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Reactions of 3,4-dihydroisoquinolines and dihydrothieno[3,2-*c*] pyridines with benzyne

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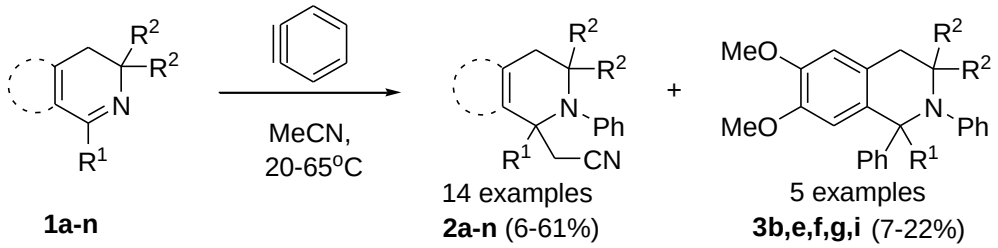
General. The aryne precursors were purchased from Sigma-Aldrich and TCI and were used without additional purification. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 (400 MHz for ^{1}H and 100.6 MHz for ^{13}C) and a JEOL JNM ECA (600 MHz and 150.9 MHz, respectively). Proton chemical shifts are reported relative to the residual solvent peak ($CDCl_3$ at δ 7.26 ppm). Carbon chemical shifts are reported relative to $CDCl_3$ at δ 77.2 ppm. Mass spectra were recorded using LCMS-8040 Shimadzu (Japan), ESI. IR spectra were recorded on FT spectrometer Infralum FT-801. For the elemental analyses, a Carlo Erba 1106 was used. Melting points were measured on SMP 10 in open capillaries. TLC on Sorbfil plates was used for the monitoring of reactions. Kieselgel from Macherey-Nagel GmbH&Co (0.04–0.06 mm/230–400 mesh), 60 Å, was used for column chromatography. All solvents were dried according to standard procedures.

1-R-6,7-dimethoxy-dihydroisoquinolines were obtained by the Bischler–Napieralsky method. In a three-necked flask were placed 2-(3,4-dimethoxyphenyl)ethylamine (14.0 g, 0.077 mol), pyridine (12.18 g, 0.154 mol), and PhMe (30 ml). The corresponding acid chloride (0.077 mol) was added dropwise. The reaction course was TLC-monitored (Alugram, EtOAc). The solvent was removed under reduced pressure; the resulting powder was used in the next step as obtained. To a flask containing $POCl_3$ (50 ml), the crude amide from the previous step (0.077 mol) was added. The mixture was heated to 50 °C for 1-2 days (TLC monitoring, Alugram, EtOH). The reaction mixture was poured into ice bath, pH was brought to 9 with ammonium carbonate, and the mixture was extracted with $CHCl_3$ (3×50ml). The organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure. The obtained powder was recrystallized from EtOAc/hexane mixture.
Spectral data f **1a** [1], **1b** [2], **1c** [2], **1d** [3], **1e** [4], **1f** [5], **1g** [6], **1h** [4], **1i** [4], **1j** [2], **1k** [7], **1m** [8] are close to the literature.

6,7-Dimethoxy-1'-methyl-4'*H*-spiro[cyclohexane-1,3'-isoquinoline] (1l). A mixture of 1,2-dimethoxybenzene (1.38 g, 10 mmol), cyclohexanecarbaldehyde (1.12 g, 10 mmol), and ethyl cyanoacetate (1.13 g, 10 mmol) was added dropwise to concentrated sulfuric acid (30 ml) at such a speed that the temperature did not exceed 30 °C. The mixture was stirred for 1 h and then was poured into water (300 ml) and extracted with toluene (2×50 ml). The water layer was heated for 1-2 h until CO_2 evolution stopped. The mixture was cooled to room temperature, ammonium carbonate was added (pH 8-9), and the mixture extracted with CH_2Cl_2 (3×50ml), the organic layer was dried over $MgSO_4$. The solvent was removed under reduced pressure, the residue was crystalized in EtOAc to afford yellow powder, yield 1.58 g (58%). ^{1}H NMR (400 MHz, $CDCl_3$), δ ppm, *J* (Hz): 1.35-1.58 (m, 10 H, H-cyclohexane), 2.36 (s, 3H, 1-CH_3), 2.64 (s, 2H, 4-CH_2),

3.87 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 6.58 (s, 1H, Ar), 6.93 (s, 1H, Ar). IR spectrum, υ, cm^{-1}: 1620, 1595, 1570, 1510, 1345, 1290, 1265, 1225, 1205, 1150, 1060, 980, 965, 835. *m/z* (*I*rel, %): 273[M]+(50), 258 [M-CH_3](17), 244 [M-2CH_3+H], 230 [M-3CH_3] (100), 217 [M-2CH_3-(CH_3-C)](21). [Found, %: C 74.47, H 8.60, N 5.70. $C_{17}H_{23}NO_2$. Calc,%: C 74.69, H 8.48, N 5.12].

1-Cyanomethyldihydroisoquinolines and 5-cyanomethyl dihydrothieno[3,2-*c*]pyridines (general procedure).

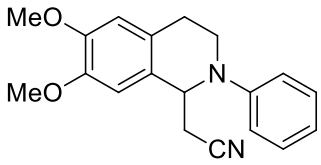


1a-n

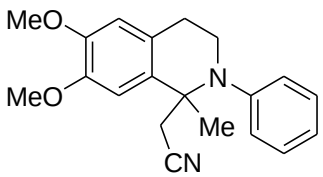
14 examples
2a-n (6-61%)

5 examples
3b,e,f,g,i (7-22%)

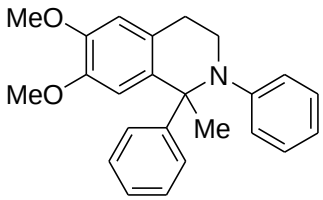
To a suspension of CsF (3 equiv.) in dry acetonitrile 2-(trimethylsilyl)phenyl trifluoromethanesulfonate (1.2 equiv.) was added and then corresponding dihydroisoquinoline or dihydrothieno[3,2-*c*]pyridine **1** (1 equiv.) was added. The reaction mixture was stirred at 65 °C (except otherwise mentioned, see Table 2 in the article) with TLC monitoring (Sorbfil, EtOAc – hexane, 1:3). The solvent was removed under the reduced pressure. To the obtained crude oil chloroform (5 ml) was added, and the precipitate of CsOTf was filtered off and washed several times with $CHCl_3$. The filtrate was concentrated, the residue was purified on SiO_2 (glass column, H=150 mm, d=20 mm), eluent gradient of EtOAc – hexane 1:30 to 1:5.



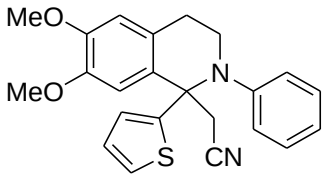
2-(6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (1a). White powder. Yield 58% (0.093 g). MP 142-145°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.74 (dd, 1H, *J* = 16.9, 5.1, C$\underline{H_2}$CN), 2.83 (dt, 1H, *J* = 16.0, 4.5, 4-CH_2), 2.89 (dd, 1H, *J* = 16.9, 5.1, C$\underline{H_2}$CN), 2.96-3.03 (m, 1H, 4-CH_2), 3.51-3.55 (m, 1H, 3-CH_2), 3.59-3.65 (m, 1H, 3-CH_2), 3.89 (s, 3H, OCH_3), 3.91 (c, 3H, OCH_3), 5.02 (t, *J* = 6.2, 1H, H-1), 6.68 (c, 1H, H-5), 6.82 (s, 1H, H-8), 6.90 (t, *J* = 7.3, 1H, Ar), 6.98 (d, *J* = 8.1, 2H, Ar), 7.32 (t, *J* = 7.3, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 22.8, 28.2, 48.4, 55.7 (2C), 59.5, 110.1, 110.5, 118.3, 118.8 (2C), 122.2, 125.5, 126.6, 129.2 (2C), 147.2 (2C), 149.8. IR spectrum, υ, cm^{-1}: 2941, 2855 (OCH_3), 2243 (CN). ESI MS $[M+H]^+$ 309. [Found, %: C, 74.12; H, 6.62; N, 9.03. $C_{19}H_{20}N_2O_2$. Calc., %: C, 73.95; H, 6.49; N, 9.12].



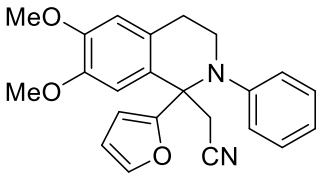
2-(6,7-Dimethoxy-1-methyl-2-phenyl-1,2,3,4-tetrahydro-isoquinolin-1-yl)acetonitrile (2b). Yellow powder. Yield 41% (0.128 g). MP 145-147°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 1.47 (s, 3H, CH_3), 2.79 (s, 2H, C$\underline{H_2}$CN), 2.83 (t, 1H, 4-CH_2), 2.94-3.04 (m, 1H, 4-CH_2), 3.39-3.45 (m, 2H, 3-CH_2), 3.89 (s, 6H, OCH_3), 6.63 (s, 1H, H-5), 6.77 (s, 1H, H-8), 7.21 (t, 1H, *J* = 7.2, Ar), 7.25 (br.s., 2H, Ar), 7.31-7.39 (m, 2H, Ar). NMR^{13}C (150 MHz, $CDCl_3$), δ ppm: 25.5, 29.9, 31.2, 47.0, 55.9, 56.3, 59.8, 109.3, 111.7, 118.5, 125.8, 128.3, 128.8 (2C), 128.8 (2C), 131.7, 147.6, 148.2, 148.8. IR spectrum, υ, cm^{-1}: 2935, 2910 (OCH_3), 2251 (CN). ESI MS $[M+H]^+$ 323. [Found, %: C, 74.36; H, 6.98; N, 8.65. $C_{20}H_{22}N_2O_2$. Calc., %: C, 74.47; H, 6.84; N, 8.72].



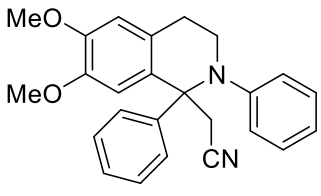
6,7-Dimethoxy-1-methyl-1,2-diphenyl-1,2,3,4-tetrahydro-isoquinoline (3b). Green oil. Yield 7% (0.025 g). R_f 0.5 (EtOAc-hexane, 1:10). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.38 (s, 3H, CH_3), 3.11-3.13 (m, 2H, 4-CH_2), 3.70 (s, 3H, OCH_3), 3.82 (s, 3H, OCH_3), 4.02-4.05 (m, 2H, 3-CH_2), 6.62 (s, 1H, H-5), 6.83 (s, 1H, H-8), 6.91 (t, 2H, *J* = 7.2, Ar), 6.95 (d, 2H, *J* = 7.6, Ar), 7.18 (t, 2H, *J*=7.2, Ar), 7.21 (t, 3H, Ar), 7.36 (t, 1H, *J* = 7.2, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 20.6, 32.1, 53.7, 56.1, 56.2, 114.4, 114.6, 121.1 (2C), 121.2 (2C), 125.5, 129.3 (2C), 129.9, 130.9, 131.4, 134.8, 137.8, 139.5, 146.7, 148.0, 151.5, 199.4. IR spectrum, *v*, cm^{-1}: 2930, 2847 (OCH_3). ESI MS $[M+H_2O]^+$ 377. [Found, %: C, 80.31; H, 6.78; N, 3.98. $C_{24}H_{25}NO_2$. Calc., %: C, 80.15; H, 6.98; N, 3.93].



(6,7-Dimethoxy-2-phenyl-1-(2-thiophene)-1,2,3,4-tetrahydro-isoquinolin-1-yl)acetonitrile (2c). Yellow powder. Yield 45% (0.128 g). MP 152-154°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.77-2.86 (m, 1H, 4-CH_2), 3.18 (d, 1H, *J* = 16.5, C$\underline{H}_2$CN), 3.21-3.29 (m, 2H, 3-CH_2), 3.44 (d, 1H, *J*=16.5, C$\underline{H}_2$CN), 3.60-3.68 (m, 1H, 4-CH_2), 3.74 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.35-6.38 (m, 1H, Ar), 6.52 (s, 1H, H-5), 6.68 (s, 1H, H-8), 6.82 (d, 3H, *J* = 7.6, Ar), 7.12 - 7.16 (m, 1H, Ar), 7.21 (t, 3H, *J* = 6.9, Ar). NMR ^{13}C (150 MHz, $CDCl_3$) δ ppm: 30.2, 31.9, 47.1, 55.9, 56.3, 64.1, 111.0, 111.3, 117.8, 125.6, 125.7, 125.8, 126.0, 128.0 (2C), 128.6 (2C), 129.1, 130.3, 147.2, 147.7, 148.4, 148.7. IR spectrum, *v*, cm^{-1}: 2930, 2826 (OCH_3), 2254 (CN). ESI MS $[M+H]^+$ 391. [Found, %: C, 70.63; H, 5.81; N, 7.15. $C_{23}H_{22}N_2O_2S$. Calc., %: C, 70.70; H, 5.64; N, 7.20].

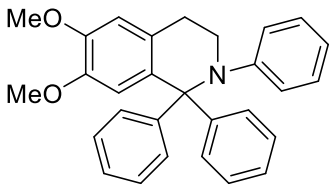


(6,7-Dimethoxy-2-phenyl-1-(2-furyl)-1,2,3,4-tetrahydro-isoquinoline-1-yl)acetonitrile (2d). White powder. Yield 49% (0.285 g). MP 190-192°C (EtOAc-hexane). NMR^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.79-2.87 (m, 2H, 4-CH_2), 3.05 (d, 1H, *J* = 16.5, C$\underline{H}_2$CN), 3.20-3.29 (m, 2H, 3-CH_2), 3.33 (d, 1H, *J* = 16.5, C$\underline{H}_2$CN), 3.74 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 5.93 (d, 1H, *J* = 2.8, Fur), 6.26-6.31 (m, 1H, Fur), 6.45 (s, 1H, H-5), 6.70 (s, 1H, H-8), 6.82 (d, 2H, *J* = 7.6, Ar), 7.13 - 7.18 (m, 1H, Ar), 7.22 (2H, t, *J* = 7.6, Ar), 7.25 (c, 1H, Fur). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 29.3, 30.3, 47.4, 55.9, 56.2, 62.8, 109.2, 110.3, 110.4, 111.2, 117.8, 124.3, 125.9, 127.5, 127.9, 128.6, 129.3, 130.1, 130.3, 130.4, 141.8, 148.5, 148.7. IR spectrum, *v*, cm^{-1}: 2934, 2833 (OCH_3), 2251 (CN). ESI MS $[M+H]^+$ 375. [Found, %: C, 73.81; H, 5.94; N, 7.48. $C_{23}H_{22}N_2O_3$. Calc., %: C, 73.74; H, 5.88; N, 7.52].

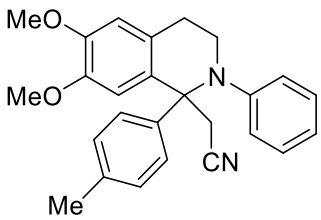


2-(6,7-Dimethoxy-1,2-diphenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2e). White powder. Yield 55% (0.157 g). MP 166-168°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.95 (d, *J* = 15.7, 1H, 4-CH_2), 3.15 (d, *J* = 16.5, 1H, C$\underline{H}_2$CN), 3.18-3.25 (m, 1H, 4-CH_2), 3.36-3.42 (m, 2H, 3-CH_2), 3.49 (d, *J* = 16.5, 1H, C$\underline{H}_2$CN), 3.68 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.38 (s, 1H, H-5), 6.67 (d, *J*=7.4, 2H, Ar), 6.71 (s, 1H, H-8), 6.90 (d, *J* = 7.4, 2H, Ar), 7.09 (d, *J* = 6.6, 1H, Ar), 7.11-7.16 (m, 2H, Ar), 7.18-7.23 (m, 2H, Ar), 7.23-7.28 (m, 1H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 29.1,

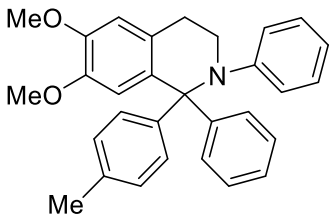
30.1, 46.9, 55.9, 56.2, 66.0, 111.0, 111.2, 118.6, 125.3, 127.6 (2C), 127.8, 127.9 (2C), 128.1, 128.5 (2C), 128.9 (2C), 130.8, 142.7, 147.7, 148.3, 148.4. IR spectrum, *ν*, cm^{-1}: 2957, 2824 (OCH_3), 2248 (CN). ESI MS $[M+H]^+$ 385. [Found, %: C, 77.93; H, 6.31; N, 7.27. $C_{25}H_{24}N_2O_2$. Calc., %: C, 78.06; H, 6.25; N, 7.32].



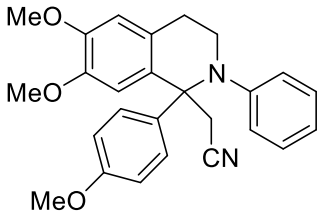
6,7-Dimethoxy-1,1,2-triphenyl-1,2,3,4-tetrahydroisoquinoline (3e). Yellow powder. Yield 13% (0.040 g). MP 88-90°C (EtOAc-hexane). NMR ^1H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 3.01 (t, *J* = 7.4, 2H, 4-CH_2), 3.81 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 3.99 (t, *J* = 7.4, 2H, 3-CH_2), 6.71 (s, 1H, H-5), 6.89 (s, 1H, H-8), 6.92-6.98 (m, 6H, Ar), 7.23 (t, *J* = 7.8, 3H, Ar), 7.46 (t, *J* = 7.8, 2H, Ar), 7.59 (t, *J* = 7.0, 2H, Ar), 7.78 (d, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 29.8, 31.5, 54.3, 56.1, 56.2, 112.9, 114.0, 118.9 (2C), 121.1 (2C), 121.6 (2C), 128.5 (2C), 129.4 (2C), 130.3 (2C), 130.7, 133.0, 133.1 (2C), 138.4 (2C), 146.6, 147.5, 150.8, 197.6. IR spectrum, *ν*, cm^{-1}: 2916, 2847 (OCH_3). ESI MS $[M+H_2O]^+$ 439. [Found, %: C, 82.67; H, 6.38; N, 3.31. $C_{29}H_{27}NO_2$. Calc., %: C, 82.59; H, 6.42; N, 3.36].



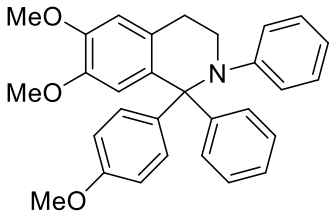
2-(6,7-Dimethoxy-2-phenyl-1-(4-tolyl)-1,2,3,4-tetrahydro-isoquinoline-1-yl)acetonitrile (2f). White powder. Yield 50% (0.141 g). MP 110-112°C (EtOAc-hexane). NMR ^1H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.32 (s, 3H, CH_3), 2.93 (d, *J* = 15.7, 1H, C$\underline{H_2}$CN), 3.13 (d, *J* = 16.5, 1H, C$\underline{H_2}$CN), 3.18 – 3.21 (m, 1H, 4-CH_2), 3.34-3.39 (m, 1H, 4-CH_2), 3.43-3.47 (m, 2H, 3-CH_2), 3.69 (s, 3H, OCH_3), 3.92 (s, 3H, OCH_3), 6.39 (s, 1H, H-5), 6.67 - 6.72 (m, 3H, H-8, Ar), 6.76 (d, *J* = 7.4, 2H, Ar), 7.00 (d, *J* = 7.4, 2H, Ar), 7.09 (t, *J* = 7.4, 1H, Ar), 7.14 (t, *J* = 7.4, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 21.1, 29.1, 30.1, 46.9, 55.9 (2C), 56.2, 66.0, 111.0, 111.1, 118.7, 125.3, 127.6 (2C), 128.1 (2C), 128.5 (4C), 128.8, 130.9, 137.4, 147.7, 148.3. IR spectrum, *ν*, cm^{-1}: 2933, 2834 (OCH_3), 2245 (CN). ESI MS $[M+H]^+$ 399. [Found, %: C, 78.22; H, 6.63; N, 7.00. $C_{26}H_{26}N_2O_2$. Calc., %: C, 78.32; H, 6.54; N, 7.07].



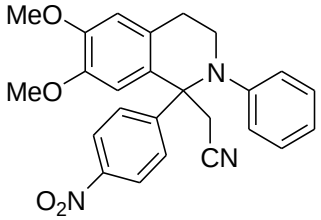
6,7-Dimethoxy-1,2-diphenyl-1-(4-tolyl)-1,2,3,4-tetrahydro-isoquinoline (3f). Beige powder. Yield 9% (0.040 g). MP 153-155°C (EtOAc-hexane). NMR ^1H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.42 (s, 3H, CH_3), 2.98 (t, 2H, *J* = 7.6, 4-CH_2), 3.79 (c, 3H, OCH_3), 3.85 (c, 3H, OCH_3), 3.96 (t, 2H, *J* = 7.2, 3-CH_2), 6.70 (s, 1H, H-5), 6.86 (s, 1H, H-8), 6.93 (t, 2H, *J* = 7.2, Ar), 6.96 (d, 4H, *J* = 7.6, Ar), 7.17-7.27 (m, 6H, Ar), 7.67 (d, 2H, *J* = 8.3, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 21.8, 31.4 (2C), 54.7, 56.1, 56.2, 112.9, 114.1, 121.3 (4C), 122.2 (2C), 129.2 (2C), 129.4 (4C), 130.4, 131.1, 132.5 (2C), 135.8, 143.9, 146.7, 147.2, 150.1, 197.3. IR spectrum, *ν*, cm^{-1}: 2924, 2853 (OCH_3). ESI MS $[M+H_2O]^+$ 453. [Found, %: C, 82.75; H, 6.57; N, 3.22. $C_{30}H_{29}NO_2$. Calc., %: C, 82.69; H, 6.68; N, 3.23].



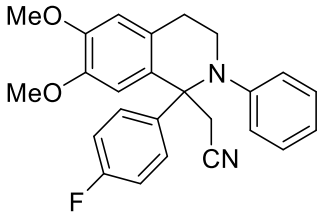
2-(6,7-Dimethoxy-2-phenyl-1-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2g). White powder. Yield 61% (0.170 g). MP 71-73°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.88-2.96 (m, 1H, 4-CH_2), 3.08-3.16 (m, 1H, C$\underline{H}_2$CN), 3.33-3.40 (m, 1H, C$\underline{H}_2$CN), 3.42-3.52 (m, 2H, 3-CH_2), 3.68 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 3.86-3.96 (m, 4H, OCH_3, 4-CH_2), 6.41 (s, 1H, H-5), 6.66 - 6.74 (m, 5H, H-8, Ar), 6.77 (d, *J* = 8.9, 2H, Ar), 7.06-7.11 (m, 1H, Ar), 7.14-7.18 (m, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 14.2, 29.1, 30.0, 32.0, 46.9, 55.3 (2C), 55.9, 56.1, 110.9 (2C), 111.1, 113.0 (2C), 118.6, 122.6, 127.7 (2C), 128.5 (2C), 129.6 (2C), 130.8, 147.6, 148.3, 159.0. IR spectrum, *ν*, cm^{-1}: 2932, 2835 (OCH_3), 2245 (CN). ESI MS $[M+H]^+$ 415. [Found, %: C, 75.44; H, 6.42; N, 6.72. $C_{26}H_{26}N_2O_3$. Calc., %: C, 75.29; H, 6.28; N, 6.79].



6,7-Dimethoxy-1,2-diphenyl-1-(4-methoxyphenyl)-1,2,3,4-tetrahydroisoquinoline (3g). Yellow oil. Yield 22% (0.067 g). R_f 0.4 (EtOAc-hexane, 1:5). 7.22 (t, *J*=7.2, 4H, Ar), 7.79 (d, *J* = 8.9, 2H, Ar). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.96 (t, *J*=7.6, 2H, 4-CH_2), 3.81 (s, 3H, OCH_3), 3.85 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3) 3.94 (t, *J*=7.2, 2H, 3-CH_2), 6.68 (s, 1H, H-5), 6.86 (s, 1H, H-8), 6.91 (d, *J*=6.9, 8H, Ar), 7.20 (t, *J*=7.2, 4H, Ar), 7.77 (d, 2H, Ar). NMR^{13}C (150 MHz, $CDCl_3$), δ ppm: 29.8, 31.3, 54.2, 55.6, 56.1, 56.2, 100.0, 112.3, 113.8 (2C), 121.1 (4C), 121.5, 129.4 (4C), 131.1, 131.4, 132.1, 132.7 (2C), 146.7, 147.6 (2C), 150.4, 163.7, 196.5. ESI MS $[M+H_2O]^+$ 469. IR spectrum, *ν*, cm^{-1}: 2931, 2847 (OCH_3). [Found, %: C, 79.68; H, 6.53; N, 3.10. $C_{30}H_{29}NO_3$. Calc., %: C, 79.76; H, 6.42; N, 3.14].

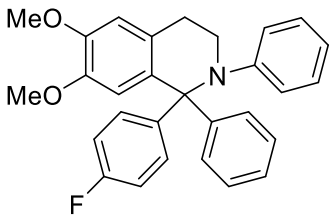


2-(6,7-Dimethoxy-2-phenyl-1-(4-nitrophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2h). Orange powder. Yield 6% (0.020 g). MP 126-128°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 3.00-3.03 (m, 1H, 4-CH_2), 3.22-3.26 (m, 2H, C$\underline{H}_2$CN, 4-CH_2), 3.45-3.48 (m, 2H, 3-CH_2), 3.55 (d, *J* = 16.5, 1H, C$\underline{H}_2$CN), 3.69 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 6.33 (s, 1H, H-5), 6.72 (d, *J*=7.4, 2H, Ar), 6.75 (s, 1H, H-8), 7.12 (d, *J* = 9.1, 2H, Ar), 7.14-7.20 (m, 3H, Ar), 8.08 (d, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm.: 29.0, 29.8, 47.1, 56.0, 56.3, 65.9, 110.9, 111.5, 111.7, 123.1 (2C), 126.1, 127.4 (2C), 128.8, 128.9 (2C), 129.1 (2C), 129.2, 147.3, 147.4, 148.1, 149.0, 149.9. IR spectrum, *ν*, cm^{-1}: 2960, 2932 (OCH_3), 2249 (CN), 1518, 1349 (NO_2). ESI MS $[M+H]^+$ 430. [Found, %: C, 70.02; H, 5.48; N, 9.75. $C_{25}H_{23}N_3O_4$. Calc., %: C, 69.89; H, 5.35; N, 9.83].

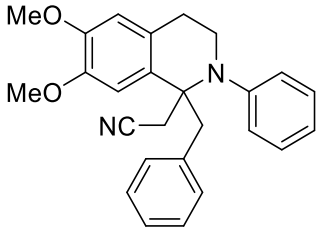


2-(6,7-Dimethoxy-2-phenyl-1-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2i). White powder. Yield 50% (0.145 g). MP 179-181°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.77-2.86 (m, 1H, 4-CH_2), 3.18 (d, 1H, *J* = 16.5, C$\underline{H}_2$CN), 3.21-3.29 (m, 2H, 3-CH_2), 3.44 (d, 1H, *J* = 16.5, C$\underline{H}_2$CN), 3.60-3.68 (m, 1H, 4-CH_2), 3.67 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.39 (s, 1H, H-5), 6.70 (s, 1H, H-8), 6.72-6.73 (m, 2H, Ar), 6.83-6.87 (m, 2H,

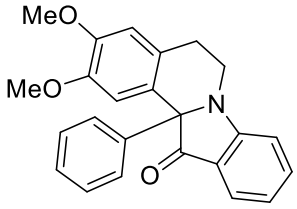
Ar), 6.85- 6.94 (m, 2H, Ar), 7.12-7.20 (m, 3H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 29.1, 29.6, 47.3 (2C), 56.0 (2C), 56.2, 66.4, 111.2 (2C), 114.7 (2C), 114.9 (2C), 118.1, 126.2, 127.5 (2C), 128.7 (2C), 130.0, 130.3, 130.4, 137.9, 161.1. IR spectrum, *v*, cm^{-1}: 2959, 2831 (OCH_3), 2248 (CN). ESI MS $[M+H]^+$ 403. [Found, %: C, 74.66; H, 5.62; N, 6.92; O. $C_{25}H_{23}FN_2O_2$. Calc., %: C, 74.57; H, 5.73; N, 7.00].



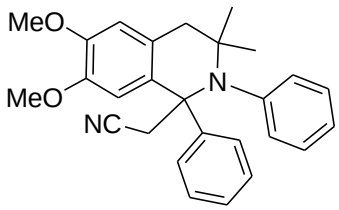
6,7-Dimethoxy-1,2-diphenyl-1-(4-fluorophenyl)-1,2,3,4-tetrahydroisoquinoline (3i). Beige powder. Yield 10% (0.031 g). MP 98-100°C (EtOAc-hexane). NMR^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.89-2.91 (m, 2H, 4-CH_2), 3.73 (s, 3H, OCH_3), 3.79 (s, 3H, OCH_3), 3.87-3.89 (m, 2H, 3-CH_2), 6.63 (s, 1H, H-5), 6.77 (s, 1H, H-8), 6.85-6.87 (m, 6H, Ar), 7.03 (t, 2H, *J* = 8.6, Ar), 7.14 (t, 4H, *J* = 7.9, Ar), 7.86 (t, 2H, *J* = 8.6, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 31.5 (2C), 54.5, 56.2 (2C), 56.3, 112.8 (2C), 114.2, 115.5 (2C), 115.7 (2C), 121.2 (2C), 121.9 (2C), 129.4, 130.5 (2C), 132.8, 132.9, 134.8 (2C), 146.8, 147.4, 151.0, 167.0, 196.0. IR spectrum, *v*, cm^{-1}: 2964, 2827 (OCH_3). ESI MS $[M+ H_2O]^+$ 457. [Found, %: C, 79.36; H, 5.83; N, 3.23. $C_{29}H_{26}FNO_2$. Calc., %: C, 79.25; H, 5.96; N, 3.19].



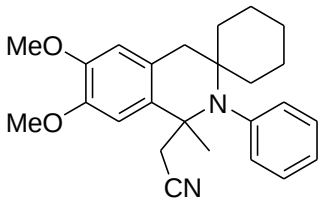
2-(1-Benzyl-6,7-Dimethoxy-2-phenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2j). Beige powder. Yield 35% (0.098 g). MP 91-93°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.73 (d, *J* = 16.1, 1H, 3-CH_2), 2.85-2.96 (d, 2H, C$\underline{H}_2$CN), 3.02-3.05 (m, 2H, 4-CH_2), 3.37 (d, *J* = 16.1, 1H, 3-CH_2), 3.44-3.51 (m, 4H, C$\underline{H}_2$Ph, OCH_3), 3.70 (br.s, 1H, C$\underline{H}_2$Ph), 3.88 (s, 3H, OCH_3), 5.93 (s, 1H, H-5), 6.61 (s, 1H, H-8), 6.88-6.93 (m, 2H, Ar), 7.16-7.21 (m, 3H, Ar), 7.24 (t, *J* = 6.4, 1H, Ar), 7.36-7.42 (m, 4H, Ar). NMR^{13}C (150 MHz, $CDCl_3$), δ ppm: 28.7, 29.3, 43.7, 47.4, 55.5 (2C), 55.8 (2C), 63.7, 110.4, 111.4, 118.2, 126.1, 126.8 (2C), 128.1, 128.2 (2C), 128.4, 129.2 (2C), 131.1 (2C), 136.7, 146.4, 148.1. IR spectrum, *v*, cm^{-1}: 2916, 2834 (OCH_3), 2251 (CN). ESI MS $[M+H]^+$ 399. [Found, %: C, 78.26; H, 6.63; N, 7.13. $C_{26}H_{26}N_2O_2$. Calc., %: C, 78.32; H, 6.54; N, 7.07].



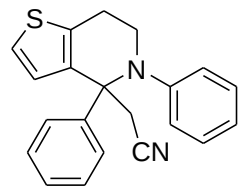
2,3-Dimethoxy-12a-phenyl-5,12a-dihydroindolo[2,1-*a*]-isoquinolin-12(6*H*)-one (4). Yellow powder. Yield 10% (0.027 g). MP 188°C (EtOAc-hexane, dec.). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.68 (d, *J* = 15.7, 1H, 5-CH_2), 2.91-2.99 (m, 1H, 5-CH_2), 3.43-3.50 (m, 2H, 6-CH_2), 3.85 (s, 3H, OCH_3), 3.87 (s, 3H, OCH_3), 6.62 (s, 1H, Ar), 6.85 (t, *J* = 7.4, 1H, Ar), 7.01 (d, *J* = 8.3, 1H, Ar), 7.10-7.14 (m, 2H, Ar), 7.27-7.31 (m, 3H, Ar), 7.37 (s, 1H, Ar), 7.54 (t, *J* = 7.6, 1H, Ar), 7.69 (d, *J* = 7.8, 1H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 26.5, 39.4, 55.9, 56.2, 74.3, 110.1, 111.1, 111.2, 118.9, 121.7, 124.7, 125.9, 127.5, 128.0, 128.3 (2C), 128.5 (2C), 137.4, 141.6, 147.5, 148.5, 160.9, 201.1. IR spectrum, *v*, cm^{-1}: 2929, 2851 (OCH_3), 1685 (C=O). ESI MS $[M+H]^+$ 372. [Found, %: C, 77.50; H, 5.77; N, 3.74. $C_{24}H_{21}NO_3$. Calc., %: C, 77.58; H, 5.67; N, 3.80].



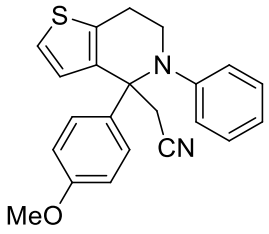
2-(6,7-Dimethoxy-3,3-dimethyl-1,2-diphenyl-1,2,3,4-tetrahydroisoquinolin-1-yl)acetonitrile (2k). White powder. Yield 44% (0.105 g). MP 151-153°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 0.92 (s, 3H, CH_3), 1.23 (s, 3H, CH_3), 2.72 (d, 1H, *J* = 15.0, CH_2), 2.87 (d, 1H, *J* = 15.8, C$\underline{H}_2$CN), 3.34 (d, 1H, *J*=15.0, CH_2), 3.43 (d, 1H, *J* = 15.8, C$\underline{H}_2$CN), 3.62 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 6.04 (d, 1H, *J* = 7.7, Ar), 6.35 (s, 1H, 5-H), 6.70 (s, 1H, 8-H), 6.82 - 6.93 (m, 3H, Ar), 7.08-7.20 (m, 4H, Ar), 7.27-7.34 (m, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 27.0, 32.3, 33.4, 46.0, 54.0, 55.9, 56.2, 66.2, 111.3, 112.1, 118.9, 126.6, 127.3, 127.4 (2C), 127.8, 128.3, 129.1 (2C), 129.2, 130.5, 134.8, 134.9, 143.2, 144.1, 147.2, 148.4. IR spectrum, *v*, cm^{-1}: 2968, 2247 (CN), 1514, 1264, 1227, 711. ESI MS [M+H] 413. [Found, %: C, 78.71; H, 6.76; N, 6.84. $C_{27}H_{28}N_2O_2$ Calc., %: C, 78.61; H, 6.84; N, 6.79].



2-(6',7'-Dimethoxy-1'-methyl-2'-phenyl-2',4'-dihydro-1'*H*-spiro[cyclohexane-1,3'-isoquinolin]-1'-yl)acetonitrile (2l). Almost white powder. Yield 38% (0.107 g). MP 144-145°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 0.87 - 1.01 (m, 2H, CH_2), 1.17-1.34 (m, 2H, CH_2), 1.41-1.53 (m, 5H, CH_2), 1.55 (s, 3H, CH_3), 1.85 (d, *J* = 12.4, 1H, CH_2), 2.40 - 2.58 (m, 2H, 4-CH_2), 2.92 (d, *J* = 14.9, 1H, C$\underline{H}_2$CN), 3.17 (d, 1H, *J*=15.7, C$\underline{H}_2$CN), 3.87 (s, 3H, OCH_3), 3.89 (s, 3H, OCH_3), 6.64 (s, 1H, 5-H), 6.77 (s, 1H, 8-H), 7.28-7.32 (m, 1H, Ar), 7.32-7.37 (m, 3H, Ar) 7.38 - 7.41 (m, 1H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 22.9, 23.8, 25.7, 28.9, 34.2, 35.3, 38.8, 38.9, 55.89, 56.4, 56.5, 59.8, 109.2, 112.1, 118.9, 126.9, 127.8, 127.9, 128.9, 130.8, 134.8, 135.8, 142.9, 147.6, 148.2. IR spectrum, *v*, cm^{-1}: 2935, 2245 (CN), 1609, 1521, 1451, 1358, 1261, 1216, 1153, 1080, 710; ESI MS [M+H] 391. [Found, %: C, 76.78; H, 7.81; N, 7.22. $C_{25}H_{30}N_2O_2$ Calc., %: C, 76.89; H, 7.74; N, 7.17].



2-(4,5-Diphenyl-4,5,6,7-tetrahydrothieno[3,2-*c*]pyridin-4-yl)-acetonitrile (2m). Yellow powder. Yield 45% (0.067 g). MP 107-110°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 3.01-3.03 (m, 1H, 7-CH_2), 3.10 (d, *J* = 16.5, 1H, C$\underline{H}_2$CN), 3.23-3.30 (m, 1H, 7-CH_2), 3.39-3.53 (m, 2H, 6-CH_2, C$\underline{H}_2$CN), 3.53-3.56 (m, 1H, 6-CH_2), 6.65 (d, *J* = 5.5, 1H, Ar), 6.72 (d, *J* = 6.9, 1H, Ar), 6.85 (d, *J* = 7.6, 2H, Ar), 7.09-7.17 (m, 4H, Ar), 7.19-7.21 (m, *J* = 7.2, 2H, Ar), 7.23-7.28 (m, 2H, Ar). NMR ^{13}C (150 MHz, $CDCl_3$), δ ppm: 26.2, 28.2, 47.4, 65.0, 118.1, 123.5, 125.5, 125.8, 127.7, 127.8 (2C), 127.9 (2C), 128.6 (2C), 129.4, 130.4, 136.8, 137.7, 141.2, 147.9. IR spectrum, *v*, cm^{-1}: 2243 (CN). ESI MS $[M+H]^+$ 331. [Found, %: C, 76.19; H, 5.61; N, 8.46. $C_{21}H_{18}N_2S$. Calc., %: C, 76.29; H, 5.44; N, 8.52].



2-(4-(4-Methoxyphenyl)-5-phenyl-4,5,6,7-tetrahydrothieno[3,2-*c*]-pyridin-4-yl)acetonitrile (2n). Beige powder. Yield 62% (0.092 g). MP 131-133°C (EtOAc-hexane). NMR ^{1}H (600 MHz, $CDCl_3$), δ ppm, *J* (Hz): 2.99-3.08 (m, 2H, 6-CH_2), 3.20-3.28 (m, 1H, 7-CH_2), 3.36-3.42 (m, 2H, C$\underline{H}_2$CN), 3.52 (br.s., 1H, 7-CH_2), 3.79 (s, 3H, OCH_3), 6.66 (d, *J* = 4.9, 1H, Ar), 6.75 (s, 6H, Ar), 7.11-7.20 (m, 4H, Ar). NMR ^{13}C

(150 MHz, $CDCl_3$), δ ppm: 26.1, 28.3, 47.4, 55.3, 64.9, 113.1 (2C), 118.3, 123.6 (2C), 125.7, 125.9 (2C), 127.9 (2C), 128.6 (2C), 129.1 (2C), 136.7, 137.8, 159.2. IR spectrum, ν, cm^{-1}: 2937, 2864 (OCH_3), 2243 (CN). ESI MS $[M+H]^+$ 361. [Found, %: C, 73.35; H, 5.43; N, 7.77; O, 4.44. $C_{22}H_{20}N_2OS$. Calc., %: C, 73.27; H, 5.54; N, 7.81; O, 4.40].

The structure of the bicyclic product **2d** was unambiguously established by X-ray diffraction study (Figure S1).

The tetrahydropyrimidine ring of **2d** adopts a slightly distorted *sofa* conformation (the C3 carbon atom deviates from the mean plane passed through the other atoms of the ring by 0.733(2) Å). The N2 nitrogen atom has a trigonal-pyramidal geometry (the sum of bond angles is 342.4(2)°). The phenyl substituent occupies the sterically favorable equatorial position. The both methoxy groups are almost coplanar to the central benzene ring.

The mutual orientation of the furyl and cyanomethyl substituents (the dihedral angle is 35.45(6)°) is apparently determined by the intermolecular hydrogen bonds C13─H13A**...*π***(O1─C12) (1-*x*, 1-*y*, 1-*z*) (the distances H13A**...**O1 and H13A**...**C12 are 2.56 and 2.77 Å, respectively), which result in the formation of the centrosymmetrical dimers (Figure S2).

In the crystal, the dimers are linked by the weak intermolecular hydrogen bonds C10─H10**...**O3 (1-*x*, 2-*y*, 1-*z*) [C**…**O 3.4985(15), H**…**O 2.58 Å, ∠C─H**…**O 162°] and C5─H5**...**N1 (1-*x*, 2-*y*, -*z*) [C**…**N 3.5541(16), H**…**N 2.62 Å, ∠C─H**…**N 167°] into layers parallel to (100) (Figure S3).

Compound **2d** is chiral and has an asymmetric center at the C1 carbon atom. The crystal of **2d** is racemic and consists of 1***RS***-enantiomeric pairs.

The crystal of **2d** ($C_{23}H_{22}N_2O_3$, M = 374.42) is triclinic, space group P-1, at T = 120 K: a = 9.8362(8) Å, b = 9.8419(8) Å, c = 11.2133(9) Å, α = 72.490(2)°, β = 86.732(2)°, γ = 63.657(2)°, V = 924.00(13) $Å^3$, Z = 2, d_{calc} = 1.346 g/cm^3, $F(000)$ = 396, μ = 0.090 mm^{-1}. 13741 total reflections (6594 unique reflections, R_{int} = 0.029) were measured on a three-circle Bruker APEX-II CCD diffractometer ($\lambda(MoK_\alpha)$-radiation, graphite monochromator, φ and ω scan mode, $2\theta_{max}$ = 65.24°) and corrected for absorption (T_{min} = 0.969; T_{max} = 0.975) [9]. The structure was determined by direct methods and refined by full-matrix least squares technique on F^2 with anisotropic displacement parameters for non-hydrogen atoms. The hydrogen atoms were placed in calculated positions and refined within riding model with fixed isotropic displacement parameters [U_{iso}(H) = 1.5U_{eq}(C) for the CH_3-groups and U_{iso}(H) = 1.2U_{eq}(C) for the other groups]. The final divergence factors were R_1 = 0.050 for 4823 independent reflections with $I > 2\sigma(I)$ and wR_2 = 0.127 for all independent reflections, S = 1.022. All calculations were carried out using the *SHELXL2014* program [10].

Crystallographic data for compound **2d** have been deposited with the Cambridge Crystallographic Data Center, CCDC 1502504. Copies of this information may be obtained free of charge from the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or www.ccdc.cam.ac.uk).

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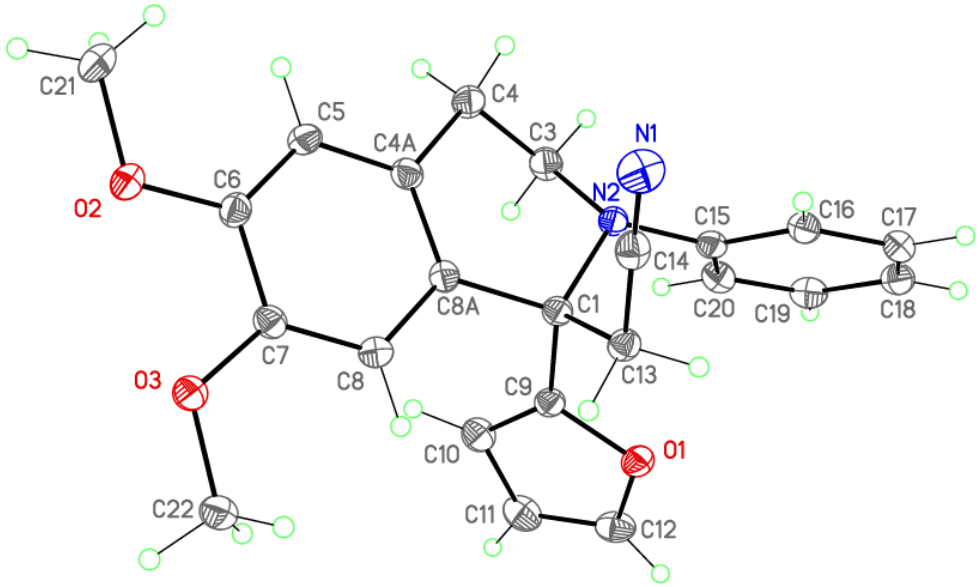


Figure S1 Molecular structure of **2d**. Displacement ellipsoids are shown at the 50% probability level. H atoms are presented as small spheres of arbitrary radius.

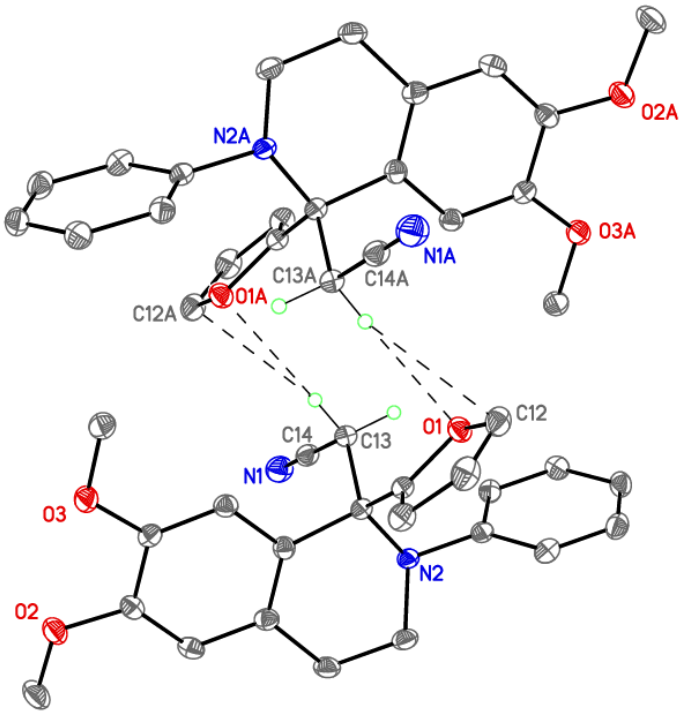
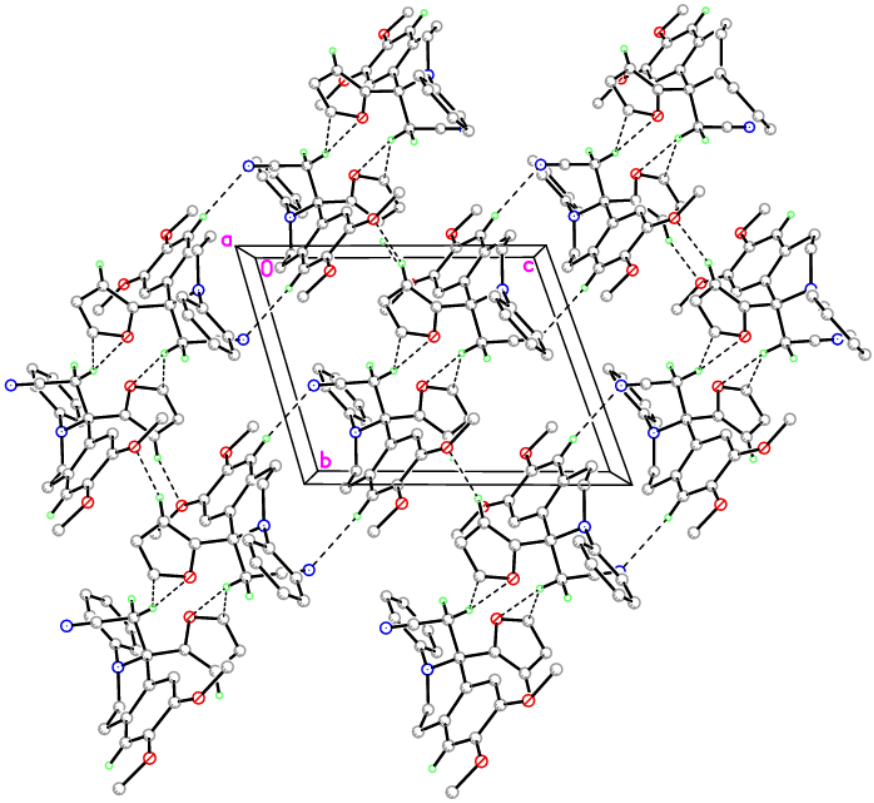


Figure S2 The centrosymmetrical dimers of **2d**. The hydrogen atoms of the ─CH_2CN groups are shown only. Dashed lines are indicative of the intermolecular hydrogen bonds C13─H13A**...π**(O1A─C12A) and C13A─H13C**...π**(O1─C12).



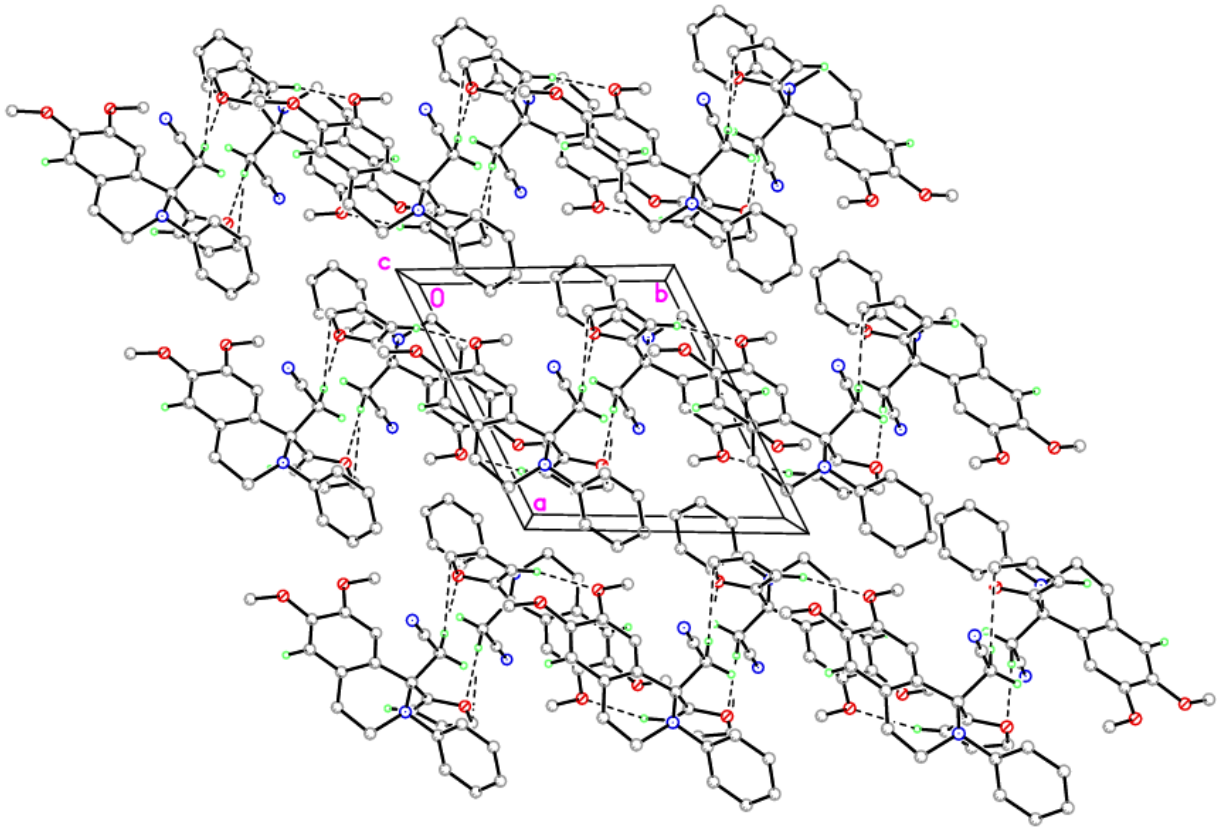
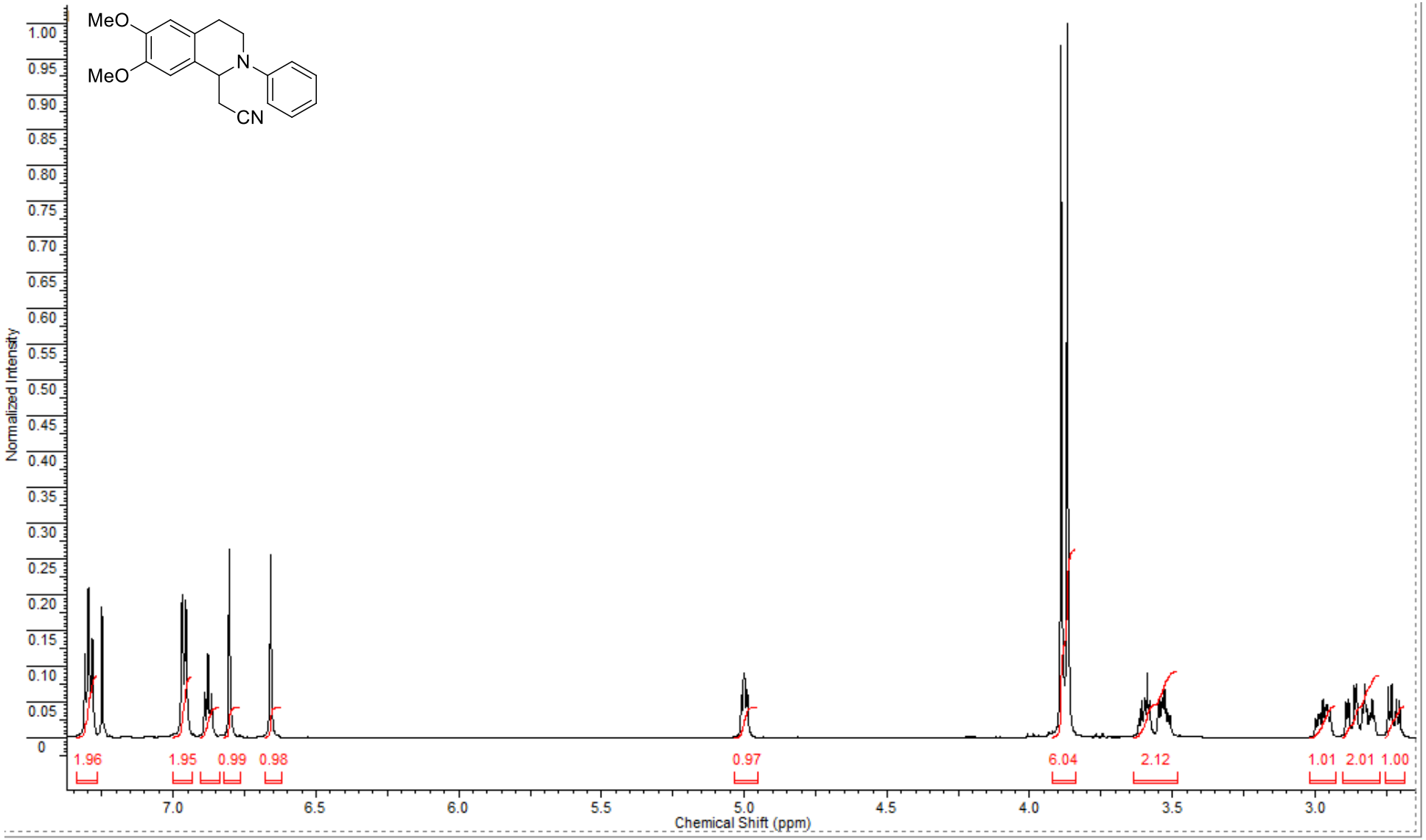


Figure S3 The layers of **2d** parallel to (100) (two projections along the ***a*** (top) and ***c*** (bottom) axes are presented). Dashed lines are indicative of the intermolecular hydrogen bonds.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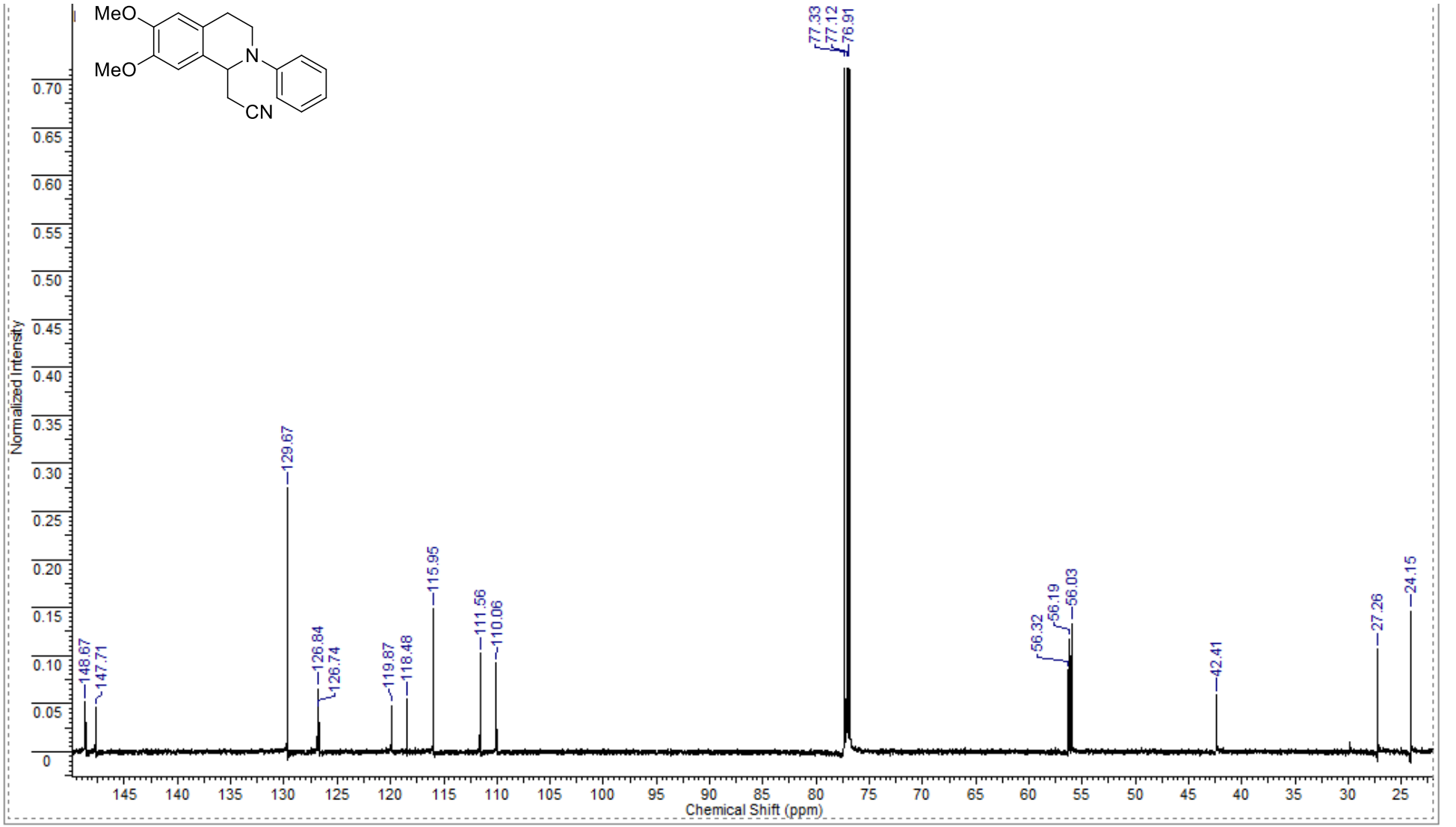
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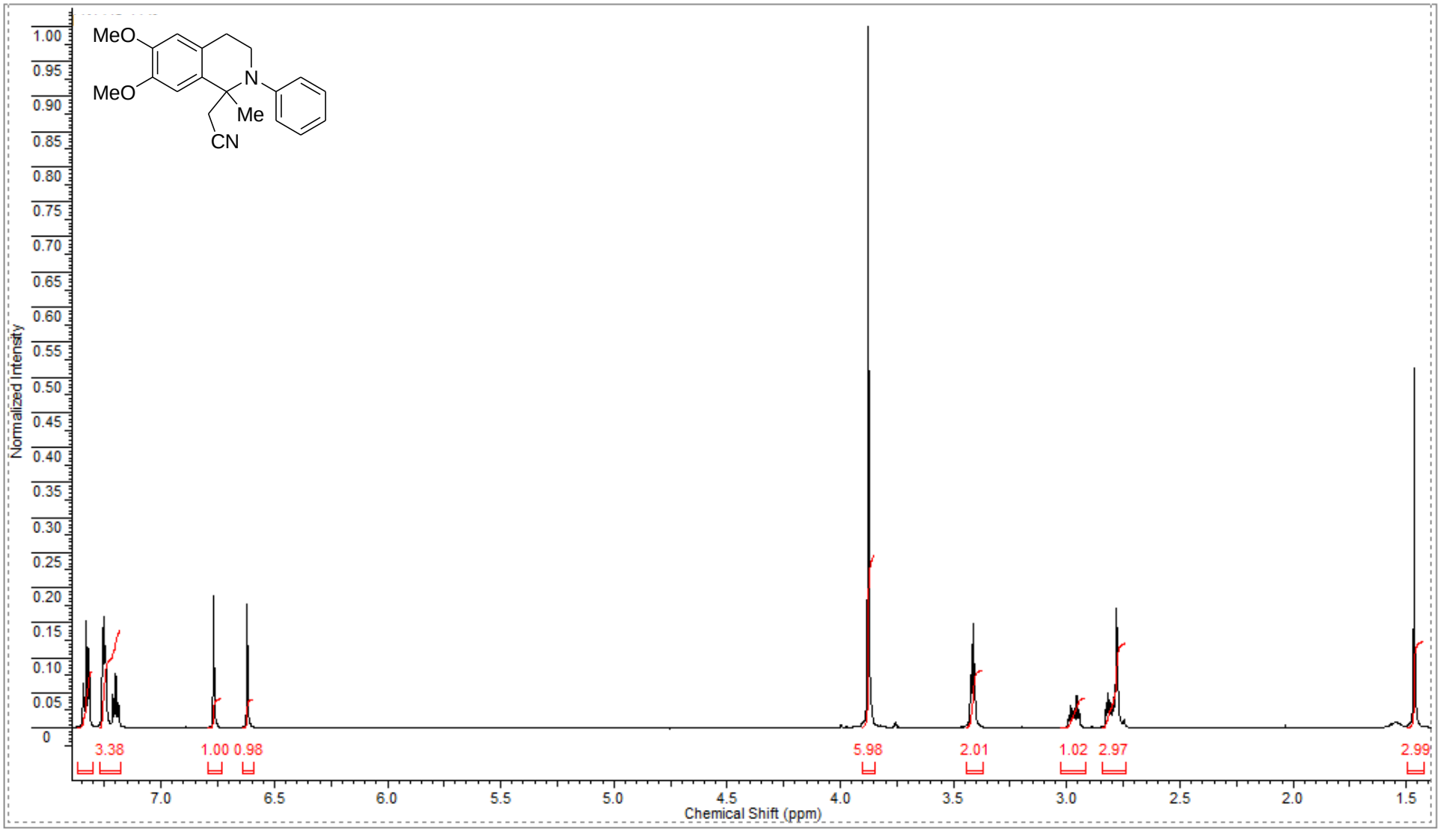
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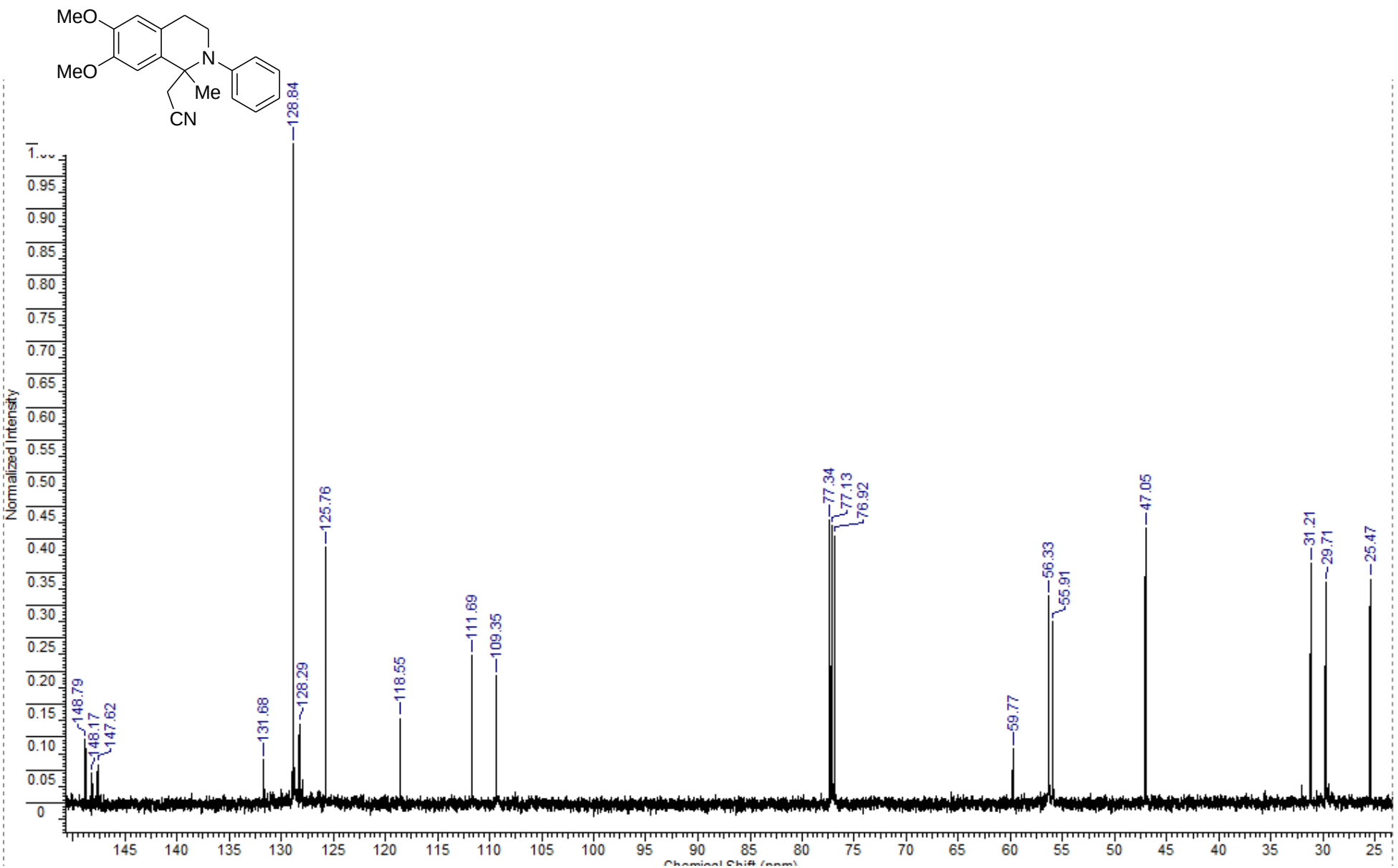
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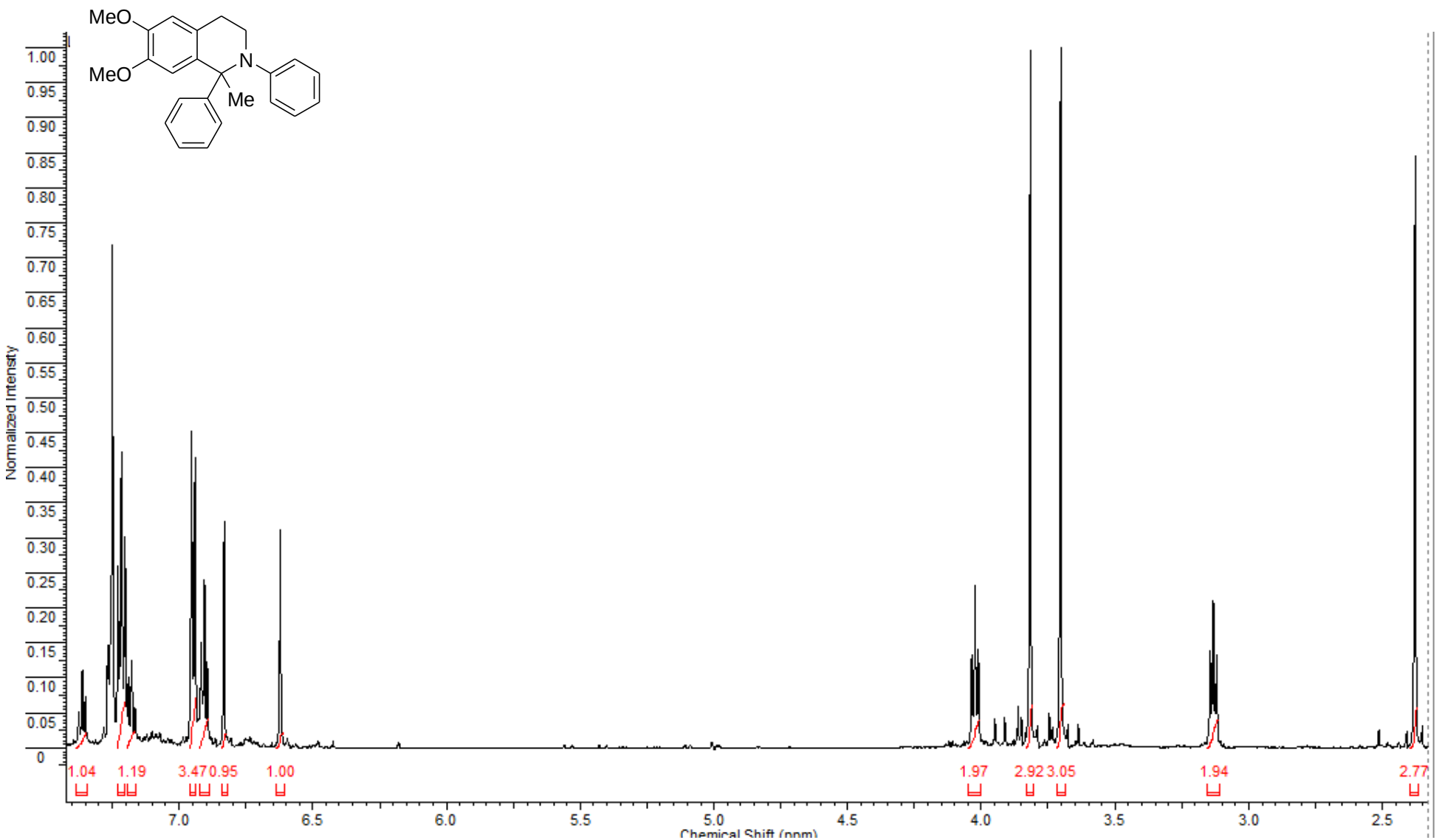
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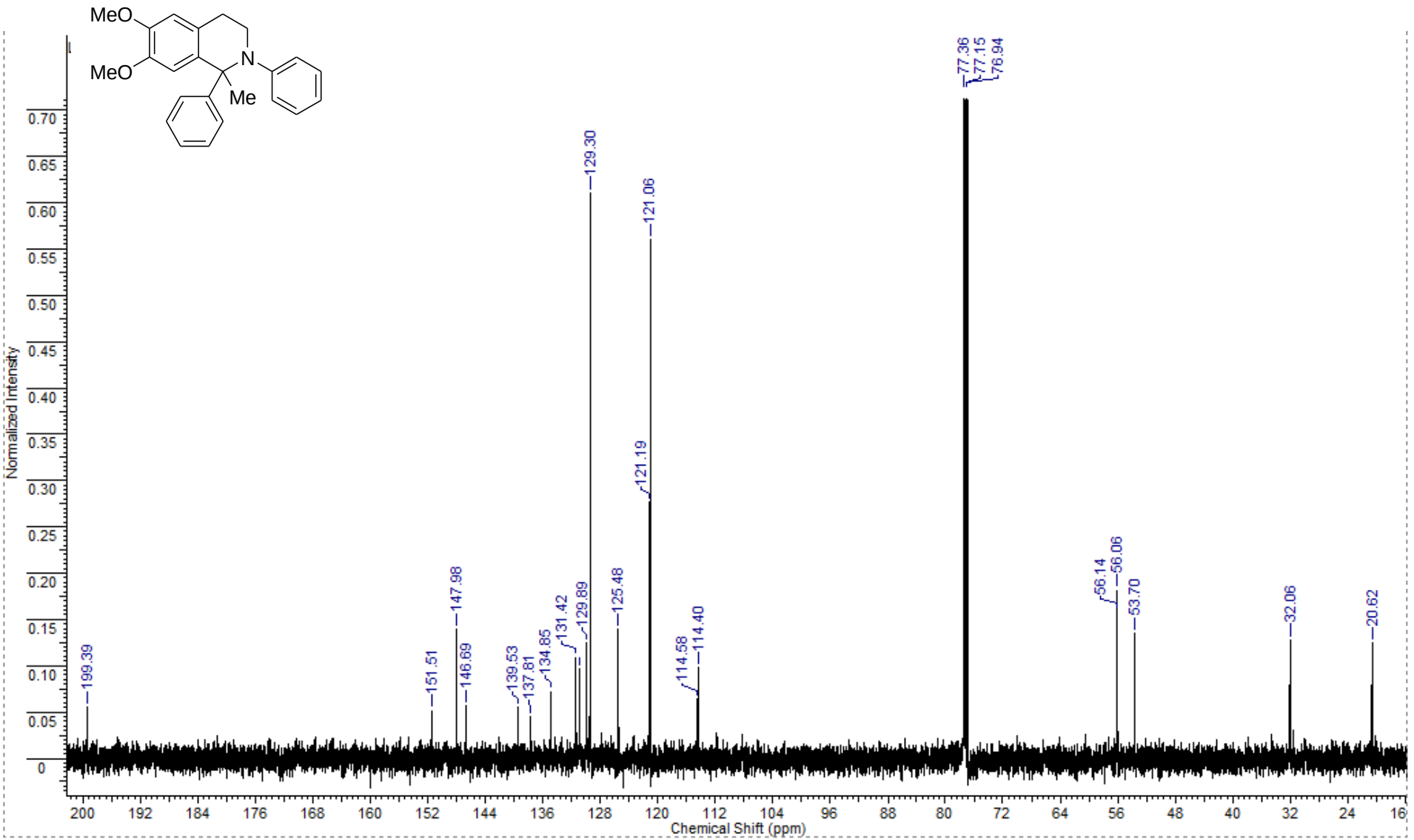
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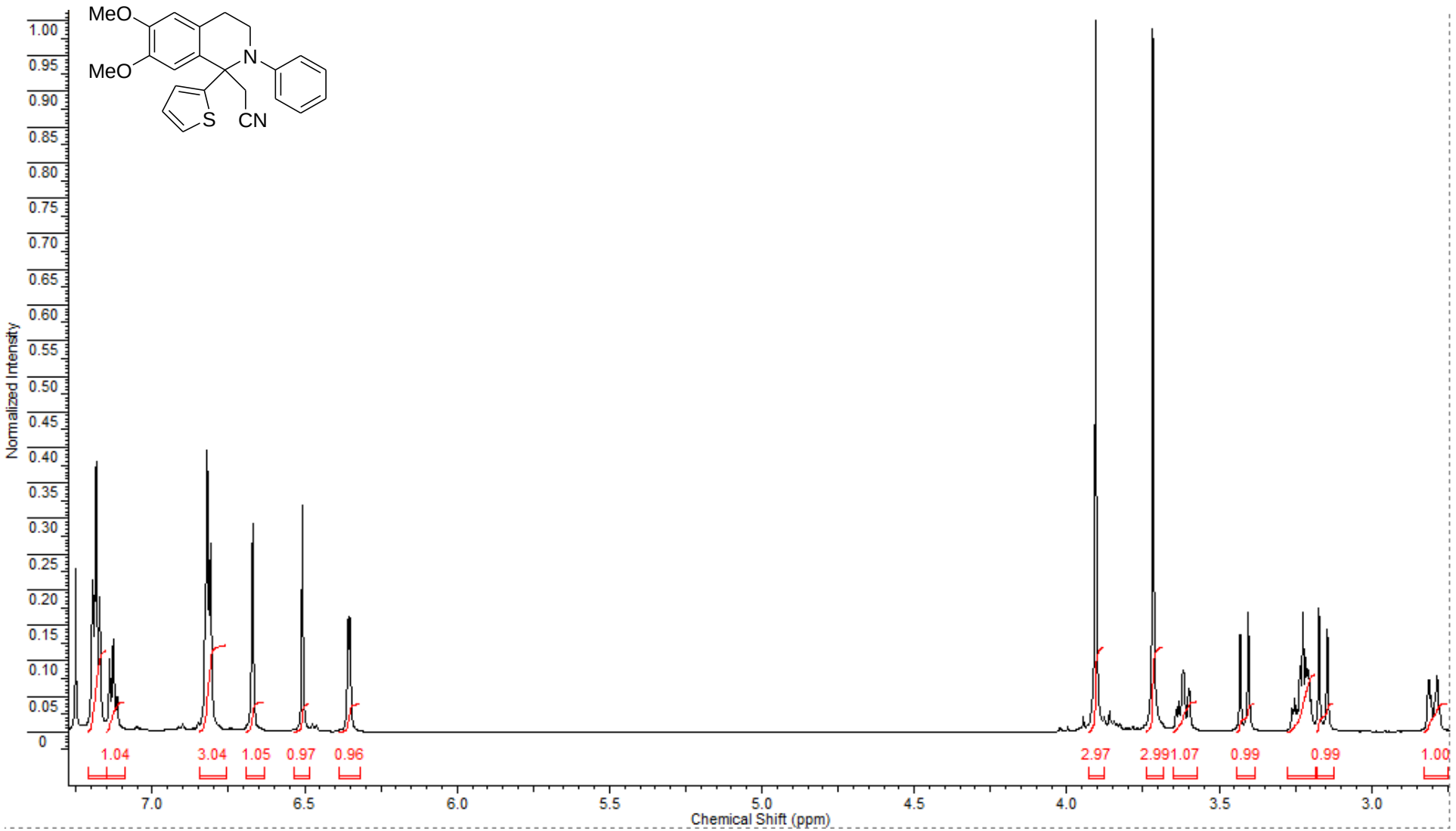
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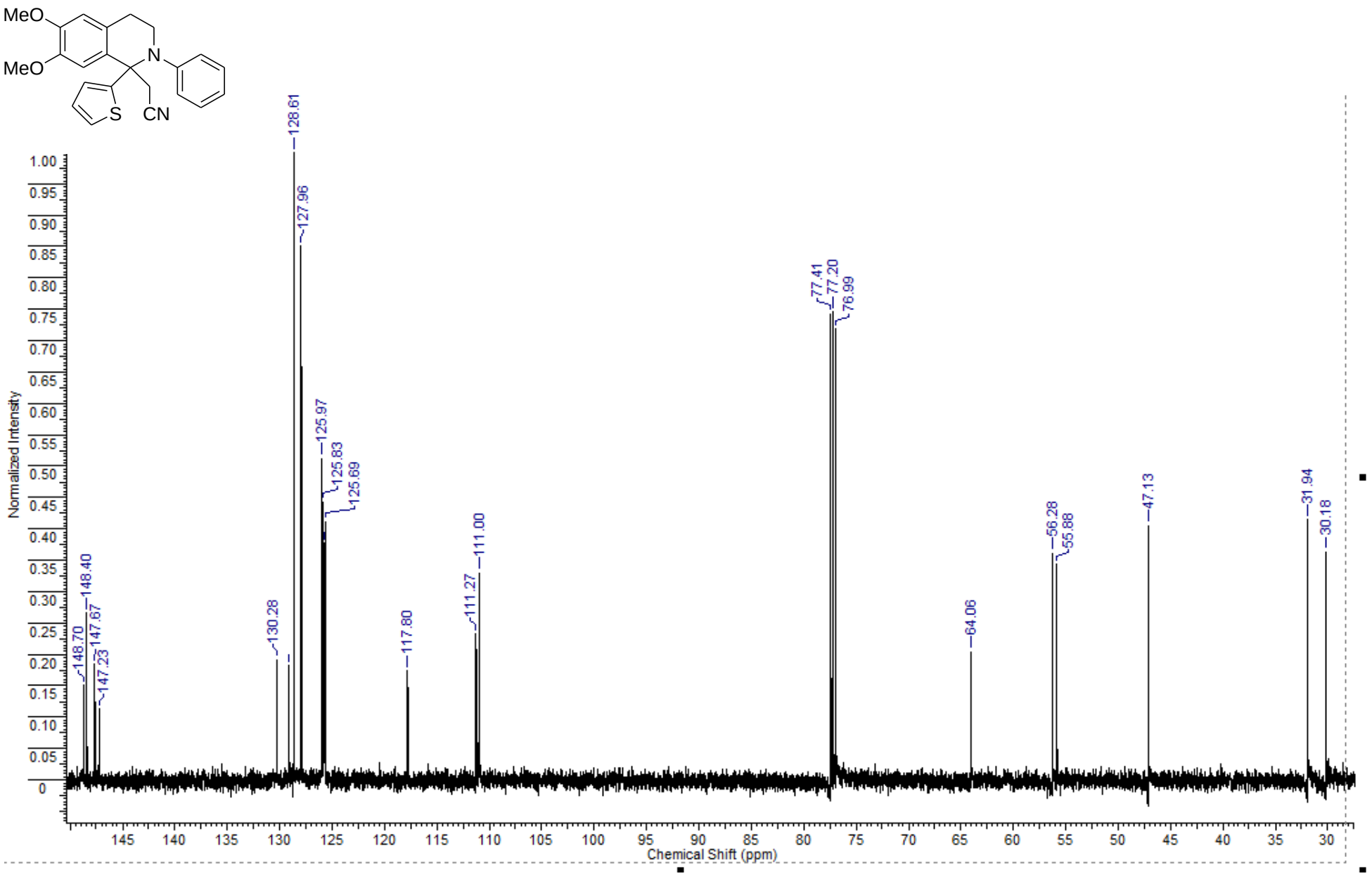
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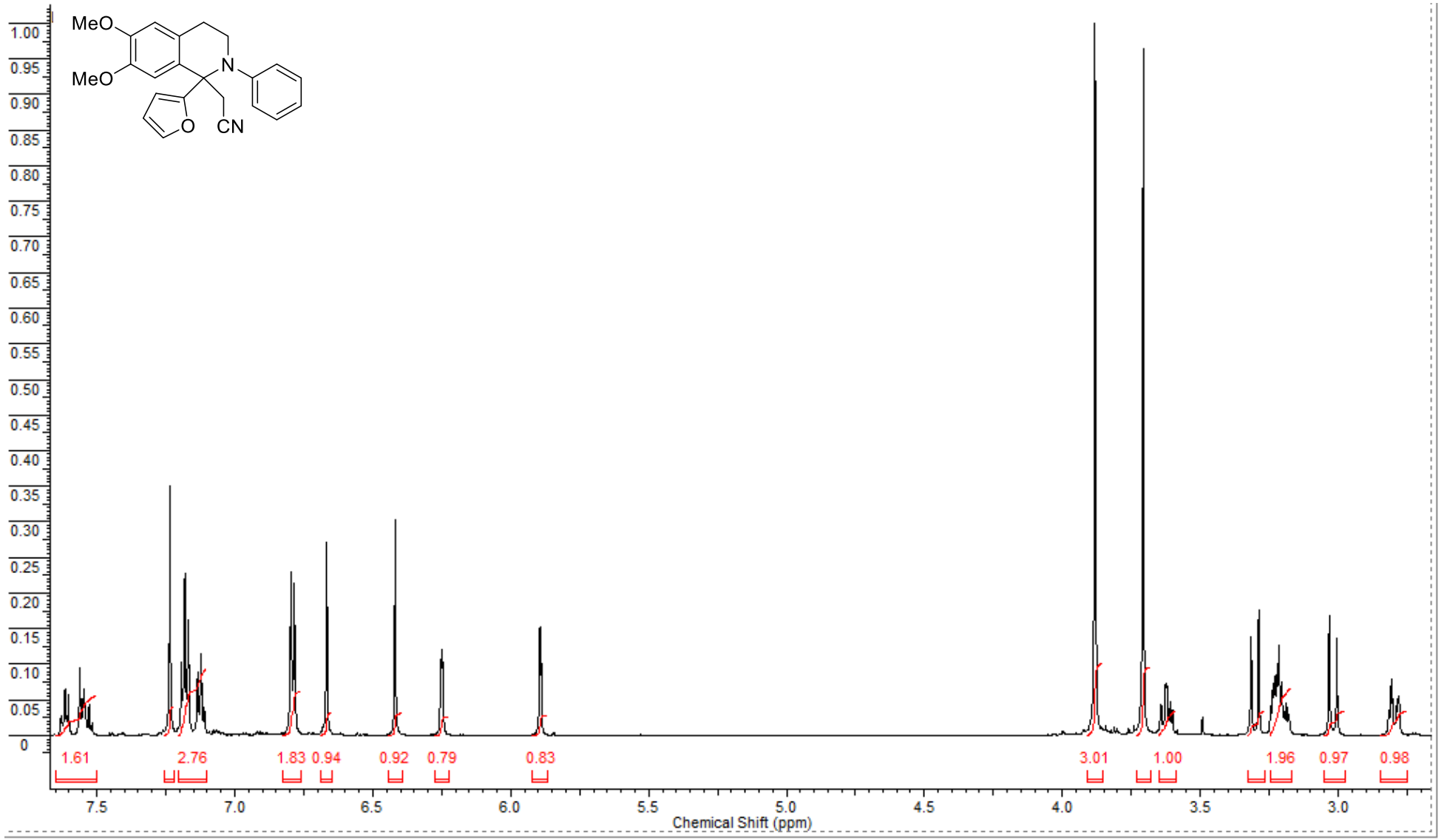
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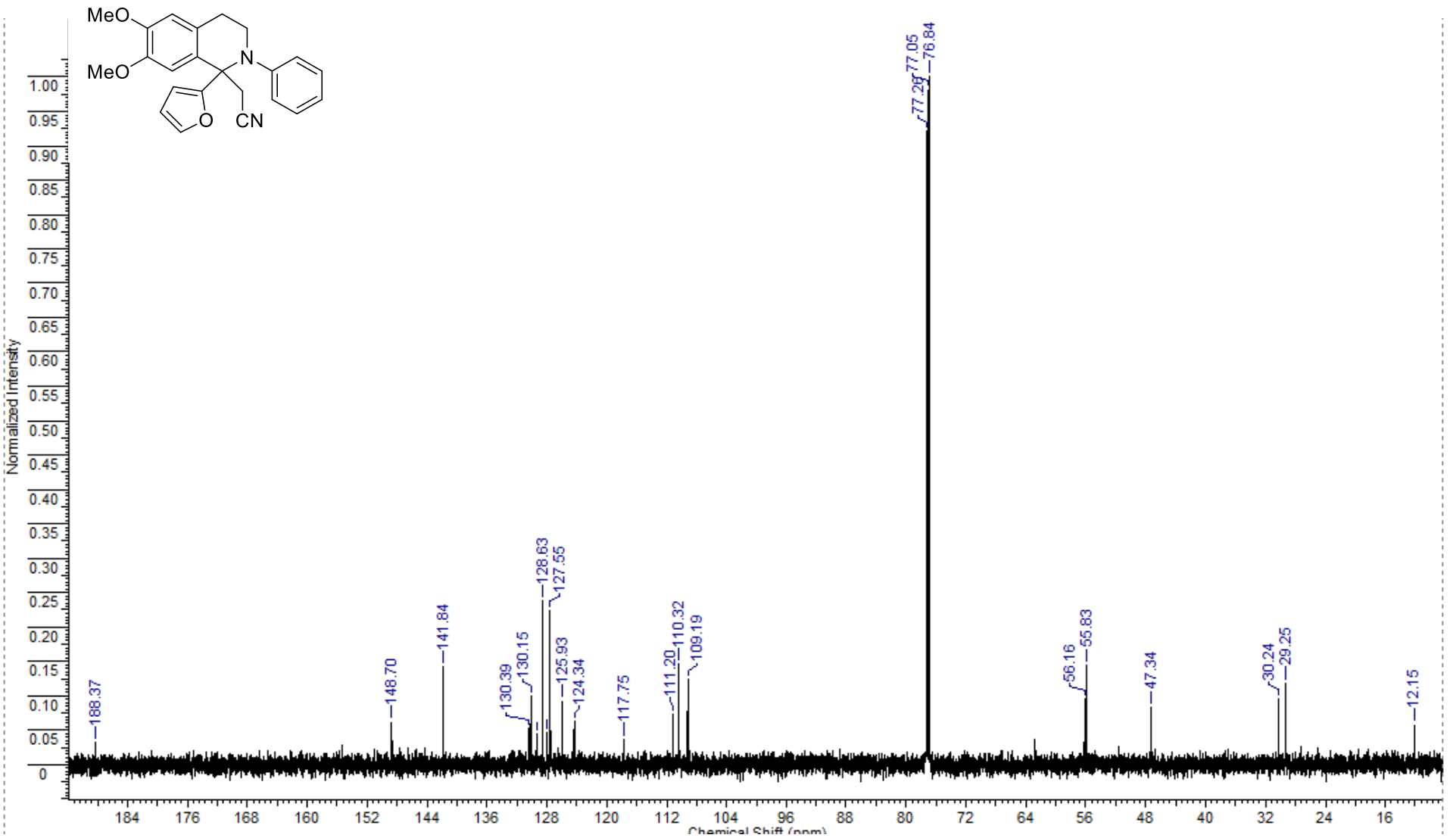
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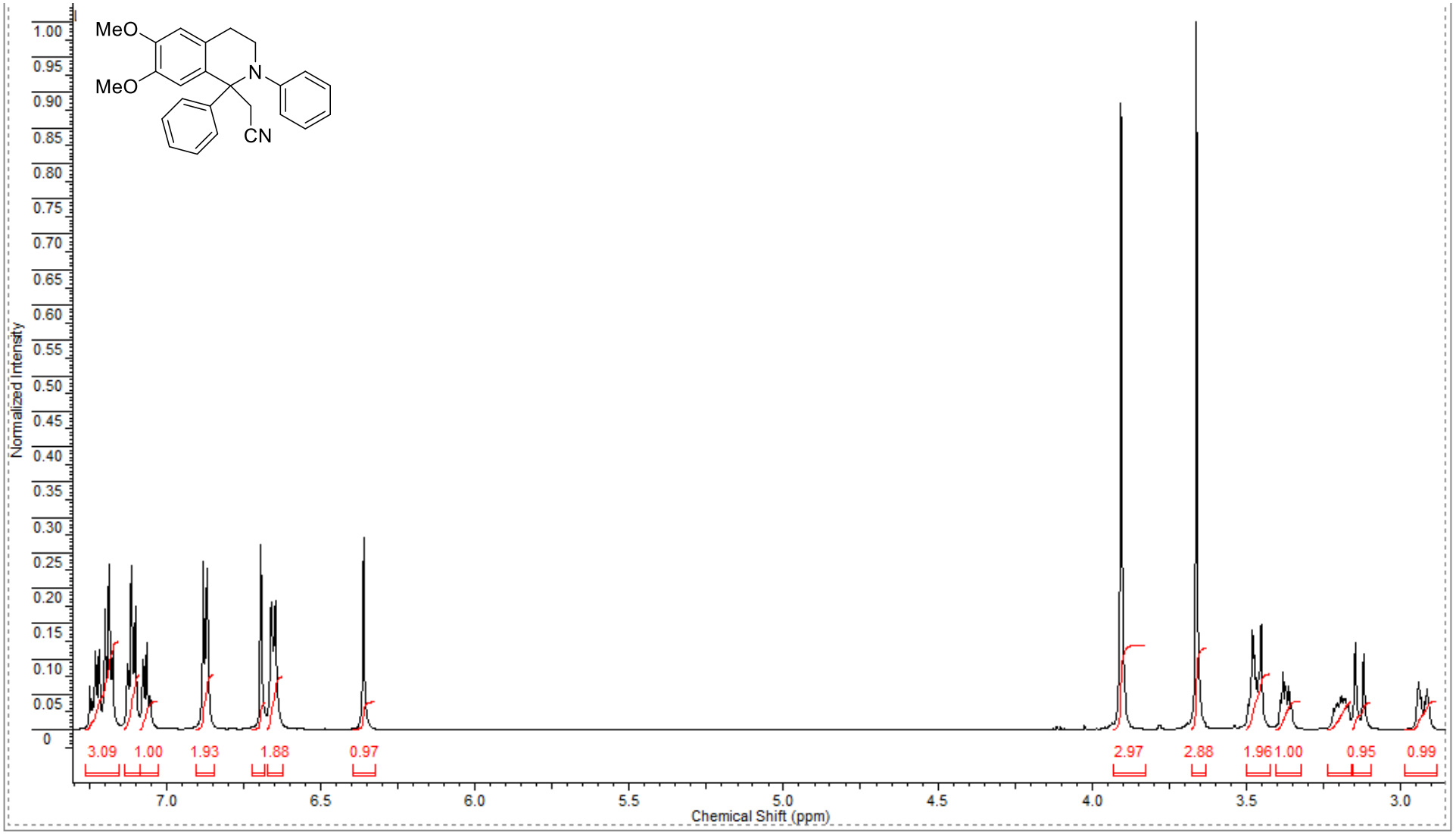
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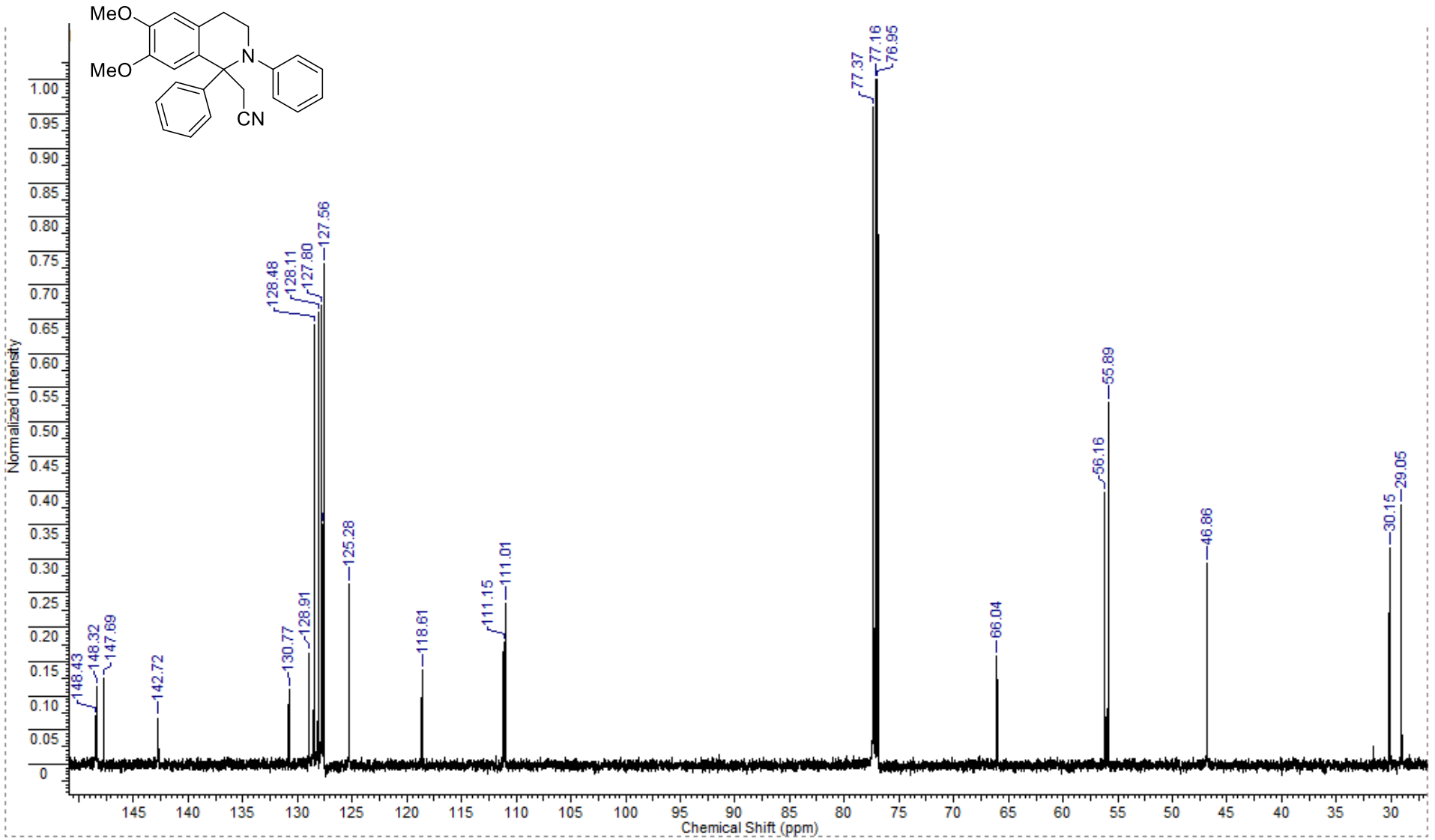
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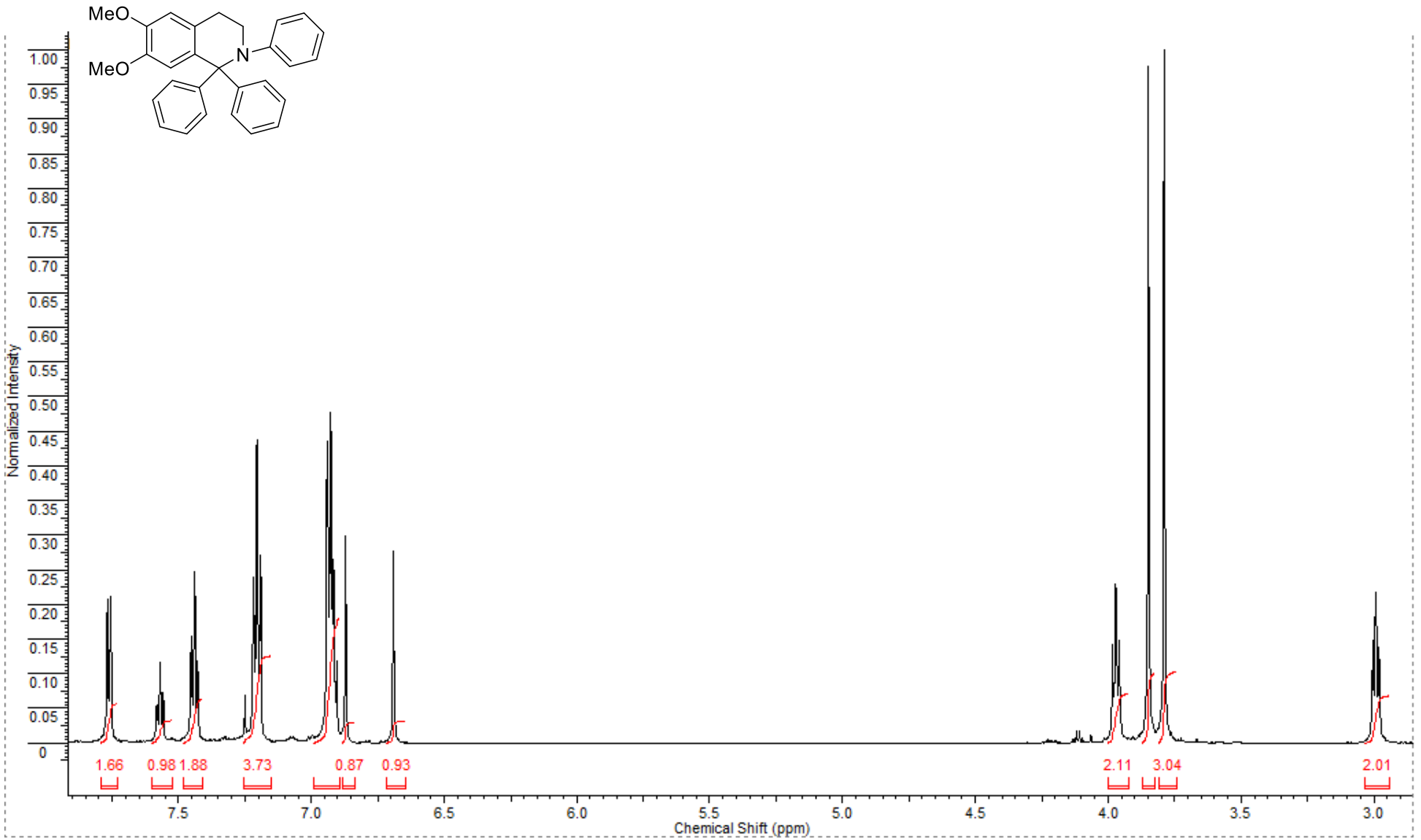
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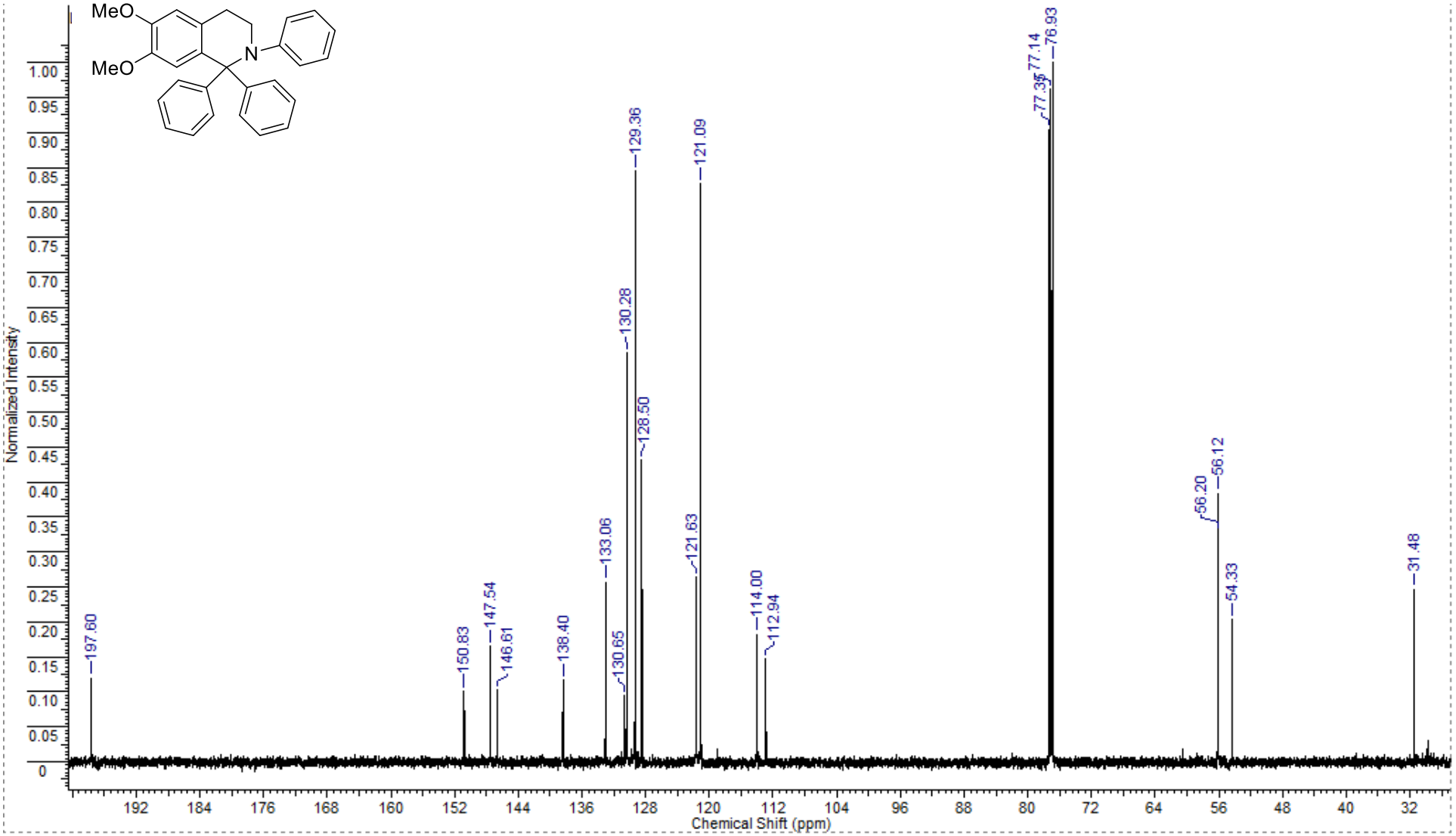
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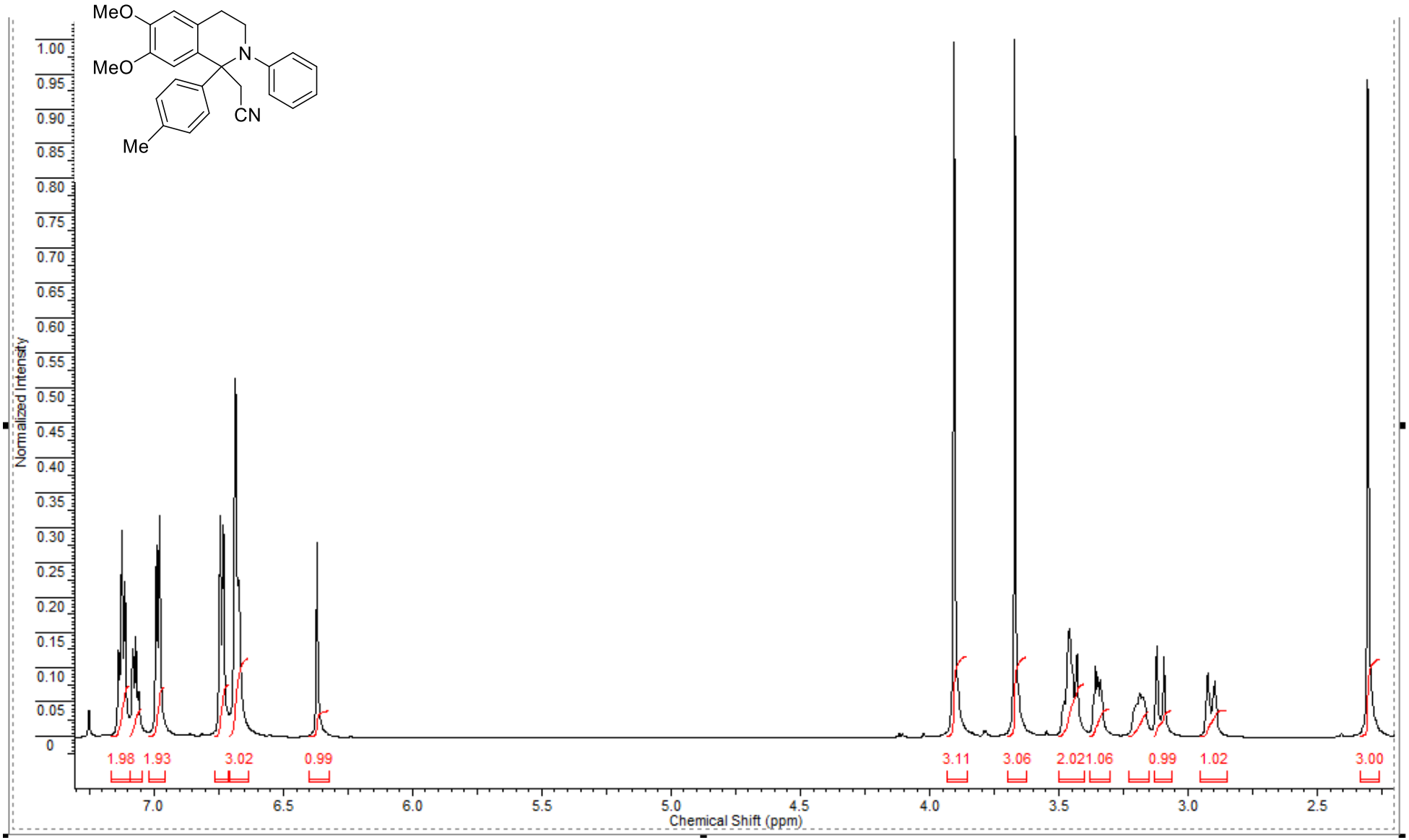
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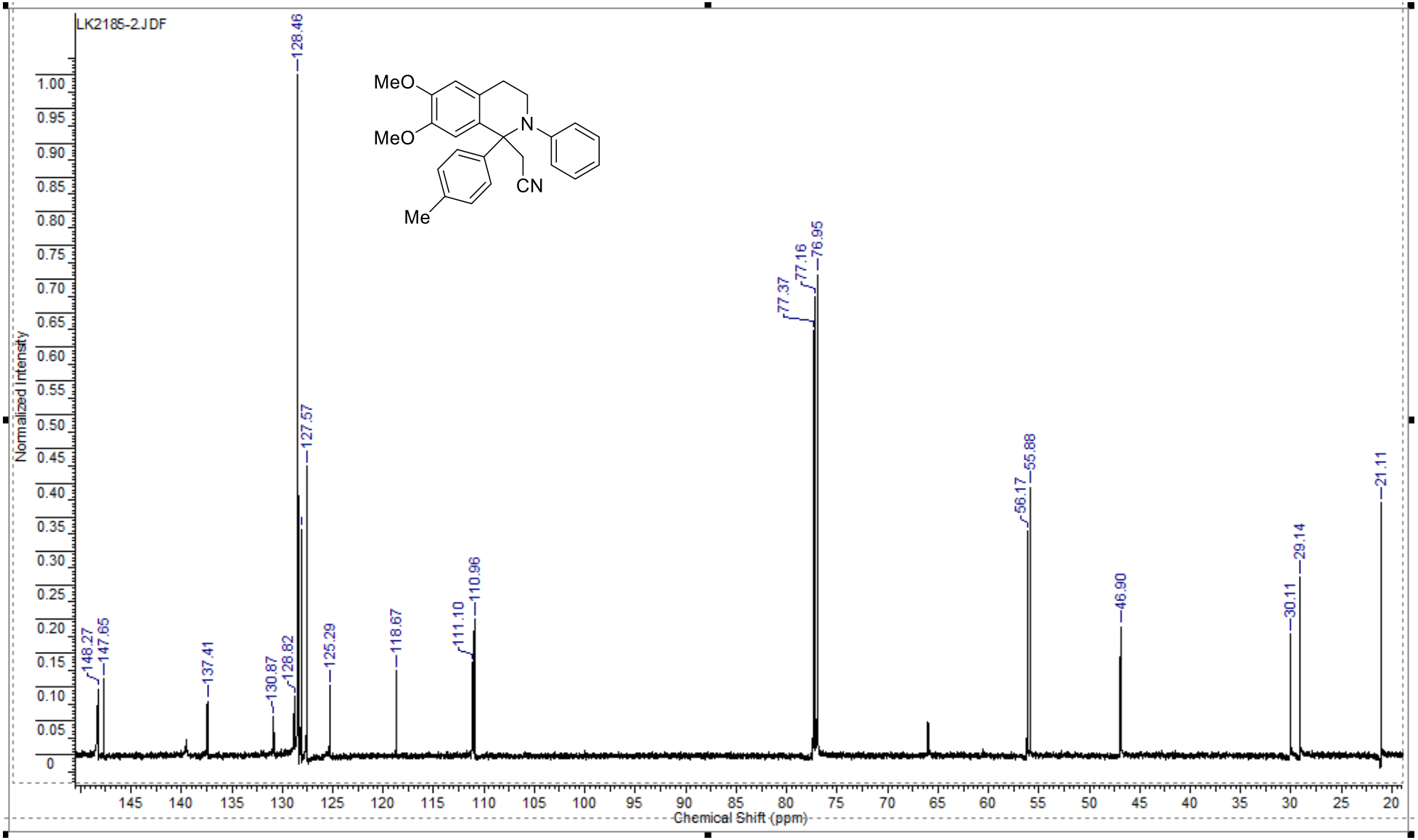
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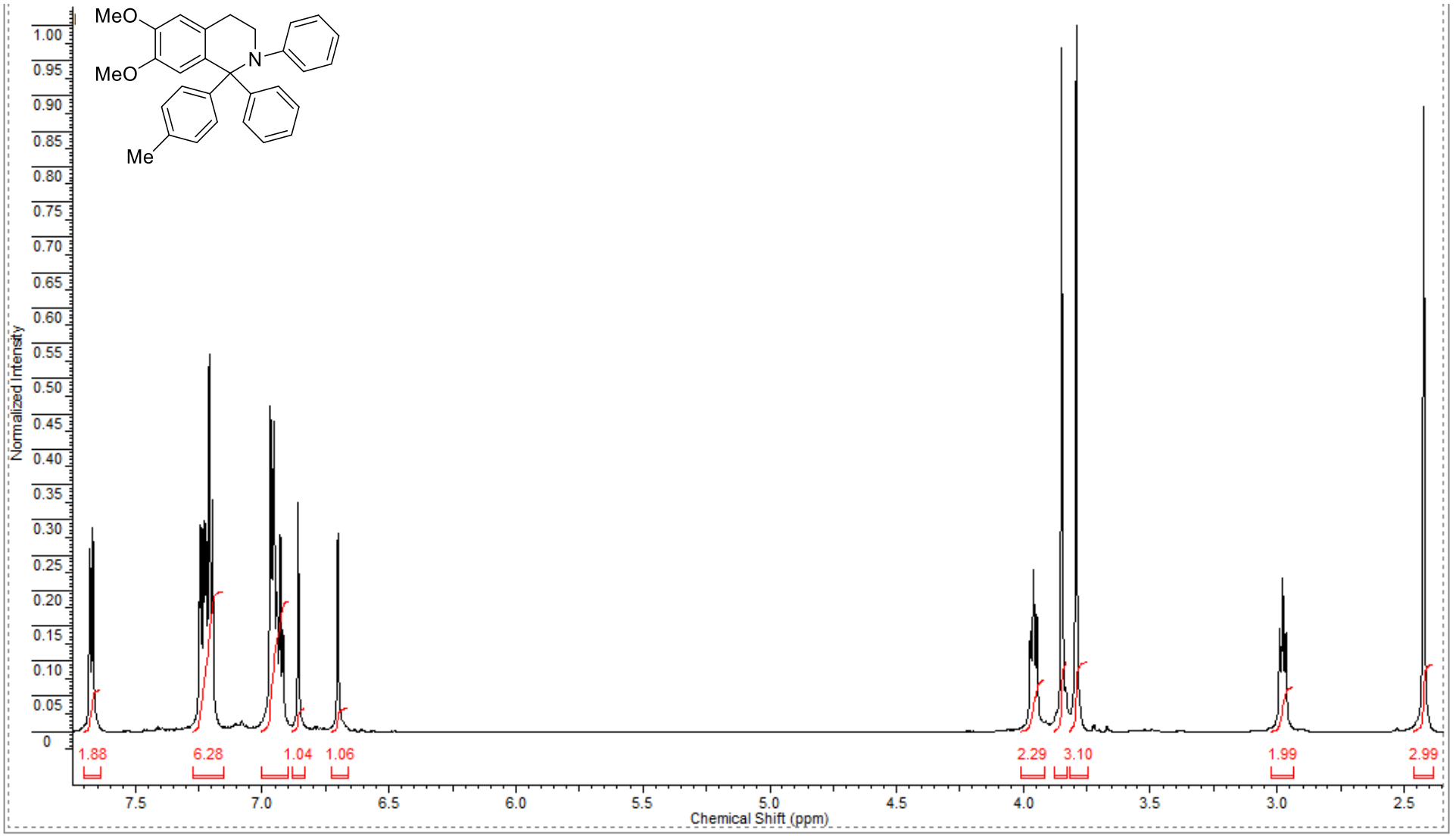
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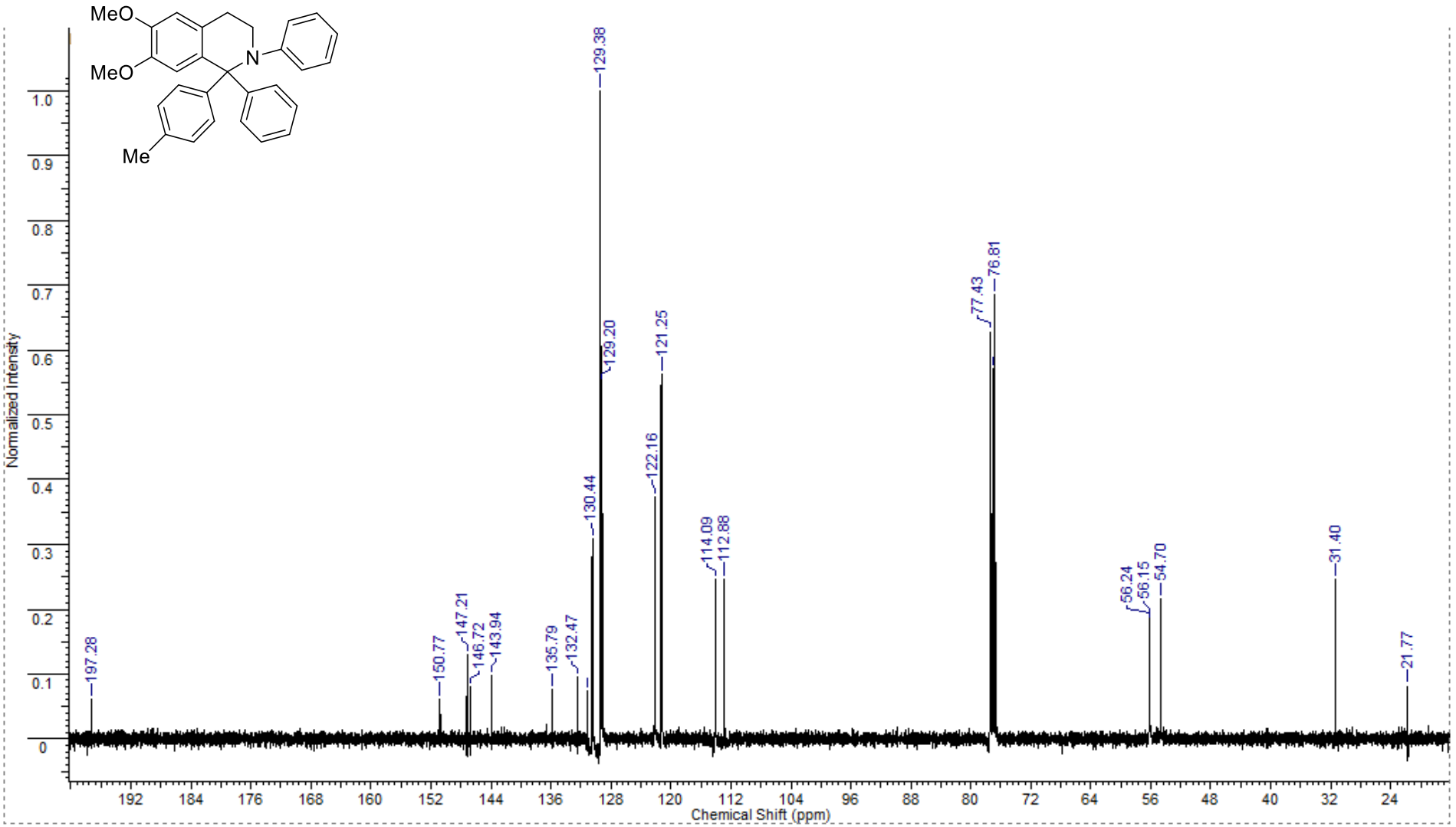
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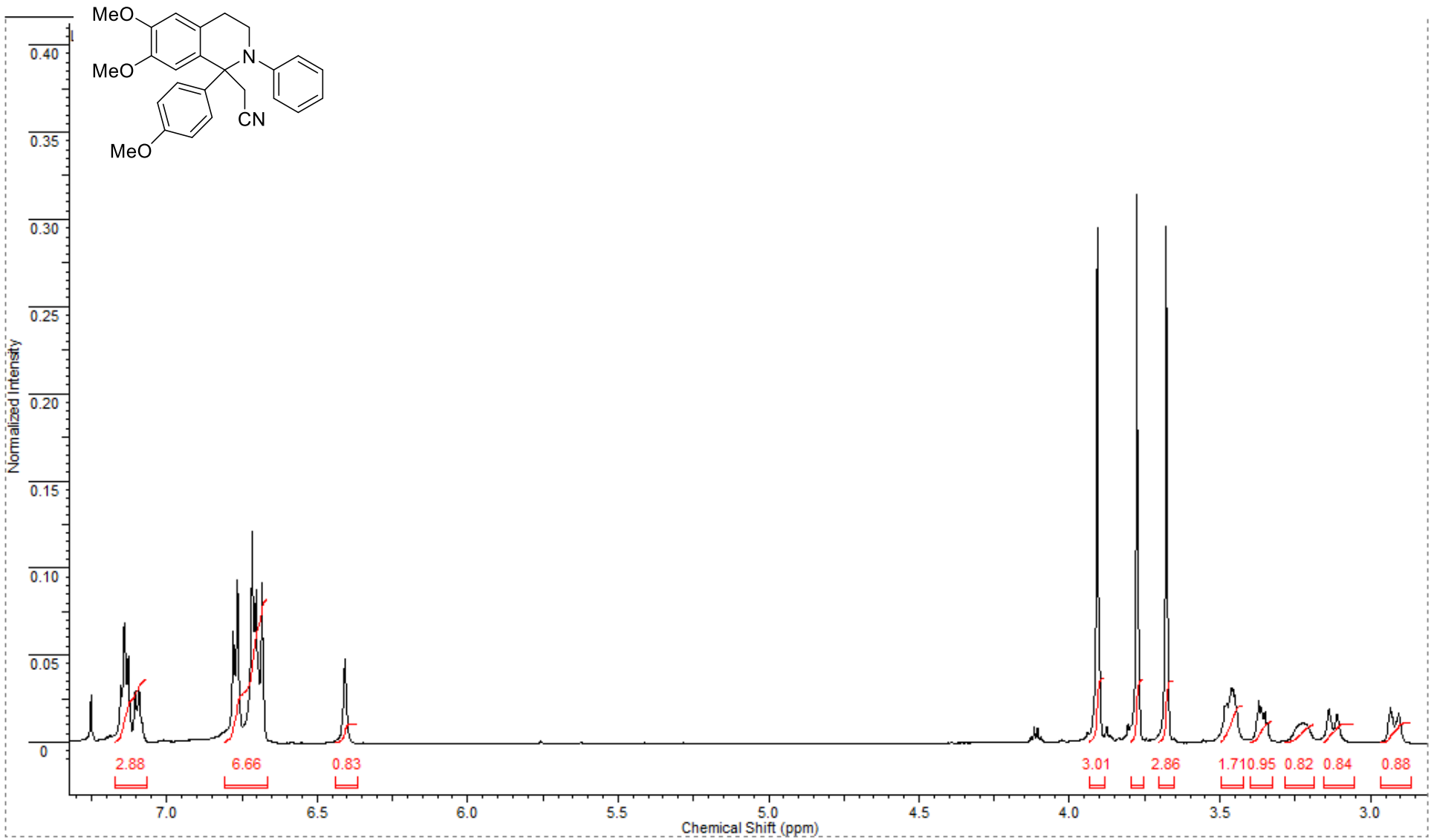
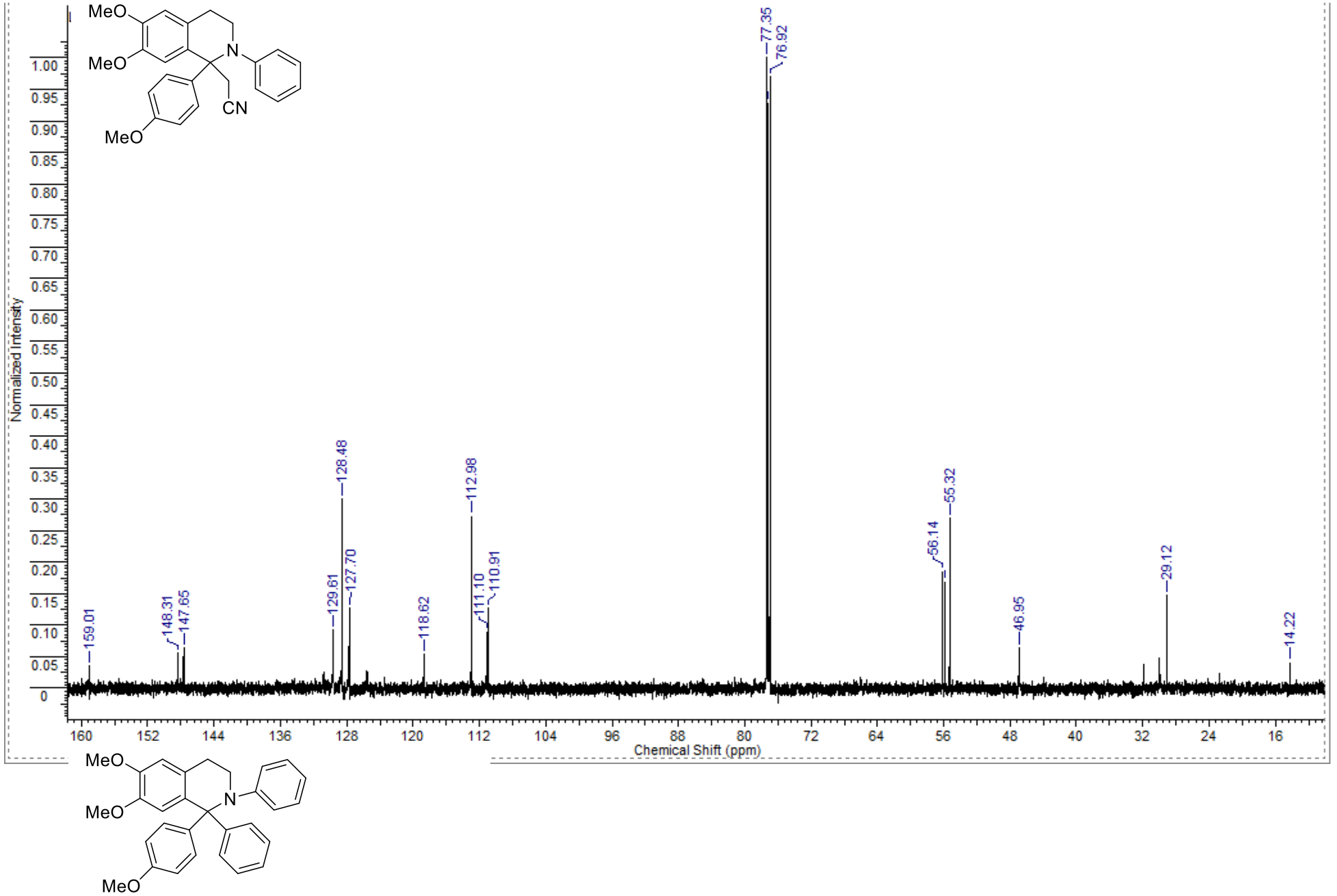
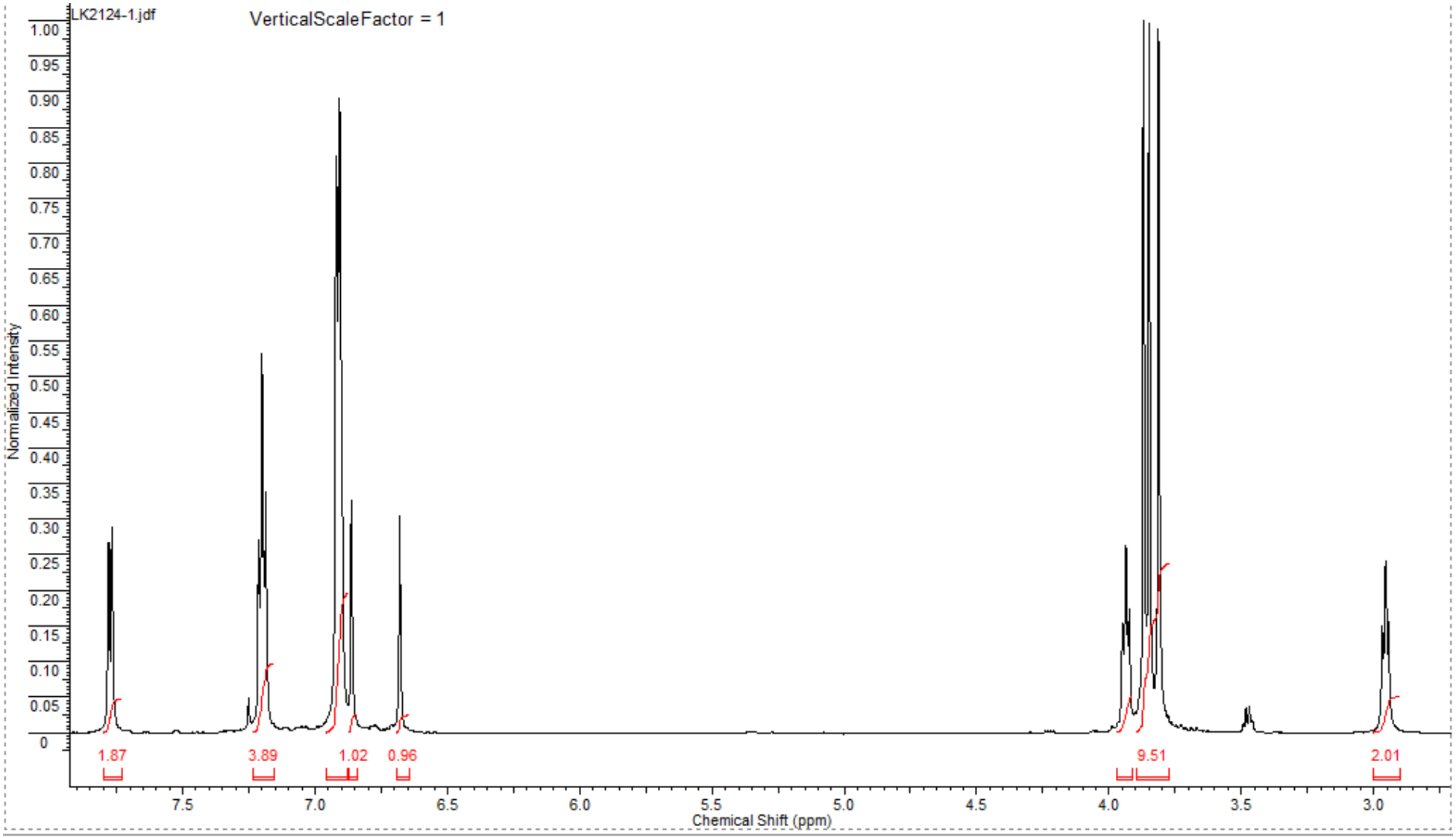
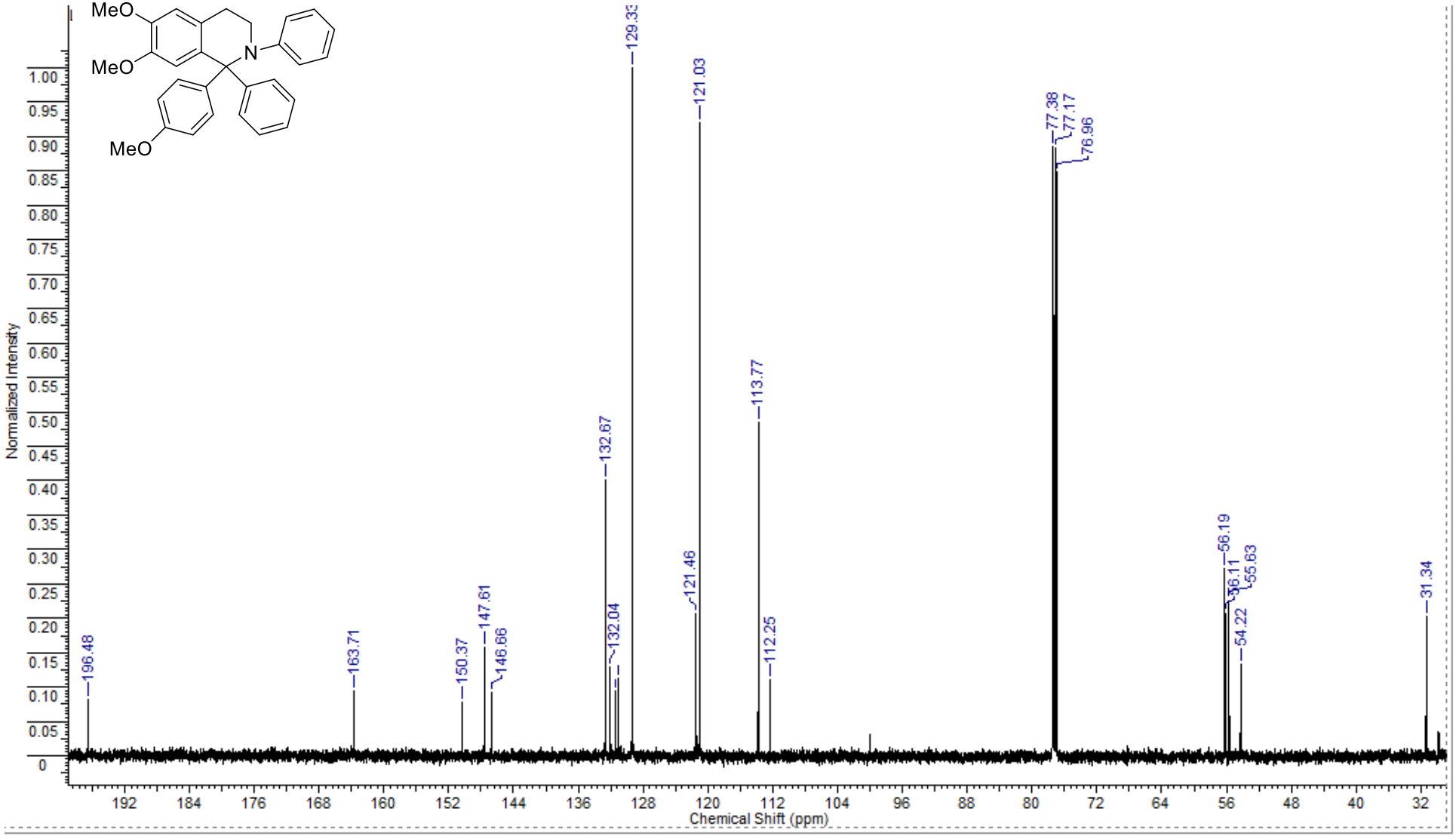
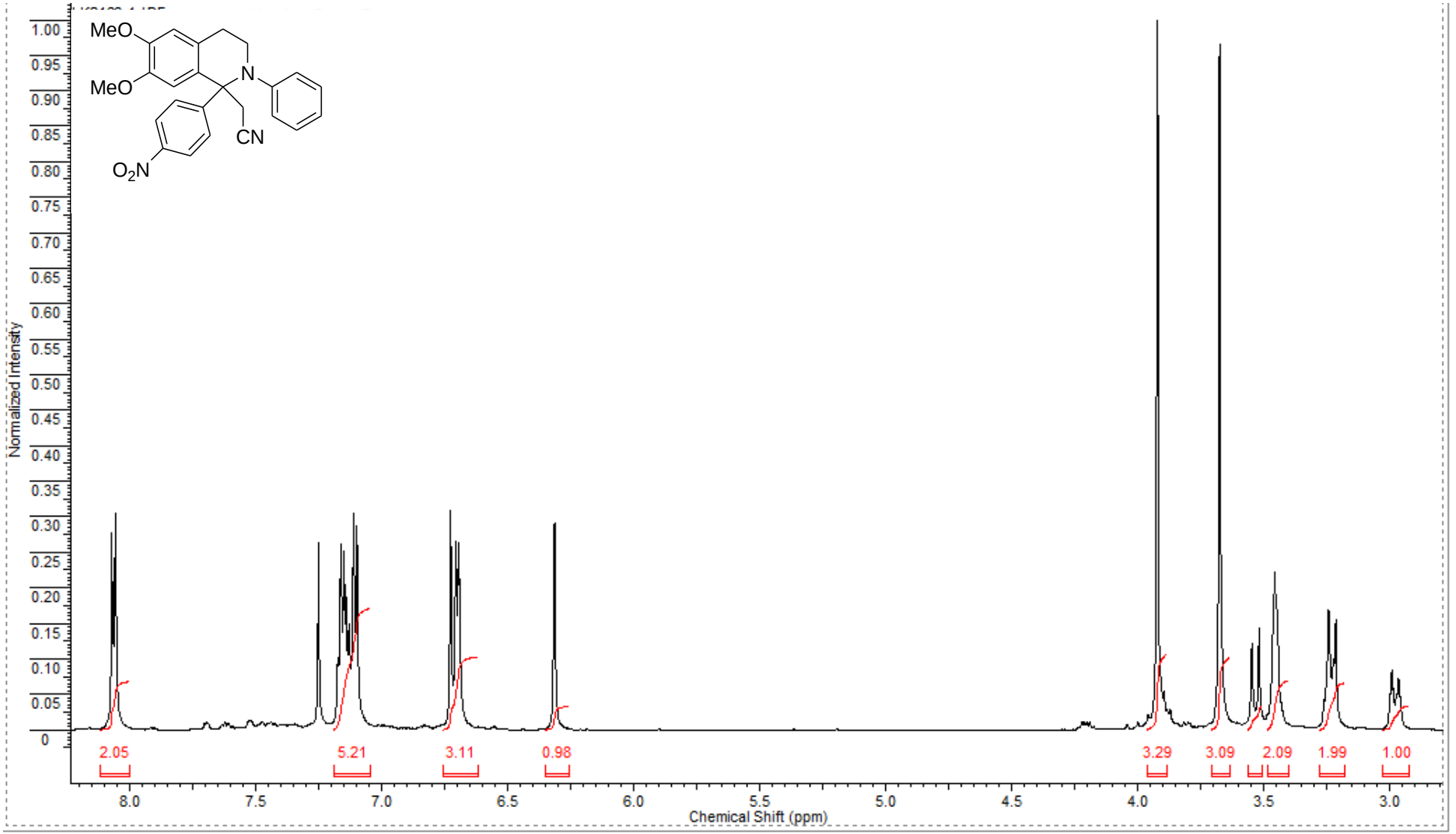
24
Chemical Shift (ppm)

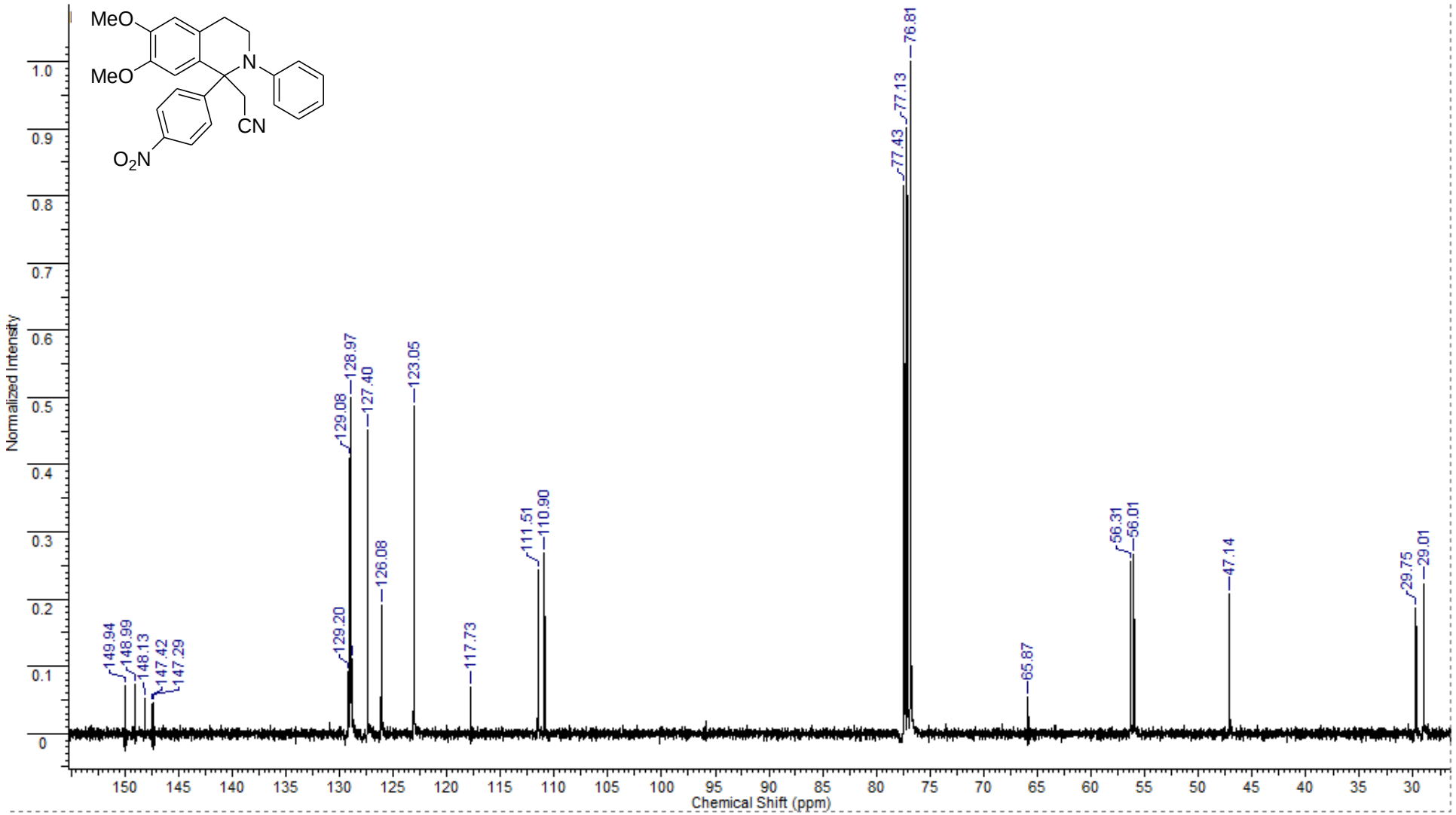

MeO
MeO
MeO
N
CN
Normalized Intensity
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
2.88
6.66
0.83
3.01
2.86
1.71
0.95
0.82
0.84
0.88
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

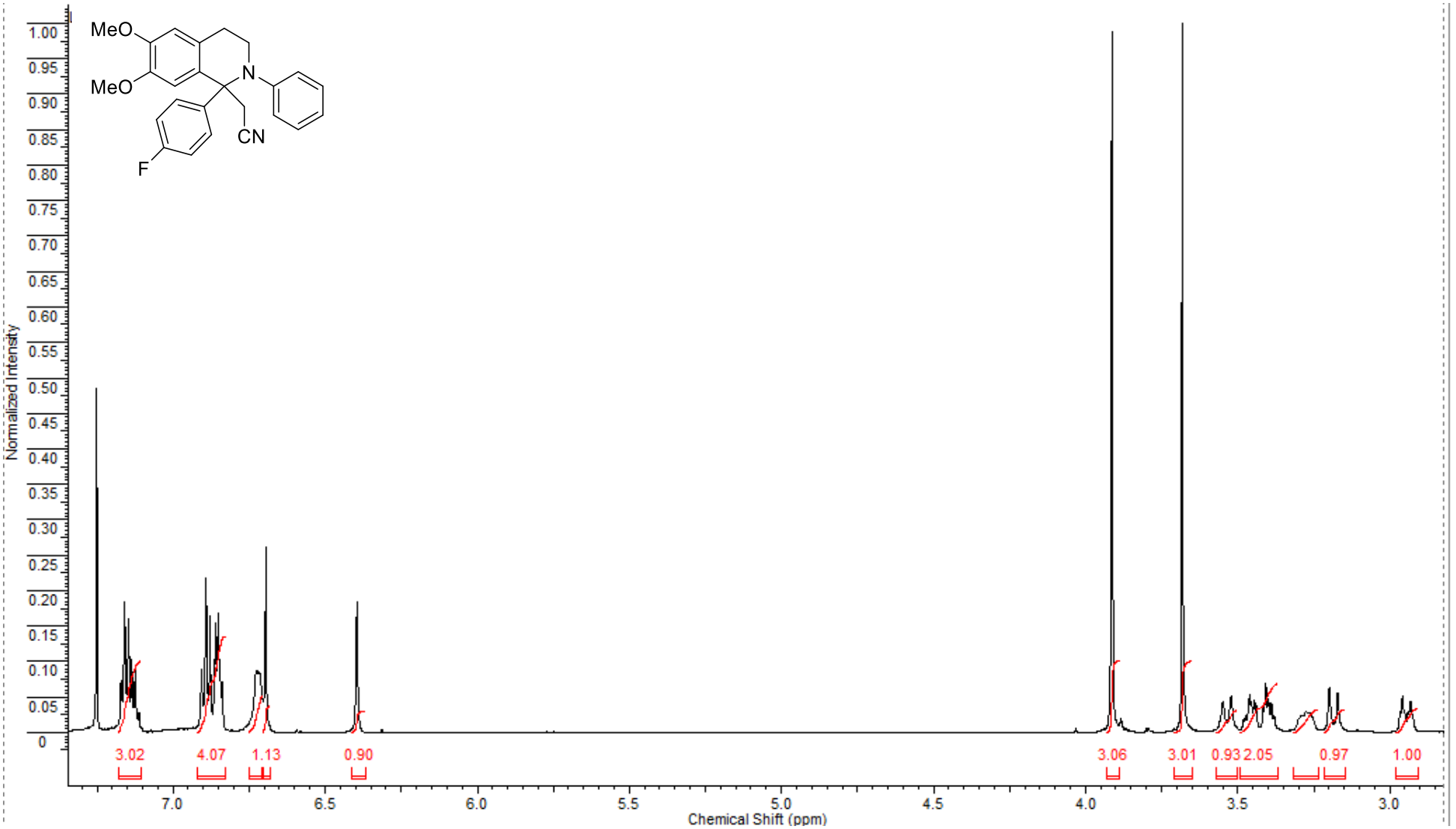

MeO
MeO
N
CN
MeO
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
159.01
148.31
147.65
129.61
128.48
127.70
118.62
112.98
111.10
110.91
77.35
76.92
56.14
55.32
46.95
29.12
14.22
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
Chemical Shift (ppm)
MeO
MeO
N
MeO

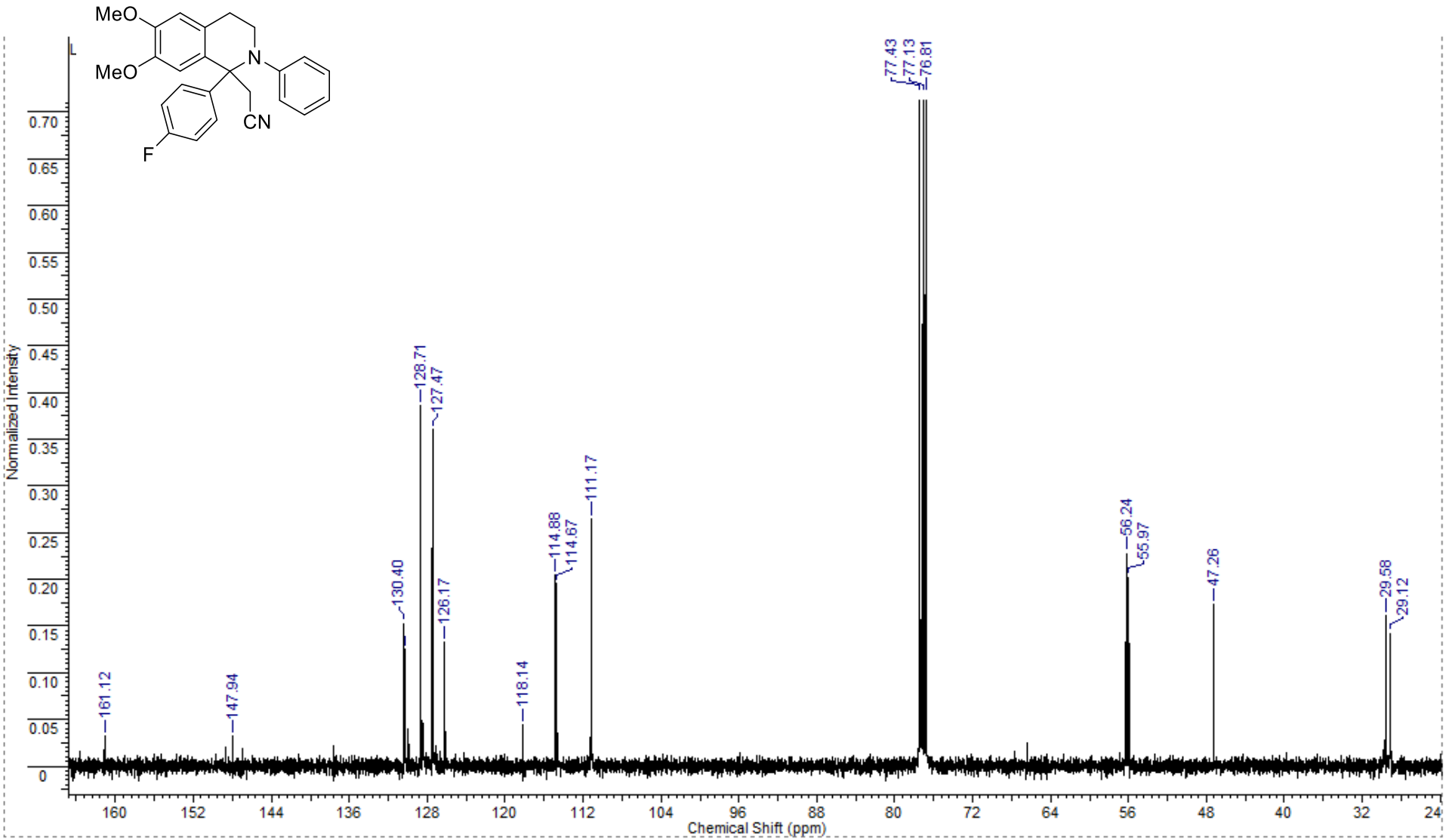

LK2124-1.jdf
VerticalScaleFactor = 1
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.87
3.89
1.02
0.96
9.51
2.01
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

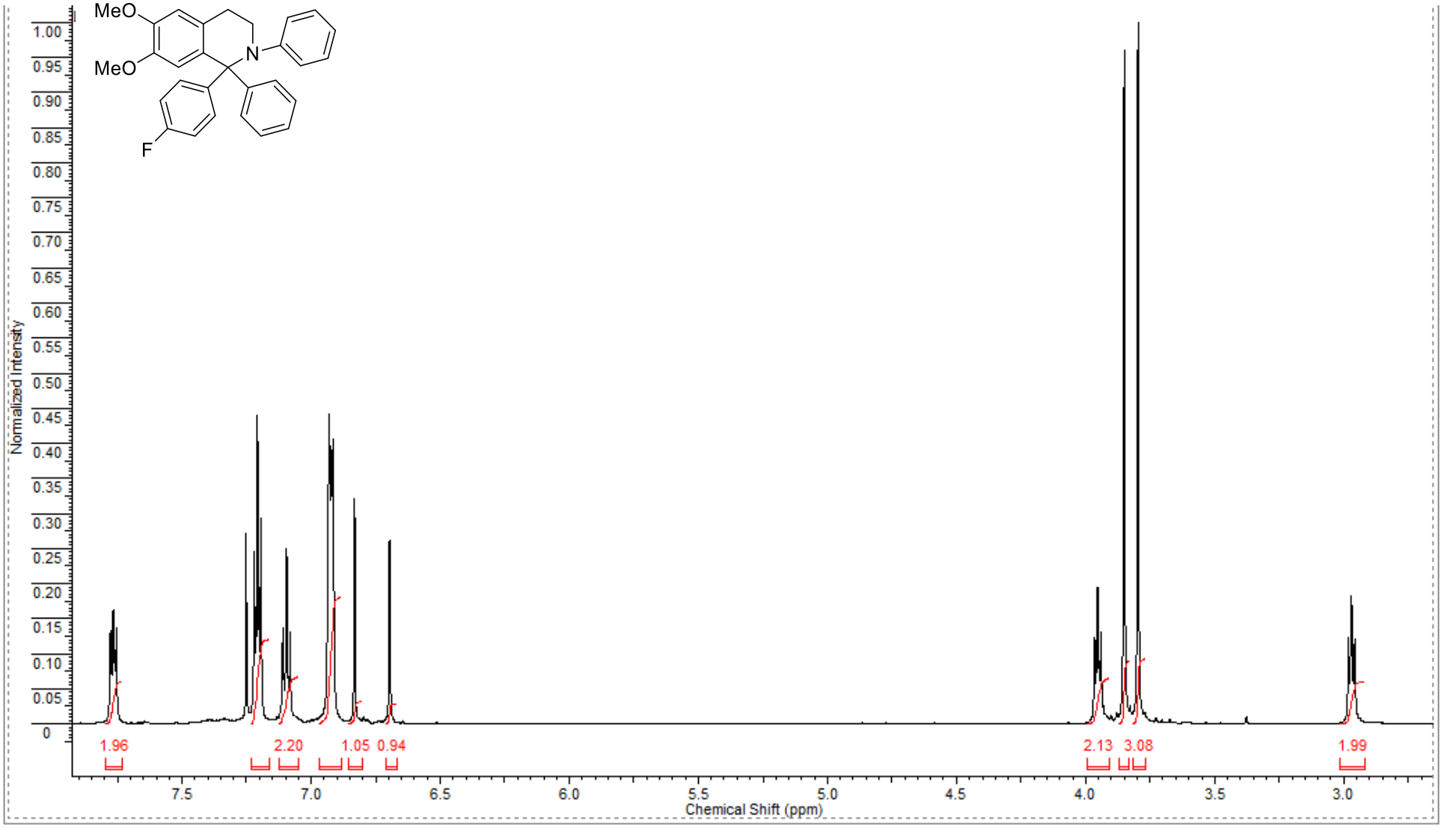

MeO
MeO
MeO
N
Normalized Intensity
Chemical Shift (ppm)
196.48
163.71
150.37
147.61
146.66
132.67
132.04
129.33
121.46
121.03
113.77
112.25
77.38
77.17
76.96
56.19
56.11
55.63
54.22
31.34

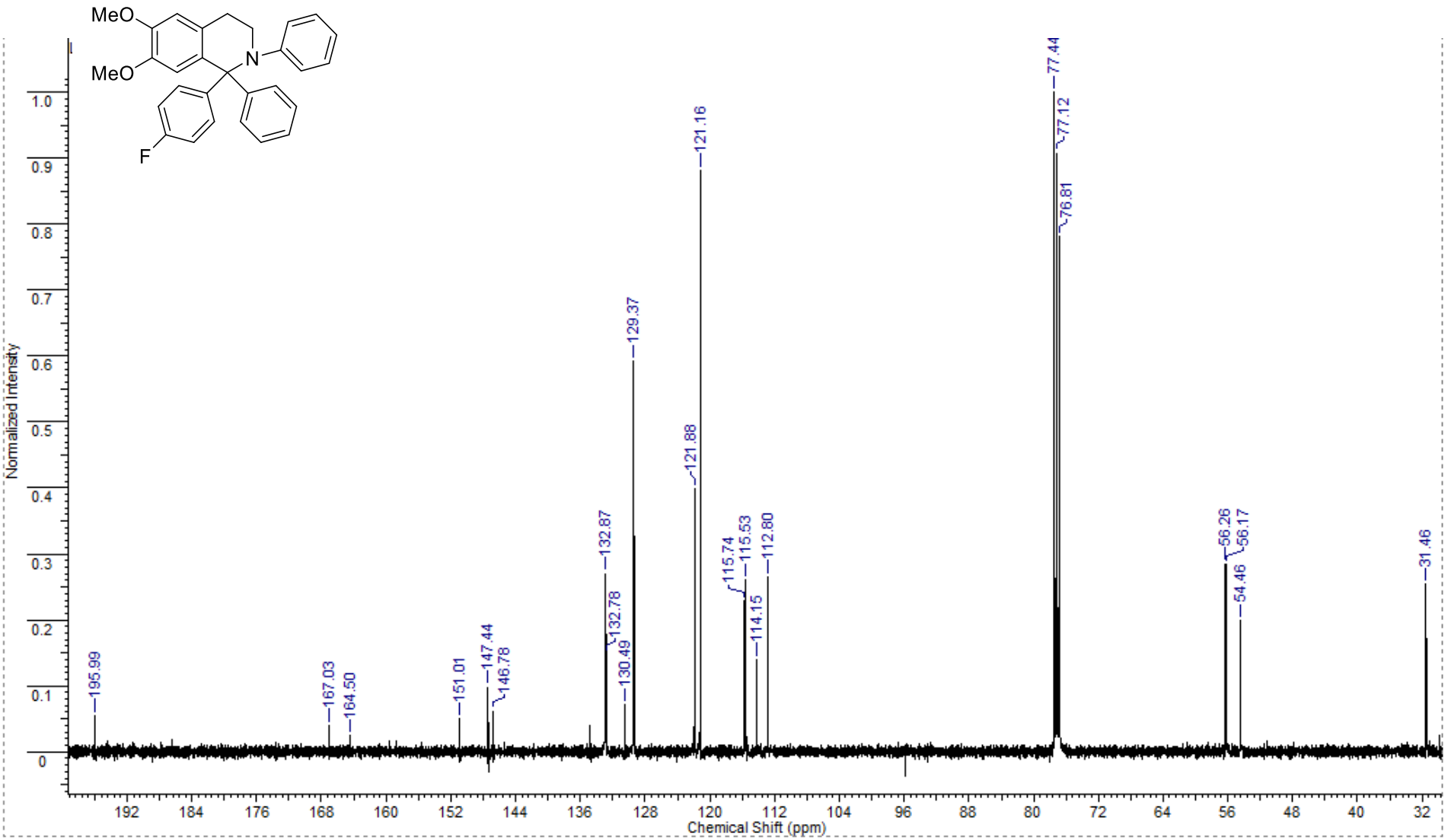

MeO
MeO
N
CN
O2N
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
2.05
5.21
3.11
0.98
3.29
3.09
2.09
1.99
1.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

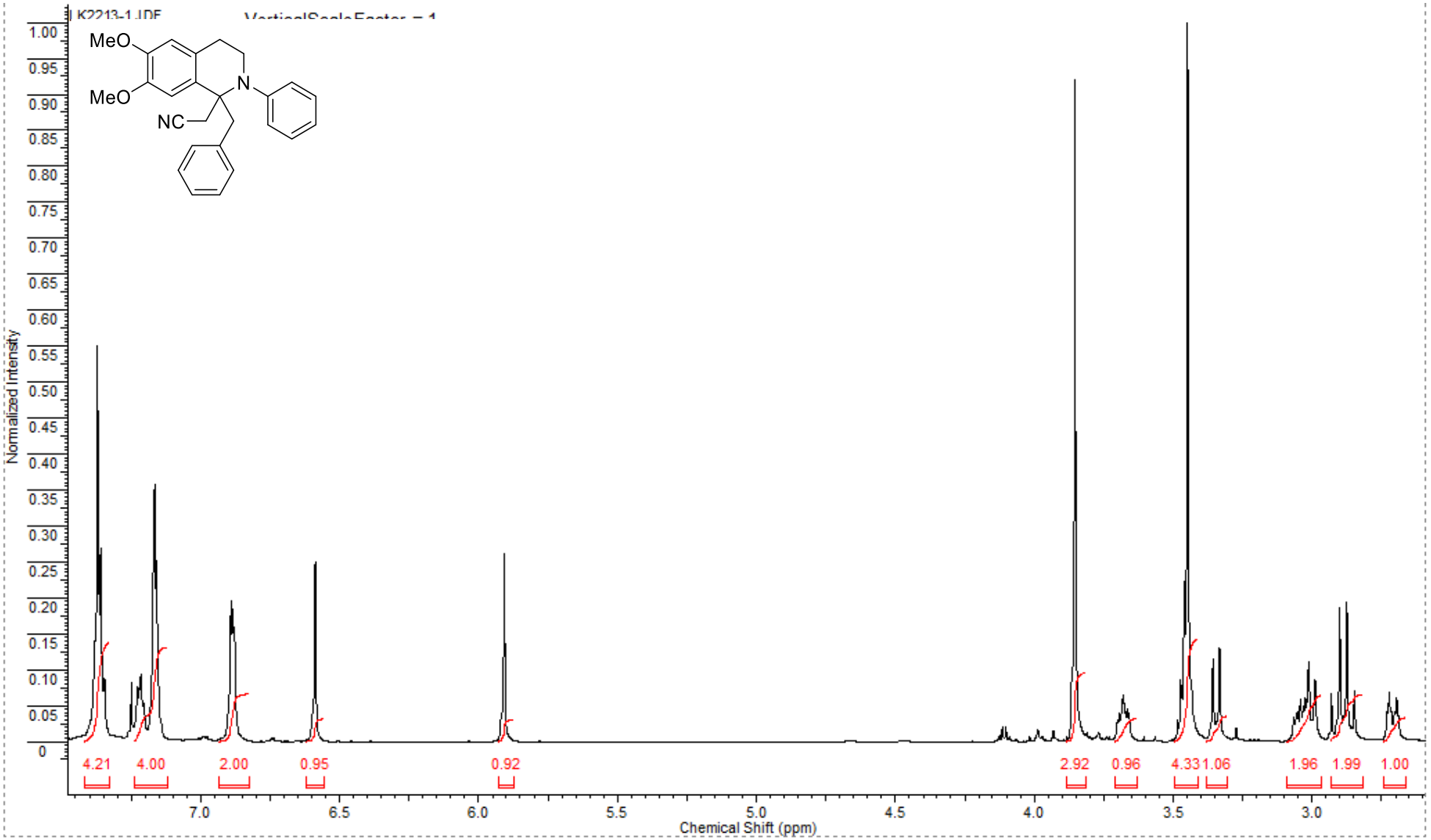

MeO
MeO
N
CN
O2N
Normalized Intensity
Chemical Shift (ppm)
149.94
148.99
148.13
147.42
147.29
129.20
129.08
128.97
127.40
126.08
123.05
117.73
111.51
110.90
77.43
77.13
76.81
65.87
56.31
56.01
47.14
29.75
29.01

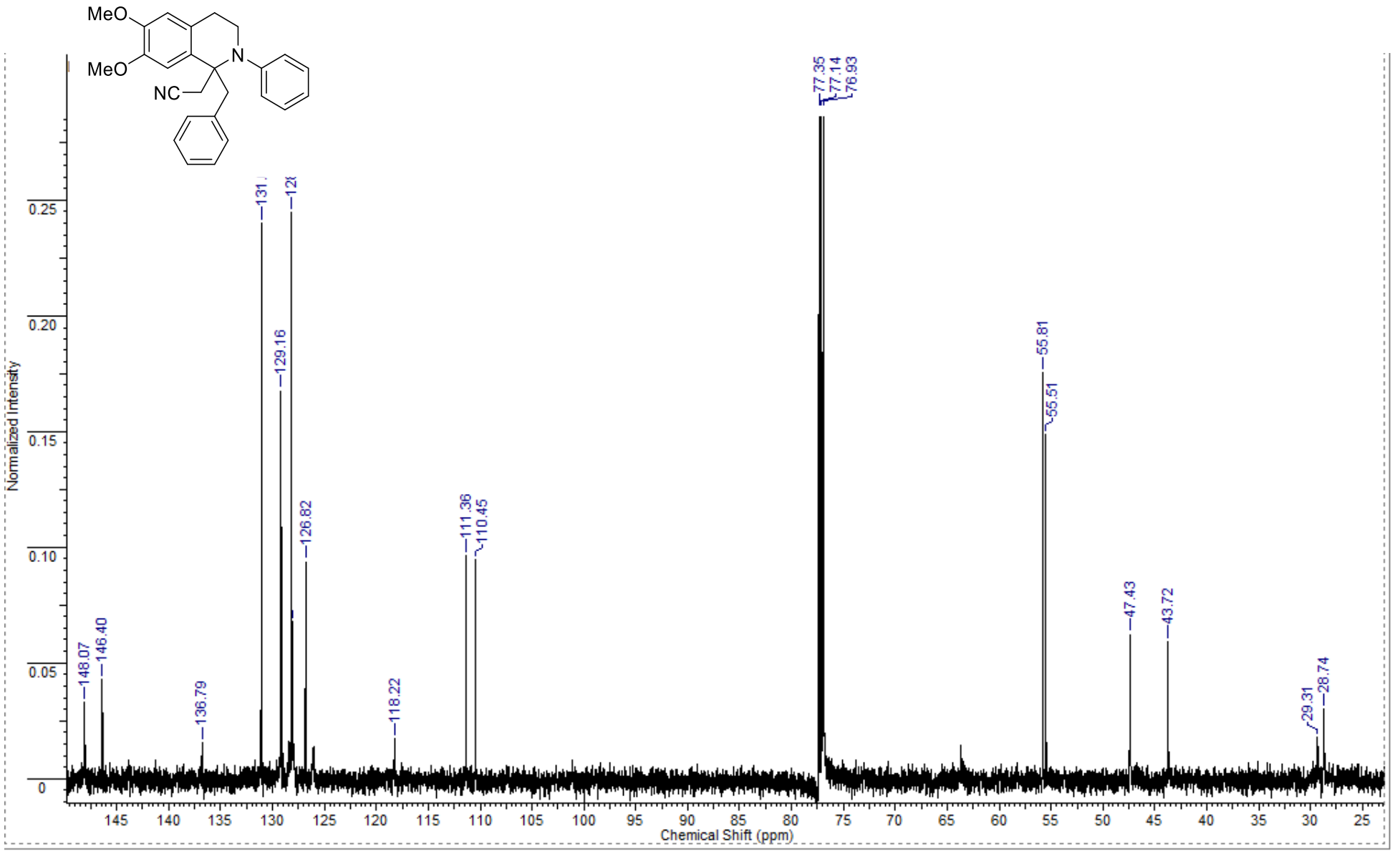

MeO
MeO
N
CN
F
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
3.02
4.07
1.13
0.90
3.06
3.01
0.93
2.05
0.97
1.00
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

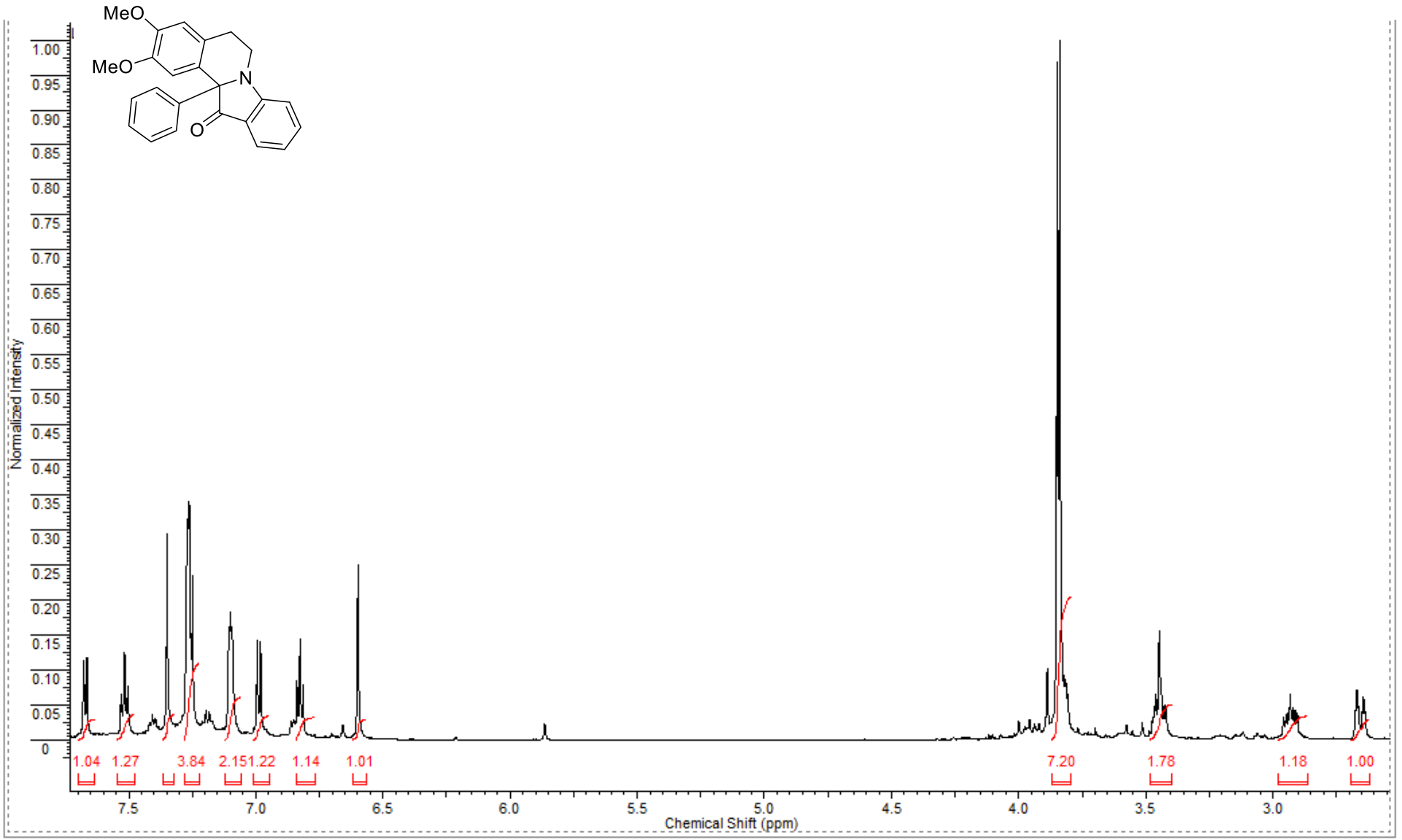

MeO
MeO
N
CN
F
Normalized Intensity
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
161.12
147.94
130.40
128.71
127.47
126.17
118.14
114.88
114.67
111.17
77.43
77.13
76.81
56.24
55.97
47.26
29.58
29.12
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

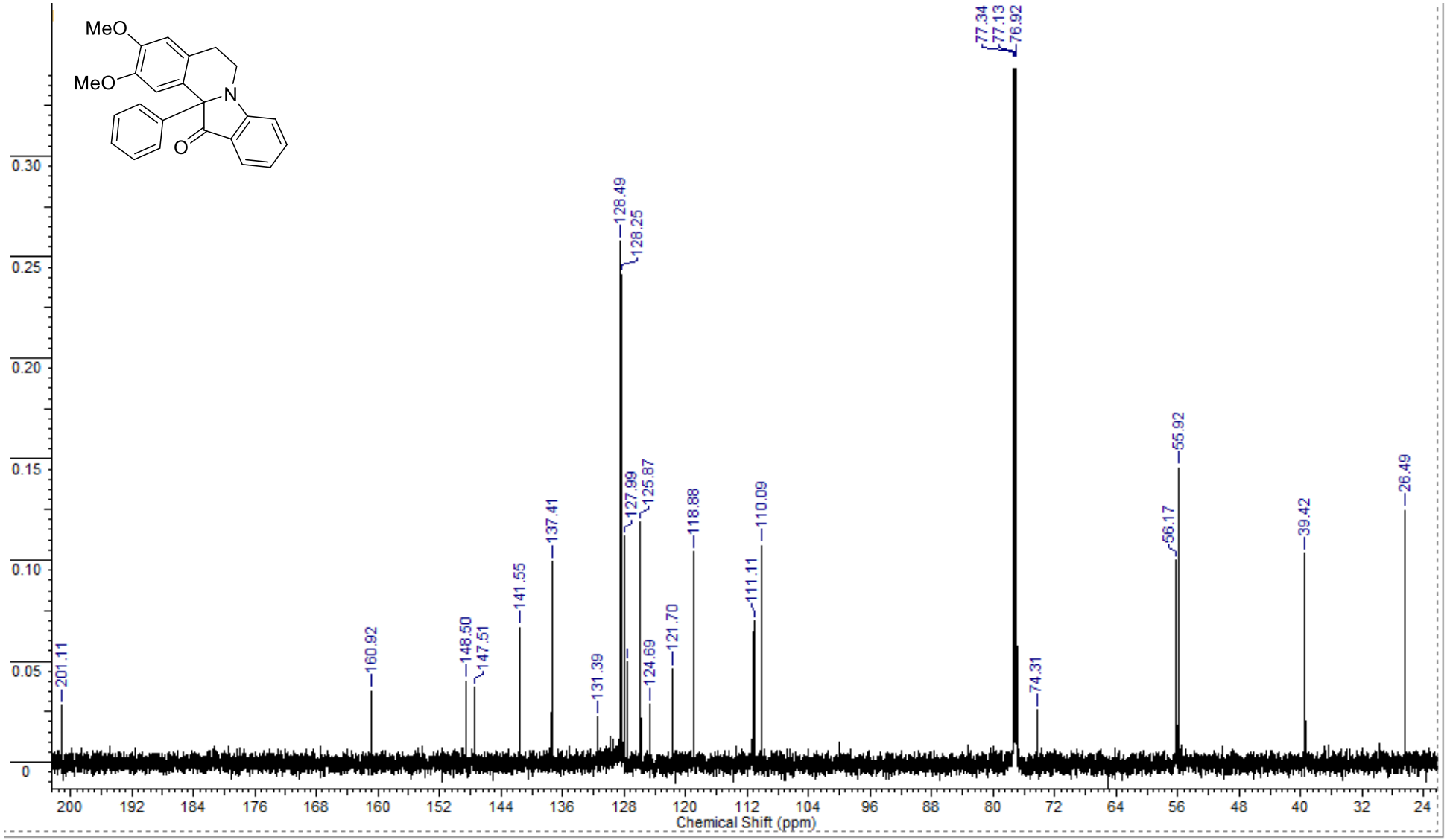

MeO
MeO
N
F
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.96
2.20
1.05
0.94
2.13
3.08
1.99
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

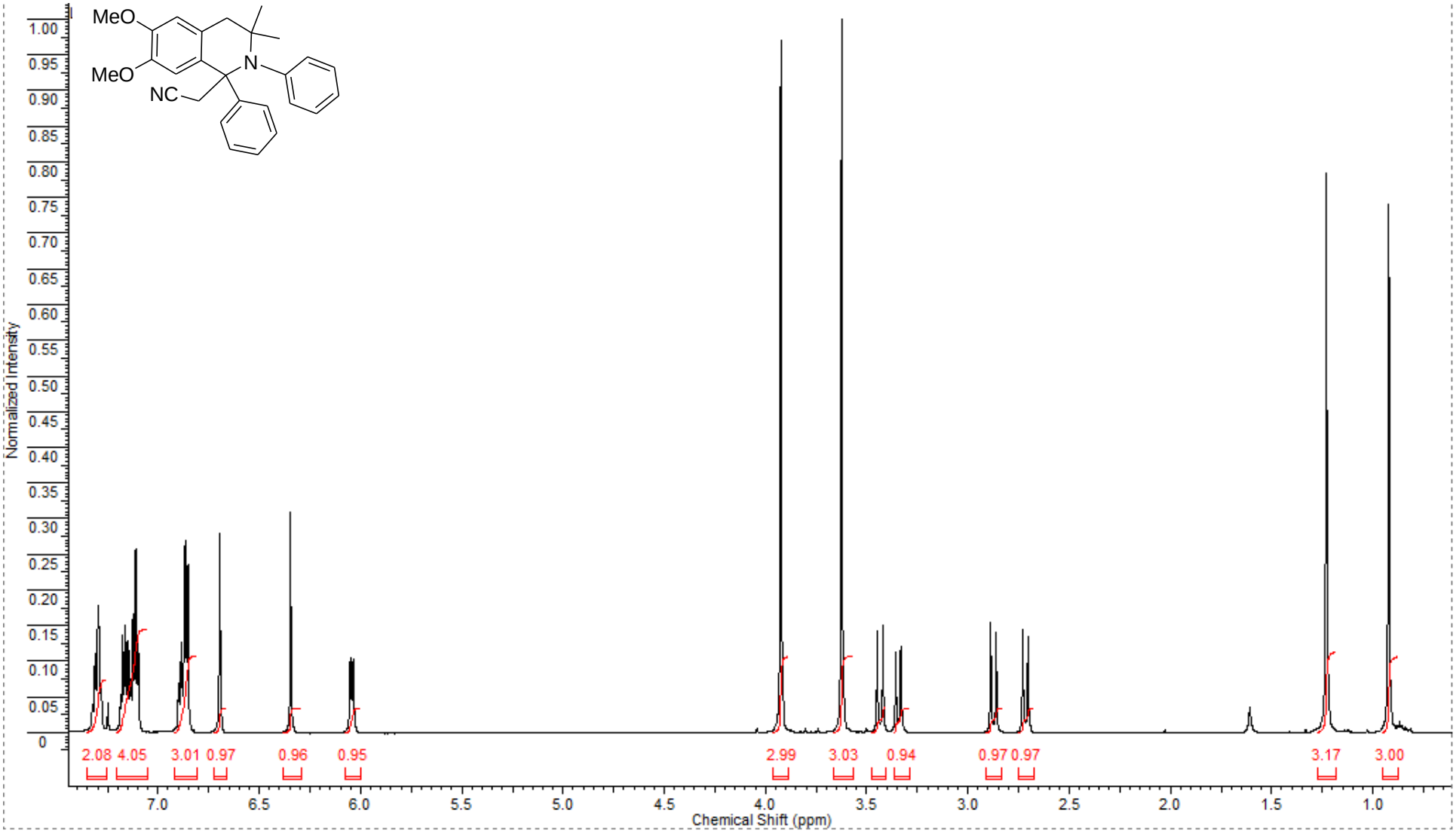

MeO
MeO
N
F
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
195.99
167.03
164.50
151.01
147.44
146.78
132.87
132.78
130.49
129.37
121.88
121.16
115.74
115.53
114.15
112.80
77.44
77.12
76.81
56.26
56.17
54.46
31.46
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
Chemical Shift (ppm)

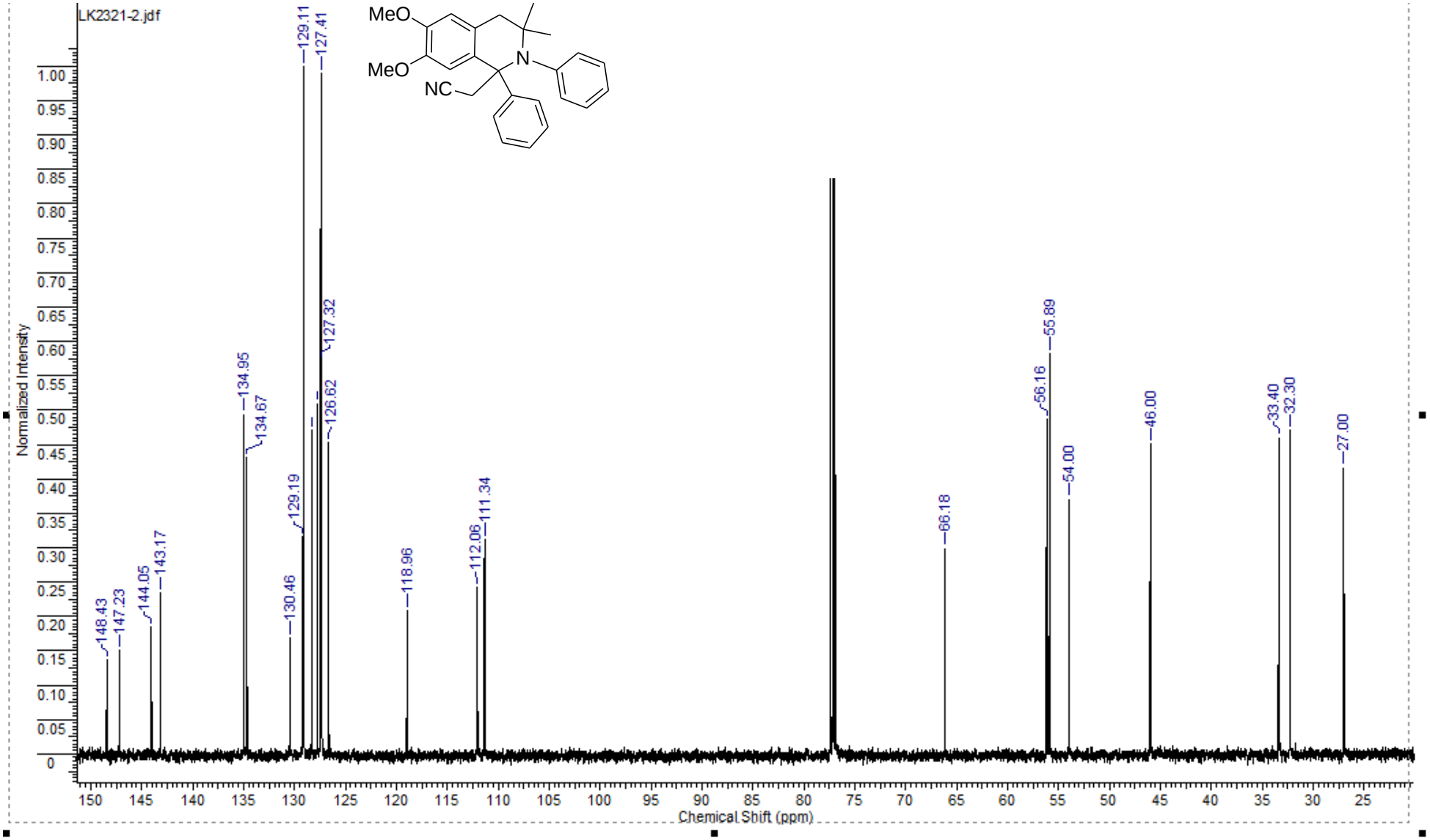

MeO
MeO
NC
N
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
4.21
4.00
2.00
0.95
0.92
2.92
0.96
4.33
1.06
1.96
1.99
1.00
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

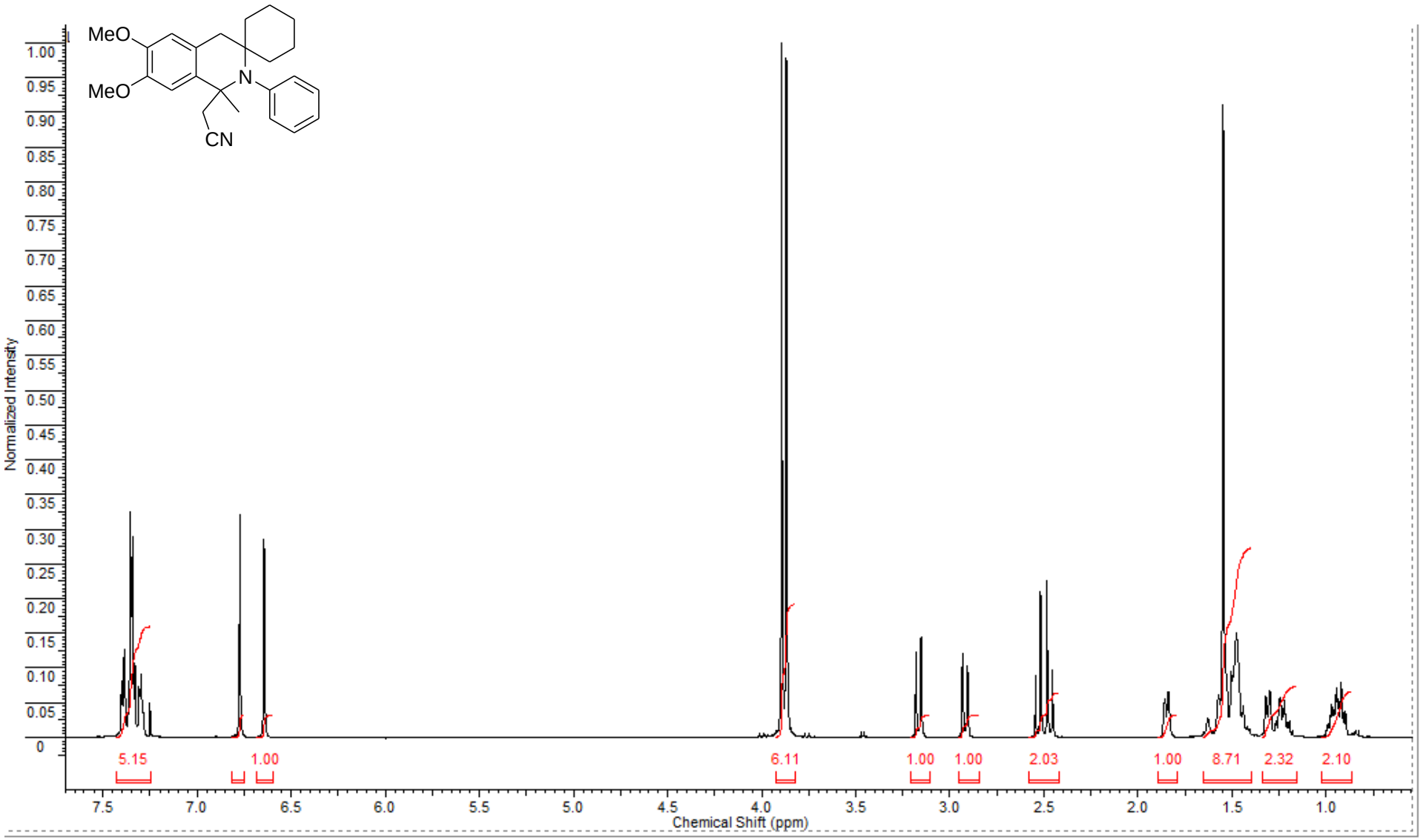

MeO
MeO
N
NC
Normalized Intensity
0.25
0.20
0.15
0.10
0.05
0
77.35
77.14
76.93
131.
12
129.16
126.82
111.36
110.45
55.81
55.51
47.43
43.72
29.31
28.74
148.07
146.40
136.79
118.22
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
Chemical Shift (ppm)

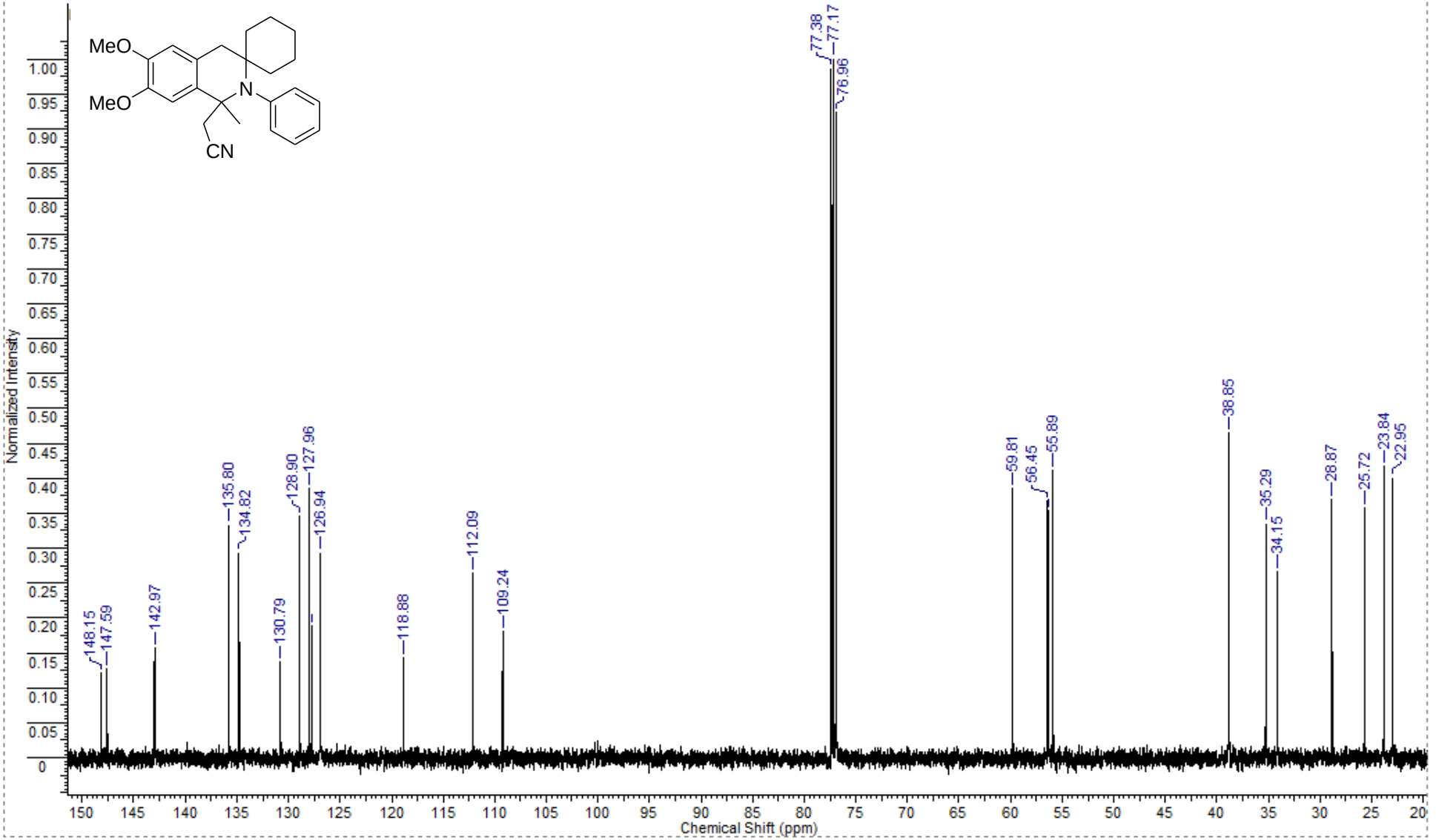

MeO
MeO
N
O
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
1.04
1.27
3.84
2.15
1.22
1.14
1.01
7.20
1.78
1.18
1.00
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)

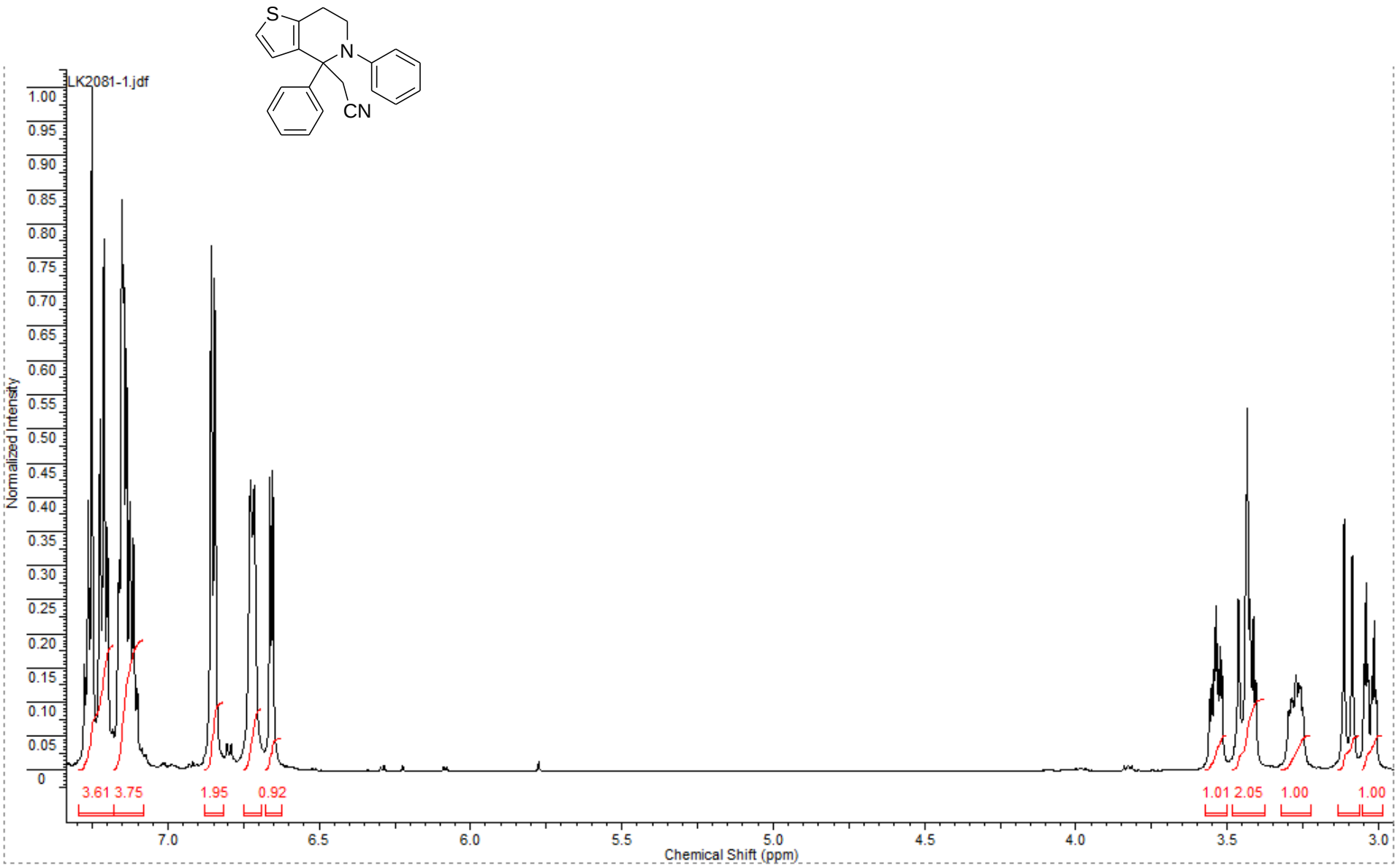

MeO
MeO
N
O
77.34
77.13
76.92
128.49
128.25
127.99
125.87
118.88
110.09
111.11
137.41
141.55
131.39
148.50
147.51
160.92
201.11
124.69
121.70
74.31
56.17
55.92
39.42
26.49
0.30
0.25
0.20
0.15
0.10
0.05
0
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)

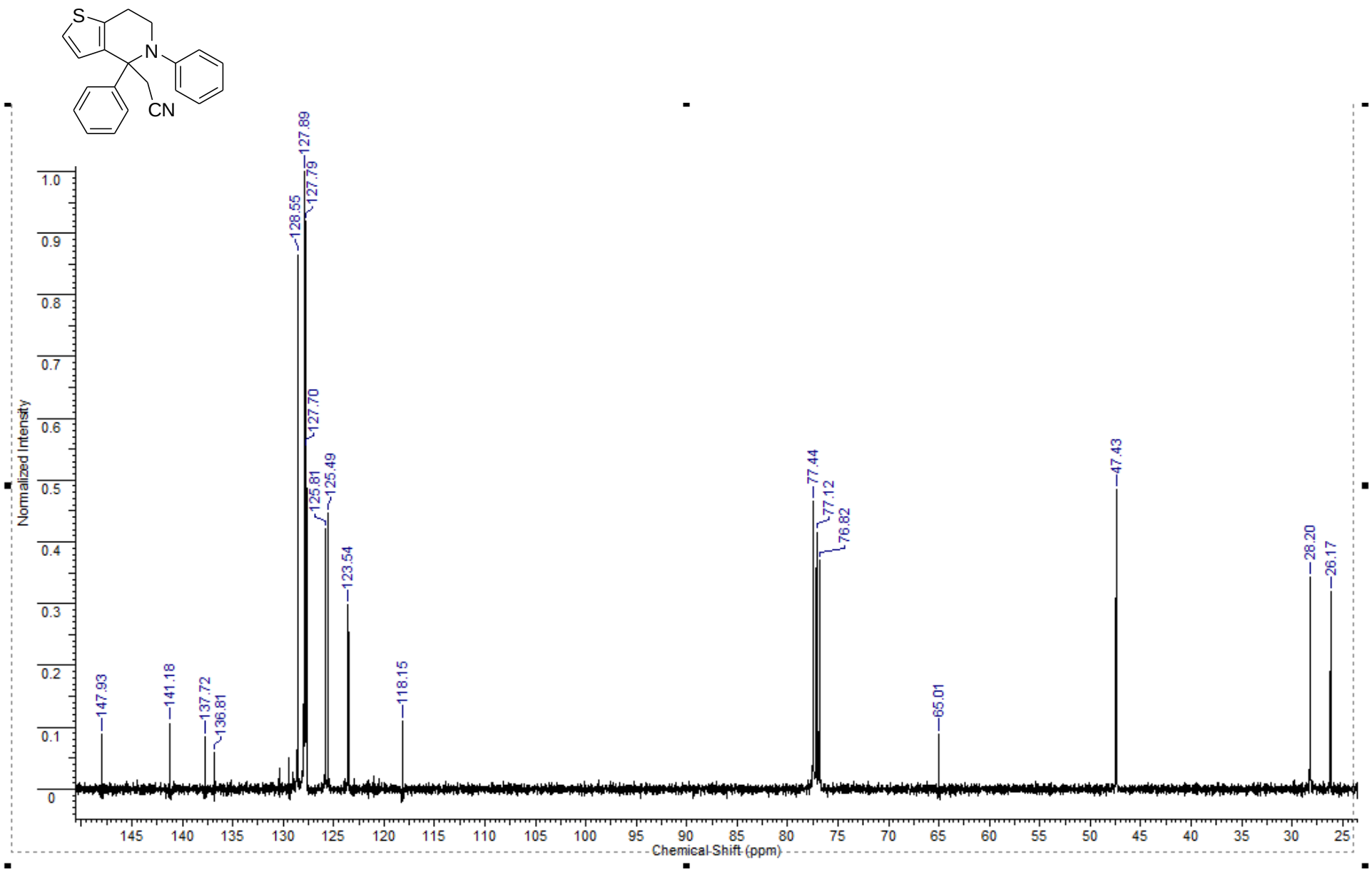

MeO
MeO
NC
N
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
2.08 4.05 3.01 0.97 0.96 0.95 2.99 3.03 0.94 0.97 0.97 3.17 3.00
7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0
Chemical Shift (ppm)

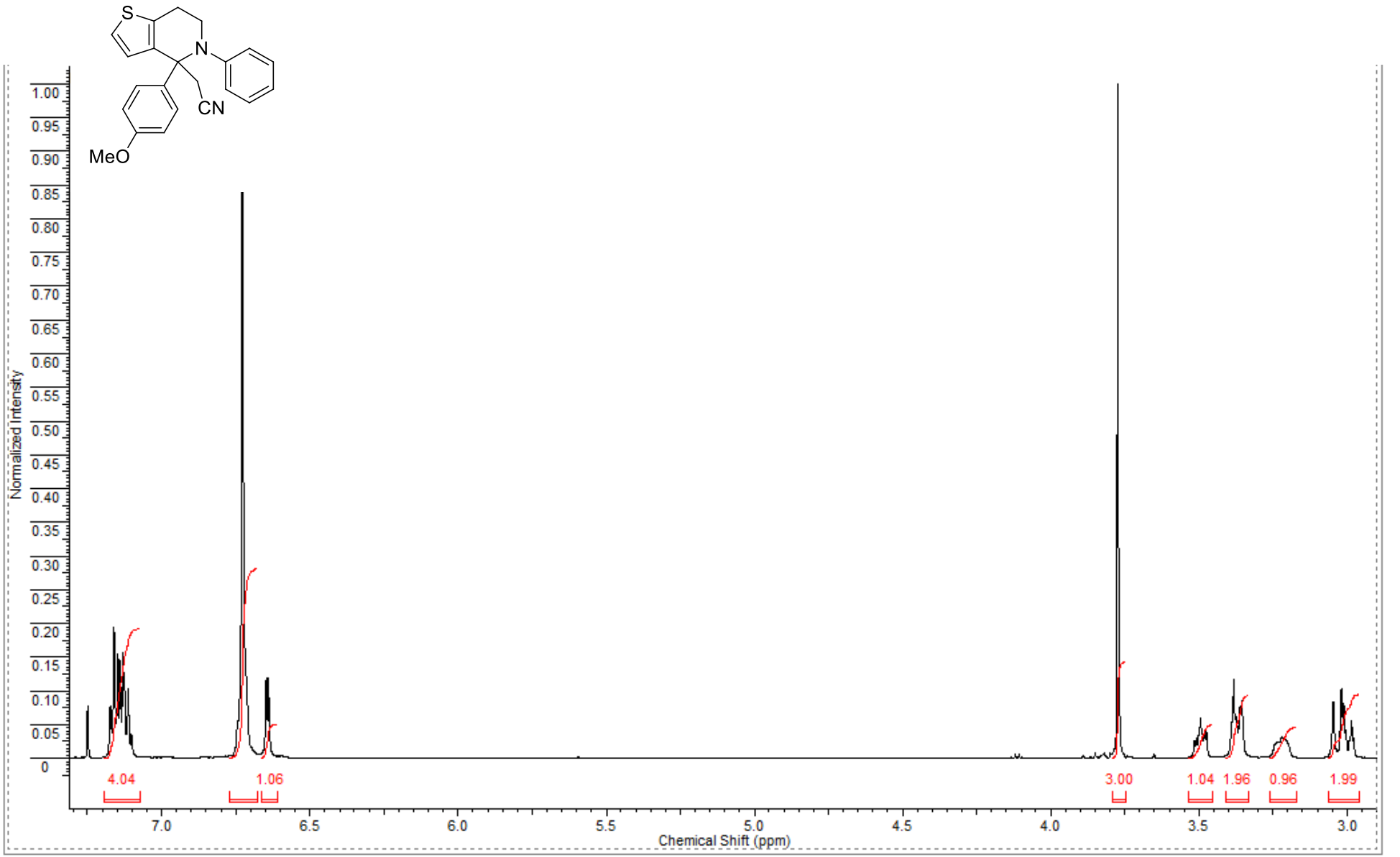

LKZ321-2.jdf
MeO
MeO
N
NC
Normalized Intensity
Chemical Shift (ppm)
148.43
147.23
144.05
143.17
134.95
134.67
130.46
129.19
129.11
127.41
127.32
126.62
118.96
112.06
111.34
66.18
56.16
55.89
54.00
46.00
33.40
32.30
27.00

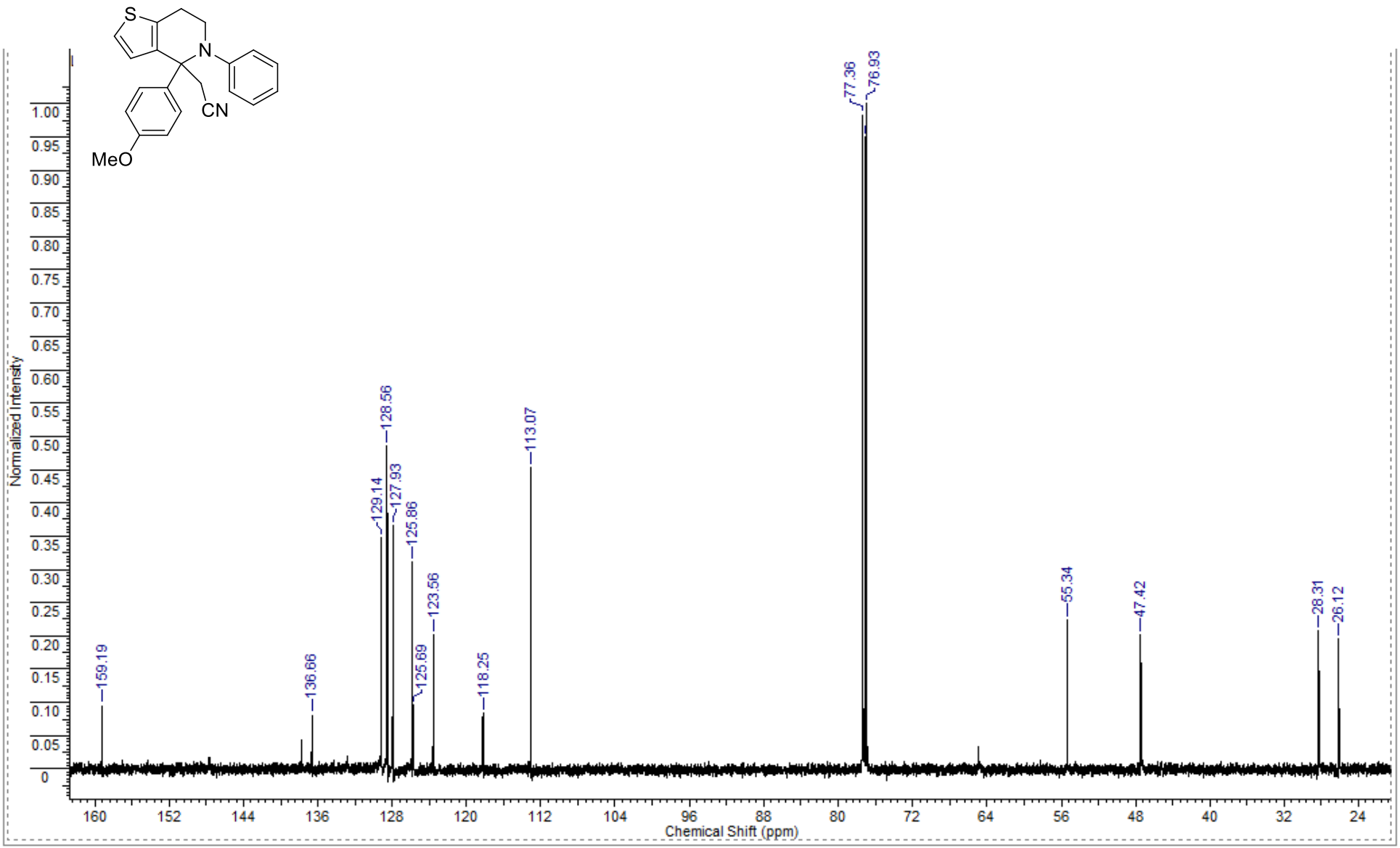

MeO
MeO
N
CN
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
5.15
1.00
6.11
1.00
1.00
2.03
1.00
8.71
2.32
2.10
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
Chemical Shift (ppm)


MeO
MeO
N
CN
Normalized Intensity
Chemical Shift (ppm)
148.15
147.59
142.97
135.80
134.82
130.79
128.90
127.96
126.94
118.88
112.09
109.24
77.38
77.17
76.96
59.81
56.45
55.89
38.85
35.29
34.15
28.87
25.72
23.84
22.95


S
N
CN
LK2081-1.jdf
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
3.61 3.75
1.95
0.92
1.01 2.05
1.00
1.00
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)


S
N
CN
Normalized Intensity
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
147.93
141.18
137.72
136.81
128.55
127.89
127.79
127.70
125.81
125.49
123.54
118.15
77.44
77.12
76.82
65.01
47.43
28.20
26.17
145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25
Chemical Shift (ppm)


S
N
CN
MeO
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
4.04
1.06
3.00
1.04
1.96
0.96
1.99
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
Chemical Shift (ppm)


S
N
CN
MeO
Normalized Intensity
1.00
0.95
0.90
0.85
0.80
0.75
0.70
0.65
0.60
0.55
0.50
0.45
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0
159.19
136.66
129.14
128.56
127.93
125.86
125.69
123.56
118.25
113.07
77.36
76.93
55.34
47.42
28.31
26.12
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
Chemical Shift (ppm)