Copper-Catalyzed Domino Cyclization of Anilines and Cyclobutanone Oxime Ethers: A Scalable and Versatile Route to Spirotetrahydroquinoline Derivatives

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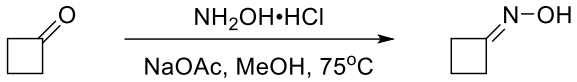
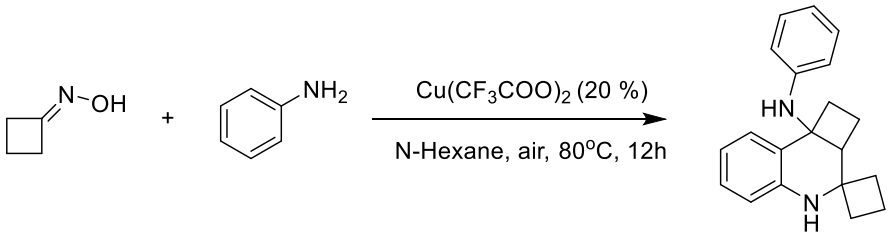
The synthesis of cyclobutanone oxime



To a mixture of hydroxylamine hydrochloride (1.2 equiv), sodium acetate (2.2 equiv), methanol (100mL) in a 250-mL two-necked flask was added cyclobutanone (1.0 equiv) and the mixture was stirred at 75 ℃ for 12 h. The reaction mixture was cooled to room temperature and then methanol was removedunder vacuum and the resulting mixture was extracted with diethyl ether. The organic layer was washedwith water and dried over MgSO4. The solvent was removed under reduced pressure and the crudematerial was subjected to column chromatography to afford cyclobutanone oxime in 95 % yield.

Reaction and method of cyclobutanone oxime with aniline

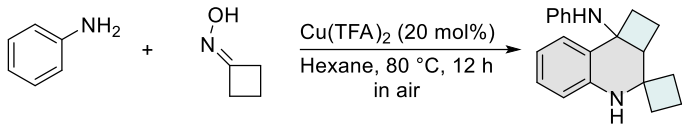


1a **2a** **3aa**, 92%

A dried straight reaction tube was charged with **1** (0.4 mmol), **2** (0.2 mmol), and $Cu(CF_3COO)_2$ (11.58 mg, 20 mol %), then dried N-Hexane (2 mL) was added by using a syringe . The reaction mixture was stirred at 80 °C for 12 h. After quenching the reaction with aqueous NH_4Cl (2 mL), the crude product was extracted with ethyl acetate (3×10 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under vacuum.

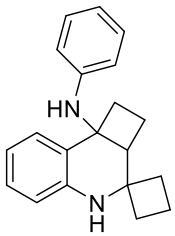
The residue was purified by flash chromatography on neutral alumina to give the desired product **3**.

Gram level reaction



1a 5.0 mmol | **2a** 2.0 equiv. | **3aa** 1.2 g, 82%

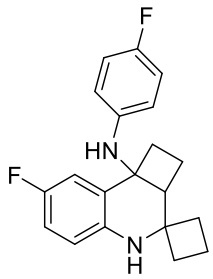
A dried two-necked flask was charged with **1a** (10 mmol), **2a** (5 mmol), and $Cu(CF_3COO)_2$ (145 mg, 20 mol %), then dried n-hexane (100 mL) was added by using a syringe. The reaction mixture was stirred at 80 °C for 12 h. After quenching the reaction with aqueous NH_4Cl (20 mL), the crude product was extracted with ethyl acetate (3×10 mL). The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was purified by flash chromatography on neutral alumina to give the desired product **3aa** (yellow solid, 1.2g, 82%).



3aa, 92%

The general procedure was applied to aniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography

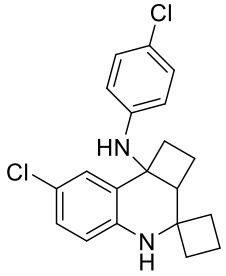
on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow solid (27 mg, 92% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.32 (dd, J = 7.6, 1.5 Hz, 1H), 7.05 (td, J = 7.3, 1.1 Hz, 3H), 6.71 (td, J = 7.5, 1.2 Hz, 1H), 6.65 (td, J = 7.7, 1.1 Hz, 2H), 6.48 (dd, J = 8.7, 1.1 Hz, 2H), 4.05 (s, 2H), 2.99 (t, J = 8.5 Hz, 1H), 2.39 – 2.30 (m, 1H), 2.20 (dddd, J = 11.5, 9.6, 4.6, 1.0 Hz, 1H), 2.05 – 1.83 (m, 5H), 1.77 – 1.68 (m, 1H), 1.68 – 1.58 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.77, 142.98, 128.79, 127.63, 127.36, 126.94, 118.92, 117.54, 115.37, 56.50, 54.77, 50.45, 37.83, 37.52, 33.84, 15.49, 12.66.



3ba, 62%

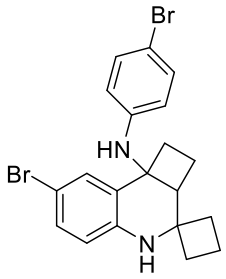
The general procedure was applied to 4-fluoroaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow liquid (21 mg, 62% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.05 (dd, J = 9.7, 3.0 Hz, 1H), 6.80 – 6.73 (m, 3H), 6.58 (dd, J = 8.7, 4.7 Hz, 1H), 6.41 – 6.35 (m, 2H), 3.92 (s, 2H), 2.88 – 2.78 (m, 1H), 2.24 – 2.13 (m, 2H), 2.06 – 1.88 (m, 3H), 1.83 – 1.72 (m, 3H), 1.61 (dtd, J = 17.2, 8.9, 8.4, 3.0 Hz, 2H).13C NMR (101 MHz, $CDCl_3$) δ 157.96,

155.61, 141.70, 139.28, 129.12, 116.77, 116.32, 115.40, 114.43, 112.96, 57.05, 55.08, 50.23, 37.63, 37.49, 33.56, 15.47, 12.63.



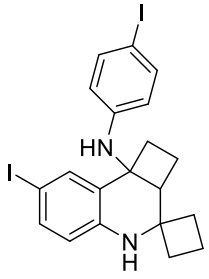
3ca, 80%

The general procedure was applied to 4-chloroaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow solid (29 mg, 80% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.24 (d, J = 2.5 Hz, 1H), 7.00 (dd, J = 8.7, 2.1 Hz, 3H), 6.57 (d, J = 8.5 Hz, 1H), 6.40 – 6.33 (m, 2H), 4.21 (s, 1H), 4.01 (s, 1H), 2.86 (t, J = 8.5 Hz, 1H), 2.28 – 2.15 (m, 2H), 2.00 (ddt, J = 14.2, 11.5, 4.4 Hz, 2H), 1.95 – 1.81 (m, 3H), 1.78 – 1.70 (m, 1H), 1.60 (dtd, J = 14.2, 6.1, 5.5, 3.0 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.93, 141.65, 128.70, 128.52, 127.55, 126.46, 123.45, 122.55, 116.63, 116.43, 56.41, 54.83, 50.59, 37.98, 37.73, 33.73, 15.53, 12.60.



3da, 57%

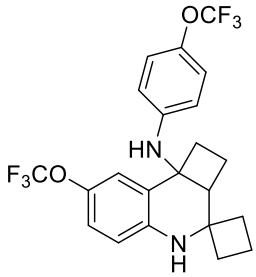
The general procedure was applied to 4-bromoaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow solid (26 mg, 57% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.36 (d, J = 2.3 Hz, 1H), 7.12 (dd, J = 8.7, 3.4 Hz, 3H), 6.52 (d, J = 8.5 Hz, 1H), 6.34 – 6.28 (m, 2H), 4.22 (s, 1H), 4.02 (s, 1H), 2.86 (t, J = 8.5 Hz, 1H), 2.28 – 2.15 (m, 2H), 2.04 – 1.95 (m, 2H), 1.94 – 1.81 (m, 3H), 1.78 – 1.69 (m, 1H), 1.63 – 1.55 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.31, 142.07, 131.57, 130.39, 129.33, 128.90, 117.04, 116.86, 110.62, 109.69,56.30, 54.76, 50.61, 38.03, 37.74, 33.74, 15.54, 12.59.



3ea, 59%

The general procedure was applied to 4-iodoaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-

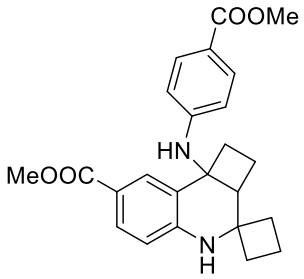
Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow solid (32 mg, 59% yield).^{1}H NMR (600 MHz, DMSO) δ = 7.25 (d, J = 8.2 Hz, 2H), 6.60 (d, J = 8.4 Hz, 1H), 6.51 (s, 1H), 6.35 (s, 1H), 6.24 (d, J = 8.3 Hz, 2H), 2.73 (t, J = 8.2 Hz, 1H), 2.47 (d, J = 9.4 Hz, 1H), 2.05 (q, J = 9.9 Hz, 1H), 1.92 (dt, J = 19.7, 8.9 Hz, 4H), 1.83 (t, J = 10.3 Hz, 1H), 1.71 (q, J = 10.2 Hz, 1H), 1.54 (q, J = 9.4 Hz, 1H), 1.44 (q, J = 8.8, 8.4 Hz, 1H).^{13}C NMR (151 MHz, DMSO) δ 145.67, 143.69, 136.54, 135.20, 133.96, 128.71, 117.51, 116.86, 78.01, 76.98, 54.74, 53.83, 50.83, 37.96, 36.14, 32.68, 15.45, 12.03.



3fa, 33%

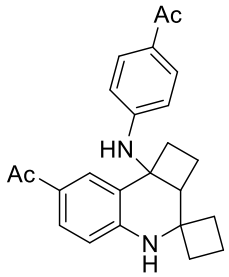
The general procedure was applied to 4-(trifluoromethoxy)aniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/20) to afford the title compound as a colorless liquid (15 mg, 33% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.13 (dd, J = 2.8, 1.0 Hz, 1H), 6.95 – 6.85 (m, 3H), 6.61 (d, J = 8.6 Hz, 1H), 6.39 – 6.34 (m, 2H), 4.11 (s, 2H), 2.92 – 2.85 (m, 1H), 2.31 – 2.17 (m, 2H), 2.06 – 1.96 (m, 2H), 1.96 – 1.82 (m, 3H), 1.79 – 1.70

(m, 1H), 1.67 – 1.57 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.02, 141.85, 141.38, 140.93, 127.83, 121.85, 120.79, 119.83, 115.94, 115.71, 56.52, 54.86, 50.60, 37.85, 37.71, 33.69, 15.46, 12.59.



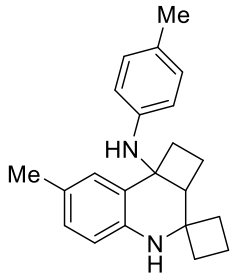
3ga, 40%

The general procedure was applied to methyl 4-aminobenzoate (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a white solid (16 mg, 40% yield).^{1}H NMR (400 MHz, DMSO) δ = 7.63 (d, J = 2.1 Hz, 1H), 7.50 (dd, J = 14.9, 8.6 Hz, 3H), 7.20 (s, 1H), 7.09 (s, 1H), 6.69 (d, J = 8.6 Hz, 1H), 6.31 (d, J = 8.4 Hz, 2H), 3.64 (d, J = 7.1 Hz, 6H), 2.79 (t, J = 8.9 Hz, 1H), 2.55 (q, J = 10.6, 10.2 Hz, 1H), 2.12 – 1.96 (m, 2H), 1.94 – 1.80 (m, 4H), 1.62 (d, J = 7.4 Hz, 1H), 1.51 (q, J = 9.5 Hz, 1H), 1.31 (p, J = 10.0 Hz, 1H).^{13}C NMR (101 MHz, DMSO) δ = 166.66, 166.64, 150.54, 148.54, 131.50, 130.60, 129.32, 123.69, 117.55, 116.56, 114.24, 113.52, 54.81, 53.92, 51.61, 51.29, 39.05, 36.68, 33.44, 15.90, 12.29.



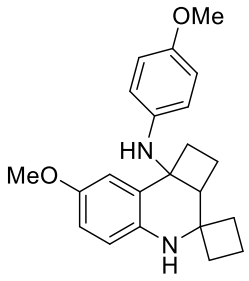
3ha, 29%

The general procedure was applied to 1-(4-aminophenyl)ethan-1-one (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a white solid (11 mg, 29% yield).^{1}H NMR (400 MHz, DMSO) δ = 7.63 (d, J = 2.1 Hz, 1H), 7.57 (dd, J = 8.6, 2.1 Hz, 1H), 7.53 (s, 1H), 7.51 (s, 1H), 7.25 (s, 1H), 7.17 (s, 1H), 6.69 (d, J = 8.5 Hz, 1H), 6.32 (d, J = 8.5 Hz, 2H), 2.81 (t, J = 8.9 Hz, 1H), 2.57 (q, J = 10.2 Hz, 1H), 2.29 (d, J = 5.2 Hz, 6H), 2.10 – 1.81 (m, 6H), 1.69 – 1.59 (m, 1H), 1.58 – 1.49 (m, 1H), 1.37 – 1.25 (m, 1H).^{13}C NMR (101 MHz, DMSO) δ = 195.53, 195.41, 150.61, 148.67, 130.06, 129.32, 128.30, 126.50, 125.47, 123.64, 113.84, 113.34, 54.86, 53.97, 51.22, 39.07, 36.64, 33.44, 26.24, 15.96, 12.32.



3ia, 96%

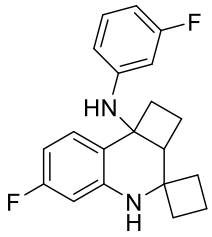
The general procedure was applied to *p*-toluidine (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a red liquid (31 mg, 96% yield).^{1}H NMR (400 MHz, cdcl3) δ = 7.20 (d, J = 2.0 Hz, 1H), 6.94 – 6.86 (m, 3H), 6.58 (d, J = 8.0 Hz, 1H), 6.47 (d, J = 8.4 Hz, 2H), 3.95 (s, 2H), 2.97 (t, J = 8.4 Hz, 1H), 2.38 – 2.30 (m, 1H), 2.22 (d, J = 4.4 Hz, 6H), 2.17 (dd, J = 11.2, 4.8 Hz, 1H), 2.06 – 1.89 (m, 4H), 1.84 (t, J = 8.9 Hz, 1H), 1.72 (tt, J = 9.5, 4.7 Hz, 1H), 1.69 – 1.58 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 143.54, 140.58, 129.38, 128.16, 128.07, 127.16, 126.97, 116.02, 115.45, 56.95, 54.89, 49.89, 37.53, 37.44, 33.76, 20.75, 20.42, 15.49, 12.73.



3ja, 97%

The general procedure was applied to 4-methoxyaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a white solid (34 mg, 97% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.01 (d, J = 2.8 Hz, 1H), 6.70 – 6.65 (m, 3H), 6.59 (d, J = 8.4 Hz, 1H),

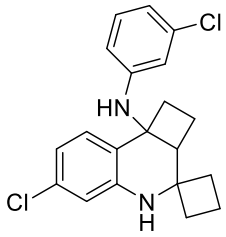
6.49 (d, J = 8.8 Hz, 2H), 3.70 (d, J = 6.2 Hz, 6H), 2.87 (t, J = 8.4 Hz, 1H), 2.25 (t, J = 9.9 Hz, 1H), 2.19 (dd, J = 10.0, 4.8 Hz, 1H), 1.99 (dd, J = 11.7, 4.1 Hz, 1H), 1.92 (ddd, J = 17.3, 8.3, 4.9 Hz, 2H), 1.71 (ddd, J = 15.2, 11.4, 7.8 Hz, 3H), 1.64 – 1.50 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 153.89, 152.72, 139.75, 137.05, 129.14, 118.04, 116.48, 114.35, 114.06, 111.52, 57.76, 55.61, 55.55, 54.98, 49.63, 37.48, 37.20, 33.60, 15.35, 12.72.



3ka, 31%

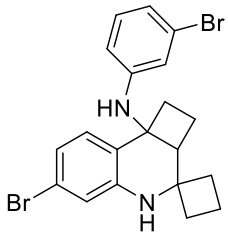
The general procedure was applied to 3-fluoroaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a white solid (10 mg, 31% yield).^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.19 (dd, J = 8.6, 6.4 Hz, 1H), 6.97 (td, J = 8.2, 6.8 Hz, 1H), 6.39 (td, J = 8.5, 2.5 Hz, 1H), 6.35 – 6.29 (m, 2H), 6.22 (ddd, J = 8.2, 2.3, 0.9 Hz, 1H), 6.08 (dt, J = 12.0, 2.4 Hz, 1H), 4.33 (s, 1H), 4.08 (s, 1H), 2.93 (t, J = 8.7 Hz, 1H), 2.33 – 2.25 (m, 1H), 2.19 – 2.12 (m, 1H), 2.04 (ddt, J = 13.0, 8.7, 4.0 Hz, 1H), 1.98 – 1.88 (m, 4H), 1.73 (dtd, J = 11.8, 9.6, 4.8 Hz, 1H), 1.63 – 1.57 (m, 2H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 163.32, 161.71, 147.31, 144.42, 129.77, 128.61, 122.03, 111.02, 105.88, 103.97, 101.59,

101.43,56.05, 54.75, 50.82, 38.16, 37.84, 33.91, 15.38, 12.58.



3la, 63%

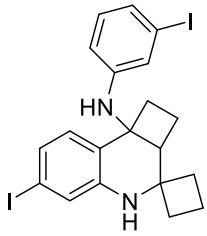
The general procedure was applied to 3-chloroaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a white solid (23 mg, 63% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.19 – 7.13 (m, 1H), 6.94 (t, J = 8.1 Hz, 1H), 6.67 – 6.59 (m, 3H), 6.40 (t, J = 2.2 Hz, 1H), 6.28 (ddd, J = 8.2, 2.3, 0.9 Hz, 1H), 4.30 (s, 1H), 4.07 (s, 1H), 2.89 (t, J = 8.5 Hz, 1H), 2.30 – 2.21 (m, 1H), 2.16 (ddd, J = 11.5, 10.1, 4.5 Hz, 1H), 2.07 – 1.89 (m, 5H), 1.76 (ddt, J = 16.2, 9.8, 4.6 Hz, 1H), 1.67 – 1.58 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.53, 144.14, 134.43, 132.92, 129.78, 128.11, 125.05, 118.92, 117.53, 114.88, 114.84, 113.18,55.94, 54.90, 50.92, 38.07, 37.70, 33.80, 15.52, 12.62.



3ma, 91%

The general procedure was applied to 3-bromoaniline (0.2 mmol),

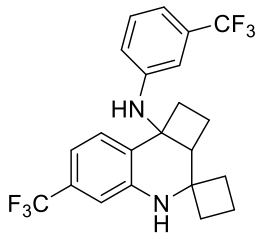
cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a white solid (41 mg, 91% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.7 Hz, 1H), 6.87 (t, J = 8.0 Hz, 1H), 6.81 – 6.75 (m, 3H), 6.56 (t, J = 2.1 Hz, 1H), 6.(dd, J = 7.7, 1.8 Hz, 1H), 4.28 (s, 1H), 4.06 (s, 1H), 2.88 (t, J = 8.530 Hz, 1H), 2.29 – 2.14 (m, 2H), 2.06 – 1.89 (m, 5H), 1.77 (ddt, J = 11.6, 9.2, 4.7 Hz, 1H), 1.61 (dtd, J = 11.8, 8.4, 2.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.63, 144.42, 132.23, 130.08, 128.34, 125.52, 122.70, 121.79, 121.05, 120.43, 117.78, 115.72, 113.49, 55.96, 54.92, 50.93, 38.07, 37.64, 33.78, 15.55, 12.63.



3na, 66%

The general procedure was applied to 3-iodoaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a white solid (36 mg, 66% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.03 – 6.91 (m, 4H), 6.78 (s, 1H), 6.73 (t, J = 8.0 Hz, 1H), 6.33 (dd, J = 8.2, 2.3 Hz, 1H), 4.24 (s, 1H), 4.13 (q, J = 7.1 Hz, 1H), 4.05 (s, 1H), 2.87

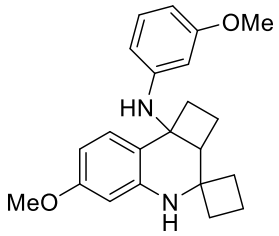
(t, J = 8.5 Hz, 1H), 2.28 – 2.11 (m, 2H), 2.05 (s, 1H), 2.03 – 1.99 (m, 1H), 1.98 – 1.94 (m, 1H), 1.89 (dd, J = 10.3, 2.4 Hz, 1H), 1.76 (ddt, J = 18.2, 9.2, 4.5 Hz, 1H), 1.61 (dt, J = 10.4, 8.4 Hz, 2H), 1.26 (t, J = 7.1 Hz, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 146.55, 144.56, 130.26, 128.49, 127.78, 126.49, 126.28, 123.77, 123.73, 114.03, 94.73, 92.81, 55.96, 54.88, 50.98, 38.09, 37.62, 33.79, 15.59, 12.66.



3oa, 58%

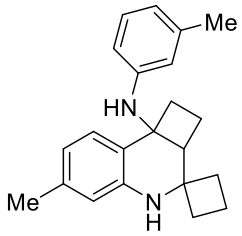
The general procedure was applied to 3-(trifluoromethyl)aniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a colorless solid (25 mg, 58% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.34 (d, J = 8.1 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 6.95 – 6.87 (m, 3H), 6.64 (s, 1H), 6.52 (dd, J = 8.2, 2.4 Hz, 1H), 4.51 (s, 1H), 4.25 (s, 1H), 2.94 (t, J = 8.6 Hz, 1H), 2.34 – 2.22 (m, 2H), 2.13 – 2.02 (m, 2H), 2.00 – 1.91 (m, 3H), 1.78 (tdd, J = 14.3, 10.2, 5.0 Hz, 1H), 1.64 (dtd, J = 17.5, 8.9, 3.1 Hz, 2H).13C NMR (101 MHz, cdcl3) δ 145.40, 143.31, 130.93, 129.72, 129.56, 129.23, 127.35, 125.56, 122.85, 117.66, 115.14, 114.06, 111.88, 111.37, 55.97, 54.76, 51.34, 38.18, 37.70, 33.85, 15.57,

12.53.



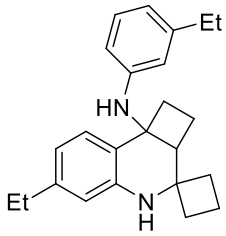
3pa, 70%

The general procedure was applied to 3-methoxyaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a colorless liquid (25 mg, 70% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.07 (ddd, J = 8.2, 3.9, 1.7 Hz, 1H), 6.82 (dq, J = 10.0, 3.9, 3.0 Hz, 1H), 6.17 (ddd, J = 6.1, 3.8, 1.8 Hz, 1H), 6.11 – 6.06 (m, 1H), 6.05 – 6.01 (m, 1H), 6.01 – 5.95 (m, 1H), 5.90 (dd, J = 4.0, 2.1 Hz, 1H), 3.96 (d, J = 84.4 Hz, 2H), 3.61 (dd, J = 4.0, 1.8 Hz, 3H), 3.52 – 3.45 (m, 3H), 2.85 (s, 1H), 2.20 (td, J = 10.5, 9.9, 3.7 Hz, 1H), 2.08 – 1.97 (m, 1H), 1.93 – 1.69 (m, 5H), 1.62 – 1.53 (m, 1H), 1.51 – 1.42 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 160.24, 159.22, 147.28, 143.95, 129.45, 128.41, 119.75, 108.43, 105.05, 103.04, 101.10, 100.03, 56.24, 55.09, 54.88, 54.67, 50.52, 38.15, 37.72, 33.98, 15.31, 12.64.



3qa, 90%

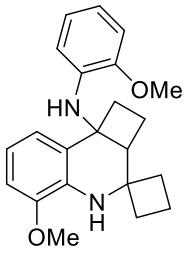
The general procedure was applied to *m*-toluidine (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a colorless liquid (29 mg, 90% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.22 (d, J = 7.8 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 6.55 (d, J = 7.8 Hz, 1H), 6.53 – 6.46 (m, 2H), 6.37 (s, 1H), 6.31 (dd, J = 8.0, 2.4 Hz, 1H), 4.02 (s, 2H), 3.00 (t, J = 8.5 Hz, 1H), 2.36 (dd, J = 19.8, 10.0 Hz, 1H), 2.28 (s, 3H), 2.21 (s, 3H), 2.20 – 2.14 (m, 1H), 2.07 – 1.86 (m, 5H), 1.77 – 1.70 (m, 1H), 1.64 (qd, J = 9.1, 8.6, 3.0 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.85, 142.83, 138.45, 137.06, 128.67, 126.82, 125.09, 120.05, 118.43, 116.34, 115.85, 112.34, 56.37, 54.85, 50.30, 37.78, 37.45, 33.87, 21.60, 21.23, 15.48, 12.74.



3ra, 29%

The general procedure was applied to 3-ethylaniline (0.2 mmol),

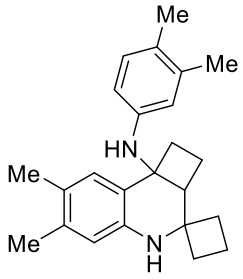
cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow liquid (10 mg, 29% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.28 (d, J = 7.9 Hz, 1H), 7.05 – 6.99 (m, 1H), 6.61 (dd, J = 7.9, 1.7 Hz, 1H), 6.55 (d, J = 7.8 Hz, 1H), 6.51 (d, J = 1.7 Hz, 1H), 6.37 (dd, J = 7.8, 1.5 Hz, 2H), 4.07 (d, J = 88.6 Hz, 2H), 3.05 (t, J = 8.6 Hz, 1H), 2.60 (q, J = 7.6 Hz, 2H), 2.52 (q, J = 7.6 Hz, 2H), 2.42 (dd, J = 20.0, 9.9 Hz, 1H), 2.26 – 2.18 (m, 1H), 2.07 – 1.96 (m, 3H), 1.92 – 1.85 (m, 1H), 1.75 – 1.58 (m, 3H), 1.32 (s, 1H), 1.26 (t, J = 7.6 Hz, 3H), 1.16 (t, J = 7.6 Hz, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 145.97, 144.77, 143.50, 142.82, 128.67, 127.14, 124.99, 118.82, 117.27, 115.24, 114.52, 112.83, 56.48, 54.66, 50.38, 37.93, 37.42, 34.00, 28.93, 28.58, 15.39, 15.37, 15.27, 12.71.



3sa, 20%

The general procedure was applied to 2-methoxyaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/40) to afford the title compound as a colorless liquid (7 mg, 20% yield).^{1}H NMR (400 MHz,

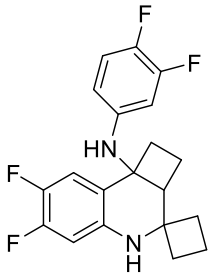
$CDCl_3$) δ = 6.99 (dd, J = 7.4, 1.8 Hz, 1H), 6.82 – 6.75 (m, 1H), 6.72 – 6.57 (m, 4H), 6.33 – 6.25 (m, 1H), 4.91 (s, 1H), 4.74 – 4.60 (m, 1H), 3.90 (d, J = 7.0 Hz, 6H), 2.97 (t, J = 8.6 Hz, 1H), 2.45 (ddd, J = 11.3, 10.0, 8.7 Hz, 1H), 2.22 (ddd, J = 11.4, 9.7, 4.1 Hz, 1H), 2.11 – 1.94 (m, 4H), 1.84 (q, J = 10.9, 10.0 Hz, 1H), 1.75 – 1.58 (m, 3H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 147.33, 146.61, 135.53, 132.90, 127.51, 120.60, 118.98, 117.32, 116.34, 113.26, 109.31, 107.56, 56.00, 55.53, 55.47, 54.11, 51.07, 38.59, 37.59, 33.82, 15.43, 12.64.



3ta, 60%

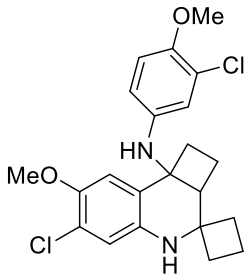
The general procedure was applied to 3,4-dimethylaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow liquid (22 mg, 60% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.13 (s, 1H), 6.84 (d, J = 8.1 Hz, 1H), 6.47 (s, 1H), 6.43 (d, J = 2.5 Hz, 1H), 6.30 (dd, J = 8.1, 2.5 Hz, 1H), 3.88 (s, 2H), 2.98 (t, J = 8.5 Hz, 1H), 2.41 – 2.33 (m, 1H), 2.20 (s, 3H), 2.15 (s, 3H), 2.13 (s, 3H), 2.12 (s, 3H), 2.01 (ddd, J = 8.8, 6.4, 3.9 Hz, 2H), 1.95 – 1.88 (m, 2H), 1.87 – 1.80 (m, 1H), 1.78 – 1.64 (m, 2H), 1.64 – 1.56 (m, 2H).^{13}C NMR (101 MHz,

$CDCl_3$) δ = 143.99, 140.73, 136.82, 135.60, 129.87, 127.72, 126.95, 125.85, 125.68, 117.86, 116.66, 113.18, 56.71, 54.80, 49.58, 37.48, 37.24, 33.81, 20.01, 19.62, 19.02, 18.70, 15.36, 12.76.



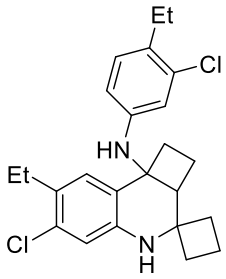
3ua, 69%

The general procedure was applied to 3,4-difluoroaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow solid (25 mg, 69% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.06 (dd, J = 11.3, 8.8 Hz, 1H), 6.90 – 6.78 (m, 1H), 6.43 (dd, J = 11.6, 6.8 Hz, 1H), 6.22 – 6.08 (m, 2H), 4.13 (s, 1H), 3.95 (s, 1H), 2.82 (t, J = 8.5 Hz, 1H), 2.22 – 2.11 (m, 2H), 2.07 – 1.91 (m, 3H), 1.88 – 1.82 (m, 2H), 1.79 – 1.72 (m, 1H), 1.64 – 1.57 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 151.57, 151.44, 150.96, 150.82, 149.14, 149.01, 148.52, 148.38, 145.33, 145.20, 144.65, 144.52, 142.96, 142.83, 142.29, 142.26, 142.24, 142.18, 142.16, 139.71, 139.69, 139.63, 139.61, 122.14, 122.10, 122.07, 117.19, 117.17, 117.01, 116.99, 115.09, 115.07, 114.91, 114.89, 110.81, 110.78, 110.76, 110.73, 104.13, 103.92, 103.68, 103.48, 56.35, 54.94, 50.58, 37.87, 33.64, 29.69, 15.31, 12.52.



3va, 31%

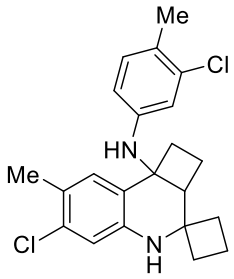
The general procedure was applied to 3-chloro-4-methoxyaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow liquid (13mg, 31% yield).^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.88 (s, 1H), 6.64 (s, 1H), 6.59 (d, J = 8.8 Hz, 1H), 6.50 (d, J = 2.8 Hz, 1H), 6.23 (dd, J = 8.8, 2.8 Hz, 1H), 3.71 (s, 3H), 3.66 (s, 3H), 2.78 – 2.68 (m, 1H), 2.15 – 2.07 (m, 2H), 1.94 – 1.85 (m, 2H), 1.81 (dt, J = 12.0, 8.8 Hz, 1H), 1.73 – 1.69 (m, 2H), 1.59 – 1.46 (m, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 148.40, 147.99, 140.15, 137.60, 126.92, 118.45, 117.10, 115.18, 113.35, 111.09, 57.25, 56.82, 56.71, 55.04, 50.36, 37.82, 37.47, 33.51, 15.35, 12.69.



3wa, 32%

The general procedure was applied to 3-chloro-4-ethylaniline (0.2 mmol),

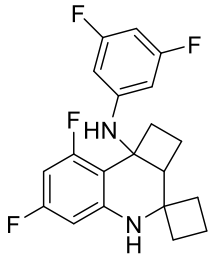
cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a red liquid (13mg, 32% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.13 (s, 1H), 6.90 (d, J = 8.3 Hz, 1H), 6.67 (s, 1H), 6.49 (d, J = 2.5 Hz, 1H), 6.31 (dd, J = 8.3, 2.4 Hz, 1H), 4.02 (d, J = 70.7 Hz, 2H), 2.90 (t, J = 8.5 Hz, 1H), 2.59 (p, J = 7.3 Hz, 4H), 2.28 (q, J = 10.0 Hz, 1H), 2.16 (td, J = 11.1, 10.6, 4.5 Hz, 1H), 2.04 – 1.85 (m, 5H), 1.74 (ddd, J = 14.1, 9.2, 4.7 Hz, 1H), 1.67 – 1.57 (m, 2H), 1.13 (dt, J = 19.2, 7.5 Hz, 6H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.60, 141.99, 133.72, 132.30, 131.77, 130.53, 129.48, 127.65, 126.19, 116.09, 115.60, 114.26, 56.45, 54.95, 50.46, 37.71, 37.59, 33.69, 26.04, 25.73, 15.44, 14.65, 14.38, 12.68.



3xa, 46%

The general procedure was applied to 3-chloro-4-methylaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a yellow solid (18mg, 46% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.11 (s, 1H), 6.88 (d, J = 8.2 Hz, 1H), 6.67 (s, 1H), 6.48 (d, J = 2.4 Hz,

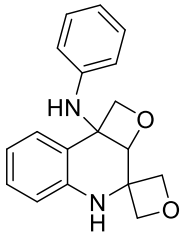
1H), 6.26 (dd, J = 8.3, 2.5 Hz, 1H), 4.01 (s, 2H), 2.86 (t, J = 8.5 Hz, 1H), 2.19 (d, J = 5.3 Hz, 8H), 2.04 – 1.85 (m, 5H), 1.74 (ddt, J = 14.0, 9.3, 4.7 Hz, 1H), 1.61 (t, J = 8.7 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 144.58, 142.01, 134.28, 132.88, 130.87, 128.76, 125.96, 125.82, 124.66, 115.77, 115.40, 113.93, 56.26, 54.99, 50.47, 37.79, 37.65, 33.70, 19.17, 18.84, 15.47, 12.65.



3ya, 39%

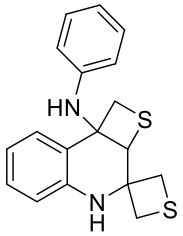
The general procedure was applied to 3,5-difluoroaniline (0.2 mmol), cyclobutanone (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 ºC for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/60) to afford the title compound as a white solid (12 mg, 39% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.14 – 5.99 (m, 3H), 5.96 – 5.82 (m, 2H), 4.53 (s, 1H), 4.39 (s, 1H), 2.97 – 2.90 (m, 1H), 2.43 – 2.29 (m, 2H), 2.08 (td, J = 7.9, 3.8 Hz, 3H), 1.99 – 1.90 (m, 2H), 1.74 – 1.60 (m, 2H), 1.52 – 1.44 (m, 1H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 164.85, 164.69, 164.08, 163.99, 163.91, 163.84, 162.43, 162.28, 161.64, 161.52, 161.48, 161.37, 147.80, 147.67, 147.54, 145.62, 145.49, 145.39, 105.80, 105.68, 105.65, 97.27, 97.18, 97.06, 96.98, 96.15, 96.12, 95.91, 95.88, 93.55, 93.29, 93.03, 92.59, 92.33, 92.07, 53.93,

53.59, 50.26, 38.93, 35.28, 34.78, 16.44, 12.29.



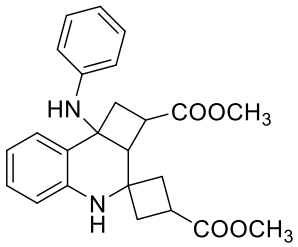
3ab, 76%

The general procedure was applied to aniline (0.2 mmol), oxetan-3-one (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/5) to afford the title compound as a white solid (22mg, 76% yield).^{1}H NMR (400 MHz, DMSO) δ = 7.00 (ddd, J = 19.9, 8.2, 6.8 Hz, 4H), 6.94 – 6.86 (m, 2H), 6.77 (s, 1H), 6.59 (t, J = 7.4 Hz, 1H), 6.52 (t, J = 7.3 Hz, 1H), 6.21 (d, J = 7.6 Hz, 2H), 5.01 (d, J = 2.0 Hz, 1H), 4.75 (d, J = 5.8 Hz, 1H), 4.57 (d, J = 6.5 Hz, 1H), 4.50 (d, J = 6.6 Hz, 1H), 4.36 (d, J = 6.0 Hz, 1H), 4.20 (dd, J = 16.1, 5.9 Hz, 2H).^{13}C NMR (101 MHz, DMSO) δ = 145.94, 143.71, 143.66, 129.19, 128.33, 125.41, 124.37, 118.88, 117.16, 116.35, 116.32, 114.24, 92.78, 82.16, 81.21, 78.21, 56.80, 55.63.



3ac, 78%

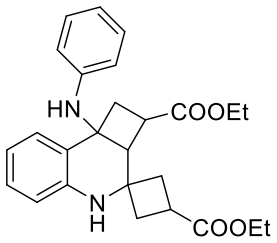
The general procedure was applied to aniline (0.2 mmol), thietan-3-one (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a white solid (25mg, 78% yield).^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.31 (dd, J = 7.8, 1.5 Hz, 1H), 7.11 (dd, J = 8.8, 7.4 Hz, 3H), 6.80 (td, J = 7.5, 1.2 Hz, 1H), 6.73 (t, J = 7.4 Hz, 2H), 6.64 (d, J = 7.5 Hz, 2H), 4.96 (s, 1H), 4.58 (s, 1H), 4.35 (s, 1H), 3.72 (d, J = 9.6 Hz, 1H), 3.14 (d, J = 10.3 Hz, 1H), 3.07 (d, J = 9.6 Hz, 1H), 2.99 (dd, J = 11.7, 2.2 Hz, 3H).^{13}C NMR (151 MHz, $CDCl_3$) δ = 144.63, 141.16, 129.48, 128.95, 127.96, 126.23, 120.77, 119.15, 116.74, 115.55, 61.02, 59.37, 56.41, 40.56, 39.12, 37.71.



3ad, 37%

The general procedure was applied to aniline (0.2 mmol), methyl 3-oxocyclobutane-1-carboxylate (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a colorless liquid (15mg, 37% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.40 (d, J = 7.7 Hz, 1H), 7.13 – 7.02 (m, 3H), 6.79 (t, J = 7.5 Hz, 1H), 6.70 (dd, J = 14.6, 7.6 Hz, 2H), 6.46 (d, J = 8.7 Hz, 2H),

4.34 (s, 1H), 4.11 (s, 1H), 3.73 (s, 3H), 3.61 (s, 3H), 3.18 – 3.06 (m, 2H), 2.84 (dt, J = 9.1, 6.9 Hz, 1H), 2.69 – 2.56 (m, 2H), 2.35 (dd, J = 12.1, 9.6 Hz, 1H), 2.26 – 2.20 (m, 1H), 2.14 (d, J = 8.6 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 175.94, 175.30, 145.41, 142.39, 128.88, 128.01, 127.71, 126.78, 120.02, 118.35, 116.26, 115.85, 56.53, 54.12, 52.91, 52.11, 51.90, 40.03, 39.80, 35.69, 32.58, 30.56.



3ae, 40%

The general procedure was applied to aniline (0.2 mmol), 3-oxocyclobutyl propionate (0.4 mmol), $Cu(CF_3COO)_2$ (11.58 mg, 0.04 mmol), N-Hexane (2 mL) at 80 °C for 12 h. The crude product was purified by column chromatography on neutral alumina (EtOAc/PE = 1/10) to afford the title compound as a white solid (17mg, 40% yield).^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.37 (d, J = 7.8 Hz, 1H), 7.12 – 7.01 (m, 3H), 6.76 (t, J = 7.5 Hz, 1H), 6.73 – 6.65 (m, 2H), 6.52 – 6.45 (m, 2H), 4.49 (s, 1H), 4.32 (s, 1H), 4.21 – 4.09 (m, 4H), 3.07 (d, J = 7.1 Hz, 1H), 2.87 – 2.79 (m, 1H), 2.75 (q, J = 7.6 Hz, 1H), 2.67 (dd, J = 11.8, 7.5 Hz, 1H), 2.47 (ddd, J = 12.3, 8.8, 3.1 Hz, 1H), 2.38 (dd, J = 11.8, 9.3 Hz, 1H), 2.28 – 2.18 (m, 2H), 2.05 (dd, J = 12.0, 7.5 Hz, 1H), 1.26 (dd, J = 15.5, 6.9 Hz, 7H).^{13}C NMR (101 MHz, $CDCl_3$) δ = 176.35, 175.56, 145.46, 142.17, 128.93, 127.83, 126.96, 126.93, 119.69,

118.24, 116.10, 115.70, 60.84, 60.79, 55.55, 54.02, 51.48, 40.64, 40.46, 36.12, 32.81, 29.65, 14.23, 14.19.

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

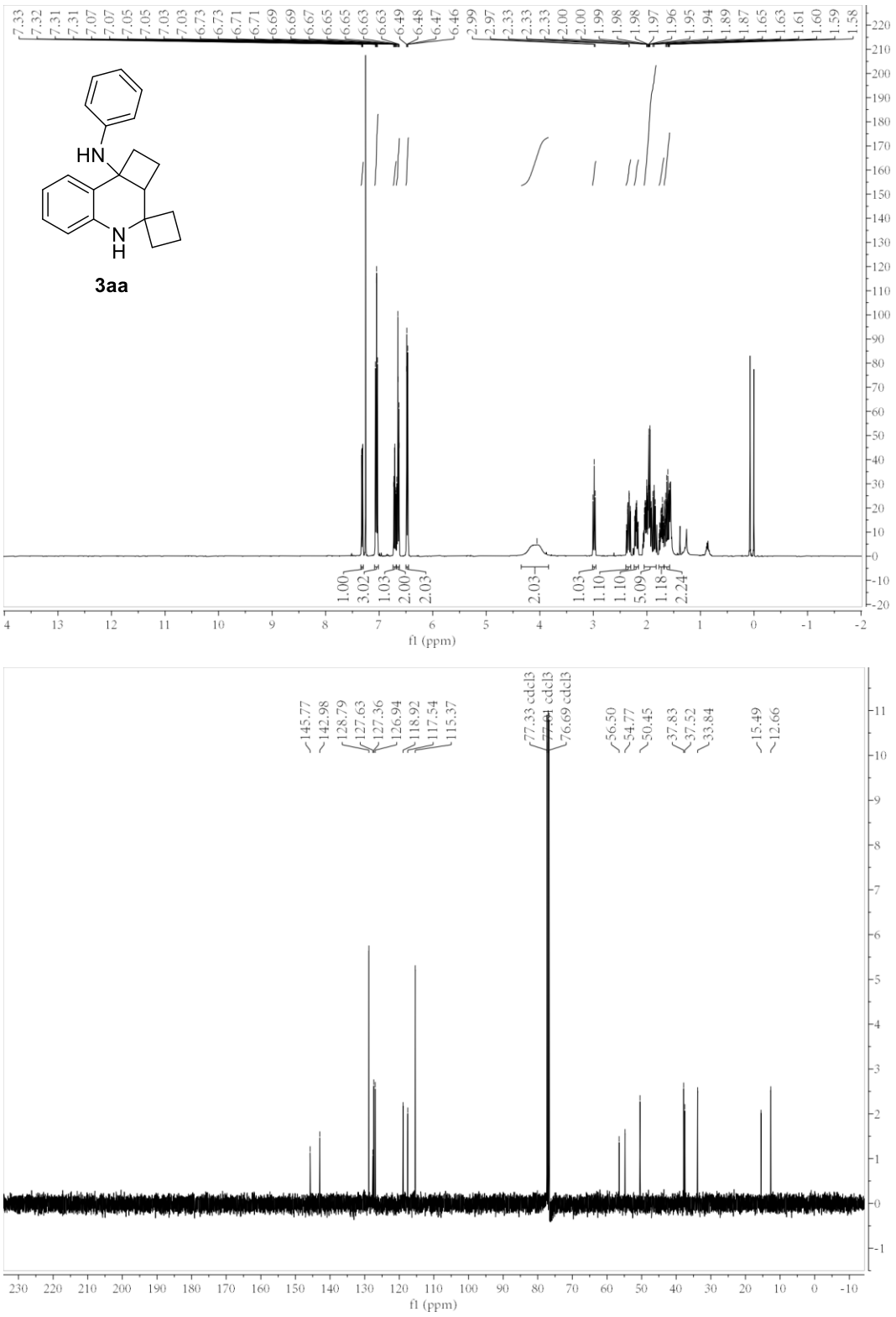


Figure S1. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3aa**

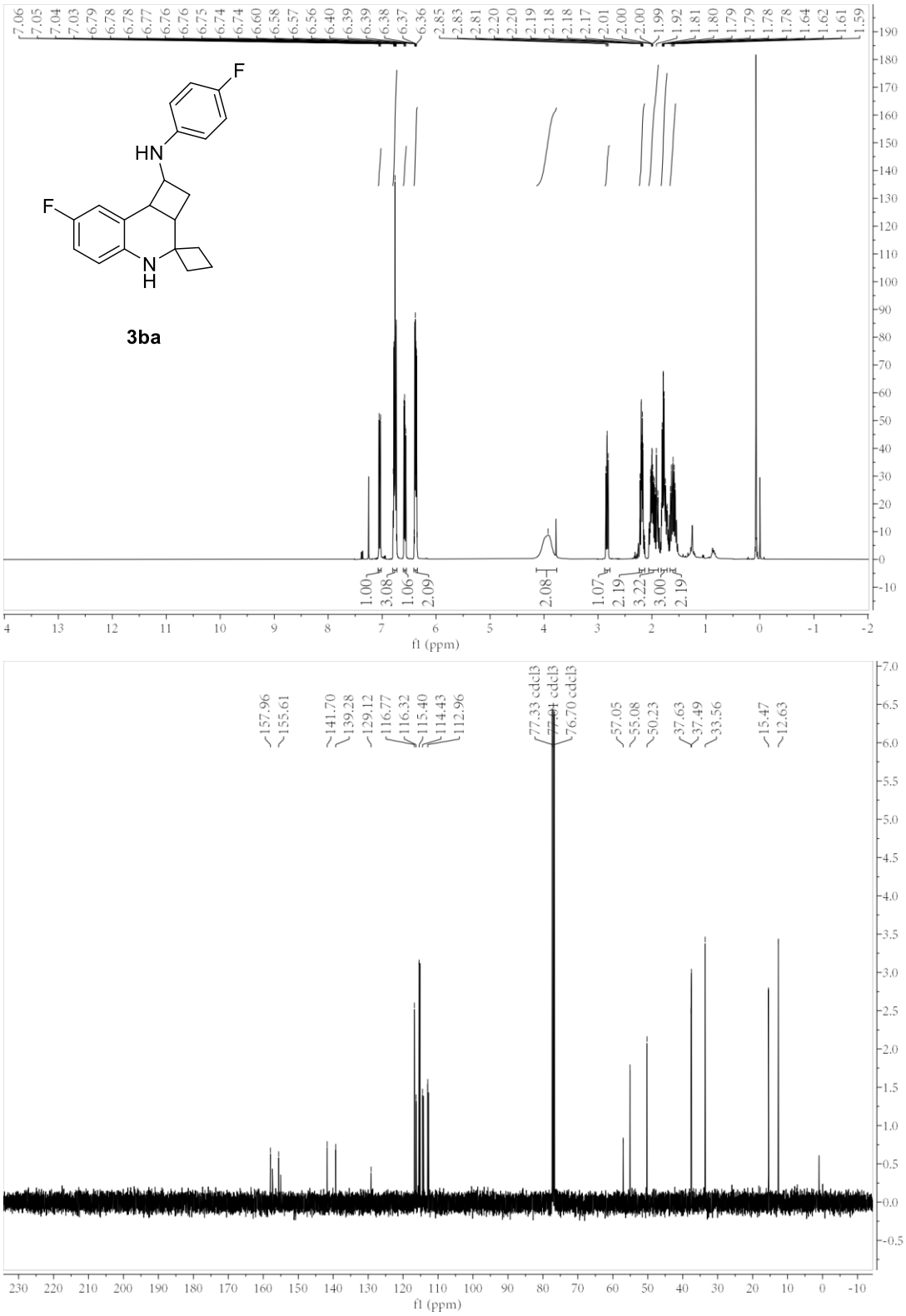


Figure S2. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ba**

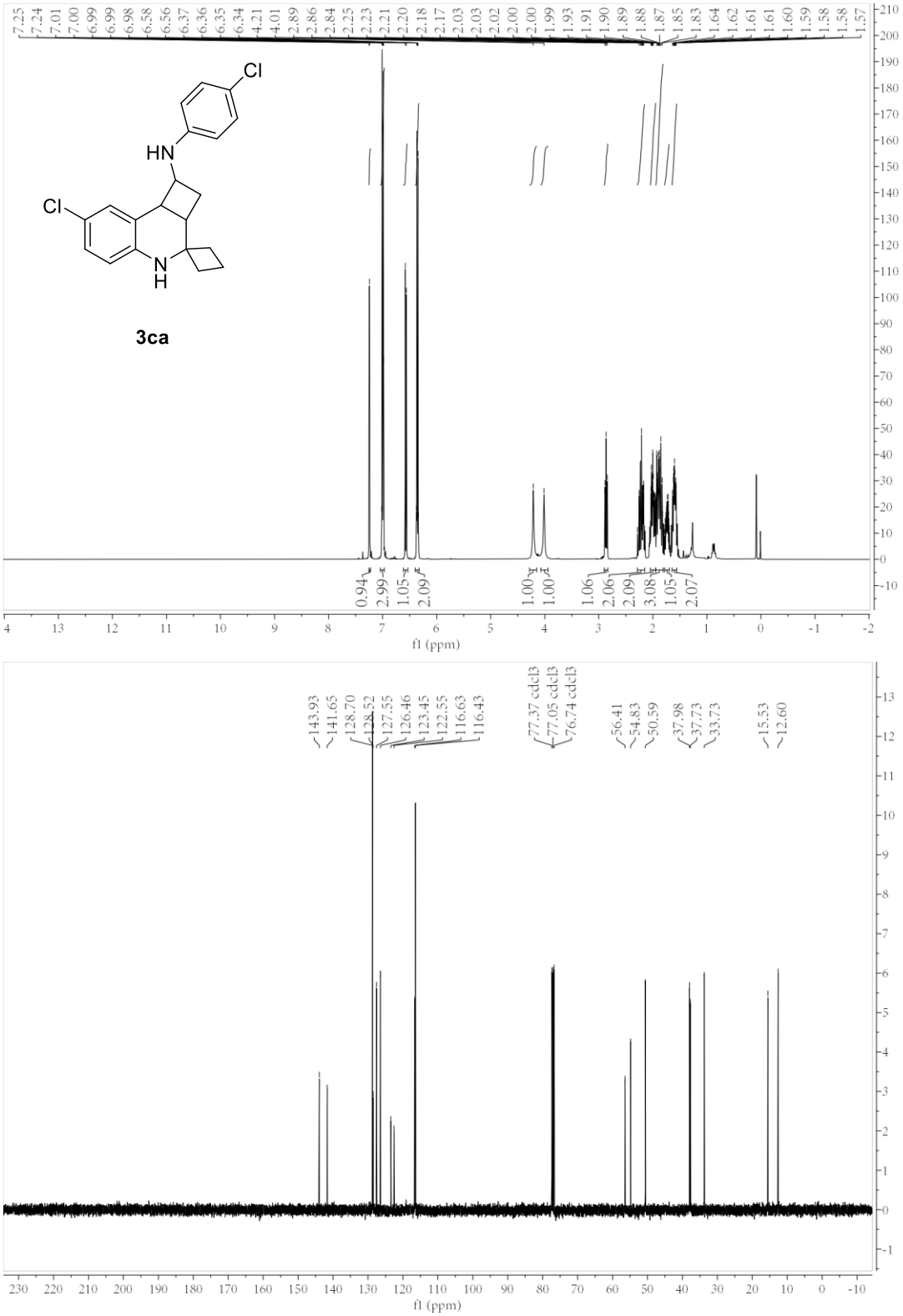


Figure S3. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ca**

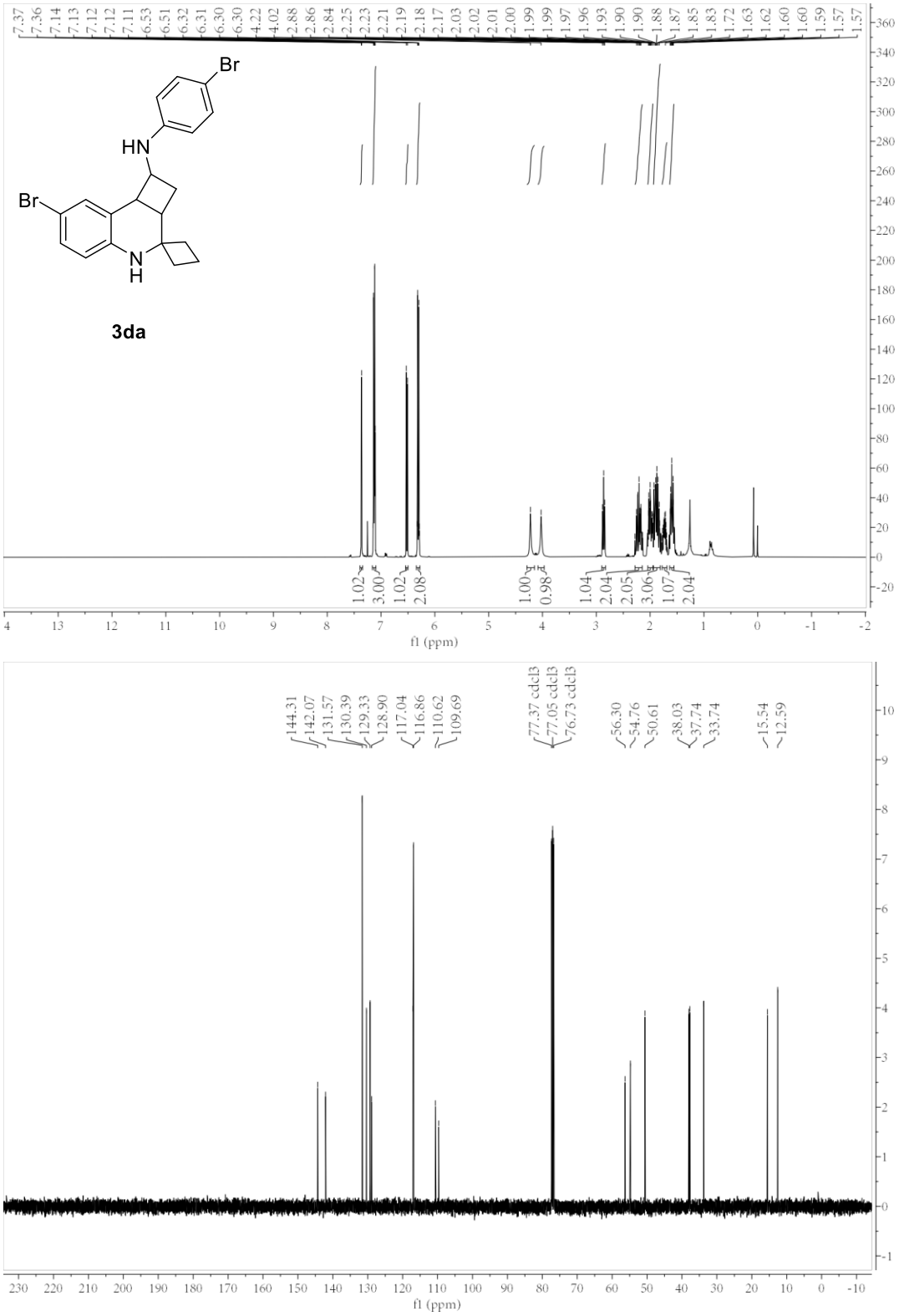


Figure S4. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3da**

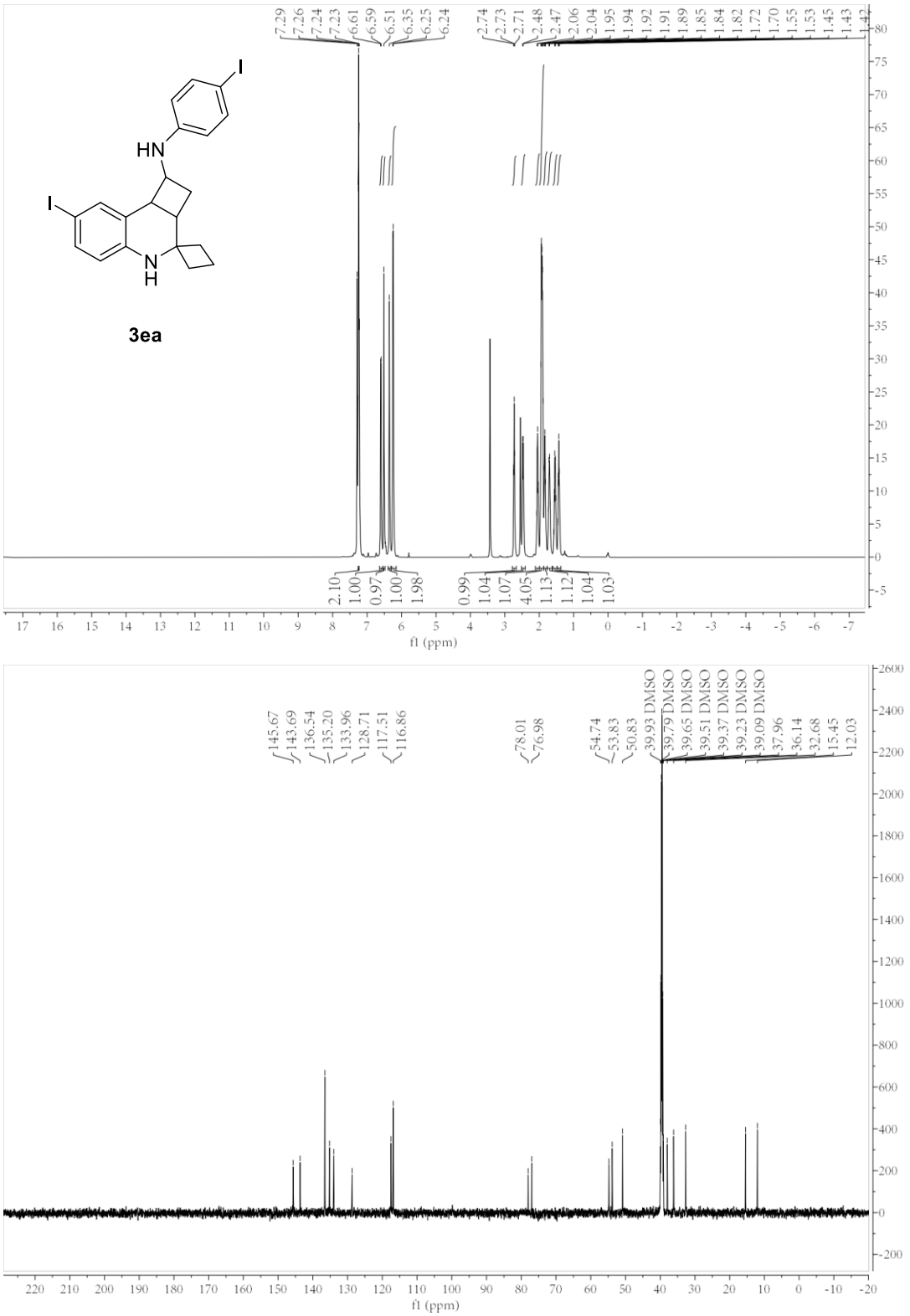


Figure S5. ^{1}H(600 MHz, DMSO) and ^{13}C (151 MHz, DMSO) NMR spectra for compound **3ea**

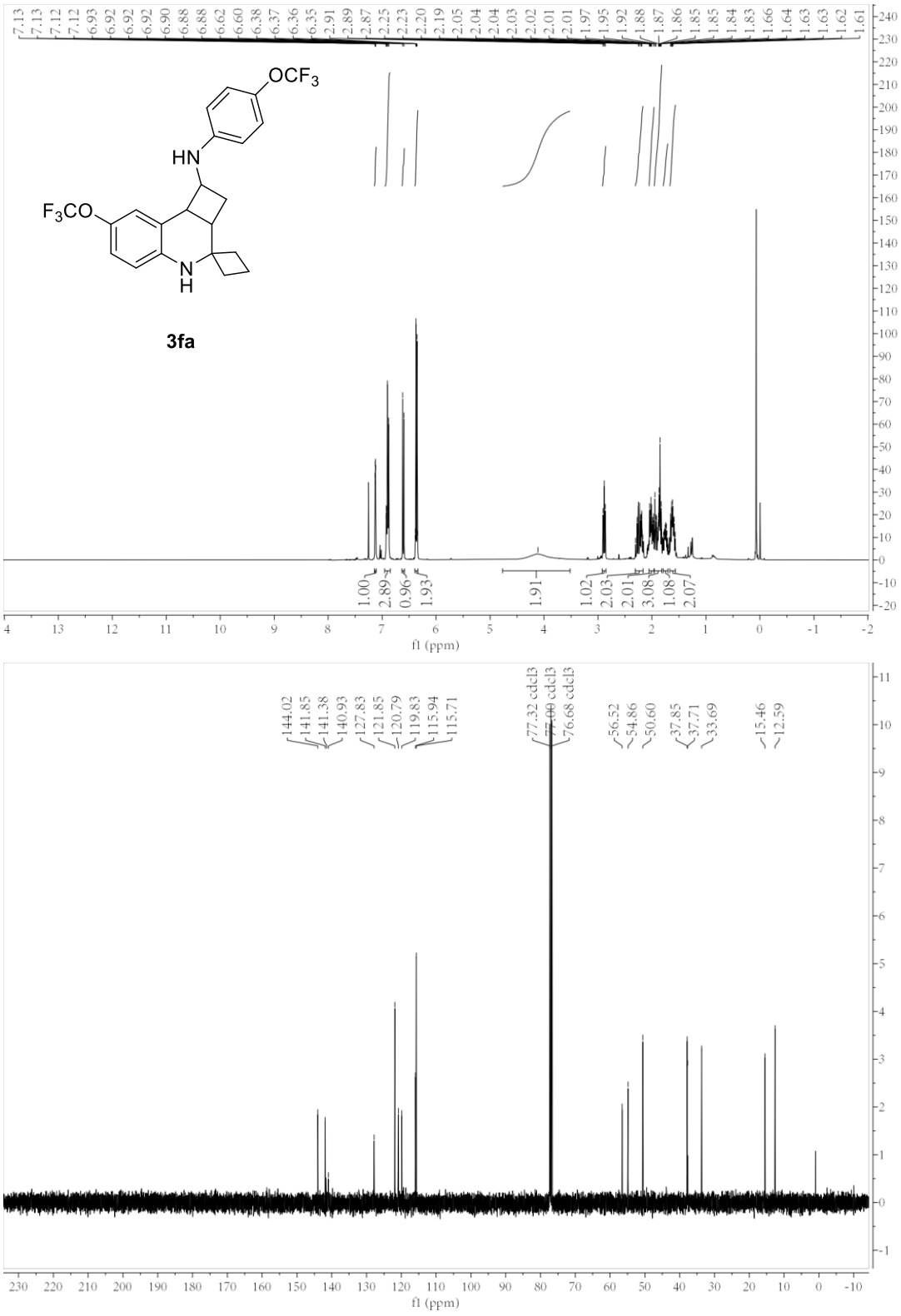


Figure S6. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3fa**

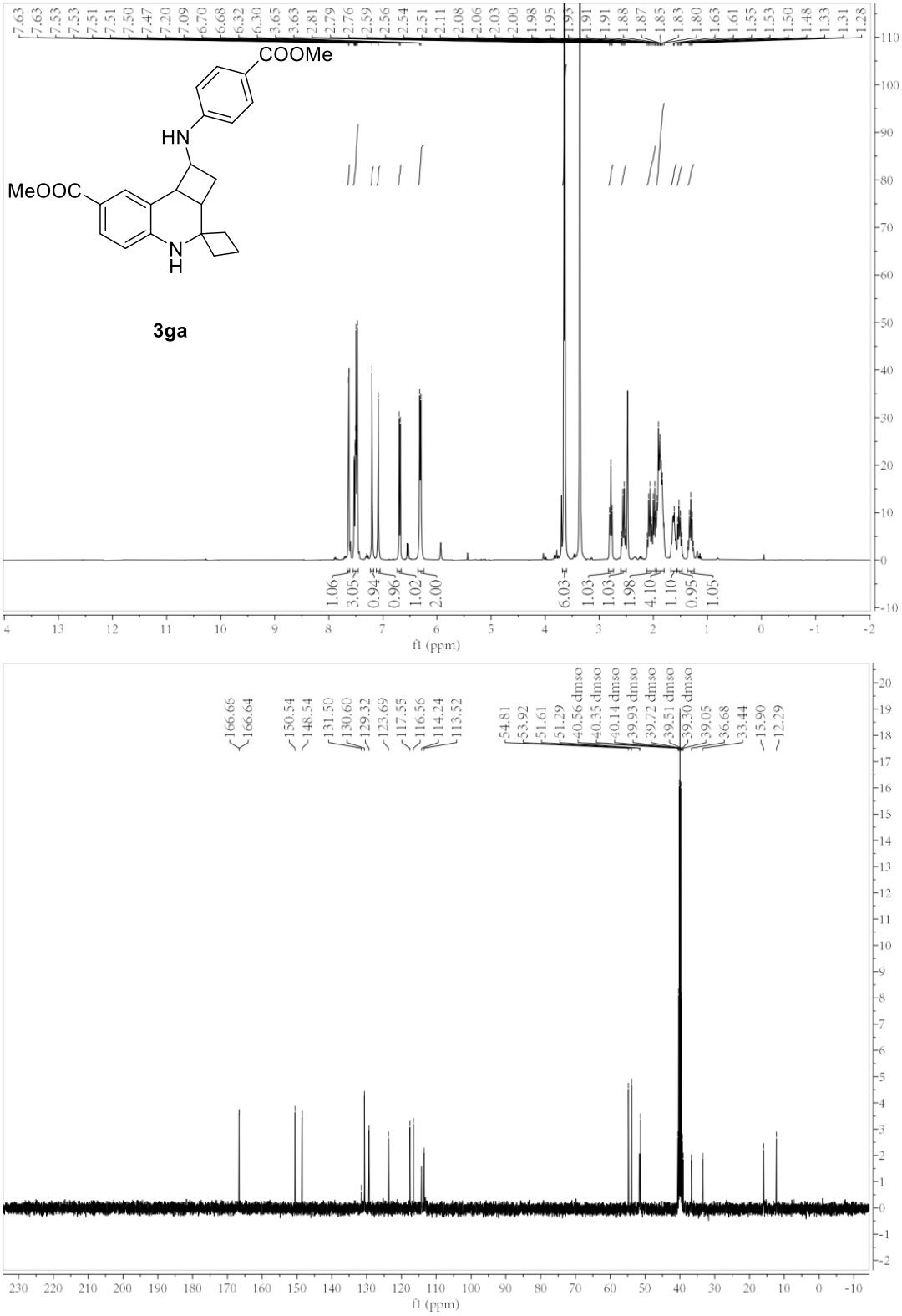


Figure S7. ^{1}H(400 MHz, DMSO) and ^{13}C (101 MHz, DMSO) NMR spectra for compound **3ga**

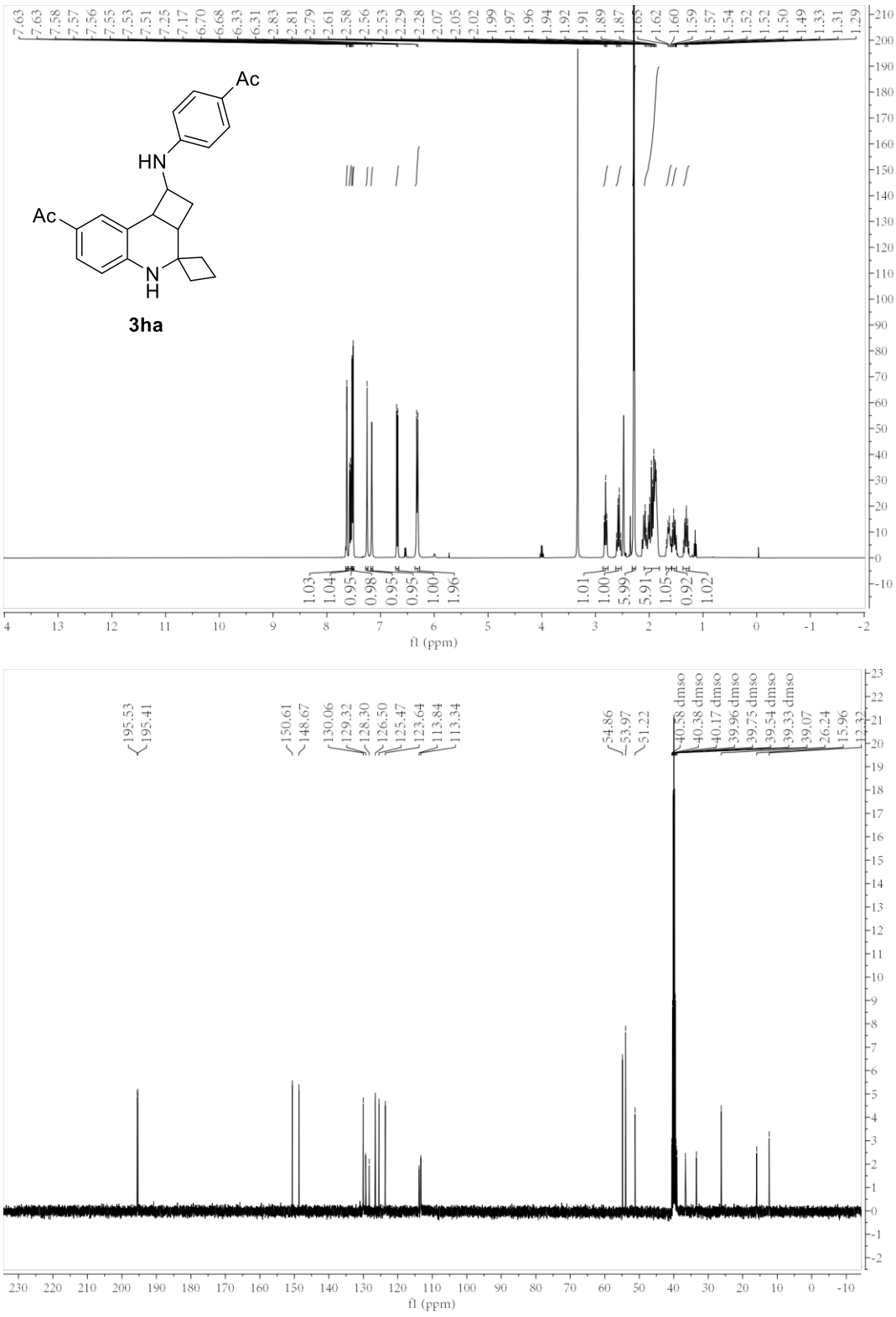


Figure S8. ^{1}H(400 MHz, DMSO) and ^{13}C (101 MHz, DMSO) NMR spectra for compound **3ha**

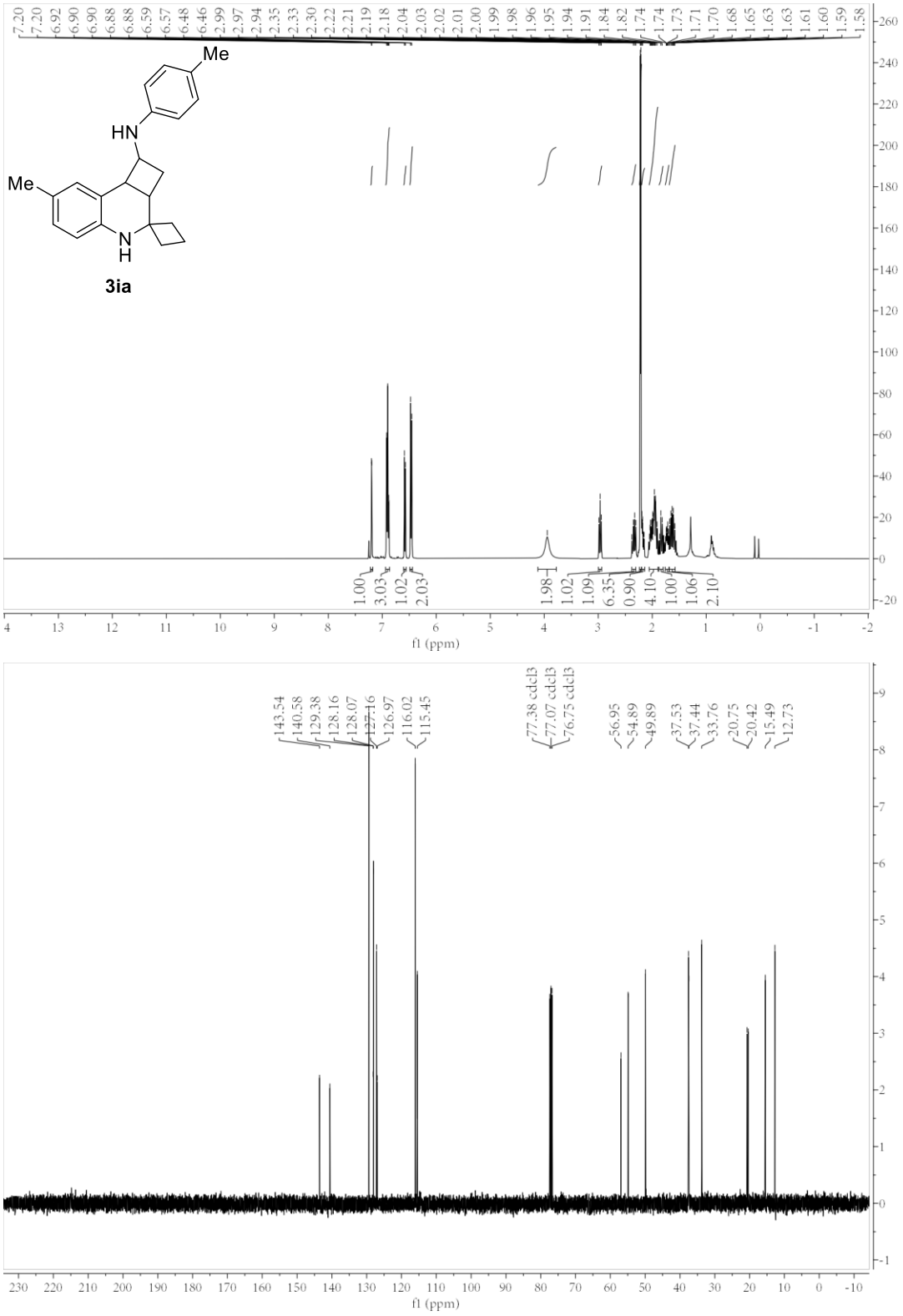


Figure S9. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ia**

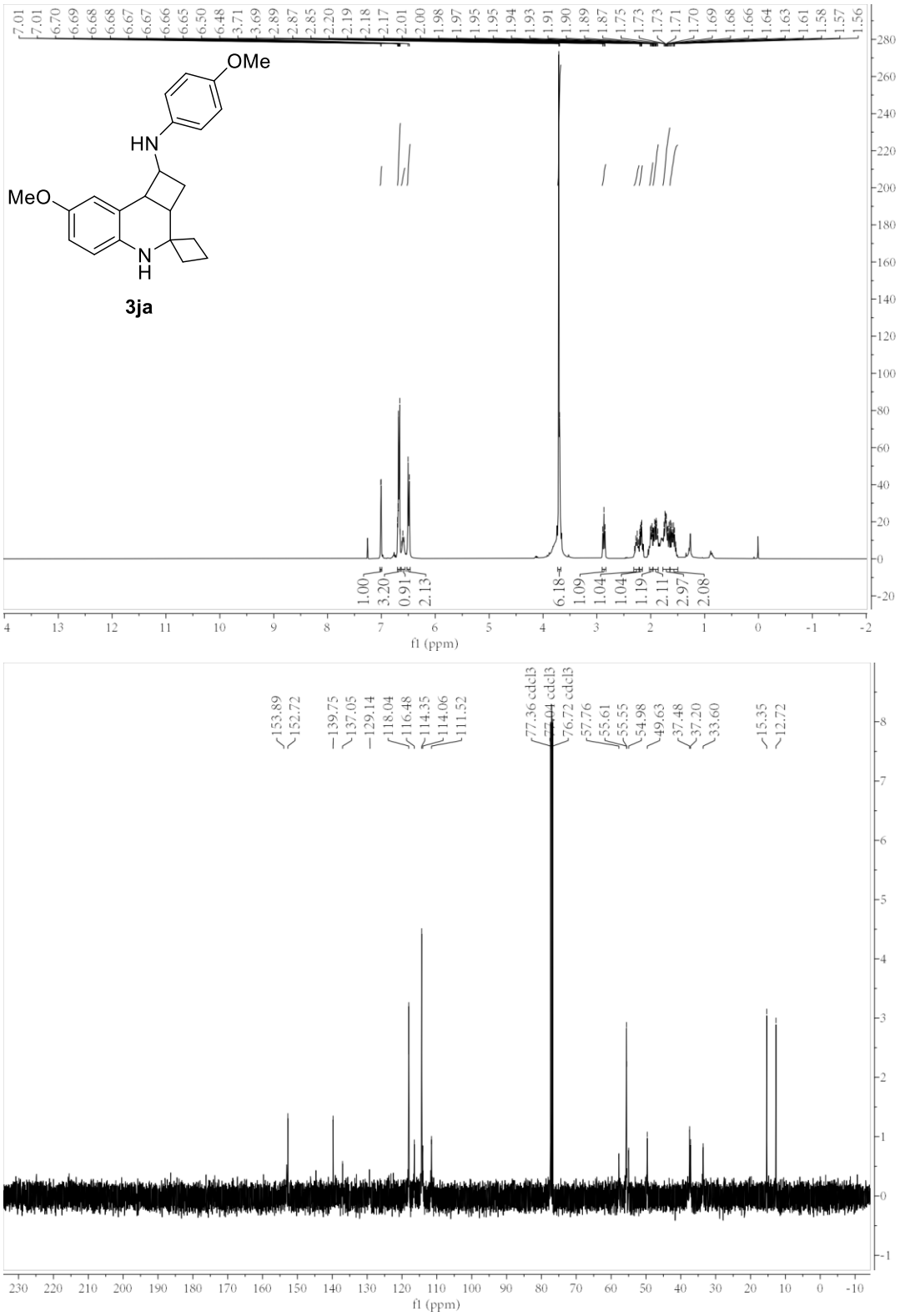


Figure S10. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ja**

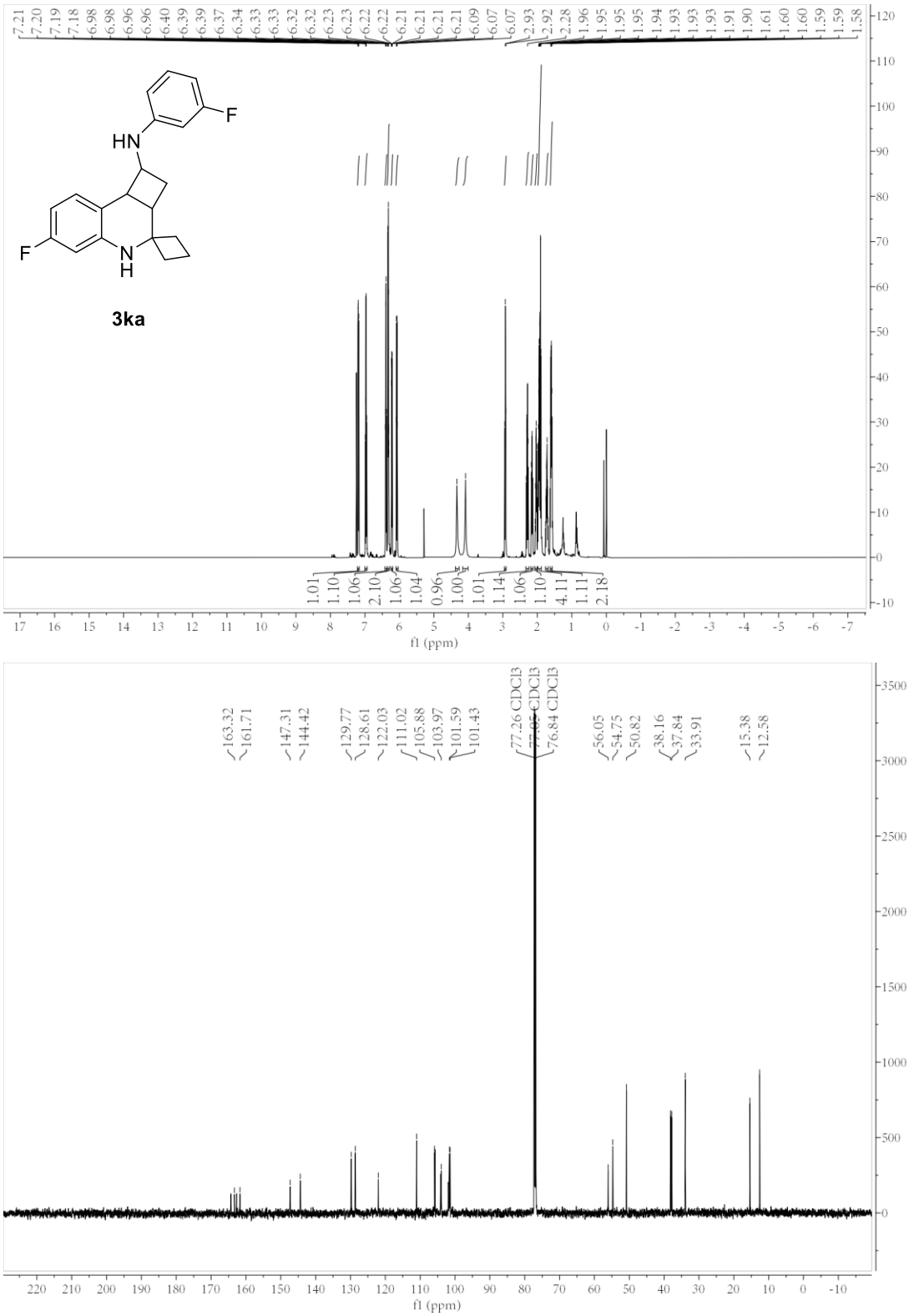


Figure S11. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ka**

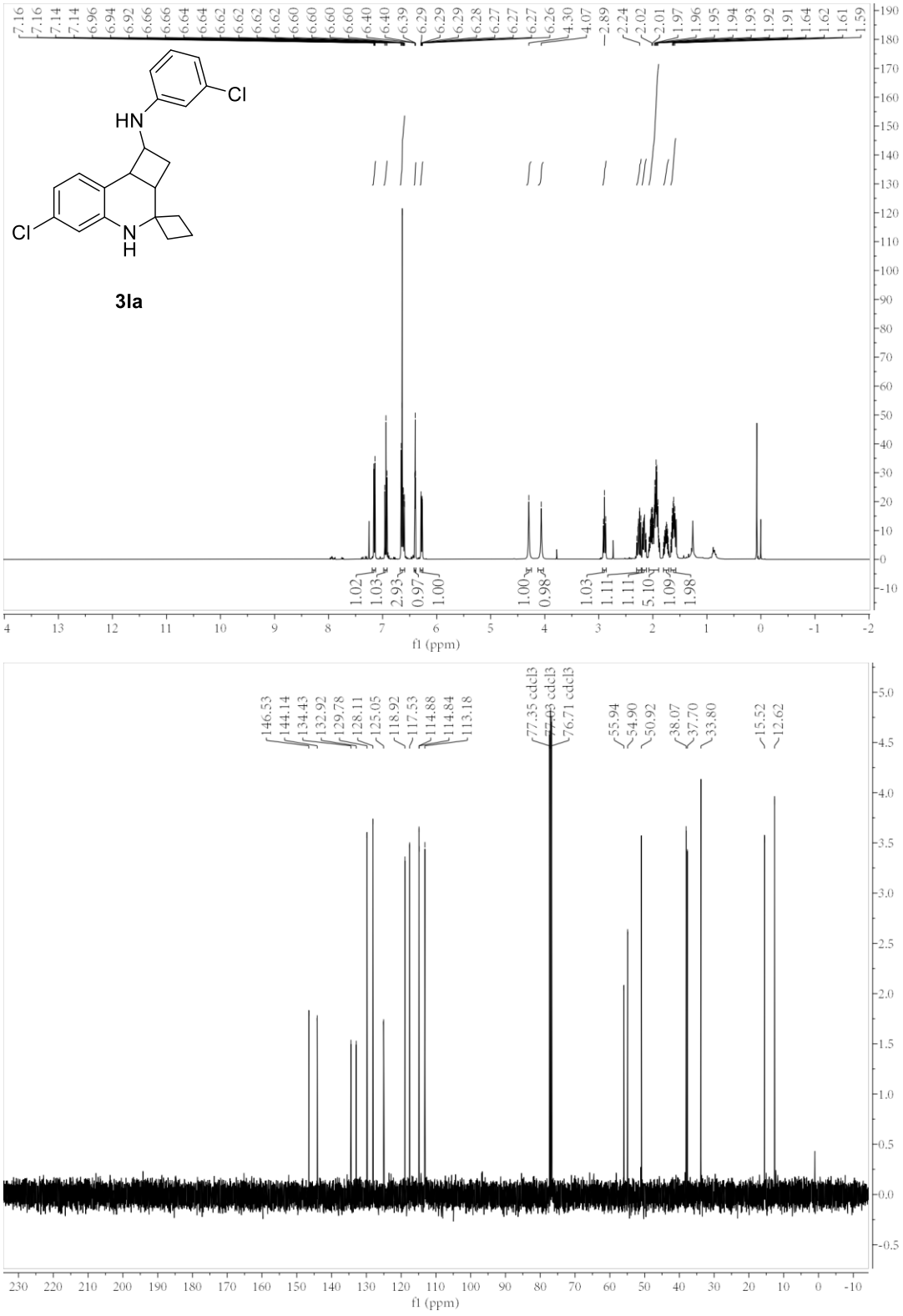


Figure S12. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3la**

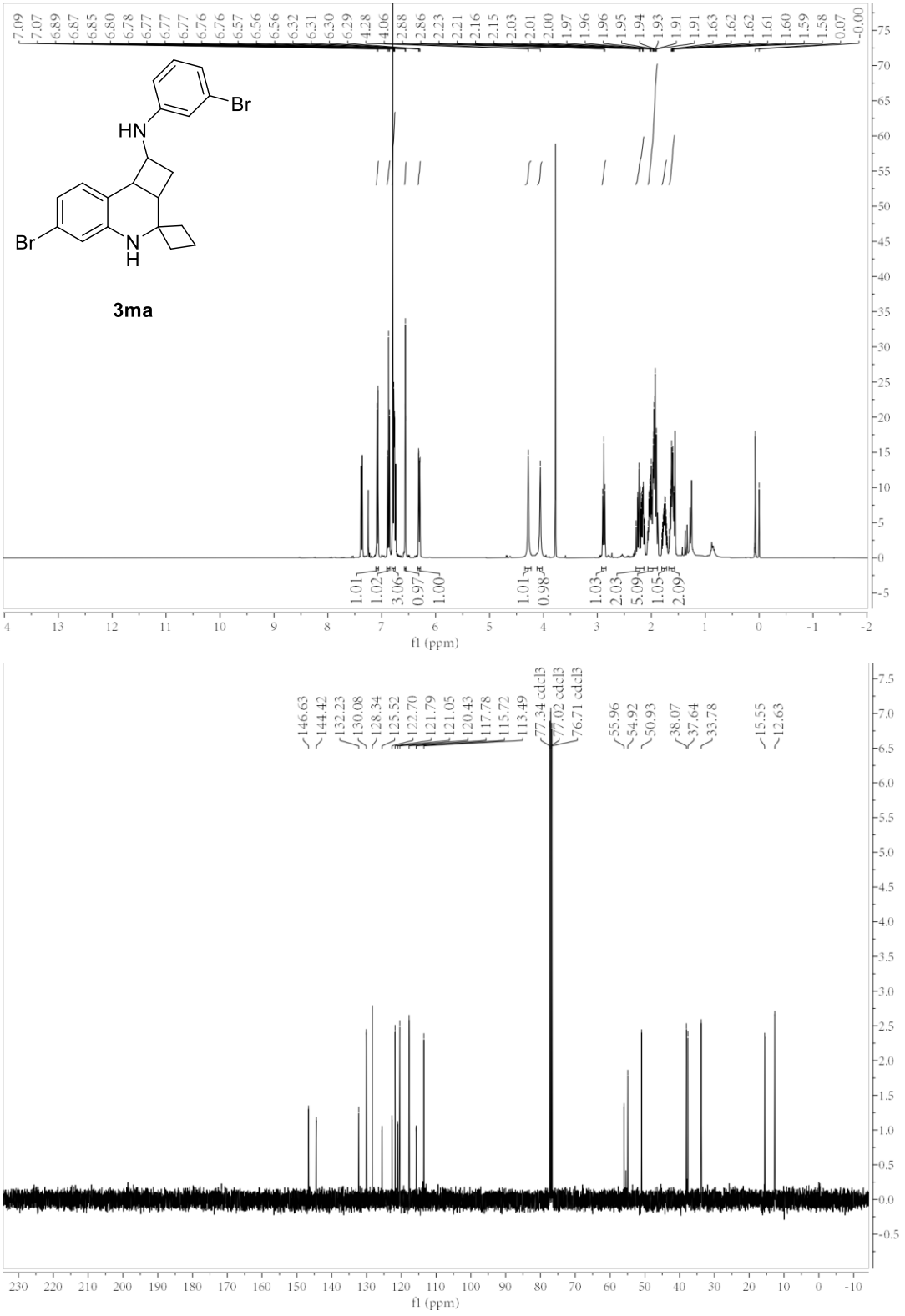


Figure S13. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ma**

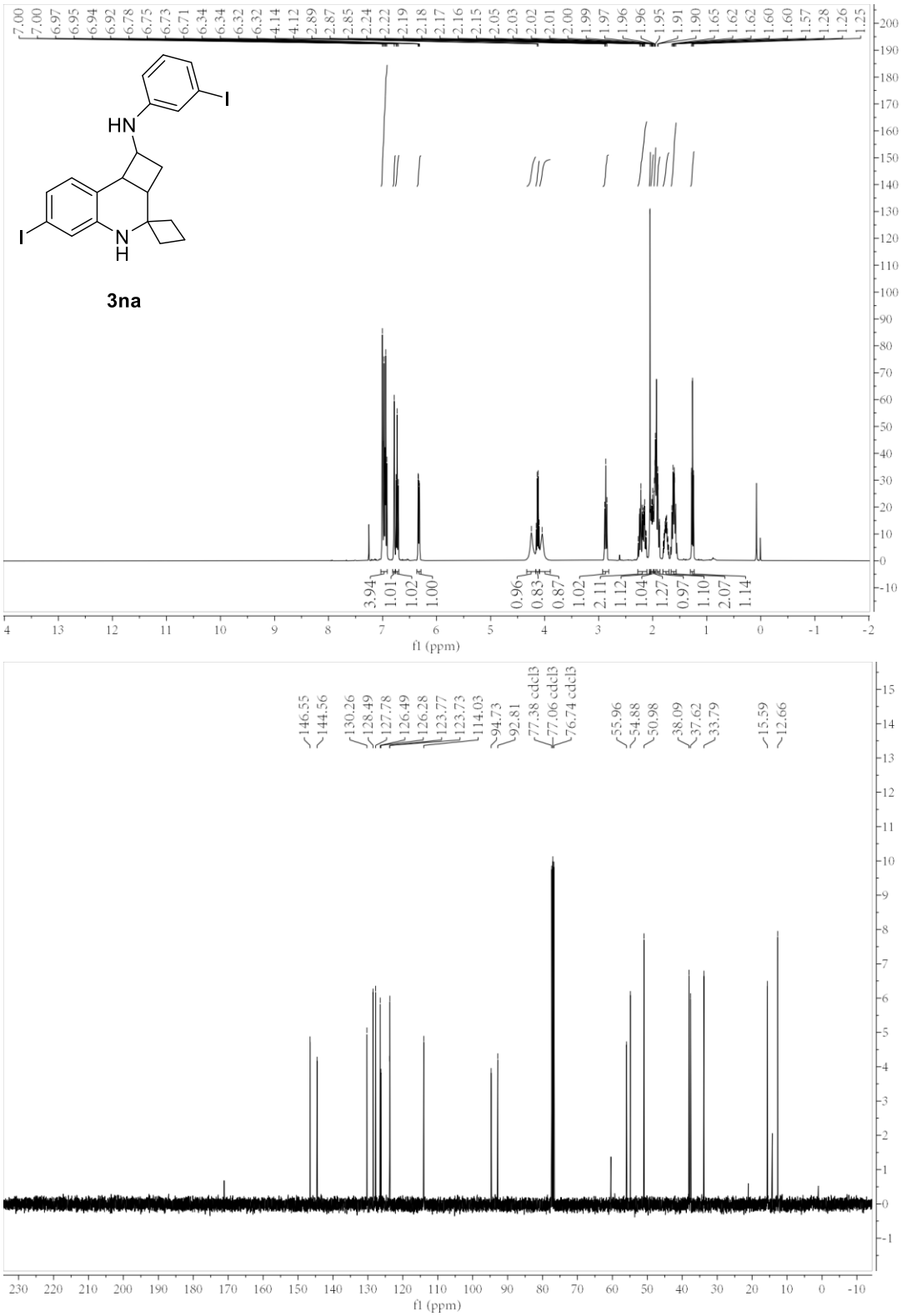


Figure S14. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3na**

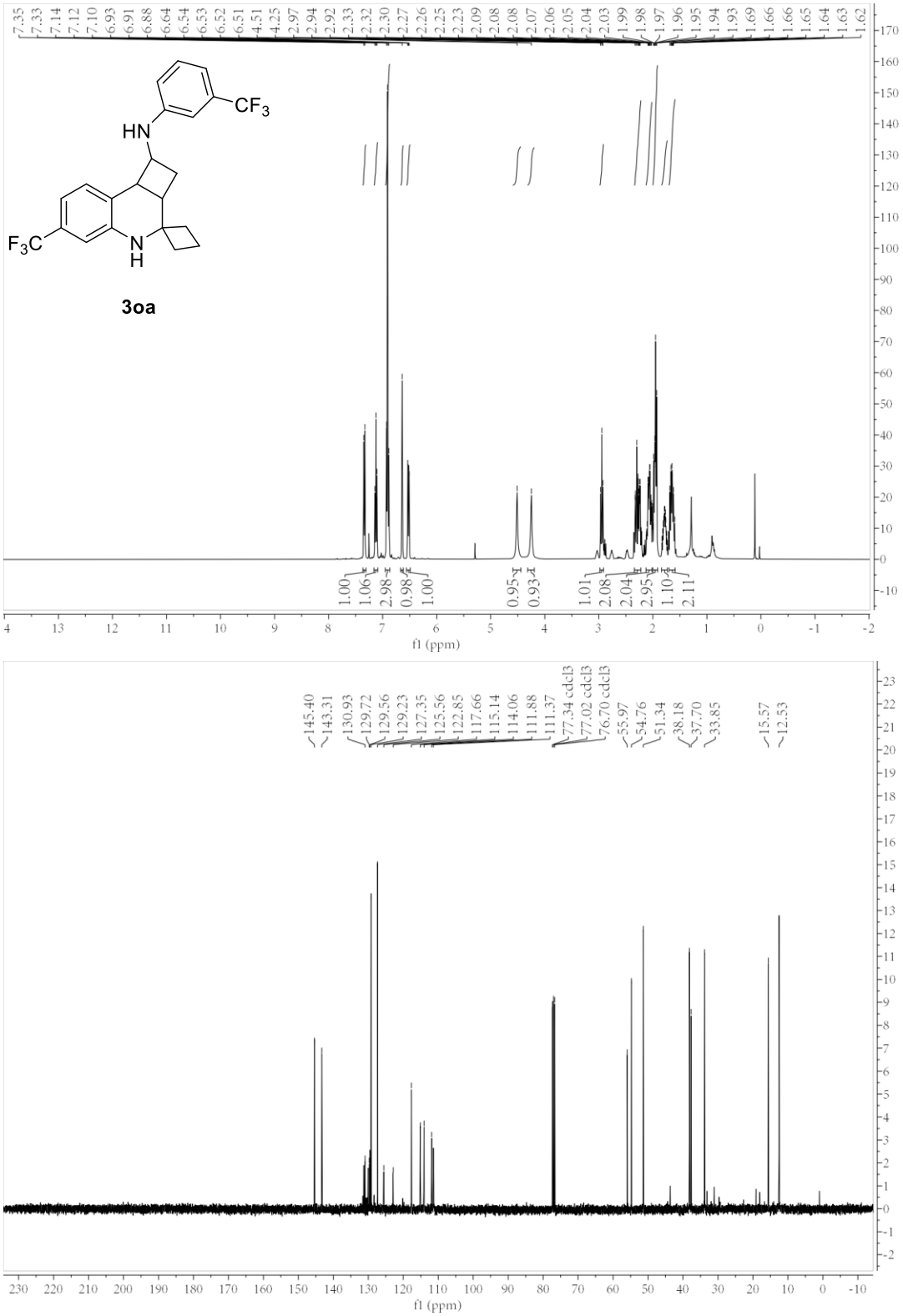


Figure S15. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3oa**

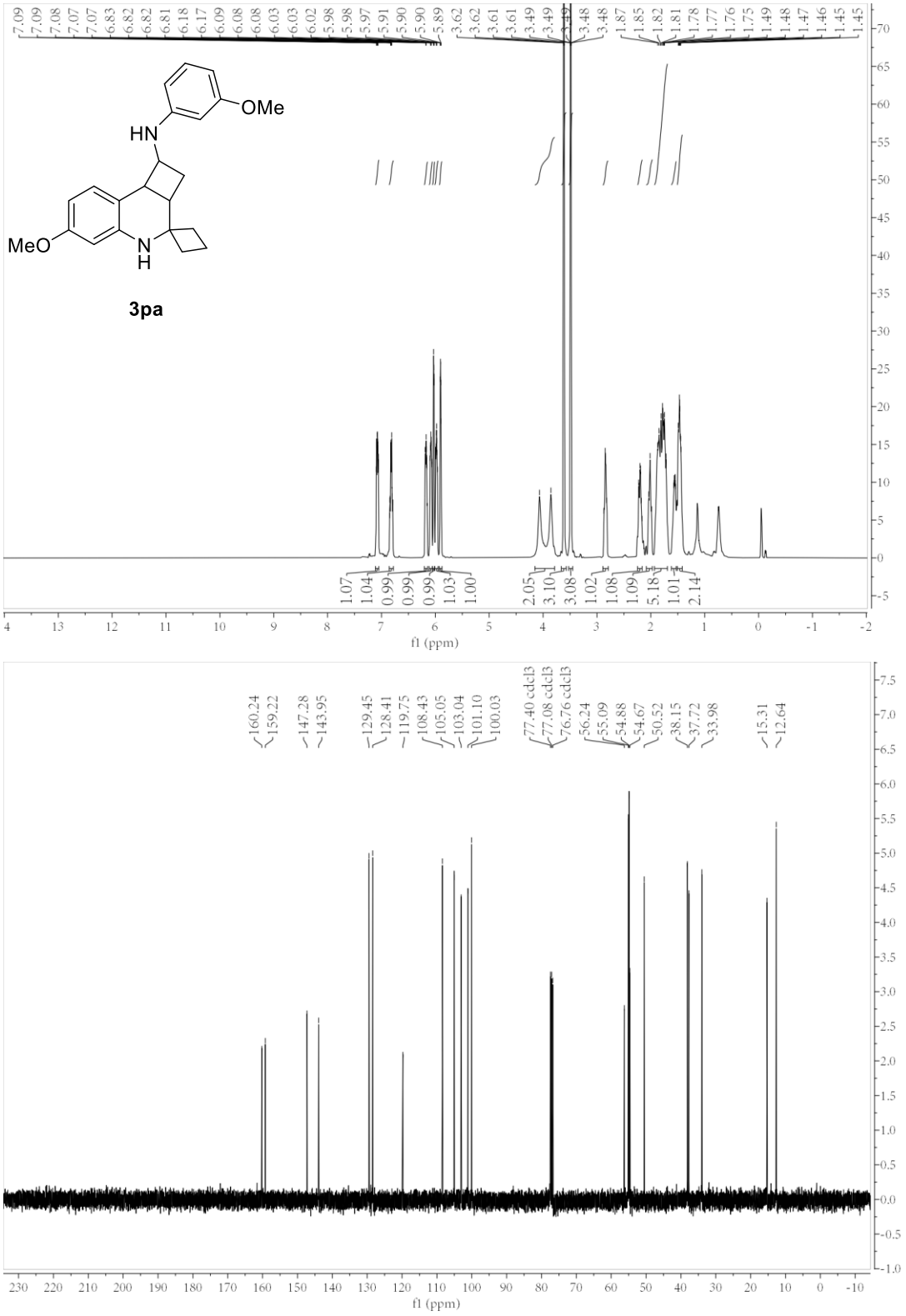


Figure S16. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3pa**

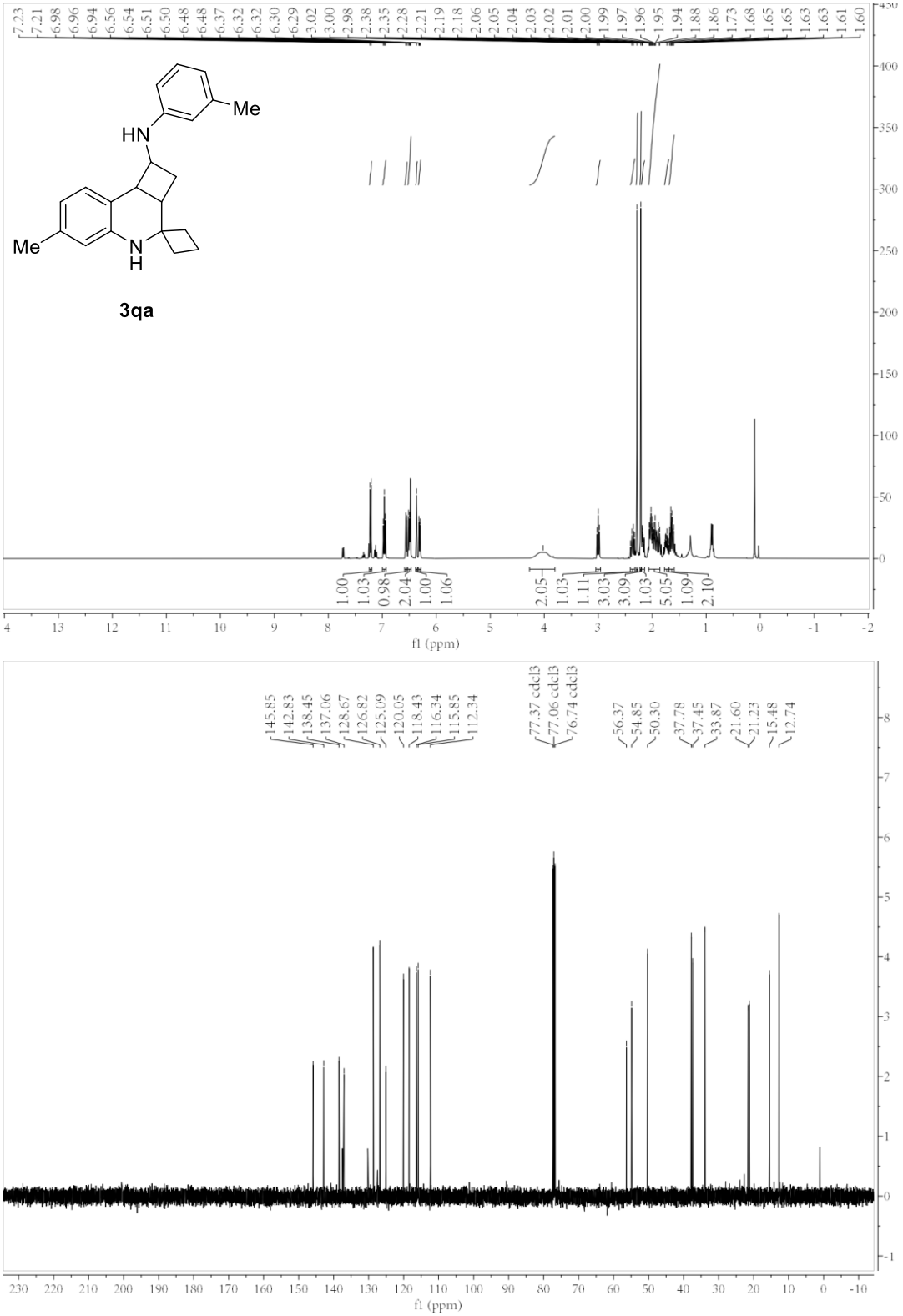


Figure S17. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3qa**

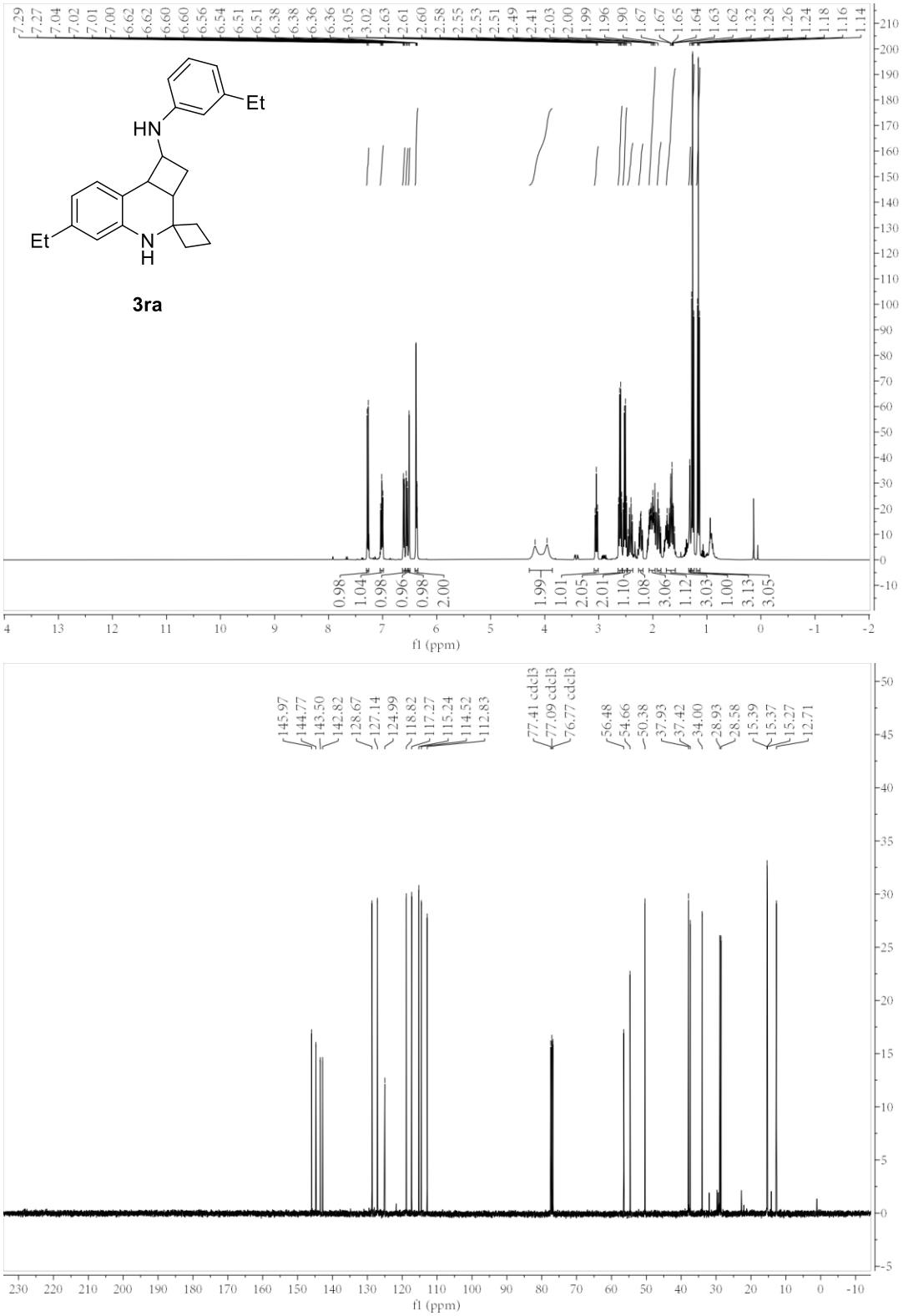


Figure S18. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ra**

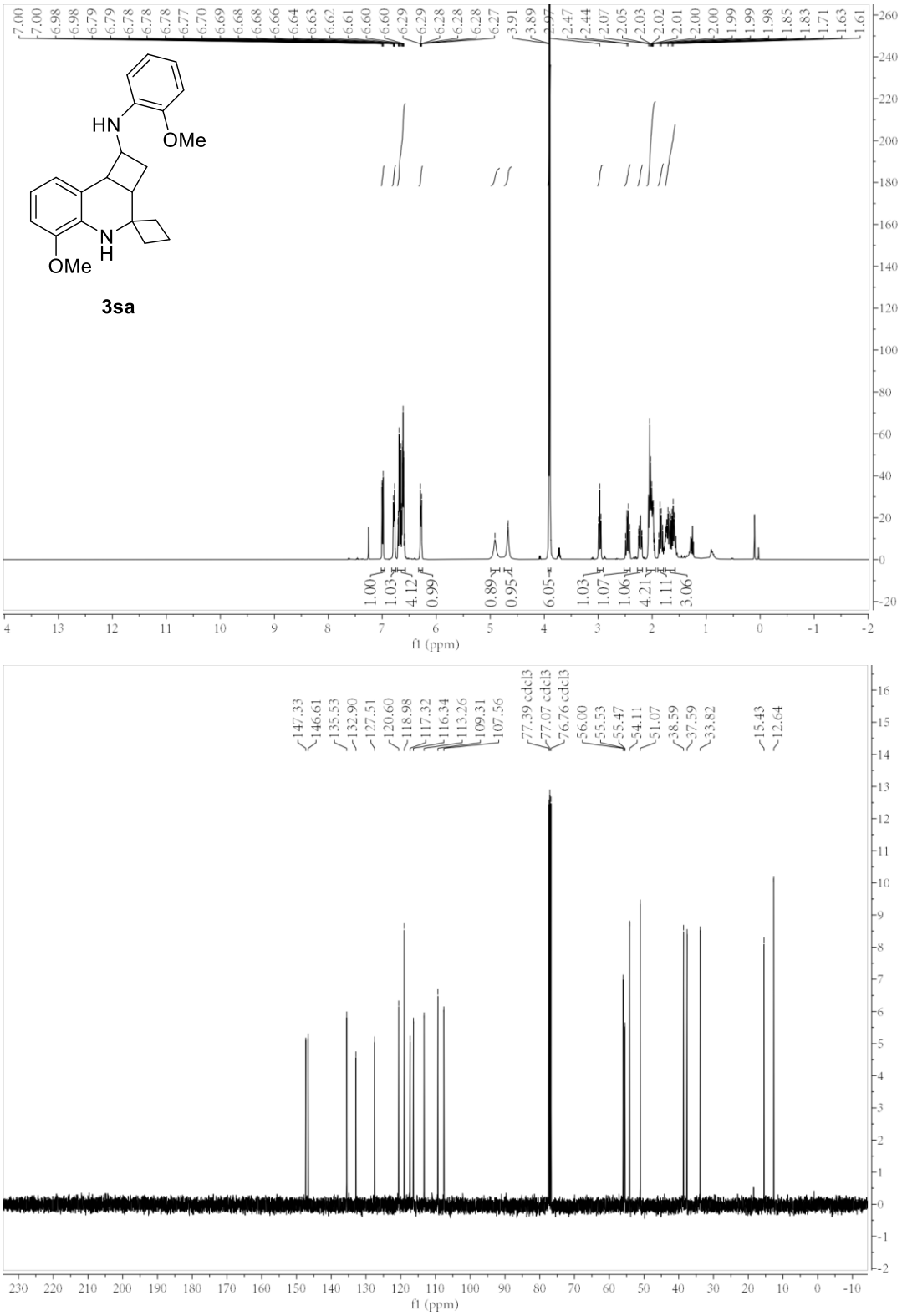


Figure S19. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3sa**

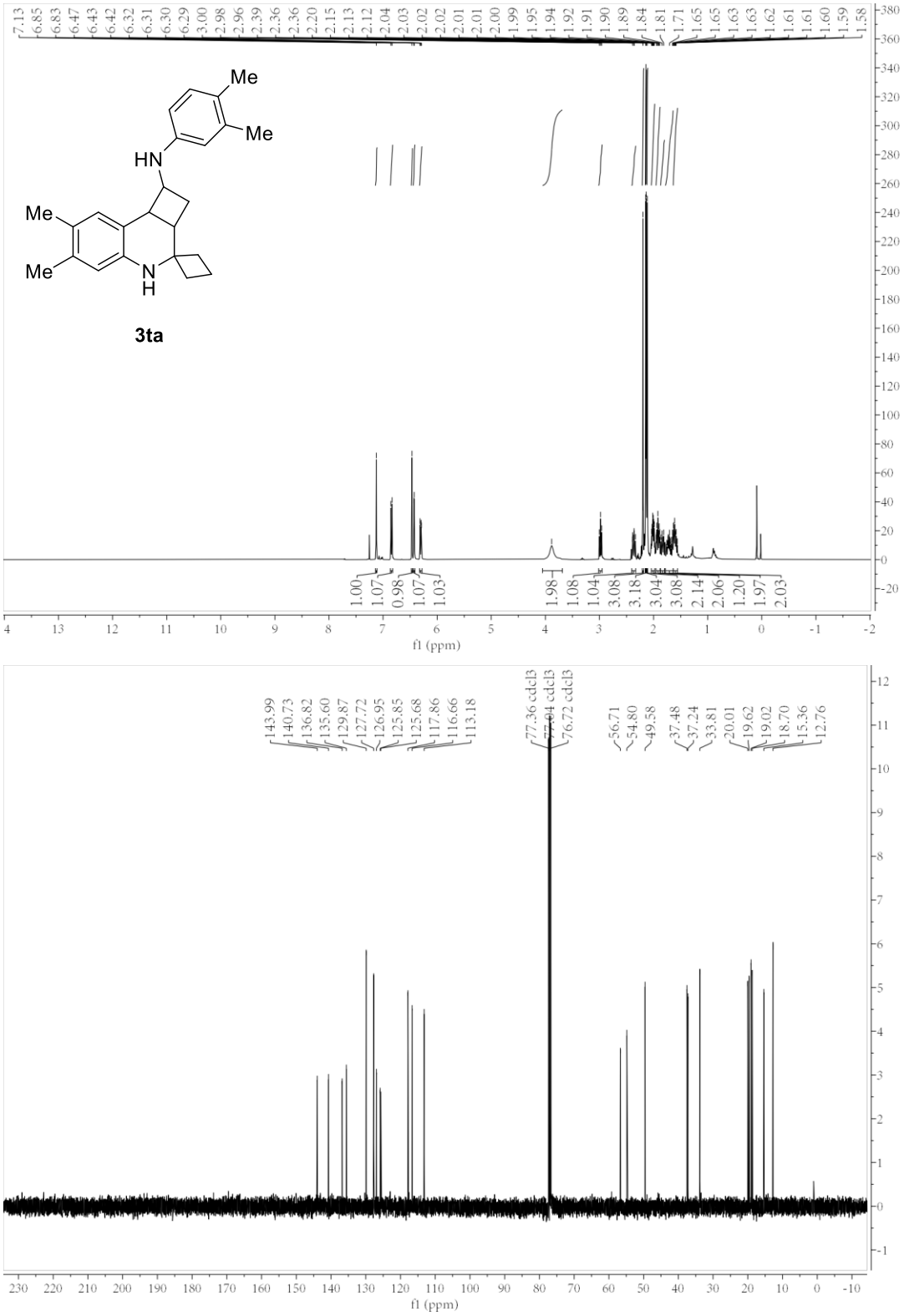


Figure S20. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ta**

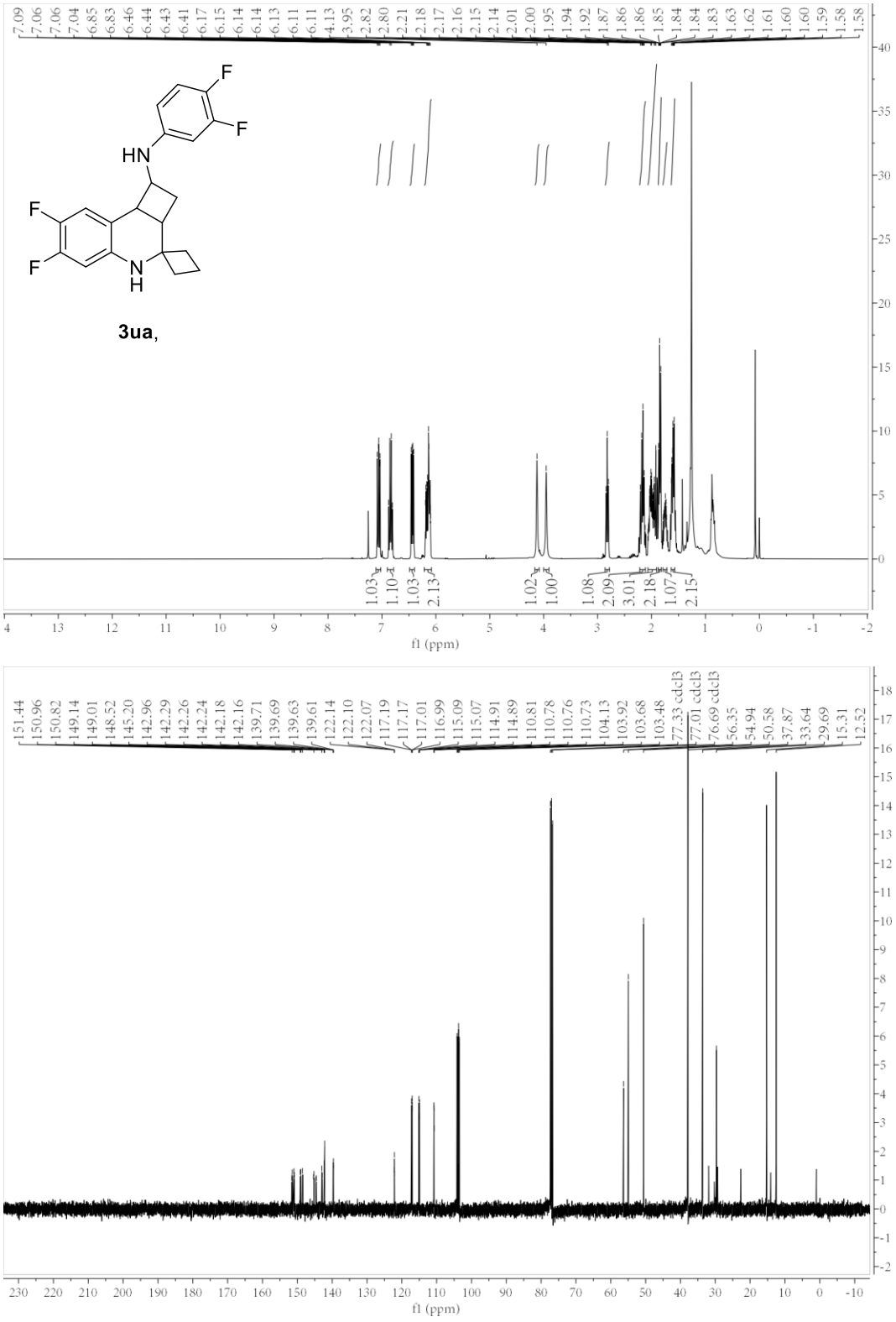


Figure S21. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ua**

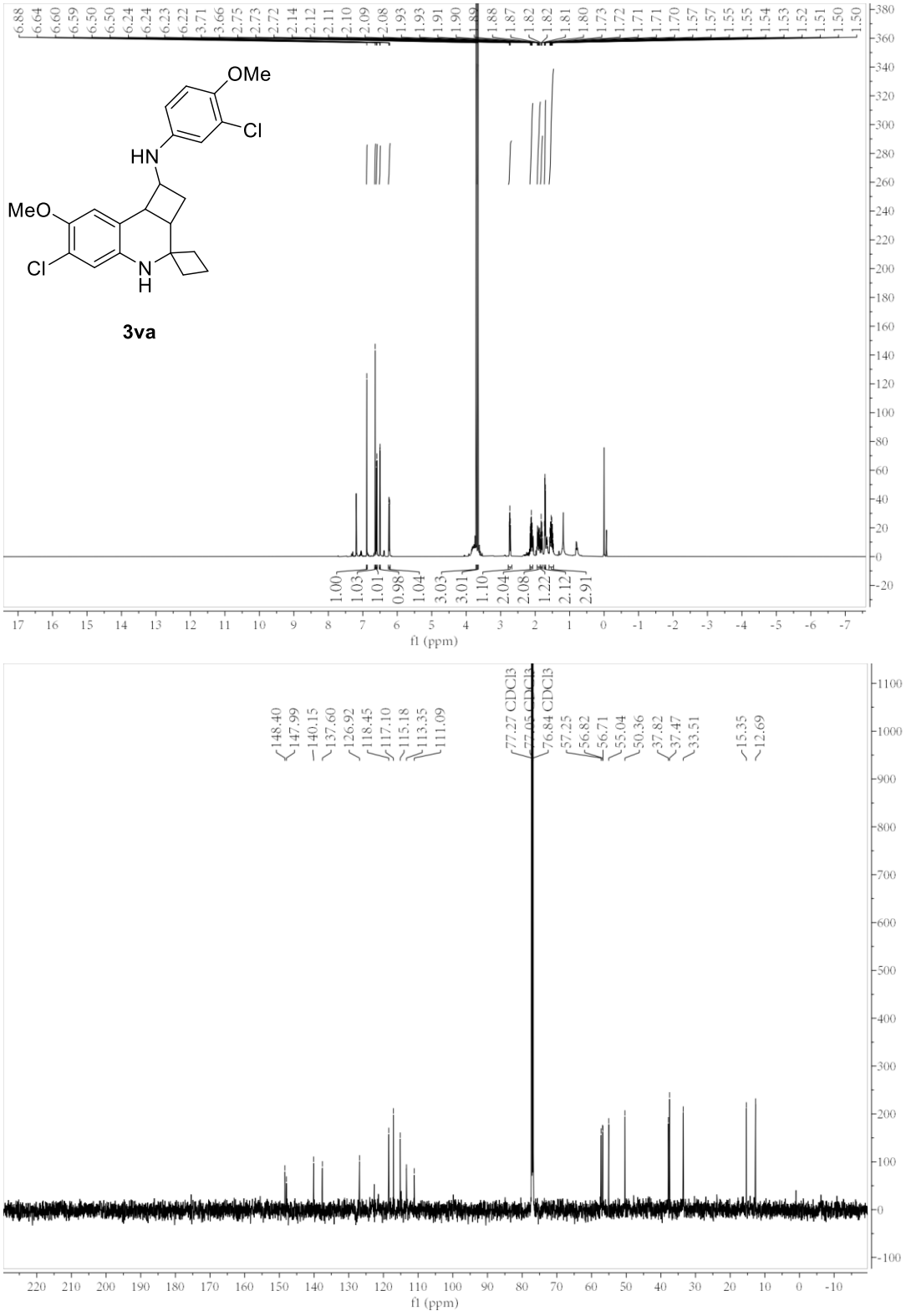


Figure S22. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3va**

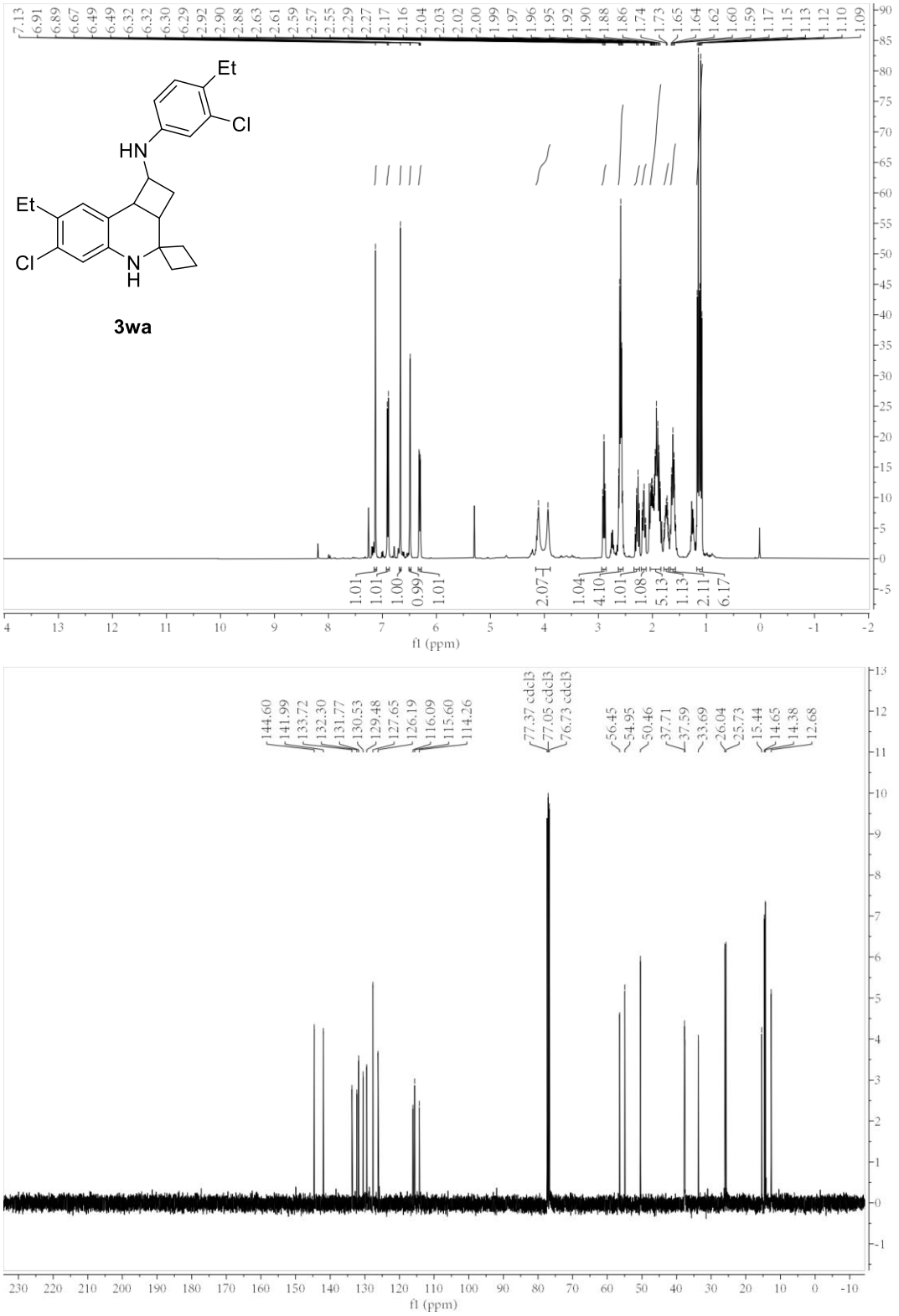


Figure S23. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3wa**

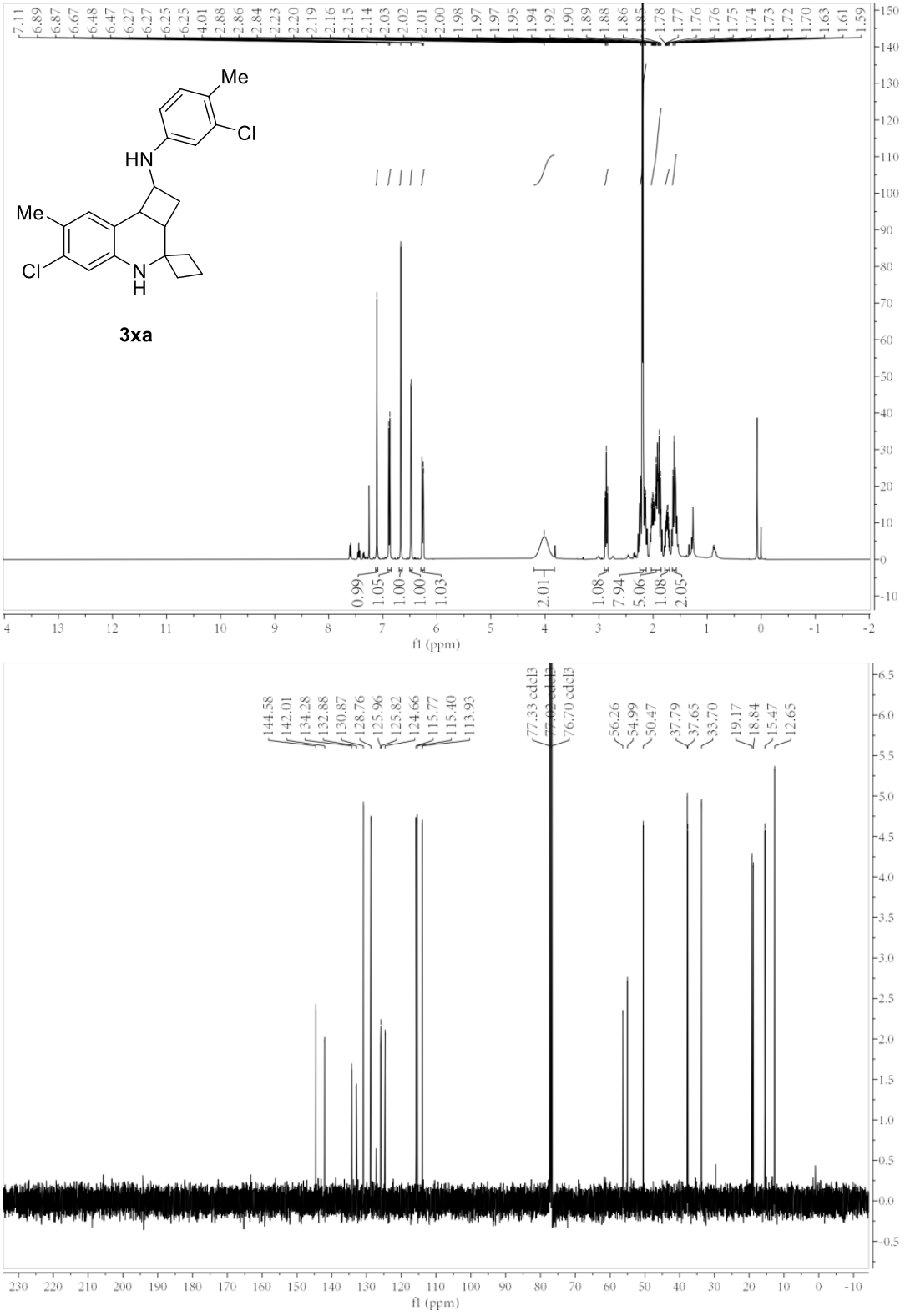


Figure S24. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3xa**

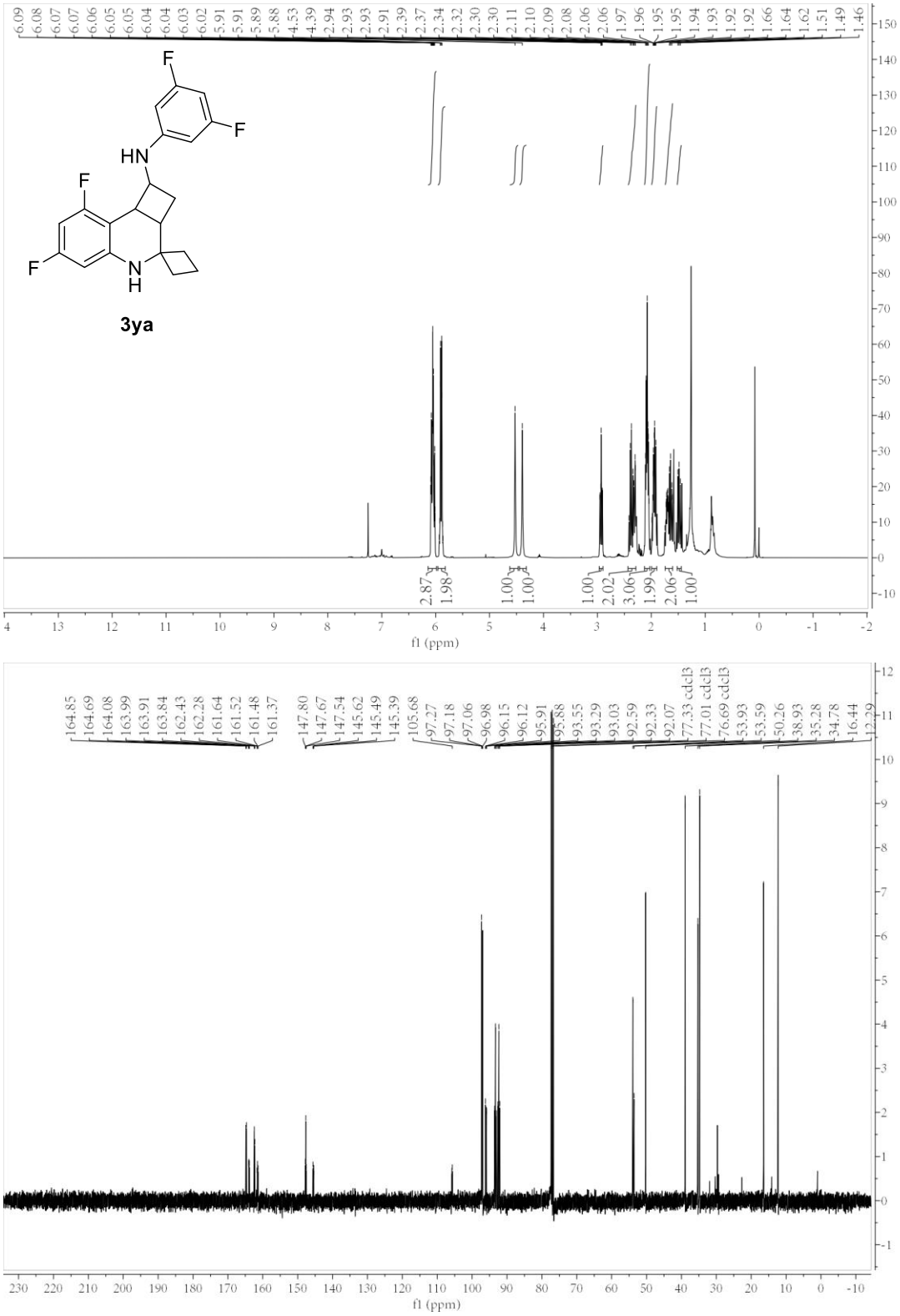


Figure S25. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ya**

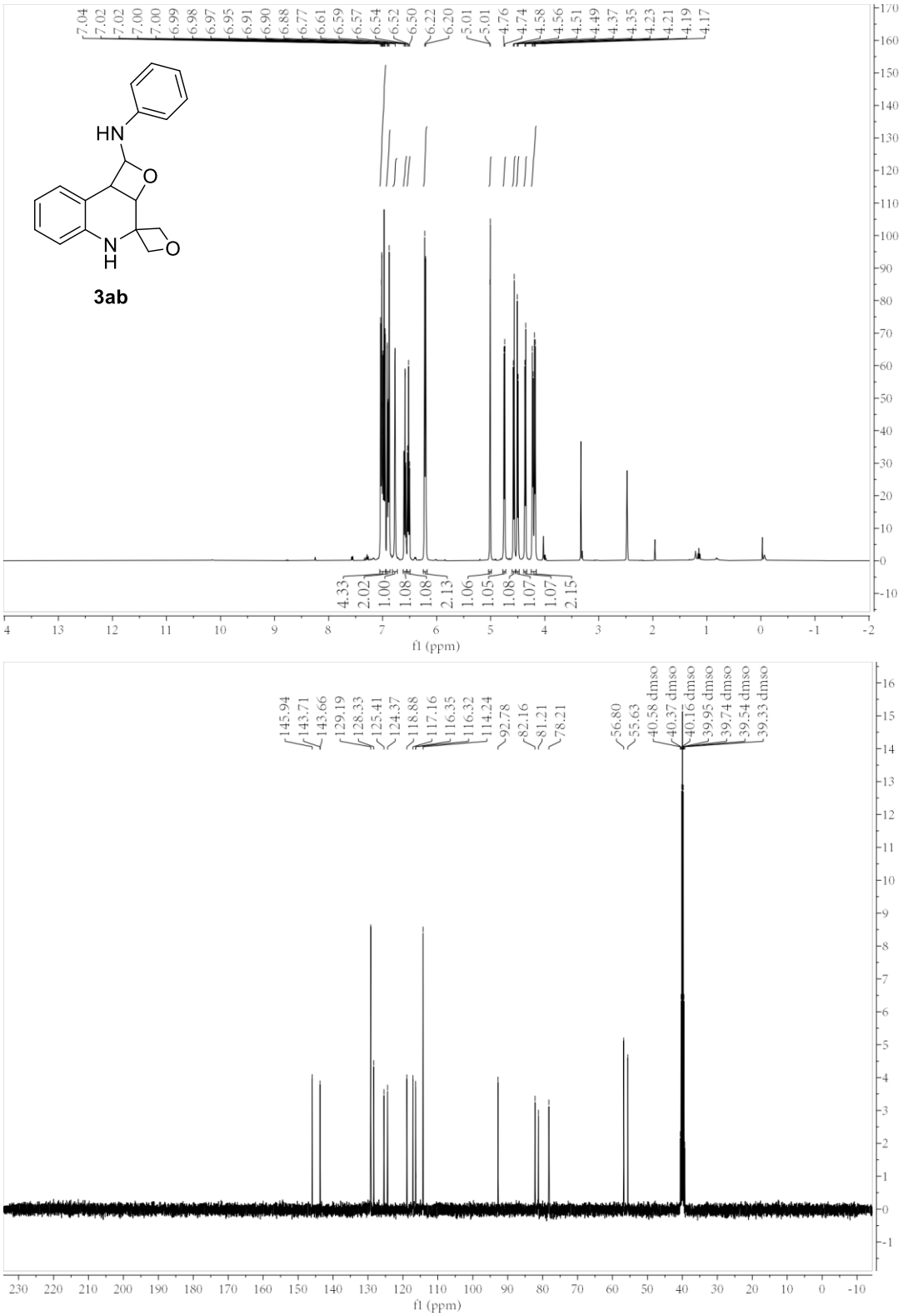


Figure S26. ^{1}H(400 MHz, DMSO) and ^{13}C (101 MHz, DMSO) NMR spectra for compound **3ab**

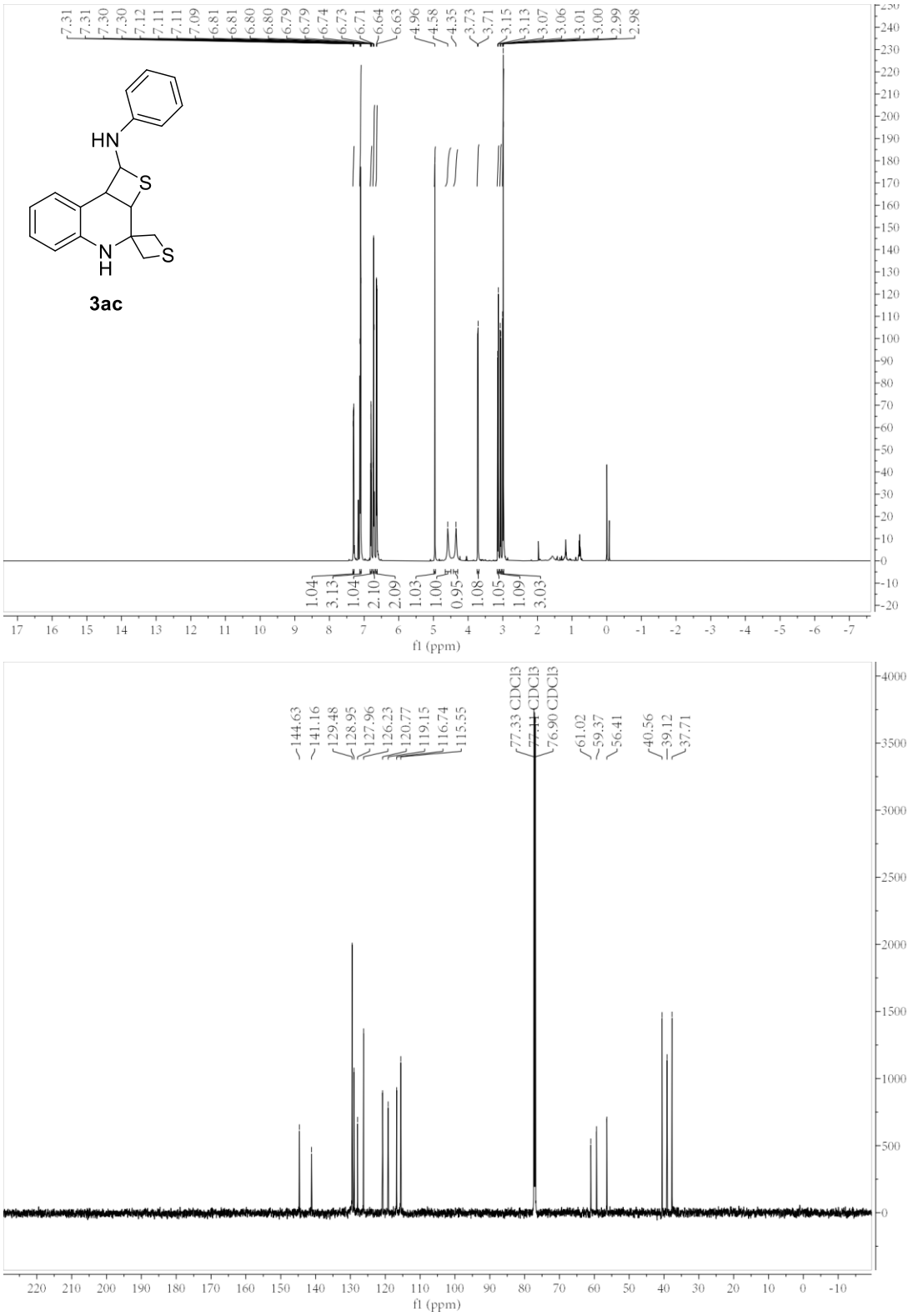


Figure S27. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ac**

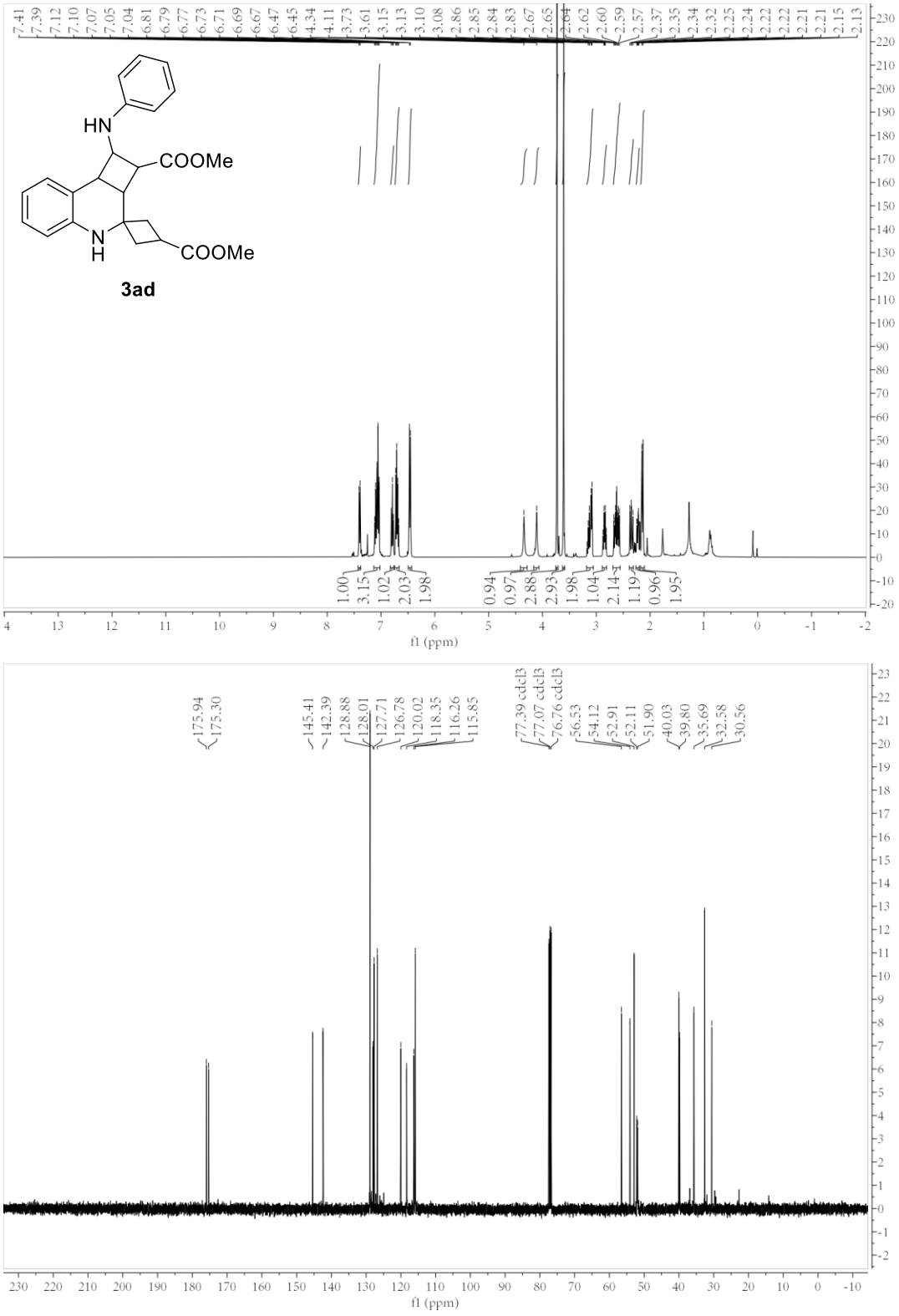


Figure S28. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ad**

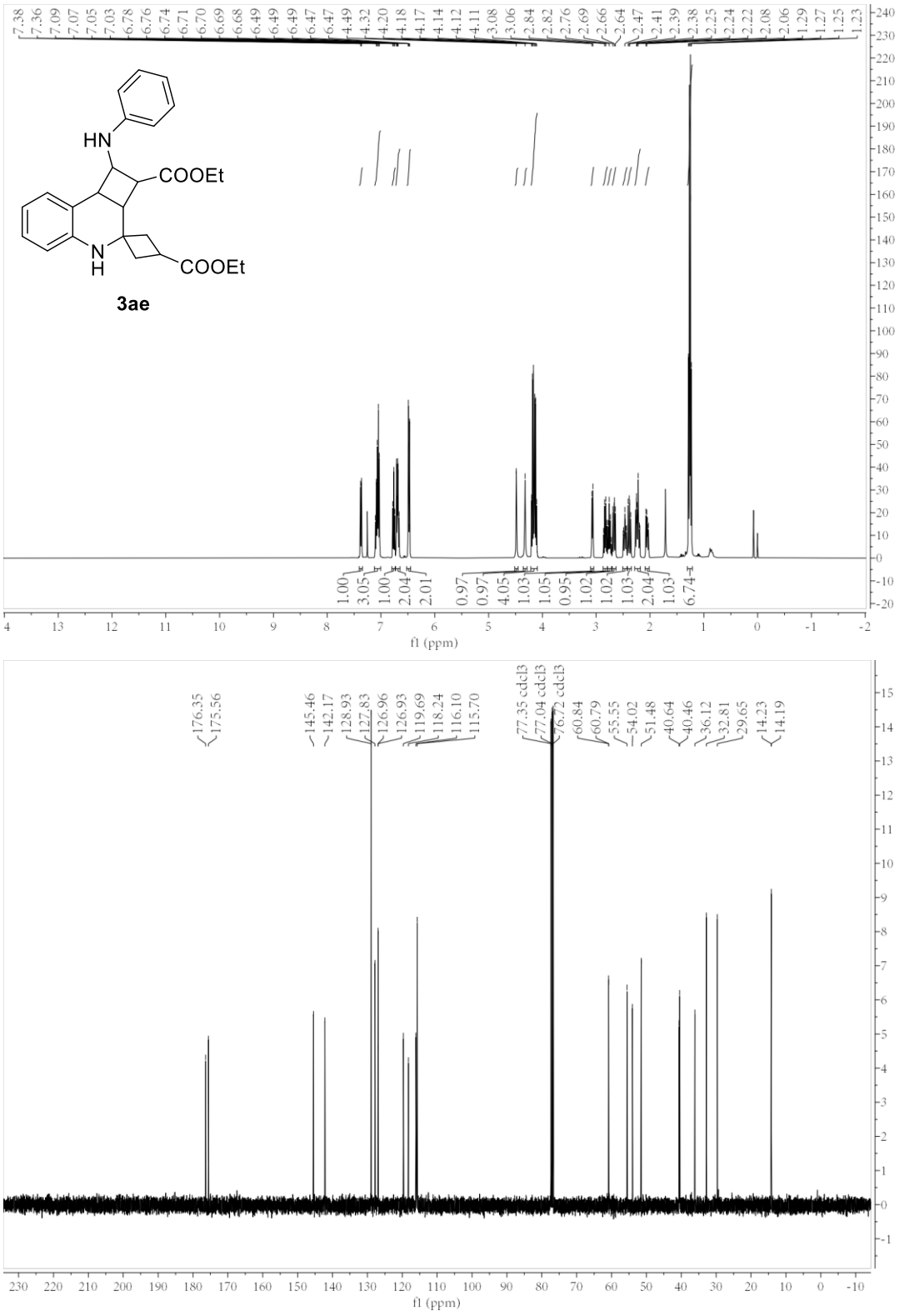


Figure S28. ^{1}H(400 MHz, $CDCl_3$) and ^{13}C (101 MHz, $CDCl_3$) NMR spectra for compound **3ad**