Supporting Information for

An Annulation Reaction for the Synthesis of Cross-Conjugated Triene-containing Hydroindanes from Acyclic Precursors

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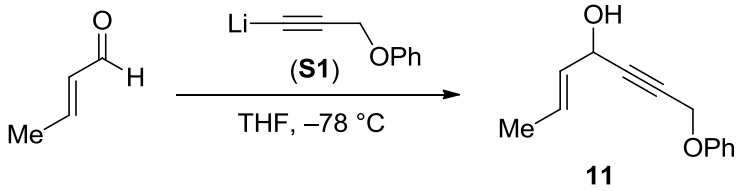
1. Materials and Methods

All reactions were conducted in flame-dried glassware under a nitrogen atmosphere with dry solvents, unless otherwise noted. All reagents and starting materials were purchased from commercial sources and used as supplied, unless otherwise indicated. Anhydrous tetrahydrofuran (THF) and toluene (PhMe) were obtained by distillation over sodium and benzophenone. Anhydrous dichloromethane (CH_2Cl_2) was purchased from Aldrich and was thoroughly degassed before use. Titanium isopropoxide ($Ti(O\textit{i}\text{-}Pr)_4$) was distilled before use. Solutions of *n*-BuLi were purchased from Aldrich and titrated against *N*-benzylbenzamide. Yields refer to chromatographically and spectroscopically (^{1}H NMR) homogeneous materials, unless otherwise stated. Flash column chromatography was performed on the Biotage® Automated Liquid Chromatography System Isolera One® using Biotage® SNAP KP-Sil 10-100 g silica gel cartridges. Thin layer chromatography (TLC) analyses were performed on EMD TLC Silica gel 60 F254 Glass Plates and the spots were visualized by UV-light (254 nm) or an aqueous solution of phosphomolybdic acid, ceric sulfate, and sulfuric acid. ^{1}H NMR data were recorded on a Varian Unity Plus 500 MHz NMR spectrometer, a Bruker Avance III 500 MHz spectrometer (TBI probe) and a Bruker Avance III 600 MHz spectrometer (BBFO probe) with calibration of spectra to $CDCl_3$ (7.26 ppm) or CD_2Cl_2 (5.32 ppm). ^{13}C NMR data were recorded at 125 MHz on a Varian Unity Plus 500 MHz NMR, a Bruker Avance III 500 MHz spectrometer (TBI probe) and at 150 MHz on a Bruker Avance III 600 MHz spectrometer (BBFO probe) with calibration to the central line of $CDCl_3$ (77.0 ppm) or CD_2Cl_2 (54.0 ppm). Two-dimensional NMR spectra, including COSY, HMQC, TOCSY and NOESY were recorded on a Varian Unity Plus 500 MHz NMR spectrometer, a Bruker Avance III 500 MHz spectrometer (TBI probe) and a Bruker Avance III 600 MHz spectrometer (BBFO probe). Infrared spectra were recorded on a JASCO FT/IRM4100 Fourier Transform Infrared Spectrometer. HRMS (ESI-TOF) analyses were performed at the Mass Spectrometry Laboratory of University of Illinois at Urbana-Champaign. All compounds purified by chromatography were sufficiently pure for use in further experiments, unless indicated otherwise.

2. Experimental Procedures

A. Synthesis of enyne substrates 15, 19, 25, 41, 31, 38

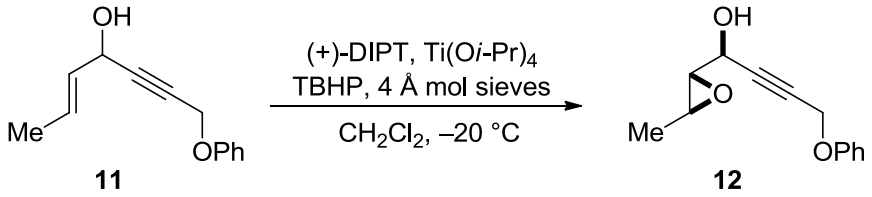


11

(±)-(*E*)-7-phenoxyhept-2-en-5-yn-4-ol (11). To a solution of phenyl propargyl ether[1] (4.55 g, 34.4 mmol) in anhydrous THF (33.0 mL) at –78 ℃ was added *n*-BuLi (2.48 M in hexanes, 12.8 mL, 31.8 mmol). After stirring at –78 ℃ for 30 min, a solution of crotonaldehyde (2.2 mL, 26.5 mmol) in anhydrous THF (20.0 mL) was added via syringe. After additional 1.5 h at –78 ℃, the reaction mixture was quenched with saturated aqueous NH_4Cl. The THF was removed *in vacuo*, and the resulting mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (silica gel, gradient 90:10 to 75:25 hexanes:EtOAc) to afford the alcohol **11** (5.15 g, 96%) as a pale yellow oil.

Data for **11**: R_f = 0.30 (75:25 hexanes:EtOAc); IR (thin film) 3376, 3032, 2916, 1857, 2224, 1991, 1673, 1644,1 1598, 1495, 1447, 1376, 1215, 1032, 754, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32–7.28 (m, 2H), 7.01–6.96 (m, 3H), 5.86 (ddq, *J* = 15.2, 6.6, 1.2 Hz, 1H), 5.61 (ddq, *J* = 15.2, 6.2, 16 Hz, 1H), 4.87 (dd, *J* = 5.9, 5.9 Hz, 1H), 4.75 (d, *J* = 1.7 Hz, 2H), 1.83 (d, *J* = 5.9 Hz, 1H), 1.72 (ddd, *J* = 6.6, 1.6, 1.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.7, 129.8, 129.6 (2C), 129.2, 121.6, 115.0 (2C), 86.9, 80.8, 62.8, 56.2, 17.6. HRMS calculated for $C_{13}H_{14}O_2Na$ [M+Na^+] 225.0891, found 225.0890.

[1] Carvalho, J. F. S.; Louvel, J.; Doornbos, M. L. J.; Klaasse, E.; Yu, Z.; Brussee, J.; IJzerman A. P. *J. Med. Chem.* **2013**, *56*, 2828–2840.



(*S*)-1-((2*S*,3*S*)-3-methyloxiran-2-yl)-4-phenoxybut-2-yn-1-ol (12). To a solution of alcohol **11** (5.13 g, 25.4 mmol) and (+)-diisopropyl L-tartrate ((+)-DIPT, 0.89 g, 3.80 mmol) in anhydrous CH_2Cl_2 (101.5 mL) was added activated 4 Å molecular sieves (1.54 g) at rt. The reaction mixture was cooled to –20 ℃ and Ti(O*i*-Pr)$_4$ (0.75 mL, 2.54 mmol) was added. After 30 min at –20 ℃, *tert*-butyl hydroperoxide (TBHP, 5.5 M in decane, 3.23 mL, 17.76 mmol) was added dropwise. The cloudy reaction mixture was stirred at –20 ℃ for another 12 h and was quenched at the same temperature with a freshly prepared solution of $FeSO_4$•$7H_2O$ (8.37 g, 30.1 mmol) and anhydrous citric acid (2.75 g, 14.3 mmol) in water (25.4 mL). This mixture was stirred without cooling for 30 min until two phases appeared. The mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (twice) and the combined organic layers were concentrated to approximately the original reaction volume (100mL). After that, a 30% NaOH in brine solution[2] (25 mL) was added and the resulting mixture was stirred vigorously at rt for 1h. Upon addition of water and separation of layers, the aqueous layer was extracted with Et_2O (twice). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated to a small volume. Finally this solution was filtered through Celite with Et_2O and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (silica gel, gradient 94:6 to 34:66 hexanes:EtOAc) to afford epoxide **12** (2.77 g, 50%, 90% *ee* by Mosher's ester[3]) as a yellow oil.

Data for **12**: R_f = 0.25 (65:35 hexanes:EtOAc); $[\alpha]_D^{23}$ = +7.7 ° (*c* 0.33, $CHCl_3$); IR (thin film) 3412, 3.63, 2972, 2925, 2867, 1598, 1495, 1378, 1215, 1032, 1014, 755, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32–7.28 (m, 2H), 7.01–6.94 (m, 3H), 4.72 (d, *J* = 1.7 Hz, 2H), 4.62–4.59 (m, 1H), 3.12 (dddd, *J* = 5.3, 5.3, 5.3, 2.2 Hz, 1H), 2.96 (dd, *J* = 3.1, 2.3 Hz, 1H), 2.61 (d, *J* = 5.4 Hz, 1H), 1.31 (d, *J* = 5.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 129.6 (2C), 121.7, 115.1 (2C), 84.0, 81,6, 61.2, 60.5, 58.1, 52.5, 17.0; HRMS (ESI-TOF) calculated for $C_{13}H_{14}O_3Na$ [M+Na^+] 241.0841, found 241.0841.

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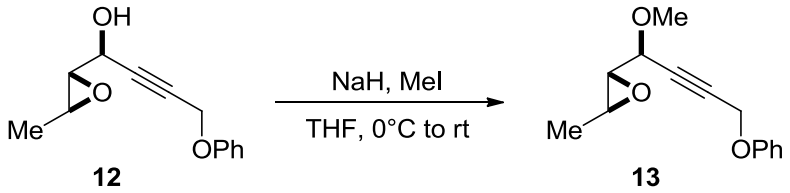
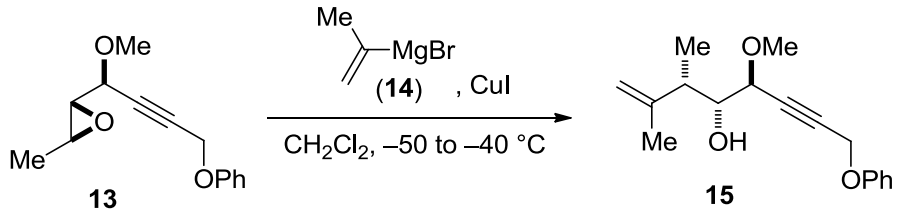
[2] Gao, Y.; Klunder, J. M.; Hanson, R. M.; Masamune, H.; Ko, S.Y.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765–5780. 100 mL of this solution was prepared by dissolving 5 g of NaCl and 30 g of NaOH in 90 mL of water. See reference 2 for more details regarding Sharpless asymmetric epoxidation and kinetic resolution reactions.

[3] Hoye, T. R.; Jeffrey, C. S.; Shao, F. *Nature Protocols* **2007**, *2*, 2451–2458.



(2*R*,3*S*)-2-((*S*)-1-methoxy-4-phenoxybut-2-yn-1-yl)-3-methyloxirane (13). To a solution of epoxy alcohol **12** (1.68 g, 7.70 mmol) in anhydrous THF (38.5 mL) at 0 ℃ was added NaH (60% dispersion in mineral oil, 0.62 g, 15.41 mmol). After 20 min at 0 ℃, MeI (1.44 mL, 23.11 mmol) was added. The reaction mixture was allowed to warm to rt and stirred for 1.5 h. Upon cooling to 0 ℃, saturated aqueous NH_4Cl was added dropwise to quench the reaction, and THF was carefully removed *in vacuo*. The mixture was then diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice) and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel, gradient 95:5 to 60:40 hexanes:EtOAc) to give methyl ether **13** (1.69 g, 94%) as a yellow oil.

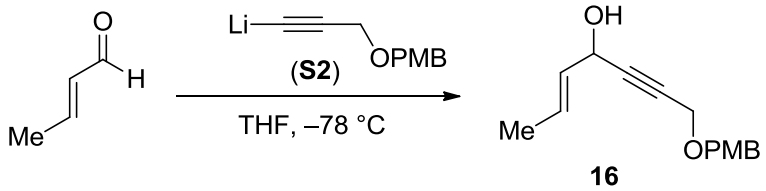
Data for **13**: R_f = 0.31 (80:20 hexanes:EtOAc); $[\alpha]_D^{25}$ = +21.6 ° (*c* 0.31, $CHCl_3$); IR (thin film) 2991, 2930, 2825, 1732, 1597, 1495, 1457, 1378, 1215, 1080, 871, 755, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.33–7.28 (m, 2H), 7.01-6.96 (m, 3H), 4.76 (d, *J* = 1.6 Hz, 2H), 4.15 (ddd, *J* = 3.6, 1.6, 1.6 Hz, 1H), 3.77 (s, 3H), 3.06 (dddd, *J* = 5.3, 5.3, 5.3, 2.1 Hz, 1H), 2.92 (dd, *J* = 3.6, 2.1 Hz, 1H), 1.32 (d, *J* = 5.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.4, 129.3 (2C), 121.4, 114.9 (2C), 82.5, 82.1, 70.6, 59.1, 56.6, 55.7, 52.0, 16.9; HRMS (ESI-TOF) calculated for $C_{14}H_{16}O_3Na$ [M+Na^+] 255.0997, found 255.0995.



(3*S*,4*R*,5*S*)-5-methoxy-2,3-dimethyl-8-phenoxyoct-1-en-6-yn-4-ol (15). To a stirred suspension of CuI (128 mg, 0.67 mmol) in anhydrous THF (4.5 mL) at –50 ℃ was added isopropenylmagnesium bromide (0.5 M in THF, 17.9 mL, 8.95 mmol) dropwise. The resulting cloudy yellow mixture was stirred between –50 and –40 ℃ for 30 min and a solution of epoxide **13** (520 mg, 2.24 mmol) in anhydrous THF (9.0 mL) was added via syringe at –40 ℃. The

reaction mixture was stirred at the same temperature for 4.5 h and quenched with saturated aqueous NH_4Cl. Upon removing THF *in vacuo*, the mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (silica gel, gradient 95:5 to 60:40 hexanes:EtOAc) provided **15** (215 mg, 35%) as a colorless oil.

Data for **15**: R_f = 0.25 (78:22 hexanes:EtOAc); $[\alpha]_D^{23}$ = +23.7 ° (*c* 0.30, $CHCl_3$); IR (thin film) 3479, 3072, 2965, 2934, 2877, 2824, 1645, 1599, 1496, 1304, 1215, 1102, 1033, 1014, 896, 754, 691 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32–7.28 (m, 2H), 7.00–6.97 (m, 3H), 4.79 (d, *J* = 1.6 Hz, 2H), 4.75–4.73 (m, 1H), 4.73–4.72 (m, 1H), 4.00 (ddd, *J* = 3.3, 1.6, 1.6 Hz, 1H), 3.67 (ddd, *J* = 9.0, 2.4, 2.4 Hz, 1H), 3.39 (s, 3H), 2.38 (dq, *J* = 8.8, 6.9 Hz, 1H), 2.10 (d, *J* = 2.6 Hz, 1H), 1.66 (dd, *J* = 1.4, 0.8 Hz, 3H), 1.10 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.6, 146.7, 129.6 (2C), 121.6, 115.2 (2C), 112.5, 83.2, 82.9, 74.8, 74.1, 57.0, 56.1, 43.6, 19.9. 15.8; HRMS (ESI-TOF) calculated for $C_{17}H_{22}O_3Na$ [M+Na^+] 297.1467, found 297.1463.



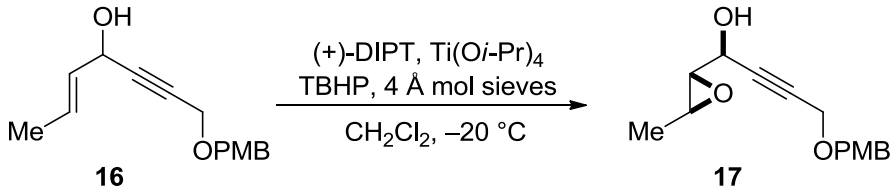
16

(±)-(*E*)-7-((4-methoxybenzyl)oxy)hept-2-en-5-yn-4-ol (16). To a solution of 1-(4-Methoxy-benzyloxy)-2-propyne[4] (3.68 g, 20.9 mmol) in anhydrous THF (16.0 mL) at –78 ℃ was added *n*-BuLi (2.30 M in hexanes, 8.4 mL, 19.3 mmol). After stirring at –78 ℃ for 30 min, a solution of crotonaldehyde (1.33 mL, 16.1 mmol) in anhydrous THF (16.0 mL) was added via syringe. After additional 1.5 h at –78 ℃, the reaction mixture was quenched with saturated aqueous NH_4Cl. The THF was removed *in vacuo*, and the resulting mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) to afford the alcohol **16** (3.63 g, 92%) as a pale yellow oil.

Data for **16**: R_f = 0.22 (75:25 hexanes:EtOAc); IR (thin film) 3408, 2937, 2914, 2854, 1612, 1514, 1442, 1355, 1303, 1250, 1175, 1071, 1033, 964, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ

[4] Takemura, A.; Fujiwara, K.; Shimawaki, K.; Murai, A.; Kawai, H.; Suzuki, T. *Tetrahedron* **2005**, *61*, 7392–7419.

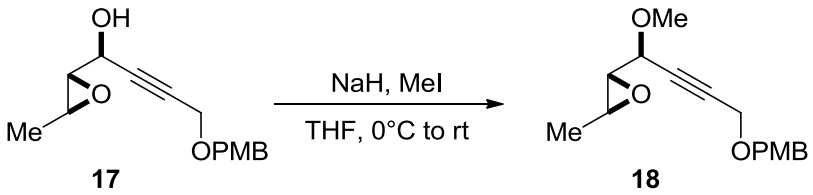
7.30–7.27 (m, 2H), 6.90-6.87 (m, 2H), 5.91 (ddq, *J* = 15.2, 6.6, 1.2 Hz, 1H), 5.64 (ddq, *J* = 15.2, 6.3, 1.7 Hz, 1H), 4.88 (dd, *J* = 6.1, 6.1 Hz, 1H), 4.53 (s, 2H), 4.20 (d, *J* = 1.7 Hz, 2H), 3.81 (s, 3H), 1.82 (d, *J* = 6.0 Hz, 1H), 1.74 (ddd, *J* = 6.6, 1.6, 1.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 130.2 129.9, 129.8, 129.4, 128.8, 113.9 (2C), 86.2, 81.8, 71.3, 62.9, 57.1, 55.3, 17.6; HRMS (ESI-TOF) calculated for $C_{15}H_{18}O_3Na$ [M+Na$^+$] 269.1154, found 269.1153.



(*S*)-4-((4-methoxybenzyl)oxy)-1-((2*S*,3*S*)-3-methyloxiran-2-yl)but-2-yn-1-ol (17). To a solution of alcohol **16** (3.28 g, 13.32 mmol) and (+)-DIPT (0.47 g, 2.00 mmol) in anhydrous CH_2Cl_2 (53.0 mL) was added activated 4 Å molecular sieves (0.98 g) at rt. The reaction mixture was cooled to –20 ℃ and Ti(O*i*-Pr)$_4$ (0.39 mL, 1.33 mmol) was added. After 30 min at –20 ℃, TBHP (5.5 M in decane, 1.70 mL, 9.32 mmol) was added dropwise. The cloudy reaction mixture was stirred at –20 ℃ for another 13 h and was quenched at the same with a freshly prepared solution of $FeSO_4$•$7H_2O$ (4.44 g, 16.0 mmol) and anhydrous citric acid (1.54 g, 8.0 mmol) in water (13.3 mL). This mixture was stirred without cooling for 30 min until two phases appeared. The mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (twice) and the combined organic layers were concentrated to approximately the original reaction volume (53 mL). After that, a 30% NaOH in brine solution[2] (13.3 mL) was added and the resulting mixture was stirred vigorously at rt for 1 h. Upon addition of water and separation of layers, the aqueous layer was extracted with Et_2O (twice). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated to a small volume. Finally this solution was filtered through Celite with Et_2O and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (silica gel, gradient 90:10 to 20:80 hexanes:EtOAc,) to afford epoxide **17** (1.56 g, 45%, 89% *ee* by Mosher's ester[3]) as a pale yellow oil.

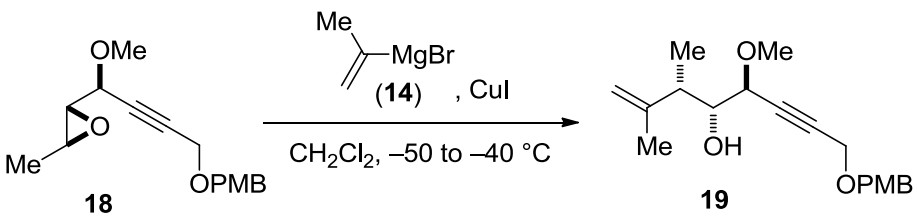
Data for **17**: R_f = 0.26 (60:40 hexanes:EtOAc); $[\alpha]_D^{26}$ = +1.8 ° (*c* 0.52, $CHCl_3$); IR (thin film) 3412, 2964, 2933, 2839, 1612, 1514, 1442, 1355, 1250, 1175, 1137, 1073, 1032, 983, 922, 872, 819, 759, 575 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.29–7.26 (m, 2H), 6.90–6.87 (m, 2H), 4.65–4.63 (m, 1H), 4.52 (s, 2H), 4.19 (d, *J* = 1.7 Hz, 2H), 3.81 (s, 3H), 3.20 (dddd, *J* = 5.3, 5.3, 5.3, 2.2 Hz, 1H), 3.00 (dd, *J* = 3.2, 2.2 Hz, 1H), 2.09 (d, *J* = 5.0 Hz, 1H), 1.37 (d, *J* = 5.3 Hz, 3H);

^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 129.9 (2C), 129.3, 113.9 (2C), 83.3, 82.6, 71.4, 61.3, 60.7, 57.0. 55.4, 52.5, 17.1; HRMS (ESI-TOF) calculated for $C_{15}H_{18}O_4Na$ [M+Na^+] 285.1103, found 285.1104.



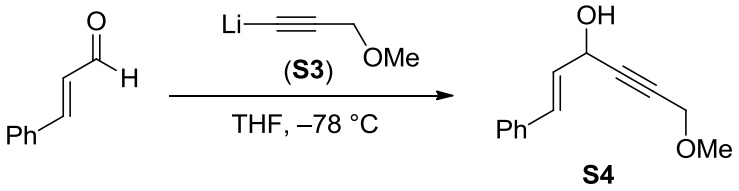
(2*R*,3*S*)-2-((*S*)-1-methoxy-4-((4-methoxybenzyl)oxy)but-2-yn-1-yl)-3-methyloxirane (18). To a solution of epoxy alcohol **17** (1.55 g, 5.91 mmol) in anhydrous THF (29.6 mL) at 0 ℃ was added NaH (60% dispersion in mineral oil, 0.47 g, 11.82 mmol). After 20 min at 0 ℃, MeI (1.1 mL, 17.73 mmol) was added. The reaction mixture was allowed to warm to rt and stirred for 1.5 h. Upon cooling to 0 ℃, saturated aqueous NH_4Cl was added dropwise to quench the reaction, and THF was carefully removed *in vacuo*. The mixture was then diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice) and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel, gradient 95:5 to 60:40 hexanes:EtOAc) to give methyl ether **18** (1.40 g, 86%) as a pale yellow oil.

Data for **18**: R_f = 0.27 (75:25 hexanes:EtOAc); $[\alpha]_D^{23}$ = +17.7 ° (*c* 0.61, $CHCl_3$); IR (thin film) 2992, 2934, 2901, 2836, 1611, 1513, 1464, 1341, 1302, 1174, 1077, 1033, 943, 871, 819, 565 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (m, 2H), 6.90–6.87 (m, 2H), 4.54 (s, 2H), 4.20 (d, *J* = 1.7 Hz, 2H), 4.18-4.16 (m, 1H), 3.81 (s, 3H), 3.45 (s, 3H), 3.12 (dddd, *J* = 5.3, 5.3, 5.3, 2.1 Hz, 1H), 2.95 (dd, *J* = 3.7, 2.1 Hz, 1H), 1.35 (d, *J* = 5.3 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.5, 129.8 (2C), 129.4, 113.9 (2C), 83.8, 81.3, 71.3, 70.9, 59.5, 57.0, 56.9, 55.3, 52.3, 17.1; HRMS (ESI-TOF) calculated for $C_{16}H_{20}O_4Na$ [M+Na^+] 299.1259, found 299.1254.



(3*S*,4*R*,5*S*)-5-methoxy-8-((4-methoxybenzyl)oxy)-2,3-dimethyloct-1-en-6-yn-4-ol (19). To a stirred suspension of CuI (289 mg, 1.52 mmol) in anhydrous THF (10.0 mL) at –50 ℃ was added isopropenylmagnesium bromide (0.5 M in THF, 40.5 mL, 20.3 mmol) dropwise. The resulting cloudy yellow mixture was stirred between –50 and –40 ℃ for 30 min and a solution of epoxide **18** (1.40 g, 5.07 mmol) in anhydrous THF (15.0 mL) was added via syringe at –40 ℃. The reaction mixture was stirred at the same temperature for 4.5 h and quenched with saturated aqueous NH_4Cl. Upon removing THF *in vacuo*, the mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (silica gel, gradient 95:5 to 50:50 hexanes:EtOAc) provided **19** (1.11 g, 68%) as a colorless oil.

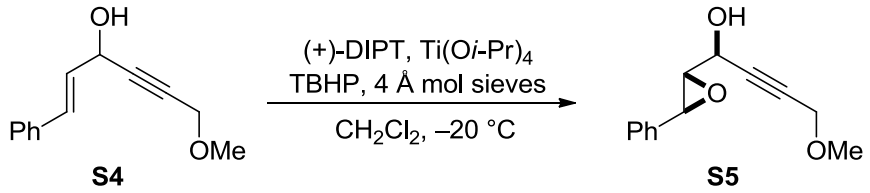
Data for **19**: R_f = 0.29 (75:25 hexanes:EtOAc); $[\alpha]_D^{26}$ = +18.9 ° (*c* 0.63, $CHCl_3$); IR (thin film) 3478, 2936, 2906, 2874, 2833, 1612, 1514, 1463, 1350, 1303, 1249, 1174, 1099, 1037, 895, 820, 776cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30–7.27 (m, 2H), 6.90–6.87 (m, 2H), 4.85–4.84 (m, 1H), 4.81–4.80 (m, 1H), 4.56 (s, 2H), 4.23 (d, *J* = 1.6 Hz, 2H), 4.05 (ddd, *J* = 3.5, 1.6, 1.6 Hz, 1H), 3.81 (s, 3H), 3.71 (ddd, *J* = 8.7, 3.5, 3.5 Hz, 1H), 3.46 (s, 3H), 2.50 (dq, *J* = 8.7, 6.9 Hz, 1H), 2.16 (d, *J* = 3.6 Hz, 1H), 1.72 (dd, *J* = 1.4, 0.8 Hz, 3H), 1.16 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.6, 146.9, 129.9 (2C), 129.6, 114.0 (2C), 112.5, 84.3, 81.9, 74.8, 74.2, 71.3, 57.2, 57.0. 55.4, 43.7, 20.1, 15.7; HRMS (ESI-TOF) calculated for $C_{19}H_{26}O_4Na$ [M+Na$^+$] 341.1729, found 341.1726.



(±)-(*E*)-7-methoxyhept-2-en-5-yn-4-ol (S4). To a solution of methyl propargyl ether (3.29 mL, 39.0 mmol) in anhydrous THF (40.0 mL) at –78 ℃ was added *n*-BuLi (2.33 M in hexanes, 15.5 mL, 36.0 mmol). After stirring at –78 ℃ for 30 min, a solution of *trans*-cinnamaldehyde (3.78 mL, 30.0 mmol) in anhydrous THF (20.0 mL) was added via syringe. After additional 1.5 h at –78 ℃, the reaction mixture was quenched with saturated aqueous NH_4Cl. The THF was removed *in vacuo*, and the resulting mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified

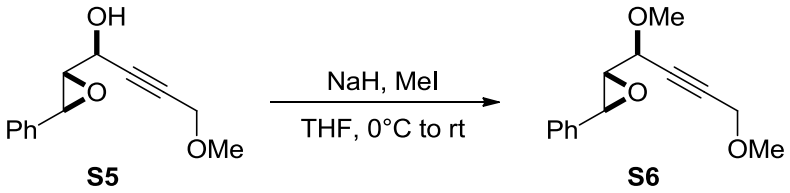
by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) to afford the alcohol **S4** (5.94 g, 98%,) as a yellow oil.

Data for **S4**: R_f = 0.23 (75:25 hexanes:EtOAc); IR (thin film) 3388, 3027, 2935, 2891, 2824, 1495, 1449, 1359, 1280, 1187, 1133, 1096, 967, 903, 869, 748, 694, 604, 547, 488 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.42–7.40 (m, 2H), 7.35–7.32 (m, 2H), 7.29–7.27 (m, 1H), 6.78 (d, *J* = 15.8 Hz, 1H), 6.31(dd, *J* = 15.8, 6.0 Hz, 1H), 5.12 (ddd, *J* = 6.1, 6.1, 1.4 Hz, 1H), 4.20 (d, *J* = 1.6 Hz, 2H), 3.41 (s, 3H), 2.12–2.02 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 131.2, 128.3 (2C), 127.9, 127.7, 126.5 (2C), 85.8, 81.3, 62.2, 59.6, 57.2; HRMS (ESI-TOF) calculated for $C_{13}H_{14}O_2Na$ [M+Na^+] 225.0891, found 225.0891.



(*S*)-4-methoxy-1-((2*S*,3*S*)-3-phenyloxiran-2-yl)but-2-yn-1-ol (S5). To a solution of alcohol **S4** (1.33 g, 6.60 mmol) and (+)-DIPT (0.23 g, 0.99 mmol) in anhydrous CH_2Cl_2 (26.0 mL) was added activated 4 Å molecular sieves (0.40 g) at rt. The reaction mixture was cooled to –20 ℃ and Ti(O*i*-Pr)$_4$ (0.20 mL, 0.66 mmol) was added. After 30 min at –20 ℃, TBHP (5.5 M in decane, 0.84 mL, 4.62 mmol) was added dropwise. The cloudy reaction mixture was stirred at –20 ℃ for another 12 h was was quenched at the same temperature with a freshly prepared solution of $FeSO_4$•$7H_2O$ (2.20 g, 7.92 mmol) and anhydrous citric acid (0.76 g, 3.96 mmol) in water (6.6 mL). This mixture was stirred without cooling for 30 min until two phases appeared. The mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (twice) and the combined organic layers were concentrated to approximately the original reaction volume (26 mL). After that, a 30% NaOH in brine solution[2] (6.6 mL) was added and the resulting mixture was stirred vigorously at rt for 1 h. Upon addition of water and separation of layers, the aqueous layer was extracted with Et_2O (twice). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated to a small volume. Finally this solution was filtered through Celite with Et_2O and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (silica gel, gradient 94:6 to 34:66 hexanes:EtOAc) to afford epoxide **S5** (675 mg, 47%, 85% *ee* by Mosher's ester[3]) as a yellow oil.

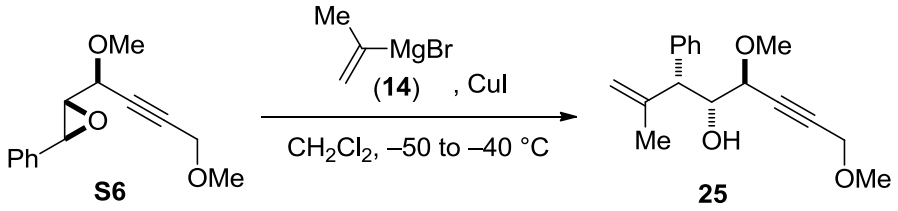
Data for **S5**: R_f = 0.31 (67:33 hexanes:EtOAc); $[\alpha]_D^{28}$ = –32.0 ° (*c* 0.54, $CHCl_3$); IR (thin film) 3397, 2992, 2935, 2824, 1497, 1463, 1359, 1285, 1188, 1133, 1096, 1030, 944, 852, 752, 699, 590 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.38–7.29 (m, 5H), 4.80–4.77 (m, 1H), 4.15 (d, *J* = 1.5 Hz, 2H), 4.06 (d, *J* = 1.8 Hz, 1H), 3.38 (s, 3H), 3.34 (dd, *J* = 4.9, 2.5 Hz, 1H), 2.36 (d, *J* = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.1, 128.5 (2C), 128.4, 125.9 (2C), 83.2, 82.3, 63.4, 61.0, 59.7, 57.6, 55.9; HRMS (ESI-TOF) calculated for $C_{13}H_{14}O_3Na$ [M+Na^+] 241.0841, found 241.0842.



S5 **S6**

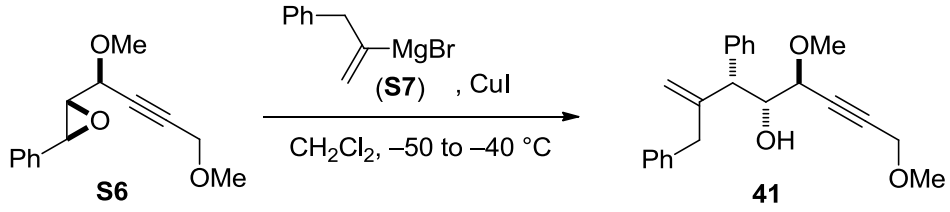
(2*R*,3*S*)-2-((*S*)-1,4-dimethoxybut-2-yn-1-yl)-3-phenyloxirane (S6). To a solution of epoxy alcohol **S5** (550 mg, 2.52 mmol) in anhydrous THF (12.6 mL) at 0 ℃ was added NaH (60% dispersion in mineral oil, 202 mg, 5.04 mmol). After 20 min at 0 ℃, MeI (0.47 mL, 7.56 mmol) was added. The reaction mixture was allowed to warm to rt and stirred for 1.5 h. Upon cooling to 0 ℃, saturated aqueous NH_4Cl was added dropwise to quench the reaction, and THF was carefully removed *in vacuo*. The mixture was then diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice) and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel, gradient 95:5 to 60:40 hexanes:EtOAc) to give methyl ether **S6** (497 mg, 85%) as a yellow oil.

Data for **S6**: R_f = 0.40 (80:20 hexanes:EtOAc); $[\alpha]_D^{21}$ = –21.0 ° (*c* 0.98, $CHCl_3$); IR (thin film) 2992, 2937, 2825, 1720, 1670, 1462, 1346, 1258, 1191, 1096, 903, 755, 699, 598 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.37–7.27 (m, 5H), 4.36–4.33 (m, 1H), 4.18 (d, *J* = 1.5 Hz, 2H), 3.99 (d, *J* = 1.7 Hz, 1H), 3.50 (s, 3H), 3.40 (s, 3H), 3.29 (dd, *J* = 3.1, 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.2, 128.3 (2C), 128.2, 125.6 (2C), 83.7, 80.8, 70.3, 62.0, 59.5, 57.4, 56.6, 55.6; HRMS (ESI-TOF) calculated for $C_{14}H_{16}O_3Na$ [M+Na^+] 255.0997, found 255.0993.



(3*R*,4*R*,5*S*)-5,8-dimethoxy-2-methyl-3-phenyloct-1-en-6-yn-4-ol (25). To a stirred suspension of CuI (107 mg, 0.56 mmol) in anhydrous THF (5.0 mL) at –50 ℃ was added isopropenylmagnesium bromide (0.5 M in THF, 15.0 mL, 7.51 mmol) dropwise. The resulting cloudy yellow mixture was stirred between –50 and –40 ℃ for 30 min and a solution of epoxide **S6** (436 mg, 1.88 mmol) in anhydrous THF (6.0 mL) was added via syringe at –40 ℃. The reaction mixture was stirred at the same temperature for 1 h and quenched with saturated aqueous NH_4Cl. Upon removing THF *in vacuo*, the mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) provided **25** (396 mg, 77%) as a colorless oil.

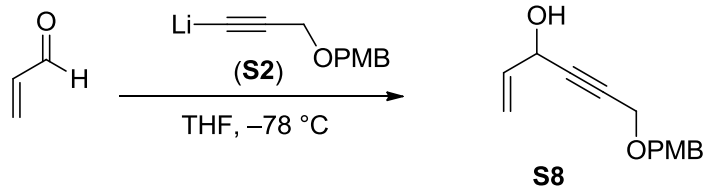
Data for **25**: R_f = 0.31 (75:25 hexanes:EtOAc); $[\alpha]_D^{24}$ = +30.5 ° (*c* 0.84, $CHCl_3$); IR (thin film) 3464, 3061, 3027, 2985, 2935, 2898, 2822, 1644, 1494, 1451, 1356, 1188, 1102, 956, 901, 749, 701, 604 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.31 (m, 4H), 7.27–7.22 (m, 1H), 5.07 (s, 1H), 4.90 (s, 1H), 4.38 (ddd, *J* = 8.8, 3.9, 3.9 Hz, 1H), 4.21 (d, *J* = 1.1 Hz, 2H), 4.12–4.10 (m, 1H), 3.63 (d, *J* = 8.8 Hz, 1H), 3.47 (s, 3H), 3.42 (s, 3H), 2.09–2.07 (m, 1H), 1.64 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.8, 139.1, 128.8 (2C), 128.1 (2C), 126.5, 112.6, 83.9, 81.7, 73.8, 72.2, 59.7, 57.3, 56.6, 55.0, 21.2; HRMS (ESI-TOF) calculated for $C_{17}H_{22}O_3Na$ [$M+Na^+$] 297.1467, found 297.1464.



(3*R*,4*R*,5*S*)-2-benzyl-5,8-dimethoxy-3-phenyloct-1-en-6-yn-4-ol (41). To a round bottom flask equipped with a reflux condenser at rt was added Mg (184 mg, 7.58 mmol) followed by

anhydrous THF (10.0 mL) and 1,2-dibromoethane (0.09 mL). After that, a solution of 2-(bromoallyl)benzene[5] (1.22 g, 6.20 mmol) in anhydrous THF (5.0 mL) was added dropwise and the resulting reaction mixture was heated at reflux for 1.5 h. After cooling to rt, this newly formed Grignard solution was added dropwise via syringe to a stirred suspension of CuI (79 mg, 0.41 mmol) in anhydrous THF (2.0 mL) at –50 ℃. After 30 min between –50 and –40 ℃, a solution of epoxide **S6** (320 mg, 1.38 mmol) in anhydrous THF (3.5 mL) was added at –40 ℃. The reaction mixture was stirred at the same temperature for 1 h and quenched with saturated aqueous NH_4Cl. Upon removing THF *in vacuo*, the mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) provided **41** (294 mg, 60%) as a colorless oil.

Data for **41**: R_f = 0.29 (75:25 hexanes:EtOAc); $[\alpha]_D^{26}$ = +41.2 ° (*c* 0.26, $CHCl_3$); IR (thin film) 3457, 3060, 3027, 2988, 2921, 2849, 2822, 1642, 1601, 1494, 1453, 1356, 1188, 1101, 957, 903, 751, 701, 614 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.31 (m, 2H), 7.28–7.24 (m, 5H), 7.21–7.18 (m, 1H), 7.09–7.07 (m 2H), 5.23 (s, 1H), 4.91 (s, 1H), 4.33–4.30 (m, 1H), 4.10 (s, 2H), 4.10–4.09 (m, 1H), 3.59 (d, *J* = 8.1 Hz, 1H), 3.39 (s, 3H), 3.37 (s, 3H), 3.27 (app. d, *J* = 15.3 Hz, 1H), 3.17 (app. d, *J* = 15.3 Hz, 1H), 2.00 (d, *J* = 4.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.9, 139.0. 138.9, 129.4 (2C), 129.3 (2C), 128.27 (2C), 128.25 (2C), 126.8, 126.2, 113.2, 84.0, 81.9, 73.6, 73.1, 59.8, 57.5, 56.6, 52.6, 42.4; HRMS (ESI-TOF) calculated for $C_{23}H_{26}O_3Na$ [M+Na^+] 373.1780, found 373.1772.



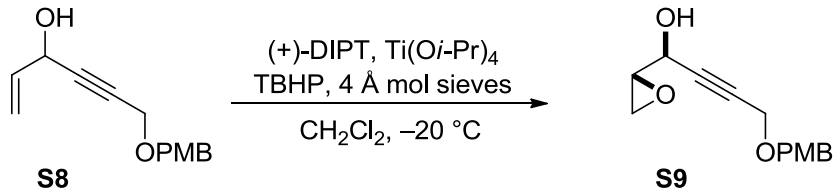
S8

(±)-6-((4-methoxybenzyl)oxy)hex-1-en-4-yn-3-ol (S8). To a solution of 1-(4-Methoxy-benzyloxy)-2-propyne[4] (1.60 g, 9.08 mmol) in anhydrous THF (15.0 mL) at –78 ℃ was added *n*-BuLi (2.35 M in hexanes, 3.9 mL, 9.08 mmol). After stirring at –78 ℃ for 30 min, a solution of acrolein (0.50 mL, 7.57 mmol) in anhydrous THF (6.0 mL) was added via syringe. After additional 1.5 h at –78 ℃, the reaction mixture was quenched with saturated aqueous NH_4Cl.

[5] Bigot, A.; Breuninger, D.; Breit, B. *Org. Lett.* **2008**, *10*, 5321–5324.

The THF was removed *in vacuo*, and the resulting mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and the solvent was removed *in vacuo*. The crude product was purified by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) to afford the alcohol **S8** (1.25 g, 71%,) as a colorless oil.

Data for **S8**: R_f = 0.25 (75:25 hexanes:EtOAc); IR (thin film) 3408, 3084, 3001, 2936, 2907, 2838, 1612, 1586, 1514, 1465, 1356, 1303, 1249, 1175, 1111, 1073, 930, 819, 669, 577, 518 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.28–7.27 (m, 2H), 6.90–6.88 (m, 2H), 5.99 (ddd, *J* = 17.0, 10.2, 5.3 Hz, 1H), 5.48 (d, *J* = 17.0 Hz, 1H), 5.25 (d, *J* = 10.2 Hz, 1H), 4.96–4.93 (m, 1H), 4.53 (s, 2H), 4.20 (d, *J* = 1.6 Hz, 2H), 3.81 (s, 3H), 1.91 (d, *J* = 6.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.0, 136.8, 129.5 (2C), 128.9, 115.8, 113.5 (2C), 85.5, 81.5, 70.7, 62.4, 56.6, 54.9; HRMS (ESI-TOF) calculated for $C_{14}H_{16}O_3Na$ [M+Na^+] 255.0997, found 255.0997.

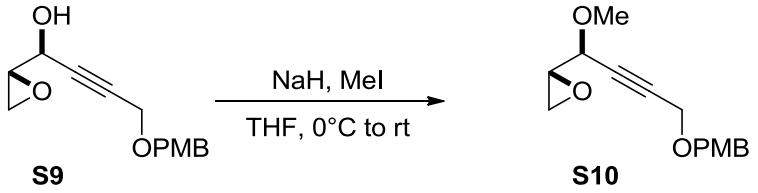


S8 **S9**

(*S*)-4-((4-methoxybenzyl)oxy)-1-((*R*)-oxiran-2-yl)but-2-yn-1-ol (S9). To a solution of alcohol **S8** (930 mg, 4.00 mmol) and (+)-DIPT (141 mg, 0.60 mmol) in anhydrous CH_2Cl_2 (16.0 mL) was added activated 4 Å molecular sieves (0.28 g) at rt. The reaction mixture was cooled to –20 ℃ and Ti(O*i*-Pr)$_4$ (0.12 mL, 0.40 mmol) was added. After 30 min at –20 ℃, TBHP (5.5 M in decane, 0.51 mL, 2.80 mmol) was added dropwise. The cloudy reaction mixture was stirred at –20 ℃ for another 87 h and was quenched at the same temperature with a freshly prepared solution of $FeSO_4$•$7H_2O$ (1.34 g, 4.8 mmol) and anhydrous citric acid (0.46 g, 2.4 mmol) in water (4.0 mL). This mixture was stirred without cooling for 30 min until two phases appeared. The mixture was transferred to a separatory funnel and the layers were separated. The aqueous phase was extracted with CH_2Cl_2 (twice) and the combined organic layers were concentrated to approximately the original reaction volume (16 mL). After that, a 30% NaOH in brine solution[2] (4 mL) was added and the resulting mixture was stirred vigorously at rt for 1 h. Upon addition of water and separation of layers, the aqueous layer was extracted with Et_2O (twice). The combined organic extracts were dried with $MgSO_4$, filtered and concentrated to a small volume. Finally this solution was filtered through Celite with Et_2O and the solvent was removed *in vacuo*. The crude

product was purified by flash chromatography (silica gel, gradient 88:12 to 0:100 hexanes:EtOAc) to afford epoxide **S9** (299 mg, 30%, 91% *ee* by Mosher's ester[3]) as a yellow oil.

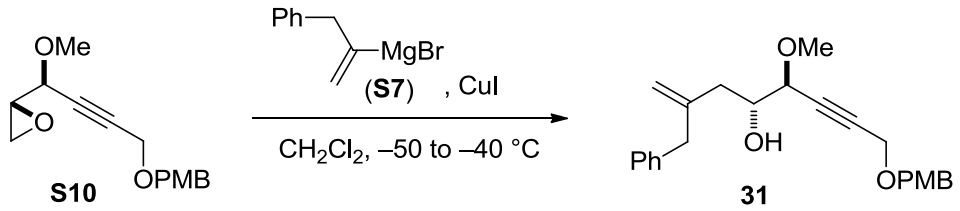
Data for **S9**: R_f = 0.34 (50:50 hexanes:EtOAc); $[\alpha]_D^{23}$ = +20.8 ° (*c* 0.52, $CHCl_3$); IR (thin film) 3415, 2999, 2933, 2900, 2838, 1611, 1513, 1464, 1355, 1302, 1249, 1175, 1129, 1069, 1031, 939, 908, 817, 583 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.27 (m, 2H), 6.90–6.87 (m, 2H), 4.72–4.69 (m, 1H), 4.52 (s, 2H), 4.19 (d, *J* = 1.5 Hz, 2H), 3.81 (s, 3H), 3.28 (ddd, *J* = 3.5, 3.0, 3.0 Hz, 1H), 2.93 (dd, *J* = 4.9, 2.6 Hz, 1H), 2.84 (dd, *J* = 4.6, 4.6 Hz, 1H), 2.09 (d, *J* = 4.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 129.8 (2C), 129.2, 113.8 (2C), 82.9, 82.5, 71.3, 61.2, 56.8, 55.2, 53.7, 44.4; HRMS (ESI-TOF) calculated for $C_{14}H_{16}O_4Na$ [M+Na^+] 271.0946, found 271.0940.



S9 **S10**

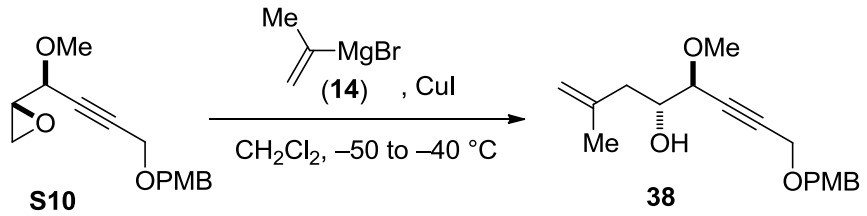
(*R*)-2-((*S*)-1-methoxy-4-((4-methoxybenzyl)oxy)but-2-yn-1-yl)oxirane (S10). To a solution of epoxy alcohol **S9** (230 mg, 0.93 mmol) in anhydrous THF (4.6 mL) at 0 ℃ was added NaH (60% dispersion in mineral oil, 74 mg, 1.85 mmol). After 20 min at 0 ℃, MeI (0.17 mL, 2.78 mmol) was added. The reaction mixture was allowed to warm to rt and stirred for 1.5 h. Upon cooling to 0 ℃, saturated aqueous NH_4Cl was added dropwise to quench the reaction, and THF was carefully removed *in vacuo*. The mixture was then diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice) and the combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude material was purified by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) to give methyl ether **S10** (187 mg, 77%) as a pale yellow oil.

Data for **S10**: R_f = 0.30 (75:25 hexanes:EtOAc); $[\alpha]_D^{24}$ = +34.7 ° (*c* 1.04, $CHCl_3$); IR (thin film) 2998, 2937, 2837, 1716, 1684, 1612, 1514, 1465, 1303, 1250, 1175, 1085, 1033, 903, 819, 761, 586, 518 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.27 (m, 2H), 6.89–6.87 (m, 2H), 4.54 (s, 2H), 4.26–4.24 (m, 1H), 4.20 (d, *J* = 1.4 Hz, 2H), 3.81 (s, 3H), 3.47 (s, 3H), 3.24 (ddd, *J* = 3.4, 3.4, 3.0 Hz, 1H), 2.85 (dd, *J* = 5.2, 2.5 Hz, 1H), 2.81 (dd, *J* = 5.0, 5.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 129.7 (2C), 129.2, 113.7 (2C), 83.8, 80.7, 71.1, 70.8, 56.74, 56.72, 55.1, 52.4, 44.2; HRMS (ESI-TOF) calculated for $C_{15}H_{18}O_4Na$ [M+Na^+] 285.1103, found 285.1102.



(4*R*,5*S*)-2-benzyl-5-methoxy-8-((4-methoxybenzyl)oxy)oct-1-en-6-yn-4-ol (31). To a round bottom flask equipped with a reflux condenser at rt was added Mg (140 mg, 5.77 mmol) followed by anhydrous THF (8.0 mL) and 1,2-dibromoethane (0.07 mL). After that, a solution of 2-(bromoallyl)benzene[5] (930 mg, 4.72 mmol) in anhydrous THF (4.0 mL) was added dropwise and the resulting reaction mixture was heated at reflux for 1.5 h. After cooling to rt, this newly formed Grignard solution was added dropwise via syringe to a stirred suspension of CuI (60 mg, 0.31 mmol) in anhydrous THF (2.0 mL) at –50 ℃. After 30 min between –50 and –40 ℃, a solution of epoxide **S10** (275 mg, 1.05 mmol) in anhydrous THF (3.0 mL) was added at –40 ℃. The reaction mixture was stirred at the same temperature for 1 h and quenched with saturated aqueous NH_4Cl. Upon removing THF *in vacuo*, the mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) provided **31** (293 mg, 73%) as a colorless oil.

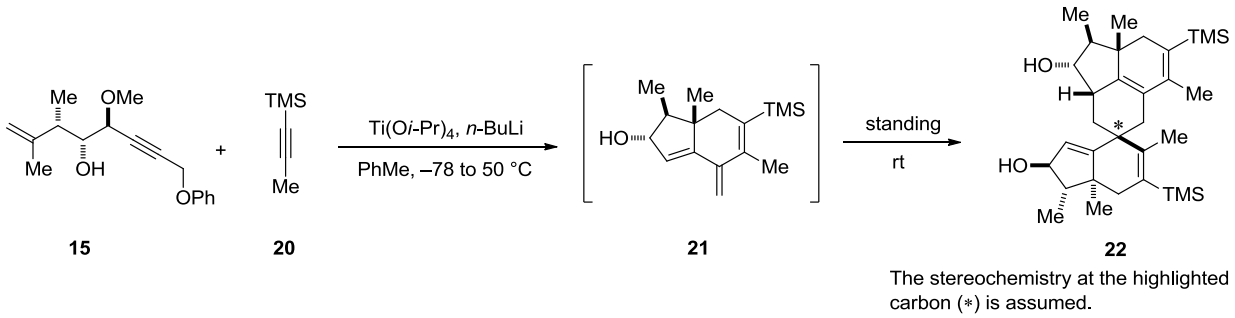
Data for **31**: R_f = 0.30 (75:25 hexanes:EtOAc); $[\alpha]_D^{23}$ = +26.5 ° (*c* 0.28, $CHCl_3$); IR (thin film) 3450, 3025, 2996, 2934, 2905, 2836, 1611, 1513, 1450, 1353, 1302, 1249, 1176, 1106, 1034, 819, 742, 700 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.25 (m, 4H), 7.22–7.17 (m, 3H), 6.90–6.87 (m, 2H), 5.00 (s, 1H), 4.91 (s, 1H), 4.51 (app. t, *J* = 15.3 Hz, 2H), 4.19 (app. t, *J* = 16.3 Hz, 2H), 4.03–4.02 (m, 1H), 3.97–3.93 (m, 1H), 3.81 (s, 3H), 3.47 (app. d, *J* = 7.4 Hz, 1H), 3.45 (s, 3H), 3.41 (app. d, *J* = 7.4 Hz, 1H), 2.37 (dd, *J* = 14.5, 4.3 Hz, 1H), 2.27 (dd, *J* = 14.5, 8.9 Hz, 1H), 2.15 (d, *J* = 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.6, 145.3, 139.4, 130.0 (2C), 129.5, 129.3 (2C), 128.6 (2C), 126.4, 114.8, 114.1 (2C), 84.4, 81.9, 75.2, 71.4, 71.3, 57.3, 57.1, 55.5, 43.2, 38.7; HRMS (ESI-TOF) calculated for $C_{24}H_{28}O_4Na$ [M+Na^+] 403.1885, found 403.1884.



(4*R*,5*S*)-5-methoxy-8-((4-methoxybenzyl)oxy)-2-methyloct-1-en-6-yn-4-ol (38). To a stirred suspension of CuI (35 mg, 0.18 mmol) in anhydrous THF (1.5 mL) at –50 ℃ was added isopropenylmagnesium bromide (0.5 M in THF, 4.9 mL, 2.44 mmol) dropwise. The resulting cloudy yellow mixture was stirred between –50 and –40 ℃ for 30 min and a solution of epoxide **S10** (160 mg, 0.61 mmol) in anhydrous THF (2.5 mL) was added via syringe at –40 ℃. The reaction mixture was stirred at the same temperature for 1 h and quenched with saturated aqueous NH_4Cl. Upon removing THF *in vacuo*, the mixture was diluted with water and CH_2Cl_2. After separation of phases, the aqueous layer was extracted with CH_2Cl_2 (twice). The combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo*. Purification by flash chromatography (silica gel, gradient 94:6 to 50:50 hexanes:EtOAc) provided **38** (173 mg, 93%) as a colorless oil.

Data for **38**: R_f = 0.24 (75:25 hexanes:EtOAc); $[\alpha]_D^{24}$ = +45.9 °(*c* 0.85, $CHCl_3$); IR (thin film) 3458, 3074, 2936, 1714, 1612, 1514, 1464, 1354, 1303, 1250, 1174, 1108, 1074, 1033, 894, 820 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.29–7.27 (m, 2H), 6.90–6.87 (m, 2H), 4.88 (s, 1H), 4.85 (s, 1H), 4.55 (s, 2H), 4.23 (d, *J* = 1.3 Hz, 2H), 4.07–4.05 (m, 1H), 3.95 (dq, *J* = 8.7, 4.4 Hz, 1H), 3.81 (s, 3H), 3.48 (S, 3H), 2.40 (dd, *J* = 14.2, 4.5 Hz, 1H), 2.31 (dd, *J* = 14.2, 8.9 Hz, 1H), 2.17 (d, *J* = 4.7 Hz, 1H), 1.79 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.3, 141.9, 129.7 (2C), 129.2, 113.7 (2C), 113.2, 84.0, 81.9, 75.1, 71.0, 70.9, 57.0, 56.8, 55.1, 40.7, 22.5; HRMS (ESI-TOF) calculated for $C_{18}H_{25}O_4$ [M+H^+] 305.1753, found 305.1749.

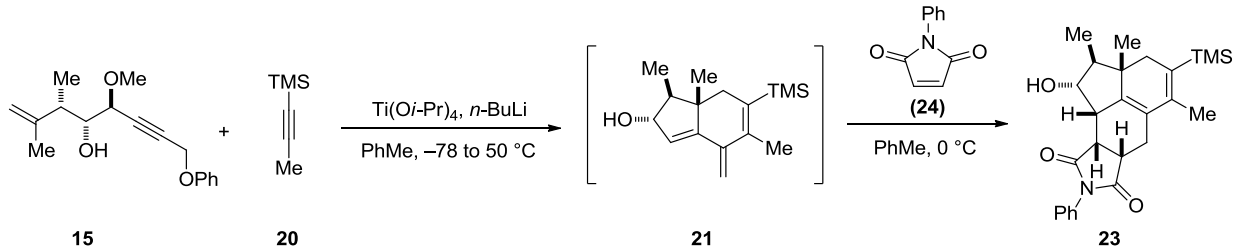
B. Synthesis of cross-conjugated triene-containing hydroindanes 22, 23, 28, 30, 32, 34, 37, 40 and tetraene 43

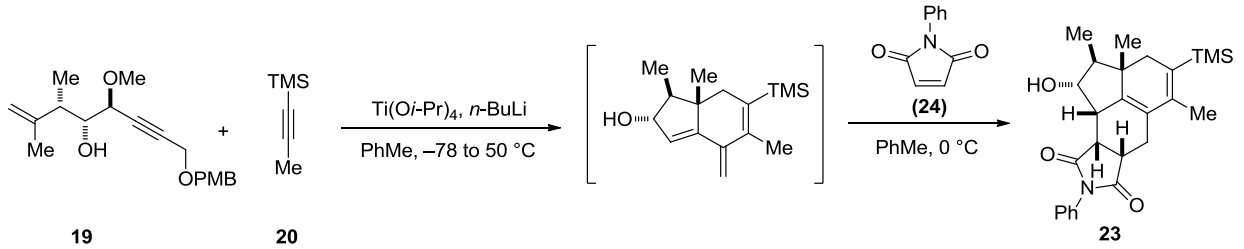


(1*S*,1'*S*,2*R*,2a*S*,2'*S*,4*S*,7a'*S*,8a*S*)-1,1',5',6,7a',8a-hexamethyl-6',7-bis(trimethylsilyl)-1',2,2a,2',3,5,7',7a',8,8a-decahydro-*1H*-spiro[acenaphthylene-4,4'-indene]-2,2'-diol (22). To a solution of alkyne **20** (125 mg, 1.11 mmol) in PhMe (7.4 mL) was added Ti(O*i*-Pr)$_4$ (0.33 mL, 1.11 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.37 M in hexanes, 0.94 mL, 2.22 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **15** (82 mg, 0.30 mmol) was dissolved in PhMe (4.0 mL), treated with *n*-BuLi (2.37 M in hexanes, 0.13 mL, 0.32 mmol) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 5 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates and the resulting solution was washed with 2 M aqueous NaOH (three times). The organic layer was separated, dried over Na_2SO_4, and concentrated *in vacuo*. Due to the reactive nature of the triene **21**, dimerization began to occur to give rise to **22** during the isolation of **21**. Purification of the crude mixture by flash chromatography (silica gel, 95:5 to 50:50 hexanes:EtOAc) afforded a mixture of **21** and **22**. Upon standing under vacuum (<1 mbar) overnight, the above isolated material was fully converted to pure **22** (31 mg, 40%) as an unstable off-white solid.

Data for **22**: R_f = 0.20 (75:25 hexanes:EtOAc); $[\alpha]_D^{23}$ = +48.7 ° (*c* 0.27, CH_2Cl_2); IR (thin film) 3383, 2956, 2913, 2869, 1711, 1668, 1447, 1376, 1248, 1020, 850, 835, 755, 685 cm^{-1}; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 5.49 (brs, 1H), 4.40 (d, *J* = 7.9 Hz, 1H), 3.47 (dd, *J* = 9.7 Hz, 1H), 2.74 (d, *J* = 9.6 Hz, 1H), 2.48 (dddd, *J* = 17.7, 7.9, 7.9, 3.3 Hz, 1H), 2.29 (dddd, *J* = 17.6, 8.6, 2.8, 2.8 Hz, 1H), 2.22 (app. d, *J* = 16.1 Hz, 1H), 2.12 (app. d, *J* = 15.7 Hz, 1H), 2.05 (ddd, *J* = 14.6, 7.8, 2.7 Hz, 1H), 1.99–1.94 (m, 5H), 1.85 (d, *J* = 2.4 Hz, 3H), 1.82 (d, *J* = 2.3 Hz, 3H), 1.64–1.58 (m, 1H), 1.58–1.52 (m, 1H), 1.08 (d, *J* = 7.0 Hz, 3H), 0.97 (d, *J* = 7.0 Hz, 3H), 0.77 (s, 3H), 0.66 (s, 3H), 0.15 (s, 9H), 0.12 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.5, 146.4, 143.8, 140.8, 133.4, 128.2, 126.6, 125.5, 82.7, 79.3, 59.4, 56.9, 52.4, 47.3, 44.1, 41.4, 40.4, 37.6, 37.4, 26.0, 22.3, 20.0, 18.2, 16.3, 11.5, 11.1, 0.6 (3C), 0.2 (3C); HRMS (ESI-TOF) calculated for $C_{32}H_{52}O_2NaSi_2$ [M+Na^+] 547.3404, found 547.3414.





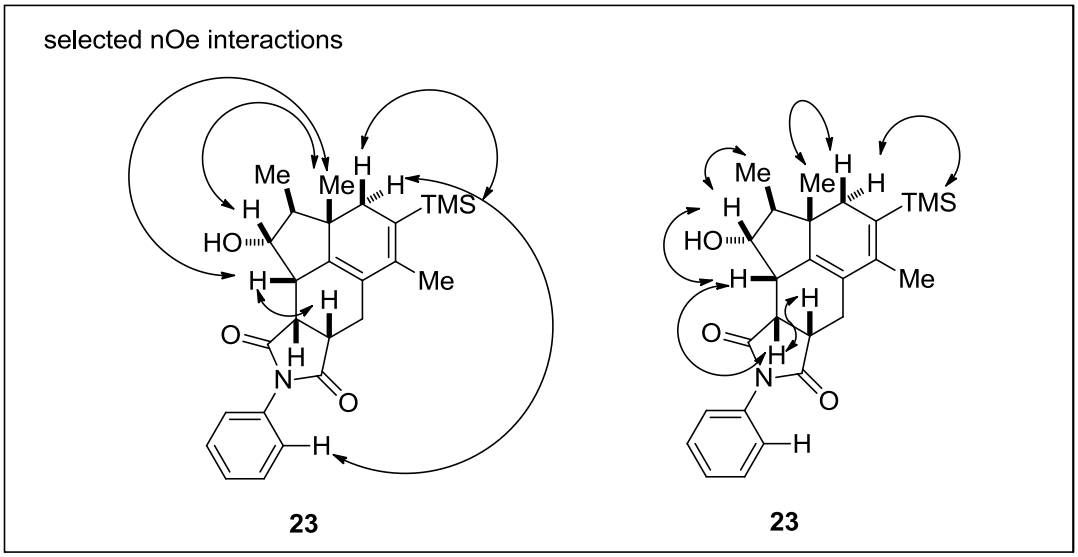
(1*R*,2*S*,2a*S*,6a*S*,9a*R*,9b*S*)-1-hydroxy-2,2a,5-trimethyl-8-phenyl-4-(trimethylsilyl)-2a,3,6,6a,9a,9b-hexahydro-1*H*-indeno[1,7-*ef*]isoindole-7,9(2*H*,8*H*)-dione (23). From enyne **15**: To a solution of alkyne **20** (179 mg, 1.59 mmol) in PhMe (9.0 mL) was added Ti(O*i*-Pr)$_4$ (0.47 mL, 1.59 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.30 M in hexanes, 1.39 mL, 3.19 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **15** (125 mg, 0.46 mmol) was dissolved in PhMe (6.0 mL), treated with *n*-BuLi (2.30 M in hexanes, 0.21 mL, 0.48 mmol) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne

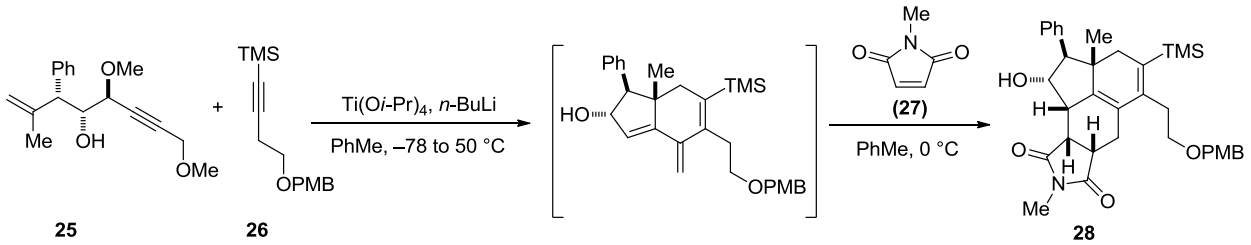
complex solution at –78 °C. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 °C for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 °C and quenched with saturated aqueous $NaHCO_3$ (approx. 6 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates and the resulting solution was washed with 2 M aqueous NaOH (three times). The organic layer was separated, dried over Na_2SO_4, and concentrated *in vacuo* to approximately the original volume of PhMe (15 mL). After cooling this solution to 0 °C, *N*-phenylmaleimide (**24**, 237 mg, 1.37 mmol) was added. After stirring for 30 min at 0 °C, the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 80:20 to 0:100 hexanes:EtOAc) afforded **23** (97 mg, 49%) as a yellow foam.

From enyne **19**: To a solution of alkyne **20** (157 mg, 1.39 mmol) in PhMe (8.3 mL) was added $Ti(O\textit{i}\text{-}Pr)_4$ (0.41 mL, 1.39 mmol) at rt. The mixture was cooled to –78 °C and *n*-BuLi (2.35 M in hexanes, 1.19 mL, 2.79 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 °C (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 °C cooling bath. In the meantime, enyne **19** (120 mg, 0.38 mmol) was dissolved in PhMe (5.1 mL), treated with *n*-BuLi (2.35 M in hexanes, 0.17 mL, 0.40 mmol,) at –78 °C, and the resulting solution was stirred at –78 °C for 15 min and then allowed to warm to between 0 °C and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 °C. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 °C for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 °C and quenched with saturated aqueous $NaHCO_3$ (approx. 6 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (13 mL). After cooling this solution to 0 °C, *N*-phenylmaleimide (196 mg, 1.13 mmol) was added. After stirring for 30 min at 0 °C, the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 80:20 to 0:100 hexanes:EtOAc) afforded **23** (74 mg, 45%) as a yellow foam.

Data for **23**: R_f = 0.26 (50:50 hexanes:EtOAc); $[\alpha]_D^{24}$ = +87.8 ° (*c* 0.40, $CHCl_3$); IR (thin film) 3429, 2956, 2914, 2871, 2806, 1770, 1695, 1499, 1445, 1393, 1248, 1189, 1085, 855, 836, 755, 690 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.46–7.37 (m, 3H), 7.07–7.04 (m, 2H), 4.63 (d, *J* = 12.5 Hz, 1H), 4.13 (ddd, *J* = 12.3, 10.8, 9.4 Hz, 1H), 3.67 (dd, *J* = 8.3, 7.3 Hz, 1H), 3.38 (ddd, *J* = 8.3, 7.3, 1.4 Hz, 1H), 3.05 (dd, *J* = 14.6, 1.3 Hz, 1H), 2.97 (dd, *J* = 8.2, 8.2 Hz, 1H), 2.28 (ddd, *J* = 14.6, 7.4, 1.9 Hz, 1H), 2.22 (app. d, *J* = 16.1 Hz, 1H), 1.90 (d, *J* = 2.6 Hz, 3H), 1.71–1.62 (m, 2H), 1.00 (d, *J* = 6.8 Hz, 3H), 0.70 (s, 3H), 0.14 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 181.2,

179.1, 146.8, 138.4, 131.8, 129.5 (2C), 129.3, 128.4, 126.8, 126.6 (2C), 80.0, 53.2, 42.2, 42.1, 41.3, 40.8, 37.8, 25.9, 18.6, 15.0, 11.8, 0.2 (3C); HRMS (ESI-TOF) calculated for $C_{26}H_{34}NO_3Si$ [M+H$^+$] 436.2308, found 436.2304.





(1*S*,2*S*,2a*S*,6a*S*,9a*R*,9b*S*)-1-hydroxy-5-(2-((4-methoxybenzyl)oxy)ethyl)-2a,8-dimethyl-2-phenyl-4-(trimethylsilyl)-2a,3,6,6a,9a,9b-hexahydro-1*H*-indeno[1,7-*ef*]isoindole-7,9(2*H*,8*H*)-dione (28). To a solution of alkyne **26**[6] (335 mg, 1.28 mmol) in PhMe (7.7 mL) was added Ti(O*i*-Pr)$_4$ (0.39 mL, 1.28 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.37 M in hexanes, 1.07 mL, 2.55 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **25** (100 mg, 0.36 mmol) was dissolved in PhMe (4.8 mL), treated with *n*-BuLi (2.37 M in hexanes, 0.16 mL, 0.38 mmol,) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to

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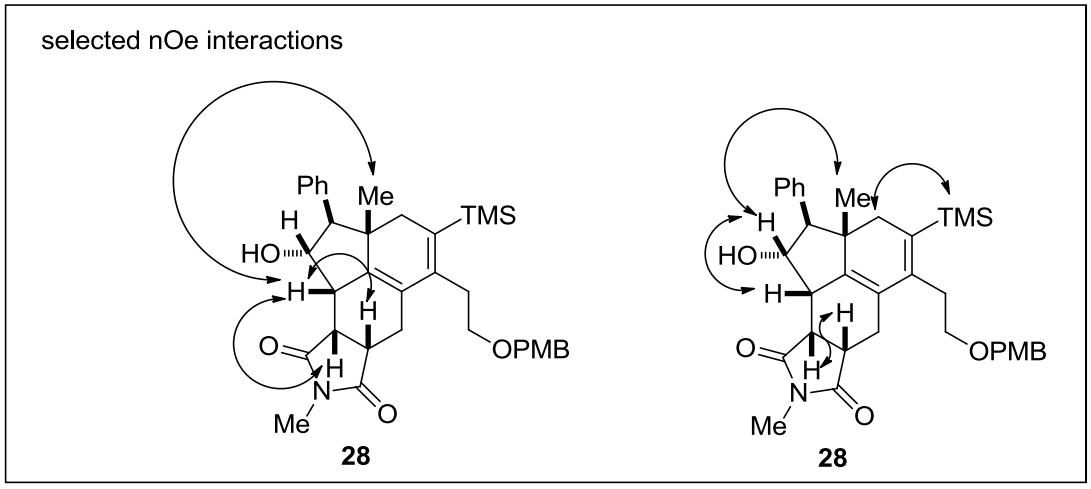
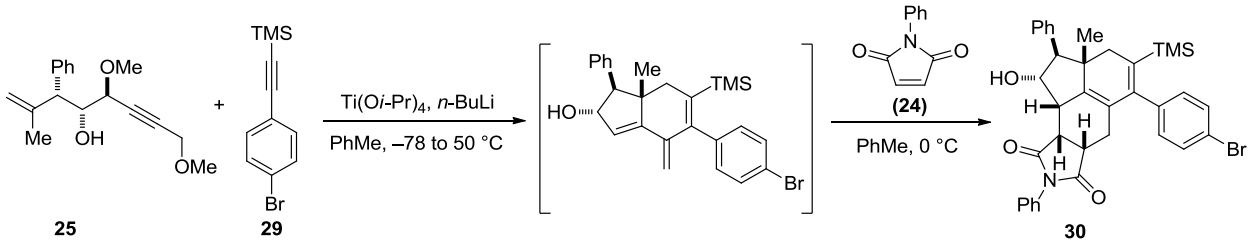
warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 6 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (12 mL). After cooling this solution to 0 ℃, *N*-methylmaleimide (**27**, 122 mg, 1.09 mmol) was added. After stirring for 30 min at 0 ℃, the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 88:12 to 0:100 hexanes:EtOAc) afforded **28** (87 mg, 41%) as a yellow oil.

Data for **28**: R_f = 0.26 (50:50 hexanes:EtOAc); $[\alpha]_D^{23}$ = +150.4 °(*c* 0.79, CH_2Cl_2); IR (thin film) 3024, 2952, 2856, 1766, 1682, 1509, 1445, 1293, 1249, 1092, 1034, 839, 704, 573 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.37–7.33 (m, 2H), 7.28–7.21 (m, 5H), 6.86 (d, *J* = 8.6 Hz, 2H), 5.02 (ddd, *J* = 11.3, 11.3, 9.5 Hz, 1H), 4.88 (d, *J* = 12.6 Hz, 1H), 4.40 (app. dd, *J* = 15.2, 11.5 Hz, 2H), 3.79 (s, 3H), 3.55 (dd, *J* = 8.0, 8.0 Hz, 1H), 3.37 (dd, *J* = 6.4, 2.8 Hz, 1H), 3.35 (dd, *J* = 7.8, 3.0 Hz, 1H), 3.27 (dd, *J* = 7.9, 7.9 Hz, 1H), 3.07 (dd, *J* = 8.2, 8.2 Hz, 1H), 2.97–2.94 (m, 1H), 2.96 (s, 3H), 2.90 (d, *J* = 11.2 Hz, 1H), 2.65–2.54 (m, 2H), 2.23 (ddd, *J* = 14.9, 7.7, 1.7 Hz, 1H), 2.17 (app. d, *J* = 15.7 Hz, 1H), 1.86 (app. d, *J* = 15.7 Hz, 1H), 0.48 (s, 3H), 0.07 (s, 9H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 182.5, 179.9, 159.7, 147.3, 140.5, 138.9, 131.4, 130.9, 129.6 (2C), 129.3 (2C), 128.7 (2C), 127.1, 127.0, 114.1 (2C), 76.0, 73.1, 70.7, 64.7, 55.8, 42.4, 41.7, 41.5, 41.0, 40.4, 32.7, 25.72, 25.67, 15.5, 0.3 (3C); HRMS (ESI-TOF) calculated for $C_{35}H_{44}NO_5Si$ $[M+H^+]$ 586.2989, found 586.2986.

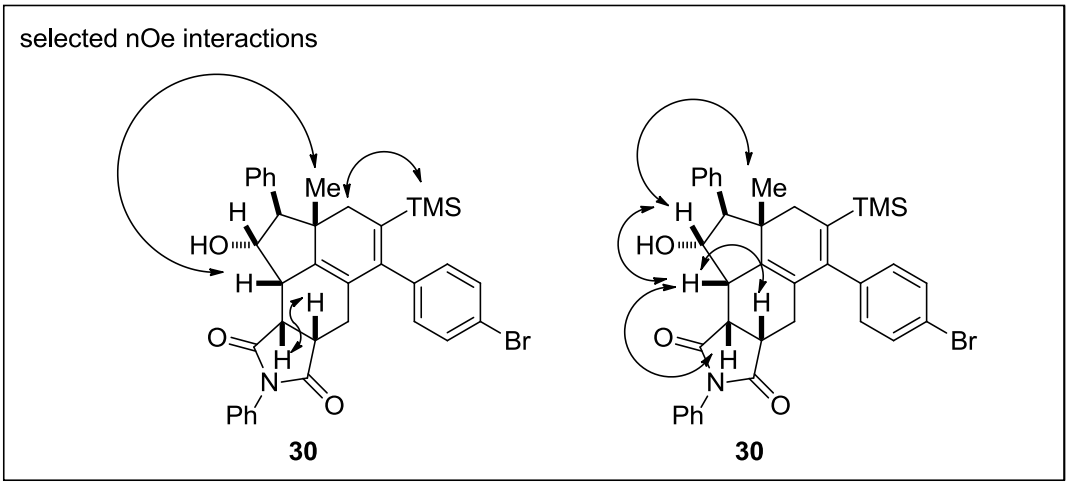


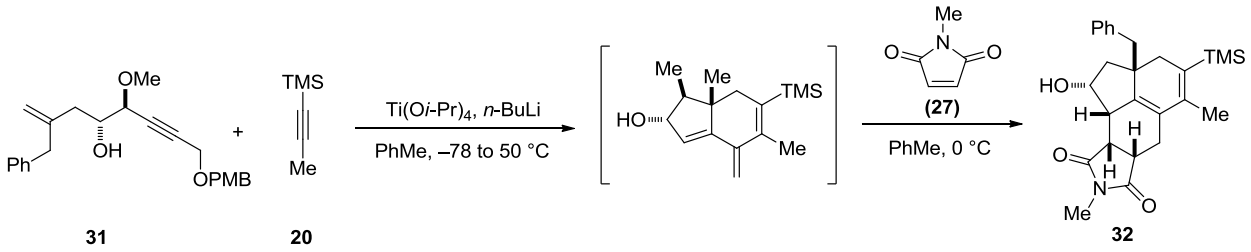


(1*S*,2*S*,2a*S*,6a*S*,9a*R*,9b*S*)-5-(4-bromophenyl)-1-hydroxy-2a-methyl-2,8-diphenyl-4-(trimethylsilyl)-2a,3,6,6a,9a,9b-hexahydro-1*H*-indeno[1,7-*ef*]isoindole-7,9(2*H*,8*H*)-dione (30). To a solution of Ti(O*i*-Pr)$_4$ (0.42 mL, 1.42 mmol) in PhMe (5.5 mL) at –78 ℃ was added *n*-BuLi (2.37 M in hexanes, 1.20 mL, 2.83 mmol) dropwise by syringe over 5 min. After another 5 min at –78 ℃, a solution of alkyne **29** (359 mg, 1.42 mmol) in PhMe (3.0 mL) was added dropwise. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **25** (111 mg, 0.40 mmol) was dissolved in PhMe (5.4 mL), treated with *n*-BuLi (2.37 M in hexanes, 0.17 mL, 0.40 mmol,) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 6 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (14 mL). After cooling this solution to 0 ℃, *N*-phenylmaleimide (**24**, 210 mg, 1.21 mmol) was added. After stirring for 30 min at 0 ℃, the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 92:8 to 34:66 hexanes:EtOAc) afforded **30** (116 mg, 45%) as a white solid.

Data for **30**: R_f = 0.26 (67:33 hexanes:EtOAc); $[\alpha]_D^{22}$ = +103.8 °(*c* 0.60, CH_2Cl_2); IR (thin film) 3422, 3029, 2955, 1770, 1694, 1600, 1498, 1444, 1391, 1248, 1097, 1011, 860, 836, 756, 691, 621 cm^{-1}; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.56–7.46 (m, 5H), 7.37–7.33 (m, 2H), 7.28–7.25 (m, 3H), 7.17 (d, *J* = 7.8 Hz, 2H), 6.95 (d, *J* = 7.4 Hz, 2H), 5.11 (ddd, *J* = 11.7, 11.7, 9.8 Hz, 1H), 4.69 (d, *J* = 12.6 Hz, 1H), 3.76 (dd, *J* = 7.8, 7.8 Hz, 1H), 3.36 (dd, *J* = 8.0, 8.0 Hz, 1H), 3.20 (dd, *J* = 8.2, 8.2 Hz, 1H), 3.03 (d, *J* = 11.3 Hz, 1H), 2.57 (d, *J* = 14.8 Hz, 1H), 2.42 (app. d, *J* = 16.0 Hz, 1H), 2.16 (app. d, *J* = 16.0 Hz, 1H), 2.05 (dd, *J* = 14.9, 7.2 Hz, 1H), 0.68 (s, 3H), –0.26 (s,

9H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 181.8, 179.2, 147.2, 144.6, 140.4, 138.7, 133.3, 132.5, 131.7 (4C), 129.9 (2C), 129.7, 129.3 (2C), 128.7 (2C), 127.3 (2C), 127.2, 126.5, 121.6, 76.1, 65.0, 42.9, 42.3, 41.9, 41.4, 40.3. 26.5, 16.4, –0.6 (3C); HRMS (ESI-TOF) calculated for $C_{36}H_{37}BrNO_3Si$ [M+H$^+$] 638.1726, found 638.1714.

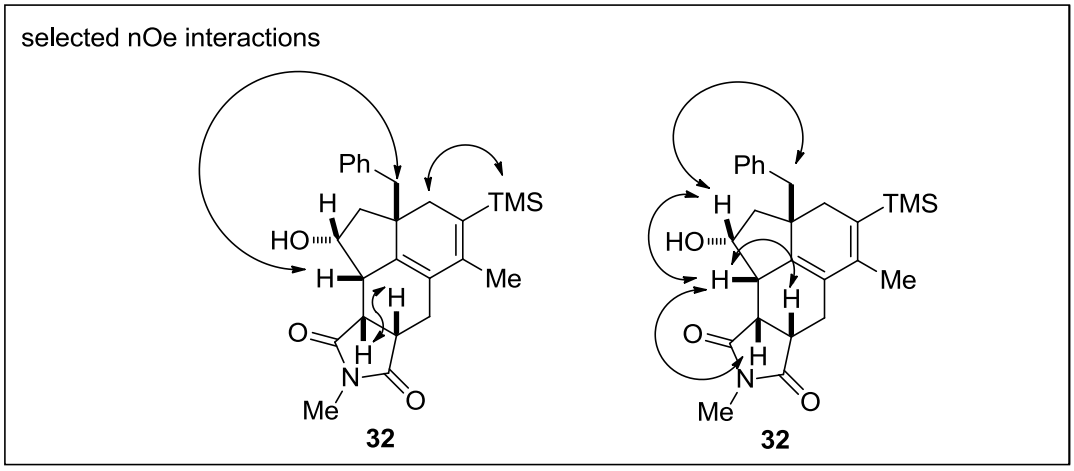


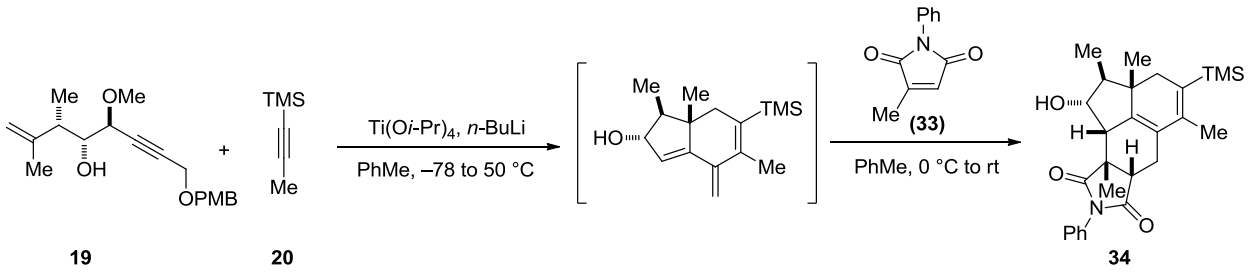


(1*R*,2a*R*,6a*S*,9a*R*,9b*S*)-2a-benzyl-1-hydroxy-5,8-dimethyl-4-(trimethylsilyl)-2a,3,6,6a,9a,9b-hexahydro-1*H*-indeno[1,7-*ef*]isoindole-7,9(2*H*,8*H*)-dione (32). To a solution of alkyne **20** (117 mg, 1.04 mmol) in PhMe (6.0 mL) was added Ti(O*i*-Pr)$_4$ (0.31 mL, 1.04 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.37 M in hexanes, 0.88 mL, 2.08 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **31** (113 mg, 0.30 mmol) was dissolved in PhMe (4.0 mL), treated with *n*-BuLi (2.37 M in hexanes, 0.13 mL, 0.31 mmol) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx.

15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 5 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (10 mL). After cooling this solution to 0 ℃, *N*-methylmaleimide (**27**, 99 mg, 0.89 mmol) was added. After stirring for 30 min at 0 ℃, the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 88:12 to 20:80 hexanes:EtOAc) afforded **32** (52 mg, 40%) as a yellow oil.

Data for **32**: R_f = 0.34 (60:40 hexanes:EtOAc); $[\alpha]_D^{22}$ = +62.8 ° (*c* 0.60, CH_2Cl_2); IR (thin film) 3420, 3025, 2952, 2856, 2807, 1769, 1684, 1441, 1386, 1294, 1250, 1125, 1087, 837, 741, 705 cm^{-1}; ^1H NMR (500 MHz, CD_2Cl_2) δ 7.26–7.18 (m, 3H), 7.05–7.02 (m, 2H), 4.66 (d, *J* = 12.4 Hz, 1H), 3.91 (ddd, *J* = 18.0, 10.8, 7.4 Hz, 1H), 3.35 (dd, *J* = 7.4, 7.4 Hz, 1H), 3.20 (dd, *J* = 7.8, 7.8 Hz, 1H), 2.92 (d, *J* = 12.9 Hz, 1H), 2.86 (s, 3H), 2.73 (app. d, *J* = 12.9 Hz, 1H), 2.57 (dd, *J* = 7.9, 7.9 Hz, 1H), 2.34 (app. d, *J* = 16.5 Hz, 1H), 2.33–2.27 (m, 2H), 2.24 (app. d, *J* = 12.9 Hz, 1H), 1.92 (d, *J* = 2.7 Hz, 3H), 1.58 (app. d, *J* = 15.9 Hz, 1H), 1.32 (dd, *J* = 12.4, 11.2 Hz, 1H), 0.16 (s, 9H); ^{13}C NMR (150 MHz, CD_2Cl_2) δ 182.3, 180.1, 146.7, 140.0. 139.9. 130.6 (2C), 129.6, 128.5 (2C), 128.0, 126.7, 74.0, 48.3, 43.7, 42.7, 42.1, 40.94, 40.87, 38.9, 26.0, 25.4, 18.8, 0.3 (3C); HRMS (ESI-TOF) calculated for $C_{26}H_{34}NO_3Si$ [M+H^+] 436.2308, found 436.2304.

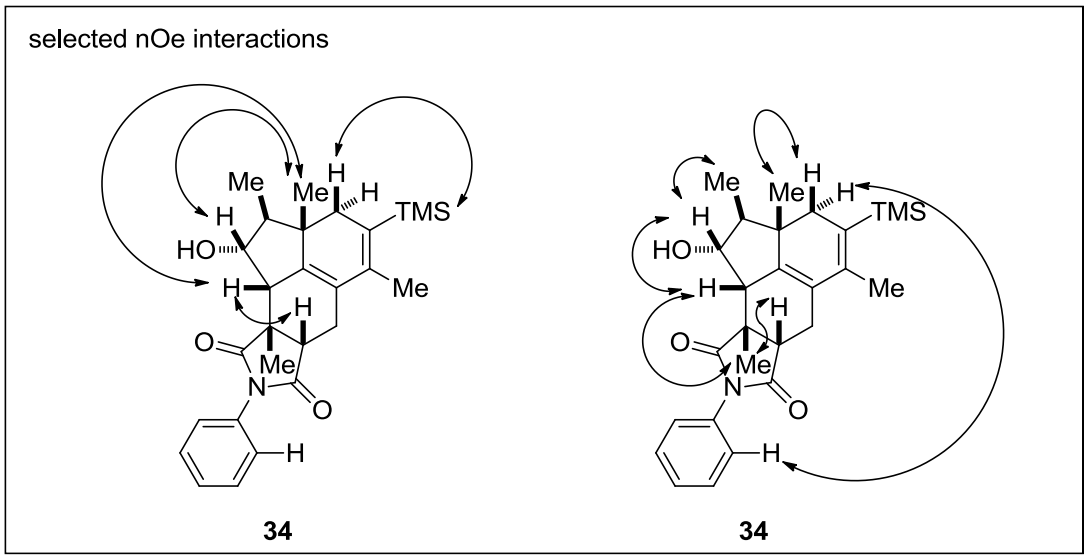


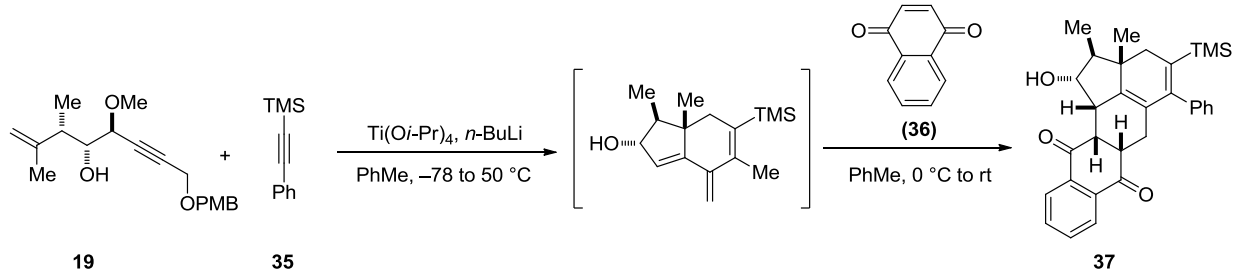


(1*R*,2*S*,2a*S*,6a*S*,9aR,9b*R*)-1-hydroxy-2,2a,5,9a-tetramethyl-8-phenyl-4-(trimethylsilyl)-2a,3,6,6a,9a,9b-hexahydro-1*H*-indeno[1,7-*ef*]isoindole-7,9(2*H*,8*H*)-dione (34). To a solution of alkyne **20** (137 mg, 1.22 mmol) in PhMe (7.3 mL) was added Ti(O*i*-Pr)$_4$ (0.36 mL, 1.22 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.35 M in hexanes, 1.04 mL, 2.44 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **19** (105 mg, 0.33 mmol) was dissolved in PhMe (4.4 mL), treated with *n*-BuLi (2.35 M in hexanes, 0.15 mL, 0.35 mmol) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 5 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (12 mL). After cooling this solution to 0 ℃, 2-methyl-*N*-phenylmaleimide (**33**, 185 mg, 0.99 mmol) was added. The reaction mixture was then warmed to rt, stirrred for 8 h and the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 94:6 to 50:50 hexanes:EtOAc) afforded **34** (64 mg, 43%) as a yellow foam.

Data for **34**: R_f = 0.37 (75:25 hexanes:EtOAc); $[\alpha]_D^{21}$ = +56.5 ° (*c* 0.26, CH_2Cl_2); IR (thin film) 3437, 2957, 2912, 2872, 2806, 1771, 1693, 1500, 1444, 1394, 1248, 1190, 1072, 852, 836, 754, 690, 607 cm^{-1}; ^{1}H NMR (500 MHz, CD_2Cl_2) δ 7.47–7.39 (m, 3H), 7.09–7.06 (m, 2H), 4.53 (d, *J* = 12.6 Hz, 1H), 4.12 (ddd, *J* = 12.1, 11.3, 9.3 Hz, 1H), 3.01 (dd, *J* = 14.5, 1.6 Hz, 1H), 2.87 (dd, *J* = 6.4, 1.6 Hz, 1H), 2.70 (d, *J* = 9.1 Hz, 1H), 2.32 (ddd, *J* = 14.5, 6.4, 1.6 Hz, 1H), 2.23 (app. d, *J* = 16.1 Hz, 1H), 1.91 (d, *J* = 2.6 Hz, 3H), 1.76 (s, 3H), 1.66 (app. d, *J* = 16.0 Hz, 1H), 1.50 (dq, *J* = 11.0, 6.7 Hz, 1H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.68 (s, 3H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, CD_2Cl_2) δ 184.8, 178.4, 147.4, 139.2, 132.5, 129.7 (2C), 129.4, 128.5, 128.1, 127.2 (2C), 81.0,

53.4, 51.7, 50.0, 48.2, 41.8, 37.8, 25.8, 25.4, 18.7, 14.9, 11.7, 0.2 (3C); HRMS (ESI-TOF) calculated for $C_{27}H_{36}NO_3Si$ [M+H$^+$] 450.2464, found 450.2460.

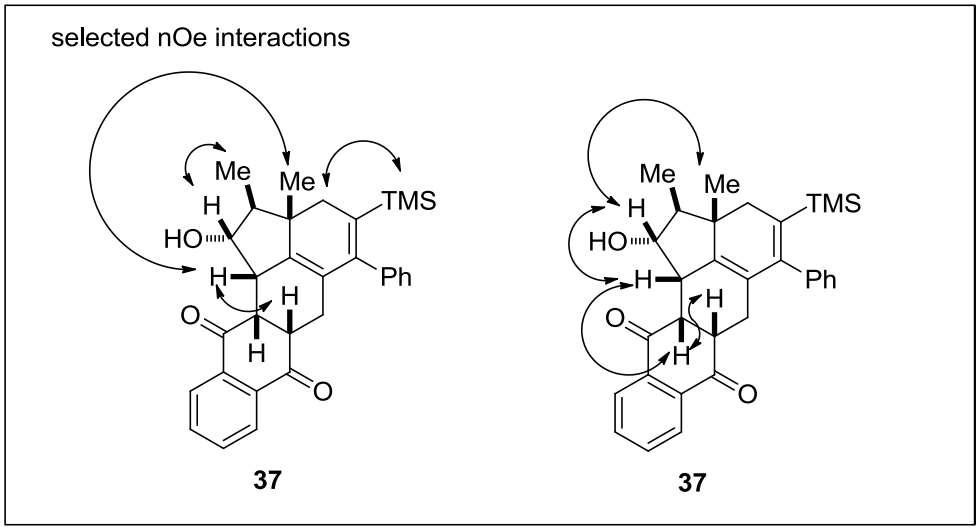


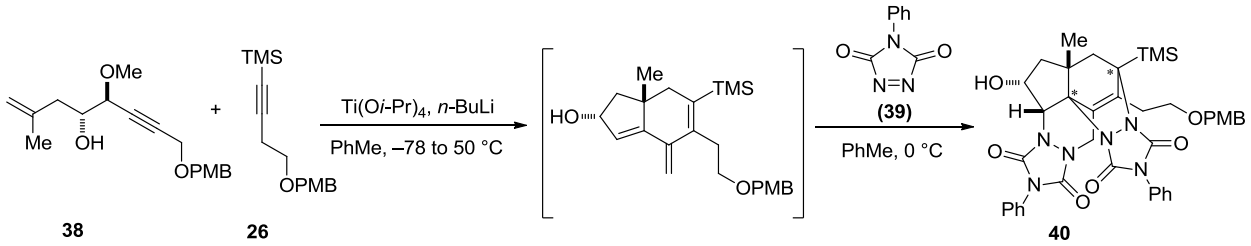


(1*R*,2*S*,2a*S*,6a*S*,12a*R*,12b*S*)-1-hydroxy-2,2a-dimethyl-5-phenyl-4-(trimethylsilyl)-1,2a,3,6,6a,12b-hexahydrocyclopenta[*de*]tetracene-7,12(2*H*,12a*H*)-dione (37). To a solution of alkyne **35** (243 mg, 1.39 mmol) in PhMe (8.3 mL) was added Ti(O*i*-Pr)$_4$ (0.41 mL, 1.39 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.35 M in hexanes, 1.19 mL, 2.79 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **19** (120 mg, 0.38 mmol) was dissolved in PhMe (5.0 mL), treated with *n*-BuLi (2.35 M in hexanes, 0.17 mL, 0.40 mmol,) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx.

15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 6 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (13 mL). After cooling this solution to 0 ℃, 1,4-naphthoquinone (**36**, 179 mg, 1.13 mmol) was added. The reaction mixture was then warmed to rt, stirrred for 3 h and the solvent was removed *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 94:6 to 50:50 hexanes:EtOAc) afforded **37** (99 mg, 54%) as a yellow foam.

Data for **37**: R_f = 0.26 (75:25 hexanes:EtOAc); $[\alpha]_D^{18}$ = +148.7 ° (*c* 0.53, $CHCl_3$); IR (thin film) 3500, 3059, 3023, 2955, 2955, 2923, 1692, 1591, 1442, 1377, 1248, 1056, 1010, 863, 835, 760, 739, 703 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.00–7.97 (m, 2H), 7.76–7.72 (m, 2H), 7.24 (dd, *J* = 7.4, 7.4 Hz, 1H), 7.18 (dd, *J* = 7.3, 7.3 Hz, 1H), 7.13 (dd, *J* = 7.3, 7.3 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.5 Hz, 1H), 4.08 (ddd, *J* = 10.6, 10.6, 10.6 Hz, 1H), 3.75 (d, *J* = 4.6, 4.6 Hz, 1H), 3.33 (ddd, *J* = 11.3, 7.2, 4.6 Hz, 1H), 3.09–3.06 (m, 1H), 3.04 (d, *J* = 12.4 Hz, 1H), 2.37 (app. d, *J* = 15.8 Hz, 1H), 2.25 (dq, *J* = 9.2, 6.9 Hz, 1H), 2.12 (app. d, *J* = 15.8 Hz, 1H), 2.06 (ddd, *J* = 18.0, 7.2, 2.6 Hz, 1H), 1.73 (ddd, *J* = 17.9, 11.4, 3.9 Hz, 1H), 1.19 (d, *J* = 6.9 Hz, 3H), 0.85 (s, 3H), –0.3 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 201.4, 198.9, 145.3, 144.2, 141.5, 135.1, 134.7, 134.6, 132.9, 130.7, 129.8, 129.3, 128.1, 127.8, 127.6, 127.1, 127.0, 121.9, 80.6, 56.8, 51.0, 48.7, 42.2, 40.7, 40.2, 27.9, 15.4, 12.0, –0.7 (3C); HRMS (ESI-TOF) calculated for $C_{31}H_{35}O_3Si$ [M+H^+] 483.2355, found 483.2344.



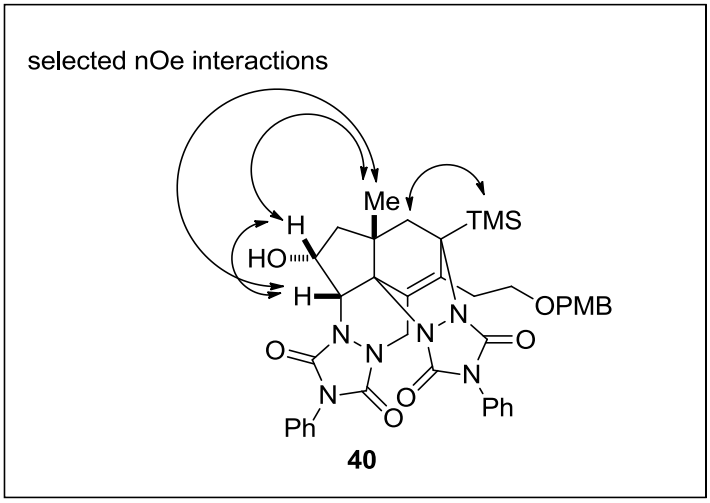


The stereochemistry at the highlighted centers (∗) is assumed.

(10*S*,13*R*)-11-hydroxy-2-(2-((4-methoxyphenyl)methoxy]ethyl)-13-methyl-7,17-diphenyl-1-(trimethylsilyl)-5,7,9,15,17,19-hexaazahexacyclo[11.6.1.0^{3,14}.0^{5,9}.0^{10,14}.0^{15,19}]icos-2-ene-6,8,16,18-tetrone. To a solution of alkyne **26** (401 mg, 1.53 mmol) in PhMe (9.2 mL) was added Ti(O*i*-Pr)$_4$ (0.45 mL, 1.53 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.23 M in hexanes, 1.37 mL, 3.06 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **38** (133 mg, 0.44 mmol) was dissolved in PhMe (5.8 mL), treated with *n*-BuLi (2.23 M in hexanes, 0.21 mL, 0.46 mmol,) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 6 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo* to approximately the original volume of PhMe (15 mL). After cooling this solution to 0 ℃, 4-phenyl-1,2,4-triazoline-3,5-dione (**39**, 230 mg, 1.31 mmol) was added. After stirring for 1 h at 0 ℃, the solvent was removed *in vacuo*. Due to the high reactivity of **39**, a second [4+2] cycloaddition occurred between the initial adduct and **39**. The facial selectively of the second [4+2] cycloaddition appeared to be high, as we were unable to identify a stereoisomeric product. The crude material was purified by flash chromatography (silica gel, 84:16 to 0:100 hexanes:EtOAc) provided only one isomer **40** (117 mg, 36%) as a white solid.

Data for **40**: R_f = 0.20 (40:60 hexanes:EtOAc); $[\alpha]_D^{24}$ = +110.0 ° (*c* 1.86, $CHCl_3$); R_f = 0.29 (75:25 hexanes:EtOAc); IR (thin film) 3438, 3063, 2959, 2934, 2901, 2860, 1766, 1714, 1612, 1504, 1412, 1317, 1250, 1140, 1092, 1030, 846, 736, 690, 647 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52–7.48 (m, 2H), 7.46–7.41 (m, 2H), 7.38–7.29 (m, 6H), 7.17 (d, *J* = 8.5 Hz, 2H), 6.81 (d, *J* = 8.5 Hz, 2H), 5.36 (d, *J* = 8.2 Hz, 1H), 4.99 (app. d, *J* = 15.7 Hz, 1H), 4.61 (ddd, *J* = 7.7, 7.7,

7.7 Hz, 1H), 4.44 (app. d, *J* = 11.6 Hz, 1H), 4.27 (app. d, *J* = 15.7 Hz, 1H), 4.19 (app. d, *J* = 11.6 Hz, 1H), 3.76 (s, 3H), 3.45 (d, *J* = 3.2 Hz, 1H), 3.38 (ddd, *J* = 7.8, 7.5, 5.7 Hz, 1H), 3.29 (ddd, *J* = 7.8, 7.8, 7.8 Hz, 1H), 2.65 (ddd, *J* = 14.2, 7.6, 7.6 Hz, 1H), 2.46 (ddd, *J* = 14.2, 6.0, 6.0 Hz, 1H), 2.19 (dd, *J* = 13.2, 7.7 Hz, 1H), 1.92 (app. d, *J* = 13.2 Hz, 1H), 1.55 (app. d, *J* = 13.2 Hz, 1H), 1.26–1.19 (m, 1H), 1.23 (s, 3H), 0.34 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 159.4, 155.9, 154.8, 153.4, 148.7, 137.2, 131.8, 131.3, 130.0, 129.8 (2C), 129.3 (2C), 129.1 (3C), 128.5, 128.3, 126.8 (2C), 125.6 (2C), 113.9 (2C), 73.1, 69.5, 67.1, 64.8, 58.8, 57.1, 55.4, 45.3, 43.6, 40.6, 39.9, 30.2, 26.2, 0.3 (3C); HRMS (ESI-TOF) calculated for $C_{40}H_{45}N_6O_7Si$ [M+H$^+$] 749.3119, found 749.3114.



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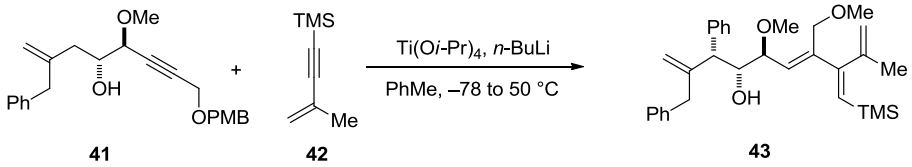


41 **42** **43**

(3*R*,4*R*,5*S*,6*Z*,8*E*)-2-benzyl-5-methoxy-7-(methoxymethyl)-9-methyl-3-phenyl-8-((trimethylsilyl)methylene)deca-1,6,9-trien-4-ol (43). To a solution of alkyne **42** (150 mg, 1.05 mmol) in PhMe (6.3 mL) was added Ti(O*i*-Pr)$_4$ (0.31 mL, 1.05 mmol) at rt. The mixture was cooled to –78 ℃ and *n*-BuLi (2.23 M in hexanes, 0.94 mL, 2.10 mmol) was added dropwise by syringe over 5 min. After this period, the cooling bath was removed and the reaction was allowed to warm to rt (approx. 15 to 20 min). The reaction mixture was then heated to 50 ℃ (no reflux condenser required) for 1 h and allowed to cool to rt before it was placed into a –78 ℃ cooling bath. In the meantime, enyne **41** (105 mg, 0.30 mmol) was dissolved in PhMe (4.0 mL), treated with *n*-BuLi

(2.23 M in hexanes, 0.14 mL, 0.31 mmol,) at –78 ℃, and the resulting solution was stirred at –78 ℃ for 15 min and then allowed to warm to between 0 ℃ and rt over 15 min. Next, this alkoxide solution was added dropwise by syringe to the above Ti-alkyne complex solution at –78 ℃. The reaction mixture was then allowed to warm slowly to rt overnight (approx. 15 h) and then heated at 50 ℃ for 2.5 h. Upon cooling to rt, the flask was further cooled down to 0 ℃ and quenched with saturated aqueous $NaHCO_3$ (approx. 5 mL) via syringe while the flask was still under N_2. The contents of the flask were filtered through Celite with Et_2O to remove the precipitates. The solution was dried over Na_2SO_4 and concentrated *in vacuo*. Purification of the crude mixture by flash chromatography (silica gel, 98:2 to 80:20 hexanes:EtOAc) afforded **43** (75 mg, 51%) as a yellow oil.

Data for **43**: R_f = 0.30 (90:10 hexanes:EtOAc); $[\alpha]_D^{22}$ = +46.6 ° (*c* 2.11, $CHCl_3$); IR (thin film) 3435, 3027, 2951, 2926, 2898, 2818, 1731, 1641, 1567, 1494, 1452, 1246, 1101, 953, 903, 863, 701 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.34–7.30 (m, 4H), 7.25–7.22 (m, 3H), 7.18–7.15 (m, 1H), 7.07–7.04 (m, 2H), 5.72 (d, *J* = 9.6 Hz, 1H), 5.56 (s, 1H), 5.40 (s, 1H), 5.03 (s, 1H), 4.89–4.86 (m, 2H), 4.09–4.04 (m, 1H), 3.84–3.80 (m, 1H), 3.64–3.56 (m, 3H), 3.20 (app. d, *J* = 15.5 Hz, 1H), 3.12 (s, 3H), 3.09 (app. d, *J* = 15.5 Hz, 1H), 2.86 (d, *J* = 6.4 Hz, 1H), 2.81 (s, 3H), 1.71 (s, 3H), 0.02 (s, 9H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.5, 150.0, 145.5, 142.3, 139.9, 139.1, 133.3, 130.8 (2C), 129.5 (2C), 128.3 (2C), 128.1 (2C), 126.8, 126.7, 126.1, 116.8, 113.3, 78.5, 72.5, 68.7, 58.2, 56.4, 52.1, 42.9, 23.2, 0.5 (3C); HRMS (ESI-TOF) calculated for $C_{31}H_{42}O_3NaSi$ [M+Na^+] 513.2801, found 513.2809.

3. Spectral Data

Figure S1: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **11**.

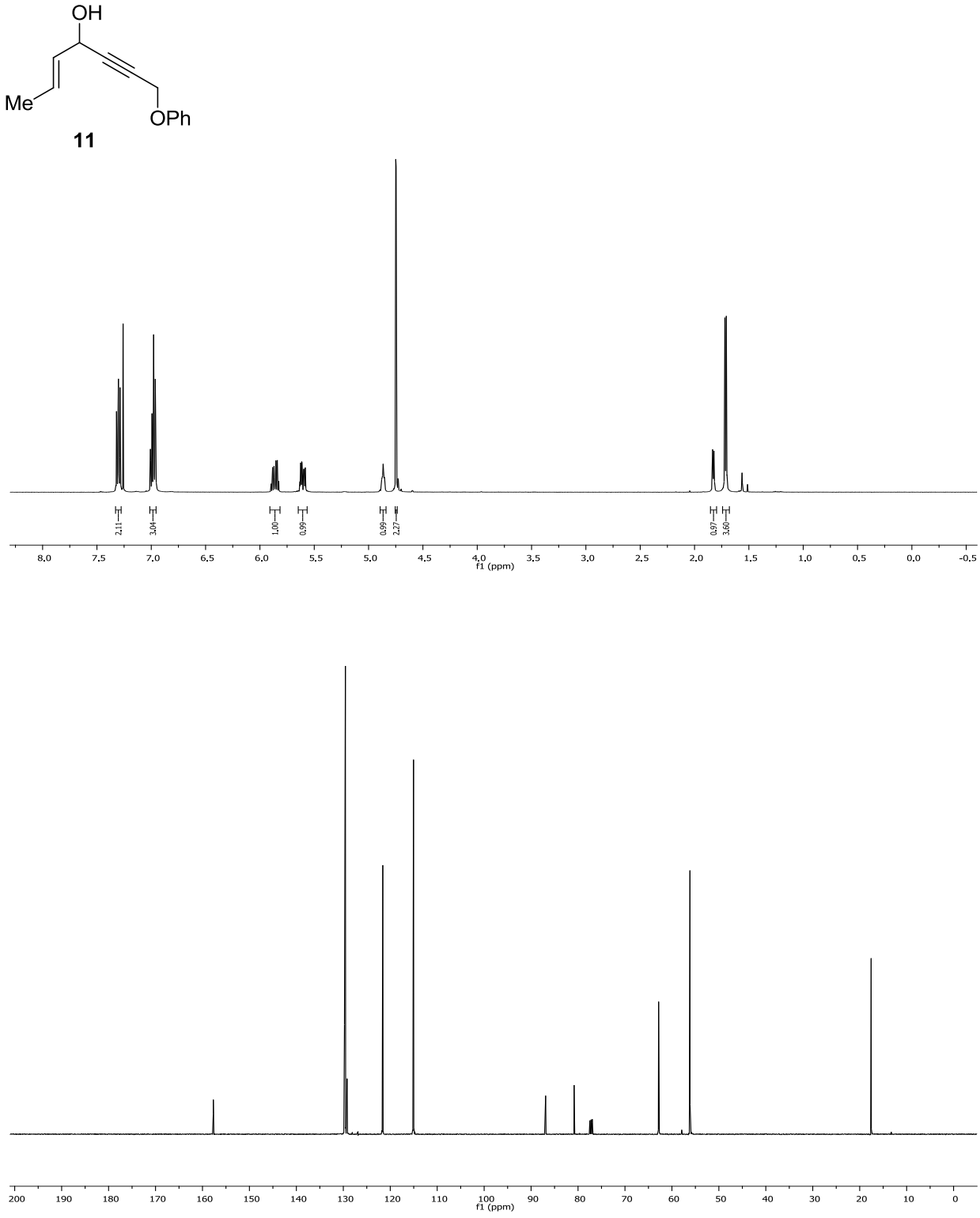


Figure S2: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **12**.

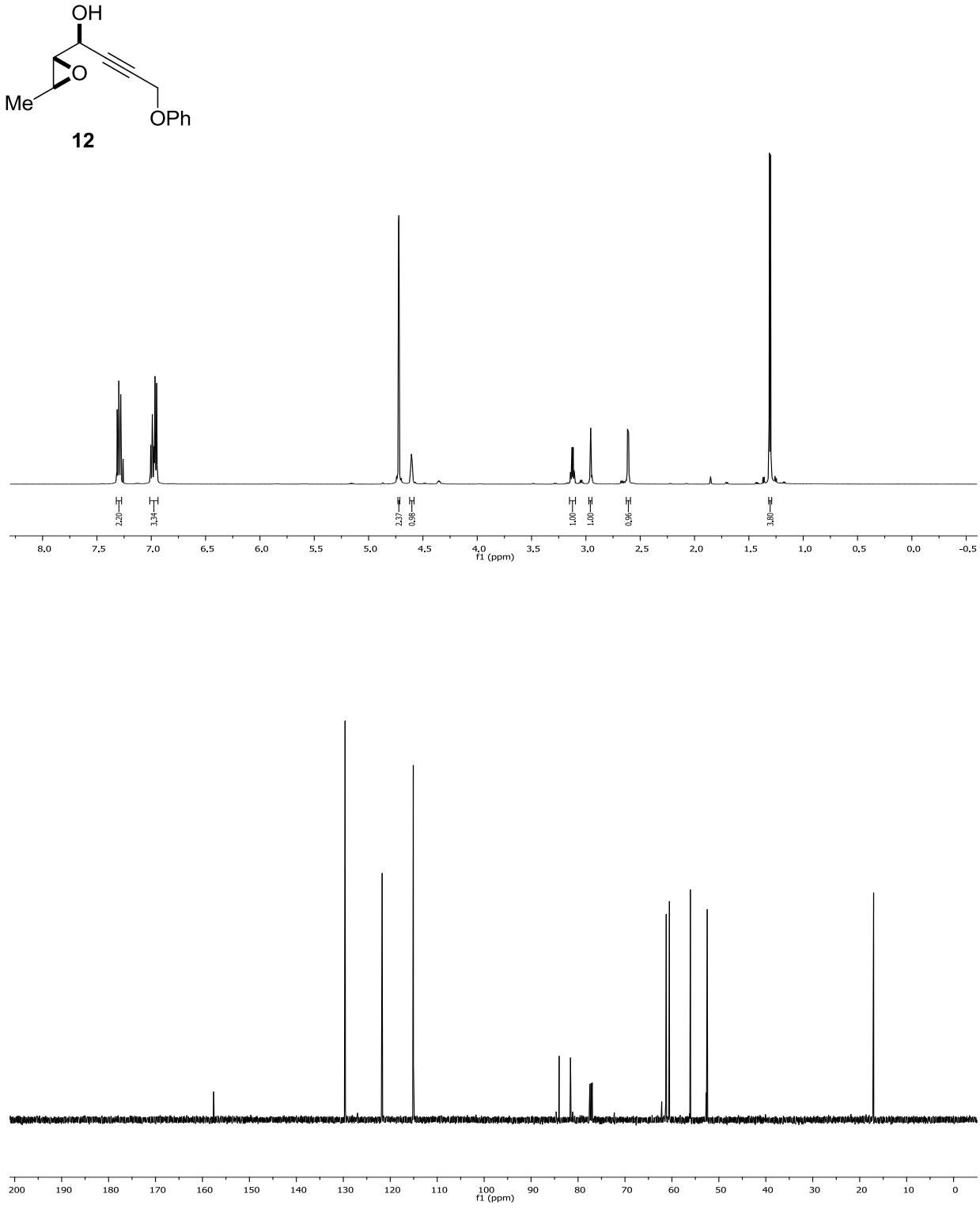


Figure S3: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **13**.

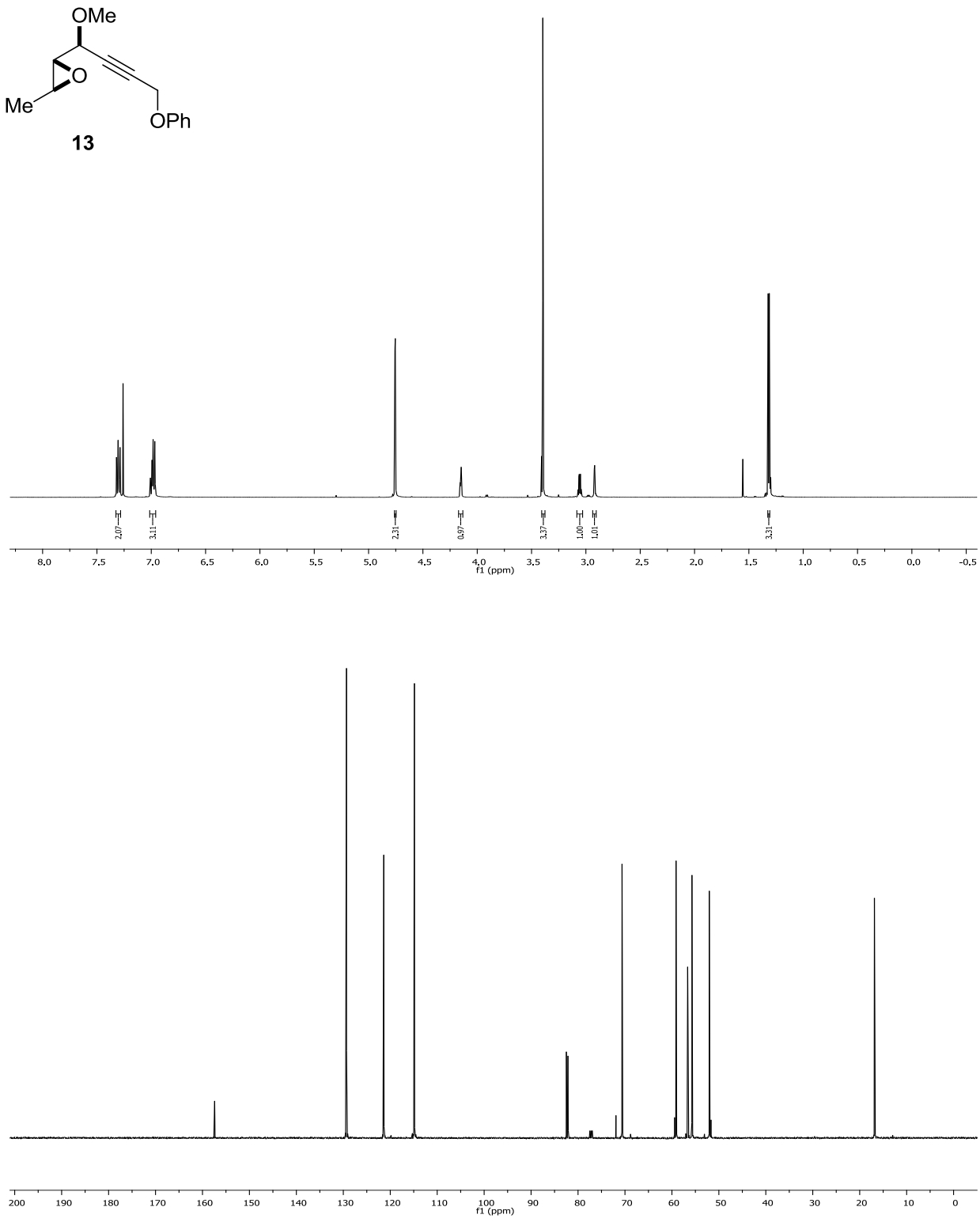


Figure S4: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **15**.

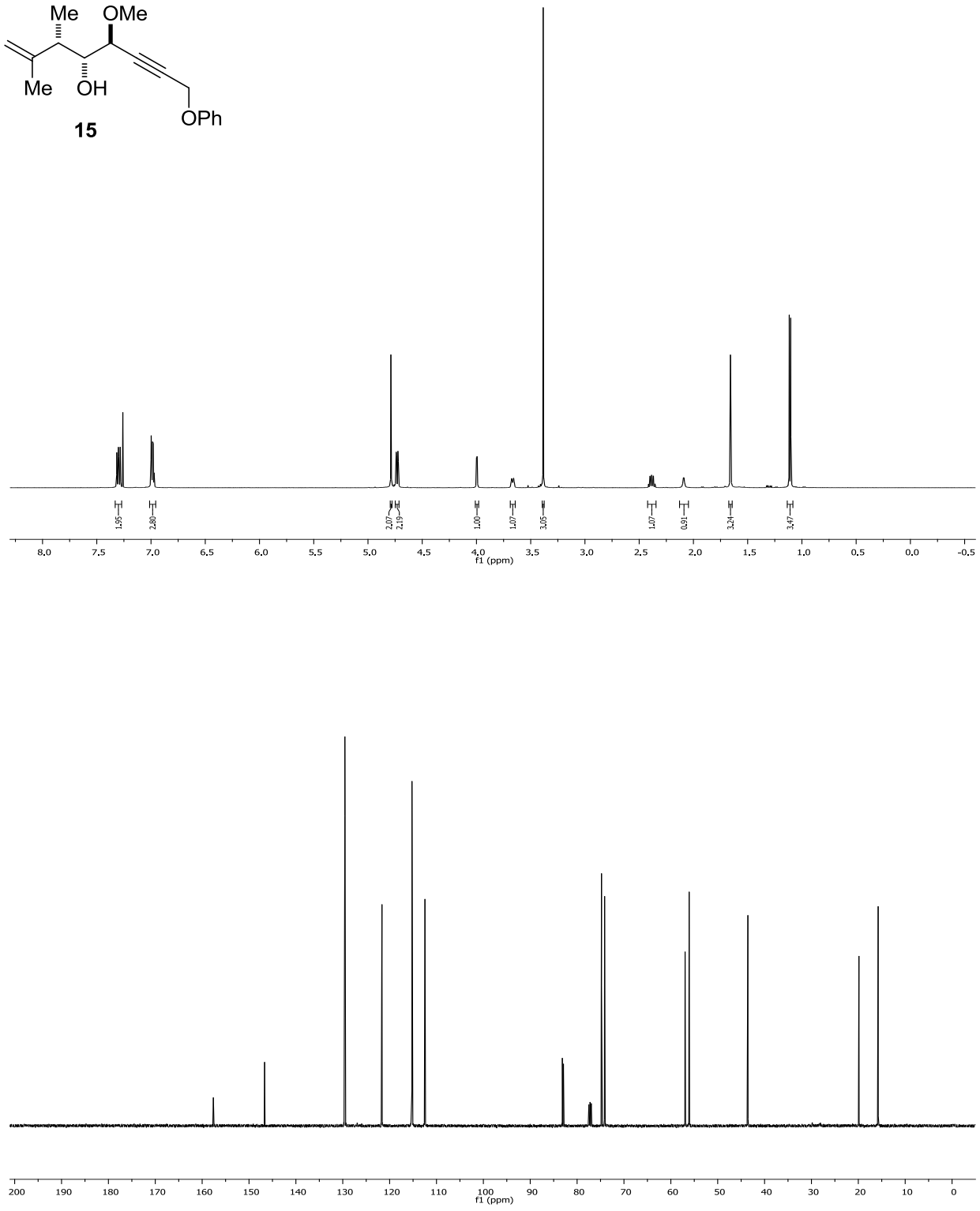


Figure S5: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **16**.

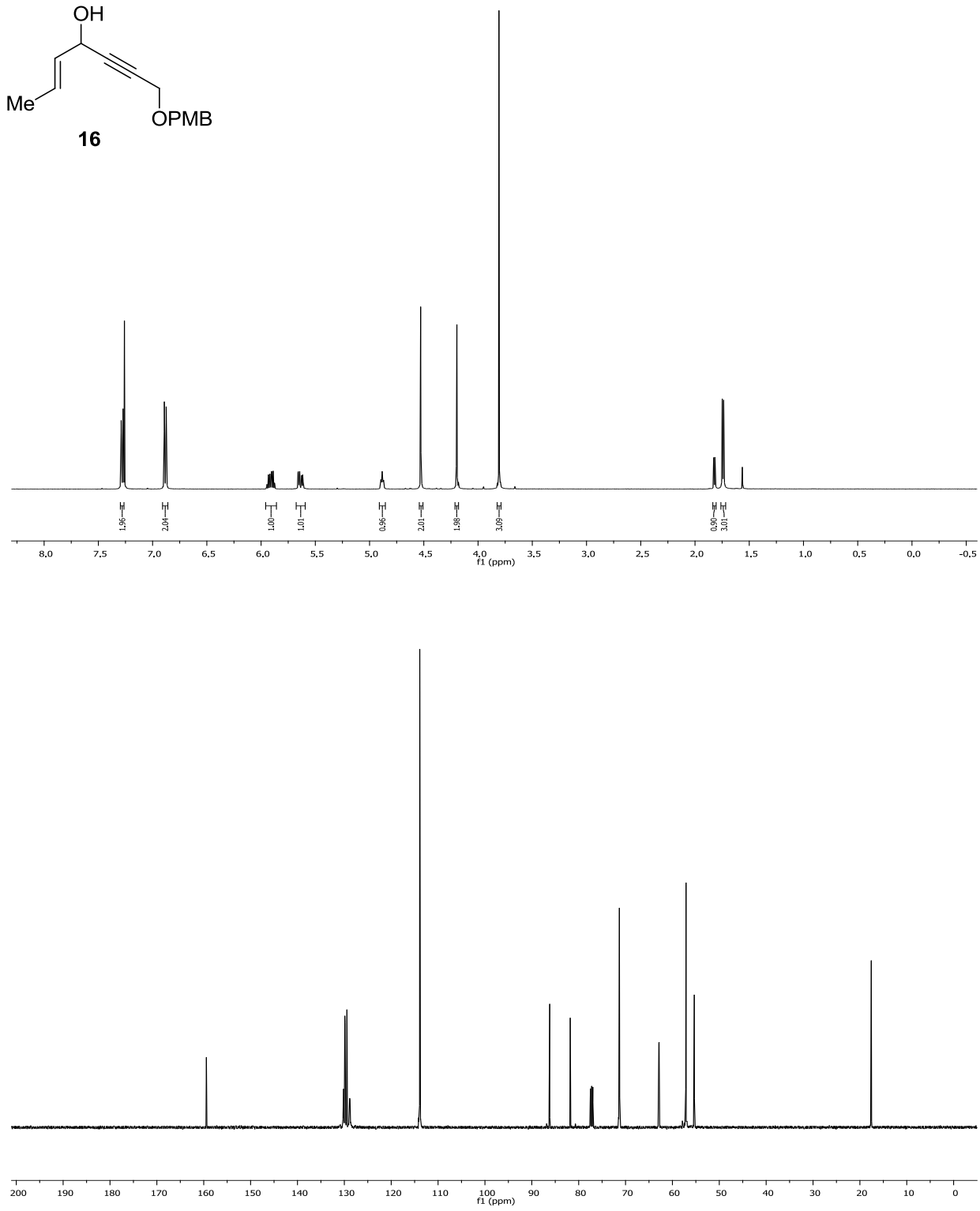
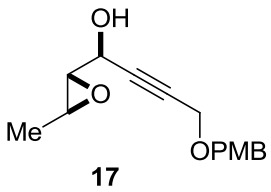
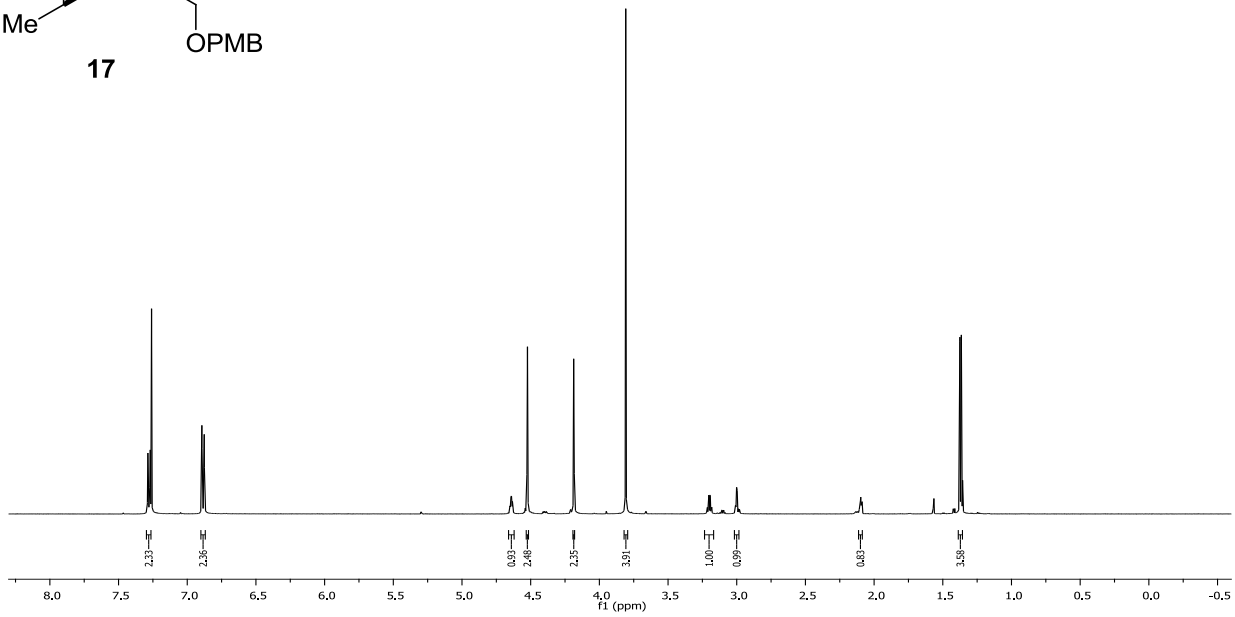


Figure S6: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **17.**



17



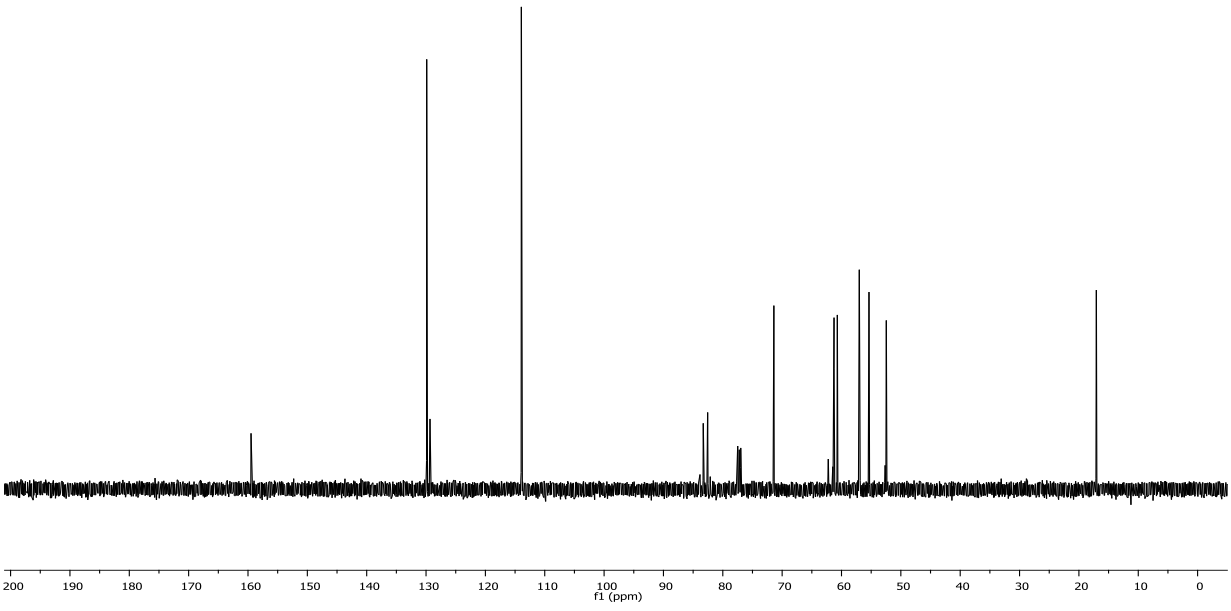
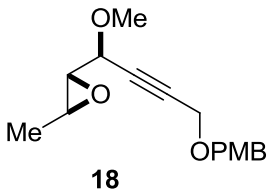
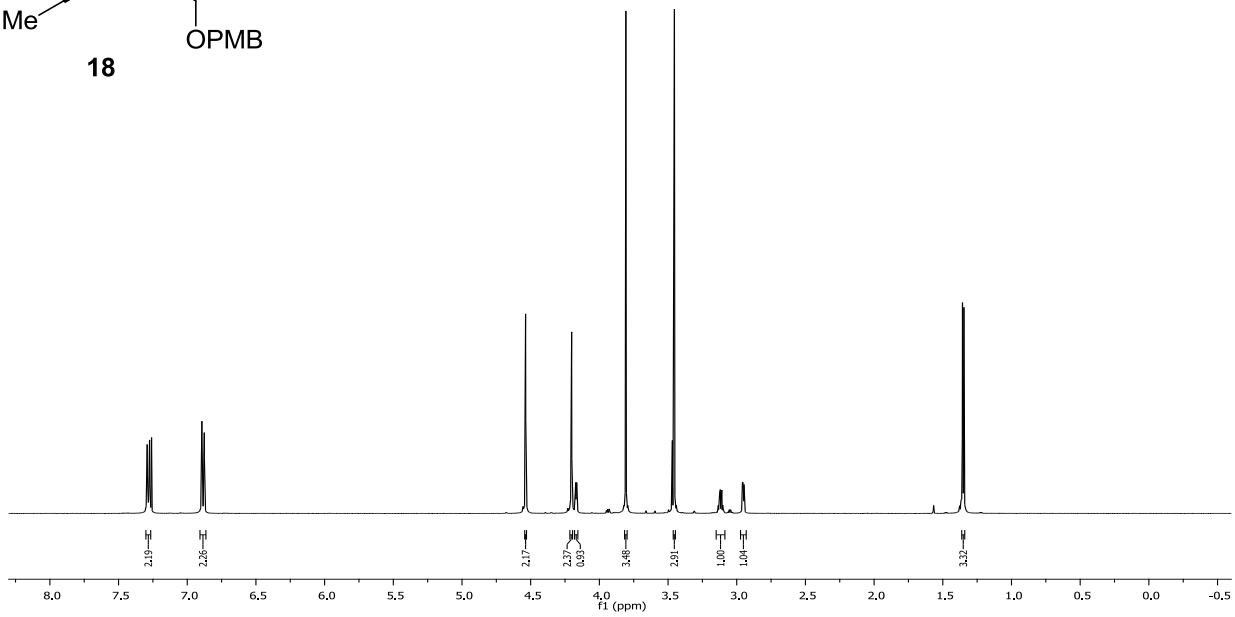


Figure S7: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **18.**



18



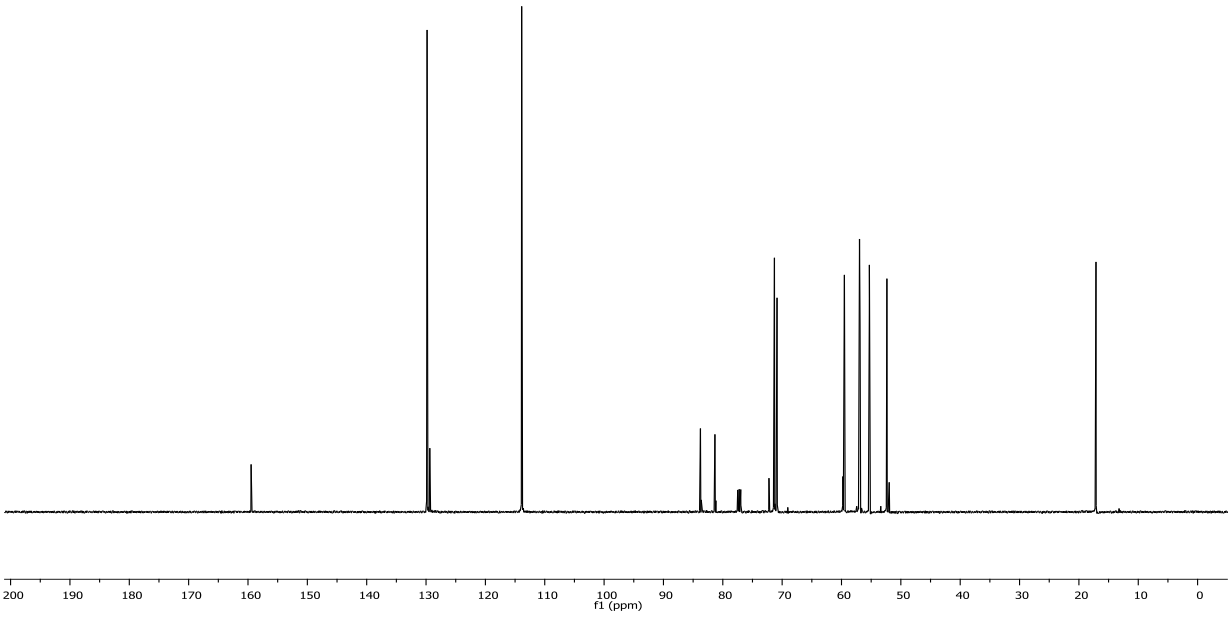


Figure S8: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **19.**

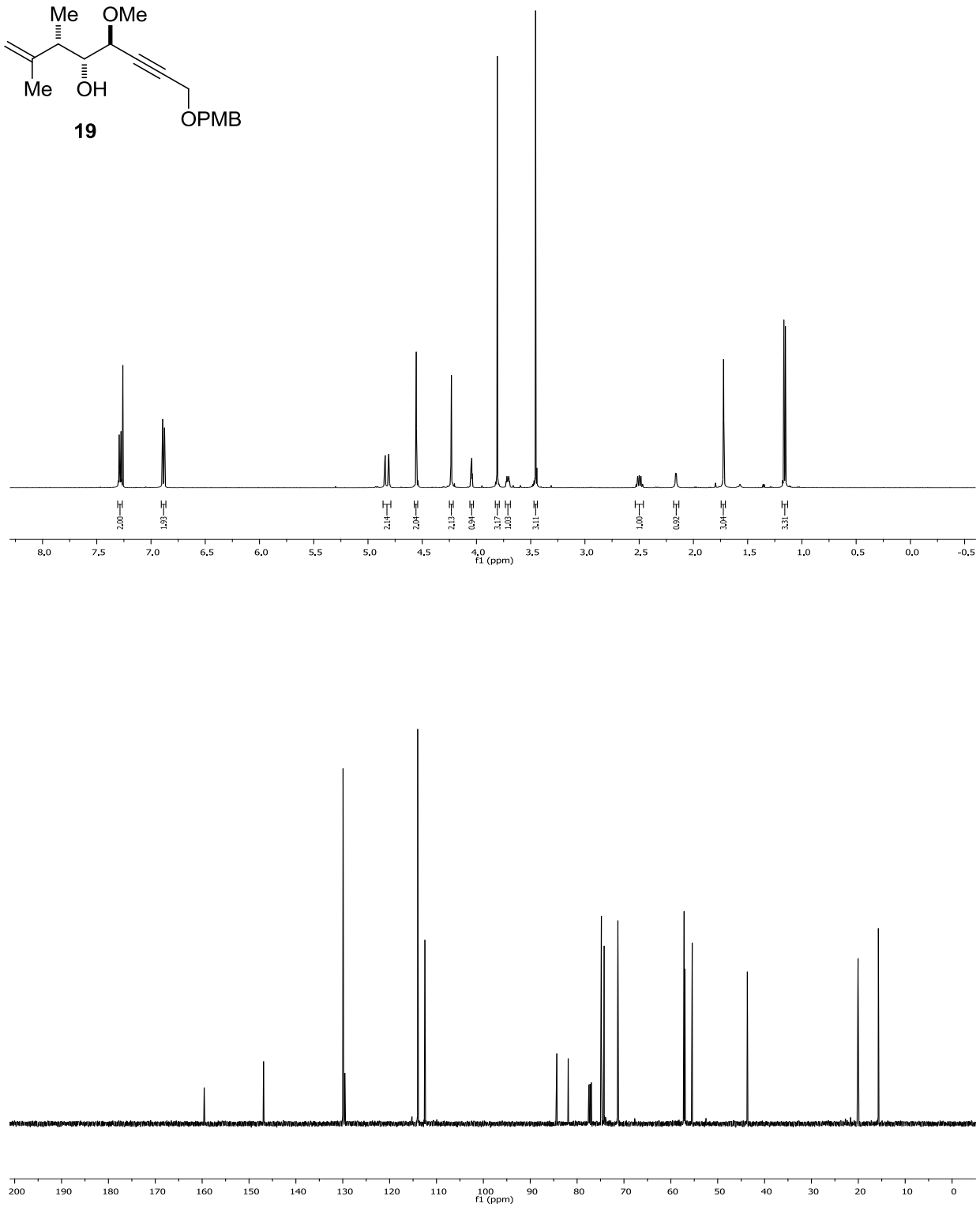


Figure S9: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **S4.**

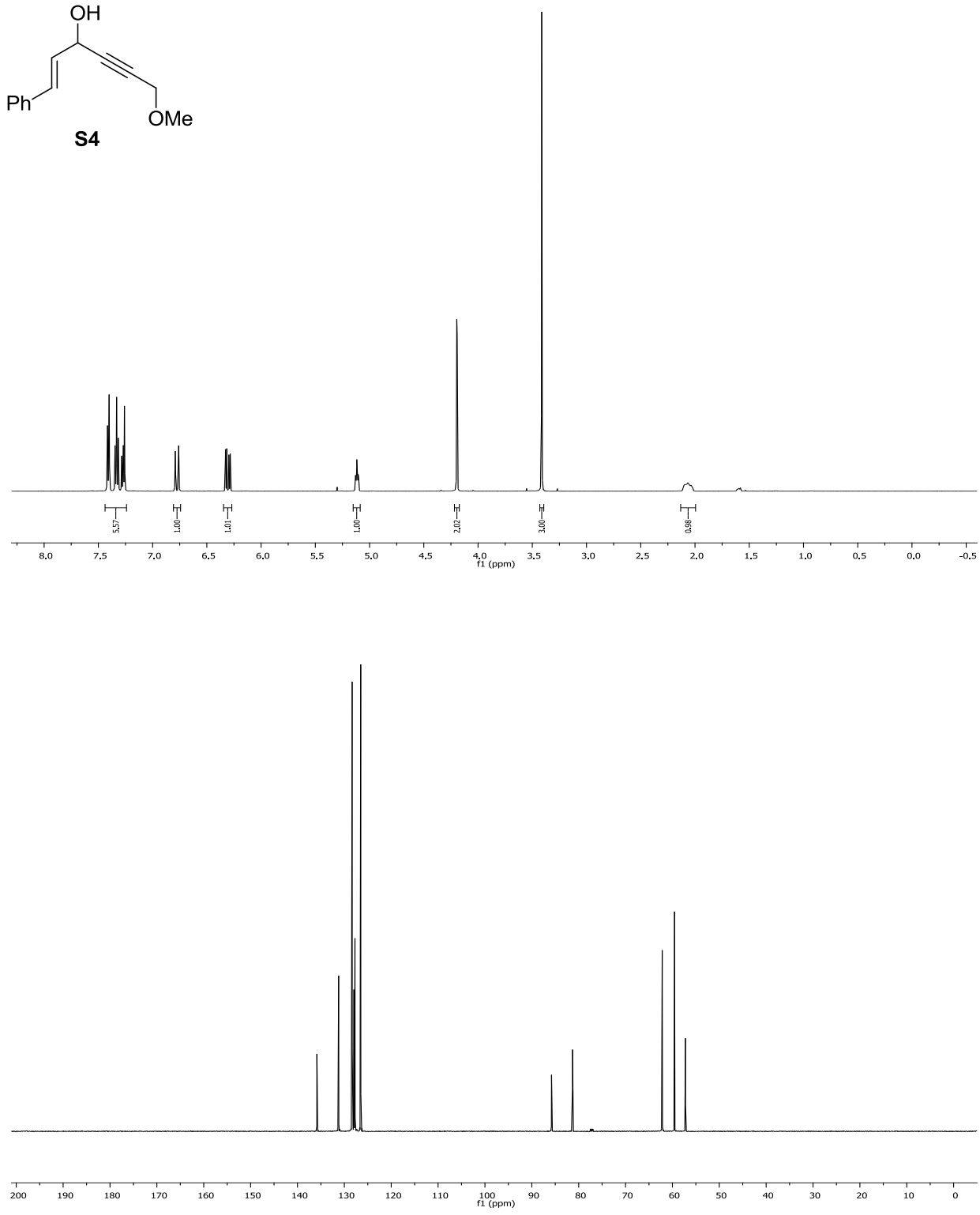
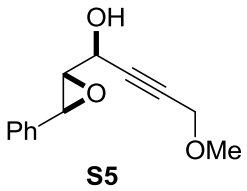
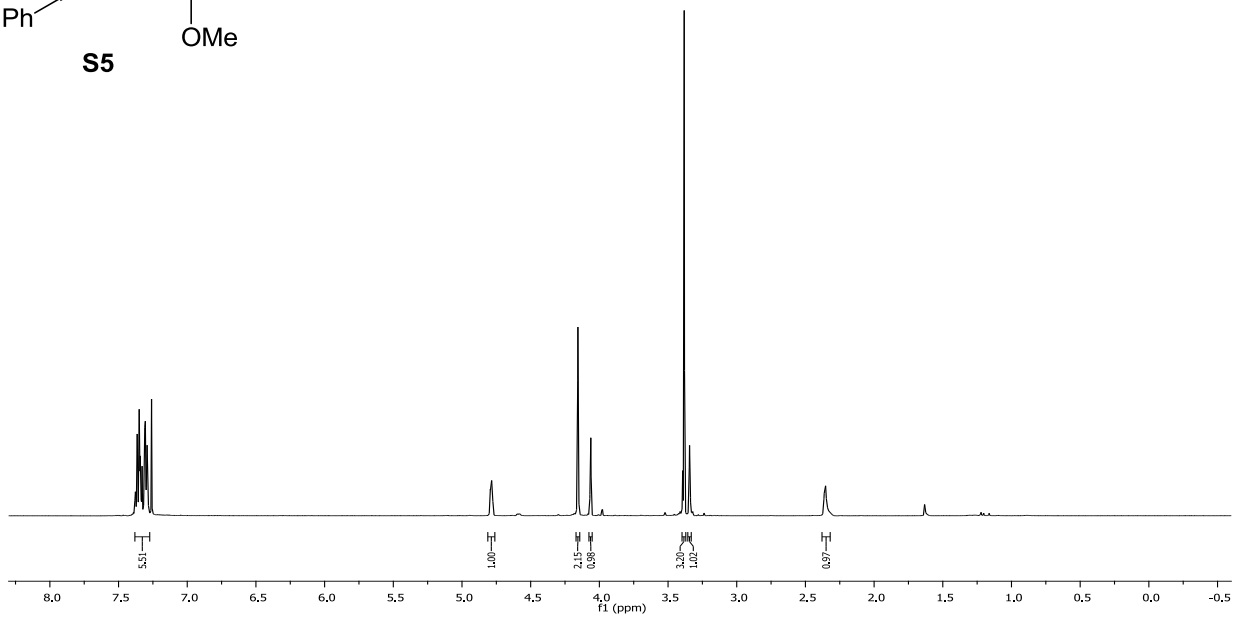


Figure S10: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **S5.**



S5



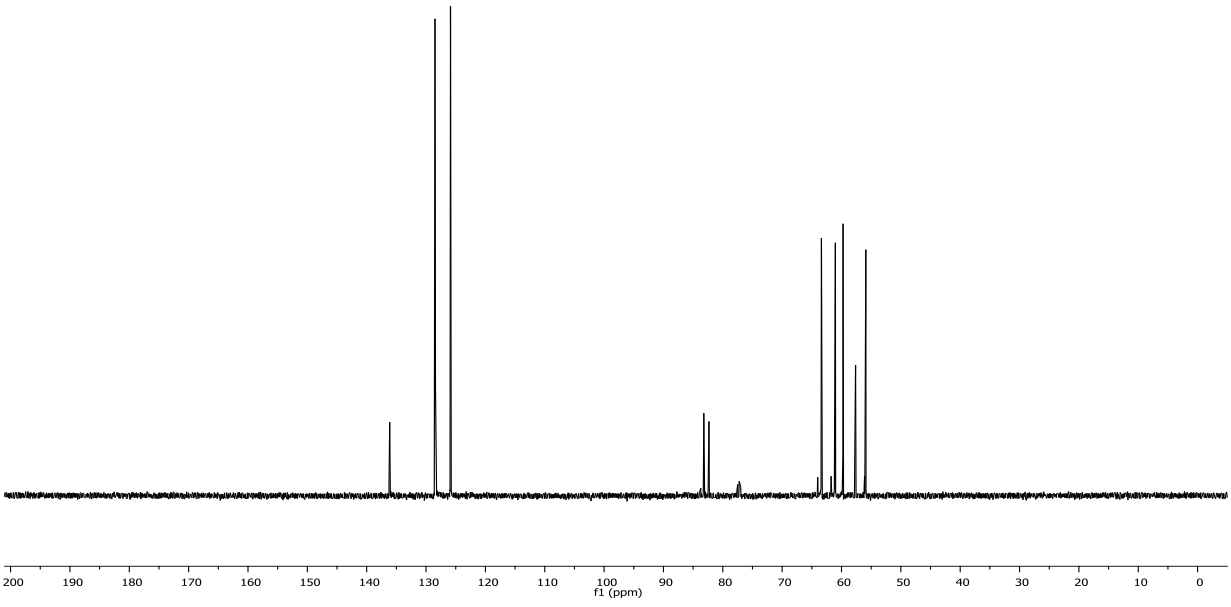


Figure S11: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **S6.**

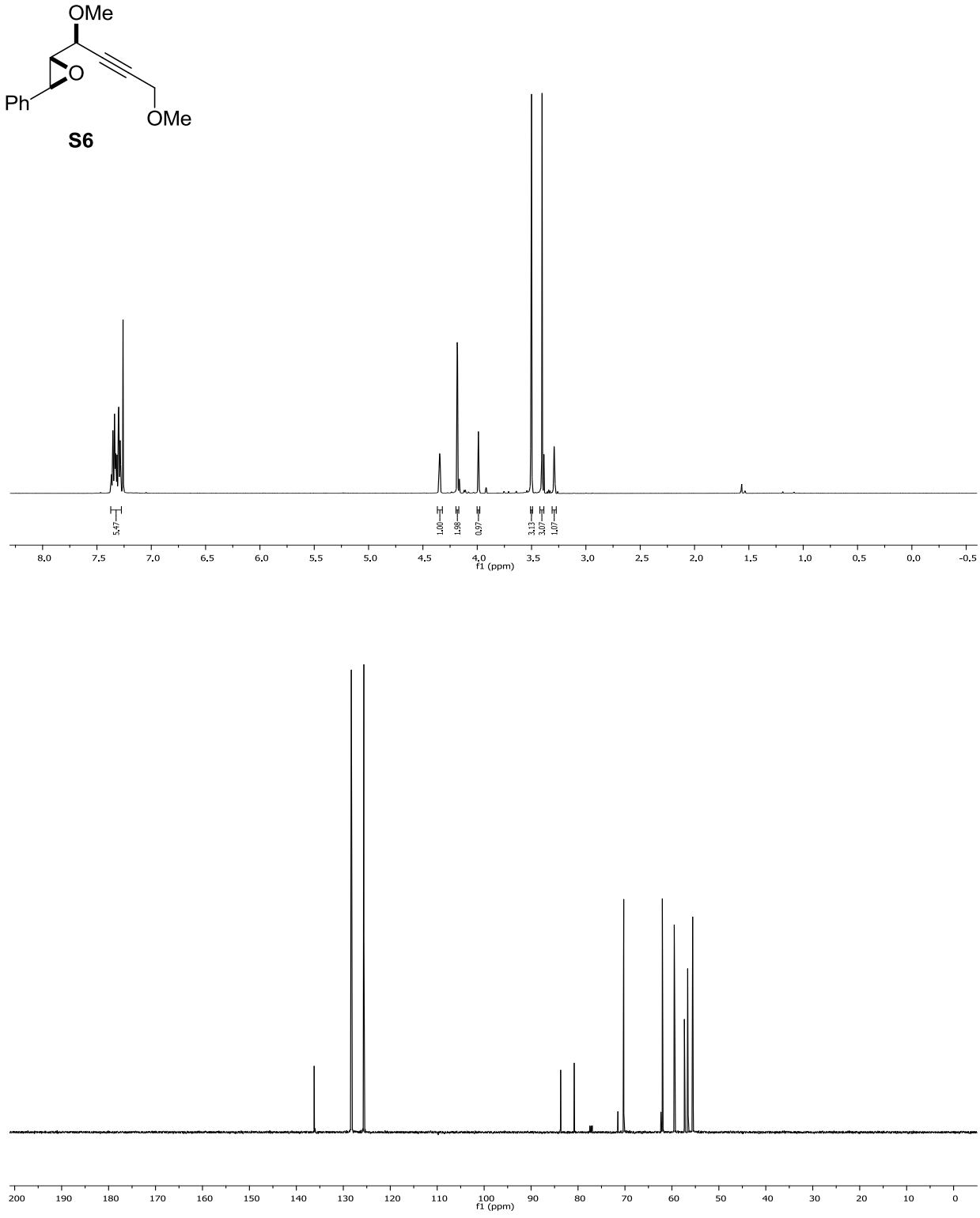


Figure S12: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **25**.

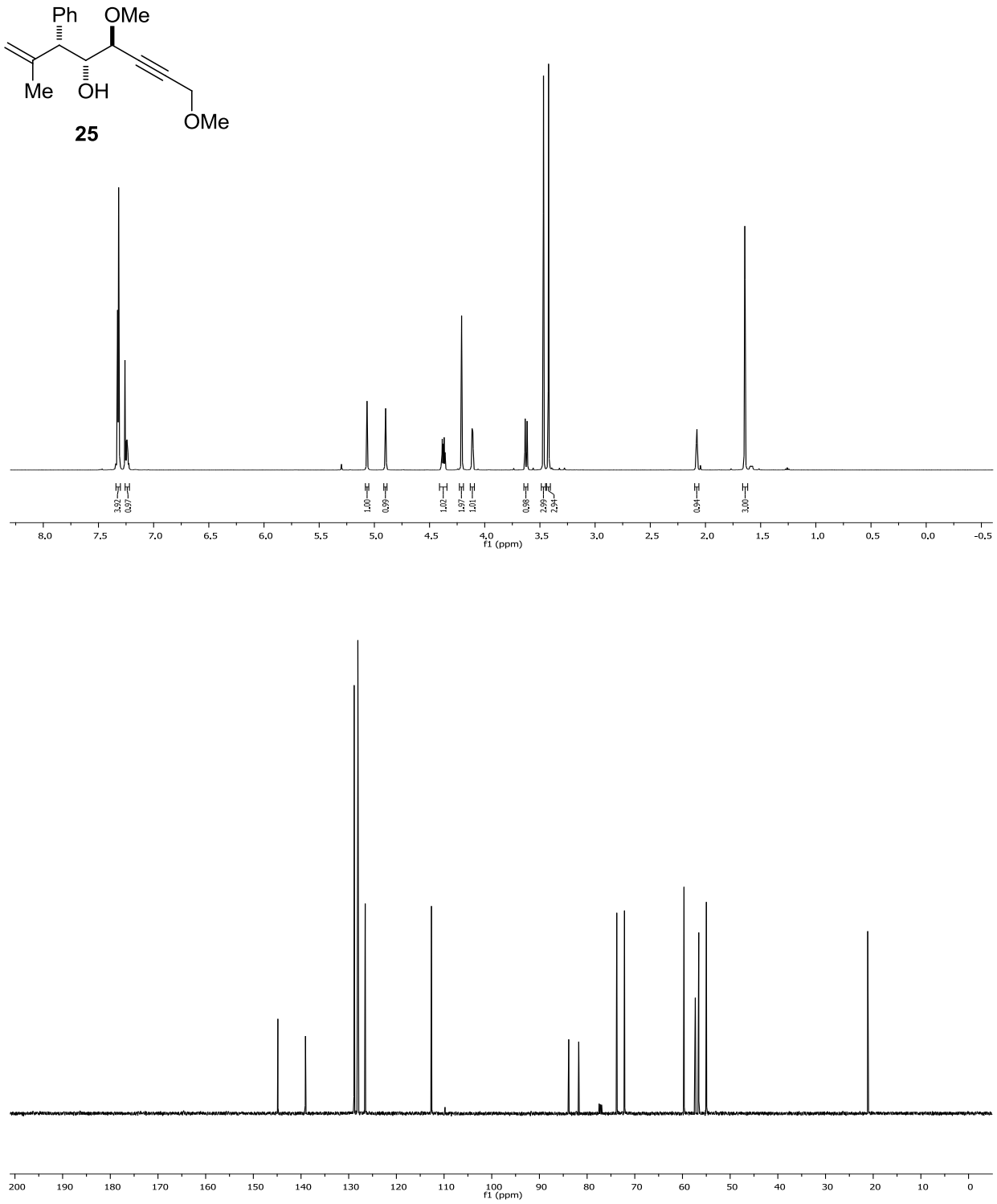


Figure S13: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **41**.

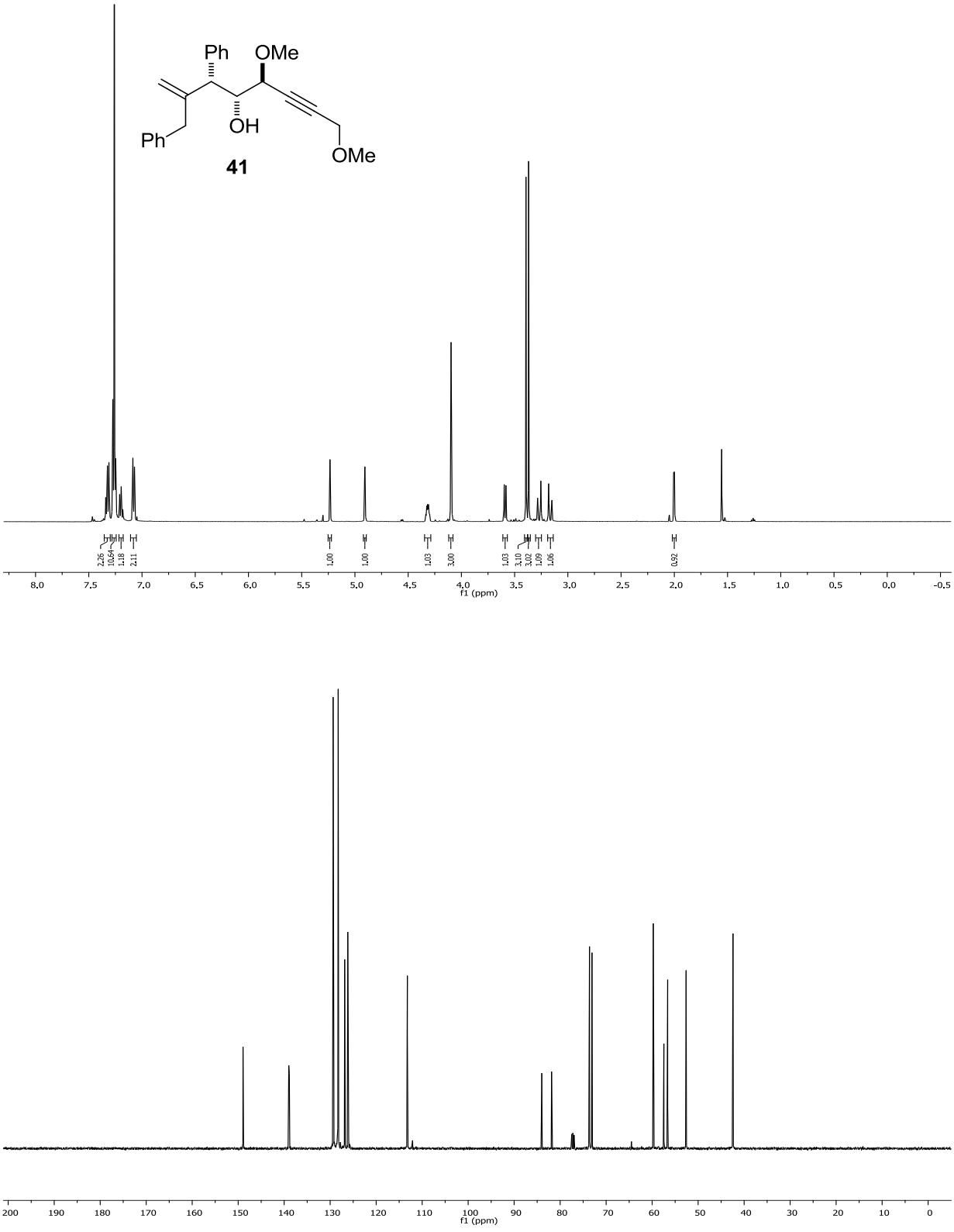


Figure S14: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **S8**.

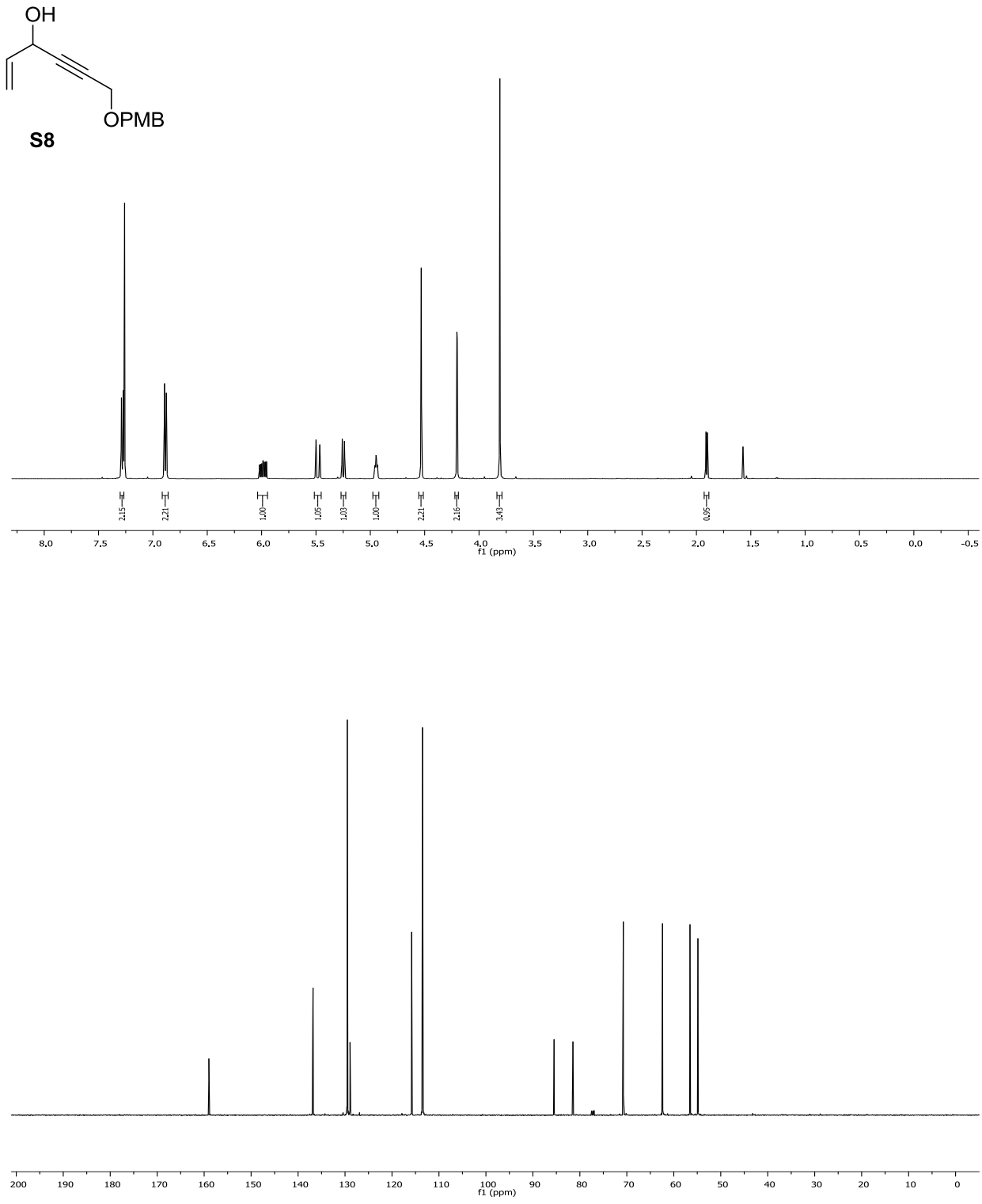
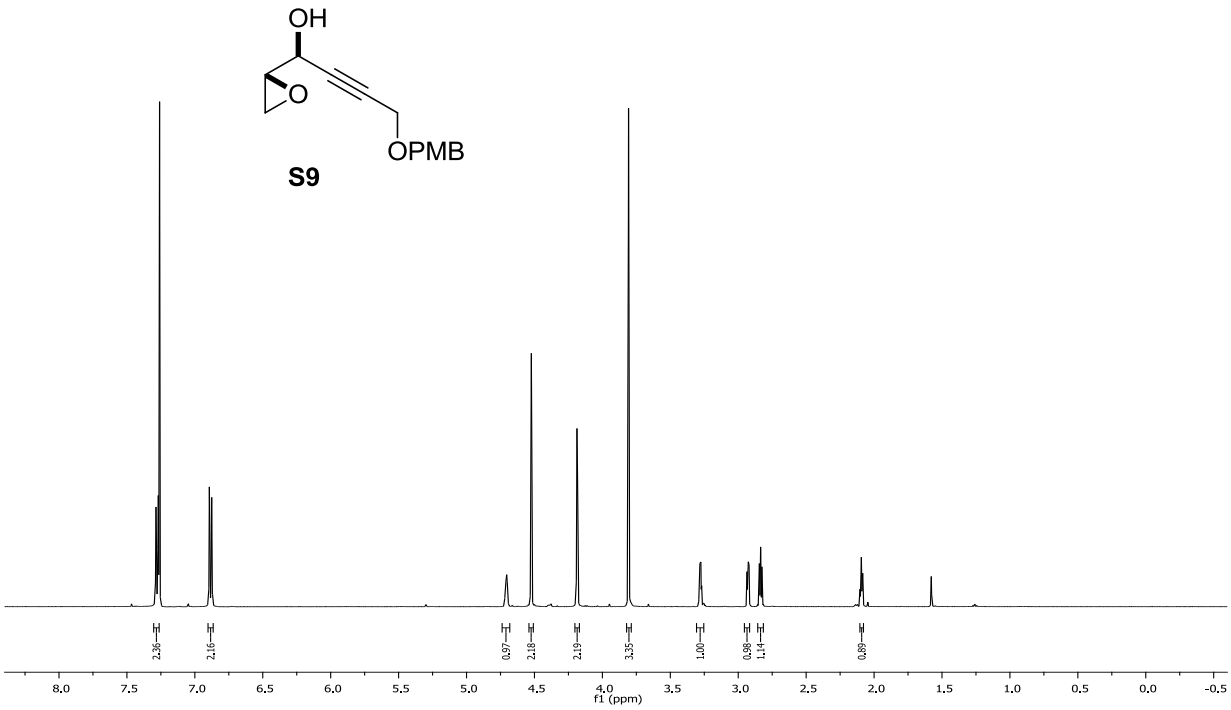


Figure S15: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **S9**.



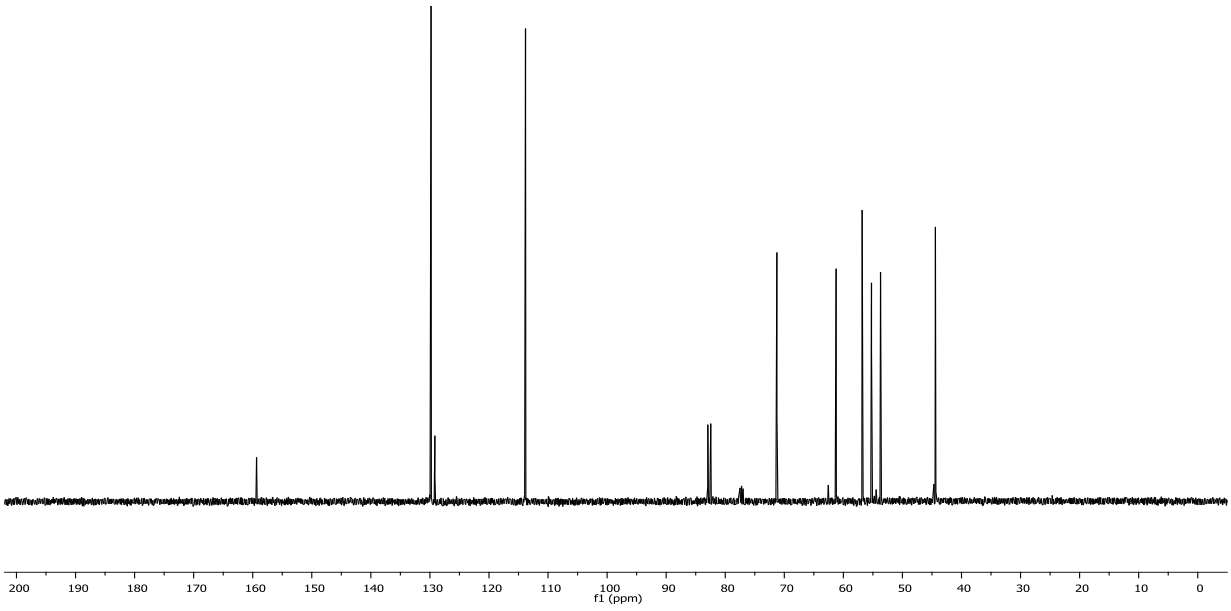


Figure S16: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **S10**.

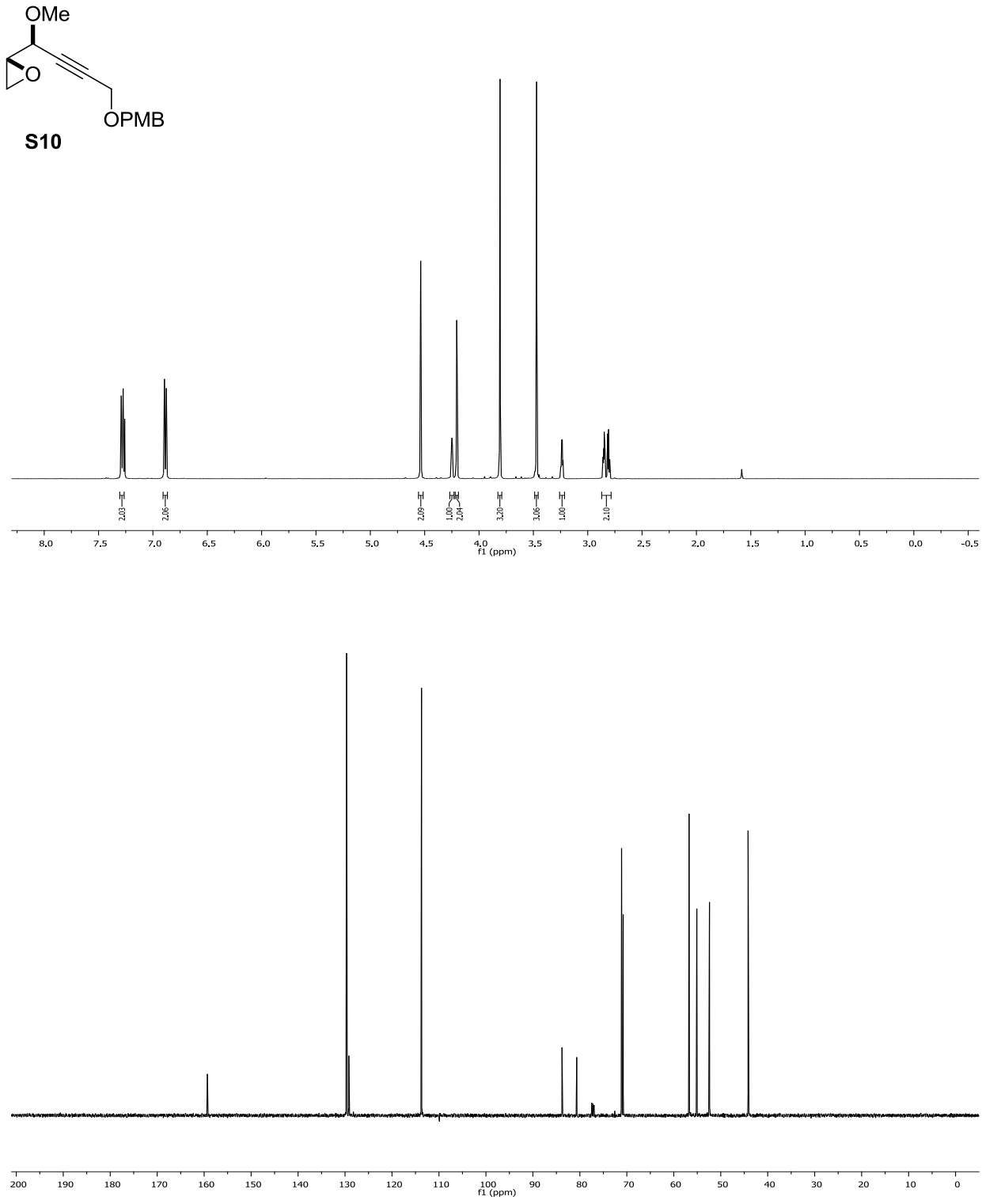


Figure S17: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **31**.

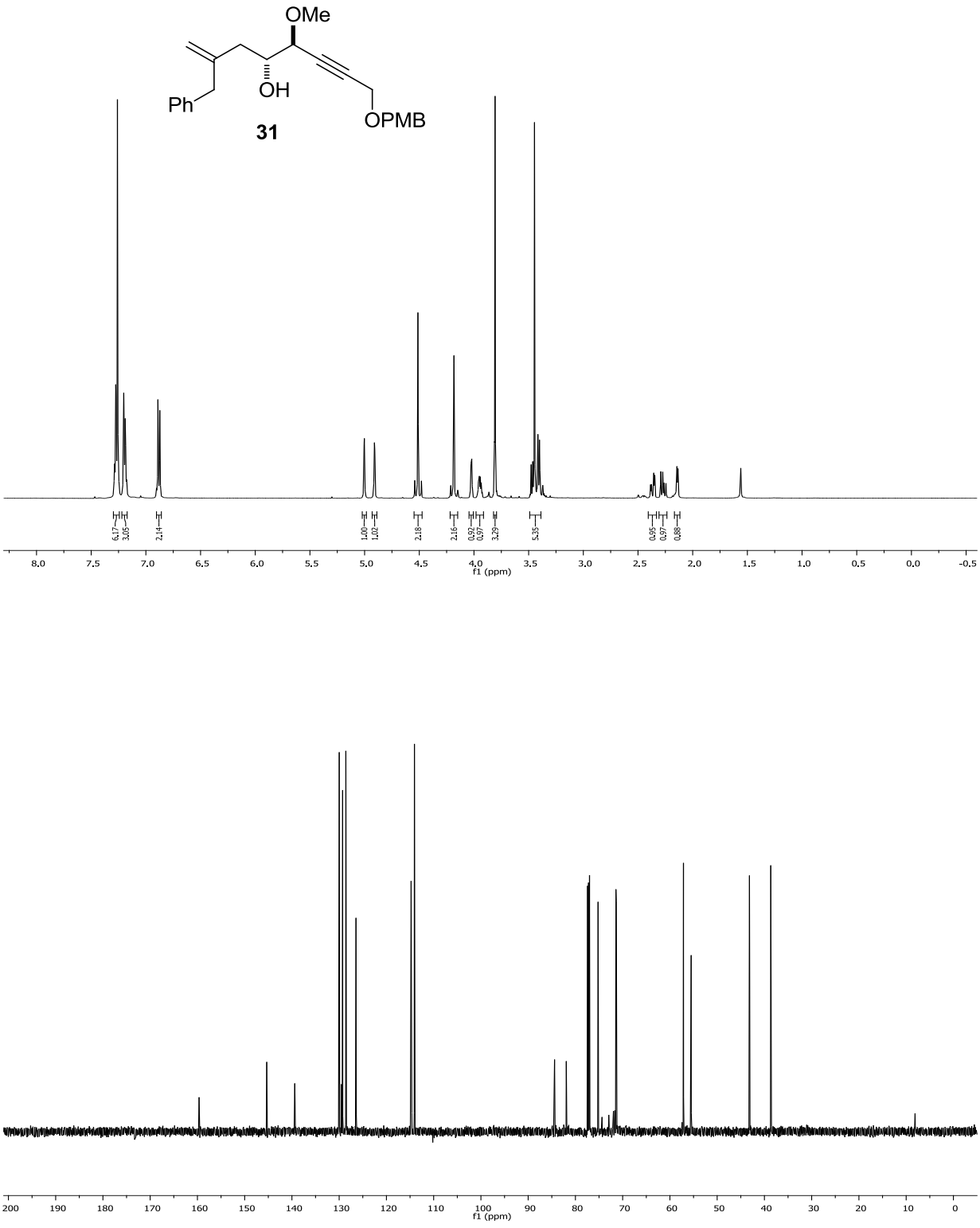


Figure S18: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **38**.

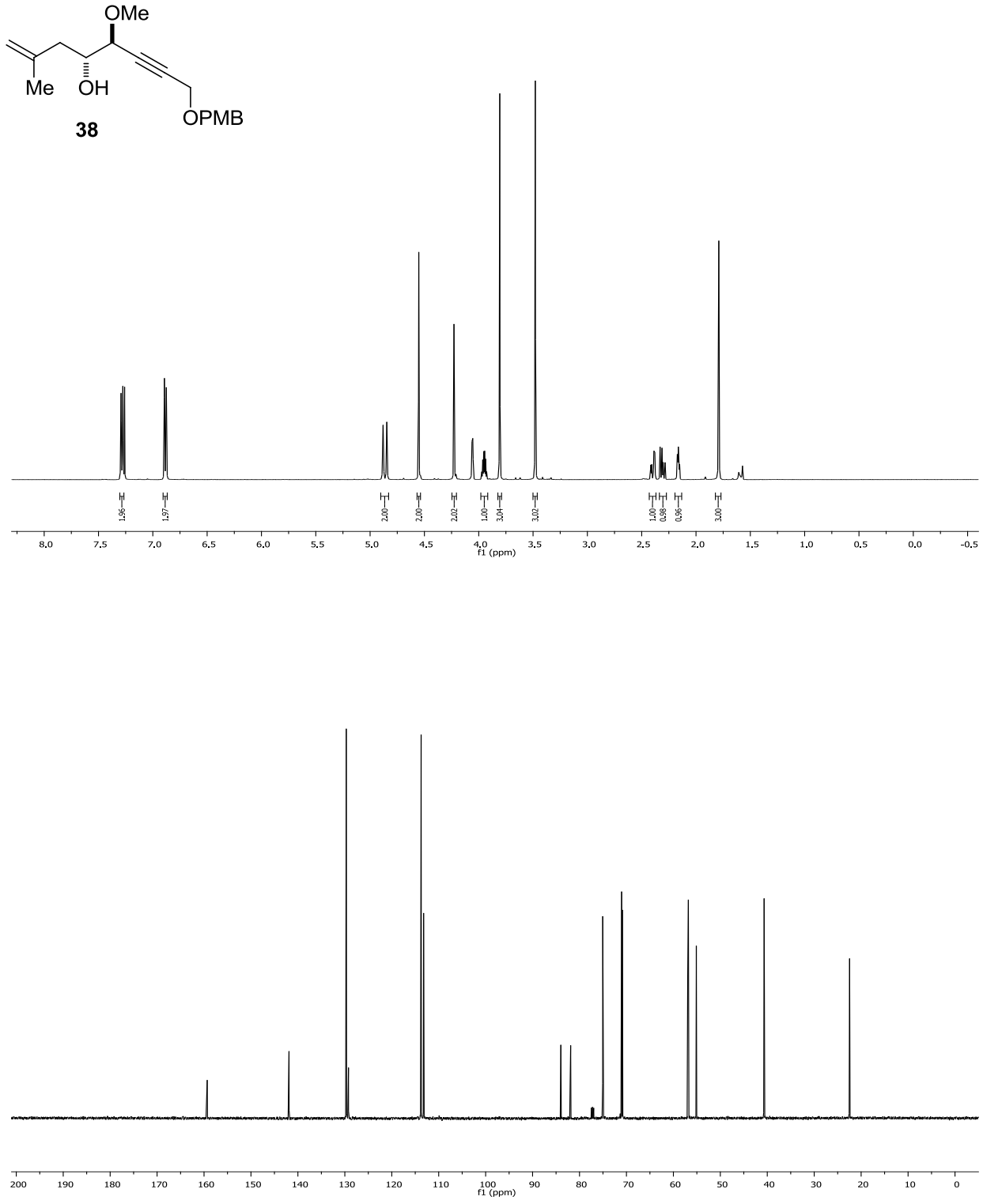
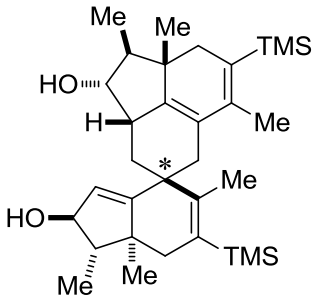


Figure S19: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **22**.



22

The stereochemistry at the highlighted carbon (∗) is assumed.

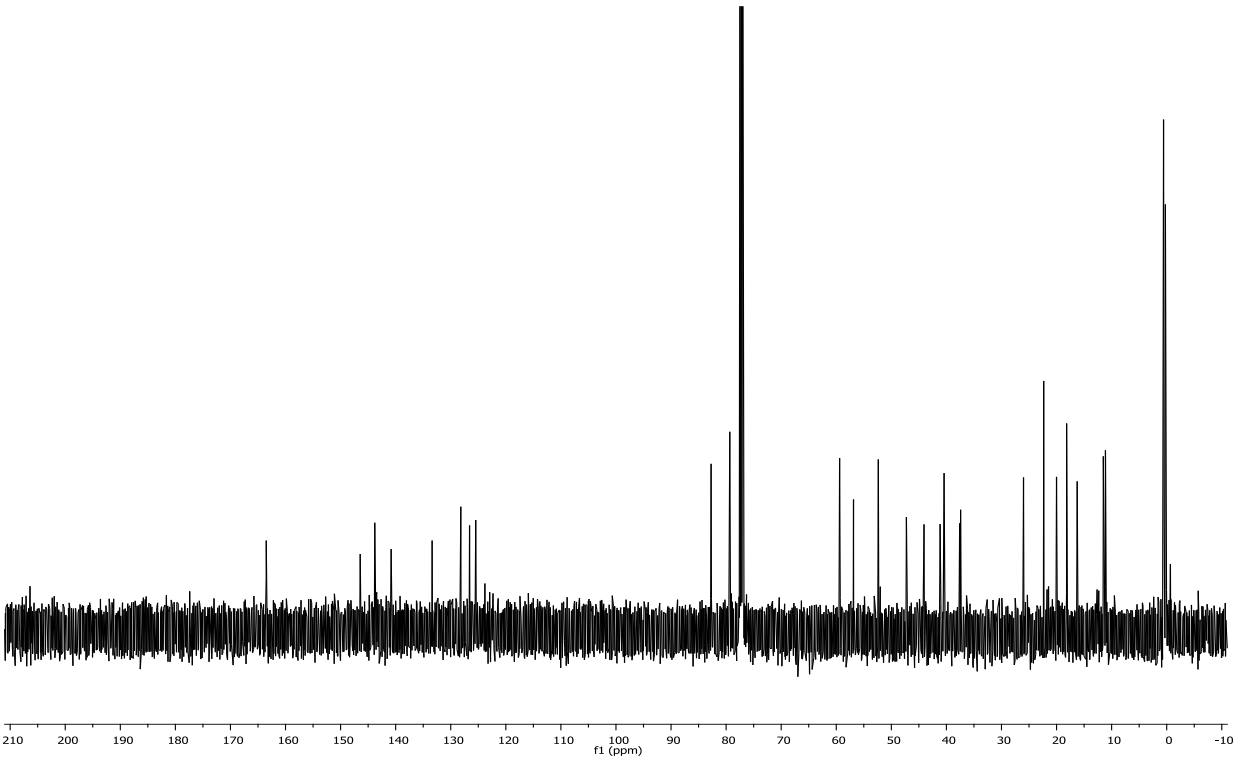


Figure S20: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **23**.

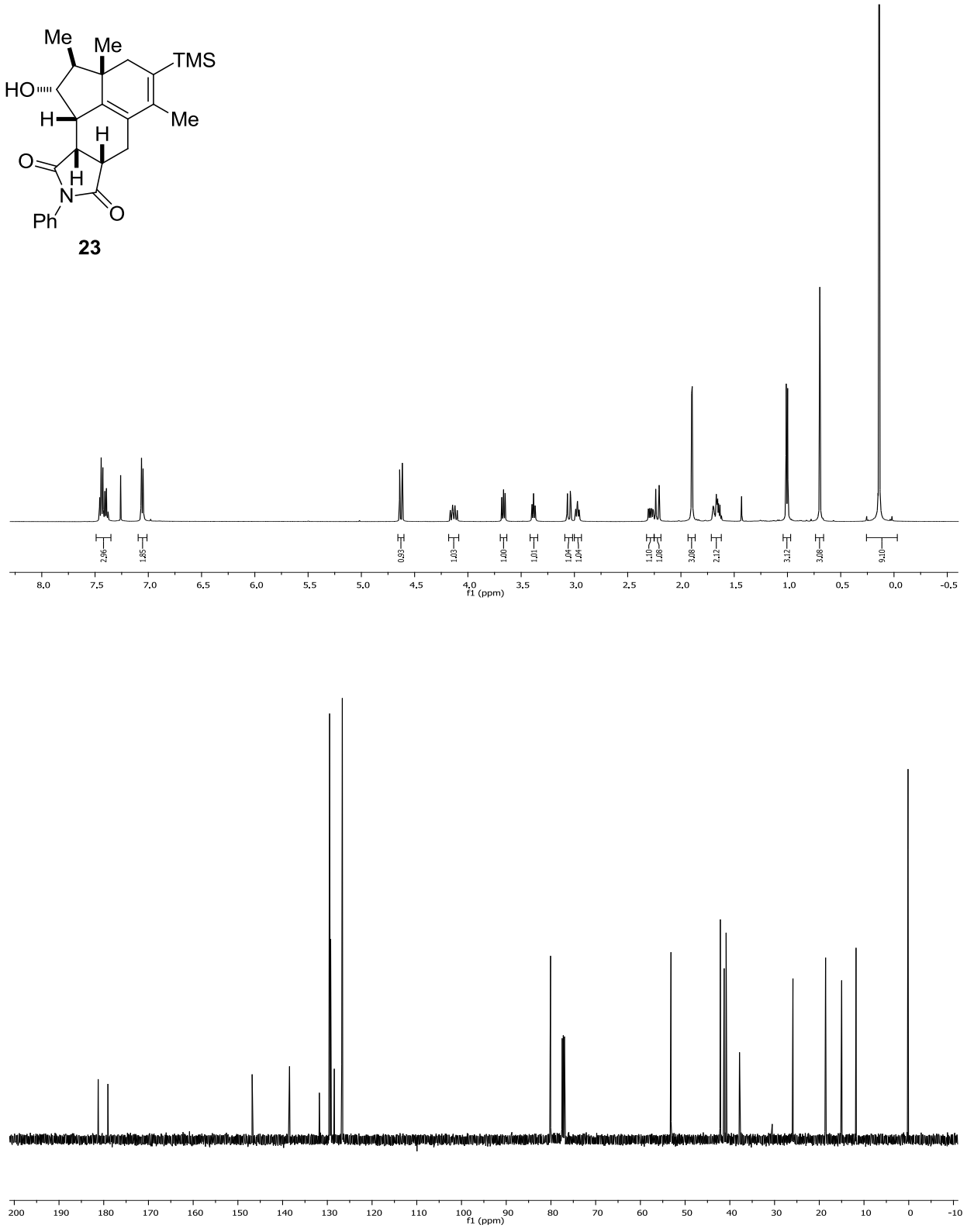
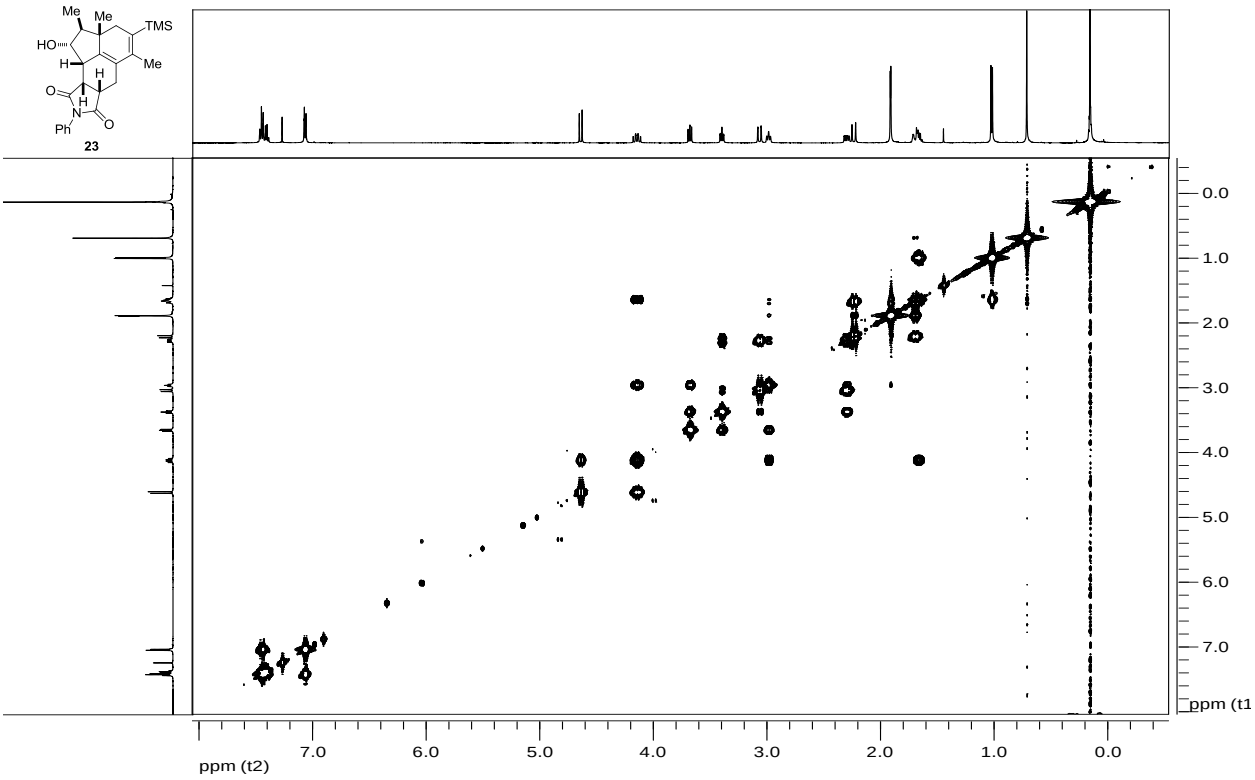


Figure S21: COSY (500 MHz, $CDCl_3$) of **23**.



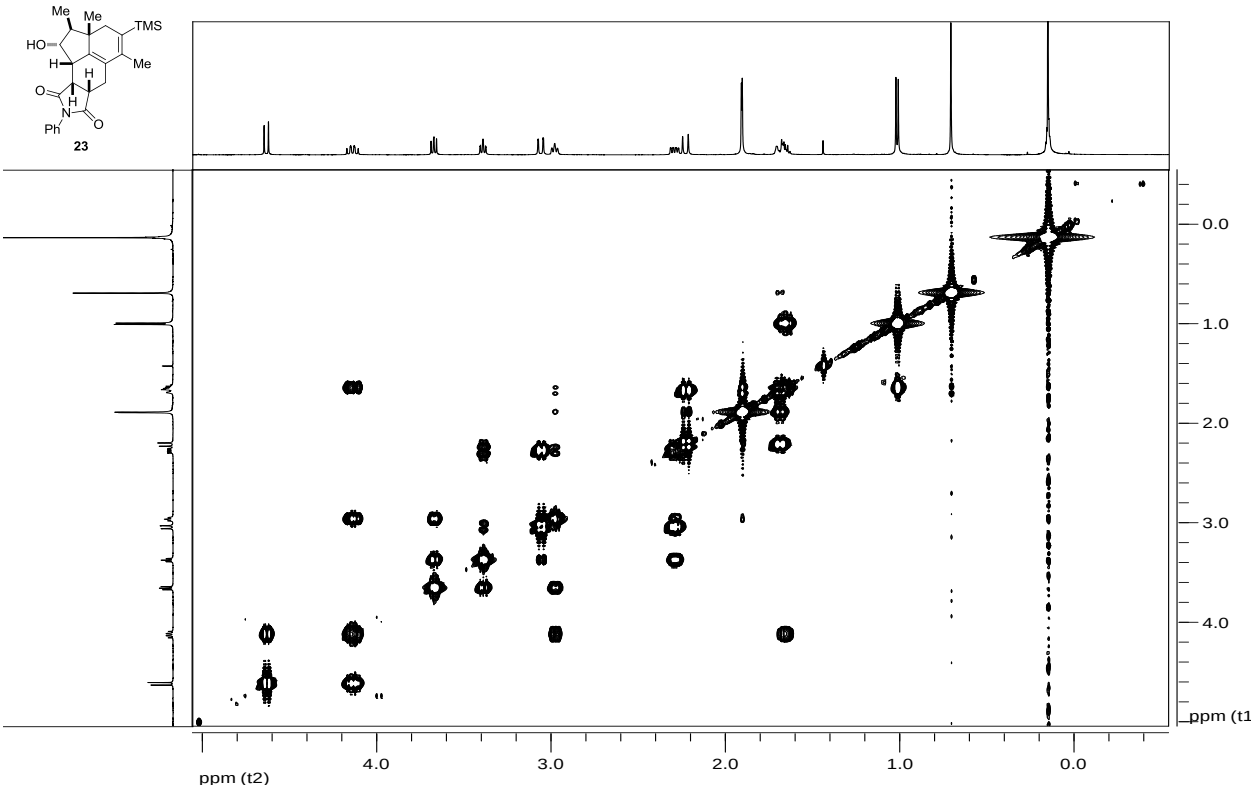


Figure S22: HMQC (500 MHz and 125 MHz, $CDCl_3$) of **23**.

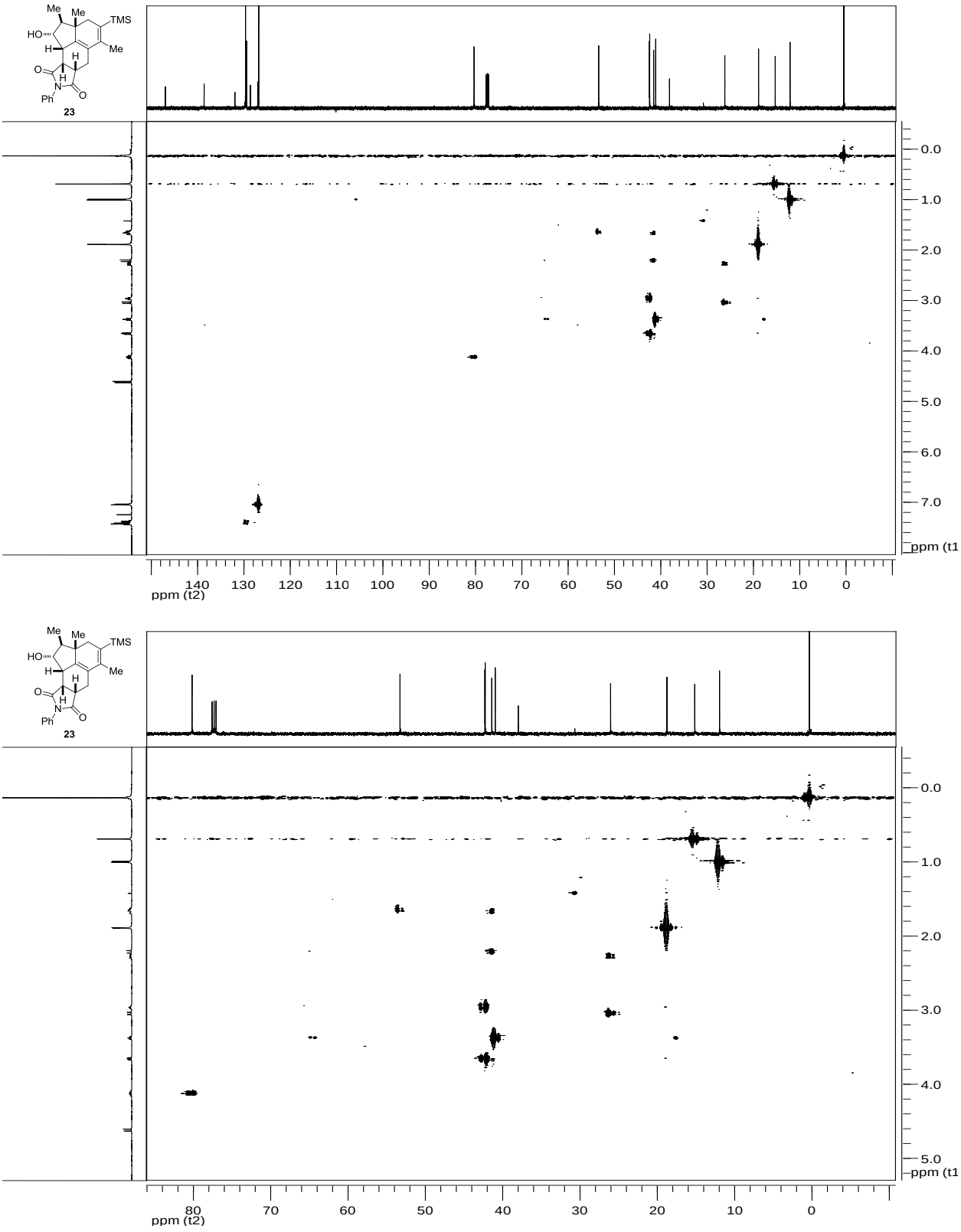


Figure S23: NOESY (500 MHz, $CDCl_3$) of **23**.

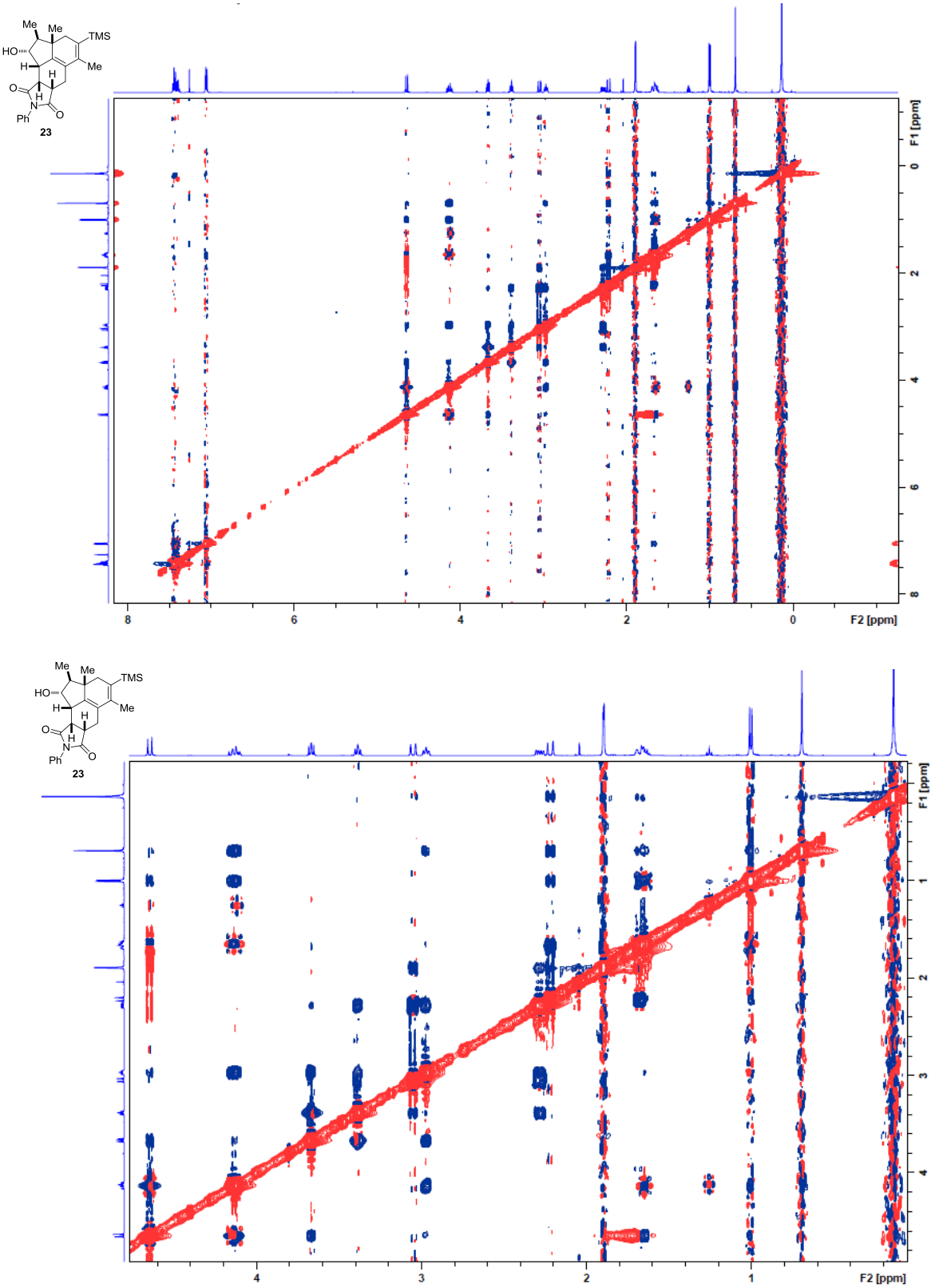


Figure S24: ^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **28**.

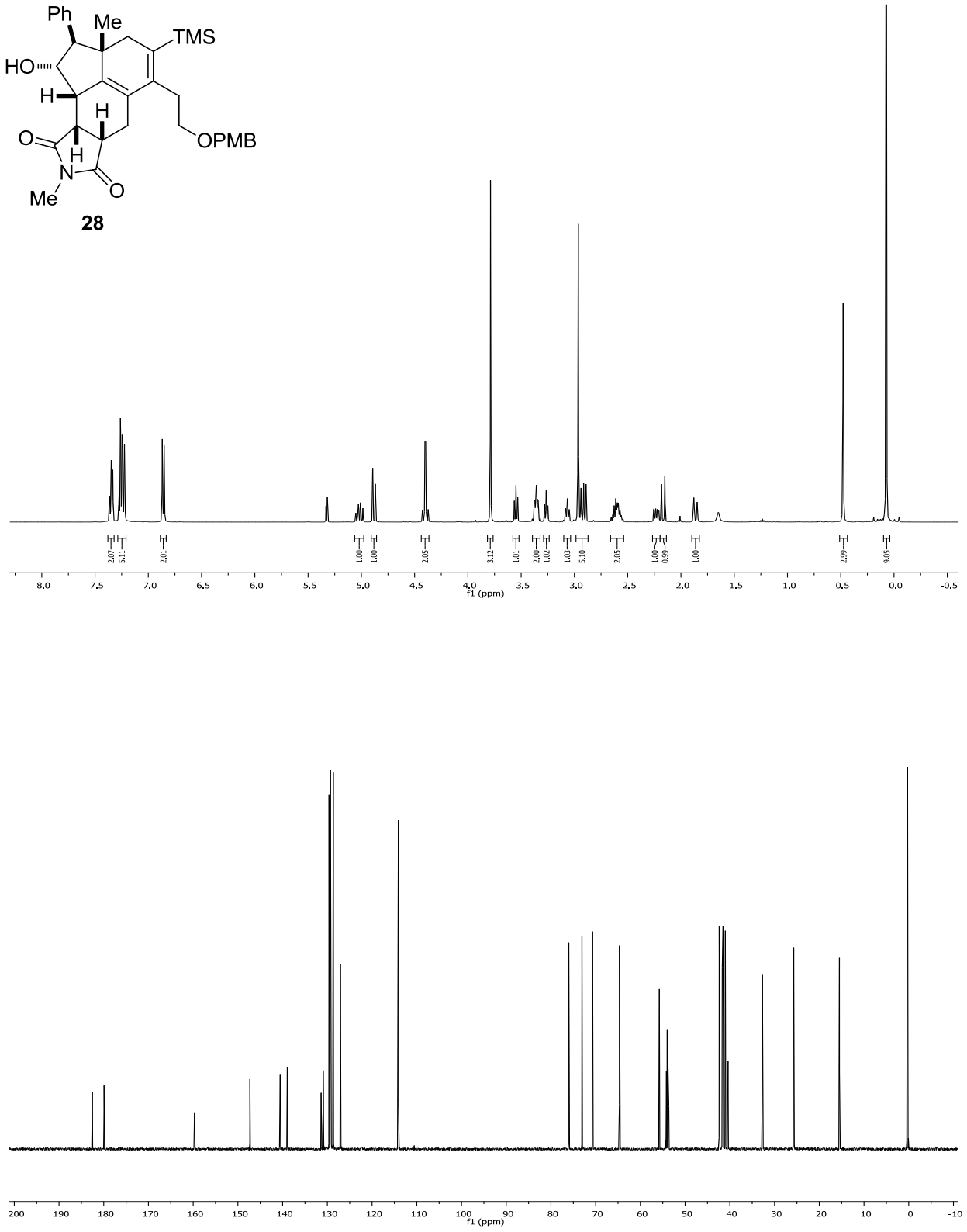


Figure S25: COSY (500 MHz, CD_2Cl_2) of **28**.

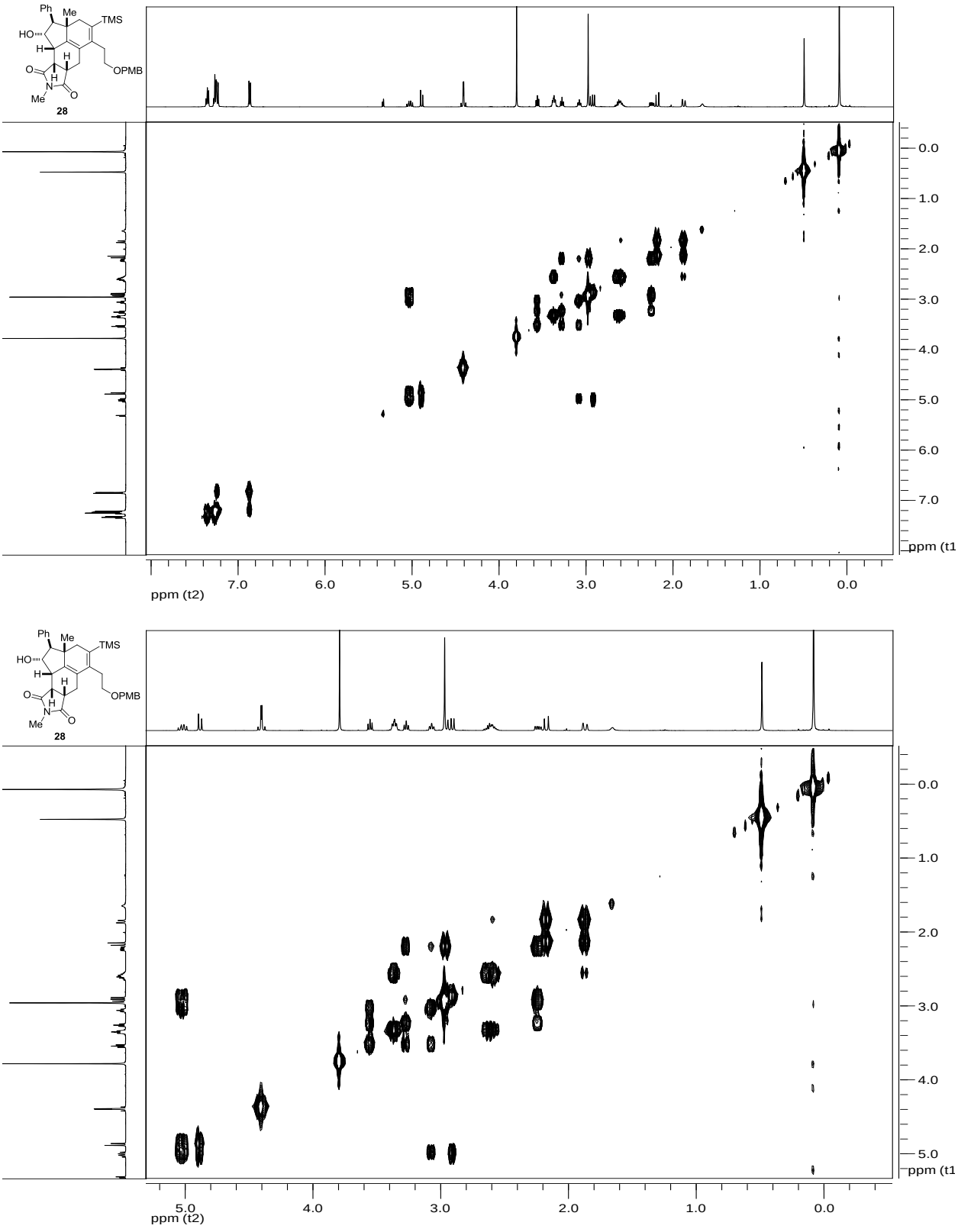


Figure S26: HMQC (500 MHz and 125 MHz, CD_2Cl_2) of **28**.

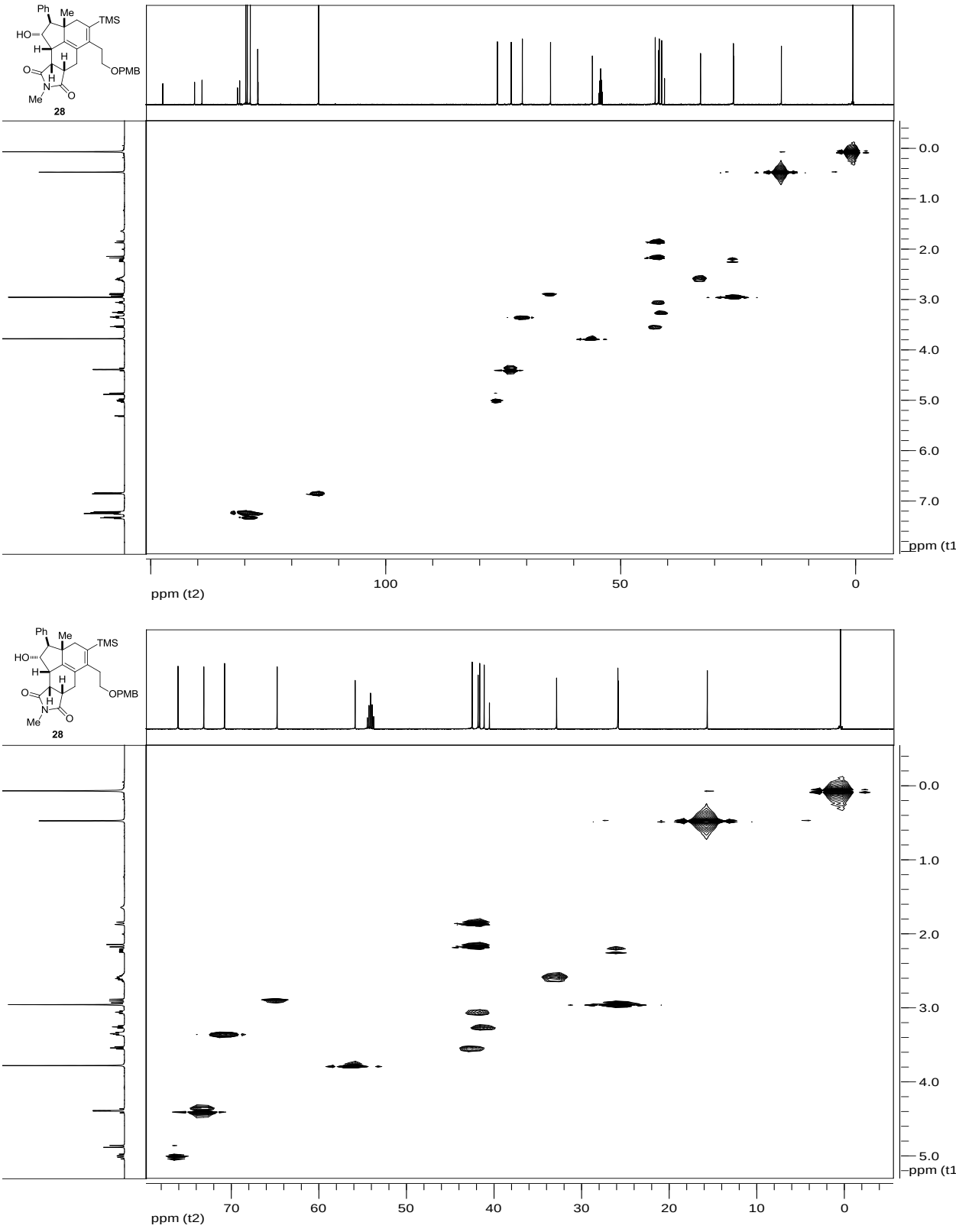


Figure S27: TOCSY (500 MHz, CD_2Cl_2) of **28**.

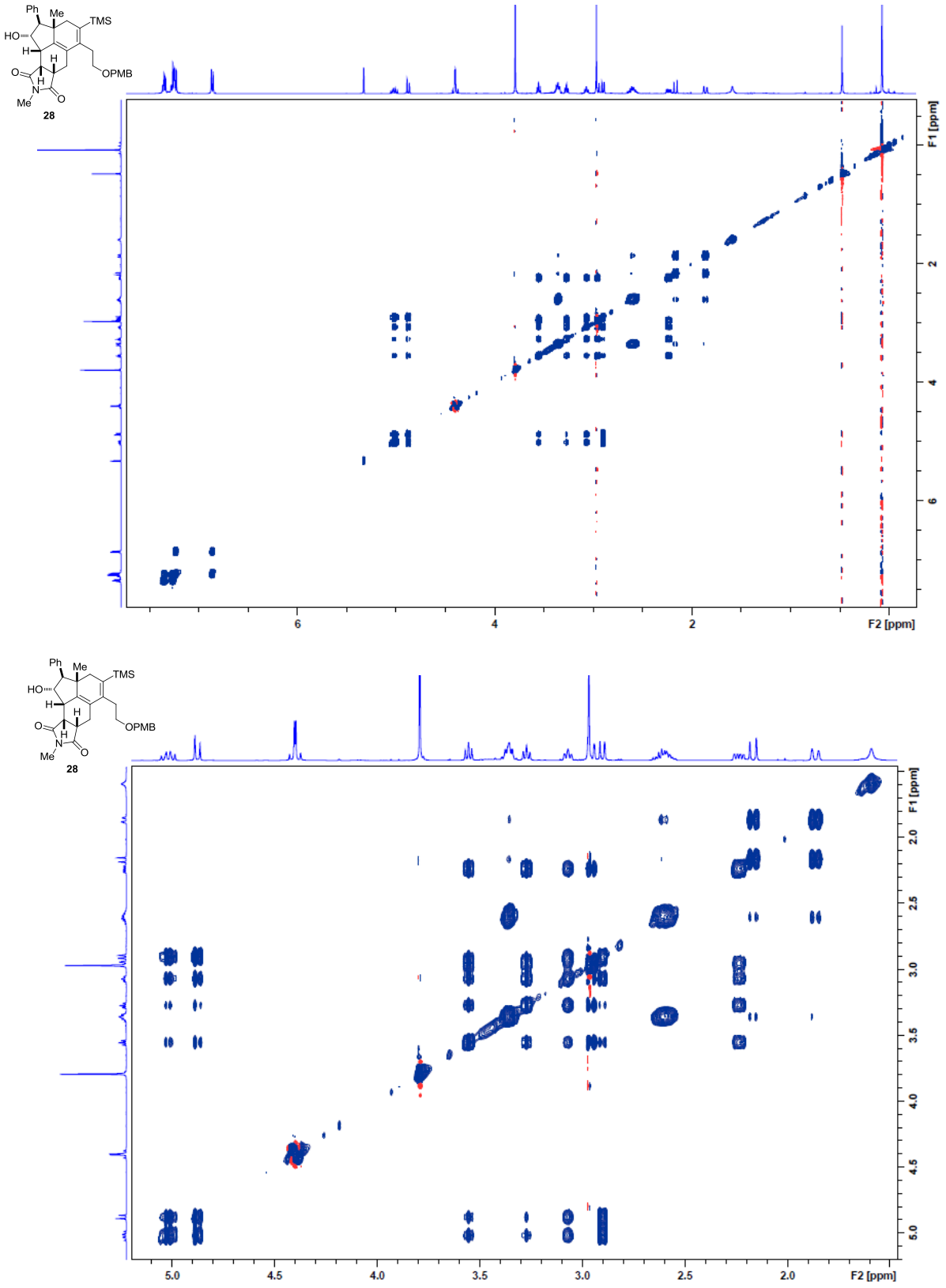


Figure S28: NOESY (500 MHz, CD_2Cl_2) of **28**.

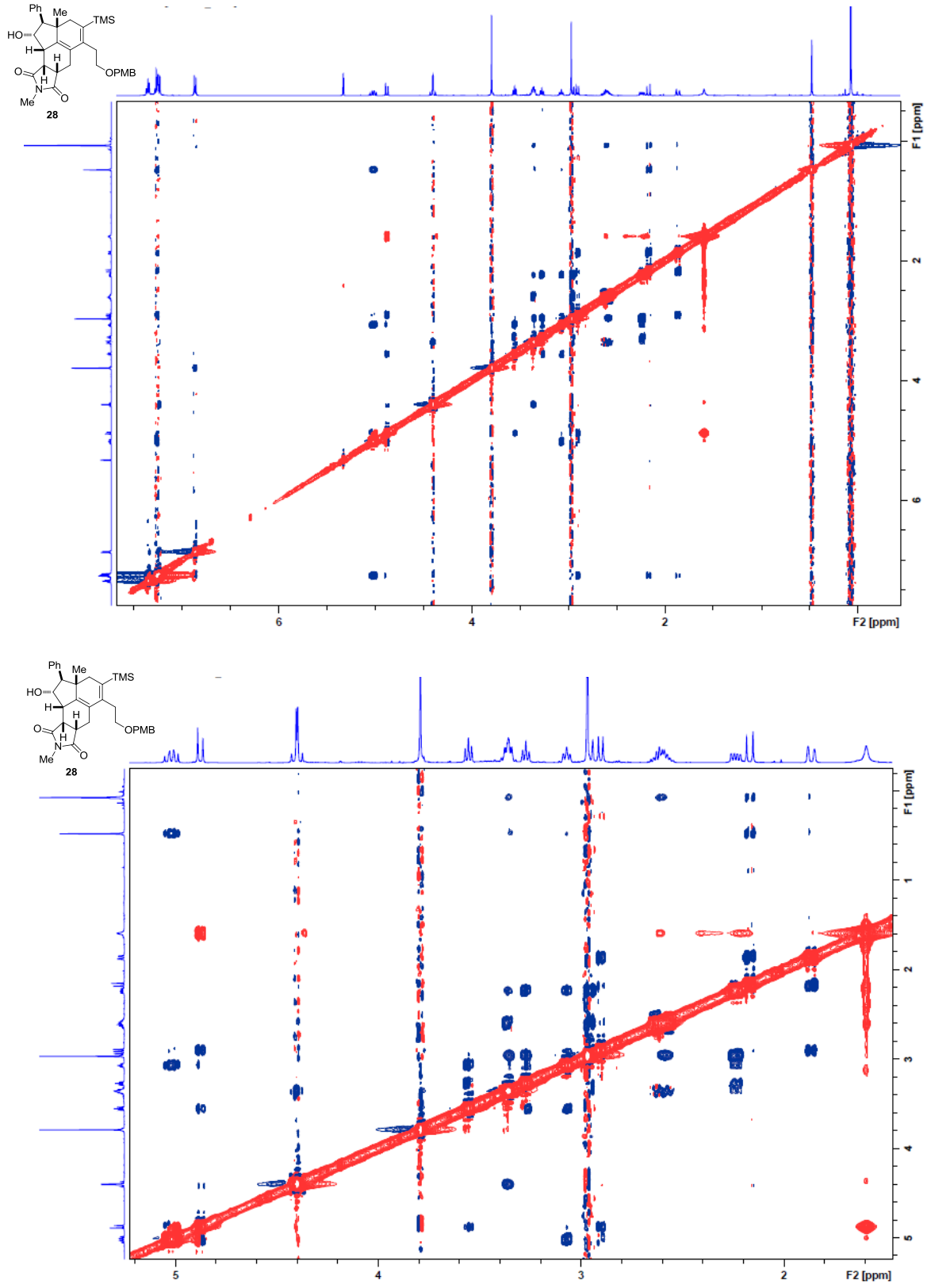


Figure S29: ^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **30**.

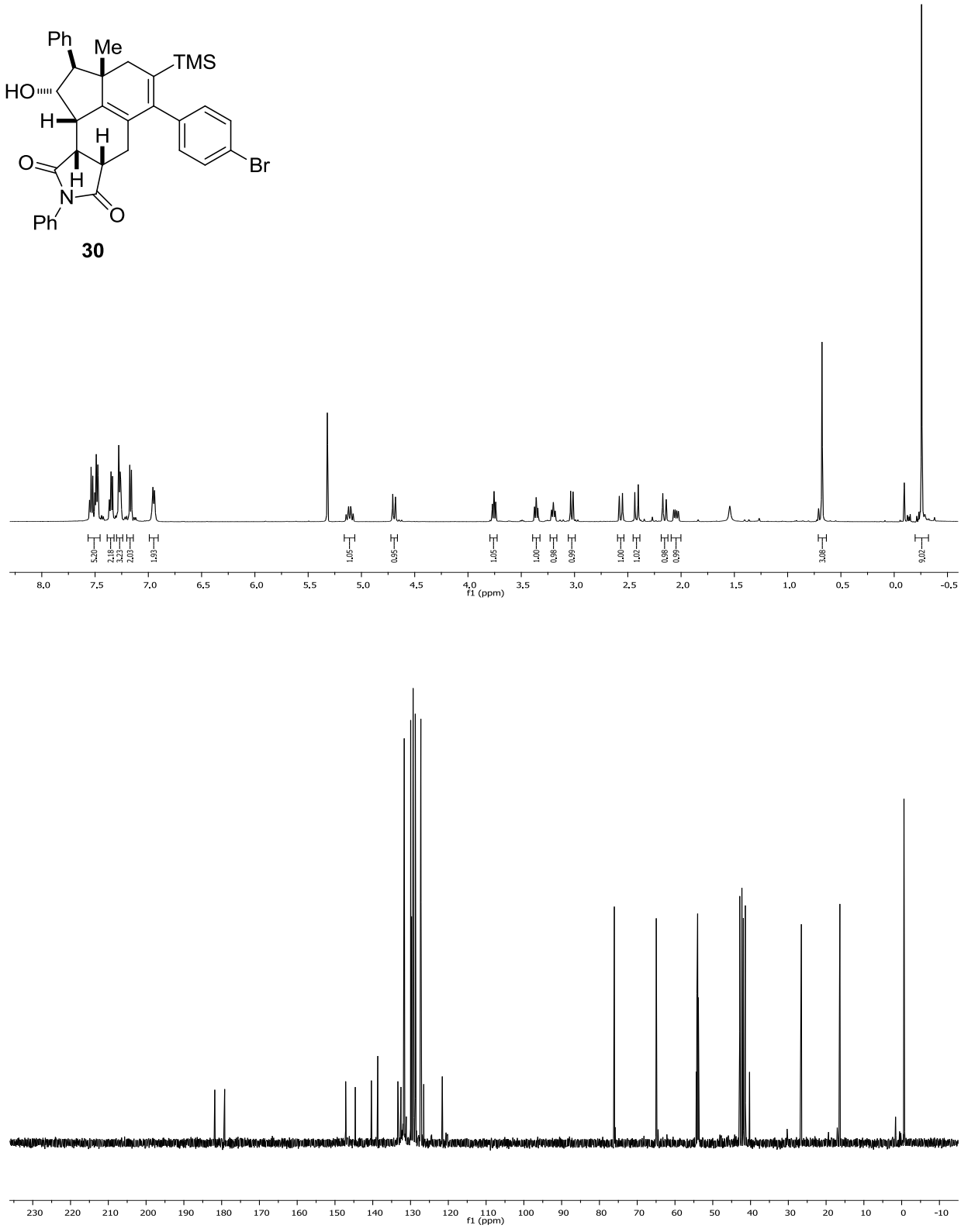


Figure S30: COSY (500 MHz, CD_2Cl_2) of **30**.

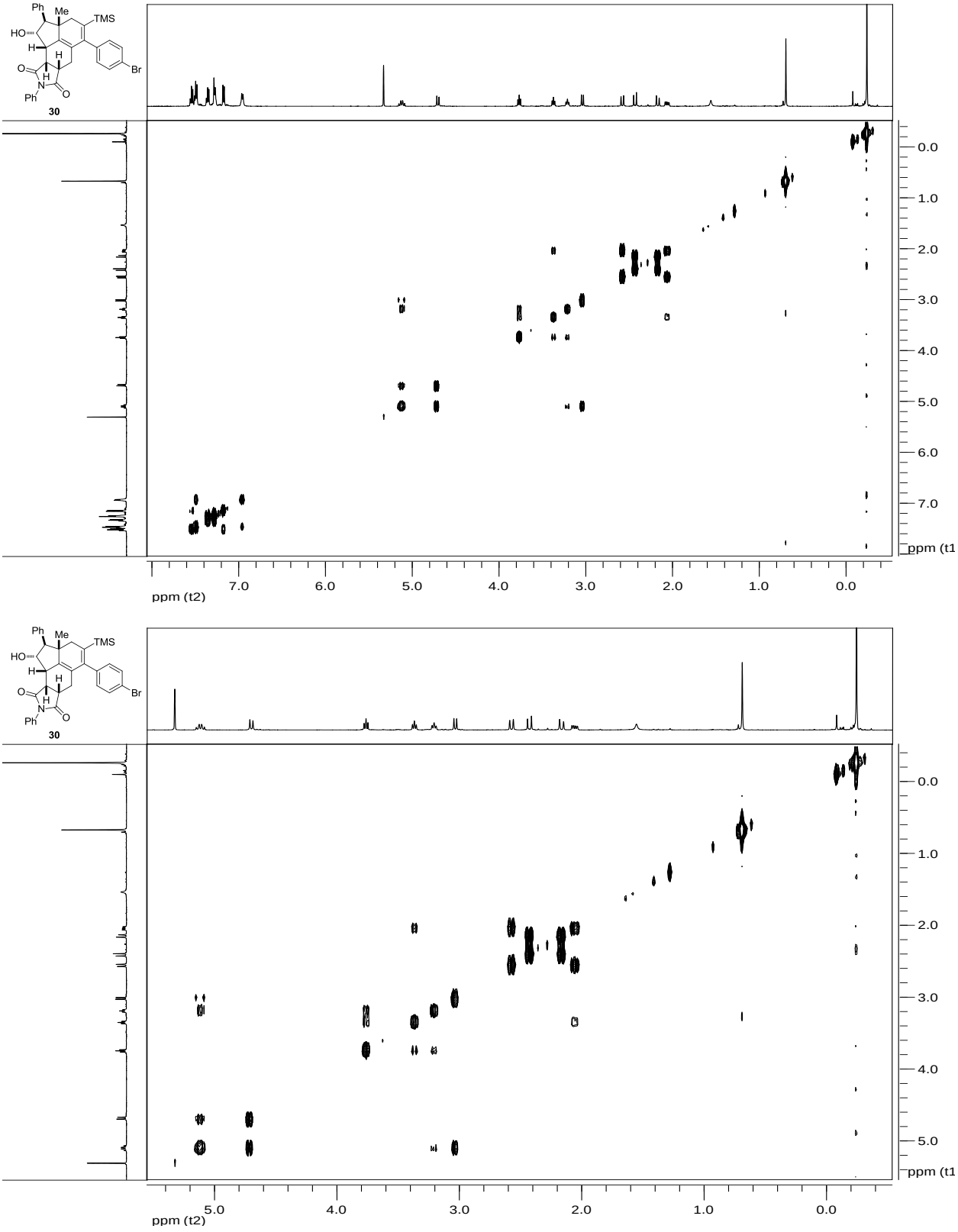


Figure S31: HMQC (500 MHz and 125 MHz, CD_2Cl_2) of **30**.

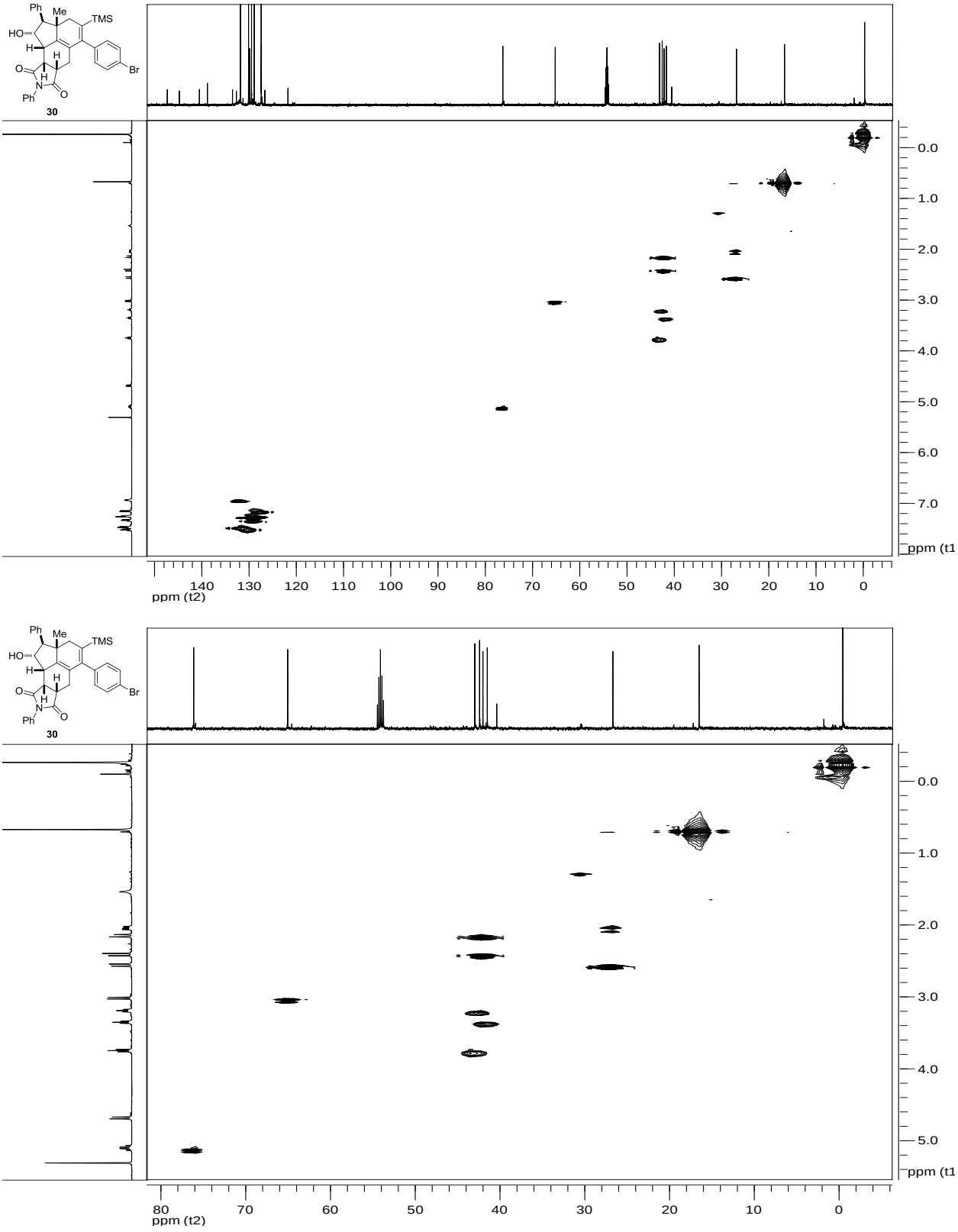
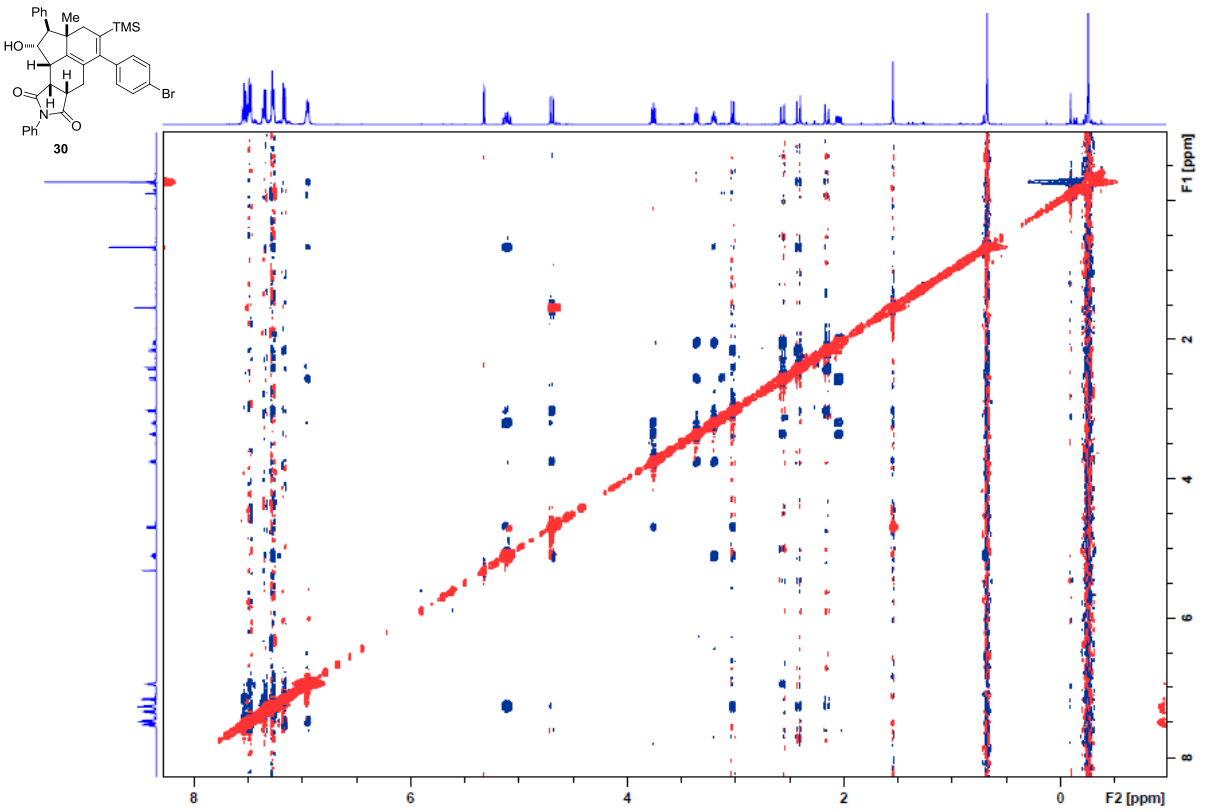


Figure S32: NOESY (500 MHz, CD_2Cl_2) of **30**.



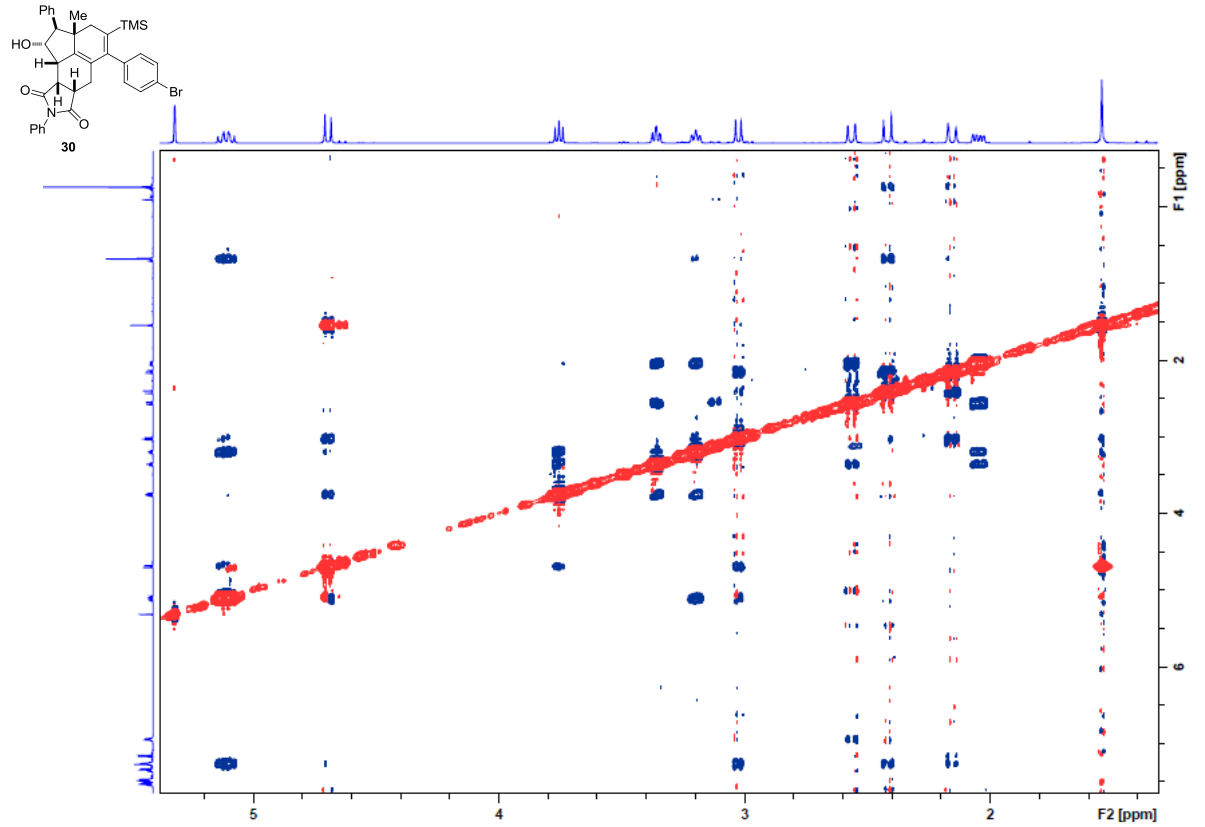


Figure S33: ^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (150 MHz, CD_2Cl_2) of **32**.

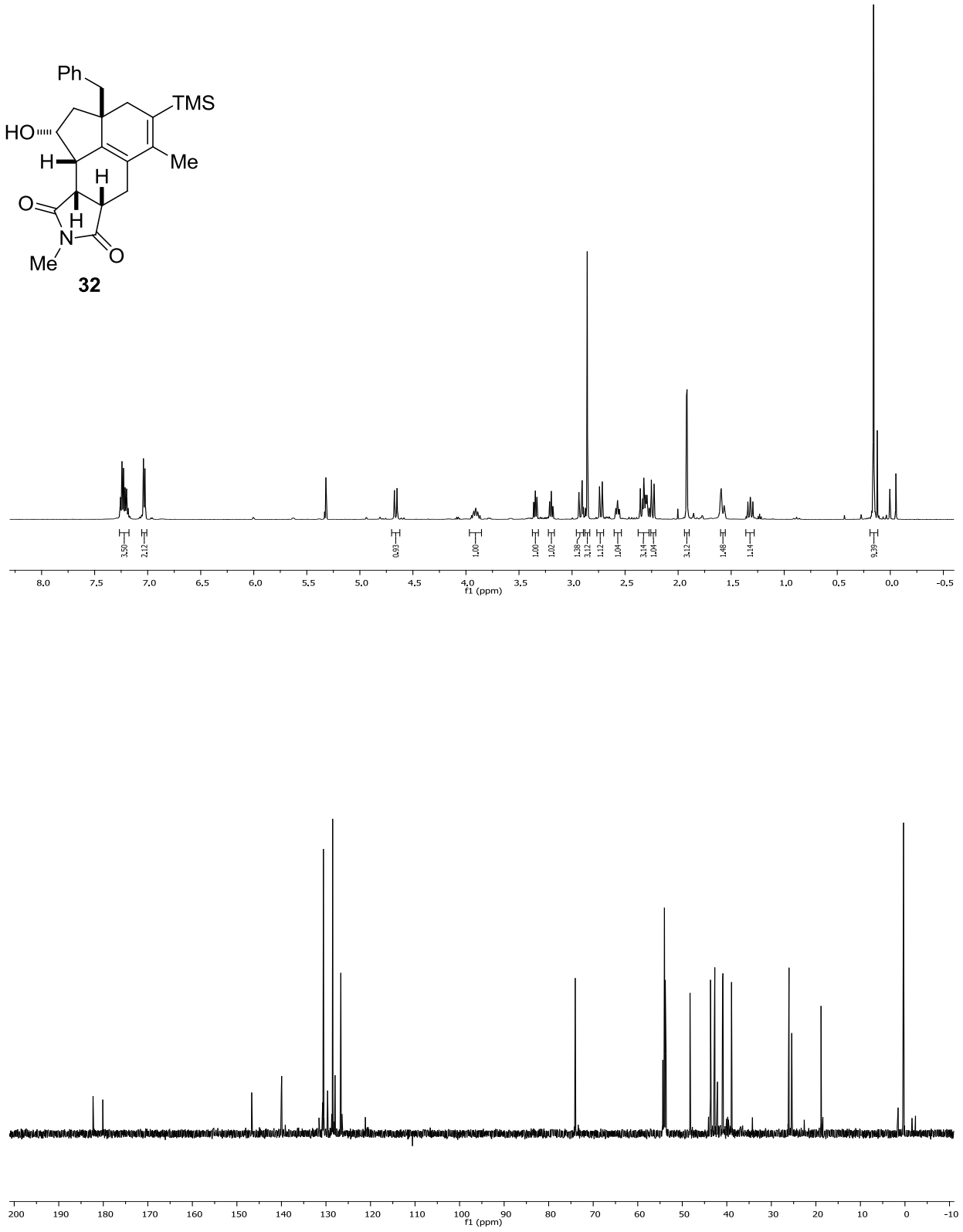


Figure S34: COSY (600 MHz, CD_2Cl_2) of **32**.

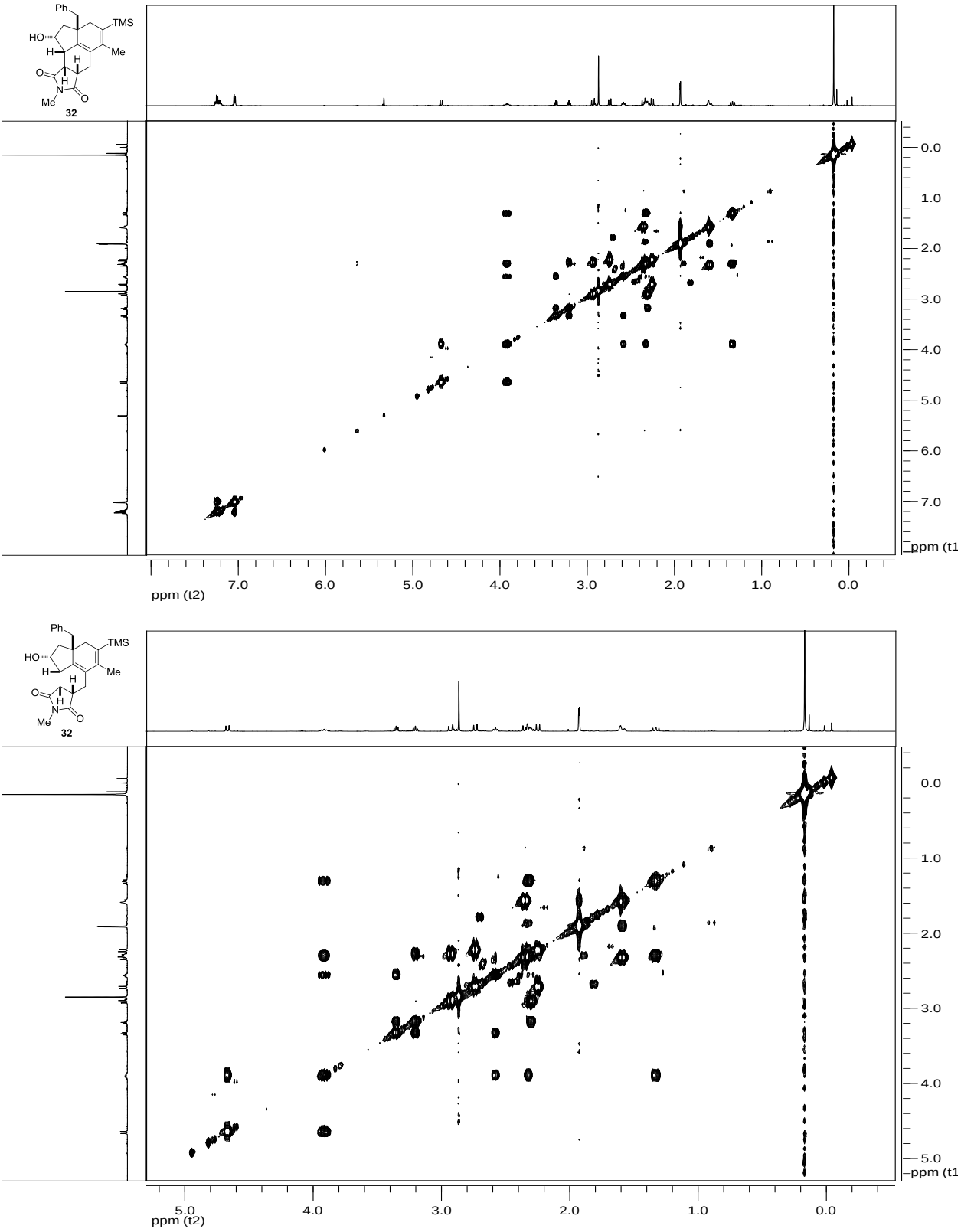


Figure S35: HMQC (500 MHz, CD_2Cl_2 and 125 MHz, CD_2Cl_2) of **32**.

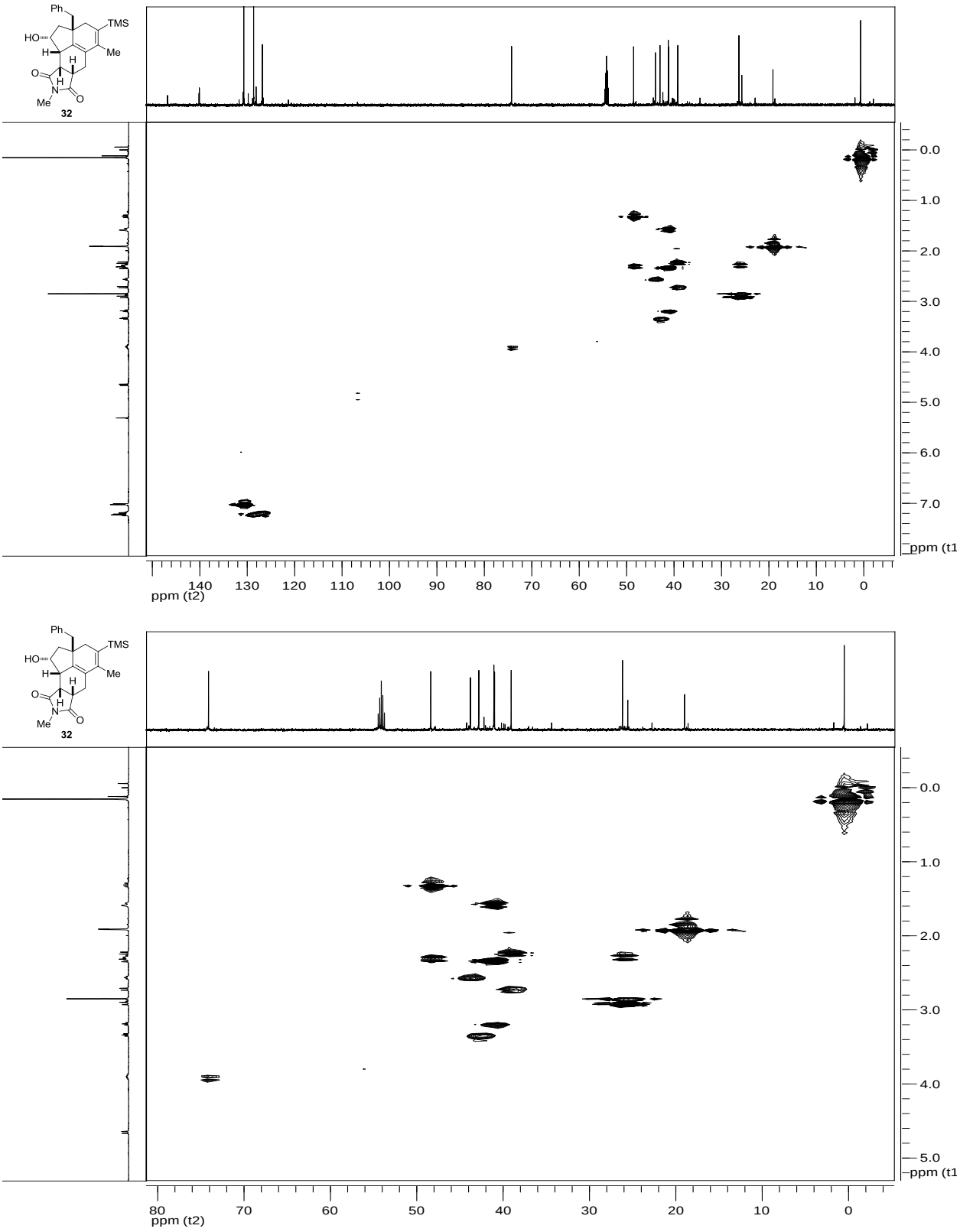


Figure S36: TOCSY (500 MHz, CD_2Cl_2) of **32**.

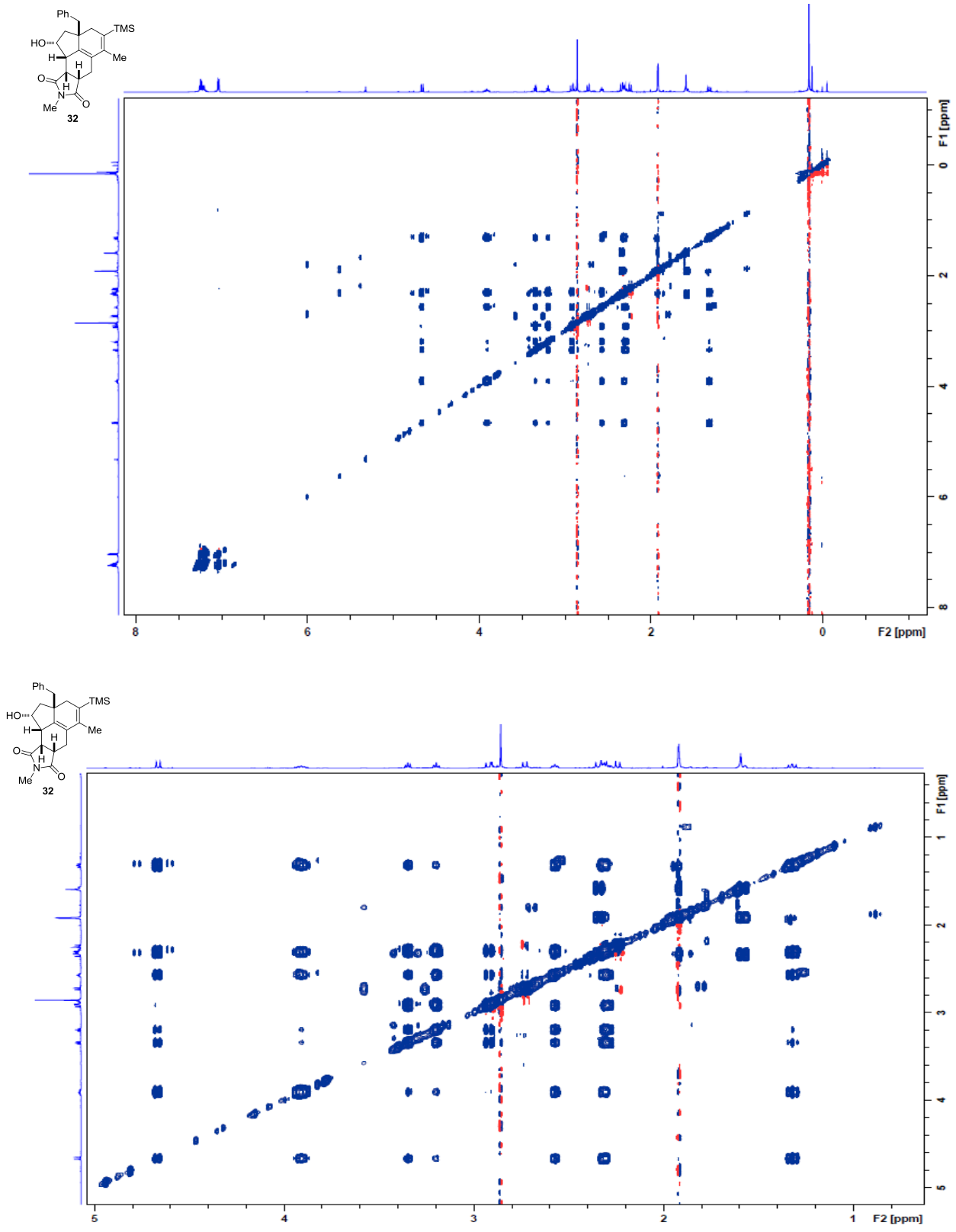


Figure S37: NOESY (500 MHz, CD_2Cl_2) of **32**.

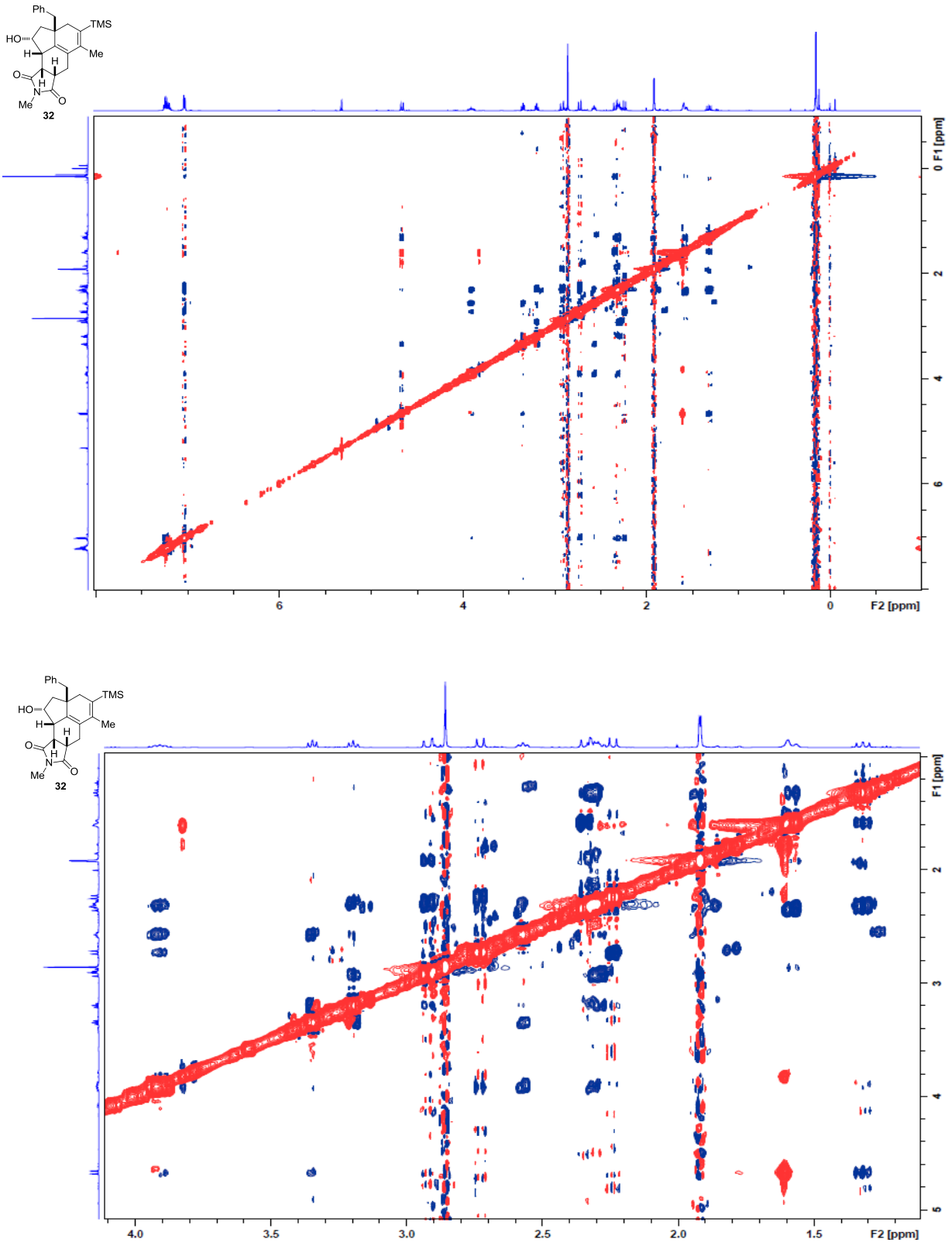


Figure S38: ^{1}H NMR (500 MHz, CD_2Cl_2) and ^{13}C NMR (125 MHz, CD_2Cl_2) of **34**.

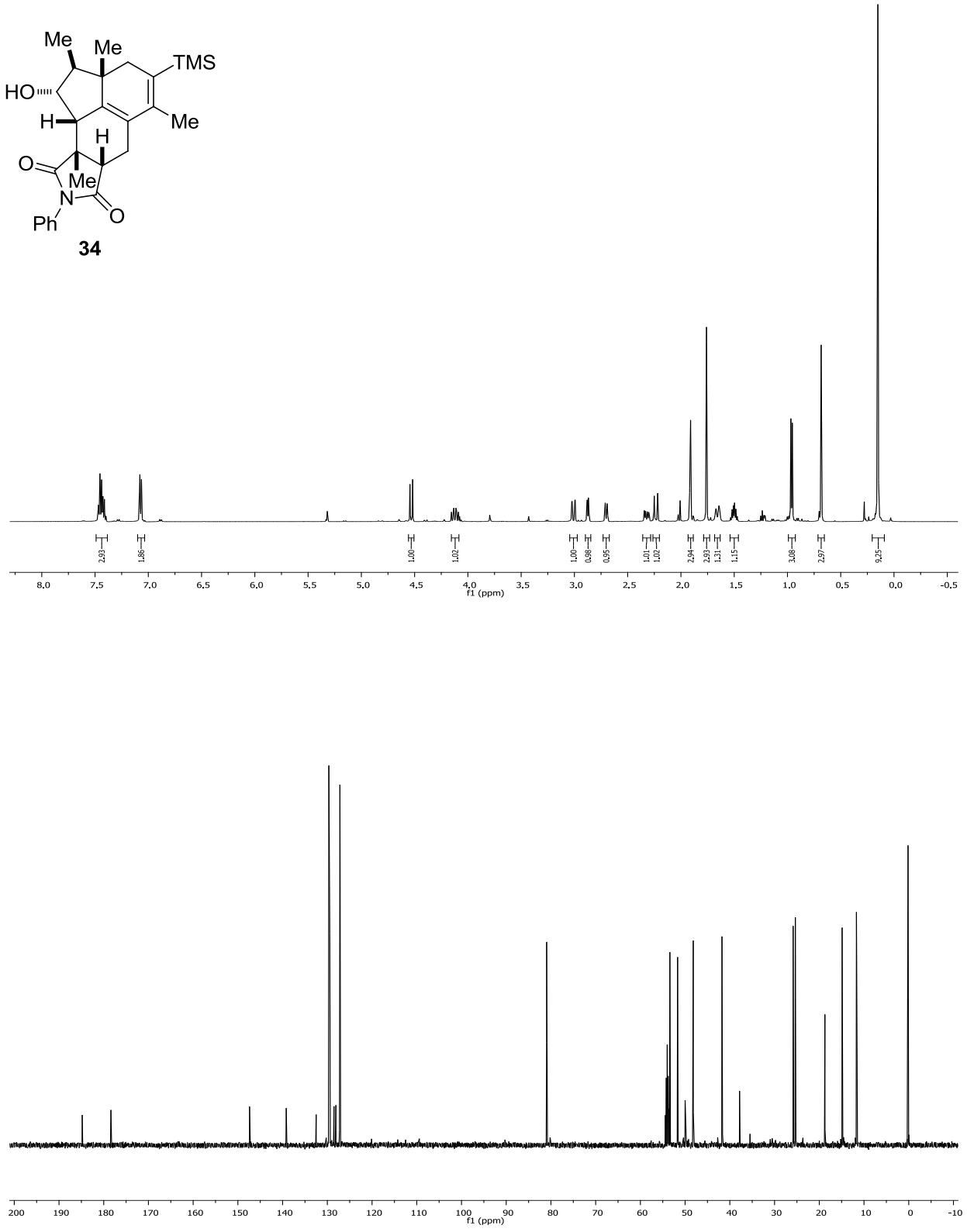


Figure S39: COSY (500 MHz, CD_2Cl_2) of **34**.

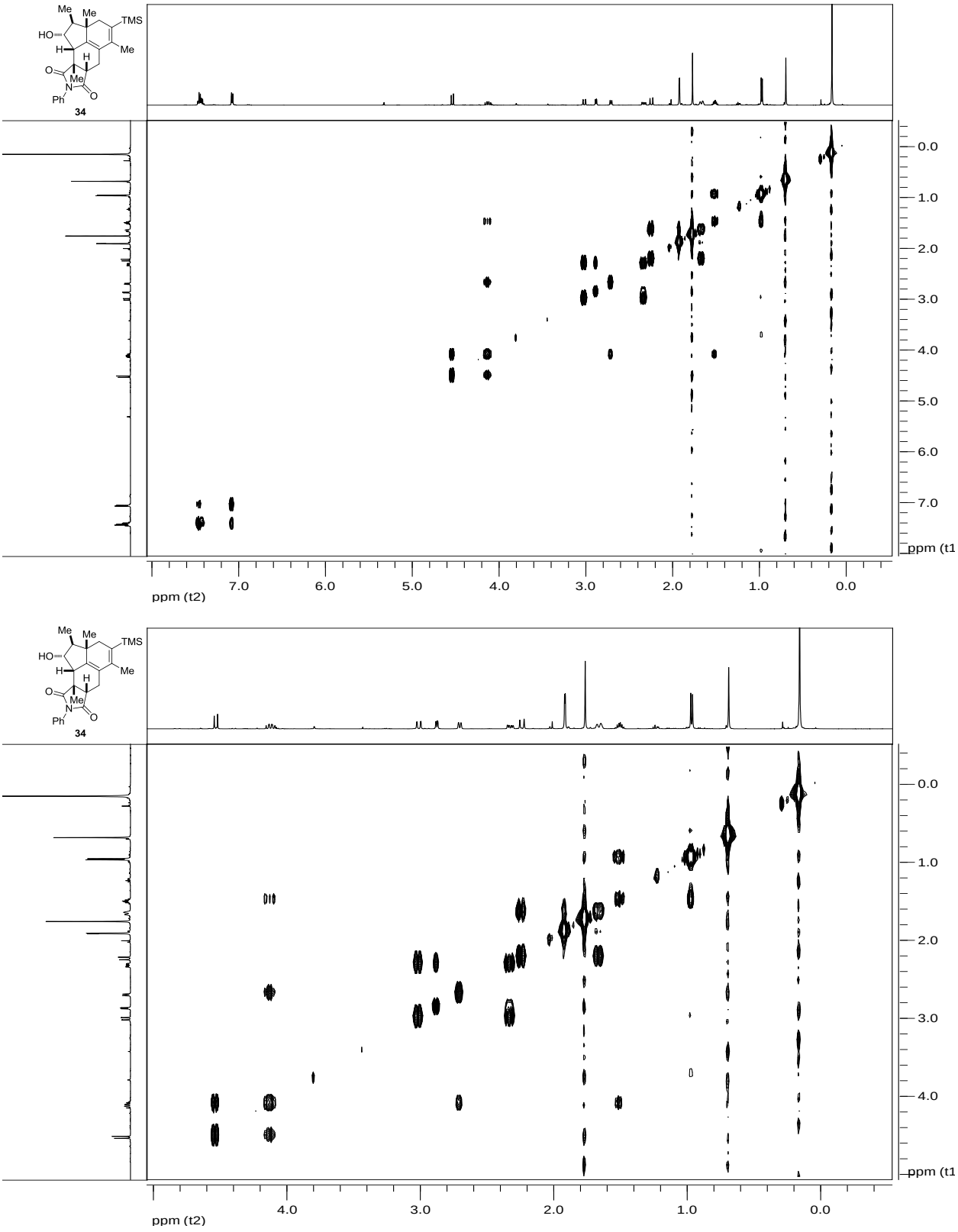


Figure S40: HMQC (500 MHz, CD_2Cl_2 and 125 MHz, CD_2Cl_2) of **34**.

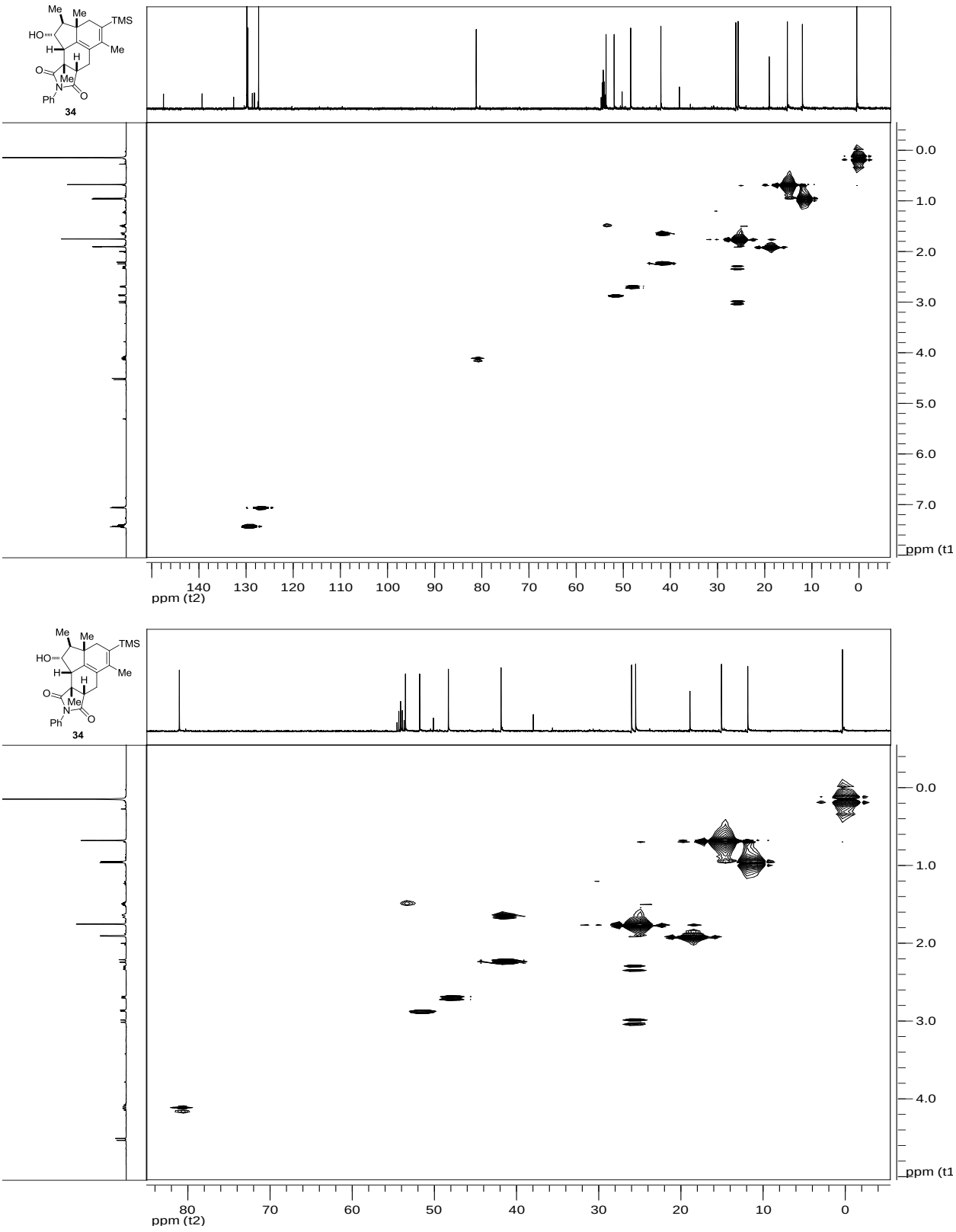


Figure S41: TOCSY (500 MHz, CD_2Cl_2) of **34**.

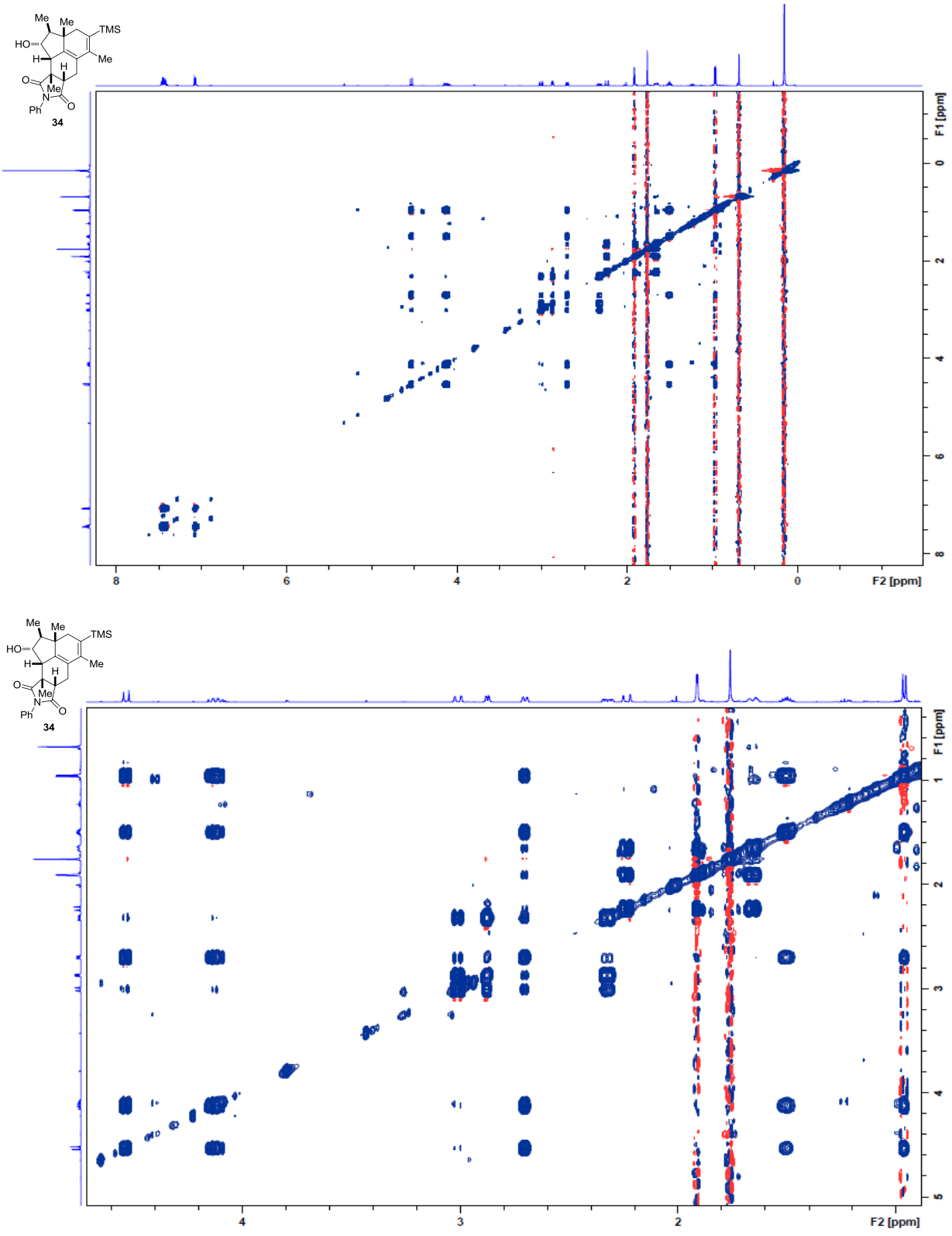


Figure S42: NOESY (500 MHz, CD_2Cl_2) of **34**.

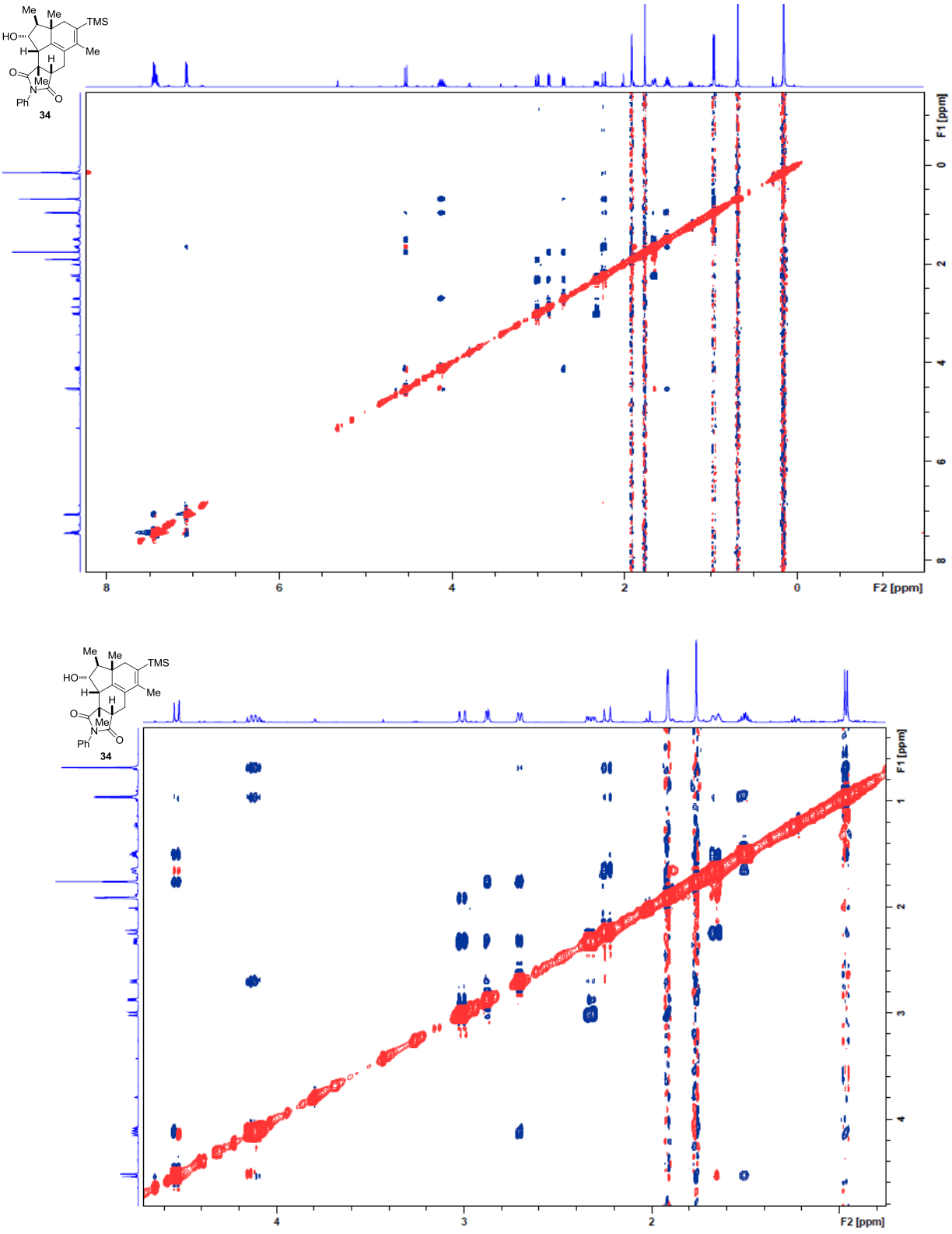


Figure S43: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **37**.

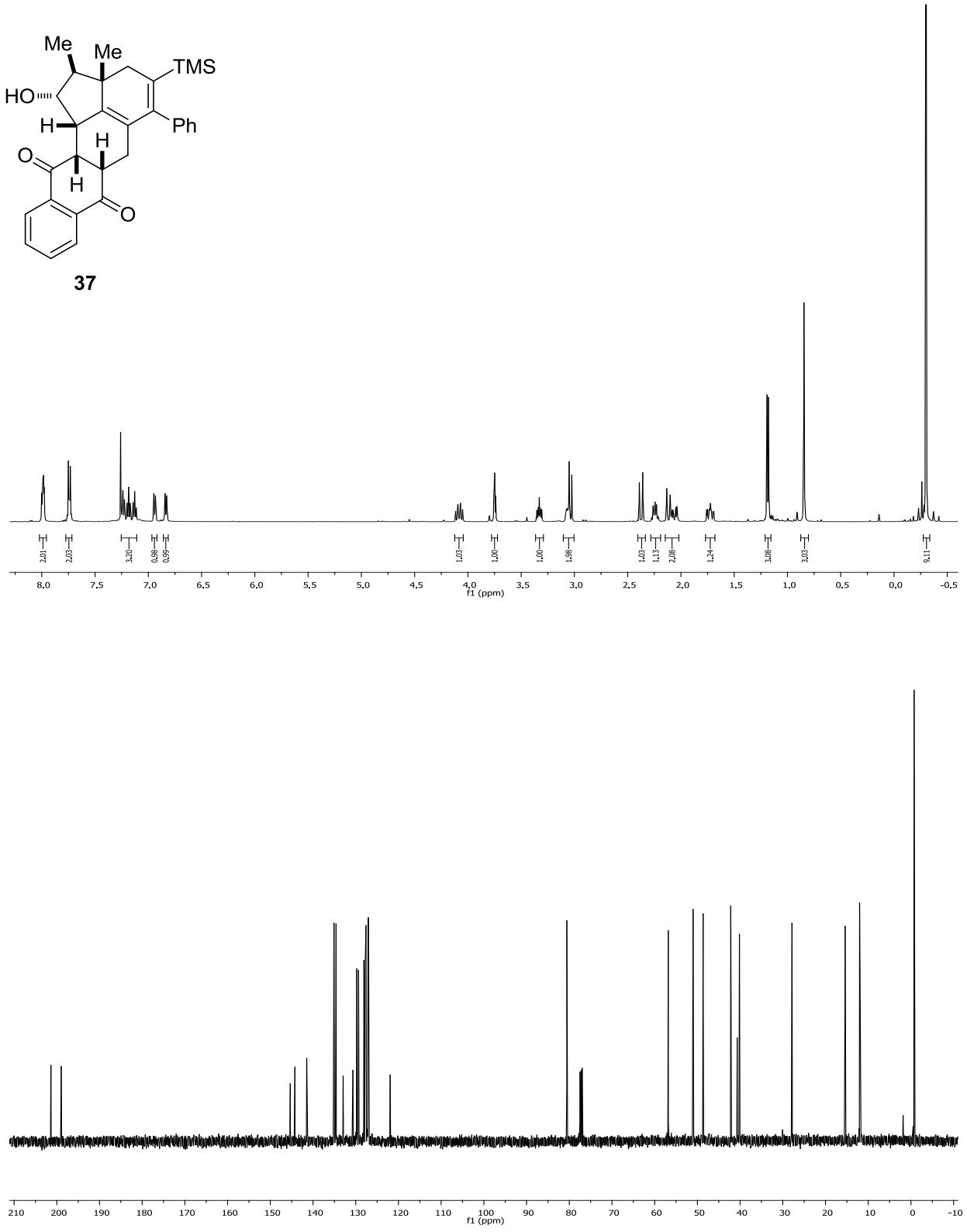


Figure S44: COSY (500 MHz, $CDCl_3$) of **37**.

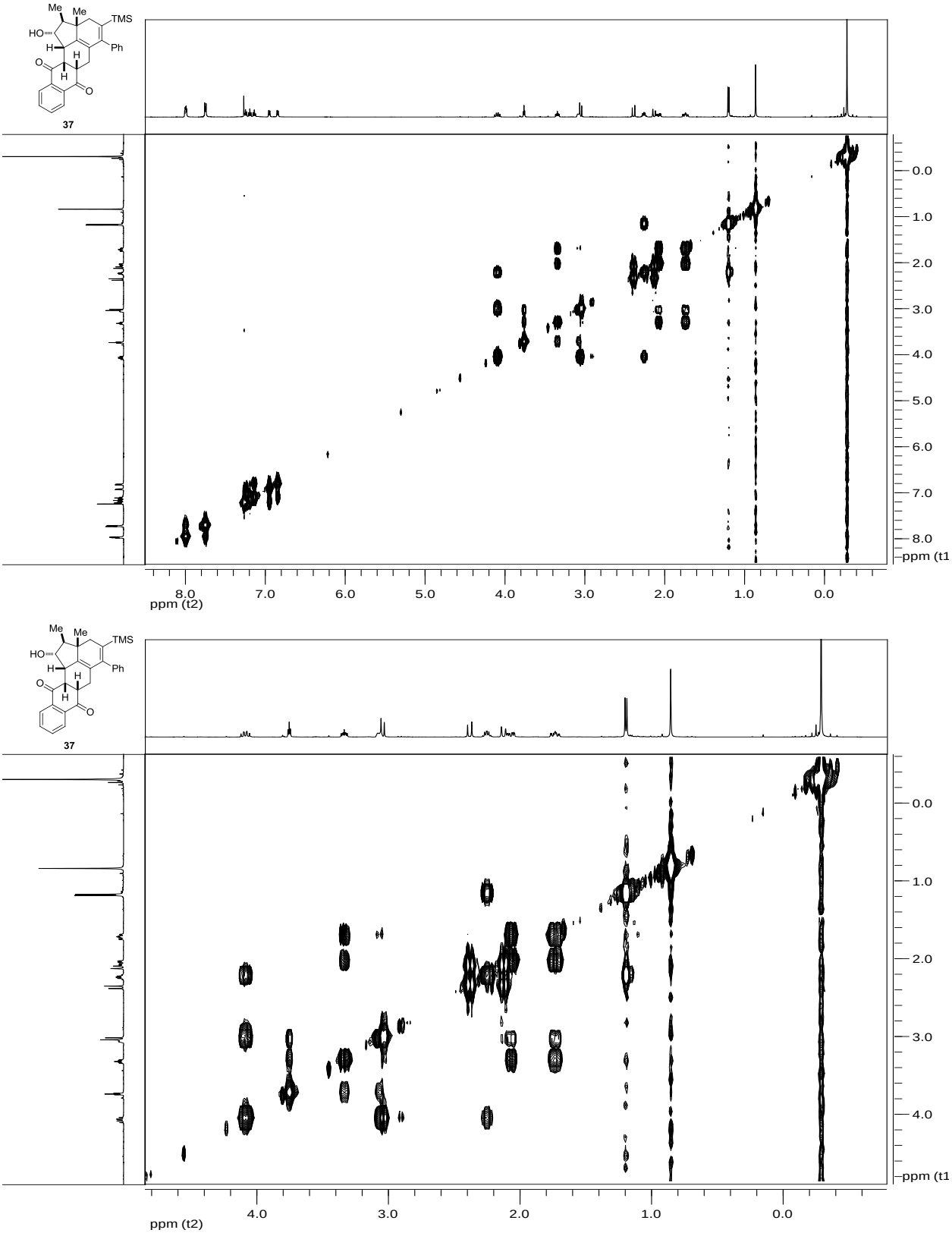


Figure S45: HMQC (500 MHz, $CDCl_3$ and 125 MHz, $CDCl_3$) of **37**.

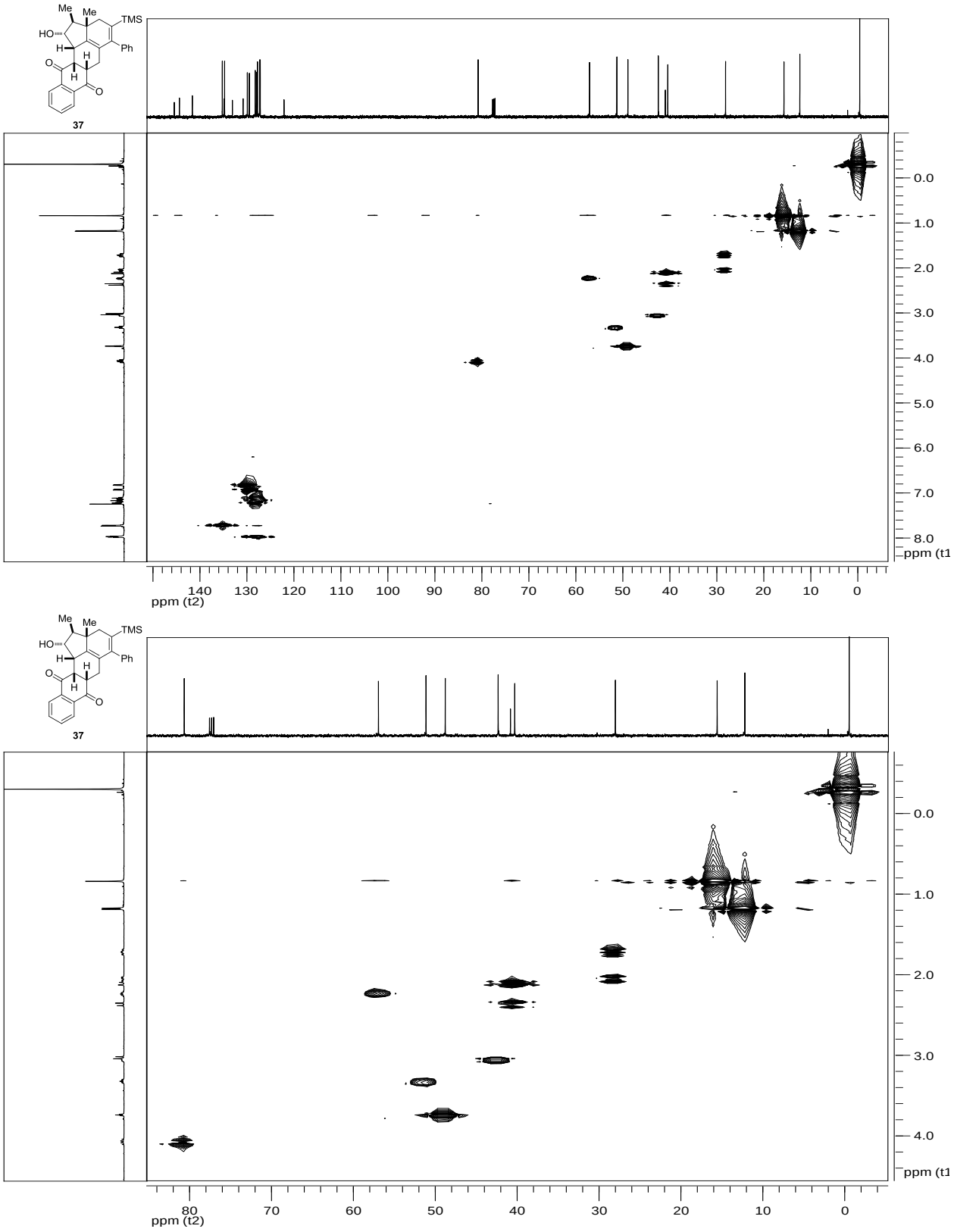


Figure S46: NOESY (500 MHz, $CDCl_3$) of **37**.

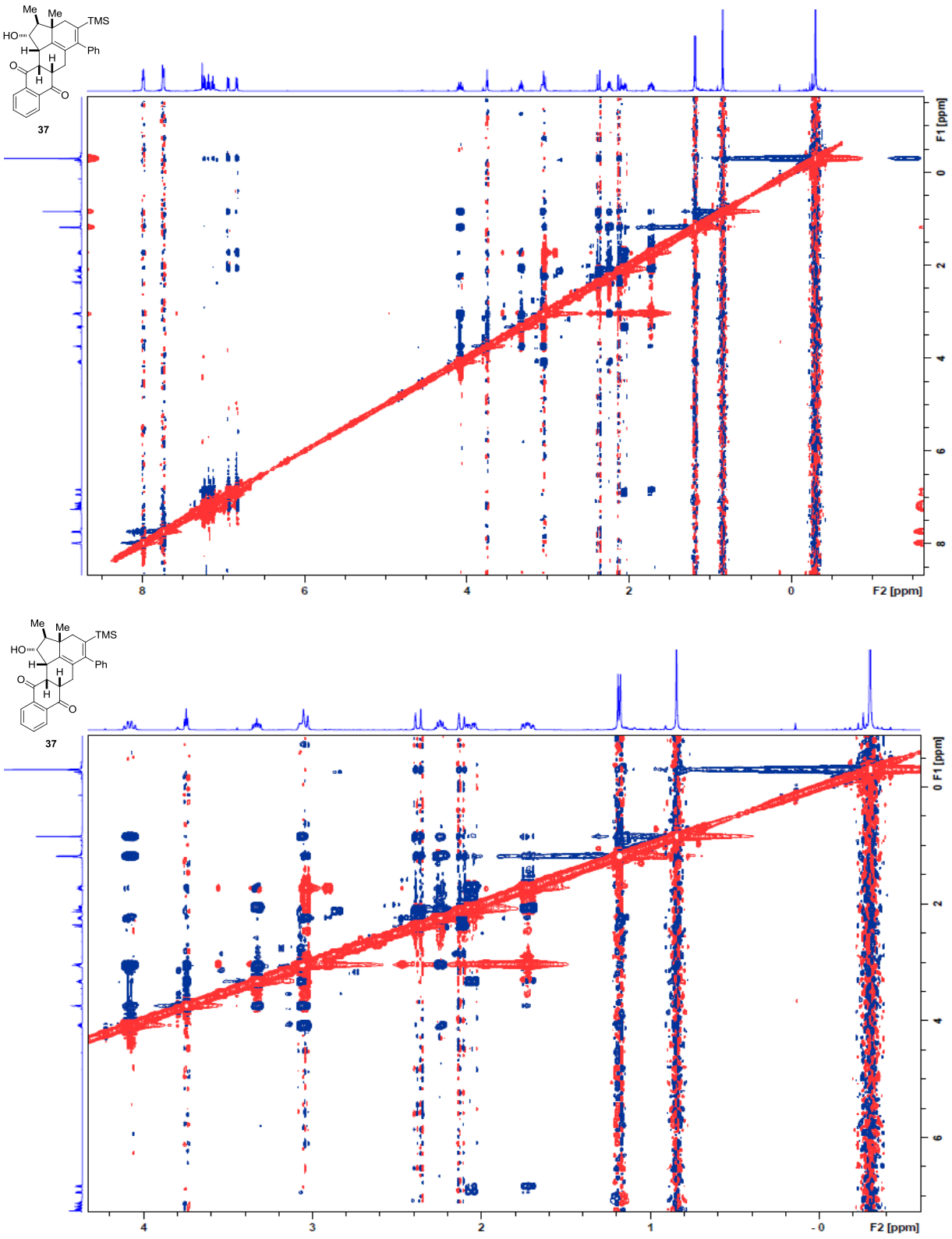
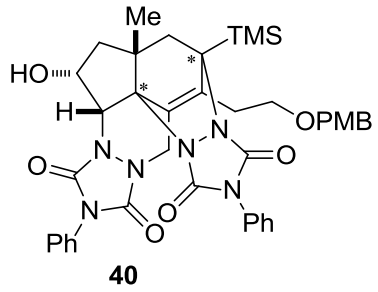


Figure S47: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (125 MHz, $CDCl_3$) of **40**.



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The stereochemistry at the highlighted centers (∗) is assumed.

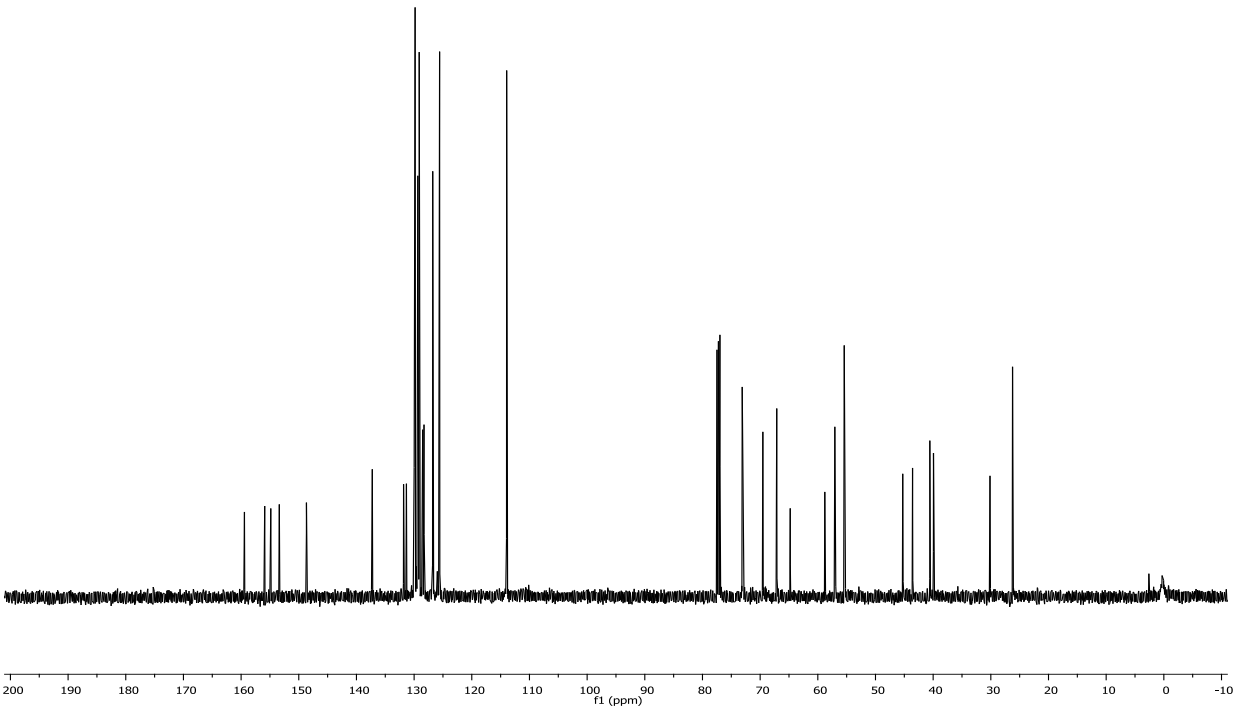


Figure S48: COSY (500 MHz, $CDCl_3$) of **40**.

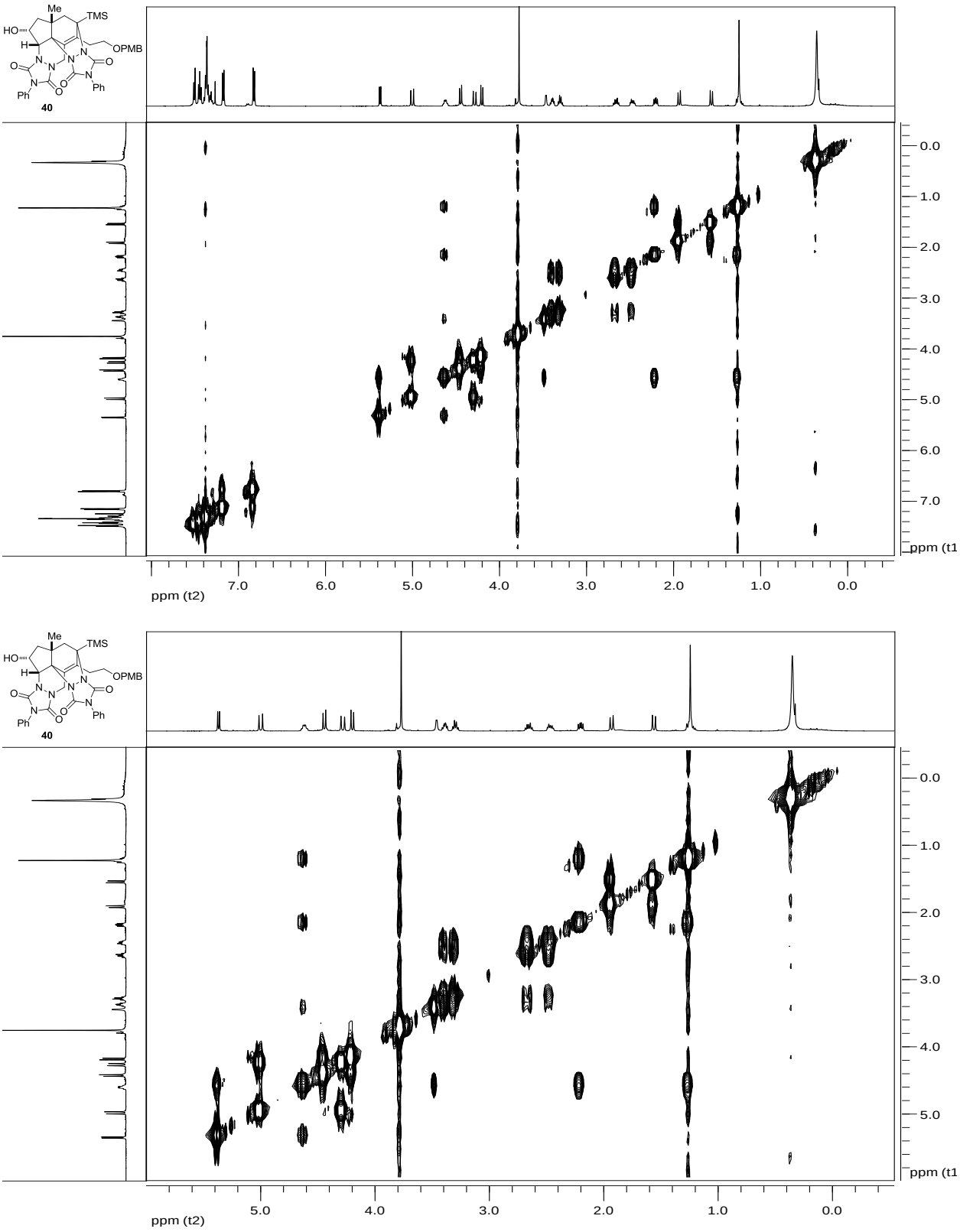


Figure S49: HMQC (500 MHz, $CDCl_3$ and 125 MHz, $CDCl_3$) of **40**.

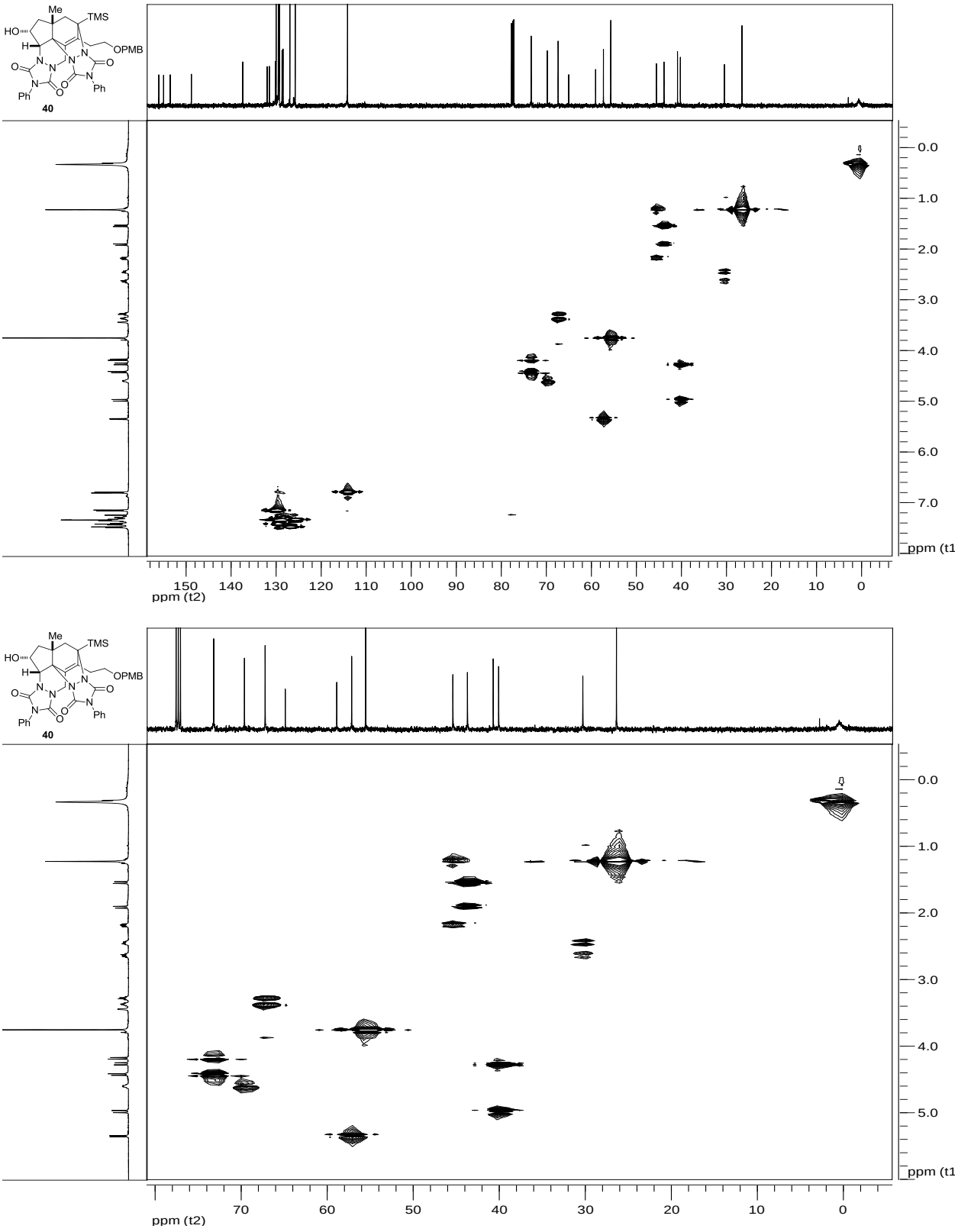


Figure S50: TOCSY (500 MHz, $CDCl_3$) of **40**.

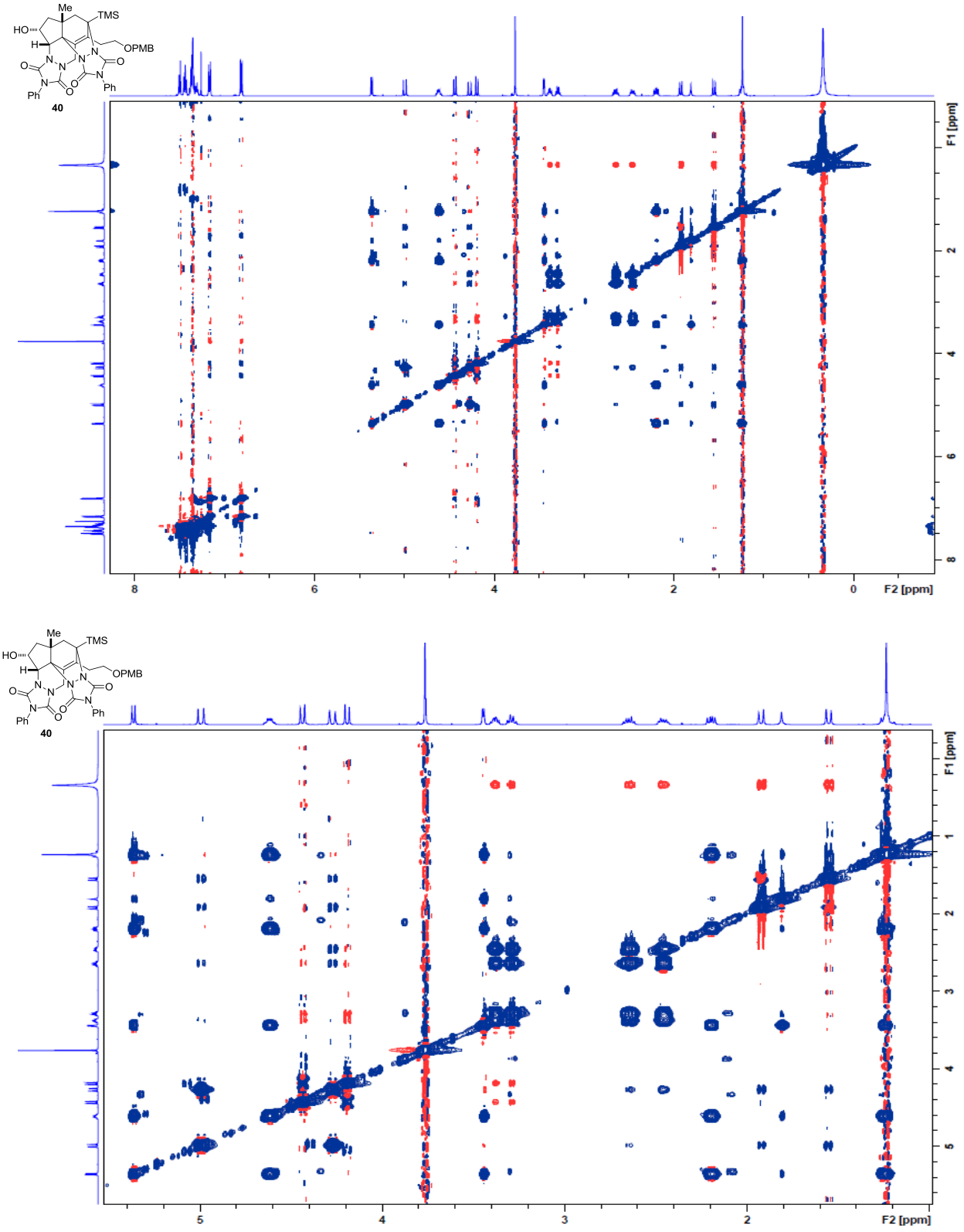
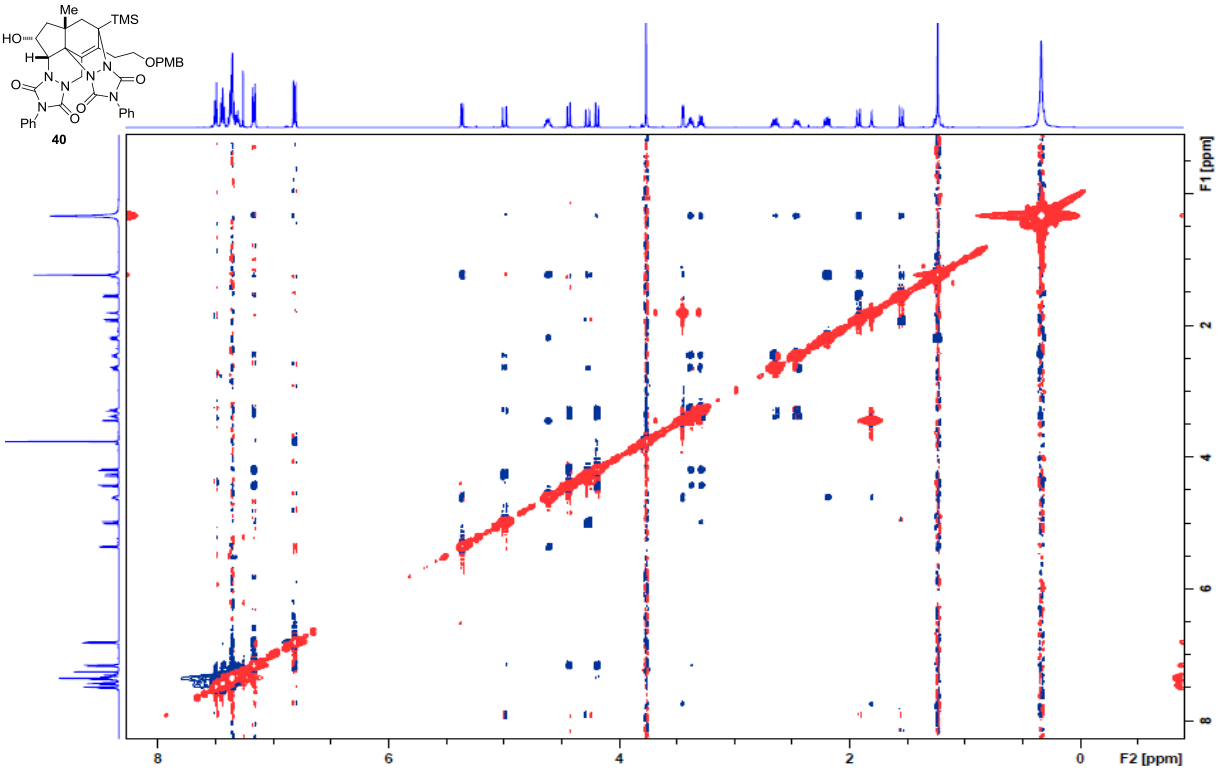


Figure S51: NOESY (500 MHz, $CDCl_3$) of **40**.



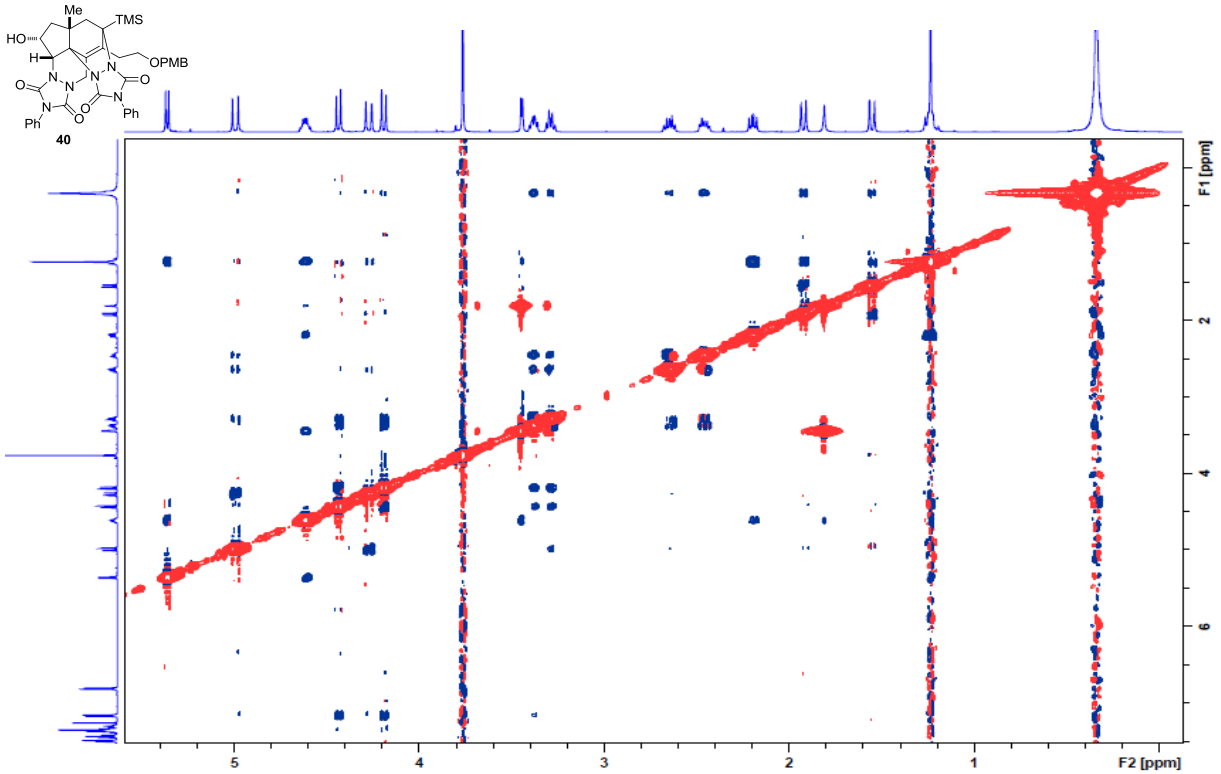
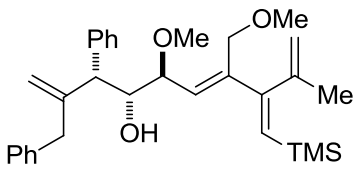


Figure S52: ^{1}H NMR (500 MHz, $CDCl_3$) and ^{13}C NMR (150 MHz, $CDCl_3$) of **43**.



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