Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information

TfOH-mediated [2+2+2] Cycloadditions of Ynamides with Two Discrete Nitriles: Access to 4-Aminopyrimidine Derivatives

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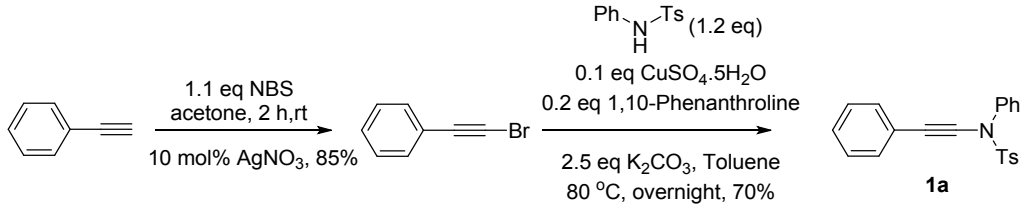
1 General Information

Unless otherwise mentioned, all reactions were performed in flame-dried glassware under air. Solvents were distilled prior to use. Reagents were used as purchased from commercial available unless otherwise noted. Chromatographic separations were performed using Kangbino 48-75 Å SiO_2. ^1H and ^{13}C NMR spectra were obtained on 500 MHz or 600 MHz spectrometers using $CDCl_3$ with TMS or residual solvent as standard unless otherwise noted. Melting points were determined using a melting point apparatus and were uncorrected/calibrated. TLC analysis was performed using Kangbino glass-backed plates (60 Å, 250 μm) and visualized using UV and Iodine stains. Low-resolution mass spectra were obtained using an Agilent 1100 series LS/MSD. All spectral data obtained for new compounds are reported here.

Experimental Section

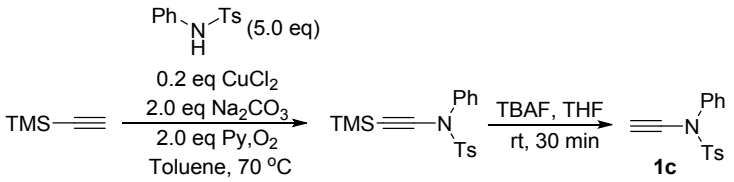
General Procedure 1 for the Synthesis of ynamides (1a, b, d –1n)



To a solution of phenylacetylene (1.00 g, 9.80 mmol) in acetone (100 mL) was added NBS (1.92 g, 10.78 mmol) and $AgNO_3$ (0.17 g, 0.98 mmol). The resulting solution was stirred under nitrogen at room temperature for 4 hours. After removing excess acetone the reaction was quenched with water, and the organic layer was extracted with EtOAc three times, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was eluted through a shout silica column (petroleum ether) to obtain the bromoalkyne (1.50 g, 85%).

To a dried flask was added 4-methyl-N-phenylbenzenesulfonamide (1.20 g, 4.85 mmol), $CuSO_4 \cdot 5H_2O$ (100 mg, 0.40 mmol), 1,10-phenanthroline (145 mg, 0.81 mmol) and K_2CO_3 (1.40 mg, 10.01 mmol), bromoalkyne (730 mg, 4.04 mmol) and this mixture was subsequently treated with anhydrous toluene (100 mL) and the bromoalkyne. The flask was charged with nitrogen, and the solution was heated at 80°C overnight. After completion, the crude reaction mixture was cooled to room temperature, filtered through CeliteTM, and concentrated in vacuo. Purification of the crude residue using silica gel flash column chromatography yielded the pure ynamide **1a** as white solid (980 mg, 57%).

General Procedure 1' for the Synthesis of ynamides (1c)



$CuCl_2$ (0.35g, 2.05 mmol), 4-methyl-N-phenylbenzenesulfonamide (12.60 g, 51.33 mmol), Na_2CO_3 (2.15 g, 20.30 mmol) were added to a flame-dried flask. The flask was purged with oxygen for 15 min and a solution of pyridine (1.61 ml, 20.30 mmol) in dry toluene (0.2 M) was heated at 70 °C. After 15 min, a solution of trimethylsilylacetylene in dry toluene (0.2 M) was added over 4 h. The mixture was allowed to stir at 70 °C for another 4 h and was then cooled to rt. The reaction mixture was concentrated under reduced pressure and the residue was purified by flash chromatography to obtain the corresponding product (1.89 g, 54%).

To a solution of the corresponding ynamide (1.89 g, 5.51 mmol) in THF (50 mL) was added the solution of TBAF (2.88 g, 11.02 mmol) in THF (30 mL) slowly at rt. Then the resulting solution was stirred at room temperature for 30 min. The reaction mixture was concentrated and the residue was purified by flash chromatography to obtained the ynamide **1c** (1.20 g, 45% over two steps).

4-methyl-*N*-phenyl-*N*-(phenylethynyl)benzenesulfonamide (1a)

Following the general procedure 1: white solid, mp: 103-105 °C, 70%; R_f = 0.4 (5% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 2H), 7.41 - 7.28 (m, 12H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.03, 138.94, 132.88, 131.47, 129.54, 129.13, 128.32, 128.29, 128.00, 126.32, 122.62, 82.98, 70.48, 21.76; mass spectrum (ESI): m/e (% relative intensity) 370.1 (100) $(M+Na)^+$; HRMS calcd for $C_{21}H_{17}NO_2SNa$ $(M+Na)^+$ 370.0878, found 370.0878.

***N*-(cyclopropylethynyl)-*N*,4-dimethylbenzenesulfonamide (1b)**

Following the general procedure 1: white solid, mp: 48-50 °C, 47%; R_f = 0.45 (30% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.4 Hz, 2H), 7.36 (d, *J* = 7.8 Hz, 2H), 2.99 (s, 3H), 2.46 (s, 3H), 1.31 - 1.24 (m, 1H), 0.82 - 0.73 (m, 2H), 0.66 - 0.58 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.33, 134.08, 130.47, 128.66, 73.79, 71.28, 40.22, 22.50, 9.55, 0.00; mass spectrum (ESI): m/e (% relative intensity) 272.1 (100) $(M+Na)^+$.

***N*-ethynyl-4-methyl-*N*-phenylbenzenesulfonamide (1c)**

Following the general procedure 1‘: pale yellow solid, mp: 69-70 °C, 45%; R_f = 0.45 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.4 Hz, 2H), 7.35 - 7.23 (m, 7H), 2.84 (s, 1H), 2.45 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.12, 138.23, 132.84, 129.57, 129.16, 128.46, 128.27, 126.32, 76.53, 58.91, 21.76; mass spectrum (ESI): m/e (% relative intensity) 294.1 (100) $(M+Na)^+$.

(*R*)-4-phenyl-3-((triisopropylsilyl)ethynyl)oxazolidin-2-one (1d)

Following the general procedure 1: colorless oil, 46%; R_f = 0.45 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 - 7.38 (m, 3H), 7.37 - 7.33 (m, 2H), 5.06 (dd, *J* = 7.8, 8.4 Hz, 1H), 4.73 (dd, *J* = 8.4, 9.0 Hz, 1H), 4.28 (dd, *J* = 7.8, 9.0 Hz, 1H), 0.90 (s, 21H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.32, 135.79, 129.47, 129.18, 127.17, 91.87, 71.98, 70.56, 62.32, 18.39, 11.05; mass spectrum (ESI): m/e (% relative intensity) 366.2 (100) $(M+Na)^+$.

(*S*)-4-benzyl-3-(phenylethynyl)oxazolidin-2-one (1e)

Following the general procedure 1: white solid, mp: 96-98 °C, 63%; R_f = 0.35 (30% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 - 7.43 (m, 2H), 7.40 - 7.27 (m, 6H), 7.27 - 7.23 (m, 2H), 4.42 - 4.33 (m, 2H), 4.21- 4.14 (m, 1H), 3.33 - 3.26 (m, 1H), 3.06 - 2.98 (m, 1H); ^{13}C NMR (150 MHz,

$CDCl_3$) δ 155.50, 134.20, 131.68, 129.43, 129.10, 128.34, 128.30, 127.59, 122.18, 77.90, 73.33, 67.48, 58.53, 38.04; mass spectrum (ESI): m/e (% relative intensity) 300.1 (100) $(M+Na)^+$.

_N_-(hex-1-yn-1-yl)-_N_,4-dimethylbenzenesulfonamide (1f)

Following the general procedure 1: colorless oil, 35%; R_f = 0.4 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.2 Hz, 2H), 7.35 (d, *J* = 7.8 Hz, 2H), 3.01 (s, 3H), 2.46 (s, 3H), 2.24 (t, *J* = 7.2 Hz, 2H), 1.49 - 1.42 (m, 2H), 1.41 - 1.32 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.44, 133.21, 129.61, 127.84, 74.84, 68.61, 39.39, 30.96, 21.83, 21.64, 18.03, 13.58; mass spectrum (ESI): m/e (% relative intensity) 288.1 (100) $(M+Na)^+$.

(*S*)-4-phenyl-3-(phenylethynyl)oxazolidin-2-one (1g)

Following the general procedure 1: white solid, mp: 144-146 °C, 50%; R_f = 0.4 (30% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.52 - 7.37 (m, 5H), 7.30 - 7.18 (m, 5H), 5.14 (dd, *J* = 7.8, 7.8 Hz, 1H), 4.78 (dd, *J* = 7.8, 7.8 Hz, 1H), 4.31 (dd, *J* = 7.8, 7.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.62, 136.03, 131.49, 129.57, 129.36, 128.18, 128.10, 126.94, 122.11, 78.02, 72.84, 70.81, 62.23; mass spectrum (ESI): m/e (% relative intensity) 286.1 (100) $(M+Na)^+$.

_N_,4-dimethyl-_N_-(phenylethynyl)benzenesulfonamide (1h)

Following the general procedure 1: white solid, mp: 79-81 °C, 49%; R_f = 0.3 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (d, *J* = 7.8 Hz, 2H), 7.40 - 7.33 (m, 4H), 7.32 - 7.26 (m, 3H), 3.15 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.87, 133.16, 131.43, 129.85, 128.30, 127.88, 122.68, 83.93, 69.02, 39.35, 21.71; mass spectrum (ESI): m/e (% relative intensity) 308.1 (100) $(M+Na)^+$.

3-(phenylethynyl)oxazolidin-2-one (1i)

Following the general procedure 1: white solid, mp: 84-85 °C, 62%; R_f = 0.25 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.47 - 7.41 (m, 2H), 7.33 - 7.28 (m, 3H), 4.48 (t, *J* = 7.8 Hz, 2H), 4.01 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.91, 131.59, 128.32, 128.22, 122.17, 78.96, 71.21, 63.05, 47.06; mass spectrum (ESI): m/e (% relative intensity) 210.1 (100) $(M+Na)^+$.

_N_-methyl-_N_-(phenylethynyl)methanesulfonamide (1j)

Following the general procedure 1: white solid, mp: 58-60 °C, 61%; R_f = 0.45 (30% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.45 - 7.38 (m, 2H), 7.33 - 7.28 (m, 3H), 3.30 (s, 3H), 3.13 (m, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 131.55, 128.35, 128.13, 122.34, 82.99, 69.47, 39.26, 36.78; mass spectrum (ESI): m/e (% relative intensity) 232.0 (100) $(M+Na)^+$.

3-(*p*-tolylethynyl)oxazolidin-2-one (1k)

Following the general procedure1: white solid, mp: 124-126 °C, 52%; R_f = 0.3 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.8 Hz, 2H), 7.11 (d, *J* = 7.8 Hz, 2H), 4.48 (t, *J* = 8.4 Hz, 2H), 4.00 (t, *J* = 8.4 Hz, 2H), 2.34 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 155.98, 138.43, 131.64, 129.08, 119.00, 78.25, 71.23, 63.01, 47.10, 21.48; mass spectrum (ESI): m/e (% relative intensity) 224.1 (100) $(M+Na)^+$.

_N_-benzyl-_N_-((4-methoxyphenyl)ethynyl)-4-methylbenzenesulfonamide (1l)

Following the general procedure 1: white solid, mp: 88-90 °C, 15%; R_f = 0.6 (30% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8 Hz, 2H), 7.36 - 7.27 (m, 7H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.77 (d, *J* = 7.8 Hz, 2H), 4.56 (s, 2H), 3.77 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 159.42, 144.54, 134.74, 134.62, 133.19, 129.68, 128.86, 128.49, 128.26, 127.77, 114.73, 113.86, 81.21, 70.95, 55.79, 55.30, 21.67; mass spectrum (ESI): m/e (% relative intensity) 414.1 (100) $(M+Na)^+$.

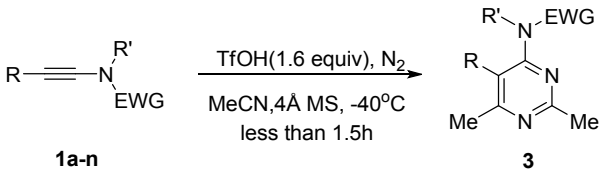
3-((4-fluorophenyl)ethynyl)oxazolidin-2-one (1m)

Following the general procedure 1: white solid, mp: 114-116 °C, 56%; R_f = 0.3 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 - 7.40 (m, 2H), 7.03 - 6.98 (m, 2H), 4.49 (t, *J* = 7.8 Hz, 2H), 4.00 (t, *J* = 7.8 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 163.35 - 161.70 (d, *J* = 247.5 Hz), 155.92, 133.72 - 133.66 (d, *J* = 9.0 Hz), 118.20 - 118.18 (d, *J* = 3.0 Hz), 115.69 - 115.54 (d, *J* = 22.5 Hz), 78.58, 70.16, 63.08, 63.06, 47.00; mass spectrum (ESI): m/e (% relative intensity) 228.0 (100) $(M+Na)^+$.

Ethyl 3-(*N*,4-dimethylphenylsulfonamido)propiolate (1n)

Following the general procedure 1: white solid, mp: 79-80 °C, 43%; R_f = 0.3 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 (d, *J* = 7.8 Hz, 2H), 7.39 (d, *J* = 7.8 Hz, 2H), 4.23 (q, *J* = 7.2 Hz, 2H), 3.17 (s, 3H), 2.47 (s, 3H), 1.31 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.14, 145.70, 133.10, 130.15, 127.87, 83.54, 0 65.95, 61.64, 38.62, 21.73, 14.17; mass spectrum (ESI): m/e (% relative intensity) 304.1 (100) $(M+Na)^+$; m/e calcd for $C_{13}H_{15}NO_4SNa$ $(M+Na)^+$ 304.0619, found 304.0632.

General Procedure A for TfOH-Mediated [2+2+2] Cycloadditions of Ynamides with Acetonitrile (3a–3n).



1a-n **3**

To a suspension of ynamide (0.15 mmol) and 4Å MS (20.0 mg) in dry acetonitrile (2.00 mL) was added TfOH dropwise (21.0 µl, 0.24 mmol) via a syringe pump at -40 °C under nitrogen atmosphere. The reaction was monitored by TLC. when progress appeared to be completed after about 1.5 h at the same temperature, the saturated sodium bicarbonate solution was added to the mixture and the resulting mixture was extracted with EtOAc. The organic layers were washed with sat aq NaCl and dried over $MgSO_4$. Filtration and concentration of the mixture in vacuo afforded the crude product that was purified by flash silica gel column chromatography [gradient eluent: EtOAc in petroleum ether] to obtain the corresponding products.

***N*-(2,6-dimethyl-5-phenylpyrimidin-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide (3a)**

Following the general procedure A: white solid, mp: 163-165 °C, 97%; R_f = 0.5 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.66 (d, *J* = 7.8 Hz, 2H), 7.32 -7.18 (m, 5H), 7.11 - 7.06 (m, 1H), 7.01 - 6.94 (m, 2H), 6.89 (d, *J* = 7.2 Hz, 2H), 6.58 (d, *J* = 7.8 Hz, 2H), 2.70 (s, 3H), 2.42 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.89, 165.69, 160.12, 143.54, 138.91, 136.57, 133.82, 129.51, 129.42, 129.05, 128.59, 128.42, 128.29, 127.64, 127.50, 127.46, 25.38, 22.96, 21.66; mass spectrum (ESI): m/e (% relative intensity) 452.1 (100) $(M+Na)^+$; HRMS calcd for $C_{25}H_{23}N_3O_2SNa$ $(M+Na)^+$ 452.1409, found 452.1429.

***N*-(5-cyclopropyl-2,6-dimethylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3b)**

Following the general procedure A: white solid, mp: 140-141 ^{o}C, 93%; R_f = 0.25 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 3.09 (s, 3H), 2.65 (s, 3H), 2.51 (s, 3H), 2.44 (s, 3H), 1.96 - 1.86 (m, 1H), 1.22 - 1.12 (m, 2H), 0.66 - 0.53 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.04, 164.48, 160.86, 143.71, 135.08, 129.25, 128.51, 127.83, 36.39, 25.15, 22.79, 21.58, 10.08, 8.52; mass spectrum (ESI): m/e (% relative intensity) 354.1 (100) $(M+Na)^+$; HRMS calcd for $C_{17}H_{21}N_3O_2SNa$ $(M+Na)^+$ 354.1252, found 354.1266.

***N*-(2,6-dimethylpyrimidin-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide (3c)**

Following the general procedure A: white solid, mp: 138-141 ^{o}C, 91%; R_f = 0.8 (50% EtOAc/Petroleum Ether); ;^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (d, *J* = 7.5 Hz, 2H), 7.55 - 7.45 (m, 3H), 7.36 - 7.26 (m, 4H), 5.94 (s, 1H), 2.57 (s, 3H), 2.43 (s, 3H), 2.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.07, 166.42, 160.83, 144.28, 137.41, 137.31, 130.48, 130.01, 129.62, 128.94, 105.53, 25.42, 24.15, 21.65; mass spectrum (ESI): m/e (% relative intensity) 376.1 (100) $(M+Na)^+$; HRMS calcd for $C_{19}H_{19}N_3O_2SNa$ $(M+Na)^+$ 376.1096, found 376.1112.

(*R*)-3-(2,6-dimethylpyrimidin-4-yl)-4-phenyloxazolidin-2-one (3d)

Following the general procedure A: colorless oil, 87%; R_f = 0.7 (50% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 (s, 1H), 7.44 - 7.25 (m, 5H), 5.88 - 5.78 (m, 1H), 4.79 (t, *J* = 8.7 Hz, 1H), 4.43 - 4.33 (m, 1H), 2.45 (s, 3H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.81, 166.78, 156.27, 154.72, 139.63, 128.91, 128.42, 126.45, 105.72, 70.34, 57.99, 25.58, 24.34; mass spectrum (ESI): m/e (% relative intensity) 292.1 (100) $(M+Na)^+$; HRMS calcd for $C_{15}H_{15}N_3O_2Na$ $(M+Na)^+$ 292.1062, found 292.1064.

3-(5-(4-fluorophenyl)-2,6-dimethylpyrimidin-4-yl)oxazolidin-2-one (3e)

Following the general procedure A: white solid, mp: 153-155 ^{o}C, 82%; R_f = 0.6 (60% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 - 7.19 (m, 2H), 7.17 - 7.07 (m, 2H), 4.33 (t, *J* = 7.8 Hz, 2H), 4.03 (t, *J* = 7.8 Hz, 2H), 2.70 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.96, 166.39, 163.12 - 161.48 (d, *J* = 246.1 Hz), 155.91, 154.44, 131.20 - 131.14 (d, *J* = 9.0 Hz), 130.50 - 130.48(d, *J* = 3.0 Hz), 125.49, 115.63 - 115.48 (d, *J* = 22.5 Hz), 62.66, 45.53, 25.60, 23.13; ^{19}F NMR (564 MHz, $CDCl_3$): δ -113.65; mass spectrum (ESI): m/e (% relative intensity) 310.1 (100) $(M+Na)^+$; HRMS calcd for $C_{15}H_{14}FN_3O_2Na$ $(M+Na)^+$ 310.0968, found 310.0981.

3-(2,6-dimethyl-5-(*p*-tolyl)pyrimidin-4-yl)oxazolidin-2-one (3f)

Following the general procedure A: white solid, mp: 103-104 ^{o}C, 93%; R_f = 0.4 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.23 (d, *J* = 7.8 Hz, 2H), 7.14 (d, *J* = 7.8 Hz, 2H), 4.29 (t, *J* = 7.8 Hz, 2H), 3.91 (t, *J* = 7.8 Hz, 2H), 2.70 (s, 3H), 2.39 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.04, 166.08, 155.88, 154.66, 137.76, 131.33, 129.25, 129.10, 126.57, 62.62, 45.63, 25.58, 23.09, 21.30; mass spectrum (ESI): m/e (% relative intensity) 306.1 (100) $(M+Na)^+$; HRMS calcd for $C_{16}H_{17}N_3O_2Na$ $(M+Na)^+$ 306.1218, found 306.1231.

(*R*)-3-(2,6-dimethyl-5-phenylpyrimidin-4-yl)-4-phenyloxazolidin-2-one (3g)

Following the general procedure A: white solid, mp: 58-60 ^{o}C, 86%; R_f = 0.3 (20% EtOAc/Petroleum

Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.63 - 7.37 (m, 4H), 7.36 - 7.30 (m, 3H), 7.28 - 7.23 (m, 2H), 6.90 - 6.57 (m, 1H), 5.56 (dd, *J* = 9.0, 9.6 Hz, 1H), 4.60 (dd, *J* = 9.0, 9.0 Hz, 1H), 4.15 (dd, *J* = 9.0, 9.6 Hz, 1H), 2.66 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.26, 166.16, 155.36, 155.06, 136.34, 134.17, 129.11, 128.82, 128.13, 128.10, 128.06, 70.06, 60.64, 25.56, 23.12; mass spectrum (ESI): m/e (% relative intensity) 368.1 (100) $(M+Na)^+$; HRMS calcd for $C_{21}H_{19}N_3O_2Na$ $(M+Na)^+$ 368.1375, found 368.1390.

(*S*)-4-benzyl-3-(2,6-dimethyl-5-phenylpyrimidin-4-yl)oxazolidin-2-one (3h)

Following the general procedure A: white solid, mp: 43-45 °C, 78%; R_f = 0.45 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.53 - 7.31 (m, 4H), 7.30 - 7.18 (m, 4H), 7.09 (d, *J* = 7.2 Hz, 2H), 4.66 - 4.56 (m, 1H), 4.13 (t, *J* = 8.5 Hz, 1H), 3.96 (t, *J* = 8.5 Hz, 1H), 3.20 - 3.15 (m, 1H), 2.74 (s, 3H), 2.67 - 2.56 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.22, 166.52, 155.16, 154.92, 135.33, 134.32, 128.86, 128.84, 128.51, 128.15, 127.87, 127.25, 67.99, 57.35, 38.97, 25.74, 23.19; mass spectrum (ESI): m/e (% relative intensity) 382.2 (100) $(M+Na)^+$; HRMS calcd for $C_{22}H_{21}N_3O_2Na$ $(M+Na)^+$ 382.1531, found 382.1538.

3-(2,6-dimethyl-5-phenylpyrimidin-4-yl)oxazolidin-2-one (3i)

Following the general procedure A: white solid, mp: 125-127 °C, 89%; R_f = 0.45 (50% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.45 - 7.40 (m, 2H), 7.39 - 7.35 (m, 1H), 7.26 (d, *J* = 7.2 Hz, 2H), 4.29 (t, *J* = 7.7 Hz, 2H), 3.93 (t, *J* = 7.7 Hz, 2H), 2.71 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.91, 166.29, 155.83, 154.62, 134.45, 129.30, 128.50, 128.03, 126.54, 62.63, 45.63, 25.60, 23.09; mass spectrum (ESI): m/e (% relative intensity) 292.1 (100) $(M+Na)^+$; HRMS calcd for $C_{15}H_{15}N_3O_2Na$ $(M+Na)^+$ 292.1062, found 292.1065.

***N*-(2,6-dimethyl-5-phenylpyrimidin-4-yl)-N-methylmethanesulfonamide (3j)**

Following the general procedure A: white solid, mp: 117-118 °C, 95%; R_f = 0.4 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.49 - 7.45 (m, 2H), 7.43 - 7.38 (m, 1H), 7.32 (d, *J* = 7.2 Hz, 2H), 3.19 (s, 3H), 2.80 (s, 3H), 2.71 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.28, 166.23, 159.98, 133.90, 129.60, 128.83, 128.26, 127.51, 39.85, 36.88, 25.65, 23.22; mass spectrum (ESI): m/e (% relative intensity) 314.1 (100) $(M+H)^+$; HRMS calcd for $C_{14}H_{17}N_3O_2SNa$ $(M+Na)^+$ 314.0939 found 314.0952.

***N*-(5-butyl-2,6-dimethylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3k)**

Following the general procedure A: white solid, mp: 91-93 °C, 84%; R_f = 0.45 (30% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.8 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 2H), 3.02 (s, 3H), 2.91 (t, *J* = 7.7 Hz, 2H), 2.56 (s, 3H), 2.46 (s, 3H), 2.45 (s, 3H), 1.57 - 1.48 (m, 2H), 1.47 - 1.39 (m, 2H), 0.98 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.67, 164.59, 160.27, 143.85, 133.92, 129.80, 129.12, 129.00, 37.34, 31.32, 26.96, 25.00, 22.89, 22.30, 21.60, 13.86; mass spectrum (ESI): m/e (% relative intensity) 370.2 (100) $(M+Na)^+$; HRMS calcd for $C_{18}H_{25}N_3O_2SNa$ $(M+Na)^+$ 370.1565, found 370.1578.

***N*-benzyl-*N*-(5-(4-methoxyphenyl)-2,6-dimethylpyrimidin-4-yl)-4-methylbenzenesulfonamide (3l)**

Following the general procedure A: pale yellow solid, mp: 146-148 °C, 91%; R_f = 0.4 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.8 Hz, 2H), 7.25 (d, *J* = 8.0 Hz,

2H), 7.20 - 7.15 (m, 1H), 7.13 - 7.07 (m, 2H), 6.85 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 7.4 Hz, 2H), 6.73 (d, J = 8.0 Hz, 2H), 4.41 (s, 2H), 3.87 (s, 3H), 2.67 (s, 3H), 2.44 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.76, 165.87, 159.18, 157.98, 143.78, 136.07, 134.70, 131.18, 130.93, 129.44, 129.13, 128.93, 128.19, 127.77, 126.05, 113.52, 55.27, 53.17, 25.38, 23.37, 21.62; mass spectrum (ESI): m/e (% relative intensity) 496.2 (100) $(M+Na)^+$; HRMS calcd for $C_{27}H_{27}N_3O_4SNa$ $(M+Na)^+$ 496.1671, found 496.1687.

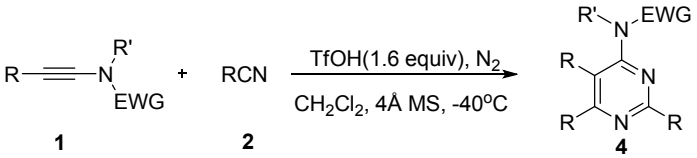
***N*-(2,6-dimethyl-5-phenylpyrimidin-4-yl)-*N*,4-dimethylbenzenesulfonamide (3m)**

Following the general procedure A: white solid, mp: 135-137 °C, 94%; R_f = 0.2 (50% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.74 (d, J = 7.8 Hz, 2H), 7.51 - 7.46 (m, 2H), 7.45 - 7.40 (m, 1H), 7.35 (d, J = 7.2 Hz, 2H), 7.28 (d, J = 7.8 Hz, 2H), 2.74 (s, 3H), 2.65 (s, 3H), 2.43 (s, 3H), 2.36 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.14, 166.22, 159.71, 143.66, 135.87, 134.27, 129.70, 129.10, 128.91, 128.71, 128.53, 128.10, 36.72, 25.37, 23.29, 21.59; mass spectrum (ESI): m/e (% relative intensity) 390.1 (100) $(M+Na)^+$; HRMS calcd for $C_{20}H_{21}N_3O_2SNa$ $(M+Na)^+$ 390.1252, found 390.1258.

Ethyl 4-(*N*,4-dimethylphenylsulfonamido)-2,6-dimethylpyrimidine-5-carboxylate (3n)

Following the general procedure A: white solid, mp: 80-82 °C, 86%; R_f = 0.35 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, J = 7.9 Hz, 2H), 7.28 (d, J = 7.9 Hz, 2H), 4.46 (q, J = 7.1 Hz, 2H), 3.13 (s, 3H), 2.66 (s, 3H), 2.56 (s, 3H), 2.43 (s, 3H), 1.44 (t, J = 7.1 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.93, 167.75, 165.85, 159.07, 144.14, 134.21, 129.47, 128.26, 121.13, 61.99, 36.36, 25.68, 23.47, 21.60, 14.02; mass spectrum (ESI): m/e (% relative intensity) 386.1 (100) $(M+Na)^+$; HRMS calcd for $C_{17}H_{21}N_3O_2SNa$ $(M+Na)^+$ 386.1150, found 386.1147.

General Procedure B for TfOH-Mediated [2+2+2] Cycloadditions of Ynamides with Various Nitrile (4a–4s).



To a stirring suspension of ynamide (0.13 mmol), nitriles (1.20 mmol) and 4Å MS (20.0 mg) in dry dichloromethane (2.00 mL) was added TfOH dropwise (21.0 μl, 0.24 mmol) via a syringe pump at –40 °C under nitrogen atmosphere. The reaction was monitored by TLC. When progress appeared to be completed after about 1.5 h at the same temperature, the saturated sodium bicarbonate solution was added to the mixture and the resulting mixture was extracted with EtOAc. The organic layers were washed with sat aq NaCl and dried over $MgSO_4$. Filtration and concentration of the mixture in vacuo afforded the crude product that was purified by flash silica gel column chromatography [gradient eluent: EtOAc in petroleum ether] to obtain corresponding product s.

4-methyl-*N*-phenyl-*N*-(2,5,6-triphenylpyrimidin-4-yl)benzenesulfonamide (4a)

Following the general procedure B: white solid, mp: 218-220 °C, 91%; R_f = 0.7 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.34 (d, J = 6.6 Hz, 2H), 7.67 (d, J = 7.2 Hz, 2H), 7.57 -7.45 (m, 3H), 7.41 (d, J = 7.2 Hz, 2H), 7.32 - 7.16 (m, 8H), 7.13 - 6.95 (m, 5H), 6.75 (d, J = 7.2 Hz, 2H), 2.49 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.33, 162.99, 161.49, 143.53, 138.64,

137.76, 137.27, 137.11, 133.93, 131.01, 130.47, 129.98, 129.17, 129.12, 129.00, 128.91, 128.84, 128.66, 128.44, 128.40, 128.33, 127.79, 127.71, 127.67, 21.76; mass spectrum (ESI): m/e (% relative intensity) 576.2 (100) $(M+Na)^+$; HRMS calcd for $C_{35}H_{27}N_3O_2SNa$ $(M+Na)^+$ 576.1722, found 576.1720.

Ethyl 4-(N,4-dimethylphenylsulfonamido)-2,6-diphenylpyrimidine-5-carboxylate (4b)

Following the general procedure B: white solid, mp: 172-174 °C, 83%; R_f = 0.5 (20% EtOAc/Petroleum Ether); ^1H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 7.2 Hz, 2H), 7.85 - 7.76 (m, 2H), 7.72 (d, *J* = 8.2 Hz, 2H), 7.53 - 7.45 (m, 4H), 7.44 - 7.38 (m, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 4.30 (q, *J* = 7.2 Hz, 2H), 3.26 (s, 3H), 2.45 (s, 3H), 1.17 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.72, 166.13, 164.09, 160.49, 144.09, 137.69, 136.18, 134.42, 131.63, 130.37, 129.51, 128.76, 128.71, 128.49, 122.84, 62.11, 37.49, 21.65, 13.73; mass spectrum (ESI): m/e (% relative intensity) 510.1 (100) $(M+Na)^+$; HRMS calcd for $C_{27}H_{25}N_3O_4SNa$ $(M+Na)^+$ 510.1463, found 510.1478.

***N*,4-dimethyl-*N*-(2,5,6-triphenylpyrimidin-4-yl)benzenesulfonamide (4c)**

Following the general procedure B: white solid, mp: 207-210 °C, 87%; R_f = 0.5 (10% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 8.28 (d, *J* = 7.8 Hz, 2H), 7.81 (d, *J* = 7.8 Hz, 2H), 7.52 - 7.40 (m, 5H), 7.39 - 7.28 (m, 8H), 7.27 - 7.22 (m, 2H), 2.87 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 167.58, 163.07, 161.46, 143.59, 138.05, 136.84, 136.20, 134.21, 130.99, 130.56, 130.04, 129.34, 129.17, 128.92, 128.86, 128.50, 128.49, 128.37, 127.96, 127.86, 37.17, 21.67; mass spectrum (ESI): m/e (% relative intensity) 514.2 (100) $(M+Na)^+$; HRMS calcd for $C_{30}H_{25}N_3O_2SNa$ $(M+Na)^+$ 514.1565, found 514.1576.

***N*-(2,6-bis(2-chlorophenyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4d)**

Following the general procedure B: white solid, mp: 89-91 °C, 60.6%; R_f = 0.7 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.93 - 7.88 (m, 1H), 7.53 -7.49 (m, 1H), 7.41 - 7.37 (m, 2H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.23 (m, 5H), 7.22 – 7.05 (m, 4H), 3.36 (s, 3H), 2.85 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ167.13, 163.12, 161.14, 137.01, 136.64, 132.92, 132.68, 132.49, 132.46, 130.87, 130.79, 130.67, 129.97, 129.86, 129.66, 129.07, 128.48, 128.33, 128.26, 127.78, 126.99, 126.44, 125.33, 40.21, 37.00.; 506.0 (100) $(M+Na)^+$; HRMS calcd for $C_{24}H_{19}Cl_2N_3O_2SNa$ $(M+Na)^+$ 506.0473, found 506.0476.

***N*-benzyl-*N*-(2,6-bis(4-chlorophenyl)-5-(4-methoxyphenyl)pyrimidin-4-yl)-4-methylbenzenesulfonamide (4e)**

Following the general procedure B: white solid, mp: 178-183 °C, 75%; R_f = 0.6 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.1 Hz, 2H), 7.67 (d, *J* = 7.7 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.35 - 7.27 (m, 4H), 7.17 (d, *J* = 8.2 Hz, 2H), 7.14 - 7.10 (m, 1H), 7.07 - 7.02 (m, 2H), 6.80 (d, *J* = 7.4 Hz, 4H), 6.76 (d, *J* = 8.0 Hz, 2H), 4.49 (s, 2H), 3.84 (s, 3H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.62, 161.49, 160.18, 159.28, 143.91, 137.32, 136.53, 136.05, 135.39, 135.19, 134.26, 132.06, 131.42, 131.05, 129.63, 129.43, 129.32, 129.08, 128.73, 128.25, 128.18, 128.09, 127.85, 125.55, 113.65, 55.25, 54.24, 21.71; mass spectrum (ESI): m/e (% relative intensity) 688.1 (100)$(M+Na)^+$; HRMS calcd for $C_{37}H_{29}Cl_2N_3O_3SNa$ $(M+Na)^+$ 688.1204, found 688.1195.

***N*-benzyl-*N*-(2,6-bis(4-chlorophenyl)-5-phenylpyrimidin-4-yl)-4-methylbenzenesulfonamide (4f)**

Following the general procedure B: white solid, mp: 276-279 °C (dec.), 90%; R_f = 0.4 (10% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 8.24 (d, *J* = 8.1 Hz, 2H), 7.62 (d, *J* = 7.8 Hz,

2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.37 - 7.23 (m, 8H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.11 (d, *J* = 7.3 Hz, 1H), 7.07 - 6.97 (m, 4H), 6.73 (d, *J* = 7.7 Hz, 2H), 2.50 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 166.13, 162.10, 161.72, 143.67, 138.51, 137.34, 137.29, 135.99, 135.58, 135.46, 133.49, 131.28, 130.28, 129.92, 129.00, 128.89, 128.84, 128.67, 128.55, 128.48, 128.11, 127.99, 127.75, 21.74; mass spectrum (ESI): m/e (% relative intensity) 644.1 (100) $(M+Na)^+$; HRMS calcd for $C_{35}H_{25}Cl_2N_3O_2SNa$ $(M+Na)^+$ 644.0942, found 644.0955

Dimethyl-2,2'-(6-(*N*-methylmethylsulfonamido)-5-phenylpyrimidine-2,4-diyl)diacetate (4g)

Following the general procedure B: pale yellow oil, 74%; R_f = 0.4 (50% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 - 7.45 (m, 2H), 7.44 - 7.41 (m, 1H), 7.34 (d, *J* = 7.3 Hz, 2H), 4.03 (s, 2H), 3.77 (s, 3H), 3.70 (s, 2H), 3.65 (s, 3H), 3.19 (s, 3H), 2.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.74, 169.72, 164.48, 162.62, 161.00, 132.76, 129.51, 129.05, 128.83, 128.69, 52.33, 52.29, 44.75, 41.58, 39.91, 37.00.; mass spectrum (ESI): m/e (% relative intensity) 430.1 (100) $(M+Na)^+$; HRMS calcd for $C_{18}H_{21}N_3O_6SNa$ $(M+Na)^+$ 430.1049, found 430.1062.

***N*-(2,6-dibutyl-5-phenylpyrimidin-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide (4h)**

Following the general procedure B: white solid, mp: 57-59 °C, 78%; R_f = 0.8 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.32 - 7.23 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 2H), 7.12 - 7.07 (m, 1H), 7.01 - 6.95 (m, 2H), 6.91 (d, *J* = 7.2 Hz, 2H), 6.59 (d, *J* = 7.8 Hz, 2H), 2.93 (t, *J* = 7.8 Hz, 2H), 2.46 (t, *J* = 7.8 Hz, 2H), 2.41 (s, 3H), 1.85 - 1.77 (m, 2H), 1.52 -1.42 (m, 4H), 1.19 - 1.11 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H), 0.72 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 171.53, 169.45, 160.12, 143.33, 139.04, 136.85, 133.82, 129.71, 129.32, 129.00, 128.58, 128.28, 128.21, 127.73, 127.52, 127.43, 38.73, 35.04, 31.23, 30.67, 22.59, 22.51, 21.60, 14.04, 13.69; mass spectrum (ESI): m/e (% relative intensity) 536.2 (100) $(M+Na)^+$; HRMS calcd for $C_{31}H_{35}N_3O_2SNa$ $(M+Na)^+$ 536.2348, found 536.2357.

***N*-(2,6-bis(2-methoxyethyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4i)**

Following the general procedure B: colorless oil, 76%; R_f = 0.45 (50% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.48 - 7.44 (m, 2H), 7.42 -7.38 (m, 1H), 7.37 - 7.32 (m, 2H), 3.93 (t, *J* = 6.2 Hz, 2H), 3.71 (t, *J* = 6.2 Hz, 2H), 3.40 (s, 3H), 3.27 - 3.22 (m, 5H), 3.19 (s, 3H), 2.89 (t, *J* = 6.3 Hz, 2H), 2.79 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.62, 166.61, 160.24, 133.41, 129.93, 128.77, 128.30, 70.77, 70.54, 58.74, 58.66, 39.82, 38.94, 36.99, 35.18; mass spectrum (ESI): m/e (% relative intensity) 402.1 (100) $(M+Na)^+$; HRMS calcd for $C_{18}H_{25}N_3O_4SNa$ $(M+Na)^+$ 402.1463 found 402.1463.

4-methyl-*N*-phenyl-*N*-(5-phenyl-2,6-di(thiophen-2-yl)pyrimidin-4-yl)benzenesulfonamide (4j)

Following the general procedure B: white solid, mp: 68-71 °C, 93%; R_f = 0.6 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.18 - 8.15 (m, 1H), 7.81 (d, *J* = 4.7 Hz, 1H), 7.64 (d, *J* = 7.7 Hz, 2H), 7.41 - 7.36 (m, 2H), 7.35 - 7.31 (m, 2H), 7.28 - 7.23 (m, 3H), 7.22 - 7.20 (m, 1H), 7.13 -7.09 (m, 2H), 7.06 (d, *J* = 7.0 Hz, 2H), 7.04 - 7.00 (m, 2H), 6.75 (d, *J* = 7.9 Hz, 2H), 2.46 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 161.53, 161.47, 160.14, 143.55, 141.40, 139.32, 138.71, 137.26, 134.36, 130.14, 129.56, 129.06, 128.92, 128.85, 128.80, 128.74, 128.45, 128.35, 128.17, 127.72, 127.63, 127.49, 125.85, 124.60, 21.71; mass spectrum (ESI): m/e (% relative intensity) 588.1 (100) $(M+Na)^+$; HRMS calcd for $C_{31}H_{23}N_3O_3S_3Na$ $(M+Na)^+$ 588.0850, found 588.0857.

***N*-(2,6-dibenzyl-5-phenylpyrimidin-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide(4l)**

Following the general procedure B: pale yellow oil, 77%; R_f = 0.7 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.8 Hz, 2H), 7.35 - 7.30 (m, 4H), 7.29 - 7.19 (m, 4H), 7.16 - 7.08 (m, 5H), 7.07 - 7.03 (m, 1H), 6.96 - 6.91 (m, 2H), 6.90 - 6.86 (m, 2H), 6.77 (d, *J* = 7.08 Hz, 2H), 6.52 (d, *J* = 7.5 Hz, 2H), 4.27 (s, 2H), 3.82 (s, 2H), 2.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.59, 167.76, 160.76, 143.39, 138.88, 138.36, 137.74, 136.61, 133.36, 129.86, 129.37, 129.32, 129.17, 129.03, 128.68, 128.42, 128.33, 128.30, 128.27, 128.19, 127.77, 127.53, 126.51, 126.33, 45.35, 41.28, 21.64; mass spectrum (ESI): m/e (% relative intensity) 604.2 (100) $(M+Na)^+$; HRMS calcd for $C_{37}H_{31}N_3O_2SNa$ $(M+Na)^+$ 604.2035, found 604.2047.

***N*-(2,6-bis(4-nitrobenzyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4m)**

Following the general procedure B: pale yellow solid, mp: 130-132 °C, 36%; R_f = 0.5 (50% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.2 Hz, 2H), 8.03 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.1 Hz, 2H), 7.49 - 7.44 (m, 3H), 7.20 (d, *J* = 5.7 Hz, 2H), 7.10 (d, *J* = 8.1 Hz, 2H), 4.39 (s, 2H), 4.07 (s, 2H), 2.95 (s, 3H), 2.77 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.48, 166.76, 161.11, 146.93, 146.76, 145.07, 144.89, 132.90, 130.44, 129.89, 129.73, 129.11, 128.90, 128.15, 123.68, 123.49, 44.94, 41.14, 39.77, 36.90; mass spectrum (ESI): m/e (% relative intensity) 556.1 (100) $(M+Na)^+$; HRMS calcd for $C_{26}H_{23}N_5O_6SNa$ $(M+Na)^+$ 556.1267, found 556.1281.

***N*-(2,6-bis(2-methylbenzyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4n)**

Following the general procedure B: white solid, mp: 141-142 °C, 75%; R_f = 0.6 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.40 - 7.33 (m, 3H), 7.27 - 7.23 (m, 1H), 7.21 - 7.10 (m, 5H), 7.10 - 6.99 (m, 3H), 6.78 (d, *J* = 7.4 Hz, 1H), 4.28 (s, 2H), 3.93 (s, 2H), 2.83 (s, 3H), 2.68 (s, 3H), 2.26 (s, 3H), 1.98 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.02, 168.02, 160.70, 137.31, 136.64, 136.57, 136.49, 133.51, 130.54, 130.26, 130.13, 129.68, 129.12, 128.80, 128.35, 127.56, 126.86, 126.50, 125.94, 125.81, 43.01, 39.52, 38.85, 37.02, 37.01, 19.81, 19.78; mass spectrum (ESI): m/e (% relative intensity) 494.2 (100) $(M+Na)^+$; HRMS calcd for $C_{28}H_{29}N_3O_2SNa$ $(M+Na)^+$ 494.1878, found 494.1888.

***N*-(2,6-bis(3-methoxybenzyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4o)**

Following the general procedure B: colourless oil, 72%; R_f = 0.5 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 - 7.37 (m, 3H), 7.24 - 7.18 (m, 3H), 7.08 (t, *J* = 7.9 Hz, 1H), 6.98 - 6.89 (m, 2H), 6.78 (d, *J* = 8.2 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.54 (s, 2H), 4.28 (s, 2H), 3.93 (s, 2H), 3.77 (s, 3H), 3.67 (s, 3H), 2.97 (s, 3H), 2.70 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.71, 168.00, 160.71, 159.74, 159.50, 139.41, 139.24, 133.50, 130.00, 129.43, 129.26, 128.72, 128.40, 127.61, 121.92, 121.35, 115.00, 114.39, 112.27, 112.21, 55.23, 55.22, 55.10, 45.44, 41.46, 39.63, 37.00; mass spectrum (ESI): m/e (% relative intensity) 526.2 (100) $(M+Na)^+$; HRMS calcd for $C_{28}H_{29}N_3O_4SNa$ $(M+Na)^+$ 526.1776, found 526.1790.

***N*-(2,6-bis(4-methoxybenzyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4p)**

Following the general procedure B: white solid, mp: 125-127 °C, 81%; R_f = 0.3 (20% EtOAc/Petroleum Ether); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.44 - 7.38 (m, 3H), 7.29 (d, *J* = 7.9 Hz, 2H), 7.18 (d, *J* = 7.0 Hz, 2H), 6.90 - 6.84 (m, 4H), 6.71 (d, *J* = 7.9 Hz, 2H), 4.24 (s, 2H), 3.89 (s, 2H), 3.79 (s, 3H), 3.75 (s, 3H), 2.98 (s, 3H), 2.71 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 170.16, 168.41, 160.59,

158.34, 158.20, 133.56, 130.55, 130.10, 129.97, 129.81, 128.68, 128.32, 127.41, 113.84, 113.70, 55.32, 55.31, 55.25, 55.23, 44.50, 40.53, 39.62, 37.02, 37.01; mass spectrum (ESI): m/e (% relative intensity) 526.2 (100) $(M+Na)^+$; HRMS calcd for $C_{28}H_{29}N_3O_4SNa$ $(M+Na)^+$ 526.1776, found 526.1800.

***N*-(2,6-bis(4-bromobenzyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4q)**

Following the general procedure B: white solid, mp: 166-168 ^oC, 94%; R_f = 0.51 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.46-7.38 (m, 5H), 7.29 (d, *J* = 7.6 Hz, 2H), 7.22 (d, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 6.5 Hz, 2H), 6.81 (d, *J* = 7.7 Hz, 2H), 4.23 (s, 2H), 3.88 (s, 2H), 2.96 (s, 3H), 2.72 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.36, 167.63, 160.76, 136.79, 136.58, 133.27, 131.53, 131.37, 131.34, 130.75, 129.85, 128.87, 128.57, 127.74, 120.57, 120.52, 44.70, 40.79, 39.66, 36.97; mass spectrum (ESI): m/e (% relative intensity) 622.0 (100) $(M+Na)^+$; HRMS calcd for $C_{26}H_{23}Br_2N_3O_2S$ $(M)^-$ 597.9878, found 597.9870.

***N*-(2,6-bis(2-fluorobenzyl)-5-phenylpyrimidin-4-yl)-*N*-methylmethanesulfonamide (4r)**

Following the general procedure B: pale yellow solid, mp: 95-97 ^oC, 91%; R_f = 0.3 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.46 - 7.35 (m, 3H), 7.31 - 7.27 (m, 1H), 7.26 -7.20 (m, 3H), 7.19 -7.13 (m, 1H), 7.11 -6.96 (m, 4H), 6.94 - 6.89 (m, 1H), 4.31 (s, 2H), 4.00 (s, 2H), 2.90 (s, 3H), 2.70 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.98, 167.02, 162.10 - 161.48 (d, *J* = 93.0 Hz), 160.71, 160.47 - 159.85 (d, *J* = 93.0 Hz), 133.18, 131.89 -131.87 (d, *J* = 3.0 Hz), 131.10 - 131.08 (d, *J* = 3.0 Hz), 129.63, 128.82, 128.45 - 128.39 (d, *J* = 9.0 Hz), 128.26, 128.20 (d, *J* = 9.0 Hz), 127.71, 124.91, 124.80, 124.01 - 123.99 (d, *J* = 3.0 Hz), 123.86 - 123.84 (d, *J* = 3.0 Hz), 115.27 - 115.14 (d, *J* = 19.5 Hz), 115.13 - 115.00 (d, *J* = 19.5 Hz), 39.48, 38.18 - 38.17 (d, *J* = 1.5 Hz), 37.02, 34.42 -34.41 (d, *J* = 1.5 Hz); ^{19}F NMR (564 MHz, $CDCl_3$): δ -116.69 –- 116.72 (m, 1F), -117.07 –- 116.10 (m, 1F); mass spectrum (ESI): m/e (% relative intensity)502.1 (100) $(M+Na)^+$; HRMS calcd for $C_{26}H_{23}F_2N_3O_2SNa$ $(M+Na)^+$ 502.1377, found 502.1381.

***N*-(2,6-bis(4-fluorobenzyl)-5-phenylpyrimidin-4-yl)-4-methyl-*N*-phenylbenzenesulfonamide (4s)**

Following the general procedure B: colorless oil, 69%; R_f = 0.8 (20% EtOAc/Petroleum Ether); ^1H NMR (600 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.2 Hz, 2H), 7.33 - 7.27 (m, 3H), 7.24 - 7.20 (m, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 7.11 - 7.06 (m, 1H), 7.03 - 6.98 (m, 2H), 6.97 - 6.93 (m, 2H), 6.80 (d, *J* = 7.2 Hz, 4H), 6.74 (d, *J* = 6.6 Hz, 2H), 6.51 (d, *J* = 6.6 Hz, 2H), 4.27 (s, 2H), 3.81 (s, 2H), 2.41 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 168.99, 167.18, 162.59 - 162.39 (d, *J* = 30.0 Hz), 161.16, 160.97 - 160.77 (d, *J* = 30.0 Hz), 143.61, 138.67, 136.44, 133.54, 132.90, 130.84 - 130.79 (d, *J* = 7.5 Hz), 130.49 - 130.44 (d, *J* = 7.5 Hz), 129.68, 129.21, 129.18, 128.71, 128.39, 128.07, 127.95, 127.69, 115.28 - 115.14 (d, *J* = 21.0 Hz), 115.06 - 114.92 (d, *J* = 21.0 Hz), 44.07, 40.07, 21.62; ^{19}F NMR (564 MHz, $CDCl_3$) δ -116.46; mass spectrum (ESI): m/e (% relative intensity) 640.2 (100) $(M+Na)^+$; HRMS calcd for $C_{37}H_{29}F_2N_3O_2SNa$ $(M+Na)^+$ 640.1846, found 640.1851.

General Procedure C for TfOH-Mediated [2+2+2] Cycloadditions of Ynamides with Two Difficult Nitriles.

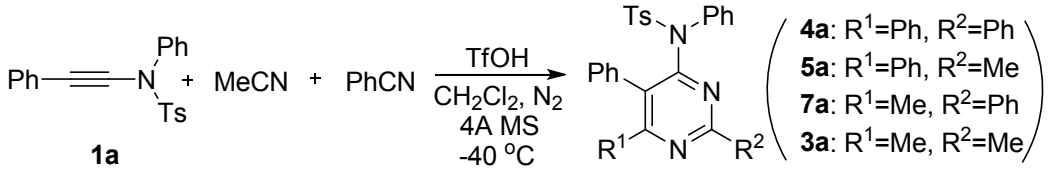
To a suspension of ynamide **1a** (0.15 mmol), acetonitrile (31.0 µl, 0.60 mmol), benzonitrile (61.0 µl,

0.60 mmol), and 4Å MS (20.0 mg) in dry CH_2Cl_2 (2.00 mL) was added TfOH dropwise (21.0 µl, 0.24 mmol) via a syringe pump at -40 °C under nitrogen atmosphere. The reaction was monitored by TLC. when progress appeared to be completed after about 1.0 h at the same temperature, the saturated sodium bicarbonate solution was added to the mixture and the resulting mixture was extracted with EtOAc. The organic layers were washed with sat aq NaCl and dried over $MgSO_4$. Filtration and concentration of the mixture in vacuo afforded the crude product that was purified by flash silica gel column chromatography [gradient eluent: EtOAc in petroleum ether] to obtain the corresponding products.

4-methyl-*N*-(6-methyl-2,5-diphenylpyrimidin-4-yl)-*N*-phenylbenzenesulfonamide (7a)

Following the general procedure C: white solid, mp: 188-190 °C, 39%; R_f = 0.55 (20% EtOAc/Petroleum Ether); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (d, *J* = 8.5 Hz, 2H), 7.25 -7.17 (m, 6H), 7.16 -7.10 (m, 4H), 7.09 - 7.03 (m, 1H), 6.99 - 6.92 (m, 2H), 6.87 (d, *J* = 7.5 Hz, 2H), 6.62 (d, *J* = 7.5 Hz, 2H), 2.79 (s, 3H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ167.01, 166.18, 161.24, 143.55, 138.67, 137.41, 136.49, 133.61, 130.35, 129.51, 128.93, 128.85, 128.57, 128.23, 128.14, 127.76, 127.46, 127.41, 126.89, 25.48, 21.62.; mass spectrum (ESI): m/e (% relative intensity) 492.0 (100) $(M+H)^+$; HRMS calcd for $C_{30}H_{25}N_3O_2SNa$ $(M+H)^+$ 492.1746, found 492.1739.

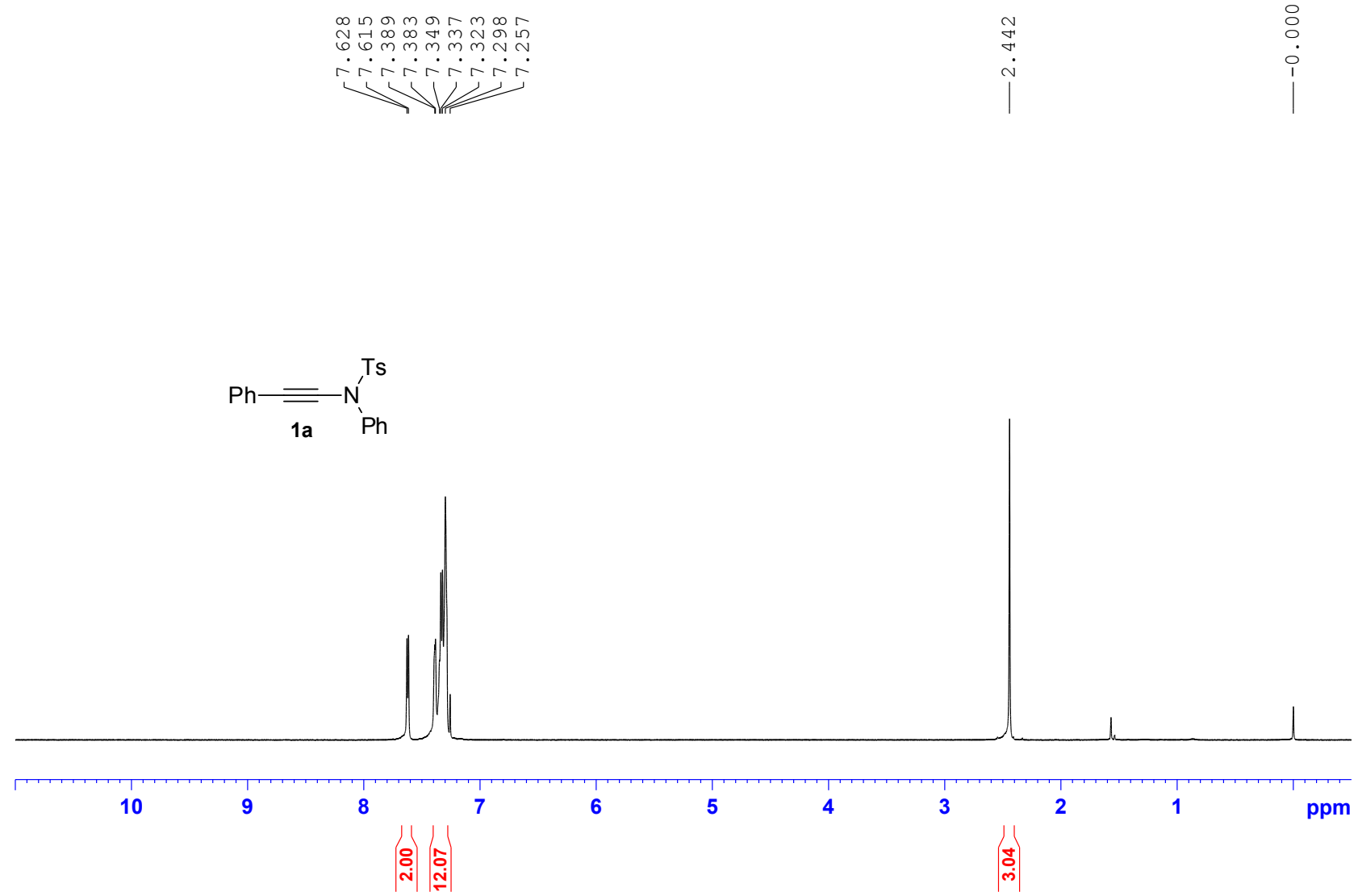
Table 1: Screening of Conditions[a]



Enter	*C*(mol/L)	MeCN (*n* equiv)	PhCN (*n* equiv)	TfOH (*n* equiv)	Yield[b] (%)
1	0.075	1.1	1.1	1.6	**4a**: 18%, **5a**: 14%, **7a**, **3a**: trace
2	0.075	2	2	1.6	**4a**: 13%, **5a**: 13%, **7a** : 26%, **3a** : <5%
3	0.075	4	4	1.6	**4a**: 15%, **5a**: 15%, **7a** : 39%, **3a**: 18%
4	0.075	6	6	1.6	**4a**: 18%, **5a**: 18%, **7a** : 28%, **3a**: 24%
5	0.075	4	3	1.6	**4a**: 16%, **5a**: 18%, **7a** : 23%, **3a**: 21%
6	0.075	3	4	1.6	**4a**: 19%, **5a**: 17%, **7a** : 25%, **3a**: 16%

[a]Ynamides **1a** (0.15 mmol), TfOH (0.24 mmol), CH_2Cl_2 (2.0 mL), 20 mg 4 Å MS, −40 °C, N_2. [b]Isolated yield; the ratio(**4a:5a**) was determined by ^{1}H NMR spectroscopic analysis of the isolated mixture..

Spectra data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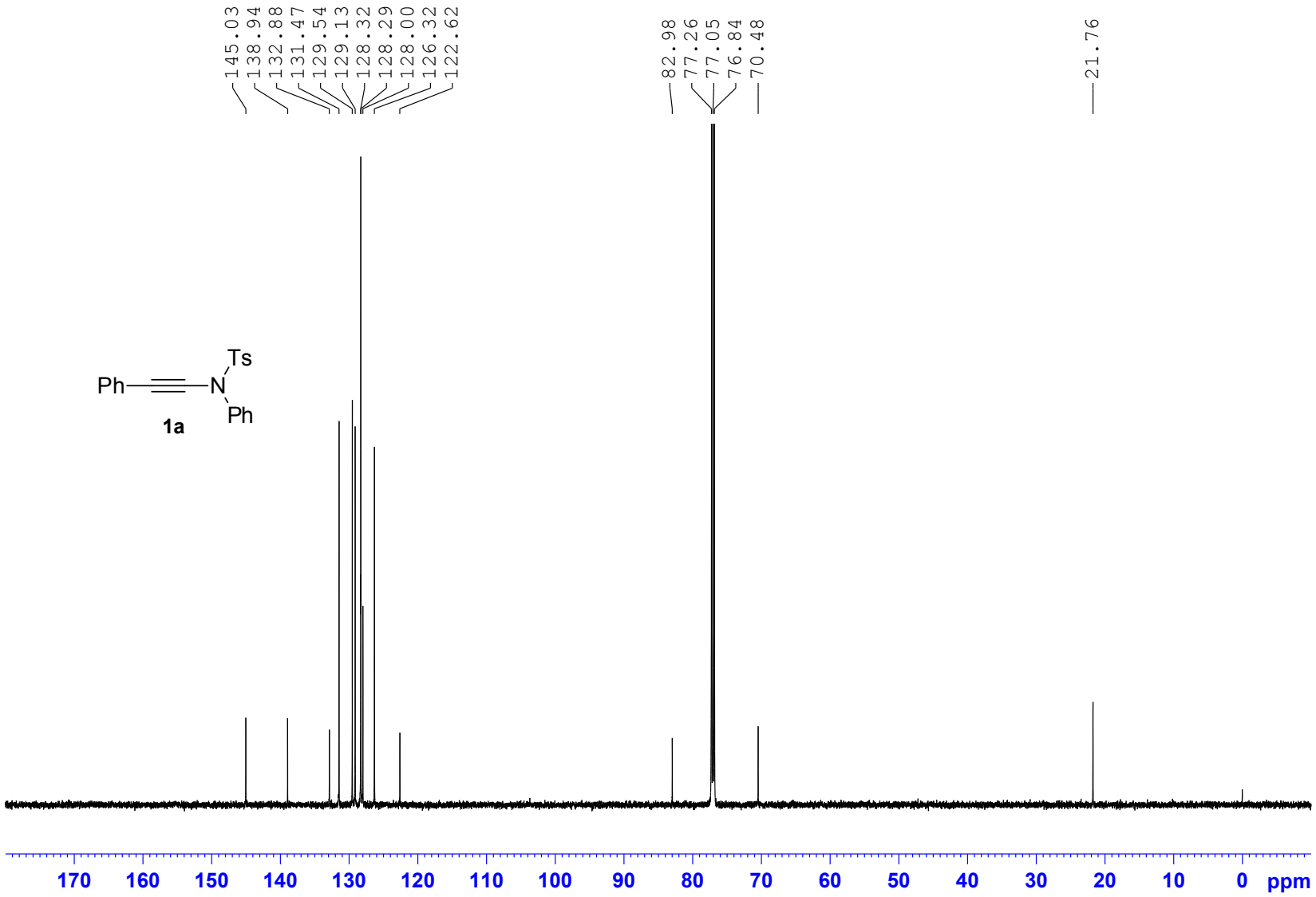
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Ph
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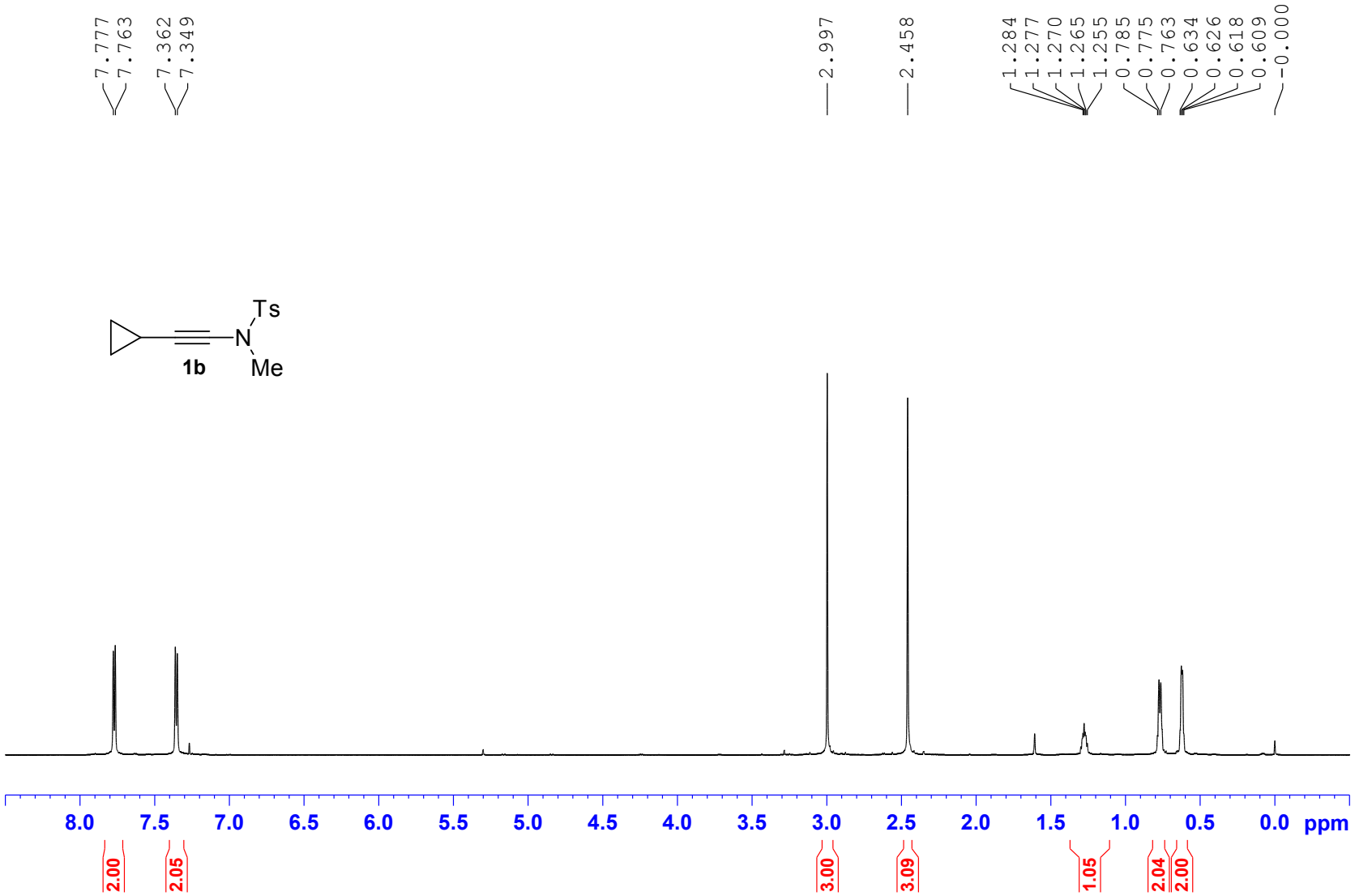
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0.609
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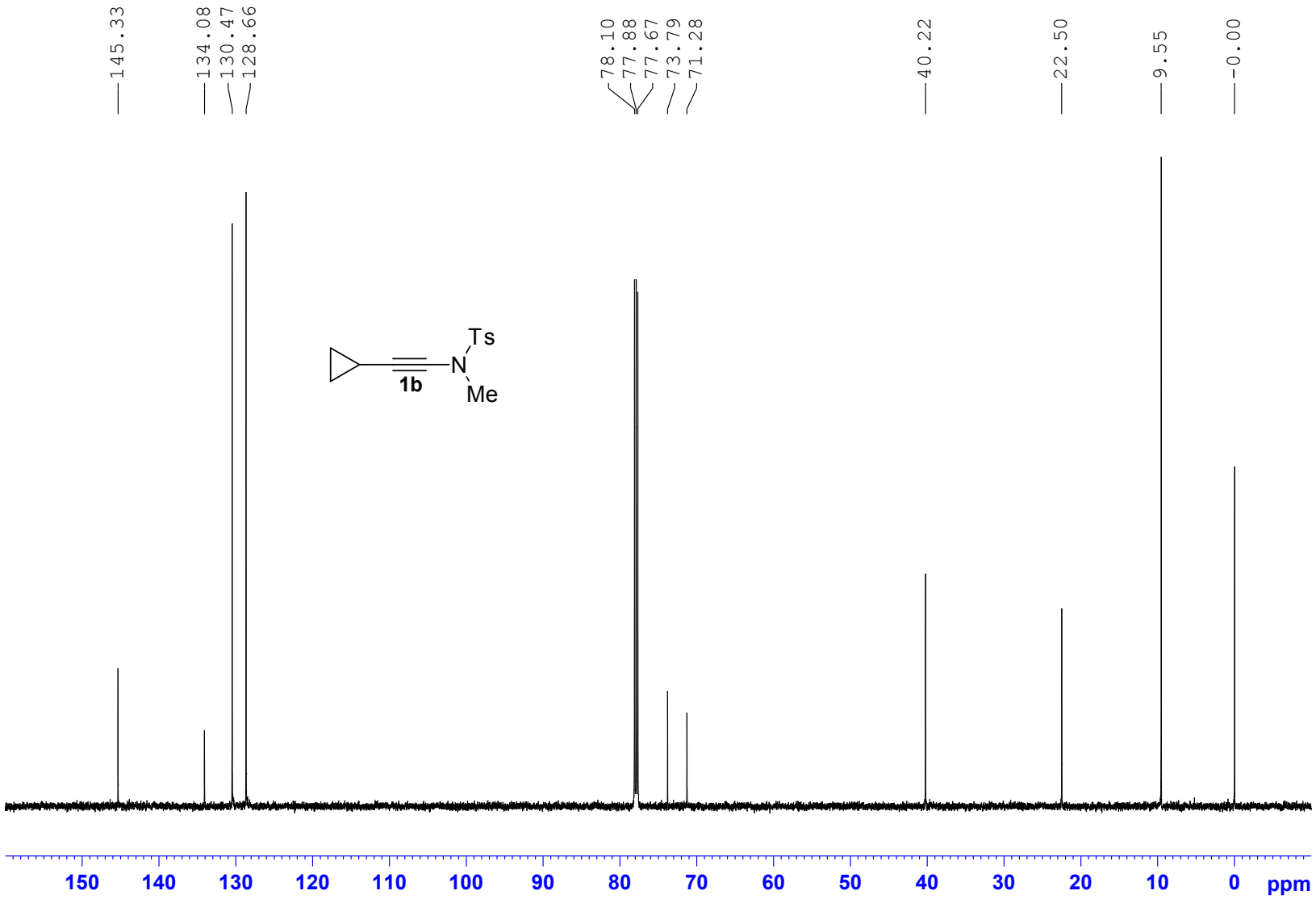
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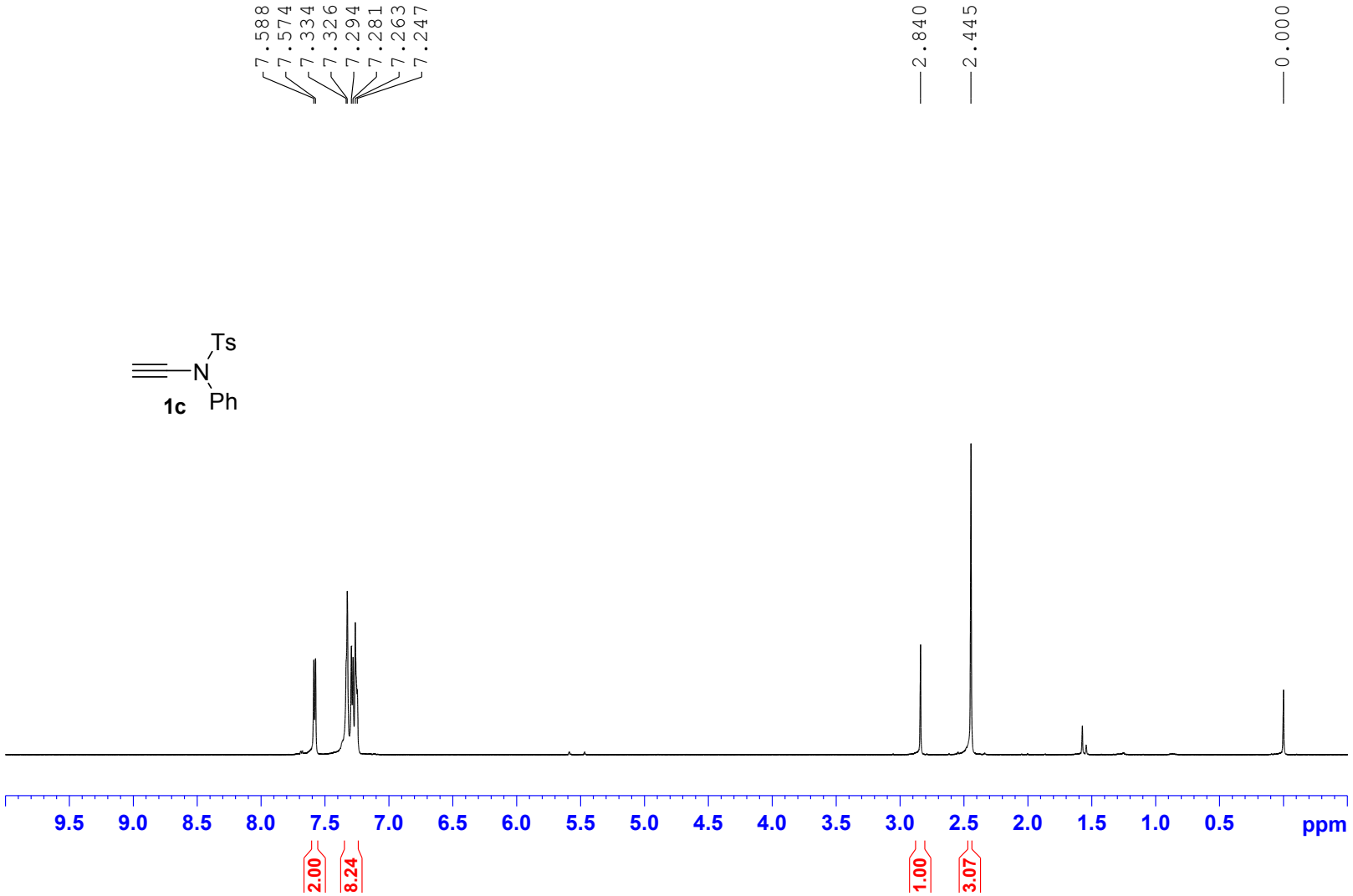
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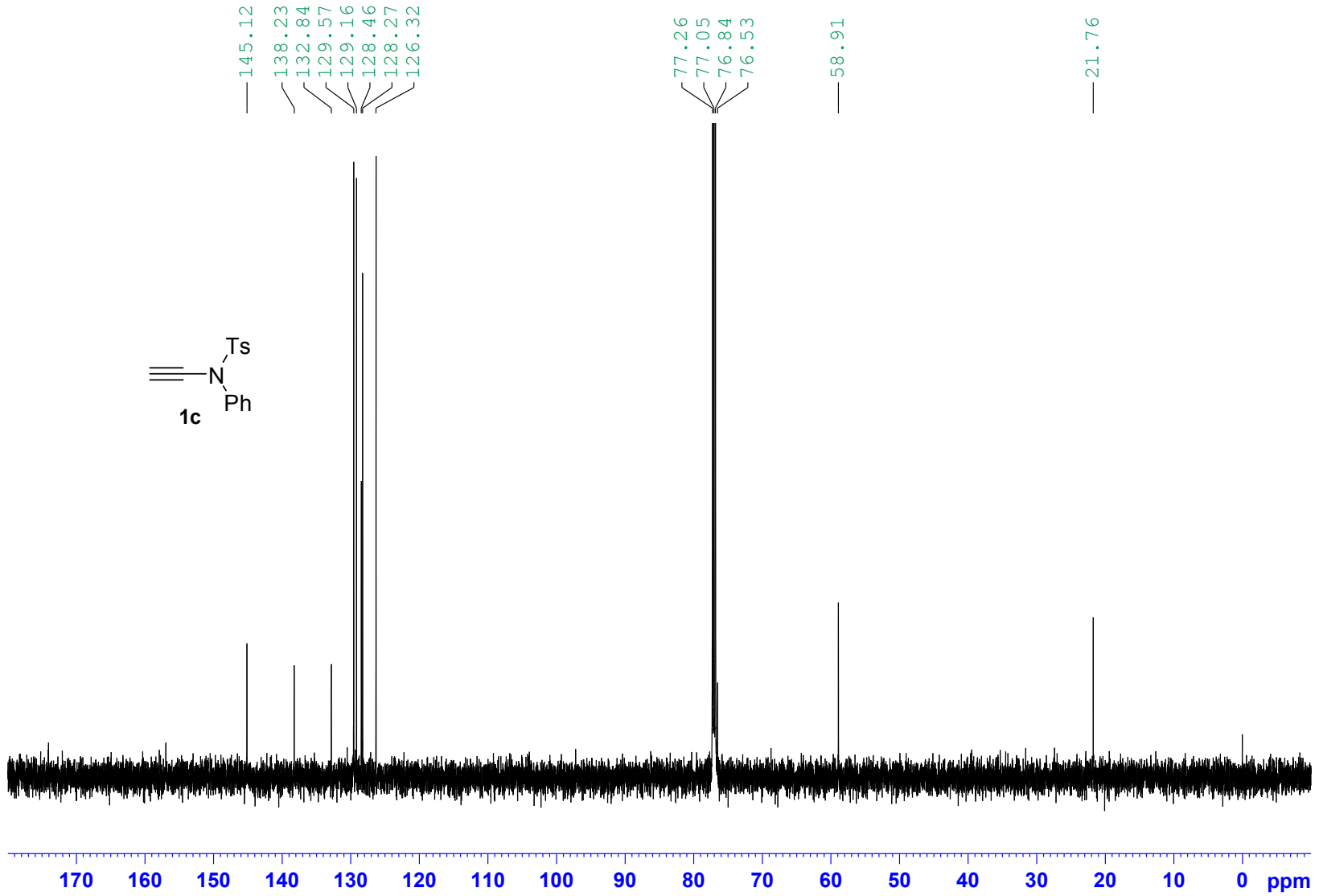
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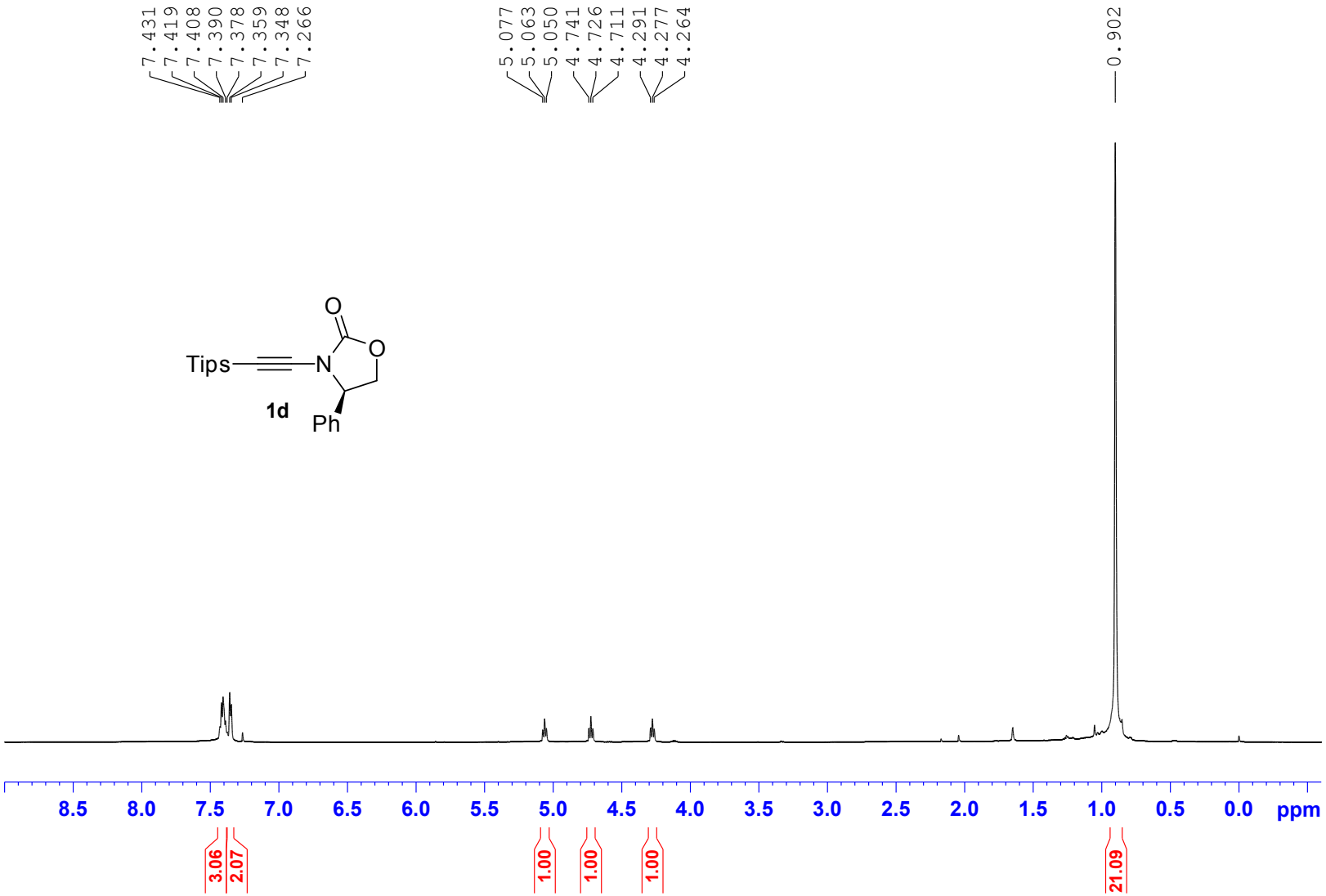
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O
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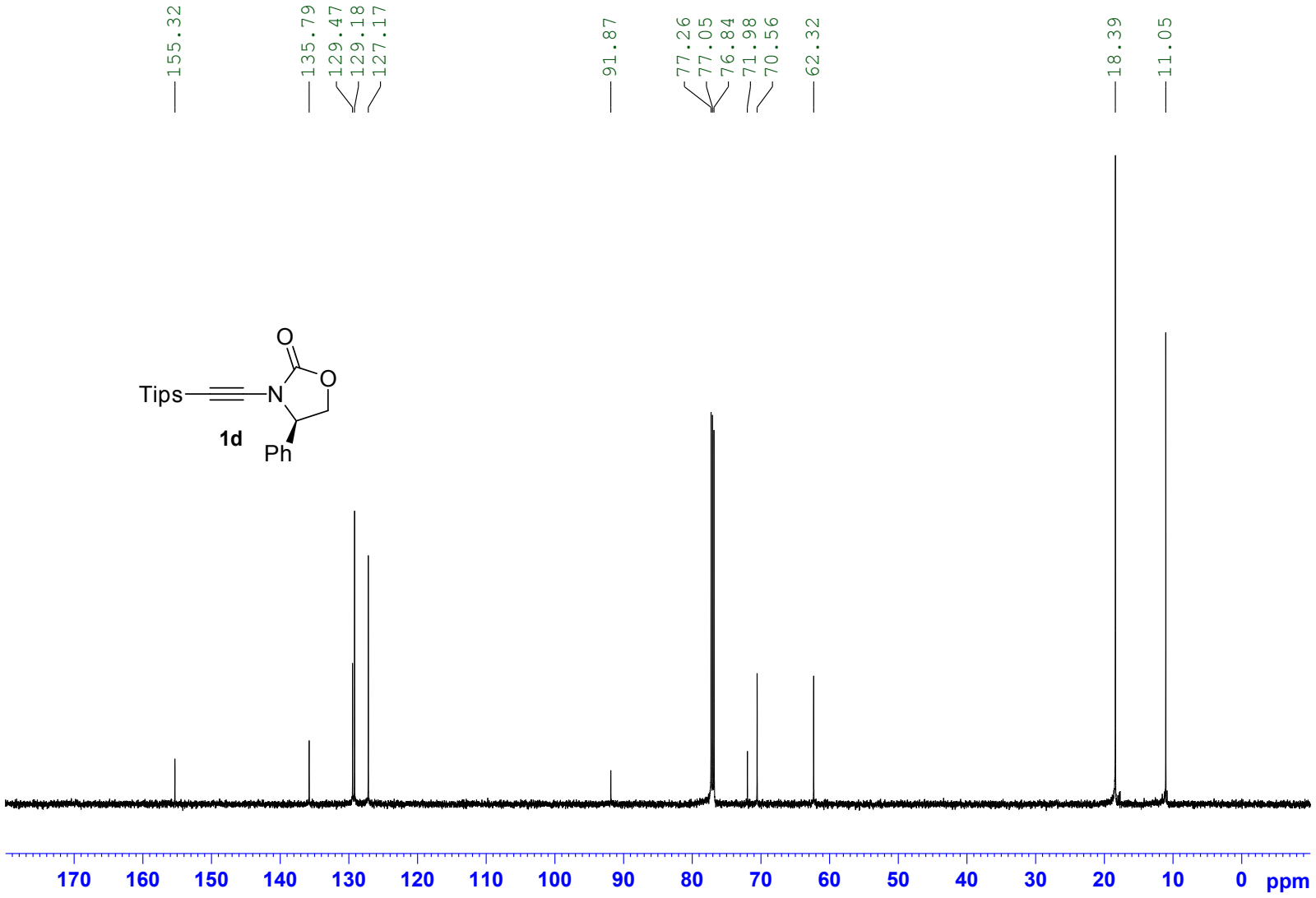
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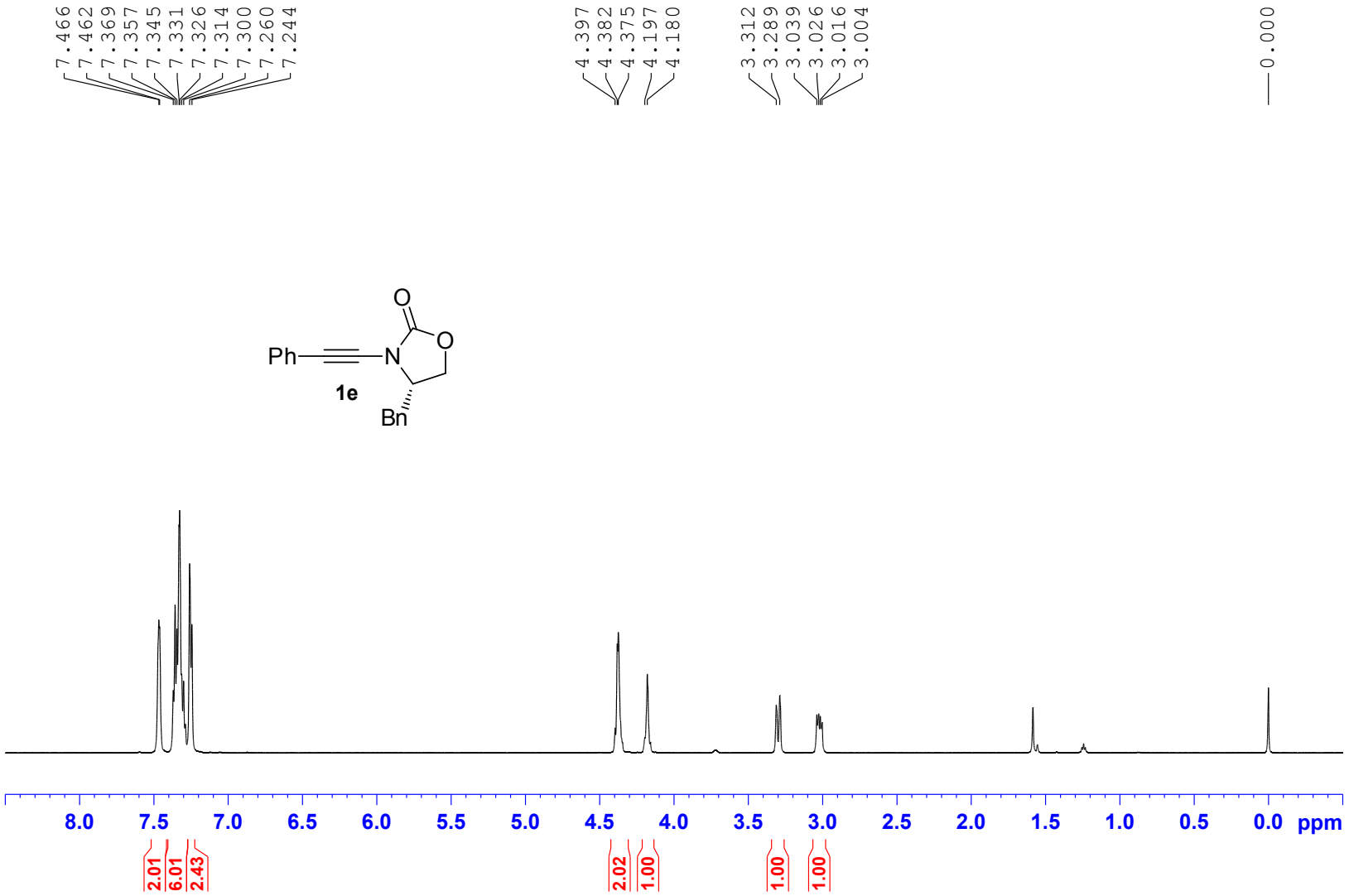
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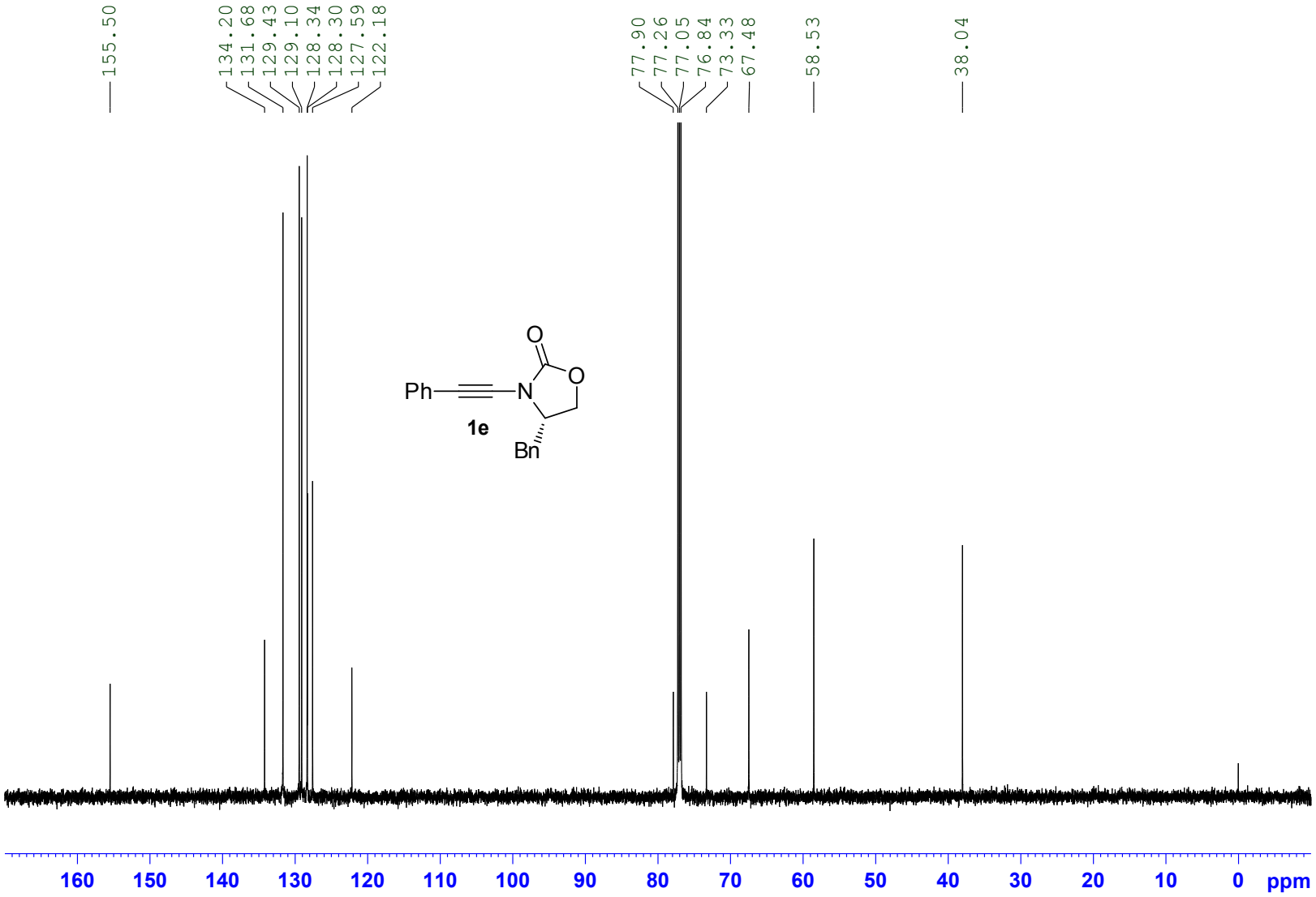
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O
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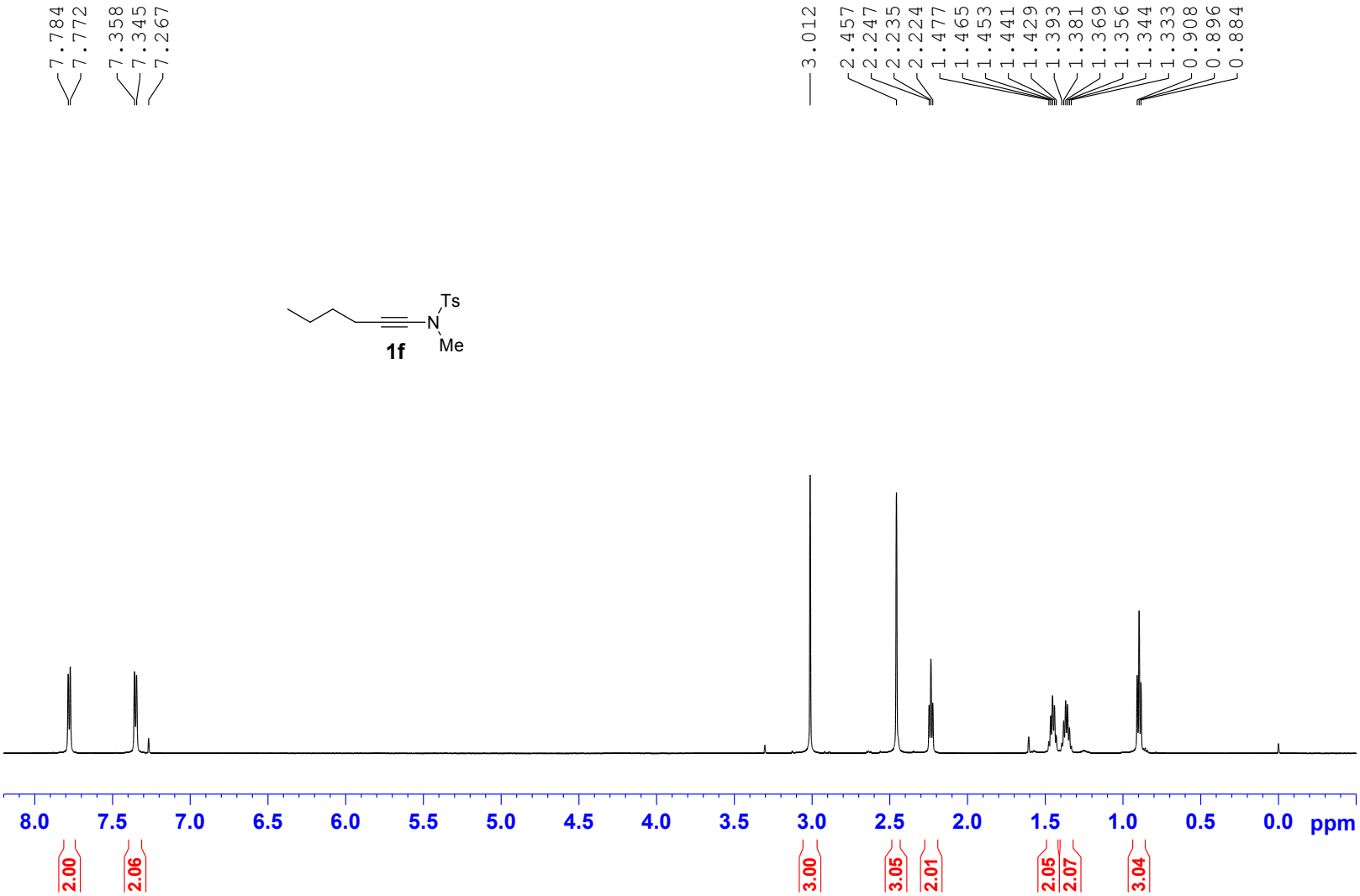
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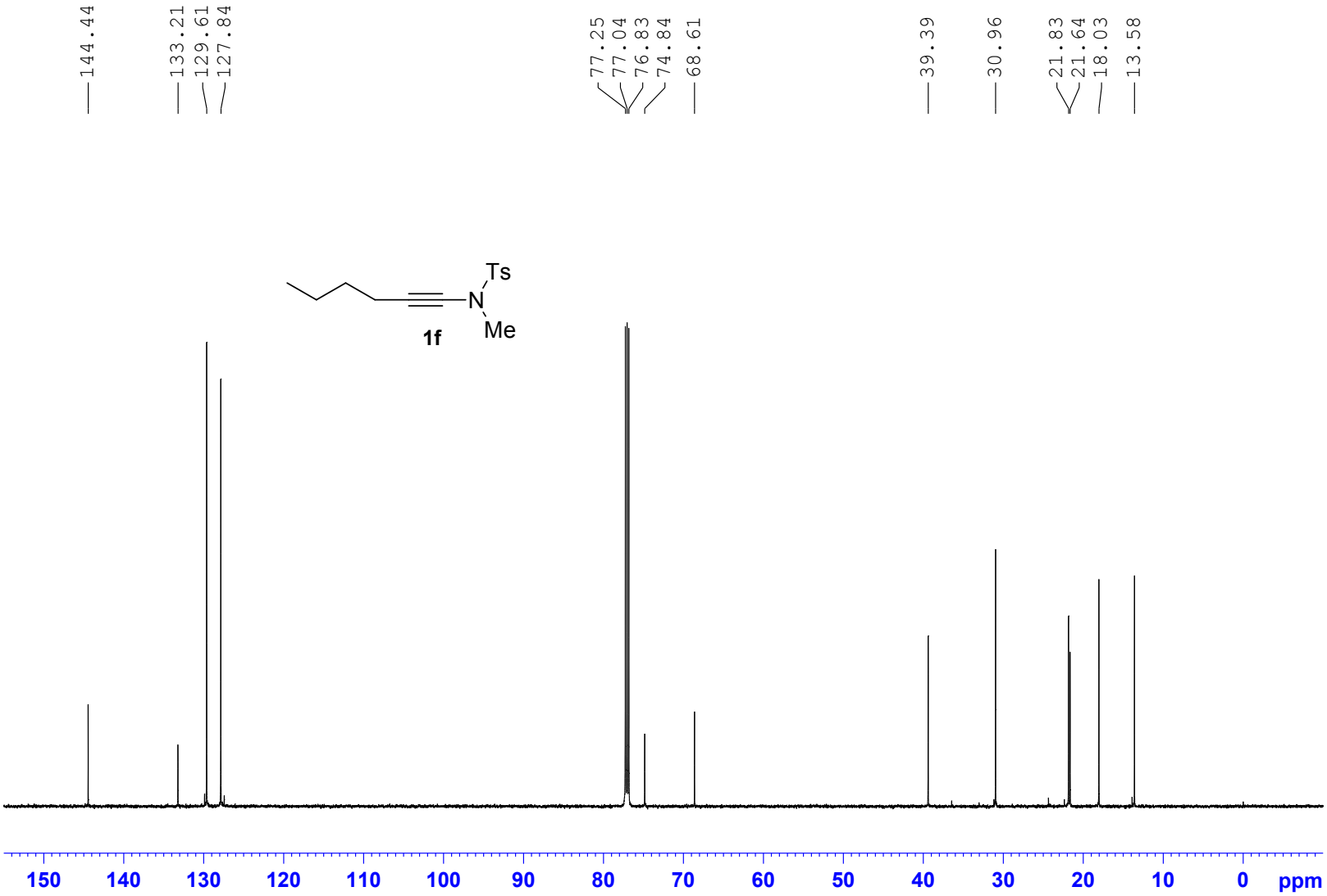
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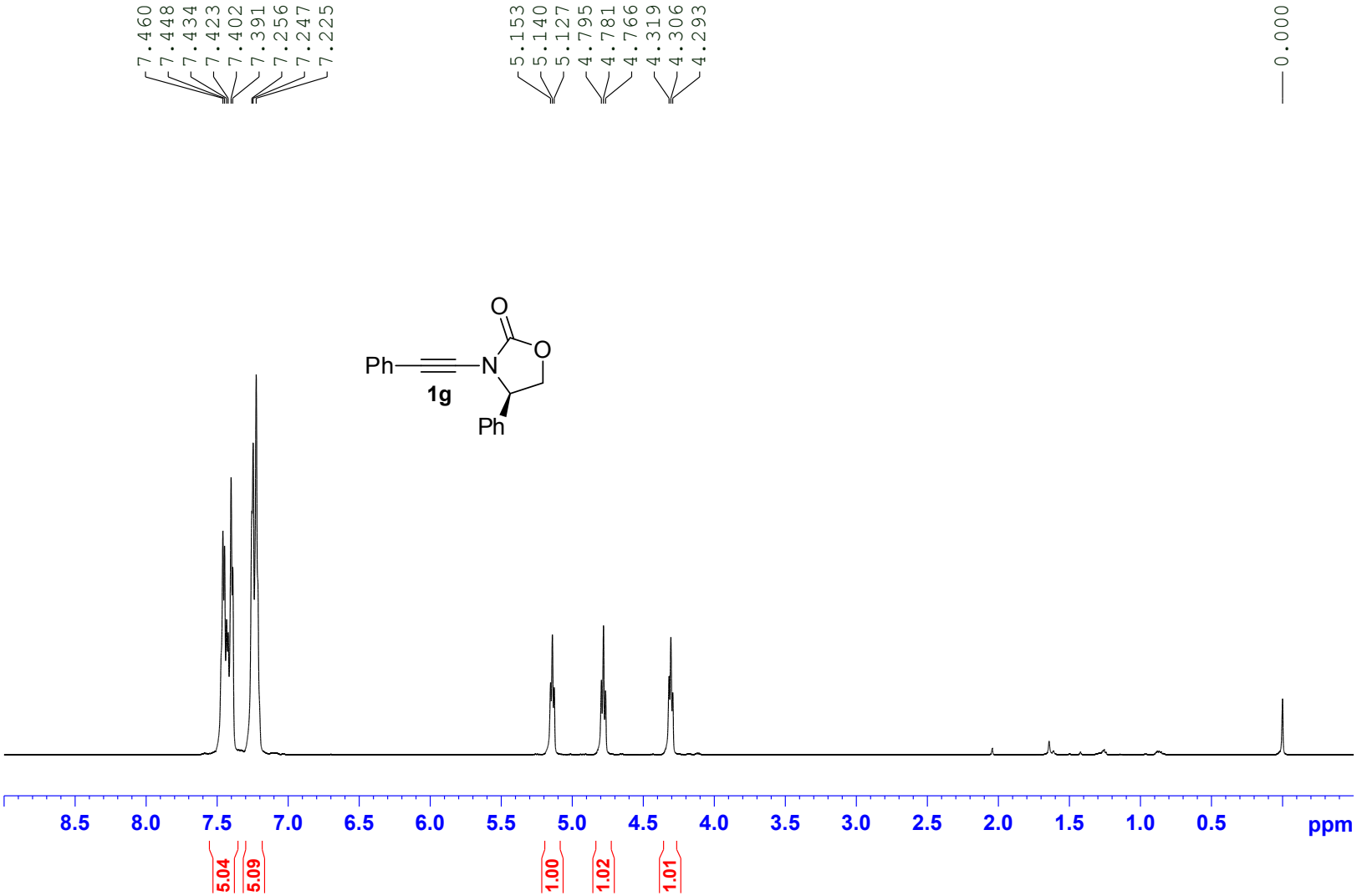
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Ph
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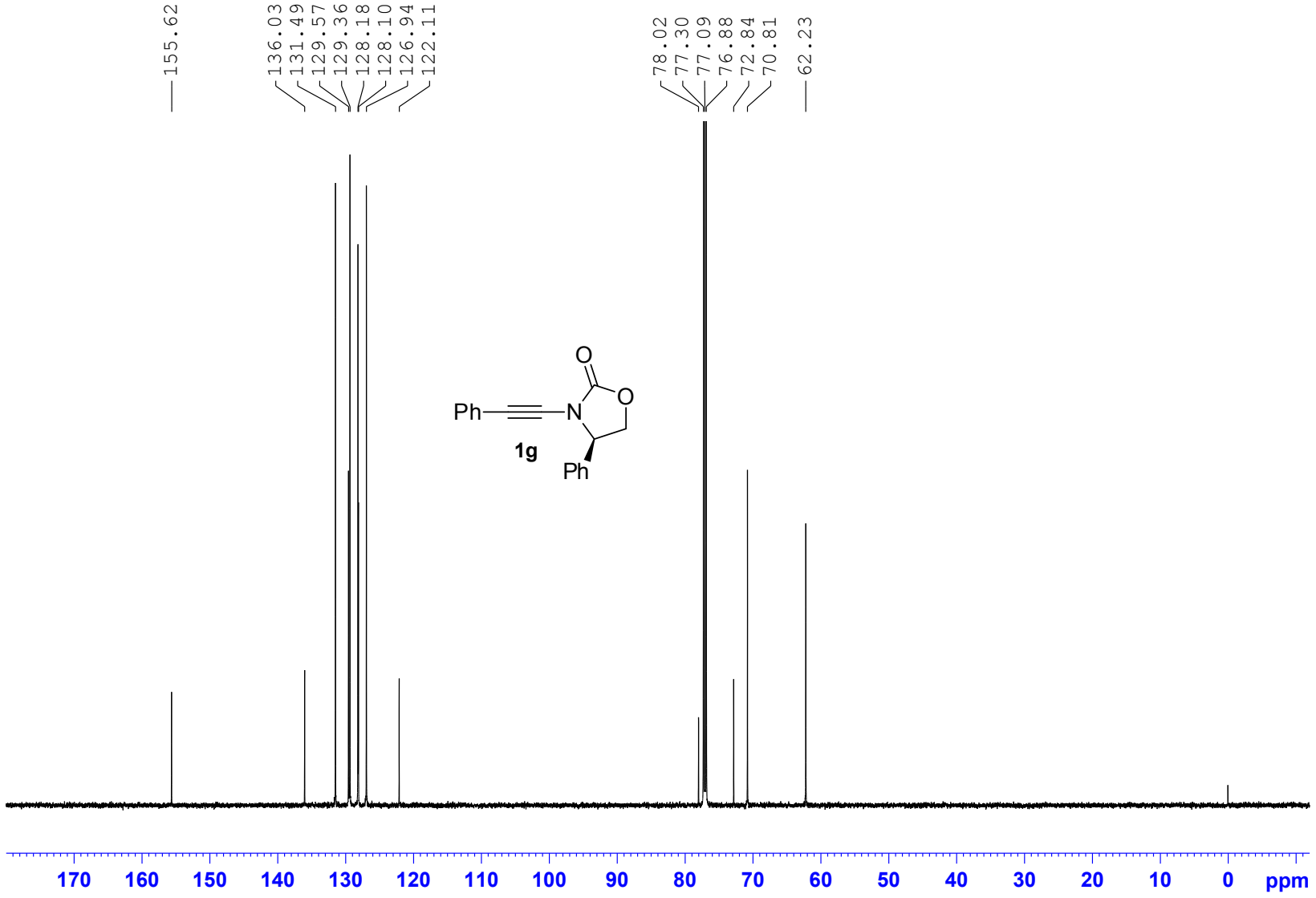
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77.30
77.09
76.88
72.84
70.81
62.23
O
O
N
Ph
Ph
1g
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130
120
110
100
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80
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60
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20
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0
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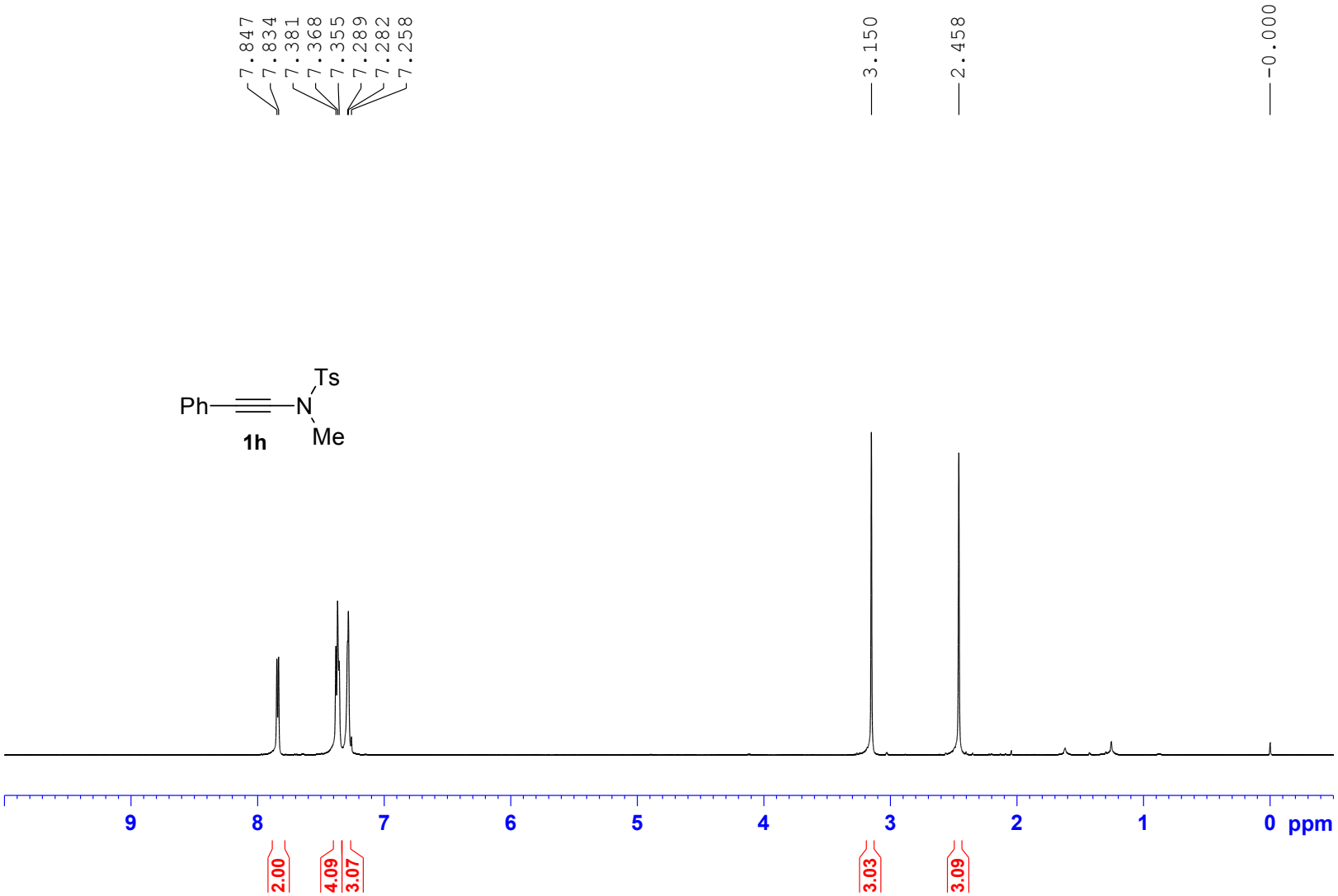
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Ts
Me
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7
6
5
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2
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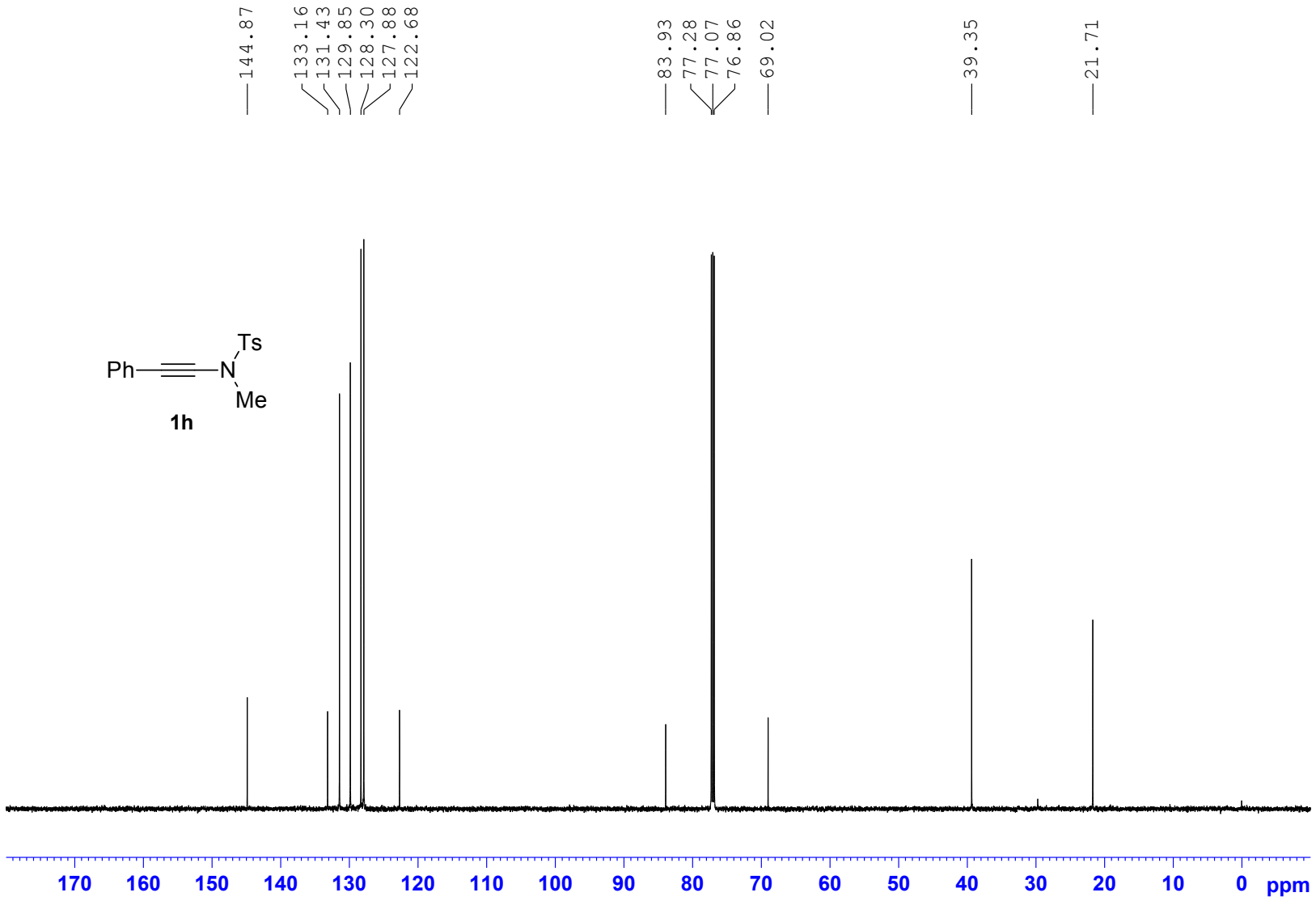
3.07
3.03
3.09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76.86
69.02
39.35
21.71
Ts
Ph
N
Me
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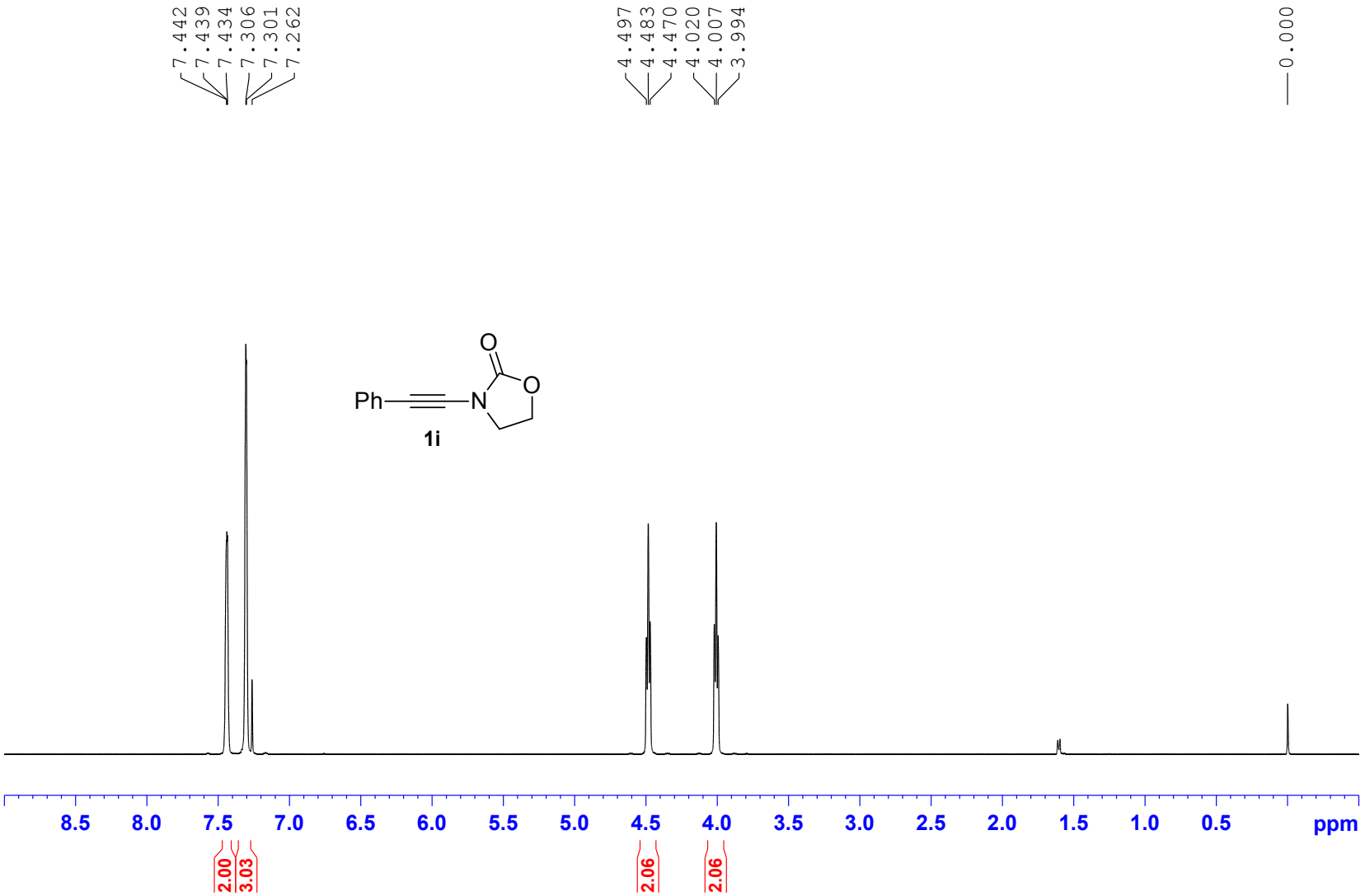
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4.497
4.483
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4.007
3.994
0.000
Ph
N
O
O
1i
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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2.5
2.0
1.5
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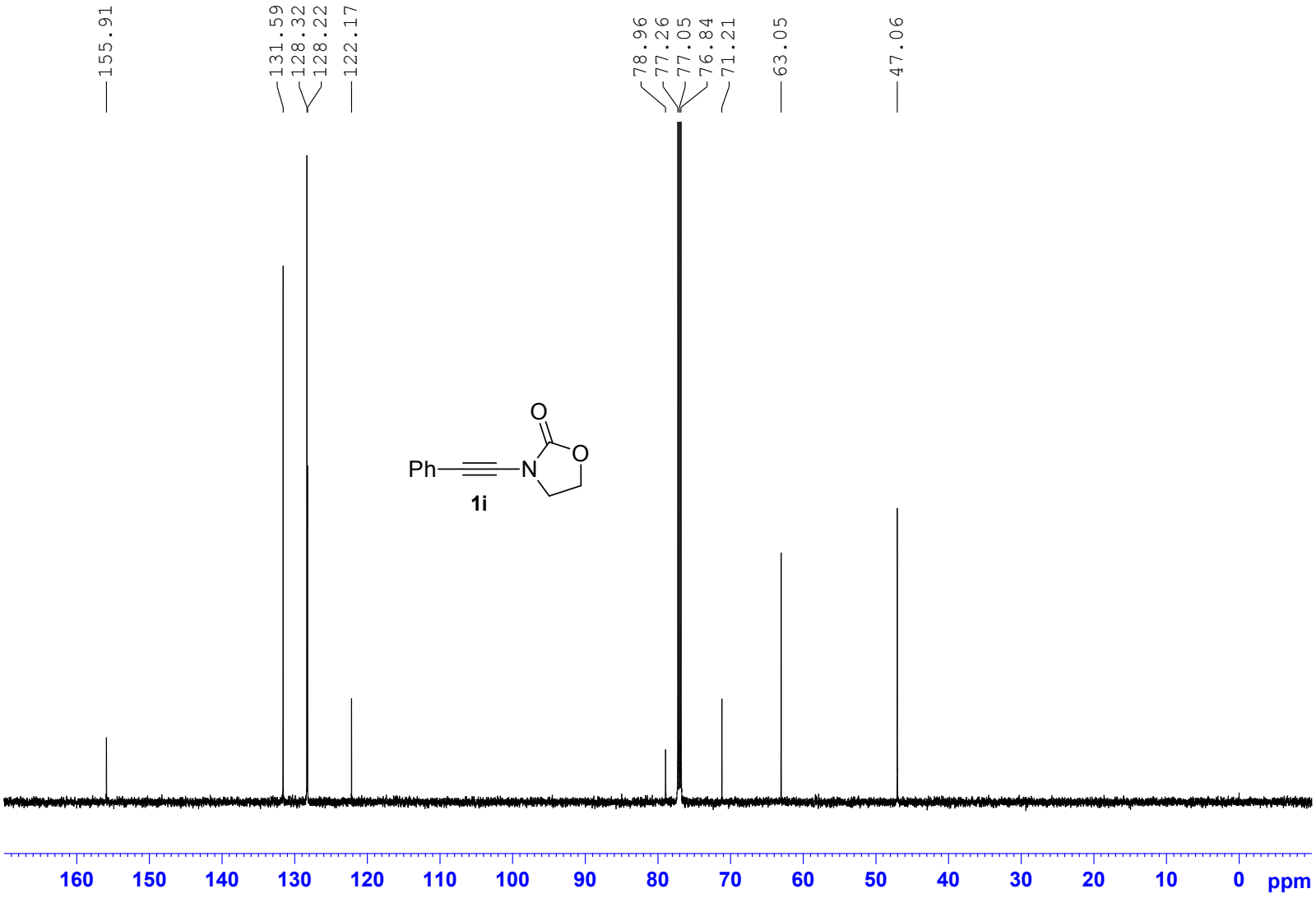
2.06
2.06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78.96
77.26
77.05
76.84
71.21
63.05
47.06
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N
O
O
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140
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120
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100
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60
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30
20
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0
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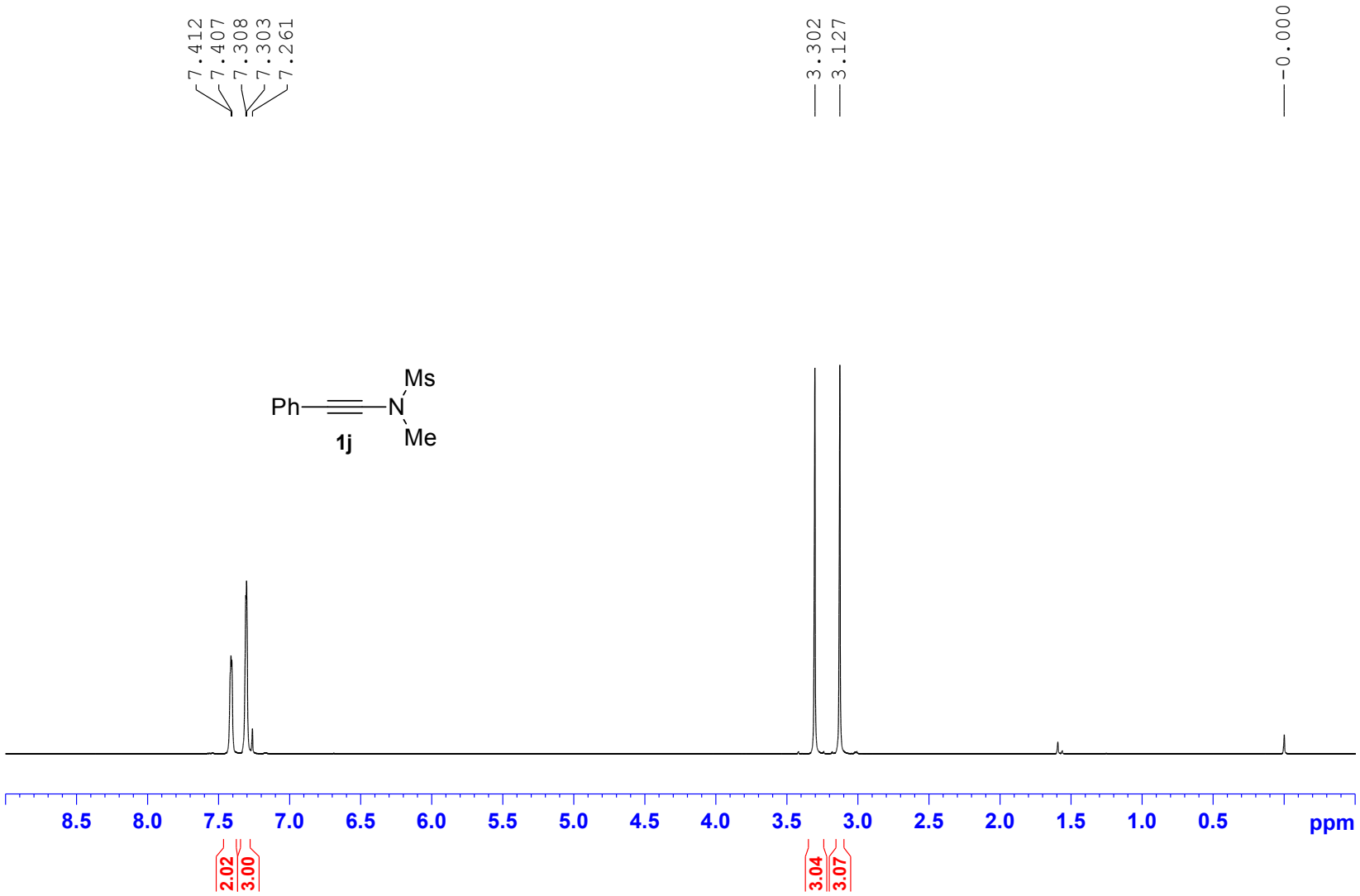
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7.261
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Ph
N
Ms
Me
1j
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
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1.5
1.0
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ppm
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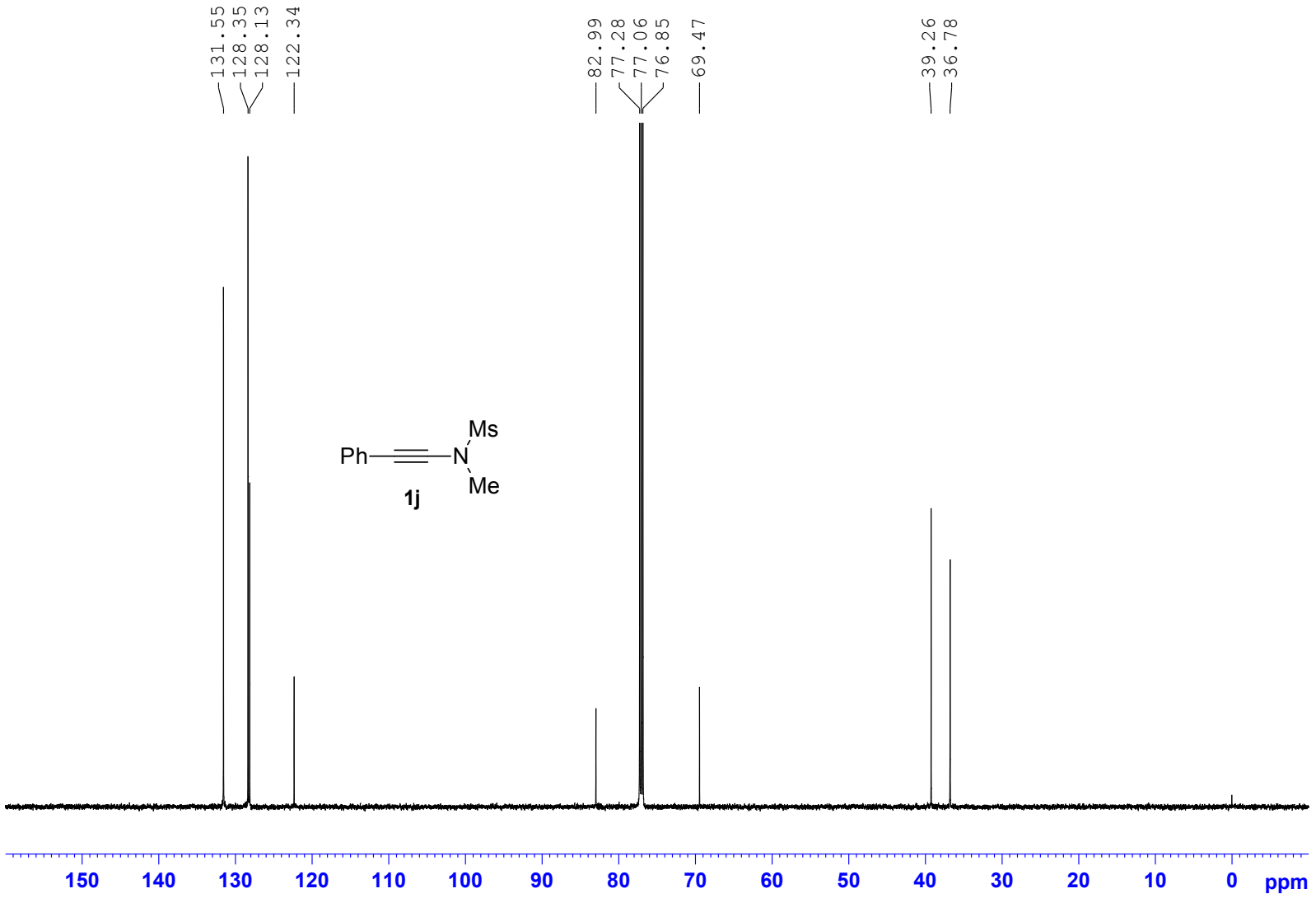
3.00
3.04
3.07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128.13
122.34
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77.28
77.06
76.85
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39.26
36.78
Ph
N
Ms
Me
1j
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140
130
120
110
100
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80
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60
50
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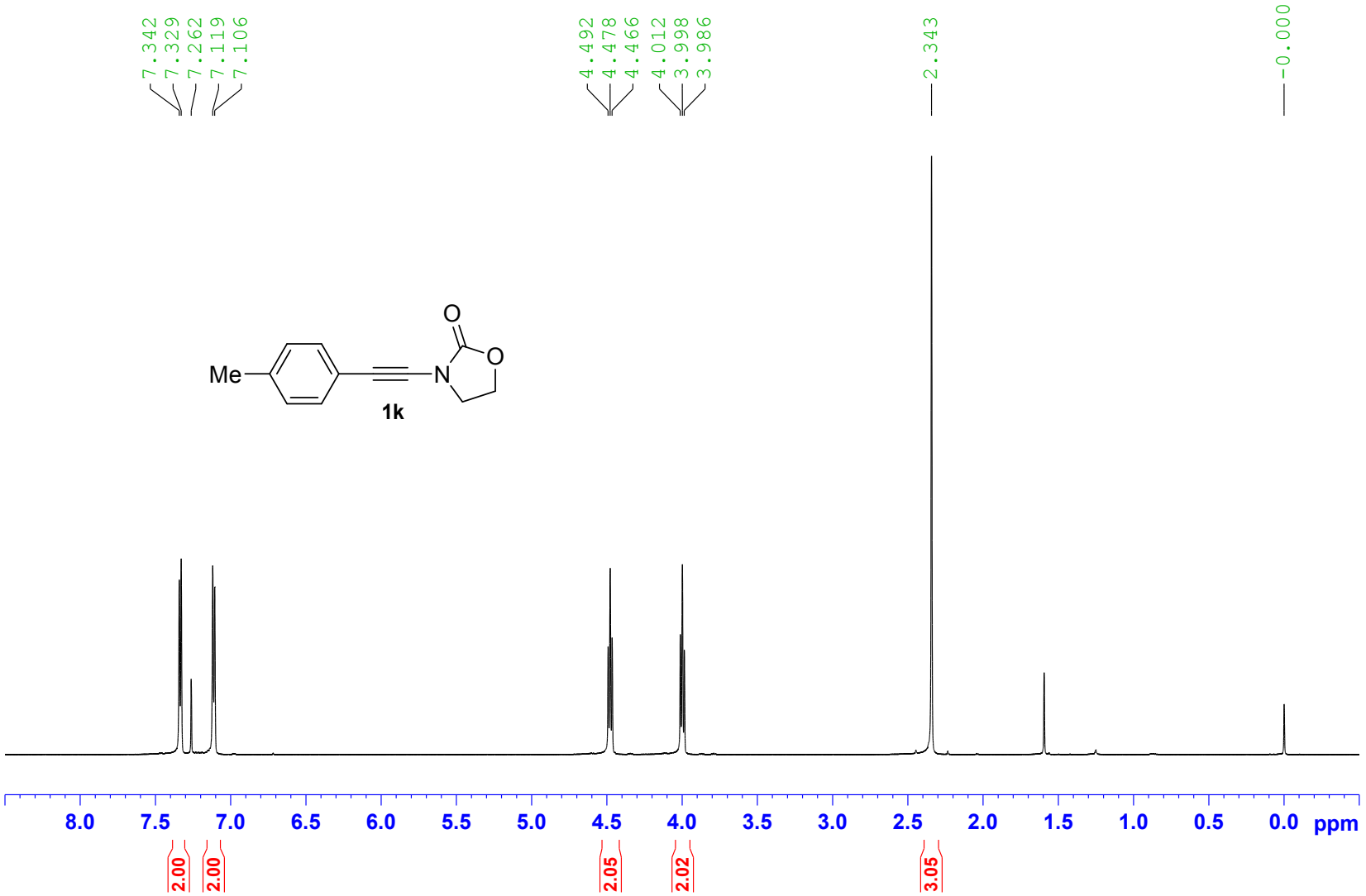
30
20
10
0
ppm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7.329
7.262
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4.466
4.012
3.998
3.986
2.343
-0.000
Me
N
O
O
1k
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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1.5
1.0
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0.0
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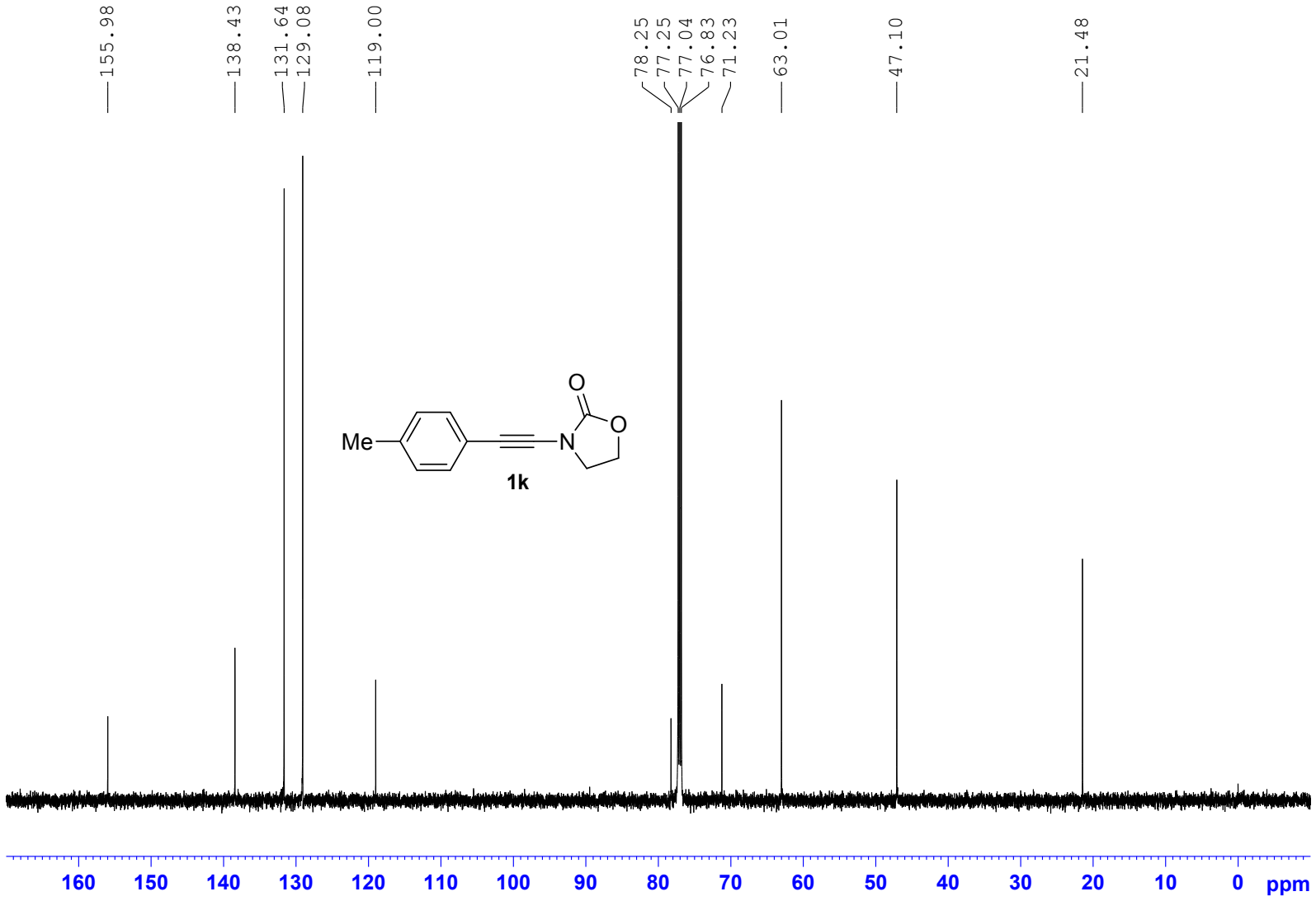
2.00
2.05
2.02
3.05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77.25
77.04
76.83
71.23
63.01
47.10
21.48
Me
N
O
O
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140
130
120
110
100
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60
50
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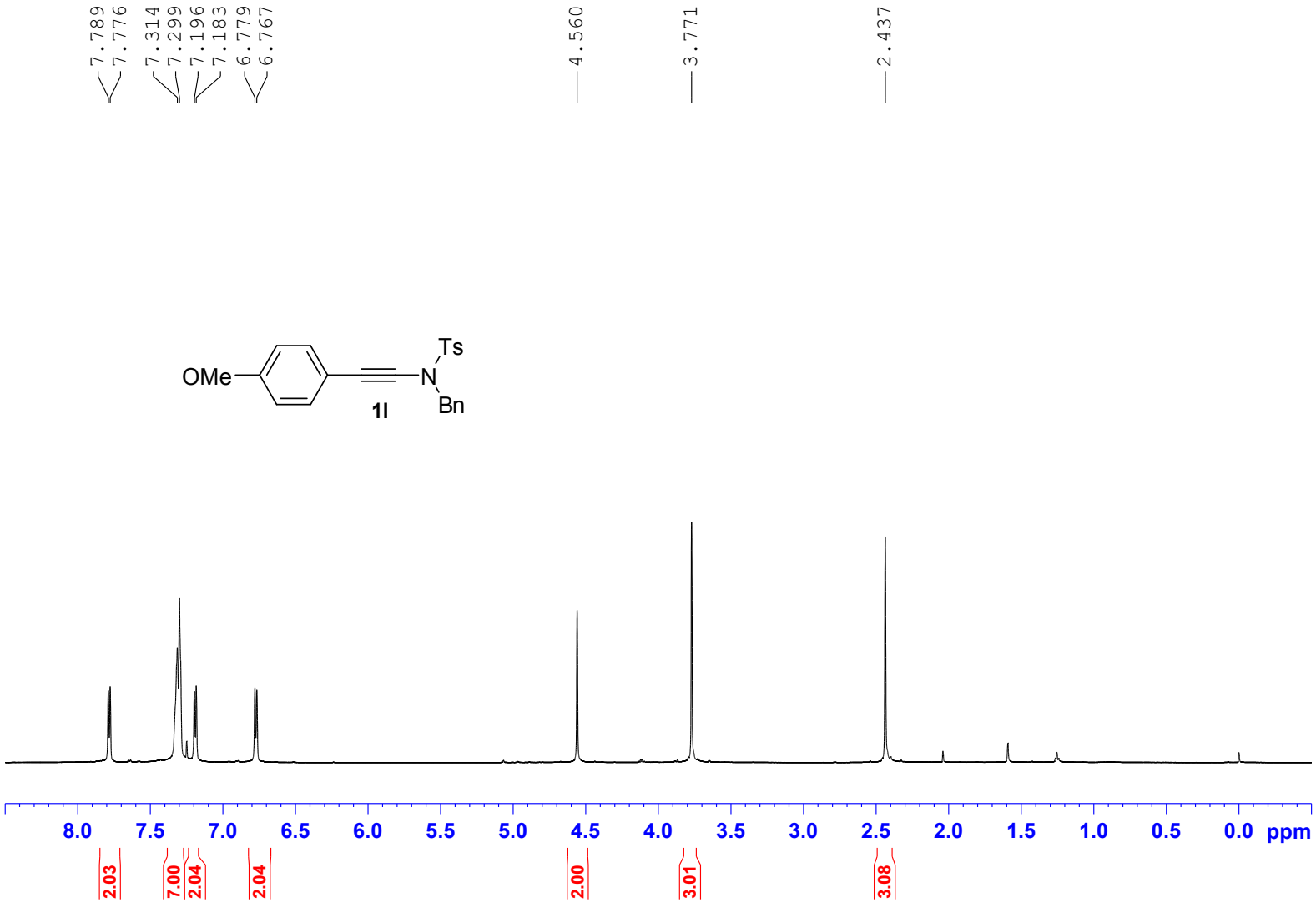
30
20
10
0
ppm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7.776
7.314
7.299
7.196
7.183
6.779
6.767
4.560
3.771
2.437
OMe
Ts
N
Bn
1l
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
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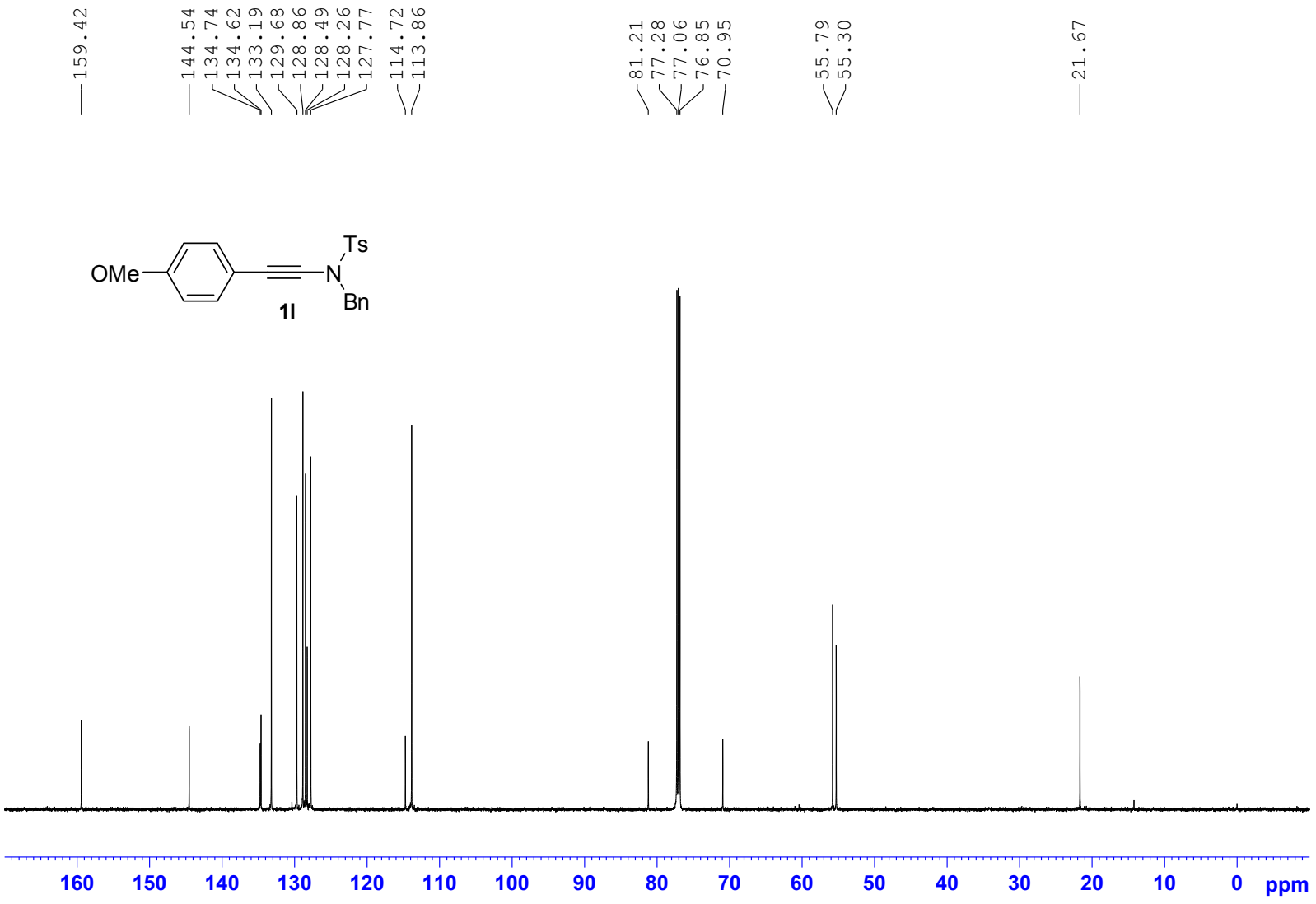
7.00
2.04
2.04
2.00
3.01
3.08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133.19
129.68
128.86
128.49
128.26
127.77
114.72
113.86
81.21
77.28
77.06
76.85
70.95
55.79
55.30
21.67
OMe
N
Ts
Bn
1l
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140
130
120
110
100
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60
50
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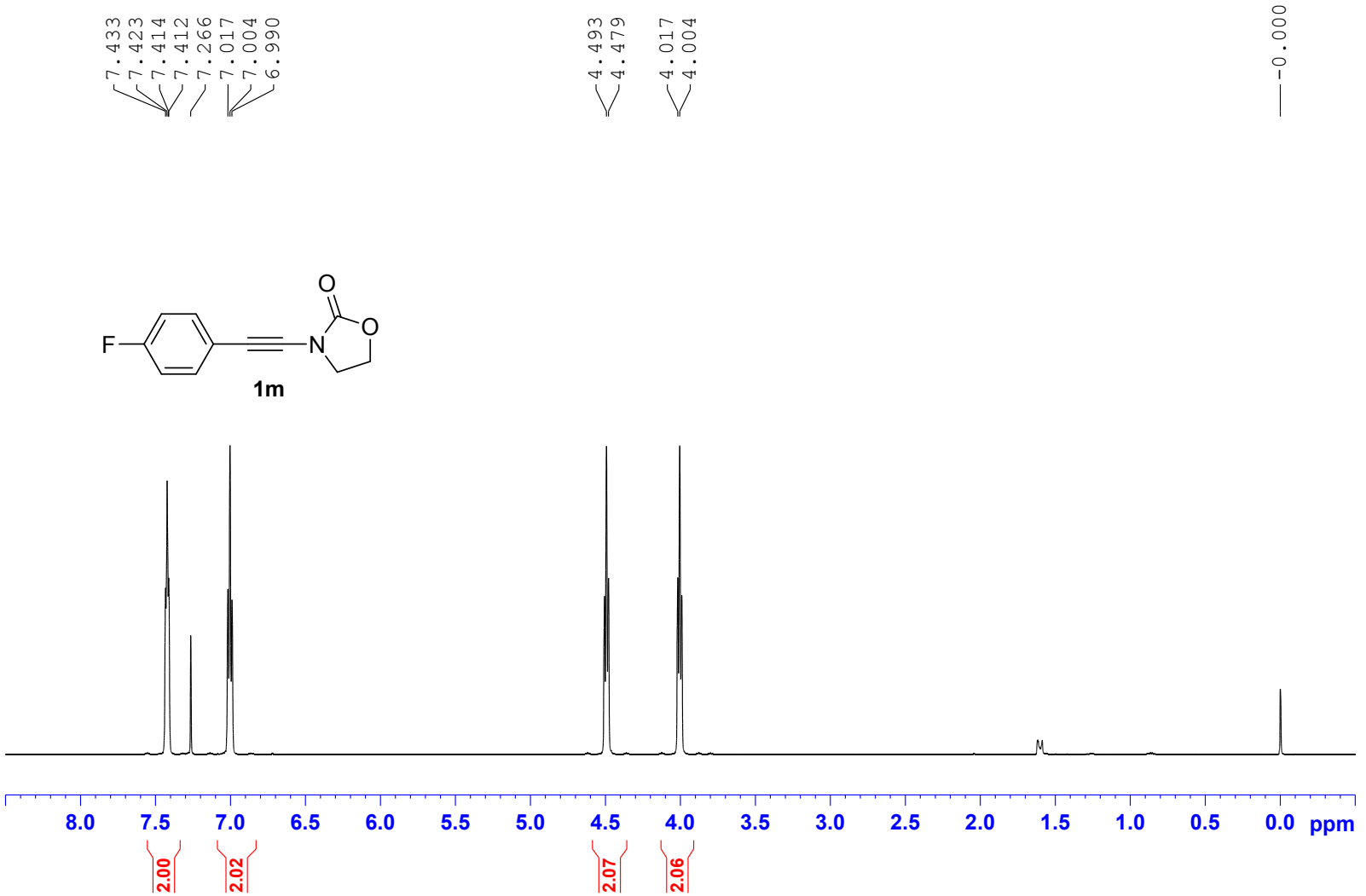
20
10
0
ppm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7.423
7.414
7.412
7.266
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7.004
6.990
4.493
4.479
4.017
4.004
0.000
O
O
F
N
1m
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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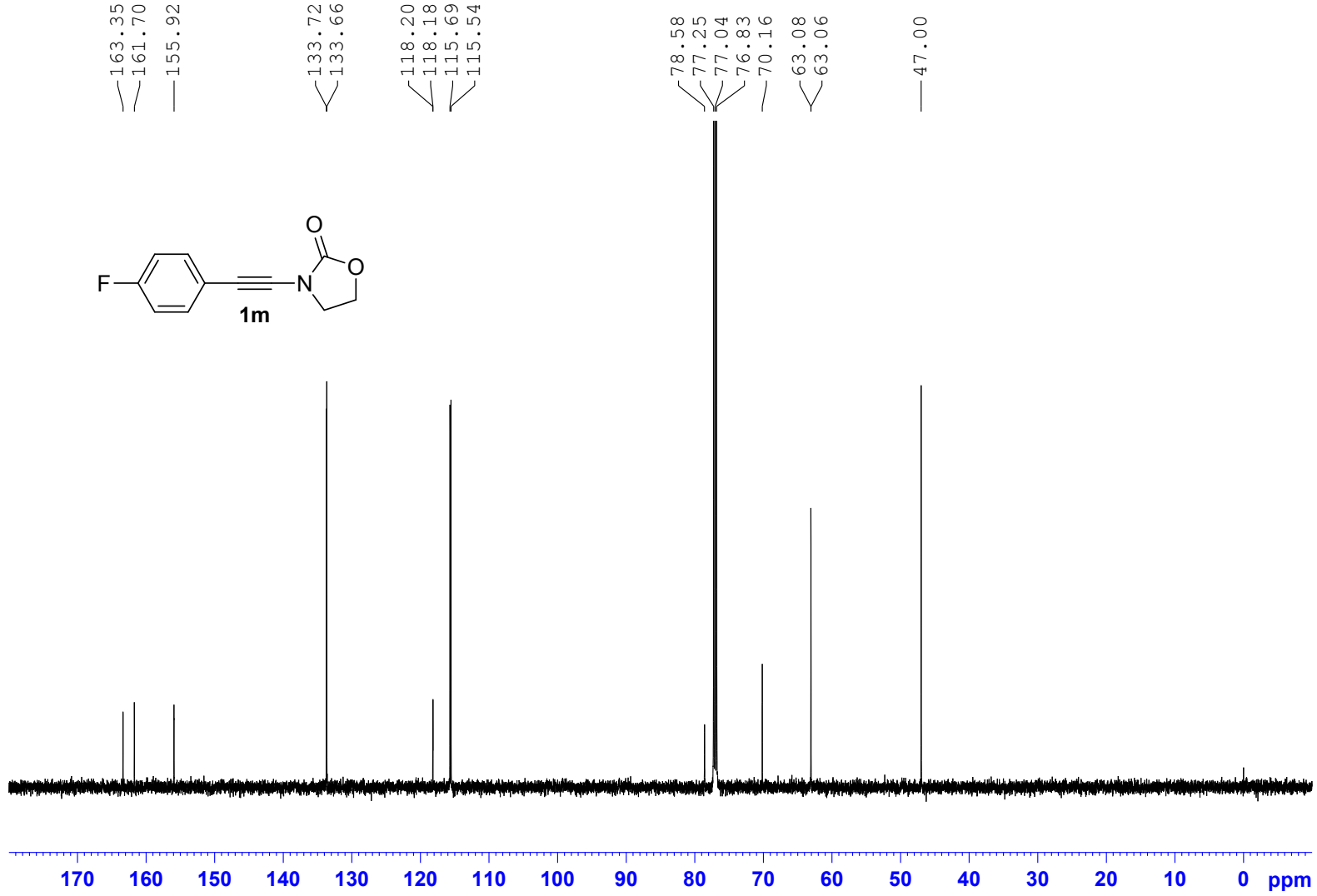
2.0
1.5
1.0
0.5
0.0
ppm
2.00
2.02
2.07
2.06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118.20
118.18
115.69
115.54
78.58
77.25
77.04
76.83
70.16
63.08
63.06
47.00
O
O
N
F
1m
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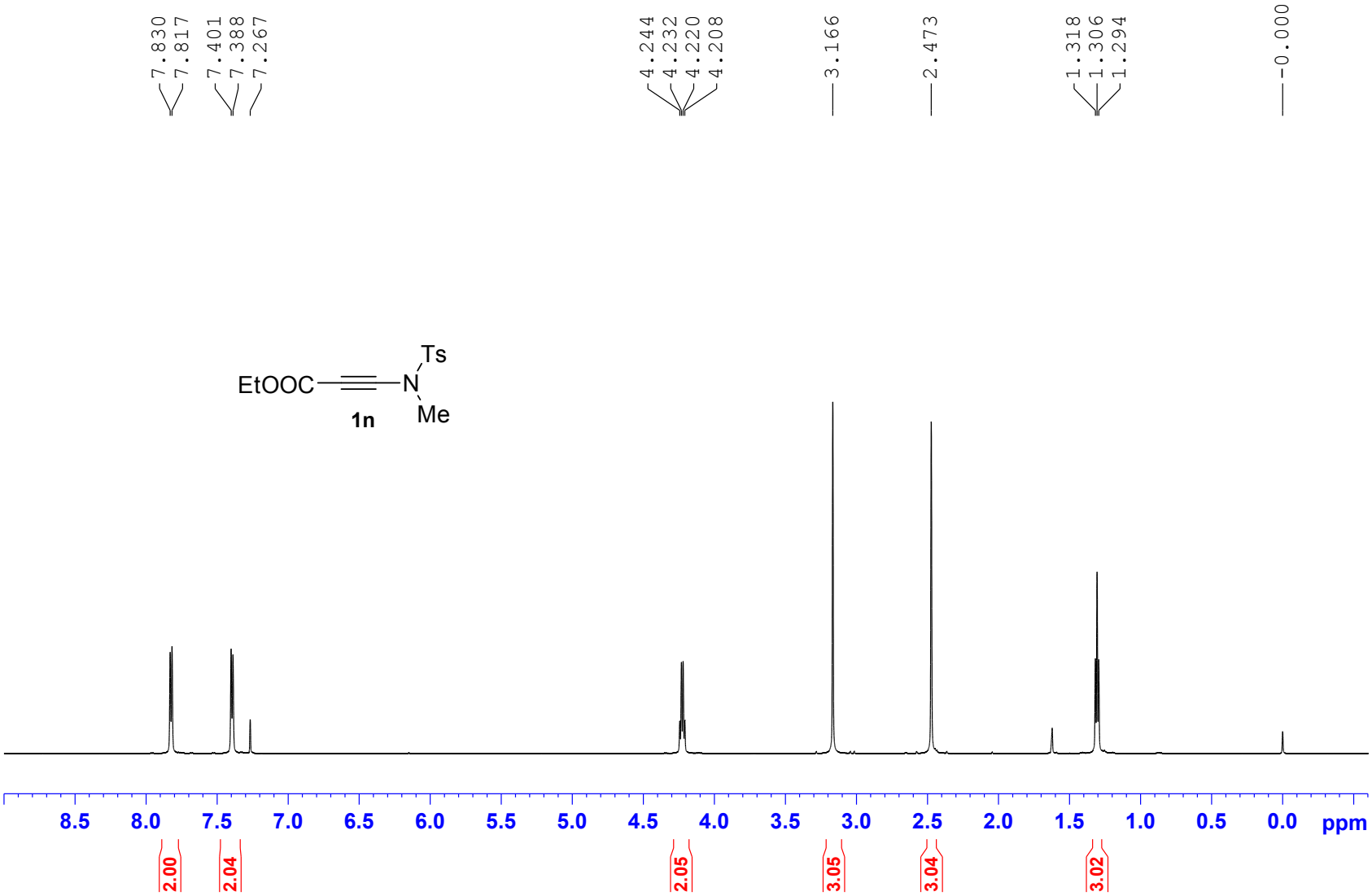
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm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4.220
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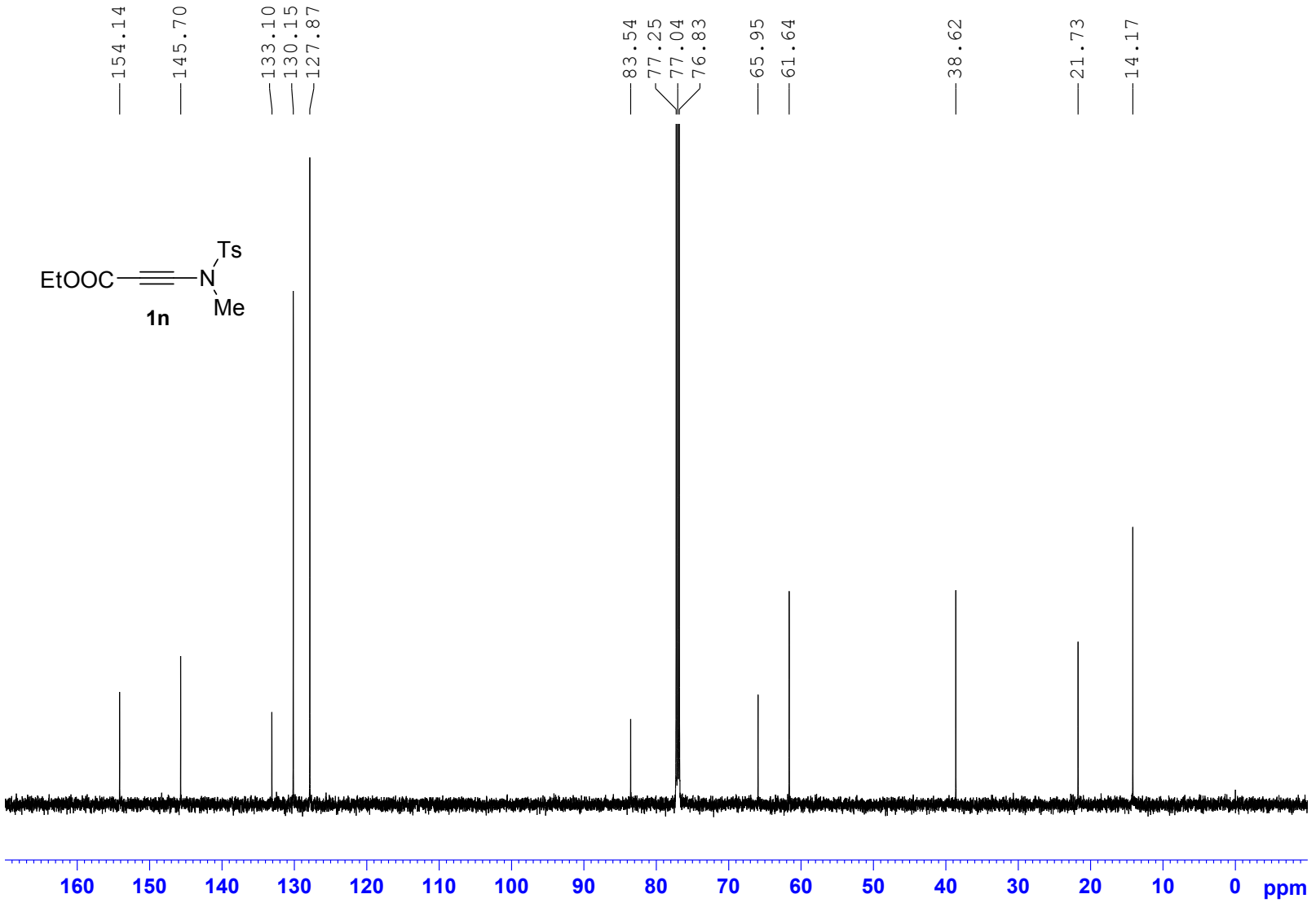
2.473
1.318
1.306
1.294
0.000
EtOOC
N
Ts
Me
1n
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
2.04
2.05
3.05
3.04
3.02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145.70
133.10
130.15
127.87
83.54
77.25
77.04
76.83
65.95
61.64
38.62
21.73
14.17
EtOOC
N
Ts
Me
1n
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140
130
120
110
100
90
80
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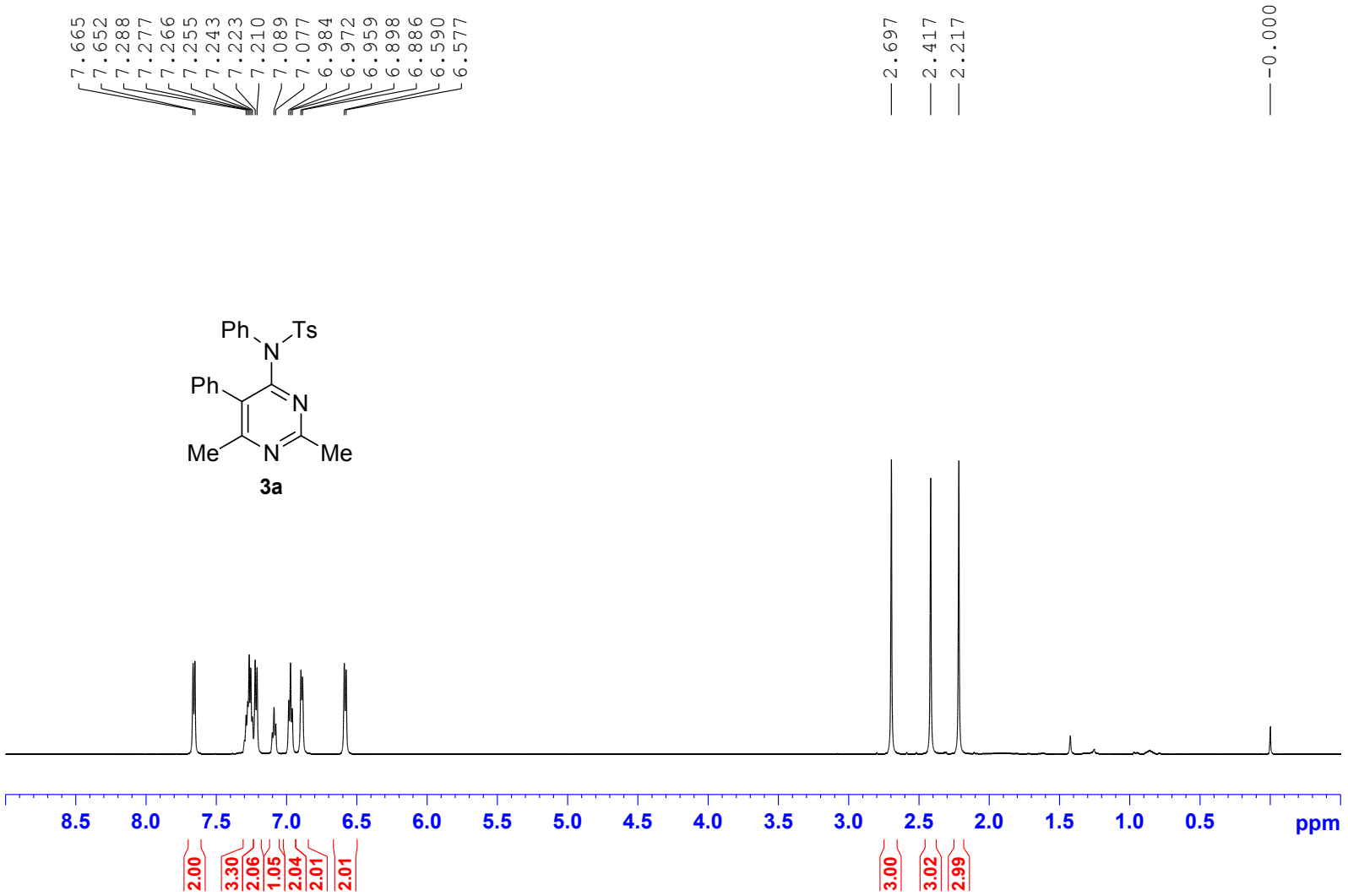
60
50
40
30
20
10
0
ppm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7.223
7.210
7.089
7.077
6.984
6.972
6.959
6.898
6.886
6.590
6.577
2.697
2.417
2.217
0.000
Ph
N
Ts
Ph
N
Me
N
Me
3a
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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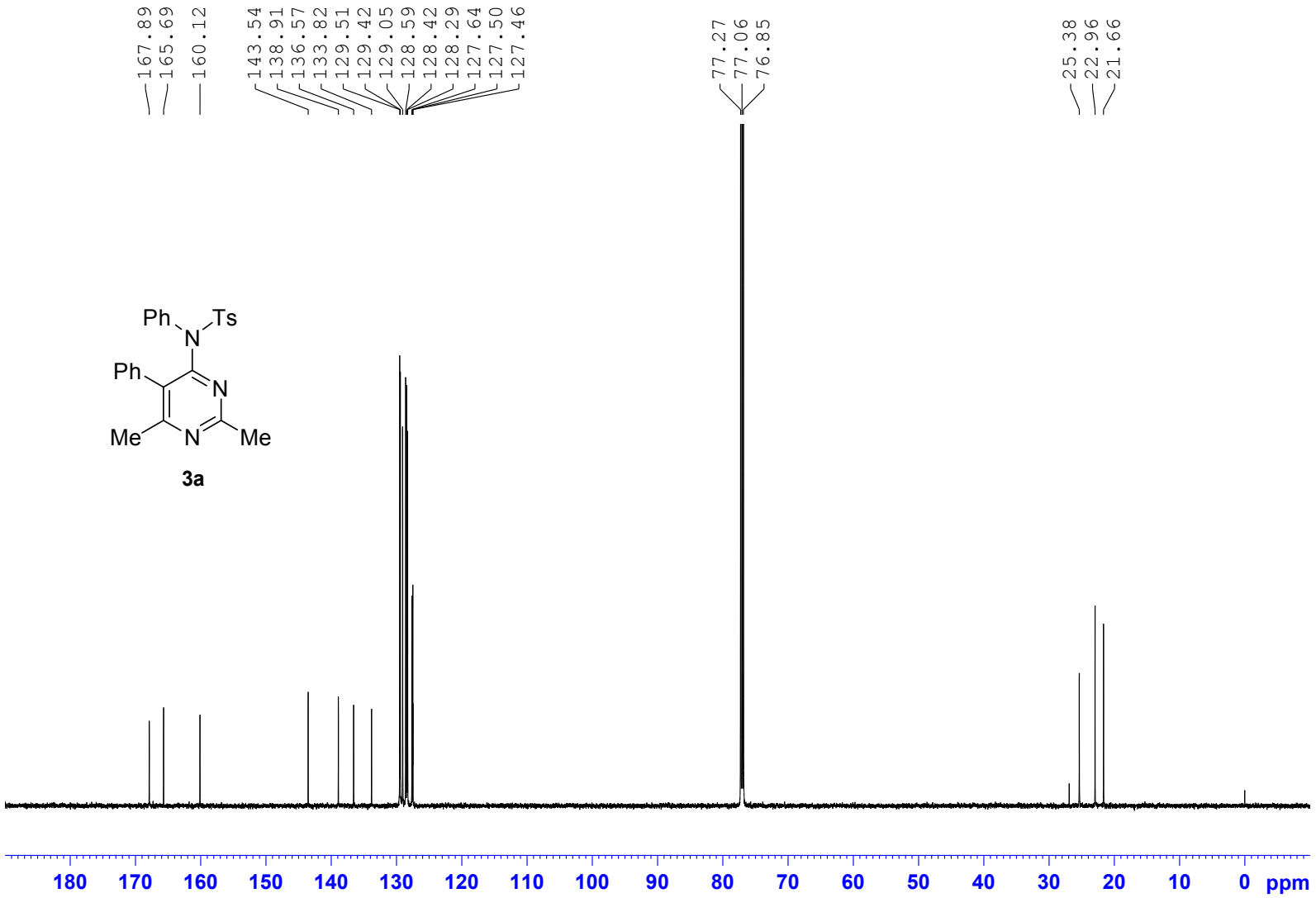
1.05
2.04
2.01
2.01
3.00
3.02
2.99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129.51
129.42
129.05
128.59
128.42
128.29
127.64
127.50
127.46
77.27
77.06
76.85
25.38
22.96
21.66
Ph
Ts
N
Ph
N
Me
N
Me
3a
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150
140
130
120
110
100
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60
50
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30
20
10
0
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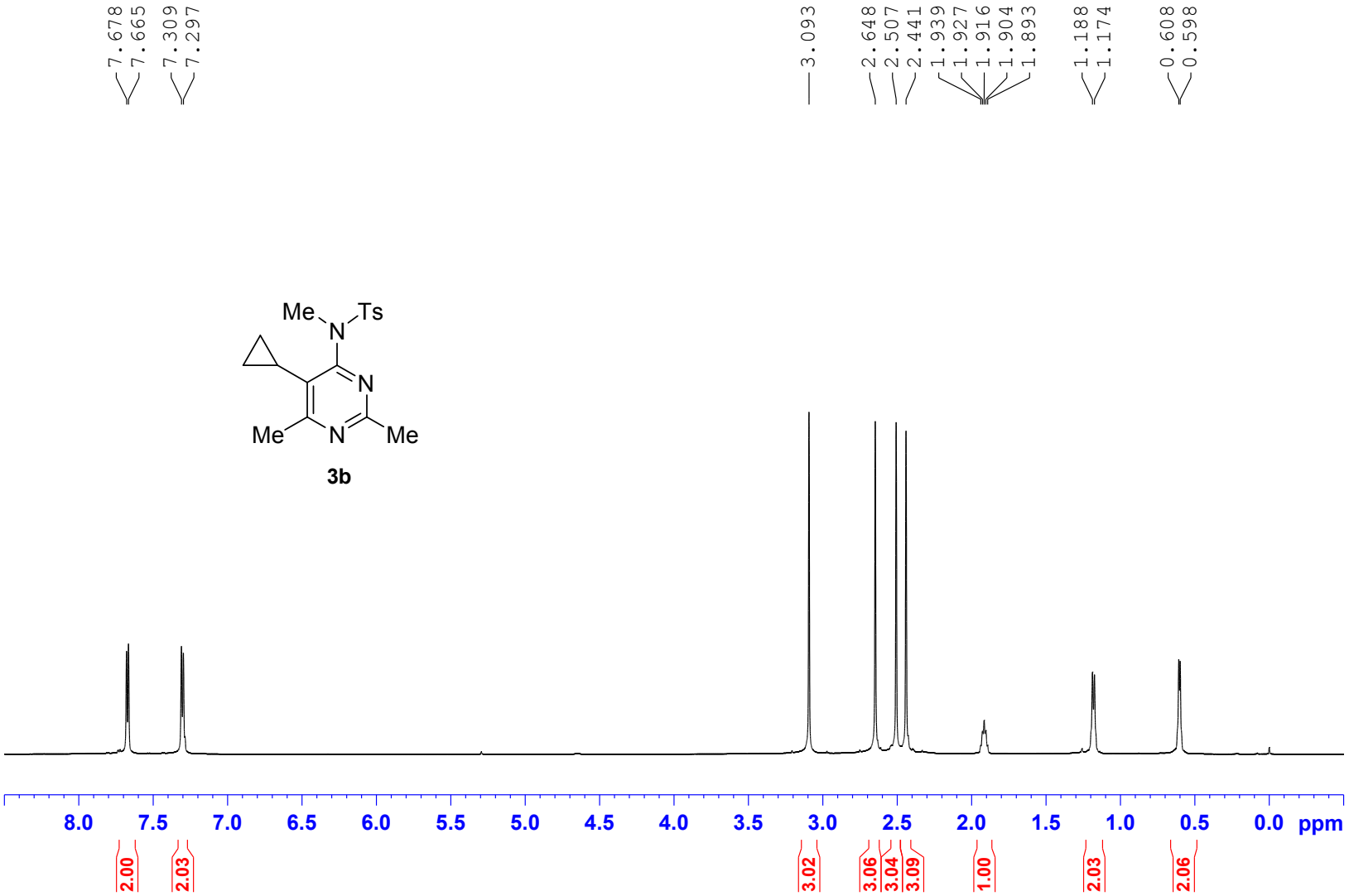
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1.904
1.893
1.188
1.174
0.608
0.598
Me
N
Ts
N
Me
N
Me
3b
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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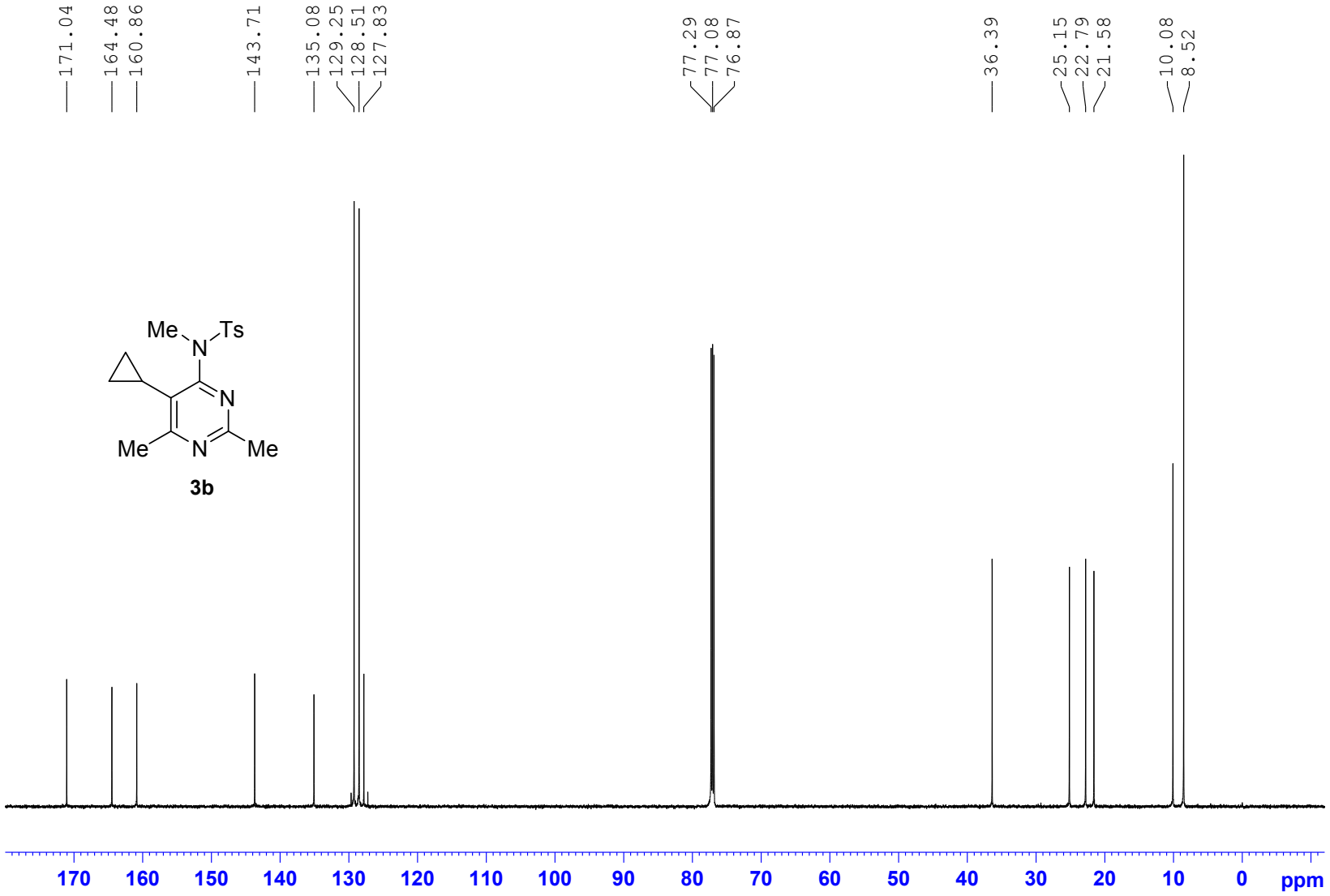
3.02
3.06
3.04
3.09
1.00
2.03
2.06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127.83
77.29
77.08
76.87
36.39
25.15
22.79
21.58
10.08
8.52
Me
N
Ts
N
Me
N
Me
3b
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150
140
130
120
110
100
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80
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60
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30
20
10
0
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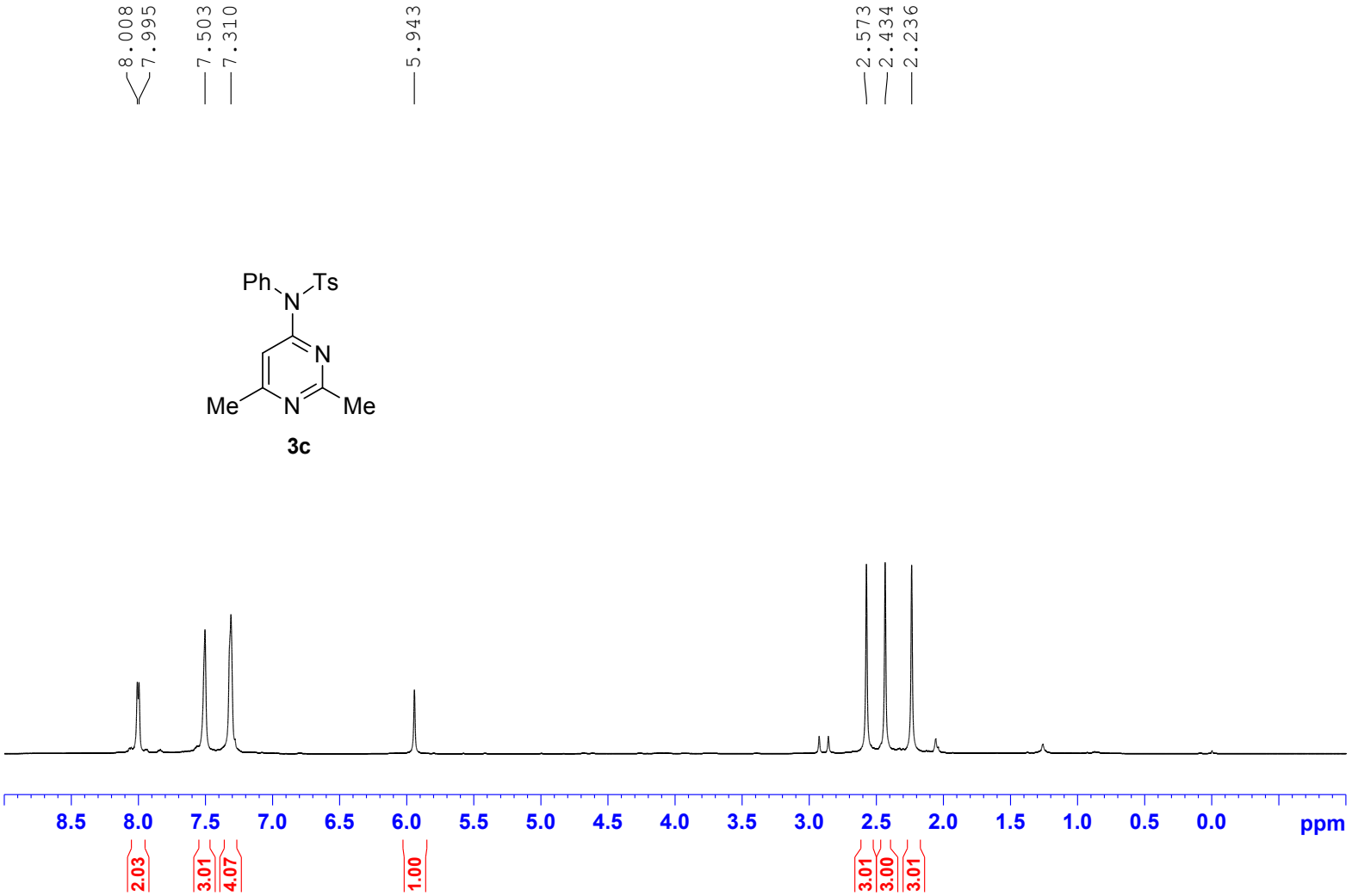
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7.310
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2.236
Ph
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Ts
N
Me
N
Me
3c
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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0.5
0.0
ppm
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4.07
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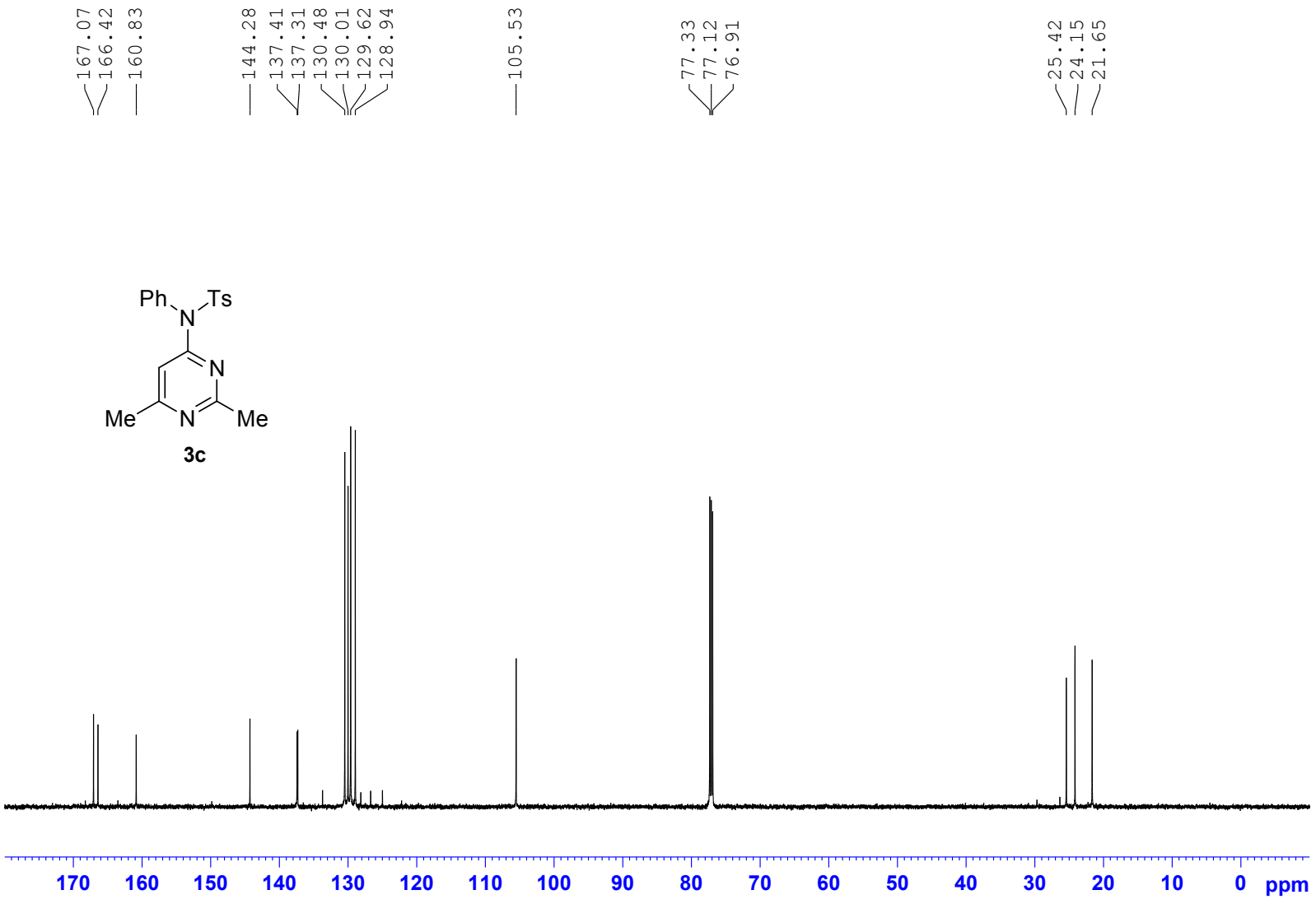
3.00
3.01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137.31
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130.01
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128.94
105.53
77.33
77.12
76.91
25.42
24.15
21.65
Ph
Ts
N
N
Me
N
Me
3c
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160
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140
130
120
110
100
90
80
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60
50
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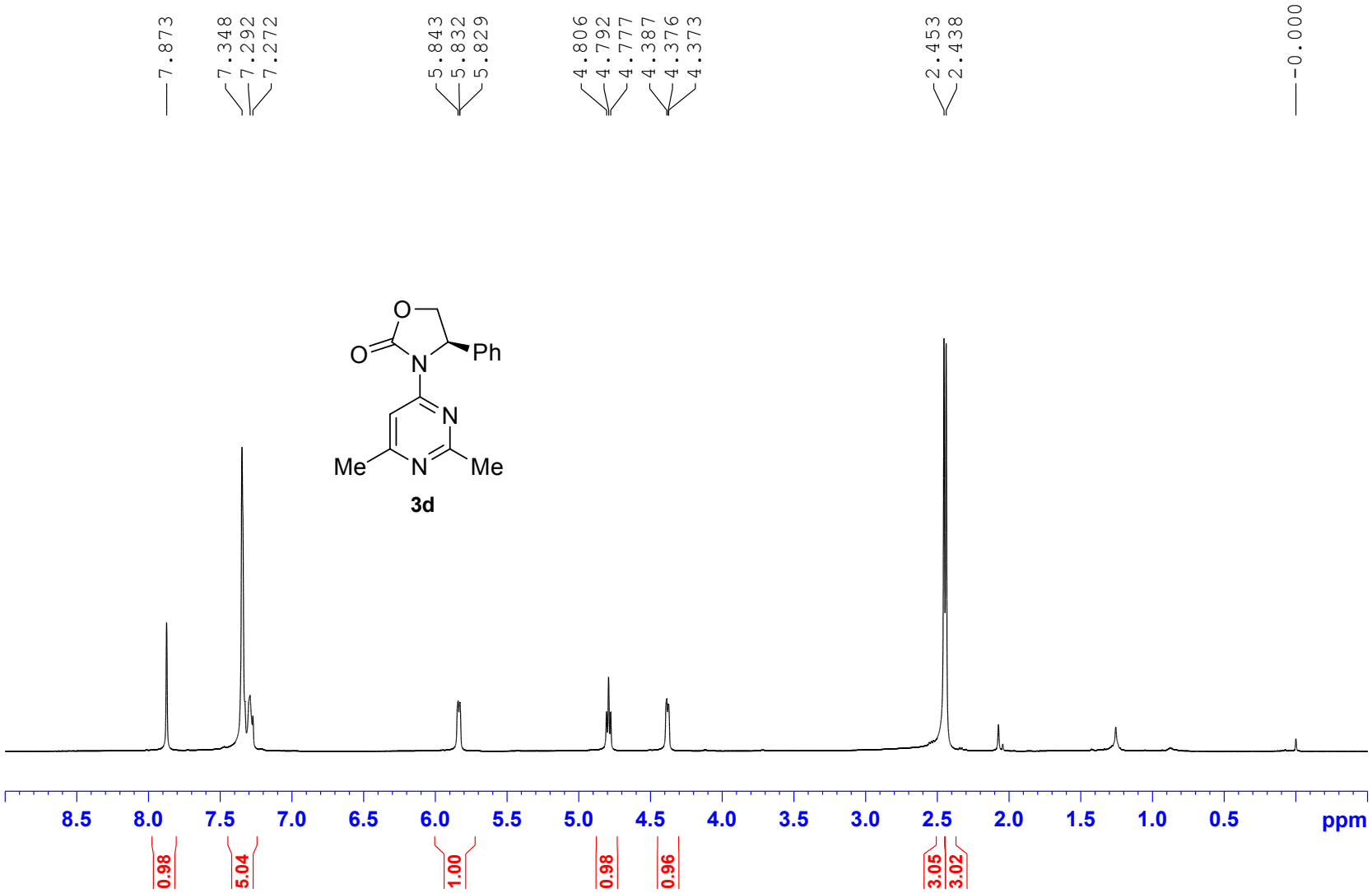
30
20
10
0
ppm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4.376
4.373
2.453
2.438
0.000
O
O
N
Ph
N
Me
N
Me
3d
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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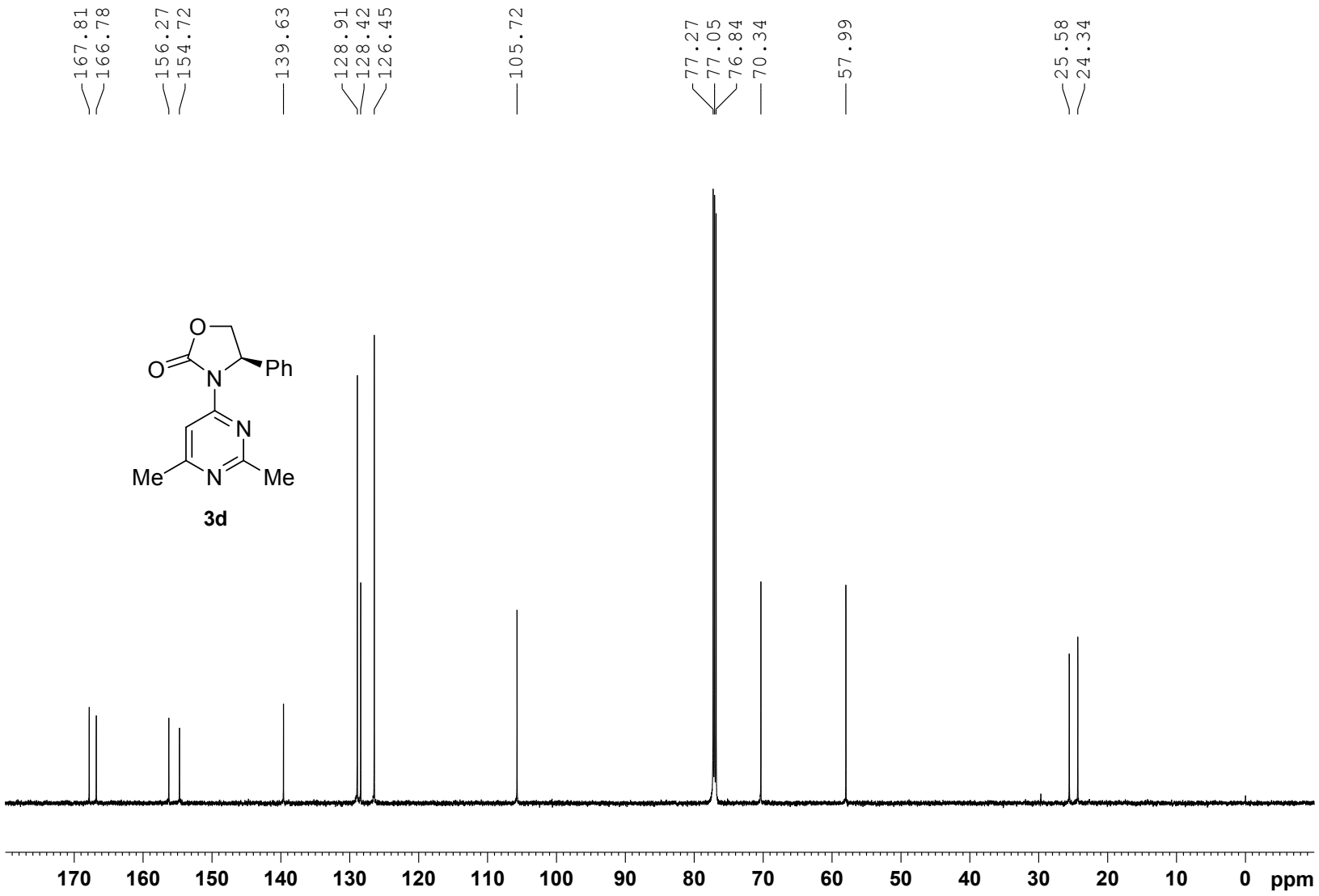
3.02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128.42
126.45
105.72
77.27
77.05
76.84
70.34
57.99
25.58
24.34
O
O
N
Ph
N
Me
N
Me
3d
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140
130
120
110
100
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60
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20
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0
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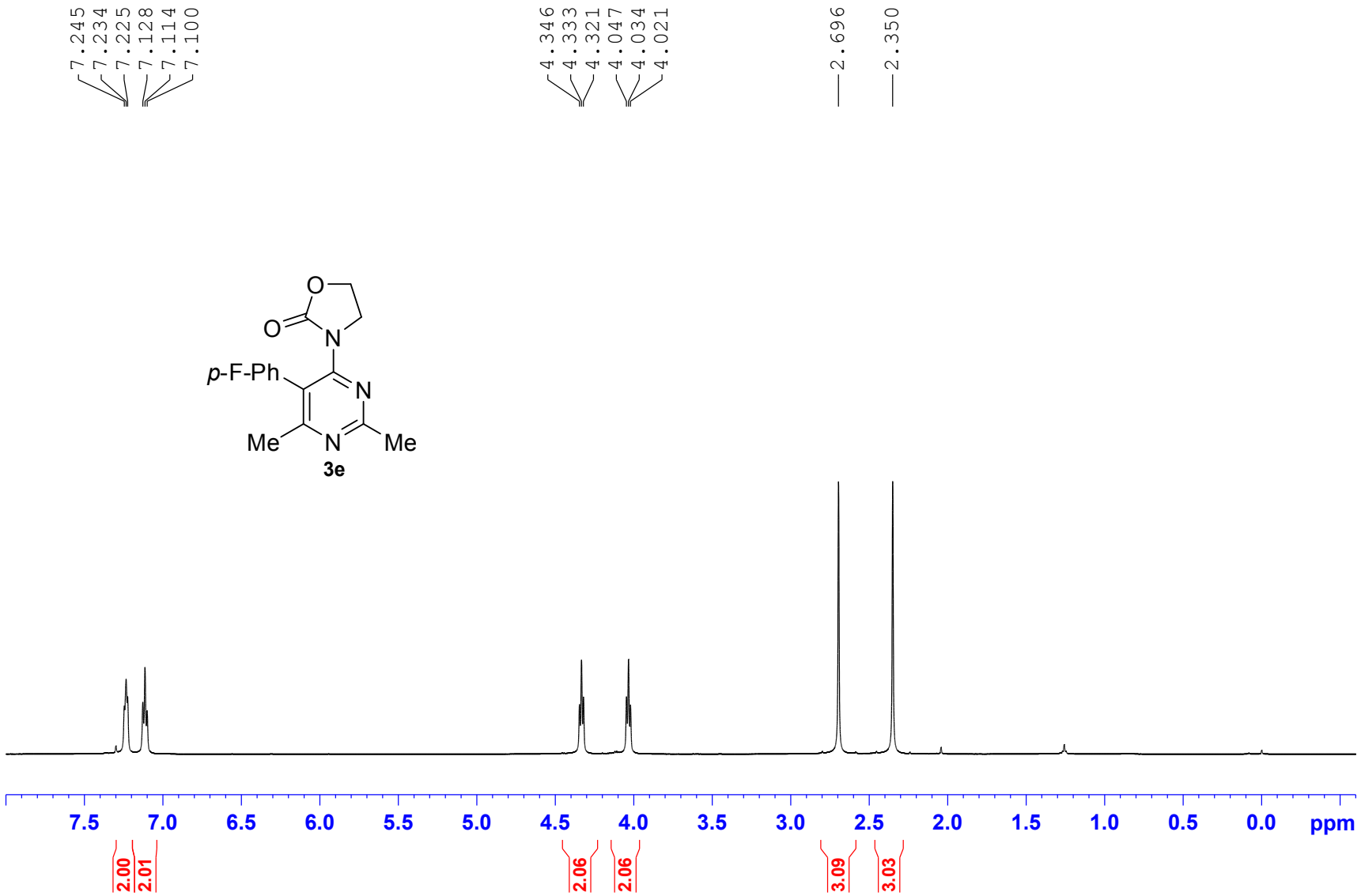
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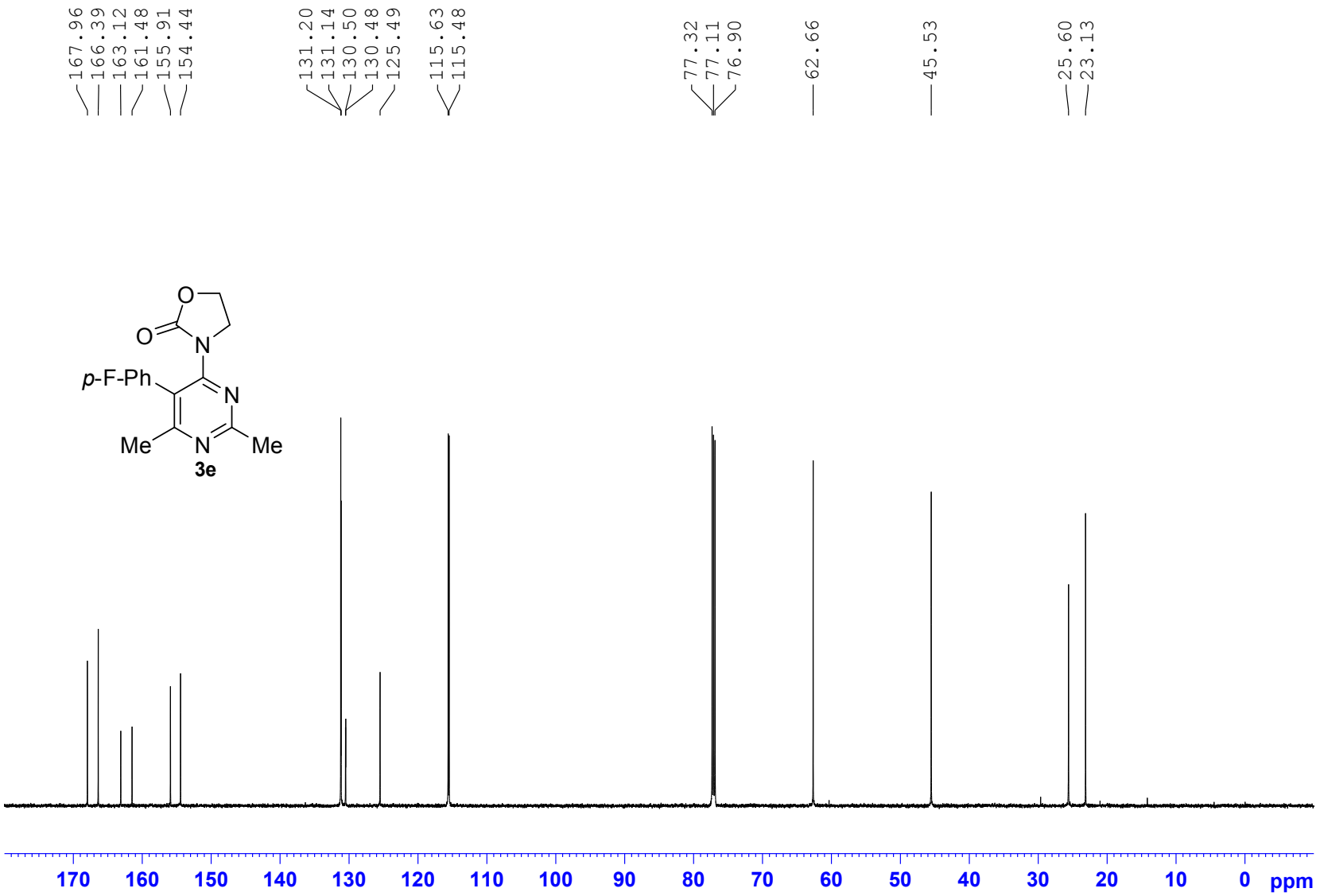
4.321
4.047
4.034
4.021
2.696
2.350
O
O
N
p-F-Ph
N
Me
N
Me
3e
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.00
2.01
2.06
2.06
3.09
3.03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131.14
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130.48
125.49
115.63
115.48
77.32
77.11
76.90
62.66
45.53
25.60
23.13
O
O
N
p-F-Ph
N
Me
N
Me
3e
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140
130
120
110
100
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60
50
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20
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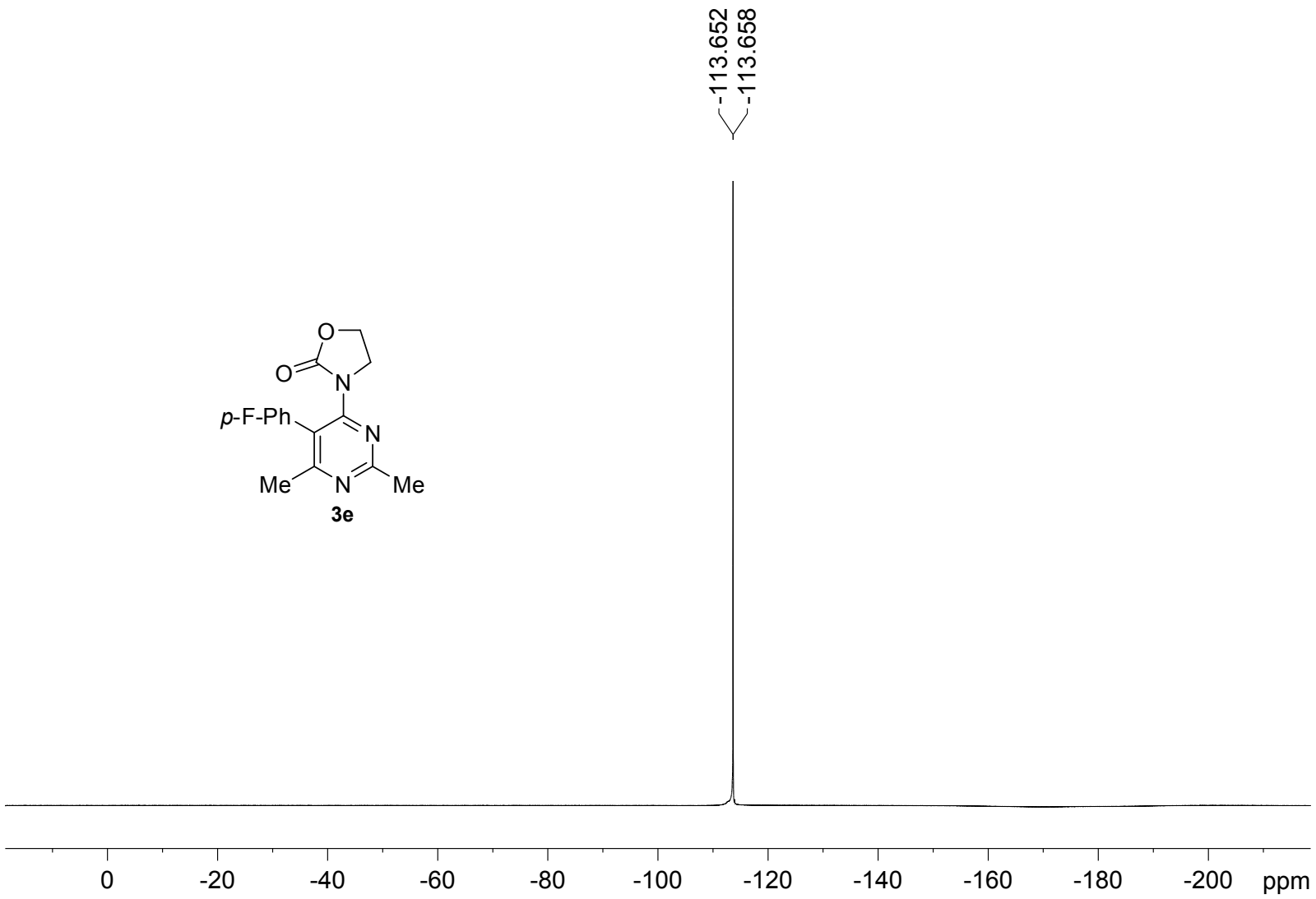
0
ppm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O
N
p-F-Ph
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N
Me
3e
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-80
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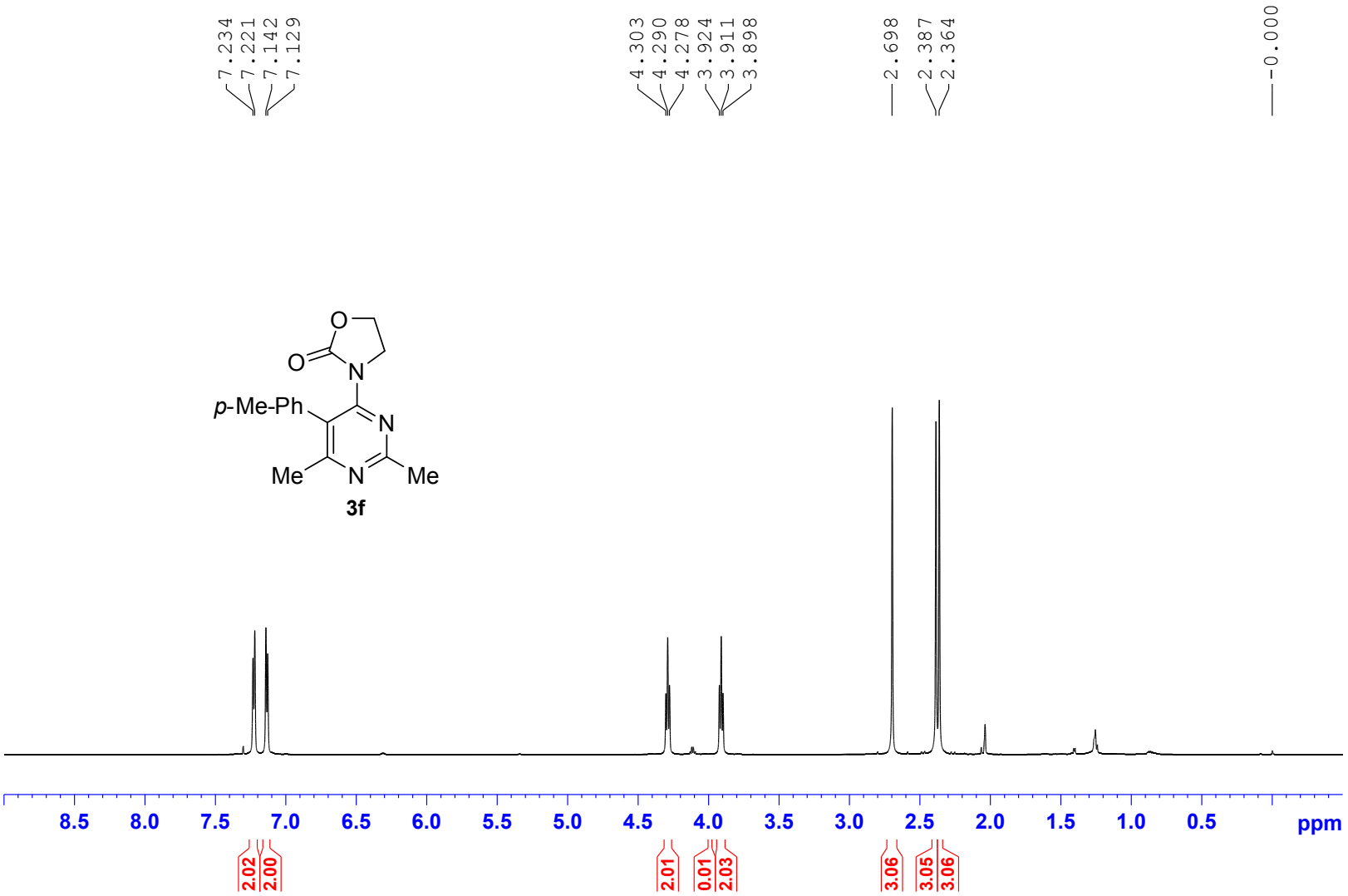
-120
-140
-160
-180
-200
ppm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3.898
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2.387
2.364
0.000
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O
N
p-Me-Ph
N
Me
N
Me
3f
8.5
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7.5
7.0
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
2.02
2.00
2.01
0.01
2.03
3.06
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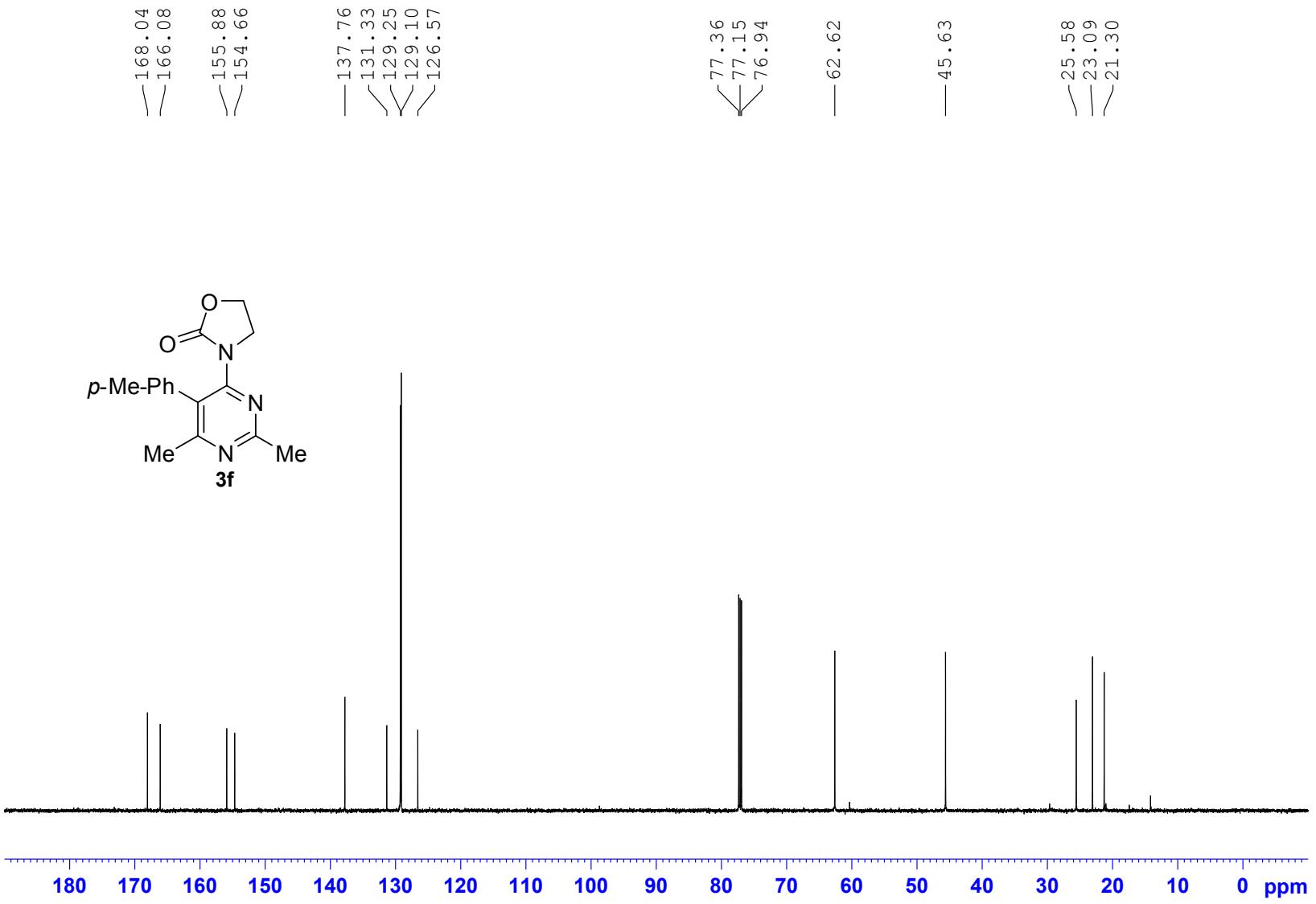
3.06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25.58
23.09
21.30
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O
N
p-Me-Ph
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Me
N
Me
3f
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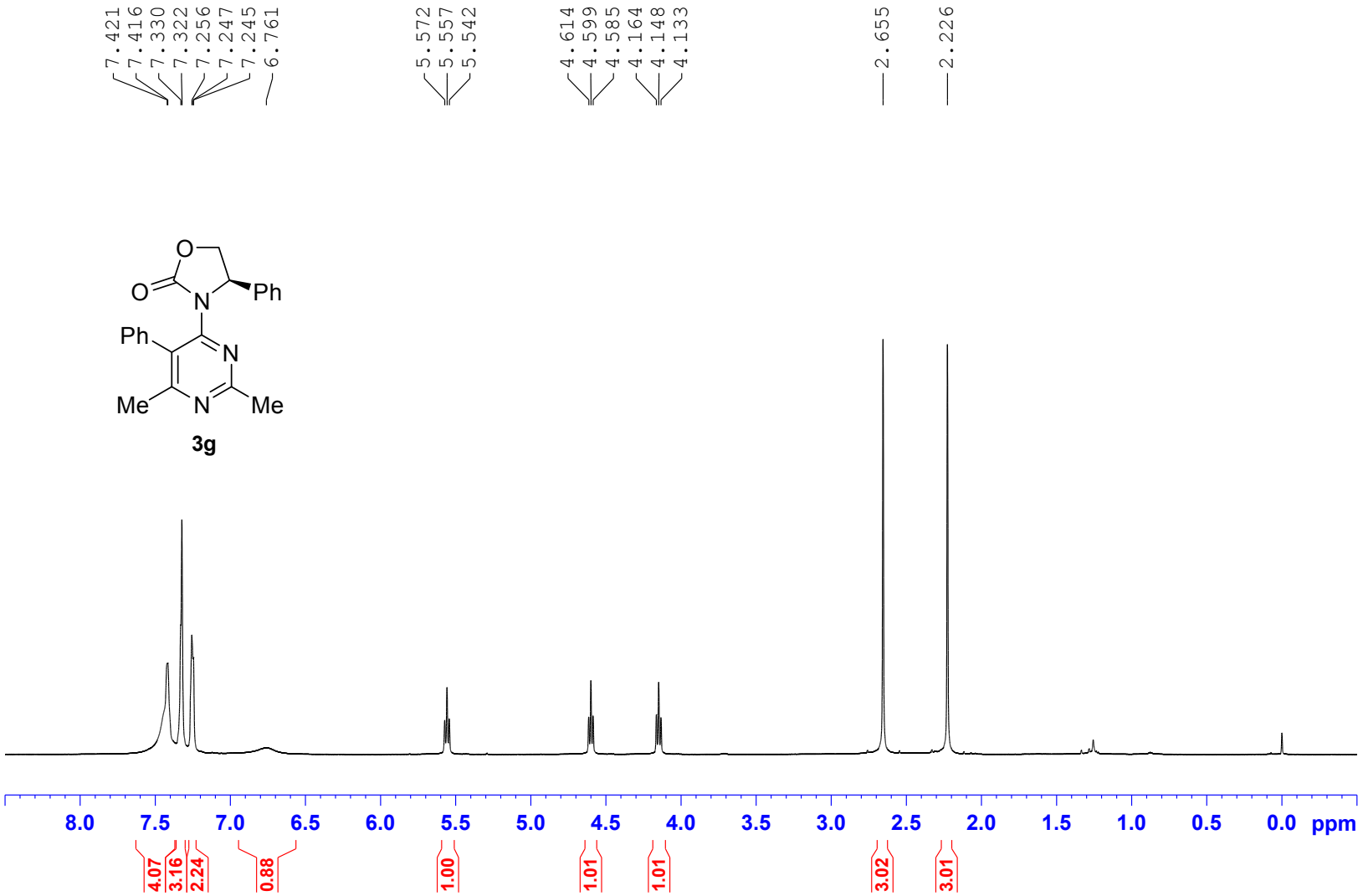
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4.148
4.133
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2.226
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O
N
Ph
Ph
N
Me
N
Me
3g
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6.0
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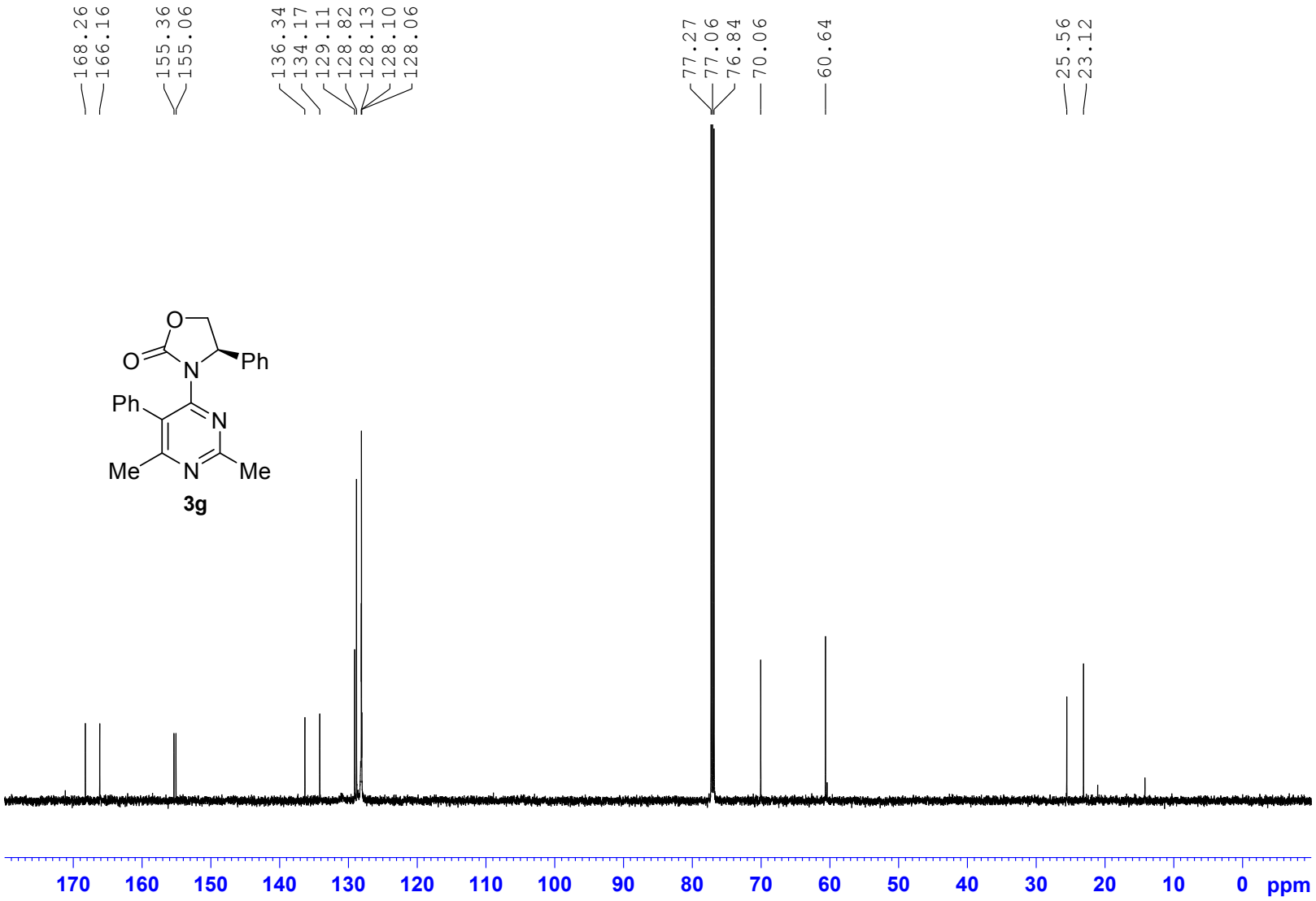
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O
N
Ph
Ph
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N
Me
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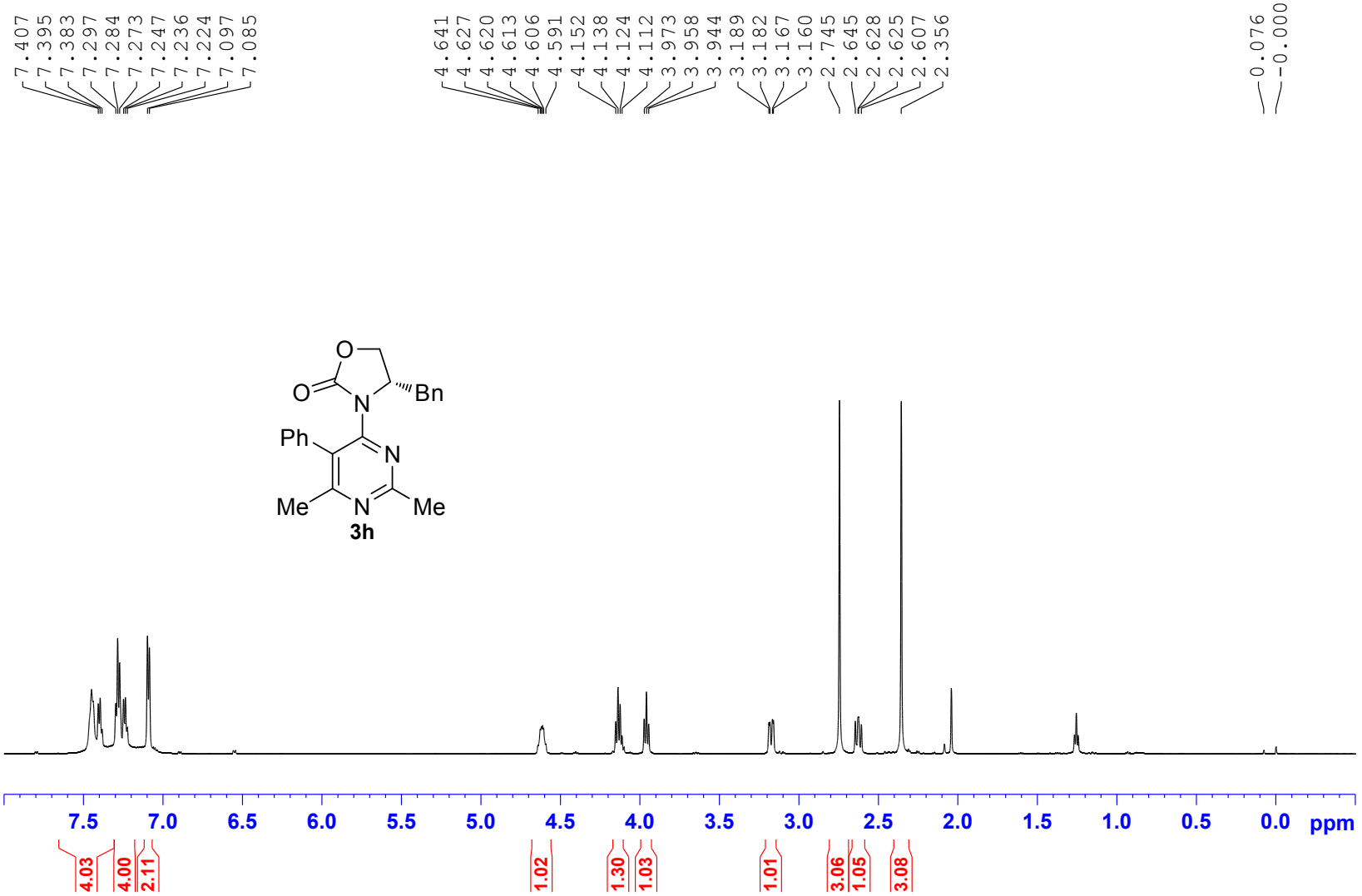
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2.625
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O
N
Bn
Ph
N
Me
N
Me
3h
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2.0
1.5
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1.03
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1.05
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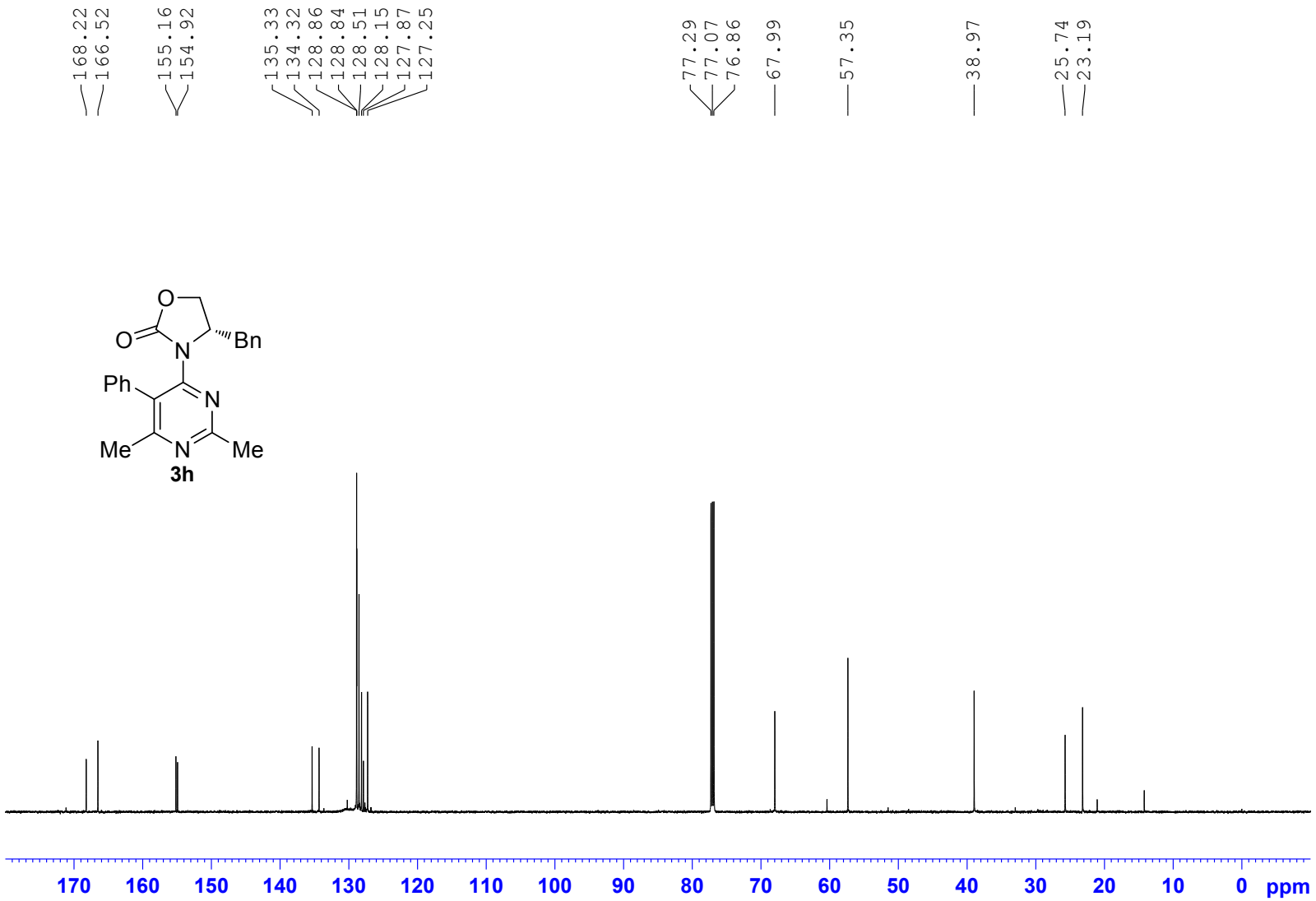
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76.86
67.99
57.35
38.97
25.74
23.19
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O
N
Bn
Ph
N
Me
N
Me
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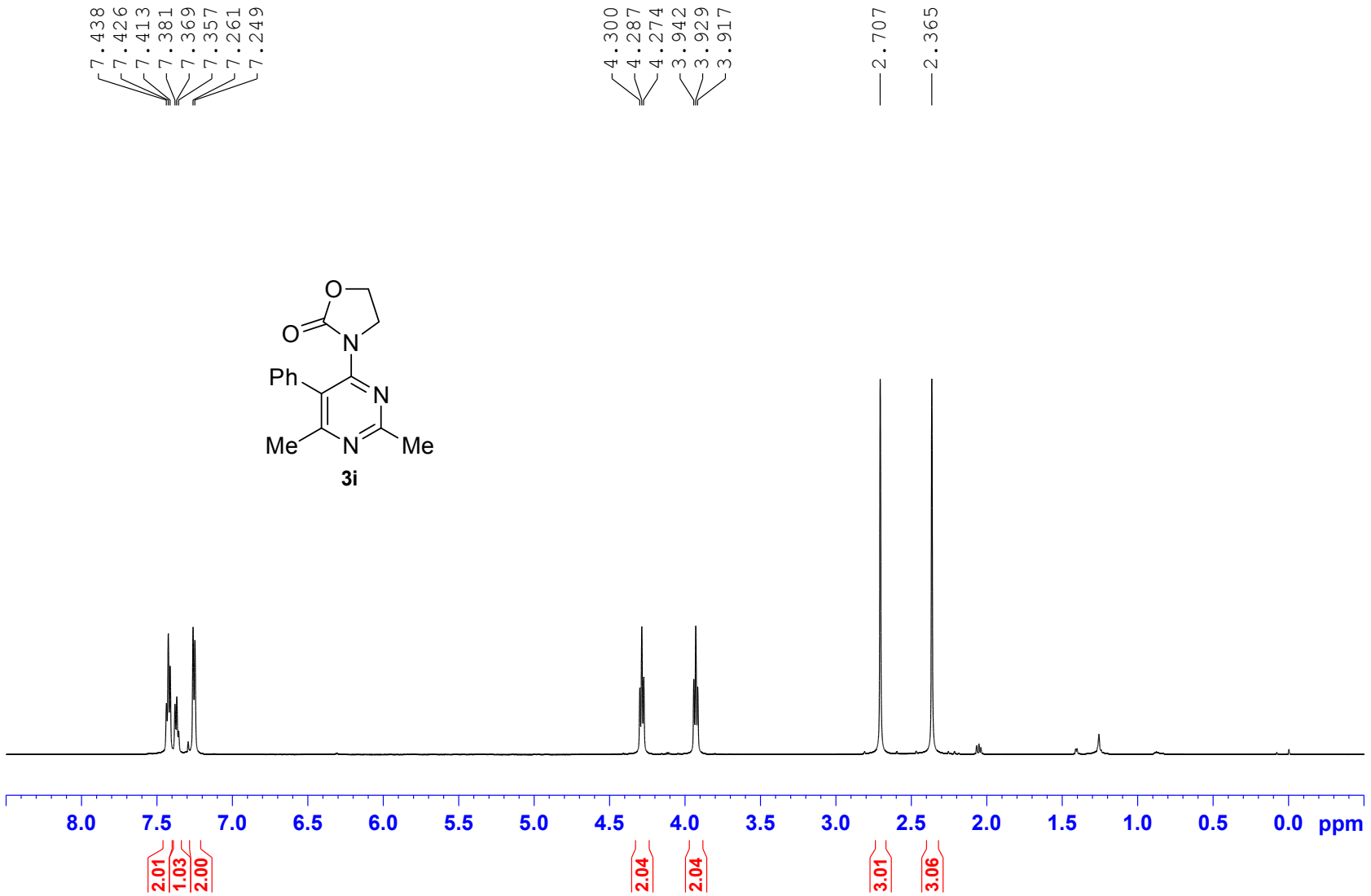
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Ph
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Me
N
Me
3i
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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2.00
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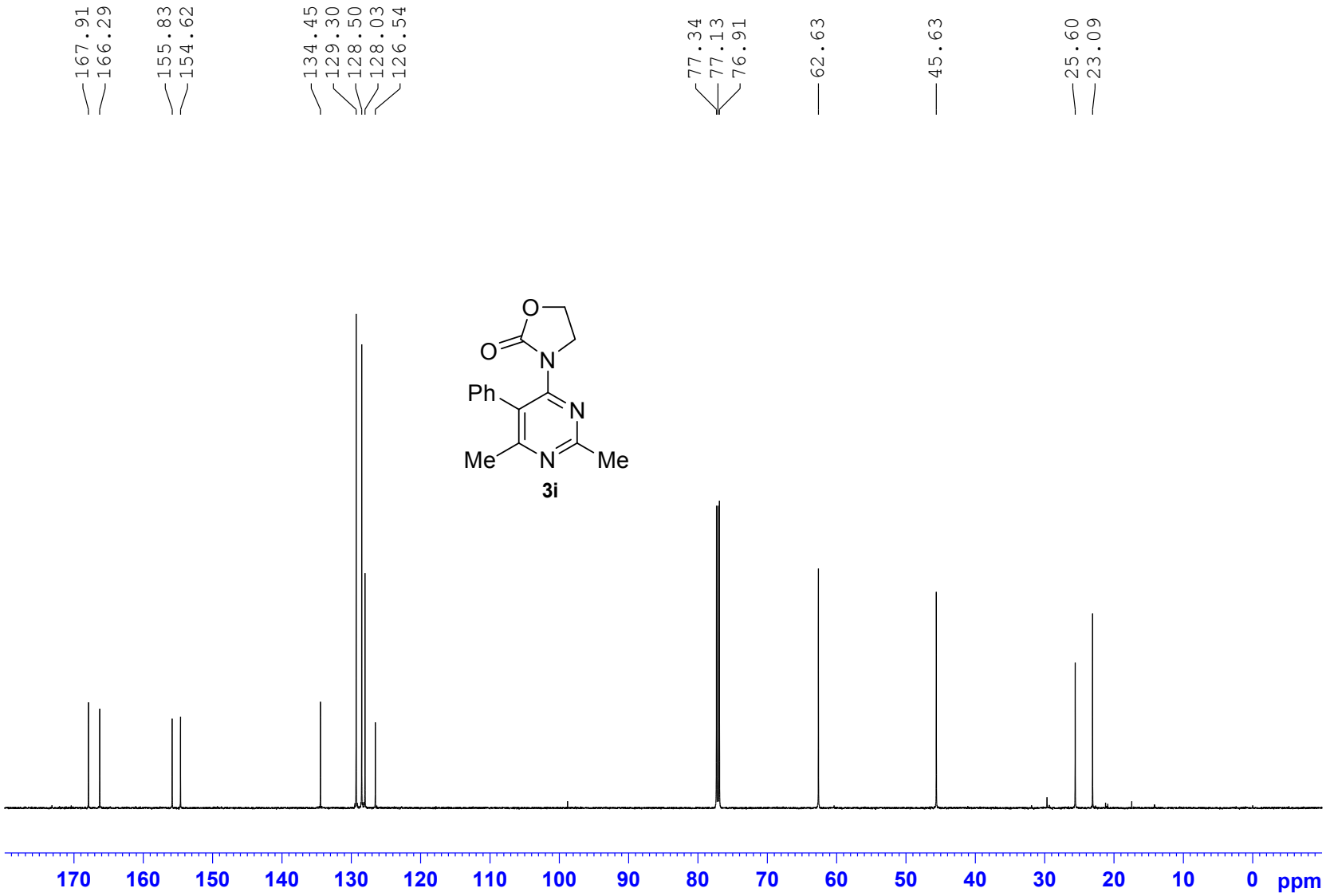
2.04
3.01
3.06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128.03
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76.91
62.63
45.63
25.60
23.09
O
O
N
Ph
N
Me
N
Me
3i
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130
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100
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60
50
40
30
20
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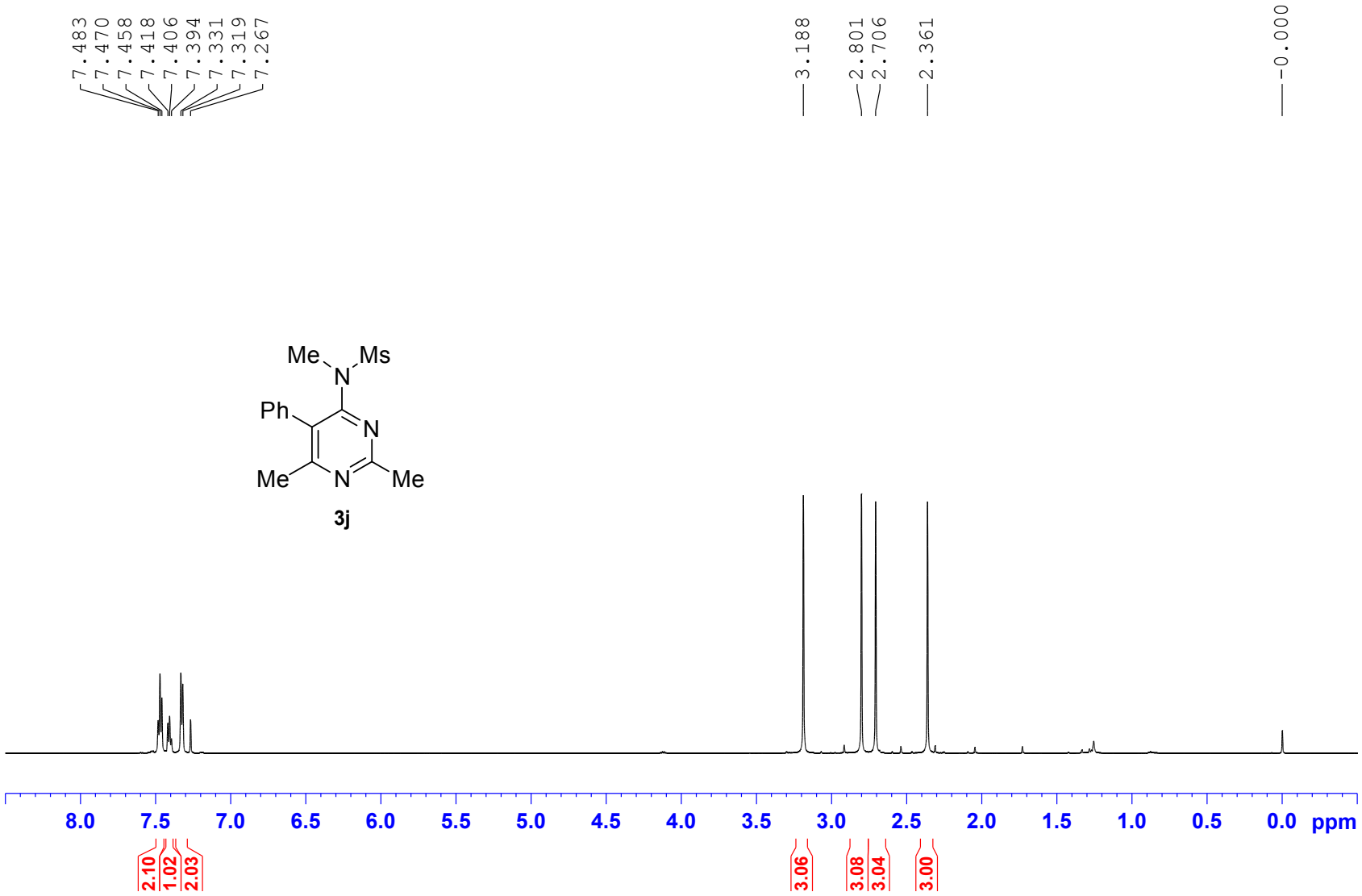
ppm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Me
Ms
N
Ph
N
Me
N
Me
3j
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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ppm
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1.02
2.03
3.06
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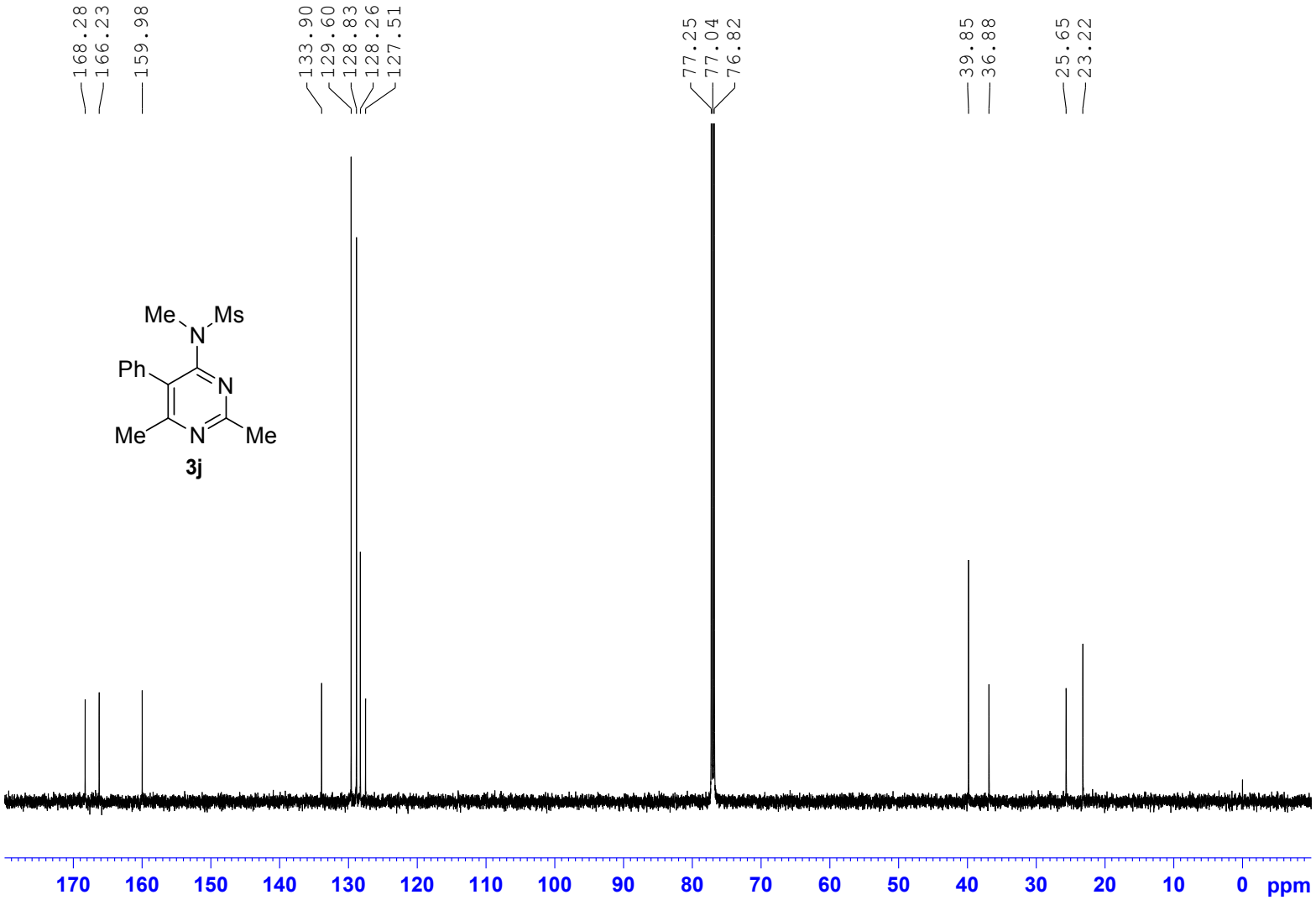
3.04
3.00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76.82
39.85
36.88
25.65
23.22
Me
N
Ms
Ph
N
Me
N
Me
3j
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140
130
120
110
100
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60
50
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30
20
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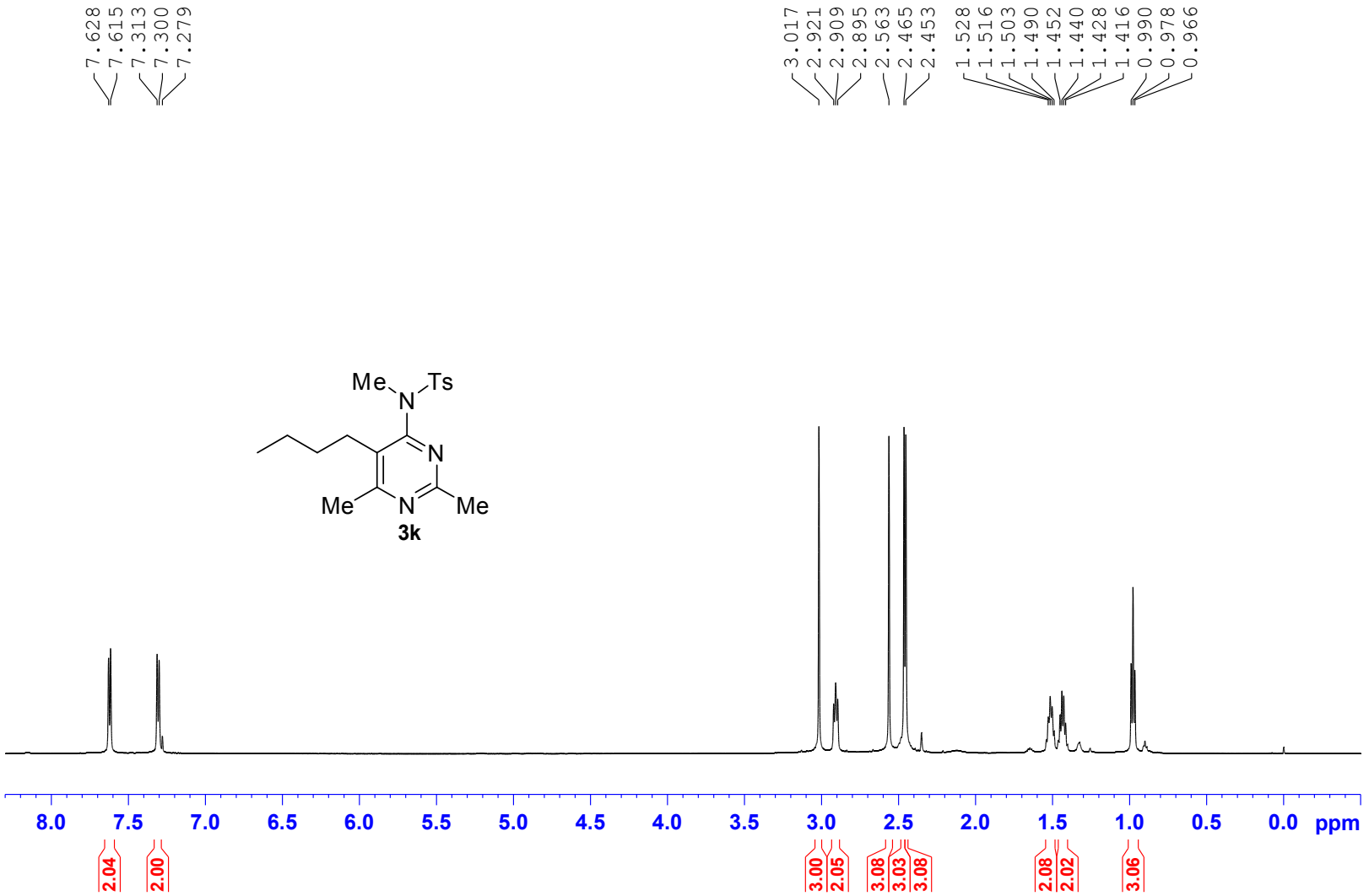
0
ppm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1.490
1.452
1.440
1.428
1.416
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0.966
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Ts
N
Me
N
Me
3k
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6.5
6.0
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4.5
4.0
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1.0
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3.08
2.08
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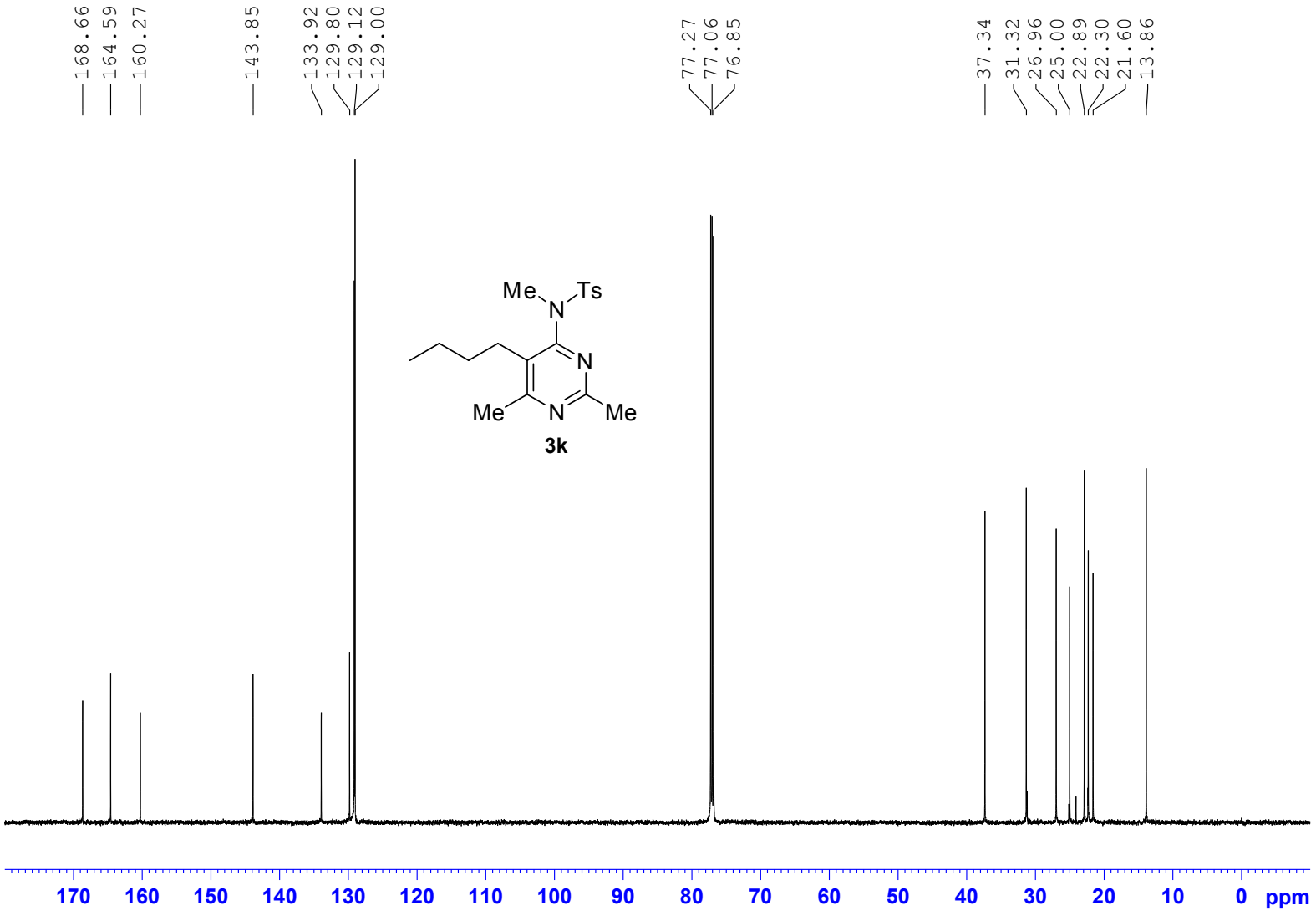
3.06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26.96
25.00
22.89
22.30
21.60
13.86
Me
N
Ts
N
Me
N
Me
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20
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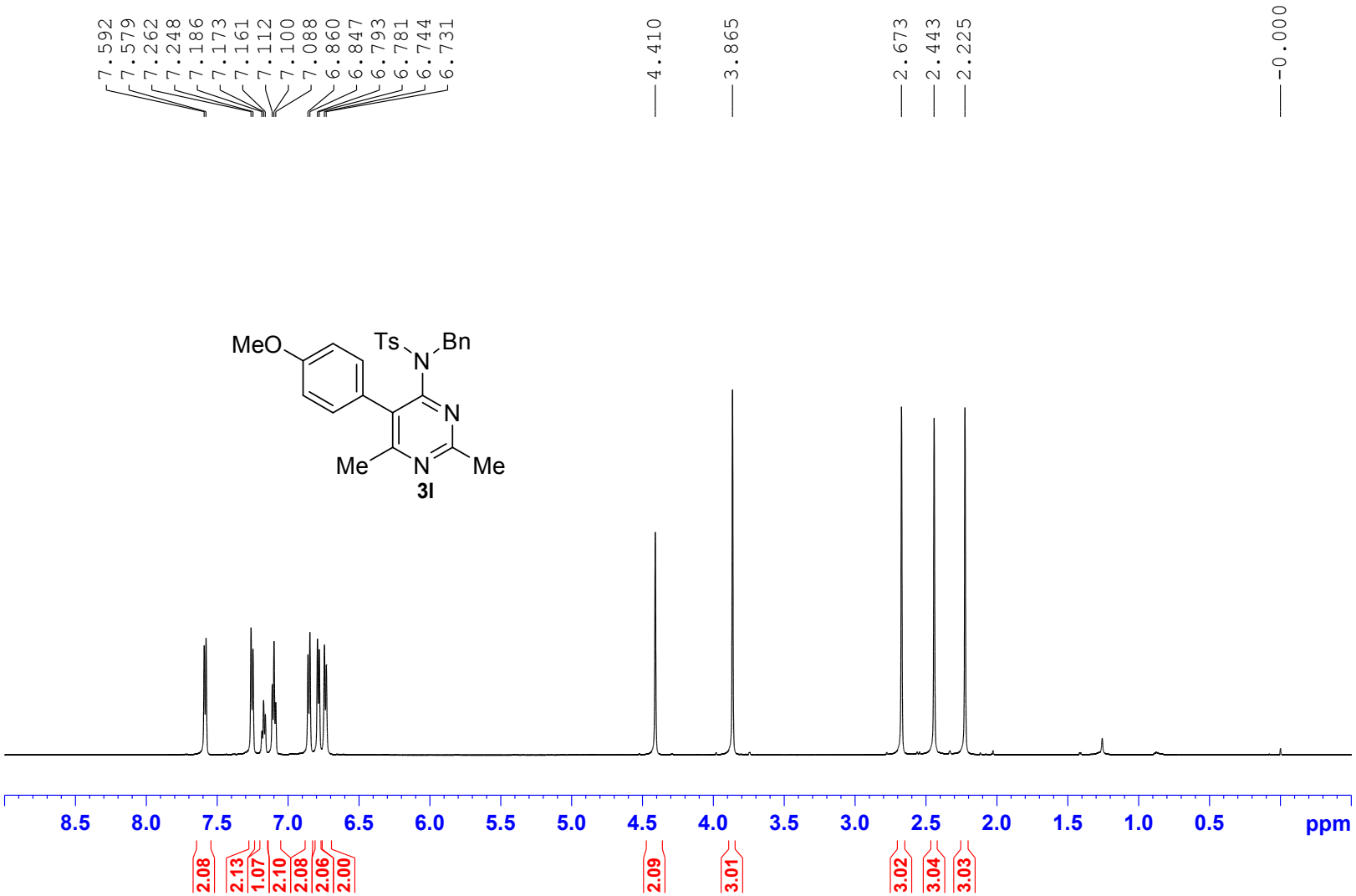
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6.731
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2.225
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MeO
Ts
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Bn
N
Me
N
Me
3l
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7.0
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6.0
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5.0
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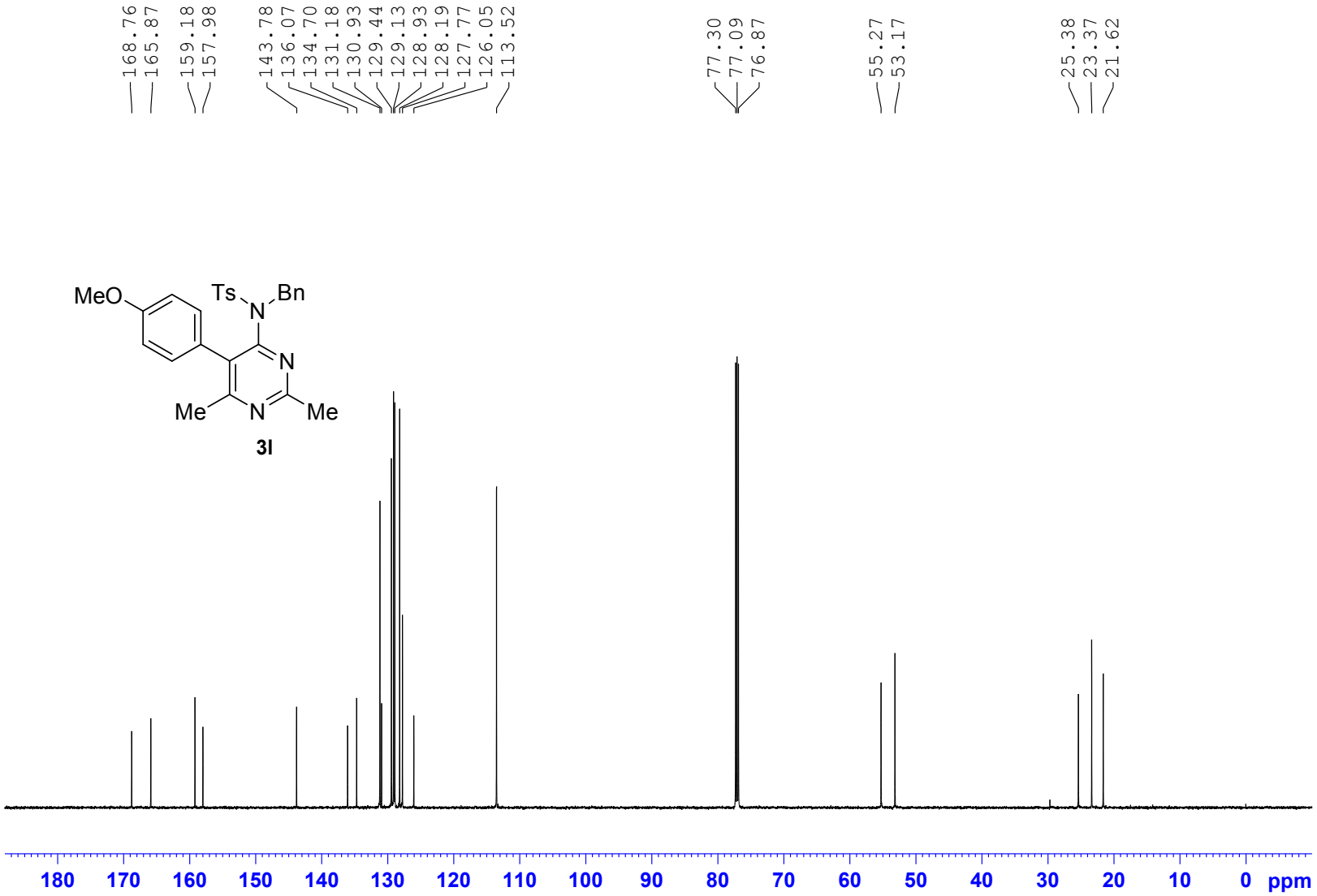
3.03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127.77
126.05
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77.30
77.09
76.87
55.27
53.17
25.38
23.37
21.62
MeO
Ts
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Bn
N
Me
N
Me
3l
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110
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50
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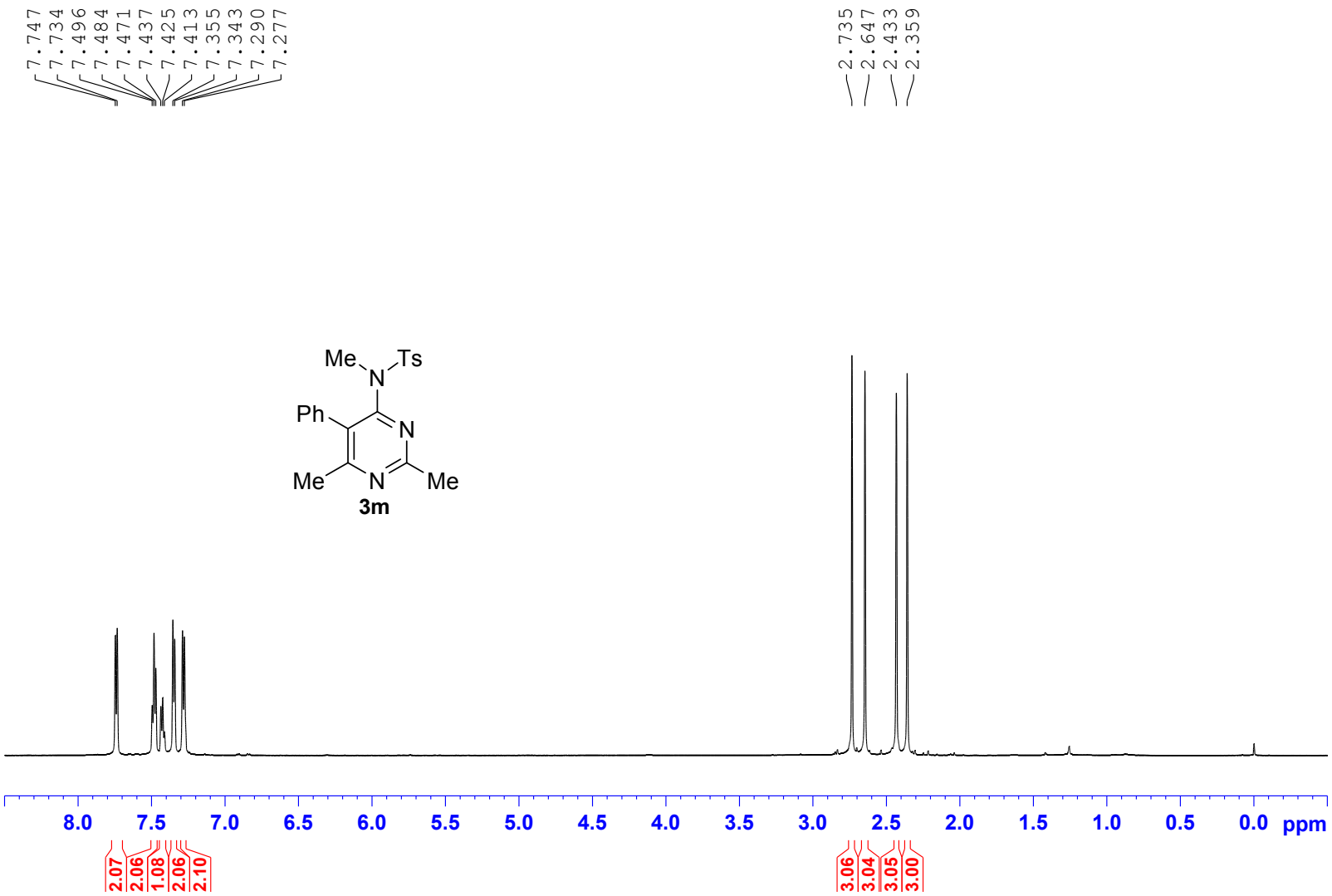
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Ph
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Me
N
Me
3m
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5.0
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4.0
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3.0
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2.0
1.5
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2.10
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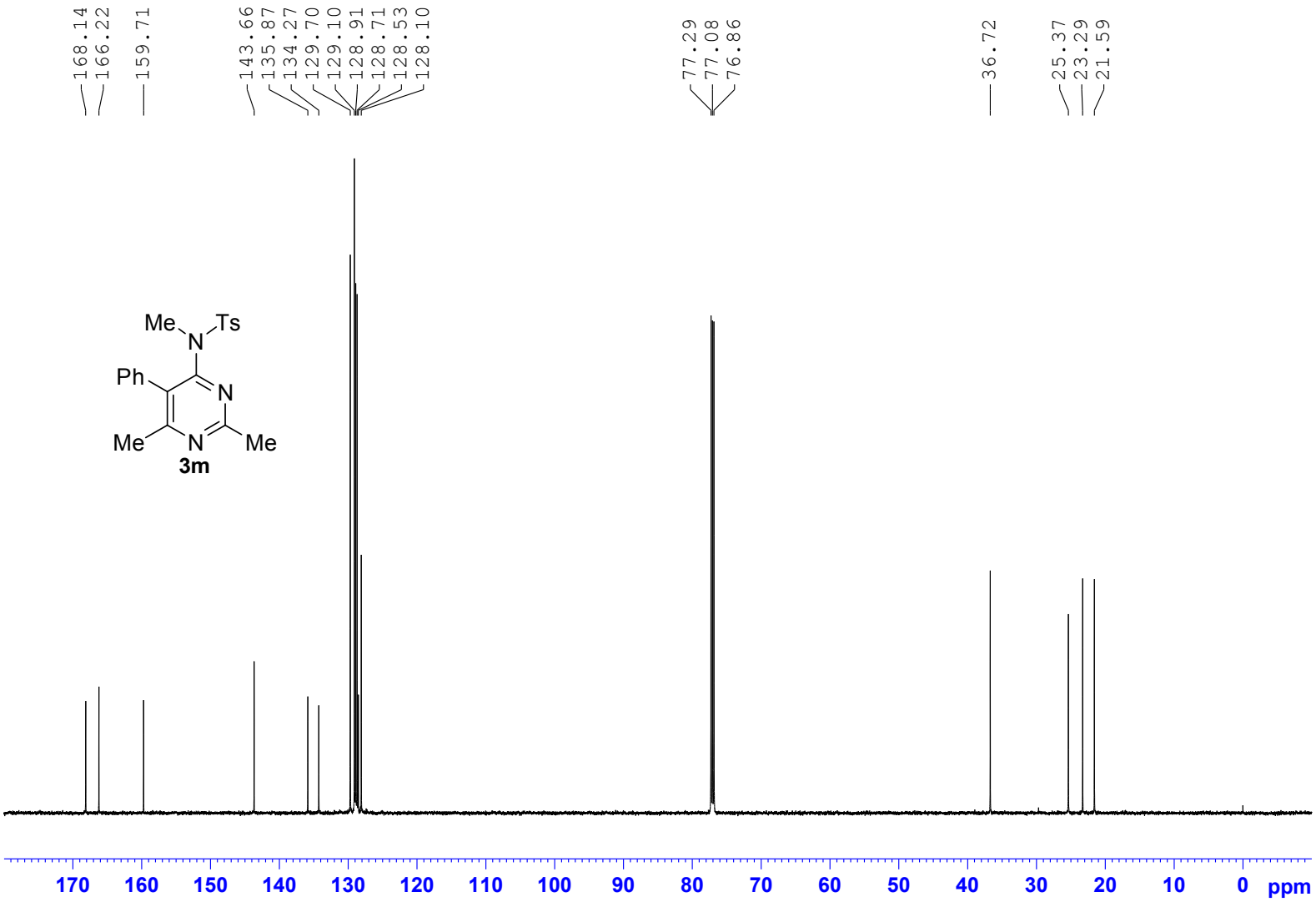
3.00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76.86
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23.29
21.59
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Ph
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Me
N
Me
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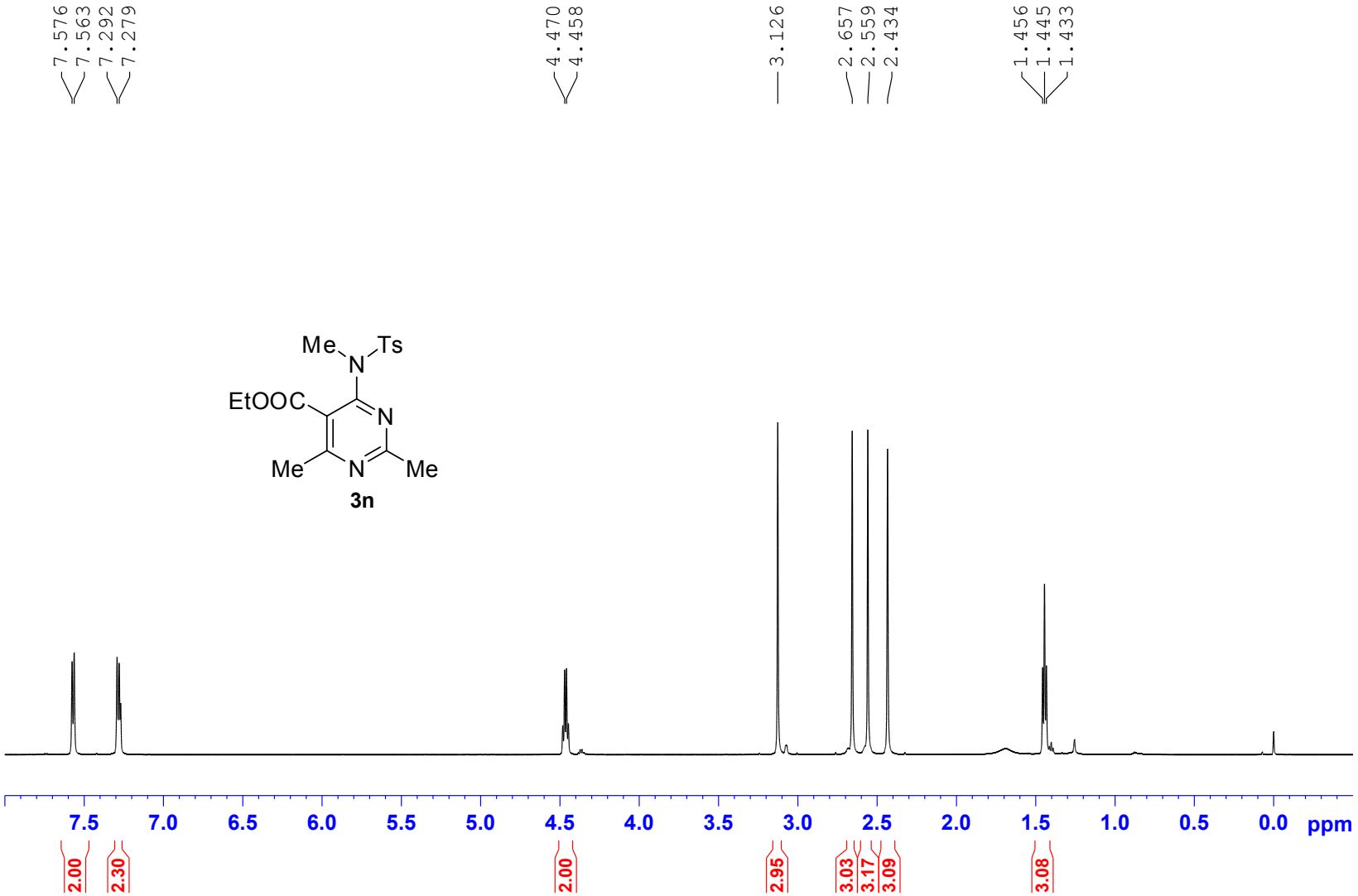
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N
Me
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4.0
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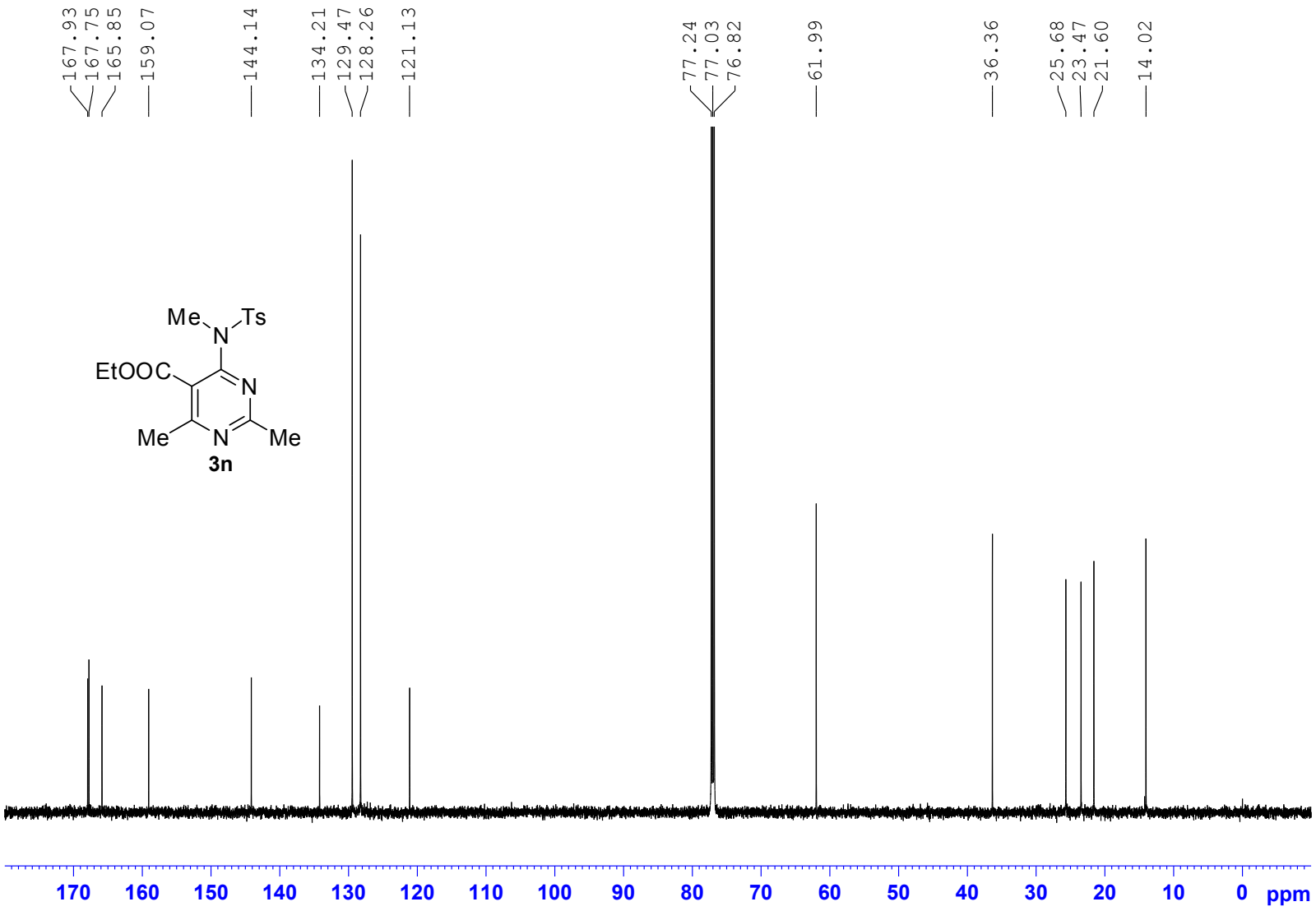
3.08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36.36
25.68
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21.60
14.02
Me
N
Ts
EtOOC
N
Me
N
Me
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20
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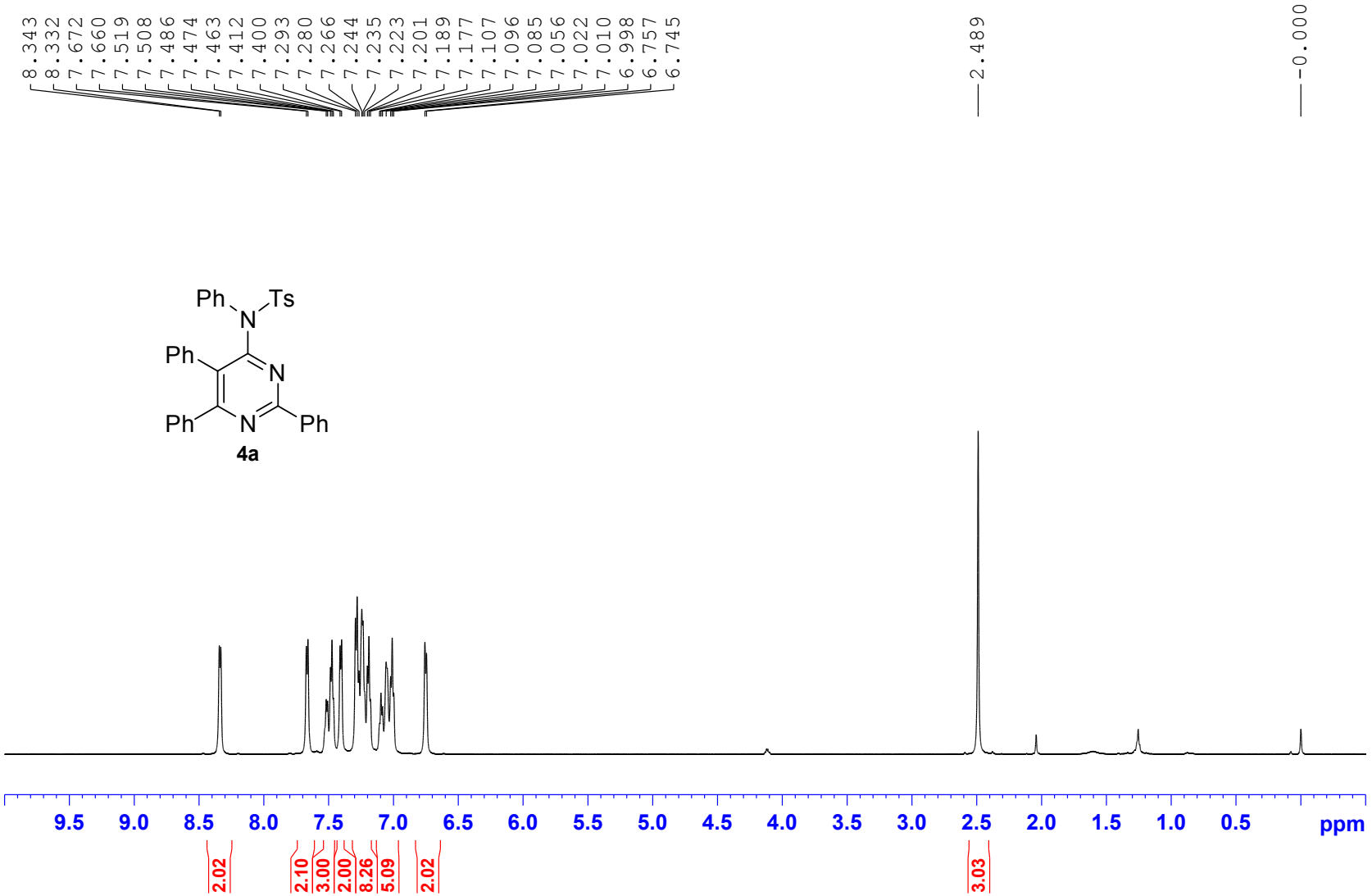
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7.223
7.201
7.189
7.177
7.107
7.096
7.085
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7.022
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6.745
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Ts
Ph
N
Ph
N
Ph
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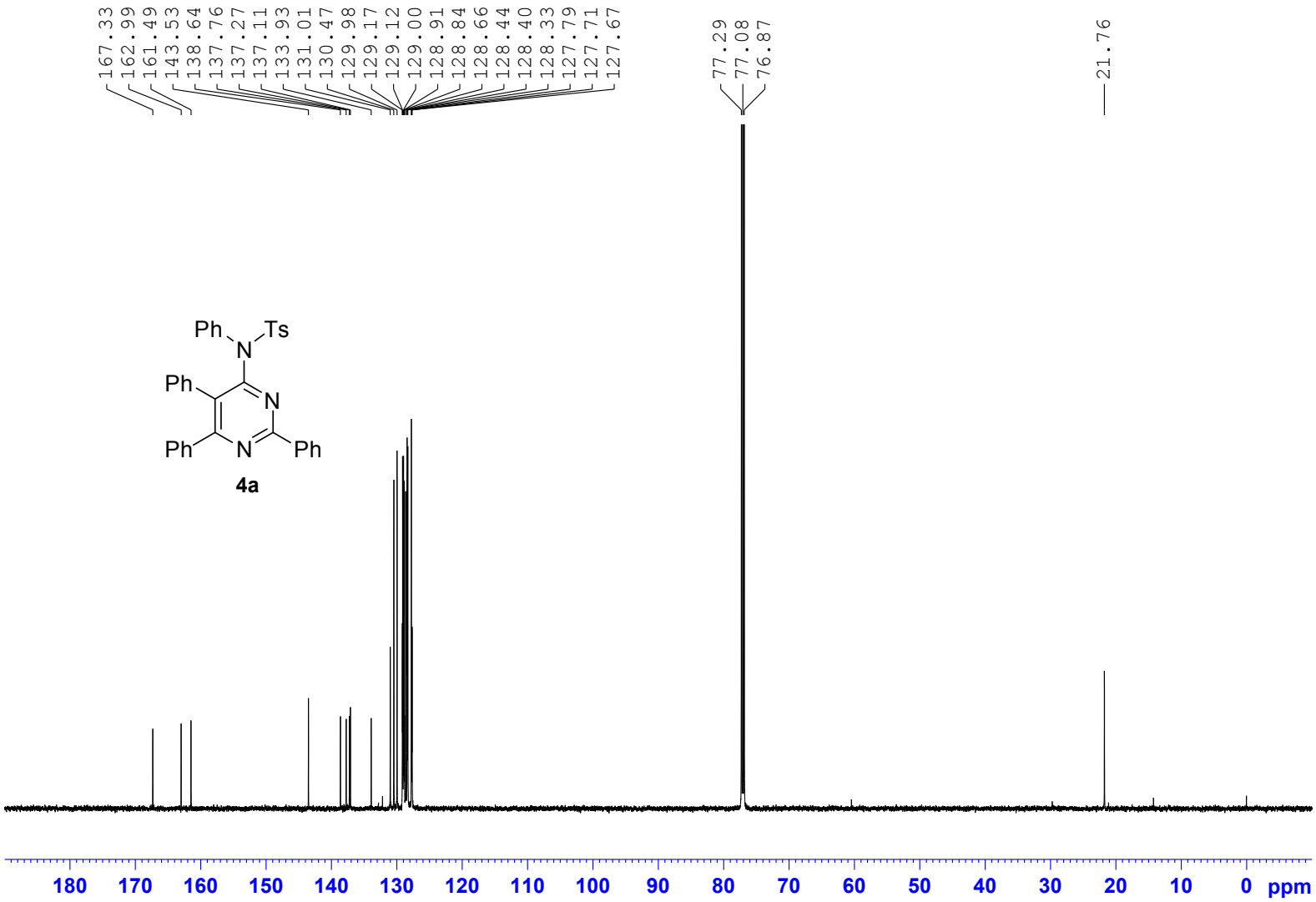
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Ph
N
Ph
N
Ph
4a
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100
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60
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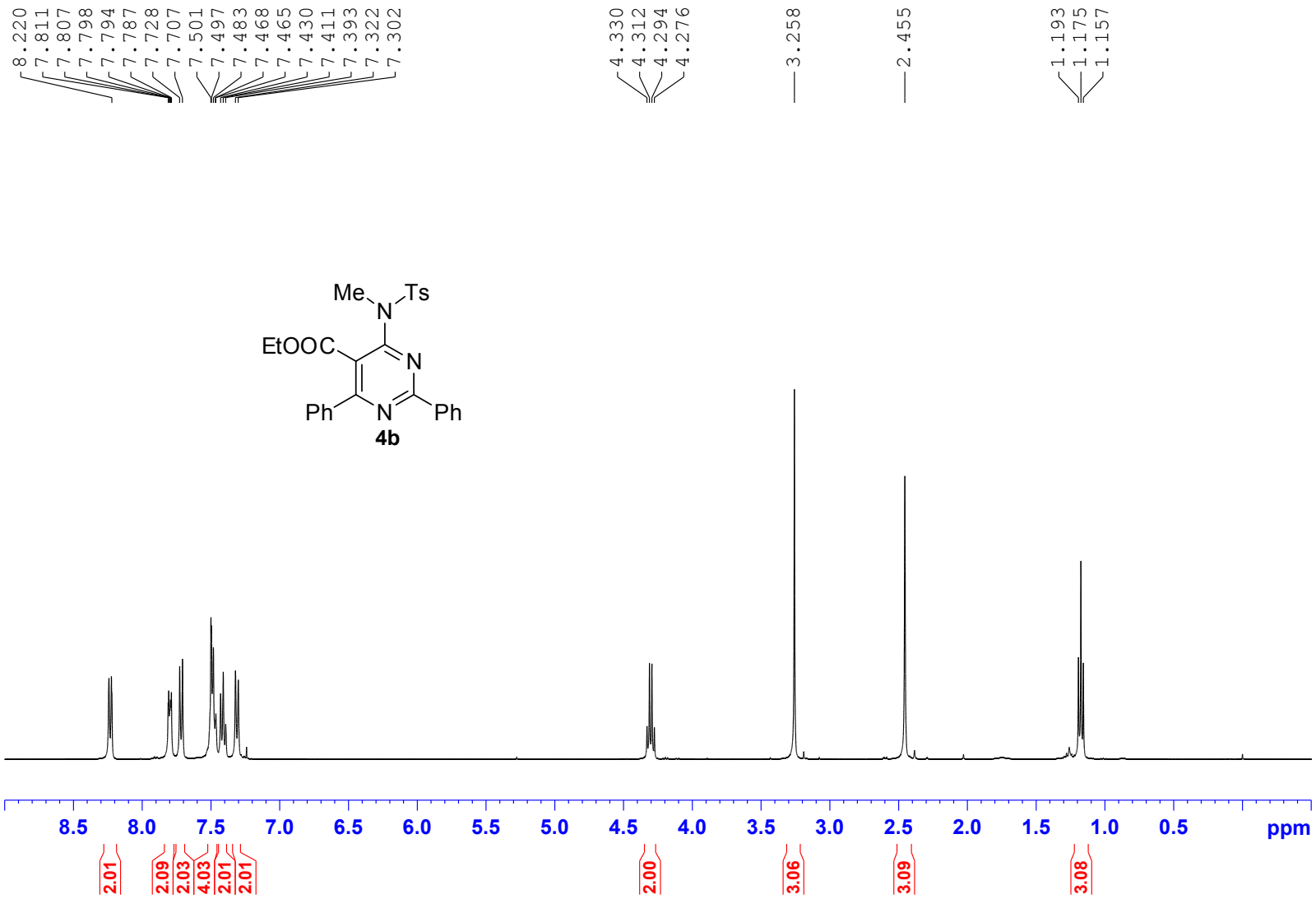
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EtOOC
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Ph
N
Ph
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6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
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2.01
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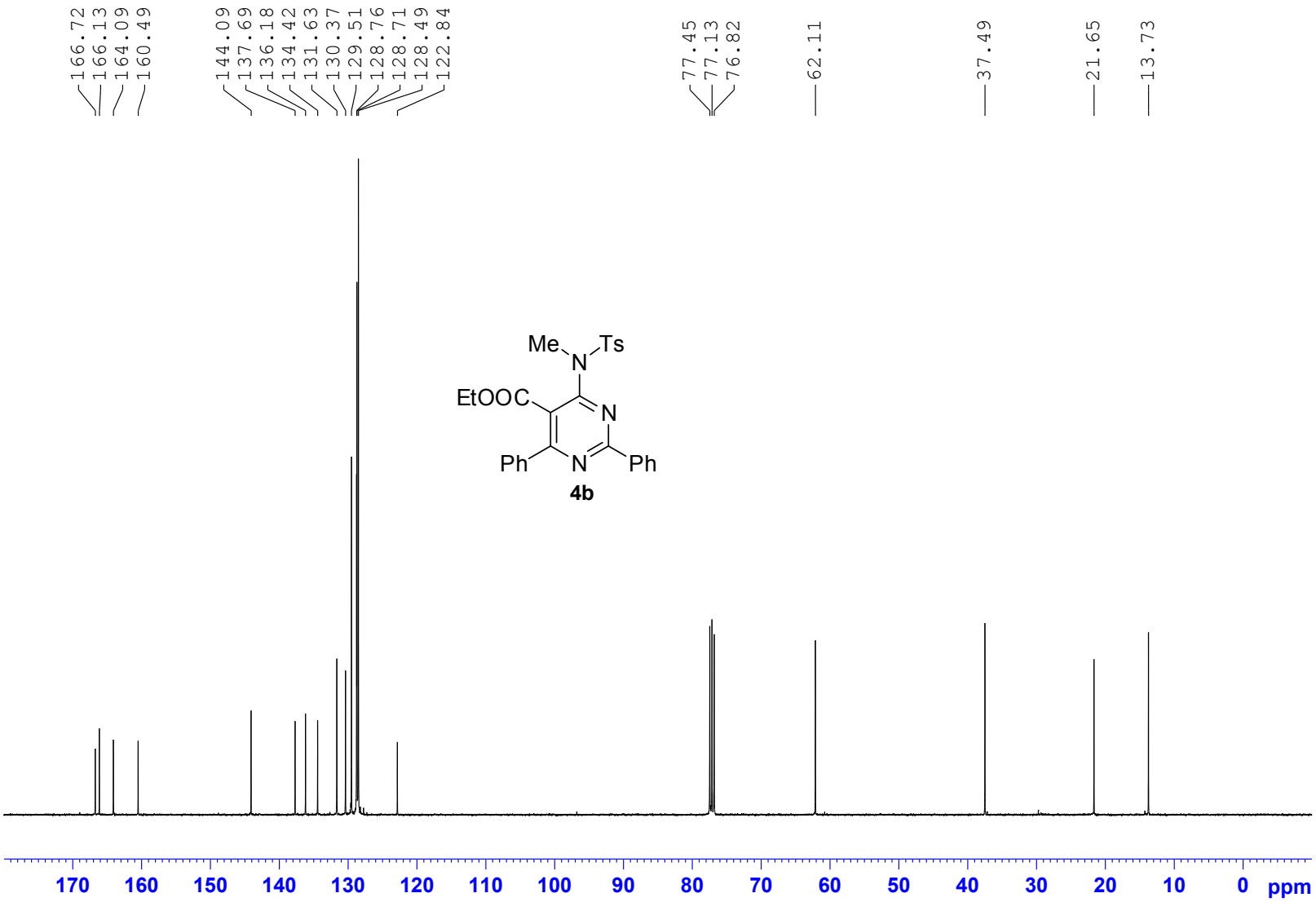
3.09
3.08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Ts
EtOOC
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Ph
N
Ph
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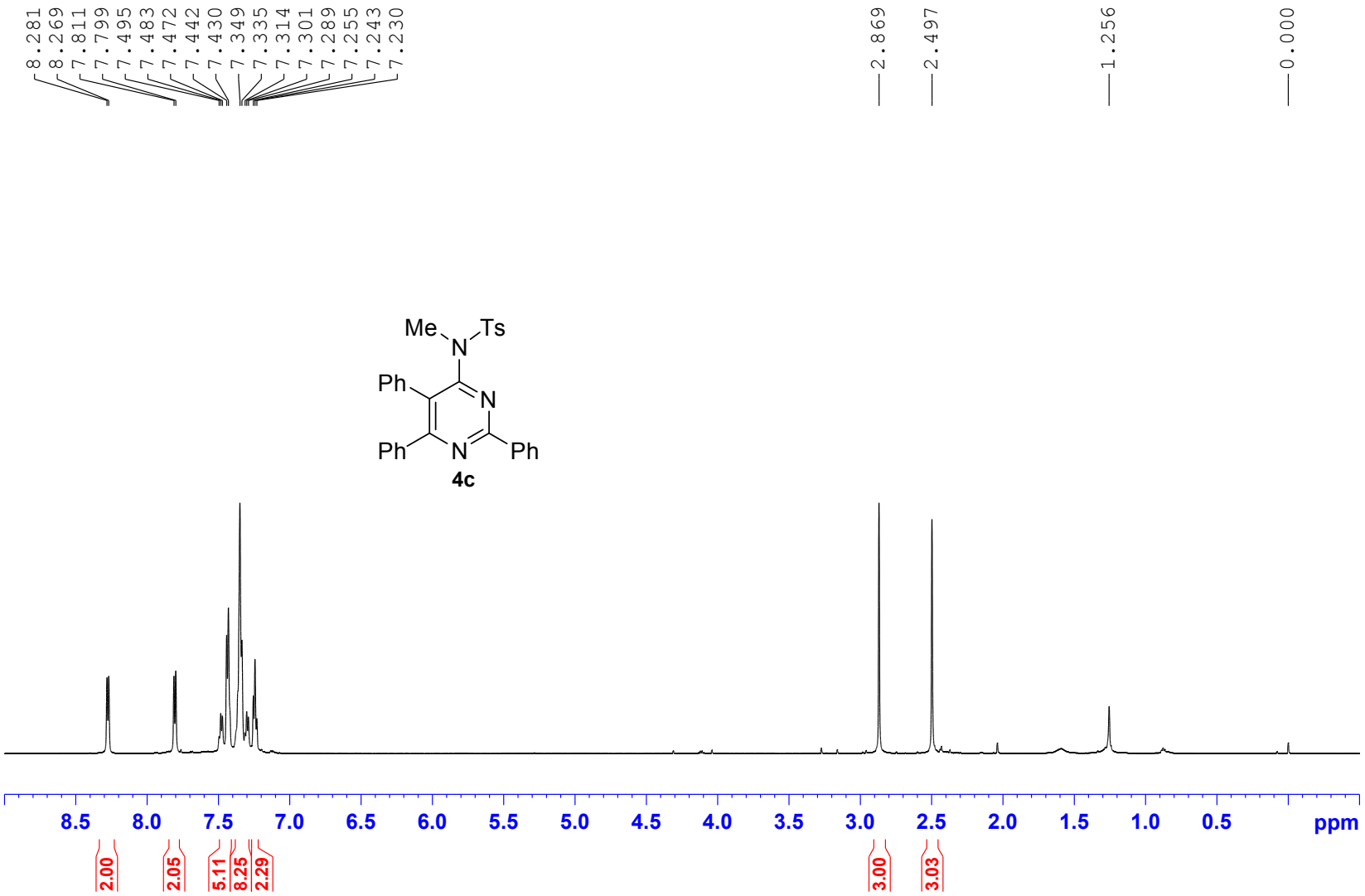
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7.230
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1.256
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Ph
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Ph
N
Ph
4c
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7.0
6.5
6.0
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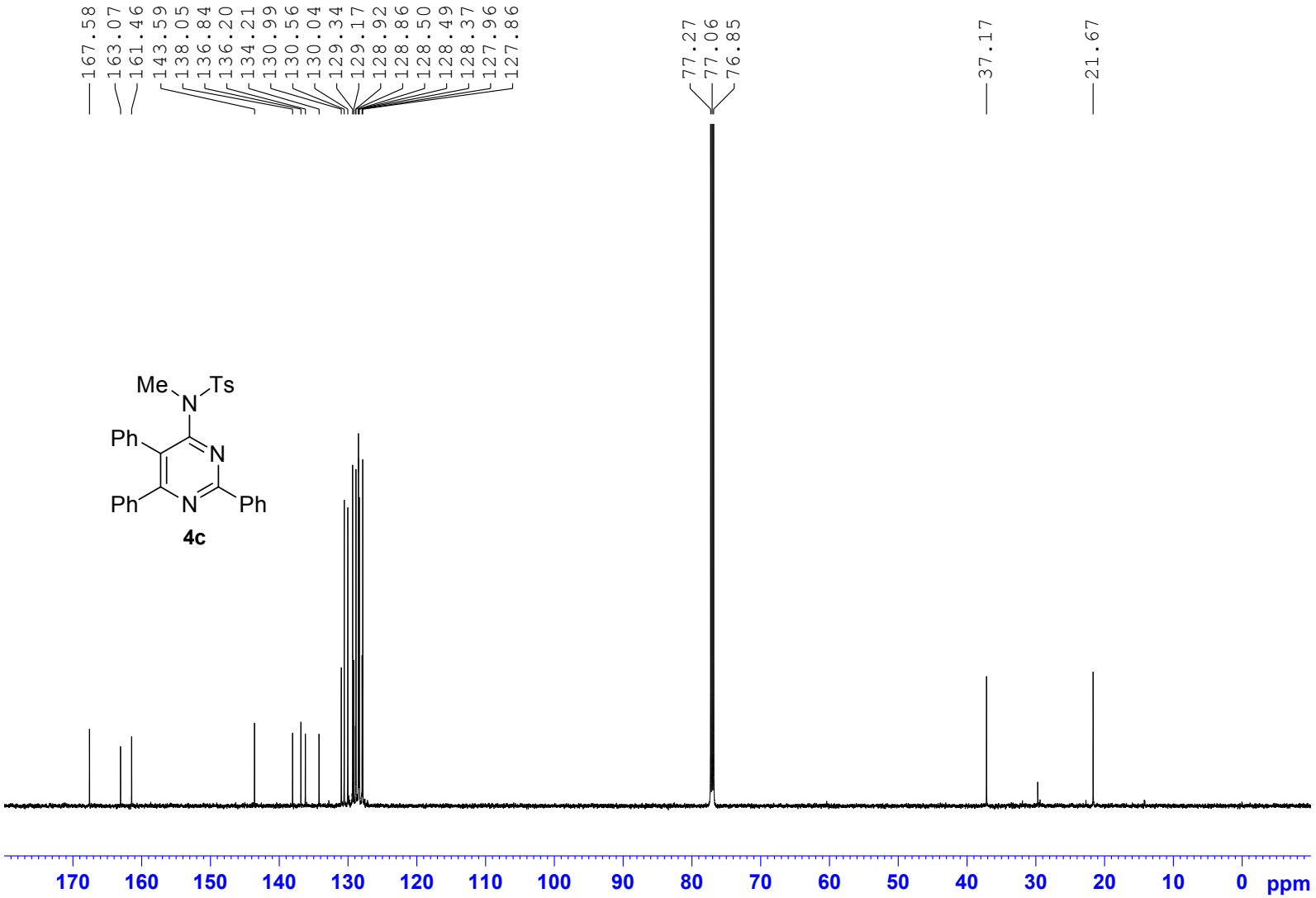
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Ph
N
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80
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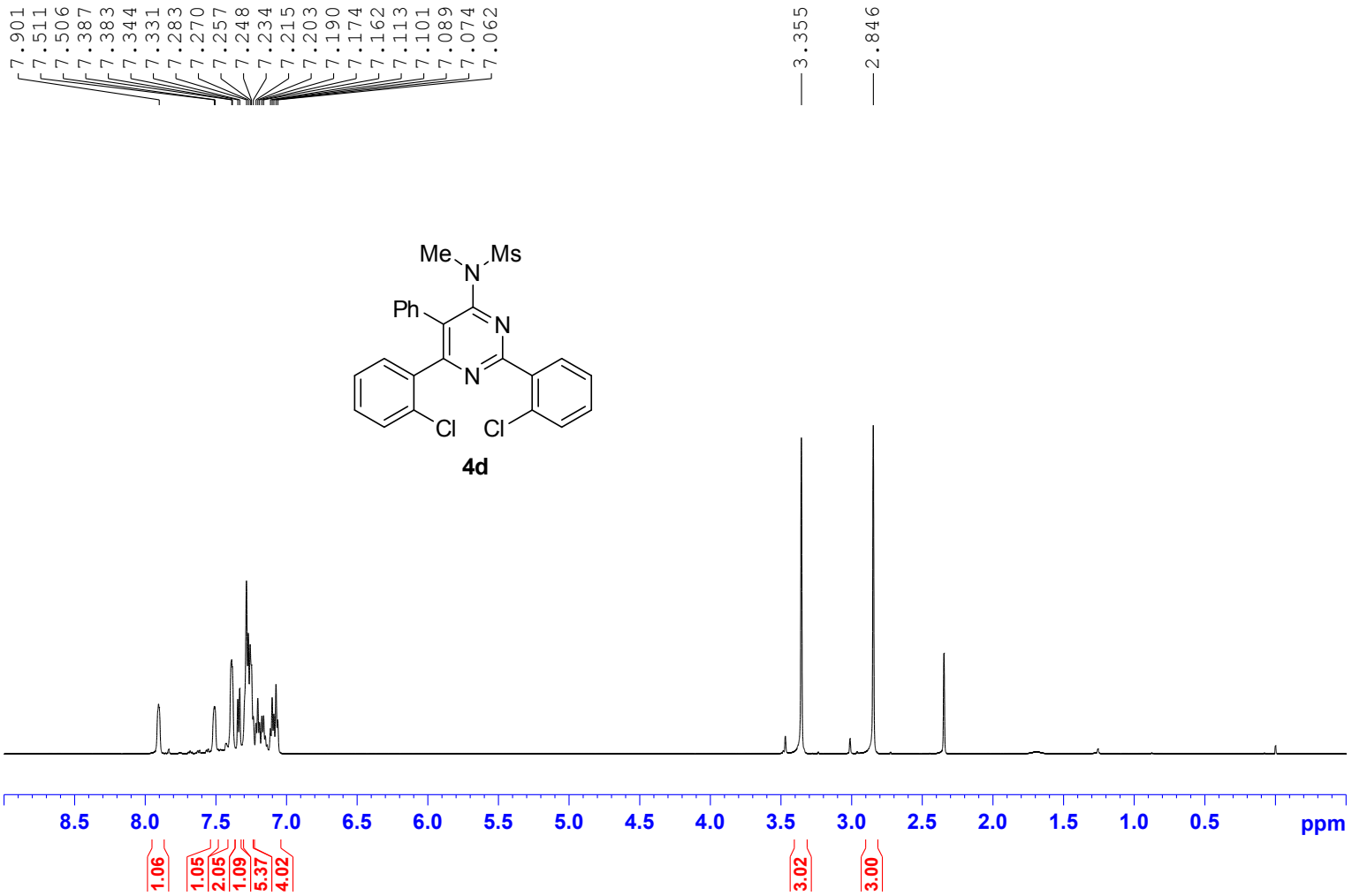
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7.190
7.174
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7.113
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7.089
7.074
7.062
3.355
2.846
Me
N
Ms
Ph
N
N
Cl
Cl
4d
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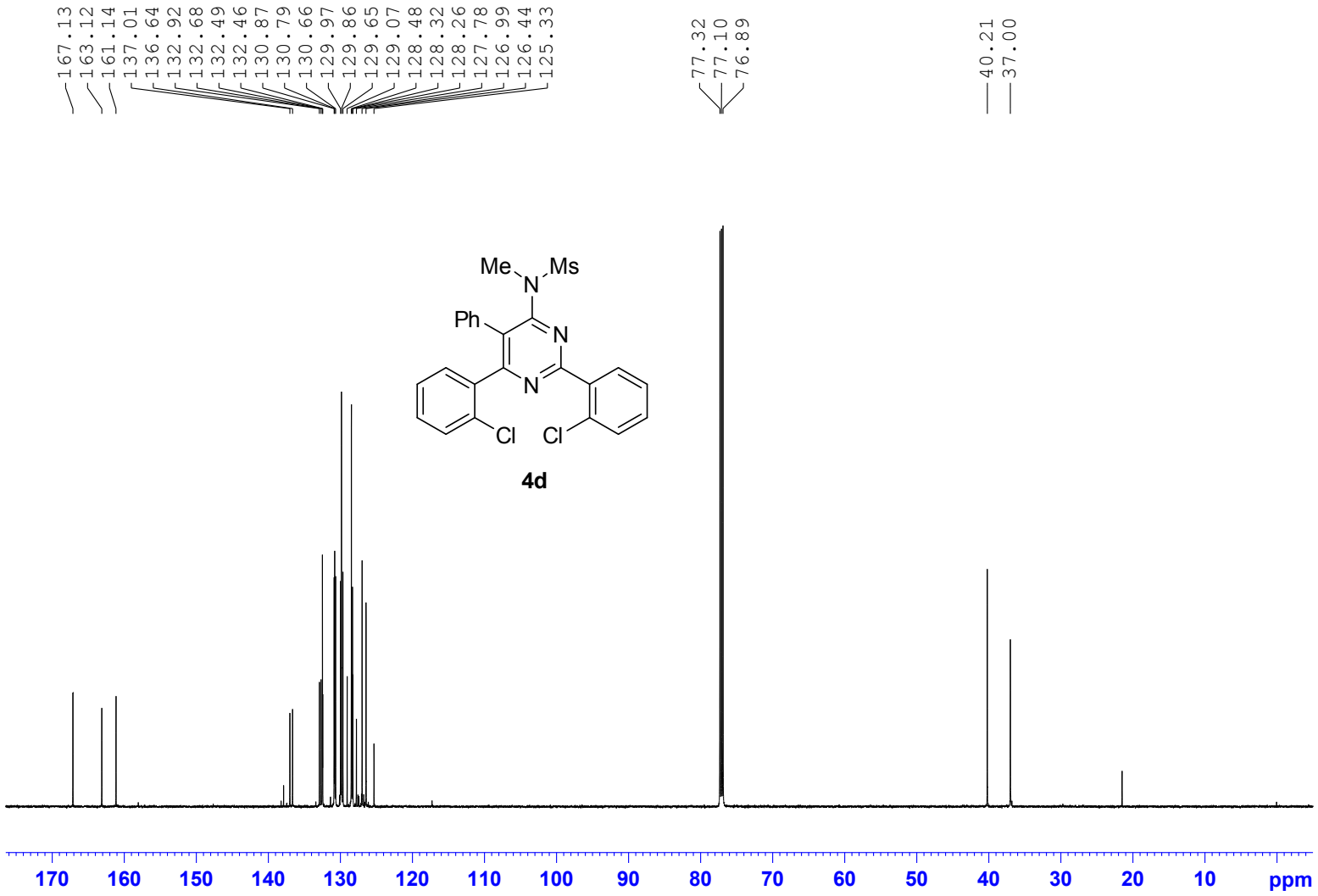
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126.44
125.33
77.32
77.10
76.89
40.21
37.00
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Ms
Ph
N
N
Cl
Cl
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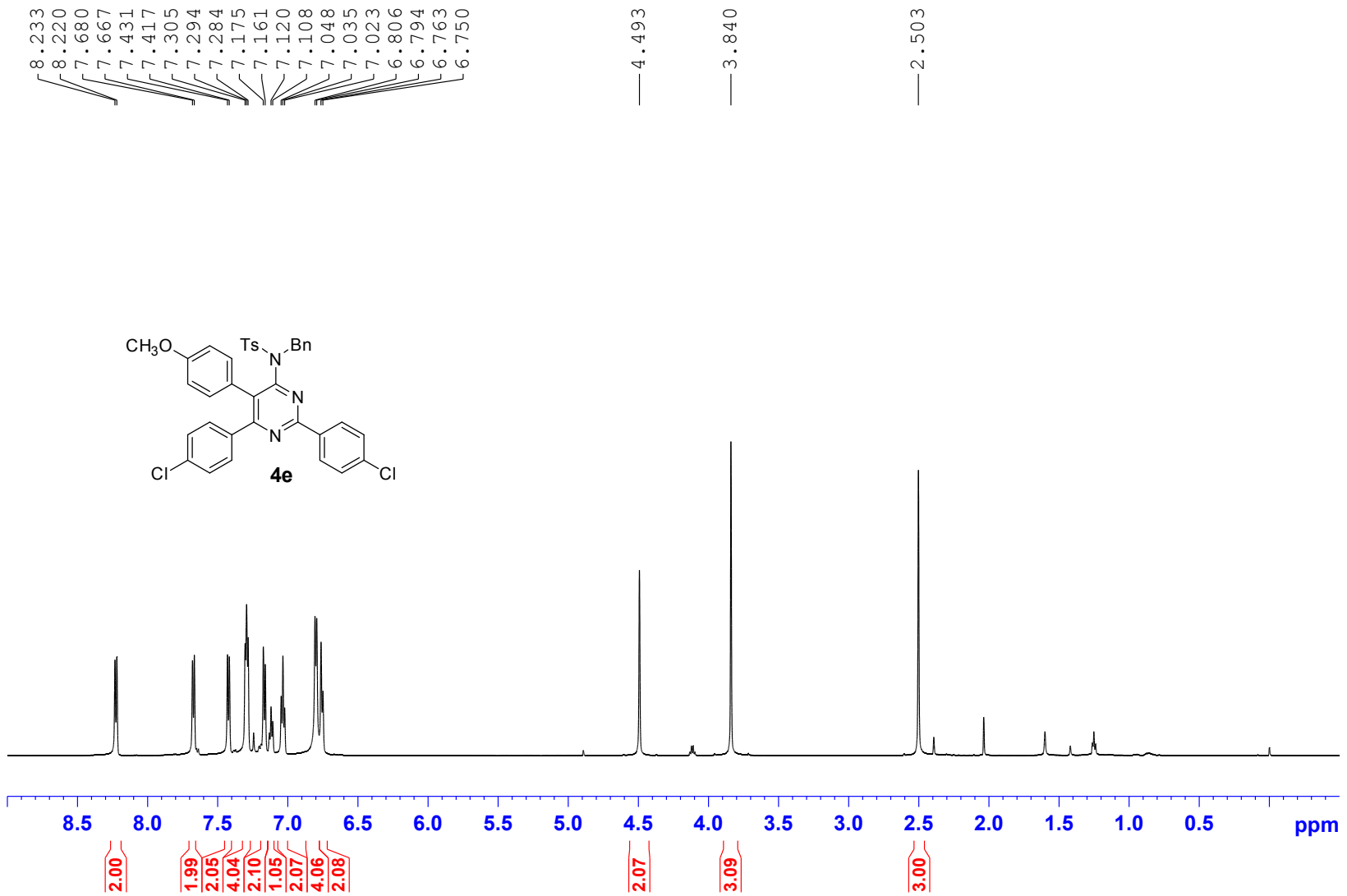
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7.048
7.035
7.023
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6.794
6.763
6.750
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3.840
2.503
CH3O
Ts
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Bn
N
N
Cl
Cl
4e
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8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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1.0
0.5
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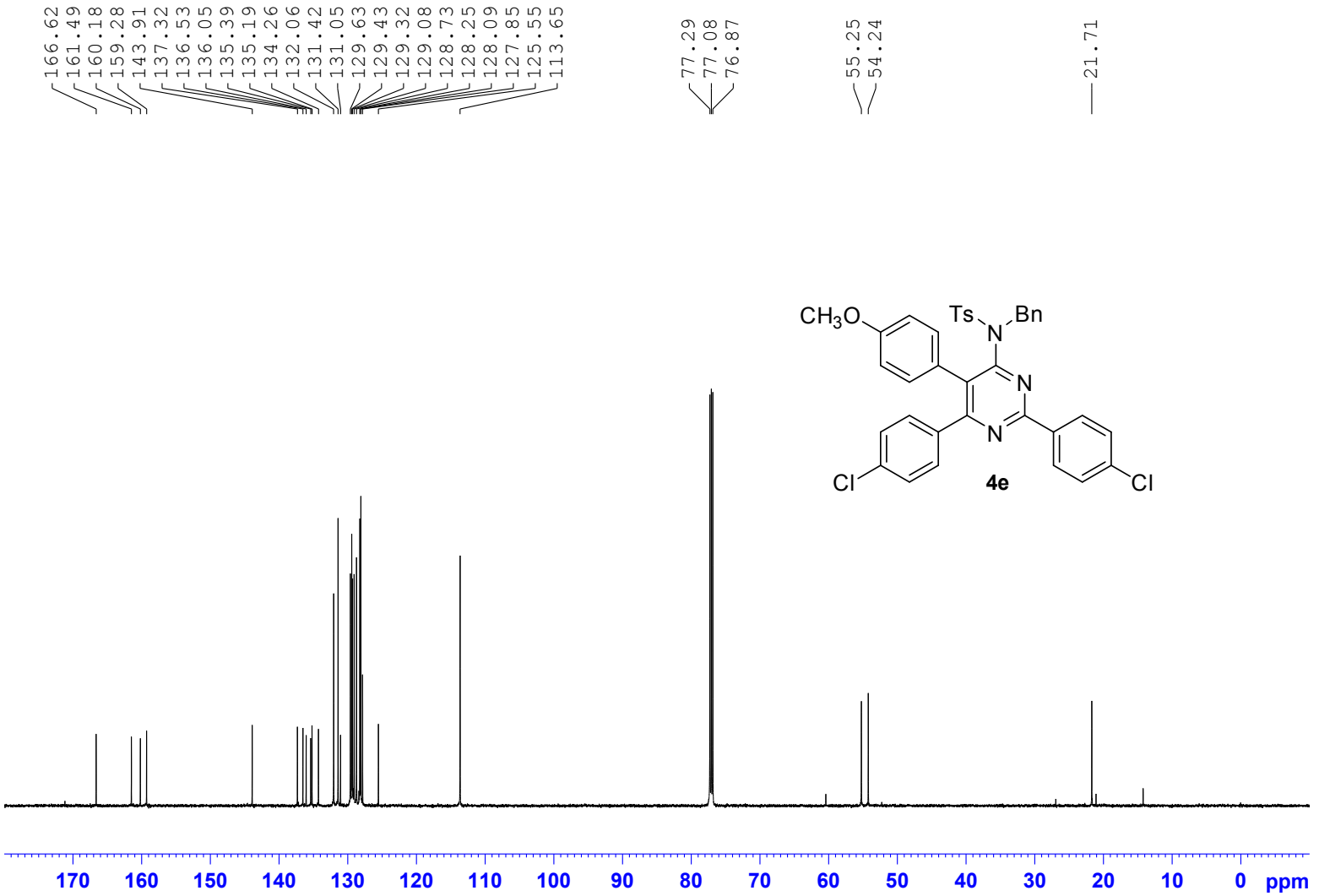
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129.43
129.32
129.08
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128.25
128.09
127.85
125.55
113.65
77.29
77.08
76.87
55.25
54.24
21.71
CH3O
Ts
N
Bn
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Cl
Cl
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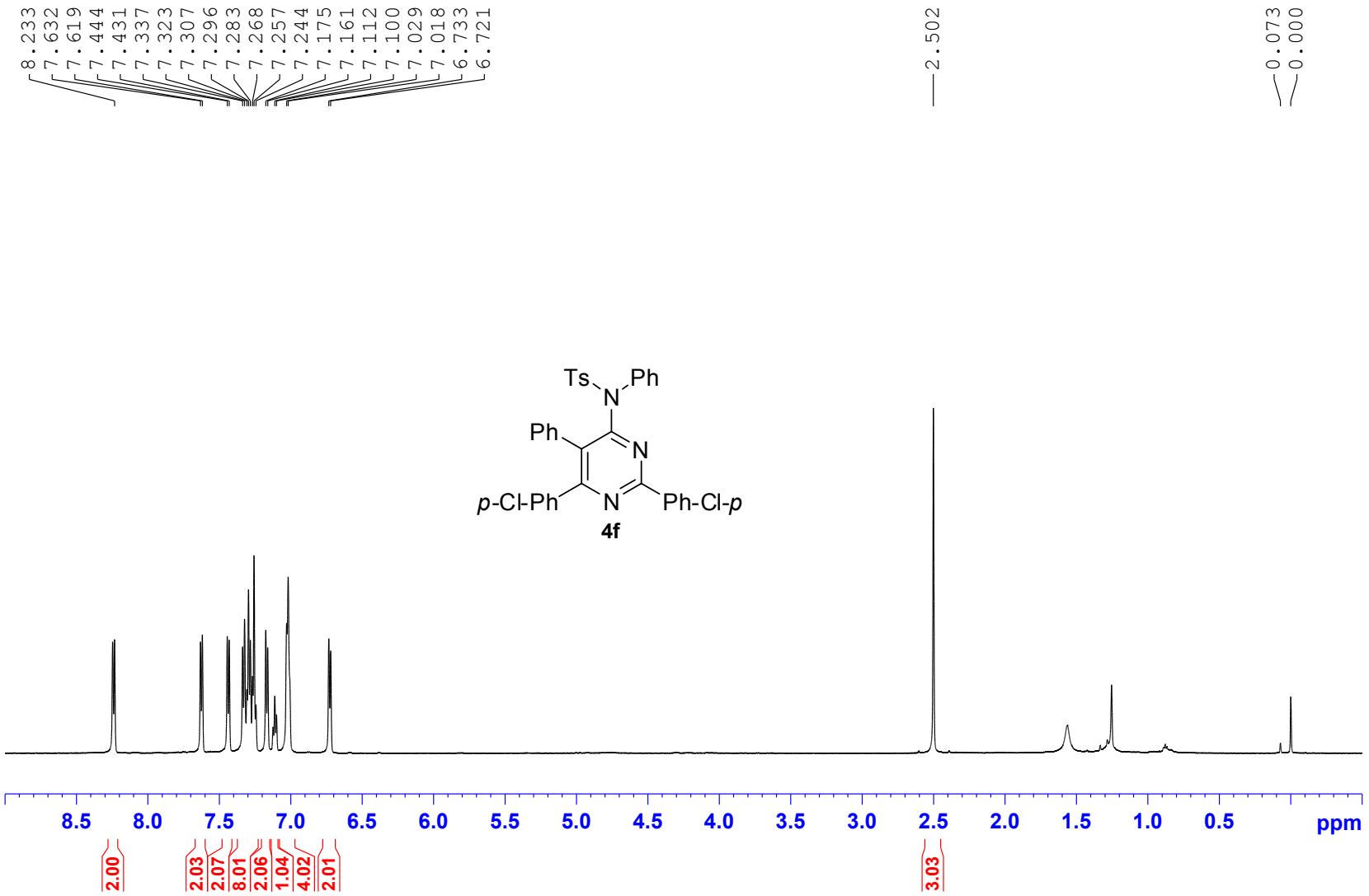
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7.244
7.175
7.161
7.112
7.100
7.029
7.018
6.733
6.721
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0.000
Ts
N
Ph
Ph
N
p-Cl-Ph
N
Ph-Cl-p
4f
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
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4.0
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3.0
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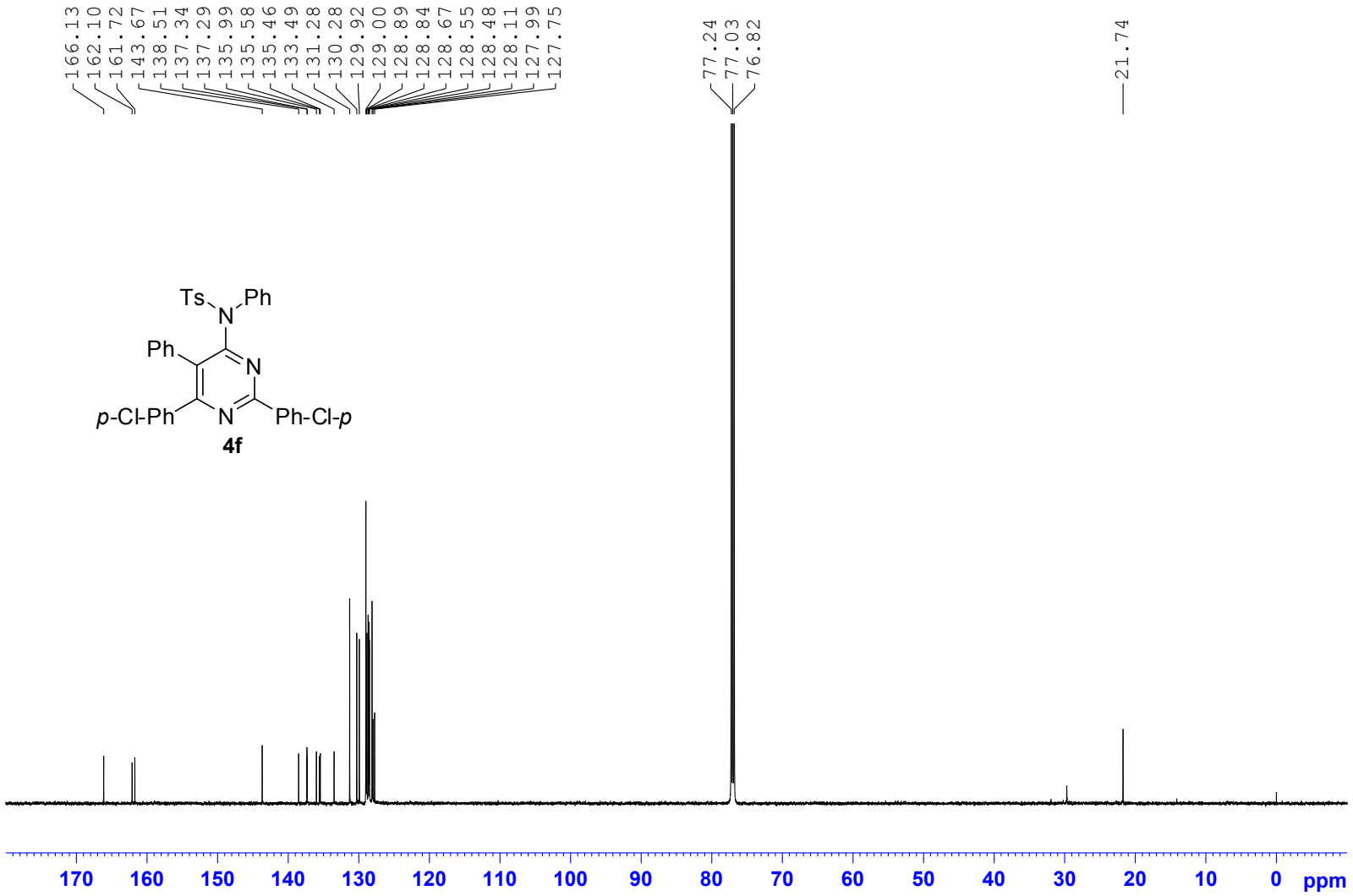
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129.92
129.00
128.89
128.84
128.67
128.55
128.48
128.11
127.99
127.75
77.24
77.03
76.82
21.74
Ts
N
Ph
Ph
N
p-Cl-Ph
N
Ph-Cl-p
4f
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140
130
120
110
100
90
80
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60
50
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30
20
10
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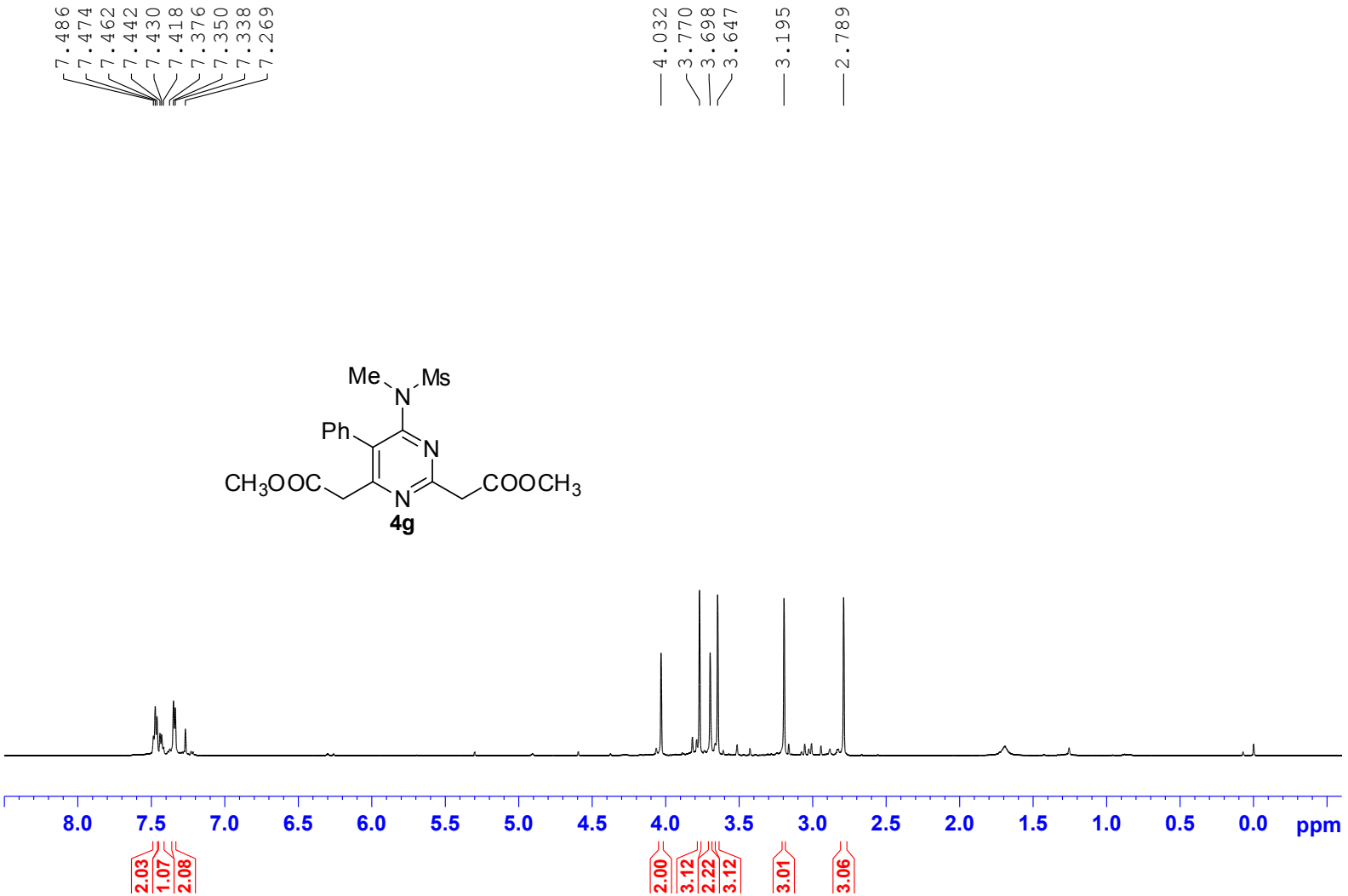
ppm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4.032
3.770
3.698
3.647
3.195
2.789
Me
N
Ms
Ph
N
CH3OOC
COOCH3
N
4g
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
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ppm
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1.07
2.08
2.00
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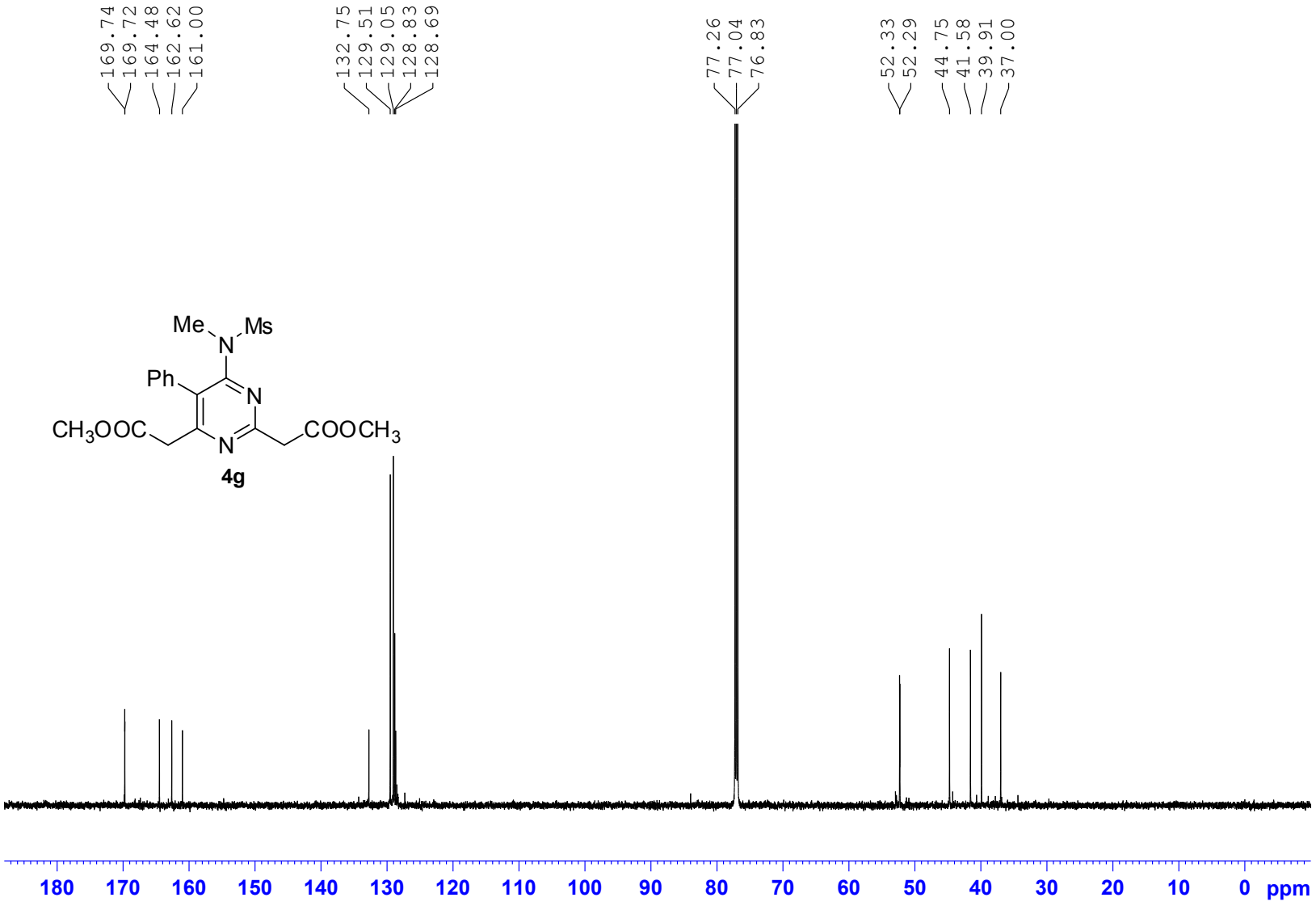
3.01
3.06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52.33
52.29
44.75
41.58
39.91
37.00
Me
N
Ms
Ph
N
CH3OOC
COOCH3
N
4g
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140
130
120
110
100
90
80
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60
50
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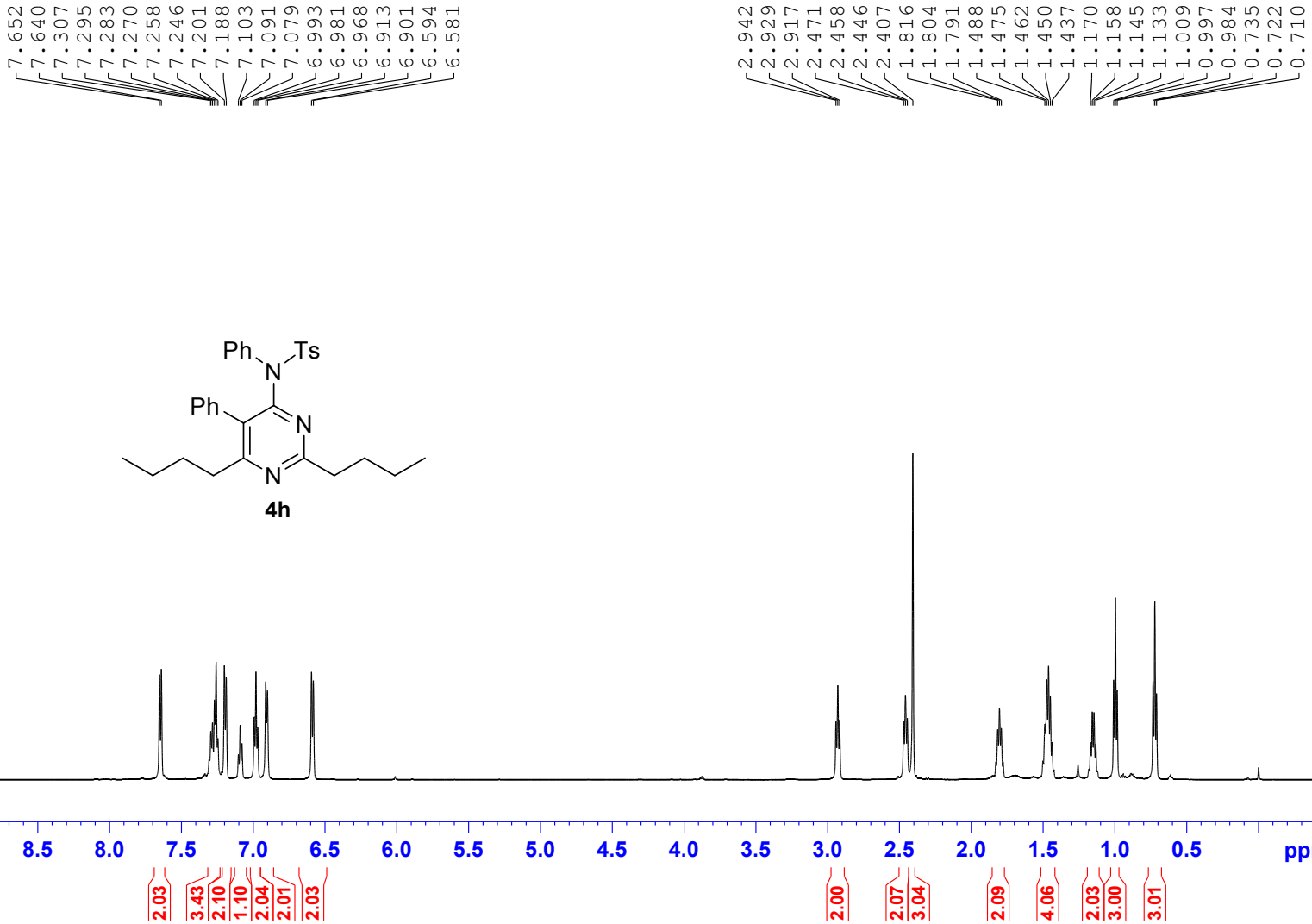
30
20
10
0
ppm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7.079
6.993
6.981
6.968
6.913
6.901
6.594
6.581
2.942
2.929
2.917
2.471
2.458
2.446
2.407
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1.791
1.488
1.475
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1.450
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1.170
1.158
1.145
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0.984
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0.710
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Ts
Ph
N
N
4h
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7.5
7.0
6.5
6.0
5.5
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3.5
3.0
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2.09
4.06
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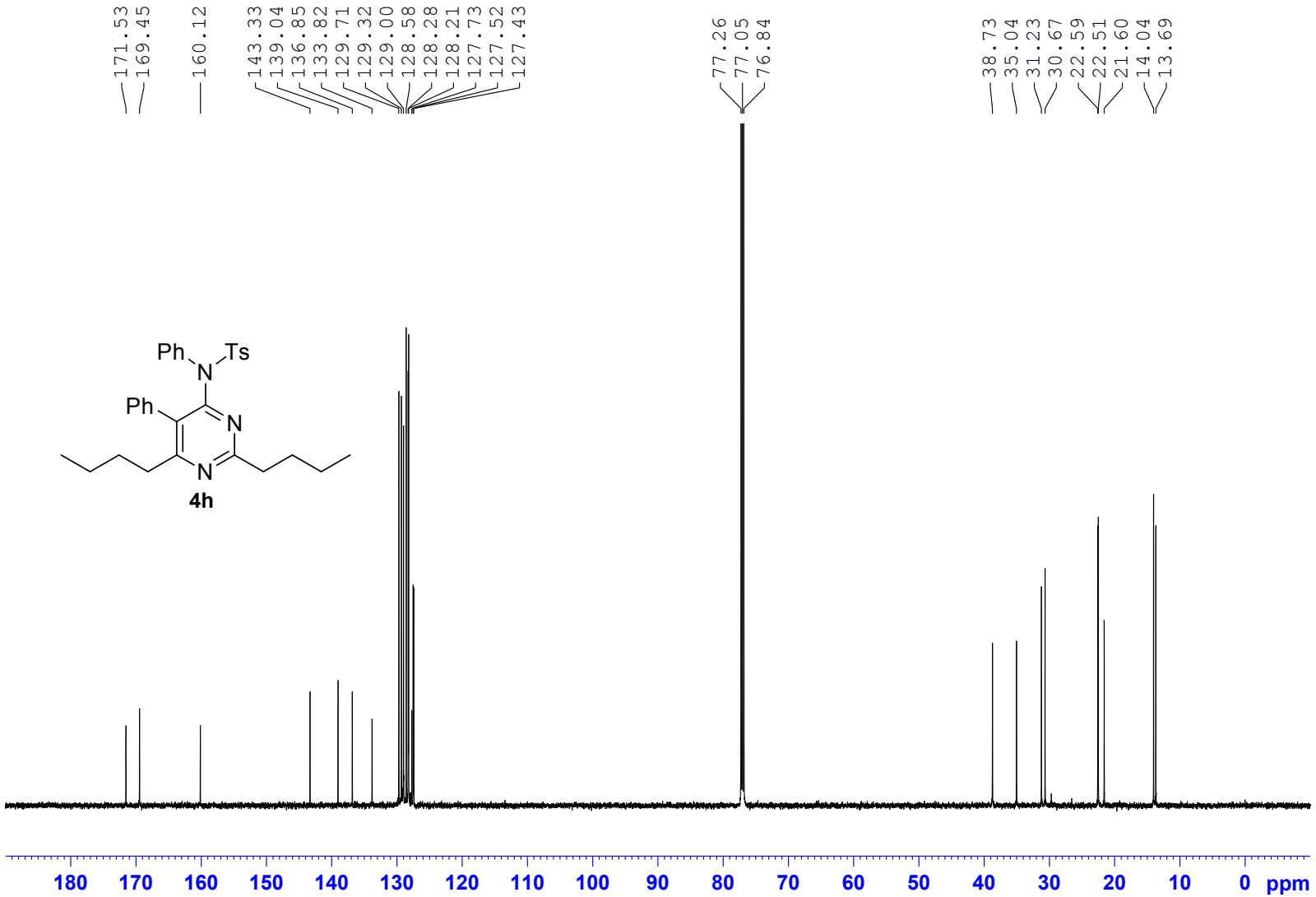
3.01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127.73
127.52
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77.26
77.05
76.84
38.73
35.04
31.23
30.67
22.59
22.51
21.60
14.04
13.69
Ph
N
Ts
Ph
N
N
4h
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50
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20
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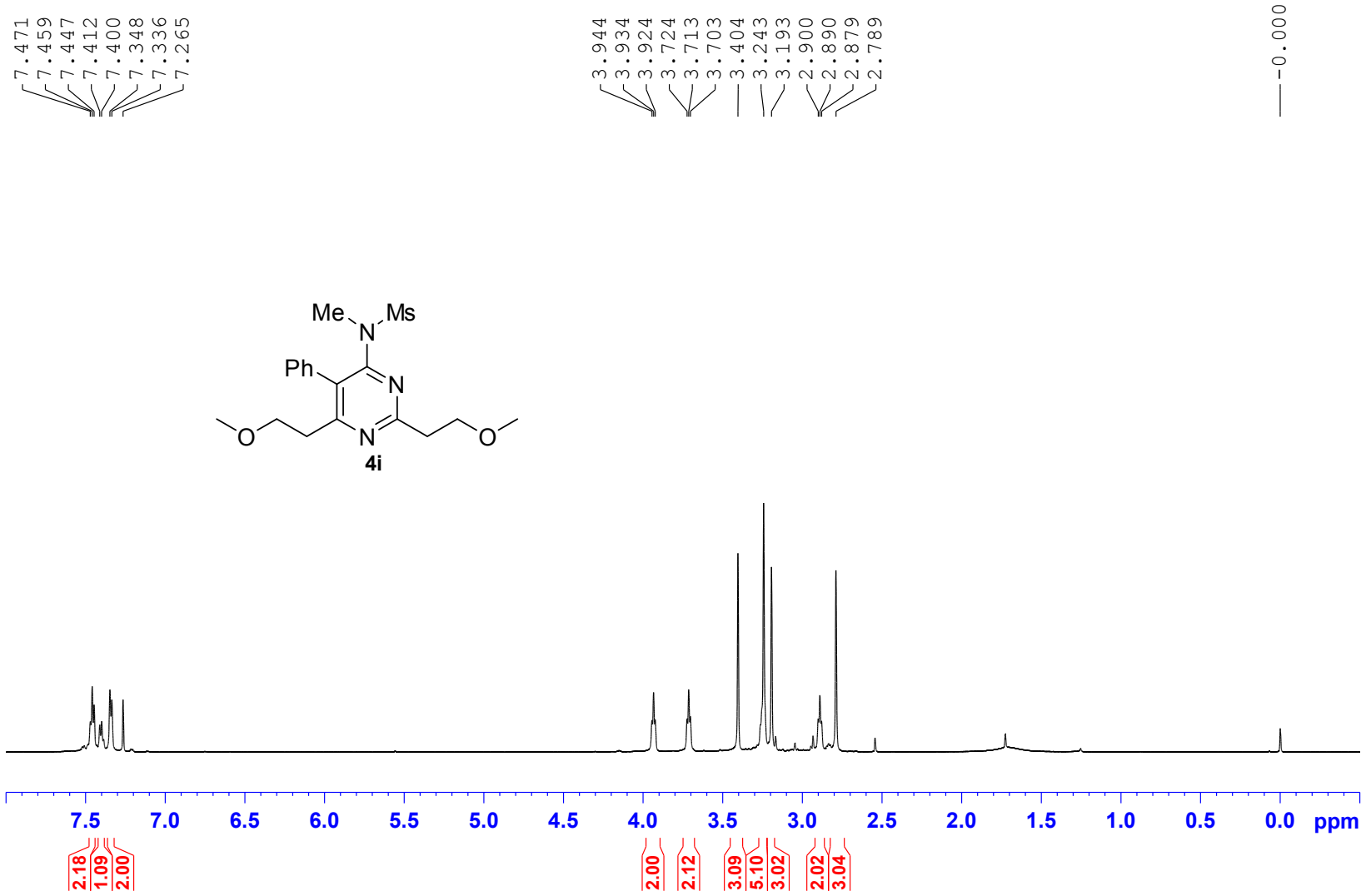
ppm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3.713
3.703
3.404
3.243
3.193
2.900
2.890
2.879
2.789
0.000
Me
N
Ms
Ph
N
O
N
O
4i
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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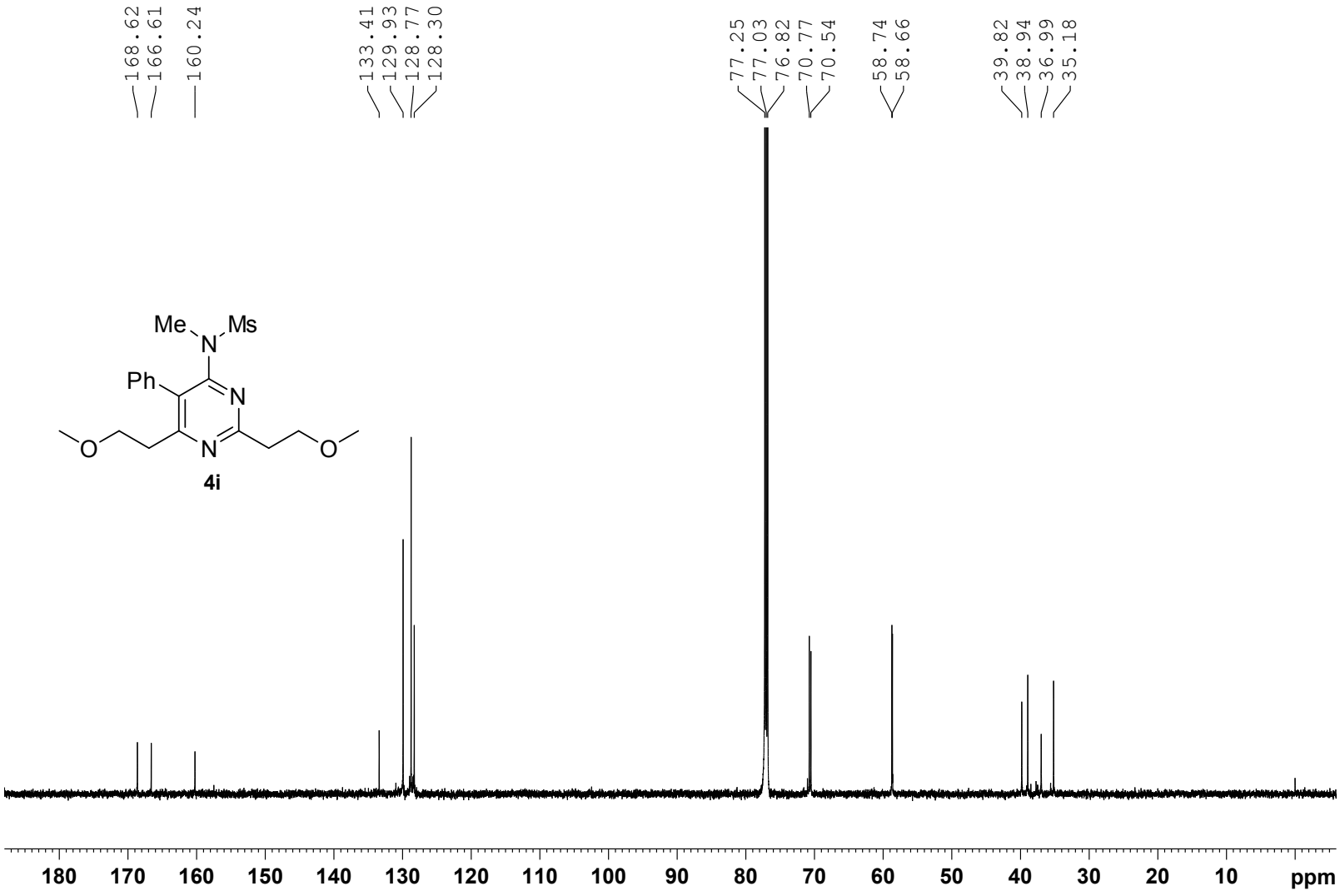
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70.54
58.74
58.66
39.82
38.94
36.99
35.18
Me
Ms
N
Ph
N
N
O
O
4i
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150
140
130
120
110
100
90
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70
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30
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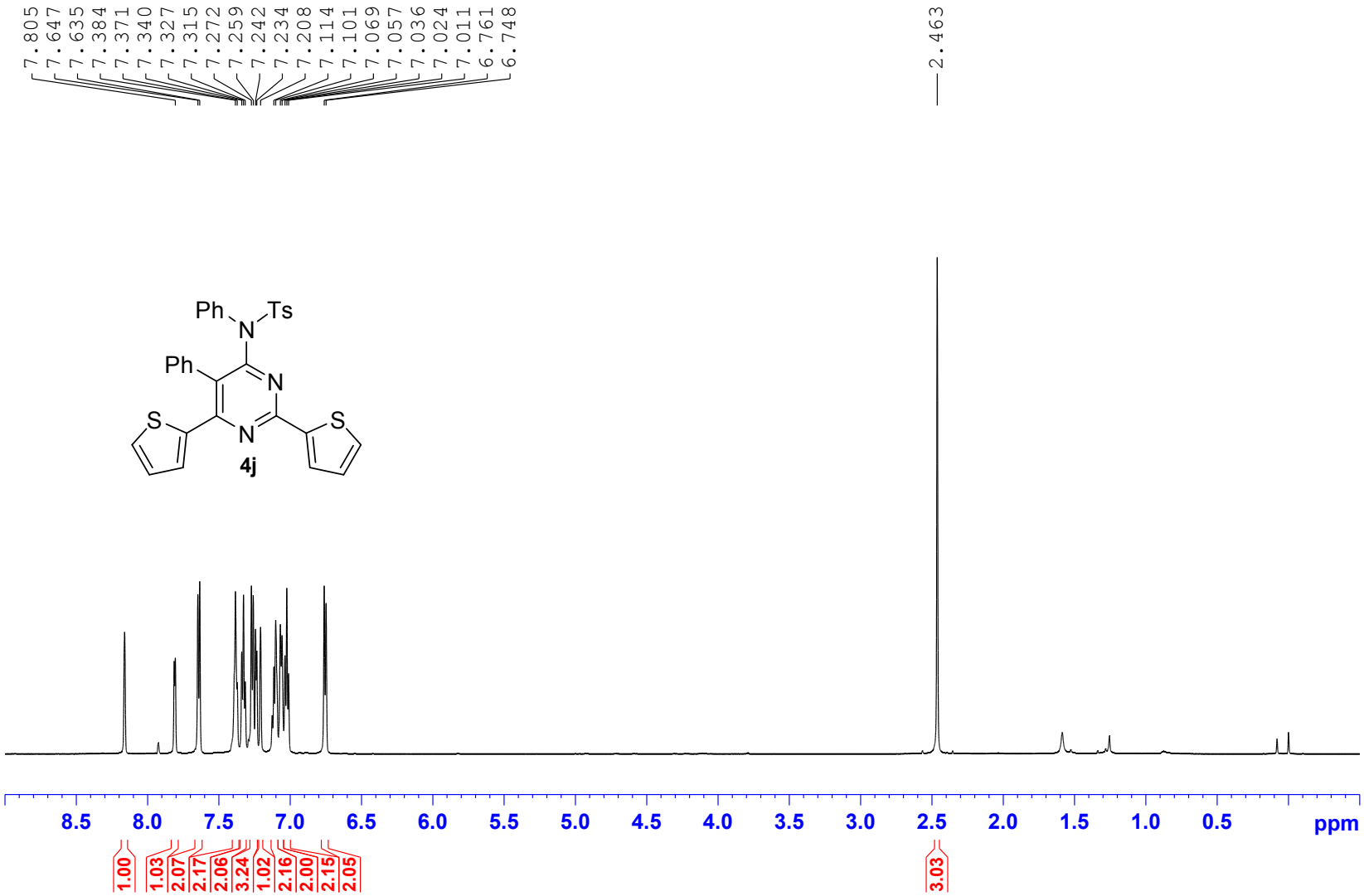
10
ppm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7.208
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7.101
7.069
7.057
7.036
7.024
7.011
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6.748
2.463
Ph
N
Ts
Ph
N
S
N
S
4j
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
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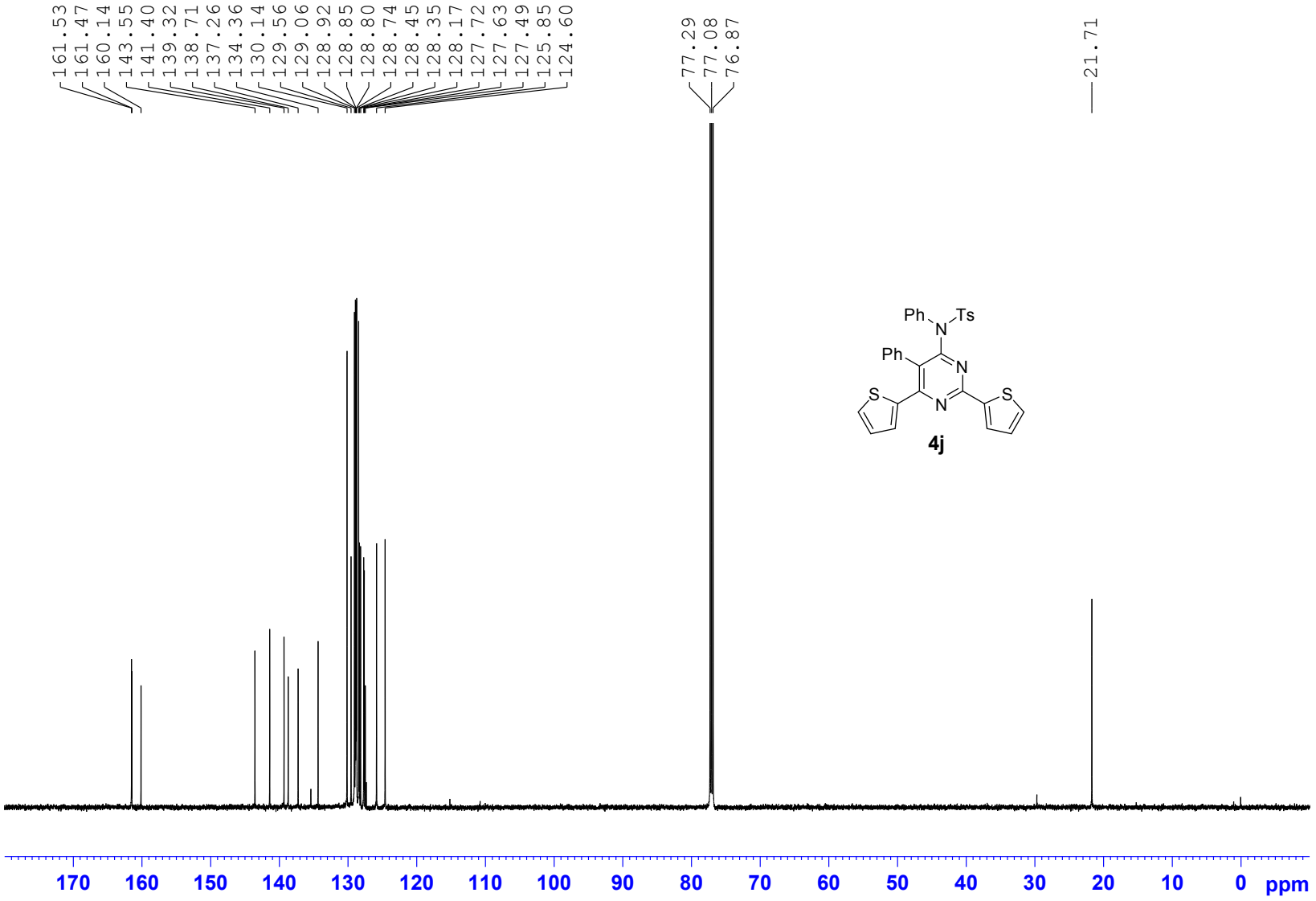
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127.49
125.85
124.60
77.29
77.08
76.87
21.71
Ph
N
Ts
Ph
N
N
S
S
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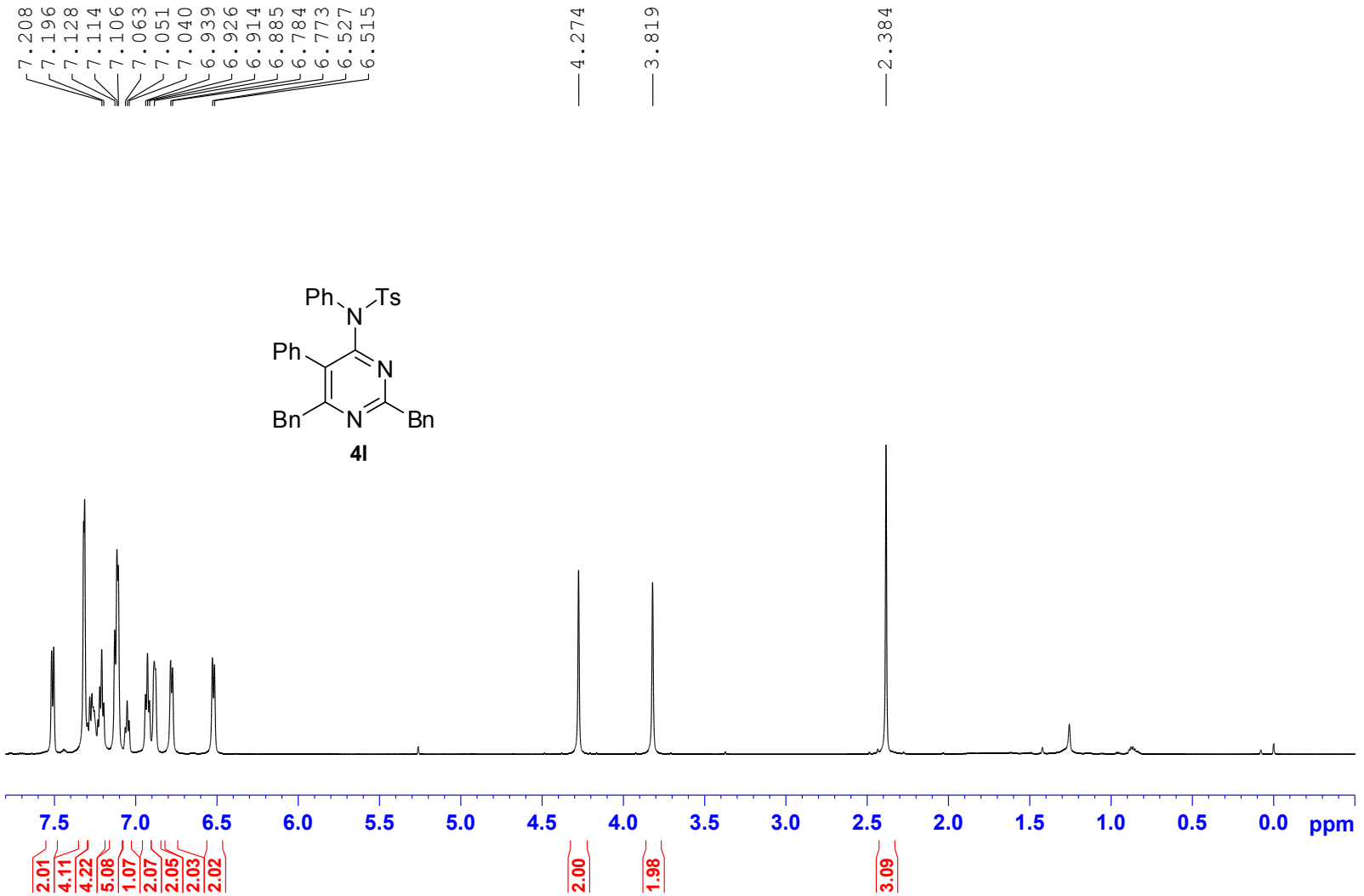
ppm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6.784
6.773
6.527
6.515
4.274
3.819
2.384
Ph
N
Ts
Ph
N
Bn
N
Bn
4l
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6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
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0.0
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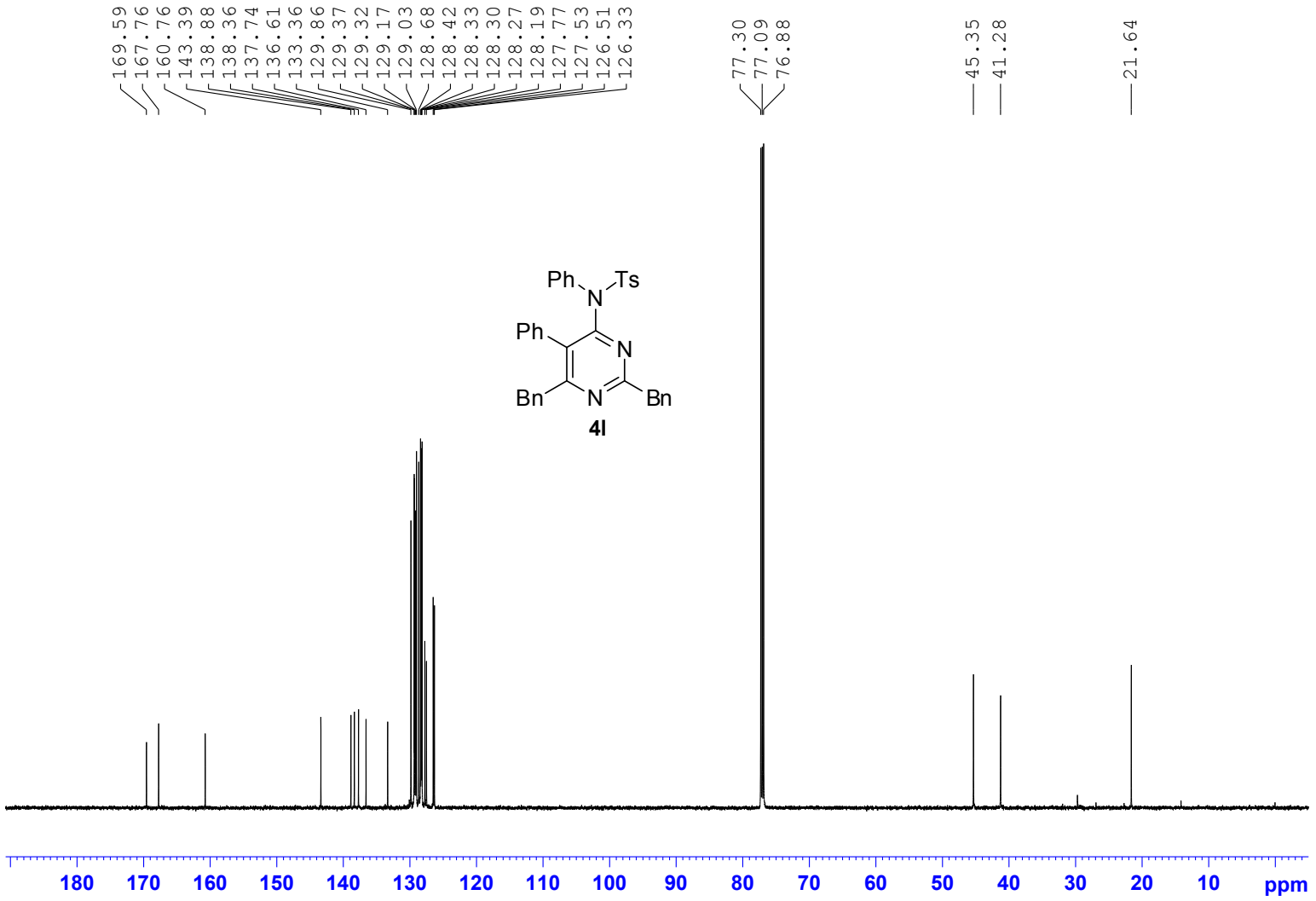
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77.09
76.88
45.35
41.28
21.64
Ph
N
Ts
Ph
N
Bn
N
Bn
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30
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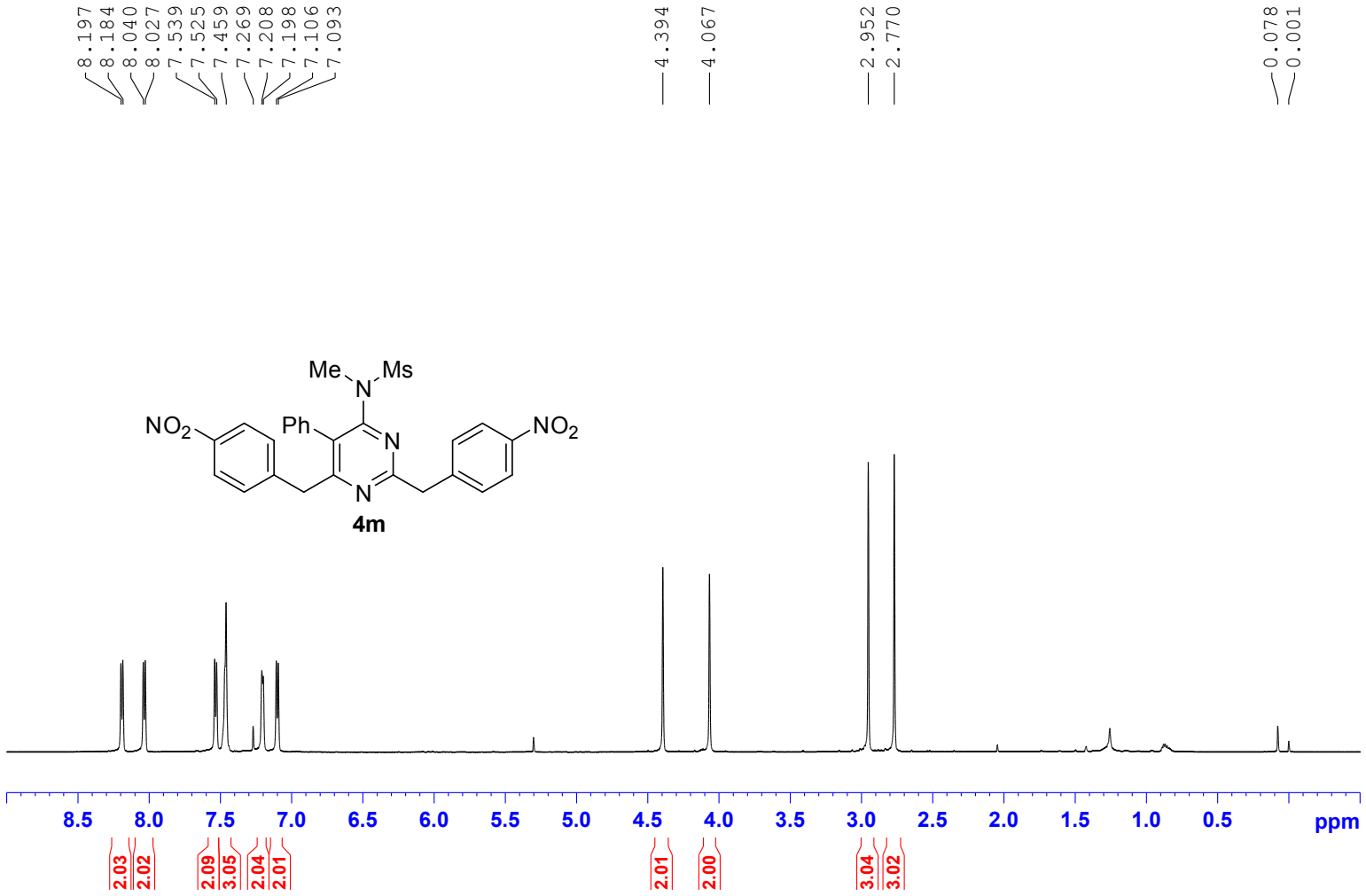
10
ppm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4.067
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0.001
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N
Ms
NO2
Ph
N
NO2
N
4m
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7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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2.5
2.0
1.5
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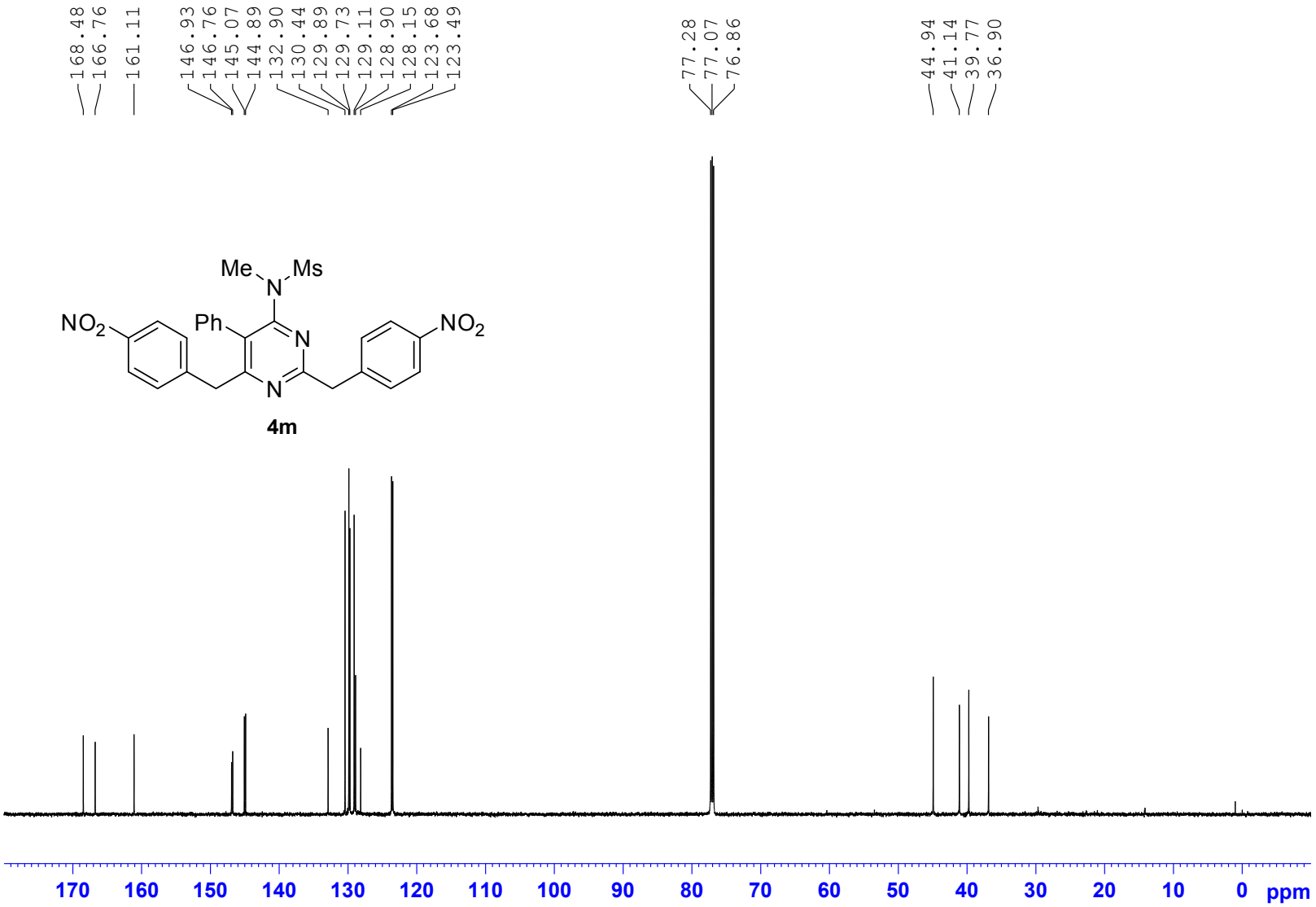
3.04
3.02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77.28
77.07
76.86
44.94
41.14
39.77
36.90
Me
Ms
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Ph
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N
NO2
NO2
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140
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50
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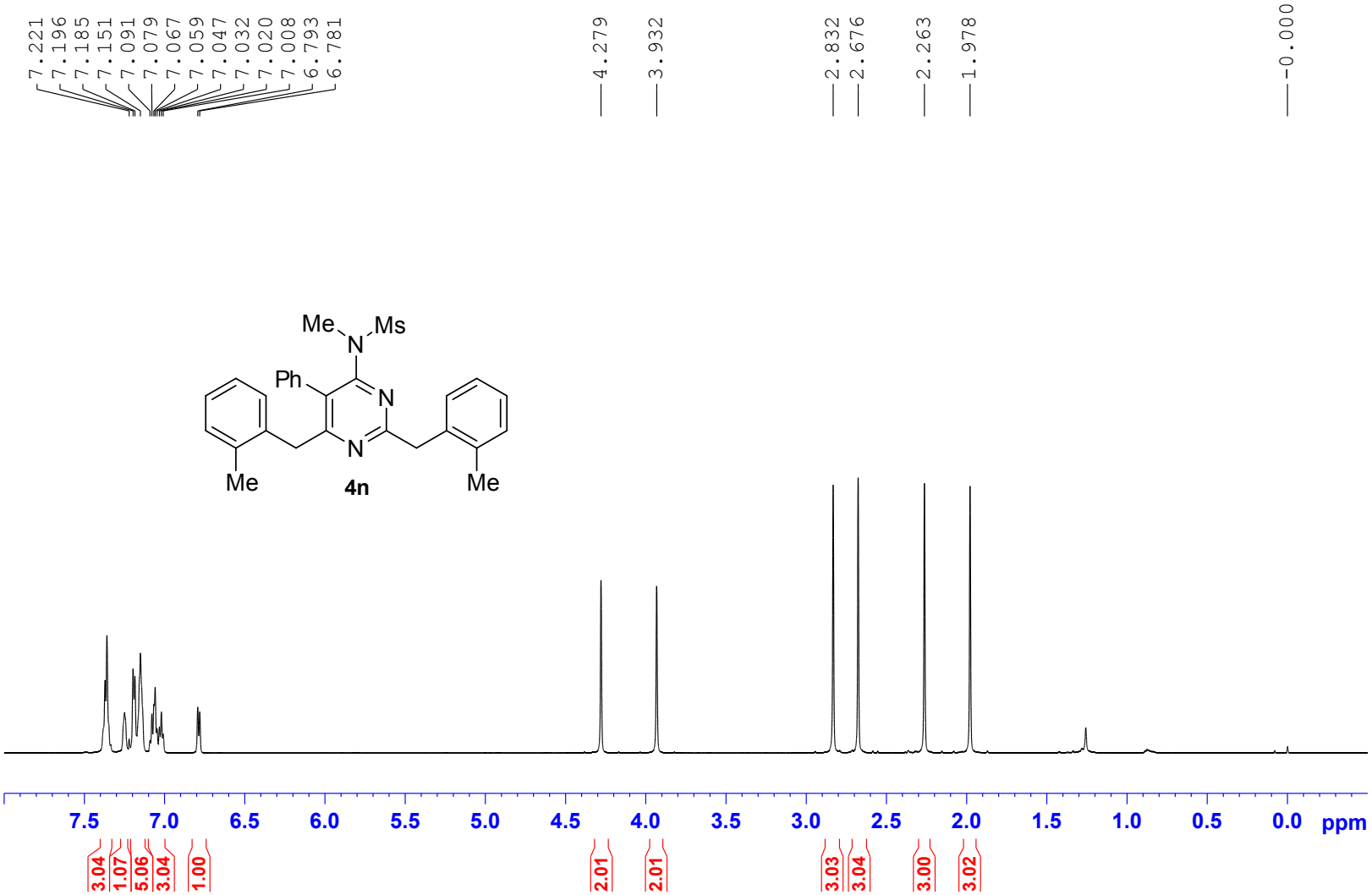
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N
Ms
Ph
N
N
Me
Me
4n
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5.0
4.5
4.0
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3.0
2.5
2.0
1.5
1.0
0.5
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2.01
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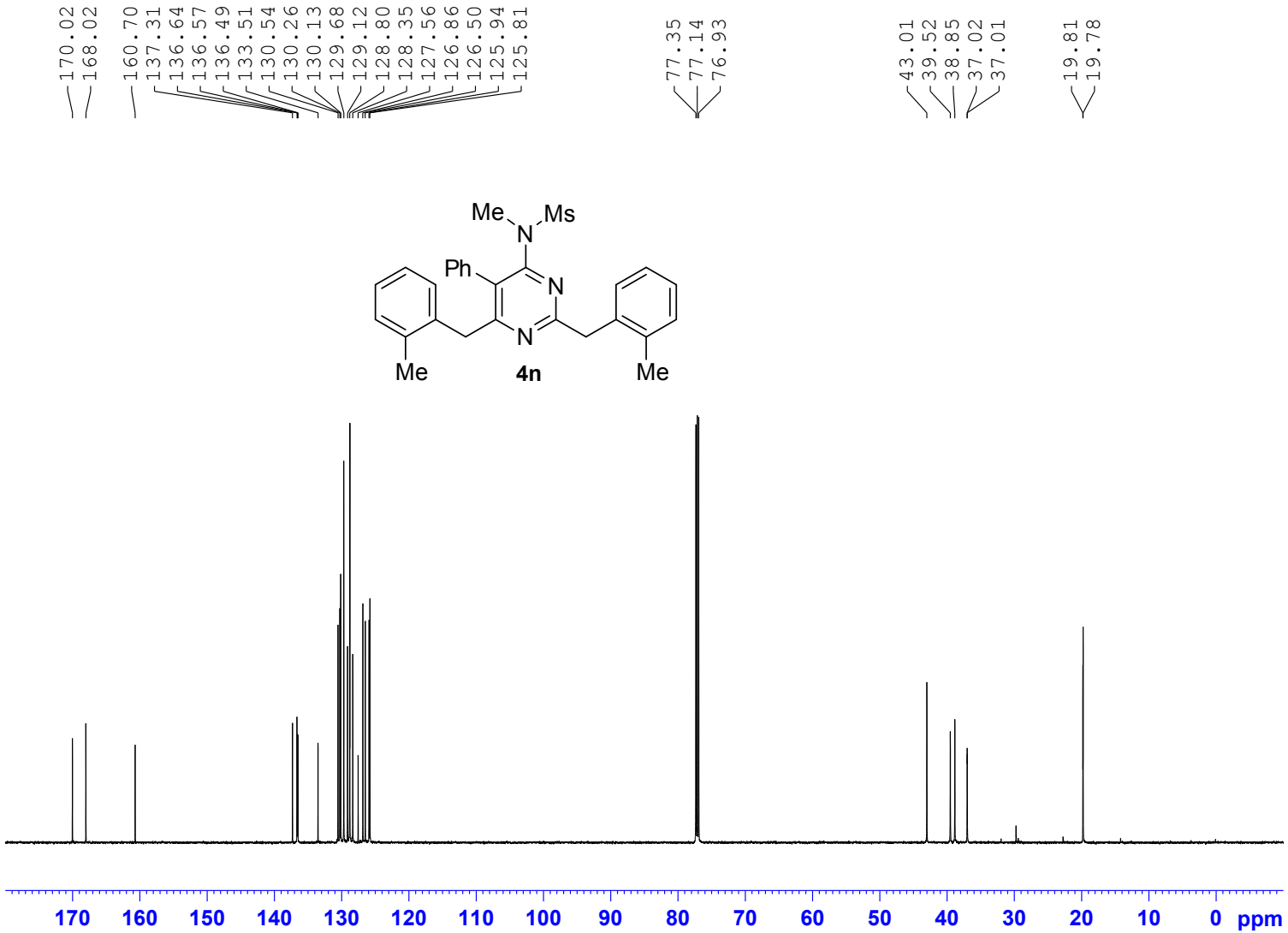
3.02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Me
Me
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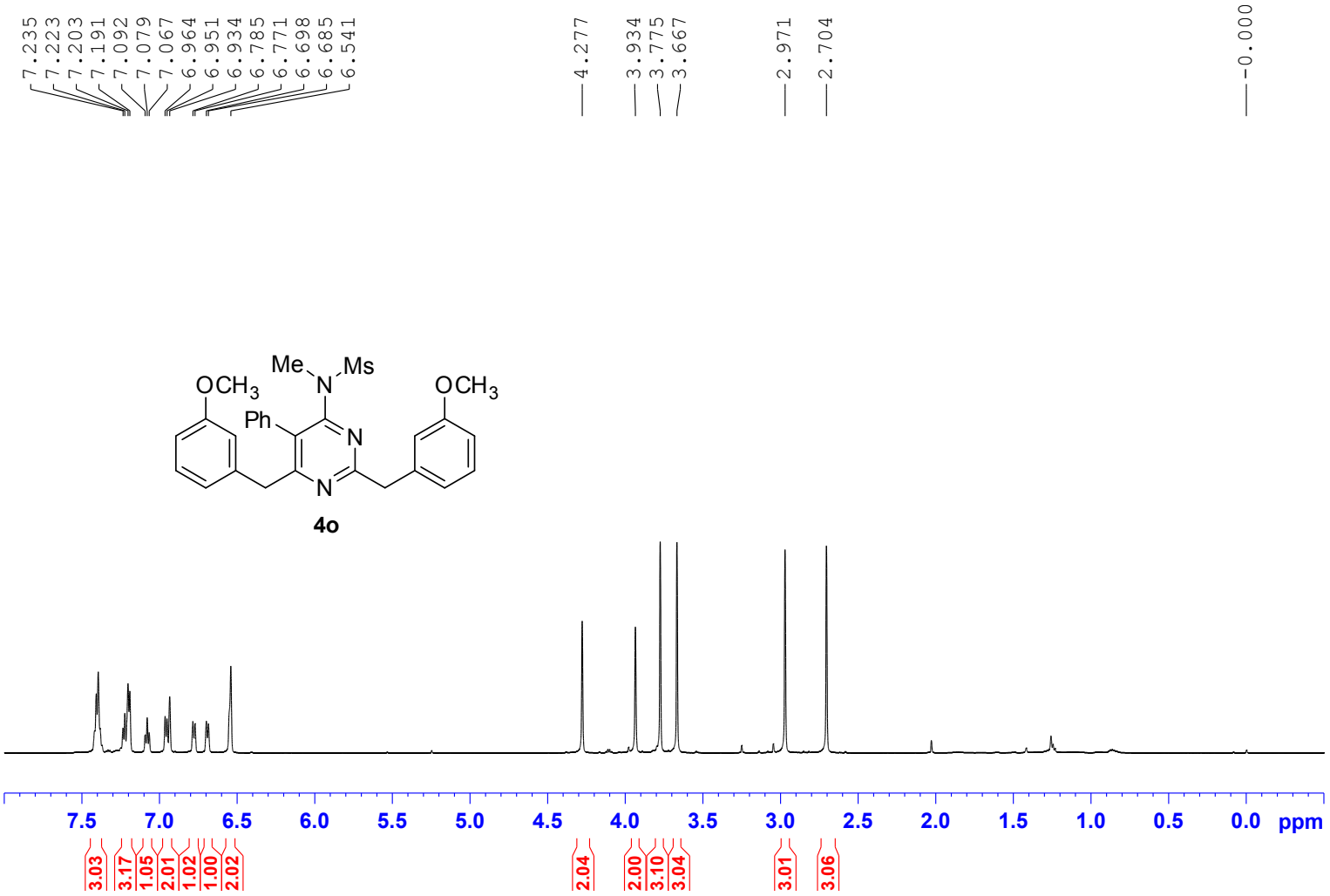
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OCH3
Ph
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2.0
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0.0
ppm
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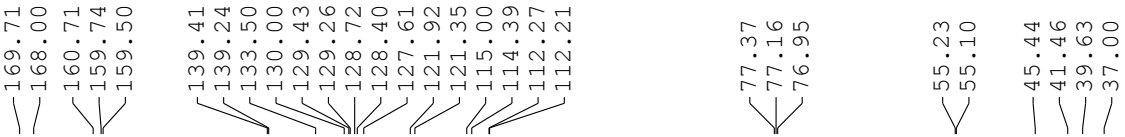
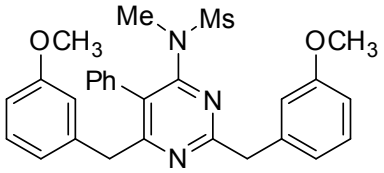
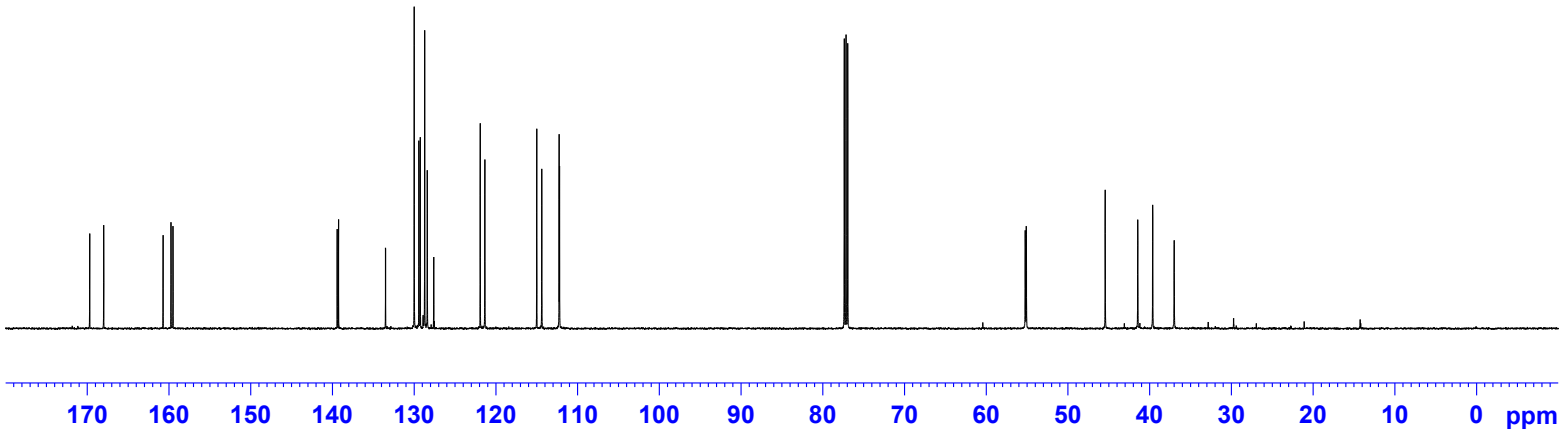
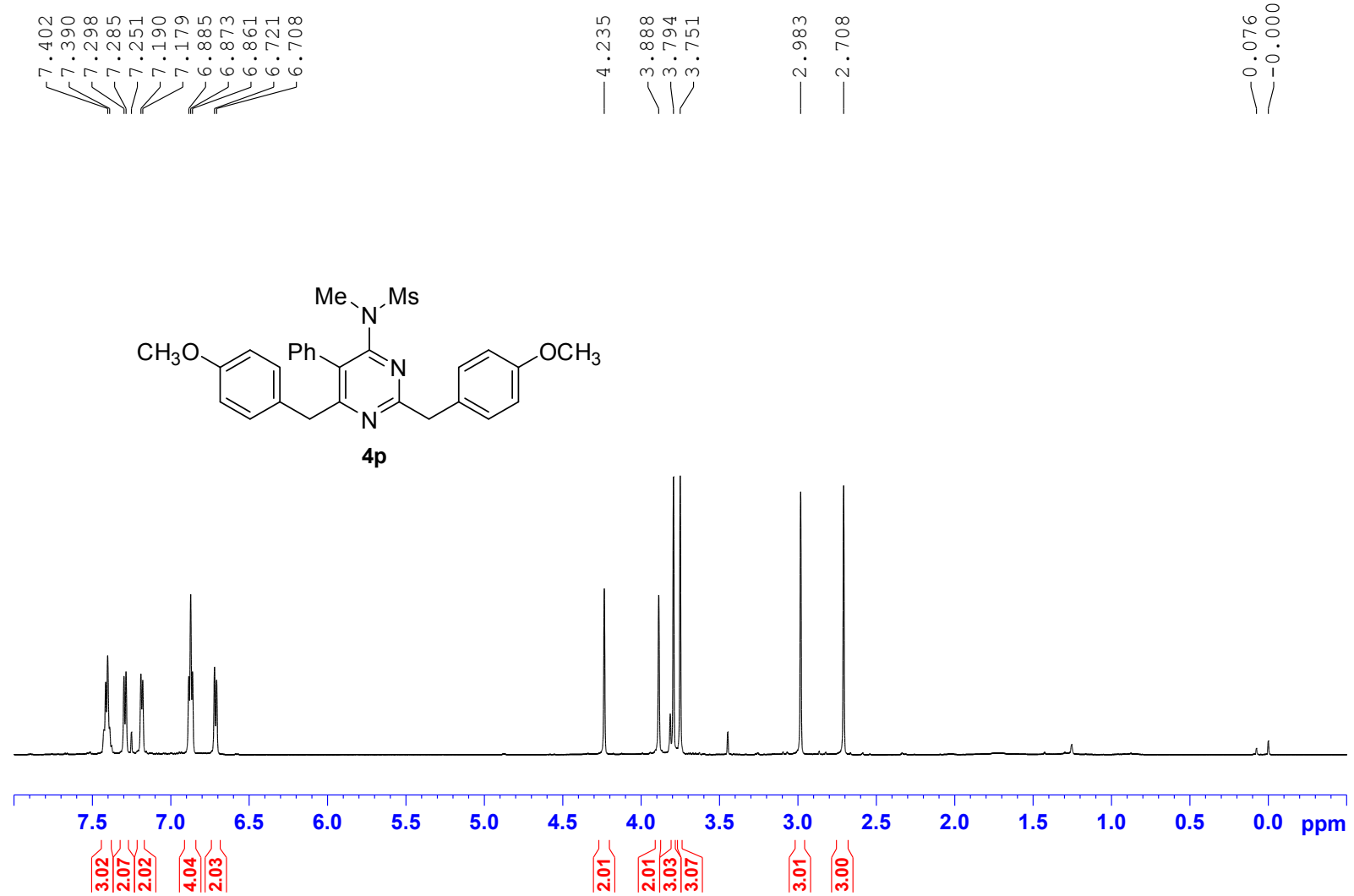
1.02
1.00
2.02
2.04
2.00
3.10
3.04
3.01
3.06

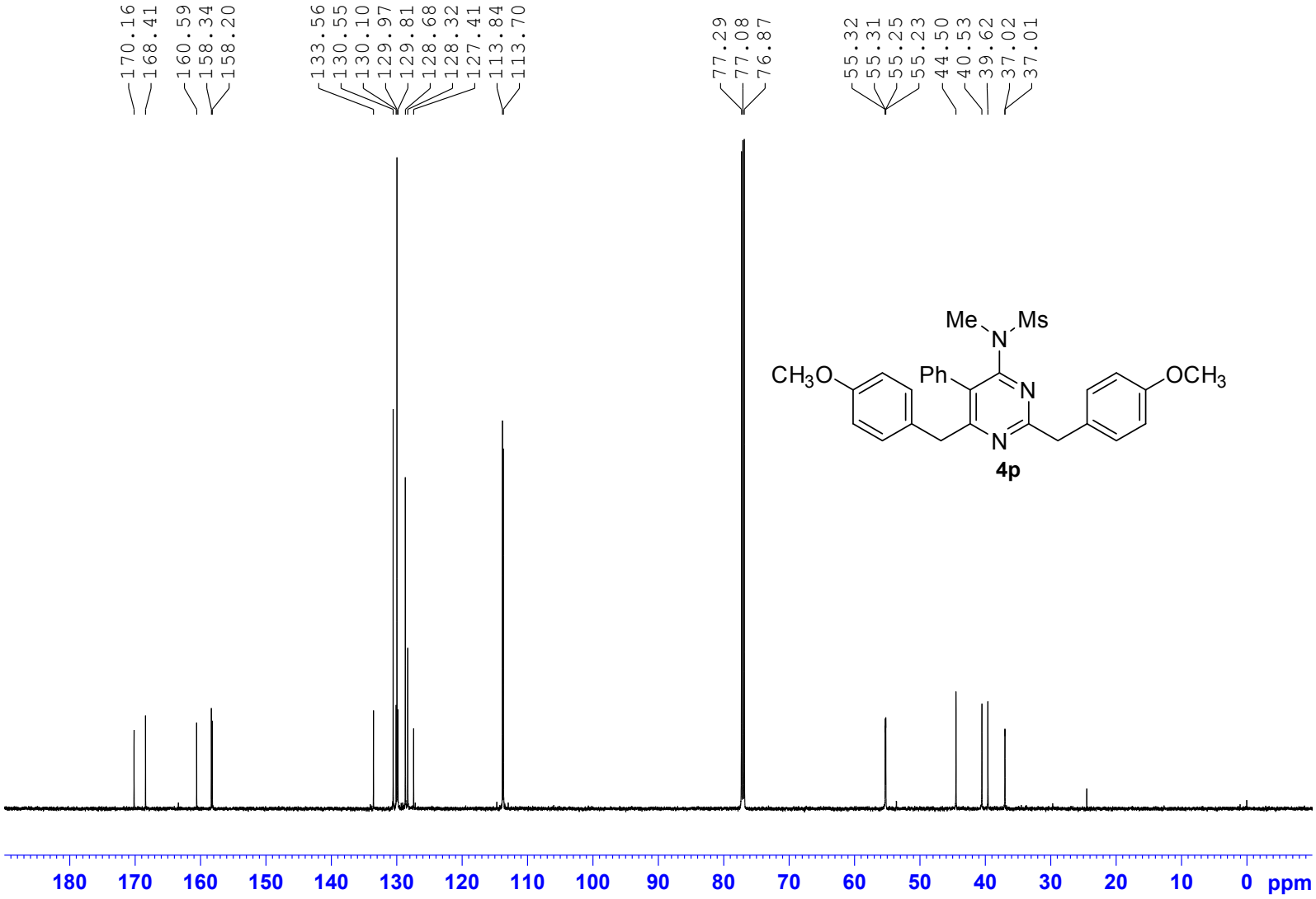

169.71
168.00
160.71
159.74
159.50
139.41
139.24
133.50
130.00
129.43
129.26
128.72
128.40
127.61
121.92
121.35
115.00
114.39
112.27
112.21
77.37
77.16
76.95
55.23
55.10
45.44
41.46
39.63
37.00

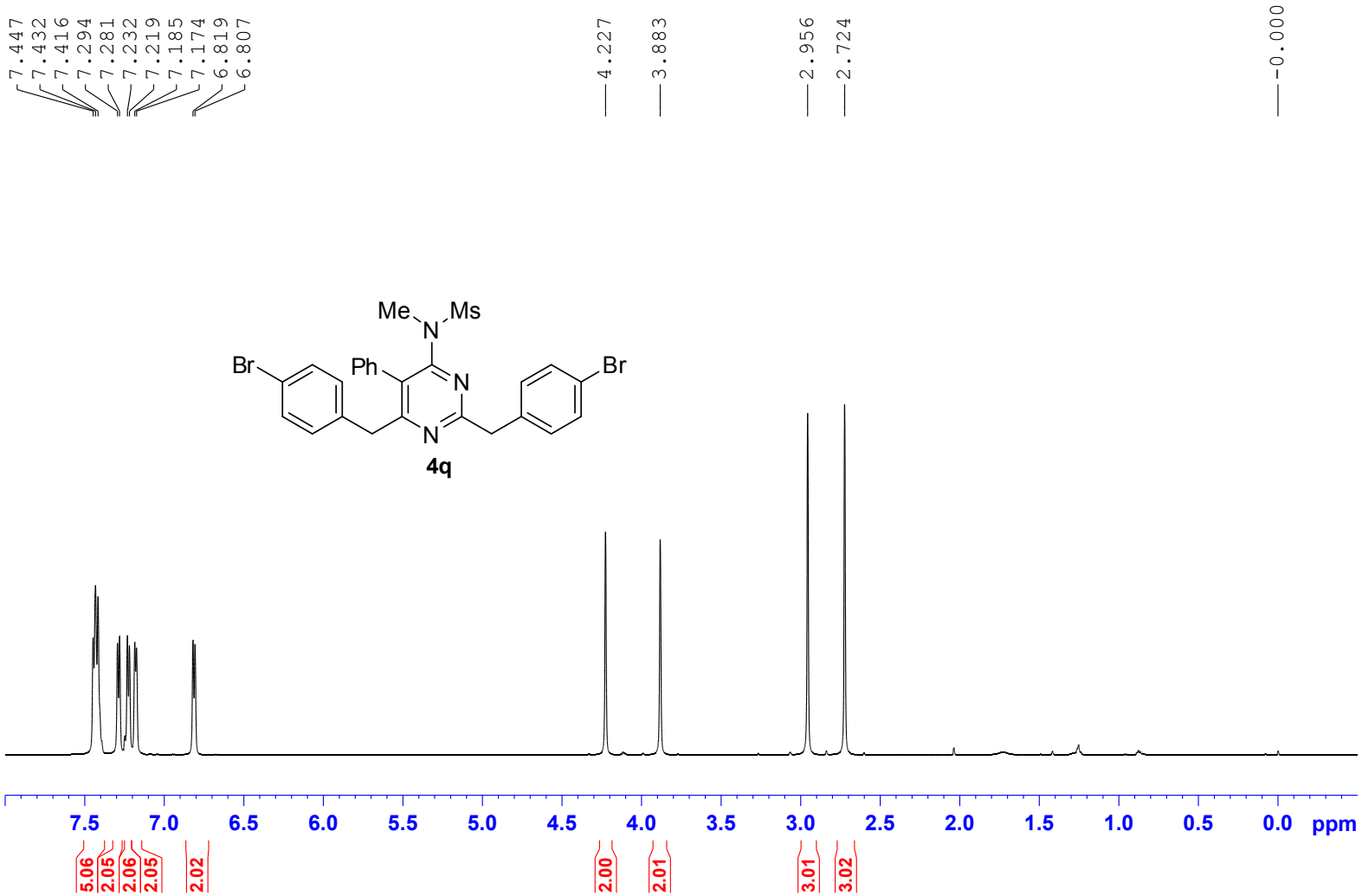

Me
N
Ms
OCH3
OCH3
Ph
N
N

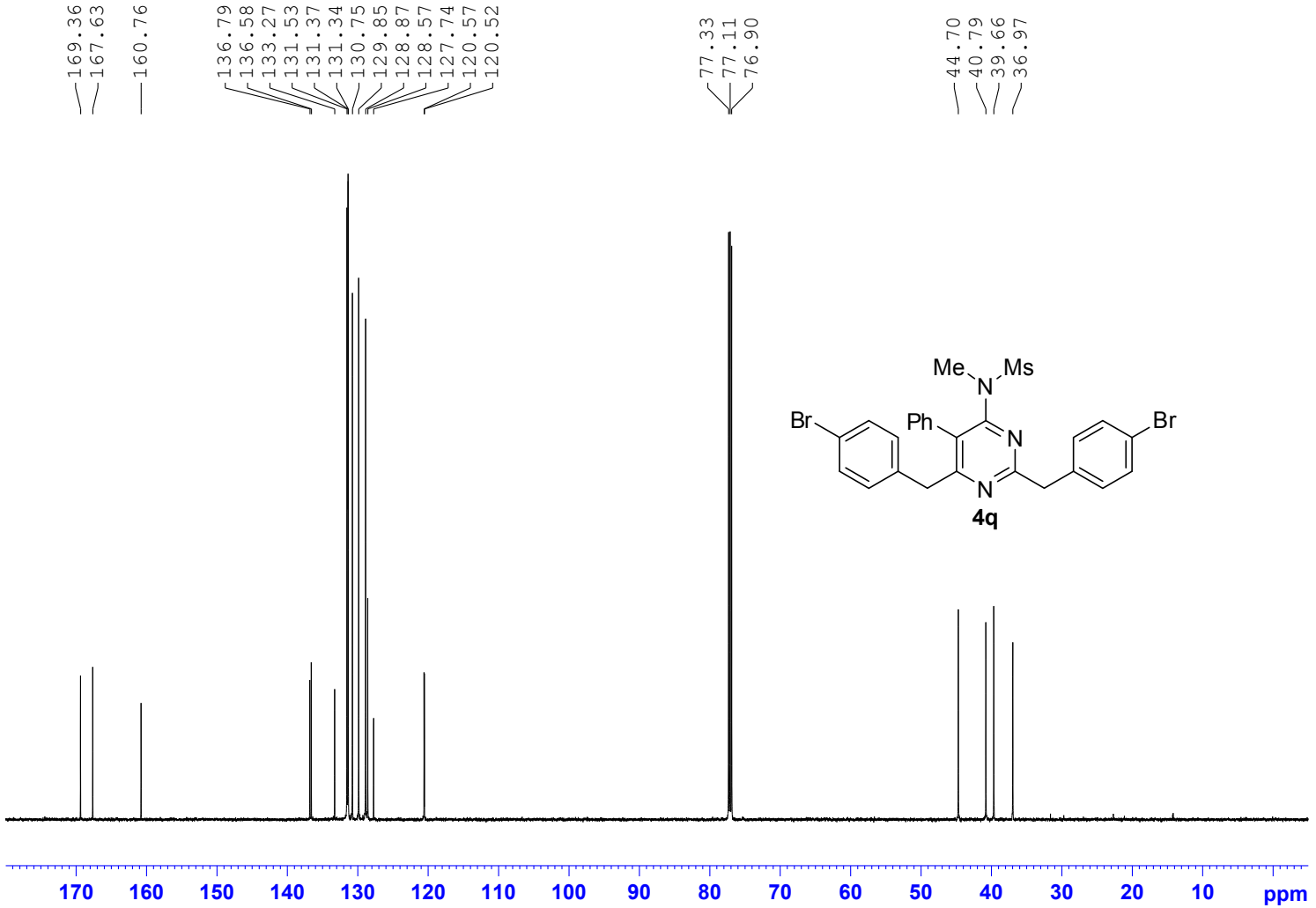
4o

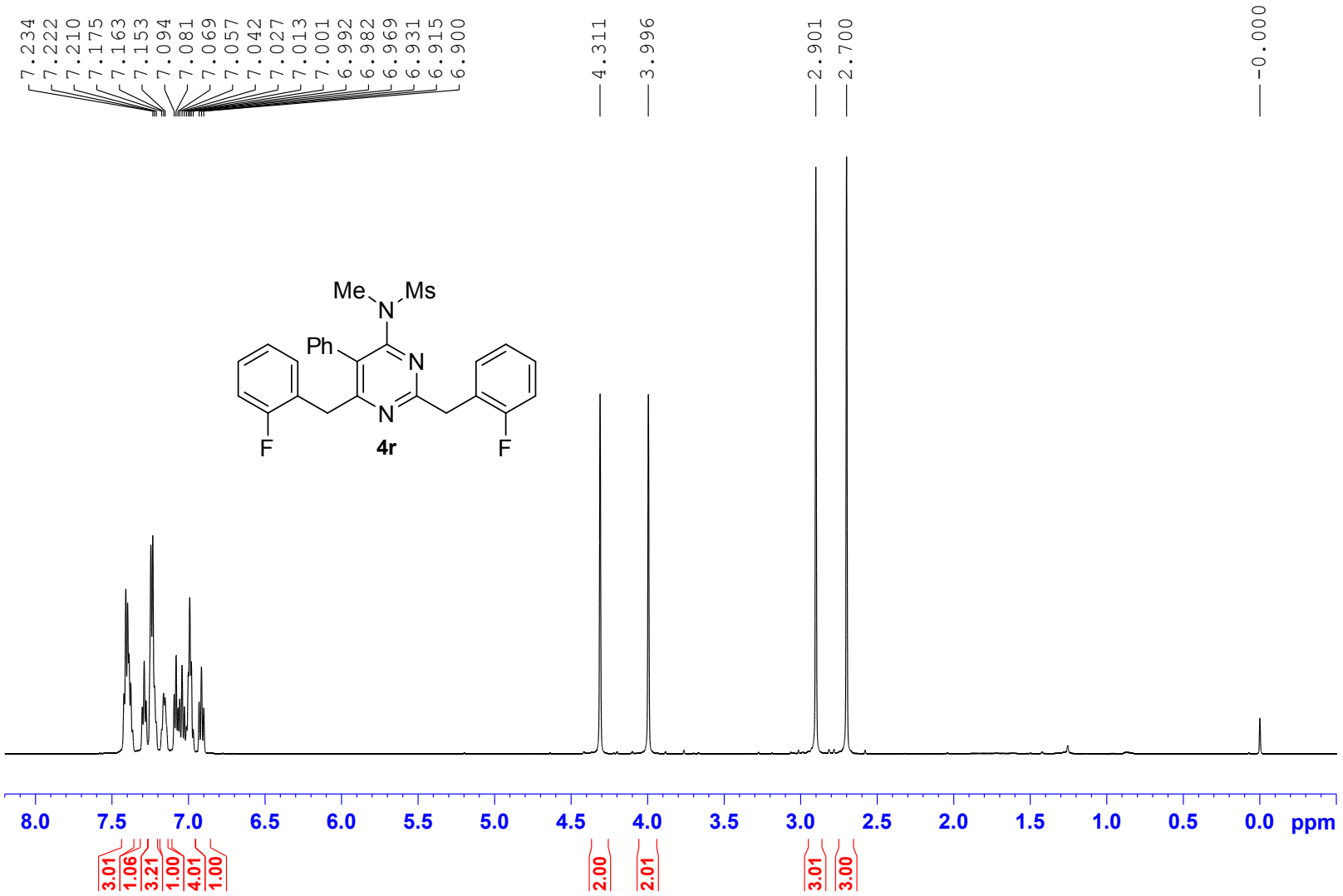

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

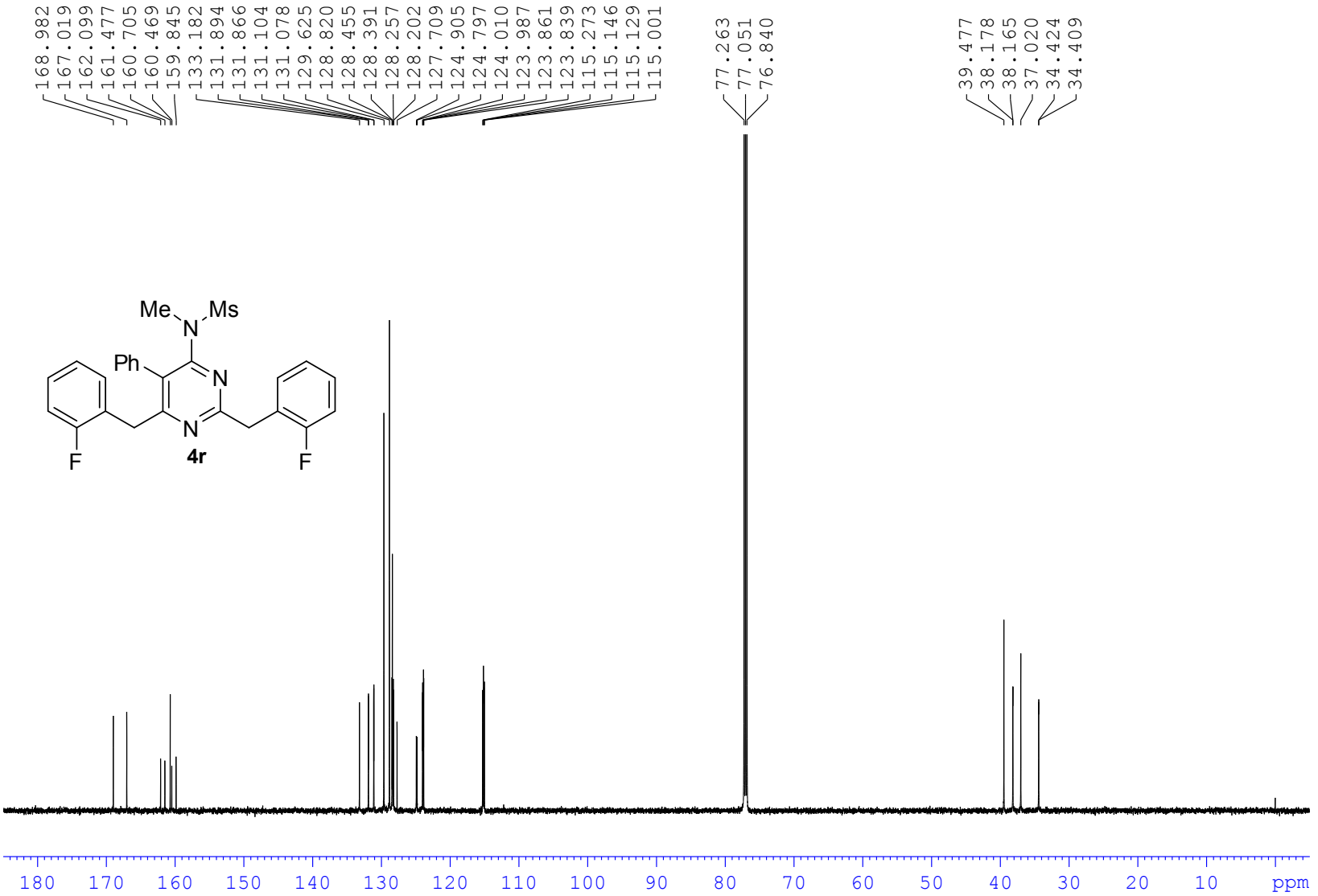

7.402
7.390
7.298
7.285
7.251
7.190
7.179
6.885
6.873
6.861
6.721
6.708
4.235
3.888
3.794
3.751
2.983
2.708
0.076
0.000
Me
N
Ms
CH3O
Ph
N
OCH3
N
4p
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.02
2.07
2.02
4.04
2.03
2.01
2.01
3.03
3.07
3.01
3.00

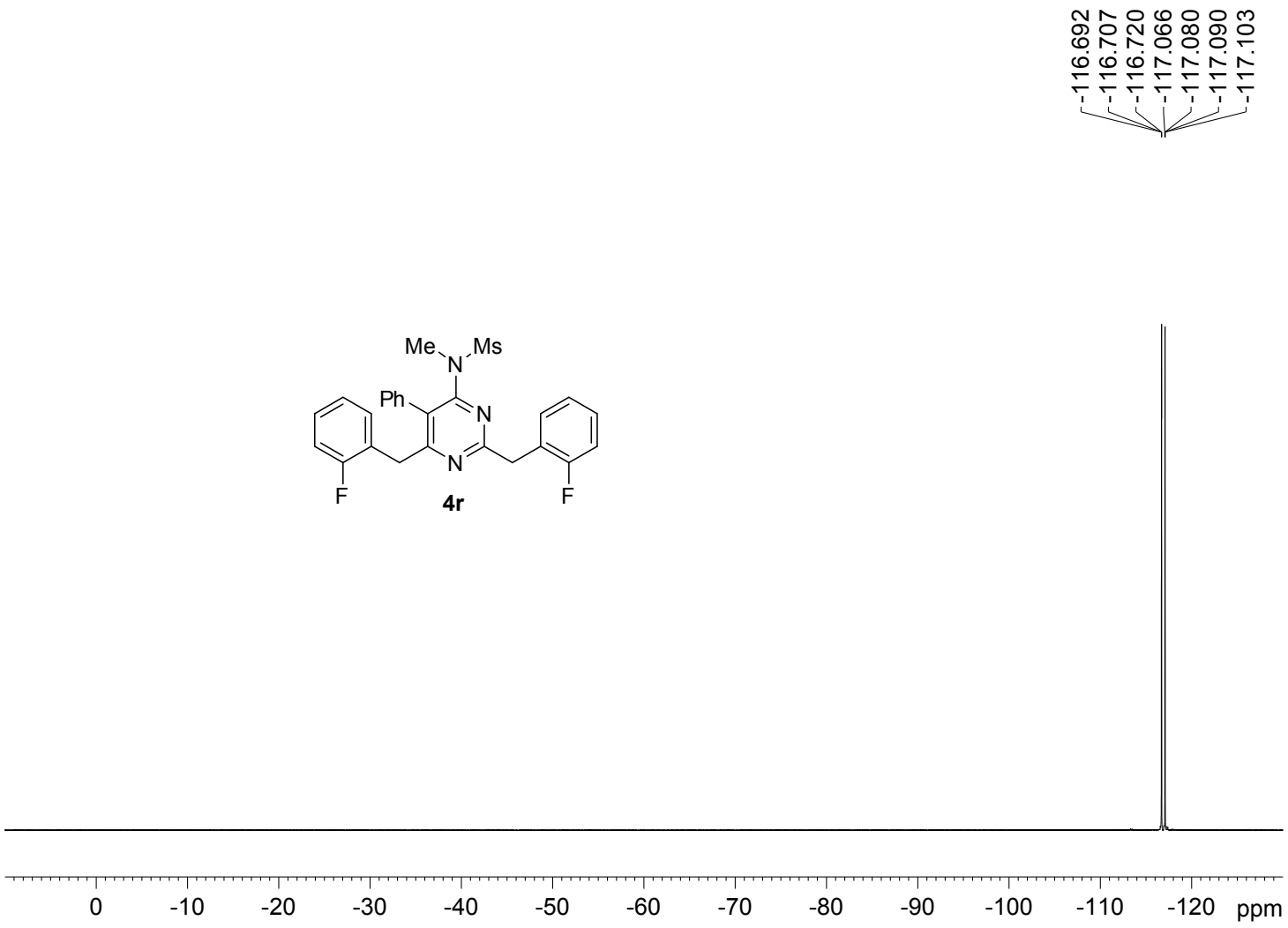

170.16
168.41
160.59
158.34
158.20
133.56
130.55
130.10
129.97
129.81
128.68
128.32
127.41
113.84
113.70
77.29
77.08
76.87
55.32
55.31
55.25
55.23
44.50
40.53
39.62
37.02
37.01
Me
Ms
N
CH3O
Ph
N
OCH3
N
4p
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm

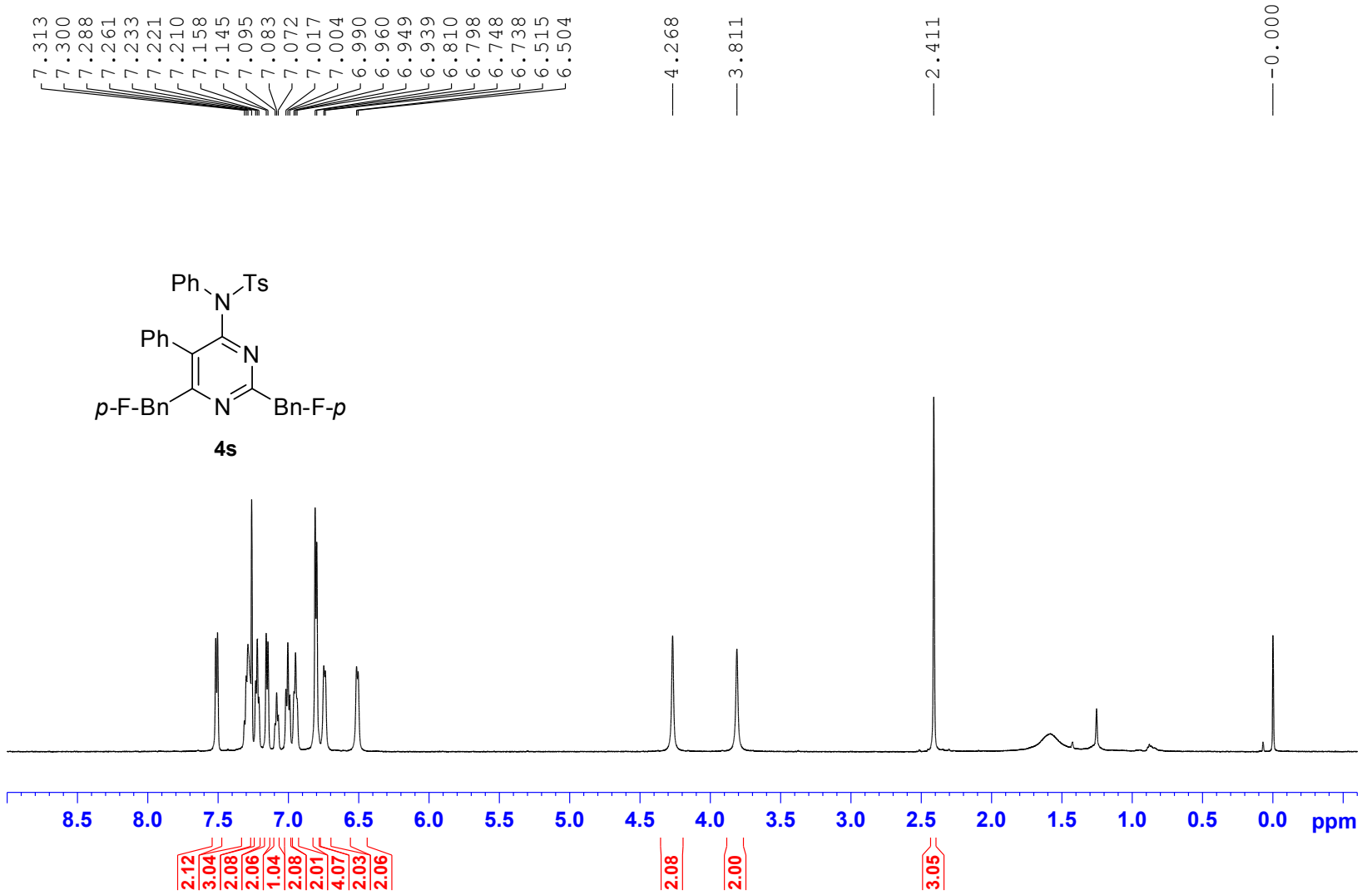

7.447
7.432
7.416
7.294
7.281
7.232
7.219
7.185
7.174
6.819
6.807
4.227
3.883
2.956
2.724
0.000
Me
N
Ms
Br
Ph
N
Br
N
4q
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
5.06
2.05
2.06
2.05
2.02
2.00
2.01
3.01
3.02

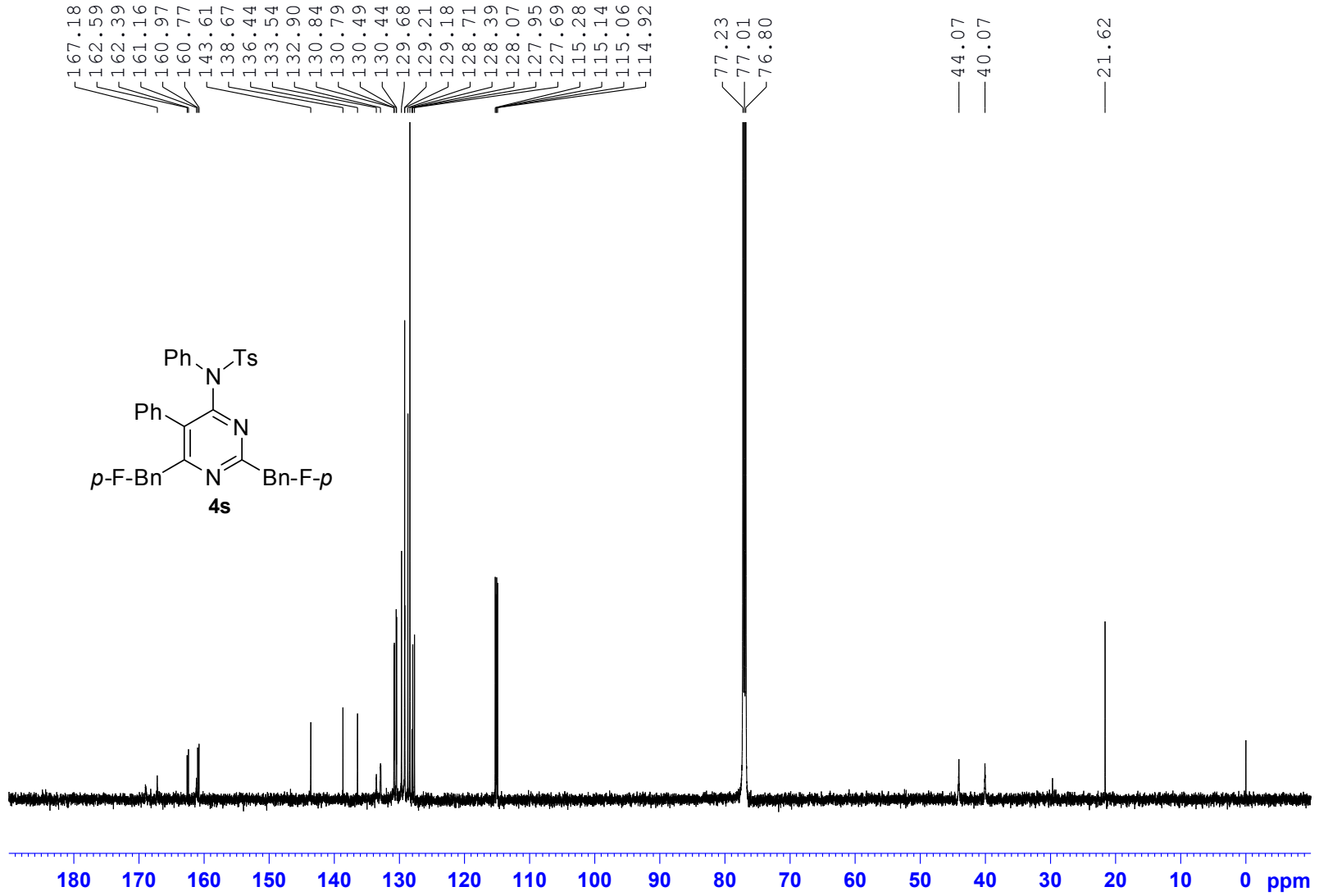

169.36
167.63
160.76
136.79
136.58
133.27
131.53
131.37
131.34
130.75
129.85
128.87
128.57
127.74
120.57
120.52
77.33
77.11
76.90
44.70
40.79
39.66
36.97
Me
N
Ms
Br
Ph
N
Br
N
4q
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

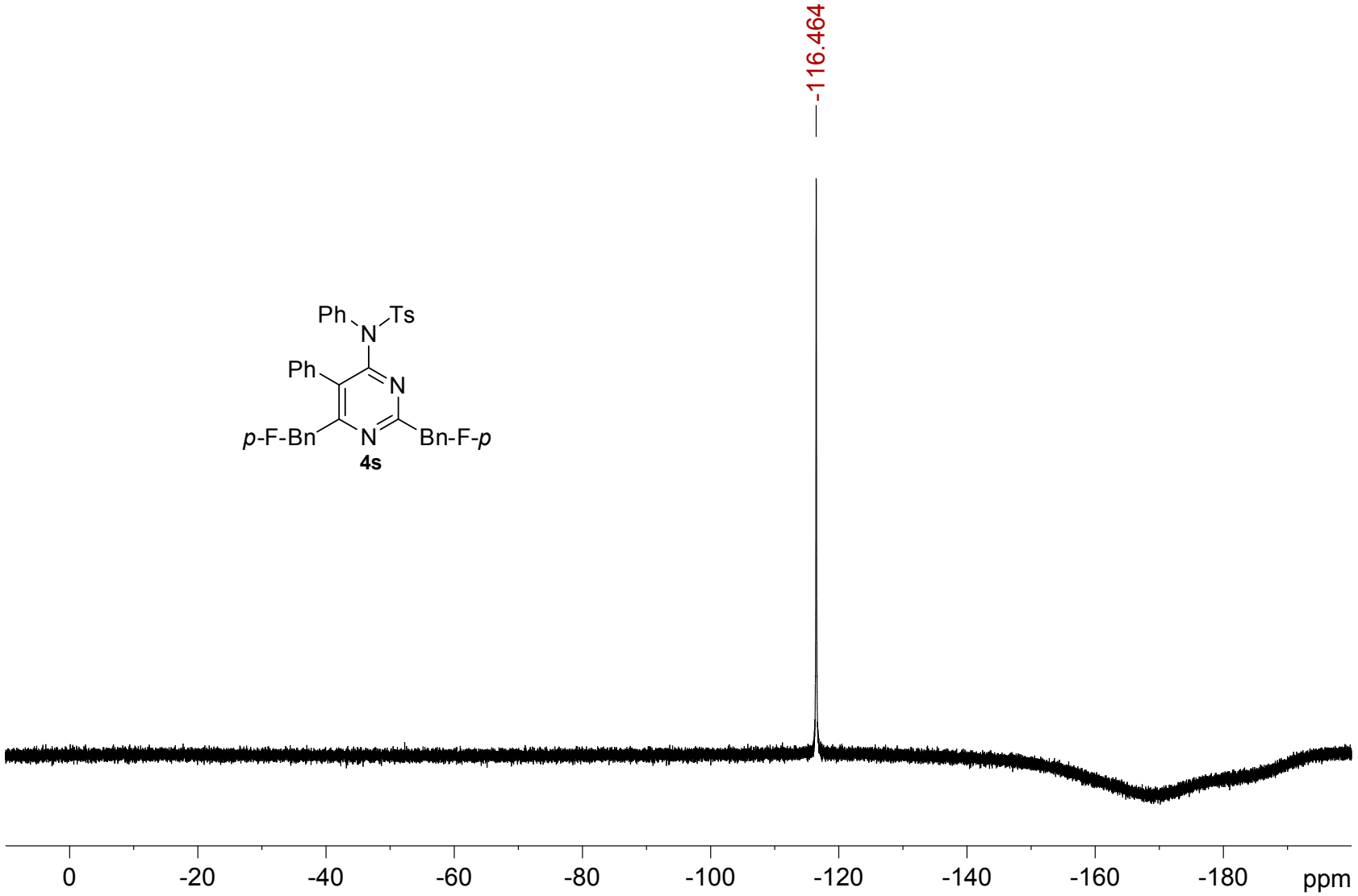

7.234
7.222
7.210
7.175
7.163
7.153
7.094
7.081
7.069
7.057
7.042
7.027
7.013
7.001
6.992
6.982
6.969
6.931
6.915
6.900
4.311
3.996
2.901
2.700
0.000
Me
Ms
N
Ph
N
N
F
F
4r
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
3.01
1.06
3.21
1.00
4.01
1.00
2.00
2.01
3.01
3.00

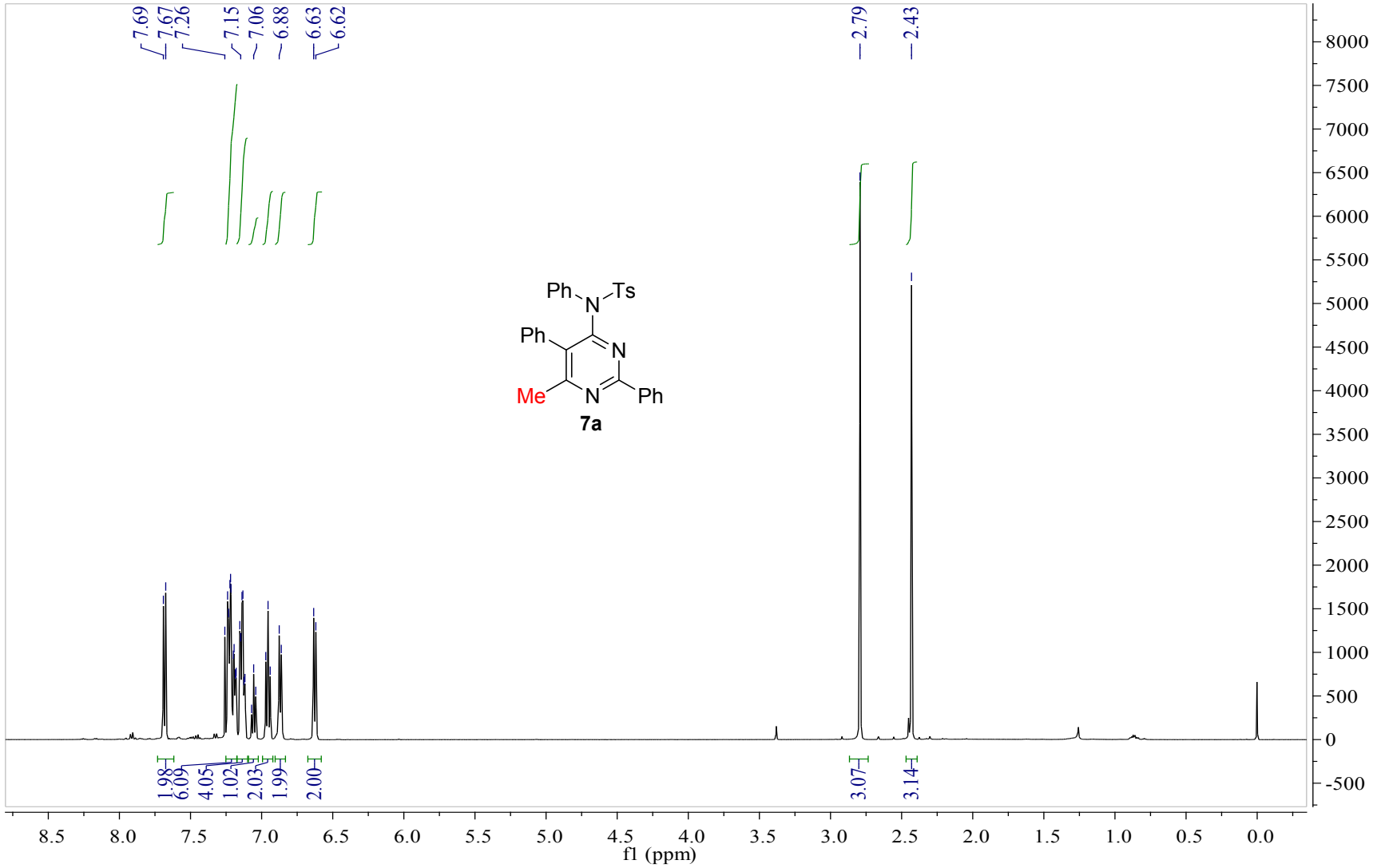

168.982
167.019
162.099
161.477
160.705
160.469
159.845
133.182
131.894
131.866
131.104
131.078
129.625
128.820
128.455
128.391
128.257
128.202
127.709
124.905
124.797
124.010
123.987
123.861
123.839
115.273
115.146
115.129
115.001
77.263
77.051
76.840
39.477
38.178
38.165
37.020
34.424
34.409
Me
N
Ms
Ph
N
N
F
F
4r
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

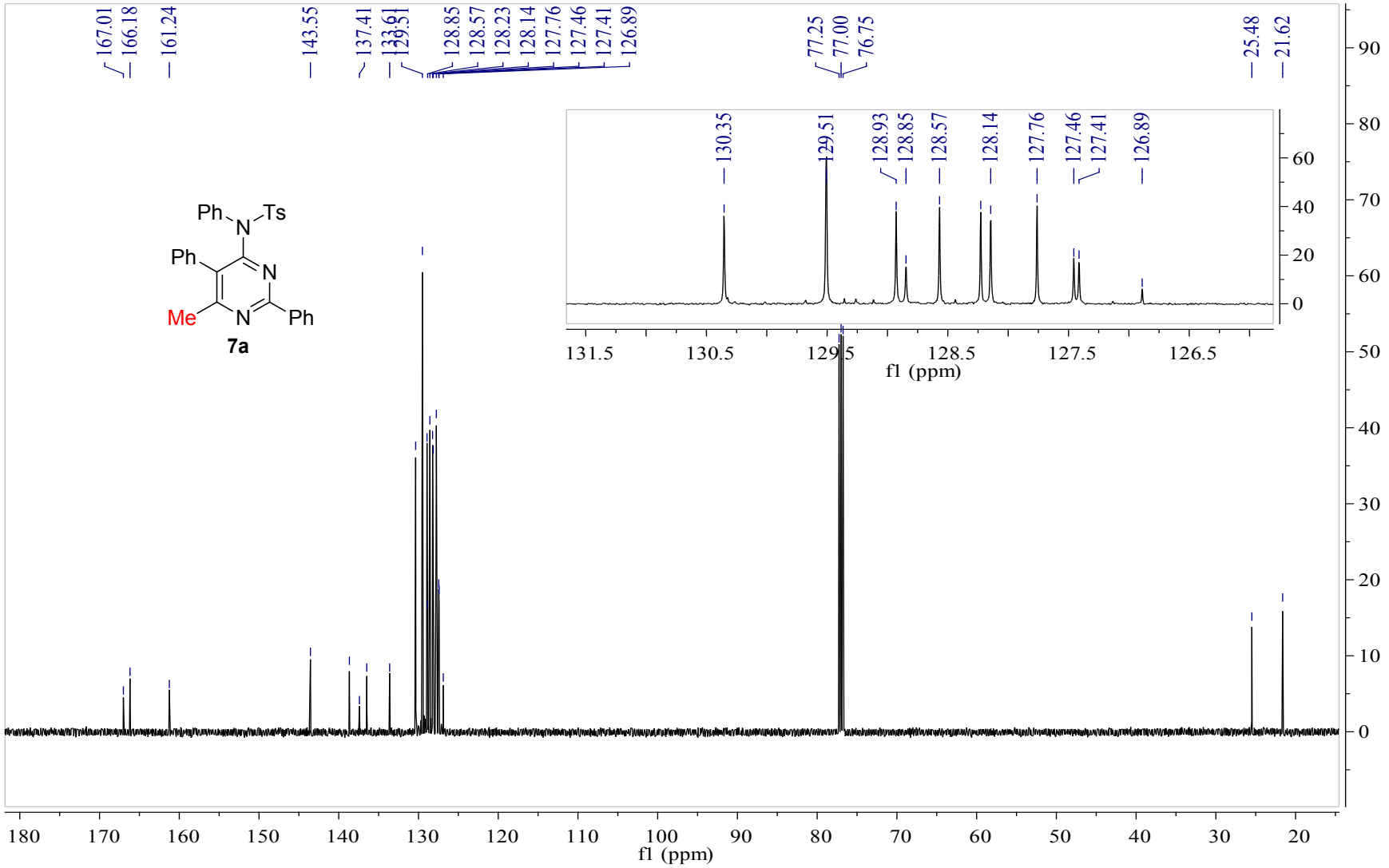

-116.692
-116.707
-116.720
-117.066
-117.080
-117.090
-117.103
Me
N
Ms
Ph
N
N
F
F
4r
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
ppm

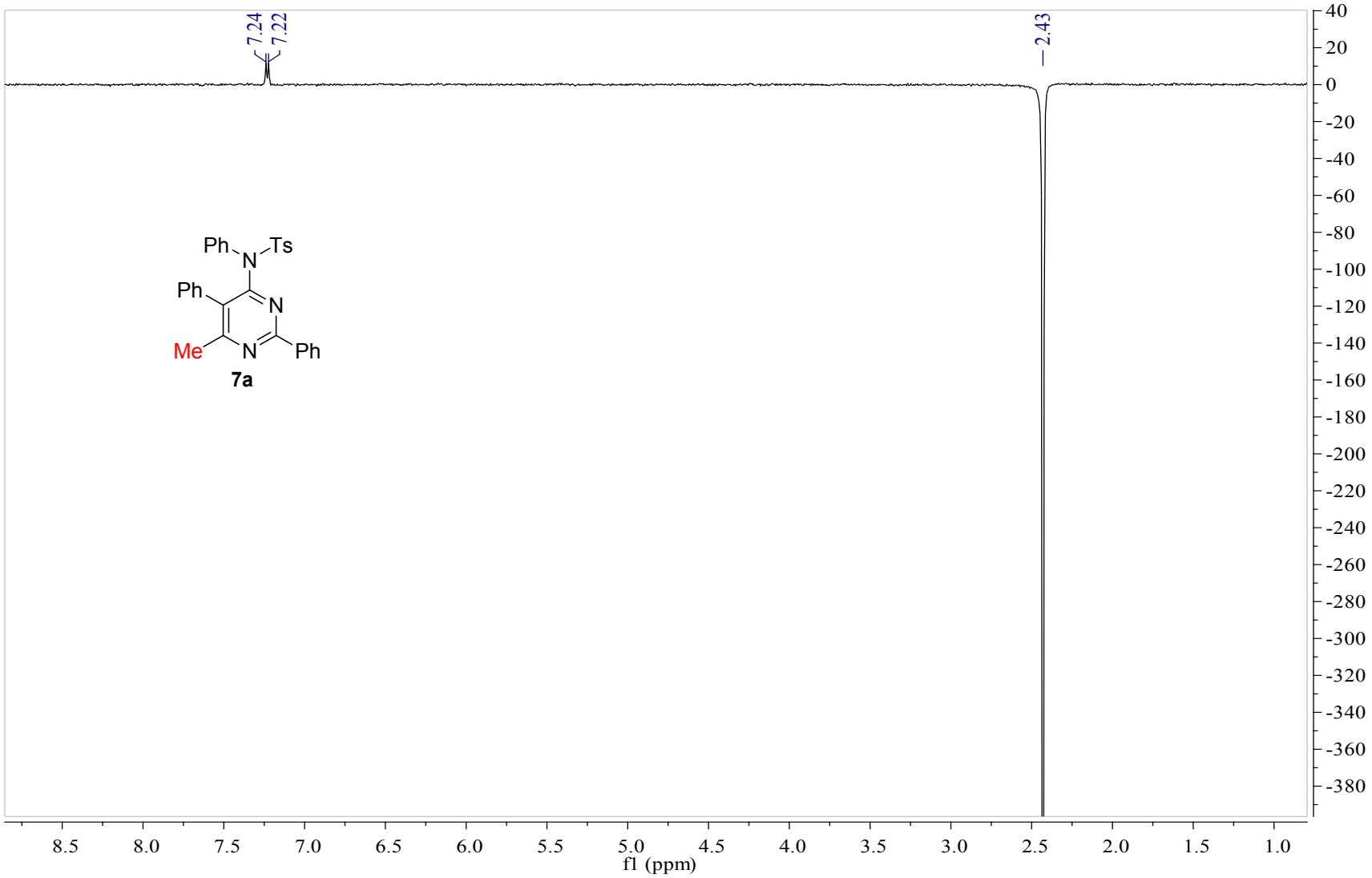

7.313
7.300
7.288
7.261
7.233
7.221
7.210
7.158
7.145
7.095
7.083
7.072
7.017
7.004
6.990
6.960
6.949
6.939
6.810
6.798
6.748
6.738
6.515
6.504
4.268
3.811
2.411
0.000
Ph
N
Ts
Ph
N
p-F-Bn
N
Bn-F-p
4s
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
ppm
2.12
3.04
2.08
2.06
1.04
2.08
2.01
4.07
2.03
2.06
2.08
2.00
3.05


167.18
162.59
162.39
161.16
160.97
160.77
143.61
138.67
136.44
133.54
132.90
130.84
130.79
130.49
130.44
129.68
129.21
129.18
128.71
128.39
128.07
127.95
127.69
115.28
115.14
115.06
114.92
77.23
77.01
76.80
44.07
40.07
21.62
Ph
N
Ts
Ph
N
p-F-Bn
N
Bn-F-p
4s
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
ppm


-116.464
Ph
N
Ts
Ph
N
p-F-Bn
N
Bn-F-p
4s
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm


7.69
7.67
7.26
7.15
7.06
6.88
6.63
6.62
2.79
2.43
Ph
N
Ts
Ph
N
Me
N
Ph
7a
1.98
6.09
4.05
1.02
2.03
1.99
2.00
3.07
3.14
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
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
f1 (ppm)


167.01
166.18
161.24
143.55
137.41
133.61
129.51
128.85
128.57
128.23
128.14
127.76
127.46
127.41
126.89
77.25
77.00
76.75
25.48
21.62
Ph
N
Ts
Ph
N
Me
N
Ph
7a
130.35
129.51
128.93
128.85
128.57
128.14
127.76
127.46
127.41
126.89
131.5
130.5
129.5
128.5
127.5
126.5
f1 (ppm)
f1 (ppm)


7.24
7.22
2.43
Ph
N
Ts
Ph
N
Me
N
Ph
7a
40
20
0
-20
-40
-60
-80
-100
-120
-140
-160
-180
-200
-220
-240
-260
-280
-300
-320
-340
-360
-380
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
f1 (ppm)