

Supporting Information

Concise and efficient one-pot copper-catalyzed synthesis of *H*-pyrazolo[5,1-*a*]isoquinolines

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General experimental procedures

All reactions were carried out under nitrogen atmosphere. Proton and carbon magnetic resonance spectra (^1H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of CDCl_3 as the internal standard (^1H NMR: TMS at 0.00 ppm, CDCl_3 at 7.26 ppm; ^{13}C NMR: CDCl_3 at 77.0 ppm) or tetramethylsilane (TMS) in the solvent of $\text{DMSO}-d_6$ as the internal standard (^1H NMR: TMS at 0.00 ppm, DMSO at 2.50 ppm; ^{13}C NMR: DMSO at 40.0 ppm).

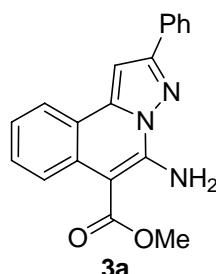
Synthesis of compounds 1a-d and 1f. Compounds **1a-d** and **1f** were prepared according to the previous procedure.¹

Synthesis of compound 1e: Compound **1e** was prepared according to the previous procedure.^{2,3}

General procedure for synthesis of compounds 3a-l. Substituted 1-(2-bromophenyl)-3-alkylprop-2-yn-1-one (0.25 mmol), hydrazine hydrochloride (0.30 mmol), alkyl 2-cyanoacetate (1.25 mmol), CuI (0.025 mmol, 4.8 mg), K_3PO_4 (1.25 mmol, 265 mg), dried DMF (2 mL) were added to a 25 mL Schlenk tube with a magnetic stirrer under nitrogen atmosphere. The mixture was allowed to stir under nitrogen atmosphere at 100 °C for 24 h. After cooled to room temperature, the resulting solution was concentrated via rotary evaporation, and the residue was purified by column chromatography on silica gel to provide the desired product (**3a-l**).

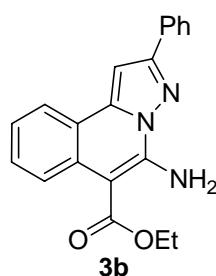
General procedure for synthesis of compounds 3m-x. Substituted 1-(2-bromophenyl)-3-alkylprop-2-yn-1-one (0.25 mmol), hydrazine hydrochloride (0.30 mmol), K_3PO_4 (1.25 mmol, 265 mg) or Cs_2CO_3 (1.25 mmol, 410 mg) (see Table 3 in Text) were added to a 25ml Schlenk tube with a magnetic stirrer under nitrogen atmosphere. The mixture was allowed to stir under nitrogen atmosphere at 80 °C for 12 h. After cooled to room temperature, malononitrile, acetylacetone or ethyl acetoacetate (1.25 mmol), and CuI (0.025 mmol, 4.8 mg) were added to the tube under nitrogen atmosphere. The mixture was allowed to stir under nitrogen atmosphere at 100 °C for 24 h. After cooled to room temperature, the resulting solution was concentrated via rotary evaporation, and the residue was purified by column chromatography on silica gel to provide the desired product.

Characterization data of compounds **3a-x** and **Ia**

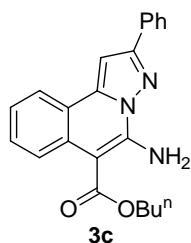


Methyl 5-amino-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3a).

Eluent: petroleum ether/ethyl acetate (10:1). Yield 63 mg (80%). Light yellow solid, mp 156-158 °C. IR ν_{\max} (KBr)/cm⁻¹ 3443 (NH), 1663 (C=O). ¹H NMR (CDCl₃, 300 MHz) δ 8.59 (d, 1H, *J* = 8.6 Hz), 7.96 (m, 3H), 7.85 (s, 2H), 7.42 (m, 4H), 7.25 (m, 1H), 7.14 (s, 1H), 3.98 (s, 3H). ¹³C NMR (CDCl₃, 75 MHz) δ 169.7, 154.3, 147.1, 140.8, 132.5, 129.0, 128.8, 126.6, 125.4, 123.9, 123.5, 118.1, 96.3, 86.9, 51.6. HR-MS (ESI) [M+H]⁺ m/z calcd for C₁₉H₁₆N₃O₂ 318.1243, found 318.1245.

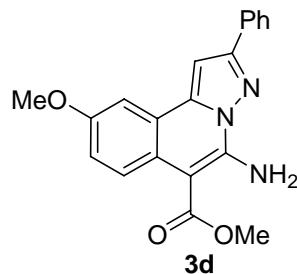


Ethyl 5-amino-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3b). Eluent: petroleum ether/ethyl acetate (10:1). Yield 67 mg (82%). Light yellow solid, mp 148-150 °C. IR ν_{\max} (KBr)/cm⁻¹ 3466 (NH), 1665 (C=O). ¹H NMR (CDCl₃, 300 MHz) δ 8.66 (d, 1H, *J* = 8.6 Hz), 7.98 (m, 3H), 7.86 (s, 2H), 7.43 (m, 4H), 7.25 (m, 1H), 7.17 (s, 1H), 4.47 (dd, 2H, *J* = 7.2 Hz), 1.49(t, 3H, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 75 MHz) δ 169.3, 154.3, 147.1, 140.7, 132.5, 129.2, 129.1, 128.9, 128.8, 126.6, 125.5, 123.9, 123.4, 118.2, 96.3, 87.0, 60.8, 14.7. HR-MS (ESI) [M+H]⁺ m/z calcd for C₂₀H₁₈N₃O₂ 332.1399, found 332.1402.

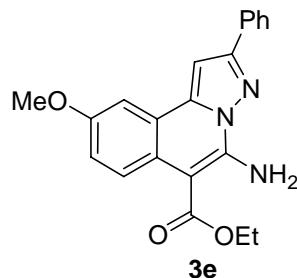


n-Butyl 5-amino-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3c).

Eluent: petroleum ether/ethyl acetate (10:1). Yield 68 mg (76%). Light yellow solid, mp 87-89 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3463 (NH), 1667 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.67 (d, 1H, J = 8.6 Hz), 7.97 (m, 3H), 7.87 (s, 2H), 7.44 (m, 4H), 7.27 (m, 1H), 7.21 (s, 1H), 4.43 (t, 2H, J = 6.9 Hz), 1.85 (m, 2H), 1.55 (m, 2H), 1.01 (t, 3H, J = 7.2 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.5, 154.3, 147.1, 140.8, 132.5, 129.2, 129.0, 128.9, 126.6, 125.5, 123.9, 123.5, 118.2, 96.3, 87.2, 64.8, 31.0, 19.7, 13.9. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{22}\text{H}_{22}\text{N}_3\text{O}_2$ 360.1712, found 360.1714.

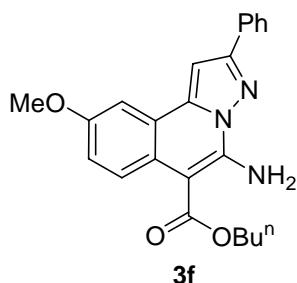


Methyl 5-amino-9-methoxy-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3d). Eluent: petroleum ether/ethyl acetate (10:1). Yield 71 mg (82%). Light yellow solid, mp 133-135 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3447 (NH), 1667 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.51 (d, 1H, J = 9.6 Hz), 7.98 (m, 2H), 7.67 (s, 2H), 7.43 (m, 3H), 7.25 (m, 1H), 7.08 (m, 2H), 3.96 (s, 3H), 3.87 (s, 3H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.6, 155.7, 154.0, 146.0, 140.4, 132.5, 129.0, 128.8, 127.2, 126.6, 122.8, 119.1, 117.9, 105.4, 96.2, 86.9, 55.4, 51.5. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{20}\text{H}_{18}\text{N}_3\text{O}_3$ 348.1348, found 348.1357.

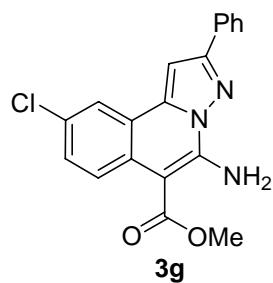


Methyl 5-amino-9-methoxy-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3e). Eluent: petroleum ether/ethyl acetate (10:1). Yield 78 mg (87%). Light yellow solid, mp 119-121 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3444 (NH), 1662 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.55 (d, 1H, J = 9.3 Hz), 7.97 (m, 2H), 7.65 (s, 2H), 7.43

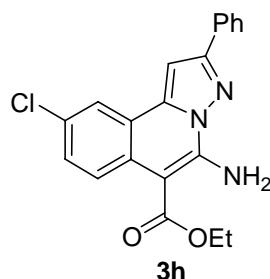
(m, 3H), 7.25 (m, 1H), 7.07 (m, 2H), 4.43 (dd, 2H, $J = 6.9$ Hz), 3.87 (s, 3H), 1.46 (t, 3H, $J = 7.2$ Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.2, 155.7, 154.0, 146.0, 140.4, 132.5, 128.9, 128.8, 127.2, 126.6, 122.9, 119.1, 117.9, 105.4, 96.1, 87.0, 60.7, 55.4, 14.7. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{21}\text{H}_{20}\text{N}_3\text{O}_3$ 362.1505, found 362.1504.



n-Butyl 5-amino-9-methoxy-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3f). Eluent: petroleum ether/ethyl acetate (10:1). Yield 85 mg (88%). Light yellow solid, mp 96-98 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3453 (NH), 1663 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.55 (d, 1H, $J = 9.6$ Hz), 7.97 (m, 2H), 7.67 (s, 2H), 7.42 (m, 3H), 7.25 (m, 1H), 7.07 (m, 2H), 4.37 (dd, 2H, $J = 6.9$ Hz), 3.87 (s, 3H), 1.81 (m, 2H), 1.50 (m, 2H), 1.00 (t, 3H, $J = 7.2$ Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.3, 155.7, 154.0, 146.0, 140.4, 132.5, 128.9, 128.8, 127.2, 126.6, 123.0, 119.1, 117.8, 105.4, 96.2, 87.1, 64.7, 55.5, 31.0, 19.7, 14.0. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{23}\text{H}_{24}\text{N}_3\text{O}_3$ 390.1818, found 390.1815.

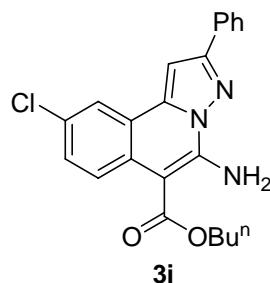


Methyl 5-amino-9-chloro-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3g). Eluent: petroleum ether/ethyl acetate (10:1). Yield 50 mg (57%). Light yellow solid, mp 165-166 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3465 (NH), 1677 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.54 (d, 1H, $J = 9.3$ Hz), 7.97 (m, 2H), 7.87 (m, 3H), 7.43 (m, 4H), 7.14 (s, 1H), 3.99 (s, 3H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.4, 154.5, 147.1, 139.6, 132.2, 129.2, 128.9, 127.4, 127.2, 126.6, 123.1, 119.2, 96.8, 86.5, 51.7. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{19}\text{H}_{15}\text{ClN}_3\text{O}_2$ 352.0853, found 352.0854.



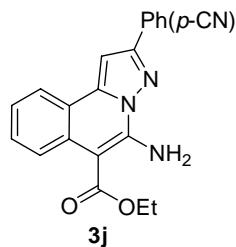
Ethyl 5-amino-9-chloro-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3h).

Eluent: petroleum ether/ethyl acetate (10:1). Yield 55 mg (61%). Light yellow solid, mp 161-163 °C. IR ν_{\max} (KBr)/cm⁻¹ 3461 (NH), 1674 (C=O). ¹H NMR (CDCl₃, 300 MHz) δ 8.54 (d, 1H, *J* = 9.3 Hz), 7.93 (m, 2H), 7.80 (m, 3H), 7.41 (m, 4H), 7.07 (s, 1H), 4.43 (dd, 2H, *J* = 7.2 Hz), 1.46 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 75 MHz) δ 168.9, 154.3, 146.9, 139.5, 132.2, 129.2, 128.9, 128.8, 127.5, 127.1, 126.6, 123.0, 119.1, 96.7, 86.5, 60.9, 14.6. HR-MS (ESI) [M+H]⁺ m/z calcd for C₂₀H₁₇ClN₃O₂ 366.1009, found 366.0997.



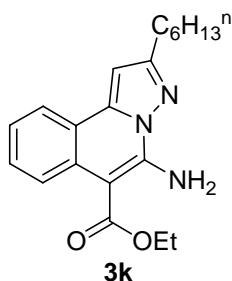
n-Butyl 5-amino-9-chloro-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carboxylate (3i).

Eluent: petroleum ether/ethyl acetate (10:1). Yield 62 mg (64%). White solid, mp 147-149 °C. IR ν_{\max} (KBr)/cm⁻¹ 3463 (NH), 1667 (C=O). ¹H NMR (CDCl₃, 300 MHz) δ 8.49 (d, 1H, *J* = 9.3 Hz), 7.91 (m, 2H), 7.75 (m, 3H), 7.40 (m, 3H), 7.30 (m, 1H), 7.00 (s, 1H), 4.35 (t, 2H, *J* = 6.9 Hz), 1.79 (m, 2H), 1.50 (m, 2H), 1.00 (t, 3H, *J* = 7.2 Hz). ¹³C NMR (CDCl₃, 75 MHz) δ 168.9, 154.2, 146.9, 139.4, 132.2, 129.1, 128.9, 128.8, 127.5, 127.0, 126.5, 122.9, 119.0, 96.6, 86.5, 64.9, 30.9, 19.6, 13.9. HR-MS (ESI) [M+H]⁺ m/z calcd for C₂₂H₂₁ClN₃O₂ 394.1322, found 394.1335.



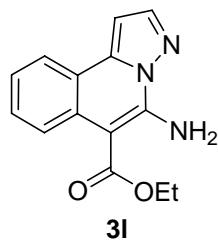
Ethyl 5-amino-2-(4-cyanophenyl) H-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3j).

Eluent: petroleum ether/ethyl acetate (7:1). Yield 47 mg (53%). Light yellow solid, mp 194-196 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3421 (NH), 2221 (CN), 1657 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.66 (d, 1H, J = 9.3 Hz), 8.03 (m, 2H), 7.92 (m, 1H), 7.78 (s, 2H), 7.68 (m, 2H), 7.50 (m, 1H), 7.32 (m, 1H), 7.17 (s, 1H), 4.48 (dd, 2H, J = 7.2 Hz), 1.50 (t, 3H, J = 7.2 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.1, 152.0, 146.7, 141.0, 136.7, 132.6, 129.2, 126.9, 125.6, 123.9, 123.7, 118.9, 118.0, 112.2, 96.6, 87.9, 61.0, 14.6. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{21}\text{H}_{17}\text{N}_4\text{O}_2$ 357.1352, found 357.1365.



Ethyl 5-amino-2-n-hexyl H-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3k).

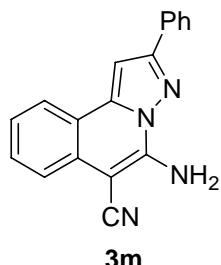
Eluent: petroleum ether/ethyl acetate (10:1). Yield 44 mg (52%). Light yellow solid, mp 59-60 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3441 (NH), 1667 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.68 (d, 1H, J = 8.6 Hz), 7.91 (m, 1H), 7.80 (s, 2H), 7.47 (m, 1H), 7.28 (m, 1H), 6.74 (s, 1H), 4.48 (dd, 2H, J = 7.2 Hz), 2.83 (t, 2H, J = 7.9 Hz), 1.79 (m, 2H), 1.49 (t, 3H, J = 7.2 Hz), 1.34 (m, 6H), 0.89 (t, 3H, J = 6.9 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.5, 157.7, 147.1, 140.2, 129.2, 128.6, 125.4, 123.9, 123.3, 118.2, 98.2, 86.8, 60.6, 31.8, 29.5, 29.2, 28.8, 22.7, 14.7, 14.2. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{20}\text{H}_{26}\text{N}_3\text{O}_2$ 340.2025, found 340.2041.



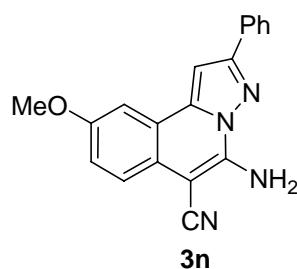
Ethyl 5-amino H-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3l). Eluent:

petroleum ether/ethyl acetate (10:1). Yield 29 mg (47%). White solid, mp 124-126 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3383 (NH), 1661 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.69 (d, 1H, J = 8.6 Hz), 7.99 (m, 2H), 7.82 (s, 2H), 7.49 (m, 1H), 7.30 (m, 1H), 6.94 (d, 1H, J

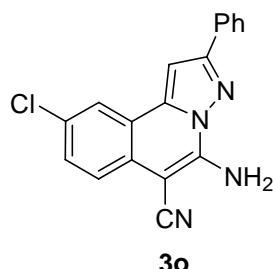
= 2.0 Hz), 4.49 (dd, 2H, J = 7.2 Hz), 1.49 (t, 3H, J = 7.2 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 169.4, 147.2, 142.8, 139.6, 129.1, 128.8, 125.4, 123.9, 123.5, 118.3, 99.2, 87.1, 60.8, 14.6. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{14}\text{H}_{14}\text{N}_3\text{O}_2$ 256.1086, found 256.1099.



5-Amino-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carbonitrile (3m). Eluent: petroleum ether/ethyl acetate (7:1). Yield 44 mg (62%). Light yellow solid, mp 225-227 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3440 (NH), 2216 (CN). ^1H NMR ($\text{DMSO}-d_6$, 300 MHz) δ 8.20 (m, 3H), 8.12 (s, 2H), 7.92 (s, 1H), 7.68 (m, 2H), 7.55 (m, 2H), 7.47 (m, 2H). ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz) δ 154.2, 147.6, 140.9, 132.4, 130.1, 129.7, 129.4, 129.1, 126.8, 124.8, 124.5, 122.0, 117.5, 98.2, 68.4. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{18}\text{H}_{13}\text{N}_4$ 285.1140, found 285.1141.

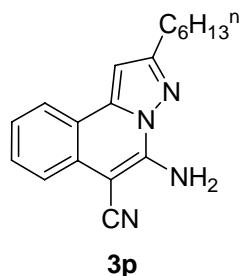


5-Amino-9-methoxy-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carbonitrile (3n). Eluent: petroleum ether/ethyl acetate (6:1). Yield 58 mg (74%). Light yellow solid, mp 213-215 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3459 (NH), 2204 (CN). ^1H NMR ($\text{DMSO}-d_6$, 300 MHz) δ 8.17 (m, 2H), 7.97 (s, 1H), 7.87 (s, 2H), 7.78 (m, 1H), 7.60 (m, 3H), 7.48 (m, 1H), 7.30 (m, 1H), 3.95 (s, 3H). ^{13}C NMR ($\text{DMSO}-d_6$, 75 MHz) δ 156.8, 154.0, 146.4, 140.6, 132.5, 129.6, 129.4, 126.8, 123.7, 122.6, 119.6, 118.5, 117.7, 106.7, 98.4, 68.4, 56.1. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{19}\text{H}_{15}\text{N}_4\text{O}$ 315.1246, found 315.1254.

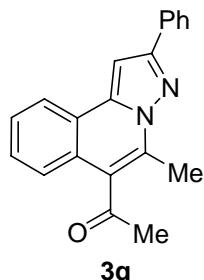


5-Amino-9-chloro-2-phenyl H-pyrazolo[5,1-a]isoquinoline-6-carbonitrile (3o).

Eluent: petroleum ether/ethyl acetate (7:1). Yield 41 mg (52%). Yellow solid, mp 278-280 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3435 (NH), 2206 (CN). ^1H NMR (DMSO- d_6 , 300 MHz) δ 8.28 (m, 1H), 8.15 (s, 2H), 8.08 (m, 2H), 7.96 (s, 1H), 7.59 (m, 2H), 7.51 (m, 2H), 7.43 (m, 1H). ^{13}C NMR (DMSO- d_6 , 75 MHz) δ 154.3, 147.7, 139.8, 132.2, 130.5, 129.8, 129.5, 128.6, 128.0, 126.8, 124.1, 123.9, 118.7, 117.3, 99.2, 68.0. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{18}\text{H}_{12}\text{ClN}_4$ 319.0750, found 319.0761.

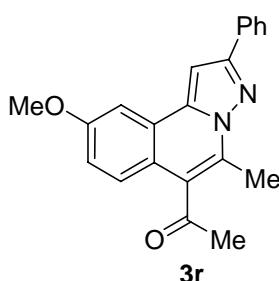


5-Amino-2-n-hexyl H-pyrazolo[5,1-a]isoquinoline-6-carbonitrile (3p). Eluent: petroleum ether/ethyl acetate (10:1). Yield 45 mg (62%). White solid, mp 119-121 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 3454 (NH), 2213 (CN). ^1H NMR (CDCl_3 , 300 MHz) δ 7.91 (d, 1H, J = 7.9 Hz), 7.76 (d, 1H, J = 8.3 Hz), 7.53 (m, 1H), 7.35 (m, 1H), 6.80 (s, 1H), 6.09 (s, 2H), 2.84 (t, 2H, J = 7.6 Hz), 1.76 (m, 2H), 1.33 (m, 6H), 0.90 (t, 3H, J = 7.2 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 158.3, 146.3, 140.1, 129.2, 128.2, 124.6, 123.9, 122.8, 117.9, 117.2, 99.1, 70.1, 31.7, 29.4, 29.2, 28.7, 22.7, 14.2. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{18}\text{H}_{21}\text{N}_4$ 293.1766, found 293.1758.



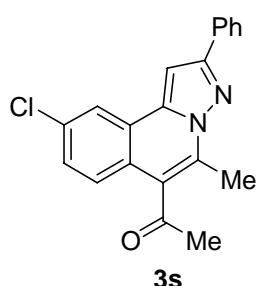
1-(5-Methyl-2-phenyl H-pyrazolo[5,1-a]isoquinolin-6-yl)ethanone (3q). Eluent:

petroleum ether/ethyl acetate (10:1). Yield 50 mg (66%). White solid, mp 128-130 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1692 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.10 (m, 1H), 8.03 (m, 2H), 7.47 (m, 5H), 7.36 (m, 1H), 7.29 (s, 1H), 2.77 (s, 3H), 2.65 (s, 3H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 204.3, 153.2, 139.8, 133.3, 130.2, 128.9, 128.6, 128.3, 127.3, 126.5, 125.7, 124.1, 124.0, 123.8, 123.5, 95.5, 33.3, 15.3. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{20}\text{H}_{17}\text{N}_2\text{O}$ 301.1341, found 301.1349.



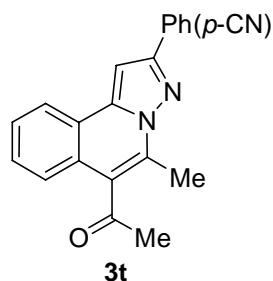
1-(9-Methoxy-5-methyl-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinolin-6-yl)ethanone (3r).

Eluent: petroleum ether/ethyl acetate (10:1). Yield 55 mg (67%). White solid, mp 116-118 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1679 (C=O). ^1H NMR (CDCl_3 , 600 MHz) δ 8.03 (m, 2H), 7.45 (m, 4H), 7.37 (m, 1H), 7.28 (s, 1H), 7.14 (m, 1H), 3.96 (s, 3H), 2.77 (s, 3H), 2.66 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 204.3, 158.7, 153.0, 139.4, 133.3, 130.0, 128.8, 128.5, 126.5, 125.7, 124.9, 123.7, 119.8, 118.0, 105.5, 95.4, 55.6, 33.3, 15.2. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_2$ 331.1447, found 331.1432.

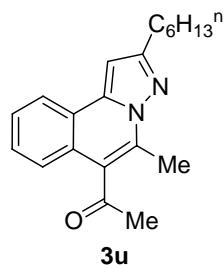


1-(9-Chloro-5-methyl-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinolin-6-yl)ethanone (3s).

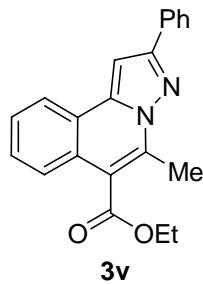
Eluent: petroleum ether/ethyl acetate (10:1). Yield 50 mg (60%). White solid, mp 148-150 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1681 (C=O). ^1H NMR (CDCl_3 , 600 MHz) δ 8.09 (s, 1H), 8.02 (m, 2H), 7.47 (m, 4H), 7.40 (m, 1H), 7.30 (s, 1H), 2.79(s, 3H), 2.66 (s, 3H). ^{13}C NMR (CDCl_3 , 150 MHz) δ 203.6, 153.5, 138.5, 133.1, 132.9, 132.7, 128.9, 128.7, 128.7, 126.5, 125.6, 124.8, 124.0, 123.5, 123.0, 95.9, 33.3, 15.4. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{20}\text{H}_{16}\text{ClN}_2\text{O}$ 335.0951, found 335.0966.



4-(6-Acetyl-5-methyl *H*-pyrazolo[5,1-*a*]isoquinolin-2-yl)benzonitrile (3t). Eluent: petroleum ether/ethyl acetate (10:1). Yield 51 mg (63%). White solid, mp 174–176 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 2221 (CN), 1684 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.10 (m, 3H), 7.70 (m, 2H), 7.54 (m, 3H), 7.34 (s, 1H), 2.77 (s, 3H), 2.68 (s, 3H). ^{13}C NMR (CDCl_3 , 75 MHz) δ 203.9, 150.9, 139.9, 137.6, 132.6, 131.9, 128.7, 127.6, 126.8, 125.7, 124.7, 124.2, 124.1, 123.4, 119.1, 111.7, 96.0, 33.3, 15.3. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{21}\text{H}_{16}\text{N}_3\text{O}$ 326.1293, found 326.1297.

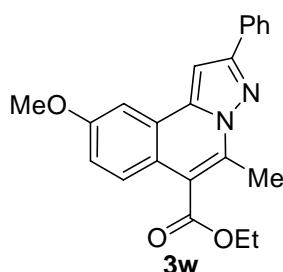


1-(2-n-Hexyl-5-methyl *H*-pyrazolo[5,1-*a*]isoquinolin-6-yl)ethanone (3u). Eluent: petroleum ether/ethyl acetate (10:1). Yield 50 mg (65%). Yellow oil. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1700 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.05 (m, 1H), 7.50 (m, 3H), 6.85 (s, 1H), 2.88 (t, 2H, J = 7.9 Hz), 2.74 (s, 3H), 2.65 (s, 3H), 1.78 (m, 2H), 1.37 (m, 6H), 0.89 (t, 3H, J = 6.9 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 204.4, 156.4, 139.0, 132.0, 128.0, 127.0, 125.7, 124.0, 123.9, 123.3, 122.9, 97.1, 33.3, 31.8, 29.9, 29.2, 28.9, 22.7, 15.5, 14.2. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{20}\text{H}_{25}\text{N}_2\text{O}$ 309.1967, found 309.1970.

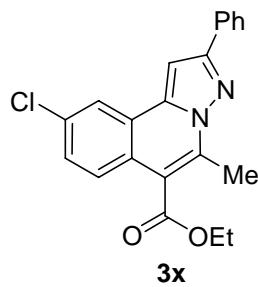


Ethyl 5-methyl-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3v).

Eluent: petroleum ether/ethyl acetate (10:1). Yield 49 mg (60%). White solid, mp 97–99 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1718 (C=O). ^1H NMR (CDCl_3 , 300 MHz) δ 8.07 (m, 3H), 7.79 (m, 1H), 7.50 (m, 4H), 7.37 (m, 1H), 7.30 (s, 1H), 4.53 (dd, 2H, J = 7.2 Hz), 2.91 (s, 3H), 1.47 (t, 3H, J = 6.9 Hz). ^{13}C NMR (CDCl_3 , 75 MHz) δ 167.8, 153.5, 139.9, 136.1, 133.2, 128.8, 128.6, 128.3, 127.2, 126.6, 126.3, 124.7, 123.8, 123.2, 115.8, 95.5, 61.8, 15.9, 14.5. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{21}\text{H}_{19}\text{N}_2\text{O}_2$ $[\text{M}+\text{H}]^+$ 331.1447, found 331.1455.

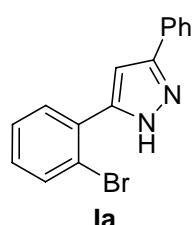


Ethyl 9-methoxy-5-methyl-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3w). Eluent: petroleum ether/ethyl acetate (10:1). Yield 55 mg (61%). Yellow oil. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1710 (C=O). ^1H NMR (CDCl_3 , 600 MHz) δ 8.04 (m, 2H), 7.75 (m, 1H), 7.47 (m, 3H), 7.38 (m, 1H), 7.29 (s, 1H), 7.17 (m, 1H), 4.53 (dd, 2H, J = 6.9 Hz), 3.97 (s, 3H), 2.90 (s, 3H), 1.47 (t, 3H, J = 6.9 Hz). ^{13}C NMR (CDCl_3 , 150 MHz) δ 167.9, 158.6, 153.2, 139.7, 133.9, 133.3, 132.4, 128.8, 128.5, 126.5, 124.5, 120.4, 118.0, 118.5, 105.1, 95.4, 61.8, 55.6, 15.7, 14.4. HR-MS (ESI) $[\text{M}+\text{H}]^+$ m/z calcd for $\text{C}_{22}\text{H}_{21}\text{N}_2\text{O}_3$ 361.1552, found 361.1552.



Ethyl 9-chloro-5-methyl-2-phenyl *H*-pyrazolo[5,1-*a*]isoquinoline-6-carboxylate (3x). Eluent: petroleum ether/ethyl acetate (10:1). Yield 52 mg (57%). Light yellow solid mp 99–101 °C. IR $\nu_{\text{max}}(\text{KBr})/\text{cm}^{-1}$ 1718 (C=O). ^1H NMR (CDCl_3 , 600 MHz) δ 8.01 (m, 3H), 7.74 (m, 1H), 7.45 (m, 3H), 7.39 (m, 1H), 7.27 (s, 1H), 4.54 (dd, 2H, J = 6.9 Hz), 2.89 (s, 3H), 1.47 (t, 3H, J = 6.9 Hz). ^{13}C NMR (CDCl_3 , 150 MHz) δ 167.4,

153.6, 138.8, 136.7, 132.9, 132.8, 128.9, 128.8, 128.6, 126.6, 126.4, 124.7, 124.2, 123.1, 115.1, 96.0, 61.9, 15.9, 14.4. HR-MS (ESI) $[M+H]^+$ m/z calcd for $C_{21}H_{18}ClN_2O_2$ 365.1057, found 365.1067.

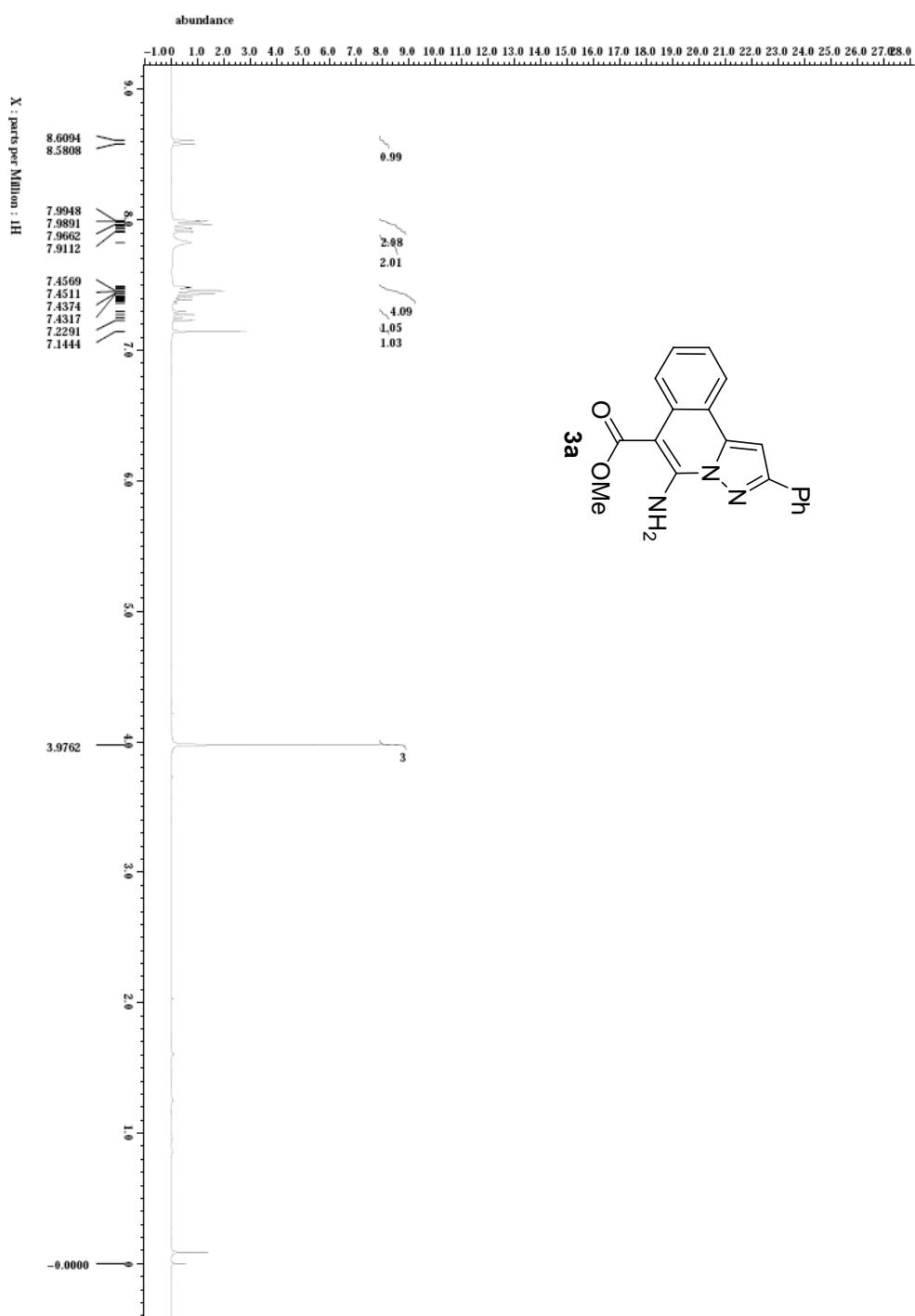


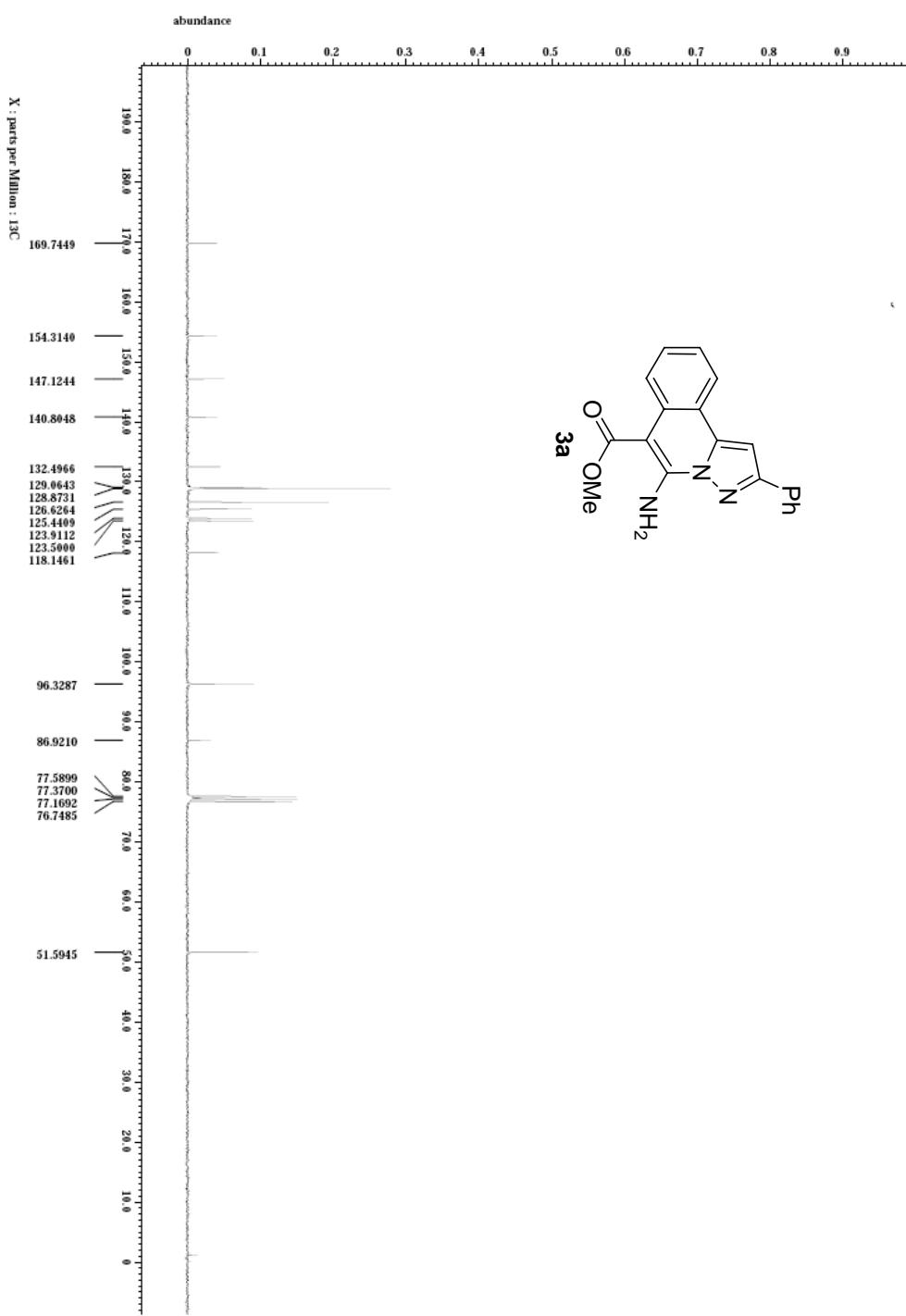
5-(2-Bromophenyl)-3-phenyl-1H-pyrazole (Ia). Eluent: petroleum ether/ethyl acetate (3:1). Yield 65 mg (87 %). Light yellow solid. 1H NMR ($CDCl_3$, 300 MHz) δ 11.30 (br, 1H), 7.70 (m, 4H), 7.30 (m, 5H), 6.94 (s, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 133.9, 130.9, 129.8, 128.9, 128.3, 127.7, 125.8, 121.6, 103.8. ESIMS $[M+H]^+$ m/z 299.2, 301.2, $[M+Na]^+$ m/z 322.0, 323.0.

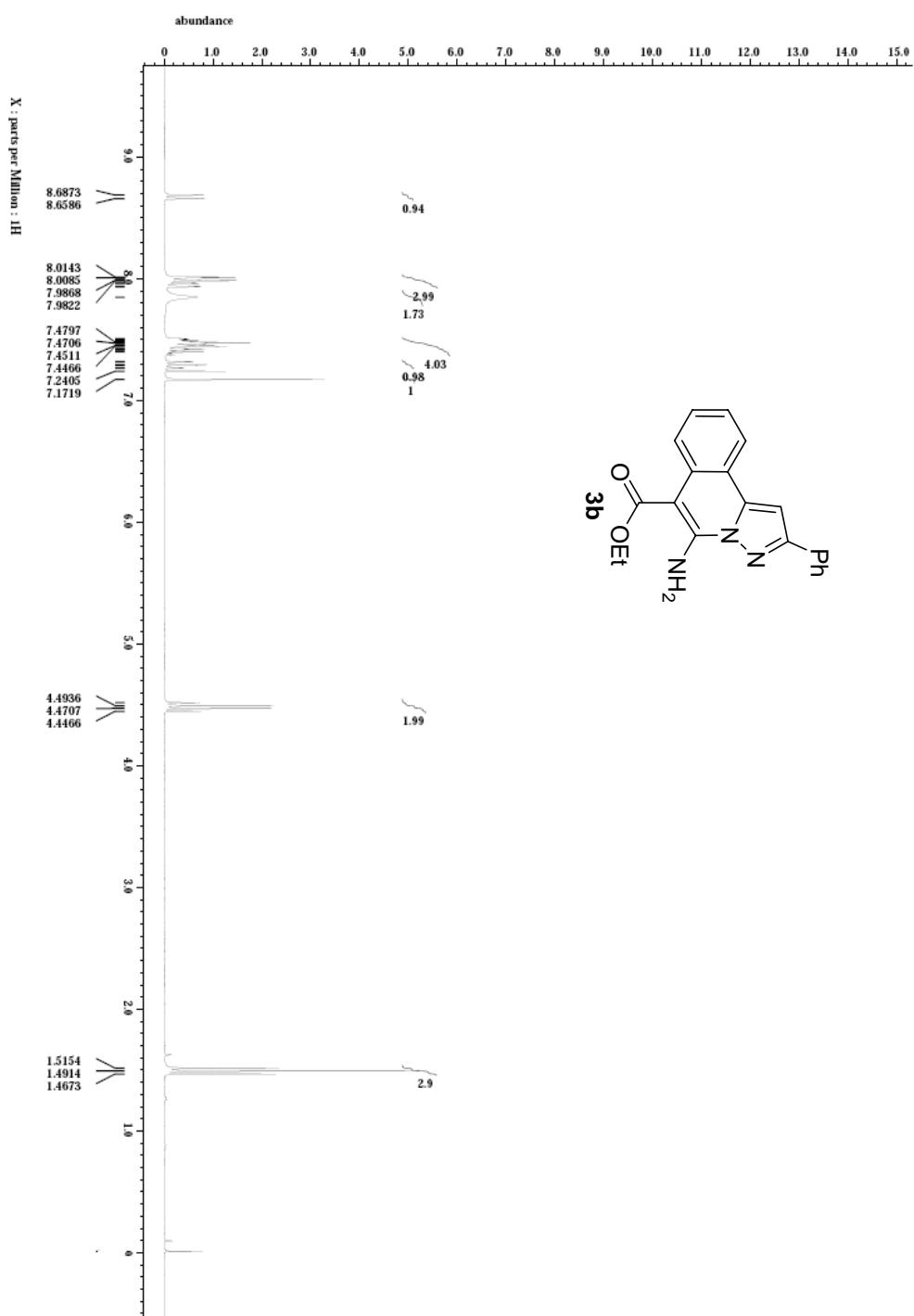
References

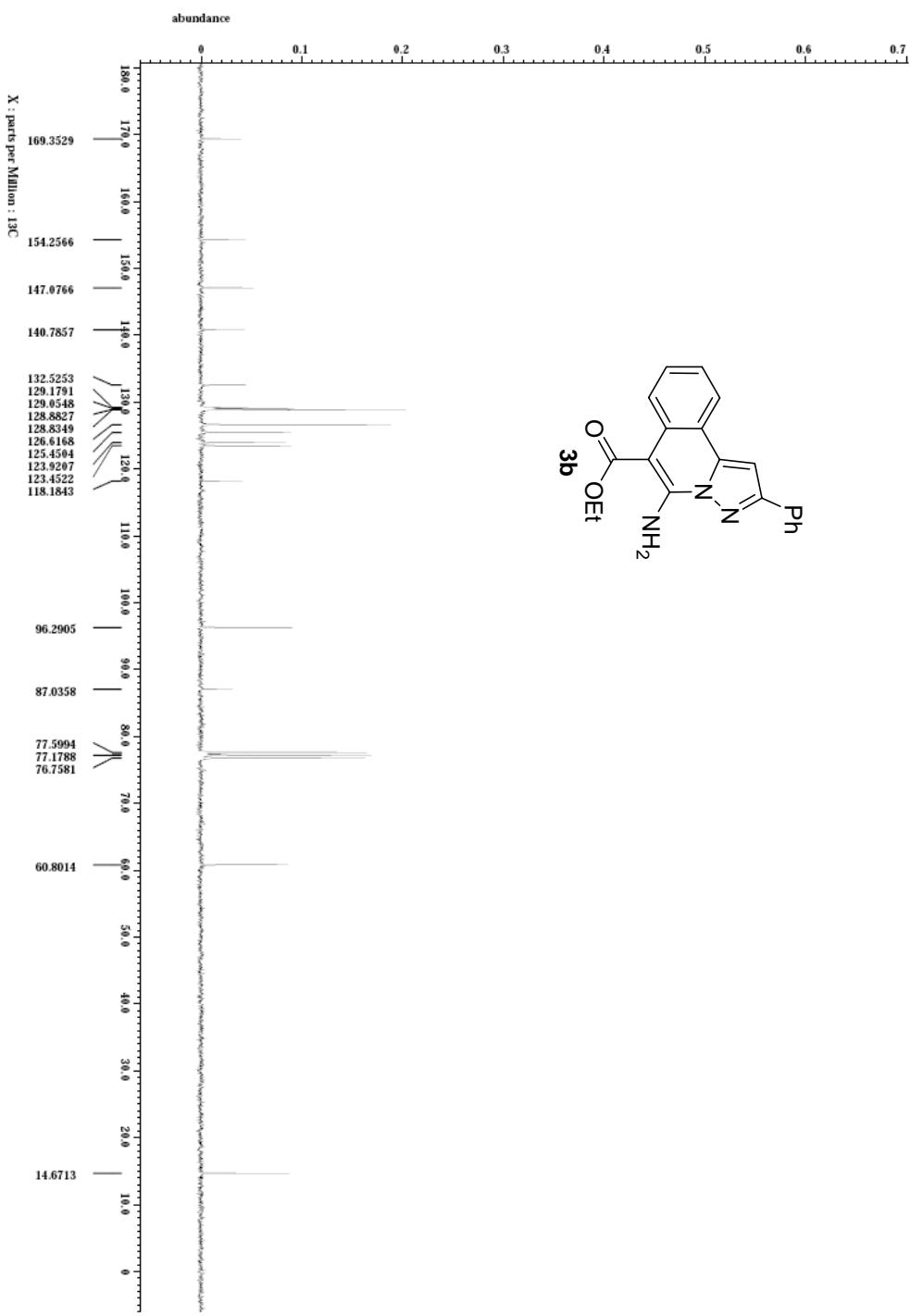
- 1 R. Bernini, S. Cacchi, G. Fabrizi, A. Sferrazza, *Synthesis*, 2009, 1209-1219.
- 2 C. Lin, T. H. Duh, W. D. Lu, J. L. Lee, C. Y. Lee, C. C. Chen, M. J. Wu, *J. Chin. Chem. Soc.*, 2004, **51**, 183-186.
- 3 S. Ma, J. Liu, S. Li, B. Chen, J. Cheng, J. Kuang, Y. Liu, B. Wan, Y. Wang, J. Ye, Q. Yu, W. Yuan, S. Yu, *Adv. Synth. Catal.*, 2011, **353**, 1005-1017.

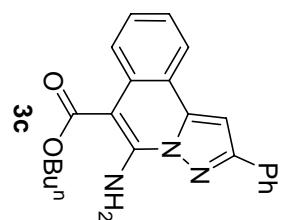
The ^1H and ^{13}C NMR spectra of compounds **3a-x** and **Ia**

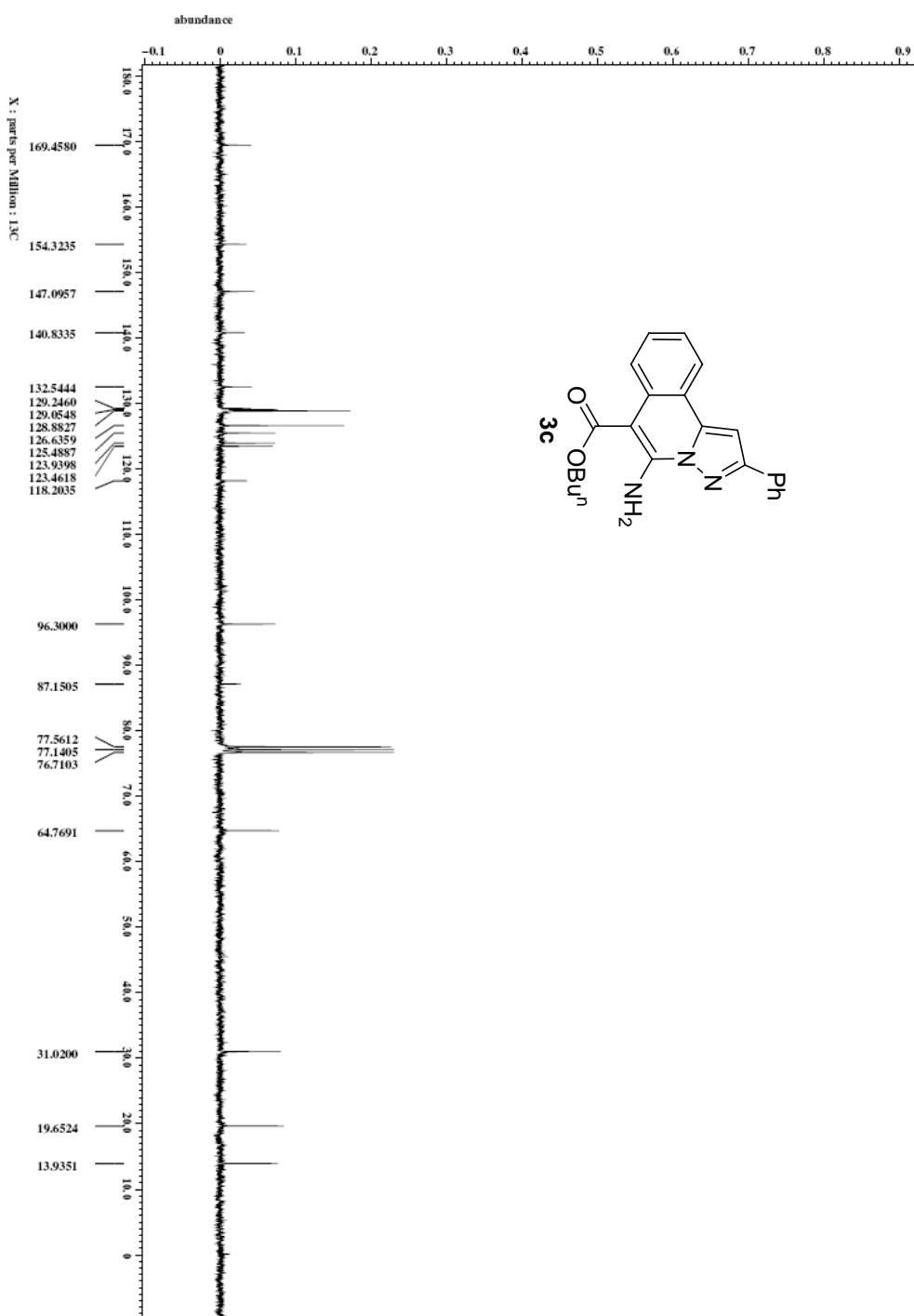




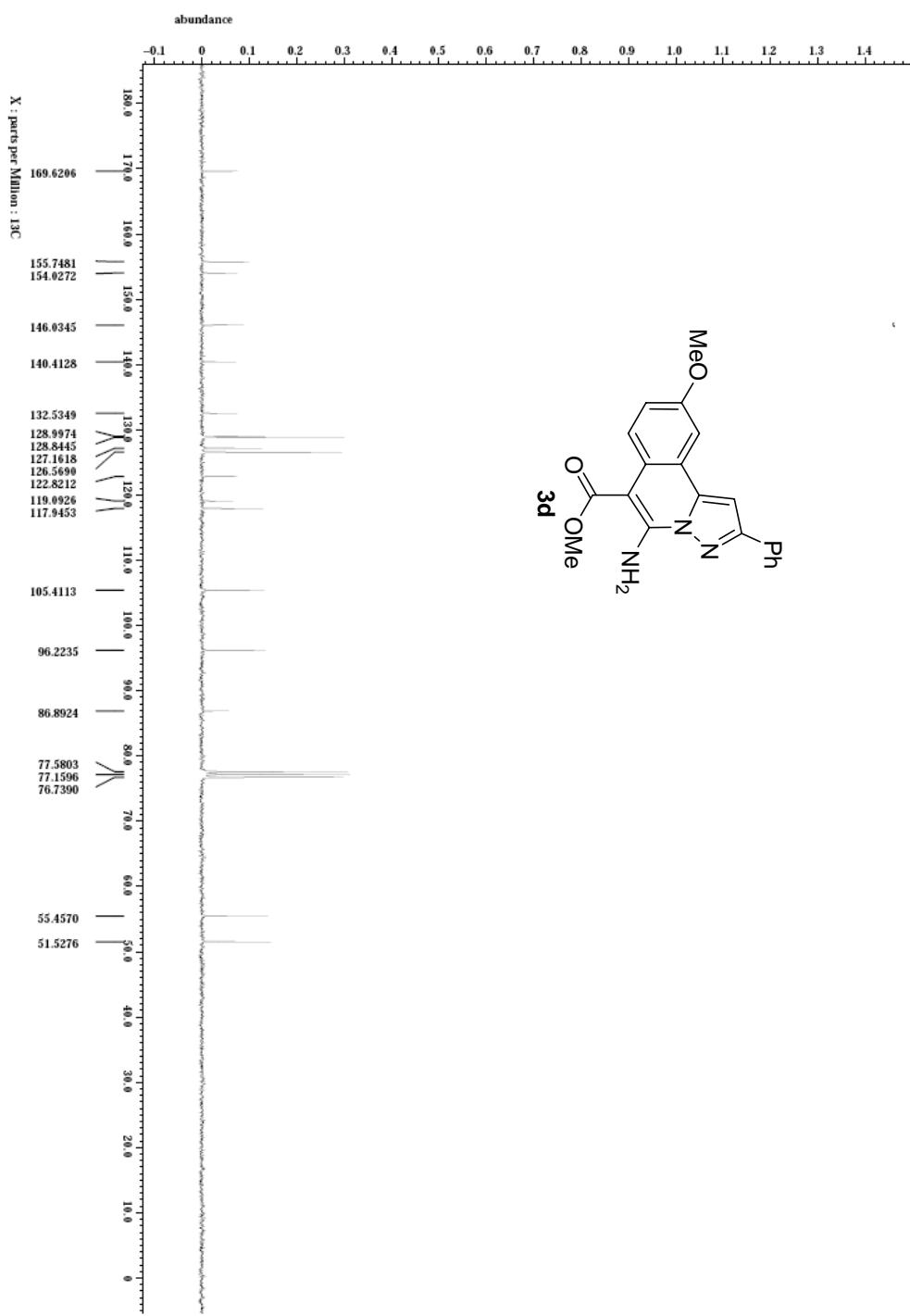


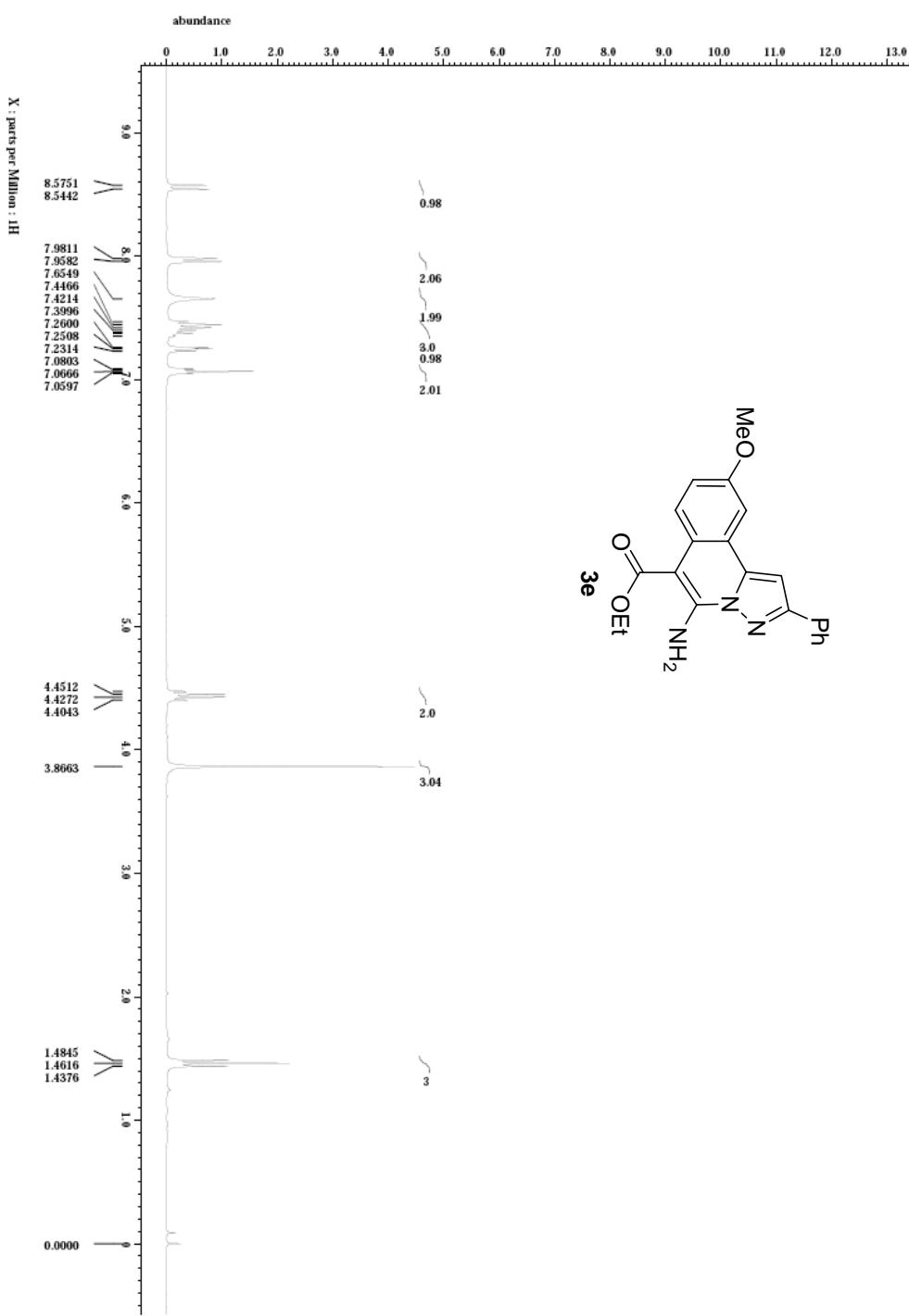


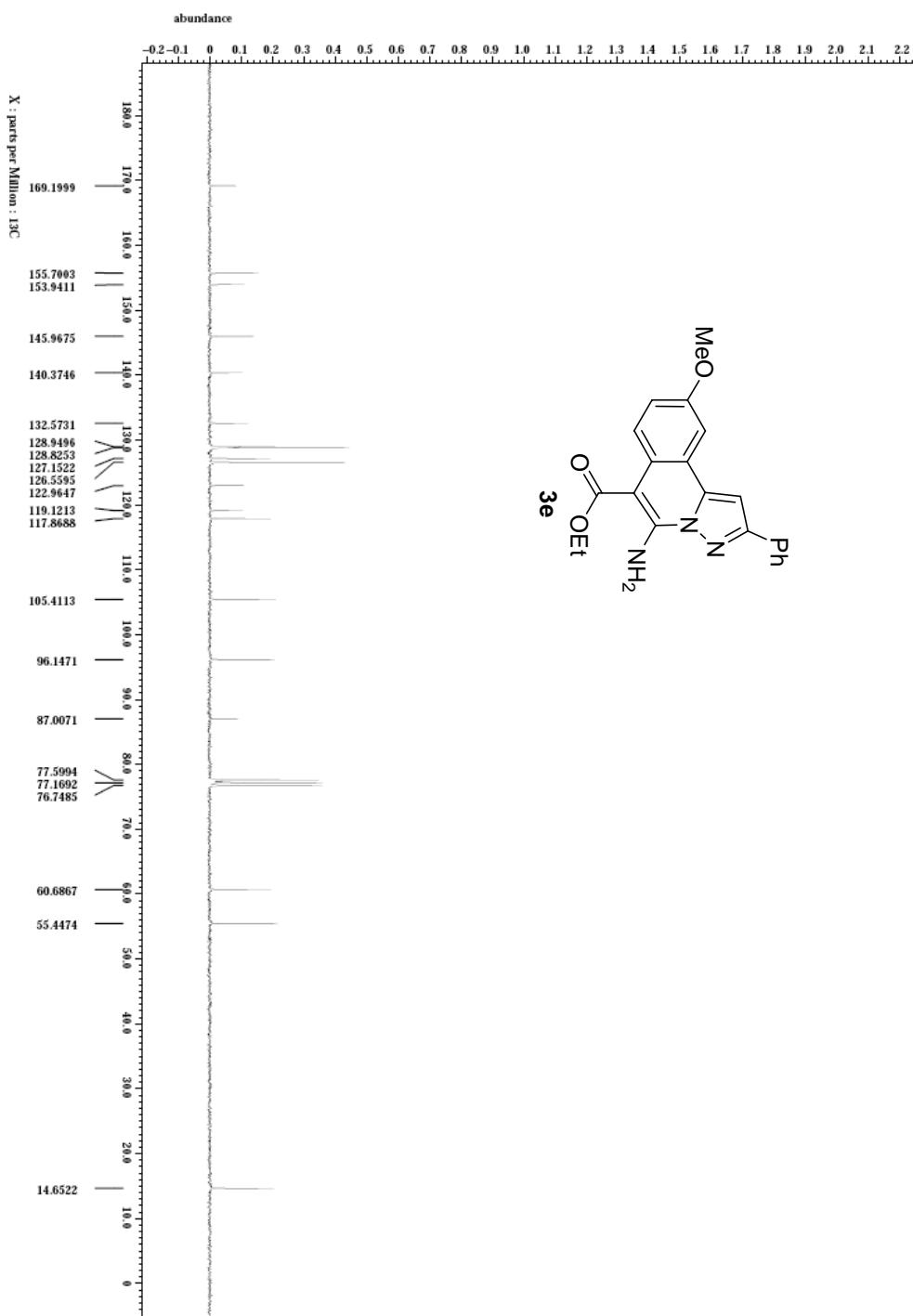


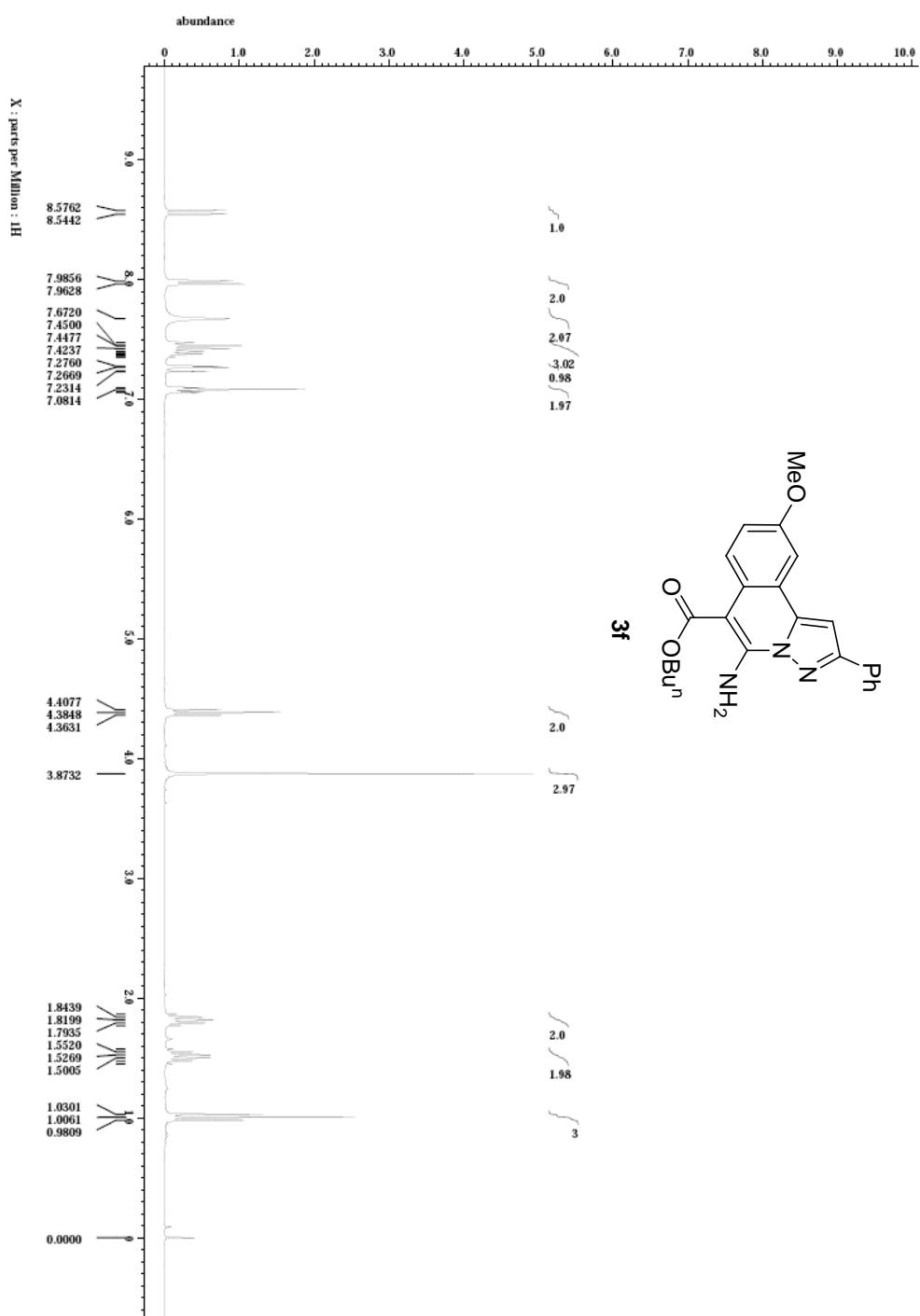


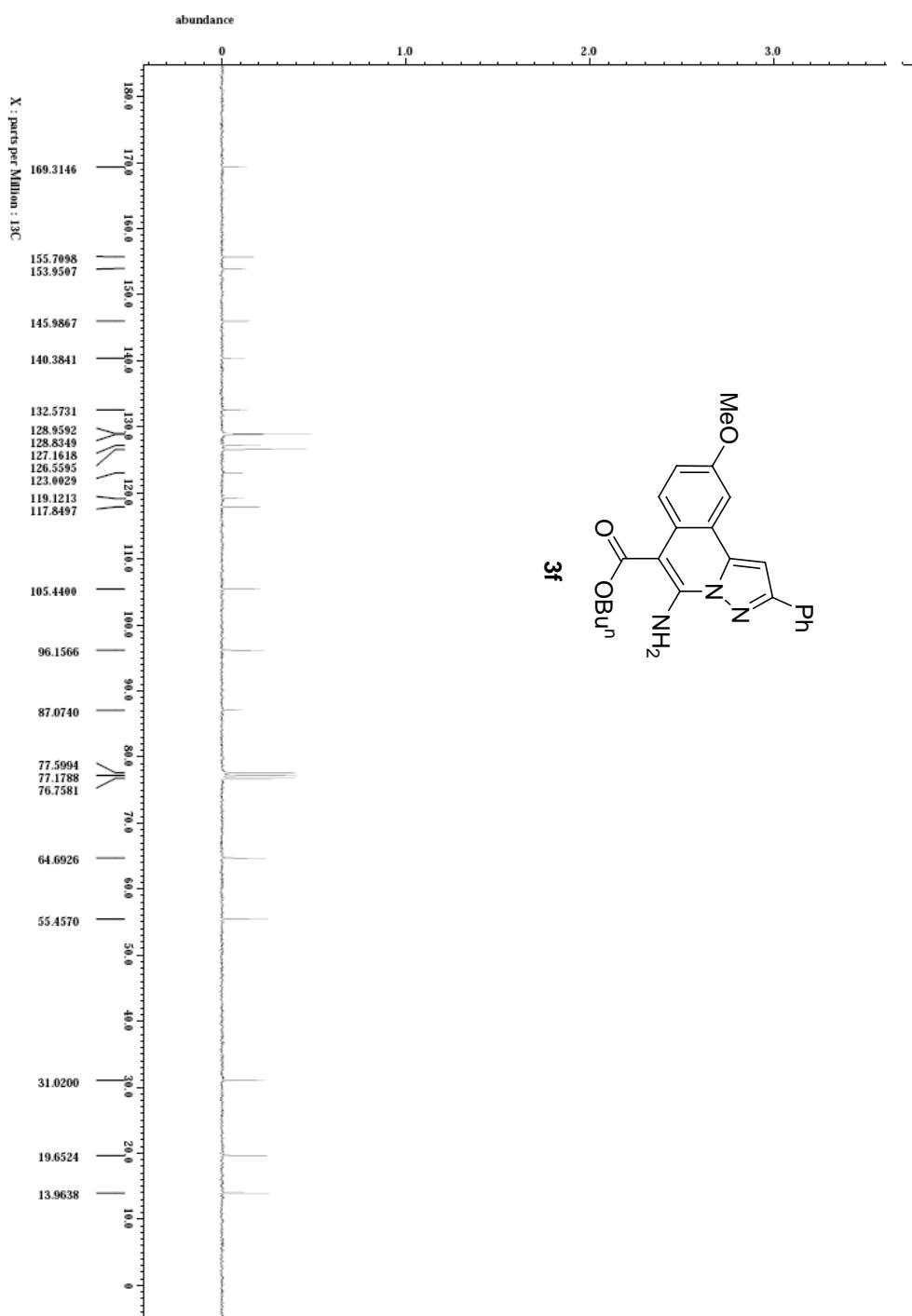


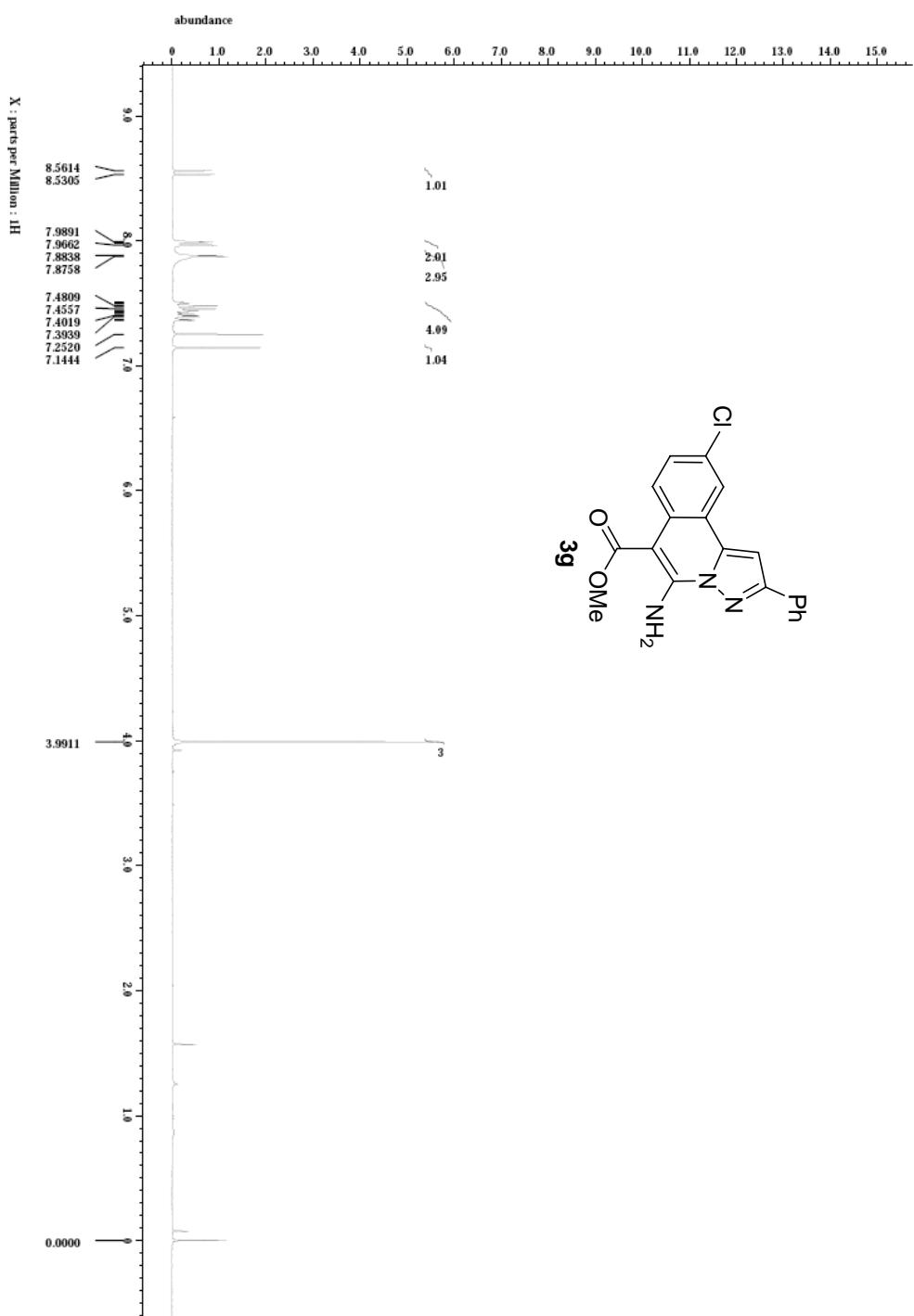




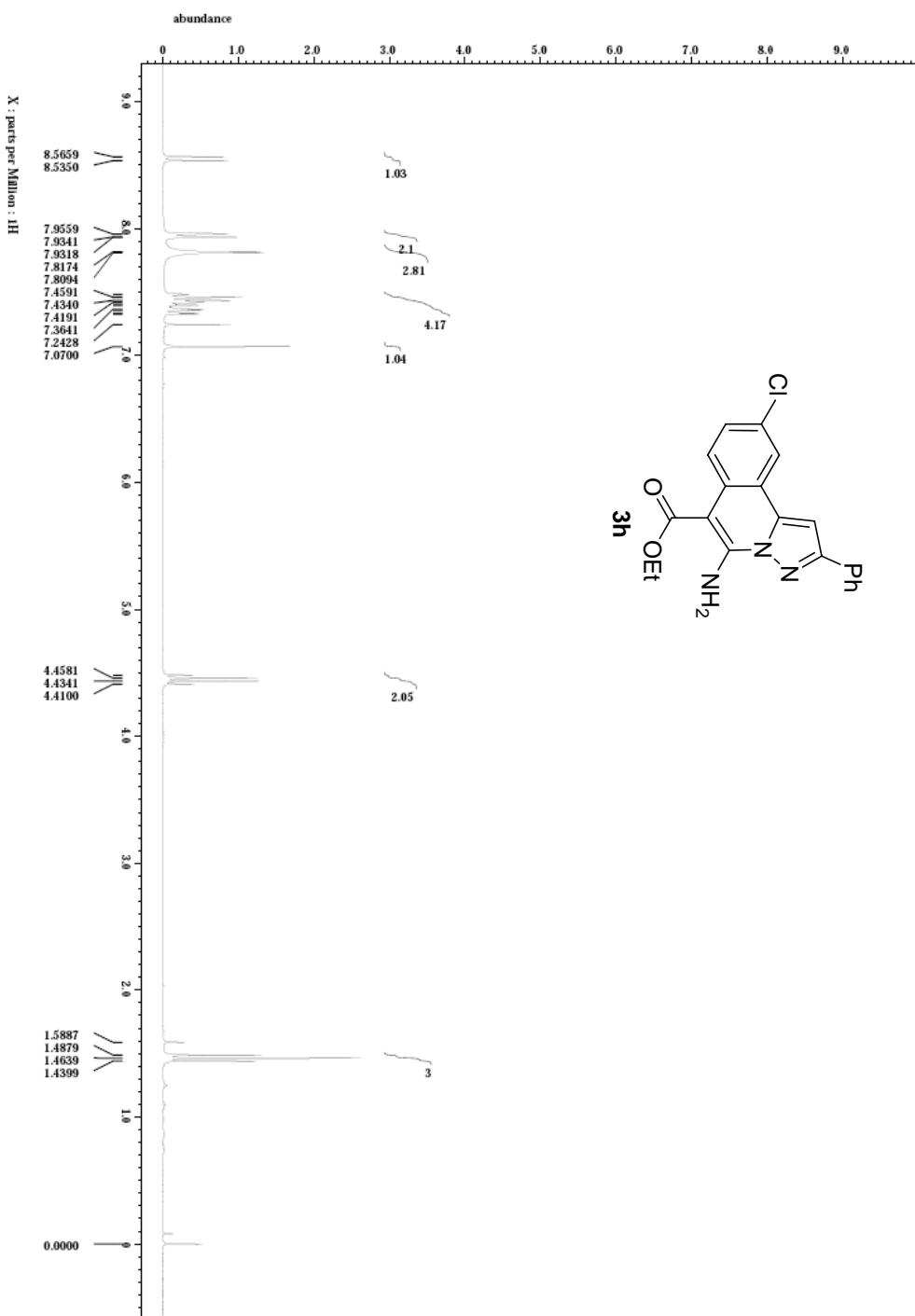


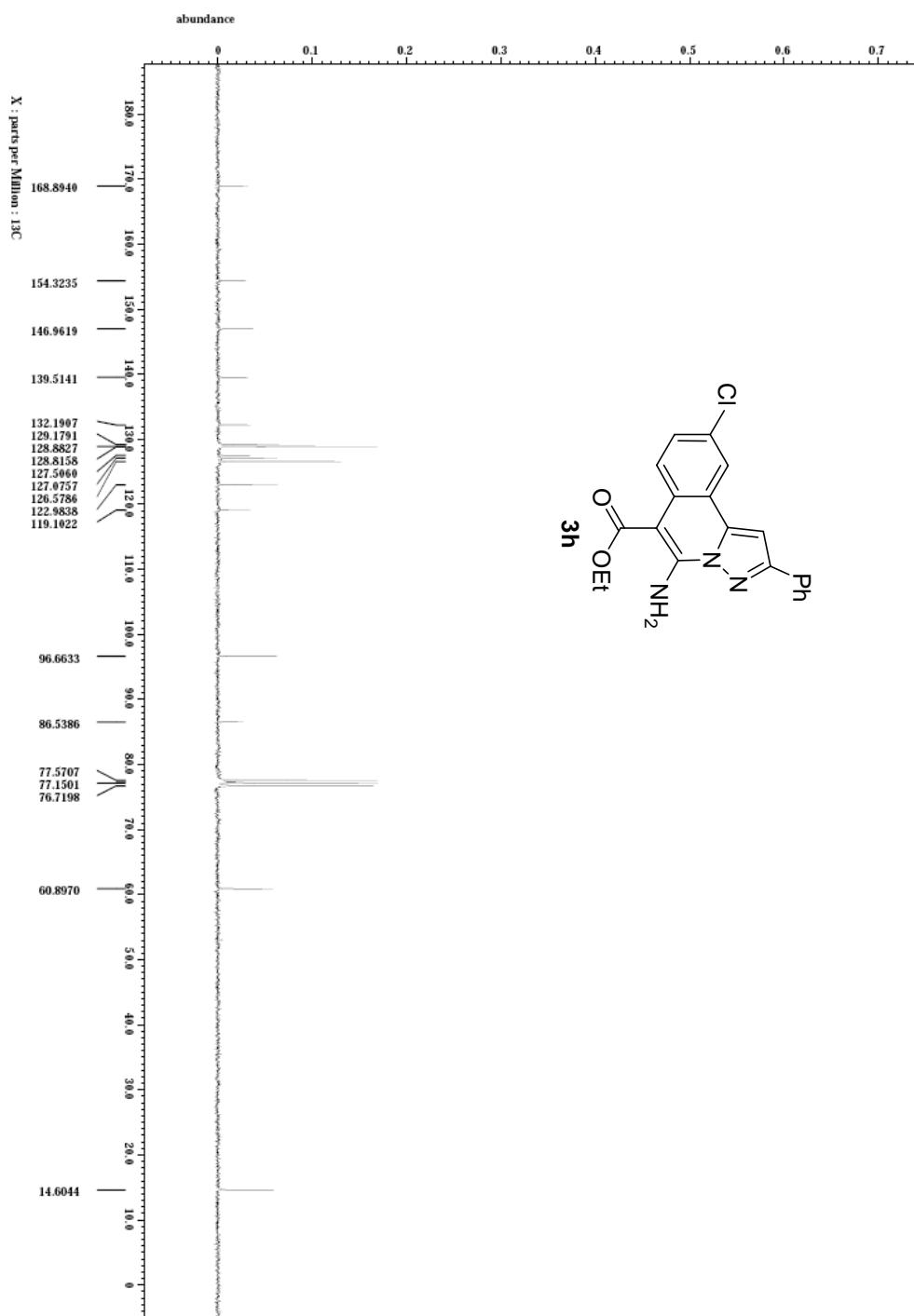


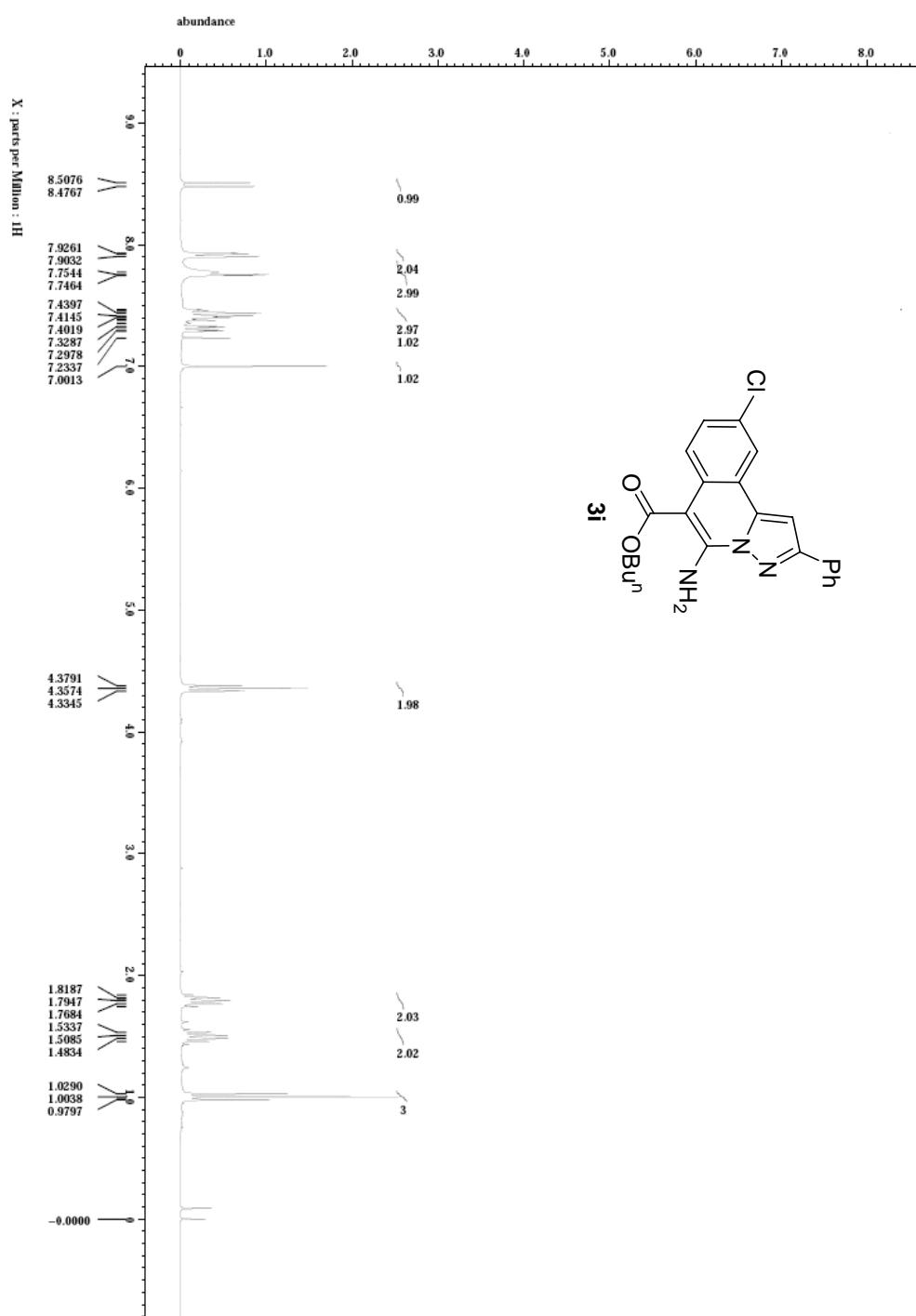


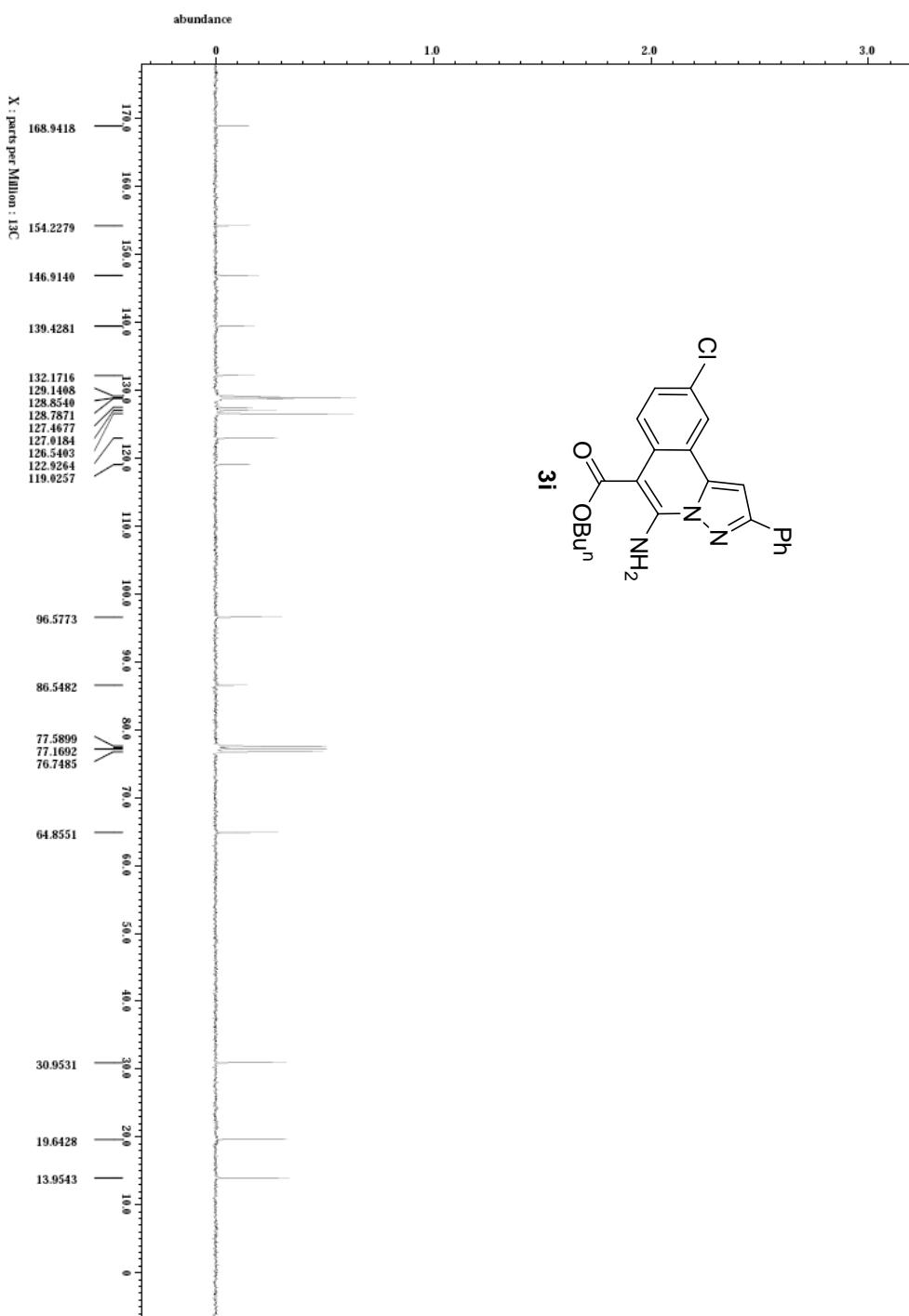


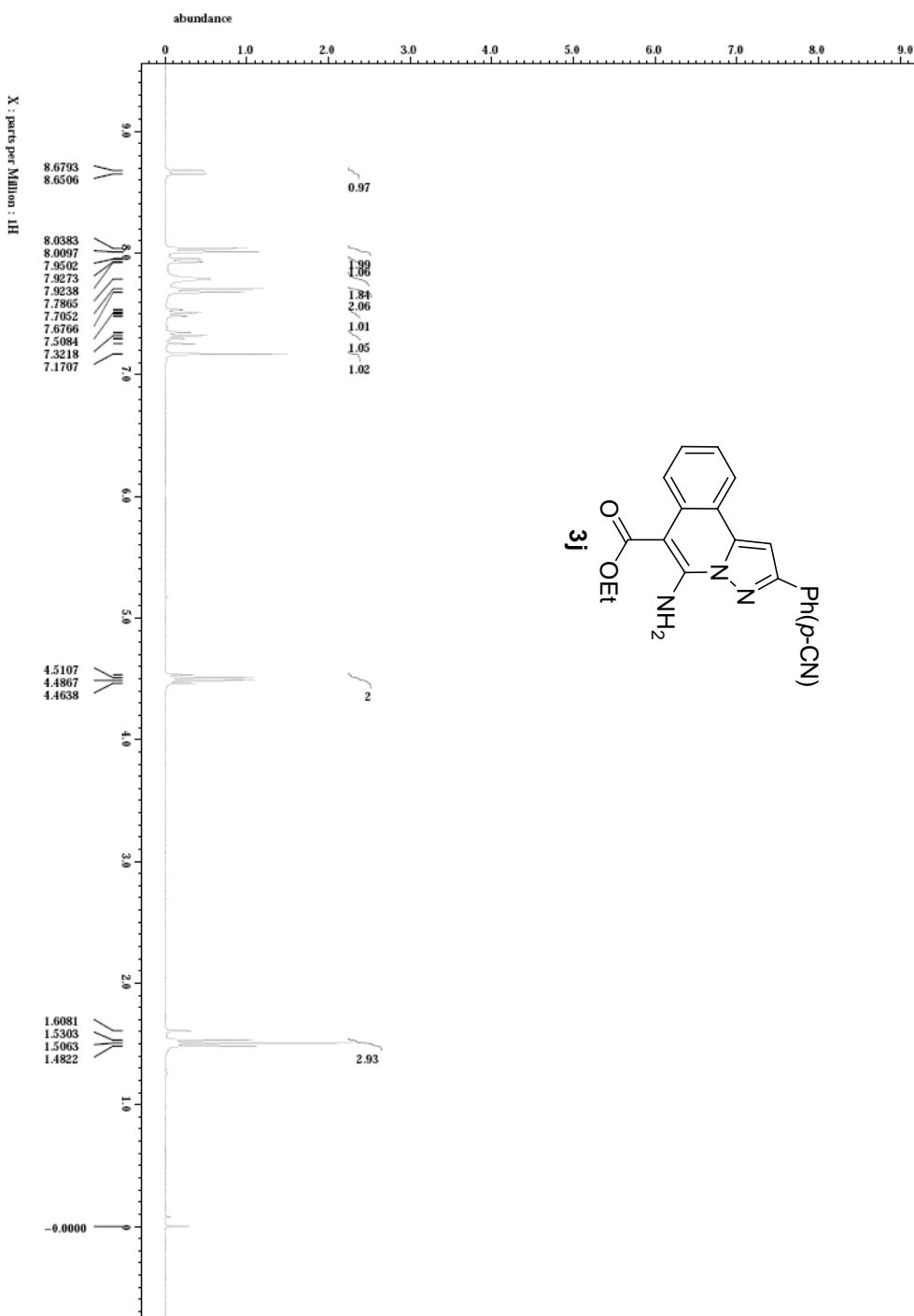


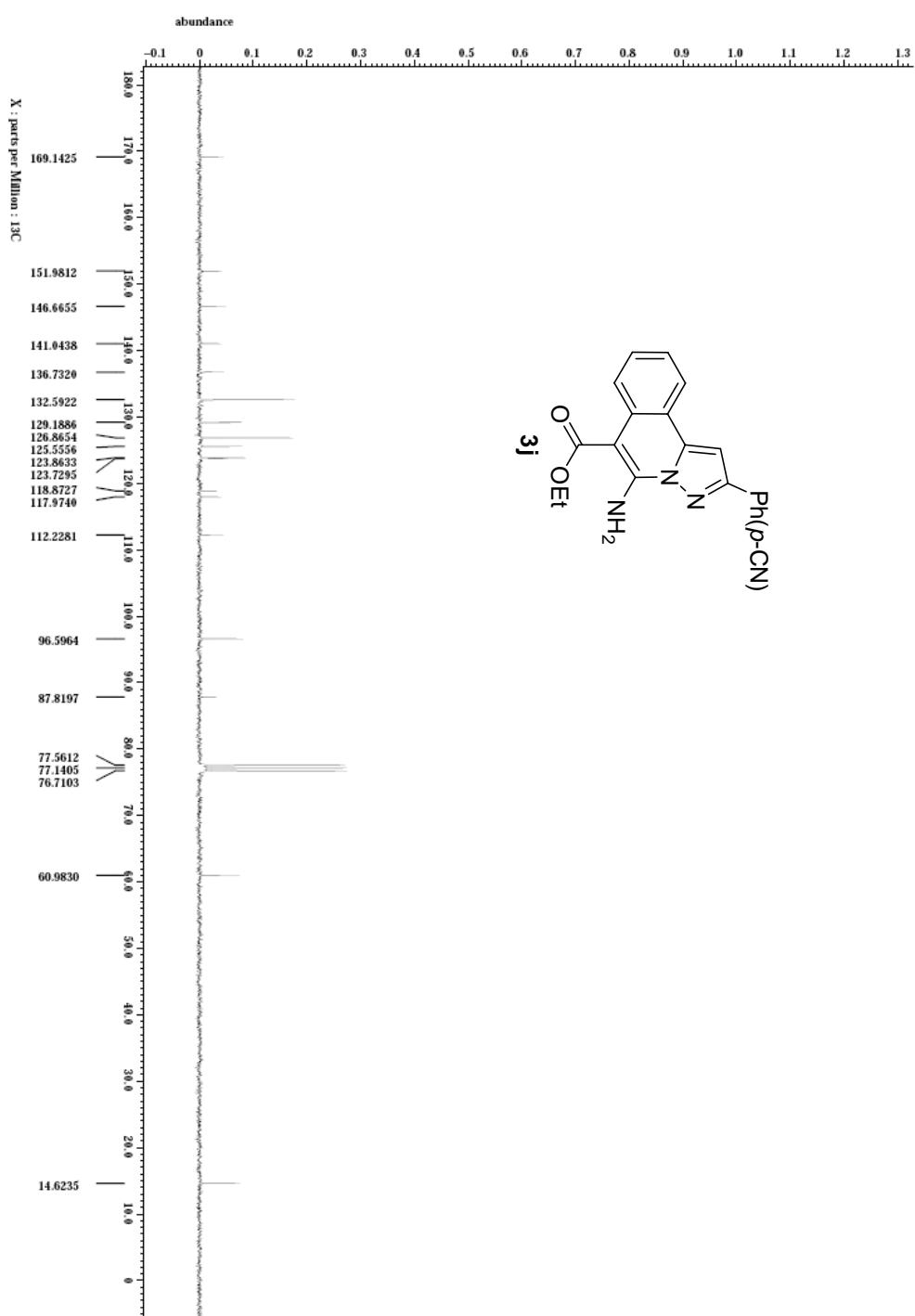




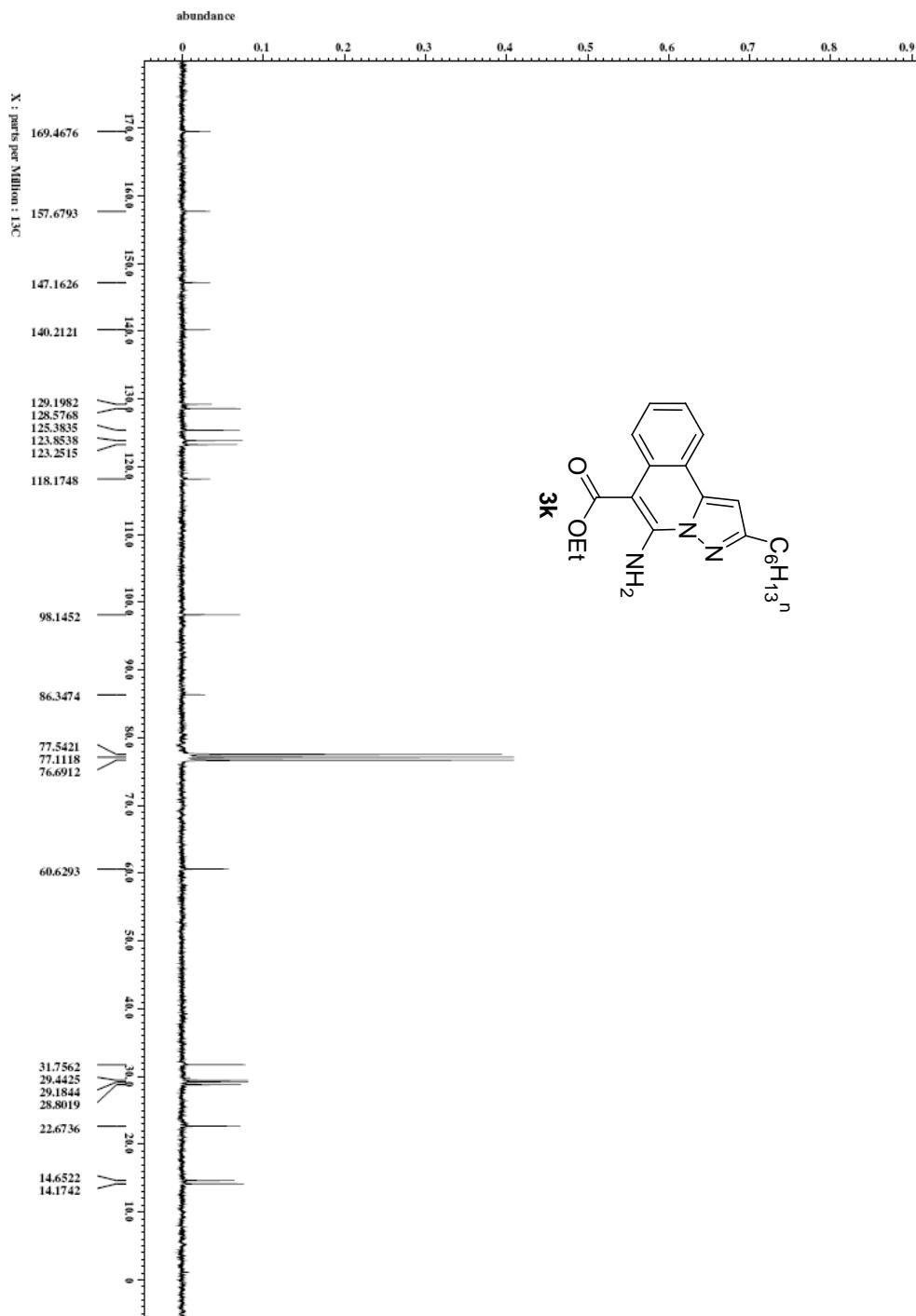


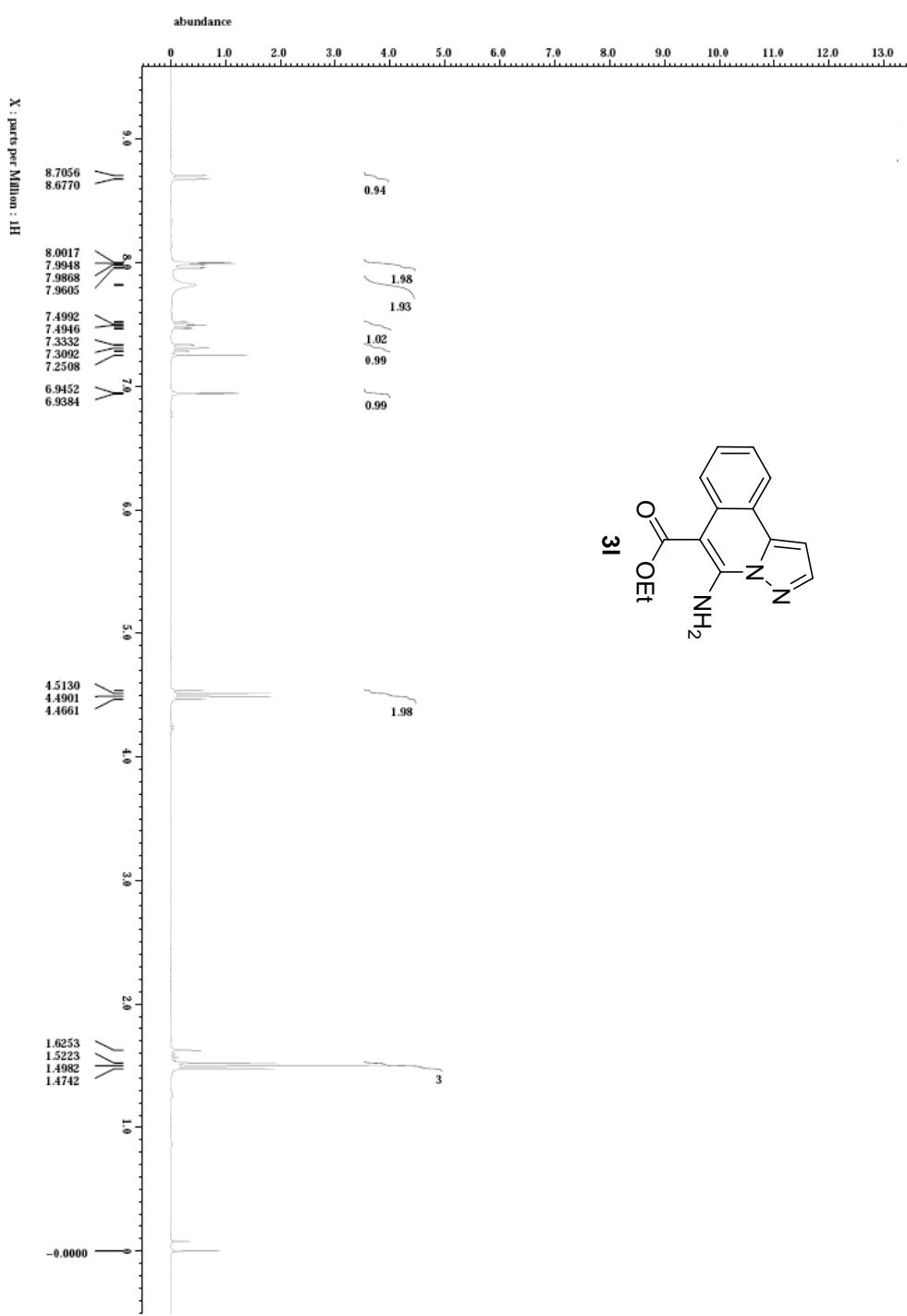


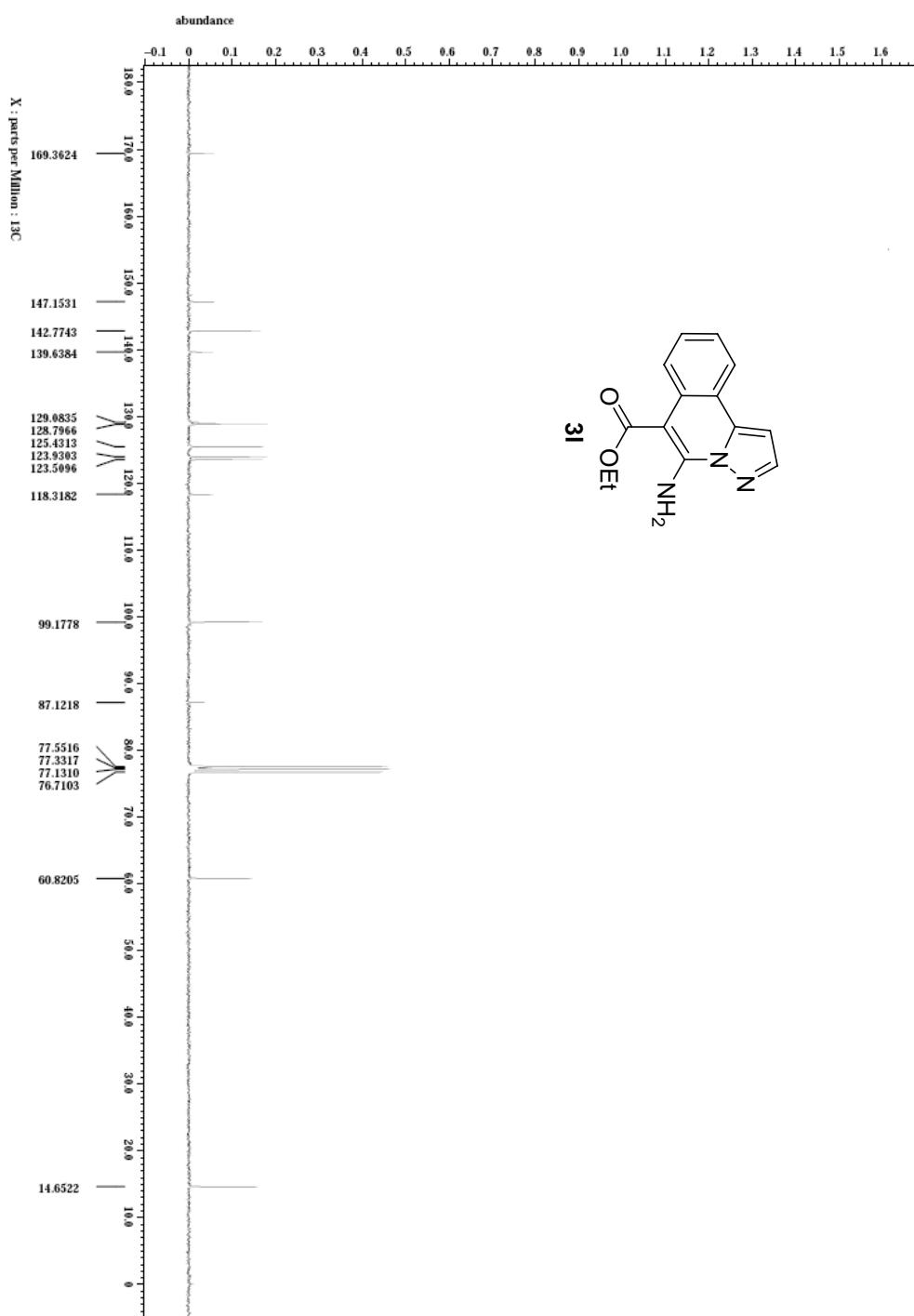


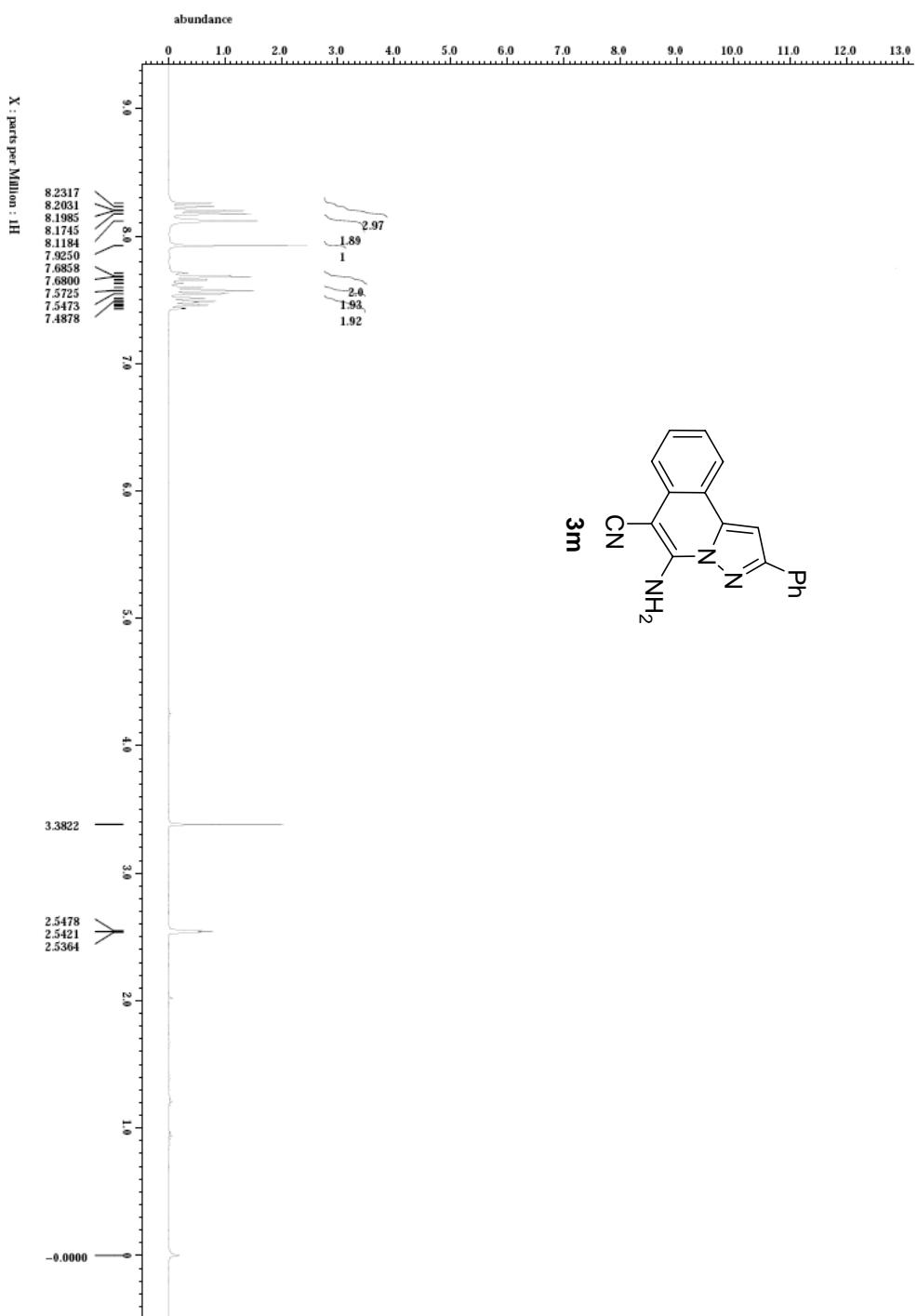


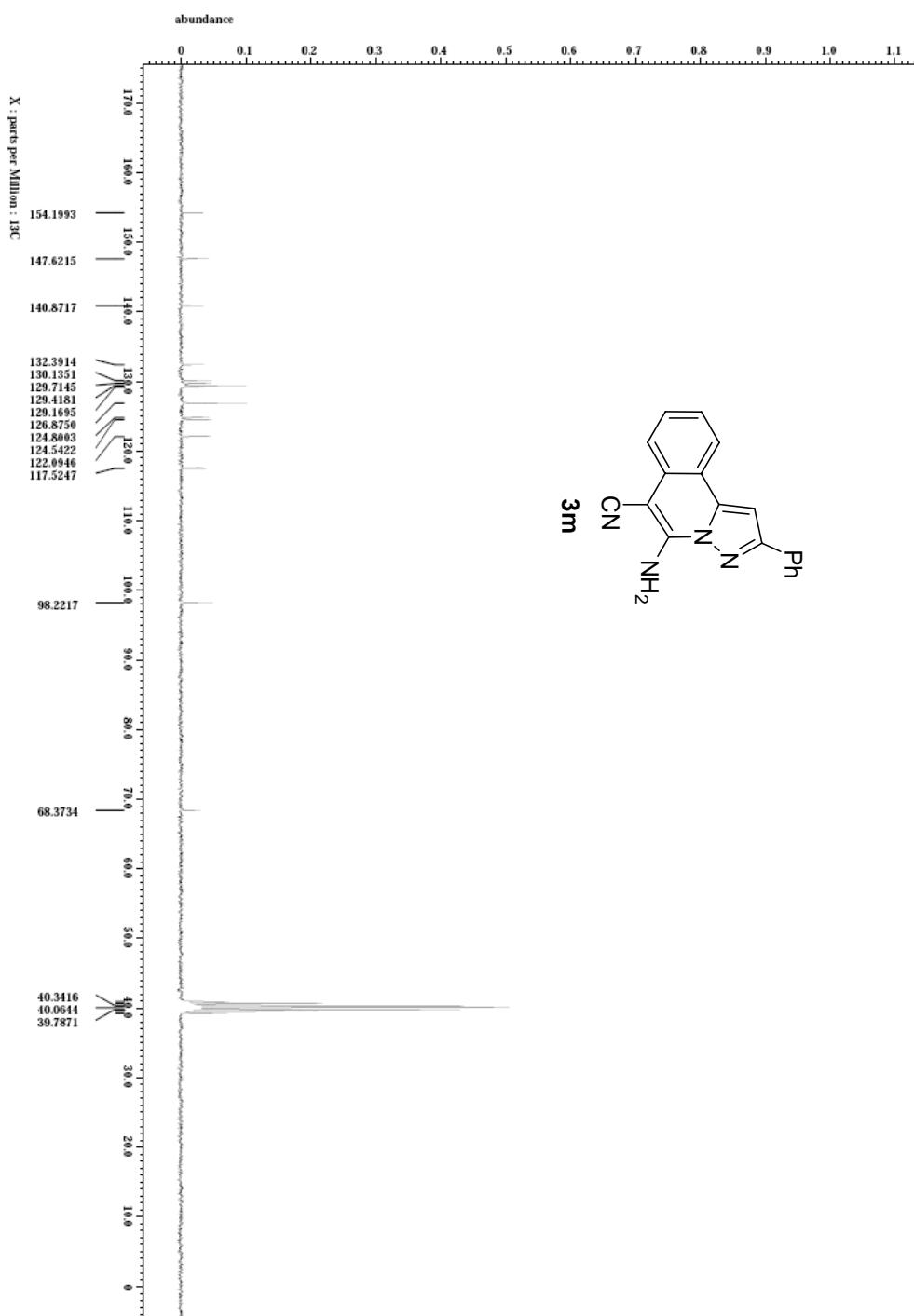


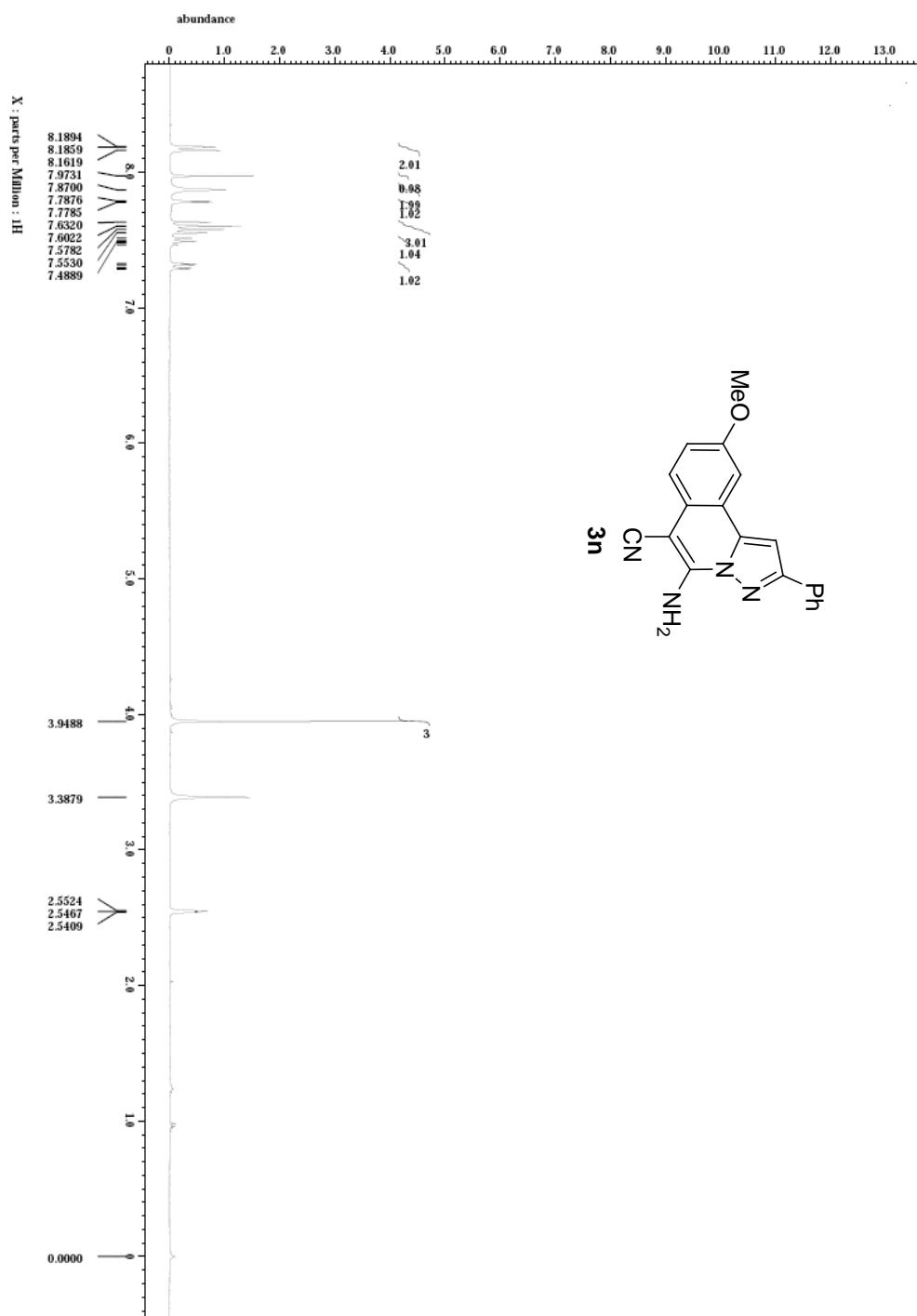


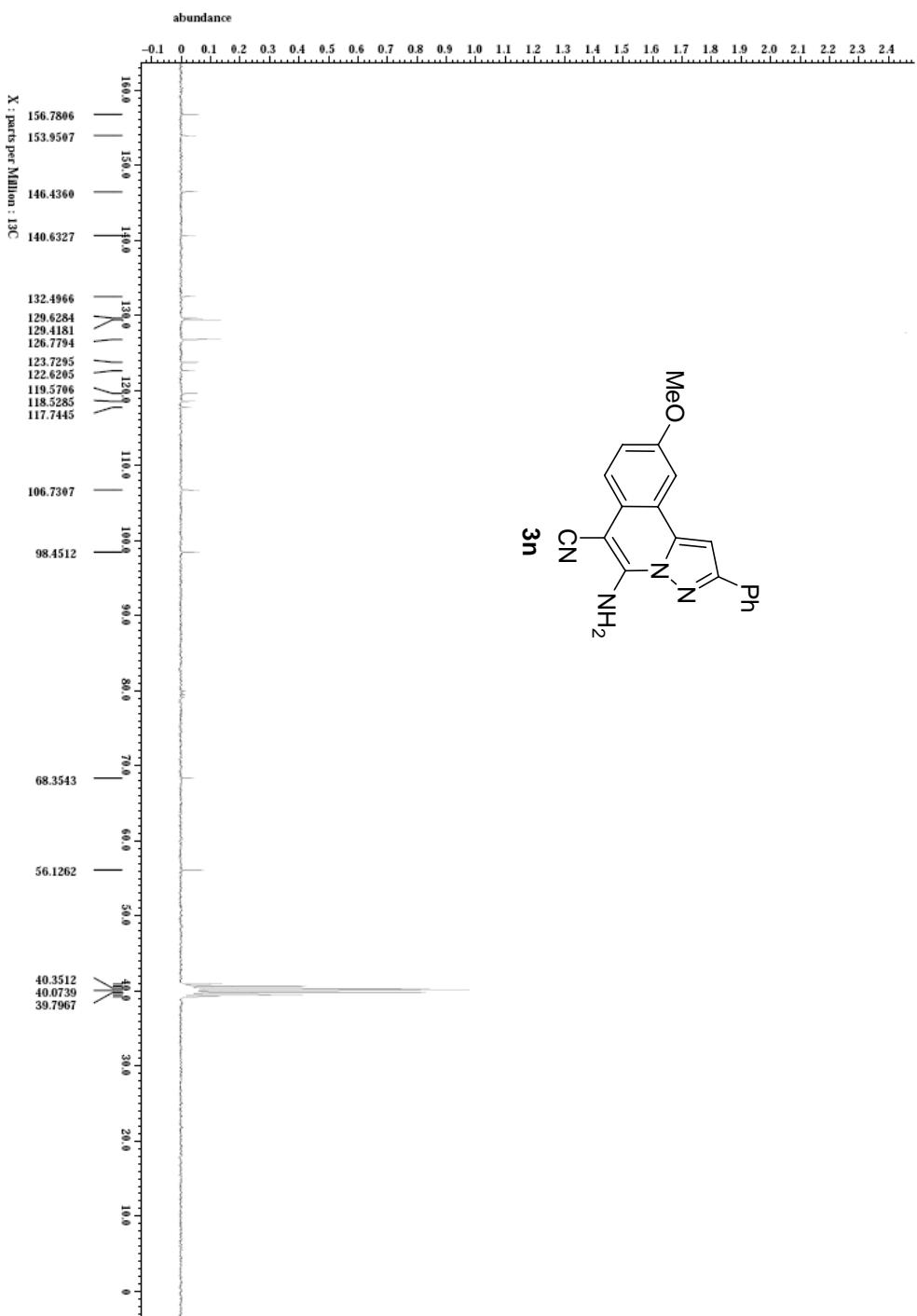


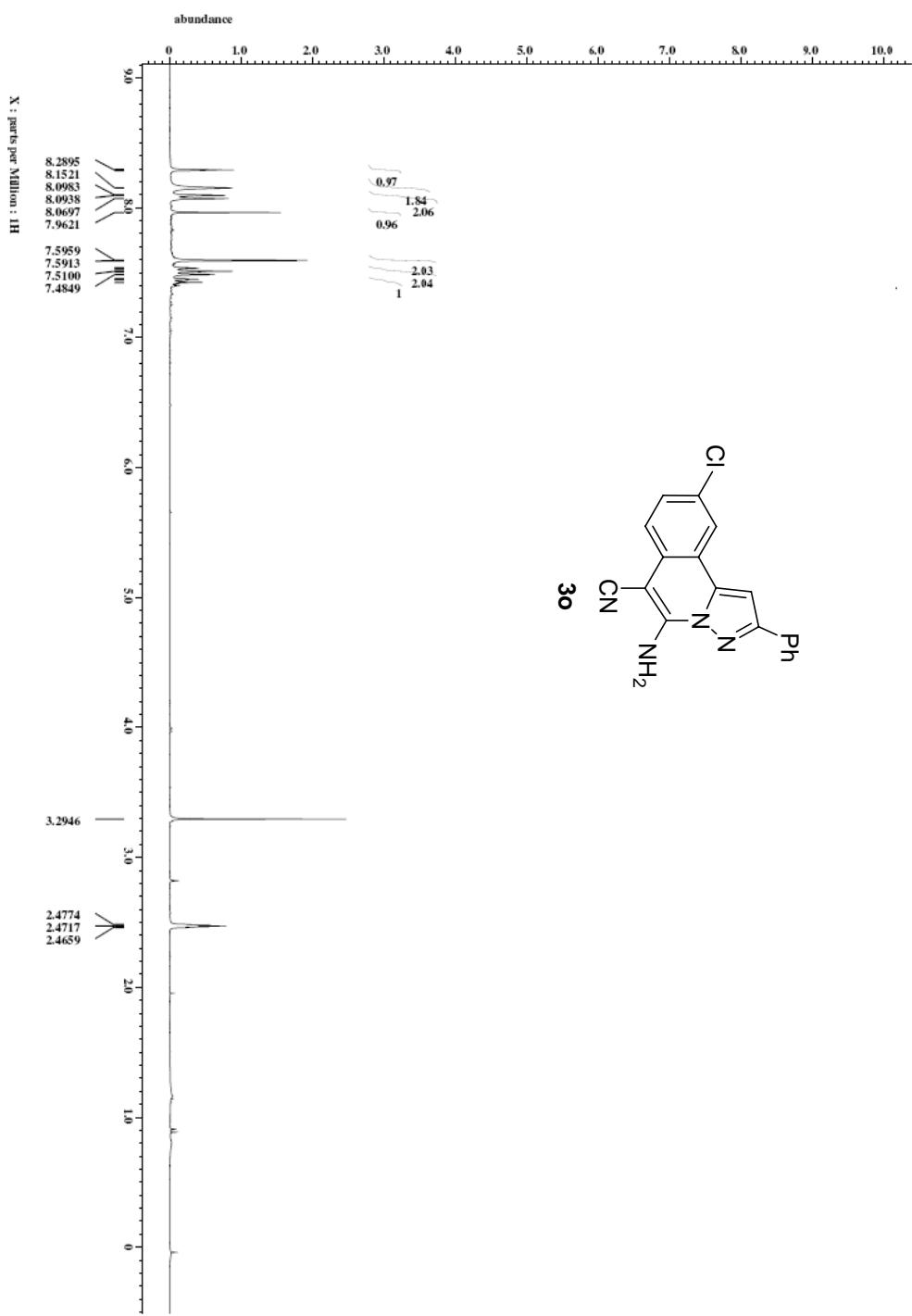


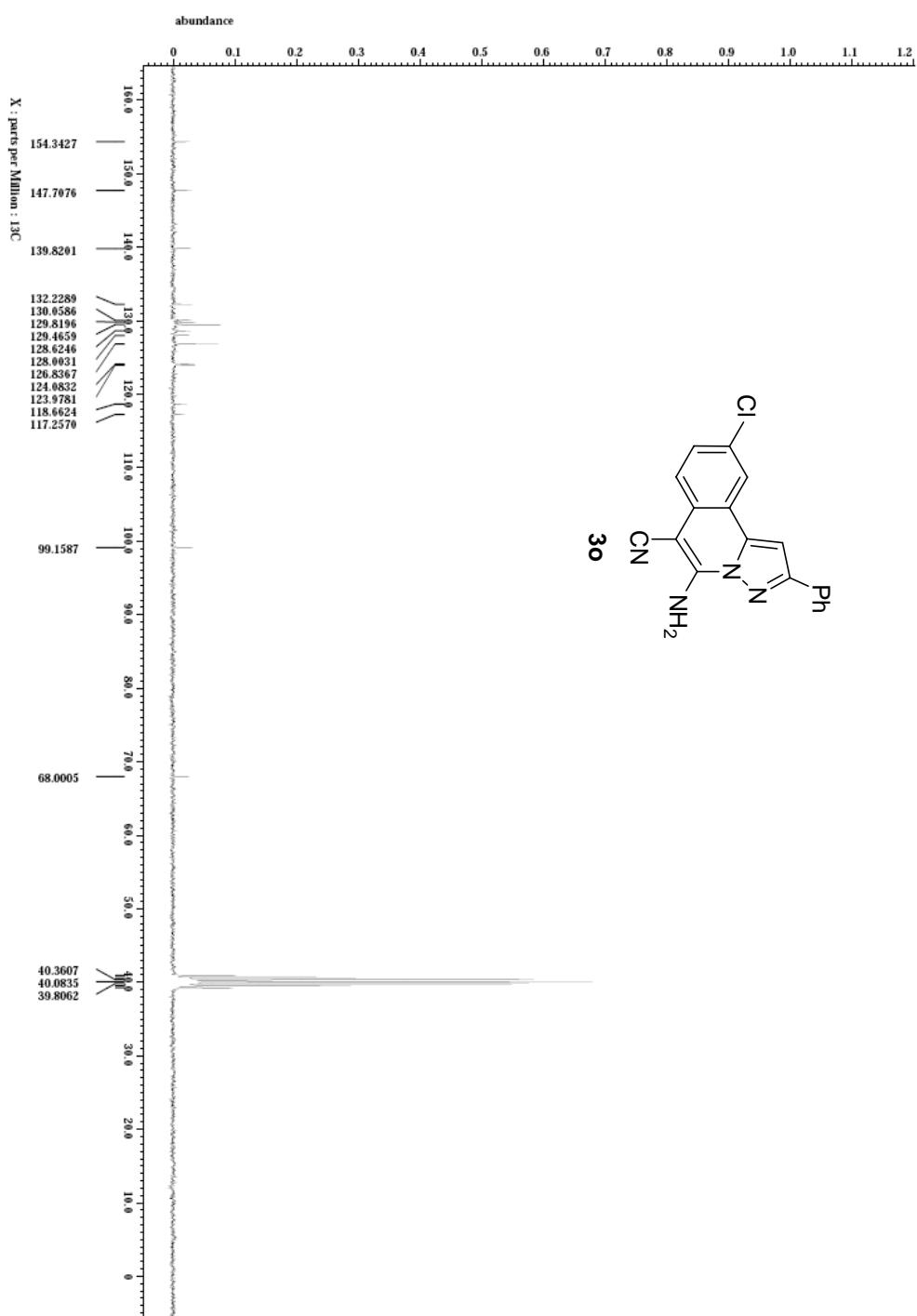


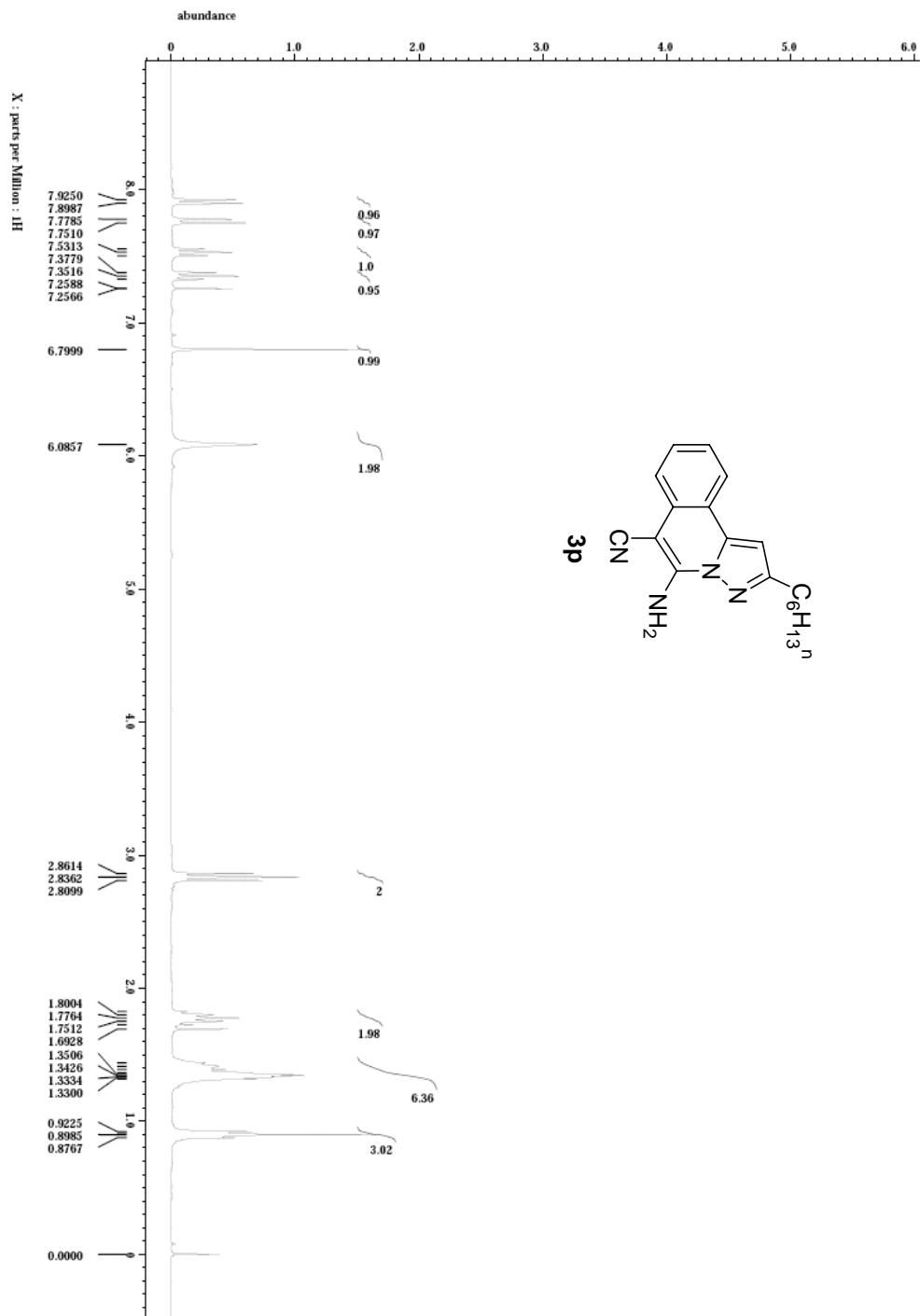


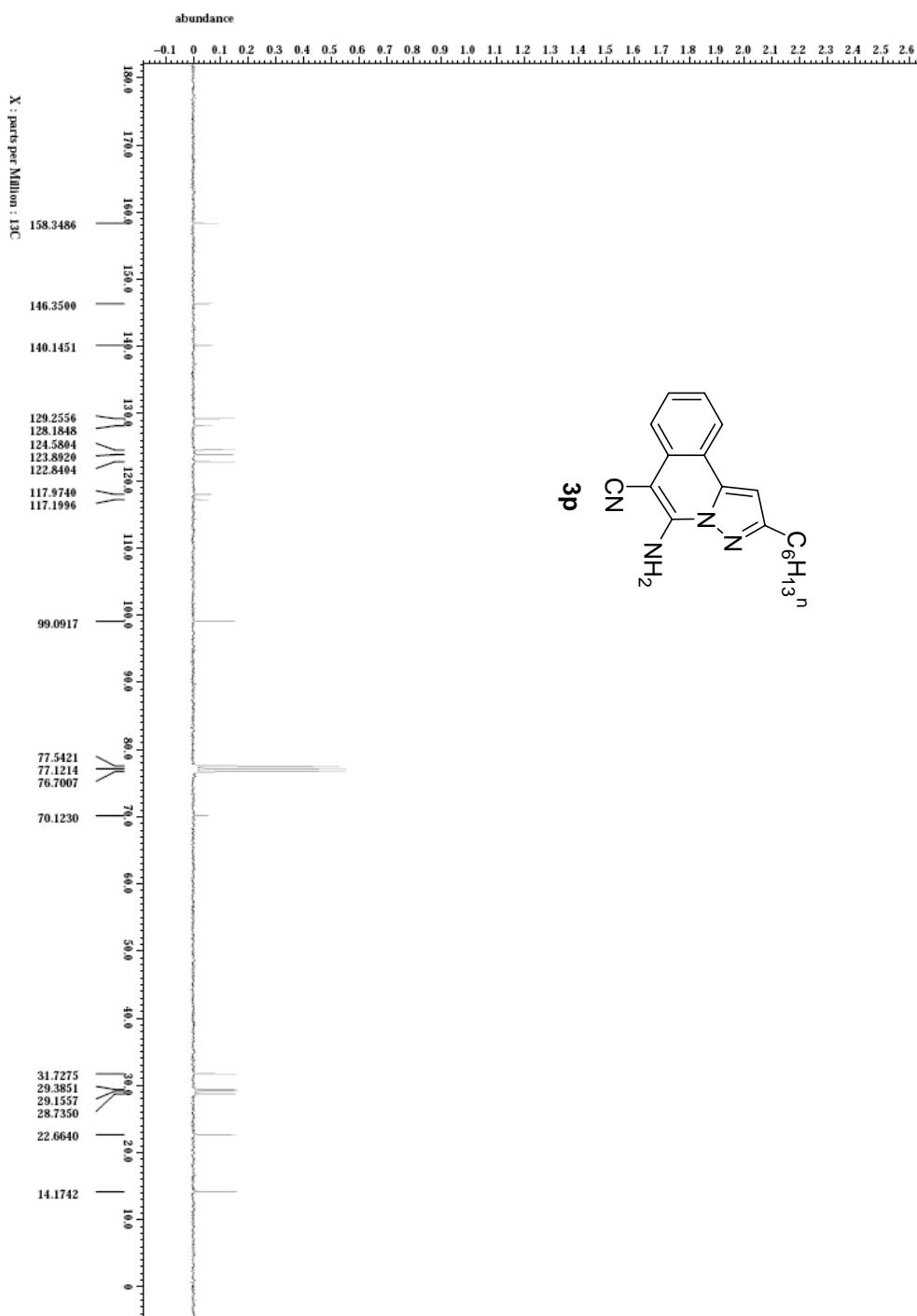


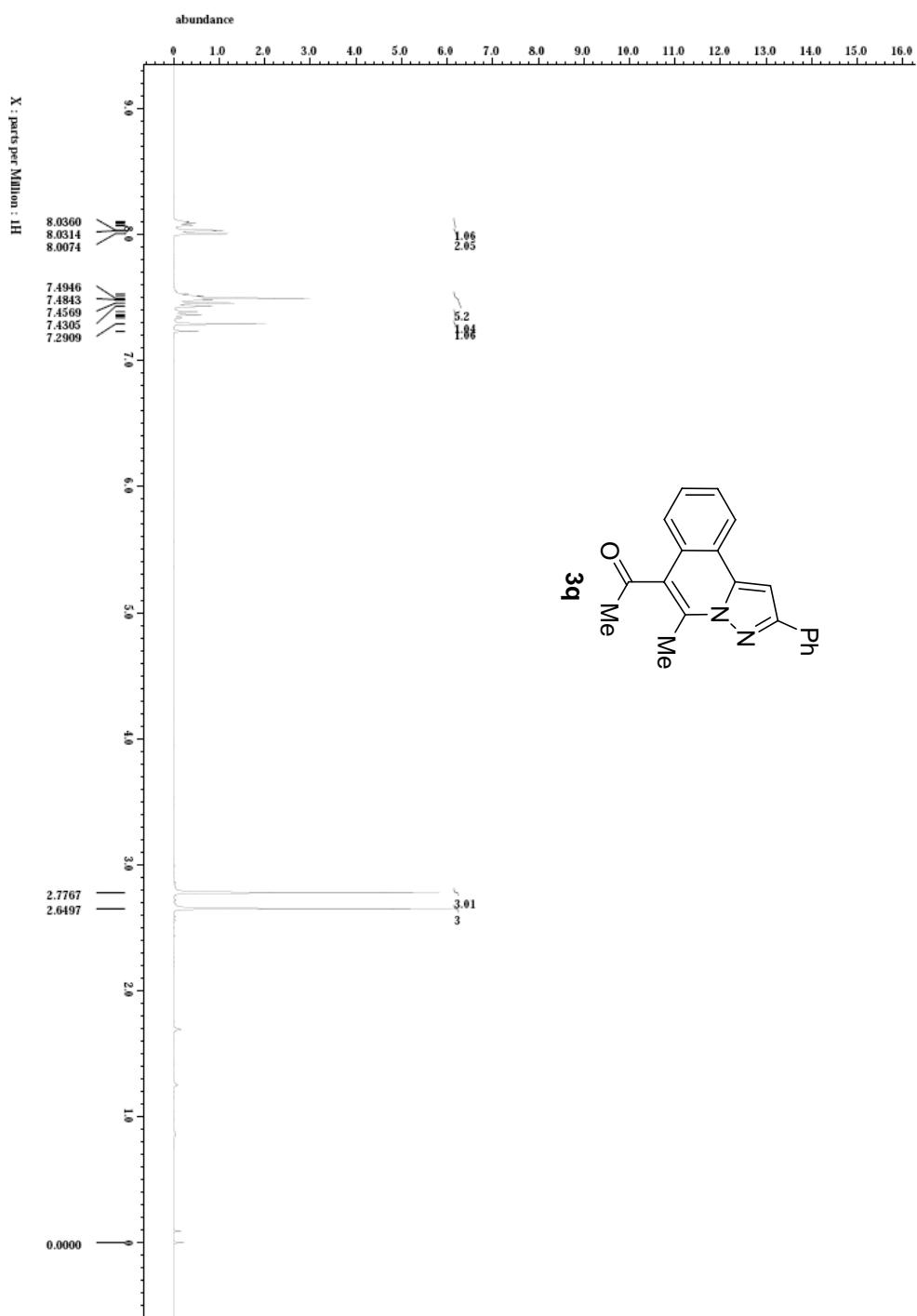


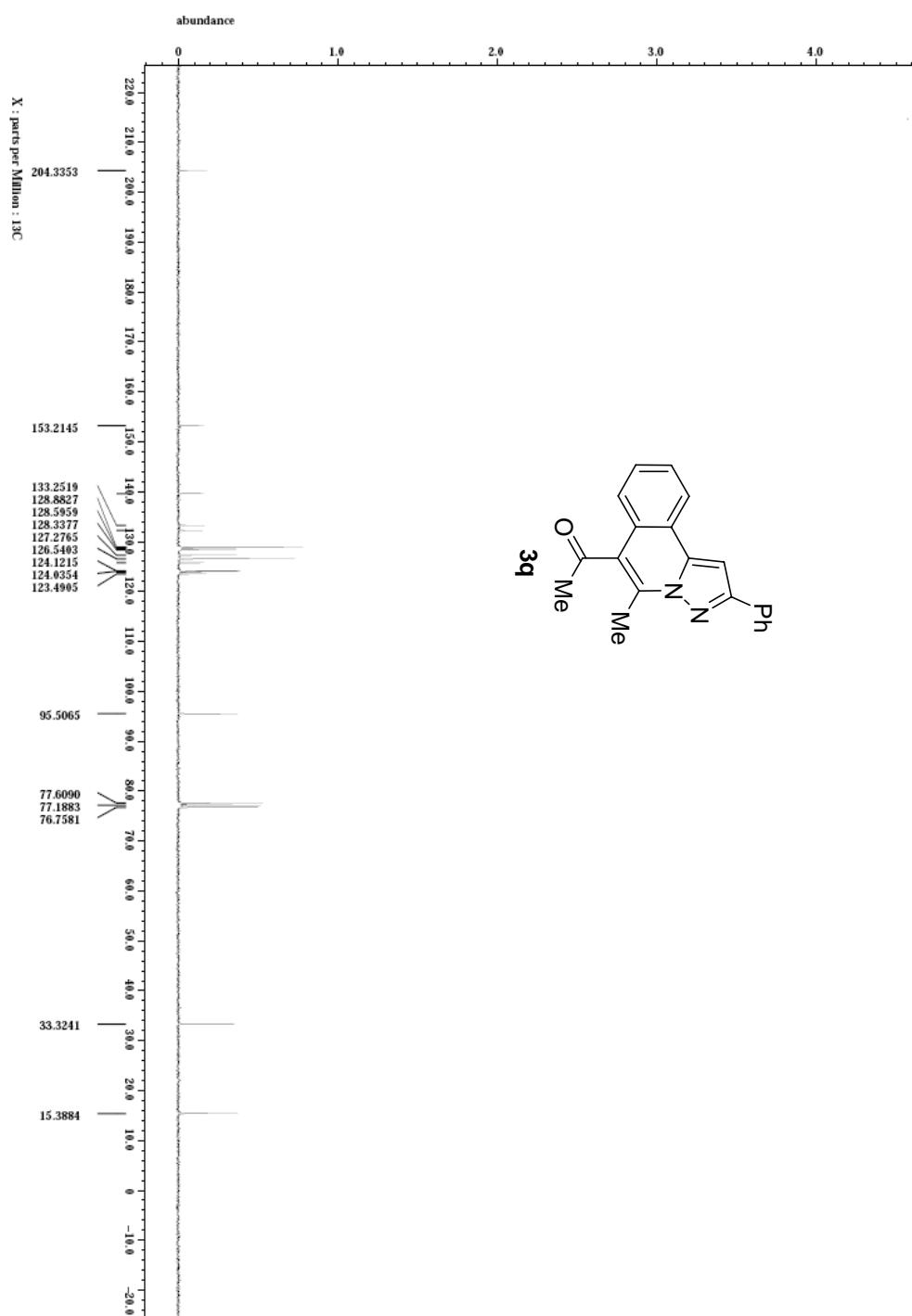


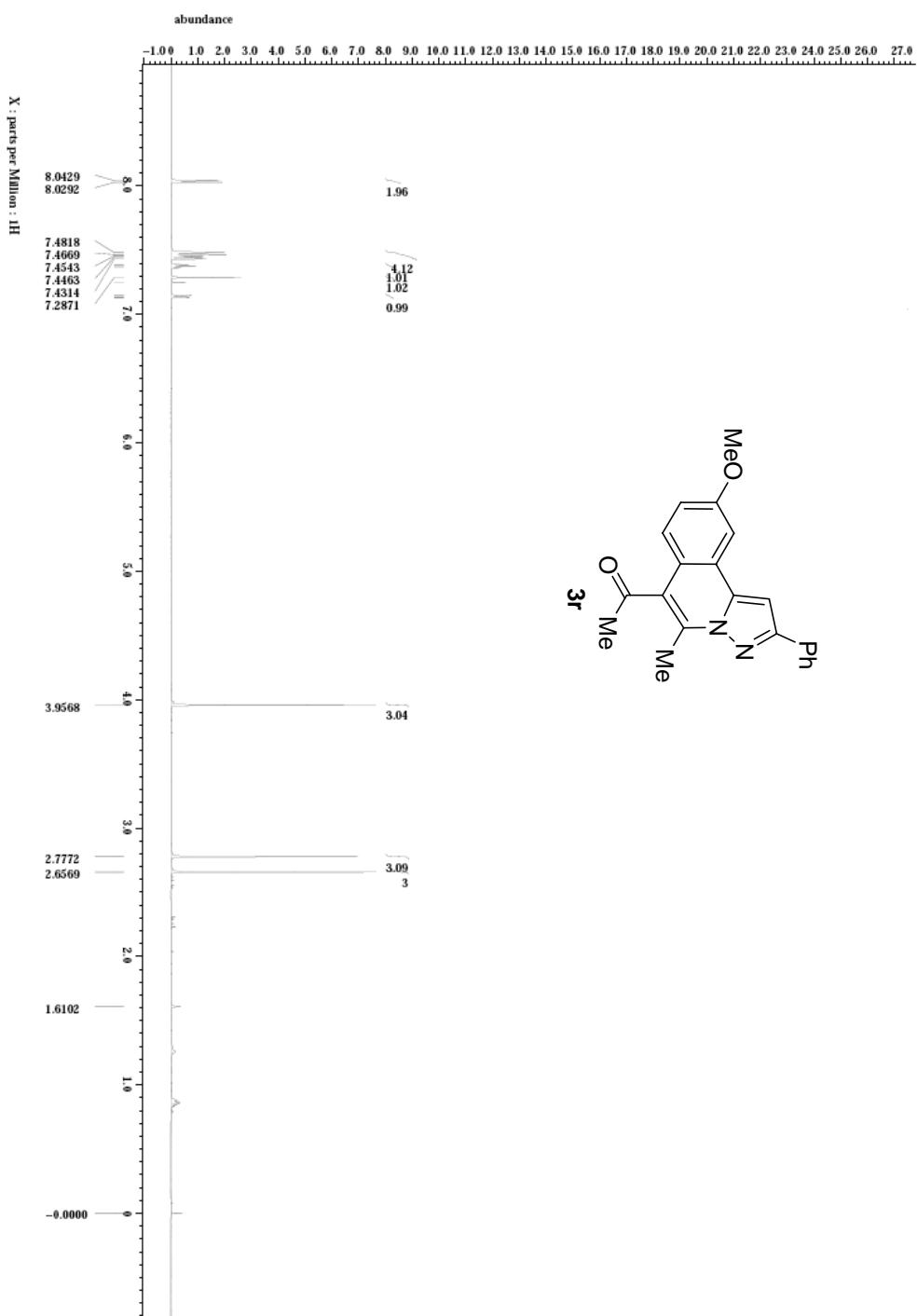


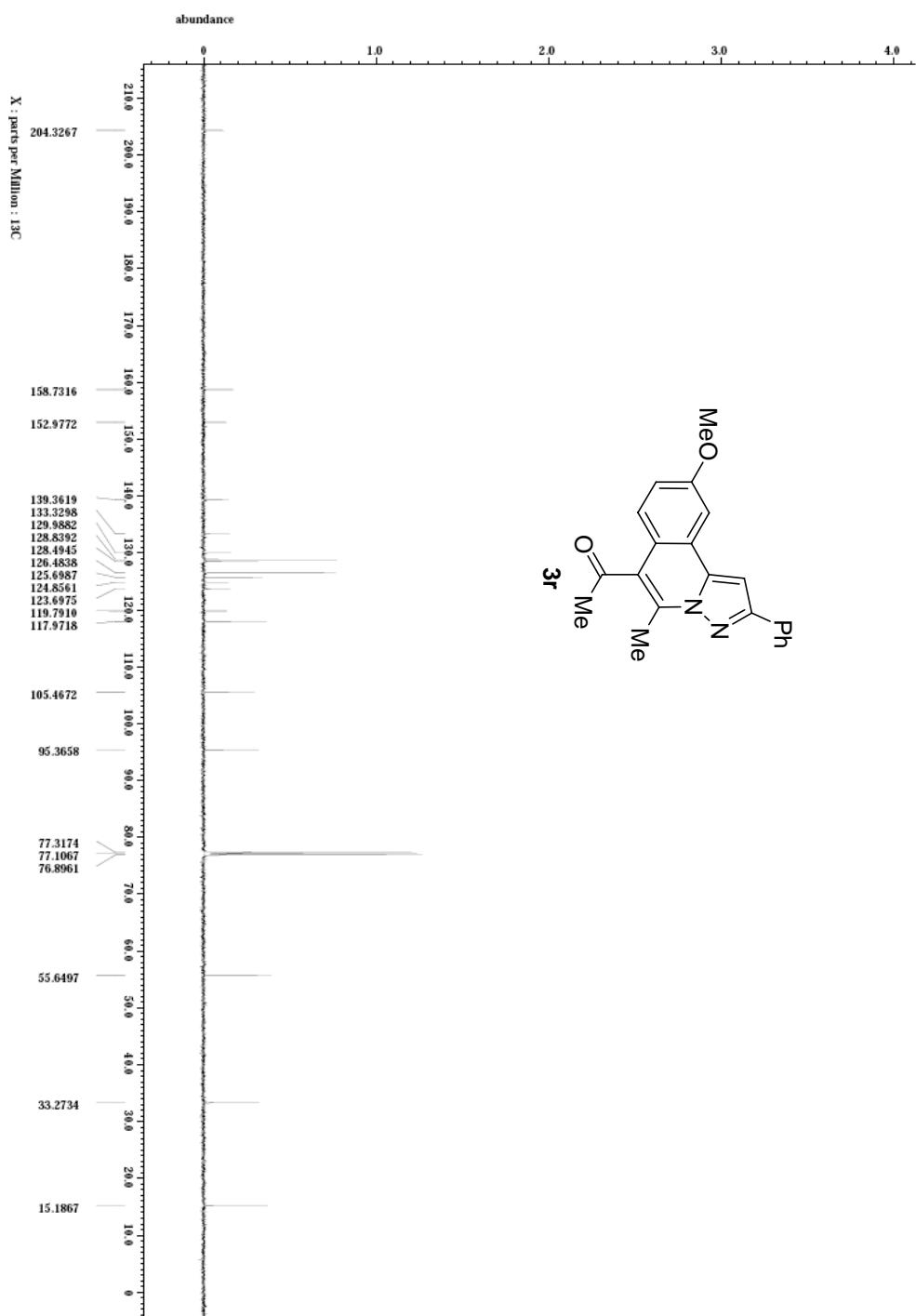






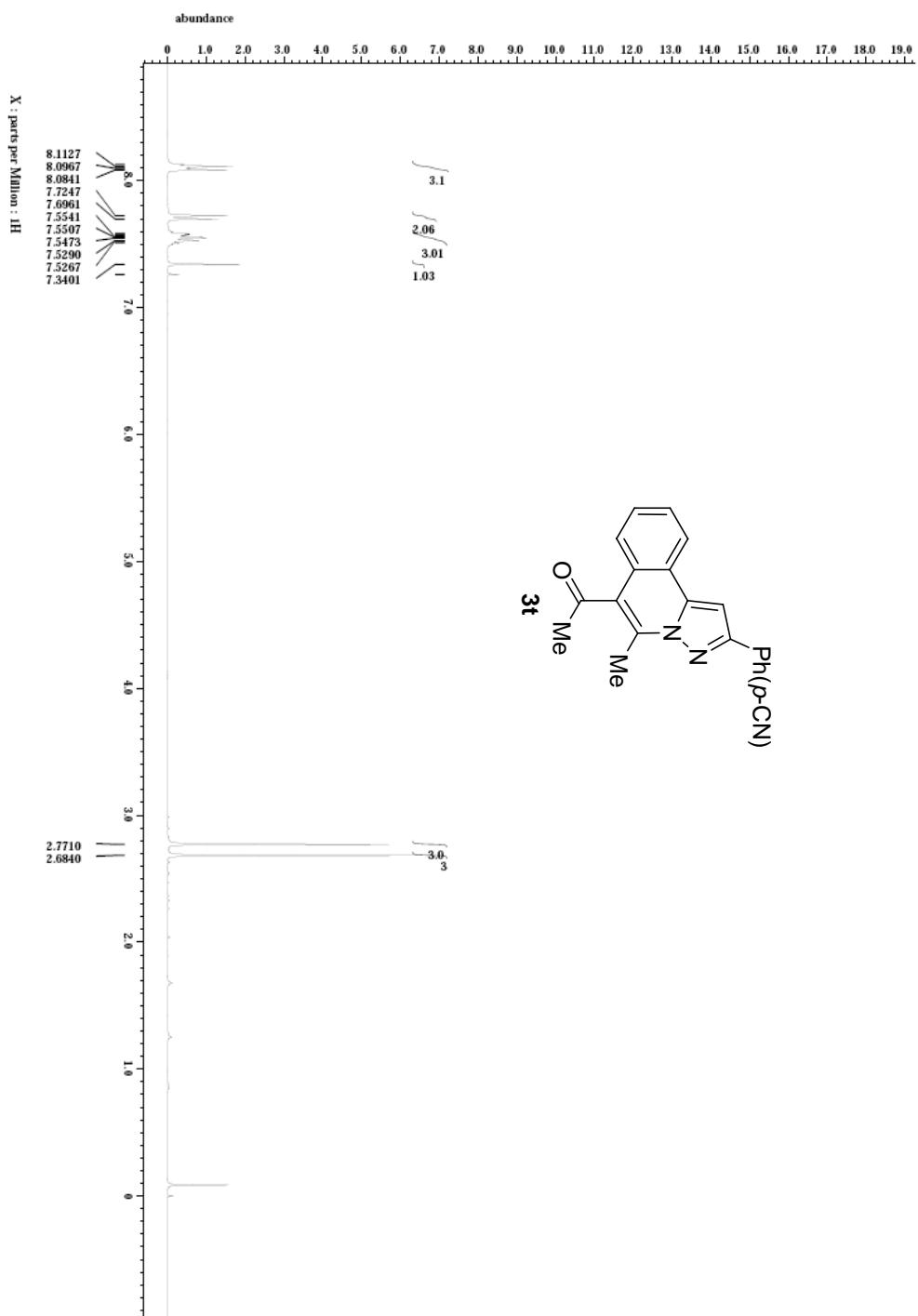


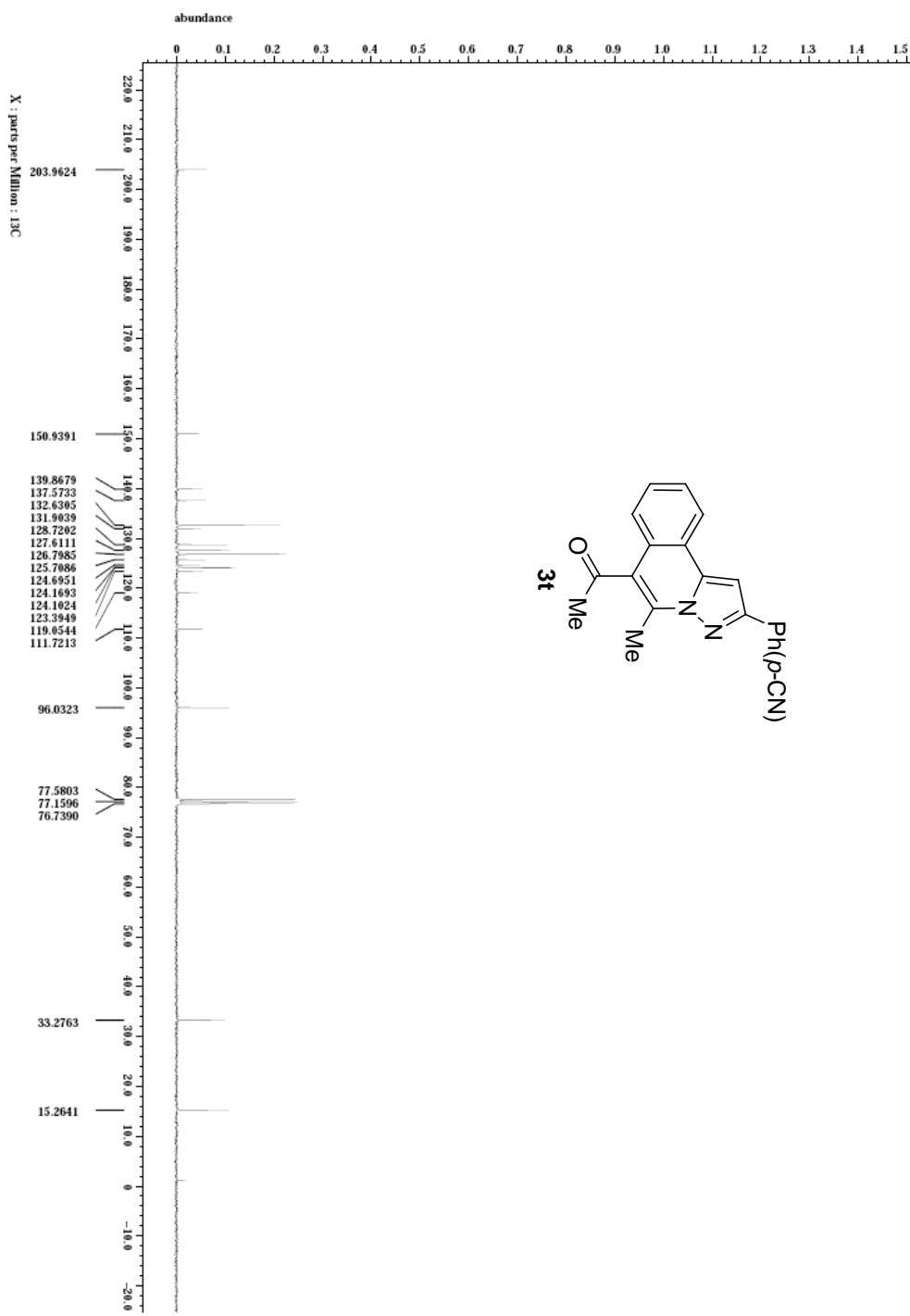




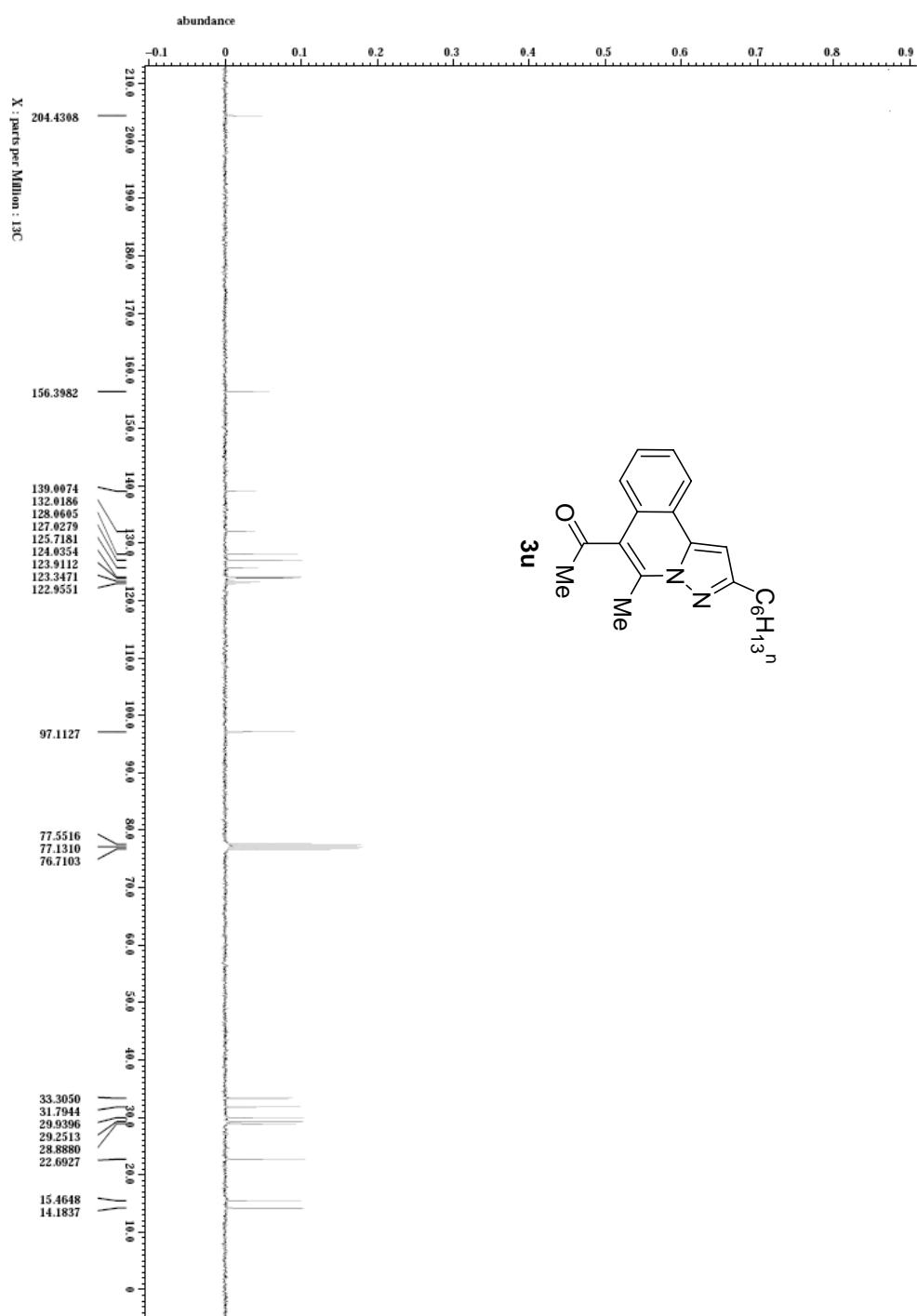


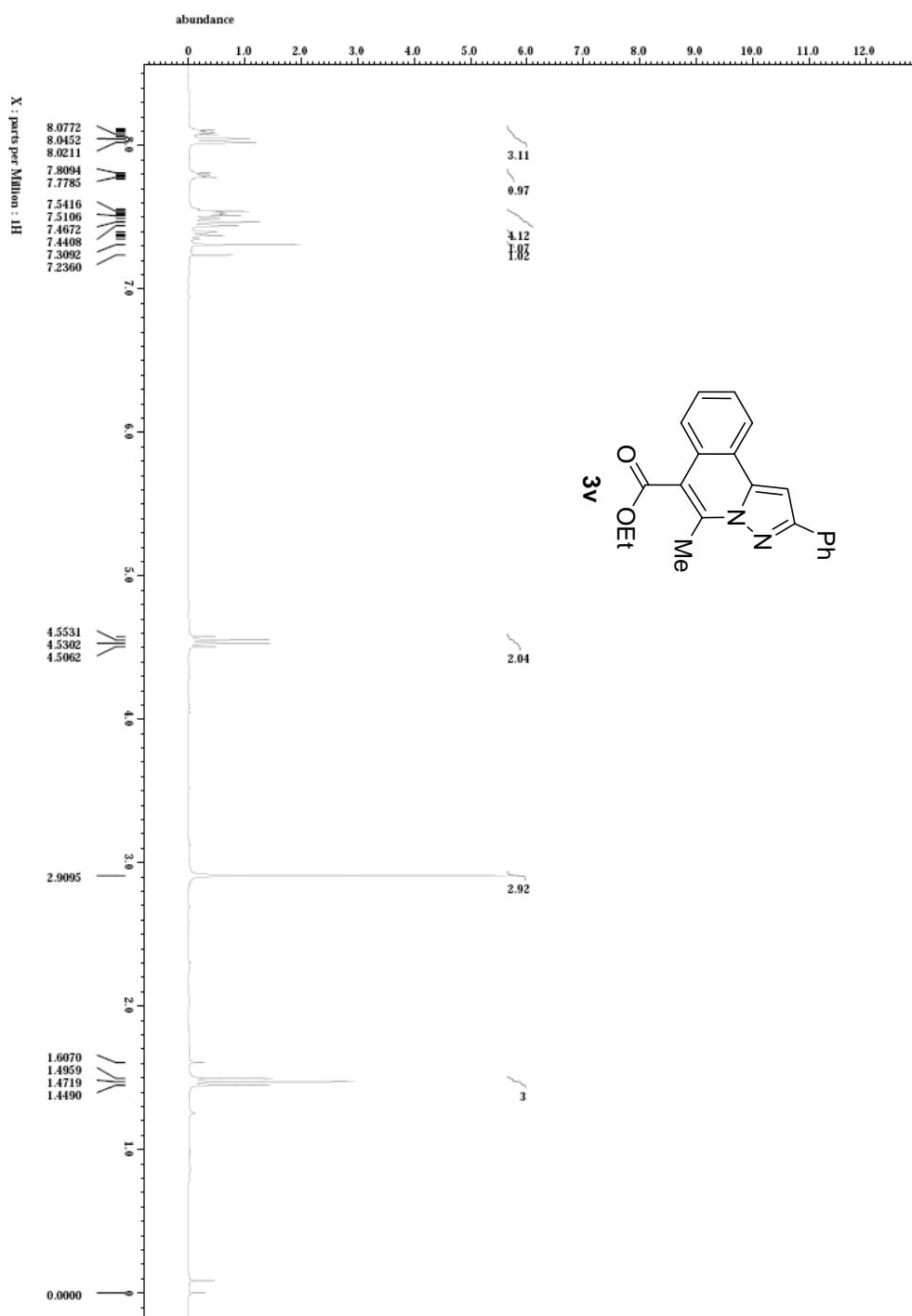


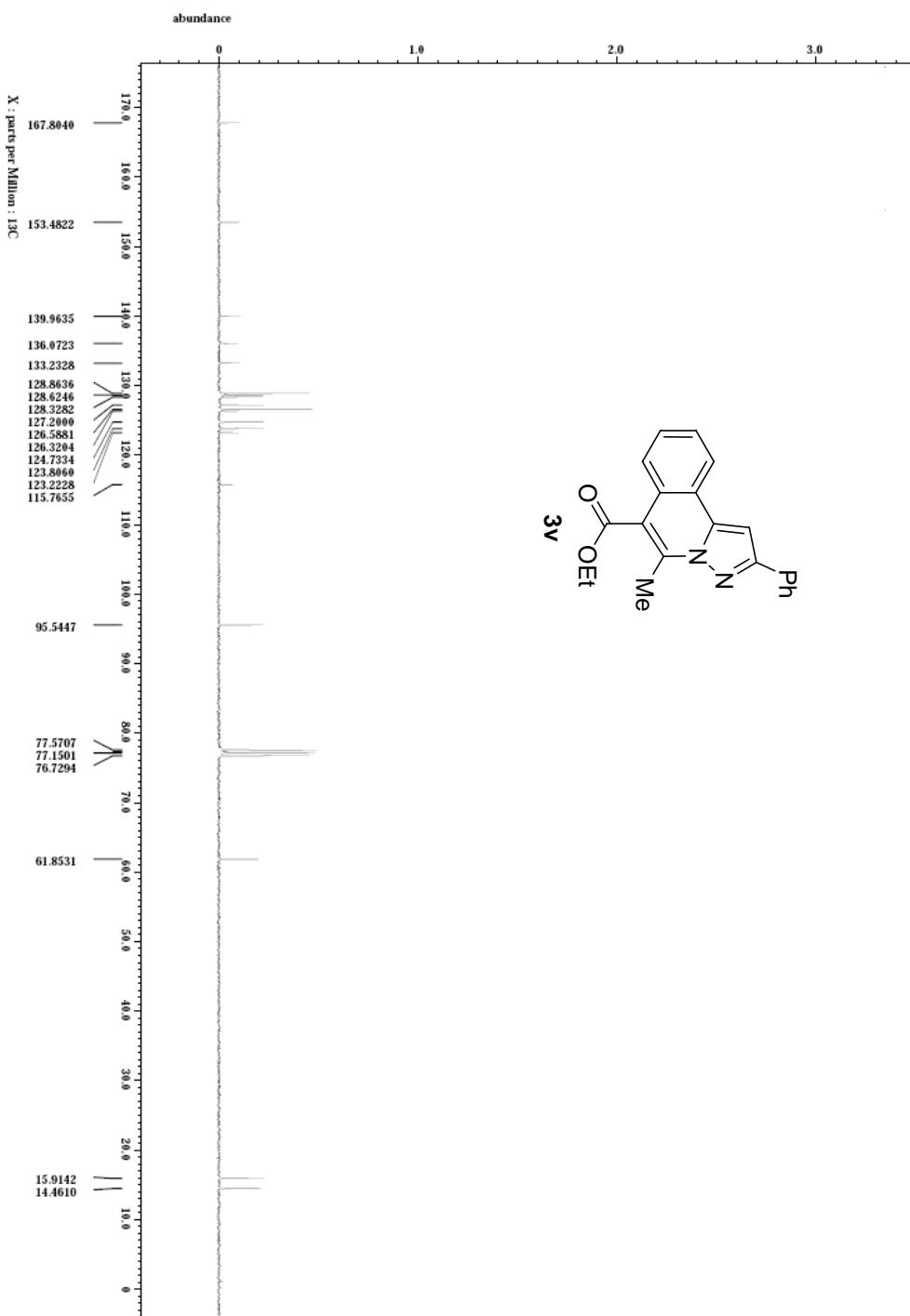


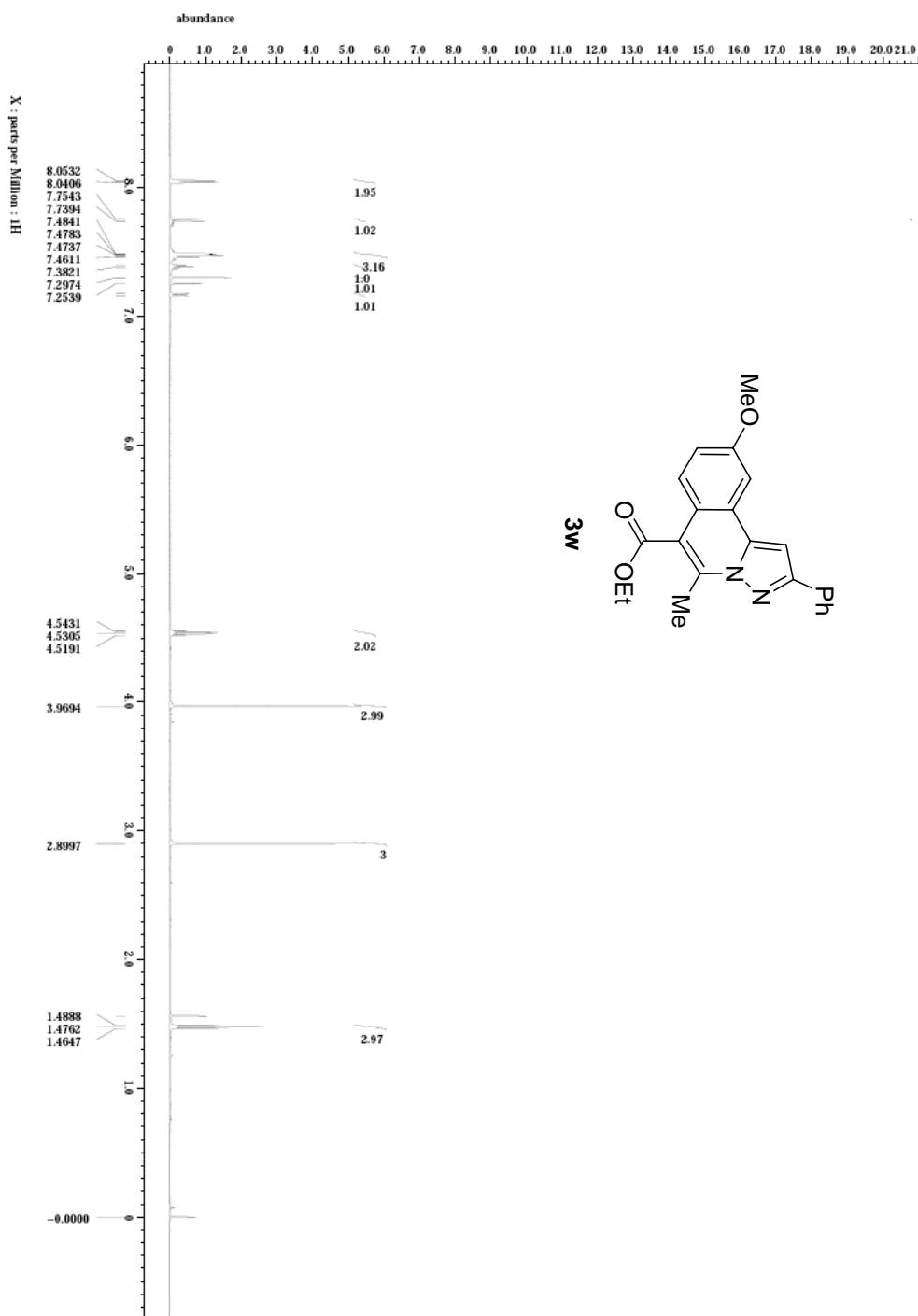


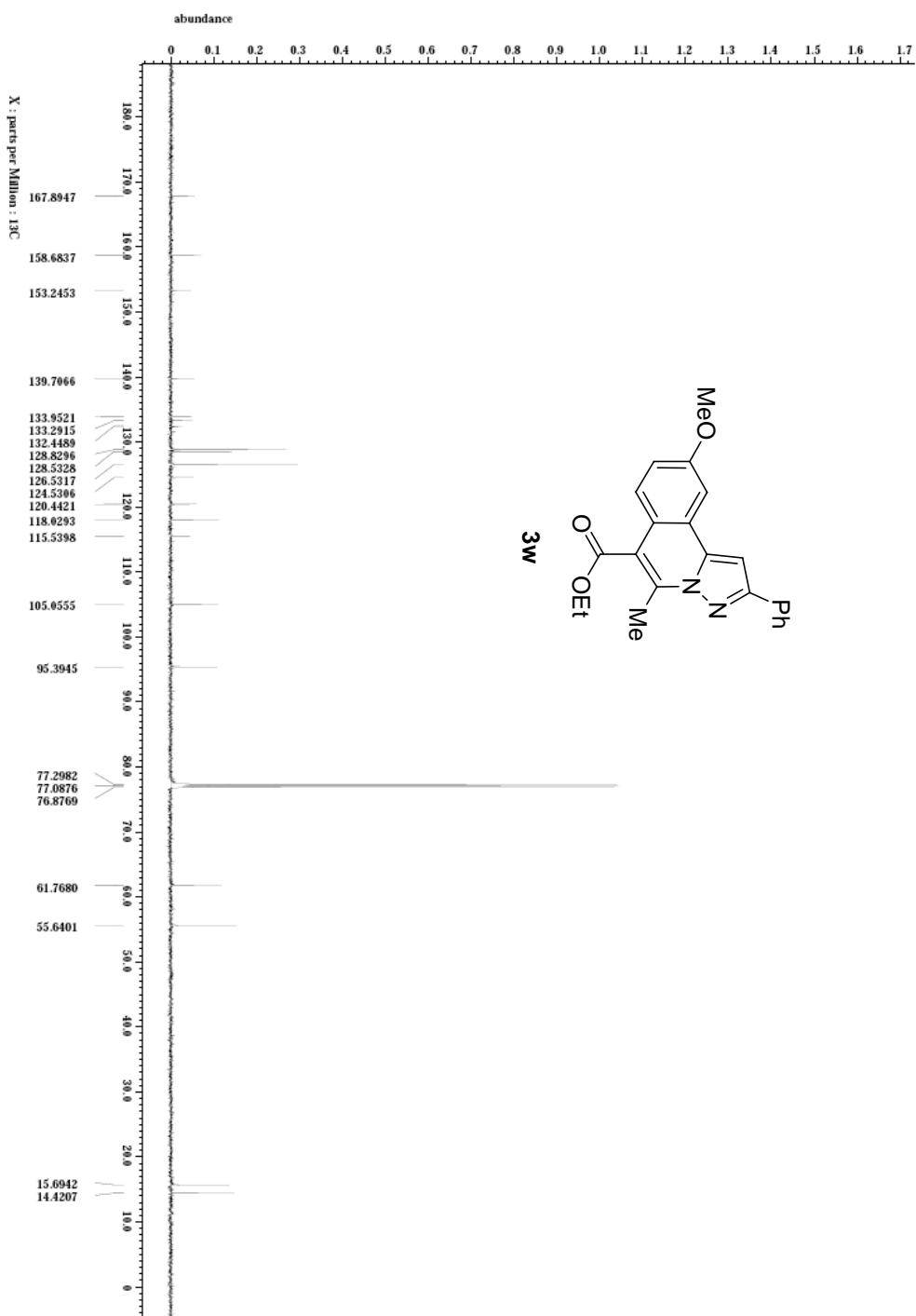






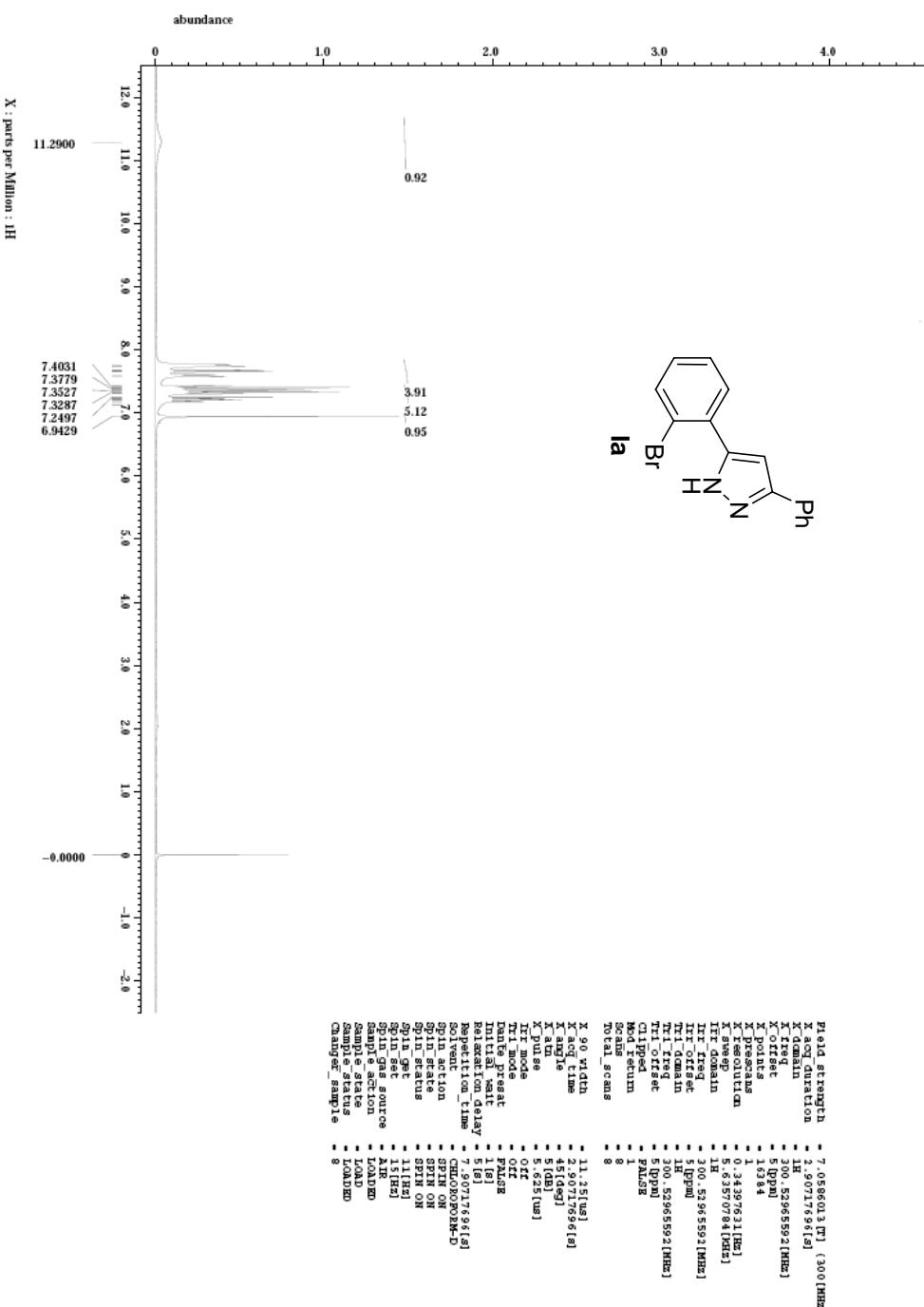


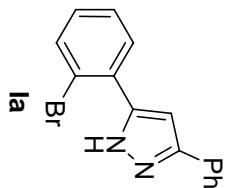
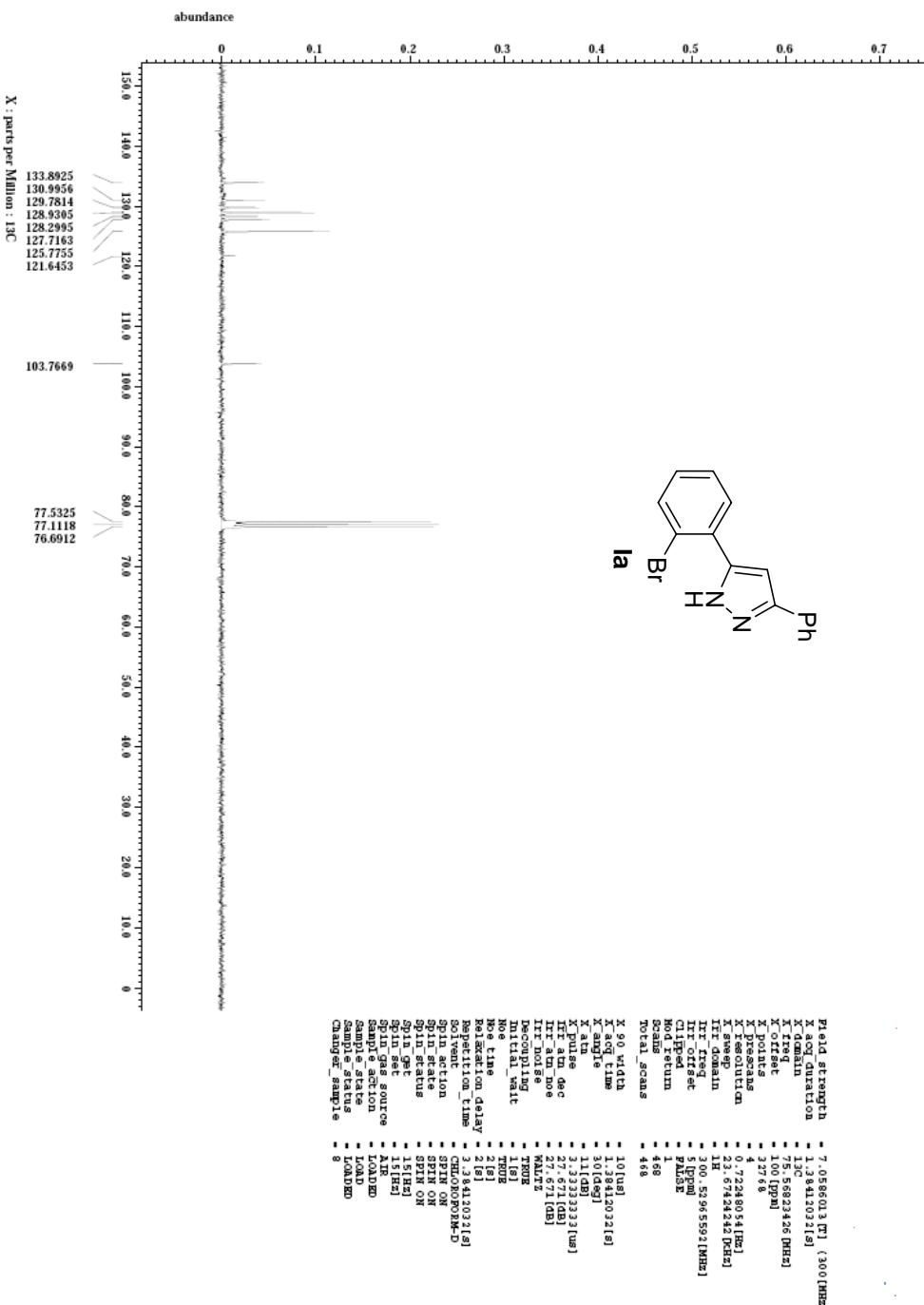












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