Supporting Information

A New Method for the Stereoselective Synthesis of α-Substituted Serine Amino Acid Analogs

Jonathan W. Lane and Randall L. Halcomb*

Department of Chemistry and Biochemistry,
University of Colorado, Boulder, Colorado 80309-0215

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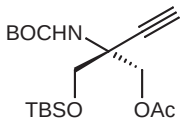
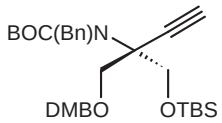
Experimental Section

Physical Properties and Spectroscopic Measurements. ^{1}H and ^{13}C NMR spectra are reported in parts per million (δ) relative to $CHCl_3$ (7.24 ppm and 77.23 ppm, respectively) or CD_3OD (3.31 ppm and 49.15 ppm, respectively) as the internal standards.



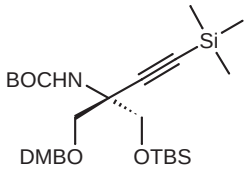
4

Compound 4. Compound **1** (0.750 g, 2.9 mmol, 1.0 equiv) was dissolved in 19 mL DMF and treated with imidazole (0.784 g, 11.5 mmol, 4.0 equiv) and TBS-Cl (1.742 g, 11.5 mmol, 4.0 equiv) at 45 °C according to the reported procedure.[8] The reaction mixture was then cooled to rt and concentrated under vacuum (0.1 torr) with a rotary evaporator. The resulting residue was dissolved in a mixture of 50 mL EtOAc and 25 mL saturated aq NH_4Cl. The phases were separated, and the aq phase was extracted with 2 × 50 mL EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was chromatographed on silica gel (3:1 hexanes/EtOAc) to give **4** as a clear oil (1.015 g, 2.72 mmol, 94%). $[\alpha]^{28}_{D}$: +4.8 (c 1.0, MeOH). IR (thin film): 3304, 2952, 1741, 1724 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.97 (s, 1H), 4.43 (d, *J* = 10.8 Hz, 1H), 4.18 (d, *J* = 10.8 Hz, 1H), 3.84-3.73 (m, 2H), 2.32 (s, 1H), 2.06 (s, 3H), 1.42 (s, 9H), 0.85 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 154.3, 81.2, 80.4, 72.8, 65.1, 64.6, 54.4, 28.5, 25.9, 21.0, 18.4, -5.3 (2C).



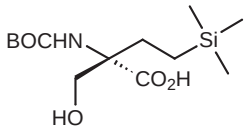
5

Compound 5. To a solution of **2** (457 mg, 0.95 mmol, 1.0 equiv) in 7.2 mL anhydrous THF at rt was added 2.4 mL DMPU. The mixture was then cooled to -50 °C, and KHMDS (0.5 M in toluene, 2.1 mL, 1.05 mmol, 1.1 equiv) was added slowly. The resulting mixture was stirred for 1.5 h at -50 °C, after which benzyl bromide (0.45 mL, 3.8 mmol, 4.0 equiv) was added dropwise. Tetrabutylammonium iodide (352 mg, 0.95 mmol, 1.0 equiv) was then added to the mixture in one portion, and the reaction was warmed to rt. The mixture was stirred for an additional 24 h at rt and was then quenched with 1 mL H_2O, followed by 1 mL saturated aq NH_4Cl. The heterogeneous mixture was diluted with 25 mL EtOAc and an additional 20 mL saturated aq NH_4Cl. The phases were separated, and the aq phase was extracted with 2 × 25 mL EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was chromatographed on silica gel (3:1 hexanes/EtOAc) to give **5** as an oil (468 mg, 0.82 mmol, 86%). $[\alpha]^{28}_D$: +6.8 (c 1.0, MeOH). IR (thin film): 2952, 2848, 1681 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.33-7.12 (m, 5H), 6.89-6.76 (m, 3H), 4.75 (AB, J = 16.8 Hz, $\Delta\nu$ = 19.1 Hz, 2H), 4.51 (AB, J = 11.8 Hz, $\Delta\nu$ = 9.6 Hz, 2H), 4.18 (d, J = 9.6 Hz, 1H), 4.05 (d, J = 9.3 Hz, 1H), 3.90 (d, J = 9.6 Hz, 1H), 3.86 (s, 3H), 3.83-3.79 (m, 1H), 3.81 (s, 3H), 2.39 (s, 1H), 1.30 (s, 9H), 0.87 (s, 9H), 0.02 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.1, 149.1, 148.6, 141.1, 131.1, 128.1, 126.8, 126.3, 120.3, 111.1, 111.0, 83.7, 80.5, 74.1, 73.6, 71.2, 65.1, 63.7, 56.1, 55.9, 51.3, 28.5, 26.0, 18.5, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.40.



6a

Compound 6a. (Condition A) To a solution of **2** (94 mg, 0.20 mmol, 1.0 equiv) in 1.5 mL anhydrous THF at rt was added 0.5 mL DMPU. The mixture was then cooled to -50 °C, and LDA (0.65 M in THF, 1.21 mL, 0.80 mmol, 4.0 equiv), kept at 0 °C, was added slowly. The resulting mixture was stirred for 15 min at -50 °C, after which TMS-Cl (100 μL, 0.80 mmol, 4.0 equiv) was added dropwise. The mixture was stirred for an additional 30 min at -50 °C and was then quenched with 0.5 mL H_2O, followed by 0.5 mL saturated aq NH_4Cl. The heterogeneous mixture was warmed to rt and was then diluted with 15 mL EtOAc and an additional 10 mL saturated aq NH_4Cl. The phases were separated, and the aq phase was extracted with 2 × 15 mL EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was chromatographed on silica gel (3:1 hexanes/EtOAc) to give **6a** as an oil (98 mg, 0.18 mmol, 91%). $[\alpha]^{28}_D$: +5.1 (c 0.90, MeOH). IR (thin film): 2947, 2924, 2848, 1719 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.88-6.78 (m, 3H), 5.02 (s, 1H), 4.57-4.48 (m, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.90-3.72 (m, 2H), 3.68 (AB, J = 9.6 Hz, Δν = 36.2 Hz, 2H), 1.42 (s, 9H), 0.85 (s, 9H), 0.12 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.7, 149.2, 148.8, 130.8, 120.5, 111.2, 111.0, 104.9, 87.9, 79.9, 73.7, 71.3, 65.2, 56.1, 56.0, 55.8, 28.5, 26.0, 18.4, 0.2, -5.1, -5.2. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.50.

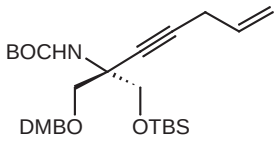


7a

Compound 7a. To remove the TBS protecting group, compound **6a** (98 mg, 0.18 mmol, 1.0 equiv) was dissolved in 5 mL 8:1:1 AcOH:H_2O:MeOH. One drop of aqueous HCl solution (2 N) was then added to the mixture, and the resulting solution was stirred for 2 h at rt. The reaction was then diluted with excess toluene, and the resulting biphasic mixture was concentrated under vacuum (0.1 torr) with a rotary evaporator at a temperature not exceeding 30 °C. To reduce the alkyne, the resulting crude product was dissolved in 10 mL anhydrous benzene, and 10% Pd/C (65 mg) was added to the stirring mixture. The flask was evacuated under aspirator vacuum, refilled with hydrogen three times, and then stirred under hydrogen (1 atm) for 12 h. The mixture was then filtered through Celite to remove the catalyst, and the filtrate was concentrated to give a crude oil. The crude product of this sequence was chromatographed on silica gel (2:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (59 mg, 0.13 mmol, 75% from **6a**). $[\alpha]^{28}_{D}$: +4.8 (c 0.50, MeOH). IR (thin film): 3419, 2947, 1714, 1687 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.85-6.79 (m, 3H), 5.04 (s, 1H), 4.47-4.39 (m, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.67-3.58 (m, 3H), 3.34 (d, *J* = 9.2 Hz, 1H), 1.75-1.62 (m, 1H), 1.53-1.40 (m, 1H), 1.40 (s, 9H), 0.41 (dt, *J* = 13.7, 4.1 Hz, 1H), 0.27 (dt, *J* = 13.8, 4.2 Hz, 1H), -0.05 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.2, 149.3, 149.0, 130.5, 120.6, 111.2, 111.1, 79.8, 73.7, 72.3, 67.0, 59.7, 56.1, 56.0, 28.5, 26.4, 9.6, -1.7. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.47.

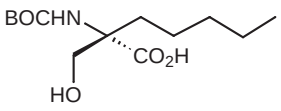
The resulting alcohol was then oxidized in two steps. To a solution of the above alcohol (59 mg, 0.13 mmol, 1.0 equiv) in 2.6 mL CH_2Cl_2 at rt was added $NaHCO_3$ (113 mg) followed by Dess-Martin periodinane (113 mg, 0.27 mmol, 2.0 equiv). The reaction mixture was stirred for 12 h after which it was quenched with 1 mL of a $Na_2S_2O_3$ solution (25g $Na_2S_2O_3$ per 100 mL). After stirring for 15 min, the mixture was diluted with 15

mL CH_2Cl_2 and 15 mL H_2O. The phases were separated, and the aq phase was extracted with 2 × 15 mL CH_2Cl_2. The combined organic phases were dried (Na_2SO_4), filtered, and concentrated. The crude oil was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the corresponding aldehyde as a clear oil. The resulting product was dissolved in 2.5 mL 4:1 *t*BuOH:H_2O. NaH_2PO_4 (55 mg, 0.40 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.5 mL, 1.0 mmol, 7.7 equiv), and $NaClO_2$ (73 mg, 0.81 mmol, 6.0 equiv) were successively added, and the solution was stirred at rt for 12 h. The reaction mixture was then diluted with 10 mL H_2O and 15 mL CH_2Cl_2. The phases were separated, and the aq phase was extracted with 2 × 15 mL CH_2Cl_2. The combined organic phases were dried (Na_2SO_4), filtered, and concentrated to give the corresponding carboxylic acid. To remove the DMB protecting group, the crude product was subsequently dissolved in 4 mL methanol, and 10% Pd/C (40 mg) was added to the stirring mixture. The flask was evacuated under aspirator vacuum, refilled with hydrogen three times, and then stirred under hydrogen (1 atm) for 24 h. The mixture was then filtered through Celite to remove the catalyst, and the filtrate was concentrated to give an oil. The resulting crude product was immediately chromatographed on silica gel (1:1 hexanes/EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **7a** as an oil (32 mg, 0.10 mmol, 78% from the alcohol product). $[\alpha]^{28}_D$: -11.6 (c 0.50, MeOH). IR (thin film): 3408, 2947, 1714, 1643 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ 4.03 (d, J = 11.0 Hz, 1H), 3.77 (d, J = 11.0 Hz, 1H), 2.10-1.98 (m, 1H), 1.78-1.65 (m, 1H), 1.45 (s, 9H), 0.43 (dt, J = 13.9, 4.0 Hz, 1H), 0.28 (dt, J = 13.9, 4.0 Hz, 1H), -0.01 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD): δ 175.9, 156.2, 80.3, 67.5, 64.4, 28.9, 26.9, 10.6, -1.7. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.50.



6b

Compound 6b. To a solution of **2** (107 mg, 0.22 mmol, 1.0 equiv) in 1.65 mL anhydrous THF at rt was added 0.55 mL DMPU. The mixture was then cooled to -50 °C, and LDA (0.65 M in THF, 1.35 mL, 0.88 mmol, 4.0 equiv), kept at 0 °C, was added slowly. The resulting mixture was stirred for 15 min at -50 °C, after which allyl bromide (76 μL, 0.88 mmol, 4.0 equiv) was added dropwise. The mixture was then stirred for an additional 6 h at -50 °C after which reaction workup was performed according to Condition A for **6a**. The crude product was chromatographed on silica gel (5:1 hexanes/EtOAc) to give **6b** as an oil (87 mg, 0.17 mmol, 75%). $[\alpha]^{28}_{D}$: +2.0 (c 0.90, MeOH). IR (thin film): 3424, 2849, 1725 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.89-6.78 (m, 3H), 5.80-5.72 (m, 1H), 5.38-5.32 (m, 1H), 5.09-5.00 (m, 1H), 5.03 (s, 1H), 4.55-4.49 (m, 2H), 3.85 (s, 6H), 3.88-3.78 (m, 2H), 3.72 (d, *J* = 9.1 Hz, 1H), 3.60 (d, *J* = 9.3 Hz, 1H), 2.98-2.94 (m, 2H), 1.41 (s, 9H), 0.84 (s, 9H), 0.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.6, 149.2, 148.8, 132.5, 130.8, 120.6, 116.3, 111.2, 111.0, 81.6, 80.5, 79.7, 73.6, 71.4, 65.2, 56.1, 56.0, 55.3, 28.6, 26.0, 23.3, 18.4, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.38.



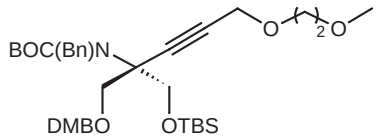
7b

Compound 7b. To reduce the alkyne, compound **6b** (134 mg, 0.26 mmol, 1.0 equiv) was dissolved in 14 mL anhydrous benzene, and 10% Pd/C (89 mg) was added to the stirring mixture. The flask was evacuated under aspirator vacuum, refilled with hydrogen three times, and then stirred under hydrogen (1 atm) for 12 h. The mixture was then

filtered through Celite to remove the catalyst, and the filtrate was concentrated to give a crude oil. To remove the TBS protecting group, the crude product was dissolved in 5 mL 8:1:1 AcOH:H_2O:MeOH. One drop of aqueous HCl solution (2 N) was then added to the mixture, and the resulting solution was stirred for 2 h at rt. The reaction was then diluted with excess toluene, and the resulting biphasic mixture was concentrated under vacuum (0.1 torr) with a rotary evaporator at a temperature not exceeding 30 °C. The crude product of this sequence was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (100 mg, 0.24 mmol, 94% from **6b**). $[\alpha]^{28}_D$: +1.7 (c 0.50, MeOH). IR (thin film): 3419, 2952, 1709, 1681 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ 6.84-6.79 (m, 3H), 5.08 (s, 1H), 4.43 (s, 2H), 3.86 (s, 3H), 3.85 (s, 3H), 3.65-3.58 (m, 2H), 3.61 (d, *J* = 9.2 Hz, 1H), 3.34 (d, *J* = 9.2 Hz, 1H), 1.73-1.62 (m, 1H), 1.57-1.44 (m, 1H), 1.40 (s, 9H), 1.32-1.10 (m, 6H), 0.87-0.80 (m, 3H). ^{13}C NMR (100 MHz, CD_3OD): δ 156.2, 149.2, 148.9, 130.4, 120.6, 111.1, 111.0, 79.8, 73.7, 72.7, 67.2, 59.0, 56.1, 56.0, 32.6, 32.4, 28.5, 23.1, 22.7, 14.2. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.45.

The resulting alcohol (75 mg, 0.18 mmol, 1.0 equiv) was oxidized in 3.6 mL CH_2Cl_2 using Dess-Martin periodinane (155 mg, 0.36 mmol, 2.0 equiv) and $NaHCO_3$ (155 mg). The crude oil was chromatographed on silica gel (2:1 hexanes/EtOAc) to give the corresponding aldehyde as a clear oil. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.58. The resulting product was further oxidized in 3.6 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (75 mg, 0.54 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.7 mL, 1.4 mmol, 7.8 equiv), and $NaClO_2$ (99 mg, 1.1 mmol, 6.0 equiv). Following oxidation, the crude carboxylic acid product was subsequently treated with 10% Pd/C (54 mg) in 5 mL methanol to remove the DMB protecting group, according to the procedure for **7a**. The resulting product was immediately chromatographed on silica gel (1:1 hexanes/EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **7b** as an oil (42 mg, 0.15 mmol, 84% from the alcohol product). $[\alpha]^{28}_D$: -2.6 (c 0.50, MeOH). IR (thin film): 3414, 2957, 1709, 1643

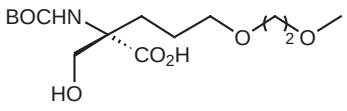
cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 4.00 (d, *J* = 11.0 Hz, 1H), 3.77 (d, *J* = 11.1 Hz, 1H), 2.07-1.94 (m, 1H), 1.77-1.64 (m, 1H), 1.45 (s, 9H), 1.38-1.10 (m, 6H), 0.94-0.84 (m, 3H). ^{13}C NMR (100 MHz, CD_3OD): δ 176.0, 156.3, 80.4, 66.0, 64.7, 33.0, 32.5, 28.9, 24.4, 23.6, 14.4. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.36.



6c

Compound 6c. (Condition B) To a solution of **5** (137 mg, 0.24 mmol, 1.0 equiv) in 1.8 mL anhydrous THF at rt was added 0.6 mL DMPU. The mixture was then cooled to -50 °C, and LDA (0.65 M in THF, 1.11 mL, 0.72 mmol, 3.0 equiv), kept at 0 °C, was added slowly. The resulting mixture was stirred for 15 min at -50 °C, after which MEM-Cl (110 μL, 0.96 mmol, 4.0 equiv) was added dropwise. The mixture was immediately warmed to rt and stirred for an additional 12 h, after which the mixture was quenched with 0.5 mL H_2O, followed by 0.5 mL saturated aq NH_4Cl. The heterogeneous mixture was then diluted with 15 mL EtOAc and an additional 10 mL saturated aq NH_4Cl. The phases were separated, and the aq phase was extracted with 2 × 15 mL EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was chromatographed on silica gel (1:1 hexanes/EtOAc) to give **6c** as an oil (132 mg, 0.20 mmol, 85%). $[\alpha]^{28}_D$: +8.0 (c 1.0, MeOH). IR (thin film): 2925, 2843, 1692 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.32-7.10 (m, 5H), 6.87-6.76 (m, 3H), 4.74 (AB, *J* = 16.9 Hz, Δν = 11.7 Hz, 2H), 4.49 (AB, *J* = 11.7 Hz, Δν = 11.1 Hz, 2H), 4.22 (d, *J* = 9.5 Hz, 1H), 4.13 (s, 2H), 4.05 (d, *J* = 9.2 Hz, 1H), 3.87 (d, *J* = 9.6 Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 3.79 (d, *J* = 9.3 Hz, 1H), 3.47-3.41 (m, 2H), 3.39-3.33 (m, 2H), 3.30 (s, 3H), 1.31 (s, 9H), 0.87 (s, 9H), 0.02 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.2, 149.1, 148.6,

141.2, 131.2, 128.1, 126.7, 126.2, 120.2, 111.1, 111.0, 86.7, 81.6, 80.3, 73.6, 71.8, 71.5, 68.5, 65.3, 64.1, 59.2, 58.8, 56.1, 56.0, 51.6, 28.5, 26.0, 18.5, -5.2 (2C). TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.54.

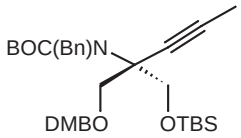


7c

Compound 7c. Compound **6c** (112 mg, 0.17 mmol, 1.0 equiv) was reduced with 10% Pd/C (75 mg) in 11 mL anhydrous benzene. Subsequent removal of the TBS protecting group was accomplished in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N) according to the procedure for **7b**. The crude product of this sequence was chromatographed on silica gel (1:2 hexanes/EtOAc then EtOAc) to give the corresponding alcohol as a clear oil (71 mg, 0.13 mmol, 76% from **6c**). $[\alpha]^{28}_D$: -1.6 (c 0.55, MeOH). IR (thin film): 3419, 2925, 1687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26-7.12 (m, 5H), 6.80-6.72 (m, 3H), 4.60-4.49 (m, 2H), 4.37-4.28 (m, 2H), 3.98 (d, *J* = 12.0 Hz, 1H), 3.85 (s, 3H), 3.83 (d, *J* = 12.3 Hz, 1H), 3.79 (s, 3H), 3.75 (d, *J* = 9.8 Hz, 1H), 3.54 (d, *J* = 9.8 Hz, 1H), 3.54-3.44 (m, 4H), 3.38-3.30 (m, 2H), 3.34 (s, 3H), 1.86-1.70 (m, 2H), 1.56-1.44 (m, 2H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.8, 149.1, 148.8, 141.2, 130.4, 128.3, 126.5, 120.5, 111.1, 111.0, 80.5, 73.6, 73.5, 72.1, 71.7, 70.1, 67.3, 65.6, 59.2, 56.1, 56.0, 49.5, 29.2, 28.4, 24.2. TLC (SiO_2, EtOAc): R_f = 0.57.

The resulting alcohol (84 mg, 0.16 mmol, 1.0 equiv) was oxidized in 3.2 mL CH_2Cl_2 using Dess-Martin periodinane 133 mg, 0.32 mmol, 2.0 equiv) and $NaHCO_3$ (133 mg). The crude oil was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the aldehyde as a clear oil. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.41. The resulting product was further oxidized in 3.0 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (65 mg, 0.48 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.6 mL, 1.2 mmol, 7.5 equiv), and

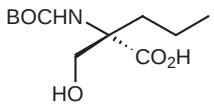
$NaClO_2$ (84 mg, 0.96 mmol, 6.0 equiv), according to the procedure for **7a**, to provide the corresponding carboxylic acid (80 mg, 0.14 mmol). To remove the benzyl and DMB protecting groups, the crude product (60 mg, 0.11 mmol) was subsequently dissolved in 2.5 mL 4:1 AcOH:EtOH, and 20% $Pd(OH)_2/C$ (Pearlman's catalyst) (50 mg) was added to the stirring mixture. The flask was evacuated under aspirator vacuum, refilled with hydrogen three times, and then stirred under hydrogen (1 atm) for 24 h. The mixture was then filtered through Celite to remove the catalyst, and the filtrate was concentrated to give a crude oil. The resulting crude product was immediately chromatographed on silica gel (9:1 EtOAc/MeOH with 0.1% AcOH then 90:8:2 EtOAc/MeOH/AcOH) to give **7c** as an oil (28 mg, 0.09 mmol, 77% from the alcohol product). $[\alpha]^{28}_D$: +3.5 (c 0.30, MeOH). IR (thin film): 3414, 2925, 1703 cm^{-1}. ^1H NMR (500 MHz, CD_3OD with $CDCl_3$ for solubility): δ 3.98 (d, *J* = 11.0 Hz, 1H), 3.79 (d, *J* = 11.0 Hz, 1H), 3.57-3.50 (m, 4H), 3.48-3.42 (m, 2H), 3.35 (s, 3H), 2.10-2.00 (m, 1H), 1.85-1.74 (m, 1H), 1.62-1.42 (m, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD with $CDCl_3$ for solubility): δ 176.6, 156.4, 80.3, 73.0, 72.2, 70.9, 65.7, 65.1, 59.3, 29.5, 28.9, 25.2. TLC (SiO_2, 10% MeOH/EtOAc with 2% AcOH): R_f = 0.28.



6d

Compound 6d. To a solution of **5** (130 mg, 0.23 mmol, 1.0 equiv) in 1.7 mL anhydrous THF at rt was added 0.6 mL DMPU. The mixture was then cooled to -50 °C, and LDA (0.65 M in THF, 1.05 mL, 0.68 mmol, 3.0 equiv), kept at 0 °C, was added slowly. The resulting mixture was stirred for 15 min at -50 °C, after which methyl iodide (57 μL, 0.91 mmol, 4.0 equiv) was added dropwise. The mixture was immediately warmed to rt and stirred for an additional 12 h, after which reaction workup was performed according to

Condition B for **6c**. The crude oil was chromatographed on silica gel (3:1 hexanes/EtOAc) to give **6d** as an oil (131 mg, 0.22 mmol, 98%). $[\alpha]^{28}_{D}$: +7.8 (c 0.95, MeOH). IR (thin film): 3419, 2930, 2854, 1687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.34-7.10 (m, 5H), 6.90-6.76 (m, 3H), 4.74 (AB, *J* = 16.8 Hz, Δν = 13.9 Hz, 2H), 4.49 (AB, *J* = 11.9 Hz, Δν = 10.6 Hz, 2H), 4.15 (d, *J* = 9.4 Hz, 1H), 4.02 (d, *J* = 9.2 Hz, 1H), 3.86 (d, *J* = 9.4 Hz, 1H), 3.85 (s, 3H), 3.82 (s, 3H), 3.78 (d, *J* = 9.2 Hz, 1H), 1.74 (s, 3H), 1.30 (s, 9H), 0.87 (s, 9H), 0.01 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.3, 149.1, 148.6, 141.5, 131.4, 128.0, 127.0, 126.2, 120.2, 111.1, 111.0, 82.0, 80.1, 79.2, 73.5, 71.8, 65.6, 64.2, 56.1, 55.9, 51.6, 28.5, 26.0, 18.5, 4.0, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.41.

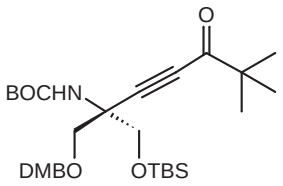


7d

Compound 7d. Compound **6d** (104 mg, 0.18 mmol, 1.0 equiv) was reduced with 10% Pd/C (69 mg) in 10 mL anhydrous benzene. Subsequent removal of the TBS protecting group was accomplished in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N) according to the procedure for **7b**. The crude product of this sequence was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (79 mg, 0.17 mmol, 94% from **6d**). $[\alpha]^{28}_{D}$: -4.5 (c 0.55, MeOH). IR (thin film): 3424, 2957, 2865, 1681 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.27-7.13 (m, 5H), 6.81-6.74 (m, 3H), 4.62-4.50 (m, 2H), 4.34 (AB, *J* = 11.7 Hz, Δν = 7.3 Hz, 2H), 3.99 (d, *J* = 12.1 Hz, 1H), 3.85 (s, 3H), 3.83 (d, *J* = 12.0 Hz, 1H), 3.80 (s, 3H), 3.77 (d, *J* = 9.9 Hz, 1H), 3.56 (d, *J* = 9.8 Hz, 1H), 1.74-1.65 (m, 2H), 1.30 (s, 9H), 1.26-1.12 (m, 2H), 0.82 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.9, 149.1, 148.8, 141.3,

130.4, 128.3, 126.5, 120.5, 111.1, 111.0, 80.4, 73.7, 73.5, 67.5, 65.8, 56.1, 56.0, 49.5, 35.4, 28.4, 17.3, 14.8. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.53.

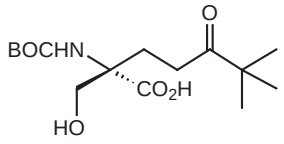
The resulting alcohol (54 mg, 0.11 mmol, 1.0 equiv) was oxidized in 2.3 mL CH_2Cl_2 using Dess-Martin periodinane (97 mg, 0.22 mmol, 2.0 equiv) and $NaHCO_3$ (97 mg). The crude oil was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the aldehyde as a clear oil. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.74. The resulting product was further oxidized in 2.5 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (47 mg, 0.34 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.5 mL, 1.0 mmol, 9.1 equiv), and $NaClO_2$ (62 mg, 0.68 mmol, 6.0 equiv). The benzyl and DMB protecting groups were subsequently removed using 20% $Pd(OH)_2$/C (Pearlman's catalyst) (45 mg) in 3 mL 4:1 AcOH:EtOH, according to the procedure for **7c**. The crude product was immediately chromatographed on silica gel (9:1 EtOAc/MeOH with 0.1% AcOH then 90:8:2 EtOAc/MeOH/AcOH) to give **7d** as an oil (17 mg, 0.07 mmol, 60% from the alcohol product). $[\alpha]^{28}_D$: +2.3 (c 0.50, MeOH). IR (thin film): 3408, 2968, 2919, 1703 cm^{-1}. ^1H NMR (400 MHz, CD_3OD with $CDCl_3$ for solubility): δ 4.02 (d, J = 10.7 Hz, 1H), 3.76 (d, J = 11.1 Hz, 1H), 2.06-1.94 (m, 1H), 1.75-1.62 (m, 1H), 1.43 (s, 9H), 1.38-1.10 (m, 2H), 0.90 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD with $CDCl_3$ for solubility): δ 175.9, 156.0, 80.2, 65.8, 64.8, 34.6, 28.8, 17.9, 14.5. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.42.



6e

Compound 6e. (Condition C) Compound **2** (123 mg, 0.26 mmol, 1.0 equiv) was dissolved in 9.5 mL anhydrous 9:1 toluene:NEt_3 at rt. Trimethylacetyl chloride (0.47

mL, 3.8 mmol, 15 equiv) was then added followed by CuI (34 mg, 0.18 mmol, 0.7 equiv), and the resulting mixture was slowly heated to 60 ^{o}C. The mixture was stirred at 60 ^{o}C for 2 h and was then cooled to rt, after which the mixture was treated with 0.5 mL MeOH, followed by 10 mL H_2O, and dilution with 15 mL EtOAc. The phases were separated, and the aq phase was extracted with 2 × 15 mL EtOAc. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The product was then chromatographed on silica gel (5:1 hexanes/EtOAc) to give **6e** as a clear oil (87 mg, 0.15 mmol, 60%). $[\alpha]^{28}_{D}$: +4.9 (c 1.0, MeOH). IR (thin film): 3435, 2952, 1719, 1665 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.87-6.78 (m, 3H), 5.10 (s, 1H), 4.55-4.45 (m, 2H), 3.93 (d, *J* = 9.7 Hz, 1H), 3.90-3.82 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.78 (d, *J* = 9.3 Hz, 1H), 3.65 (d, *J* = 9.1 Hz, 1H), 1.41 (s, 9H), 1.16 (s, 9H), 0.85 (s, 9H), 0.04 (s, 3H), 0.03 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 194.1, 154.4, 149.2, 148.9, 130.3, 120.6, 111.2, 111.0, 92.7, 80.8, 80.2, 73.8, 70.6, 64.6, 56.1, 56.0, 55.6, 45.2, 28.5, 26.1, 26.0, 18.4, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.41.

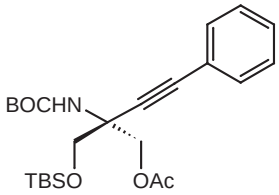


7e

Compound 7e. Compound **6e** (77 mg, 0.14 mmol, 1.0 equiv) was reduced with 10% Pd/C (51 mg) in 8 mL anhydrous benzene according to the procedure for **7b**. To remove the TBS group, the crude product was dissolved in 2.7 mL anhydrous THF, and tetrabutylammonium fluoride (1.0 M in hexanes, 0.27 mL, 0.27 mmol, 2.0 equiv) was added dropwise. The solution was stirred at rt for 6 h, after which the reaction mixture was chromatographed on silica gel (1:1 hexanes/EtOAc). To oxidize the resulting alcohol, the product was then dissolved in 2.7 mL CH_2Cl_2 at rt, and Dess-Martin periodinane (114 mg, 0.27 mmol, 2.0 equiv) was added to the mixture. The reaction was

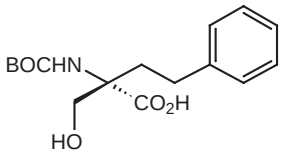
stirred for 12 h after which workup was performed according to the procedure for **7a**. The crude product was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the corresponding aldehyde as a clear oil (53 mg, 0.12 mmol, 86% from **6e**). $[\alpha]^{28}_{D}$: -5.4 (c 0.25, MeOH). IR (thin film): 3392, 2974, 2914, 1698 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.29 (s, 1H), 6.79-6.75 (m, 3H), 5.45 (s, 1H), 4.39 (AB, *J* = 11.9 Hz, Δν = 28.1 Hz, 2H), 3.88-3.78 (m, 1H), 3.84 (s, 3H), 3.83 (s, 3H), 3.65 (d, *J* = 9.5 Hz, 1H), 2.46-2.29 (m, 2H), 2.22-2.10 (m, 1H), 2.10-1.99 (m, 1H), 1.39 (s, 9H), 1.04 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 215.1, 198.8, 154.8, 149.2, 148.9, 130.1, 120.5, 111.0, 110.9, 80.0, 73.6, 69.4, 65.7, 56.0, 55.9, 44.2, 30.2, 28.4, 26.5, 24.0. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.61. HRMS: Calcd for $C_{24}H_{37}NO_7Si$ $(M + Na)^+$: 474.2462. Found: 474.2469.

The resulting aldehyde (44 mg, 0.10 mmol, 1.0 equiv) was oxidized in 2.0 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (40 mg, 0.29 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.4 mL, 0.8 mmol, 8.0 equiv), and $NaClO_2$ (53 mg, 0.58 mmol, 6.0 equiv). Following oxidation, the crude carboxylic acid product was subsequently treated with 10% Pd/C (30 mg) in 3 mL methanol to remove the DMB protecting group, according to the procedure for **7a**. The resulting product was immediately chromatographed on silica gel (98:2 EtOAc/AcOH) to give **7e** as an oil (28 mg, 0.09 mmol, 90% from the aldehyde product). Compound **7e** was found to exist in equilibrium with the corresponding hemiketal, and the position of this equilibrium was shown to be highly solvent-dependent. Therefore, characterization by NMR spectroscopy was performed in a solvent combination which effectively suppressed formation of the hemiketal. $[\alpha]^{28}_{D}$: +3.0 (c 0.50, MeOH). IR (thin film): 2974, 1741, 1709 cm^{-1}. ^{1}H NMR (500 MHz, CD_3OD with D_2O and 1 drop AcOH): δ 3.95 (d, *J* = 10.7 Hz, 1H), 3.80 (d, *J* = 10.2 Hz, 1H), 2.64-2.42 (m, 2H), 2.26-2.12 (m, 1H), 2.08-1.94 (m, 1H), 1.44 (s, 9H), 1.12 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD with D_2O and 1 drop AcOH): δ 218.8, 176.2, 156.5, 81.0, 65.0, 64.7, 45.5, 32.3, 28.8, 27.4, 26.9. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.30.



8a

Compound 8a. (Condition D) Compound **4** (94 mg, 0.25 mmol, 1.0 equiv) was dissolved in 2 mL anhydrous 4:1 DMF:NEt_3 at rt. Iodobenzene (56 μL, 0.50 mmol, 2.0 equiv) was then added followed by CuI (10 mg, 0.05 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (29 mg, 0.02 mmol, 0.1 equiv). The resulting mixture was stirred for 12 h and was then filtered through a short column of silica gel (5:1 hexanes/EtOAc). The product was then further chromatographed on silica gel (5:1 hexanes/EtOAc) to give **8a** as a clear oil (108 mg, 0.24 mmol, 95%). $[\alpha]^{28}_D$: -2.6 (c 0.50, MeOH). IR (thin film): 3365, 2947, 1747, 1725 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40-7.36 (m, 2H), 7.29-7.25 (m, 3H), 5.04 (s, 1H), 4.53 (d, *J* = 10.8 Hz, 1H), 4.30 (d, *J* = 10.6 Hz, 1H), 3.89 (AB, *J* = 9.6 Hz, Δν = 13.2 Hz, 2H), 2.09 (s, 3H), 1.45 (s, 9H) 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.8, 154.5, 132.0, 128.5, 128.4, 122.9, 86.9, 84.4, 80.4, 65.4, 64.8, 55.3, 28.6, 26.0, 21.1, 18.5, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.55.



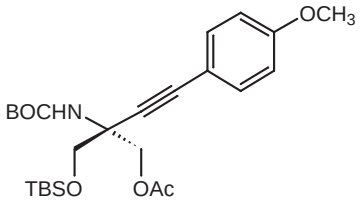
9a

Compound 9a. To reduce the alkyne, compound **8a** (79 mg, 0.18 mmol, 1.0 equiv) was dissolved in 8 mL anhydrous benzene, and 10% Pd/C (50 mg) was added to the stirring mixture. The flask was evacuated under aspirator vacuum, refilled with hydrogen three times, and then stirred under hydrogen (1 atm) for 12 h. The mixture was then filtered

through Celite to remove the catalyst, and the filtrate was concentrated to give a crude oil. To remove the acetate group, the product was subsequently dissolved in 2 mL of a saturated solution of ammonia in MeOH, and the reaction was stirred for 12 h after which the mixture was concentrated under vacuum (aspirator pressure) with a rotary evaporator. The crude product of this sequence was chromatographed on silica gel (3:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (70 mg, 0.17 mmol, 97% from **8a**). $[\alpha]^{28}_{D}$: +7.2 (c 0.50, MeOH). IR (thin film): 3414, 2952, 1714, 1687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28-7.22 (m, 2H), 7.19-7.12 (m, 3H), 5.15 (s, 1H), 3.87 (d, *J* = 10.0 Hz, 1H), 3.74-3.66 (m, 2H), 3.54 (d, *J* = 9.9 Hz, 1H), 2.64 (dt, *J* = 12.9, 4.8 Hz, 1H), 2.50 (dt, *J* = 12.7, 5.0 Hz, 1H), 2.03 (dt, *J* = 13.1, 4.6 Hz, 1H), 1.76-1.65 (m, 1H), 1.43 (s, 9H), 0.90 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 142.4, 128.6, 128.5, 126.0, 79.8, 67.4, 66.5, 59.0, 34.3, 30.1, 28.6, 26.0, 18.4, -5.3, -5.4. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.58.

The resulting alcohol was then oxidized in two steps. To a solution of the above alcohol (53 mg, 0.13 mmol, 1.0 equiv) in 2.6 mL CH_2Cl_2 at rt was added $NaHCO_3$ (110 mg) followed by Dess-Martin periodinane (110 mg, 0.26 mmol, 2.0 equiv). The reaction mixture was stirred for 12 h after which it was quenched with 1 mL of a $Na_2S_2O_3$ solution (25g $Na_2S_2O_3$ per 100 mL). After stirring for 15 min, the mixture was diluted with 15 mL CH_2Cl_2 and 15 mL H_2O. The phases were separated, and the aq phase was extracted with 2 × 15 mL CH_2Cl_2. The combined organic phases were dried (Na_2SO_4), filtered, and concentrated. The crude oil was chromatographed on silica gel (5:1 hexanes/EtOAc) to give the aldehyde as a clear oil. The resulting product was dissolved in 3 mL 4:1 *t*BuOH:H_2O. NaH_2PO_4 (53mg, 0.38 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.6 mL, 1.2 mmol, 9.2 equiv), and $NaClO_2$ (70 mg, 0.76 mmol, 6.0 equiv) were successively added, and the solution was stirred at rt for 12 h. The reaction mixture was then diluted with 10 mL H_2O and 15 mL CH_2Cl_2. The phases were separated, and the aq phase was extracted with 2 × 15 mL CH_2Cl_2. The combined organic phases were dried

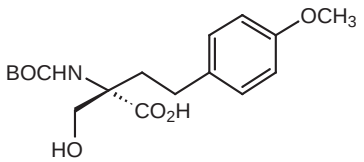
(Na_2SO_4), filtered, and concentrated to give the corresponding carboxylic acid. To remove the TBS group, the crude product was subsequently dissolved in 5 mL 8:1:1 AcOH:H_2O:MeOH. One drop of aqueous HCl solution (2 N) was then added to the mixture, and the resulting solution was stirred for 2 h at rt. The reaction was then diluted with excess toluene, and the resulting biphasic mixture was concentrated under vacuum (0.1 torr) with a rotary evaporator at a temperature not exceeding 30 °C. The resulting crude product was immediately chromatographed on silica gel (EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **9a** as an oil (31 mg, 0.10 mmol, 78% from alcohol product). $[\alpha]^{28}_D$: -1.7 (c 1.0, MeOH). IR (thin film): 3403, 2974, 2925, 1703 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ 7.28-7.21 (m, 2H), 7.18-7.11 (m, 3H), 4.03 (d, *J* = 11.1 Hz, 1H), 3.80 (d, *J* = 11.1 Hz, 1H), 2.55 (dt, *J* = 12.9, 4.9 Hz, 1H), 2.51-2.39 (m, 1H), 2.39-2.24 (m, 1H), 2.10-1.96 (m, 1H), 1.48 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD): δ 175.7, 156.4, 143.1, 129.6, 129.5, 127.1, 80.5, 66.0, 64.8, 35.0, 31.4, 28.9. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.44.



8b

Compound 8b. Compound **4** (127 mg, 0.34 mmol, 1.0 equiv) was coupled with 4-iodoanisole (159 mg, 0.68 mmol, 2.0 equiv) in 2.7 mL anhydrous 4:1 DMF:NEt_3 using CuI (13 mg, 0.07 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (36 mg, 0.03 mmol, 0.1 equiv) according to Condition D for **8a**. The product was purified according to the chromatography protocol for **8a** using 5:1 hexanes/EtOAc. Compound **8b** was produced as a clear oil (148 mg, 0.31 mmol, 91%). $[\alpha]^{28}_D$: -2.6 (c 0.50, MeOH). IR (thin film): 2952, 2854, 1747, 1725 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 7.31 (d, *J* = 8.9 Hz, 1H),

6.79 (d, *J* = 8.9 Hz, 1H), 5.03 (s, 1H), 4.52 (d, *J* = 10.7 Hz, 1H), 4.29 (d, *J* = 10.3 Hz, 1H), 3.92-3.82 (m, 2H), 3.78 (s, 3H), 2.08 (s, 3H), 1.44 (s, 9H) 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 159.8, 154.6, 133.4, 115.0, 114.0, 85.4, 84.3, 80.2, 65.4, 64.8, 55.5, 55.3, 28.6, 26.0, 21.1, 18.5, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.53.



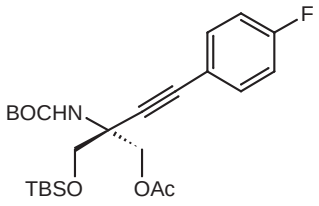
9b

Compound 9b. Compound **8b** (121 mg, 0.25 mmol, 1.0 equiv) was reduced with 10% Pd/C (80 mg) in 10 mL anhydrous benzene. Subsequent deacetylation was accomplished in 15 mL of a saturated solution of ammonia in MeOH according to the procedure for **9a**. The crude product of this sequence was chromatographed on silica gel (3:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (111 mg, 0.25 mmol, 100% from **8b**). $[\alpha]^{28}_D$: +6.1 (c 0.50, MeOH). IR (thin film): 3414, 2925, 1714, 1692 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.08 (d, *J* = 8.5 Hz, 1H), 6.79 (d, *J* = 8.7 Hz, 1H), 5.14 (s, 1H), 3.86 (d, *J* = 9.9 Hz, 1H), 3.76 (s, 3H), 3.72-3.66 (m, 2H), 3.53 (d, *J* = 9.9 Hz, 1H), 2.58 (dt, *J* = 12.9, 4.8 Hz, 1H), 2.44 (dt, *J* = 12.9, 5.2 Hz, 1H), 2.00 (dt, *J* = 13.3, 4.0 Hz, 1H), 1.66 (dt, *J* = 12.7, 5.2 Hz, 1H), 1.43 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 158.0, 156.1, 134.4, 129.4, 114.0, 79.7, 67.4, 66.4, 59.0, 55.5, 34.5, 29.2, 28.6, 26.0, 18.4, -5.3, -5.4. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.45. HRMS: Calcd for $C_{23}H_{41}NO_5Si$ $(M + Na)^+$: 462.2646. Found: 462.2651.

The resulting alcohol was then oxidized in two steps. A solution of oxalyl chloride (51 μL, 0.58 mmol, 3.0 equiv) in 3 mL CH_2Cl_2 was cooled to -78 °C, and

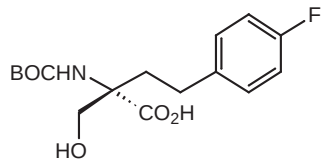
DMSO (55 μL, 0.78 mmol, 4.0 equiv) was then added dropwise. The resulting mixture was stirred an additional 15 min at -78 °C. A solution of the above alcohol (86 mg, 0.20 mmol, 1.0 equiv) in 2 mL of CH_2Cl_2 at -78 °C was then added dropwise, and the mixture continued to stir at -78 °C for 2 h. NEt_3 (0.22 mL, 1.6 mmol, 8.0 equiv) was then added dropwise, and the solution was stirred for 20 min at -78 °C and an additional 30 min at 0 °C. The reaction was treated with 1 mL saturated aq $NaHCO_3$ and was then diluted with 15 mL CH_2Cl_2. The resulting layers were separated and the aq phase was extracted with 2 × 15 mL CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated to give the corresponding aldehyde. The resulting product was dissolved in 3.5 mL 4:1 *t*BuOH:H_2O. NaH_2PO_4 (81 mg, 0.58 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.7 mL, 1.4 mmol, 7.0 equiv), and $NaClO_2$ (106 mg, 1.2 mmol, 6.0 equiv) were successively added, and the solution was stirred at rt for 12 h. The reaction mixture was then diluted with 10 mL H_2O and 15 mL CH_2Cl_2. The phases were separated, and the aq phase was extracted with 2 × 15 mL CH_2Cl_2. The combined organic phases were dried (Na_2SO_4), filtered, and concentrated to give the corresponding carboxylic acid. To remove the TBS group, the crude product was subsequently dissolved in 5 mL 8:1:1 AcOH:H_2O:MeOH. One drop of aqueous HCl solution (2 N) was then added to the mixture, and the resulting solution was stirred for 2 h at rt. The reaction was then diluted with excess toluene, and the resulting biphasic mixture was concentrated under vacuum (0.1 torr) with a rotary evaporator at a temperature not exceeding 30 °C. The resulting crude product was immediately chromatographed on silica gel (EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **9b** as an oil (31 mg, 0.10 mmol, 59% from the alcohol product). $[\alpha]^{28}_D$: -4.0 (c 2.0, MeOH). IR (thin film): 3414, 2968, 1703 cm^{-1}. ^1H NMR (400 MHz, CD_3OD): δ 7.05 (d, *J* = 8.4 Hz, 1H), 6.80 (d, *J* = 8.5 Hz, 1H), 4.04 (d, *J* = 10.2 Hz, 1H), 3.80 (d, *J* = 11.0 Hz, 1H), 3.74 (s, 3H), 2.50 (dt, *J* = 13.2, 5.0 Hz, 1H), 2.45-2.34 (m, 1H), 2.34-2.22 (m, 1H), 2.06-1.94 (m, 1H),

1.47 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD): δ 175.7, 159.5, 156.3, 134.9, 130.4, 115.0, 80.5, 65.9, 64.8, 55.7, 35.1, 30.4, 28.9. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.34.



8c

Compound 8c. Compound **4** (116 mg, 0.31 mmol, 1.0 equiv) was coupled with 1-flouro-4-iodobenzene (72 μL, 0.62 mmol, 2.0 equiv) in 2.5 mL anhydrous 4:1 DMF:NEt_3 using CuI (12 mg, 0.06 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (36 mg, 0.03 mmol, 0.1 equiv) according to Condition D for **8a**. The product was purified according to the chromatography protocol for **8a** using 5:1 hexanes/EtOAc. Compound **8c** was produced as a clear oil (127 mg, 0.27 mmol, 87%). $[\alpha]^{28}_D$: -2.3 (c 0.50, MeOH). IR (thin film): 3365, 2952, 1747, 1719 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38-7.33 (m, 2H), 6.99-6.93 (m, 2H), 5.04 (s, 1H), 4.52 (d, *J* = 10.7 Hz, 1H), 4.29 (d, *J* = 10.5 Hz, 1H), 3.92-3.82 (m, 2H), 2.09 (s, 3H), 1.44 (s, 9H) 0.88 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.7, 162.7 (d, J_{CF} = 249.4 Hz), 154.4, 133.9 (d, J_{CF} = 8.2 Hz), 118.9 (d, J_{CF} = 3.7 Hz), 115.7 (d, J_{CF} = 22.0 Hz), 86.6, 83.4, 80.4, 65.3, 64.7, 55.2, 28.6, 26.0, 21.1, 18.5, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.66.

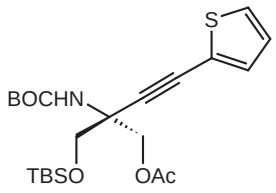


9c

Compound 9c. Compound **8c** (105 mg, 0.22 mmol, 1.0 equiv) was reduced with 10% Pd/C (67 mg) in 10 mL anhydrous benzene. Subsequent deacetylation was accomplished in 15 mL of a saturated solution of ammonia in MeOH according to the procedure for **9a**. The crude product of this sequence was chromatographed on silica gel (3:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (89 mg, 0.21 mmol, 92% from **8c**). $[\alpha]^{28}_{D}$: +2.7 (c 0.35, MeOH). IR (thin film): 3419, 2952, 1719, 1687 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.14-7.07 (m, 2H), 6.96-6.88 (m, 2H), 5.16 (s, 1H), 3.86 (d, J = 9.9 Hz, 1H), 3.68 (AB, J = 11.7 Hz, $\Delta\nu$ = 15.8 Hz, 2H), 3.52 (d, J = 9.9 Hz, 1H), 2.61 (dt, J = 12.9, 4.8 Hz, 1H), 2.46 (dt, J = 12.9, 5.2 Hz, 1H), 2.01 (dt, J = 13.3, 4.4 Hz, 1H), 1.71-1.62 (m, 1H), 1.43 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 161.5 (d, J_{CF} = 243.0 Hz), 156.0, 137.9 (d, J_{CF} = 3.2 Hz), 129.9 (d, J_{CF} = 7.8 Hz), 115.3 (d, J_{CF} = 21.5 Hz), 79.8, 67.4, 66.5, 58.9, 34.3, 29.3, 28.6, 26.0, 18.4, -5.3, -5.4. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.33. HRMS: Calcd for $C_{22}H_{38}FNO_4Si$ $(M + Na)^+$: 450.2446. Found: 450.2453.

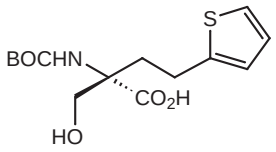
The resulting alcohol (67 mg, 0.16 mmol, 1.0 equiv) was oxidized in CH_2Cl_2 using oxalyl chloride (41 μL, 0.48 mmol, 3.0 equiv), DMSO (44 μL, 0.64 mmol, 4.0 equiv), and NEt_3 (0.17 mL, 1.3 mmol, 8.0 equiv). The resulting product was further oxidized in 3.0 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (65 mg, 0.47 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.6 mL, 1.2 mmol, 7.5 equiv), and $NaClO_2$ (85 mg, 0.94 mmol, 6.0 equiv). Subsequent silyl deprotection was performed in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N), according to the procedure for **9b**. The product was chromatographed on silica gel (EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **9c** as an oil (47 mg, 0.14 mmol, 91% from the alcohol

product). $[\alpha]^{28}_{D}$: -4.8 (c 1.0, MeOH). IR (thin film): 3408, 2974, 2930, 1709 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.19-7.12 (m, 2H), 7.01-6.92 (m, 2H), 4.03 (d, *J* = 11.1 Hz, 1H), 3.80 (d, *J* = 11.1 Hz, 1H), 2.55 (dt, *J* = 13.3, 5.3 Hz, 1H), 2.45 (dt, *J* = 12.1, 4.8 Hz, 1H), 2.36-2.24 (m, 1H), 2.08-1.97 (m, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD): δ 175.8, 162.9 (d, J_{CF} = 242.1 Hz), 156.4, 138.9 (d, J_{CF} = 3.2 Hz), 131.1 (d, J_{CF} = 7.8 Hz), 116.1 (d, J_{CF} = 21.0 Hz), 80.5, 65.8, 64.8, 34.9, 30.5, 28.9. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.39.



8d

Compound 8d. Compound **4** (116 mg, 0.31 mmol, 1.0 equiv) was coupled with 2-iodothiophene (69 μL, 0.62 mmol, 2.0 equiv) in 2 mL anhydrous 4:1 DMF:NEt_3 using CuI (12 mg, 0.06 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (36 mg, 0.03 mmol, 0.1 equiv) according to Condition D for **8a**. The product was purified according to the chromatography protocol for **8a** using 5:1 hexanes/EtOAc. Compound **8d** was produced as a clear oil (122 mg, 0.27 mmol, 86%). $[\alpha]^{28}_{D}$: -2.3 (c 0.50, MeOH). IR (thin film): 2952, 2854, 1747, 1698 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.23-7.19 (m, 1H), 7.17-7.13 (m, 1H), 6.92 (dd, *J* = 5.1, 3.7 Hz, 1H), 5.03 (s, 1H), 4.51 (d, *J* = 10.8 Hz, 1H), 4.29 (d, *J* = 10.7 Hz, 1H), 3.93-3.80 (m, 2H), 2.09 (s, 3H), 1.45 (s, 9H) 0.89 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 154.5, 132.4, 127.3, 127.0, 122.8, 90.8, 80.5, 77.8, 65.3, 64.6, 55.5, 28.6, 26.0, 21.1, 18.5, -5.2 (2C). TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.46.

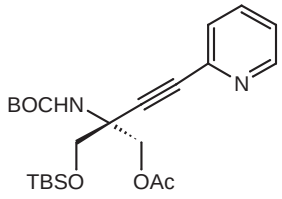


9d

Compound 9d. Compound **8d** (100 mg, 0.22 mmol, 1.0 equiv) was reduced with 10% Pd/C (66 mg) in 10 mL anhydrous benzene. Subsequent deacetylation was accomplished in 15 mL of a saturated solution of ammonia in MeOH according to the procedure for **9a**. The crude product of this sequence was chromatographed on silica gel (3:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (86 mg, 0.21 mmol, 94% from **8d**). $[\alpha]^{28}_{D}$: +3.3 (c 0.50, MeOH). IR (thin film): 3419, 2952, 1714, 1687 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.08 (dd, *J* = 5.2, 1.2 Hz, 1H), 6.79 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.78-6.76 (m, 1H), 5.14 (s, 1H), 3.83 (d, *J* = 9.9 Hz, 1H), 3.68 (AB, *J* = 11.7 Hz, $\Delta\nu$ = 12.7 Hz, 2H), 3.54 (d, *J* = 9.9 Hz, 1H), 2.93-2.84 (m, 1H), 2.80-2.71 (m, 1H), 2.17-2.06 (m, 1H), 1.85-1.76 (m, 1H), 1.42 (s, 9H), 0.89 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 156.1, 145.1, 127.0, 124.3, 123.2, 79.9, 67.2, 66.3, 58.9, 34.4, 28.6, 26.0, 24.3, 18.4, -5.3, -5.4. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.48. HRMS: Calcd for $C_{20}H_{37}NO_4SSi$ $(M + Na)^+$: 438.2105. Found: 438.2098.

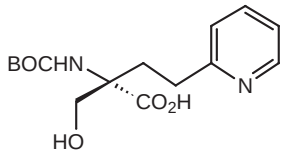
The resulting alcohol (69 mg, 0.16 mmol, 1.0 equiv) was oxidized in CH_2Cl_2 using oxalyl chloride (43 μL, 0.48 mmol, 3.0 equiv), DMSO (47 μL, 0.64 mmol, 4.0 equiv), and NEt_3 (0.18 mL, 1.3 mmol, 8.0 equiv). The resulting product was further oxidized in 3.0 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (68 mg, 0.49 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.6 mL, 1.2 mmol, 7.5 equiv), and $NaClO_2$ (90 mg, 1.0 mmol, 6.0 equiv). Subsequent silyl deprotection was performed in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N), according to the procedure for **9b**. The resulting crude product was immediately chromatographed on silica gel (EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **9d** as an oil (31 mg, 0.10 mmol, 59% from the alcohol product). $[\alpha]^{28}_{D}$: -3.6 (c 1.0, MeOH). IR (thin film):

3397, 2925, 1709 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 7.19-7.13 (m, 1H), 6.92-6.86 (m, 1H), 6.82-6.76 (m, 1H), 4.03 (d, *J* = 10.9 Hz, 1H), 3.80 (d, *J* = 10.9 Hz, 1H), 2.86-2.75 (m, 1H), 2.75-2.64 (m, 1H), 2.46-2.33 (m, 1H), 2.19-2.07 (m, 1H), 1.47 (s, 9H). ^{13}C NMR (100 MHz, CD_3OD): δ 175.5, 156.4, 145.4, 127.9, 125.5, 124.3, 80.6, 65.6, 64.7, 35.1, 28.9, 25.4. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.54.



8e

Compound 8e. (Condition E) Compound **4** (101 mg, 0.27 mmol, 1.0 equiv) was dissolved in 2.5 mL anhydrous 4:1 CH_3CN:NEt_3 at rt. 2-bromopyridine (77 μL, 0.81 mmol, 3.0 equiv) was then added followed by CuI (10 mg, 0.05 mmol, 0.2 equiv) and $PdCl_2(PPh_3)$ (19 mg, 0.03 mmol, 0.1 equiv). The resulting mixture was stirred for 12 h and was then filtered through a short column of silica gel (1:1 hexanes/EtOAc). The product was then further chromatographed on silica gel (2:1 hexanes/EtOAc then 1:1 hexanes/EtOAc) to give **8e** as a clear oil (89 mg, 0.20 mmol, 73%). $[\alpha]^{28}_{D}$: -1.8 (c 0.50, MeOH). IR (thin film): 2952, 2854, 1747, 1714 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.58-8.48 (m, 1H), 7.66-7.56 (m, 1H), 7.42-7.34 (m, 1H), 7.24-7.16 (m, 1H), 5.07 (s, 1H), 4.57 (d, *J* = 10.7 Hz, 1H), 4.26 (d, *J* = 9.5 Hz, 1H), 4.00-3.86 (m, 2H), 2.08 (s, 3H), 1.44 (s, 9H) 0.87 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 154.3, 149.9, 142.9, 136.3, 127.7, 123.2, 87.0, 83.8, 80.4, 65.1, 64.4, 55.0, 28.5, 26.0, 21.1, 18.5, -5.3 (2C). TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.50.

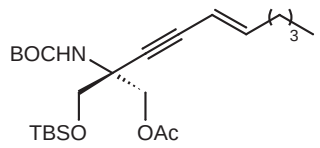


9e

Compound 9e. Compound **8e** (89 mg, 0.20 mmol, 1.0 equiv) was reduced with 10% Pd/C (59 mg) in 9 mL anhydrous benzene. Subsequent deacetylation was accomplished in 15 mL of a saturated solution of ammonia in MeOH according to the procedure for **9a**. The crude product of this sequence was chromatographed on silica gel (1:2 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (71 mg, 0.17 mmol, 87% from **8e**). $[\alpha]^{28}_{D}$: +6.8 (c 0.50, MeOH). IR (thin film): 3419, 2947, 2849, 1709 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.45 (d, J = 4.6 Hz, 1H), 7.56 (dt, J = 7.6, 1.7 Hz, 1H), 7.14 (d, J = 7.8 Hz, 1H), 7.10-7.02 (m, 1H), 5.30 (s, 1H), 3.89 (d, J = 10.0 Hz, 1H), 3.74-3.65 (m, 2H), 3.60 (d, J = 9.9 Hz, 1H), 2.87-2.72 (m, 2H), 2.21-2.09 (m, 1H), 1.90-1.80 (m, 1H), 1.41 (s, 9H), 0.86 (s, 9H), 0.04 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2, 156.0, 149.1, 136.8, 123.2, 121.3, 79.5, 66.9, 66.2, 59.1, 32.1, 31.9, 28.6, 26.0, 18.4, -5.3, -5.4. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.18.

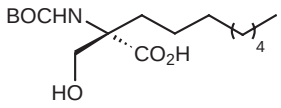
The resulting alcohol (71 mg, 0.17 mmol, 1.0 equiv) was oxidized in 3.5 mL CH_2Cl_2 using Dess-Martin periodinane (146 mg, 0.34 mmol, 2.0 equiv) and $NaHCO_3$ (146 mg). The crude oil was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the aldehyde as a clear oil. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.42. The resulting product was further oxidized in 2.5 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (48 mg, 0.35 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.5 mL, 1.0 mmol, 5.9 equiv), and $NaClO_2$ (63 mg, 0.70 mmol, 6.0 equiv). Subsequent silyl deprotection was performed in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N), according to the procedure for **9a**. The resulting crude product was immediately chromatographed on silica gel (EtOAc then 80:18:2 EtOAc/MeOH/AcOH) to give **9e** as an oil (27 mg, 0.09 mmol, 50% from the alcohol product). $[\alpha]^{28}_{D}$: +0.48 (c 1.0, MeOH). IR (thin film):

3392, 2968, 1698 cm^{-1}. ^1H NMR (500 MHz, CD_3OD): δ 8.34-8.42 (m, 1H), 7.72 (dt, *J* = 7.5, 1.6 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.24-7.16 (m, 1H), 4.02 (d, *J* = 10.5 Hz, 1H), 3.82 (d, *J* = 10.5 Hz, 1H), 2.75 (dt, *J* = 13.3, 5.2 Hz, 1H), 2.68 (dt, *J* = 11.9, 4.8 Hz, 1H), 2.42 (dt, *J* = 12.3, 5.2 Hz, 1H), 2.12-2.02 (m, 1H), 1.44 (s, 9H). ^{13}C NMR (125 MHz, CD_3OD): δ 172.7, 163.4, 156.5, 149.5, 138.8, 124.6, 122.8, 80.0, 66.2 (2C), 33.9, 33.2, 29.0. TLC (SiO_2, 20% MeOH/EtOAc with 2% AcOH): R_f = 0.15.



8f

Compound 8f. Compound **4** (107 mg, 0.29 mmol, 1.0 equiv) was coupled with (E)-1-iodo-1-hexene (122 mg, 0.58 mmol, 2.0 equiv) in 2.3 mL anhydrous 4:1 DMF:NEt_3 using CuI (11 mg, 0.06 mmol, 0.2 equiv) and $Pd(PPh_3)_4$ (33 mg, 0.03 mmol, 0.1 equiv) according to Condition D for **8a**. The product was purified according to the chromatography protocol for **8a** using 5:1 hexanes/EtOAc. Compound **8f** was produced as a clear oil (107 mg, 0.24 mmol, 82%). $[\alpha]^{28}_D$: +1.2 (c 0.30, MeOH). IR (thin film): 2952, 2925, 1747, 1719 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ 6.09 (td, *J* = 15.9, 6.9 Hz, 1H), 5.43 (td, *J* = 15.9, 1.6 Hz, 1H), 4.96 (s, 1H), 4.43 (d, *J* = 10.7 Hz, 1H), 4.20 (d, *J* = 10.5 Hz, 1H), 3.83-3.74 (m, 2H), 2.07 (s, 3H), 2.10-2.03 (m, 2H), 1.43 (s, 9H), 1.37-1.22 (m, 4H), 0.87 (s, 9H), 0.92-0.82 (m, 3H), 0.05 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$): δ 170.8, 154.5, 145.7, 109.1, 85.0, 83.4, 80.2, 65.4, 64.9, 55.1, 32.9, 30.9, 28.5, 26.0, 22.3, 21.1, 18.5, 14.1, -5.2, -5.3. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.59. HRMS: Calcd for $C_{24}H_{43}NO_5Si$ $(M + Na)^+$: 476.2803. Found: 476.2790.

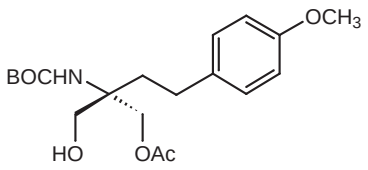


9f

Compound 9f. Compound **8f** (88 mg, 0.19 mmol, 1.0 equiv) was reduced with 10% Pd/C (59 mg) in 9 mL anhydrous benzene. Subsequent deacetylation was accomplished in 15 mL of a saturated solution of ammonia in MeOH according to the procedure for **9a**. The crude product of this sequence was chromatographed on silica gel (3:1 hexanes/EtOAc) to give the corresponding alcohol as a clear oil (73 mg, 0.17 mmol, 90% from **8f**). $[\alpha]^{28}_{D}$: +4.7 (c 0.50, MeOH). IR (thin film): 3419, 2952, 1719, 1687 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.04 (s, 1H), 3.80 (d, *J* = 10.0 Hz, 1H), 3.67-3.56 (m, 2H), 3.51 (d, *J* = 9.9 Hz, 1H), 1.71-1.61 (m, 1H), 1.41 (s, 9H), 1.46-1.10 (m, 13H), 0.87 (s, 9H), 0.91-0.81 (m, 3H), 0.04 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.1, 79.6, 67.6, 66.4, 59.1, 32.3, 32.0, 30.3, 29.7, 29.4, 28.6, 26.0, 23.4, 22.9, 18.4, 14.3, -5.3, -5.4. TLC (SiO_2, 25% EtOAc/hexanes): R_f = 0.59.

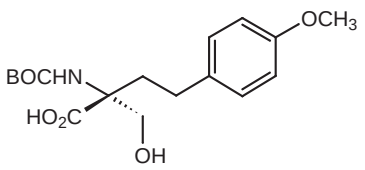
The resulting alcohol (53 mg, 0.13 mmol, 1.0 equiv) was oxidized in CH_2Cl_2 using oxalyl chloride (33 μL, 0.38 mmol, 3.0 equiv), DMSO (36 μL, 0.52 mmol, 4.0 equiv), and NEt_3 (0.14 mL, 1.0 mmol, 7.7 equiv). The resulting product was further oxidized in 2.3 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (52 mg, 0.38 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.5 mL, 1.0 mmol, 7.7 equiv), and $NaClO_2$ (68 mg, 0.75 mmol, 6.0 equiv). Subsequent silyl deprotection was performed in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N), according to the procedure for **9b**. The resulting crude product was immediately chromatographed on silica gel (EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **9f** as an oil (30 mg, 0.09 mmol, 75% from the alcohol product). $[\alpha]^{28}_{D}$: -5.0 (c 1.0, MeOH). IR (thin film): 3408, 2930, 1709, 1643 cm^{-1}. ^{1}H NMR (400 MHz, CD_3OD): δ 4.00 (d, *J* = 10.8 Hz, 1H), 3.77 (d, *J* = 11.1 Hz, 1H), 2.07-1.94 (m, 1H), 1.78-1.65 (m, 1H), 1.45 (s, 9H), 1.38-

1.10 (m, 12H), 0.94-0.85 (m, 3H). ^{13}C NMR (100 MHz, CD_3OD): δ 176.0, 156.3, 80.4, 66.0, 64.7, 33.1, 32.6, 30.7, 30.6, 30.4, 28.9, 24.7, 23.9, 14.6. TLC (SiO_2, EtOAc with 2% AcOH): R_f = 0.43.



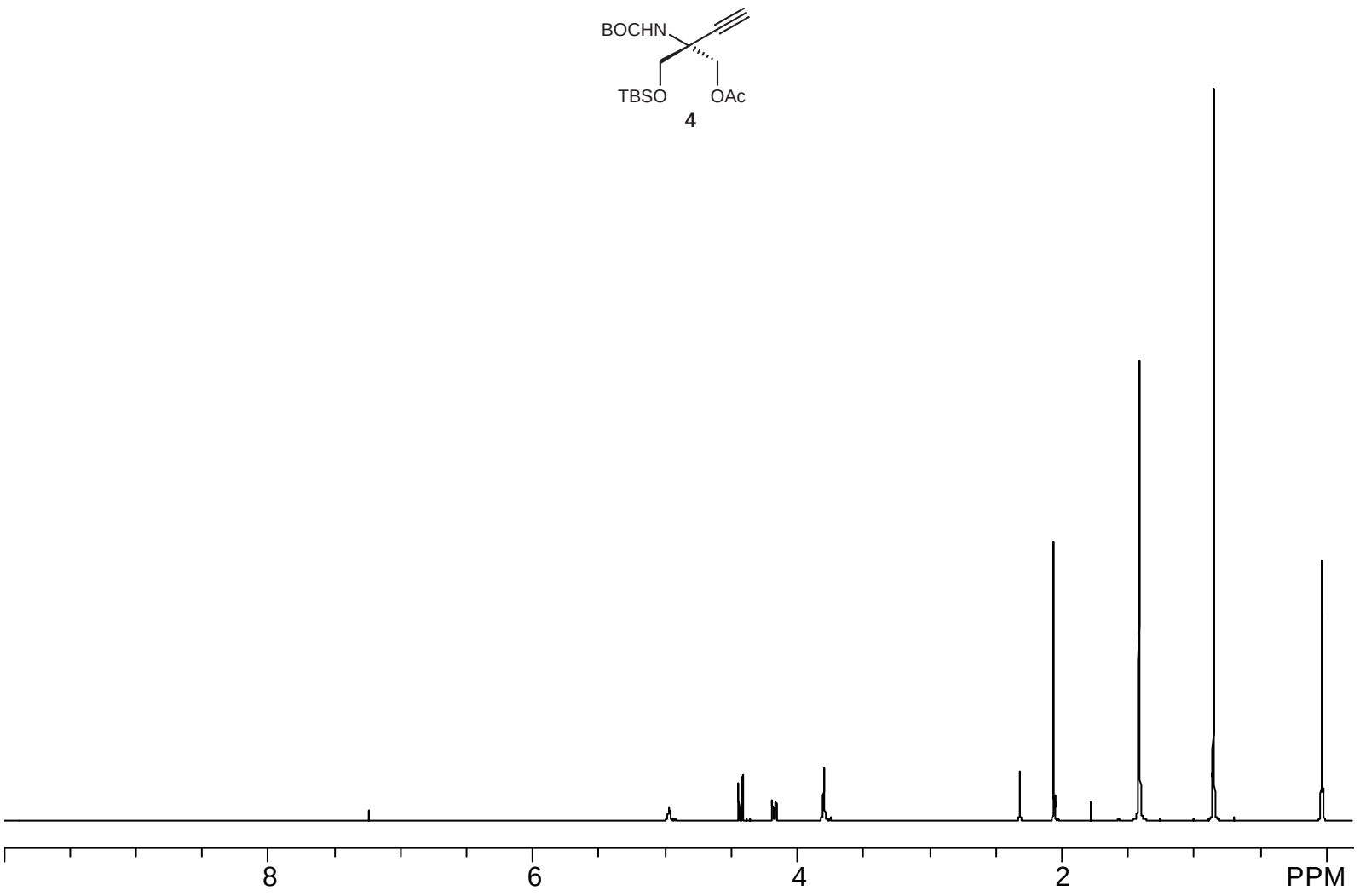
10

Compound 10. Compound **8b** (80 mg, 0.17 mmol, 1.0 equiv) was reduced with 10% Pd/C (80 mg) in 8 mL anhydrous benzene, and subsequent silyl deprotection was performed in 5 mL 8:1:1 AcOH:H_2O:MeOH with one drop of aqueous HCl solution (2 N), according to the procedure for **7b**. The resulting crude product was immediately chromatographed on silica gel (1:1 hexanes/EtOAc) to give **10** as an oil (61 mg, 0.16 mmol, 99% from **8b**). $[\alpha]^{28}_D$: +4.8 (c 0.50, MeOH). IR (thin film): 3414, 2925, 1741, 1714 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.7 Hz, 2H), 4.85 (s, 1H), 4.31 (d, *J* = 11.3 Hz, 1H), 4.14 (d, *J* = 11.3 Hz, 1H), 3.76 (s, 3H), 3.69 (AB, *J* = 11.9 Hz, Δν = 21.7 Hz, 2H), 2.58 (dt, *J* = 13.3, 5.0 Hz, 1H), 2.49 (dt, *J* = 12.2, 5.4 Hz, 1H), 2.09 (s, 3H), 2.08-1.98 (m, 1H), 1.89-1.78 (m, 1H), 1.43 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.4, 158.1, 155.9, 133.8, 129.4, 114.1, 80.4, 65.4, 65.3, 58.8, 55.5, 35.2, 28.8, 28.5, 21.1. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.37.



11

Compound 11. Compound **10** (61 mg, 0.16 mmol, 1.0 equiv) was oxidized in 3.3 mL CH_2Cl_2 using Dess-Martin periodinane (140 mg, 0.32 mmol, 2.0 equiv) and $NaHCO_3$ (140 mg). The crude oil was chromatographed on silica gel (1:1 hexanes/EtOAc) to give the aldehyde as a clear oil. TLC (SiO_2, 50% EtOAc/hexanes): R_f = 0.72. The resulting product was further oxidized in 3.0 mL 4:1 *t*BuOH:H_2O using NaH_2PO_4 (68 mg, 0.49 mmol, 3.0 equiv), 2-methyl-2-butene (2.0 M in THF, 0.6 mL, 1.2 mmol, 7.5 equiv), and $NaClO_2$ (89 mg, 1.0 mmol, 6.0 equiv), according to the procedure for **9a**. To remove the acetate group, the product was subsequently dissolved in 8 mL of a saturated solution of ammonia in MeOH, and the reaction was stirred for 12 h after which the mixture was concentrated under vacuum (aspirator pressure) with a rotary evaporator. The resulting crude product was immediately chromatographed on silica gel (EtOAc then 90:8:2 EtOAc/MeOH/AcOH) to give **11** as an oil (40 mg, 0.12 mmol, 71% from **23**). $[\alpha]^{28}_D$: +3.7 (c 2.0, MeOH).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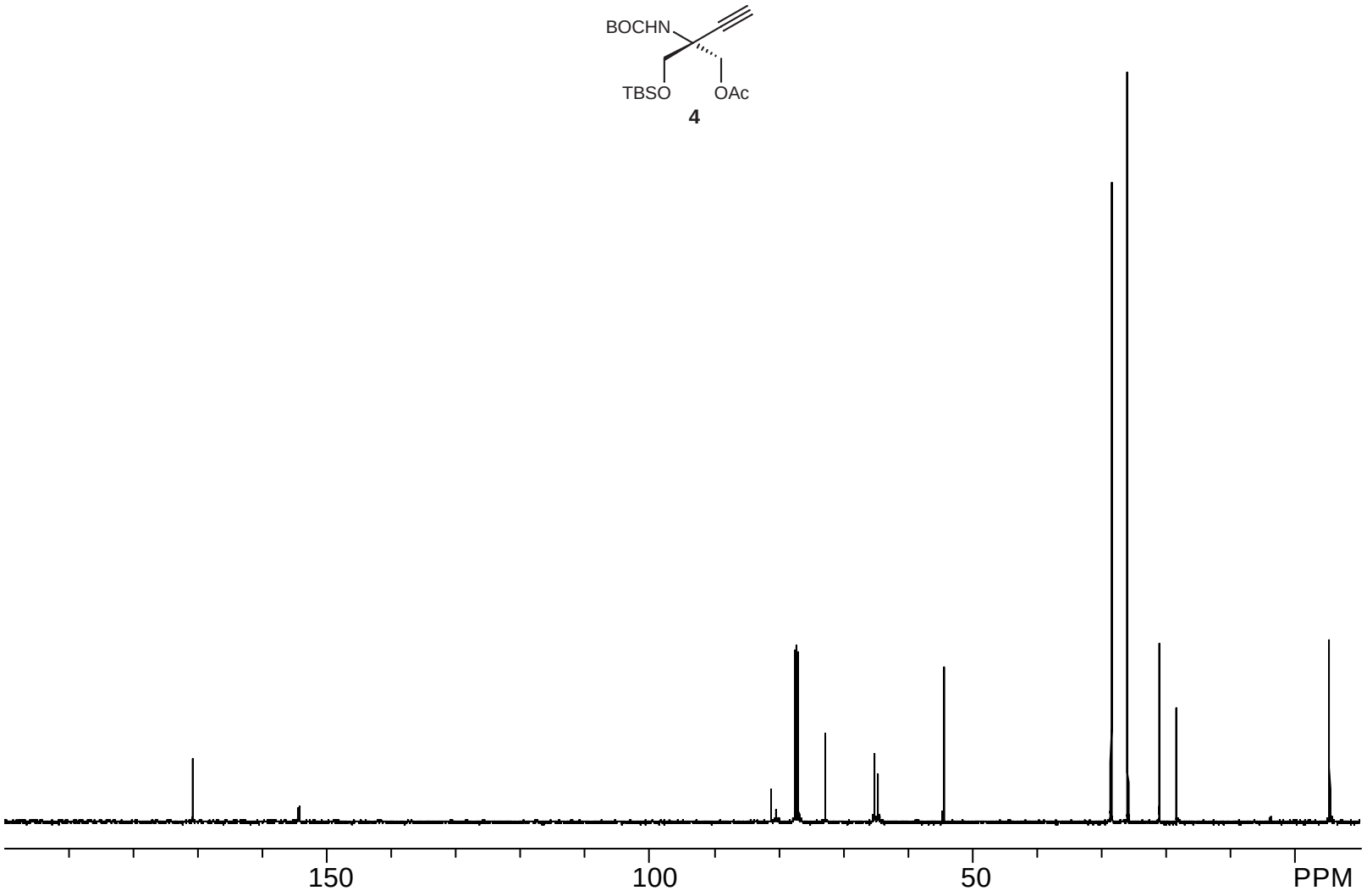
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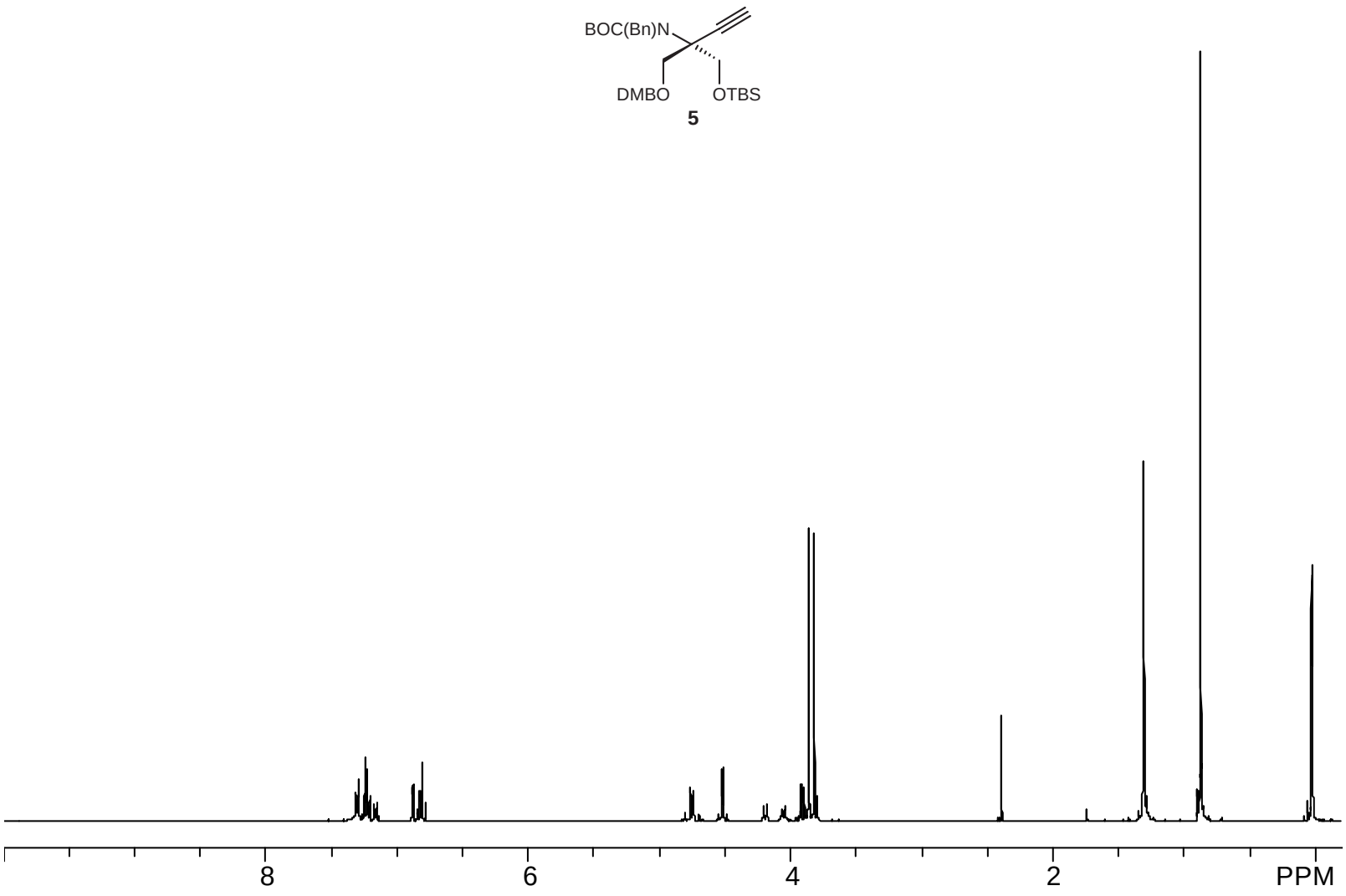
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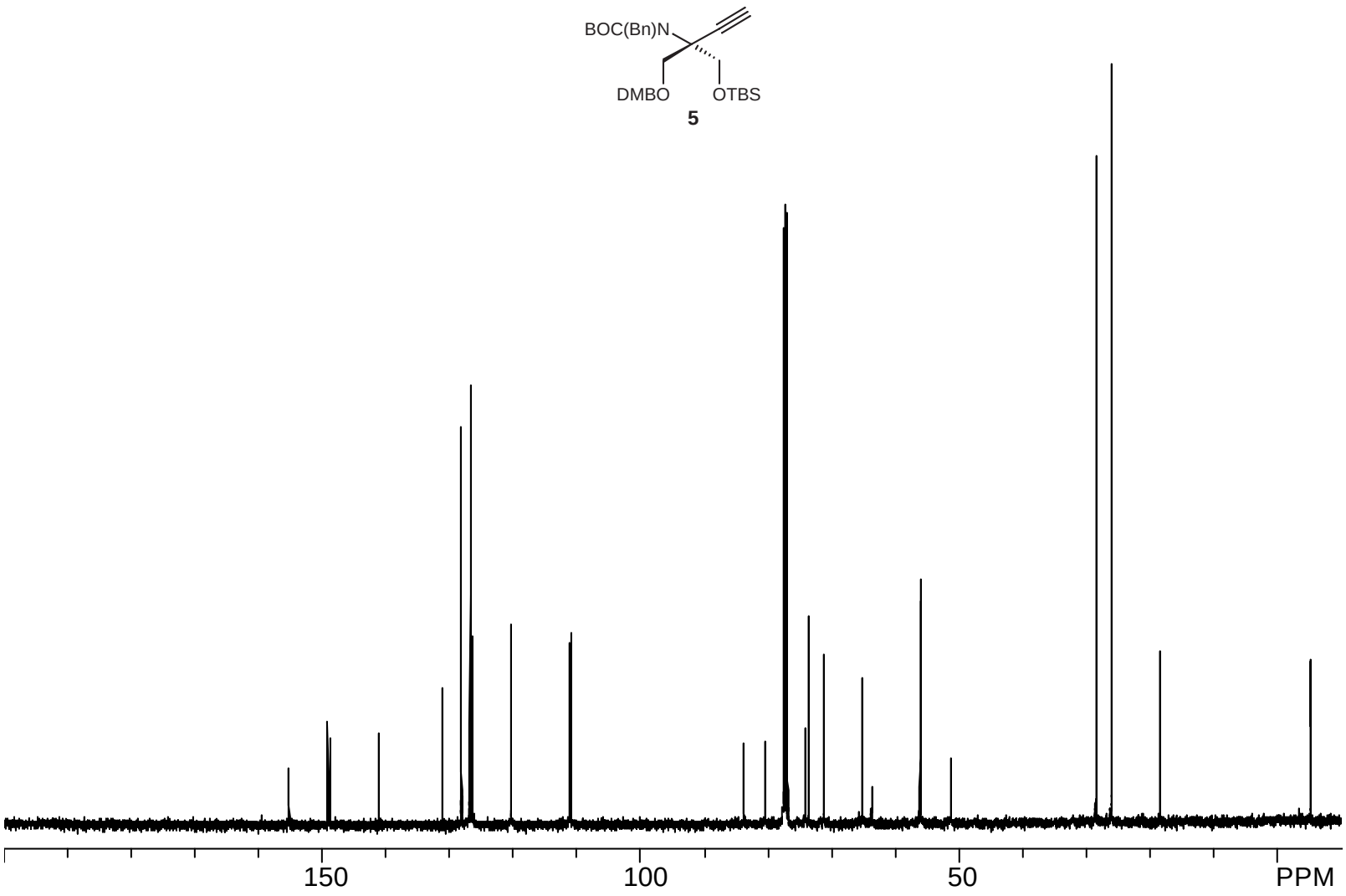
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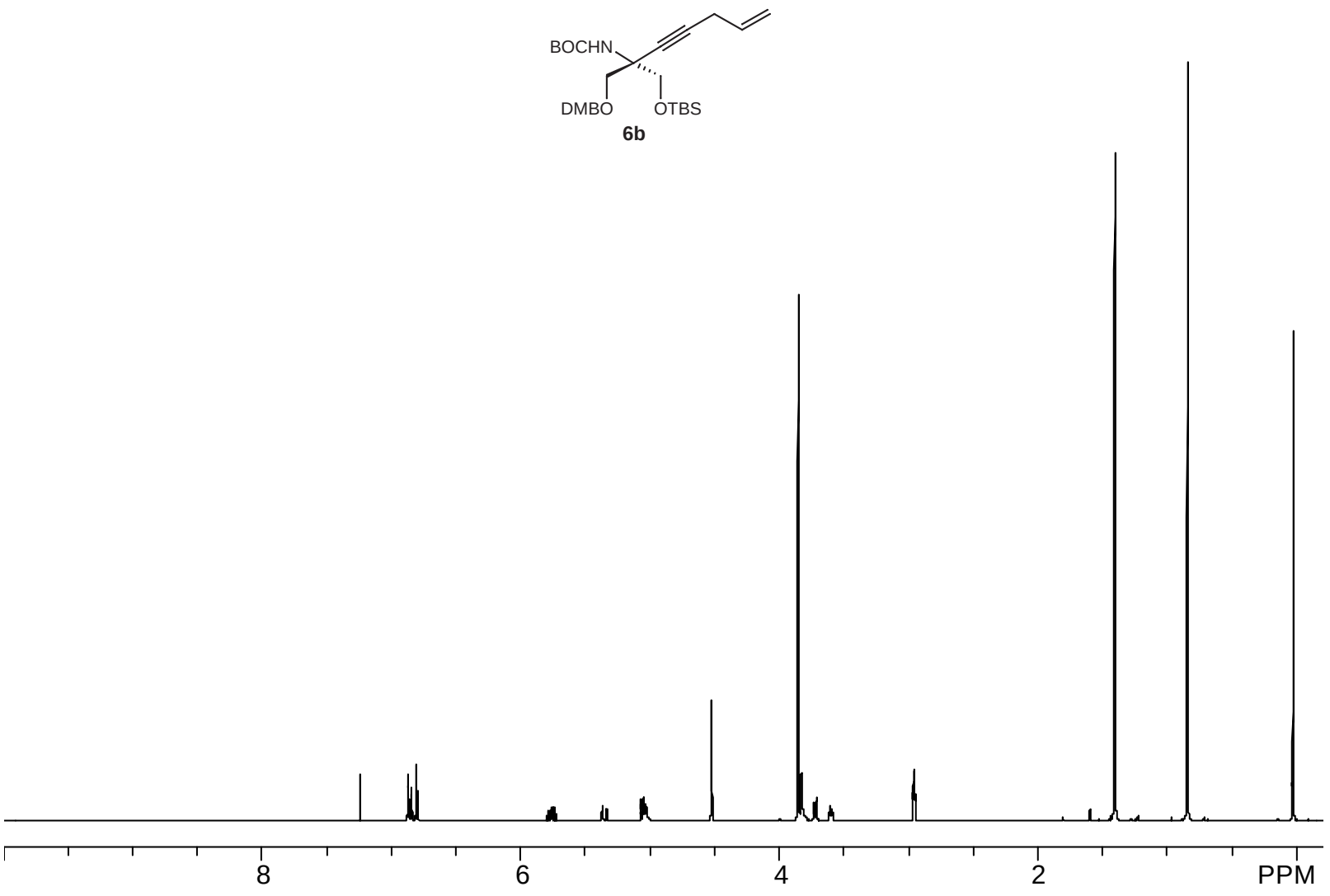
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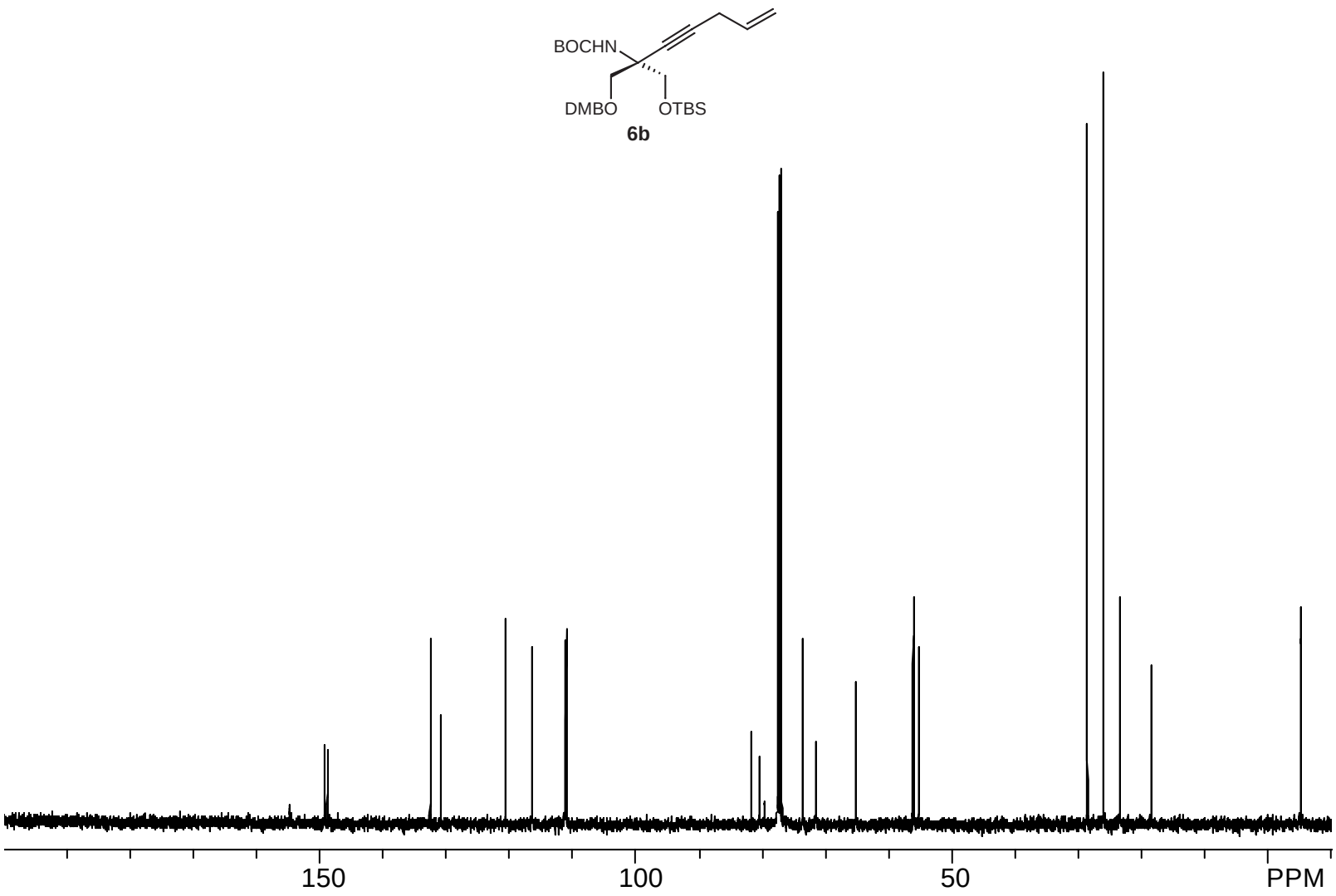
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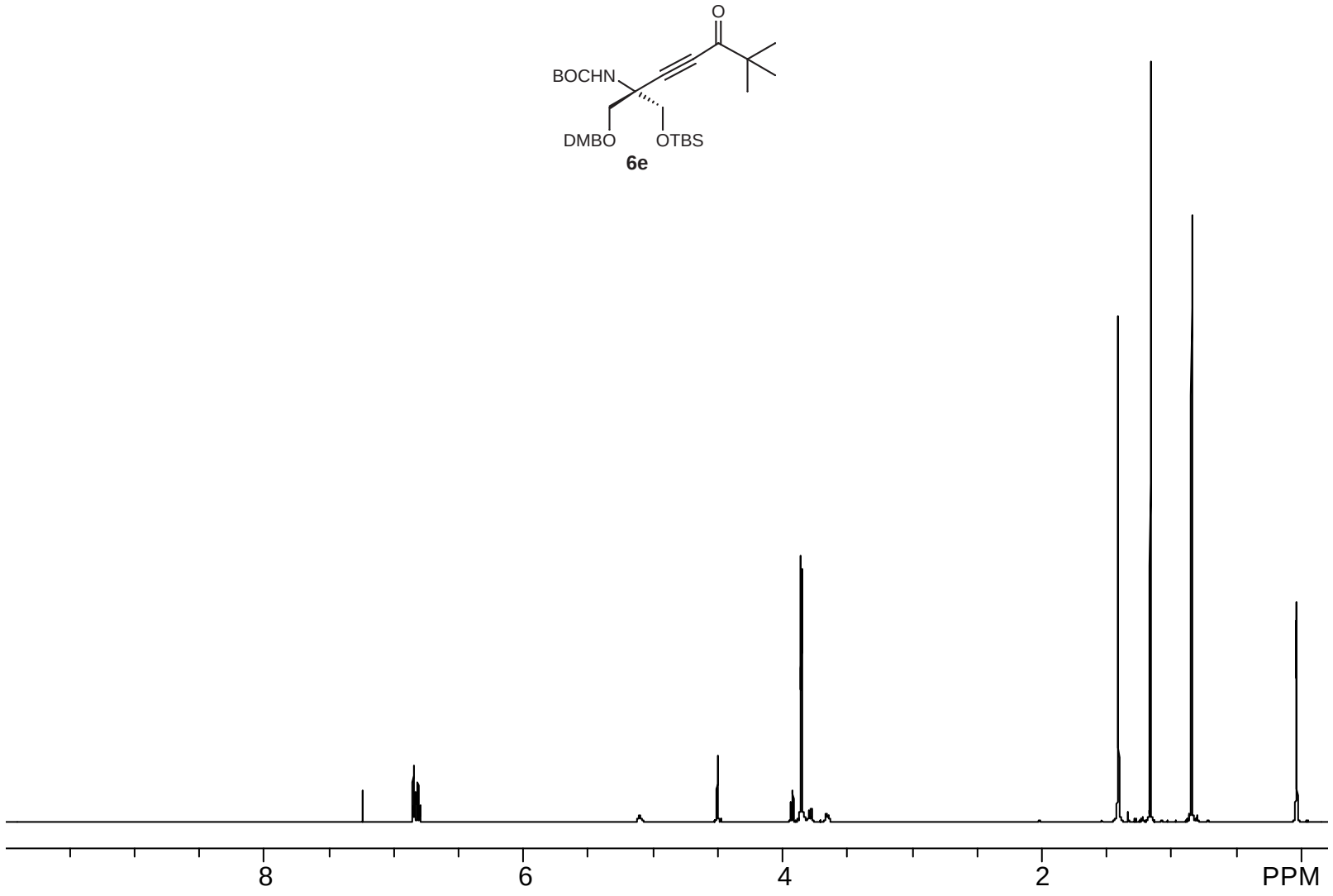
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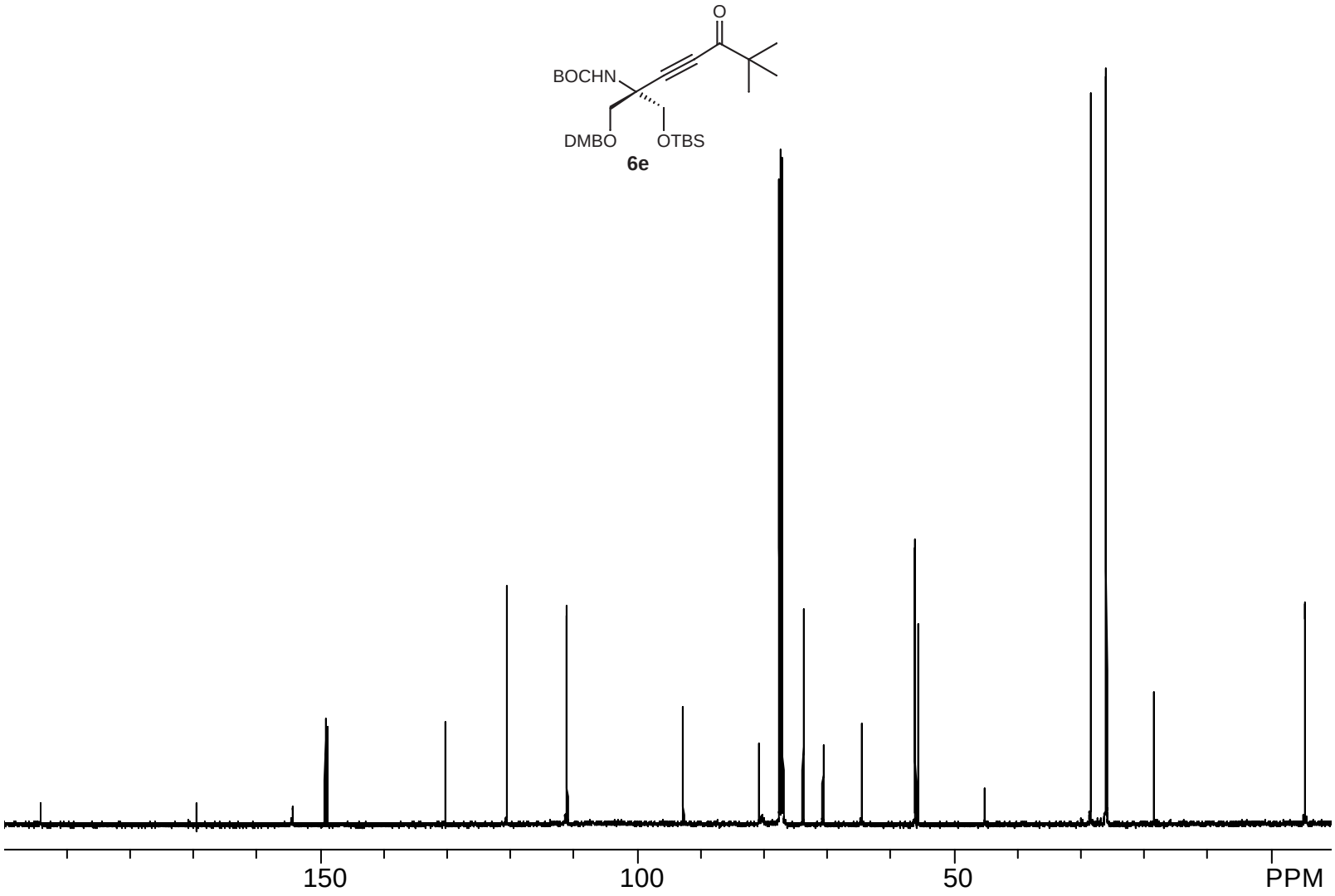
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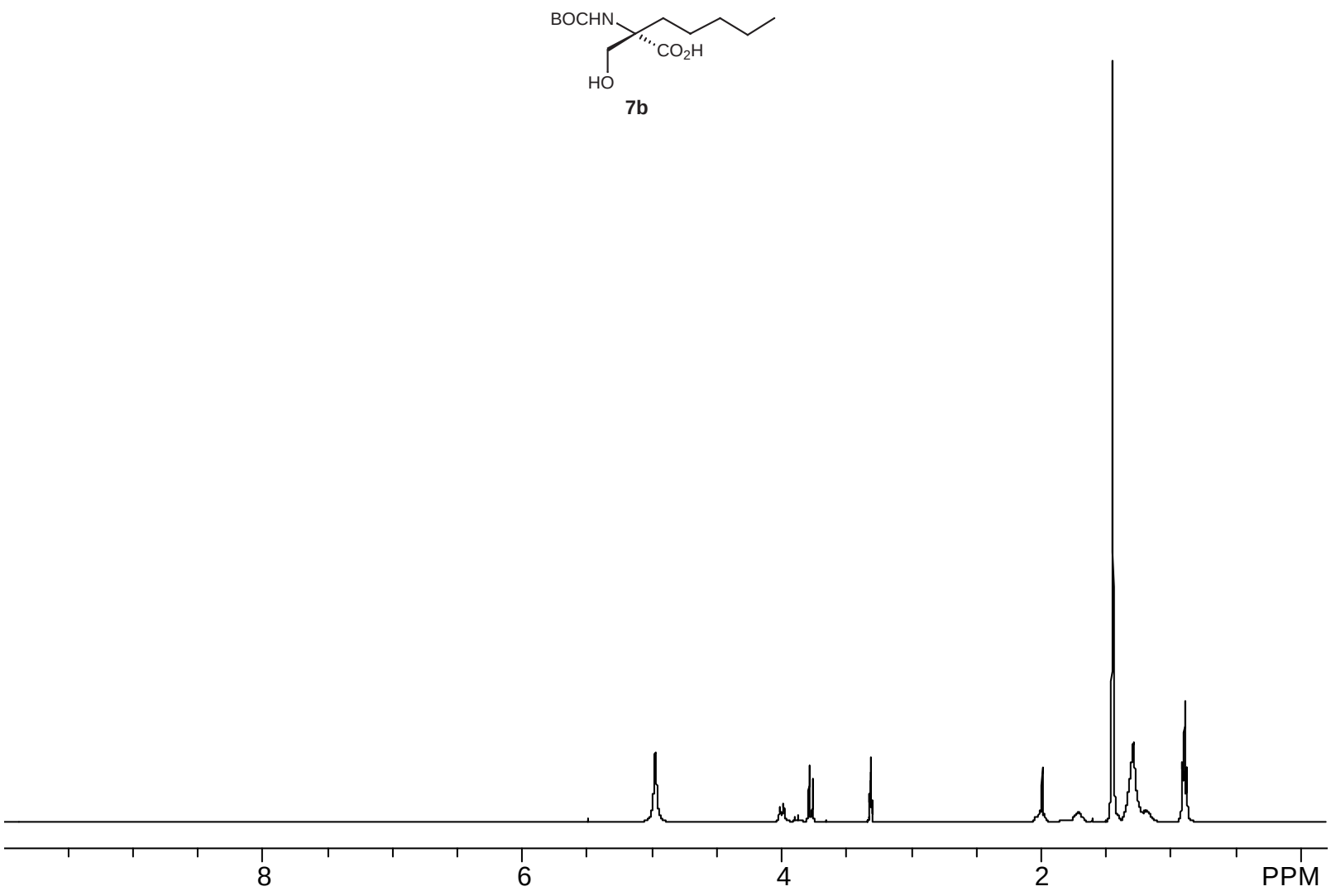
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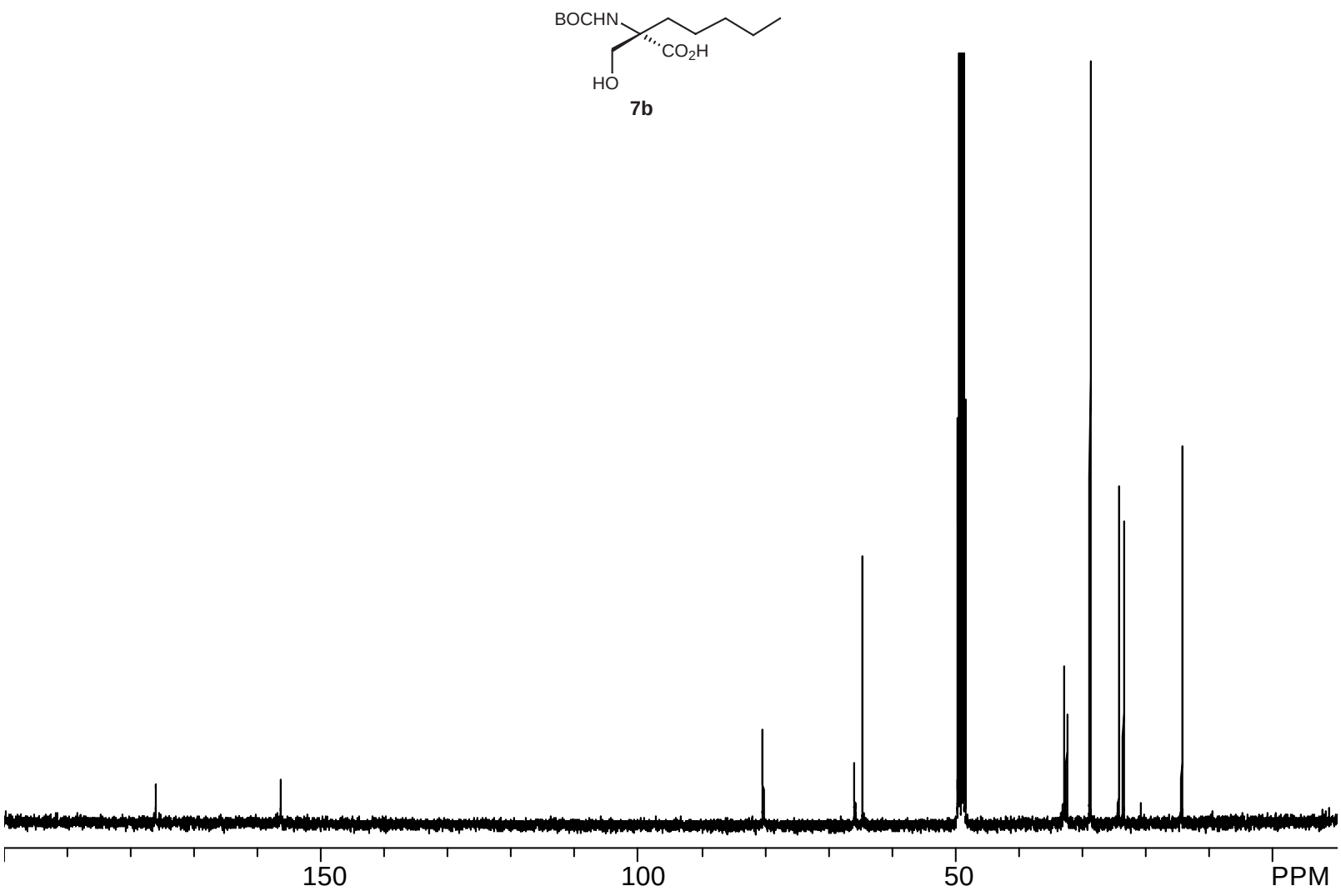
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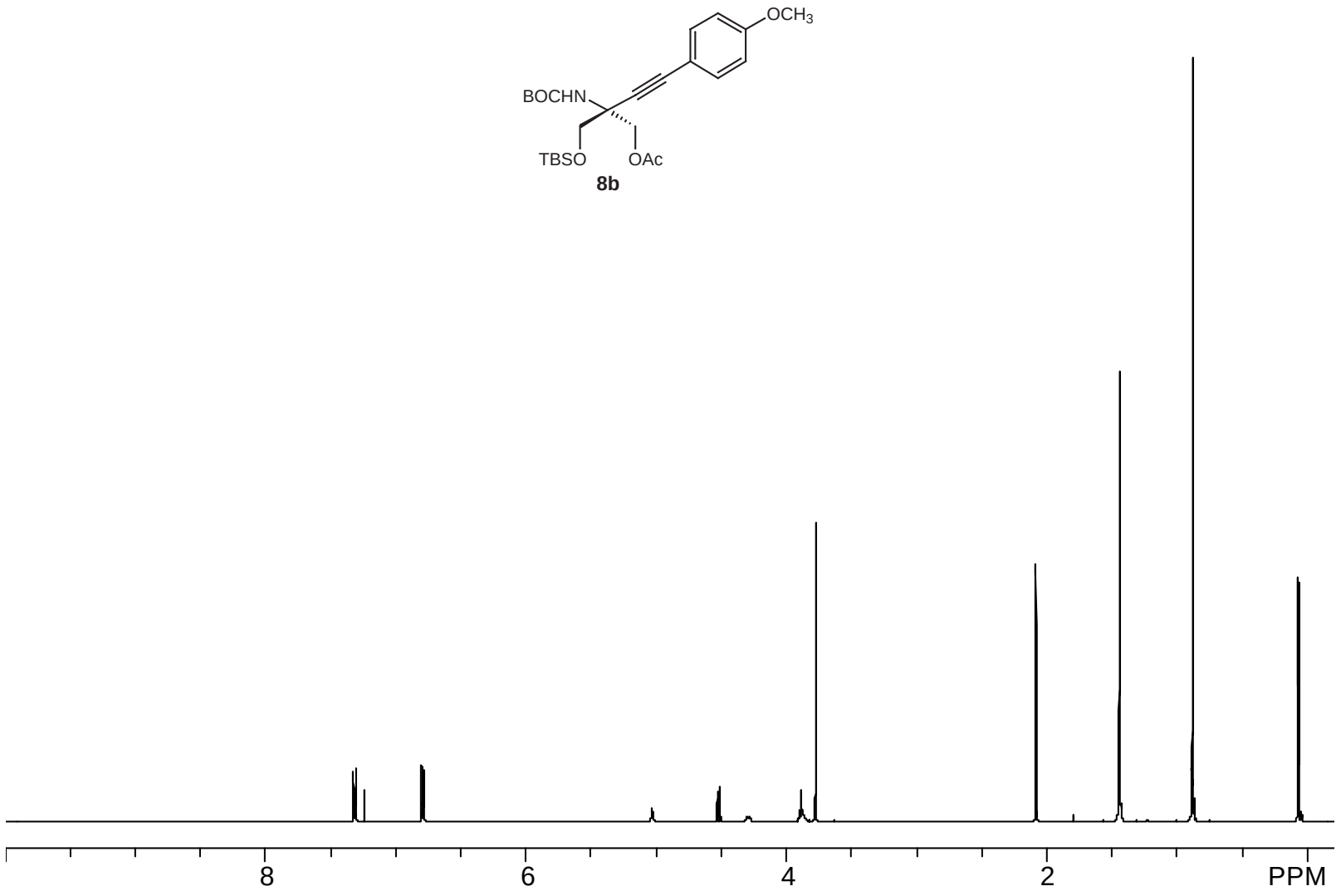
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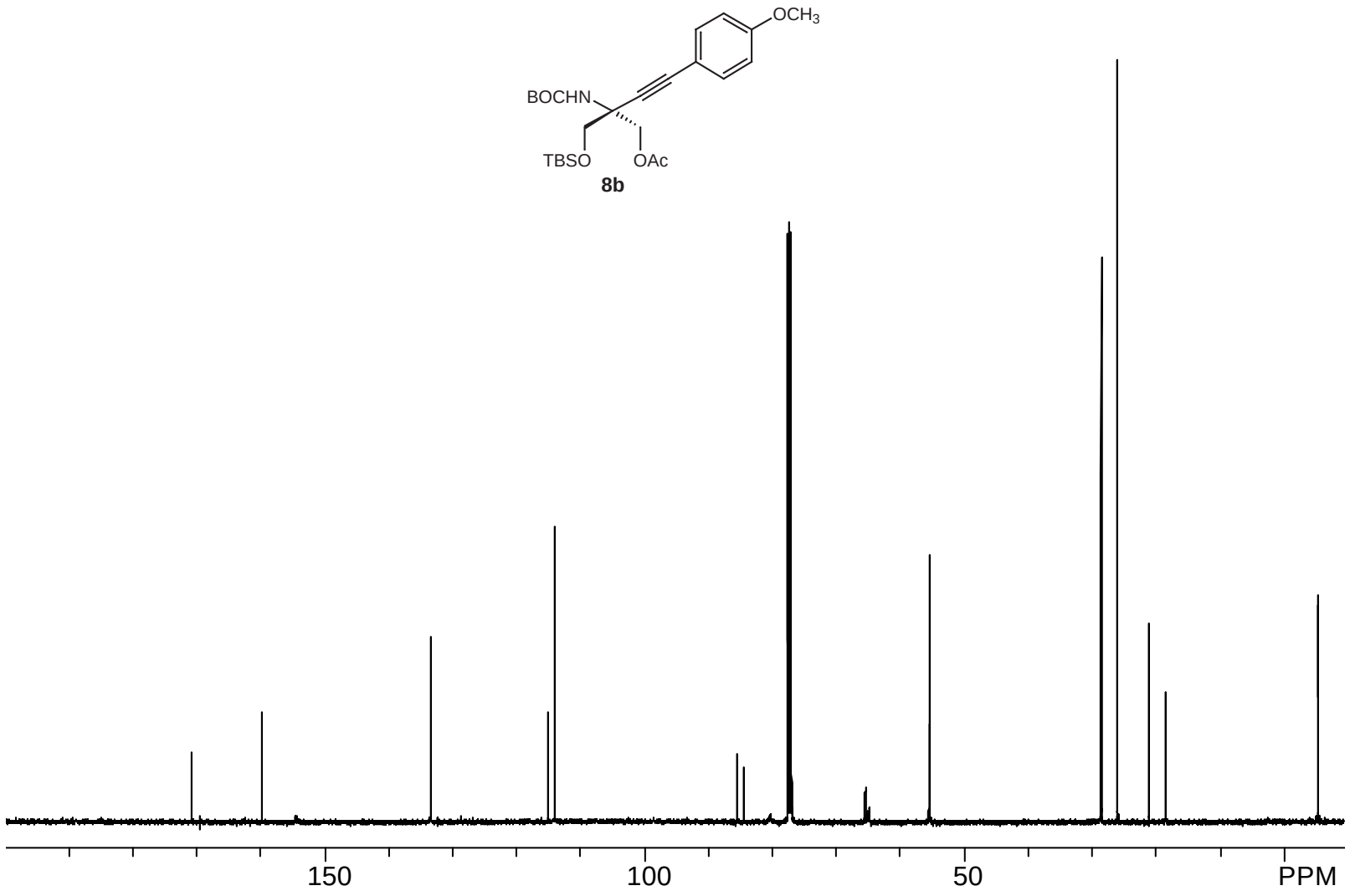
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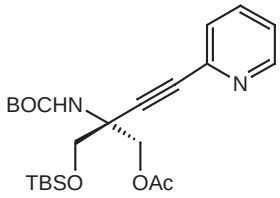

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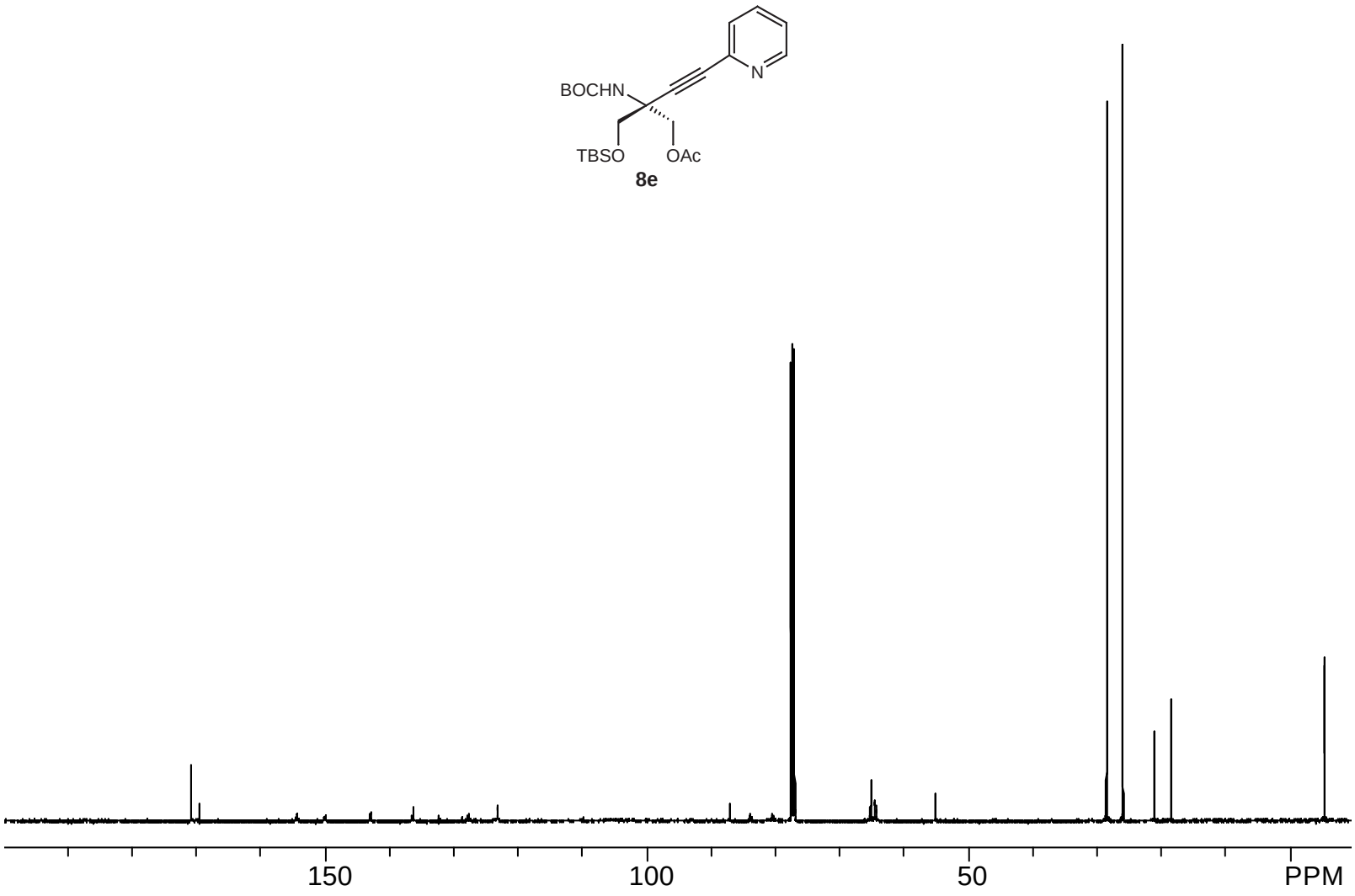
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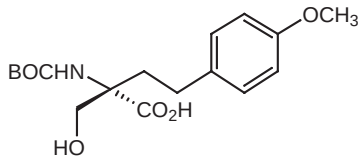

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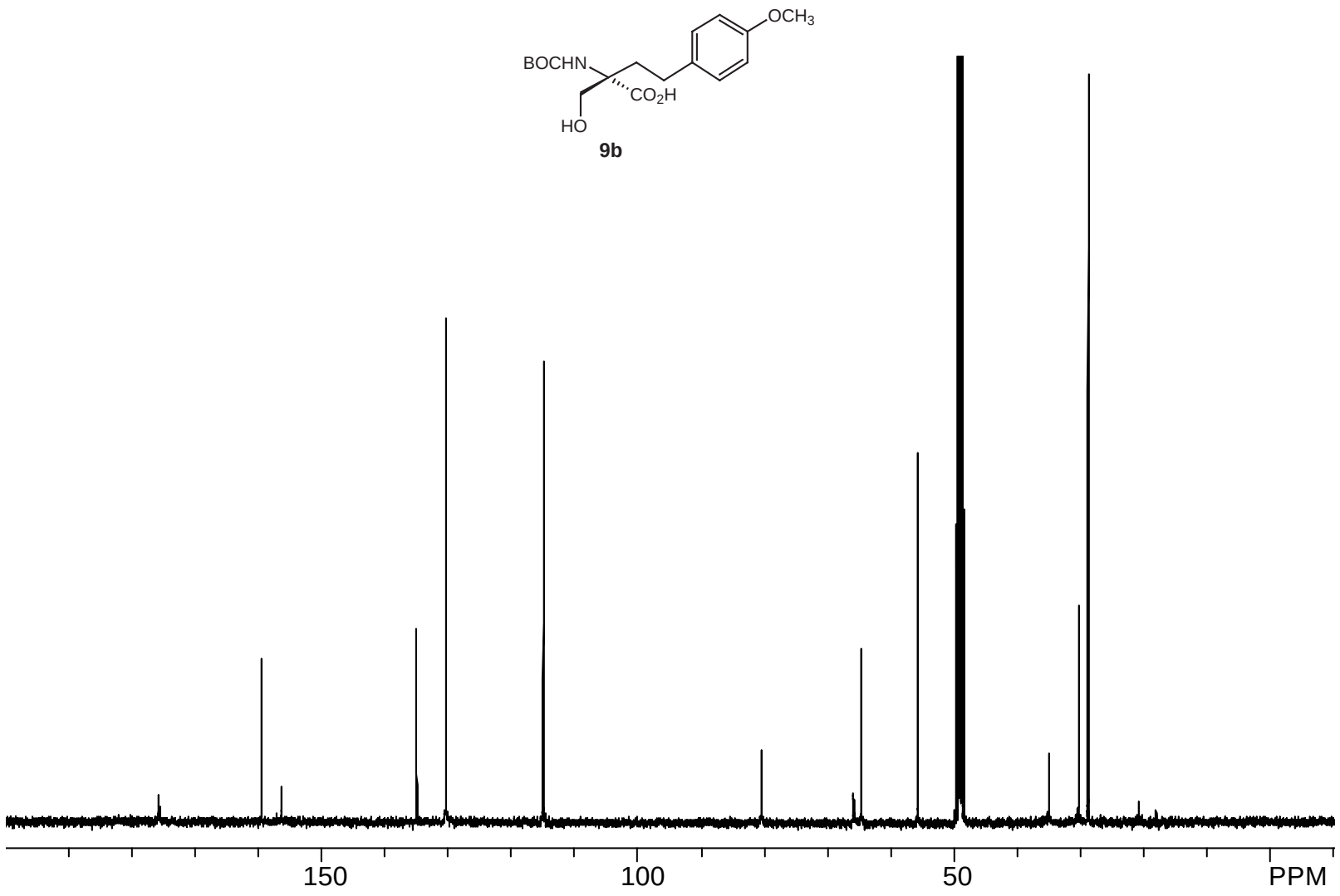
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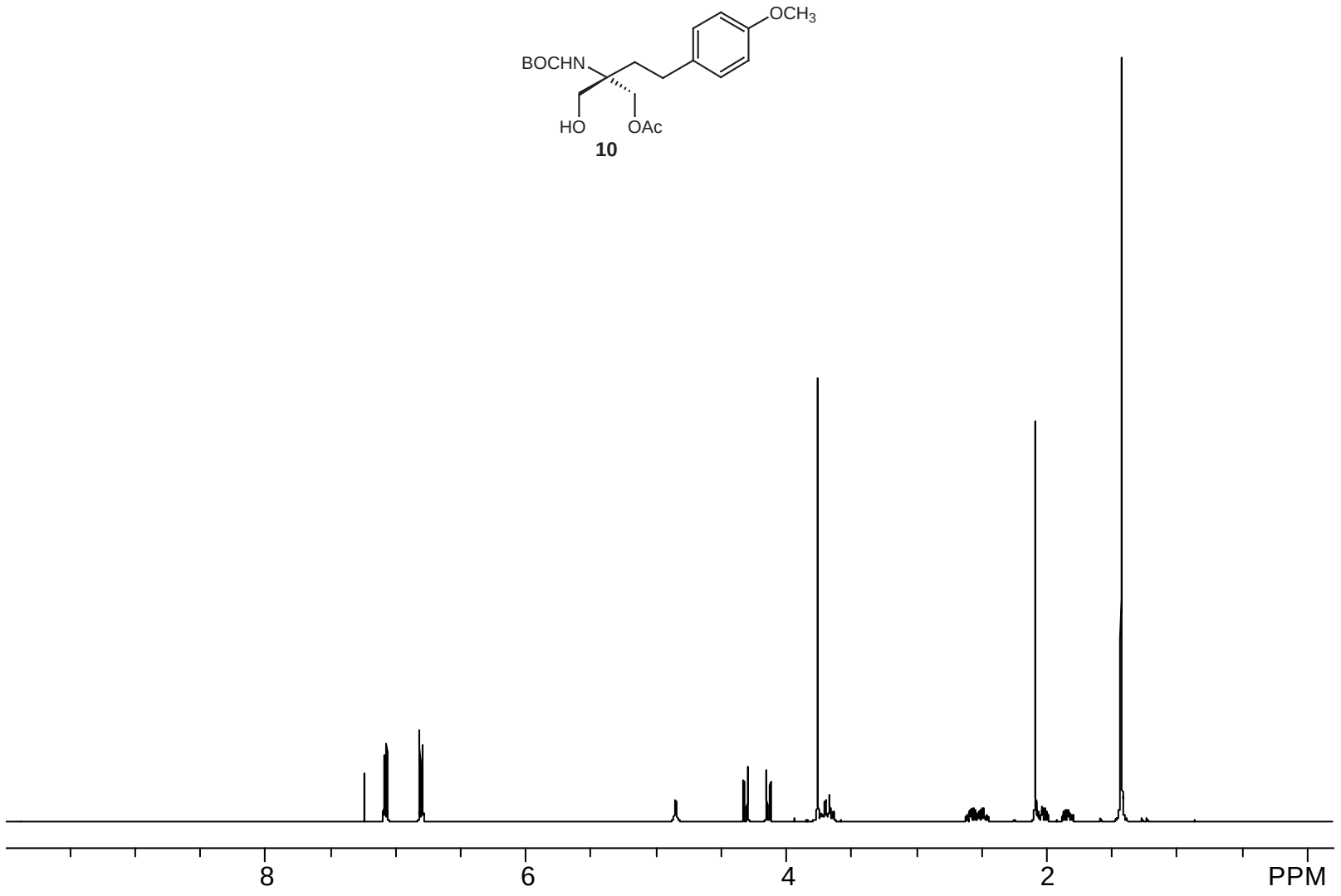
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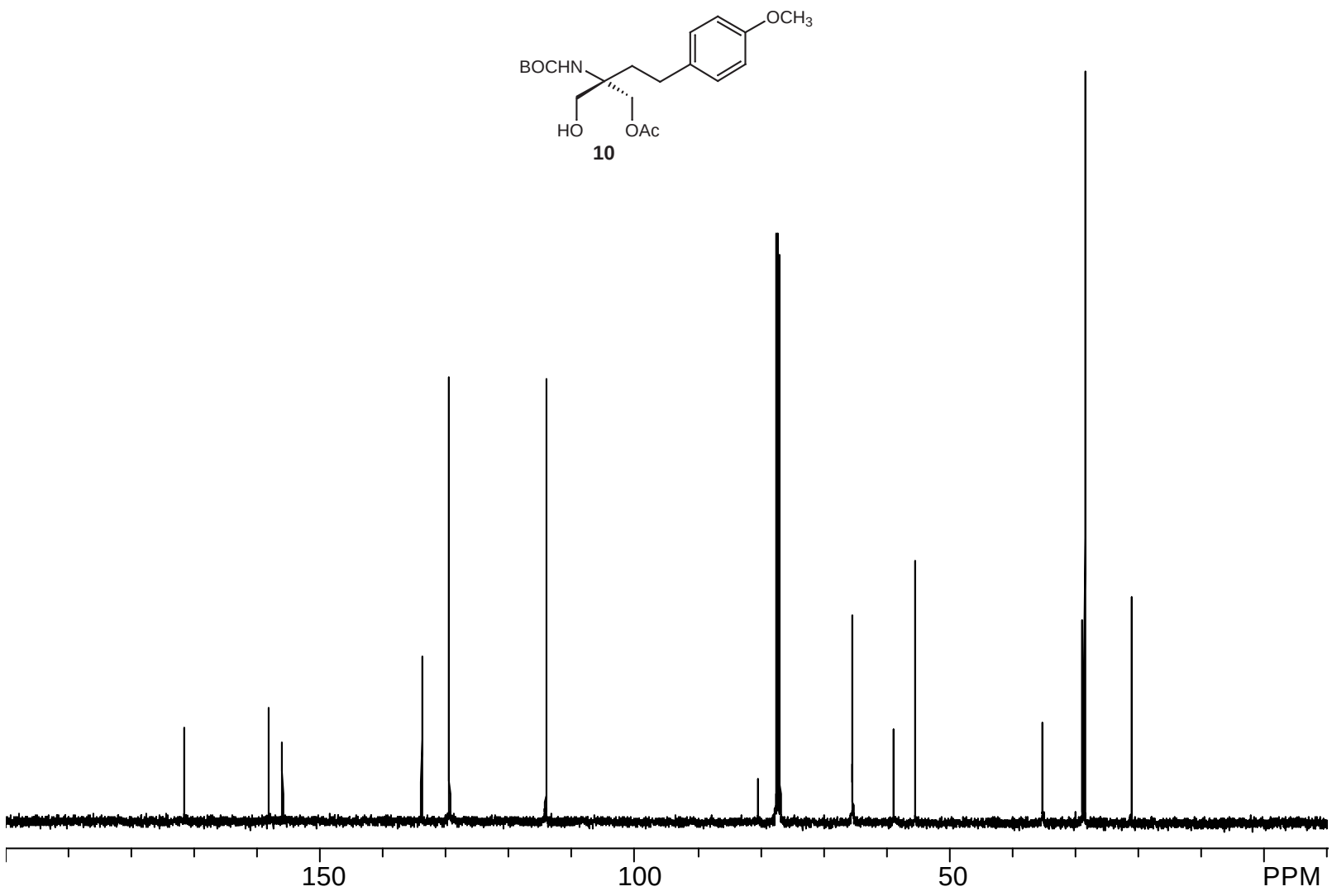
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