Supporting Information

A One-pot, Metal-free Approach to Bicyclic 2-Pyridones

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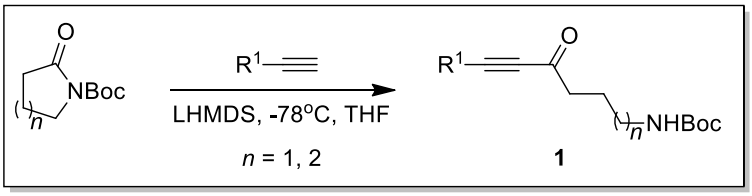
1. General information

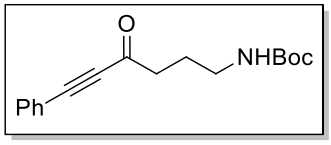
Unless otherwise noted, all commercial reagents were used without further purification. Anhydrous solvents and reagents were purified and dried according to the standard procedures. Column chromatography was carried out using silica gel. Thin layer chromatography (TLC) was carried out on glass plates precoated with 0.25 mm silica gel 60 F_{254}. Flash chromatography column were performed on 230-400 mesh silica gel. ^{1}H NMR spectra were recorded on a 300 MHz NMR instrument. Chemical shifts (δ values) for ^{1}H nuclear magnetic resonance (NMR) spectra were reported in parts per million (ppm) downfield from tetramethylsilane (δ = 0.00 ppm) as internal reference and coupling constants (*J* values) in Hz. Multiplicity was indicated using the following abbreviations: singlet (s), doublet (d), triplet (t), quartet (q), pentet (pent), multiplet (m), broad (br). ^{13}C Spectra were recorded on a 75 MHz NMR spectrometer with $CDCl_3$ (δ = 77.00 ppm) as internal reference and complete proton decoupling. Infrared (IR) spectra were obtained using Universal Attenuated Total Reflectance (UATR) technique and reported in wavenumbers (cm^{-1}). High resolution mass spectrometry (HRMS) was performed using time-of-flight (TOF). Optical rotations were recorded on a Jasco P-1020 polarimeter. Melting points (mp) were determined and reported without correction. HPLC analysis was performed on a chiral column at 254 nm.

2. General procedure for the preparation of internal ynones 1



Lithium hexamethyldisilazane (LHMDS, 1 M in THF, 1.5 equiv) was added dropwise to a solution of alkynes (1.2 equiv) in THF (5 mL) at -78°C and further stirred for 45 min. Then, the solution of lactam (3 mmol, 1.0 equiv) in THF (10 mL) was added dropwise and the mixture was stirred for an additional 4 h. The reaction was quenched with saturated NH_4Cl solution, gradually warmed up to room temperature and extracted with EtOAc. The combined organic part was washed with water, dried over Na_2SO_4, and the solvent was concentrated under reduced pressure. Crude products were purified by column chromatography on silica gel using hexanes and an increasing proportion of EtOAc as eluents to afford compounds **1**.

***tert*-Butyl 4-oxo-6-phenylhex-5-ynylcarbamate (1a)**[1)]



81% yield, white solid, m.p. 69.5–70.5°C

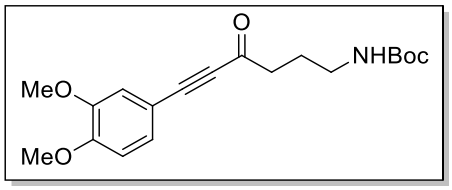
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.35 (m, 5H), 4.64 (br s, 1H), 3.20 (br q, *J* = 6.5 Hz, 2H), 2.74 (t, *J* =7.2 Hz, 2H), 1.92 (pent, *J* = 7.0 Hz, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.12, 155.93, 132.96, 130.67, 128.54, 119.75, 90.96, 87.62, 79.15, 42.64, 39.71, 28.29, 24.33

IR (UATR) ν_{max} 3361, 2976, 2201, 1669, 1513, 1365, 1249, 1166, 1052, 758, 689 cm^{-1}

HRMS (ESI^+) calcd for $C_{17}H_{21}N_1Na_1O_3$ $(M+Na)^+$ 310.1414, found 310.1416.

***tert*-Butyl 6-(3,4-dimethoxyphenyl)-4-oxohex-5-ynylcarbamate (1b)**



75% yield, white solid, m.p. 80.1–80.5°C

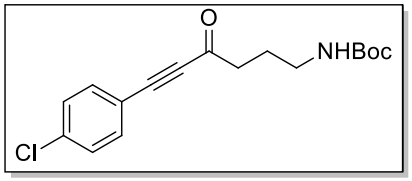
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.06 (d, *J* = 1.3 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 4.65 (br s, 1H), 3.92 (s, 3H), 3.90 (s, 3H), 3.20 (br q, *J* = 6.4 Hz, 2H), 2.73 (t, *J* =7.2 Hz, 2H), 1.92 (pent, *J* = 7.0 Hz, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.79, 155.73, 151.30, 148.43, 127.14, 115.03, 111.23, 110.76, 91.83, 87.04, 78.67, 55.59, 55.57, 42.23, 39.46, 28.02, 24.13

IR (UATR) ν_{max} 3391, 2974, 2186, 1709, 1663, 1596, 1513, 1249, 1170, 1023, 855, 810, 763 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{25}N_1Na_1O_5$ $(M+Na)^+$ 370.1625, found 370.1623.

***tert*-Butyl 6-(4-chlorophenyl)-4-oxohex-5-ynylcarbamate (1c)**



79% yield, white solid, m.p. 104.3–105°C

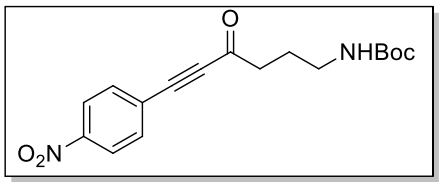
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.6 Hz, 2H), 7.36 (d, *J* = 8.6 Hz, 2H), 4.75 (br s, 1H), 3.19 (br q, *J* = 6.5 Hz, 2H), 2.73 (t, *J* = 7.2 Hz, 2H), 1.91 (pent, *J* = 7.0 Hz, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.85, 155.91, 137.05, 134.13, 129.00, 118.24, 89.41, 88.28, 79.17, 42.60, 39.70, 28.29, 24.30

IR (UATR) ν_{max} 3316, 2977, 2202, 1684, 1669, 1533, 1365, 1289, 1167, 1088, 822, 758 cm^{-1}

HRMS (ESI^+) calcd for $C_{17}H_{20}Cl_1N_1Na_1O_3$ $(M+Na)^+$ 344.1024, found 344.1022.

***tert*-Butyl 6-(4-nitrophenyl)-4-oxohex-5-ynylcarbamate (1d)**



73% yield, yellow solid, m.p. 120.1–121.0°C

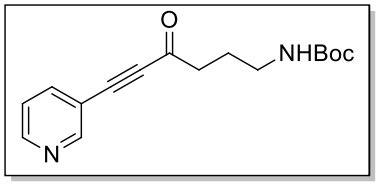
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.9 Hz, 2H), 7.73 (d, *J* = 8.9 Hz, 2H), 4.62 (br s, 1H), 3.20 (br q, *J* = 6.5 Hz, 2H), 2.77 (t, *J* =7.2 Hz, 2H), 1.93 (pent, *J* = 7.0 Hz, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.48, 155.94, 148.37, 133.56, 126.45, 123.65, 90.41, 86.94, 79.21, 42.65, 39.60, 28.27, 24.17

IR (UATR) ν_{max} 3306, 2973, 2207, 1681, 1674, 1521, 1348, 1286, 1172, 1036, 857, 750, 685 cm^{-1}

HRMS (ESI^+) calcd for $C_{17}H_{20}N_2Na_1O_5$ $(M+Na)^+$ 355.1264, found 355.1264.

***tert*-Butyl 4-oxo-6-(pyridin-3-yl)hex-5-ynylcarbamate (1e)**



71% yield, brown solid, m.p. 79.3–80.0°C

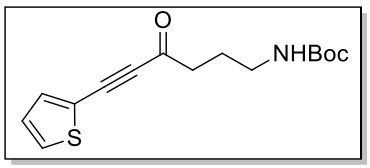
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.79 (d, *J* = 1.4 Hz, 1H), 8.66 (dd, *J* = 4.9, 1.5 Hz, 1H), 7.86 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.34 (ddd, *J* = 7.9, 4.9, 0.7 Hz, 1H), 4.71 (br s, 1H), 3.20 (br q, *J* = 6.5 Hz, 2H), 2.76 (t, *J* =7.2 Hz, 2H), 1.92 (pent, *J* = 7.0 Hz, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.65, 155.95, 153.24, 150.71, 139.82, 123.20, 117.21, 90.11, 86.79, 79.28, 42.66, 39.69, 28.33, 24.27

IR (UATR) ν_{max} 3347, 2976, 2206, 1694, 1674, 1516, 1366, 1250, 1167, 808, 703 cm^{-1}

HRMS (ESI^+) calcd for $C_{16}H_{20}N_2Na_1O_3$ $(M+Na)^+$ 311.1366, found 311.1375.

***tert*-Butyl 4-oxo-6-(thiophen-2-yl)hex-5-ynylcarbamate (1f)**



76% yield, white solid, m.p. 77.1–77.4°C

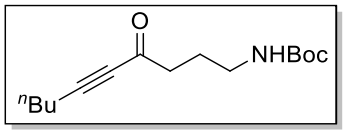
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 3.0, 1.0 Hz, 1H), 7.34 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.22 (dd, *J* = 5.0, 1.0 Hz, 1H), 4.66 (br s, 1H), 3.19 (br q, *J* = 6.5 Hz, 2H), 2.72 (t, *J* =7.2 Hz, 2H), 1.91 (pent, *J* = 7.0 Hz, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.99, 155.87, 133.81, 130.09, 126.11, 119.00, 87.85, 86.27, 79.06, 42.47, 39.68, 28.27, 24.31

IR (UATR) ν_{max} 3372, 2977, 2195, 1699, 1667, 1516, 1365, 1250, 1169, 787 cm^{-1}

HRMS (ESI^+) calcd for $C_{15}H_{19}N_1Na_1O_3S_1$ $(M+Na)^+$ 316.0978, found 316.0989.

tert-Butyl 4-oxodec-5-ynylcarbamate (1g)



71% yield, colorless oil

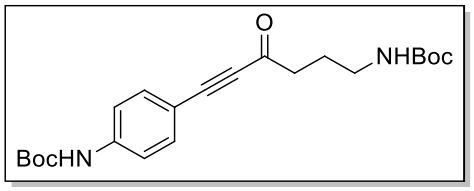
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.63 (br s, 1H), 3.14 (br q, *J* = 6.2 Hz, 2H), 2.59 (t, *J* = 7.2 Hz, 2H), 2.37 (t, *J* = 7.0 Hz, 2H), 1.83 (pent, *J* = 7.0 Hz, 2H), 1.55 (sext, *J* = 7.2 Hz, 2H), 1.50–1.36 (m, 2H), 1.44 (s, 9H), 0.93 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.28, 155.82, 94.55, 80.55, 78.87, 42.53, 39.54, 29.46, 28.16, 24.14, 21.72, 18.39, 13.26

IR (UATR) ν_{max} 3368, 2934, 2211, 1702, 1677, 1509, 1367, 1250, 1166 cm^{-1}

HRMS (ESI^+) calcd for $C_{15}H_{25}N_1Na_1O_3$ $(M+Na)^+$ 290.1727, found 290.1719.

tert-Butyl 4-oxo-6-{4-(_N_-_tert_-butoxycarbonyl)aminophenyl}hex-5-ynylcarbamate (1h)



74% yield, white solid, m.p. 139.3–140.0°C

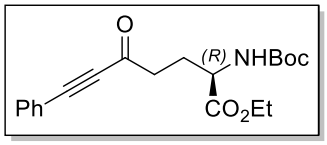
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.8 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 6.61 (br s, 1H), 4.61 (br s, 1H), 3.19 (br q, *J* = 6.7 Hz, 2H), 2.71 (t, *J* = 7.2 Hz, 2H), 1.91 (pent, *J* = 7.0 Hz, 2H), 1.53 (s, 9H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.16, 155.98, 152.28, 141.22, 134.18, 117.94, 113.11, 92.10, 87.57, 80.93, 79.11, 42.47, 39.68, 28.26, 28.12, 24.34,

IR (UATR) ν_{max} 3336, 2978, 2194, 1692, 1520, 1587, 1233, 1155, 1050, 840, 774 cm^{-1}

HRMS (ESI^+) calcd for $C_{22}H_{30}N_2Na_1O_5$ $(M+Na)^+$ 425.2047, found 425.2060.

(_R_)-Ethyl 2-(tert-butoxycarbonylamino)-5-oxo-7-phenylhept-6-ynoate (1i)



81% yield, yellow solid, m.p. 45.0–46.0°C, $[\alpha]^D_{28}$ +10.8 (*c* 1.1, MeOH)

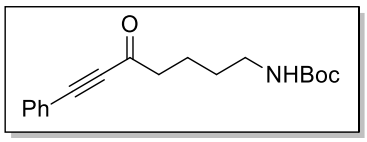
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.55 (m, 2H), 7.50–7.35 (m, 3H), 5.19 (d, *J* = 7.7 H, 1H), 4.38–4.30 (br m, 1H), 4.21 (q, *J* = 7.1 Hz, 2H), 2.91–2.70 (m, 2H), 2.35–2.22 (m, 1H), 2.14–1.98 (m, 1H), 1.45 (s, 9H), 1.29 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.14, 172.04, 155.32, 132.99, 130.74, 128.56, 119.70, 91.24, 87.48, 79.93, 61.52, 52.78, 41.34, 28.20, 26.70, 14.07

IR (UATR) ν_{max} 3365, 2979, 2202, 1742, 1713, 1671, 1490, 1368, 1252, 1160, 1027, 759, 690 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{25}N_1Na_1O_5$ $(M+Na)^+$ 382.1625, found 382.1636.

<u>*tert*-Butyl 5-oxo-7-phenylhept-6-ynylcarbamate (1j)</u>[1)]



78% yield, white solid, m.p. 57.0–57.9°C

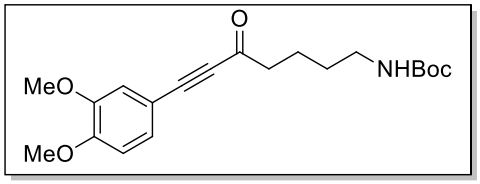
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.32 (m, 5H), 4.78 (br s, 1H), 3.15 (br q, *J* = 6.4 Hz, 2H), 2.70 (t, *J* =7.2 Hz, 2H), 1.82–1.70 (m, 2H), 1.62–1.50 (m, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.38, 155.85, 132.84, 130.55, 128.45, 119.69, 90.62, 87.56, 78.82, 44.76, 39.94, 29.16, 28.22, 20.97

IR (UATR) ν_{max} 3362, 2933, 2202, 1694, 1669, 1510, 1366, 1248, 1169, 1066, 758, 690 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{23}N_1Na_1O_3$ $(M+Na)^+$ 324.1570, found 324.1586.

<u>*tert*-Butyl 7-(3,4-dimethoxyphenyl)-5-oxohept-6-ynylcarbamate (1k)</u>



72% yield, white solid, m.p. 70.3–71.0°C

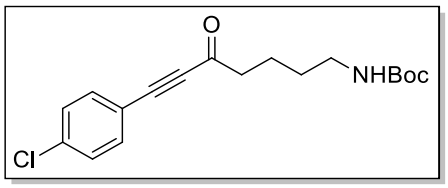
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21 (dd, *J* = 8.4, 1.7 Hz, 1H), 7.05 (d, *J* = 1.7 Hz, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 5.03 (br s, 1H), 3.91 (s, 3H), 3.88 (s, 3H), 3.16 (br q, *J* = 6.3 Hz, 2H), 2.70 (t, *J* =7.2 Hz, 2H), 1.83–1.70 (m, 2H), 1.63–1.52 (m, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.51, 155.95, 151.63, 148.81, 127.45, 115.40, 111.68, 111.04, 91.97, 87.42, 79.11, 55.98, 55.95, 44.77, 40.13, 29.35, 28.37, 21.18

IR (UATR) ν_{max} 3393, 2936, 2186, 1702, 1665, 1514, 1250, 1170, 1023, 856, 763 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{27}N_1Na_1O_5$ $(M+Na)^+$ 384.1781, found 384.1796.

tert-Butyl 7-(4-chlorophenyl)-5-oxohept-6-ynylcarbamate (1l)



71% yield, white solid, m.p. 81.1–82.0°C

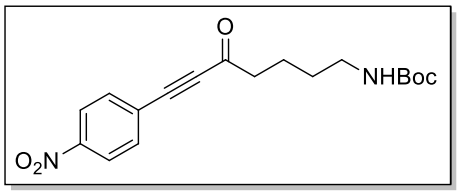
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.7 Hz, 2H), 7.36 (d, *J* = 8.7 Hz, 2H), 4.85 (br s, 1H), 3.16 (br q, *J* = 6.4 Hz, 2H), 2.70 (t, *J* =7.2 Hz, 2H), 1.82–1.70 (m, 2H), 1.62–1.50 (m, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.85, 155.68, 136.59, 133.81, 128.65, 117.95, 88.76, 88.01, 78.42, 44.49, 39.66, 28.92, 28.00, 20.68,

IR (UATR) ν_{max} 3362, 2933, 2202, 1694, 1670, 1489, 1366, 1248, 1167, 1090, 829, 765 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{22}Cl_1N_1Na_1O_3$ $(M+Na)^+$ 358.1180, found 358.1186.

tert-Butyl 7-(4-nitrophenyl)-5-oxohept-6-ynylcarbamate (1m)



69% yield, white solid, m.p. 105.3–106.0°C

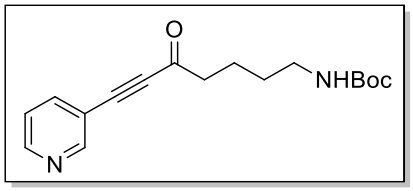
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.26 (d, *J* = 8.9 Hz, 2H), 7.74 (d, *J* = 8.7 Hz, 2H), 4.68 (br s, 1H), 3.17 (br q, *J* = 6.5 Hz, 2H), 2.75 (t, *J* =7.2 Hz, 2H), 1.84–1.71 (m, 2H), 1.63–1.51 (m, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.80, 155.92, 148.39, 133.56, 126.51, 123.67, 90.51, 86.76, 79.08, 44.87, 39.97, 29.26, 28.30, 20.81

IR (UATR) ν_{max} 3364, 2936, 2208, 1694, 1677, 1595, 1522, 1345, 1250, 1168, 858, 750, 687 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{22}N_2Na_1O_5$ $(M+Na)^+$ 369.1421, found 369.1420.

tert-Butyl 7-(pyridin-3-yl)-5-oxohept-6-ynylcarbamate (1n)



74% yield, yellow solid, m.p. 69.3–70.0°C

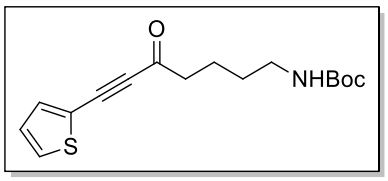
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (dd, *J* = 1.9, 0.8 Hz, 1H), 8.67 (dd, *J* = 4.9, 1.7 Hz, 1H), 7.86 (dt, *J* = 7.9, 1.9 Hz, 1H), 7.34 (ddd, *J* = 7.9, 4.9, 0.8 Hz, 1H), 4.58 (br s, 1H), 3.16 (br q, *J* = 6.5 Hz, 2H), 2.73 (t, *J* =7.2 Hz, 2H), 1.83–1.71 (m, 2H), 1.62–1.51 (m, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 186.67, 155.75, 152.75, 150.28, 139.52, 122.96, 116.89, 89.82, 86.17, 78.51, 44.54, 39.66, 28.92, 28.01, 20.62

IR (UATR) ν_{max} 3348, 2933, 2206, 1702, 1674, 1516, 1366, 1249, 1169, 808, 704 cm^{-1}

HRMS (ESI^+) calcd for $C_{17}H_{22}N_2Na_1O_3$ $(M+Na)^+$ 325.1523, found 325.1537.

***tert*-Butyl 7-(thiophen-2-yl)-5-oxohept-6-ynylcarbamate (1o)**



71% yield, white solid, m.p. 65.4–65.7°C

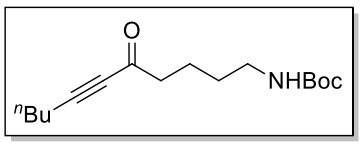
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (dd, *J* = 3.0, 1.1 Hz, 1H), 7.34 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.22 (dd, *J* = 5.0, 1.1 Hz, 1H), 4.58 (br s, 1H), 3.15 (br q, *J* = 6.5 Hz, 2H), 2.69 (t, *J* =7.2 Hz, 2H), 1.81–1.70 (m, 2H), 1.61–1.49 (m, 2H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.41, 155.88, 133.78, 130.12, 126.11, 119.05, 87.89, 86.10, 78.96, 44.69, 40.02, 29.24, 28.29, 21.04

IR (UATR) ν_{max} 3363, 2933, 2190, 1698, 1667, 1510, 1365, 1249, 1169, 1063, 787 cm^{-1}

HRMS (ESI^+) calcd for $C_{16}H_{21}N_1Na_1O_3S_1$ $(M+Na)^+$ 330.1134, found 330.1137.

***tert*-Butyl 5-oxoundec-6-ynylcarbamate (1p)**



72% yield, colorless oil

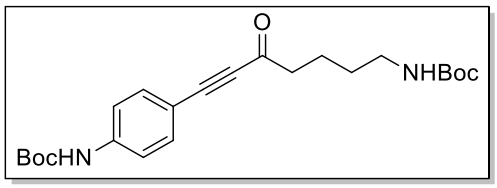
^{1}H NMR (300 MHz, $CDCl_3$) δ 4.82 (br s, 1H), 3.12 (br q, *J* = 6.2 Hz, 2H), 2.57 (t, *J* = 7.2 Hz, 2H), 2.37 (t, *J* = 6.8 Hz, 2H), 1.75–1.35 (m, 8H), 1.44 (s, 9H), 0.93 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.61, 155.79, 94.26, 80.56, 78.70, 44.71, 39.87, 29.45, 29.06, 28.15, 21.68, 20.87, 18.34, 13.22

IR (UATR) ν_{max} 3361, 2934, 2212, 1694, 1673, 1515, 1366, 1249, 1166 cm^{-1}

HRMS (ESI^+) calcd for $C_{16}H_{27}N_1Na_1O_3$ $(M+Na)^+$ 304.1883, found 304.1895.

***tert*-Butyl 7-{4-(*N*-*tert*-butoxycarbonyl)aminophenyl}-5-oxohept-6-ynylcarbamate (1q)**



75% yield, white solid, m.p. 120.7–121.4°C

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, *J* = 8.8 Hz, 2H), 7.40 (d, *J* = 8.8 Hz, 2H), 6.75 (br s, 1H), 4.59 (br s, 1H), 3.15 (br q, *J* = 6.4 Hz, 2H), 2.68 (t, *J* = 7.2 Hz, 2H), 1.82–1.69 (m, 2H), 1.61–1.49 (m, 2H), 1.52 (s, 9H), 1.44 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 187.46, 155.92, 152.30, 141.32, 133.97, 117.86, 112.82, 91.92, 87.45, 80.56, 78.75, 44.54, 39.85, 29.03, 28.14, 27.97, 20.95

IR (UATR) ν_{max} 3334, 2977, 2192, 1689,1586, 1518, 1231, 1152, 1050, 839, 773 cm^{-1}

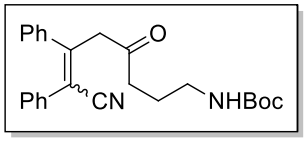
HRMS (ESI^+) calcd for $C_{23}H_{32}N_2Na_1O_5$ $(M+Na)^+$ 439.2203, found 439.2186.

3. General procedure for Michael reaction

*3.1 Screening of bases, solvents, and reaction conditions for Michael reaction between alkynone **1a** and benzyl cyanide **2c***

A solution of alkynone **1a** (0.35 mmol) in solvent (1.0 mL) were added to a mixture of benzyl cyanide **2c** (1.1 equiv.) and base (1.1 equiv.) in solvent (1.0 mL) at room temperature. The reaction was stirred at room temperature for 1-2 h. Then, the mixture was cooled down under ice-bath and neutralized with 1 N HCl. The products were extracted with EtOAc. The combined organic layers were washed with water, successively, dried over Na_2SO_4, and the solvent was concentrated under reduced pressure. The crude products were purified by column chromatography on silica gel using hexanes and increasing proportion of EtOAc as eluents to afford compound **3c**.

***tert*-Butyl 7-cyano-4-oxo-6,7-diphenylhept-6-enylcarbamate (3c)**



81% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 7.52–7.36 (m, 10H), 7.23–7.02 (m, 10H), 4.79 (br s, 1H), 4.67 (br s, 1H), 4.03 (s, 2H), 3.67 (s, 2H), 3.06 (br q, *J* = 6.4 Hz, 2H), 2.94 (br q, *J* = 6.4 Hz, 2H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.26 (t, *J* = 7.1 Hz, 2H), 1.74 (pent, *J* = 7.0 Hz, 2H), 1.58 (pent, *J* = 7.0 Hz, 2H), 1.42 (s, 9H), 1.40 (s, 9H)

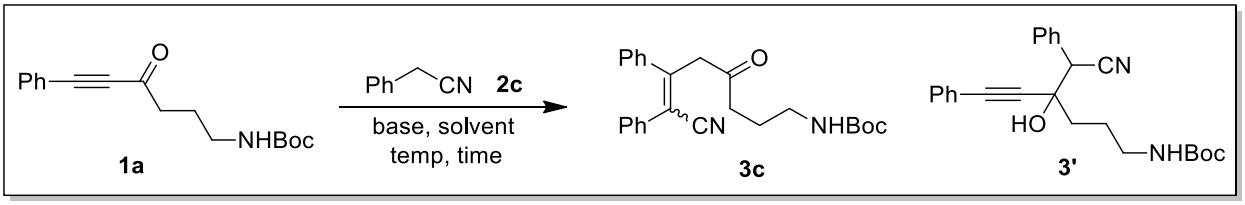
^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 205.41, 204.40, 155.89, 155.83, 152.59, 151.21, 138.79, 137.71, 133.82, 132.93, 129.67, 129.27, 129.19, 129.02, 128.86, 128.61, 128.52,

128.36, 128.35, 128.24, 128.16, 128.09, 127.59, 118.50, 118.42, 115.33, 115.11, 78.87, 51.99, 48.38, 40.14, 39.91, 39.38, 39.30, 28.17, 28.15, 23.71, 23.59

IR (UATR) ν_{max} 3384, 2976, 2214, 1708, 1510, 1366, 1249, 1167, 763, 698 cm^{-1}

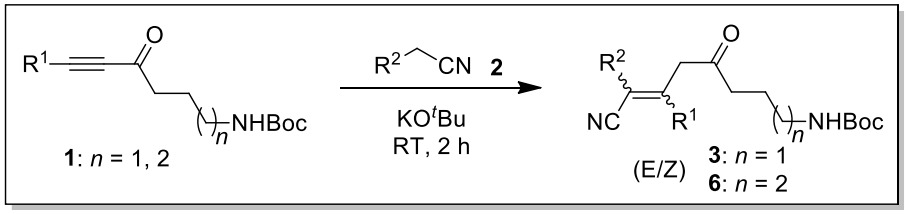
HRMS (ESI^+) calcd for $C_{25}H_{28}N_2Na_1O_3$ $(M+Na)^+$ 427.1992, found 427.1978.

Table S1. Screening of bases, solvents, and reaction conditions



Entry	Base	Solvent	Temp (^oC)	Time (h)	Conversion ratio of **1a** : **3c**	Isomer ratio of **3c**	Yield of **3c** (%)
1	LHMDS	THF	– 78	1	compound **3'**	-	as **3'**: 89
2	NaH	DMF	RT	2	4:96	10 : 13	89
3	K_2CO_3	MeCN	RT	2	100:0	-	-
4	NaOMe	MeCN	RT	2	100:0	-	-
5	LiO^tBu	MeCN	RT	2	100:0	-	-
6	NaO^tBu	MeCN	RT	2	81:19	10 : 13	-
7	KO^tBu	MeCN	RT	2	51:49	10 : 15	-
8	KO^tBu	THF	RT	2	29:71	7 : 5	63
9	KO^tBu	DME	RT	2	23:77	6 : 5	69
10	KO^tBu	DMF	RT	2	0:100	10 : 13	91
11	KO^tBu	NMP	RT	2	18:82	5 : 6	75
12	KO^tBu	1,4-dioxane	RT	2	23:77	10 : 15	66
13	LiO^tBu	DMF	RT	2	20:80	10 : 13	75
14	NaO^tBu	DMF	RT	2	29:71	5 : 7	65
15	DBU	DMF	RT	2	65:35	1 : 1	-

*3.2 General procedure for Michael reaction between various internal ynones **1** and nitriles **2***

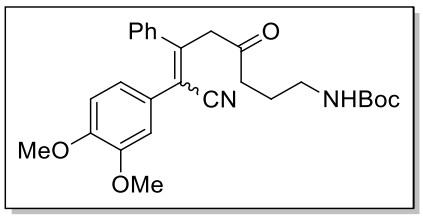


A solution of alkyne carbamate **1** (0.35 mmol) in DMF (1 mL) were added to a mixture of nitrile **2** (1.1 equiv) and KO^tBu (1.1 equiv) in DMF (1 mL) at room temperature. The reaction was stirred at room temperature for 2 h. Then, the mixture was cooled down under ice-bath and neutralized with 1

N HCl. The products were extracted with EtOAc. The combined organic layers were washed with water, successively, dried over Na_2SO_4, and the solvent was concentrate under reduced pressure. Crude products were purified by column chromatography on silica gel using hexanes and an increasing proportion of EtOAc as eluents to afford compound **3** or **6**.

Note: (1) For the synthesis of nitro compounds (**3p**, **3q**, **6p**, and **6q**), K_2CO_3 was used as base, instead of KO^{t}Bu, and the reaction was stirred at room temperature for 4 h. (2) Due to stability, compound **3s** was used in the next reaction without purification.

***tert*-Butyl 7-(3,4-dimethoxyphenyl)-7-cyano-4-oxo-6-phenylhept-6-enylcarbamate (3d)**



75% yield, yellow oil

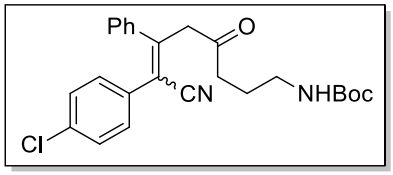
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 7.51–7.39 (m, 5H), 7.29–7.22 (m, 3H), 7.10 (dd, *J* = 8.7, 2.0 Hz, 2H), 7.00–6.95 (m, 2H), 6.90 (d, *J* = 8.7 Hz, 1H), 6.87 (dd, *J* = 8.4, 2.0 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.47 (d, *J* = 2.0 Hz, 1H), 4.62 (br s, 1H), 4.50 (br s, 1H), 4.02 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H), 3.72 (s, 2H), 3.48 (s, 3H), 3.09 (br q, *J* = 6.4 Hz, 2H), 2.98 (br q, *J* = 6.4 Hz, 2H), 2.58 (t, *J* = 7.1 Hz, 2H), 2.31 (t, *J* = 7.1 Hz, 2H), 1.77 (pent, *J* = 7.0 Hz, 2H), 1.61 (pent, *J* = 7.0 Hz, 2H), 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 205.83, 204.69, 155.97, 155.89, 151.78, 149.69, 149.50, 149.08, 148.22, 138.99, 138.47, 129.41, 128.73, 128.68, 128.59, 128.29, 127.75, 126.43, 125.34, 122.26, 121.23, 118.64, 115.40, 115.34, 112.32, 111.60, 111.21, 110.62, 79.17, 55.94, 55.89, 55.71, 55.36, 52.26, 48.76, 40.52, 40.07, 39.58, 39.52, 28.31, 28.28, 23.89, 23.83

IR (UATR) ν_{max} 3391, 2975, 2213, 1709, 1600, 1515, 1366, 1262, 1171, 1025, 765, 701 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{27}H_{32}N_2Na_1O_5$ $(M+Na)^+$ 487.2203, found 487.2196.

***tert*-Butyl 7-(4-chlorophenyl)-7-cyano-4-oxo-6-phenylhept-6-enylcarbamate (3e)**



87% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 7.50–7.33 (m, 9H), 7.26–7.18 (m, 3H), 7.14 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 7.07–7.02 (m, 2H), 4.76 (br s, 1H), 4.65 (br s, 1H), 4.03 (s, 2H), 3.67 (s, 2H), 3.08 (br q, *J* = 6.2 Hz, 2H), 2.97 (br q, *J* = 6.2 Hz, 2H), 2.56 (t, *J* = 7.1

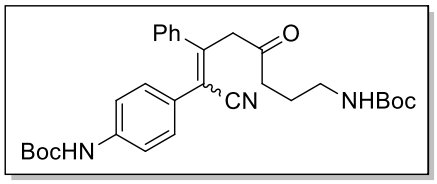
Hz, 2H), 2.30 (t, *J* = 7.1 Hz, 2H), 1.75 (pent, *J* = 7.0 Hz, 2H), 1.60 (pent, *J* = 7.0 Hz, 2H), 1.42 (s, 19H), 1.41 (s, 19H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 205.28, 204.24, 155.94, 155.89, 153.17, 151.99, 138.60, 137.50, 135.19, 134.27, 132.25, 131.48, 130.56, 129.88, 129.49, 129.15, 128.88, 128.63, 128.58, 128.47, 128.15, 127.57, 118.15, 118.11, 114.26, 114.17, 78.98, 52.05, 48.41, 40.27, 40.03, 39.40, 39.27, 28.20, 28.18, 23.78, 23.69

IR (UATR) ν_{max} 3378, 2977, 2214, 1707, 1512, 1366, 1250, 1168, 1093, 833, 767, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{25}H_{27}Cl_1N_2Na_1O_3$ $(M+Na)^+$ 461.1602, found 461.1595.

tert-Butyl 7-cyano-7-{4-(*N*-_tert_-butoxycarbonyl)aminophenyl}-4-oxo-6-phenylhept-6-enyl carbamate (3f)



81% yield, yellow oil

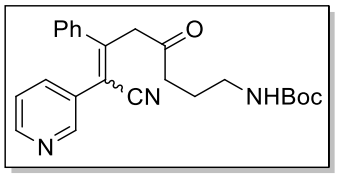
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 43:57) 7.50–7.38 (m, 7H), 7.31 (d, *J* = 8.8 Hz, 2H), 7.24–7.16 (m, 5H), 7.09–7.04 (m, 2H), 7.04 (d, *J* = 8.8 Hz, 2H), 6.84 (br s, 1H), 6.66 (br s, 1H), 4.63 (br s, 1H), 4.55 (br s), 4.01 (s, 2H), 3.68 (s, 2H), 3.08 (br q, *J* = 6.4 Hz, 2H), 2.96 (br q, *J* =6.6 Hz, 2H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.76 (pent, *J* = 6.9 Hz, 2H), 1.60 (pent, *J* =7.0 Hz, 2H), 1.52 (s, 9H), 1.48 (s, 9H), 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 43:57) 205.61, 204.68, 155.99, 155.93, 152.53, 152.36, 152.11, 150.09, 139.36, 139.04, 138.60, 138.05, 130.11, 129.39, 129.31, 128.72, 128.70, 128.62, 128.33, 128.30, 127.74, 127.31, 118.67, 118.60, 117.83, 115.11, 115.02, 80.87, 80.74, 79.15, 52.24, 48.61, 40.37, 40.05, 39.55, 28.33, 28.32, 28.24, 28.21, 23.88, 23.81

IR (UATR) ν_{max} 3335, 2978, 2213, 1701, 1522, 1234, 1156, 1054, 841, 772, 699 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{30}H_{37}N_3Na_1O_5$ $(M+Na)^+$ 542.2625, found 542.2606.

tert-Butyl 7-cyano-7-(pyridin-3-yl)-4-oxo-6-phenylhept-6-enylcarbamate (3g)



73% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 60:40) 8.67 (d, *J* = 2.0 Hz, 1H), 8.65 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.42 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.34 (d, *J* = 1.7 Hz, 1H), 7.79 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.52–7.42 (m, 6H), 7.39 (dd, *J* = 8.0, 4.9 Hz, 1H), 7.28–7.19 (m, 3H), 7.15 (dd, *J* = 8.0, 4.9 Hz,

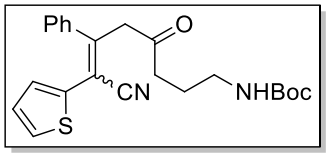
1H), 7.08–7.01 (m, 2H), 4.82 (br s, 1H), 4.74 (br s, 1H), 4.08 (s, 2H), 3.69 (s, 2H), 3.09 (br q, *J* = 6.4 Hz, 2H), 2.97 (br q, *J* = 6.4 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 2.32 (t, *J* = 7.0 Hz, 2H), 1.77 (pent, *J* = 7.0 Hz, 2H), 1.61 (pent, *J* = 6.8 Hz, 2H), 1.43 (s, 9H), 1.40 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 60:40) 204.93, 203.95, 155.94, 154.57, 153.77, 151.12, 149.92, 149.05, 149.03, 138.41, 137.13, 136.45, 136.20, 130.10, 129.71, 129.38, 129.16, 128.73, 128.72, 128.14, 127.53, 123.65, 122.96, 117.84, 117.75, 112.19, 112.05, 78.97, 52.05, 48.40, 40.35, 40.13, 39.41, 39.22, 28.22, 28.19, 23.83, 23.73

IR (UATR) ν_{max} 3336, 2977, 2156, 1702, 1626, 1525, 1366, 1248, 1168, 767, 702 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{27}N_3Na_1O_3$ $(M+Na)^+$ 428.1945, found 428.1945.

***tert*-Butyl 7-cyano-7-(thiophen-2-yl)-4-oxo-6-phenylhept-6-enylcarbamate (3h)**



70% yield, yellow oil

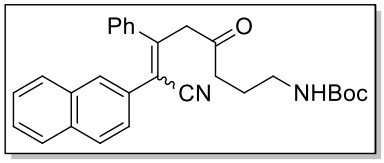
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 55:45) 7.49–7.36 (m, 9H), 7.29 (dd, *J* = 3.6, 1.2 Hz, 1H), 7.23–7.18 (m, 3H), 7.11 (dd, *J* = 5.1, 1.2 Hz, 1H), 7.08 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.88 (dd, *J* = 5.1, 3.7 Hz, 1H), 4.63 (br s, 1H), 4.56 (br s, 1H), 3.97 (s, 2H), 3.93 (s, 2H), 3.08 (br q, *J* = 6.6 Hz, 2H), 3.03 (br q, *J* = 6.6 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H), 2.43 (t, *J* = 7.1 Hz, 2H), 1.75 (pent, *J* = 7.0 Hz, 2H), 1.68 (pent, *J* = 7.0 Hz, 2H), 1.42 (s, 18H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 55:45) 204.56, 204.18, 155.82, 151.92, 148.21, 139.22, 137.71, 135.22, 134.87, 129.71, 129.42, 129.34, 129.14, 129.06, 128.52, 128.00, 127.75, 127.60, 127.33, 126.05, 117.67, 117.09, 110.70, 109.03, 78.84, 52.58, 49.37, 40.04, 39.98, 39.39, 28.16, 23.70, 23.64

IR (UATR) ν_{max} 3385, 2976, 2219, 1706, 1513, 1366, 1249, 1168, 765, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{26}N_2Na_1O_3S_1$ $(M+Na)^+$ 433.1556, found 433.1551.

***tert*-Butyl 7-cyano-7-(naphthalen-2-yl)-4-oxo-6-phenylhept-6-enylcarbamate (3i)**



99% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 7.92–7.79 (m, 5H), 7.73–7.67 (m, 2H), 7.40–7.57 (m, 11H), 7.23–7.14 (m, 3H), 7.11 (d, *J* = 1.6 Hz, 1H), 7.09 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.04 (dd, *J* = 8.6, 1.8 Hz, 1H), 4.68 (br s, 1H), 4.52 (br s, 1H), 4.08 (s, 2H), 3.72 (s, 2H), 3.10 (br q,

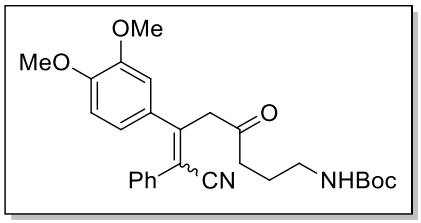
J = 6.4 Hz, 2H), 2.94 (br q, *J* = 6.4 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.26 (t, *J* = 7.1 Hz, 2H), 1.77 (pent, *J* = 7.0 Hz, 2H), 1.58 (pent, *J* = 7.0 Hz, 2H), 1.43 (s, 9H), 1.39 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 205.54, 204.51, 155.98, 155.86, 152.84, 151.31, 138.89, 137.84, 133.07, 132.92, 132.78, 132.61, 131.26, 130.50, 129.44, 129.10, 128.83, 128.67, 128.53, 128.44, 128.12, 128.10, 128.04, 127.72, 127.64, 127.42, 127.03, 126.79, 126.38, 126.35, 125.56, 118.72, 118.53, 115.40, 115.30, 79.02, 52.19, 48.59, 40.27, 40.03, 39.49, 39.40, 28.26, 28.21, 23.83, 23.73

IR (UATR) ν_{max} 3386, 2976, 2212, 1707, 1506, 1366, 1249, 1166, 861, 820, 750, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{29}H_{30}N_2Na_1O_3$ $(M+Na)^+$ 477.2149, found 477.2150.

tert-Butyl 7-cyano-6-(3,4-dimethoxyphenyl)-4-oxo-7-phenylhept-6-enylcarbamate (3j)



89% yield, yellow oil

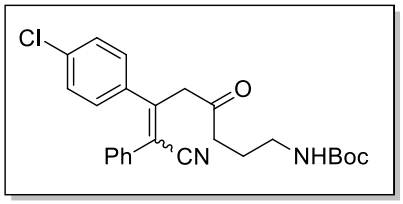
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 7.47–7.33 (m, 5H), 7.25–7.14 (m, 5H), 7.12 (d, *J* = 1.7 Hz, 1H), 7.09 (dd, *J* = 8.3, 1.7 Hz, 1H), 6.91 (d, *J* = 8.6 Hz, 1H), 6.73 (s, 2H), 6.48 (s, 1H), 4.77 (br s, 1H), 4.66 (br s, 1H), 4.05 (s, 2H), 3.93 (s, 3H), 3.90 (s, 3H), 3.82 (s, 3H), 3.68 (s, 2H), 3.49 (s, 3H), 3.09 (br q, *J* = 6.4 Hz, 2H), 2.97 (br q, *J* = 6.4 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.29 (t, *J* = 7.1 Hz, 2H), 1.76 (pent, *J* = 7.0 Hz, 2H), 1.61 (pent, *J* = 7.0 Hz, 2H), 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 205.70, 204.79, 155.95, 155.87, 152.17, 150.87, 150.00, 149.47, 148.69, 148.28, 134.25, 133.62, 131.09, 129.76, 129.27, 128.98, 128.93, 128.50, 128.41, 128.22, 121.21, 120.56, 118.95, 118.88, 114.07, 113.99, 112.30, 111.16, 110.91, 110.71, 79.05, 55.96, 55.75, 55.62, 55.41, 51.77, 48.35, 40.12, 39.86, 39.45, 28.23, 28.21, 23.88, 23.79

IR (UATR) ν_{max} 3379, 2932, 2211, 1699, 1513, 1366, 1249, 1168, 766, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{27}H_{32}N_2Na_1O_5$ $(M+Na)^+$ 487.2203, found 487.2186

tert-Butyl 7-cyano-6-(4-chlorophenyl)-4-oxo-7-phenylhept-6-enylcarbamate (3k)



90% yield, yellow oil

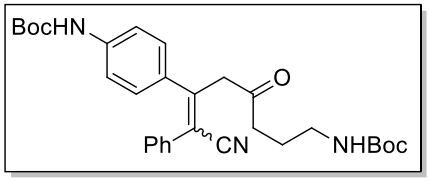
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 7.48–7.32 (m, 9H), 7.24–7.10 (m, 7H), 7.00 (d, *J* = 8.5 Hz, 2H), 4.77 (br s, 1H), 4.66 (br s, 1H), 4.02 (s, 2H), 3.66 (s, 2H), 3.09 (br q, *J* = 6.4 Hz, 2H), 2.98 (br q, *J* = 6.4 Hz, 2H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.75 (pent, *J* = 7.0 Hz, 2H), 1.60 (pent, *J* = 7.0 Hz, 2H), 1.42 (s, 9H), 1.40 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 205.27, 204.33, 155.93, 155.85, 151.41, 149.93, 137.33, 136.23, 135.27, 134.61, 133.54, 132.68, 129.79, 129.21, 129.19, 129.12, 128.95, 128.82, 128.65, 128.52, 128.39, 128.29, 118.26, 118.18, 115.90, 115.69, 78.97, 51.73, 48.31, 40.06, 39.94, 39.32, 28.19, 28.17, 23.81, 23.71

IR (UATR) ν_{max} 3365, 2977, 2215, 1704, 1492, 1366, 1249, 1165, 1093, 833, 765, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{27}Cl_1N_2Na_1O_3$ $(M+Na)^+$ 461.1602, found 461.1591.

tert-Butyl 7-cyano-6-{4-(*N*-*tert*-butoxycarbonyl)aminophenyl}-4-oxo-7-phenylhept-6-enyl carbamate (3l)



91% yield, white foam

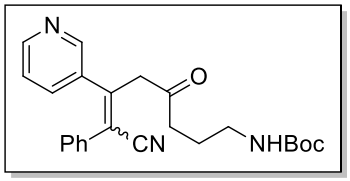
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 54:46) 7.45 (s, 4H), 7.43–7.35 (m, 5H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.22–7.14 (m, 5H), 6.98 (d, *J* = 8.7 Hz, 2H), 6.77 (br s, 1H), 6.64 (br s, 1H), 4.64 (br s, 1H), 4.53 (br s, 1H), 4.02 (s, 2H), , 3.66 (s, 2H), 3.08 (br q, *J* = 6.5 Hz, 2H), 2.97 (br q, *J* = 6.5 Hz, 2H), 2.57 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.75 (pent, *J* = 7.0 Hz, 2H), 1.60 (pent, *J* = 7.0 Hz, 2H), 1.52 (s, 9H), 1.49 (s, 9H), 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 54:46) 205.62, 204.73, 155.95, 155.89, 152.48, 152.37, 152.16, 150.72, 139.81, 139.18, 134.13, 133.26, 132.83, 131.63, 129.36, 129.27, 128.98, 128.90, 128.55, 128.46, 128.34, 128.24, 118.83, 118.80, 118.16, 117.89, 114.42, 114.16, 80.58, 79.01, 51.91, 48.27, 40.18, 39.89, 39.46, 28.24, 28.23, 28.14, 28.10, 23.79, 23.69

IR (UATR) ν_{max} 3344, 2977, 2209, 1705, 1589, 1520, 1234, 1155, 1052, 840, 765, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{30}H_{37}N_3Na_1O_5$ $(M+Na)^+$ 542.2625, found 542.2641.

tert-Butyl 7-cyano-6-(pyridin-3-yl)-4-oxo-7-phenylhept-6-enylcarbamate (3m)



75% yield, yellow oil

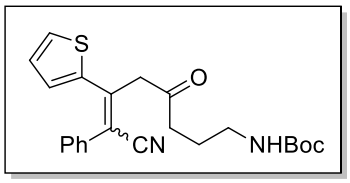
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 8.71 (d, *J* = 1.9 Hz, 1H), 8.64 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.45 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.30 (d, *J* = 1.7 Hz, 1H), 7.90 (ddd, *J* = 8.0, 2.2, 1.7 Hz, 1H), 7.46–7.34 (m, 7H), 7.23–7.10 (m, 6H), 4.81 (br s, 1H), 4.71 (br s, 1H), 4.07 (s, 2H), 3.72 (s, 2H), 3.11 (br q, *J* = 6.4 Hz, 2H), 2.99 (br q, *J* = 6.4 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 1.78 (pent, *J* = 7.0 Hz, 2H), 1.63 (pent, *J* = 7.0 Hz, 2H), 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 205.16, 204.30, 156.05, 155.97, 150.08, 149.32, 149.28, 148.81, 148.01, 147.85, 136.20, 135.90, 135.18, 134.13, 133.24, 132.35, 129.49, 129.36, 129.08, 128.86, 128.61, 128.32, 123.43, 123.17, 117.94, 117.83, 117.30, 117.21, 79.14, 51.49, 48.35, 40.07, 39.38, 28.26, 28.24, 23.93, 23.84

IR (UATR) ν_{max} 3332, 2976, 2156, 1701, 1634, 1522, 1367, 1250, 1168, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{27}N_3Na_1O_3$ $(M+Na)^+$ 428.1945, found 428.1950.

***tert*-Butyl 7-cyano-6-(thiophen-2-yl)-4-oxo-7-phenylhept-6-enylcarbamate (3n)**



92% yield, yellow oil

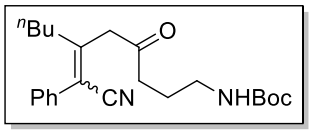
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 44:56) 7.71 (d, *J* = 1.4 Hz, 1H), 7.46–7.16 (m, 13H), 7.07 (dd, *J* = 5.0, 3.0 Hz, 1H), 6.56 (d, *J* = 5.0 Hz, 1H), 4.86 (br s, 1H), 4.77 (br s, 1H), 4.03 (s, 2H), 3.65 (s, 2H), 3.08 (br q, *J* = 6.3 Hz, 2H), 2.98 (br q, *J* = 6.3 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.31 (t, *J* = 7.1 Hz, 2H), 1.76 (pent, *J* = 6.9 Hz, 2H), 1.62 (pent, *J* = 6.9 Hz, 2H) 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 44:56) 205.55, 204.71, 155.88, 155.81, 145.98, 145.25, 138.75, 137.90, 134.03, 133.44, 128.98, 128.92, 128.84, 128.59, 128.47, 128.36, 127.46, 126.83, 126.73, 126.31, 126.16, 125.52, 119.00, 118.65, 113.92, 112.59, 78.81, 51.55, 48.05, 39.69, 39.48, 39.25, 28.12, 23.72, 23.63

IR (UATR) ν_{max} 3378, 2976, 2211, 1708, 1687, 1595, 1515, 1366, 1249, 1167, 1046, 765, 698 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{26}N_2Na_1O_3S_1$ $(M+Na)^+$ 433.1556, found 433.1572.

***tert*-Butyl 7-cyano-6-butyl-4-oxo-7-phenylhept-6-enylcarbamate (3o)**



94% yield, yellow oil

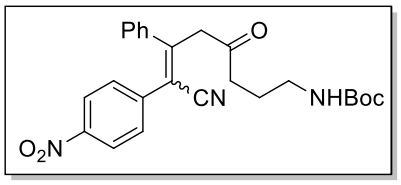
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 23:77) 7.43–7.19 (m, 10H), 4.94 (br s, 1H), 4.85 (br s, 1H), 3.71 (s, 2H), 3.33 (s, 2H), 3.15 (br q, *J* = 6.4 Hz, 2H), 3.05 (br q, *J* = 6.3 Hz, 2H), 2.64 (t, *J* = 7.1 Hz, 2H), 2.58 (dd, *J* = 8.0, 7.5 Hz, 2H), 2.35 (t, *J* = 7.1 Hz, 2H), 2.24 (dd, *J* = 8.0, 7.5 Hz, 2H), 1.82 (pent, *J* = 6.9 Hz, 2H), 1.68 (pent, *J* = 6.9 Hz, 2H), 1.59–1.13 (m, 4H), 1.44 (s, 9H), 1.42 (s, 9H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 23:77) 205.57, 204.73, 155.86, 155.16, 133.50, 133.08, 128.64, 128.55, 128.48, 128.38, 128.31, 118.21, 117.76, 114.23, 113.82, 78.76, 48.39, 45.49, 39.76, 39.73, 39.25, 36.32, 32.55, 29.62, 29.33, 28.09, 28.08, 23.78, 23.72, 22.22, 22.16, 13.56, 13.33

IR (UATR) ν_{max} 3390, 2966, 2202, 1680, 1615, 1509, 1413, 1364, 1252, 1165, 1096, 708 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{33}N_2O_3$ $(M+H)^+$ 385.2486, found 385.2499.

***tert*-Butyl 7-cyano-7-(4-nitrophenyl)-4-oxo-6-phenylhept-6-enylcarbamate (3p)**



70% yield, yellow oil

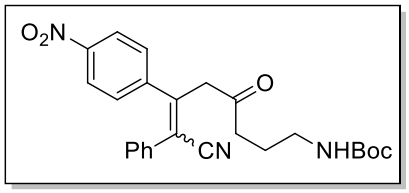
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 60:40) 8.29 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.53–7.42 (m, 5H), 7.35–7.22 (m, 5H), 7.05 (dd, *J* = 8.0, 1.6 Hz, 2H), 4.74 (br s, 1H), 4.63 (br s, 1H), 4.10 (s, 2H), 3.72 (s, 2H), 3.10 (br q, *J* = 6.4 Hz, 2H), 3.00 (br q, *J* = 6.3 Hz, 2H), 2.51 (t, *J* = 7.1 Hz, 2H), 2.35 (t, *J* = 7.0 Hz, 2H), 1.78 (pent, *J* = 7.0 Hz, 2H), 1.62 (pent, *J* = 6.8 Hz, 2H), 1.43 (s, 9H), 1.39 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 60:40) 204.93, 203.82, 155.94, 154.94, 147.94, 147.08, 140.11, 139.66, 138.29, 137.08, 130.30, 129.86, 129.78, 129.43, 128.81, 128.76, 128.11, 127.53, 124.11, 123.41, 117.58, 117.54, 113.53, 79.01, 52.19, 48.46, 40.34, 40.18, 39.39, 39.12, 28.21, 28.14, 23.86, 23.82

IR (UATR) ν_{max} 3363, 2977, 2213, 1705, 1636, 1518, 1344, 1246, 1166, 1044, 854, 768, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{27}N_3Na_1O_5$ $(M+Na)^+$ 472.1843, found 472.1842.

***tert*-Butyl 7-cyano-6-(4-nitrophenyl)-4-oxo-7-phenylhept-6-enylcarbamate (3q)**



68% yield, yellow oil

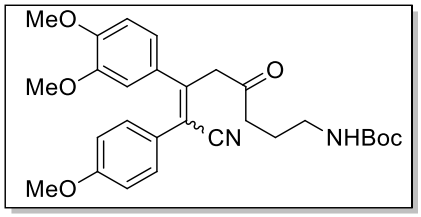
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 46:54) 8.27 (d, *J* = 8.7 Hz, 2H), 8.05 (d, *J* = 8.7 Hz, 2H), 7.70 (d, *J* = 8.7 Hz, 2H), 7.48–7.34 (m, 5H), 7.28 (d, *J* = 8.7 Hz, 2H), 7.27–7.08 (m, 5H), 4.80 (br s, 1H), 4.69 (br s, 1H), 4.10 (s, 2H), 3.76 (s, 2H), 3.11 (br q, *J* = 6.4 Hz, 2H), 3.00 (br q, *J* = 6.4 Hz, 2H), 2.62 (t, *J* = 7.1 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 1.78 (pent, *J* = 7.0 Hz, 2H), 1.63 (pent, *J* = 7.0 Hz, 2H), 1.42 (s, 9H), 1.40 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 46:54) 205.10, 204.18, 155.98, 155.90, 150.52, 148.94, 147.83, 147.21, 145.54, 144.68, 132.89, 132.10, 129.57, 129.18, 129.06, 129.01, 128.57, 128.20, 123.75, 123.50, 117.68, 117.59, 117.20, 78.99, 51.34, 48.24, 39.92, 39.85, 39.23, 28.16, 28.14, 23.87, 23.78

IR (UATR) ν_{max} 3363, 2977, 2215, 1701, 1597, 1521, 1346, 1249, 1167, 857, 763, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{27}N_3Na_1O_5$ $(M+Na)^+$ 472.1843, found 472.1835.

<u>*tert*-Butyl 7-cyano-6-(3,4-dimethoxyphenyl)-7-(4-methoxyphenyl)-4-oxohept-6-enylcarbamate (3r)</u>



91% yield, yellow oil

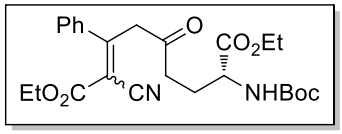
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 7.32 (d, *J* = 8.8 Hz, 2H), 7.10 (d, *J* = 8.8 Hz, 2H), 7.06 (dd, *J* = 8.4, 2.1 Hz, 2H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.77–6.68 (m, 4H), 6.53 (d, *J* = 1.8 Hz, 1H), 4.64 (br s, 1H), 4.54 (br s, 1H), 4.02 (s, 2H), 3.94 (s, 3H), 3.91 (s, 3H), 3.844 (s, 3H), 3.837 (s, 3H), 3.76 (s, 3H), 3.69 (s, 2H), 3.57 (s, 3H), 3.10 (br q, *J* = 6.5 Hz, 2H), 3.00 (br q, *J* = 6.5 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.77 (pent, *J* = 7.0 Hz, 2H), 1.63 (pent, *J* = 7.0 Hz, 2H), 1.43 (s, 9H), 1.41 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 205.91, 205.02, 160.04, 159.42, 155.98, 155.91, 151.29, 149.99, 149.39, 149.31, 148.77, 148.49, 131.33, 130.66, 130.20, 129.93, 126.54, 125.81, 121.23, 120.59, 119.18, 119.07, 114.33, 113.93, 113.83, 112.15, 111.26, 110.99, 110.85, 79.12, 56.04, 55.82, 55.70, 55.59, 55.28, 55.18, 51.97, 48.50, 40.25, 39.90, 39.57, 28.31, 28.28, 23.96, 23.90

IR (UATR) ν_{max} 3393, 2936, 2155, 1709, 1606, 1513, 1252, 1174, 1026, 836, 767 cm^{-1}

HRMS (ESI^+) calcd for $C_{28}H_{34}N_2Na_1O_6$ $(M+Na)^+$ 517.2309, found 517.2305.

(*R*)-Diethyl 8-[(*tert*-butoxycarbonyl)amino]-2-cyano-5-oxo-3-phenylnon-2-enedioate (3s)

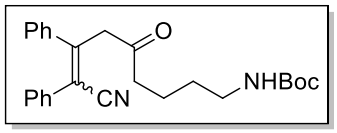


Quantitative yield, yellow oil (using in the next step without purification)

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (s, 5H), 5.21 (d, *J* = 8.2 Hz, 1H), 4.29 (t, *J* = 7.1 Hz, 2H), 4.28–4.20 (m, 3H), 4.17 (t, *J* = 7.1 Hz, 2H), 2.80–2.59 (m, 2H), 2.30–2.10 (m, 1H), 1.95–1.80 (m, 1H), 1.42 (s, 9H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.26 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 202.63, 172.07, 167.66, 161.89, 155.29, 139.36, 130.40, 128.57, 127.33, 115.49, 106.77, 79.65, 62.10, 61.25, 52.49, 49.93, 38.41, 28.05, 13.92, 13.81

***tert*-Butyl 8-cyano-7,8-diphenyl-5-oxooct-7-enylcarbamate (6c)**



89% yield, yellow oil

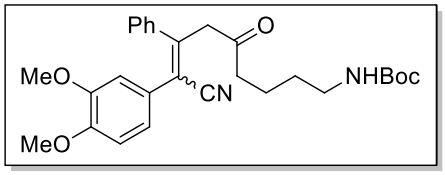
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 7.52–7.36 (m, 11H), 7.23–7.02 (m, 9H), 4.71 (br s, 1H), 4.64 (br s, 1H), 4.02 (s, 2H), 3.66 (s, 2H), 3.06 (br q, *J* = 6.3 Hz, 2H), 2.97 (br q, *J* = 6.3 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H), 2.26 (t, *J* = 7.1 Hz, 2H), 1.65–1.52 (m, 2H), 1.52–1.32 (m, 4H), 1.42 (s, 18H), 1.32–1.20 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 45:55) 205.71, 204.65, 155.82, 152.67, 151.25, 138.87, 137.77, 133.88, 132.96, 129.27, 129.22, 129.05, 128.85, 128.61, 128.54, 128.38, 128.37, 128.26, 128.23, 128.18, 127.60, 118.50, 118.42, 115.40, 115.15, 78.86, 52.06, 48.44, 42.51, 42.32, 39.82, 39.66, 29.04, 28.96, 28.20, 20.39, 20.25

IR (UATR) ν_{max} 3382, 2934, 2215, 1710, 1512, 1366, 1249, 1169, 764, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{26}H_{30}N_2Na_1O_3$ $(M+Na)^+$ 441.2149, found 441.2154.

***tert*-Butyl 8-cyano-8-(3,4-dimethoxyphenyl)-5-oxo-7-phenyloct-7-enylcarbamate (6d)**



74% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 7.50–7.39 (m, 5H), 7.27–7.23 (m, 3H), 7.13–7.07 (m, 2H), 7.00–6.95 (m, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 6.87 (dd, *J* = 8.4, 2.1 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 2.1 Hz, 1H), 4.58 (br s, 1H), 4.53 (br s, 1H), 4.01 (s, 2H), 3.91 (s, 3H), 3.88 (s, 3H), 3.83 (s, 3H), 3.70 (s, 2H), 3.48 (s, 3H), 3.08 (br q, *J* = 6.4 Hz, 2H), 2.99 (br q, *J* =

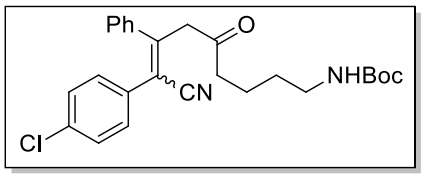
6.4 Hz, 2H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.30 (t, *J* = 7.1 Hz, 2H), 1.68–1.55 (m, 2H), 1.51–1.24 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 206.08, 204.89, 155.88, 151.92, 149.73, 149.54, 149.11, 148.26, 139.07, 138.52, 129.37, 128.71, 128.68, 128.57, 128.27, 127.74, 126.50, 125.38, 122.27, 121.24, 118.62, 115.44, 115.32, 112.38, 111.69, 111.25, 110.67, 79.02, 55.96, 55.91, 55.72, 55.38, 52.31, 48.78, 42.87, 42.45, 39.99, 39.86, 29.21, 28.33, 28.32, 20.55, 20.42

IR (UATR) ν_{max} 3391, 2935, 2212, 1706, 1599, 1513, 1365, 1247, 1169, 1024, 861, 765, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{28}H_{34}N_2Na_1O_5$ $(M+Na)^+$ 501.2360, found 501.2347

tert-Butyl 8-cyano-8-(4-chlorophenyl)-5-oxo-7-phenyloct-7-enylcarbamate (6e)



81% yield, yellow oil

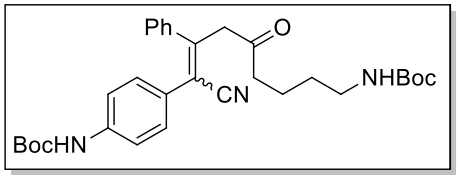
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 7.49–7.33 (m, 9H), 7.27–7.20 (m, 3H), 7.15 (d, *J* = 8.6 Hz, 2H), 7.06 (d, *J* = 8.6 Hz, 2H), 7.06–7.01 (m, 2H), 4.65 (br s, 1H), 4.59 (br s, 1H), 4.02 (s, 2H), 3.65 (s, 2H), 3.07 (br q, *J* = 6.4 Hz, 2H), 2.99 (br q, *J* = 6.4 Hz, 2H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.29 (t, *J* = 7.1 Hz, 2H), 1.66–1.55 (m, 2H), 1.52–1.37 (m, 2H), 1.43 (s, 9H), 1.42 (s, 9H), 1.35–1.24 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 205.54, 204.44, 155.86, 155.83, 153.24, 152.03, 138.68, 137.59, 135.27, 134.33, 132.35, 131.54, 130.61, 129.91, 129.51, 129.16, 128.90, 128.67, 128.62, 128.51, 128.16, 127.59, 118.16, 118.10, 114.37, 114.23, 78.96, 52.14, 48.48, 42.74, 42.45, 39.87, 39.70, 29.13, 29.08, 28.26, 20.46, 20.27

IR (UATR) ν_{max} 3382, 2976, 2213, 1710, 1507, 1366, 1249, 1169, 1093, 834, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{26}H_{29}Cl_1N_2Na_1O_3$ $(M+Na)^+$ 475.1759, found 475.1754.

tert-Butyl 8-{4-(_N-tert_-butoxycarbonyl)aminophenyl}-8-cyano-5-oxo-7-phenyloct-7-enyl carbamate (6f)



85% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 7.50–7.37 (m, 7H), 7.31 (d, *J* = 8.7 Hz, 2H), 7.24–7.16 (m, 5H), 7.08–7.02 (m, 4H), 6.89 (br s, 1H), 6.65 (br s, 1H), 4.59 (br s, 2H), 4.00 (s, 2H),

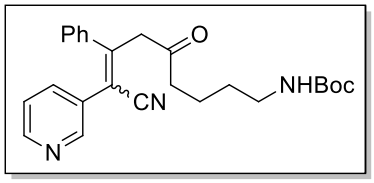
3.67 (s, 2H), 3.07 (br q, *J* = 6.4 Hz, 2H), 2.99 (br q, *J* =6.4 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.66–1.25 (m, 8H), 1.52 (s, 9H), 1.48 (s, 9H), 1.43 (s, 18H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 205.94, 204.90, 155.94, 152.57, 152.36, 152.22, 150.13, 139.39, 139.12, 138.58, 138.09, 130.12, 129.35, 129.29, 128.69, 128.62, 128.33, 127.74, 127.34, 118.66, 118.60, 117.82, 115.14, 115.01, 80.87, 80.75, 79.08, 52.29, 48.64, 42.71, 42.44, 39.98, 39.91, 29.20, 28.35, 28.25, 28.21, 20.53

IR (UATR) ν_{max} 3344, 2977, 2213, 1709, 1521, 1235, 1158, 1054, 841, 771, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{31}H_{39}N_3Na_1O_5$ $(M+Na)^+$ 556.2782, found 556.2768.

tert-Butyl 8-cyano-8-(pyridin-3-yl)-5-oxo-7-phenyloct-7-enylcarbamate (6g)



79% yield, yellow oil

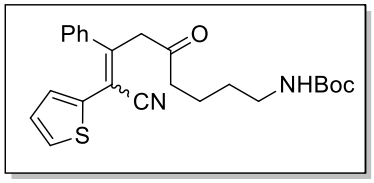
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 55:45) 8.67 (d, *J* = 1.7 Hz, 1H), 8.65 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.43 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.34 (d, *J* = 1.7 Hz, 1H), 7.79 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.52–7.42 (m, 6H), 7.39 (dd, *J* = 8.0, 4.9 Hz, 1H), 7.30–7.19 (m, 3H), 7.15 (ddd, *J* = 8.0, 4.9, 0.6 Hz, 1H), 7.07–7.01 (m, 2H), 4.66 (br s, 2H), 4.07 (s, 2H), 3.67 (s, 2H), 3.08 (br q, *J* = 6.4 Hz, 2H), 2.99 (br q, *J* = 6.4 Hz, 2H), 2.57 (t, *J* = 7.1 Hz, 2H), 2.31 (t, *J* = 7.0 Hz, 2H), 1.68–1.56 (m, 2H), 1.51–1.37 (m , 4H), 1.43 (s, 9H), 1.42 (s, 9H), 1.36–1.25 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 55:45) 205.26, 204.23, 155.92, 154.66, 153.86, 150.18, 149.95, 149.05, 138.48, 137.20, 136.54, 136.29, 130.21, 129.76, 129.45, 129.21, 128.80, 128.78, 128.16, 127.57, 123.69, 123.03, 117.86, 117.78, 112.30, 112.05, 78.98, 52.15, 48.48, 42.83, 42.56, 39.87, 39.71, 29.15, 29.06, 28.29, 20.47, 20.34,

IR (UATR) ν_{max} 3341, 2933, 2212, 1704, 1634, 1516, 1365, 1249, 1168, 767, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{29}N_3Na_1O_3$ $(M+Na)^+$ 442.2101, found 442.2097

tert-Butyl 8-cyano-8-(thiophen-2-yl)-5-oxo-7-phenyloct-7-enylcarbamate (6h)



75% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 60:40) 7.47–7.37 (m, H), 7.29 (dd, *J* = 3.6, 1.1 Hz, 1H), 7.24–7.18 (m, 4H), 7.12 (dd, *J* = 5.1, 1.1 Hz, 1H), 7.08 (dd, *J* = 4.7, 3.7 Hz, 1H), 6.88 (dd, *J* =

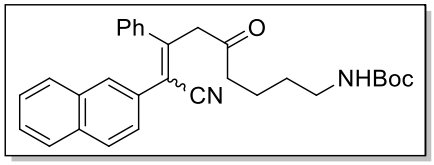
5.1, 3.7 Hz, 1H), 4.53 (br s, 2H), 3.96 (s, 2H), 3.91 (s, 2H), 3.13–2.99 (m, 4H), 2.57 (t, *J* = 7.1 Hz, 2H), 2.42 (t, *J* = 7.1 Hz, 2H), 1.67–1.32 (m, 8H), 1.43 (s, 18H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 60:40) 204.80, 204.41, 155.82, 152.08, 148.27, 139.32, 137.83, 135.31, 134.95, 129.77, 129.46, 129.38, 129.18, 129.11, 128.59, 128.03, 127.82, 127.64, 127.63, 127.35, 126.10, 117.69, 117.13, 110.82, 109.13, 78.86, 52.69, 49.44, 42.45, 42.41, 39.85, 39.78, 29.11, 28.24, 20.45, 20.30

IR (UATR) ν_{max} 3378, 2933, 2218, 1706, 1509, 1365, 1247, 1167, 851, 766, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{28}N_2Na_1O_3S_1$ $(M+Na)^+$ 447.1713, found 447.1726

***tert*-Butyl 8-cyano-8-(naphthalen-2-yl)-5-oxo-7-phenyloct-7-enylcarbamate (6i)**



95% yield, yellow oil

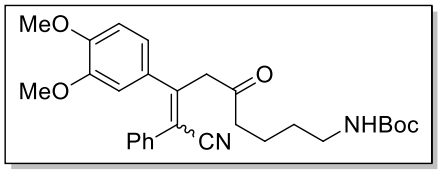
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 7.90–7.77 (m, 5H), 7.70–7.64 (m, 2H), 7.55–7.37 (m, 11H), 7.21–7.12 (m, 3H), 7.10–7.05 (m, 2H), 7.03 (dd, *J* = 8.6, 1.8 Hz, 1H), 4.68 (br s, 1H), 4.54 (br s, 1H), 4.06 (s, 2H), 3.69 (s, 2H), 3.07 (br q, *J* = 6.4 Hz, 2H), 2.92 (br q, *J* = 6.4 Hz, 2H), 2.55 (t, *J* = 7.1 Hz, 2H), 2.22 (t, *J* = 7.1 Hz, 2H), 1.68–1.54 (m, 2H), 1.49–1.33 (m , 4H), 1.43 (s, 9H), 1.41 (s, 9H), 1.28–1.17 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 50:50) 205.71, 204.63, 155.85, 155.77, 152.91, 151.32, 138.94, 137.83, 133.02, 132.88, 132.73, 132.55, 131.28, 130.49, 129.33, 129.04, 128.76, 128.73, 128.59, 128.46, 128.36, 128.04, 128.01, 127.98, 127.66, 127.64, 127.60, 127.37, 126.98, 126.74, 126.33, 126.29, 125.52, 118.64, 118.46, 115.37, 115.19, 78.81, 52.17, 48.58, 42.55, 42.36, 39.85, 39.66, 29.09, 28.99, 28.23, 28.21, 20.43, 20.32

IR (UATR) ν_{max} 3384, 2932, 2208, 1709, 1505, 1365, 1248, 1169, 751, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{30}H_{32}N_2Na_1O_3$ $(M+Na)^+$ 491.2305, found 491.2304

***tert*-Butyl 8-cyano-7-(3,4-dimethoxyphenyl)-5-oxo-8-phenyloct-7-enylcarbamate (6j)**



82% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 7.45–7.35 (m, 5H), 7.24–7.15 (m, 5H), 7.11 (d, *J* = 2.1 Hz, 1H), 7.06 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.91 (d, *J* = 8.3 Hz, 1H), 6.74 (d, *J* = 8.4 Hz, 1H), 6.70 (dd, *J* = 8.4, 1.8 Hz, 1H), 6.46 (d, *J* = 1.8 Hz, 1H), 4.65 (br s, 1H), 4.58 (br s, 1H), 4.04,

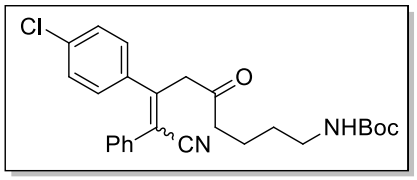
3.94 (s, 2H), 3.90 (s, 3H), 3.83 (s, 3H), 3.66 (s, 2H), 3.49 (s, 3H), 3.08 (br q, *J* = 6.4 Hz, 2H), 3.00 (br q, *J* = 6.4 Hz, 2H), 2.57 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.68–1.57 (m, 2H), 1.52–1.24 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 205.91, 204.96, 155.87, 155.83, 152.22, 150.86, 150.02, 149.49, 148.72, 148.32, 134.28, 133.64, 131.18, 129.81, 129.28, 128.99, 128.91, 128.51, 128.41, 128.22, 121.14, 120.53, 118.93, 118.85, 114.16, 114.07, 112.35, 111.23, 110.96, 110.75, 78.96, 55.98, 55.77, 55.64, 55.44, 51.83, 48.38, 42.53, 42.30, 39.91, 39.76, 29.18, 29.11, 28.25, 20.46, 20.32

IR (UATR) ν_{max} 3362, 2932, 2213, 1699, 1493, 1367, 1250, 1168, 1093, 1014, 834, 765, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{28}H_{34}N_2Na_1O_5$ $(M+Na)^+$ 501.2360, found 501.2344.

tert-Butyl 7-(4-chlorophenyl)-8-cyano-5-oxo-8-phenyloct-7-enylcarbamate (6k)



93% yield, yellow oil

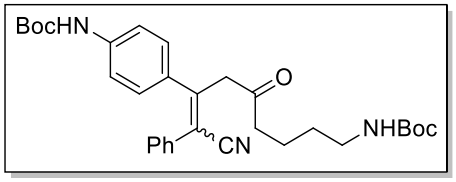
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 47:53) 7.47–7.33 (m, 9H), 7.22–7.10 (m, 7H), 7.00 (d, *J* = 8.6 Hz, 2H), 4.76 (br s, 1H), 4.69 (br s, 1H), 4.01 (s, 2H), 3.65 (s, 2H), 3.10 (br q, *J* = 6.3 Hz, 2H), 3.00 (br q, *J* = 6.3 Hz, 2H), 2.56 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.0 Hz, 2H), 1.67–1.53 (m, 2H), 1.43 (s, 9H), 1.42 (s, 9H), 1.50–1.25 (m, 6H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 47:53) 205.55, 204.55, 155.78, 151.46, 149.92, 137.34, 136.20, 135.18, 134.54, 133.51, 132.63, 129.71, 129.18, 129.14, 129.07, 128.88, 128.76, 128.60, 128.48, 128.34, 128.23, 118.21, 118.14, 115.88, 115.62, 78.79, 51.71, 48.29, 42.39, 42.32, 39.74, 39.58, 29.02, 28.96, 28.16, 20.34, 20.20

IR (UATR) ν_{max} 3363, 2932, 2213, 1703, 1510, 1493, 1366, 1249, 1167, 1093, 833, 764, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{26}H_{29}Cl_1N_2Na_1O_3$ $(M+Na)^+$ 475.1759, found 475.1747.

tert-Butyl 7-{4-(_N-tert_-butoxycarbonyl)aminophenyl}-8-cyano-5-oxo-8-phenyl-oct-7-enyl carbamate (6l)



92% yield, white foam

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 57:43) 7.43 (s, 4H), 7.43–7.35 (m, 5H), 7.22 (d, *J* = 8.7 Hz, 2H), 7.22–7.14 (m, 5H), 6.97 (d, *J* = 8.7 Hz, 2H), 6.78 (br s, 1H), 6.65 (br s, 1H), 4.60 (br s,

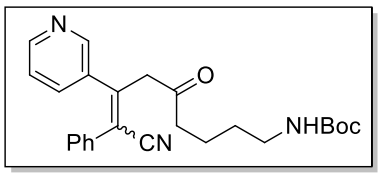
1H), 4.55 (br s, 1H), 4.01 (s, 2H), , 3.65 (s, 2H), 3.07 (br q, *J* = 6.4 Hz, 2H), 3.00 (br q, *J* = 6.4 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.67–1.24 (m, 8H), 1.52 (s, 9H), 1.49 (s, 9H), 1.43 (s, 18H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 57:43) 205.88, 204.92, 155.89, 155.86, 152.51, 152.39, 152.23, 150.74, 139.79, 139.17, 134.13, 133.25, 132.85, 131.61, 129.30, 129.25, 128.95, 128.85, 128.50, 128.43, 128.30, 128.21, 118.80, 118.78, 118.18, 117.90, 114.40, 114.11, 80.52, 78.85, 51.92, 48.27, 42.53, 42.26, 39.88, 39.74, 29.07, 29.01, 28.23, 28.12, 28.08, 20.41, 20.28

IR (UATR) ν_{max} 3343, 2977, 2212, 1708, 1590, 1520, 1234, 1155, 1052, 840, 765, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{31}H_{39}N_3Na_1O_5$ $(M+Na)^+$ 556.2782, found 556.2807.

***tert*-Butyl 8-cyano-5-oxo-8-phenyl-7-(pyridin-3-yl)oct-7-enylcarbamate (6m)**



79% yield, yellow oil

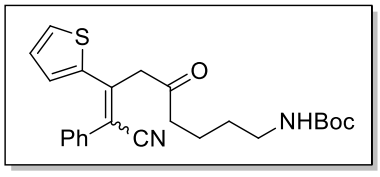
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 47:53) 8.71 (d, *J* = 1.8 Hz, 1H), 8.62 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.44 (dd, *J* = 4.8, 1.5 Hz, 1H), 8.29 (d, *J* = 1.7 Hz, 1H), 7.88 (dt, *J* = 8.0, 1.8 Hz, 1H), 7.46–7.33 (m, 7H), 7.22–7.14 (m, 6H), 4.91 (br s, 1H), 4.85 (br s, 1H), 4.06 (s, 2H), 3.70 (s, 2H), 3.09 (br q, *J* = 6.4 Hz, 2H), 3.00 (br q, *J* =6.3 Hz, 2H), 2.58 (t, *J* = 7.10 Hz, 2H), 2.31 (t, *J* = 7.1 Hz, 2H), 1.68–1.28 (m, 8H), 1.43 (s, 9H), 1.42 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 47:53) 205.37, 204.41, 155.82, 155.78, 149.92, 149.28, 149.19, 148.66, 147.93, 147.80, 135.95, 135.62, 135.07, 133.96, 133.12, 132.24, 129.35, 129.19, 128.91, 128.69, 128.45, 128.15, 123.24, 123.00, 117.78, 117.71, 117.11, 116.95, 78.73, 51.36, 48.21, 42.36, 42.31, 39.69, 39.54, 29.00, 28.94, 28.13, 20.35, 20.21

IR (UATR) ν_{max} 3357, 2930, 2155, 1702, 1627, 1522, 1366, 1245, 1168, 1045, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{29}N_3Na_1O_3$ $(M+Na)^+$ 442,2101, found 442.2096.

***tert*-Butyl 8-cyano-5-oxo-8-phenyl-7-(thiophen-2-yl)oct-7-enylcarbamate (6n)**



97% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 46:54) 7.69 (dd, *J* = 2.9, 1.4 Hz, 1H), 7.43–7.33 (m, 7H), 7.31–7.22 (m, 5H), 7.13 (dd, *J* = 2.9, 1.4 Hz, 1H), 7.10 (dd, *J* = 5.0, 2.9 Hz, 1H), 6.58 (dd, *J* = 5.0, 1.4 Hz, 1H), 4.65 (br s, 1H), 4.60 (br s, 1H), 4.02 (s, 2H), 3.64 (s, 2H), 3.08 (br q, *J* = 6.3 Hz,

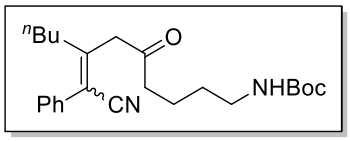
2H), 3.01 (br q, *J* = 6.3 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 2.32 (t, *J* = 7.1 Hz, 2H), 1.69–1.57 (m, 2H), 1.55–1.30 (m, 6H), 1.43 (s, 18H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 46:54) 205.82, 204.97, 155.80, 146.06, 145.30, 138.83, 137.96, 134.11, 133.49, 129.05, 129.00, 128.88, 128.65, 128.52, 128.44, 127.50, 126.76, 126.68, 126.25, 126.22, 125.63, 119.01, 118.68, 114.17, 112.85, 78.83, 51.70, 48.15, 42.21, 41.99, 39.81, 39.66, 29.02, 28.21, 20.40, 20.28

IR (UATR) ν_{max} 3393, 2928, 2206, 1708, 1513, 1366, 1244, 1167, 1045, 768, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{28}N_2Na_1O_3S_1$ $(M+Na)^+$ 447.1713, found 447.1709.

***tert*-Butyl 8-cyano-5-oxo-8-phenyl-7-butyloct-7-enylcarbamate (6o)**



83% yield, yellow oil

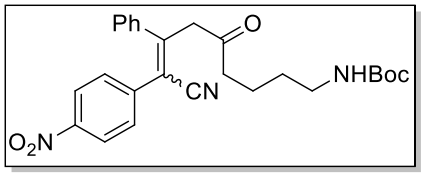
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 27:73) 7.42–7.29 (m, 5H), 7.25–7.20 (m, 5H), 4.62 (br s, 1H), 4.56 (br s, 1H), 3.69 (s, 2H), 3.31 (s, 2H), 3.14 (br q, *J* = 6.4 Hz, 2H), 3.07 (br q, *J* = 6.4 Hz, 2H), 2.63 (t, *J* = 7.0 Hz, 2H), 2.58 (dd, *J* = 8.0, 7.0 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 2.24 (dd, *J* = 8.0, 7.0 Hz, 2H), 1.73–1.13 (m, 8H), 1.44 (s, 18H), 0.92 (t, *J* = 7.1 Hz, 3H), 0.79 (t, *J* = 7.2 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 27:73) 205.84, 204.98, 155.81, 155.78, 155.08, 154.96, 133.56, 133.13, 128.66, 128.59, 128.52, 128.41, 128.36, 118.22, 117.78, 114.31, 113.90, 78.74, 48.47, 45.55, 42.26, 39.79, 39.65, 36.38, 32.56, 29.64, 29.38, 29.07, 28.14, 22.26, 22.20, 20.43, 20.34, 13.58, 13.36

IR (UATR) ν_{max} 3374, 2933, 2131, 1709, 1511, 1366, 1249, 1169, 766, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{34}N_2Na_1O_3$ $(M+Na)^+$ 421.2462, found 421.2465.

***tert*-Butyl 8-cyano-8-(4-nitrophenyl)-5-oxo-7-phenyloct-7-enylcarbamate (6p)**



68% yield, yellow oil

^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 65:35) 8.30 (d, *J* = 8.8 Hz, 2H), 8.03 (d, *J* = 8.8 Hz, 2H), 7.66 (d, *J* = 8.8 Hz, 2H), 7.53–7.42 (m, 5H), 7.35–7.22 (m, 5H), 7.05 (dd, *J* = 7.6, 1.6 Hz, 2H),

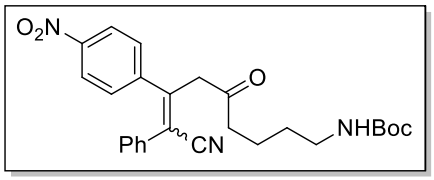
4.72 (br s, 1H), 4.66 (br s, 1H), 4.10 (s, 2H), 3.70 (s, 2H), 3.09 (br q, *J* = 6.3 Hz, 2H), 3.00 (br q, *J* = 6.4 Hz, 2H), 2.59 (t, *J* = 7.1 Hz, 2H), 2.35 (t, *J* = 7.1 Hz, 2H), 1.70–1.58 (m, 2H), 1.53–1.38 (m, 4H), 1.43 (s, 9H), 1.42 (s, 9H), 1.38–1.27 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 65:35) 205.29, 204.07, 155.81, 154.96, 147.92, 147.02, 140.14, 139.62, 138.21, 137.05, 130.27, 129.84, 129.72, 129.38, 128.78, 128.73, 128.04, 127.48, 124.05, 123.38, 117.50, 113.52, 113.39, 78.83, 52.19, 48.39, 42.87, 42.53, 39.76, 39.56, 29.04, 28.98, 28.19, 28.17, 20.38, 20.11

IR (UATR) ν_{max} 3361, 2934, 2354, 1709, 1597, 1520, 1346, 1249, 1168, 855, 769, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{26}H_{29}N_3Na_1O_5$ $(M+Na)^+$ 486.1999, found 486.1994.

<u>*tert*-Butyl 8-cyano-7-(4-nitrophenyl)-5-oxo-8-phenyloct-7-enylcarbamate (6q)</u>



67% yield, yellow oil

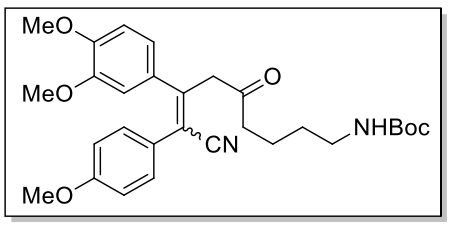
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 8.28 (d, *J* = 8.8 Hz, 2H), 8.06 (d, *J* = 8.8 Hz, 2H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.42–7.48 (m, 3H), 7.34–7.39 (m, 2H), 7.17–7.30 (m, 5H), 7.14 (dd, *J* = 7.8, 1.7 Hz, 2H), 4.68 (br s, 1H), 4.62 (br s, 1H), 4.07 (s, 2H), 3.72 (s, 2H), 3.09 (br q, *J* = 6.4 Hz, 2H), 3.01 (br q, *J* = 6.4 Hz, 2H), 2.60 (t, *J* = 7.1 Hz, 2H), 2.33 (t, *J* = 7.1 Hz, 2H), 1.71–1.58 (m, 2H), 1.56–1.32 (m, 6H), 1.43 (s, 9H), 1.42 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 48:52) 205.36, 204.43, 155.87, 150.52, 148.92, 147.95, 147.32, 145.60, 144.77, 132.97, 132.13, 129.64, 129.54, 129.23, 129.10, 129.07, 129.01, 128.62, 128.25, 126.44, 123.84, 123.59, 117.78, 117.68, 117.57, 117.35, 79.00, 51.46, 48.36, 42.49, 42.37, 39.80, 39.64, 29.16, 29.11, 28.24, 28.23, 20.44, 20.29

IR (UATR) ν_{max} 3362, 2933, 2213, 1701, 1598, 1521, 1347, 1249, 1168, 857, 763, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{26}H_{29}N_3Na_1O_5$ $(M+Na)^+$ 486.1999, found 486.1980.

<u>*tert*-Butyl 8-cyano-7-(3,4-dimethoxyphenyl)-8-(4-methoxyphenyl)-5-oxooct-7-enylcarbamate (6r)</u>



92% yield, yellow oil

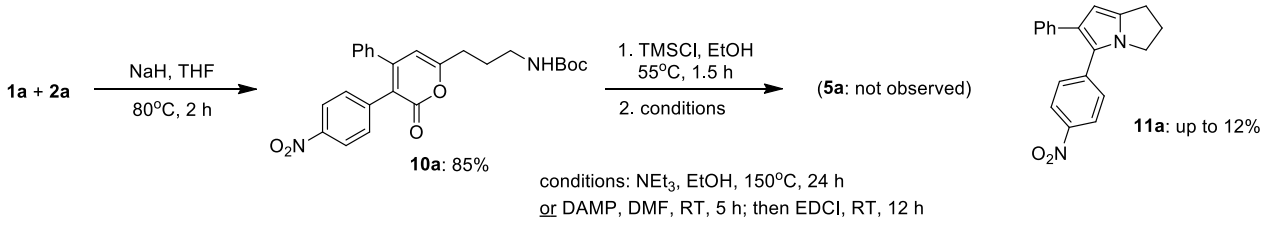
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 46:54) 7.29 (d, *J* = 8.8 Hz, 2H), 7.08 (d, *J* = 8.8 Hz, 3H), 7.02 (dd, *J* = 8.3, 2.1 Hz, 1H), 6.91 (d, *J* = 8.8 Hz, 3H), 6.86 (s, 1H), 6.75–6.64 (m, 3H), 6.50 (d, *J* = 1.8 Hz, 1H), 4.66 (br s, 1H), 4.60 (br s, 1H), 4.02 (s, 2H), 3.98 (s, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 3.81 (s, 3H), 3.80 (s, 3H), 3.72 (s, 3H), 3.65(s, 2H), 3.53 (s, 3H), 3.05 (br q, *J* = 6.4 Hz, 2H), 2.98 (br q, *J* = 6.4 Hz, 2H), 2.54 (t, *J* = 7.1 Hz, 2H), 2.28 (t, *J* = 7.1 Hz, 2H), 1.64–1.53 (m, 2H), 1.52–1.22 (m, 6H), 1.40 (s, 18H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 46:54) 206.09, 205.13, 159.95, 159.32, 155.83, 151.35, 149.88, 149.30, 149.27, 148.66, 148.40, 131.33, 130.55, 130.13, 129.81, 126.46, 125.74, 121.10, 120.48, 119.09, 118.95, 114.22, 113.85, 113.80, 113.74, 112.12, 111.24, 110.93, 110.80, 78.92, 55.94, 55.72, 55.61, 55.49, 55.18, 55.07, 51.89, 48.40, 42.54, 42.22, 39.89, 39.75, 29.12, 28.22, 20.44, 20.30

IR (UATR) ν_{max} 3390, 2936, 2208, 1709, 1606, 1513, 1251, 1174, 1025, 836, 767 cm^{-1}

HRMS (ESI^+) calcd for $C_{29}H_{36}N_2Na_1O_6$ $(M+Na)^+$ 531.2466, found 531.2474.

4. Trial for the transformation of 2-pyrone to bicyclic 2-pyridone



Employing the reported conditions for the intramolecular lactamization for 2-pyrone **10a** gave contrasting results to our observed data, in which the pyrrolizine **11a** was formed in low yield, instead of the corresponding bicyclic 2-pyridone.

I) A 2-pyrone **10a** were prepared using literature reported methodologies.[2)]

A solution of alkynone **1a** (0.35 mmol) in THF (1.0 mL) were added to a mixture of active methylene (**2a)** (1.1 equiv.) and NaH (0.25 equiv.) in THF (1.0 mL) at room temperature. The reaction was further stirred at refluxing for 5 h., then, cooled down to room temperature and neutralized with sat. NH_4Cl solution. The products were extracted with EtOAc. The combined organic layers were washed with water, dried over Na_2SO_4, and the solvent was concentrated under reduced pressure to obtain crude product which was purified by silica gel column chromatography using hexanes and increasing proportion of EtOAc as eluents to afford 2-pyrone **10a**.

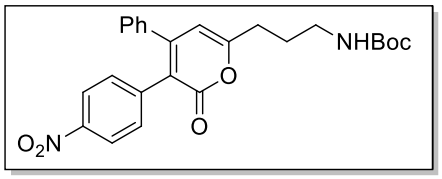
II) Trial for transformation of 2-pyrone **10a** to the corresponding 2-pyridone **5a** was performed using modified procedures according to literatures.[3-5)]

Under thermal base condition: In a round-bottomed flask, a solution of compound **10a** (103 mg, 0.23 mmol) in ethanol (3 mL) was added trimethylsilyl chloride (5 equiv.) at room temperature and

heated at 55°C for 1.5 h. The reaction was cooled down to room temperature and concentrated under reduced pressure. Then, the un-purified de-Boc product (**deBoc-10a**) was transferred to a pressure tube and ethanol (3 mL) and NEt_3 (1.6 mL, 50 equiv.) were added. The mixture was heated at 150°C for 24 h. The reaction was cooled down to room temperature, diluted with water and extracted with EtOAc. The organic solvent was washed with water, dried over Na_2SO_4, and the solvent was concentrated under reduced pressure. The obtained solid was purified by column chromatography on silica gel using hexanes and EtOAc as eluents to give pyrrolizine **11a**.

Employing EDCI as carboxyl activating agent: A solution of the un-purified de-Boc product (**deBoc-10a**, from **10a** 148.5 mg, 0.33 mmol) in DMF (1 mL) was added DMAP (50.4 mg, 1.3 equiv.) and the reaction was stirred at room temperature for 5 h. After that, EDCI (62.0 mg, 1.3 equiv.) was directly added and the mixture was further stirred at room temperature for 12 h. The reaction was diluted with water and extracted with EtOAc. The combined organic phase was washed with water, dried over Na_2SO_4, and the solvent was concentrated to dryness under reduced pressure. The obtained solid was purified by column chromatography on silica gel using hexanes and EtOAc as eluents to give pyrrolizine **11a**.

6-[3-(*tert*-Butoxycarbonylamino)propyl]-3-(4-nitrophenyl)-4-phenyl-*2H*-pyran-2-one (10a)



85% yield, white solid, m.p. 145.5–147.1°C

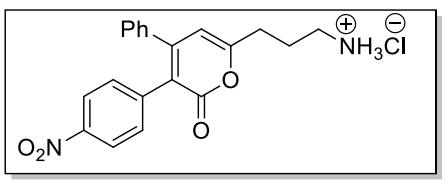
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.9 Hz, 2H), 7.33 (d, *J* = 8.9 Hz, 1H), 7.30–7.22 (m, 3H), 7.10–7.05 (m, 2H), 6.25 (s, 1H), 4.61 (br s, 1H), 3.25 (br q, *J* = 6.3 Hz, 2H), 2.64 (t, *J* =7.5 Hz, 2H), 1.95 (pent, *J* = 7.0 Hz, 2H), 1.45 (s, 9H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 164.11, 162.36, 155.93, 154.17, 146.75, 141.04, 136.47, 131.91, 129.33, 128.60, 128.47, 122.98, 119.88, 106.80, 79.30, 39.58, 31.00, 28.29, 27.39

IR (UATR) ν_{max} 3359, 2976, 1702, 1637, 1516, 1344, 1247, 1165, 949, 852, 768, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{27}N_2O_6$ $(M+H)^+$ 451.1864, found 451.1869.

6-(3-Aminopropyl)-3-(4-nitrophenyl)-4-phenyl-*2H*-pyran-2-one hydrochloride (deBoc-10a)



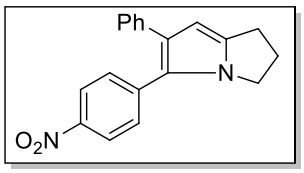
^{1}H NMR (300 MHz, $CDCl_3$+CD_3OD) δ 8.07 (d, *J* = 8.9 Hz, 2H), 7.32 (d, *J* = 8.9 Hz, 1H), 7.33–7.22 (m, 3H), 7.10–7.05 (m, 2H), 6.38 (s, 1H), 3.11 (t, *J* = 7.1 Hz, 2H), 2.80 (t, *J* =7.4 Hz, 2H), 2.24 (pent, *J* = 7.0 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$+CD_3OD) δ 162.79, 162.51, 154.64, 146.69, 140.69, 135.99, 131.76, 129.38, 128.50, 128.37, 122.89, 120.05, 107.50, 38.68, 30.39, 24.35

IR (UATR) ν_{max} 3392, 2924, 1702, 1635, 1598, 1519, 1346, 1109, 946, 853, 771, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{19}N_2O_4$ $(M+H)^+$ 351.1339, found 351.1339.

5-(4-Nitrophenyl)-6-phenyl-2,3-dihydro-*1H*-pyrrolizine (11a)



up to 12% yield, brown foam

^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, *J* = 9.0 Hz, 2H), 7.30 (d, *J* = 9.0 Hz, 2H), 7.20–7.10 (m, 5H), 6.02 (s, 1H), 3.98 (t, *J* = 7.0 Hz, 2H), 2.90 (t, *J* = 7.2 Hz, 2H), 2.49 (tt, *J* = 7.2, 7.0 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 145.51, 139.90, 139.83, 136.59, 129.65, 128.74, 128.54, 128.50, 126.13, 123.82, 122.64, 102.30, 46.82, 27.47, 24.50

IR (UATR) ν_{max} 2923, 1592, 1513, 1340, 1325, 1109, 852, 761, 703 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{17}N_2O_2$ $(M+H)^+$ 305.1285, found 305.1295.

5. General procedure for the synthesis of amidine 5c and bicyclic 2-pyridones 5/7

*5.1 General procedure for the synthesis of amidine **5c***

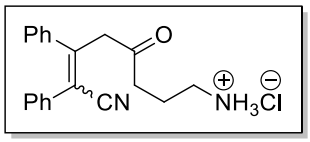
In a round-bottomed flask, a solution of Michael products **3** (0.2 mmol) in ethanol (3 mL) was added trimethylsilyl chloride (5 equiv.) at room temperature and then, the mixture was heated at 55 ^{o}C for 1.5 h. The reaction was cooled down to room temperature and concentrated under reduced pressure. Then, the mixture was added CH_2Cl_2 (10 mL), silica gel (3 g) and stirred at room temperature for 3 h. After that, the solid suspension was filtered out though a paper pad and successively washed with a solvent mixture of 10% methanol in CH_2Cl_2. The combined filtrate was concentrated under reduced pressure. The obtained solid was purified by column chromatography on silica gel using hexanes and an increasing proportion of EtOAc as eluents to afford **5c**.

*5.2 General procedure for the synthesis of bicyclic 2-pyridones **5/7***

In a pressure tube, a solution of compound **3** (0.2 mmol) in ethylene glycol (3 mL) was added trimethylsilyl chloride (5 equiv.) at room temperature and heated at 55^{o}C for 1.5 h. Then, the reaction was cooled down to room temperature, 30% aq. KOH solution (3 mL) was added dropwise and the mixture was heated at 190^{o}C for 2 h. The reaction was cooled down under ice-bath, diluted

with water and extracted with EtOAc. The combined organic part was washed successively with water, dried over Na_2SO_4, and the solvent was concentrate under reduced pressure. The obtained solid was purified by the combined techniques of crystallization from EtOAc and column chromatography on silica gel using hexanes and EtOAc as eluents to afford the desired 2-pyridones. Note: Only intermediate **4c**, from Michael adduct **3c**, was characterized.

7-Cyano-4-oxo-6,7-diphenylhept-6-enylamonium chloride (4c)



Quantitative yield, yellow solid, m.p. 157.2–158.9°C

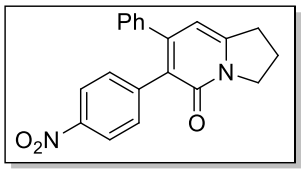
^{1}H NMR (300 MHz, $CDCl_3$) δ (isomeric ratio 58:42) 8.20 (br s, 3H), 7.70–7.00 (m, 20H), 4.06 (br s, 2H), 3.70, (br s, 2H), 2.98 (br s, 2H), 2.86 (br s, 2H), 2.74 (br s, 2H), 2.43 (br s, 2H), 2.02 (br s, 2H), 1.87 (br s, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ (isomeric ratio 58:42) 205.05, 204.18, 152.58, 151.44, 138.86, 137.75, 133.90, 133.05, 129.31, 129.17, 129.08, 129.01, 128.77, 128.65, 128.47, 128.40, 128.34, 128.22, 127.90, 127.86, 118.68, 118.64, 115.28, 115.13, 52.08, 48.44, 39.86, 39.76, 39.00, 38.94, 21.21, 21.09

IR (UATR) ν_{max} 3392, 2923, 2213, 1716, 1602, 1493, 1445, 1310, 1074, 763, 734, 697 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{20}H_{21}N_2O_1$ $(M+H)^+$ 305.1648, found 305.1642.

6-(4-Nitrophenyl)-7-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5a)



85% yield, yellow solid, m.p. 200.8–202.0°C

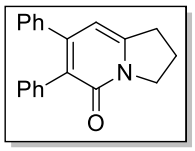
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03 (d, *J* = 8.9 Hz, 2H), 7.32 (d, *J* = 8.9 Hz, 2H), 7.25–7.19 (m, 3H), 7.08–7.03 (m, 2H), 6.29 (s, 1H), 4.25 (t, *J* = 7.3 Hz, 2H), 3.19 (t, *J* = 7.7 Hz, 2H), 2.29 (tt, *J* = 7.7, 7.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.61, 151.88, 149.98, 146.22, 143.34, 138.99, 132.28, 128.79, 128.32, 128.12, 124.22, 122.68, 103.96, 49.28, 31.99, 21.32

IR (UATR) ν_{max} 3058, 2928, 1643, 1597, 1513, 1342, 852, 770, 707 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{20}H_{17}N_2O_3$ $(M+H)^+$ 333.1234, found 333.1237.

6,7-Diphenyl-2,3-dihydroindolizin-5(*1H*)-one (5b)



81% yield, white solid, m.p. 213.3–213.7°C

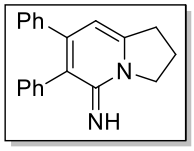
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20–7.05 (m, 10H), 6.24 (s, 1H), 4.23 (t, *J* = 7.2 Hz, 2H), 3.15 (t, *J* = 7.8 Hz, 2H), 2.25 (tt, *J* = 7.8, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.32, 150.62, 148.32, 139.85, 135.65, 131.18, 128.86, 127.81, 127.43, 127.35, 126.60, 126.48, 103.71, 49.07, 31.76, 21.34

IR (UATR) ν_{max} 2924, 1643, 1582, 1528, 1440, 1234, 1071, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{20}H_{18}N_1O_1$ $(M+H)^+$ 288.1383, found 288.1376.

6,7-Diphenyl-2,3-dihydroindolizin-5(*1H*)-imine (5c)



Yellow solid, m.p. 201.7–203.5°C;

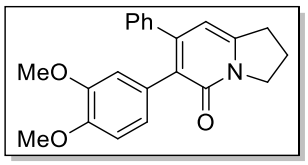
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.00 (m, 10H), 5.86 (s, 1H), 4.12 (t, *J* = 7.2 Hz, 2H), 3.04 (t, *J* = 7.7 Hz, 2H), 2.24 (tt, *J* = 7.7, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 159.59, 148.14, 145.67, 140.24, 136.41, 130.97, 128.65, 128.59, 127.68, 127.15, 127.01, 125.11, 100.02, 49.76, 31.33, 21.34

IR (UATR) ν_{max} 3327, 1636, 1557, 1516, 1239, 1014, 768, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{20}H_{19}N_2$ $(M+H)^+$ 287.1543, found 287.1557.

6-(3,4-Dimethoxyphenyl)-7-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5d)



65% yield, white solid, m.p. 145.1–146.0°C

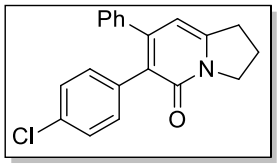
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20–7.07 (m, 5H), 6.78 (dd, *J* = 8.3, 1.9 Hz, 1H), 6.70 (d, *J* = 8.3 Hz, 1H), 6.62 (d, *J* = 1.9 Hz, 1H), 6.24 (s, 1H), 4.23 (t, *J* = 7.2 Hz, 2H), 3.81 (s, 3H), 3.60 (s, 3H), 3.14 (t, *J* = 7.6 Hz, 2H), 2.24 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.42, 150.44, 148.00, 147.85, 147.57, 140.16, 128.73, 127.97, 127.92, 127.28, 126.13, 123.89, 114.75, 110.39, 103.77, 55.60, 55.49, 49.10, 31.73, 21.38

IR (UATR) ν_{max} 2935, 1638, 1579, 1526, 1464, 1249, 1026, 727 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{22}H_{22}N_1O_3$ $(M+H)^+$ 348.1594, found 348.1607.

6-(4-Chorophenyl)-7-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5e)



78% yield, white solid, m.p. 231.0–231.9°C

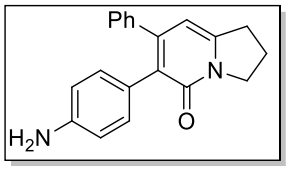
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23–7.05 (m, 9H), 6.24 (s, 1H), 4.22 (t, *J* = 7.2 Hz, 2H), 3.15 (t, *J* = 7.6 Hz, 2H), 2.25 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.14, 150.90, 148.74, 139.60, 134.22, 132.64, 132.38, 128.86, 128.09, 127.75, 127.64, 125.32, 103.77, 49.15, 31.86, 21.39

IR (UATR) ν_{max} 3053, 2927, 1640, 1582, 1525, 1088, 845, 700 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{20}H_{17}Cl_1N_1O_1$ $(M+H)^+$ 322.0993, found 322.0989.

6-(4-Aminophenyl)-7-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5f)



59% yield, brown solid, m.p. 275.0–276.2°C;

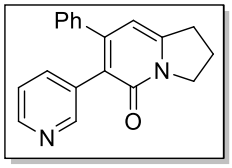
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.08 (m, 5H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.49 (d, *J* = 8.4 Hz, 2H), 6.20 (s, 1H), 4.21 (t, *J* = 7.3 Hz, 2H), 3.53 (br s, 2H), 3.12 (t, *J* = 7.7 Hz, 2H), 2.23 (tt, *J* = 7.7, 7.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.74, 149.86, 147.49, 144.89, 140.42, 132.19, 128.96, 127.89, 127.17, 126.68, 125.72, 114.48, 103.73, 49.06, 31.76, 21.46

IR (UATR) ν_{max} 3402, 3339, 3240, 2958, 1642, 1588, 1533, 1237, 770, 698 cm^{-1}

HRMS (ESI$^+$) calcd for $C_{20}H_{18}N_2Na_1O_1$ $(M+Na)^+$ 325.1311, found 325.1317.

7-Phenyl-6-(pyridin-3-yl)-2,3-dihydroindolizin-5(*1H*)-one (5g)



65% yield, yellow solid, m.p. 199.4–200.1°C

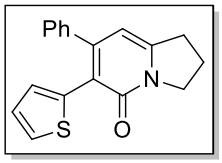
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 4.8, 1.6 Hz, 1H), 8.26 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.59 (dt, *J* = 7.9, 1.8 Hz, 1H), 7.25–7.18 (m, 3H), 7.15 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.09–7.03 (m, 2H), 6.28 (s, 1H), 4.24 (t, *J* = 7.2 Hz, 2H), 3.18 (t, *J* = 8.0 Hz, 2H), 2.28 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.16, 151.87, 151.76, 149.38, 147.46, 139.21, 138.71, 131.82, 128.95, 128.27, 127.95, 123.01, 122.47, 103.92, 49.23, 31.95, 21.420

IR (UATR) ν_{max} 2929, 1637, 1592, 1373, 1239, 1023, 768 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{17}N_2O_1$ $(M+H)^+$ 289.1335, found 289.1334.

7-Phenyl-6-(thiophen-2-yl)-2,3-dihydroindolizin-5(*1H*)-one (5h)



78% yield, white solid, m.p. 172.2–172.9°C

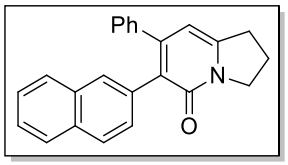
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.18 (m, 6H), 6.78 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.65 (dd, *J* = 3.7, 1.1 Hz, 1H), 6.20 (s, 1H), 4.26 (t, *J* = 7.2 Hz, 2H), 3.15 (t, *J* = 7.6 Hz, 2H), 2.26 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 160.62, 150.71, 147.89, 140.57, 136.38, 129.03, 128.36, 128.35, 127.81, 125.99, 125.54, 119.62, 104.31, 49.31, 31.80, 21.38

IR (UATR) ν_{max} 2925, 1637, 1588, 1228, 768, 698 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{16}N_1O_1S_1$ $(M+H)^+$ 294.0947, found 294.0950

6-(Naphthalen-2-yl)-7-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5i)



85% yield, white solid, m.p. 175.4–176.1°C

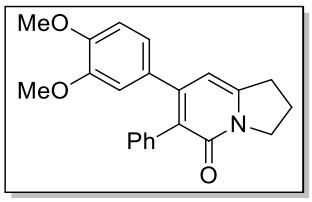
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74–7.62 (m, 3H), 7.60 (d, *J* = 8.5 Hz, 1H), 7.41–7.31 (m, 2H), 7.19 (dd, *J* = 8.5, 1.6 Hz, 1H), 7.15–7.06 (m, 5H), 6.28 (s, 1H), 4.25 (t, *J* = 7.2 Hz, 2H), 3.17 (t, *J* = 7.6 Hz, 2H), 2.26 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.49, 150.91, 148.49, 139.85, 133.25, 133.12, 132.23, 130.49, 129.34, 128.93, 128.02, 127.98, 127.47, 127.37, 126.77, 126.39, 125.49, 125.29, 103.88, 49.15, 31.85, 21.41

IR (UATR) ν_{max} 3053, 1637, 1577, 1525, 1437, 1221, 830, 744 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{20}N_1O_1$ $(M+H)^+$ 338.1539, found 338.1547.

7-(3,4-Dimethoxyphenyl)-6-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5j)



78% yield, white solid, m.p. 127.0–127.9°C

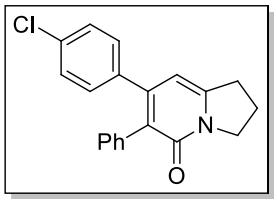
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25–7.09 (m, 5H), 6.81 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.75 (d, *J* = 8.3 Hz, 1H), 6.44 (d, *J* = 2.0 Hz, 1H), 6.28 (s, 1H), 4.22 (t, *J* = 7.2 Hz, 2H), 3.84 (s, 3H), 3.47 (s, 3H), 3.16 (t, *J* = 7.6 Hz, 2H), 2.25 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.35, 150.00, 148.35, 148.28, 147.88, 136.19, 132.07, 131.06, 127.68, 126.44, 126.13, 121.17, 112.96, 110.43, 103.47, 55.63, 55.40, 48.99, 31.75, 21.36

IR (UATR) ν_{max} 2935, 1639, 1590, 1514, 1257, 1137, 1024, 807, 746, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{22}H_{21}N_1Na_1O_3$ $(M+Na)^+$ 370.1414, found 370.1404

7-(4-Chorophenyl)-6-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5k)



73% yield, white solid, m.p. 255.0–256.0°C

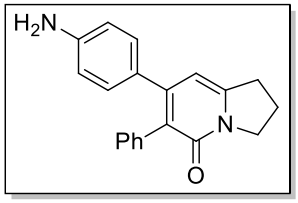
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23–7.09 (m, 7H), 7.00 (d, *J* = 8.6 Hz, 2H), 6.19 (s, 1H), 4.20 (t, *J* = 7.2 Hz, 2H), 3.13 (t, *J* = 7.6 Hz, 2H), 2.23 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.20, 149.22, 148.61, 138.32, 135.37, 133.41, 131.12, 130.25, 128.11, 127.66, 127.72, 103.25, 49.11, 31.81, 21.36

IR (UATR) ν_{max} 2927, 1640, 1577, 1492, 1239, 1090, 830, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{17}Cl_1N_1O_1$ $(M+H)^+$ 322.0993, found 322.1001.

7-(4-Aminophenyl)-6-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5l)



65% yield, yellow solid, m.p. 233.4–234.4°C

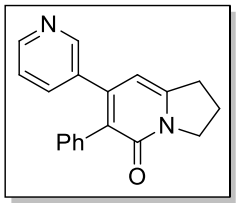
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.11 (m, 5H), 6.87 (d, *J* = 8.4 Hz, 2H), 6.47 (d, *J* = 8.4 Hz, 2H), 6.24 (s, 1H), 4.20 (t, *J* = 7.2 Hz, 2H), 3.71 (br s, 2H), 3.13 (t, *J* = 7.6 Hz, 2H), 2.24 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.53, 150.59, 148.00, 145.88, 136.33, 131.31, 130.25, 129.74, 127.58, 126.34, 125.85, 114.37, 103.82, 49.01, 31.79, 21.44

IR (UATR) ν_{max} 3411, 3340, 3233, 2927, 1634, 1609, 1570, 1521, 1307, 823, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{18}N_2Na_1O_1$ $(M+Na)^+$ 325.1311, found 325.1322.

6-Phenyl-7-(pyridin-3-yl)- 2,3-dihydroindolizin-5(*1H*)-one (5m)



68% yield, yellow solid, m.p. 220.5–221.5°C

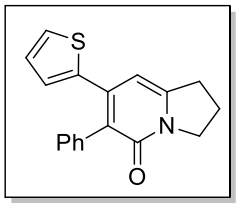
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.42 (dd, *J* = 4.9, 1.5 Hz, 1H), 8.40 (d, *J* = 2.0 1H), 7.31 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.23–7.10 (m, 5H), 7.08 (dd, *J* = 7.9, 4.9 Hz, 1H), 6.22 (s, 1H), 4.24 (t, *J* = 7.3 Hz, 2H), 3.18 (t, *J* = 7.6 Hz, 2H), 2.27 (tt, *J* = 7.6, 7.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.13, 149.41, 149.04, 148.55, 146.92, 136.30, 135.68, 134.92, 131.21, 127.81, 127.53, 127.02, 122.64, 102.96, 49.21, 31.90, 21.38

IR (UATR) ν_{max} 3030, 1638, 1578, 1527, 1439, 1371, 1231, 1023, 791, 705 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{17}N_2O_1$ $(M+H)^+$ 289.1335, found 289.1346

6-Phenyl-7-(thiophen-2-yl)-2,3-dihydroindolizin-5(*1H*)-one (5n)



80% yield, white solid, m.p. 222.0–223.0°C

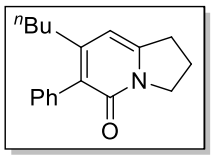
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.15 (m, 5H), 7.08 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.02 (dd, *J* = 3.0, 1.2 Hz, 1H), 6.65 (dd, *J* = 5.0, 1.2 Hz, 1H), 6.31 (s, 1H), 4.20 (t, *J* = 7.2 Hz, 2H), 3.14 (t, *J* = 7.6 Hz, 2H), 2.24 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.44, 148.36, 144.76, 140.13, 136.21, 130.82, 128.27, 127.85, 126.90, 126.39, 124.81, 124.73, 103.03, 49.03, 31.80, 21.42

IR (UATR) ν_{max} 2925, 1644, 1606, 1238, 1082, 781, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{16}N_1O_1S_1$ $(M+H)^+$ 294.0947, found 294.0953.

7-(*n*-Butyl)-6-phenyl-2,3-dihydroindolizin-5(*1H*)-one (5o)



66% yield, white solid, m.p. 121.0–122.7°C

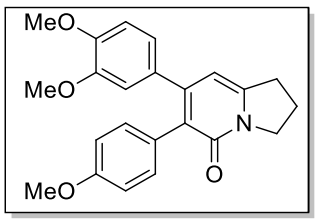
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.18 (m, 5H), 6.11 (s, 1H), 4.12 (t, *J* = 7.2 Hz, 2H), 3.06 (t, *J* = 7.7 Hz, 2H), 2.30 (dd, *J* = 8.0, 7.6 Hz, 2H), 2.16 (tt, *J* = 7.7, 7.2 Hz, 2H), 1.49–1.36 (m, 2H), 1.19 (sext, *J* = 7.3 Hz, 2H), 0.77 (t, *J* = 7.3 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.29, 152.15, 147.80, 136.18, 130.13, 127.88, 127.58, 126.75, 102.69, 48.71, 32.97, 32.03, 31.48, 22.26, 21.27, 13.58

IR (UATR) ν_{max} 2957, 1645, 1575, 1441, 1268, 1088, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{22}N_1O_1$ $(M+H)^+$ 268.1696, found 268.1702.

7-(3,4-Dimethoxyhenyl)-6-(4-methoxyphenyl)-2,3-dihydroindolizin-5(*1H*)-one (5r)[6)]



78% yield, white solid, m.p. 146.0–146.4°C

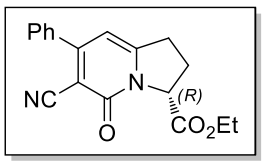
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.7 Hz, 2H), 6.82–6.72 (m, 4H), 6.49 (d, *J* = 1.6 Hz, 1H), 6.26 (s, 1H), 4.21 (t, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H), 3.53 (s, 3H), 3.13 (t, *J* = 7.6 Hz, 2H), 2.24 (tt, *J* = 7.6, 7.2 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.49, 158.09, 149.64, 148.23, 147.92, 147.85, 132.35, 132.12, 128.36, 125.71, 121.18, 113.19, 112.84, 110.45, 103.38, 55.60, 55.42, 55.02, 48.91, 31.67, 21.34

IR (UATR) ν_{max} 2927, 1639, 1574, 1511, 1464, 1241, 1025, 807, 732 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{24}N_1O_4$ $(M+H)^+$ 378.16998, found 378.1700.

(*R*)-Ethyl 6-cyano-5-oxo-7-phenyl-2,3-tetrahydroindolizine-3-carboxylate (5s)



77% yield, brown solid, m.p. 155.0–157.0°C, $[\alpha]^D_{28}$ +247.2 (*c* 1.1, MeOH), > 99.9 % ee (HPLC)

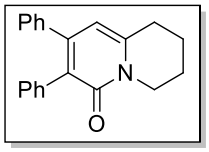
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.60–7.44 (m, 5H), 6.31 (s, 1H), 5.18 (dd, *J* = 9.6, 3.0 Hz, 1H), 4.36–4.21 (m, 2H), 3.36–3.15 (m, 2H), 2.68–2.53 (m, 1H), 2.41–2.30 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 169.20, 161.03, 159.32, 155.28, 135.90, 130.42, 128.77, 127.95, 115.66, 103.10, 99.40, 62.18, 62.06, 31.29, 25.76, 13.97

IR (UATR) ν_{max} 2983, 2219, 1742, 1651, 1599, 1518, 1448, 1377, 1196, 1019, 766, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{18}H_{16}N_2Na_1O_3$ $(M+Na)^+$ 331.1053, found 331.1062.

2,3-Diphenyl-6,7,8,9-tetrahydroquinolizin-4-one (7b)



80% yield, white solid, m.p. 188.6–189.3°C

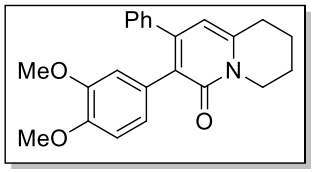
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–7.05 (m, 10H), 6.13 (s, 1H), 4.07 (t, *J* = 6.3 Hz, 2H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.01 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.85 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.77, 149.01, 145.57, 139.56, 136.14, 131.19, 128.90, 127.87, 127.51, 127.42, 126.50, 125.89, 107.46, 42.26, 28.91, 22.43, 18.81

IR (UATR) ν_{max} 2954, 1634, 1584, 1536, 1444, 1250, 1019, 767, 698 cm^{-1}

HRMS (ESI^+) calcd for $C_{21}H_{20}N_1O_1$ $(M+H)^+$ 302.1539, found 302.1530.

3-(3,4-Dimethoxyphenyl)-2-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7d)



68% yield, white solid, m.p. 158.2–158.9°C

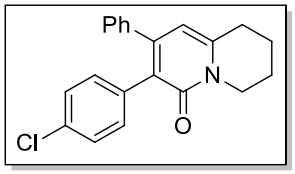
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.22–7.06 (m, 5H), 6.79 (dd, *J* = 8.3, 1.9 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 6.62 (d, *J* = 1.9 Hz, 1H), 6.12 (s, 1H), 4.08 (t, *J* = 6.3 Hz, 2H), 3.82 (s, 3H), 3.60 (s, 3H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.02 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.85 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.84, 148.85, 147.95, 147.62, 145.30, 139.91, 128.78, 128.54, 127.98, 127.35, 125.44, 123.90, 114.81, 110.50, 107.44, 55.70, 55.57, 42.27, 28.89, 22.45, 18.83

IR (UATR) ν_{max} 2948, 1635, 1575, 1535, 1443, 1260, 1139, 1027, 764, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{23}N_1Na_1O_3$ $(M+Na)^+$ 384.1570, found 384.1567.

3-(4-Chorophenyl)-2-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7e)



76% yield, white solid, m.p. 218.1–219.2°C

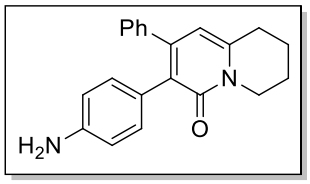
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.21–7.06 (m, 9H), 6.12 (s, 1H), 4.06 (t, *J* = 6.3 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H), 2.02 (tt, *J* = 6.5, 6.3 Hz, 2H), 1.86 (tt, *J* = 6.5, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.58, 149.29, 146.01, 139.28, 134.66, 132.63, 132.36, 128.87, 128.11, 127.78, 127.68, 124.54, 107.54, 42.35, 28.96, 22.42, 18.78

IR (UATR) ν_{max} 2949, 1634, 1574, 1534, 1253, 1090, 835, 767, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{21}H_{18}Cl_1N_1Na_1O_1$ $(M+Na)^+$ 358.0969, found 358.0960.

3-(4-Aminophenyl)-2-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7f)



59% yield, brown solid, m.p. 260.0–261.7°C;

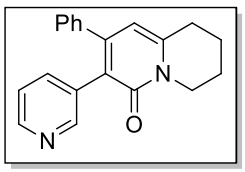
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.23–7.08 (m, 5H), 6.93 (d, *J* = 8.2 Hz, 1H), 6.51 (d, *J* = 8.2 Hz, 1H), 6.09 (s, 1H), 4.06 (t, *J* = 6.3 Hz, 2H), 3.49 (br s, 2H), 2.83 (t, *J* = 6.5 Hz, 2H), 2.00 (tt, *J* = 6.5, 6.3 Hz, 2H), 1.84 (tt, *J* = 6.5, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.15, 148.37, 144.82, 144.77, 140.05, 132.16, 128.96, 127.91, 127.22, 126.24, 125.90, 114.52, 107.55, 42.27, 28.89, 22.50, 18.88

IR (UATR) ν_{max} 3342, 3225, 2926, 1634, 1571, 1542, 1252, 1179, 835, 766, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{21}H_{20}N_2Na_1O_1$ $(M+Na)^+$ 339.1468, found 339.1478.

2-Phenyl-3-(pyridin-3-yl)-6,7,8,9-tetrahydroquinolizin-4-one (7g)



62% yield, yellow solid, m.p. 179.1–180.0°C

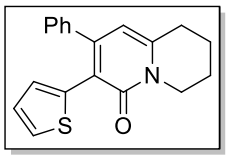
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, *J* = 4.9, 1.6 Hz, 1H), 8.27 (dd, *J* = 2.0, 0.6 Hz, 1H), 7.60 (dt, *J* = 7.9, 2.0 Hz, 1H), 7.24–7.18 (m, 3H), 7.13 (dd, *J* = 7.9, 4.9 Hz, 1H), 7.11–7.03 (m, 2H), 6.16 (s, 1H), 4.08 (t, *J* = 6.3 Hz, 2H), 2.88 (t, *J* = 6.6 Hz, 2H), 2.04 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.87 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.56, 151.83, 150.11, 147.39, 146.64, 138.86, 138.70, 132.21, 128.92(2C), 128.24(2C), 127.94, 122.46, 122.12, 107.67, 42.40, 28.98, 22.36, 18.71

IR (UATR) ν_{max} 2929, 1633, 1576, 1538, 1256, 1123, 798, 701 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{19}N_2O_1$ $(M+H)^+$ 303.1492, found 303.1506.

2-Phenyl-3-(thiophen-2-yl)-6,7,8,9-tetrahydroquinolizin-4-one (7h)



79% yield, white solid, m.p. 165.4–166.1°C

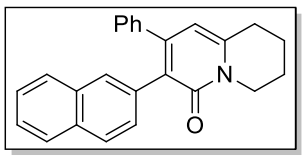
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33–7.18 (m, 6H), 6.76 (dd, *J* = 5.1, 3.7 Hz, 1H), 6.61 (dd, *J* = 3.7, 1.1 Hz, 1H), 6.07 (s, 1H), 4.09 (t, *J* = 6.3 Hz, 2H), 2.83 (t, *J* = 6.6 Hz, 2H), 2.00 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.83 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 161.96, 149.02, 145.15, 140.22, 136.71, 128.85, 128.30, 128.28, 127.76, 125.85, 125.41, 118.68, 108.12, 42.53, 28.77, 22.36, 18.69

IR (UATR) ν_{max} 2947, 1630, 1580, 1574, 1442, 1244, 844, 763, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{18}N_1O_1S_1$ $(M+H)^+$ 308.1104, found 308.1115.

3-(Naphthalen-2-yl)-2-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7i)



81% yield, white solid, m.p. 157.2–157.9°C

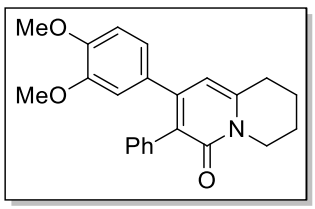
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75–7.62 (m, 3H), 7.63 (d, *J* = 8.5 Hz, 1H), 7.41–7.31 (m, 2H), 7.24 (dd, *J* = 8.5, 1.7 Hz, 1H), 7.15–7.08 (m, 5H), 6.16 (s, 1H), 4.09 (t, *J* = 6.3 Hz, 2H), 2.86 (t, *J* = 6.6 Hz, 2H), 2.02 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.85 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.89, 149.30, 145.74, 139.52, 133.72, 133.17, 132.25, 130.38, 129.38, 128.91, 128.03, 127.98, 127.47, 127.37, 126.78, 125.60, 125.44, 125.25, 107.60, 42.27, 28.93, 22.44, 18.81

IR (UATR) ν_{max} 3054, 2948, 1635, 1574, 1538, 1442, 1264, 819, 734, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{25}H_{22}N_1O_1$ $(M+H)^+$ 352.1696, found 352.1683.

2-(3,4-Dimethoxyphenyl)-3-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7j)



75% yield, white solid, m.p. 122.0–122.7°C

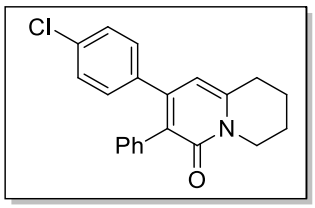
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25–7.10 (m, 5H), 6.81 (dd, *J* = 8.3, 1.9 Hz, 1H), 6.71 (d, *J* = 8.3 Hz, 1H), 6.44 (d, *J* = 1.9 Hz, 1H), 6.16 (s, 1H), 4.05 (t, *J* = 6.3 Hz, 2H), 3.82 (s, 3H), 3.46 (s, 3H), 2.84 (t, *J* = 6.6 Hz, 2H), 1.99 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.83 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.64, 148.32, 148.27, 147.83, 145.45, 136.57, 131.65, 130.95, 127.60, 126.30, 125.24, 121.07, 112.89, 110.40, 107.10, 55.56, 55.33, 42.03, 28.76, 22.27, 18.67

IR (UATR) ν_{max} 2924, 1632, 1577, 1514, 1457, 1261, 1135, 1026, 791, 702 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{24}N_1O_3$ $(M+H)^+$ 362.1751, found 362.1745.

2-(4-Chorophenyl)-3-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7k)



75% yield, white solid, m.p. 212.6–213.5°C

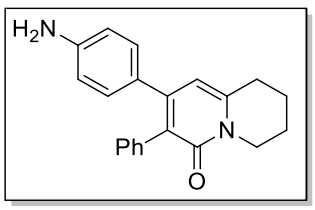
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.09 (m, 7H), 7.01 (d, *J* = 8.6 Hz, 2H), 6.07 (s, 1H), 4.06 (t, *J* = 6.3 Hz, 2H), 2.84 (t, *J* = 6.6 Hz, 2H), 2.01 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.85 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.63, 147.64, 145.87, 137.99, 135.82, 133.46, 131.09, 130.25, 128.13, 127.68, 126.69, 125.96, 106.98, 42.27, 28.90, 22.37, 18.75

IR (UATR) ν_{max} 2925, 1631, 1568, 1537, 1491, 1248, 1085, 827, 697 cm^{-1}

HRMS (ESI^+) calcd for $C_{21}H_{19}Cl_1N_1O_1$ $(M+H)^+$ 336.1150, found 336.1146.

2-(4-Aminophenyl)-3-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7l)



60% yield, yellow solid, m.p. 224.6–225.6°C

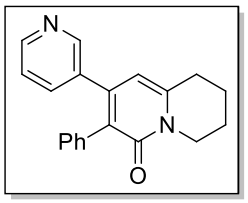
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24–7.11 (m, 5H), 6.88 (d, *J* = 8.6 Hz, 2H), 6.47 (d, *J* = 8.6 Hz, 2H), 6.12 (s, 1H), 4.05 (t, *J* = 6.3 Hz, 2H), 3.67 (br s, 2H), 2.84 (t, *J* = 6.6 Hz, 2H), 2.00 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.84 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.89, 148.89, 145.91, 145.20, 136.77, 131.25, 130.21, 129.33, 127.57, 126.27, 125.08, 114.35, 107.55, 42.14, 28.91, 22.48, 18.88

IR (UATR) ν_{max} 3337, 3225, 2926, 1636, 1607, 1571, 1524, 1374, 1283, 1182, 820, 735, 699 cm^{-1}

HRMS (ESI^+) calcd for $C_{21}H_{21}N_2O_1$ $(M+H)^+$ 317.1648, found 317.1651.

3-Phenyl-2-(pyridin-3-yl)-6,7,8,9-tetrahydroquinolizin-4-one (7m)



65% yield, yellow solid, m.p. 178.4–179.4°C

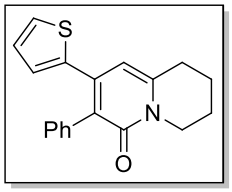
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.43 (br d, *J* = 1.7 Hz, 1H), 7.33 (dt, *J* = 8.0, 2.0 Hz, 1H), 7.26–7.11 (m, 5H), 7.10 (ddd, *J* = 8.0, 4.9, 0.7 Hz, 1H), 6.13 (s, 1H), 4.10 (t, *J* = 6.3 Hz, 2H), 2.90 (t, *J* = 6.6 Hz, 2H), 2.05 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.89 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.52, 149.41, 148.56, 146.31, 145.35, 136.28, 135.35, 135.32, 131.14, 127.80, 126.94, 126.61, 122.62, 106.65, 42.34, 28.93, 22.33, 18.68

IR (UATR) ν_{max} 2949, 1634, 1584, 1535, 1258, 1015, 767, 702 cm^{-1}

HRMS (ESI^+) calcd for $C_{20}H_{18}N_2Na_1O_1$ $(M+Na)^+$ 325.1311, found 325.1321.

3-Phenyl-2-(thiophen-2-yl)-6,7,8,9-tetrahydroquinolizin-4-one (7n)



78% yield, white solid, m.p. 189.8–190.5°C

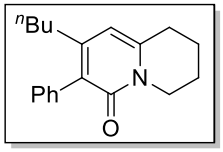
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30–7.16 (m, 5H), 7.08 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.03 (dd, *J* = 3.0, 1.3 Hz, 1H), 6.67 (dd, *J* = 5.0, 1.3 Hz, 1H), 6.20 (s, 1H), 4.05 (t, *J* = 6.3 Hz, 2H), 2.85 (t, *J* = 6.5 Hz, 2H), 2.01 (tt, *J* = 6.5, 6.3 Hz, 2H), 1.85 (tt, *J* = 6.5, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.87, 145.58, 143.17, 139.76, 136.65, 130.75, 128.23, 127.90, 126.87, 125.57, 124.87, 124.74, 106.77, 42.19, 28.91, 22.42, 18.83

IR (UATR) ν_{max} 2947, 1634, 1584, 1543, 1254, 1021, 846, 783, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{18}N_1O_1S_1$ $(M+H)^+$ 308.1104, found 308.1097.

2-(*n*-Butyl)-3-phenyl-6,7,8,9-tetrahydroquinolizin-4-one (7o)



65% yield, white solid, m.p. 104.3–105.0°C

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43–7.34 (m, 2H), 7.33–7.27 (m, 1H), 7.24–7.18 (m, 2H), 5.97 (s, 1H), 3.99 (t, *J* = 6.3 Hz, 2H), 2.79 (t, *J* = 6.6 Hz, 2H), 2.27 (dd, *J* = 8.0, 7.7 Hz, 2H), 1.96 (pent, *J* =

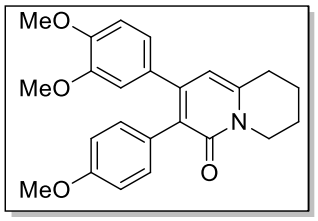
6.6 Hz, 2H), 1.82 (pent, *J* = 6.6 Hz, 2H), 1.48–1.36 (m, 2H), 1.20 (sext, *J* = 7.3 Hz, 2H), 0.78 (t, *J* = 7.3 Hz, 3H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 162.63, 150.63, 144.94, 136.57, 130.10, 127.93, 127.09, 126.73, 106.63, 41.86, 32.65, 31.96, 28.67, 22.35, 22.31, 18.77, 13.63

IR (UATR) ν_{max} 2955, 2869, 1638, 1550, 1443, 1260, 1099, 700 cm^{-1}

HRMS (ESI^+) calcd for $C_{19}H_{24}N_1O_1$ $(M+H)^+$ 282.1852, found 282.1857.

2-(3,4-Dimethoxyhenyl)-3-(4-methoxyphenyl)-6,7,8,9-tetrahydroquinolizin-4-one (7r)



75% yield, white solid, m.p. 144.2–144.9°C

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.08 (d, *J* = 8.7, 1.8 Hz, 2H), 6.83–6.72 (m, 4H), 6.49 (d, *J* = 1.8 Hz, 1H), 6.14 (s, 1H), 4.06 (t, *J* = 6.3 Hz, 2H), 3.85 (s, 3H), 3.75 (s, 3H), 3.53 (s, 3H), 2.85 (t, *J* = 6.6 Hz, 2H), 2.01 (tt, *J* = 6.6, 6.3 Hz, 2H), 1.85 (tt, *J* = 6.6, 6.3 Hz, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 163.01, 158.16, 148.34, 148.18, 148.00, 145.16, 132.16, 132.04, 128.85, 125.06, 121.21, 113.30, 112.88, 110.51, 107.25, 55.69, 55.50, 55.13, 42.17, 28.88, 22.42, 18.82

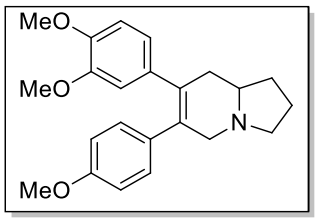
IR (UATR) ν_{max} 2949, 1634, 1574, 1509, 1464, 1242, 1139, 1024, 833, 761 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{25}N_1Na_1O_4$ $(M+Na)^+$ 414.1676, found 414.1672.

6. Synthesis of (±)-*seco*-antofine (8) and (±)-julandine (9)

General procedure for reduction of 2-pyridone: A solution of 2-pyridone **5r** or **7r** (2.0 mmol) in THF (14 mL) was added slowly to a suspension of $LiAlH_4$ (13 equiv.) and $AlCl_3$ (10 equiv.) in THF (14 mL) at 0 °C. The reaction was allowed to further stir at room temperature for 20 h. The yellow suspension was quenched with EtOH (1 mL) at 0 °C to destroy the excess reagent and poured onto ice-crashed water. The mixture was basified to pH 12 and extracted with AcOEt. The combined organic layers were washed with water, dried over Na_2SO_4, and the solvent was concentrated under reduced pressure. Crude products were purified by column chromatography on silica gel using AcOEt and an increasing proportion of MeOH as eluents to afford **8** or **9**.

(±)-*seco*-Antofine (8)[7)]



75% yield, yellow foam

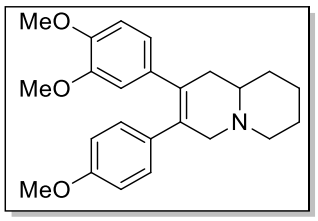
^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, *J* = 8.8 Hz, 2H), 6.72–6.65 (m, 4H), 6.47 (d, *J* = 0.9 Hz, 1H), 3.88 (d, *J* = 16.0 Hz, 1H), 3.80 (s, 3H), 3.72 (s, 3H), 3.54 (s, 3H), 3.32 (td, *J* = 8.6, 2.1 Hz, 1H), 3.11 (dd, *J* = 16.0, 3.8 Hz, 1H), 2.73 (dd, *J* = 12.9, 2.1 Hz, 1H), 2.53–2.37 (m, 2H), 2.35–2.24 (m, 1H), 2.18–2.04 (m, 1H), 2.00–1.80 (m, 2H), 1.66–1.51 (m 1H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.95, 147.82, 147.13, 134.78, 133.25, 132.51, 132.24, 130.13, 120.60, 113.33, 112.99, 110.38, 60.34, 57.40, 55.60, 55.41, 55.04, 53.95, 37.97, 30.57, 21.38

IR (UATR) ν_{max} 2925, 1607, 1510, 1464, 1246, 1169, 1028, 832, 763 cm^{-1}

HRMS (ESI^+) calcd for $C_{23}H_{28}N_1O_3$ $(M+H)^+$ 366.2064, found 366.2068.

(±)-Julandine (9)[7)]



77% yield, yellow foam

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, *J* = 8.8 Hz, 2H), 6.72–6.65 (m, 4H), 6.46 (s, 1H), 3.80 (s, 3H), 3.73 (s, 3H), 3.63 (d, *J* = 16.8 Hz, 1H), 3.53 (s, 3H), 3.16–3.01 (m, 2H), 2.60–2.29 (m, 4H), 2.18–2.07 (m, 1H), 1.90–1.69 (m, 4H), 1.43–1.32 (m, 2H)

^{13}C NMR (75 MHz, $CDCl_3$) δ 157.99, 147.87, 147.18, 134.44, 133.18, 131.38, 131.25, 130.14, 120.51, 113.38, 112.98, 110.43, 60.32, 57.89, 55.67, 55.52, 55.45, 55.12, 39.48, 33.26, 25.84, 24.32

IR (UATR) ν_{max} 2933, 1606, 1509, 1463, 1245, 1169, 1026, 833, 763 cm^{-1}

HRMS (ESI^+) calcd for $C_{24}H_{30}N_1O_3$ $(M+H)^+$ 380.2220, found 380.2233.

7. References

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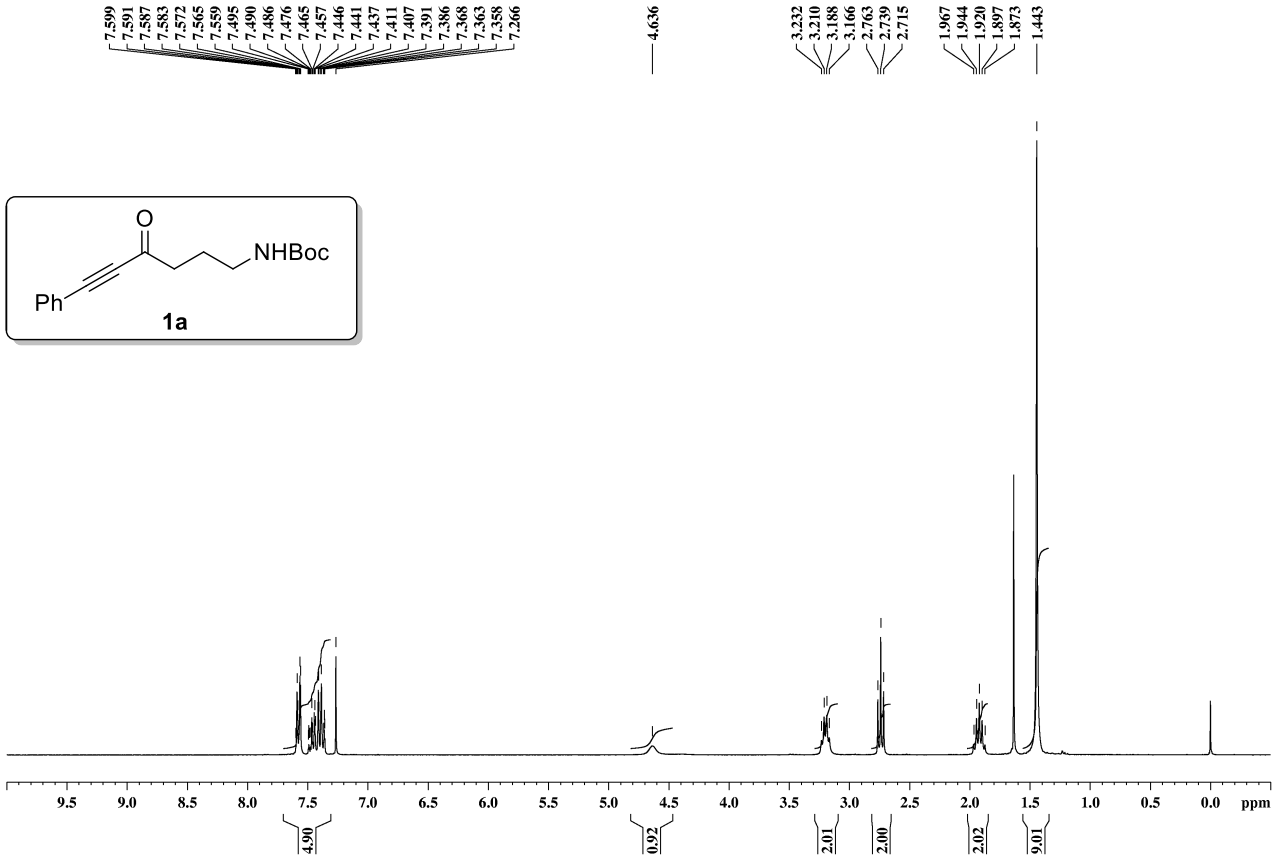
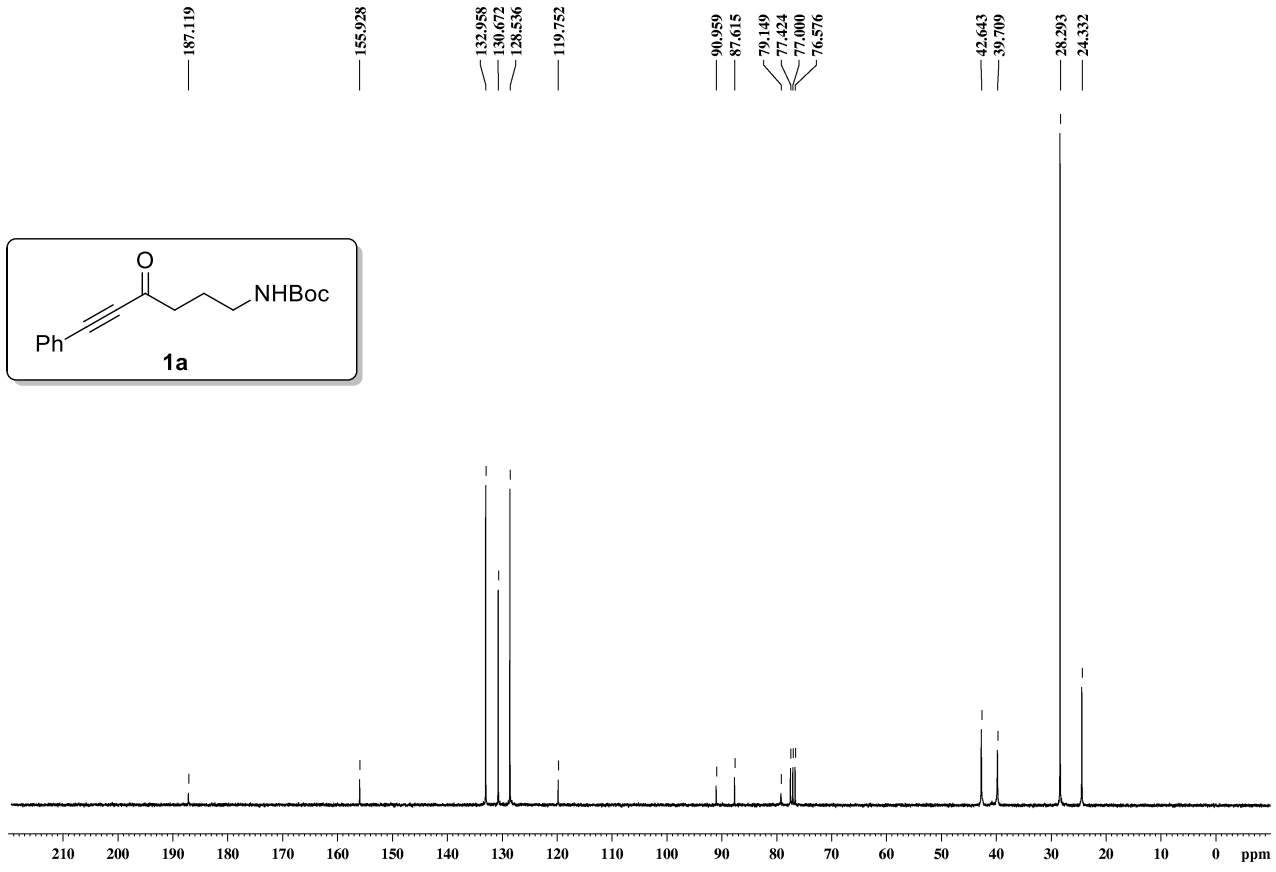
8. ^{1}H and ^{13}C NMR spectra

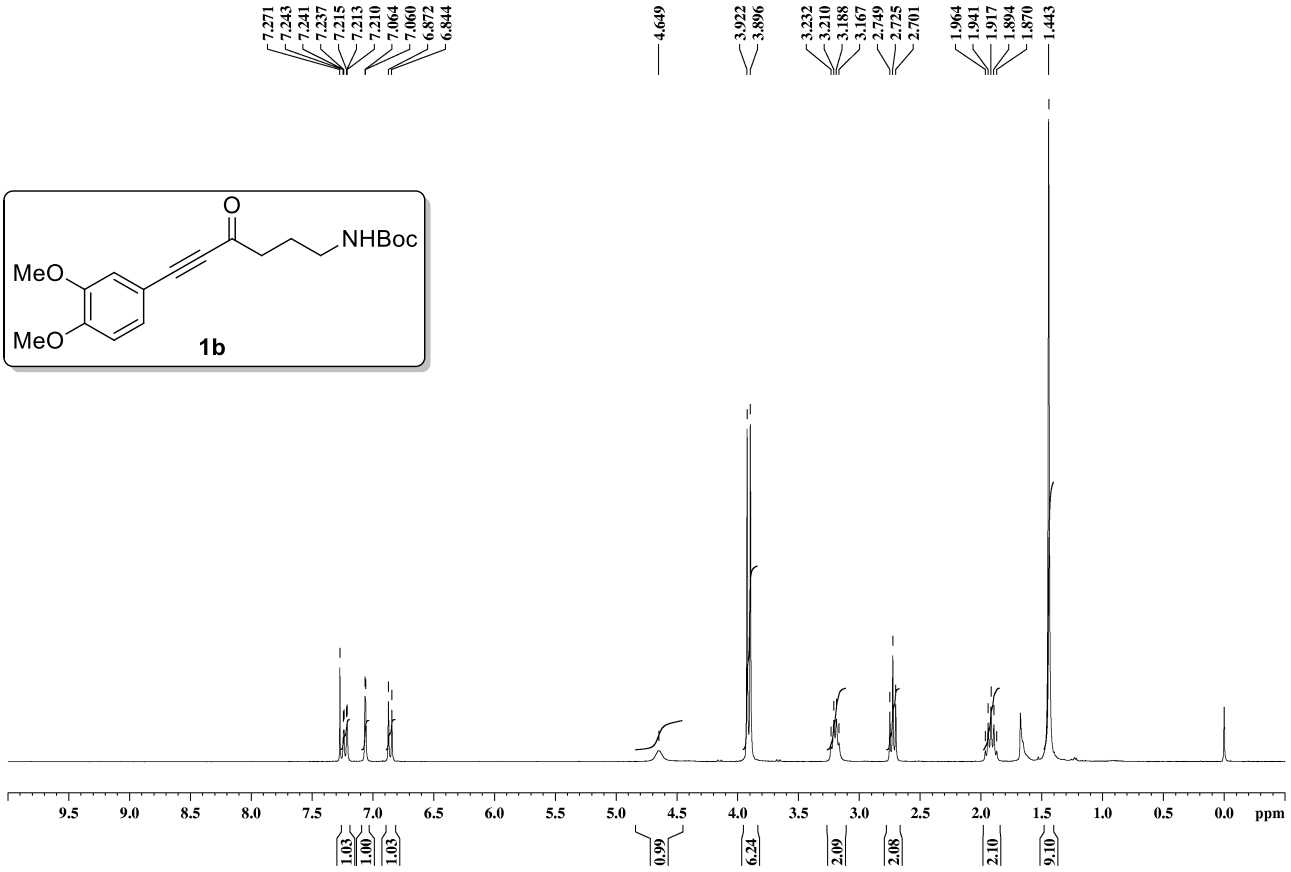
^{1}H NMR (300 MHz, $CDCl_3$); **1a**



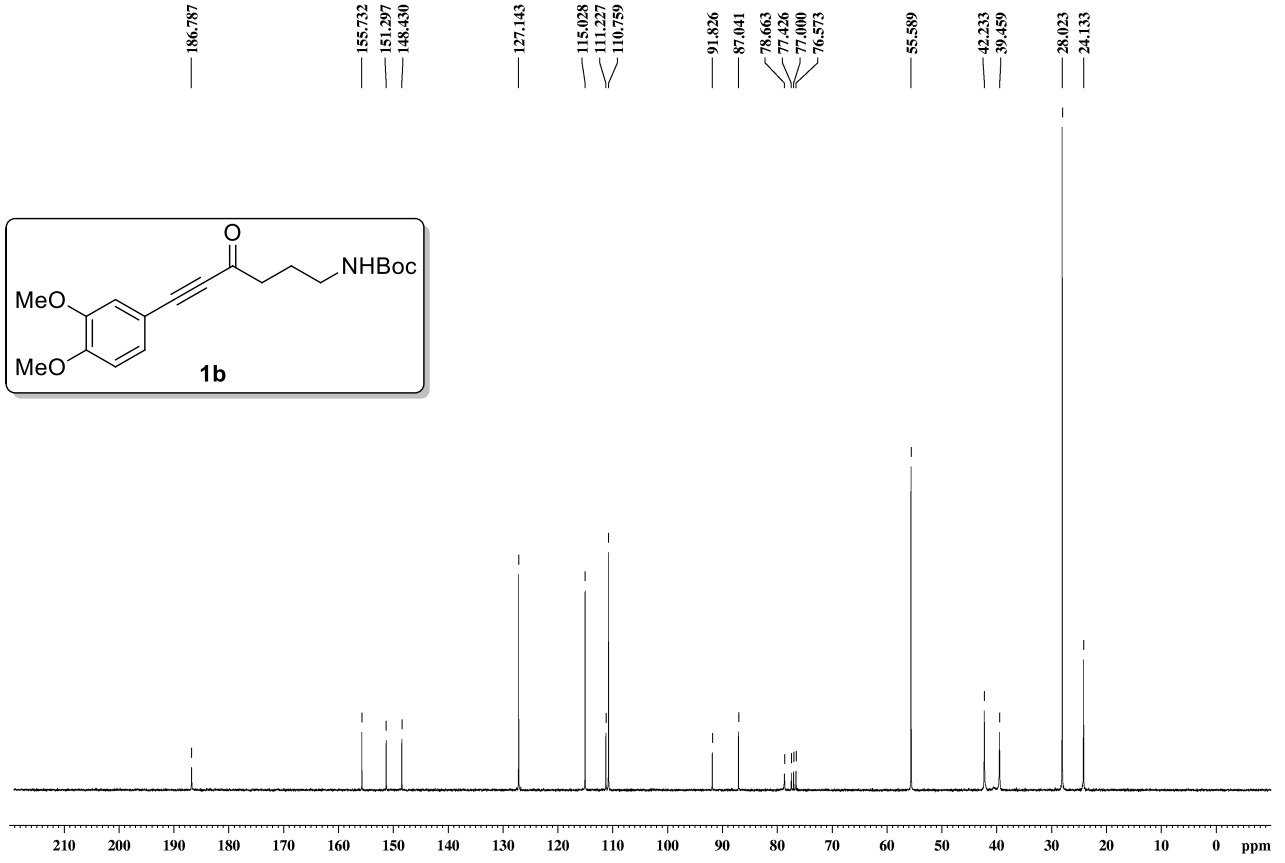
^{13}C NMR (75 MHz, $CDCl_3$); **1a**



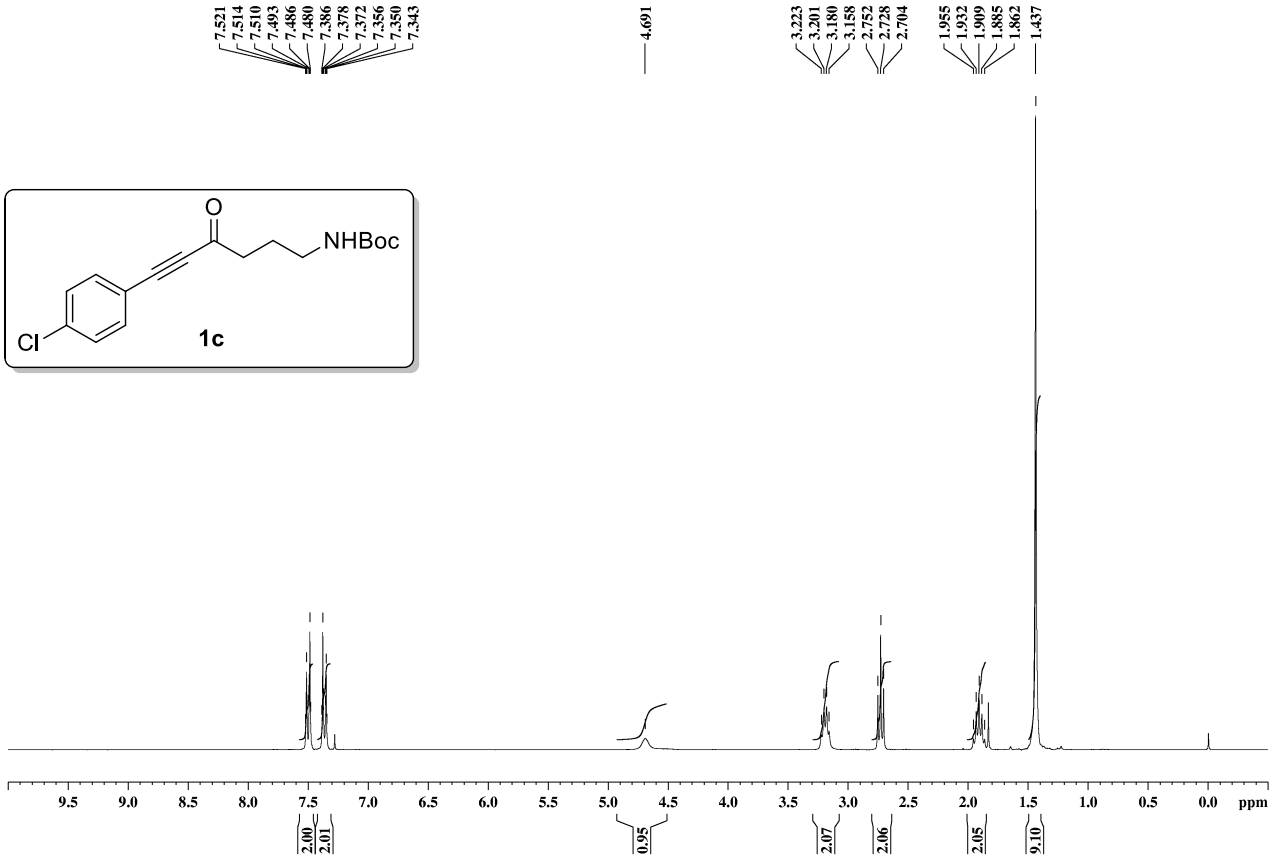
^{1}H NMR (300 MHz, $CDCl_3$); **1b**



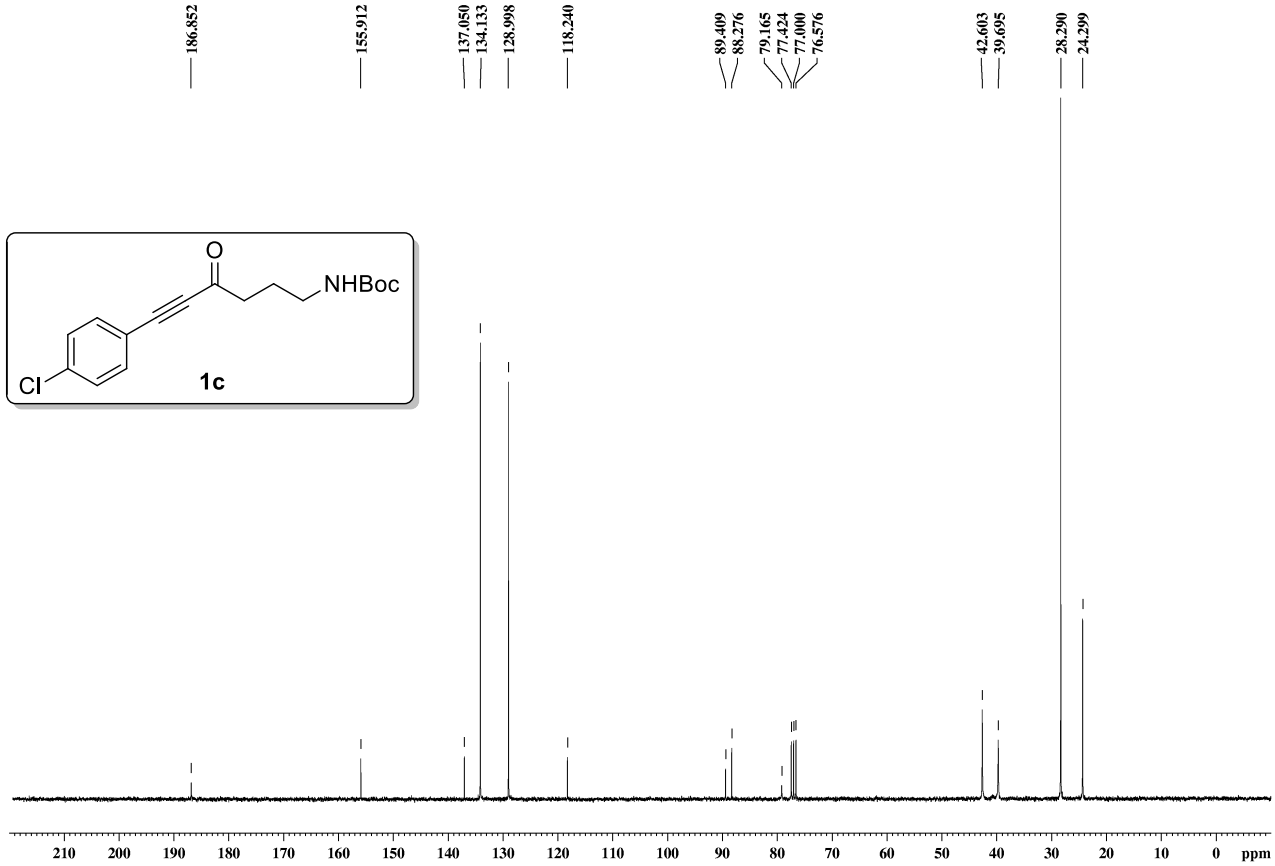
^{13}C NMR (75 MHz, $CDCl_3$); **1b**



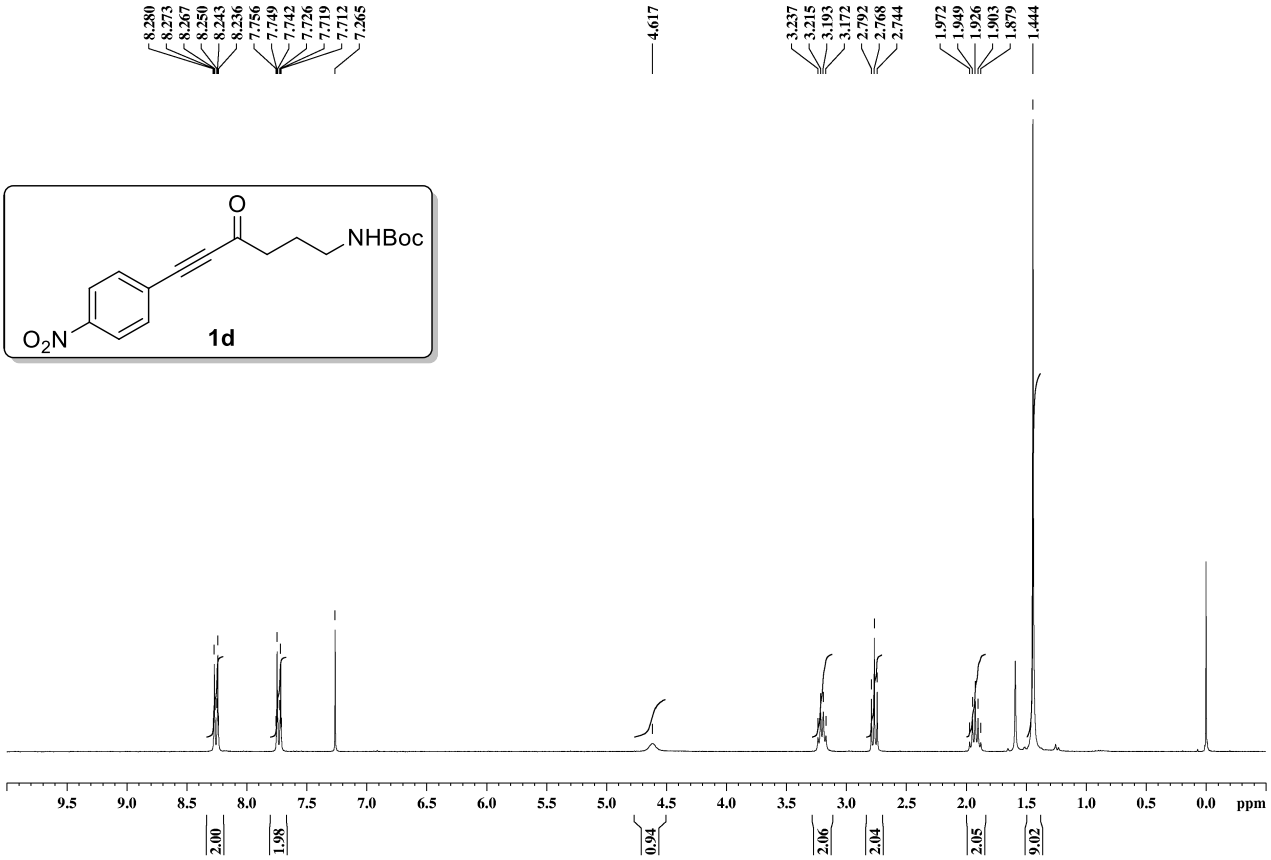
^{1}H NMR (300 MHz, $CDCl_3$); **1c**



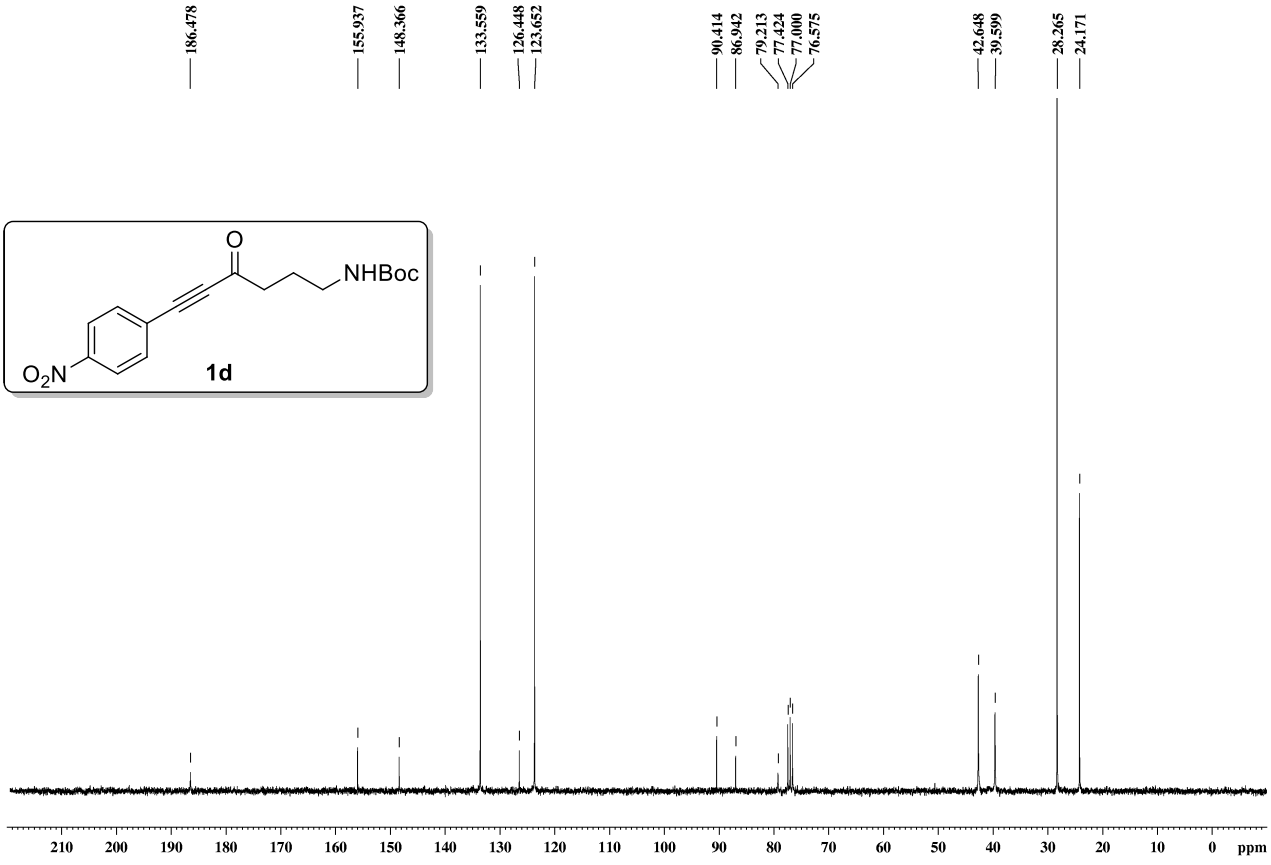
^{13}C NMR (75 MHz, $CDCl_3$); **1c**



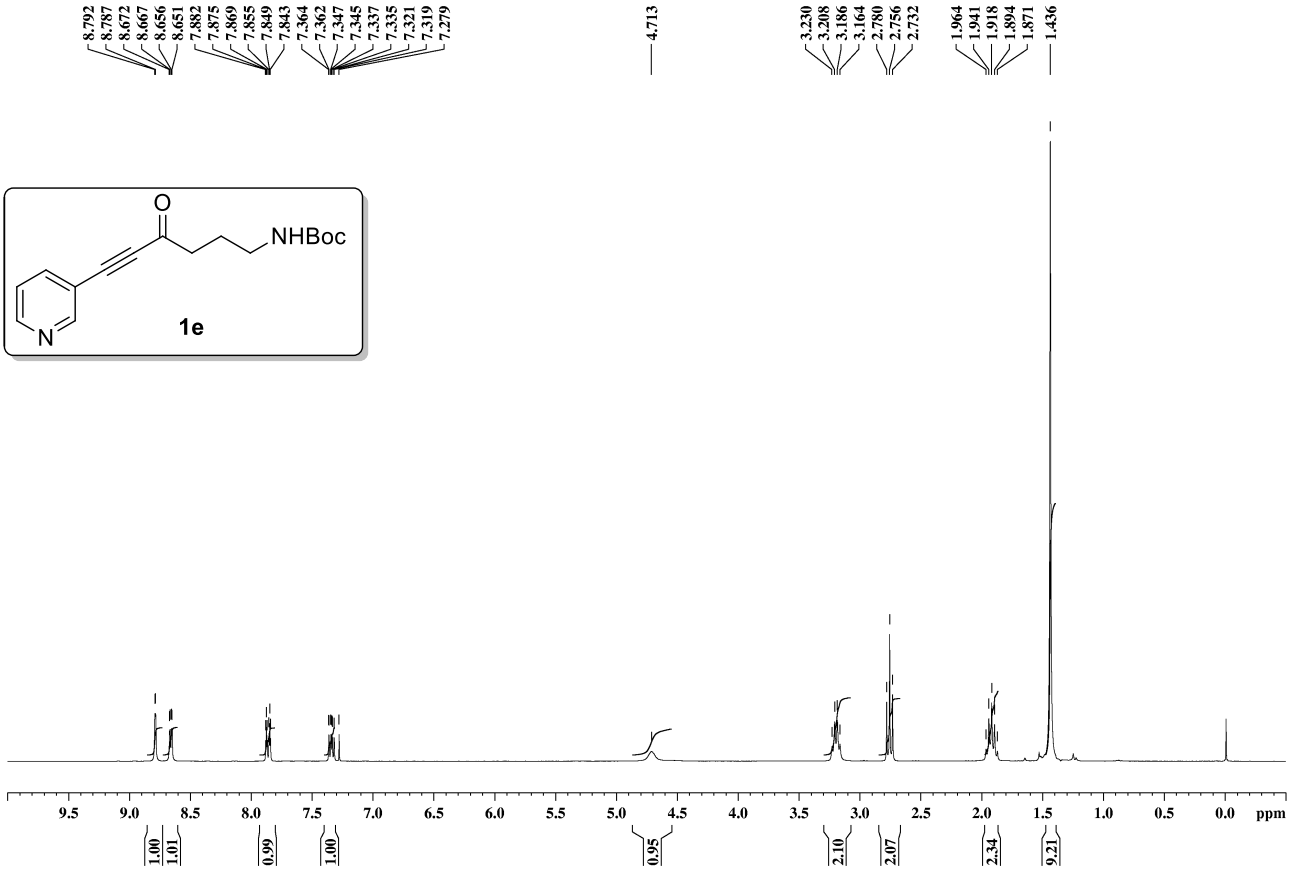
^{1}H NMR (300 MHz, $CDCl_3$); **1d**



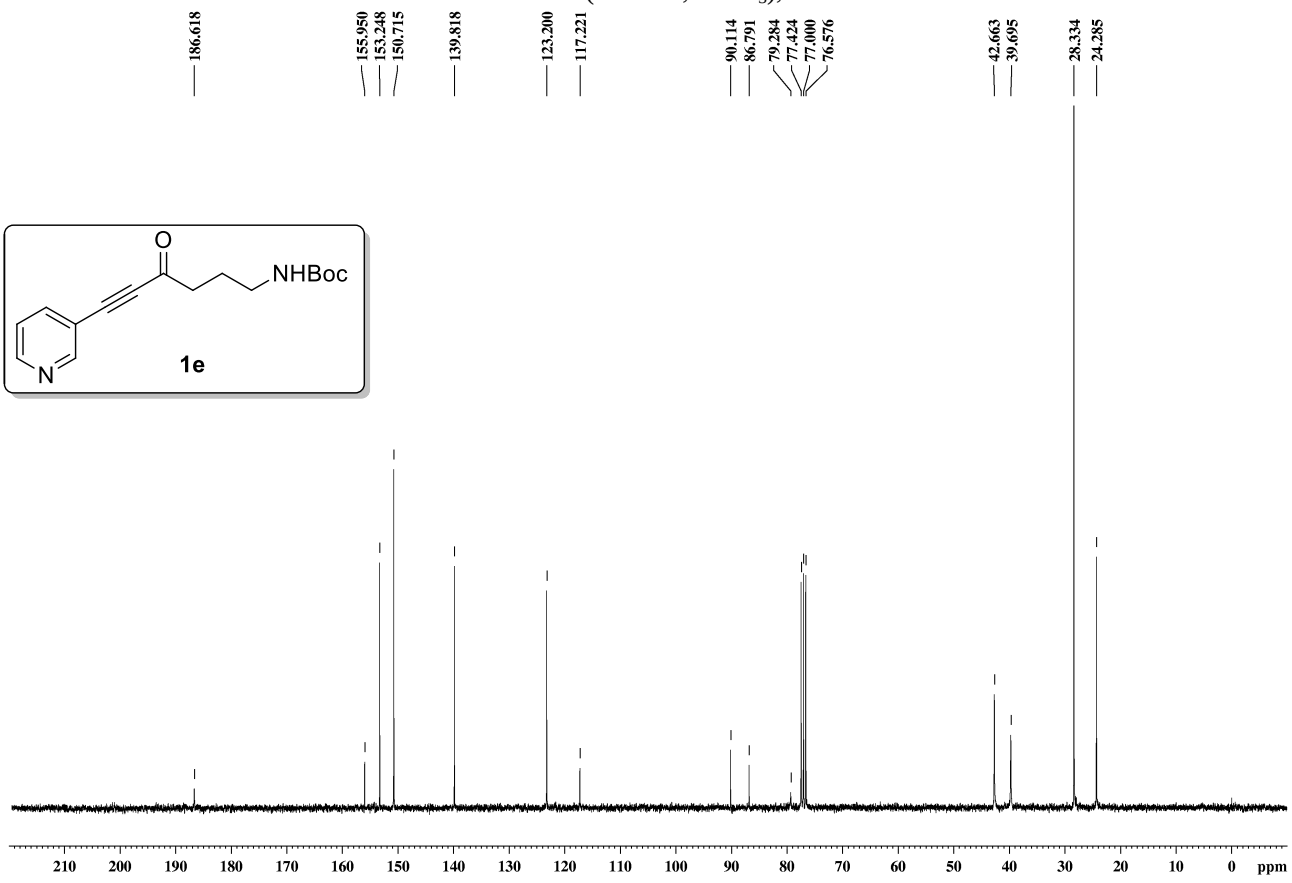
^{13}C NMR (75 MHz, $CDCl_3$); **1d**



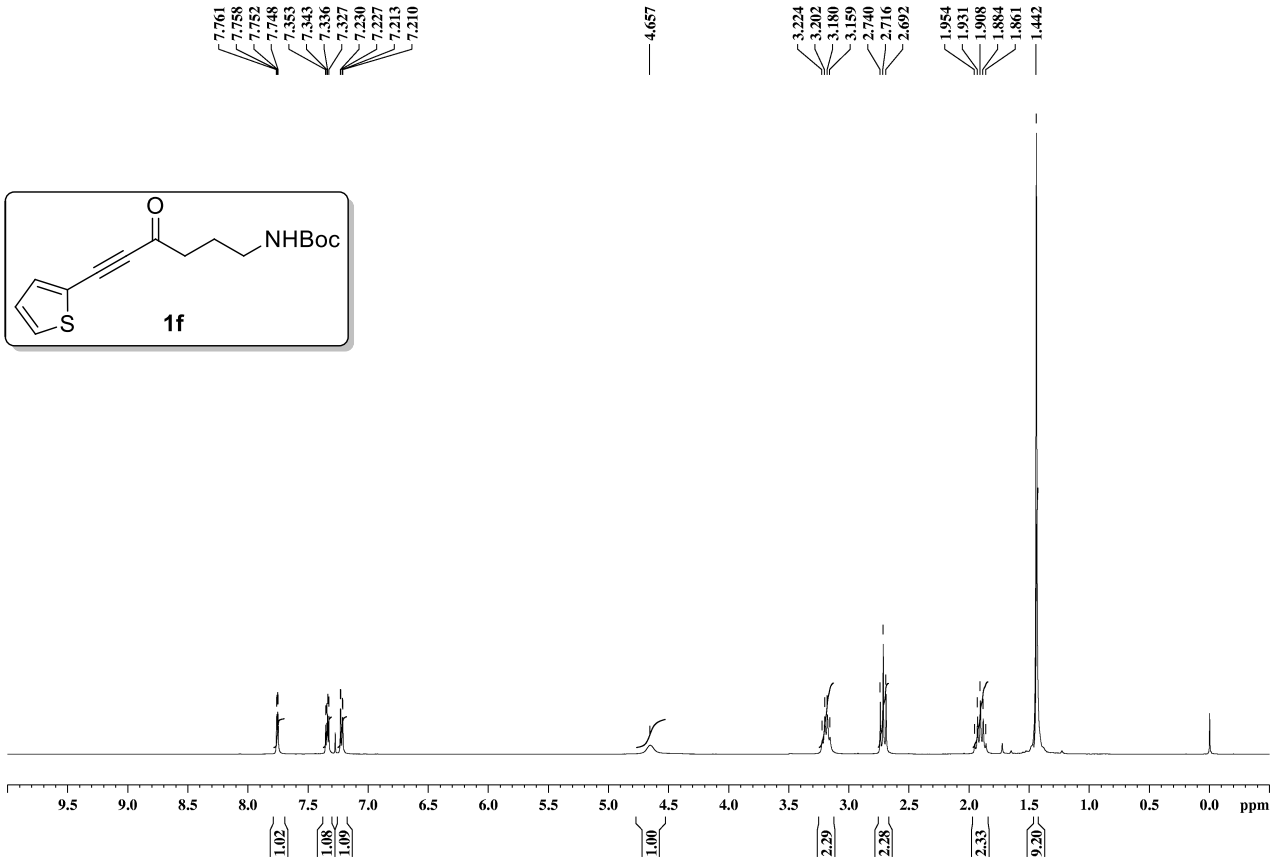
^{1}H NMR (300 MHz, $CDCl_3$); **1e**



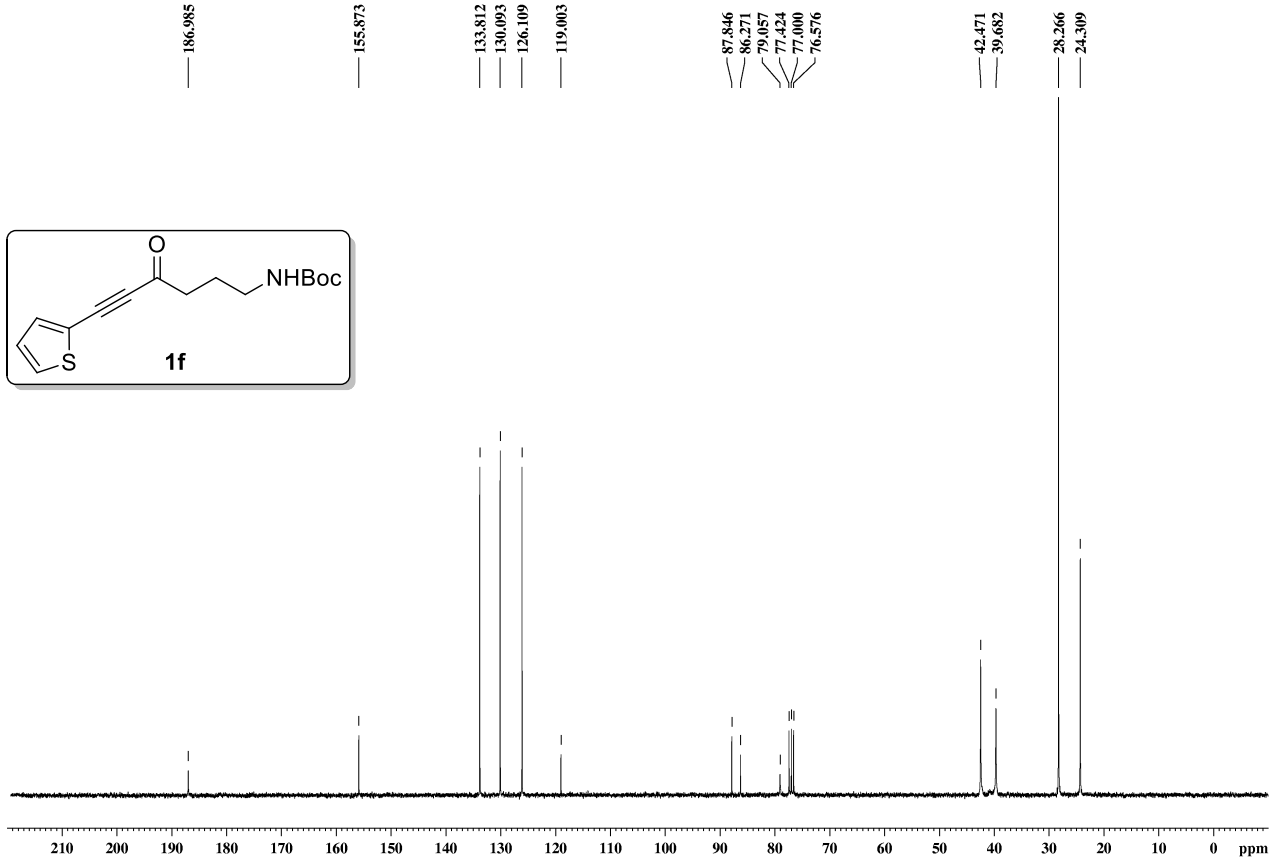
^{13}C NMR (75 MHz, $CDCl_3$); **1e**



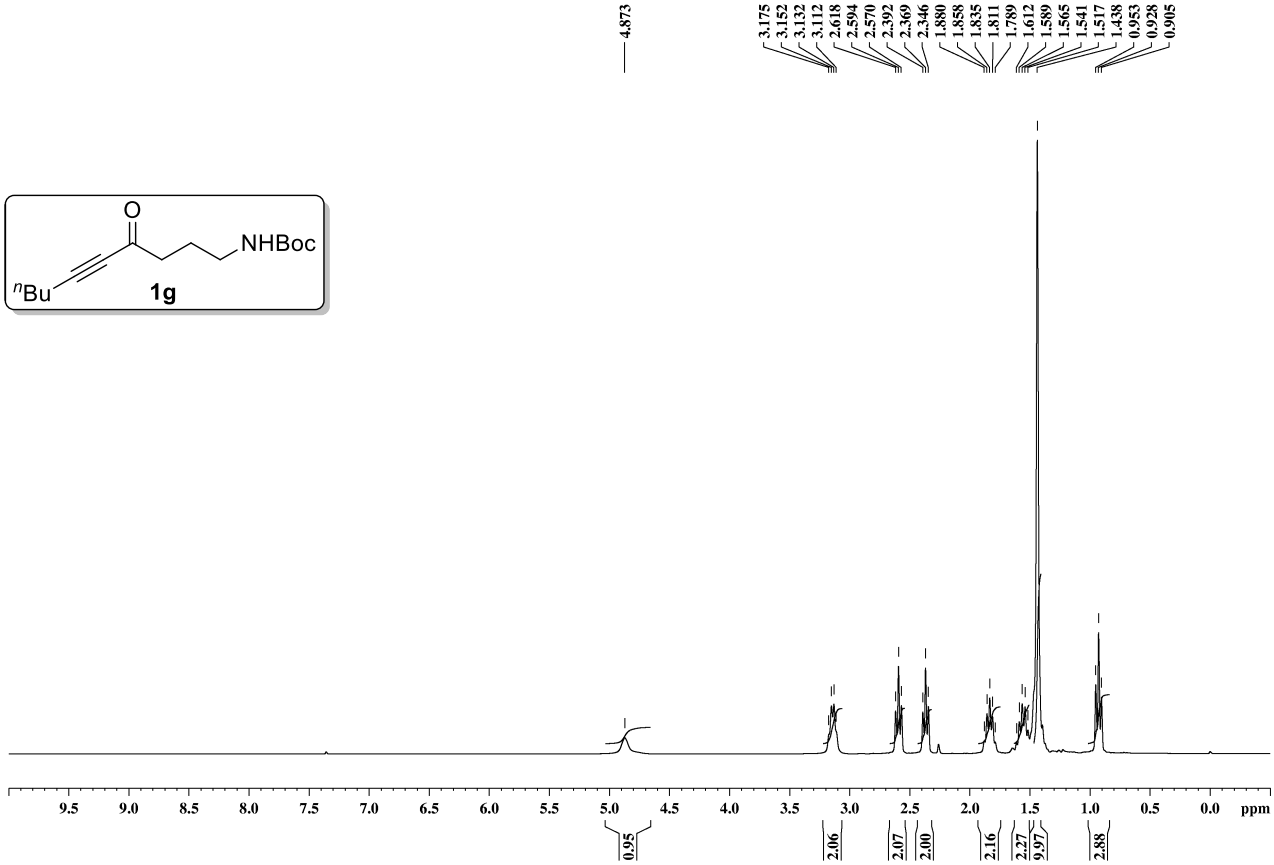
^{1}H NMR (300 MHz, $CDCl_3$); **1f**



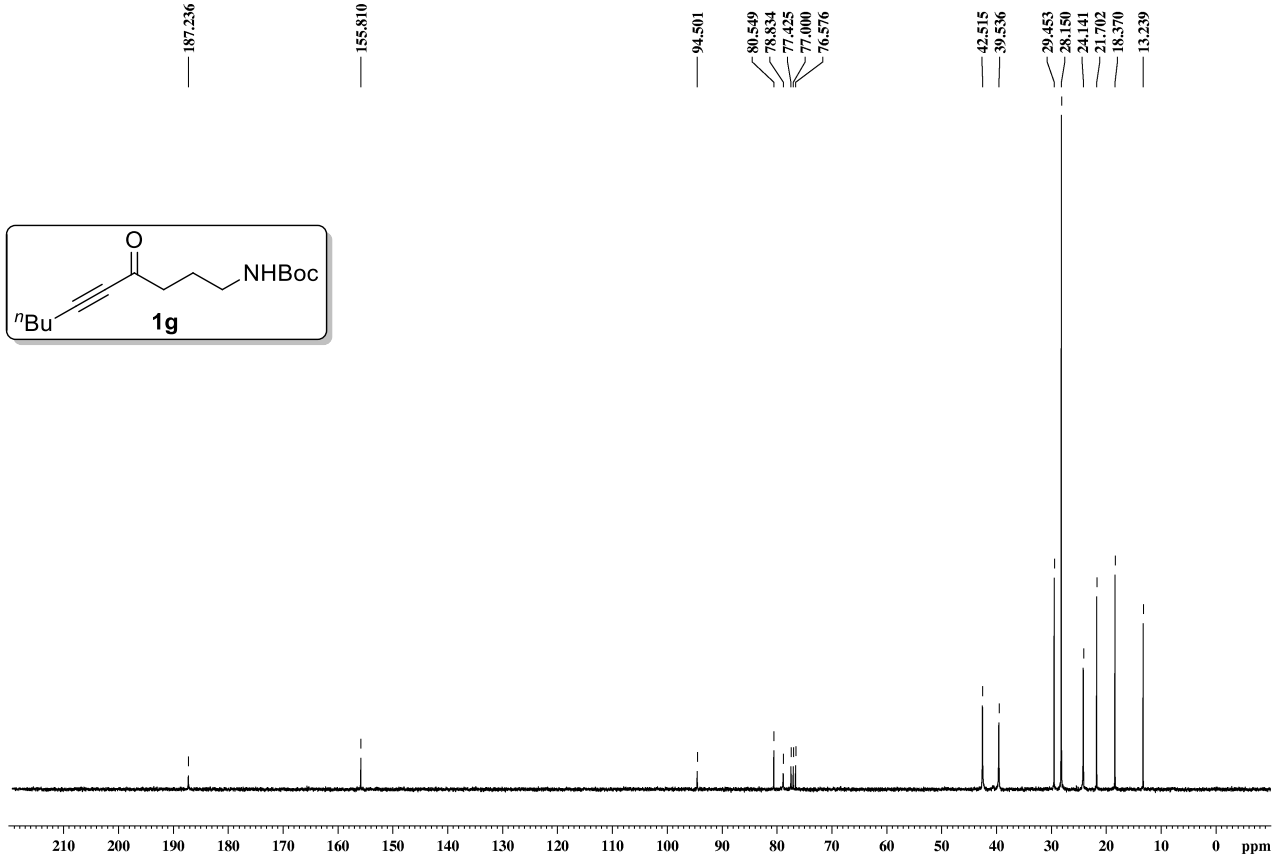
^{13}C NMR (75 MHz, $CDCl_3$); **1f**



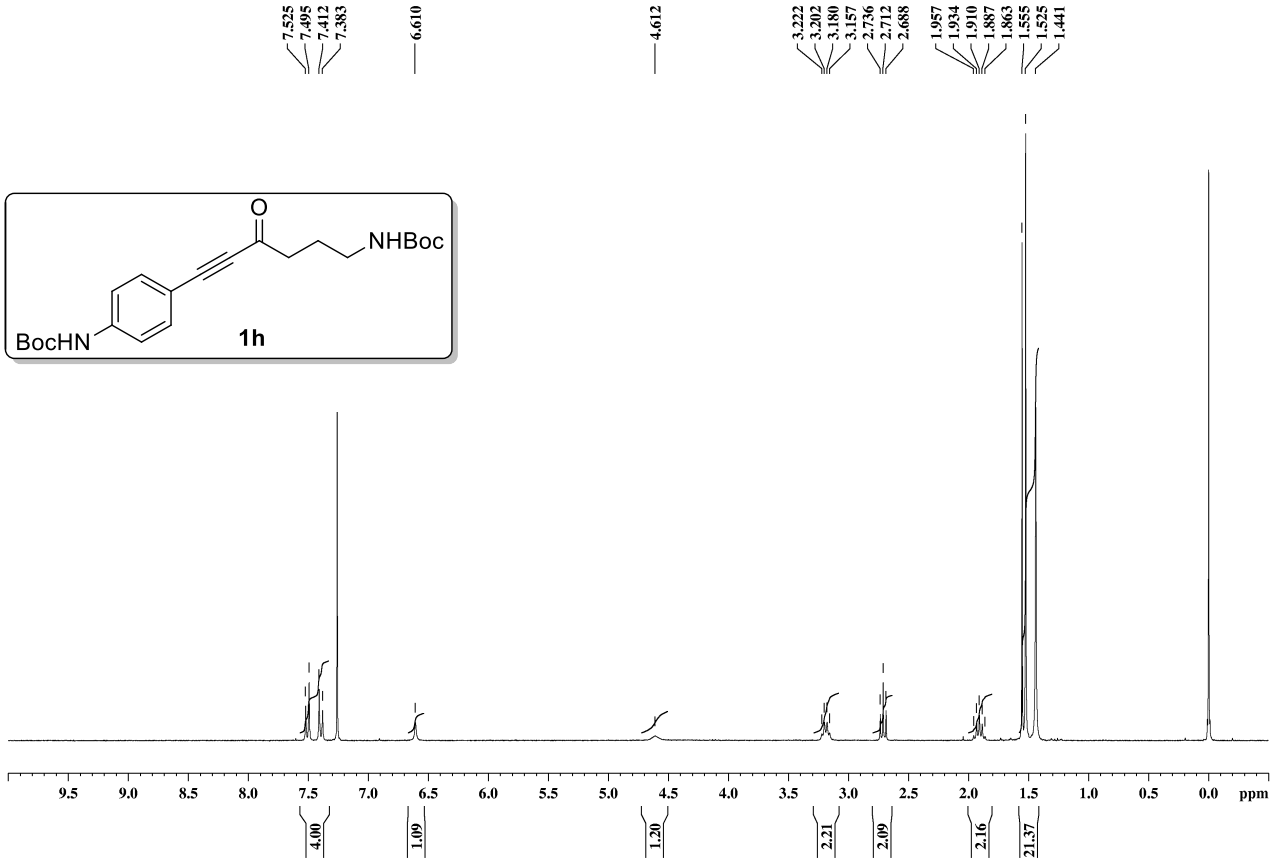
^{1}H NMR (300 MHz, $CDCl_3$); **1g**



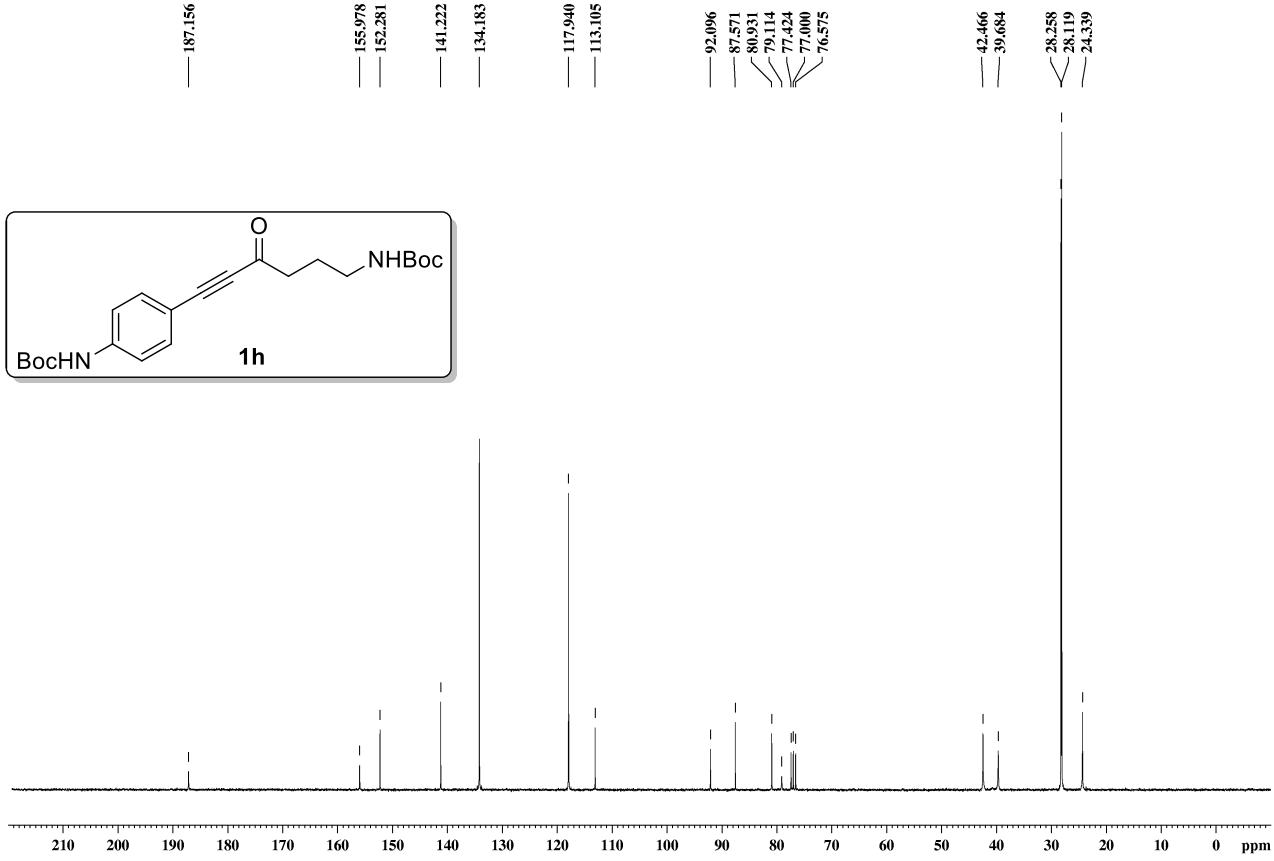
^{13}C NMR (75 MHz, $CDCl_3$); **1g**



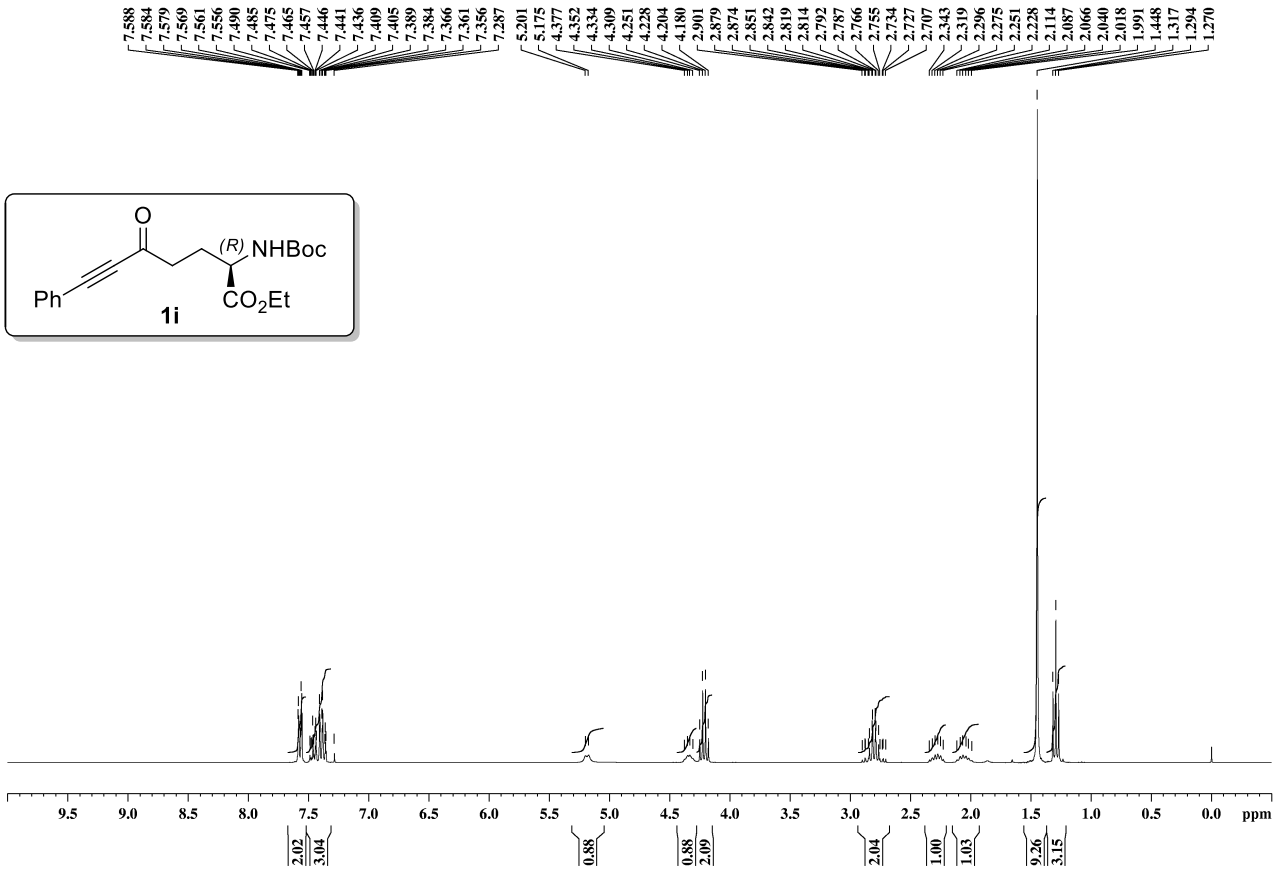
^{1}H NMR (300 MHz, $CDCl_3$); **1h**



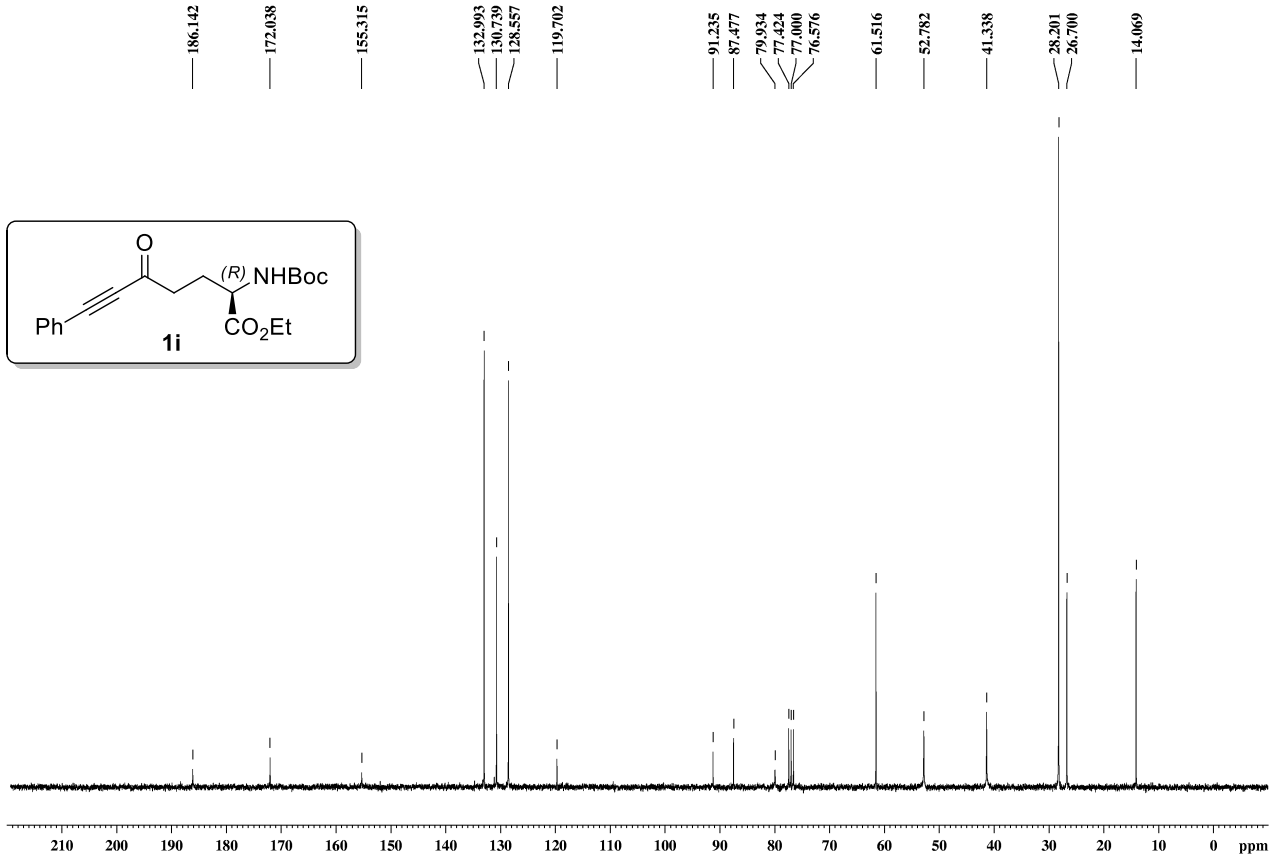
^{13}C NMR (75 MHz, $CDCl_3$); **1h**



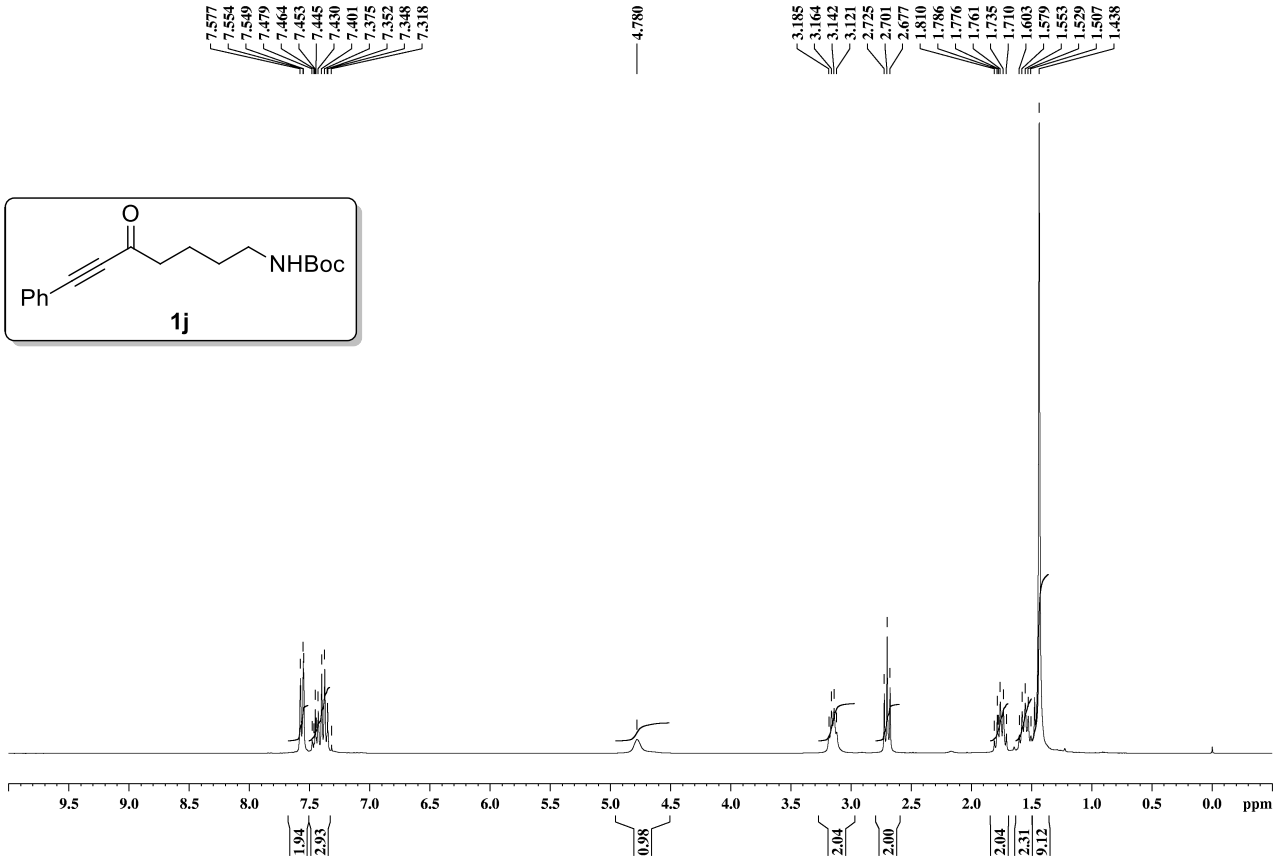
^{1}H NMR (300 MHz, $CDCl_3$); **1i**



^{13}C NMR (75 MHz, $CDCl_3$); **1i**



^{1}H NMR (300 MHz, $CDCl_3$); **1j**



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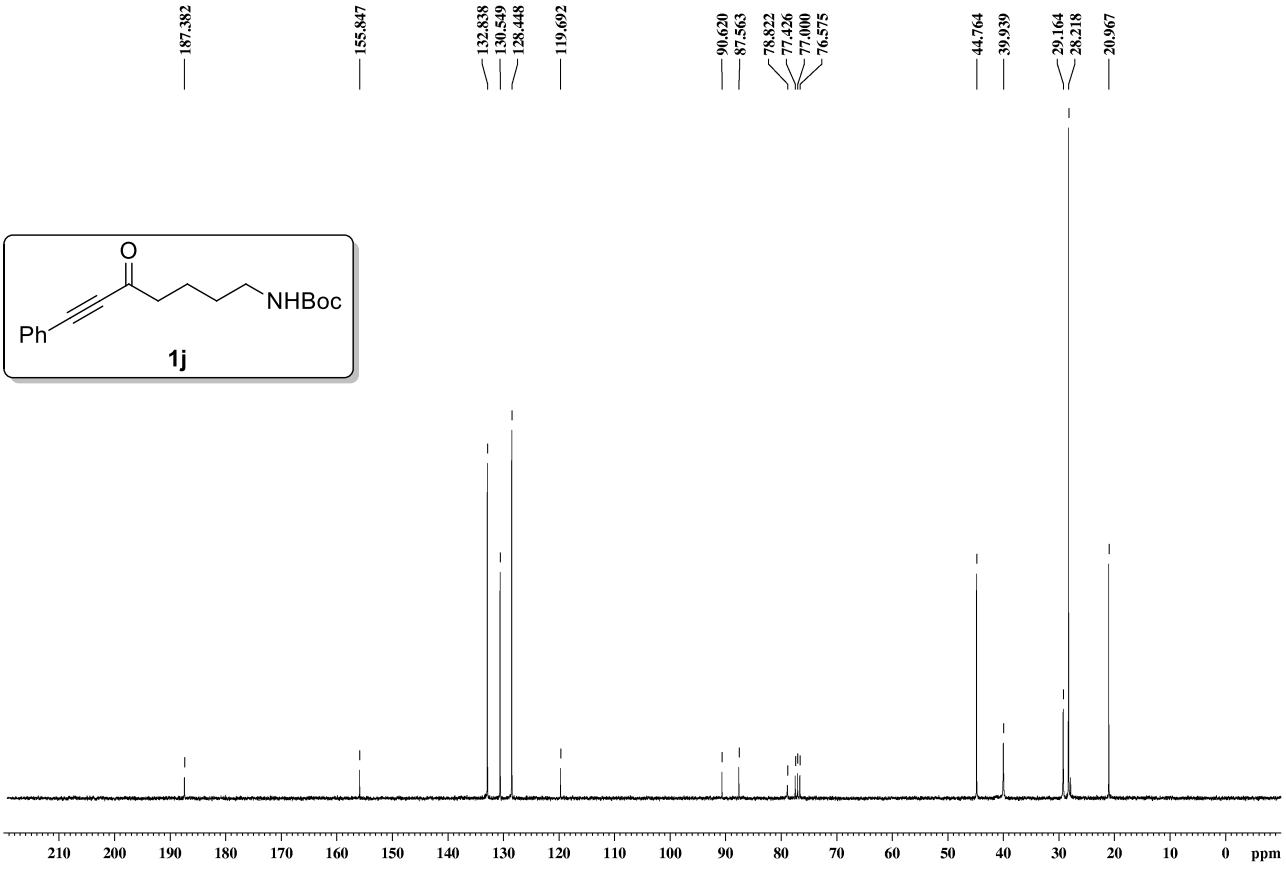

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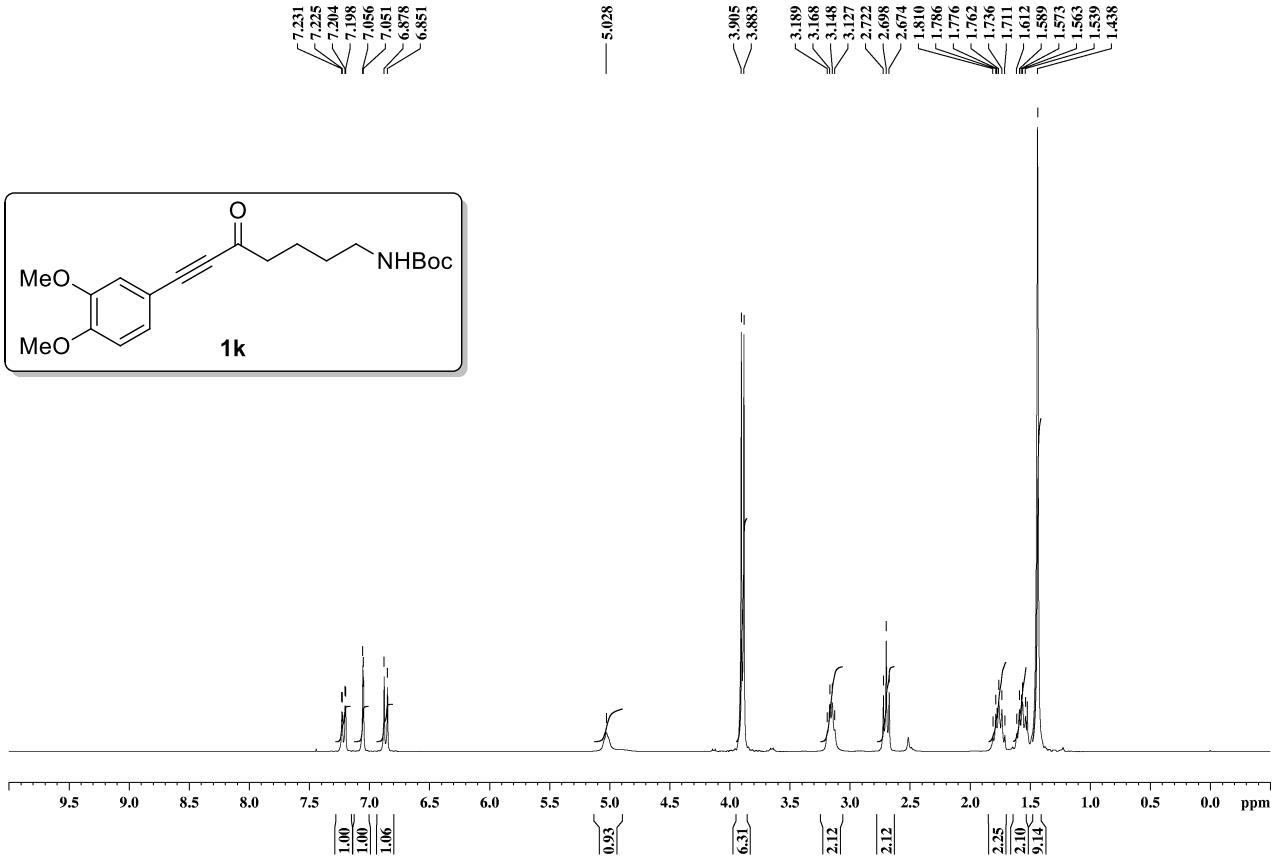
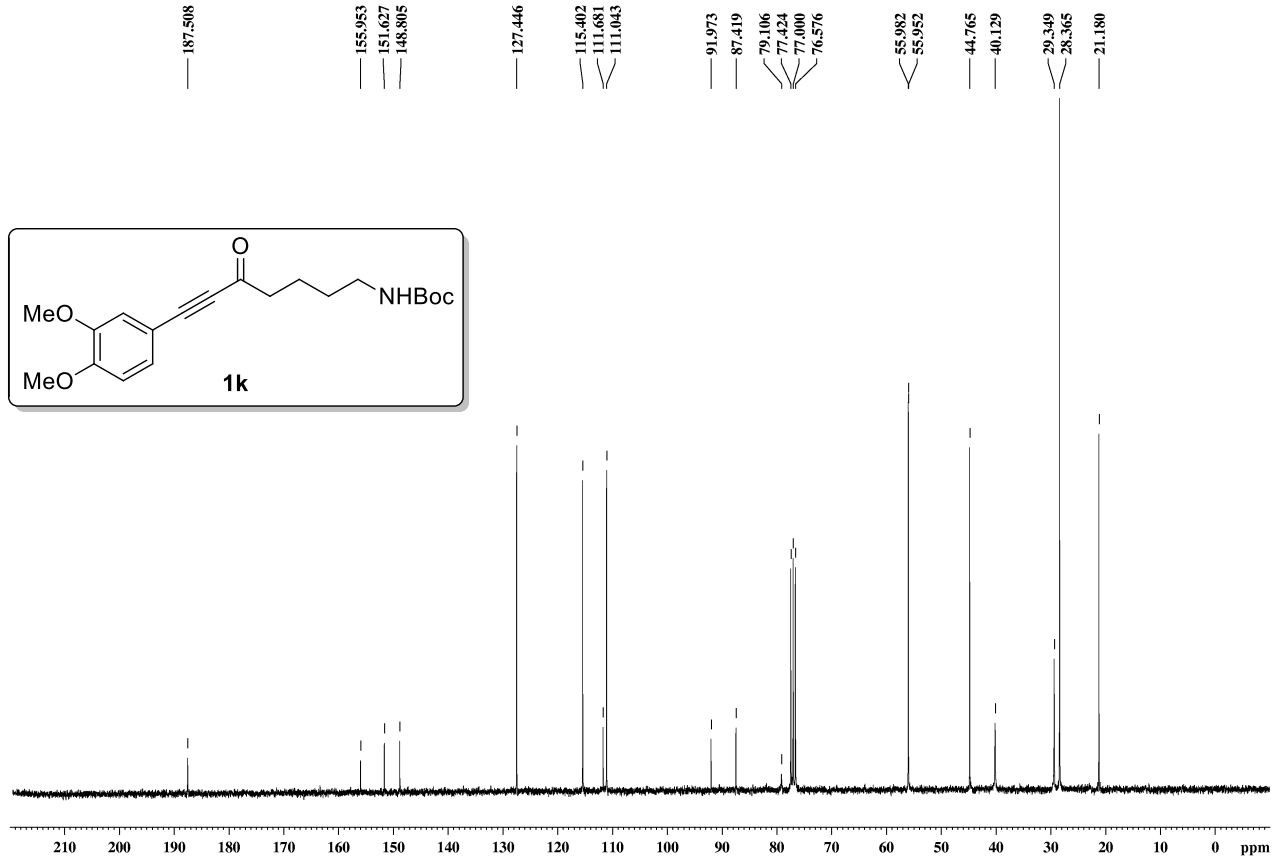


^{13}C NMR (75 MHz, $CDCl_3$); **1k**



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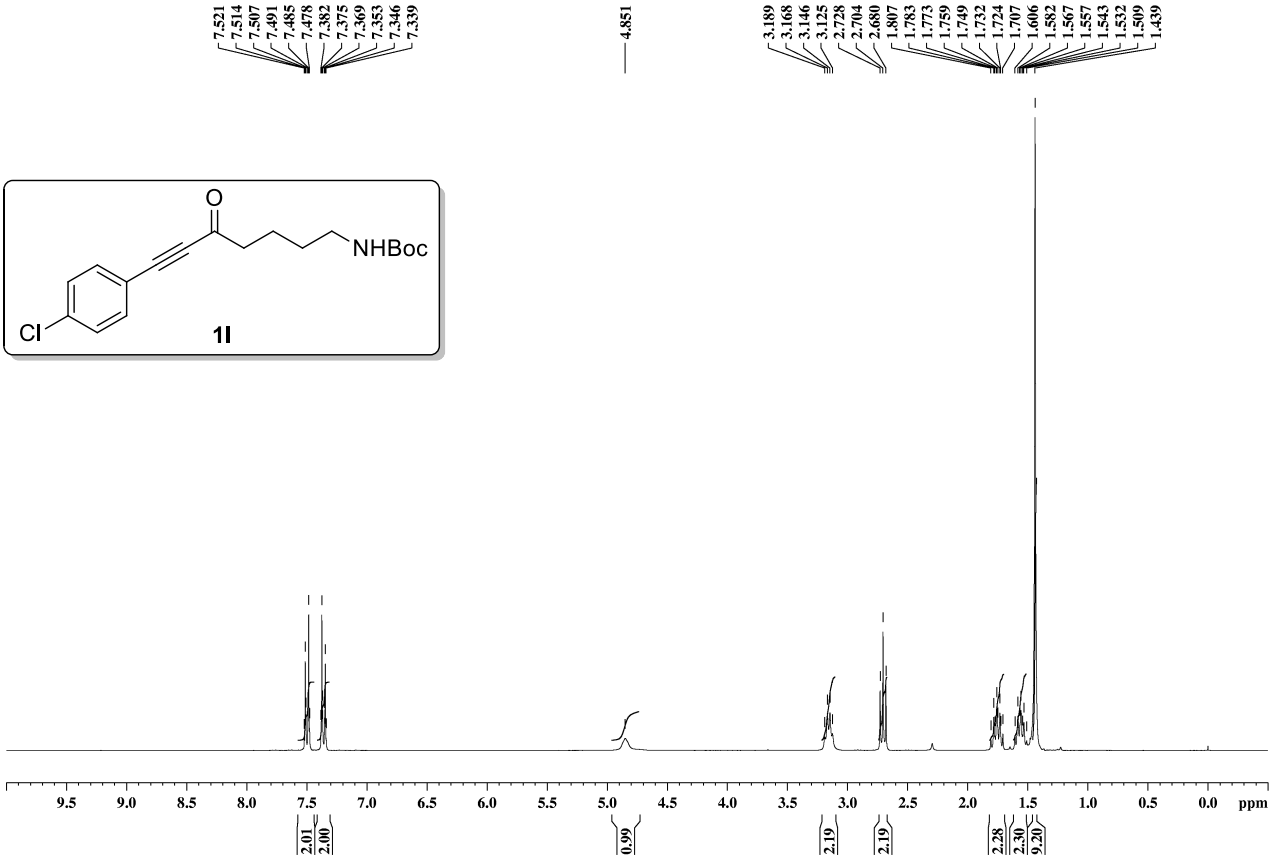
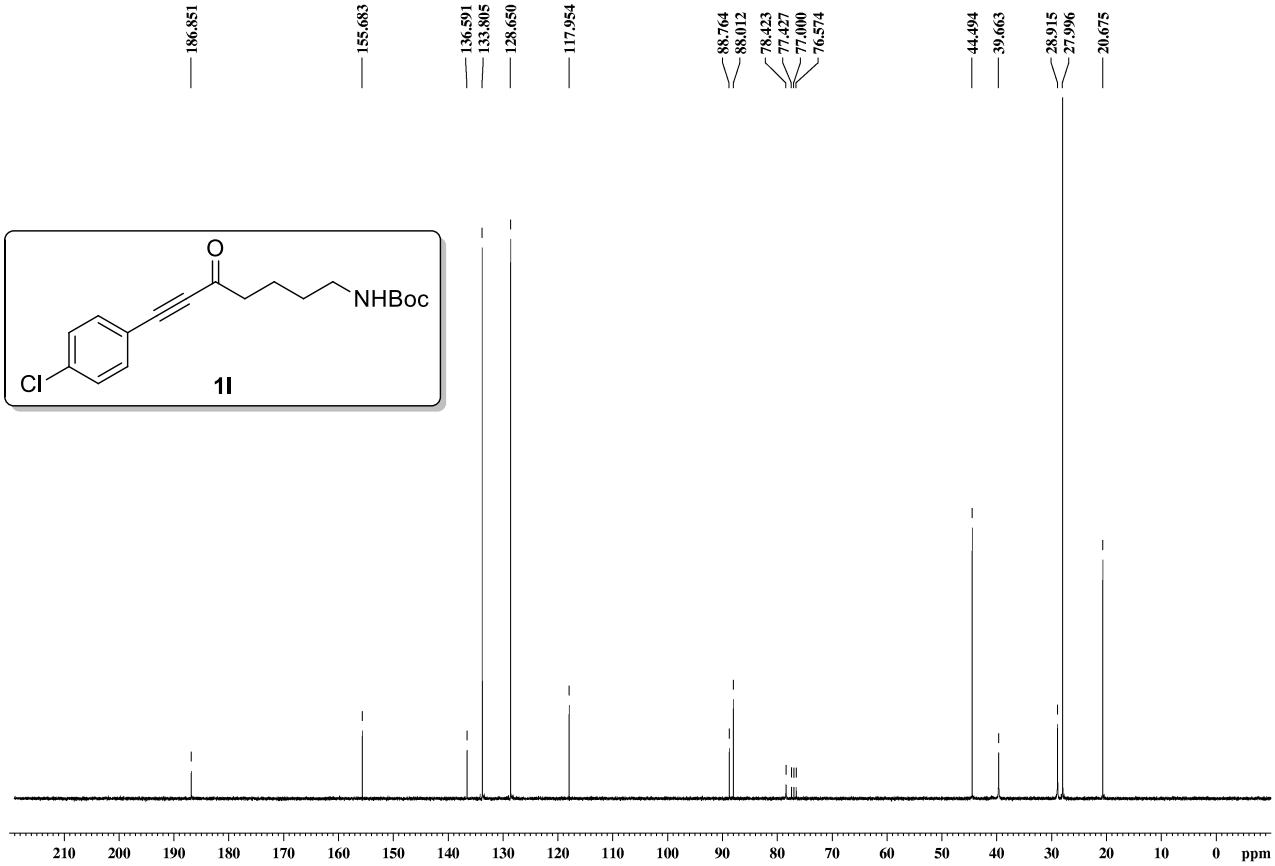


^{13}C NMR (75 MHz, $CDCl_3$); **1l**



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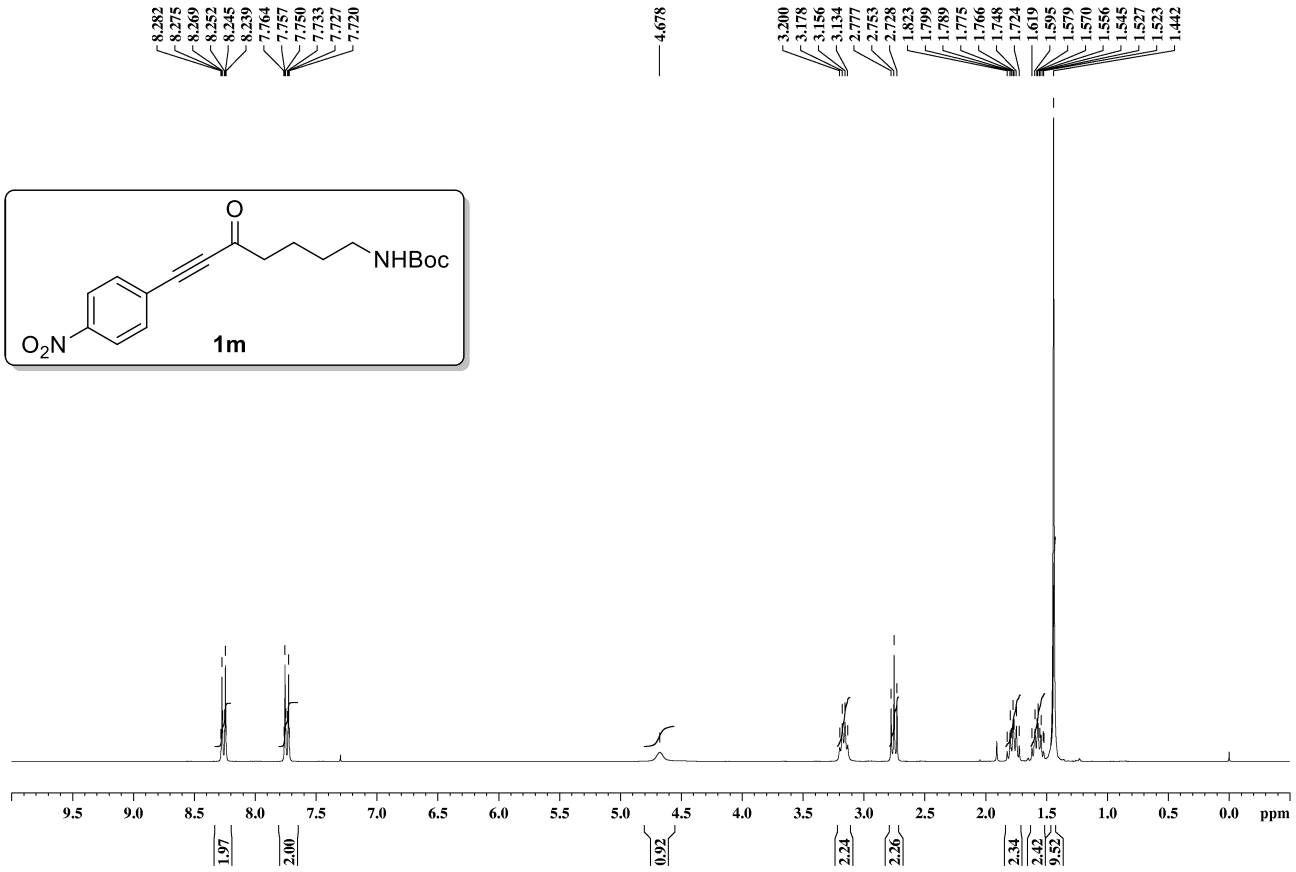
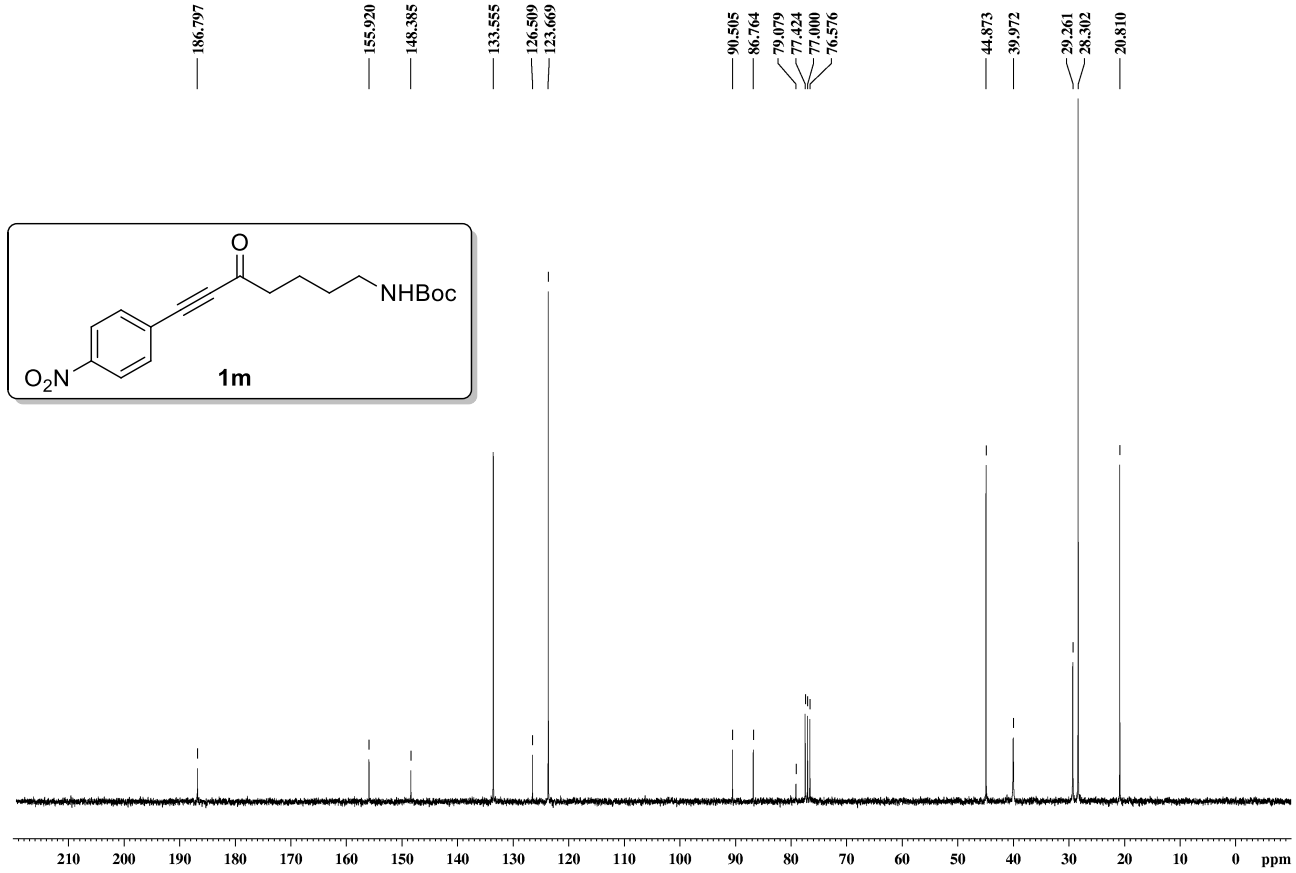


^{13}C NMR (75 MHz, $CDCl_3$); **1m**



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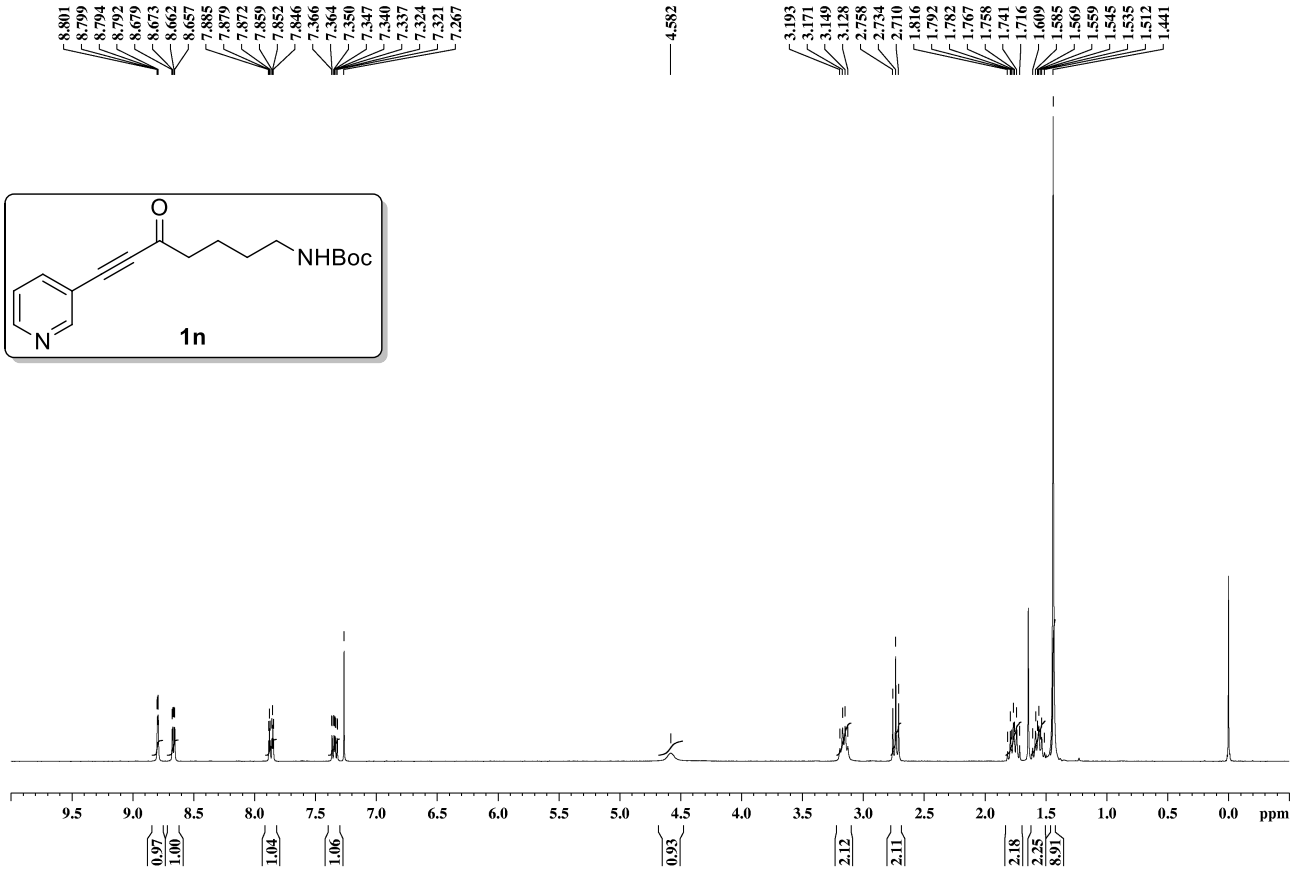

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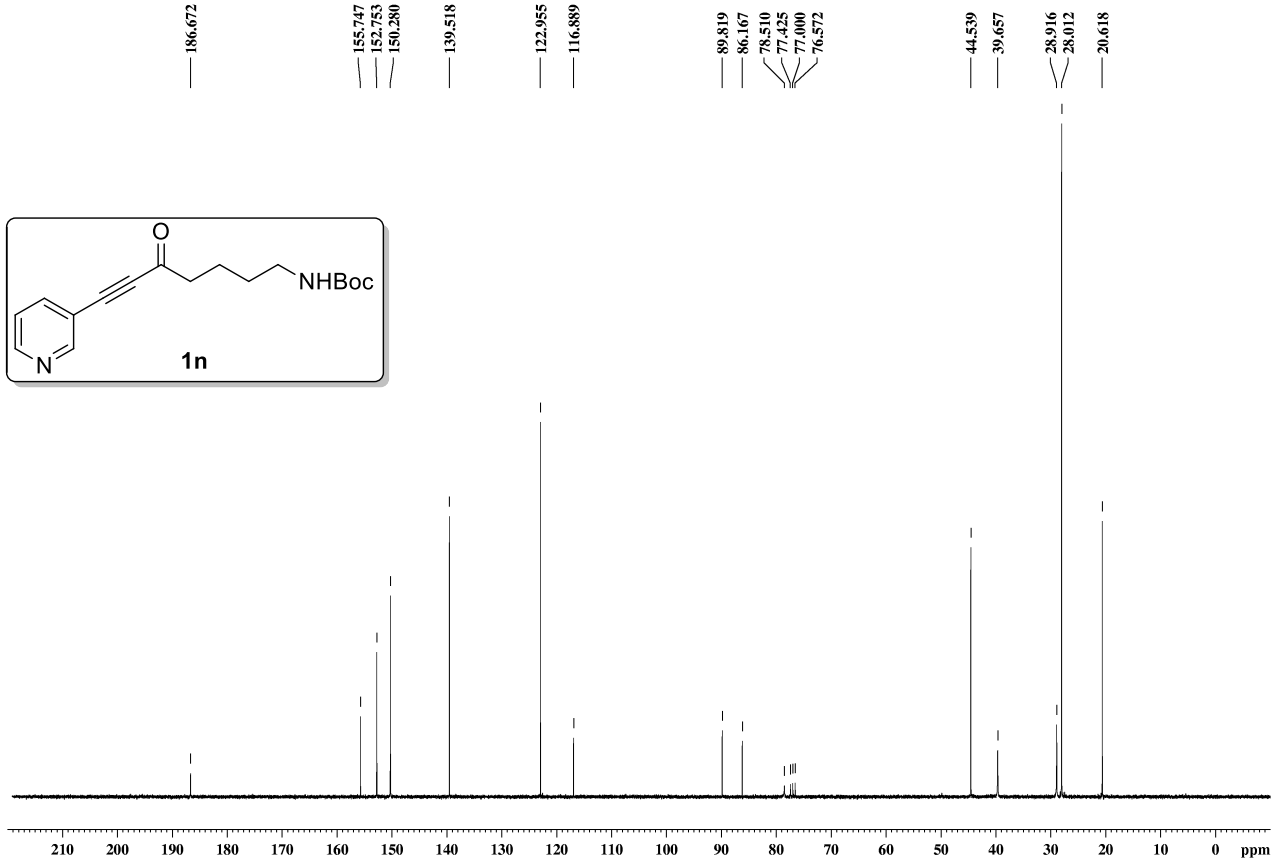

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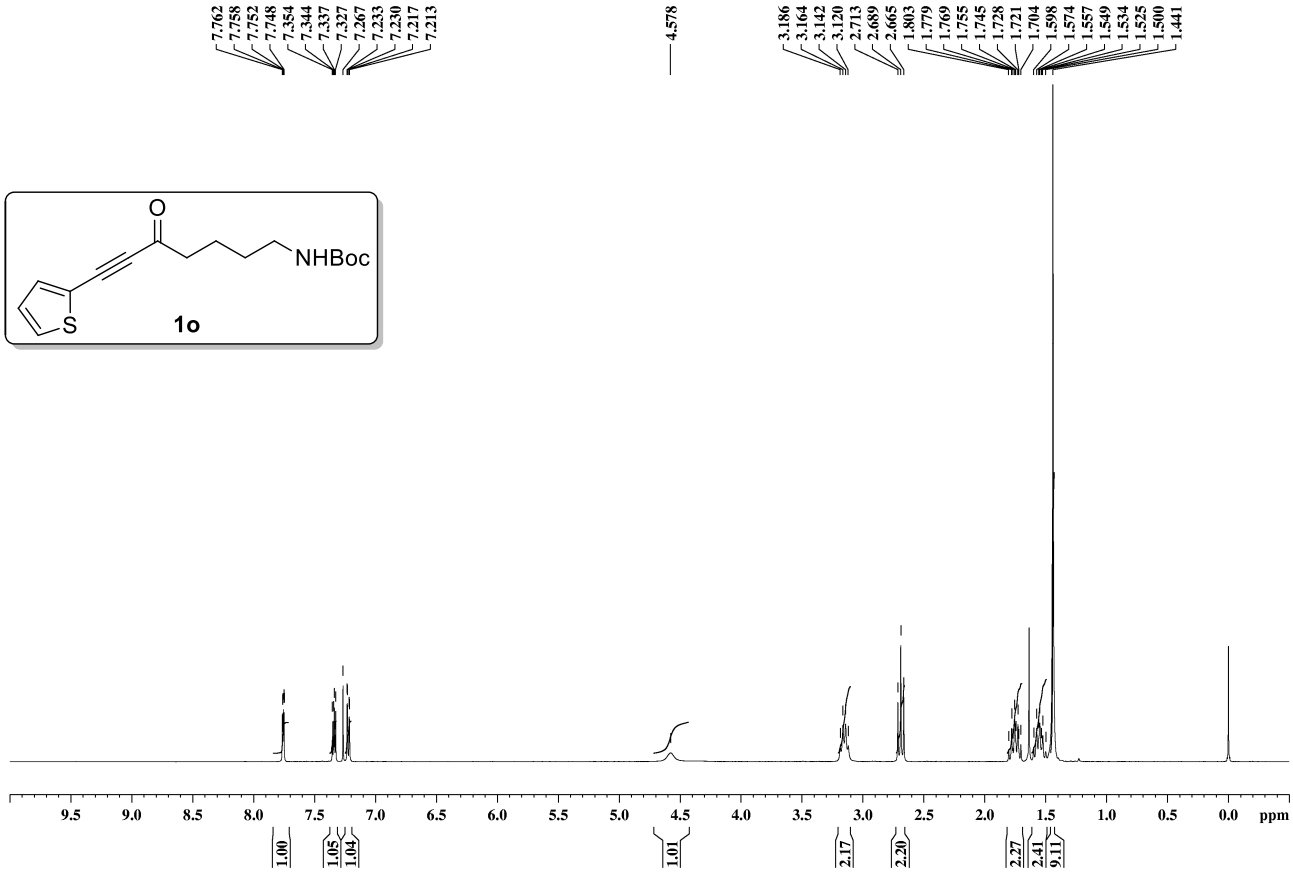
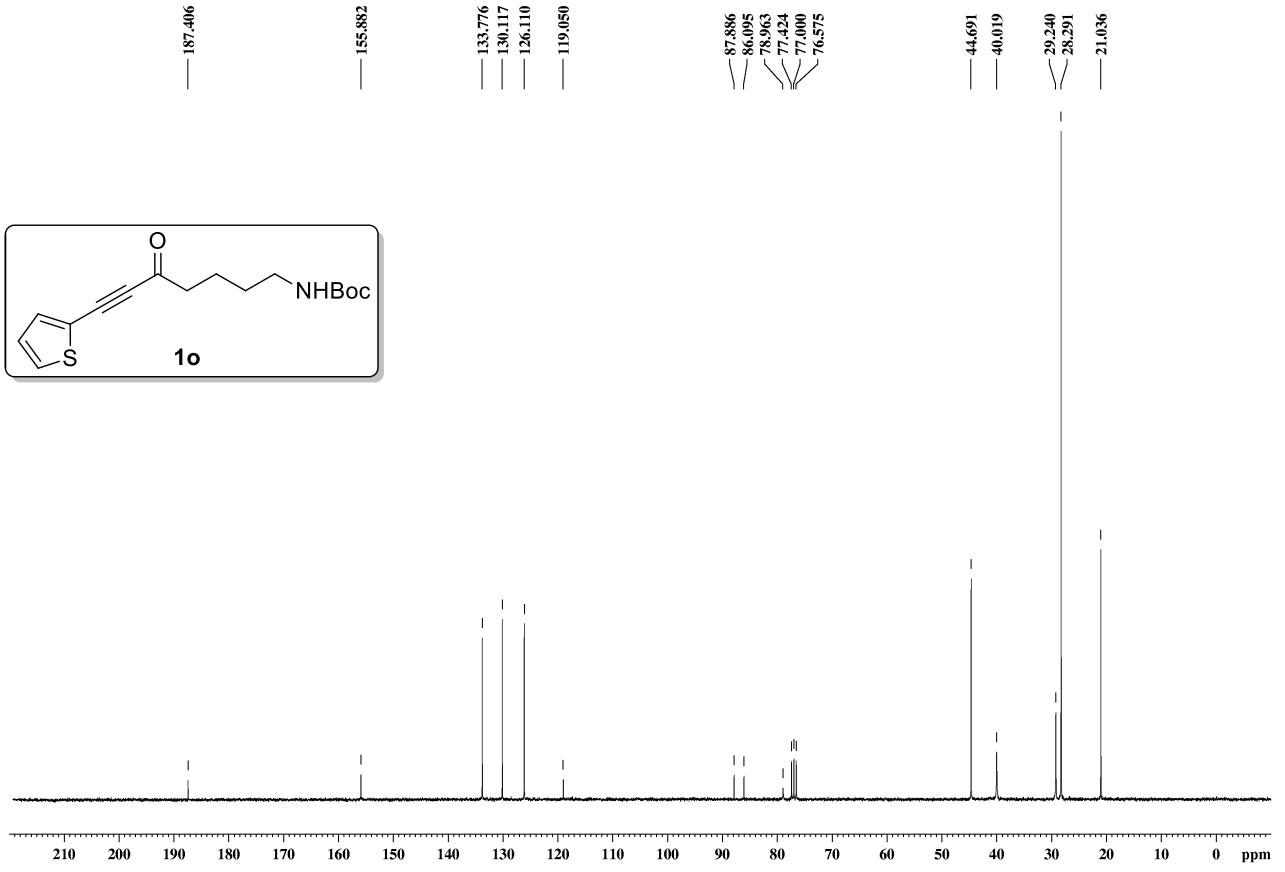


^{13}C NMR (75 MHz, $CDCl_3$); **1o**



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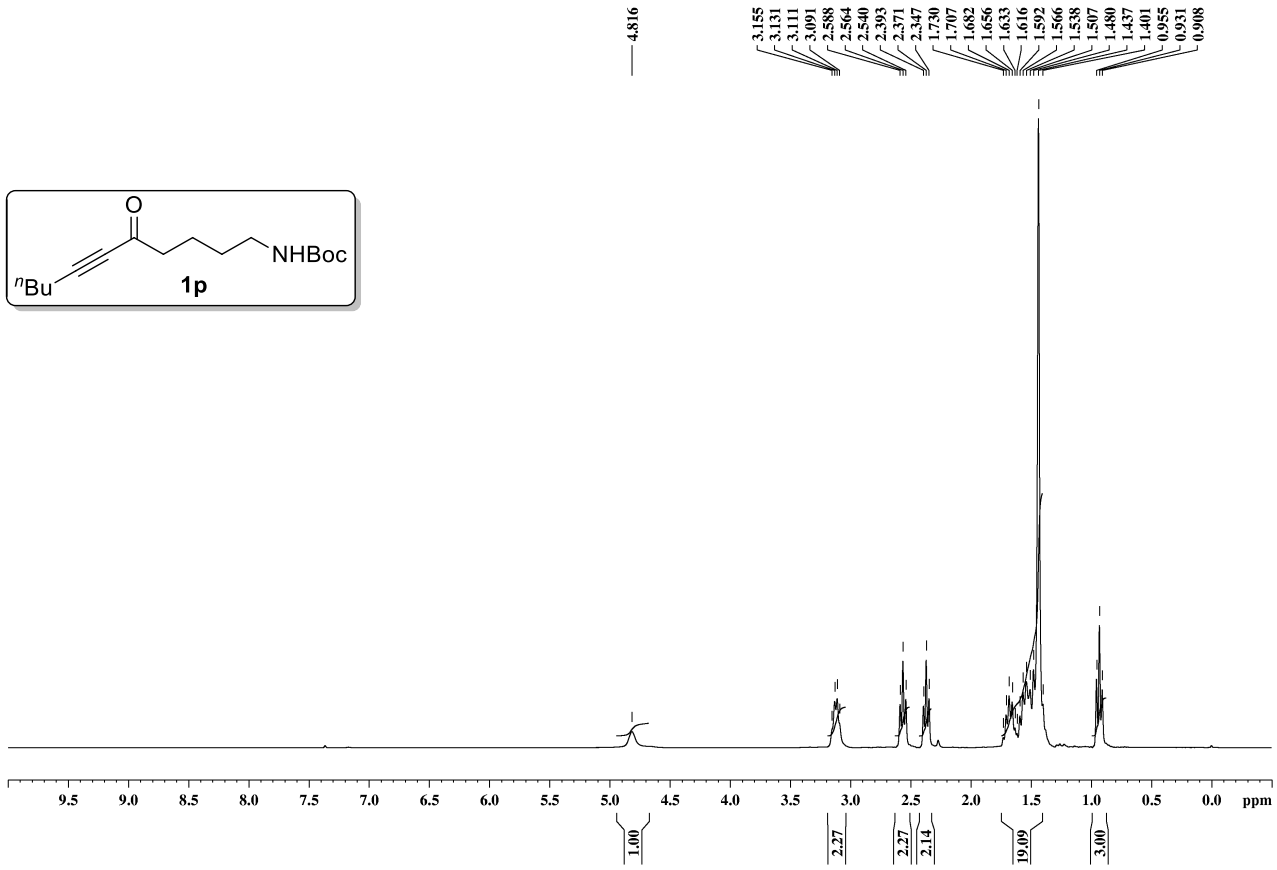
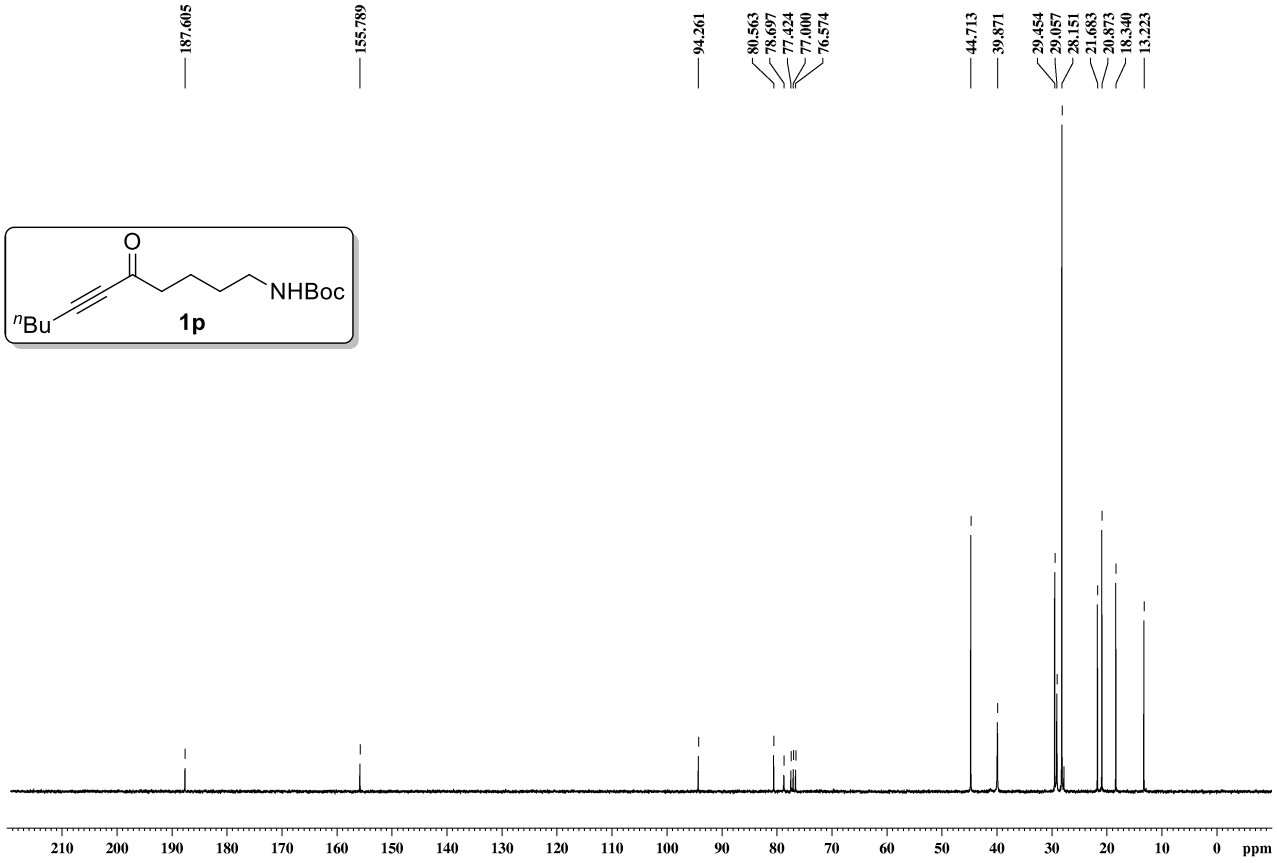


^{13}C NMR (75 MHz, $CDCl_3$); **1p**



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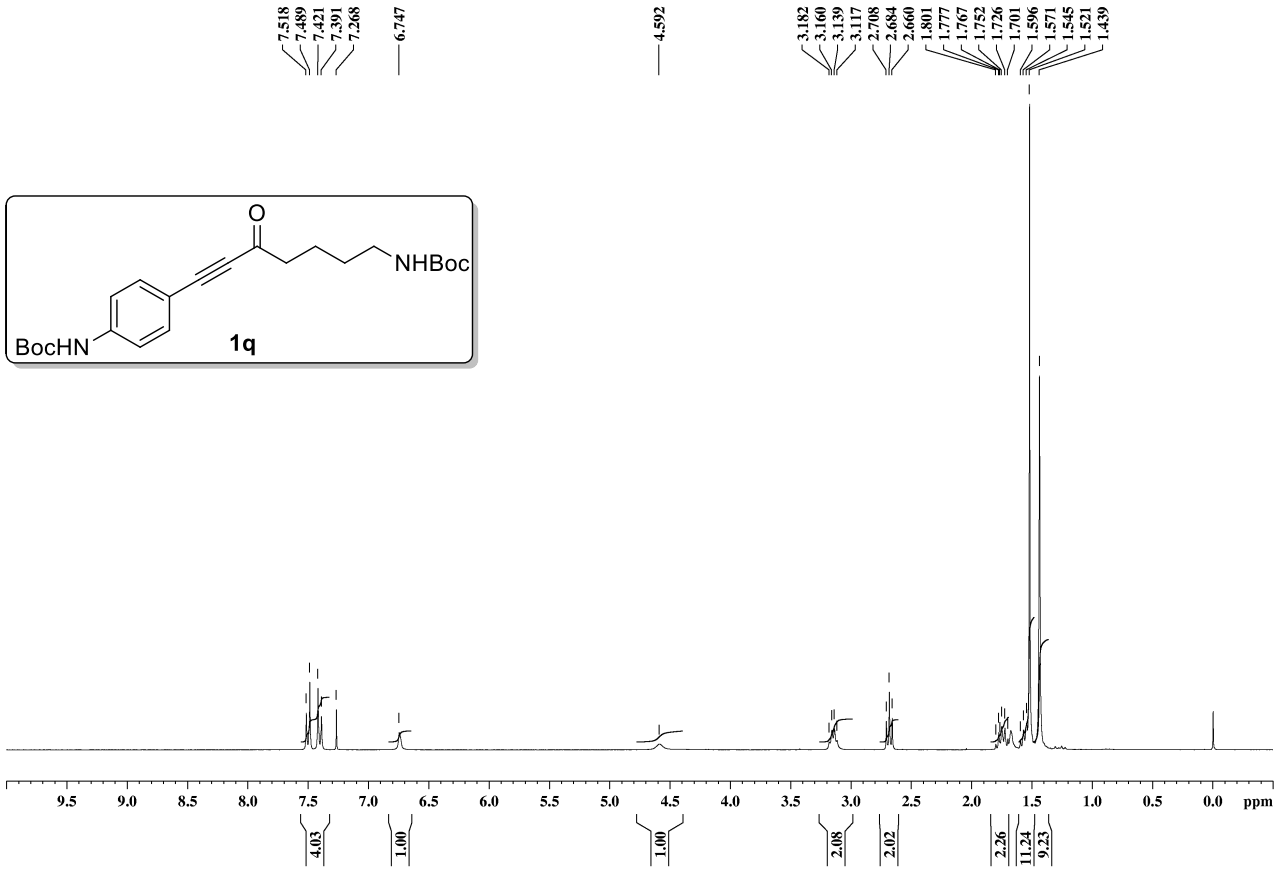
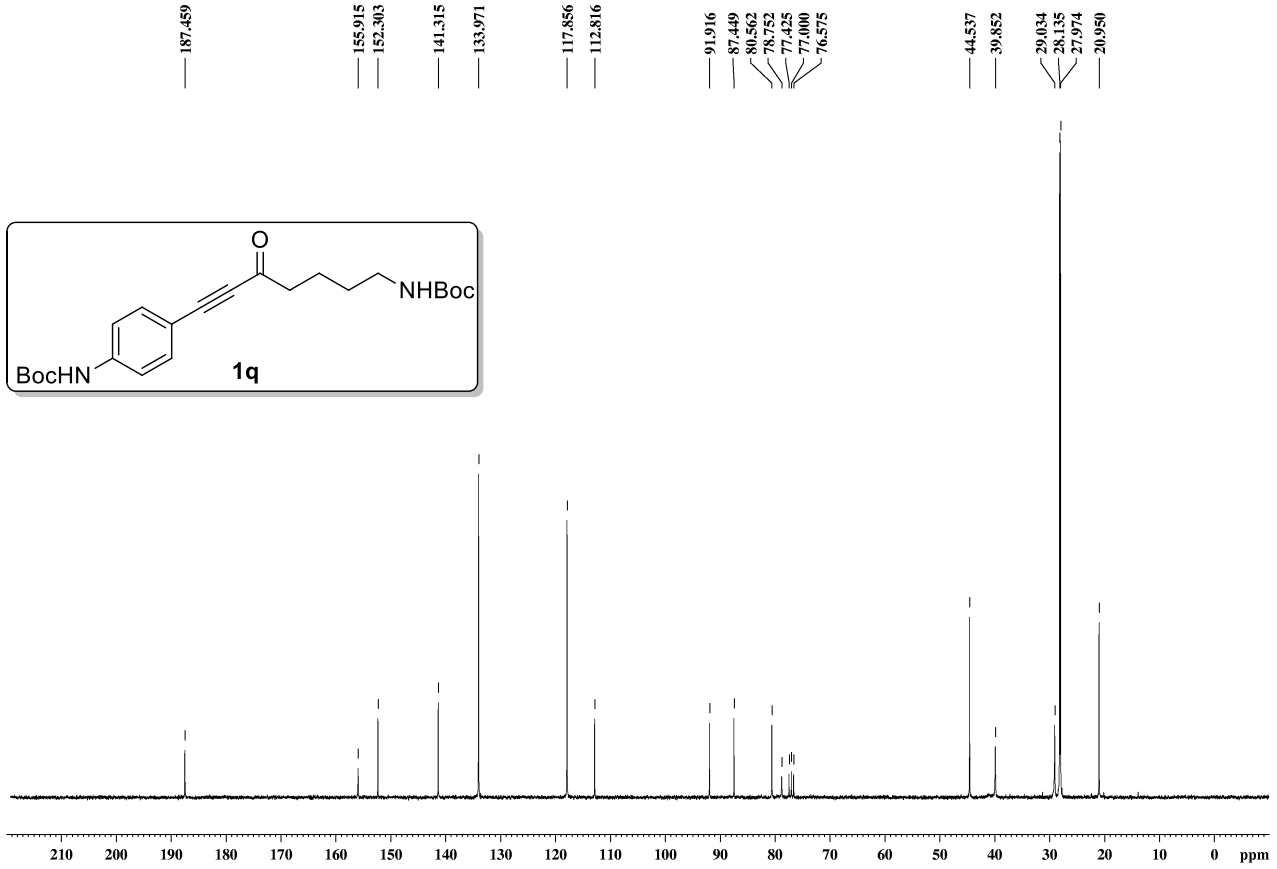
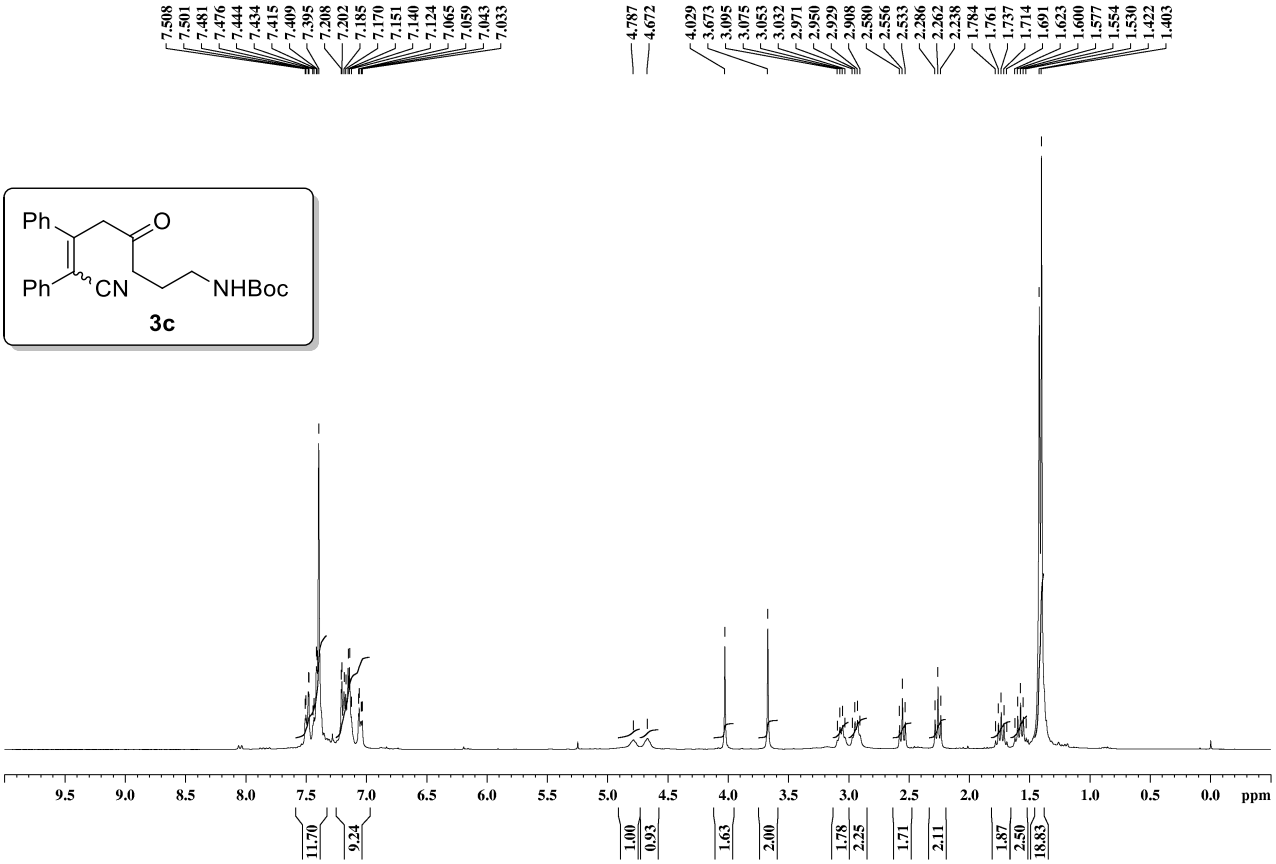


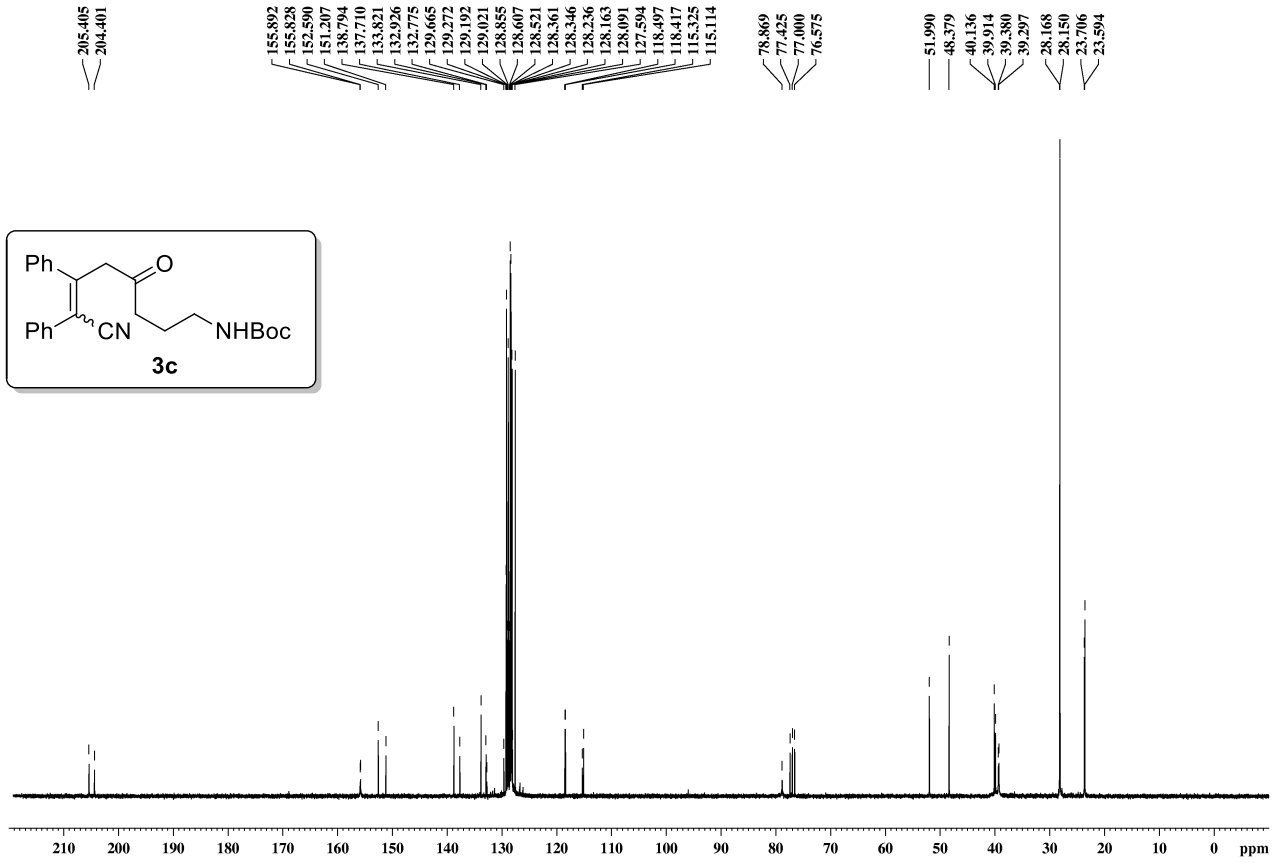
^{13}C NMR (75 MHz, $CDCl_3$); **1q**



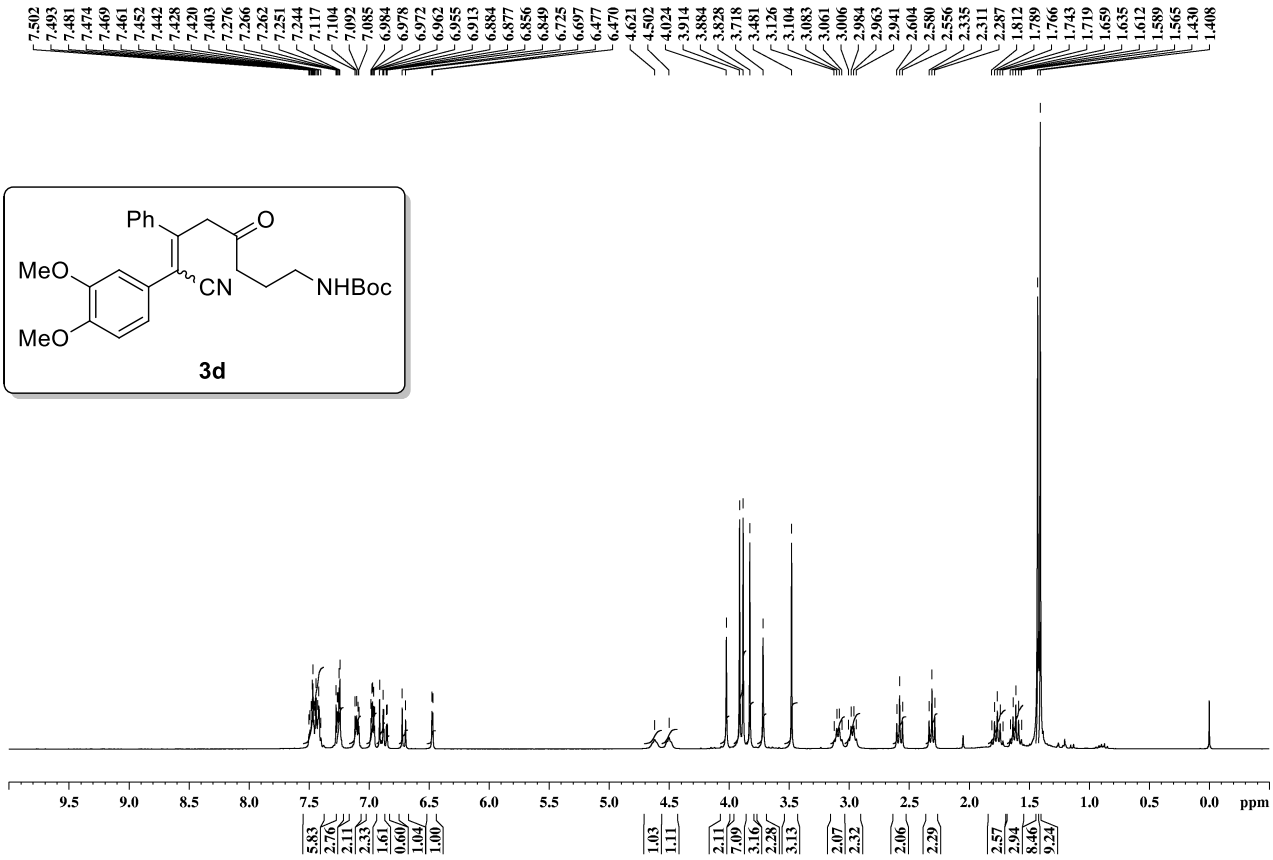
^{1}H NMR (300 MHz, $CDCl_3$); **3c**



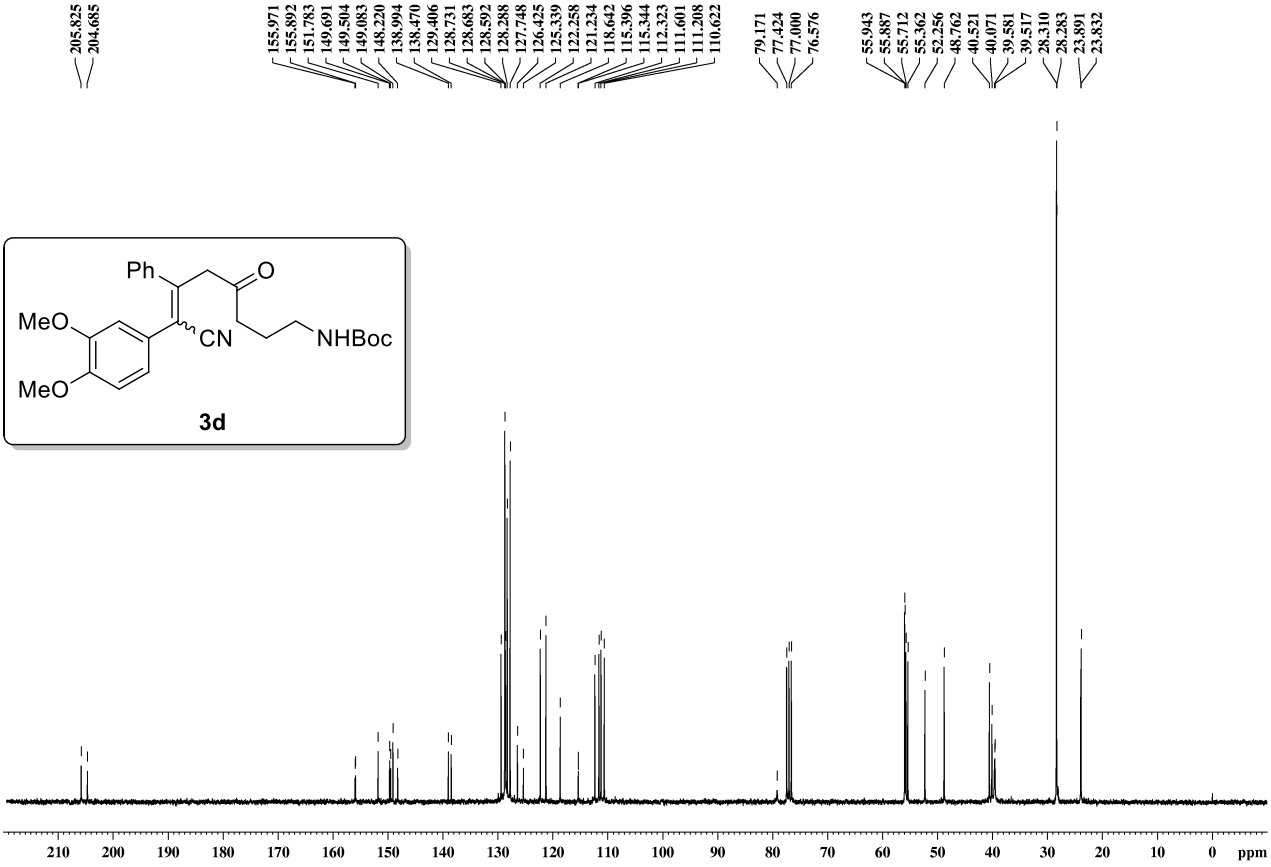
^{13}C NMR (75 MHz, $CDCl_3$); **3c**



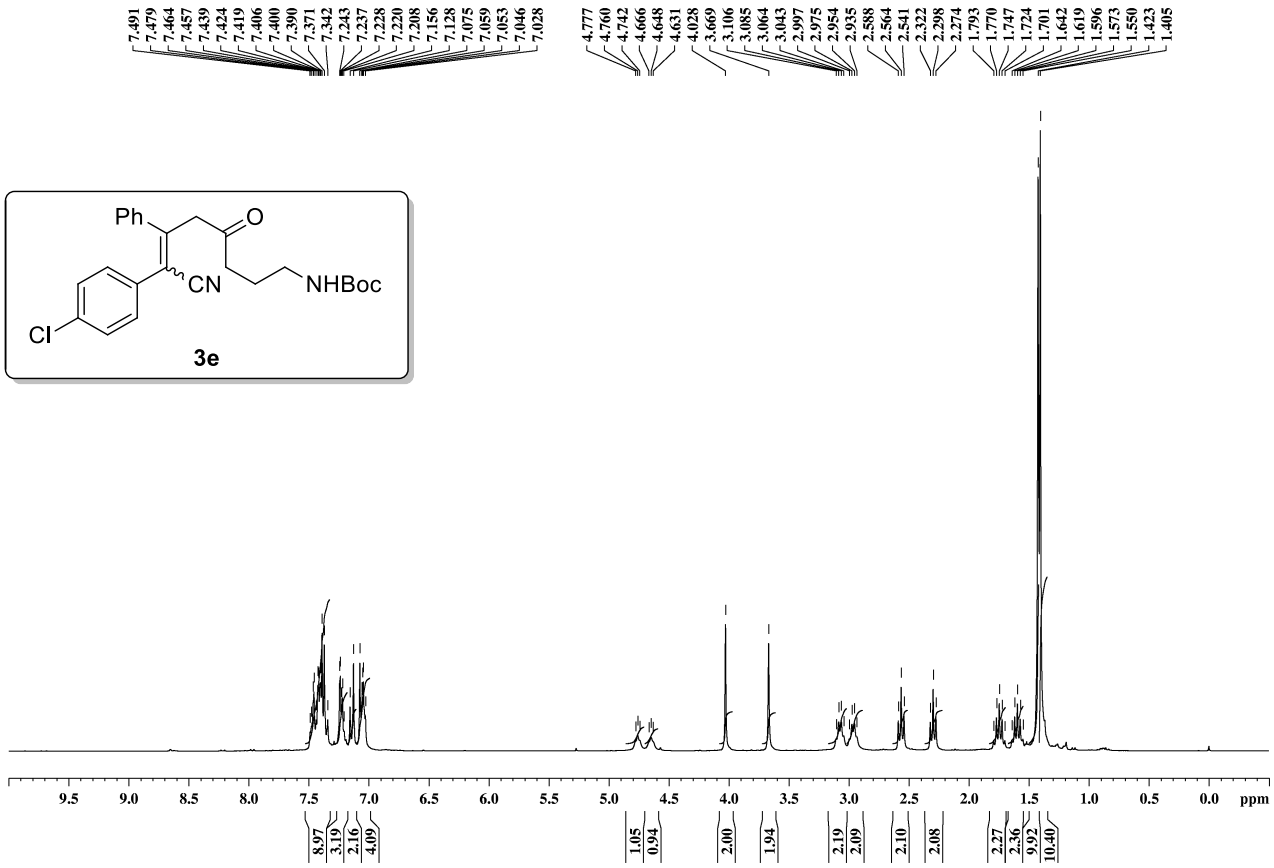
^{1}H NMR (300 MHz, $CDCl_3$); **3d**



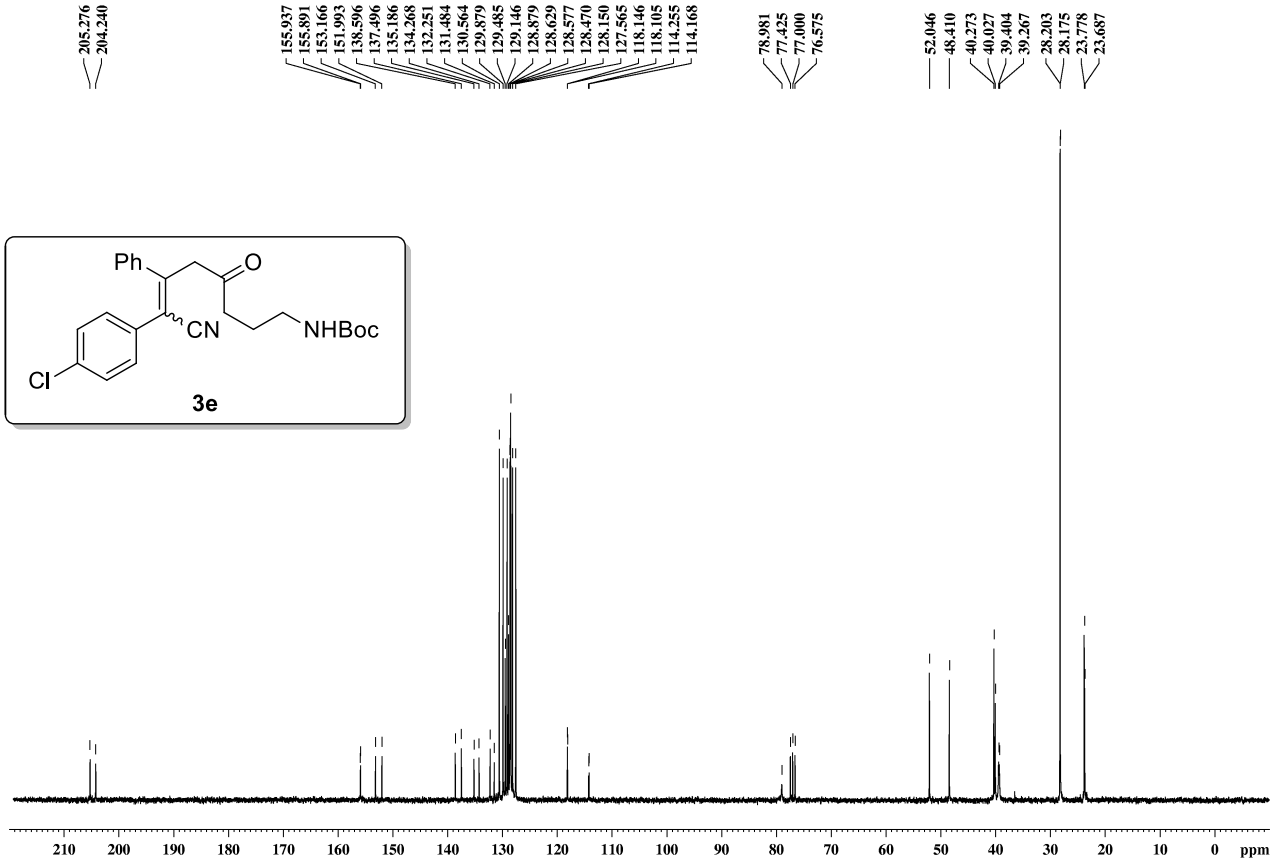
^{13}C NMR (75 MHz, $CDCl_3$); **3d**



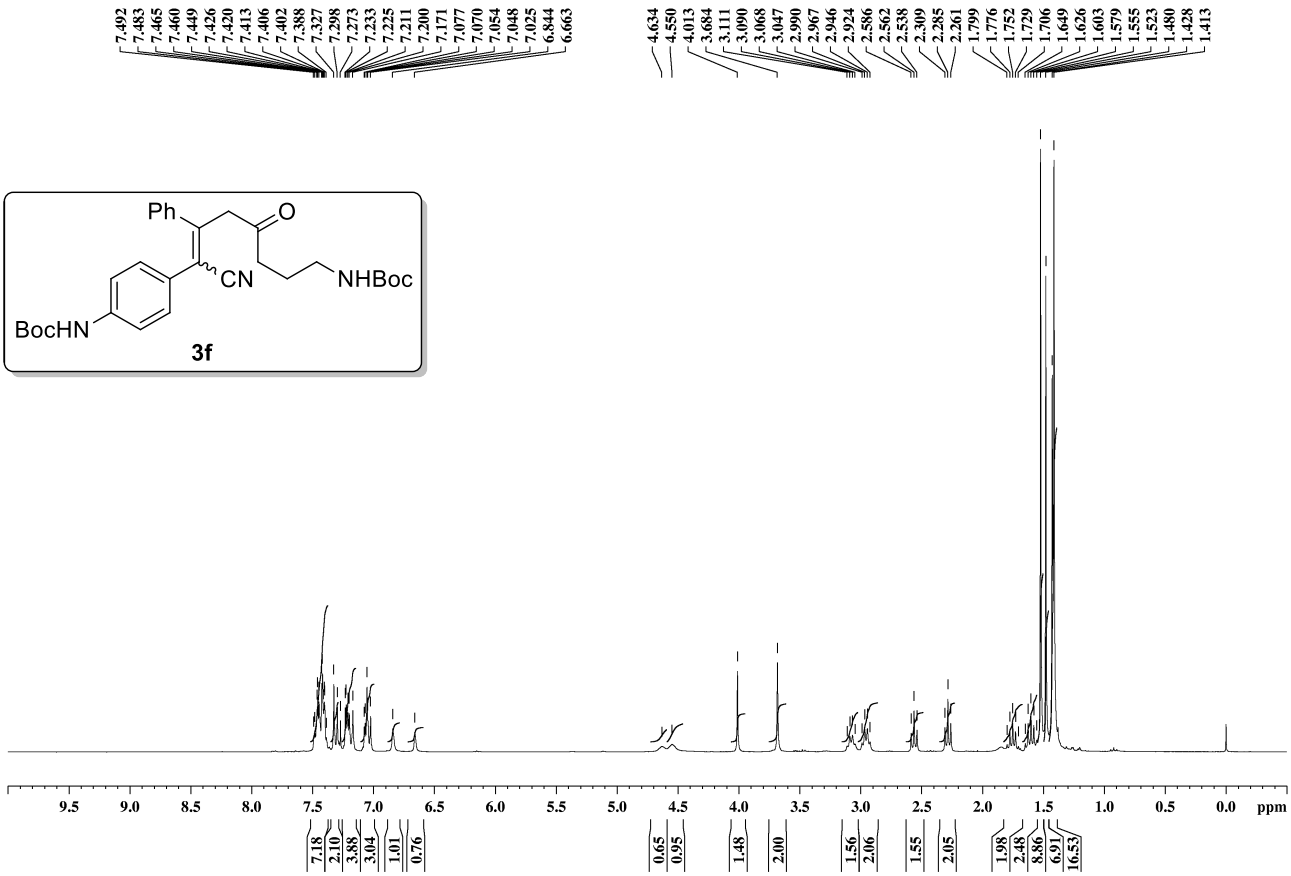
^{1}H NMR (300 MHz, $CDCl_3$); **3e**



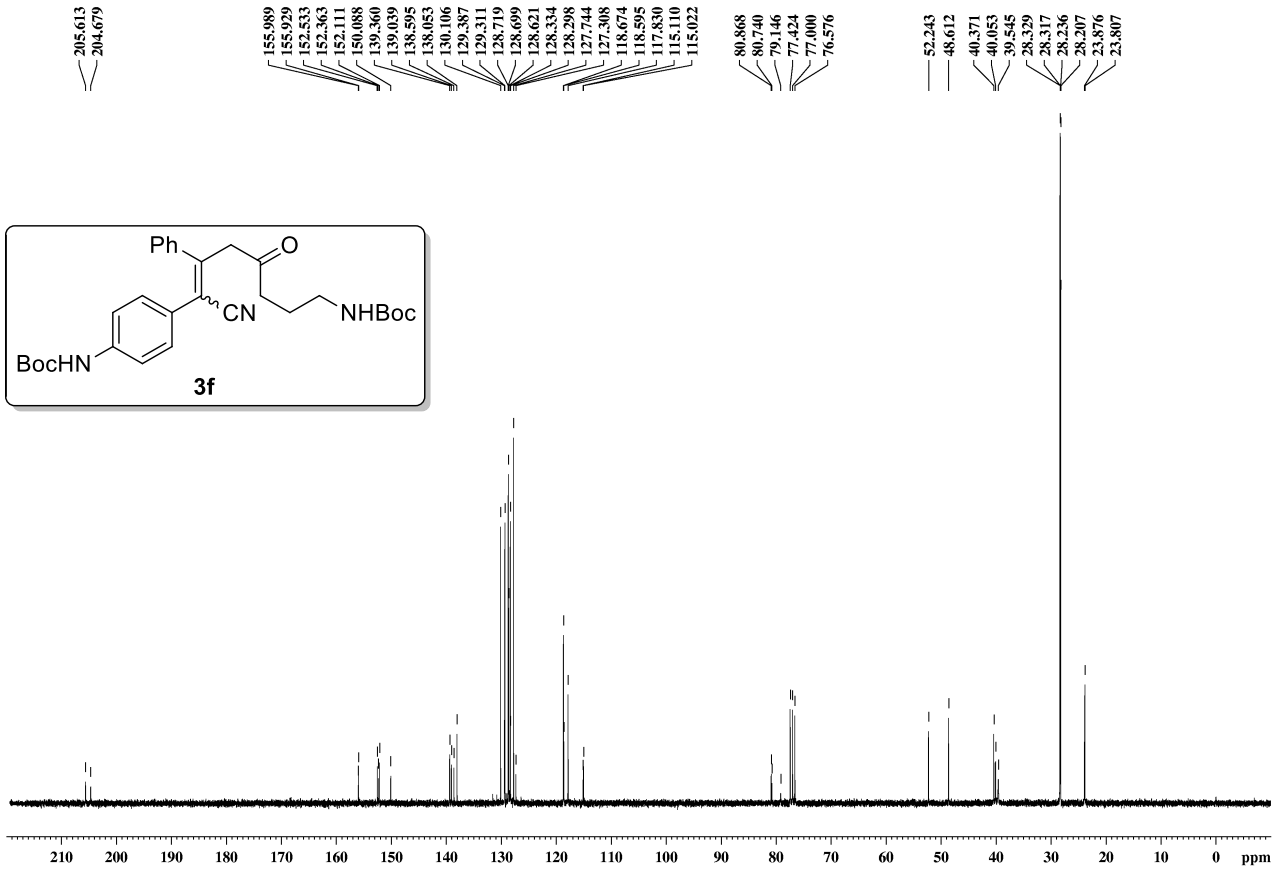
^{13}C NMR (75 MHz, $CDCl_3$); **3e**



^{1}H NMR (300 MHz, $CDCl_3$); **3f**



^{13}C NMR (75 MHz, $CDCl_3$); **3f**



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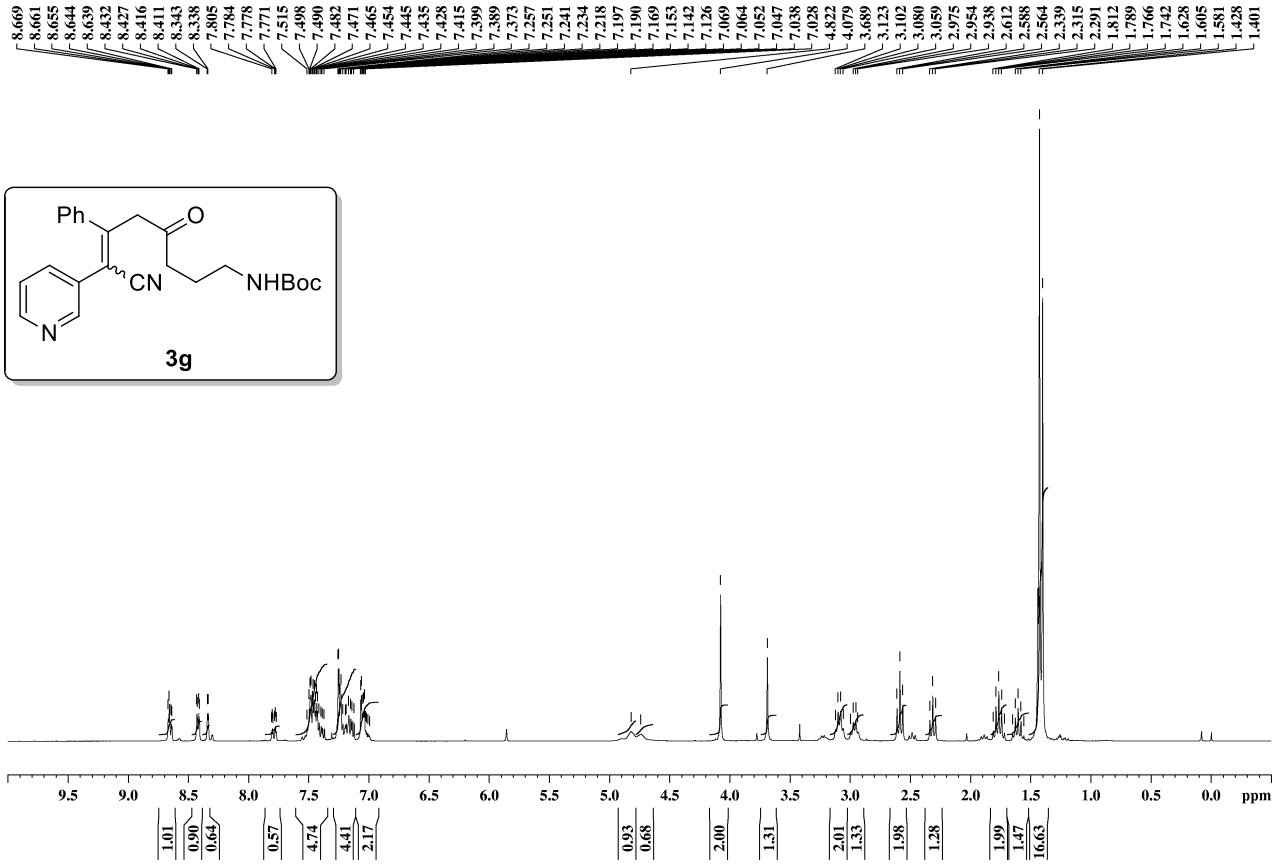
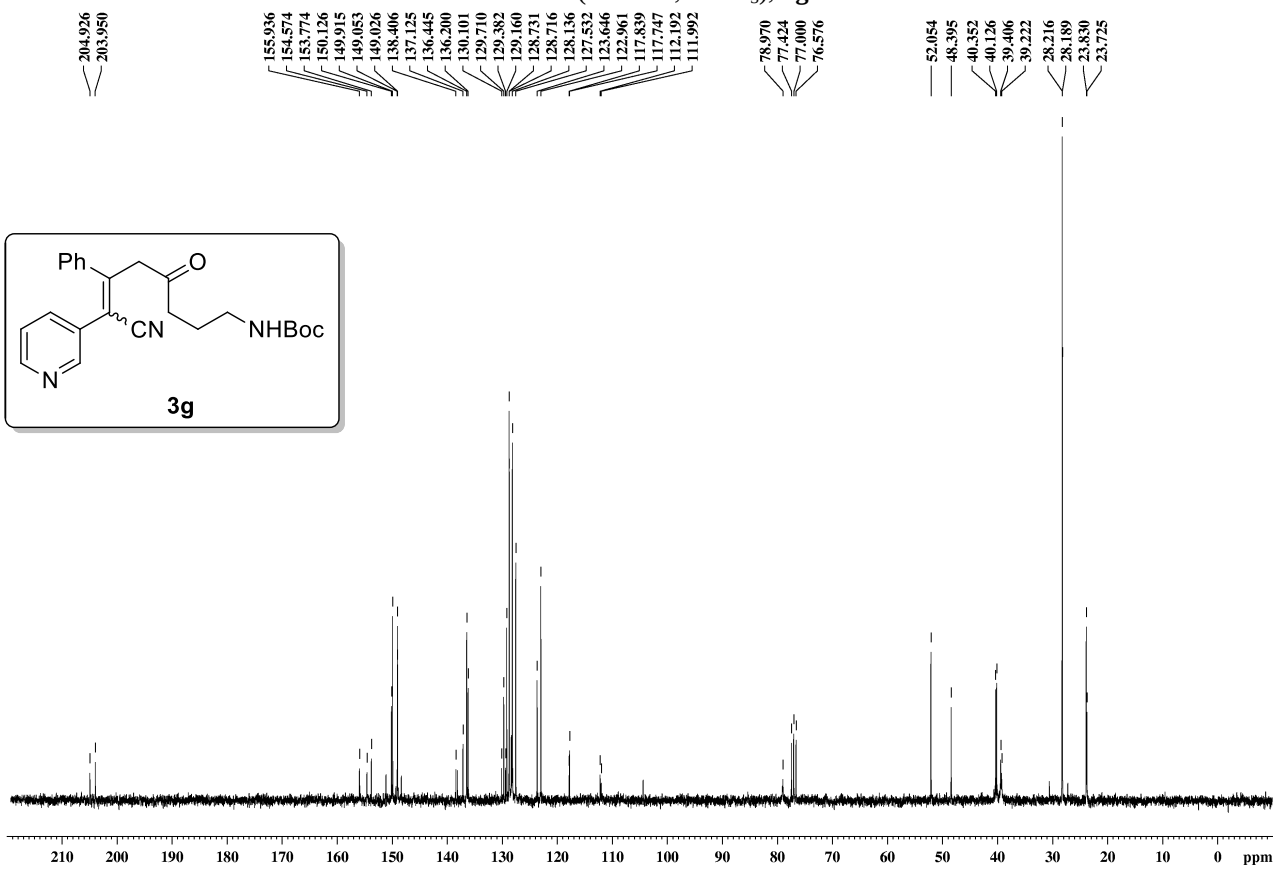
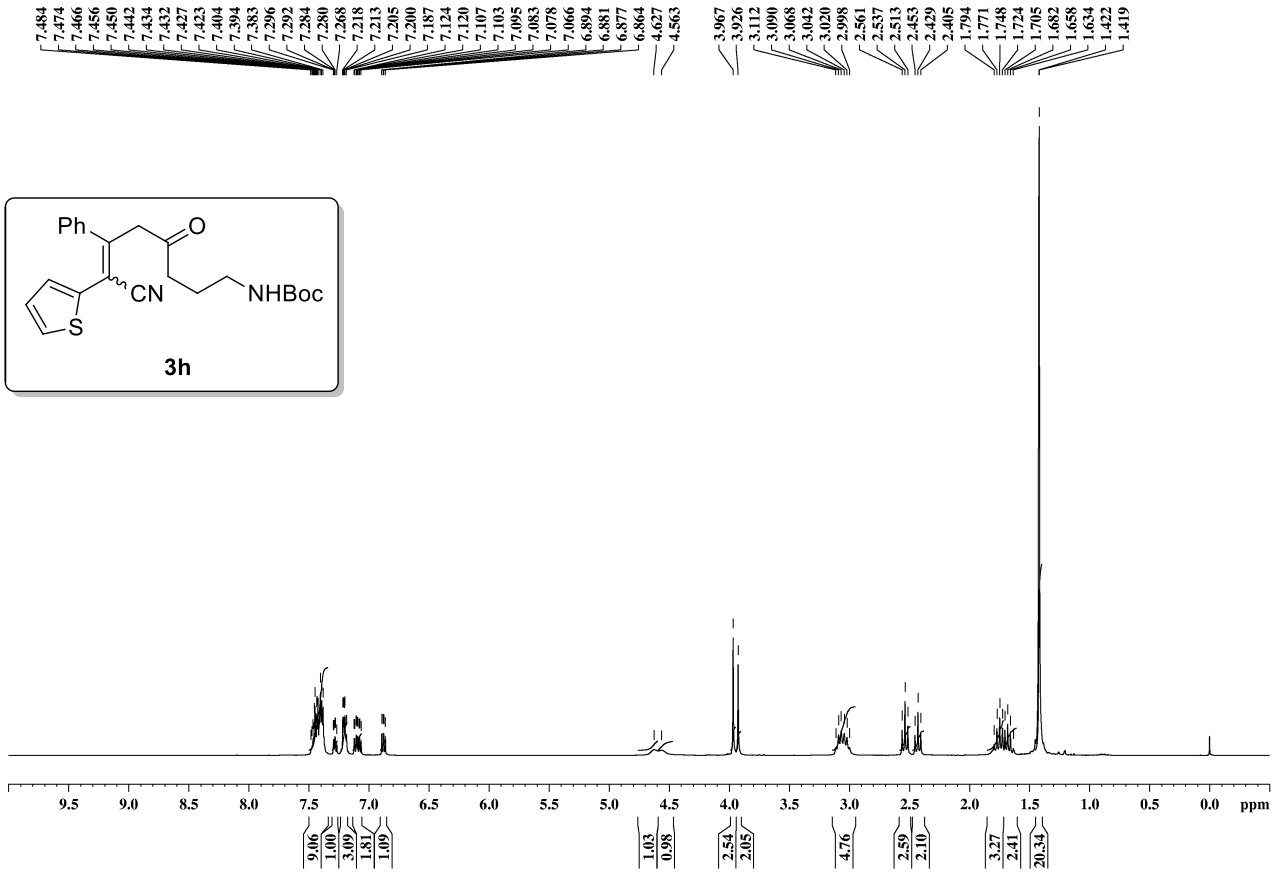


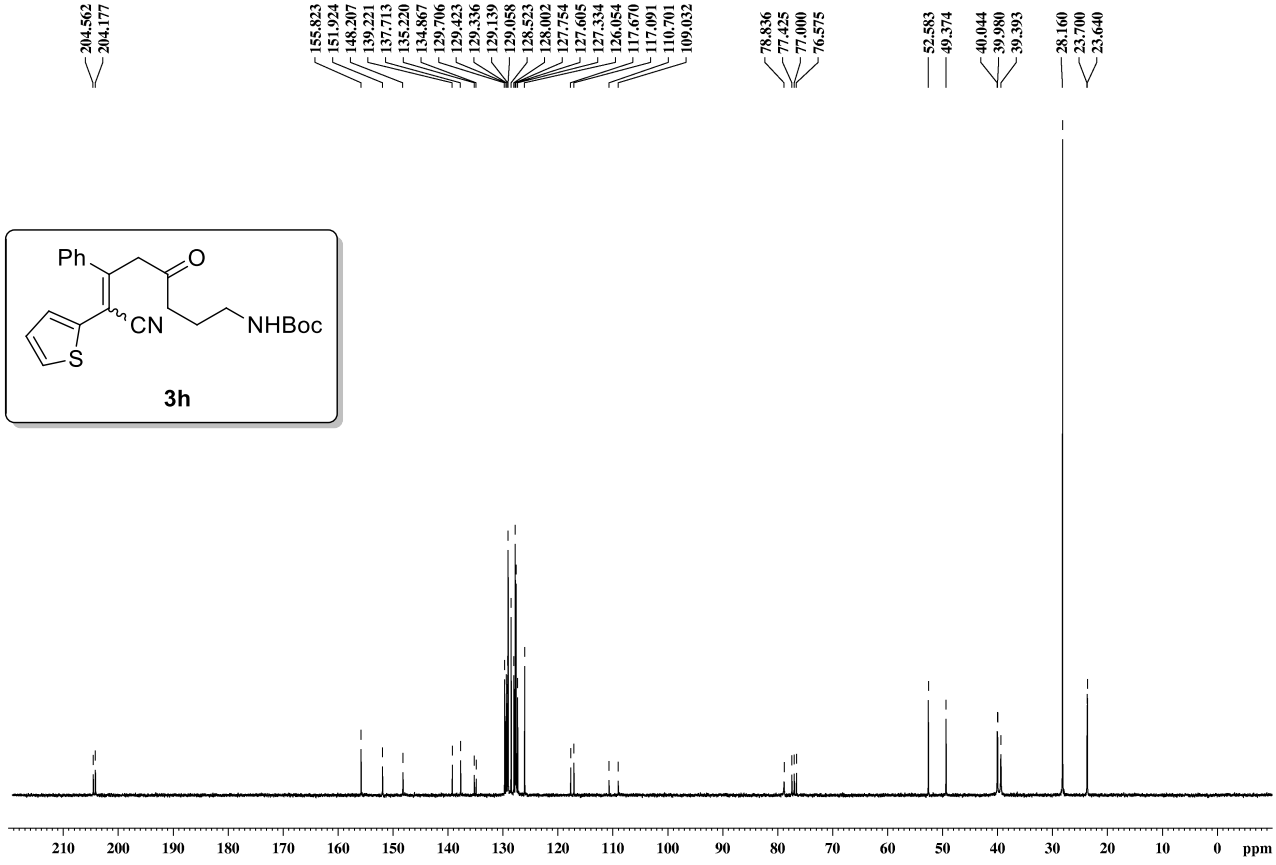
^{13}C NMR (75 MHz, $CDCl_3$); **3g**



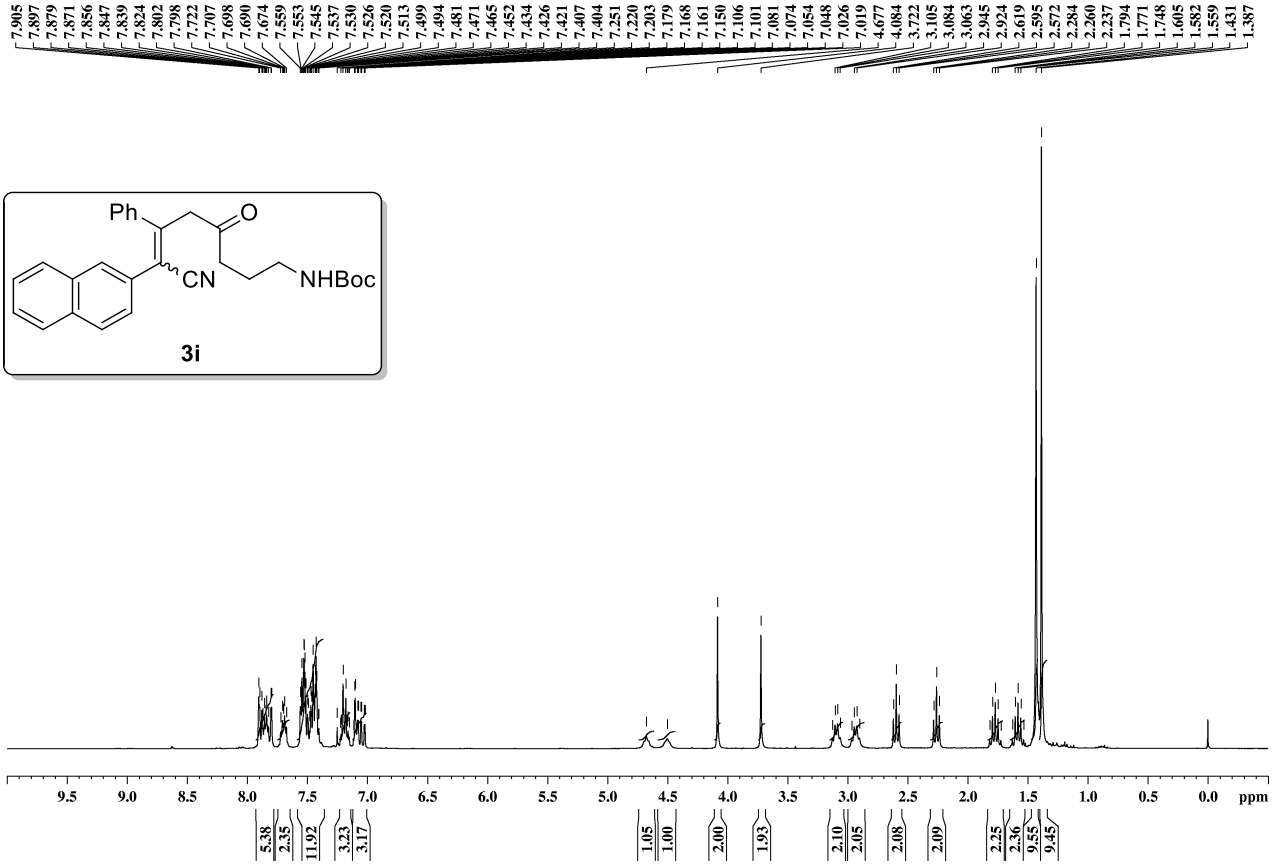
^{1}H NMR (300 MHz, $CDCl_3$); **3h**



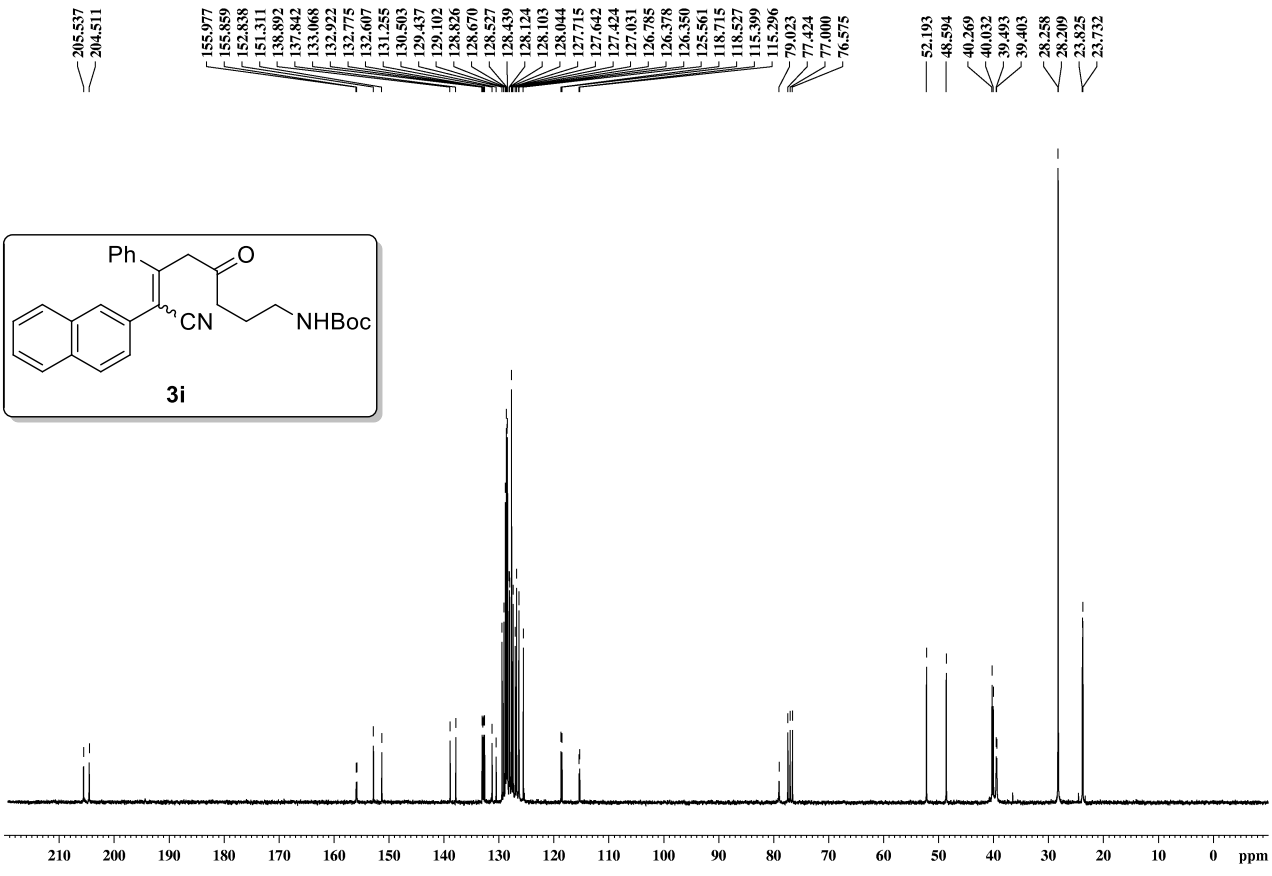
^{13}C NMR (75 MHz, $CDCl_3$); **3h**



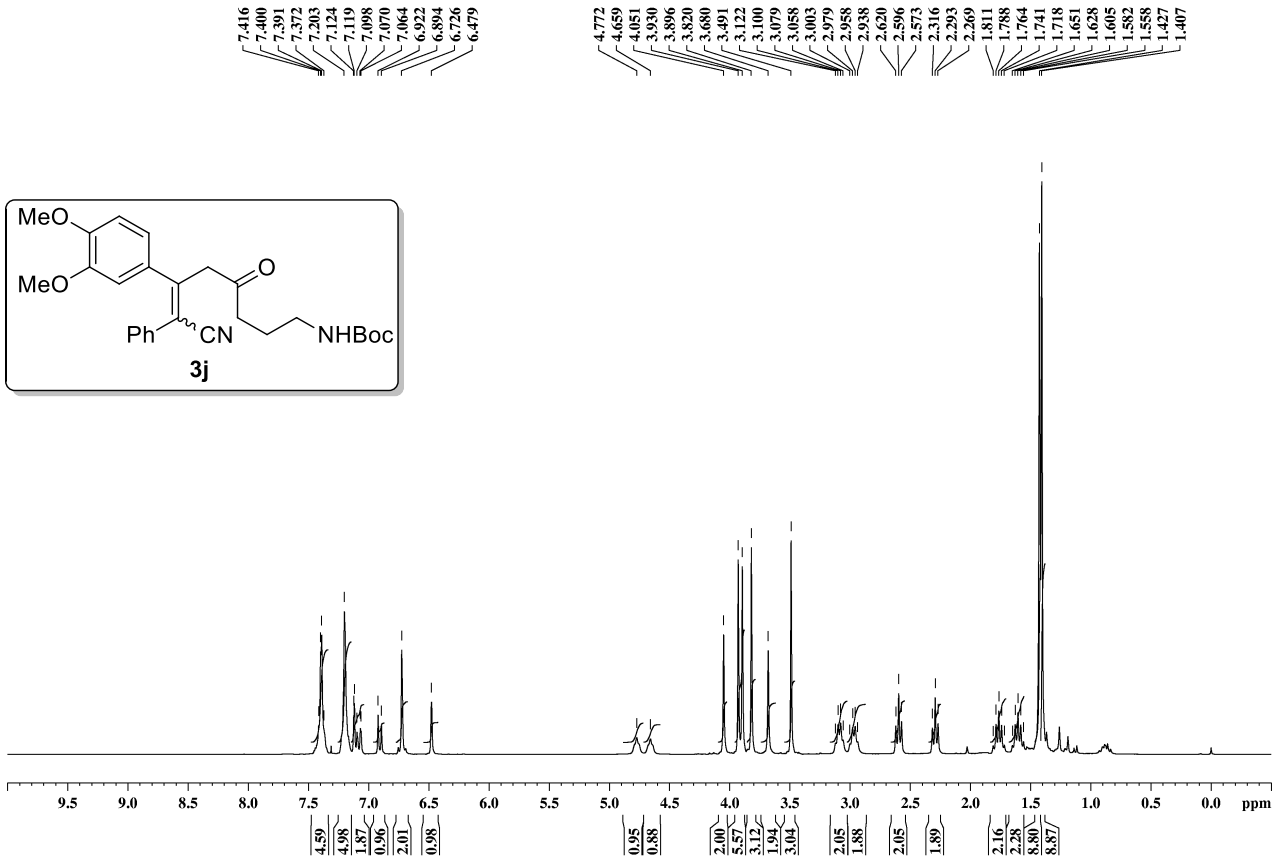
^{1}H NMR (300 MHz, $CDCl_3$); **3i**



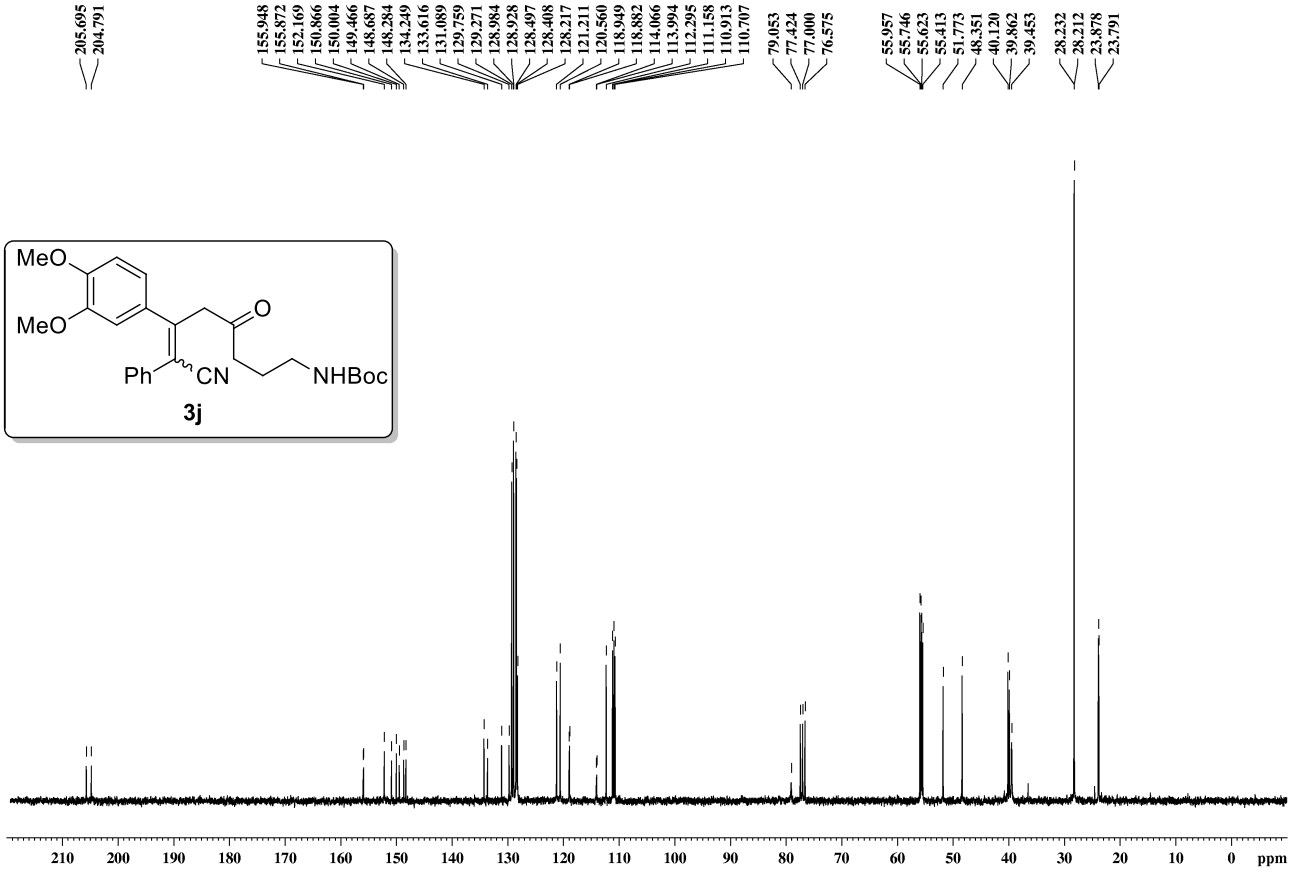
^{13}C NMR (75 MHz, $CDCl_3$); **3i**



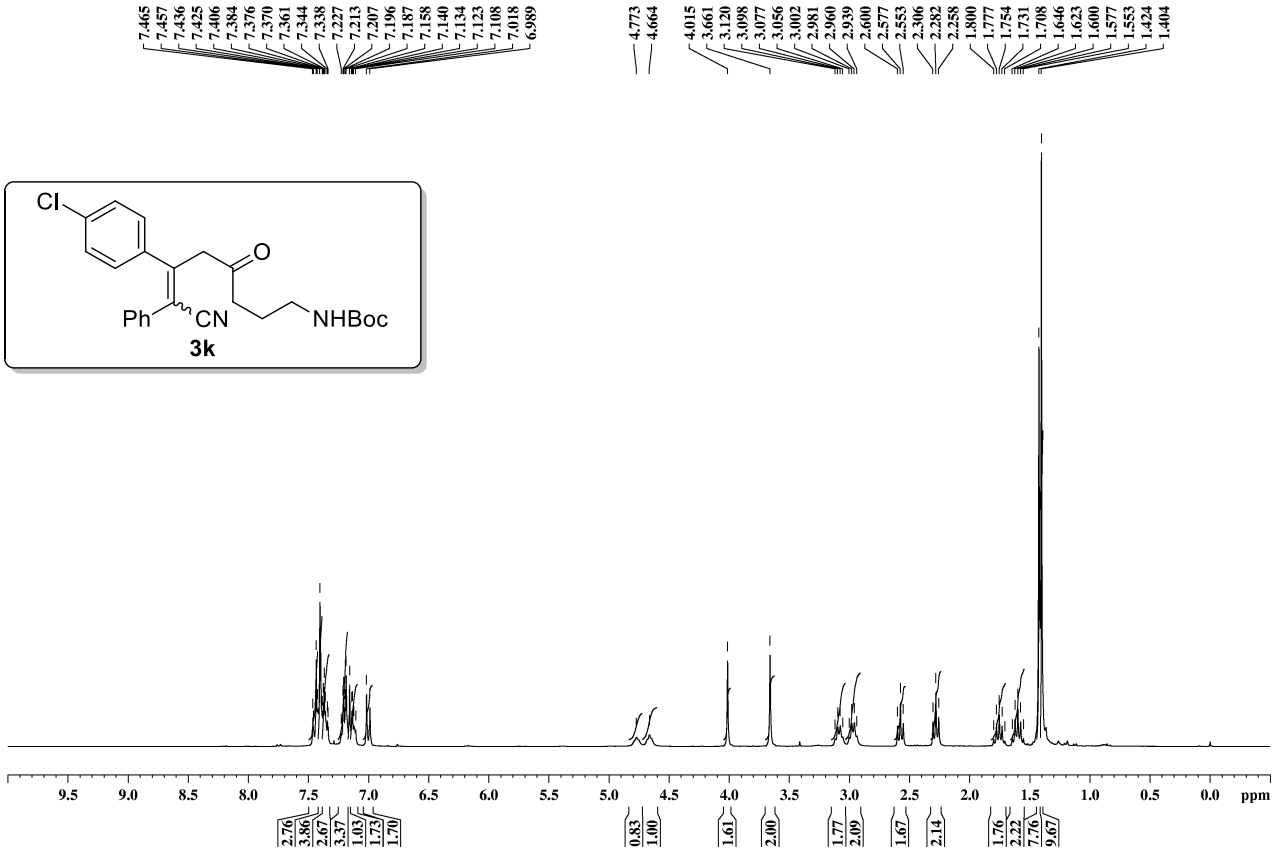
^{1}H NMR (300 MHz, $CDCl_3$); **3j**



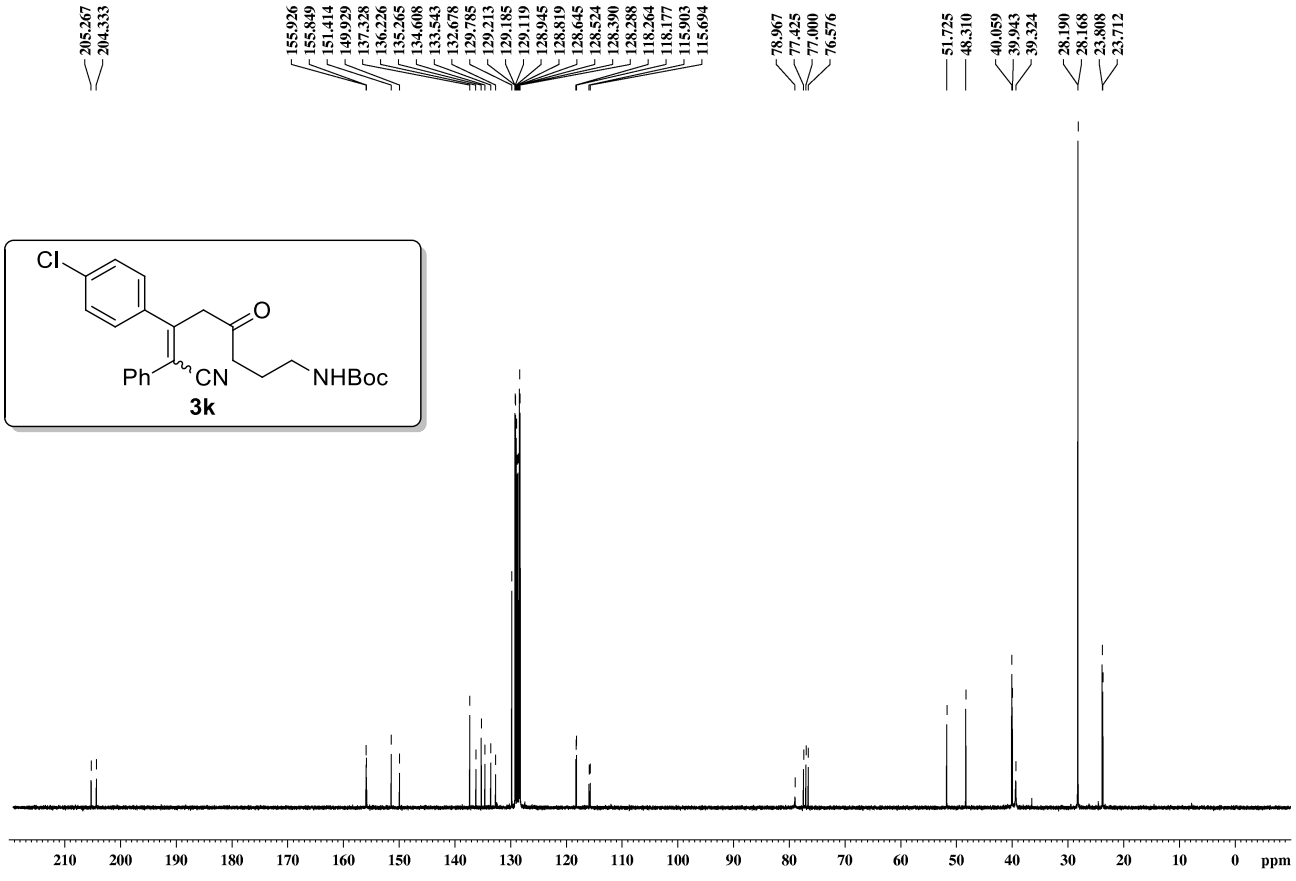
^{13}C NMR (75 MHz, $CDCl_3$); **3j**



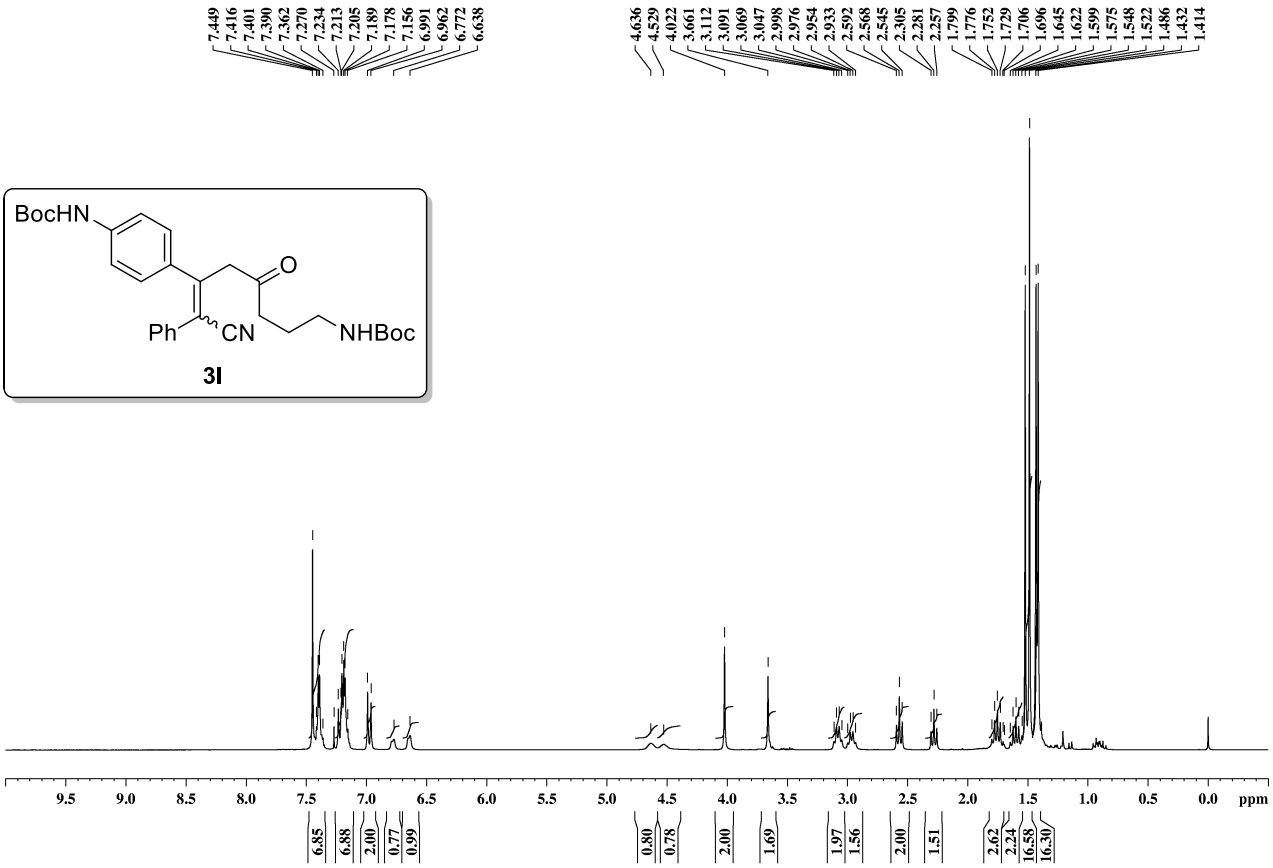
^{1}H NMR (300 MHz, $CDCl_3$); **3k**



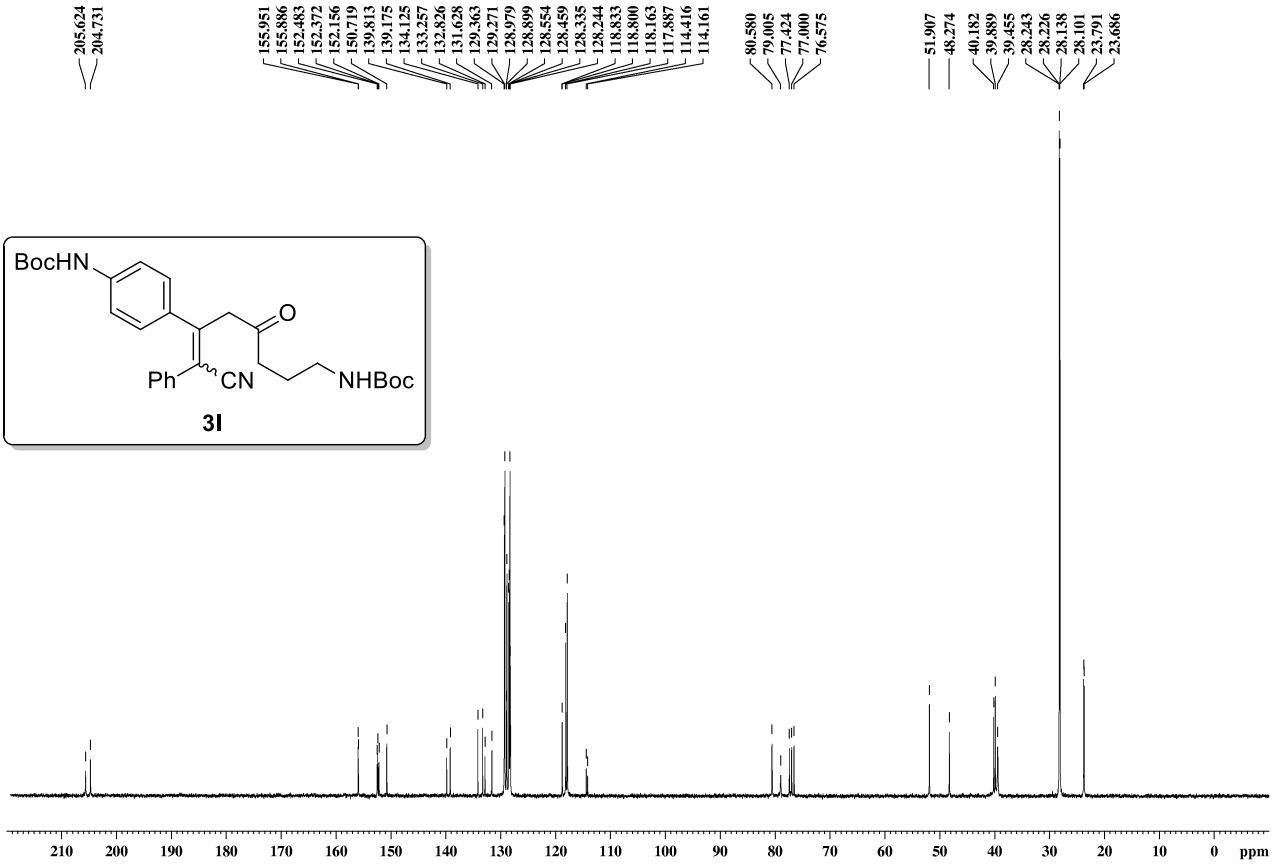
^{13}C NMR (75 MHz, $CDCl_3$); **3k**



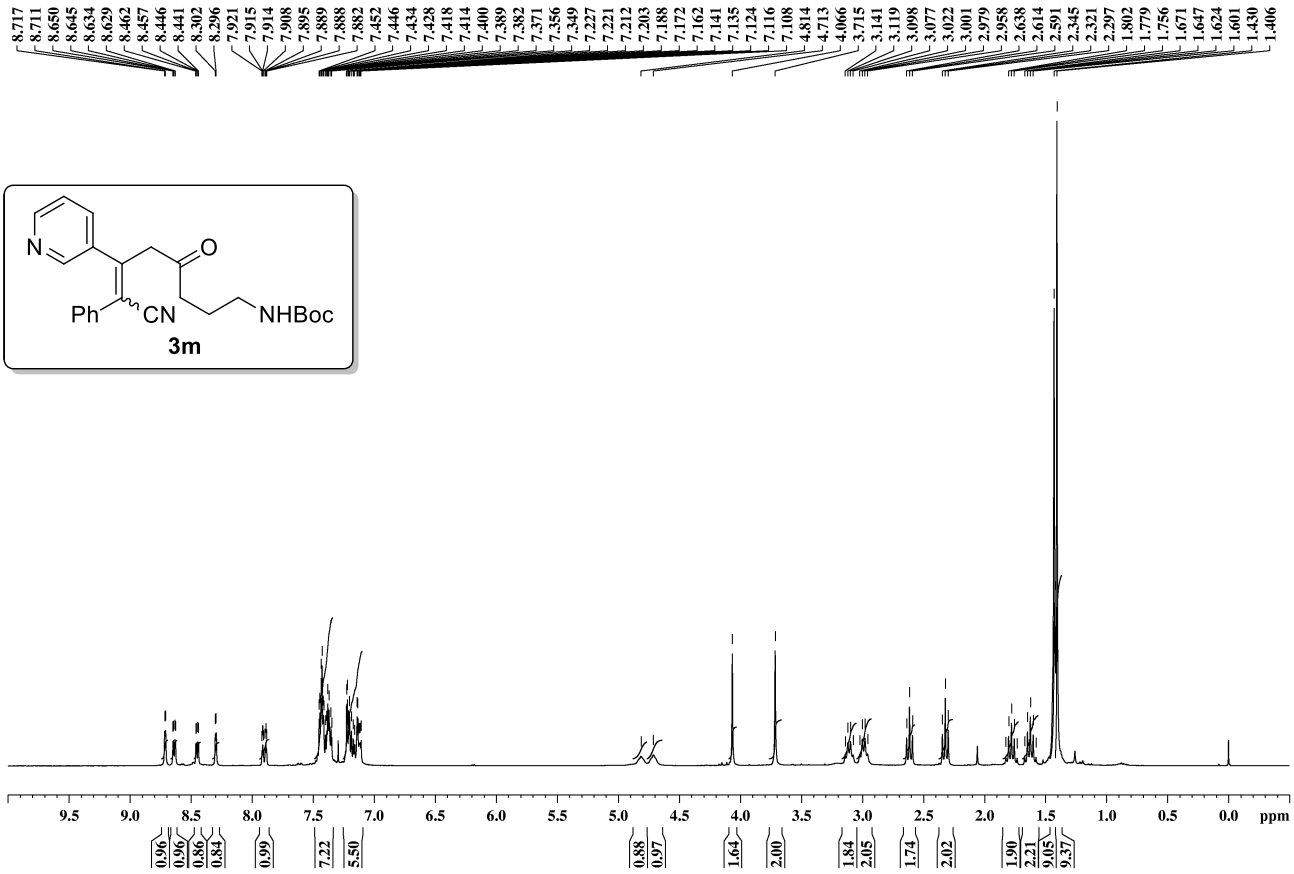
^{1}H NMR (300 MHz, $CDCl_3$); **3l**



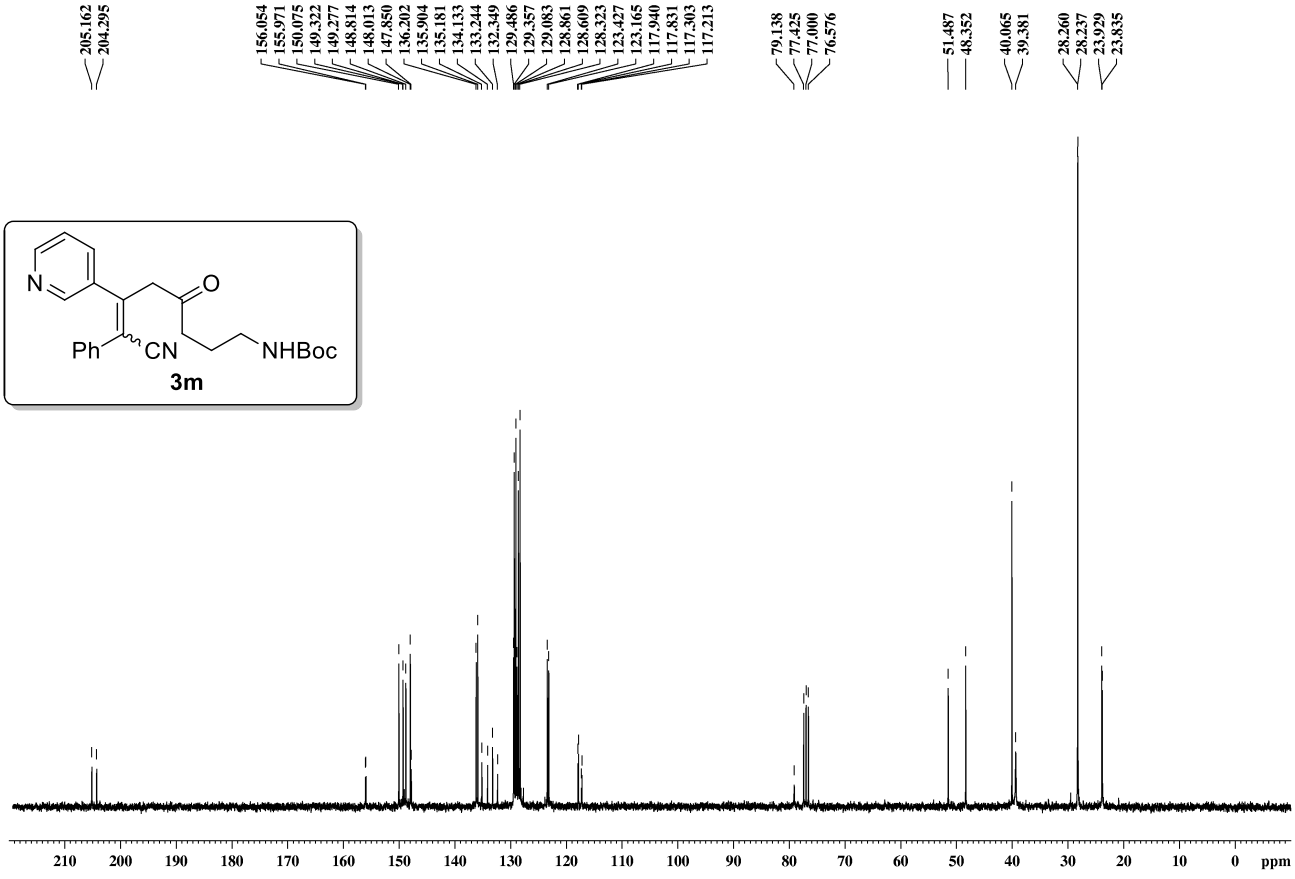
^{13}C NMR (75 MHz, $CDCl_3$); **3l**



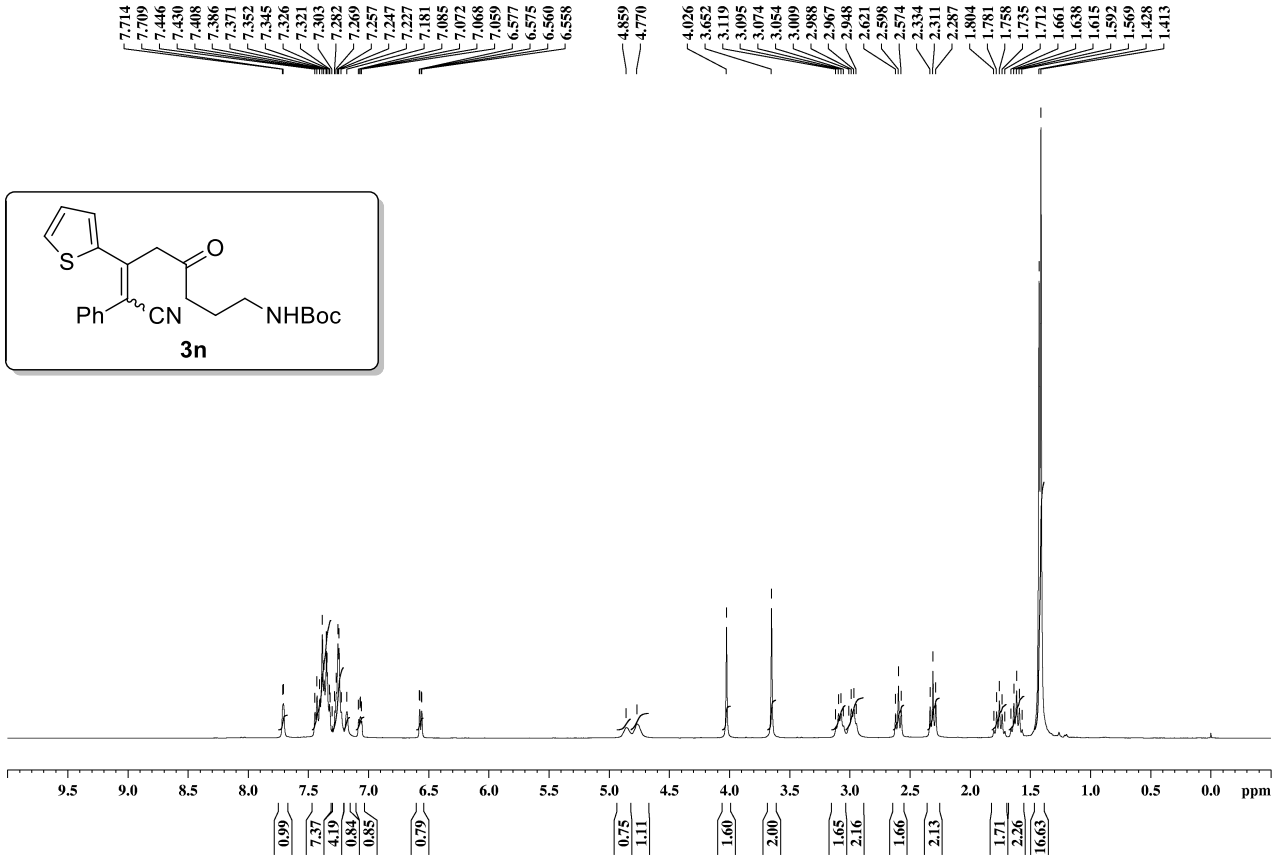
^{1}H NMR (300 MHz, $CDCl_3$); **3m**



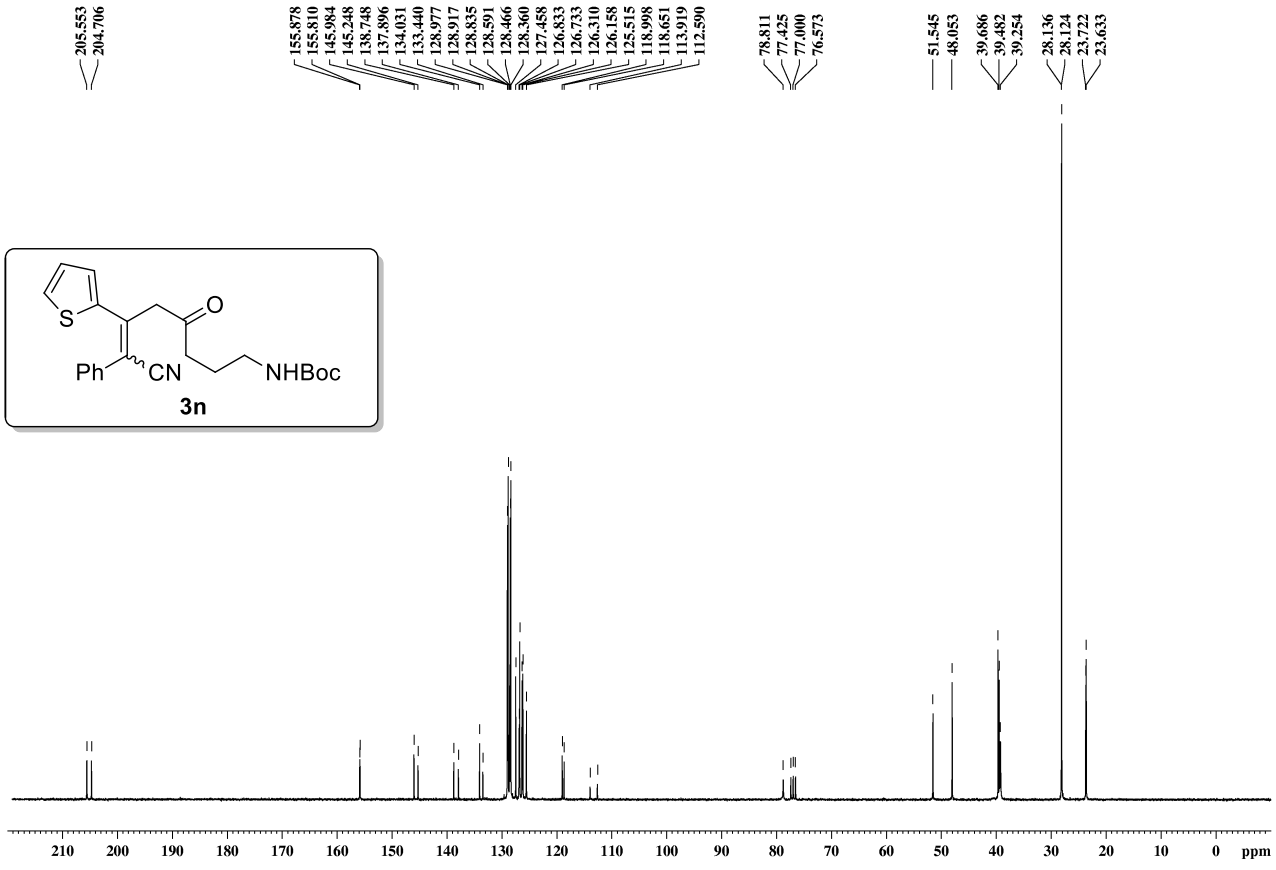
^{13}C NMR (75 MHz, $CDCl_3$); **3m**



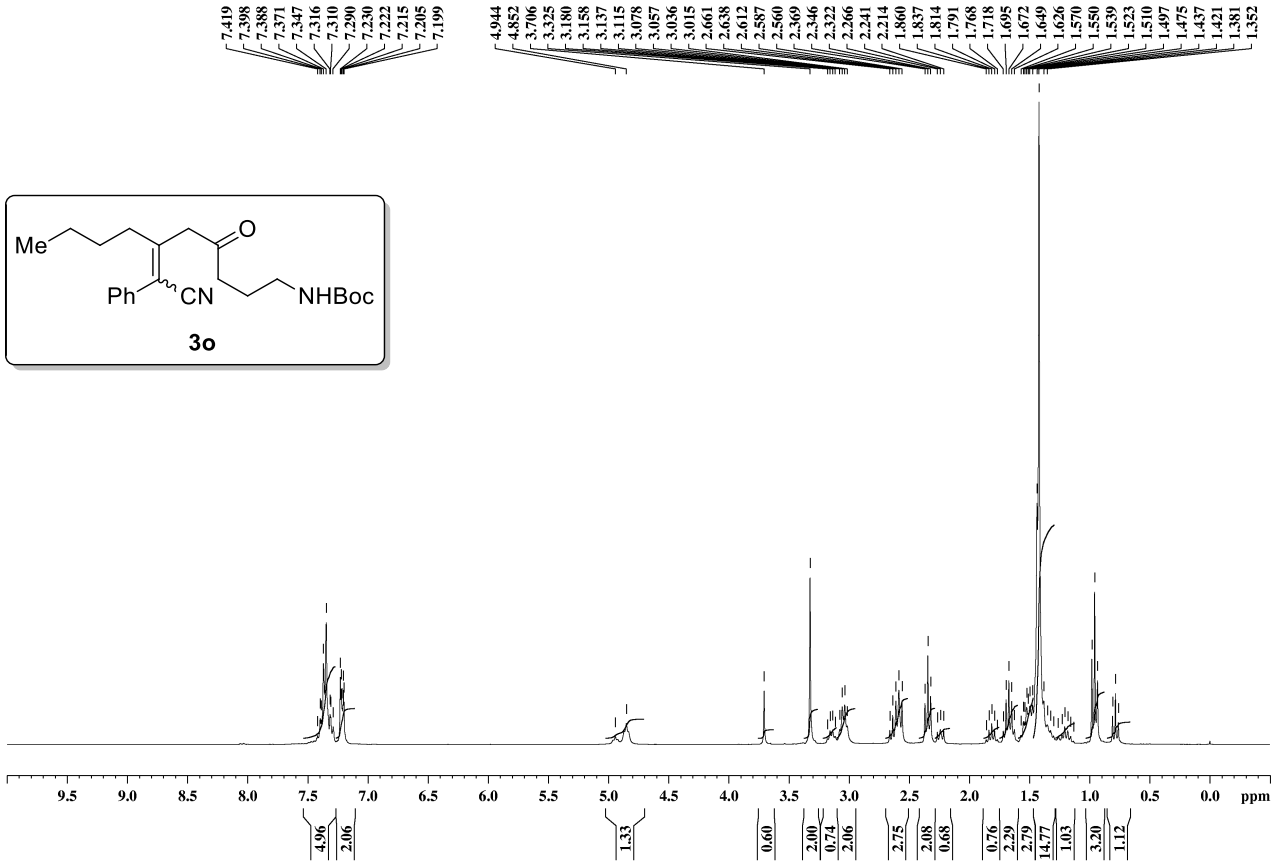
^{1}H NMR (300 MHz, $CDCl_3$); **3n**



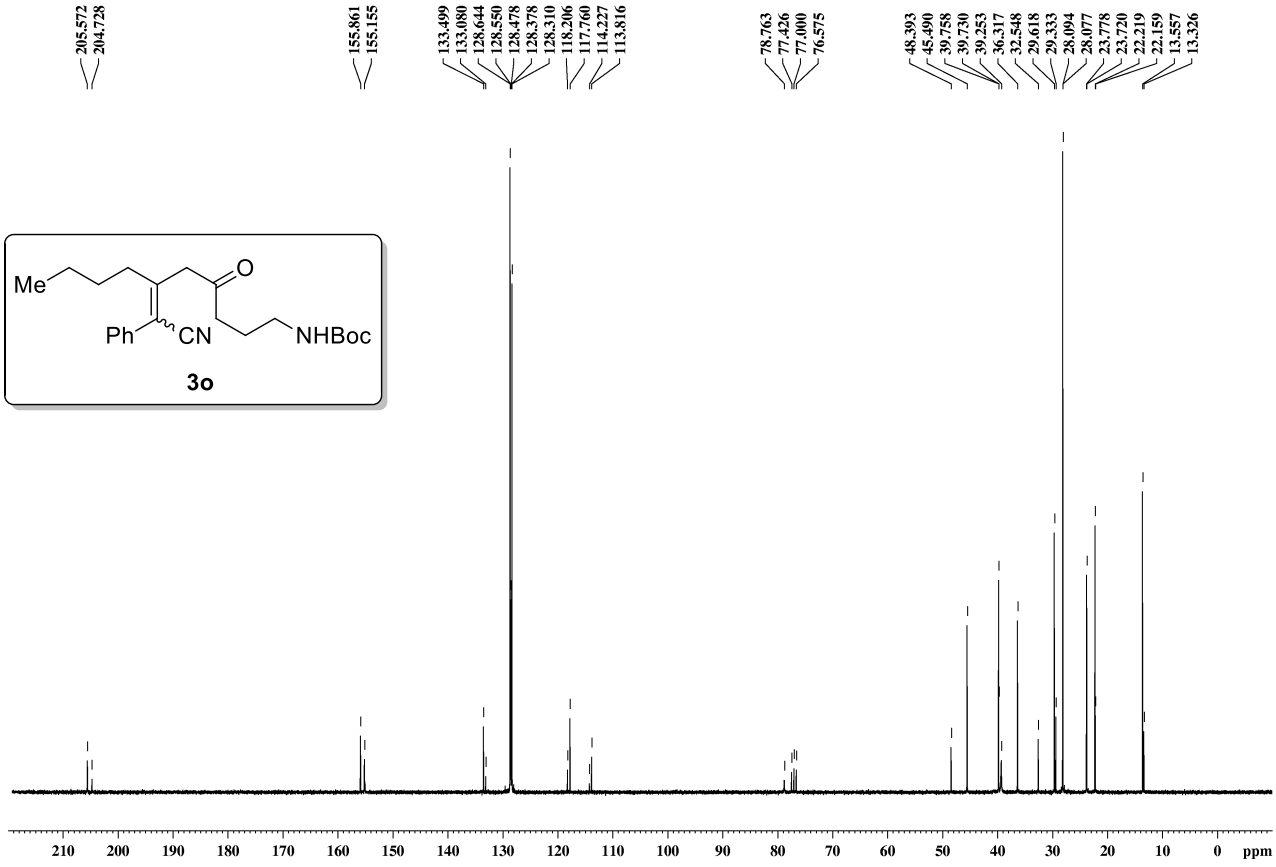
^{13}C NMR (75 MHz, $CDCl_3$); **3n**



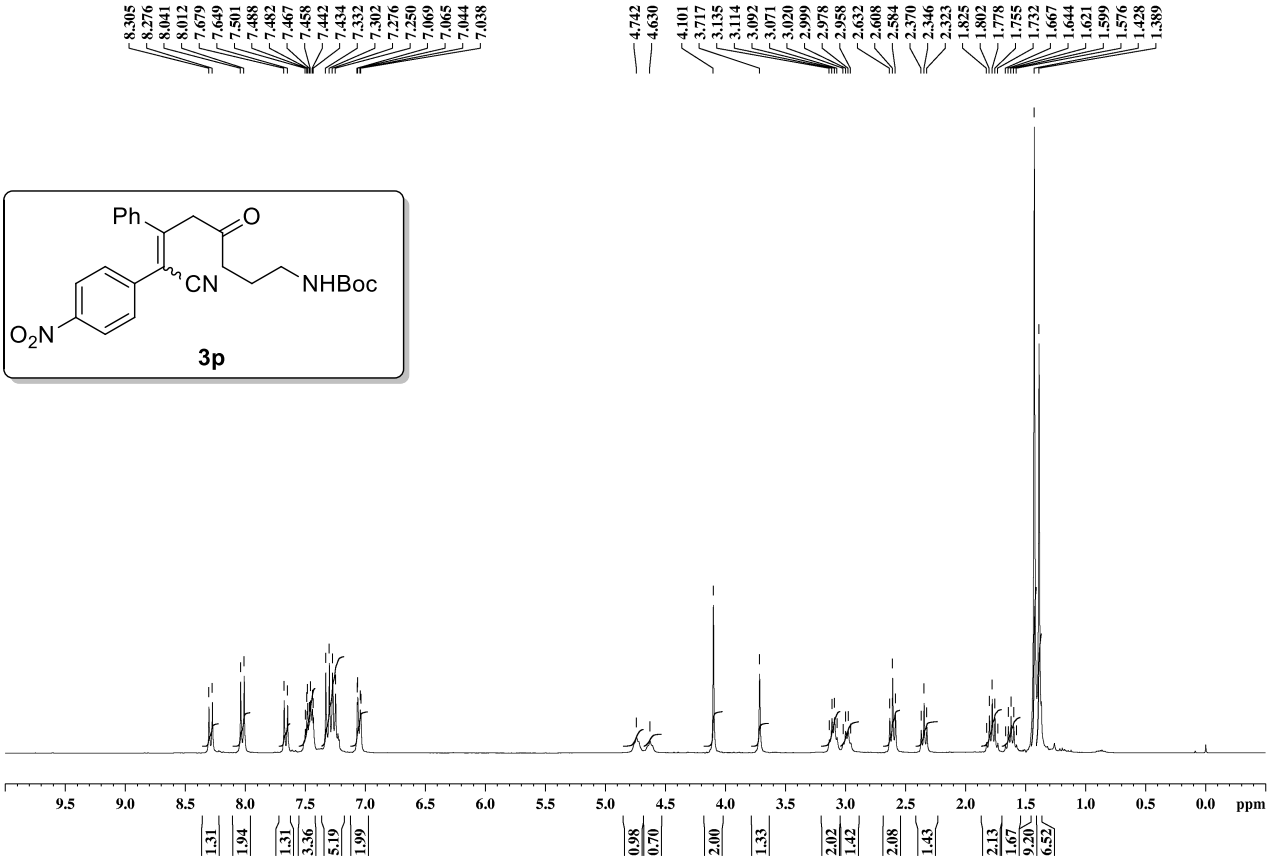
^{1}H NMR (300 MHz, $CDCl_3$); **3o**



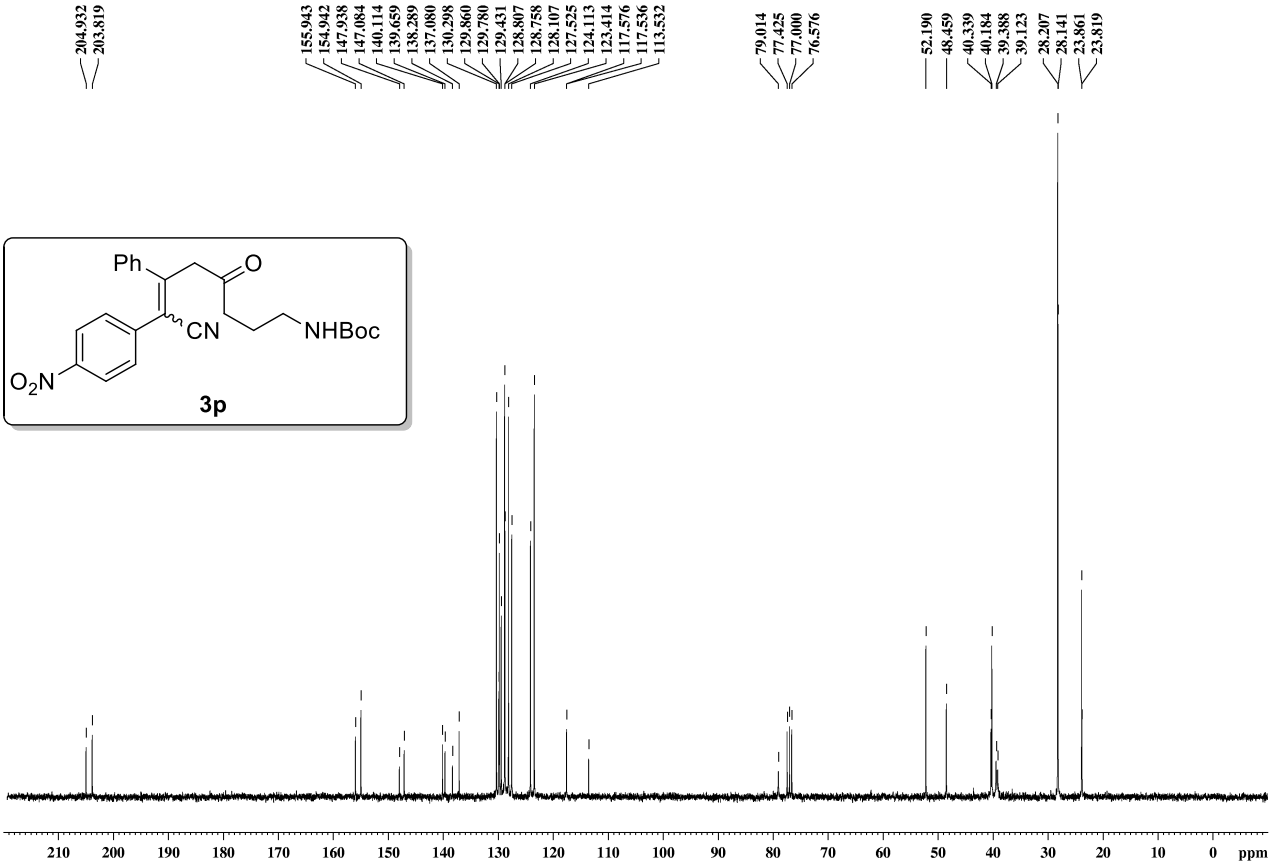
^{13}C NMR (75 MHz, $CDCl_3$); **3o**



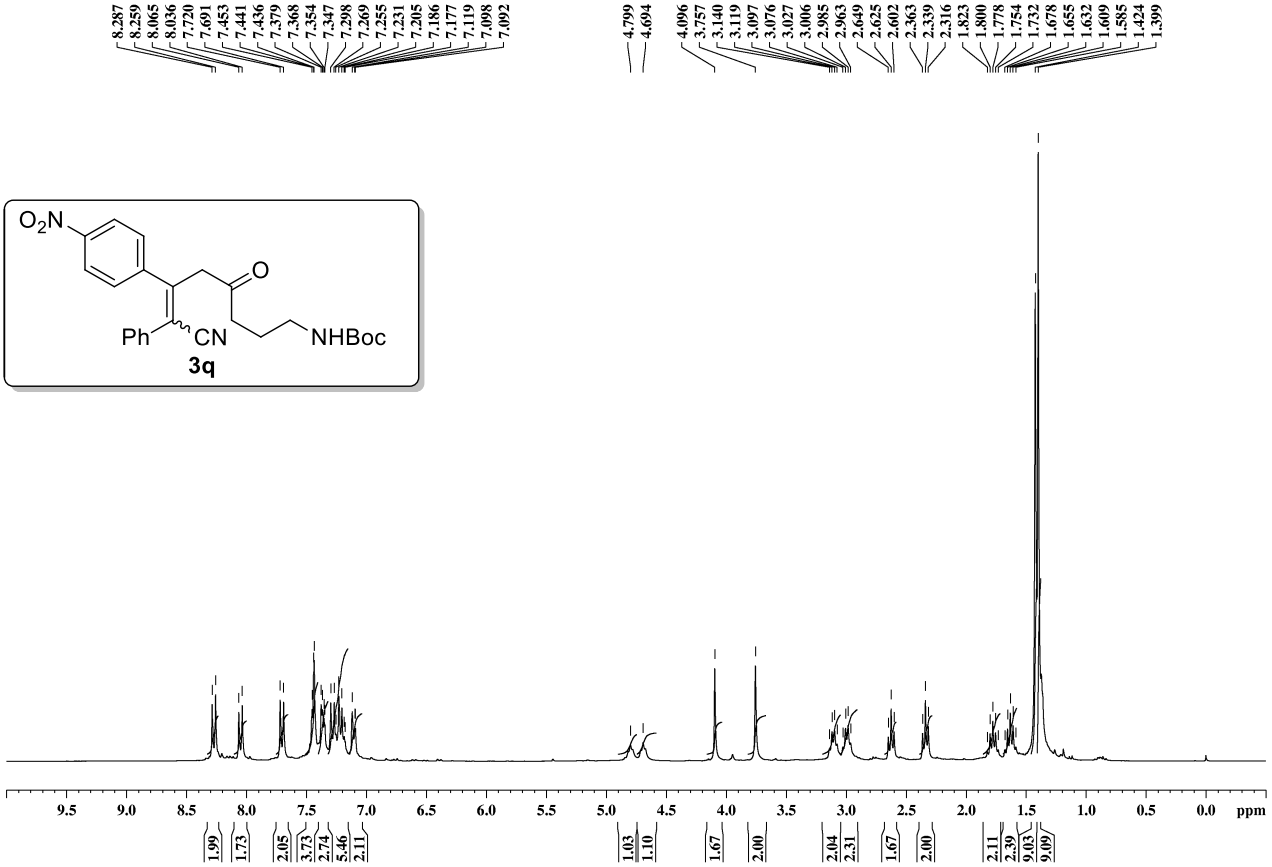
^{1}H NMR (300 MHz, $CDCl_3$); **3p**



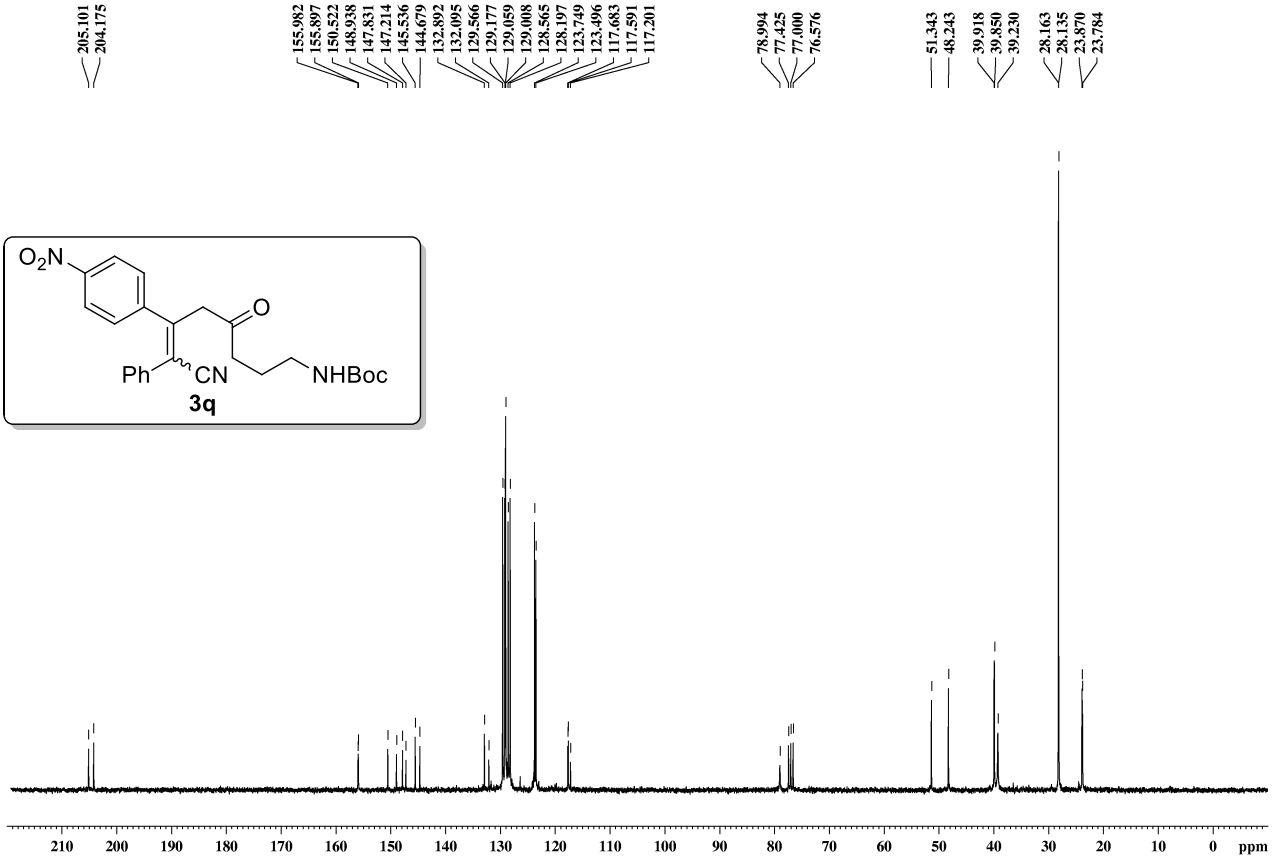
^{13}C NMR (75 MHz, $CDCl_3$); **3p**



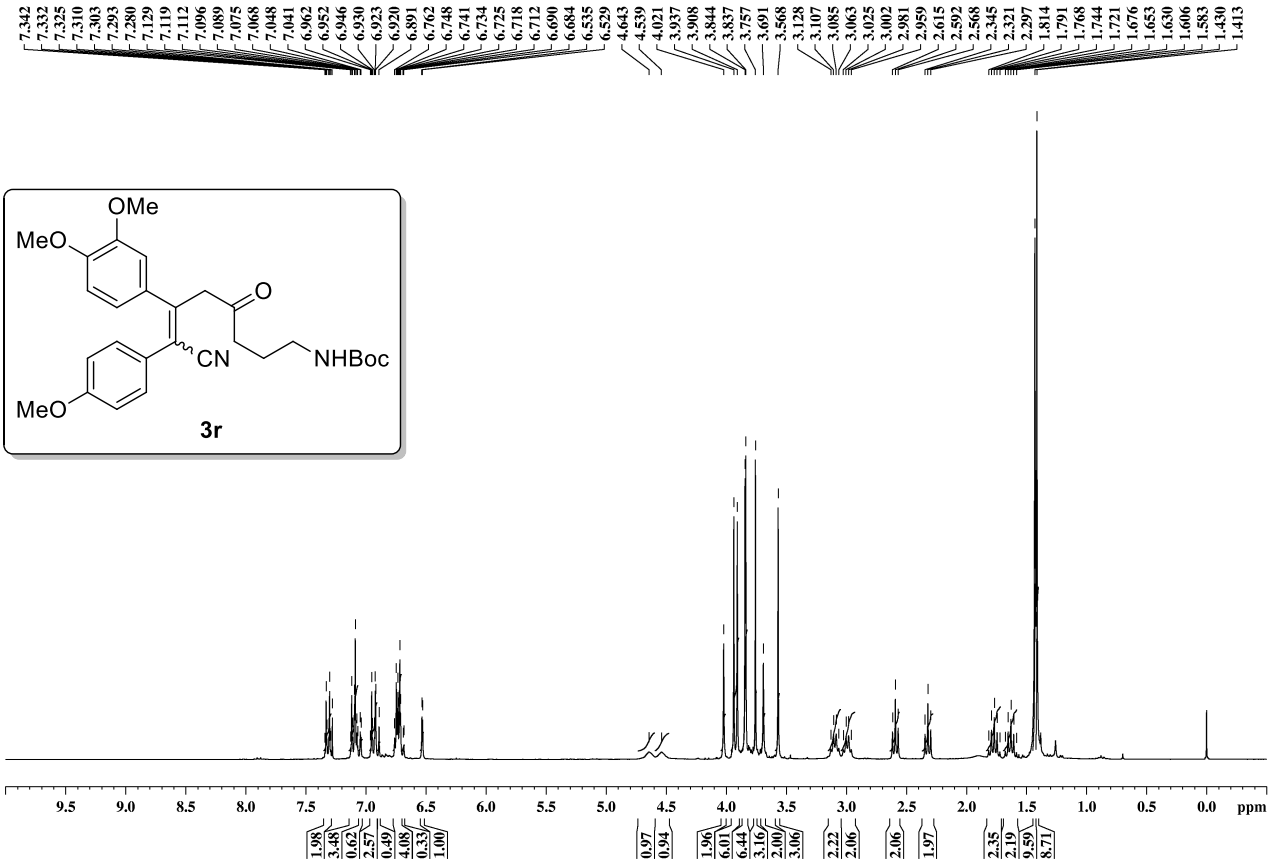
^{1}H NMR (300 MHz, $CDCl_3$); **3q**



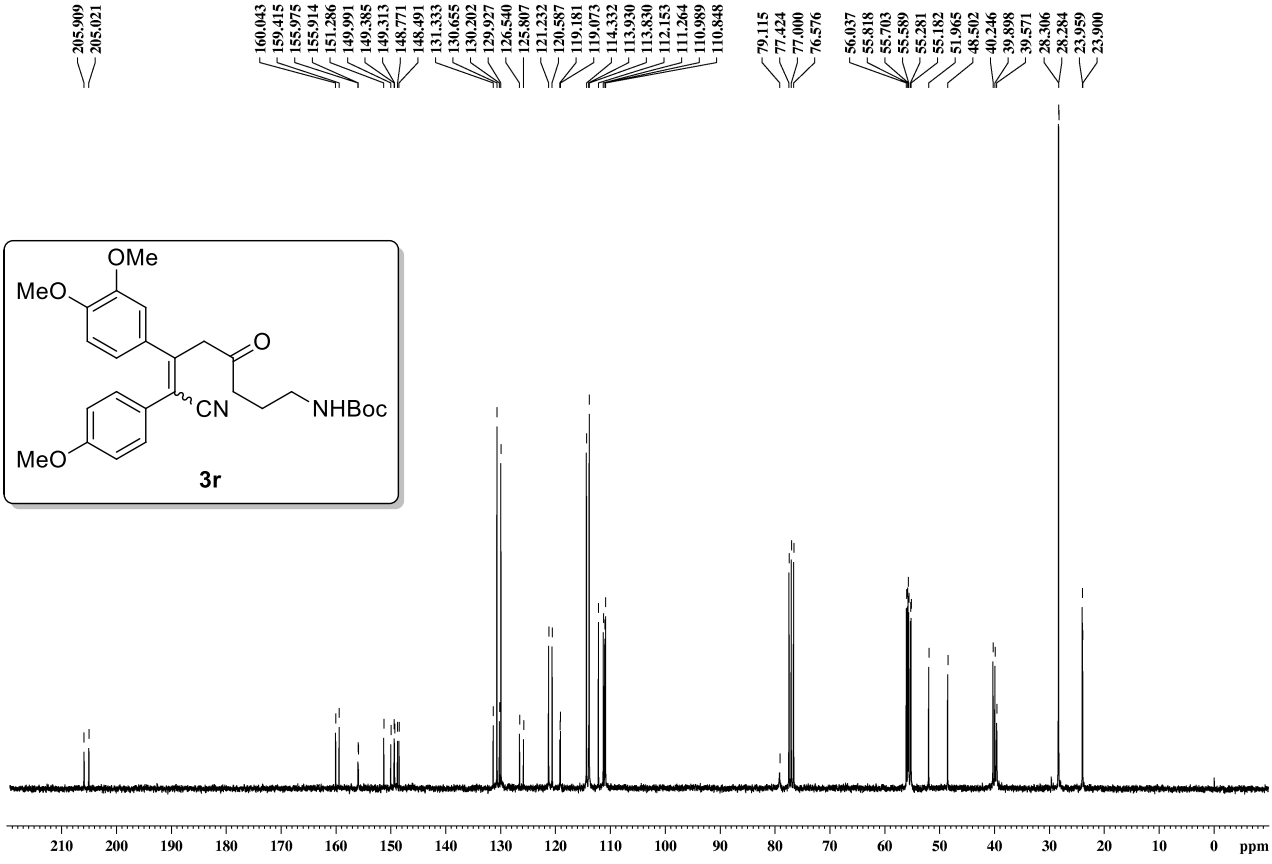
^{13}C NMR (75 MHz, $CDCl_3$); **3q**



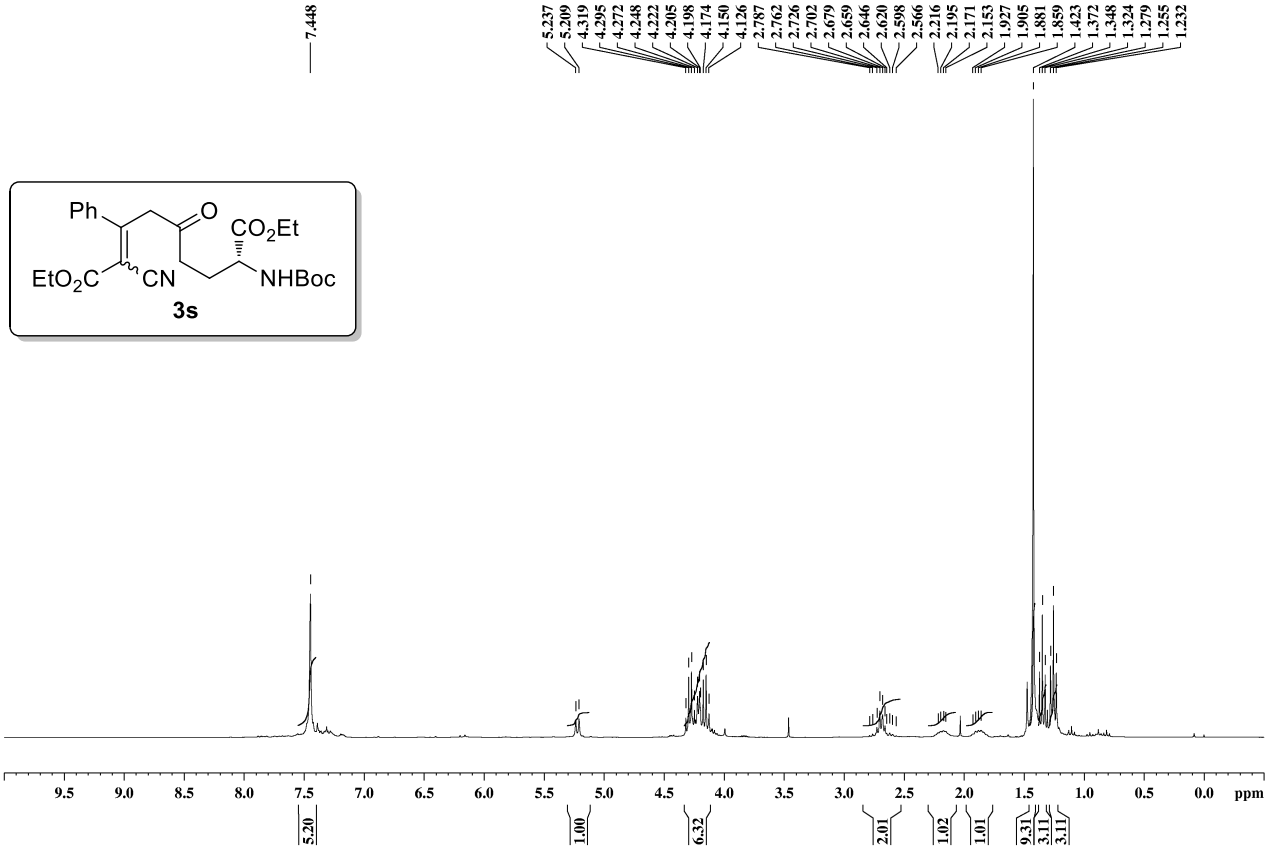
^{1}H NMR (300 MHz, $CDCl_3$); **3r**



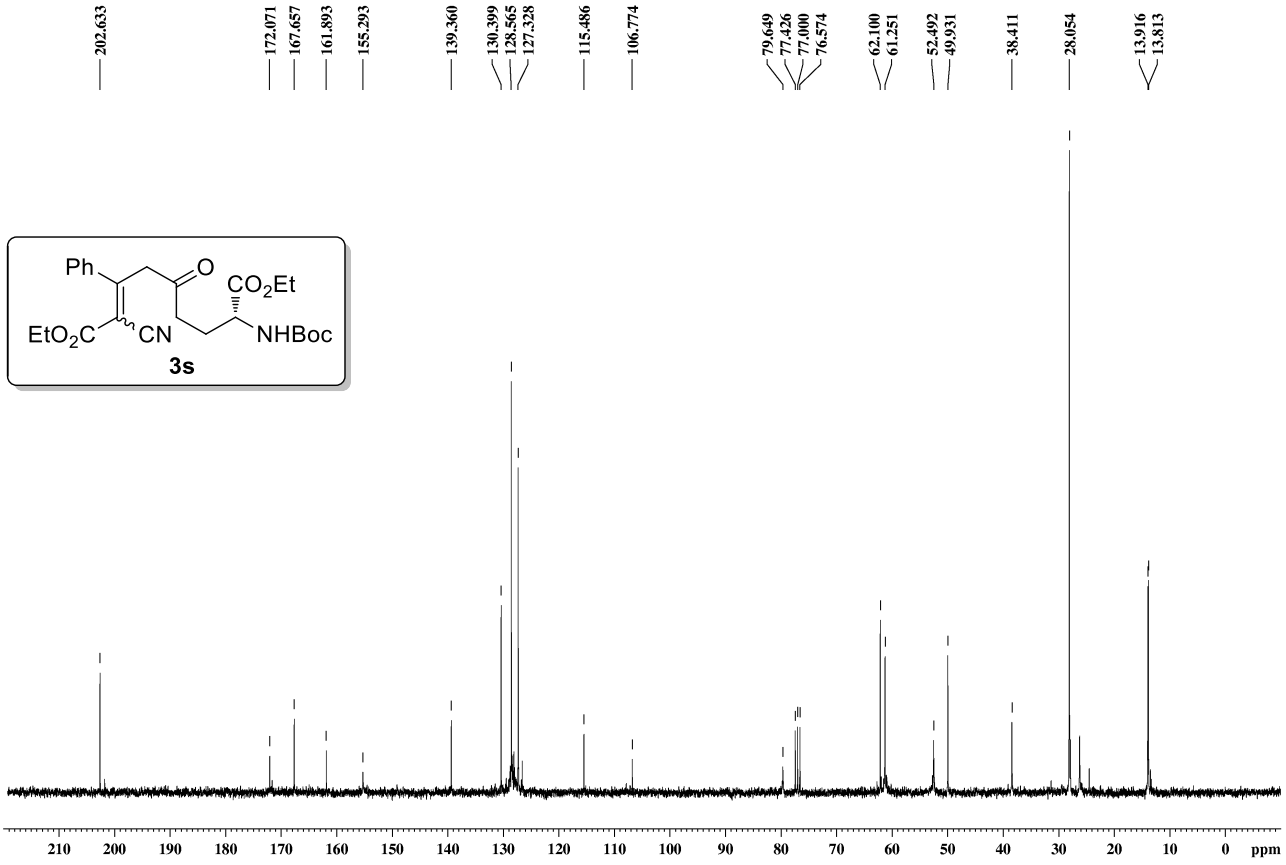
^{13}C NMR (75 MHz, $CDCl_3$); **3r**



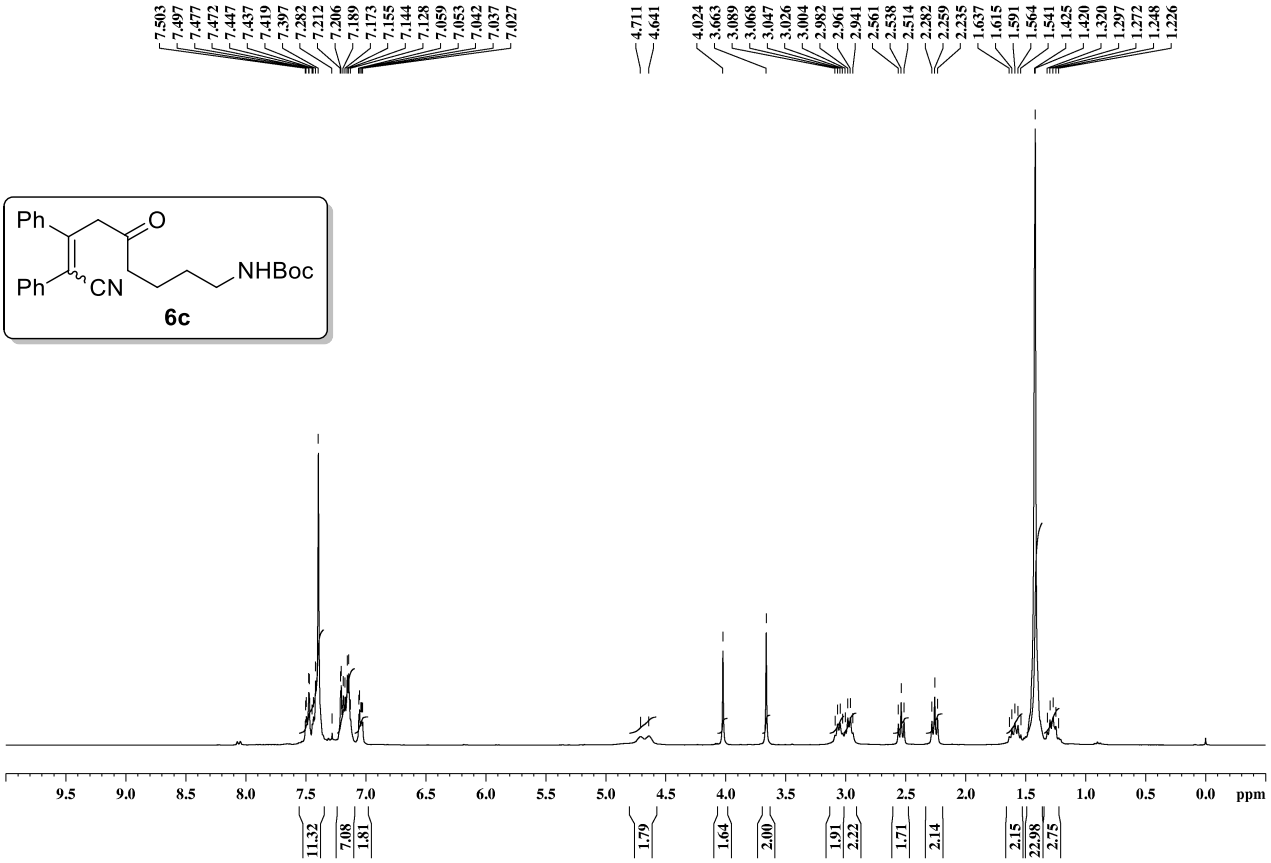
^{1}H NMR (300 MHz, $CDCl_3$); **3s**



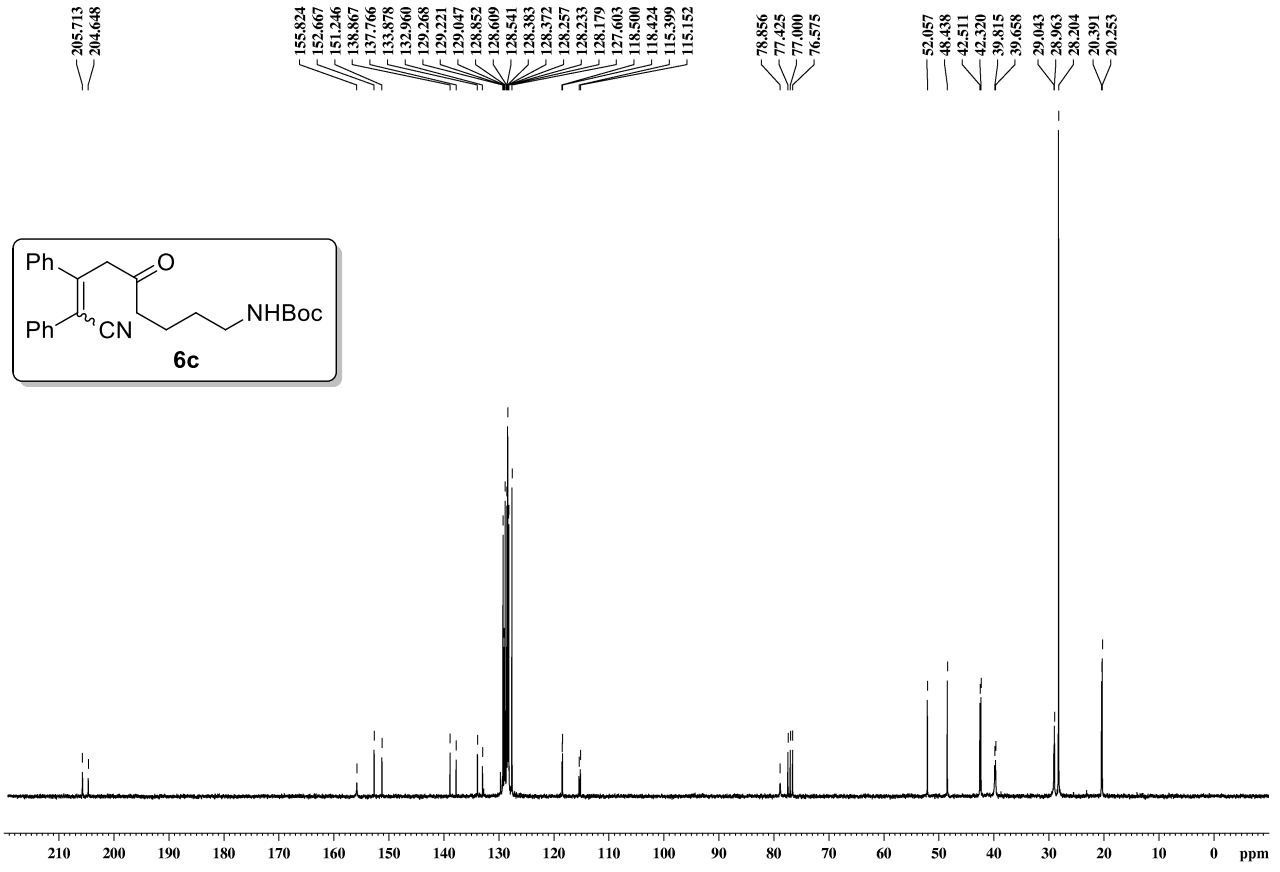
^{13}C NMR (75 MHz, $CDCl_3$); **3s**



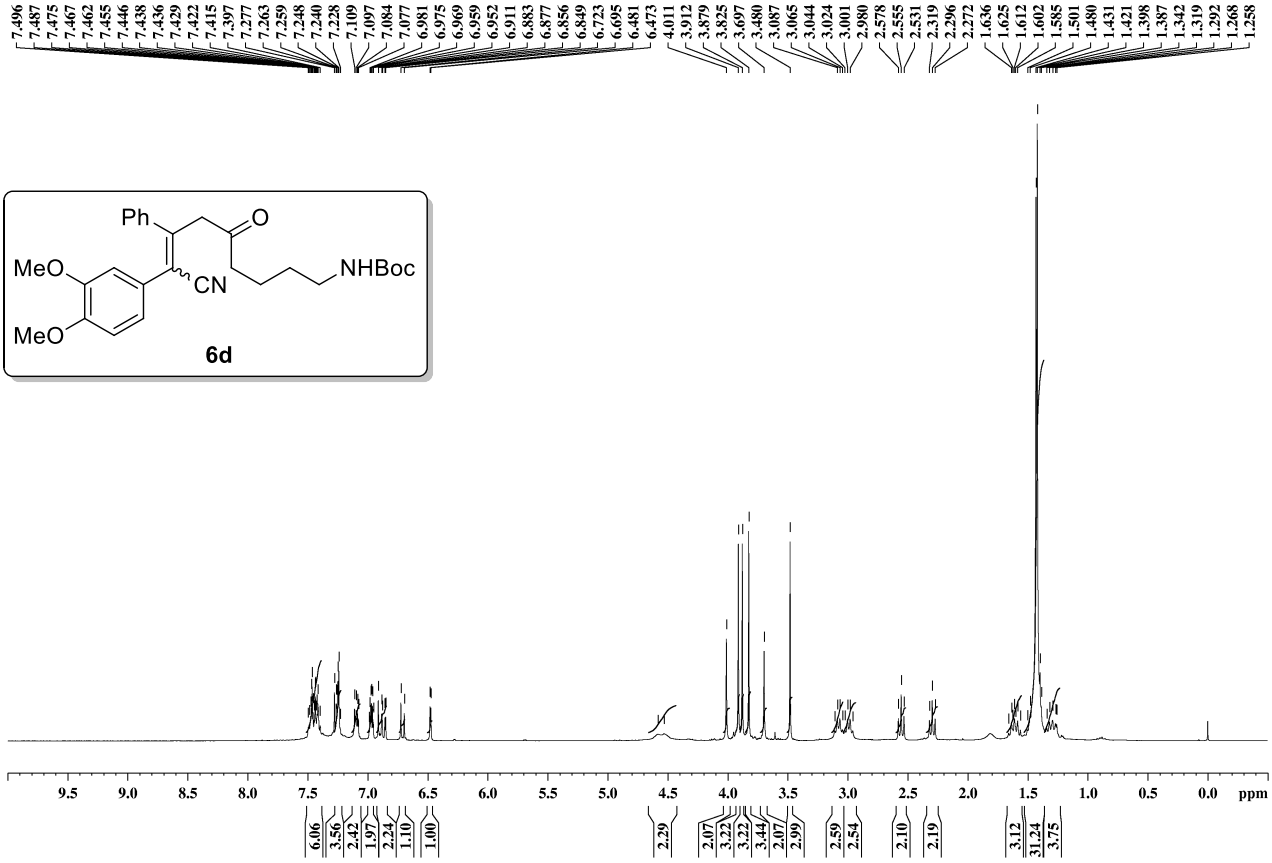
^{1}H NMR (300 MHz, $CDCl_3$); **6c**



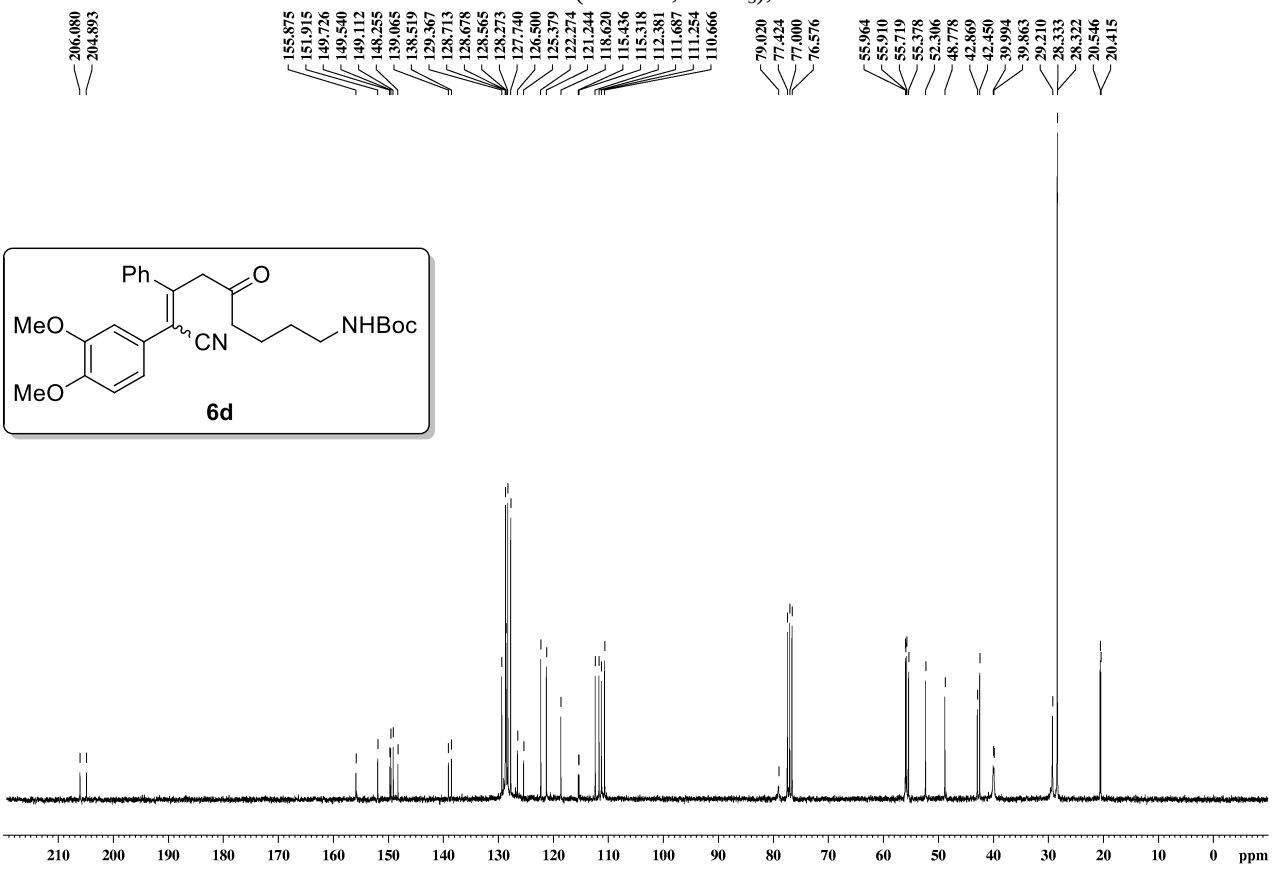
^{13}C NMR (75 MHz, $CDCl_3$); **6c**



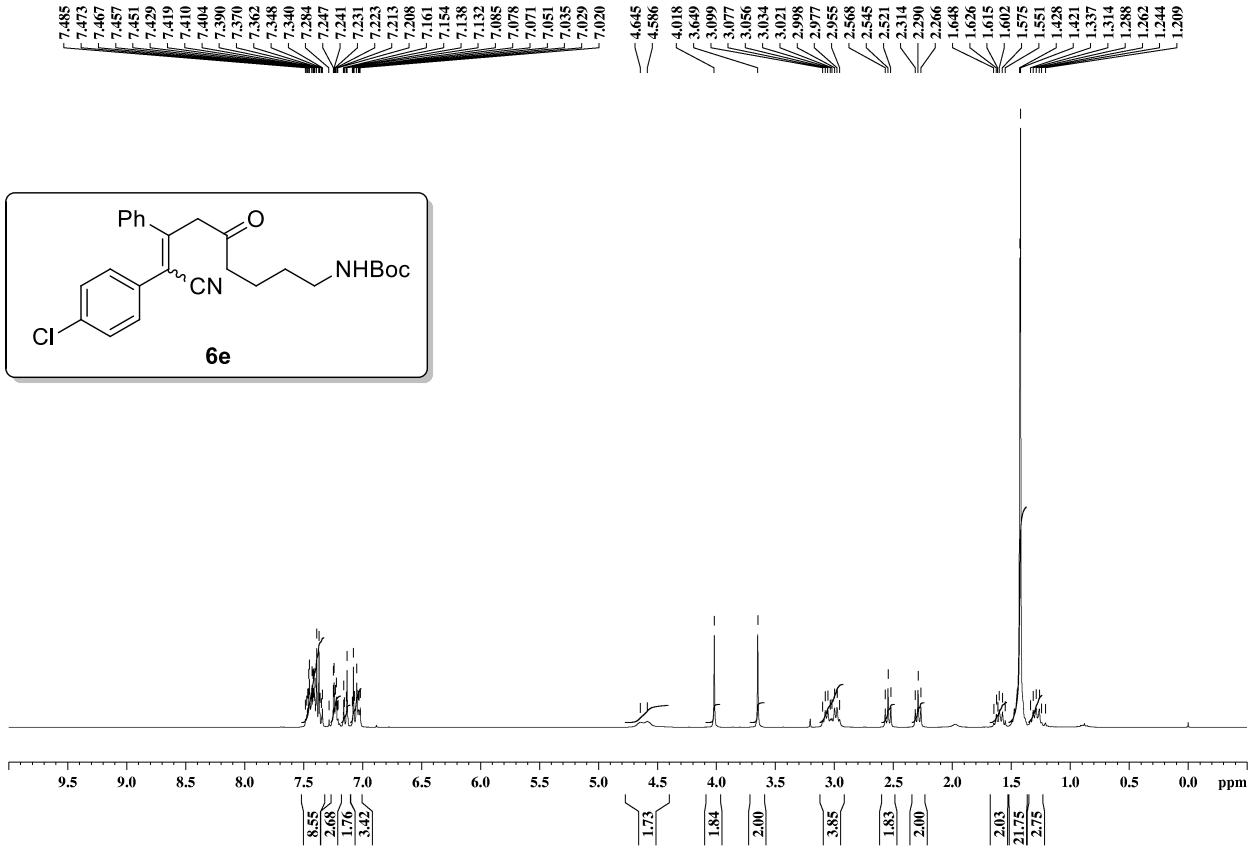
^{1}H NMR (300 MHz, $CDCl_3$); **6d**



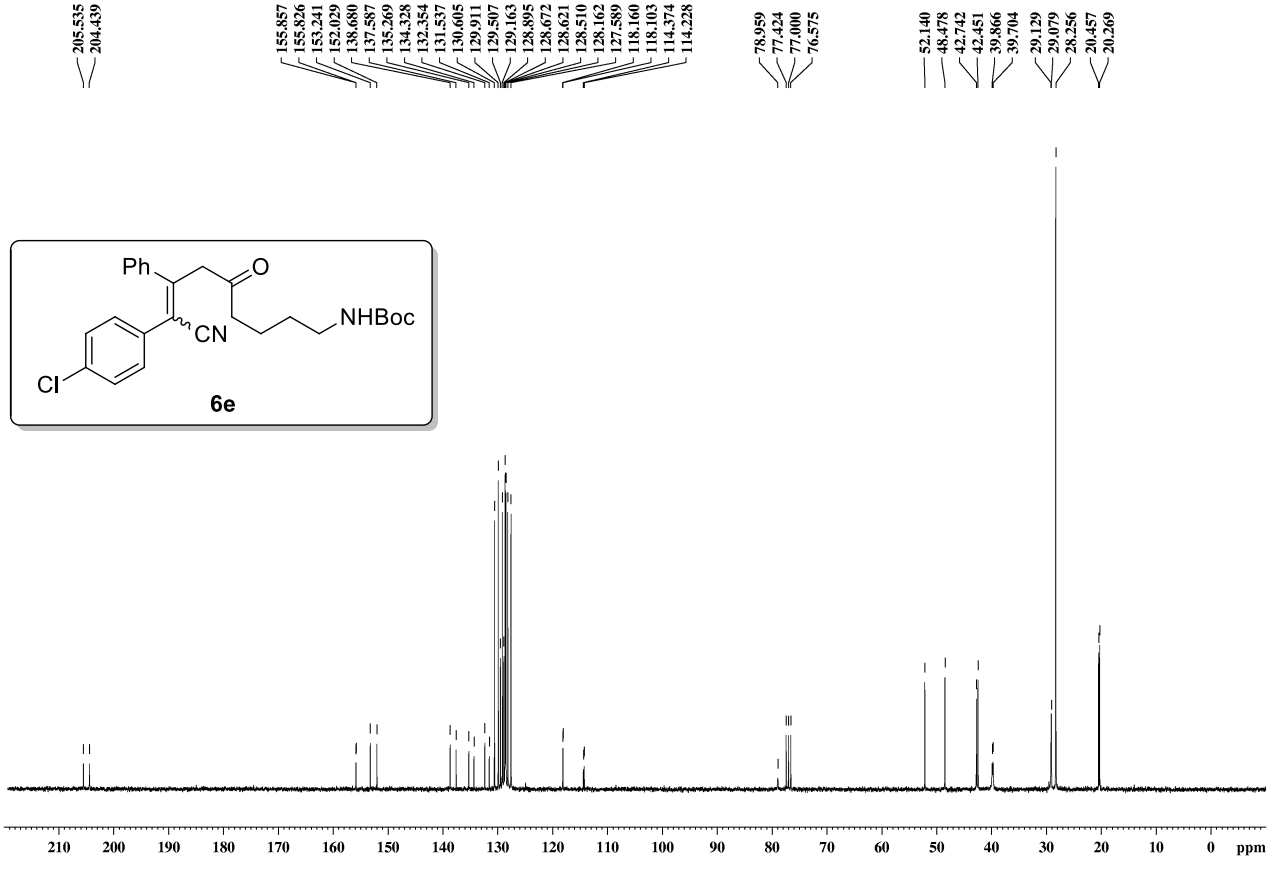
^{13}C NMR (75 MHz, $CDCl_3$); **6d**



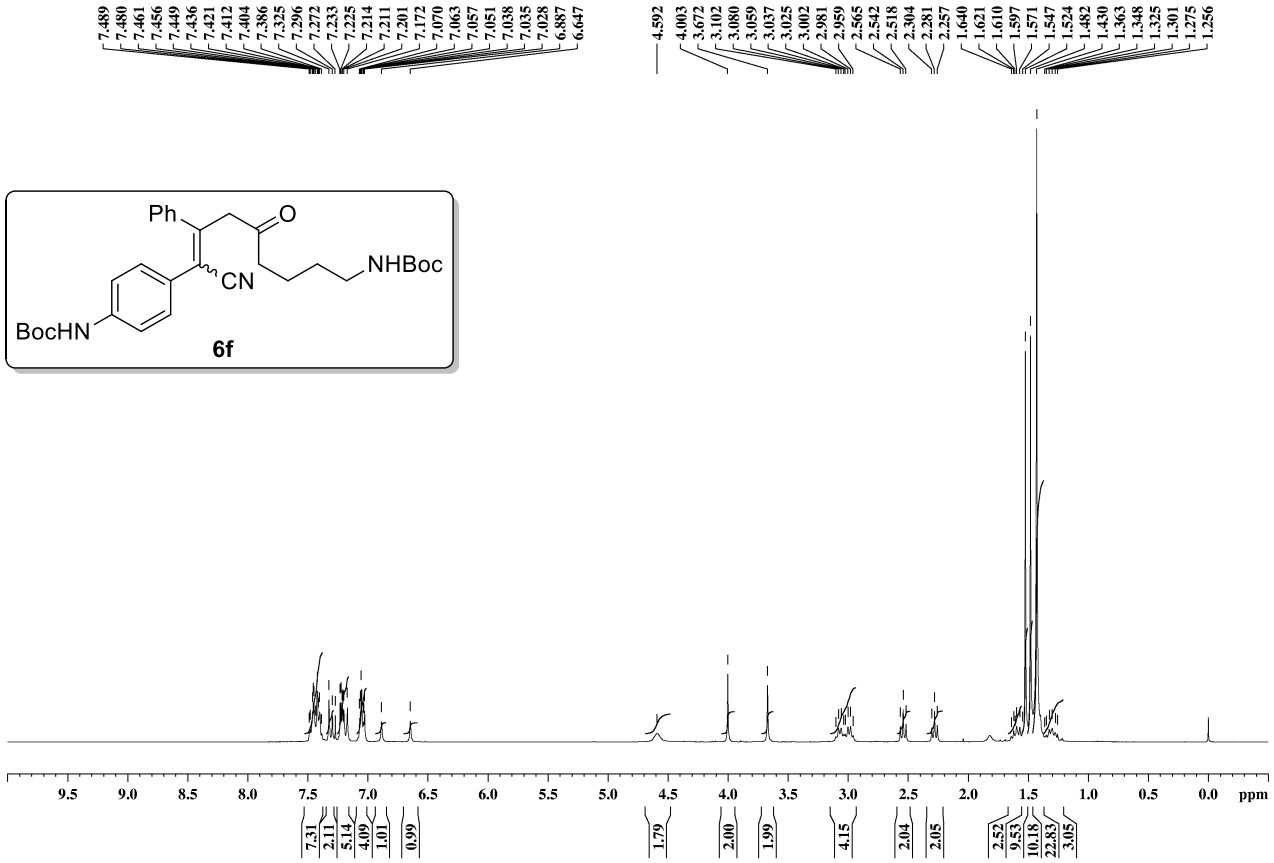
^{1}H NMR (300 MHz, $CDCl_3$); **6e**



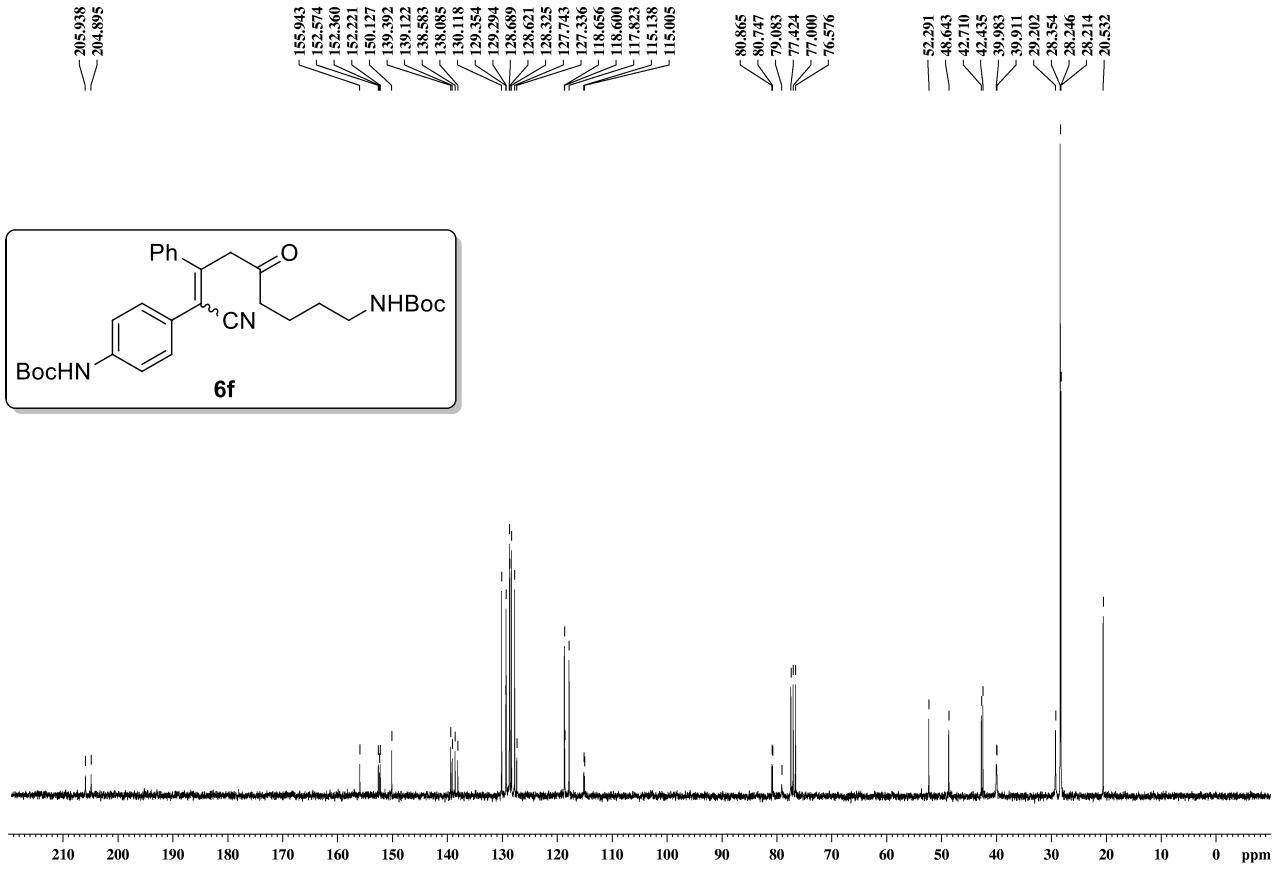
^{13}C NMR (75 MHz, $CDCl_3$); **6e**



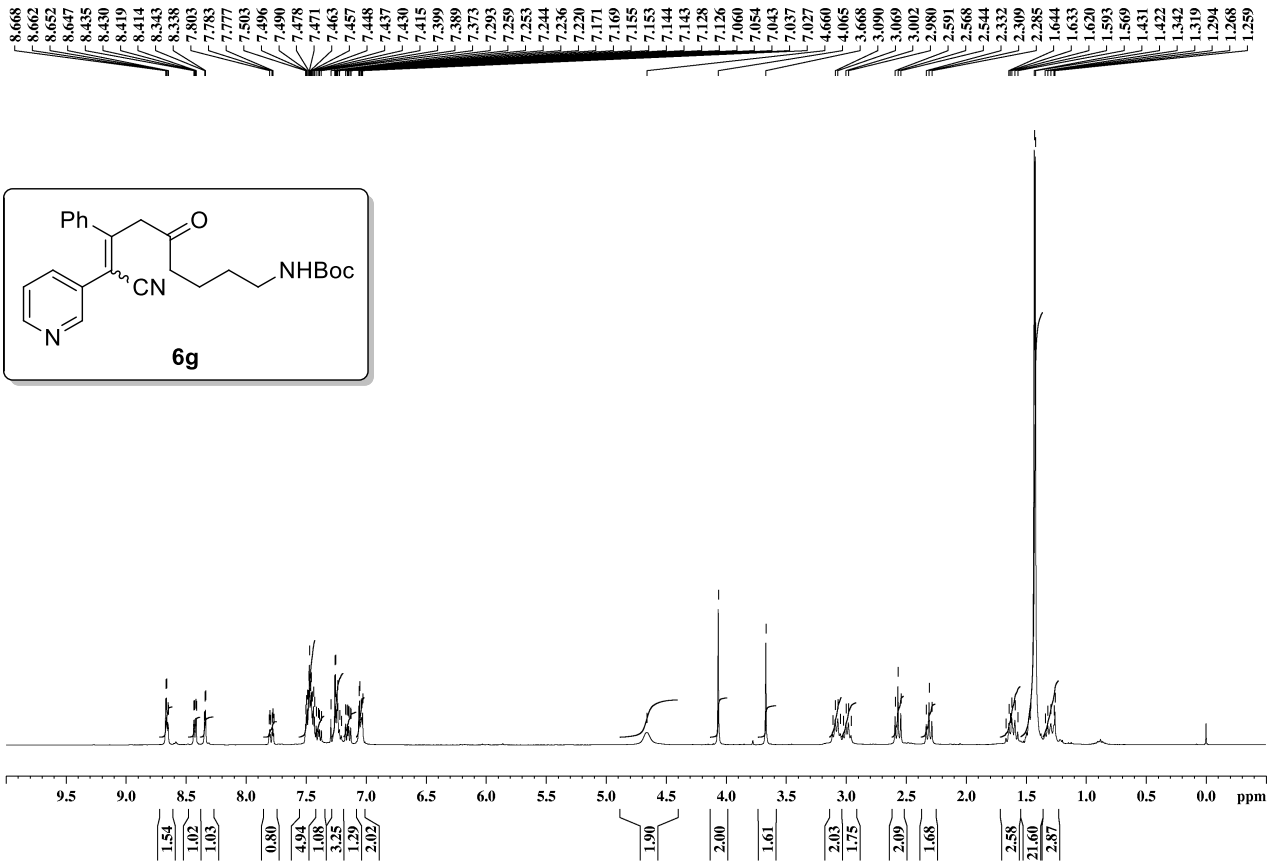
^{1}H NMR (300 MHz, $CDCl_3$); **6f**



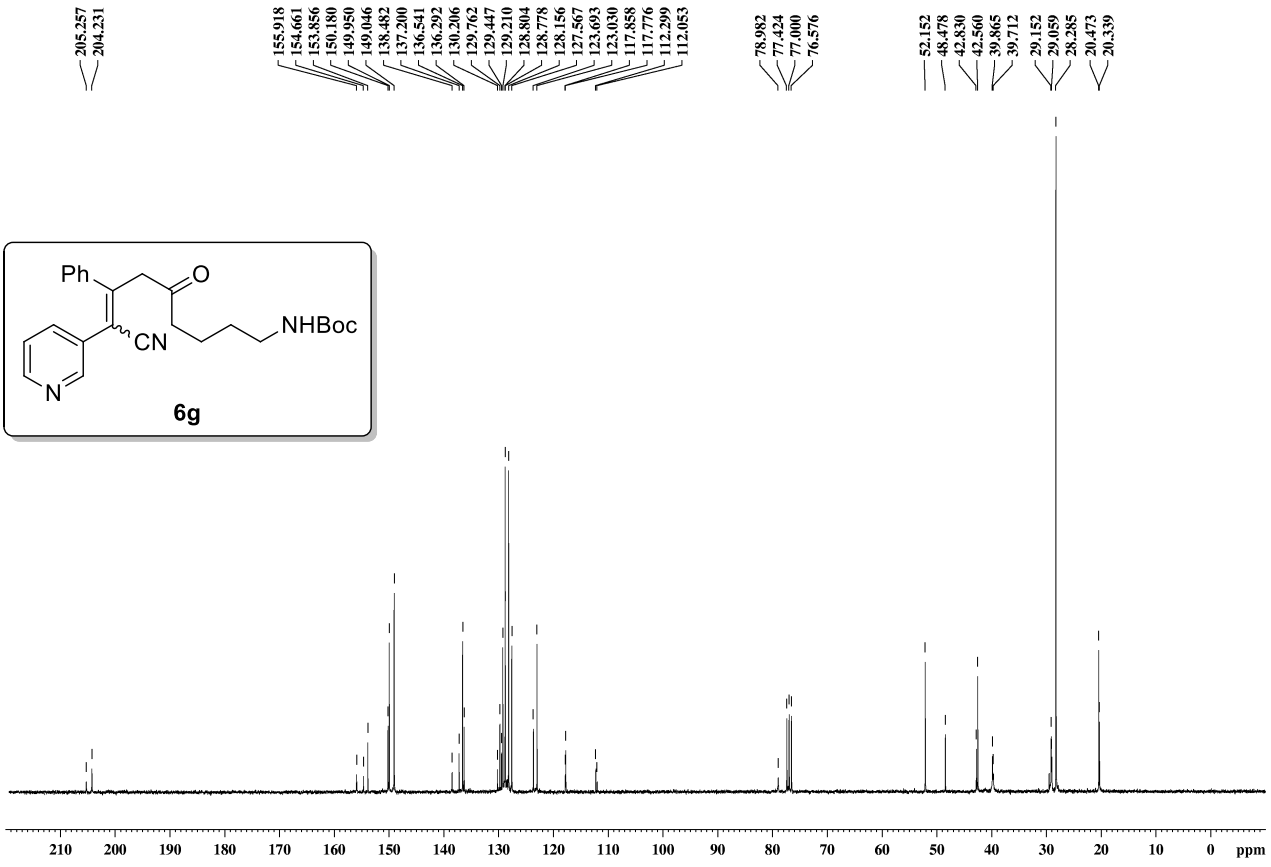
^{13}C NMR (75 MHz, $CDCl_3$); **6f**



^{1}H NMR (300 MHz, $CDCl_3$); **6g**



^{13}C NMR (75 MHz, $CDCl_3$); **6g**



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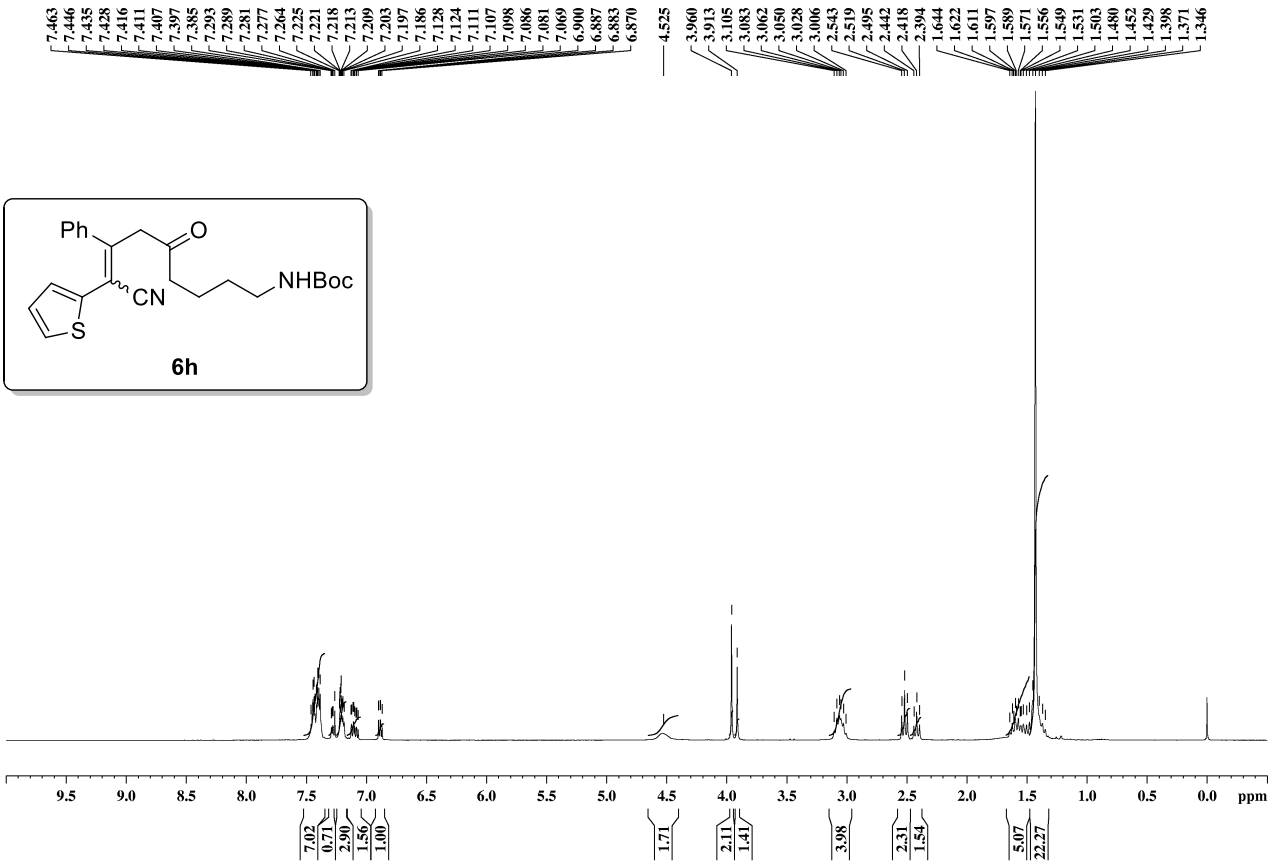
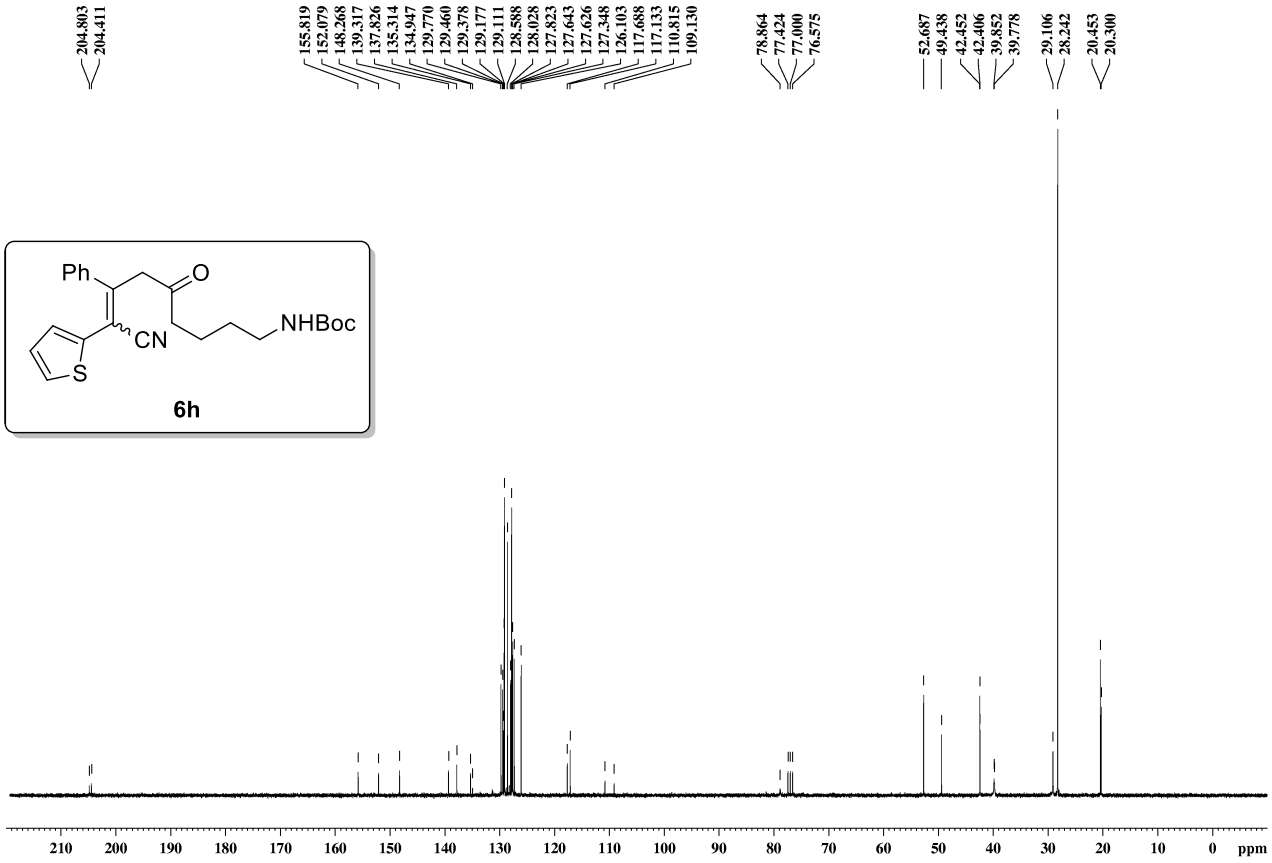
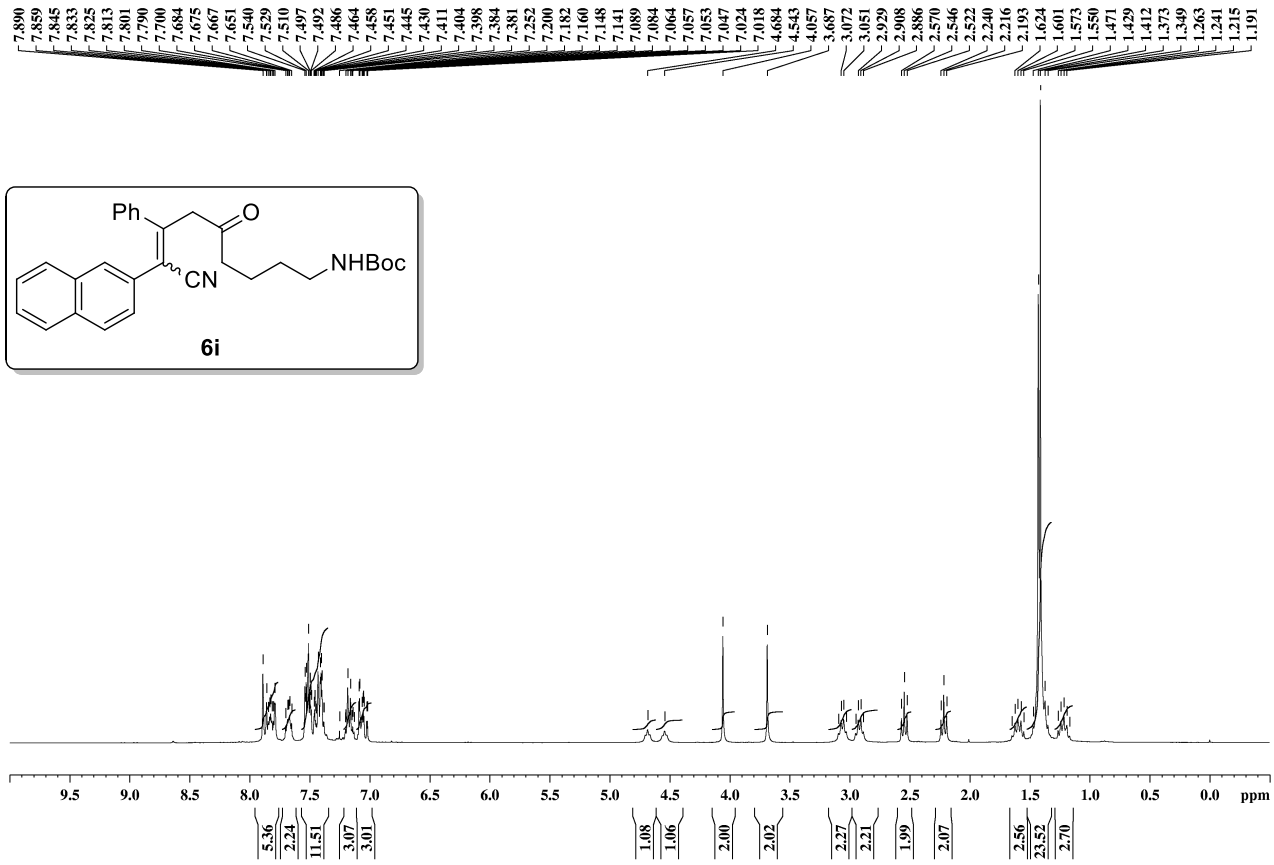


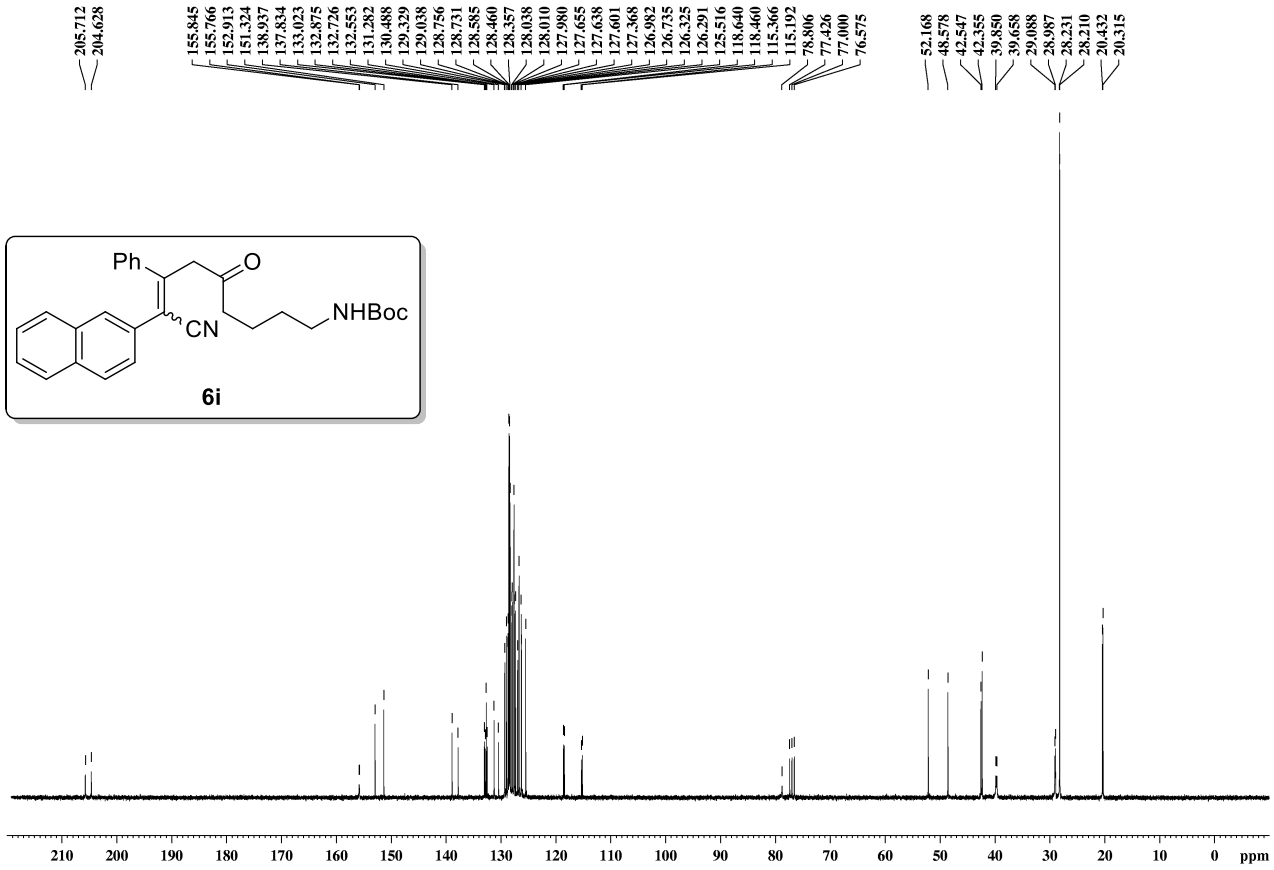
^{13}C NMR (75 MHz, $CDCl_3$); **6h**



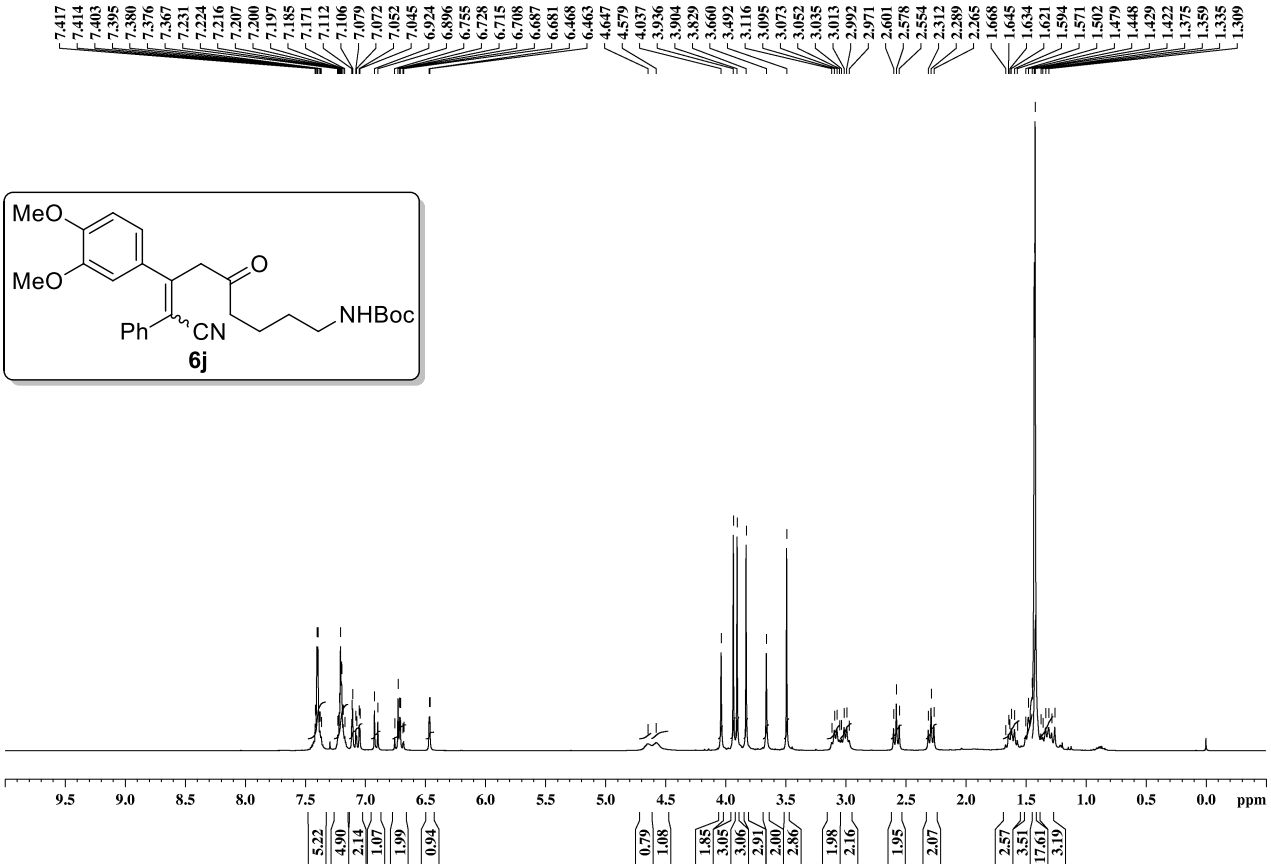
^{1}H NMR (300 MHz, $CDCl_3$); **6i**



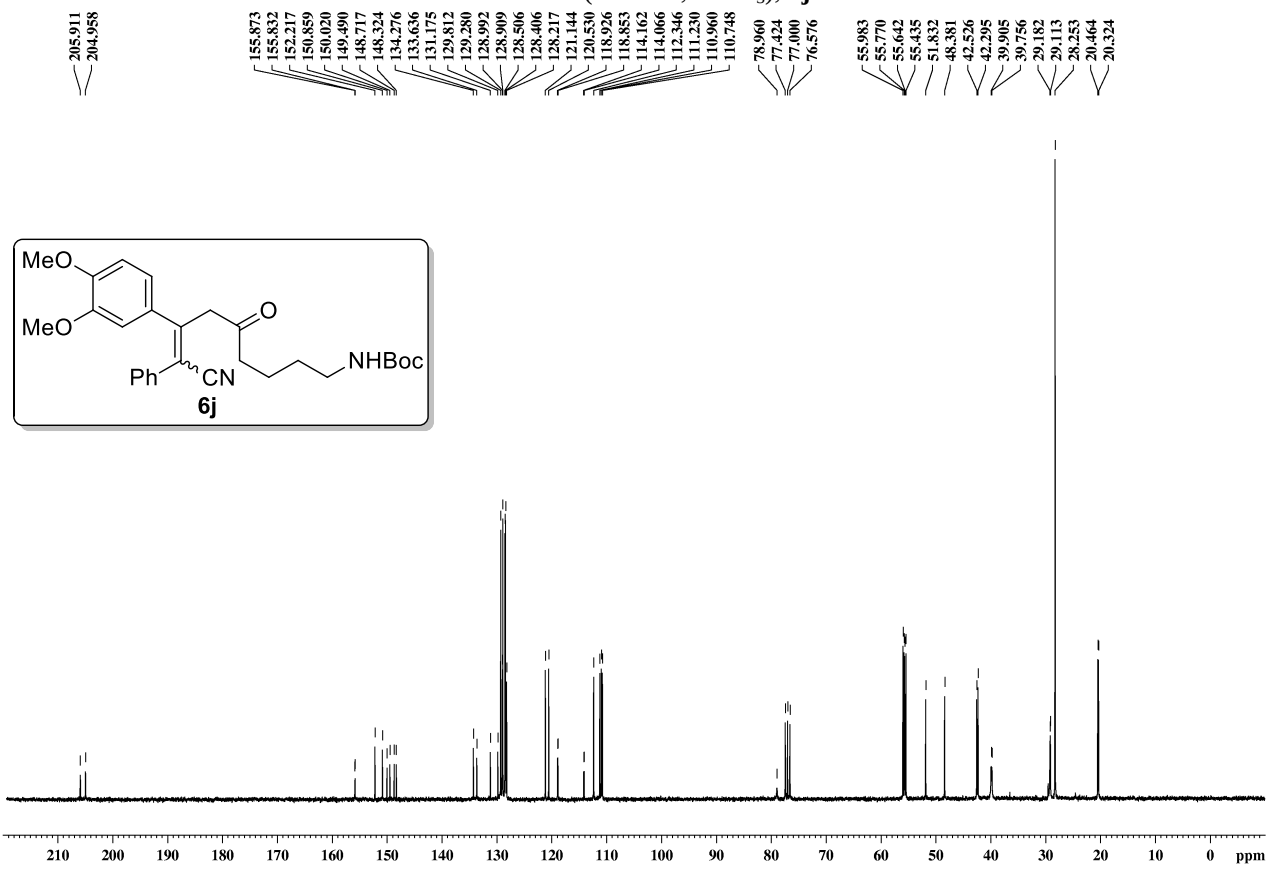
^{13}C NMR (75 MHz, $CDCl_3$); **6i**



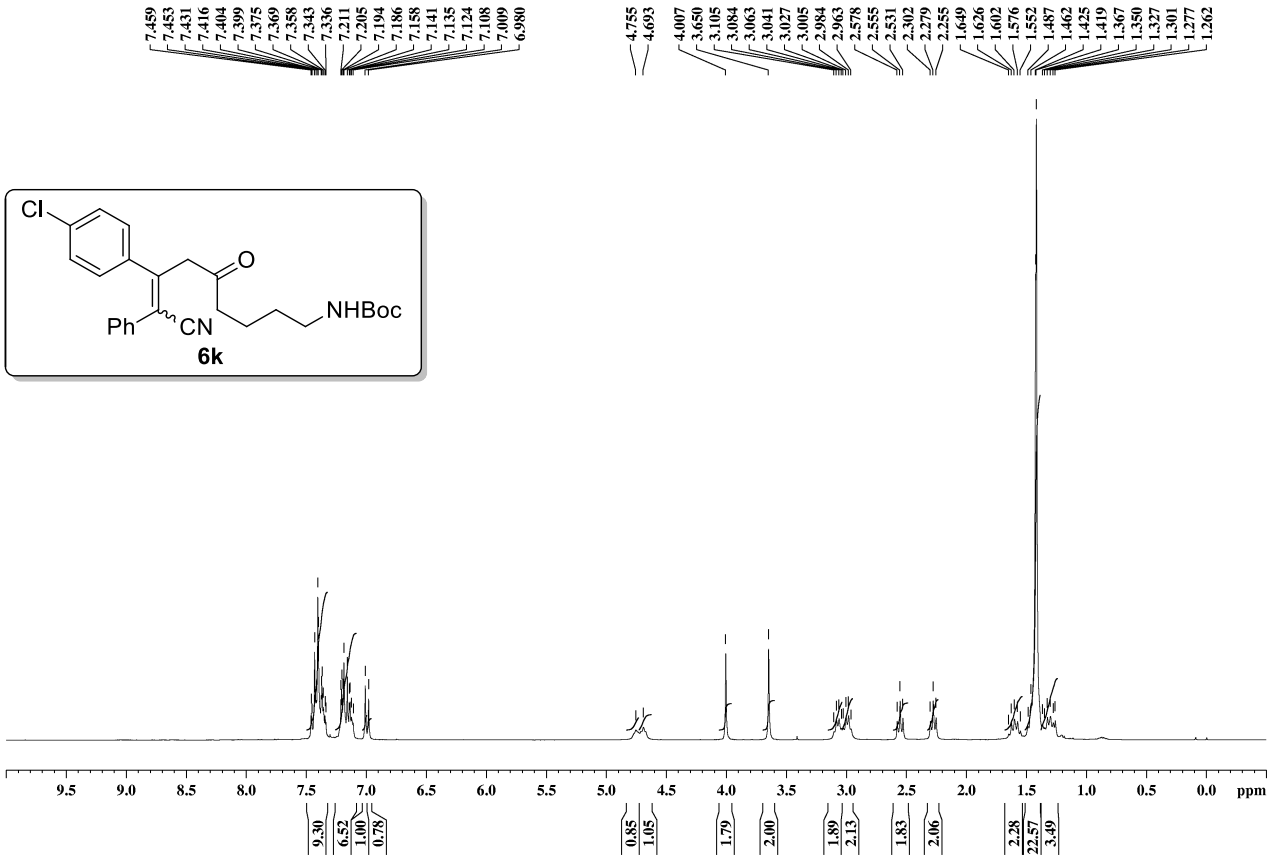
^{1}H NMR (300 MHz, $CDCl_3$); **6j**



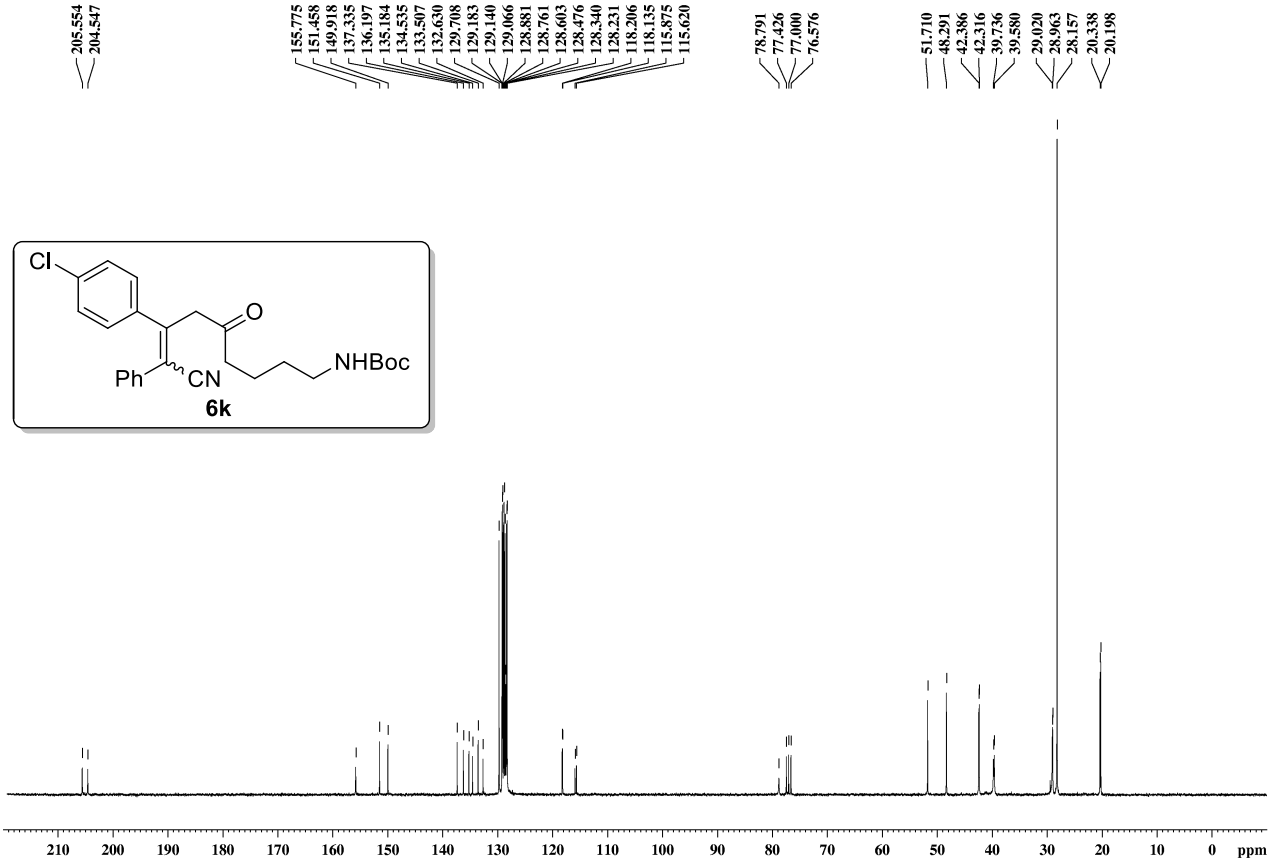
^{13}C NMR (75 MHz, $CDCl_3$); **6j**



^{1}H NMR (300 MHz, $CDCl_3$); **6k**



^{13}C NMR (75 MHz, $CDCl_3$); **6k**



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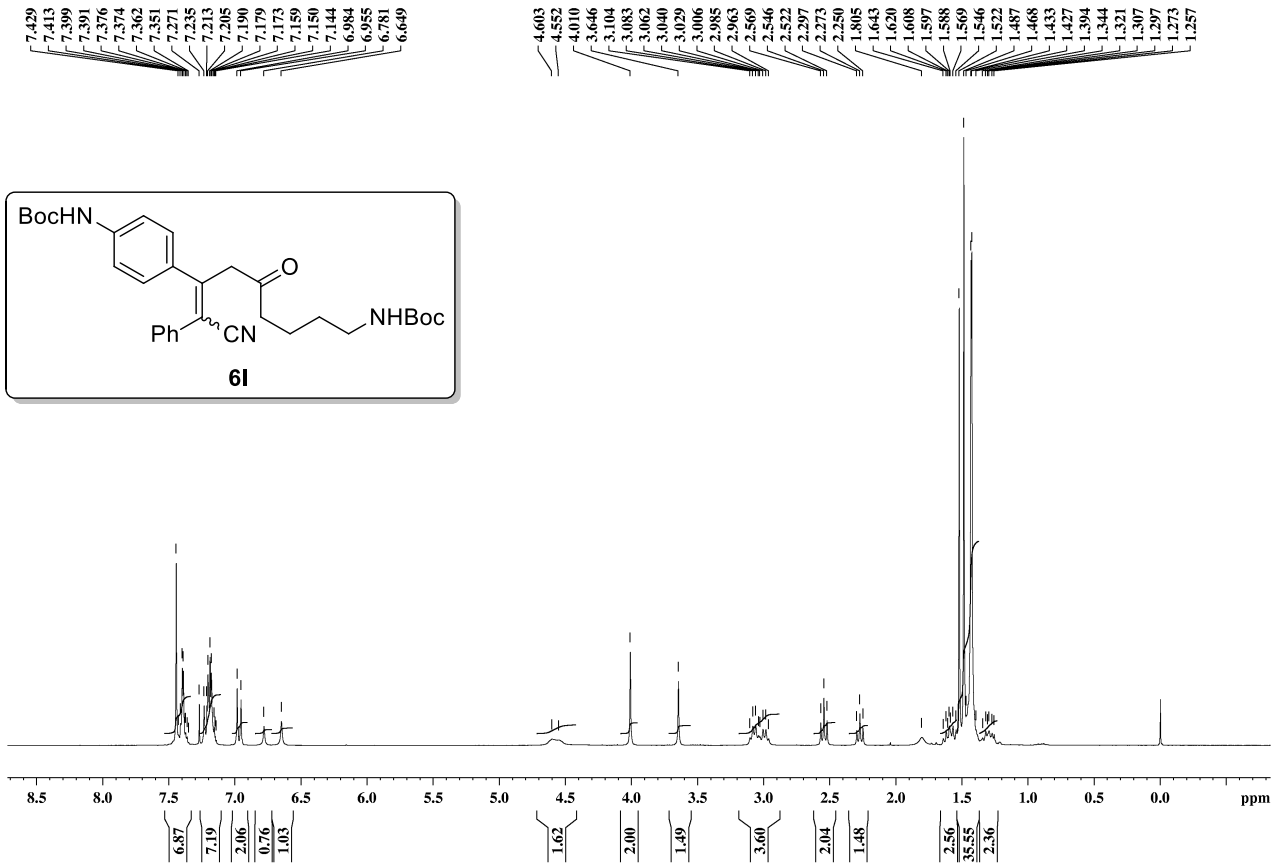
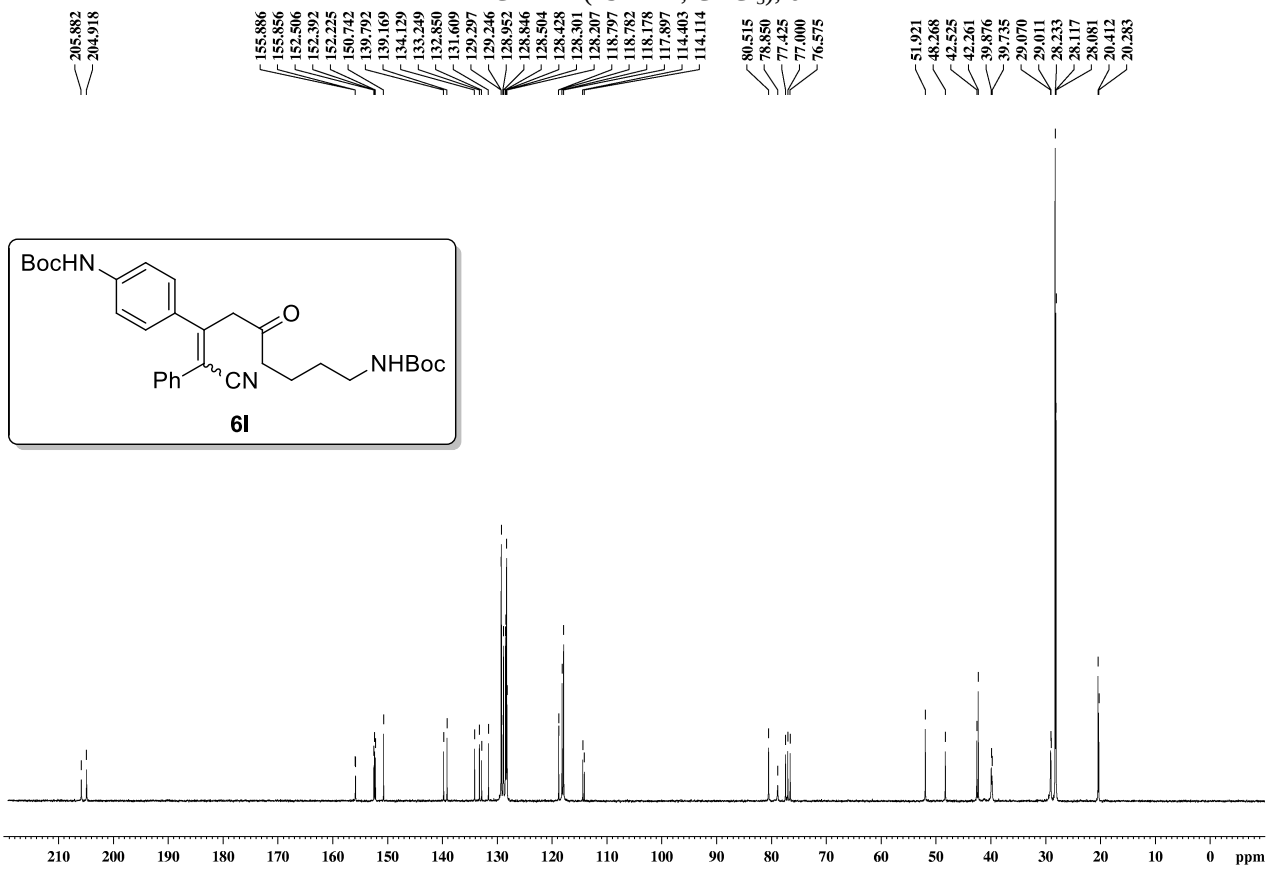
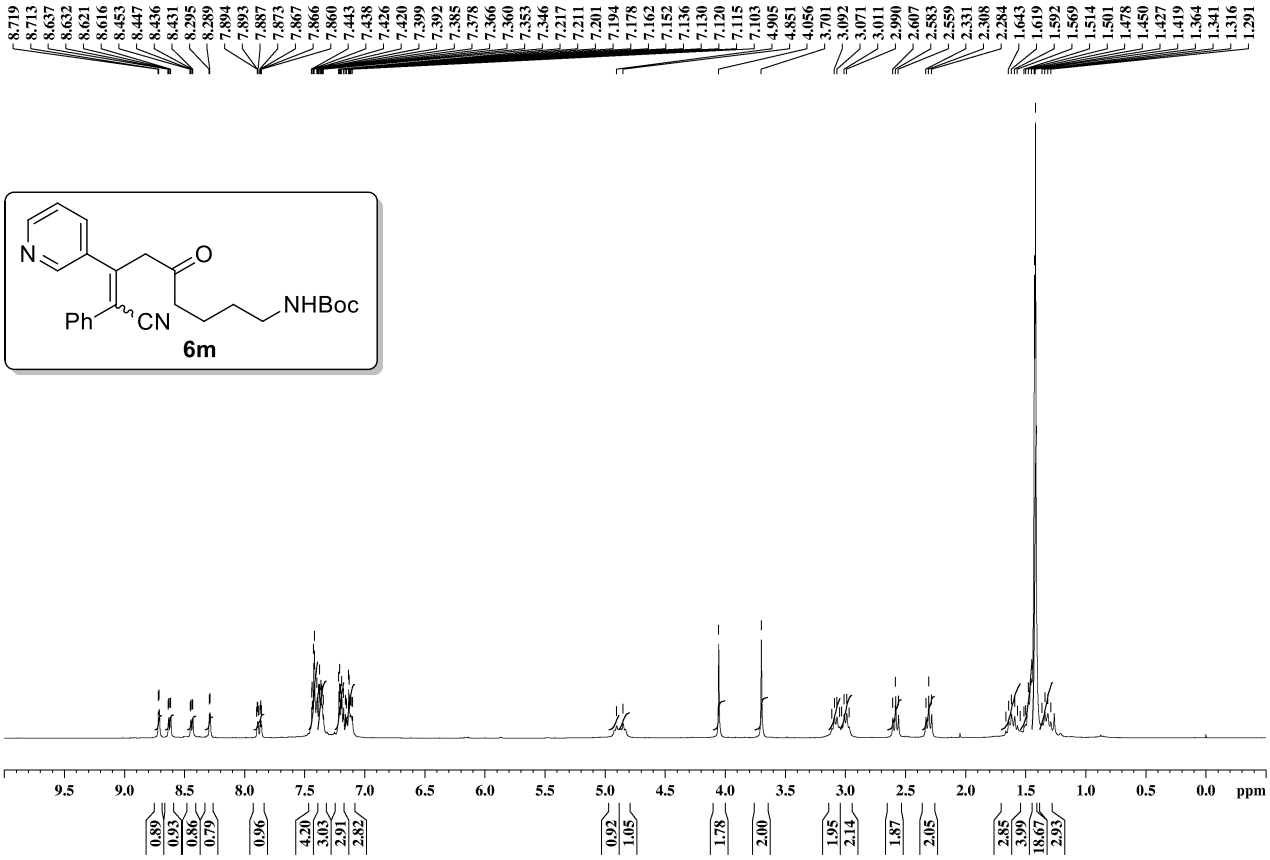


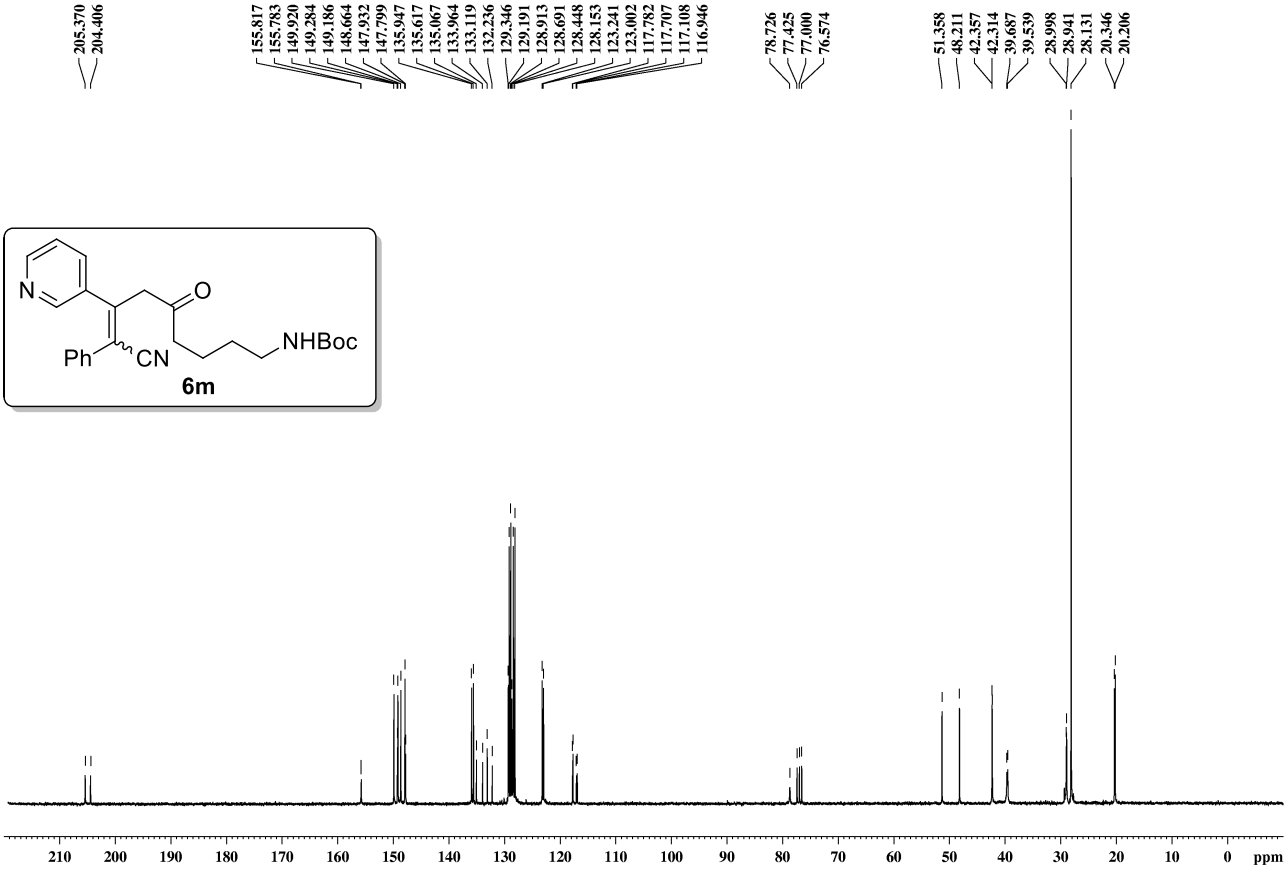
^{13}C NMR (75 MHz, $CDCl_3$); **6l**



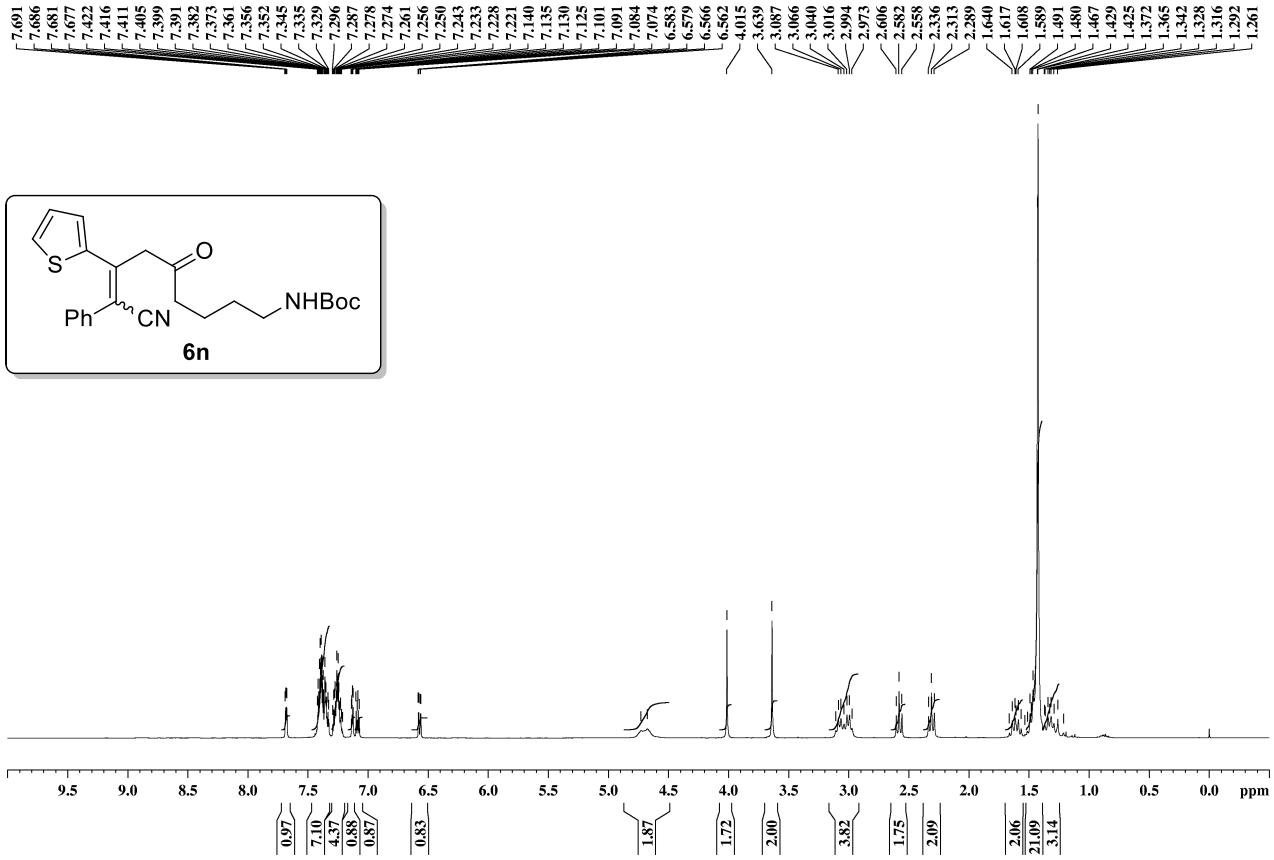
^{1}H NMR (300 MHz, $CDCl_3$); **6m**



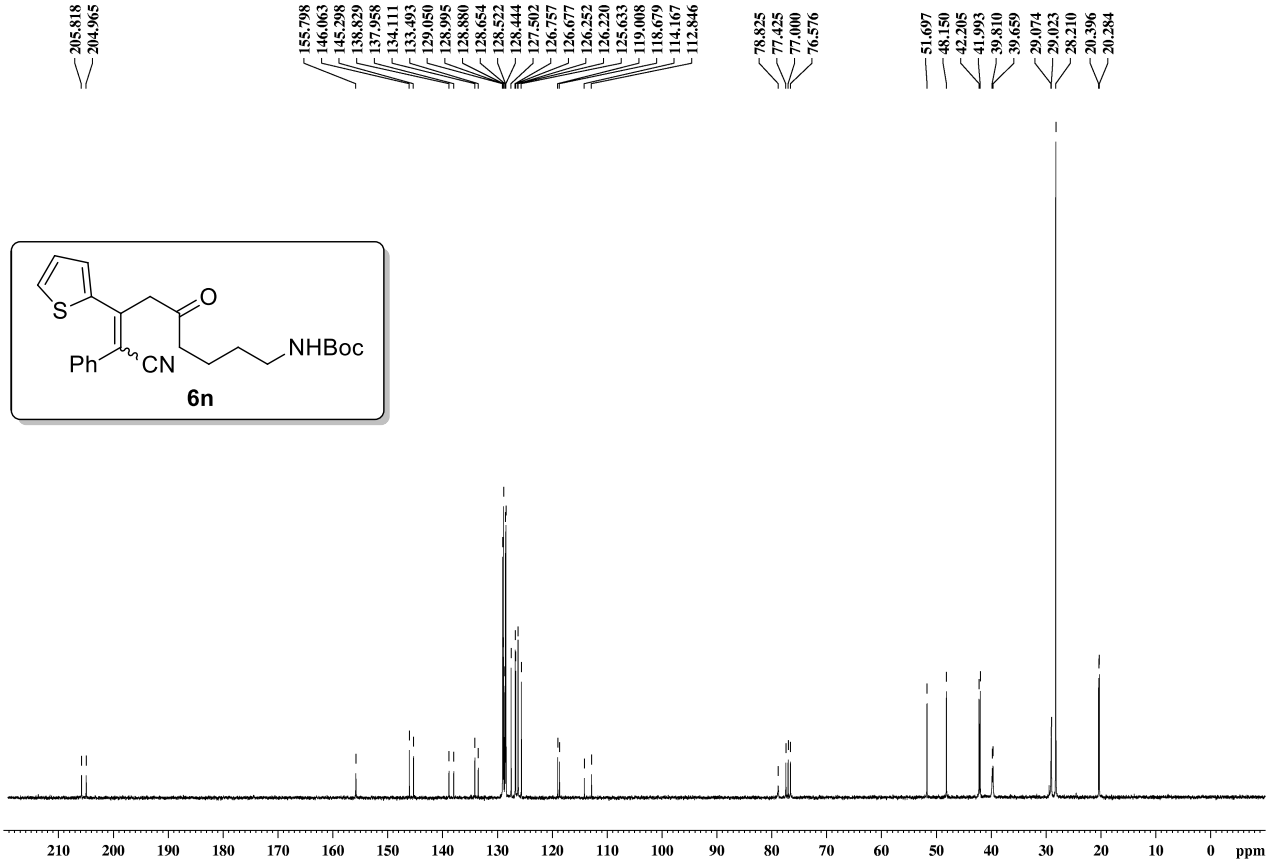
^{13}C NMR (75 MHz, $CDCl_3$); **6m**



^{1}H NMR (300 MHz, $CDCl_3$); **6n**



^{13}C NMR (75 MHz, $CDCl_3$); **6n**



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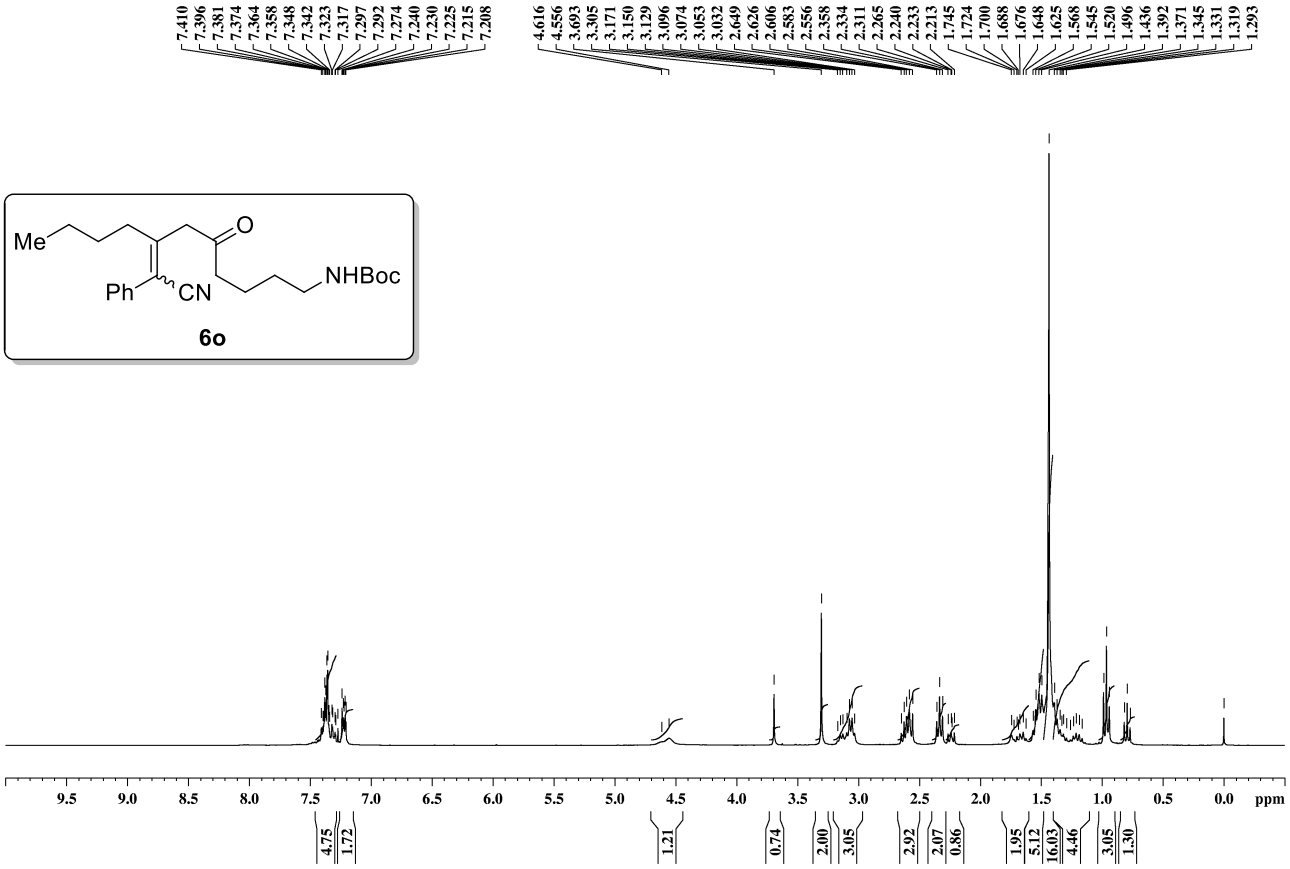
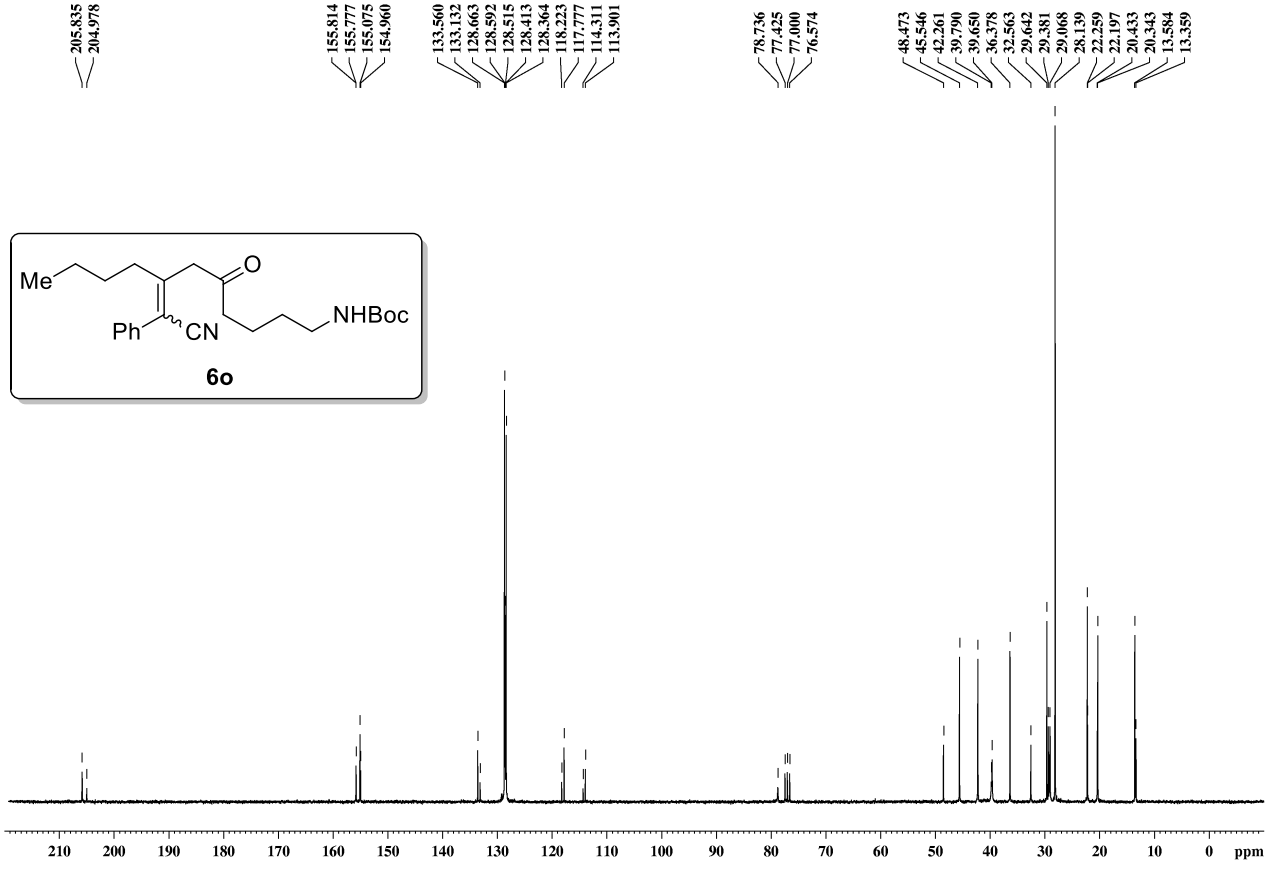


^{13}C NMR (75 MHz, $CDCl_3$); **6o**



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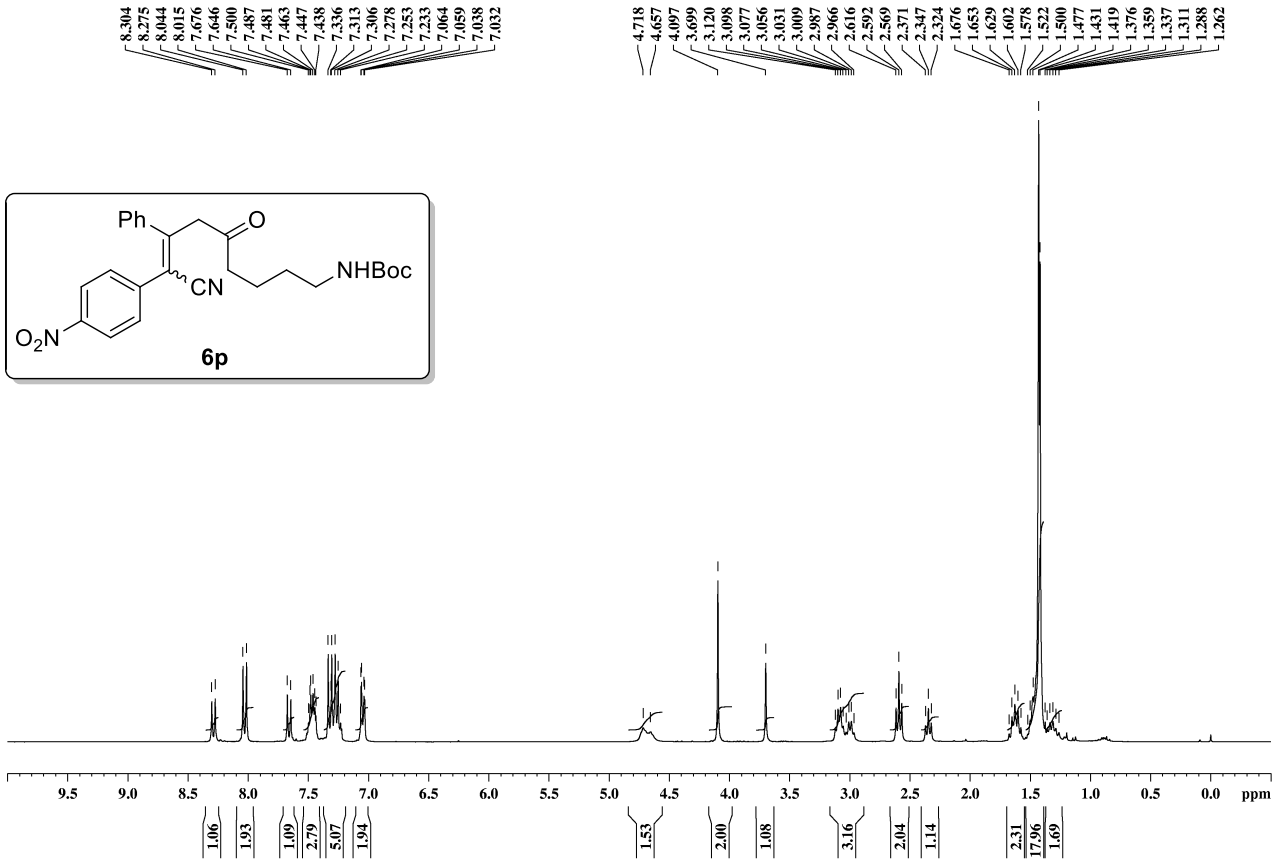
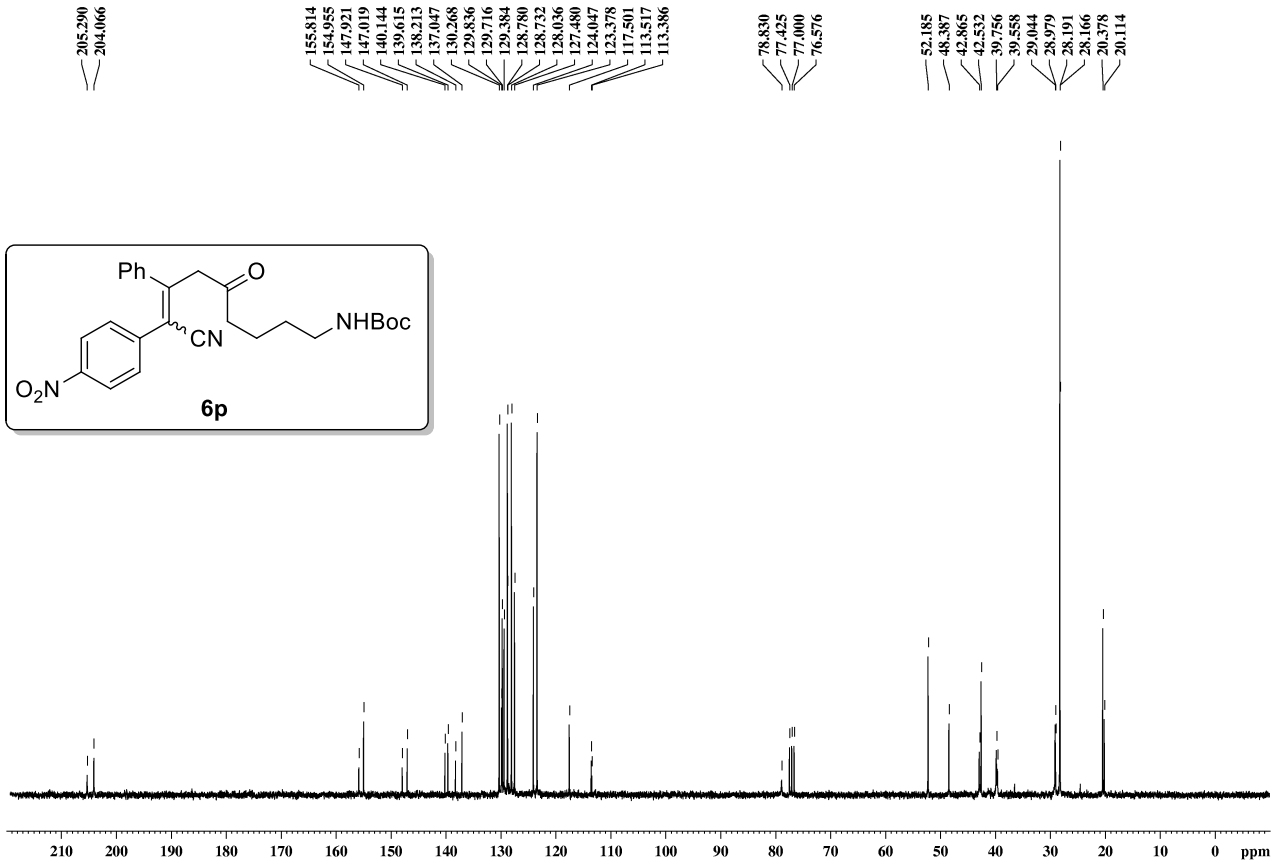


^{13}C NMR (75 MHz, $CDCl_3$); **6p**



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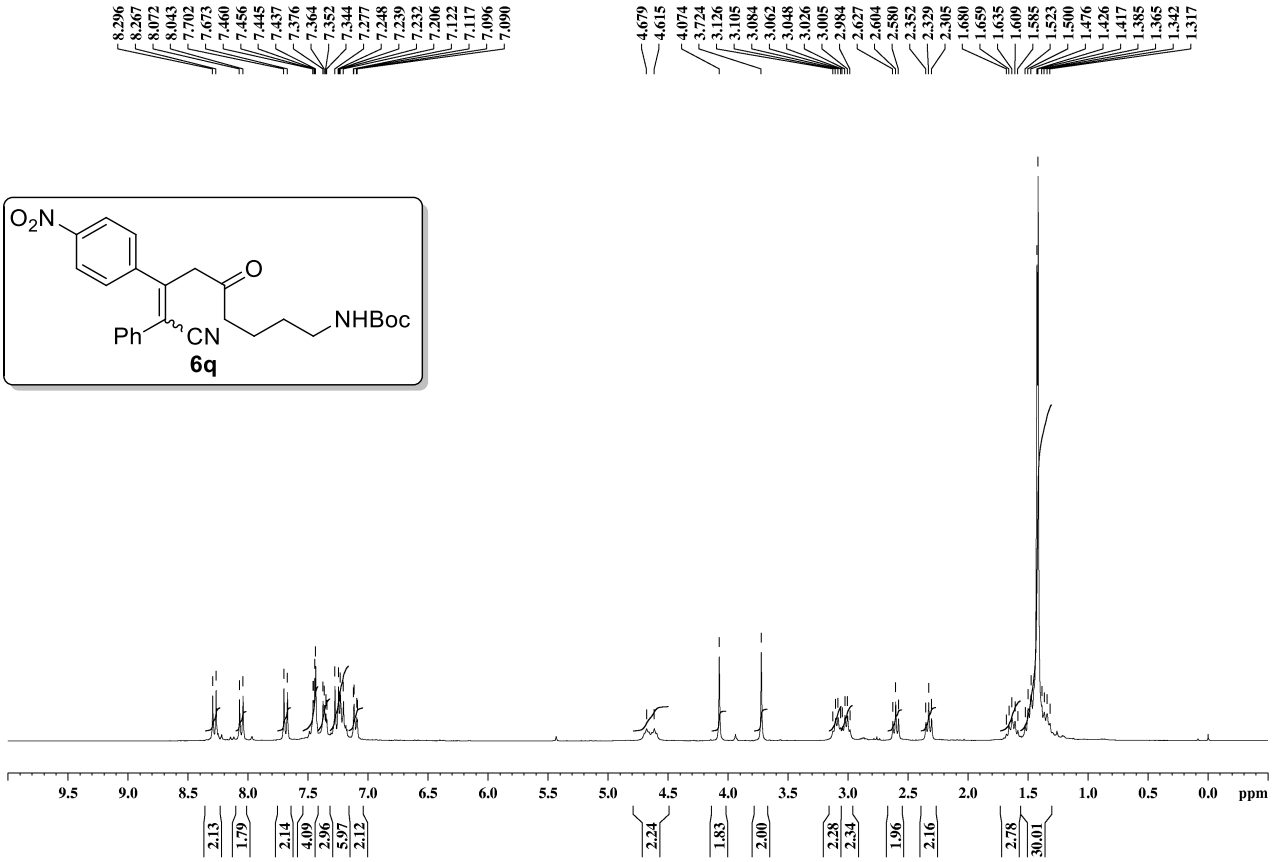
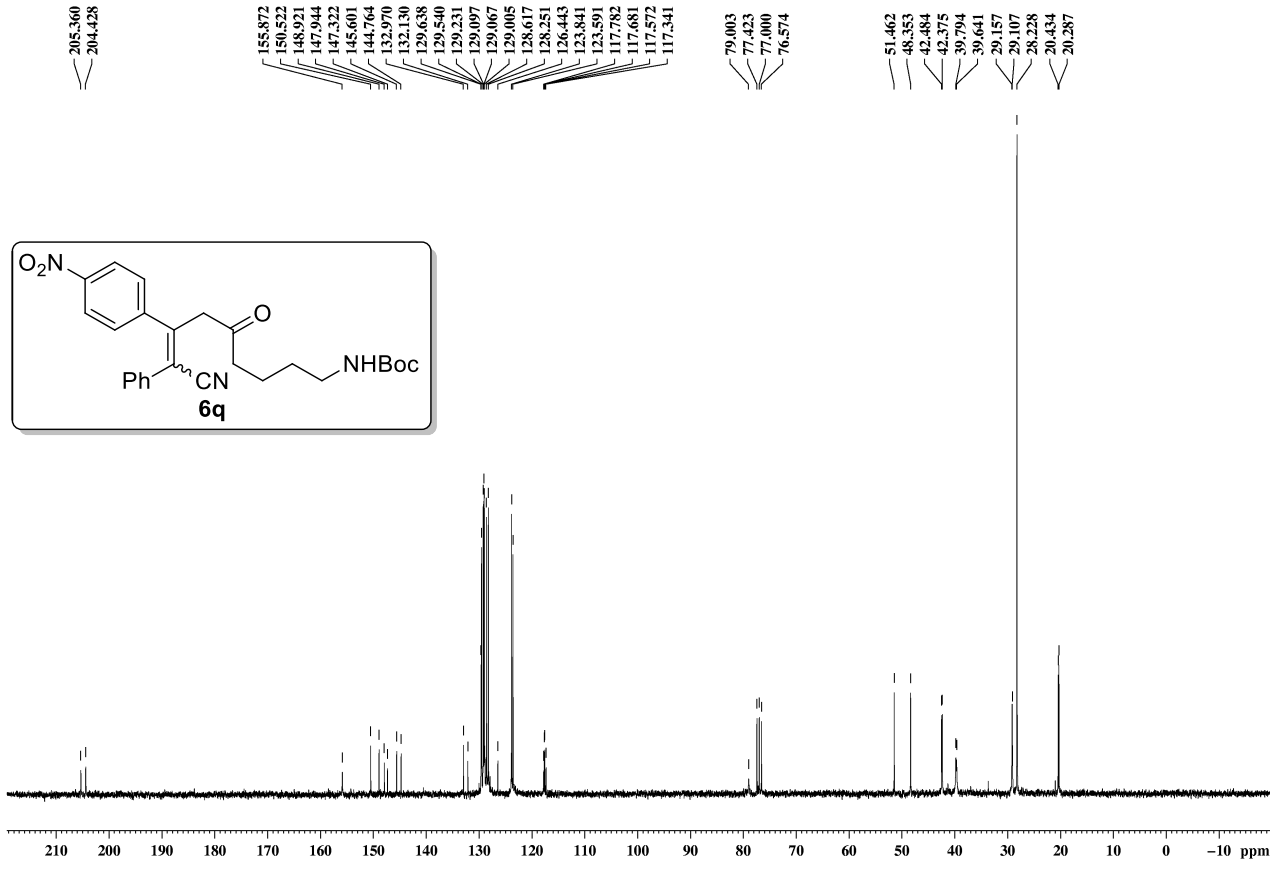
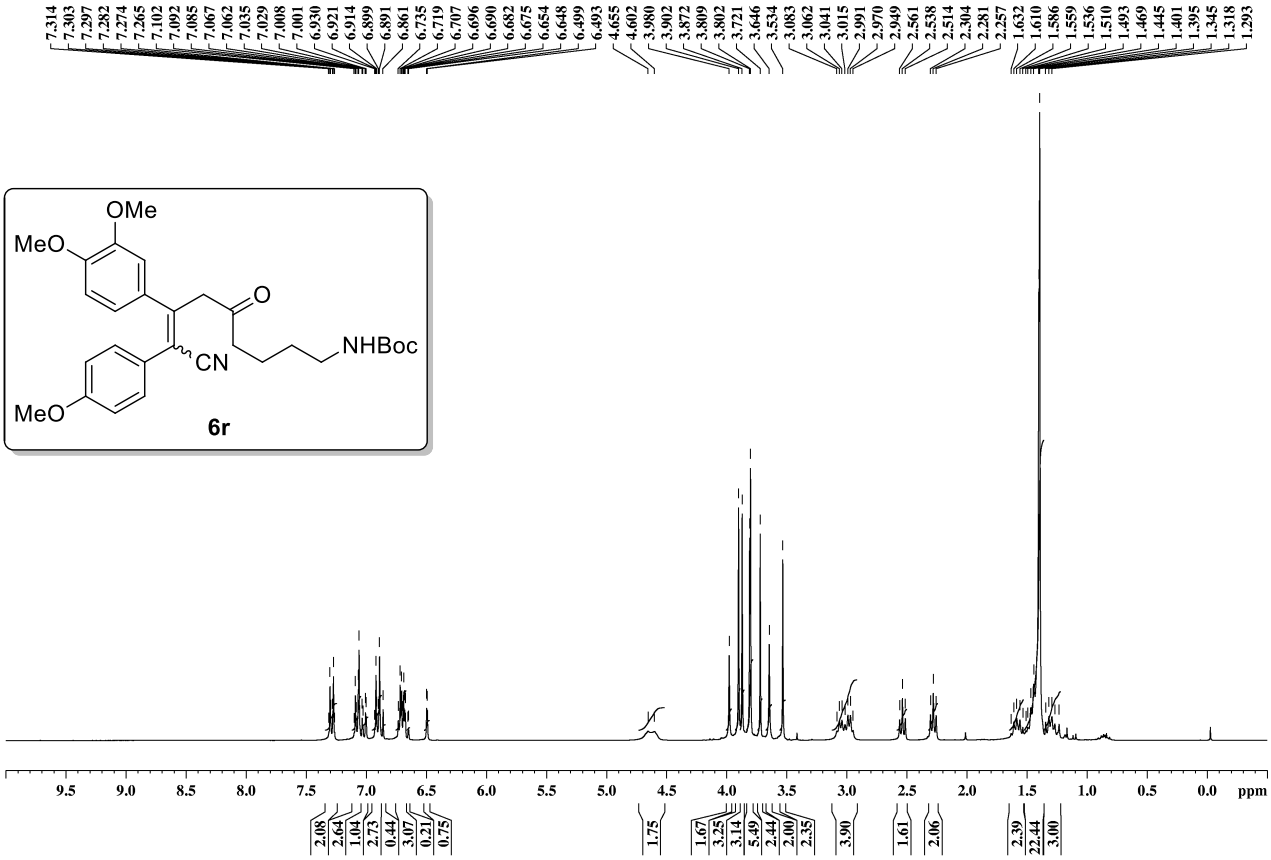


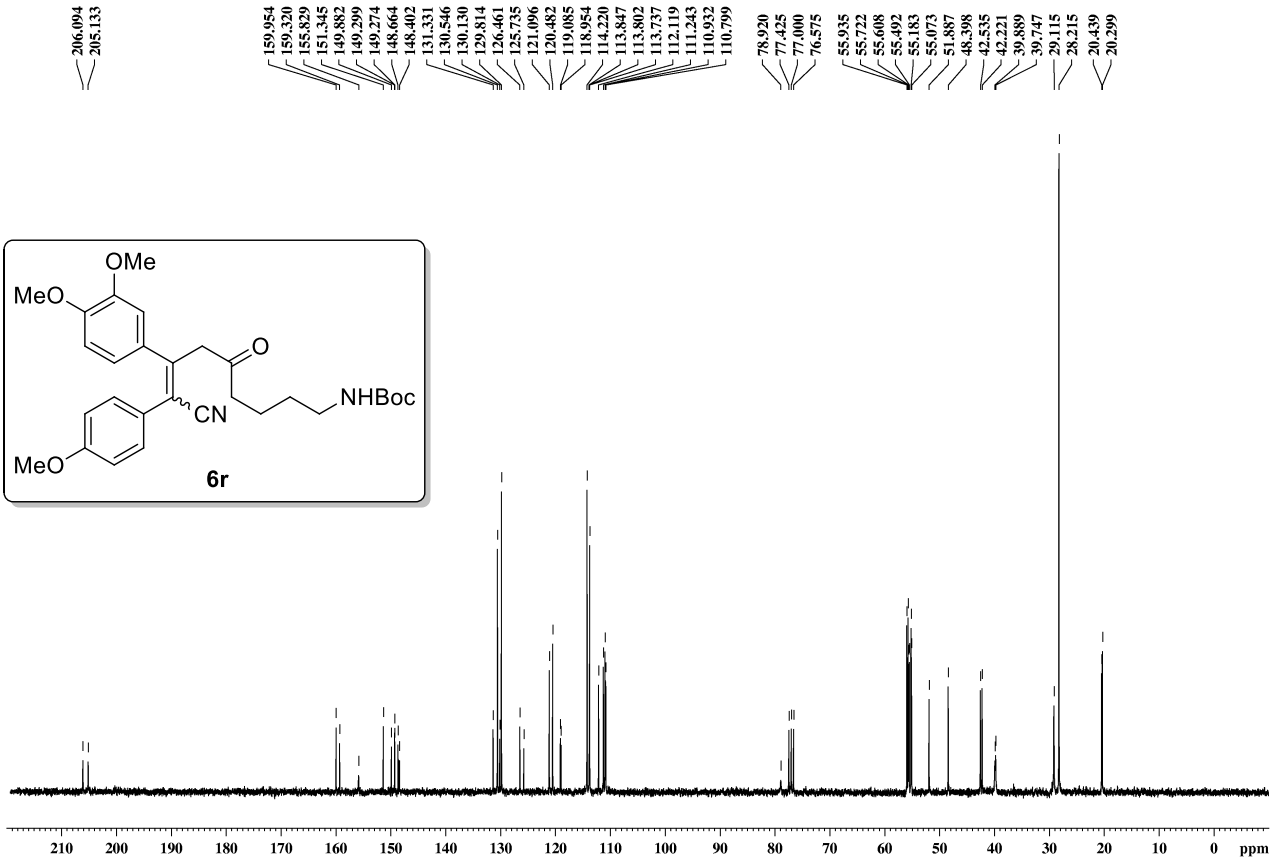
^{13}C NMR (75 MHz, $CDCl_3$); **6q**



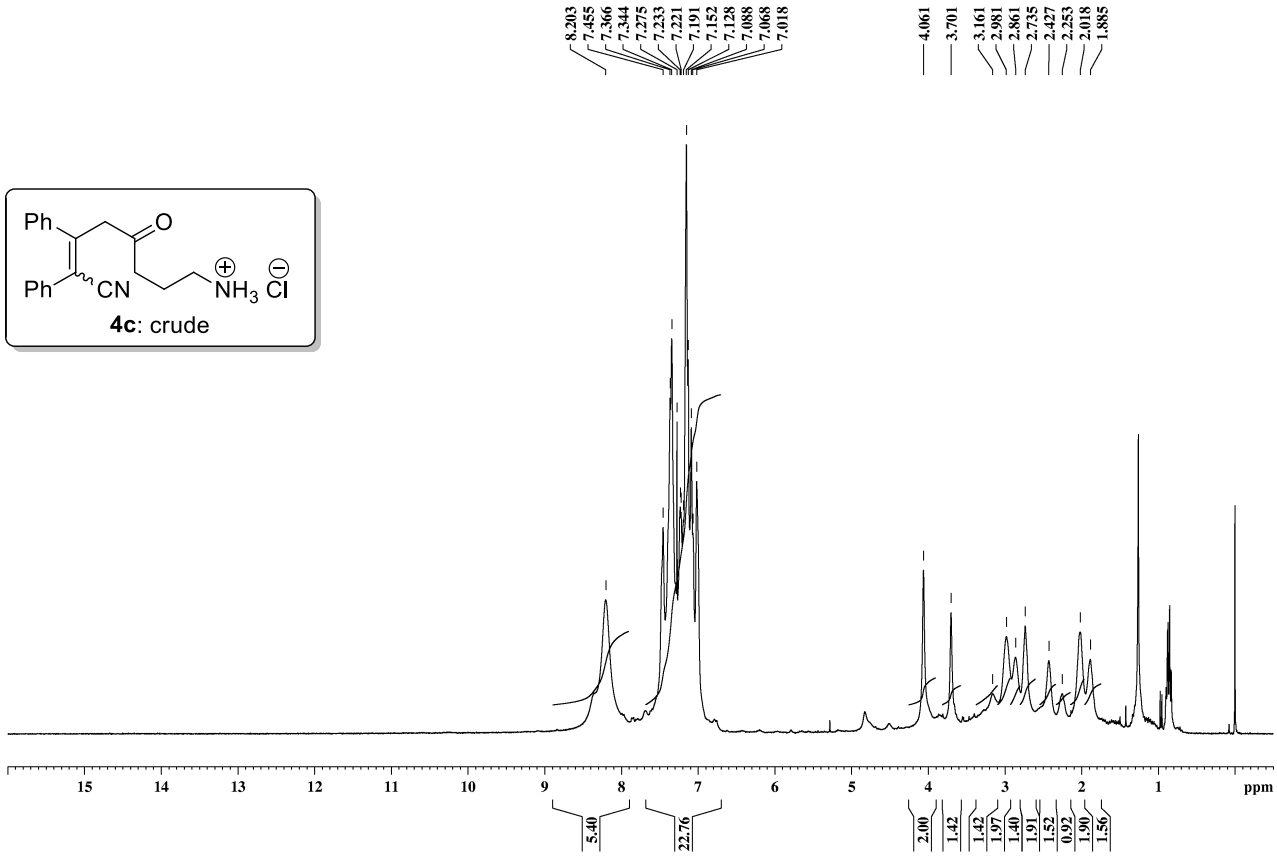
^{1}H NMR (300 MHz, $CDCl_3$); **6r**



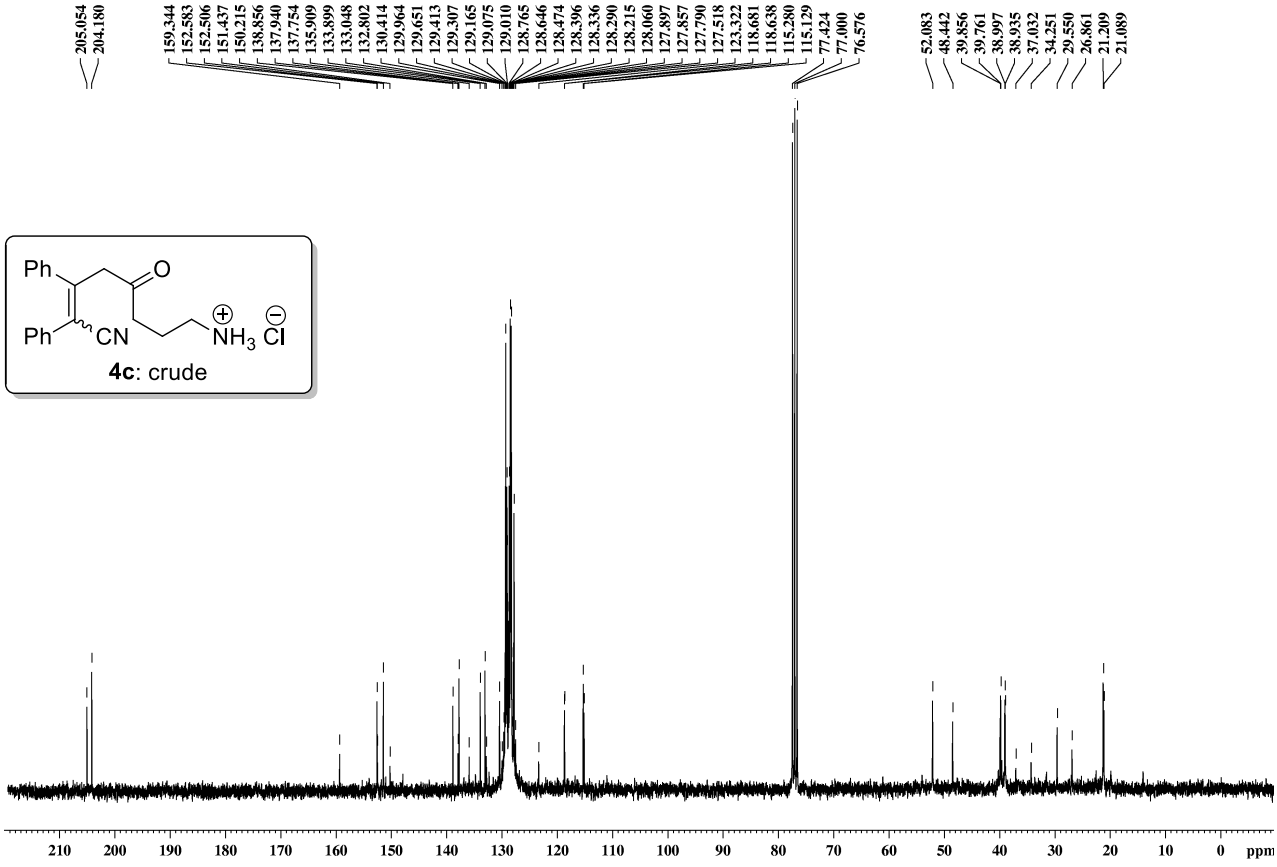
^{13}C NMR (75 MHz, $CDCl_3$); **6r**



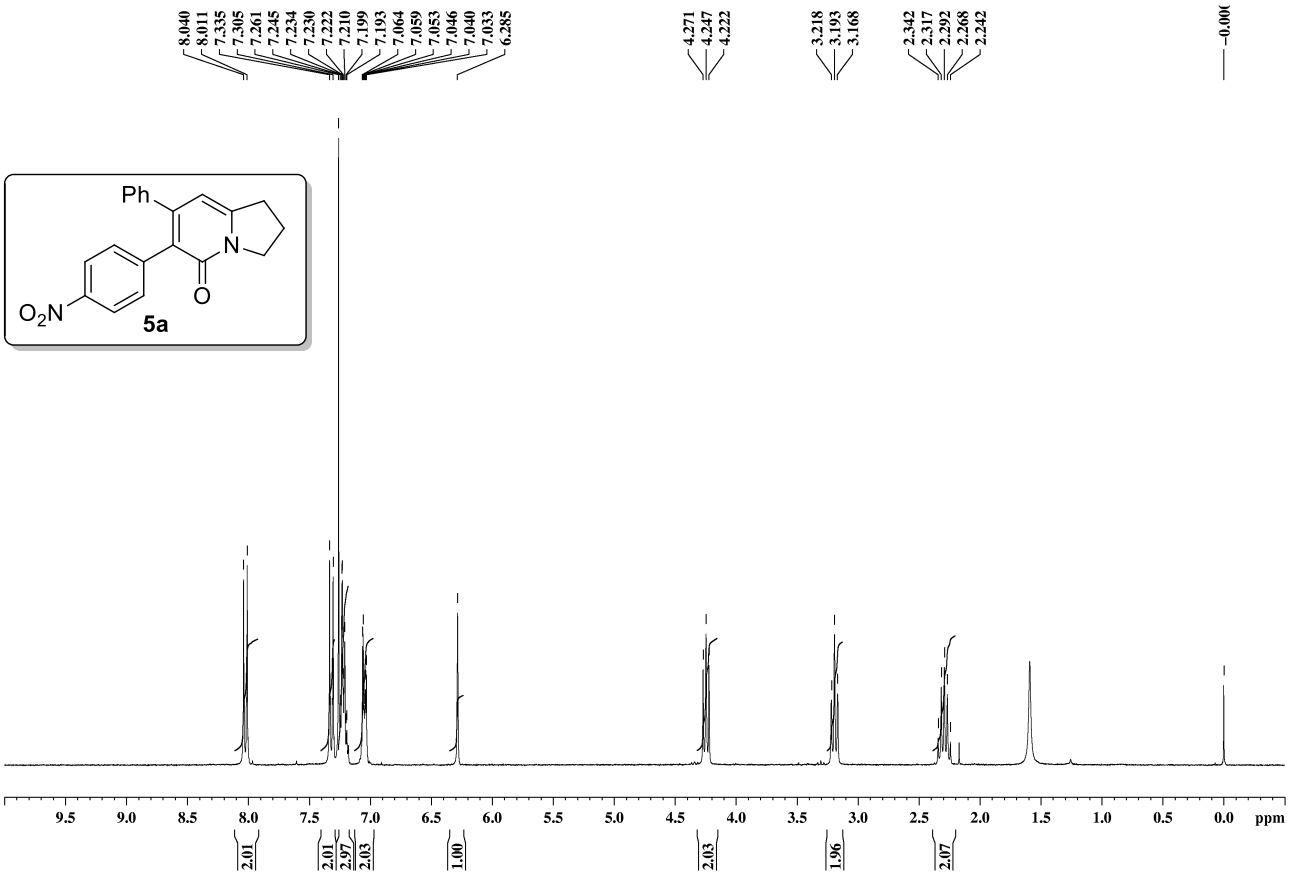
^{1}H NMR (300 MHz, $CDCl_3$); **4c**



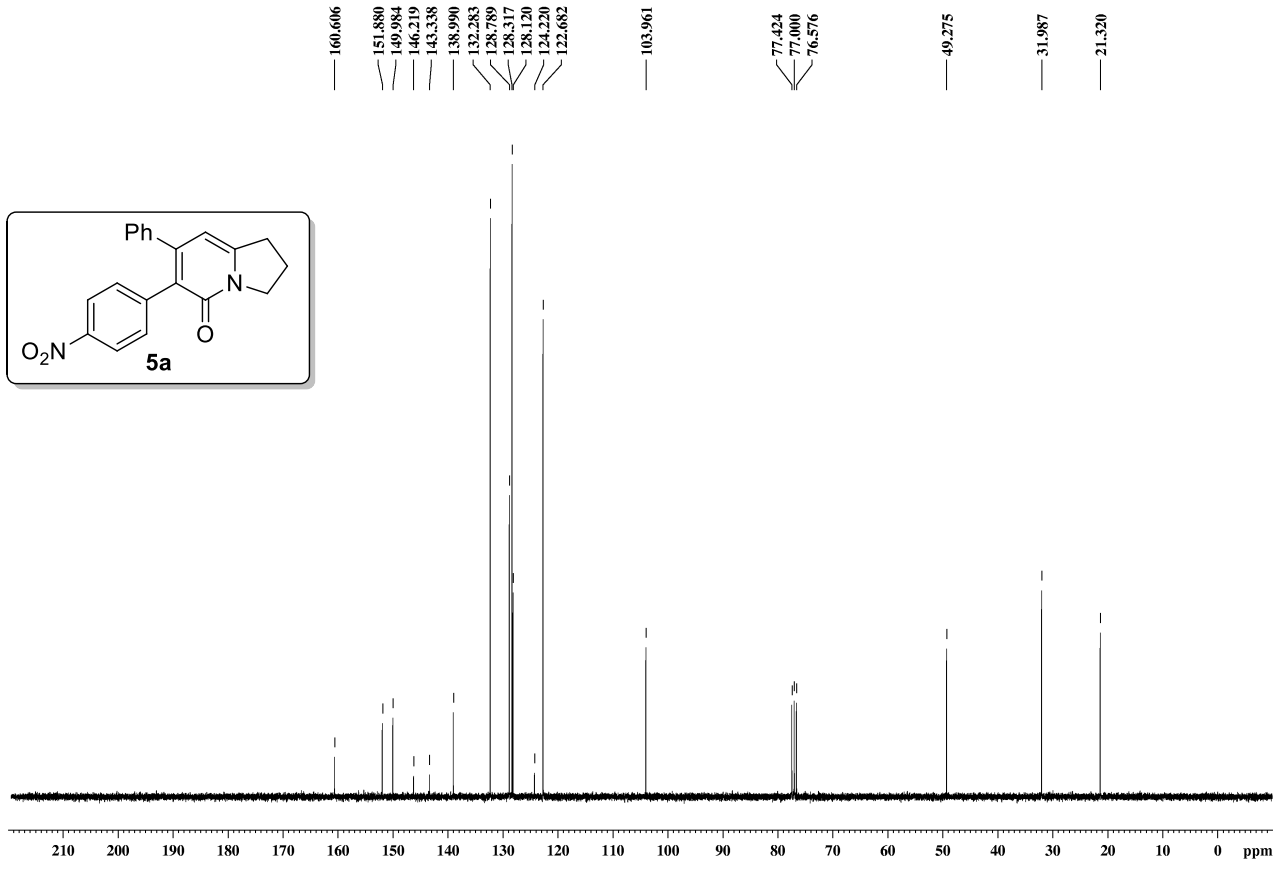
^{13}C NMR (75 MHz, $CDCl_3$); **4c**



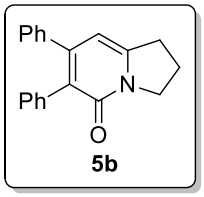
^{1}H NMR (300 MHz, $CDCl_3$); **5a**

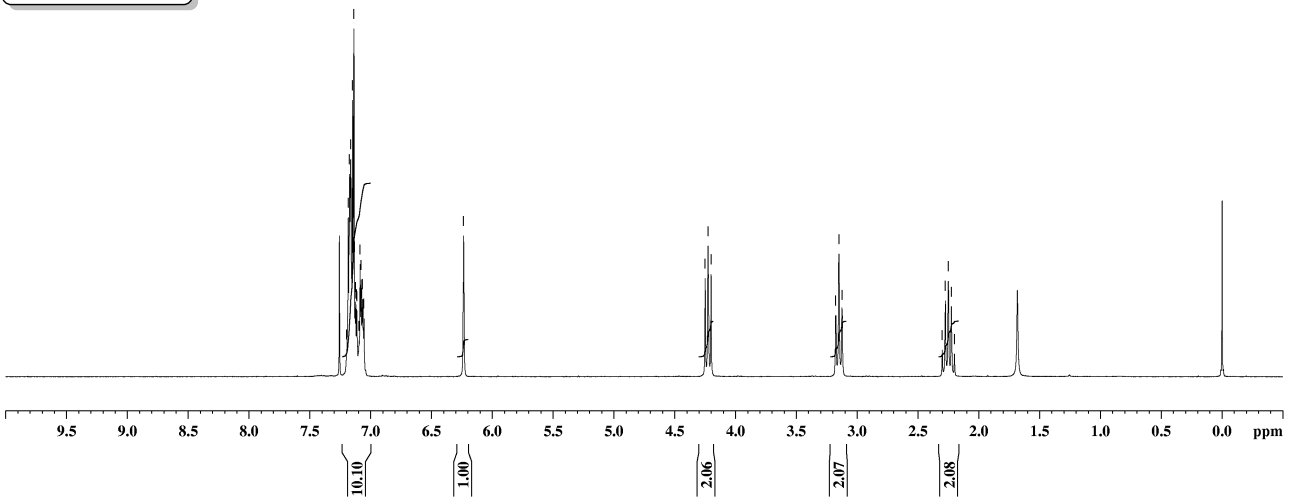


^{13}C NMR (75 MHz, $CDCl_3$); **5a**

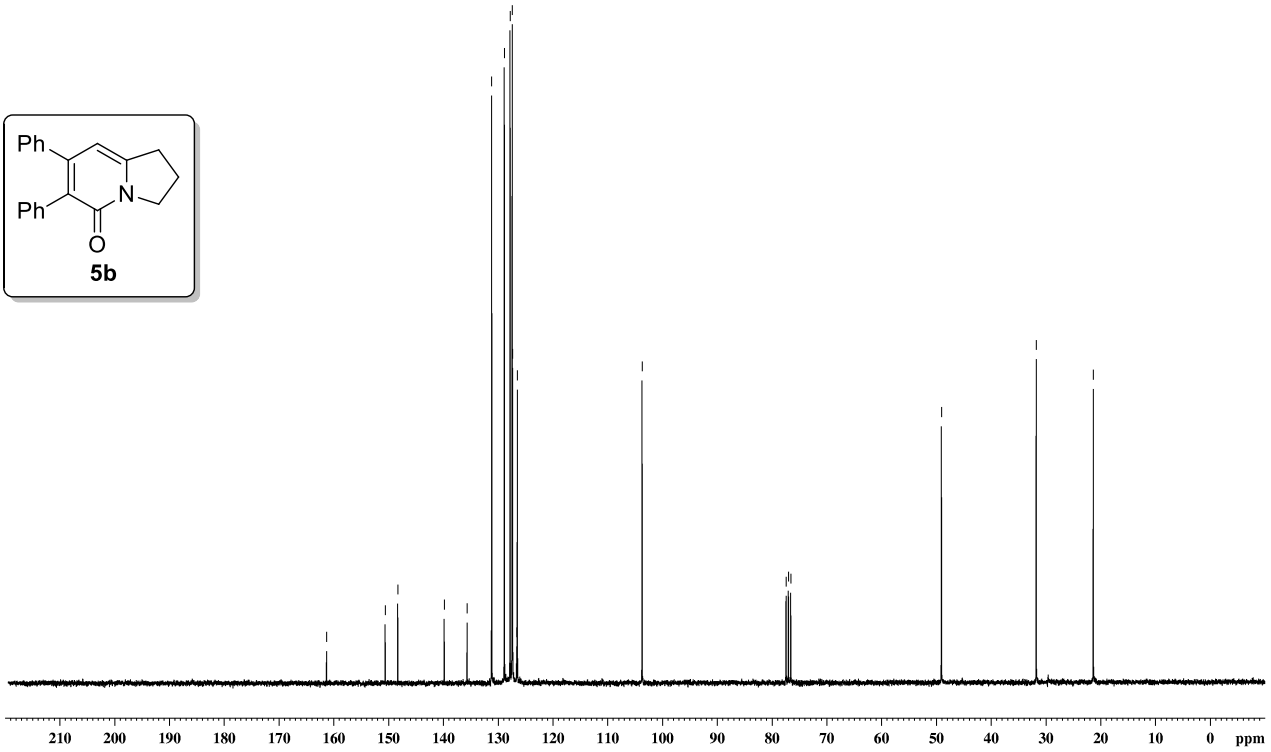


^{1}H NMR (300 MHz, $CDCl_3$); **5b**

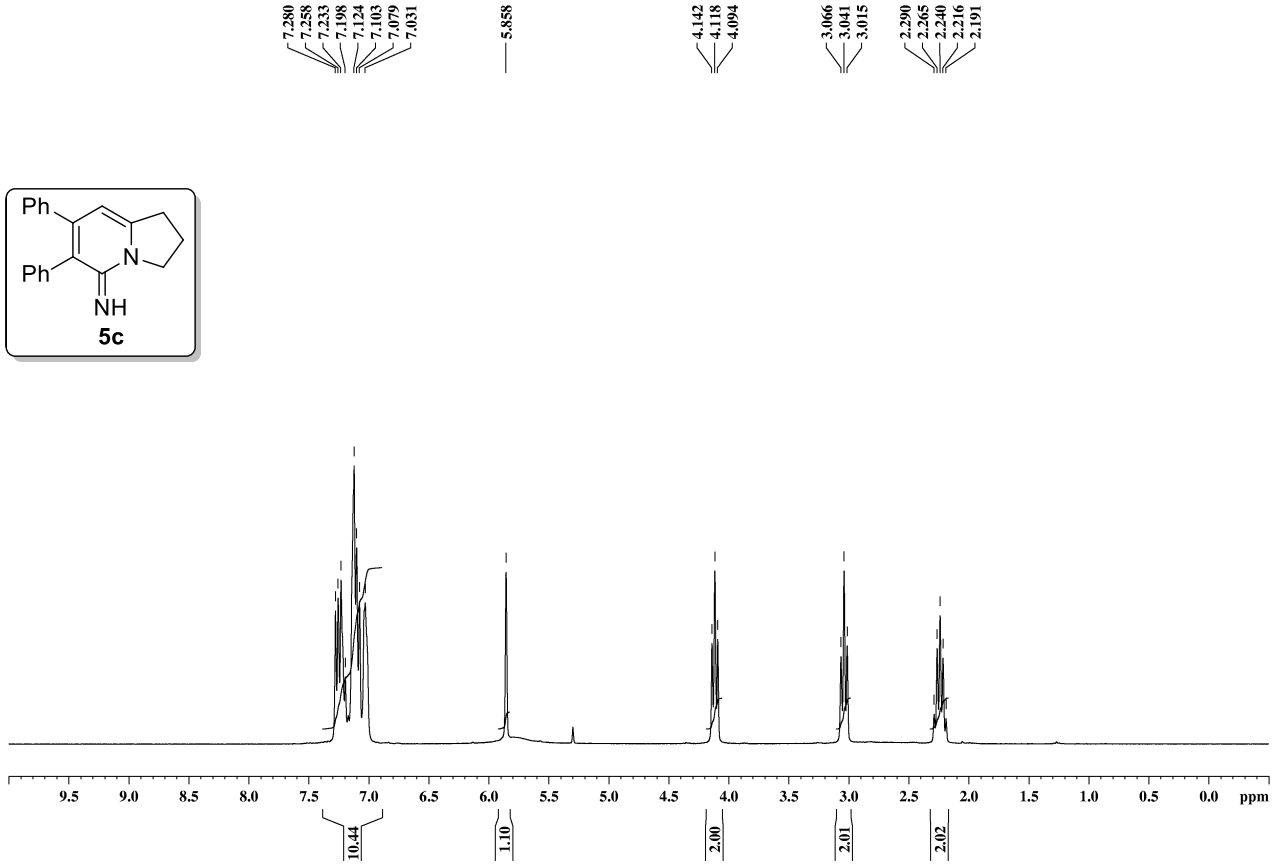




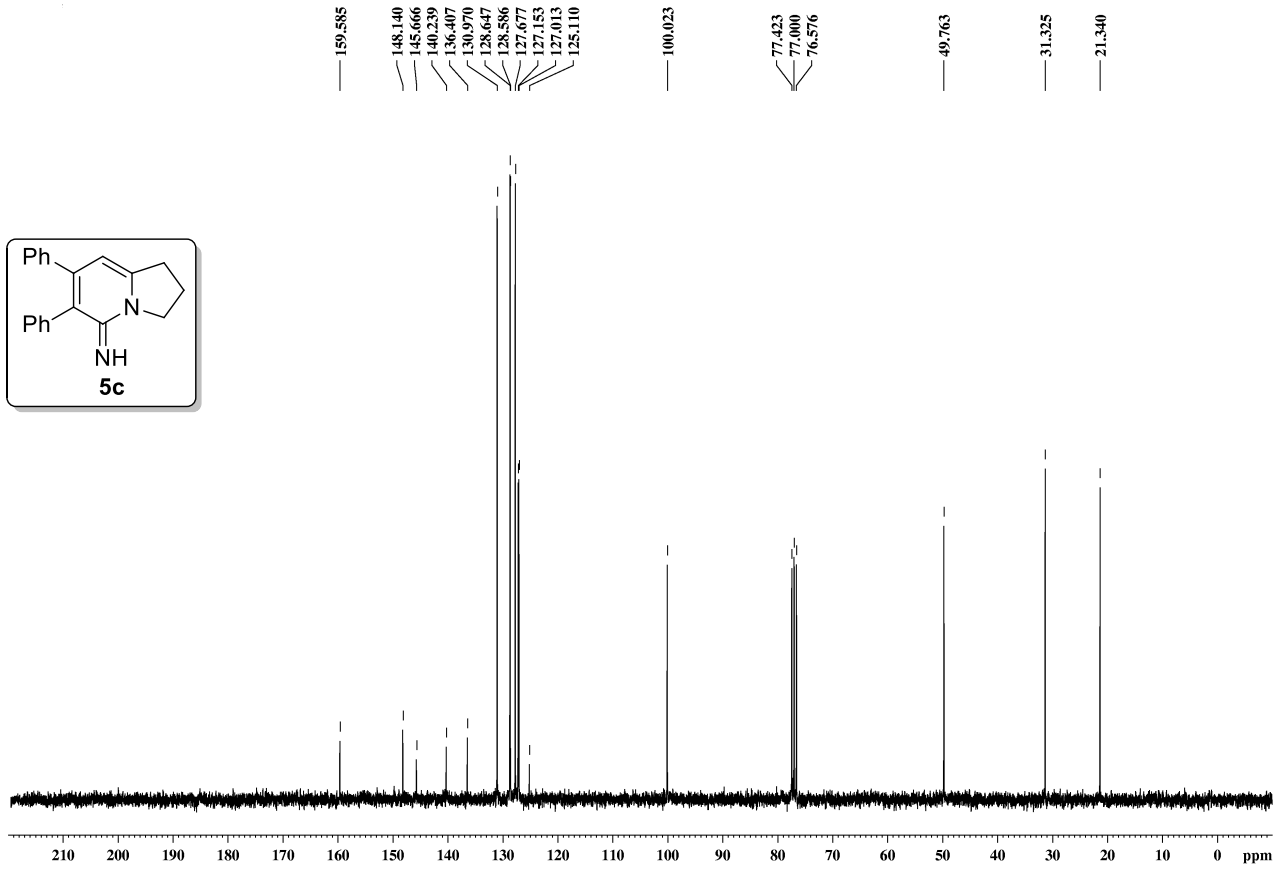
^{13}C NMR (75 MHz, $CDCl_3$); **5b**



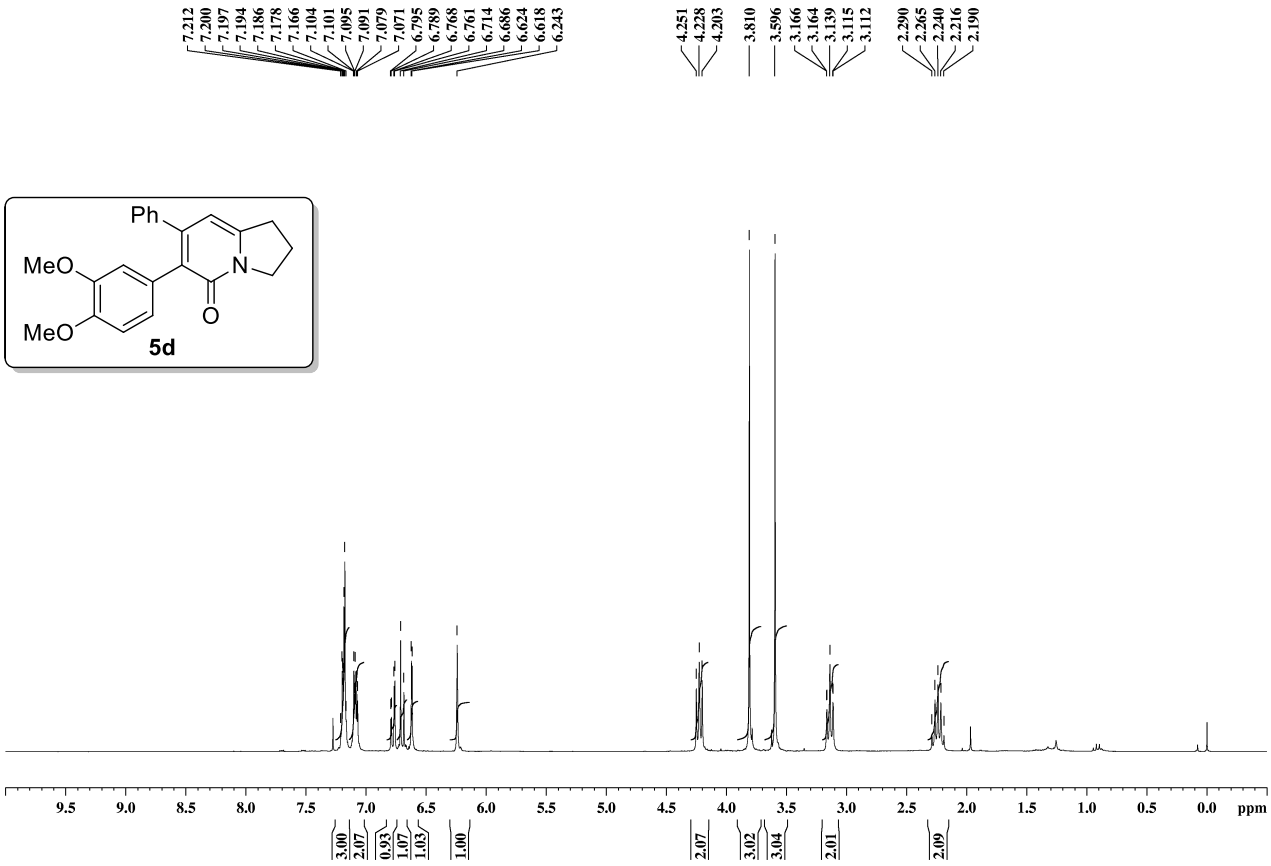
^{1}H NMR (300 MHz, $CDCl_3$); **5c**



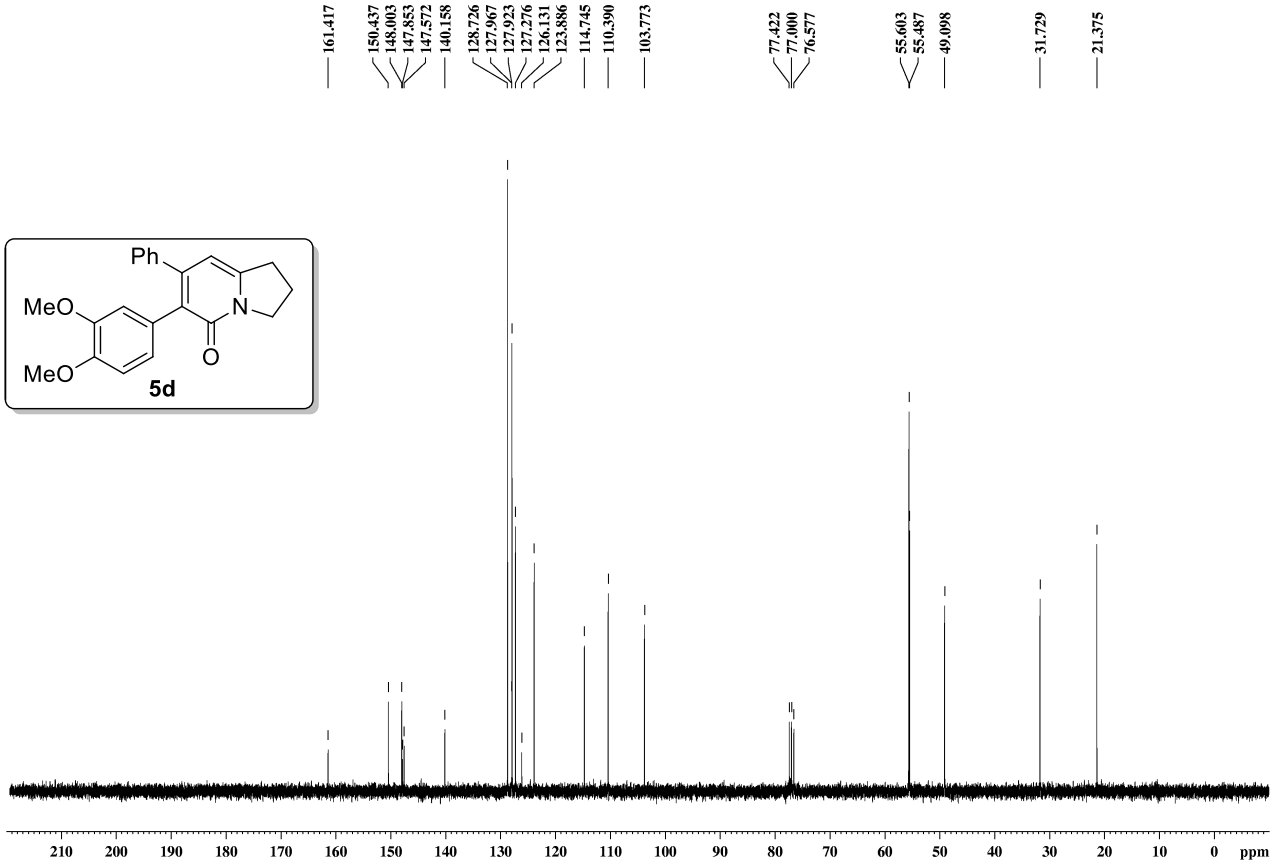
^{13}C NMR (75 MHz, $CDCl_3$); **5c**



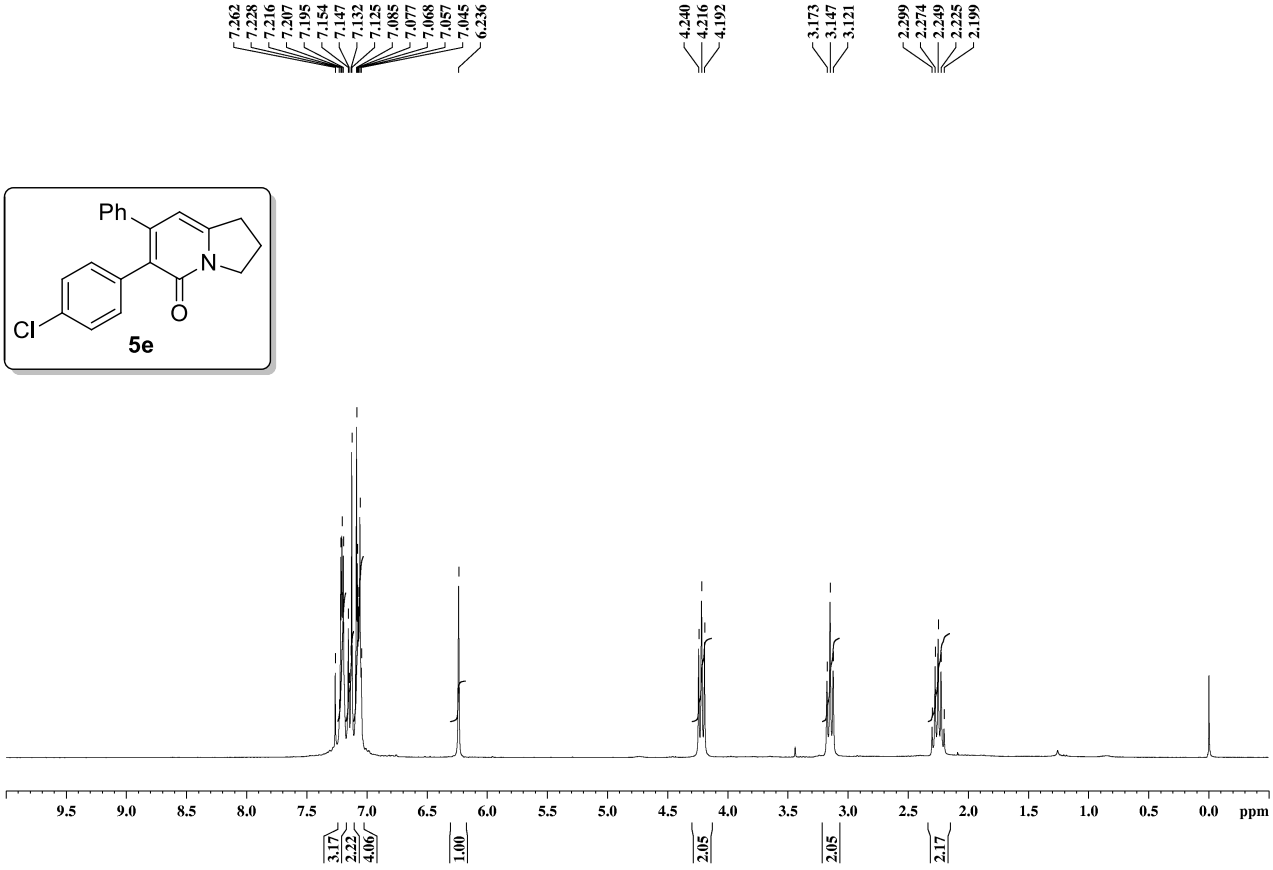
^{1}H NMR (300 MHz, $CDCl_3$); **5d**



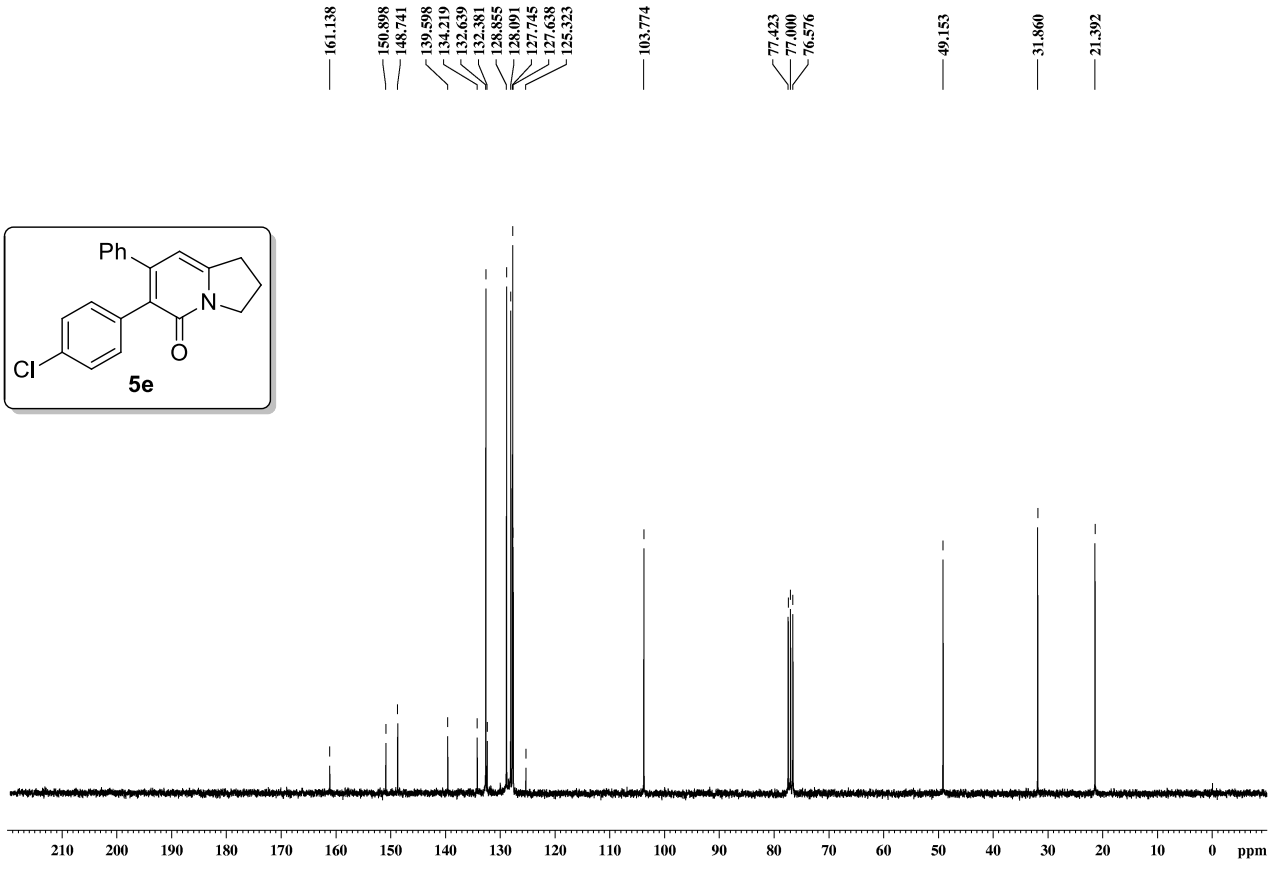
^{13}C NMR (75 MHz, $CDCl_3$); **5d**



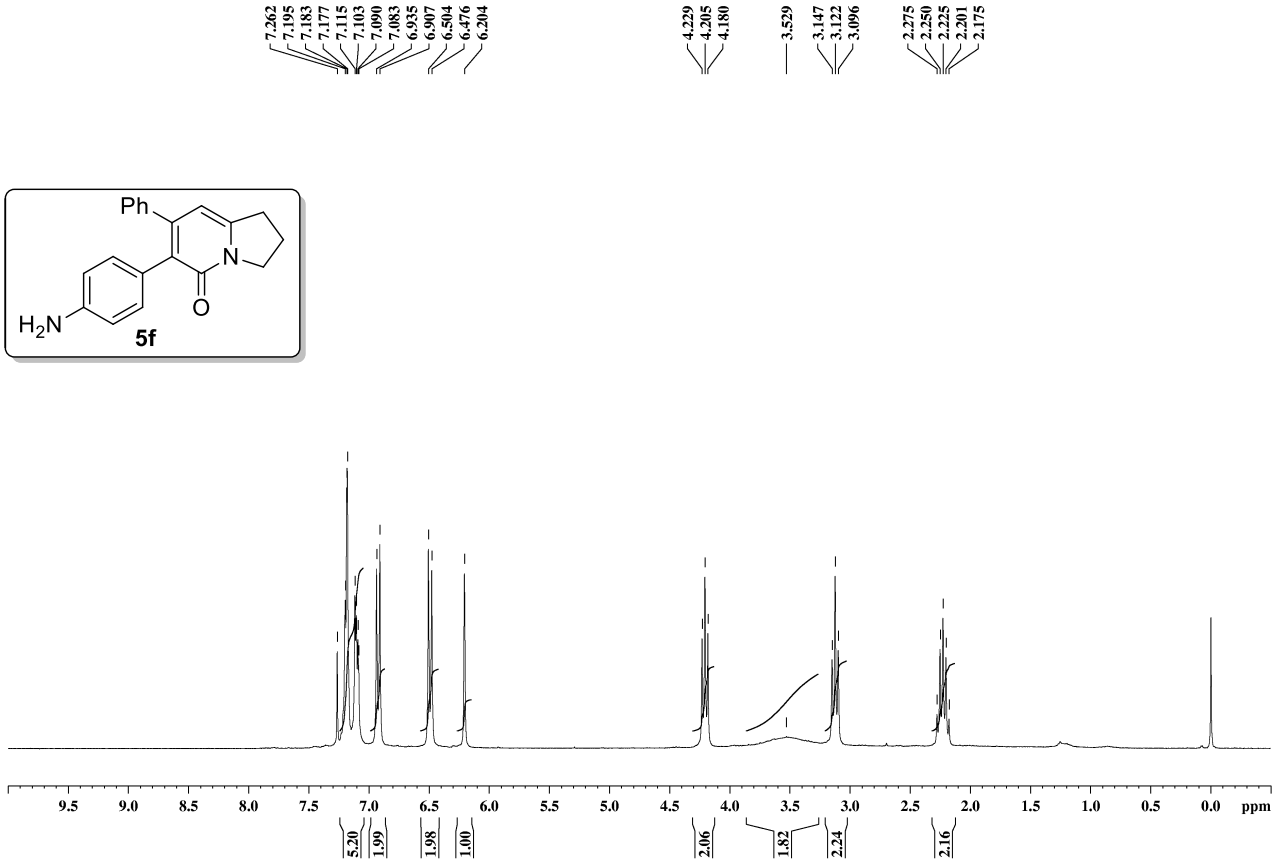
^{1}H NMR (300 MHz, $CDCl_3$); **5e**



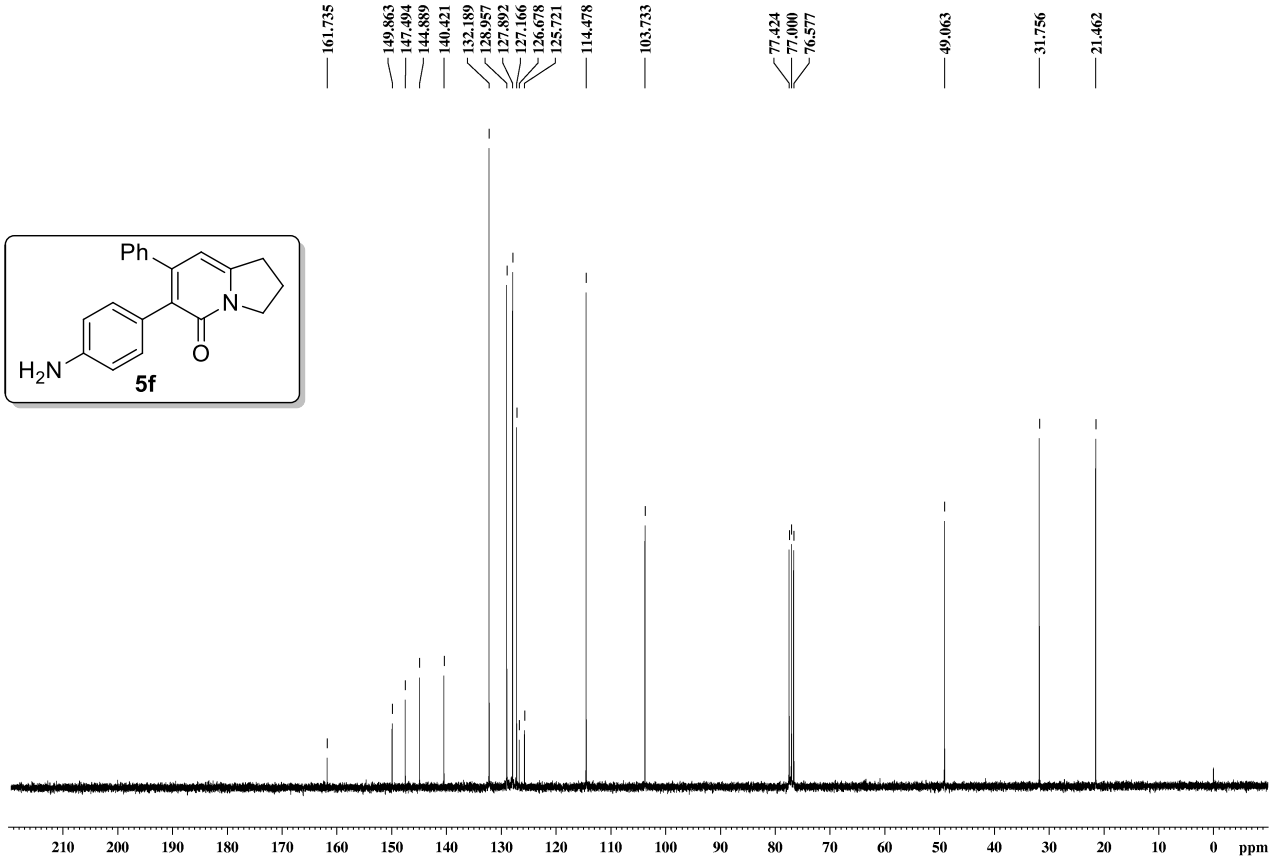
^{13}C NMR (75 MHz, $CDCl_3$); **5e**



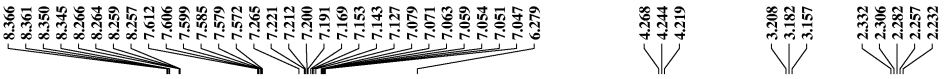
^{1}H NMR (300 MHz, $CDCl_3$); **5f**

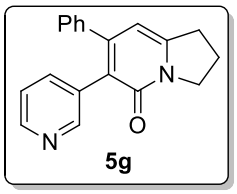


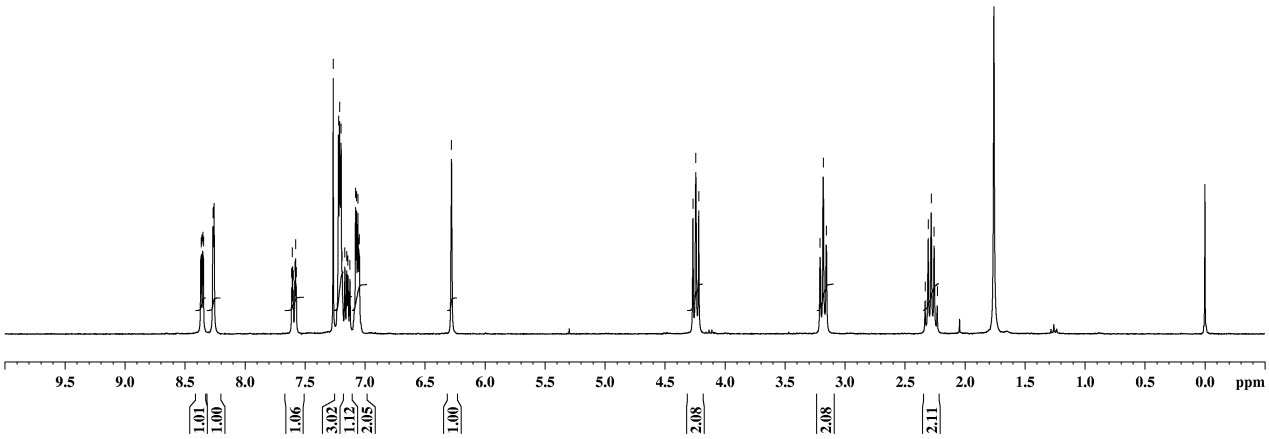
^{13}C NMR (75 MHz, $CDCl_3$); **5f**



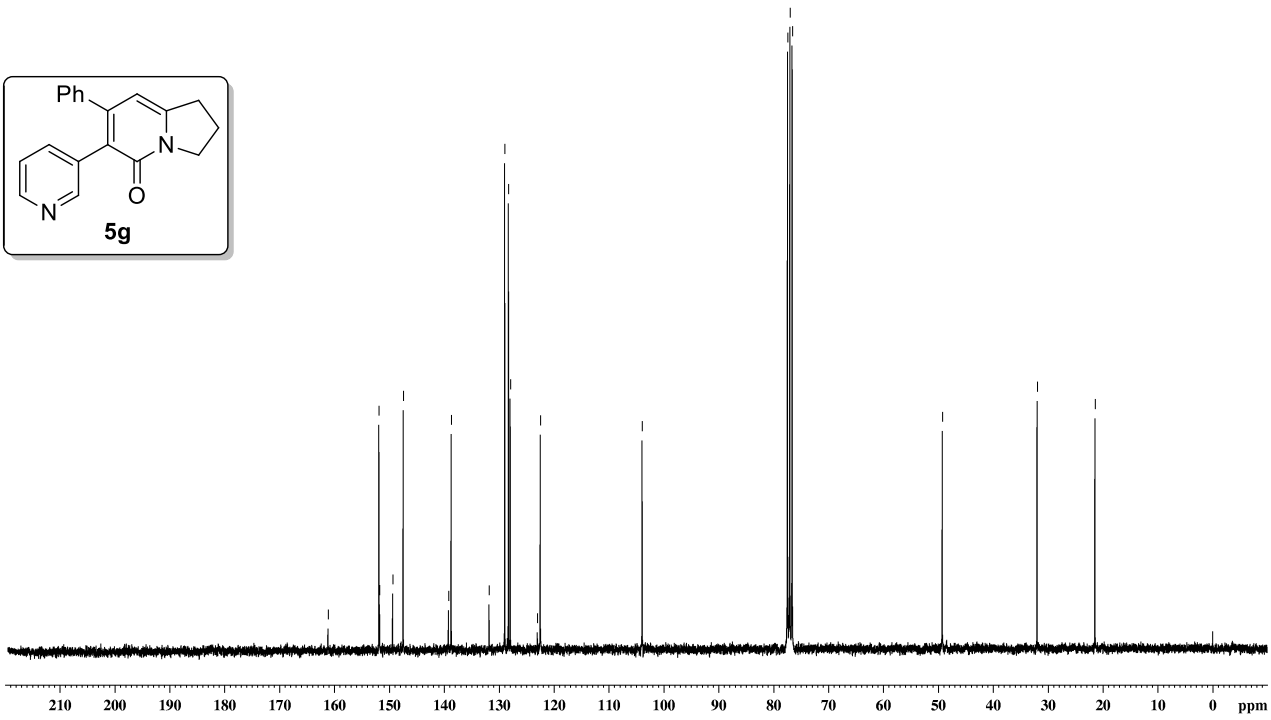
^{1}H NMR (300 MHz, $CDCl_3$); **5g**



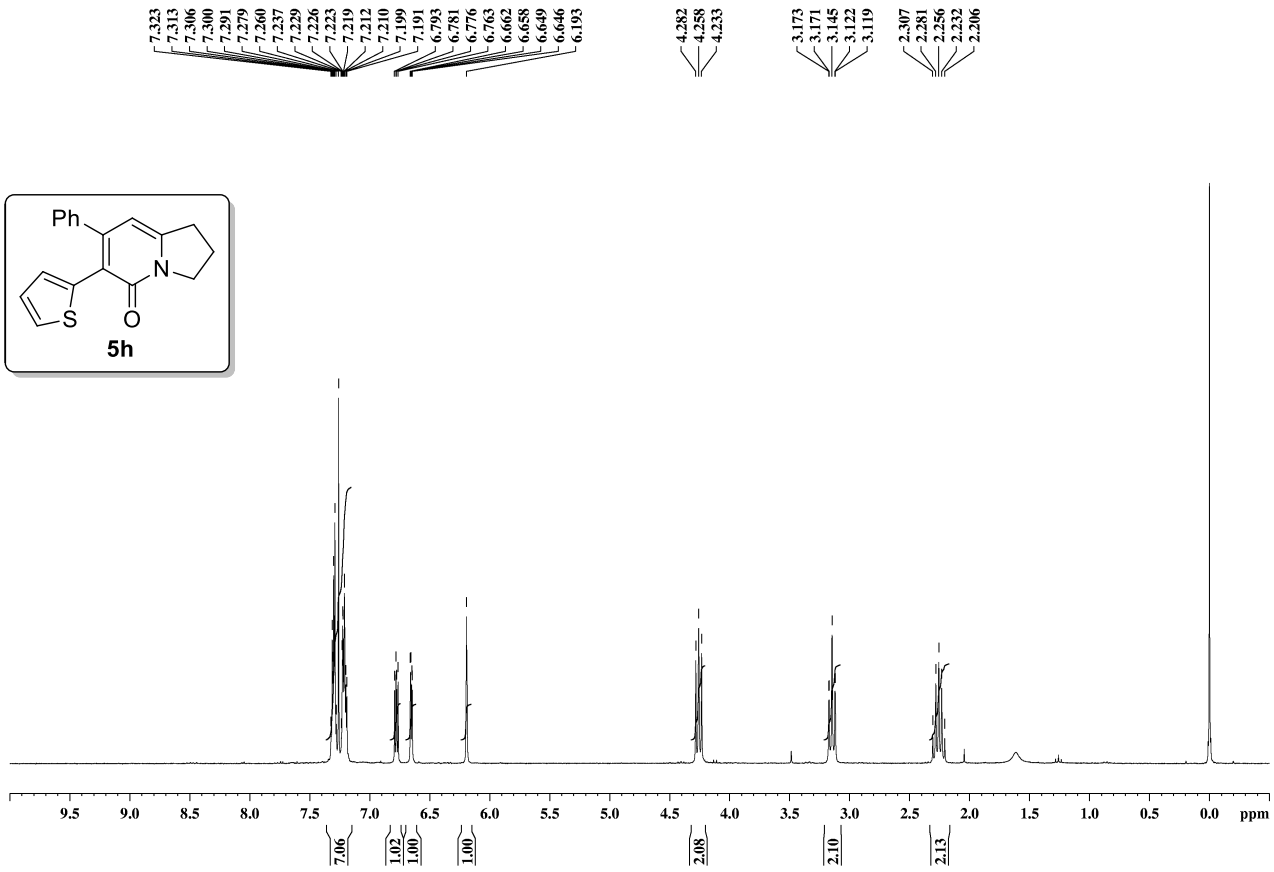




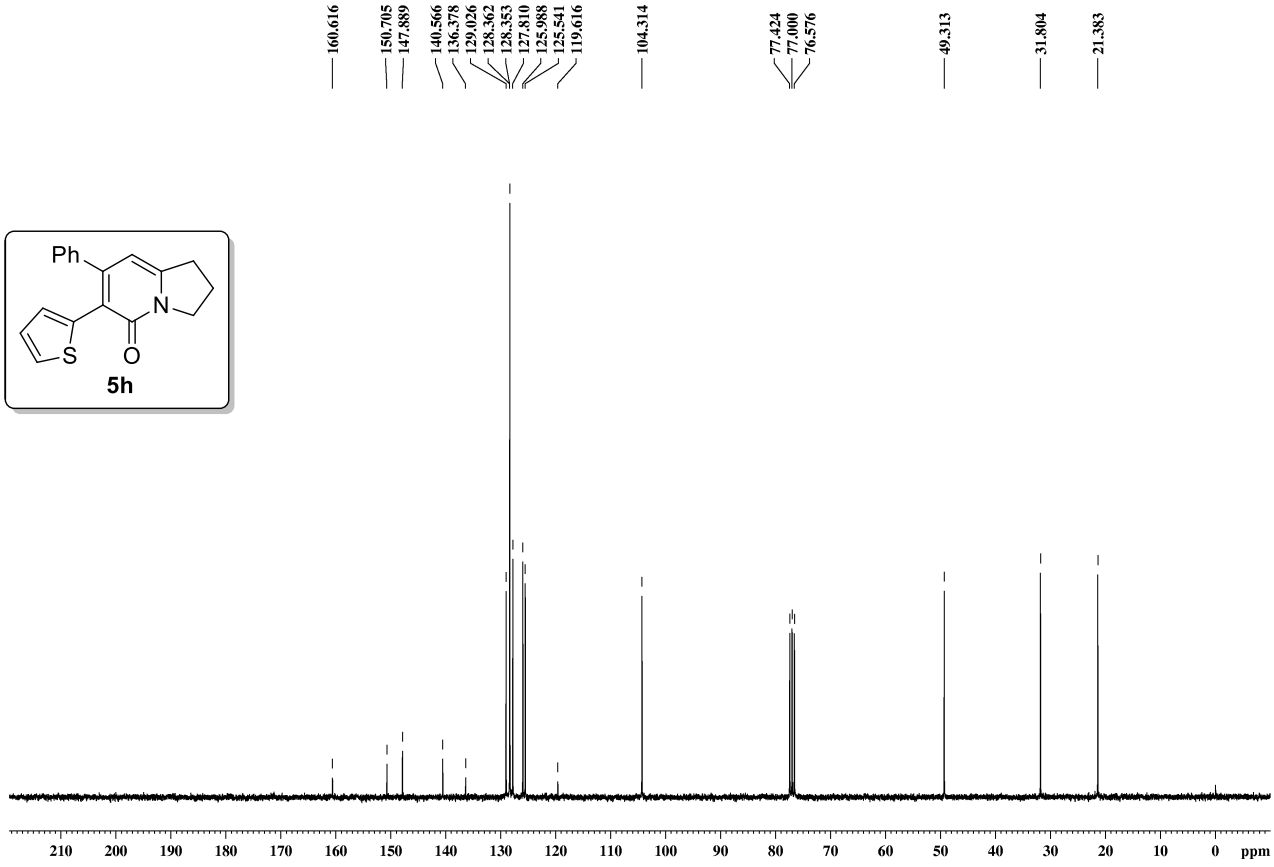
^{13}C NMR (75 MHz, $CDCl_3$); **5g**



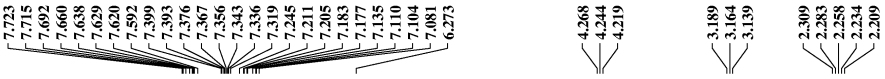
^{1}H NMR (300 MHz, $CDCl_3$); **5h**

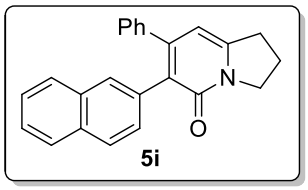


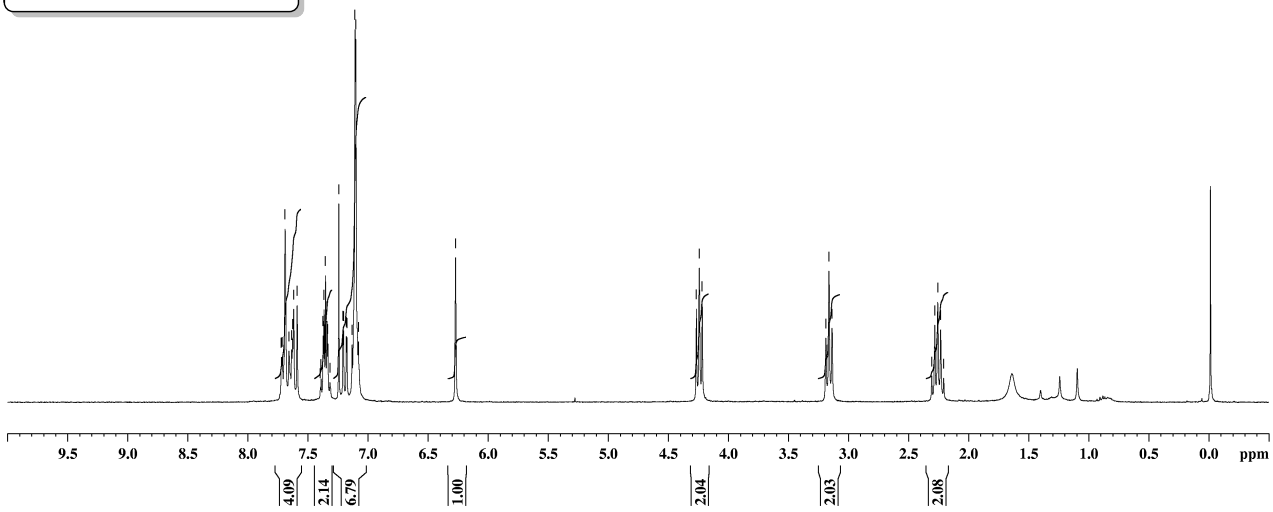
^{13}C NMR (75 MHz, $CDCl_3$); **5h**



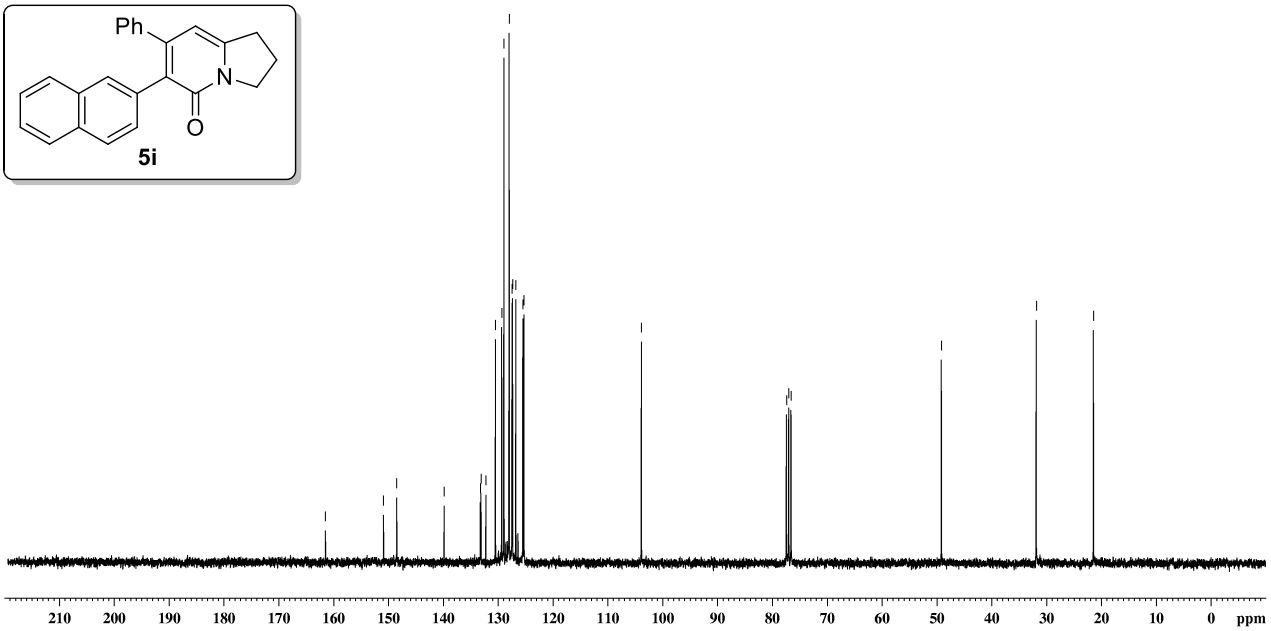
^{1}H NMR (300 MHz, $CDCl_3$); **5i**



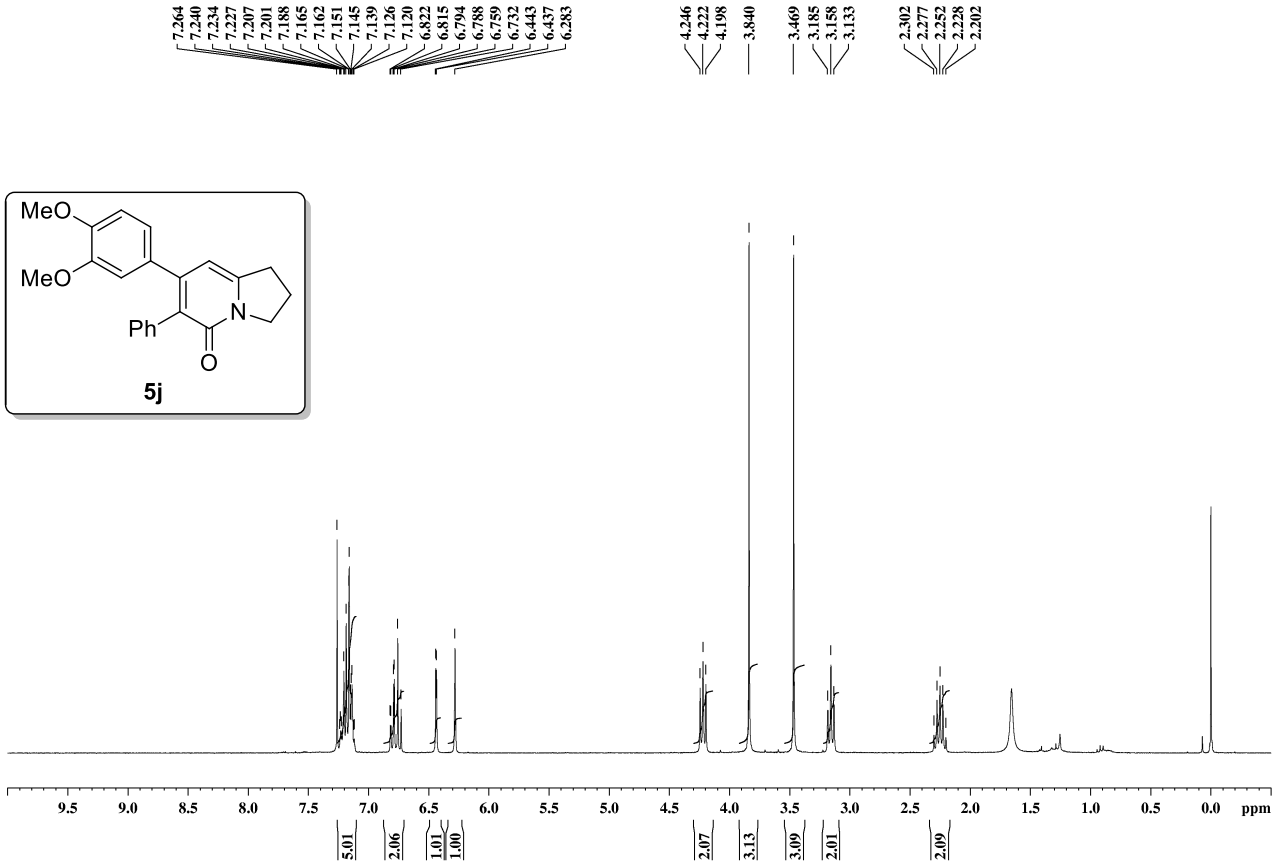




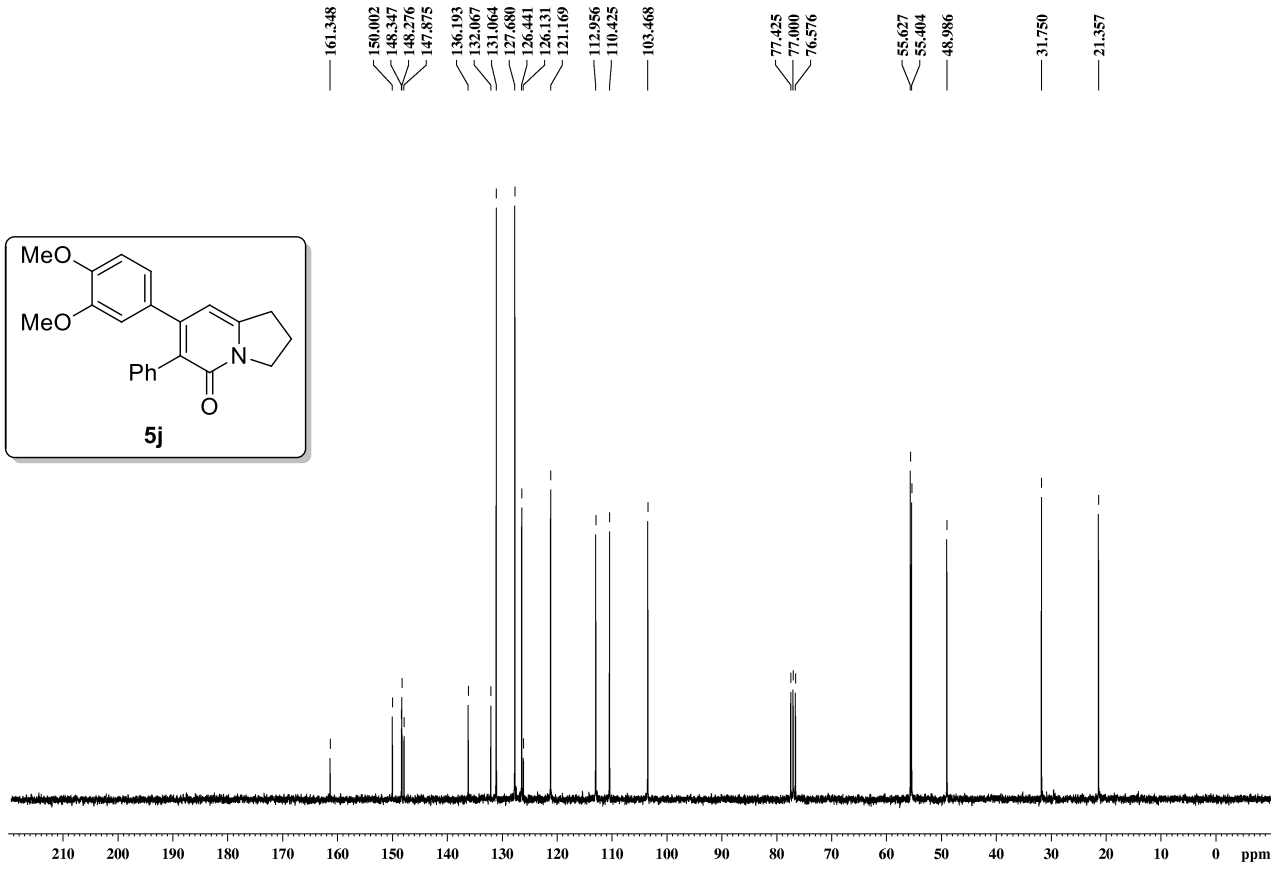
^{13}C NMR (75 MHz, $CDCl_3$); **5i**



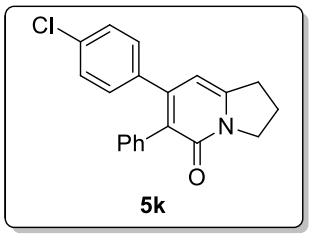
^{1}H NMR (300 MHz, $CDCl_3$); **5j**

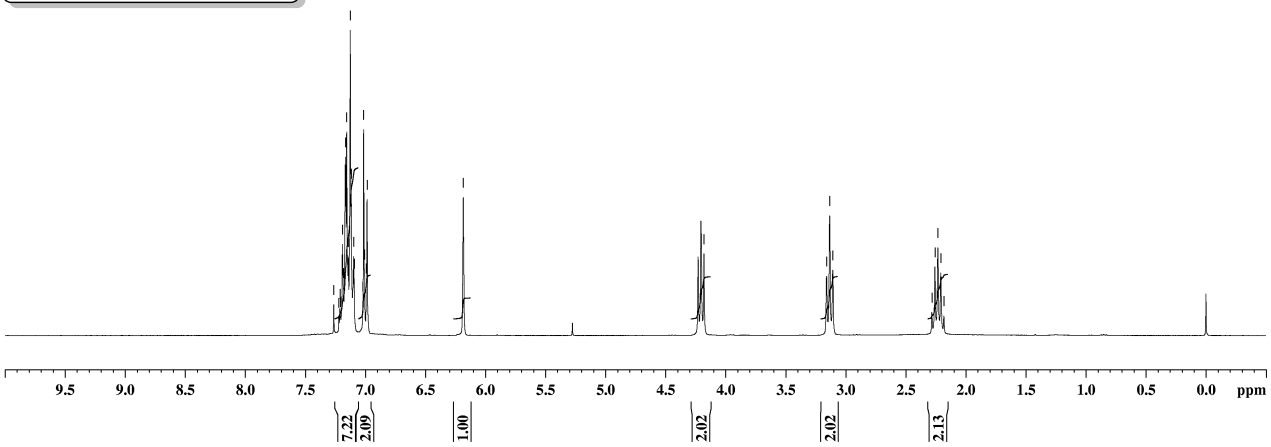


^{13}C NMR (75 MHz, $CDCl_3$); **5j**

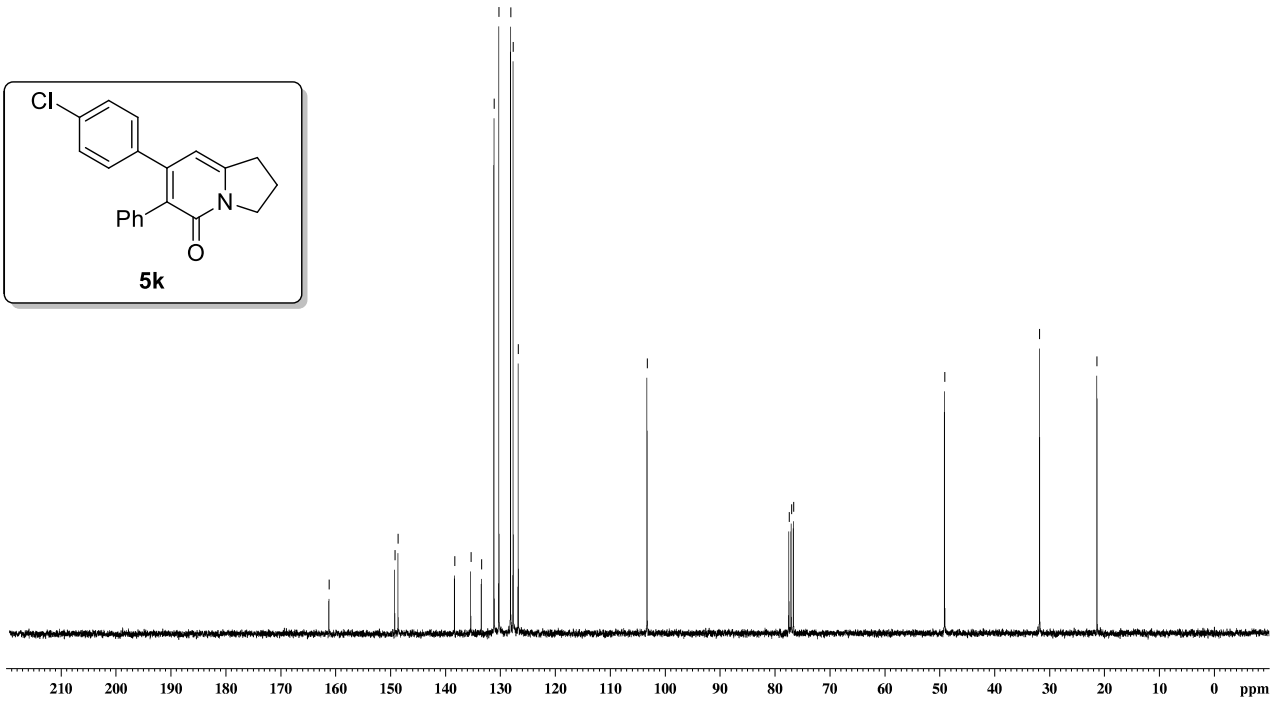


^{1}H NMR (300 MHz, $CDCl_3$); **5k**

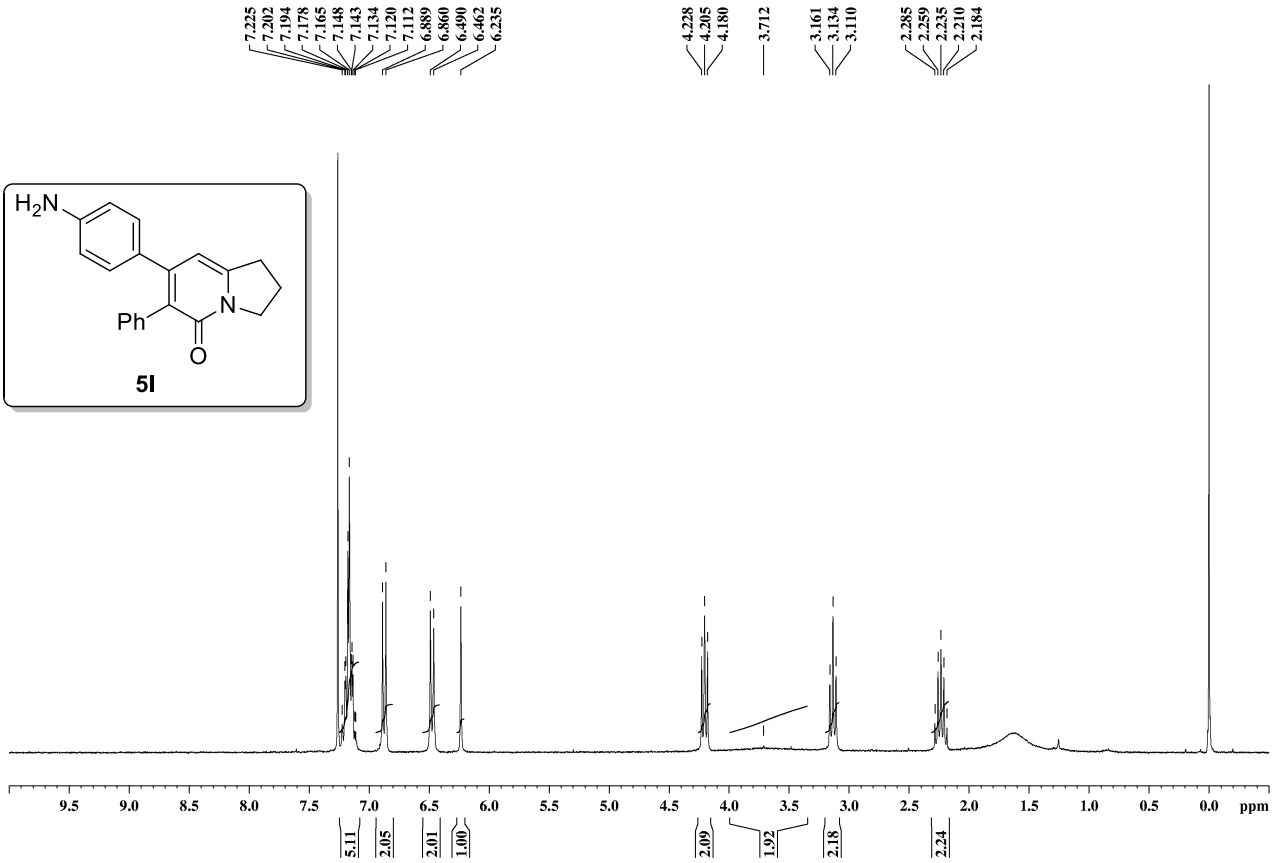




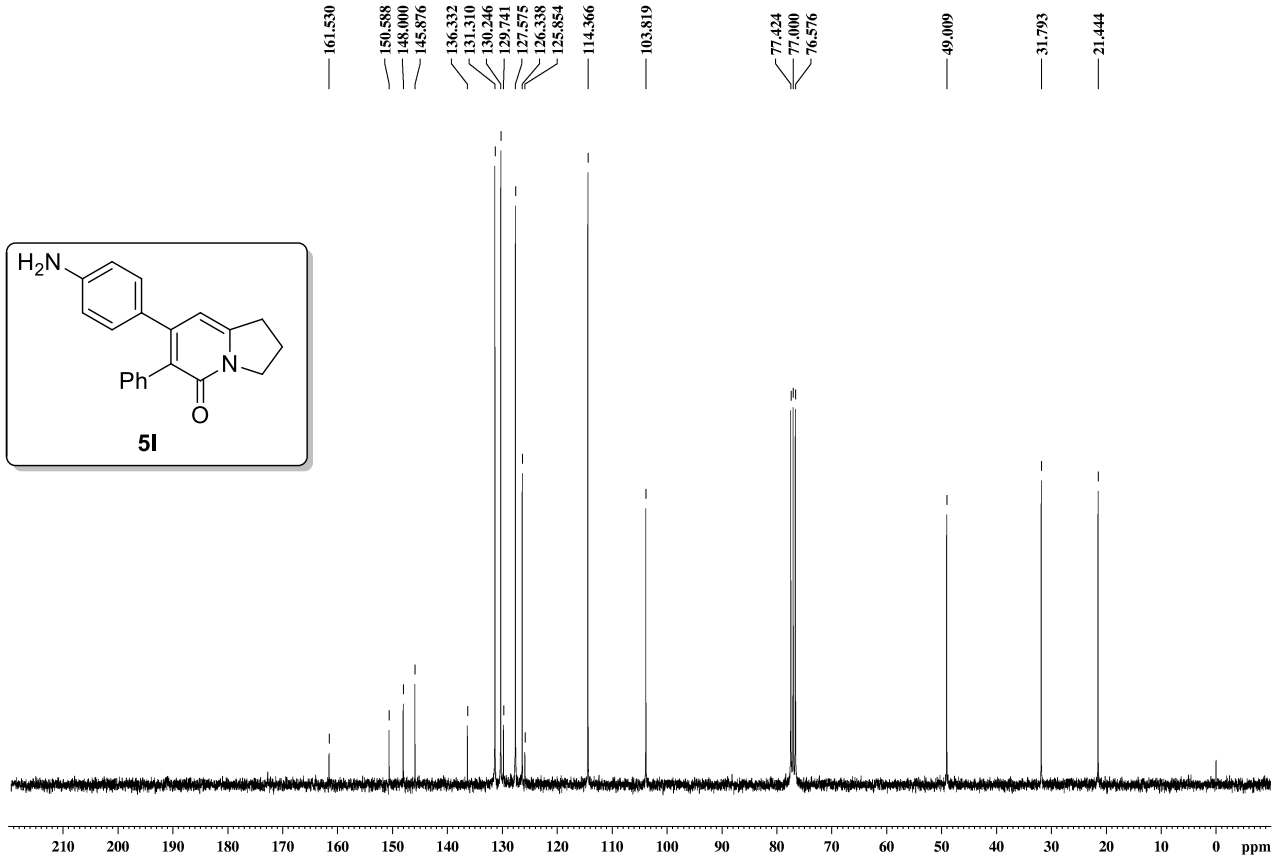
^{13}C NMR (75 MHz, $CDCl_3$); **5k**



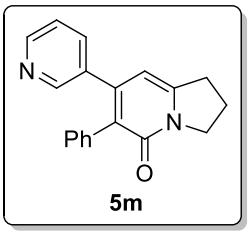
^{1}H NMR (300 MHz, $CDCl_3$); **5l**

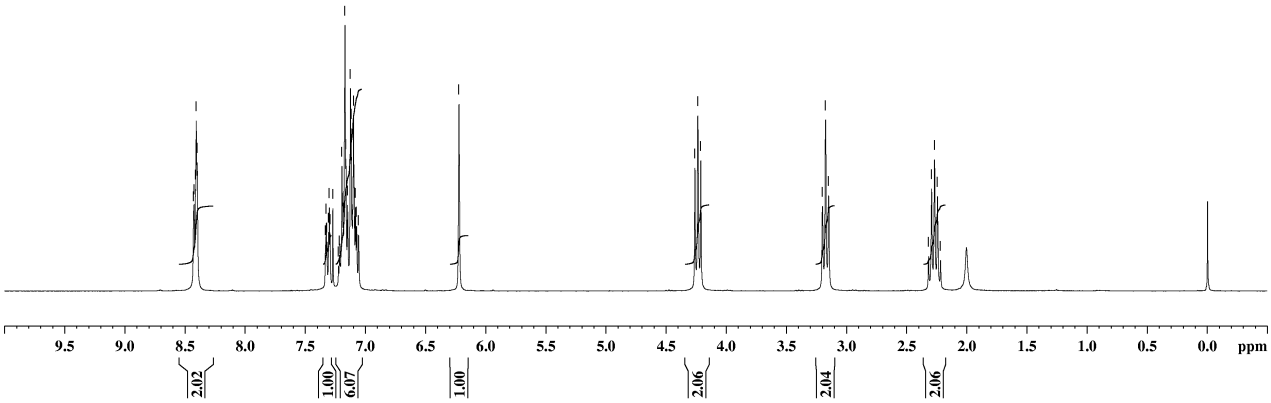


^{13}C NMR (75 MHz, $CDCl_3$); **5l**

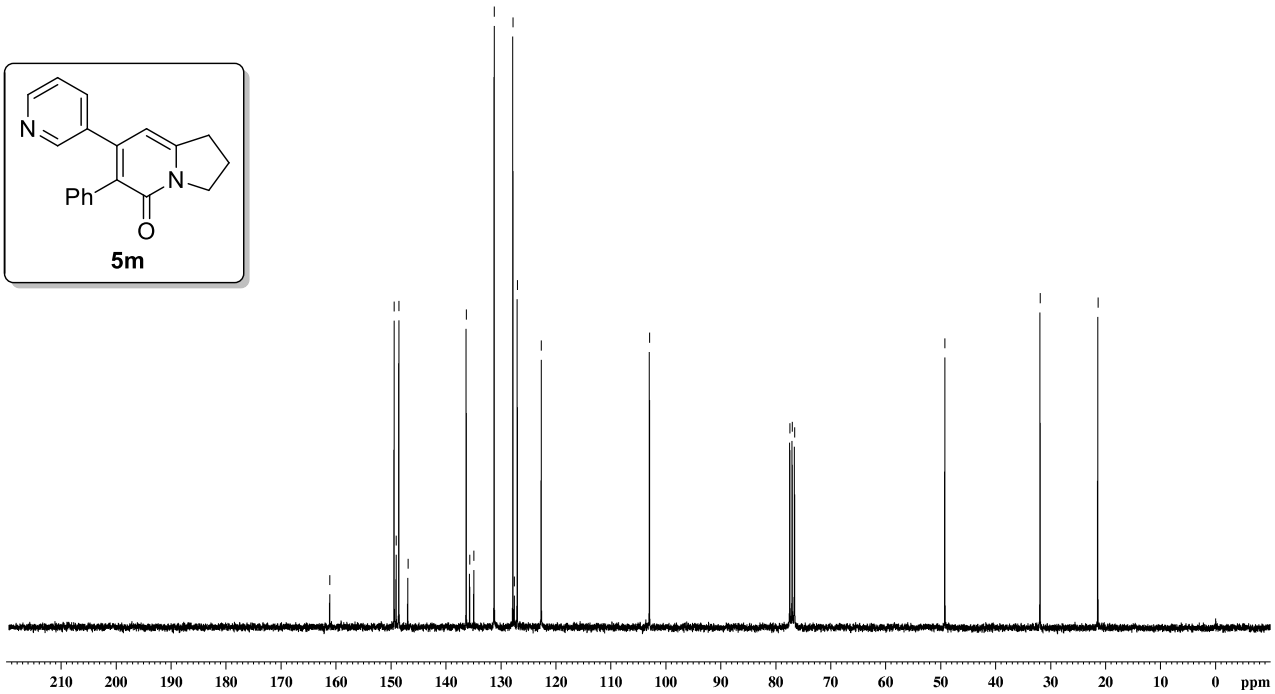


^{1}H NMR (300 MHz, $CDCl_3$); **5m**

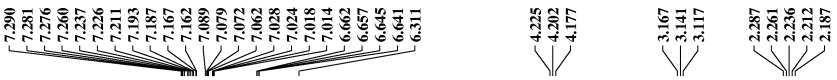


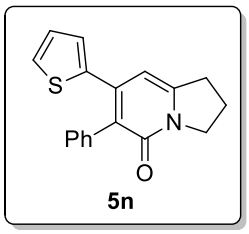


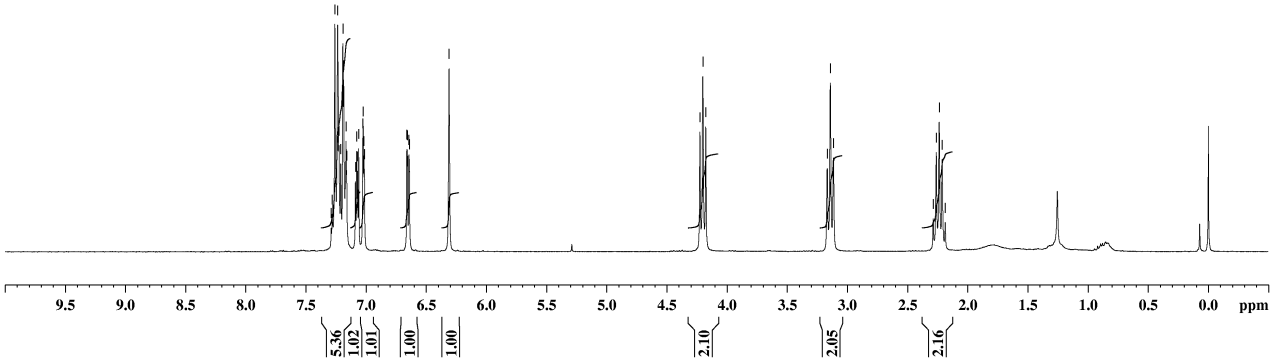
^{13}C NMR (75 MHz, $CDCl_3$); **5m**



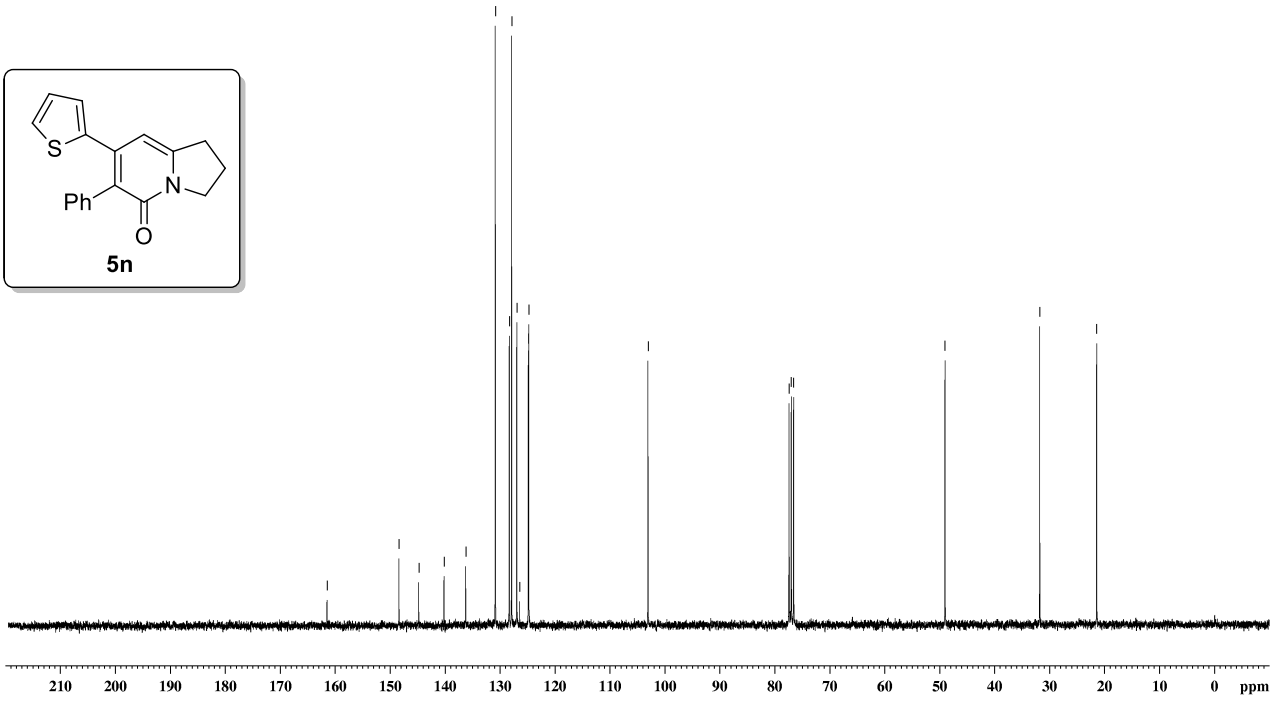
^{1}H NMR (300 MHz, $CDCl_3$); **5n**



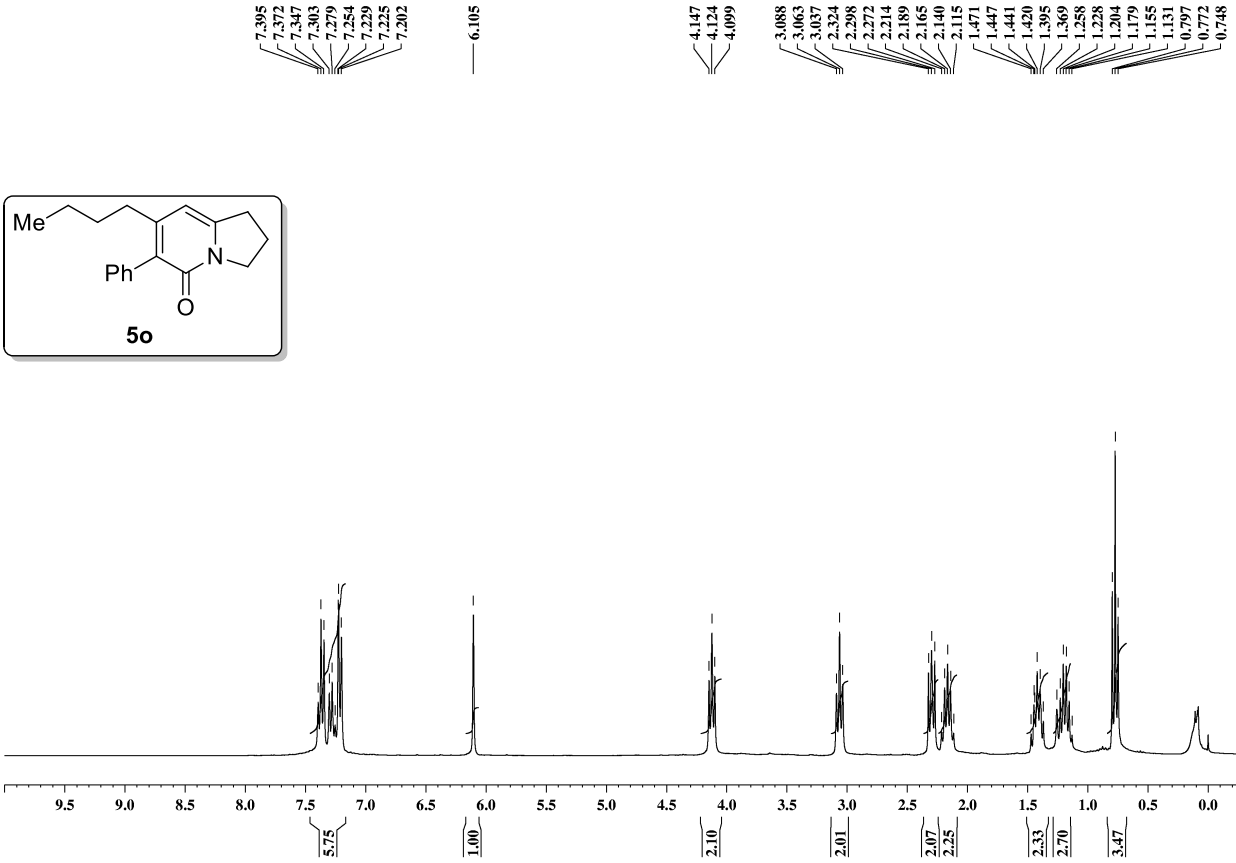




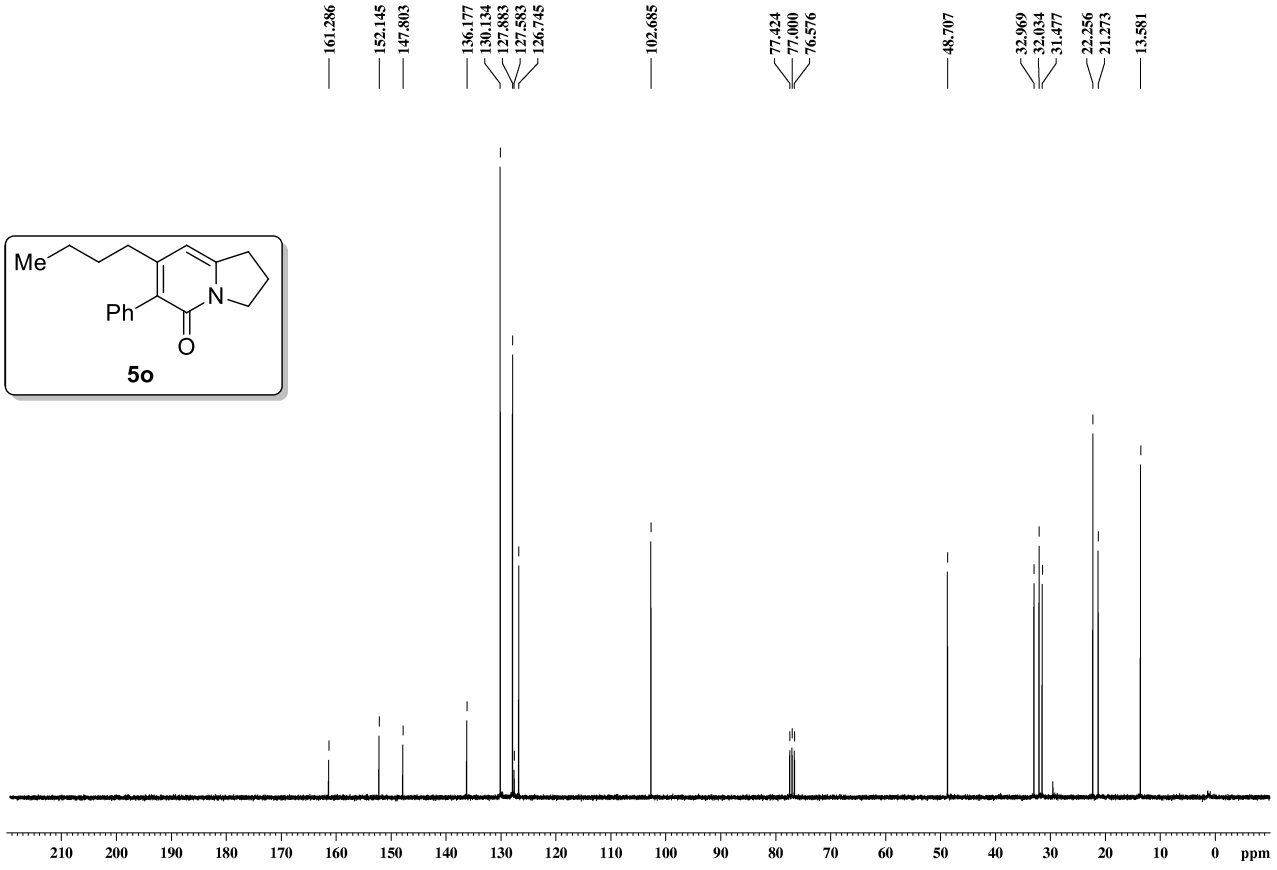
^{13}C NMR (75 MHz, $CDCl_3$); **5n**



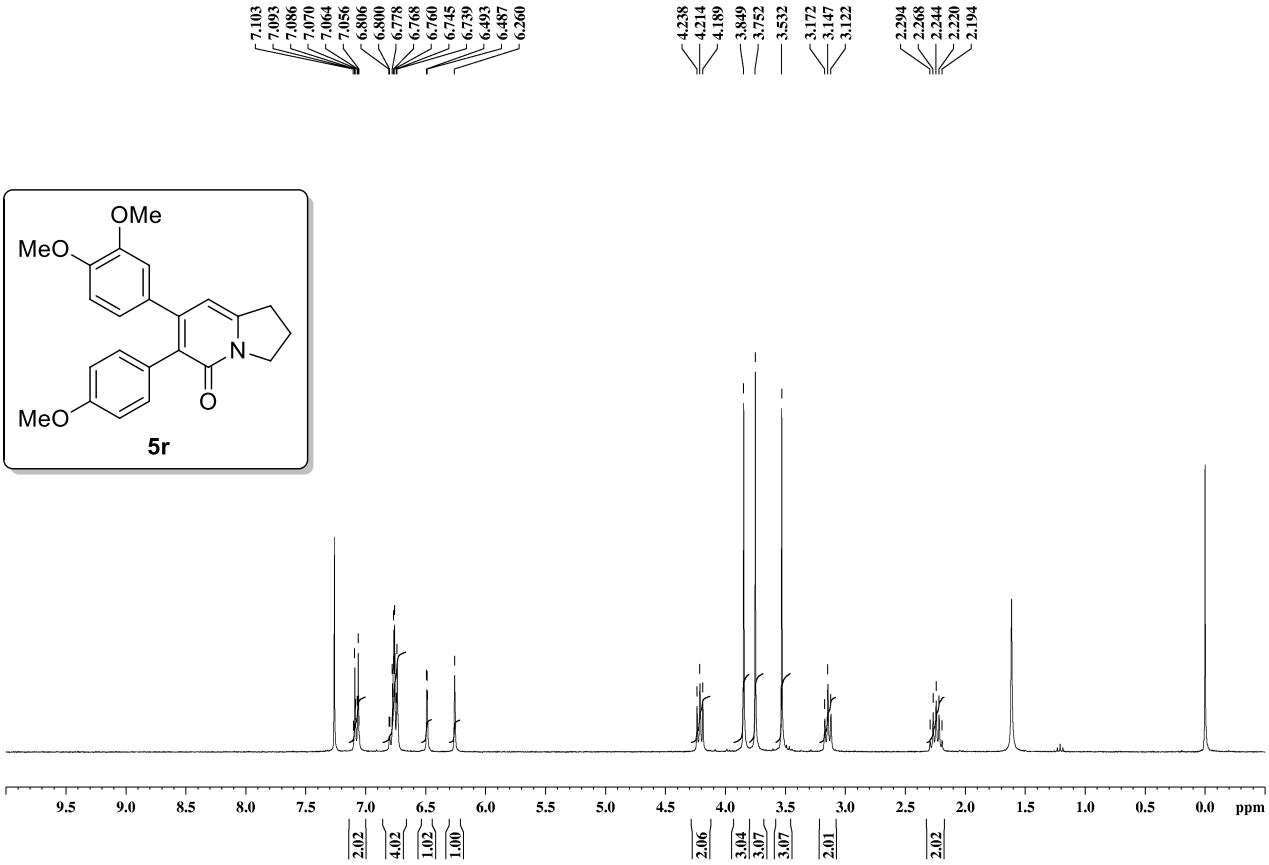
^{1}H NMR (300 MHz, $CDCl_3$); **5o**



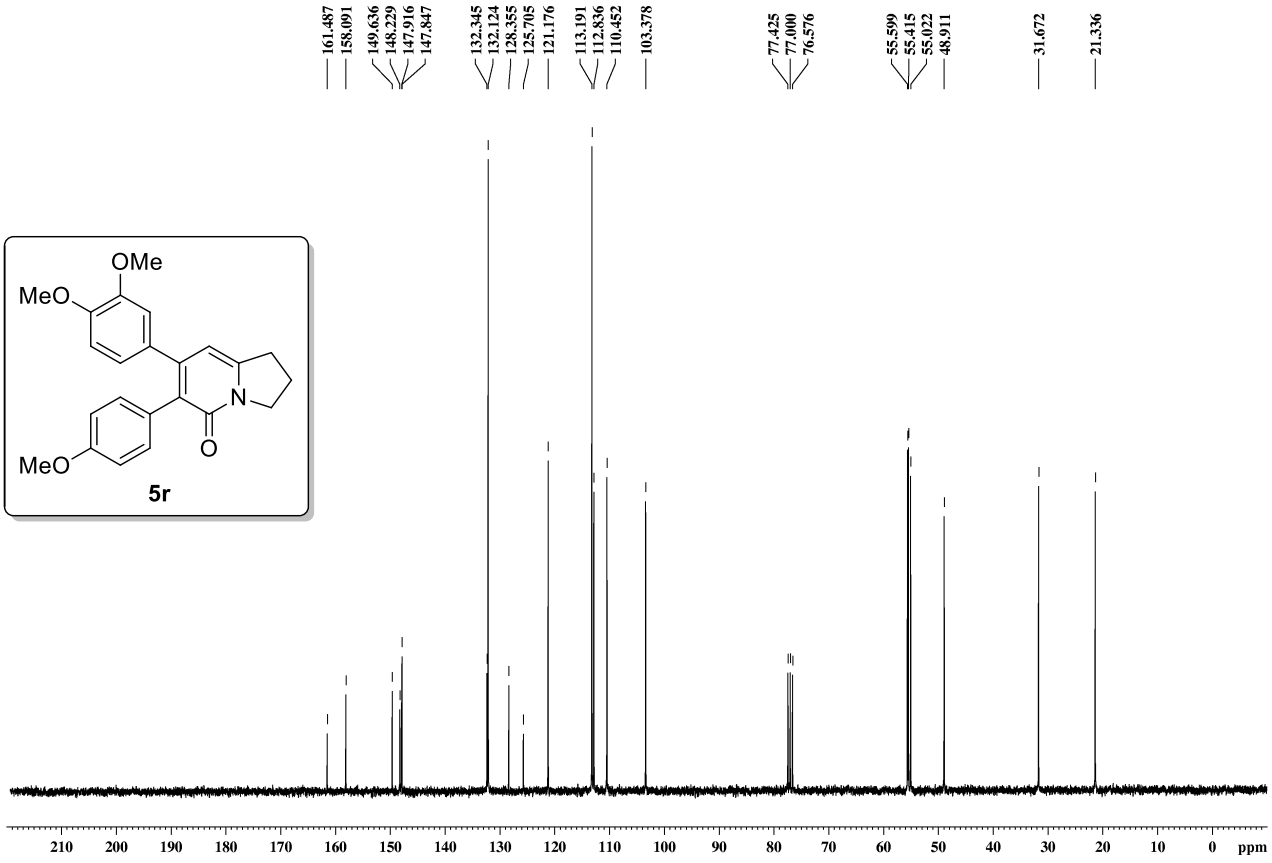
^{13}C NMR (75 MHz, $CDCl_3$); **5o**



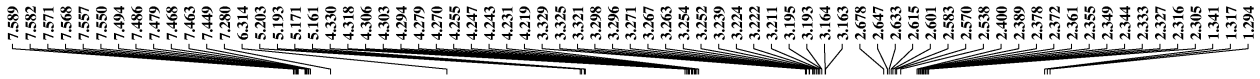
^{1}H NMR (300 MHz, $CDCl_3$); **5r**

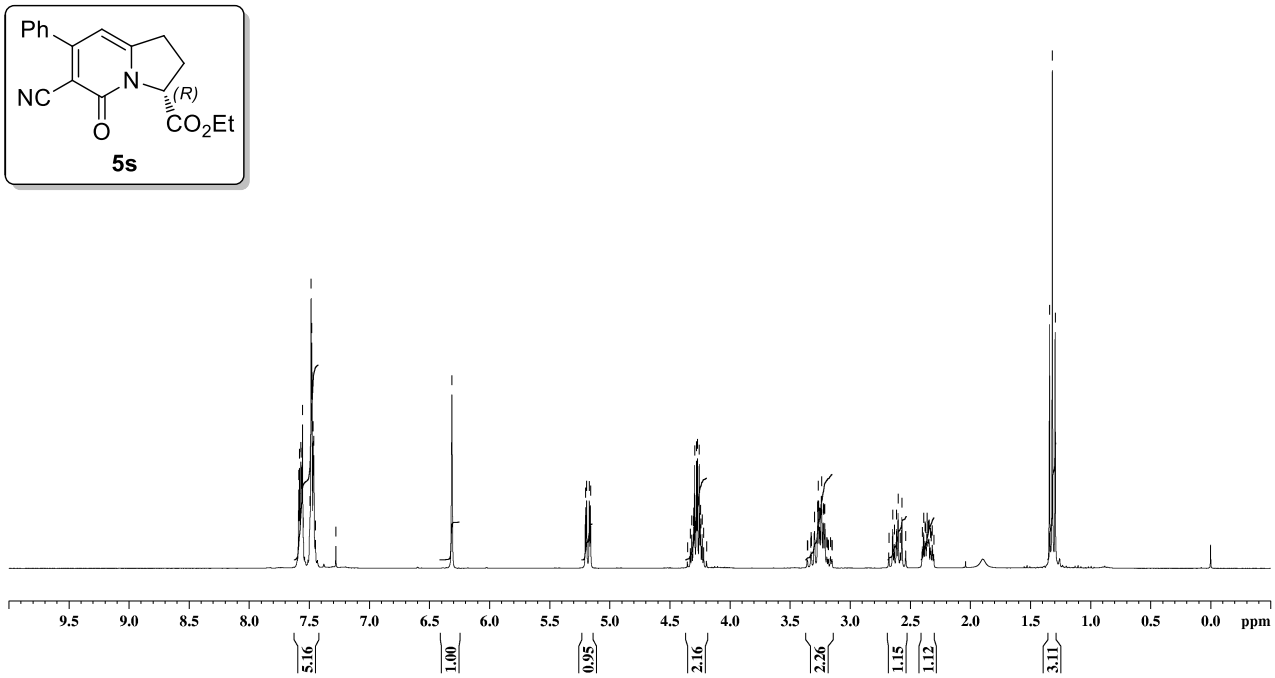


^{13}C NMR (75 MHz, $CDCl_3$); **5r**

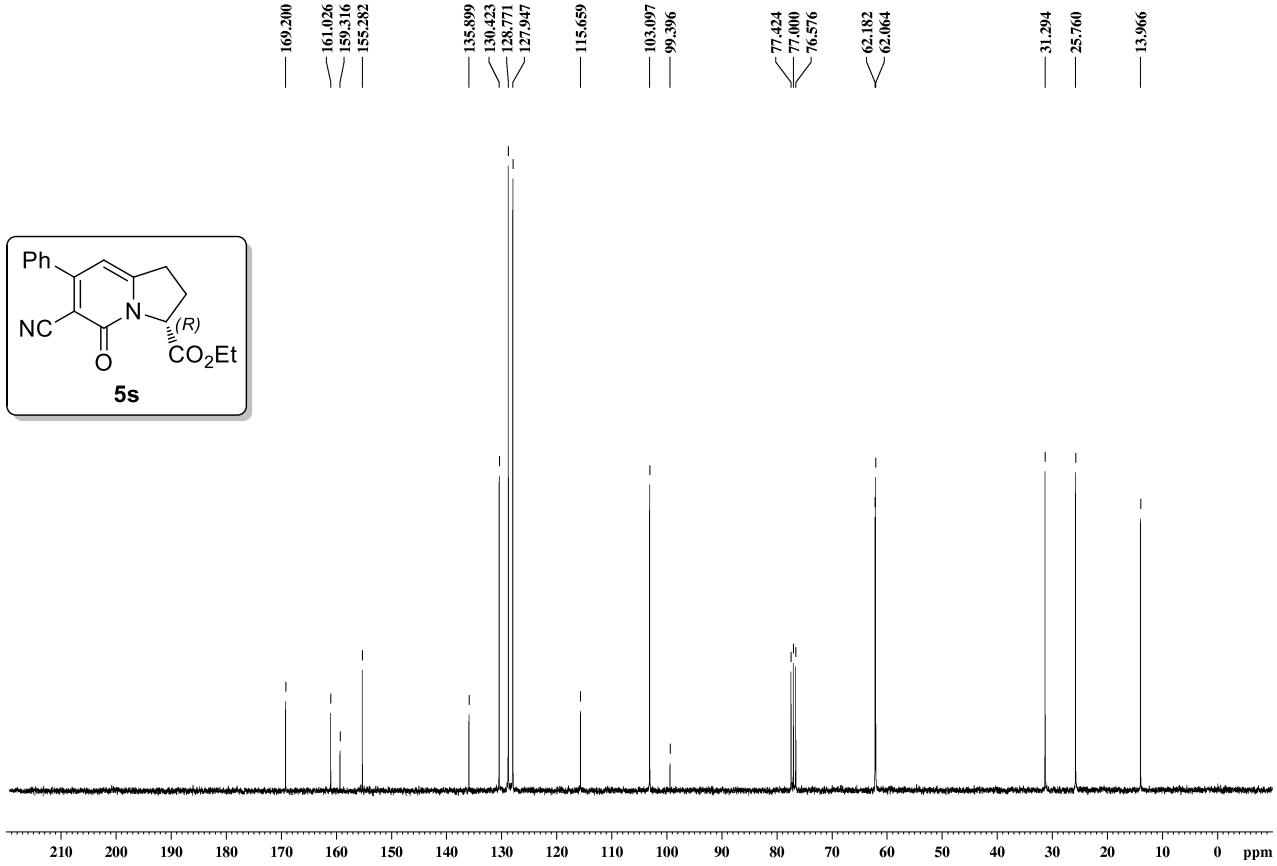


^{1}H NMR (300 MHz, $CDCl_3$); **5s**

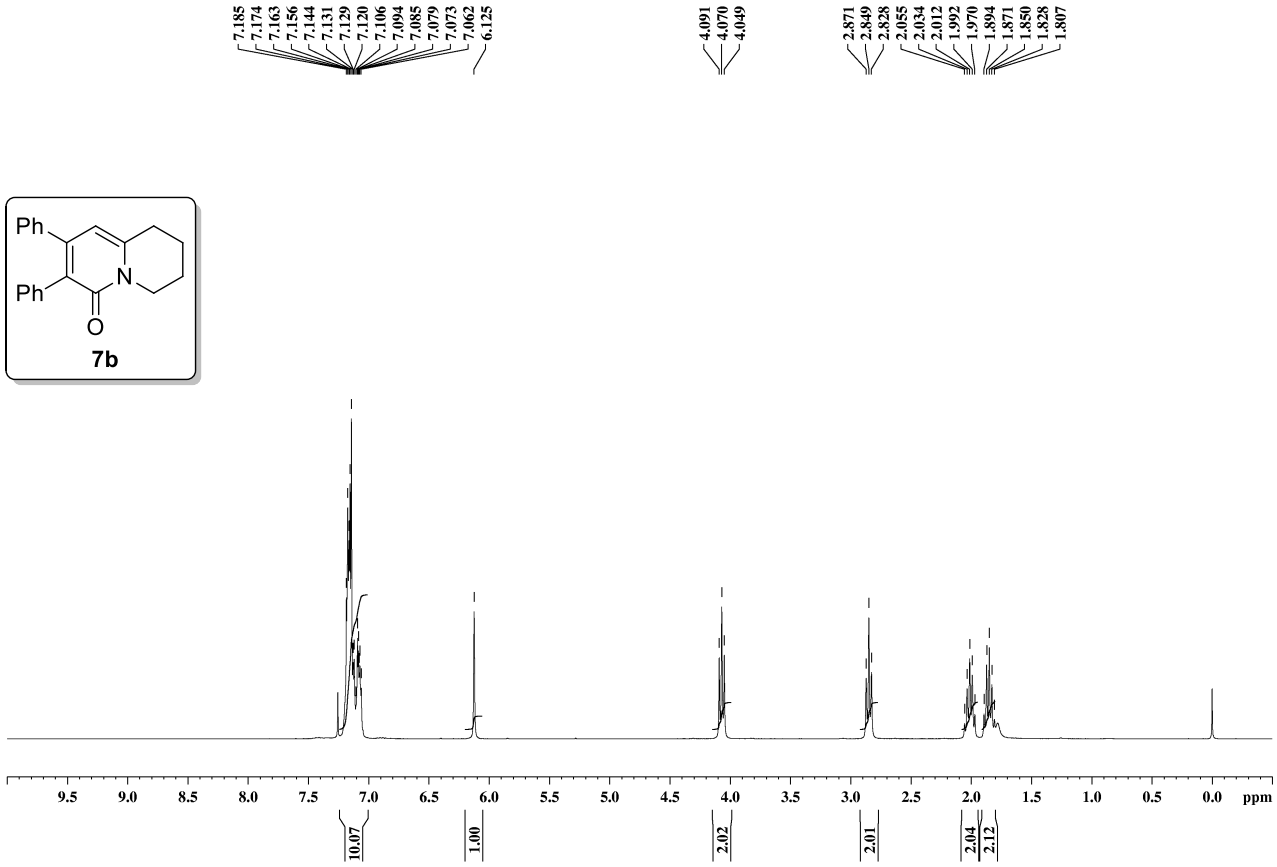




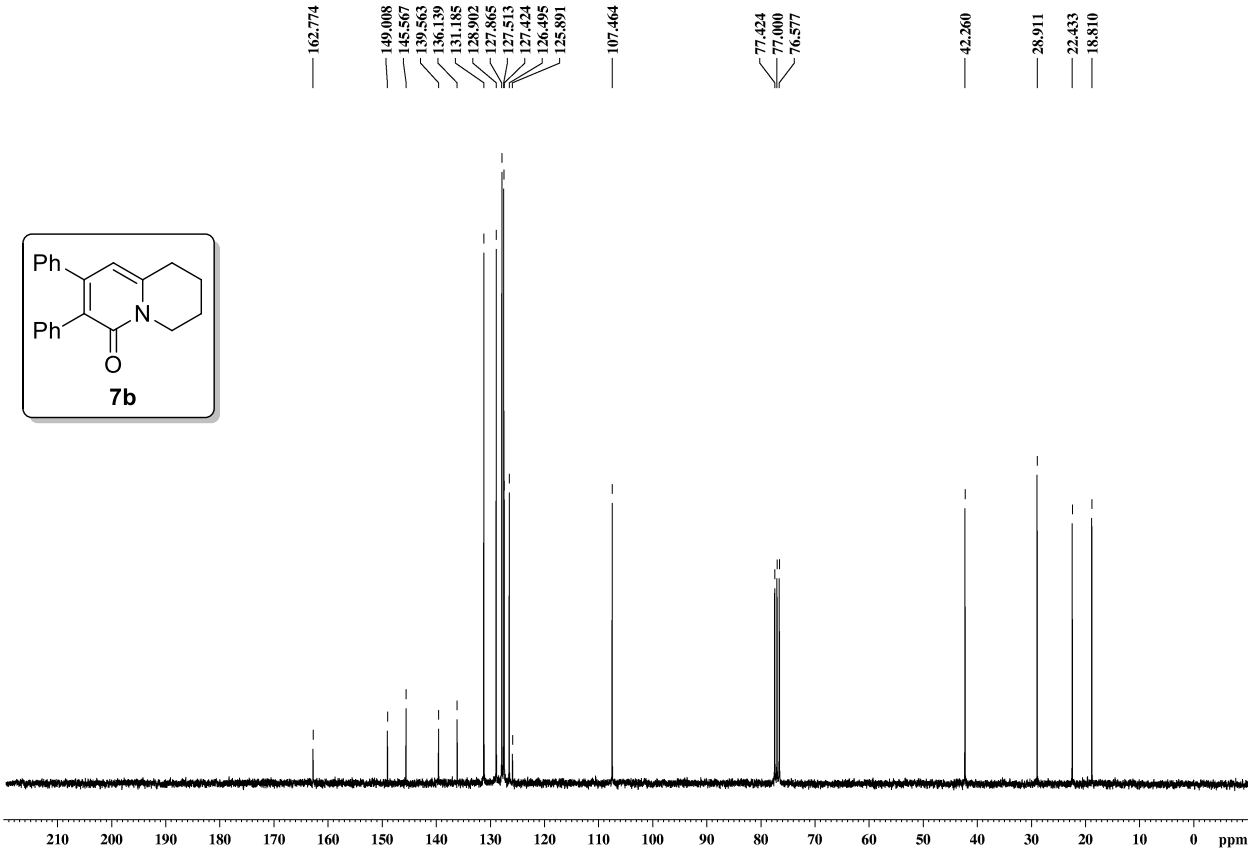
^{13}C NMR (75 MHz, $CDCl_3$); **5s**



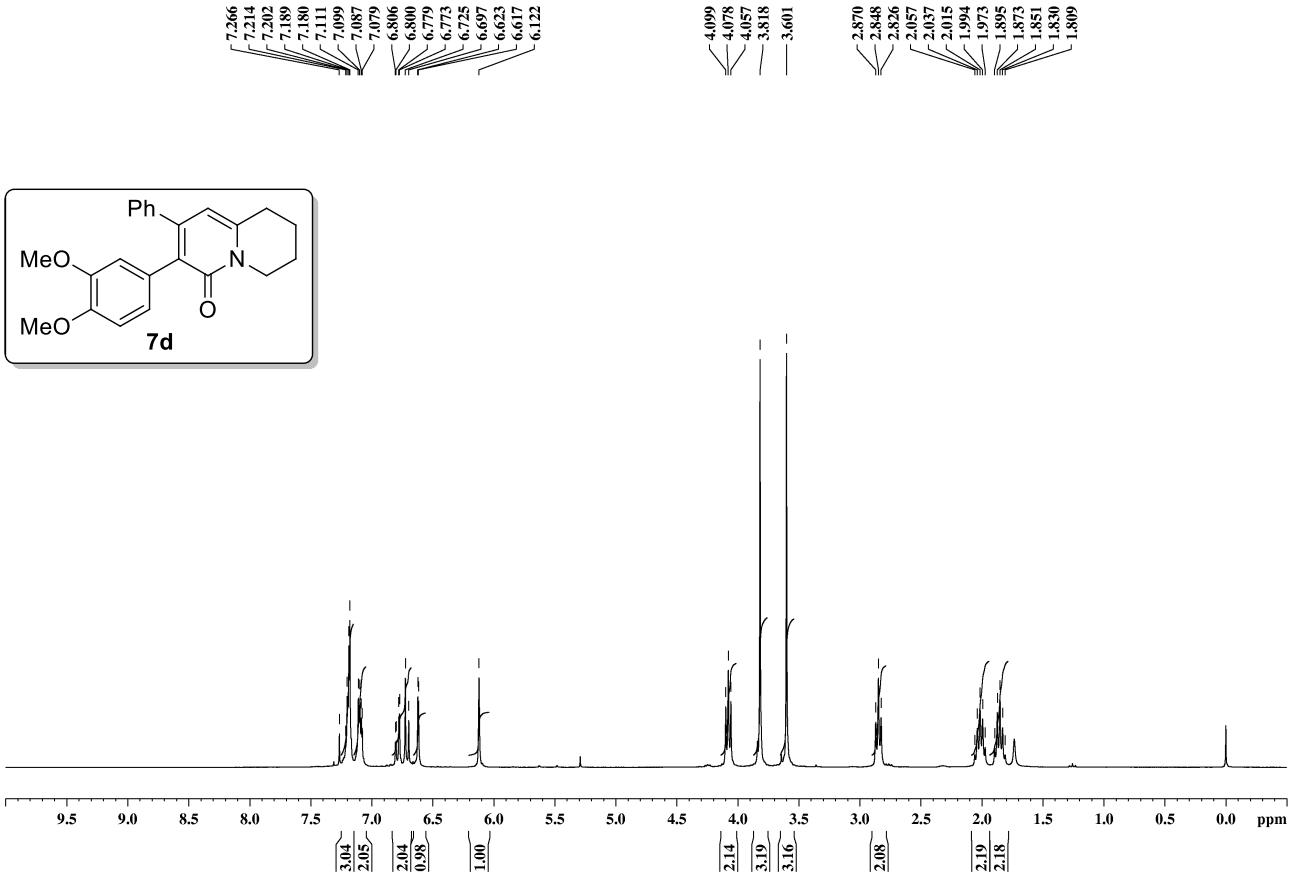
^{1}H NMR (300 MHz, $CDCl_3$); **7b**



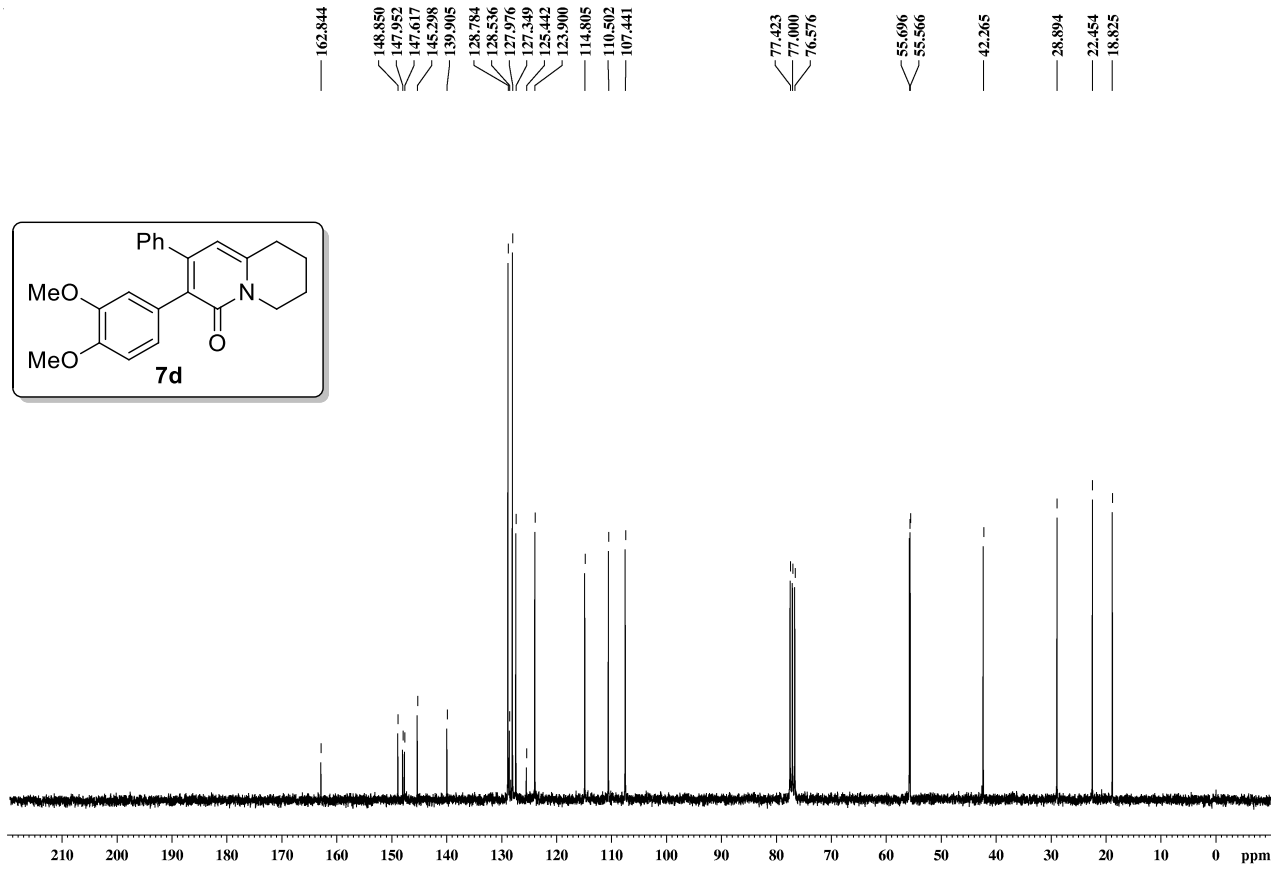
^{13}C NMR (75 MHz, $CDCl_3$); **7b**



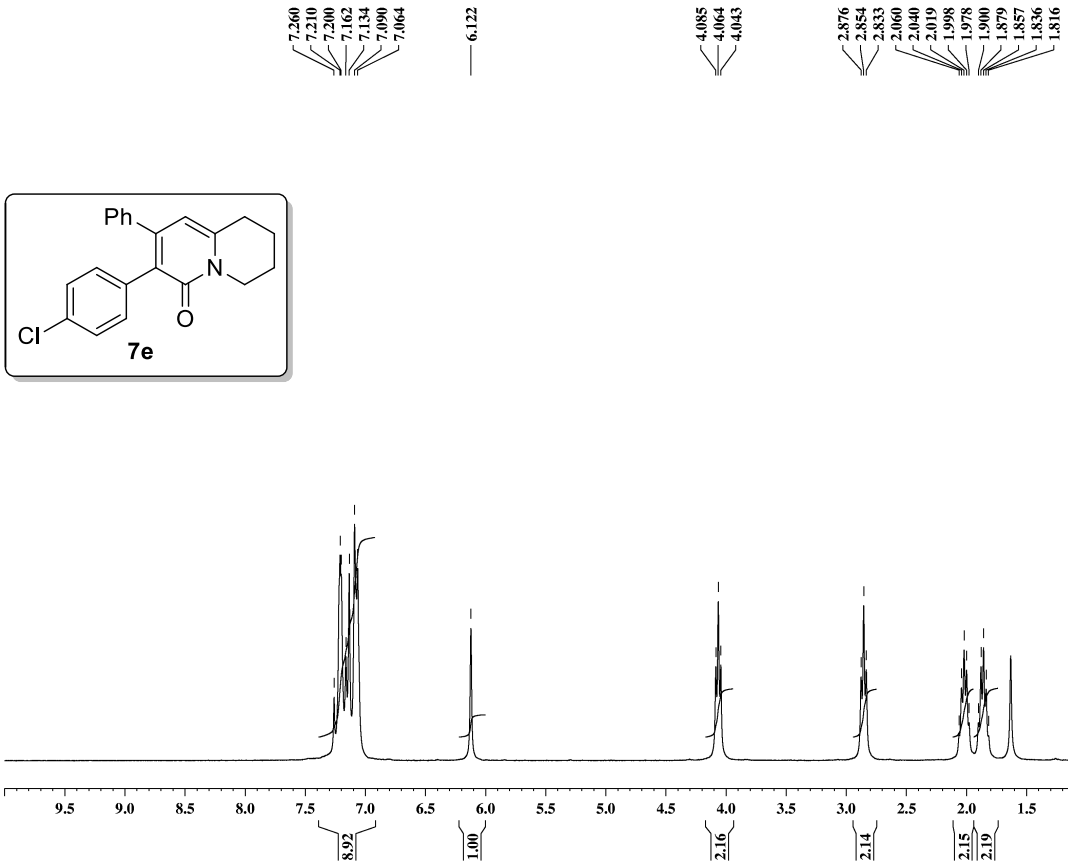
^{1}H NMR (300 MHz, $CDCl_3$); **7d**



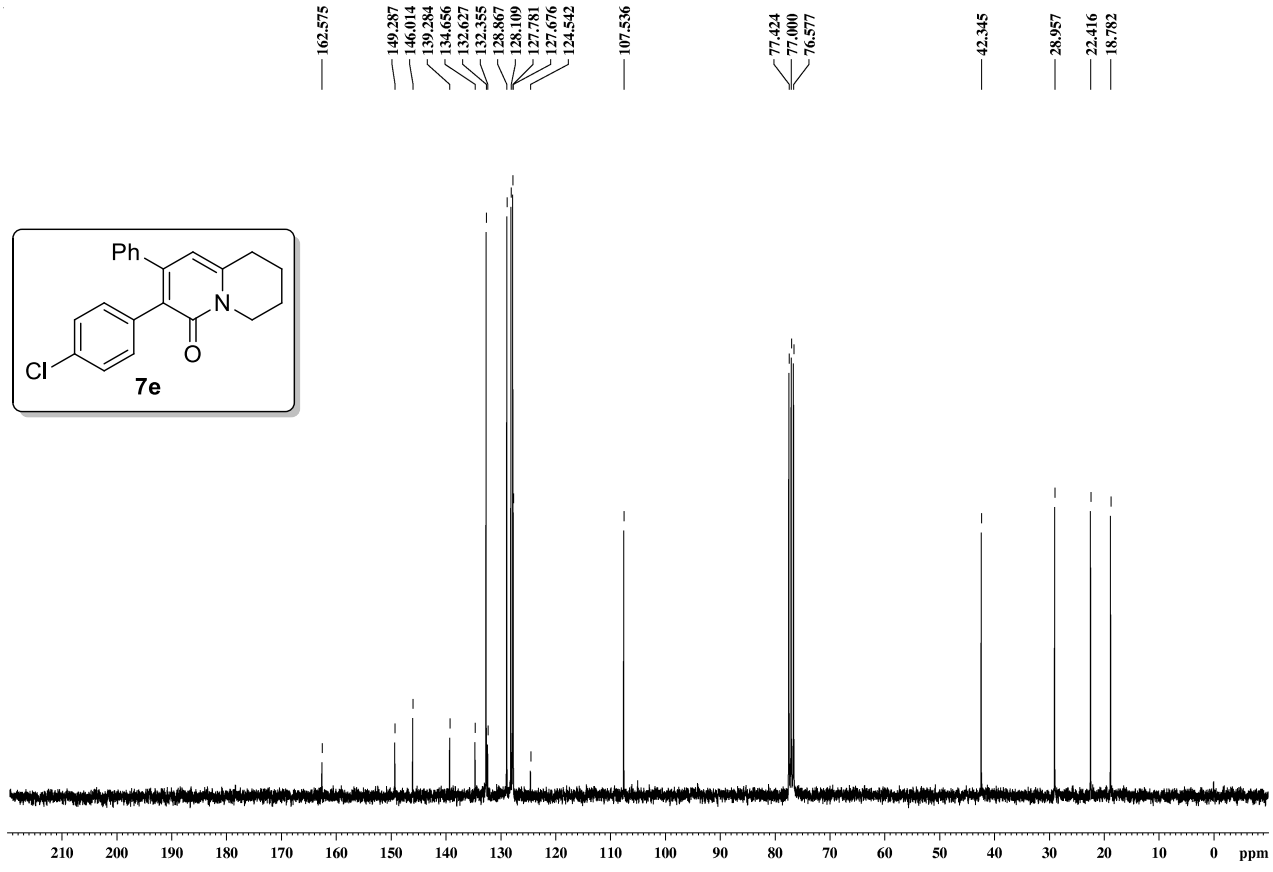
^{13}C NMR (75 MHz, $CDCl_3$); **7d**



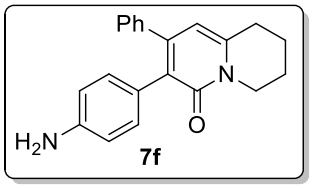
^{1}H NMR (300 MHz, $CDCl_3$); **7e**

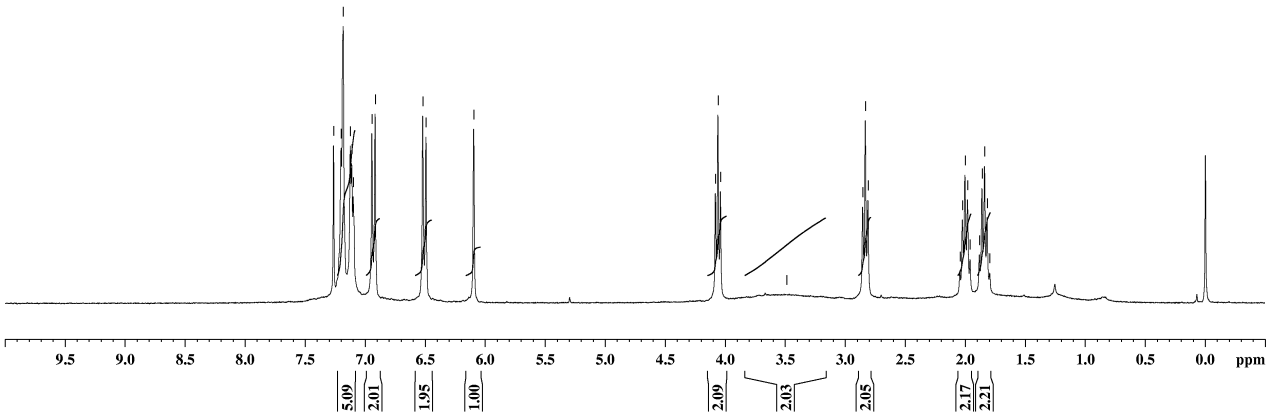


^{13}C NMR (75 MHz, $CDCl_3$); **7e**

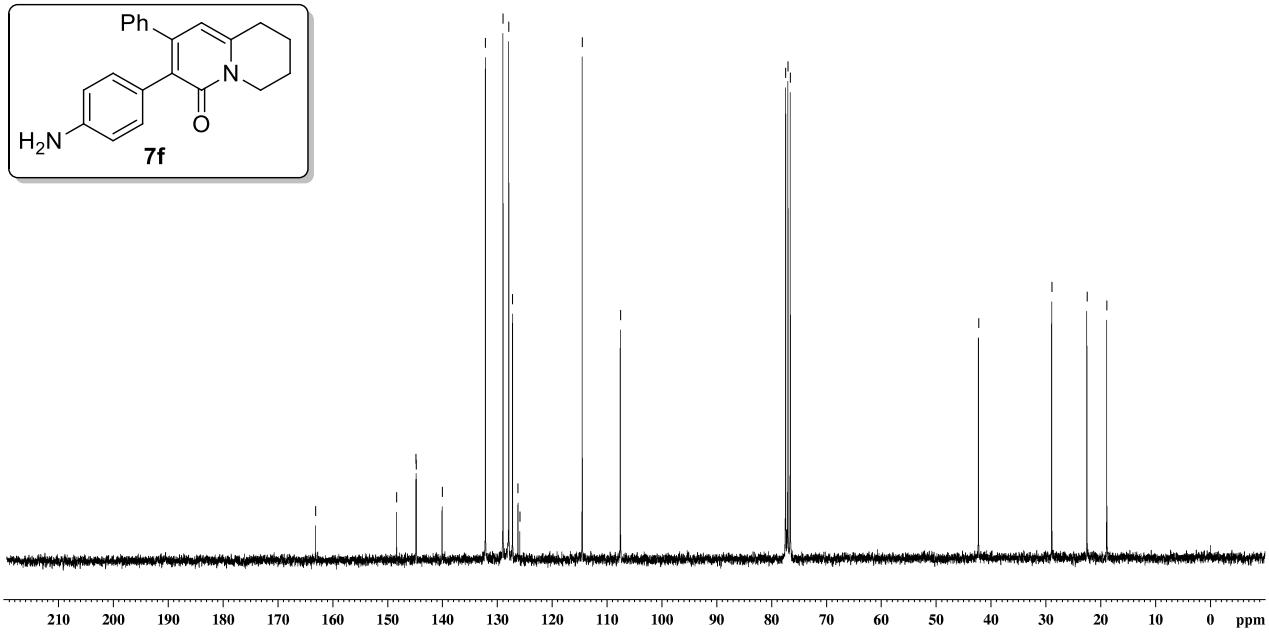


^{1}H NMR (300 MHz, $CDCl_3$); **7f**

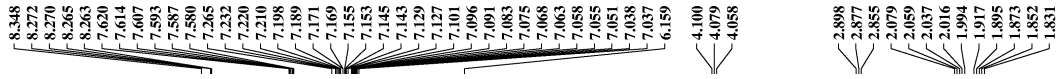


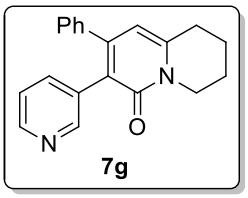


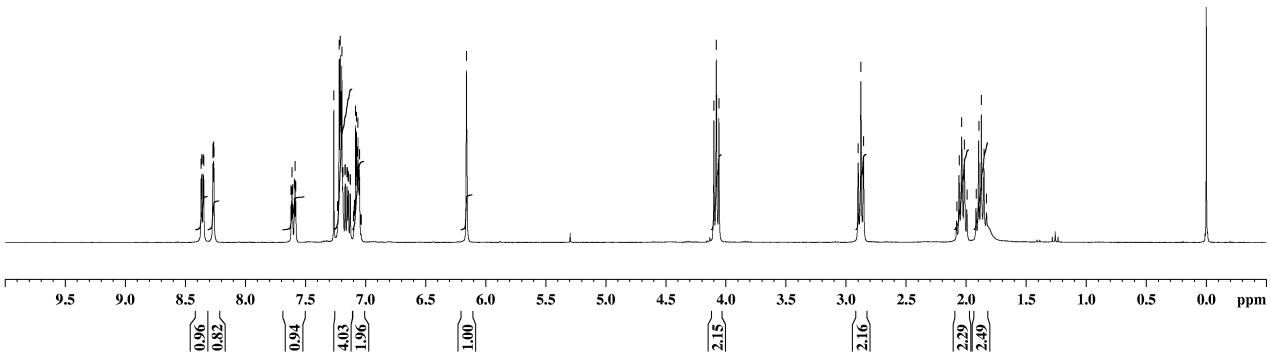
^{13}C NMR (75 MHz, $CDCl_3$); **7f**



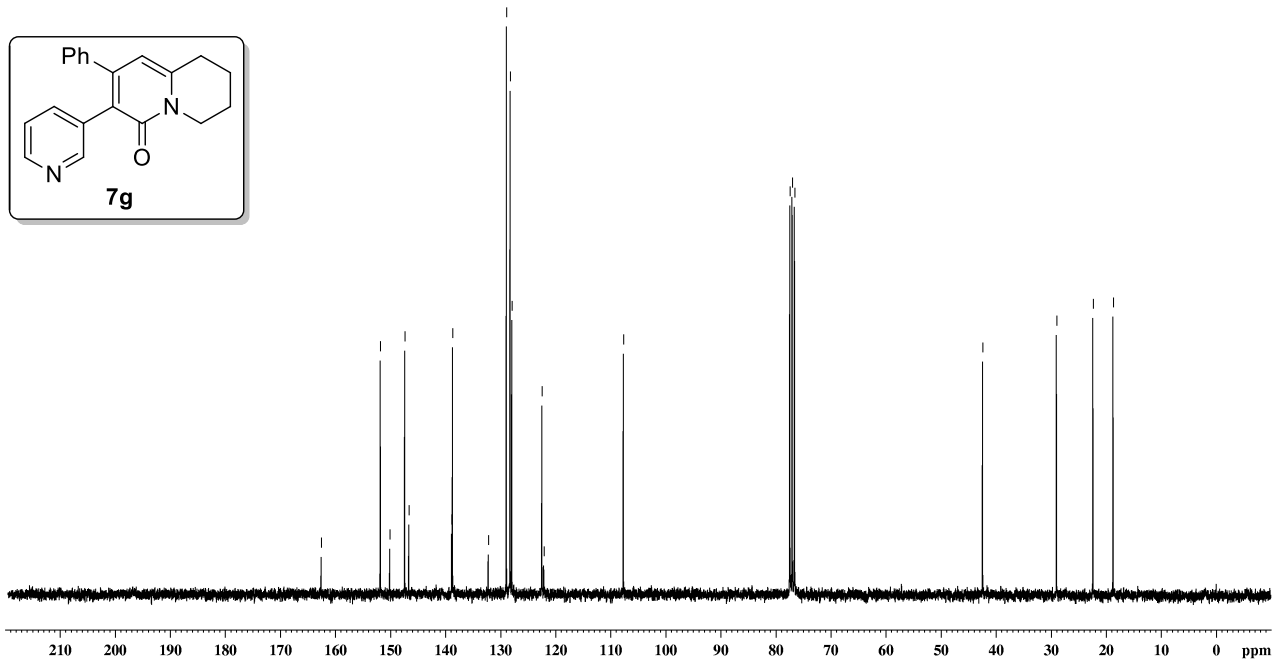
^{1}H NMR (300 MHz, $CDCl_3$); **7g**



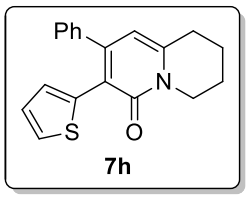




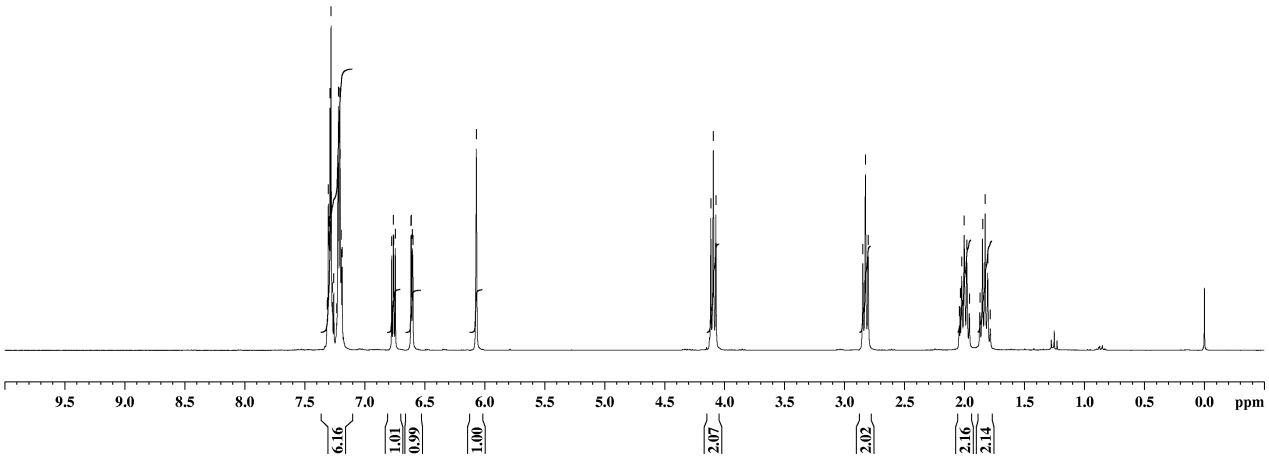
^{13}C NMR (75 MHz, $CDCl_3$); **7g**



^{1}H NMR (300 MHz, $CDCl_3$); **7h**

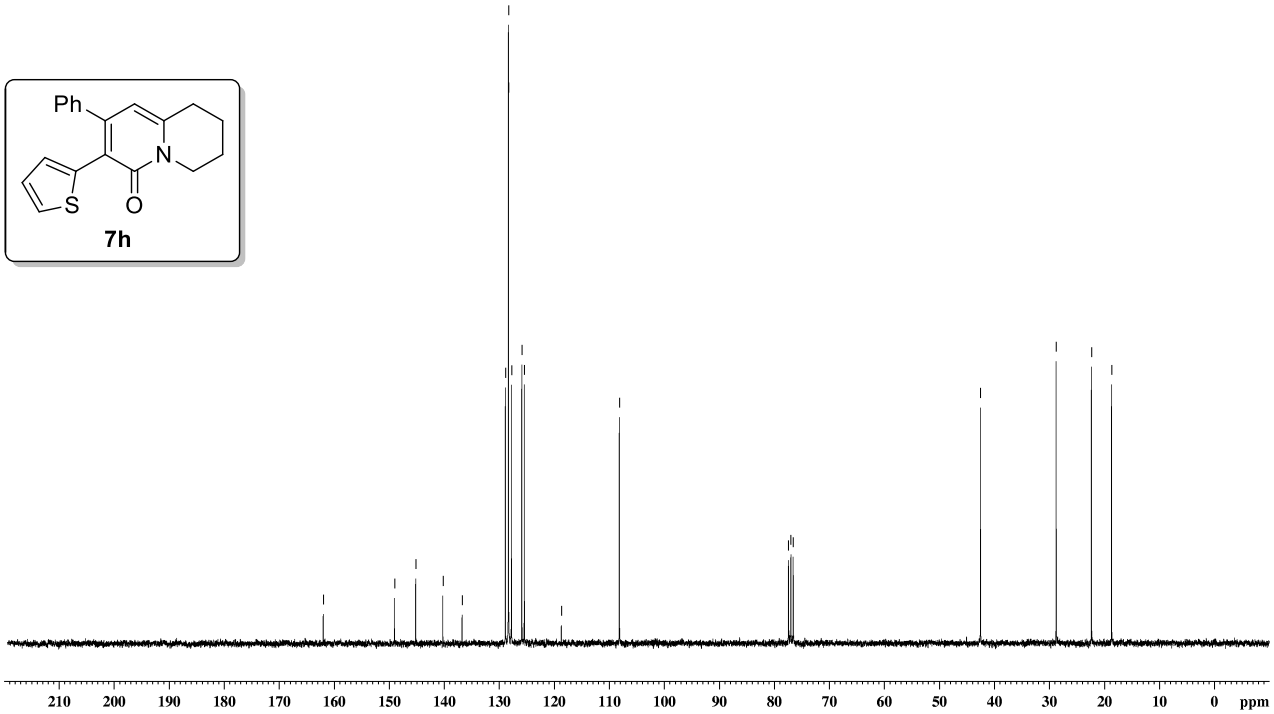


7h

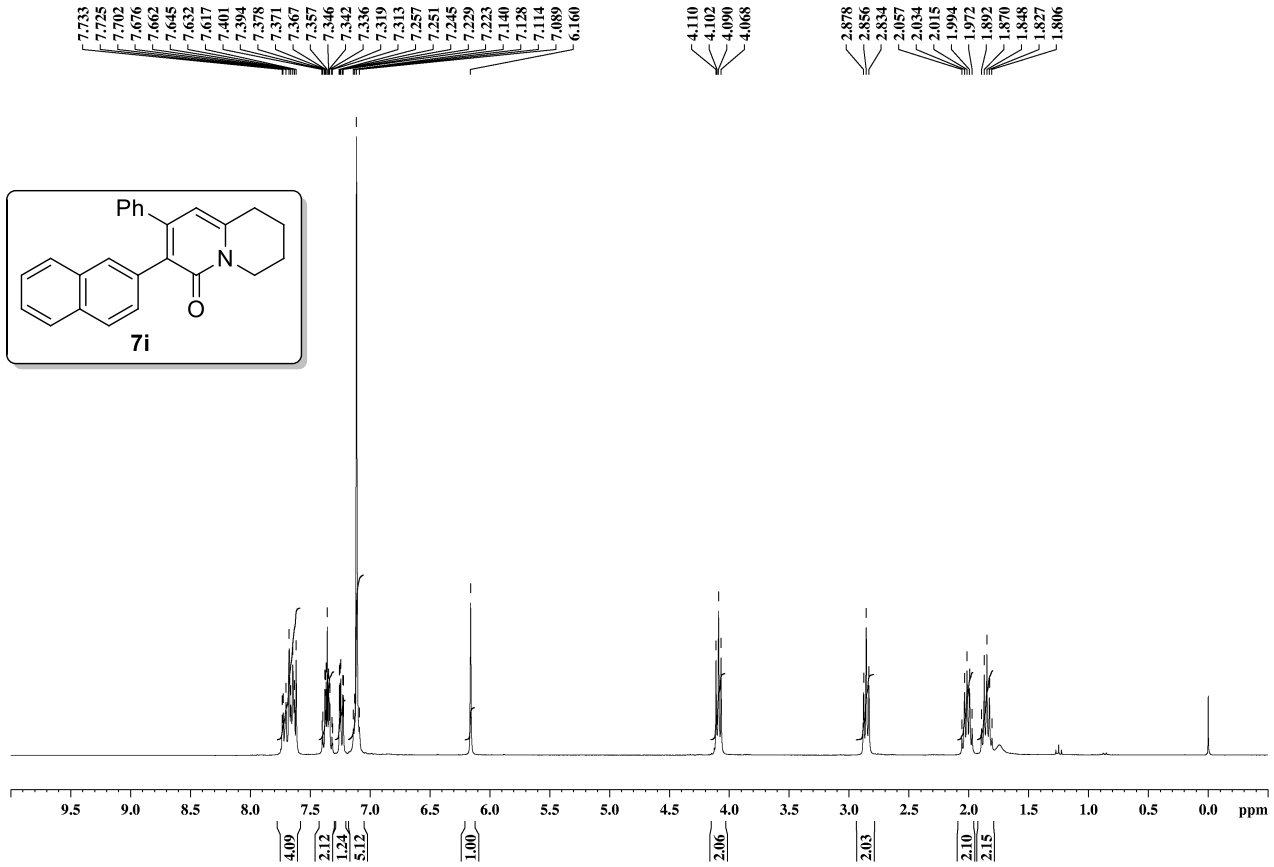


^{13}C NMR (75 MHz, $CDCl_3$); **7h**

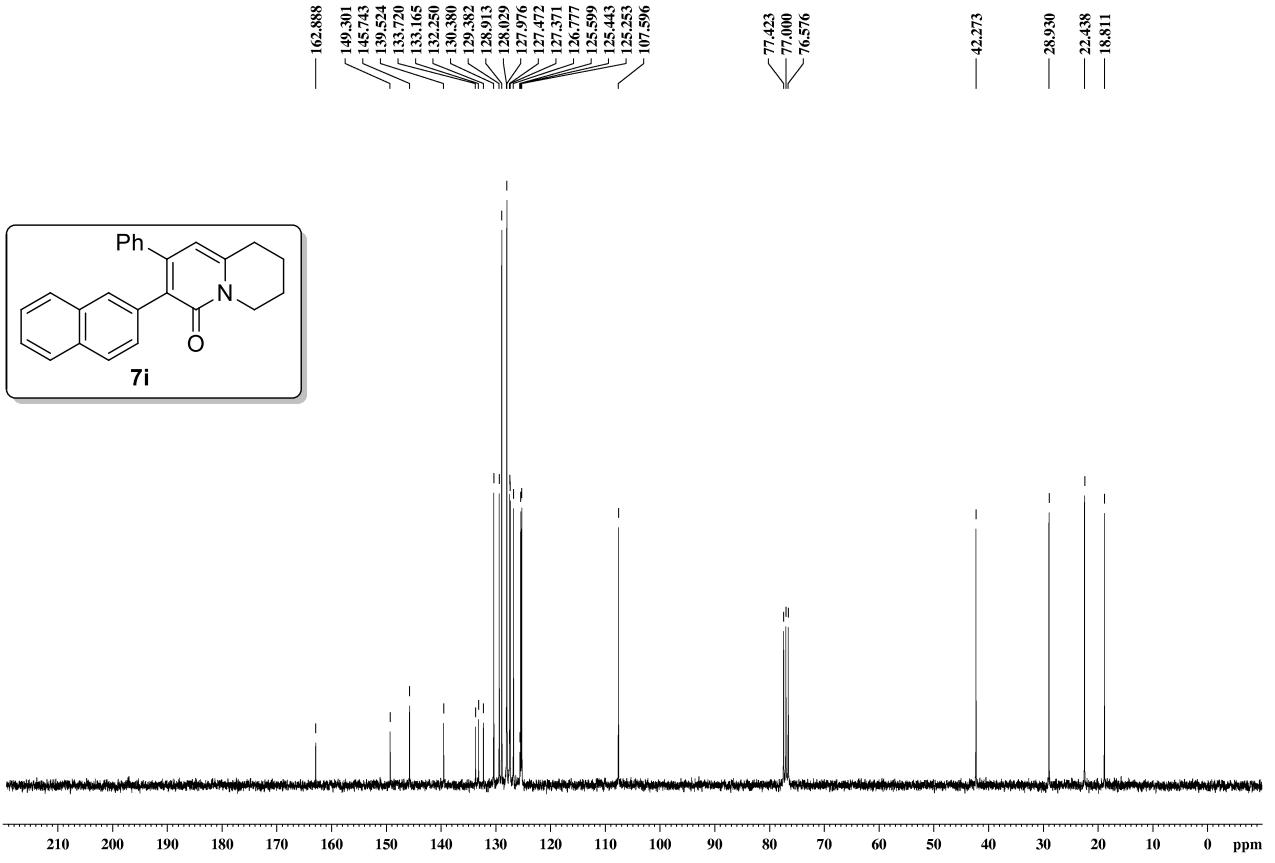
7h



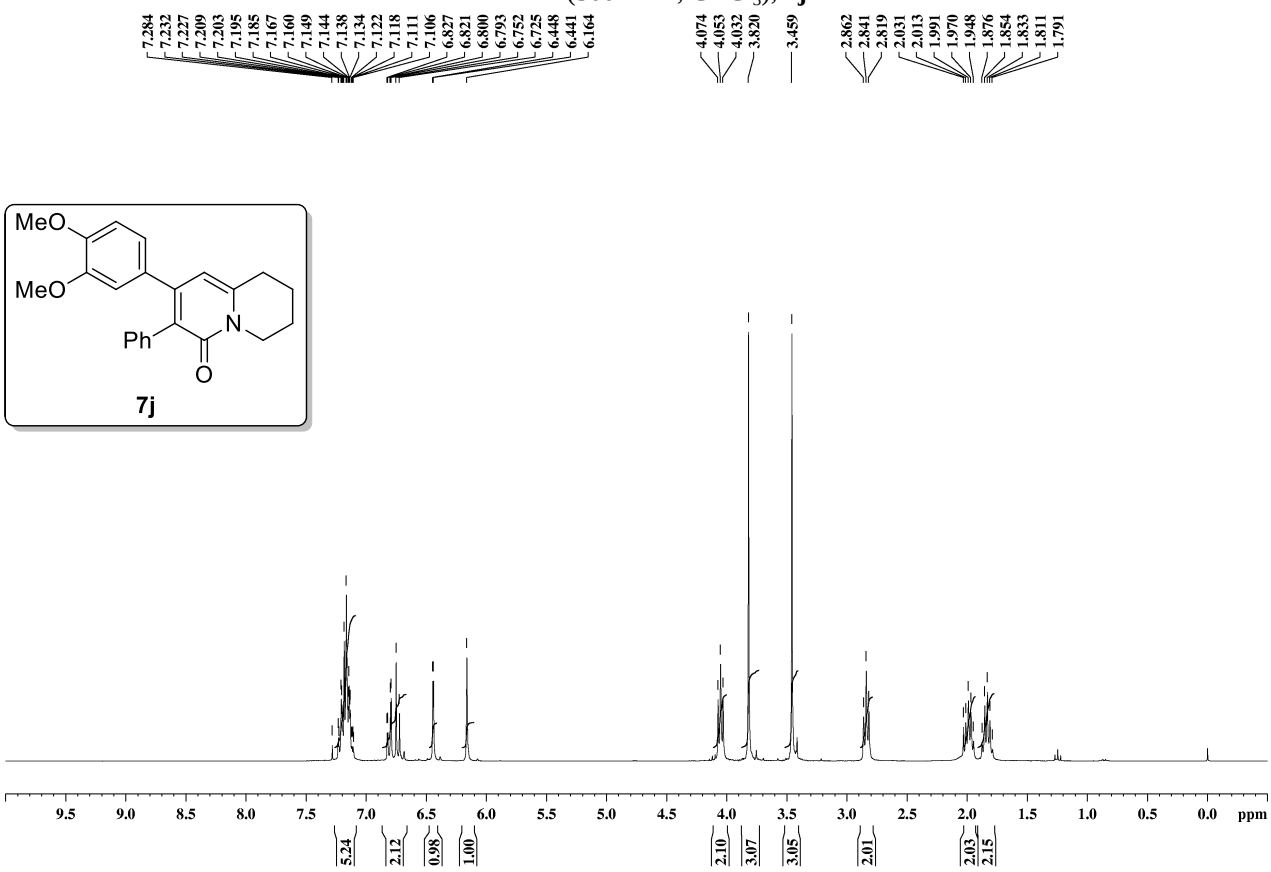
^{1}H NMR (300 MHz, $CDCl_3$); **7i**



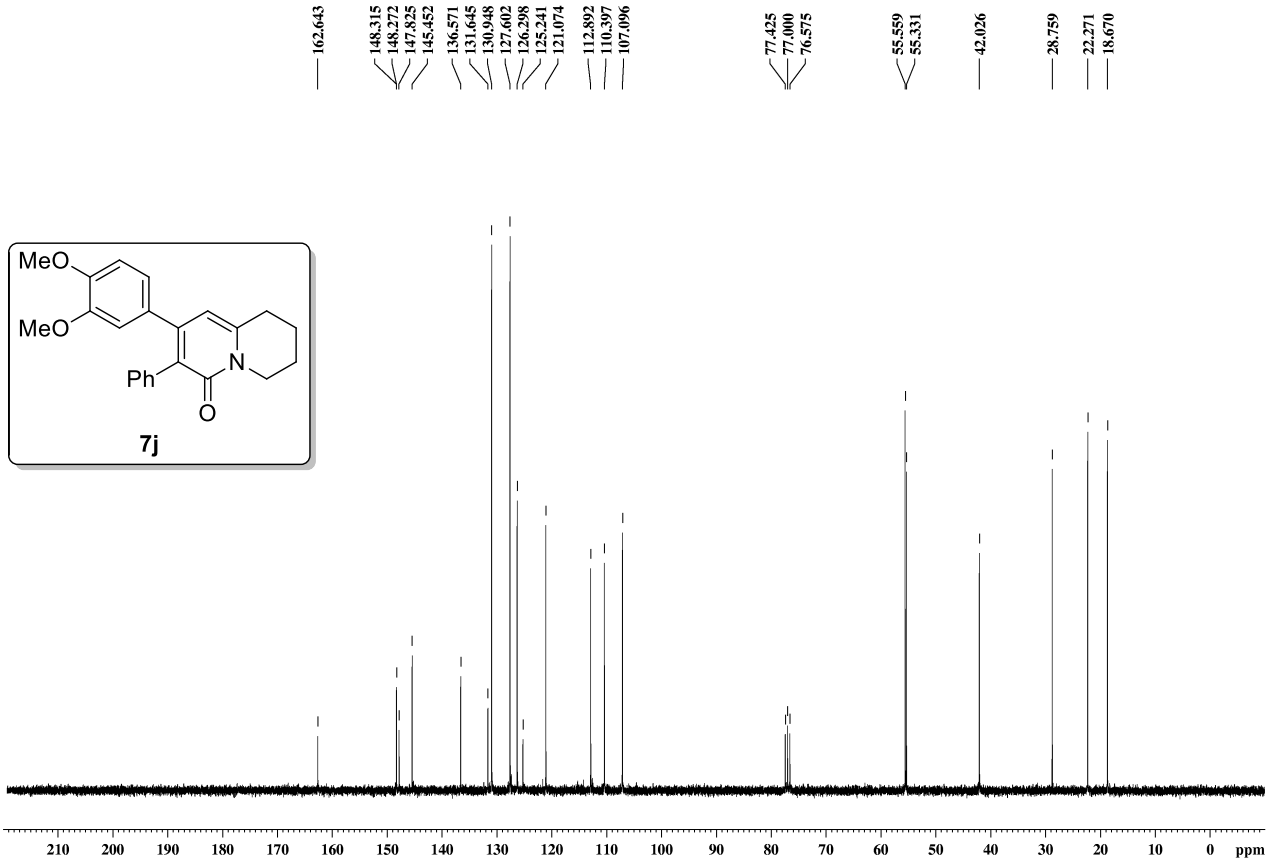
^{13}C NMR (75 MHz, $CDCl_3$); **7i**



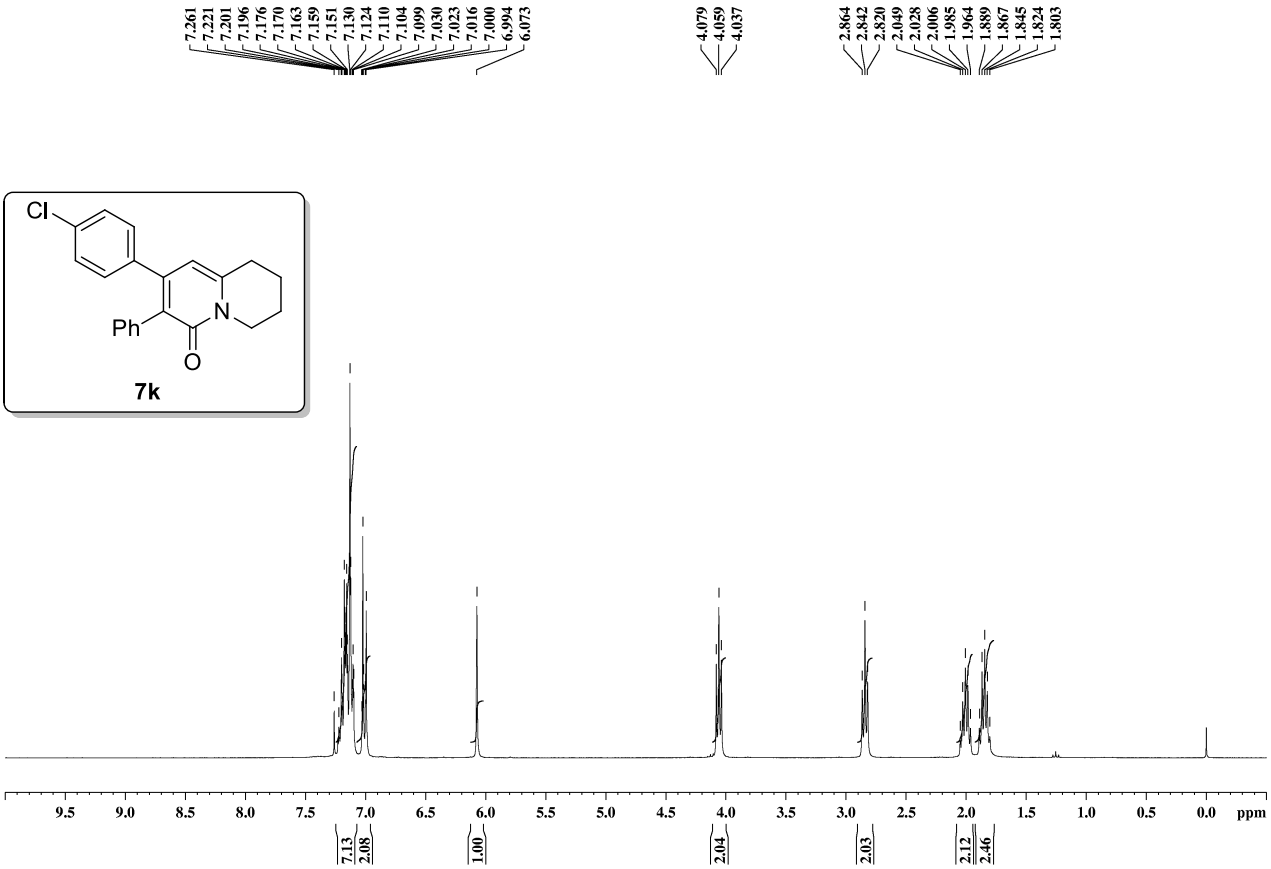
^{1}H NMR (300 MHz, $CDCl_3$); **7j**



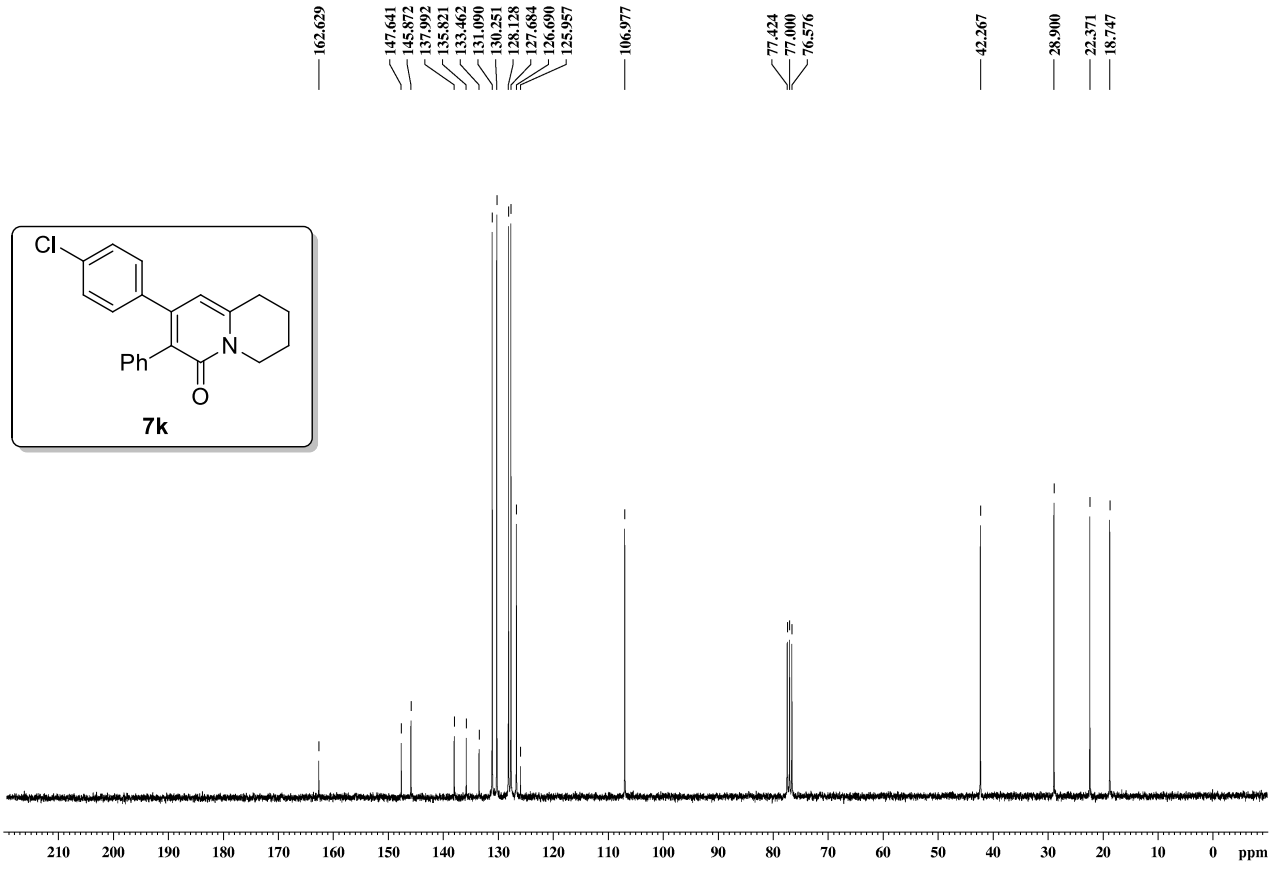
^{13}C NMR (75 MHz, $CDCl_3$); **7j**



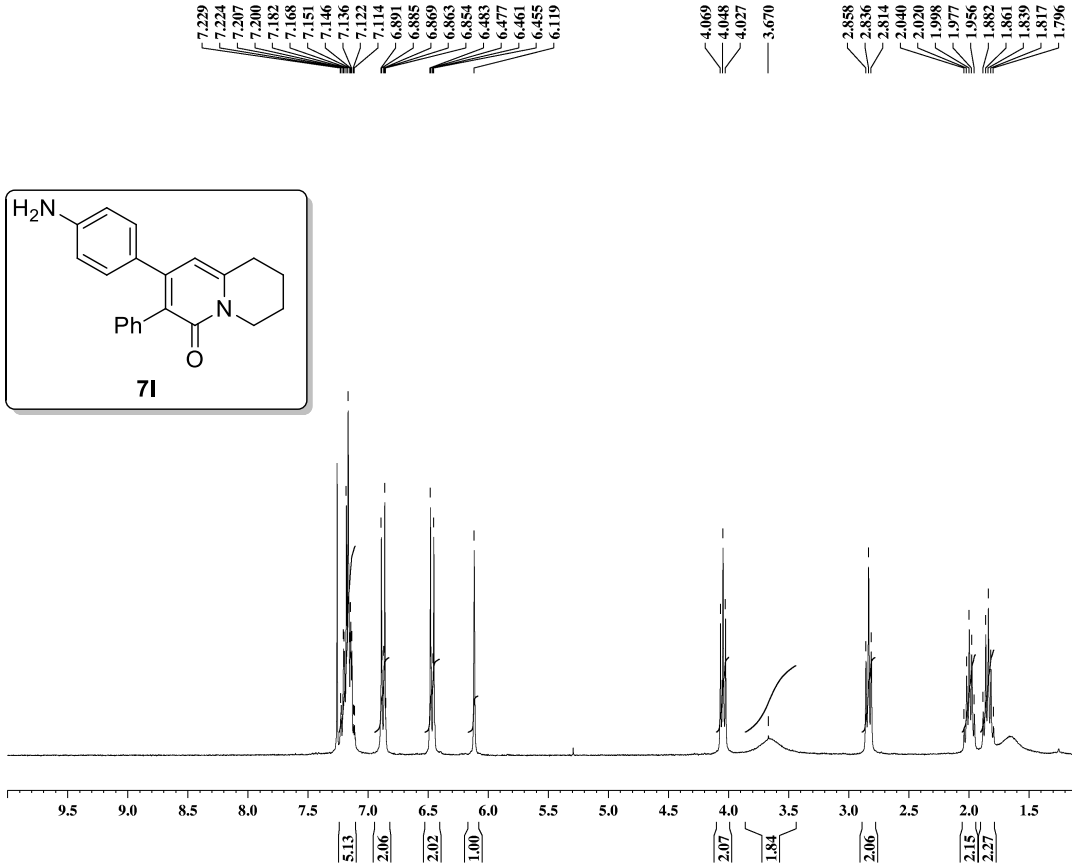
^{1}H NMR (300 MHz, $CDCl_3$); **7k**



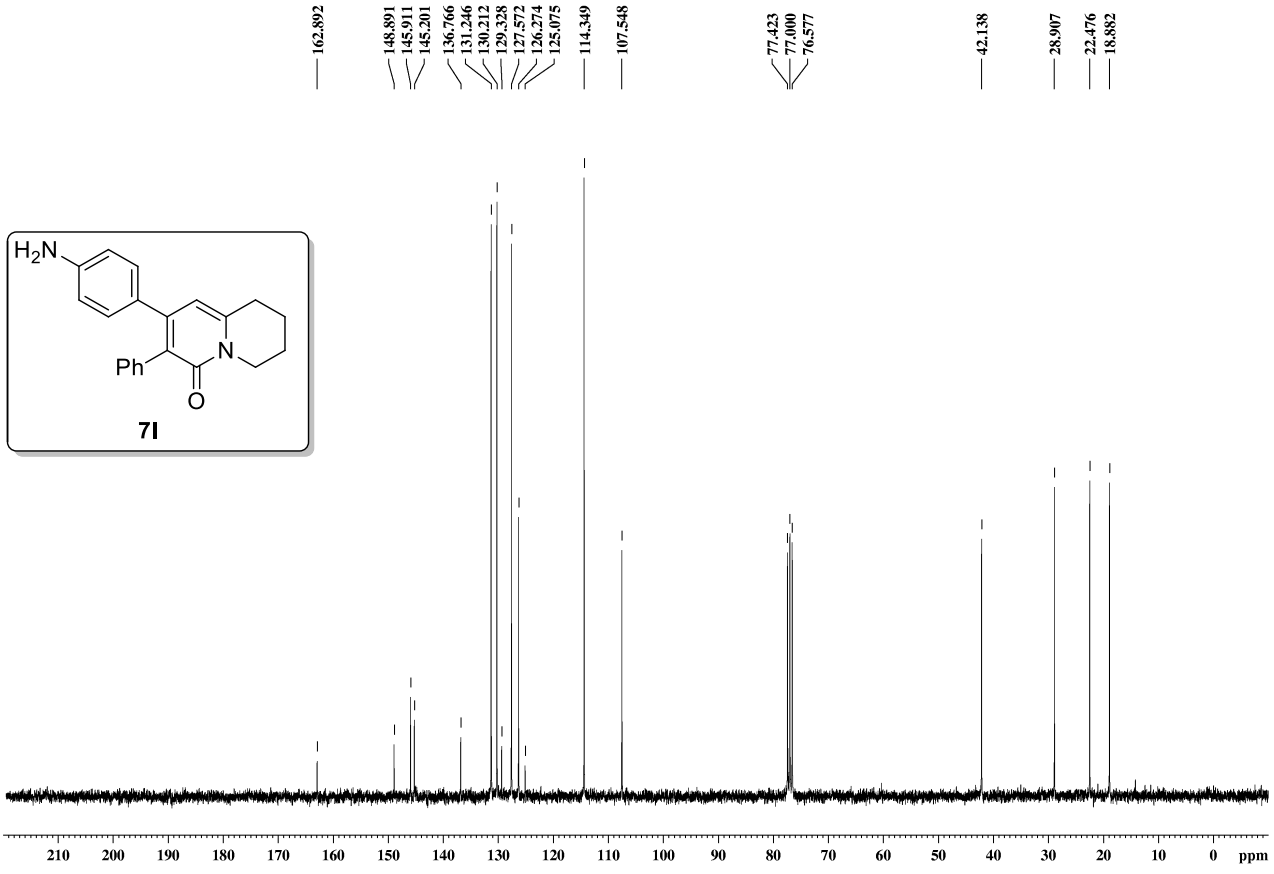
^{13}C NMR (75 MHz, $CDCl_3$); **7k**



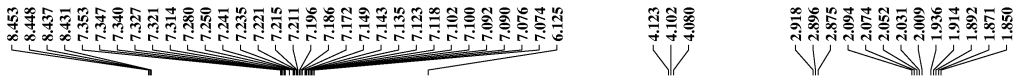
^{1}H NMR (300 MHz, $CDCl_3$); **7l**

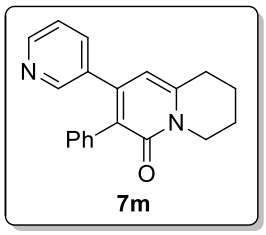


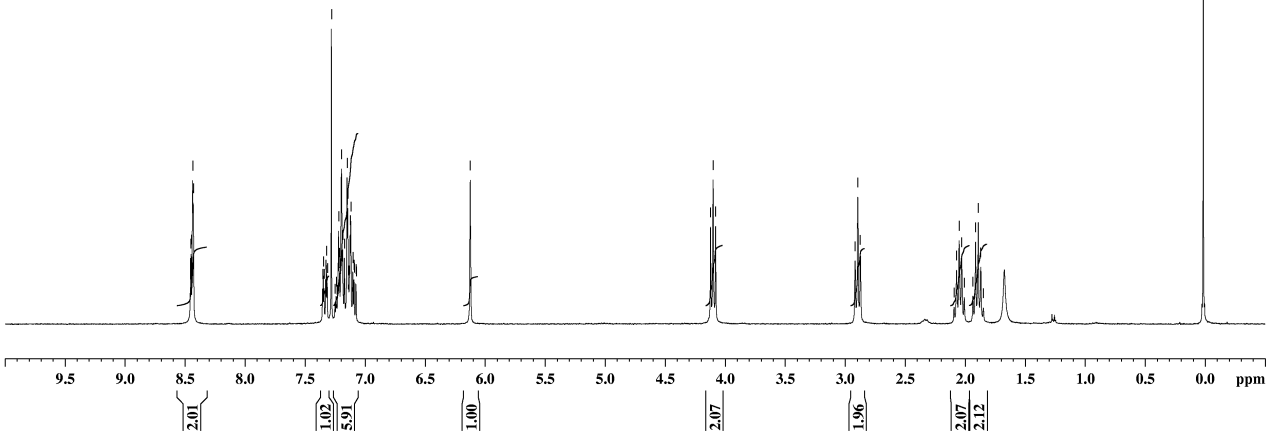
^{13}C NMR (75 MHz, $CDCl_3$); **7l**



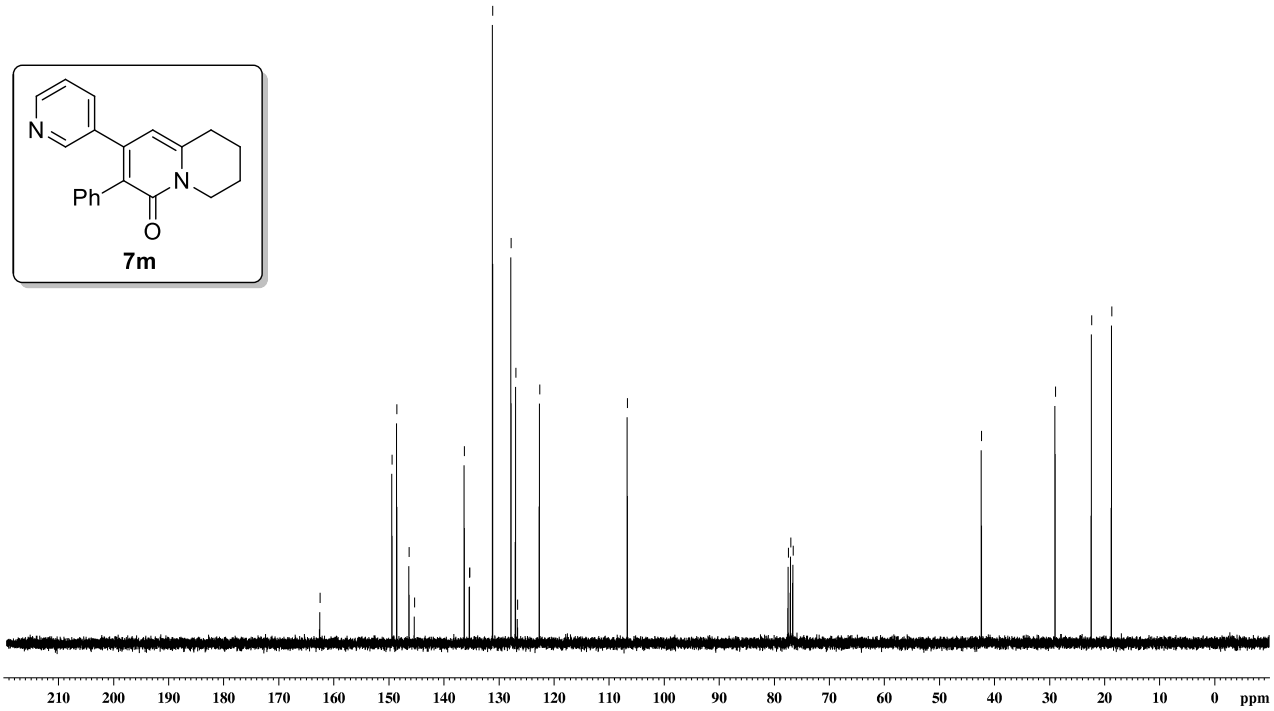
^{1}H NMR (300 MHz, $CDCl_3$); **7m**



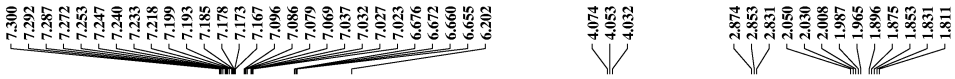


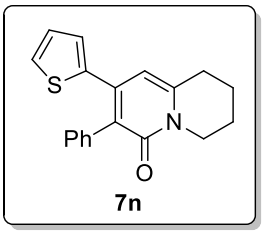


^{13}C NMR (75 MHz, $CDCl_3$); **7m**

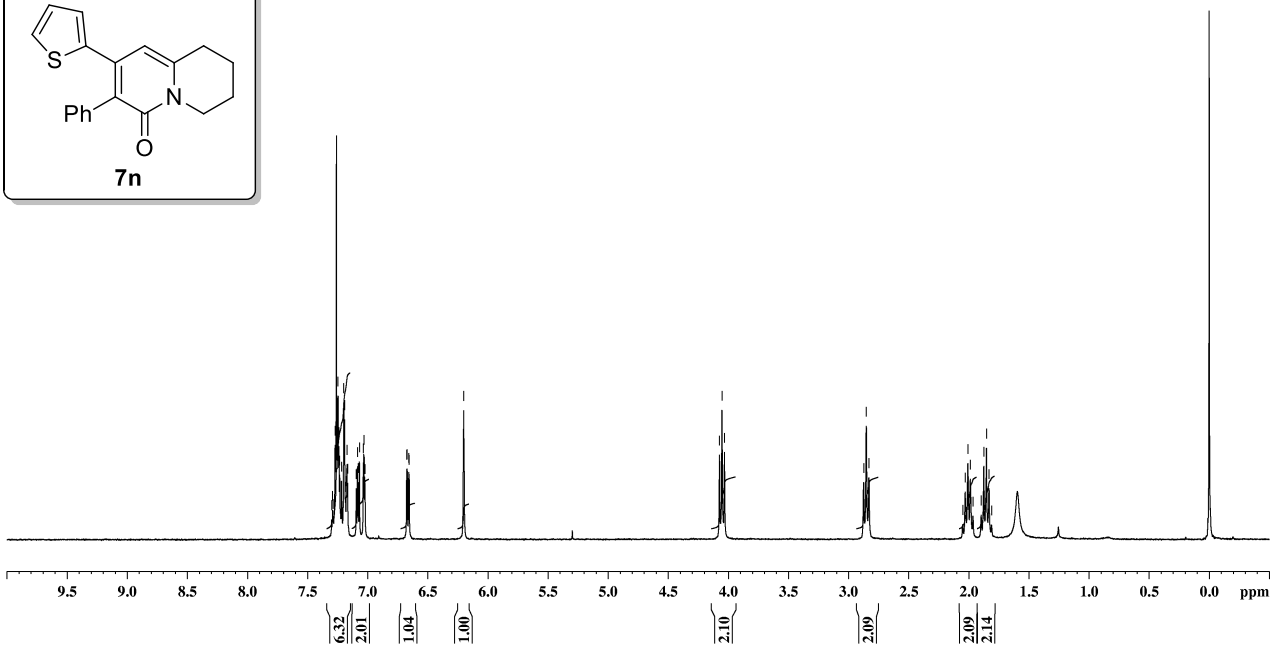


^{1}H NMR (300 MHz, $CDCl_3$); **7n**



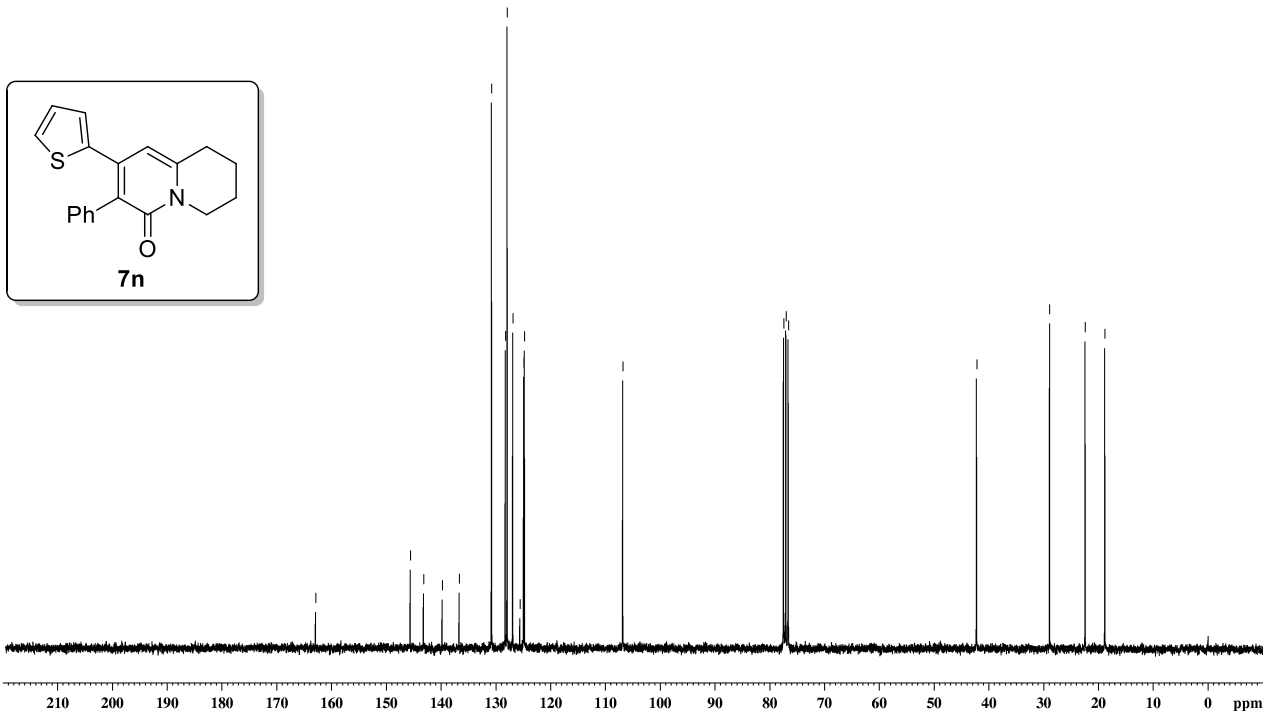


7n

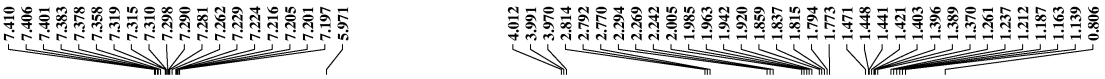


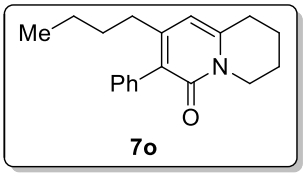
^{13}C NMR (75 MHz, $CDCl_3$); **7n**

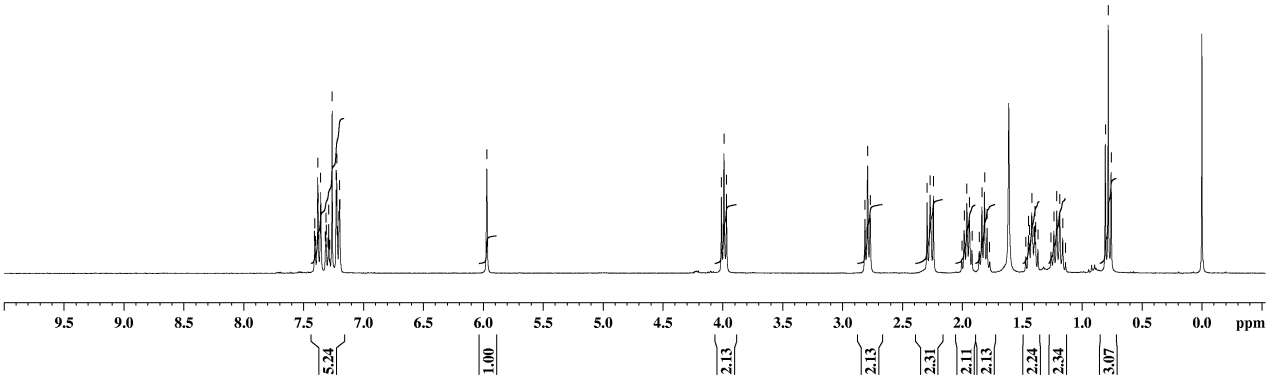
7n



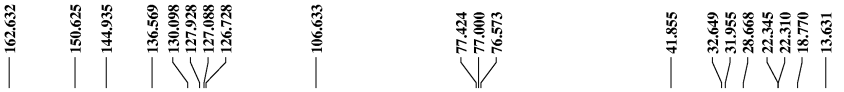
^{1}H NMR (300 MHz, $CDCl_3$); **7o**

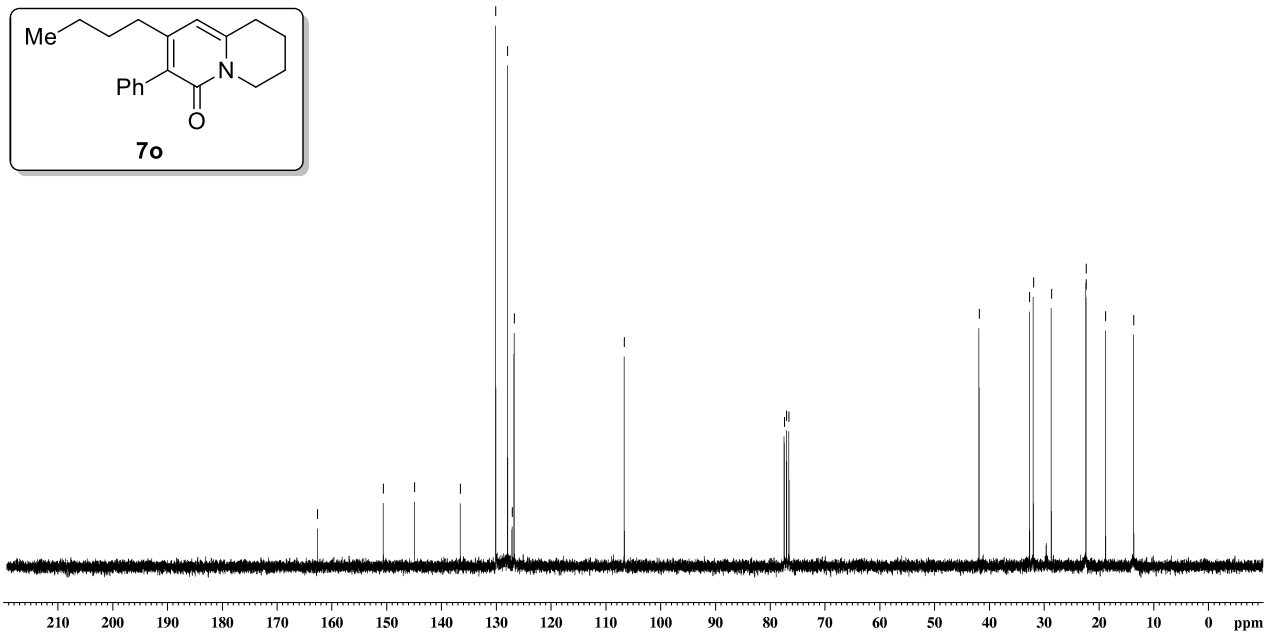




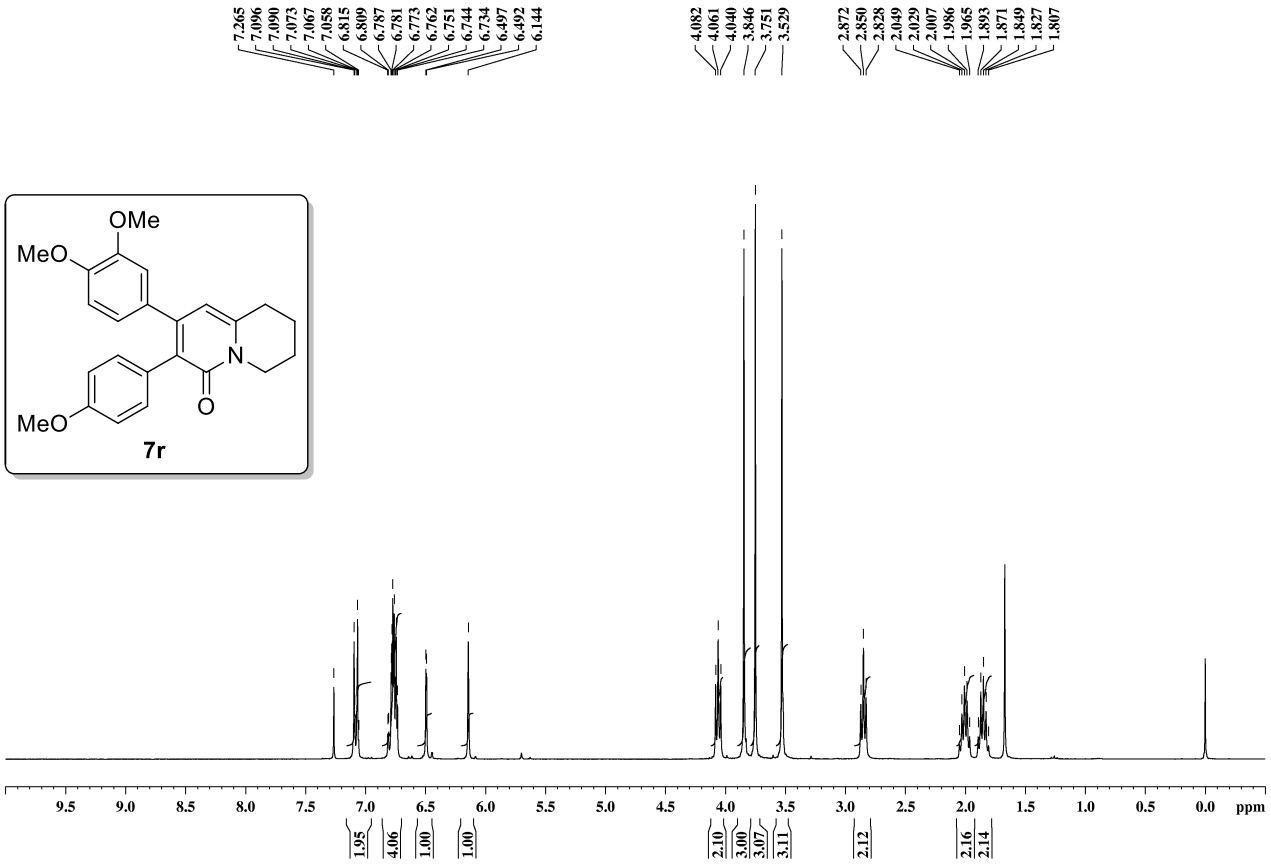


^{13}C NMR (75 MHz, $CDCl_3$); **7o**

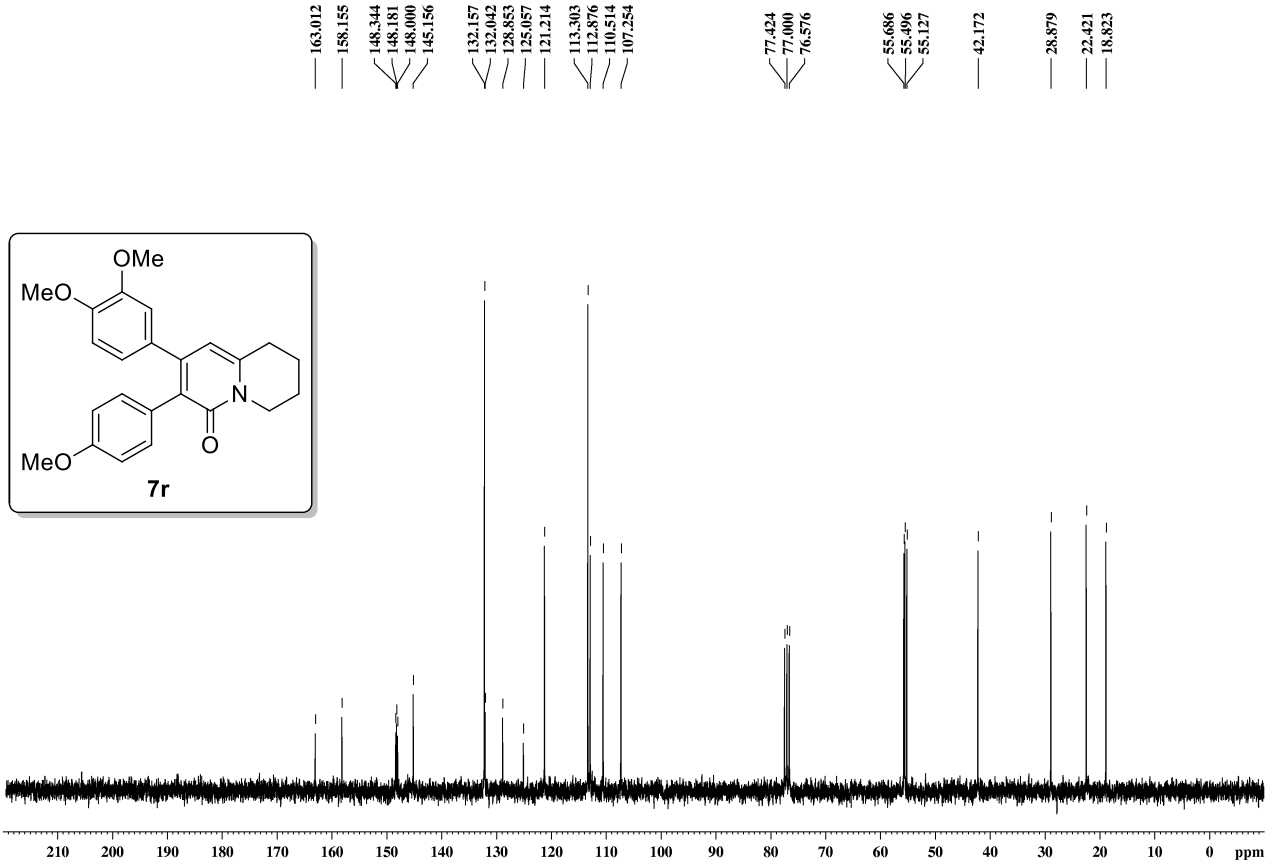




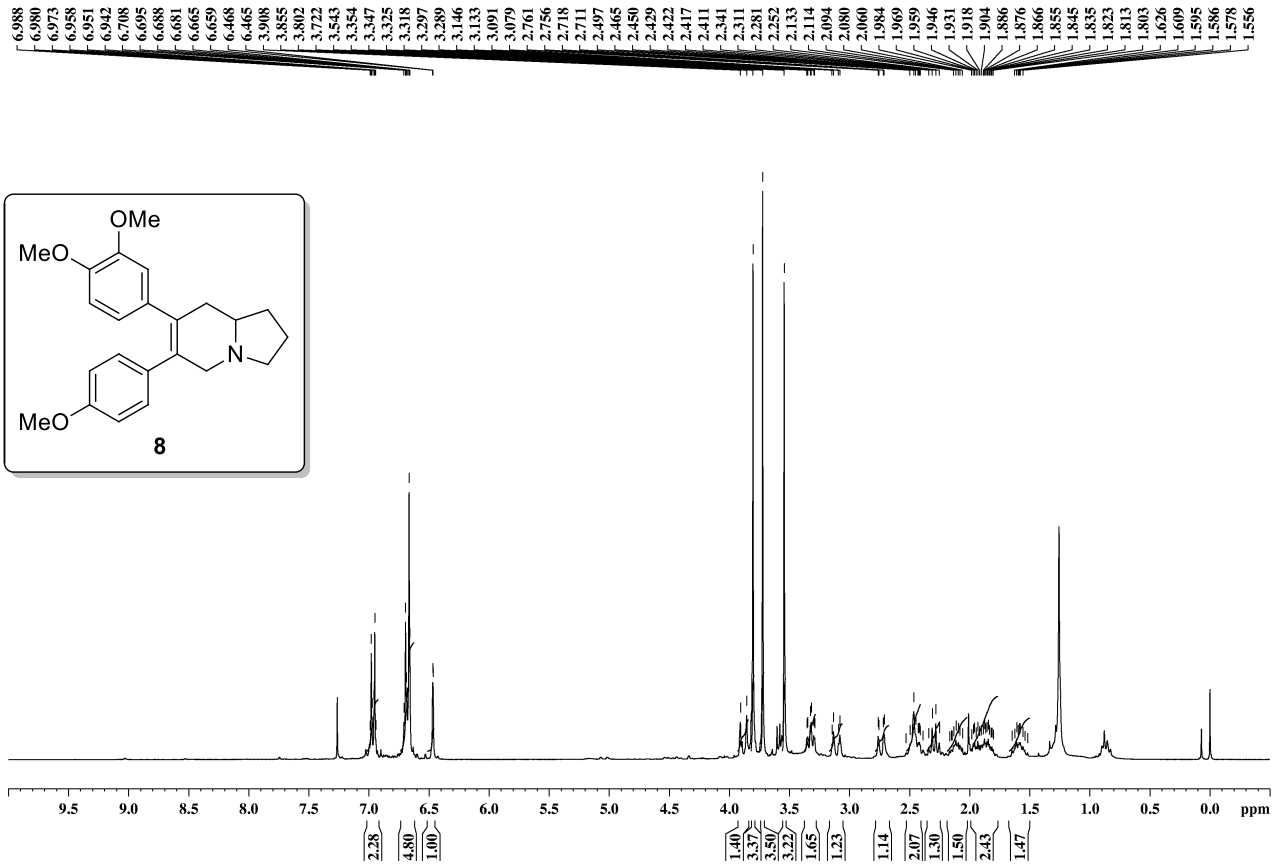
^{1}H NMR (300 MHz, $CDCl_3$); **7r**



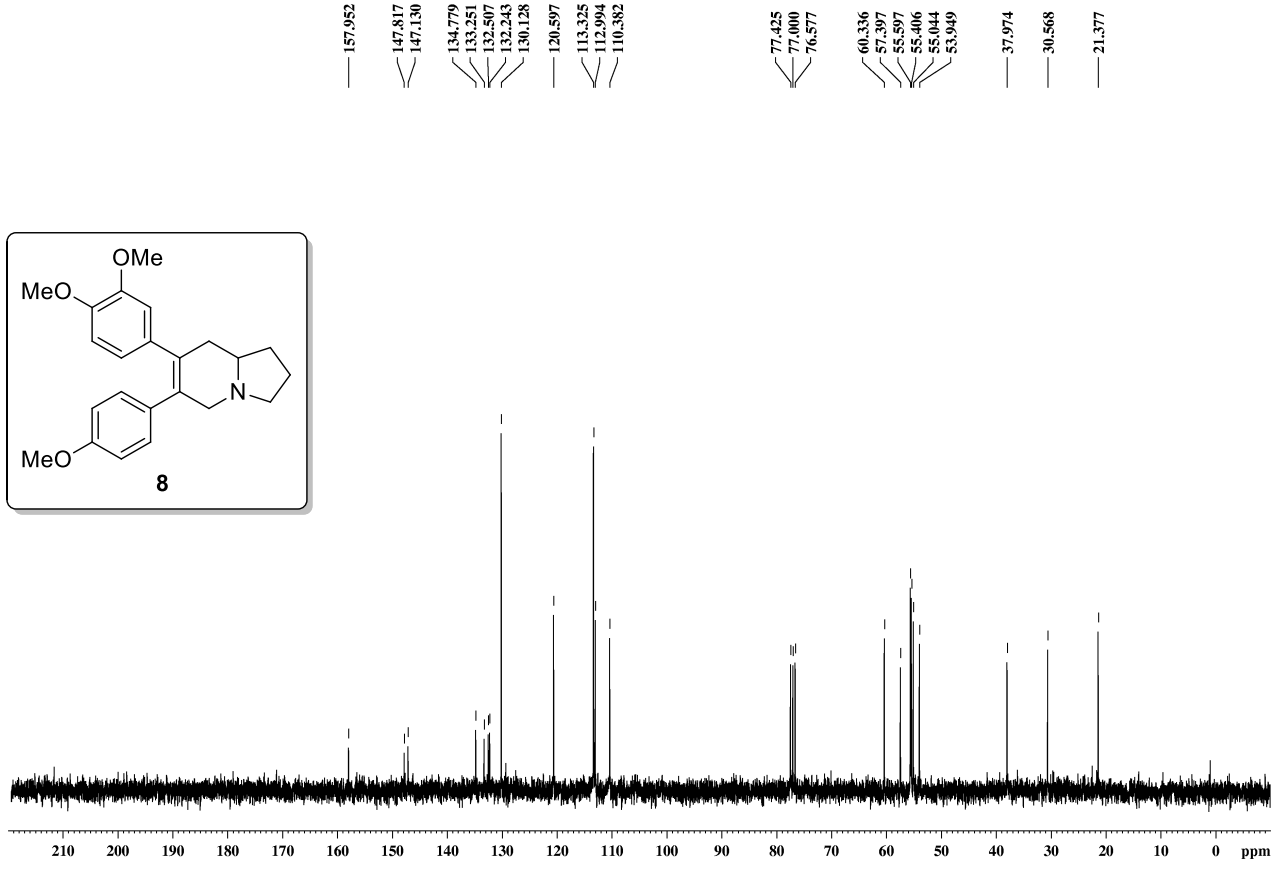
^{13}C NMR (75 MHz, $CDCl_3$); **7r**



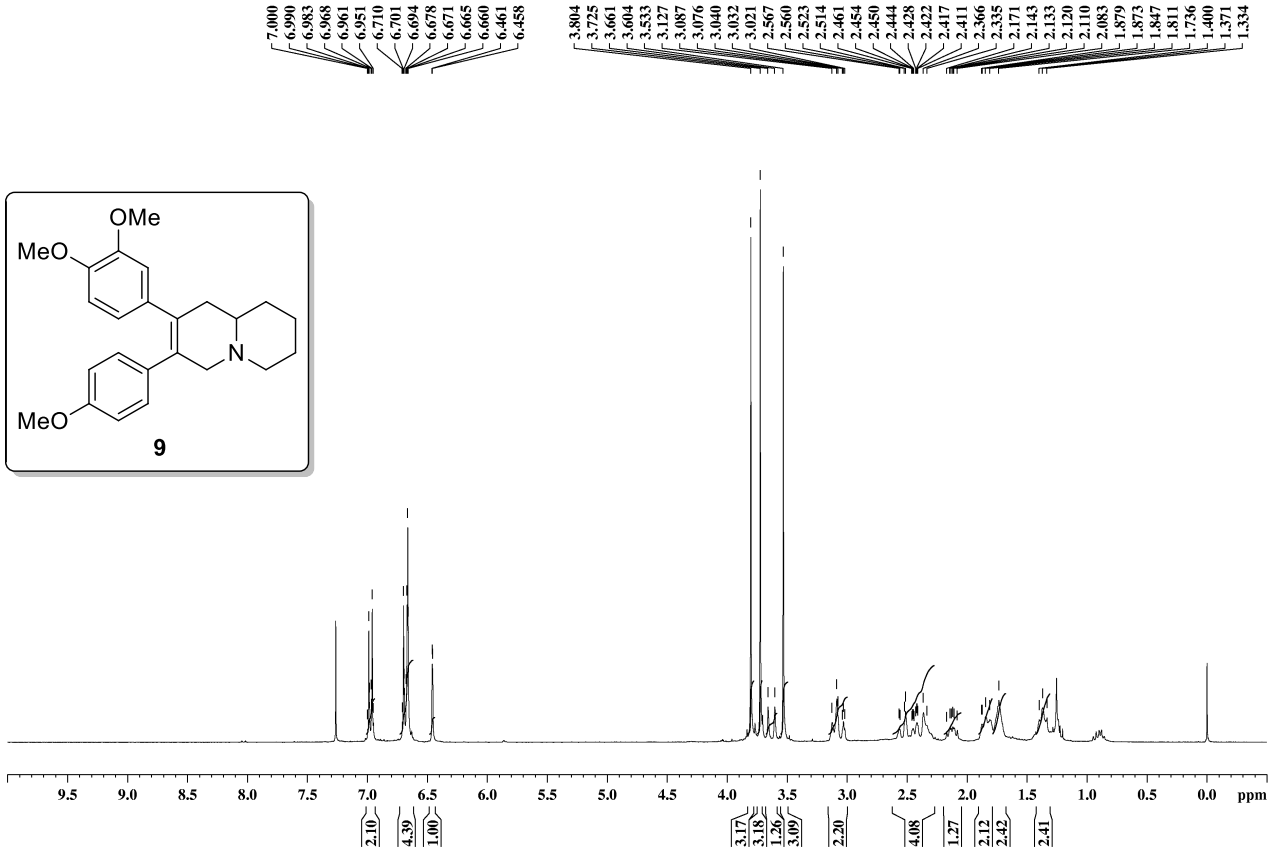
^{1}H NMR (300 MHz, $CDCl_3$); **(±)-8**



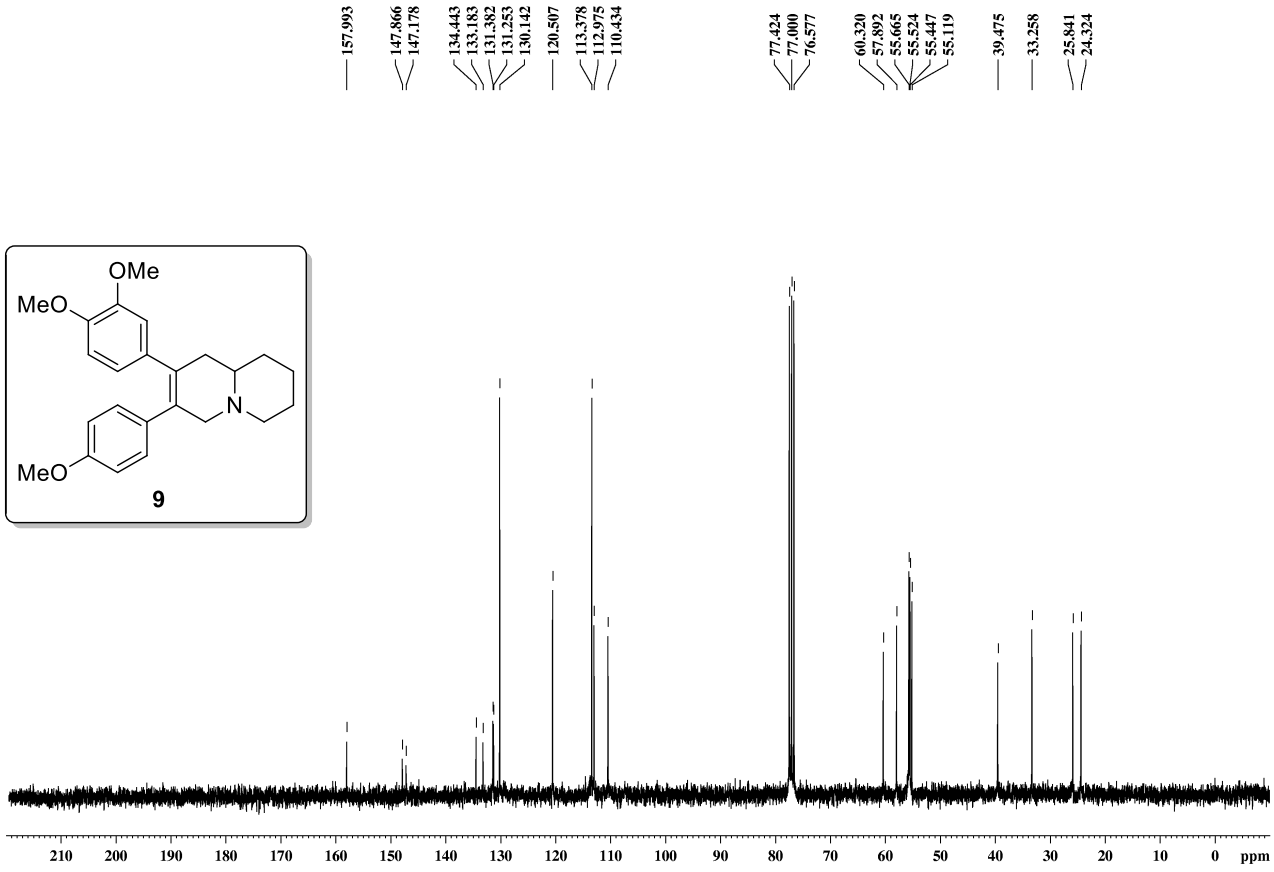
^{13}C NMR (75 MHz, $CDCl_3$); (±)-**8**



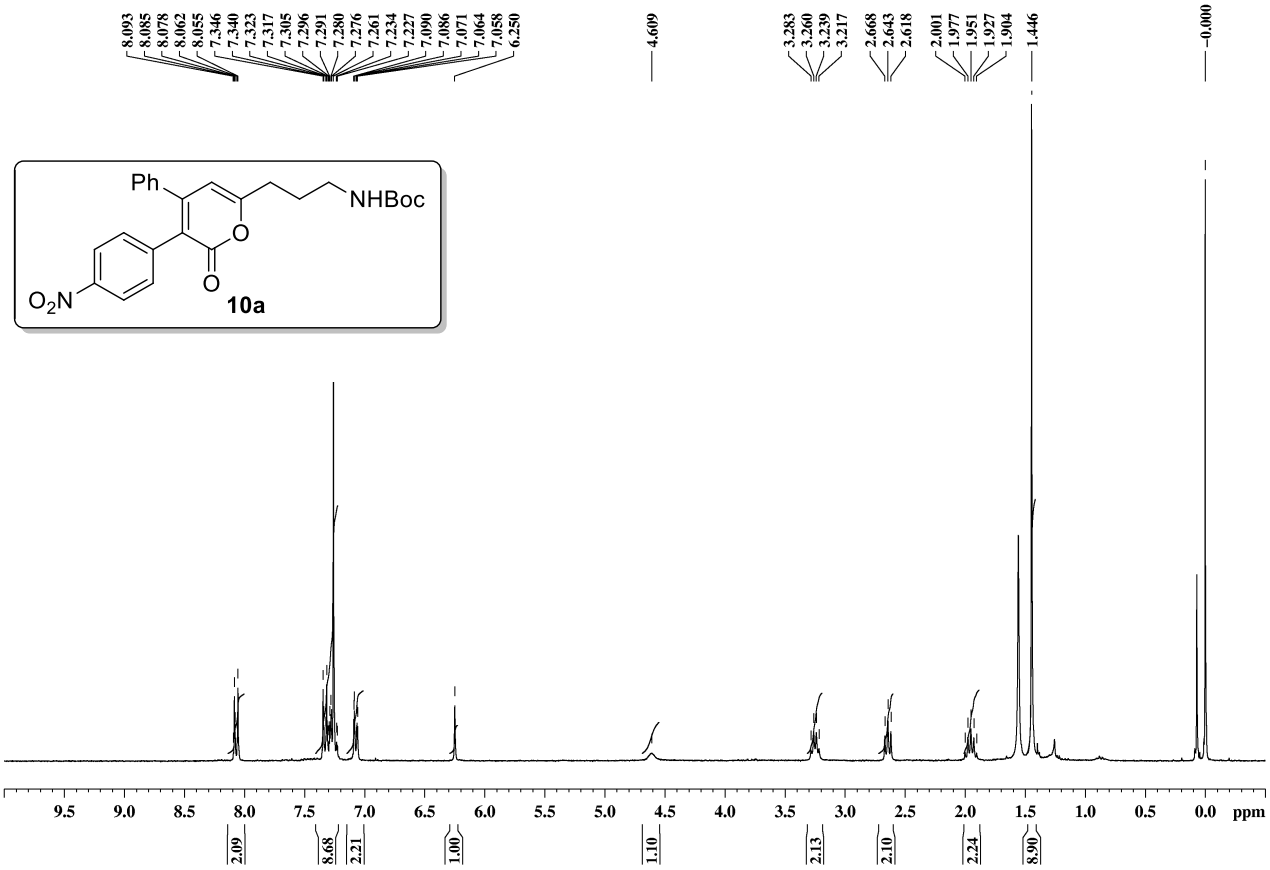
^{1}H NMR (300 MHz, $CDCl_3$); **(±)-9**



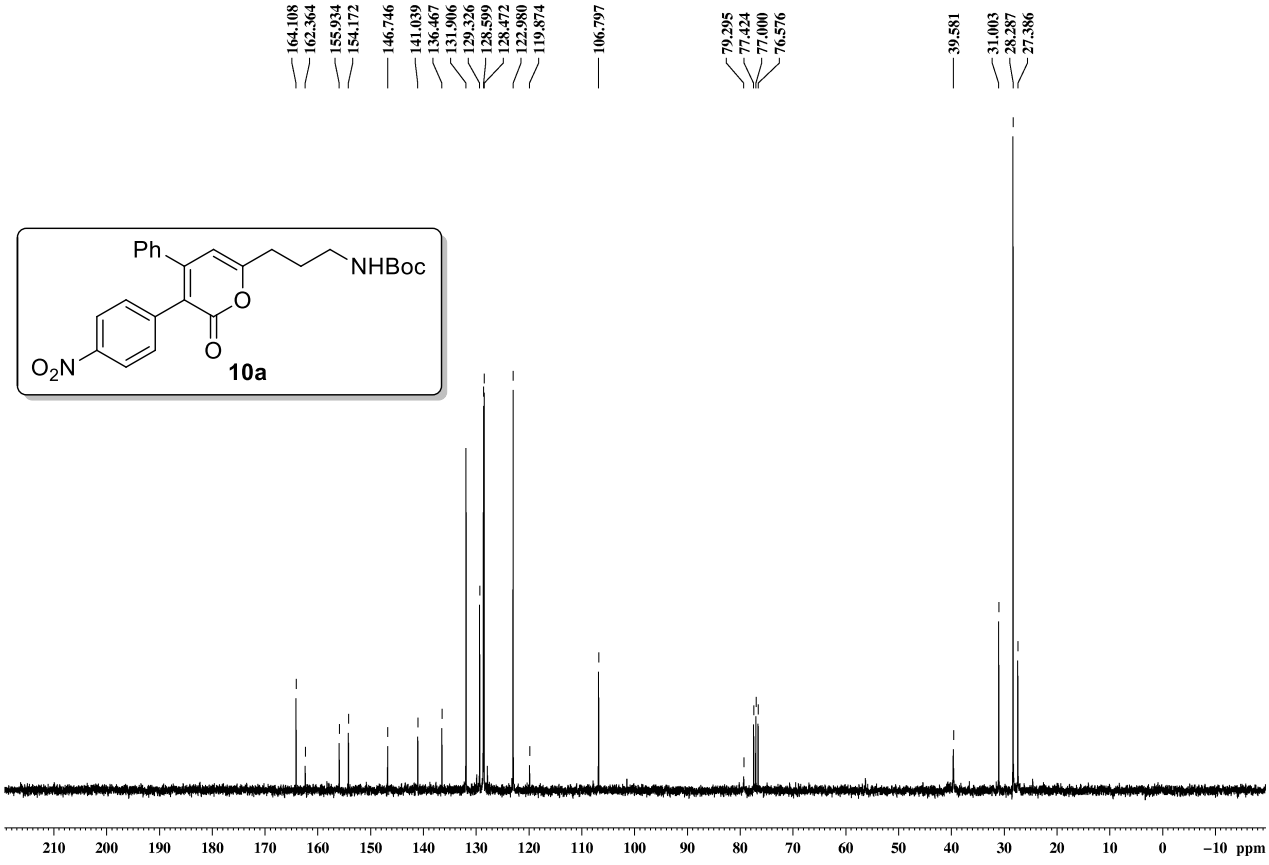
^{13}C NMR (75 MHz, $CDCl_3$); (±)-**9**



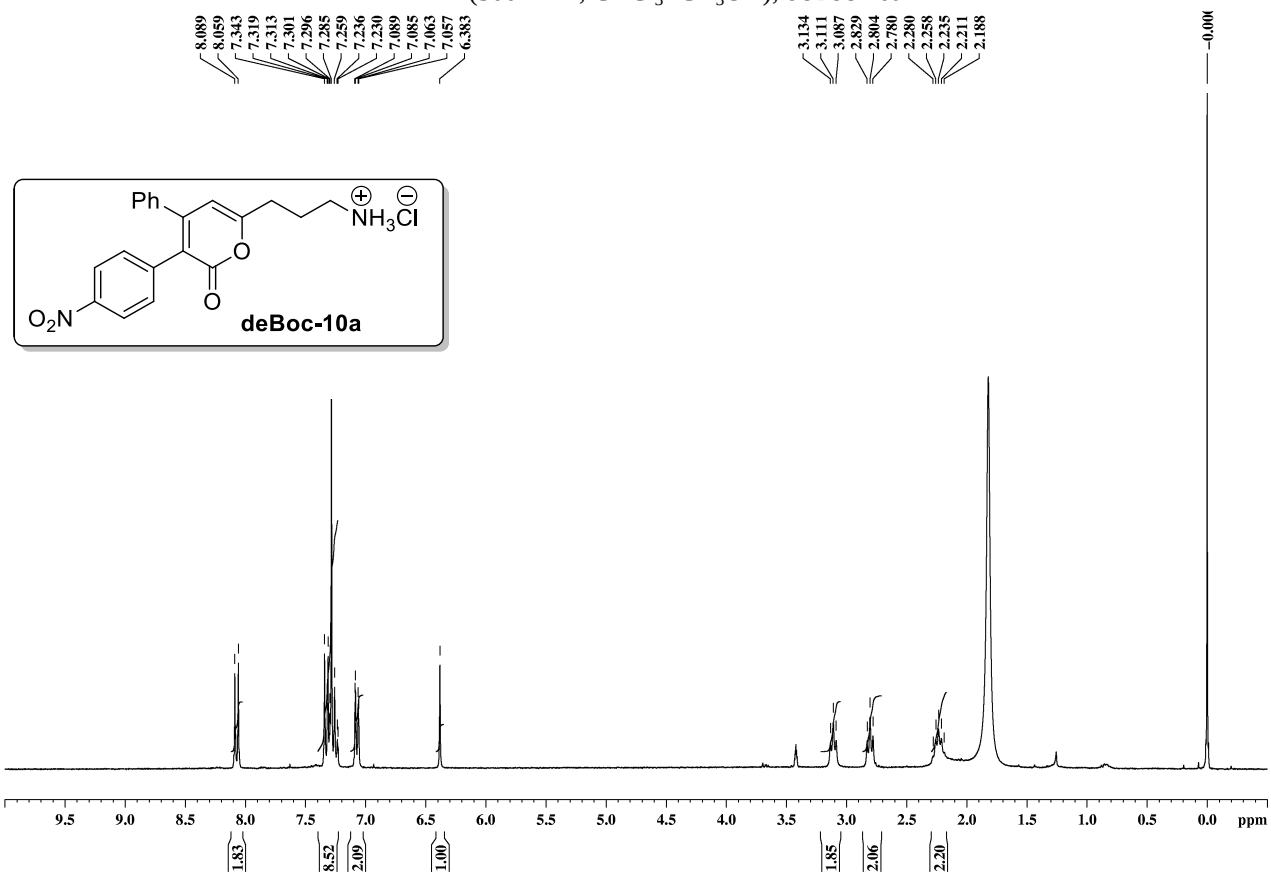
^{1}H NMR (300 MHz, $CDCl_3$); **10a**



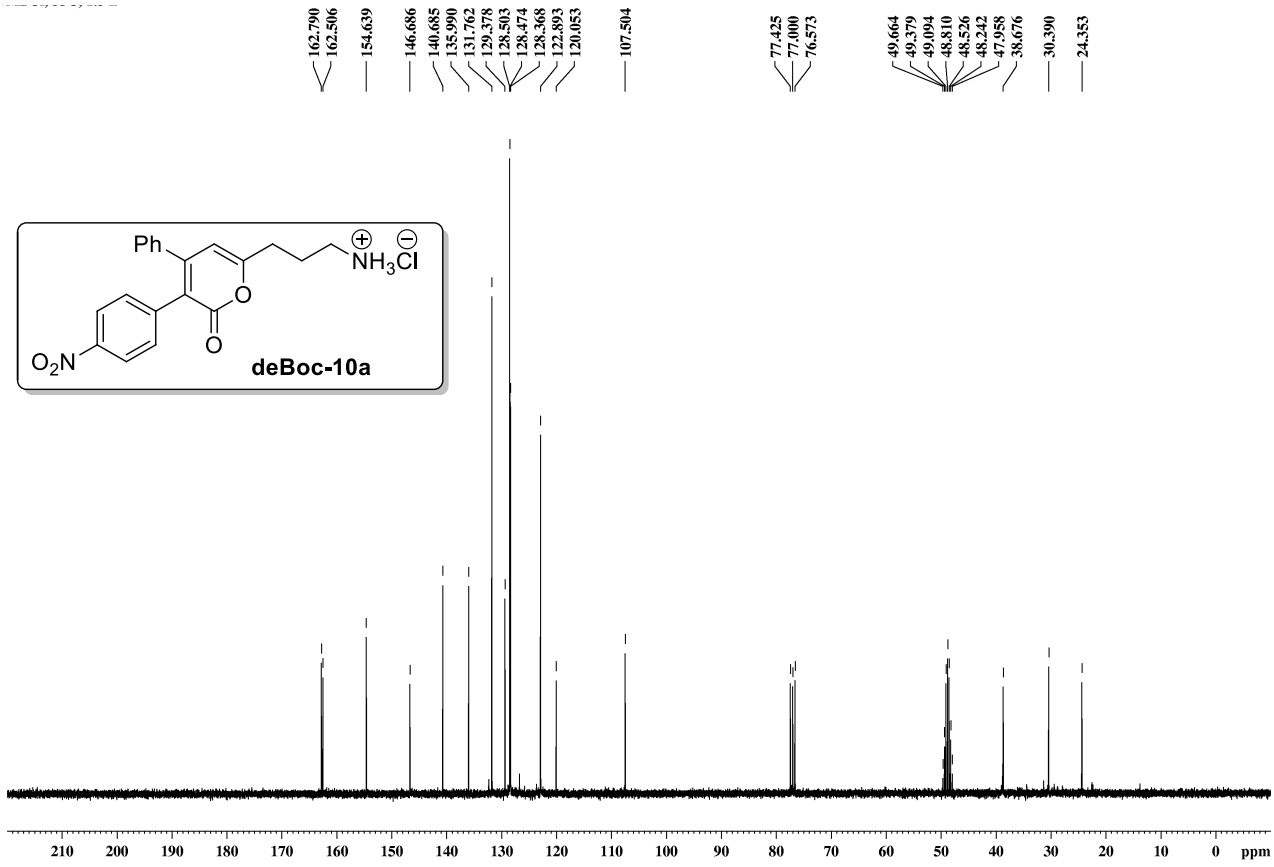
^{13}C NMR (75 MHz, $CDCl_3$); **10a**



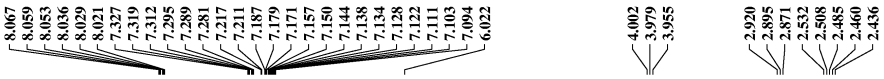
^{1}H NMR (300 MHz, $CDCl_3$+CD_3OD); **deBoc-10a**

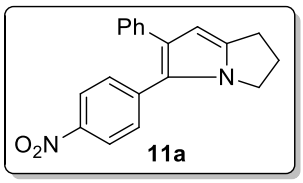


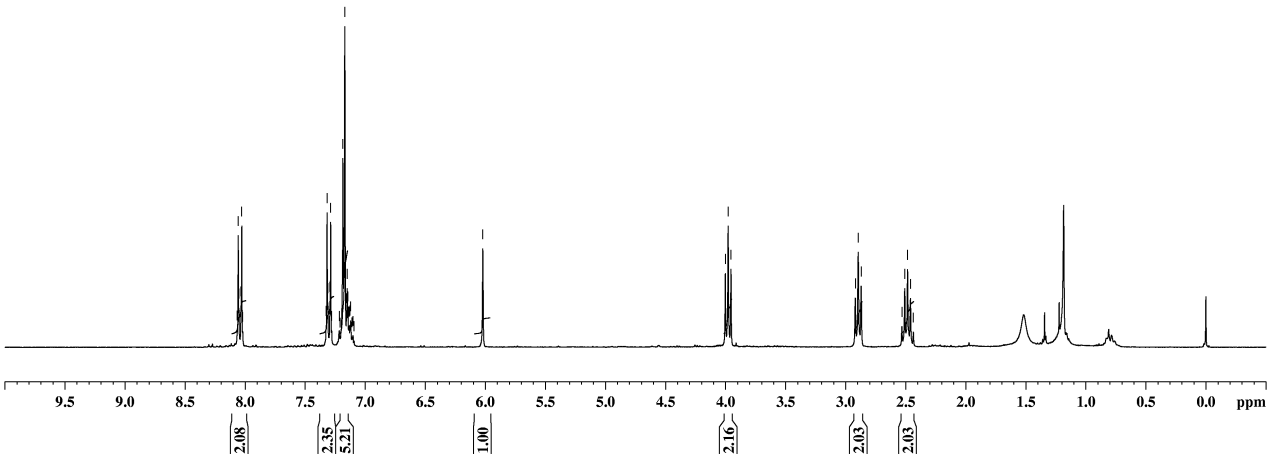
^{13}C NMR (75 MHz, $CDCl_3$+CD_3OD); **deBoc-10a**



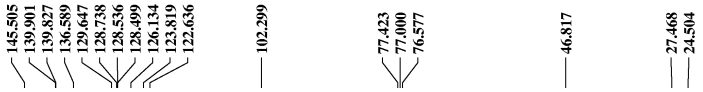
^{1}H NMR (300 MHz, $CDCl_3$); **11a**

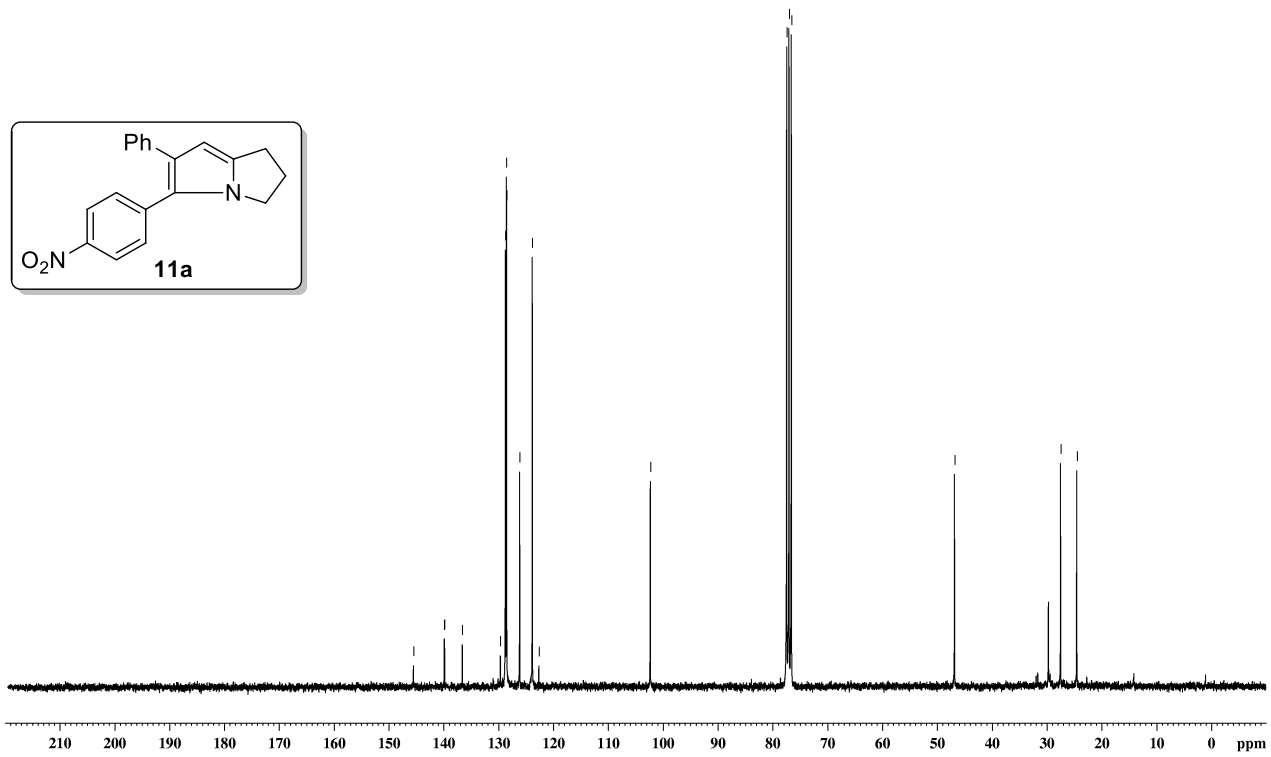






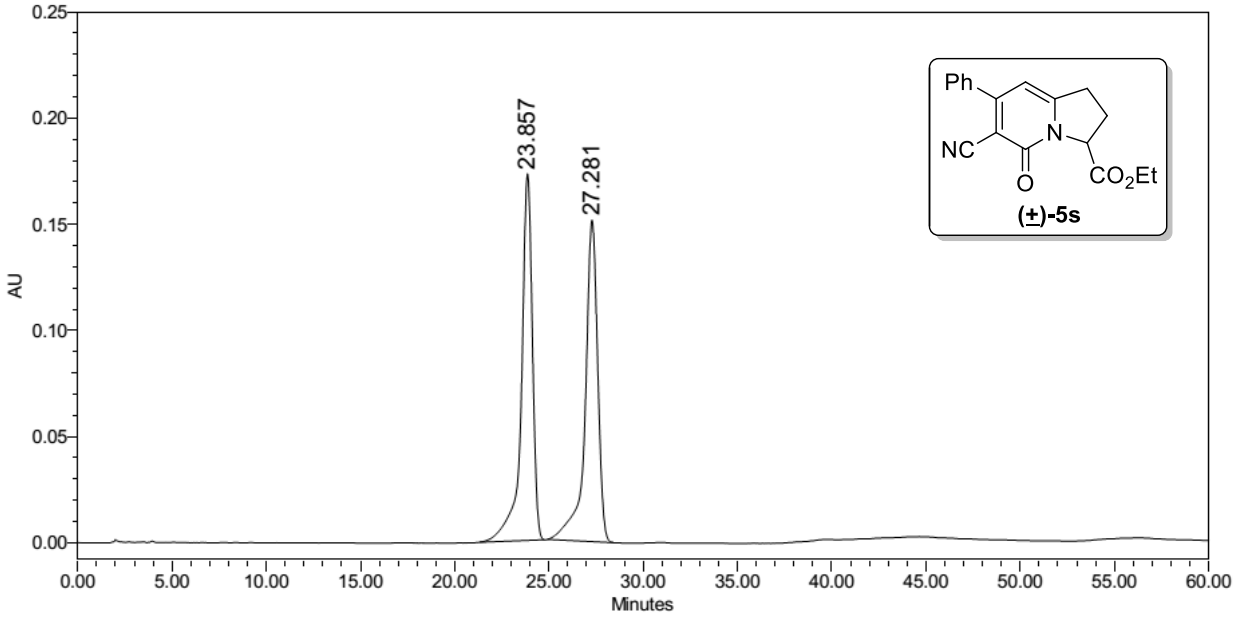
^{13}C NMR (75 MHz, $CDCl_3$); **11a**





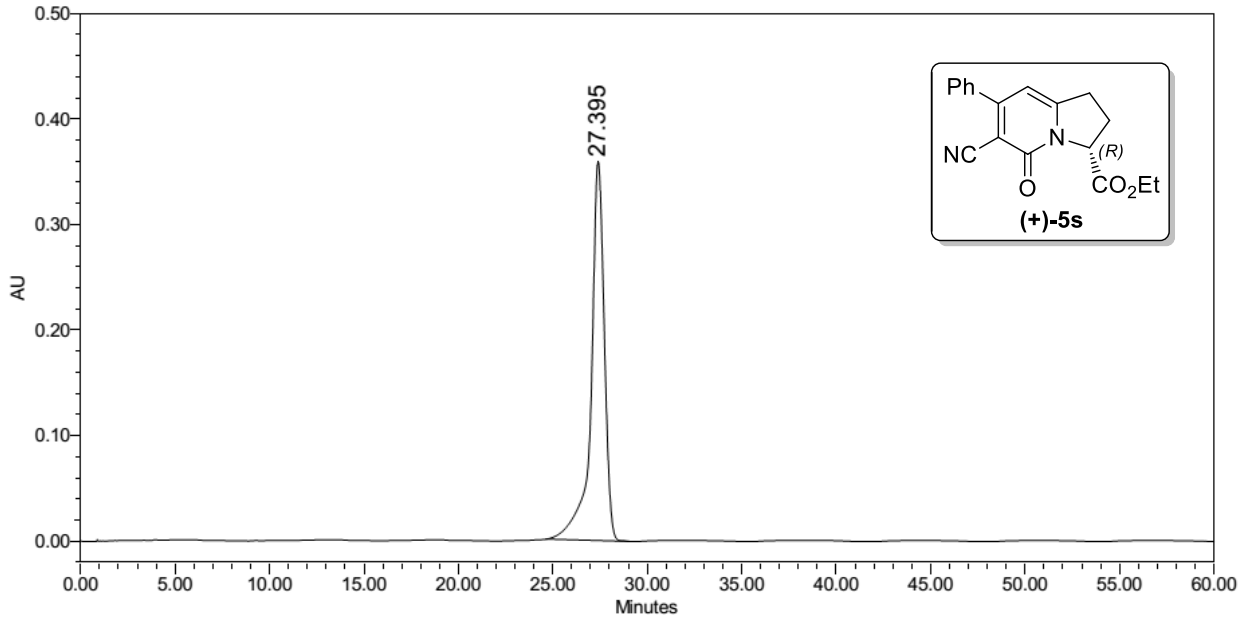
9. HPLC spectra for compound 5s

HPLC analysis of **5s** was performed on a DAICEL chiral column (type IC-3) with UV/VIS detection at 254 nm using 40% acetonitrile in water as eluents at flow rate 0.5 mL/min, 25^{o}C.



LC Peak Results

	RT	Area	% Area	Height	% Height
1	23.857	7039652	50.01	172741	53.27
2	27.281	7036180	49.99	151524	46.73



LC Peak Results

	RT	Area	% Area	Height	% Height
1	27.395	17498312	100.00	359249	100.00