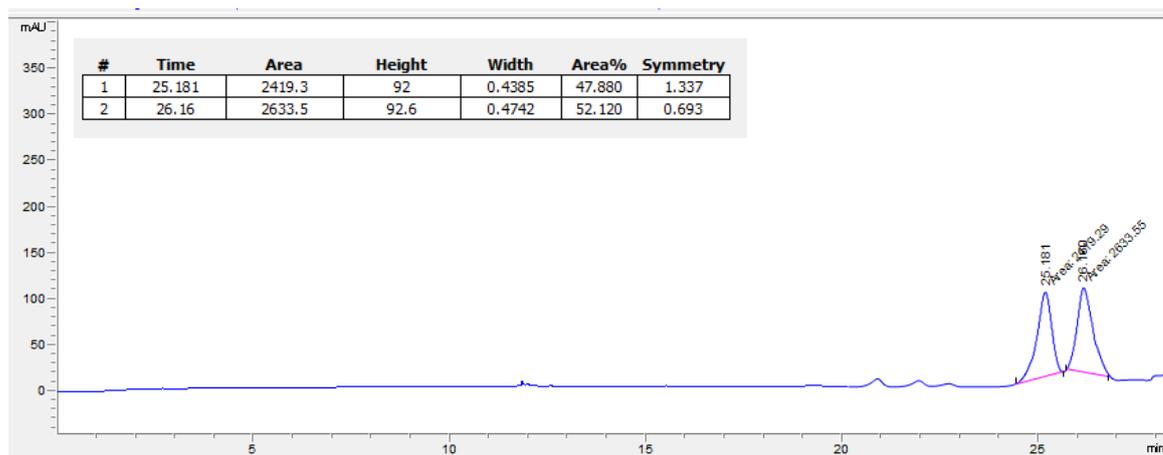


To a solution of $\text{Pd}(\text{OAc})_2$ (10.6 mg, 0.474 mmol, 0.05 equiv.) in THF (63.2 mL) at -78 °C, was added PPh_3 (12.4 mg, 0.474 mmol, 0.05 equiv.), and the resulting mixture was stirred for 5 min. A solution of aldehyde **15** (1.84 g, 9.47 mmol, 1.0 equiv.) and mesylate **16** (2.18 g, 14.7 mmol, 1.55 equiv.) in THF (3.9 mL) was added. After stirring at -78 °C for 5 min, Et_2Zn (28.4 mL, 1.0 M in hexane, 28.4 mmol, 3.0 equiv.) was added dropwise. The mixture was stirred for another 5 min and then warmed to -20 °C (colour changed to dark brown). After stirring at -20 °C overnight, the reaction mixture was quenched with sat. aq. NH_4Cl solution (50 mL). The layers were separated and the aqueous layer was extracted with diethyl ether (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane to 20% EtOAc/pentane) to afford alcohol **20** (1.27 g, 5.11 mmol, 54%, 95% *ee*, 16:1 *dr*) as a yellow oil.

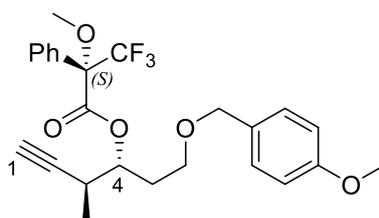
R_f 0.50 (30% EtOAc /pentane); $[\alpha]_{\text{D}}^{25} -8.8$ ($c = 0.50$, CHCl_3); **IR** (thin film, ν_{\max} / cm^{-1}) 3420, 3288, 2979, 2936, 2871, 1613, 1513, 1248, 1092, 821; **¹H NMR** (400 MHz, CDCl_3) δ 7.25 (2H, d, $J = 8.5$ Hz, ArH), 6.88 (2H, d, $J = 8.7$ Hz, ArH), 4.46 (2H, s, H7), 3.80 (3H, s, H8), 3.78-3.69 (2H, m, H4 and H6), 3.63 (1H, ddd, $J = 9.4, 7.8, 4.6$ Hz, H6'), 2.81 (1H, d, $J = 4.4$ Hz, OH), 2.56 (1H, qdd, $J = 7.0, 4.4, 2.5$ Hz, H3), 2.12 (1H, d, $J = 2.5$ Hz, H1), 1.93-1.78 (2H, m, H5), 1.23 (3H, d, $J = 7.0$ Hz,

C3-Me); ^{13}C NMR (101 MHz, CDCl_3) δ 159.4, 130.2, 129.5, 114.0, 85.7, 73.3, 73.1, 70.6, 68.5, 55.4, 34.2, 32.8, 16.9; HRMS (ESI $^+$) calc. for $\text{C}_{15}\text{H}_{20}\text{O}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 271.1305, found 271.1305.

HPLC for compound **17**: [CHIRALPAK-IC, eluent system: 100% isopropanol-10% isopropanol/*n*-hexane (0-20 min), 10% isopropanol/*n*-hexane-15% isopropanol/*n*-hexane (20-40 min), injection volume: 5 μL , flow rate: 1.0 mL/min, λ = 260 nm]: t_{R} = 23.9 min (major), 24.7 min (minor); 95% *ee*



(3*R*,4*S*)-1-((4-Methoxybenzyl)oxy)-4-methylhex-5-yn-3-yl (S)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (17-*S*-ester)

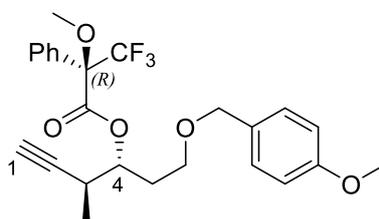


To a solution of alcohol **17** (5.9 mg, 0.0238 mmol, 1.0 equiv.) in CH_2Cl_2 (0.35 mL) was added

anhydrous pyridine (11.9 μL , 0.147 mmol, 6.2 equiv.) and (*R*)-(-)- α -Methoxy- α -(trifluoromethyl)phenylacetyl chloride (16.9 μL , 0.0903 mmol, 3.8 equiv.) at room temperature. After stirring at room temperature overnight, the reaction was quenched with water (1 mL) and extracted with CH_2Cl_2 (3 x 1 mL). The combined organic layers were washed with brine (1 mL), dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane to 10% EtOAc/pentane) to afford alcohol **17-S-ester** (9.0 mg, 0.0194 mmol, 82%) as a yellow oil.

R_f 0.50 (10% EtOAc /pentane); $[\alpha]_D^{25}$ -5.1 ($c = 1.0$, CHCl_3); **IR** (thin film, $\nu_{\text{max}} / \text{cm}^{-1}$) 3293, 2954, 2850, 1745, 1612, 1514, 1249, 1170, 1082, 994, 719; **$^1\text{H NMR}$** (500 MHz, CDCl_3 , ^{19}F decoupled) δ 7.56 (2H, d, $J = 6.1$ Hz, ArH), 7.41-7.35 (3H, m, ArH), 7.25 (2H, d, $J = 8.5$ Hz, ArH), 6.87 (2H, d, $J = 8.6$ Hz, ArH), 5.29 (1H, dt, $J = 8.4, 4.1$ Hz, H4), 4.40 (2H, s, H7), 3.80 (3H, s, OCH_3), 3.50 (3H, s, OCH_3), 3.49-3.41 (2H, m, H6), 2.82 (1H, qdd, $J = 7.0, 4.0, 2.6$ Hz, H3), 2.12 (1H, dddd, $J = 14.2, 7.9, 6.2, 4.2$ Hz, H5), 2.05 (1H, d, $J = 2.5$ Hz, H1), 2.04-1.98 (1H, m, H5'), 1.07 (3H, d, $J = 7.1$ Hz, C3-Me); **$^{13}\text{C NMR}$** (126 MHz, CDCl_3) δ 166.3, 159.4, 132.1, 130.3, 129.7, 129.5, 128.5, 127.6, 123.5 (q, $J = 289$ Hz), 114.0, 84.7 (q, $J = 28$ Hz), 83.8, 75.7, 72.9, 70.9, 65.9, 55.6, 55.4, 31.4, 29.8, 16.2; **$^{19}\text{F NMR}$** (470 Hz, CDCl_3) δ -71.5; **HRMS** (ES^+) calc. for $\text{C}_{25}\text{H}_{27}\text{O}_5\text{F}_3\text{Na}$ $[\text{M}+\text{Na}]^+$ 487.1703, found 487.1699.

(3*R*,4*S*)-1-((4-Methoxybenzyl)oxy)-4-methylhex-5-yn-3-yl (*R*)-3,3,3-trifluoro-2-methoxy-2-phenylpropanoate (17-*R*-ester)



To solution of alcohol **17** (5.5 mg, 0.0221 mmol, 1.0 equiv.) in CH_2Cl_2 (0.33 mL) was added anhydrous pyridine (11.1 μL , 0.137 mmol, 6.2 equiv.) and (*S*)-(+)- α -Methoxy- α -(trifluoromethyl)phenylacetyl chloride (15.7 μL , 0.0842 mmol, 3.8 equiv.) at room temperature. After stirring at room temperature overnight, the reaction was quenched with water (1 mL) and extracted with CH_2Cl_2 (3 x 1 mL). The combined organic layers were washed with brine (1 mL), dried over

Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane to 10% EtOAc/pentane) to afford alcohol **20-R-ester** (8.1 mg, 0.0174 mmol, 81%) as a yellow oil.

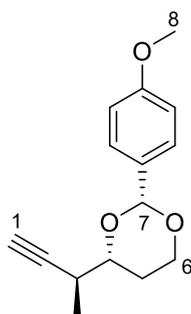
R_f 0.50 (10% EtOAc /pentane); **[α]_D²⁵** +43.7 (*c* = 1.0, CHCl₃); **IR** (thin film, ν_{max} / cm⁻¹) 3291, 2981, 2856, 1746, 1613, 1514, 1249, 1170, 1082, 1018, 717; **¹H NMR** (500 MHz, CDCl₃, ¹⁹F decoupled) δ 7.59 (2H, dd, *J* = 8.1 Hz, ArH), 7.42-7.35 (3H, m, ArH), 7.23 (2H, d, *J* = 8.6 Hz, ArH), 6.87 (2H, d, *J* = 8.6 Hz, ArH), 5.33 (1H, dt, *J* = 8.5, 4.2 Hz, H4), 4.32 (2H, s, H7), 3.80 (3H, s, OCH₃), 3.58 (3H, s, OCH₃), 3.39-3.33 (1H, m, H6), 3.27 (1H, ddd, *J* = 9.6, 8.1, 5.5 Hz, H6'), 2.83 (1H, qdd, *J* = 7.1, 4.2, 2.5 Hz, H3), 2.09 (1H, d, *J* = 2.5 Hz, H1), 2.07-1.92 (2H, m, H5), 1.20 (3H, d, *J* = 7.1 Hz, H3-Me); **¹³C NMR** (126 MHz, CDCl₃) δ 166.3, 159.4, 132.3, 130.4, 129.7, 129.4, 128.5, 127.6, 123.5 (q, *J* = 289 Hz) 114.0, 84.7, 84.0 (q, *J* = 28 Hz), 75.6, 72.8, 71.1, 65.7, 55.8, 55.4, 31.8, 30.4, 16.9; **¹⁹F NMR** (470 Hz, CDCl₃) δ -71.3; **HRMS** (ES⁺) calc. for C₂₅H₂₇O₅F₃Na [M+Na]⁺ 487.1703, found 487.1697.

Comparison of ¹H NMR data of two Mosher ester derivatives is shown below:

Proton position	S-17-ester (ppm)	R-17-ester (ppm)	Δδ _{SR}
H1	2.05	2.09	-0.04
H3	2.82	2.83	-0.01
H3'	1.07	1.02	-0.13
H5	2.02	2.00	+0.02
H6	3.44	3.36	+0.08
H6	3.44	3.27	+0.17
H7	4.40	4.32	+0.08

Negative values obtained for alkyne portion and positive values obtained for PMB portion. Analysis of all the values reveals the C4 centre is of R configuration.

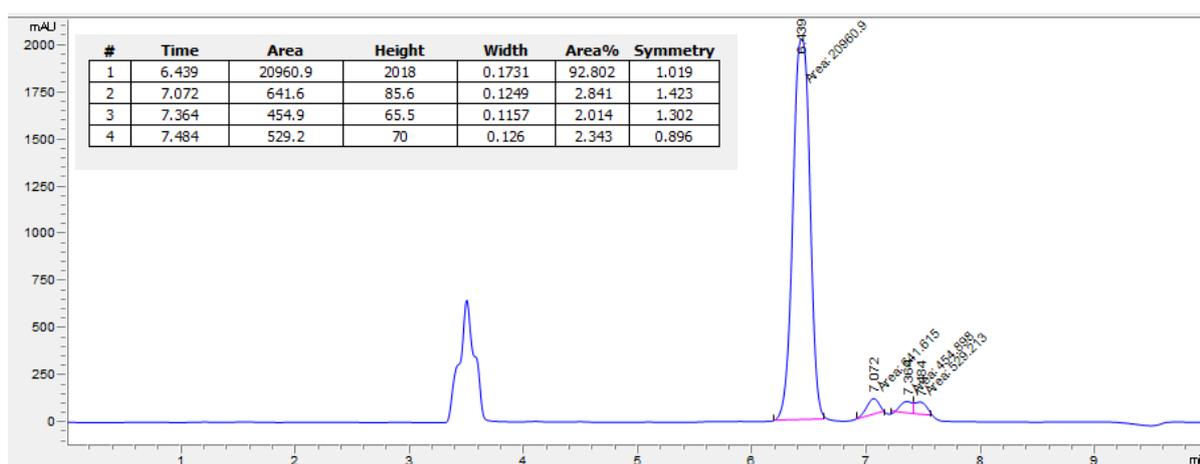
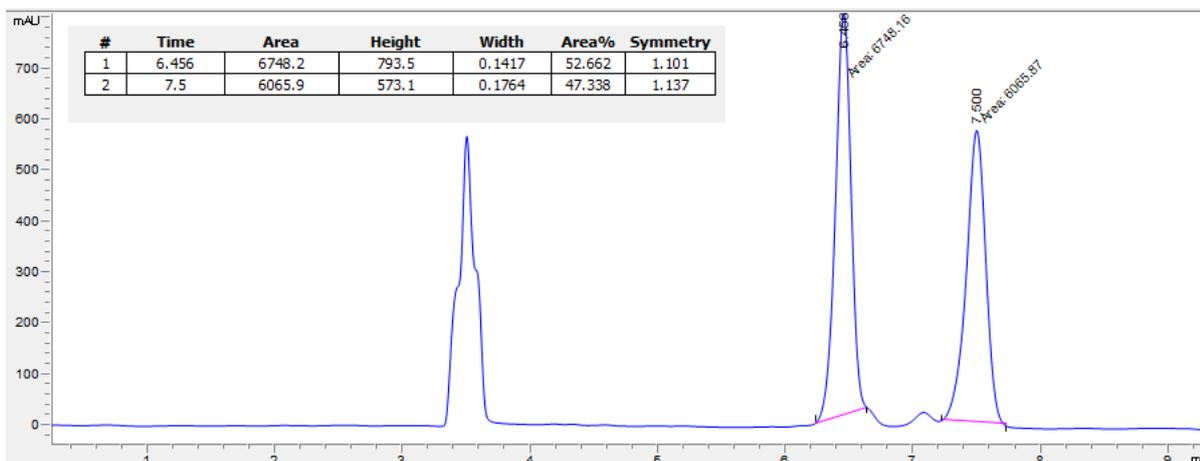
(2*R*,4*R*)-4-((*S*)-But-3-yn-2-yl)-2-(4-methoxyphenyl)-1,3-dioxane (4)



To a solution of alcohol **20** (1.25 g, 5.03 mmol, 1.0 equiv.) and 3Å molecular sieves (3.7 g) in CH₂Cl₂ (25.0 mL) was added 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (1.48 g, 6.54 mmol, 1.3 equiv.) in three portions at 0 °C. After stirring at 0 °C for 2 h, the reaction mixture was quenched with sat. aq. NaHCO₃ solution (50 mL) and filtered through celite. The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 100 mL). The combined organic layers were washed with brine (100 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane to 10% EtOAc/pentane) to afford title PMP alkyne **4** (0.81 g, 3.29 mmol, 65%, 95% *ee*, 19:1 *dr*) as a white solid.

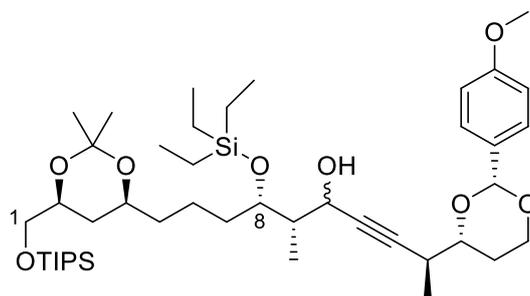
m.p. 67-68 °C; **R_f** 0.50 (10% EtOAc /pentane); **[α]_D²⁵** -12.3 (*c* = 0.55, CHCl₃); **IR** (thin film, ν_{max}/cm⁻¹) 3289, 2979, 2936, 2851, 1615, 1518, 1248, 1102, 1034, 829; **¹H NMR** (400 MHz, CDCl₃) δ 7.43 (2H, d, *J* = 8.4 Hz, ArH), 6.89 (2H, d, *J* = 8.8 Hz, ArH), 5.48 (1H, s, H7), 4.30 (1H, ddd, *J* = 11.4, 5.1, 1.4 Hz, H4), 3.96 (1H, td, *J* = 12.1, 2.5 Hz, H6), 3.91-3.85 (1H, m, H6'), 3.80 (3H, s, H8), 2.77 (1H, qdd, *J* = 7.2, 5.0, 2.5 Hz, H3), 2.10 (1H, d, *J* = 2.5 Hz, H1), 1.99 (1H, dddd, *J* = 13.1, 12.3, 11.3, 5.0 Hz, H5), 1.59 (1H, m, dtd, *J* = 13.2, 2.5, 1.4 Hz, H5'), 1.27 (3H, d, *J* = 7.1 Hz, C3-Me); **¹³C NMR** (101 MHz, CDCl₃) δ 160.1, 131.4, 127.5, 113.7, 101.3, 85.5, 78.7, 70.0, 67.0, 55.4, 31.1, 27.1, 15.7; **HRMS** (ESI⁺) calc. for C₁₅H₁₈O₃Na [M+Na]⁺ 269.1148, found 269.1146.

HPLC for compound 4 (CHIRALPAK-IC, eluent system: 10% isopropanol/*n*-hexane, injection volume: 5 μ L, flow rate: 1.0 mL/min, λ = 222 nm): t_R = 6.4 min (product), 7.5 min (enantiomer of product); 95% *ee*, 19:1 *dr*^a



^aPeak at 3.5 min is the residual solvent peak for both graphs. In the second graph, peak 2 and 3 are diastereomers of product. In addition, peak 4 is the enantiomer of product and the enantioselectivity originates from previous allenyl zinc addition step.

(2*S*,6*S*,7*S*)-10-(((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-2-((4*R*)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl)-6-methyl-7-((triethylsilyl)oxy)dec-3-yn-5-ol (18)

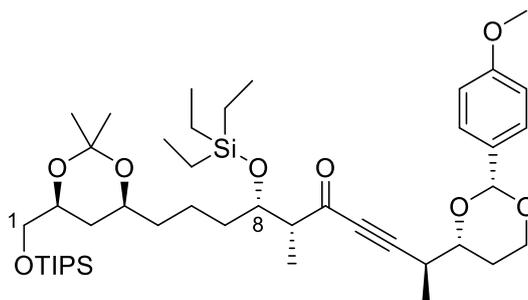


To a solution of alkyne **4** (0.38 g, 1.56 mmol, 1.6 equiv.) in THF (2.1 mL) at -78 °C under argon was added *n*-butyllithium (0.58 mL, 2.5 M in hexanes, 1.46 mmol, 1.4 equiv.) dropwise. After stirring at -78 °C for 1 h, the reaction mixture was warmed to 0 °C and stirred for another 1 h. The reaction mixture was recooled to -78 °C and a solution of aldehyde **3** (0.53 g, 0.973 mmol, 1.0 equiv.) in THF (0.4 mL) was added dropwise. After stirring at -78 °C for 1 h, the reaction was slowly warmed to 0 °C. After stirring at 0 °C for 1 h, the mixture was warmed to room temperature and stirred for a further 1 h. The reaction mixture was quenched with sat. aq. NH₄Cl solution (10 mL) and extracted with Et₂O (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% EtOAc/pentane to 30% EtOAc/pentane) to afford title compound **18** (0.66 g, 0.834 mmol, 86%) as a colourless oil and inseparable mixture of diastereomers (1:1), along with recovered alkyne **4** (0.12 g, 0.49 mmol).

R_f 0.45 (20% EtOAc /pentane); **IR** (thin film, ν_{\max} / cm⁻¹) 3464, 2942, 2867, 1616, 1518, 1463, 1379, 1249, 1109, 1009, 883, 742; **¹H NMR** (400 MHz, CDCl₃) δ 7.41 (2H, d, J = 8.9 Hz, ArH), 6.87 (2H, d, J = 8.7 Hz, ArH), 5.46 (1H, s, PMP acetal), 4.48 (0.5H, br s, H10), 4.40-4.35 (0.5H, m, H10), 4.28 (1H, ddd, J = 11.3, 5.0, 1.4 Hz, H14), 4.03-3.81 (5H, m, H2, H4, H8 and H16), 3.80 (3H, s, OMe), 3.76 (1H, dd, J = 9.7, 5.0 Hz, H1), 3.63 (0.5H, d, J = 4.4 Hz, OH), 3.52 (1H, dd, J = 9.7, 6.8 Hz, H1'), 2.88 (0.5H, d, J = 3.7 Hz, OH), 2.81 (1H, tdd, J = 6.9, 5.0, 2.1 Hz, H9),) 2.04-1.91(1H, qd, J = 12.4, 5.0 Hz, H13), 1.90-1.72 (1H, m, H3), 1.71-1.44 (7H, m, H3', H5, H7 and H15), 1.43 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.35-1.26 (2H, m, H6), 1.24 (3H, d, J = 7.1 Hz, C9-Me), 1.15-0.99 (24H, m, TIPS and C13-Me), 0.95 (9H, t, J = 7.9 Hz, TES), 0.62 (6H, q, J = 8.0 Hz, TES); **¹³C NMR** (101 MHz, CDCl₃) δ 160.0, 131.4, 127.6, 113.7, 101.3, 98.5, 86.4, 86.3, 82.9, 82.8, 78.9, 78.9,

75.9, 75.0, 70.2, 68.9, 68.8, 67.4, 67.1, 66.6, 65.9, 55.4, 43.4, 42.8, 36.7, 34.9, 34.5, 32.9, 31.3, 31.2, 30.2, 27.1, 26.9, 21.9, 21.4, 20.0, 18.1, 15.7, 15.6, 12.1, 7.9, 7.0, 5.4, 5.3; HRMS (ESI⁺) calc. for C₄₄H₇₈O₈NaSi₂ [M+Na]⁺ 813.5127, found 813.5120.

(2*S*,6*R*,7*S*)-10-((4*S*,6*S*)-2,2-Dimethyl-6-(((triisopropylsilyloxy)methyl)-1,3-dioxan-4-yl)-2-((4*R*)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl)-6-methyl-7-((triethylsilyloxy)dec-3-yn-5-one (S4)

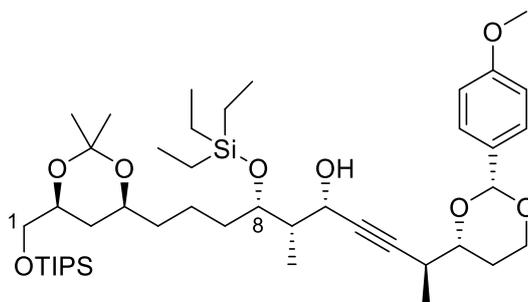


To a solution of the diastereomers **18** (0.66 g, 0.834 mmol, 1.0 equiv.) in CH₂Cl₂ (5.6 mL) and *tert*-butanol (70.0 μL), was added solid NaHCO₃ (0.70 g, 8.34 mmol, 10.0 equiv.) and Dess-Martin periodinane (0.53 g, 1.25 mmol, 1.5 equiv.). After stirring at room temperature for 2 h, the reaction mixture was quenched with sat. aq. NaHCO₃ solution (5 mL) and sat. aq. Na₂S₂O₃ solution (5 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 10 mL) and the combined organic layers were washed with brine (10 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% EtOAc/pentane) to afford title compound **S4** (0.59 g, 0.748 mmol, 90%) as a colourless oil.

R_f 0.50 (10% EtOAc/pentane); [α]_D²⁵ -9.1 (*c* = 0.27, CHCl₃); **IR** (thin film, ν_{max} / cm⁻¹) 2951, 2867, 1676, 1518, 1380, 1250, 1111, 1011, 882, 829, 744; **¹H NMR** (400 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.7 Hz, ArH), 6.88 (2H, d, *J* = 8.8 Hz, ArH), 5.48 (1H, s, PMP acetal), 4.33-4.22 (2H, m, H8 and H14), 3.99-3.89 (4H, m, H2, H4 and H16), 3.80 (3H, s, OCH₃), 3.75 (1H, dd, *J* = 9.7, 5.0 Hz, H1), 3.52 (1H, dd, *J* = 9.7, 6.7 Hz, H1'), 2.93 (1H, qd, *J* = 7.1, 5.1 Hz, H9), 2.58 (1H, qd, *J* = 6.9, 4.1 Hz, H13), 2.02-1.92 (1H, m, H7), 1.67-1.45 (7H, m, H3, H5, H7' and H15), 1.43 (3H, s, acetonide), 1.36 (3H, s, acetonide), 1.31 (3H, d, *J* = 7.1 Hz, H9-Me), 1.14 (3H, d, *J* = 6.9 Hz, H13-Me), 1.15-1.03 (23H, m, H6 and TIPS), 0.93 (9H, t, *J* = 7.9 Hz, TES), 0.57 (6H, q, *J* = 7.7 Hz, TES); **¹³C NMR** (101 MHz, CDCl₃) δ 190.8, 160.1, 131.1, 127.5, 113.7, 101.4, 98.5, 95.0, 81.9, 78.2, 72.7, 70.2, 68.8, 67.4,

66.8, 55.4, 53.3, 36.7, 35.8, 34.5, 31.8, 30.2, 27.6, 21.2, 19.9, 18.1, 15.1, 12.1, 9.8, 7.1, 5.3; **HRMS** (ESI⁺) calc. for C₄₄H₇₆O₈NaSi₂ [M+Na]⁺ 811.4971, found 811.4966.

(2S,5S,6S,7S)-10-((4S,6S)-2,2-Dimethyl-6-(((triisopropylsilyl)oxy)methyl)-1,3-dioxan-4-yl)-2-((4R)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl)-6-methyl-7-(((triethylsilyl)oxy)dec-3-yn-5-ol (19)

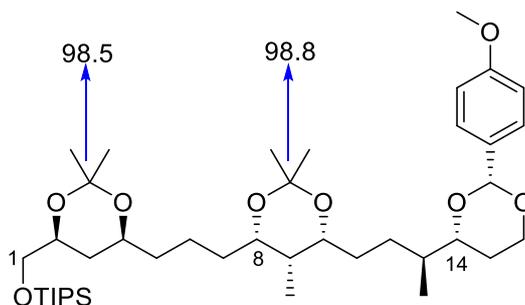


To a solution of ketone **S4** (0.59 g, 0.748 mmol, 1.0 equiv.) in degassed 2-propanol (7.5 mL), was added a solution of Ru[(1*S*,2*S*)-*p*-TsNCH(C₆H₅)CH(C₆H₅)NH](η^6 -*p*-cymene)² (50.0 mg, 0.0748 mmol, 0.1 equiv.) in degassed CH₂Cl₂ (0.65 mL) dropwise. The resulting mixture was stirred at room temperature for 2 h and then concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% ethyl acetate/pentane) to afford title compound **19** (0.54 g, 0.682 mmol, 92%, >20:1 *dr*) as a yellow oil.

R_f 0.45 (20% EtOAc/pentane); [α]_D²⁵ -4.7 (*c* = 0.45, CHCl₃); **IR** (thin film, ν_{max} / cm⁻¹) 3461, 2943, 2868, 1616, 1518, 1462, 1379, 1249, 1109, 1010, 883, 828, 741; **¹H NMR** (400 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.7 Hz, ArH), 6.87 (2H, d, *J* = 8.8 Hz, ArH), 5.47 (1H, s, PMP acetal), 4.48 (1H, brs, H10), 4.28 (1H, ddd, *J* = 11.3, 5.0, 1.4 Hz, H14), 3.98-3.85 (5H, m, H2, H4, H8 and H16), 3.80 (3H, s, OCH₃), 3.76 (1H, dd, *J* = 9.7, 5.0 Hz, H1), 3.52 (1H, dd, *J* = 9.7, 6.7 Hz, H1'), 2.88 (1H, d, *J* = 3.7 Hz, OH), 2.82 (1H, ddt, *J* = 10.3, 7.1, 3.1 Hz, H9), 1.97 (1H, qd, *J* = 12.4, 5.0 Hz, H13), 1.82-1.75 (1H, m, H3), 1.65 (1H, dt, *J* = 12.9, 2.5 Hz, H3'), 1.62-1.46 (6H, m, H5, H7 and H15), 1.43 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.35-1.27 (2H, m, H6), 1.24 (3H, d, *J* = 7.0 Hz, H9-Me), 1.15-1.03 (21H, m, TIPS), 1.02 (3H, d, *J* = 6.9 Hz, H13-Me), 0.96 (9H, t, *J* = 7.9 Hz, TES), 0.61 (6H, q, *J* = 8.0 Hz, TES); **¹³C NMR** (101 MHz, CDCl₃) δ 160.1, 131.4, 127.6, 113.7, 101.3, 98.5, 86.4, 82.8, 78.9, 75.9, 70.2, 68.8, 67.4, 67.1, 66.6, 55.4, 42.8, 36.7, 34.9, 34.5, 31.2, 30.3, 26.9, 21.4, 20.0, 18.1, 15.6, 12.1, 7.9, 7.0, 5.4; **HRMS** (ESI⁺) calc. for C₄₄H₇₈O₈NaSi₂ [M+Na]⁺ 813.5127, found 813.5107.

67.3, 55.4, 40.5, 38.0, 36.2, 35.2, 34.5, 32.7, 30.2, 28.9, 28.2, 22.0, 20.0, 18.1, 15.1, 12.1, 4.3; HRMS (ESI⁺) calc. for C₃₈H₆₈O₈NaSi [M+Na]⁺ 703.4576, found 703.4557.

Triisopropyl(((4*S*,6*S*)-6-(3-((4*S*,5*R*,6*R*)-6-((3*S*)-3-((4*R*)-2-(4-methoxyphenyl)-1,3-dioxan-4-yl)butyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propyl)-2,2-dimethyl-1,3-dioxan-4-yl)methoxy)silane
(2)

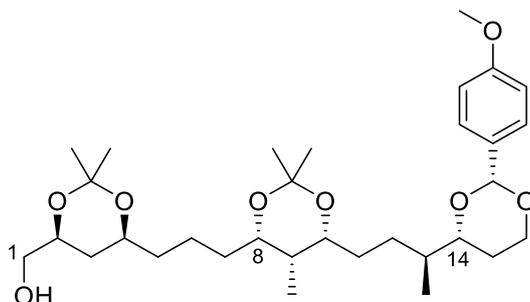


To a solution of diol **20** (0.35 g, 0.514 mmol, 1.0 equiv.) in CH₂Cl₂ (10.3 mL), was added 2,2-dimethoxypropane (10.3 mL) and pyridinium *p*-toluenesulfonate (25.8 mg, 0.103 mmol, 0.2 equiv.). The resulting mixture was stirred at room temperature for 2 h. The reaction mixture was quenched with sat. aq. NaHCO₃ solution (10 mL) and extracted with CH₂Cl₂ (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% EtOAc/pentane) to afford title compound **2** (0.33 g, 0.458 mmol, 88%) as a colourless oil.

R_f 0.45 (10% EtOAc/pentane); [**α**]_D²⁵ -6.2 (*c* = 0.70, CHCl₃); **IR** (thin film, *v*_{max} / cm⁻¹) 2941, 2865, 1615, 1518, 1462, 1379, 1249, 1112, 1010, 882; **¹H NMR** (500 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.7 Hz, ArH), 6.88 (2H, d, *J* = 8.7 Hz, ArH), 5.44 (1H, s, PMP acetal), 4.27 (1H, ddd, *J* = 11.4, 5.0, 1.4 Hz, H14), 3.95-3.90 (2H, m, H2 and H4), 3.86-3.81 (3H, m, H8 and H16), 3.80 (3H, s, OCH₃), 3.76 (1H, dd, *J* = 9.7, 5.0 Hz, H1), 3.61 (1H, ddd, *J* = 11.3, 6.8, 2.3 Hz, H10), 3.52 (1H, dd, *J* = 9.7, 6.7 Hz, H1'), 1.85-1.76 (1H, m, H13), 1.76-1.62 (3H, m, H3 and H9), 1.61-1.45 (8H, m, H5, H7, H11 and H15), 1.44 (3H, s, acetonide), 1.41 (3H, s, acetonide), 1.39 (3H, s, acetonide), 1.37 (3H, s, acetonide), 1.36-1.30 (4H, m, H6 and H12), 1.16-1.03 (21H, m, TIPS), 0.95 (3H, d, *J* = 6.8 Hz, H9-Me), 0.82 (3H, d, *J* = 6.8 Hz, H13-Me); **¹³C NMR** (126 MHz, CDCl₃) δ 159.9, 131.7, 127.5, 113.7, 101.2, 98.8, 98.5, 81.1, 73.8, 73.4, 70.2, 69.0, 67.4, 67.3, 55.4, 37.9, 36.7, 34.4, 34.2, 33.0, 30.3, 30.2,

29.9, 28.1, 27.6, 21.1, 20.0, 19.9, 18.1, 15.0, 12.1, 4.6; **HRMS** (ESI⁺) calc. for C₄₁H₇₂O₈NaSi [M+Na]⁺ 743.4889, found 743.4867.

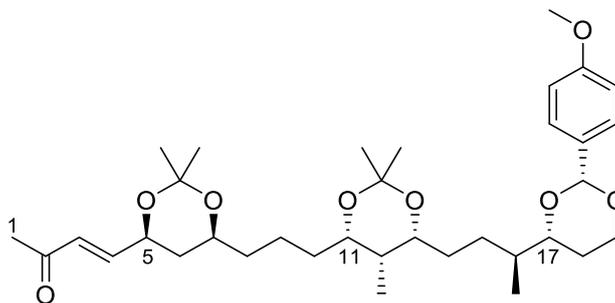
((4*S*,6*S*)-6-(3-((4*S*,5*R*,6*R*)-6-((3*S*)-3-((4*R*)-2-(4-Methoxyphenyl)-1,3-dioxan-4-yl)butyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propyl)-2,2-dimethyl-1,3-dioxan-4-yl)methanol (S5**)**



To a solution of acetonide **2** (97.7 mg, 0.135 mmol, 1.0 equiv.) in THF (2.1 mL) was added tetra-*n*-butylammonium fluoride (0.271 mL, 1.0 M in THF, 0.271 mmol, 2.5 equiv.). After stirring at room temperature overnight, the reaction was quenched with sat. aq. NH₄Cl solution (2 mL) and extracted with Et₂O (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (30% EtOAc/pentane) to afford primary alcohol **S5** (67.1 mg, 0.119 mmol, 88%) as a colourless oil.

R_f 0.30 (30% EtOAc/pentane); [α]_D²⁵ -11.6 (*c* = 0.45, CHCl₃); **IR** (thin film, ν_{max} / cm⁻¹) 3483, 2981, 2863, 1615, 1518, 1380, 1250, 1170, 1104, 1010, 829; **¹H NMR** (400 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.7 Hz, ArH), 6.88 (2H, d, *J* = 8.8 Hz, ArH), 5.44 (1H, s, PMP acetal), 4.27 (1H, ddd, *J* = 11.3, 5.0, 1.4 Hz, H14), 4.01-3.92 (2H, m, H2, H4), 3.91-3.81 (3H, m, H8, H16), 3.80 (3H, s, OCH₃), 3.63-3.57 (2H, m, H1, H10), 3.51-3.46 (1H, m, H1'), 1.96 (1H, t, *J* = 6.3 Hz, OH), 1.86-1.67 (2H, m, H9 and H13), 1.66-1.47 (6H, m, H3, H5 and H7), 1.45 (3H, s, acetonide), 1.41 (3H, s, acetonide), 1.40 (3H, s, acetonide), 1.38 (3H, s, acetonide), 1.36-1.10 (8H, m, H6, H11, H12 and H15), 0.94 (3H, d, *J* = 6.8 Hz, H9-Me), 0.80 (3H, d, *J* = 6.9 Hz, H13-Me); **¹³C NMR** (101 MHz, CDCl₃) δ 160.0, 131.7, 127.5, 113.7, 101.2, 98.8, 98.8, 81.0, 73.8, 73.4, 69.8, 68.6, 67.3, 66.3, 55.4, 37.9, 36.6, 34.1, 33.0, 32.5, 30.3, 30.2, 29.8, 28.2, 27.6, 21.1, 20.1, 19.9, 15.0, 4.6; **HRMS** (ESI⁺) calc. for C₃₂H₅₂O₈Na [M+Na]⁺ 587.3554, found 587.3539.

(E)-4-((4*S*,6*S*)-6-(3-((4*S*,5*R*,6*R*)-6-((3*S*)-3-((4*R*)-2-(4-Methoxyphenyl)-1,3-dioxan-4-yl)butyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propyl)-2,2-dimethyl-1,3-dioxan-4-yl)but-3-en-2-one (21)



To a solution of alcohol **S5** (67.1 mg, 0.119 mmol, 1.0 equiv.) in CH₂Cl₂ (0.80 mL), was added solid NaHCO₃ (99.8 mg, 1.19 mmol, 10.0 equiv.) and Dess-Martin periodinane (75.6 mg, 0.178 mmol, 1.5 equiv.). After stirring at room temperature for 1 h, the reaction mixture was cooled to 0 °C and quenched with sat. aq. NaHCO₃ solution (1 mL) and sat. aq. Na₂S₂O₃ solution (1 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄ and concentrated under reduced pressure to afford the corresponding aldehyde (61.2 mg, 0.109 mmol, 91%) as a colourless oil. **R_f**0.50 (10% EtOAc/pentane); The crude residue was used for the next step directly without further purification.

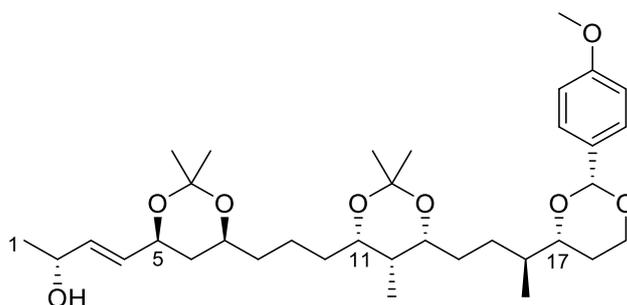
To a suspension of sodium hydride (8.7 mg, 60% dispersion in mineral oil, 0.218 mmol, 2.0 equiv.) in THF (2.2 mL) at 0 °C, was slowly added dimethyl (2-oxopropyl) phosphonate (31.6 μL, 0.228 mmol, 2.1 equiv.) and then the resulting mixture was warmed to room temperature. After stirring at room temperature for 1 h, the reaction mixture was cooled to -78 °C and a solution of crude aldehyde (61.2 mg, 0.109 mmol, 1.0 equiv.) in THF (1.1 mL) was added dropwise. The resulting mixture was allowed to warm slowly to room temperature and was stirred for 2 h. The mixture was quenched with water (1 mL) and diluted with Et₂O (1 mL). The layers were separated and the aqueous layer was extracted with Et₂O (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% EtOAc/pentane to 30% EtOAc/pentane) to afford enone **21** (45.1 mg, 0.0746 mmol, 63% over two steps) as a colourless oil.

R_f0.50 (25% EtOAc/pentane); **[α]_D²⁵** +6.5 (*c* = 0.14, CHCl₃); **IR** (thin film, ν_{max} / cm⁻¹) 2940, 2859, 1678, 1615, 1518, 1461, 1379, 1250, 1170, 1104, 1035, 829; **¹H NMR** (500 MHz, CDCl₃) δ 7.41 (2H, d, *J* = 8.7 Hz, ArH), 6.88 (2H, d, *J* = 8.8 Hz, ArH), 6.68 (1H, dd, *J* = 16.0, 4.6 Hz, H₄)^b, 6.26 (1H, d,

$J = 16.0$ Hz, H3), 5.44 (1H, s, PMP acetal), 4.56-4.52 (1H, m, H5), 4.27 (1H, ddd, $J = 11.3, 5.1, 1.4$ Hz, H17), 3.95-3.85 (3H, m, H11, H19), 3.85-3.81 (1H, m, H7), 3.80 (3H, s, OCH₃), 3.61 (1H, ddd, $J = 11.3, 6.8, 2.3$ Hz, H13), 2.27 (3H, s, H1), 1.84-1.69 (3H, m, H6, H12 and H16), 1.65-1.48 (9H, m, H6', H8, H10, H14, H18), 1.47 (3H, s, acetonide), 1.44 (3H, s, acetonide), 1.41 (3H, s, acetonide), 1.39 (3H, s, acetonide), 1.35-1.30 (4H, m, H9, H15), 0.94 (3H, d, $J = 6.8$ Hz, H12-Me), 0.80 (3H, d, $J = 6.8$ Hz, H16-Me); ¹³C NMR (126 MHz, CDCl₃) δ 198.7, 159.9, 146.1, 131.7, 129.4, 127.5, 113.7, 101.2, 99.0, 98.8, 81.0, 73.8, 73.4, 68.8, 68.5, 67.3, 55.4, 37.9, 36.4, 36.3, 34.2, 33.0, 30.2, 30.2, 29.8, 28.2, 27.6, 27.5, 21.1, 19.9, 19.9, 15.0, 4.6; HRMS (ESI⁺) calc. for C₃₅H₅₄O₈Na [M+Na]⁺ 625.3711, found 625.3701.

^bThe value of the coupling constant indicates the alkene is in trans configuration.

(2*R,E*)-4-((4*S,6S*)-6-(3-((4*S,5*R,6R*)-6-((3*S*)-3-((4*R*)-2-(4-Methoxyphenyl)-1,3-dioxan-4-yl)butyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propyl)-2,2-dimethyl-1,3-dioxan-4-yl)but-3-en-2-ol*
(22a)

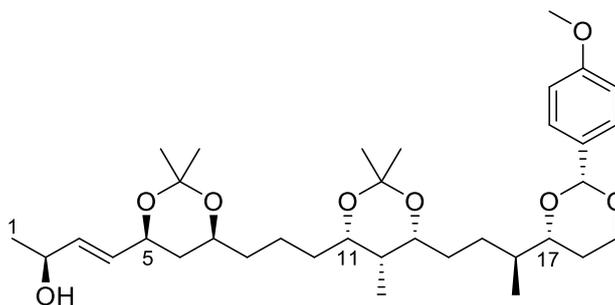


To a solution of (*S*)-(-)-2-methyl-CBS-oxazaborolidine (39.8 μ L, 1.0 M in toluene, 0.0398 mmol, 1.0 equiv.) in THF (0.6 mL) at 0 °C was added borane dimethyl sulfide complex solution (100 μ L, 1.0 M in THF, 0.1 mmol, 2.5 equiv.) dropwise. After stirring at 0 °C for 30 min, a solution of enone **26** (24.1 mg, 0.0398 mmol, 1.0 equiv.) in THF (0.2 mL) was added slowly and stirred for 1 h at 0 °C. The reaction was quenched with sat. aq. NH₄Cl solution (1 mL) and extracted with Et₂O (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (20% EtOAc/pentane to 40% EtOAc/pentane) to afford enol **27a** (22.0 mg, 0.036 mmol, 91%, >20:1 *dr*) as a colourless oil.

R_f 0.35 (30% EtOAc/pentane); [α]_D²⁵ -3.5 ($c = 0.35$, CHCl₃); **IR** (thin film, ν_{\max} / cm⁻¹) 3415, 2941,

2861, 1615, 1518, 1379, 1258, 1104, 971, 828; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.41 (2H, d, $J = 8.7$ Hz, ArH), 6.88 (2H, d, $J = 8.8$ Hz, ArH), 5.77 (1H, dd, $J = 15.6, 6.0$ Hz, H3), 5.65 (1H, dd, $J = 15.6, 6.0$ Hz, H4), 5.44 (1H, s, PMP acetal), 4.36-4.25 (3H, m, H2, H5, H17), 3.92 (1H, td, $J = 11.9, 2.6$ Hz, H11), 3.86-3.81 (3H, m, H7, H19), 3.80 (3H, s, OCH_3), 3.61 (1H, ddd, $J = 11.3, 6.8, 2.3$ Hz, H13), 1.84-1.62 (4H, m, H6, H12, H16), 1.61-1.48 (8H, m, H8, H10, H14, H18), 1.46 (3H, s, acetonide), 1.42 (3H, s, acetonide), 1.41 (3H, s, acetonide), 1.39 (3H, s, acetonide), 1.36-1.31 (4H, m, H9, H15), 1.27 (3H, d, $J = 6.5$ Hz, H1), 0.94 (3H, d, $J = 6.8$ Hz, C12-Me), 0.80 (3H, d, $J = 6.8$ Hz, C16-Me); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 159.9, 135.4, 131.7, 130.6, 127.5, 113.6, 101.2, 98.8, 98.7, 81.0, 73.8, 73.4, 69.6, 68.8, 68.3, 67.3, 55.4, 37.9, 37.1, 36.5, 34.1, 33.0, 30.4, 30.2, 29.8, 28.1, 27.5, 23.2, 21.1, 20.0, 19.9, 15.0, 4.6; **HRMS** (ESI^+) calc. for $\text{C}_{35}\text{H}_{56}\text{O}_8\text{Na}$ $[\text{M}+\text{Na}]^+$ 627.3867, found 627.3862.

(2*S*,*E*)-4-((4*S*,6*S*)-6-(3-((4*S*,5*R*,6*R*)-6-((3*S*)-3-((4*R*)-2-(4-Methoxyphenyl)-1,3-dioxan-4-yl)butyl)-2,2,5-trimethyl-1,3-dioxan-4-yl)propyl)-2,2-dimethyl-1,3-dioxan-4-yl)but-3-en-2-ol
(22b)

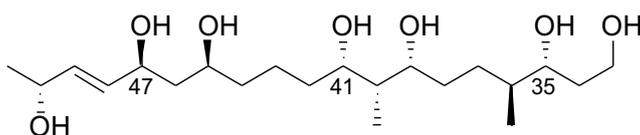


To a solution of (*R*)-(+)-2-methyl-CBS-oxazaborolidine (34.8 μL , 1.0 M in toluene, 0.0348 mmol, 1.0 equiv.) in THF (0.55 mL) at 0 $^\circ\text{C}$ was added borane dimethyl sulfide complex solution (87.1 μL , 1.0 M in THF, 0.0871 mmol, 2.5 equiv.) dropwise. After stirring at 0 $^\circ\text{C}$ for 30 min, a solution of enone **26** (21.0 mg, 0.0348 mmol, 1.0 equiv.) in THF (0.15 mL) was added slowly and stirred for 1 h at 0 $^\circ\text{C}$. The reaction was quenched with sat. aq. NH_4Cl solution (1 mL) and extracted with Et_2O (3 x 5 mL). The combined organic layers were washed with brine (5 mL), dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (20% EtOAc /pentane-40% EtOAc /pentane) to afford enol **21s** (19.0 mg, 0.031 mmol, 90%, >20:1 *dr*) as a colourless oil.

R_f 0.35 (30% EtOAc /pentane); $[\alpha]_{\text{D}}^{25}$ -2.5 ($c = 0.30$, CHCl_3); **IR** (thin film, ν_{max} / cm^{-1}) 3454, 2938,

2857, 1615, 1518, 1379, 1250, 1104, 969, 828; $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 7.41 (2H, d, $J = 8.8$ Hz, ArH), 6.88 (2H, d, $J = 8.7$ Hz, ArH), 5.77 (1H, dd, $J = 15.6, 6.1$ Hz, H3), 5.64 (1H, dd, $J = 15.6, 6.0$ Hz, H4), 5.44 (1H, s, PMP acetal), 4.36-4.25 (3H, m, H2, H5, H17), 3.92 (1H, td, $J = 11.9, 2.6$ Hz, H11), 3.86-3.81 (3H, m, H7, H19), 3.80 (3H, s, OCH_3), 3.61 (1H, ddd, $J = 11.3, 6.9, 2.3$ Hz, H13), 1.84-1.63 (4H, m, H6, H12, H16), 1.62-1.47 (8H, m, H8, H10, H14, H18), 1.46 (3H, s, acetonide), 1.42 (3H, s, acetonide), 1.41 (3H, s, acetonide), 1.39 (3H, s, acetonide), 1.36-1.30 (4H, m, H9, H15), 1.27 (3H, d, $J = 6.4$ Hz, H1), 0.94 (3H, d, $J = 6.8$ Hz, H12-Me), 0.80 (3H, d, $J = 6.8$ Hz, H16-Me); $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 159.9, 135.4, 131.7, 130.6, 127.5, 113.7, 101.2, 98.8, 98.8, 81.0, 73.8, 73.4, 69.6, 68.8, 68.4, 67.3, 55.4, 37.9, 37.1, 36.5, 34.1, 33.0, 30.4, 30.2, 29.8, 28.1, 27.6, 23.2, 21.1, 20.0, 19.9, 15.0, 4.6; **HRMS** (ESI^+) calc. for $\text{C}_{35}\text{H}_{56}\text{O}_8\text{Na}$ $[\text{M}+\text{Na}]^+$ 627.3867, found 627.3863.

(3*R*,4*S*,7*R*,8*R*,9*S*,13*S*,15*S*,18*S*,*E*)-4,8-Dimethylnonadec-16-ene-1,3,7,9,13,15,18-heptaol (1a)

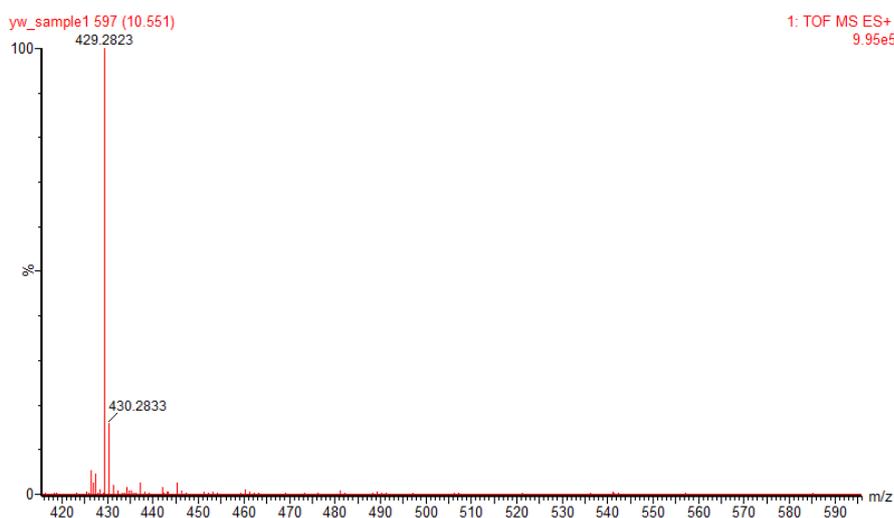
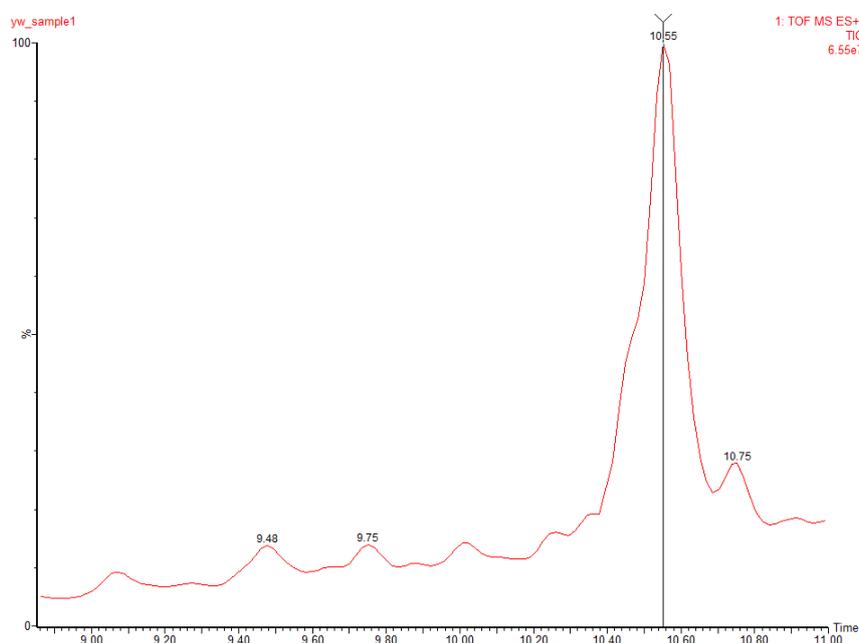


To a solution of enol **22a** (22.0 mg, 0.0364 mmol, 1.0 equiv.) in methanol (2.4 mL) and THF (1.2 mL), was added aq. HCl solution (2.4 mL, 0.1 M). After stirring at room temperature for 3 h, the reaction mixture was quenched with sat. aq. NaHCO_3 solution (3 mL) and extracted with chloroform/2-propanol (3:1) (3 x 15 mL). The combined organic layers were dried over Na_2SO_4 , filtered and concentrated under reduced pressure. The residue was purified by reverse phase HPLC (100% water to 25% acetonitrile/water gradient over 45 min) to give **1a** (8.1 mg, 0.0199 mmol, 55%) as a colourless oil. HPLC: Product peak is visible at 210 nm and the retention time is 18.2 min. In addition, other conditions (TFA, PTSA, CSA and high concentration aqueous HCl) were attempted to achieve deprotection but various byproducts were observed due to the vulnerability of the allylic alcohol.

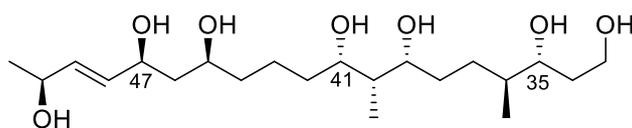
$R_f = 0.10$ (20% EtOH/ CH_2Cl_2); $[\alpha]_{\text{D}}^{25} +3.9$ ($c = 0.69$, MeOH); **IR** (thin film, $\nu_{\text{max}} / \text{cm}^{-1}$) 3366, 2981, 2889, 1647, 1382, 1252, 1151, 1071, 956; $^1\text{H NMR}$ (600 MHz, MeOD) δ 5.72 (1H, ddd, $J = 15.5, 5.8, 0.9$ Hz, H48), 5.61 (1H, ddd, $J = 15.5, 6.6, 1.1$ Hz, H49), 4.28-4.21 (2H, m, H47 and H50), 3.74-3.67 (5H, m, H33, H39, H41, H45), 3.58 (1H, ddd, $J = 9.9, 5.2, 2.6$ Hz, H35), 1.72-1.56 (6H, m, H34,

H37, H42 and H46), 1.54-1.39 (9H, m, H36, H38, H40, H42, H43, H44), 1.23 (3H, d, $J = 6.5$ Hz, H51), 1.13-1.09 (1H, m, H37'), 0.93 (3H, d, $J = 2.5$ Hz, 36-Me), 0.92 (3H, d, $J = 2.7$ Hz, C40-Me); ^{13}C NMR (151 MHz, MeOD) δ 136.1, 133.2, 76.4, 75.9, 73.8, 71.7, 70.6, 68.7, 60.8, 45.3, 42.8, 40.6, 38.7, 36.6, 36.0, 33.8, 29.7, 23.6, 23.0, 15.7, 7.0; HRMS (ES⁺) calc. for C₂₁H₄₂O₇Na [M+Na]⁺ 429.2823, found 429.2822.

LC-MS analysis of crude 1a before purification [LC: XDB-C18 column (150 mm x 4.6 mm, 5 μ m), 100% (water + 0.1% formic acid)-50% (acetonitrile + 0.1 formic acid)/(water + 0.1% formic acid) (0-40 min), MS: ESI⁺ positive mode, m/z range from 100-1000]; calc. for C₂₁H₄₂O₇Na [M+Na]⁺ 429.2823, found 429.2823. ($t = 10.55$ min)



(3*R*,4*S*,7*R*,8*R*,9*S*,13*S*,15*S*,18*R*,*E*)-4,8-Dimethylnonadec-16-ene-1,3,7,9,13,15,18-heptaol (1b**)**



To a solution of enol **22b** (19.0 mg, 0.0314 mmol, 1.0 equiv.) in methanol (2.0 mL) and THF (1.0 mL) was added aq. HCl solution (2.0 mL, 0.1 M). After stirring at room temperature for 3 h, the reaction mixture was quenched with sat. aq. NaHCO₃ solution (2 mL) and extracted with chloroform/2-propanol (3:1) (5 x 10 mL). The combined organic layers were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The residue was purified by reverse phase HPLC (100% water to 10% acetonitrile/water gradient over 45 min)^f to give **1b** (6.6 mg, 0.0162 mmol, 52%) as a colourless oil. HPLC: Product peak is visible at 210 nm and the retention time is 13.0 min.

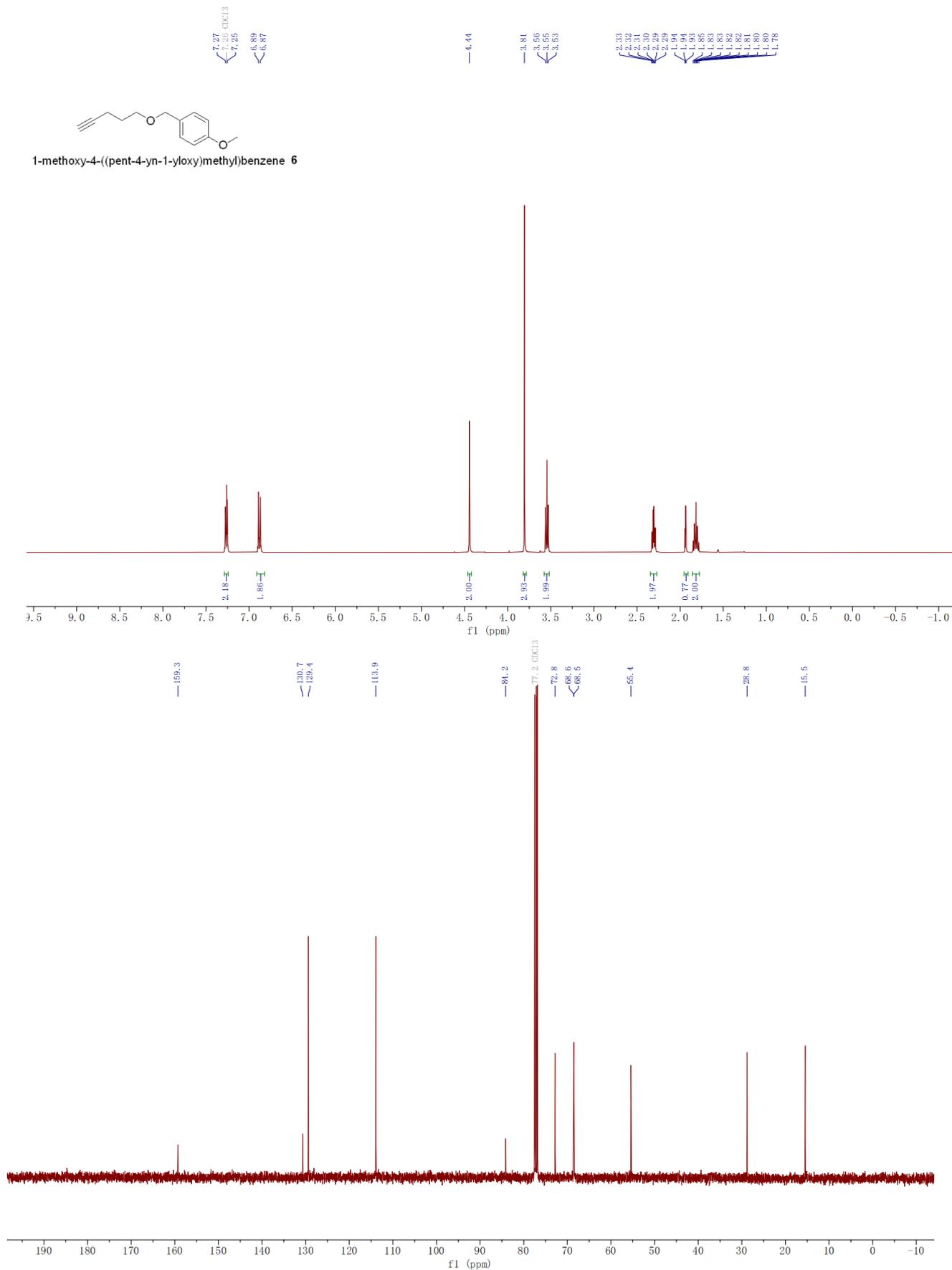
R_f = 0.10 (20% EtOH/DCM); $[\alpha]_D^{25}$ +9.9 (c = 0.76, MeOH); IR (thin film, ν_{\max} / cm⁻¹) 3344, 2981, 2889, 1653, 1382, 1252, 1150, 1071, 955; ¹H NMR (600 MHz, MeOD) δ 5.72 (1H, dd, J = 15.5, 5.9 Hz, H48), 5.61 (1H, ddd, J = 15.5, 6.6, 1.1 Hz, H49), 4.28-4.21 (2H, m, H47 and H50), 3.74-3.67 (5H, m, H33, H39, H41, H45), 3.58 (1H, ddd, J = 10.0, 5.2, 2.6 Hz, H35), 1.72-1.56 (6H, m, H34, H37, H42 and H46), 1.54-1.39 (9H, m, H36, H38, H40, H42, H43, H44), 1.23 (3H, d, J = 6.4 Hz, H51), 1.13-1.09 (1H, m, H37'), 0.93 (3H, d, J = 3.0 Hz, 36-Me), 0.92 (3H, d, J = 3.2 Hz, C40-Me); ¹³C NMR (151 MHz, MeOD) δ 136.0, 133.1, 76.4, 75.9, 73.8, 71.7, 70.6, 68.7, 60.8, 45.3, 42.8, 40.6, 38.7, 36.6, 36.0, 33.8, 29.7, 23.7, 23.1, 15.7, 7.0; HRMS (ESI⁺) calc. for C₂₁H₄₂O₇Na [M+Na]⁺ 429.2823, found 429.2823.

3. NMR data comparison of stambomycin D and two diastereomeric C33-C51 fragments 1a and 1b

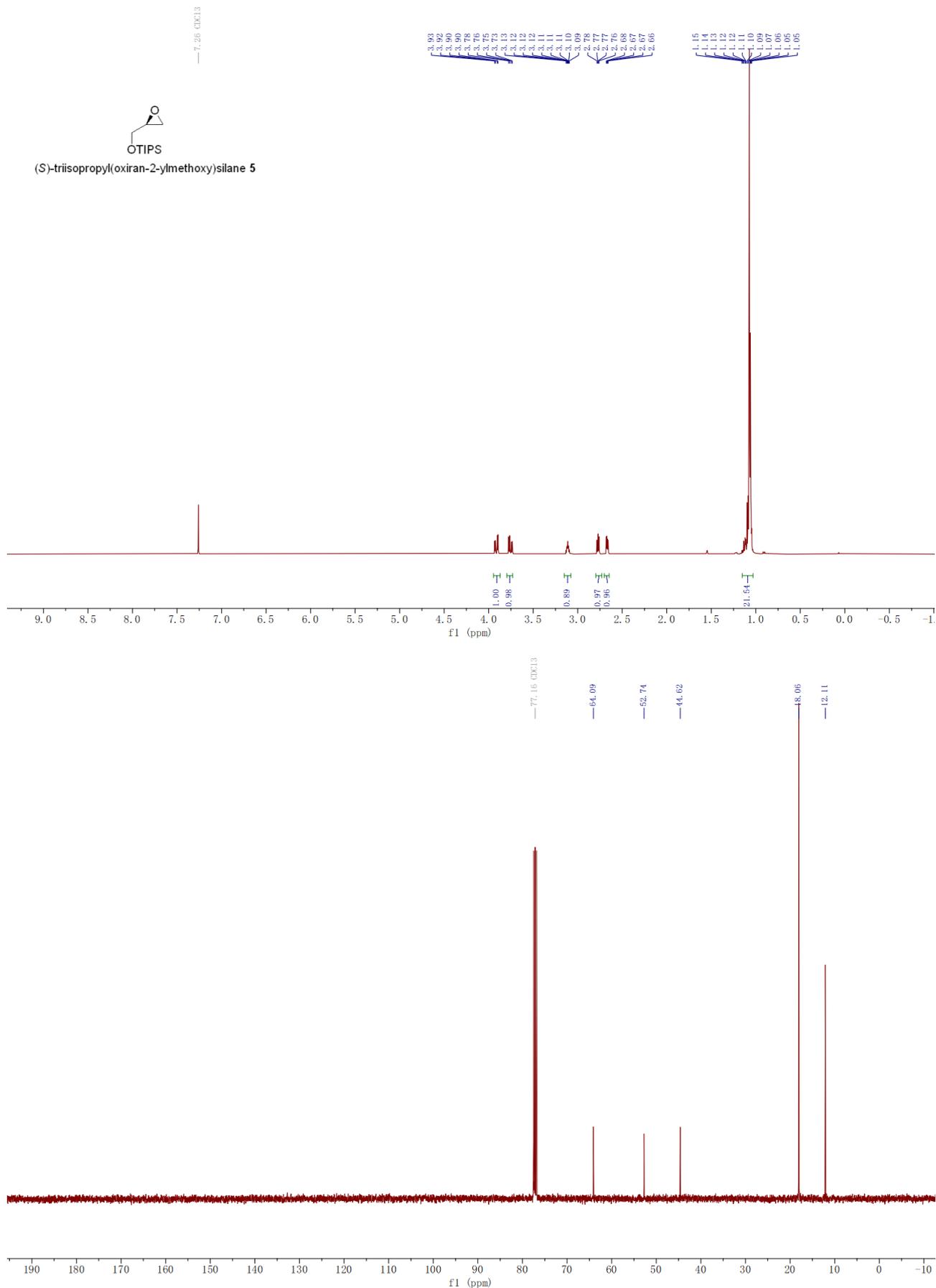
Position	Stambomycin D (MeOD, 700 MHz)		C50(<i>R</i>)-C33–C51 Fragment 1a (MeOD, 600 MHz)		C50(<i>S</i>)-C33–C51 Fragment 1b (MeOD, 600 MHz)	
	δ_C (ppm)	δ_H (ppm)	δ_C (ppm)	δ_H (ppm)	δ_C (ppm)	δ_H (ppm)
33	66.8	4.06	60.8	3.71	60.8	3.71
34	42.0	1.48, 1.50	36.6	1.57, 1.69,	36.6	1.57, 1.69,
35	72.9	3.74	73.8	3.58	73.8	3.58
36	40.8	1.48	40.6	1.53	40.6	1.53
36-Me	15.6	0.92	15.7	0.93	15.7	0.93
37	29.8	1.12, 1.28	29.7	1.10, 1.62	29.7	1.10, 1.62
38	36.0	1.50	36.0	1.48	36.0	1.48
39	76.3	3.72	76.4	3.71	76.4	3.71
40	42.3	1.51	42.8	1.50	42.8	1.50
40-Me	7.0	0.91	7.0	0.92	7.0	0.92
41	75.9	3.71	75.9	3.71	75.9	3.71
42	33.8	1.43, 1.62	33.8	1.41, 1.60	33.8	1.41, 1.60
43	22.9	1.43	23.0	1.46	23.1	1.46
44	38.8	1.45, 1.46	38.7	1.48	38.7	1.48
45	70.6	3.67	70.6	3.69	70.6	3.69
46	44.8	1.60, 1.65	45.3	1.57, 1.64	45.3	1.57, 1.64
47	71.1	4.28	71.7	4.25	71.7	4.25
48	136.7	5.80	136.1	5.72	136.0	5.72
49	130.8	5.72	133.2	5.63	133.1	5.63
50	72.8	5.43	68.7	4.25	68.7	4.25
51	20.8	1.33	23.6	1.23	23.7	1.23

4. Copies of NMR spectra

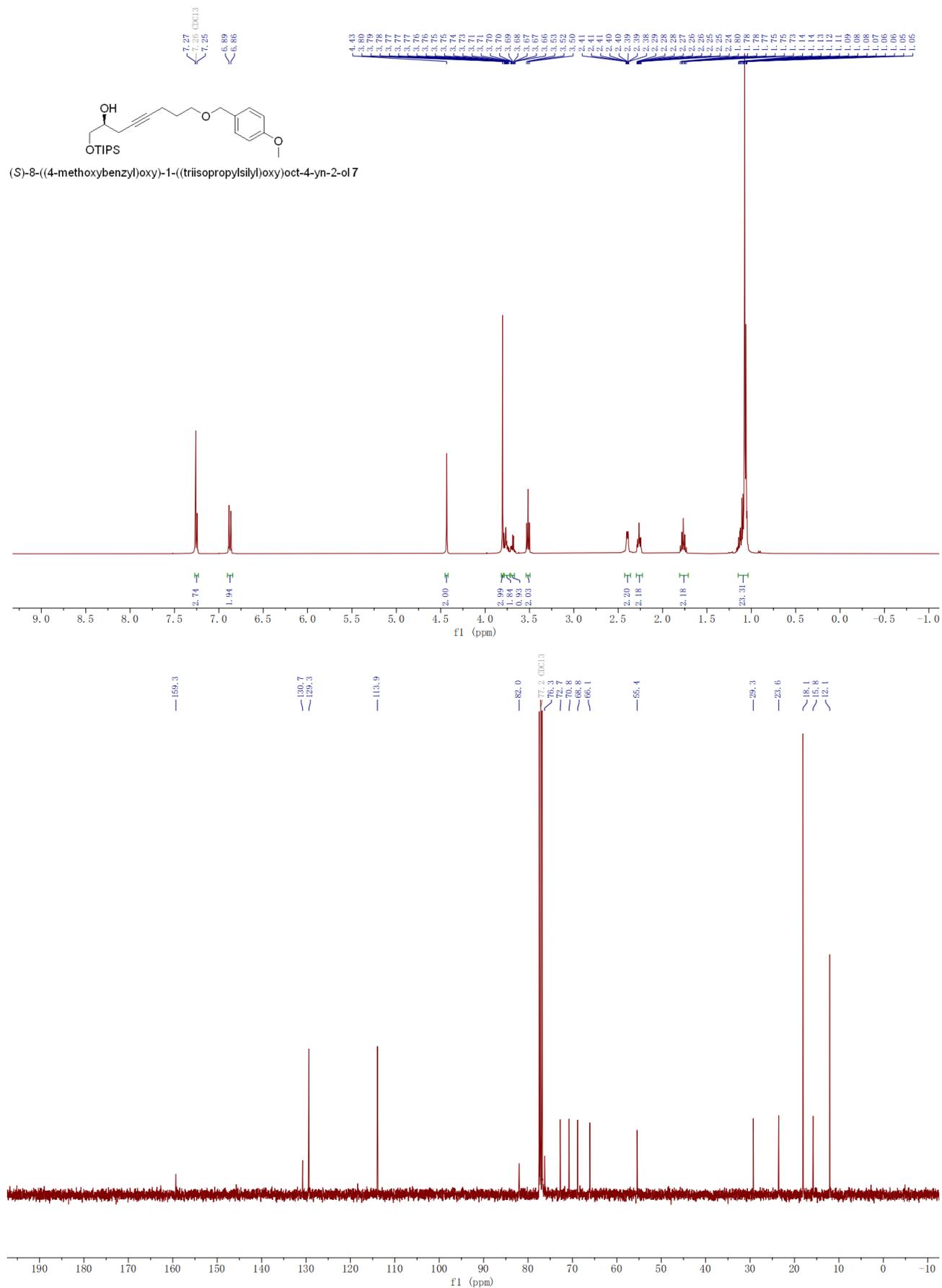
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 6



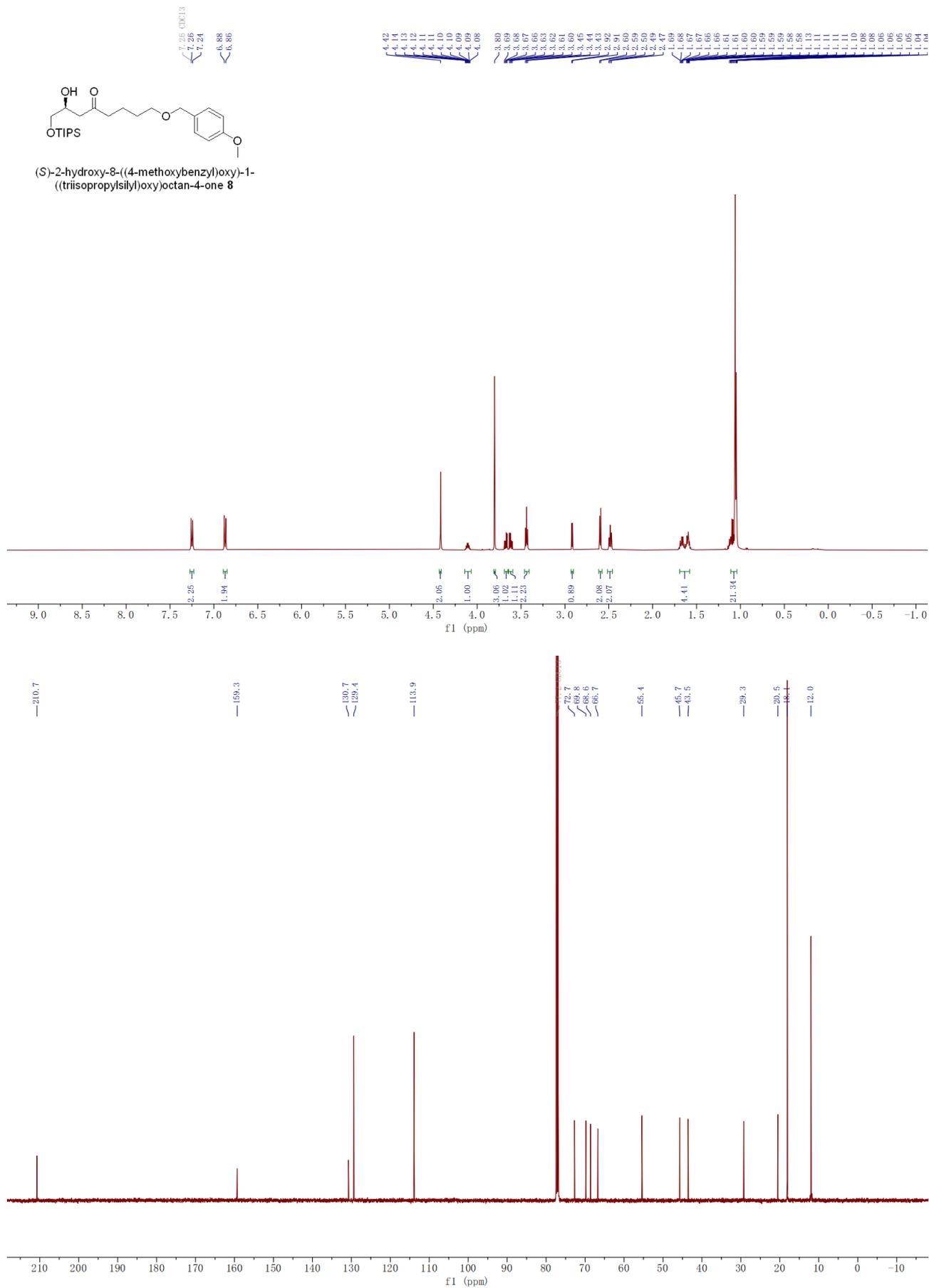
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 5



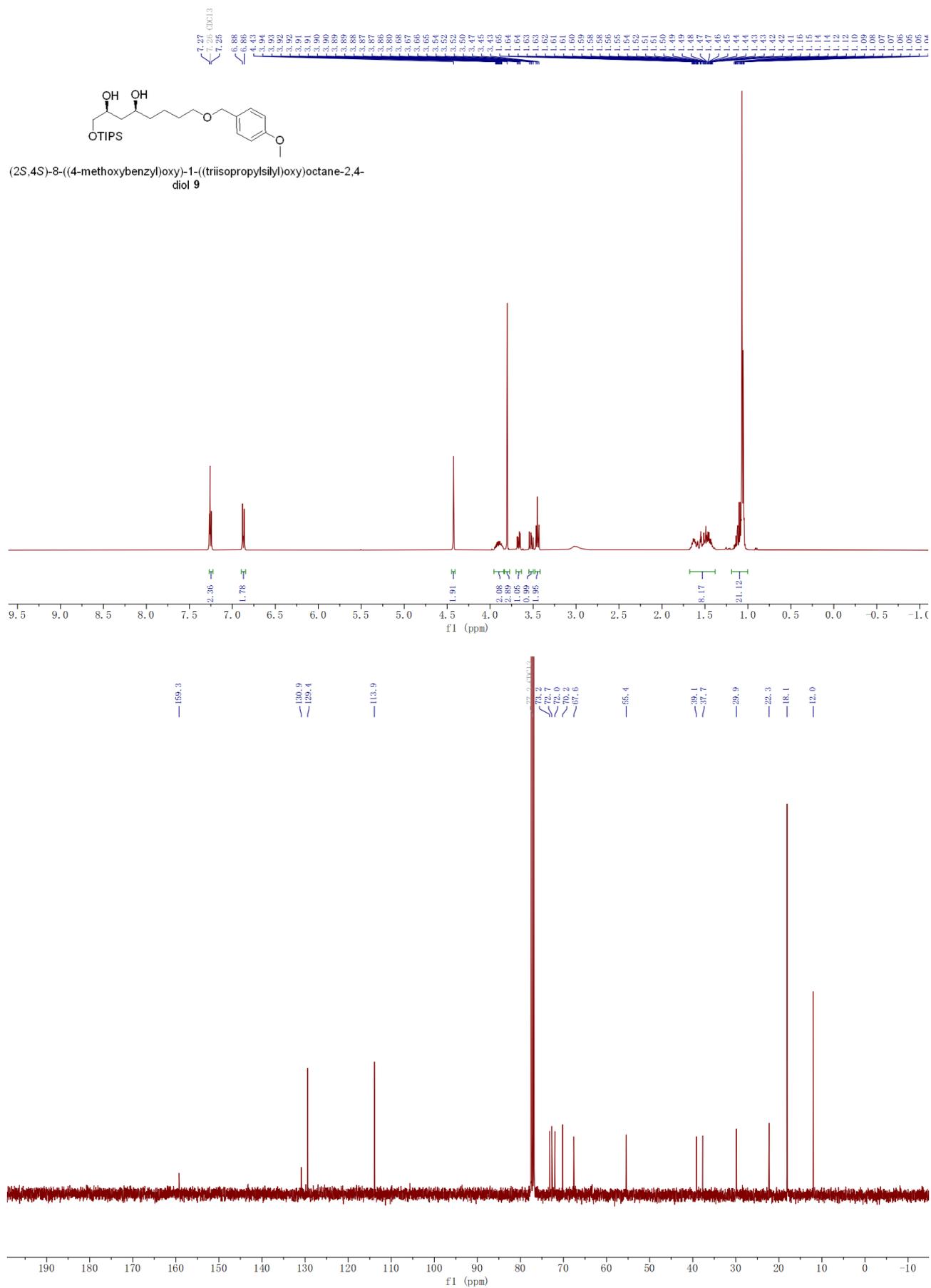
¹H (400 MHz, CDCl₃) and ¹³C (101 MHz, CDCl₃) NMR spectra of compound 7



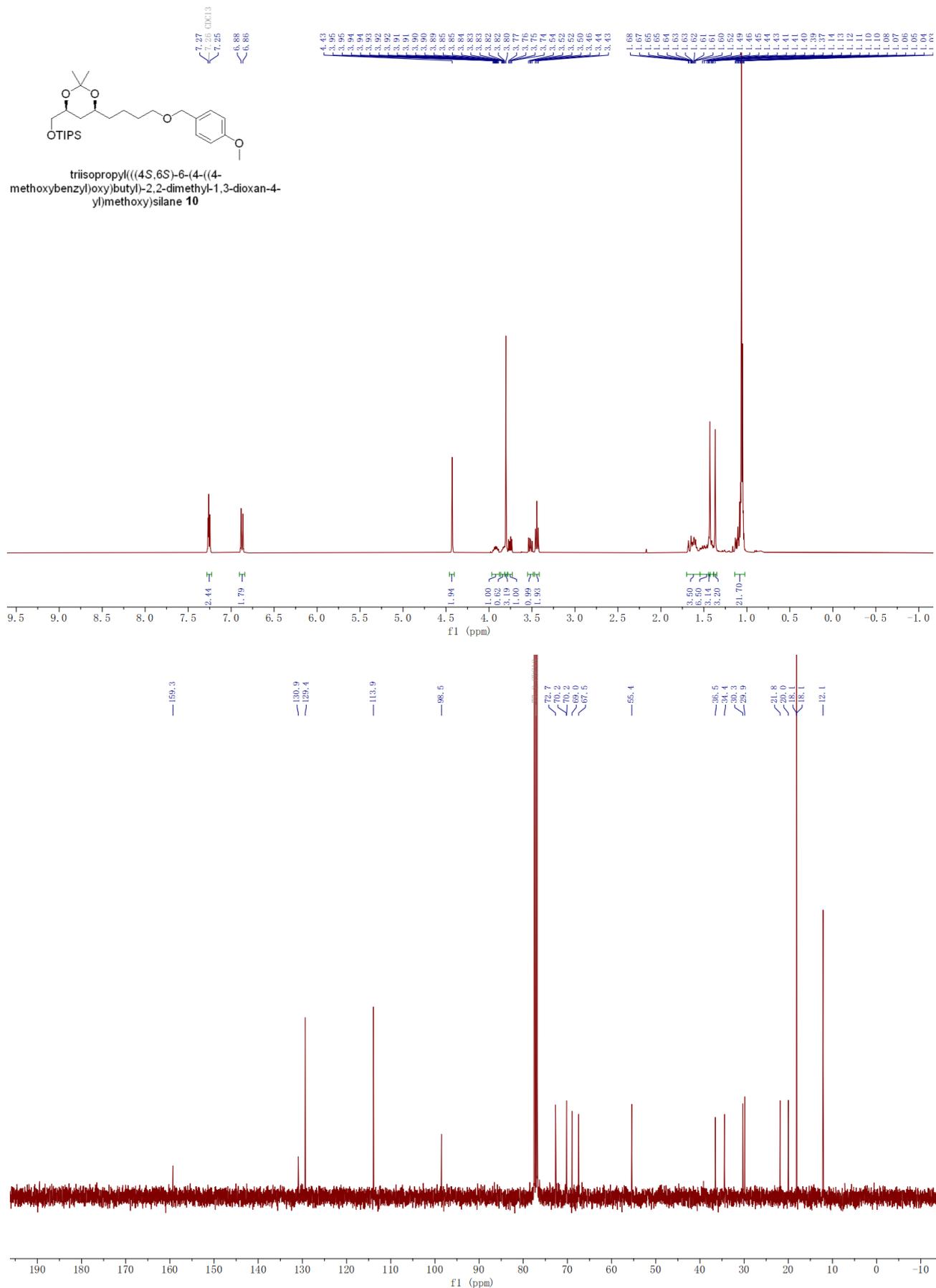
^1H (500 MHz, CDCl_3) and ^{13}C (126 MHz, CDCl_3) NMR spectra of compound 8



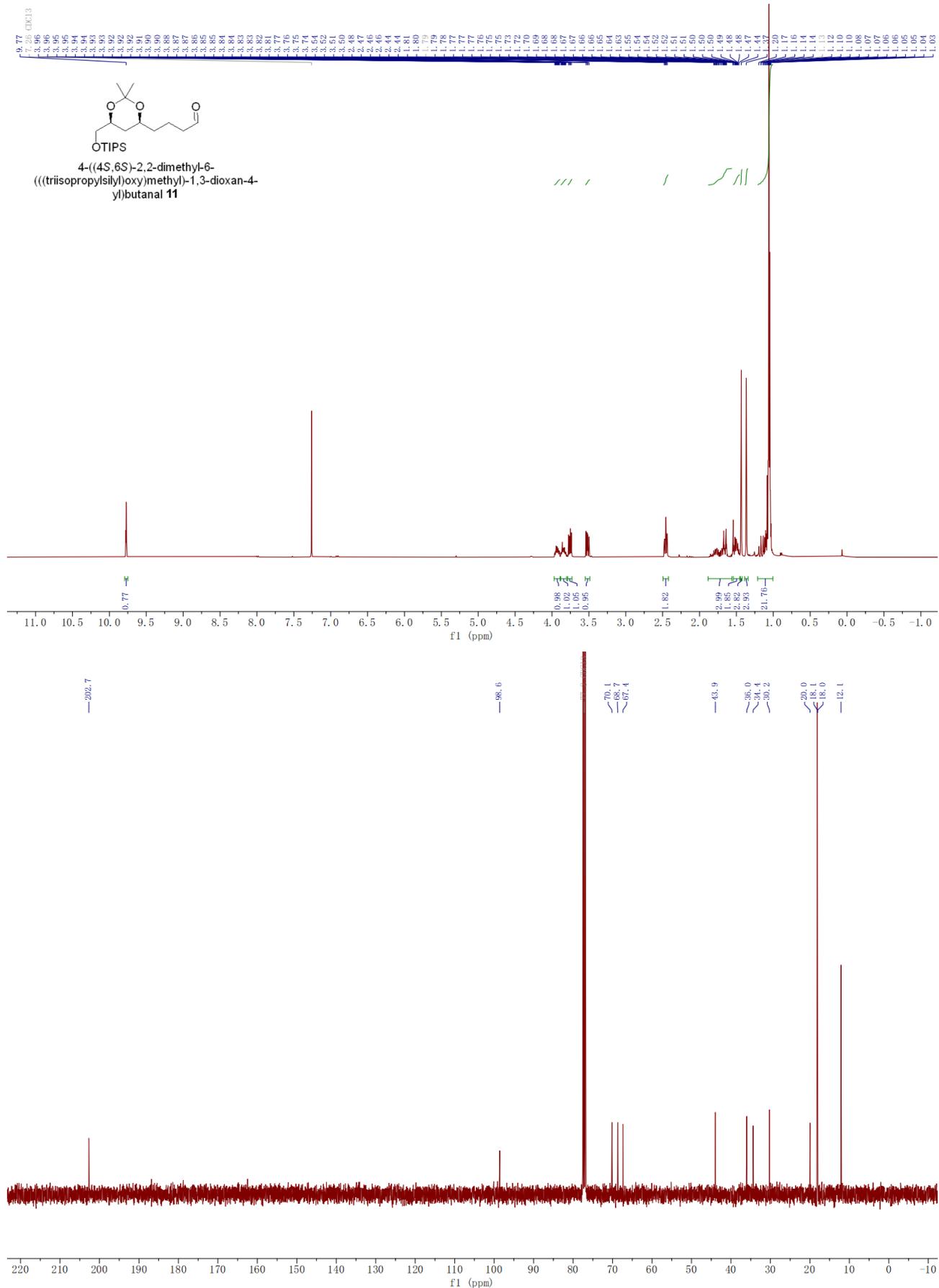
^1H (400 MHz, CDCl_3) and ^{13}C (101MHz, CDCl_3) NMR spectra of compound 9



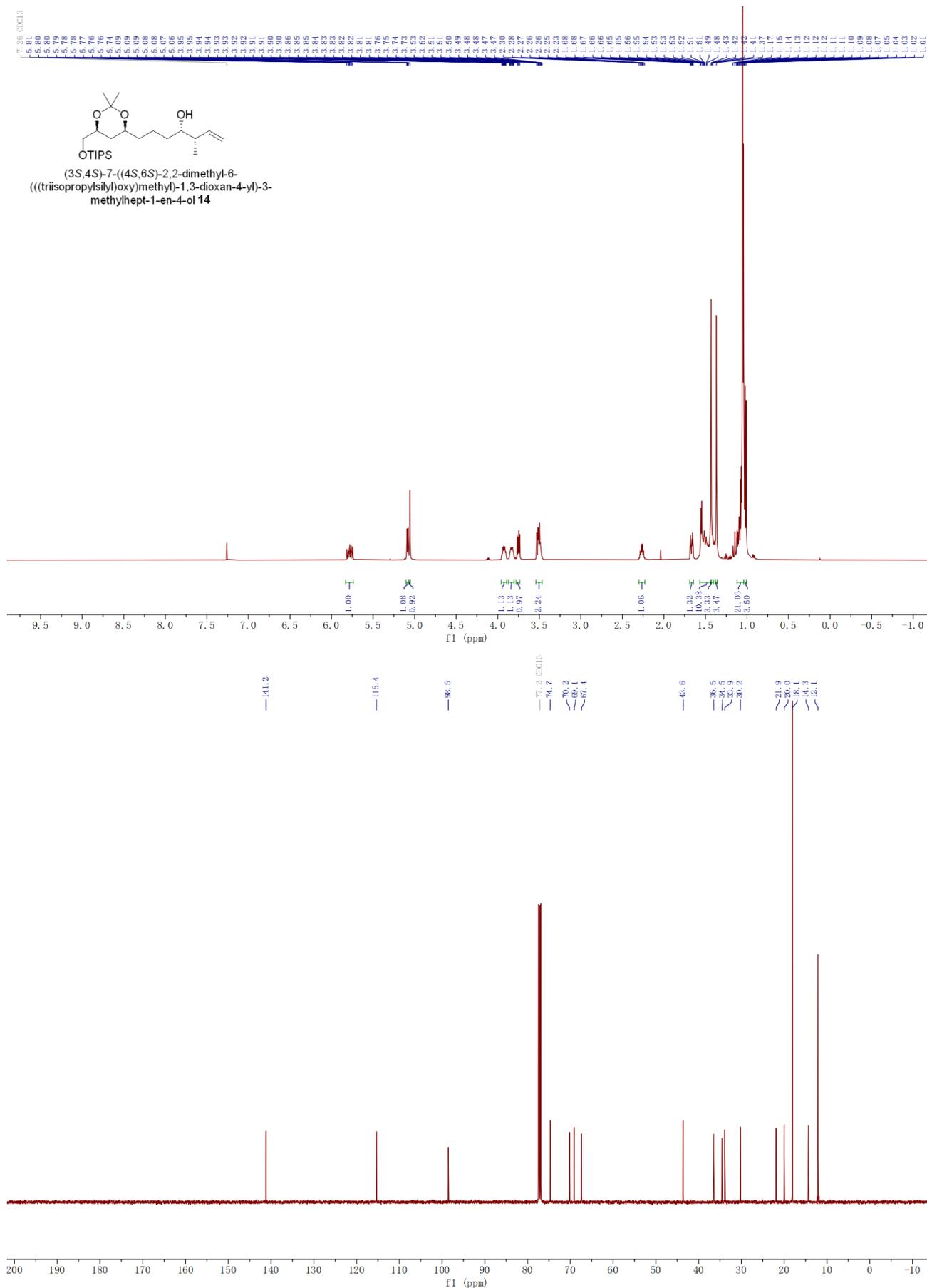
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 10



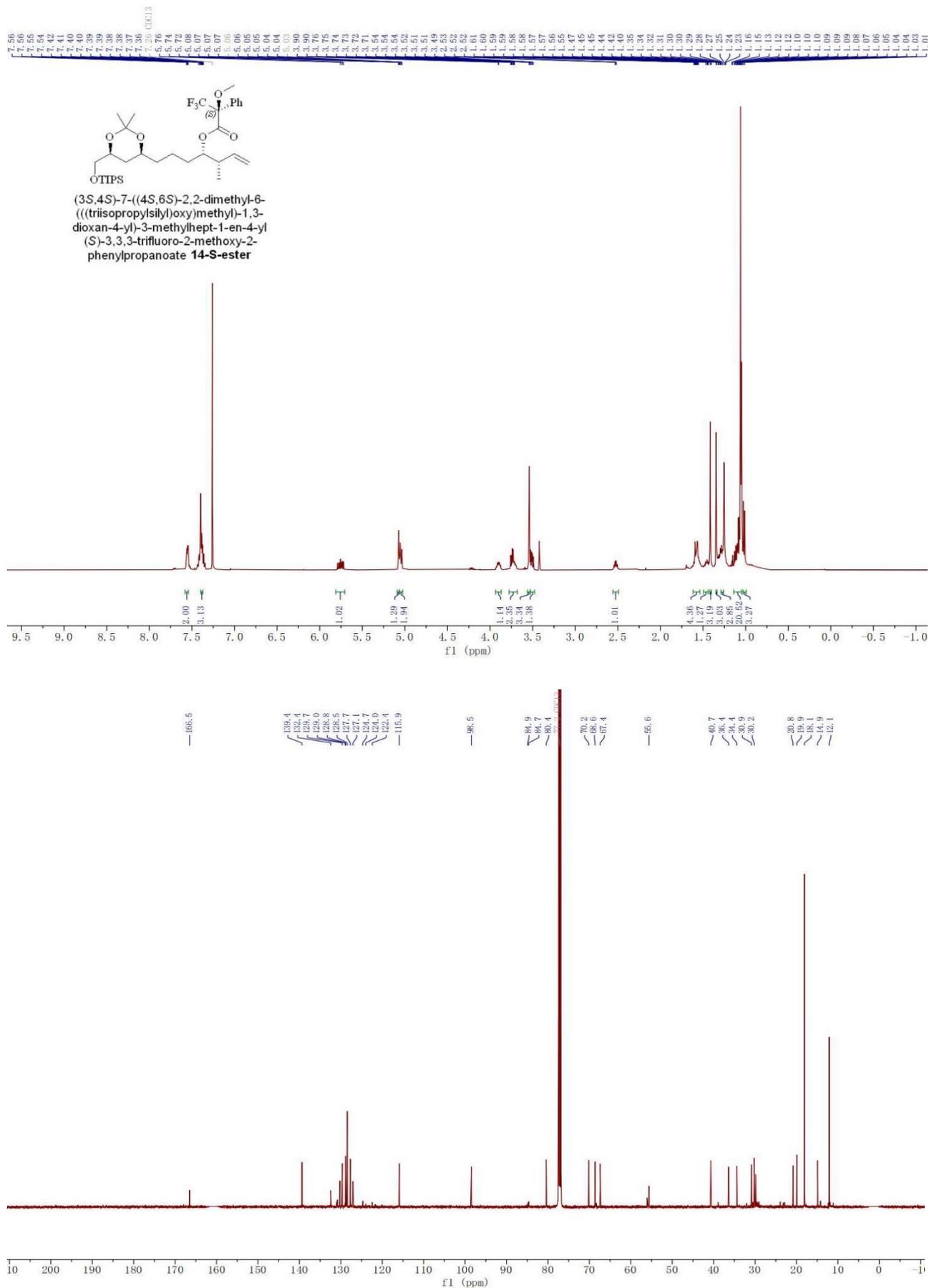
¹H (400 MHz, CDCl₃) and ¹³C (101 MHz, CDCl₃) NMR spectra of compound 11



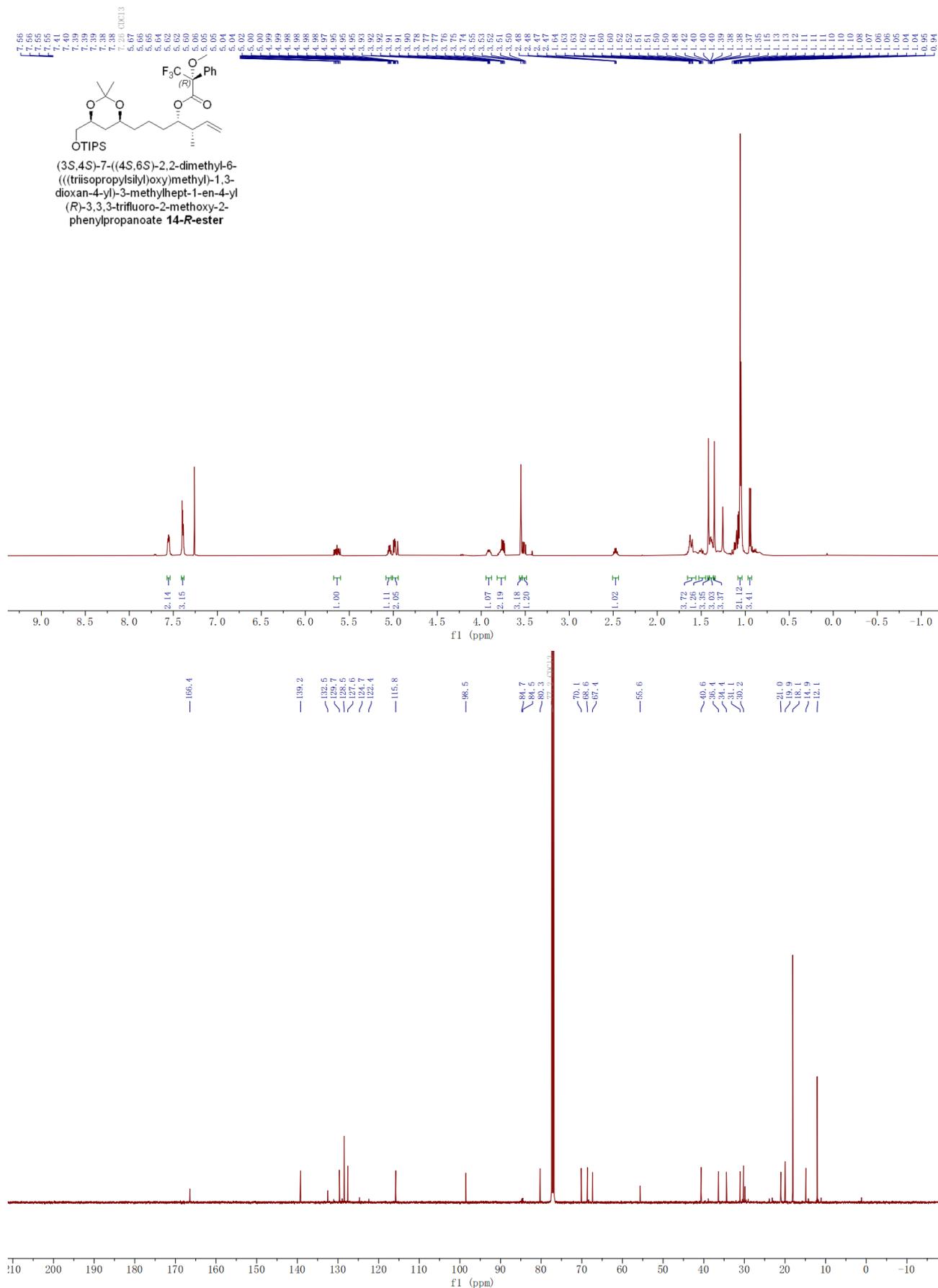
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 14



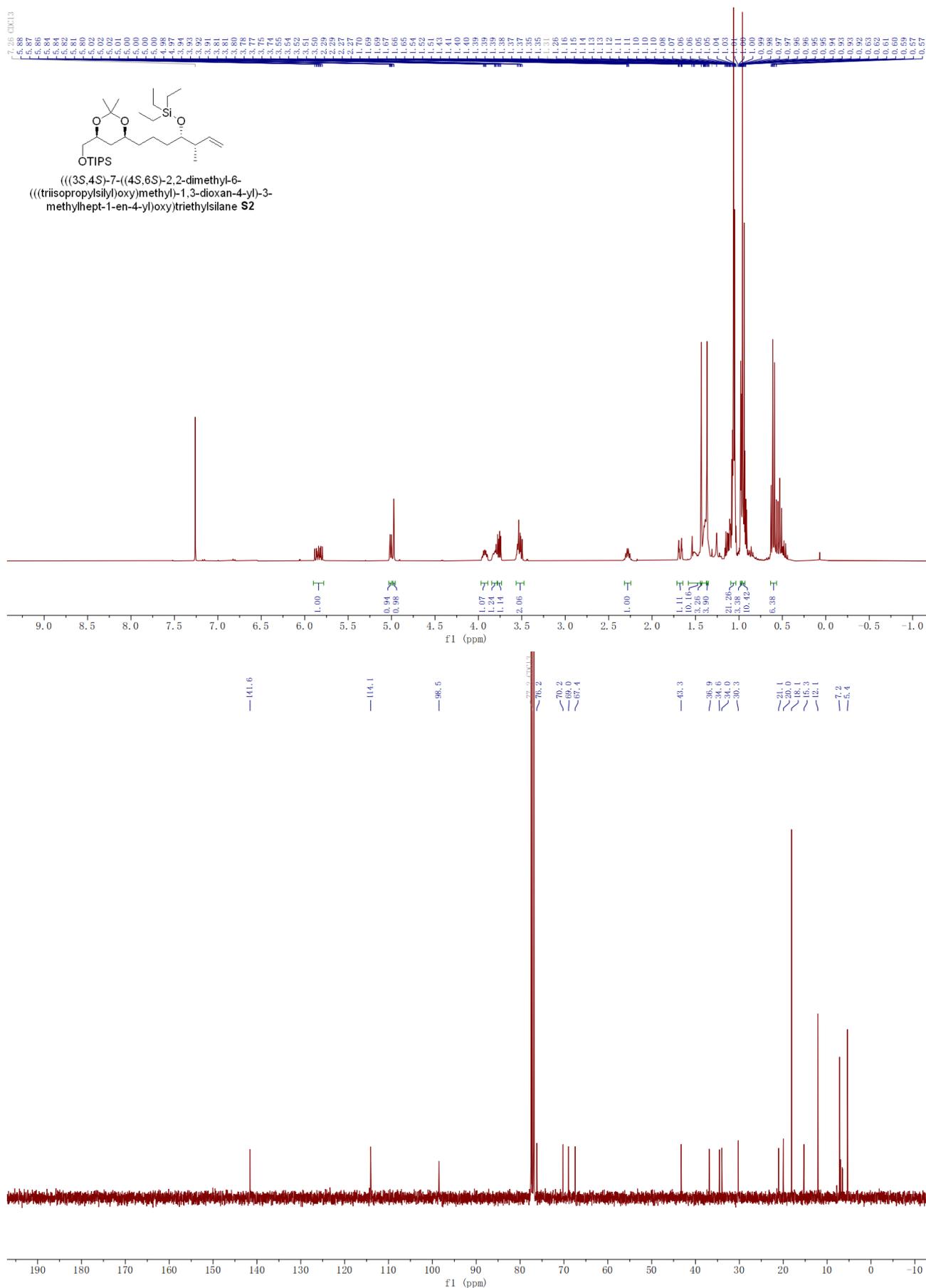
¹H (500 MHz, CDCl₃) and ¹³C (126 MHz, CDCl₃) NMR spectra of compound 14-S-ester



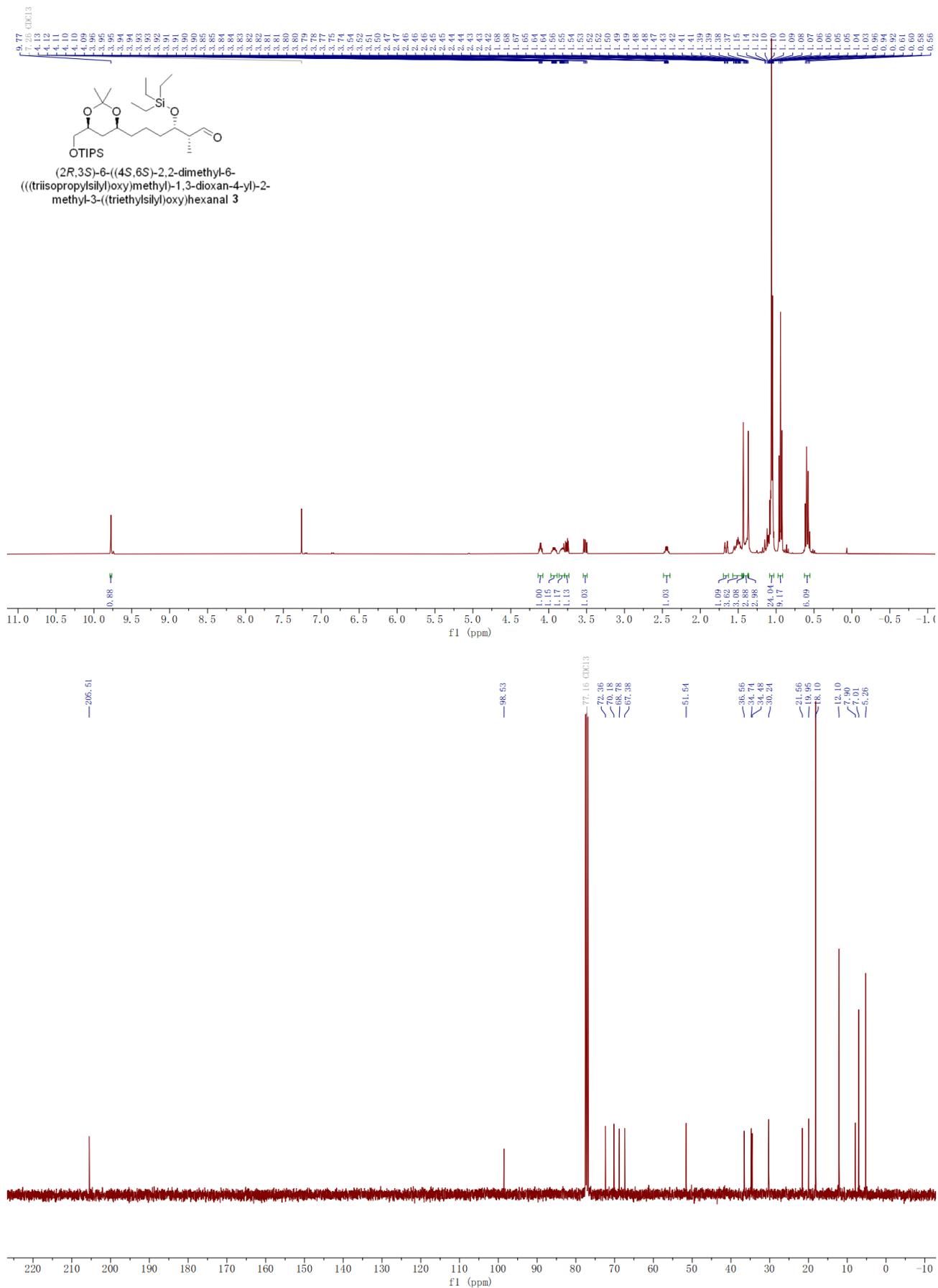
^1H (500 MHz, CDCl_3) and ^{13}C (126 MHz, CDCl_3) NMR spectra of compound 14-*R*-ester



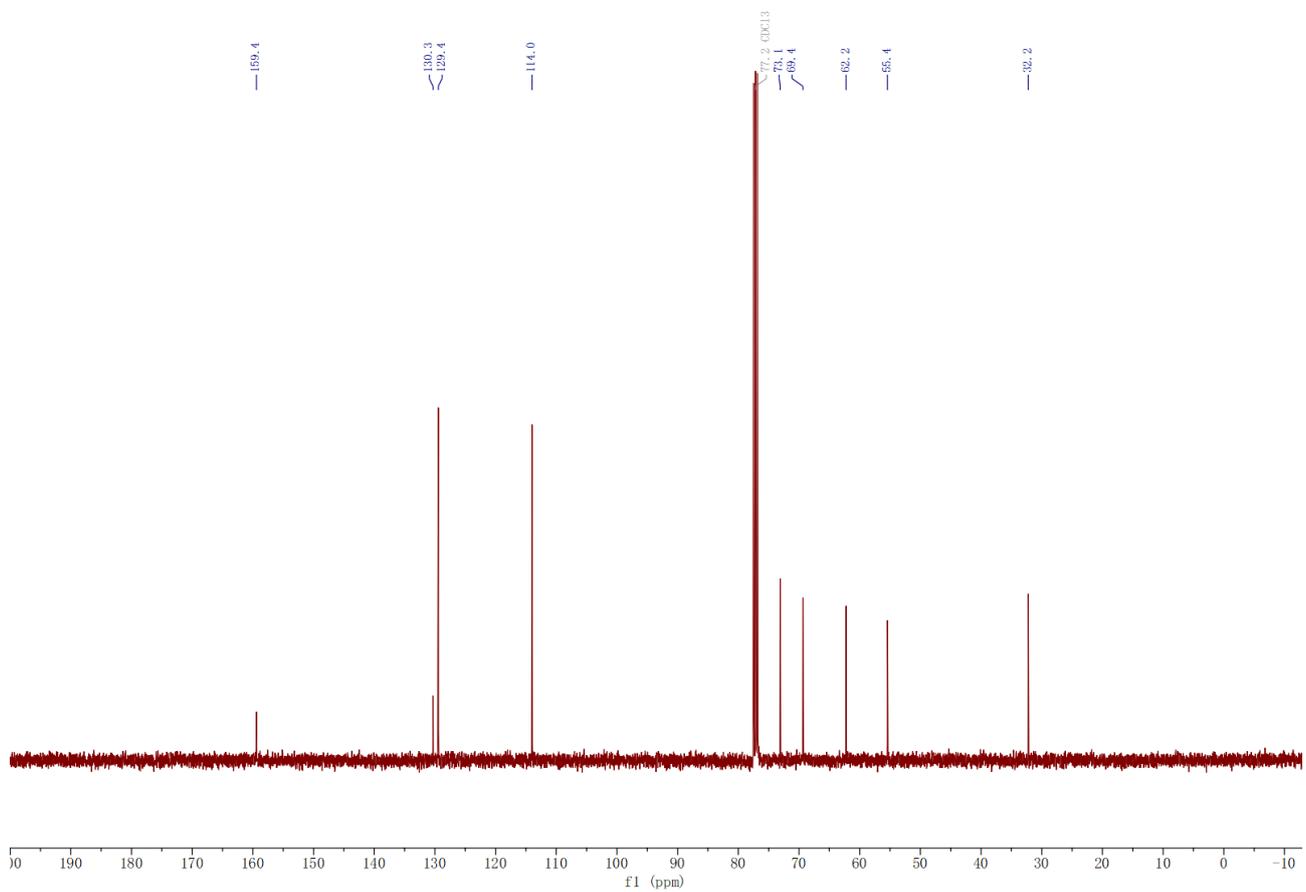
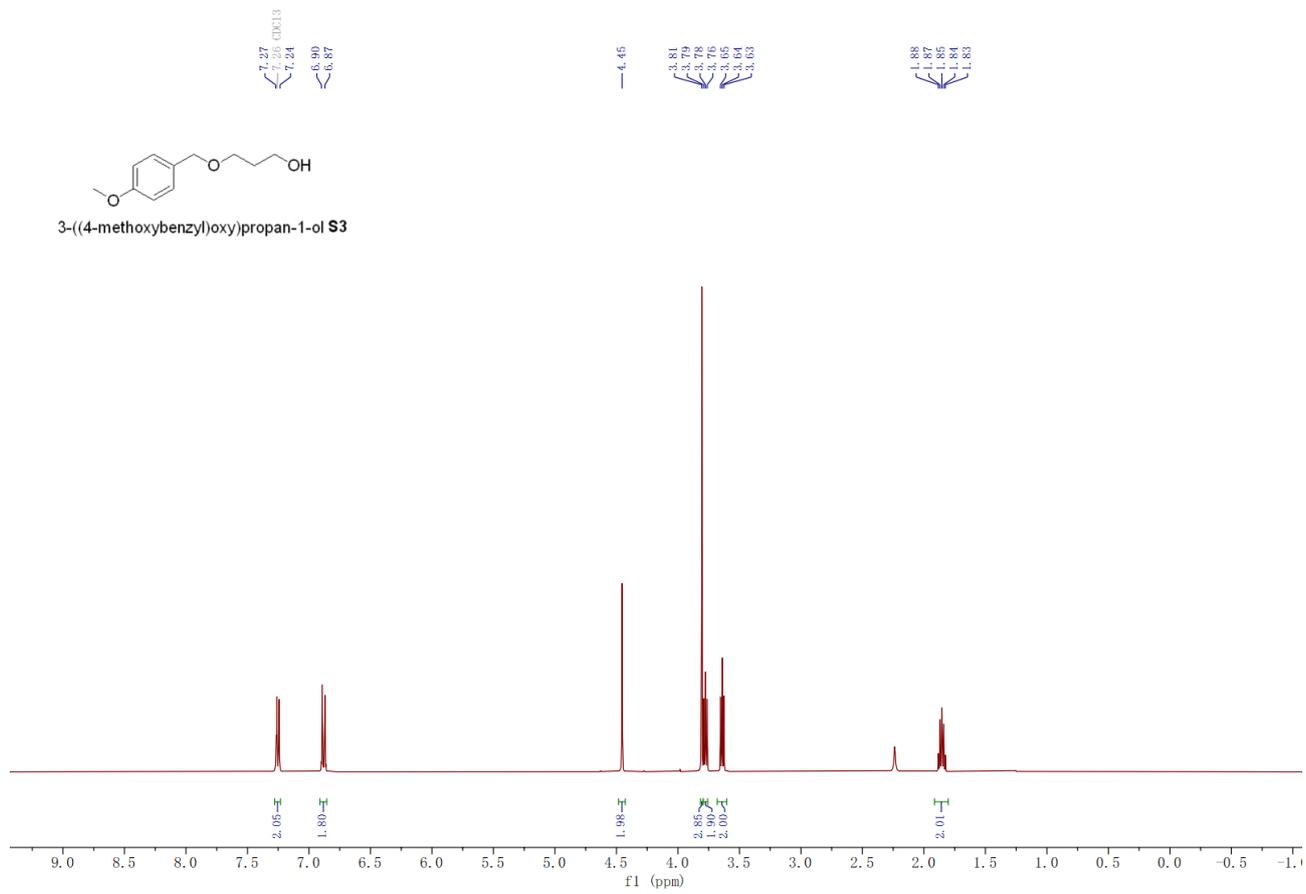
¹H (400 MHz, CDCl₃) and ¹³C (101 MHz, CDCl₃) NMR spectra of compound S2



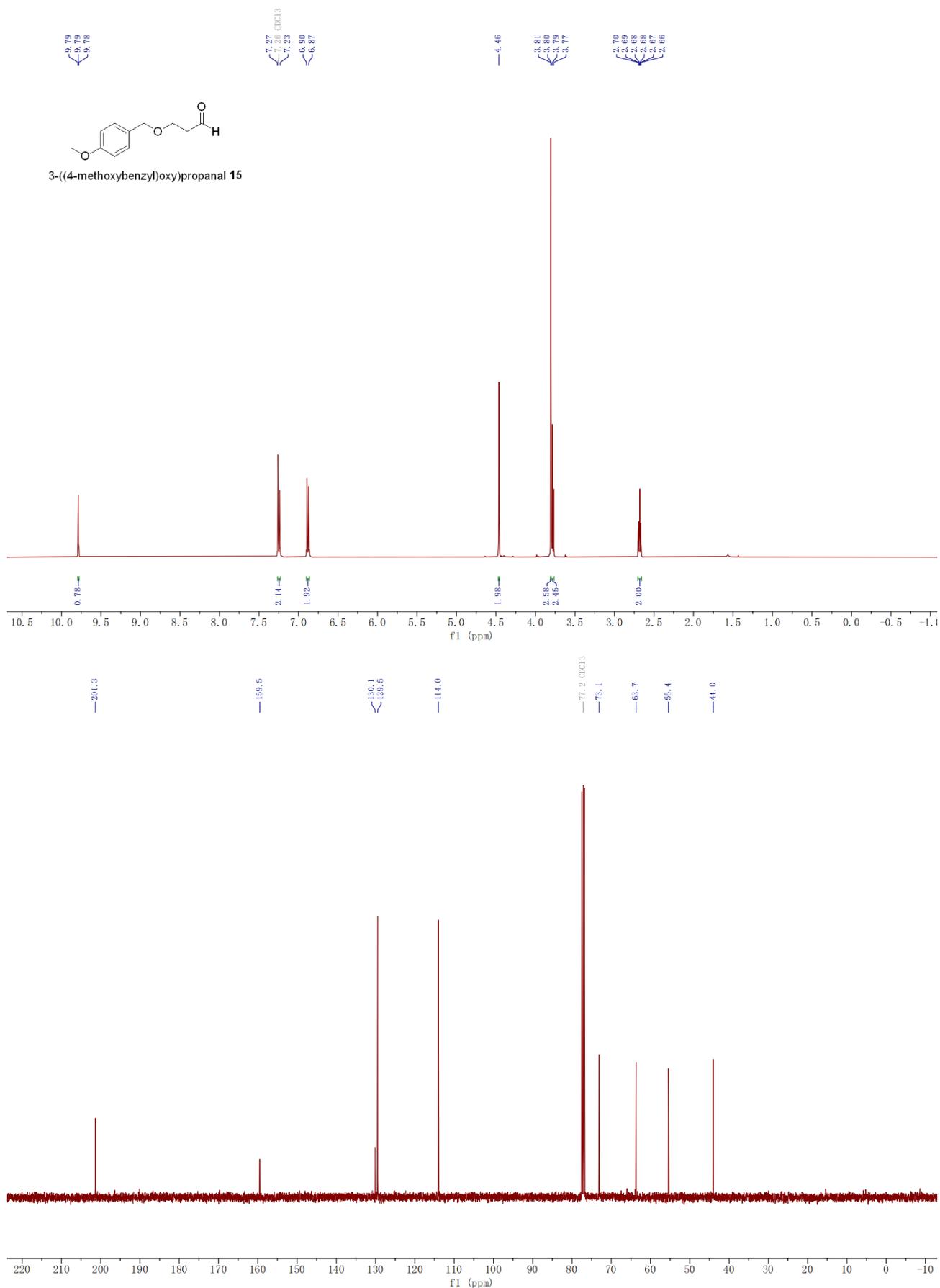
¹H (400 MHz, CDCl₃) and ¹³C (101 MHz, CDCl₃) NMR spectra of compound 3



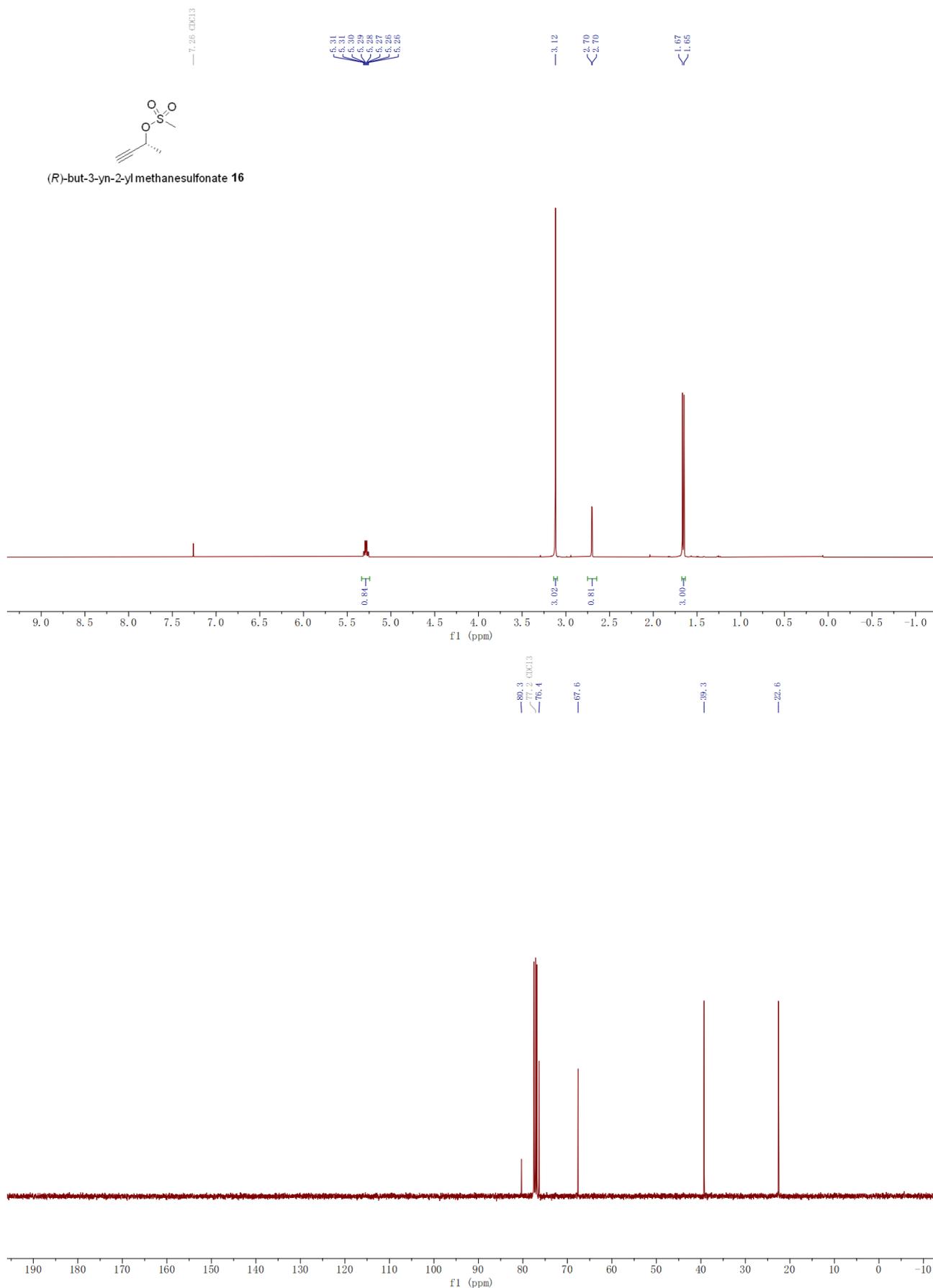
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound S3



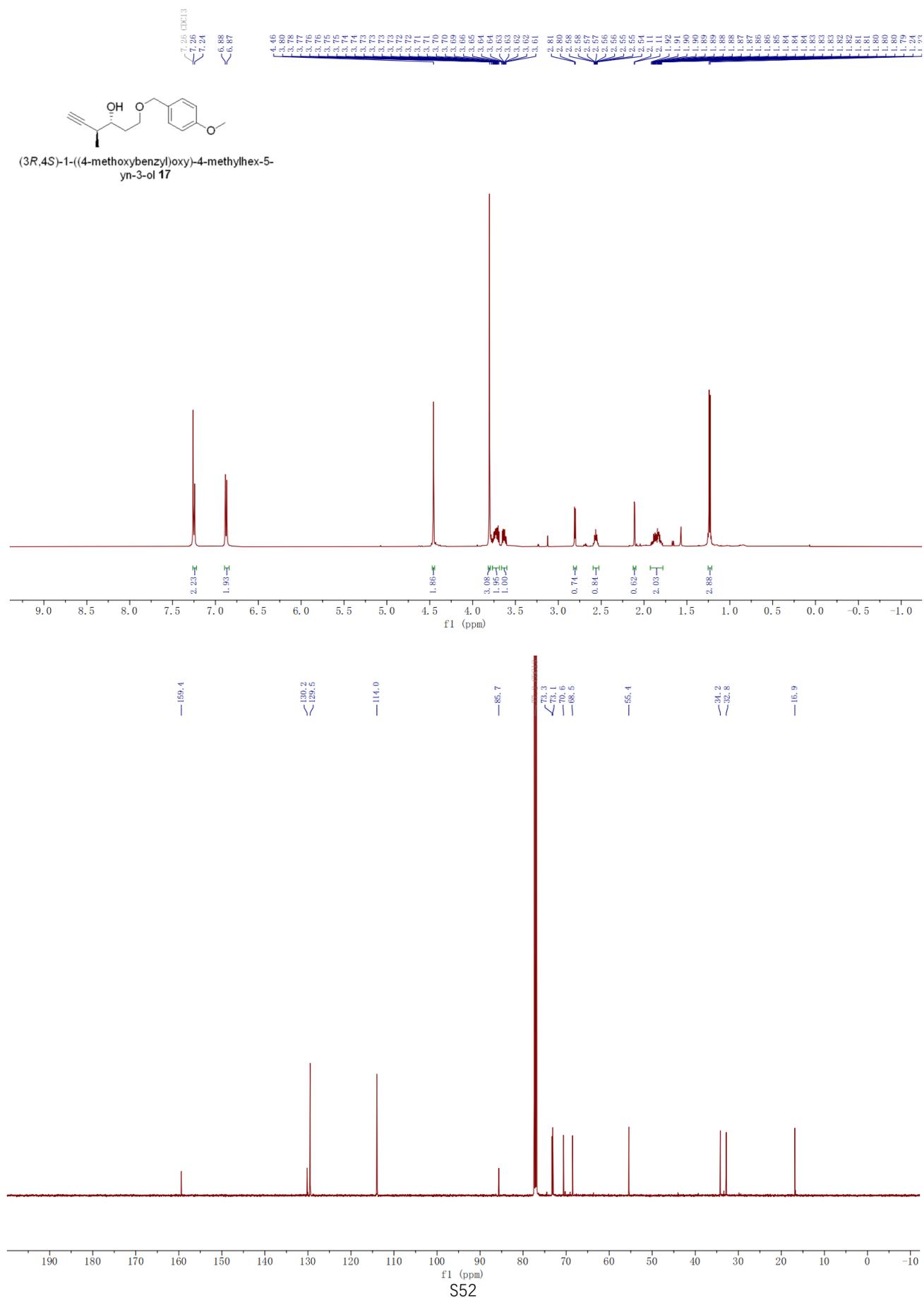
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 15



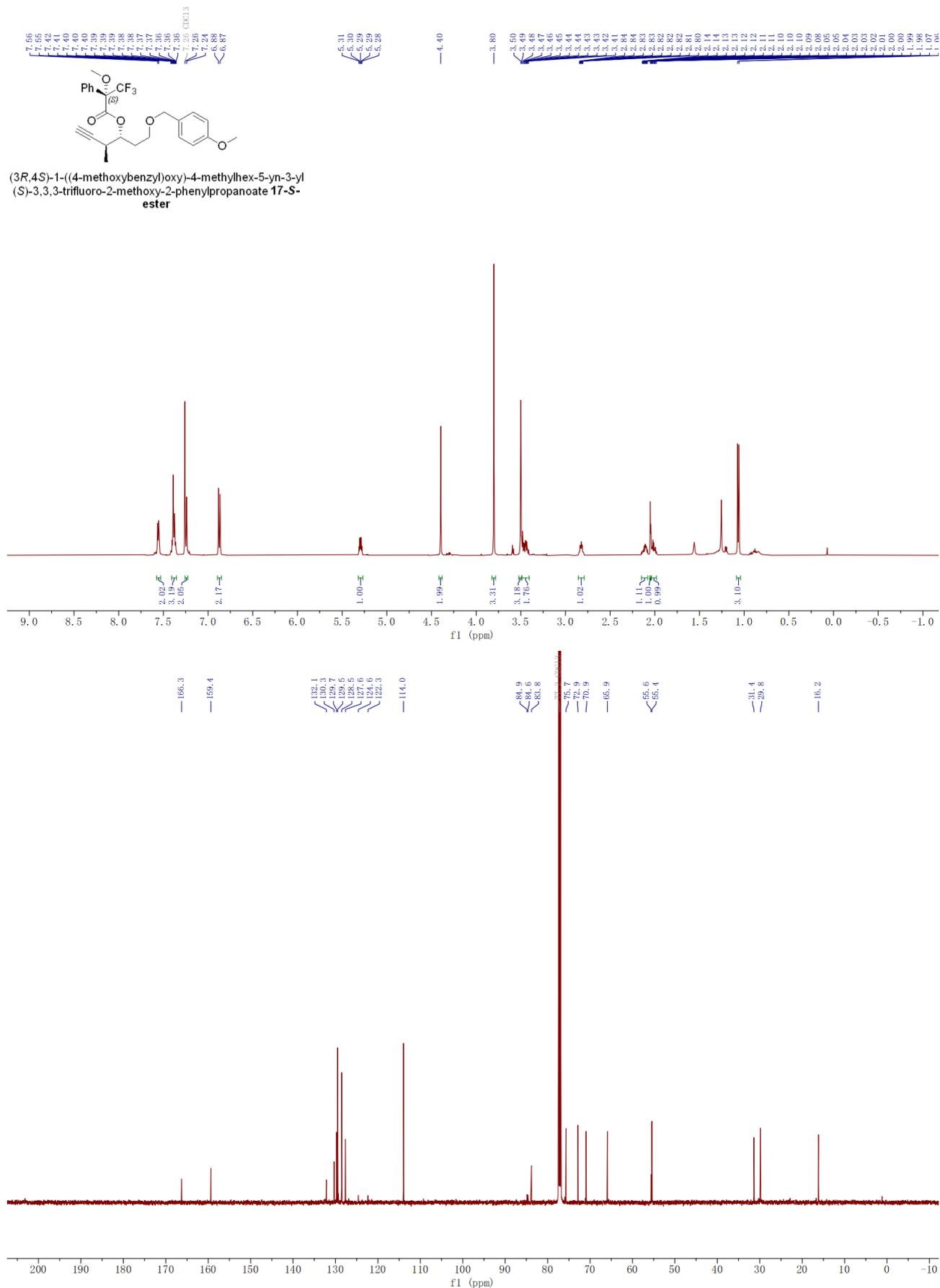
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 16



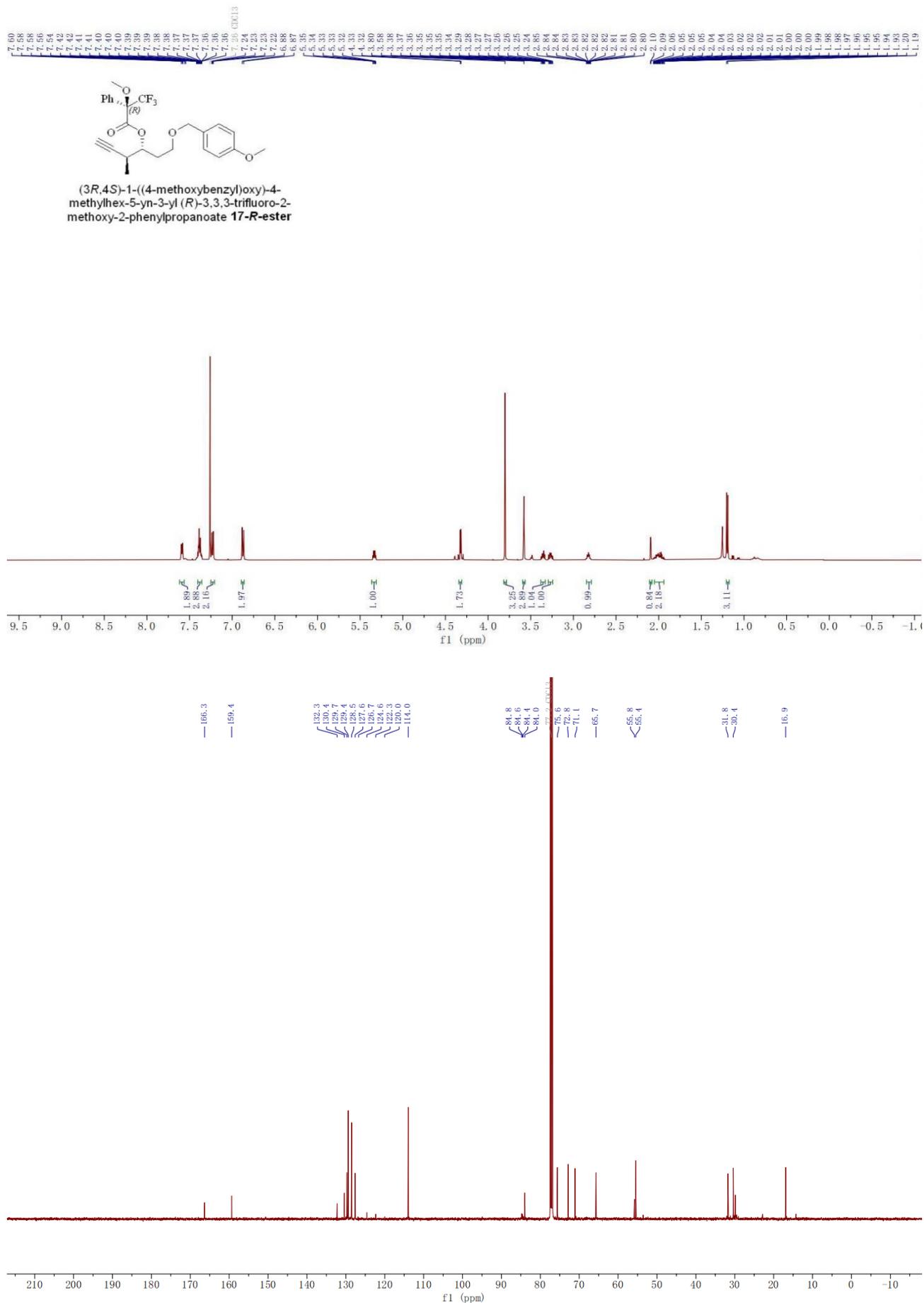
¹H (400 MHz, CDCl₃) and ¹³C (101 MHz, CDCl₃) NMR spectra of compound 17



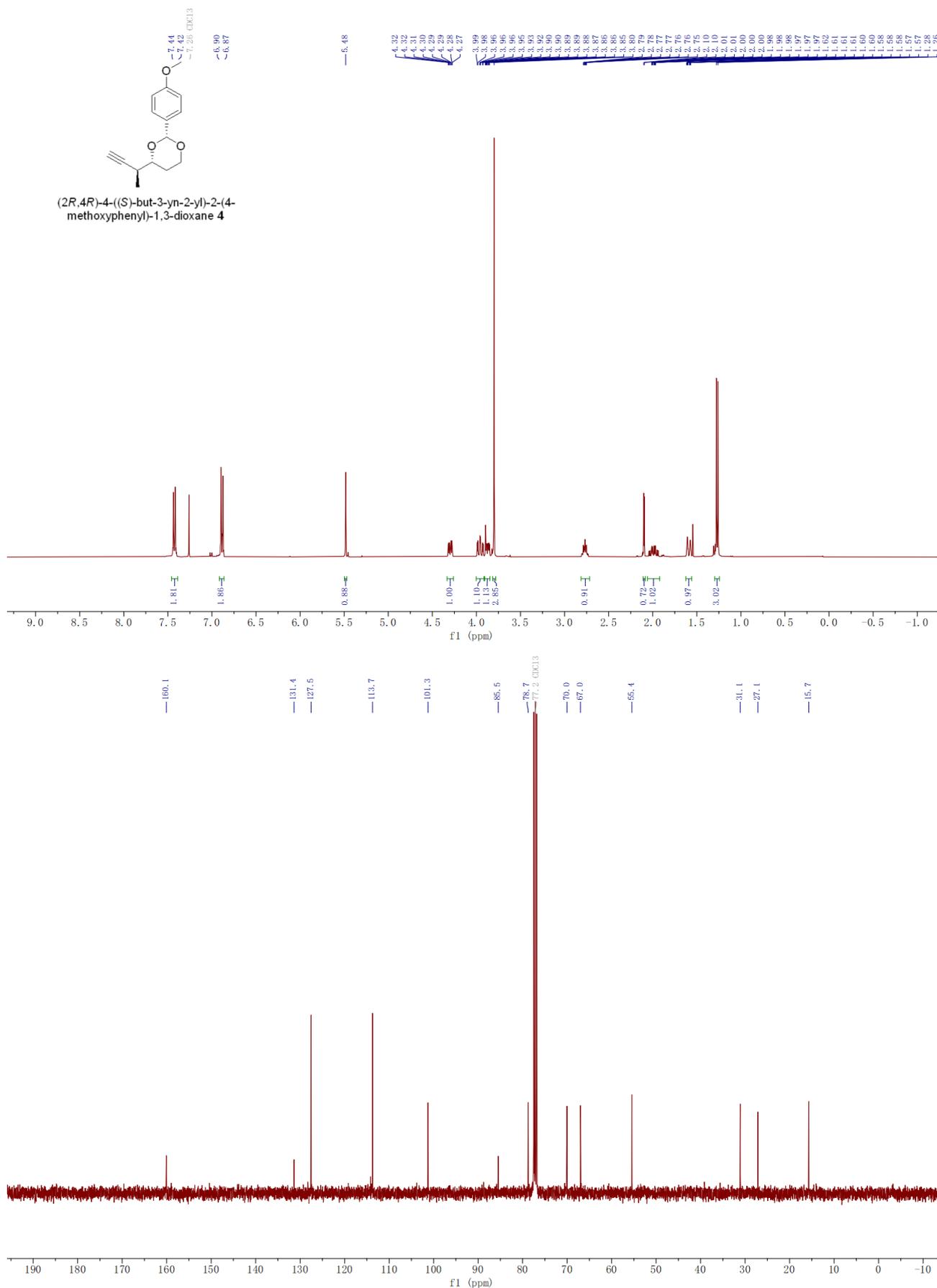
^1H (500 MHz, CDCl_3) and ^{13}C (126 MHz, CDCl_3) NMR spectra of compound 17-S-ester



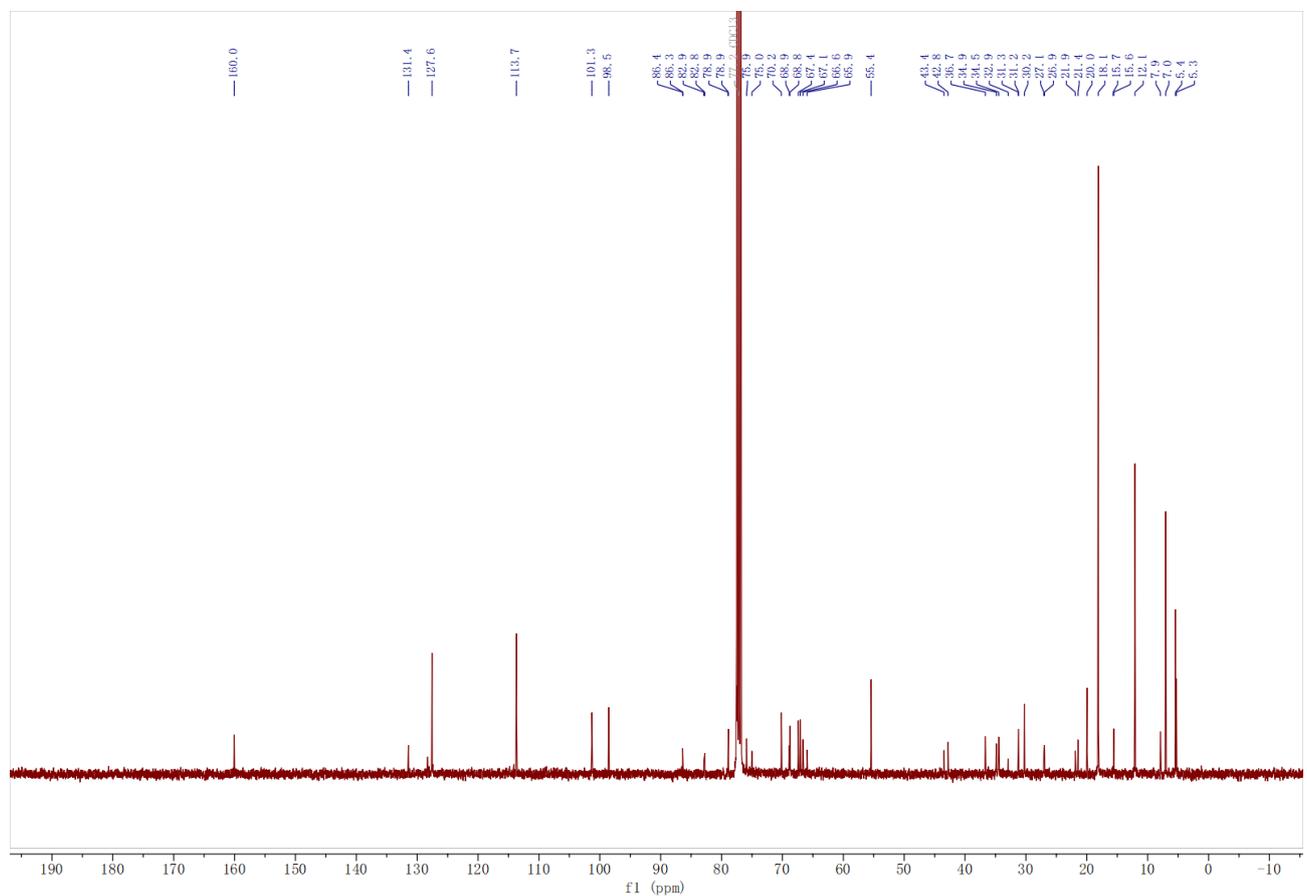
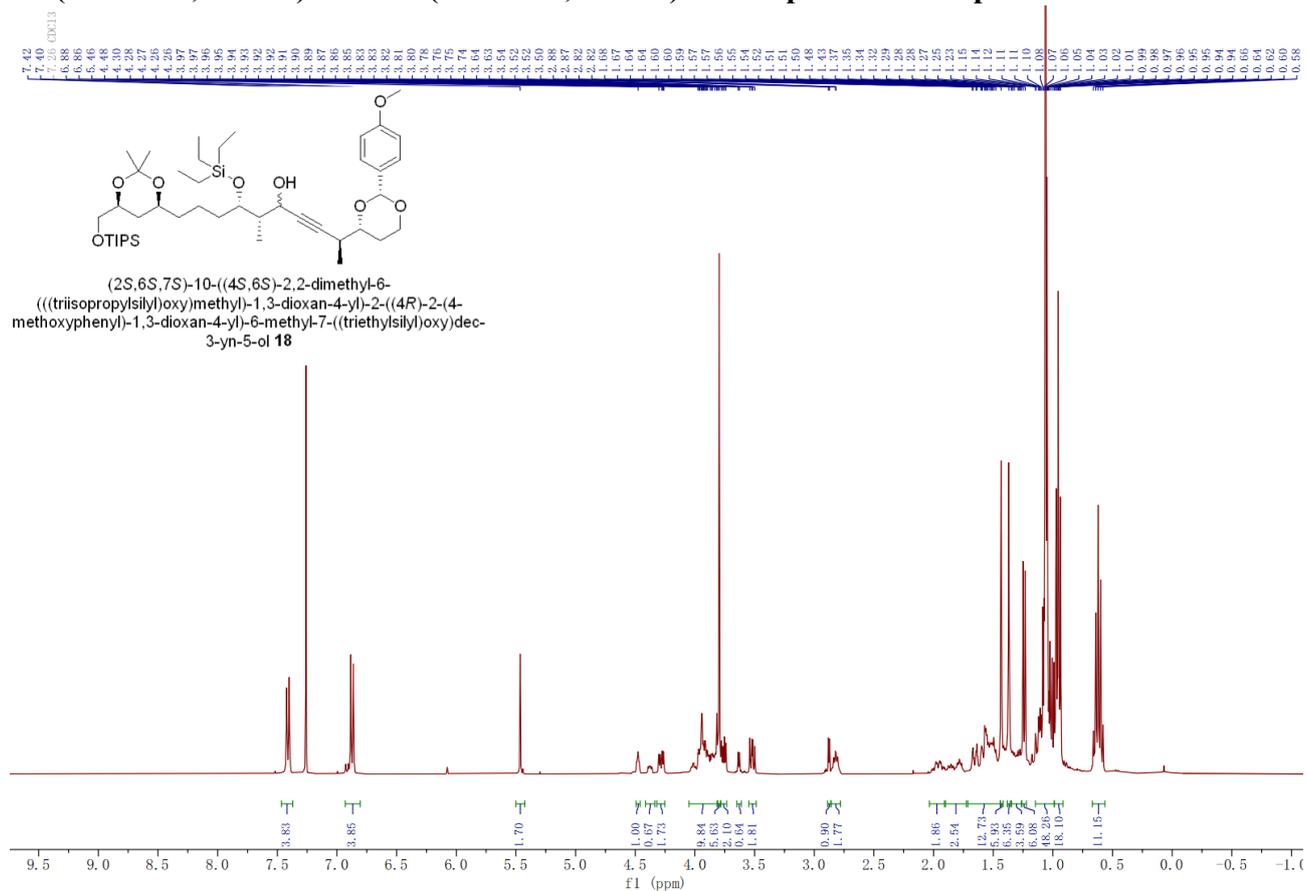
¹H (500 MHz, CDCl₃) and ¹³C (126 MHz, CDCl₃) NMR spectra of compound 17-*R*-ester



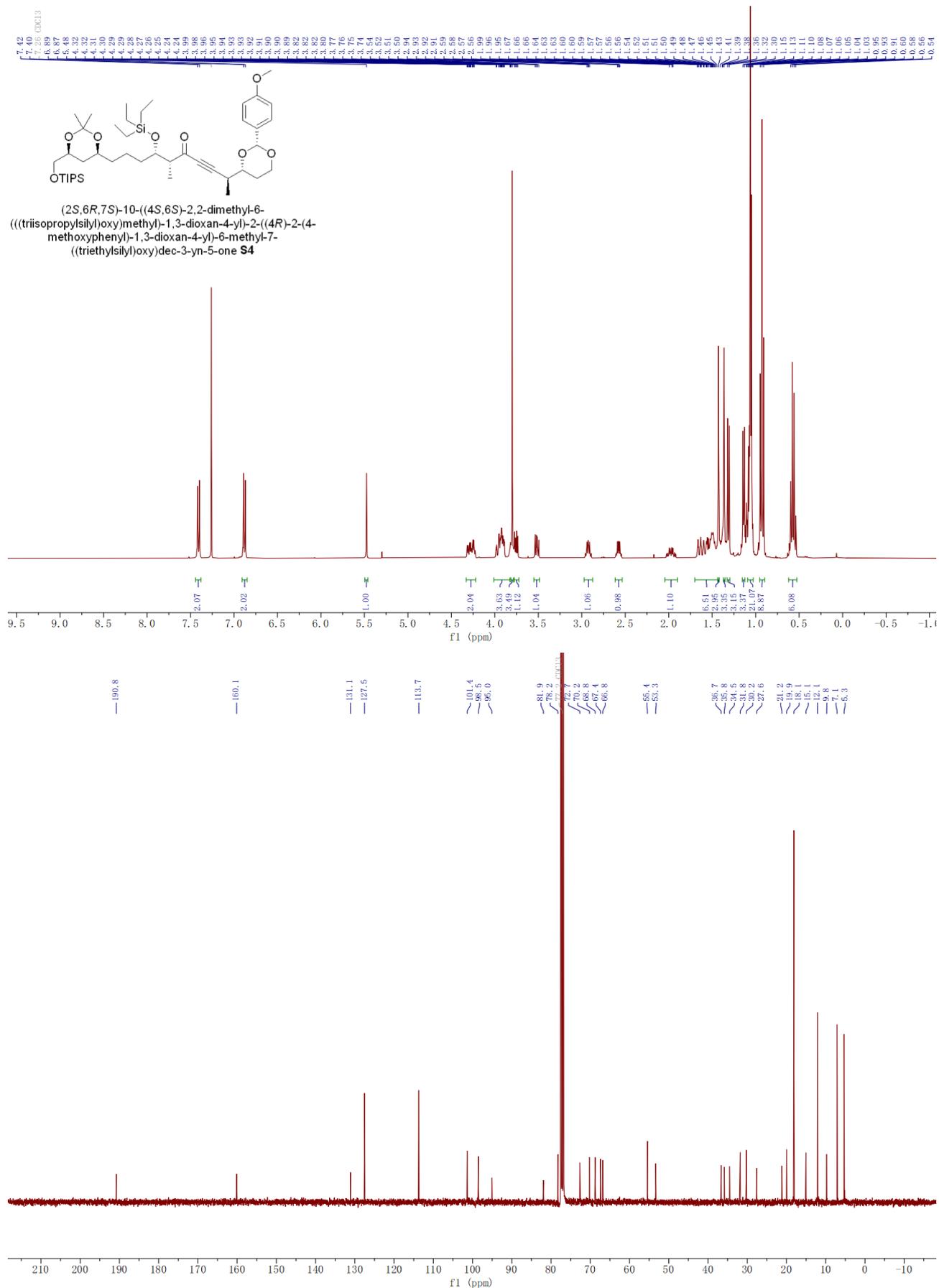
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 4



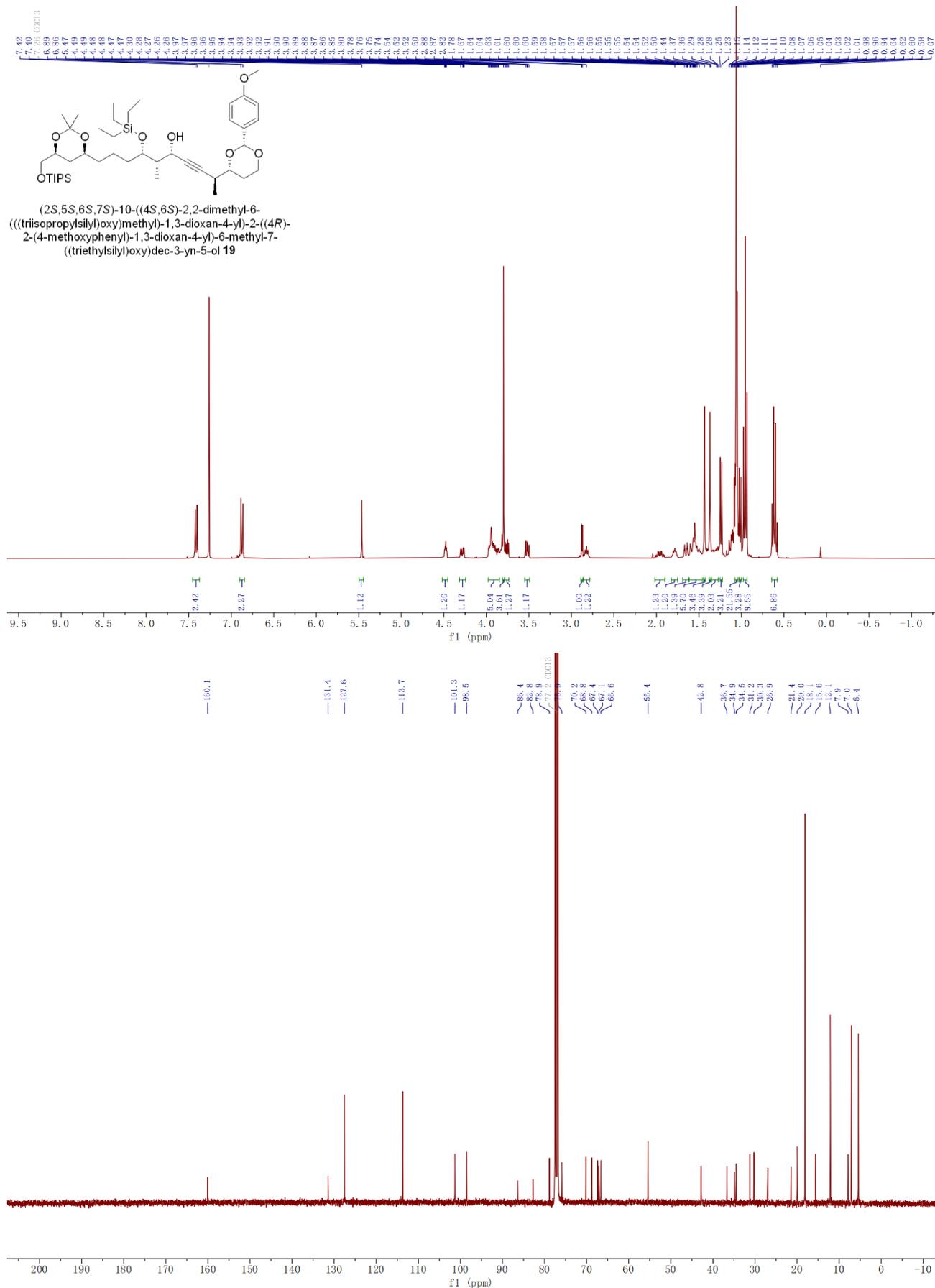
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 18



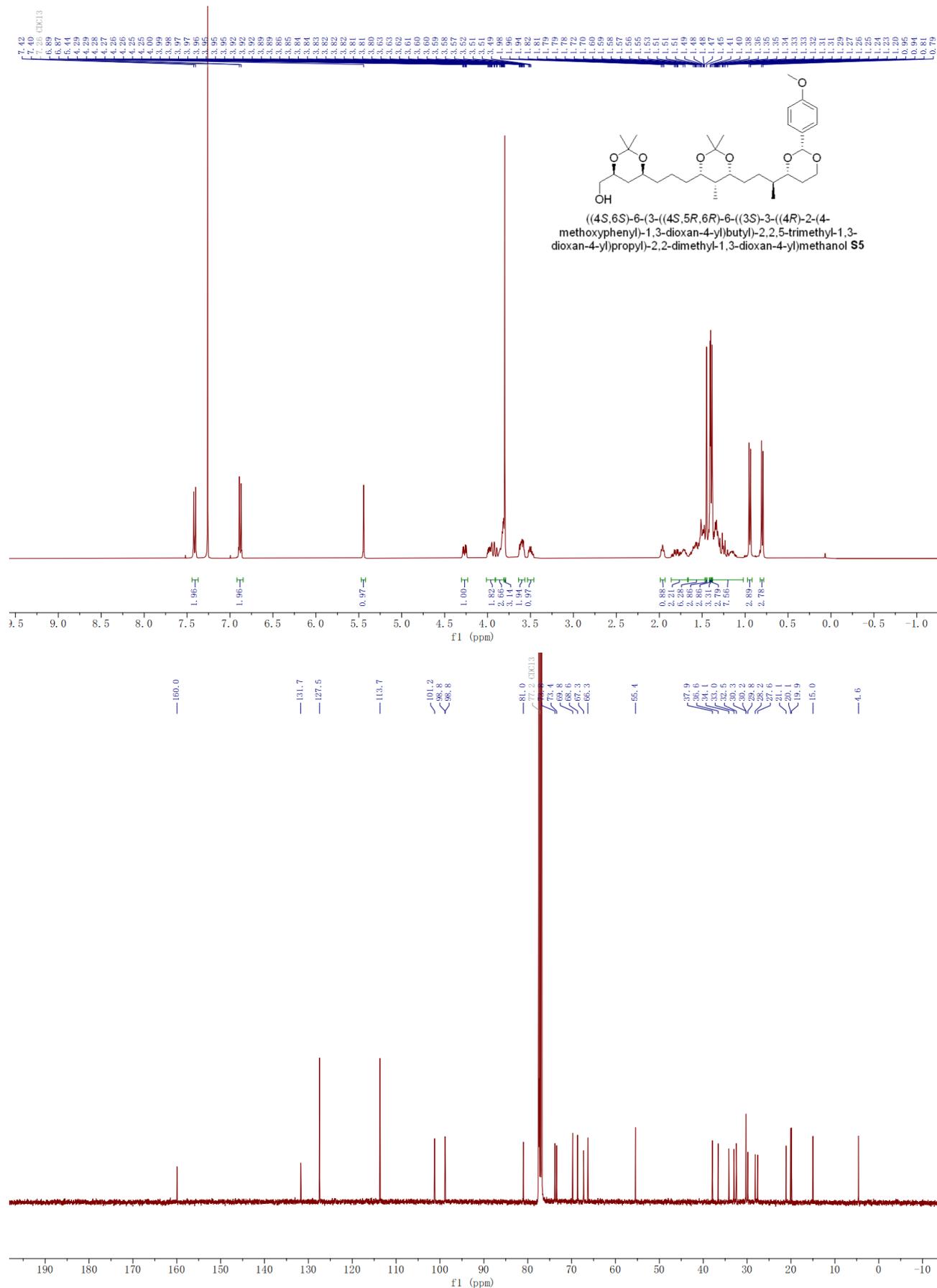
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound S4



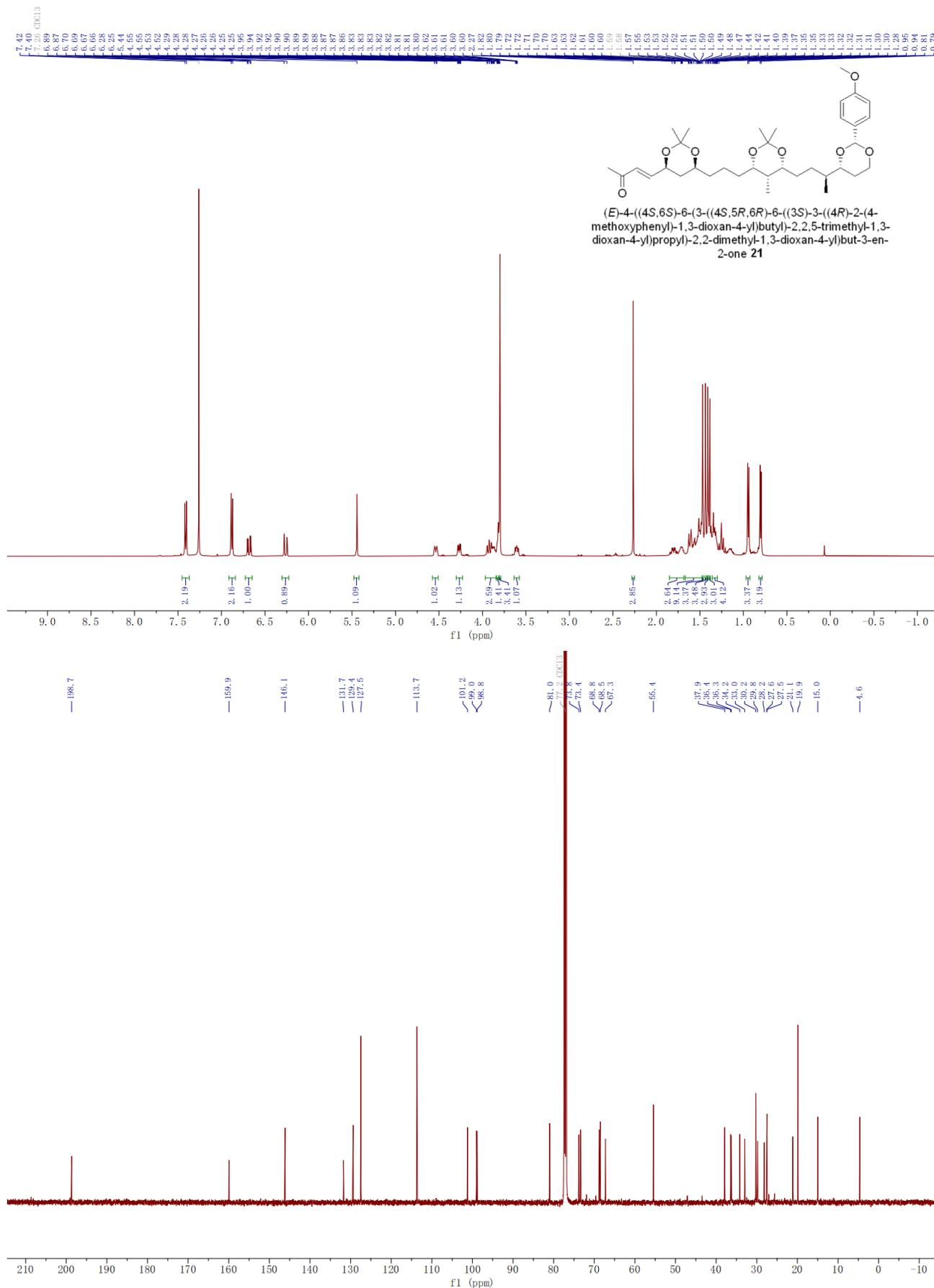
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound 19



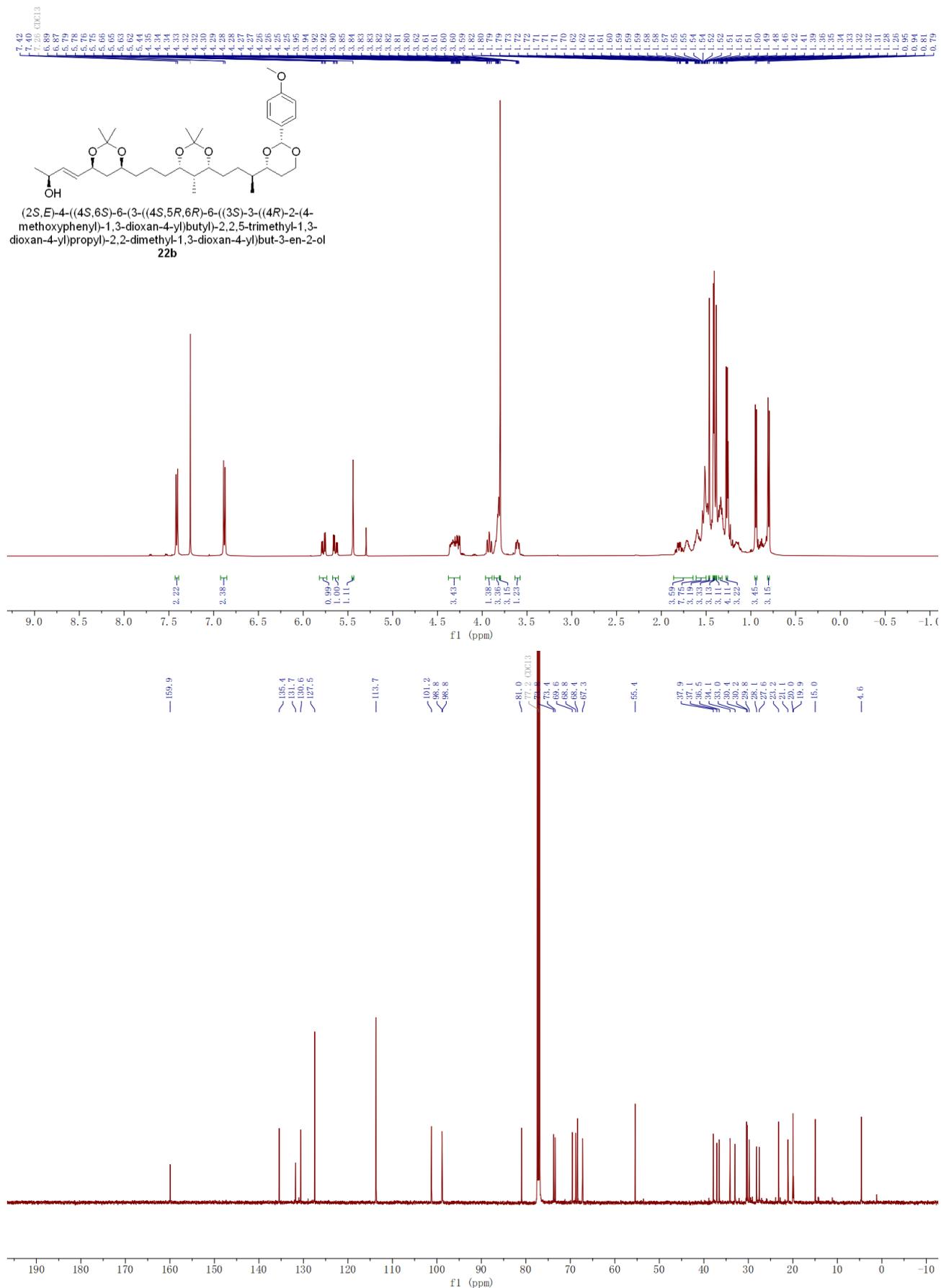
^1H (400 MHz, CDCl_3) and ^{13}C (101 MHz, CDCl_3) NMR spectra of compound S5



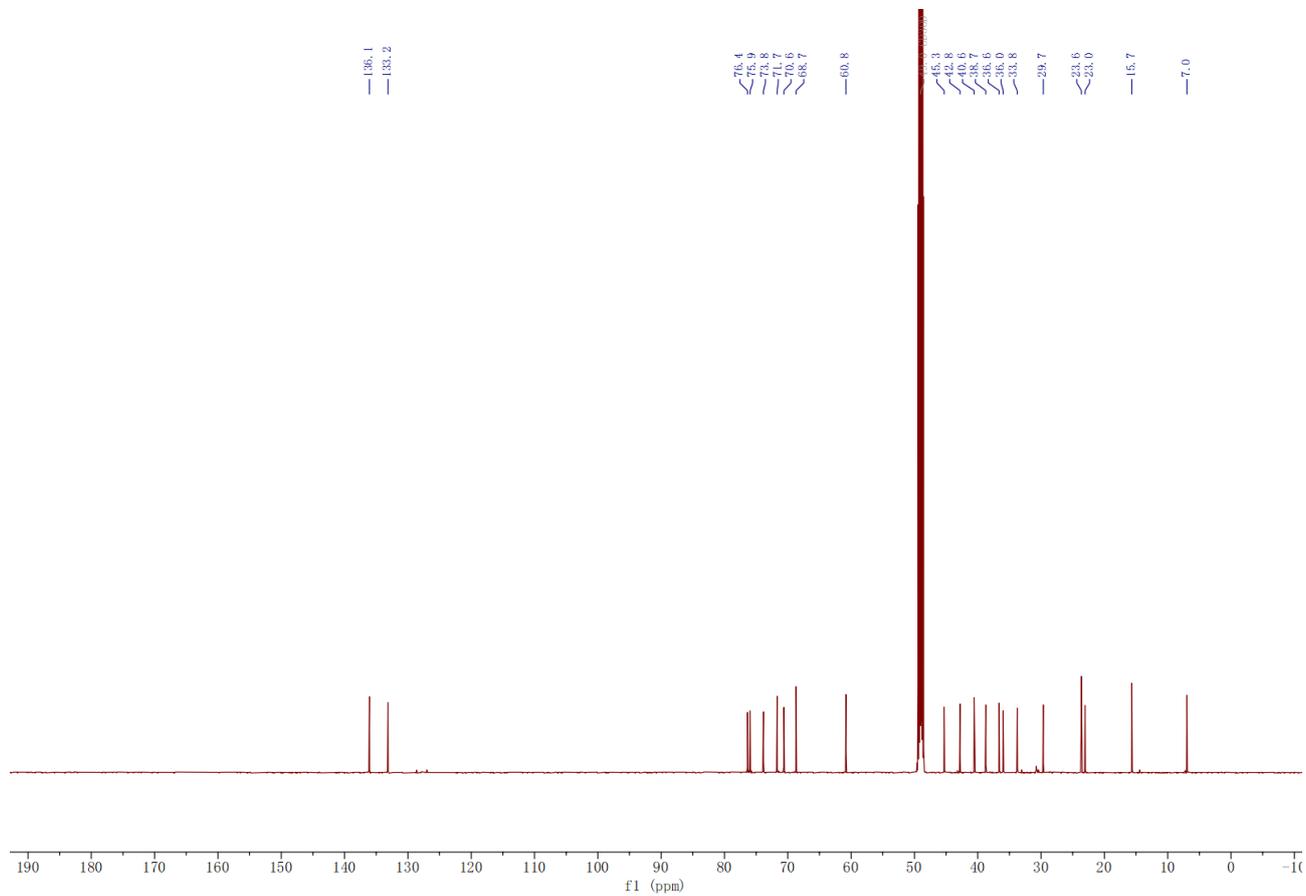
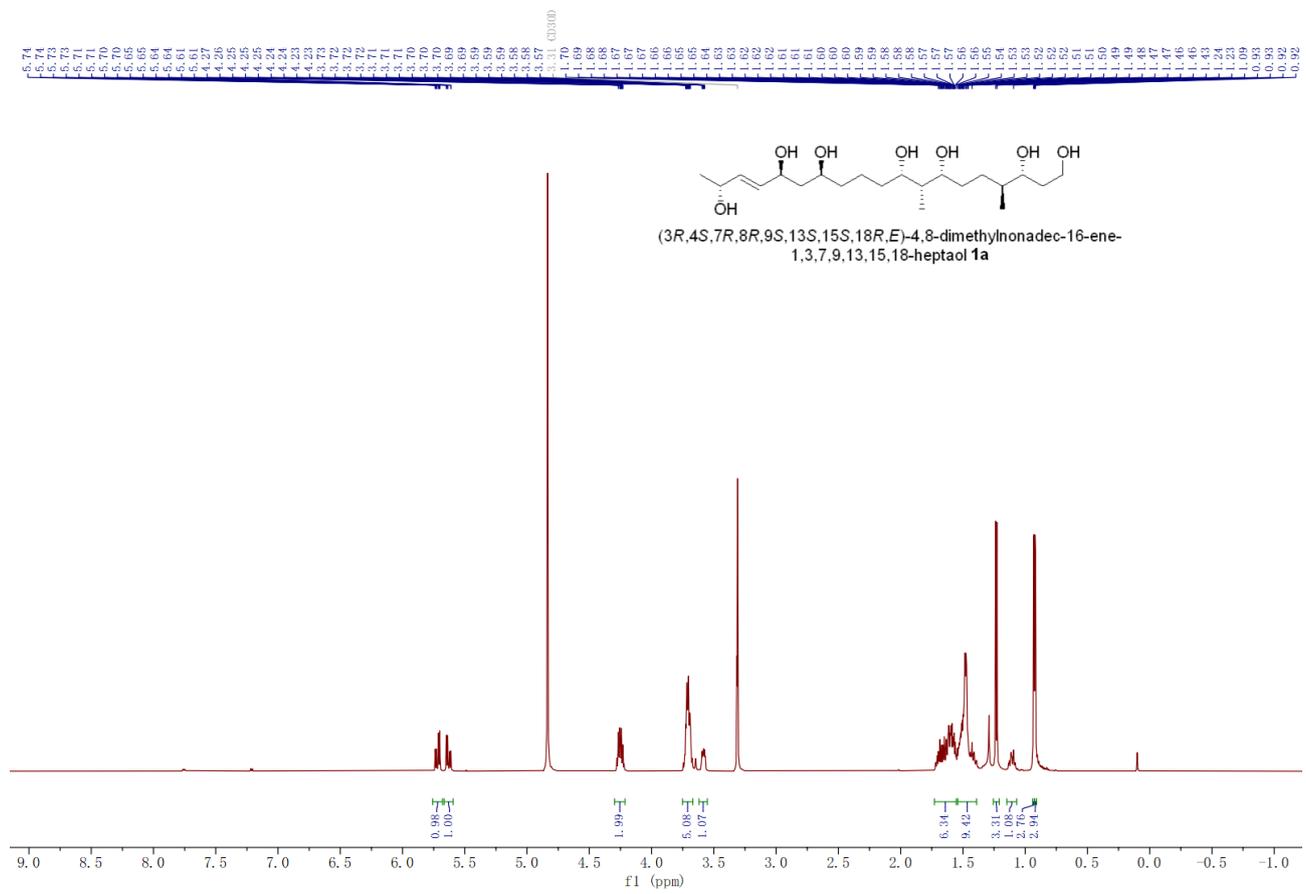
^1H (500 MHz, CDCl_3) and ^{13}C (126 MHz, CDCl_3) NMR spectra of compound 21



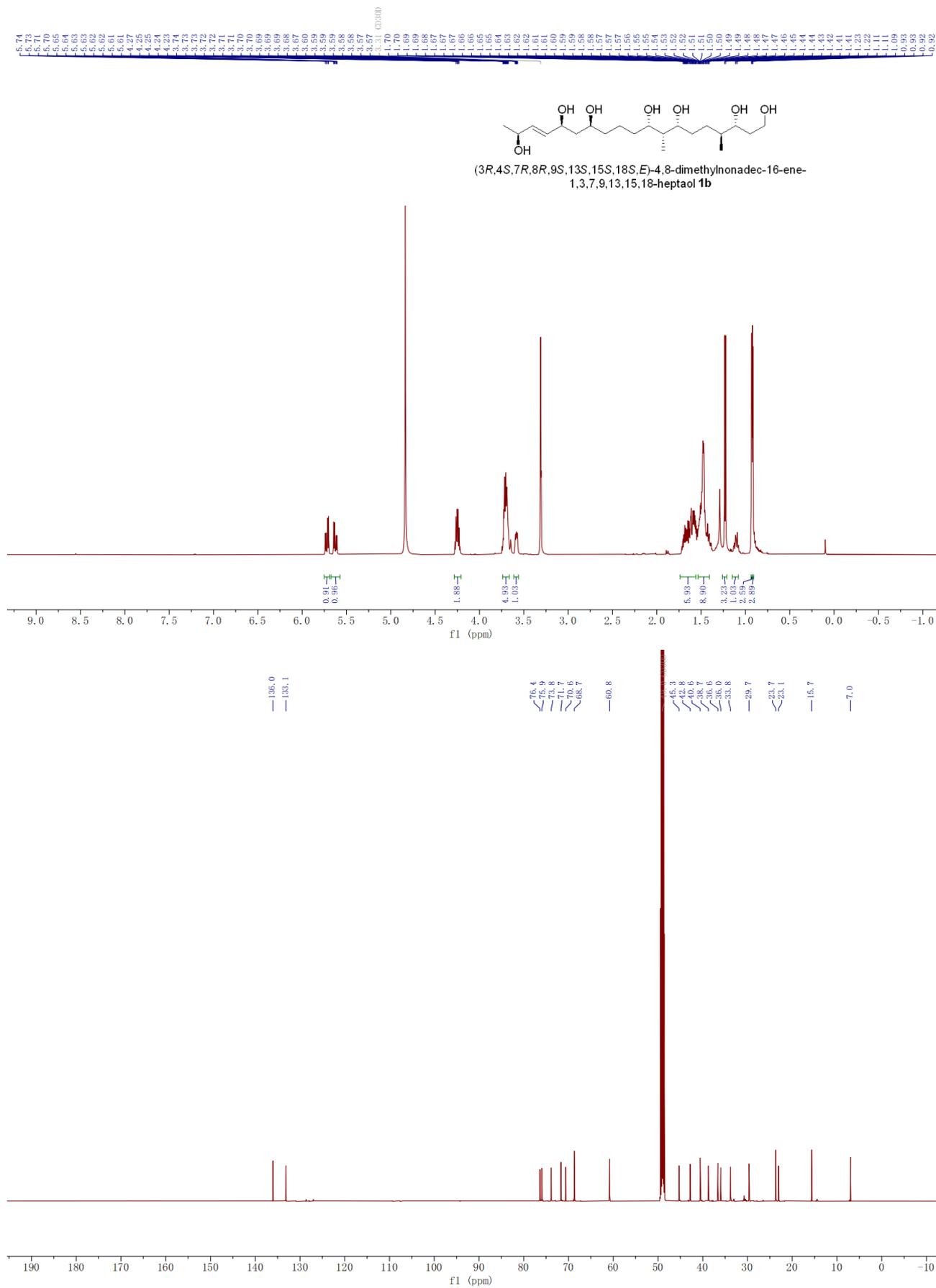
^1H (500 MHz, CDCl_3) and ^{13}C (126 MHz, CDCl_3) NMR spectra of compound 22b



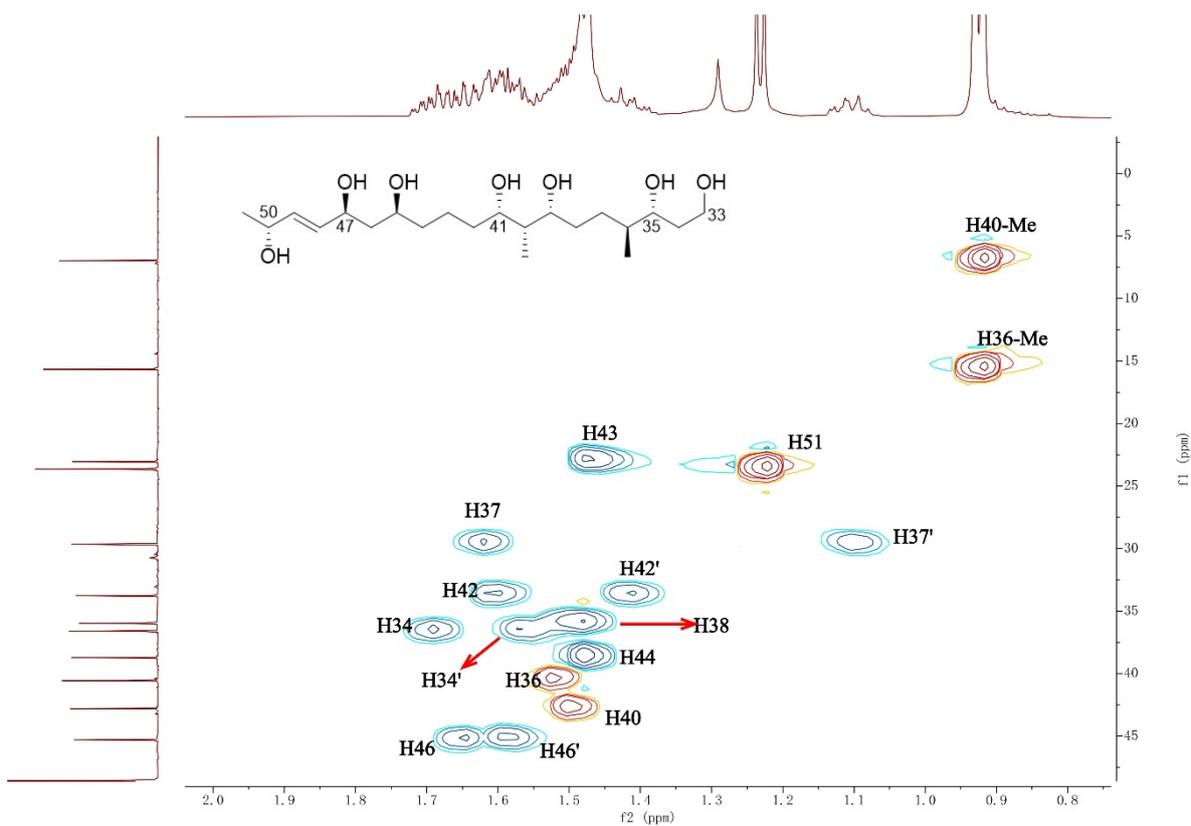
^1H (600 MHz, MeOD) and ^{13}C (151MHz, MeOD) NMR spectra of compound 1a



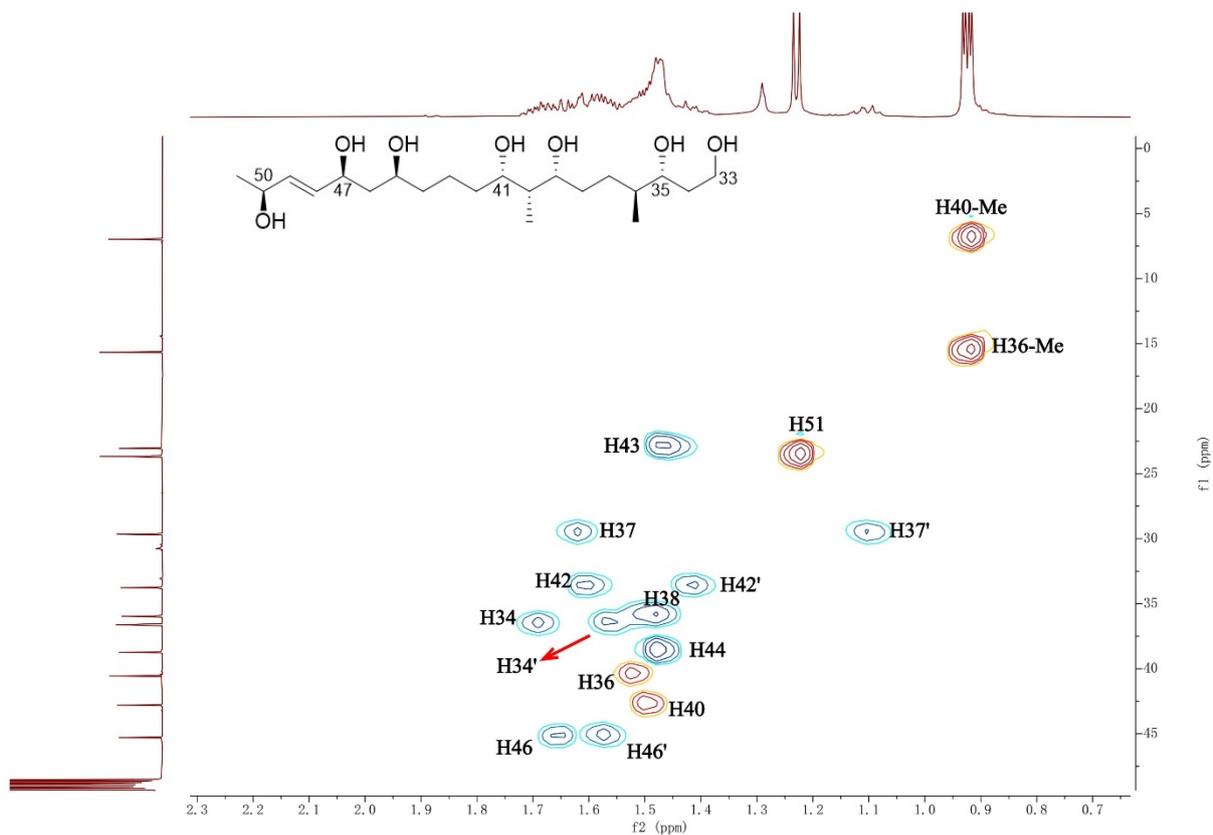
^1H (600 MHz, MeOD) and ^{13}C (151 MHz, MeOD) NMR spectra of compound **1b**



HSQC spectrum of 1a



HSQC spectrum of 1b



5. References

1. Lim, J.; Chintalapudi, V.; Gudmundsson, H. G.; Tran, M.; Bernasconi, A.; Blanco, A.; Song, L.; Challis, G. L.; Anderson, E. A., Synthesis of the C1–C27 Fragment of Stambomycin D Validates Modular Polyketide Synthase-Based Stereochemical Assignments. *Org. Lett.* **2021**, <https://doi.org/10.1021/acs.orglett.1c02650>.
2. Haack, K.J.; Hashiguchi, S.; Fujii, A.; Ikariya, T.; Noyori, R., The Catalyst Precursor, Catalyst, and Intermediate in the RuII-Promoted Asymmetric Hydrogen Transfer between Alcohols and Ketones. *Angew. Chem.* **1997**, *36*, 285-288.