Electronic supplementary materials *Mendeleev Commun.*, 2023, **33**, 328–330

Acyclic enediynes fused to triazole and benzothiophene containing propargylamine moieties

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General information

Solvents, reagents, and chemicals used for reactions were purchased from commercial suppliers. The chemicals were used without further purification. Catalyst $Pd(PPh_3)_4$ was purchased from Sigma-Aldrich. Ethyl 2-[5-iodo-4-(3-methoxyprop-1-yn-1-yl)-1*H*-1,2,3-triazol-1-yl]acetate (**1**),[S1] 3-iodo-2-(3-methoxyprop-1-yn-1-yl)benzo[*b*]thiophene (**3**),[S2] di(*N*-piperidino)methane (**5a**)[S3] bis(4-methylpiperazin-1-yl)methane (**5b**),[S4] dimorpholinomethane (**5c**)[S5] were synthesized by known procedures without any modification. Solvents were dried under standard conditions. Thin-layer chromatography (TLC) was carried out on silica gel plates (Silica gel 60, UV 254) with detection by UV or staining with a basic aqueous solution of $KMnO_4$. Normal-phase silica gel (Silica gel 60, 230−400 mesh) was used for preparative column chromatography. Melting points (mp) determined are uncorrected. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, at 25 °C in $CDCl_3$ or acetone-d_6 without an internal standard. The ^1H NMR data are reported as chemical shifts (δ), multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constants (*J*, given in Hz), and number of protons. The ^{13}C NMR data are reported as the chemical shifts (δ). Chemical shifts for ^1H and ^{13}C are reported as δ values (ppm) and referenced to residual solvents ($\delta = 7.26$ ppm for ^1H; $\delta = 77.16$ ppm for ^{13}C – for spectra recorded in $CDCl_3$ and $\delta = 2.05$ ppm for ^1H; $\delta = 29.84$ ppm for ^{13}C – for spectra recorded in acetone-d_6). High-resolution mass spectra (HRMS) were determined for solutions of all compounds in MeOH using electrospray ionization (ESI) in the mode of positive ion registration with a TOF mass analyzer.

Bis[bis(2-hydroxyethyl)amino]methane 5d. Diethanolamine (2.50 g, 23.8 mmol) was added to paraformaldehyde (0.714 g, 23.8 mmol) in dioxane (6 ml) at room temperature. The mixture was heated to 70 °C with reflux condenser for 2 h until full dissolution of paraformaldehyde. The reaction mixture was then filtered. Evaporation of the solvent *in vacuo* provided 4.5 g (85%) of crude product **5d** (light yellow liquid) which was used in the syntheses of **6d** and **7d** without additional purification.

Ethyl 2-[4-(3-methoxyprop-1-yn-1-yl)-5-trimethylsilylethynyl-1*H*-1,2,3-triazol-1-yl]acetate 1′. 5-Iodo-1*H*-1,2,3-triazole **1** (120 mg, 0.345 mmol, 1.00 equiv.), CuI (6.6 mg, 0.035 mmol, 10 mol %), K_3PO_4 (80.6 mg, 0.380 mmol, 1.10 equiv.), and $Pd(PPh_3)_4$ (19.9 mg, 0.017 mmol, 5 mol %) were placed in a vial. The vial was sealed, evacuated and flushed with Ar several times. THF was added (3.5 ml to provide $C = 0.1$ M), the mixture was stirred at room temperature for 10 min, and then an ethynyltrimethylsilane (TMSA, 50.9 mg, 0.518 mmol, 1.50 equiv.) was added. The vial with the reaction mixture was placed into a preheated vial block (65 °C) and stirred at this temperature until full conversion as indicated by TLC. After cooling to room temperature, the reaction mixture was filtered through a silica gel pad and the pad was washed with DCM (3 × 10 ml). The solvent was removed under reduced pressure. Purification of the crude product by column chromatography (eluent: hexane/acetone = 5:1) gave **1′** (89 mg, 80 %) as a brown oil. ^1H NMR (400 MHz, $CDCl_3$, δ) 5.12 (s, 2H, $-C\underline{H}_2-CO_2Et$), 4.39 (s, 2H, $\equiv C-C\underline{H}_2-$), 4.26 (q, $J = 7.1$ Hz, 2H, $-COOC\underline{H}_2CH_3$), 3.48 (s, 3H, $-OC\underline{H}_3$), 1.28 (t, $J = 7.1$ Hz, 3H, $-COOCH_2C\underline{H}_3$), 0.27 (s, 9H, $-Si(C\underline{H}_3)_3$). ^{13}C NMR (100 MHz, $CDCl_3$, δ) 165.3, 133.2, 124.9, 111.7, 91.7, 87.3, 75.3, 62.6, 60.3, 57.8, 50.1, 14.2, -0.5. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{15}H_{22}N_3O_3Si^+$ 320.1425; Found 320.1429.

Ethyl 2-[5-ethynyl-4-(3-methoxyprop-1-yn-1-yl)-1*H*-1,2,3-triazol-1-yl]acetate 2. The removal of trimethylsilyl group of **1'** was carried out as described before.[S6] To a solution of product **1′** (95.0 mg, 0.297 mmol) in DMF (1.1 ml) and H_2O (0.11 ml) was added KF (25.9 mg, 0.446 mmol). The reaction mixture was stirred for 5 min and quenched with saturated aqueous NH_4Cl. The mixture was extracted with EtOAc, washed with brine, dried over Na_2SO_4, and concentrated. The crude product was purified with flash column chromatography to give **2** (63.6 mg) in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ) 5.16 (s, 2H, $-C\underline{H}_2-CO_2Et$), 4.38 (s, 2H, $\equiv C-C\underline{H}_2-$), 4.27 (q, *J* = 7.1 Hz, 2H, $-COOC\underline{H}_2CH_3$), 3.83 (s, 1H, $-C\equiv C-\underline{H}$), 3.47 (s, 3H, $-OC\underline{H}_3$), 1.29 (t, *J* = 7.1 Hz, 3H, $-COOCH_2C\underline{H}_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.3, 134.1, 124.0, 92.1, 92.0, 74.8, 67.7, 62.7, 60.3, 57.9, 50.1, 14.2. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{12}H_{14}N_3O_3^+$ 248.1030; Found 248.1033.

{[2-(3-Methoxyprop-1-yn-1-yl)benzo[*b*]thiophen-3-yl]ethynyl}trimethylsilane 3′. To a stirred degassed solution of 3-iodo-2-(3-methoxyprop-1-yn-1-yl)benzo[*b*]thiophene **3** (0.200 g, 0.609 mmol, 1.00 equiv.) in anhydrous DMF (6 ml) in a vial were added ethynyltrimethylsilane (89.8 mg, 0.914 mmol, 1.5 equiv.), DIPA (246.7 mg, 2.44 mmol, 4.00 equiv.), $Pd(PPh_3)_4$ (35.2 mg, 0.031 mmol, 5 mol%), and CuI (11.6 mg, 0.061 mmol, 10 mol%) under atmosphere of an Ar. The reaction vessel was sealed, degassed, and flushed with Ar. The reaction mixture was stirred at 40 °C for the required time (TLC monitoring). After completion of the reaction, the mixture was cooled, poured into a saturated aqueous solution of NH_4Cl, and extracted with ethyl acetate. The combined organic layers were washed two times with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. Purification of the crude product by column chromatography (eluent: hexane/EtOAc = 20:1) gave the title product (152 mg, 83 %) as a light brown oil. ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.89 – 7.79 (m, 1H, Ar−H), 7.73 – 7.70 (m, 1H, Ar−H), 7.46 – 7.38 (m, 2H, Ar−H), 4.45 (s, 2H, $\equiv C-C\underline{H}_2-$), 3.52 (s, 3H, $-OC\underline{H}_3$), 0.32 (s, 9H, $-Si(C\underline{H}_3)_3$). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 138.7, 138.5, 126.49, 126.46, 125.3, 123.7, 123.4, 122.2, 102.0, 97.6, 95.4, 79.5, 60.6, 57.8, 0.2. HRMS (ESI) m/z: $[M+Ag]^+$ Calcd for $C_{17}H_{18}OSSiAg^+$ 404.9893; Found 404.9887.

3-Ethynyl-2-(3-methoxyprop-1-yn-1-yl)benzo[*b*]thiophene 4. The removal of trimethylsilyl group of **3'** was carried out as described before.[S6] To a solution of product **3′** (150 mg, 0.503 mmol) in DMF (4.5 ml) and H_2O (0.45 ml) was added KF (43.8 mg, 0.754 mmol). The mixture was stirred at room temperature for 15 min, and quenched with saturated aqueous NH_4Cl. The mixture was extracted with EtOAc. The combined organic layers were washed two times with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. The crude product was purified with column chromatography (eluent: hexane/ EtOAc = 10:1) to give product **4** (111.8 mg) in 98% yield. ^{1}H NMR (400 MHz, $CDCl_3$, δ) 7.94 – 7.85 (m, 1H, Ar−H), 7.78 – 7.70 (m, 1H, Ar−H), 7.50 – 7.38 (m, 2H, Ar−H), 4.45 (s, 2H, $\equiv C-C\underline{H}_2-$), 3.56 (s, 1H, $-C\equiv C-H$), 3.50 (s, 3H, $-OC\underline{H}_3$).^{13}C NMR (101 MHz, $CDCl_3$, δ) 138.8, 138.5, 127.2, 126.5, 125.4, 123.5, 122.2, 122.0, 95.6, 84.0, 79.1, 76.7, 60.6, 58.0. HRMS (ESI) m/z: $[M+Ag]^+$ Calcd for $C_{14}H_{10}OSAg^+$ 332.9498; Found 332.9499.

General procedure for the synthesis of 6a-d and 7a-d. A mixture of acetylene **2** or **4** (1.0 equiv.), diaminomethane (1.0 equiv.), and CuCl (0.25 equiv.) in dioxane (15 ml) was stirred at 50 – 70 °C for 1–2 h under argon (TLC monitoring). After completion of the reaction, the mixture was cooled, poured into a saturated aqueous solution of NH_4Cl, and extracted with ethyl acetate. The organic layers were washed two times with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure. Purification of the crude product was performed by column chromatography.

Ethyl 2-{4-(3-methoxyprop-1-yn-1-yl)-5-[3-(piperidin-1-yl)prop-1-yn-1-yl]-1*H*-1,2,3-triazol-1-yl}acetate (6a). This compound was prepared in accordance with the general procedure from alkyne **2** (70.0 mg, 0.283 mmol), di(*N*-piperidino)methane **5a** (51.6 mg, 0.283 mmol), and CuCl (7.0 mg, 0.07 mmol) in dioxane (5 ml) with a reaction time of 1 h at 70 °C. The crude product was purified by column chromatography (eluent: hexane/acetone = 2:1) to afford a beige solid (78 mg, 80% yield), mp 51 – 53 °C. ^{1}H NMR (400 MHz, $CDCl_3$, δ) 5.12 (s, 2H, $-C\underline{H}_2-CO_2Et$), 4.35 (s, 2H, $\equiv C-C\underline{H}_2-OMe$), 4.24 (q, J = 7.1 Hz, 2H, $-COOC\underline{H}_2CH_3$), 3.59 (s, 2H, $\equiv C-C\underline{H}_2-N$), 3.44 (s, 3H, $-OC\underline{H}_3$), 2.52 (t, J = 5.5 Hz, 4H, piperidine), 1.61 (p, J = 5.5 Hz, 4H, piperidine), 1.47 – 1.38 (m, 2H, piperidine), 1.26 (t, J = 7.1 Hz, 3H, $-COOCH_2C\underline{H}_3$). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 165.4, 133.2, 125.1, 100.6, 91.5, 75.4, 69.2, 62.6, 60.3, 57.8, 53.3, 50.0, 48.6, 26.0, 23.8, 14.2. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{18}H_{25}N_4O_3^+$ 345.1921; Found 345.1922.

Ethyl 2-{4-(3-methoxyprop-1-yn-1-yl)-5-[3-(4-methylpiperazin-1-yl)prop-1-yn-1-yl]-1*H*-1,2,3-triazol-1-yl}acetate 6b. This compound was prepared in accordance with the general procedure from alkyne **2** (70.0 mg, 0.283 mmol), bis(4-methylpiperazin-1-yl)methane **5b** (60.1 mg, 0.283 mmol), and CuCl (7.0 mg, 0.07 mmol) in dioxane (5 ml) with a reaction time of 1 h at 70 °C. The crude product was purified by column chromatography (eluent: DCM/MeOH = 20:1) to afford a beige solid (75 mg, 74% yield), mp 42 – 44 °C. ^{1}H NMR (400 MHz, $CDCl_3$, δ) 5.11 (s, 2H, $-C\underline{H}_2-CO_2Et$), 4.35 (s, 2H, $\equiv C-C\underline{H}_2-OMe$), 4.24 (q, J = 7.1 Hz, 2H, $-COOC\underline{H}_2CH_3$), 3.60 (s, 2H, $\equiv C-C\underline{H}_2-N$), 3.44 (s, 3H, $-OC\underline{H}_3$), 2.62 (m, 4H, piperazine), 2.52 – 2.40 (m, 4H, piperazine), 2.27 (s, 3H, $-NC\underline{H}_3$), 1.26 (t, J = 7.1 Hz, 3H, $-COOCH_2C\underline{H}_3$). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 165.4, 133.4, 124.9, 100.1, 91.6, 75.3, 69.4, 62.6, 60.3, 57.8, 55.0, 52.0, 50.0, 47.8, 46.0, 14.2. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{18}H_{26}N_5O_3^+$ 360.2030; Found 360.2023.

Ethyl 2-[4-(3-methoxyprop-1-yn-1-yl)-5-(3-morpholinoprop-1-yn-1-yl)-1*H*-1,2,3-triazol-1-yl]acetate 6c. This compound was prepared in accordance with the general procedure from alkyne **2** (55.0 mg, 0.222 mmol), dimorpholinomethane **5c** (41.4 mg, 0.222 mmol), and CuCl (5.5 mg, 0.056 mmol) in dioxane (3 ml) with a reaction time of 1 h at 70 °C. The crude product was purified by column chromatography (eluent: hexane/acetone = 2:1) to afford a beige solid (65 mg, 85% yield), mp 64 – 67 °C. ^{1}H NMR (400 MHz, $CDCl_3$, δ). 5.14 (s, 2H, $-C\underline{H}_2-CO_2Et$), 4.37 (s, 2H, $\equiv C-C\underline{H}_2-OMe$), 4.27 (q, J = 7.1 Hz, 2H, $-COOC\underline{H}_2CH_3$), 3.77 – 3.70 (m, 4H, morpholine), 3.63 (s, 2H, $\equiv C-C\underline{H}_2-N$), 3.46 (s, 3H, $-OC\underline{H}_3$), 2.63 – 2.56 (m, 4H, morpholine), 1.29 (t, J = 7.1 Hz, 3H, $-COOCH_2C\underline{H}_3$).^{13}C NMR (101 MHz, $CDCl_3$, δ) 165.4, 133.4, 124.8, 99.6, 91.7, 75.2, 69.7, 66.8, 62.7, 60.3, 57.9, 52.2, 50.0, 48.1, 14.2. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{17}H_{23}N_4O_4^+$ 347.1714; Found 347.1716.

Ethyl 2-{5-[3-bis(2-hydroxyethyl)aminoprop-1-yn-1-yl]-4-(3-methoxyprop-1-yn-1-yl)-1*H*-1,2,3-triazol-1-yl}acetate 6d). This compound was prepared in accordance with the general procedure from alkyne **2** (70.0 mg, 0.283 mmol), diaminomethane **5d** (62.9 mg, 0.283 mmol), and CuCl (7.0 mg, 0.07 mmol) in dioxane (5.6 ml) with a reaction time of 1 h at 70 °C. The crude product was purified by column chromatography (eluent: DCM/MeOH = 20:1) to afford a beige viscous oil (52 mg, 50% yield). ^{1}H NMR (400 MHz, $CDCl_3$, δ) 5.14 (s, 2H, $-C\underline{H}_2-CO_2Et$), 4.35 (s, 2H, $\equiv C-C\underline{H}_2-OMe$), 4.25 (q, J = 7.1 Hz, 2H, $-COOC\underline{H}_2CH_3$), 3.84 (s, 2H, $\equiv C-C\underline{H}_2-N$), 3.70 (t, J = 5.2 Hz, 4H, $-N-CH_2-C\underline{H}_2-OH$), 3.44 (s, 3H, $-OC\underline{H}_3$), 3.02 (s, 2H, $-OH$), 2.82 (t, J = 5.2 Hz, 4H, $-N-C\underline{H}_2-CH_2-OH$), 1.27 (t, J = 7.1 Hz, 3H, $-COOCH_2C\underline{H}_3$). ^{13}C NMR (101 MHz, $CDCl_3$, δ) 165.5, 133.6, 124.8, 99.8, 91.7, 75.2, 69.6, 62.7, 60.4, 59.4, 58.0, 55.7, 50.1, 44.1, 14.2. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{17}H_{25}N_4O_5^+$ 365.1820; Found 365.1819.

1-{3-[2-(3-Methoxyprop-1-yn-1-yl)benzo[*b*]thiophen-3-yl]prop-2-yn-1-yl}piperidine 7a. This compound was prepared in accordance with the general procedure from alkyne **4** (50.0 mg, 0.221 mmol), di(*N*-piperidino)methane **5a** (40.3 mg, 0.221 mmol), and CuCl (5.5 mg, 0.055 mmol) in dioxane (4.4 ml) with a reaction time of 1 h at 50 °C. The crude product was purified by column chromatography (eluent: hexane/acetone = 5:1) to afford a beige solid (60.3 mg, 84% yield), mp 48 – 50 °C. ^{1}H NMR (400 MHz, Acetone-d$_6$, δ) 7.97 – 7.81 (m, 2H, Ar−H), 7.59 – 7.44 (m, 2H, Ar−H), 4.44 (s, 2H, ≡C−C$\underline{H}_2$−OMe), 3.65 (s, 2H, ≡C−C$\underline{H}_2$−N), 3.44 (s, 3H, −OC$\underline{H}_3$), 2.62 (t, *J* = 5.5 Hz, 4H, piperidine), 1.61 (p, *J* = 5.5 Hz, 4H, piperidine), 1.46 – 1.40 (m, 2H, piperidine). ^{13}C NMR (101 MHz, Acetone-d$_6$, δ) 139.4, 139.1, 127.6, 126.4, 125.7, 124.2, 124.1, 123.4, 96.6, 93.8, 79.5, 78.3, 60.7, 57.8, 53.8, 49.0, 26.8, 24.8. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{20}H_{22}NOS^+$ 324.1417; Found 324.1418.

1-{3-[2-(3-Methoxyprop-1-yn-1-yl)benzo[*b*]thiophen-3-yl]prop-2-yn-1-yl}-4-methylpiperazine 7b. This compound was prepared in accordance with the general procedure from alkyne **4** (80.0 mg, 0.354 mmol), bis(4-methylpiperazin-1-yl)methane **5b** (75.1 mg, 0.354 mmol), and CuCl (8.8 mg, 0.088 mmol) in dioxane (7 ml) with a reaction time of 1.5 h at 50 °C. The crude product was purified by column chromatography (eluent: DCM/MeOH = 10:1) to afford a brown oil (111.6 mg, 93% yield). ^{1}H NMR (400 MHz, CDCl$_3$, δ) 7.89 – 7.81 (m, 1H, Ar−H), 7.75 – 7.67 (m, 1H, Ar−H), 7.40 – 7.37 (m, 2H, Ar−H), 4.43 (s, 2H, ≡C−C$\underline{H}_2$−OMe), 3.68 (s, 2H, ≡C−C$\underline{H}_2$−N), 3.48 (s, 3H, −OC$\underline{H}_3$), 2.77 (m, 4H, piperazine), 2.53 (m, 4H, piperazine), 2.31 (s, 3H, −NC$\underline{H}_3$). ^{13}C NMR (101 MHz, CDCl$_3$, δ) 138.7, 138.5, 126.4, 125.6, 125.3, 123.7, 123.3, 122.2, 95.1, 91.5, 79.6, 78.6, 60.7, 57.9, 55.2, 52.0, 48.1, 46.1. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{20}H_{23}N_2OS^+$ 339.1526; Found 339.1530.

4-{3-[2-(3-Methoxyprop-1-yn-1-yl)benzo[*b*]thiophen-3-yl]prop-2-yn-1-yl}morpholine 7c. This compound was prepared in accordance with the general procedure from alkyne **4** (50.0 mg, 0.221 mmol), di(*N*-morpholino)methane **5c** (41.2 mg, 0.221 mmol), and CuCl (5.5 mg, 0.055 mmol) in dioxane (4.4 ml) with a reaction time of 1 h at 50 °C. The crude product was purified by column chromatography (eluent: hexane/acetone = 3:1) to afford a beige solid (59.2 mg, 82% yield), mp 66 – 68 °C. ^{1}H NMR (400 MHz, CDCl$_3$, δ) 7.89 – 7.82 (m, 1H, Ar−H), 7.75 – 7.69 (m, 1H, Ar−H), 7.47 – 7.36 (m, 2H, Ar−H), 4.43 (s, 2H, ≡C−C$\underline{H}_2$−OMe), 3.81 – 3.76 (m, 4H, morpholine), 3.69 (s, 2H, ≡C−C$\underline{H}_2$−N), 3.48 (s, 3H, −OC$\underline{H}_3$), 2.76 – 2.69 (m, 4H, morpholine). ^{13}C NMR (101 MHz, CDCl$_3$, δ) 138.64, 138.57, 126.4, 125.7, 125.3, 123.5, 123.2, 122.3, 95.2, 91.0, 79.5, 78.9, 67.1, 60.7, 57.93, 52.3, 48.4. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{19}H_{20}NO_2S^+$ 326.1209; Found 326.1207.

2,2'-({3-[2-(3-Methoxyprop-1-yn-1-yl)benzo[*b*]thiophen-3-yl]prop-2-yn-1-yl}azanediyl)diethanol 7d. This compound was prepared in accordance with the general procedure from alkyne **4** (80.0 mg, 0.354 mmol), diaminomethane **5d** (78.6 mg, 0.354 mmol), and CuCl (8.8 mg, 0.088 mmol) in dioxane (7 ml) with a reaction time of 3 h at 50 °C. The crude product was purified by column chromatography (eluent: hexane/acetone = 1:2) to afford a brown oil (91.3 mg, 75% yield). ^{1}H NMR (400 MHz, CDCl$_3$, δ) 7.86 – 7.79 (m, 1H, Ar−H), 7.76 – 7.67 (m, 1H, Ar−H), 7.46 – 7.37 (m, 2H, Ar−H), 4.41 (s, 2H, ≡C−C$\underline{H}_2$−OMe), 3.88 (br.s, 2H, ≡C−C$\underline{H}_2$−N), 3.75 (m, 4H, −N−CH$_2$−C$\underline{H}_2$−OH), 3.47 (s, 3H, −OC$\underline{H}_3$), 3.11 (br.s, 2H, −O$\underline{H}$), 2.93 (m, 4H, −N−C$\underline{H}_2$−CH$_2$−OH). ^{13}C NMR (101 MHz, CDCl$_3$, δ) 138.6, 138.5, 126.5, 125.8, 125.4, 123.4, 123.0, 122.3, 95.1, 90.8, 79.5, 78.8, 60.7, 59.4, 58.0, 55.7, 43.8. HRMS (ESI) m/z: [M+H]$^+$ Calcd for $C_{19}H_{22}NO_3S^+$ 344.1315; Found 344.1318.

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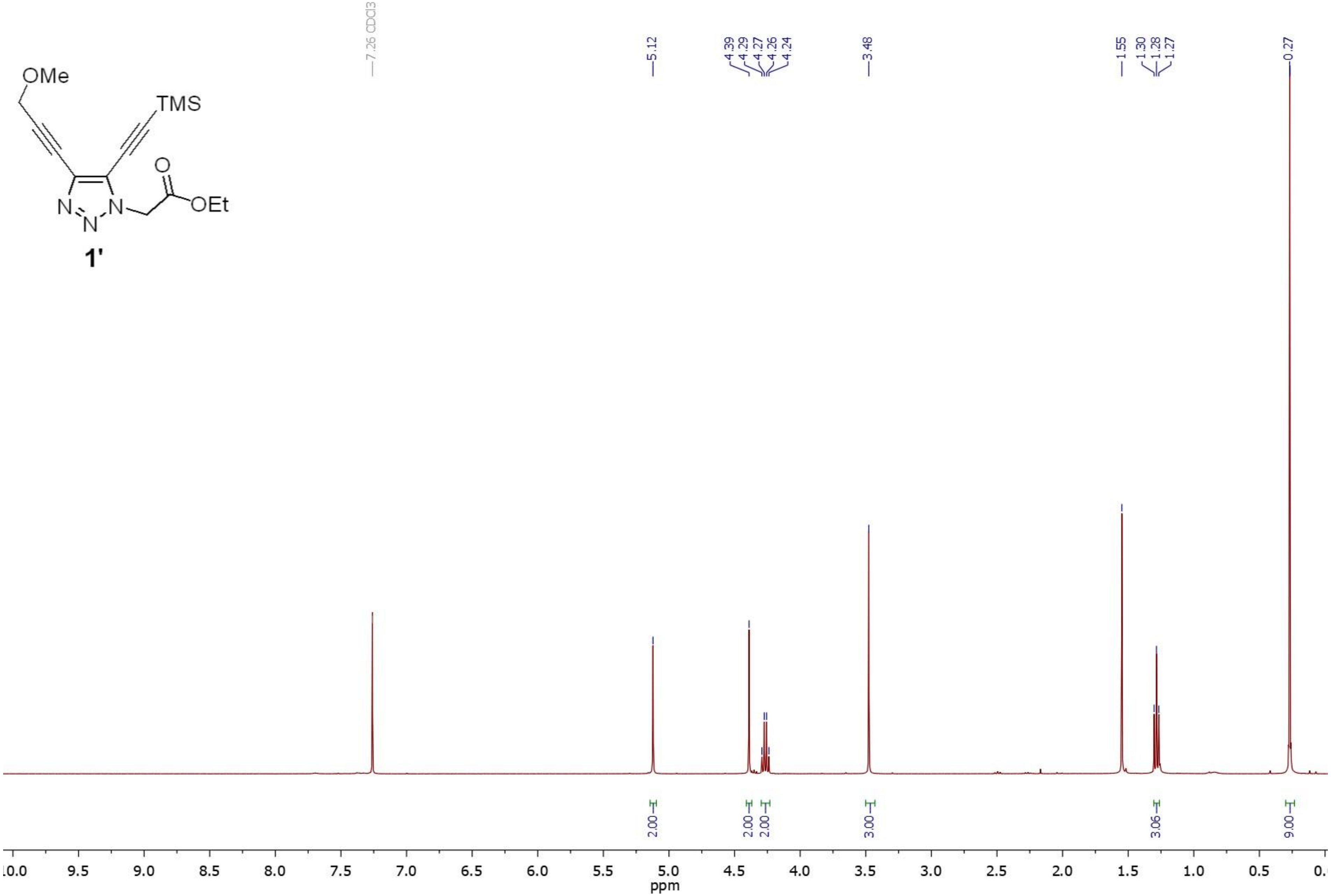
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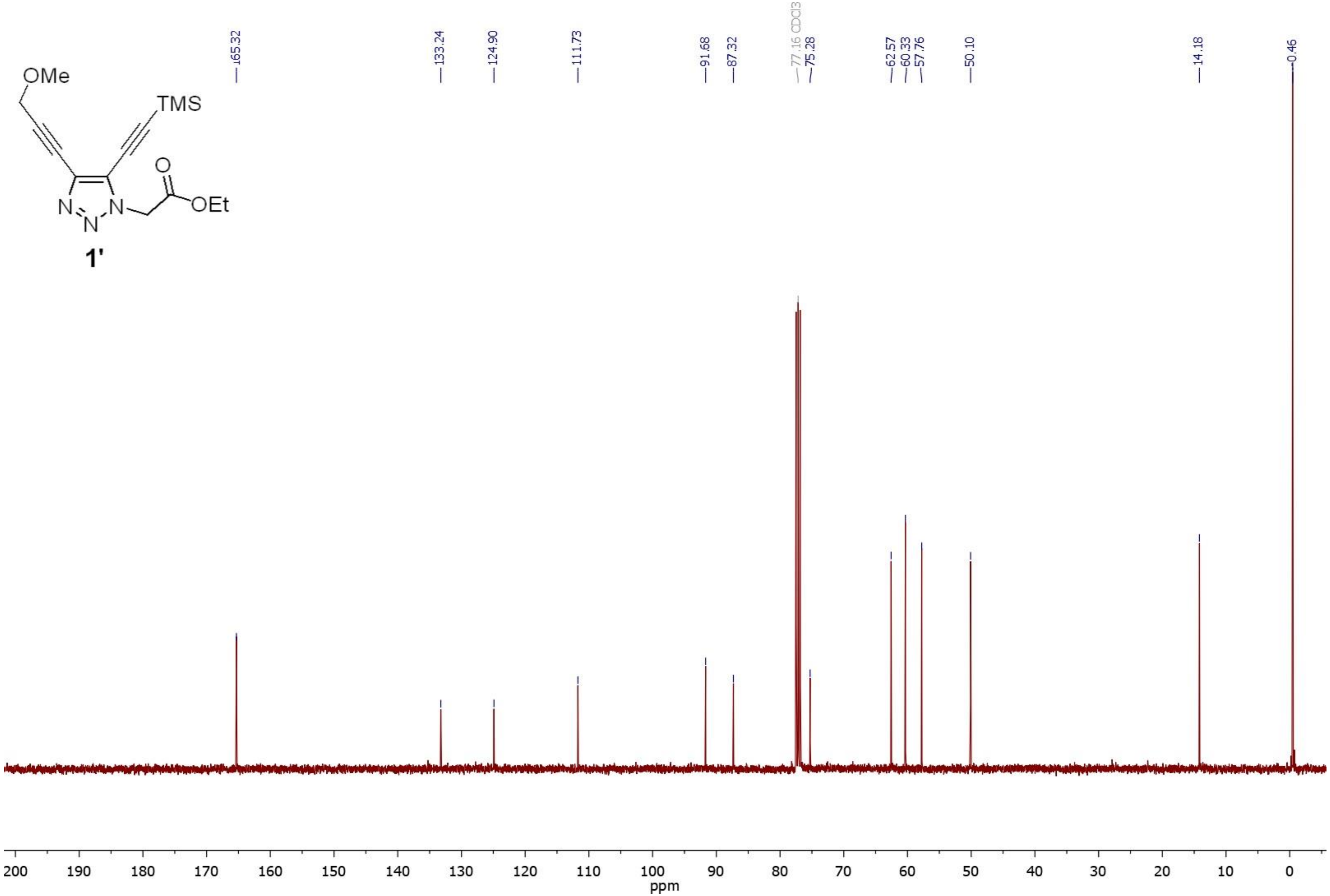
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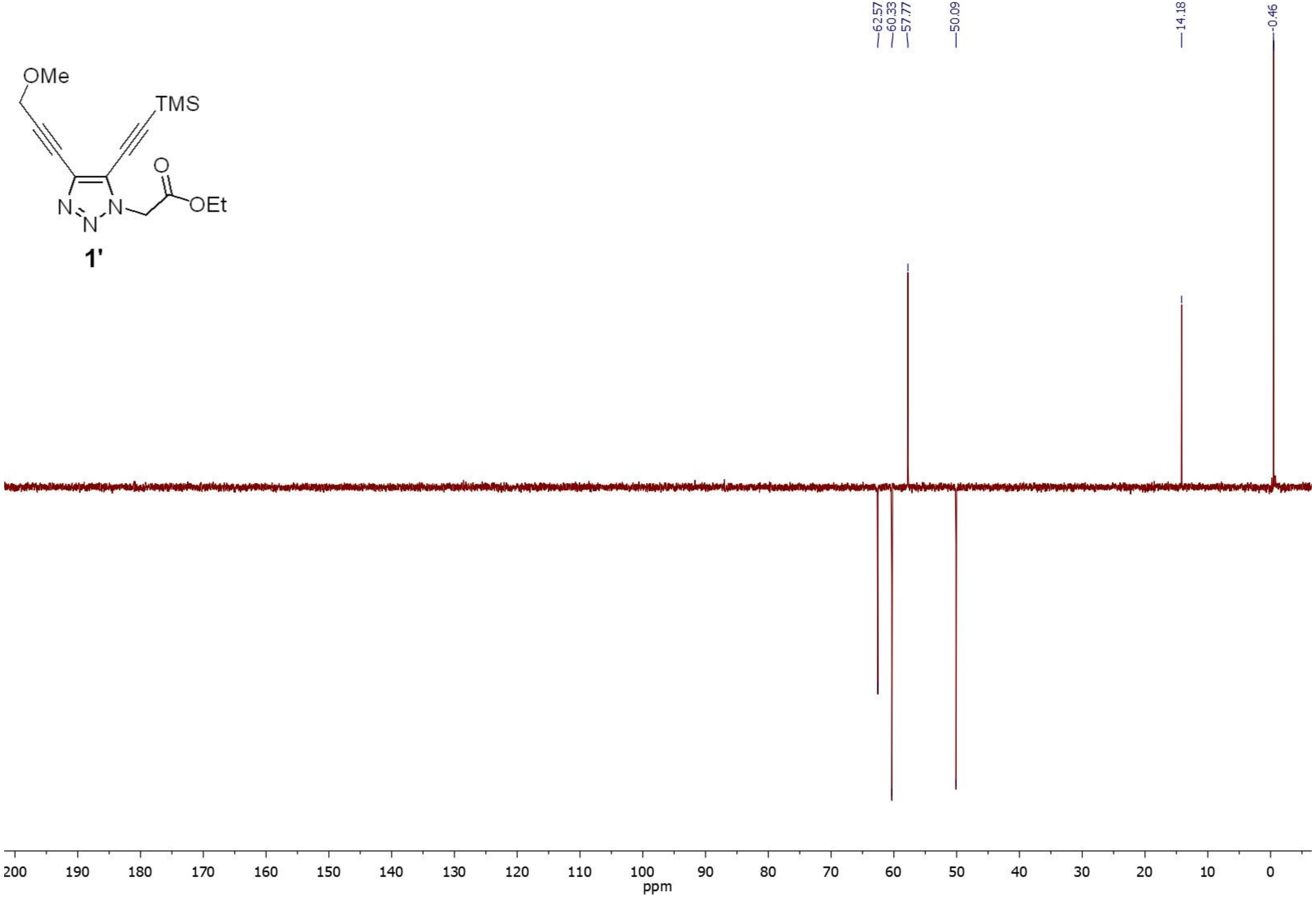
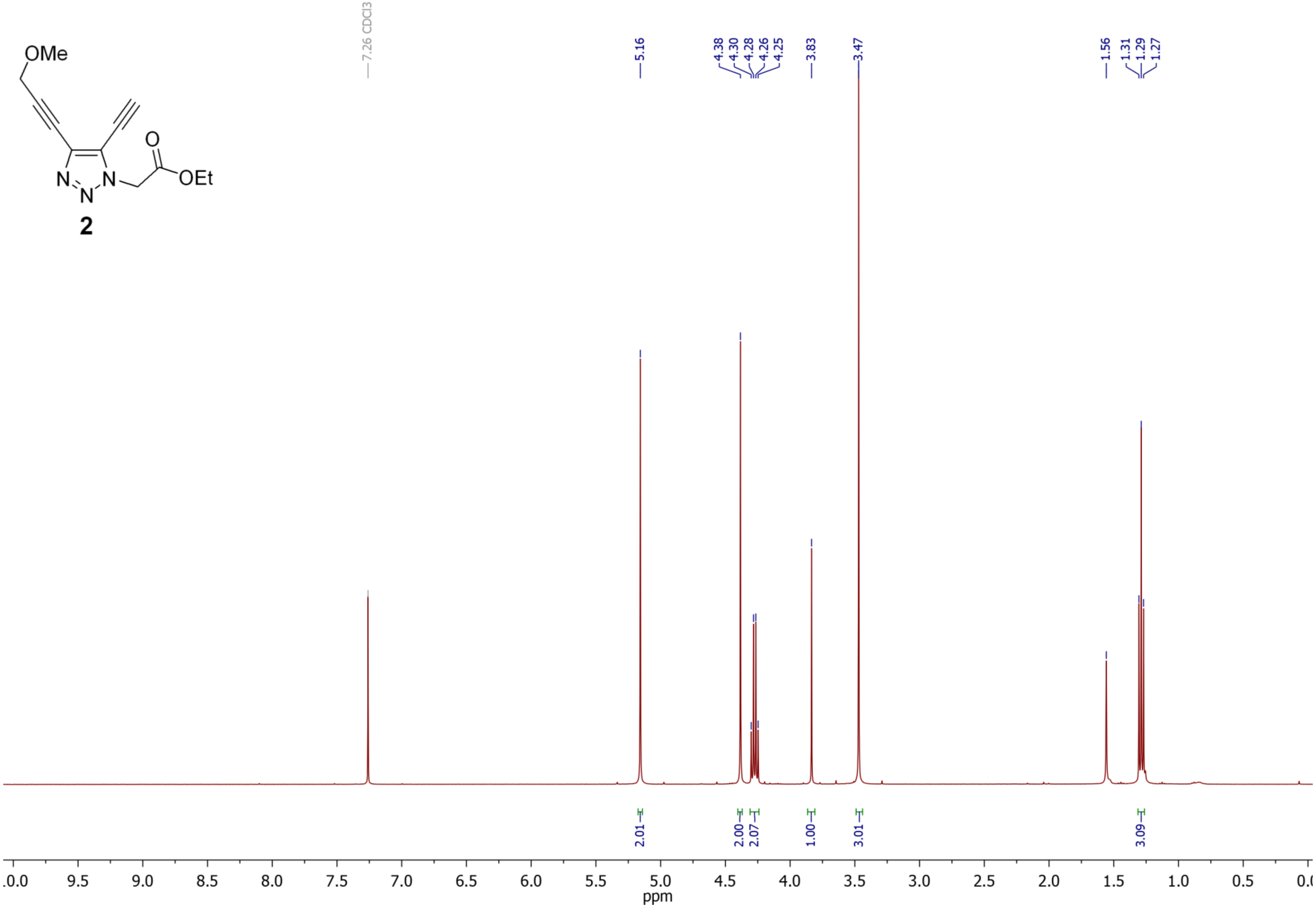
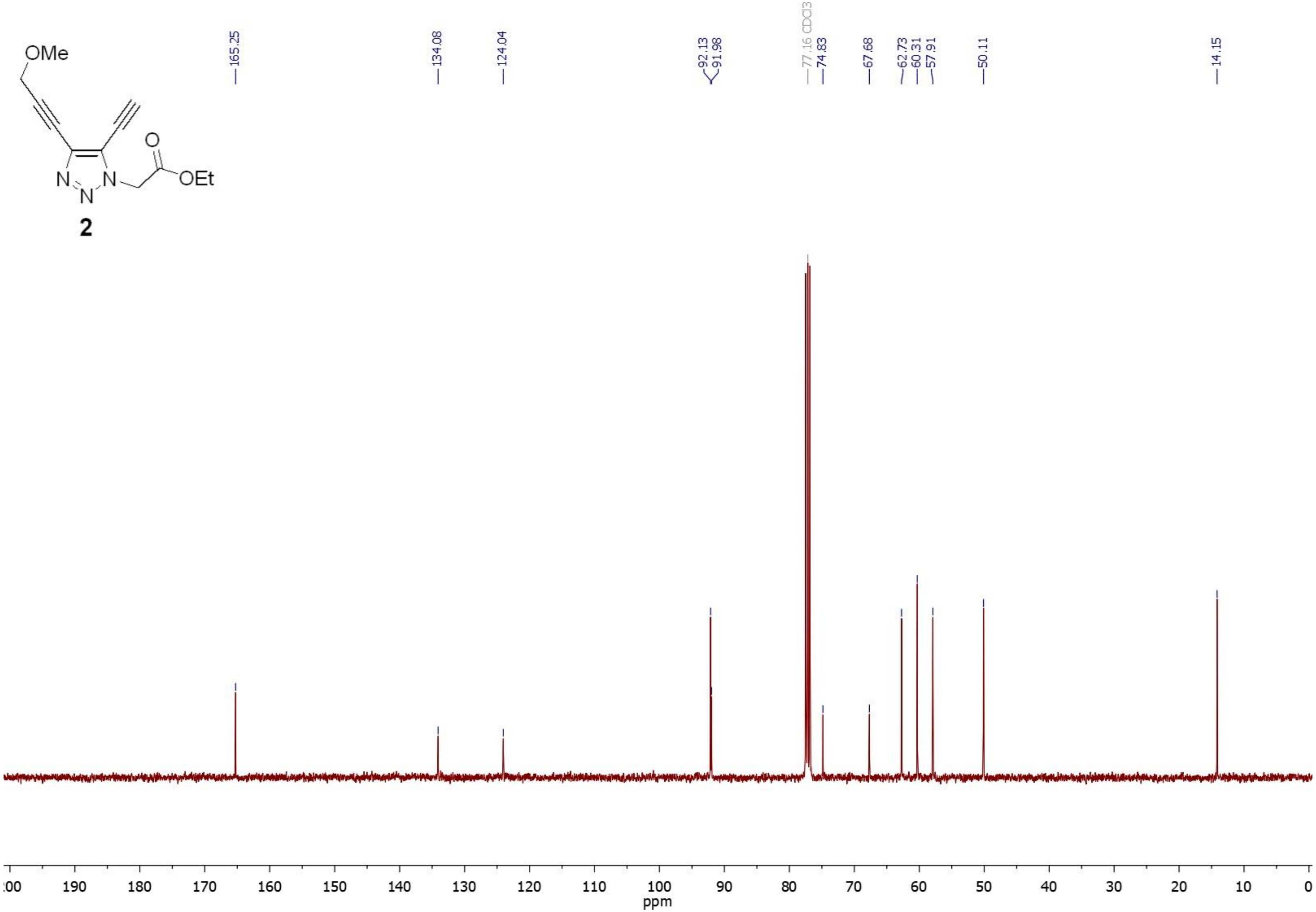
ppm

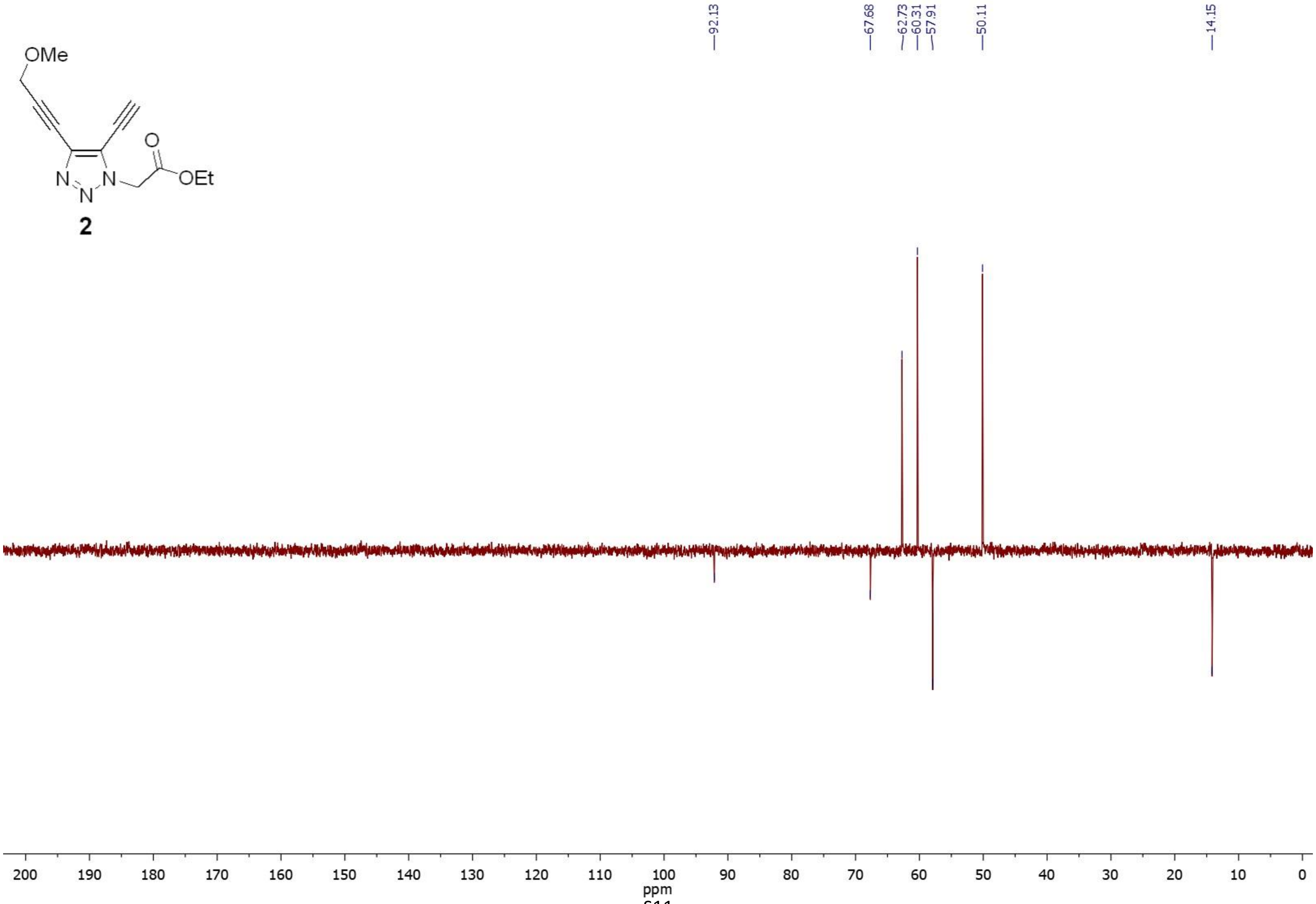
1'


OMe
TMS
O
OEt
N
N
N
1'
62.57
60.33
57.77
50.09
14.18
-0.46
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

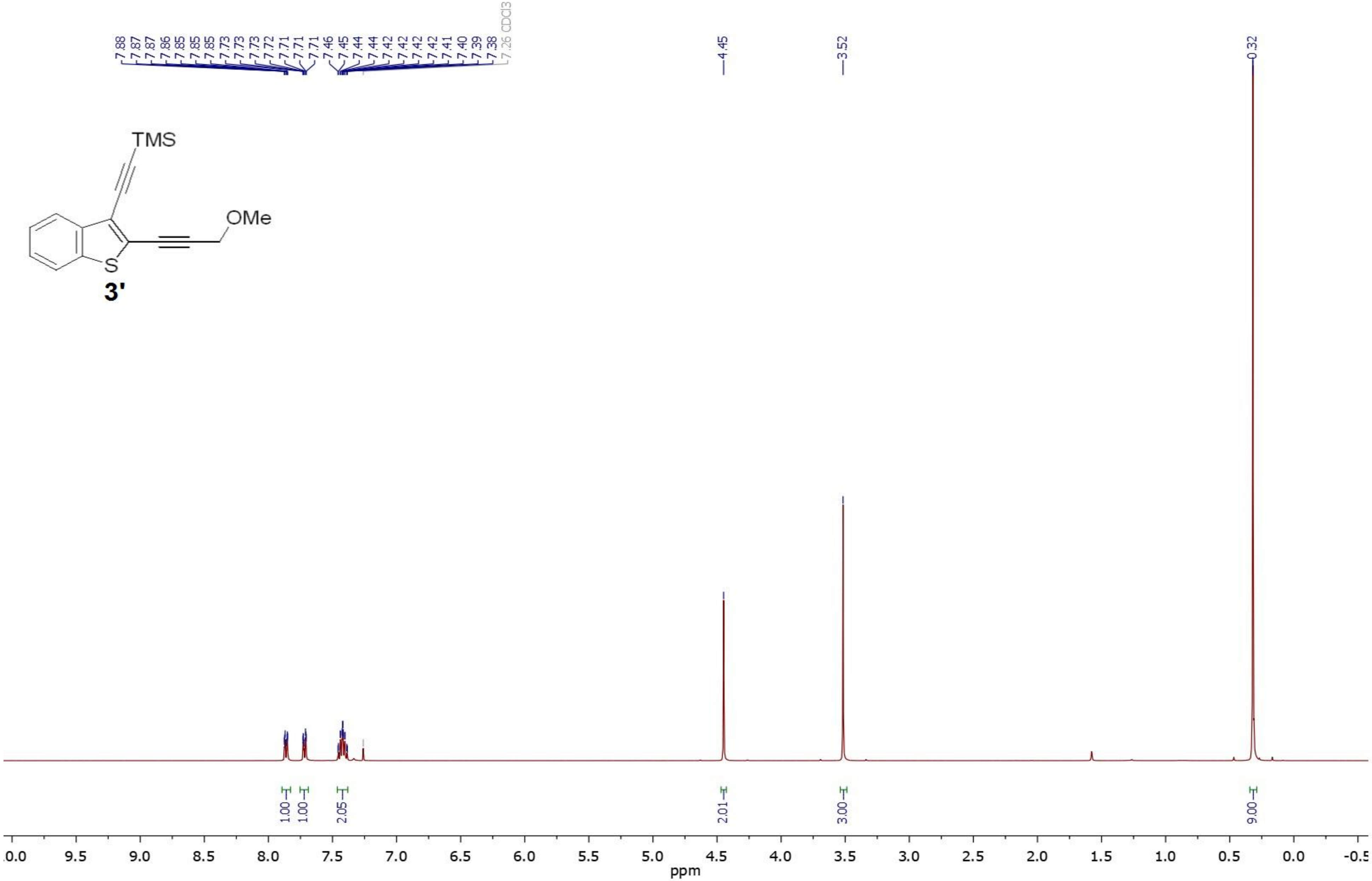

OMe
O
OEt
N
N
N
7.26 CDCl3
5.16
4.38
4.30
4.28
4.26
4.25
3.83
3.47
1.56
1.31
1.29
1.27
2.01
2.00
2.07
1.00
3.01
3.09
.0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
ppm

2

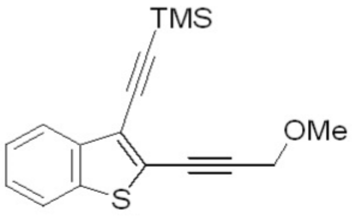

OMe
O
OEt
N
N
N
2
165.25
134.08
124.04
92.13
91.98
77.16 CDCl3
74.83
67.68
62.73
60.31
57.91
50.11
14.15
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
OEt
N
N
N
92.13
67.68
62.73
60.31
57.91
50.11
14.15
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

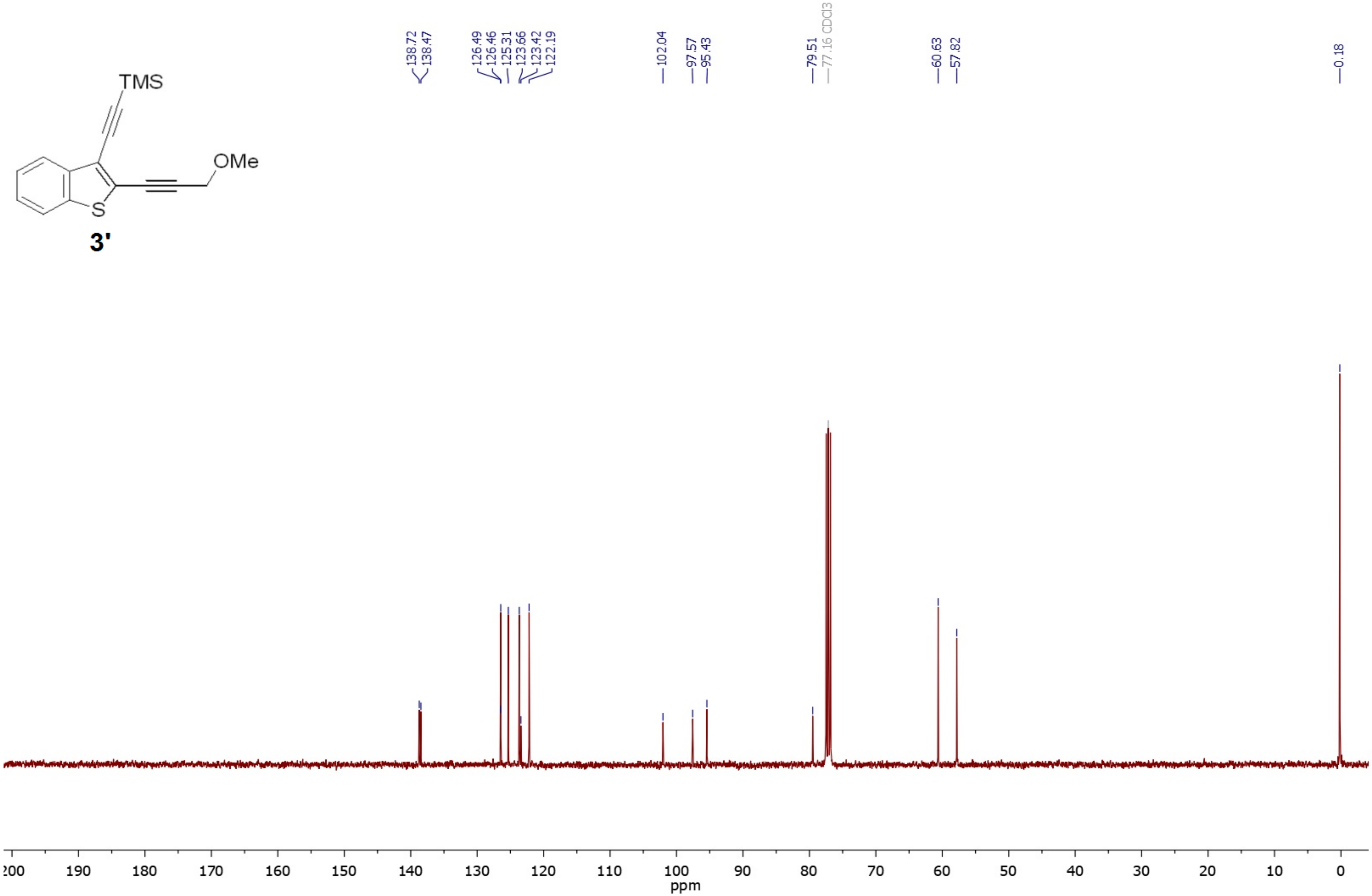
2

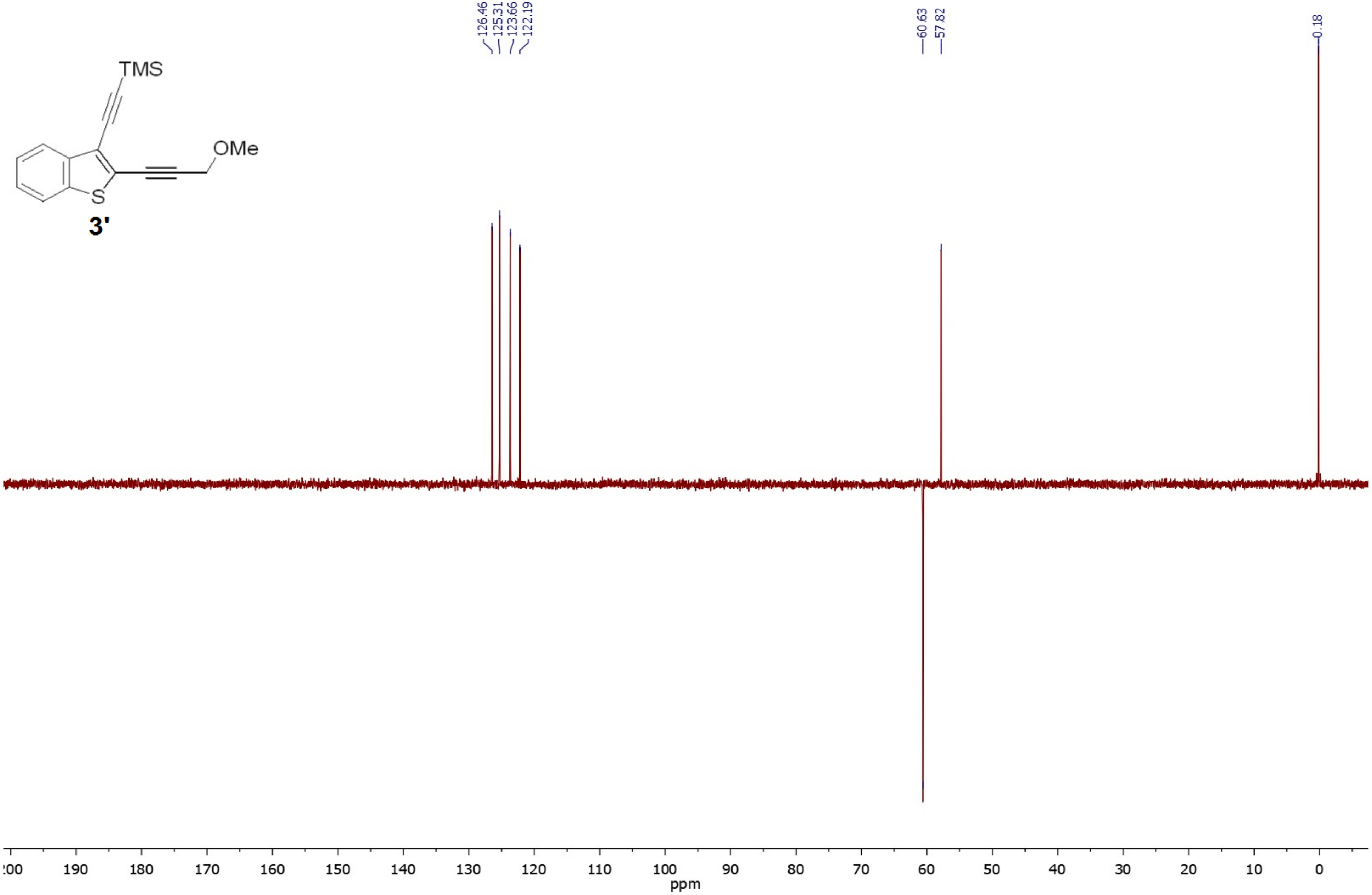

7.88
7.87
7.87
7.86
7.85
7.85
7.85
7.73
7.73
7.73
7.72
7.71
7.71
7.71
7.46
7.45
7.44
7.44
7.42
7.42
7.42
7.42
7.41
7.40
7.39
7.38
7.26 CDCl3
4.45
3.52
0.32
TMS
OMe
S
1.00
1.00
2.05
2.01
3.00
9.00
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
ppm

3'


TMS
OMe
S

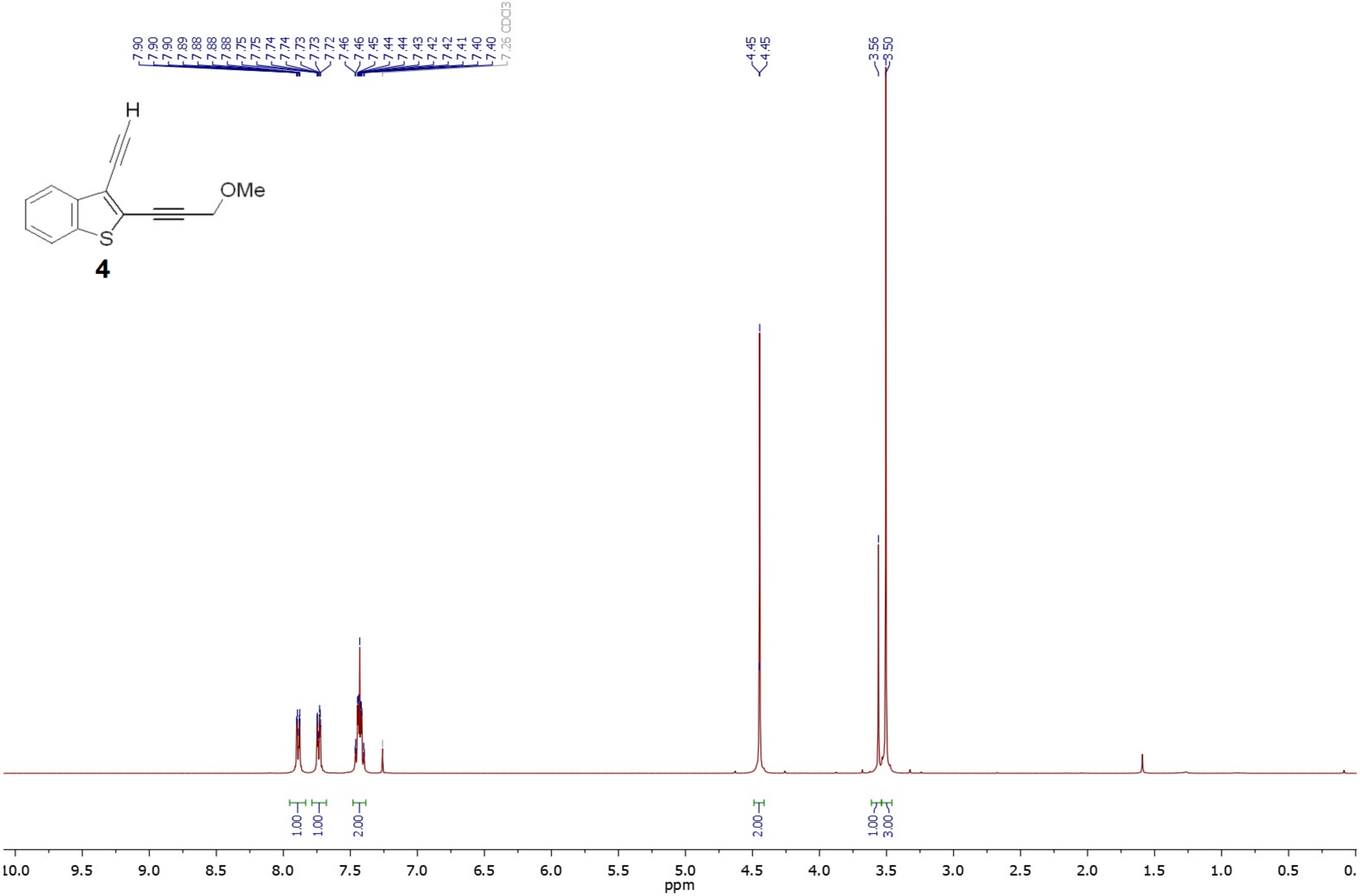
3'

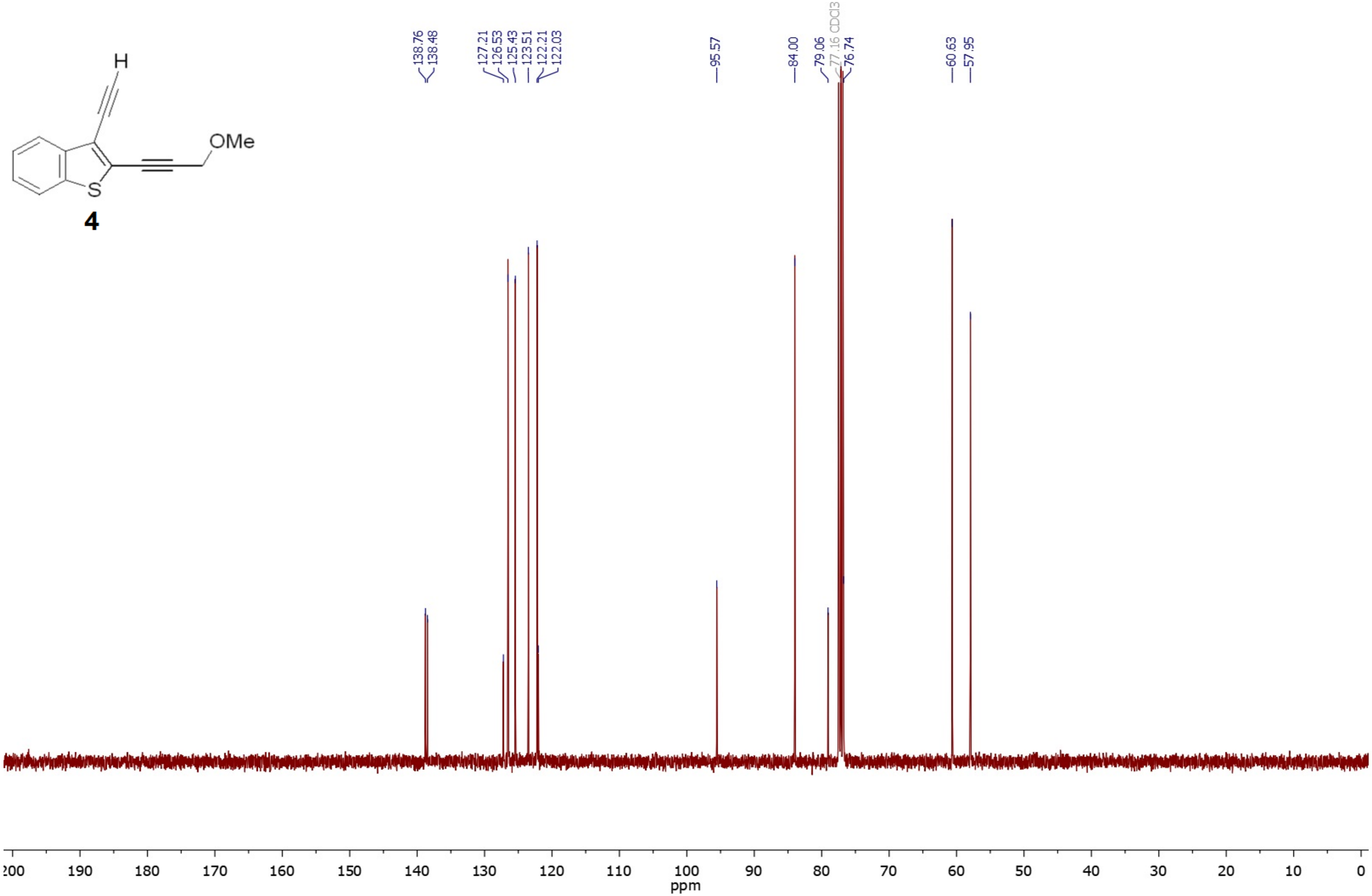

138.72
138.47
126.49
126.46
125.31
123.66
123.42
122.19
102.04
97.57
95.43
79.51
77.16 CDCl3
60.63
57.82
0.18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm



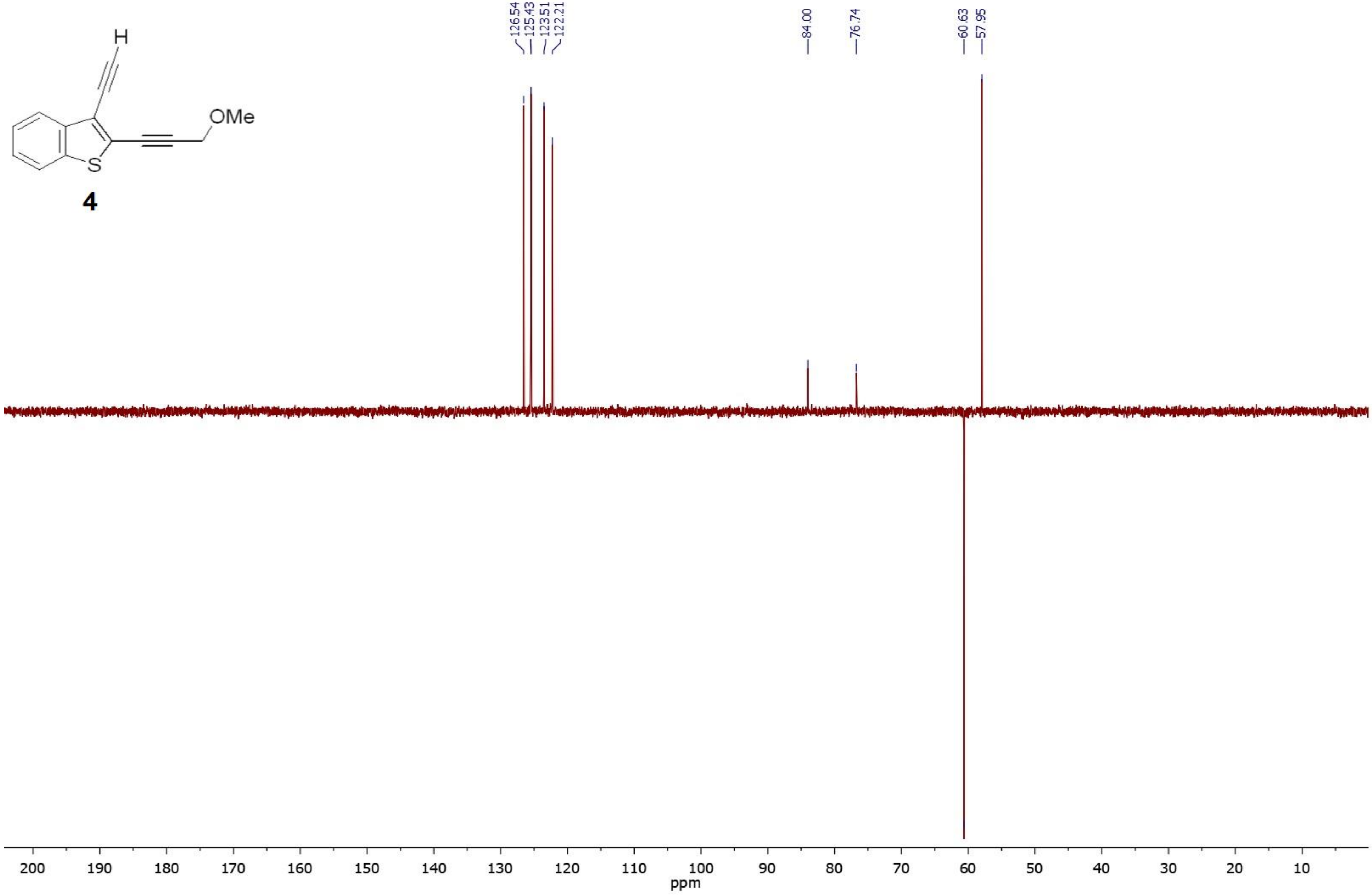
3'

TMS
OMe
S
126.46
125.31
123.66
122.19
60.63
57.82
0.18
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.90
7.90
7.90
7.89
7.88
7.88
7.88
7.75
7.75
7.74
7.74
7.73
7.73
7.72
7.46
7.46
7.45
7.44
7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.26 CDCl3
4.45
4.45
3.56
3.50
H
OMe
S
4
1.00
1.00
2.00
2.00
1.00
3.00
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.
ppm

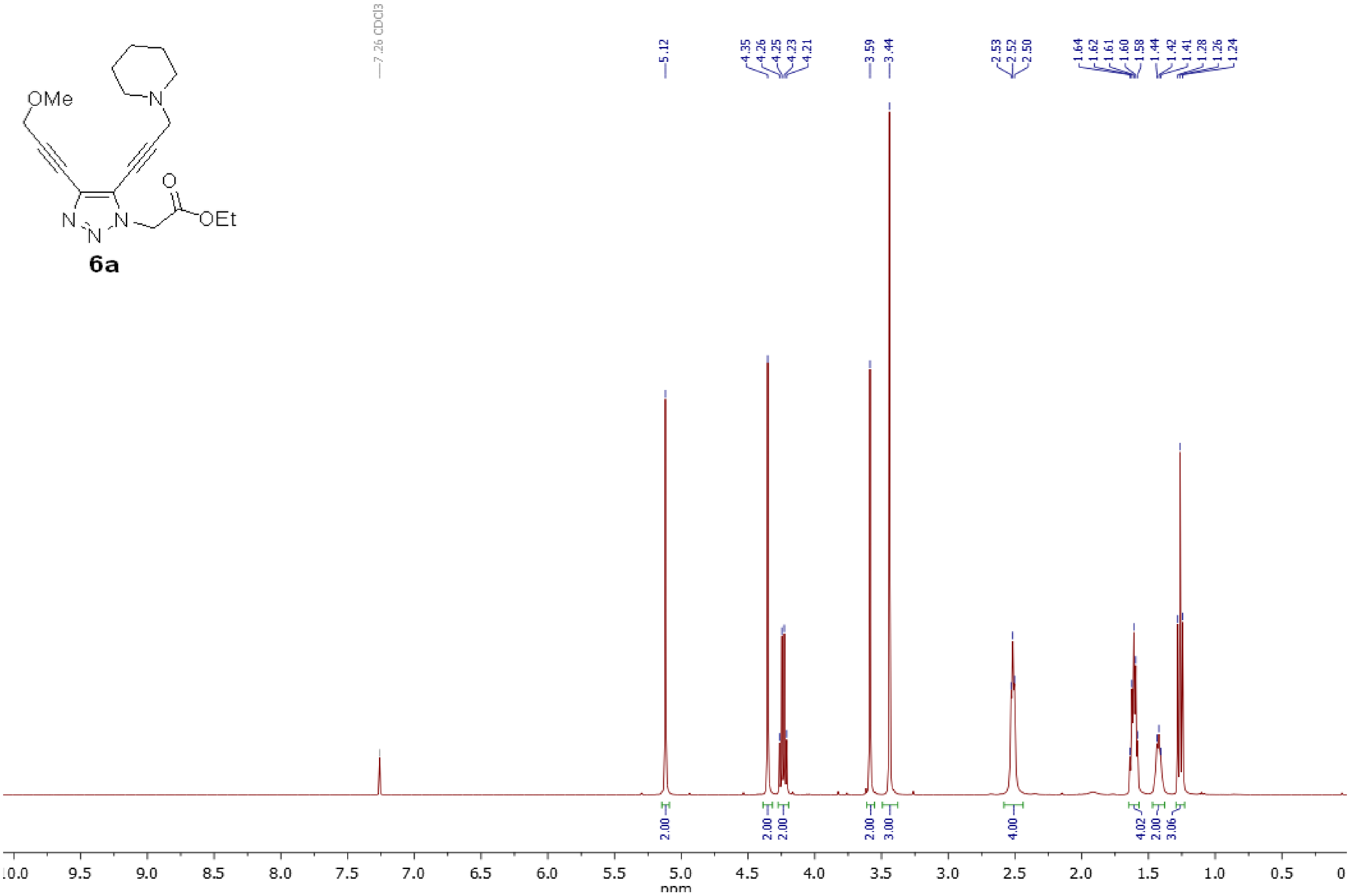

H
OMe
S
138.76
138.48
127.21
126.53
125.43
123.51
122.21
122.03
95.57
84.00
79.06
77.16 CDCl3
76.74
60.63
57.95
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

4



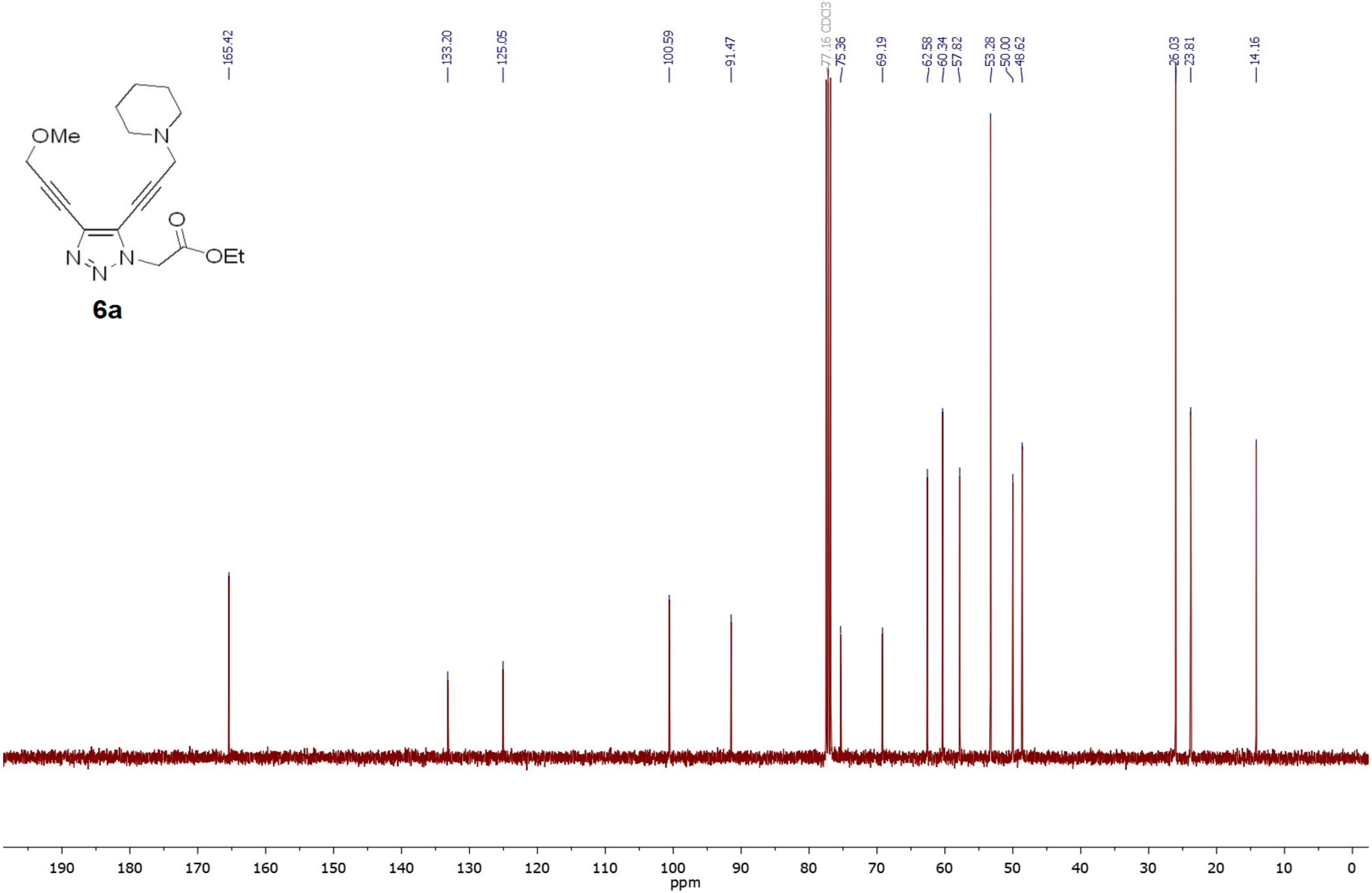
4

OMe
H
S
126.54
125.43
123.51
122.21
84.00
76.74
60.63
57.95
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm



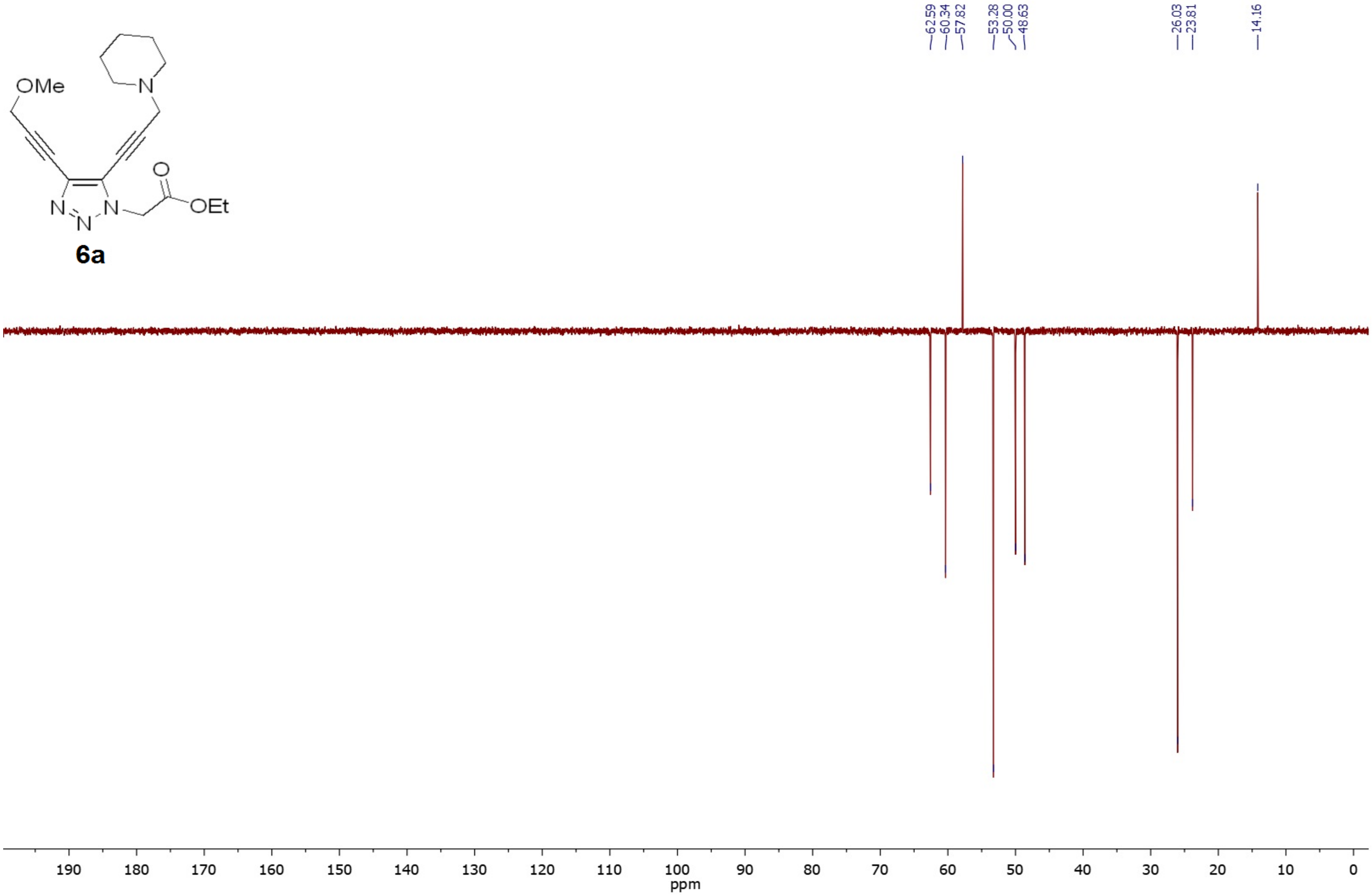
6a

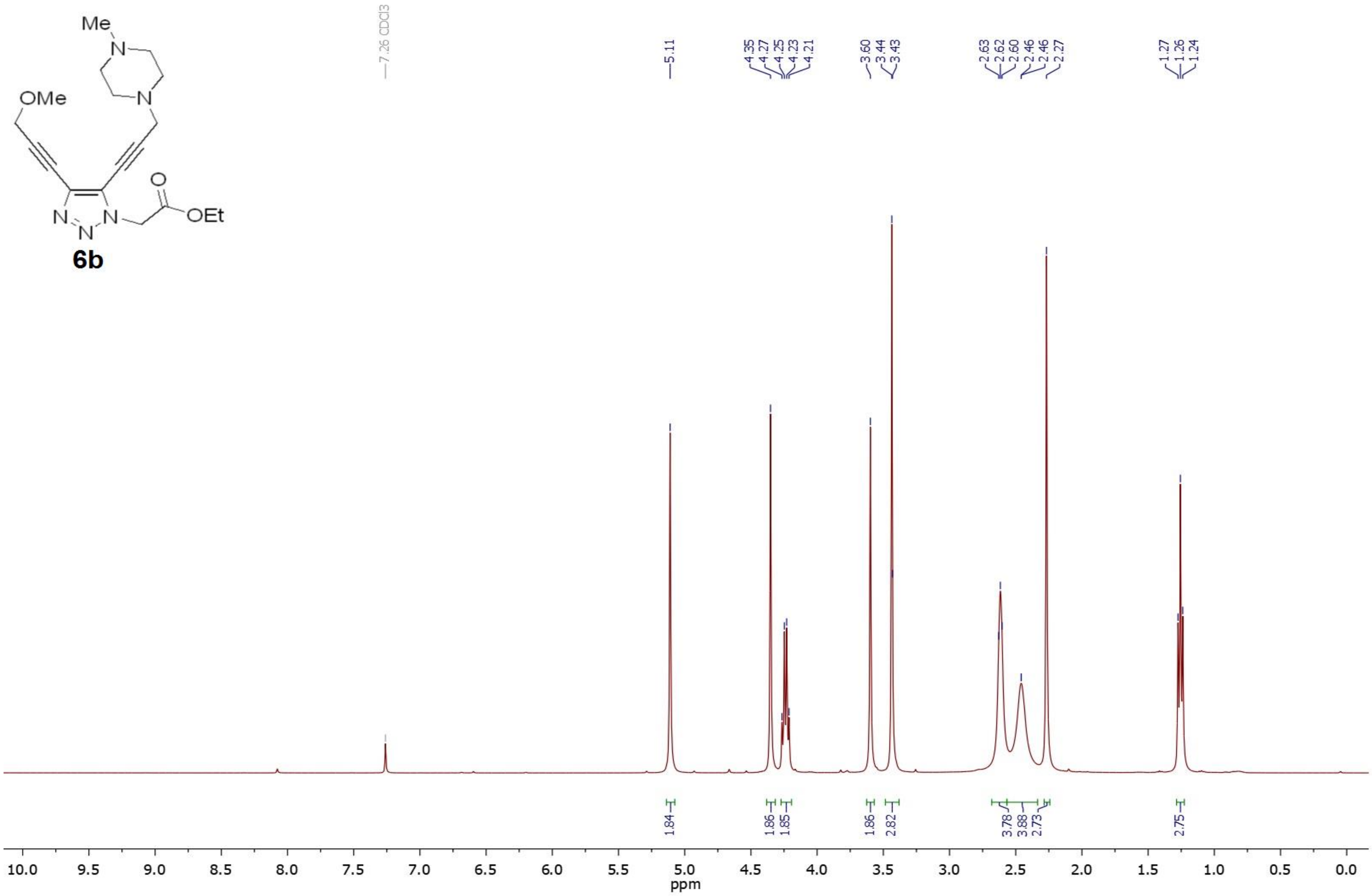
OMe
N
O
OEt
N
N
N
7.26 CDCl3
5.12
4.35
4.26
4.25
4.23
4.21
3.59
3.44
2.53
2.52
2.50
1.64
1.62
1.61
1.60
1.58
1.44
1.42
1.41
1.28
1.26
1.24
2.00
2.00
2.00
2.00
3.00
4.00
4.02
2.00
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0
ppm



6a

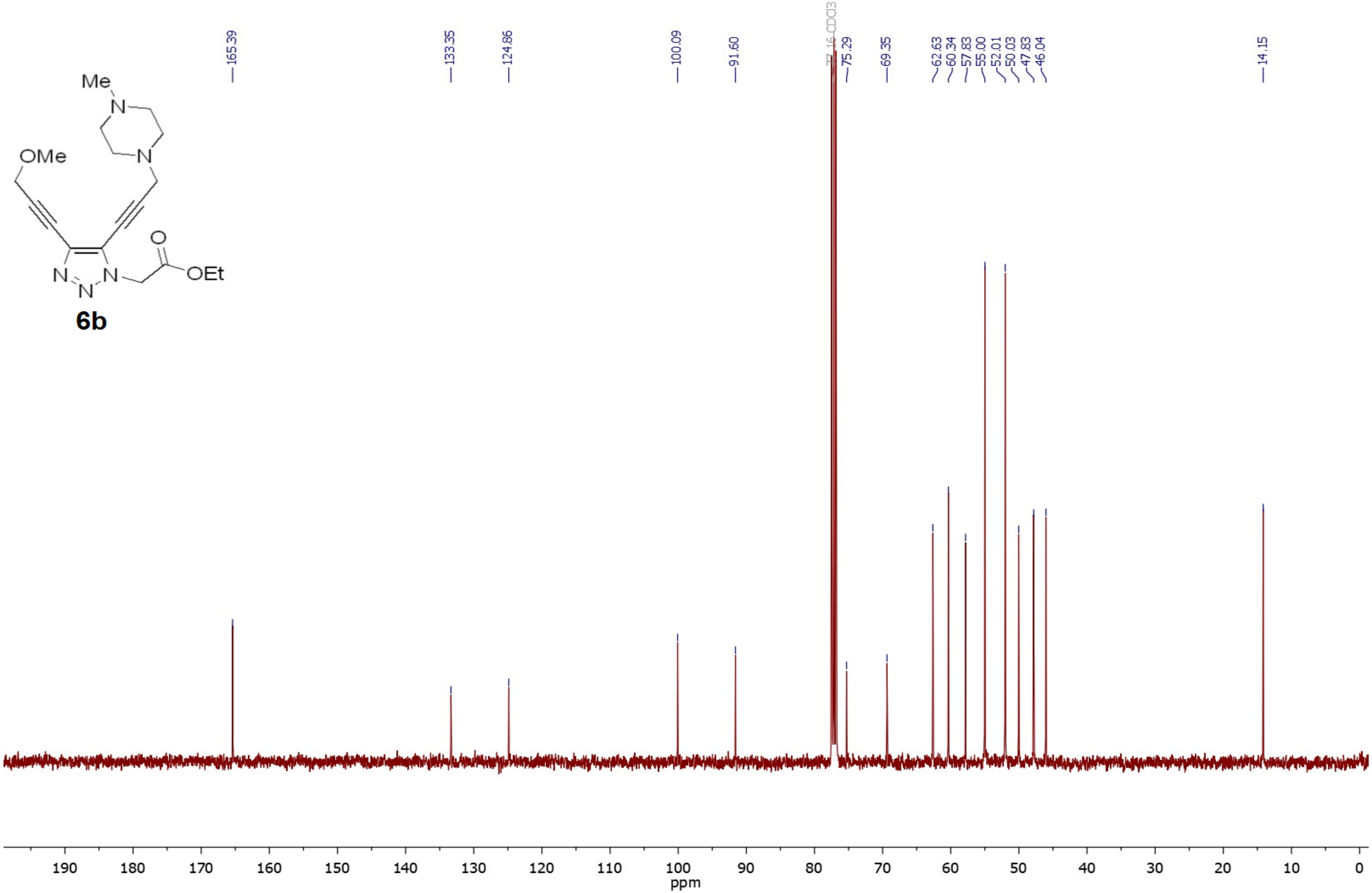
OMe
N
O
OEt
N
N
N
165.42
133.20
125.05
100.59
91.47
77.16 CDCl3
75.36
69.19
62.58
60.34
57.82
53.28
50.00
48.62
26.03
23.81
14.16
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
N
O
OEt
N
N
N
6a
62.59
60.34
57.82
53.28
50.00
48.63
26.03
23.81
14.16
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

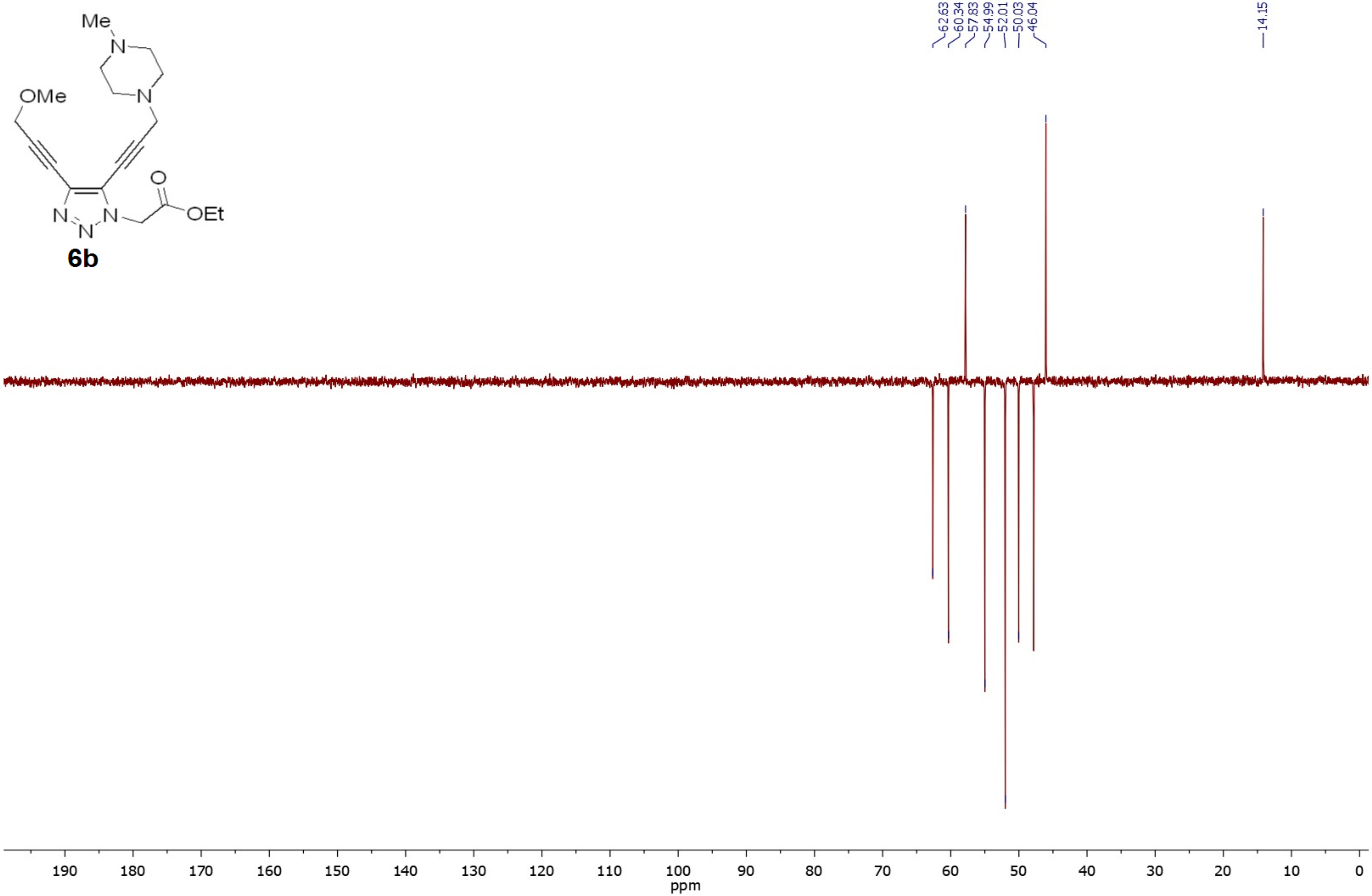


6b

Me
N
N
OMe
O
OEt
N
N
N
7.26 CDCl3
5.11
4.35
4.27
4.25
4.23
4.21
3.60
3.44
3.43
2.63
2.62
2.60
2.46
2.46
2.27
1.27
1.26
1.24
1.84
1.86
1.85
1.86
2.82
3.78
3.88
2.73
2.75
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm

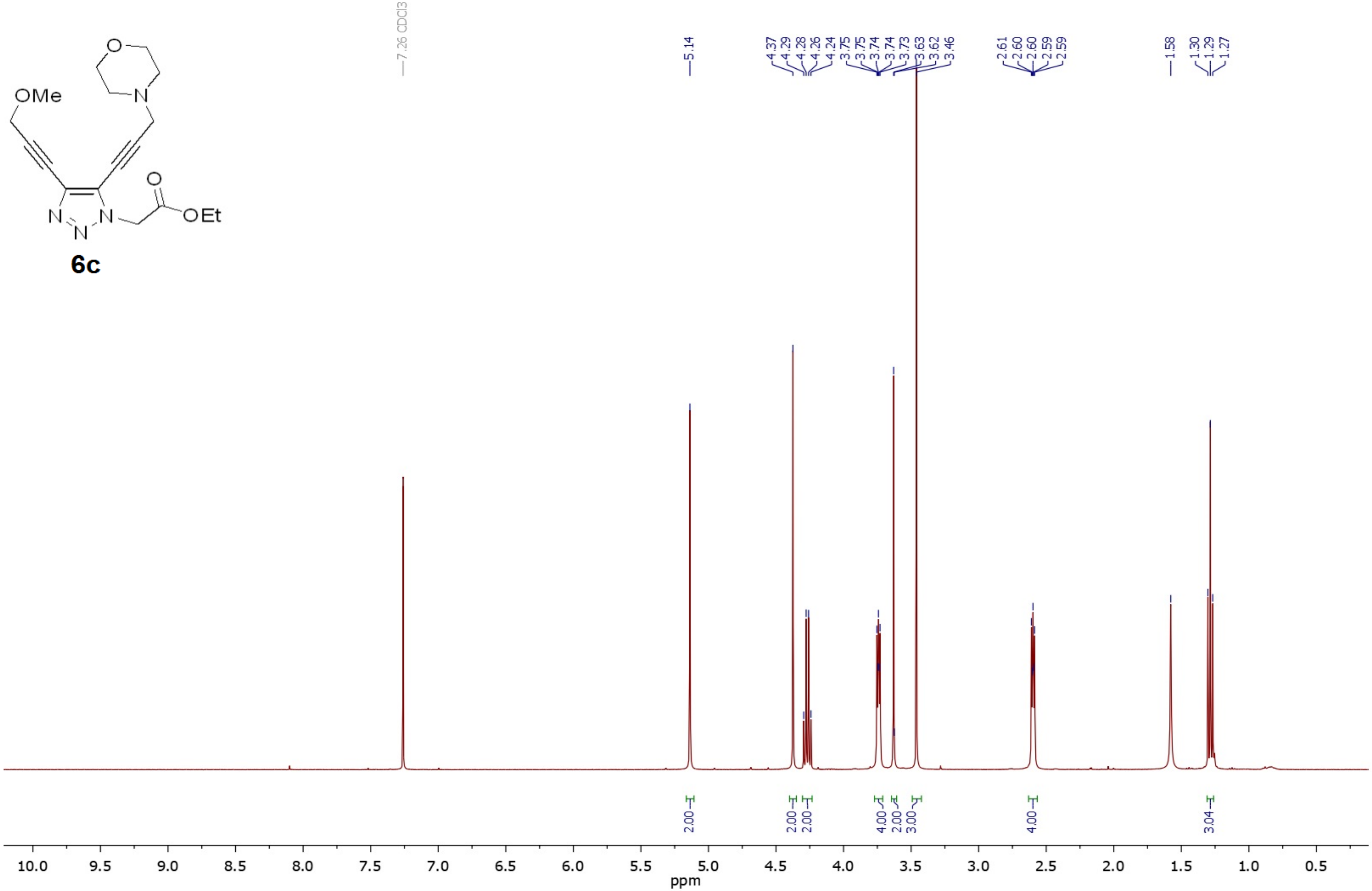

165.39
133.35
124.86
100.09
91.60
77.16 CDCl3
75.29
69.35
62.63
60.34
57.83
55.00
52.01
50.03
47.83
46.04
14.15
Me
N
N
OMe
O
OEt
N
N
N
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

6b



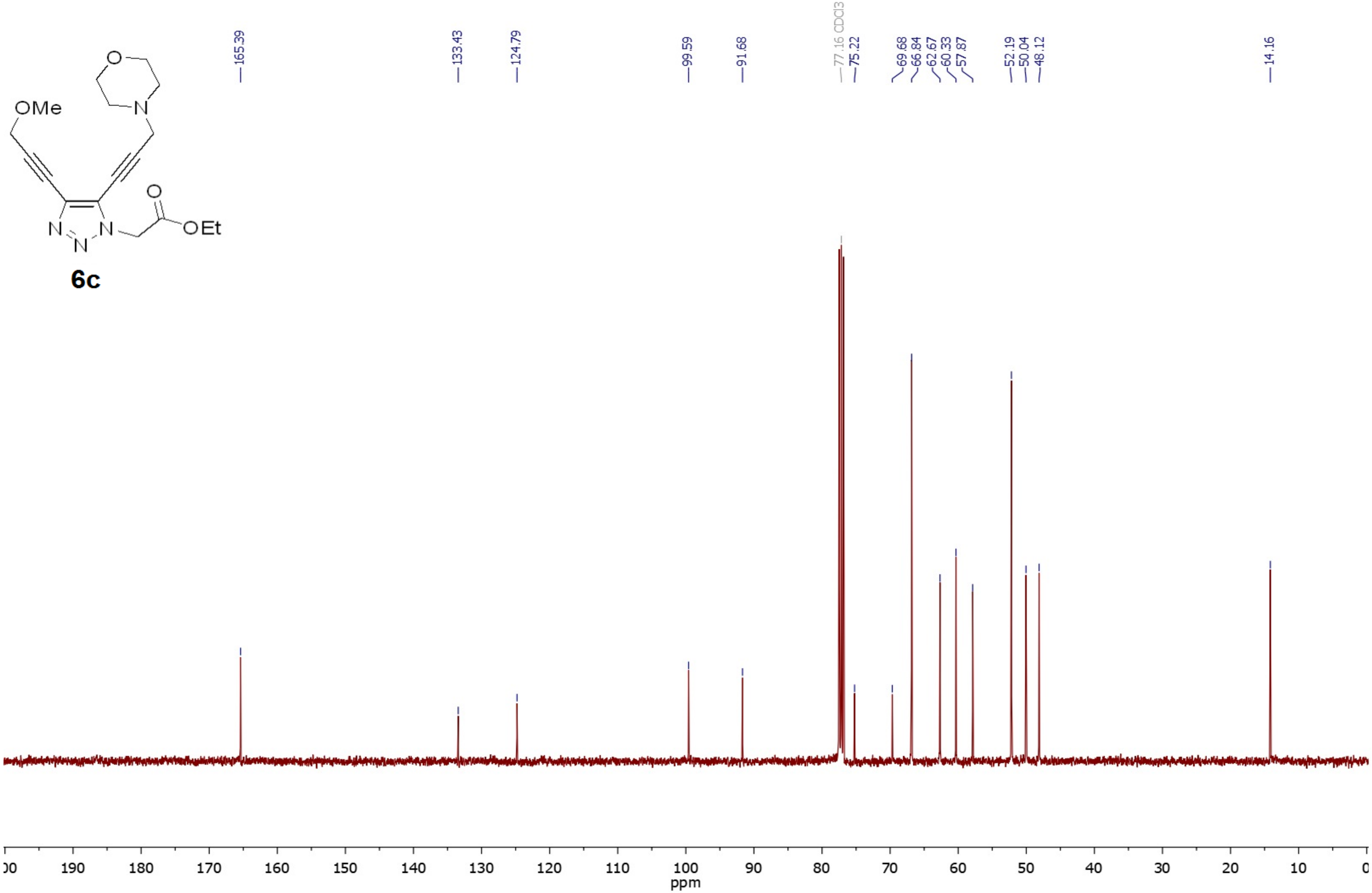
6b

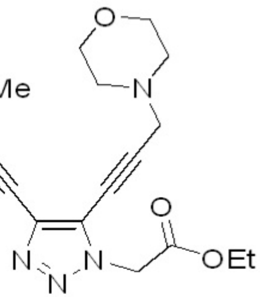
62.63
60.34
57.83
54.99
52.01
50.03
46.04
14.15
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


OMe
O
N
O
OEt
N
N
N

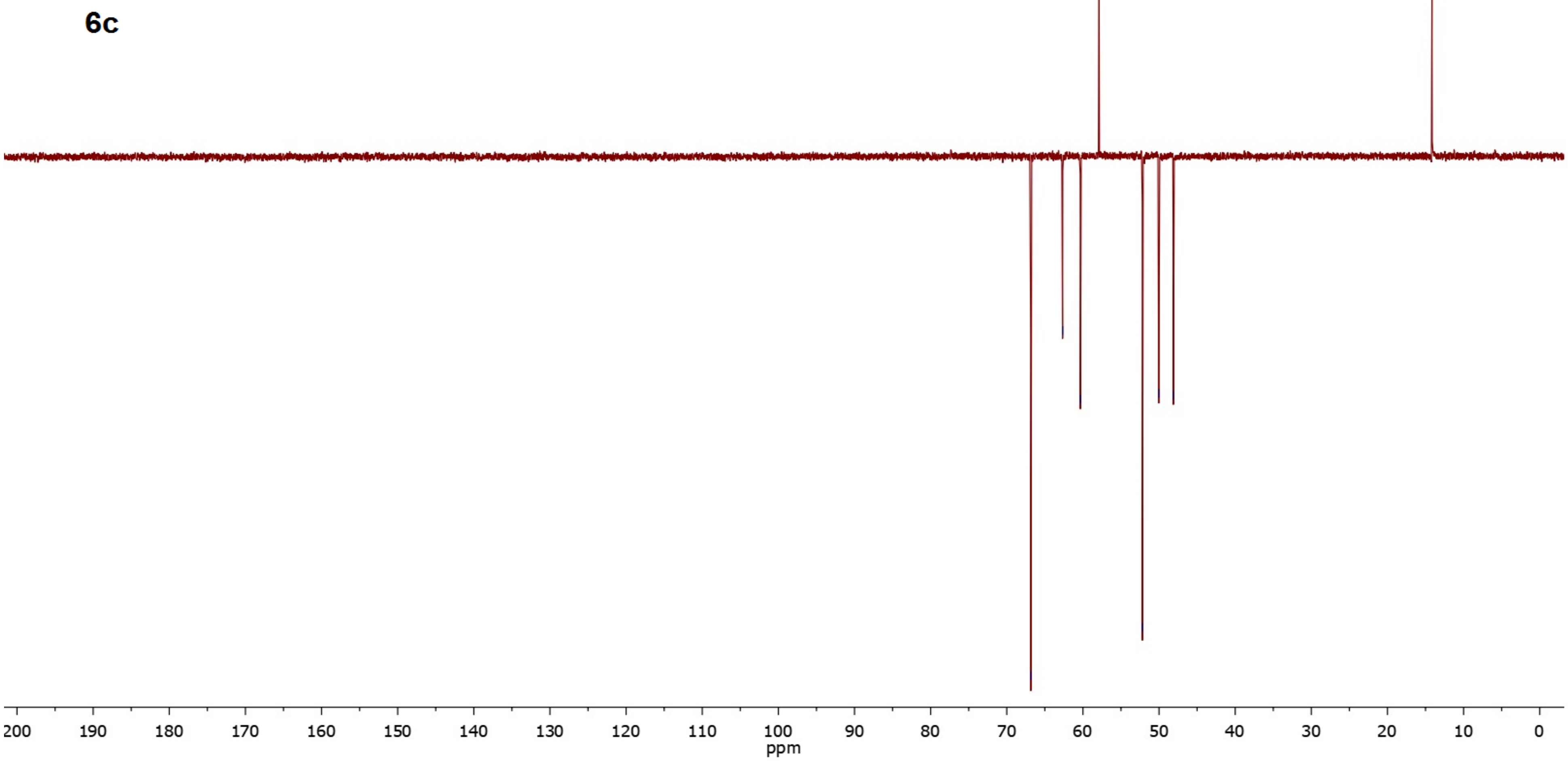
6c

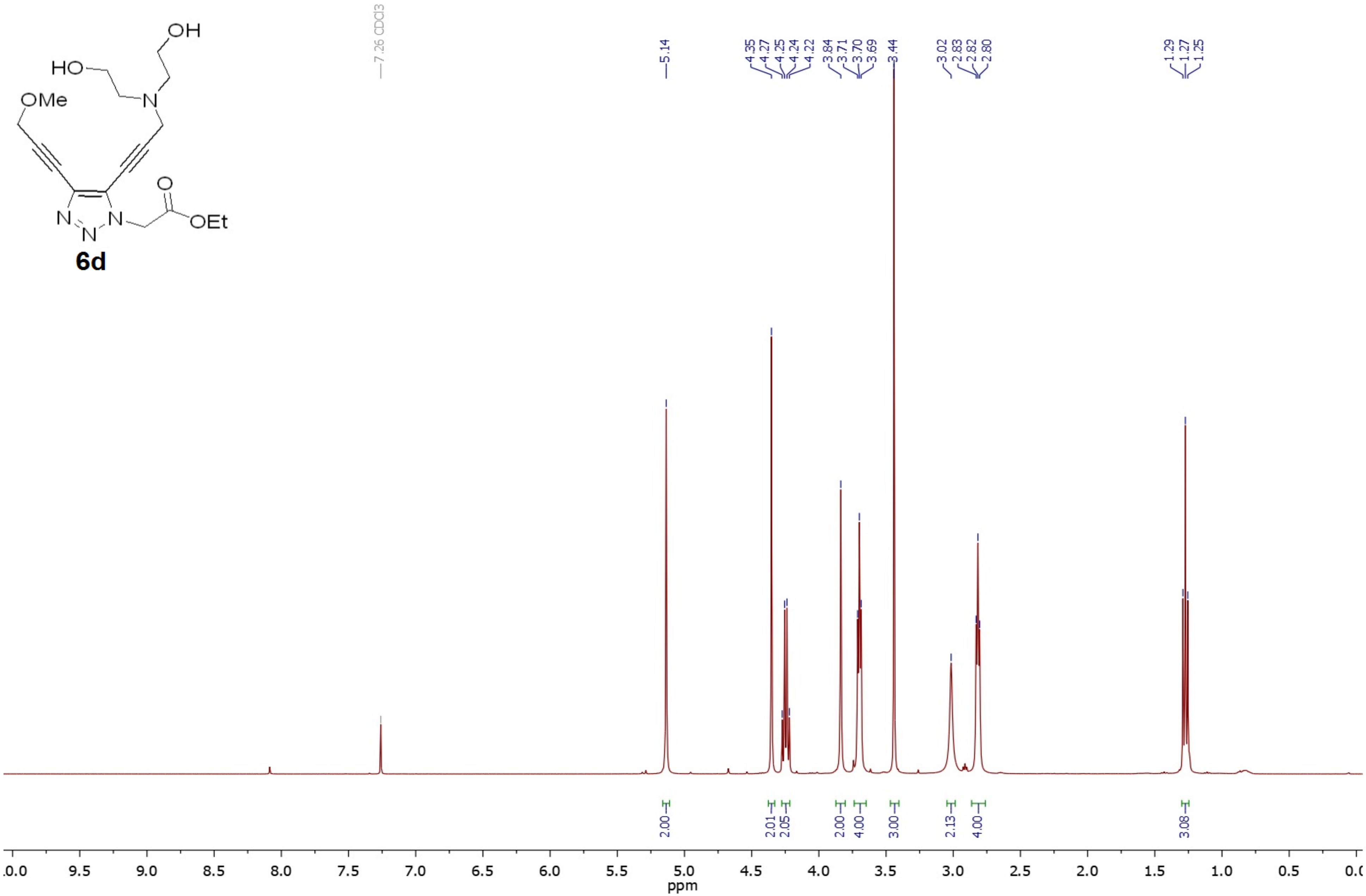
7.26 CDCl3
5.14
4.37
4.29
4.28
4.26
4.24
3.75
3.75
3.74
3.74
3.73
3.63
3.62
3.46
2.61
2.60
2.60
2.59
2.59
1.58
1.30
1.29
1.27
2.00
2.00
2.00
4.00
2.00
3.00
4.00
3.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


OMe
O
N
O
N
N
N
OEt
6c
165.39
133.43
124.79
99.59
91.68
77.16 CDCl3
75.22
69.68
66.84
62.67
60.33
57.87
52.19
50.04
48.12
14.16
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

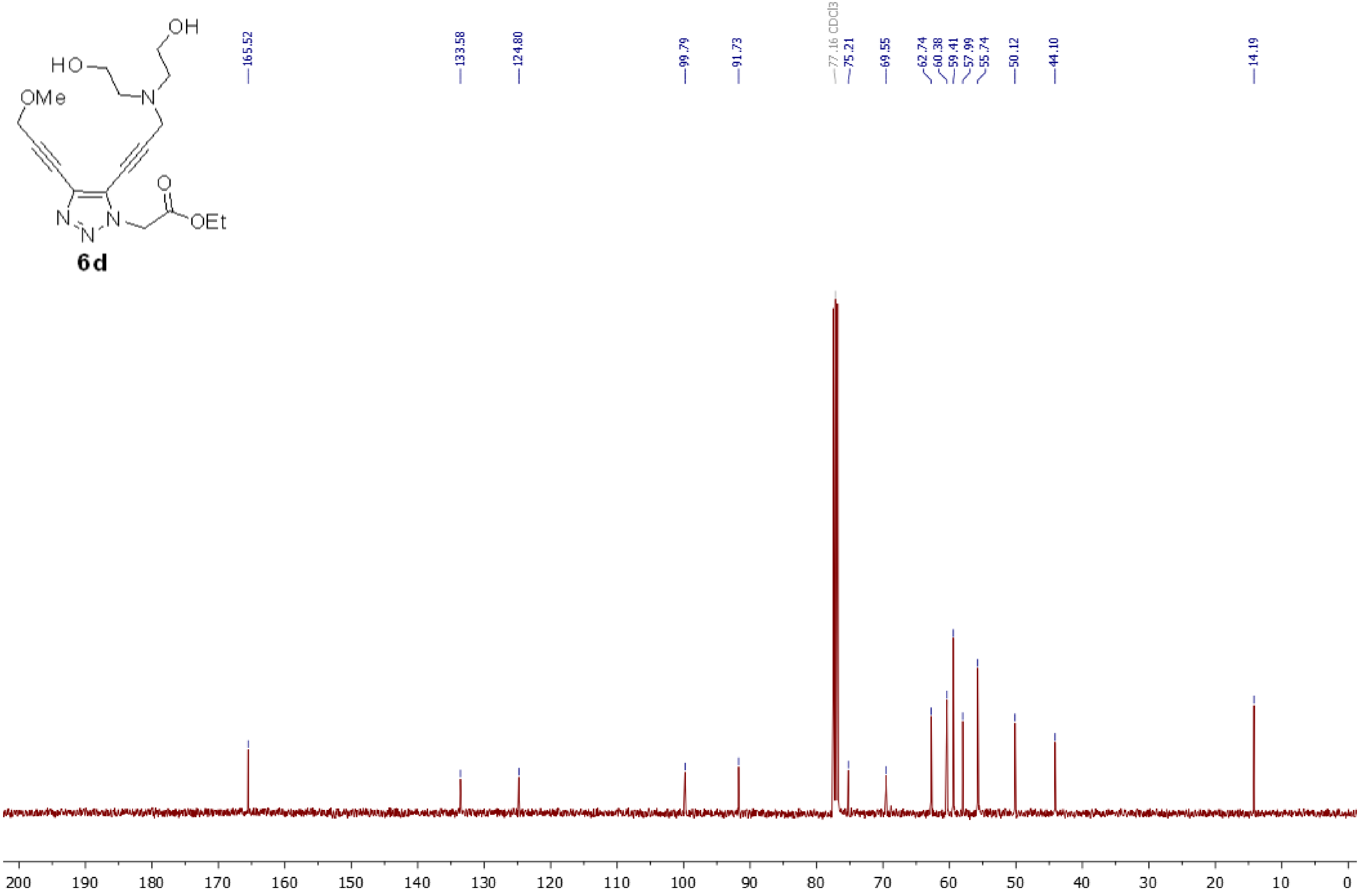


6c

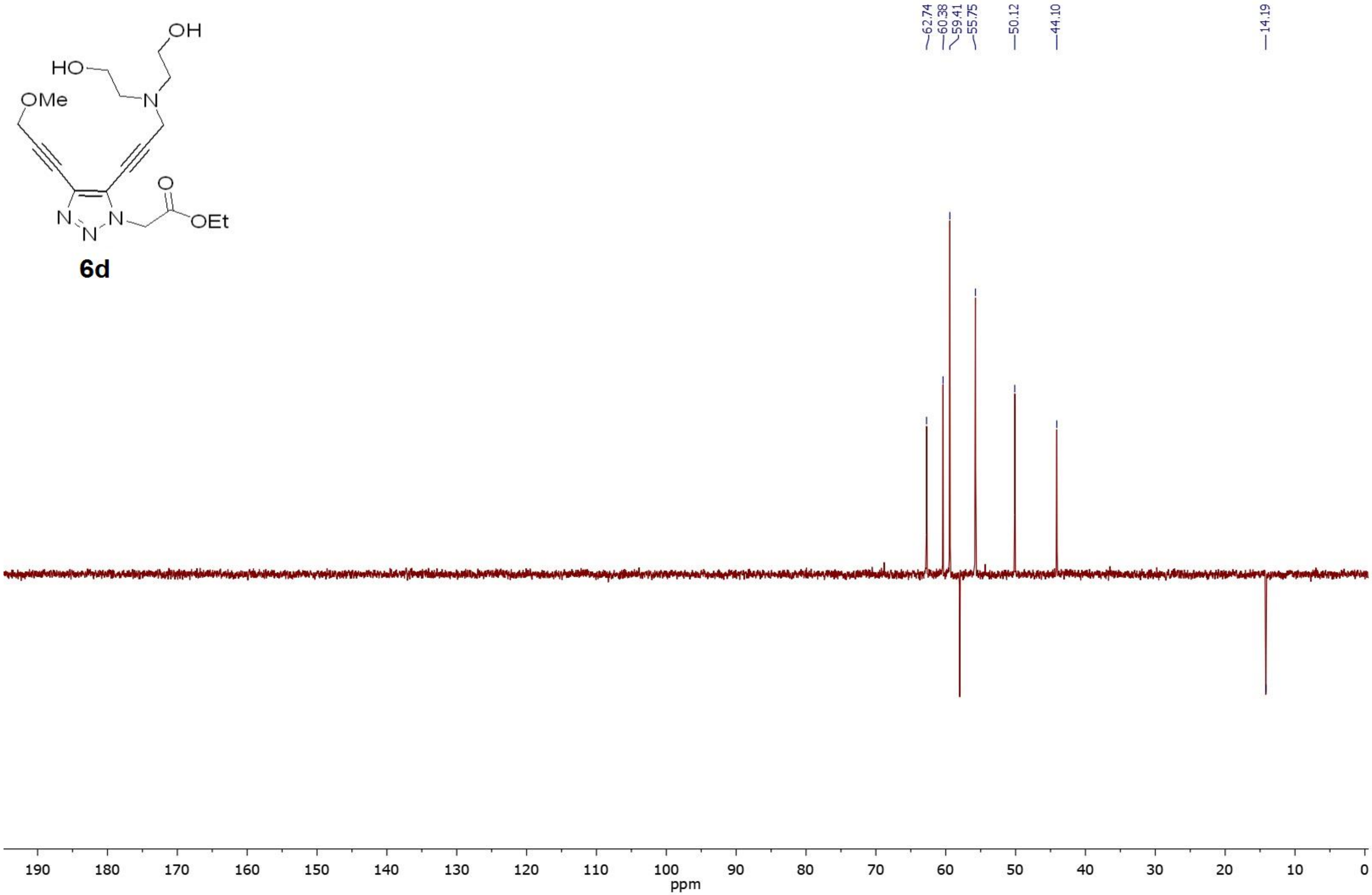

66.84
62.67
60.33
57.87
52.19
50.04
48.12
14.16
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

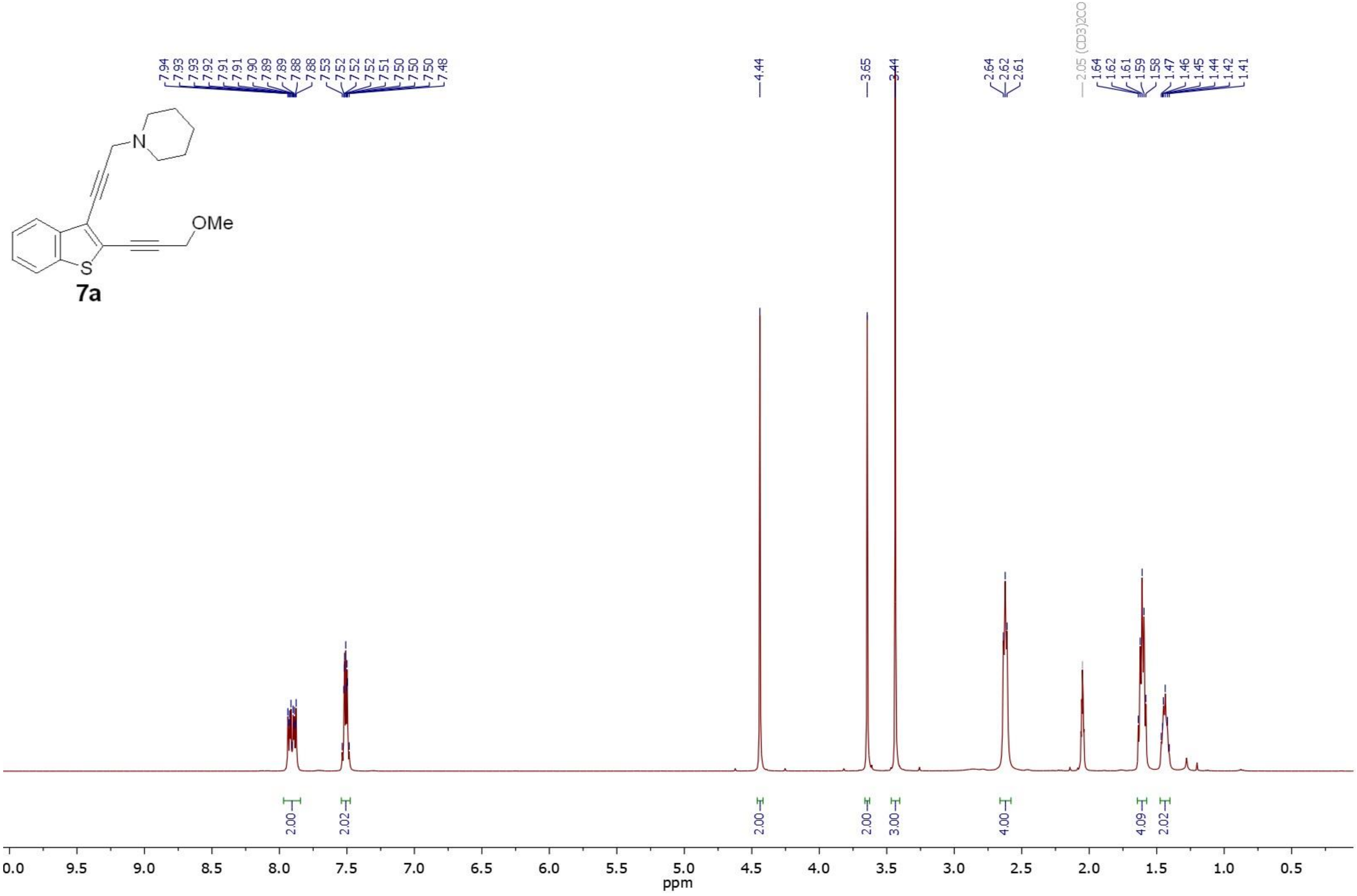

OH
HO
N
OMe
O
N
N
N
OEt
7.26 CDCl3
5.14
4.35
4.27
4.25
4.24
4.22
3.84
3.71
3.70
3.69
3.44
3.02
2.83
2.82
2.80
1.29
1.27
1.25
2.00
2.01
2.05
2.00
4.00
3.00
2.13
4.00
3.08
.0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.(
ppm

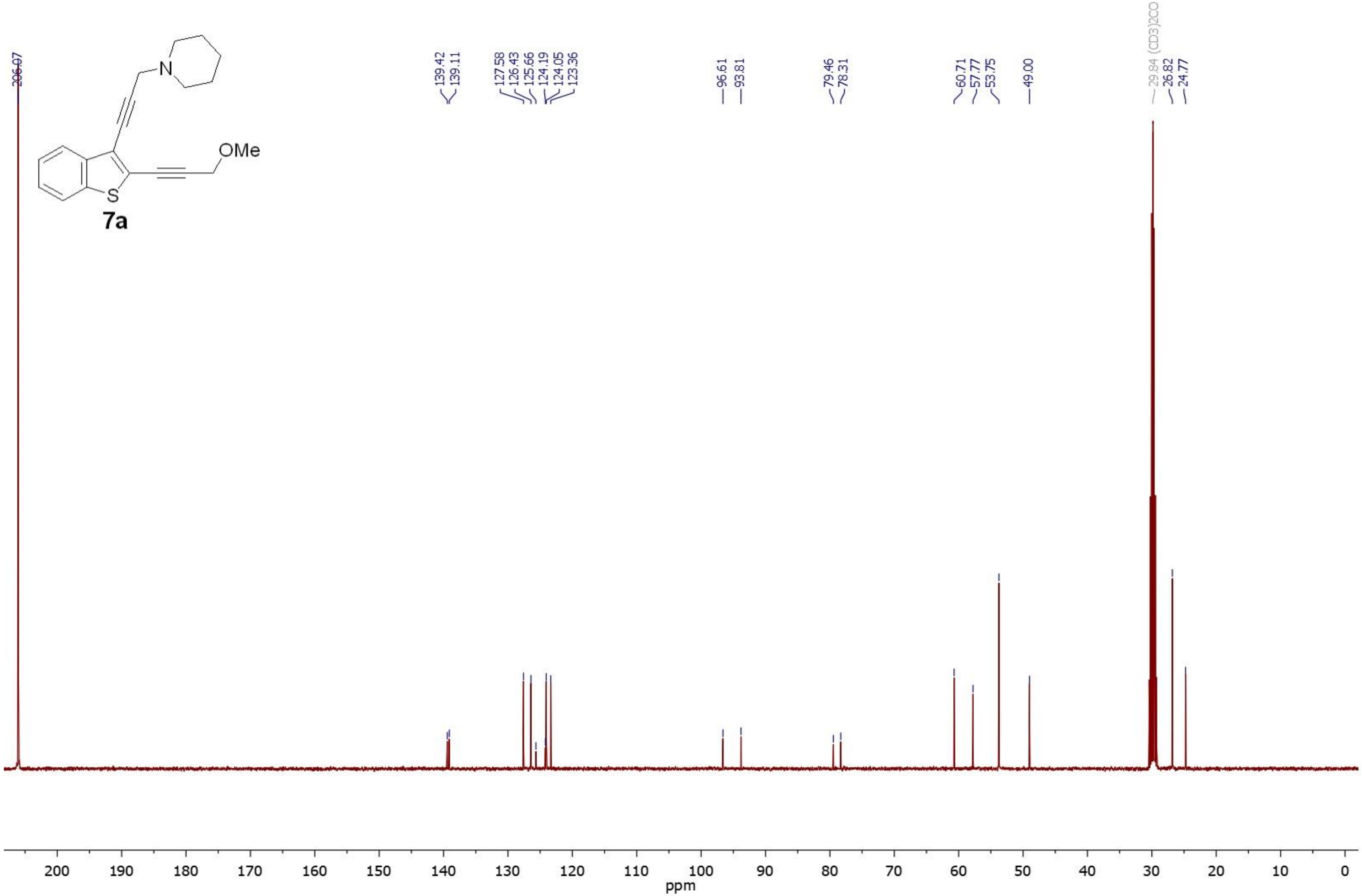
6d

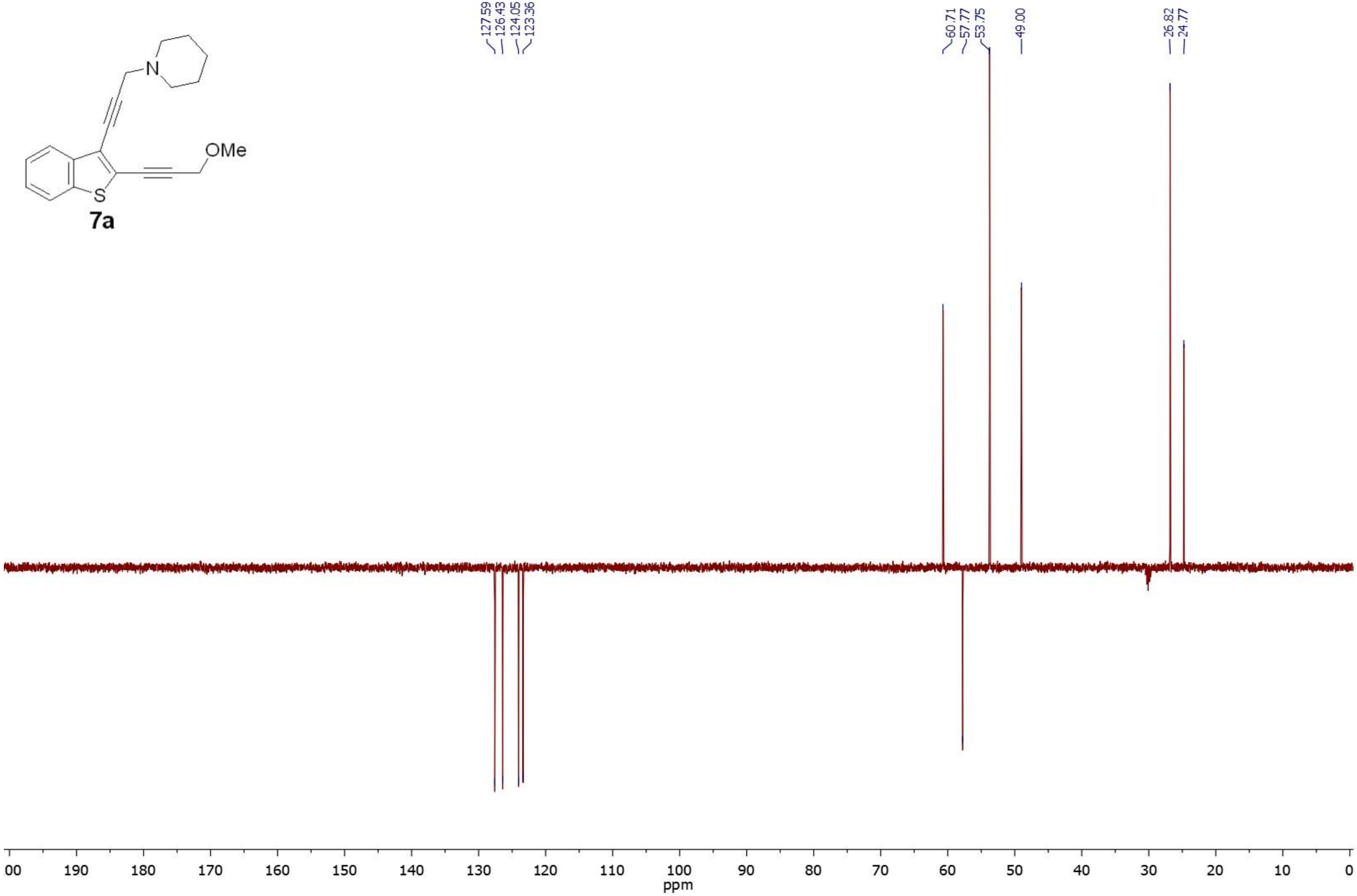

6d

OH
HO
N
OMe
O
OEt
N
N
N
165.52
133.58
124.80
99.79
91.73
77.16 CDCl3
75.21
69.55
62.74
60.38
59.41
57.99
55.74
50.12
44.10
14.19
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

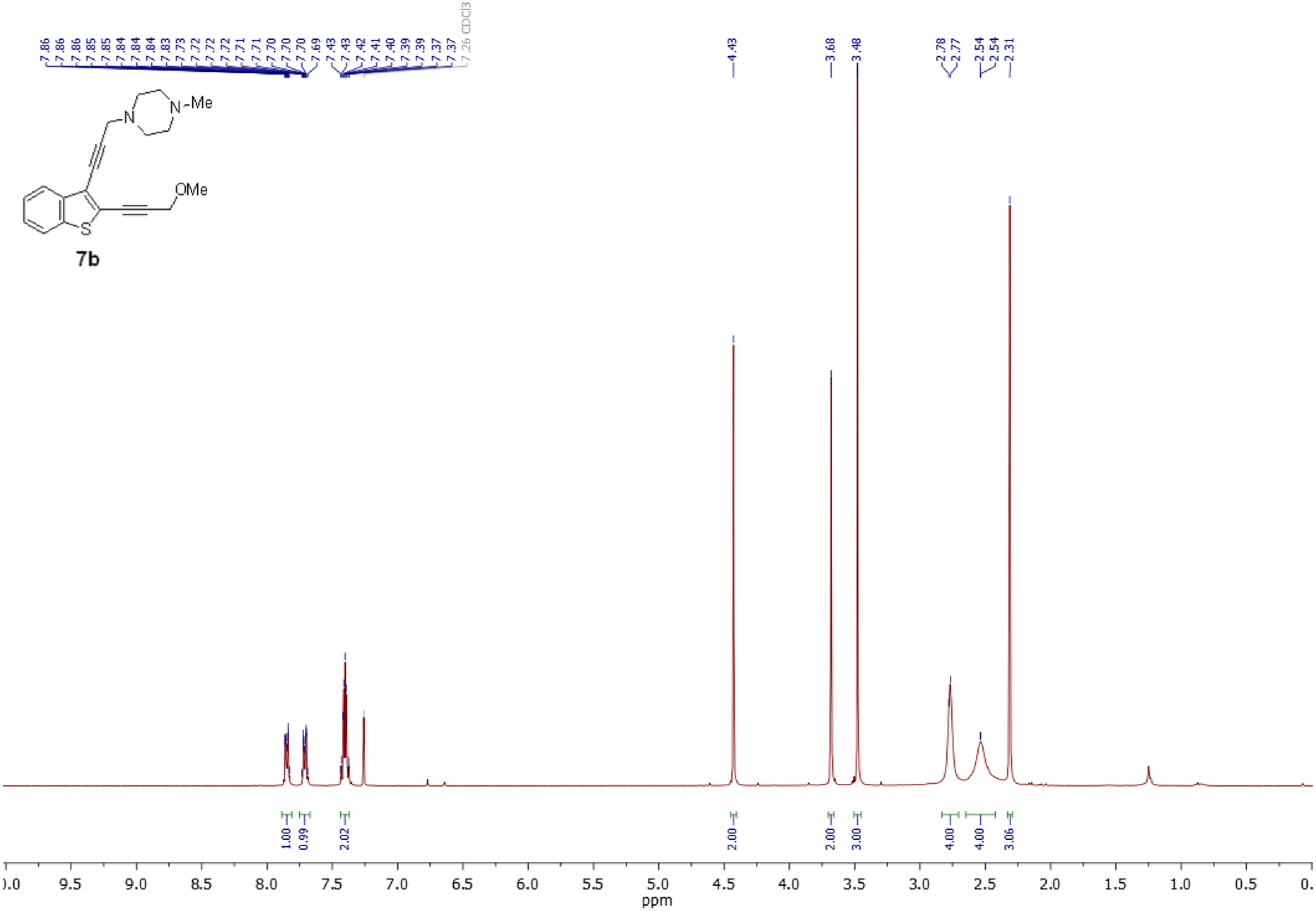

OH
HO
OMe
N
O
N
N
N
OEt
6d
62.74
60.38
59.41
55.75
50.12
44.10
14.19
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


7.94
7.93
7.93
7.92
7.91
7.91
7.90
7.89
7.89
7.88
7.88
7.53
7.52
7.52
7.52
7.51
7.50
7.50
7.50
7.48
4.44
3.65
3.44
2.64
2.62
2.61
2.05 (CD3)2CO
1.64
1.62
1.61
1.59
1.58
1.47
1.46
1.45
1.44
1.42
1.41
N
OMe
S
7a
2.00
2.02
2.00
2.00
3.00
4.00
4.09
2.02
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
ppm


206.07
139.42
139.11
127.58
126.43
125.66
124.19
124.05
123.36
96.61
93.81
79.46
78.31
60.71
57.77
53.75
49.00
29.84 (CD3)2CO
26.82
24.77
N
OMe
S
7a
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


N
OMe
S
127.59
126.43
124.05
123.36
60.71
57.77
53.75
49.00
26.82
24.77
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

7a


7.86
7.86
7.86
7.85
7.85
7.84
7.84
7.84
7.83
7.73
7.72
7.72
7.72
7.71
7.71
7.70
7.70
7.70
7.69
7.43
7.43
7.42
7.41
7.40
7.39
7.39
7.37
7.37
7.26 CDCl3
4.43
3.68
3.48
2.78
2.77
2.54
2.54
2.31
N
N
-Me
OMe
S
7b
1.00
0.99
2.02
2.00
2.00
3.00
4.00
4.00
3.06
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
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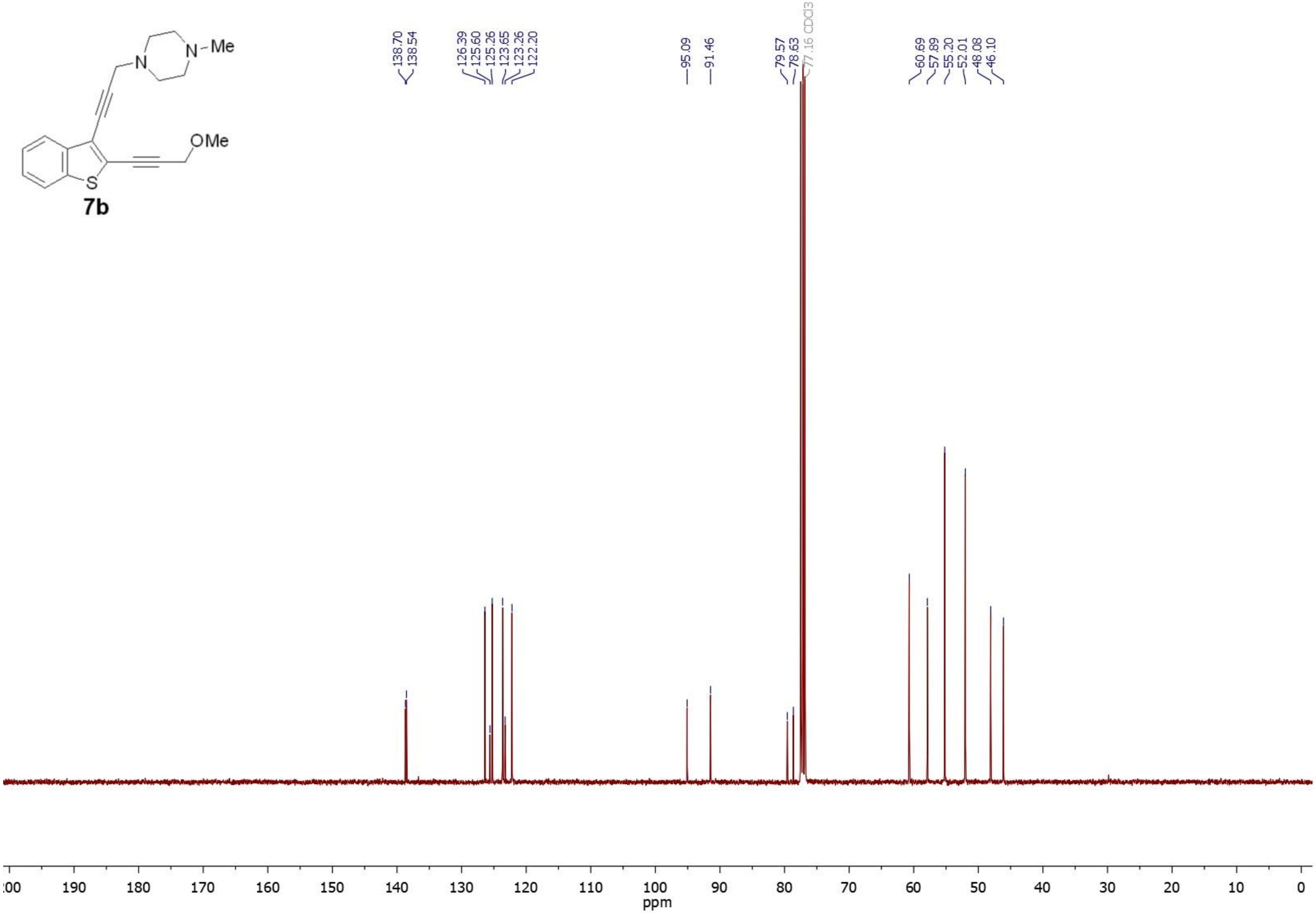
ppm



7b

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Me
OMe
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125.26
123.65
123.26
122.20
95.09
91.46
79.57
78.63
77.16 CDCl3
60.69
57.89
55.20
52.01
48.08
46.10
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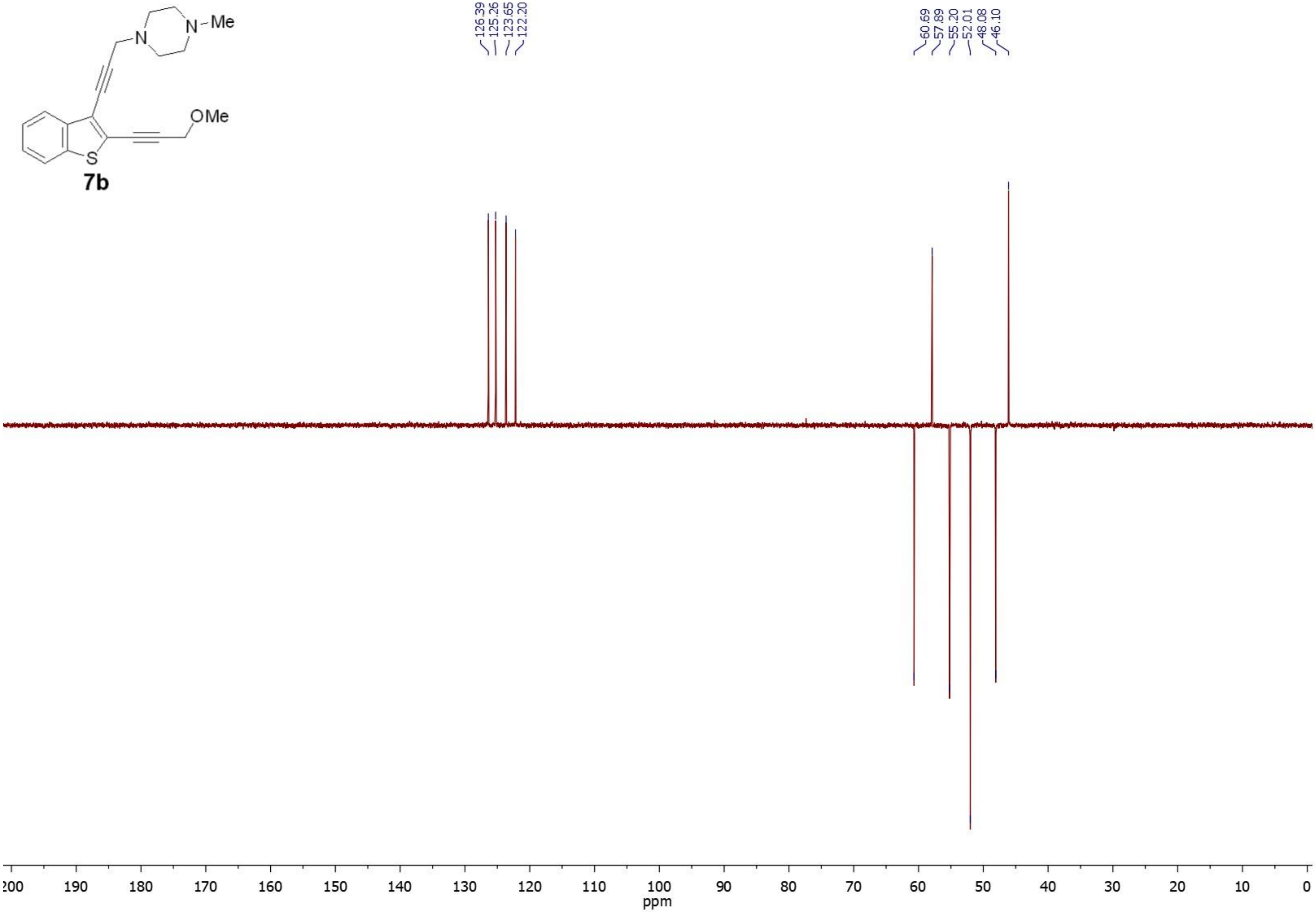
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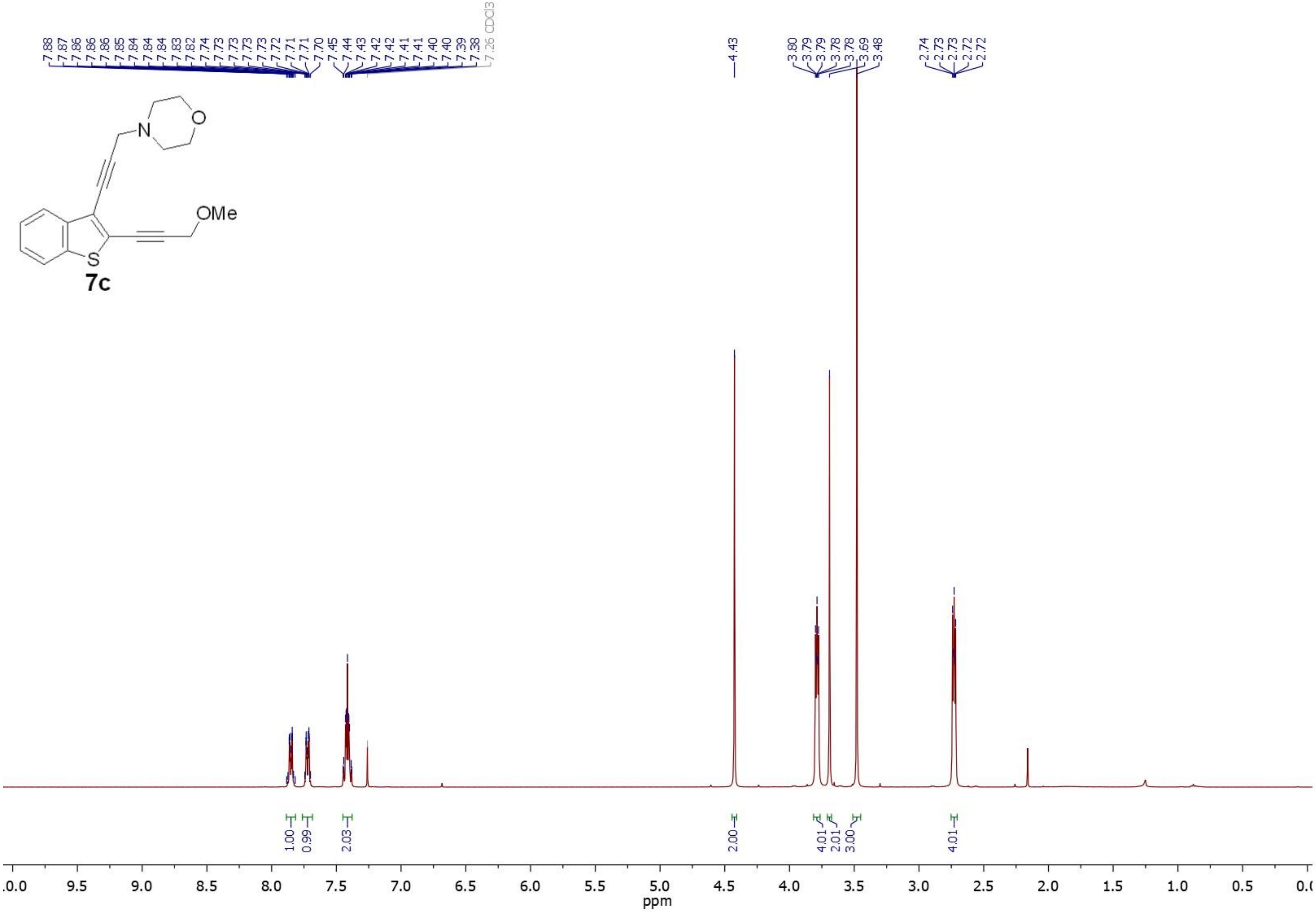
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7.43
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7.41
7.40
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7.38
7.26 CDCl3
4.43
3.80
3.79
3.79
3.78
3.78
3.69
3.48
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2.73
2.72
2.72
N
O
OMe
S
7c
1.00
0.99
2.03
2.00
4.01
2.01
3.00
4.01
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9.5
9.0
8.5
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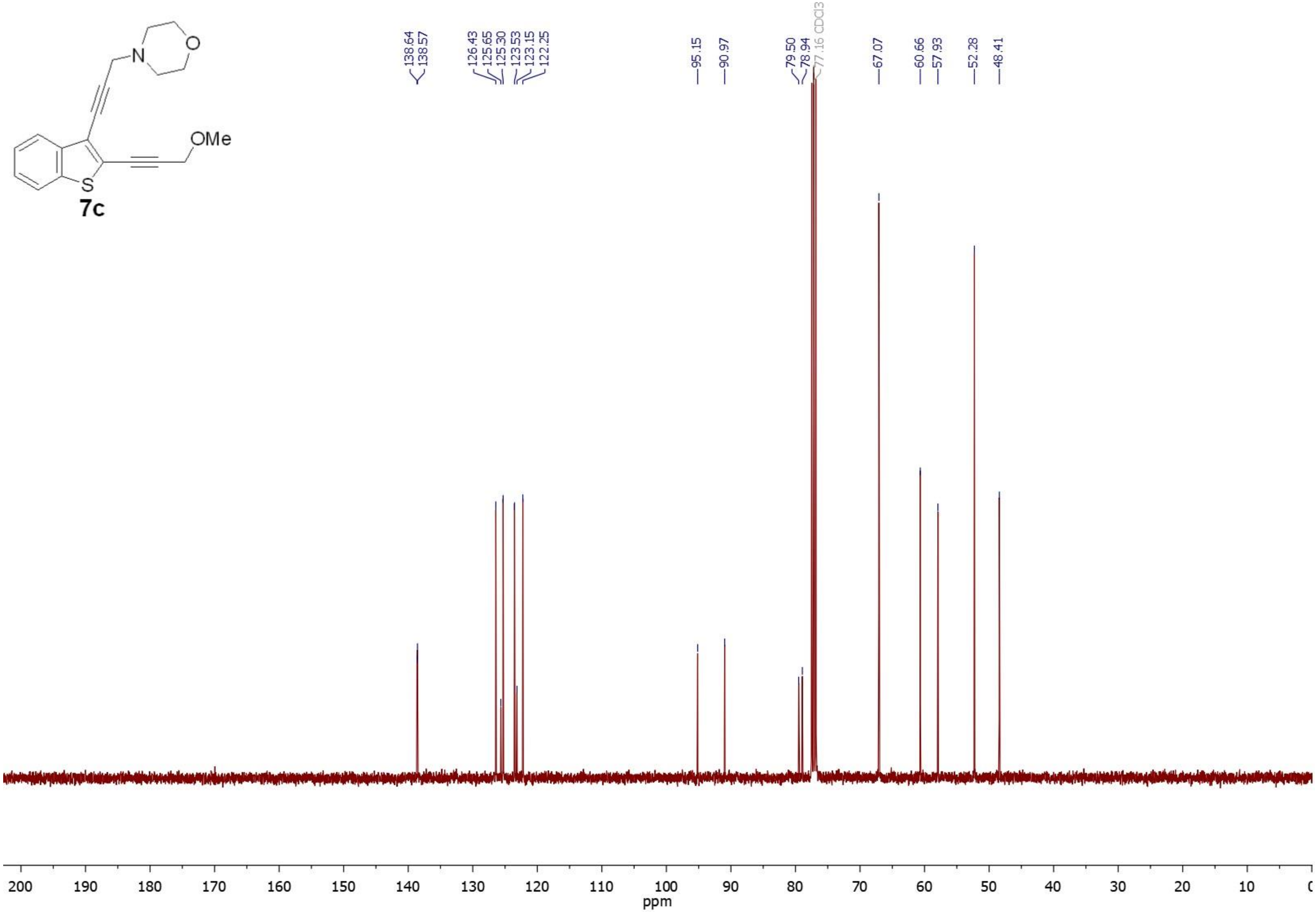
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200
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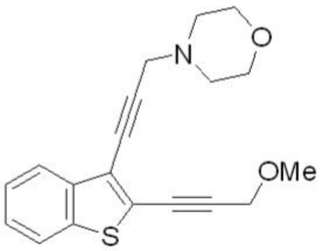
OMe
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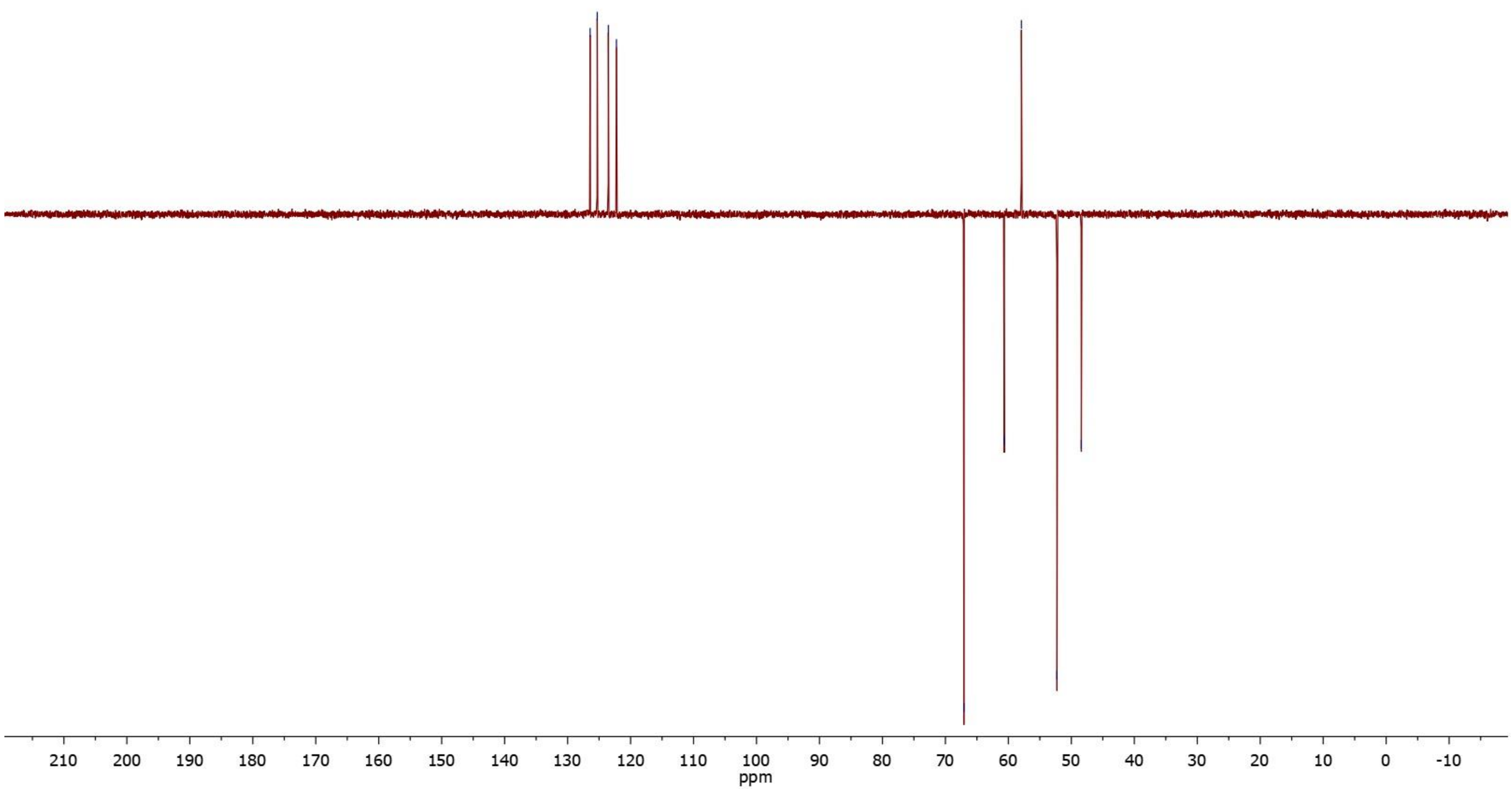
S

7c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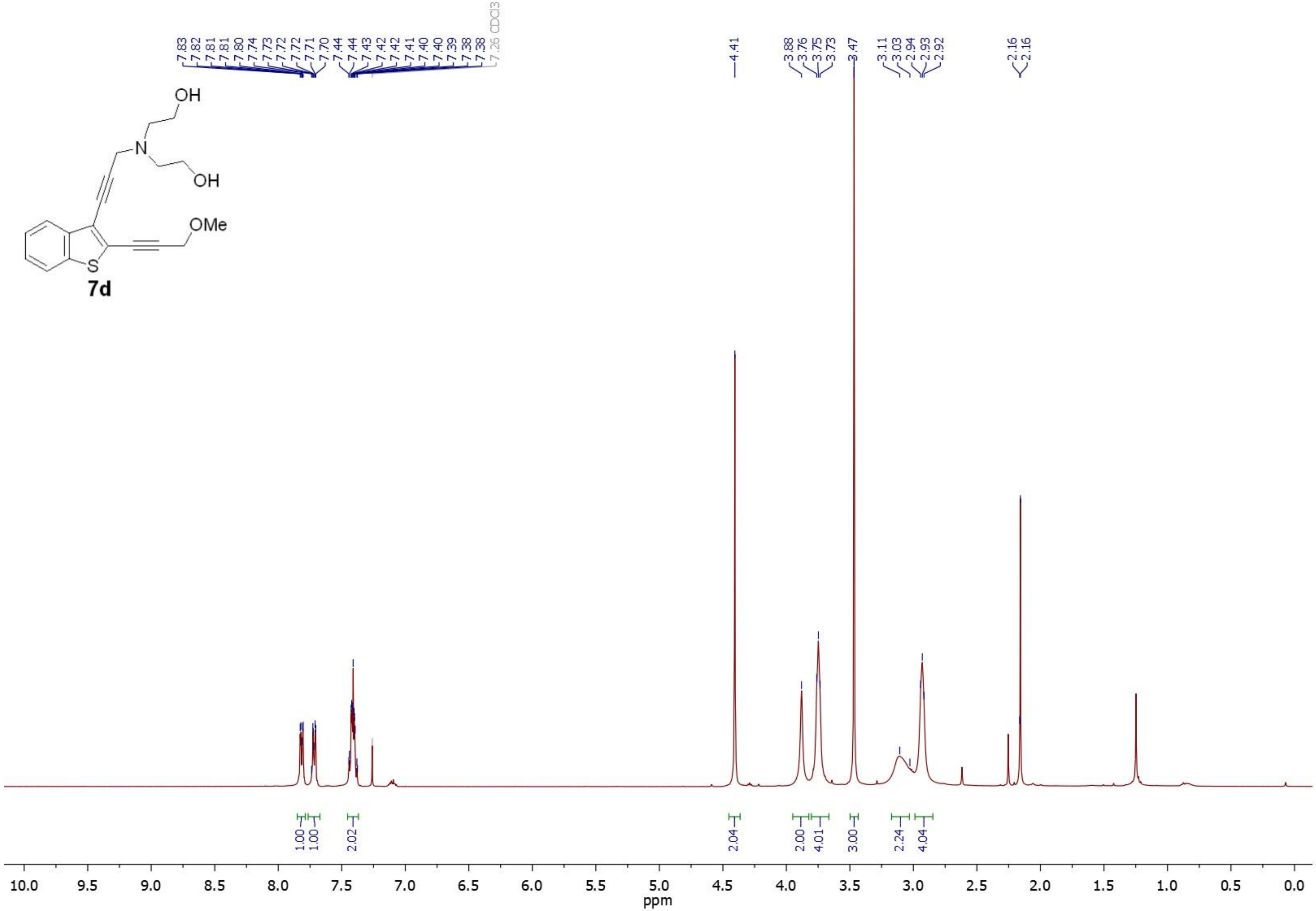
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7.44
7.43
7.42
7.42
7.41
7.40
7.40
7.39
7.38
7.38
7.26 CDCl3
4.41
3.88
3.76
3.75
3.73
3.47
3.11
3.03
2.94
2.93
2.92
2.16
2.16
OH
N
OH
OMe
S
7d
1.00
1.00
2.02
2.04
2.00
4.01
3.00
2.24
4.04
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
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4.0
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3.0
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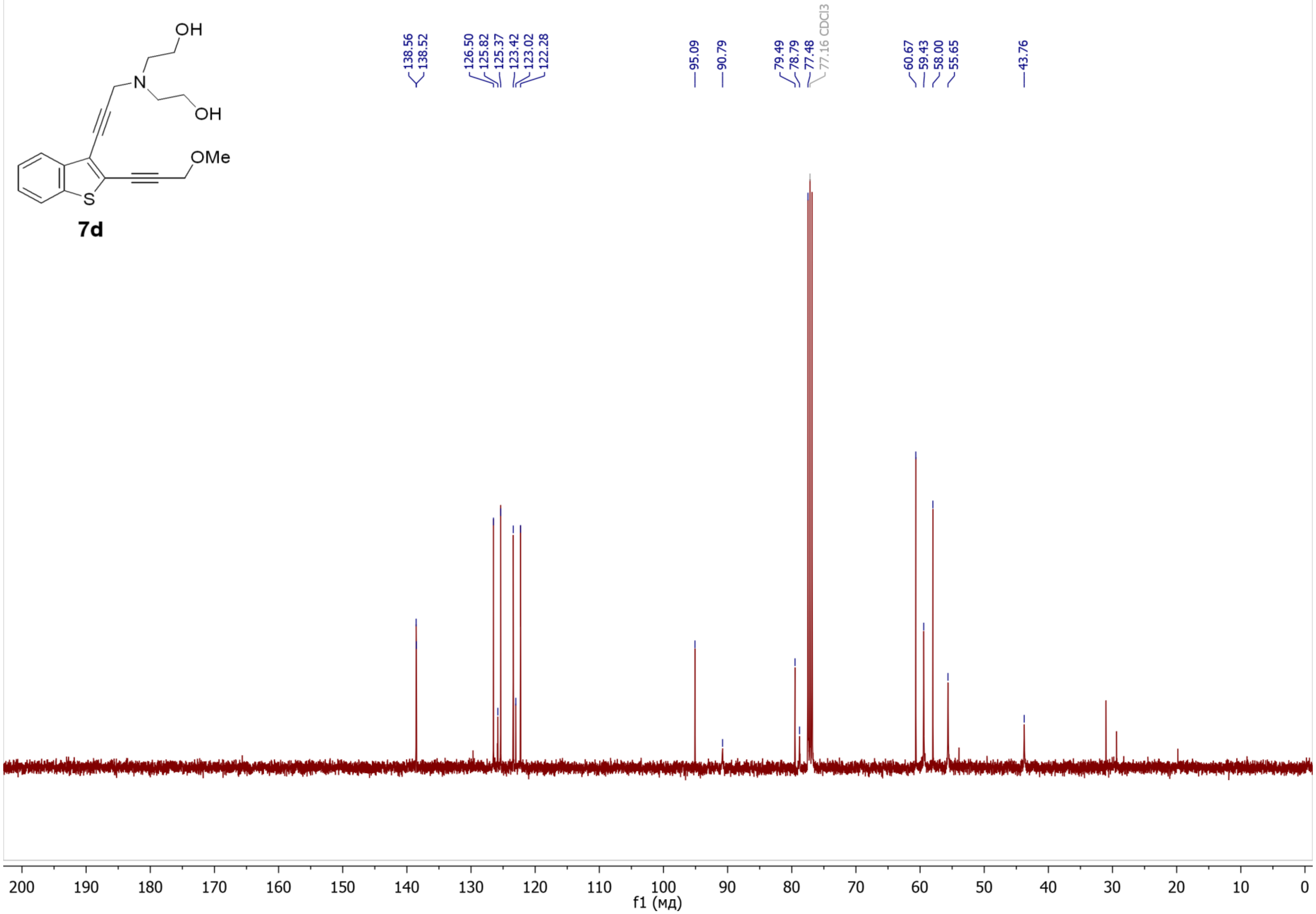
2.0
1.5
1.0
0.5
0.0
ppm


OH
N
OH
OMe
S
7d
138.56
138.52
126.50
125.82
125.37
123.42
123.02
122.28
95.09
90.79
79.49
78.79
77.48
77.16 CDCl3
60.67
59.43
58.00
55.65
43.76
200
190
180
170
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120
110
100
90
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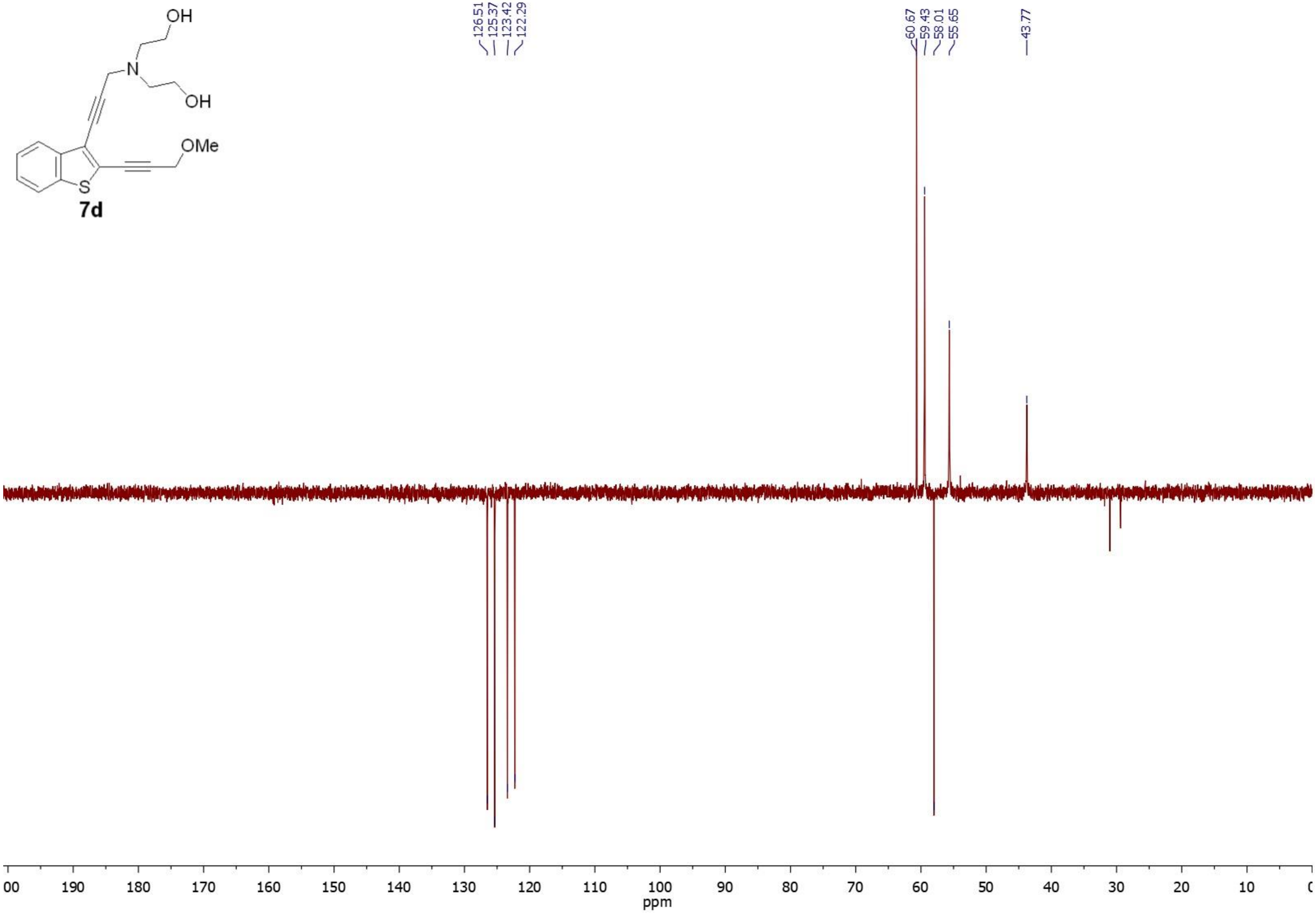
0
f1 (мд)


7d

OH
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OH
OMe
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59.43
58.01
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190
180
170
160
150
140
130
120
110
100
ppm
90
80
70
60
50
40
30
20
10
(