

Supporting Information

C(sp³)-H Dehydrogenation and C(sp²)-H Alkoxy Carbonylation of Inactivated Cyclic Amines towards Functionalized *N*-Heterocycles

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I. General Experimental Information

Commercial reagents were used without further purification, and the solvents were dried before using. *N*-Substituted piperidines (**1**), *N*-substituted pyrrolidines (**4**) and *N*-substituted azepanes (**6**) were prepared based on a literature procedure.¹ The 5:1 mixture of CO with O₂ was made by filling 2.5 MPa of CO and then 0.5 MPa of O₂ into a high-pressure reactor. The pre-made mixture of CO with O₂ was then introduced into a balloon from the high-pressure reactor for following uses. The ¹H NMR spectra were recorded at 400 MHz or 600 MHz. The ¹³C NMR spectra were recorded at 100 MHz or 150 MHz. Chemical shifts were expressed in parts per million (δ) downfield from the internal standard tetramethylsilane, and were reported as s (singlet), d (doublet), t (triplet), quint (quintuplet), dd (doublet of doublet), m (multiplet), etc. The coupling constants *J* were given in Hz. High resolution mass spectra (HRMS) were obtained *via* ESI mode by using a MicrOTOF mass spectrometer. The conversion of starting materials was monitored by thin layer chromatography (TLC) using silica gel plates (silica gel 60 F254 0.25 mm), and components were visualized by observation under UV light (254 and 365 nm).

II. Experimental Procedures and Spectroscopic Data

1. Typical Procedure for the Synthesis of **3a** and Spectroscopic Data of **3a-3x**

A schlenk tube (25 mL) containing 1-benzylpiperidine (**1a**, 88 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), Cu(OAc)₂ (18 mg, 0.1 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with CO/O₂ in balloon (5:1) for three times. Then CH₃CN (5 mL) and EtOH (**2a**, 292 μ L, 5 mmol) were added via syringe, and resulting mixture was stirred at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **3a** in 75% yield. **3b-3x** were obtained in a similar manner.

Ethyl 1-benzyl-1,4,5,6-tetrahydropyridine-3-carboxylate (**3a**)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (92 mg, 75%). ¹H NMR (400 MHz, CDCl₃) δ 1.28 (t, J = 7.2 Hz, 3H), 1.79-1.82 (m, 2H), 2.31 (t, J = 6.4 Hz, 2H), 3.00 (t, J = 6.0 Hz, 2H), 4.16 (q, J = 7.2 Hz, 2H), 4.30 (s, 2H), 7.23 (d, J = 6.8 Hz, 2H), 7.31-7.36 (m, 3H), 7.56 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 14.7, 20.0, 21.3, 45.4, 58.9, 59.7, 94.9, 127.4, 127.7, 128.7, 137.1, 146.2, 168.8. HRMS calcd for C₁₅H₂₀NO₂: 246.1489 [M+H]⁺, found: 246.1492.

Ethyl 1-(2-methylbenzyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (**3b**)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (97 mg, 75%). ¹H NMR (400 MHz, CDCl₃) δ 1.25-1.29 (m, 3H), 1.83 (t, J = 5.6 Hz, 2H), 2.30-2.34 (m, 5H), 2.97-3.02 (m, 2H), 4.12-4.18 (m, 2H), 4.30 (s, 2H), 7.15-7.23 (m, 4H), 7.50 (s, 1H). ¹³C NMR (100 MHz, CDCl₃) δ 14.7, 19.2, 20.1, 21.3, 45.6, 57.5, 58.9, 94.7, 126.2, 127.8, 128.0, 130.7, 134.8, 136.4, 146.2, 168.8. HRMS calcd for C₁₆H₂₁NO₂Na: 282.1465 [M+Na]⁺, found: 282.1462.

Ethyl 1-(3-fluorobenzyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (**3c**)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (101 mg, 77%). ^1H NMR (400 MHz, CDCl_3) δ 1.27-1.30 (m, 3H), 1.82 (t, $J = 5.6$ Hz, 2H), 2.31 (t, $J = 6.0$ Hz, 2H), 3.01 (t, $J = 6.4$ Hz, 2H), 4.17 (q, $J = 7.2$ Hz, 2H), 4.29 (s, 2H), 6.92-7.02 (m, 3H), 7.32-7.34 (m, 1H), 7.52 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 19.9, 21.2, 45.5, 59.1, 59.2, 95.4, 114.2 (d, $^2J_{\text{C-F}} = 21.0$ Hz), 114.7 (d, $^2J_{\text{C-F}} = 20.8$ Hz), 122.9, 130.3 (d, $^3J_{\text{C-F}} = 9.1$ Hz), 139.9 (d, $^4J_{\text{C-F}} = 6.2$ Hz), 146.0, 163.1 (d, $^1J_{\text{C-F}} = 245.5$ Hz), 168.7. HRMS calcd for $\text{C}_{15}\text{H}_{19}\text{FNO}_2$: 264.1394 $[\text{M}+\text{H}]^+$, found: 264.1395.

Ethyl 1-(4-methoxybenzyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3d)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (117 mg, 85%). ^1H NMR (400 MHz, CDCl_3) δ 1.28 (t, $J = 7.2$ Hz, 3H), 1.77-1.80 (m, 2H), 2.29 (t, $J = 6.0$ Hz, 2H), 2.97 (t, $J = 6.0$ Hz, 2H), 3.82 (s, 3H), 4.16 (q, $J = 6.8$ Hz, 2H), 4.23 (s, 2H), 6.88 (d, $J = 8.8$ Hz, 2H), 7.15 (d, $J = 8.8$ Hz, 2H), 7.55 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 20.0, 21.3, 45.2, 55.3, 58.9, 59.2, 94.5, 114.1, 128.8, 129.0, 146.1, 159.2, 168.8. HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_3$: 276.1594 $[\text{M}+\text{H}]^+$, found: 276.1595.

Ethyl 1-(4-chlorobenzyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3e)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (110 mg, 79%). ^1H NMR (400 MHz, CDCl_3) δ 1.26-1.30 (m, 3H), 1.79-1.82 (m, 2H), 2.30 (t, $J = 6.4$ Hz, 2H), 2.97 (t, $J = 6.0$ Hz, 2H), 4.16 (q, $J = 7.2$ Hz, 2H), 4.26 (s, 2H), 7.16 (d, $J = 8.4$ Hz, 2H), 7.33 (d, $J = 8.0$ Hz, 2H), 7.52 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 20.0, 21.2, 45.4, 59.0, 95.4, 117.2, 119.4, 126.3, 128.8, 128.9, 133.6, 135.6, 145.9, 168.7. HRMS calcd for $\text{C}_{15}\text{H}_{18}\text{ClNO}_2\text{Na}$: 302.0918 $[\text{M}+\text{Na}]^+$, found: 302.0921.

Ethyl 1-(4-cyanobenzyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3f)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (95 mg, 70%). ^1H NMR (400 MHz, CDCl_3) δ 1.26-1.30 (m, 3H), 1.82 (s, 2H), 2.31 (s, 2H), 2.99 (s, 2H), 4.16 (q, $J = 6.8$ Hz, 2H), 4.35 (s, 2H), 7.34 (d, $J = 7.6$ Hz, 2H), 7.49 (s, 1H), 7.66 (d, $J = 7.2$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 19.9, 21.2, 30.9, 45.8, 59.2, 96.3, 111.7, 118.6, 127.9, 132.6, 142.8, 145.6, 168.6. HRMS calcd for $\text{C}_{16}\text{H}_{19}\text{N}_2\text{O}_2$: 271.1441 $[\text{M}+\text{H}]^+$, found: 271.1443.

Ethyl 1-phenethyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3g)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (101 mg, 78%). ^1H NMR (400 MHz, CDCl_3) δ 1.25 (t, $J = 7.2$ Hz, 3H), 1.75-1.81 (m, 2H), 2.25 (t, $J = 6.4$ Hz, 2H), 2.83 (t, $J = 7.2$ Hz, 2H), 3.07 (t, $J = 5.6$ Hz, 2H), 3.34 (t, $J = 7.2$ Hz, 2H), 4.12 (q, $J = 7.2$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 2H), 7.21-7.32 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 20.0, 21.4, 35.6, 46.3, 57.6, 58.8, 94.3, 126.6, 128.6, 128.8, 138.6, 145.5, 168.7. HRMS calcd for $\text{C}_{16}\text{H}_{21}\text{NO}_2\text{Na}$: 282.1465 $[\text{M} + \text{Na}]^+$, found: 282.1479.

Ethyl 1-ethyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3h)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (75 mg, 82%). ^1H NMR (400 MHz, CDCl_3) δ 1.14-1.18 (m, 3H), 1.24-1.29 (m, 3H), 1.79-1.85 (m, 2H), 2.26-2.29 (m, 2H), 3.09 (t, $J = 6.0$ Hz, 2H), 3.15-3.21 (m, 2H), 4.11-4.17 (m, 2H), 7.38 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 13.9, 14.7, 20.1, 21.4, 29.7, 45.2, 50.4, 58.8, 93.8, 145.5, 168.8. HRMS calcd for $\text{C}_{10}\text{H}_{18}\text{NO}_2$: 184.1332 $[\text{M} + \text{H}]^+$, found: 184.1343.

Ethyl 1-octyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3i)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (112 mg, 84%). ^1H NMR (400 MHz, CDCl_3) δ 0.88 (t, $J = 7.2$ Hz, 3H), 1.24-1.32 (m, 13H), 1.53 (t, $J = 6.8$ Hz, 2H), 1.76-1.84 (m, 2H), 2.27 (t, $J = 6.0$ Hz, 2H), 3.08 (q, $J = 6.8$ Hz, 4H), 4.13 (q, $J = 6.8$ Hz, 2H), 7.35 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.1, 14.7, 20.1, 21.4, 22.6, 26.6, 28.5, 29.2, 29.3, 31.8, 45.7, 56.0, 58.8, 93.3, 146.0, 168.8. HRMS calcd for $\text{C}_{16}\text{H}_{29}\text{NO}_2\text{Na}$: 290.2091 $[\text{M} + \text{Na}]^+$, found: 290.2112.

Ethyl 1-cyclopentyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3j)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (61 mg, 55%). ^1H NMR (400 MHz, CDCl_3) δ 1.20-1.27 (m, 3H), 1.56-1.87 (m, 10H), 2.28 (t, $J = 6.4$ Hz, 2H), 3.07 (t, $J = 5.6$ Hz, 2H), 3.59 (t, $J = 8.0$ Hz, 1H), 4.13 (q, $J = 7.2$ Hz, 2H), 7.47 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.8, 20.6, 21.6, 23.9, 29.9, 43.4, 58.8, 65.8, 93.6, 144.8, 168.9. HRMS calcd for $\text{C}_{13}\text{H}_{21}\text{NO}_2\text{Na}$: 246.1465 $[\text{M} + \text{Na}]^+$, found: 246.1484.

Ethyl 1-phenyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3k)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (75 mg, 65%). ^1H NMR (400 MHz, CDCl_3) δ 1.29 (t, $J = 7.2$ Hz, 3H), 1.97-2.00 (m, 2H), 2.39 (t, $J = 6.4$ Hz, 2H), 3.60 (t, $J = 5.6$ Hz, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 7.06 (t, $J = 7.6$ Hz, 3H), 7.32-7.36 (m, 2H), 7.89 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.6, 20.6, 21.5, 46.1, 53.4, 59.4, 101.2, 117.4, 122.6, 129.4, 140.5, 145.9, 168.6. HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_2$: 232.1332 $[\text{M}+\text{H}]^+$, found: 232.1342.

Ethyl 1-(*o*-tolyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3l)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (69 mg, 56%). ^1H NMR (400 MHz, CDCl_3) δ 1.23-1.28 (m, 3H), 1.94-2.01 (m, 2H), 2.28 (s, 3H), 2.41 (t, $J = 6.4$ Hz, 2H), 3.43 (t, $J = 5.6$ Hz, 2H), 4.15 (q, $J = 7.2$ Hz, 2H), 7.07 (dd, $J_1 = 7.2$ Hz, $J_2 = 1.2$ Hz, 1H), 7.14-7.24 (m, 3H), 7.47 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.6, 18.2, 20.5, 21.7, 48.8, 59.1, 97.9, 125.7, 126.4, 127.0, 131.5, 133.5, 144.6, 146.2, 168.7. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$: 246.1489 $[\text{M}+\text{H}]^+$, found: 246.1488.

Ethyl 1-(*p*-tolyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3m)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (86 mg, 70%). ^1H NMR (400 MHz, CDCl_3) δ 1.25-1.30 (m, 3H), 1.95-1.98 (m, 2H), 2.31 (s, 3H), 2.38 (t, $J = 6.4$ Hz, 2H), 3.57 (t, $J = 5.6$ Hz, 2H), 4.18 (q, $J = 7.2$ Hz, 2H), 6.97 (dd, $J_1 = 6.8$ Hz, $J_2 = 2.0$ Hz, 2H), 7.14 (d, $J = 8.0$ Hz, 2H), 7.85 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 20.5, 20.6, 21.5, 46.3, 53.4, 59.3, 100.3, 117.6, 129.9, 132.3, 140.9, 143.7, 168.6. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$: 246.1489 $[\text{M}+\text{H}]^+$, found: 246.1493.

Ethyl 1-(4-methoxyphenyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3n)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (104 mg, 80%). ^1H NMR (400 MHz, CDCl_3) δ 1.25-1.30 (m, 3H), 1.95-1.98 (m, 2H), 2.38 (t, $J = 6.4$ Hz, 2H), 3.55 (t, $J = 5.6$ Hz, 2H), 3.80 (s, 3H), 4.18 (q, $J = 7.2$ Hz, 2H), 6.88 (dd, $J_1 = 6.8$ Hz, $J_2 = 2.0$ Hz, 2H), 7.01 (dd, $J_1 = 6.8$ Hz, $J_2 = 2.4$ Hz, 2H), 7.78 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 20.4, 21.5, 46.8, 55.6, 59.3, 99.6, 114.6, 119.5, 140.0, 141.4, 155.7, 168.7. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_3$: 262.1438 $[\text{M}+\text{H}]^+$, found: 262.1439.

Ethyl 1-(4-fluorophenyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3o)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (62 mg, 50%). ^1H NMR (400 MHz, CDCl_3) δ 1.25-1.30 (m, 3H), 1.96-1.99 (m, 2H), 2.38 (t, $J = 6.4$ Hz, 2H), 3.56 (t, $J = 5.6$ Hz, 2H), 4.18 (q, $J = 7.2$ Hz, 2H), 7.00-7.03 (m, 4H), 7.78 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.6, 20.4, 21.4, 46.6, 59.4, 101.0, 115.9, 116.0 (d, $^2J_{\text{C-F}} = 21.8$ Hz), 119.2 (d, $^3J_{\text{C-F}} = 8.0$ Hz), 140.7, 142.4 (d, $^4J_{\text{C-F}} = 2.9$ Hz), 158.7 (d, $^1J_{\text{C-F}} = 241.5$ Hz), 168.5. HRMS calcd for $\text{C}_{14}\text{H}_{17}\text{FNO}_2$: 250.1238 $[\text{M}+\text{H}]^+$, found: 250.1243.

Ethyl 1-mesityl-1,4,5,6-tetrahydropyridine-3-carboxylate (3p)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (104 mg, 76%). ^1H NMR (400 MHz, CDCl_3) δ 1.23 (t, $J = 7.2$ Hz, 3H), 1.98-2.01 (m, 2H), 2.19 (s, 6H), 2.28 (s, 1H), 2.41 (t, $J = 6.0$ Hz, 2H), 3.29 (t, $J = 5.6$ Hz, 2H), 4.12 (q, $J = 7.2$ Hz, 2H), 6.90 (s, 2H), 7.30 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 17.9, 20.3, 20.9, 21.5, 47.6, 58.9, 95.3, 129.3, 136.0, 137.2, 141.9, 145.4, 168.8. HRMS calcd for $\text{C}_{17}\text{H}_{24}\text{NO}_2$: 274.1802 $[\text{M}+\text{H}]^+$, found: 274.1805.

Ethyl 1-benzyl-6-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3q)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (91 mg, 70%). ^1H NMR (600 MHz, CDCl_3) δ 1.06 (d, $J = 6.0$ Hz, 3H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.61-1.66 (m, 2H), 2.17-2.25 (m, 1H), 2.42-2.45 (m, 1H), 3.28 (s, 1H), 4.13-4.18 (m, 2H), 4.32-4.38 (m, 2H), 7.21-7.36 (m, 5H), 7.50 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 16.5, 17.3, 27.1, 48.9, 57.4, 59.0, 94.1, 127.3, 127.7, 128.7, 137.6, 145.5, 168.8. HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_2$: 260.1645 $[\text{M}+\text{H}]^+$, found: 260.1652.

Ethyl 6-methyl-1-(2-methylbenzyl)-1,4,5,6-tetrahydropyridine-3-carboxylate (3r)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (90 mg, 66%). ^1H NMR (600 MHz, CDCl_3) δ 1.05 (d, $J = 6.0$ Hz, 3H), 1.25 (t, $J = 7.2$ Hz, 3H), 1.68-1.70 (m, 2H), 2.22-2.25 (m, 1H), 2.29 (s, 3H), 2.43-2.46 (m, 1H), 3.27-3.28 (m, 1H), 4.13-4.16 (m, 1H), 4.27 (d, $J = 15.6$ Hz, 1H), 4.39 (d, $J = 15.6$ Hz, 1H), 7.13-7.21 (m, 4H), 7.43 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 16.4, 17.1, 19.2, 27.0, 49.0, 55.3,

58.9, 94.1, 126.2, 127.8, 128.0, 130.7, 135.2, 136.4, 145.3, 168.8. HRMS calcd for $C_{17}H_{24}NO_2$: 274.1802 $[M+H]^+$, found: 274.1805.

Ethyl 1-(4-methoxybenzyl)-6-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3s)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (113 mg, 78%). 1H NMR (600 MHz, $CDCl_3$) δ 1.04 (d, $J = 6.6$ Hz, 3H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.58-1.71 (m, 2H), 2.18-2.24 (m, 1H), 2.40-2.44 (m, 1H), 3.26-3.28 (m, 1H), 3.80 (s, 3H), 4.12-4.18 (m, 2H) 4.25 (d, $J = 15.6$ Hz, 1H), 4.29 (d, $J = 15.6$ Hz, 1H), 6.87 (d, $J = 8.4$ Hz, 2H), 7.14 (d, $J = 8.4$ Hz, 2H), 7.49 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.7, 16.5, 17.3, 27.1, 48.7, 55.3, 56.9, 58.9, 93.8, 114.1, 128.7, 129.5, 145.4, 159.2, 168.8. HRMS calcd for $C_{17}H_{23}NO_3Na$: 312.1570 $[M+Na]^+$, found: 312.1600.

Ethyl 1-benzyl-4-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3t)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (95 mg, 73%). 1H NMR (600 MHz, $CDCl_3$) δ 1.04 (d, $J = 6.6$ Hz, 3H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.56-1.59 (m, 1H), 1.70-1.75 (m, 1H), 2.76-2.78 (m, 1H), 2.91-2.93 (m, 1H), 3.03-3.07 (m, 1H), 4.12-4.19 (m, 2H) 4.29-4.35 (m, 2H), 7.21 (d, $J = 7.8$ Hz, 2H), 7.28-7.36 (m, 3H), 7.53 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.7, 22.0, 24.1, 27.9, 41.1, 58.8, 59.8, 100.4, 127.3, 127.7, 128.8, 137.2, 145.6, 168.6. HRMS calcd for $C_{16}H_{22}NO_2$: 260.1645 $[M+H]^+$, found: 260.1652.

Ethyl 1-(4-methoxybenzyl)-4-methyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3u)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (118 mg, 82%). 1H NMR (600 MHz, $CDCl_3$) δ 1.02 (d, $J = 6.6$ Hz, 3H), 1.27 (t, $J = 7.2$ Hz, 3H), 1.55-1.57 (m, 1H), 1.68-1.73 (m, 1H), 2.74-2.76 (m, 1H), 2.90-2.92 (m, 1H), 2.99-3.04 (m, 1H), 3.80 (s, 3H), 4.11-4.28 (m, 4H), 6.87 (d, $J = 8.4$ Hz, 2H), 7.13 (d, $J = 8.4$ Hz, 2H), 7.53 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 14.7, 22.0, 24.1, 27.9, 40.9, 55.3, 58.8, 59.3, 100.2, 114.1, 128.7, 129.0, 145.5, 159.2, 168.7. HRMS calcd for $C_{17}H_{23}NO_3Na$: 312.1570 $[M+Na]^+$, found: 312.1564.

Methyl 1-benzyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3v)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (83 mg, 72%). ^1H NMR (400 MHz, CDCl_3) δ 1.79-1.82 (m, 2H), 2.30 (t, $J = 6.0$ Hz, 2H), 3.01 (t, $J = 5.6$ Hz, 2H), 3.70 (s, 3H), 4.30 (s, 2H), 7.22-7.37 (m, 5H), 7.56 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 20.0, 21.3, 45.4, 50.6, 59.8, 94.5, 127.4, 127.8, 128.8, 137.0, 146.3, 169.2. HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_2$: 232.1332 $[\text{M}+\text{H}]^+$, found: 232.1332.

Propyl 1-benzyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3w)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (78 mg, 60%). ^1H NMR (400 MHz, CDCl_3) δ 0.97 (t, $J = 7.2$ Hz, 3H) 1.65-1.71 (m, 2H), 1.81 (t, $J = 6.0$ Hz, 2H), 2.31 (t, $J = 6.0$ Hz, 2H), 3.00 (t, $J = 5.6$ Hz, 2H), 4.07 (t, $J = 6.4$ Hz, 2H), 4.31 (s, 2H), 7.22-7.38 (m, 5H), 7.56 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 10.6, 20.0, 21.3, 22.4, 45.4, 59.8, 64.7, 94.8, 127.4, 127.7, 128.8, 137.1, 146.1, 169.0. HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_2\text{Na}$: 282.1465 $[\text{M}+\text{Na}]^+$, found: 282.1462.

Benzyl 1-benzyl-1,4,5,6-tetrahydropyridine-3-carboxylate (3x)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (83 mg, 54%). ^1H NMR (600 MHz, CDCl_3) δ 1.80 (t, $J = 6.0$ Hz, 2H), 2.33 (t, $J = 6.0$ Hz, 2H), 3.00 (t, $J = 6.0$ Hz, 2H), 4.28 (s, 2H), 5.16 (s, 2H), 7.20-7.39 (m, 5H), 7.59 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 20.0, 21.2, 30.9, 45.5, 59.8, 64.8, 94.4, 127.4, 127.6, 127.8, 127.9, 128.4, 128.8, 136.9, 137.7, 146.6, 168.4. HRMS calcd for $\text{C}_{20}\text{H}_{21}\text{NO}_2\text{Na}$: 330.1465 $[\text{M}+\text{Na}]^+$, found: 330.1460.

2. Typical Procedure for the Synthesis of 5a and Spectroscopic Data of 5a-5l'

To a schlenk tube containing 1-benzylpyrrolidine (**4a**, 81 mg, 0.5 mmol) were added with PdCl_2 (9 mg, 0.05 mmol), $\text{Cu}(\text{OAc})_2$ (91 mg, 0.5 mmol), KI (83 mg, 0.5 mmol), CH_3CN (5 mL), and EtOH (**2a**, 292 μL , 5 mmol). The mixture was then stirred under CO in balloon at 80 $^\circ\text{C}$ for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **5a** in 68% yield. **5b-5l'** were obtained in a similar manner.

Ethyl 1-benzyl-4,5-dihydro-1H-pyrrole-3-carboxylate (5a)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (79 mg, 68%). ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3H), 2.79 (t, $J = 10.0$ Hz, 2H), 3.37 (t, $J = 10.4$ Hz, 2H), 4.14 (q, $J = 7.2$ Hz, 2H), 4.23 (s, 2H), 7.17 (s, 1H), 7.25-7.37 (m, 5H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 27.7, 54.0, 54.6, 58.9, 101.4, 127.1, 128.0, 128.8, 136.6, 151.3, 166.6. HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_2$: 232.1332 $[\text{M}+\text{H}]^+$, found: 232.1342.

Ethyl 1-(2-methylbenzyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5b)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (77 mg, 63%). ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3H), 2.32 (s, 3H), 2.79 (t, $J = 10.0$ Hz, 2H), 3.40 (t, $J = 10.0$ Hz, 2H), 4.13 (q, $J = 7.2$ Hz, 2H), 4.19 (s, 2H), 7.09 (s, 1H), 7.20-7.23 (m, 4H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 19.1, 27.6, 52.2, 52.7, 58.9, 101.1, 126.2, 128.0, 128.9, 130.7, 134.4, 136.7, 151.1, 166.6. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$: 246.1489 $[\text{M}+\text{H}]^+$, found: 246.1494.

Ethyl 1-(3-fluorobenzyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5c)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (75 mg, 60%). ^1H NMR (400 MHz, CDCl_3) δ 1.25-1.28 (m, 3H), 2.79 (t, $J = 10.0$ Hz, 2H), 3.36 (t, $J = 10.0$ Hz, 2H), 4.12-4.18 (m, 2H), 4.21 (s, 2H), 6.96-7.05 (m, 3H), 7.14 (d, $J = 0.8$ Hz, 1H), 7.32-7.34 (m, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 27.7, 51.8, 54.2, 59.0, 102.1, 114.7 (d, $^2J_{\text{C-F}} = 20.9$ Hz), 119.0, 123.4 (d, $^4J_{\text{C-F}} = 3.8$ Hz), 130.3 (d, $^3J_{\text{C-F}} = 7.9$ Hz), 139.3, 151.1, 163.1 (d, $^1J_{\text{C-F}} = 245.0$ Hz), 166.5. HRMS calcd for $\text{C}_{14}\text{H}_{17}\text{FNO}_2$: 250.1238 $[\text{M}+\text{H}]^+$, found: 250.1241.

Ethyl 1-(4-methoxybenzyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5d)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (99 mg, 76%). ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3H), 2.77 (t, $J = 10.0$ Hz, 2H), 3.34 (t, $J = 9.6$ Hz, 2H), 3.82 (s, 3H), 4.13 (q, $J = 7.2$ Hz, 2H), 4.15 (s, 2H), 6.89 (d, $J = 8.8$ Hz, 2H), 7.15 (d, $J = 8.4$ Hz, 2H), 7.18 (s, 1H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 27.6, 51.6, 54.0, 55.3, 58.9, 101.2, 114.1, 128.5, 129.3, 151.2, 159.2, 166.6. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_3$: 262.1438 $[\text{M}+\text{H}]^+$, found: 262.1442.

Ethyl 1-(4-chlorobenzyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5e)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (81 mg, 61%). ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3H), 2.78 (t, $J = 10.0$ Hz, 2H), 3.34 (t, $J = 10.0$ Hz, 2H), 4.14 (q, $J = 7.2$ Hz, 2H), 4.18 (s, 2H), 7.14 (s, 1H), 7.19 (d, $J = 8.4$ Hz, 2H), 7.34 (d, $J = 8.4$ Hz, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 27.7, 51.7, 54.0, 59.0, 102.0, 128.9, 129.3, 133.6, 135.1, 151.1, 166.5. HRMS calcd for $\text{C}_{14}\text{H}_{17}\text{ClNO}_2$: 266.0942 $[\text{M}+\text{H}]^+$, found: 266.0945.

Ethyl 1-phenethyl-4,5-dihydro-1H-pyrrole-3-carboxylate (5f)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (55 mg, 45%). ^1H NMR (400 MHz, CDCl_3) δ 1.22-1.26 (m, 3H), 2.74-2.85 (m, 4H), 3.28-3.32 (m, 2H), 3.45 (t, $J = 10.0$ Hz, 2H), 4.11 (q, $J = 7.2$ Hz, 2H), 7.00 (s, 1H), 7.18 (d, $J = 8.0$ Hz, 2H), 7.23-7.31 (m, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 27.6, 35.1, 52.1, 53.4, 58.8, 100.7, 126.6, 128.2, 128.65, 128.67, 138.7, 151.2, 166.5. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$: 246.1489 $[\text{M}+\text{H}]^+$, found: 246.1493.

Ethyl 1-cyclopentyl-4,5-dihydro-1H-pyrrole-3-carboxylate (5g)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (52 mg, 50%). ^1H NMR (400 MHz, CDCl_3) δ 1.23-1.31 (m, 3H), 1.56-1.59 (m, 4H), 1.70-1.72 (m, 2H), 1.85-1.88 (m, 2H), 2.72-2.77 (m, 2H), 3.43 (t, $J = 10.0$ Hz, 3H), 4.13 (q, $J = 7.2$ Hz, 2H), 7.14 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 23.6, 27.2, 29.7, 30.9, 51.0, 53.4, 58.8, 60.7, 100.8, 150.0, 166.8. HRMS calcd for $\text{C}_{12}\text{H}_{20}\text{NO}_2$: 210.1489 $[\text{M}+\text{H}]^+$, found: 210.1495.

Ethyl 1-(*p*-tolyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5h)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (60 mg, 52%). ^1H NMR (400 MHz, CDCl_3) δ 1.30 (t, $J = 7.2$ Hz, 3H), 2.29 (s, 3H), 2.92-2.97 (m, 2H), 3.93 (t, $J = 9.6$ Hz, 2H), 4.19 (q, $J = 7.2$ Hz, 2H), 6.79 (d, $J = 8.4$ Hz, 2H), 7.10 (d, $J = 8.0$ Hz, 2H), 7.69-7.70 (m, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 20.5, 49.8, 53.4, 59.3, 106.1, 113.9, 130.0, 130.4, 139.3, 142.4, 166.3. HRMS calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_2$: 232.1332 $[\text{M}+\text{H}]^+$, found: 232.1343.

Ethyl 1-(4-chlorophenyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5i)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (55 mg, 44%). ^1H NMR (600 MHz, CDCl_3) δ 1.29-1.33 (m, 3H), 2.96 (t, $J = 10.2$ Hz, 2H), 3.91 (t, $J = 10.2$ Hz, 2H), 4.20 (q, $J = 7.2$ Hz, 2H), 6.80 (d, $J = 8.4$ Hz, 2H), 7.24 (d, $J = 8.4$ Hz, 2H), 7.64 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.6, 49.7, 53.4, 59.6, 65.6, 107.9, 114.9, 129.5, 130.9, 140.3, 141.5, 166.1. HRMS calcd for $\text{C}_{13}\text{H}_{15}\text{ClNO}_2$: 252.0786 $[\text{M}+\text{H}]^+$, found: 252.0792.

Ethyl 1-mesityl-4,5-dihydro-1H-pyrrole-3-carboxylate (5j)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (78 mg, 60%). ^1H NMR (400 MHz, CDCl_3) δ 1.26 (t, $J = 7.2$ Hz, 3H), 2.22 (s, 6H), 2.27 (s, 3H), 2.95-3.00 (m, 2H), 3.76 (t, $J = 10.0$ Hz, 2H), 4.16 (q, $J = 7.6$ Hz, 2H), 6.88 (s, 2H). ^{13}C NMR (100 MHz, CDCl_3) δ 14.7, 18.0, 20.9, 27.8, 53.1, 58.9, 100.9, 129.3, 136.4, 137.0, 137.3, 151.0, 166.9. HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_2$: 260.1645 $[\text{M}+\text{H}]^+$, found: 260.1652.

Ethyl 1-benzyl-5-methyl-4,5-dihydro-1H-pyrrole-3-carboxylate (5k)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (31 mg, 25%). ^1H NMR (600 MHz, CDCl_3) δ 1.22-1.25 (m, 6H), 2.39-2.43 (m, 1H), 2.96-3.00 (m, 1H), 3.70-3.73 (m, 1H), 4.11-4.15 (m, 2H), 4.16 (d, $J = 15.0$ Hz, 1H), 4.30 (d, $J = 15.0$ Hz, 1H), 7.10 (s, 1H), 7.23-7.36 (m, 5H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 19.3, 36.2, 51.7, 58.6, 58.8, 99.5, 127.8, 127.9, 128.8, 136.9, 150.6, 166.6. HRMS calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_2$: 246.1489 $[\text{M}+\text{H}]^+$, found: 246.1491.

Ethyl (*E*)-2-(1-benzylpyrrolidin-2-ylidene)acetate (5k')²

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (64 mg, 52%). ^1H NMR (600 MHz, CDCl_3) δ 1.24 (t, $J = 7.2$ Hz, 3H), 1.95-2.00 (m, 2H), 3.24 (t, $J = 7.8$ Hz, 2H), 3.35 (t, $J = 7.8$ Hz, 2H), 4.08 (q, $J = 7.2$ Hz, 2H), 4.36 (s, 2H), 4.69 (s, 1H), 7.18 (d, $J = 7.8$ Hz, 2H), 7.26-7.28 (m, 1H), 7.33 (t, $J = 7.2$ Hz, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 21.1, 32.6, 50.0, 52.4, 58.3, 78.4, 127.2, 127.5, 128.8, 136.1, 165.3, 169.6. MS: m/z 246 $[\text{M}+\text{H}]^+$.

Ethyl 5-methyl-1-(2-methylbenzyl)-4,5-dihydro-1H-pyrrole-3-carboxylate (5l)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (26 mg, 20%). ^1H NMR (600 MHz, CDCl_3) δ 1.21-1.25 (m, 6H), 2.31 (s, 3H), 2.40-2.44 (m, 1H), 3.00-3.04 (m, 1H), 3.74-3.77 (m, 1H), 4.09-4.14 (m, 3H), 4.24 (d, $J = 14.4$ Hz, 1H), 6.94 (s, 1H), 7.18-7.23 (m, 4H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 19.2, 19.5, 36.3, 49.8, 58.8, 59.4, 99.3, 126.2, 128.0, 129.1, 130.8, 134.6, 136.7, 150.0, 166.7. HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_2$: 260.1645 $[\text{M}+\text{H}]^+$, found: 260.1655.

Ethyl (*E*)-2-(1-(2-methylbenzyl)pyrrolidin-2-ylidene)acetate (5l')

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (57 mg, 44%). ^1H NMR (600 MHz, CDCl_3) δ 1.21-1.25 (m, 3H), 1.97-1.99 (m, 2H), 2.25 (s, 3H), 3.25-3.28 (m, 4H), 4.08 (q, $J = 7.2$ Hz, 2H), 4.30 (s, 2H), 4.60 (s, 1H), 7.02 (d, $J = 7.2$ Hz, 1H), 7.15-7.20 (m, 4H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.7, 19.0, 21.1, 32.6, 48.3, 52.2, 58.4, 78.5, 126.2, 126.9, 127.6, 130.5, 133.5, 136.1, 165.3, 169.6. HRMS calcd for $\text{C}_{16}\text{H}_{22}\text{NO}_2$: 260.1645 $[\text{M}+\text{H}]^+$, found: 260.1655.

3. Typical Procedure for the Synthesis of 7a and Spectroscopic Data of 7a and 7b

A schlenk tube containing 1-(*o*-tolyl)azepane (**6a**, 95 mg, 0.5 mmol), PdCl_2 (9 mg, 0.05 mmol), $\text{Cu}(\text{OAc})_2$ (18 mg, 0.1 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with CO/O_2 in balloon (5:1) for three times. Then CH_3CN (5 mL) and EtOH (**2a**, 292 μL , 5 mmol) were added via syringe, and the resulting mixture was stirred at 80 $^\circ\text{C}$ for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **7a** in 60% yield. **7b** was obtained in a similar manner.

Ethyl 1-(*o*-tolyl)-4,5,6,7-tetrahydro-1*H*-azepine-3-carboxylate (7a)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (78 mg, 60%). ^1H NMR (400 MHz, CDCl_3) δ 1.15 (t, $J = 7.2$ Hz, 3H), 1.84-1.85 (m, 4H), 2.21 (d, $J = 3.2$ Hz, 3H), 2.59 (t, $J = 6.0$ Hz, 2H), 3.57 (t, $J = 6.0$ Hz, 2H), 4.04 (q, $J = 7.2$ Hz, 2H), 7.05-7.14 (m, 4H), 7.33 (s, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.6, 18.2,

25.4, 26.7, 28.9, 54.2, 59.6, 102.4, 126.1, 126.4, 127.0, 131.4, 134.1, 148.5, 149.3, 170.2. HRMS calcd for C₁₆H₂₂NO₂: 260.1645 [M+H]⁺, found: 260.1642.

Ethyl 1-(4-bromophenyl)-4,5,6,7-tetrahydro-1H-azepine-3-carboxylate (7b)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (82 mg, 51%). ¹H NMR (600 MHz, CDCl₃) δ 1.28 (t, *J* = 7.2 Hz, 3H), 1.82-1.89 (m, 4H), 2.62 (t, *J* = 6.0 Hz, 2H), 3.86 (t, *J* = 6.0 Hz, 2H), 4.18 (q, *J* = 7.2 Hz, 2H), 6.92 (d, *J* = 9.0 Hz, 2H), 7.40 (d, *J* = 9.0 Hz, 2H), 7.62 (s, 1H). ¹³C NMR (150 MHz, CDCl₃) δ 14.5, 24.9, 25.2, 27.4, 50.1, 60.0, 109.7, 115.0, 119.7, 132.2, 145.0, 145.6, 169.5. HRMS calcd for C₁₅H₁₉BrNO₂: 324.0594 [M+H]⁺, found: 324.0596.

4. Typical Procedure for the Synthesis of 8a and Spectroscopic Data of 8a-8f

To a schlenk tube containing 1-benzyl-4,5-dihydro-1H-pyrrole-3-carboxylate (**5a**, 46 mg, 0.2 mmol) was added DMSO (2 mL). The tube was then evacuated and back-filled with O₂ in balloon for three times, and the resulting mixture was stirred at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na₂SO₄, and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **8a** in 92% yield. **8b-8f** were obtained in a similar manner.

Ethyl 1-benzyl-1H-pyrrole-3-carboxylate (8a) ³

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (42 mg, 92%). ¹H NMR (400 MHz, CDCl₃) δ 1.32-1.36 (m, 3H), 4.28 (q, *J* = 7.2 Hz, 2H), 5.07 (s, 2H), 6.64 (d, *J* = 0.8 Hz, 2H), 7.15 (d, *J* = 7.2 Hz, 2H), 7.34-7.38 (m, 4H). ¹³C NMR (100 MHz, CDCl₃) δ 14.5, 53.9, 59.7, 110.5, 116.6, 122.1, 126.3, 127.3, 128.1, 128.9, 136.8, 164.9. MS: *m/z* 230 [M+H]⁺.

Ethyl 1-(2-methylbenzyl)-1H-pyrrole-3-carboxylate (8b)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (44 mg, 90%). ¹H NMR (600 MHz, CDCl₃) δ 1.32 (t, *J* = 7.2 Hz, 3H), 2.25 (s, 3H), 4.25 (q, *J* = 7.2 Hz, 2H), 5.05 (s, 2H), 6.57 (s, 1H), 6.60 (s, 1H), 6.96 (d, *J* =

7.8 Hz, 1H), 7.17-7.25 (m, 4H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.5, 18.9, 52.0, 59.7, 110.3, 116.4, 122.0, 126.2, 126.5, 128.4, 130.7, 134.4, 136.2, 164.9. HRMS calcd for $\text{C}_{15}\text{H}_{18}\text{NO}_2$: 244.1332 $[\text{M}+\text{H}]^+$, found: 244.1342.

Ethyl 1-(4-chlorobenzyl)-1*H*-pyrrole-3-carboxylate (8c)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (46 mg, 88%). ^1H NMR (600 MHz, CDCl_3) δ 1.32 (t, $J = 7.2$ Hz, 3H), 4.26 (q, $J = 7.2$ Hz, 2H), 5.03 (s, 2H), 6.59-6.60 (m, 1H), 6.616-6.623 (m, 1H), 7.06 (d, $J = 8.4$ Hz, 2H), 7.29-7.32 (m, 3H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.5, 53.1, 59.7, 110.7, 116.9, 122.0, 126.2, 128.6, 129.1, 134.1, 135.3, 164.8. HRMS calcd for $\text{C}_{14}\text{H}_{15}\text{ClNO}_2$: 264.0786 $[\text{M}+\text{H}]^+$, found: 264.0788.

Ethyl 1-mesityl-1*H*-pyrrole-3-carboxylate (8d)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (46 mg, 91%). ^1H NMR (600 MHz, CDCl_3) δ 1.35 (t, $J = 7.2$ Hz, 3H), 2.00 (s, 6H), 2.33 (s, 3H), 4.30 (q, $J = 7.2$ Hz, 2H), 6.53 (s, 1H), 6.74 (s, 1H), 6.94 (s, 2H), 7.23 (d, $J = 1.2$ Hz, 1H). ^{13}C NMR (150 MHz, CDCl_3) δ 14.5, 17.2, 21.0, 59.7, 110.3, 116.9, 122.8, 126.9, 135.4, 136.4, 138.4, 165.1. HRMS calcd for $\text{C}_{16}\text{H}_{20}\text{NO}_2$: 258.1489 $[\text{M}+\text{H}]^+$, found: 258.1493.

Ethyl 1-benzyl-5-methyl-1*H*-pyrrole-3-carboxylate (8e)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (41 mg, 85%). ^1H NMR (600 MHz, CDCl_3) δ 1.32 (t, $J = 7.2$ Hz, 3H), 2.11 (s, 3H), 4.25 (q, $J = 7.2$ Hz, 2H), 5.02 (s, 2H), 6.36 (s, 1H), 7.02 (d, $J = 7.2$ Hz, 2H), 7.26-7.34 (m, 4H). ^{13}C NMR (150 MHz, CDCl_3) δ 11.9, 14.5, 51.0, 59.6, 108.6, 115.0, 126.4, 126.5, 127.8, 128.9, 130.0, 136.9, 149.4, 165.0. HRMS calcd for $\text{C}_{15}\text{H}_{18}\text{NO}_2$: 244.1332 $[\text{M}+\text{H}]^+$, found: 244.1335.

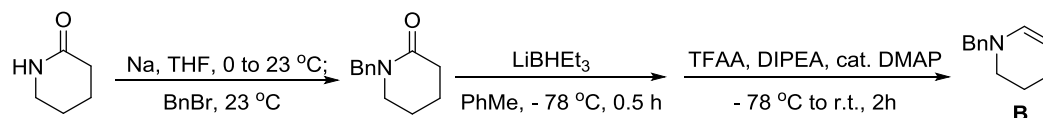
Ethyl 5-methyl-1-(2-methylbenzyl)-1*H*-pyrrole-3-carboxylate (8f)

Eluent: ethyl acetate/hexanes (1:20). Yellow liquid (42 mg, 82%). ^1H NMR (600 MHz, CDCl_3) δ 1.31 (t, $J = 7.2$ Hz, 3H), 2.13 (s, 3H), 2.29 (s, 3H), 4.24 (q, $J = 7.2$ Hz, 2H), 4.96 (s, 2H), 6.39 (s, 1H), 6.62 (d, $J = 7.2$ Hz, 1H), 7.14-7.21 (m, 4H). ^{13}C NMR (150 MHz, CDCl_3) δ 11.8, 14.5, 19.0, 48.9, 59.5, 108.4, 115.0,

126.2, 126.6, 126.8, 127.9, 130.1, 130.4, 134.8, 135.2, 165.1. HRMS calcd for $C_{16}H_{20}NO_2$: 258.1489 $[M+H]^+$, found: 258.1452.

5. Control Experiments

5.1 Synthesis of 1-benzyl-1,2,3,4-tetrahydropyridine (intermediate B)



5.1.1 Synthetic procedure and spectroscopic data of 1-benzylpiperidin-2-one

To a flame-dried round-bottom flask with a magnetic stir bar were added sodium hydride (60% dispersion in mineral oil, 226 mg, 5.65 mmol) and THF (2 mL). The flask was capped with a rubber septum, put under a nitrogen atmosphere, and cooled to 0 $^\circ\text{C}$ using an ice water bath. Then, a solution of piperidin-2-one (495 mg, 5 mmol) in THF (8 mL) was added with syringe, and the resulting mixture was allowed to warm to 23 $^\circ\text{C}$ and stirred for 2 h. Next, benzyl bromide (635 μL , 5.35 mmol) was added dropwise with syringe, and the mixture was stirred for another 2 h. Upon completion (as determined by TLC analysis), the suspension was diluted with water (30 mL) and extracted with ethyl acetate (3×30 mL). The combined organic layer was washed with brine (1×30 mL), dried over anhydrous Na_2SO_4 , filtered, and concentrated under reduced pressure. The crude residue was purified by column chromatography on silica gel with ethyl acetate/hexane (1:1) as the eluent to give 1-benzylpiperidin-2-one (851 mg, 90%).⁴

1-Benzylpiperidin-2-one⁴

Eluent: ethyl acetate/hexanes (1:1). Colorless liquid (851 mg, 90%). ^1H NMR (600 MHz, CDCl_3) δ 1.75-1.81 (m, 4H), 2.47 (t, $J = 6.0$ Hz, 2H), 3.19 (t, $J = 6.0$ Hz, 2H), 1.60 (s, 2H), 7.24-7.26 (m, 3H), 7.32 (t, $J = 7.2$ Hz, 2H). ^{13}C NMR (150 MHz, CDCl_3) δ 21.4, 23.2, 32.4, 47.3, 50.1, 127.3, 128.1, 128.6, 137.3, 170.0. MS: m/z 190 $[M+H]^+$.

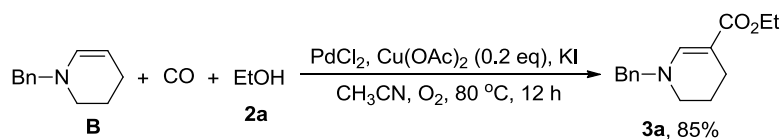
5.1.2 Synthetic procedure and spectroscopic data of 1-benzyl-1,2,3,4-tetrahydropyridine (**B**)

To a solution of 1-benzylpiperidin-2-one (756 mg, 4.0 mmol) in toluene (8 mL) was added super-hydride (1.0 M in THF, 4.24 mL) dropwise at -78 °C. After being stirred at -78 °C for 30 min, it was added with DIPEA (4.0 mL, 22.8 mmol), DMAP (10 mg, 0.08 mmol) and TFAA (0.68 mL, 4.8 mmol). The mixture was allowed to warm to room temperature and then stirred for 2 h. It was then quenched with H₂O (10 mL). The organic layer was separated and washed with H₂O (2 × 10 mL), dried over magnesium sulfate, filtered, and concentrated in vacuo. The crude residue was purified by column chromatography on silica gel with ethyl acetate/hexane (1:5) as the eluent to give **B** (346 mg, 50%).⁵

1-Benzyl-1,2,3,4-tetrahydropyridine (**B**)

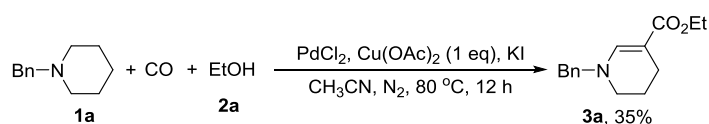
Eluent: ethyl acetate/hexanes (1:5). Yellow liquid (346 mg, 50%). ¹H NMR (600 MHz, CDCl₃) δ 1.80-1.89 (m, 2H), 2.04-2.19 (m, 2H), 2.89-2.94 (m, 2H), 4.06 (s, 2H), 4.23 (q, *J* = 7.2 Hz, 1H), 6.51 (d, *J* = 7.2 Hz, 1H), 7.22-7.34 (m, 5H). ¹³C NMR (150 MHz, CDCl₃) δ 20.0, 46.2, 59.1, 127.0, 127.4, 127.8, 128.5, 138.1, 138.2. MS: *m/z* 174 [M+H]⁺.

5.2 A schlenk tube containing 1-benzyl-1,2,3,4-tetrahydropyridine (**B**, 87 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), Cu(OAc)₂ (18 mg, 0.1 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with CO/O₂ in balloon (5:1) for three times. Then, CH₃CN (5 mL) and EtOH (**2a**, 292 μL, 5 mmol) were added via syringe, and the resulting mixture was stirred at 80 °C for 12 h. Upon completion, it was diluted with brine (10 mL) and extracted with EtOAc (10 mL × 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give ethyl **3a** (104 mg, 85%).

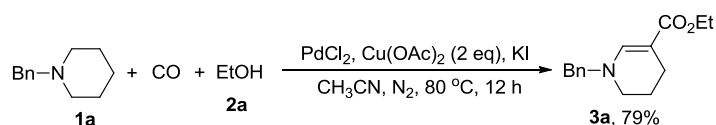


5.3 A schlenk tube containing 1-benzylpiperidine (**1a**, 88 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), Cu(OAc)₂ (91 mg, 0.5 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with N₂ in

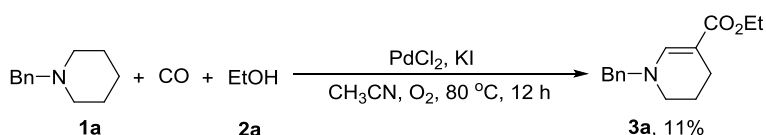
balloon for three times. Then, CH₃CN (5 mL) and EtOH (**2a**, 292 μ L, 5 mmol) were added via syringe, and the resulting mixture was stirred under CO in balloon at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **3a** (43 mg, 35%).



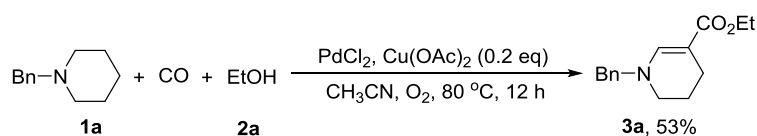
5.4 A schlenk tube containing 1-benzylpiperidine (**1a**, 88 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), Cu(OAc)₂ (181 mg, 1 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with N₂ in balloon for three times. Then, CH₃CN (5 mL) and EtOH (**2a**, 292 μ L, 5 mmol) were added via syringe, and the resulting mixture was stirred under CO in balloon at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **3a** (97 mg, 79%).



5.5. A schlenk tube containing 1-benzylpiperidine (**1a**, 88 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with CO/O₂ in balloon (5:1) for three times. Then, CH₃CN (5 mL) and EtOH (**2a**, 292 μ L, 5 mmol) were added via syringe, and the resulting mixture was stirred at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **3a** (13 mg, 11%).

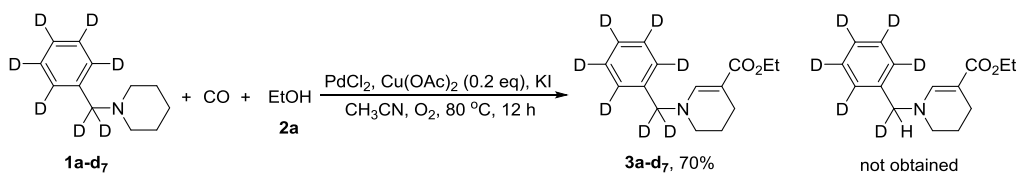


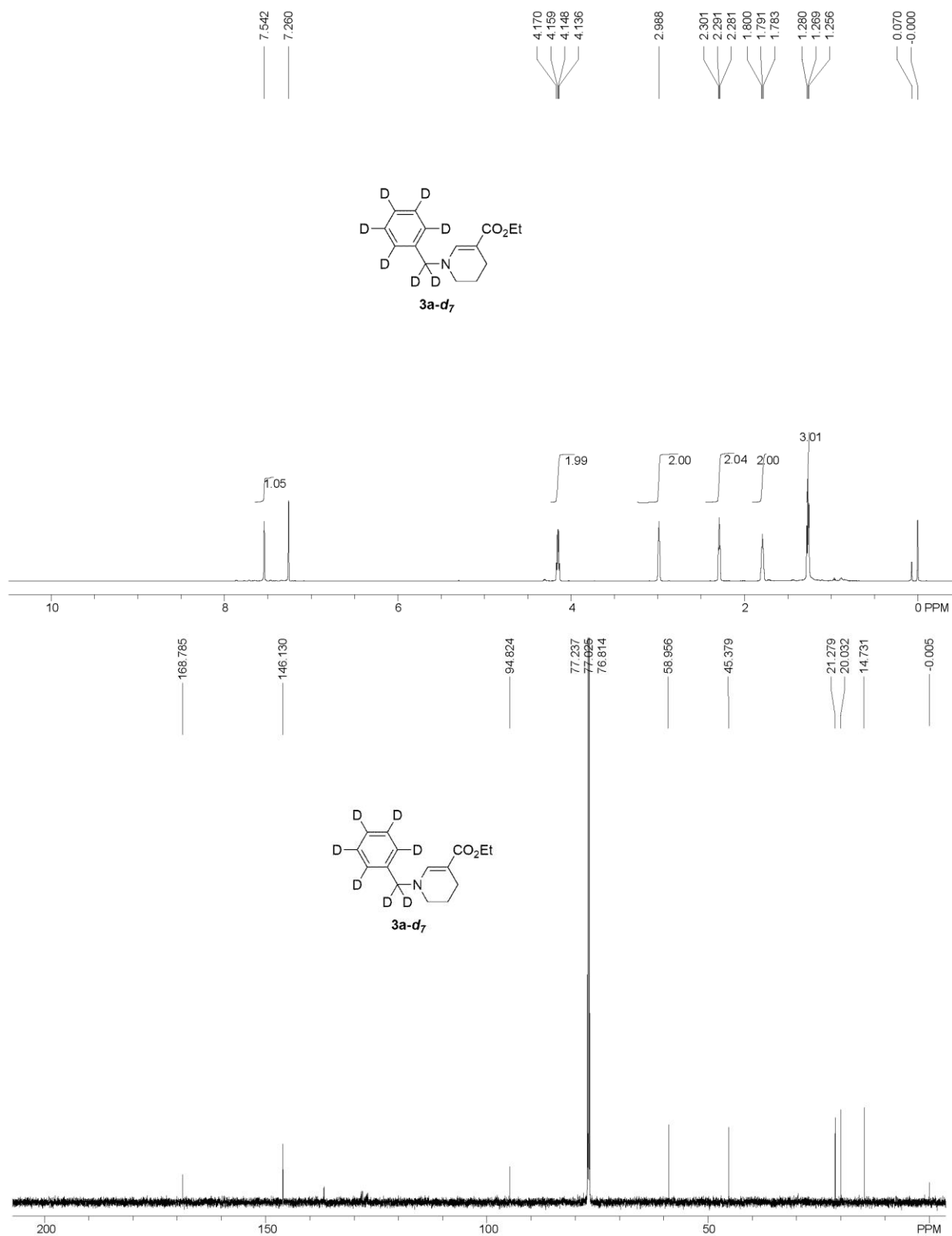
5.6. A schlenk tube containing 1-benzylpiperidine (**1a**, 88 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), and Cu(OAc)₂ (18 mg, 0.1 mmol) was evacuated and back-filled with CO/O₂ in balloon (5:1) for three times. Then, CH₃CN (5 mL) and EtOH (**2a**, 292 μ L, 5 mmol) were added via syringe, and the resulting mixture was stirred at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give **3a** (65 mg, 53%).



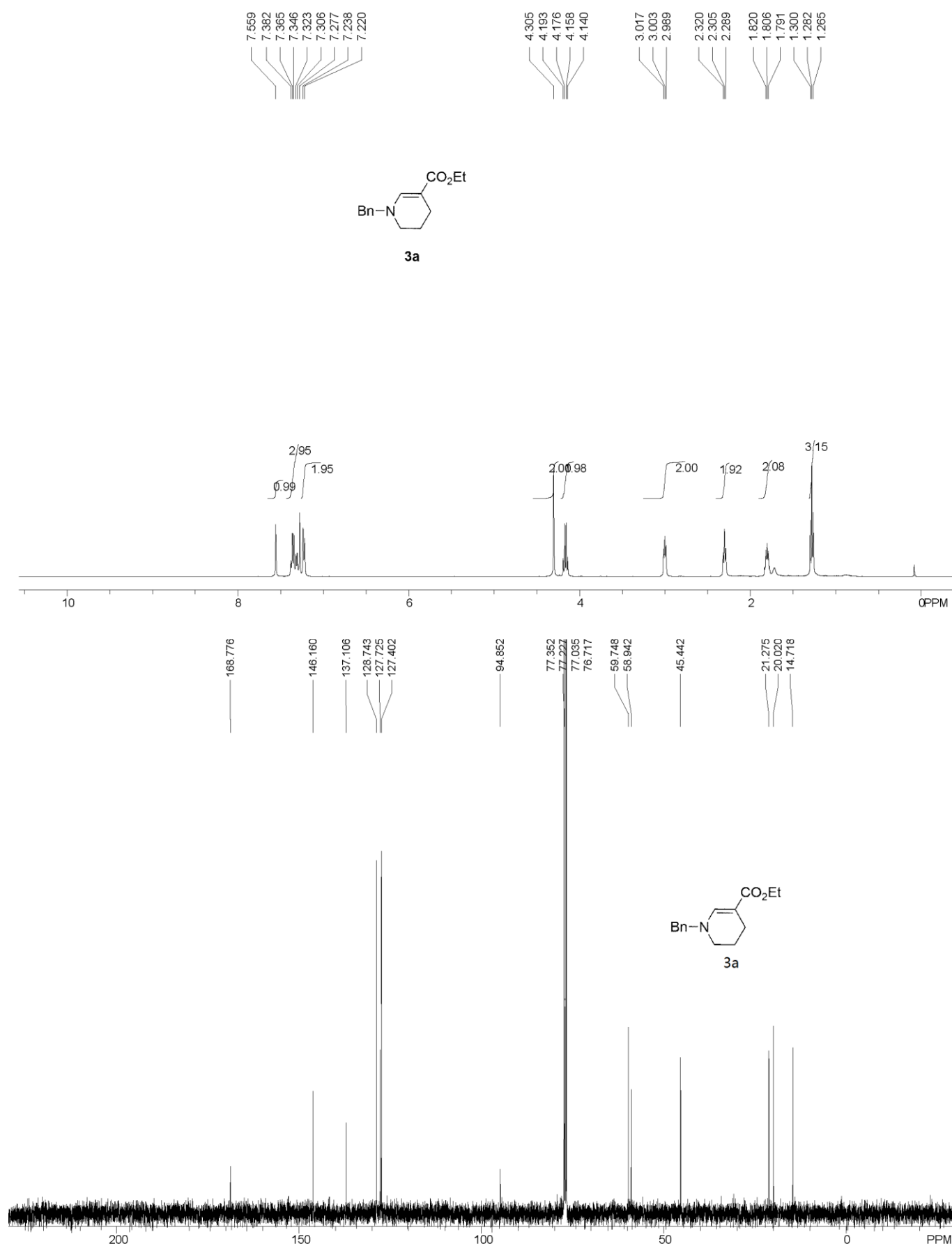
6. Deuterium Experiments

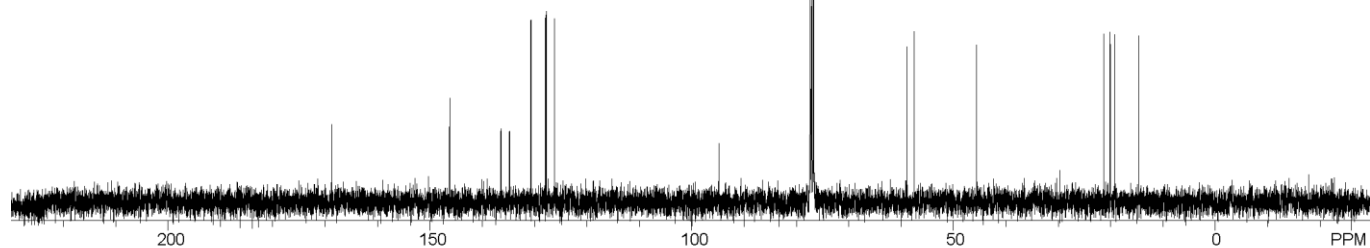
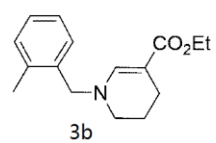
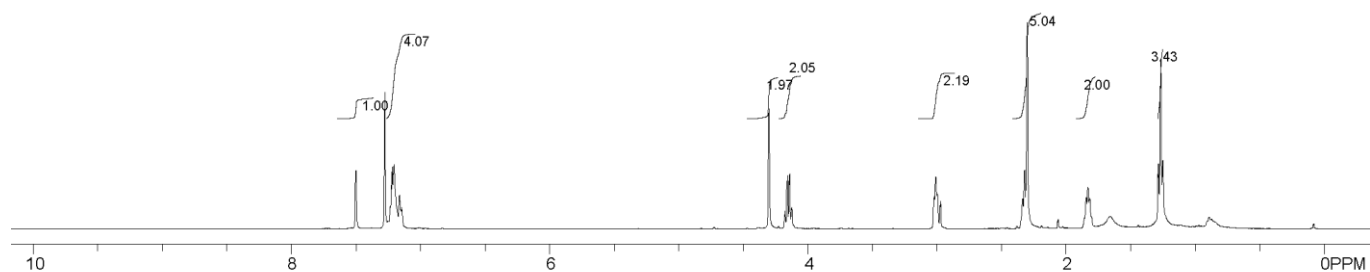
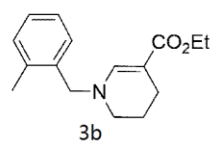
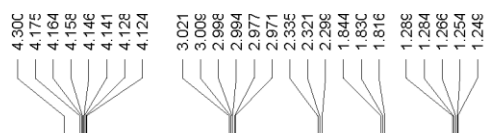
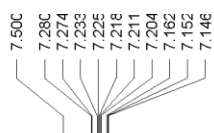
A schlenk tube containing 1-((phenyl-*d*₅)methyl-*d*₂)piperidine (**1a-d₇**, 92 mg, 0.5 mmol), PdCl₂ (9 mg, 0.05 mmol), Cu(OAc)₂ (18 mg, 0.1 mmol), and KI (83 mg, 0.5 mmol) was evacuated and back-filled with CO/O₂ in balloon (5:1) for three times. Then, CH₃CN (5 mL) and EtOH (**2a**, 292 μ L, 5 mmol) were added via syringe, and the resulting mixture was stirred at 80 °C for 12 h. Upon completion, it was diluted with saturated brine (10 mL) and extracted with EtOAc (10 mL \times 3). The combined organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel with EtOAc/hexane (1:20) as the eluent to give ethyl 1-((phenyl-*d*₅)methyl-*d*₂)-1,4,5,6-tetrahydropyridine-3-carboxylate (**3a-d₇**, 88 mg, 70%).

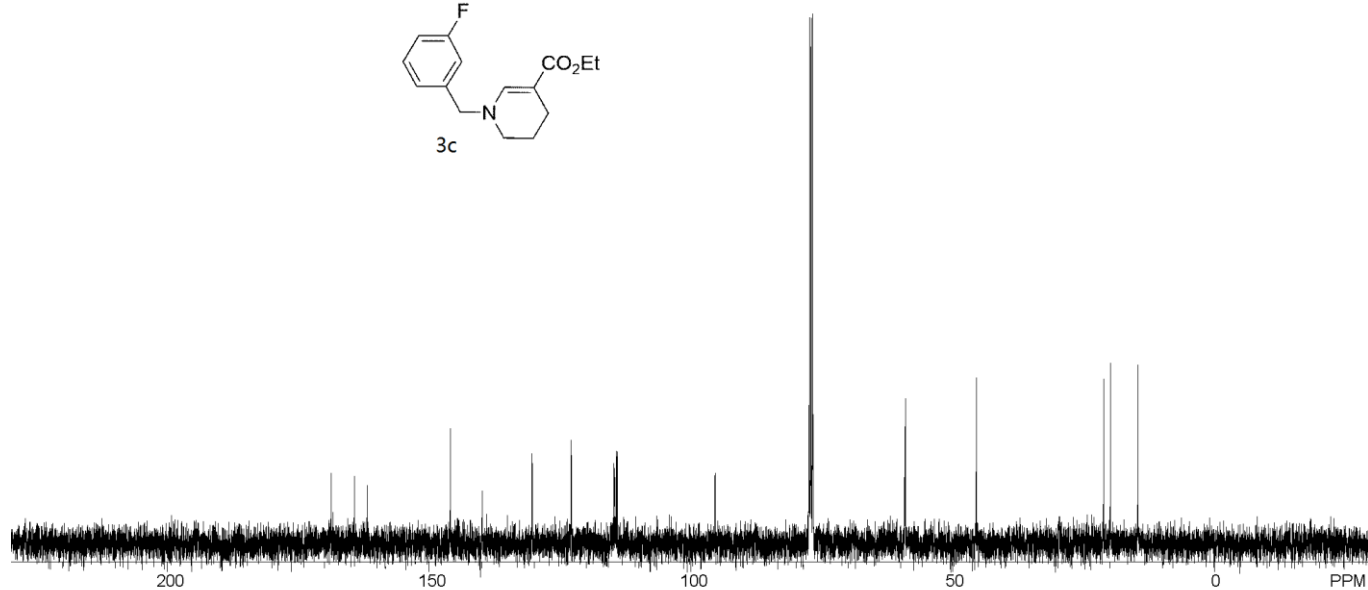
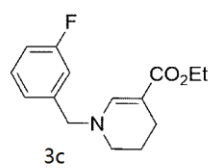
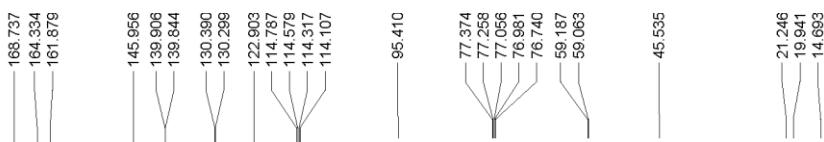
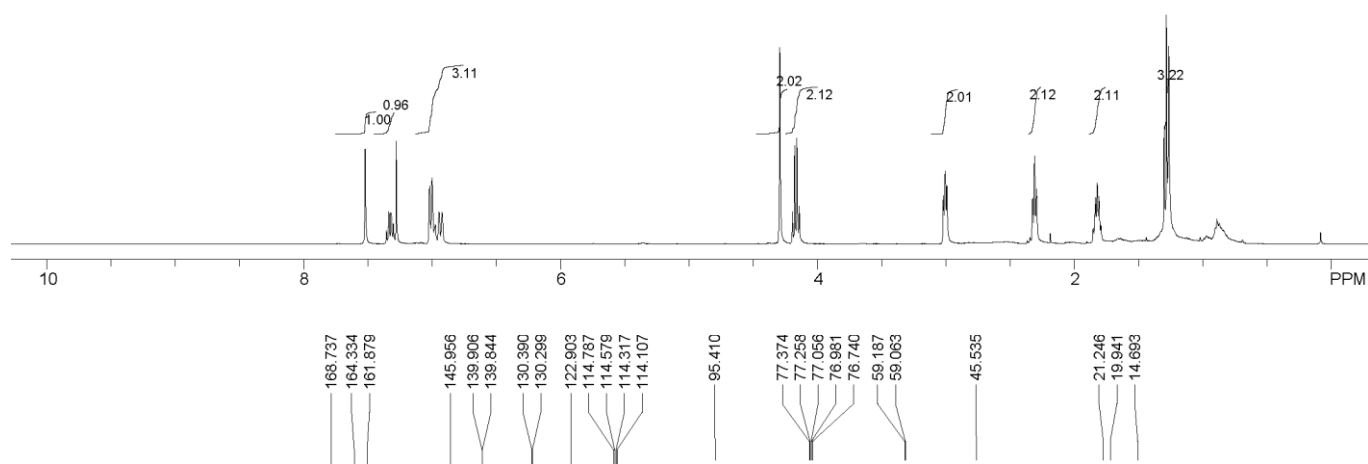
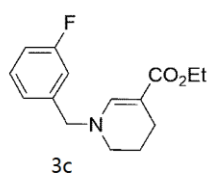
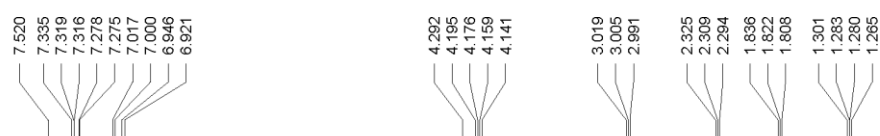


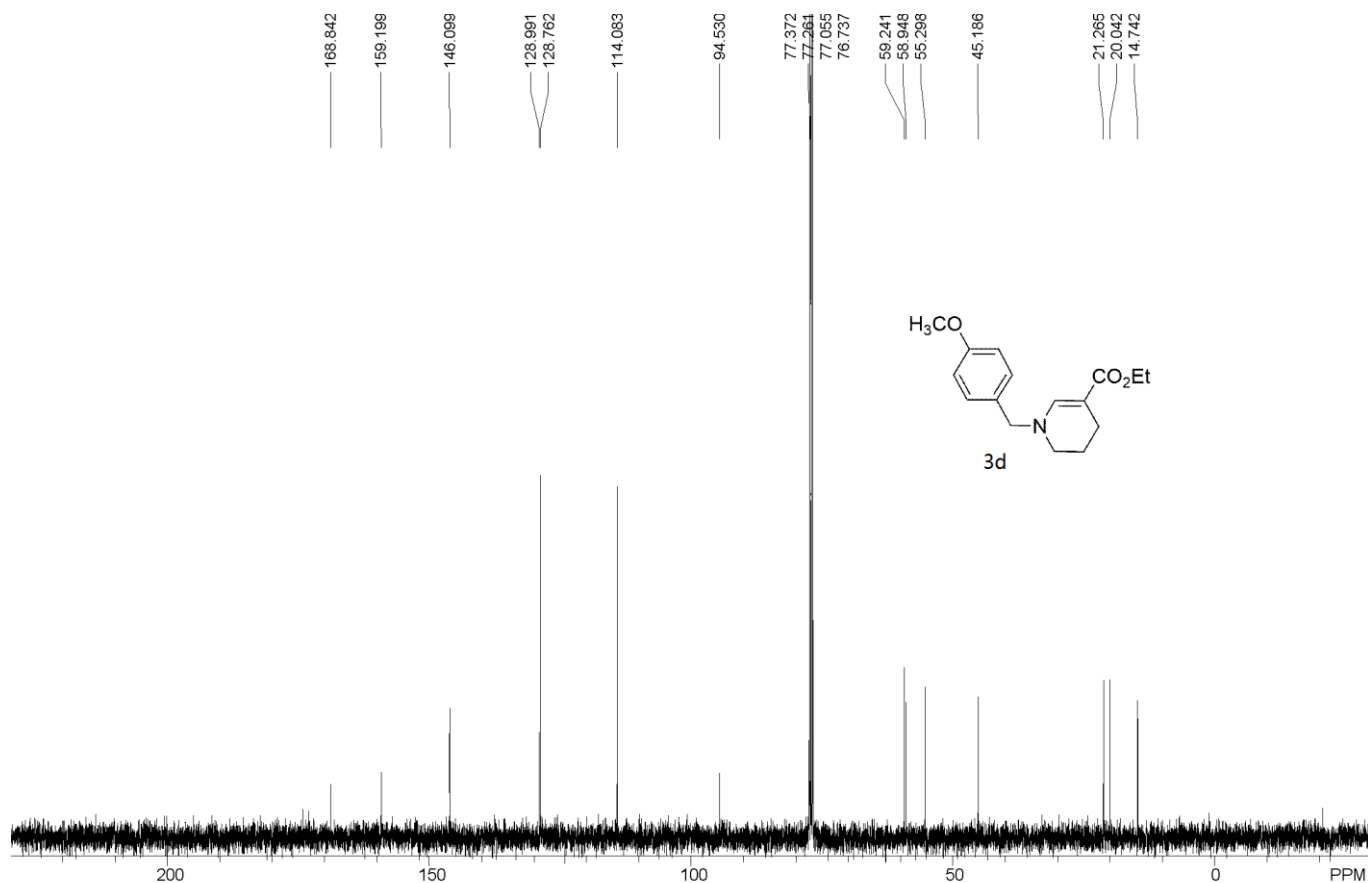
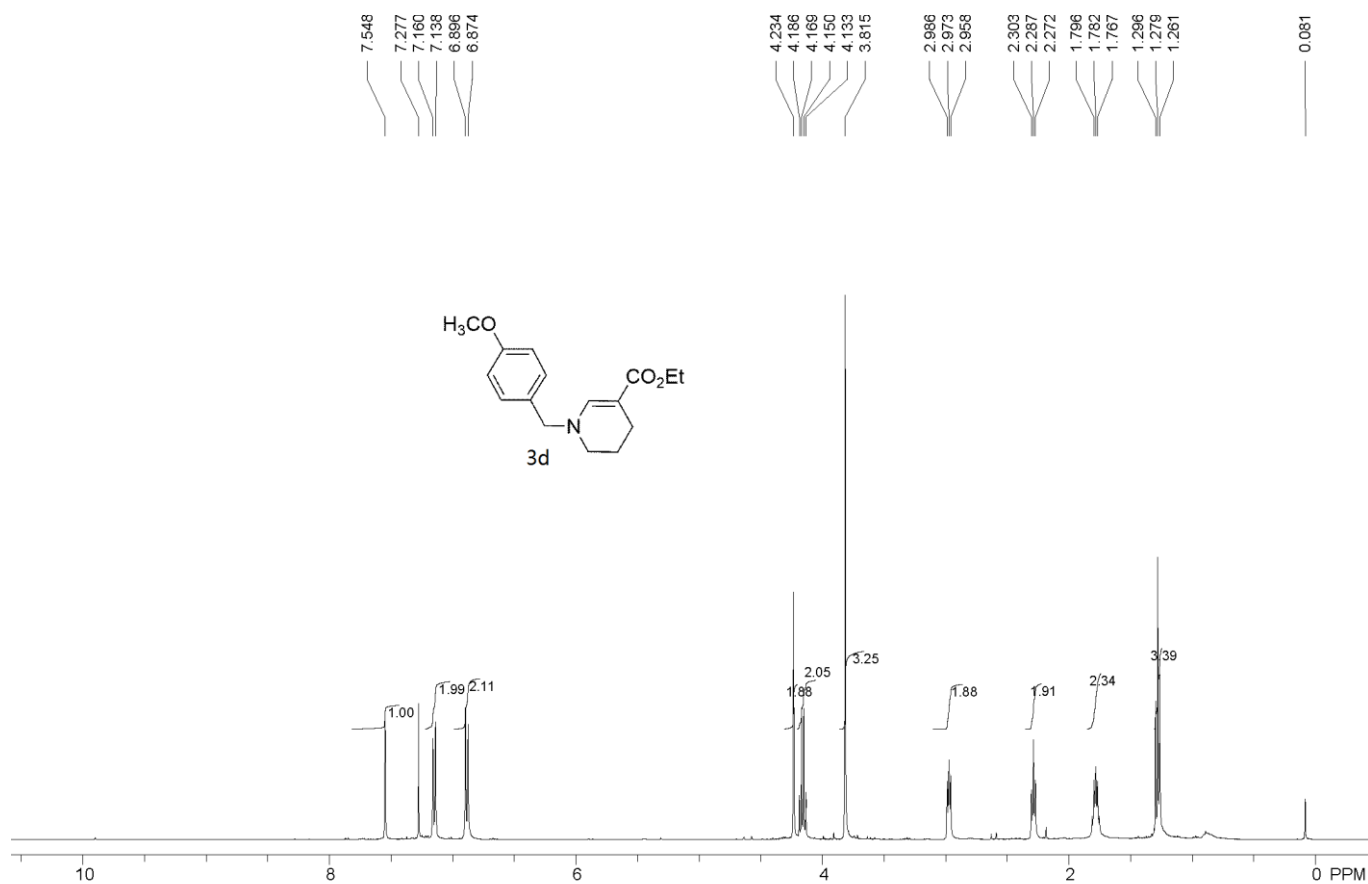


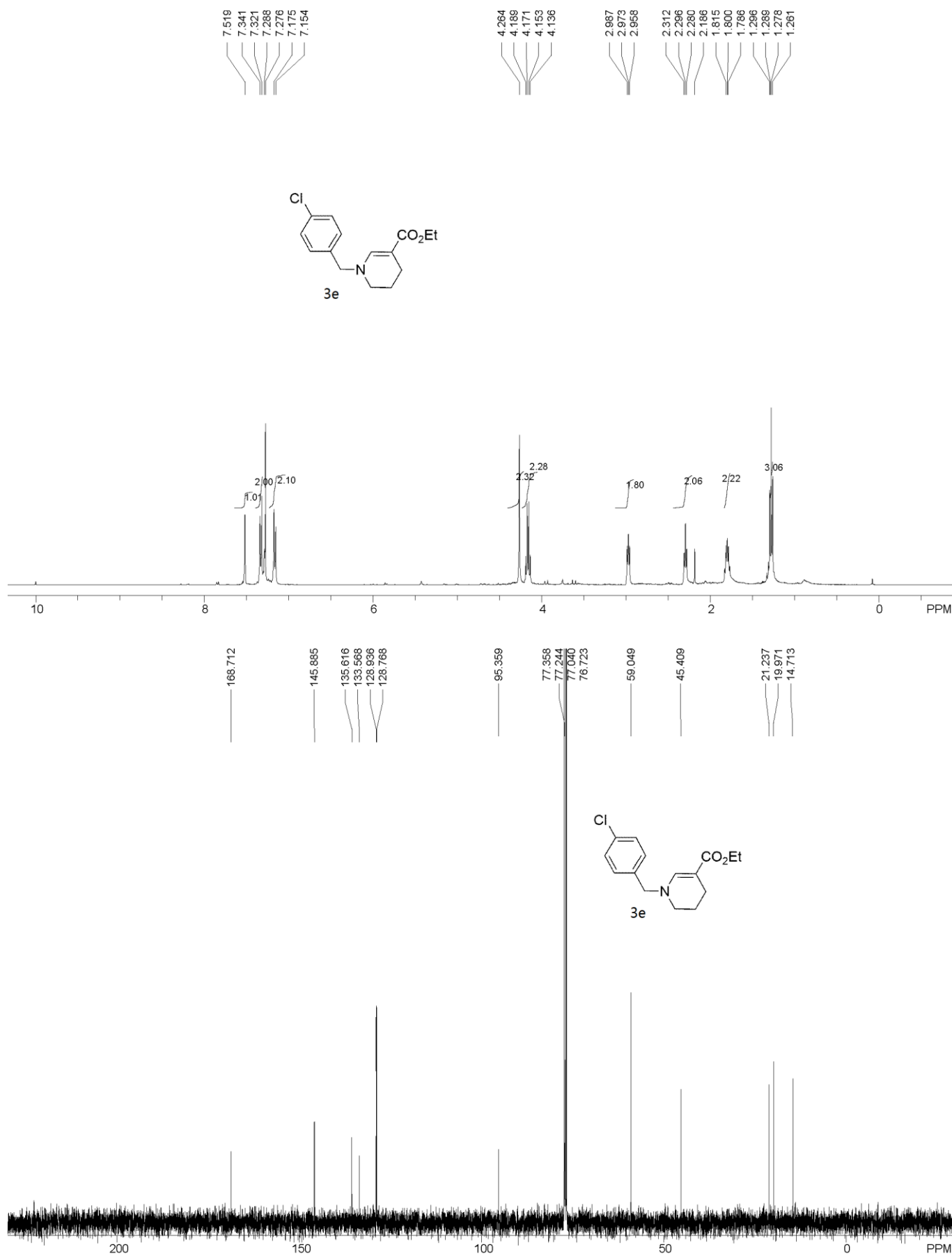
III. Copies of ^1H and ^{13}C NMR Spectra of 3a-3x

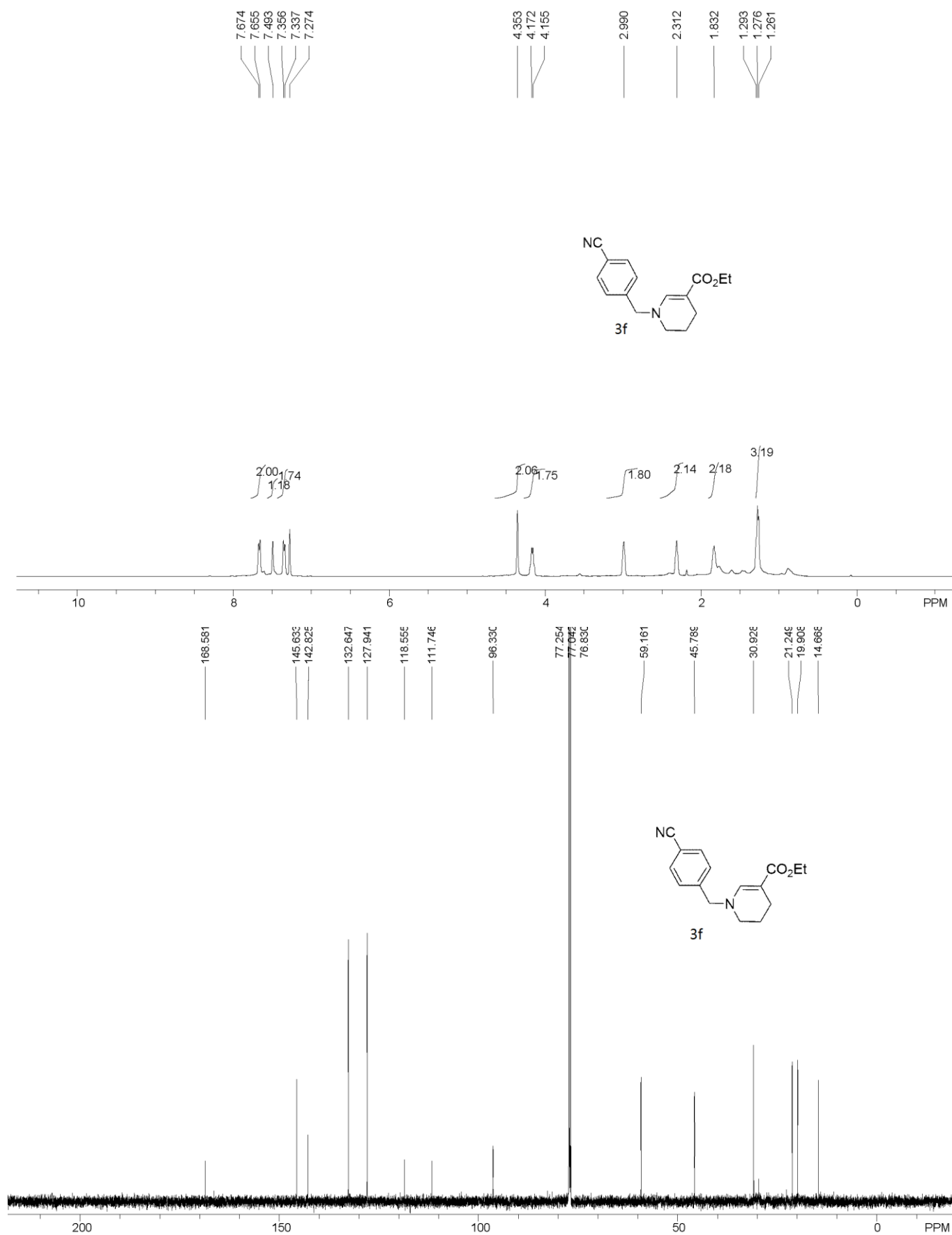


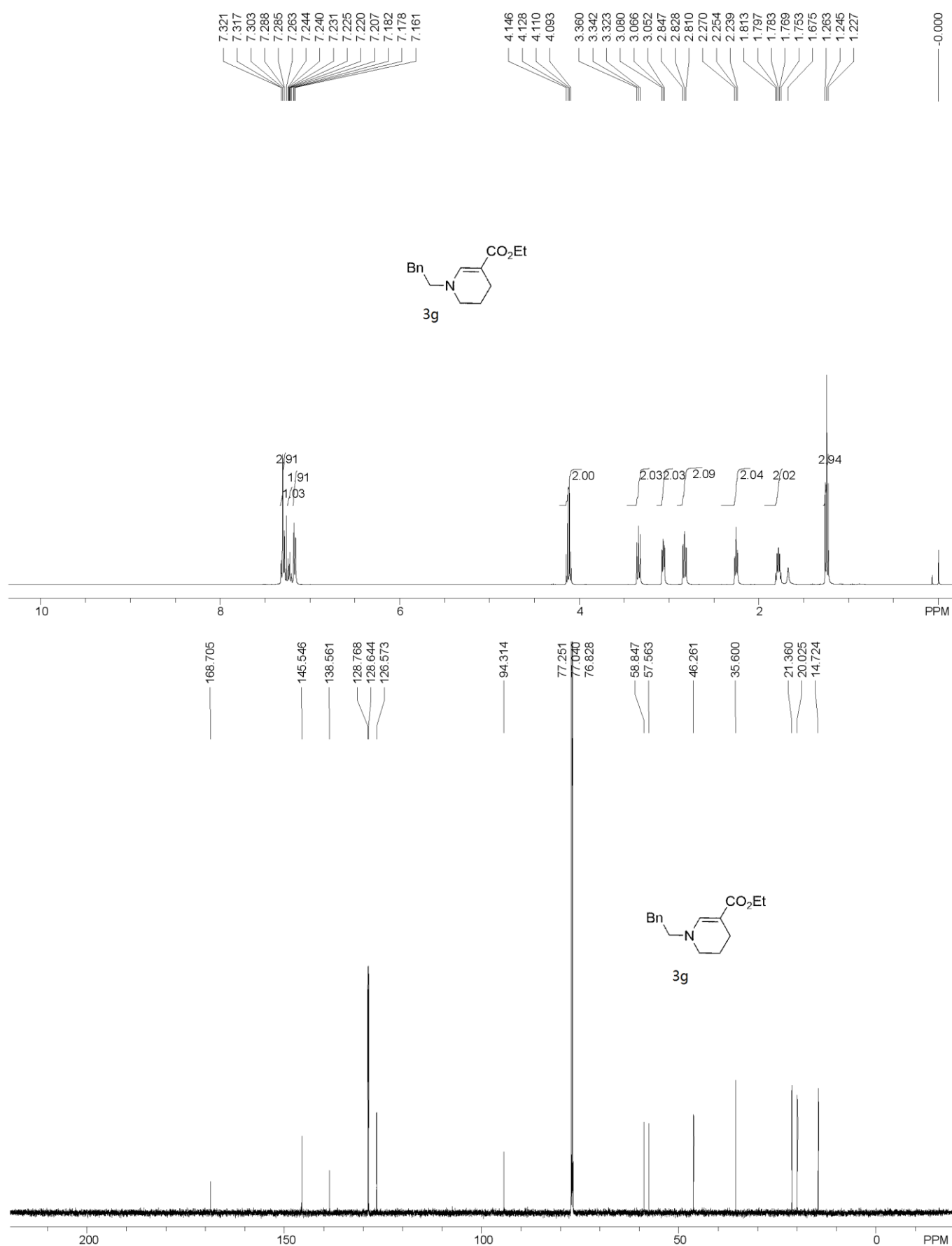


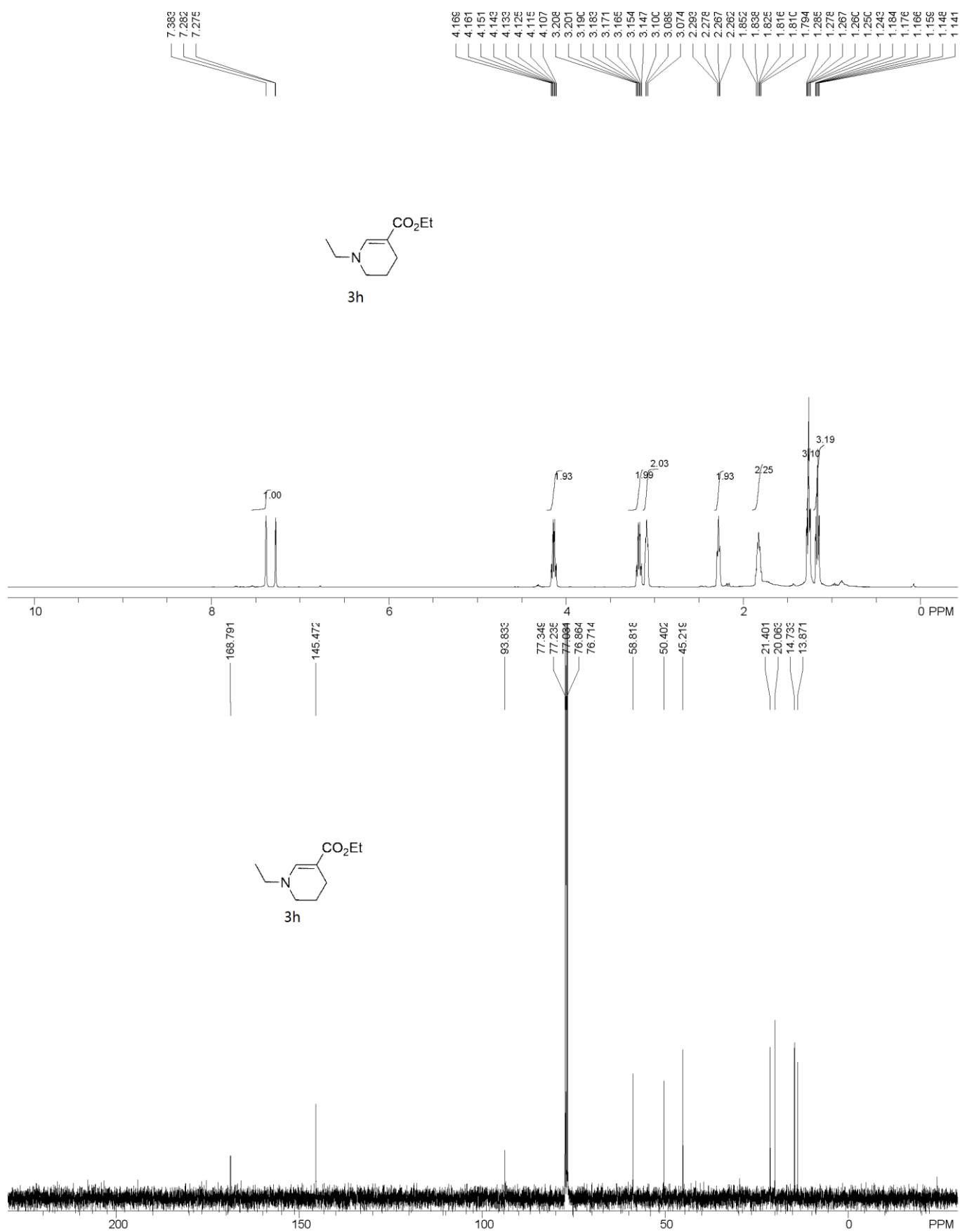


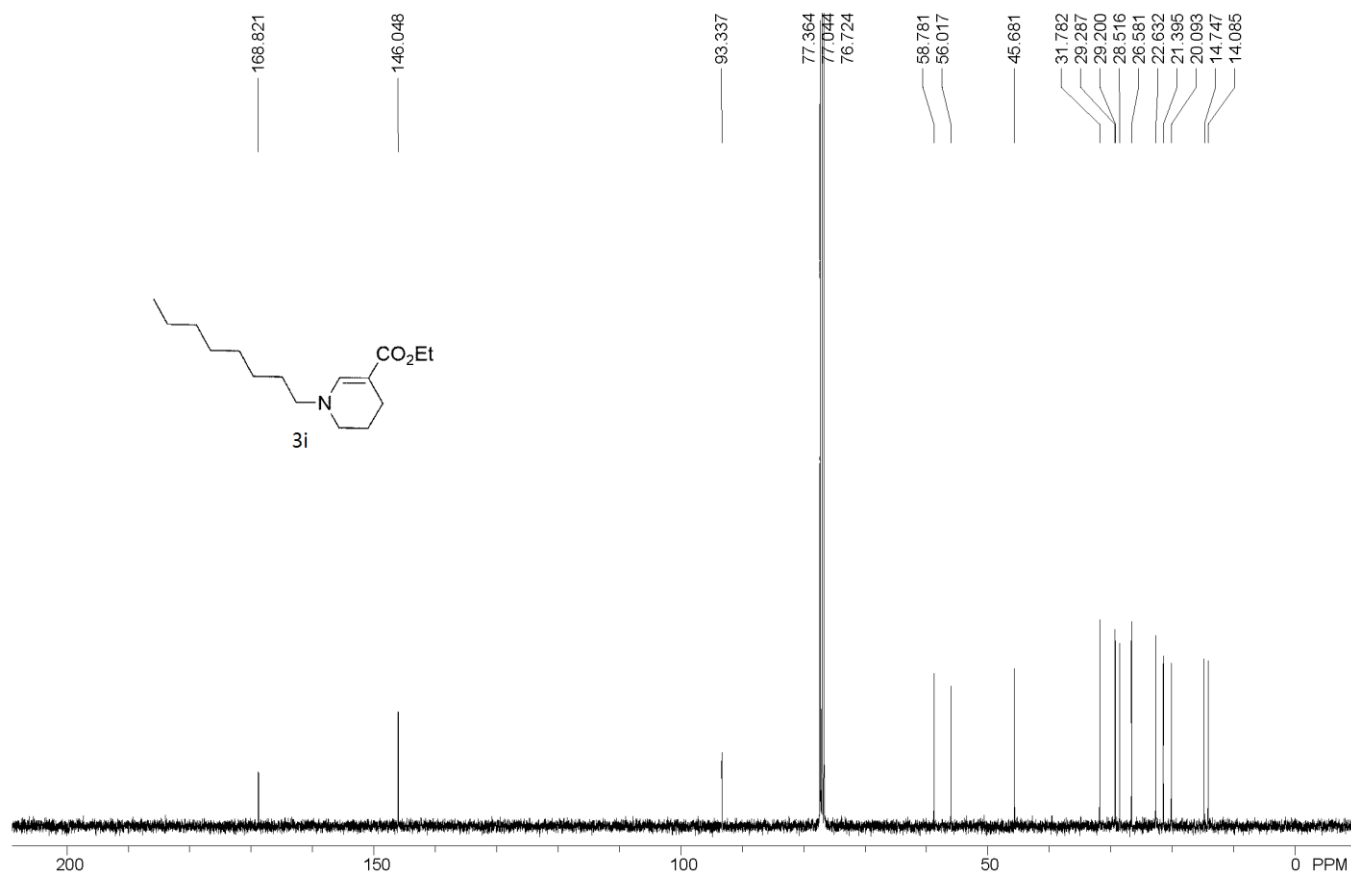
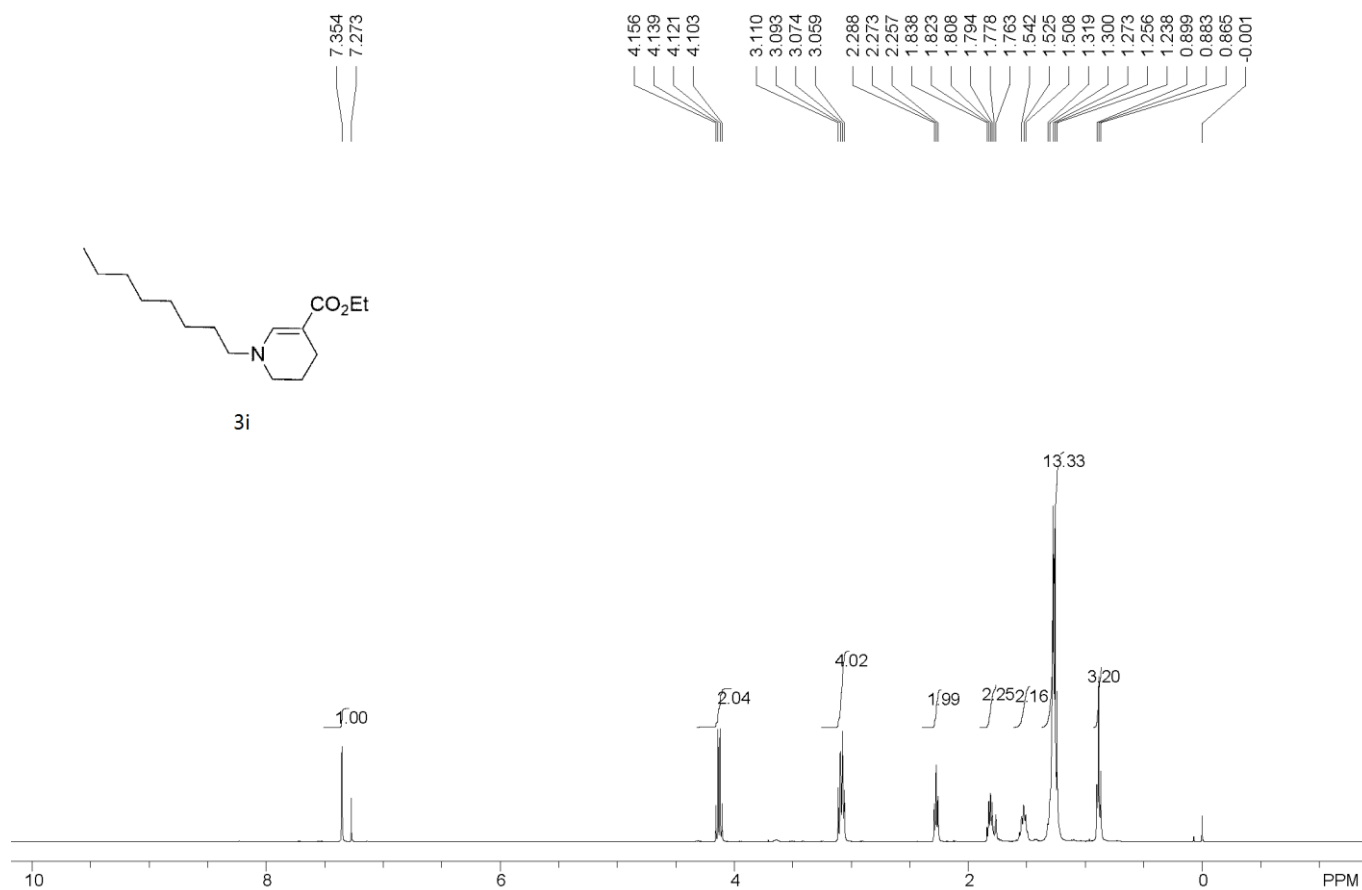


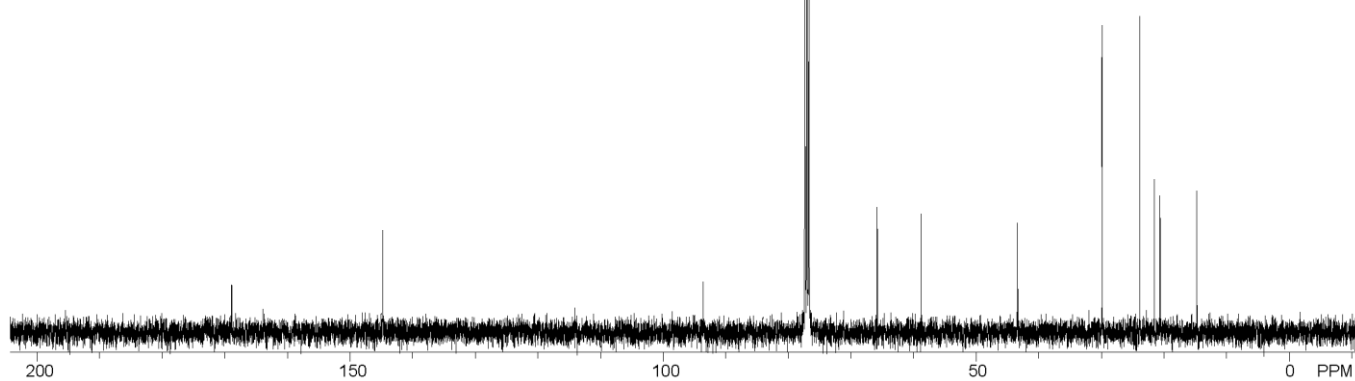
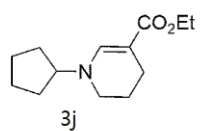
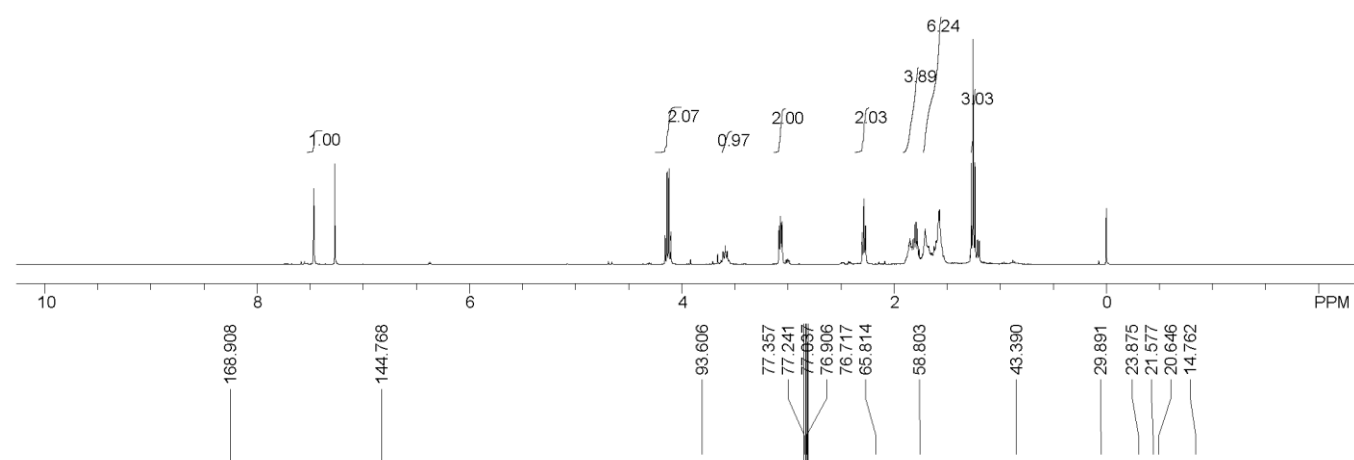
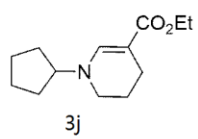


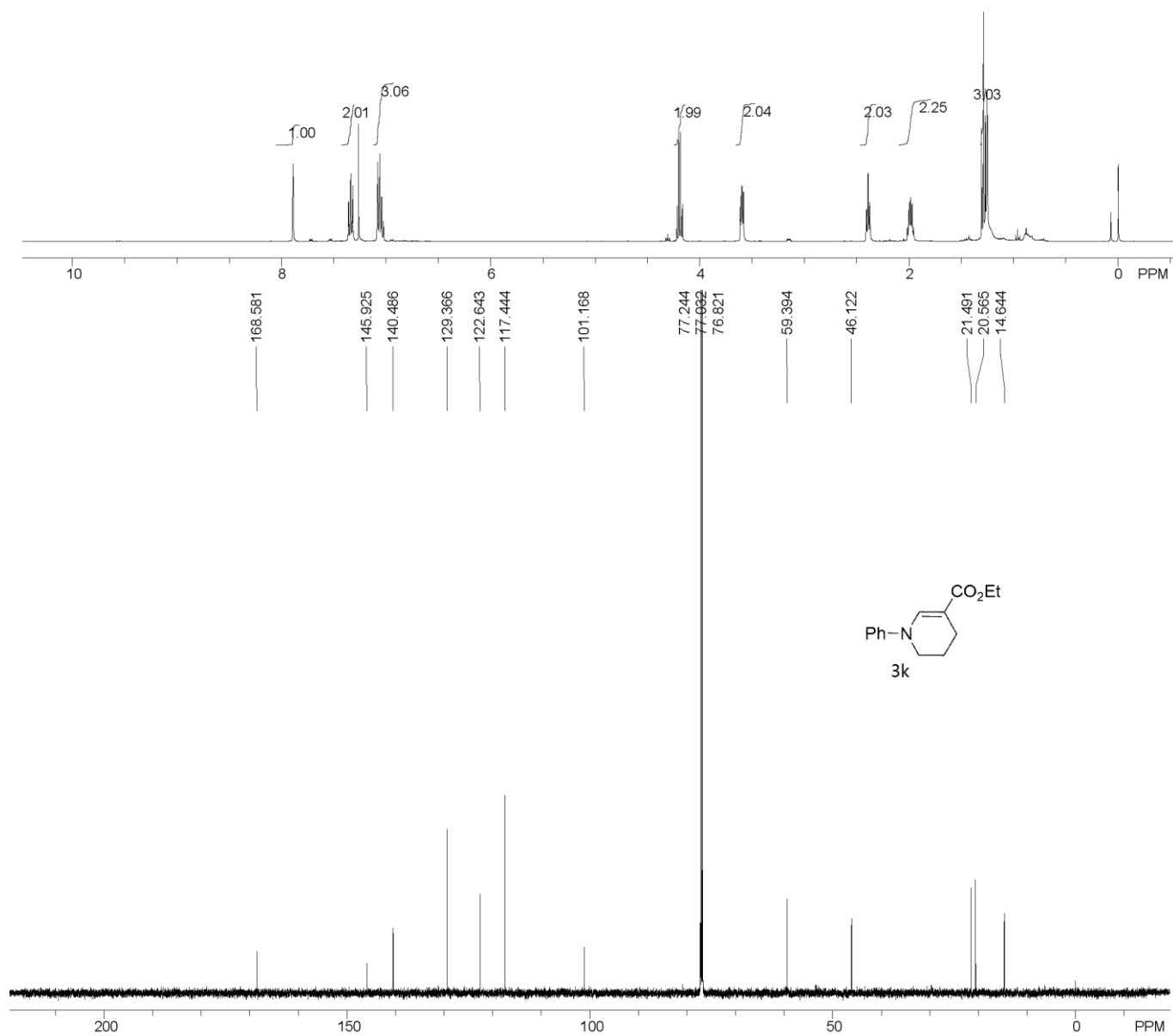
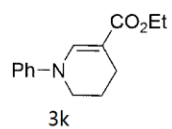
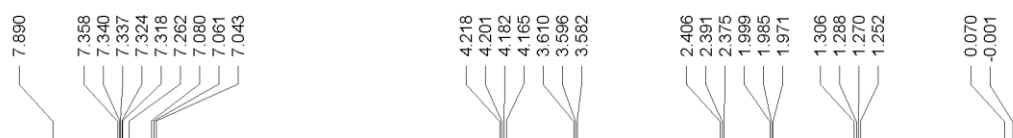


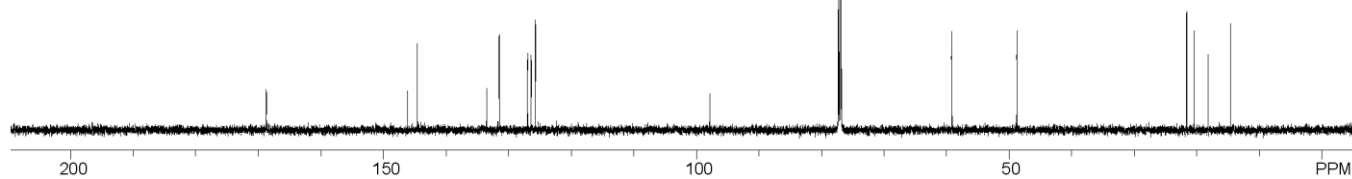
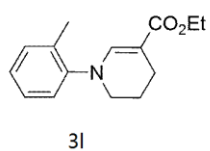
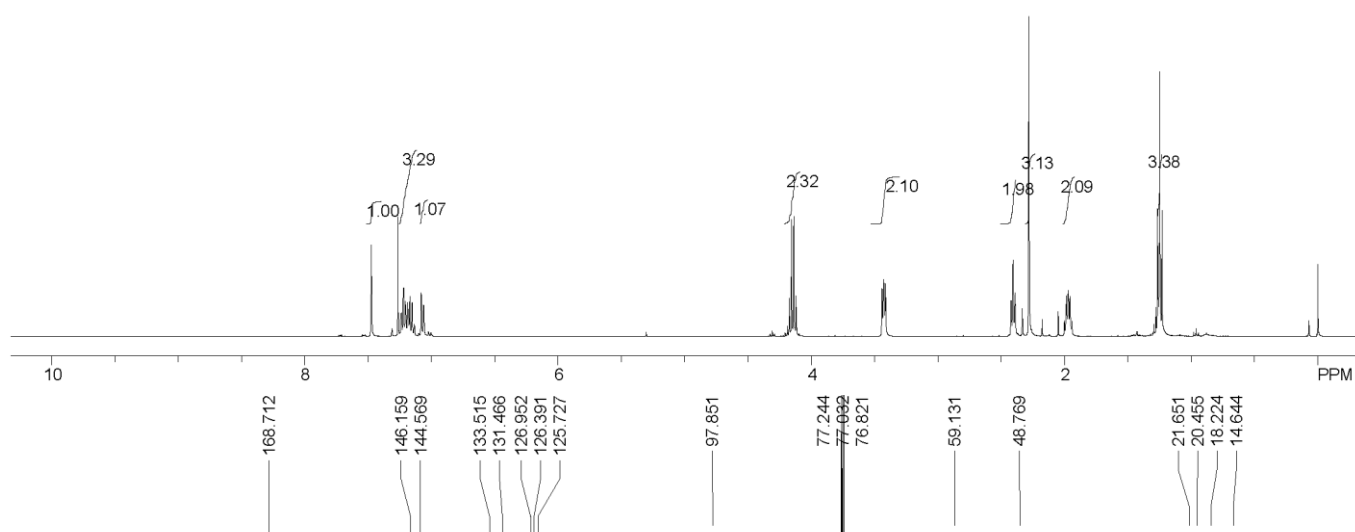
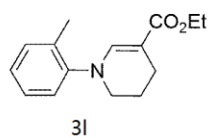
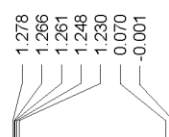
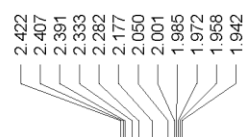
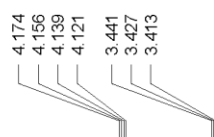
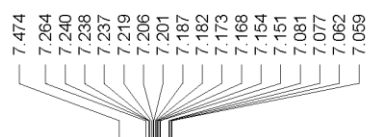


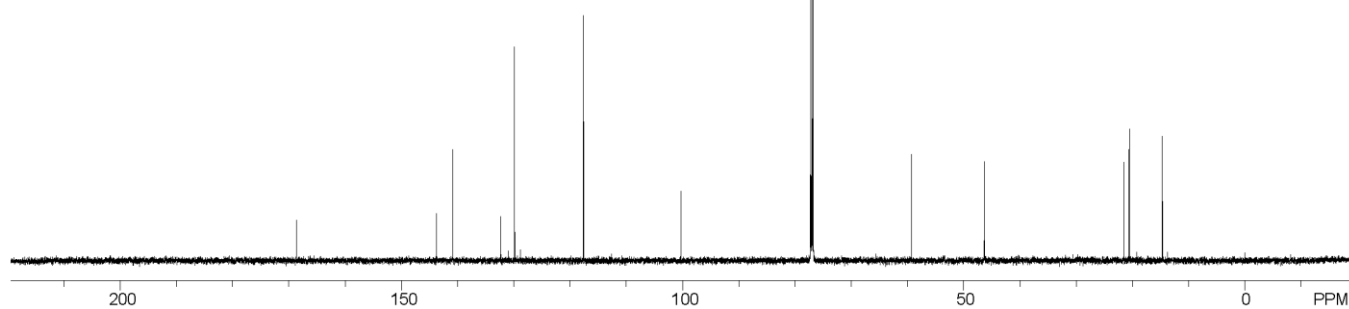
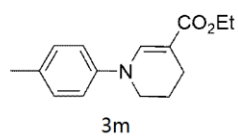
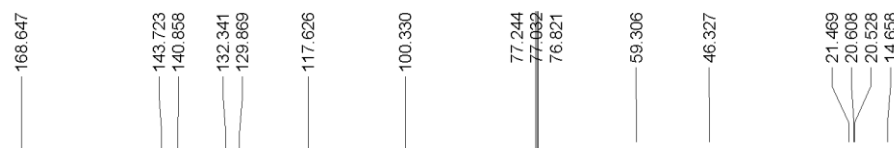
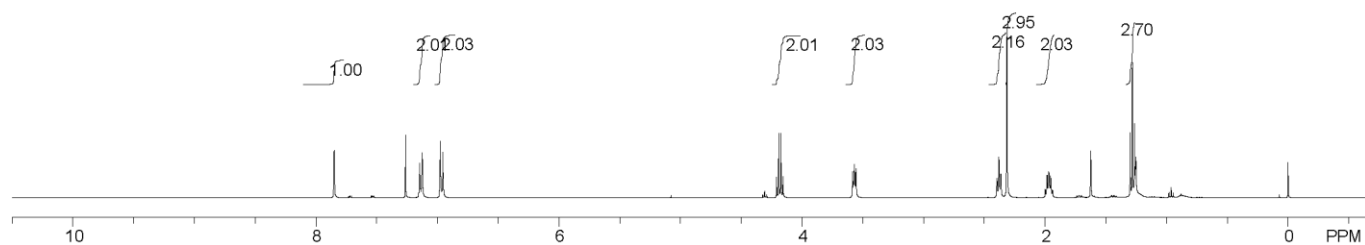
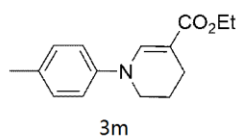
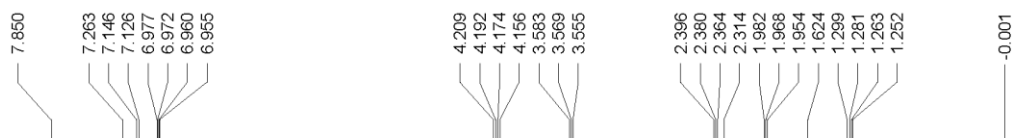


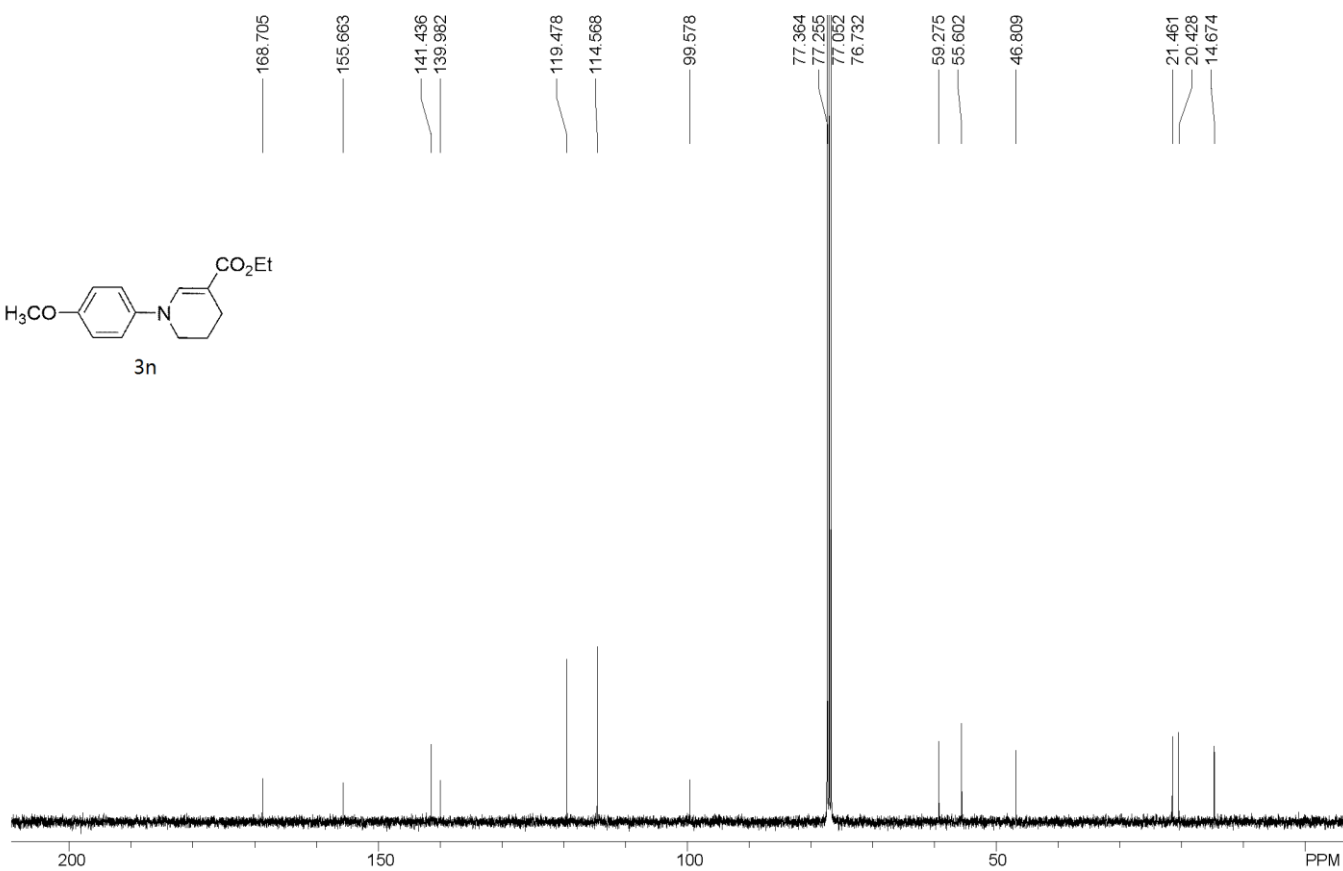
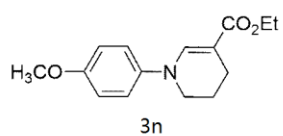
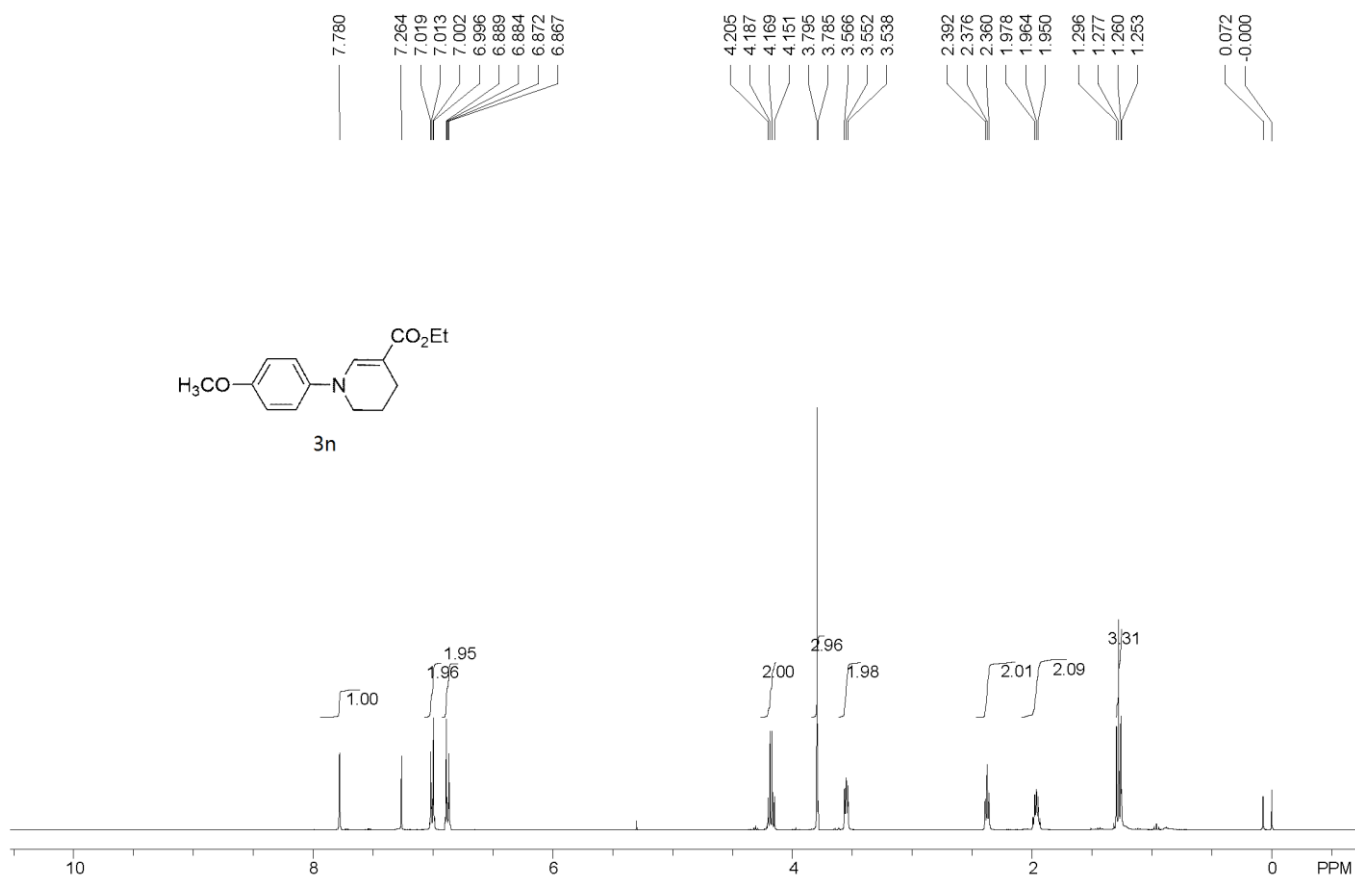
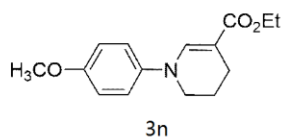


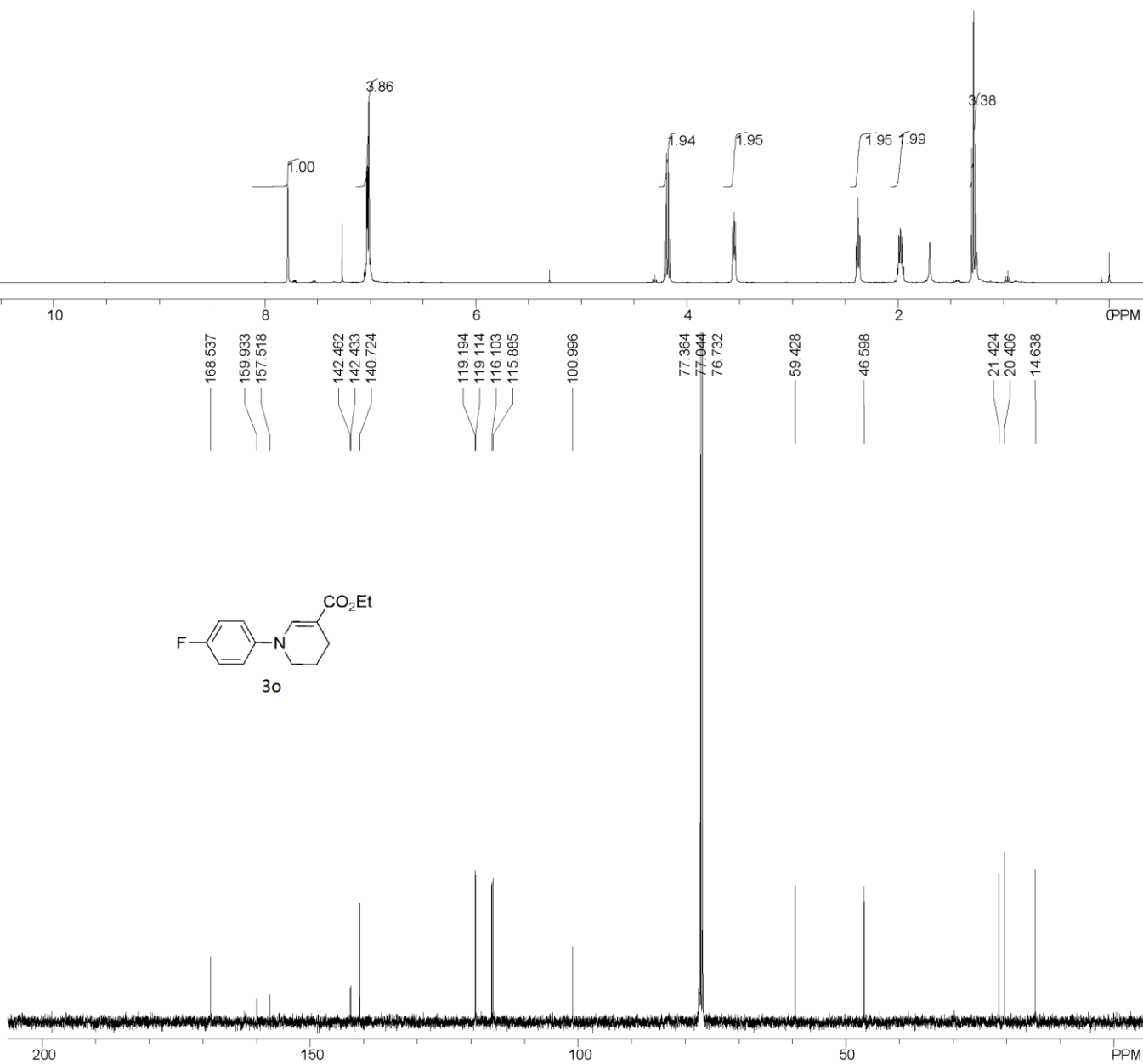
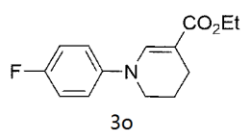
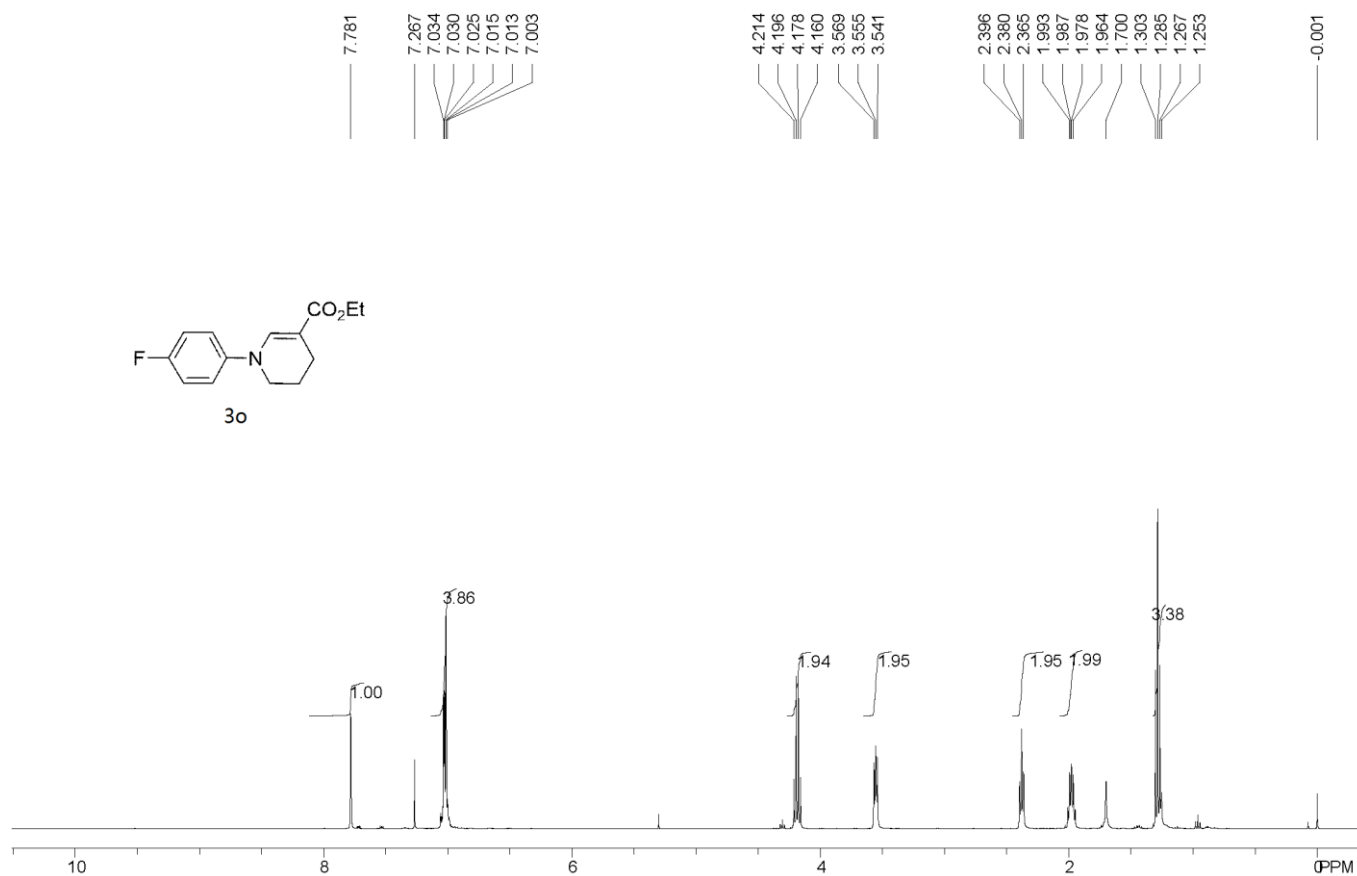
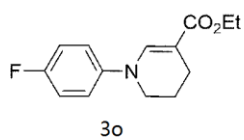


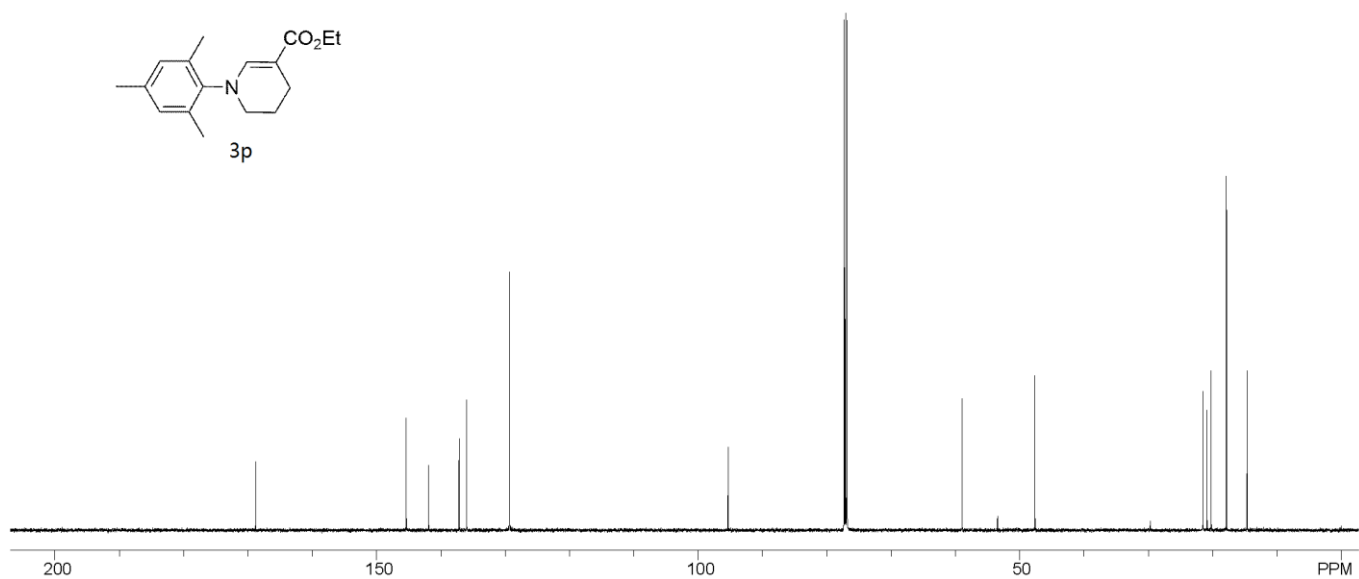
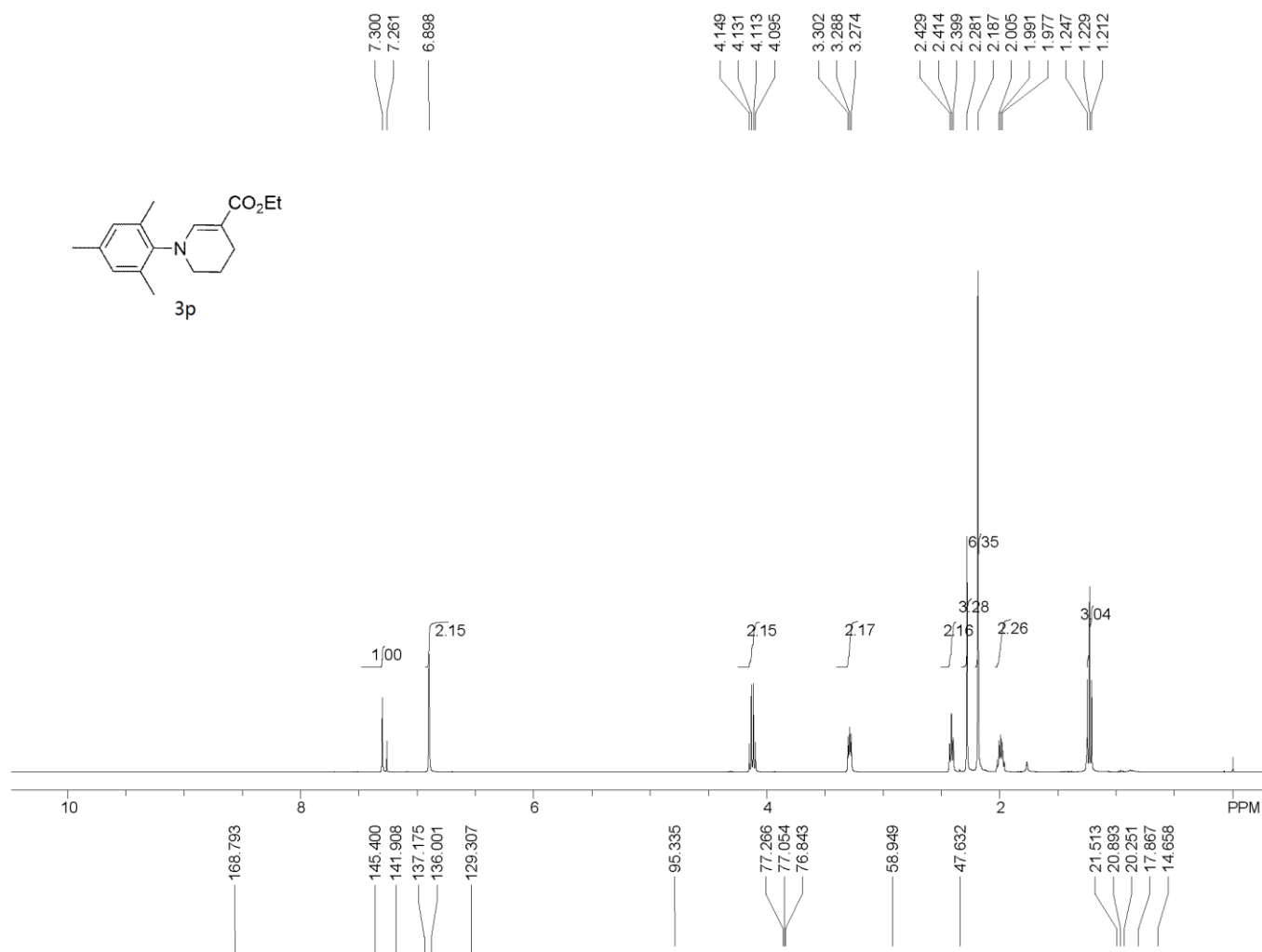


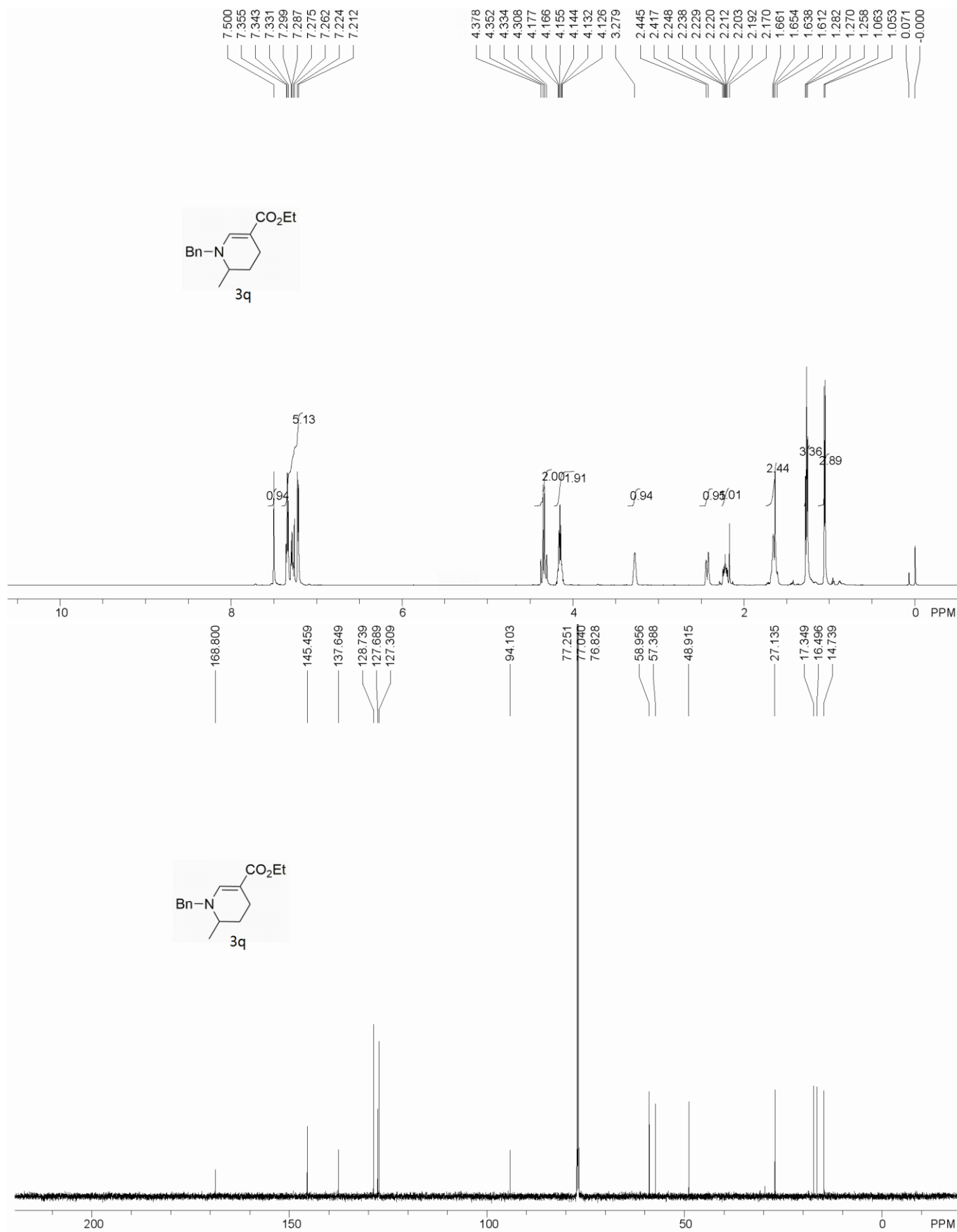


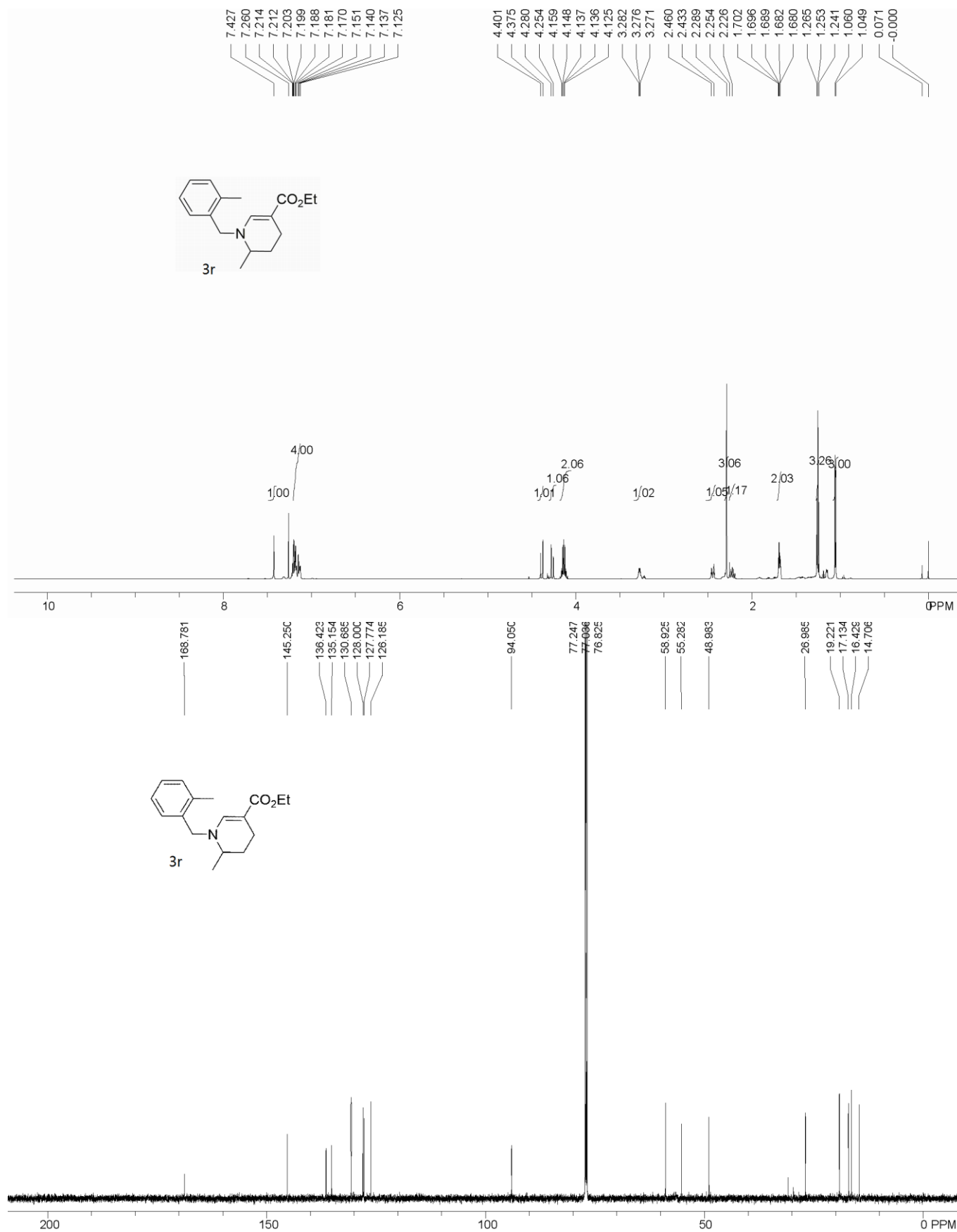


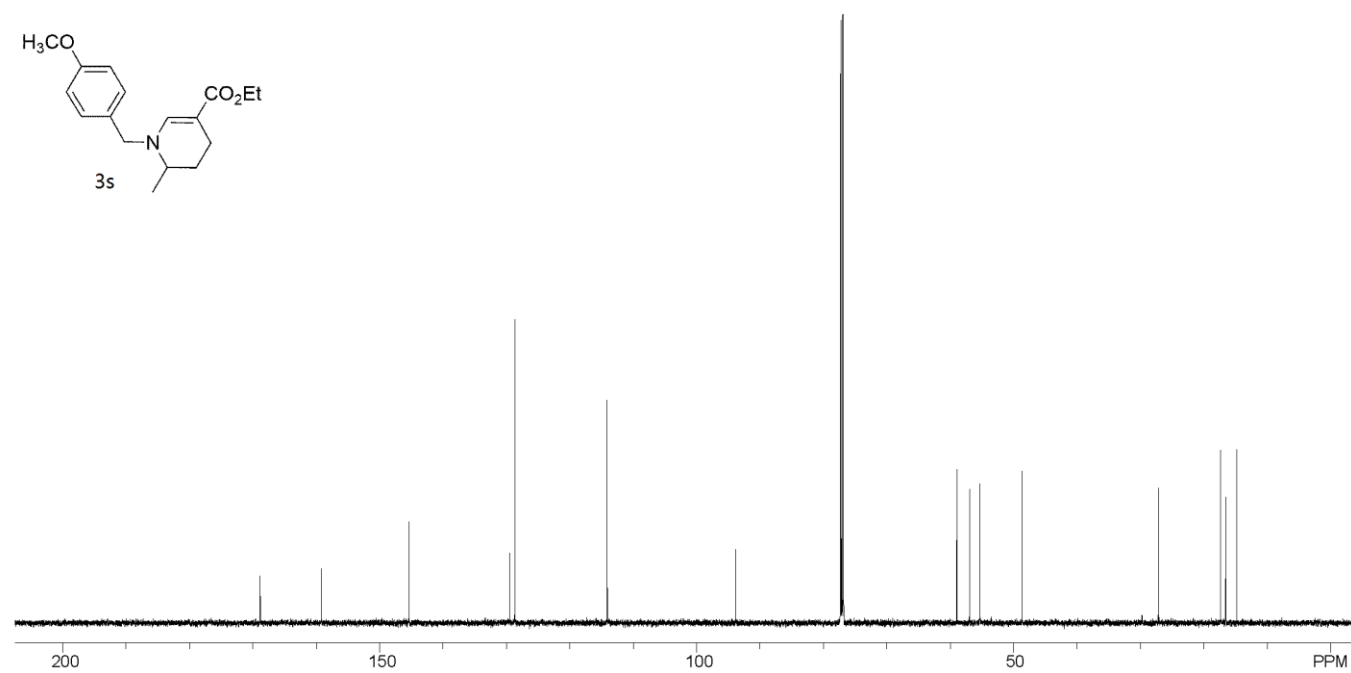
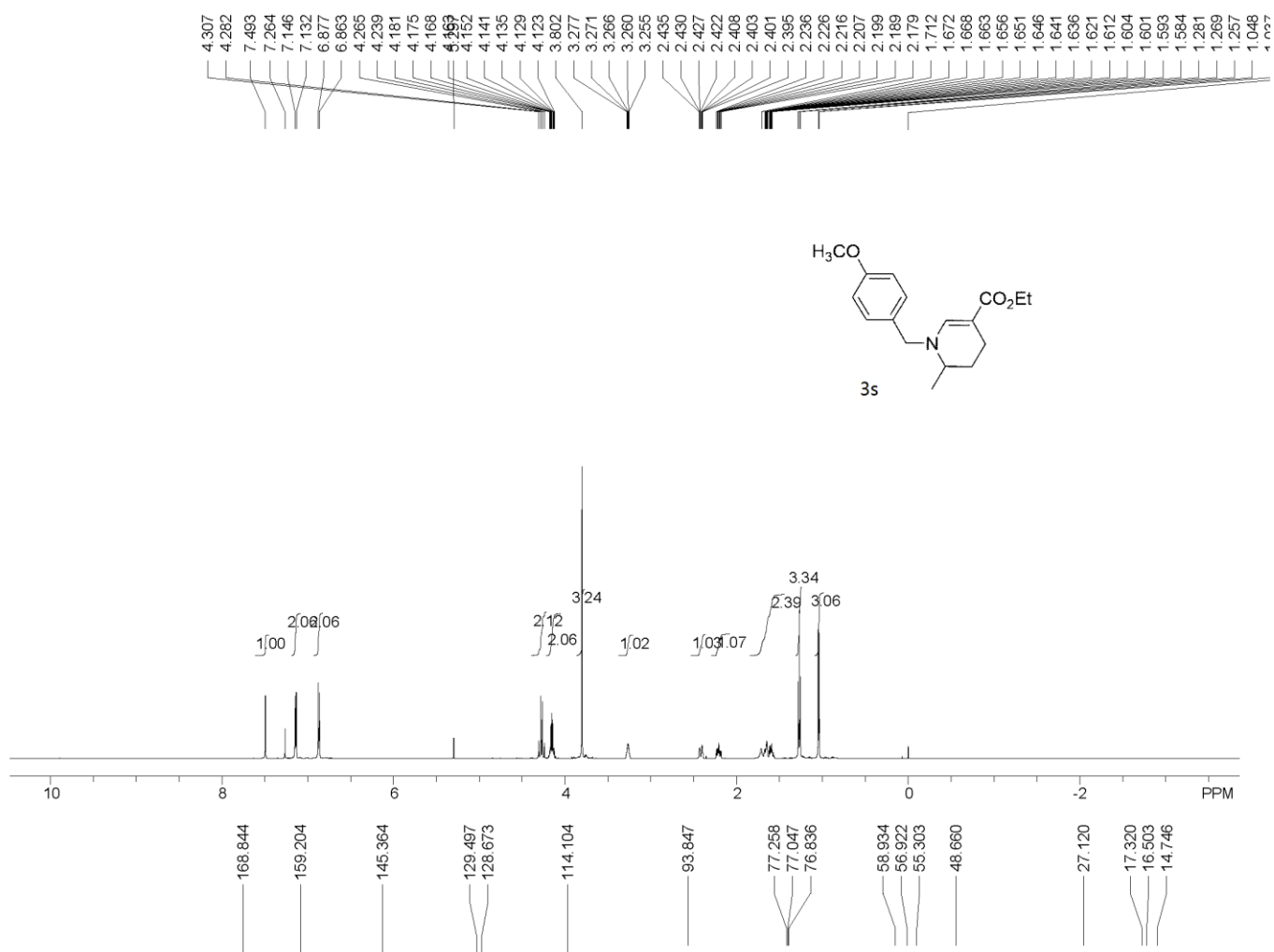


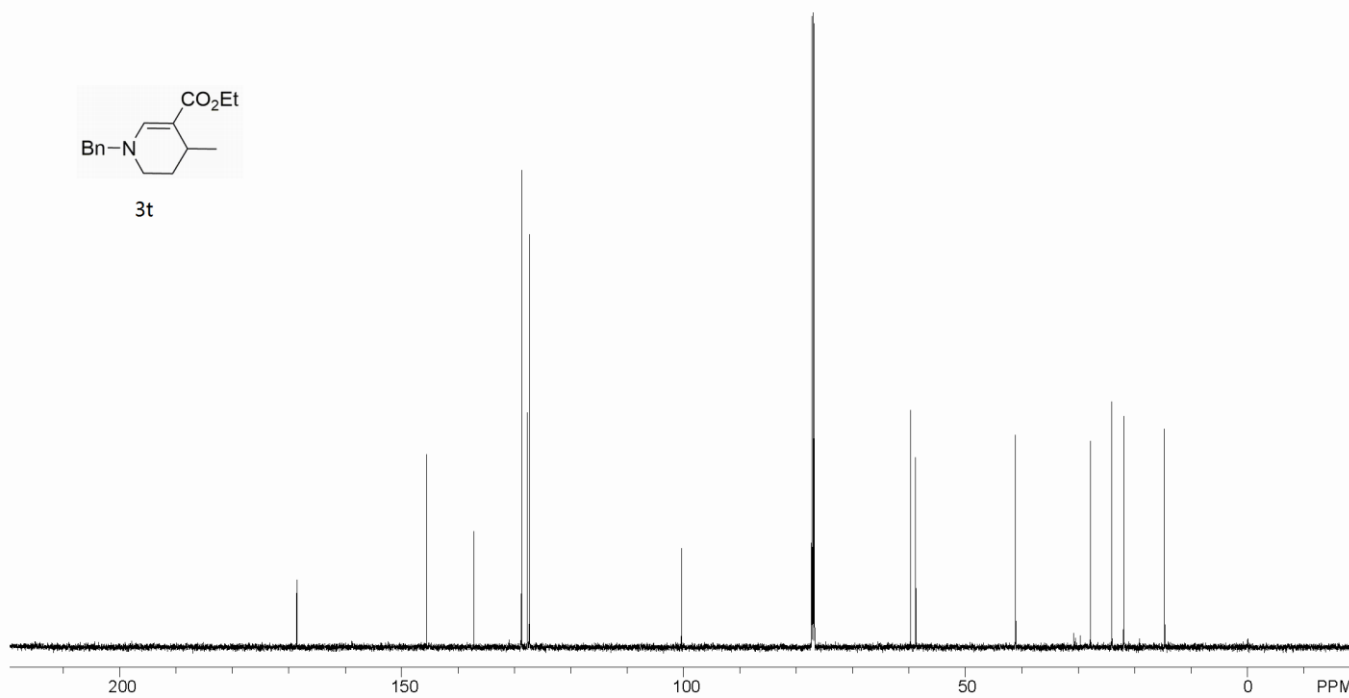
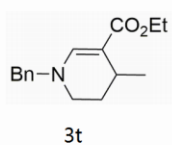
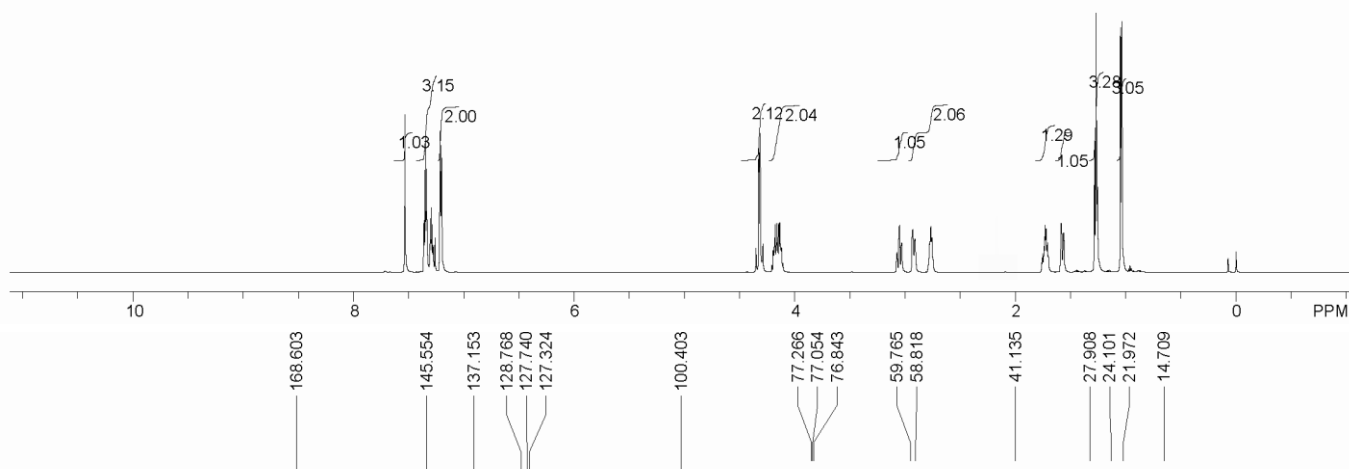
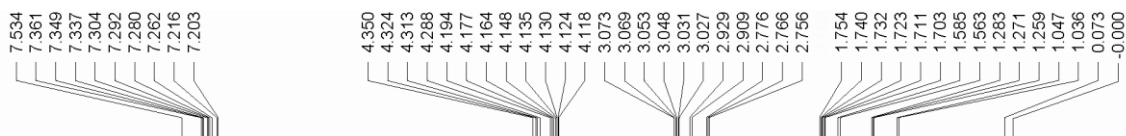
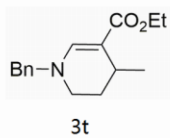


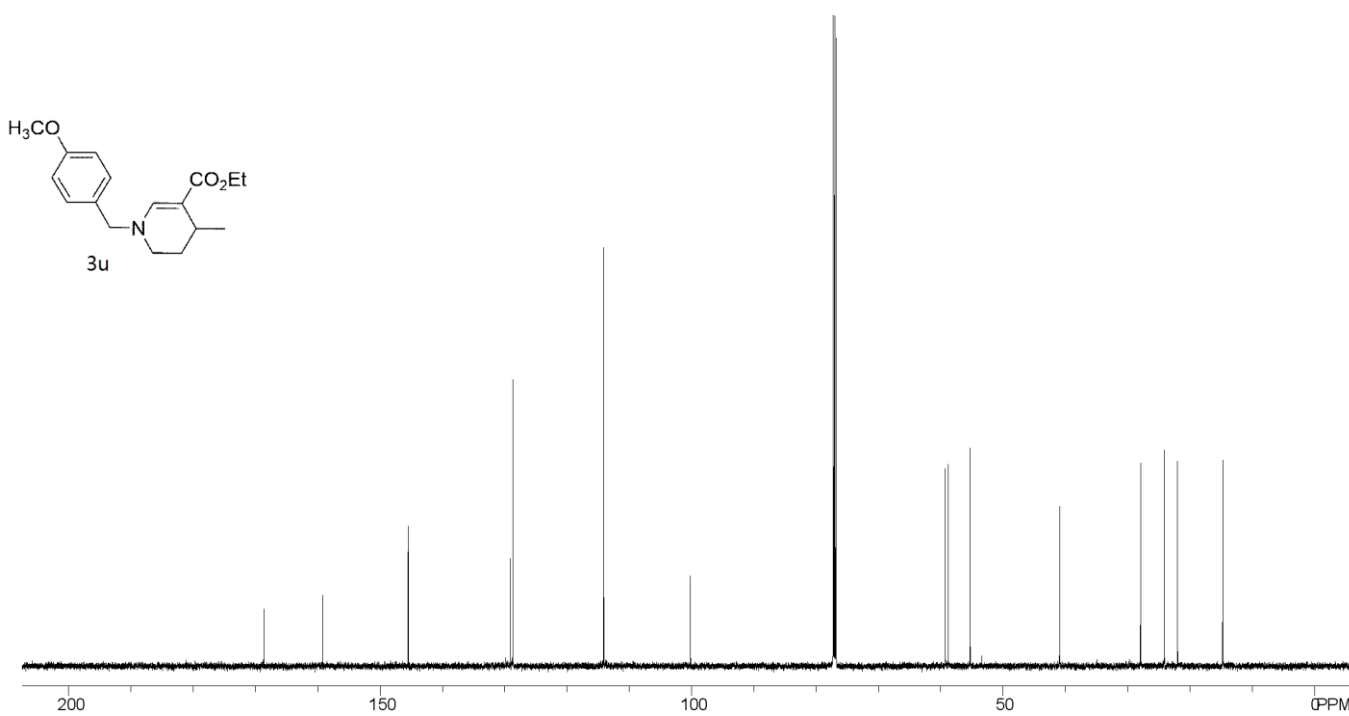
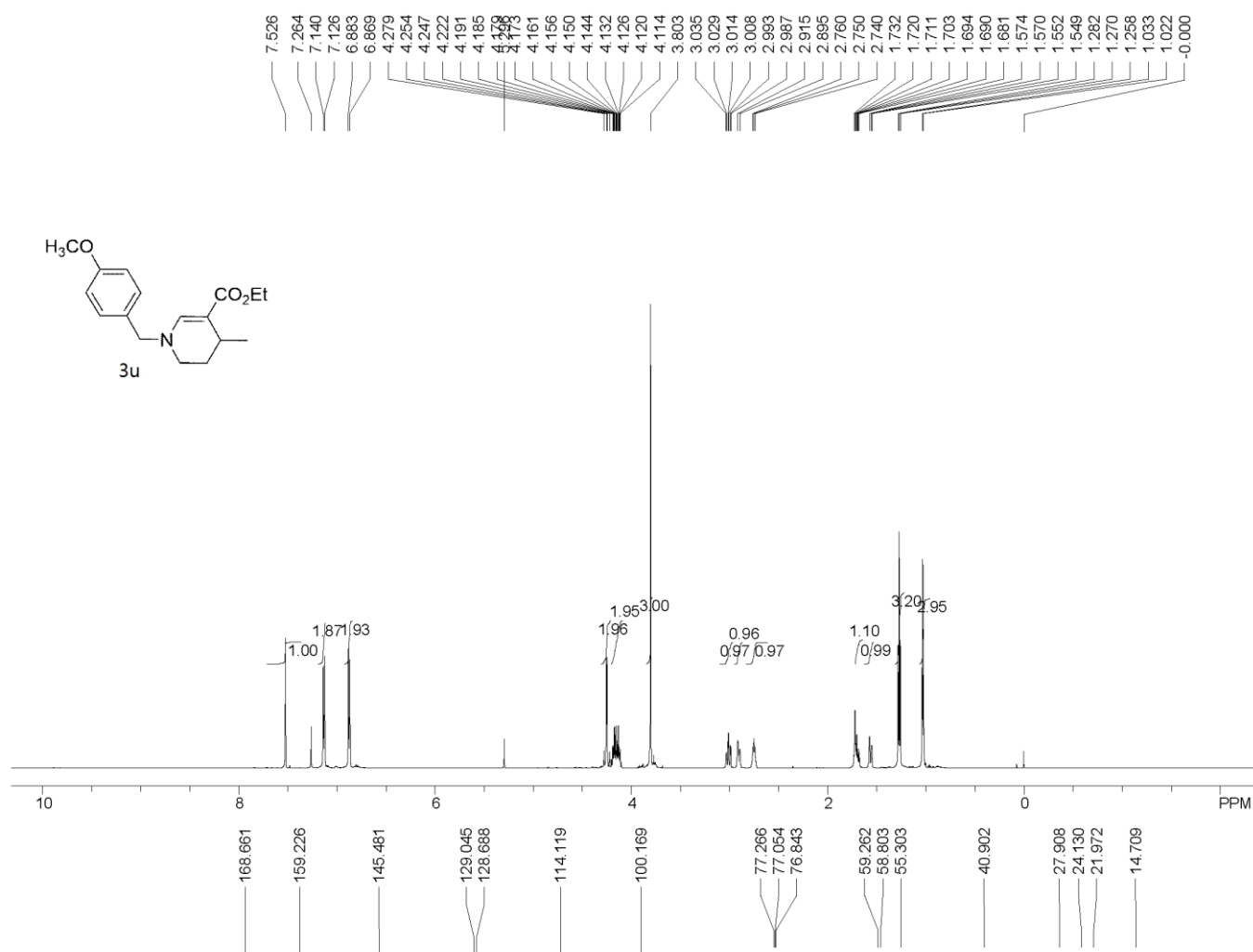


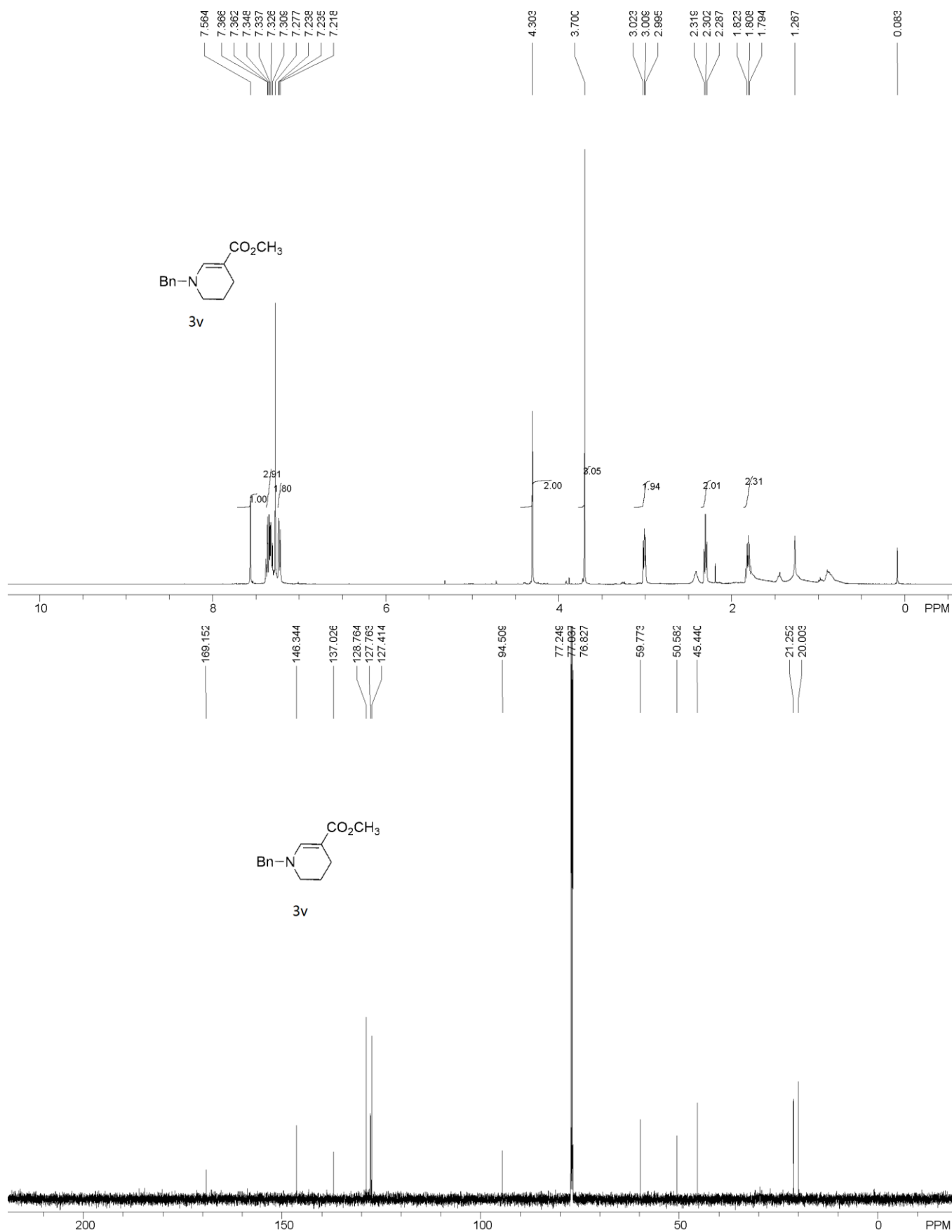


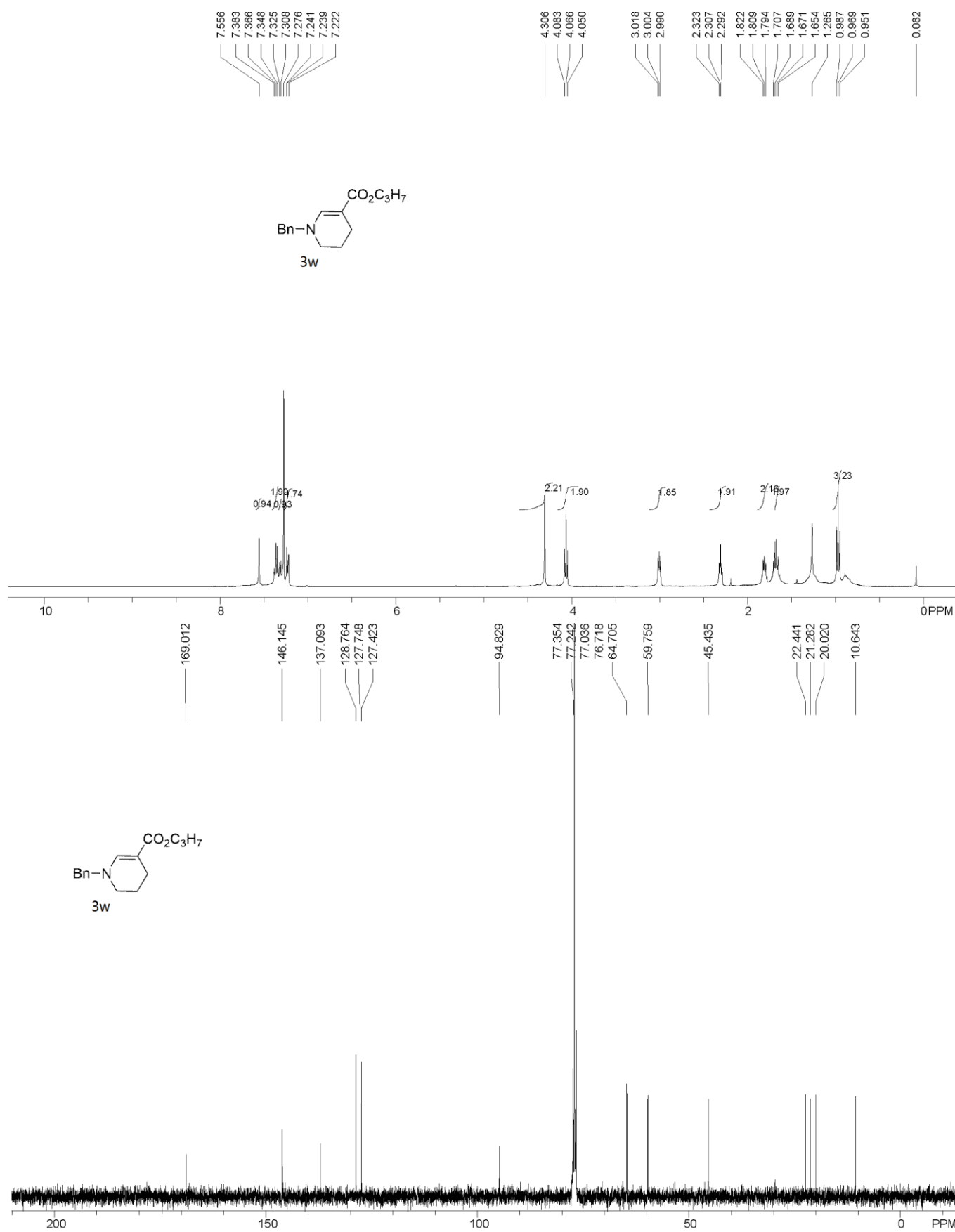


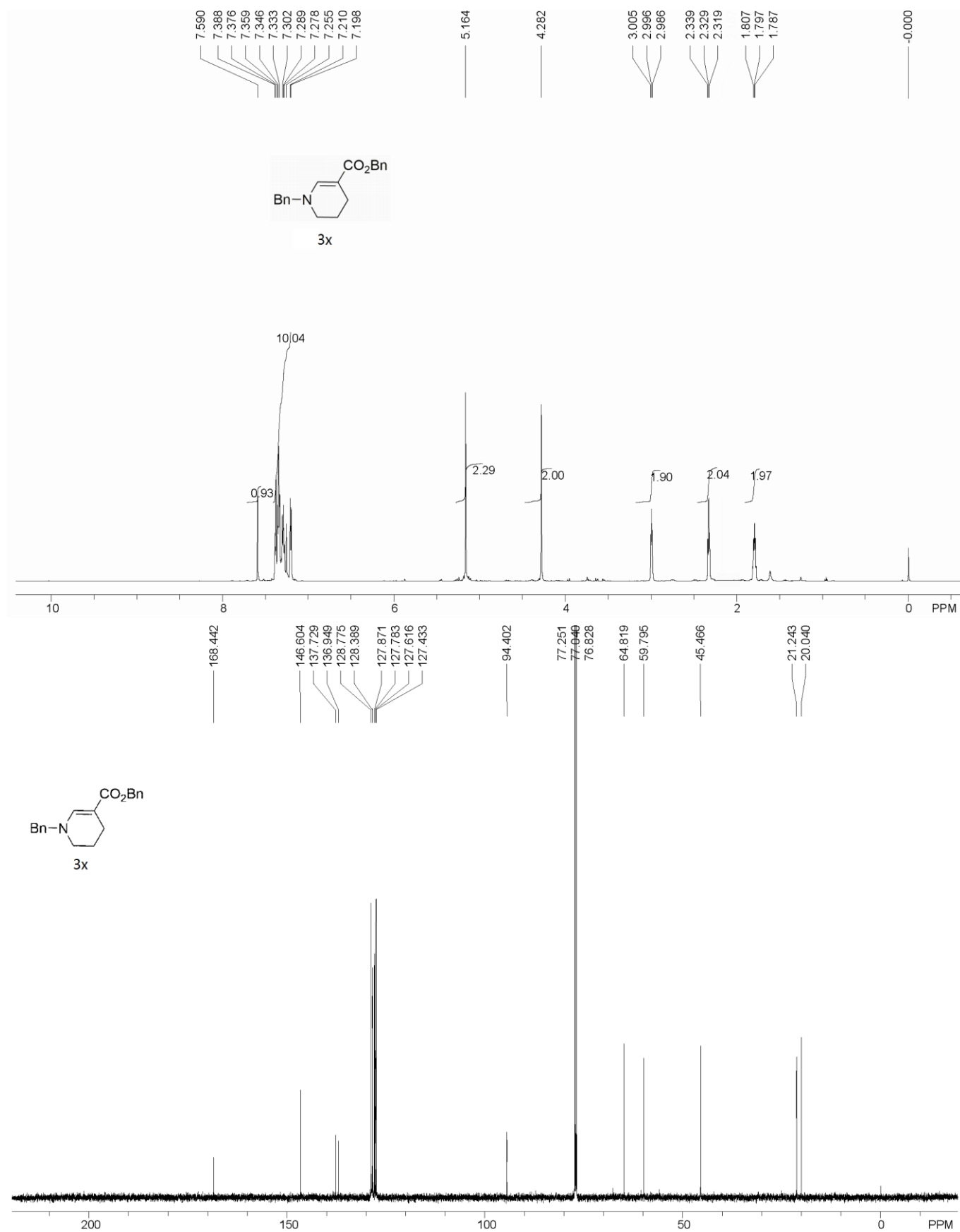




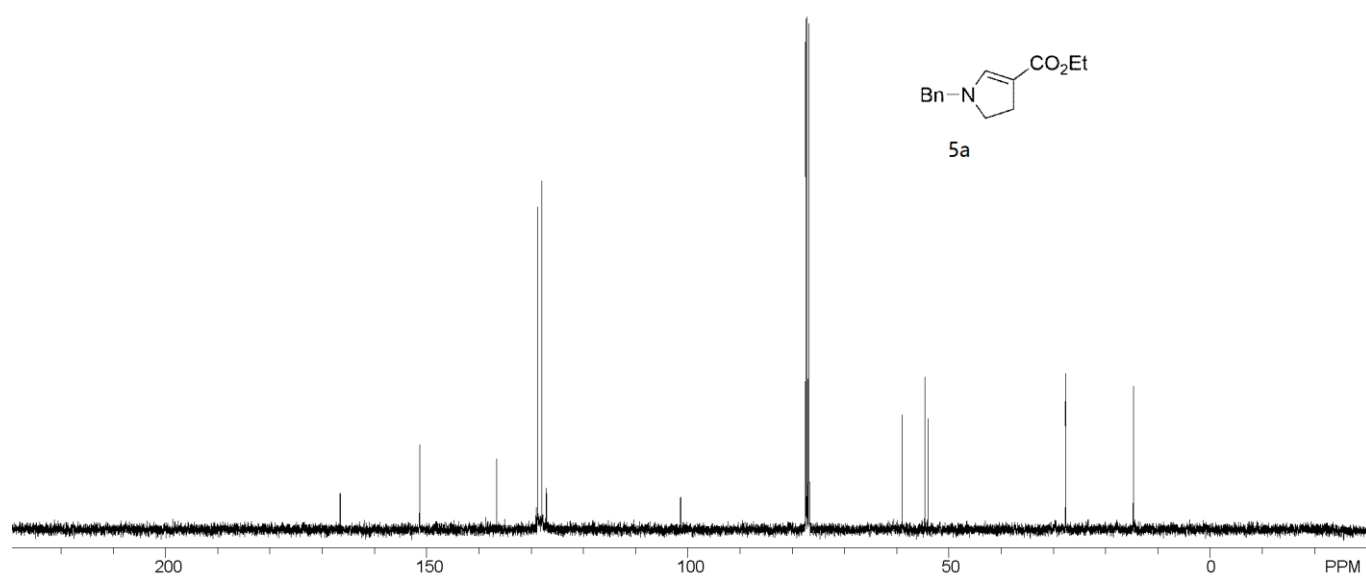
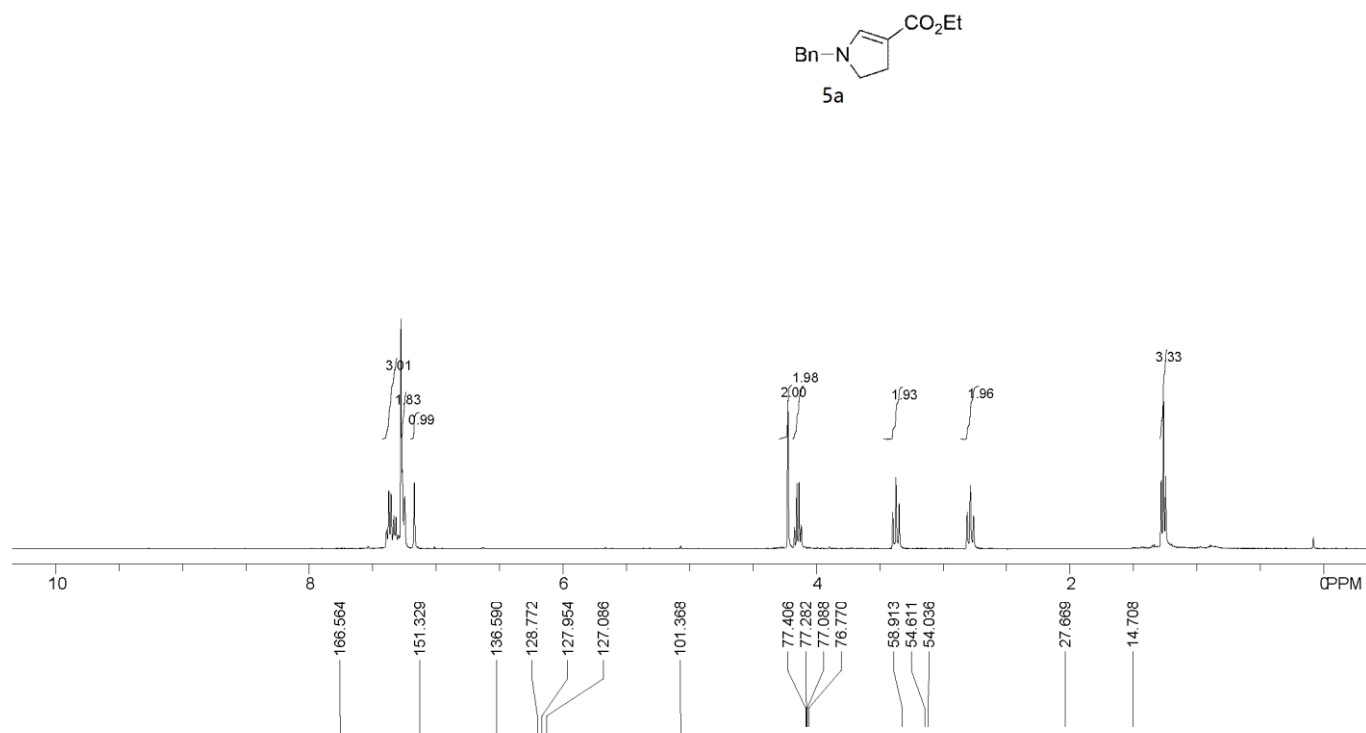
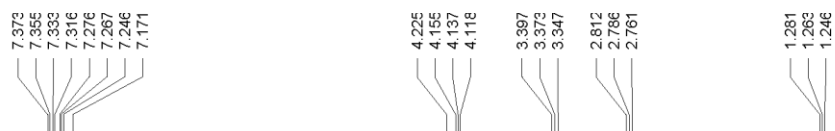




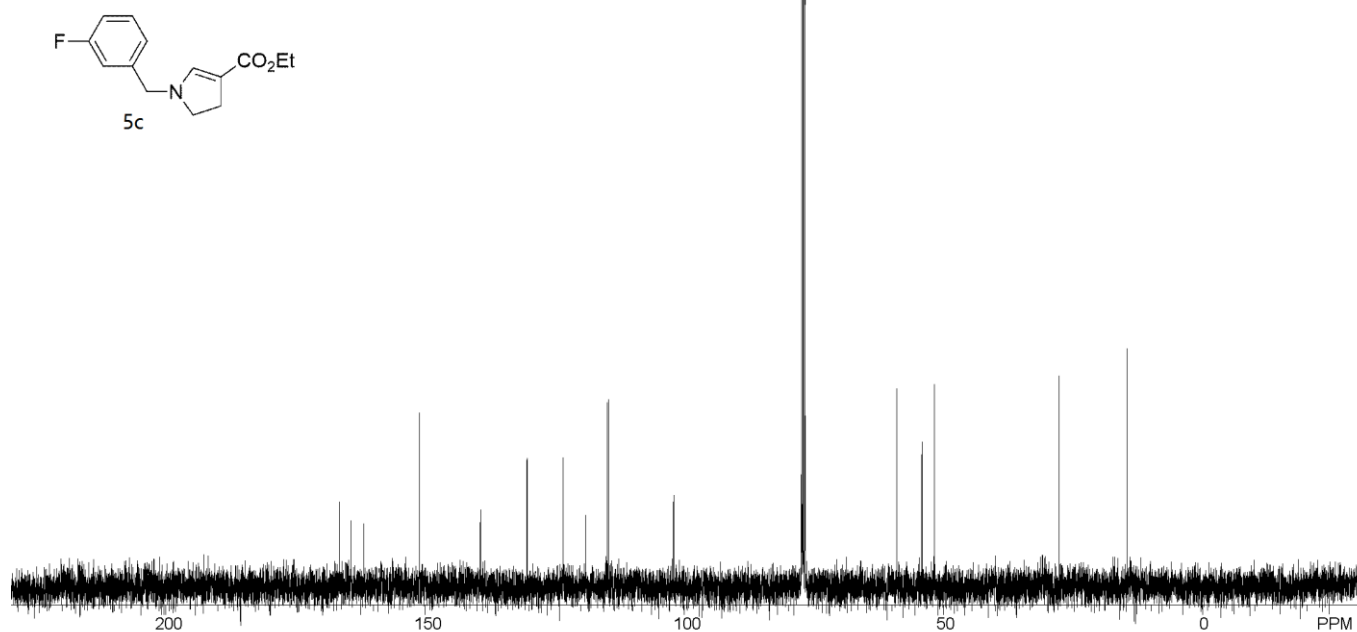
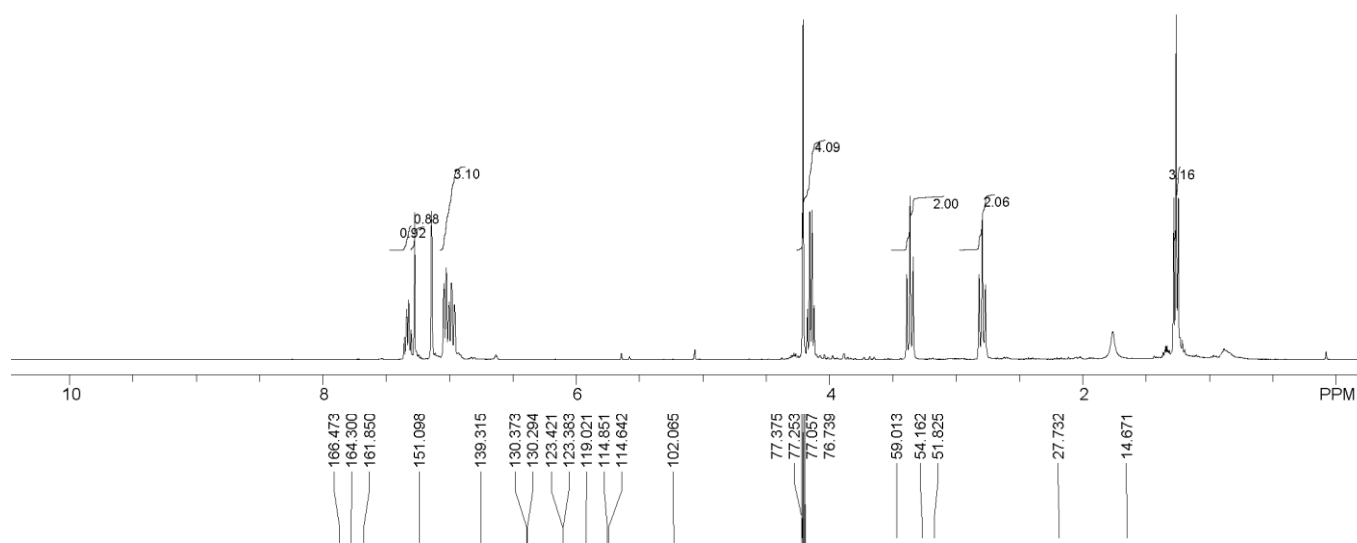
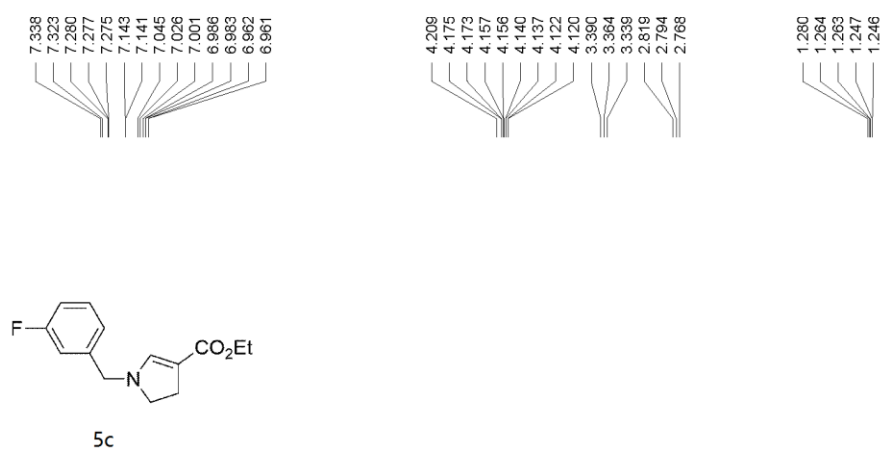


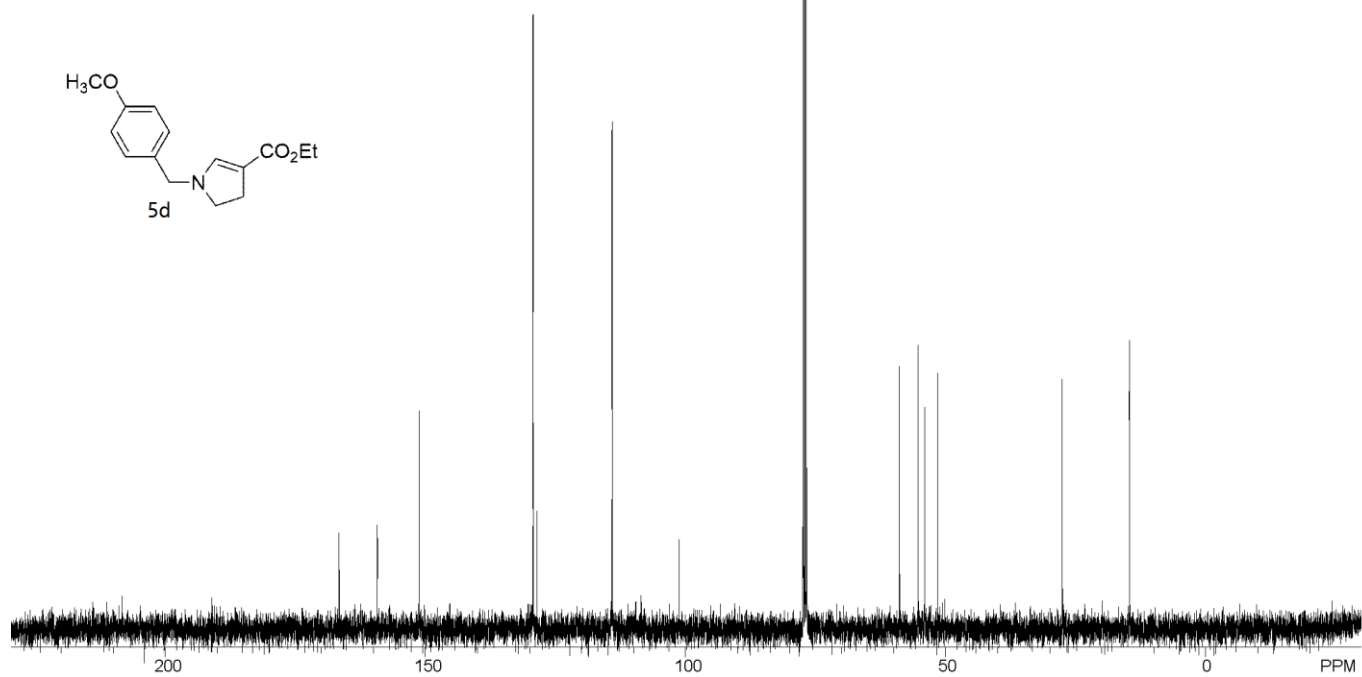
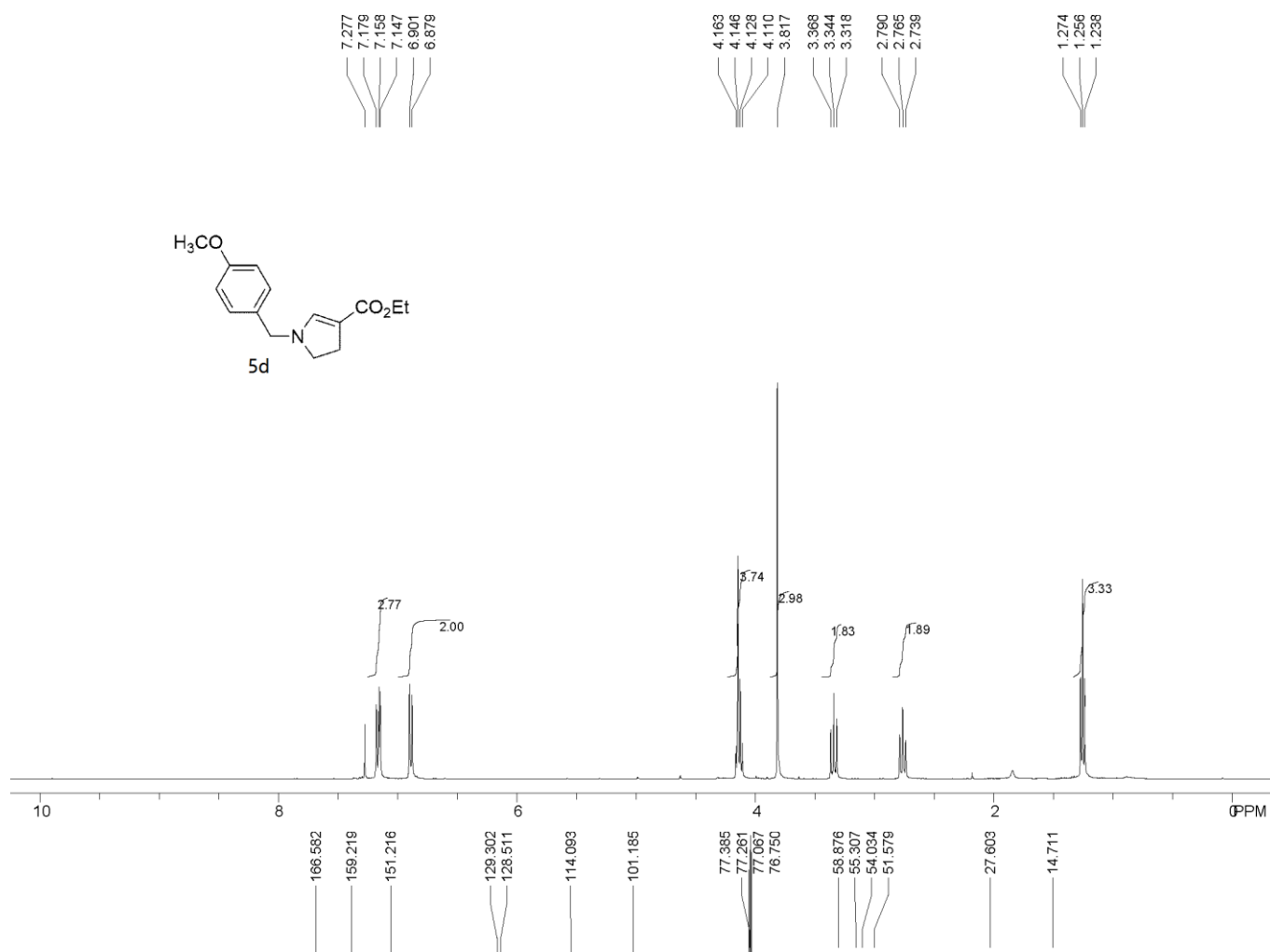


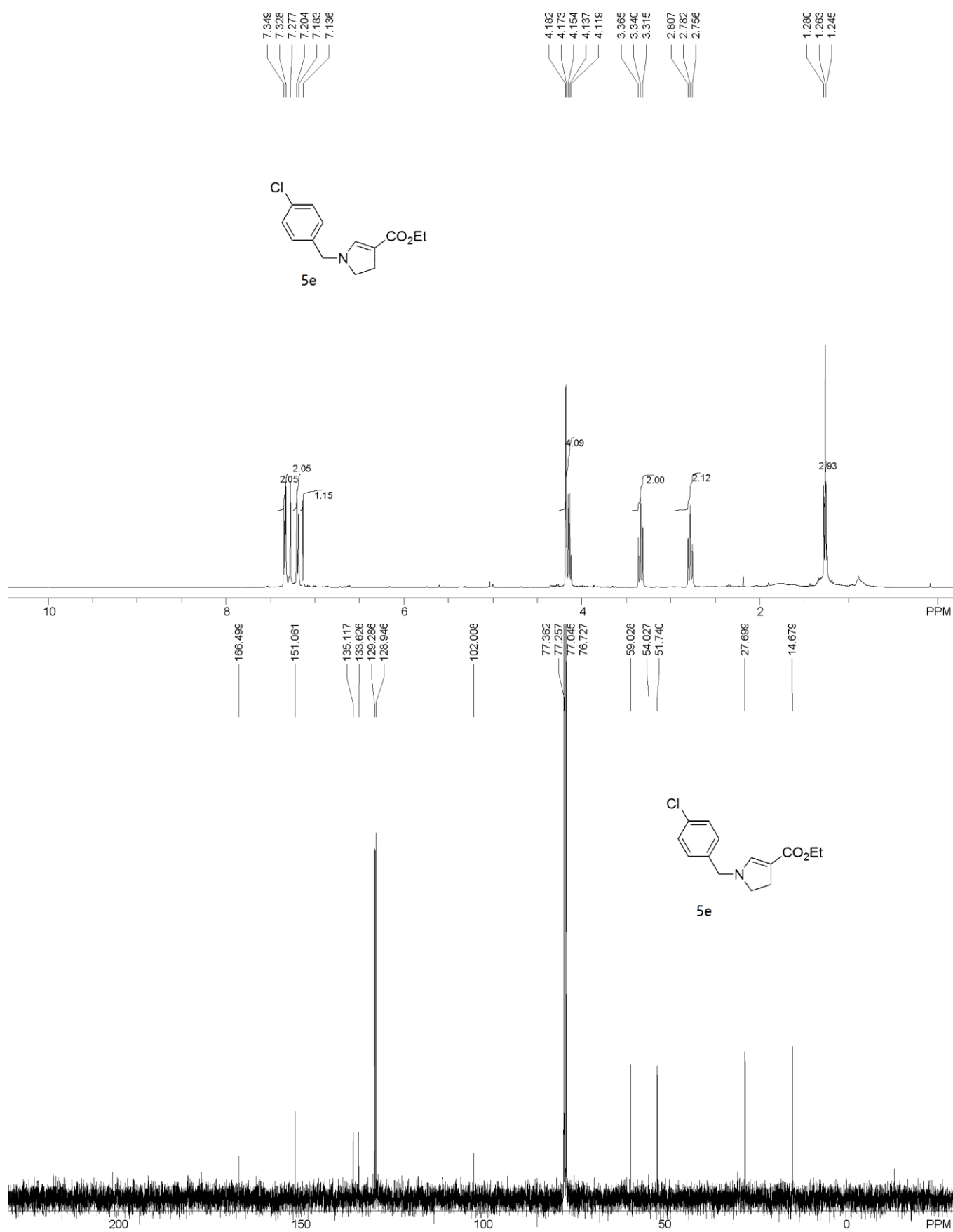
IV. Copies of ^1H and ^{13}C NMR Spectra of 5a-5l'

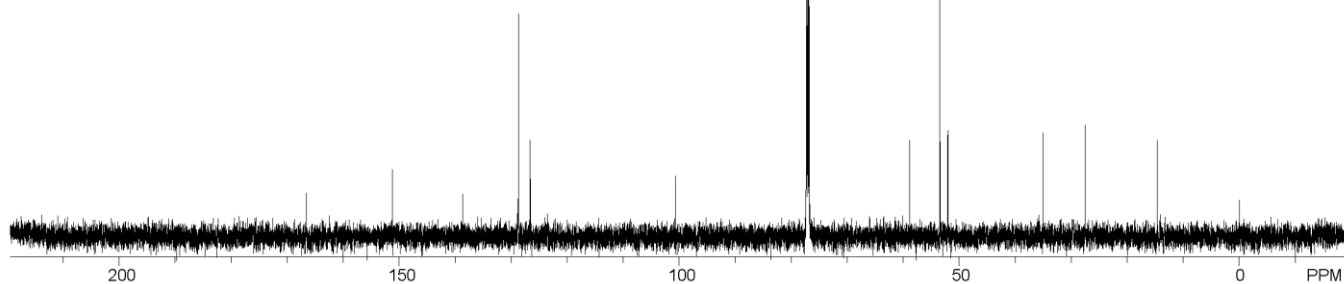
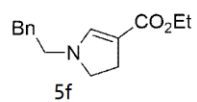
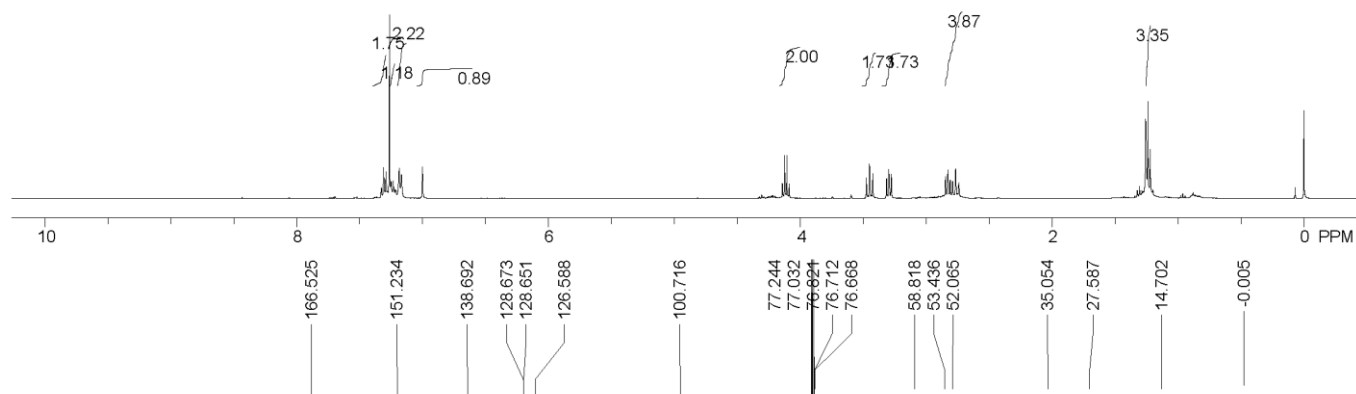
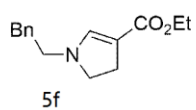
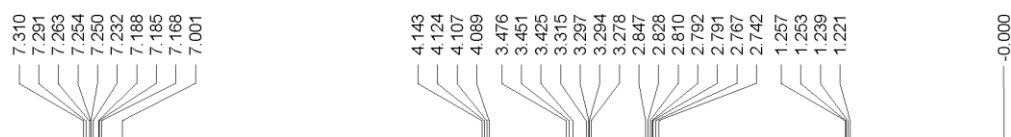


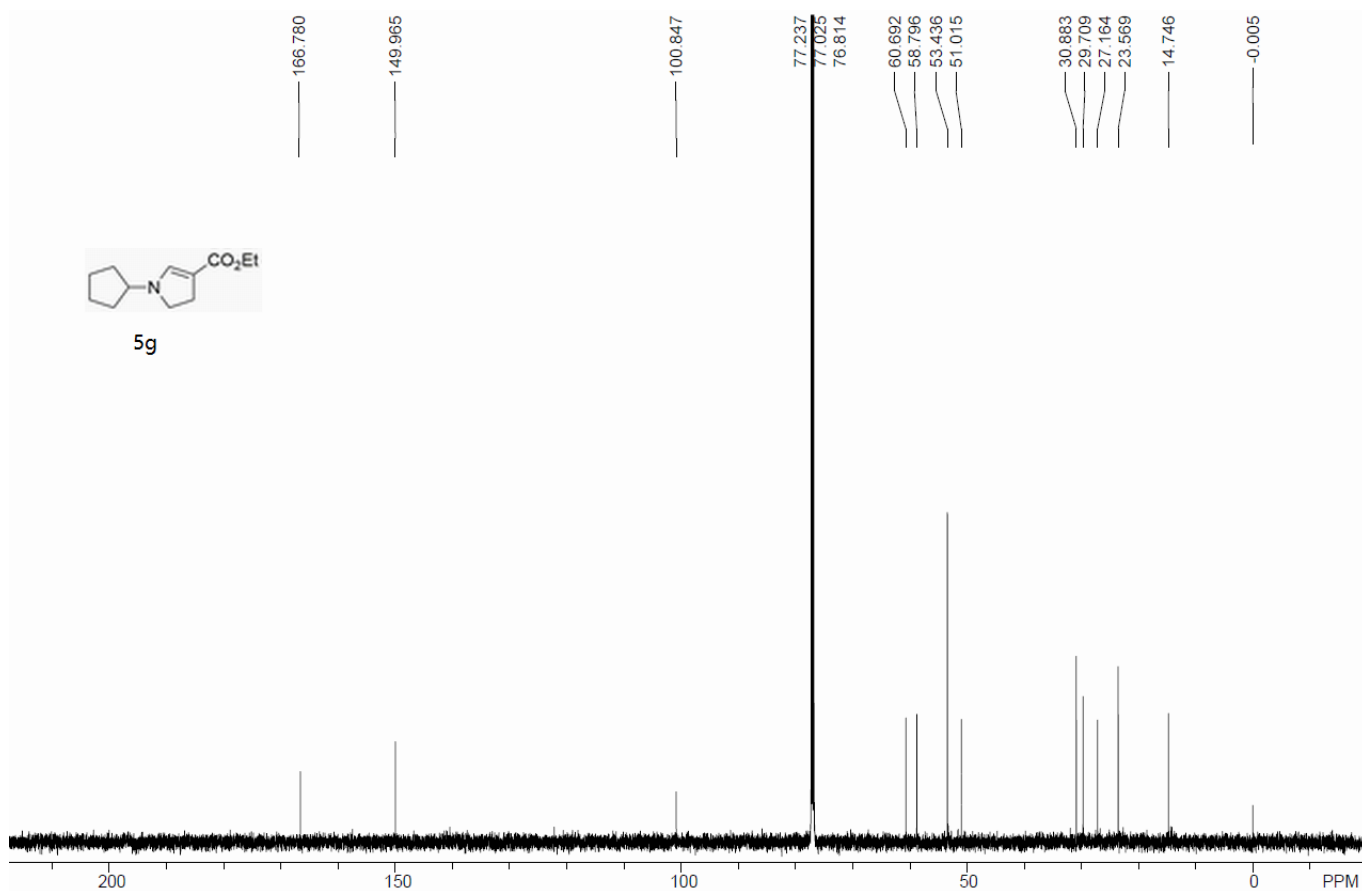
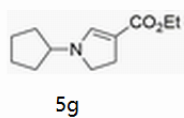
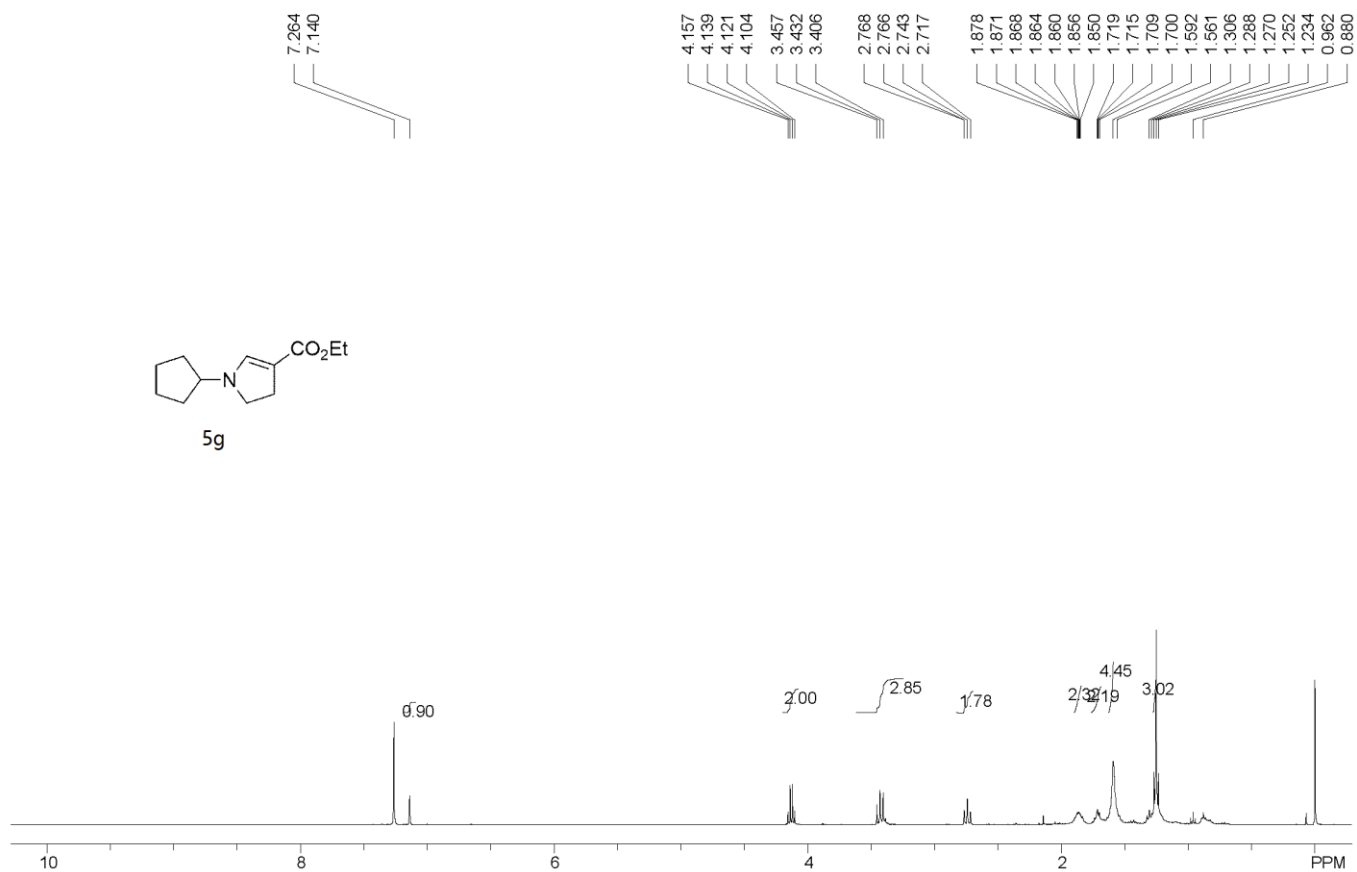
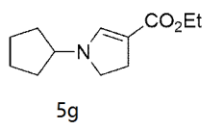


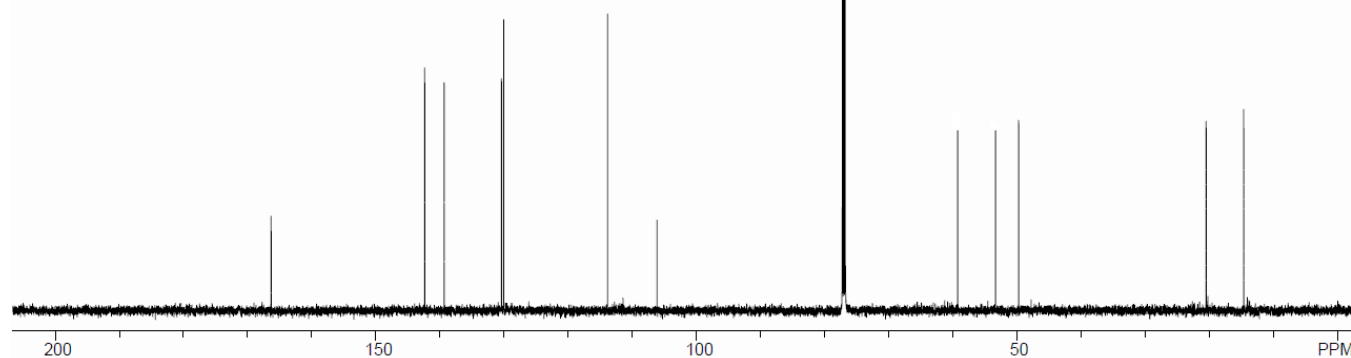
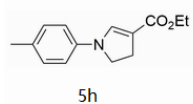
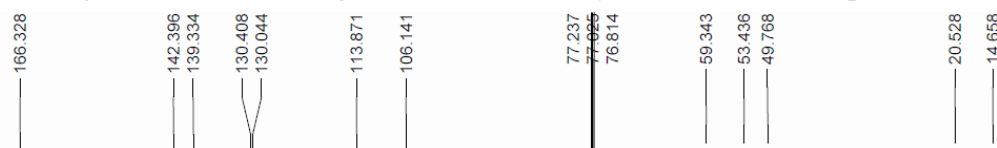
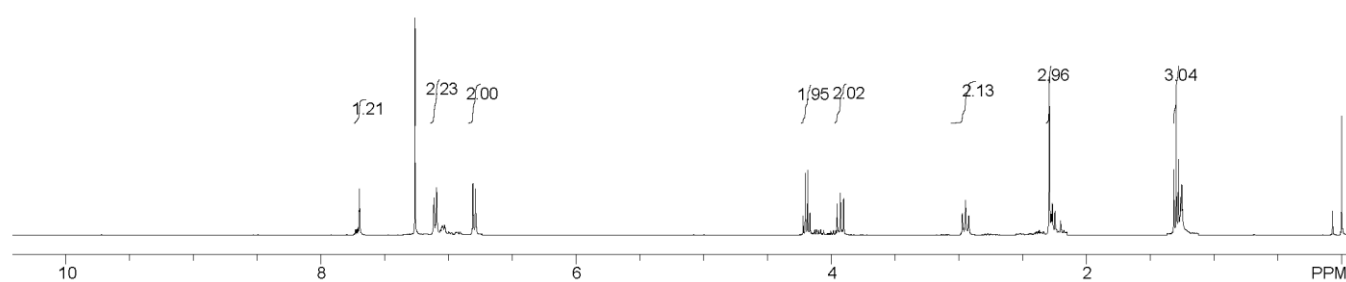
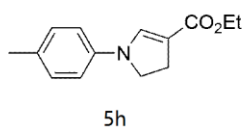
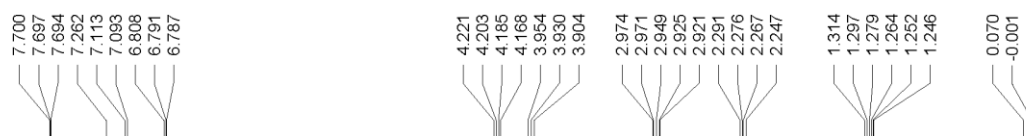


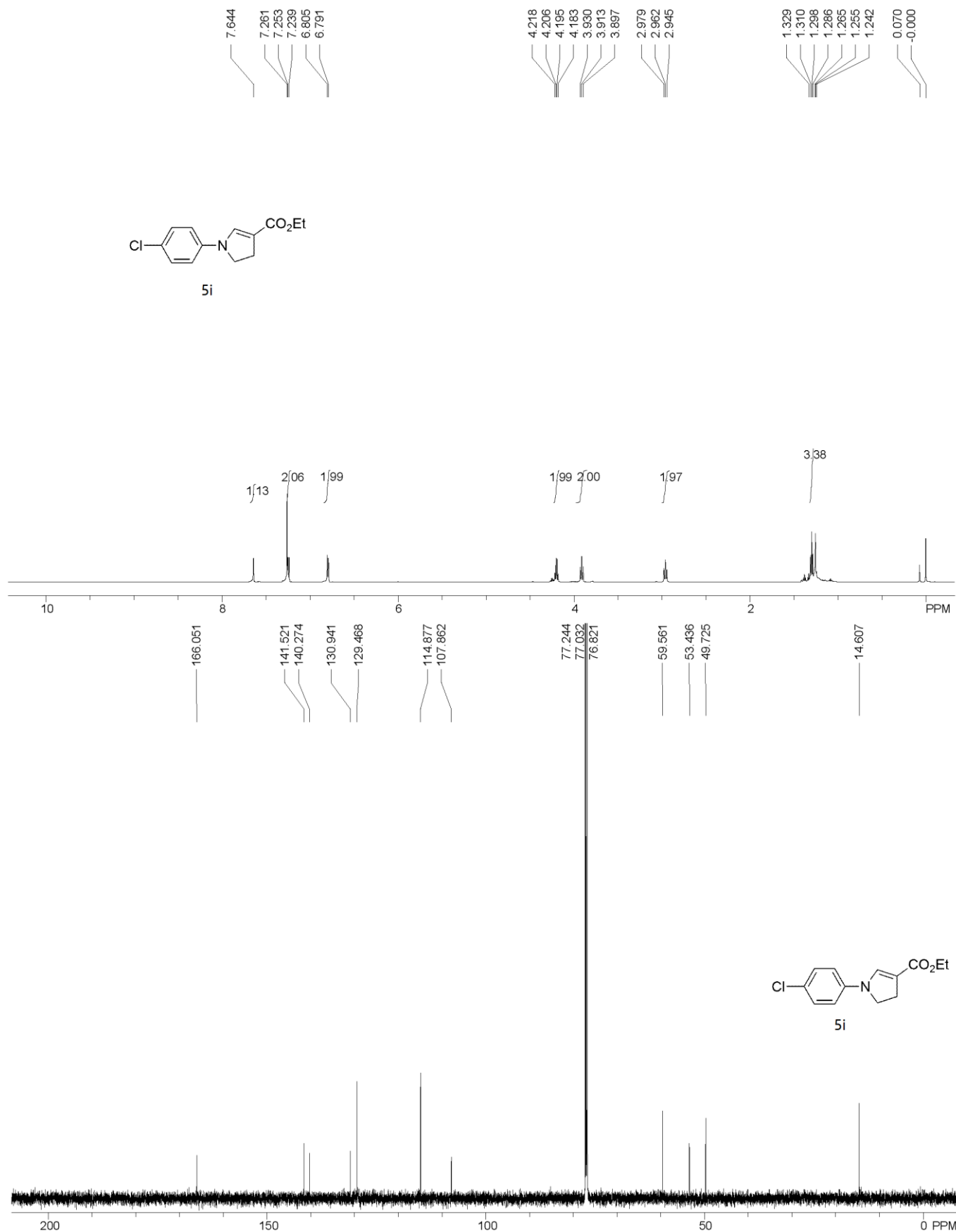
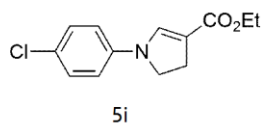


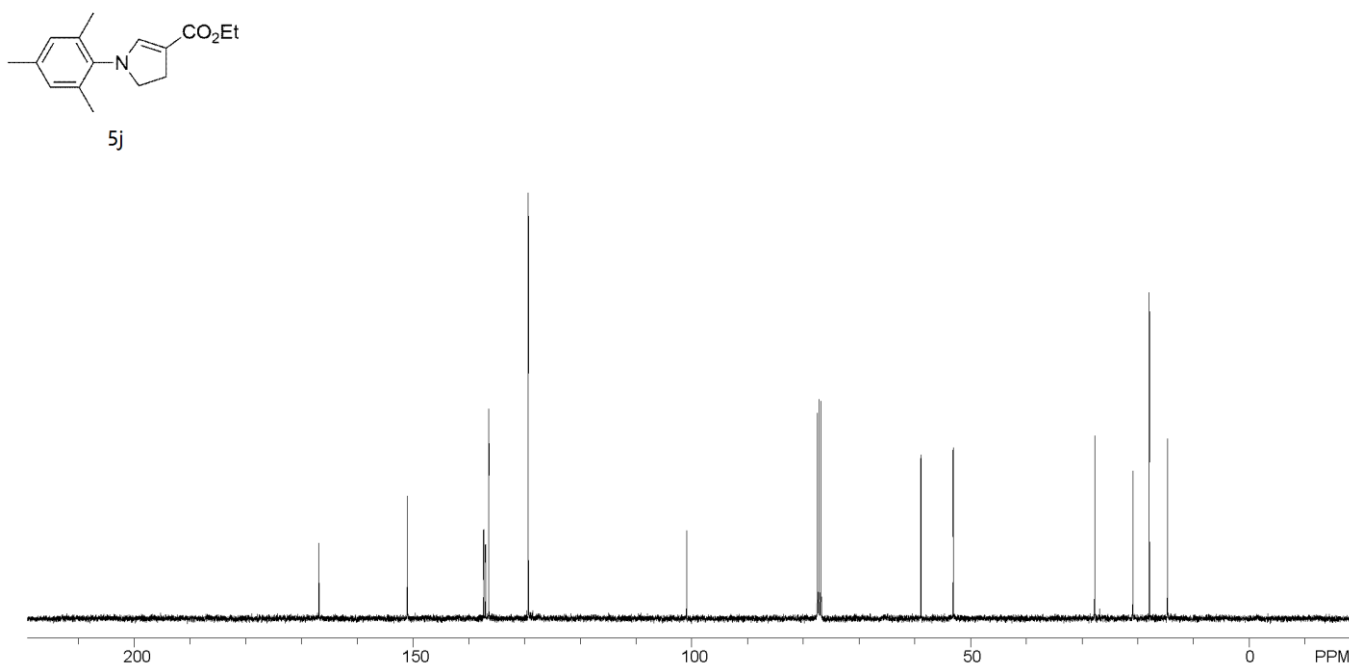
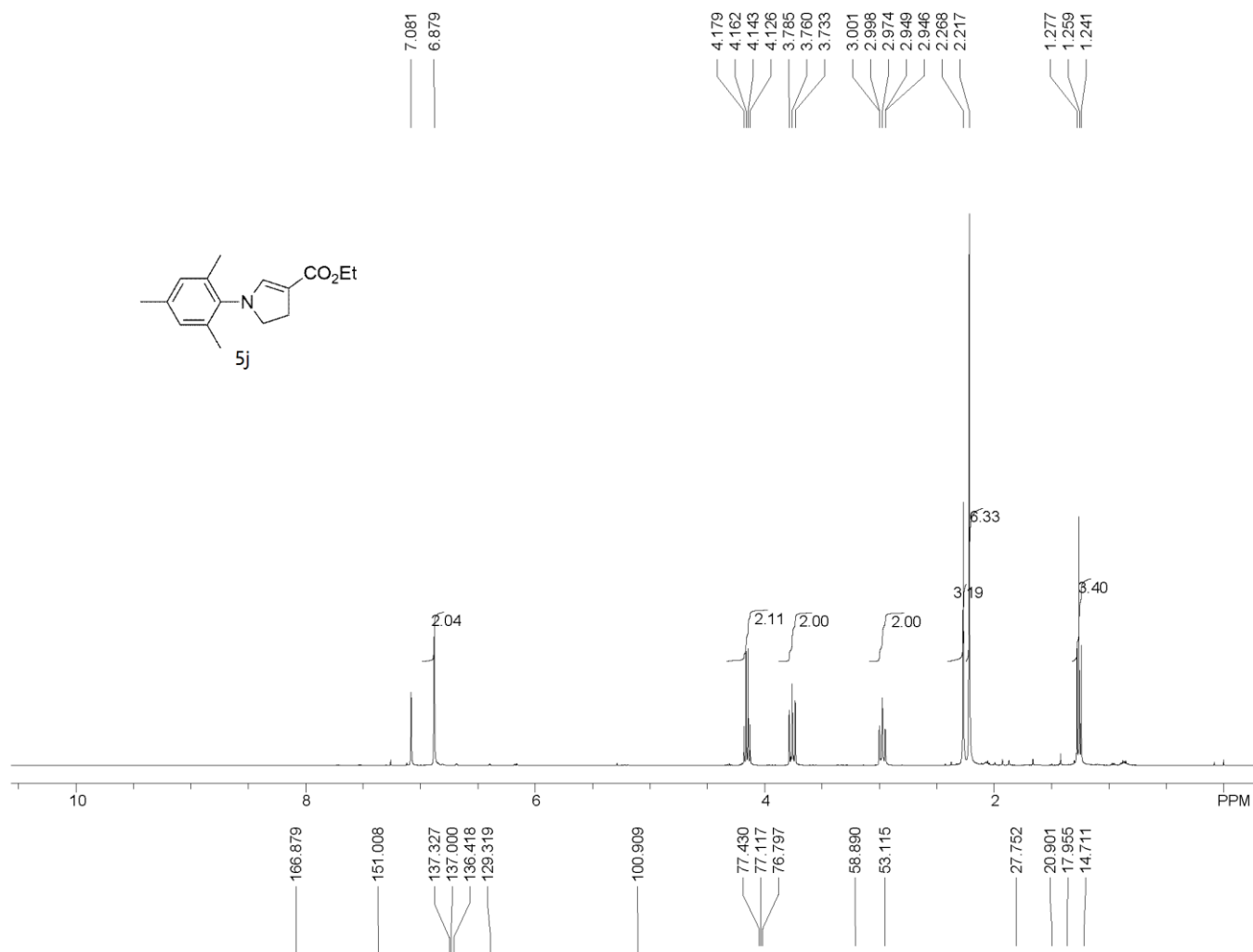


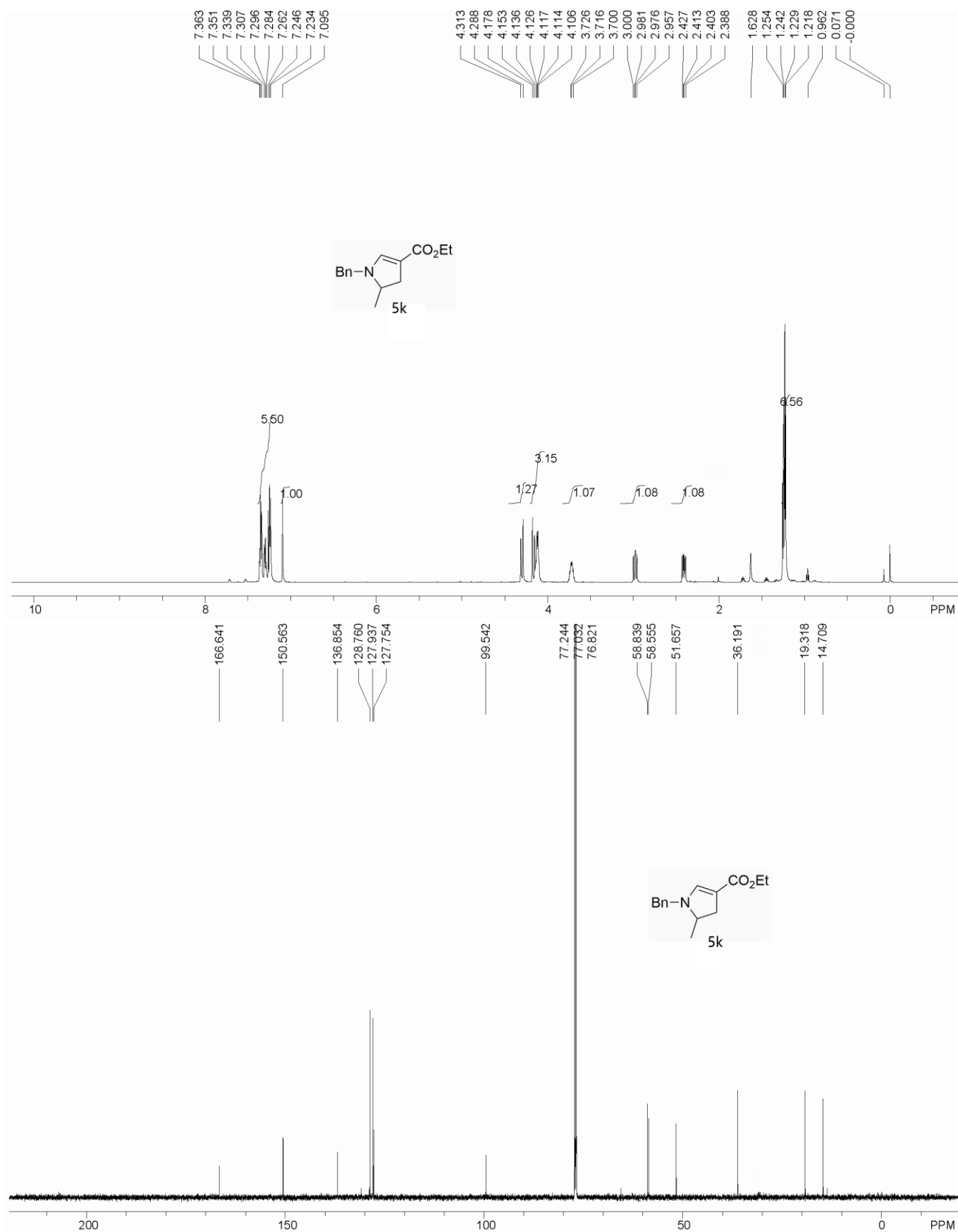


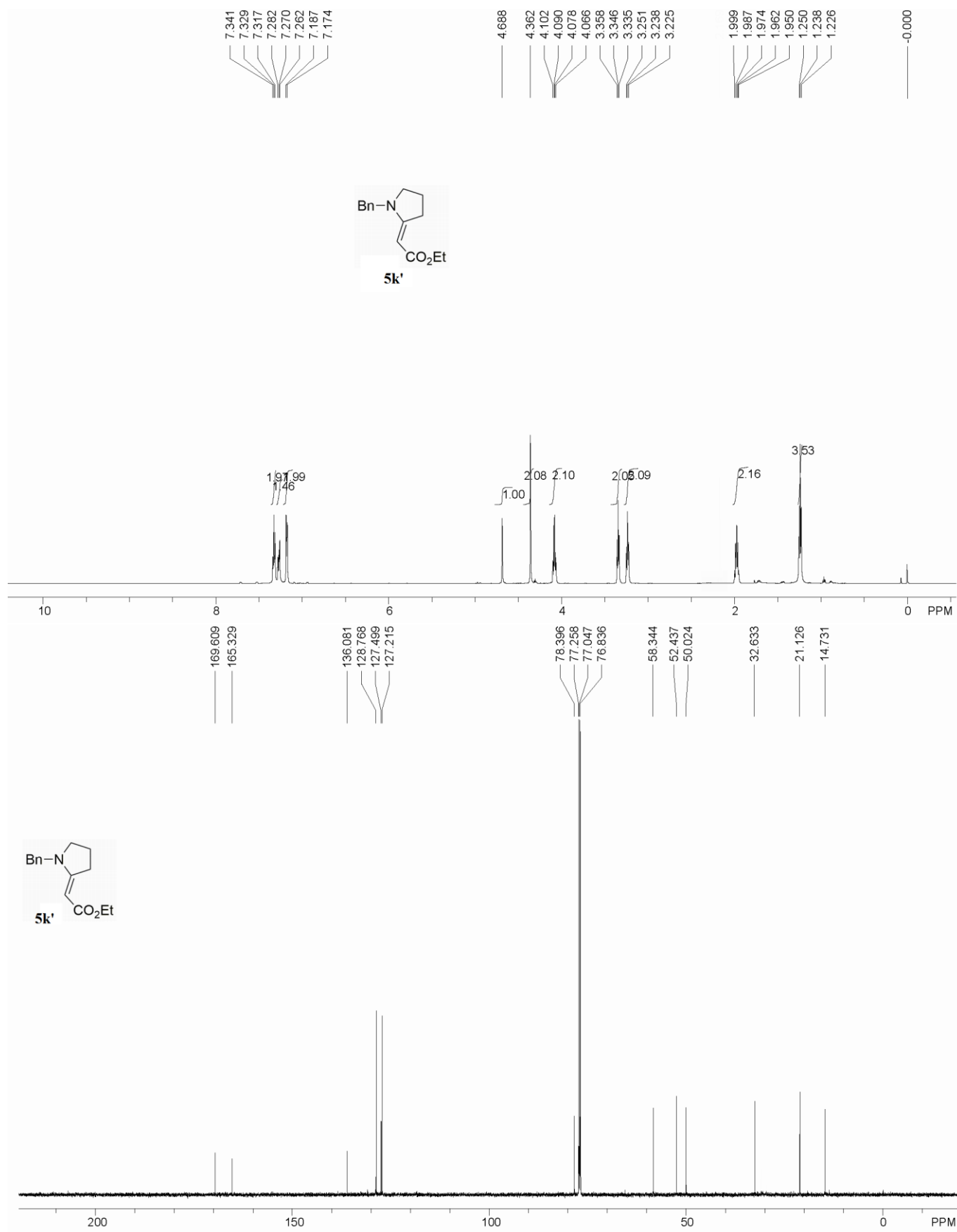


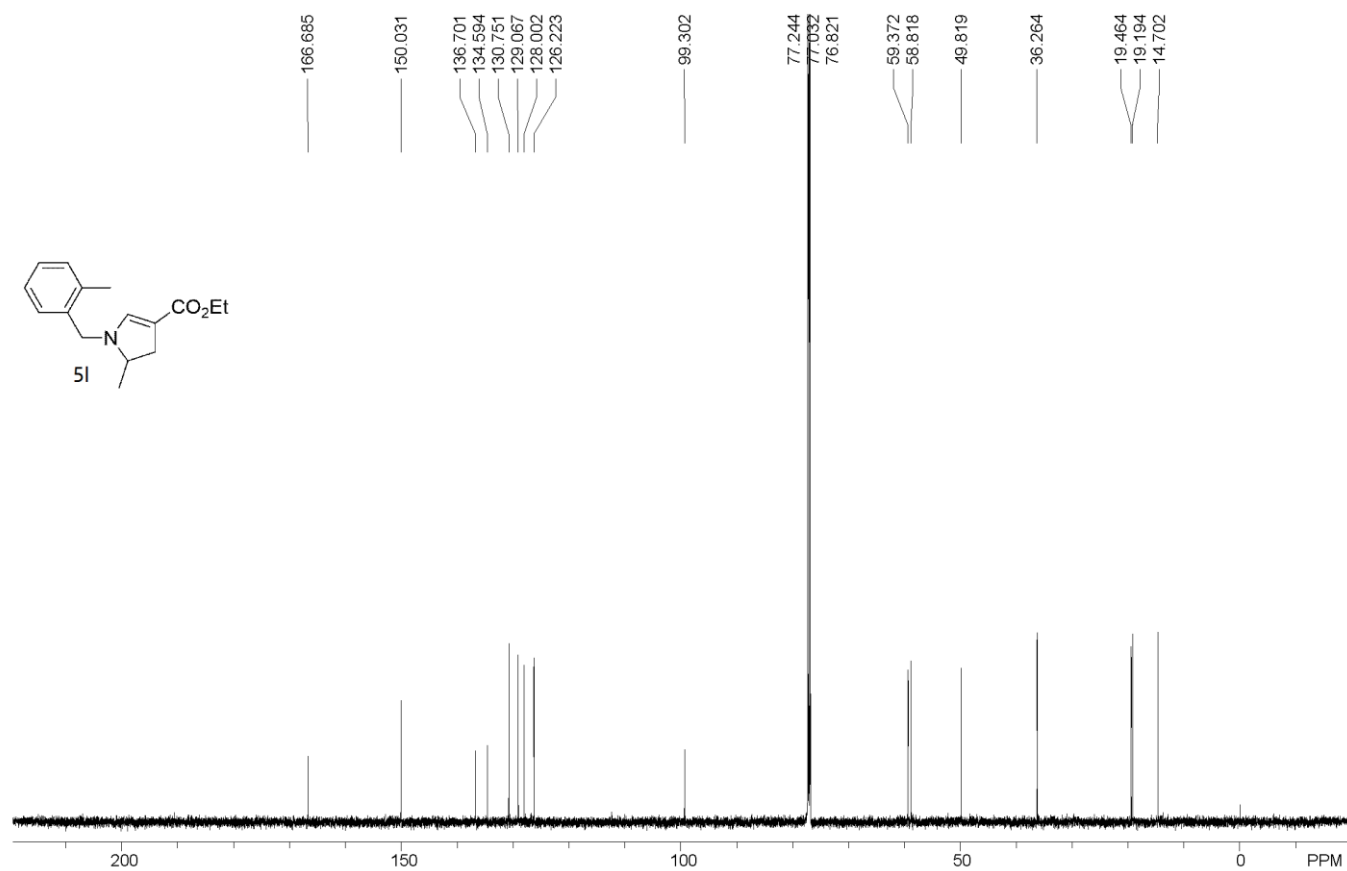
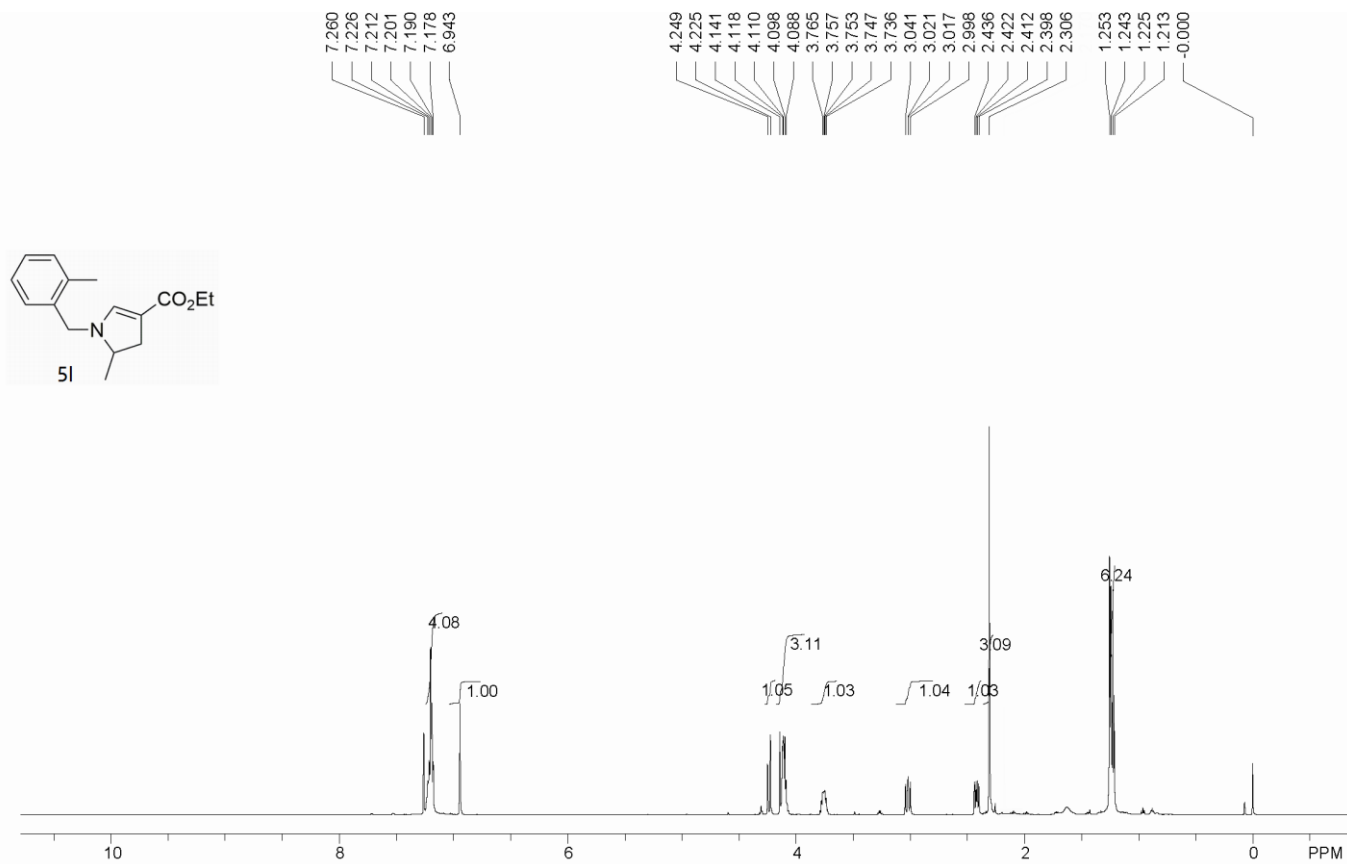


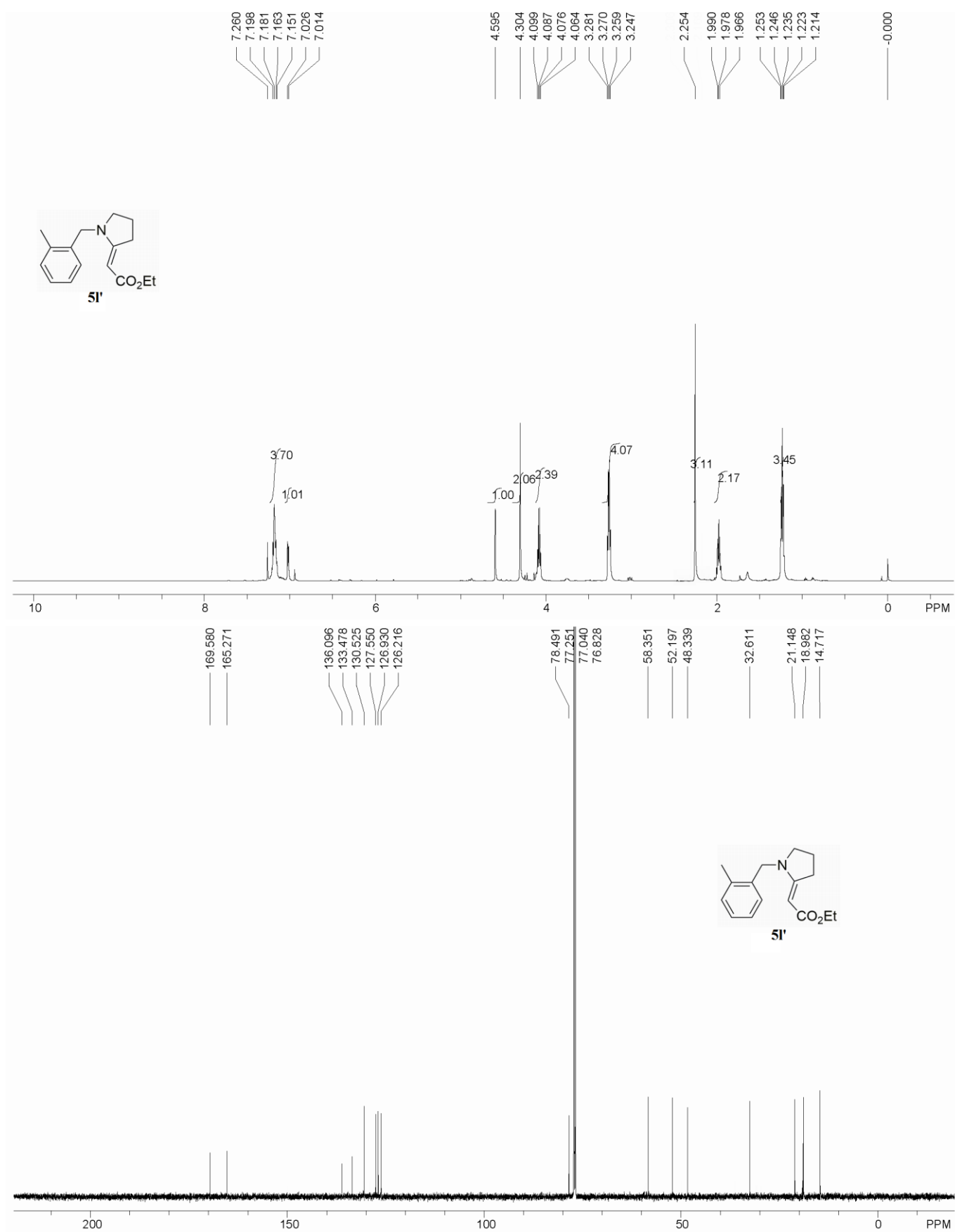




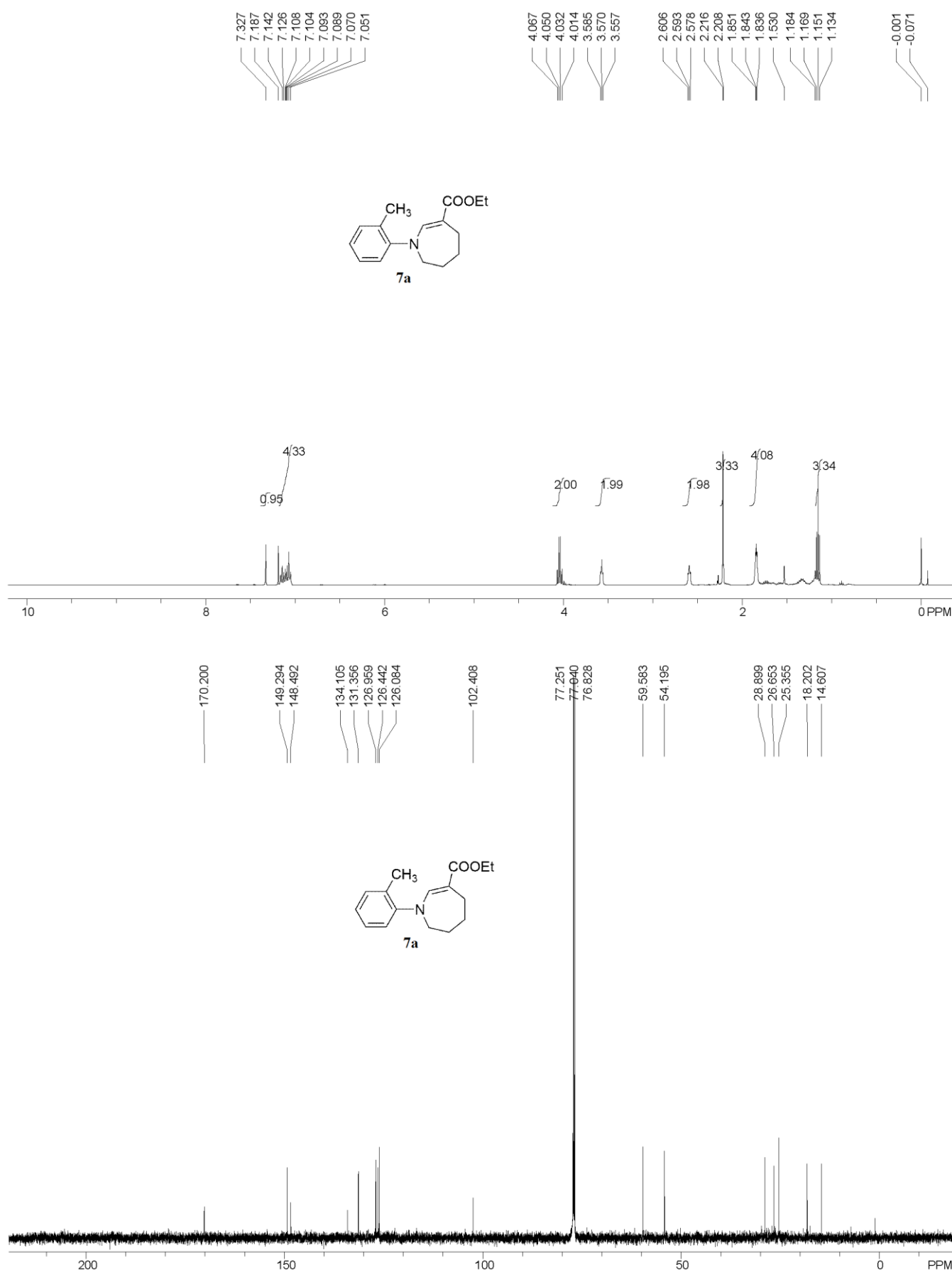


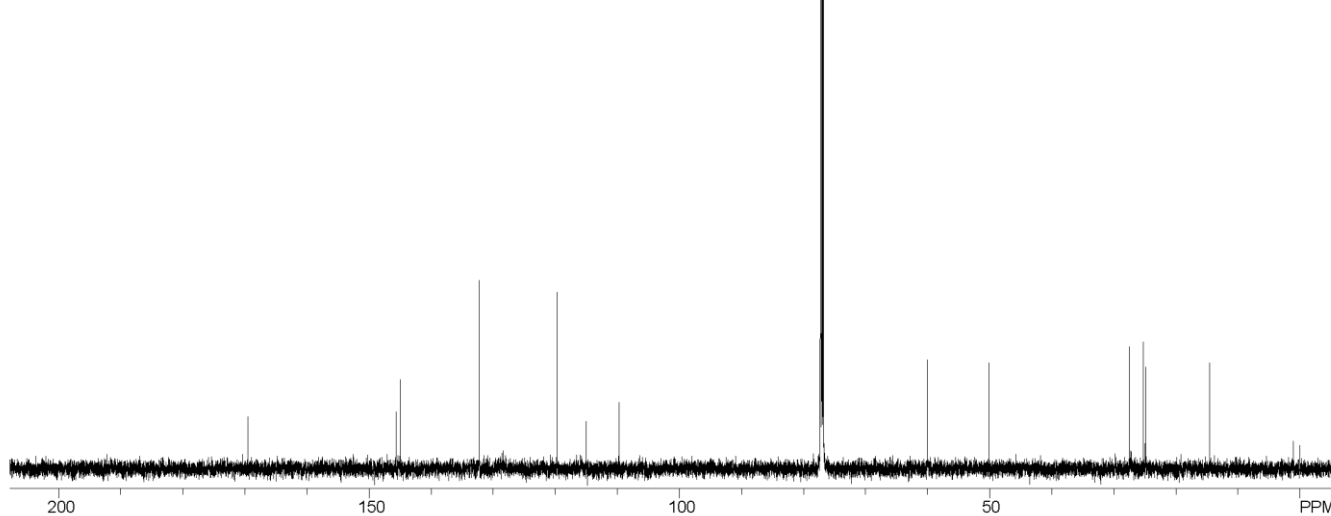
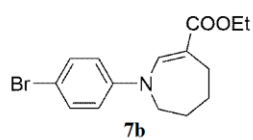
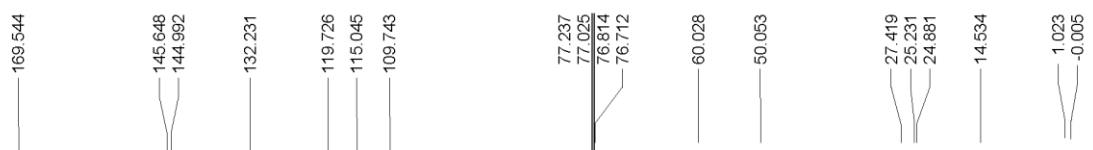
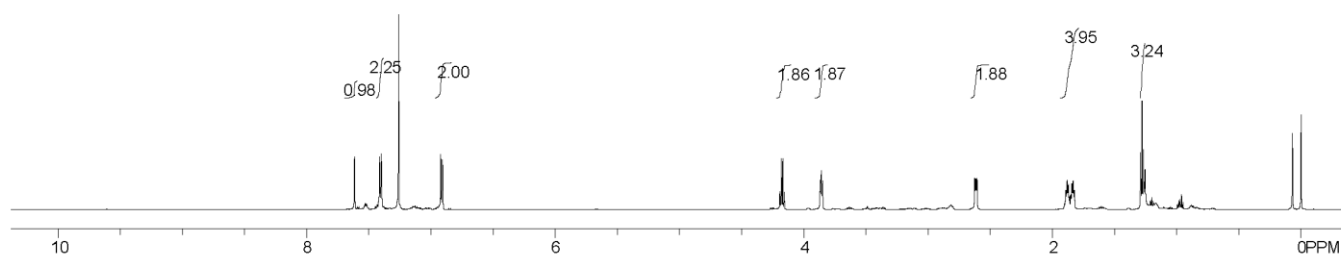
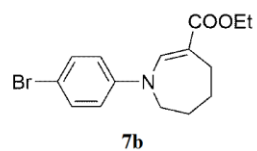
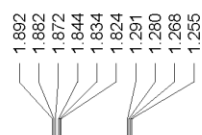
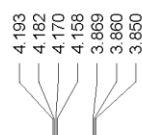
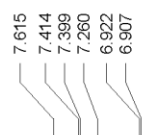




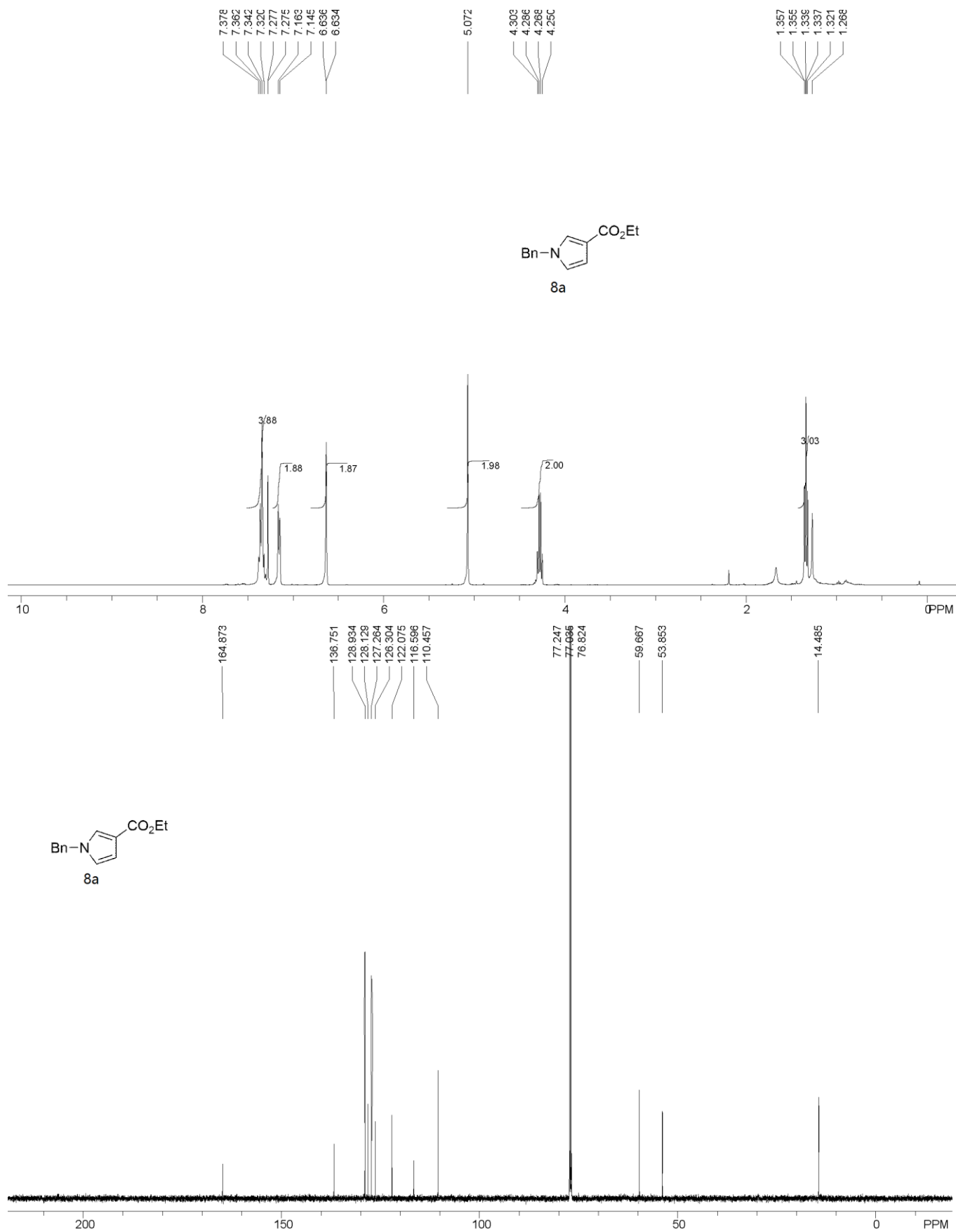


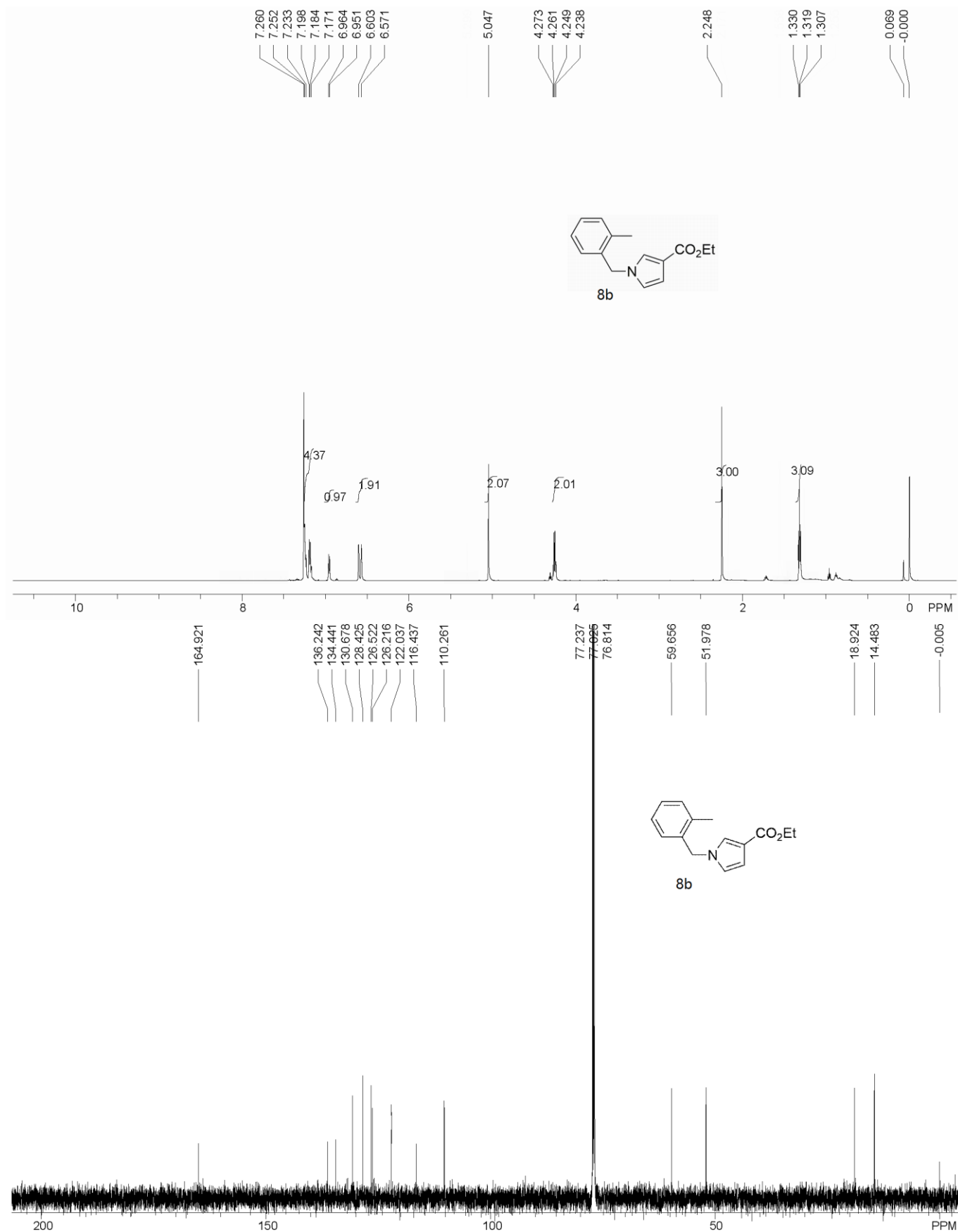
V. Copies of ^1H and ^{13}C NMR Spectra of 7a and 7b

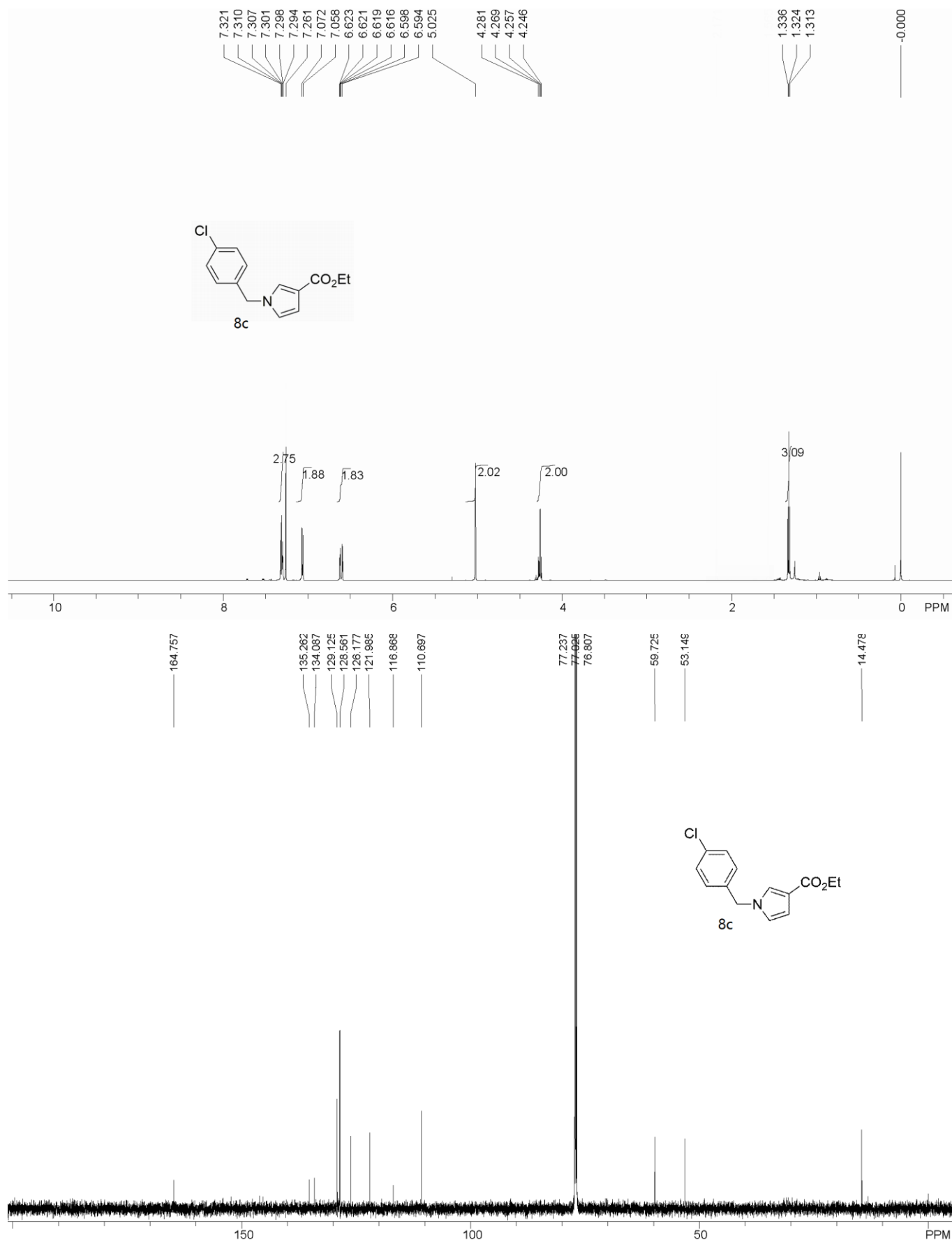


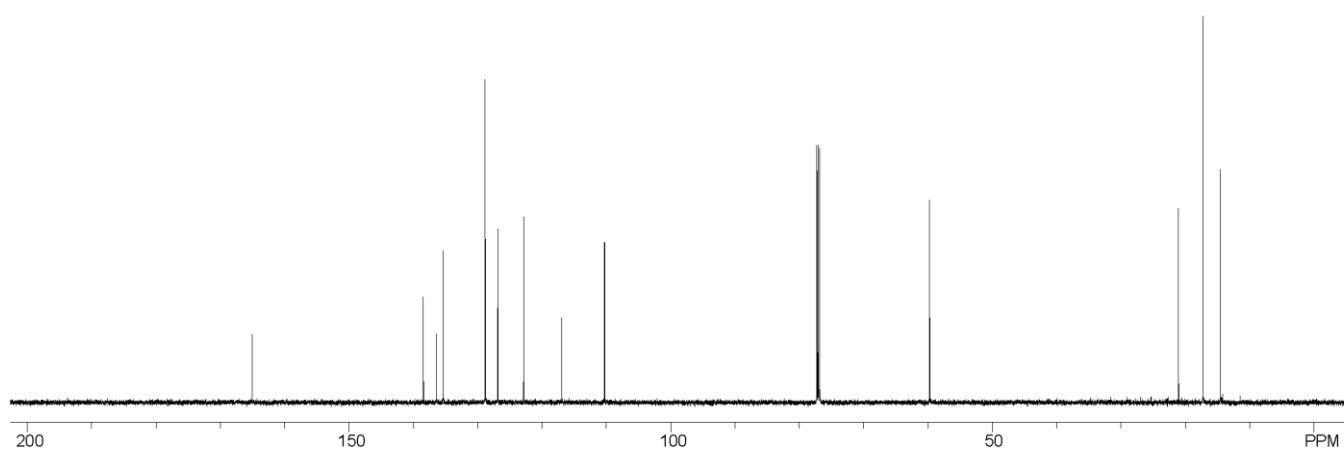
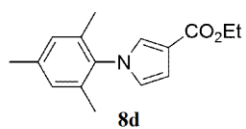
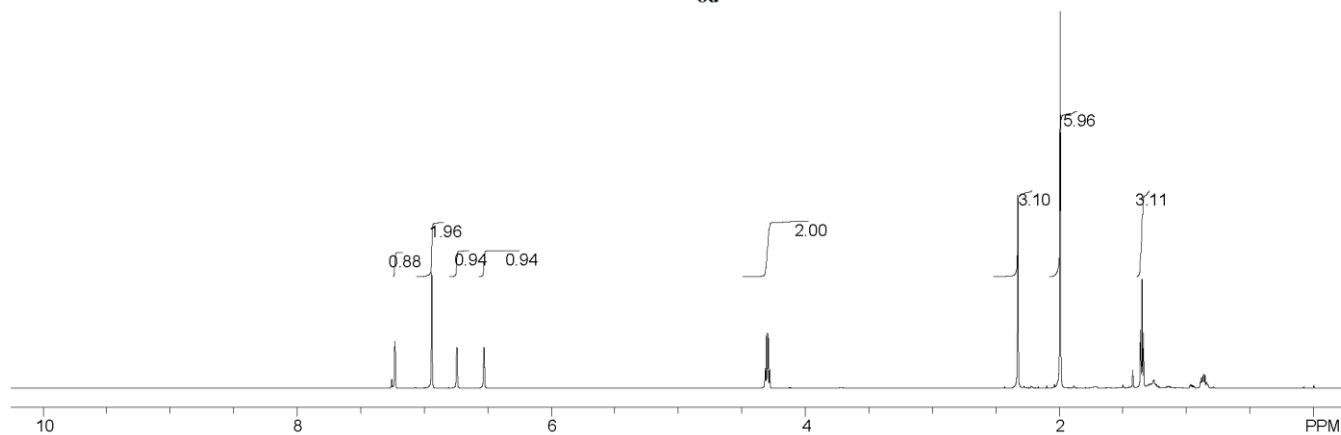
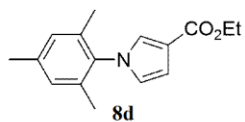
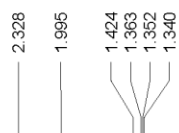
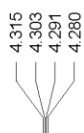
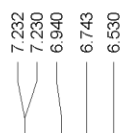


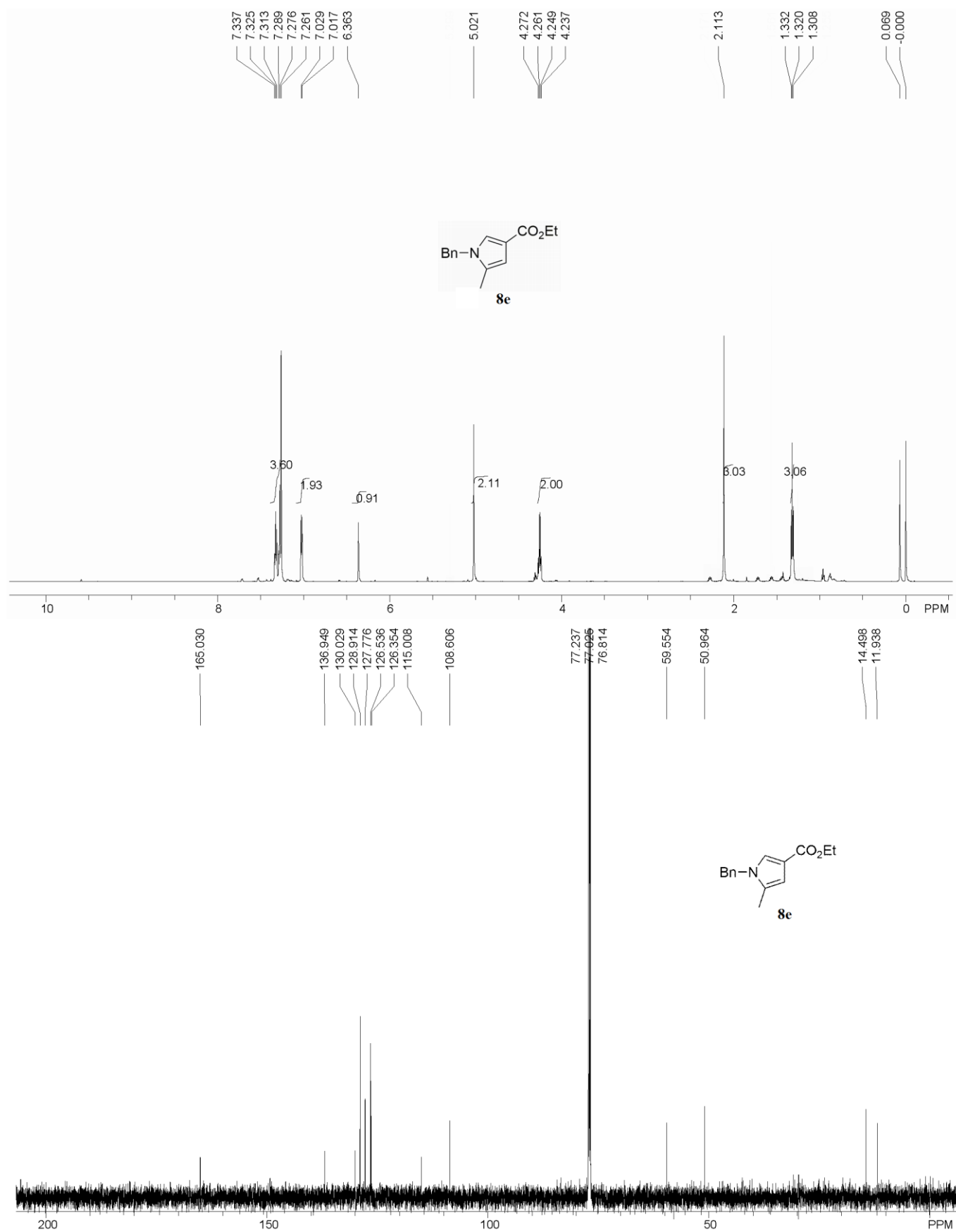
VI. Copies of ^1H and ^{13}C NMR Spectra of 8a-8f

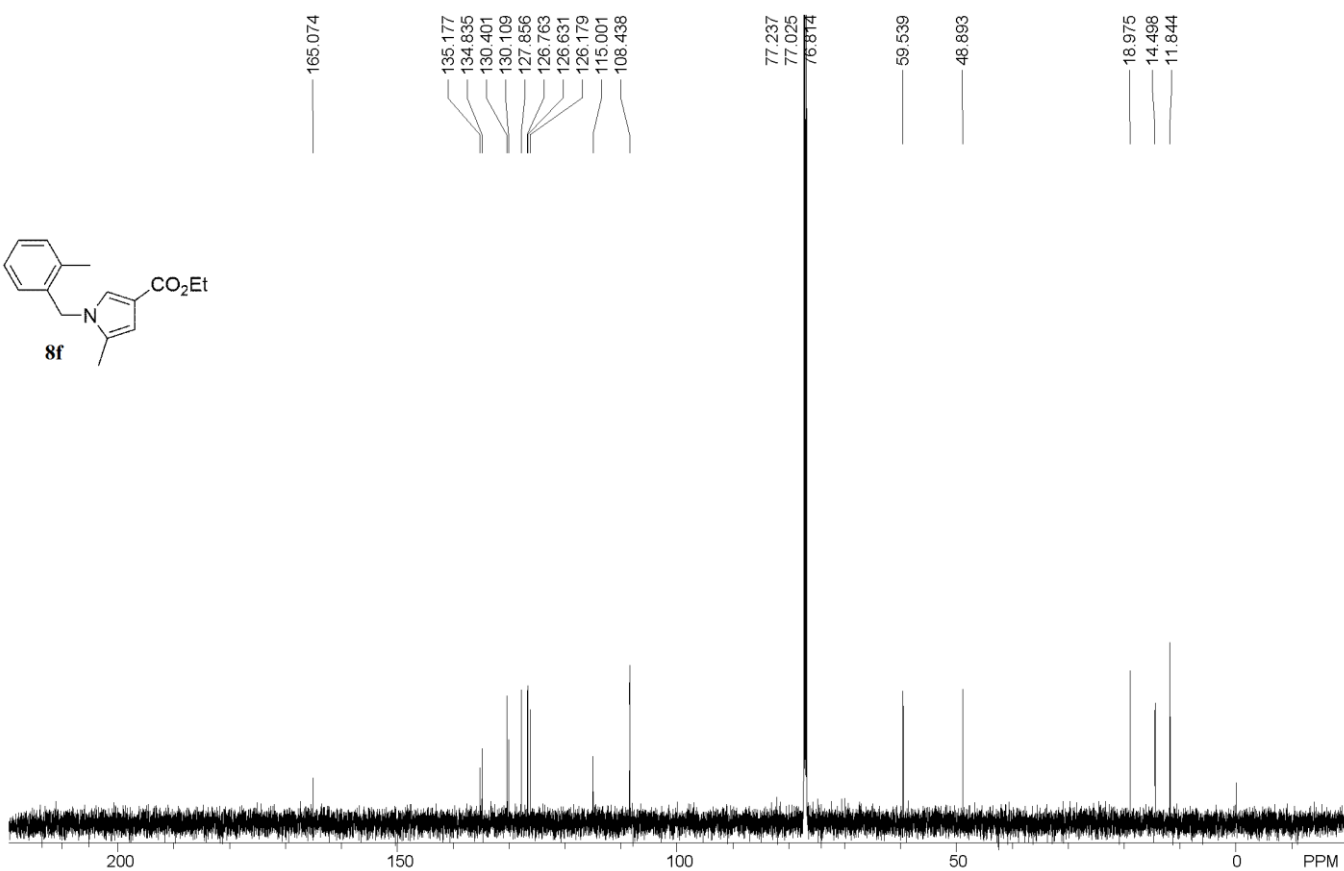
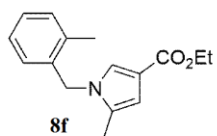
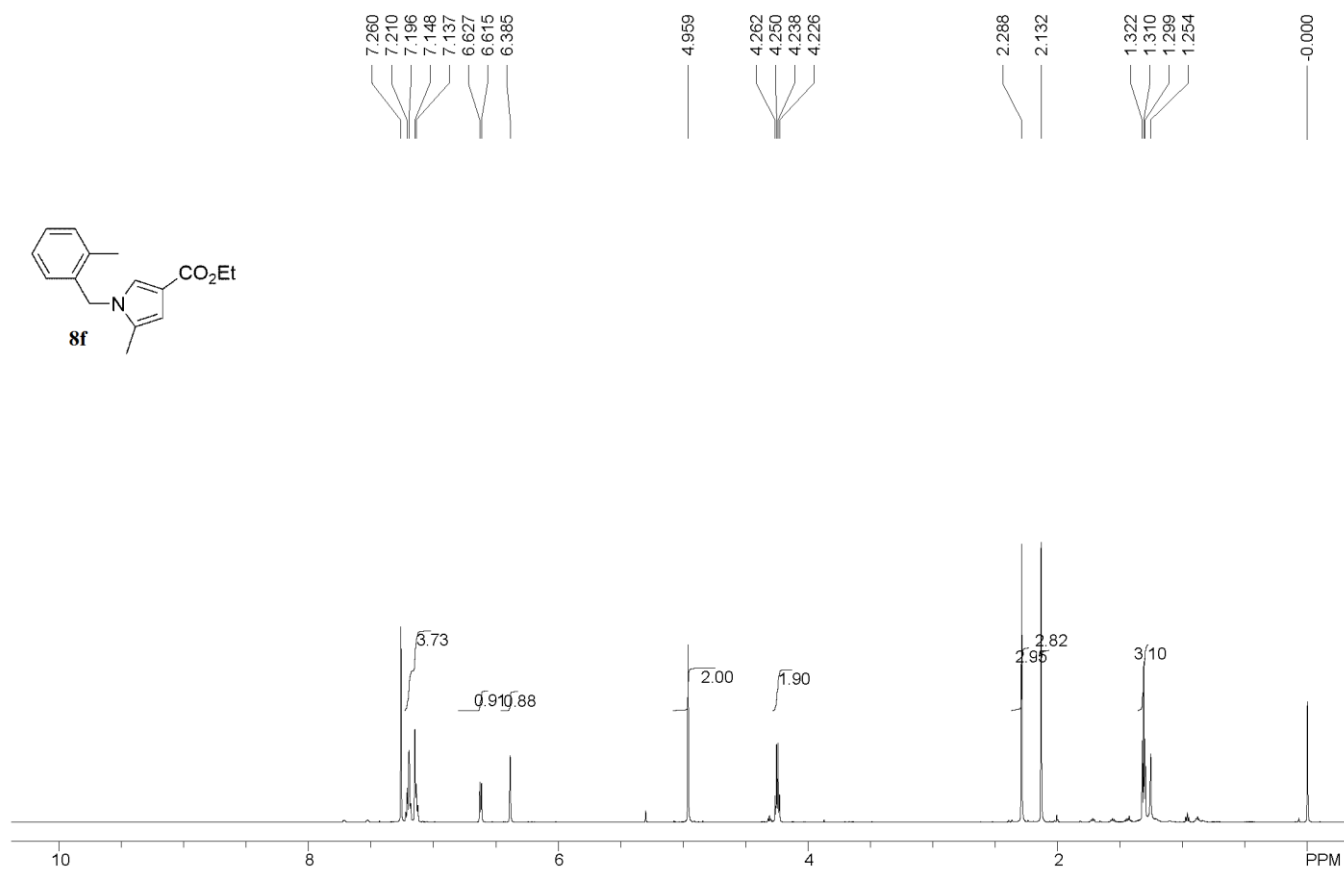
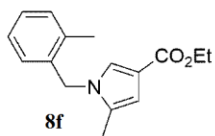




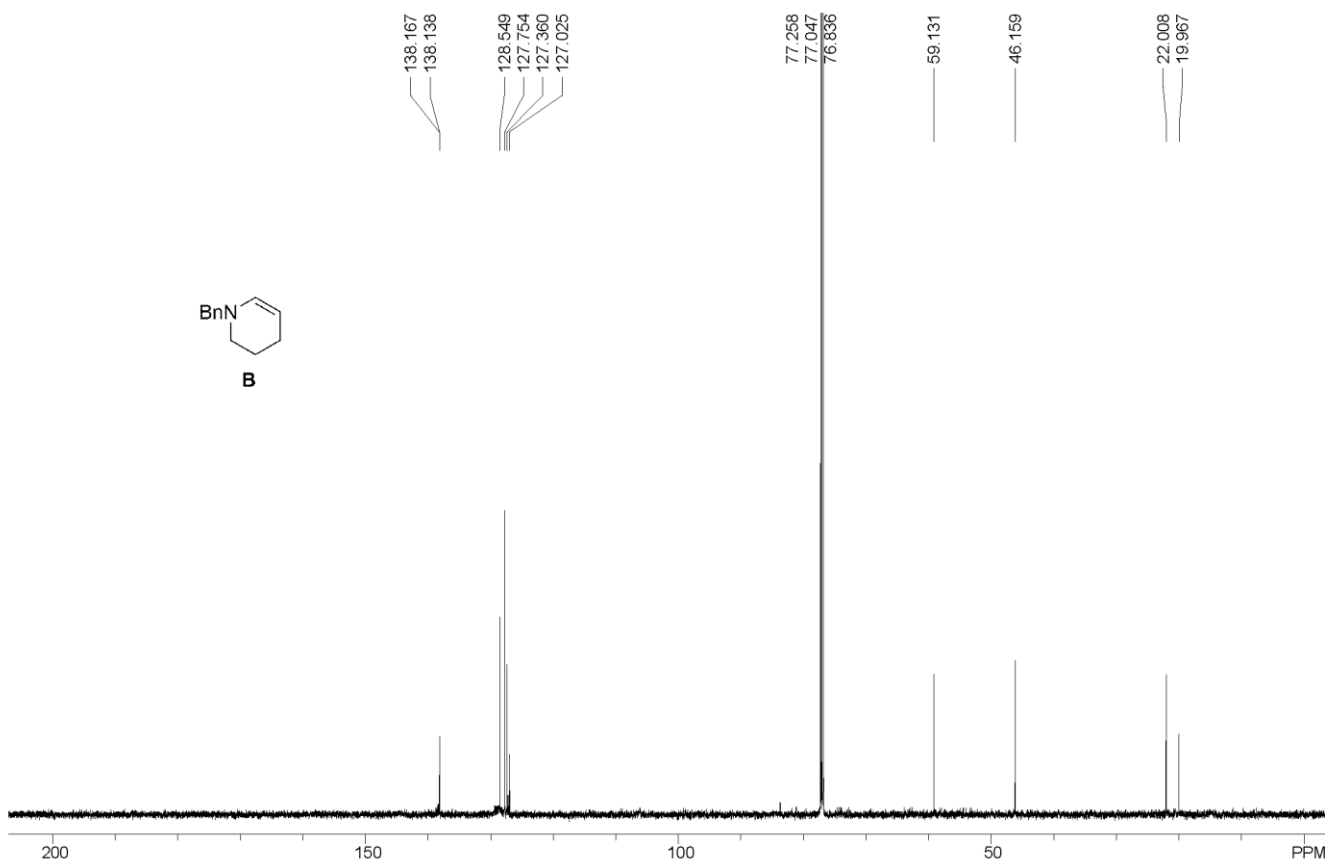
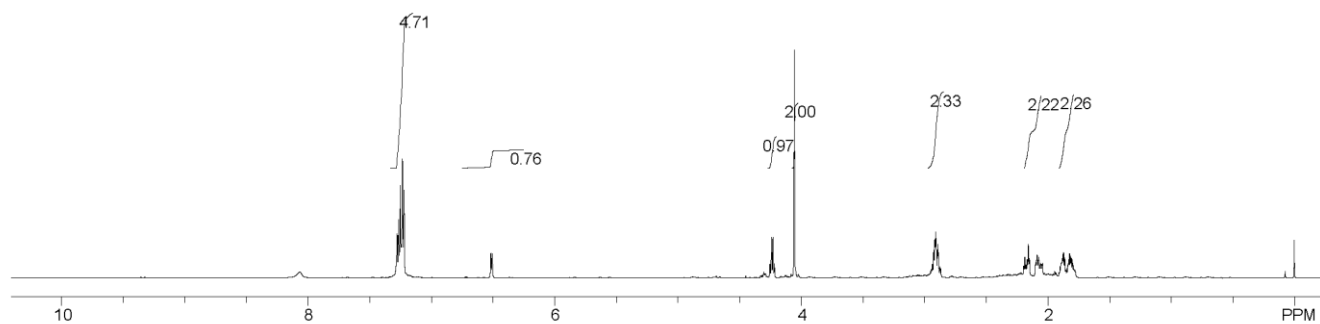
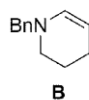
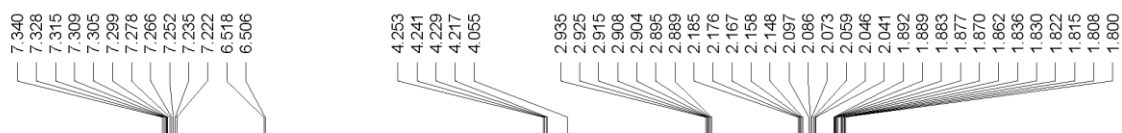








VII. Copies of ^1H and ^{13}C NMR Spectra of B



VIII. References

- (1) N. Takasu, K. Oisaki and M. Kanai, *Org. Lett.*, 2013, **15**, 1918.
- (2) P.-Q. Huang, W. Ou, K.-J. Xiao and A.-E. Wang, *Chem. Commun.*, 2014, **50**, 8761.
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