Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information for

Thermal 1, 3-Dipolar Cycloaddition Reactions of Azomethine Imines with active Esters

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General information.

Solvents were purified and dried by standard methods prior to use. All commercially available reagents were used without further purification unless otherwise noted. Oxygen- and moisture-sensitive reactions were carried out under argon atmosphere. Column chromatography was generally performed on silica gel (200-300 mesh) and reactions were monitored by thin layer chromatography (TLC) using silica gel GF254 plates with UV light to visualize the course of reaction. Melting points were determined with a digital Koffer apparatus and were uncorrected. ^{1}H and ^{13}C NMR data were recorded on a 400 MHz spectrometer using $CDCl_3$ as solvent at room temperature. The chemical shifts (δ) are reported in ppm and coupling constants (J) in Hz. High-resolution mass spectra (HRMS) were obtained on a FT-ICR spectrometer.

Diastereomeric ratios were determined by ^{1}H-NMR analysis of the crude mixtures.

Typical procedure

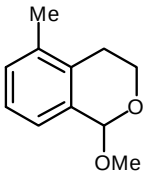
a) Synthesis of ester substrates and imines

Esters were synthesized according to the reported method [1].

Azomethine imines were prepared according to literature procedures [2a].

The physical data of benzoyl(3,4-dihydroisoquinolin-2-ium-2-yl)amide (**2a**), benzoyl(7-methyl-3,4-dihydroisoquinolin-2-ium-2-yl)amide (**2b**), benzoyl(7-methoxy-3,4-dihydroisoquinolin-2-ium-2-yl)amide (**2c**) and benzoyl(7-bromo-3,4-dihydroisoquinolin-2-ium-2-yl)amide (**2d**) are in accordance with those described in the literature.[2b,c]

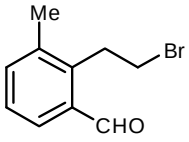
1-Methoxy-5-methylisochroman



To a solution of DDQ (3.34 g, 14.72 mmol, 1.2 eq.) in CH_2Cl_2 (30 mL) was added anhydrous MeOH (0.60 mL, 14.72 mmol, 1.2 eq.) and then 5-methylisochroman [3] (1.82 g, 12.26 mmol, 1.0 eq.) at room temperature. The resulting dark green-blue solution was vigorously stirred at room temperature over 20 h and then quenched by addition of $NaHCO_3$ (aq. sat., 30 mL). The heterogeneous mixture was filtered through celite which was then rinsed with CH_2Cl_2 (20 mL).The aqueous layer was separated and extracted twice with CH_2Cl_2 (30 mL) and the combined organic layers were washed once with $NaHCO_3$ (aq. sat., 80 mL), once with brine (80 mL), dried over $MgSO_4$ and evaporated under reduced pressure. The crude material was purified by flash chromatography (PE/EtOAc = 10/1) to give 1-methoxy-5-methylisochroman (1.55 g, 8.70 mmol, 71%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (dq, *J* = 14.2, 7.1 Hz, 3H), 5.43 (s, 1H), 4.14 (td, *J* = 11.6, 3.6 Hz, 1H), 3.95 (ddd, *J* = 11.3, 6.3, 1.4 Hz, 1H), 3.54 (s, 3H), 2.87 – 2.73 (m, 1H), 2.53 (dd, *J* = 16.8, 2.5 Hz, 1H), 2.22 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 135.9, 133.8, 132.4, 129.4, 125.9, 125.0, 97.9, 57.4, 55.2, 25.6, 18.8.

2-(2-Bromoethyl)-3-methylbenzaldehyde

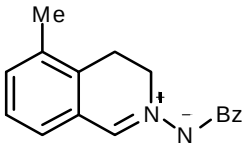


To a solution of 1-methoxy-5-methylisochroman (1.55 g, 8.69 mmol, 1.0 equiv.) in toluene (0.1 M) were added tetrabutylammonium bromide(2.80 g, 8.69 mmol, 1.0 equiv.) and trimethylsilyl bromide (2.28 mL,17.37 mmol, 2.0 equiv.) at room temperature. Then the reaction mixture was stirred at 80 °C. After 8 h, $NaHCO_3$ (aq. sat. 30ml) was added, followed by extraction with EtOAc . The combined organic layers

were dried over $MgSO_4$ and concentrated *in vacuo*. Flash chromatography (PE/ EtOAc = 5/1) of the crude material afforded the desired benzaldehyde derivative (1.66 g, 7.30 mmol, 84%) as a light brown oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 10.16 (s, 1H), 7.67 (d, *J* = 7.5 Hz, 1H), 7.44 (d, *J* = 6.9 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 3.60 (d, *J* = 7.7 Hz, 2H), 3.55 – 3.47 (m, 2H), 2.44 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 193.1, 138.8, 138.5, 136.1, 134.3, 132.5, 127.3, 31.8, 31.0, 19.5.

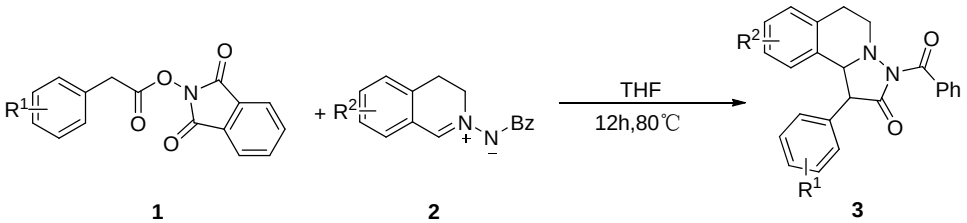
Benzoyl(5-methyl-3,4-dihydroisoquinolin-2-ium-2-yl)amide (2e)



To a solution of 2-(2-bromoethyl)-3-methylbenzaldehyde (1.66 g, 7.30 mmol , 1.0 equiv.) in MeOH (0.05 M) was added benzoylhydrazine (0.94 g, 6.94 mmol, 1.0 equiv.) at room temperature. After the formation of a white suspension, the mixture was heated to reflux and stirred for an additional 1 h to give a clear solution. After cooling to room temperature, Et_3N (1.50 ml, 10.95 mmol,1.5 equiv.) was added and the mixture was stirred for another 10 min at room temperature. Then water was added and the mixture was carefully stirred for 30 min to give a white precipitate. This solid material was washed with cold Et_2O and then dissolved in CH_2Cl_2 to give a yellow solution, which was dried over $MgSO_4$. Evaporation *in vacuo* afforded azomethine imine (1.52 g, 5.77 mmol, 79%) **2e** as a yellow solid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 9.63 (s, 1H), 8.11 (dd, *J* = 7.5, 1.9 Hz, 2H), 7.43 – 7.35 (m, 3H), 7.35 – 7.31 (m, 1H), 7.25 (d, *J* = 4.9 Hz, 2H), 4.25 (t, *J* = 7.8 Hz, 2H), 3.13 (t, *J* = 7.7 Hz, 2H), 2.31 (s, 3H).
^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 149.1, 137.5, 135.6, 134.9, 131.8, 130.0, 127.7, 127.7, 127.6, 126.5, 54.3, 23.7, 18.5.

b) General procedure for [3+2] annulations of esters and azomethine imines (*GP*)



1 **2** **3**

To a solution of the corresponding ester derivative (1.0 eq.) in THF (0.05 M) was added azomethine imine (2.0 eq.). The reaction mixture was stirred for 12 h at reflux. Then the mixture

was diluted with EtOAc and washed with $NaHCO_3$ (aq. sat.) and water, dried over $MgSO_4$ and concentrated *in vacuo*. The crude material was purified by flash chromatography (PE/EtOAc=5/1) to give the desired pyrazolidinone.

3-benzoyl-1-phenyl-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3a)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-phenylacetate (**1a**) (42.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2a**) (75.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc=5/1) afforded the desired pyrazolidinone **3a** (45.0 mg, 81%) as a colorless solid.

MP: 195-196℃. **^{1}H NMR** (400 MHz, $CDCl_3$):δ 7.76 – 7.70 (m, 2H), 7.52 (m, 1H), 7.47 – 7.36 (m, 5H), 7.26 – 7.18(m, 4H), 6.97 (m, 1H), 6.34 (d, *J* = 7.8 Hz, 1H), 5.03 (d, *J* = 12.0 Hz, 1H), 4.16 (d, *J* = 12.0 Hz, 1H), 3.80 – 3.67 (m, 1H), 3.39 – 3.22 (m, 2H), 2.90 (m, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.5, 166.2, 134.9, 133.6, 132.6, 132.5, 132.0, 129.5, 129.1, 128.8, 128.5, 128.2, 127.9, 127.5, 126.9, 126.0, 65.3, 55.4, 48.5, 28.8. **HRMS (ESI)** *m/z* = 369.1598 calcd. for $C_{24}H_{20}N_2O_2H^+$ $[M+H]^+$; found: 369.1595.

3-benzoyl-1-(p-tolyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3b)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(p-tolyl)acetate (**1b**) (44.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2a**) (75.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc=5/1) afforded the desired pyrazolidinone **3b** (44.0 mg, 76%) as a colorless solid.

MP: 191-192℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.3 Hz, 2H), 7.52 (t, *J* = 7.4 Hz, 1H), 7.42 (m, 2H), 7.25 – 7.19 (m, 4H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.98 (dt, *J* = 8.4, 4.2 Hz, 1H), 6.39 (d, *J* = 7.8 Hz, 1H), 5.01 (d, *J* = 12.0 Hz, 1H), 4.12 (d, *J* = 12.0 Hz, 1H), 3.82 – 3.65 (m, 1H), 3.40 – 3.18 (m, 2H), 2.96 – 2.81 (m, 1H), 2.39 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.8, 166.3, 138.0, 133.7, 132.7, 132.0, 131.8, 129.9, 129.3, 128.9, 128.5, 127.9, 127.5, 126.9, 126.0, 65.2, 55.1, 48.5, 28.8, 21.2. **HRMS (ESI)** *m/z* = 405.1573 calcd. for $C_{25}H_{22}N_2O_2Na^+$ $[M+Na]^+$; found: 405.1578.

3-benzoyl-1-(4-bromophenyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3c)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-bromophenyl)acetate (**1c**) (54.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine (**2a**) (75.0 mg, 0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3c** (58.0 mg, 86%) as a colorless solid.

MP: 192-193℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.3 Hz, 2H), 7.54 (m, 3H), 7.43 (m, 2H),

7.25 – 7.18 (m, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 7.05 – 6.96 (m, 1H), 6.34 (d, *J* = 7.8 Hz, 1H), 4.97 (d, *J* = 12.0 Hz, 1H), 4.14 (d, *J* = 12.0 Hz, 1H), 3.69 m, 1H), 3.30 (m, 2H), 2.96 – 2.82 (m, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.9, 166.1, 133.9, 133.5, 132.7, 132.3, 132.2, 131.2, 128.9, 128.7, 127.9, 127.7, 126.8, 126.1, 122.4, 65.2, 54.9, 48.6, 28.7. **HRMS (ESI)** *m/z* = 469.0522 calcd. for $C_{24}H_{19}Br_1N_2O_2Na^+$ $[M+Na]^+$; found: 469.0528.

3-benzoyl-1-(3-bromophenyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3d)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(3-bromophenyl)acetate (**1d**) (54.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine (**2a**) (75.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3d** (51.0 mg, 76%) as a colorless solid.

MP: 175-176℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.5 Hz, 2H), 7.52 (d, *J* = 6.6 Hz, 2H), 7.41 (m, 3H), 7.31 (m, 1H), 7.19 (m, 3H), 7.06 – 6.96 (m, 1H), 6.35 (d, *J* = 7.8 Hz, 1H), 4.99 (d, *J* = 12.0 Hz, 1H), 4.13 (d, *J* = 12.0 Hz, 1H), 3.77 – 3.60 (m, 1H), 3.38 – 3.18 (m, 2H), 2.95 – 2.79 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.8, 166.1, 137.1, 133.6, 132.7, 132.6, 132.2, 132.1, 131.4, 130.7, 128.9, 128.7, 128.1, 127.9, 127.8, 126.8, 126.2, 65.2, 55.1, 48.7, 28.7. **HRMS (ESI)** *m/z* = 469.0522 calcd. for $C_{24}H_{19}Br_1N_2O_2Na^+$ $[M+Na]^+$; found: 469.0527.

3-benzoyl-1-(thiophen-2-yl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3e)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(thiophen-2-yl)acetate (**1e**) (43.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2a**) (75.0 mg, 0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3e** (46.0 mg, 81%) as a colorless solid.

MP:165-167℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.4 Hz, 2H), 7.50 (m, 1H), 7.46 – 7.34 (m, 3H), 7.20 (m, 2H), 7.04 (m, 3H), 6.60 (d, *J* = 7.6 Hz, 1H), 5.04 (d, *J* = 11.8 Hz, 1H), 4.44 (d, *J* = 11.8 Hz, 1H), 3.73 (d, *J* = 5.8 Hz, 1H), 3.40 – 3.13 (m, 2H), 2.87 (d, *J* = 15.9 Hz, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.3, 166.2, 136.8, 133.5, 132.7, 132.3, 132.1, 128.9, 128.5, 128.3, 127.9, 127.7, 127.4, 126.8, 126.2, 65.8, 50.9, 48.7, 28.8. **HRMS (ESI)** *m/z* = 397.0981 calcd. for $C_{22}H_{18}N_2O_2S_1Na^+$ $[M+Na]^+$; found: 397.0985.

3-benzoyl-1-(4-fluorophenyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3f)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-fluorophenyl)acetate (**1f**) (45.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2a**) (75.0 mg, 0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3f** (41.0 mg, 71%) as a colorless solid.

MP: 157-159℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 2H), 7.52 (m, 1H), 7.42 (m, 2H), 7.20 (m, 4H), 7.13 (m, 2H), 7.03 – 6.93 (m, 1H), 6.32 (d, *J* = 7.8 Hz, 1H), 4.95 (d, *J* = 12.0 Hz, 1H), 4.15 (d, *J* = 12.1 Hz, 1H), 3.72 – 3.64 (m, 1H), 3.36 – 3.22 (m, 2H), 2.89 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.3, 166.1, 162.5 (d, *J* = 247.5 Hz,), 133.6, 132.7, 132.3, 132.1, 131.1 (d, *J* = 8.2 Hz), 130.6 (d, *J* = 3.3 Hz), 128.8, 128.6, 127.9, 127.6, 126.8, 126.0, 116.2 (d, *J* = 21.7 Hz), 65.3 , 54.7, 48.5, 28.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.5 (s). **HRMS (ESI)** *m/z* = 409.1323 calcd. for $C_{24}H_{19}F_1N_2O_2Na^+$ $[M+Na]^+$; found: 409.1328.

3-benzoyl-1-(4-(trifluoromethyl)phenyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3g)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-(trifluoromethyl)phenyl)acetate (**1g**) (52.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine (**2a**) (75.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3g** (49.0 mg, 75%) as a colorless solid.

MP: 174-176℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 – 7.67 (m, 4H), 7.53 (m 1H), 7.43 (m, 2H), 7.37 (m, 2H), 7.24 – 7.18 (m, 2H), 7.04 – 6.97 (m, 1H), 6.28 (d, *J* = 7.8 Hz, 1H), 5.04 (d, *J* = 12.0 Hz, 1H), 4.25 (d, *J* = 12.0 Hz, 1H), 3.77 – 3.67 (m, 1H), 3.37 – 3.25 (m, 2H), 2.97 – 2.84 (m, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.8, 166.2, 138.9, 133.4, 132.7, 132.3, 132.0, 130.5 (d, *J* = 32.8 Hz), 130.0, 128.9, 128.8, 128.0, 127.8, 126.7, 126.2,126.1 (d, *J* = 3.8Hz), 65.3, 55.3, 48.8, 28.7. **HRMS (ESI)** *m/z* = 459.1291 calcd. for $C_{25}H_{19}F_3N_2O_2Na^+$ $[M+Na]^+$; found: 459.1298.

3-benzoyl-9-methoxy-1-phenyl-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3h)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-phenylacetate (**1a**) (42.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2b**) (84.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3h** (39.0 mg, 65%) as a colorless solid.

MP: 156-157℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.3 Hz, 2H), 7.52 (m, 1H), 7.47 – 7.33 (m, 5H), 7.25 (m, 2H), 7.09 (d, *J* = 8.5 Hz, 1H), 6.76 (m, 1H), 5.79 (d, *J* = 2.1 Hz, 1H), 4.95 (d, *J* = 12.0 Hz, 1H), 4.16 (d, *J* = 12.0 Hz, 1H), 3.71 (m, 1H), 3.42 (s, 3H), 3.30 – 3.15 (m, 2H), 2.81 (m, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.4, 166.2, 157.5, 135.0, 133.7, 133.4, 132.1, 129.6, 129.5, 129.2, 128.8, 128.2, 127.9, 124.6, 114.8, 110.7, 65.7, 55.4, 54.8, 48.8, 28.0. **HRMS (ESI)** *m/z* = 399.1703 calcd. for $C_{25}H_{22}N_2O_3H^+$ $[M+H]^+$; found: 399.1698.

3-benzoyl-1-(4-bromophenyl)-9-methoxy-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3i)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-bromophenyl)acetate (**1c**) (54.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2b**) (84.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3i** (44.0 mg, 61%) as a colorless solid.

MP: 193-194℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 2H), 7.61 – 7.50 (m, 3H), 7.42 (dd, *J* = 10.5, 4.7 Hz, 2H), 7.17 – 7.08 (m, 3H), 6.78 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.83 (d, *J* = 2.6 Hz, 1H), 4.94 (d, *J* = 12.0 Hz, 1H), 4.15 (d, *J* = 12.0 Hz, 1H), 3.69 (m, 1H), 3.50 (s, 3H), 3.25 (m, 2H), 2.83 (m, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.8, 166.4, 157.6, 134.0, 133.4, 133.1, 132.4, 131.3, 129.7, 129.0, 128.0, 124.5, 122.5, 114.5, 111.2, 65.5, 55.0, 54.9, 49.1, 27.9. **HRMS (ESI)** *m/z* = 499.0628 calcd. for $C_{25}H_{21}Br_1N_2O_3Na^+$ $[M+Na]^+$; found: 499.0635.

3-benzoyl-9-methyl-1-(thiophen-2-yl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3j)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(thiophen-2-yl)acetate (**1e**) (43.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2c**) (79.0 mg, 0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3j** (48.0 mg, 82%) as a colorless solid.

MP: 154-155℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 – 7.66 (m, 2H), 7.50 (d, *J* = 7.5 Hz, 1H), 7.44 – 7.37 (m, 3H), 7.11 – 7.05 (m, 2H), 7.05 – 6.98 (m, 2H), 6.36 (s, 1H), 4.98 (d, *J* = 11.8 Hz, 1H), 4.43 (d, *J* = 11.8 Hz, 1H), 3.75 – 3.66 (m, 1H), 3.22 (ddd, *J* = 13.0, 10.4, 3.0 Hz, 2H), 2.83 (m, 1H), 2.13 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.4, 166.3, 136.8, 135.7, 133.4, 132.1, 129.5, 128.9, 128.6, 128.3, 128.2, 127.9, 127.4, 127.2, 126.2, 65.8, 50.9, 48.9, 28.3, 21.0. **HRMS (ESI)** *m/z* = 389.1318 calcd. for $C_{23}H_{20}N_2O_2S_1H^+$ $[M+H]^+$; found: 389.1325.

3-benzoyl-1-(4-bromophenyl)-9-methyl-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3k)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-bromophenyl)acetate (**1c**) (54.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2c**) (79.0 mg, 0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3k** (69.0 mg, 88%) as a colorless solid.

MP: 189-190℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.3 Hz, 2H), 7.60 – 7.49 (m, 3H), 7.41 (m, 2H), 7.09 (m, 3H), 7.01 (d, *J* = 7.8 Hz, 1H), 6.13 (s, 1H), 4.90 (d, *J* = 11.9 Hz, 1H), 4.11 (d, *J* = 11.9 Hz, 1H), 3.67 (m, 1H), 3.28 – 3.14 (m, 2H), 2.84 (m, 1H), 2.11 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ

173.1, 166.1, 135.7, 134, 133.6, 132.2, 132.1, 132.1, 131.2, 129.5, 128.9, 128.6, 128.5, 127.9, 127.2, 122.3, 65.3, 55.0, 48.8, 28.3, 20.9. **HRMS (ESI)** *m/z* = 461.0859 calcd. for $C_{25}H_{21}Br_1N_2O_2H^+$ $[M+H]^+$; found: 461.0866.

3-benzoyl-9-methyl-1-phenyl-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3l)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-phenylacetate (**1a**) (42.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2c**) (79.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3l** (37.0 mg, 63%) as a colorless solid.

MP: 187-188℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.5 Hz, 2H), 7.51 (m, 1H), 7.46 – 7.36 (m, 5H), 7.23 (m, 2H), 7.07 (d, *J* = 7.8 Hz, 1H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.09 (s, 1H), 4.95 (d, *J* = 11.9 Hz, 1H), 4.12 (d, *J* = 11.9 Hz, 1H), 3.76 – 3.64 (m, 1H), 3.32 – 3.17 (m, 2H), 2.91 – 2.76 (m, 1H), 2.05 (m, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.6, 166.2, 135.5, 135.0, 133.8, 132.4, 132.0, 129.5, 129.5, 129.1, 128.8, 128.4, 128.3, 128.2, 127.9, 127.4, 65.4, 55.5, 48.7, 28.4, 20.9. **HRMS (ESI)** *m/z* = 383.1754 calcd. for $C_{25}H_{22}N_2O_2H^+$ $[M+H]^+$; found: 383.1749.

3-benzoyl-9-bromo-1-(4-bromophenyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3m)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-bromophenyl)acetate (**1c**) (54.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2d**) (98.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3m** (51.0 mg, 65%) as a colorless solid.

MP: 178-179℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 – 7.67 (m, 2H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.54 (m, 1H), 7.43 (m, 2H), 7.34 (dd, *J* = 8.2, 1.9 Hz, 1H), 7.09 (m, 3H), 6.47 (d, *J* = 1.7 Hz, 1H), 4.90 (d, *J* = 11.9 Hz, 1H), 4.10 (d, *J* = 11.9 Hz, 1H), 3.81 – 3.67 (m, 1H), 3.32 – 3.14 (m, 2H), 2.96 – 2.78 (m, 1H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.5, 166.1, 134.4, 133.4, 132.5, 132.3, 131.8, 131.0, 130.9, 130.4, 129.6, 128.9, 128.0, 122.7, 119.7, 64.7, 54.8, 48.4, 28.3. **HRMS (ESI)** *m/z* = 526.9787 calcd. for $C_{24}H_{18}Br_2N_2O_2H^+$ $[M+H]^+$; found: 526.9796.

3-benzoyl-9-bromo-1-(4-(trifluoromethyl)phenyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one(3n)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(4-(trifluoromethyl)phenyl)acetate (**1g**) (52.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2d**) (98.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3n** (59.0 mg, 76%) as a colorless solid.

MP: 170-171℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 – 7.67 (m, 4H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.6 Hz, 2H), 7.35 (m, 3H), 7.09 (d, *J* = 8.2 Hz, 1H), 6.39 (d, *J* = 1.3 Hz, 1H), 4.97 (d, *J* = 11.9 Hz, 1H), 4.22 (d, *J* = 11.9 Hz, 1H), 3.79 – 3.68 (m, 1H), 3.33 – 3.17 (m, 2H), 2.95 – 2.78 (m, 1H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.2, 166.2, 138.4, 134.1, 133.2, 132.5, 131.7, 131.0, 130.4, 129.9, 129.5, 128.9, 128.0, 126.3 (d, *J* = 3.7 Hz), 119.7, 64.8, 55.2, 48.5, 28.2. **HRMS (ESI)** *m/z* = 537.0396 calcd. for $C_{25}H_{18}Br_1F_3N_2O_2Na^+$ $[M+Na]^+$; found:537.0402.

3-benzoyl-7-methyl-1-(thiophen-2-yl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3o)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(thiophen-2-yl)acetate (**1e**) (43.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine (**2e**) (79.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3o** (49.0 mg, 84%) as a colorless solid.

MP:192-193℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 – 7.66 (m, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.41 (m, 3H), 7.12 – 7.04 (m, 2H), 7.04 – 6.92 (m, 2H), 6.45 (d, *J* = 7.7 Hz, 1H), 5.03 (d, *J* = 11.8 Hz, 1H), 4.48 (d, *J* = 11.8 Hz, 1H), 3.79 (m, , 1H), 3.26 – 3.14 (m, 1H), 3.13 – 3.01 (m, 1H), 2.88 (m, 1H), 2.28 (s, 3H).**^{13}C NMR** (100 MHz, $CDCl_3$) δ 172.5, 166.4, 136.9, 136.2, 133.3, 132.2, 132.1, 131.2, 129.1, 129.0, 128.3, 127.9, 127.5, 126.2, 126.1, 124.6, 66.1, 50.8, 48.6, 26.2, 19.5. **HRMS (ESI)** *m/z* = 411.1138 calcd. for $C_{23}H_{20}N_2O_2S_1Na^+$ $[M+Na]^+$; found:411.1134.

3-benzoyl-7-methyl-1-phenyl-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one (3p)

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-phenylacetate (**1a**) (42.0 mg, 0.15 mmol, 1.0 eq.), azomethine imine(**2e**) (79.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3p** (44.0 mg, 77%) as a colorless solid.

MP: 209-211℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 7.1 Hz, 2H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.48 – 7.36 (m, 5H), 7.25 (m, 2H), 7.07 (d, *J* = 7.3 Hz, 1H), 6.89 (t, *J* = 7.6 Hz, 1H), 6.17 (d, *J* = 7.8 Hz, 1H), 5.00 (d, *J* = 12.0 Hz, 1H), 4.19 (d, *J* = 12.0 Hz, 1H), 3.82 – 3.69 (m, 1H), 3.37 – 3.19 (m, 1H), 3.15 – 2.98 (m, 1H), 2.89 (m, 1H), 2.28 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.8, 166.3, 136.2, 135.0, 133.6, 132.3, 132.1, 131.2, 129.5, 129.1, 128.9, 128.8, 128.1, 127.9, 125.8, 124.7, 65.6, 55.4, 48.4, 26.3, 19.5. **HRMS (ESI)** *m/z* = 383.1754 calcd. for $C_{25}H_{22}N_2O_2H^+$ $[M+H]^+$; found: 383.1757.

3-benzoyl-7-methyl-1-(o-tolyl)-1,5,6,10b-tetrahydropyrazolo[5,1-a]isoquinolin-2(3H)-one（3q）

According to ***GP*** with 1,3-dioxoisoindolin-2-yl 2-(p-tolyl)acetate (**1h**) (44.0 mg, 0.15 mmol, 1.0 eq.),azomethine imine(**2e**) (79.0 mg,0.30 mmol, 2.0 eq.). FC (PE/EtOAc = 5/1) afforded the desired pyrazolidinone **3q** (49.0 mg, 83%) as a colorless solid.

MP:189-190℃.**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77 – 7.71 (m, 2H), 7.53 (m, 1H), 7.43 (m, 2H), 7.35 – 7.27 (m, 2H), 7.27 – 7.24 (m, 1H), 7.20 (m, 1H), 7.05 (m, 1H), 6.88 (t, *J* = 7.6 Hz, 1H), 6.20 (m, 1H), 5.03 (d, *J* = 11.8 Hz, 1H), 4.50 (d, *J* = 11.9 Hz, 1H), 3.79 (ddd, *J* = 10.2, 5.3, 2.1 Hz, 1H), 3.40 – 3.25 (m, 1H), 3.08 (ddd, *J* = 17.2, 12.1, 5.3 Hz, 1H), 2.89 (m, 1H), 2.28 (s, 3H), 2.07 (s, 3H). **^{13}C NMR** (100 MHz, $CDCl_3$) δ 173.9, 166.3, 137.6, 136.1, 133.7, 133.5, 132.3, 132.0, 131.1, 130.8, 130.1, 128.8, 128.4, 127.9, 127.9, 127.0, 126.0, 124.1, 65.5, 51.4, 48.4, 26.2, 20.0, 19.5. **HRMS (ESI)** *m/z* = 419.1730 calcd. for $C_{26}H_{24}N_2O_2Na^+$ $[M+Na]^+$; found:419.1733.

Crystal structure determination of 3a

Crystal Data for $C_{24}H_{20}N_2O_2$ (*M* =368.42 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), *a* = 7.6135(8) Å, *b* = 13.282(2) Å, *c* = 18.5374(11) Å, *V* = 1874.5(4) Å^3, *Z* = 4, *T* = 291.89(10) K, μ(MoKα) = 0.084 mm^{-1}, *Dcalc* = 1.305 g/cm^3, 5870 reflections measured (6.92° ≤ 2Θ ≤ 52.04°), 3323 unique (R_{int} = 0.0689, R_{sigma} = 0.1321) which were used in all calculations. The final R_1 was 0.0640 (>2sigma(I)) and wR_2 was 0.1357 (all data)

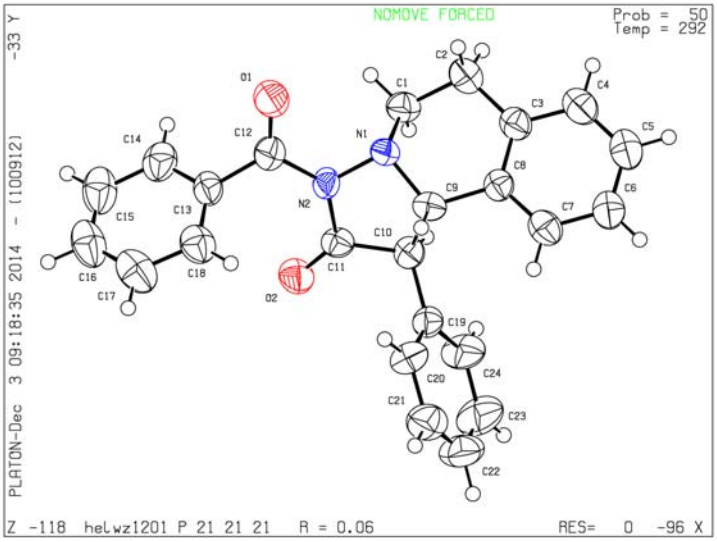
Crystal data and structure refinement for 3a

Identification code	3a
Empirical formula	$C_{24}H_{20}N_2O_2$
Formula weight	368.42
Temperature/K	291.89(10)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	7.6135(8)
b/Å	13.282(2)
c/Å	18.5374(11)
α/°	90.00
β/°	90.00
γ/°	90.00
Volume/Å^3	1874.5(4)
Z	4
ρ_{calc}g/cm^3	1.305
μ/mm^{-1}	0.084
F(000)	776.0
Crystal size/mm^3	0.27 × 0.15 × 0.12
Radiation	MoKα (λ = 0.71073)

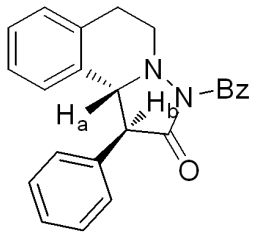
2Θ range for data collection/°	6.92 to 52.04
Index ranges	-9 ≤ h ≤ 9, -16 ≤ k ≤ 11, -21 ≤ l ≤ 22
Reflections collected	5870
Independent reflections	3323 [R_{int} = 0.0689, R_{sigma} = 0.1321]
Data/restraints/parameters	3323/0/253
Goodness-of-fit on F^2	0.975
Final R indexes [I>=2σ (I)]	R_1 = 0.0640, wR_2 = 0.0989
Final R indexes [all data]	R_1 = 0.1492, wR_2 = 0.1357
Largest diff. peak/hole / e $Å^{-3}$	0.19/-0.17
Flack parameter	-2(3)

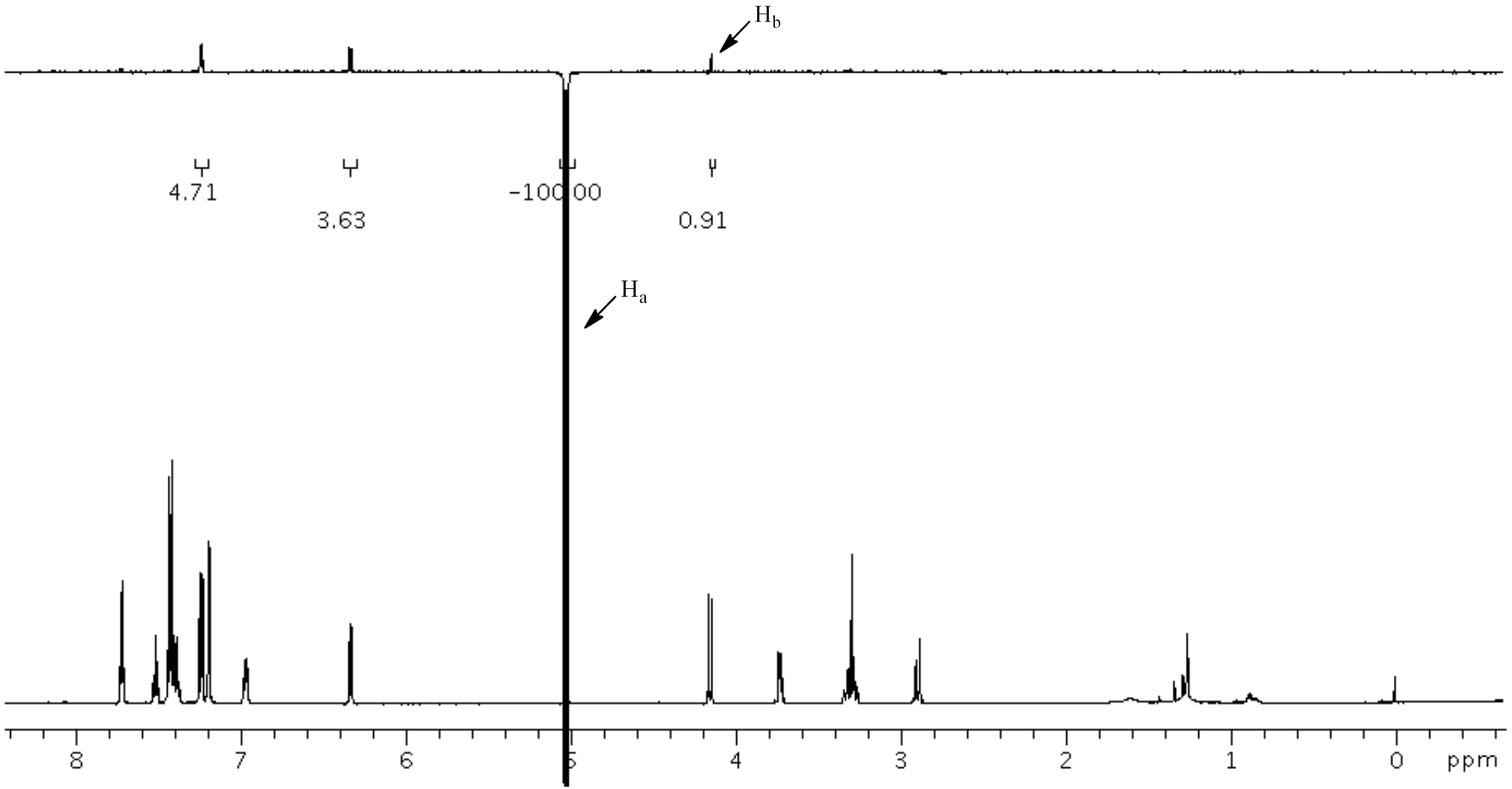
X-ray structure of pyrazolidinone 3a

CCDC 1456450



Spectra of NOE and the new compounds


N
N–Bz
Ha
Hb
O


Hb
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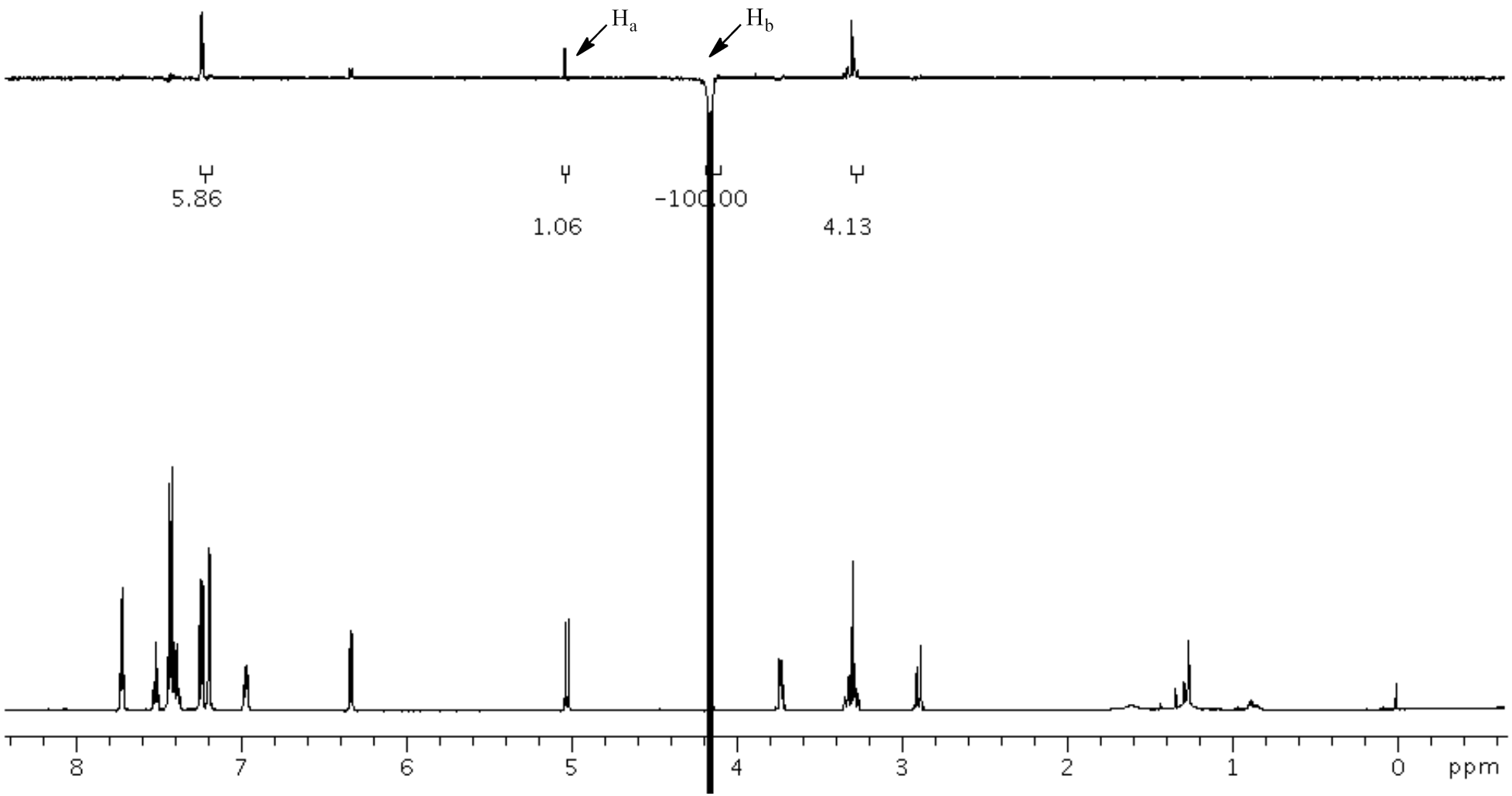
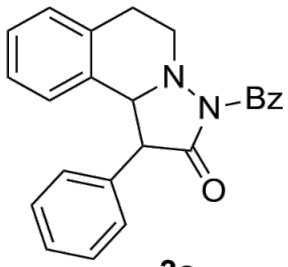
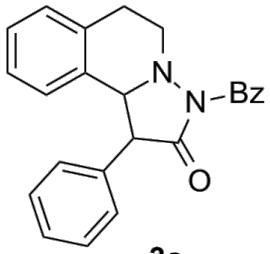
3.63
-100.00
0.91
Ha
8
7
6
5
4
3
2
1
0
ppm


Ha
Hb
5.86
1.06
-100.00
4.13
8
7
6
5
4
3
2
1
0
ppm



3a

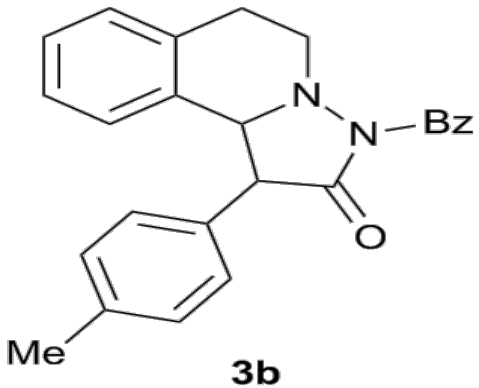
^{1}H NMR,400M,$CDCl_3$



3a

^{13}C NMR,100M,$CDCl_3$

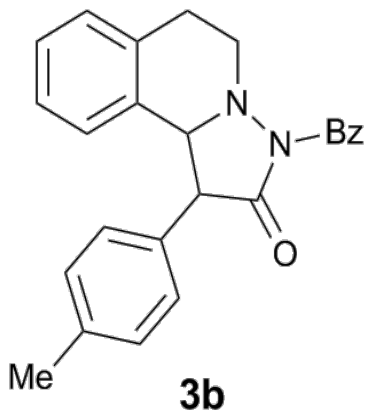
3b



3b

^{1}H NMR 400M $CDCl_3$

3b



3b

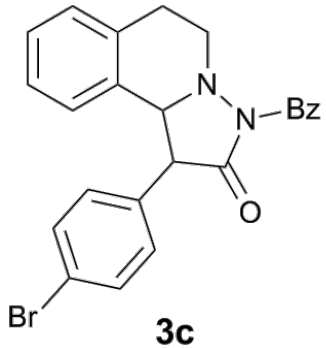
^{1}C NMR 100M $CDCl_3$

137.98
133.71
132.68
132.00
131.84
129.91
129.29
128.85
128.52
127.88
127.47
126.94
126.00
173.75
166.26
65.19
55.07
48.53
28.82
21.19

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1

f1 (ppm)

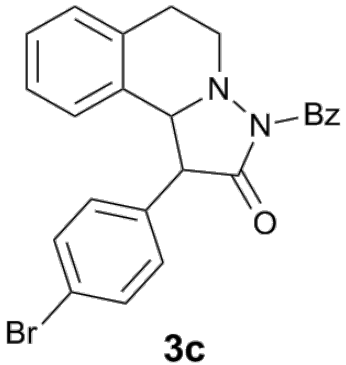
3c H



3c

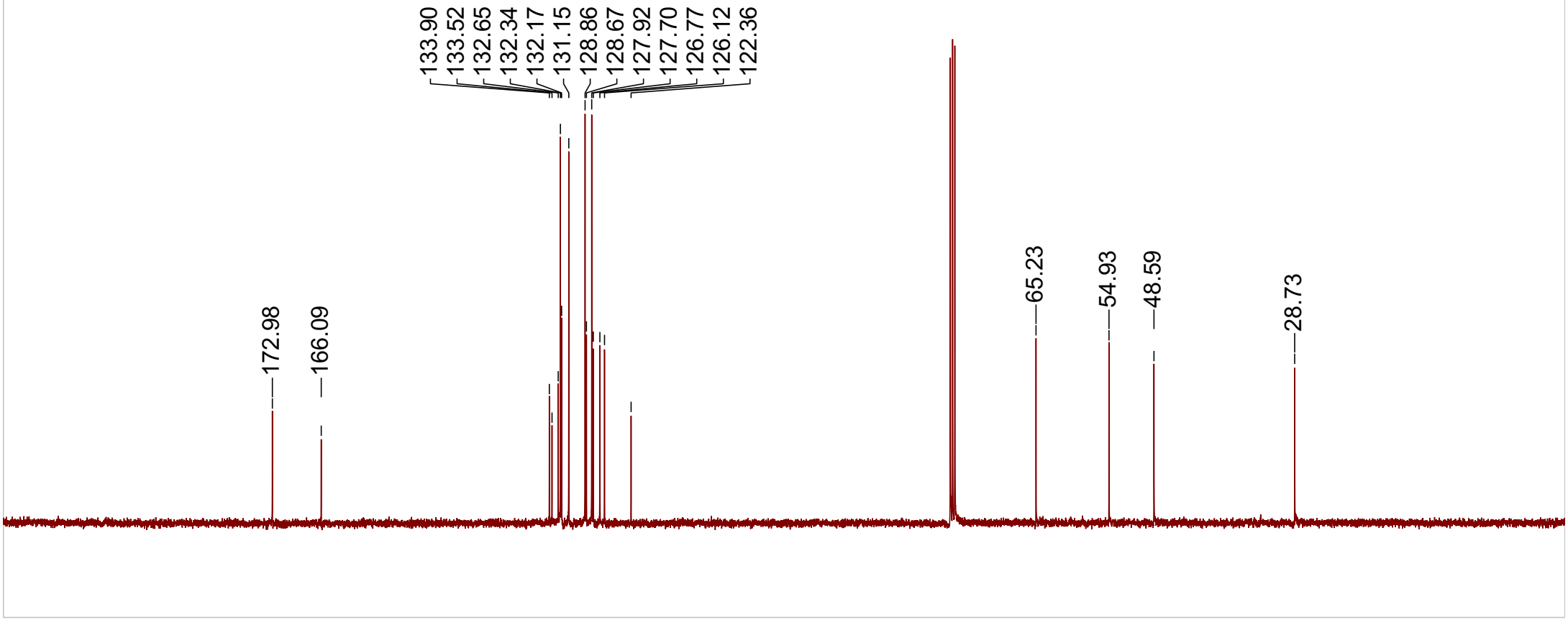
^{1}H NMR 400M $CDCl_3$

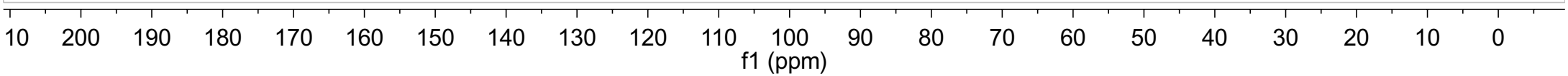
3c C



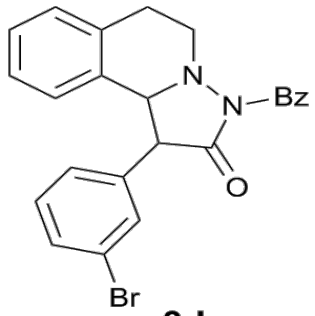
3c

^{13}C NMR 100M $CDCl_3$



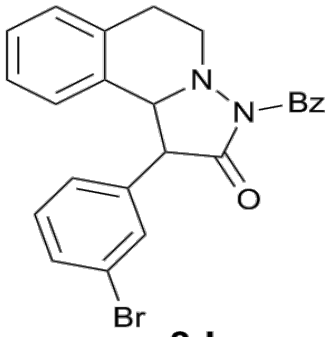


3d H



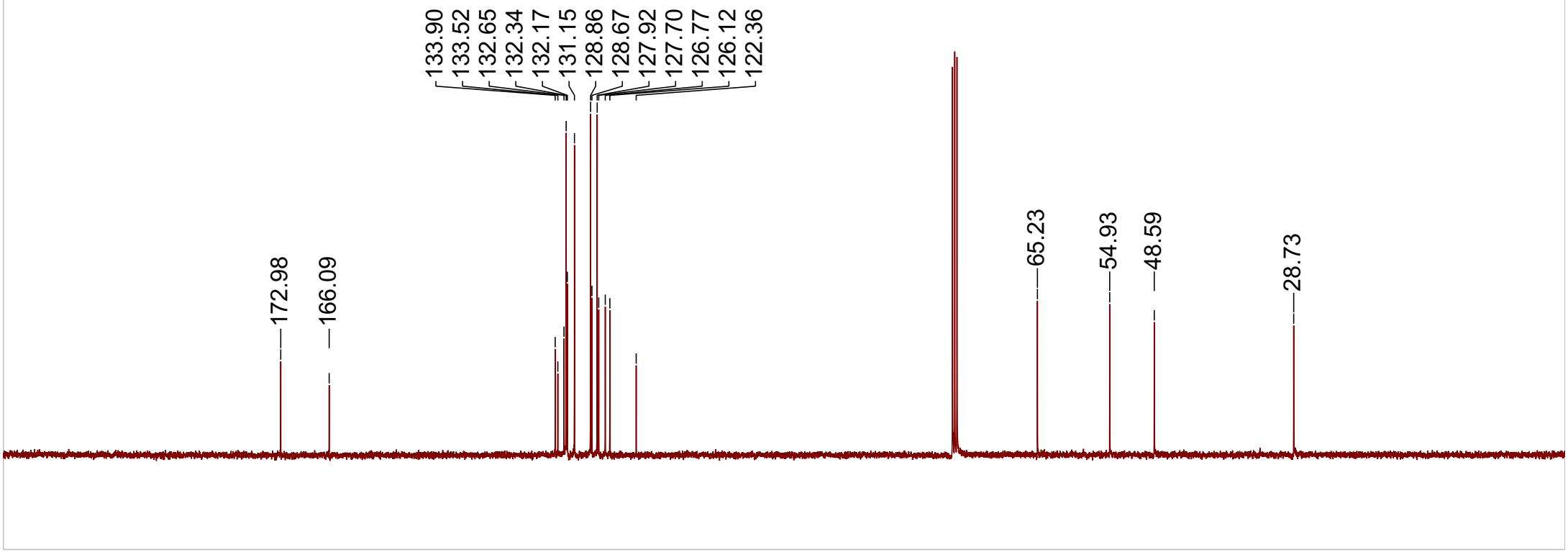
3d

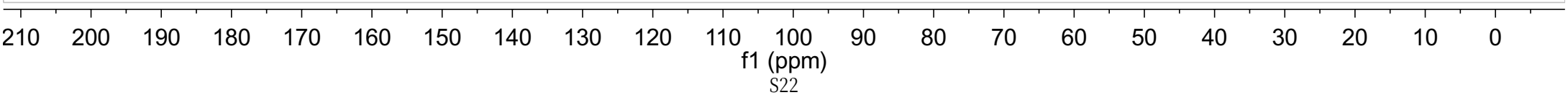
^{1}H NMR 400M $CDCl_3$



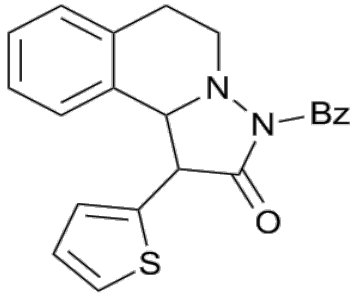
3d

^{13}C NMR 100M $CDCl_3$





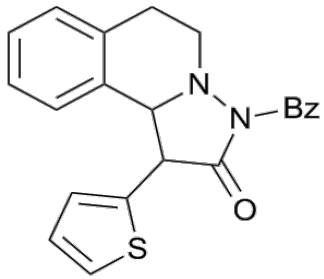
3e



3e

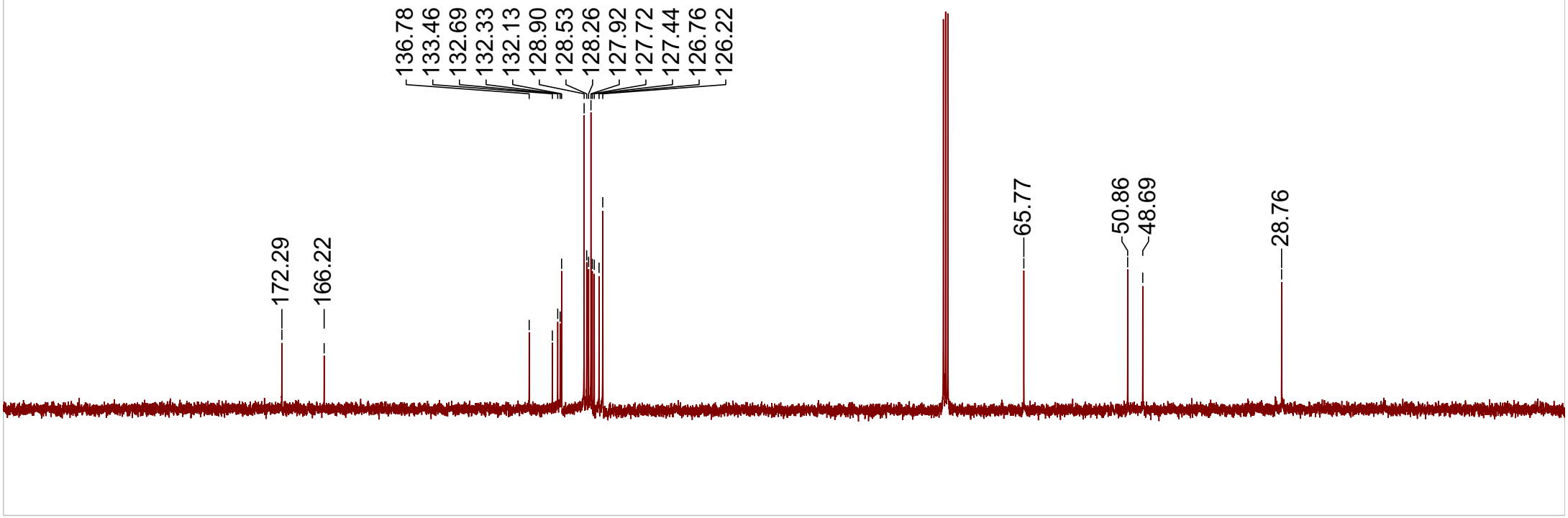
^{1}H NMR 400M $CDCl_3$

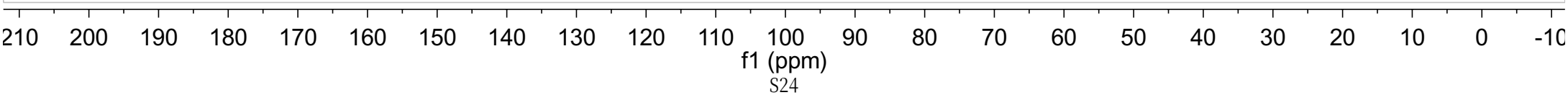
3e

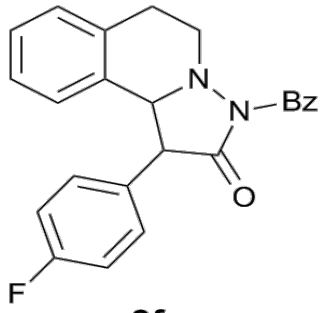


3e

^{13}C NMR 100M $CDCl_3$

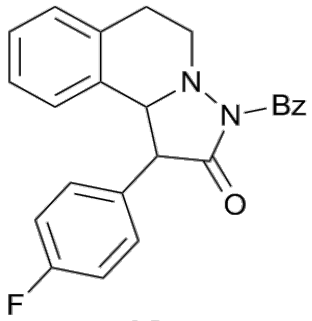






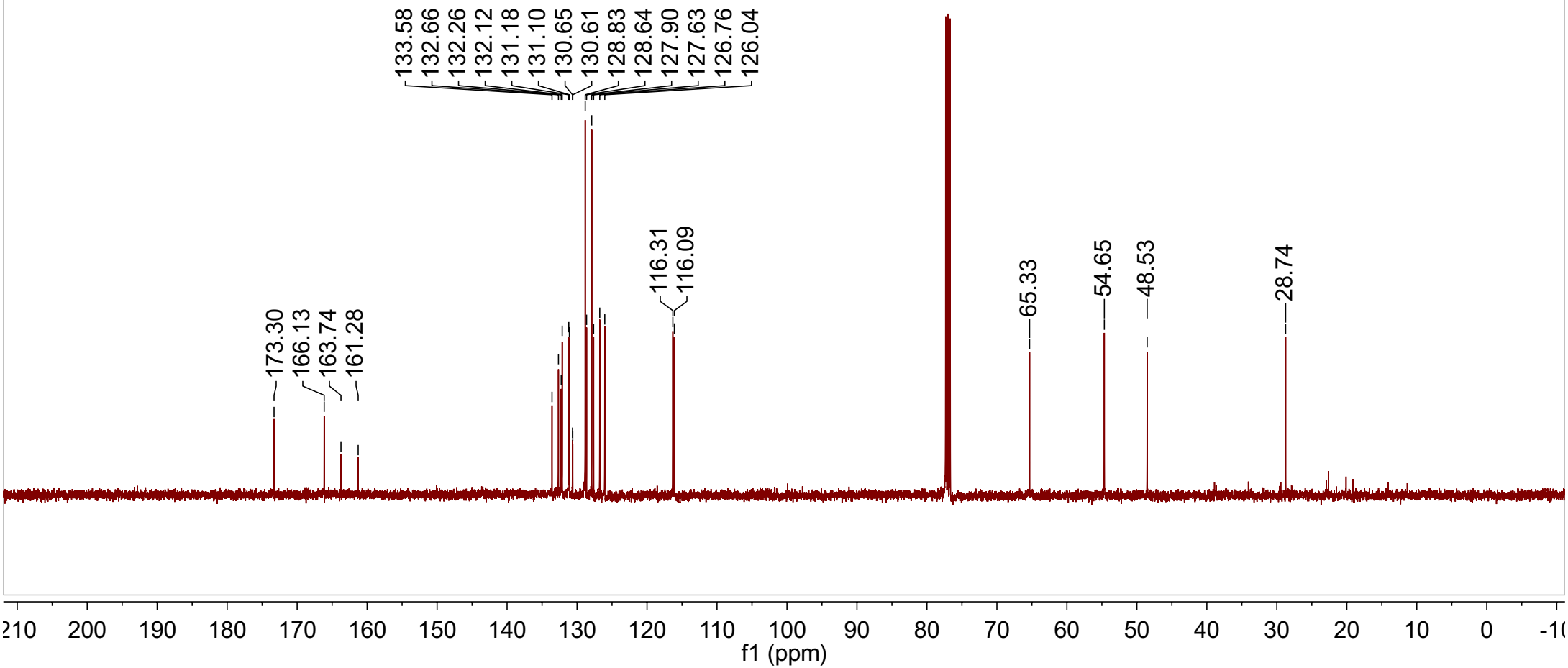
3f

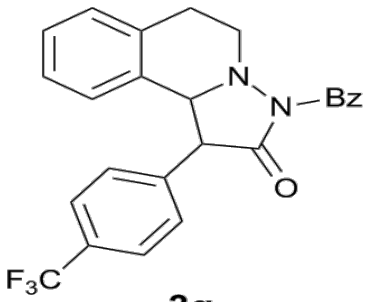
^{1}H NMR 400M $CDCl_3$



3f

^{13}C NMR 100M $CDCl_3$

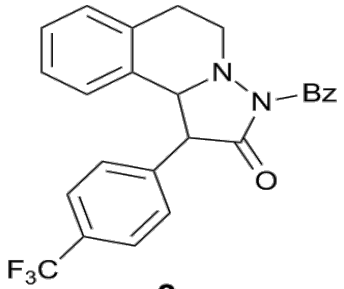




3g

^{1}H NMR 400M $CDCl_3$

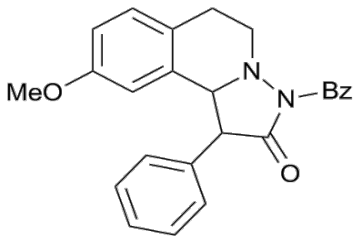
3g



3g

^{13}C NMR 100M $CDCl_3$

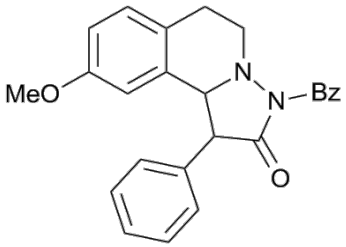
3h H



3h

^{1}H NMR 400M $CDCl_3$

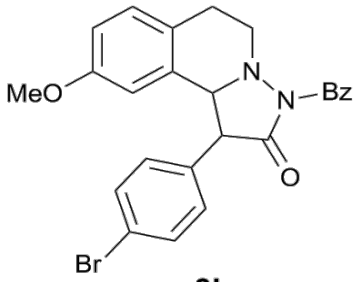
3h C



3h

^{13}C NMR 100M $CDCl_3$

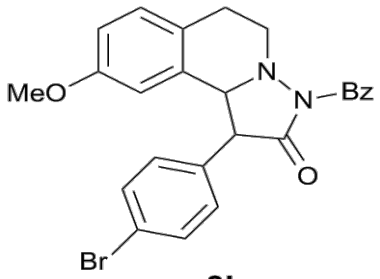
3i



3i

^{1}H NMR 400M $CDCl_3$

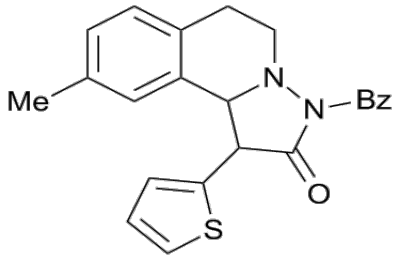
3i



3i

^{13}C NMR 100M $CDCl_3$

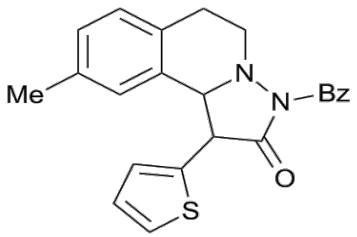
3j



3j

^{1}H NMR 400M $CDCl_3$

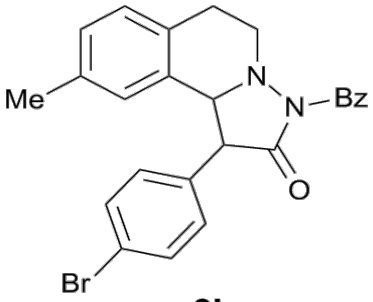
3j



3j

^{13}C NMR 100M $CDCl_3$

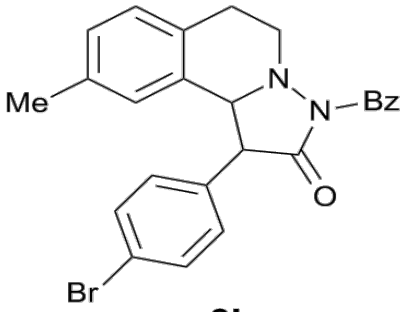
3k



3k

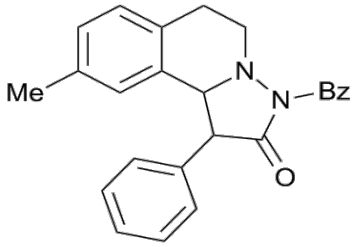
^{1}H NMR 400M $CDCl_3$

3k



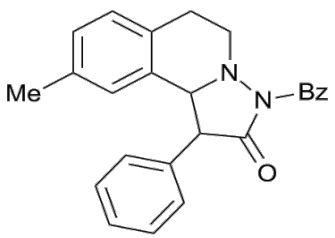
3k

^{13}C NMR 100M $CDCl_3$



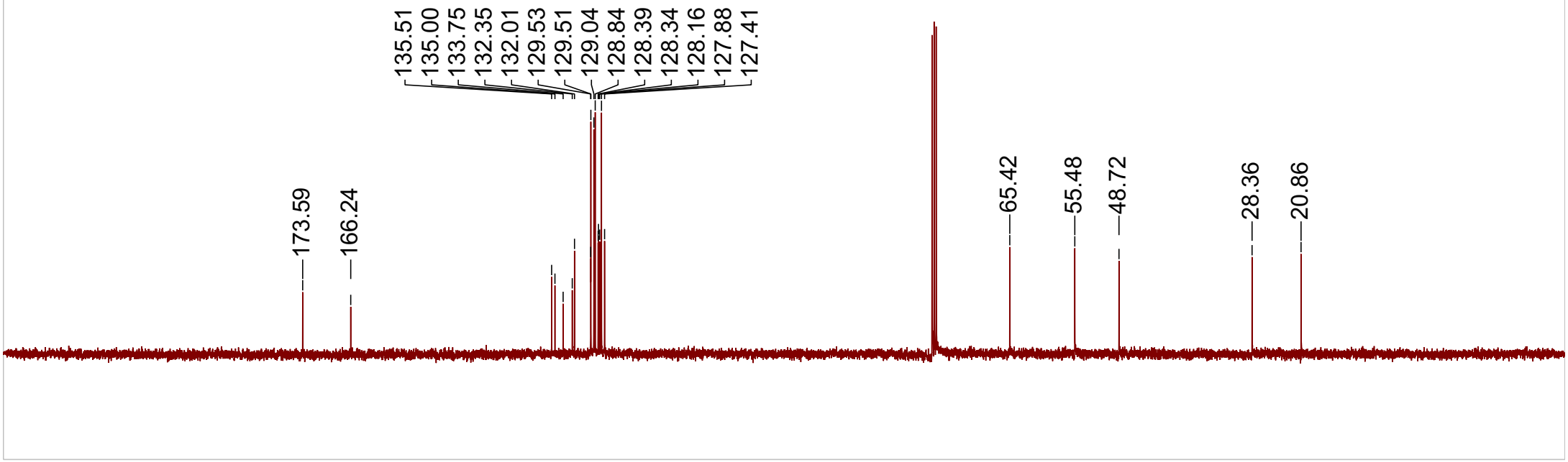
3l

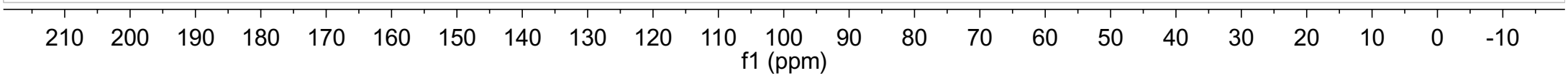
^{1}H NMR 400M $CDCl_3$



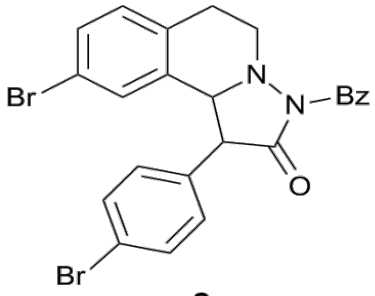
3l

^{13}C NMR 100M $CDCl_3$





3m H



3m

^{1}H NMR 400M $CDCl_3$

7.71 7.69 7.69 7.61 7.59 7.56 7.54 7.52 7.45 7.43 7.41 7.35 7.35 7.33 7.33 7.12 7.09 7.07

4.12 4.09 3.74 3.73 3.72 3.72 3.71 3.25 3.25 3.23 3.20 2.87 2.86 2.84

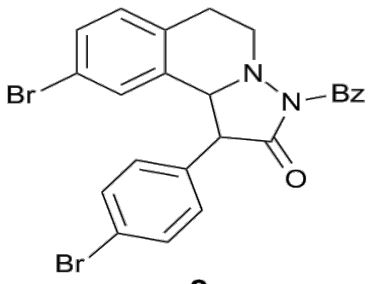
4.91 4.88

1.94 1.89 1.08 2.00 1.00 2.96 1.00 1.00 1.00 1.02 2.02 1.06

13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0

f1 (ppm)

3m C



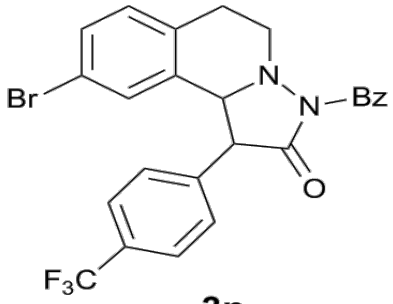
3m

^{13}C NMR 100M $CDCl_3$

134.35
133.38
132.51
132.31
131.76
131.02
130.91
130.36
129.60
128.87
127.99
122.71
119.70
172.53
166.06
64.74
54.81
48.36
28.29

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

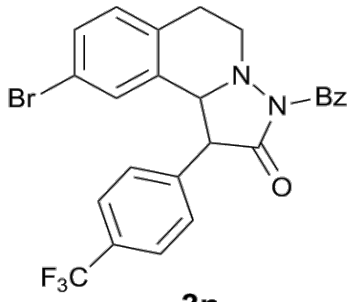
f1 (ppm)



3n

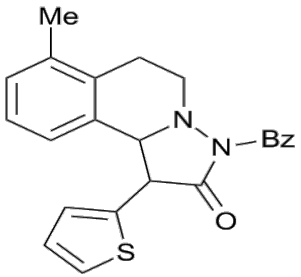
^{1}H NMR 400M $CDCl_3$

3n



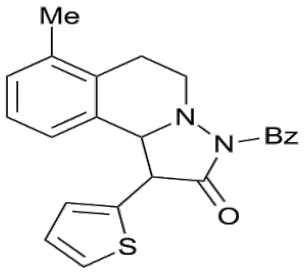
3n

^{13}C NMR 100M $CDCl_3$



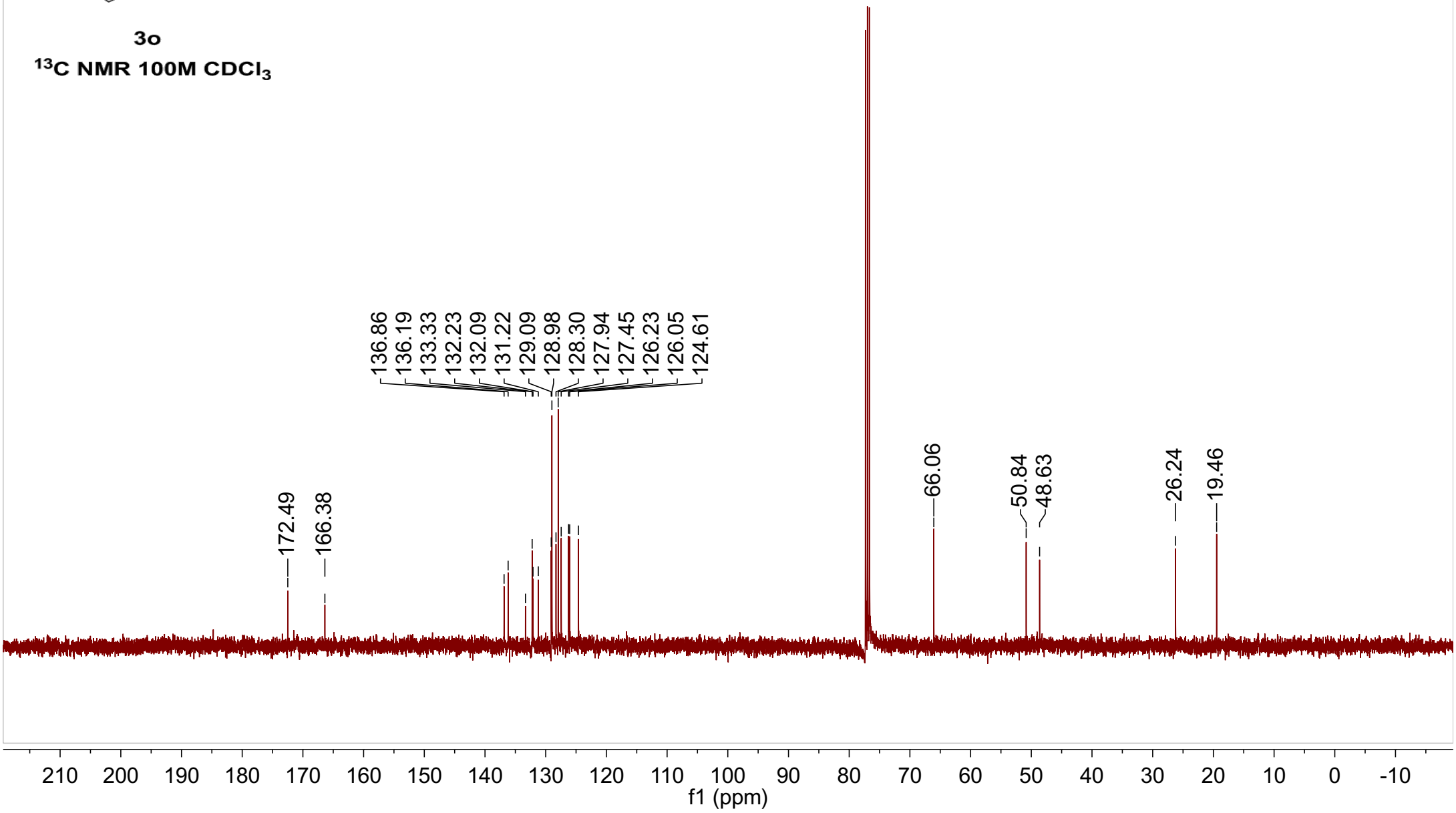
3o

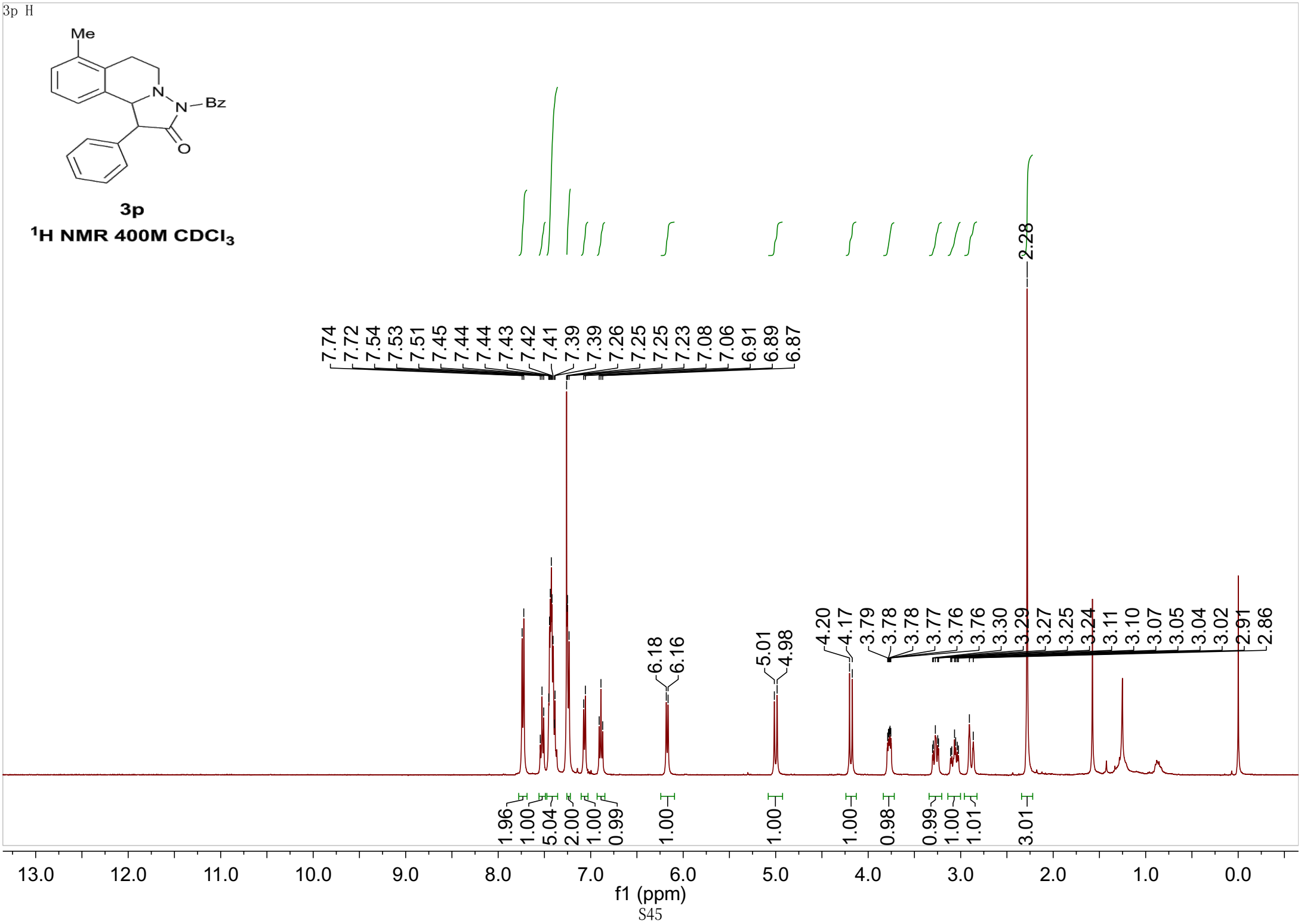
^{1}H NMR 400M $CDCl_3$



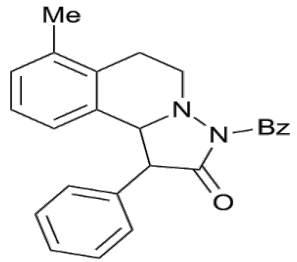
3o

^{13}C NMR 100M $CDCl_3$



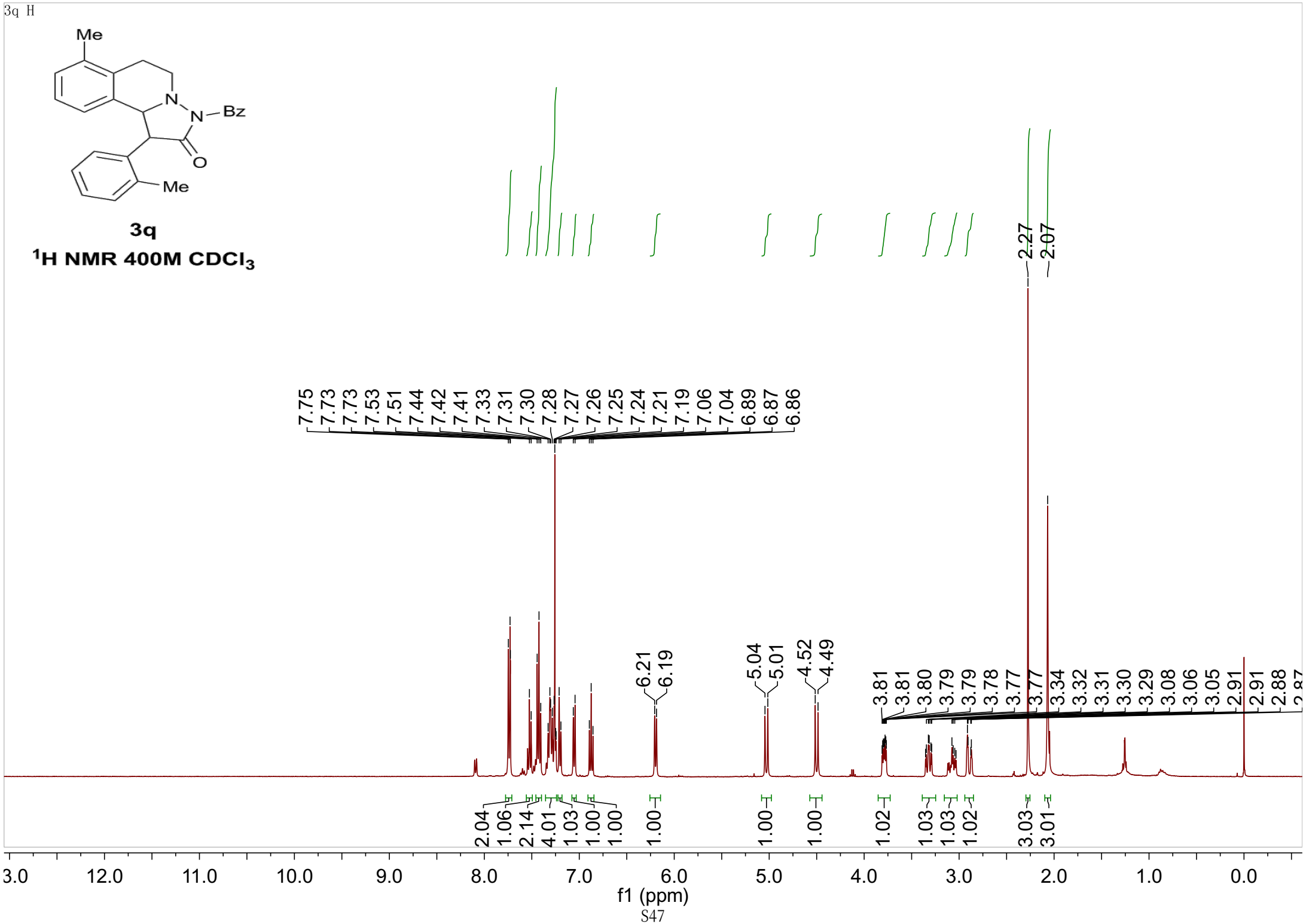

3p H
Me
N
N
Bz
O
3p
1H NMR 400M CDCl3
7.74
7.72
7.54
7.53
7.51
7.45
7.44
7.44
7.43
7.42
7.41
7.39
7.39
7.26
7.25
7.25
7.23
7.08
7.06
6.91
6.89
6.87
6.18
6.16
5.01
4.98
4.20
4.17
3.79
3.78
3.78
3.77
3.76
3.76
3.30
3.29
3.27
3.25
3.24
3.11
3.10
3.07
3.05
3.04
3.02
2.91
2.86
2.28
1.96
1.00
5.04
2.00
1.00
0.99
1.00
1.00
1.00
0.98
0.99
1.00
1.01
3.01
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

3p C

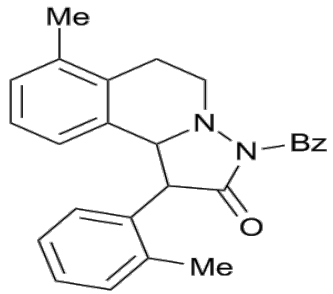


3p

^{13}C NMR 100M $CDCl_3$


3q H
Me
N
N
Bz
O
Me
3q
1H NMR 400M CDCl3
7.75
7.73
7.73
7.53
7.51
7.44
7.42
7.41
7.33
7.31
7.30
7.28
7.27
7.26
7.25
7.24
7.21
7.19
7.06
7.04
6.89
6.87
6.86
6.21
6.19
5.04
5.01
4.52
4.49
3.81
3.81
3.80
3.79
3.79
3.78
3.77
3.77
3.34
3.32
3.31
3.30
3.29
3.08
3.06
3.05
2.91
2.91
2.27
2.07
2.04
1.06
2.14
4.01
1.03
1.00
1.00
1.00
1.00
1.00
1.02
1.03
1.03
1.02
3.03
3.01
3.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

3q C



3q

^{13}C NMR 100M $CDCl_3$

137.63
136.11
133.69
132.30
131.98
131.09
130.77
130.09
128.82
128.36
127.92
127.87
127.00
125.99
124.09
173.92
166.28
65.51
51.35
48.37
26.23
20.01
19.45

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10

f1 (ppm)

Literature

1) E. Grochowski and J. Jurczak, *Synth. Commun.*, 1977, **7**, 1277.

2a) T. Hashimoto, Y. Maeda, M. Omote, H. Nakatsu, K. Maruoka, *J. Am. Chem. Soc.*, 2010,**132**, 4076; 2b) S. E. Reisman, A. G. Doyle, E. N. Jacobsen, *J. Am. Chem. Soc.*, 2008, **130**,7198;

2c) Lena Hesping, Anup Biswas, Constantin G. Daniliuc, Christian Mück-Lichtenfeld and Armido Studer, *Chem. Sci.*, 2015, **6**, 1252-1257.

3) X. Liu, B. Sun, Z. Xie, X. Qin,L. Liu, H. Lou, *J. Org. Chem.*, 2013, **78**, 3104.