Two Distinct Protocols for the Synthesis of Unsymmetrical 3,4-Disubstituted Maleimides Based on Transition-Metal Catalysts

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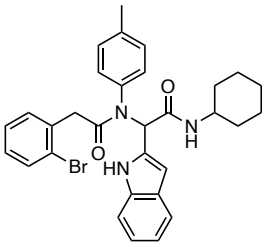
1. Experimental Details

Starting materials and solvents were purchased from commercial suppliers (Merck and Aldrich) and used without further purification unless otherwise stated. The Ugi-adducts **1** were prepared by following the literature report.[1] Melting points are determined by an Electrothermal 9100 apparatus and are uncorrected. FT-IR spectra were recorded based on a Shimadzu Infra-Red Spectroscopy IR-435. Nuclear magnetic resonance (NMR) spectra were recorded based on a Bruker AVANCE Spectrometer 400 MHz for ^{1}H,100 MHz for $^{13}C\{^{1}H\}$ in DMSO-d_6 as solvent. Mass spectra were recorded Bruker Maxis Impact mass spectrometer using electrospray ionization (ESI+) and a Leco CHNS, model 932 was used for elemental analysis.

Typical procedure for the synthesis of Ugi adduct 1a. To a stirred solution of 2-formylindole (145 mg, 1.00 mmol) and *p*-toluidine (107 mg, 1.00 mmol) in MeOH (5 mL), 2-bromophenyl acetic acid (213 mg, 1.00 mmol) and cyclohexyl isocyanide (109 mg, 1.00 mmol) were added under reflux in an oil bath. The reaction process was monitored by TLC. After 24 h, the residue was filtered and washed with methanol and Et_2O. The solid was dried and collected as pure product **1a** and used for further reactions (465 mg, 73%).

White powder, mp: 200–202 ºC. ^{1}H-NMR (300 MHz, $CDCl_3$): δ 9.75 (s, 1H), 7.62 (d, 1H, J = 7.8 Hz), 7.53 (d, 1H, J = 7.8 Hz), 7.36–7.39 (m, 1H), 7.14–7.23 (m, 9H), 6.49 (s, 1H), 5.71 (d, 1H, J = 7.8 Hz), 5.37 (s, 1H), 3.79-3.82 (m, 1H), 3.50-3.65 (q, 2H, J = 16.8 Hz) 2.37 (s, 3H), 1.85 (m, 2H), 1.55–1.69 (m, 3H), 1.29–1.33 (m, 2H), 1.00–1.07 (m, 3H); $^{13}C\{^{1}H\}$-NMR (75 MHz, $CDCl_3$): δ 172.0, 166.7, 140.0, 138.8, 136.7, 136.0, 135.8, 133.0, 132.0, 130.5, 128.7, 128.1, 127.5, 127.2, 125.0, 122.6, 120.6, 119.9, 111.8, 104.9, 76.7, 49.1, 42.5, 32.9, 32.8, 25.4, 24.9, 21.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) =1624, 3371. Elem. Anal. calcd for $C_{31}H_{32}BrN_3O_2$ C, 66.67; H, 5.78; N, 7.52 found: C, 66.53; H, 5.72; N, 7.55.

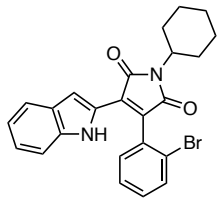


1a

General procedure for synthesis of various 4-aryl-3-pyrrolo-maleimides 2a–j. A mixture of Ugi product **1** (1 mmol), $Pd(OAc)_2$ (11.2 mg, 50 µmol, 5 mol%), PPh_3 (26.2 mg, 100µmol, 10 mol%), and K_2CO_3 (276 mg, 2.00 mmol) were dissolved in DMSO (5.0 mL) and stirred for 2 h at 100 °C in an oil bath. The progress of the reaction was monitored by TLC. After completion, the reaction was quenched by the addition of CH_2Cl_2 (20 mL), and the organic phase was washed by water and brine, and dried over Na_2SO_4 (ca 5g). The solvent was removed under reduced pressure,

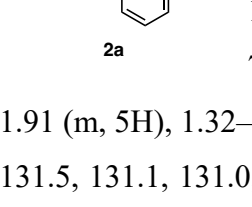
and the residue was purified by column chromatography using *n*-hexane as eluent and silica gel as stationary phase.

3-(2-Bromophenyl)-1-cyclohexyl-4-(1*H*-indol-2-yl)-1*H*-pyrrole-2,5-dione (**2a**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 86% (385 mg, 0.856 mmol) from the corresponding Ugi product (559 mg, 1.00 mmol); mp 161–163 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.23 (s, 1H), 7.83 (d, 1H, J = 7.8 Hz), 7.41–7.56 (m, 5H), 7.27 (t, 1H, J = 7.5 Hz), 7.11 (t, 1H, J = 7.5 Hz), 6.52 (d, 1H, J = 0.9 Hz), 4.09–4.19 (m, 1H), 2.18–2.30 (m, 2H), 1.75–1.91 (m, 5H), 1.32–1.49 (m, 3H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 171.9; 169.6, 137.6, 133.6, 131.5, 131.1, 131.0, 130.8, 129.1, 128.1, 127.7, 127.2, 125.2, 123.4, 121.7, 120.9, 111.8, 109.3, 51.5, 30.1, 26.0, 25.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) =1326, 1524, 1637, 1697, 3385; HR-MS (ESI) [M+H]$^{+}$: *m*/*z* calcd for $C_{24}H_{21}{}^{81}BrN_2O_2^{+}$ 451.0846 found: 451.0839. Supplementary crystallographic data for **2a** have been deposited at the Cambridge Crystallographic Data Center. CCDC: 1976139.



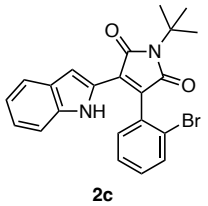
2a

3-(2-Bromophenyl)-1-butyl-4-(1*H*-indol-2-yl)-1*H*-pyrrole-2,5-dione (**2b**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 81% (342 mg, 0.807 mmol) from the corresponding Ugi product (533 mg, 1.00 mmol); mp 154–156 ˚C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 11.32 (s, 1H), 7.87–7.90 (m, 1H), 7.58–7.64 (m, 2H), 7.46–7.55 (m, 3H), 7.20 (t, 1H, J = 7.5 Hz), 7.00 (t, 1H, J = 7.5 Hz), 6.37 (d, 1H, J = 1.5 Hz), 3.62 (t, 2H, J = 6.9 Hz), 1.59–1.68 (m, 2H), 1.30–1.42 (m, 2H), 0.94 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6): δ 170.8, 169.9, 138.6, 133.5, 132.2, 132.0, 131.7, 129.9, 128.9, 127.5, 126.8, 124.8, 123.1, 121.5, 120.8, 113.5, 108.3, 38.0, 30.5, 19.9, 14.0; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1326, 1524, 1632, 1699, 3395; HR-MS (ESI) [M+H]$^{+}$: *m*/*z* calcd for $C_{22}H_{19}{}^{81}BrN_2O_2^{+}$ 423.0710, found: 423.0697.



2b

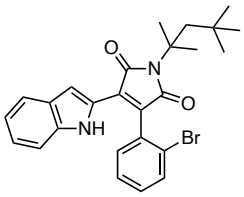
3-(2-Bromophenyl)-1-(*tert*-butyl)-4-(1*H*-indol-2-yl)-1*H*-pyrrole-2,5-dione (**2c**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 83% (350 mg, 0.826 mmol) from the corresponding Ugi product (532 mg, 1.00 mmol); mp 145–147 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.16 (s, 1H), 7.71 (d, 1H, J = 7.2 Hz), 7.38–7.47 (m, 3H), 7.28–7.35 (m, 2H) 7.17 (t, 1H, J = 7.5 Hz), 6.98 (t, 1H, J = 7.5 Hz), 6.34 (d, 1H, J = 1.2 Hz), 1.64 (s, 9H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 172.8, 167.9, 137.4, 133.6, 132.6, 131.2, 131.5, 131.1, 129.0, 128.2, 125.2, 121.8, 120.9, 111.9,



2c

109.2, 58.3, 29.3; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1329, 1524, 1638, 1697, 3388; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{22}H_{19}{}^{81}BrN_2O_2^+$ 423.0710 found: 423.0705.

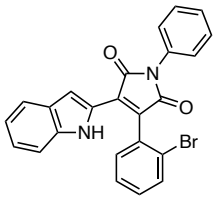
3-(2-Bromophenyl)-4-(1*H*-indol-2-yl)-1-(2,4,4-trimethylpentan-2-yl)-1*H*-pyrrole-2,5-dione (**2d**):



2d

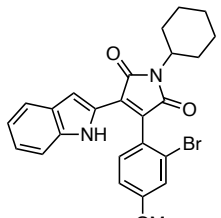
Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 77% (368 mg, 0.768 mmol) from the corresponding Ugi product (589 mg, 1.00 mmol); mp 172–174 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.18 (s, 1H), 7.71 (d, 1H, *J* = 8.0 Hz), 7.37–7.42 (m, 2H), 7.24–7.33 (m, 3H), 7.17 (t, 1H, *J* = 8.2 Hz) 6.93 (t, 1H, *J* = 7.6 Hz), 6.33 (d, 1H, *J* = 1.2 Hz), 1.86–2.00 (m, 2H), 1.70–1.71 (m, 2H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 173.5, 171.3, 137.4, 133.5, 131.6, 131.5, 131.0, 130.8, 128.8, 128.0, 127.6, 127.1, 125.0, 123.3, 121.6, 120.7, 111.7, 109.1, 61.6, 50.9, 31.6, 31.2, 30.1; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1359, 1508, 1647, 1693, 3407; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{26}H_{27}{}^{81}BrN_2O_2^+$ 481.1309 found: 481.1312.

3-(2-Bromophenyl)-4-(1*H*-indol-2-yl)-1-phenyl-1*H*-pyrrole-2,5-dione (**2e**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 75% (331 mg, 0.747 mmol) from the corresponding Ugi product (553 mg, 1.00 mmol); mp 180–182 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.19 (s, 1H), 7.86–7.89 (m, 1H), 7.54–7.57 (m, 6H), 7.42–7.51 (m, 4H), 7.29–7.34 (m, 1H), 7.10–7.16 (m, 1H), 6.62 (d, 1H, *J* = 1.2 Hz); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 170.7, 168.4, 137.8, 133.7, 131.5, 131.4, 131.2, 131.0, 130.9, 129.5, 129.2, 128.2, 128.0, 127.8, 126.9, 126.2, 125.6, 123.4, 121.9, 121.1, 111.9, 110.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1394, 1523, 1630, 1709, 3394; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{24}H_{15}BrN_2O_2^+$ 443.0397 found: 443.2236.



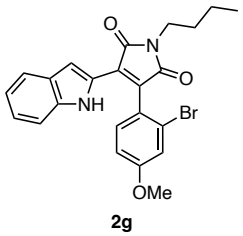
2e

3-(2-Bromo-5-methoxyphenyl)-1-cyclohexyl-4-(1*H*-indol-2-yl)-1*H*-pyrrole-2,5-dione (**2f**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 86% (411 mg, 0.857 mmol) from the corresponding Ugi product (559 mg, 1.00 mmol); mp 168–170 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.20 (s, 1H), 7.54 (d, 1H, *J* = 7.8 Hz), 7.26–7.44 (m, 4H), 7.05–7.13 (m, 2H), 6.60 (d, 1H, *J* = 1.2 Hz), 4.11 (m, 1H), 3.94 (s, 3H), 2.16–2.28 (m, 2H), 1.84–1.95 (m, 4H), 1.28–1.45 (m, 4H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 172.0, 169.9, 161.1, 137.5, 131.5, 131.1, 129.1, 127.7, 127.4, 125.1, 124.0, 123.2, 121.7, 120.8, 118.8, 114.4, 111.7, 109.1, 55.7, 51.4, 30.1, 30.0, 26.0, 25.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1286, 1593, 1637, 1697, 3408; Elem. Anal. calcd for $C_{25}H_{23}BrN_2O_3$: C, 62.64; H, 4.84; N, 5.84 found: C, 62.52; H, 4.87; N, 5.78.



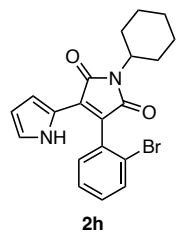
2f

3-(2-Bromo-5-methoxyphenyl)-1-butyl-4-(1*H*-indol-2-yl)-1*H*-pyrrole-2,5-dione (**2g**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 81% (366 mg, 0.807 mmol) from the corresponding Ugi product (563 mg, 1.00 mmol); mp 111–113 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.18 (s, 1H), 7.55 (d, 1H, J = 7.8 Hz), 7.27–7.44 (m, 4H), 7.05–7.14 (m, 2H), 6.64 (s, 1H), 3.93 (s, 3H$_3$), 3.73 (t, 2H, J = 6.9 Hz), 1.70–1.80 (m, 2H), 1.39–1.52 (m, 2H), 1.03 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 172.0, 170.0, 161.2, 137.6, 131.5, 131.1, 129.3, 127.8, 127.4, 125.2, 124.0, 123.1, 121.7, 120.9, 118.8, 114.5, 111.8, 109.2, 55.7, 38.2, 30.7, 20.1, 13.7; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1324, 1595, 1634, 1699, 3383; Elem. Anal. calcd for $C_{23}H_{21}BrN_2O_3$ C, 60.94; H, 4.67; N, 6.18 found: C, 60.88; H, 4.63; N, 6.15.



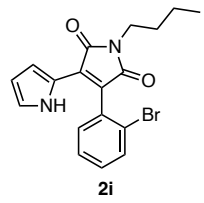
2g

4'-(2-Bromophenyl)-1'-cyclohexyl-1*H*,1'*H*-[2,3'-bipyrrole]-2',5'-dione (**2h**): Flash column chromatography (in *n*-hexane) yielded the title compound as yellow powder in 84% (334 mg, 0.837 mmol) from the corresponding Ugi product (509 mg, 1.00 mmol); mp 193–195 ˚C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ δ 11.28 (s, 1H), 7.81–7.84 (m, 1H), 7.52–7.58 (m, 1H), 7.43–7.49 (m, 2H), 7.09–7.12 (m, 1H), 6.13–6.16 (m, 1H), 5.96–5.99 (m, 1H), 3.88–3.98 (m, 1H), 1.99–2.11 (m, 2H), 1.65–1.98 (m, 5H), 1.36–1.40 (m, 3H); ^{13}C{^{1}H}-NMR (75 MHz, DMSO-d_6): δ 171.1, 170.2, 133.3, 132.4, 131.9, 131.5, 129.5, 128.8, 126.2, 125.6, 123.6, 121.5, 116.1, 111.4, 50.8, 30.1, 26.0, 25.4; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1386, 1585, 1632, 1685, 3406; HR-MS (ESI) [M+H]$^+$: *m*/*z* calcd for $C_{20}H_{19}{}^{81}BrN_2O_2^+$ 399.0710 found: 399.0705.



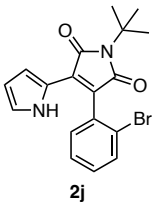
2h

4'-(2-Bromophenyl)-1'-butyl-1*H*,1'*H*-[2,3'-bipyrrole]-2',5'-dione (**2i**): Flash column chromatography (in *n*-hexane) yielded the title compound as yellow powder in 79% (294 mg, 0.787 mmol) from the corresponding Ugi product (482 mg, 1.00 mmol); mp 98–100 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.51 (s, 1H), 7.76–7.79 (m, 1H), 7.45–7.51 (m, 1H), 7.35–7.41 (m, 2H), 7.07 (d, 1H, J = 1.2 Hz), 6.21–6.25 (m, 2H), 3.68 (t, 2H, J = 7.2 Hz), 1.65–1.75 (m, 2H), 1.36–1.48 (m, 2H), 1.00 (t, 3H, J = 7.2 Hz,); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 172.4, 170.3, 133.4, 131.8, 131.1, 130.7, 129.0, 127.9, 125.5, 124.0, 123.7, 122.8, 116.3, 111.7, 38.0, 30.6, 20.0, 13.7; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1405, 1441, 1629, 1689, 3408; HR-MS (ESI) [M+H]$^+$: *m*/*z* calcd for $C_{18}H_{17}{}^{81}BrN_2O_2^+$ 375.0526 found: 375.0524.



2i

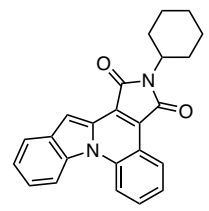
4'-(2-Bromophenyl)-1'-(tert-butyl)-1*H*,1'*H*-[2,3'-bipyrrole]-2',5'-dione (**2j**): Flash column chromatography (in *n*-hexane) yielded the title compound as yellow powder in 85% (316 mg, 0.847 mmol) from the corresponding Ugi product (482 mg, 1.00 mmol); mp 181–183 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 10.57 (s, 1H), 7.75–7.78 (m, 1H), 7.45–7.50 (m, 1H), 7.34–7.38 (m, 2H), 7.04 (d, 1H, J = 1.5 Hz), 6.17–6.21 (m, 2H), 1.73 (s, 9H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 173.4, 171.5, 133,3, 132.1, 131.1, 130.6, 128.6, 127.8, 126.0, 123.8, 123.6, 122.6, 116.0, 111.3, 57.9, 29.1; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1349, 1466, 1644, 1693, 3411; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{18}H_{17}{}^{81}BrN_2O_2^+$ 373.0553 found: 373.0550.



2j

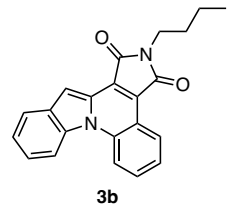
General procedure for synthesis of various maleimide-fused pyrrolo[1,2-a]quinolines 3a–l). A mixture of Ugi product **1** (1 mmol), CuI (10 mol%), L-proline (20 mol%), and K_2CO_3 (2 equiv.) were dissolved in DMSO (5.0 mL) and stirred for 4 h at 130 °C. The progress of the reaction was monitored by TLC. After completion, the reaction was quenched by the addition of CH_2Cl_2 (20 mL), and the organic phase was washed by water and brine, and dried over Na_2SO_4. The solvent was removed under reduced pressure, and the residue was purified by column chromatography using *n*-hexane as eluent and silica gel as stationary phase.

2-Cyclohexyl-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3a**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 87% (320 mg, 0.869 mmol) from the corresponding Ugi product (559 mg, 1.00 mmol); mp 270–272 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.82 (dd, 1H, J = 1.5 Hz), 8.61 (d, 1H, J = 8.7 Hz), 8.46 (d, 1H, J = 8.7 Hz), 7.98 (d, 1H, J = 8.1 Hz), 7.73–7.79 (m, 1H) 7.59 (s, 1H), 7.46–7.56 (m, 3H), 4.11–4.22 (m, 1H), 2.22–2.34 (m, 2H), 1.76–1.98 (m, 5H), 1.29–1.48 (m, 3H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 169.2, 167.8, 138.2, 133.9, 131.2, 130.9, 128.0, 127.1, 125.1, 124.1, 123.9, 123.4, 122.8, 122.6, 117.6, 116.0, 114.4, 100.5, 51.0, 30.1, 26.1, 25.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1371, 1610, 1697, 3432; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{24}H_{20}N_2O_2^+$ 369.1605, found: 369.1597.



3a

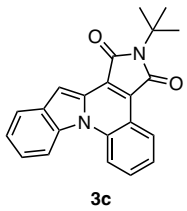
2-Butyl-1H-indolo[1,2-*a*]pyrrolo[3,4-c]quinoline-1,3(*2H*)-dione (**3b**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 78% (267 mg, 0.779 mmol) from the corresponding Ugi product (532 mg, 1.00 mmol); mp 170–172 ˚C; ^{1}H-NMR (300 MHz, DMSO-d_6): δ 8.87 (d, 1H, J = 8.7 Hz), 8.75 (d, 1H, J = 8.7 Hz), 8.70 (d, 1H, J = 7.8 Hz), 8.07 (d, 1H, J = 7.8 Hz), 7.89 (t, 1H, J = 7.9 Hz), 7.49–7.62 (m, 4H), 3.62 (t, 2H, J = 6.9 Hz), 1.60–1.70 (m, 2H), 1.31–



3b

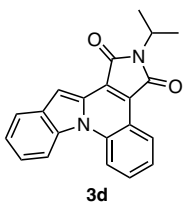
1.44 (m, 2H), 0.95 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$-NMR (75 MHz, DMSO-d_6): δ 169.1, 167.7, 137.8, 133.7, 132.4, 130.7, 128.0, 126.7, 125.0, 124.8, 124.7, 124.0, 123.4, 122.8, 117.4, 117.0, 115.4, 100.2, 37.7, 30.6, 20.0, 14.0; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1096, 1609, 1694, 2856, 2923; HR-MS (ESI) $[M+H]^+$: m/z calcd for $C_{22}H_{18}N_2O_2^+$ 343.1448, found 343.1438.

2-(*tert*-Butyl)-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3c**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 81% (277 mg, 0.809 mmol) from the corresponding Ugi product (533 mg, 1.00 mmol); mp 165–167 ˚C; ^1H-NMR (300 MHz, $CDCl_3$): δ 8.86 (d, 1H, J = 7.8 Hz), 8.64 (d, 1H, J = 8.7 Hz), 8.50 (d, 1H, J = 8.4 Hz), 8.00 (d, 1H, J = 7.8 Hz), 7.74–7.79 (m, 1H), 7.76–7.61 (m, 4H), 1.79 (s, 9H); $^{13}C\{^1H\}$-NMR (75 MHz, DMSO-d_6): δ 170.2, 168.6, 137.8, 133.5, 132.2, 130.7, 127.8, 126.7, 124.7, 124.6, 123.3, 122.7, 117.2, 116.9, 115.3, 100.1, 57.6, 29.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1287, 1645, 1700, 2923, 2960; Elem. Anal. calcd for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18, found: C, 77.23; H, 5.33; N, 8.24.



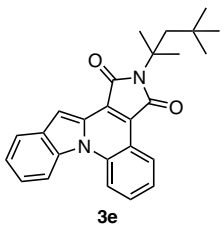
3c

2-Isopropyl-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3d**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 82% (269 mg, 0.819 mmol) from the corresponding Ugi product (518 mg, 1.00 mmol); mp 228–231 ˚C; ^1H-NMR (300 MHz, $CDCl_3$): δ 8.79 (dd, 1H, J = 1.5 Hz, J = 1.5 Hz), 8.55 (d, 1H, J = 8.4 Hz), 8.41 (d, 1H, J = 8.4 Hz), 7.96 (d, 1H, J = 7.2 Hz), 7.70–7.76 (m, 1H), 7.44–7.55 (m, 4), 4.55–4.64 (m, 1H), 1.60 (d, 6H, J = 6.9 Hz); $^{13}C\{^1H\}$-NMR (75 MHz, $CDCl_3$): δ 169.1, 167.7, 138.2, 133.8, 131.1, 130.9, 127.9, 127.1, 125.1, 124.1, 123.9, 123.5, 122.8, 122.6, 117.6, 115.9, 114.4, 100.5, 43.1, 20.3; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1362, 1610, 1701, 2873, 2931; Elem. Anal. calcd for $C_{21}H_{16}N_2O_2$: C, 76.81; H, 4.91; N, 8.53, found: C, 76.53; H, 4.87; N, 8.42.



3d

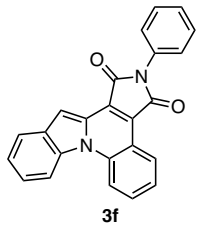
2-(2,4,4-Trimethylpentan-2-yl)-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3e**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 75% (298 mg, 0.748 mmol) from the corresponding Ugi product (575 mg, 1.00 mmol); mp 201–203 ˚C; ^1H-NMR (400 MHz, $CDCl_3$): δ 8.91 (dd, 1H, J = 1.5 Hz, J = 1.5 Hz), 8.71 (d, 1H, J = 8.4 Hz), 8.51–8.57 (m, 1H), 8.04 (d, 1H, J = 7.8 Hz), 7.80–7.86 (m, 1H), 7.73 (s, 1H), 7.47–7.64 (m, 8H); $^{13}C\{^1H\}$-NMR (100 MHz, $CDCl_3$): δ 170.8, 169.3, 138.4, 133.9, 131.1, 131.0, 127.9, 127.2, 125.1, 124.0, 123.9, 123.3, 122.8, 122.6, 117.5, 116.0, 114.4, 100.7, 61.3, 51.1, 31.7, 31.1,



3e

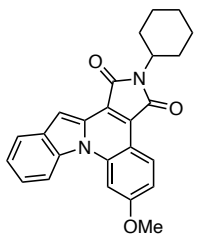
30.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1351, 1610, 1703, 2855, 2926; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{26}H_{26}N_2O_2^+$ 399.2074, found: 399.2063.

2-Phenyl-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3f**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 75% (271 mg, 0.749 mmol) from the corresponding Ugi product (575 mg, 1.00 mmol); mp 198–200 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.92 (dd, 1H, *J* = 1.5 Hz, *J* = 1.5 Hz), 8.72 (d, 1H, *J* = 8.4 Hz), 8.56 (d, 1H, *J* = 8.7 Hz), 8.05 (d, 1H, *J* = 7.8 Hz), 7.78–7.87 (m, 1H), 7.73 (s, 1H), 7.52–7.64 (m, 6H), 7.44–7.50 (m, 2H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 182.0, 181.9, 138.5, 134.1, 131.6, 131.0, 129.2, 128.0, 127.5, 127.3, 126.5, 124.5, 124.2, 123.5, 123.1, 122.8, 121.3, 117.5, 116.1, 114.5, 112.3, 101.3; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1382, 1641, 1709, 2853, 2923; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{24}H_{14}N_2O_2^+$ 363.1135, found: 363.1131.



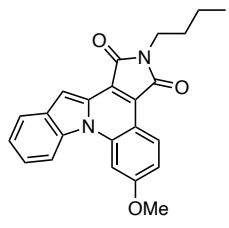
3f

2-Cyclohexyl-5-methoxy-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*) dione (**3g**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 88% (350 mg, 0.878 mmol) from the corresponding Ugi product (589 mg, 1.00 mmol); mp 245–247 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.69 (d, 1H, *J* = 8.7 Hz), 8.30 (d, 1H, *J* = 7.8 Hz), 7.93–7.98 (m, 2H), 7.45–7.51 (m, 3H), 7.01 (dd, 1H, *J* = 2.4 Hz, *J* = 2.1 Hz), 4.14 (m, 1H), 4.02 (s, 1H), 2.21–2.34 (m, 2H), 1.76–1.97 (m, 5H), 1.36–1.48 (m, 3H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 169.3, 168.0, 162.3, 139.8, 133.5, 131.2, 128.4, 128.3, 124.1, 123.5, 122.8, 122.3, 121.7, 114.1, 111.2, 110.4, 101.7, 99.8, 55.8, 50.9, 30.2, 29.7, 26.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1350, 1613, 1701, 2852, 2923; Elem. Anal. calcd for $C_{25}H_{22}N_2O_3$: C, 75.36; H, 5.57; N, 7.03, found: C, 75.21; H, 5.51; N, 7.11.



3g

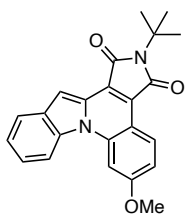
2-Butyl-5-methoxy-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3h**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 85% (316 mg, 0.849 mmol) from the corresponding Ugi product (563 mg, 1.00 mmol); mp 190–192 °C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.39 (d, 1H, *J* = 8.7 Hz), 7.95–7.98 (m, 1H), 7.77–7.80 (m, 1H), 7.55 (s, 1H), 7.32–7.39 (m, 2H), 7.21 (s, 1H), 6.78 (dd, 1H, *J* = 1.5 Hz, *J* = 1.8 Hz), 3.88 (s, 3H), 3.62 (t, 2H, *J* = 7.2 Hz), 1.66–1.76 (m, 2H), 1.39–1.52 (m, 2H), 1.03 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 169.0, 167.7, 162.0, 139.2, 133.0, 130.9, 128.0, 127.9, 123.8, 123.4, 122.6, 122.1, 121.2, 113.9, 110.7, 110.2, 101.0, 99.6, 55.6, 37.6, 30.9, 20.2, 13.7; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1356,



3h

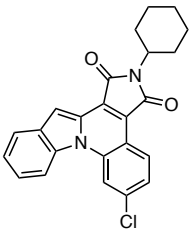
1617, 1700, 2860, 2925; Elem. Anal. calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52, Found: C, 74.08; H, 5.44; N, 7.48.

2-(*tert*-Butyl)-5-methoxy-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3i**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 79% (294 mg, 0.789 mmol) from the corresponding Ugi product (562 mg, 1.00 mmol); mp 249–251 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.75 (d, 1H, J = 9 Hz), 8.39 (d, 1H, J = 7.8 Hz), 8.08 (s, 1H), 7.95–7.98 (m, 1H), 7.44–7.53 (m, 3H), 7.03 (dd, 1H, J = 2.1 Hz, J = 2.1 Hz), 4.05 (s, 3H), 1.79 (s, 9H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 170.6, 169.2, 162.2, 140.0, 133.5, 131.2, 128.5, 128.3, 124.0, 123.5, 122.8, 122.4, 121.9, 114.2, 111.1, 110.3, 101.8, 99.9, 57.7, 55.8, 29.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1349, 1614, 1700, 2853, 2923; Elem. Anal. calcd for $C_{23}H_{20}N_2O_3$: C, 74.18; H, 5.41; N, 7.52, found: C, 75.01; H, 5.37; N, 7.47.



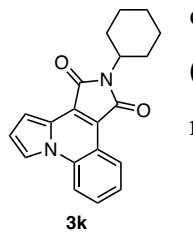
3i

6-Chloro-2-cyclohexyl-1*H*-indolo[1,2-*a*]pyrrolo[3,4-*c*]quinoline-1,3(2*H*)-dione (**3**j: Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 72% (291 mg, 0.722 mmol) from the corresponding Ugi product (593 mg, 1.00 mmol); mp 183–185 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.58 (d, 1H, J = 9.3 Hz), 8.34 (s, 1H), 8.15 (d, 1H, J = 8.1 Hz), 7.19–7.46 (m, 4H), 3.99–4.14 (m, 1H), 2.14–2.18 (m, 1H), 1.68–1.87 (m, 3H, 1.18–1.26 (m, 5H), 0.80–0.84 (m, 1H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 137.5, 136.2, 132.6, 129.9, 126.8, 126.8, 123.5, 123.2, 122.2, 121.7, 114.9, 114.8, 113.0, 110.1, 50.0, 29.1, 28.7, 25.1, 24.2; IR (KBr) $\tilde{\nu}$ (cm^{-1}) = 1378, 1642, 1701, 2867, 2944; MS (ESI) $[M+H]^+$: m/z calcd for $C_{24}H_{20}ClN_2O_2^+$ 403.11, found: 403.13. Elem. Anal. calcd for $C_{24}H_{19}ClN_2O_2$: C, 71.55; H, 4.75; N, 6.95; Found C, 71.38; H, 4.68; N, 7.01.



3j

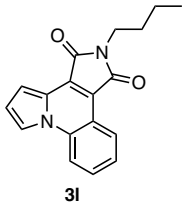
2-Cyclohexyl-1*H*-dipyrrolo[1,2-*a*:3',4'-*c*]quinoline-1,3(2*H*)-dione (**3k**): Flash column chromatography (in *n*-hexane) yielded the title compound as orange powder in 84% (267 mg, 0.839 mmol) from the corresponding Ugi product (509 mg, 1.00 mmol); mp 275–277 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.78 (d, 1H, J = 8.1 Hz), 8.1 (s, 1H), 7.78 (d, 1H, J = 8.4 Hz), 7.68–7.69 (m, 1H), 7.51–7.54 (m, 1H) 7.30–7.34 (m, 1H), 7.03–7.06 (m, 1H), 4.09–4.18 (m, 1H), 2.21–2.33 (m, 2H), 1.91–1.95 (m, 2H), 1.74–1.85 (m, 3H), 1.38–1.50 (m, 3H); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 169.7, 168.1, 134.3, 130.2, 126.8, 125.1, 123.6, 118.9, 118.6, 117.5, 116.2, 115.8, 114.8, 106.8, 50.8, 30.2, 26.1, 25.2;



3k

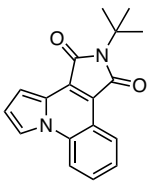
IR (KBr) ṽ (cm^{-1}) = 1349, 1624, 1698, 2851, 2920; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{20}H_{18}N_2O_2^+$ 319.1448, found 319.1439.

2-Butyl-1*H*-dipyrrolo[1,2-*a*:3',4'-*c*]quinoline-1,3(2*H*)-dione (**3l**): Flash column chromatography (in *n*-hexane) yielded the title compound as violet powder in 82% (239 mg, 0.818 mmol) from the corresponding Ugi product (482 mg, 1.00 mmol); mp 116–118 ˚C; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 8.77 (dd, 1H, *J* = 1.2 Hz, *J* = 1.2 Hz), 8.09 (dd, 1H, *J* = 1.2 Hz, *J* = 0.9 Hz), 7.97 (d, 1H, *J* = 8.4 Hz), 7.65–7.71 (m, 1H), 7.48–7.54 (m, 1H), 7.33 (dd, 1H, *J* = 0.9 Hz, *J* = 1.2 Hz), 7.04 (dd, 1H, *J* = 2.7 Hz, *J* = 2.7 Hz), 3.70–3.75 (m, 2H), 1.68–1.78 (m, 2H), 1.40–1.48 (m, 2H), 1.00 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H}-NMR (75 MHz, $CDCl_3$): δ 169.7, 168.1, 134.2, 130.3, 126.8, 125.2, 125.1, 123.6, 118.8, 117.5, 116.3, 115.8, 114.7, 106.9, 37.7, 30.9, 20.1, 13.7; IR (KBr) ṽ (cm^{-1}) = 1362, 1625, 1704, 2854, 2925; HR-MS (ESI) $[M+H]^+$: *m*/*z* calcd for $C_{18}H_{16}N_2O_2^+$ 393.1292, found: 393.1285.



3l

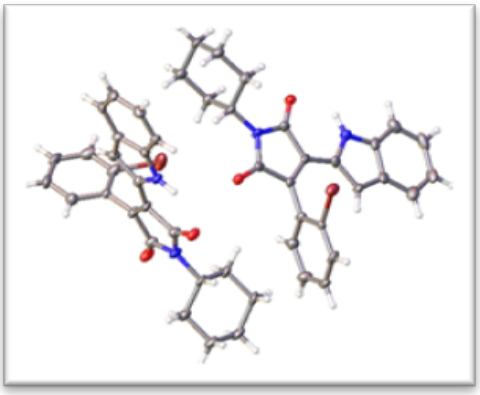
2-(tert-Butyl)-1H-dipyrrolo[1,2-a:3',4'-c]quinoline-1,3(2H)-dione (**3m**): Flash column chromatography (in n-hexane) yielded the title compound as orange powder in 86% (250 mg, 0.855 mmol) from the corresponding Ugi product (482 mg, 1.00 mmol); mp 198–200 ˚C; 1H-NMR (300 MHz, CDCl3): δ 8.78 (d, 1H, J = 8.1 Hz), 8.06 (s, 1H), 7.95 (d, 1H, J = 8.4 Hz), 7.64–7.69 (m, 1H), 7.47–7.52 (m, 1H), 7.30 (d, 1H, J = 3.0 Hz), 7.00–7.03 (m, 1H), 1.77 (s, 9H); 13C{1H}-NMR (75 MHz, CDCl3): 171.0,169.2, 134.4, 130.1, 126.8, 125.1, 125.0, 123.4, 118.5, 117.4, 116.0, 115.6, 114.7, 106.7, 57.6, 29.2; IR (KBr) ṽ (cm–1) = 1355, 1612, 1697, 2850, 2953; HR-MS (ESI) [M+H]+: m/z calcd for C18H16N2O2+ 293.1292, found: 293.1283.



3m

2. Details of the Crystallographic Studies

Single crystals of **2a** were prepared by slow evaporation of a n-hexane solution. Crystallographic single crystal X-ray data were collected on a SuperNova instrument with a micro-focus sealed X-ray tube (Mo K-alpha radiation: λ = 0.71073 Å) or a Bruker Kappa Apex2 diffractometer with a micro-focus sealed X-ray tube (Ag K-alpha radiation: λ = 0.56086 Å). Absorption correction was done with SADABS. Cell refinement and data reduction were done in SAINT-plus.[2] The structures were solved and refined with SHELXT and SHELXL, respectively, in Olex2.[3]



Item	Value
Molecular formula	C24 H21 Br N2 O2
Formula weight	449.34
Crystal system	triclinic
Space Group	P -1
a (Å)	12.1123
b (Å)	13.4106
c (Å)	15.0272
α (°)	90.102
β (°)	111.664
γ (°)	113.639
Volume ($Å^3$)	2045.7
Z	4
T (K)	153
ρ ($g\ cm^{-1}$)	1.459
λ (Å)	0.71073
μ (mm^{-1})	2.032
# measured refl	15127
# unique refl	6435
R_{int}	0.1047
# parameters	523
$R(F^2)$, all refl	0.0941
$R_w(F^2)$, all refl	0.2834
Goodness of fit	1.209

Crystal data for [**2a**]: C24 H21 Br N2 O2, M = 449.34, triclinic, Space group P -1 (no. 2), a = 12.1123(7) Å, b = 13.4106(9) Å, c = 15.0272(7) Å, α = 90.102(5)°, β = 111.664(5)°, γ = 113.639(6)°, V = 2045.7(2) $Å^3$, T = 153 K, Z = 4, d_c = 1.459 g cm^{-3}, μ(Mo Kα, λ = 0.71073 Å) = 2.032 mm^{-1}, 15127 reflections collected, 6435 unique [R_{int} = 0.1047], which were used in all calculations. Refinement on F^2, final R(F) = 0.0941, R_w(F2) = 0.2834. CCDC number unknown. CCDC: 1976139.

3. Details of the Computational Investigations

The conformational space for each structure was explored by using the OPLS3 force field[4] and a modified Monte Carlo search algorithm implemented in MacroModel.[5] An energy cutoff of 100 kJ mol^{-1} was employed for the conformational analysis, and structures with heavy-atom root mean-square deviations (RMSD) of up to 1.5 Å after the initial force-field optimizations were considered to be the same conformer. The remaining structures were then optimized with the PBE0 functional,[6] Grimme's D3 correction with Becke-Johnson damping,[7] and the triple-ζ basis set def2-TZVP.[8] The calculations an extremely fine grid with 99 radial shells per atom and 974 angular points per shell for the numerical integration of the density. Vibrational analysis verified that each structure was a minimum or a transition state and for the latter, following the intrinsic reaction coordinates (IRC) confirmed that all transition states connected the corresponding reactants and products on the potential energy surface. Thermal corrections were obtained from unscaled harmonic vibrational frequencies at the same level of theory for a standard state of 1 mol L^{-1} and 298.15 K. Entropic contributions to free energies were obtained from partition functions evaluated with Grimme's quasi-harmonic approximation.[9] This method employs the free-rotor approximation for all frequencies below 100 cm^{-1}, the rigid-rotor-harmonic-oscillator (RRHO) approximation for all frequencies above 100 cm^{-1}, and a damping function to interpolate between the two expressions. Similar results were obtained from partition functions evaluated with Cramer's and Truhlar's quasiharmonic approximation.[10] Electronic energies were subsequently calculated with the double-hybrid functional DSD-BLYP,[11] the triple-ζ basis set def2-TZVPPD,[8] Grimme's D3 correction with Becke-Johnson damping,[7] and the SMD solvation model for DMSO.[12] The calculations were performed with Gaussian16[13] and ORCA.[14]

Starting Material: 2-(2-Bromophenyl)acetic Acid

SCF energy:	–3032.670824 hartree
Zero-point correction:	+0.133948 hartree
Enthalpy correction:	+0.144920 hartree
Free energy correction:	+0.095684 hartree
Truhlar's Delta G correction:	+0.097966 hartree
Grimme's Delta G correction:	+0.097538 hartree

Cartesian Coordinates

C	2.69492	1.65062	-0.04704
C	1.38961	1.88204	-0.44633
C	3.07985	0.37771	0.34237
C	2.15852	-0.65693	0.33388
C	0.85718	-0.40440	-0.06582
C	0.44359	0.86304	-0.46655
H	3.40977	2.46446	-0.03881
H	1.08604	2.87926	-0.74593
H	4.09836	0.18347	0.65688
H	2.44346	-1.65553	0.63880
Br	-0.37649	-1.84004	-0.05088
C	-0.96241	1.13841	-0.88770
C	-1.92660	1.24390	0.28497
H	-1.30889	0.36861	-1.58391
H	-1.01005	2.09618	-1.41603
O	-1.60380	1.49669	1.40365
O	-3.22572	1.08633	-0.03569
H	-3.31336	0.83439	-0.96080

Starting Material: Pyrrole-2-carbaldehyde

SCF energy:	–323.253475 hartree
Zero-point correction:	+0.093054 hartree
Enthalpy correction:	+0.099650 hartree
Free energy correction:	+0.063591 hartree
Truhlar's Delta G correction:	+0.063591 hartree
Grimme's Delta G correction:	+0.063604 hartree

Cartesian Coordinates

C	-1.60635	-0.90883	0.00006
C	-1.97990	0.42238	-0.00008
N	-0.25924	-0.96946	-0.00002
C	0.26402	0.29324	0.00001
C	-0.79891	1.18198	0.00006
H	-2.21091	-1.80207	0.00009
H	-2.99296	0.79166	-0.00015
H	-0.71431	2.25793	0.00008
C	1.68823	0.50333	0.00001
O	2.50105	-0.39809	-0.00002
H	2.00386	1.56482	-0.00005
H	0.31813	-1.79392	-0.00004

Starting Material: 2-Isocyano-2-methylpropane

SCF energy:	–250.436995 hartree
Zero-point correction:	+0.129949 hartree
Enthalpy correction:	+0.138268 hartree
Free energy correction:	+0.099688 hartree
Truhlar's Delta G correction:	+0.099688 hartree
Grimme's Delta G correction:	+0.099684 hartree

Cartesian Coordinates

C	-0.72911	-1.34281	-0.54621
C	-0.25354	-0.00006	-0.00000
H	-1.82044	-1.36784	-0.55629
H	-0.36654	-2.16179	0.07667
H	-0.36669	-1.49428	-1.56403
C	-0.72827	0.19806	1.43621
H	-1.81953	0.20074	1.46345
H	-0.36664	1.14755	1.83366
H	-0.36486	-0.60698	2.07657
C	-0.72957	1.14460	-0.88932
H	-1.82091	1.16562	-0.90566
H	-0.36725	1.01514	-1.91021
H	-0.36733	2.10178	-0.51144
N	1.17802	0.00001	-0.00064
C	2.34284	0.00020	-0.00038

Starting Material: Toluidine

SCF energy:	–326.626194 hartree
Zero-point correction:	+0.144788 hartree
Enthalpy correction:	+0.153443 hartree
Free energy correction:	+0.111932 hartree
Truhlar's Delta G correction:	+0.113456 hartree
Grimme's Delta G correction:	+0.112991 hartree

Cartesian Coordinates

C	-0.71626	-1.19554	-0.00819
C	-1.43423	0.00000	-0.00447
C	0.66762	-1.18724	-0.01070
C	1.39277	0.00001	-0.00915
C	0.66761	1.18724	-0.01070
C	-0.71628	1.19554	-0.00819
N	-2.82206	-0.00001	-0.06304
C	2.89119	-0.00000	0.02234
H	3.29901	0.88341	-0.47325
H	3.29905	-0.88256	-0.47478
H	3.26975	-0.00089	1.04980
H	-1.25073	-2.14031	-0.01771
H	1.19832	-2.13435	-0.01541
H	1.19831	2.13436	-0.01541
H	-1.25074	2.14031	-0.01770
H	-3.26154	-0.83438	0.29005
H	-3.26156	0.83437	0.29003

Ugi Adduct ***1i****: 2-(2-Bromophenyl)-N-(2-(tert-butylamino)-2-oxo-1-(1H-pyrrol-2-yl)ethyl)-N-(p-tolyl)acetamide*

SCF energy:	–3856.678127 hartree
Zero-point correction:	+0.487390 hartree
Enthalpy correction:	+0.518266 hartree
Free energy correction:	+0.423937 hartree
Truhlar's Delta G correction:	+0.432477 hartree
Grimme's Delta G correction:	+0.431135 hartree

Cartesian Coordinates

C	0.94926	-0.00881	2.32834
C	1.40878	-0.54129	1.02210
C	2.74338	0.03594	0.52469
N	3.37447	-0.79022	-0.32145
C	4.56528	-0.45980	-1.10837
C	4.88730	-1.69962	-1.93115
H	5.10203	-2.55205	-1.28217
H	5.76281	-1.51666	-2.55608
H	4.05129	-1.96534	-2.58380
C	5.73241	-0.13428	-0.18242
H	5.93532	-0.97625	0.48300
H	5.51210	0.74365	0.42338
H	6.62988	0.06122	-0.77381
C	4.27046	0.71788	-2.03457
H	3.45980	0.46607	-2.72353
H	5.15536	0.96168	-2.62682
H	3.98507	1.59722	-1.45686
O	3.13717	1.15267	0.83620
H	2.84655	-1.61546	-0.58863
C	0.08951	-0.57824	3.24294
C	-0.12156	0.37179	4.26792
C	0.62129	1.48578	3.94767
N	1.25418	1.24165	2.77357
H	-0.35129	-1.56019	3.16108
H	-0.73439	0.25160	5.14735
H	0.75771	2.41640	4.47426
H	1.92664	1.81562	2.28439
N	0.40759	-0.34231	-0.05159
H	1.50728	-1.62376	1.10581
C	-0.15708	0.95122	-0.22647
C	-1.12937	1.42847	0.64472
C	0.28939	1.75554	-1.26313
C	-0.26645	3.01066	-1.45899
C	-1.25658	3.49269	-0.61181
C	-1.66642	2.68511	0.44849
H	-2.43307	3.04371	1.12716
H	-1.46189	0.80532	1.46478
H	0.08448	3.62863	-2.27871
C	-1.87802	4.83767	-0.82823
H	1.07860	1.39614	-1.91388
H	-1.36679	5.39078	-1.61713
H	-1.84743	5.43928	0.08339
H	-2.92955	4.73979	-1.11408
C	0.26203	-1.34149	-0.96028
O	1.01176	-2.30877	-0.98377
C	-0.86616	-1.25046	-1.97829

C	-2.18148	-0.67988	-1.54294
H	-0.99053	-2.27982	-2.32134
H	-0.49444	-0.67705	-2.83186
C	-2.71919	0.42252	-2.20276
C	-2.92976	-1.22186	-0.50034
C	-4.14129	-0.67643	-0.10683
C	-4.63916	0.43224	-0.77053
C	-3.92818	0.97901	-1.82752
H	-2.15191	0.86585	-3.01316
Br	-2.30077	-2.74405	0.43006
H	-4.68711	-1.12229	0.71468
H	-5.58453	0.86186	-0.46095
H	-4.31046	1.84460	-2.35517

*Iminium Intermediate **4**:*

SCF energy:	–3855.890165 hartree
Zero-point correction:	+0.475634 hartree
Enthalpy correction:	+0.506591 hartree
Free energy correction:	+0.412984 hartree
Truhlar's Delta G correction:	+0.420717 hartree
Grimme's Delta G correction:	+0.419648 hartree

Cartesian Coordinates

C	1.00453	2.55706	-0.27402
C	1.06729	1.32285	0.36495
C	2.50672	0.84687	0.61054
N	2.92412	-0.10835	-0.22268
C	4.25682	-0.74807	-0.17915
C	4.24800	-1.80639	-1.27174
H	3.49467	-2.57406	-1.07287
H	5.21797	-2.30221	-1.31240
H	4.05452	-1.36392	-2.25244
C	4.47836	-1.39386	1.18302
H	3.70890	-2.14032	1.38832
H	4.45706	-0.64884	1.97769
H	5.45160	-1.88794	1.19688
C	5.32693	0.29707	-0.47079
H	5.16315	0.75555	-1.44907
H	6.30894	-0.17884	-0.48070
H	5.33247	1.07409	0.29324
O	3.15033	1.46094	1.43010
H	2.22456	-0.56165	-0.79095
C	2.12157	3.26327	-0.78546
C	1.67309	4.45420	-1.31439
C	0.28968	4.48601	-1.12320
N	-0.09788	3.36639	-0.51545
H	3.14107	2.91607	-0.73558
H	2.26187	5.22787	-1.77946
H	-0.42565	5.25007	-1.38914
H	-1.04677	3.13920	-0.26585
N	0.02271	0.59858	0.79389
C	-1.31997	1.01984	0.51359
C	-1.84323	0.83981	-0.75987
C	-2.07016	1.62160	1.50958
C	-3.36647	2.02978	1.22860

C	-3.92133	1.84685	-0.03533
C	-3.13372	1.25343	-1.02498
H	-3.54616	1.10174	-2.01596
H	-1.24209	0.36962	-1.52866
H	-3.95497	2.50049	2.00789
C	-5.33217	2.24533	-0.32535
H	-1.64134	1.78011	2.49286
H	-5.71502	2.94217	0.42003
H	-5.98149	1.36469	-0.32167
H	-5.42183	2.70611	-1.31049
C	0.23313	-0.57272	1.62406
O	1.30376	-0.75502	2.11371
C	-0.95125	-1.46847	1.90481
C	-1.91321	-1.82349	0.81022
H	-1.50698	-1.00333	2.72521
H	-0.49242	-2.36894	2.32024
C	-3.28048	-1.66001	1.01943
C	-1.51736	-2.37471	-0.40529
C	-2.42940	-2.72465	-1.38689
C	-3.78210	-2.53527	-1.15502
C	-4.20837	-2.00799	0.05431
H	-3.61647	-1.24386	1.96264
Br	0.32069	-2.67048	-0.76297
H	-2.08207	-3.15214	-2.31867
H	-4.49911	-2.81526	-1.91719
H	-5.26538	-1.87371	0.24916

*Intermediate **5***

SCF energy:	–3855.430838 hartree
Zero-point correction:	+0.463056 hartree
Enthalpy correction:	+0.493555 hartree
Free energy correction:	+0.399833 hartree
Truhlar's Delta G correction:	+0.408705 hartree
Grimme's Delta G correction:	+0.407175 hartree

Cartesian Coordinates

C	-0.37040	0.17531	2.06217
C	0.47981	0.71447	1.02417
C	1.97578	0.49923	1.13475
N	2.71151	0.53849	-0.06816
C	3.68520	1.65817	-0.29855
C	3.59822	2.66619	0.84209
H	2.58030	3.04661	0.96174
H	4.23770	3.51138	0.58498
H	3.93663	2.25474	1.79158
C	3.28588	2.38180	-1.58426
H	2.24847	2.71499	-1.51650
H	3.39618	1.74029	-2.45434
H	3.92702	3.25713	-1.70833
C	5.10037	1.10117	-0.37574
H	5.36362	0.60499	0.56071
H	5.80321	1.92158	-0.53814
H	5.19958	0.39347	-1.19692
O	2.52327	0.40034	2.20629
C	-1.75307	0.02935	2.13051
C	-2.04757	-0.67190	3.30660
C	-0.84806	-0.93569	3.93921

N	0.14572	-0.43259	3.18222
H	-2.45915	0.37329	1.39430
H	-3.02496	-0.96109	3.65793
H	-0.64169	-1.43313	4.87342
H	1.12840	-0.40346	3.40343
N	0.14430	1.40606	0.00323
C	-1.15275	1.89516	-0.17053
C	-1.62662	2.94764	0.61062
C	-1.96406	1.37886	-1.17469
C	-3.24131	1.88265	-1.35932
C	-3.73319	2.92697	-0.58340
C	-2.89639	3.45228	0.39866
H	-3.24959	4.27126	1.01733
H	-0.99429	3.35685	1.38999
H	-3.86882	1.45147	-2.13307
C	-5.09989	3.49397	-0.81811
H	-1.59687	0.56678	-1.78815
H	-5.75943	2.75957	-1.28388
H	-5.05764	4.36365	-1.48151
H	-5.56117	3.82071	0.11616
C	2.53454	-0.44926	-1.00244
O	3.15544	-0.48452	-2.04520
C	1.59728	-1.58570	-0.64458
C	0.36052	-1.68138	-1.49657
H	1.30652	-1.58052	0.40637
H	2.19016	-2.49743	-0.77951
C	0.29362	-1.12249	-2.77143
C	-0.76350	-2.37456	-1.04660
C	-1.91543	-2.48131	-1.81072
C	-1.95606	-1.90776	-3.07002
C	-0.84463	-1.23436	-3.55212
H	1.16219	-0.60092	-3.15138
Br	-0.75463	-3.24558	0.63580
H	-2.76864	-3.01910	-1.41815
H	-2.85416	-1.99395	-3.67018
H	-0.86168	-0.78711	-4.53881

*Maleimide **2i**: 4'-(2-Bromophenyl)-1'-(tert-butyl)-1H,1'H-[2,3'-bipyrrole]-2',5'-dione*

SCF energy:	–3528.832924 hartree
Zero-point correction:	+0.316641 hartree
Enthalpy correction:	+0.338459 hartree
Free energy correction:	+0.265289 hartree
Truhlar's Delta G correction:	+0.269946 hartree
Grimme's Delta G correction:	+0.269308 hartree

Cartesian Coordinates

C	-2.06006	3.55347	-0.99147
C	-0.88371	4.22153	-0.69712
N	0.07195	3.30513	-0.45564
C	-1.78828	2.18244	-0.91956
C	-0.44430	2.03898	-0.58274
H	-2.47954	1.37389	-1.09254
C	0.36637	0.88523	-0.39990
C	0.06430	-0.42980	-0.44442
C	1.84877	1.00199	-0.13991

O	2.44925	2.04756	-0.01761
O	1.44088	-2.39240	-0.30663
C	1.31632	-1.19436	-0.27606
N	2.36329	-0.27259	-0.07436
C	-1.21484	-1.10748	-0.65399
C	-1.40336	-1.87099	-1.80682
C	-2.59817	-2.52244	-2.05353
C	-3.63413	-2.43201	-1.13641
C	-3.46583	-1.70310	0.02918
C	-2.26327	-1.05576	0.26621
H	-0.58822	-1.94017	-2.51700
H	-2.71934	-3.10180	-2.96076
H	-4.57509	-2.93752	-1.31883
H	-4.25885	-1.64156	0.76319
Br	-2.06550	-0.12879	1.89910
H	1.04594	3.45523	-0.23245
C	3.76363	-0.70646	0.16556
C	4.69286	0.48200	0.37903
C	4.24348	-1.49012	-1.05425
C	3.79176	-1.57783	1.41965
H	4.73339	1.13734	-0.48936
H	5.69211	0.07775	0.55434
H	4.40693	1.07969	1.24312
H	3.44146	-1.00981	2.28442
H	4.81884	-1.89337	1.61409
H	3.17233	-2.46526	1.30404
H	4.21759	-0.85886	-1.94548
H	3.63124	-2.37364	-1.22587
H	5.27576	-1.80810	-0.89408
H	-3.00534	4.01535	-1.22724
H	-0.67375	5.27787	-0.64492

Copper-Proline Complex

SCF energy:	–2040.485357 hartree
Zero-point correction:	+0.134957 hartree
Enthalpy correction:	+0.144503 hartree
Free energy correction:	+0.099381 hartree
Truhlar's Delta G correction:	+0.100910 hartree
Grimme's Delta G correction:	+0.100607 hartree

Cartesian Coordinates

C	1.02329	-1.81773	-0.27337
C	2.05837	-0.84260	-0.81628
N	0.15610	-1.00766	0.63470
H	1.50448	-2.61196	0.30431
H	0.42997	-2.28759	-1.05789
C	0.78723	0.34872	0.78031
C	2.22340	0.15081	0.32306
H	2.83005	-0.28390	1.12423
H	2.66047	1.10043	0.02243
H	1.67080	-0.32787	-1.69967
H	2.98311	-1.34597	-1.10023
C	0.08756	1.50952	-0.00957
H	0.71910	0.64608	1.82998
O	0.75563	2.51612	-0.15014
O	-1.12501	1.34549	-0.39521
Cu	-1.66036	-0.46104	-0.03694

H	0.13562	-1.45053	1.54324

*Cu-Substrate Complex **6***

SCF energy:	–5569.345045 hartree
Zero-point correction:	+0.452212 hartree
Enthalpy correction:	+0.484607 hartree
Free energy correction:	+0.386110 hartree
Truhlar's Delta G correction:	+0.395200 hartree
Grimme's Delta G correction:	+0.393968 hartree

Cartesian Coordinates

C	-0.78098	-2.18171	3.28776
C	-1.41501	-0.96707	3.40781
N	-0.77846	-0.05950	2.57673
C	0.28512	-2.02532	2.38305
C	0.30412	-0.70969	1.96554
H	0.96309	-2.79292	2.04506
C	1.14613	0.01215	1.07292
C	1.97775	-0.40790	0.09814
C	1.25130	1.50943	1.16716
O	0.62648	2.19339	1.94938
O	3.54276	0.80481	-1.27220
C	2.68589	0.78874	-0.42797
N	2.17506	1.92217	0.23415
C	2.24672	-1.74192	-0.42821
C	3.57183	-2.18651	-0.47664
C	3.89513	-3.44528	-0.94545
C	2.89208	-4.29015	-1.39644
C	1.57454	-3.86534	-1.38915
C	1.25582	-2.60025	-0.91822
H	4.35130	-1.52022	-0.12926
H	4.92980	-3.76525	-0.96103
H	3.13197	-5.27930	-1.76806
H	0.78568	-4.50633	-1.76132
Br	-0.56015	-2.08732	-1.01062
C	2.67648	3.29551	-0.04442
C	4.15830	3.34888	0.31898
C	1.92877	4.34021	0.77442
C	2.46896	3.60075	-1.52651
H	4.29887	3.12553	1.37896
H	4.53914	4.35472	0.13156
H	4.73949	2.64456	-0.27414
H	3.00858	2.90169	-2.16190
H	2.83051	4.60953	-1.73463
H	1.40742	3.56625	-1.78185
H	2.06844	4.20696	1.84541
H	0.85925	4.33855	0.56796
H	2.33073	5.31500	0.49117
H	-1.08066	-3.09427	3.77724
H	-2.23210	-0.65512	4.03786
Cu	-2.15116	-0.18811	1.10989
O	-3.52621	-0.92746	-0.00420
N	-2.01783	1.30476	-0.48051
C	-3.43569	1.27627	-0.89140
C	-1.61876	2.69475	-0.71520
C	-2.38171	3.15380	-1.97612
C	-3.48608	2.09628	-2.17143

C	-3.97558	-0.16022	-0.93764
O	-4.77448	-0.46564	-1.80075
H	-1.51151	0.72575	-1.14948
H	-0.53492	2.76466	-0.81108
H	-1.91044	3.28502	0.15696
H	-1.71882	3.19718	-2.84269
H	-2.79128	4.15622	-1.83816
H	-3.27685	1.44258	-3.02081
H	-4.47054	2.52957	-2.34228
H	-3.99519	1.79551	-0.10118
H	-0.68390	0.94011	2.75448

Deprotonated Cu-Substrate Complex 7

SCF energy:	–5568.890495 hartree
Zero-point correction:	+0.438713 hartree
Enthalpy correction:	+0.470953 hartree
Free energy correction:	+0.371833 hartree
Truhlar's Delta G correction:	+0.381820 hartree
Grimme's Delta G correction:	+0.380000 hartree

Cartesian Coordinates

C	0.43501	4.56004	-0.68099
C	-0.70216	3.78302	-0.40734
N	-0.37889	2.51015	-0.16088
C	1.51369	3.69968	-0.59910
C	0.99642	2.42134	-0.26966
H	2.55595	3.92724	-0.74055
C	1.74700	1.25424	-0.00661
C	1.44132	0.01742	0.50351
C	3.23498	1.22870	-0.29643
O	3.90306	2.09850	-0.80804
O	2.80440	-1.81494	1.23313
C	2.67618	-0.75171	0.67043
N	3.72982	0.00663	0.11618
C	0.19956	-0.53872	1.03720
C	-0.52440	0.14714	2.02338
C	-1.64601	-0.40042	2.62407
C	-2.07115	-1.67010	2.26475
C	-1.39160	-2.36936	1.27789
C	-0.28600	-1.79692	0.66582
H	-0.17355	1.12747	2.32078
H	-2.20769	0.18094	3.34268
H	-2.95275	-2.10251	2.72285
H	-1.72771	-3.34920	0.96192
Br	0.47555	-2.73988	-0.79206
C	5.15181	-0.36034	-0.02989
C	5.52630	-0.29718	-1.51185
C	5.43148	-1.77508	0.46552
C	6.00285	0.61569	0.78225
H	6.57639	-0.57551	-1.63243
H	5.37764	0.70244	-1.91548
H	4.91744	-1.00351	-2.08114
H	5.86065	1.63915	0.43871
H	7.05904	0.35304	0.68058
H	5.73553	0.55538	1.83984
H	6.49188	-1.97286	0.28577
H	4.84163	-2.51886	-0.06850

H	5.22492	-1.88953	1.52745
H	0.45321	5.61754	-0.90037
H	-1.73641	4.09817	-0.37456
Cu	-1.79566	1.22408	-0.03118
O	-3.58419	1.46478	1.14157
N	-2.93780	-0.27325	-0.81586
C	-4.32876	0.19445	-0.68978
C	-2.92214	-0.99584	-2.08648
C	-4.27677	-1.73045	-2.15685
C	-5.17458	-0.98950	-1.14221
C	-4.56107	0.77975	0.71667
O	-5.63336	0.54876	1.27316
H	-2.79599	-0.96384	-0.07747
H	-2.05486	-1.65499	-2.13830
H	-2.83574	-0.26112	-2.89130
H	-4.15915	-2.78204	-1.88317
H	-4.68585	-1.70908	-3.16990
H	-5.40851	-1.60888	-0.27371
H	-6.12695	-0.67152	-1.56700
H	-4.44219	1.02320	-1.40073

Transition State Oxidative Addition ***TS1***

SCF energy:	–5568.879720 hartree
Zero-point correction:	+0.437825 hartree
Enthalpy correction:	+0.469146 hartree
Free energy correction:	+0.373933 hartree
Truhlar's Delta G correction:	+0.382119 hartree
Grimme's Delta G correction:	+0.380725 hartree
Imaginary Frequency:	139.2 *i*cm^{-1}

Cartesian Coordinates

C	0.42390	-2.39869	3.23832
C	1.24925	-1.36544	2.77060
N	0.62003	-0.62399	1.84936
C	-0.77607	-2.28090	2.54456
C	-0.63522	-1.16284	1.69829
H	-1.66361	-2.88513	2.63988
C	-1.62252	-0.53685	0.89904
C	-1.70318	0.72857	0.40045
C	-2.89732	-1.23844	0.51909
O	-3.19547	-2.38769	0.75295
O	-3.44743	1.91477	-0.74318
C	-3.00701	0.90308	-0.24878
N	-3.68837	-0.33409	-0.17068
C	-0.78432	1.85632	0.54892
C	-1.20210	3.00374	1.21996
C	-0.35999	4.08905	1.40071
C	0.93352	4.04961	0.89998
C	1.37669	2.94146	0.19769
C	0.52529	1.85319	0.05764
H	-2.21355	3.02652	1.60854
H	-0.71565	4.96479	1.93136
H	1.60621	4.88817	1.04240
H	2.38301	2.88784	-0.19541
C	-5.00223	-0.70372	-0.73115
C	-4.80869	-1.84683	-1.72864
C	-5.66166	0.46023	-1.46247

C	-5.92141	-1.13788	0.41095
H	-5.77543	-2.12613	-2.15538
H	-4.37129	-2.71982	-1.24729
H	-4.15448	-1.52640	-2.54278
H	-5.50653	-1.99047	0.94604
H	-6.89887	-1.41538	0.00798
H	-6.06250	-0.31261	1.11295
H	-6.61761	0.09544	-1.84827
H	-5.05930	0.81468	-2.29723
H	-5.84771	1.30732	-0.80486
H	0.67215	-3.12652	3.99758
H	2.27036	-1.13822	3.05111
Cu	1.59502	0.17170	0.27701
O	3.52249	0.87061	0.53836
N	2.65545	-1.65156	-0.11447
C	4.07876	-1.31137	-0.28247
C	2.20801	-2.47008	-1.25861
C	3.43793	-2.63656	-2.14845
C	4.27940	-1.42069	-1.78848
C	4.47183	0.08003	0.25103
O	5.67785	0.30242	0.31869
H	2.48926	-2.12994	0.76179
H	1.41568	-1.93791	-1.79398
H	1.79305	-3.42104	-0.91713
H	3.17594	-2.68865	-3.20763
H	3.97932	-3.55261	-1.89003
H	3.87642	-0.52399	-2.27013
H	5.33345	-1.50575	-2.04832
H	4.72021	-2.04527	0.22027
Br	0.73513	0.80053	-1.84194

*Intermediate Copper Complex **8***

SCF energy:	–5568.892340 hartree
Zero-point correction:	+0.439984 hartree
Enthalpy correction:	+0.471502 hartree
Free energy correction:	+0.376463 hartree
Truhlar's Delta G correction:	+0.384124 hartree
Grimme's Delta G correction:	+0.382933 hartree

Cartesian Coordinates

C	0.67685	-1.74005	3.51626
C	1.45434	-0.82478	2.80453
N	0.72018	-0.28641	1.81520
C	-0.58130	-1.76656	2.90710
C	-0.53424	-0.84107	1.85676
H	-1.44847	-2.34016	3.19247
C	-1.56925	-0.36922	1.00609
C	-1.69725	0.82847	0.37564
C	-2.80517	-1.16229	0.73264
O	-3.05761	-2.27564	1.13257
O	-3.48969	1.76990	-0.92920
C	-3.00959	0.85504	-0.30546
N	-3.62915	-0.39097	-0.07597
C	-0.80843	1.97642	0.43680
C	-1.32721	3.27415	0.55469
C	-0.49181	4.36290	0.72052
C	0.88423	4.18681	0.77230

C	1.43141	2.91785	0.62895
C	0.57667	1.85427	0.43810
H	-2.40099	3.40574	0.52370
H	-0.91857	5.35490	0.81949
H	1.54333	5.03746	0.91002
H	2.50185	2.75140	0.64552
C	-4.92222	-0.88948	-0.58605
C	-4.67009	-2.15539	-1.40622
C	-5.61622	0.12843	-1.48412
C	-5.83642	-1.19071	0.60154
H	-5.61928	-2.52962	-1.79779
H	-4.20913	-2.93359	-0.80051
H	-4.01562	-1.93015	-2.25133
H	-5.39526	-1.94062	1.25617
H	-6.79760	-1.56226	0.23731
H	-6.01773	-0.27958	1.17661
H	-6.54774	-0.33053	-1.82624
H	-5.01401	0.38632	-2.35377
H	-5.85236	1.05086	-0.95706
H	0.99276	-2.30096	4.38378
H	2.49036	-0.54379	2.92809
Cu	1.44975	0.20569	0.10984
O	3.45142	0.67014	0.68158
N	2.29262	-1.66011	-0.09369
C	3.75991	-1.52700	-0.17863
C	1.84982	-2.54356	-1.19392
C	2.99833	-2.54872	-2.21271
C	4.00284	-1.52831	-1.68020
C	4.29950	-0.25489	0.50047
O	5.49671	-0.24765	0.76938
H	2.02993	-2.05290	0.80436
H	0.92755	-2.15083	-1.62129
H	1.65268	-3.54737	-0.80636
H	2.64203	-2.28518	-3.20939
H	3.45102	-3.54249	-2.26755
H	3.77474	-0.53644	-2.07524
H	5.03929	-1.76840	-1.91450
H	4.24519	-2.39609	0.28110
Br	1.07494	0.62268	-2.17277

Transition State Reductive Elimination ***TS2***

SCF energy:	–5568.887846 hartree
Zero-point correction:	+0.439106 hartree
Enthalpy correction:	+0.470217 hartree
Free energy correction:	+0.376083 hartree
Truhlar's Delta G correction:	+0.383323 hartree
Grimme's Delta G correction:	+0.382401 hartree
Imaginary Frequency:	196.6 *i*cm^{-1}

Cartesian Coordinates

C	1.11371	-1.42009	3.28035
C	1.67969	-0.38773	2.54008
N	0.81044	-0.02022	1.57583
C	-0.14672	-1.69275	2.73434
C	-0.33236	-0.78936	1.68786
H	-0.87870	-2.41084	3.06790
C	-1.48161	-0.43542	0.94329

C	-1.76335	0.78508	0.41362
C	-2.65910	-1.31583	0.72975
O	-2.78356	-2.46433	1.08819
O	-3.75184	1.65530	-0.63051
C	-3.13209	0.74318	-0.14097
N	-3.61119	-0.57221	0.03859
C	-0.92746	1.95037	0.53520
C	-1.44175	3.25289	0.60393
C	-0.61508	4.32366	0.88220
C	0.74582	4.12643	1.10212
C	1.29621	2.85821	1.01137
C	0.45716	1.81378	0.66938
H	-2.50322	3.39400	0.44793
H	-1.03446	5.32143	0.94386
H	1.39151	4.96860	1.32629
H	2.35987	2.68000	1.12360
C	-4.89742	-1.15337	-0.39729
C	-4.60965	-2.35873	-1.29352
C	-5.73381	-0.15968	-1.19562
C	-5.68999	-1.57770	0.83873
H	-5.55425	-2.78996	-1.63396
H	-4.04663	-3.12343	-0.76164
H	-4.03948	-2.04571	-2.17104
H	-5.14094	-2.31557	1.42192
H	-6.64412	-2.01232	0.53012
H	-5.89750	-0.70958	1.46881
H	-6.64218	-0.68318	-1.50536
H	-5.21333	0.19033	-2.08601
H	-6.01367	0.71224	-0.60802
H	1.57730	-1.91299	4.12225
H	2.65255	0.07410	2.60331
Cu	1.39342	0.40122	-0.19582
O	3.52894	0.88425	0.28797
N	2.40299	-1.25548	-0.82477
C	3.57909	-1.45146	0.02802
C	1.90567	-2.60692	-1.07466
C	3.16952	-3.49268	-1.17677
C	4.31193	-2.61606	-0.61891
C	4.30647	-0.11927	0.27143
O	5.51773	-0.15199	0.47082
H	2.71072	-0.85657	-1.71113
H	1.27917	-2.61519	-1.96695
H	1.28745	-2.90212	-0.22332
H	3.36275	-3.78786	-2.21062
H	3.04297	-4.41125	-0.59951
H	4.95548	-2.23798	-1.41728
H	4.95391	-3.14204	0.08694
H	3.19465	-1.77091	1.00589
Br	0.80903	0.98976	-2.43081

*Final Product **3i***

SCF energy:	–954.749448 hartree
Zero-point correction:	+0.305416 hartree
Enthalpy correction:	+0.324269 hartree
Free energy correction:	+0.260095 hartree
Truhlar's Delta G correction:	+0.262205 hartree
Grimme's Delta G correction:	+0.262106 hartree

Cartesian Coordinates

C	2.63044	3.32149	-0.00048
C	3.30139	2.11772	-0.00026
N	2.38322	1.11096	0.00021
C	1.25235	3.05978	-0.00019
C	1.10492	1.68587	0.00015
H	0.43787	3.76498	-0.00016
C	0.02121	0.79703	0.00004
C	0.18821	-0.54593	-0.00014
C	-1.43201	1.09580	0.00014
O	-1.94369	2.18721	0.00033
O	-1.38895	-2.36142	-0.00049
C	-1.15209	-1.18027	-0.00046
N	-2.09227	-0.13360	-0.00005
C	1.48528	-1.13937	-0.00006
C	1.70917	-2.52344	-0.00021
C	2.98925	-3.02794	-0.00008
C	4.07867	-2.15805	0.00032
C	3.88856	-0.79232	0.00047
C	2.59815	-0.26633	0.00023
H	0.84711	-3.17742	-0.00043
H	3.14979	-4.09908	-0.00022
H	5.08797	-2.55230	0.00048
H	4.74644	-0.13372	0.00088
C	-3.57528	-0.22414	0.00007
C	-4.05660	-1.66978	0.00003
C	-4.10275	0.46330	-1.25802
C	-4.10253	0.46314	1.25835
H	-3.72616	-2.21651	-0.88141
H	-5.14843	-1.64030	0.00020
H	-3.72591	-2.21662	0.88132
H	-3.71888	-0.03519	2.15151
H	-3.82036	1.51406	1.28896
H	-5.19228	0.39604	1.27443
H	-3.82059	1.51423	-1.28852
H	-5.19250	0.39621	-1.27393
H	-3.71924	-0.03489	-2.15132
H	3.10256	4.29151	-0.00085
H	4.35907	1.92181	-0.00033

Auxiliary Material: Carbonate Ion

SCF energy:	–263.871431 hartree
Zero-point correction:	+0.013981 hartree
Enthalpy correction:	+0.018107 hartree
Free energy correction:	–0.011565 hartree
Truhlar's Delta G correction:	–0.011565 hartree
Grimme's Delta G correction:	–0.011565 hartree

Cartesian Coordinates

O	0.47615	-1.20828	0.00000
C	0.00000	0.00020	-0.00000
O	0.80849	1.01649	-0.00000
O	-1.28463	0.19163	0.00000

Auxiliary Material: Hydrogen Carbonate Ion

SCF energy:	–264.403717 hartree
Zero-point correction:	+0.026624 hartree
Enthalpy correction:	+0.031063 hartree
Free energy correction:	+0.000886 hartree
Truhlar's Delta G correction:	+0.000886 hartree
Grimme's Delta G correction:	+0.000885 hartree

Cartesian Coordinates

O	1.22350	0.40229	0.00000
C	-0.00000	0.16761	0.00000
O	-0.98471	0.90413	-0.00000
O	-0.31002	-1.22981	-0.00000
H	0.56986	-1.61857	-0.00000

Auxiliary Material: Water

SCF energy:	–76.396408 hartree
Zero-point correction:	+0.021501 hartree
Enthalpy correction:	+0.025280 hartree
Free energy correction:	+0.003866 hartree
Truhlar's Delta G correction:	+0.003866 hartree
Grimme's Delta G correction:	+0.003866 hartree

Cartesian Coordinates

O	0.00000	0.00000	0.11670
H	0.00000	0.76161	-0.46679
H	-0.00000	-0.76161	-0.46679

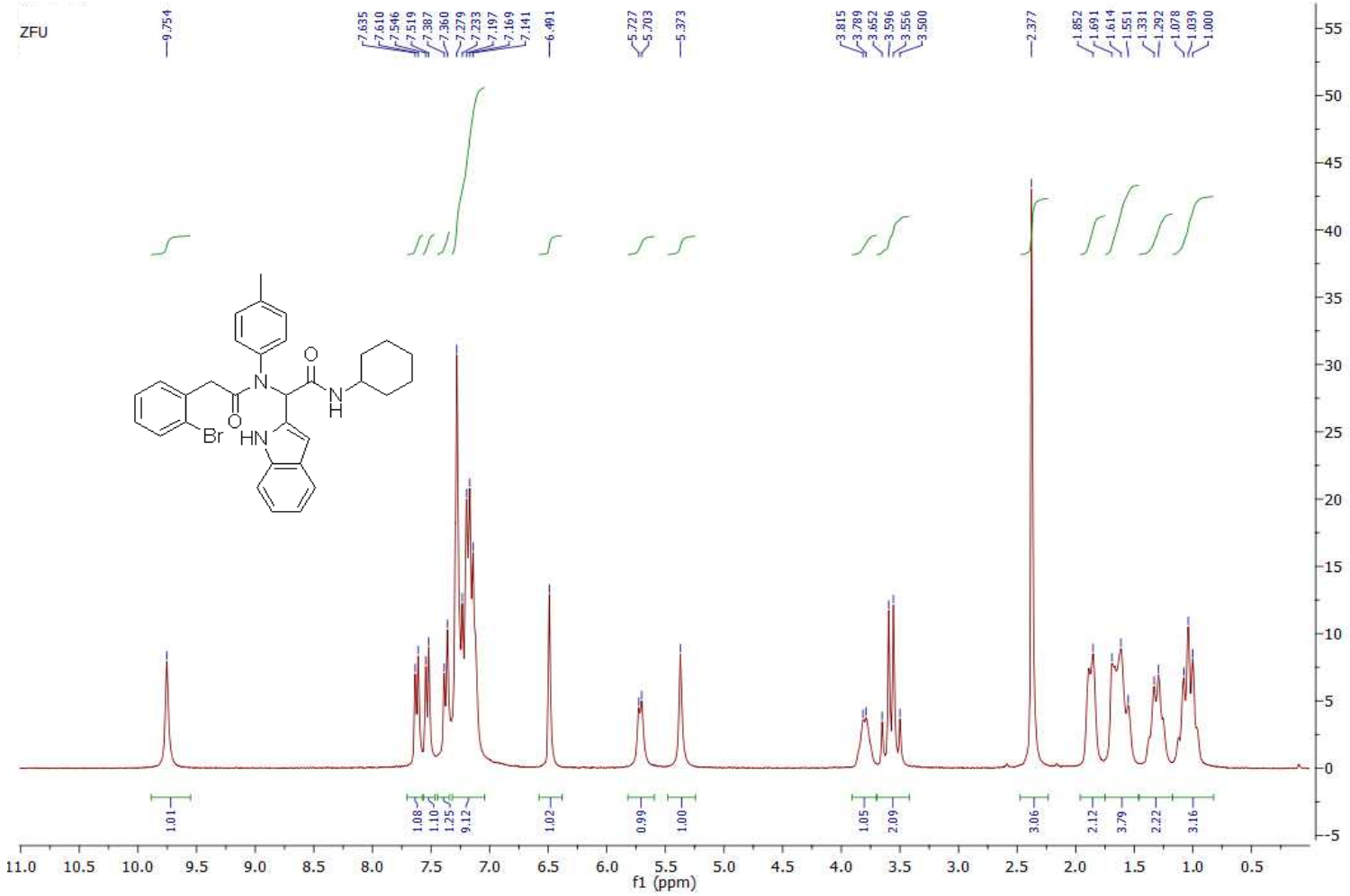
Auxiliary Material: Bromide Ion

SCF energy:	–2573.653732 hartree
Zero-point correction:	+0.000000 hartree
Enthalpy correction:	+0.002360 hartree
Free energy correction:	–0.016176 hartree
Truhlar's Delta G correction:	–0.016176 hartree
Grimme's Delta G correction:	–0.016176 hartree

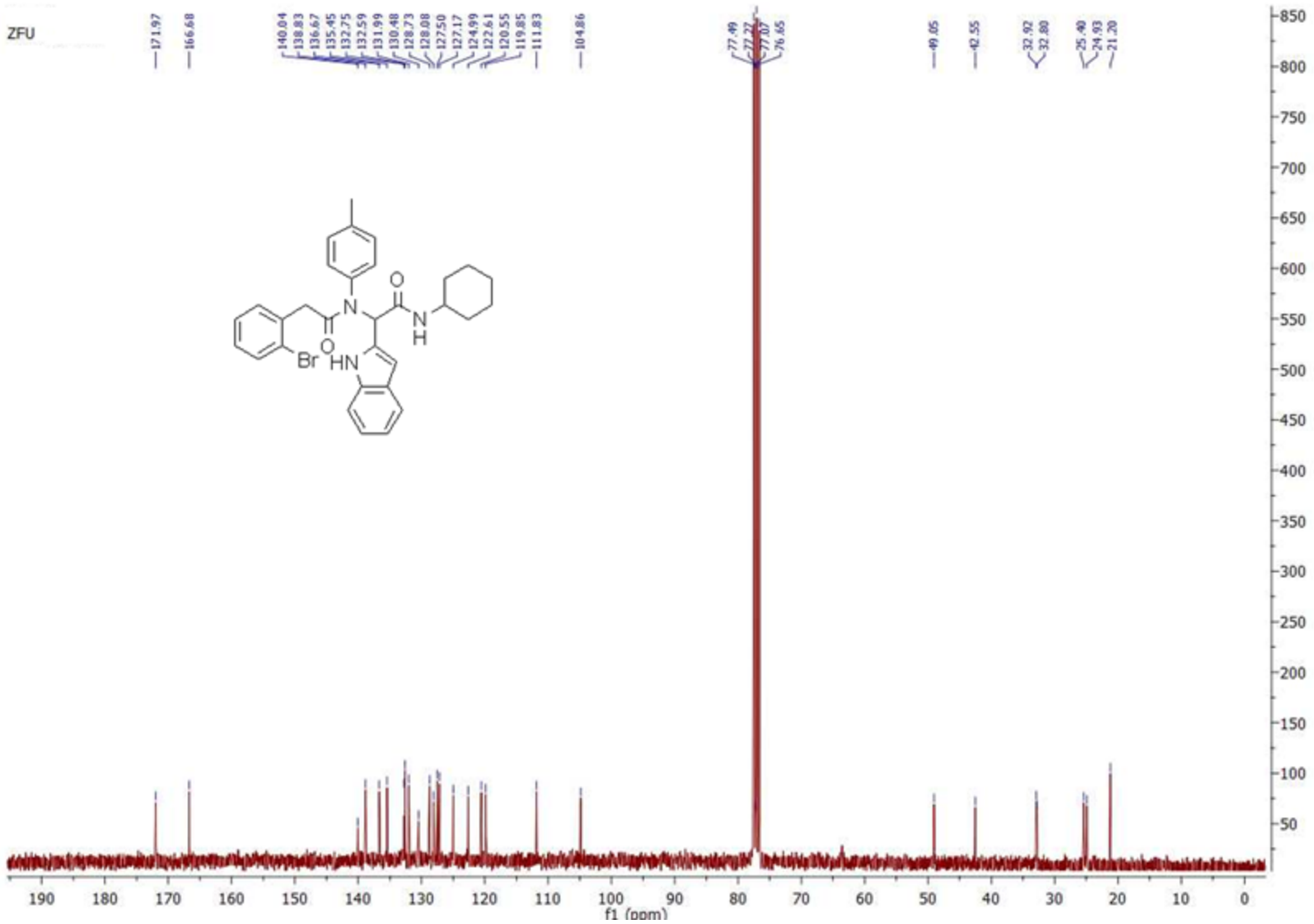
Cartesian Coordinates

Br	0.00000	0.00000	0.00000

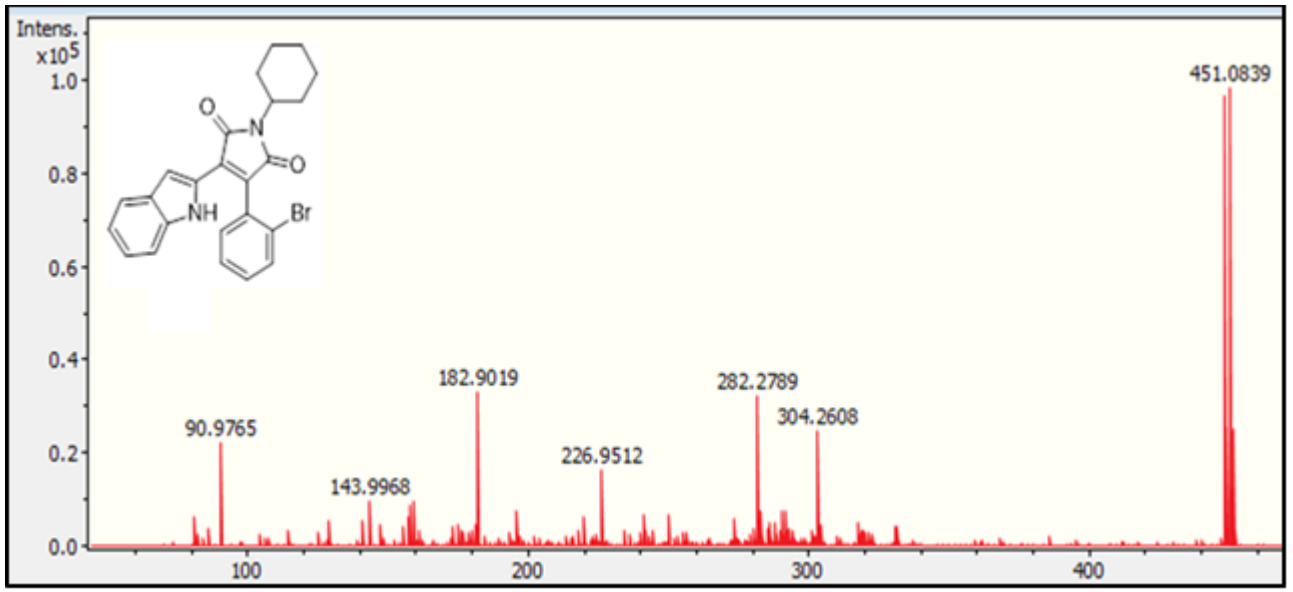
4. Copies of NMR Spectra



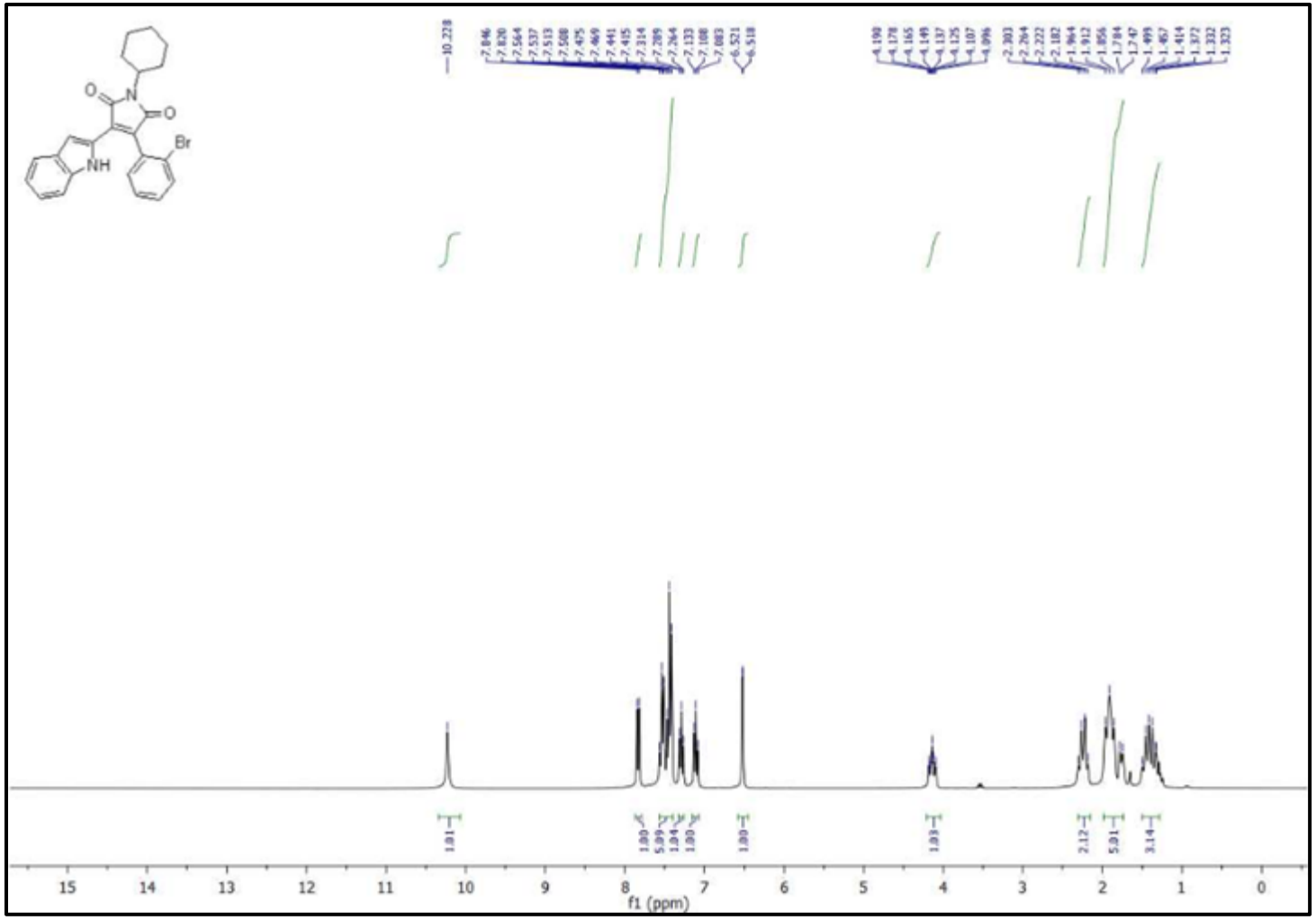
1H-NMR (300 MHz) of **1*a*** in $CDCl_3$



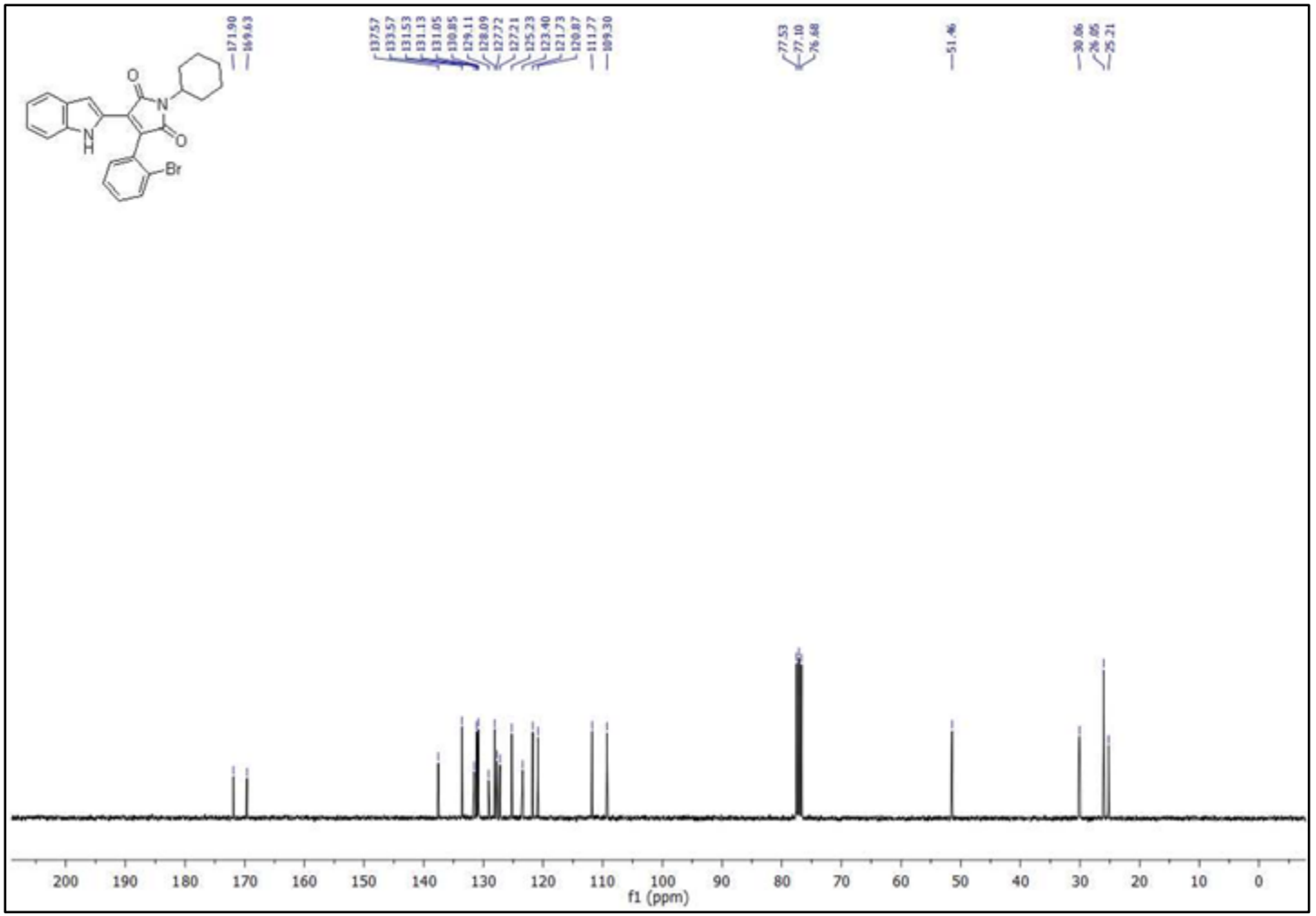
^{13}C-NMR (300 MHz) of **1*a*** in $CDCl_3$



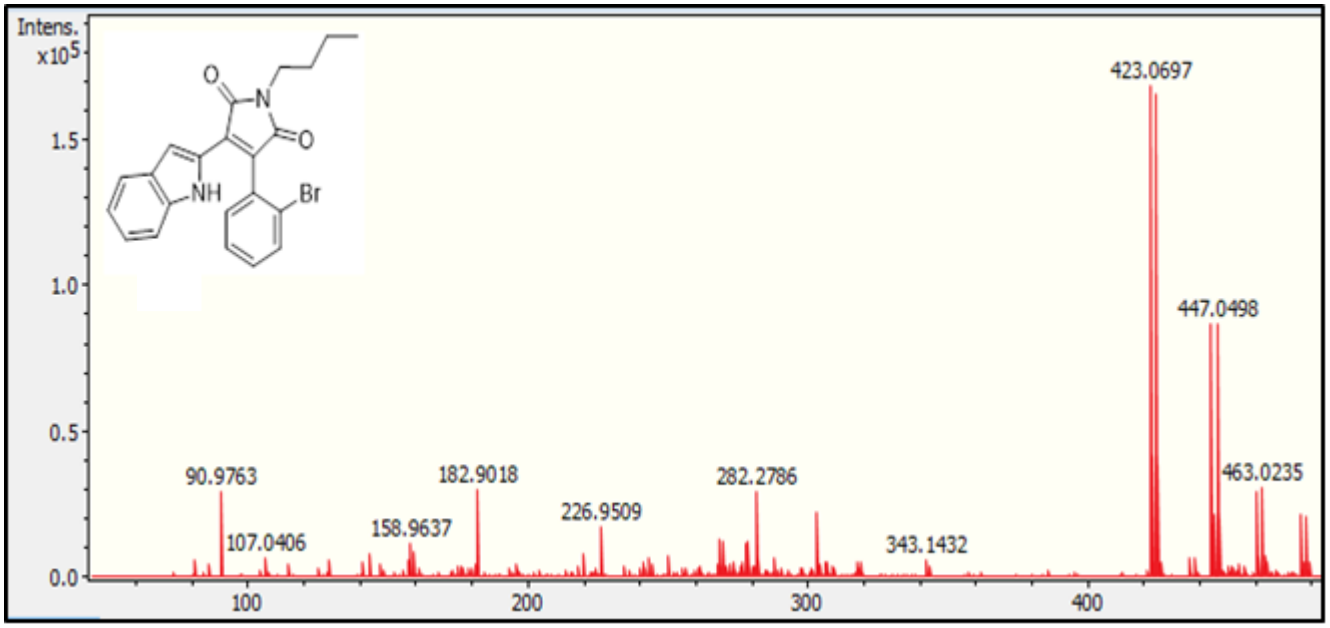
HRMS of **2*a*** ($C_{24}H_{21}{}^{81}BrN_2O_2$ $[M+H]^+$ = 451.0866)



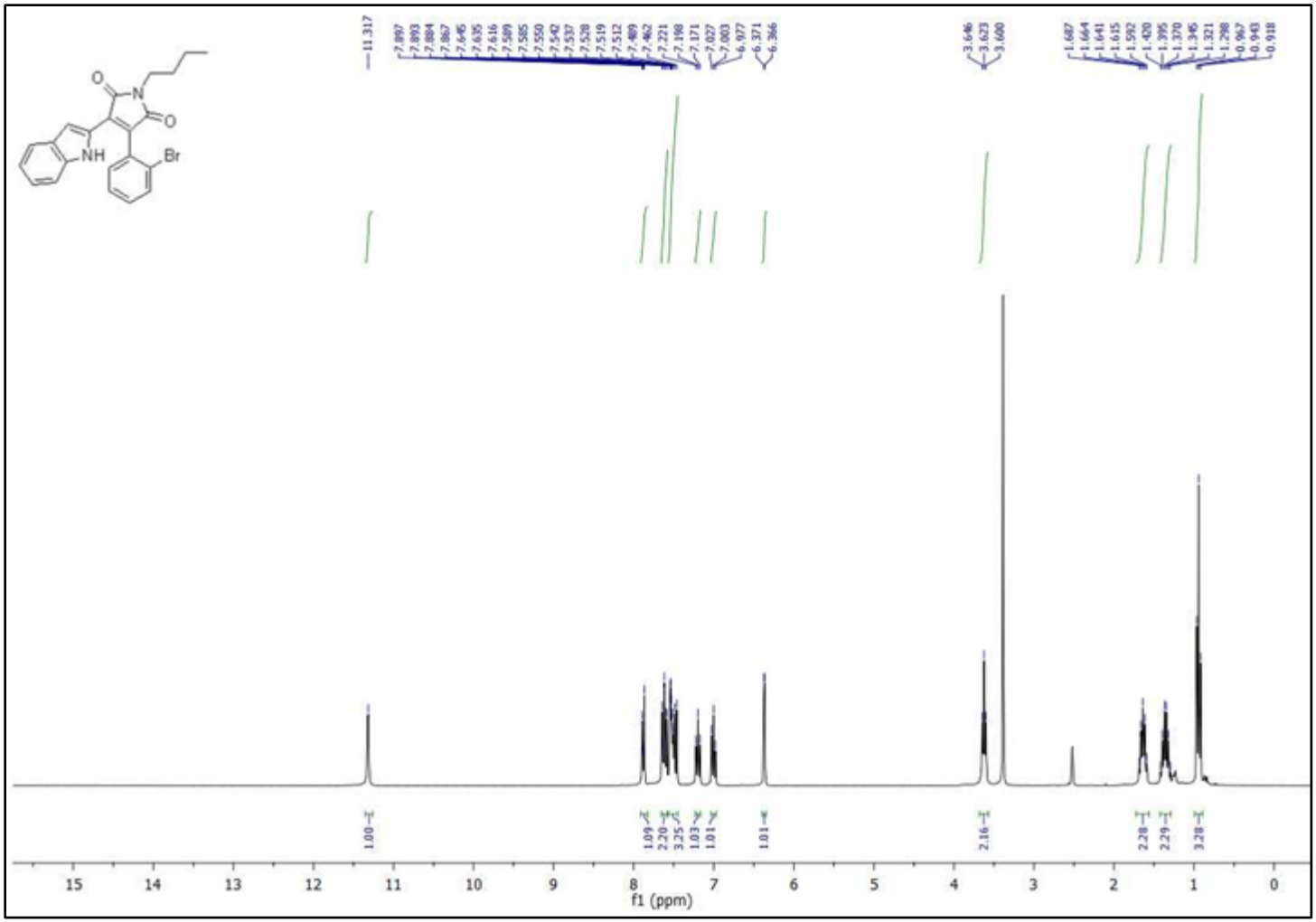
1H-NMR (300 MHz) of **2*a*** in $CDCl_3$



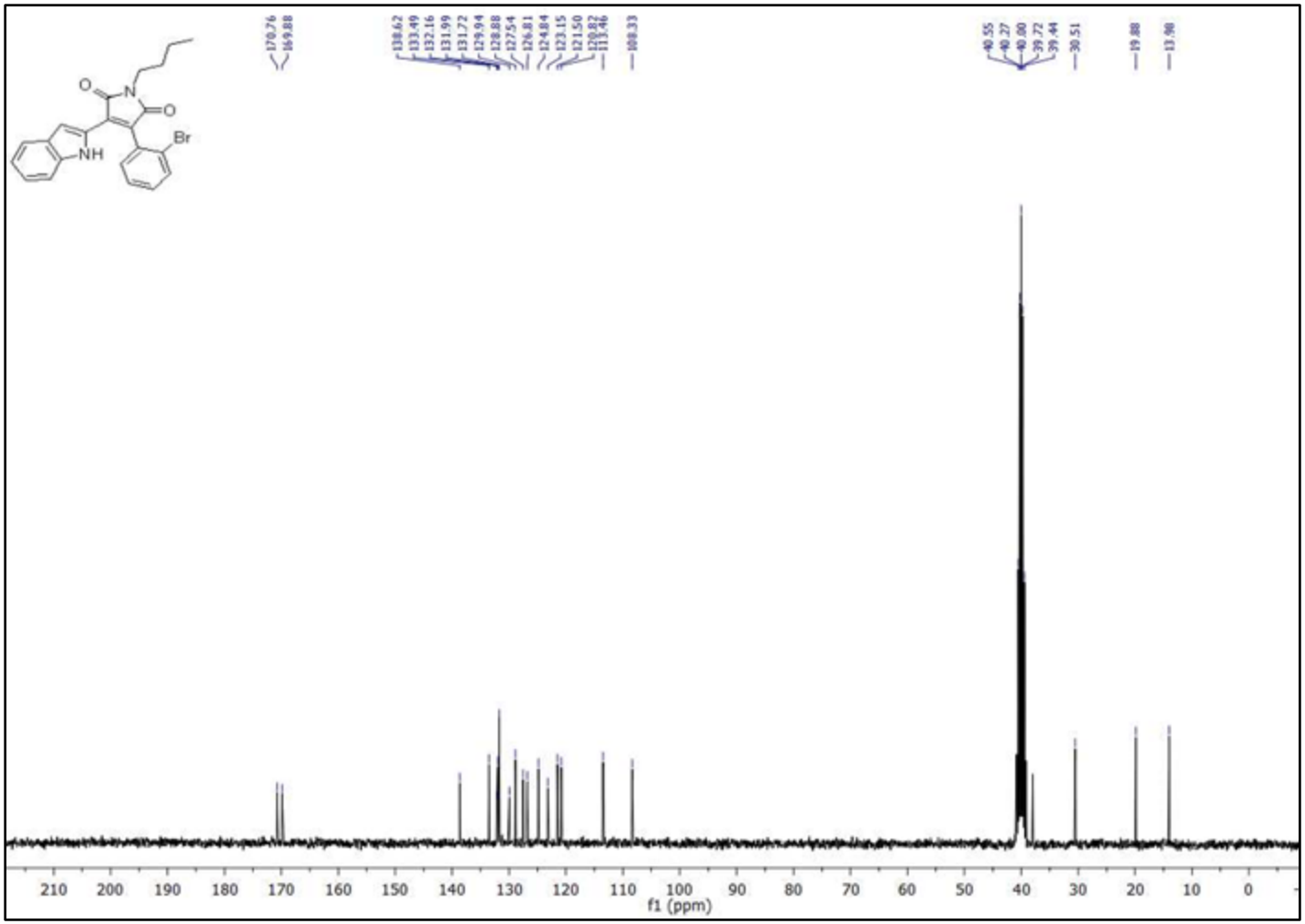
^{13}C-NMR (75 MHz) of ***2a*** in $CDCl_3$



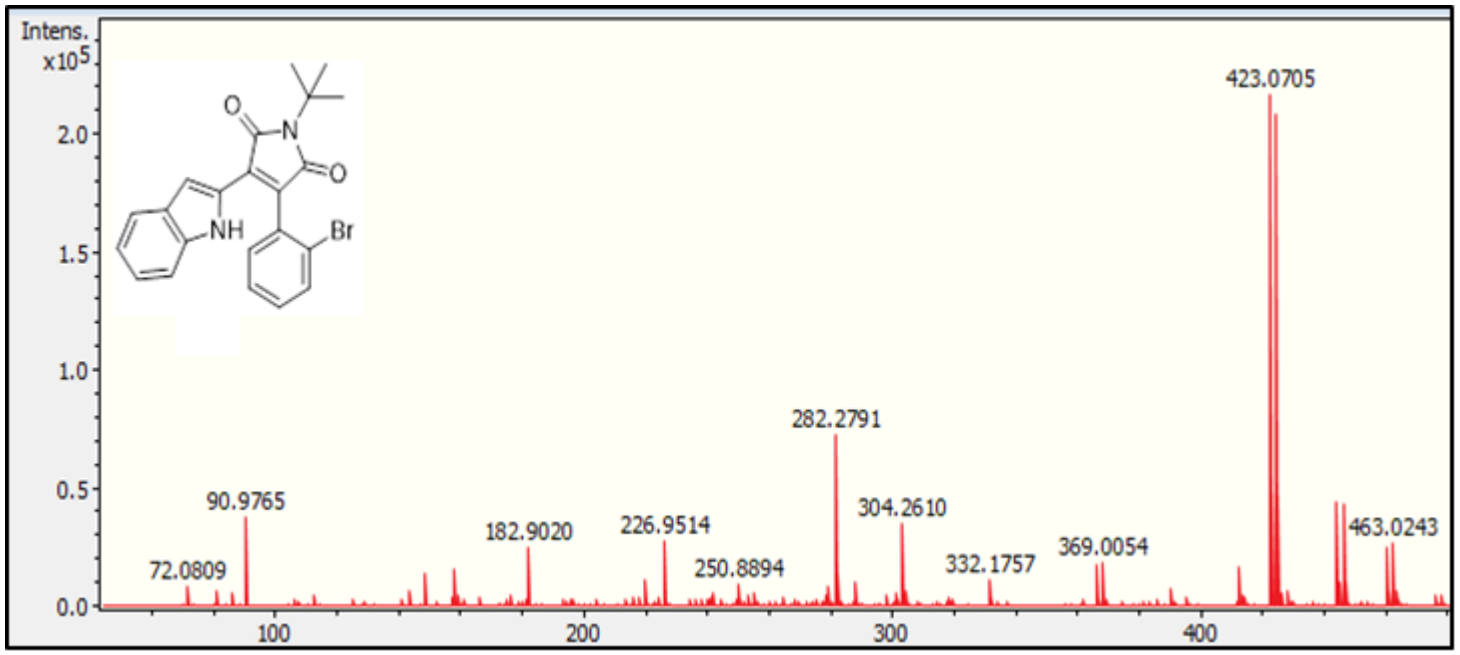
HRMS of **2*b*** ($C_{22}H_{19}BrN_2O_2$ $[M+H]^+$ = 423.0710)



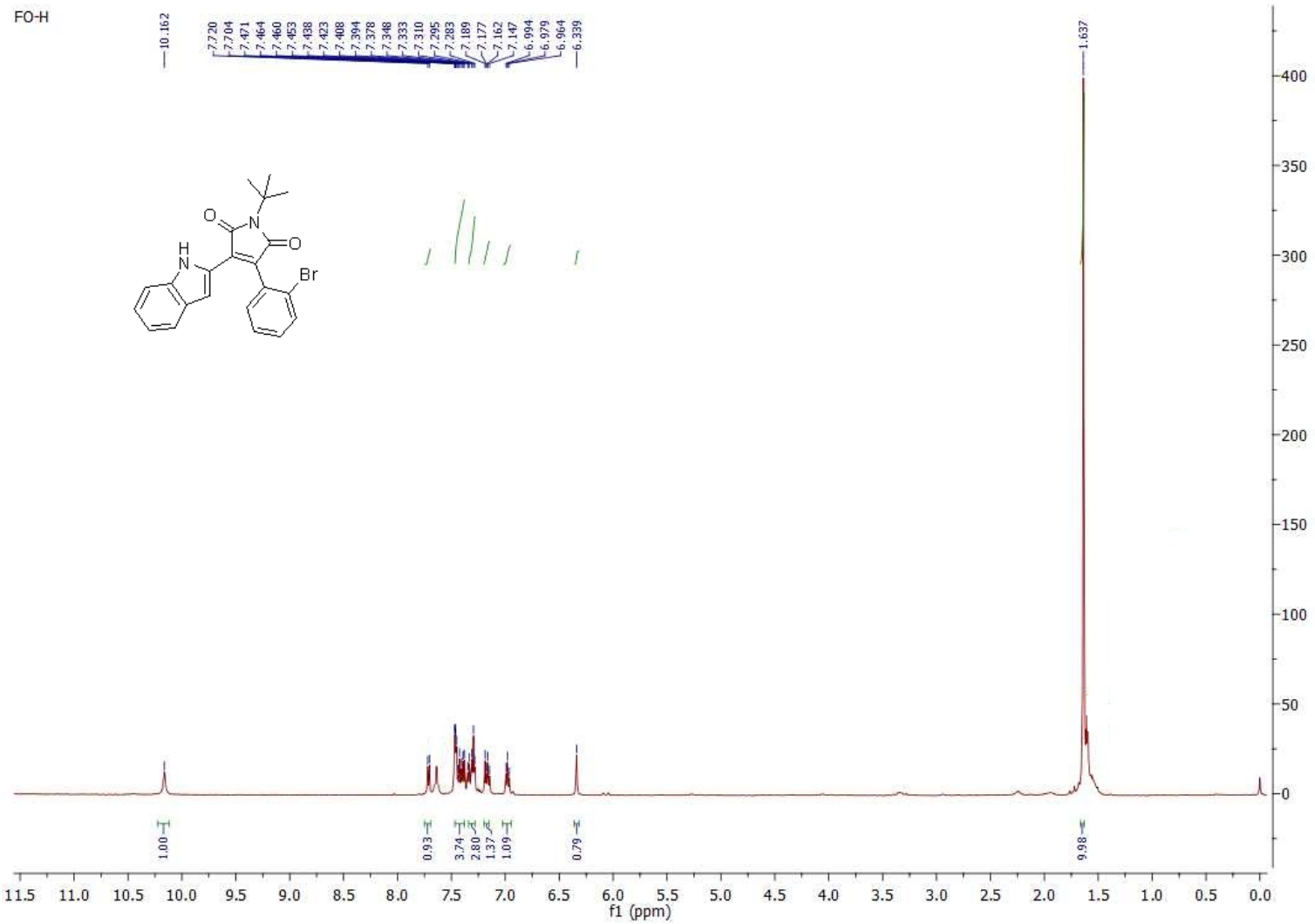
1H-NMR (300 MHz) of **2*b*** in DMSO-d_6



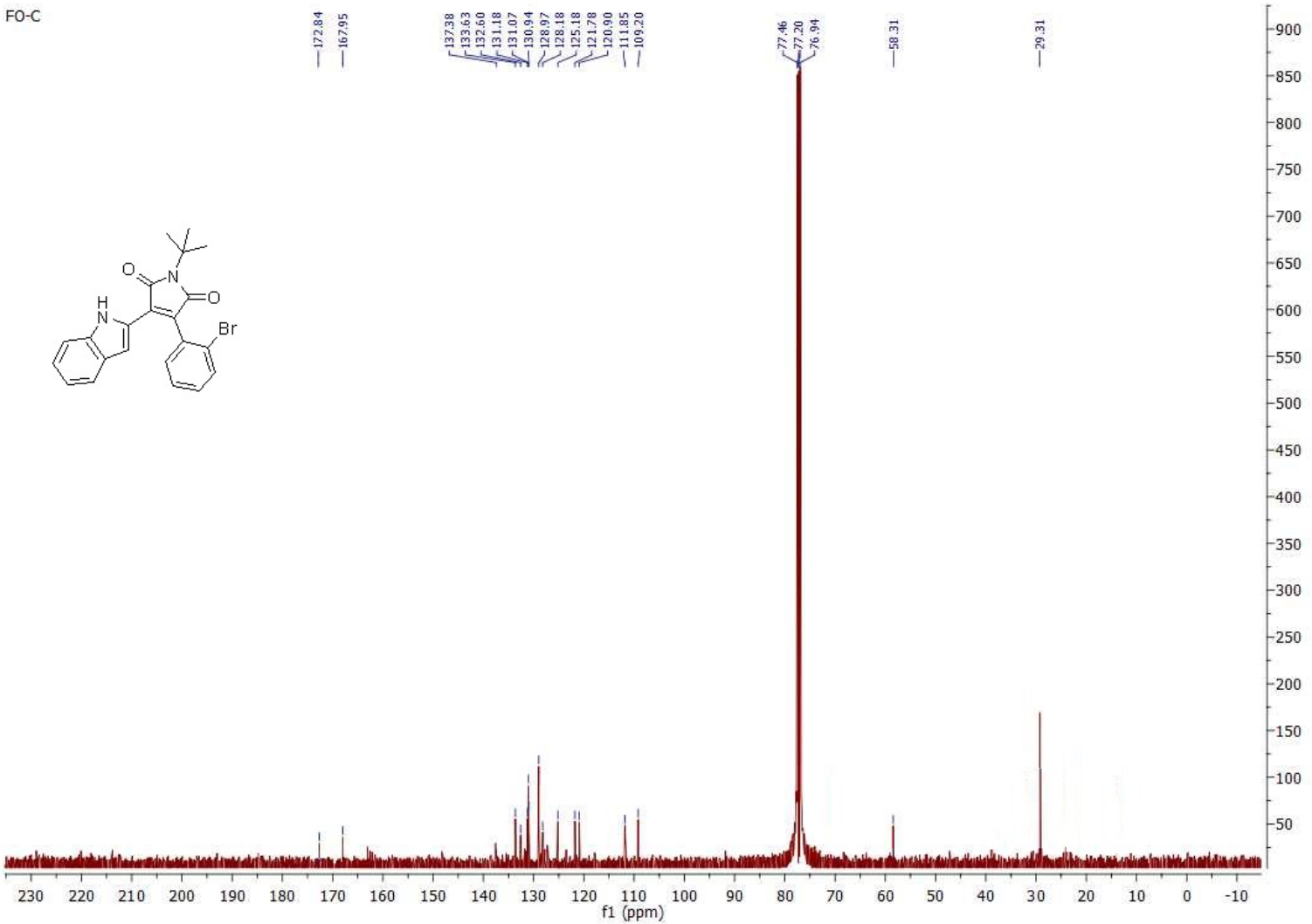
^{13}C-NMR (75 MHz) of **2*b*** in DMSO-d_6



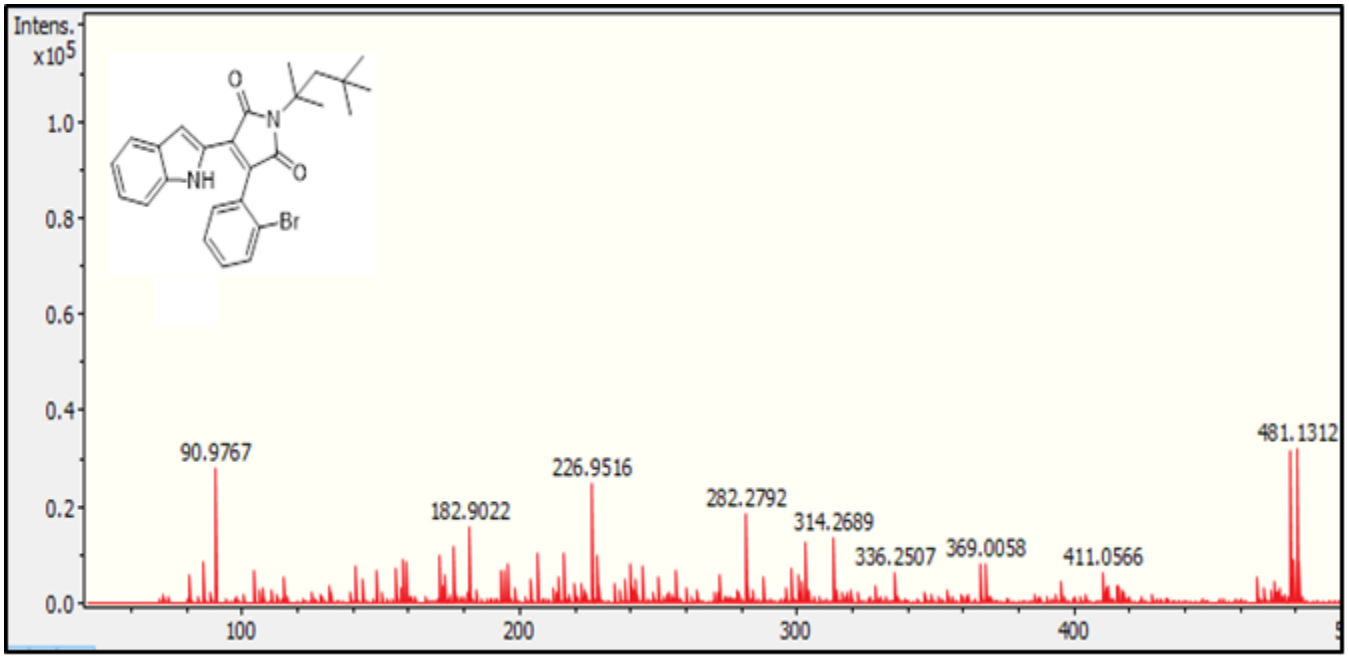
HRMS of **2*c*** ($C_{22}H_{19}BrN_2O_2$ $[M+H]^+$ = 423.0710)



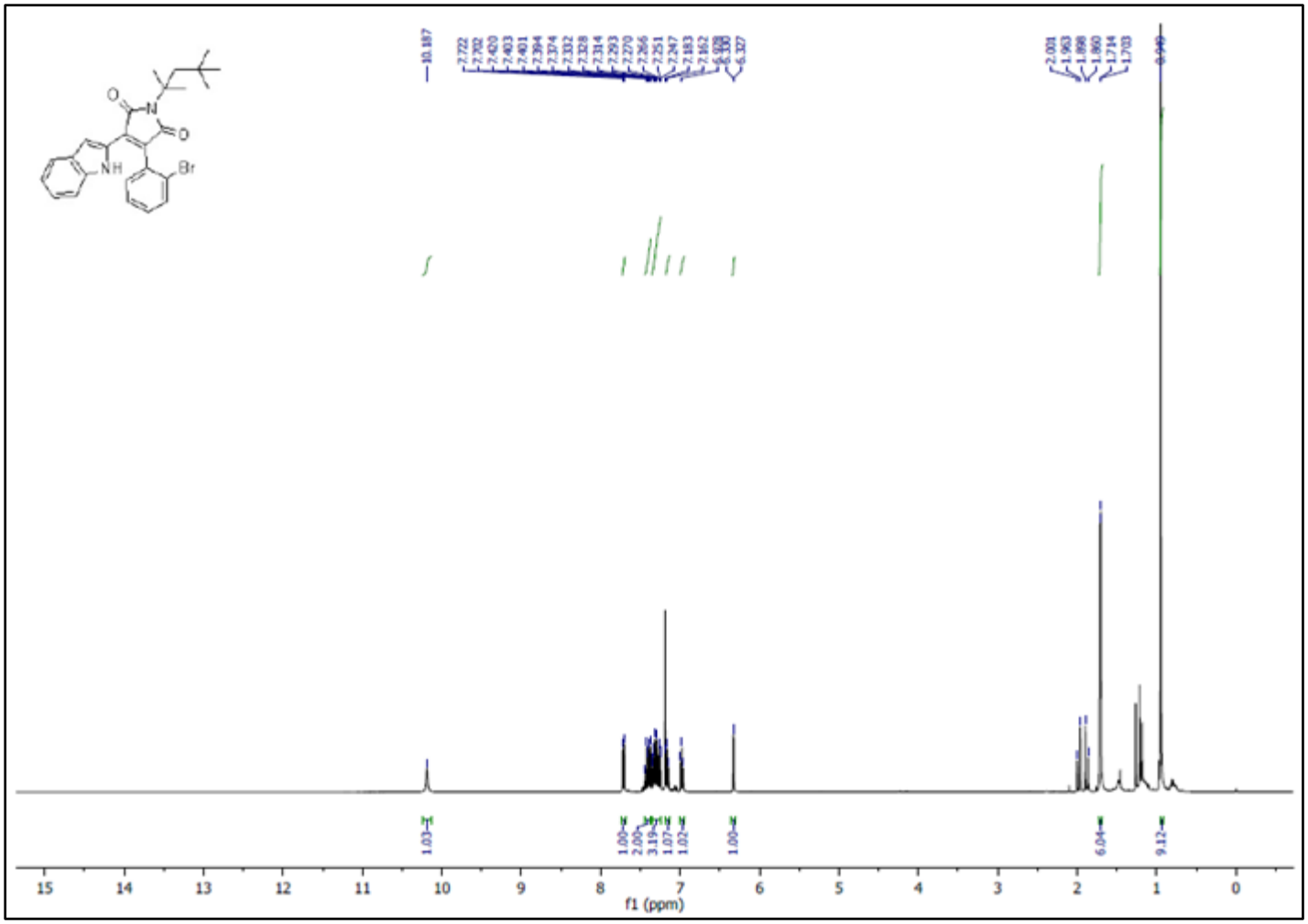
^{1}H-NMR (300 MHz) of ***2c*** in $CDCl_3$



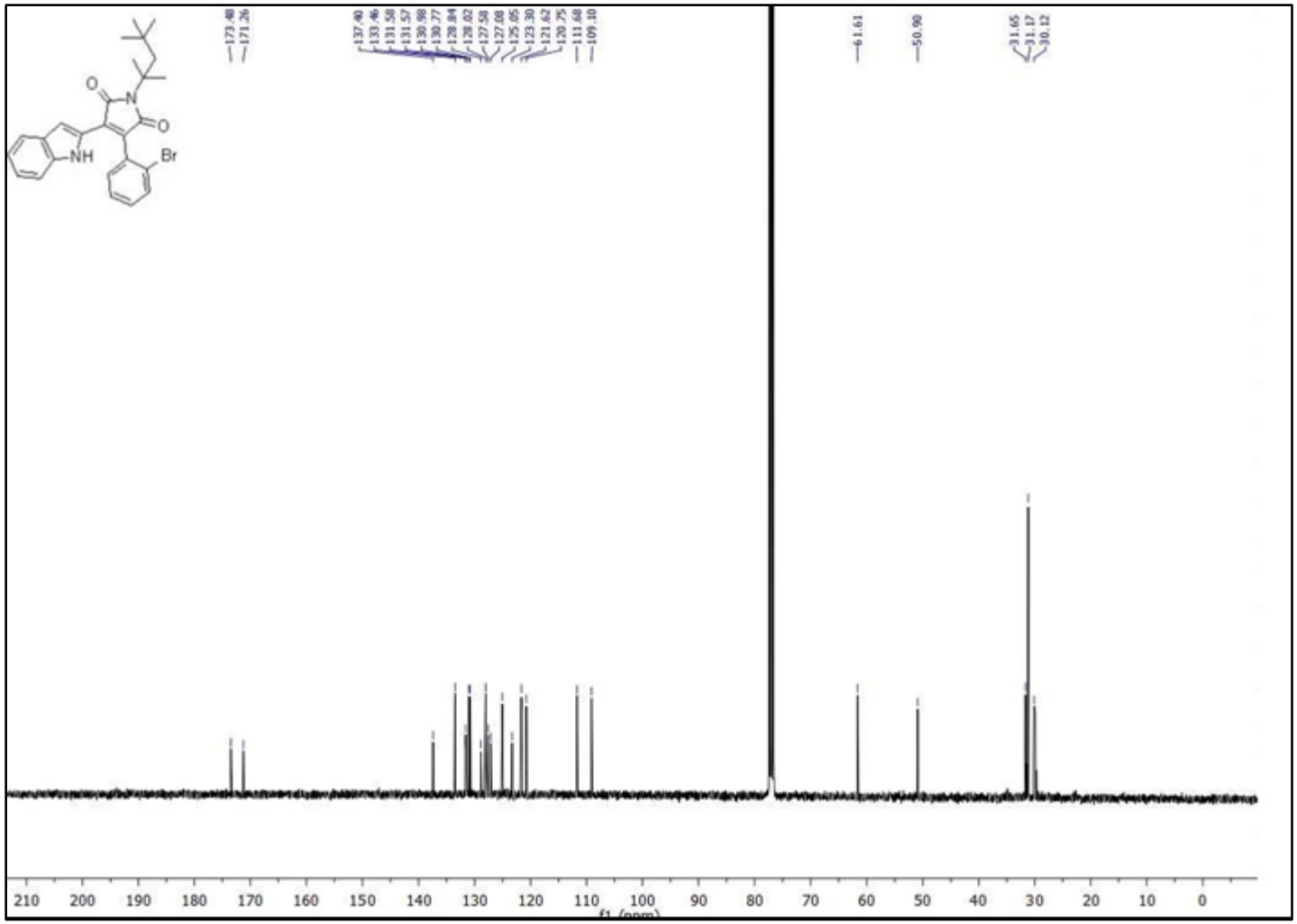
^{13}C-NMR (75 MHz) of ***2c*** in $CDCl_3$



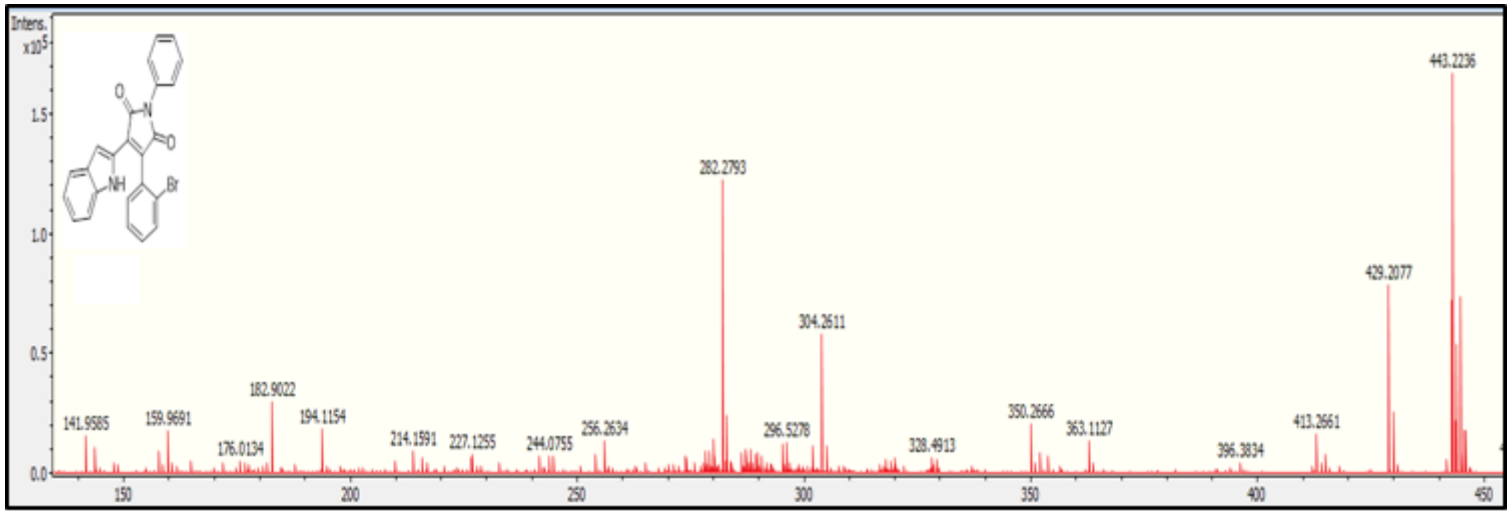
HRMS of **2*d*** $C_{26}H_{27}{}^{81}BrN_2O_2$ $[M+H]^+$ = 481.1309**)**



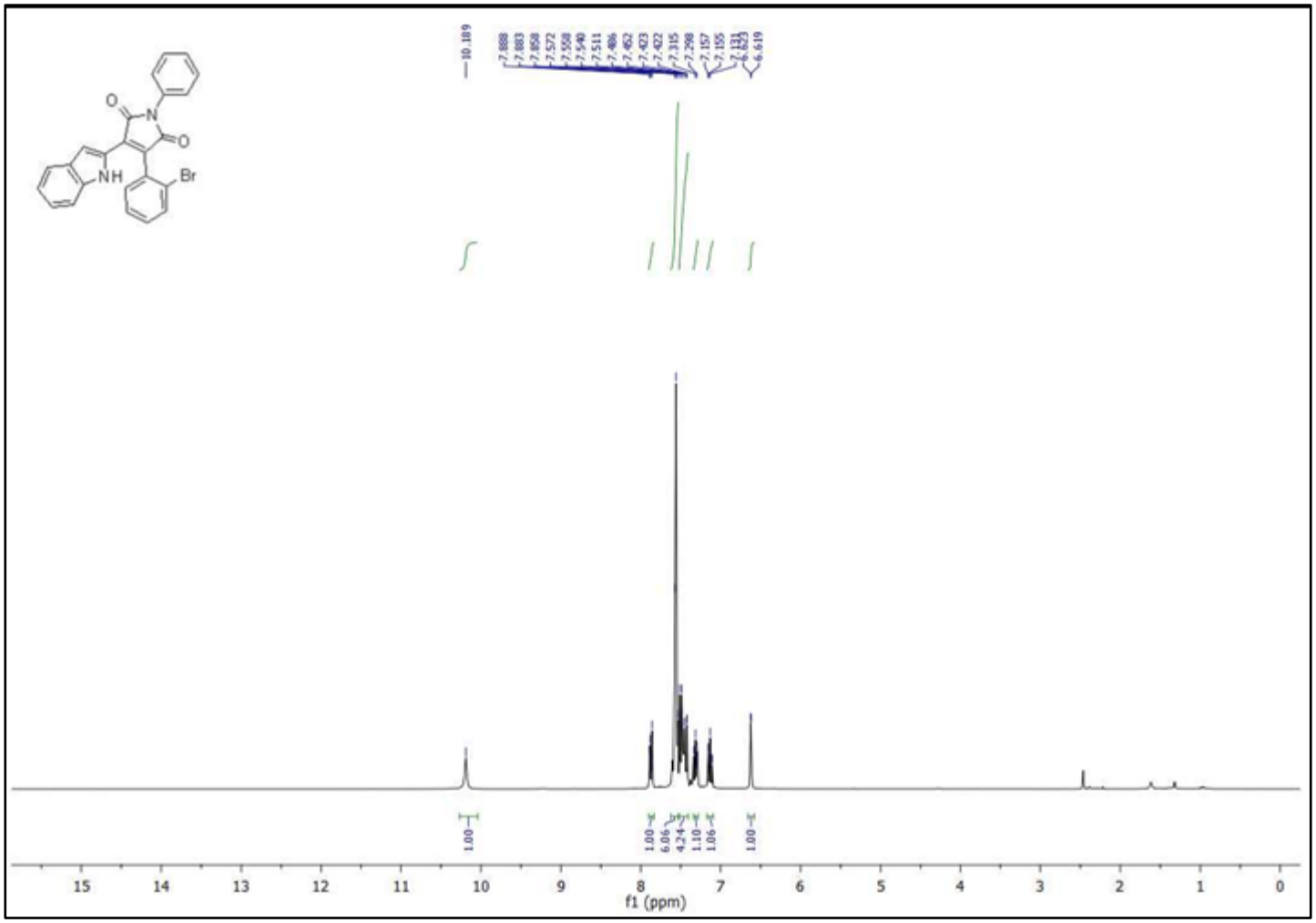
^{1}H-NMR (400 MHz) of **2*d*** in $CDCl_3$



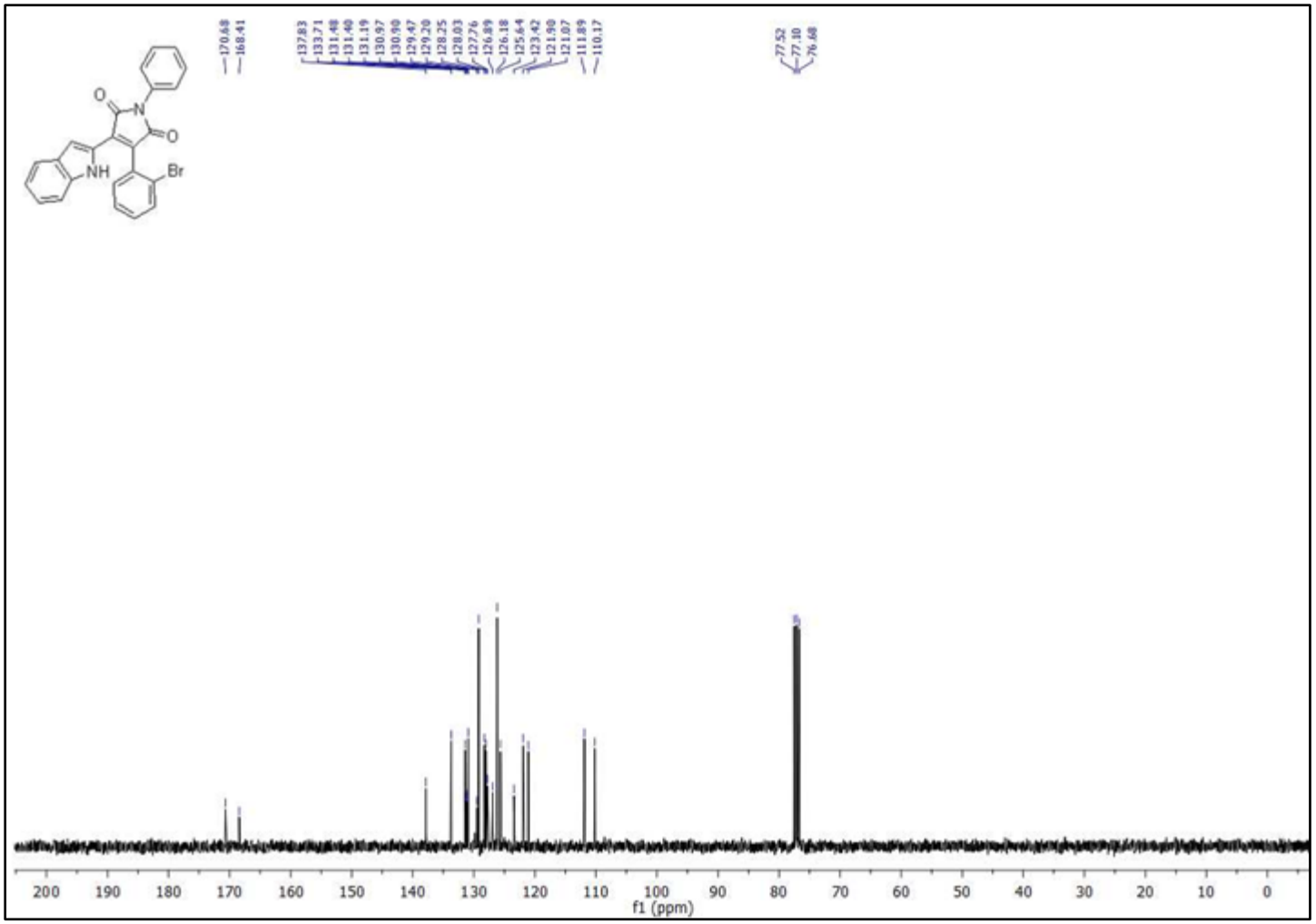
^{13}C-NMR (100 MHz) of ***2d*** in $CDCl_3$



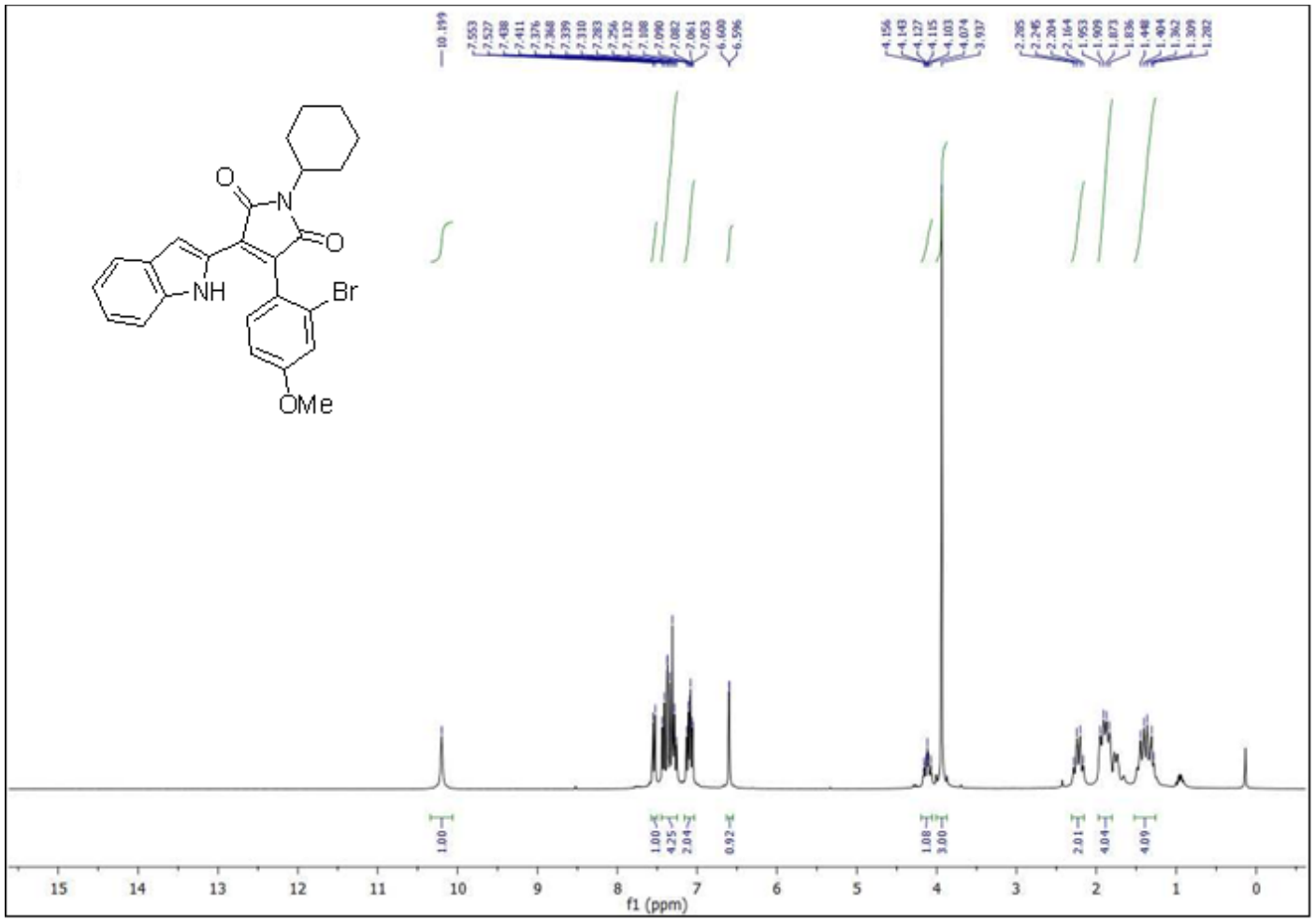
HRMS of **2*e*** **(**$C_{24}H_{15}BrN_2O_2$ $[M+H]^+$ = 443.0397**)**



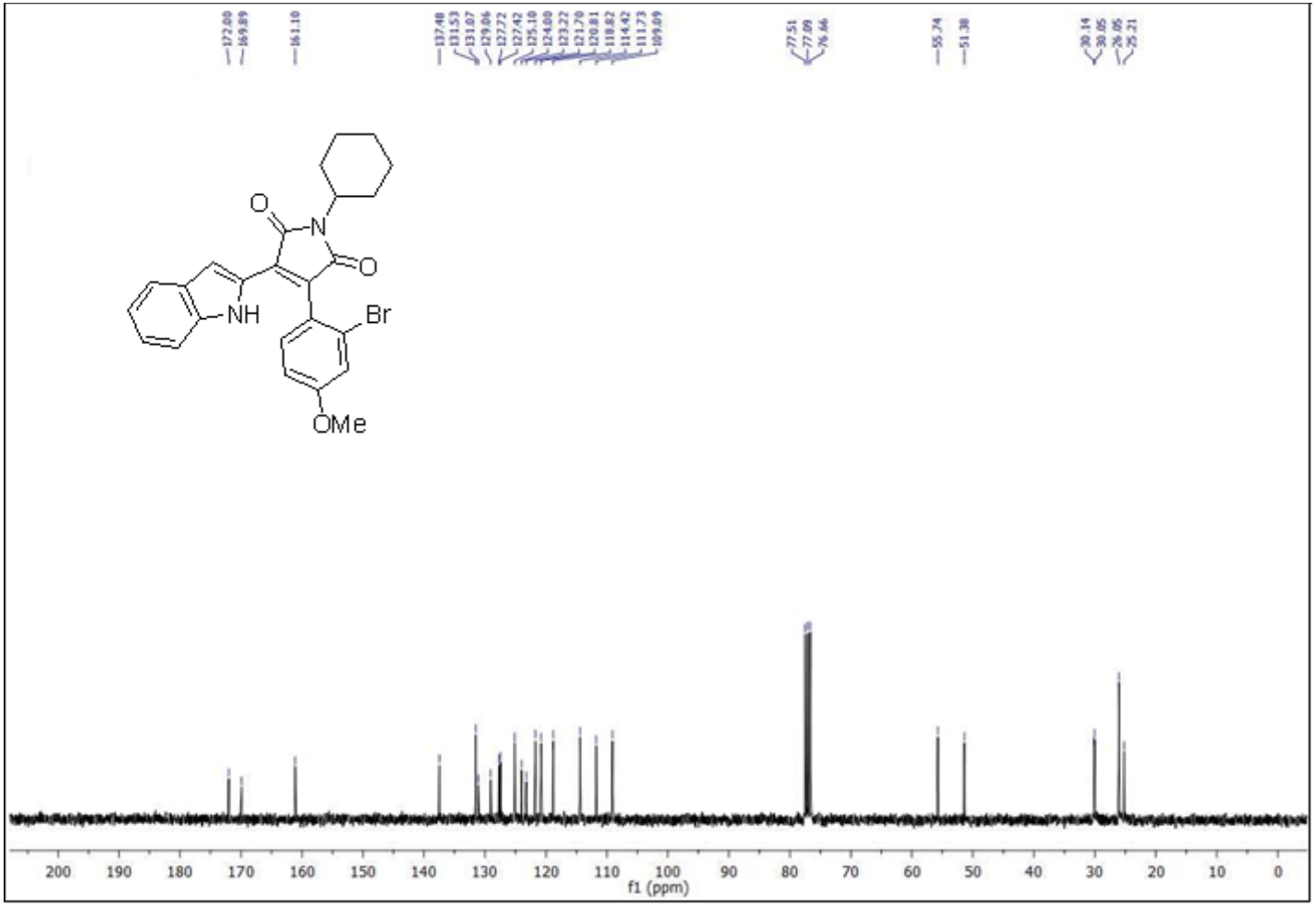
^{1}H-NMR (300 MHz) of ***2e*** in $CDCl_3$



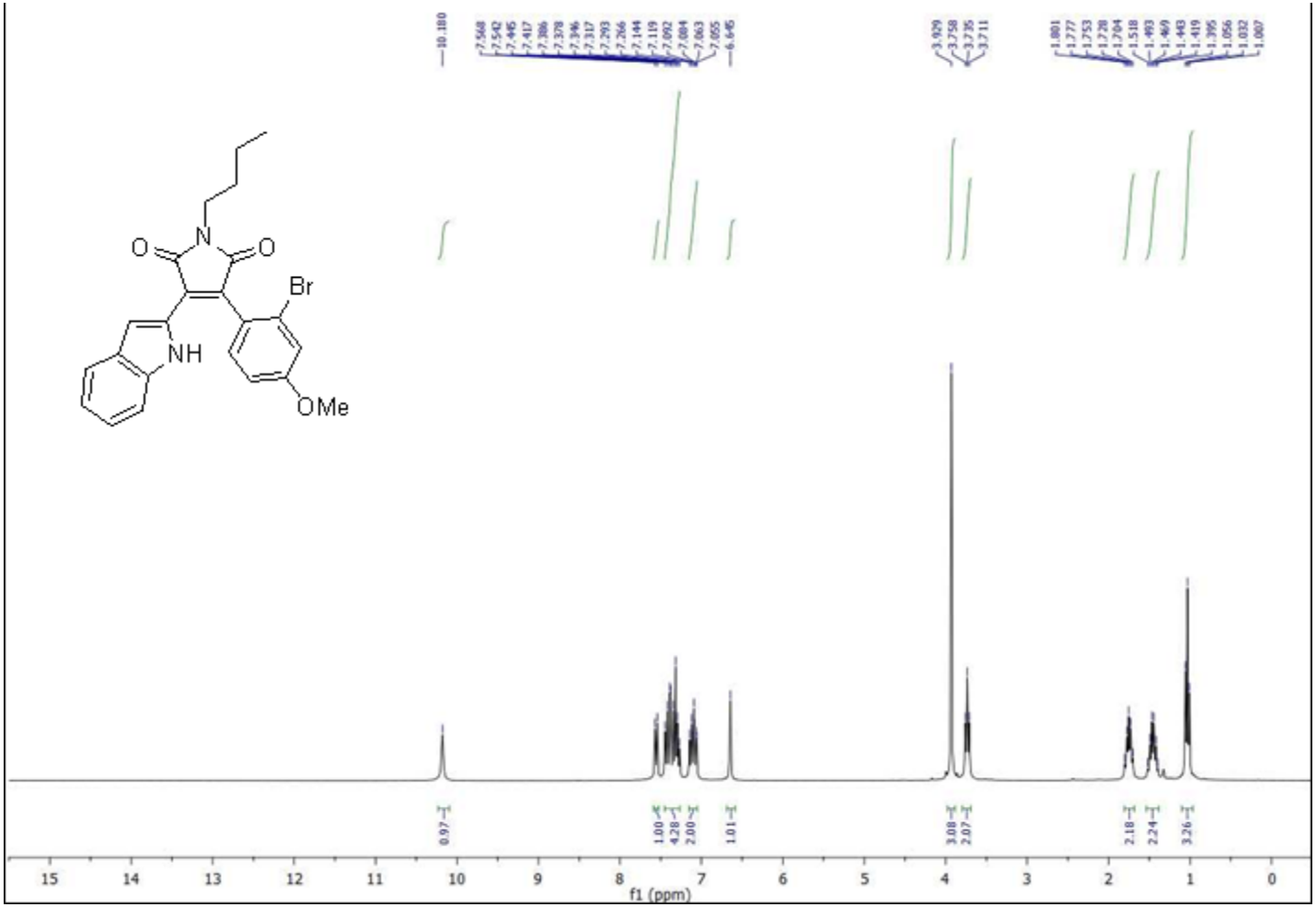
^{13}C-NMR (75 MHz) of **2*e*** in $CDCl_3$



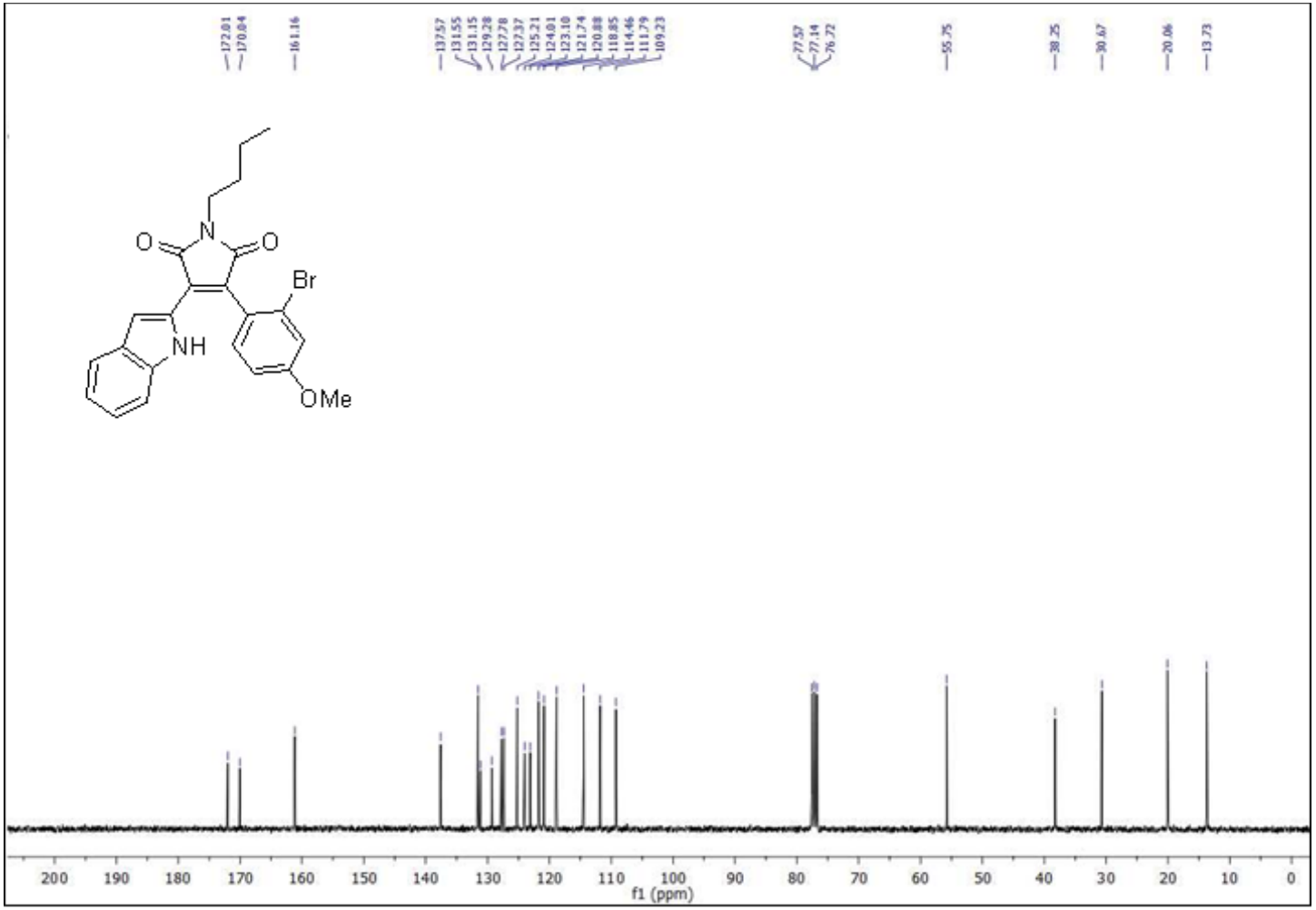
^{1}H-NMR (300 MHz) of ***2f*** in $CDCl_3$



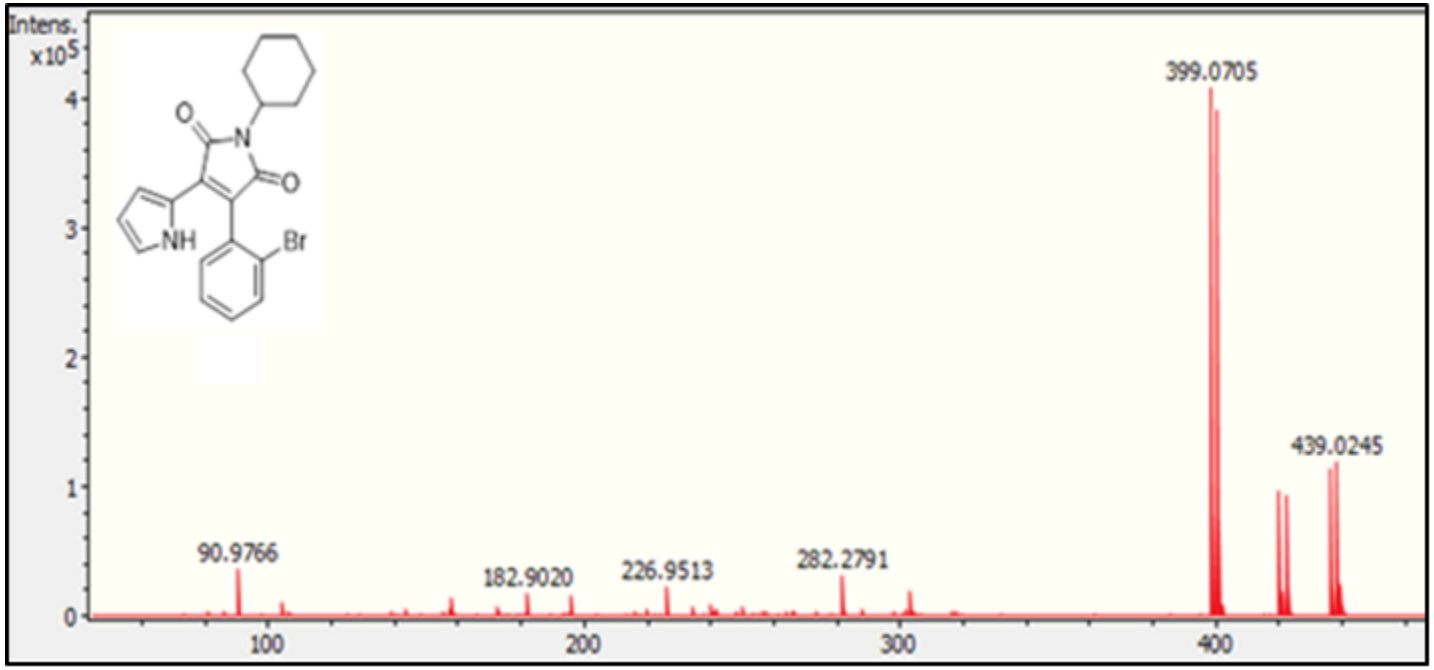
^{13}C-NMR (75 MHz) of ***2f*** in $CDCl_3$



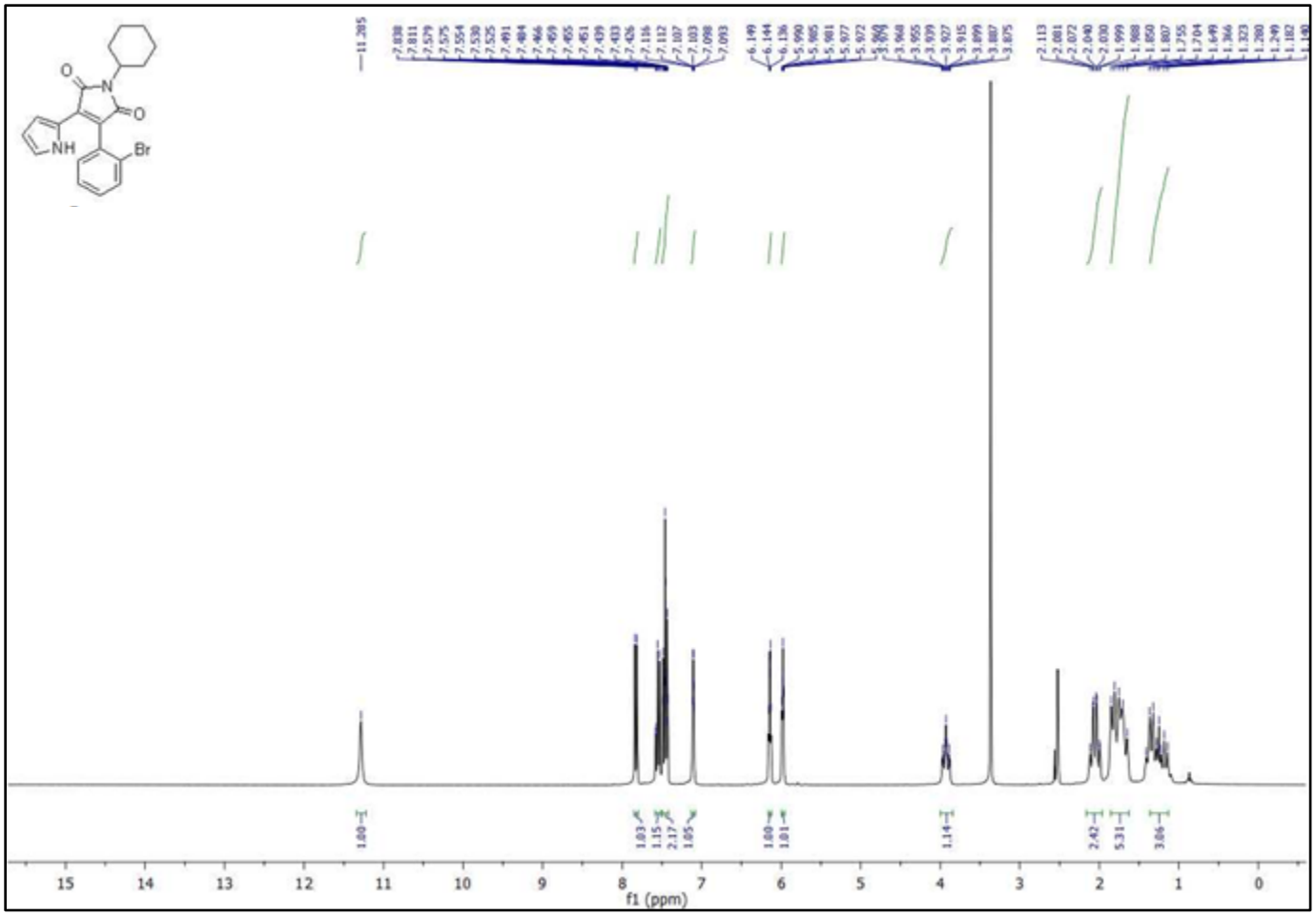
^{1}H-NMR (300 MHz) of ***2g*** in $CDCl_3$



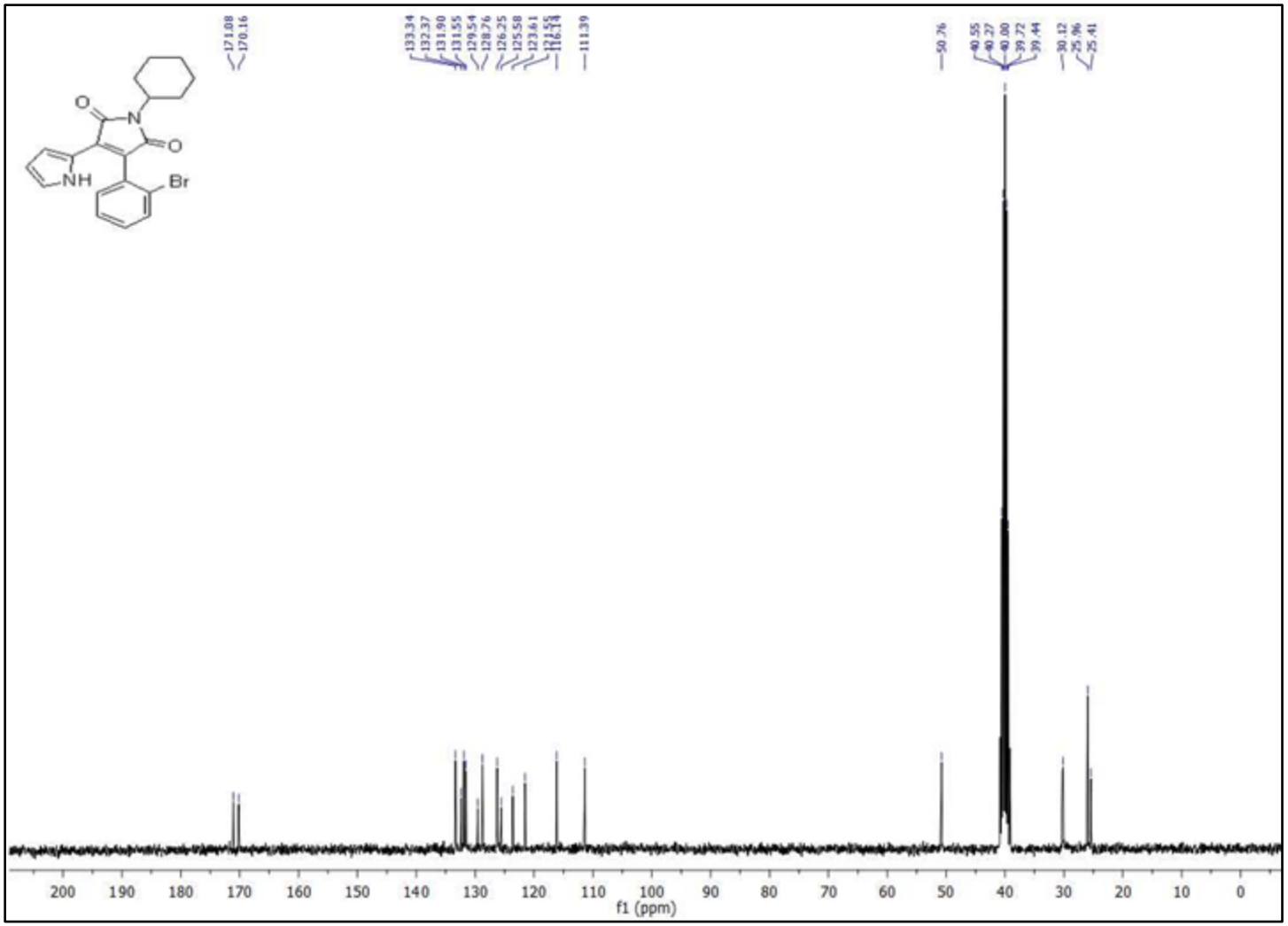
^{13}C-NMR (75 MHz) of ***2g*** in $CDCl_3$



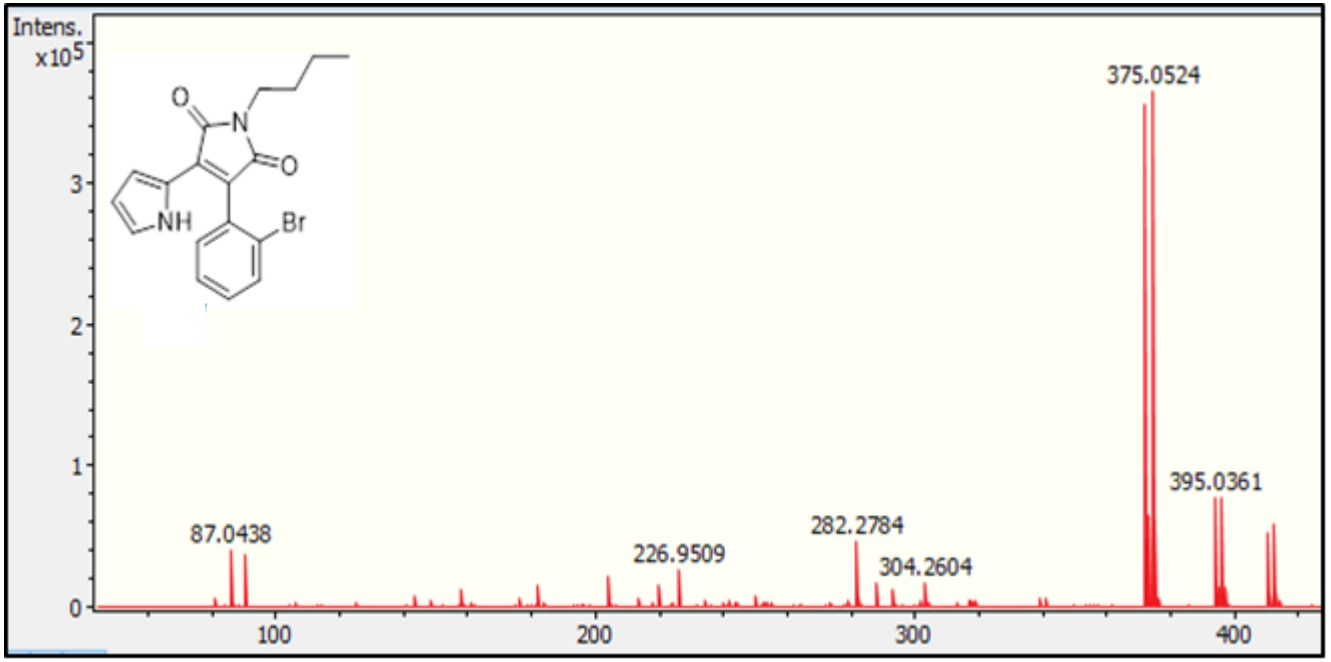
HRMS of **2*h*** ($C_{20}H_{19}BrN_2O_2$ $[M+H]^+$ = 399.0710)



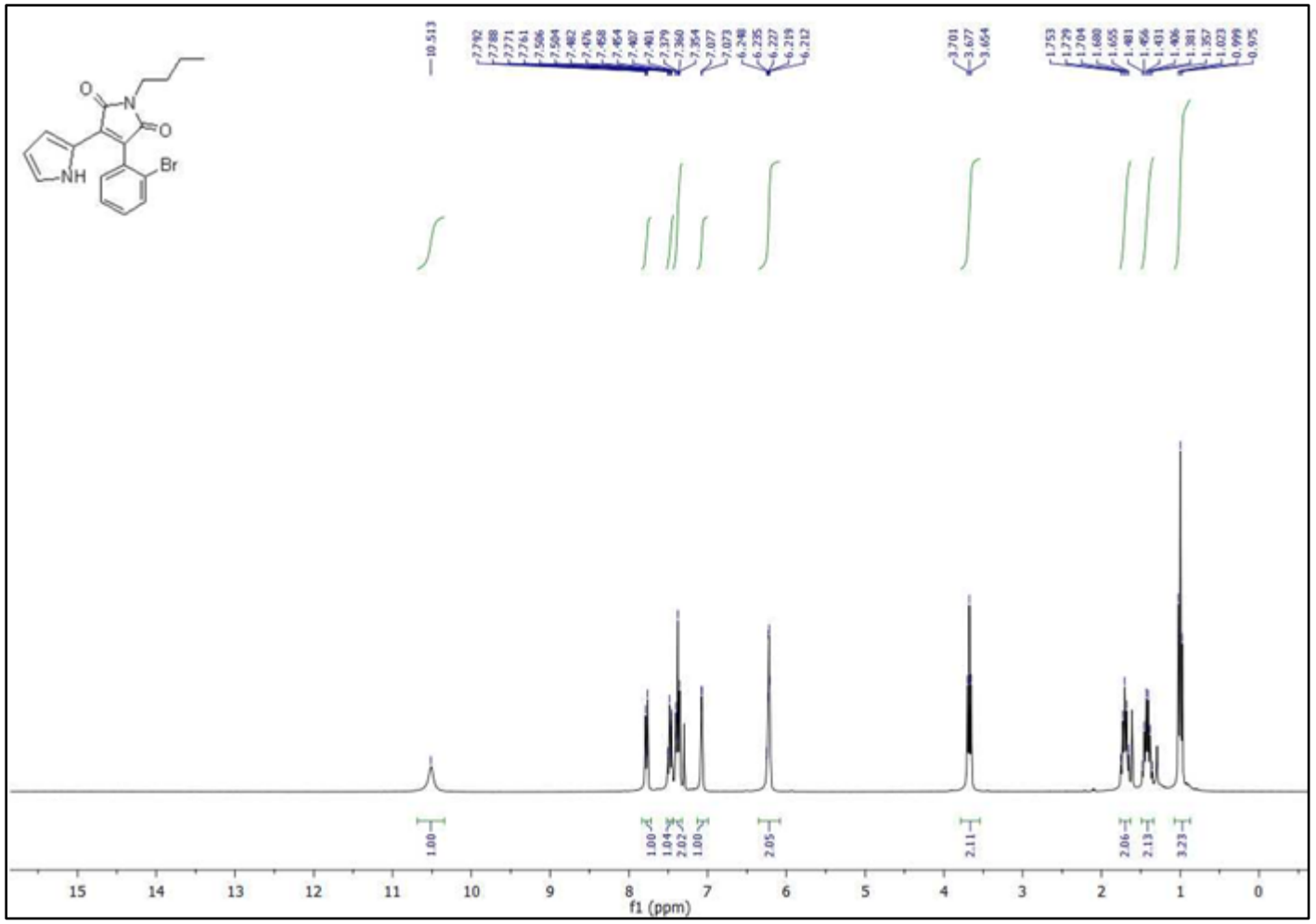
^{1}H-NMR (300 MHz) of ***2h*** in DMSO-d_6



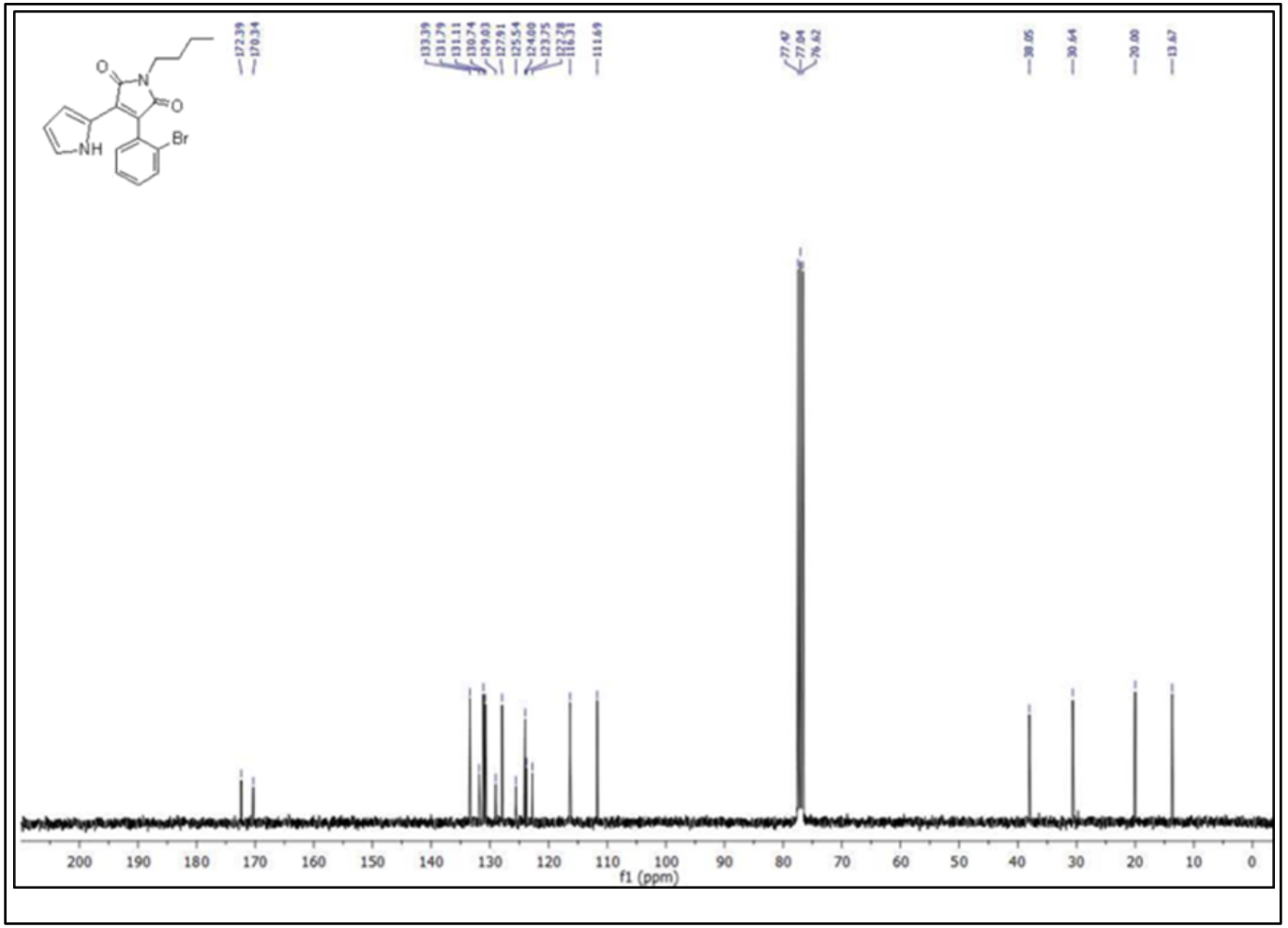
^{13}C-NMR (75 MHz) of ***2h*** in DMSO-d_6



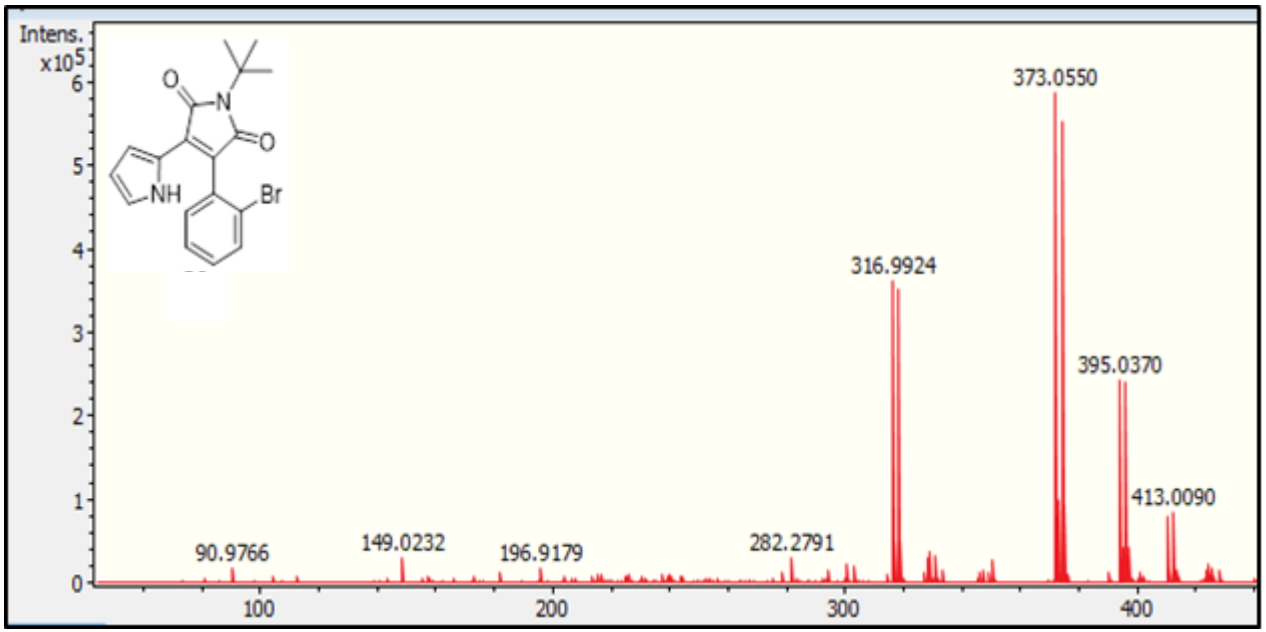
HRMS of ***2i*** ($C_{18}H_{17}{}^{81}BrN_2O_2$ $[M+H]^+$ = 375.0526**)**



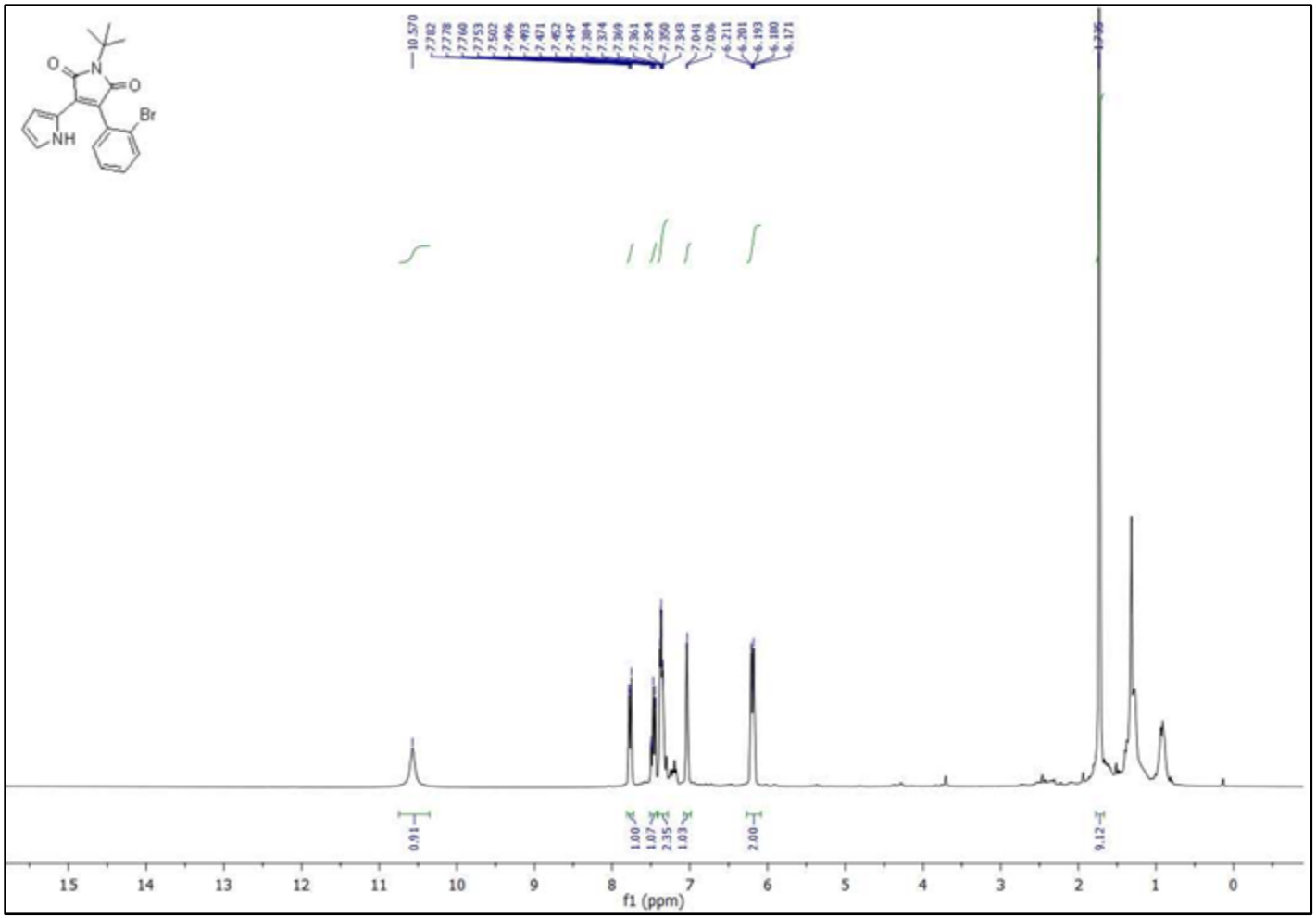
^{1}H-NMR (300 MHz) of ***2i*** in $CDCl_3$



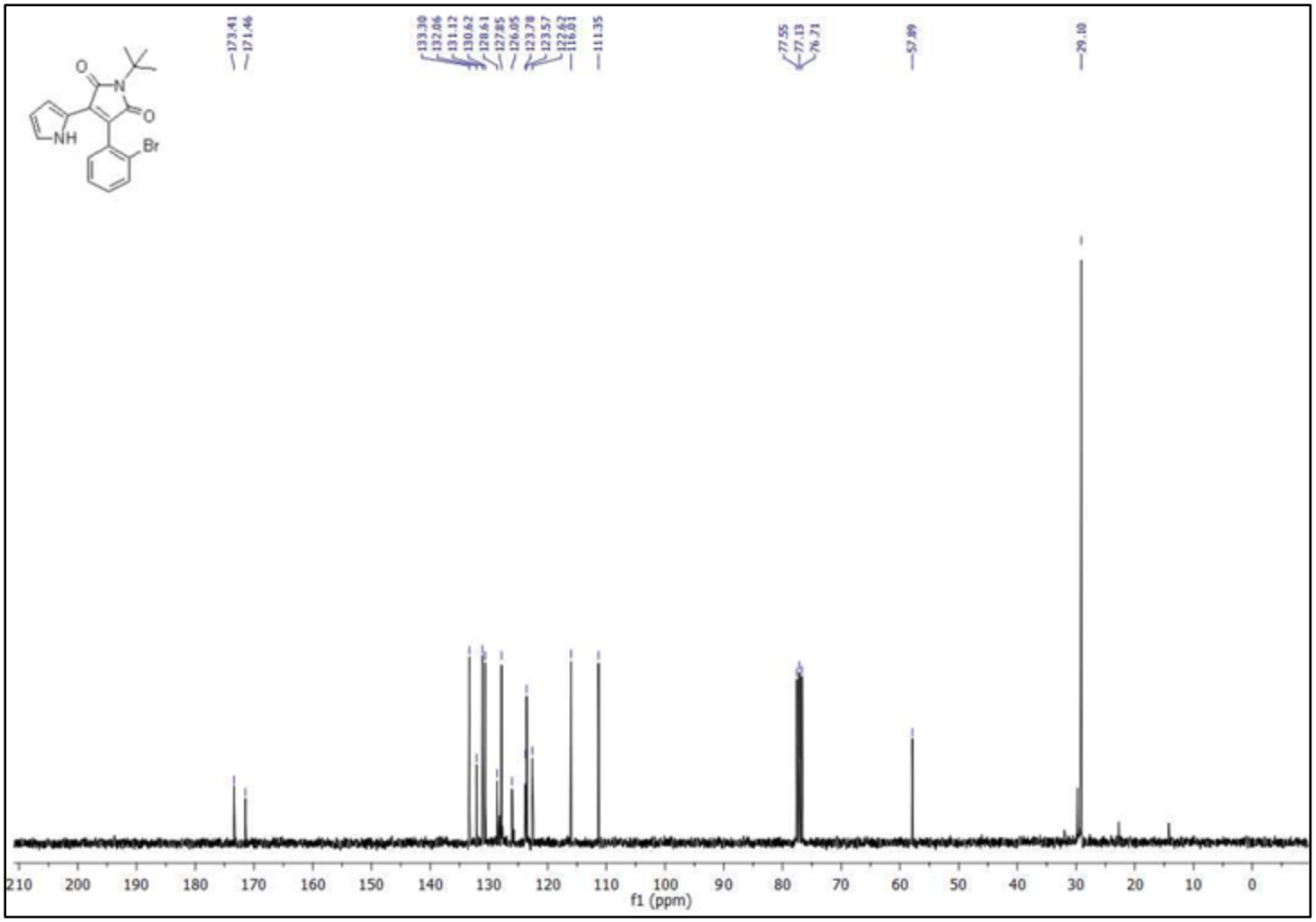
^{13}C-NMR (75 MHz) of ***2i*** in $CDCl_3$



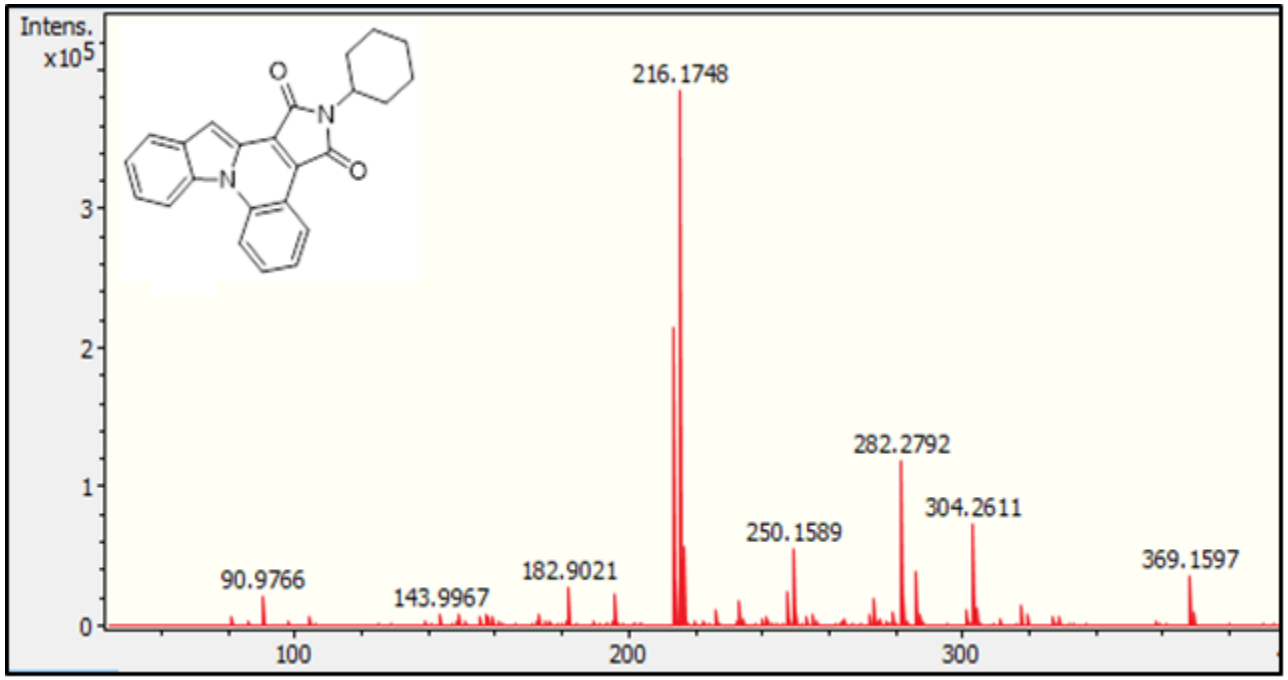
HRMS of **2*j*** ($C_{18}H_{17}BrN_2O_2$ $[M+H]^+$ = 373.0553)



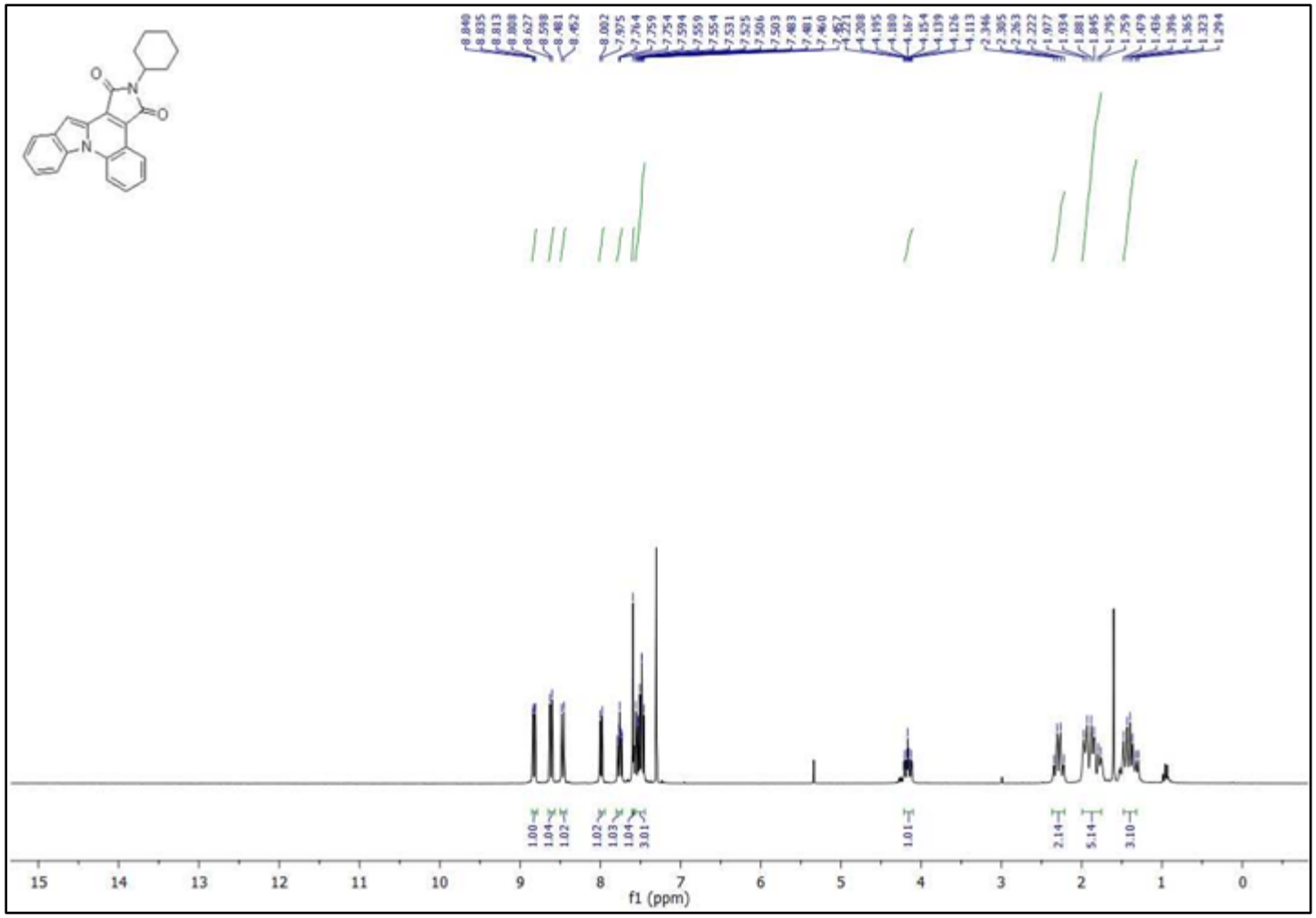
^{1}H-NMR (300 MHz) of ***2j*** in $CDCl_3$



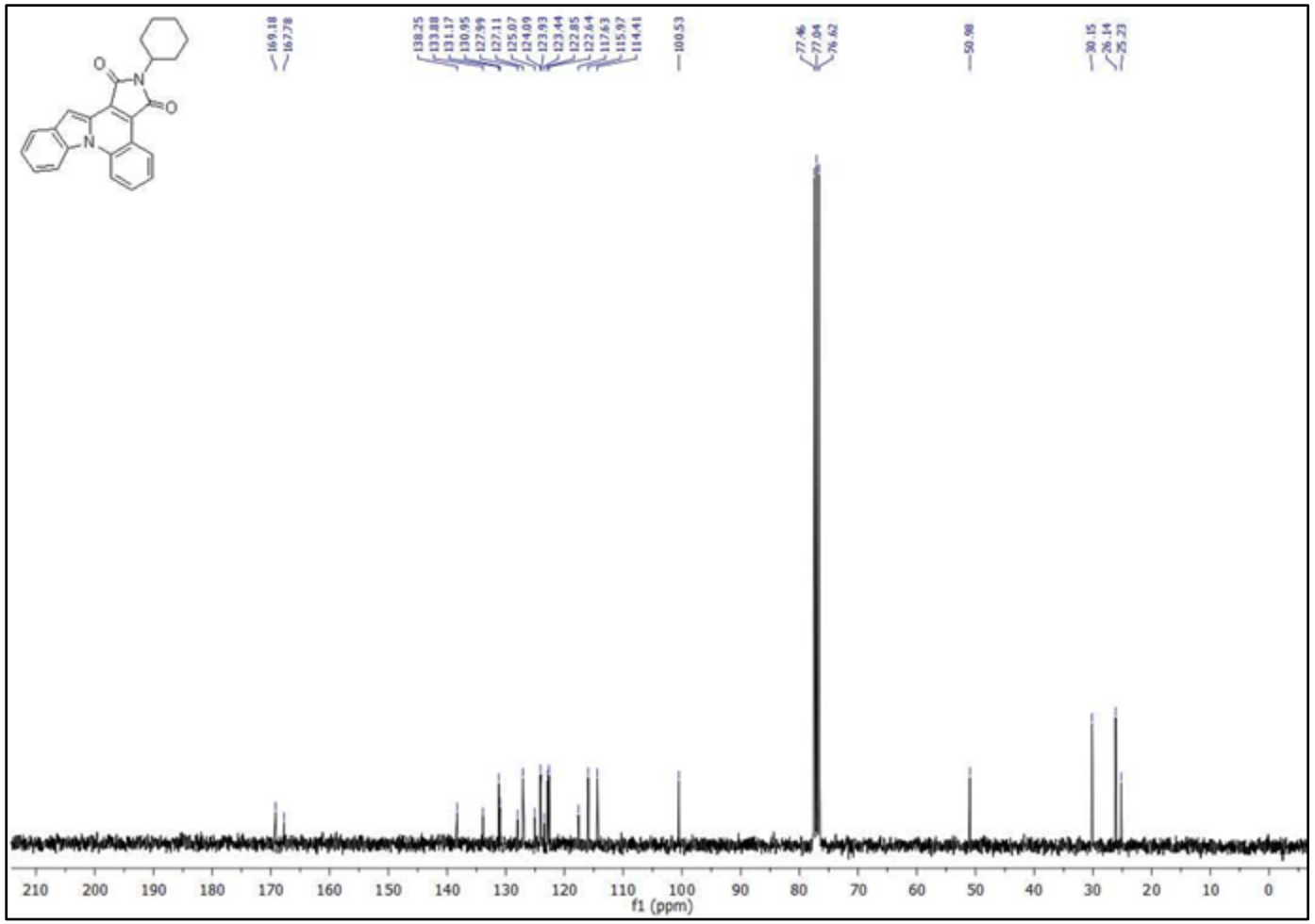
^{13}C-NMR (75 MHz) of ***2j*** in $CDCl_3$



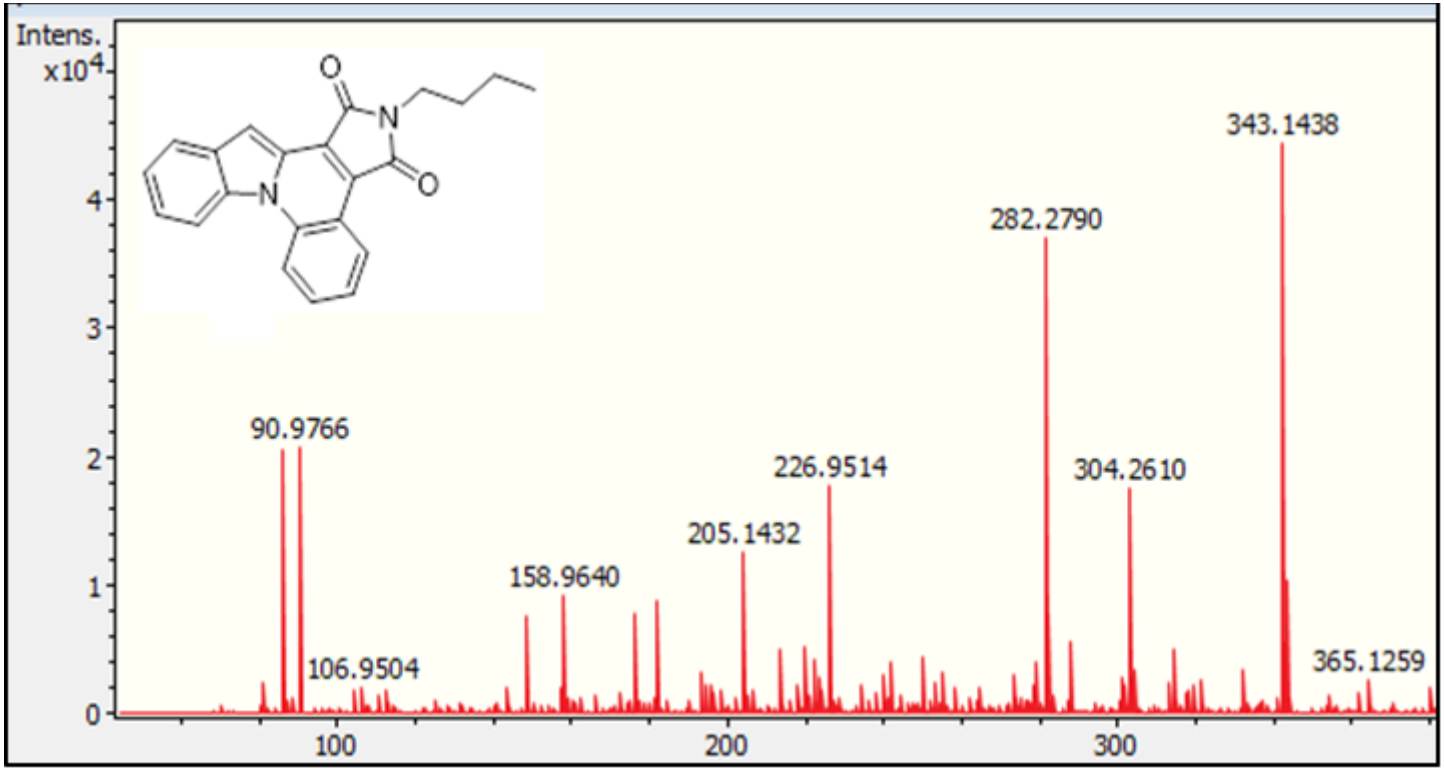
HRMS of ***3a*** ($C_{24}H_{20}N_2O_2$ $[M+H]^+$ = 369.1605)



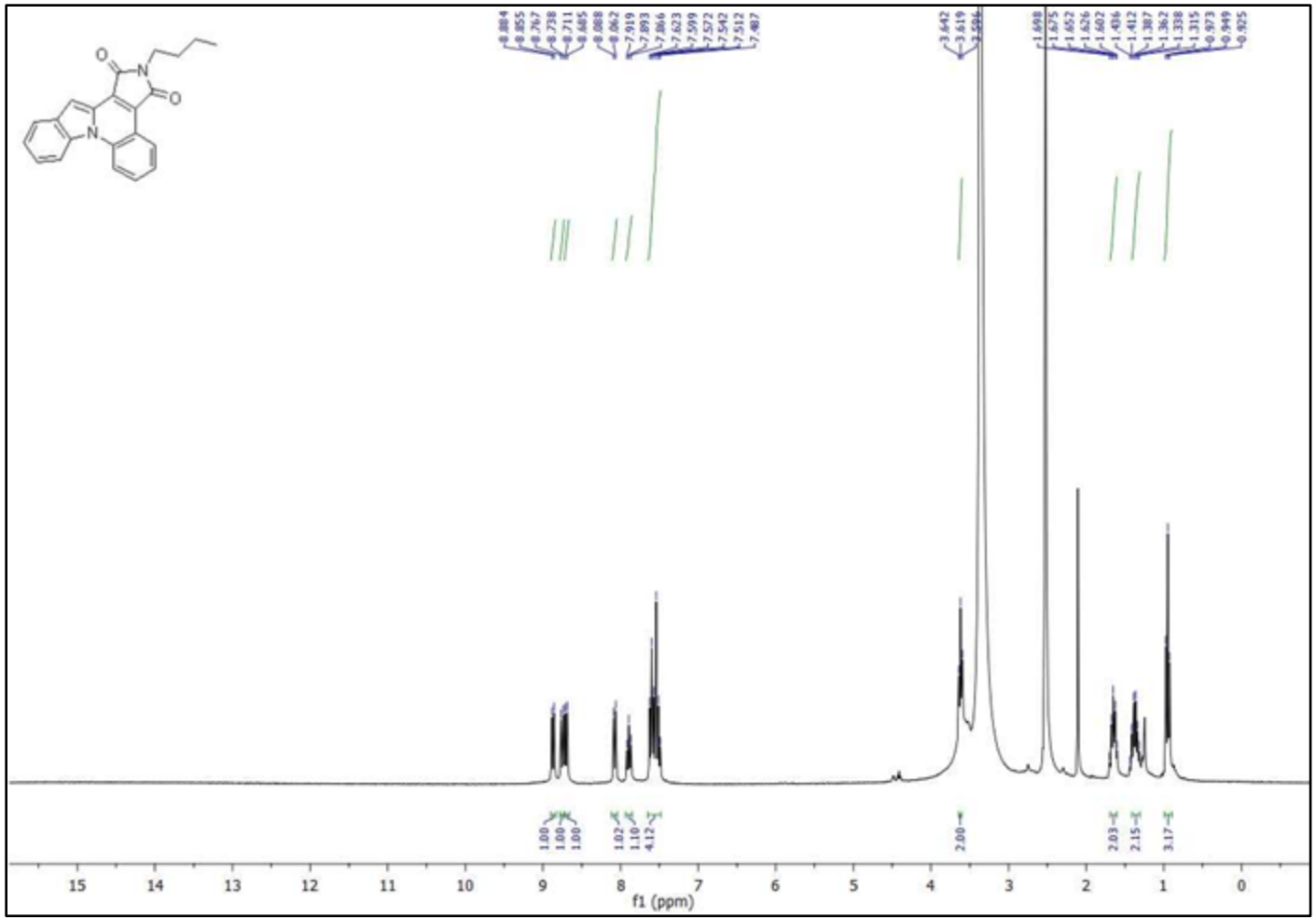
^{1}H-NMR (300 MHz) of ***3a*** in $CDCl_3$



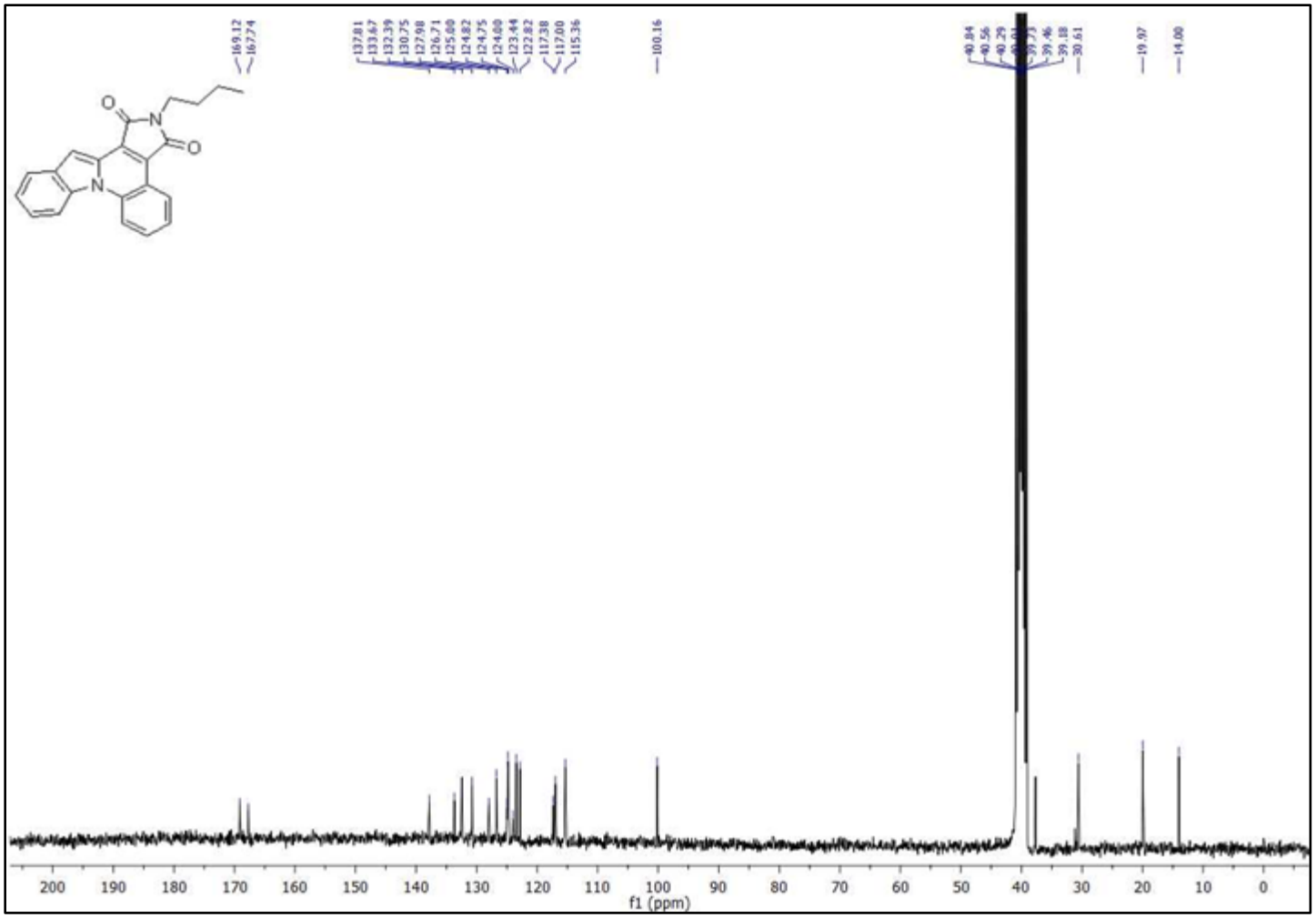
^{13}C-NMR (75 MHz) of ***3a*** in $CDCl_3$



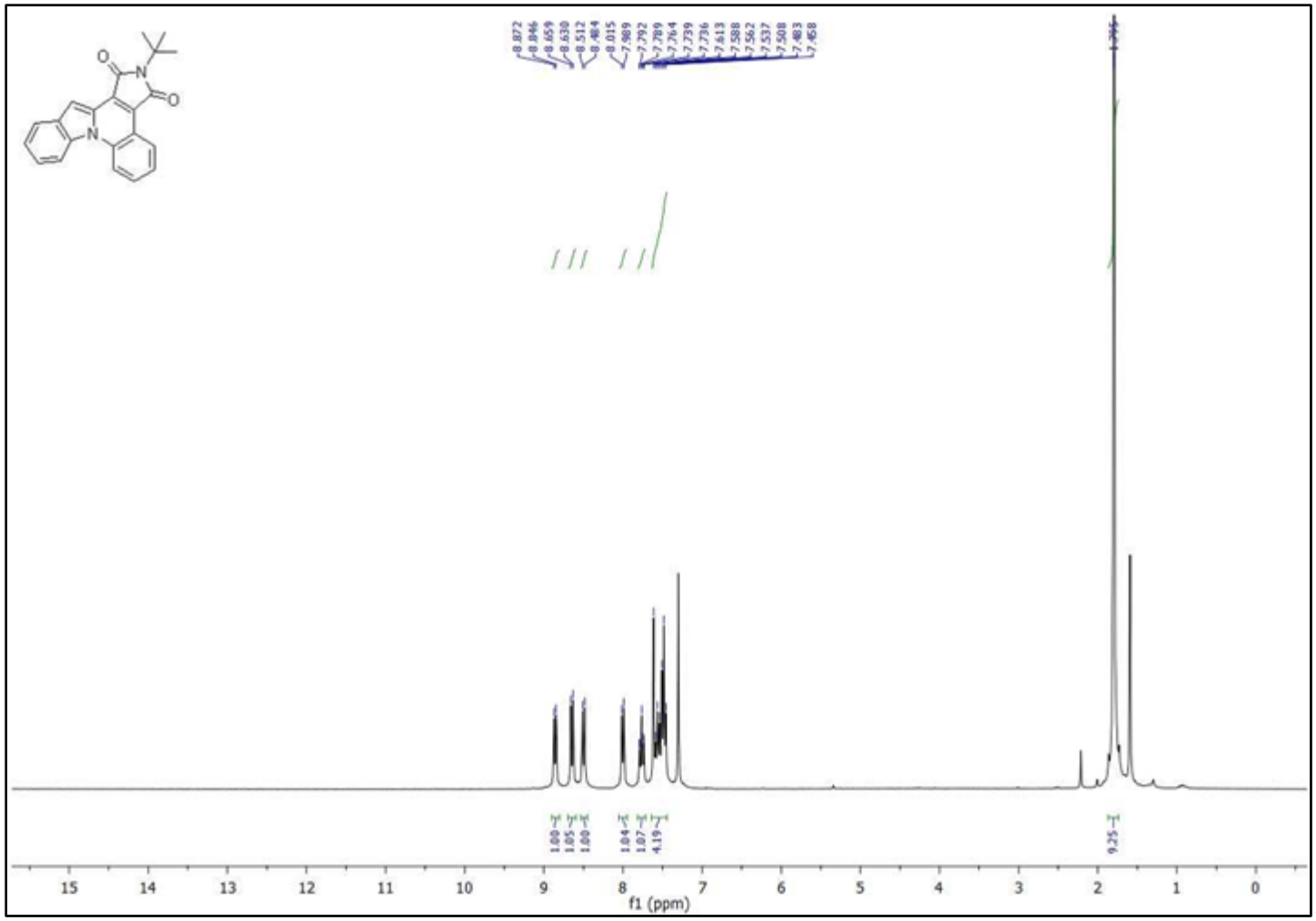
HRMS of ***3b*** ($C_{22}H_{18}N_2O_2$ $[M+H]^+$ = 343.1448)



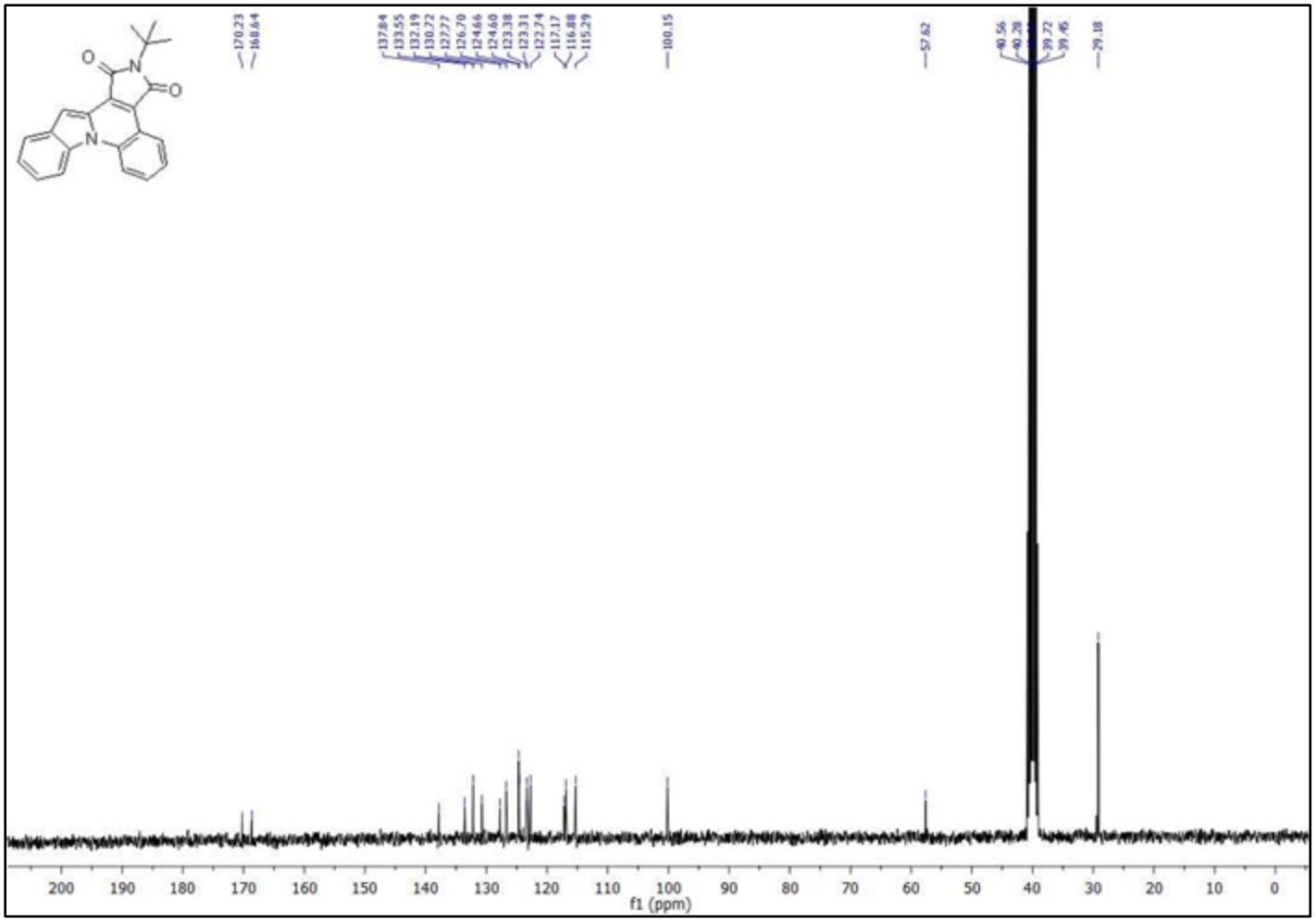
^{1}H-NMR (300 MHz) of ***3b*** in DMSO-d_6



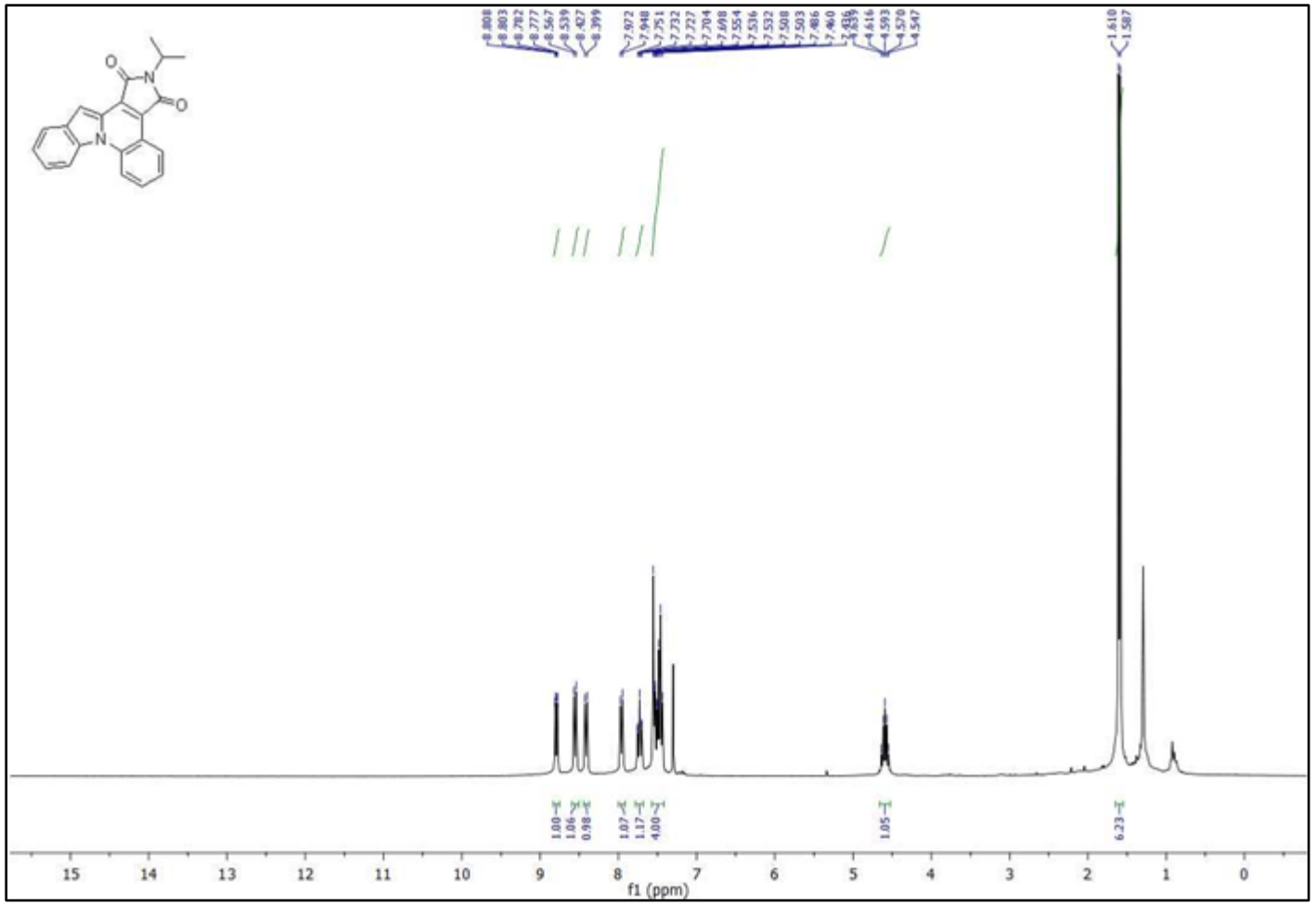
^{13}C-NMR (75 MHz) of ***3b*** in DMSO-d_6



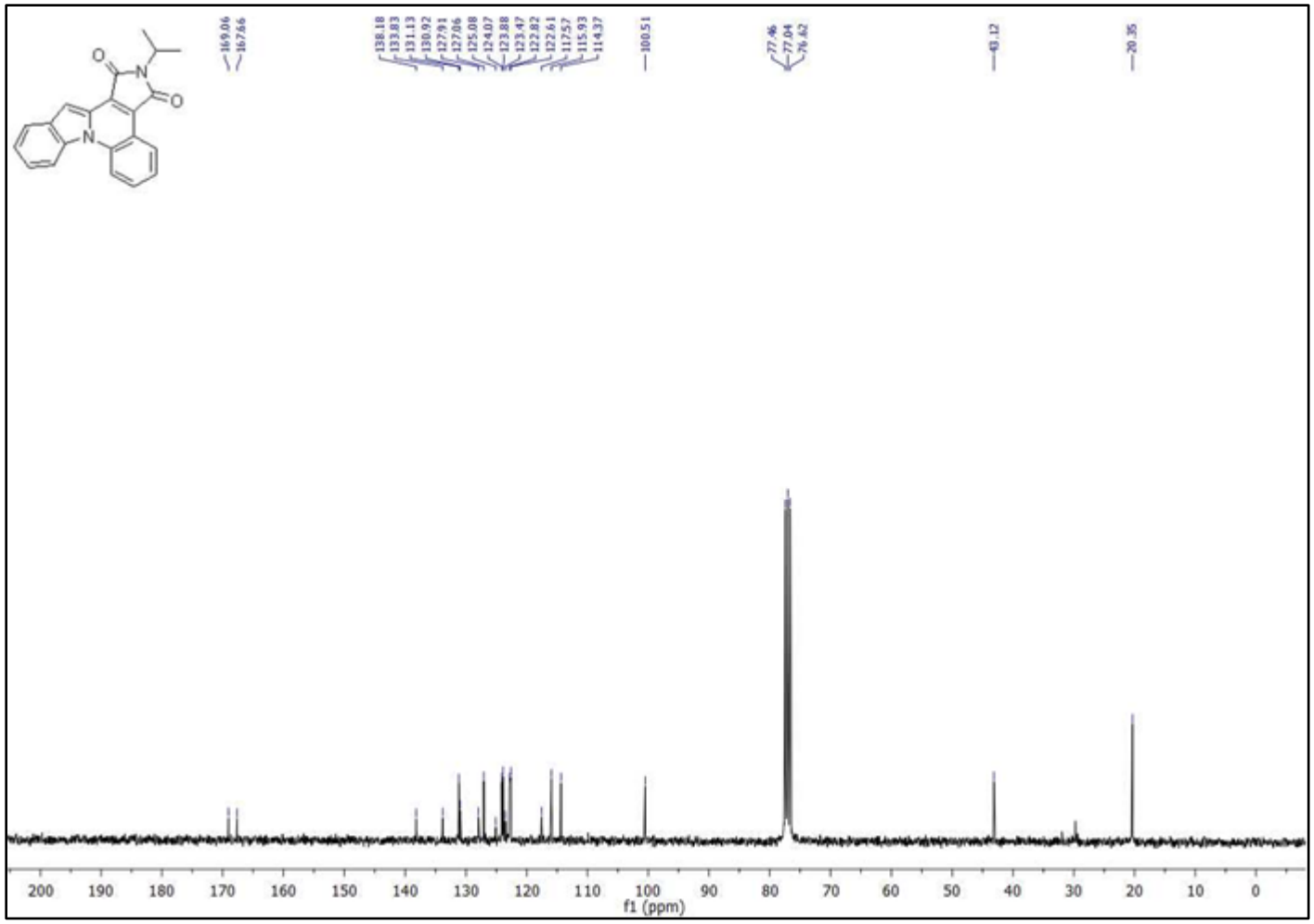
^{1}H-NMR (300 MHz) of ***3c*** in $CDCl_3$



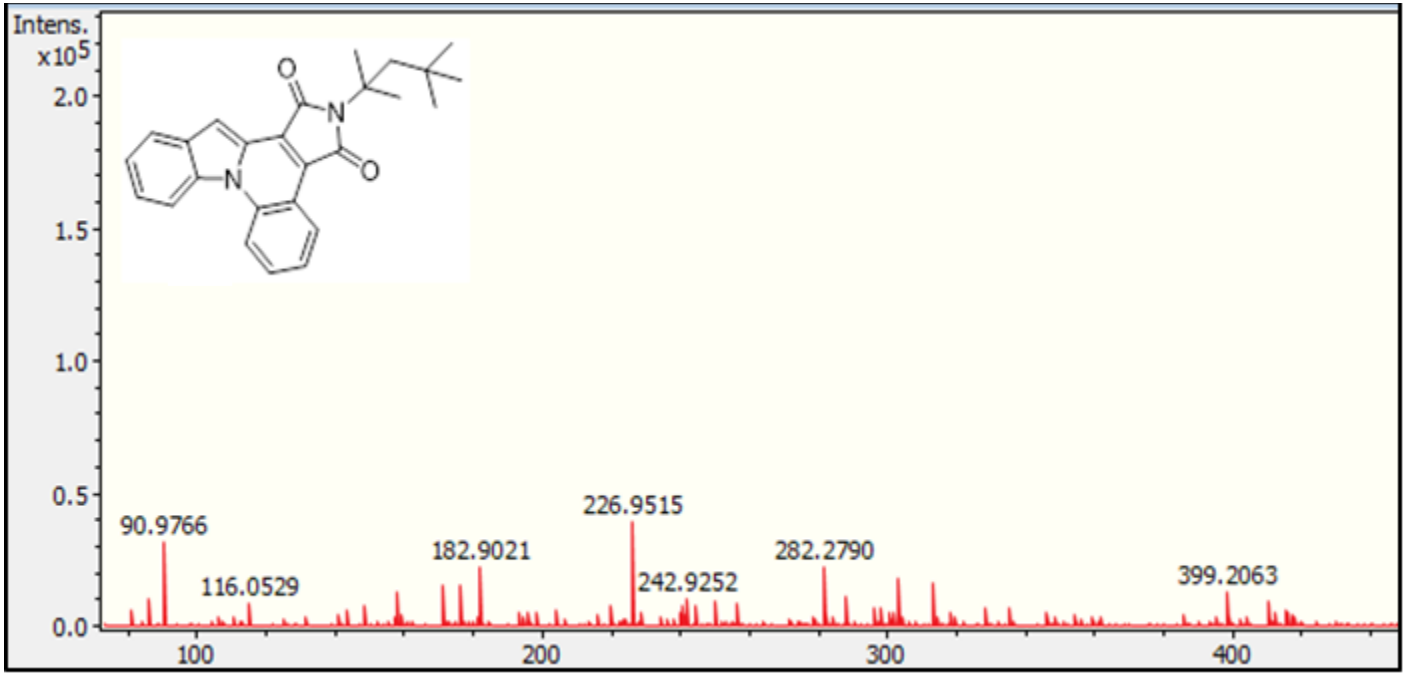
^{13}C-NMR (75 MHz) of **3*c*** in DMSO-d_6



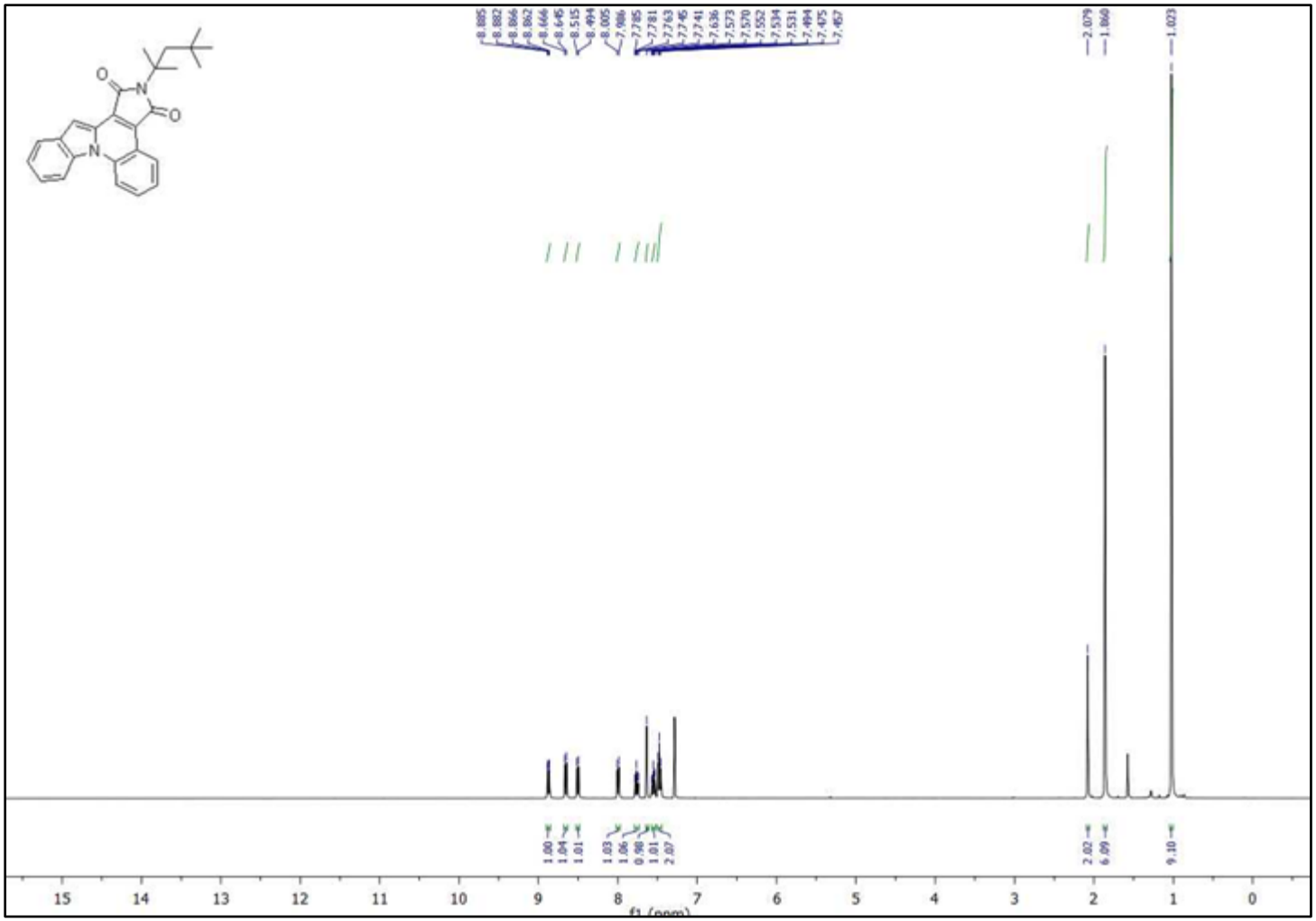
^{1}H-NMR (300 MHz) of ***3d*** in $CDCl_3$



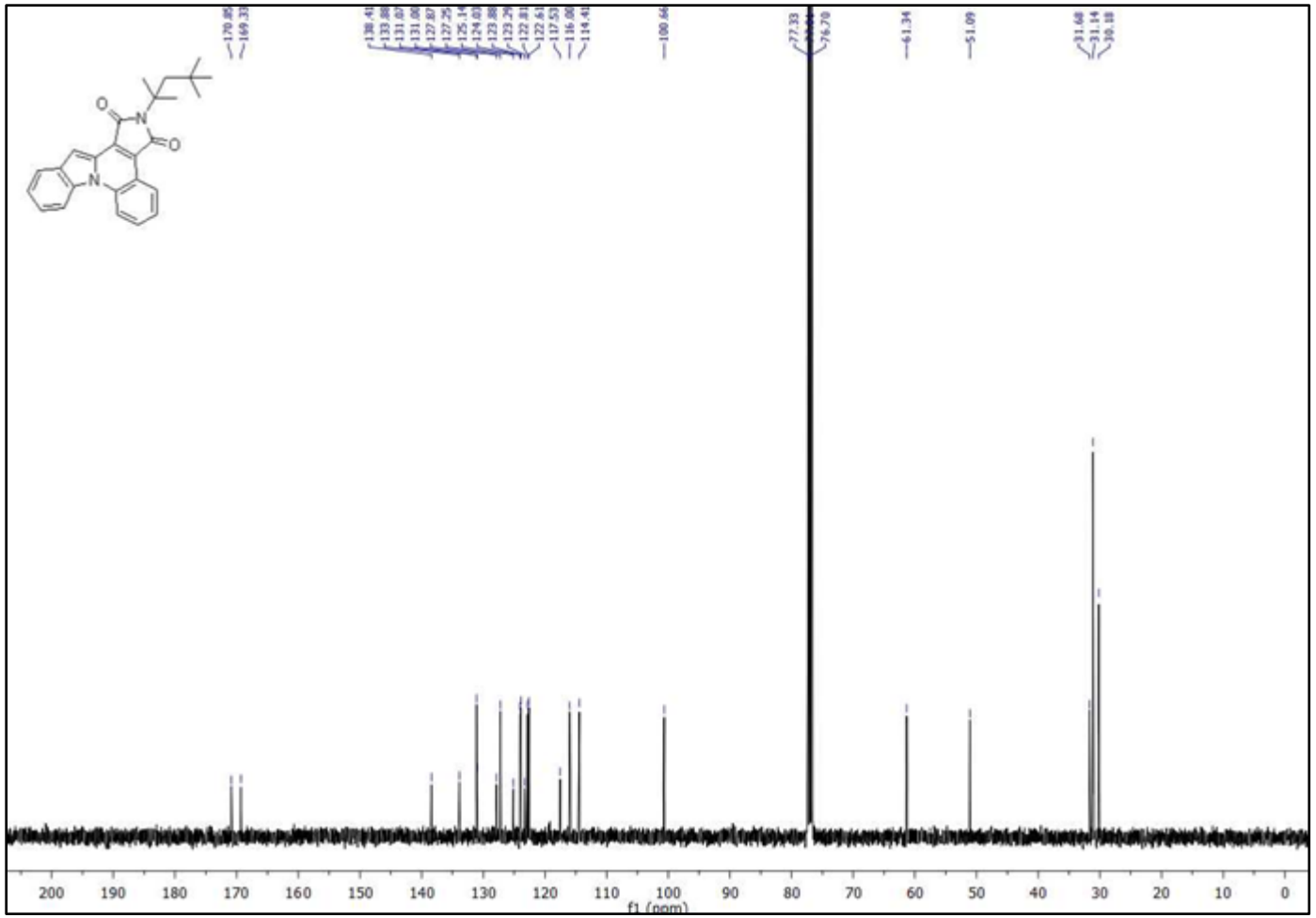
^{13}C-NMR (75 MHz) of ***3d*** in $CDCl_3$



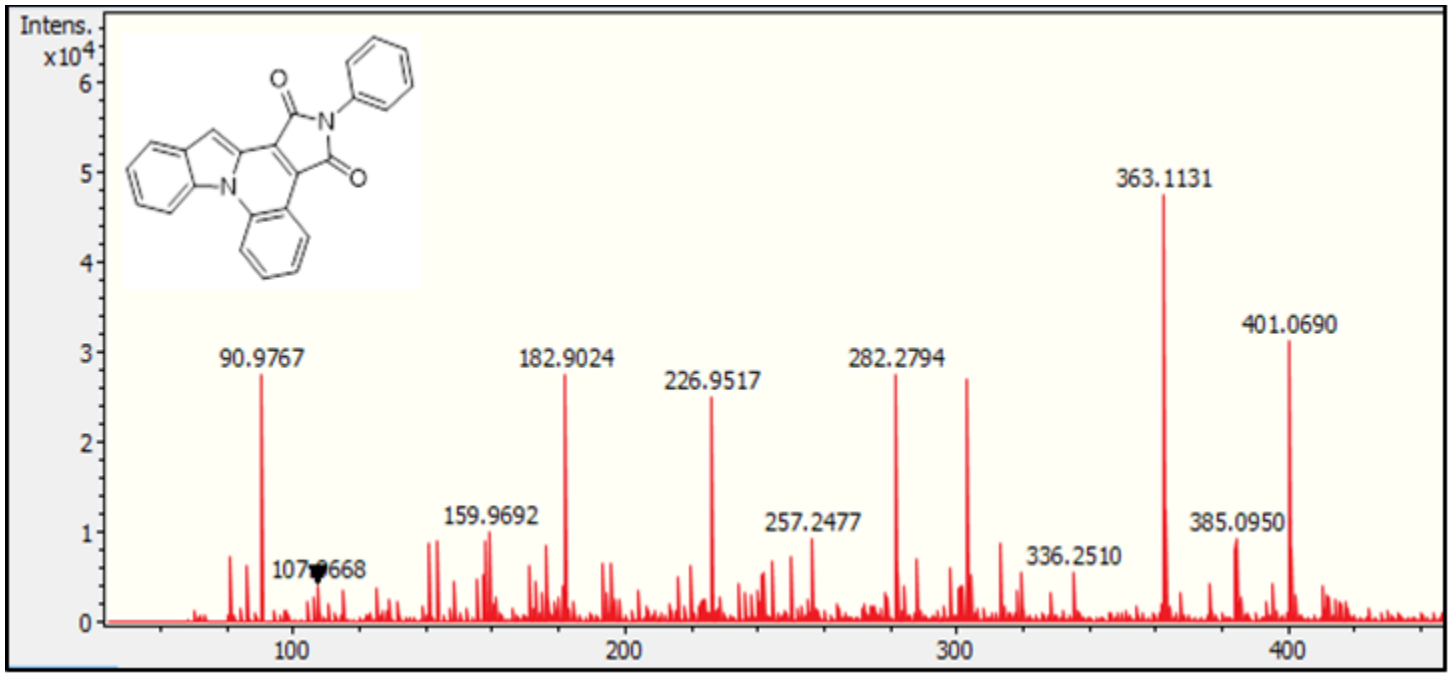
HRMS of ***3e*** ($C_{26}H_{26}N_2O_2$ $[M+H]^+$ = 399.2074)



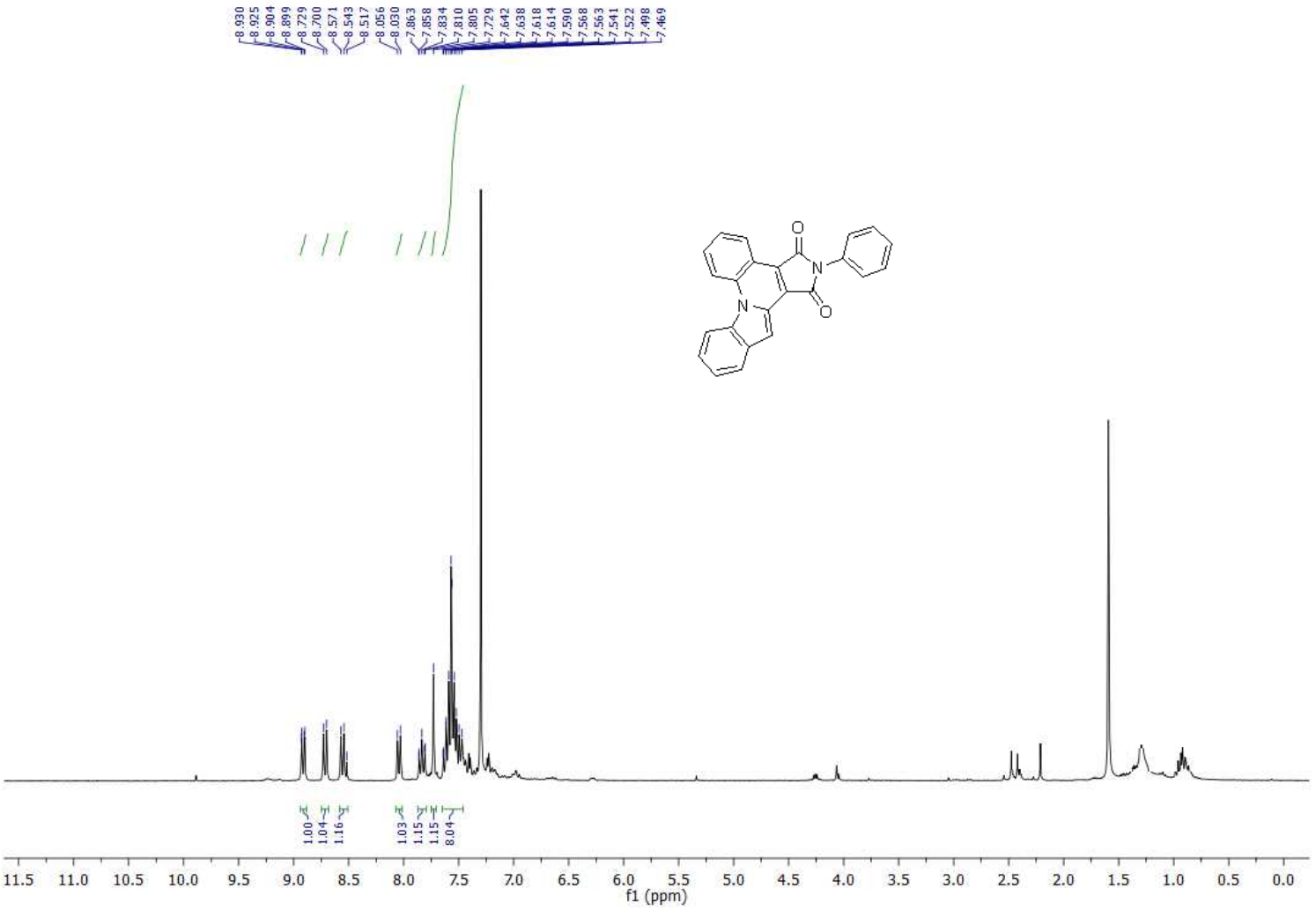
^{1}H-NMR (400 MHz) of ***3e*** in DMSO-d_6



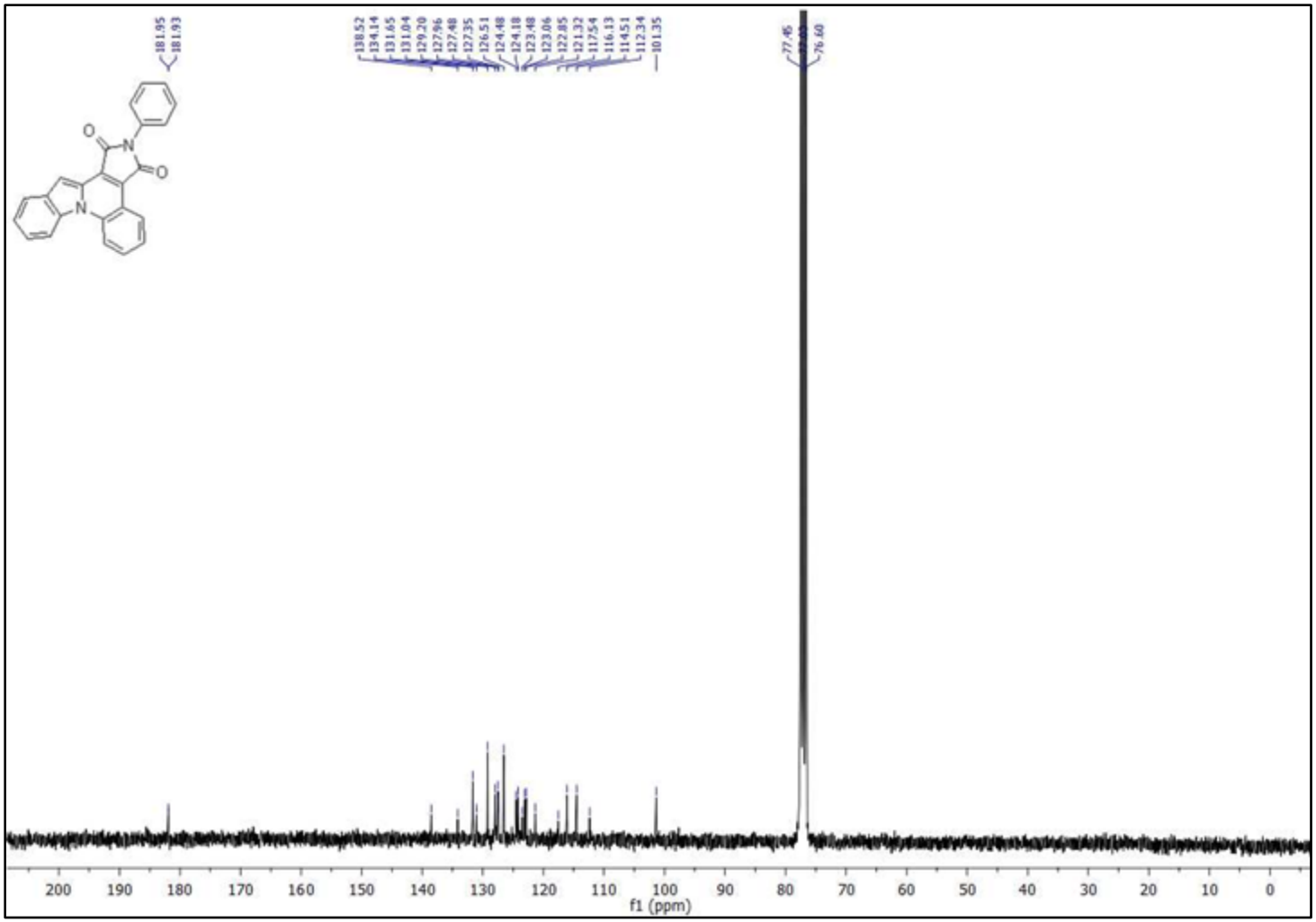
^{13}C-NMR (100 MHz) of ***3e*** in DMSO-d_6



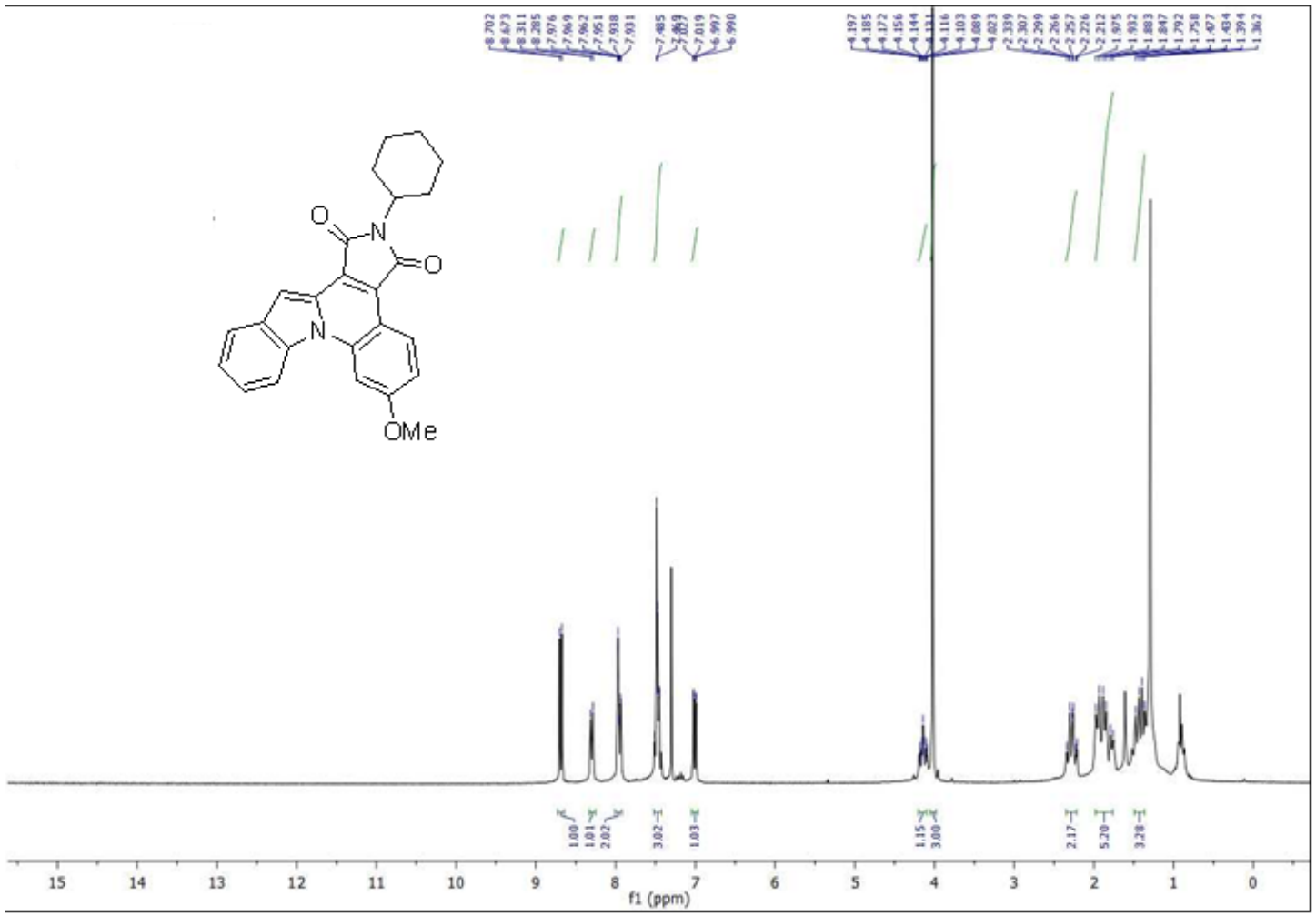
HRMS of ***3f*** **(**$C_{24}H_{14}N_2O_2$ $[M+H]^+$ = 363.1135**)**



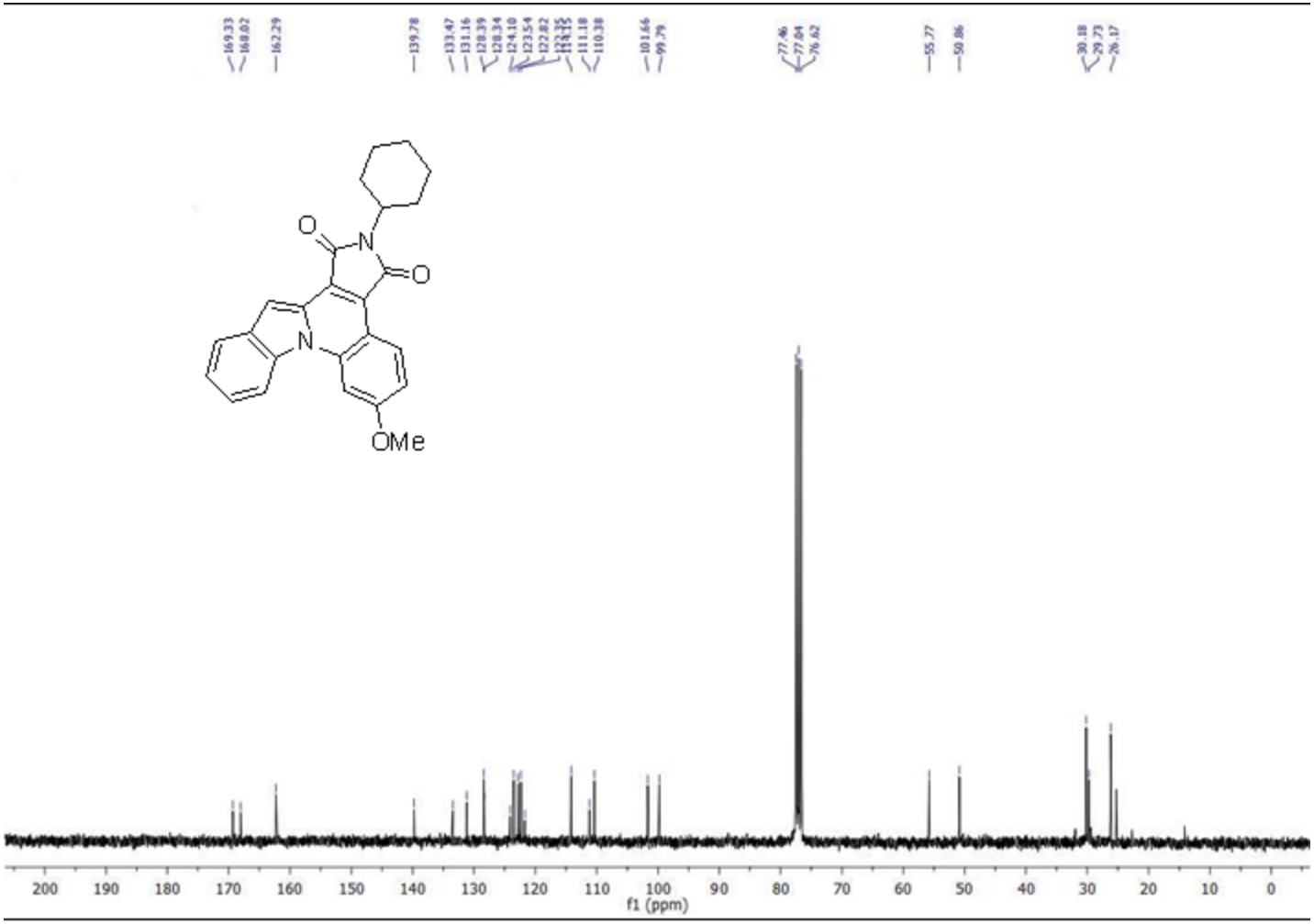
^{1}H-NMR (300 MHz) of ***3f*** in $CDCl_3$



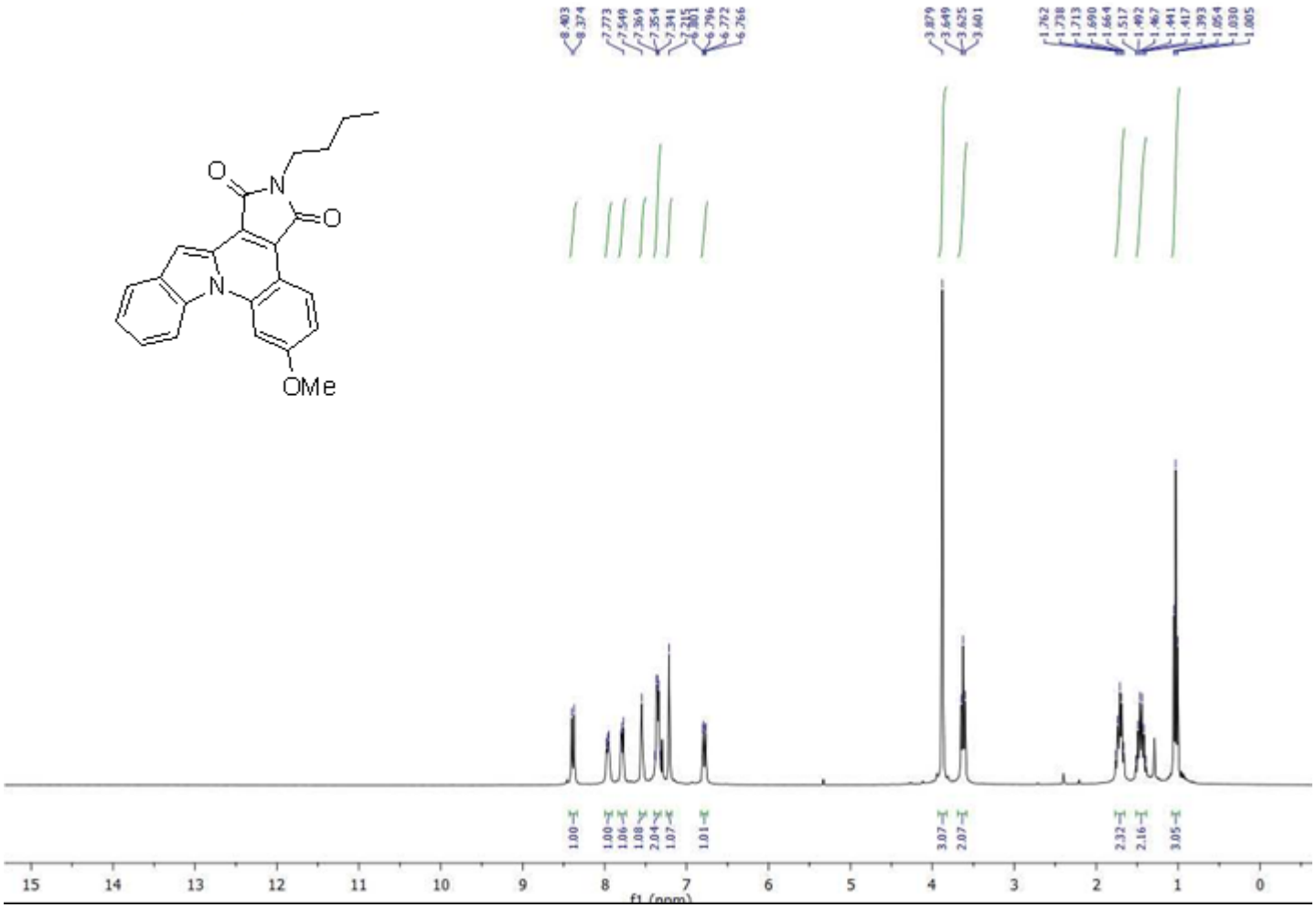
^{13}C-NMR (75 MHz) of ***3f*** in $CDCl_3$



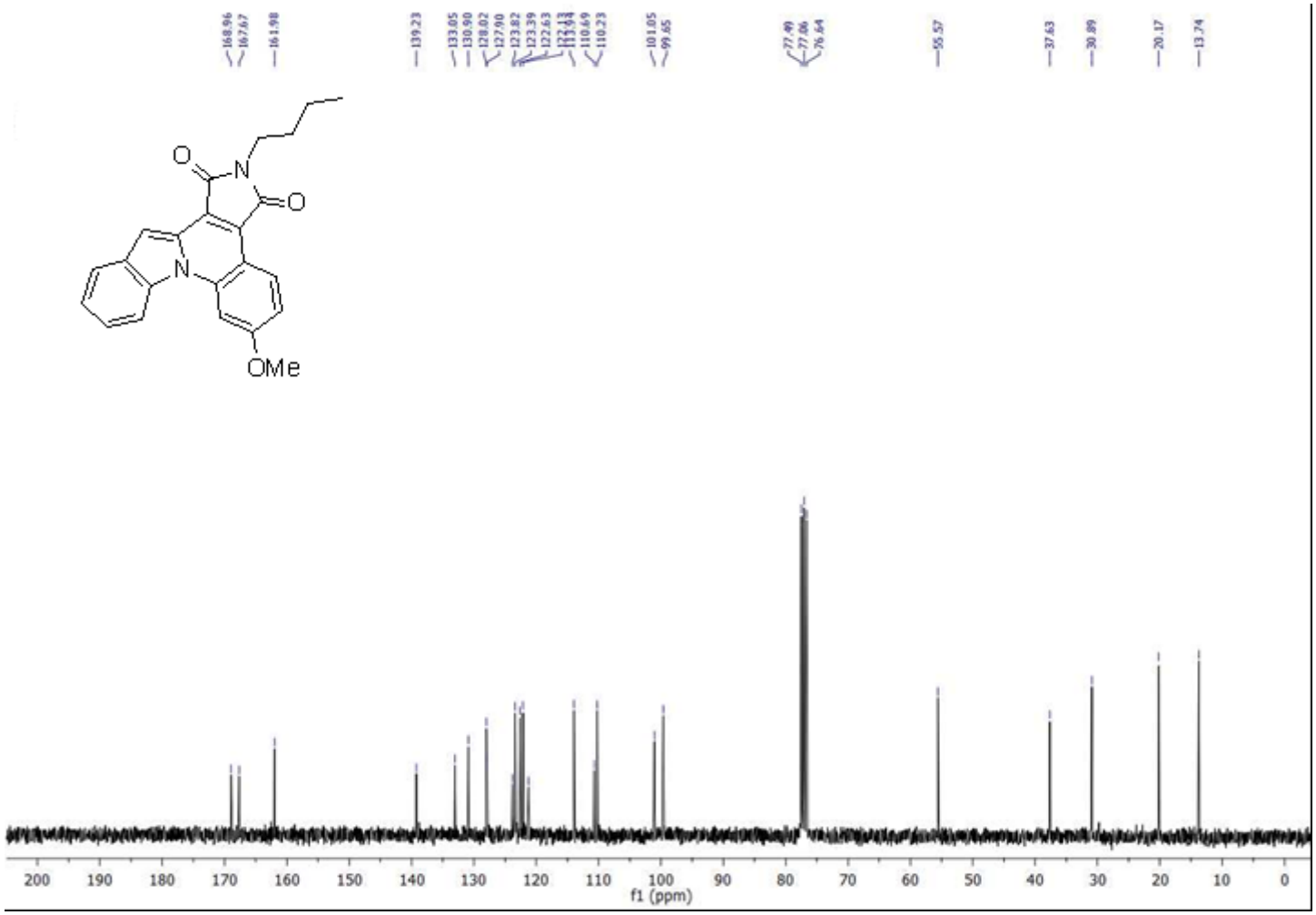
^{1}H-NMR (300 MHz) of ***3g*** in $CDCl_3$



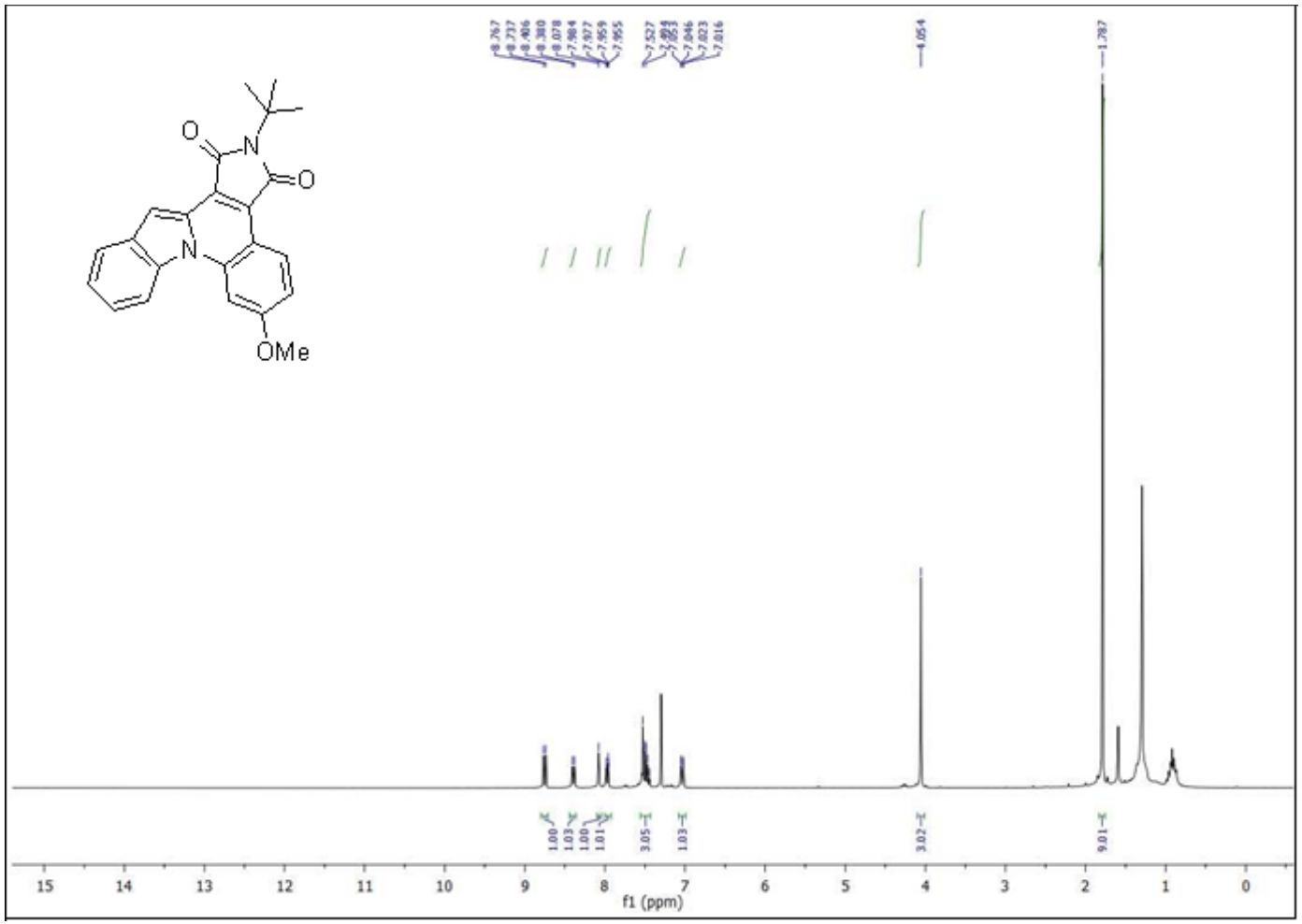
^{13}C-NMR (75 MHz) of ***3g*** in $CDCl_3$



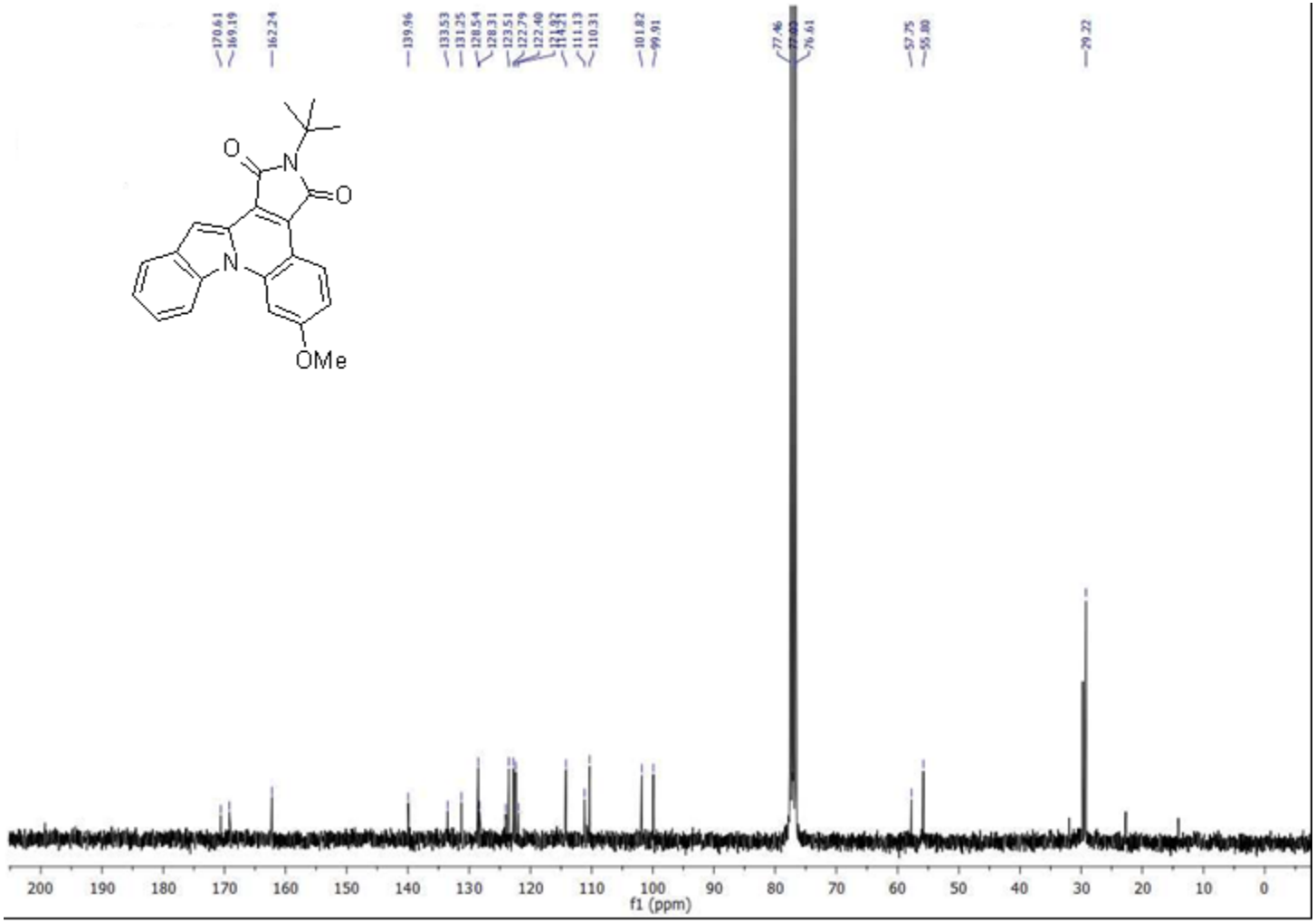
^{1}H-NMR (300 MHz) of ***3h*** in $CDCl_3$



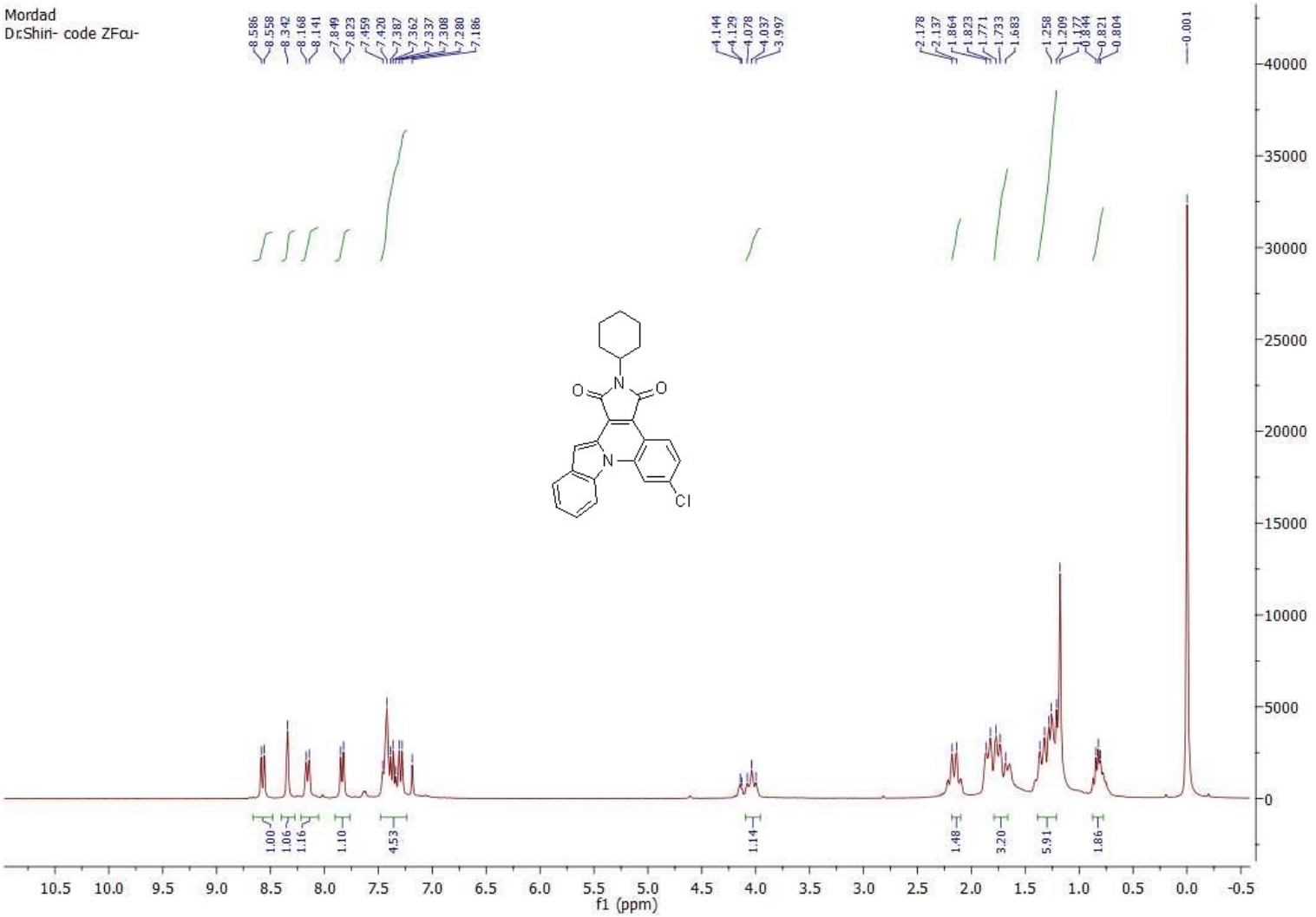
^{13}C-NMR (75 MHz) of ***3h*** in $CDCl_3$



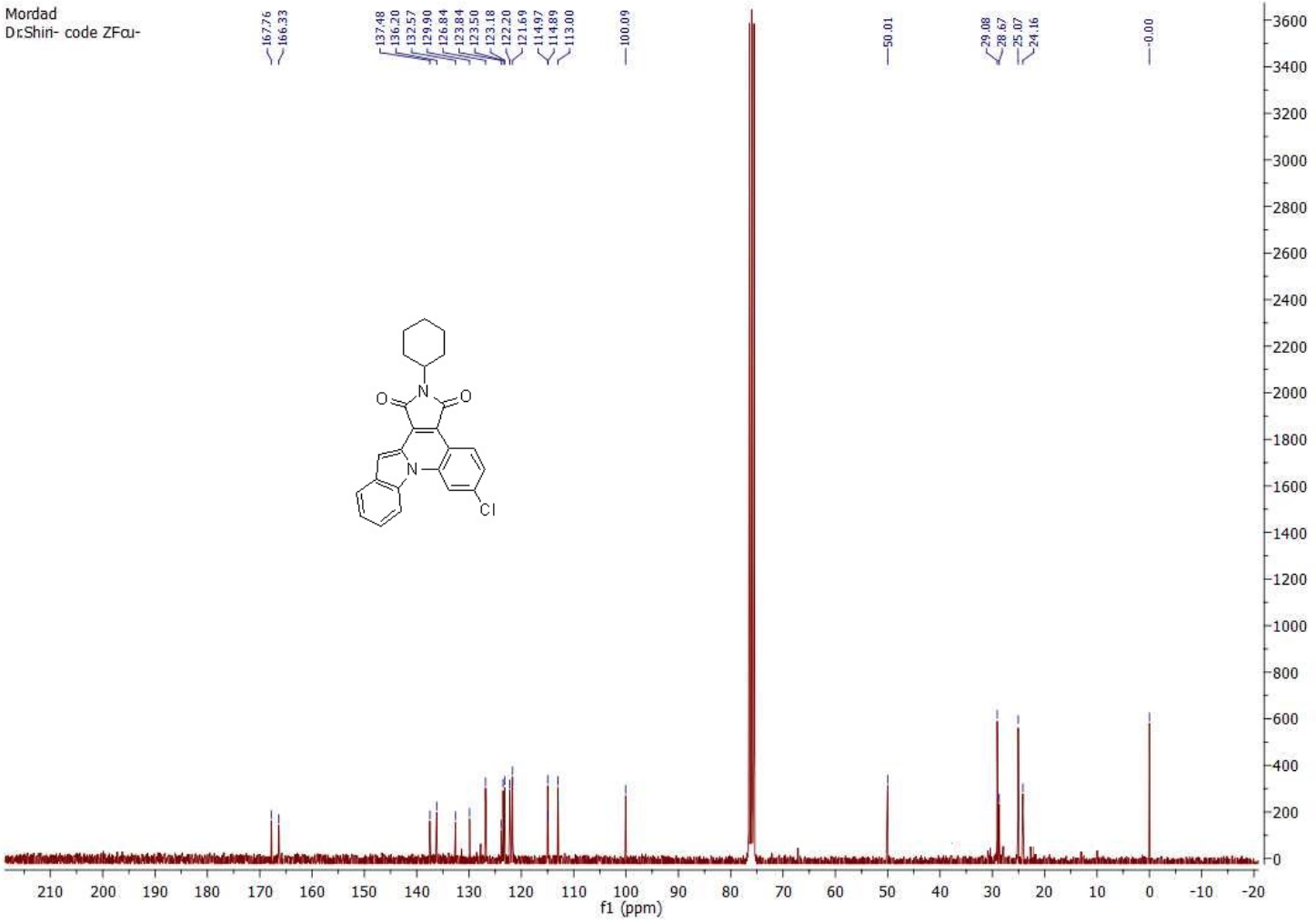
^{1}H-NMR (300 MHz) of ***3i*** in $CDCl_3$



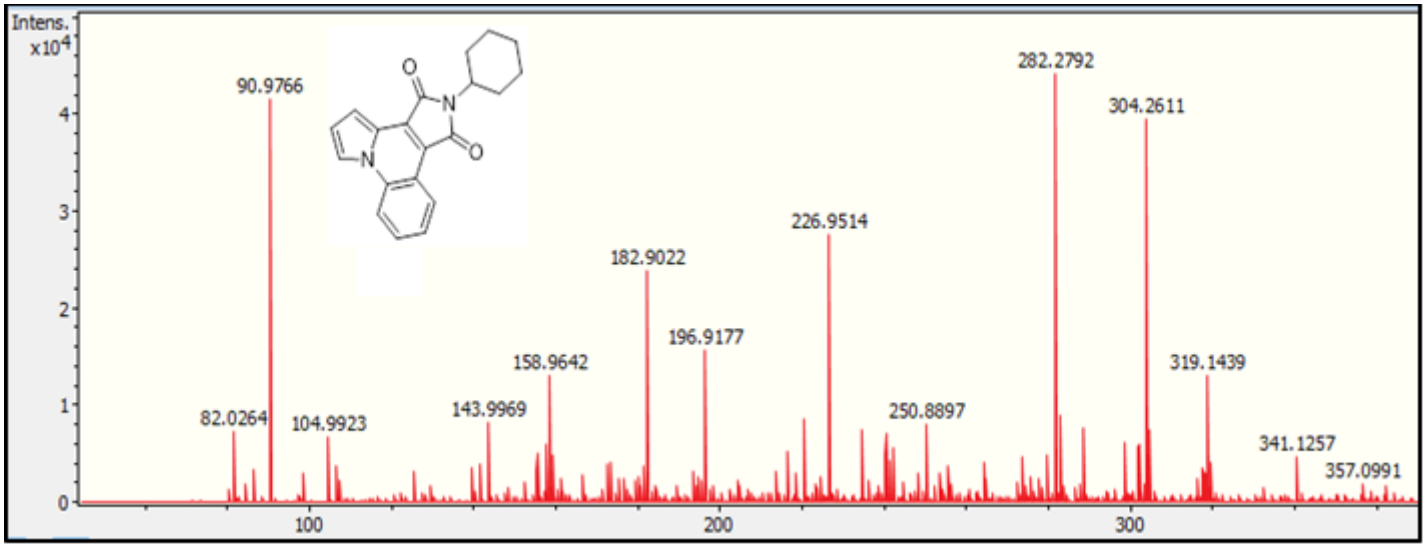
^{13}C-NMR (75 MHz) of ***3i*** in $CDCl_3$



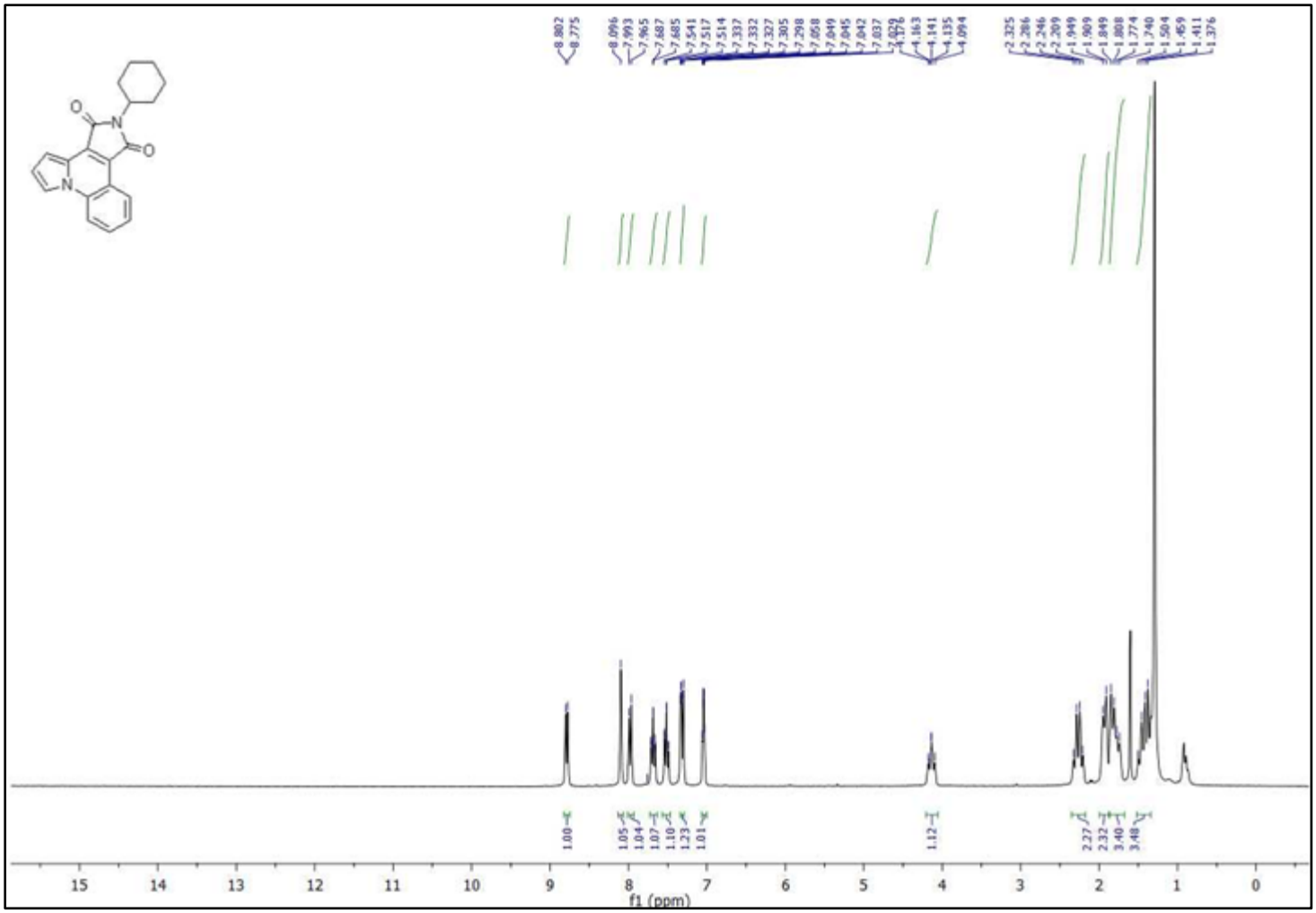
^{1}H-NMR (300 MHz) of ***3j*** in $CDCl_3$



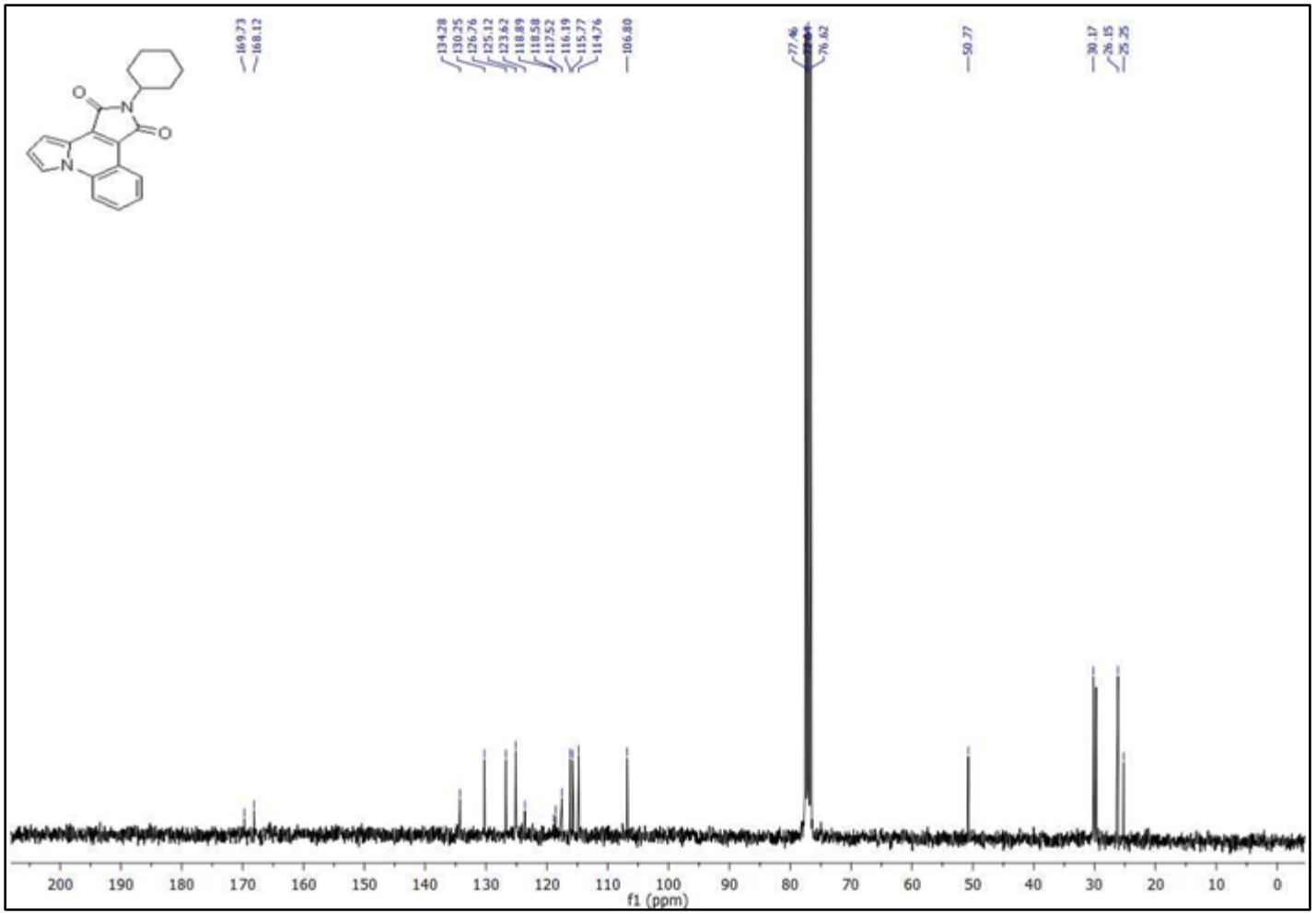
^{13}C-NMR (75 MHz) of ***3j*** in $CDCl_3$



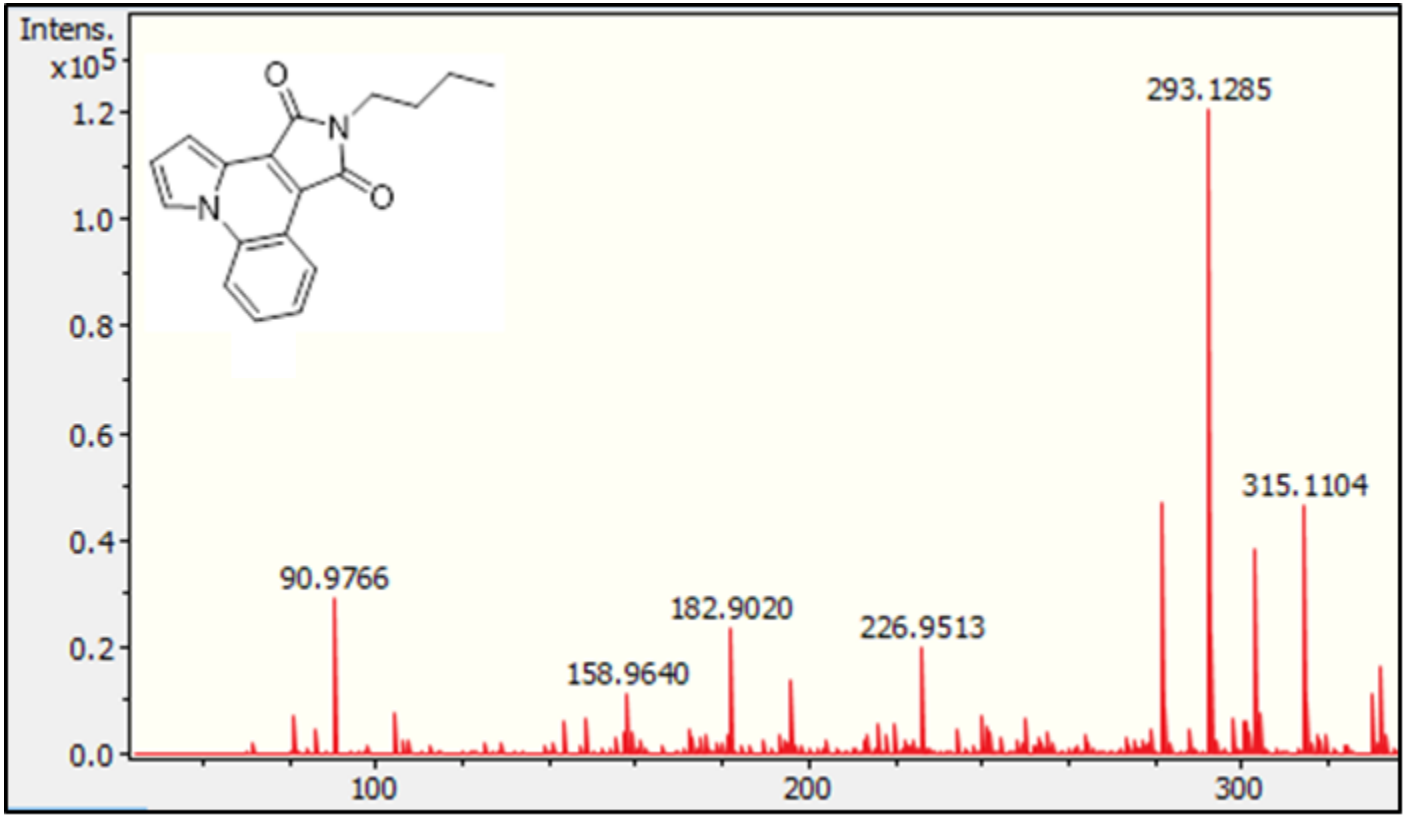
HRMS of ***3k*** ($C_{20}H_{18}N_2O_2$ $[M+H]^+$ = 319.1448)



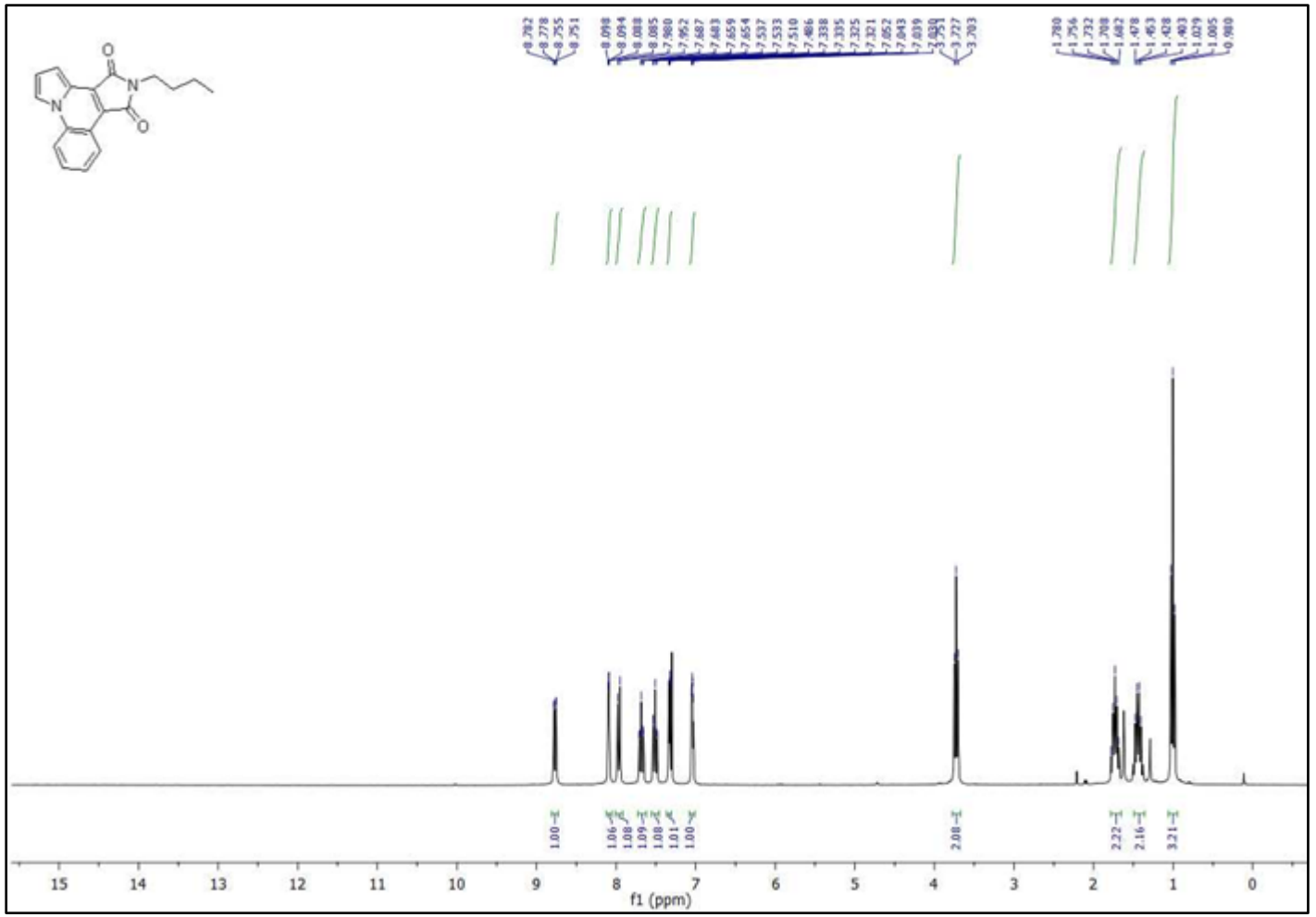
^{1}H-NMR (300 MHz) of ***3k*** in $CDCl_3$



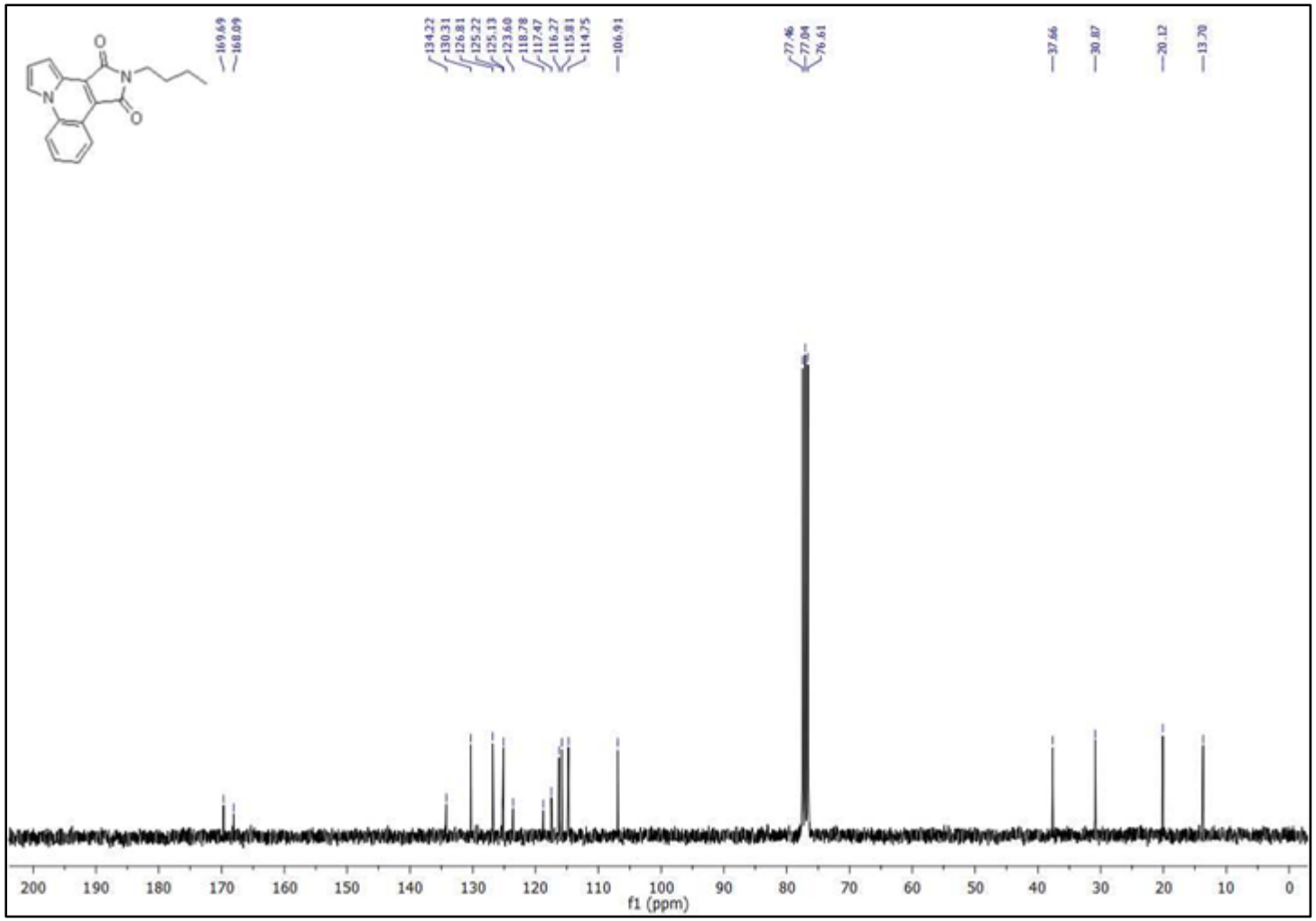
^{13}C-NMR (75 MHz) of ***3k*** in $CDCl_3$



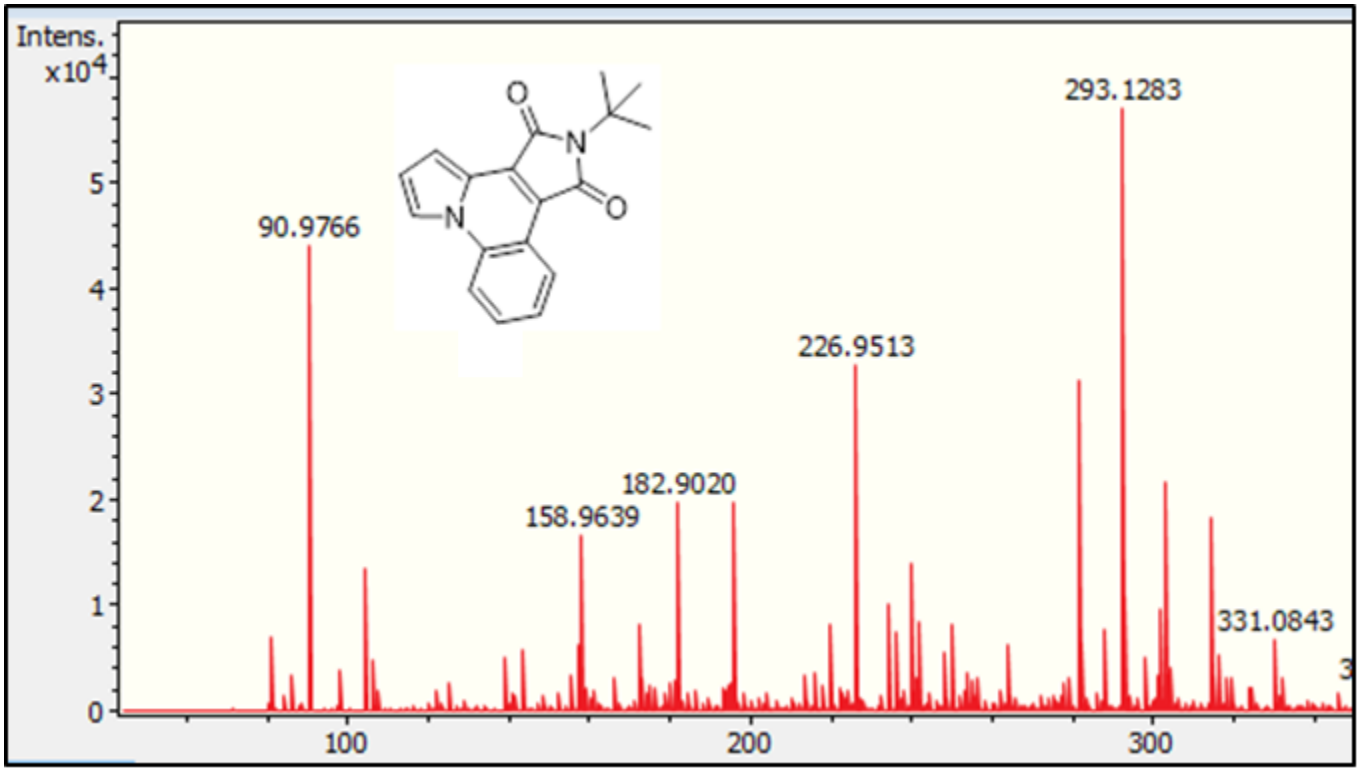
HRMS of ***3l*** **(**$C_{18}H_{16}N_2O_2$ $[M+H]^+$ = 393.1292**)**



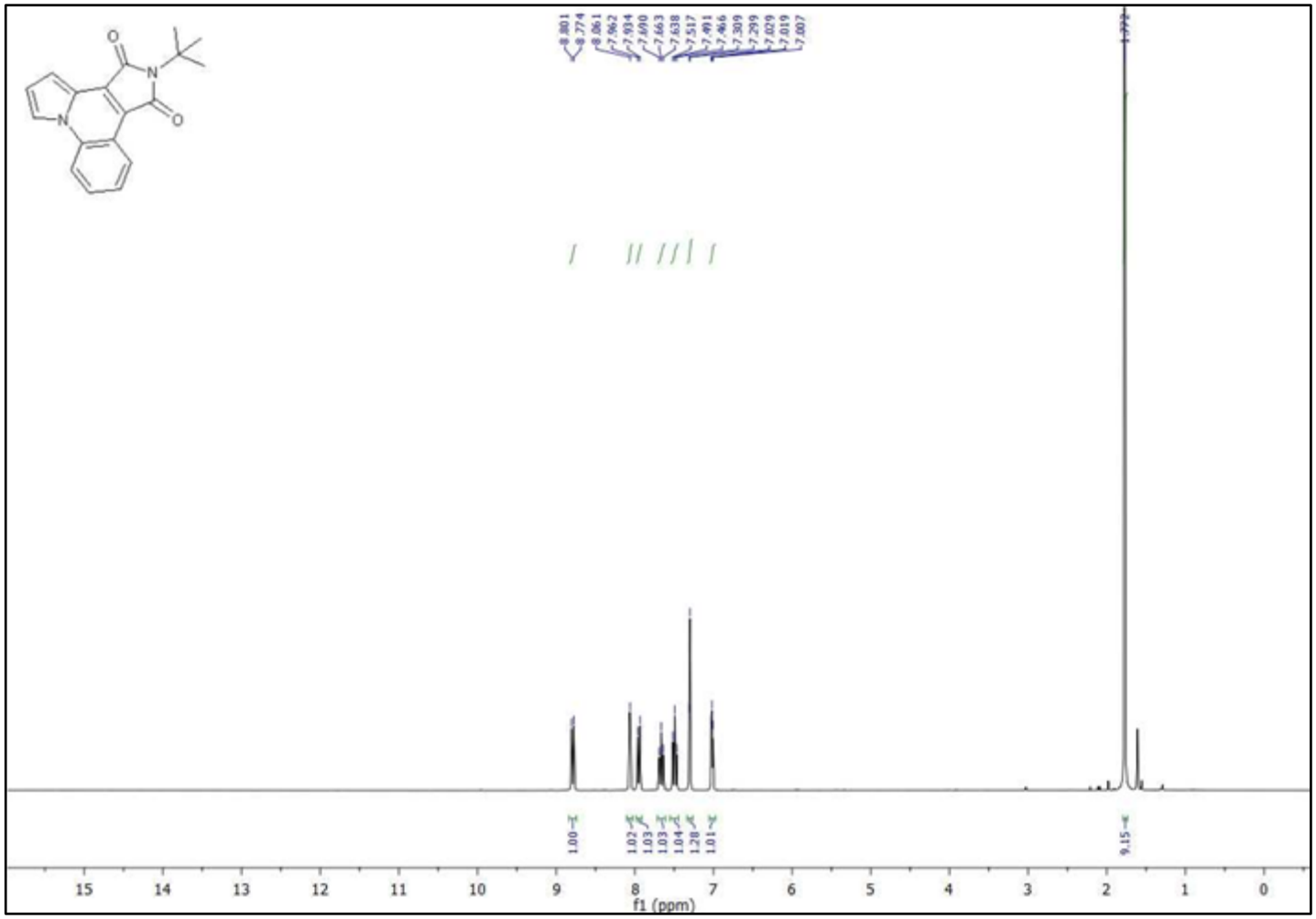
^{1}H-NMR (300 MHz) of ***3l*** in $CDCl_3$



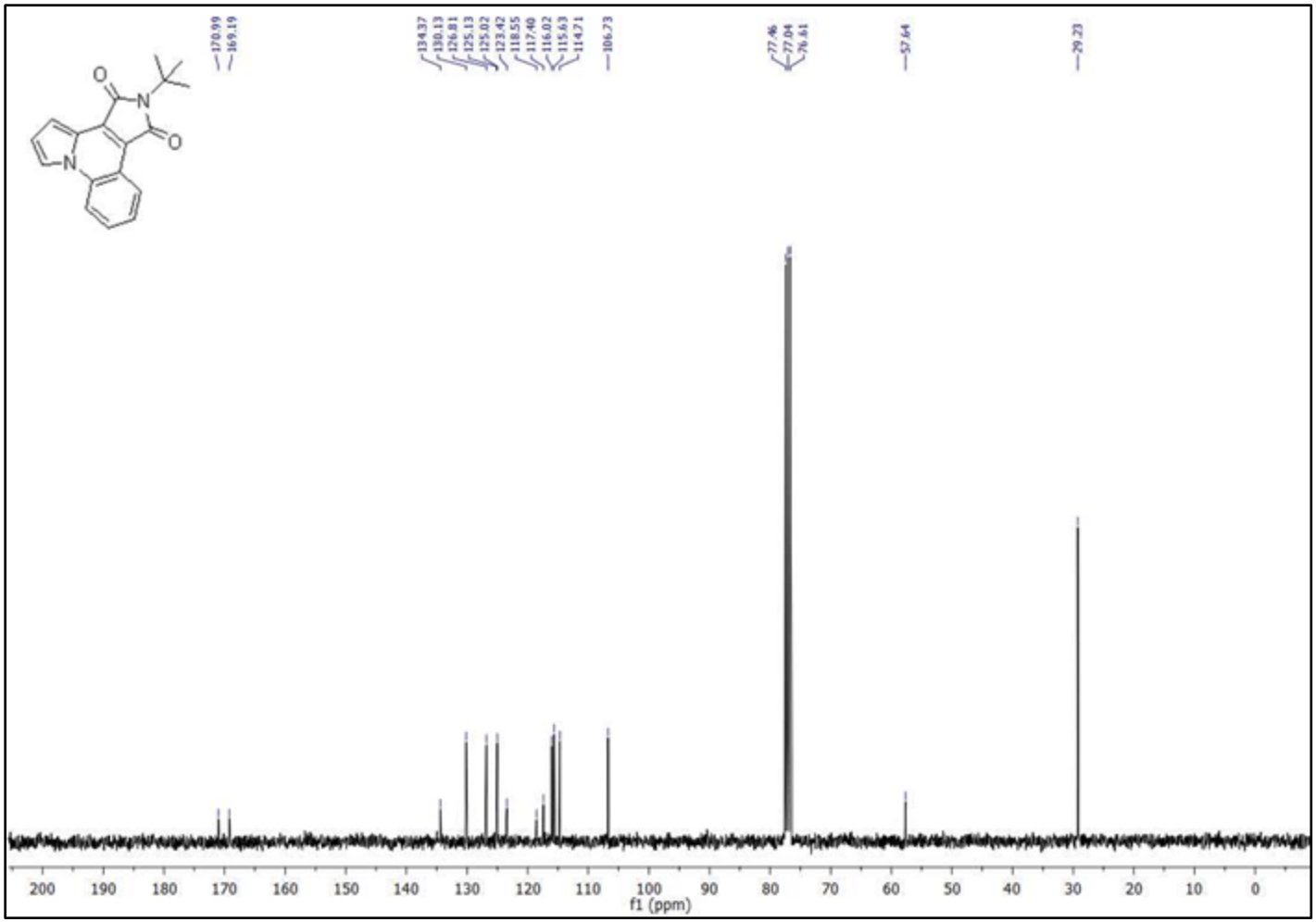
^{13}C-NMR (75 MHz) of ***3l*** in $CDCl_3$



HRMS of ***3m*** ($C_{18}H_{16}N_2O_2$ $[M+H]^+$ = 293.1292)



^{1}H-NMR (300 MHz) of ***3m*** in $CDCl_3$



^{13}C-NMR (75 MHz) of **3*m*** in $CDCl_3$

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