Gold-catalyzed Intermolecular Hetero-Dehydro-Diels-Alder Cycloaddition of Captodative Dienynes with Nitriles: A New Reaction and a Regioselective Direct Access to Pyridines

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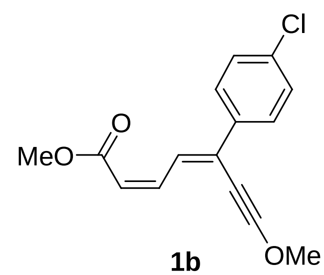
Supporting Information

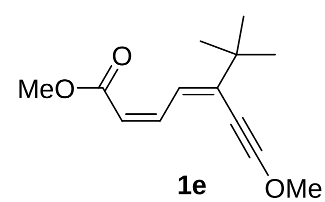
General Considerations: All reactions involving air sensitive compounds were carried out under a N_2 atmosphere (99.99%). All glassware was oven-dried (120 °C), evacuated and purged with nitrogen. All common reagents and solvents were obtained from commercial suppliers and used without any further purification unless otherwise indicated. Captodative 1,3-dien-5-ynes **1a**,**c**,**d**,**f**,**g** and **7** have previously reported and were prepared following described procedures.[1] Enynes **4**[2] and **5**[3] have been previously described. Commercial nitriles were distilled prior to use. Both components of the catalytic system ($AgSbF_6$ and $AuClPEt_3$) were acquired from commercial suppliers. 1,2-Dichloroethane, toluene, THF and 1,2-dimethoxyethane were dried by standard methods. TLC was performed on aluminum-backed plates coated with silica gel 60 with F_{254} indicator; the chromatograms were visualized under ultraviolet light and/or by staining with a Ce/Mo reagent, potassium permanganate or phosphomolibdic acid solutions and subsequent heating. R_f values are reported on silica gel. Flash column chromatography was carried out on silica gel 60, 230-240 mesh. Routine NMR measurements were recorded on Bruker AC-300, DPX-300 or AV-400 spectrometers. ^{1}H NMR: splitting pattern abbreviations are: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; hex, hextuplet; hept, heptuplet; m, multiplet. ^{13}C NMR: multiplicities were determined by DEPT, abbreviations are: q, CH_3; t, CH_2; d, CH; s, quaternary carbons. COSY, HSQC, HMBC and NOESY experiments were carried out on Bruker DPX-300 or AV-400 spectrometer. Standard pulse sequences were employed for the DEPT experimentss. FT-IR were performed with a Mattson 3000 FT-IR spectrometer. Mass spectra were determined by Universidad de Oviedo and Universidad de Vigo (CACTI) services, with a Finnigan Mat95, and a VG AutoSpec M Mass Spectrometers respectively for high resolution mass spectra (HRMS); low resolution mass spectra were obtained with a Hewlett-Packard 5880 A Spectrometer. Electron impact (70 eV) or fast atom bombardment (FAB) techniques were employed. Melting points were determined on a Büchi-Tottoli apparatus and are uncorrected.

General procedure for the synthesis of captodative 1,3-dien-5-ynes 1b,e.[1] 2-Methoxyfuran (2 equiv) was added to a solution of the corresponding carbene complex (1 equiv, 1 mmol) in dry THF (10 mL) at 0ºC. The temperature was raised to r.t. and the mixture stirred until complete disappearance of the carbene complex was observed by TLC (6-12 h). Solvent was removed under reduced pressure, and the residue purified by flash chromatography (hexane/AcOEt); the corresponding dienyne **1b** or **1e** was isolated in the yield reported below.



1b

Dienyne 1b. 72% Yield. Yellow oil. R_f = 0.37 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 2249, 1712, 1602. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.21 (d, *J* = 11.6 Hz, 1 H), 7.69 (d, *J* = 8.4 Hz, 2 H), 7.34-7.25 (m, 3 H), 5.81 (d, *J* = 11.6 Hz, 1 H), 4.08 (s, 3 H), 3.76 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.1 (s), 142.2 (d), 136.7 (s), 134.7 (s), 130.8 (s), 128.5 (d, 2 CH), 128.1 (d, 2 CH), 127.2 (d), 117.8 (d), 110.7 (s), 66.6 (q), 51.2 (q), 36.3 (s).



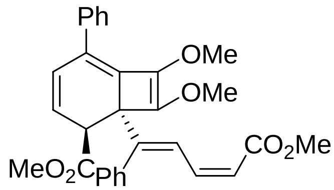
1e

Dienyne 1e. 86% Yield. Yellow oil. R_f = 0.45 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 2238, 1713, 1610. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (d, *J* = 11.4 Hz, 1 H), 7.10 (t, *J* = 11.4 Hz, 1 H), 5.61 (d, *J* = 11.4 Hz, 1 H), 3.96 (s, 3 H), 3.67 (s, 3 H), 1.14 (s, 9 H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 167.1 (s), 144.9 (s), 143.5 (d), 124.1 (d), 115.8 (d), 110.7 (s), 66.3 (q), 50.9 (q), 37.0 (s), 36.5 (s), 29.2 (q, 3 CH_3). MS (*m/z*) 222 (M^+, 14), 207 (15), 191 (14), 163 (60), 151 (97), 57 (100). HRMS (EI) calcd for $C_{13}H_{18}O_3$ $[M]^+$, 222.1251. Found: 222.1247.

Formation of dimer 2a. 1,3-Dien-5-yne **1a** evolves spontaneously when neat to yield dimer **2a**. The reaction does not go to completion, even at long reaction times, but the dimer is easily separated from the starting dienyne by flash column chromatography on silica gel (hexane/AcOEt : 5/1 as eluent).

[1] Barluenga, J.; García-García, P.; de Sáa, D.; Fernández-Rodríguez, M.A.; Bernardo de la Rúa, R.; Ballesteros, A.; Aguilar, E.; Tomás, M. *Angew. Chem. Int. Ed.* **2007**, *46*, 2610-2612.
[2] Kang, S.-K.; Kim, W.-Y.; Jiao, X. *Synthesis* **1998**, 1252-1254.
[3] Takeuchi, R.; Tanabe, K.; Tanaka, S. *J. Org. Chem.* **2000**, *65*, 1558-1561.

The formation of **2a** was also observed when **1a** was heated at 85 ºC or treated with different catalytic systems (Pt, Cu, Ag, Pd) in the presence of acetonitrile.

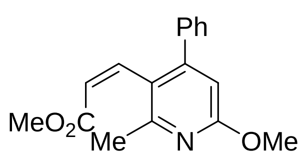


2a

Methyl (1*R,2*S**)-7,8-dimethoxy-1-[(1*Z*,3*Z*)-4-(methoxycarbonyl)-1-phenylbuta-1,3-dienyl]-5-phenylbicyclo[4.2.0]octa-3,5,7-triene-2-carboxylate. Dimer 2a:** 33% Yield. Yellow oil. R_f = 0.14 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1737, 1711, 1615. ^1H NMR ($CDCl_3$, 300 MHz) δ 7.46-7.39 (m, 2 H), 7.32-7.13 (m, 10 H), 6.32 (d, *J* = 8.9 Hz, 1 H), 5.87-5.78 (m, 2 H), 4.14 (s, 3 H), 3.79 (d, *J* = 7.0 Hz, 1 H), 3.71 (s, 3 H), 3.64 (s, 3 H), 3.25 (s, 3 H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.7 (s), 166.7 (s), 150.6 (s), 149.6 (s), 141.8 (s), 140.3 (d), 138.0 (s), 132.6 (s), 131.5 (s), 131.0 (d), 128.0 (d, 2 CH), 127.9 (d), 127.5 (d, 2 CH), 127.0 (d), 126.8 (d, 2 CH), 126.6 (d, 2 CH), 126.3 (d), 121.8 (d), 117.7 (s), 117.4 (d), 61.2 (q), 59.3 (q), 51.7 (q), 51.1 (q), 49.31 (s), 49.28 (d). MS (*m/z*) 484 (M^+, 100), 425 (25), 393 (49), 289 (68). HRMS (EI) calcd for $C_{30}H_{28}O_6$ $[M]^+$, 484.1880. Found: 484.1879.

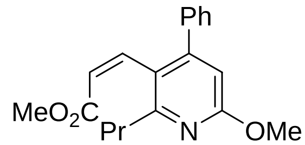
Catalyst screening for the synthesis of pyridine 3a. The metal catalyst (5 mol%) was added to a solution of dienyne **1a** (0.2 mmol, 48 mg) in dry acetonitrile (2 mL). The reaction mixture was stirred at 85 ºC until complete disappearance of dyenine was observed by TLC or GC/MS. Solvent was removed under reduced pressure and the yield of pyridine **3a** was estimated by ^1H NMR (400 MHz) of the crude mixture adding ^{t}BuOAc (0.2 mmol, 27 µL) as internal standard.

General procedure for the synthesis of pyridines 3 or 8. $AuClPEt_3$ (5 mol%, 9 mg) and $AgSbF_6$ (5 mol%, 9 mg) were added to a solution of the corresponding dienyne **1** (0.5 mmol) and the appropriate nitrile (20 equiv., 10 mmol) in dry 1,2-dichloroethane (5 mL). The reaction mixture was stirred at 85 ºC until complete disappearance of dyenine was observed by TLC or GC/MS. Solvent was removed under reduced pressure and the crude mixture was purified by flash chromatography on silica gel using mixtures of hexane and AcOEt. The corresponding pyridines **3** or **8** were isolated in the yields reported in Table 2 and equation 1.



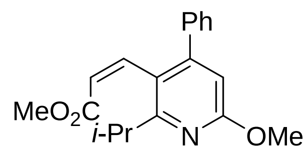
3a

Pyridine 3a: 70% Yield. White solid. Mp = 76-78 ºC. R_f = 0.33 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1727, 1590. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.34 (m, 3 H), 7.30-7.27 (m, 2 H), 6.90 (d, *J* = 11.8 Hz, 1 H), 6.56 (s, 1 H), 5.96 (d, *J* = 11.8 Hz, 1 H), 3.97 (s, 3 H), 3.56 (s, 3 H), 2.43 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.7 (s), 162.6 (s), 153.3 (s), 151.4 (s), 141.9 (d), 139.1 (s), 128.9 (d, 2 CH), 127.9 (d, 2 CH), 127.8 (d), 123.0 (d), 122.4 (s), 107.6 (d), 53.3 (q), 51.2 (q), 22.9 (q). MS (*m/z*) 283 (M^+, 27), 282 ($[M–1]^+$, 54), 224 (100), 222 (73), 194 (30). HRMS (EI) calcd for $C_{17}H_{17}NO_3$ $[M]^+$, 283.1208. Found: 283.1201.



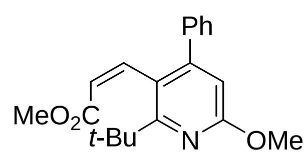
3b

Pyridine 3b: 64% Yield. Colorless oil. R_f = 0.40 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1727, 1588. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.37-7.33 (m, 3 H), 7.29-7.26 (m, 2 H), 6.98 (d, *J* = 11.8 Hz, 1 H), 6.55 (s, 1 H), 5.91 (d, *J* = 11.8 Hz, 1 H), 3.98 (s, 3 H), 3.51 (s, 3 H), 2.68 (t, *J* = 7.5 Hz, 2 H), 1.76 (hex, *J* = 7.5 Hz, 2 H), 0.97 (t, *J* = 7.5 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5 (s), 162.8 (s), 156.6 (s), 151.5 (s), 141.7 (d), 139.4 (s), 129.0 (d, 2 CH), 127.8 (d, 2 CH), 127.7 (d), 123.2 (d), 122.1 (s), 107.5 (d), 53.2 (q), 51.0 (q), 37.6 (t), 21.7 (t), 13.9 (q). MS (*m/z*) 311 (M^+, 6), 310 ($[M–1]^+$, 20), 283 (62), 252 (100), 236 (19). HRMS (EI) calcd for $C_{19}H_{21}NO_3$ $[M]^+$, 311.1521. Found: 311.1534.



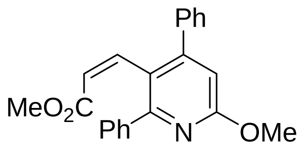
3c

Pyridine 3c: 60% Yield. White solid. Mp = 56-58 ºC. R_f = 0.45 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1727, 1589. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.34 (m, 3 H), 7.28-7.25 (m, 2 H), 7.02 (d, *J* = 11.6 Hz, 1 H), 6.53 (s, 1 H), 5.91 (d, *J* = 11.6 Hz, 1 H), 3.99 (s, 3 H), 3.50 (s, 3 H), 3.13 (hept, *J* = 6.7 Hz, 1 H), 1.25 (d, *J* = 6.7 Hz, 6 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5 (s), 163.0 (s), 160.9 (s), 151.5 (s), 141.7 (d), 139.6 (s), 129.0 (d, 2 CH), 127.8 (d, 2 CH), 127.6 (d), 123.4 (d), 121.1 (s), 107.6 (d), 53.1 (q), 51.0 (q), 32.7 (d), 21.7 (q, 2 CH_3). MS (*m/z*) 311 (M^+, 11), 268 (16), 252 (100), 236 (20). HRMS (EI) calcd for $C_{19}H_{21}NO_3$ $[M]^+$, 311.1521. Found: 311.1529.



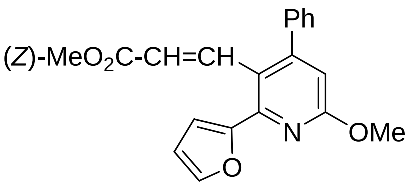
3d

Pyridine 3d: 55% Yield. Colorless oil. R_f = 0.41 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1727, 1585. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.36 (d, *J* = 11.7 Hz, 1 H), 7.33-7.28 (m, 3 H), 7.18-7.15 (m, 2 H), 6.53 (s, 1 H), 5.74 (d, *J* = 11.7 Hz, 1 H), 3.97 (s, 3 H), 3.44 (s, 3 H), 1.41 (s, 9 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.3 (s), 161.8 (s), 161.2 (s), 153.2 (s), 144.3 (d), 140.4 (s), 129.1 (d, 2 CH), 127.7 (d, 2 CH), 127.4 (d), 122.7 (d), 122.0 (s), 108.0 (d), 53.1 (q), 51.0 (q), 39.8 (s), 30.0 (q, 3 CH_3). MS (*m/z*) 325 (M^+, <5), 324 [$(M–1)^+$, 19], 310 (12), 268 (100), 266 (87). HRMS (EI) calcd for $C_{20}H_{22}NO_3$ $[M–1]^+$, 324.1594. Found: 324.1590.



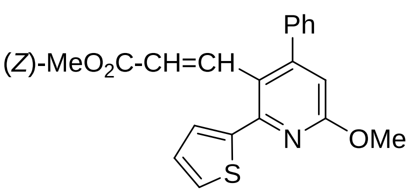
3e

Pyridine 3e: 67% Yield. White solid. Mp = 82-84 ºC. R_f = 0.29 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1723, 1587. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63-7.60 (m, 2 H), 7.40-7.30 (m, 8 H), 6.87 (d, *J* = 11.8 Hz, 1 H), 6.71 (s, 1 H), 5.72 (d, *J* = 11.8 Hz, 1 H), 4.03 (s, 3 H), 3.38 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6 (s), 162.9 (s), 154.8 (s), 152.4 (s), 141.1 (d), 140.2 (s), 139.1 (d), 129.8 (d, 2 CH), 129.0 (d, 2 CH), 128.0 (d), 127.85 (d, 2 CH), 127.78 (d), 127.6 (d, 2 CH), 123.2 (d), 121.8 (s), 109.6 (d), 53.4 (q), 50.9 (q). MS (*m/z*) 345 (M^+, 10), 286 (61), 97 (20), 69 (100). HRMS (EI) calcd for $C_{22}H_{19}NO_3$ $[M]^+$, 345.1365. Found: 345.1354.



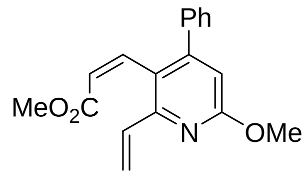
3f

Pyridine 3f: 69% Yield. White solid. Mp = 81-83 ºC. R_f = 0.26 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1725, 1593. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.51 (dd, *J* = 0.9 and 1.8 Hz, 1 H), 7.36-7.25 (m, 6 H), 7.02 (dd, *J* = 0.9 and 3.4 Hz, 1 H), 6.63 (s, 1 H), 6.50 (dd, *J* = 1.8 and 3.4 Hz, 1 H), 5.84 (d, *J* = 11.7 Hz, 1 H), 4.03 (s, 3 H), 3.39 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6 (s), 162.8 (s), 153.8 (s), 153.3 (s), 143.5 (s), 143.2 (d), 141.4 (d), 139.2 (s), 129.2 (d, 2 CH), 127.8 (d, 3 CH), 122.8 (d), 120.2 (s), 111.9 (d), 111.5 (d), 110.0 (d), 53.4 (q), 51.0 (q). MS (*m/z*) 335 (M^+, 36), 318 (100), 276 (49), 204 (37). HRMS (EI) calcd for $C_{20}H_{17}NO_4$ $[M]^+$, 335.1152. Found: 335.1151.



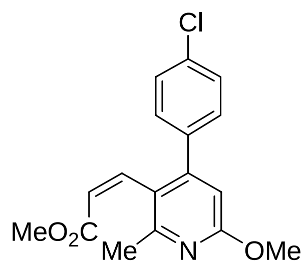
3g

Pyridine 3g: 73% Yield. White solid. Mp = 113-115 ºC. R_f = 0.29 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1725, 1584. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.53 (dd, *J* = 1.0 and 3.7 Hz, 1 H), 7.42 (dd, *J* = 1.0 and 5.1 Hz, 1 H), 7.39-7.35 (m, 3 H), 7.29-7.27 (m, 2 H), 7.18 (d, *J* = 11.7 Hz, 1 H), 7.09 (dd, *J* = 3.7 and 5.1 Hz, 1 H), 6.66 (s, 1 H), 5.92 (d, *J* = 11.7 Hz, 1 H), 4.07 (s, 3 H), 3.41 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.4 (s), 162.4 (s), 153.4 (s), 146.7 (s), 145.1 (s), 141.2 (d), 139.2 (s), 129.2 (d, 2 CH), 128.2 (d), 128.0 (d), 127.9 (d, 3 CH), 127.6 (d), 124.1 (d), 120.3 (s), 110.0 (d), 53.6 (q), 51.2 (q). MS (*m/z*) 351 (M^+, 20), 292 (100), 277 (22), 260 (25). HRMS (EI) calcd for $C_{20}H_{17}NO_3S$ $[M]^+$, 351.0924. Found: 351.0925.



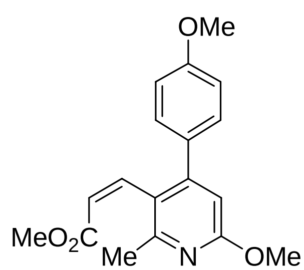
3h

Pyridine 3h: 75% Yield. White solid. Mp = 72-74 ºC. R_f = 0.41 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1727, 1582. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.41-7.36 (m, 3 H), 7.32-7.29 (m, 2 H), 6.92-6.85 (m, 2 H), 6.64 (s, 1 H), 6.50 (dd, *J* = 2.3 and 16.8 Hz, 1 H), 6.05 (d, *J* = 11.8 Hz, 1 H), 5.44 (dd, *J* = 2.3 and 10.6 Hz, 1 H), 4.04 (s, 3 H), 3.56 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.7 (s), 162.5 (s), 151.9 (s), 149.2 (s), 140.8 (d), 138.8 (s), 133.3 (d), 128.9 (d, 2 CH), 128.0 (d, 3 CH), 124.1 (d), 122.1 (s), 119.3 (t), 110.1 (d), 53.1 (q), 51.4 (q). MS (*m/z*) 295 (M^+, 11), 236 (100), 204 (30). HRMS (EI) calcd for $C_{18}H_{17}NO_3$ $[M]^+$, 295.1208. Found: 295.1202.



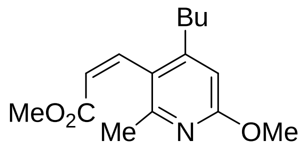
3i

Pyridine 3i: 62% Yield. Colorless oil. R_f = 0.29 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1726, 1560. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33 (d, *J* = 8.2 Hz, 2 H), 7.21 (d, *J* = 8.2 Hz, 2 H), 6.87 (d, *J* = 11.8 Hz, 1 H), 6.51 (s, 1 H), 5.96 (d, *J* = 11.8 Hz, 1 H), 3.96 (s, 3 H), 3.56 (s, 3 H), 2.41 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.6 (s), 162.7 (s), 153.5 (s), 150.2 (s), 141.7 (d), 137.6 (s), 134.0 (s), 130.3 (d, 2 CH), 128.2 (d, 2 CH), 123.3 (d), 122.2 (s), 107.6 (d), 53.4 (q), 51.3 (q), 23.0 (q). MS (*m/z*) 317 (M^+, 45), 316 ($[M–1]^+$, 82), 258 (100). HRMS (EI) calcd for $C_{17}H_{15}ClNO_3$ $[M–1]^+$, 316.0735. Found: 316.0732.



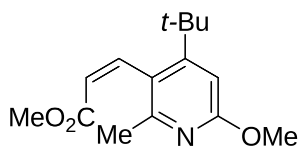
3j

Pyridine 3j: 66% Yield. Colorless oil. R_f = 0.21 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1726, 1590, 1514. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.24 (d, *J* = 8.5 Hz, 2 H), 6.91-6.86 (m, 3 H), 6.53 (s, 1 H), 5.99 (d, *J* = 11.8 Hz, 1 H), 3.96 (s, 3 H), 3.83 (s, 3 H), 3.58 (s, 3 H), 2.41 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9 (s), 162.8 (s), 159.5 (s), 153.3 (s), 151.2 (s), 142.4 (d), 131.6 (s), 130.3 (d, 2 CH), 123.0 (d), 122.6 (s), 113.5 (d, 2 CH), 107.5 (d), 55.3 (q), 53.4 (q), 51.3 (q), 23.0 (q). MS (*m/z*) 313 (M^+, 51), 312 ([M–1]$^+$, 60), 254 (100), 252 (62). HRMS (EI) calcd for $C_{18}H_{18}NO_4$ [M–1]$^+$, 312.1230. Found: 312.1230.



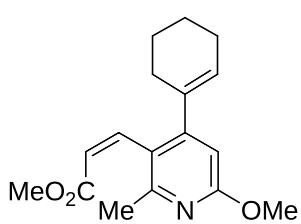
3k

Pyridine 3k: 71% Yield. Colorless oil. R_f = 0.32 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1731, 1596. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.04 (d, *J* = 11.8 Hz, 1 H), 6.43 (s, 1 H), 6.16 (d, *J* = 11.8 Hz, 1 H), 3.91 (s, 3 H), 3.61 (s, 3 H), 2.45 (t, *J* = 7.6 Hz, 2 H), 2.33 (s, 3 H), 1.49 (m, 2 H), 1.32 (m, 2 H), 0.90 (t, *J* = 7.3 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.7 (s), 162.8 (s), 152.1 (s), 151.9 (s), 142.3 (d), 123.5 (s), 123.3 (d), 106.6 (d), 53.2 (q), 51.4 (q), 32.9 (t), 31.5 (t), 22.9 (q), 22.4 (t), 13.9 (q). MS (*m/z*) 263 (M$^+$, 46), 262 ([M–1]$^+$, 51), 232 (23), 204 (20), 190 (100), 160 (47). HRMS (EI) calcd for $C_{15}H_{20}NO_3$ [M–1]$^+$, 262.1438. Found: 262.1434.



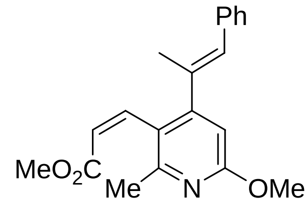
3l

Pyridine 3l: 61% Yield. Yellow solid. Mp = 53-55 ºC. R_f = 0.33 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1727, 1587. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.35 (d, *J* = 11.8 Hz, 1 H), 6.62 (s, 1 H), 6.16 (d, *J* = 11.8 Hz, 1 H), 3.91 (s, 3 H), 3.58 (s, 3 H), 2.32 (s, 3 H), 1.29 (s, 9 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.7 (s), 162.9 (s), 158.8 (s), 152.3 (s), 145.4 (d), 123.3 (d), 104.9 (d), 53.1 (q), 51.3 (q), 36.1 (s), 30.1 (q, 3 CH_3), 23.6 (q) –a signal for a C(s) around 123-124 ppm was not observed– MS (*m/z*) 263 (M$^+$, 33), 262 [(M–1)$^+$, 32), 248 (23), 206 (100), 204 (53). HRMS (EI) calcd for $C_{15}H_{20}NO_3$ [M–1]$^+$, 262.1438. Found: 262.1435.



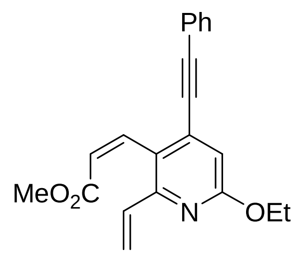
3m

Pyridine 3m: 75% Yield. Colorless oil. R_f = 0.35 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1731, 1589. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.99 (d, *J* = 11.8 Hz, 1 H), 6.37 (s, 1 H), 6.03 (d, *J* = 11.8 Hz, 1 H), 5.61 (bs, 1 H), 3.91 (s, 3 H), 3.59 (s, 3 H), 2.35 (s, 3 H), 2.13-2.09 (m, 4 H), 1.68-1.60 (m, 4 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.1 (s), 162.8 (s), 154.2 (s), 152.8 (s), 142.3 (d), 136.5 (s), 128.5 (d), 122.2 (d), 122.0 (s), 105.9 (d), 53.3 (q), 51.3 (q), 28.8 (t), 25.3 (t), 22.9 (q), 22.8 (t), 21.8 (t). MS (*m/z*) 287 (M$^+$, 23), 286 ([M–1]$^+$, 16), 228 (100). HRMS (EI) calcd for $C_{17}H_{20}NO_3$ [M–1]$^+$, 286.1438. Found: 286.1434.



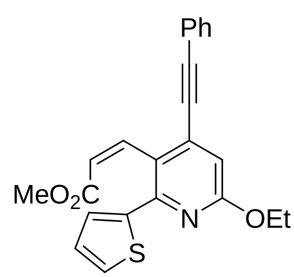
3n

Pyridine 3n: 64% Yield. Yellow oil. R_f = 0.32 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1728, 1588. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.40-7.36 (m, 2 H), 7.32-7.25 (m, 3 H), 7.08 (d, *J* = 11.7 Hz, 1 H), 6.53 (s, 1 H), 6.42 (s, 1 H), 6.09 (d, *J* = 11.7 Hz, 1 H), 3.96 (s, 3 H), 3.59 (s, 3 H), 2.41 (s, 3 H), 2.10 (s, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.0 (s), 162.9 (s), 155.5 (s), 153.1 (s), 142.1 (d), 137.3 (s), 136.4 (s), 131.0 (d), 128.9 (d, 2 CH), 128.3 (d, 2 CH), 126.9 (d), 122.8 (d), 121.9 (s), 106.1 (d), 53.4 (q), 51.4 (q), 23.0 (q), 19.0 (q). MS (*m/z*) 323 (M$^+$, 18), 322 ([M–1]$^+$, 7), 264 (100). HRMS (EI) calcd for $C_{20}H_{21}NO_3$ [M]$^+$, 323.1516. Found: 323.1508.



8a

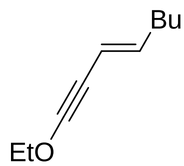
Pyridine 8a: 65% Yield. Yellow oil. R_f = 0.35 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1731, 1573. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.52-7.50 (m, 2 H), 7.38-7.36 (m, 3 H), 7.15 (d, *J* = 11.8 Hz, 1 H), 6.86-6.79 (m, 2 H), 6.44 (dd, *J* = 2.2 and 16.9 Hz, 1 H), 6.28 (d, *J* = 11.8 Hz, 1 H), 5.46 (dd, *J* = 2.2 and 10.5 Hz, 1 H), 4.46 (q, *J* = 7.1 Hz, 2 H), 3.59 (s, 3 H), 1.43 (t, *J* = 7.1 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9 (s), 162.3 (s), 149.5 (s), 139.3 (d), 133.2 (d), 133.1 (s), 131.9 (d, 2 CH), 129.1 (d), 128.4 (d, 2 CH), 124.3 (d), 124.0 (s), 122.3 (s), 119.8 (t), 112.3 (d), 95.8 (s), 86.2 (s), 61.8 (t), 51.5 (q), 14.6 (q). MS (*m/z*) 333 (M$^+$, 53), 318 (31), 274 (18), 105 (92), 84 (100). HRMS (EI) calcd for $C_{21}H_{19}NO_3$ [M]$^+$, 333.1359. Found: 333.1360.



8b

Pyridine 8b: 66% Yield. Yellow oil. R_f = 0.33 (Hexane/AcOEt : 5/1). IR ν (cm^{-1}) 1728, 1574. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54-7.52 (m, 3 H), 7.45 (dd, *J* = 1.0 and 5.1 Hz, 1 H), 7.39-7.37 (m, 3 H), 7.13-7.10 (m, 2 H), 6.85 (s, 1 H), 6.35 (d, *J* = 11.7 Hz, 1

H), 4.49 (q, J = 7.1 Hz, 2 H), 3.59 (s, 3 H), 1.46 (t, J = 7.1 Hz, 3 H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.4 (s), 162.1 (s), 147.0 (s), 144.8 (s), 139.8 (d), 134.0 (s), 131.9 (d, 2 CH), 129.1 (d), 128.8 (d), 128.4 (d, 3 CH), 127.8 (d), 124.2 (d), 122.3 (s), 122.1 (s), 111.9 (d), 95.3 (s), 86.6 (s), 62.2 (t), 51.4 (q), 14.6 (q). MS (*m/z*) 389 (M^+, 75), 374 (29), 330 (30), 302 (60), 105 (100). HRMS (EI) calcd for $C_{23}H_{19}NO_3S$ $[M]^+$, 389.1080. Found: 389.1082.



6

Synthesis of (*E*)-1-ethoxyoct-3-en-1-yne 6. Prepared as previously reported for other electron-rich enynes:[4] To a solution of tetrakis(triphenylphosphine) palladium (500 mg, 0.558 mmol) in isopropyl amine was added (E)-l-iodo-1-hexene (1.80 g, 8.56 mmol), ethoxyacetylene (1.5 equiv., 2.57 mL of a solution 5M in hexane, 12.84 mmol), and a solution of copper (I) iodide (163 mg, 1.12 mmol) in isopropylamine (5 mL). The resulting orange solution was stirred in the dark for 6 h. The reaction was diluted with hexane and thoroughly washed with ammonium chloride (sat. aq.). The aqueous layers were combined and extracted with hexane. The combined organic layers were dried over sodium sulfate, concentrated, and purified by flash chromatography (100% hexane, Et_3N pretreated silica) to afford a 35% yield of **6**. Colorless oil. R_f = 0.23 (Hexane). ^{1}H NMR (C_6D_6, 400 MHz) δ 6.17 (m, 1 H), 5.72 (m, 1 H), 3.72 (q, J = 7.1 Hz, 2 H), 2.02 (m, 2 H), 1.29 (m, 4 H), 1.02 (t, J = 7.1 Hz, 3 H), 0.90 (m, J = 7.1 Hz, 3 H). ^{13}C NMR (C_6D_6, 100 MHz) δ 140.9 (d), 109.9 (d), 97.8 (s), 74.1 (t), 39.0 (s), 32.7 (t), 31.3 (t), 22.2 (t), 14.0 (q), 13.8 (q).

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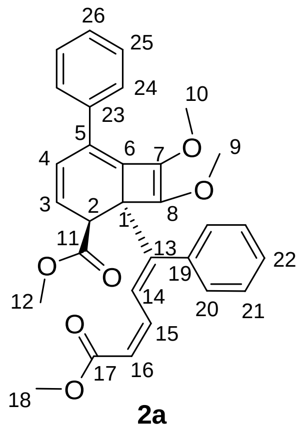
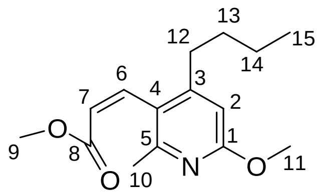
[4] Dussault, P. H.; Han, Q.; Sloss, D. G.; Symonsbergen, D. J. *Tetrahedron* **1999**, *55*, 11437-11454.

Tables with 2D-NMR (HSQC, COSY, HMBC and NOESY) experiments for 2a (400 MHz) and for 3k (300 MHz)



2a

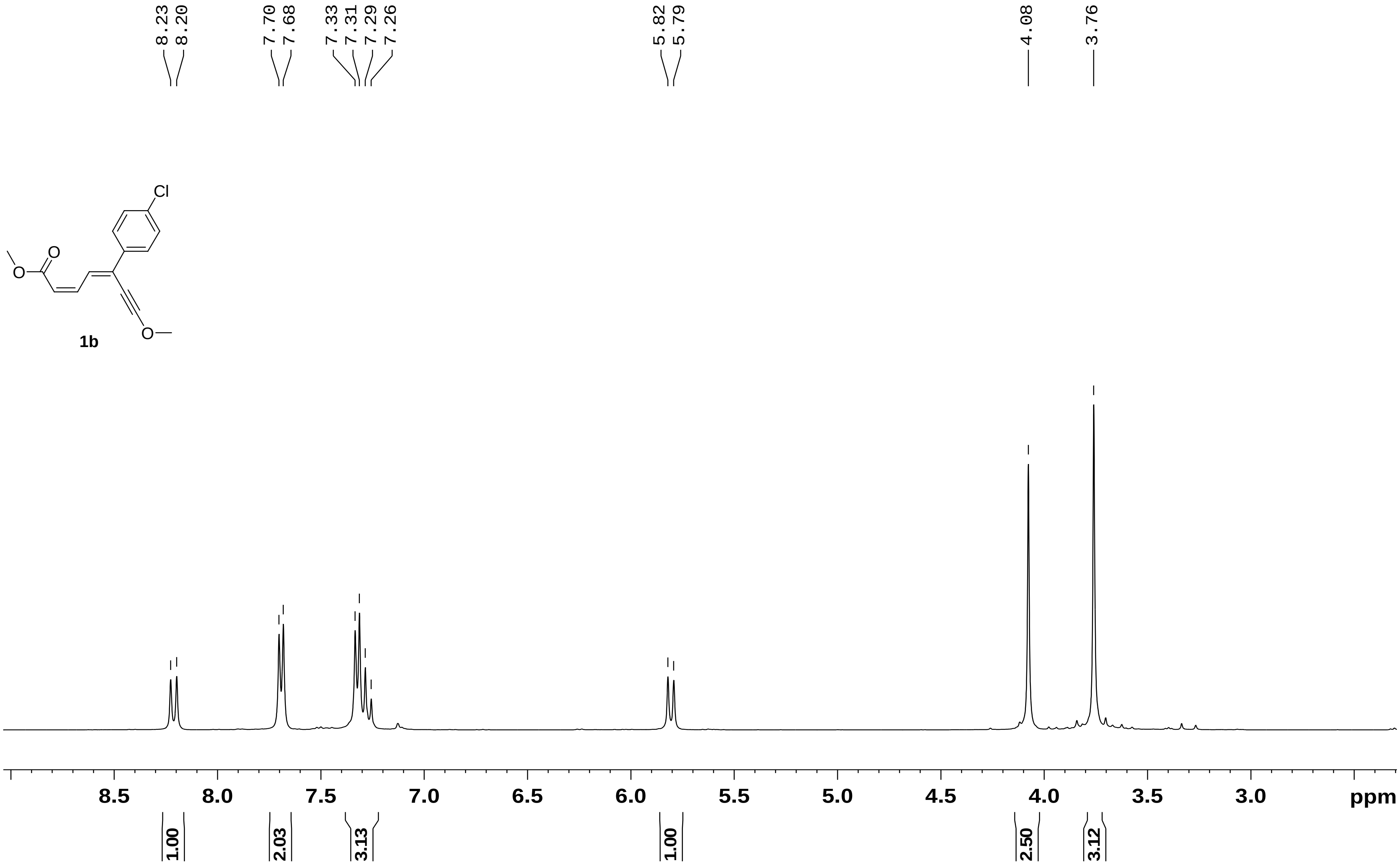
Site	^{13}C-NMR (ppm)	DEPT	^{1}H-NMR	COSY	HMBC	NOESY (selected)
1	49.31	C				
2	49.28	CH	3.79 (d, *J* = 7.0 Hz, 1H)	5.85	49.31, 121.8, 131.0, 132.6, 150.6, 170.7	5.85, 7.45, 7.32-7.13
3	121.8	CH	5.85 (m, 1H)	3.79, 6.32	49.31/49.28, 117.7	3.79, 6.32
4	131.0	CH	6.32 (d, *J* = 8.0 Hz, 1H)	5.85	49.28, 132.6	5.85, 7.32-7.13
5	117.7	C				
6	132.6	C				
7	131.5	C				
8	149.6	C				
9	59.3	CH_3	4.14 (s, 3H)		149.6	3.25
10	61.2	CH_3	3.25 (s, 3H)		131.5	4.14, 7.32-7.13
11	170.7	C				
12	51.7	CH_3	3.64 (s, 3H)		170.7	
13	150.6	C				
14	127.9	CH	7.32-7.13 (m,1 H)			
15	140.3	CH	7.45 (m, 1 H)	5.80	166.7, 150.6, 141.8, 49.31	3.79, 5.80, 7.32-7.13
16	117.4	CH	5.80 (m, 1H)	7.45	127.9, 166.7	7.45
17	166.7	C				
18	51.1	CH_3	3.71 (s, 3H)		166.7	
19	141.8	C				
20	126.6/126.8/127.5/128.0	CH	7.32-7.13/7.46-7.39 (m, 2 H)			
21	126.6/126.8/127.5/128.0	CH	7.32-7.13/7.46-7.39 (m, 2 H)			
22	126.3/127.0	CH	7.46-7.39 (m, 1 H)			
23	138.0.0	C				
24	126.6/126.8/127.5/128.0	CH	7.32-7.13/7.46-7.39 (m, 2 H)			
25	126.6/126.8/127.5/128.0	CH	7.32-7.13/7.46-7.39 (m, 2 H)			
26	126.3/127.0	CH	7.46-7.39 (m, 1 H)			



3k

Site	^{13}C-NMR (ppm)	DEPT	^{1}H-NMR	COSY	HMBC	NOESY (selected)
1	162.8	C				
2	106.6	CH	6.43 (s, 1H)	2.45	32.9, 123.5, 162.8	1.32, 1.49, 2.45, 3.91
3	151.9	C				
4	123.5	C				
5	152.1	C				
6	142.3	CH	7.04 (d, J = 11.8 Hz, 1H)		151.9, 152.1, 165.7	1.49, 2.33, 2.45
7	123.3	CH	6.16 (d, J = 11.8 Hz, 1H)		151.9, 152.1, 165.7	
8	165.7	C				
9	51.4	CH_3	3.61 (s, 3H)		165.7	
10	22.9	CH_3	2.33 (s, 3H)		123.5, 152.1	
11	53.2	CH_3	3.91 (s, 3H)		162.8	
12	32.9	CH_2	2.45 (t, J = 7.6 Hz, 2H)	1.49, 6.43	22.4, 31.5, 106.6, 123.5, 151.9	
13	31.5	CH_2	1.49 (m, 2H)	1.32, 2.45	13.9, 22.4, 32.9, 151.9	
14	22.4	CH_2	1.32 (m, 2H)	0.90, 1.49	13.9, 31.5, 32.9	
15	13.9	CH_3	0.90 (t, J = 7.3 Hz, 3H)	1.32	22.4, 31.5	

^{1}H and ^{13}C NMR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O
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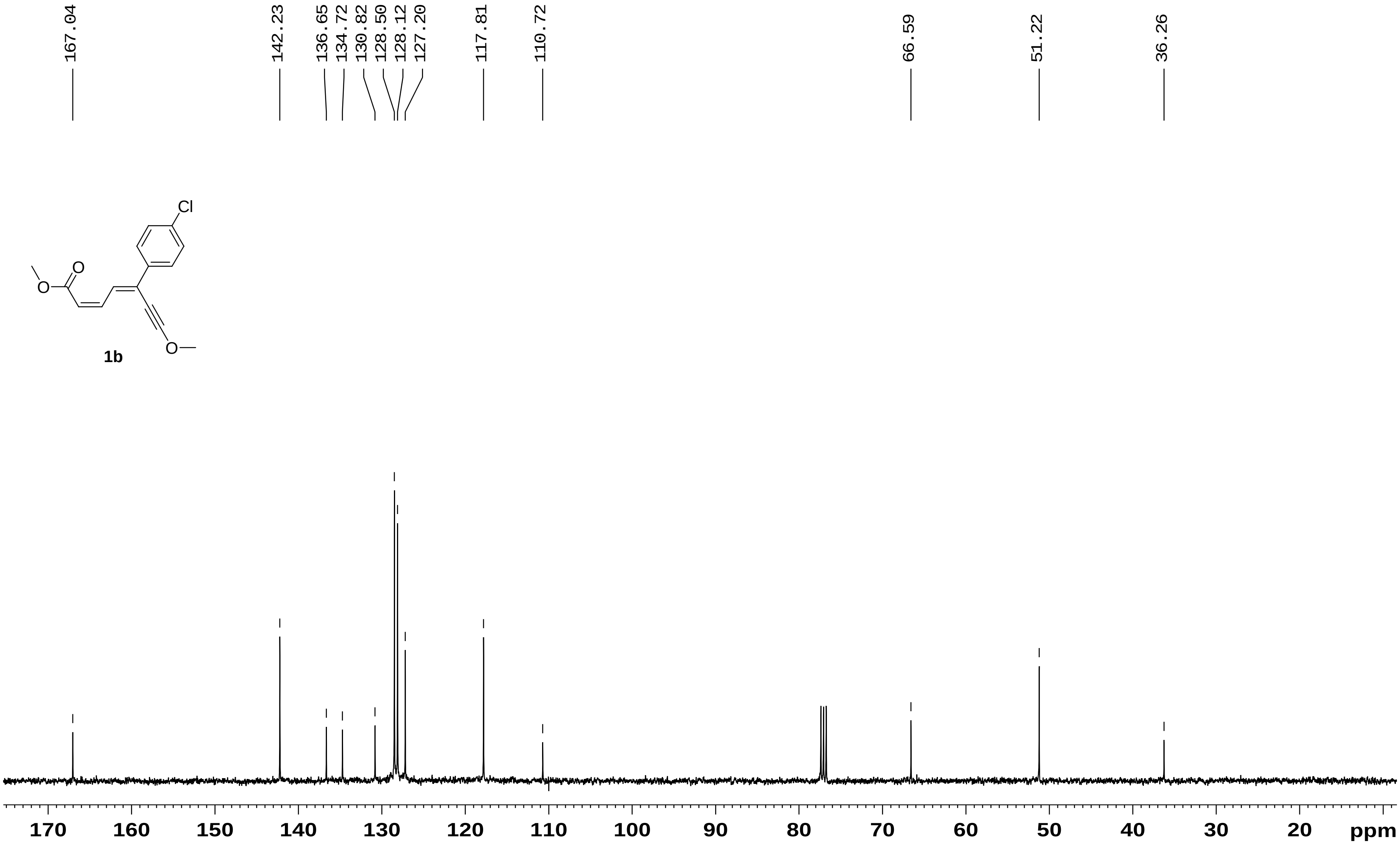
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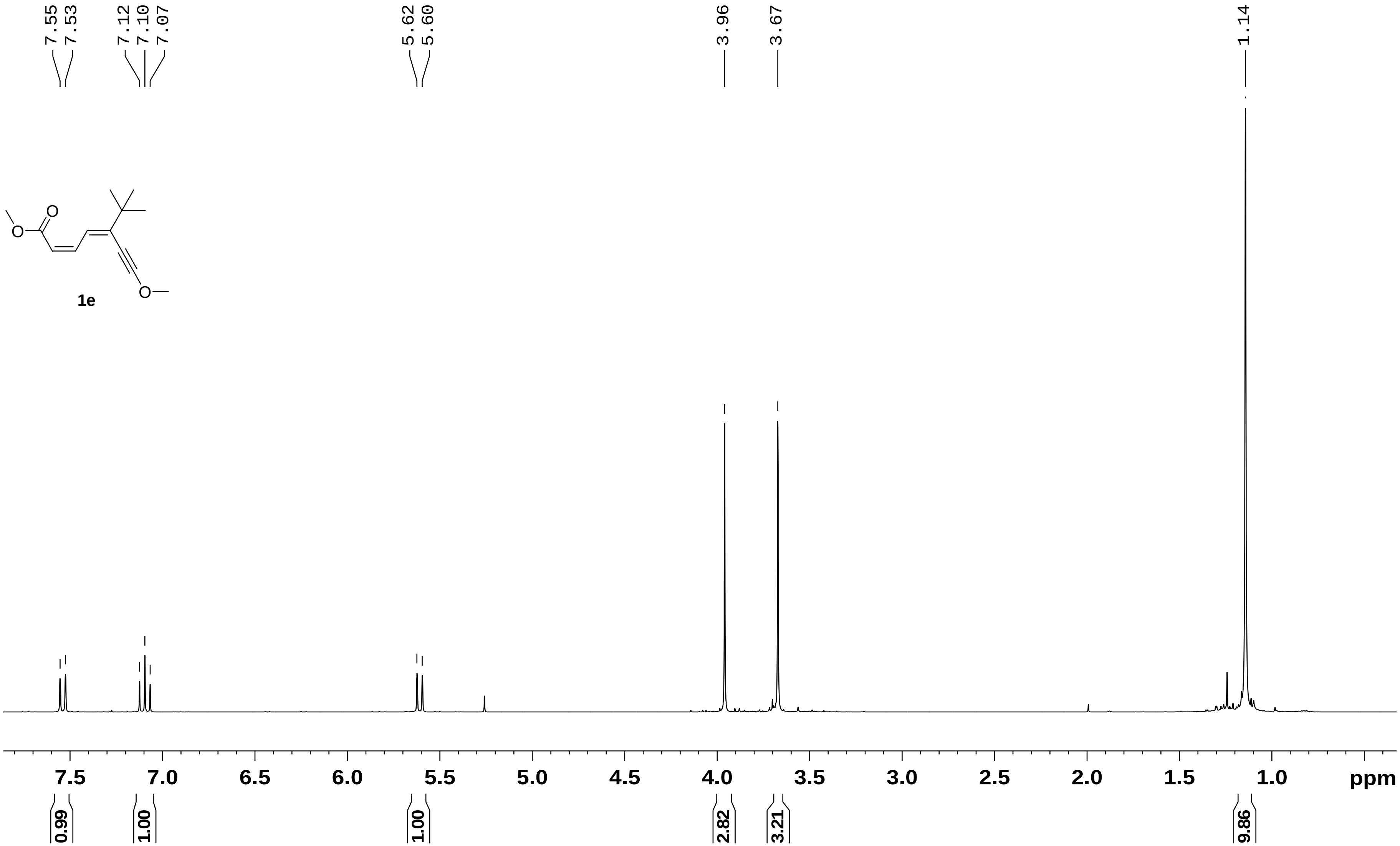
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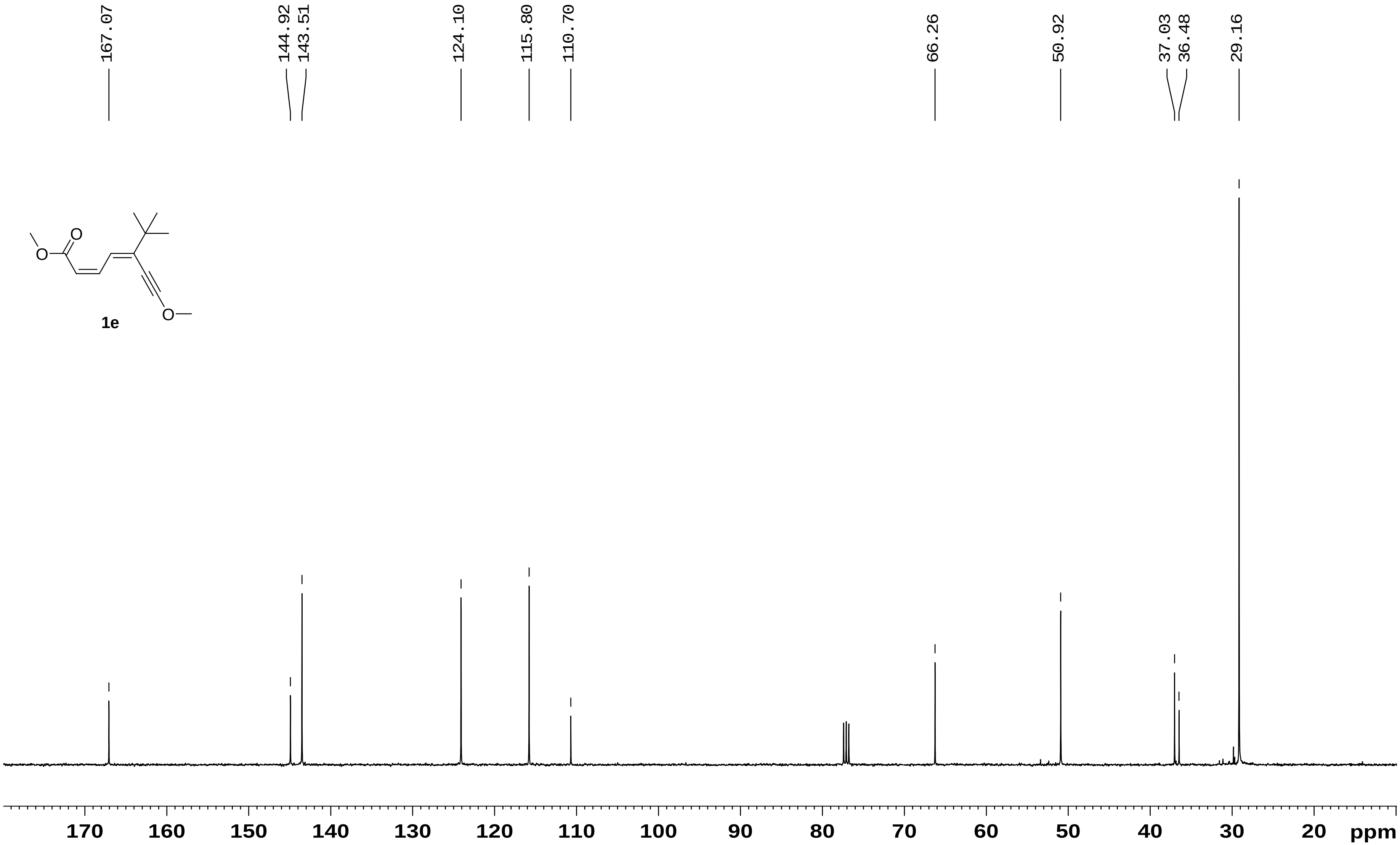
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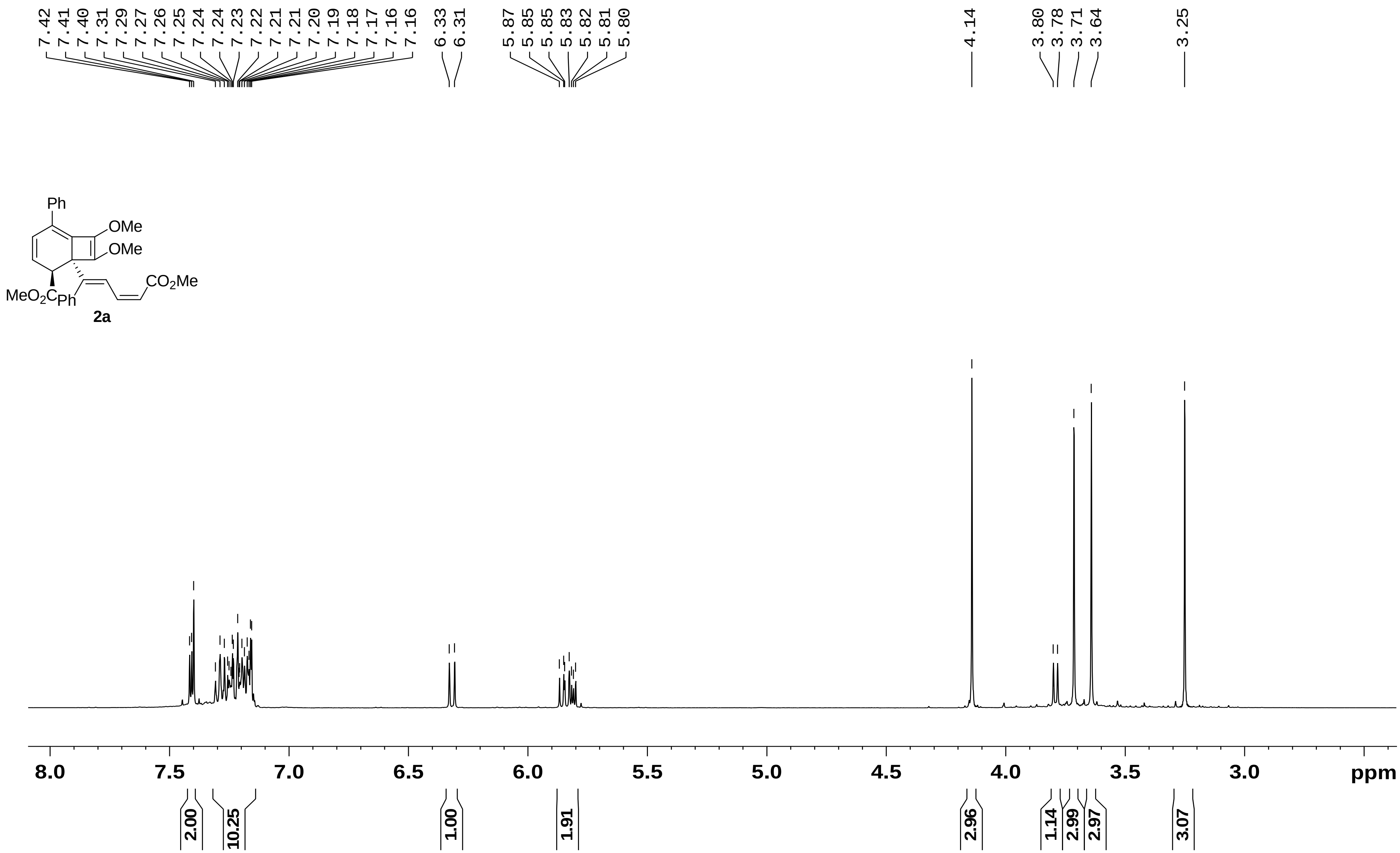
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6.33 6.31
5.87 5.85 5.85 5.83 5.82 5.81 5.80
4.14
3.80 3.78 3.71 3.64
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Ph
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CO2Me
MeO2C
Ph
2a
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 ppm
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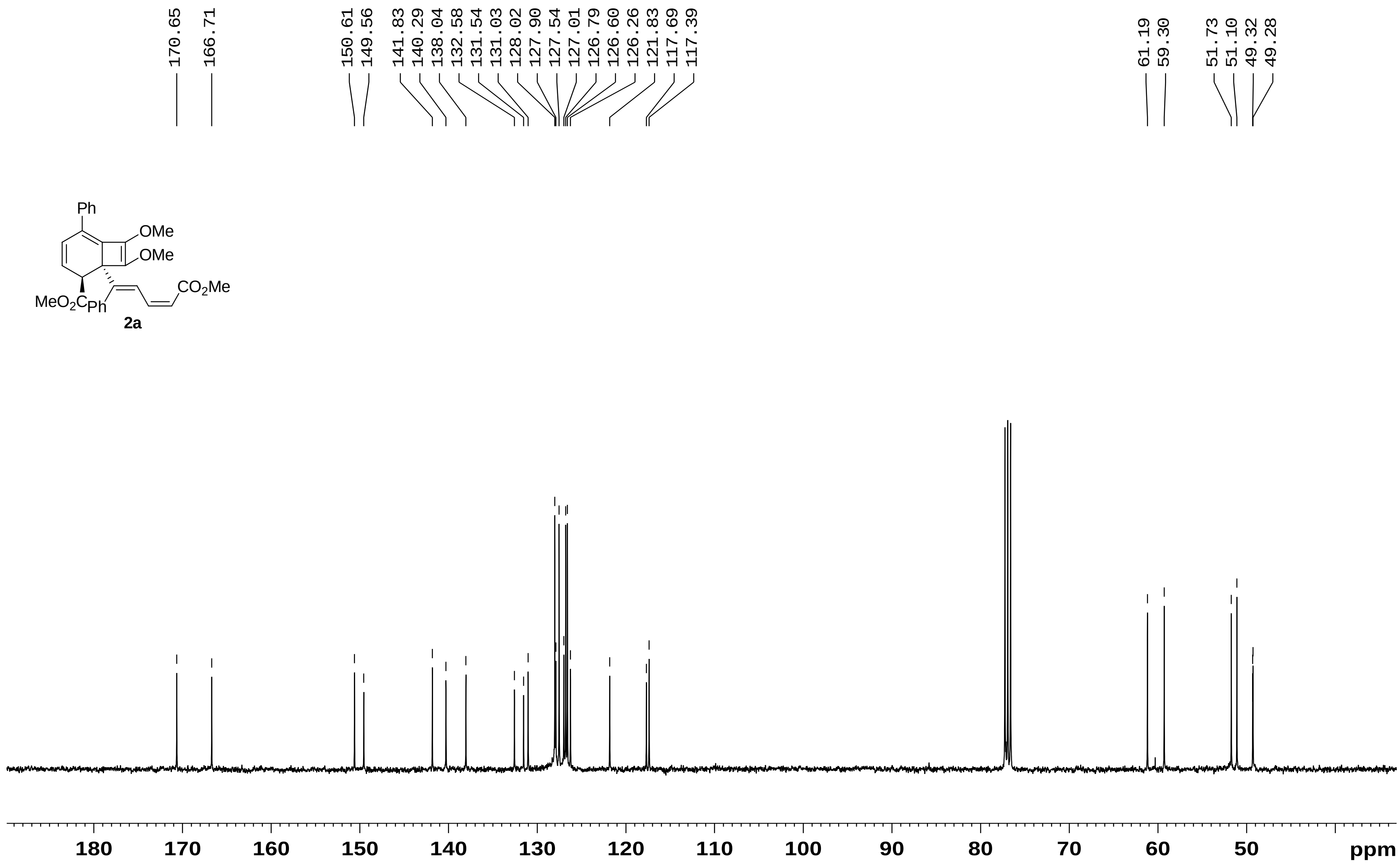
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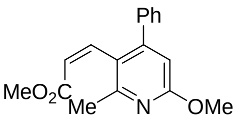
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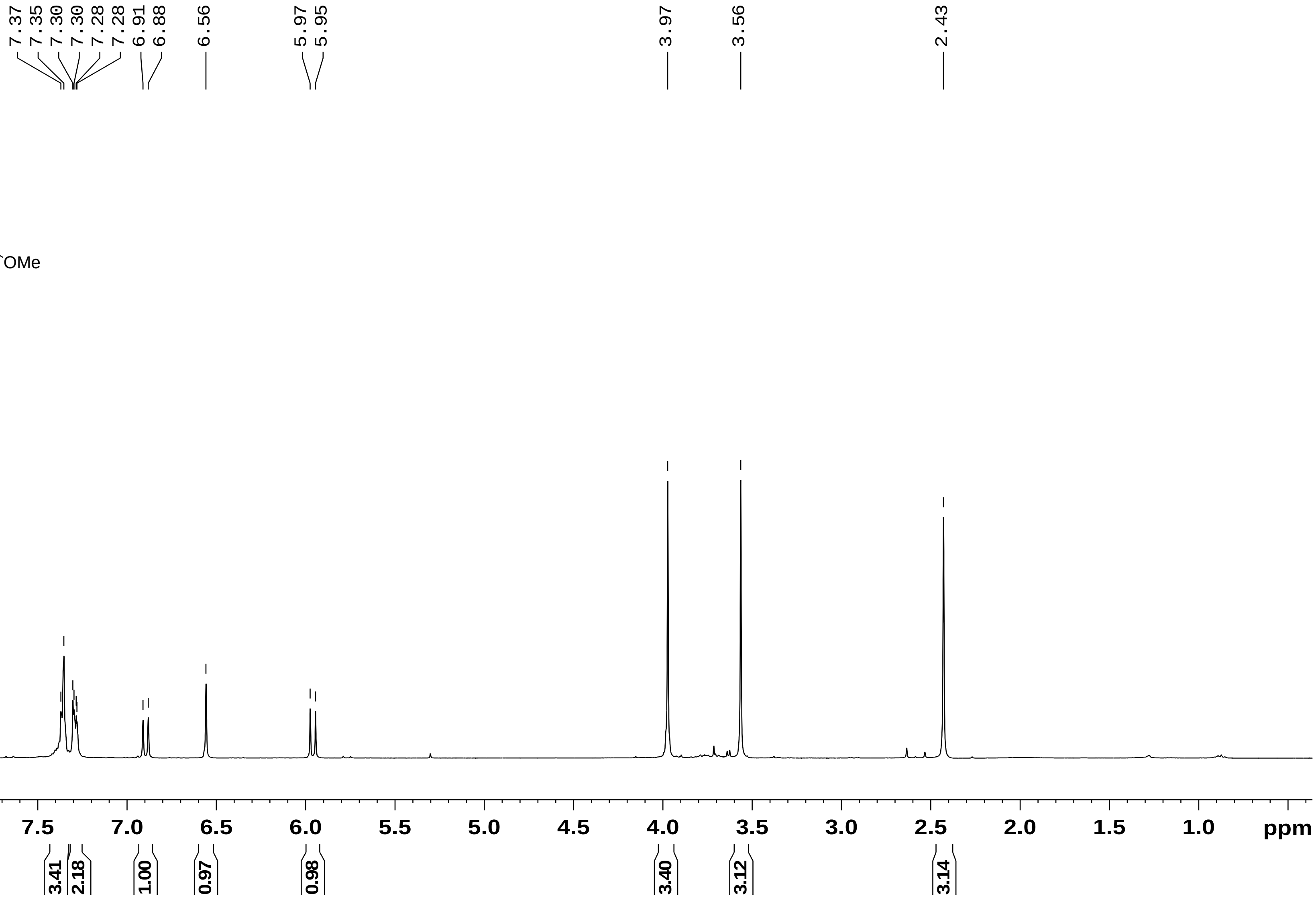
3a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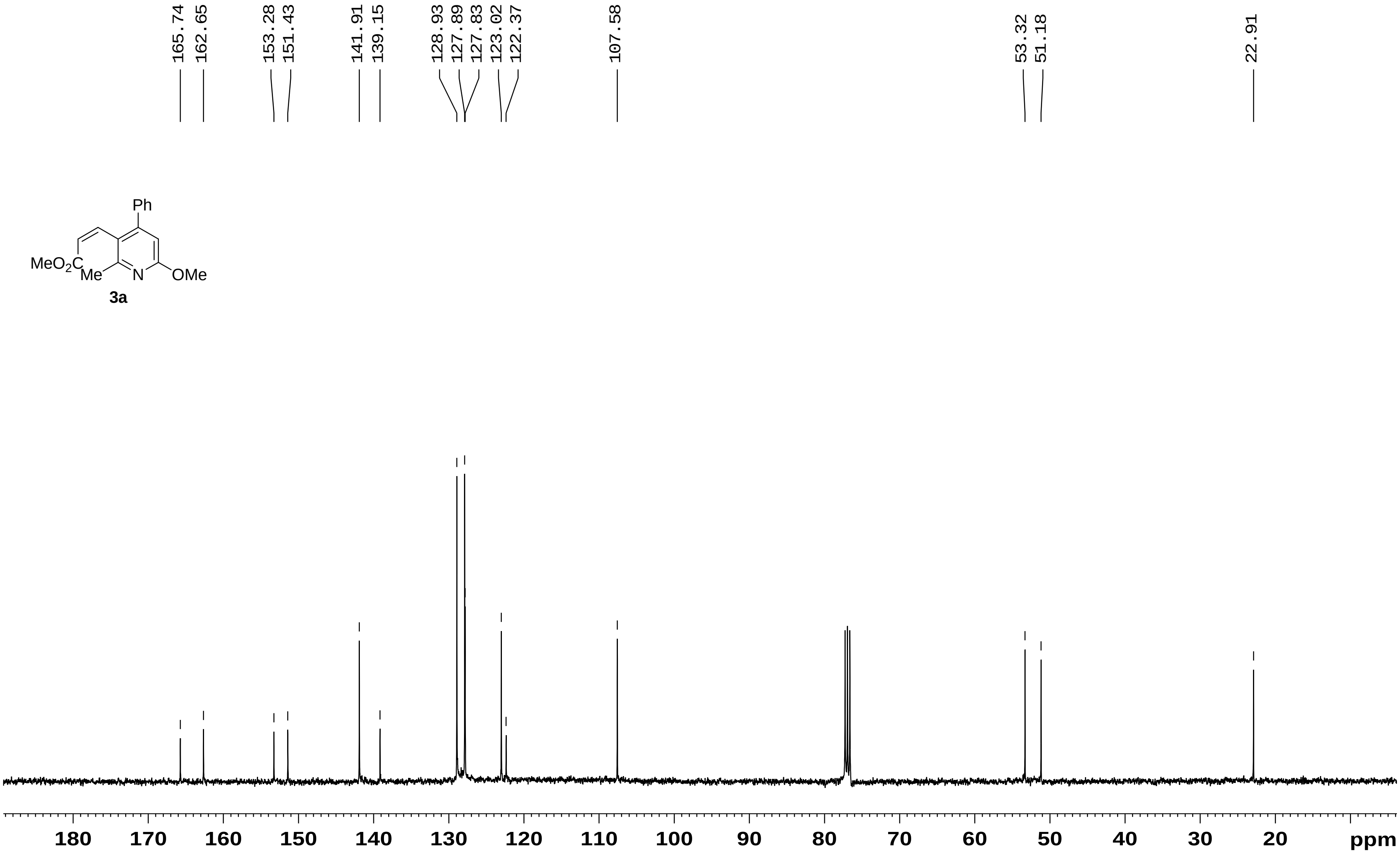

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140
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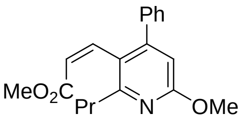
Me
N
OMe

3a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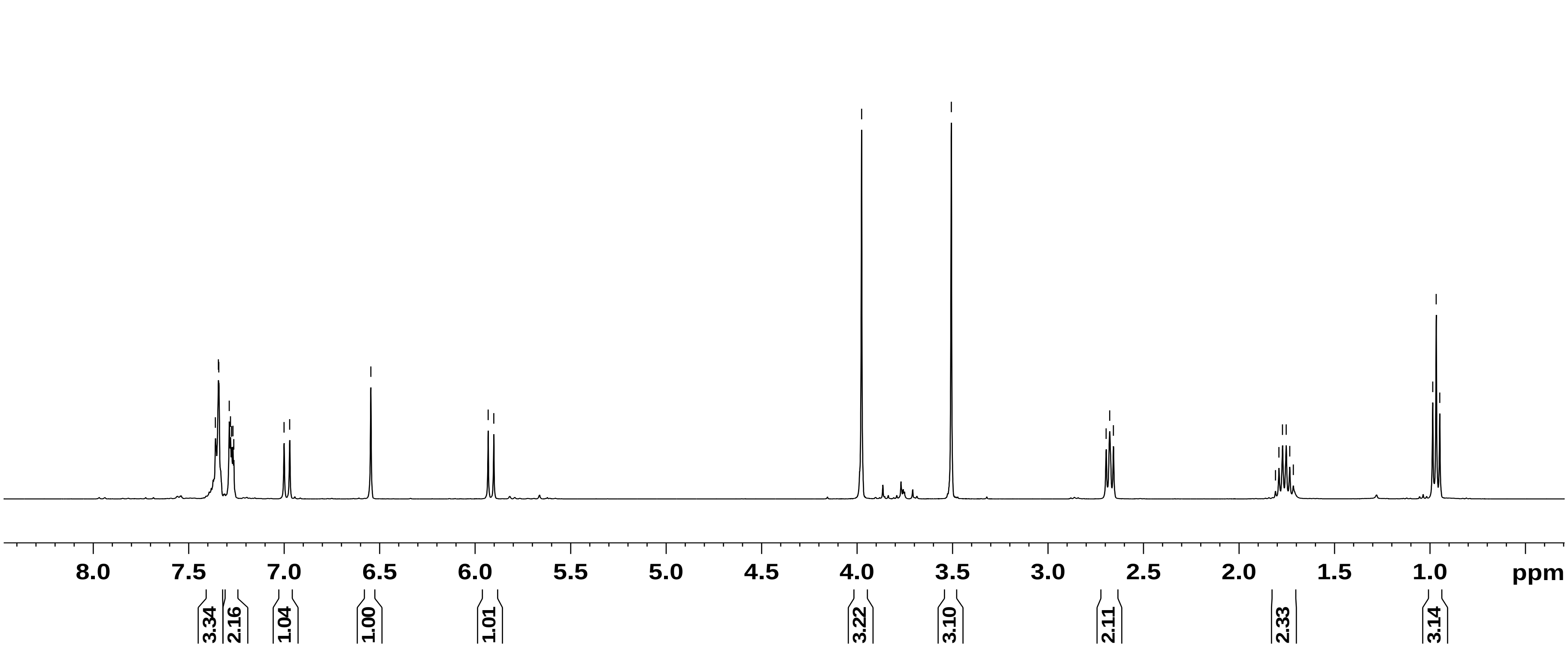
3b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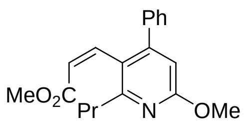
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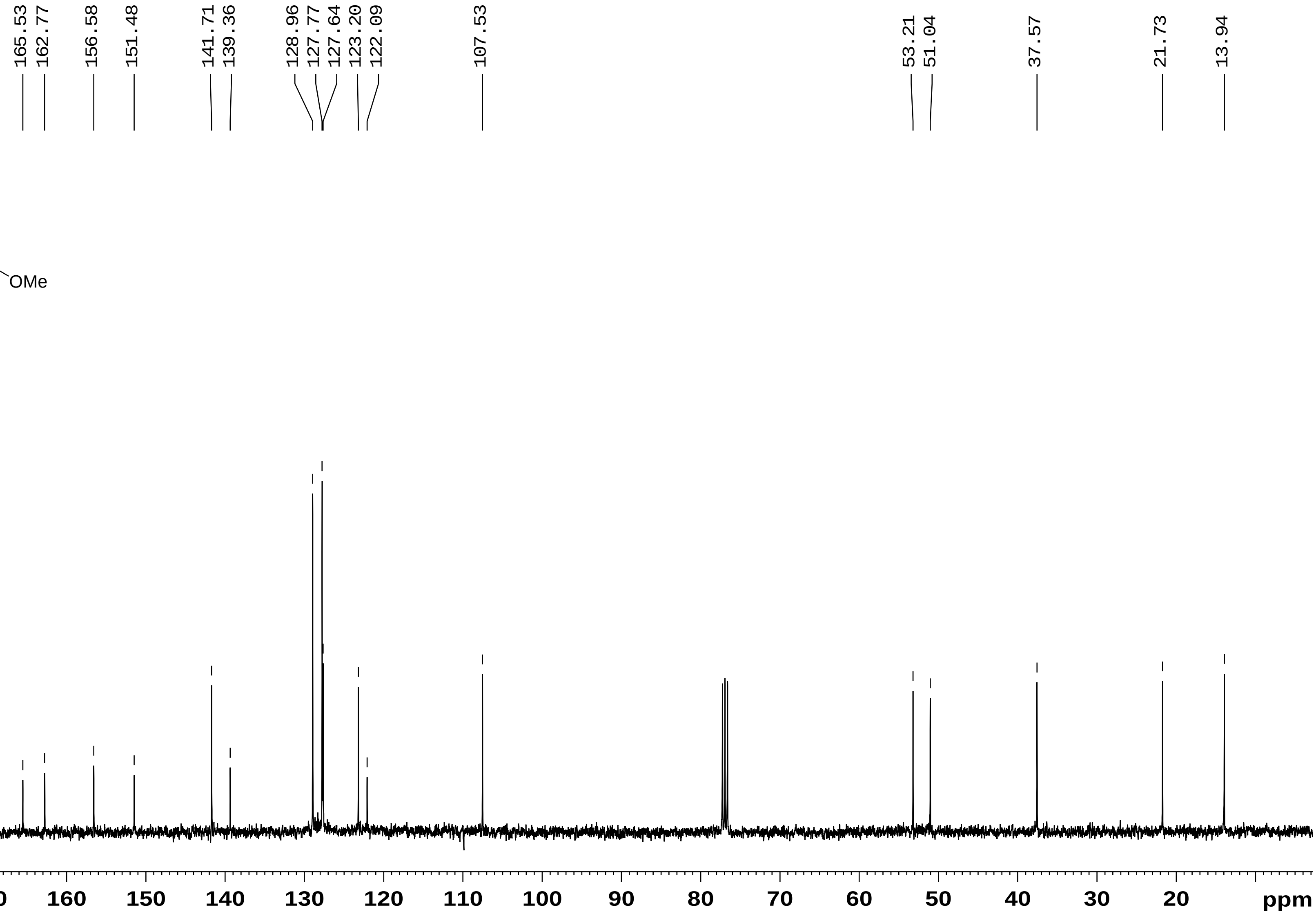
3b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140
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120
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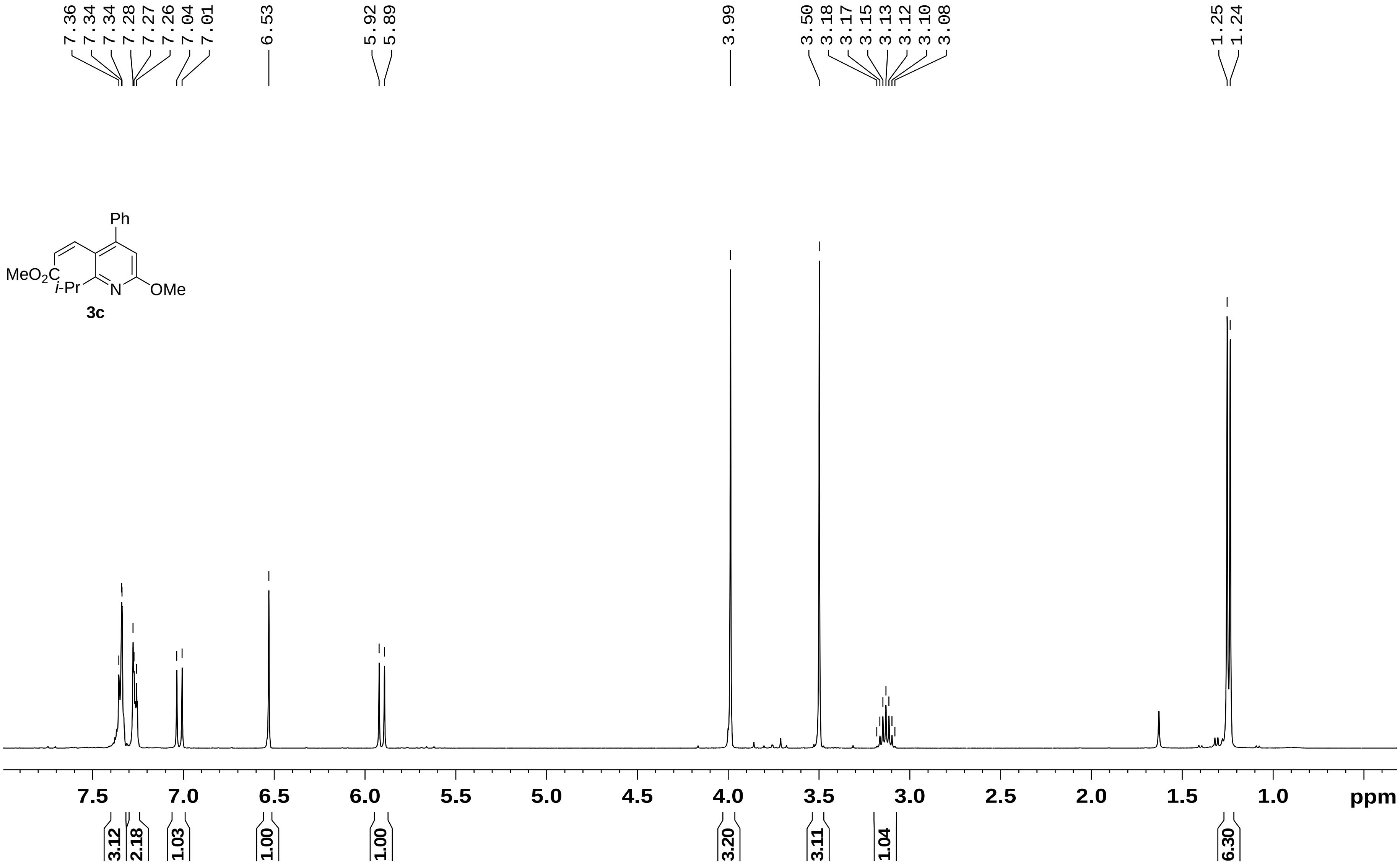
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1.25 1.24
Ph
MeO2C
i-Pr
N
OMe
3c
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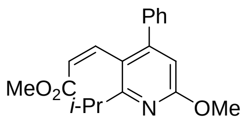
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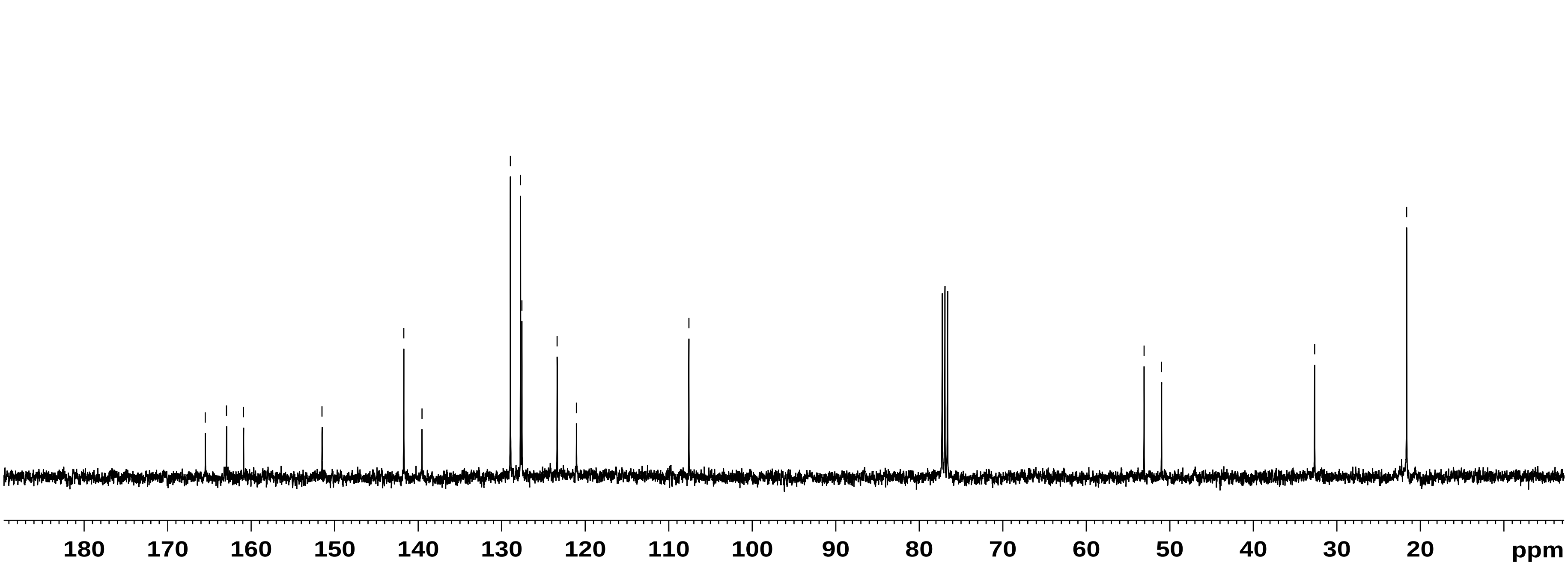
i-Pr
N
OMe

3c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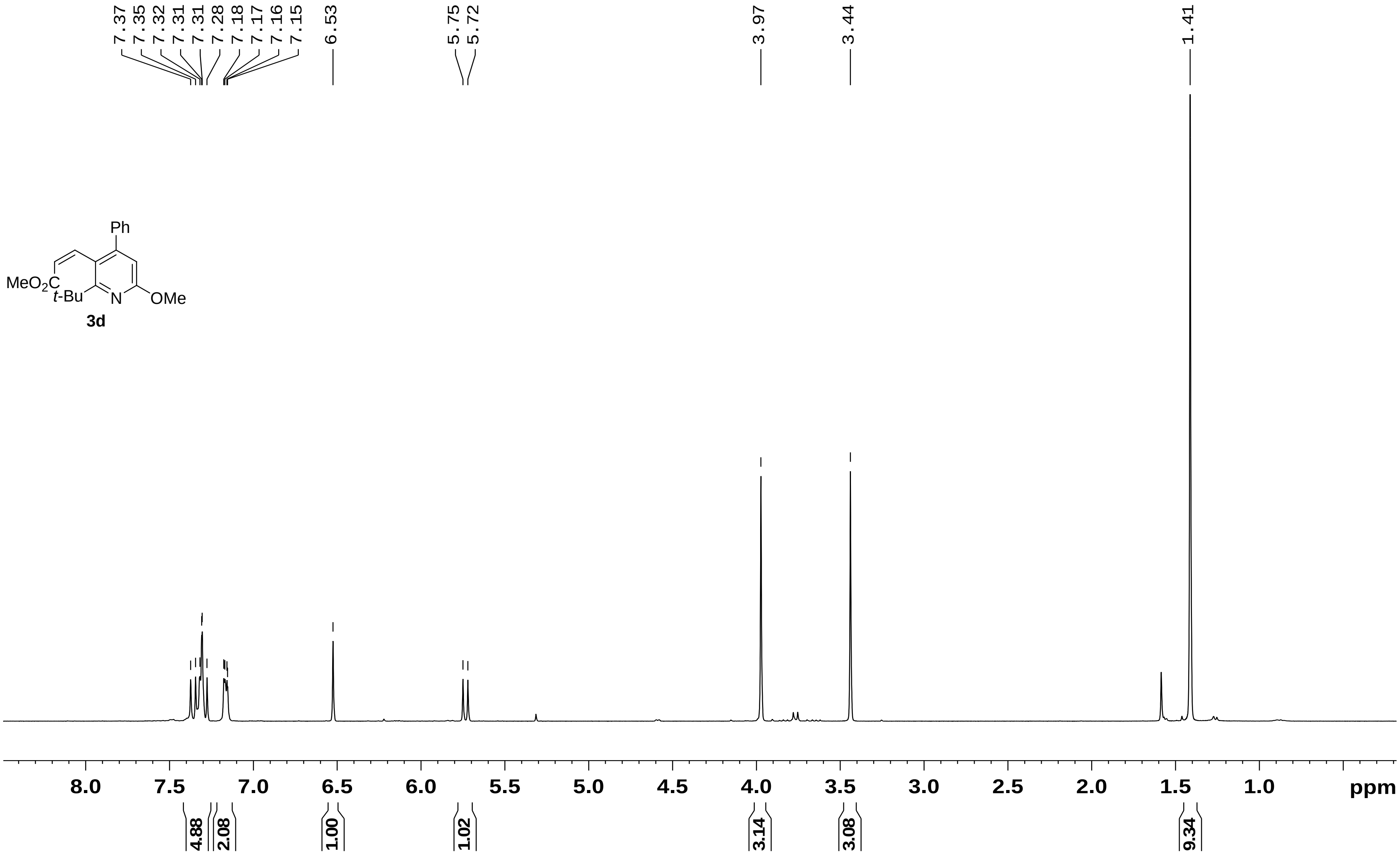
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5.72
3.97
3.44
1.41
Ph
MeO2C
t-Bu
N
OMe
3d
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6.0
5.5
5.0
4.5
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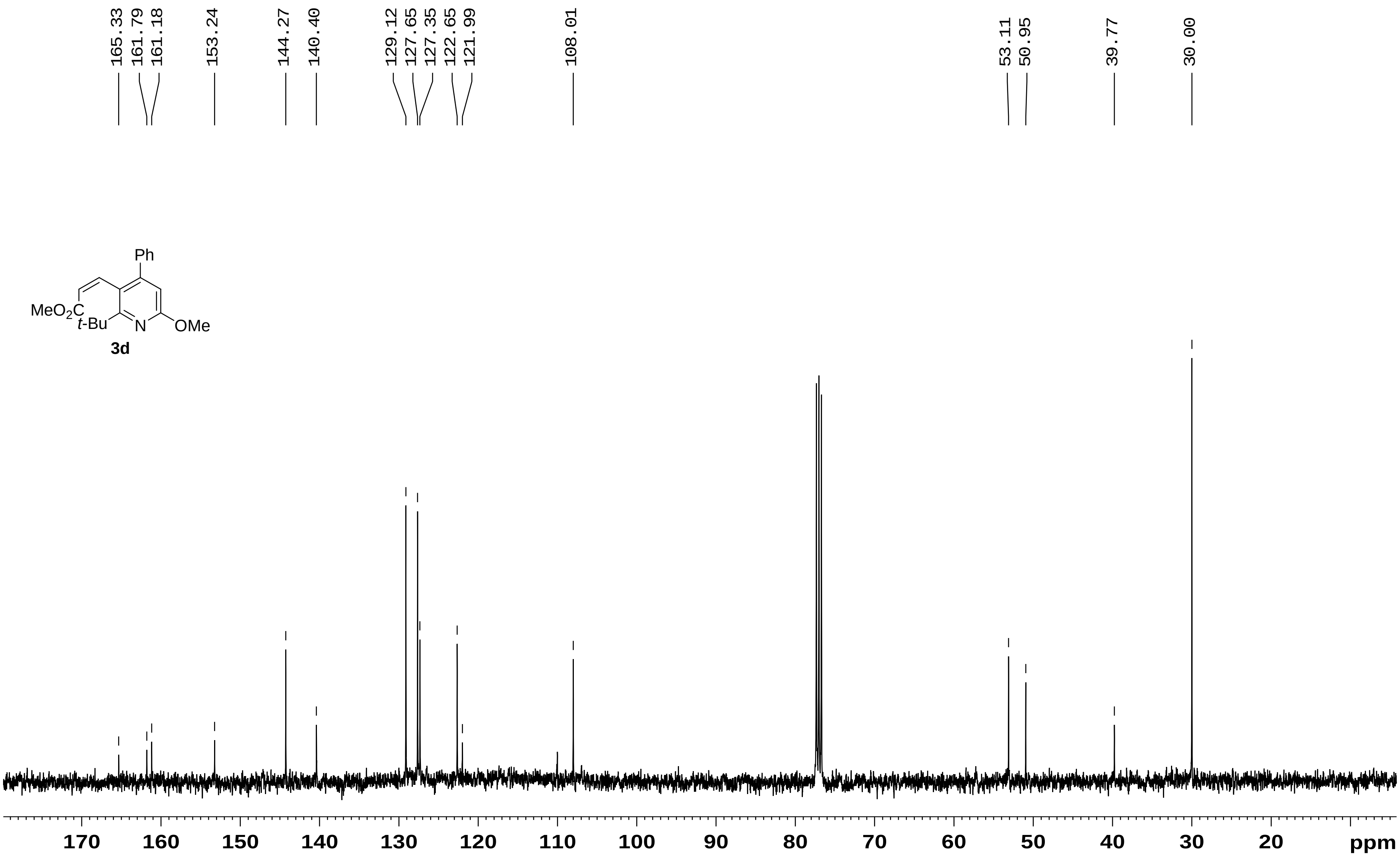
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Ph
MeO2C
t-Bu
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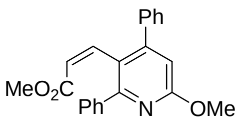
ppm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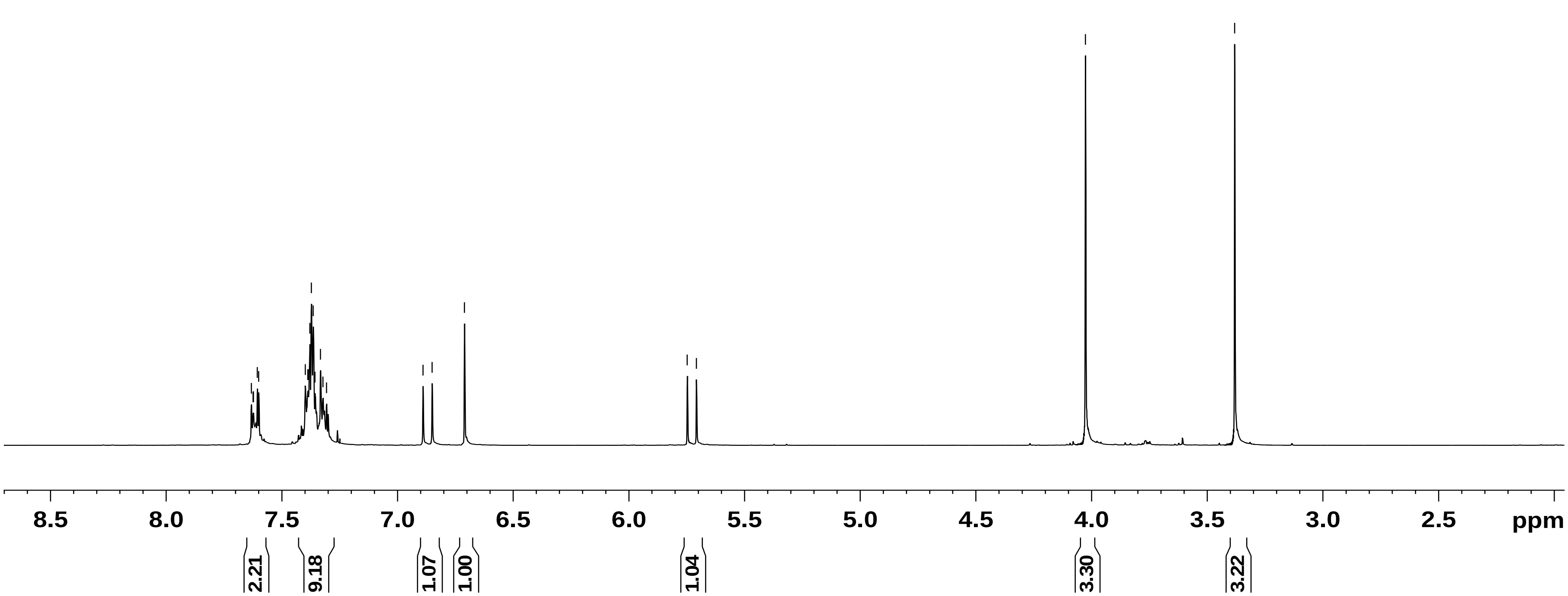
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5.75 5.71
4.03
3.38
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 ppm
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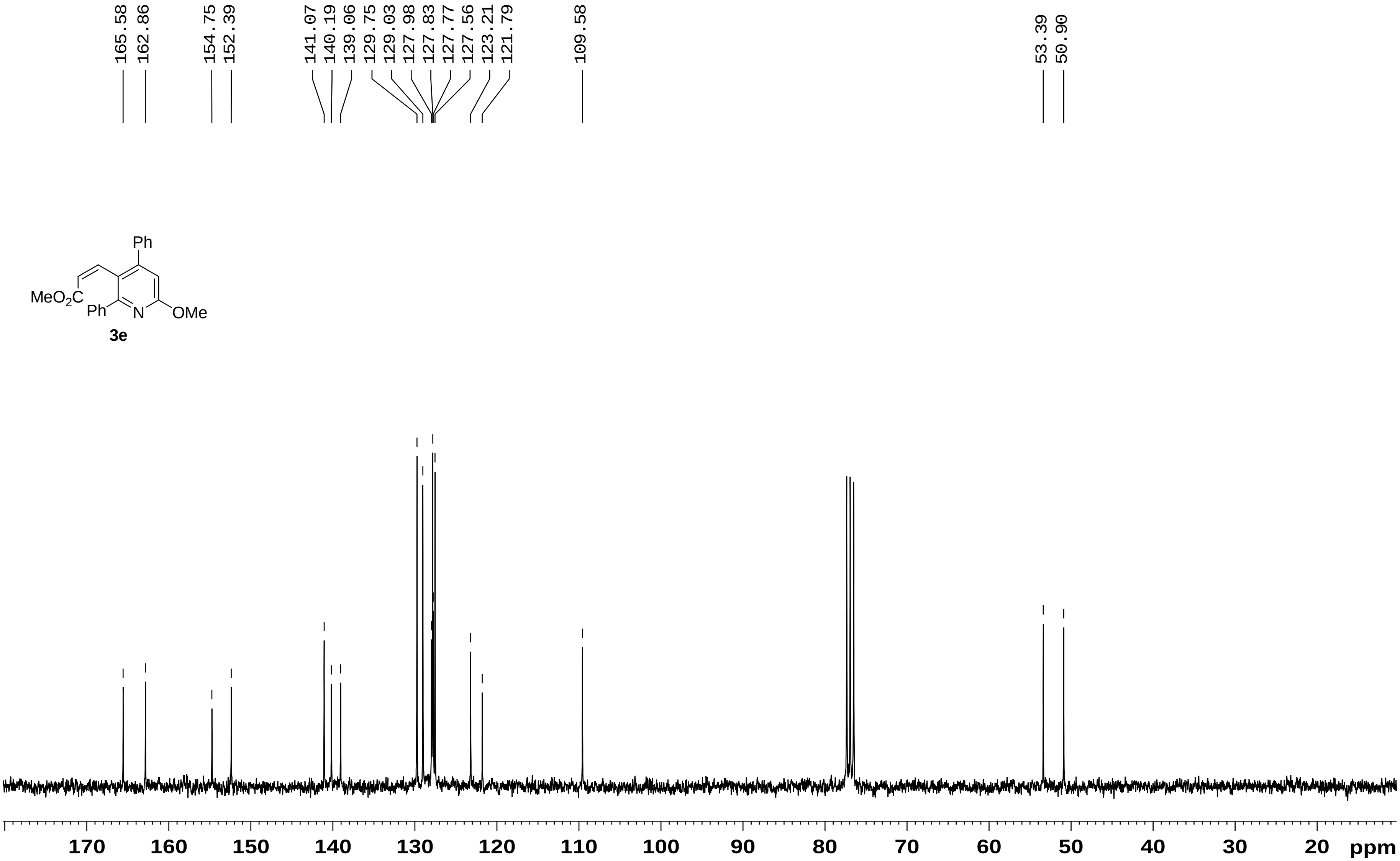
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53.39
50.90
Ph
MeO2C
Ph
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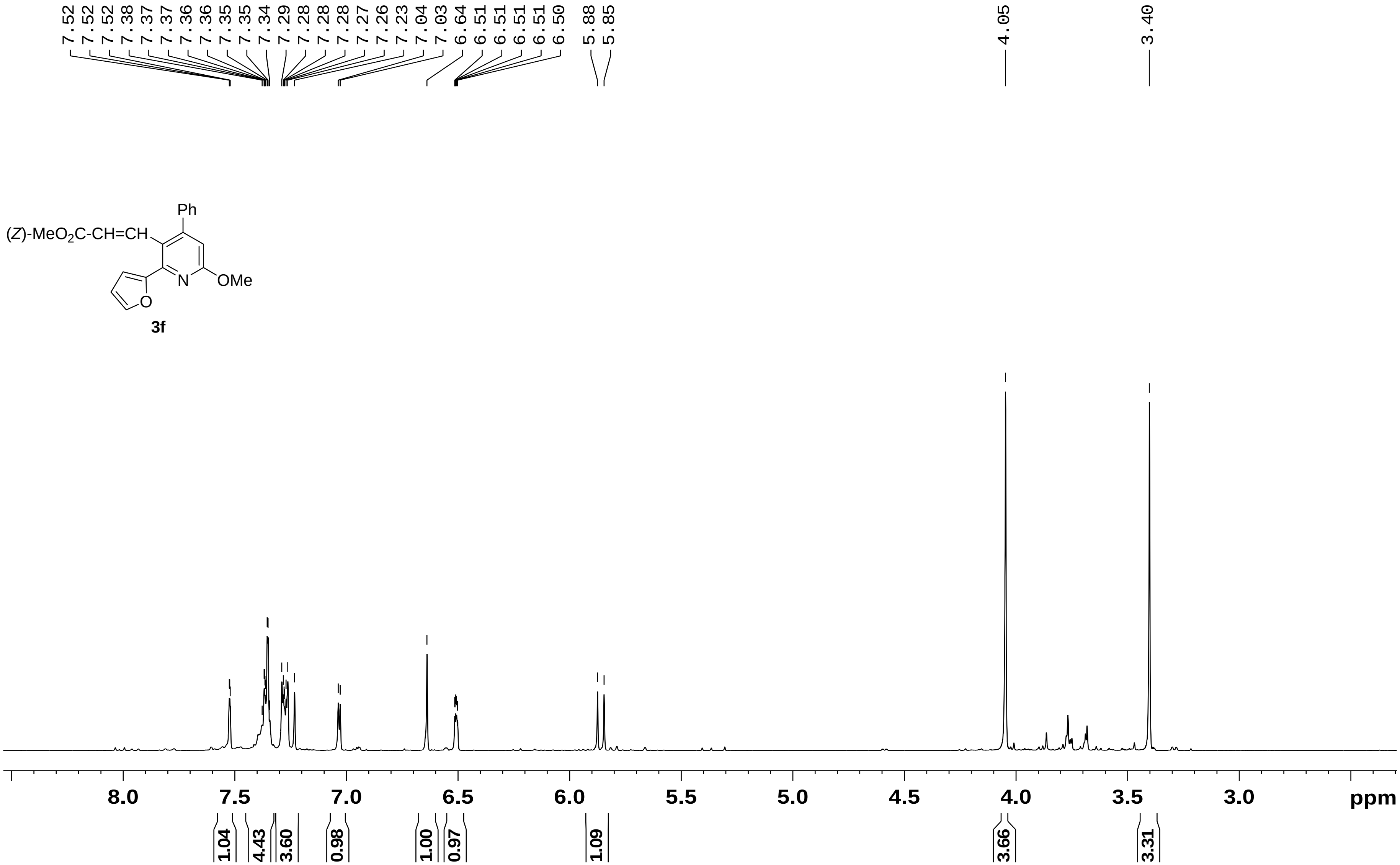
ppm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4.05
3.40
Ph
(Z)-MeO2C-CH=CH
N
OMe
O
3f
8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 ppm
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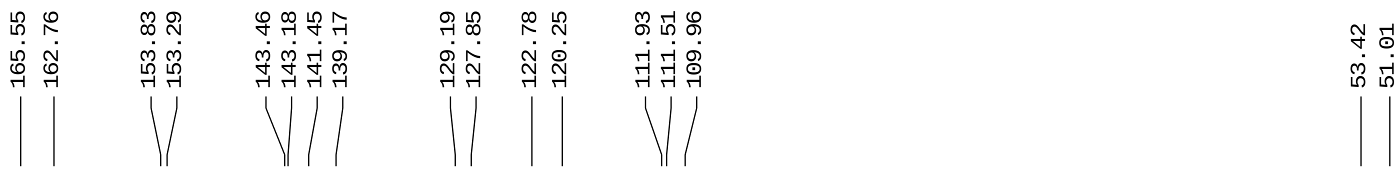
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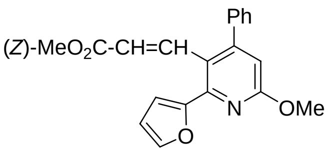
51.01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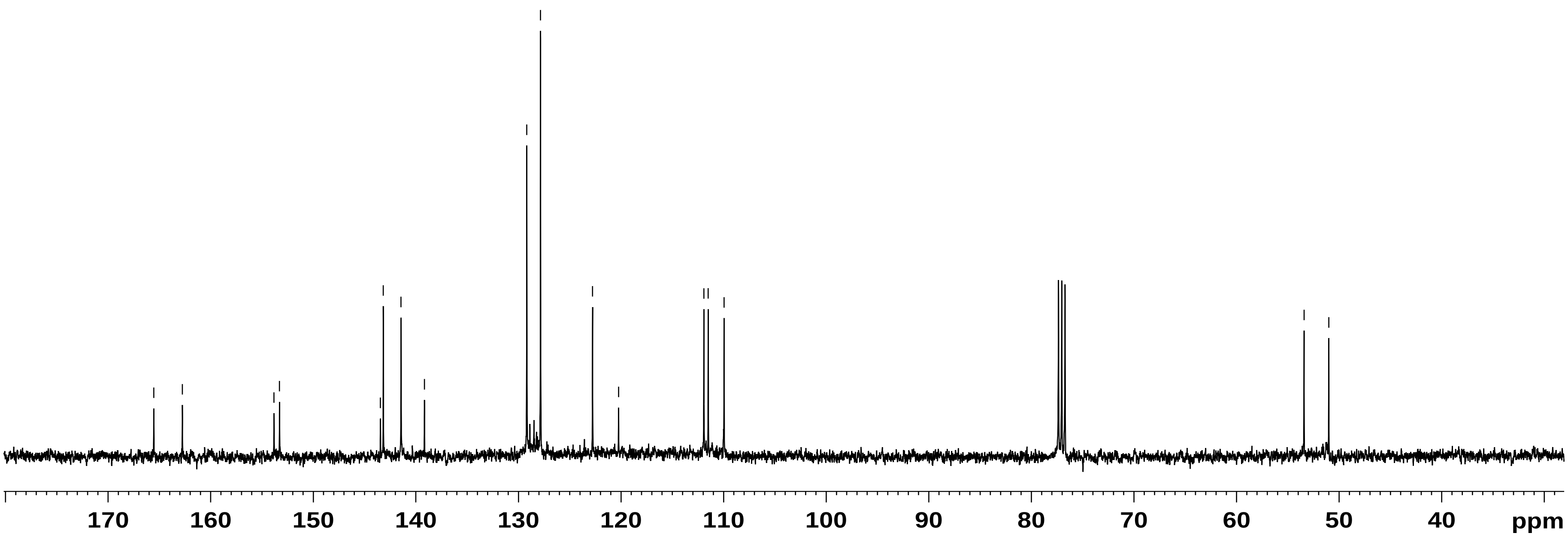
N
OMe
O

3f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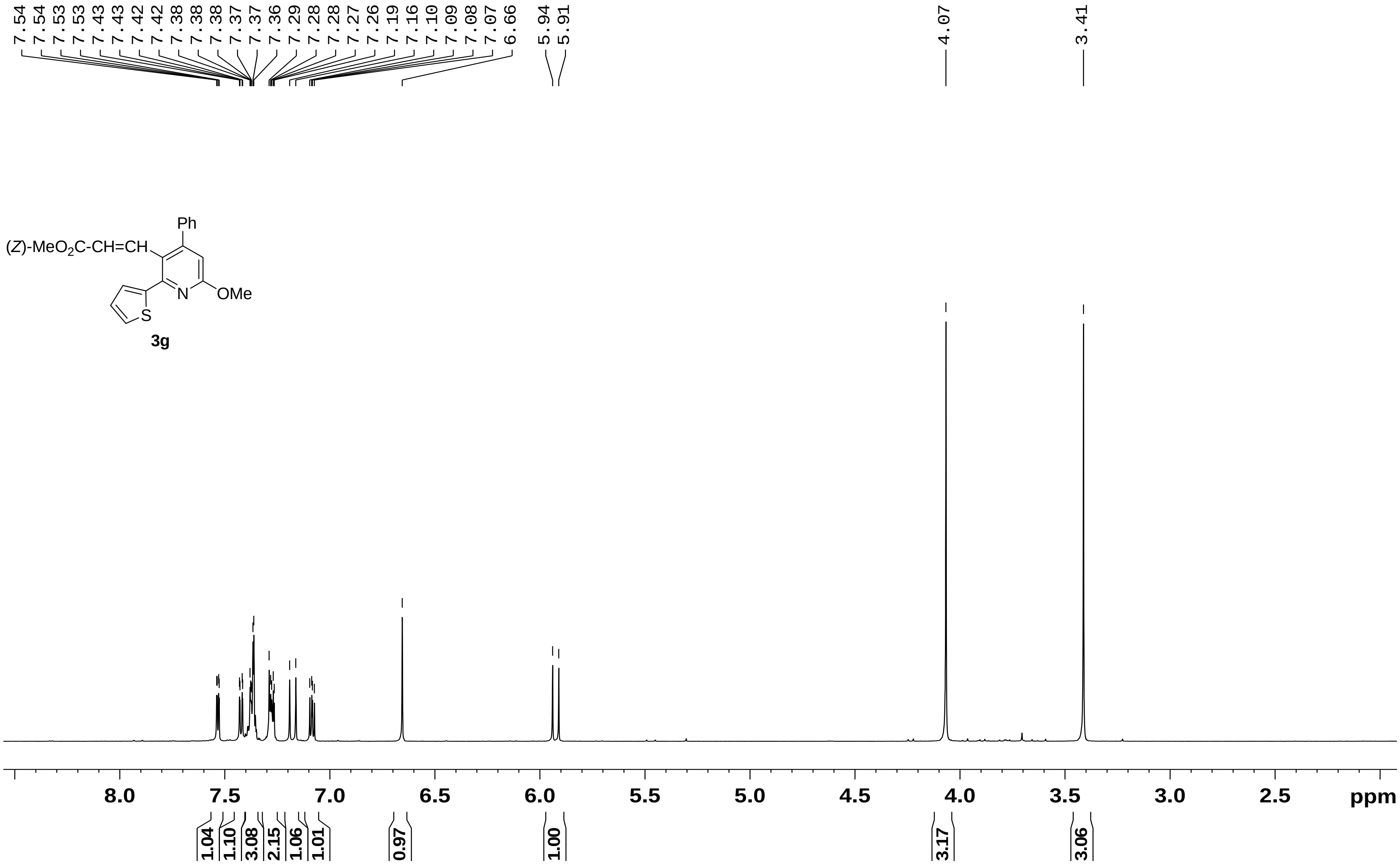
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7.36
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7.28
7.27
7.26
7.19
7.16
7.10
7.09
7.08
7.07
6.66
5.94
5.91
4.07
3.41
(Z)-MeO2C-CH=CH
Ph
N
OMe
S
3g
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
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1.10
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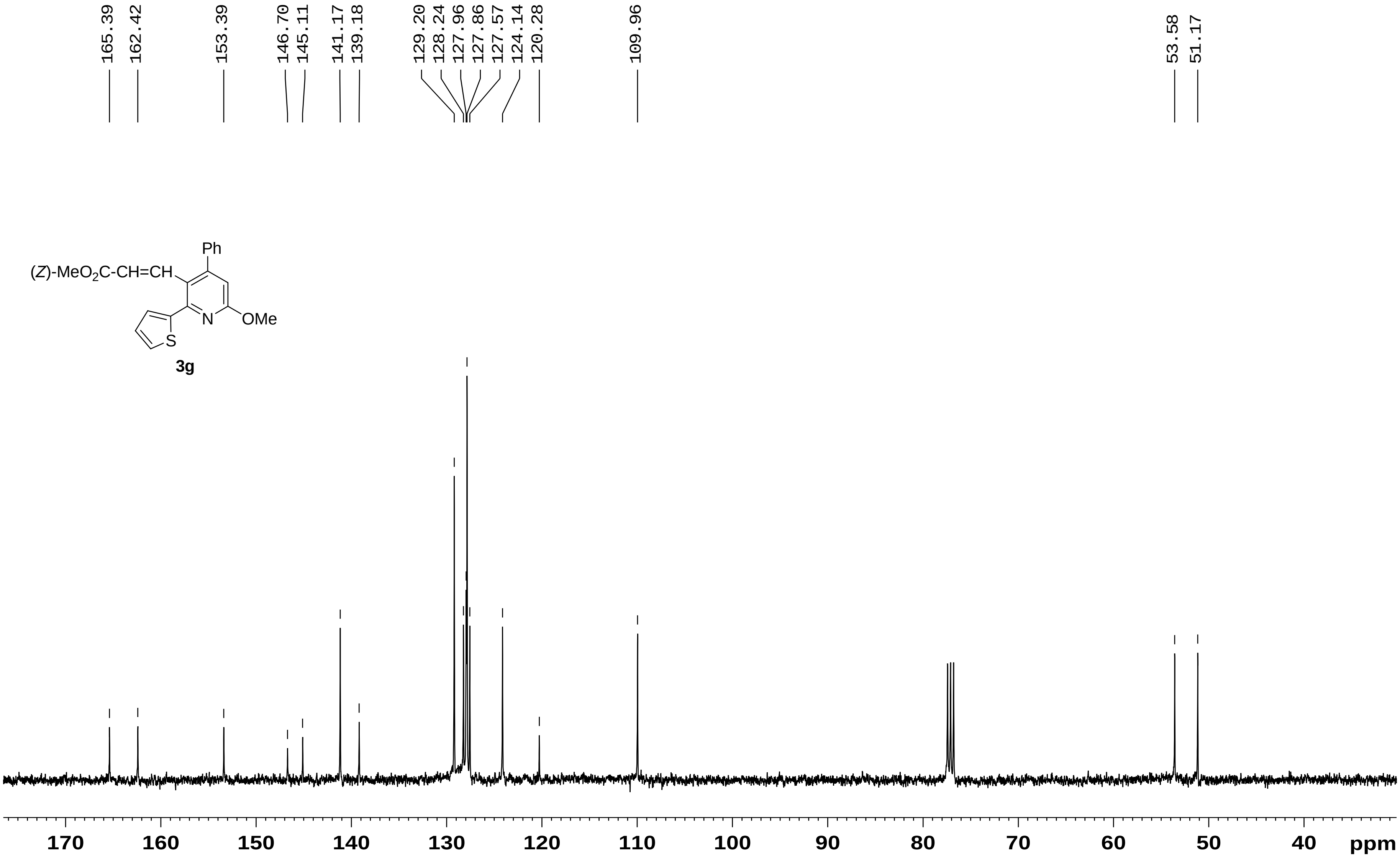
1.06
1.01
0.97
1.00
3.17
3.06



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109.96
53.58
51.17
Ph
(Z)-MeO2C-CH=CH
N
OMe
S
3g
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150
140
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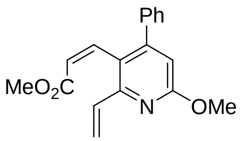
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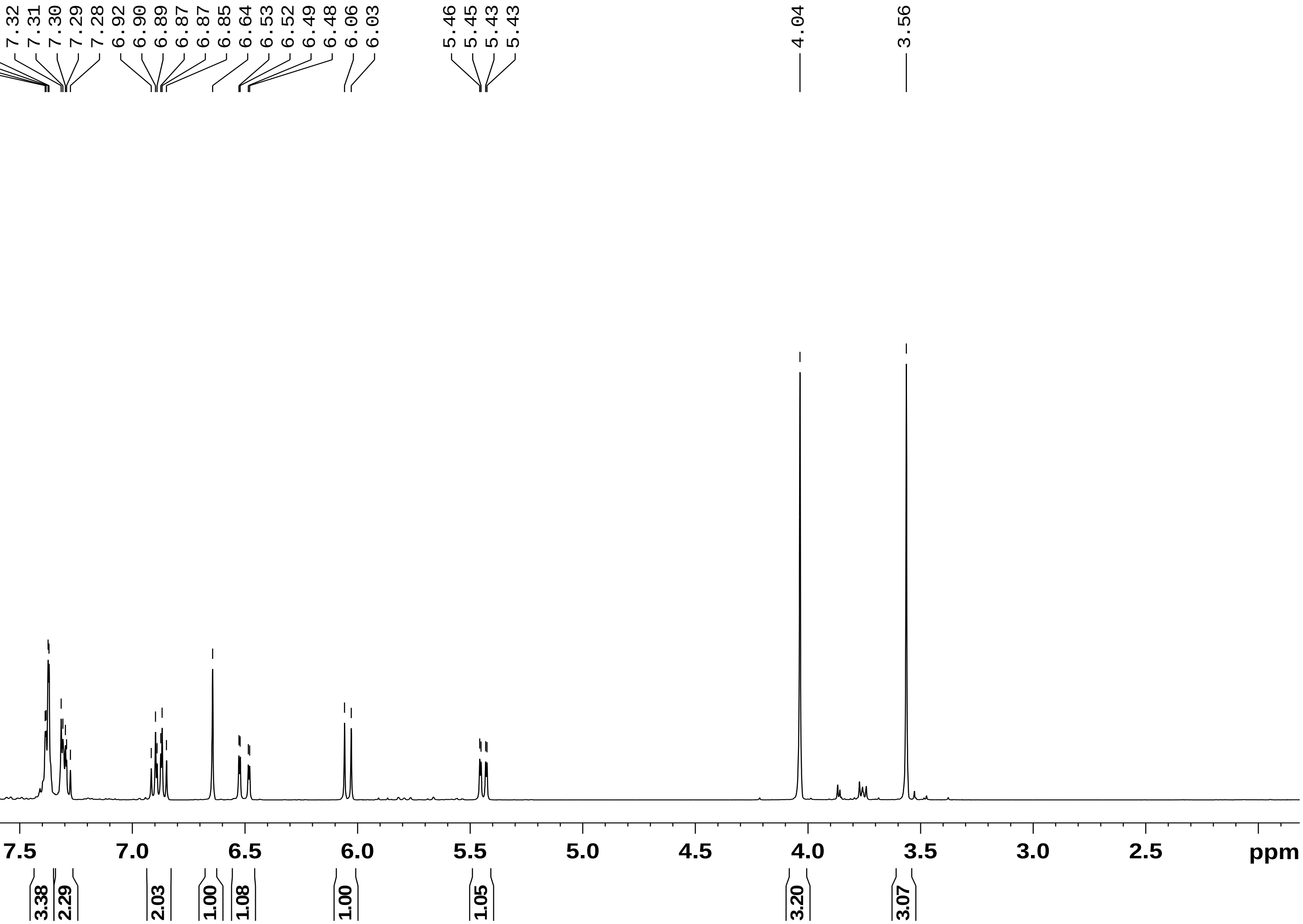
N
OMe

3h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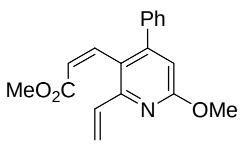
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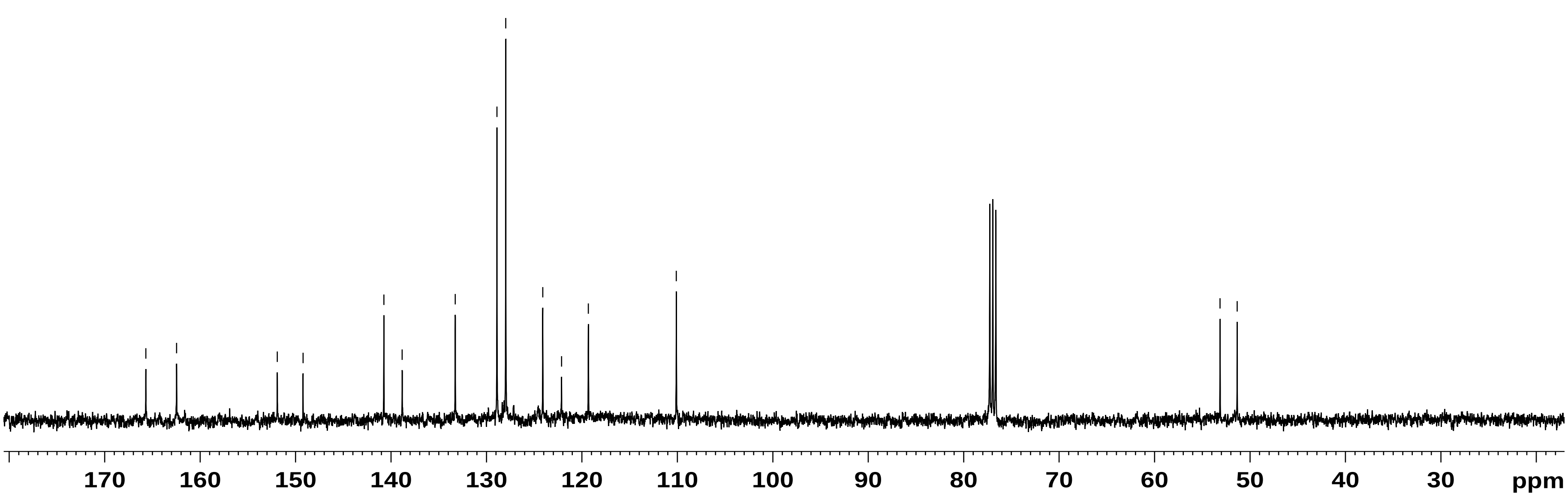
3h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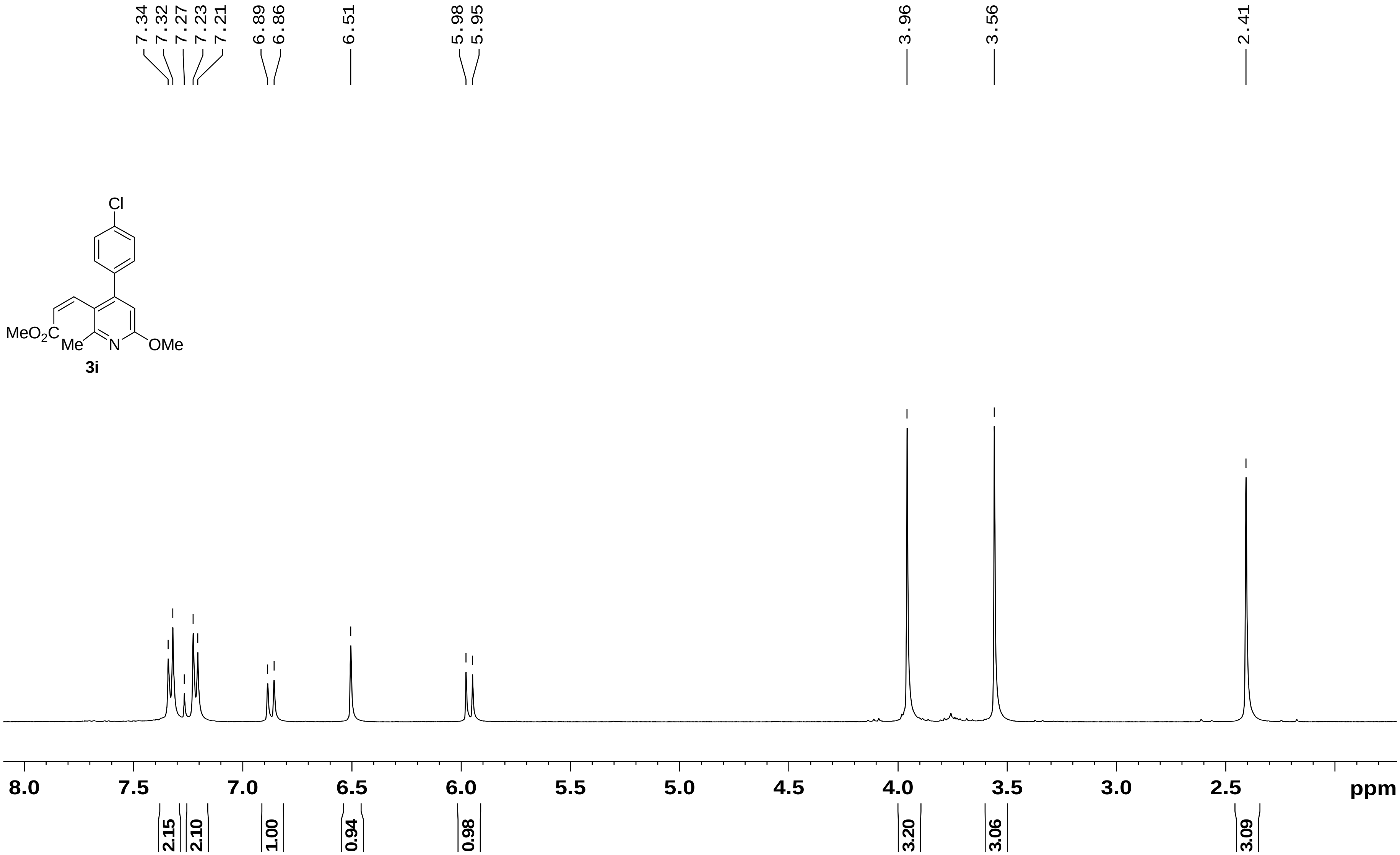
ppm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2.41
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MeO2C
Me
N
OMe
3i
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7.5
7.0
6.5
6.0
5.5
5.0
4.5
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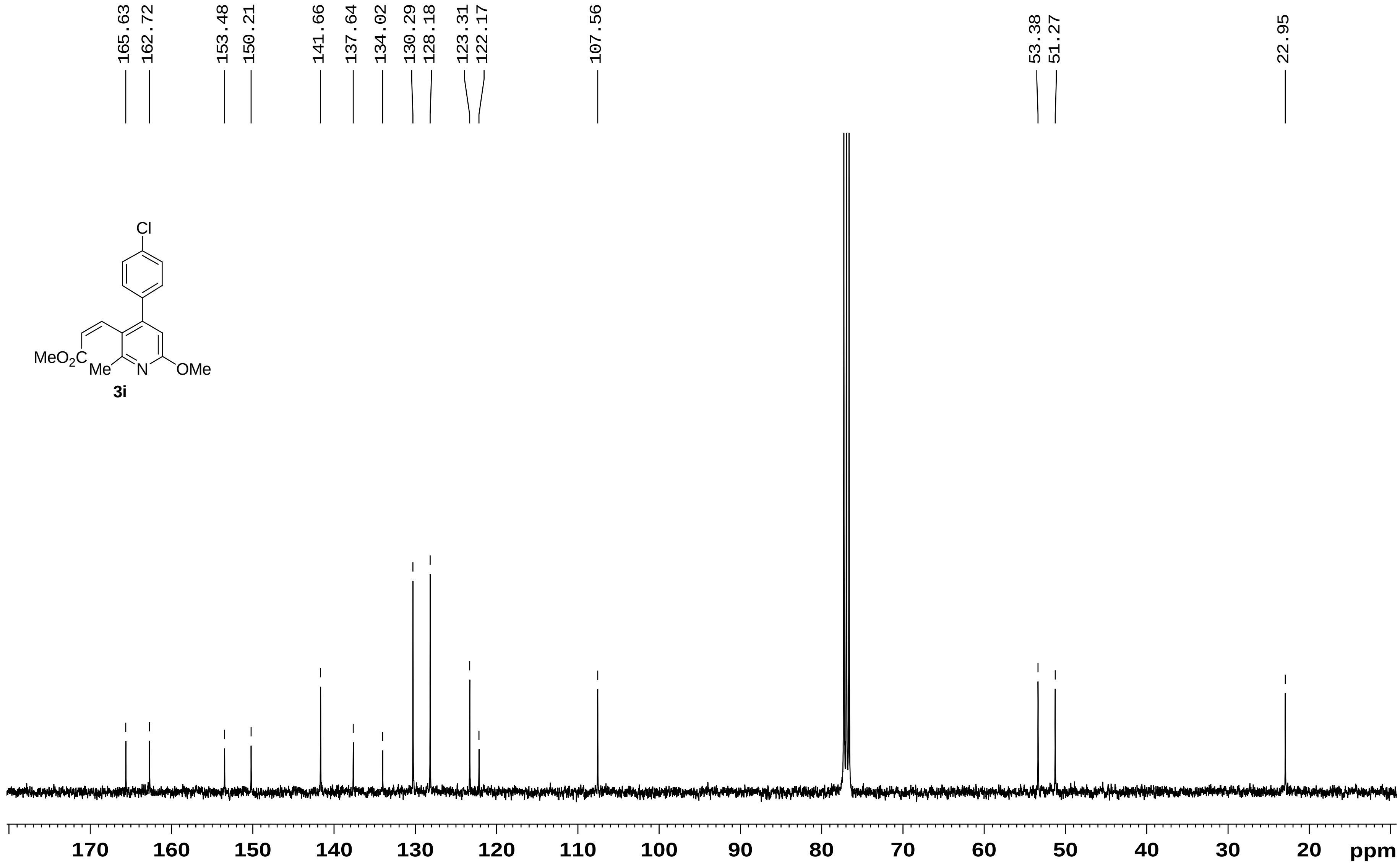
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22.95
Cl
MeO2C
Me
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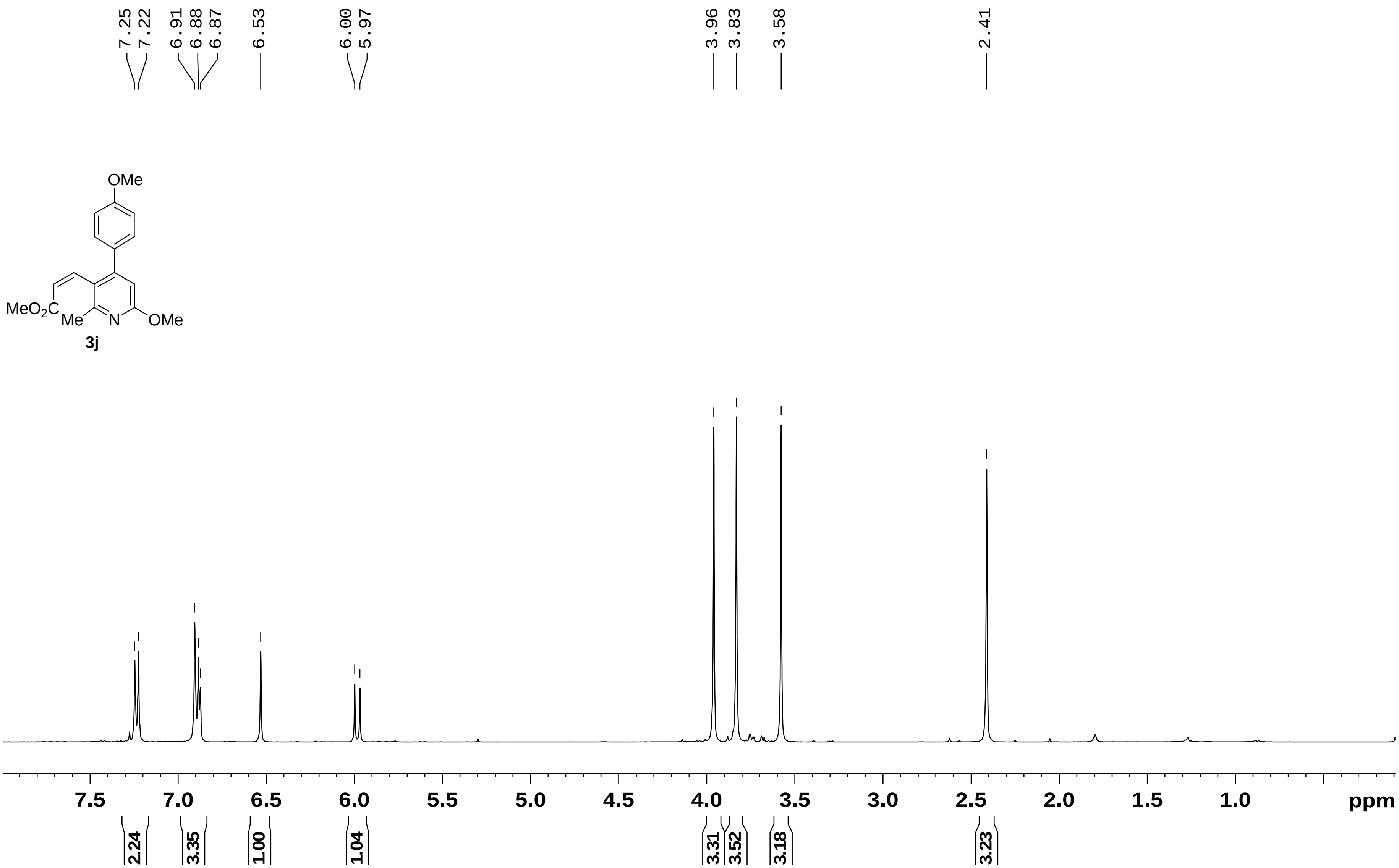
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OMe
MeO$_2$C
Me
N
OMe
3j
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6.0
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5.0
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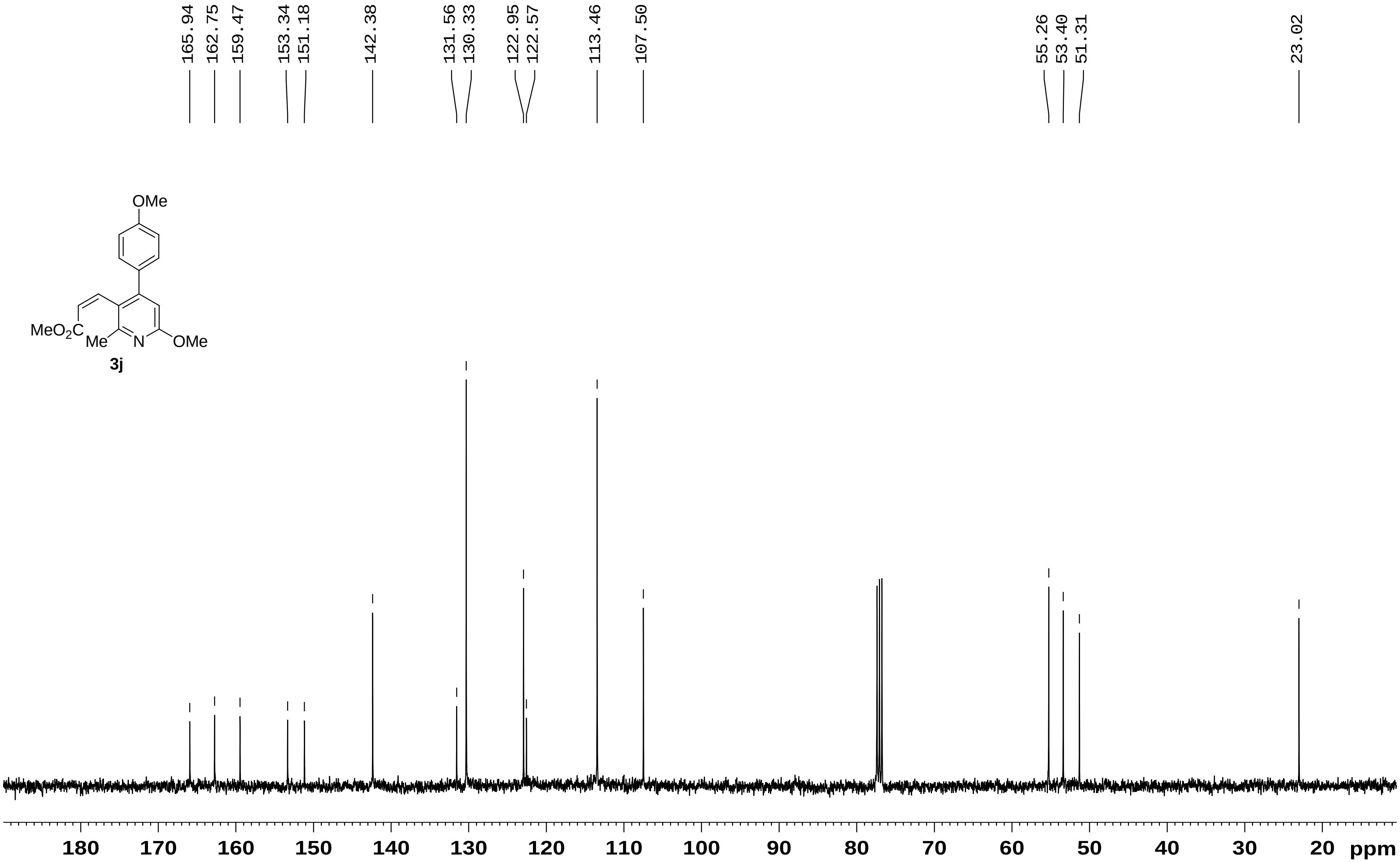
3.23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23.02
OMe
MeO2C
Me
N
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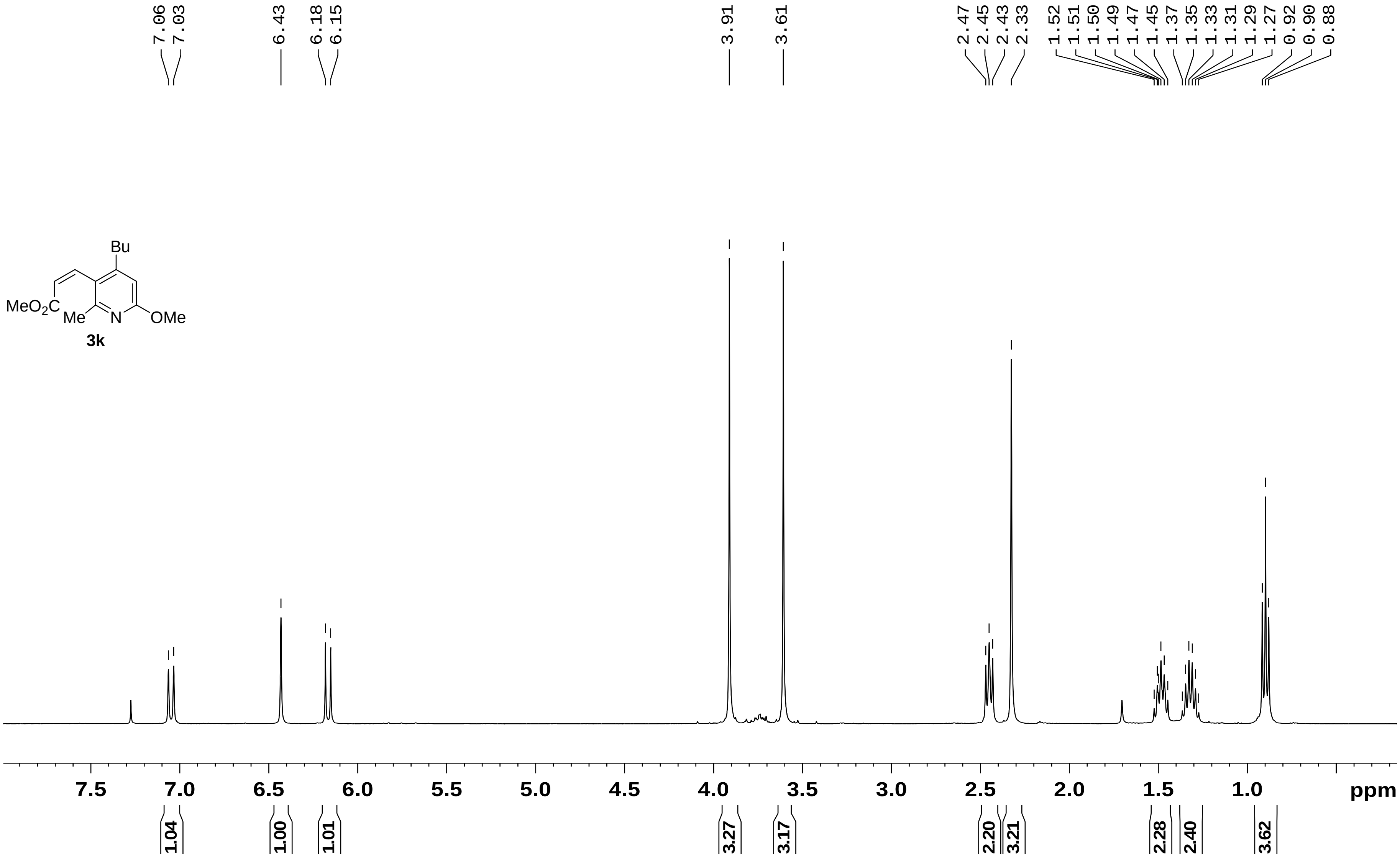
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0.88
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MeO2C
Me
N
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3k
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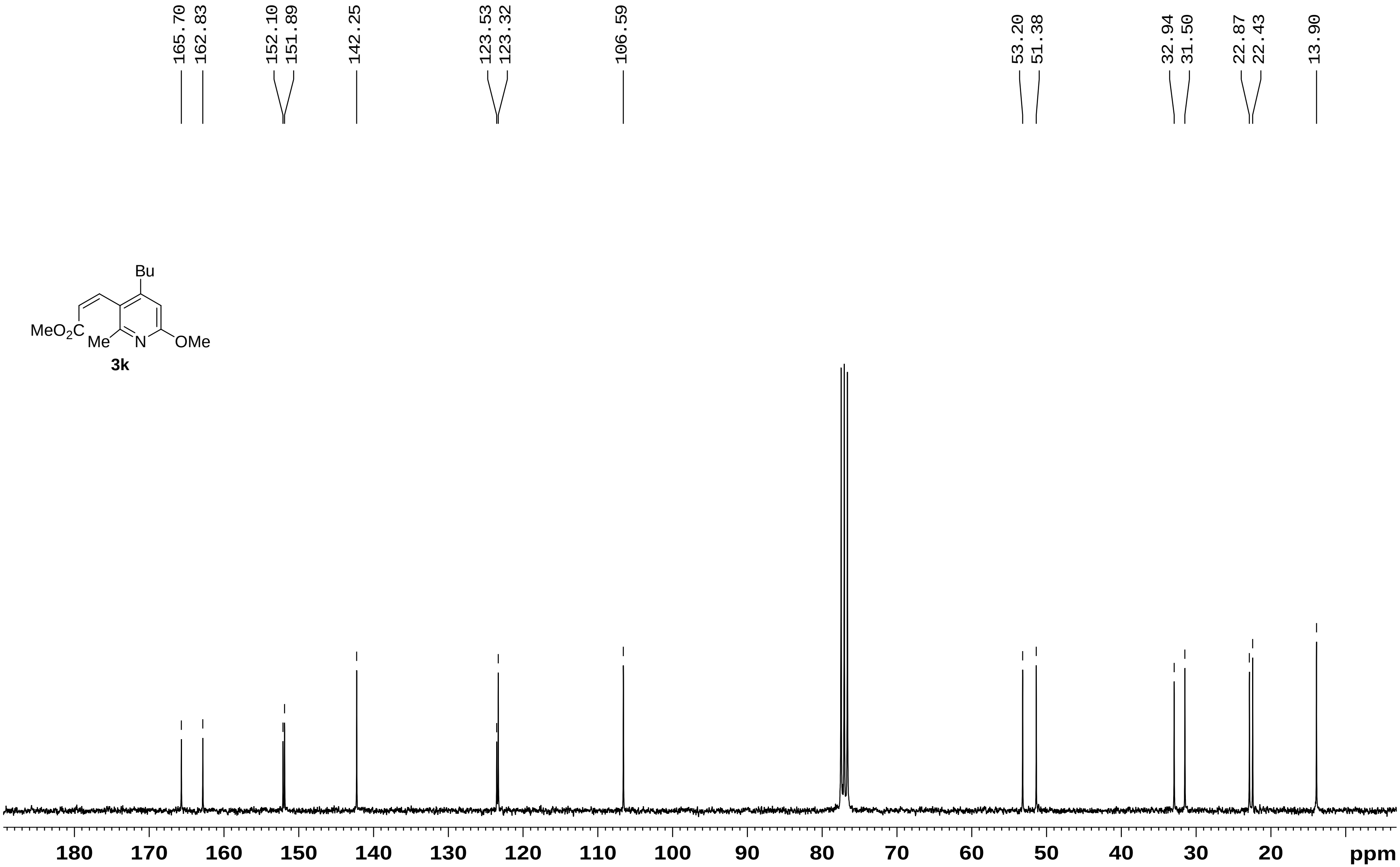
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Bu
MeO2C
Me
N
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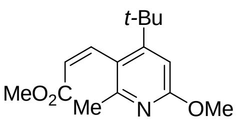
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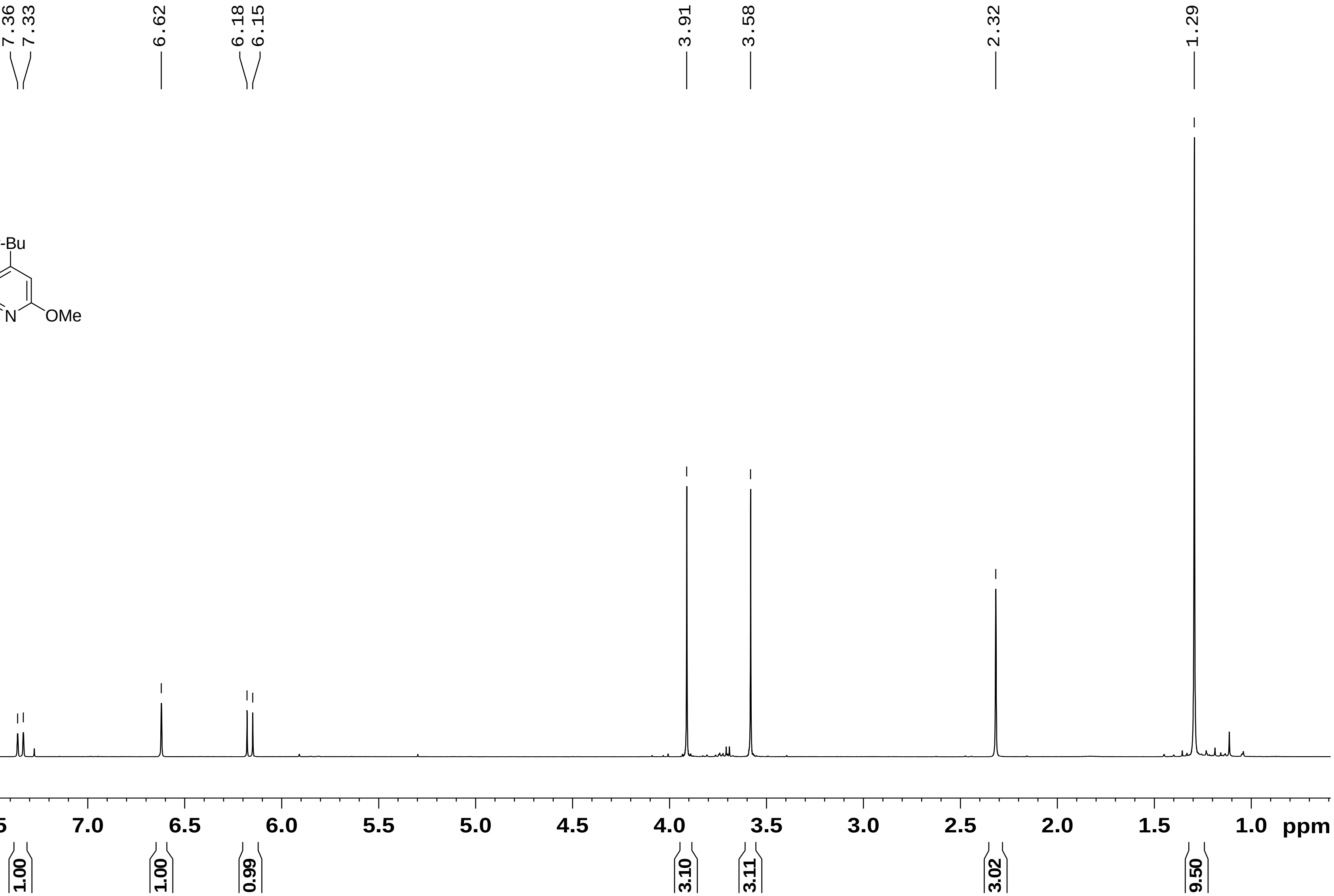
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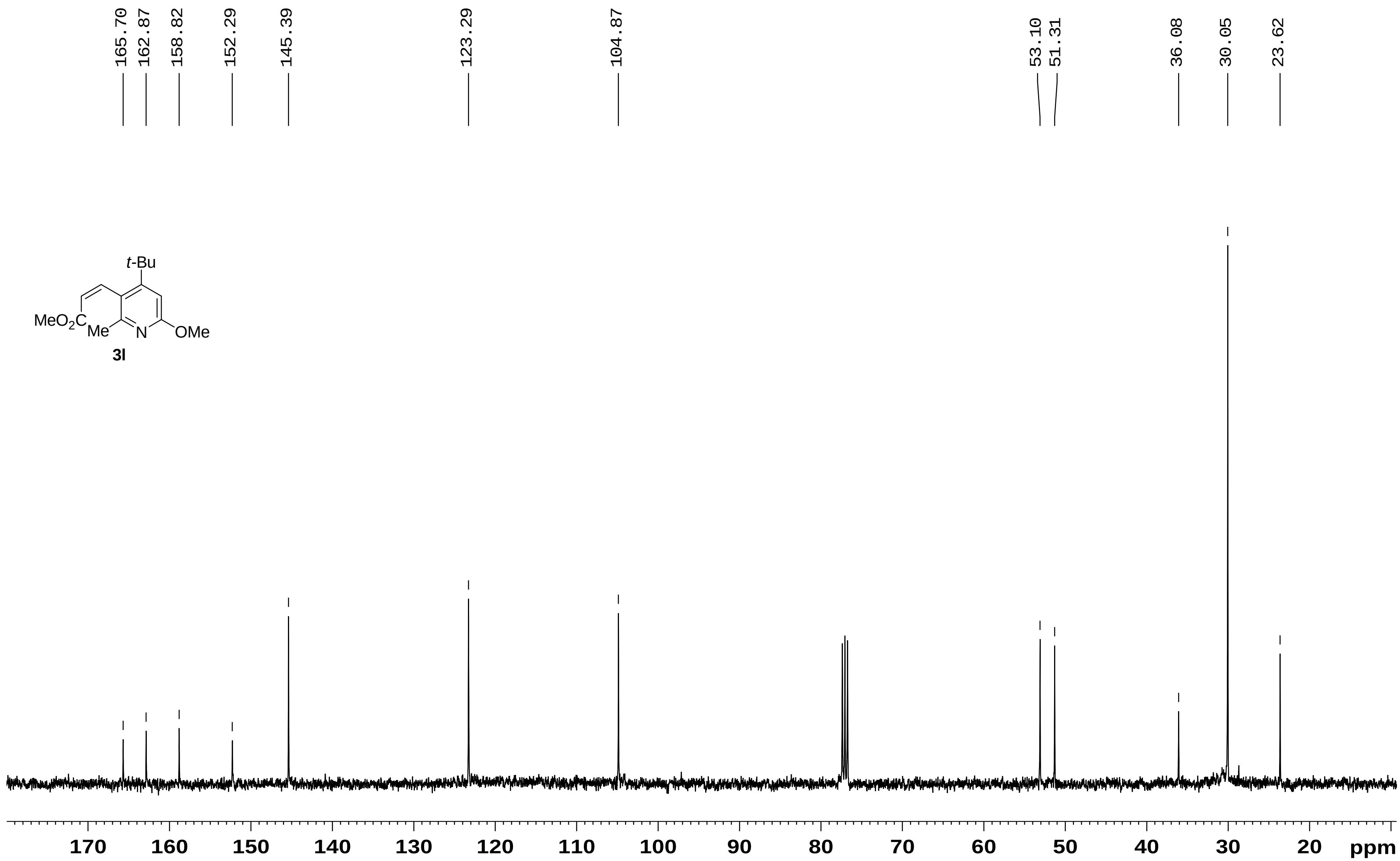
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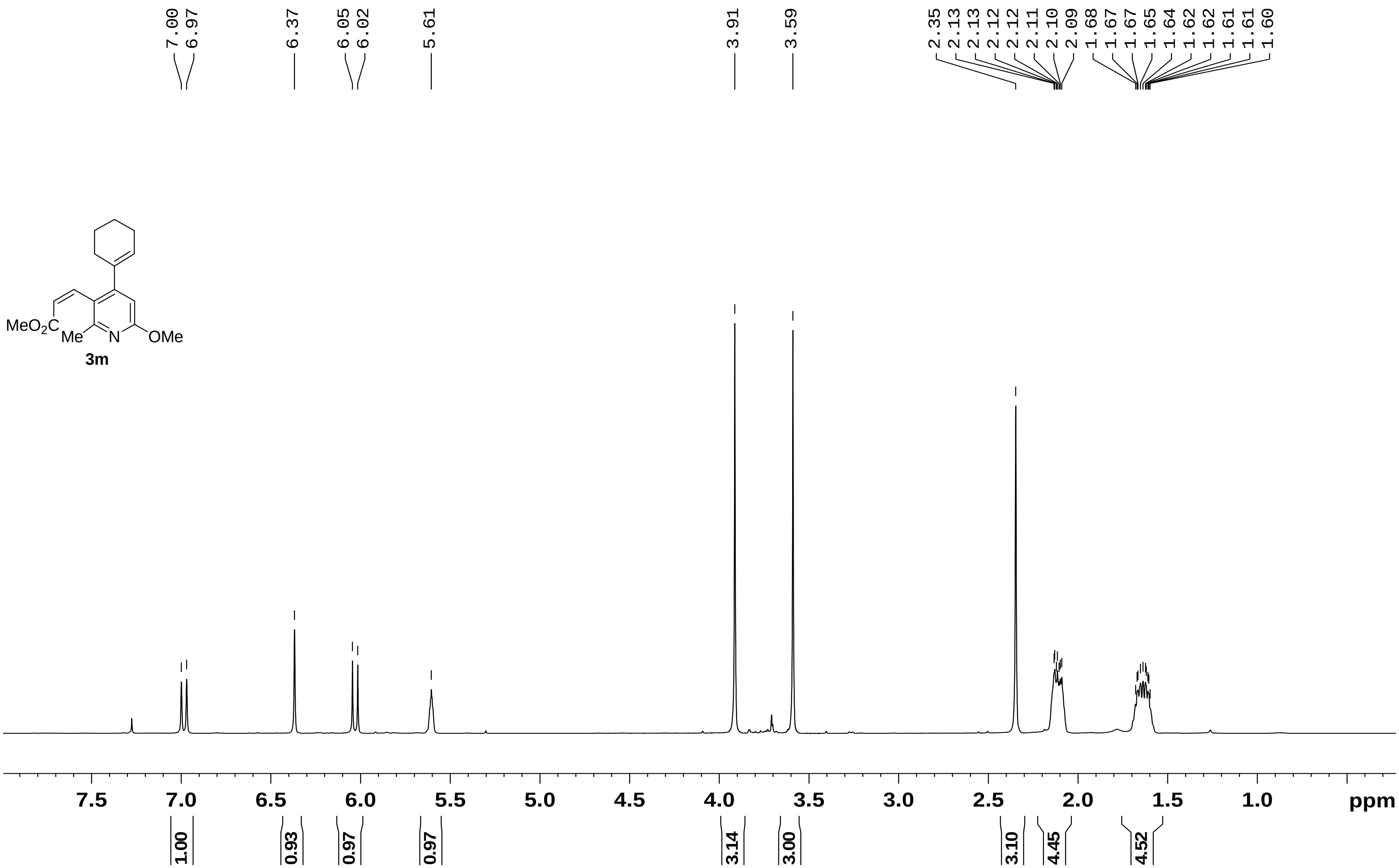
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Me
N
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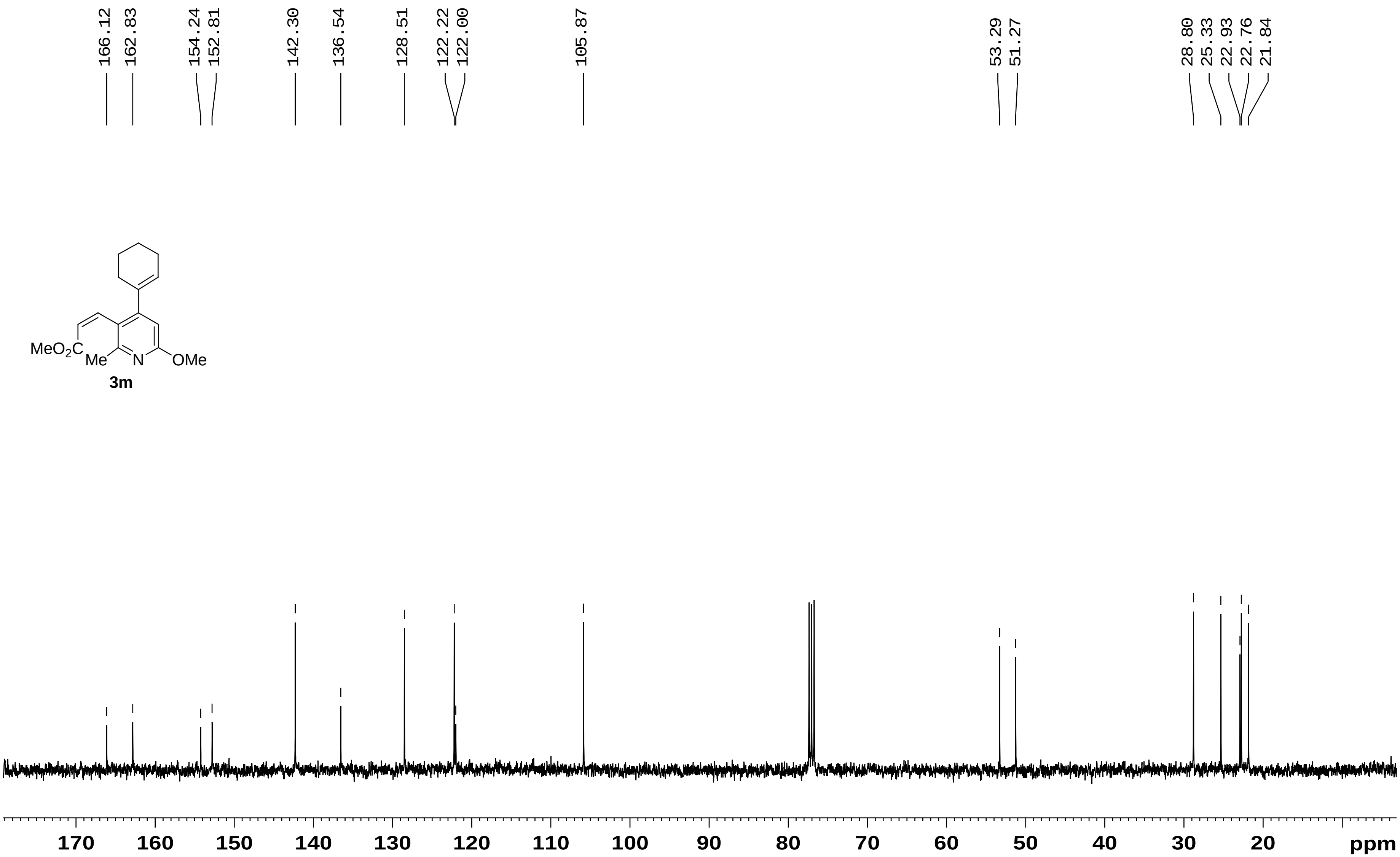
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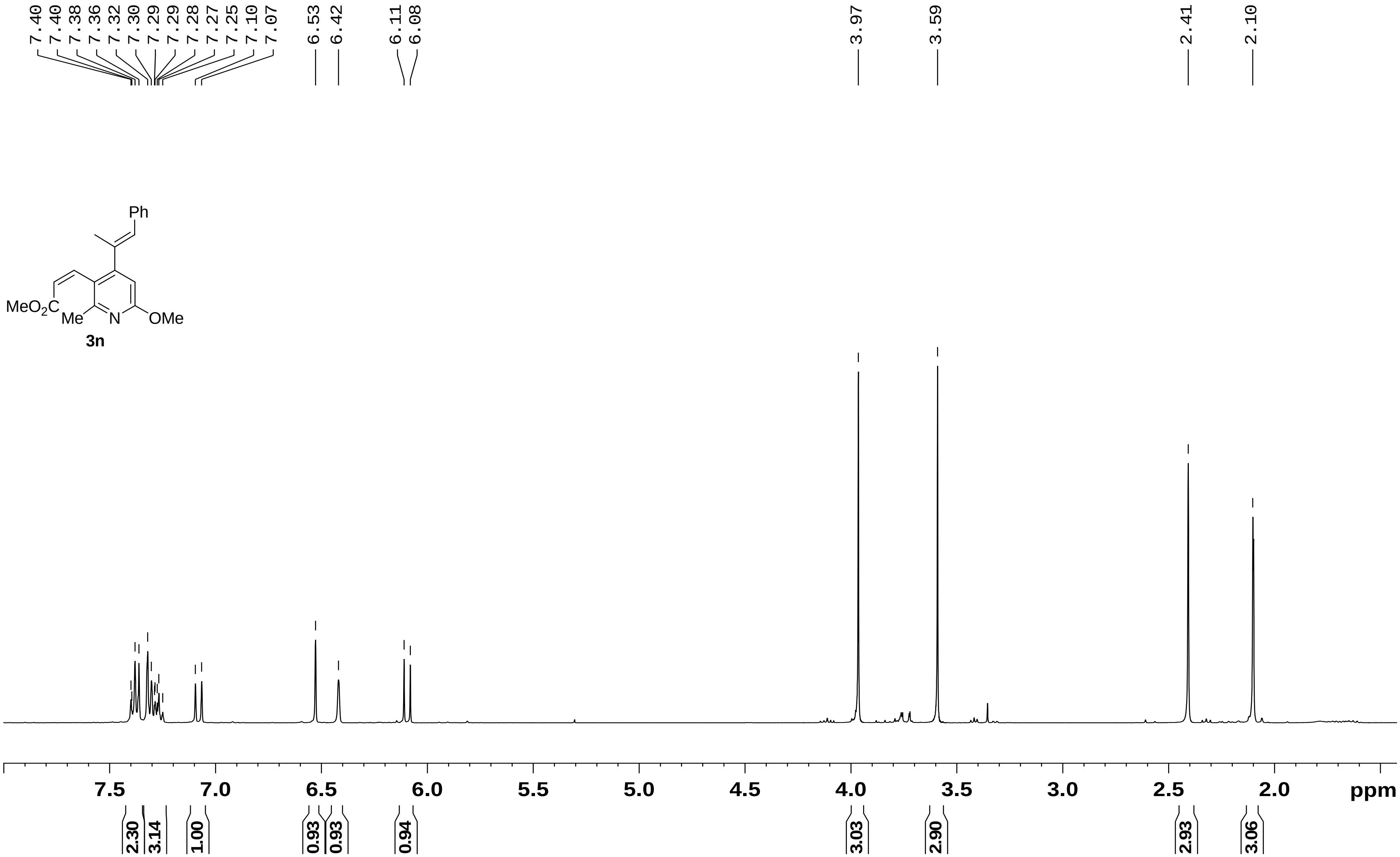
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6.08
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Ph
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Me
N
OMe
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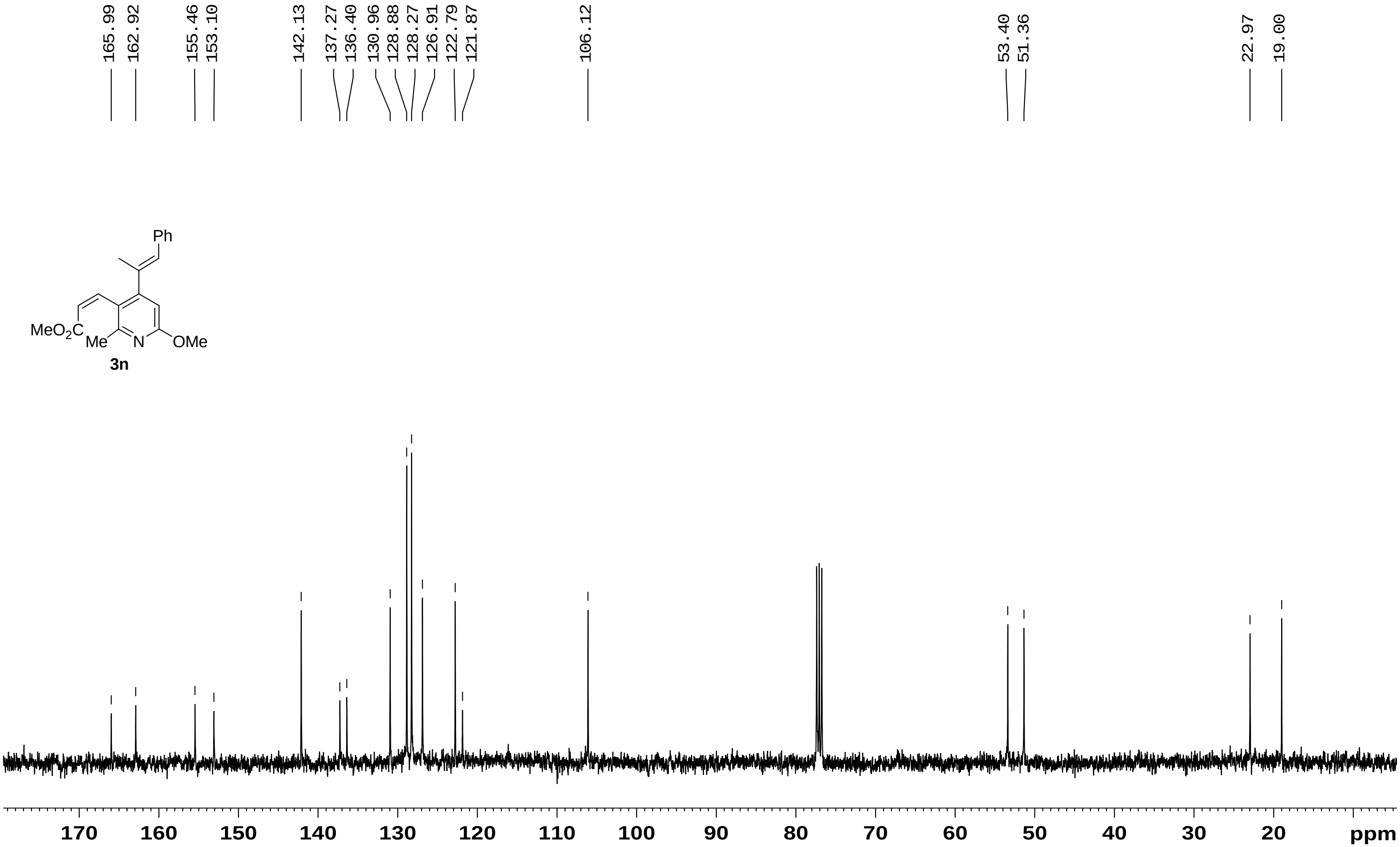
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22.97
19.00
Ph
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Me
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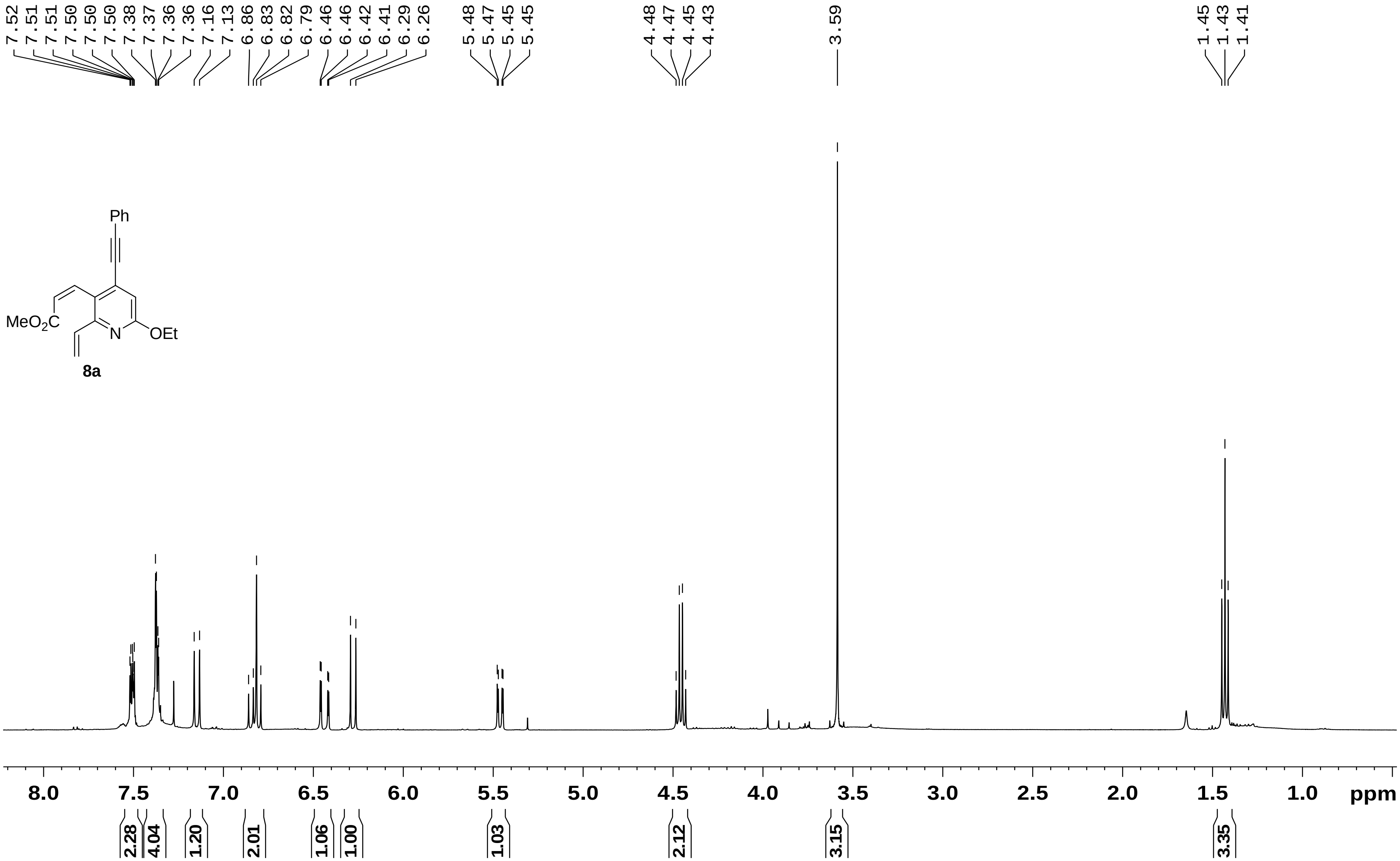
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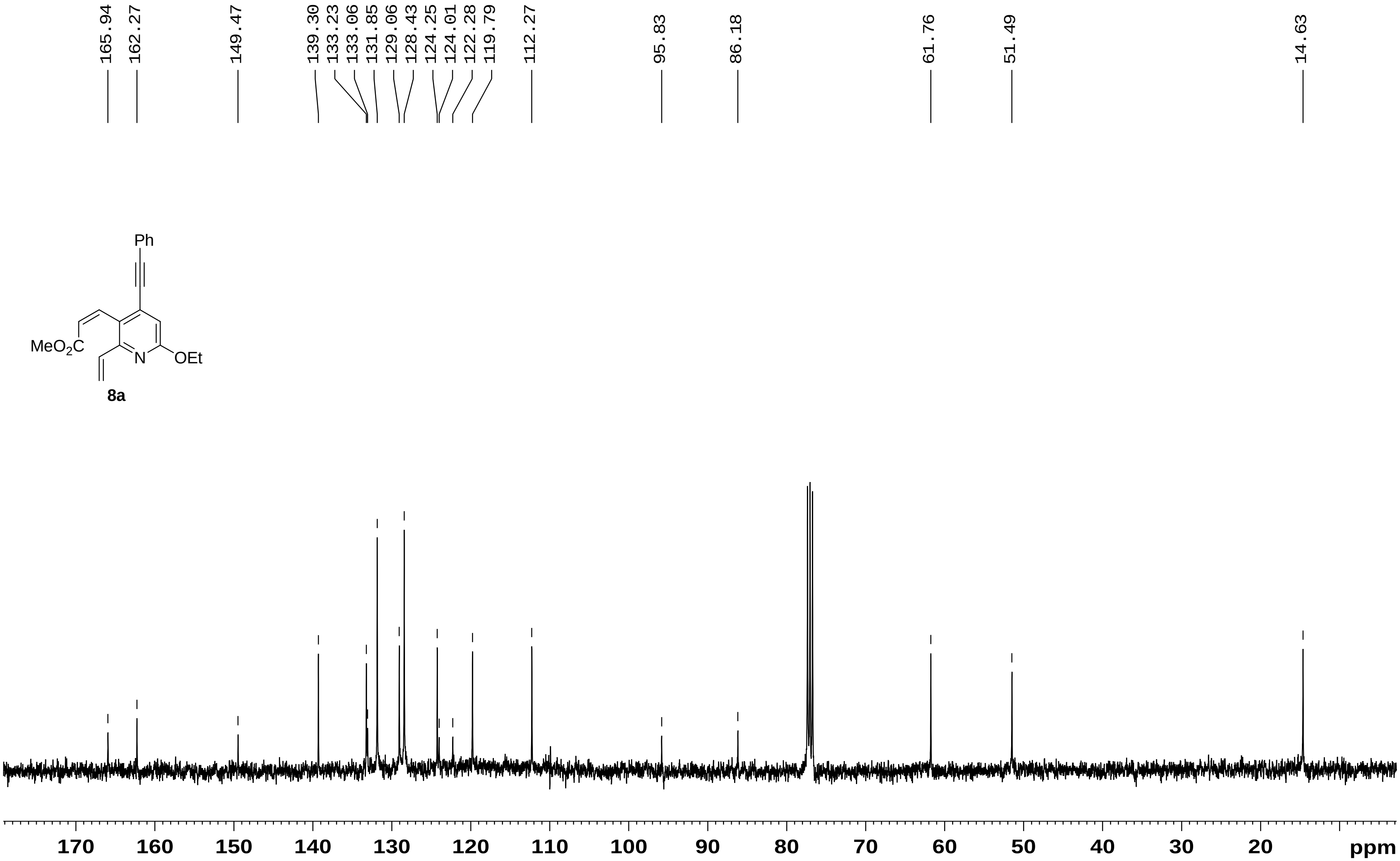
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86.18
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14.63
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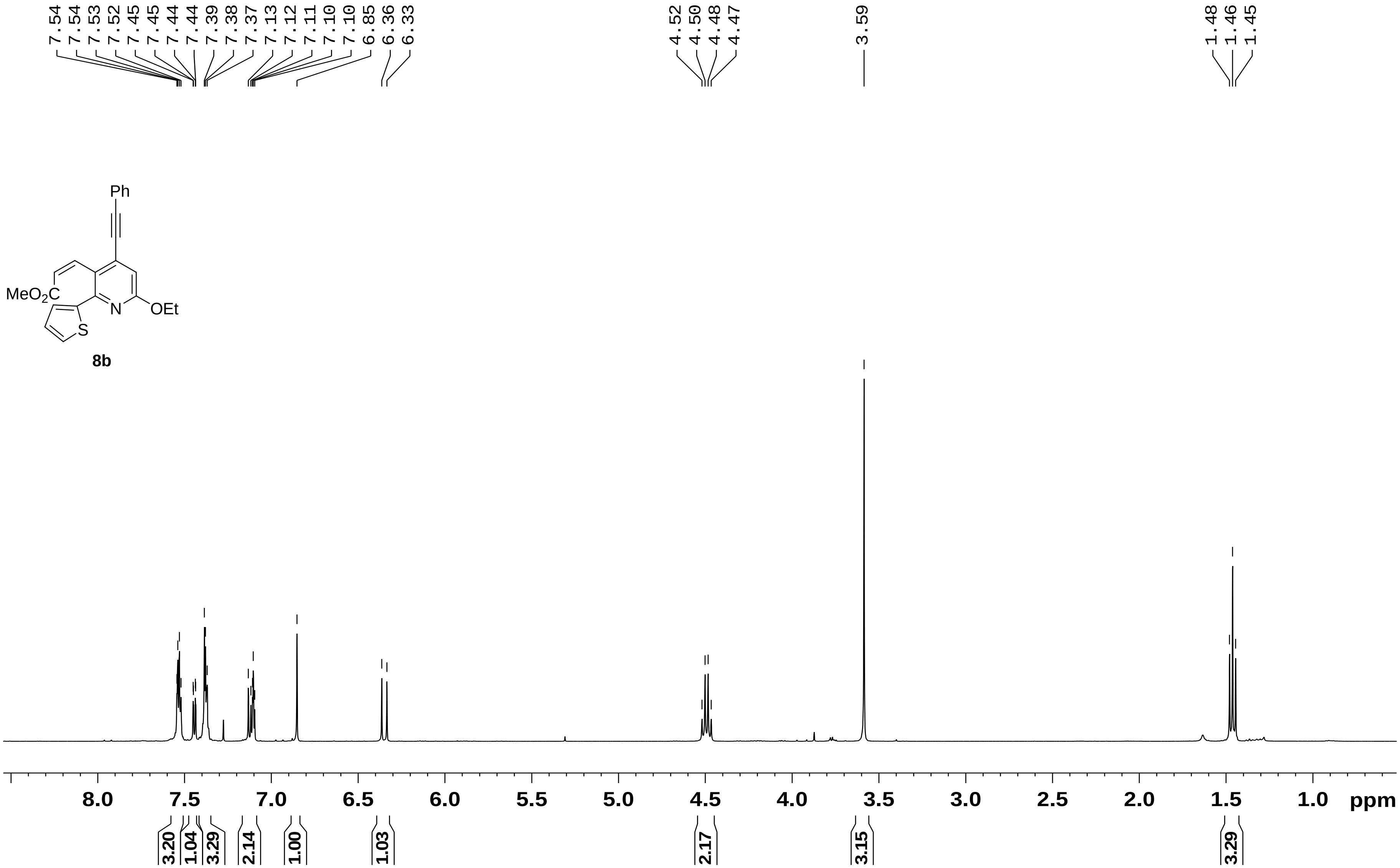
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7.11
7.10
7.10
6.85
6.36
6.33
4.52
4.50
4.48
4.47
3.59
1.48
1.46
1.45
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MeO2C
N
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S
8b
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6.5
6.0
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4.0
3.5
3.0
2.5
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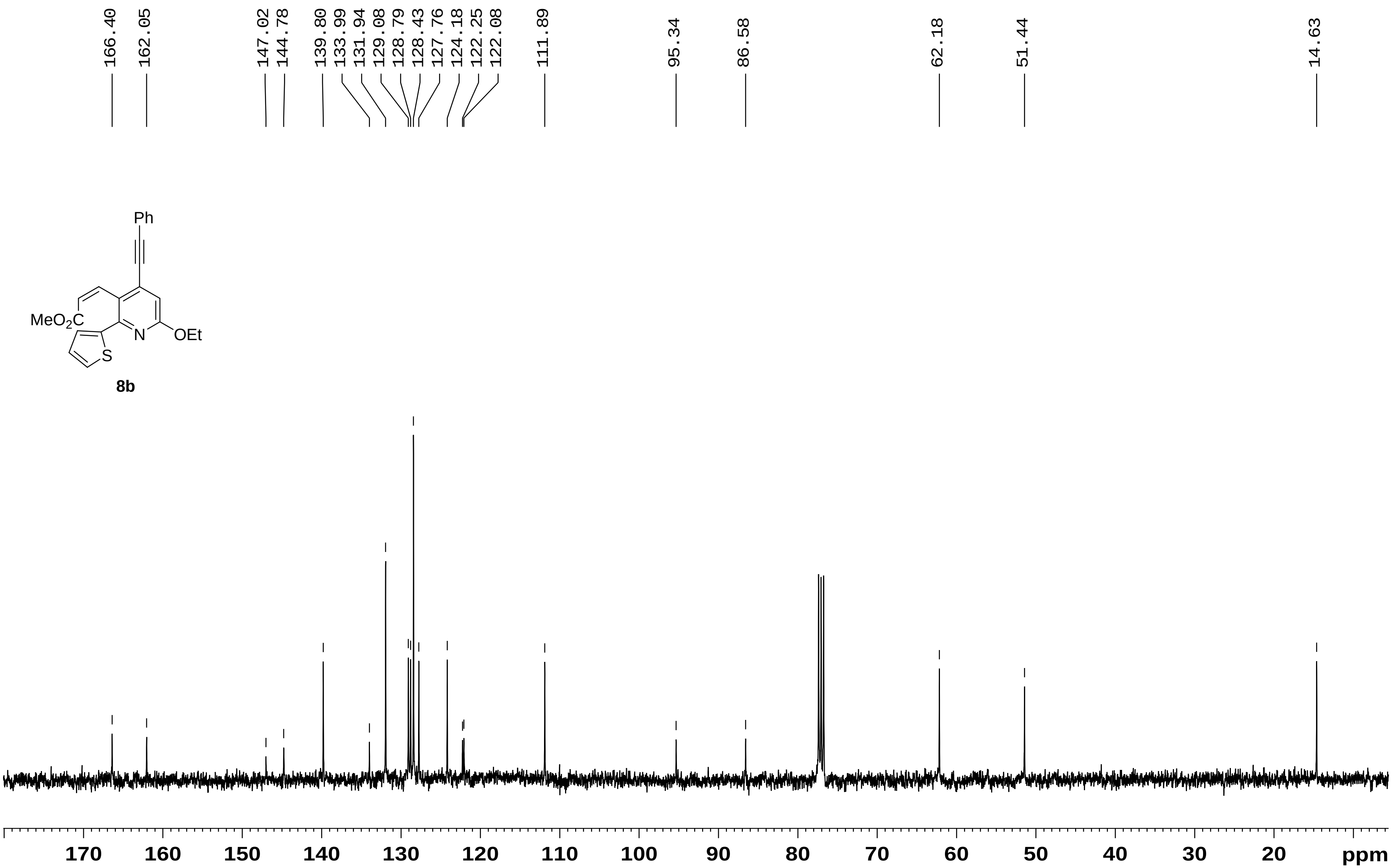
3.29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122.08
111.89
95.34
86.58
62.18
51.44
14.63
Ph
MeO2C
N
OEt
S
8b
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150
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120
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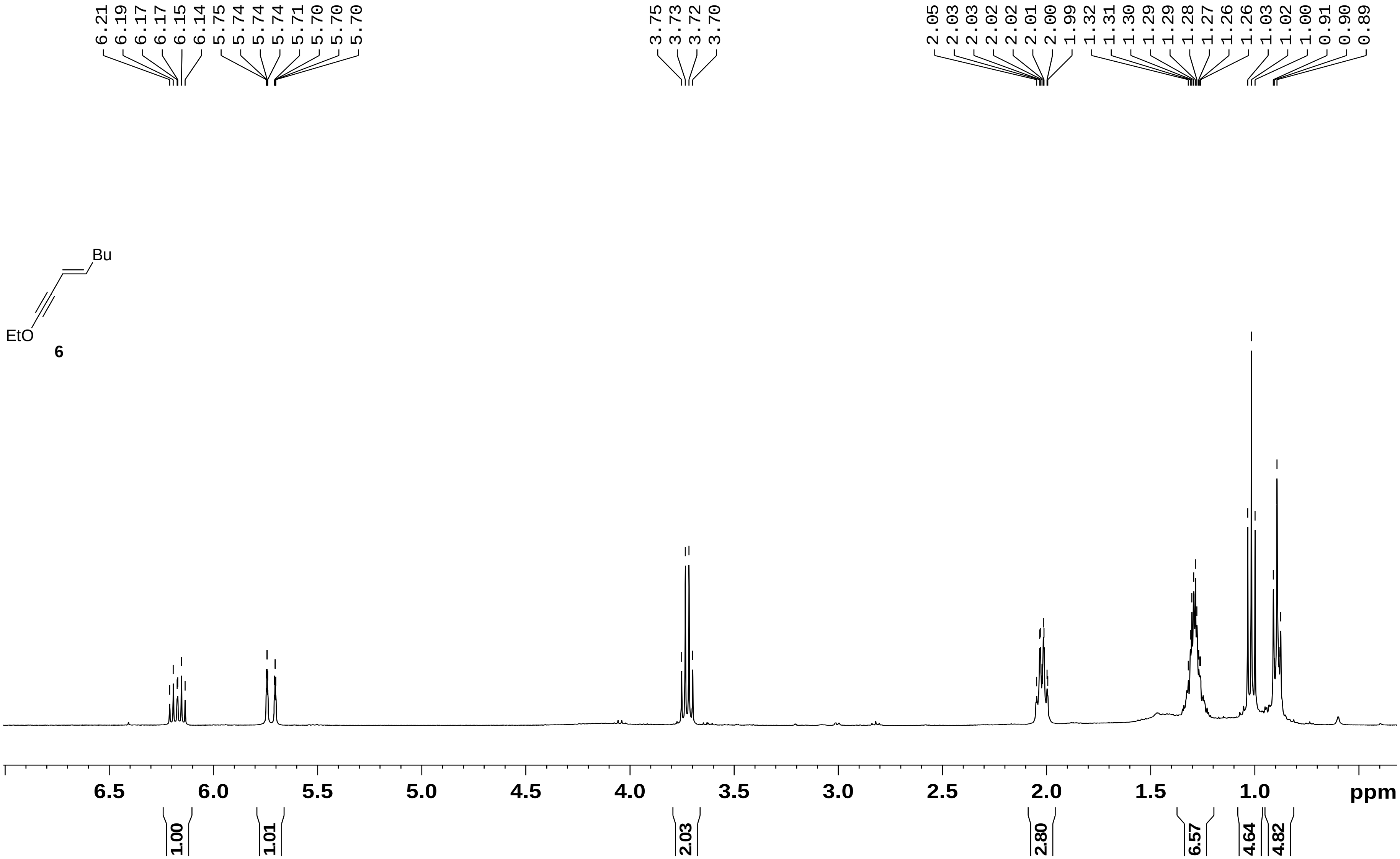
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3.75 3.73 3.72 3.70
2.05 2.03 2.03 2.02 2.02 2.01 2.00 1.99 1.32 1.31 1.30 1.29 1.29 1.28 1.27 1.26 1.26 1.03 1.02 1.00 0.91 0.90 0.89
Bu
EtO
6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 ppm
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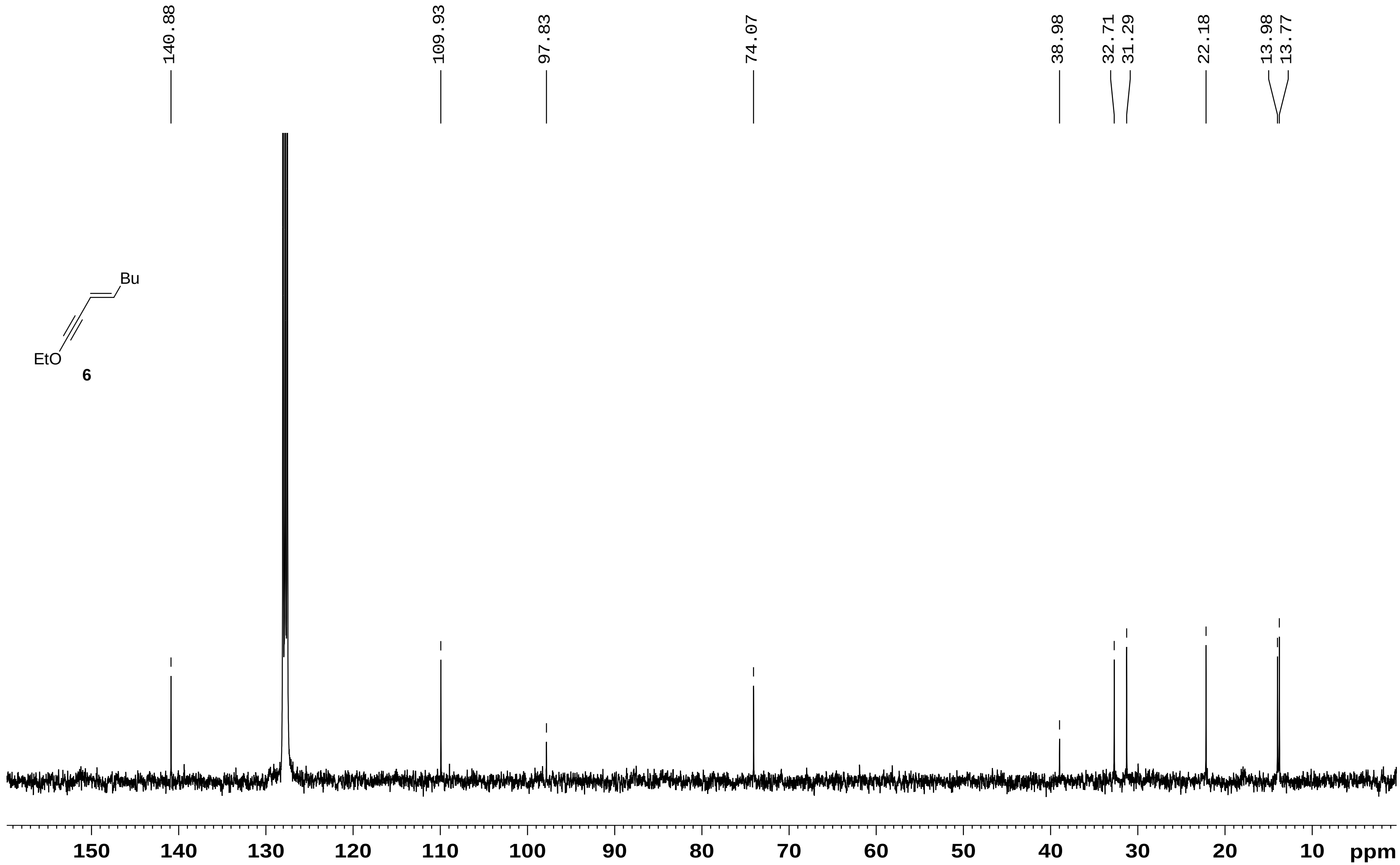
6



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97.83
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22.18
13.98
13.77
Bu
EtO
6
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm