

Supporting Information

Studies toward the Synthesis of Macrotermycin C: Stereoselective Construction of Acyclic Skeleton of the Aglycon

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Contents

1. General Experimental Section.....2
2. Experimental procedure of compounds **12, 13, 15, 16, 9, 20, 21** and **23**.....3-14
3. Photo Copies of Spectra.....15-38

General Experimental Section: All moisture sensitive reactions were performed in oven or flame-dried glassware with Teflon coated magnetic stirring bar under argon atmosphere using dry, freshly distilled solvents, unless otherwise noted. Air and moisture-sensitive liquids were transferred via a gastight syringe and a stainless-steel needle. Reactions were monitored by thin layer chromatography (TLC, Silica gel 60 F₂₅₄) plates with UV light, ethanolic anisaldehyde (with 1% AcOH and 3.3% conc. H₂SO₄) heat and aqueous KMnO₄ (with K₂CO₃ 10% aqueous NaOH solution) as developing agents. All workup and purification procedures were carried out with reagent-grade solvents under ambient atmosphere unless otherwise stated. Column chromatography was performed using silica gel 60-120 mesh, 100-200 mesh and 230-400 mesh. Yields mentioned as chromatographically and spectroscopically homogeneous materials unless otherwise stated. Optical rotations were measured using sodium (589, D line) lamp and are reported as follows: $[\alpha]^{25}_D$ ($c = \text{mg}/100 \text{ ml}$, solvent). Melting points of solids were measured in melting point apparatus. IR spectra were recorded as thin films (for liquids). HRMS were taken using Quadruple-TOF (Q-TOF) micro MS system using electrospray ionization (ESI) technique. ¹H spectra were recorded on 300 and 400 MHz spectrometers in appropriate solvents and calibrated using residual undertreated solvent as an internal reference and the chemical shift are shown in δ ppm scales. Multiplicities of NMR signals are designated as s (singlet), d (doublet), t (triplet), q (quartet), br (broad), m (multiplet, for unresolved lines) etc. ¹³C, 2D NMR spectra were recorded on 75 and 100 MHz spectrometers.

Experimental procedure:

((4*R*,5*S*)-5-((*R*)-1-((*tert*-Butyldiphenylsilyl)oxy)propan-2-yl)-2,2-dimethyl-1,3-dioxolan-4-yl)methanol (12): To a stirred ice cold solution of compound **11** (5.5 g, 22.9 mmol, 1 equiv) in anhydrous CH₂Cl₂ (50 mL) under argon, imidazole (2.37 g, 34.35 mmol, 1.5 equiv.) was added. The mixture was stirred for 15 min and TBDPSCl (7.1 mL, 27.48 mmol, 1.2 equiv) was then added. The resultant suspension was stirred at the room temperature for 4 h. The completion of the reaction was monitored by TLC. The reaction was quenched with saturated aqueous NH₄Cl solution (15 mL), extracted with CH₂Cl₂ (2 x 100 mL), washed with water, brine, dried (Na₂SO₄) and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO₂, 100-200 mesh, 6% EtOAc in hexane as eluent) provided the corresponding pure TBDPS protected diol (10.7 g, 98%) as a colorless liquid: $R_f = 0.3$ (20% EtOAc in hexane); $[\alpha]_D^{25} = -17.0$ (c 0.8, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 7.67-7.64 (m, 4H), 7.43-7.29 (m, 11H), 4.57 (d, $J = 1.8$ Hz, 2H), 4.07-4.04 (m, 2H), 3.64-3.56 (m, 4H), 2.95 (d, $J = 3.6$ Hz, 1H), 2.88 (d, $J = 3.0$ Hz, 1H), 1.87-1.82 (m, 1H), 1.06 (s, 9H), 0.95 (d, $J = 6.9$ Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 138.0, 135.8, 135.7, 133.4, 133.3, 129.9, 128.6, 128.0, 127.9, 73.8, 73.5, 72.6, 70.7, 67.1, 38.3, 27.0, 19.4, 11.9 ppm; IR (neat) ν_{max} 3361, 2931, 2857, 1428, 1121 cm⁻¹; HRMS (ESI) m/z calcd for C₂₉H₃₈O₄SiNa [M + Na]⁺ 501.2437, found 501.2434.

To an ice-cold solution of the above diol (10.5 g, 22.0 mmol, 1.0 equiv) in anhydrous CH₂Cl₂ (1 mL) under argon was added 2,2-DMP (4.1 mL, 32.9 mmol, 1.6 equiv) and CSA (511 mg, 2.2 mmol, 0.1 equiv) sequentially. The reaction mixture was warmed slowly to the room temperature and stirred further for 1 h before quenching by Et₃N (0.32 mL, 0.11 equiv). The mixture was concentrated in *vacuo* and purified by flash column chromatography (SiO₂, 60-120

mesh, 2% EtOAc in hexane as eluent) to provide the corresponding acetonide protected compound (12.71 g, 94%) as a colorless oil: $R_f = 0.6$ (5% EtOAc in hexane); $[\alpha]_D^{25} = -15.1$ (c 2.2, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 7.68-7.64 (m, 4H), 7.43-7.29 (m, 11H), 4.57 (d, $J = 1.8$ Hz, 2H), 4.07-4.04 (m, 2H), 3.64-3.56 (m, 4H), 1.91-1.83 (m, 1H), 1.41 (s, 3H), 1.40 (s, 3H), 1.06 (s, 9H), 0.95 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 75 MHz) δ 138.2, 135.8, 135.7, 133.9, 133.8, 129.8, 129.7, 128.5, 127.8, 127.8, 127.7, 108.9, 78.3, 73.7, 71.5, 66.4, 37.7, 27.3, 27.0, 19.4, 11.4 ppm; IR (neat) ν_{max} 2957, 2858, 1469, 1273, 1214 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{32}\text{H}_{42}\text{O}_4\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 541.2750, found 541.2751.

To a solution of naphthalene (15.5 g, 121.55 mmol, 5 equiv) in anhydrous THF (280 mL) under argon was added Li (0.83 mg, 121.6 mmol, 5 equiv) as small pieces. After stirring for 1 h at the room temperature, the reaction mixture was cooled to -40 °C and subsequently a solution of above compound (12.6 g, 24.31 mmol, dissolved in 40 mL of anhydrous THF, 1.0 equiv) was cannulated into it. The reaction was continued further for 1 h at the same temperature and then quenched with saturated aqueous solution of NH_4Cl (20 mL). The resultant mixture was extracted with EtOAc (2 x 200 mL), washed with water and brine, dried over anhydrous Na_2SO_4 , and concentrated under reduced pressure. The residue was purified by flash column chromatography (SiO_2 , 60-120 mesh, 5-20% EtOAc in hexane as eluent) to give compound **12** (10.41 g, 83%) as yellowish oil: $R_f = 0.3$ (10% EtOAc in hexane); $[\alpha]_D^{25} = -40.0$ (c 0.22, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 7.68-7.66 (m, 4H), 7.46-7.37 (m, 6H), 4.02-4.00 (m, 2H), 3.77 (t, $J = 4.8$ Hz, 1H), 3.65-3.61 (m, 3H), 2.14 (s, 1H), 1.88-1.78 (m, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 1.07 (s, 9H), 0.97 (d, $J = 6.6$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 75 MHz) δ 135.8, 135.7, 133.7, 133.7, 129.8, 127.8, 127.8, 108.6, 79.3, 77.8, 66.3, 63.0, 38.1, 27.3, 27.0, 19.4, 12.0 ppm; IR (neat) ν_{max} 3462, 2931,

2858, 1379 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{25}\text{H}_{36}\text{O}_4\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 451.2281, found 451.2283.

***tert*-Butyl((*R*)-2-((4*S*,5*R*)-5-((*E*)-2-iodovinyl)-2,2-dimethyl-1,3-dioxolan-4-yl)propoxy)**

diphenylsilane (13): To a stirred solution of $(\text{COCl})_2$ (3.0 mL, 35.03 mmol, 1.5 equiv.) in anhydrous CH_2Cl_2 (80 mL) under argon at $-78\text{ }^\circ\text{C}$, DMSO (4.98 mL, 70.1 mmol, 3.0 equiv.) was added drop wise over 2 min. After 15 min, a solution of compound **12** (10 g, 23.35 mmol, dissolved in 40 mL anhydrous CH_2Cl_2 , 1.0 equiv.) was cannulated into the reaction mixture and stirred further for 30 min at the same temperature. Et_3N (16.3 mL, 116.75 mmol, 5.0 equiv.) was then added and stirred further for 15 min at the same temperature. The reaction mixture was then warmed to $0\text{ }^\circ\text{C}$ and quenched with saturated aqueous solution of NH_4Cl (10 mL). The resultant mixture was extracted with CH_2Cl_2 ($2 \times 150\text{ mL}$), washed with water, brine, dried over Na_2SO_4 and concentrated in *vacuo*. Flash column chromatography of the crude residue using a short pad of silica gave the corresponding aldehyde (quantitative) as a colorless liquid which was taken for the next step without further characterizations.

To a stirred suspension of CrCl_2 (22.96 g, 186.8 mmol, 8 equiv) in anhydrous THF (400 mL) at $0\text{ }^\circ\text{C}$ under argon, a THF (60 mL) solution of the above aldehyde (23.4 mmol, 1 equiv.) and iodoform (27.6 g, 70.05 mmol, 3 equiv) was cannulated. The reaction was continued further for 2 h at the room temperature prior to quench with water. The resultant mixture was extracted with EtOAc ($2 \times 500\text{ mL}$), washed with brine, dried (Na_2SO_4), filtered, and concentrated. The crude product was purified by column chromatography (SiO_2 , 60-120 mesh, 3-5% EtOAc in hexane as eluent) to yield pure compound **13** (7.67 g, 60% yield) as a yellowish liquid: $R_f = 0.7$

(5% EtOAc in hexane); $[\alpha]_D^{25} = -11$ (c 2.8, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 7.68-7.64 (m, 4H), 7.44-7.37 (m, 6H), 6.56 (dd, $J = 6.6, 14.4$ Hz, 1H), 6.43 (d, $J = 14.7$ Hz, 1H), 4.17 (dd, $J = 6.8, 8.3$ Hz, 1H), 3.90 (dd, $J = 4.4, 8.3$ Hz, 1H), 3.65-3.54 (m, 2H), 1.87-1.79 (m, 1H), 1.39 (s, 3H), 1.38 (s, 3H), 1.07 (s, 9 H), 0.95 (d, $J = 6.6$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 75 MHz) δ 143.6, 135.8, 133.7, 129.8, 127.9, 127.8, 108.9, 80.9, 80.3, 80.2, 66.1, 37.1, 27.1, 27.0, 26.9, 19.4, 11.8 ppm; IR (neat) ν_{max} 2952, 2855, 1578, 1453, 1162 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{26}\text{H}_{35}\text{O}_3\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 573.1298, found 573.1295.

(R)-2-((4S,5R)-5-((1E,3Z)-Hexa-1,3,5-trien-1-yl)-2,2-dimethyl-1,3-dioxolan-4-yl) propan-1-ol (15): To an ice cold solution of compound **14** (4.5 g, 9.37 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (30 mL), NaHCO_3 (3.12 g, 37.48 mol, 4.0 equiv.) and DMP (6.0 g, 14.0 mmol, 1.5 equiv.) were added sequentially. The reaction mixture was warmed gradually to the room temperature and stirred further for 1 h. The reaction was then quenched with saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (5 ml) and NaHCO_3 (5 mL), then diluted with CH_2Cl_2 (20 mL) and stirred until the two phases were separated. The resultant mixture was extracted with CH_2Cl_2 (2 x 50 mL), washed with water, brine, dried over Na_2SO_4 and concentrated in *vacuo*. The crude residue was subjected to flash column chromatography (using a short pad of 60-120 silica and EtOAc as eluent) to get the corresponding aldehyde (quantitative) as a colorless liquid which was taken for the next reaction without further characterizations.

To a suspension of $\text{Ph}_3\text{PCH}_3\text{Br}$ (6.69 g, 18.74 mmol, 2.0 equiv.) in anhydrous THF (40 mL) at 0 °C under argon was added $^t\text{BuOK}$ (2.0 g, 17.80 mmol, 1.9 equiv), and the mixture was stirred for 30 min at the same temperature. The reaction mixture was cooled to -78 °C, and the

above aldehyde (9.37 mmol, dissolved in 15 mL of anhydrous THF, 1.0 equiv) was cannulated into it. The reaction mixture was stirred for another 1.5 h at -78 °C and then warmed to the room temperature prior to quench with saturated aqueous NH₄Cl solution (10 mL). The resultant mixture was extracted with EtOAc (2 x 100 mL), washed with water and brine, dried (Na₂SO₄), and concentrated in *vacuo*. Flash column chromatography (SiO₂, 60-120 mesh, 5% EtOAc in hexane as eluent) of the crude residue yielded the corresponding Wittig olefination product (3.25 g, 73%) as a yellowish oil: $R_f = 0.6$ (2% EtOAc in hexane); $[\alpha]_D^{24} = -9.65$ (c 11.6, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 7.66-7.62 (m, 4H), 7.42-7.34 (m, 6H), 6.83-6.69 (m, 2H), 6.07-5.95 (m, 2H), 5.70 (dd, $J = 7.8, 15.3$ Hz, 1H), 5.30-5.16 (m, 2H), 4.28 (t, $J = 8.1$ Hz, 1H), 3.92 (dd, $J = 4.2, 8.4$ Hz, 1H), 3.66-3.54 (m, 2H), 1.89-1.81 (m, 1H), 1.42 (s, 3H), 1.40 (s, 3H), 1.05 (s, 9H), 0.98 (d, $J = 6.9$ Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 135.8, 133.8, 132.1, 131.8, 131.1, 129.7, 129.1, 128.9, 127.8, 118.9, 108.6, 81.0, 79.7, 66.2, 37.0, 27.2, 27.0, 19.4, 11.8 ppm; IR (neat) ν_{max} 2956, 2930, 2857, 1111 cm⁻¹; HRMS (ESI) m/z calcd for C₃₀H₄₀O₃SiNa [M + Na]⁺ 499.2644, found 499.2643.

To an ice-cold solution of the above Wittig product (3 g, 6.30 mmol, 1.0 equiv) in anhydrous THF (18 mL) under argon was added TBAF (9.45 mL, 9.45 mmol, 1 M solution in THF, 1.5 equiv) over 2 min. The reaction mixture was stirred for 4 h at the room temperature prior to quench with saturated aqueous NH₄Cl solution (5 mL). The mixture was extracted with EtOAc (2 x 50 mL), washed with water and brine, dried over Na₂SO₄, and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO₂, 60-120 mesh, 5-20% EtOAc in hexane as eluent) gave compound **15** (1.26 g, 84% yield) as a colorless oil: $R_f = 0.6$

(2% EtOAc in hexane); $[\alpha]_D^{25} = -3.2$ (c 6.8, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 6.82-6.74 (m, 2H), 6.04-5.99 (m, 2H), 5.67 (dd, $J = 7.8, 15.0$ Hz, 1H), 5.30-5.18 (m, 2H), 4.32 (t, $J = 7.8$ Hz, 1H), 3.86 (dd, $J = 3.6, 8.7$ Hz, 1H), 3.66-3.64 (m, 2H), 1.97-1.91 (m, 1H), 1.42 (s, 6H), 1.01 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 75 MHz) δ 131.9, 131.5, 131.2, 129.2, 128.7, 119.2, 108.9, 82.6, 79.1, 66.4, 35.7, 27.2, 27.1, 11.5 ppm; IR (neat) v_{max} 3424, 2985, 2928, 1379, 1218 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{14}\text{H}_{22}\text{O}_3\text{Na}$ $[\text{M} + \text{Na}]^+$ 261.1467, found 261.1465.

(4*S*,5*R*)-4-((*R*)-1-Azidopropan-2-yl)-5-((1*E*,3*Z*)-hexa-1,3,5-trien-1-yl)-2,2-dimethyl-1,3-

dioxolane (16): A solution of compound **15** (1 g, 4.2 mmol, 1equiv.) and TsCl (961 mg, 5.04 mmol, 1.2 equiv.) in anhydrous CH_2Cl_2 (10 mL) under argon in the presence of Et_3N (0.88 mL, 6.30 mmol, 1.5 equiv.) was stirred at the ambient temperature for 2 h. The mixture was treated with saturated aqueous NH_4Cl solution (3 mL) and extracted with CH_2Cl_2 . (2×30 mL), washed with water and brine, dried over Na_2SO_4 , and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2 , 60-120 mesh, 3-5% EtOAc in hexane as eluent) afforded the corresponding tosylated compound (1.23 g, 89% yield) as a colorless oil: $R_f = 0.7$ (5% EtOAc in hexane); $[\alpha]_D^{24} = -23.5$ (c 0.97, CHCl_3); $^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ 7.77 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.1$ Hz, 2H), 6.84-6.69 (m, 2H), 6.09-5.94 (m, 2H), 5.59 (dd, $J = 10.8, 15.0$ Hz, 1H), 5.31-5.19 (m, 2H), 4.22 (t, $J = 8.1$ Hz, 1H), 4.03-3.91 (m, 2H), 3.68 (dd, $J = 3.5, 8.4$ Hz, 1H), 2.44 (s, 3H), 2.06-1.98 (m, 1H), 1.35 (s, 6H), 0.98 (d, $J = 6.9$ Hz, 3H); $^{13}\text{C NMR}$ (CDCl_3 , 75 MHz) δ 144.9, 133.1, 131.9, 131.6, 130.6, 130.0, 129.7, 128.6, 128.1, 119.3, 109.0, 80.1, 79.2, 72.4, 33.8, 27.1, 27.0, 21.8, 11.32 ppm; IR (neat) v_{max} 2985, 2929, 1363, 1177 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{21}\text{H}_{28}\text{O}_5\text{SNa}$ $[\text{M} + \text{Na}]^+$ 415.1555, found 415.1553.

To a stirred solution of the above tosylated compound (1.2 g, 3.66 mmol, 1 equiv.) in anhydrous DMF (15 mL) under argon at 70 °C, NaN₃ (475 mg, 7.31 mmol, 2 equiv.) was added. The reaction mixture was stirred for 12 h at the same temperature. After being cooled to the room temperature, the mixture was treated with water and extracted with Et₂O. The ethereal solution was washed with brine and dried over Na₂SO₄. The solvent was evaporated and the resultant mixture was extracted with EtOAc (2 x 20 mL), washed with water and brine, dried over Na₂SO₄, and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO₂, 60-120 mesh, 2-6% EtOAc in hexane as eluent) provided azide **16** (660 mg, 69% yield) as a yellowish oil: $R_f = 0.4$ (5% EtOAc in hexane); $[\alpha]_D^{24} = -93.3$ (c 0.2, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 6.82-6.73 (m, 2H), 6.09-6.00 (m, 2H), 5.66 (dd, $J = 7.8, 15.0$ Hz, 1H), 5.31-5.18 (m, 2H), 4.26 (t, $J = 8.3$ Hz, 1H), 3.75 (dd, $J = 3.9, 8.4$ Hz, 1H), 3.38 (dd, $J = 6.6, 12$ Hz, 1H), 3.24 (dd, $J = 6.9, 12$ Hz, 1H), 1.94-1.85 (m, 1H), 1.42 (s, 3H), 1.41 (s, 3H), 1.04 (d, $J = 6.6$ Hz, 3H); ¹³C NMR (CDCl₃, 75 MHz) δ 131.9, 131.6, 130.9, 129.6, 128.6, 119.3, 108.9, 81.2, 79.3, 55.1, 34.4, 27.1, 27.1, 12.6 ppm; IR (neat) ν_{max} 2927, 2099, 1920 cm⁻¹; HRMS (ESI) m/z calcd for C₁₄H₂₁O₂N₃Na [M + Na]⁺ 286.1531, found 286.1533.

***tert*-Butyl(((4*R*,5*S*)-5-((*E*)-2-iodovinyl)-2,2,5-trimethyl-1,3-dioxolan-4-yl)methoxy)**

diphenylsilane (9): Following the same the Swern oxidation procedure as describe in the preparation of compound **13**, compound **17** (10 g, 24.1 mmol) was converted to the corresponding aldehyde (quantitative, purification by flash column chromatography, SiO₂, 60-120 mesh, EtOAc as eluent) as a colorless oil which was directly use for the next step without further characterizations.

Following the same synthetic procedure of compound **13**, the above aldehyde (24.1 mmol, 1 equiv.) was converted to compound **9** (9.45 g, 73%, purification by flash column chromatography, SiO₂, 60-120 mesh, 2-3% EtOAc in hexane as eluent) as a yellowish oil: $R_f = 0.7$ (3% EtOAc in hexane); $[\alpha]_D^{20} = +4.4$ (c 7.1, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 7.68 (d, $J = 6.0$ Hz, 4H), 7.45-7.41 (m, 6H), 6.70 (d, $J = 14.1$ Hz, 1H), 6.41 (d, $J = 14.4$ Hz, 1H), 3.99 (dd, $J = 5.0, 8.3$ Hz, 1H), 3.84 (q, $J = 5.1$ Hz, 1H), 3.64 (t, $J = 9.3$ Hz, 1H), 1.46 (s, 3H), 1.43 (s, 3H), 1.39 (s, 3H), 1.08 (s, 9H); ¹³C NMR (CDCl₃, 75 MHz) δ 147.1, 135.7, 135.7, 132.9, 130.0, 128.0, 127.9, 108.8, 85.2, 83.2, 77.4, 62.8, 28.0, 27.0, 27.6, 26.0, 19.3 ppm; IR (neat) v_{max} 2930, 1428, 1092 cm⁻¹; HRMS (ESI) m/z calcd for C₂₅H₃₃O₃SiNa [M + Na]⁺ 549.1141, found 549.1142.

(2E,4E)-5-((4S,5R)-5-(Hydroxymethyl)-2,2,4-trimethyl-1,3-dioxolan-4-yl)penta-2,4-dien-1-yl pivalate (20): To an ice-cold solution of alcohol **19** (4.1 g, 8.79 mmol, 1.0 equiv.) in anhydrous CH₂Cl₂ (30 mL) under argon, Et₃N (1.35 mL, 9.67 mmol, 1.1 equiv), PivCl (1.17 mL, 9.67 mmol, 1.1 equiv), and DMAP (68 mg, 0.44 mmol, 0.05 equiv) were added sequentially. The reaction mixture was warmed slowly to the room temperature and stirred further for 2 h before quenching it with saturated aqueous solution of NH₄Cl (3 mL). The resultant mixture was extracted with CH₂Cl₂ (2 x 50 mL), washed with water and brine, dried over Na₂SO₄, and evaporated under reduced pressure. Flash column chromatographic purification (SiO₂, 100-200 mesh, 5-10% EtOAc in hexane as eluent) of the crude residue gave the corresponding pivaloyl protected compound (4.55 g, 95%) as a colorless oil: $R_f = 0.4$ (5% EtOAc in hexane); $[\alpha]_D^{24} = +7.7$ (c 6.3, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 7.68-7.64 (m, 4H), 7.44-7.35 (m, 6H), 6.35-

6.18 (m, 2H), 5.80-5.70 (m, 2H), 4.60 (d, $J = 6.3$ Hz, 2H), 4.02 (dd, $J = 5.1, 8.1$ Hz, 1H), 3.82 (dd, $J = 5.1, 10.2$ Hz, 1H), 3.62 (dd, $J = 8.0, 10.4$ Hz, 1H), 1.46 (s, 3H), 1.45 (s, 3H), 1.40 (s, 3H), 1.22 (s, 9H), 1.07 (m, 9H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 178.4, 136.0, 135.8, 133.4, 133.2, 133.1, 129.9, 128.9, 127.9, 127.0, 83.8, 82.4, 64.7, 63.0, 38.9, 28.1, 27.4, 26.9, 26.8, 26.2, 19.3 ppm; IR (neat) ν_{max} 2960, 2932, 2859, 1728, 1280, 1149 cm^{-1} ; HRMS (ESI) m/z calcd for $\text{C}_{33}\text{H}_{46}\text{O}_5\text{SiNa}$ $[\text{M} + \text{Na}]^+$ 573.3012, found 573.3011.

To an ice-cold solution of the above pivaloyl compound (4.5 g, 8.17 mmol, 1.0 equiv) in anhydrous THF (20 mL) under argon, TBAF (12.3 mL, 12.3 mmol, 1 M solution in THF, 1.5 equiv) was added slowly. The reaction mixture was stirred for 6 h at the room temperature prior to quench with saturated aqueous NH_4Cl solution (5 mL). The mixture was extracted with EtOAc (2 x 50 mL), washed with water and brine, dried over Na_2SO_4 , and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO_2 , 60-120 mesh, 5-25% EtOAc in hexane as eluent) afforded the TBDPS deprotected alcohol **20** (2.14 g, 84%) as a colorless oil: $R_f = 0.4$ (20% EtOAc in hexane); $[\alpha]_D^{25} = -7.58$ (c 1.9, CHCl_3); ^1H NMR (CDCl_3 , 300 MHz) δ 6.31-6.19 (m, 2H), 5.78-5.61 (m, 2H), 4.56 (d, $J = 5.7$ Hz, 2H), 4.01 (q, $J = 4.4$ Hz, 1H), 3.71-3.56 (m, 2H), 1.49 (s, 3H), 1.42 (s, 3H), 1.41 (s, 3H), 1.19 (s, 9H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 178.4, 135.2, 132.9, 129.0, 127.6, 108.9, 84.8, 81.4, 64.6, 62.1, 38.9, 28.3, 27.3, 26.9, 25.5 ppm; IR (neat) ν_{max} 3483, 2979, 2933, 1728, 1194; HRMS (ESI) m/z calcd for $\text{C}_{17}\text{H}_{28}\text{O}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 335.1834, found 335.1832.

(2E,4E)-5-((4S,5R)-5-((Z)-2-Iodovinyl)-2,2,4-trimethyl-1,3-dioxolan-4-yl)penta-2,4-dien-1-yl pivalate (21): Following the same DMP oxidation procedure of compound **15**, compound **20**

(2 g, 6.4 mmol) was converted to the corresponding aldehyde (quantitative, purification by flash column chromatography, SiO₂, 60-120 mesh, EtOAc as eluent) as a colorless oil, which was directly use for the next step without further characterizations.

To a suspension of Ph₃PCH₂I₂ [(iodomethyl)-triphenylphosphonium iodide] (6.8 g, 12.8 mmol, 2 equiv.) in anhydrous THF (30 mL) at 0 °C under argon atmosphere was added NaHMDS (1 M in THF, 23.0 mL, 23.0 mmol, 1.8 equiv.) dropwise and the reaction mixture was stirred for 30 min at the same temperature. The resultant dark red solution was cooled to -78 °C, and aldehyde (6.4 mmol, 1 equiv. dissolved in anhydrous 15 mL of THF) from the above step was cannulated into it. After 30 min of stirring at -78 °C, the reaction mixture was warmed to the room temperature and stirred further for another 1.5 h. The reaction mixture was quenched with saturated aqueous NH₄Cl solution (5 mL) and extracted with EtOAc (2 x 50 mL), washed with water and brine, dried (Na₂SO₄), and concentrated in *vacuo*. Flash column chromatography (SiO₂, 60-120 mesh, 5% EtOAc in hexane as eluent) of the resultant crude residue afforded compound **21** (2.1 g, 77%) as a colorless liquid. $R_f = 0.5$ (3% EtOAc in hexane); $[\alpha]_D^{25} = -170.0$ (c 4.3, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 6.57 (dd, $J = 0.45, 7.7$ Hz, 1H), 6.28-6.22 (m, 2H), 6.19-6.12 (m, 1H), 5.81-5.59 (m, 2H), 4.70-4.67 (m, 1H), 4.58-4.54 (m, 2H), 1.52 (s, 3H), 1.49 (s, 3H), 1.47 (s, 3H), 1.20 (s, 9H); ¹³C NMR (CDCl₃, 75 MHz) δ 178.4, 137.0, 135.9, 132.9, 128.9, 127.6, 109.5, 86.4, 85.8, 83.6, 64.6, 38.9, 28.2, 27.3, 27.0, 25.6 ppm; IR (neat) ν_{max} 2979, 2933, 2874, 1727, 1277 cm⁻¹; HRMS (ESI) m/z calcd for C₁₈H₂₇O₄INa [M + Na]⁺ 457.0852, found 457.0854.

(2E,4E,6S,7R,8Z)-6,7-Bis((tert-butyldimethylsilyloxy)-9-iodo-6-methylnona-2,4,8-trien-1-ol (23): Compound **21** (100 mg) was treated with 80% acetic acid (2 mL) and stirred for 2 days at the room temperature. Acetic acid was removed under reduced pressure, and the resultant residue was extracted with EtOAc (2 x 15 mL). The organic layers were washed with saturated aqueous NH₄Cl solution, water, and brine, dried (Na₂SO₄), and concentrated under reduced pressure. Purification by flash column chromatography (SiO₂, 100-200 mesh, 30% EtOAc in hexane as eluent) gave the corresponding diol (58 mg, 73%) as a colorless liquid: $R_f = 0.2$ (50% EtOAc in hexane); $[\alpha]_D^{20} = -7.5$ (*c* 3.7, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 6.53 (d, *J* = 7.8 Hz, 1H), 6.34-6.22 (m, 3H), 5.84-5.75 (m, 2H), 4.59 (d, *J* = 5.7 Hz, 2H), 4.28 (d, *J* = 8.7 Hz, 1H), 2.40-2.20 (m, 2H), 1.38 (s, 3H), 1.21 (s, 9H); ¹³C NMR (CDCl₃, 75 MHz) δ 178.4, 139.2, 136.1, 132.9, 129.4, 128.0, 86.6, 80.0, 75.2, 64.5, 39.0, 27.4, 24.7 ppm; IR (neat) ν_{max} 3361, 2979, 2933, 2874, 1729, 1277 cm⁻¹; HRMS (ESI) *m/z* calcd for C₁₅H₂₃O₄INa [M + Na]⁺ 417.0539, found 417.0537.

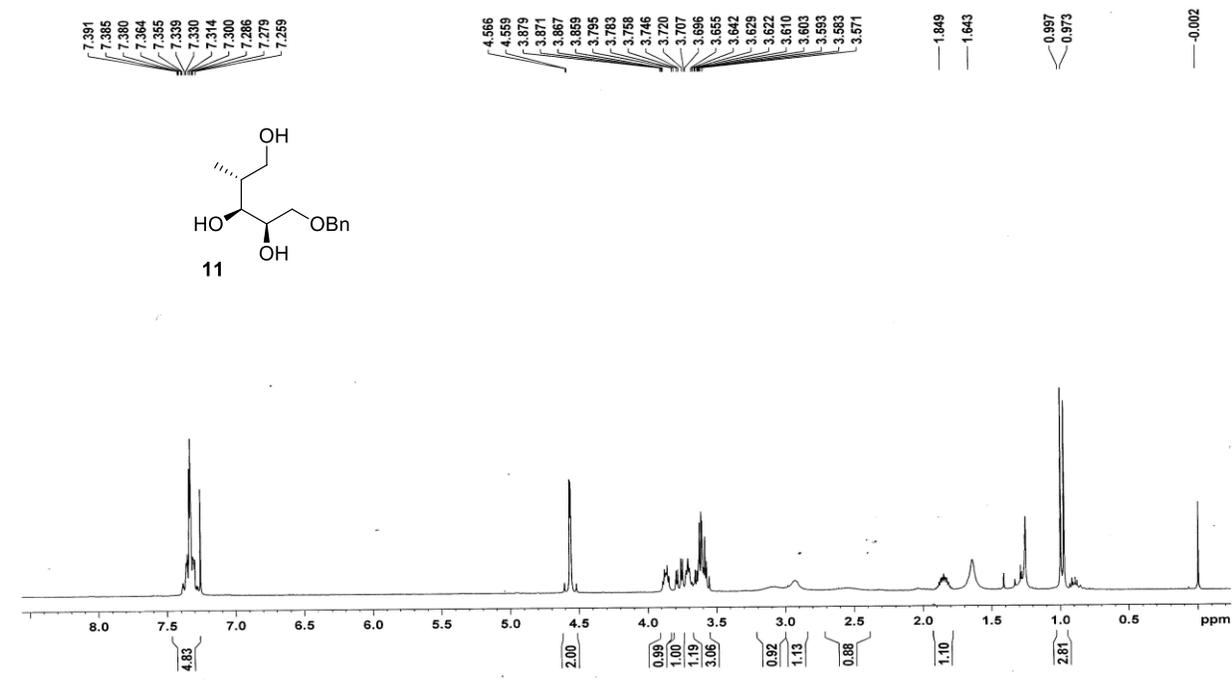
To an ice cold solution of the above diol (50 mg, 0.15mmol, 1 equiv.) in anhydrous CH₂Cl₂ (2 mL) under argon, 2,6-lutidine (0.05 mL, 0.44 mmol, 3.0 equiv.) was added. The reaction mixture was stirred for 10 min and TBSOTf (0.1 mL, 0.44 mmol, 3 equiv.) was then added. The reaction was continued at the same temperature for 45 min and subsequently quenched by saturated aqueous solution of NaHCO₃ (1 mL). The resultant mixture was extracted with CH₂Cl₂ (2 x 10 mL), washed with aqueous CuSO₄, water, brine, dried (Na₂SO₄) and concentrated in *vacuo*. Purification of the crude residue by flash column chromatography (SiO₂, 100-200 mesh, 1.0-1.5% EtOAc in hexane as eluent) furnished di-TBS protected compound (83 mg, 89%) as a yellowish liquid: $R_f = 0.7$ (5% EtOAc in hexane); $[\alpha]_D^{25} = -47.9$ (*c* 0.4, CHCl₃); ¹H

NMR (CDCl₃, 300 MHz) δ 6.32 (d, J = 5.7 Hz, 1H), 6.28-6.11 (m, 3H), 5.82-5.70 (m, 2H), 4.59 (d, J = 4.5 Hz, 2H), 4.07 (d, J = 6.3 Hz, 1H), 1.26 (s, 3H), 1.21 (s, 9H), 0.88 (s, 9H), 0.86 (s, 9H), 0.07-0.04 (m, 12H); ¹³CNMR (CDCl₃, 100 MHz) δ 178.4, 141.2, 140.4, 133.7, 128.6, 126.8, 83.8, 81.4, 78.4, 64.7, 38.9, 27.8, 26.2, 26.0, 23.1, 18.6, 18.2, -1.8, -1.9, -3.8, -4.5, ppm; IR (neat) v_{max} 2966, 2874, 1726, 1387, 1141 cm⁻¹; HRMS (ESI) m/z calcd for C₂₇H₅₁O₄Si₂INa [M + Na]⁺ 645.2268, found 645.2270.

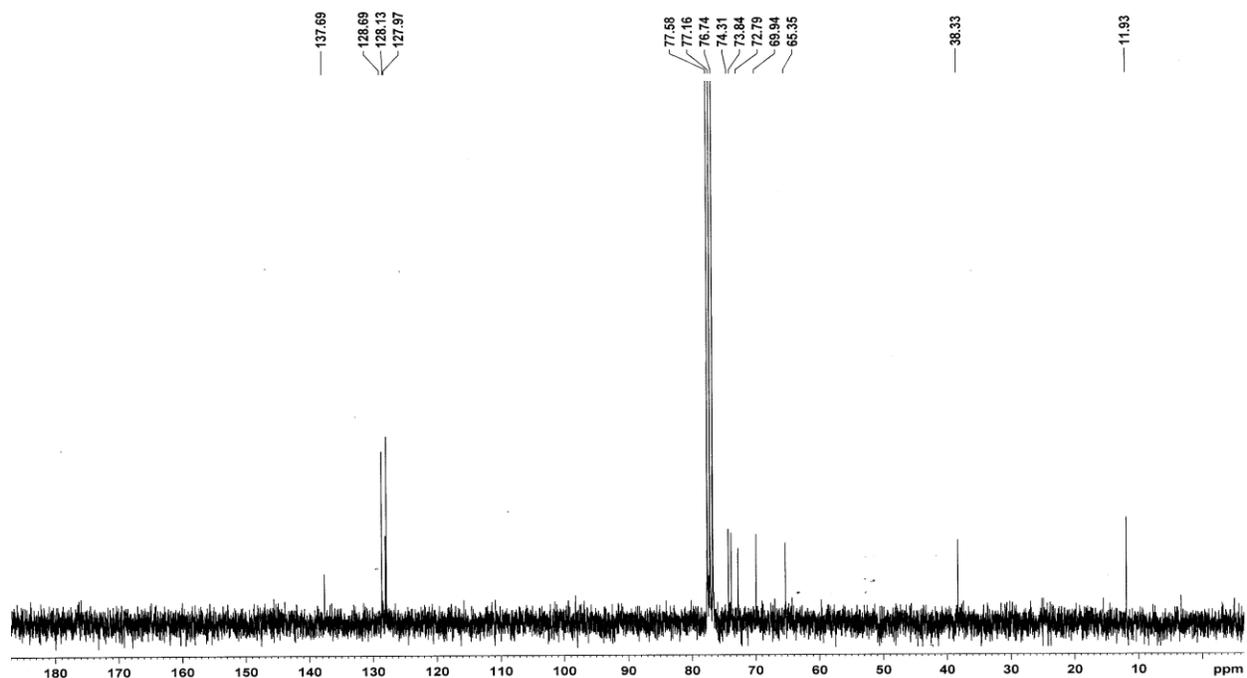
Following the same DIBAL-H reduction conditions described in the preparation of compound **7**, the above TBS protected compound (80 mg) was converted to the corresponding alcohol **23** (57 mg, 83%, purification by flash column chromatography, SiO₂, 60-120 mesh, 5-15% EtOAc in hexane as eluent) as a yellowish oil: R_f = 0.2 (10% EtOAc in hexane); $[\alpha]_D^{25}$ = -24.0 (c 0.8, CHCl₃); ¹H NMR (CDCl₃, 300 MHz) δ 6.32 (d, J = 5.7 Hz, 1H), 6.30-6.11 (m, 3H), 5.87-5.71 (m, 2H), 4.10 (d, J = 7.2 Hz, 2H), 4.03 (d, J = 12.3 Hz, 1H), 1.36 (s, 3H), 0.88 (s, 9H), 0.87 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H), 0.04 (s, 6H); ¹³C NMR (CDCl₃, 75 MHz) δ 141.3, 139.5, 131.8, 131.4, 128.8, 83.8, 81.4, 78.4, 63.6, 26.2, 26.0, 23.1, 18.5, 18.2, -1.8, -3.8, -4.5 ppm; IR (neat) v_{max} 3351, 2955, 2928, 2856, 1471, 1254 cm⁻¹; HRMS (ESI) m/z calcd for C₂₂H₄₃O₃Si₂INa [M + Na]⁺ 561.1693, found 561.1694.

Photo Copies of Spectra:

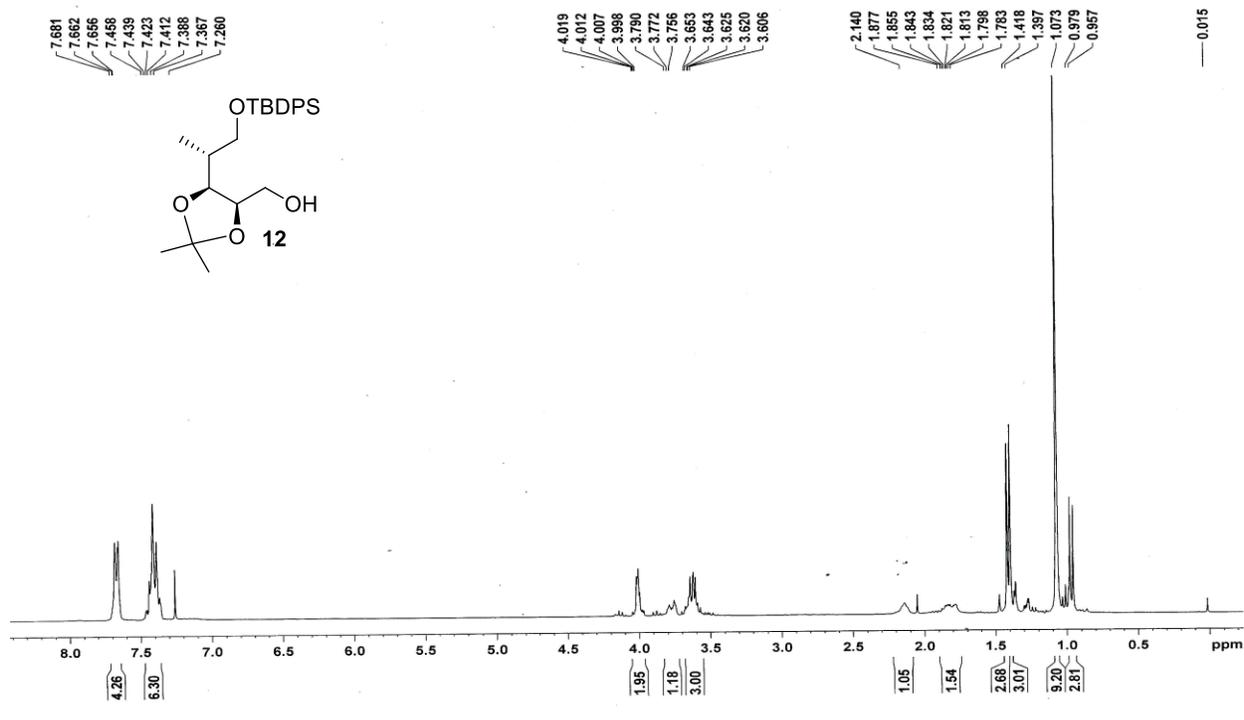
^1H NMR Spectra of 11 (300 MHz, CDCl_3):



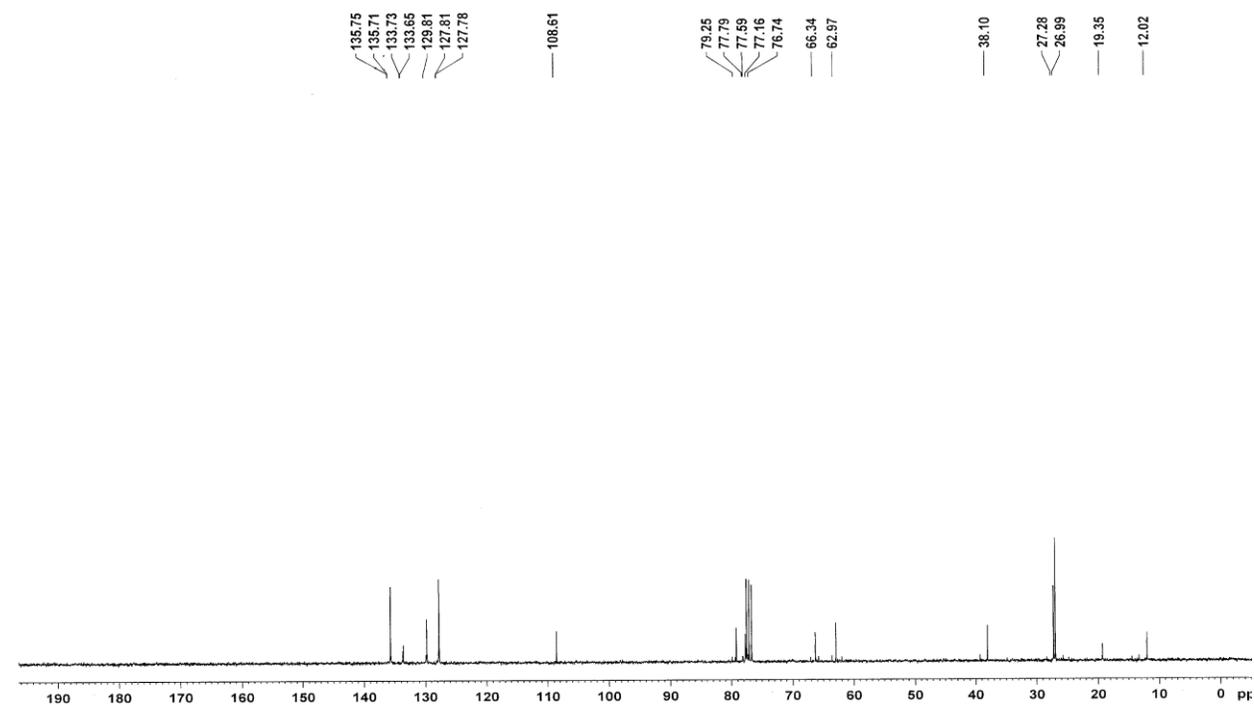
^{13}C NMR Spectra of 11 (75 MHz, CDCl_3):



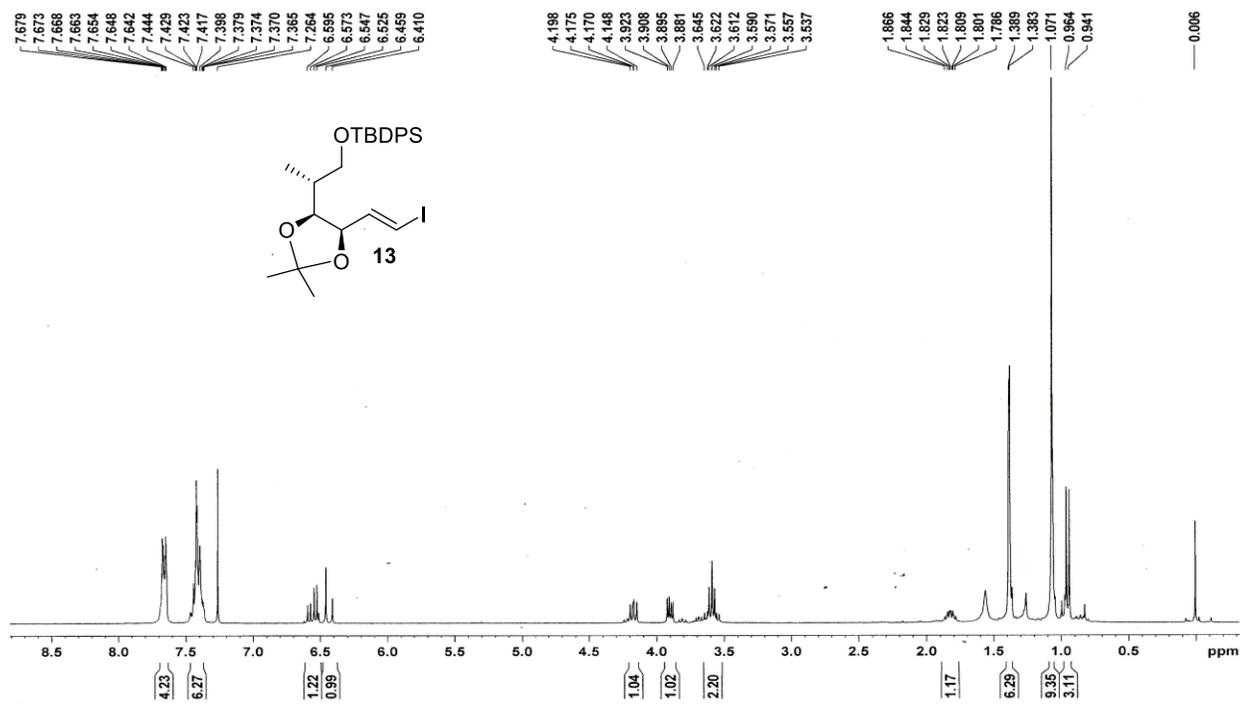
¹H NMR Spectra of 12 (300 MHz, CDCl₃):



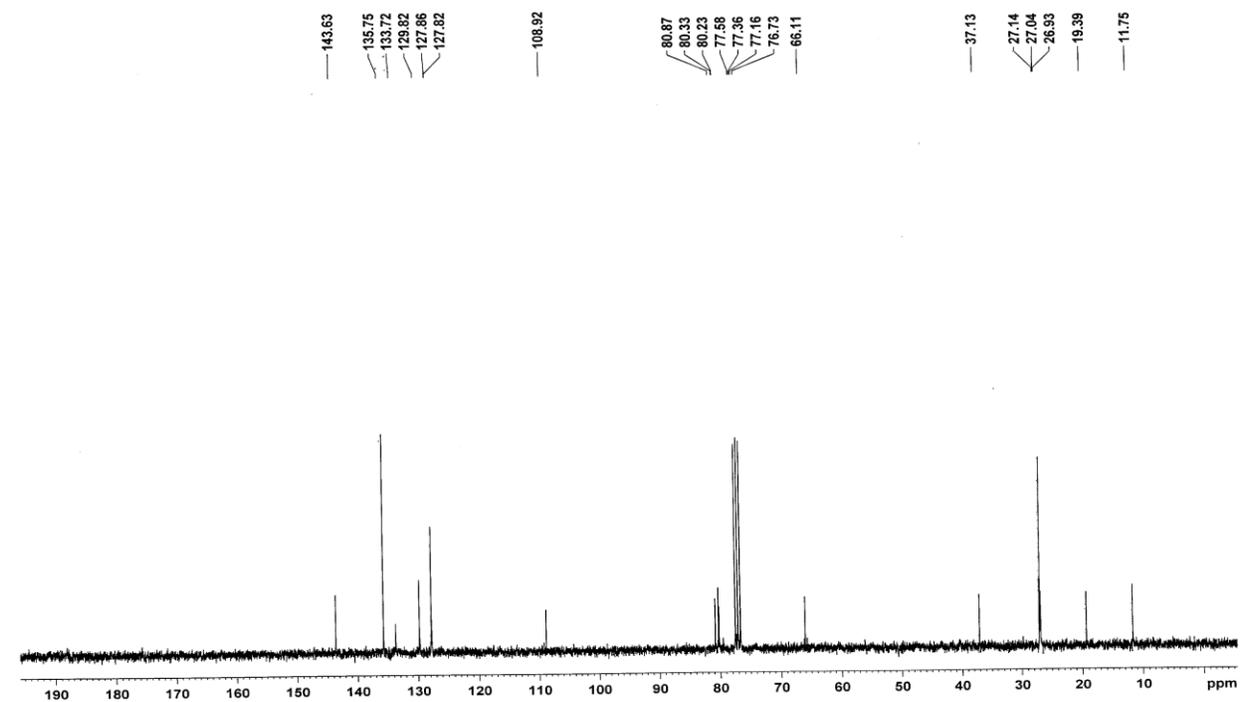
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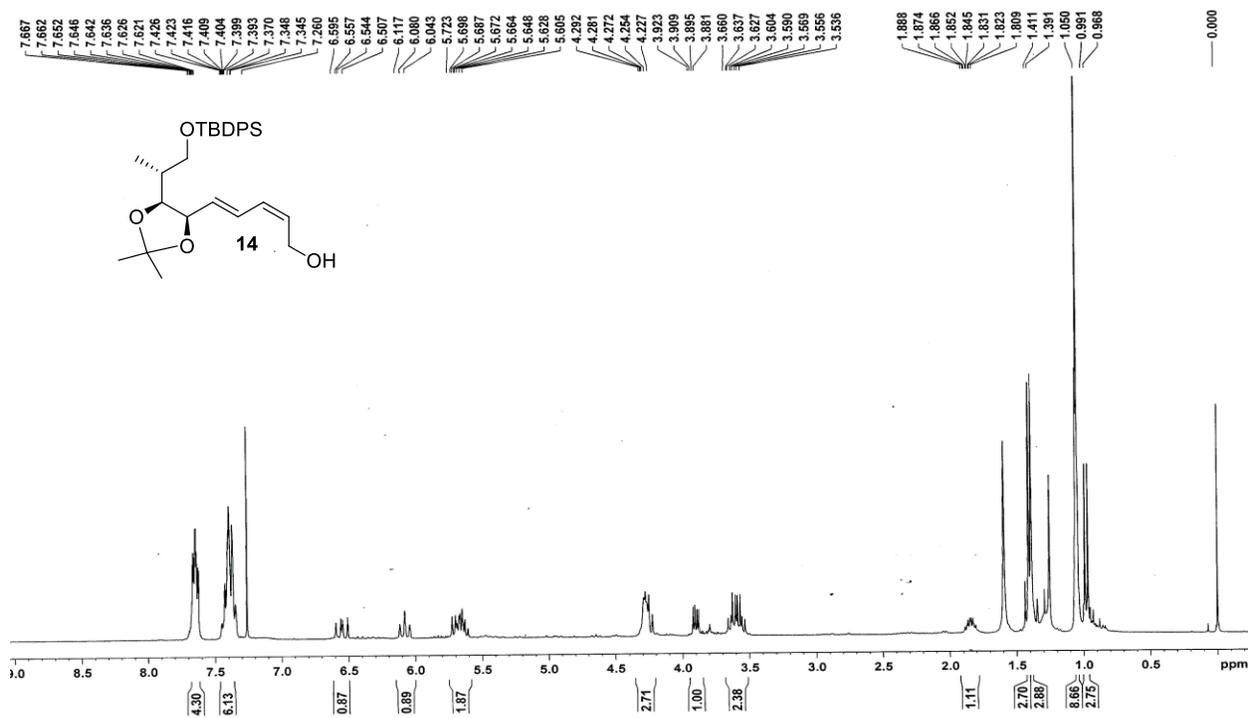
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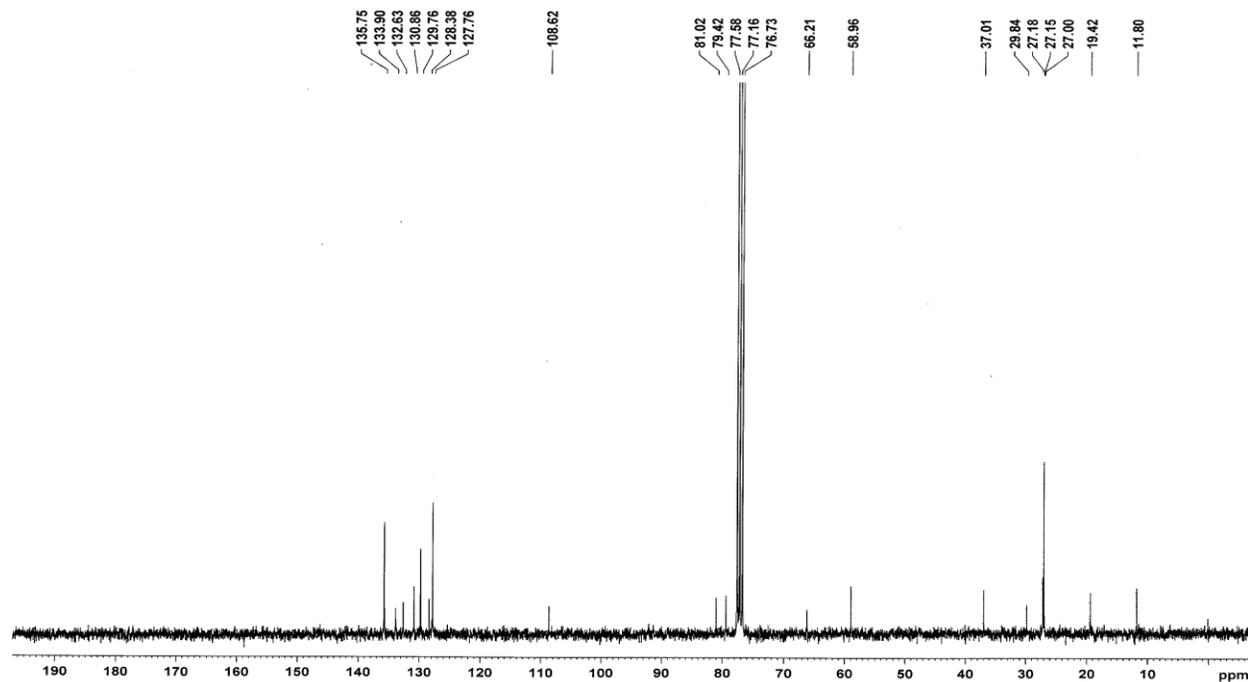
¹³C NMR Spectra of 13 (75 MHz, CDCl₃):



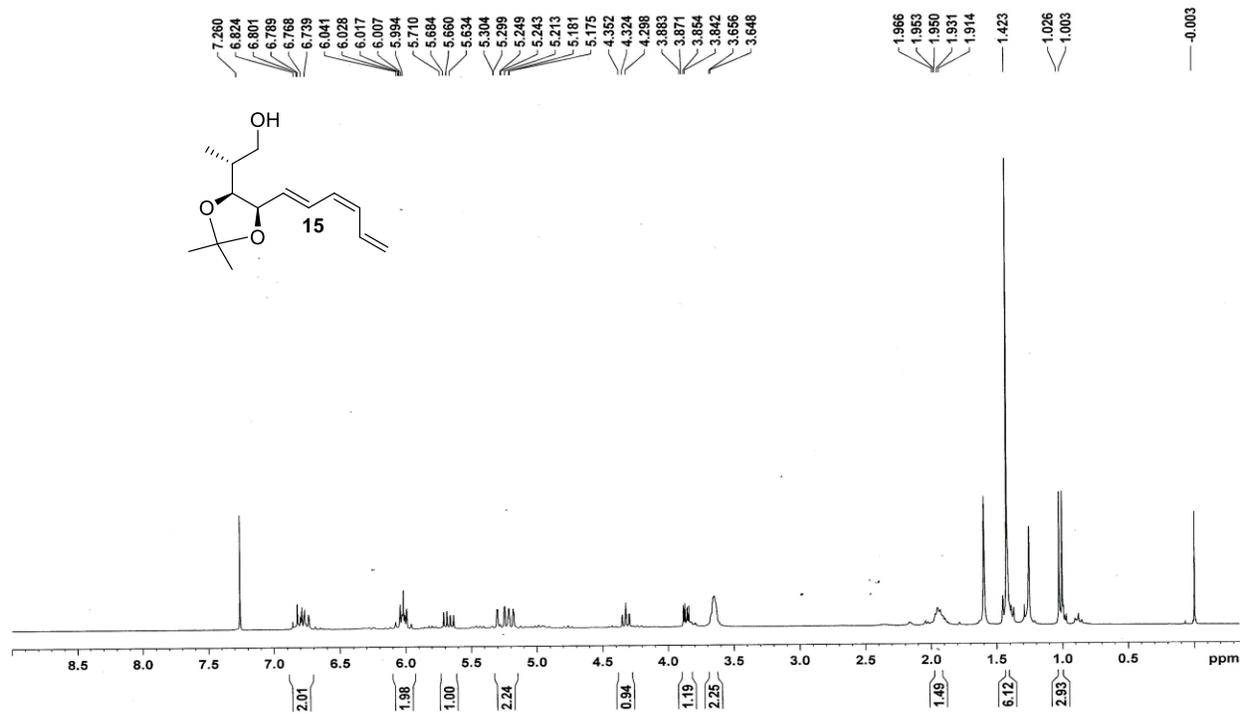
¹H NMR Spectra of 14 (300 MHz, CDCl₃):



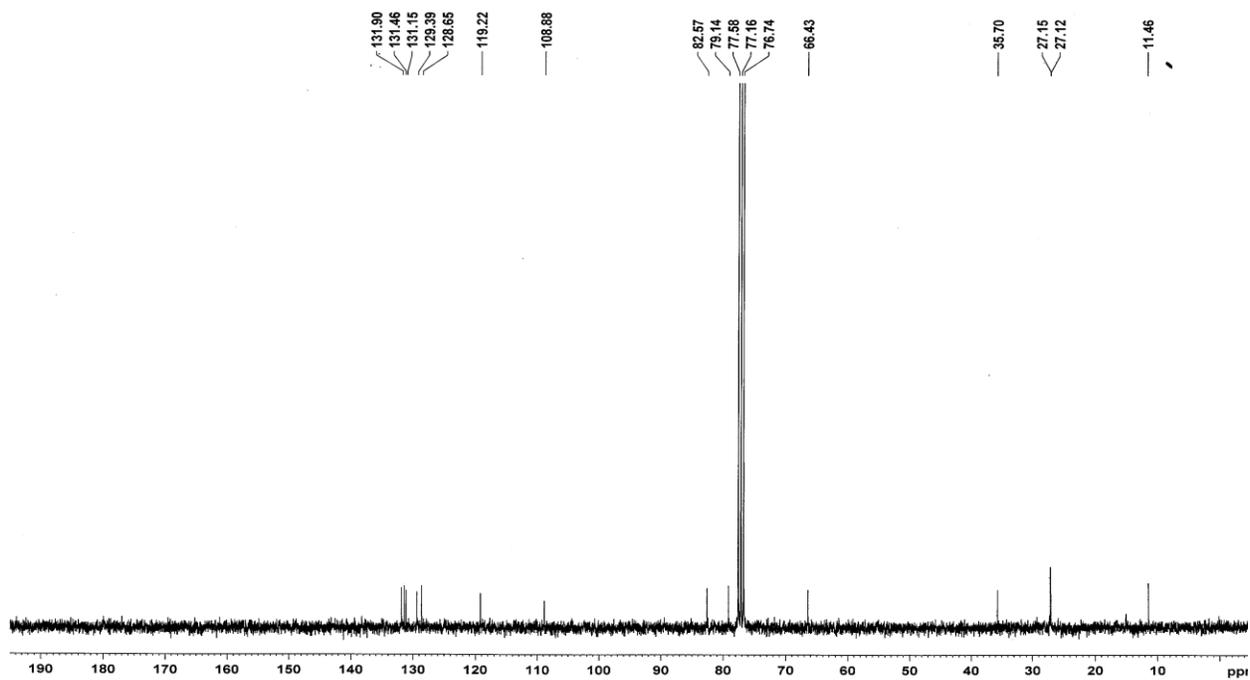
¹³C NMR Spectra of 14 (75 MHz, CDCl₃):



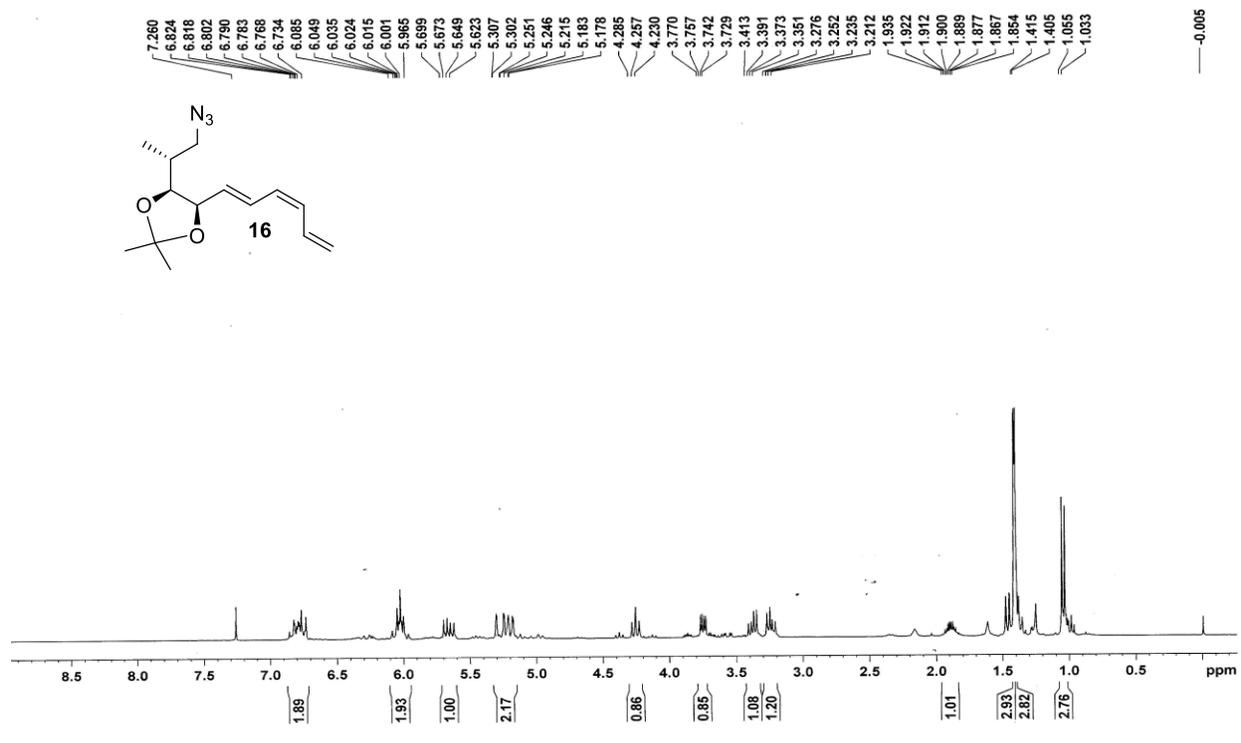
¹H NMR Spectra of 15 (300 MHz, CDCl₃):



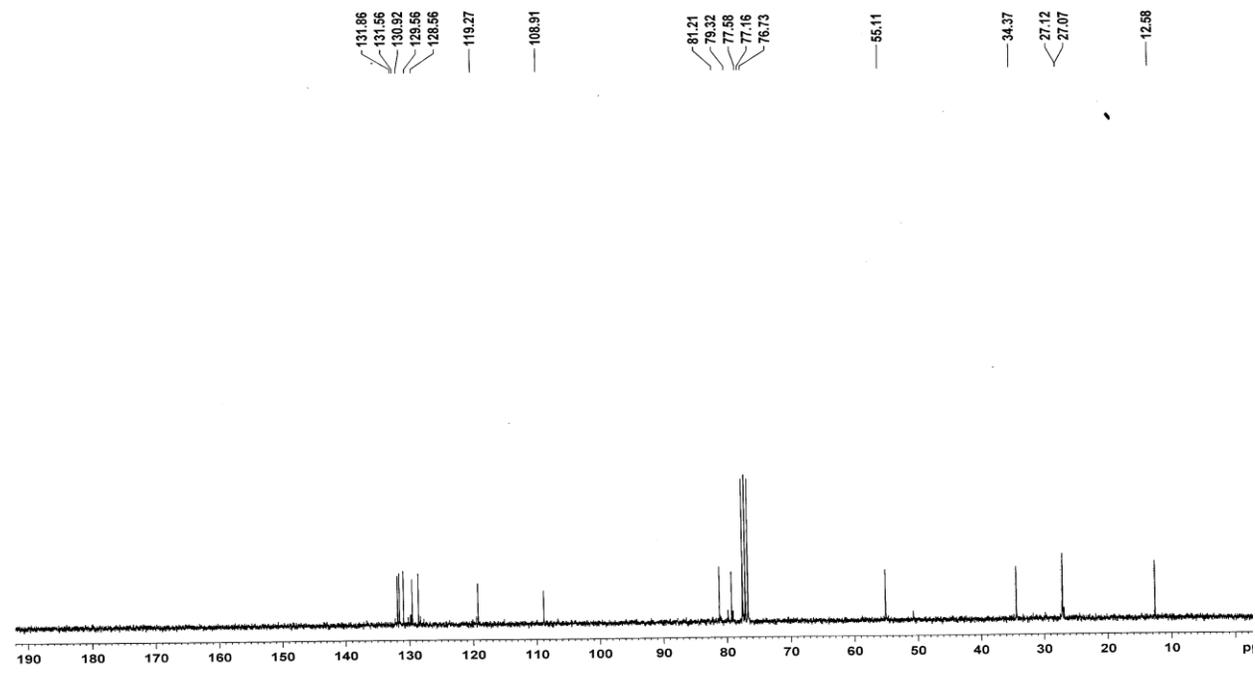
¹³C NMR Spectra of 15 (75 MHz, CDCl₃):



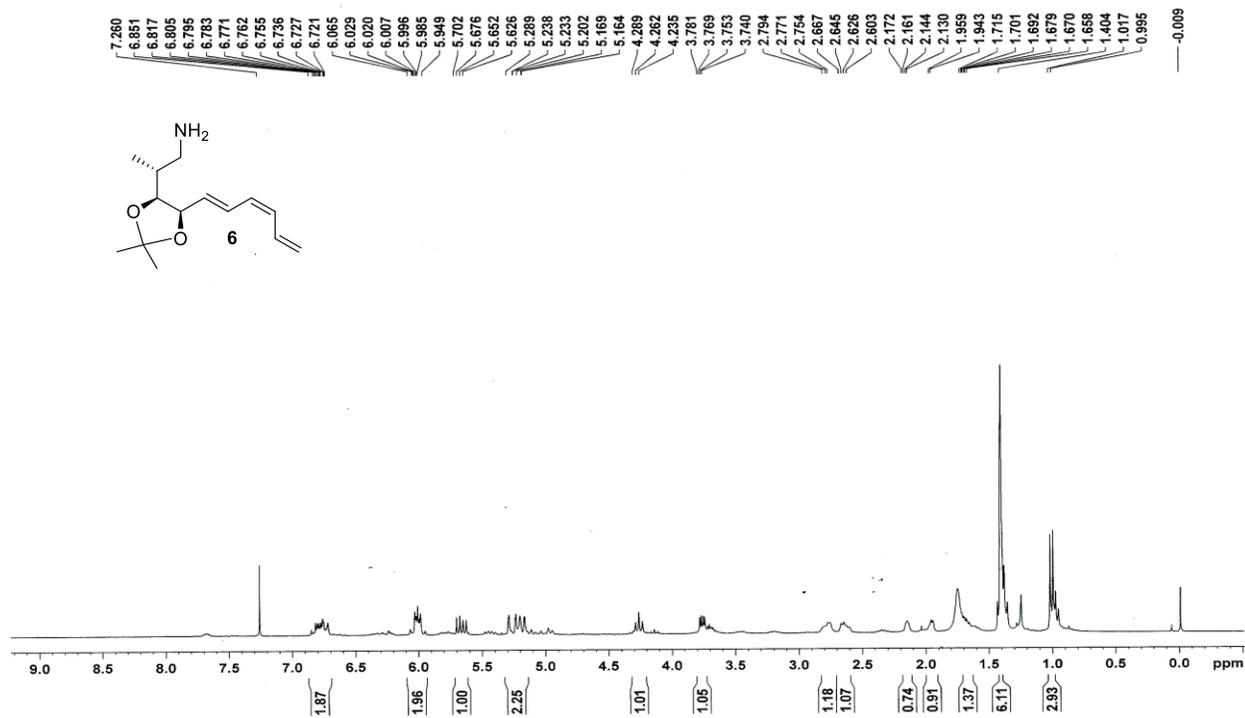
¹H NMR Spectra of 16 (75 MHz, CDCl₃):



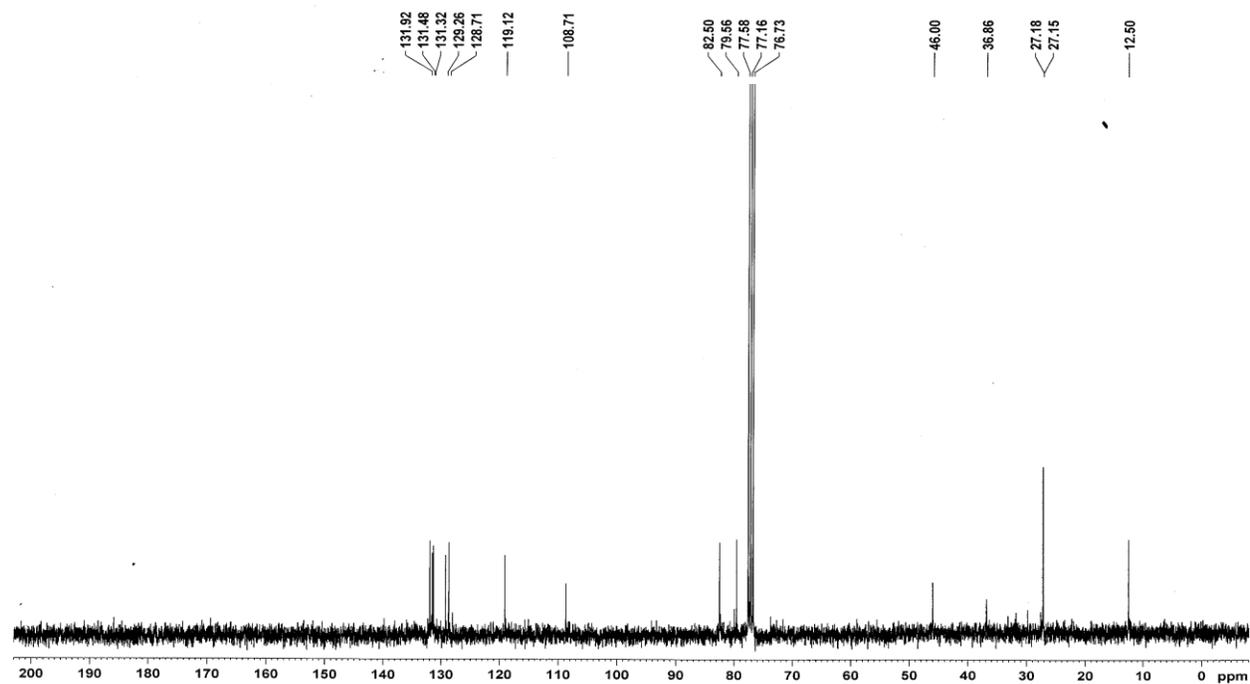
¹³C NMR Spectra of 16 (75 MHz, CDCl₃):



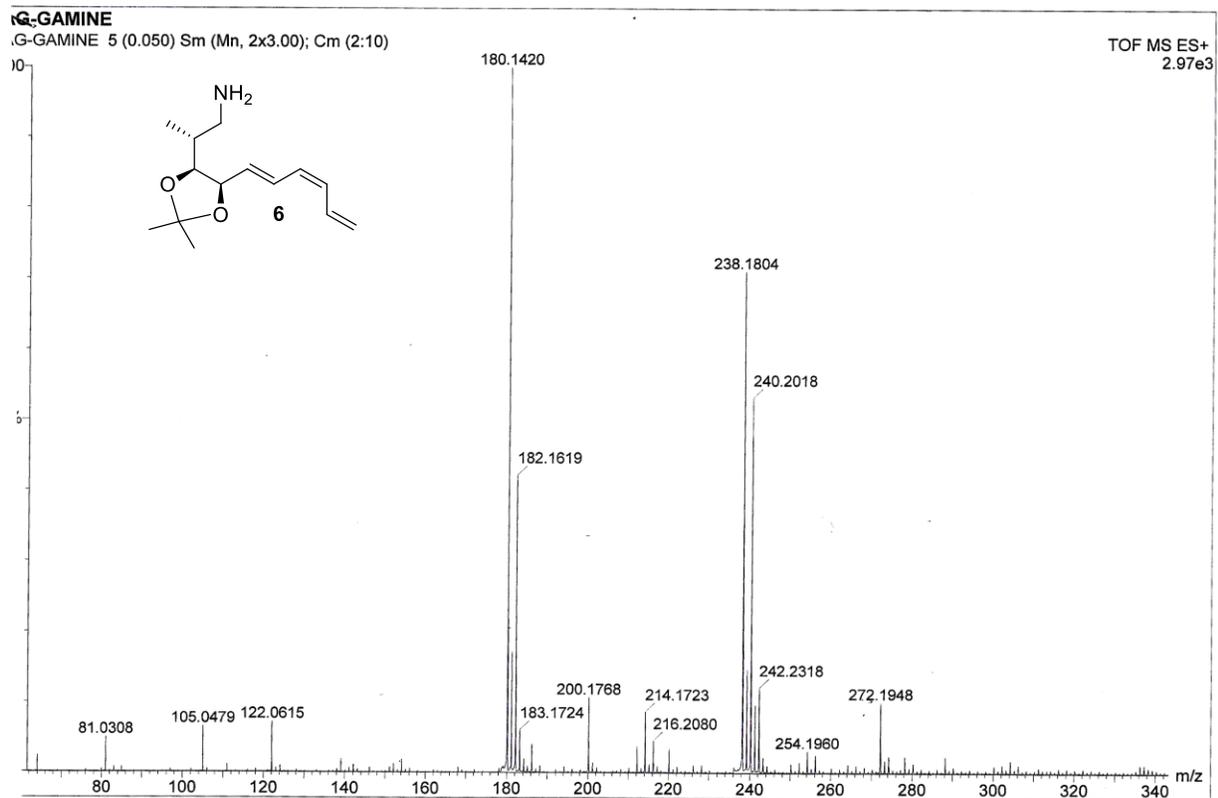
¹H NMR Spectra of 6 (300 MHz, CDCl₃):



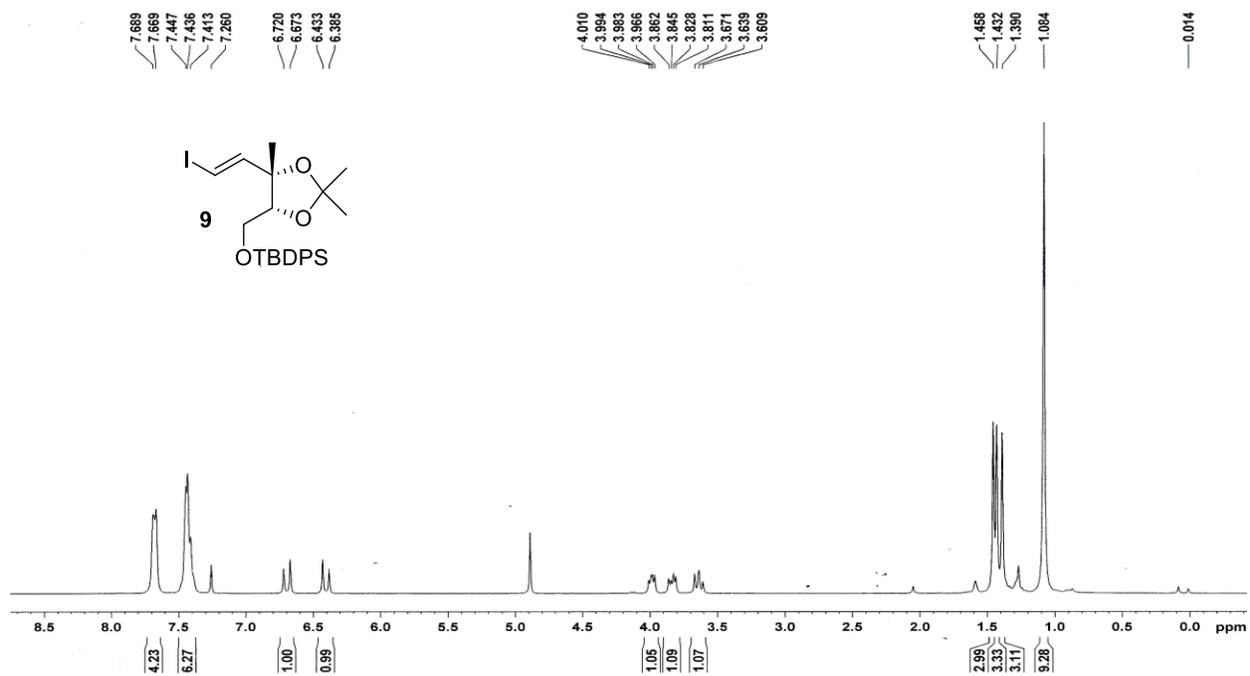
¹³C NMR Spectra of 6 (75 MHz, CDCl₃):



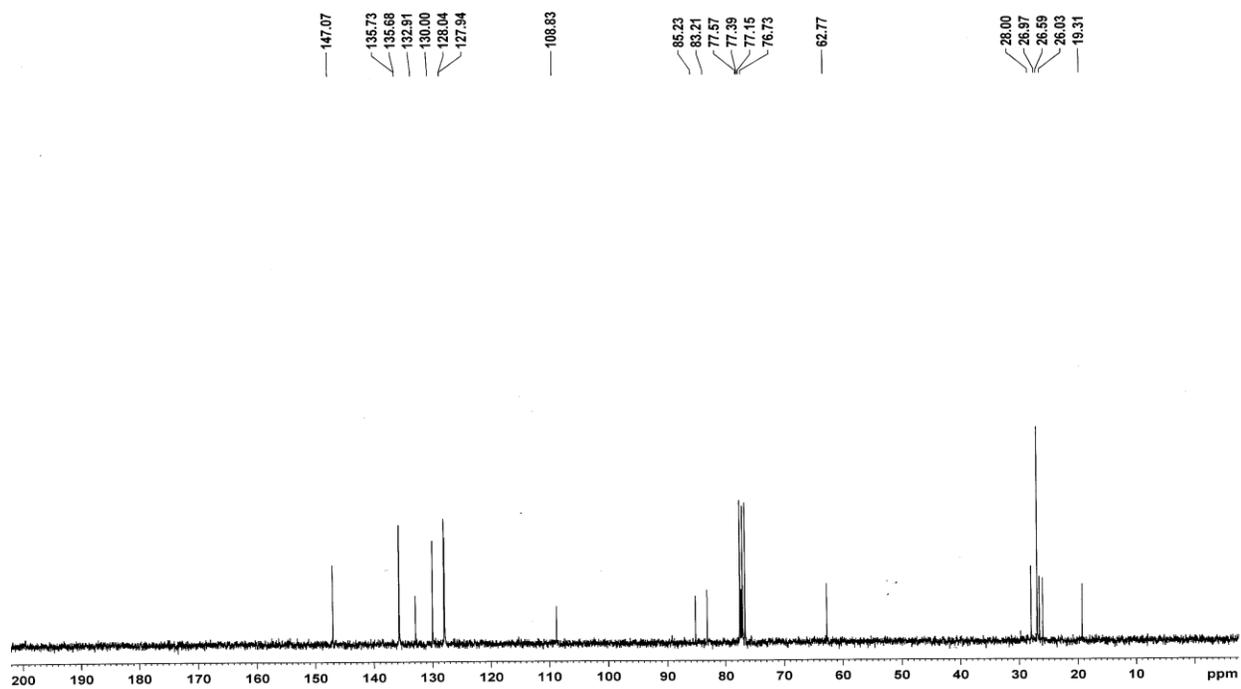
HRMS spectra of 6:



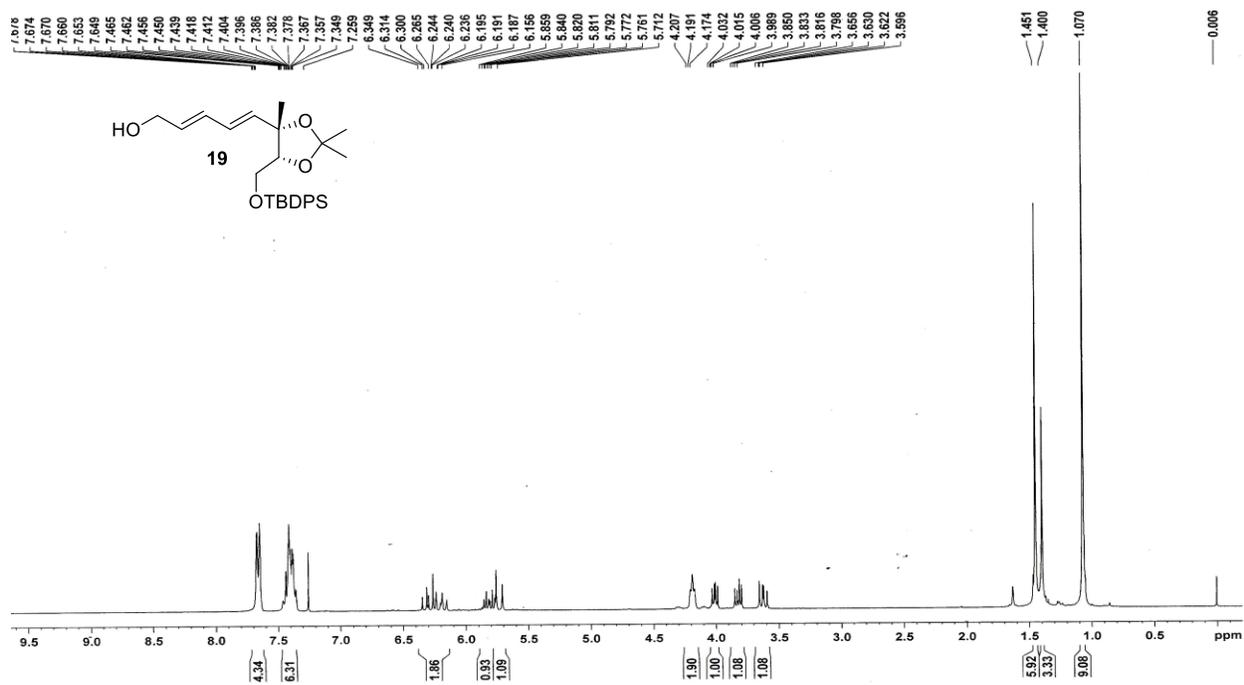
¹H NMR Spectra of 9 (300 MHz, CDCl₃):



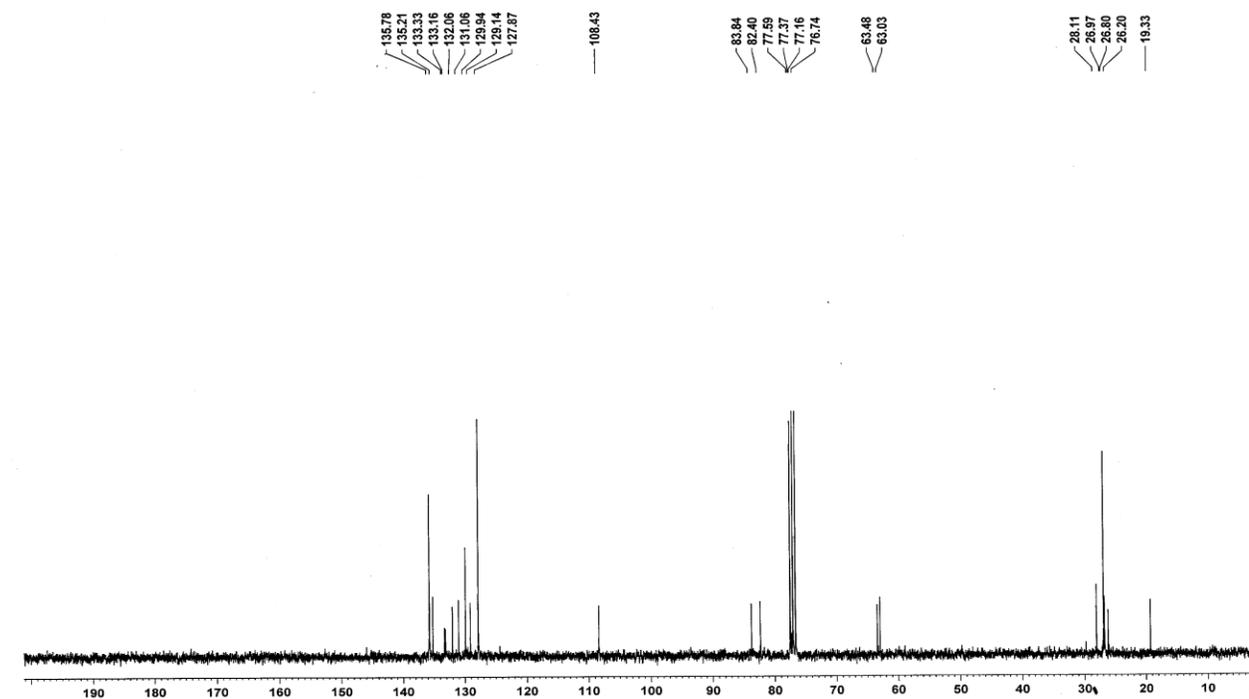
¹³C NMR Spectra of 9 (75 MHz, CDCl₃):



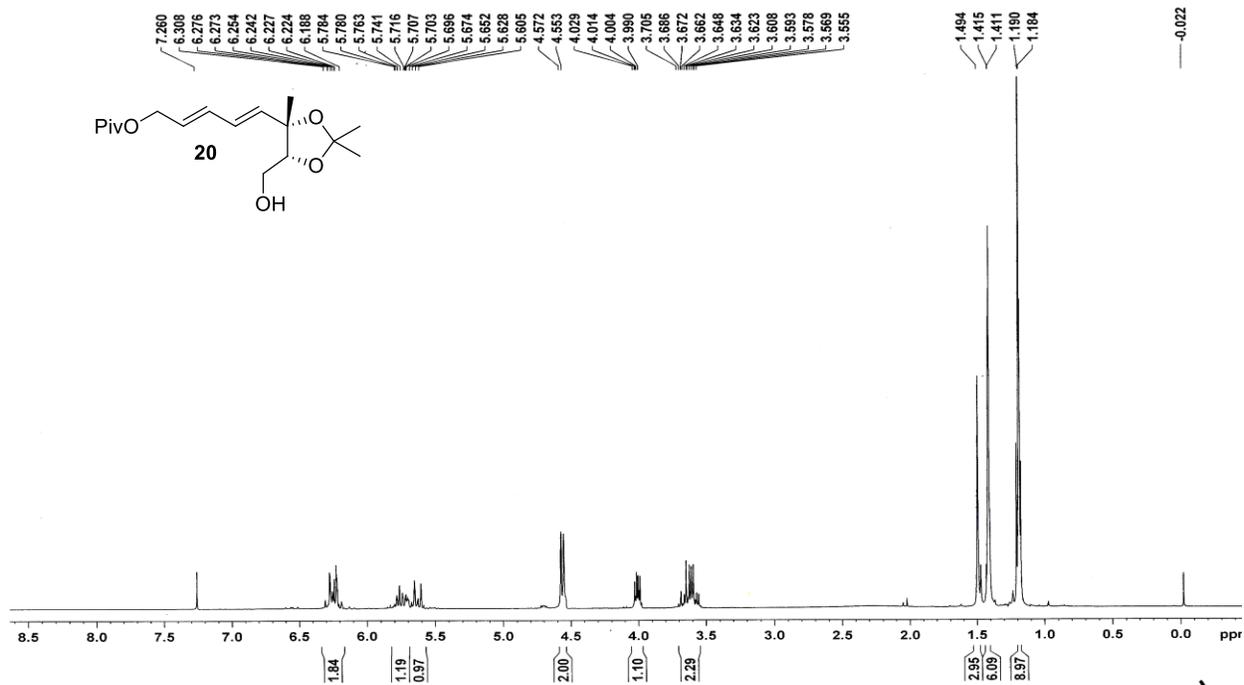
¹H NMR Spectra of 19 (300 MHz, CDCl₃):



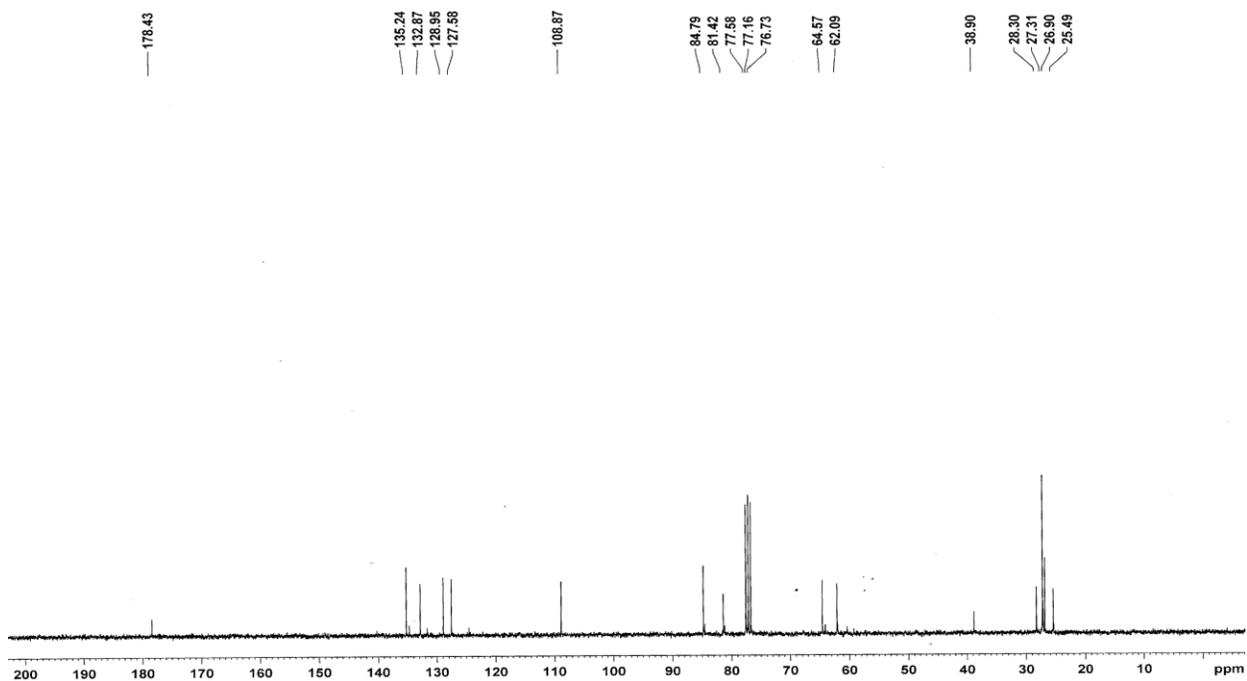
¹³C NMR Spectra of 19 (75 MHz, CDCl₃):



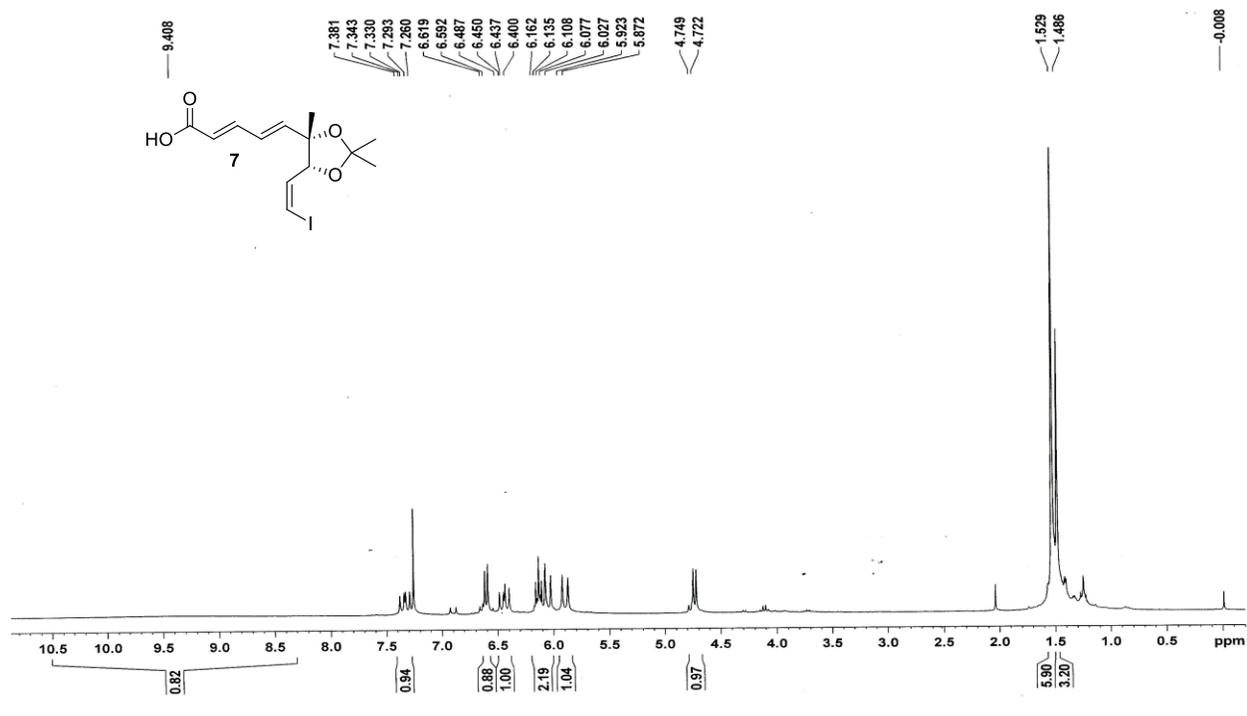
¹H NMR Spectra of 20 (300 MHz, CDCl₃):



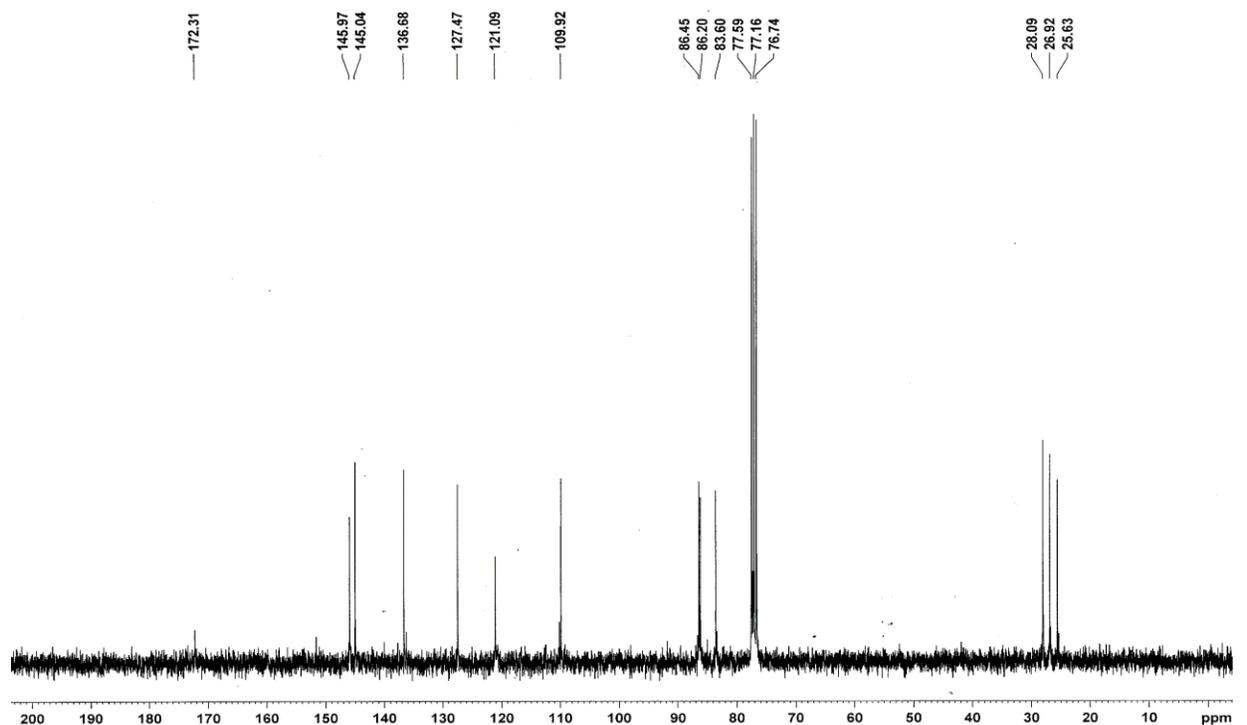
¹³C NMR Spectra of 20 (75 MHz, CDCl₃):



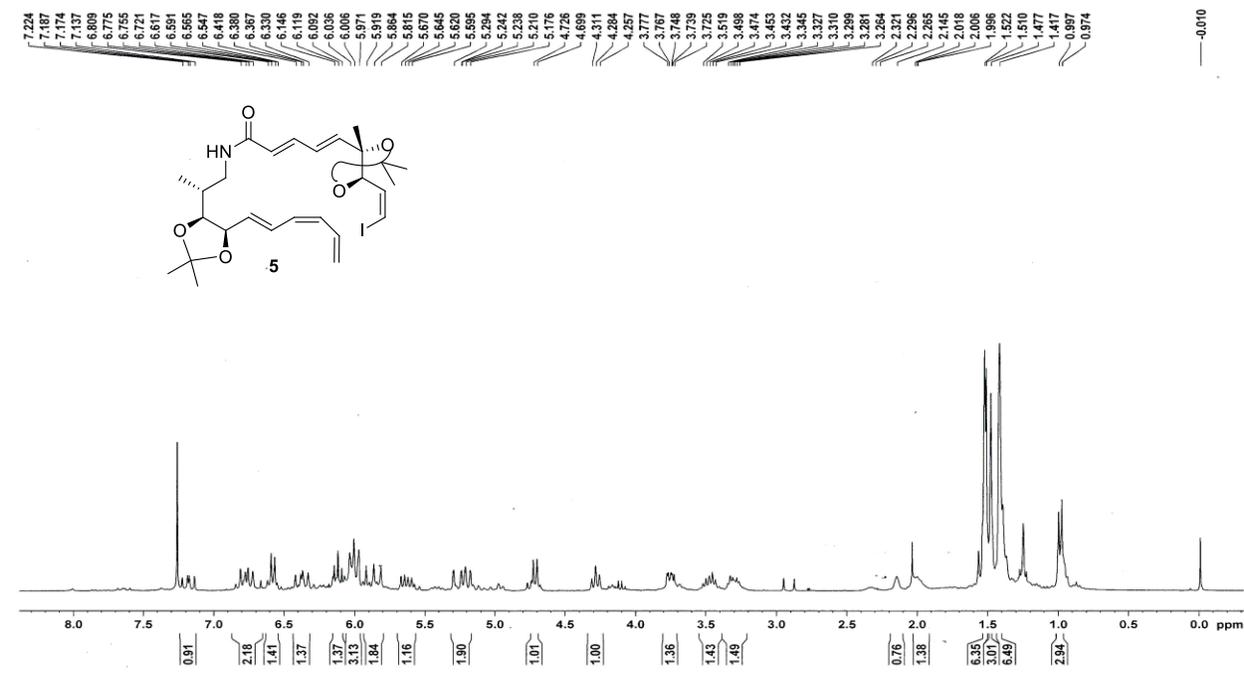
¹H NMR Spectra of 7 (300 MHz, CDCl₃):



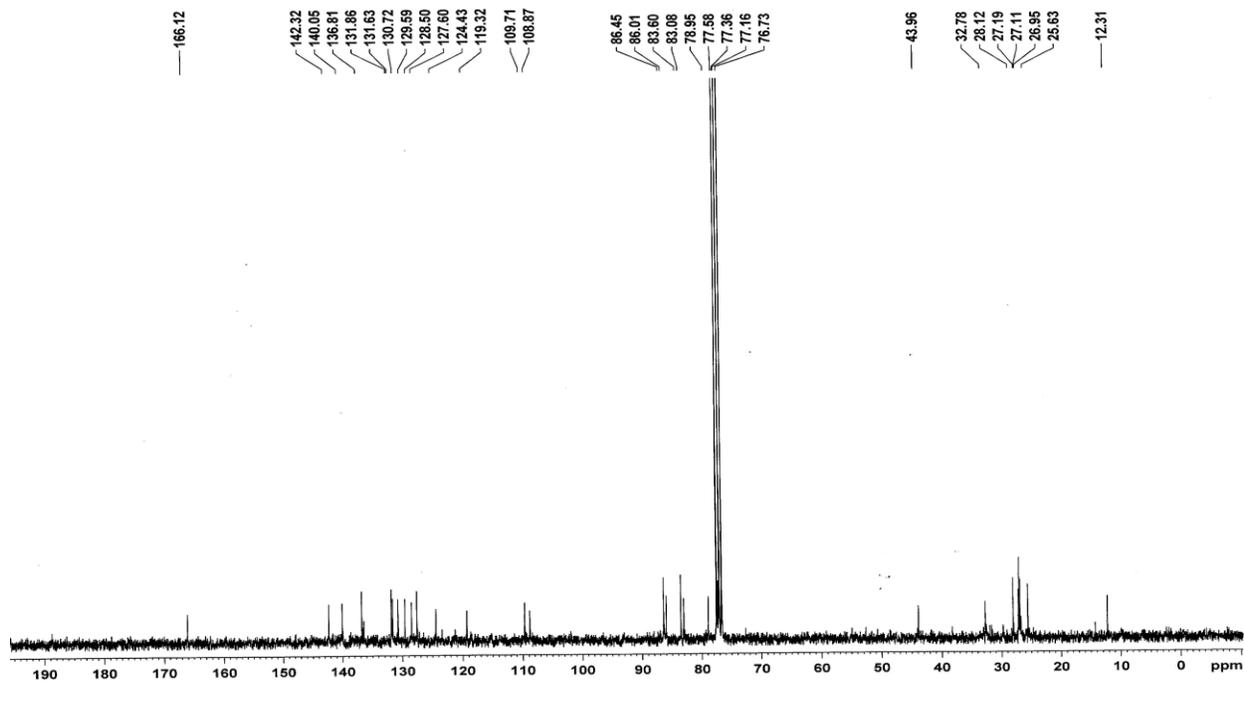
¹³C NMR Spectra of 7 (75 MHz, CDCl₃):



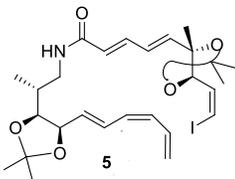
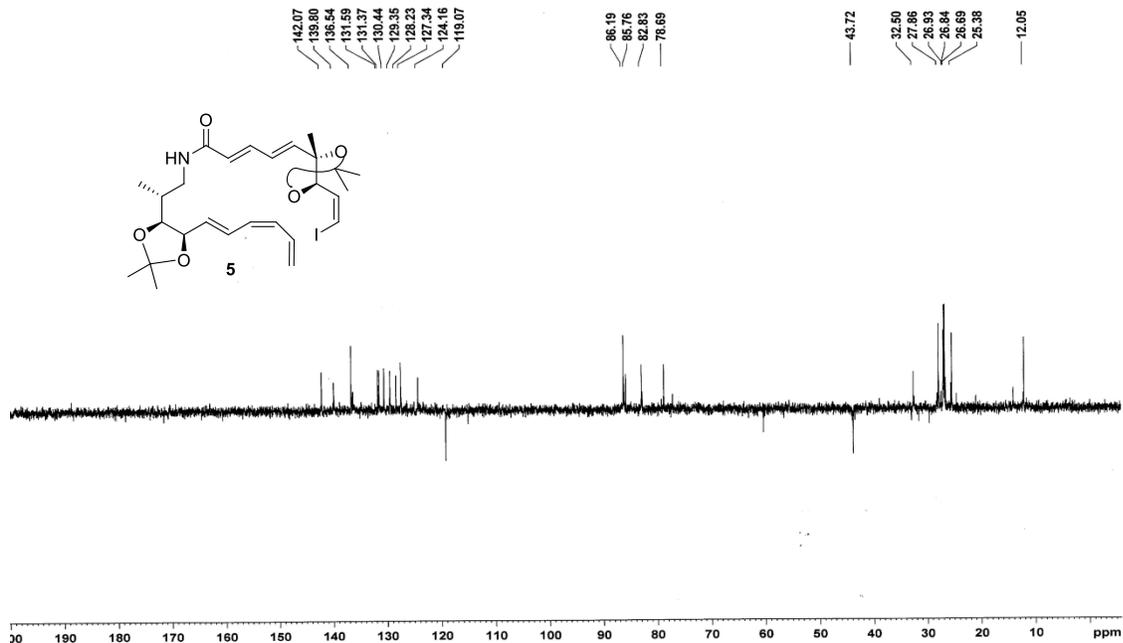
¹H NMR Spectra of 5 (300 MHz, CDCl₃):



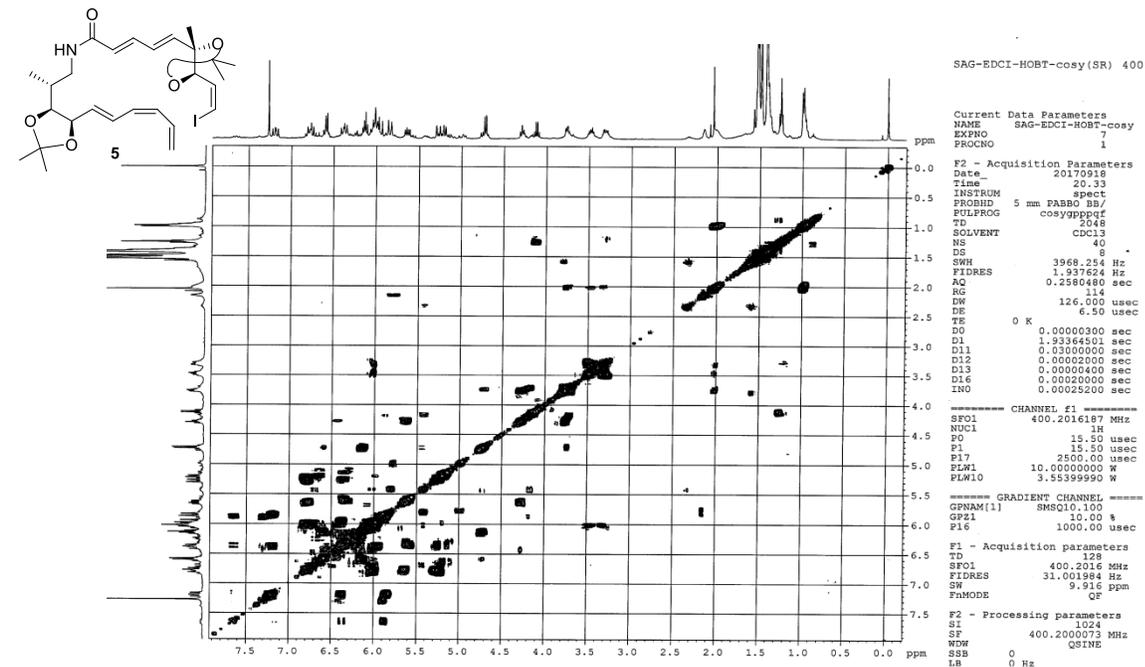
¹³C NMR Spectra of 5 (75 MHz, CDCl₃):



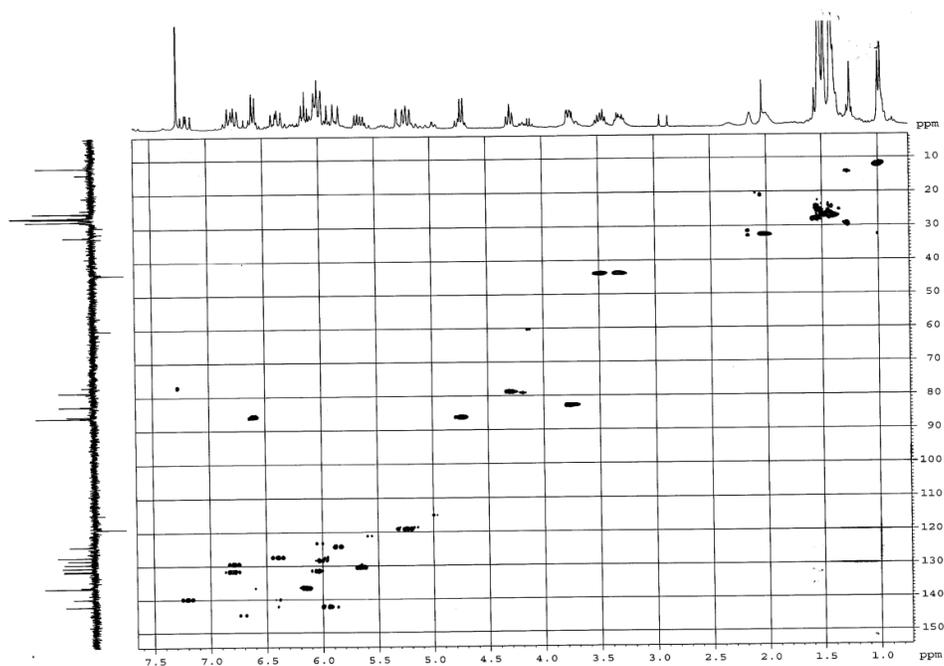
DEPT Spectra of 5 (75 MHz, CDCl₃):



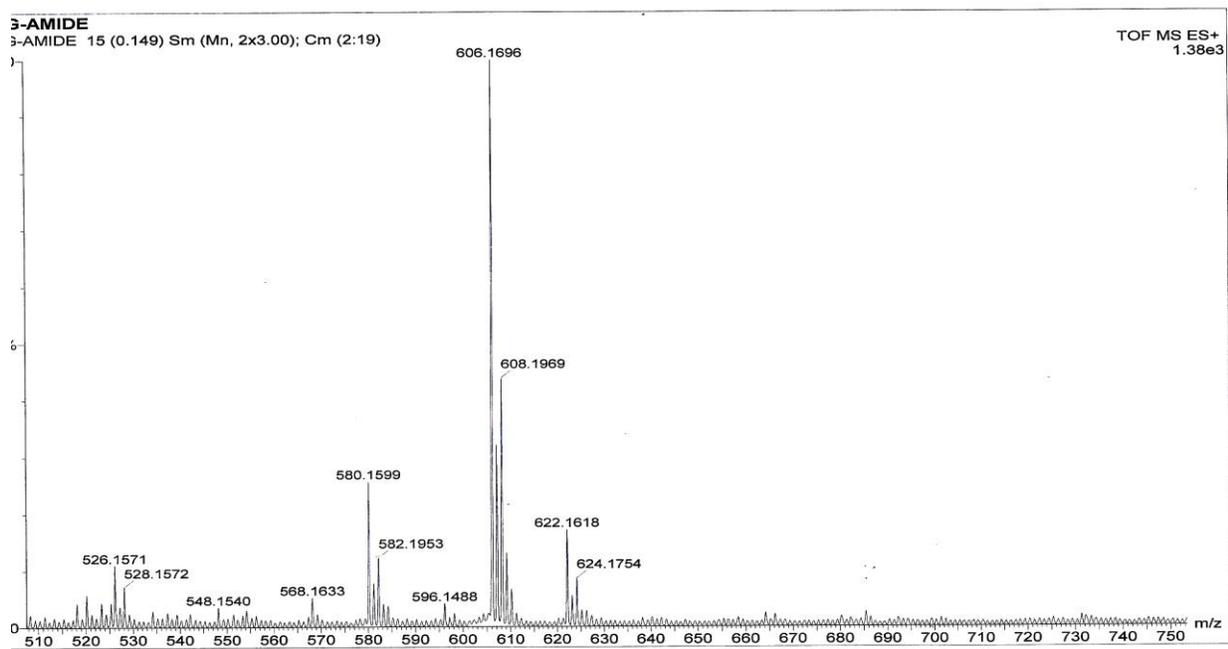
COSEY NMR of compound 5 (400 MHz, CDCl₃):



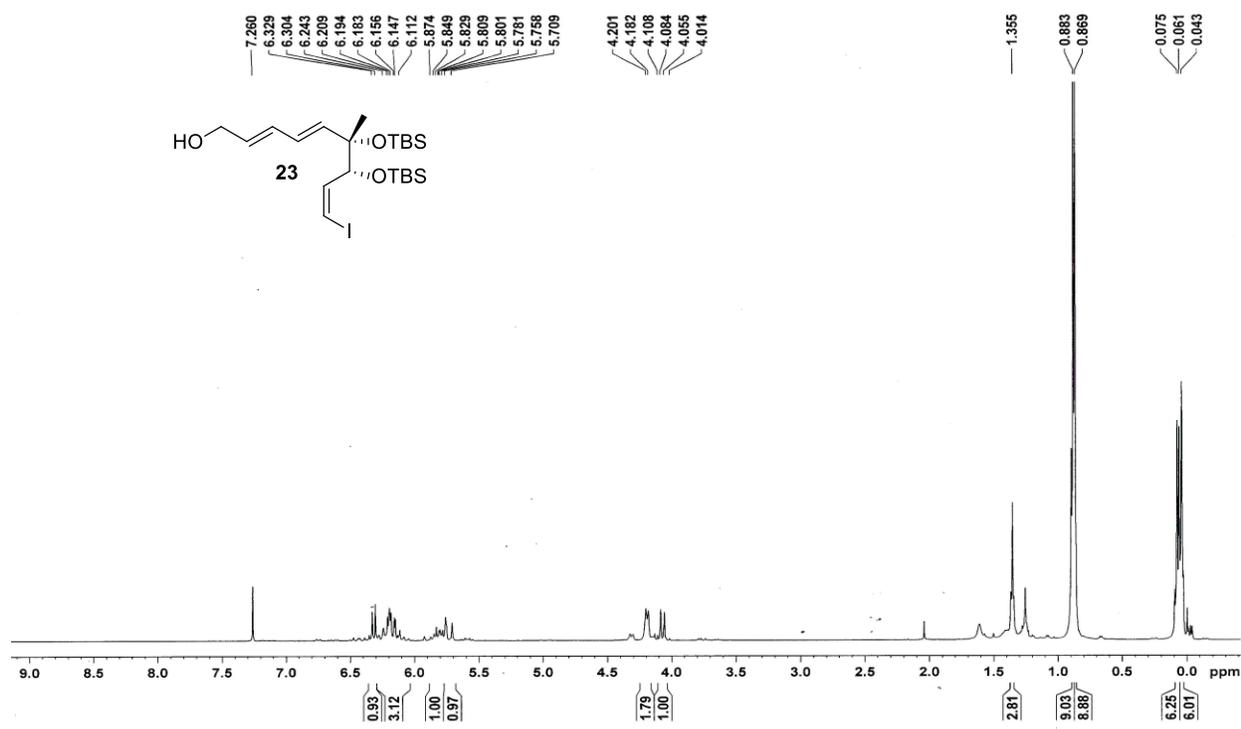
HSQC-NMR spectra of compound 5 (300 MHz, CDCl₃):



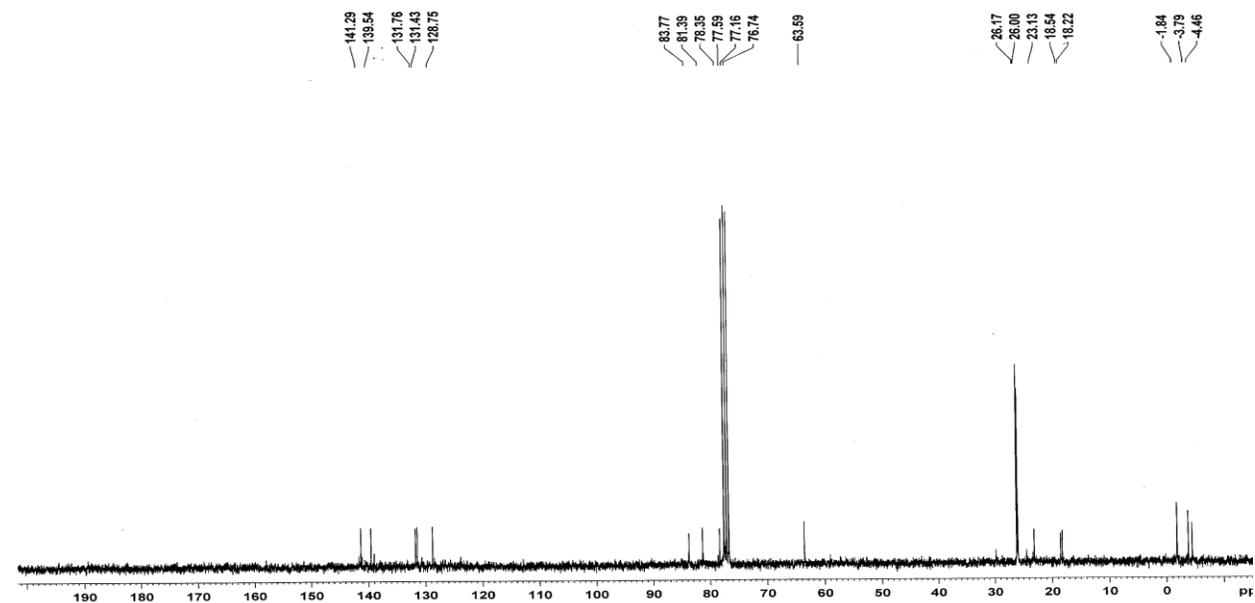
HRMS spectra of 5:



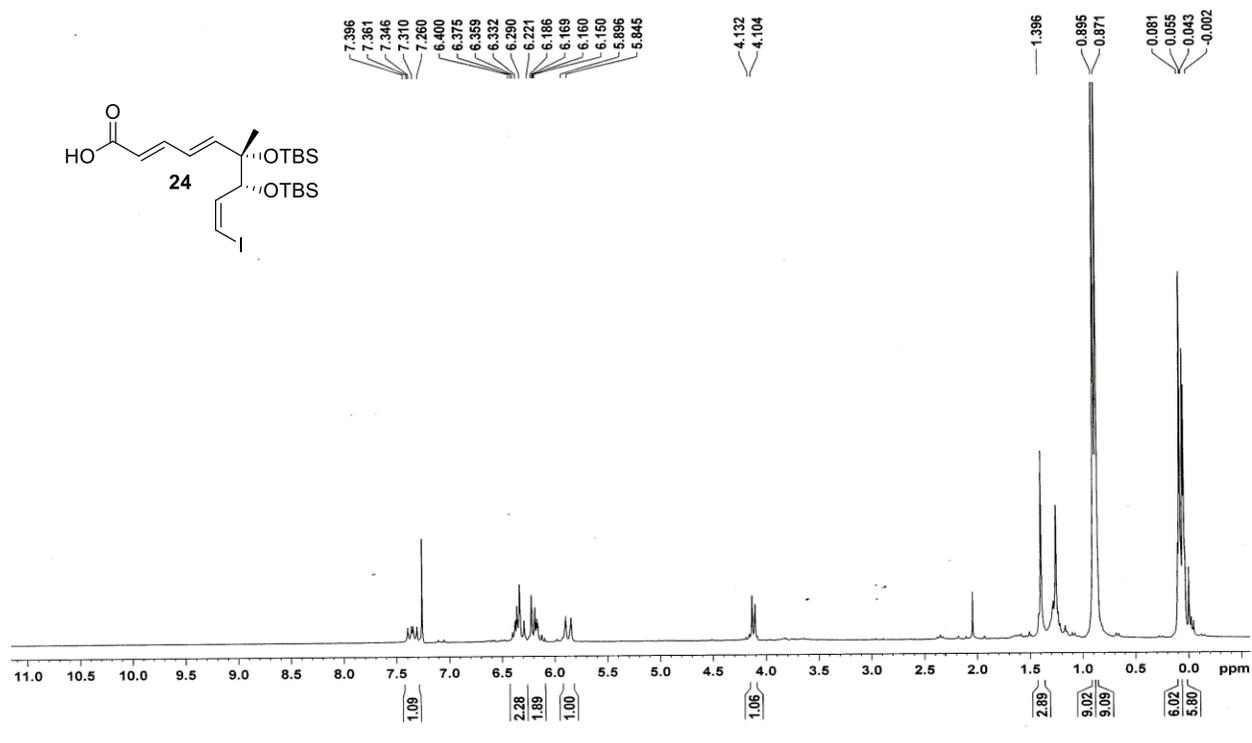
¹H NMR Spectra of 23 (75 MHz, CDCl₃):



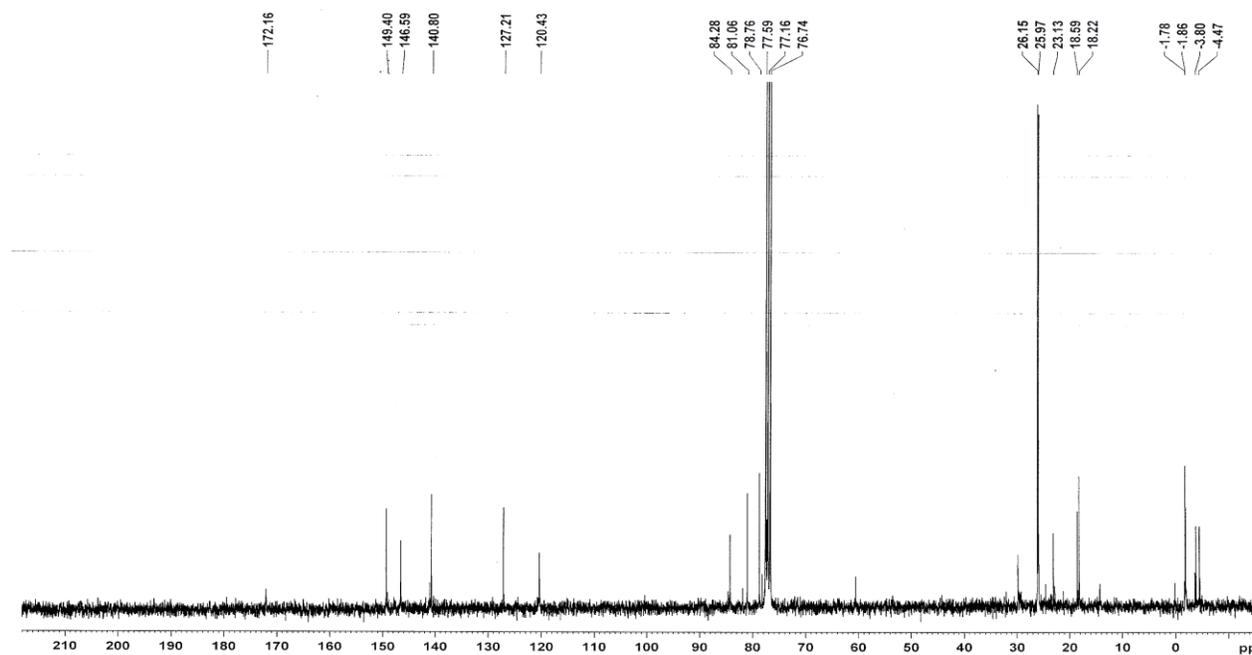
¹³C NMR Spectra of 23 (75 MHz, CDCl₃):



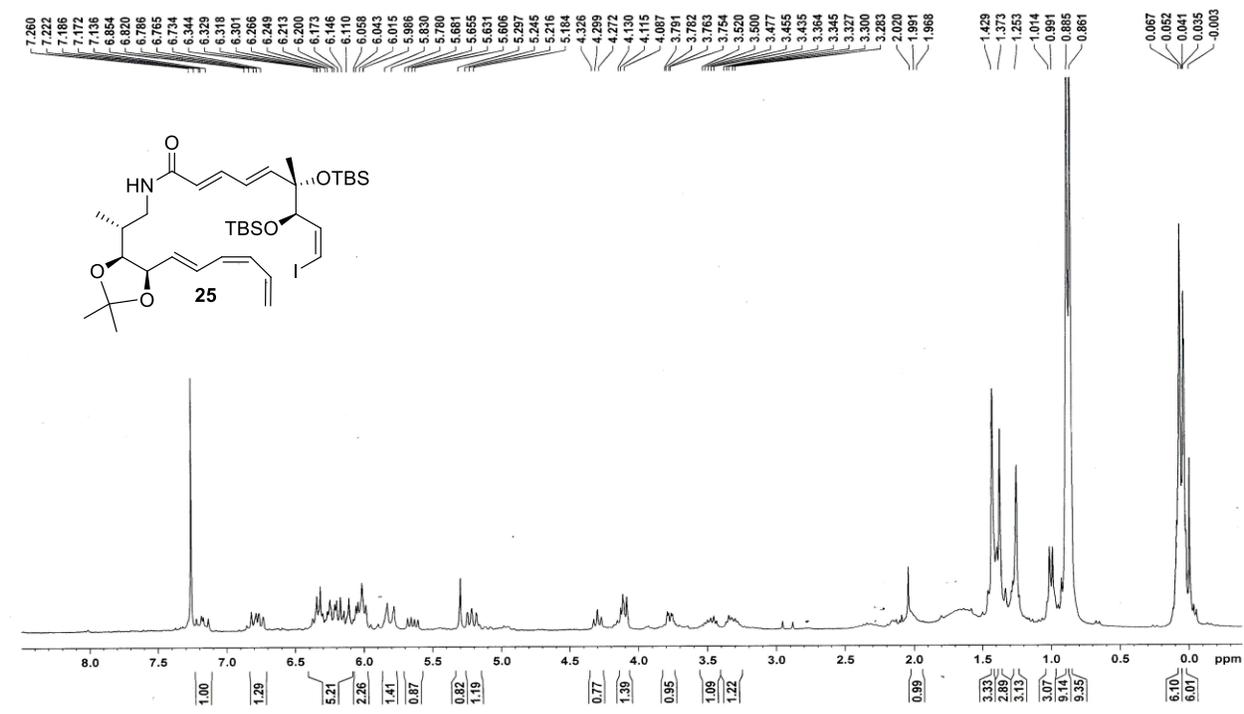
¹H NMR Spectra of 24 (300 MHz, CDCl₃):



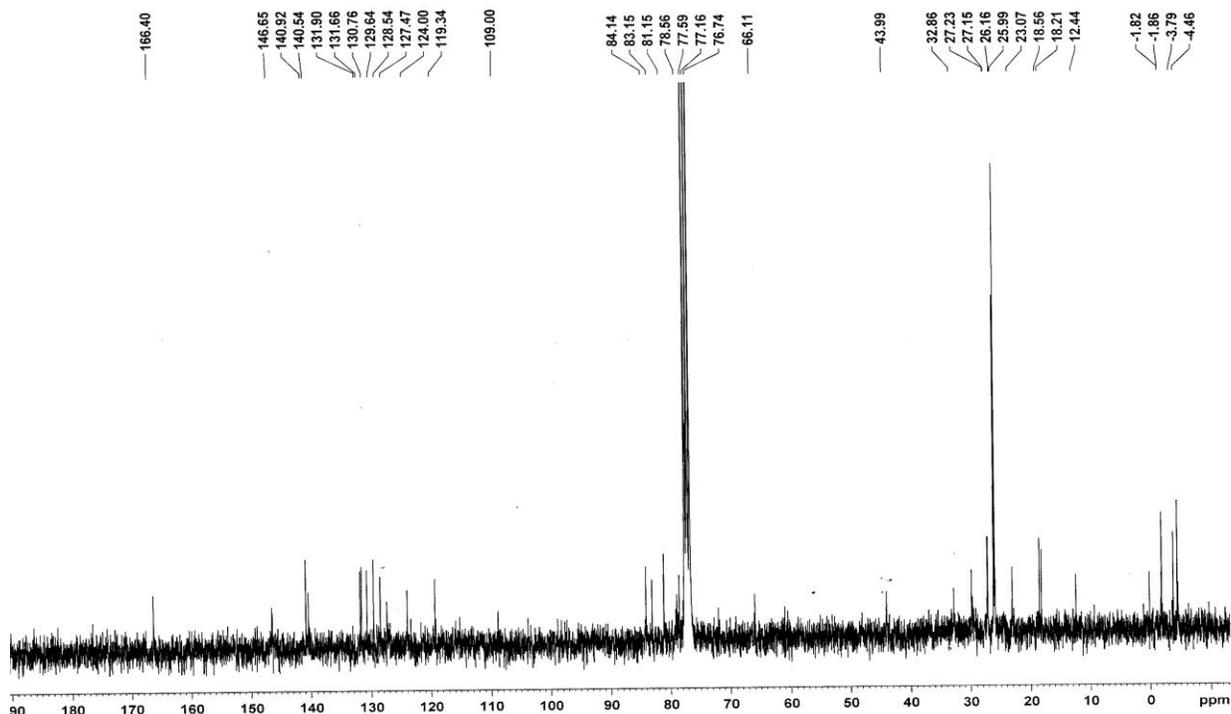
¹³C NMR Spectra of 24 (100 MHz, CDCl₃):



¹H NMR Spectra of 25 (300 MHz, CDCl₃):



¹³C NMR Spectra of 25 (75 MHz, CDCl₃):



HRMS spectra of 25:

SAG-AMIDE-TBS 9 (0.169) Sm (SG, 2x3.00); Cm (1:9)

TOF MS ES+
5.00e4

