Supporting Information

Copper-Catalyzed Aerobic Decarboxylative Coupling between Cyclic α-Amino Acids and Diverse C–H Nucleophiles with Low Catalyst Loading

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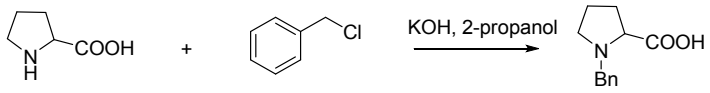
1. General information

All the commercial reagents were used as such without further purification. All solvents were used as commercial anhydrous grade without further purification. The flash column chromatography was carried out over silica gel (230-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 MHz spectrometer. Chemical shifts in ^{1}H NMR spectra were reported in parts per million (ppm, δ) downfield from the internal standard Me_4Si (TMS, δ = 0 ppm). Chemical shifts in ^{13}C NMR spectra were reported relative to the central line of the chloroform signal (δ = 77.0 ppm). Peaks were labeled as singlet (s), doublet (d), triplet (t), quartet (q), and multiplet (m). High resolution mass spectra were obtained with a Shimadzu LCMS-IT-TOF mass spectrometer. Chemical yields refer to pure isolated substances.

2. General Procedure for the Synthesis of Substrates

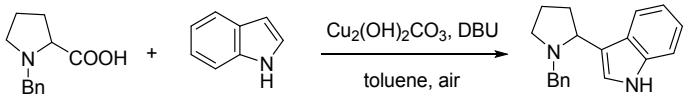
(a) General synthetic method of proline derivatives[1]



1at **1a**

To a dry 250 mL round-bottom flask, proline (17.3 g, 150 mmol) and potassium hydroxide (25.4 g, 450 mmol) were dissolved in isopropanol (150 mL) and heated to 40 °C. Benzyl chloride (18.9 mL, 160 mmol) was added over 3 h via syringe pump. The mixture was stirred for an additional 5 h (8 h in total), then cooled to room temperature. Concentrated HCl was added to adjust the pH to 4-5. Chloroform (40 mL) was added and the solution was allowed to stir at room temperature for 10 h. The formed white precipitate was filtered off and washed with chloroform (3×20 mL). The resulting organic solution was combined and concentrated under reduced pressure. The residue was further washed with acetone (4×20 mL), dried over P_2O_5 to afford crude benzylated acid as yellow solid.

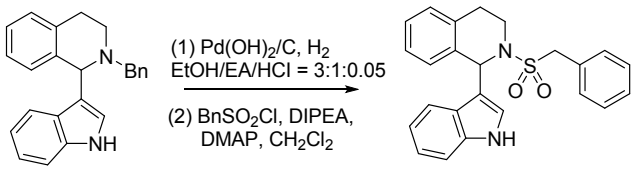
(b) General procedure for the synthesis of products



1a **2a** **3a**

To a solution of **1a** (82 mg, 0.4 mmol) and **2a** (23.4 mg, 0.2 mmol) in toluene (2 mL) was added $Cu_2(OH)_2CO_3$ (0.44 mg, 0.002 mmol) and DBU (91.2 mg. 0.6 mmol). The reaction mixture was stirred at 110 °C for 24 h under air, then extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography on silica gel to afford compound **3a**.

(c) Synthesis of IBR2 analogue 4a[2]



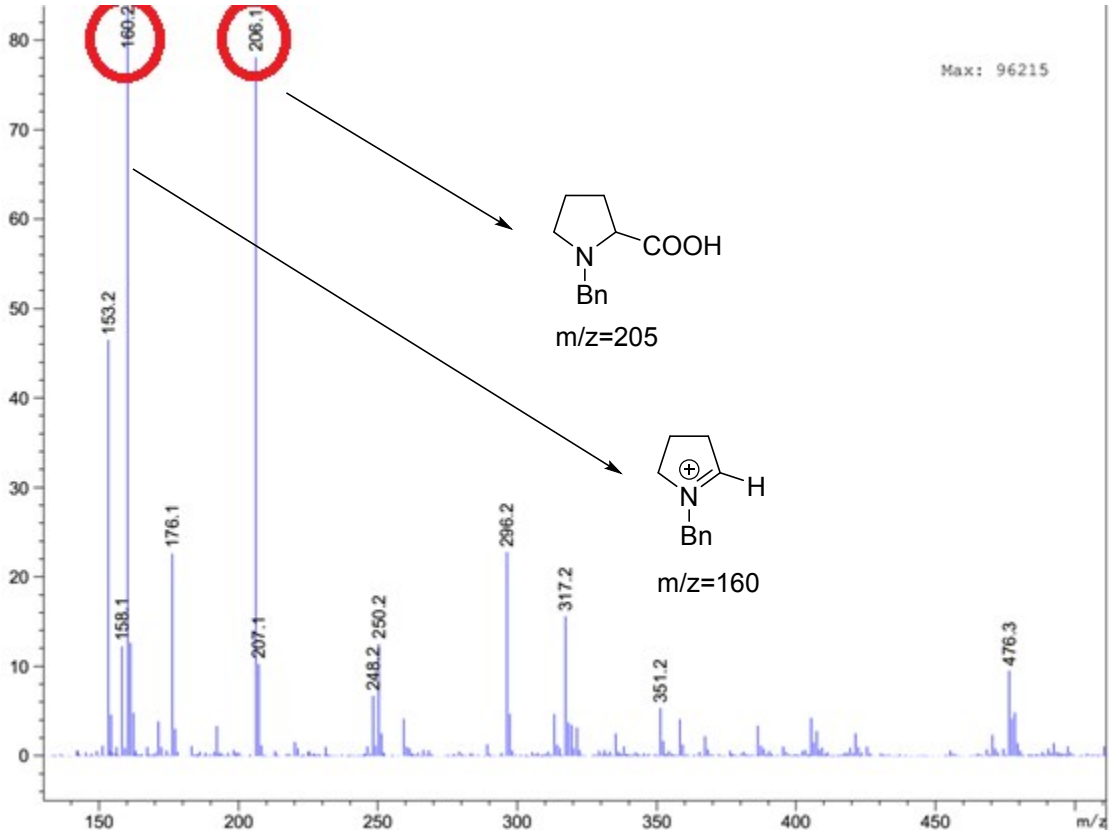
3aq **4a 85%**

IBR2 analogue

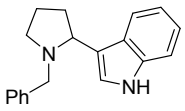
3aq (67.7 mg, 0.2 mmol), HCl (2.0 *N*, 1.25 mL, 0.24 mmol), palladium hydroxide on carbon (23 mg, 40 wt%) and EtOH/EtOAc (3:1, 2 mL) were added into a round-bottom flask. The hydrogenolysis was performed at room temperature under H_2 (1 atm) for 24 h. After carefully releasing the hydrogen, aqueous $NaHCO_3$ was added and the mixture was stirred for 30 min. The organic layer was extracted with CH_2Cl_2 for three times, the combined organic extracts were dried over Na_2SO_4 and concentrated *in vacuo* to afford crude product.

The above crude product, DMAP (3 mg), DIPEA (0.24 mmol) and CH_2Cl_2 (3 mL) were added into a round-bottom flask at 0 °C. Then a solution of $BnSO_2Cl$ (0.24 mmol) in CH_2Cl_2 (2 mL) was added dropwise. The resulting mixture was stirred at room temperature for 15 min, then concentrated *in vacuo.* The residue was purified by flash column chromatography on silica gel to afford **4a** (68 mg, 85%) as a white foam.

3. Mass Spectrum of Reactive Intermediates

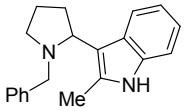


4. Characterization Data of New Products



3a

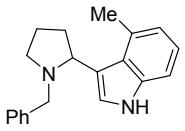
3-(1-Benzylpyrrolidin-2-yl)-1*H*-indole (3a). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 35.8 mg, 65%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.99 (s, 1H), 7.81 (m, 1H), 7.30–7.25 (m, 1H), 7.19–7.15 (m, 5H), 7.13–7.09 (m, 2H), 7.05 (m, 1H), 3.93 (m, 1H), 3.63 (m, 1H), 3.09–2.95 (m, 2H), 2.17–2.09 (m, 2H), 1.98 (m, 1H), 1.91–1.83 (m, 1H), 1.78–1.70 (m, 1H).



3b

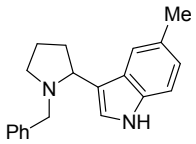
3-(1-Benzylpyrrolidin-2-yl)-2-methyl-1*H*-indole (3b). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 40.6 mg, 70%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.16–7.91 (m, 1H), 7.75 (s, 1H), 7.36–7.25 (m, 5H), 7.23 (m, 1H),

7.21–7.13 (m, 2H), 3.95 (m, 1H), 3.65 (m, 1H), 3.17 (m, 1H), 3.01 (m, 1H), 2.51 (s, 3H), 2.26–2.09 (m, 3H), 2.09–1.96 (m, 1H), 1.92–1.80 (m, 1H).



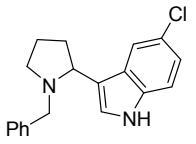
3c

3-(1-Benzylpyrrolidin-2-yl)-4-methyl-1*H*-indole (3c). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 35.4 mg, 61%. Yellow oil. ^{1}H NMR (500 MHz, chloroform-*d*) δ: 8.08 (s, 1H), 7.35 (d, *J* = 21.8 Hz, 4H), 7.23 (d, *J* = 7.8 Hz, 3H), 7.07 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.1 Hz, 1H), 4.15 (s, 1H), 3.99 (s, 1H), 3.13 (m, 2H), 2.75 (s, 3H), 2.44–2.09 (m, 2H), 1.93–1.67 (m, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ: 140.1, 137.0, 130.6, 128.7, 128.7, 128.2, 128.2, 126.7, 125.9, 121.8, 121.8, 121.2, 121.2, 109.1, 62.7, 58.7, 53.6, 35.8, 22.3, 21.4. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{20}H_{23}N_2$: 291.1856; found: 291.1869.



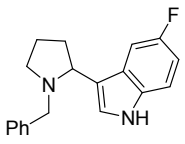
3d

3-(1-Benzylpyrrolidin-2-yl)-5-methyl-1*H*-indole (3d). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 30.8 mg, 53%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.91 (s, 1H), 7.58 (s, 1H), 7.27–7.15 (m, 5H), 7.13 (m, 2H), 6.95 (m, 1H), 3.96 (s, 1H), 3.59 (m, 1H), 3.13–2.86 (m, 2H), 2.41 (s, 3H), 2.18–2.05 (m, 2H), 1.95 (m, 2H), 1.73 (m, 1H).



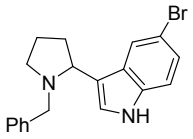
3e

3-(1-Benzylpyrrolidin-2-yl)-5-chloro-1*H*-indole (3e). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 42.1 mg, 68%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data; ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.12 (s, 1H), 7.88 (m, 1H), 7.33–7.06 (m, 8H), 3.94 (m, 1H), 3.62 (m, 1H), 3.29–2.85 (m, 2H), 2.18 (m, 2H), 2.07–1.78 (m, 3H).



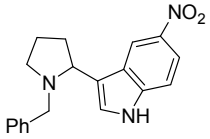
3f

3-(1-Benzylpyrrolidin-2-yl)-5-fluoro-1*H*-indole (3f). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 42.3 mg, 72%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.13 (s, 1H), 7.56 (m, 1H), 7.39–7.07 (m, 7H), 6.93 (m, 1H), 3.94 (s, 1H), 3.60 (d, *J* = 8.0 Hz, 1H), 3.18–2.90 (m, 2H), 2.27–2.05 (m, 2H), 2.04–1.63 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 158.6, 156.3, 140.0, 133.4, 128.8, 128.8, 128.1, 128.1, 127.0 (d, *J* = 40.0 Hz), 126.9, 126.7, 124.0, 118.1 (d, *J* = 16.0 Hz), 111.8（d, *J* = 40.0 Hz), 110.5（d, *J* = 104.0 Hz), 105.3 （d, *J* = 92.0 Hz), 62.4, 58.4, 53.5, 32.8, 22.3. ^{19}F NMR (376 MHz, chloroform-*d*) δ: -124.85 (m, 1F). ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{20}FN_2$: 295.1605; found: 295.1616.



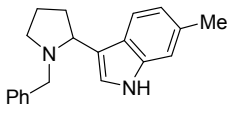
3g

3-(1-Benzylpyrrolidin-2-yl)-5-bromo-1*H*-indole (3g). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 51.6 mg, 73%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.02 (s, 1H), 7.97 (m, 1H), 7.23–7.14 (m, 5H), 7.14–7.08 (m, 3H), 3.86 (m, 1H), 3.54 (m, 1H), 3.09–2.85 (m, 2H), 2.20–2.02 (m, 2H), 1.94–1.80 (m, 2H), 1.75–1.67 (m, 1H).



3h

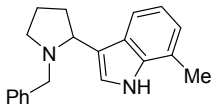
3-(1-Benzylpyrrolidin-2-yl)-5-nitro-1*H*-indole (3h). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 47.5 mg, 74%. Yellow oil. ^{1}H NMR (500 MHz, chloroform-*d*) δ: 8.93 (s, 1H), 8.59 (s, 1H), 8.11 (d, *J* = 8.9 Hz, 1H), 7.44–7.30 (m, 2H), 7.29–7.12 (m, 5H), 3.93 (d, *J* = 13.2 Hz, 1H), 3.71 (s, 1H), 3.24–2.90 (m, 2H), 2.22 (m, 2H), 2.06–1.91 (m, 2H), 1.84 (q, *J* = 10.4 Hz, 1H). ^{13}C NMR (126 MHz, chloroform-*d*) δ: 141.3, 139.9, 139.7, 128.6, 128.6, 128.2, 128.2, 126.7, 125.9, 125.1, 121.1, 117.8, 117.8, 111.1, 62.1, 58.4, 53.5, 33.5, 22.3. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{20}N_3O_2$: 322.1550; found: 322.1566.



3i

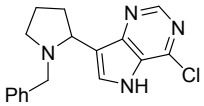
3-(1-Benzylpyrrolidin-2-yl)-6-methyl-1*H*-indole (3i). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 34.8 mg, 60%. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.09 (s, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.40–7.08 (m, 7H), 6.98 (m, 1H), 4.03 (d, *J* = 13.0 Hz, 1H), 3.76 (s, 1H), 3.14 (d, *J* = 11.0 Hz, 2H), 2.47 (s, 3H), 2.35–1.74

(m, 5H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 137.2, 131.9, 129.1, 129.1, 128.7, 128.2, 128.2, 127.0, 124.5, 122.0, 121.2, 119.5, 111.3, 111.3, 62.7, 58.2, 53.4, 32.7, 22.0, 21.7. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{20}H_{23}N_2$: 291.1856; found: 291.1865.



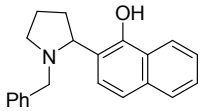
3j

3-(1-Benzylpyrrolidin-2-yl)-7-methyl-1*H*-indole (3j). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 35.9 mg, 62%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.99 (s, 1H), 7.77–7.67 (m, 1H), 7.29–7.22 (m, 5H), 7.19 (m, 1H), 7.07–6.97 (m, 2H), 4.01 (d, *J* = 13.1 Hz, 1H), 3.70 (m, 1H), 3.19–2.98 (m, 2H), 2.49 (s, 3H), 2.24–2.17 (m, 2H), 2.07–1.87 (m, 3H).



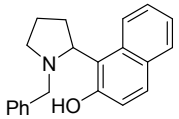
3k

7-(1-Benzylpyrrolidin-2-yl)-4-chloro-5*H*-pyrrolo[3,2-d] pyrimidine (3k). The general method was followed. Purification by chromatography (50% EtOAc/PE) provided pure product. Yield: 54.9 mg, 88%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.81 (s, 1H), 7.76 (s, 1H), 7.35–7.16 (m, 5H), 3.95 (m, 1H), 3.30 (m, 1H), 3.16 (m, 1H), 2.95 (m, 1H), 2.44–2.25 (m, 2H), 2.02–1.83 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 149.9, 149.8, 142.5, 139.4, 129.9, 128.6, 128.6, 128.1, 128.1, 126.1, 125.2, 120.6, 59.8, 58.6, 53.6, 33.6, 22.4. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{17}H_{18}ClN_4$: 313.1215; found: 313.1227.



3l

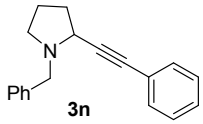
2-(1-Benzylpyrrolidin-2-yl)naphthalen-1-ol (3l). The general method was followed. Purification by chromatography (2% EtOAc/PE) provided pure product. Yield: 53.9 mg, 89%. Colorless oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.39–8.31 (m, 1H), 7.83–7.74 (m, 1H), 7.55–7.43 (m, 2H), 7.41–7.28 (m, 5H), 7.27 (s, 1H), 7.17 (m, 1H), 4.12 (d, *J* = 12.7 Hz, 1H), 3.76 (m, 1H), 3.25 (d, *J* = 12.7 Hz, 1H), 3.16 (m, 1H), 2.44–2.21 (m, 2H), 2.09–1.88 (m, 3H).



3m

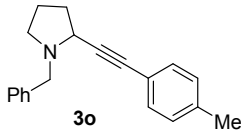
1-(1-Benzylpyrrolidin-2-yl)naphthalen-2-ol (3m). The general method was followed. Purification by chromatography (2% EtOAc/PE) provided pure product. Yield: 50.9 mg, 84%.

Colorless oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.05 (s, 1H), 7.93 (m, 1H), 7.43–7.37 (m, 1H), 7.32–7.25 (m, 5H), 7.22 (m, 2H), 7.16 (m, 1H), 4.04 (m, 1H), 3.73 (m, 1H), 3.19–3.00 (m, 2H), 2.32–2.15 (m, 2H), 2.13–1.92 (m, 2H), 1.90–1.78 (m, 1H).



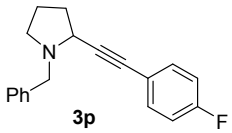
3n

1-Benzyl-2-(phenylethynyl)pyrrolidine (3n). The general method was followed. Purification by chromatography (1-2% EtOAc/PE) provided pure product. Yield: 37.1 mg, 71%. Colorless oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.50–6.90 (m, 10H), 3.97 (m, 1H), 3.52 (m, 2H), 2.46 (m, 1H), 2.13–1.51 (m, 5H).



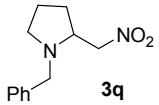
3o

1-Benzyl-2-(*p*-tolylethynyl)pyrrolidine (3o). The general method was followed. Purification by chromatography (1-2% EtOAc/PE) provided pure product. Yield: 38.5 mg, 70%. Colorless oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.52–7.45 (m, 2H), 7.37–7.26 (m, 5H), 7.16 (m, 2H), 4.04 (m, 1H), 3.74–3.50 (m, 2H), 2.81 (m,1H), 2.57 (m,1H), 2.36 (s, 3H), 2.27–2.10 (m, 1H), 2.12–2.03 (m, 1H), 2.00–1.88 (m, 1H), 1.89–1.78 (m, 1H).



3p

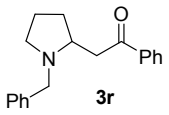
1-Benzyl-2-((4-fluorophenyl)ethynyl)pyrrolidine (3p). The general method was followed. Purification by chromatography (1-2% EtOAc/PE) provided pure product. Yield: 41.8 mg, 75%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.46–7.35 (m, 3H), 7.31 (m, 2H), 7.27–7.23 (m, 2H), 7.04–6.95 (m, 2H), 4.05 (m, 1H), 3.68–3.45 (m, 2H), 2.78 (m, 1H), 2.54 (m, 1H), 2.31–2.09 (m, 1H), 2.07–1.79 (m, 3H).



3q

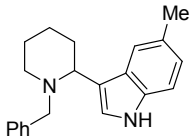
Benzyl-2-(nitromethyl)pyrrolidine (3q). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 33.9 mg, 77%. Colorless oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.31–7.12 (m, 5H), 4.25 (m, 1H), 4.17 (m, 1H), 3.82 (d, J = 13.0 Hz, 1H), 3.46

(d, *J* = 13.0 Hz, 1H), 3.25 (m, 1H), 2.88 (m, 1H), 2.36–2.17 (m, 1H), 2.09–1.85 (m, 1H), 1.80–1.60 (m, 3H).



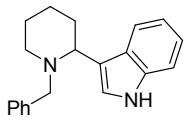
3r

2-(1-Benzylpyrrolidin-2-yl)-1-phenylethan-1-one (3r). The general method was followed. Purification by chromatography (30% EtOAc/PE) provided pure product. Yield: 30.1 mg, 54%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.92 (d, *J* = 7.0 Hz, 1H), 7.61–7.51 (m, 1H), 7.45 (m, 2H), 7.37–7.24 (m, 6H), 3.98 (m, 1H), 3.43–3.23 (m, 2H), 3.11 (m, 1H), 3.06–2.90 (m, 2H), 2,09–2.07 (m, 2H), 1.72 (m, 3H).



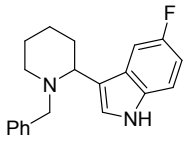
3x

3-(1-Benzylpiperidin-2-yl)-5-methyl-1*H*-indole (3x). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 37.7 mg, 62%. Colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.87 (s, 1H), 7.76 (s, 1H), 7.25–7.17 (m, 5H), 7.16–7.12 (m, 1H), 7.10 (d, *J* = 2.2 Hz, 1H), 6.99 (m, 1H), 3.95 (d, *J* = 13.4 Hz, 1H), 3.43 (m, 1H), 3.00 (m, 1H), 2.86 (d, *J* = 13.4 Hz, 1H), 2.48 (s, 3H), 1.98 (m, 2H), 1.88–1.75 (m, 2H), 1.62 (m, 2H), 1.46–1.35 (m, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 140.2, 134.9, 129.0, 129.0, 128.3, 127.9, 127.9, 126.8, 126.4, 123.6, 121.9, 120.0, 119.6, 110.8, 61.4, 59.8, 53.8, 35.5, 26.2, 25.5, 21.6. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{21}H_{25}N_2$: 305.2012; found: 305.2025.



3y

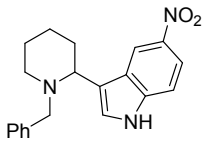
3-(1-Benzylpiperidin-2-yl)-1*H*-indole (3y). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 37.7 mg, 65%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.26 (s, 1H), 7.86 (m, 1H), 7.29 (m, 1H), 7.20–7.01 (m, 8H), 3.92 (m, 1H), 3.48 (m, 1H), 2.96 (m, 2H), 2.01 (d, *J* = 30.3 Hz, 2H), 1.84–1.52 (m, 5H).



3z

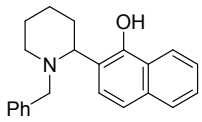
3-(1-Benzylpiperidin-2-yl)-5-fluoro-1*H*-indole (3z). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 40.6 mg, 66%.

Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.99 (s, 1H), 7.69 (m, 1H), 7.40–7.01 (m, 7H), 6.91 (m, 1H), 3.90 (d, *J* = 13.4 Hz, 1H), 3.37 (dd, *J* = 11.3, 2.6 Hz, 1H), 2.91 (dd, *J* = 52.8, 12.4 Hz, 2H), 2.14–1.51 (m, 6H), 1.40 (m, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 158.7, 156.3, 140.0, 133.1, 128.9, 128.0, 128.0, 126.7 (d, *J* = 40.0 Hz), 126.5, 123.5, 120.3 (d, *J* = 8.0 Hz), 111.7 (d, *J* = 40.0 Hz), 110.6 (d, *J* = 108.0 Hz), 105.6 (d, *J* = 96.0 Hz), 61.5, 59.8, 53.7, 35.1, 26.1, 25.4. ^{19}F NMR (376 MHz, chloroform-*d*) δ: -124.77 (s, 1F). ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{20}H_{22}FN_2$: 309.1762; found: 309.1776.



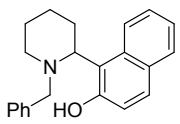
3aa

3-(1-Benzylpiperidin-2-yl)-5-nitro-1*H*-indole (3aa). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 46.9 mg, 70%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 9.06 (d, *J* = 2.2 Hz, 1H), 8.51 (s, 1H), 8.08 (m, 1H), 7.58–6.72 (m, 7H), 3.86 (d, *J* = 13.5 Hz, 1H), 3.49 (m, 1H), 3.17–2.68 (m, 2H), 2.17–1.53 (m, 6H), 1.44 (m, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 141.4, 139.7, 139.6, 128.6, 128.6, 128.1, 128.1, 126.6, 125.7, 124.6, 122.9, 118.1, 117.8, 111.1, 61.3, 59.9, 53.7, 35.6, 26.0, 25.2. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{20}H_{22}N_3O_2$: 336.1707; found: 336.1722.



3ab

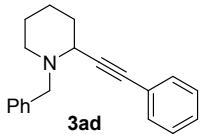
2-(1-Benzylpiperidin-2-yl)naphthalen-1-ol (3ab). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 31.7 mg, 50%. Colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 11.86 (s, 1H), 8.59–8.10 (m, 1H), 7.76 (m, 1H), 7.56–7.39 (m, 2H), 7.38–7.21 (m, 6H), 7.13 (d, *J* = 8.2 Hz, 1H), 4.07 (d, *J* = 12.9 Hz, 1H), 3.39 (m, 1H), 3.07 (dd, *J* = 12.3, 4.3 Hz, 2H), 2.11–1.74 (m, 4H), 1.72–1.49 (m, 2H), 1.46–1.28 (m, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 151.6, 136.7, 133.7, 129.9, 129.9, 128.3, 128.3, 127.3, 127.3, 126.3, 125.9, 125.2, 124.8, 122.3, 120.5, 118.8, 68.4, 60.3, 52.2, 32.8, 25.5, 24.4. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{22}H_{24}NO$: 318.1852; found: 318.1866.



3ac

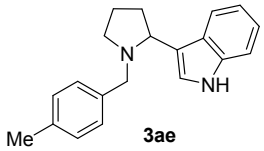
1-(1-Benzylpiperidin-2-yl)naphthalen-2-ol (3ac). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 50.7 mg, 80%. Colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 12.33 (s, 1H), 7.89 (d, *J* = 8.6 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.46 (m, 1H), 7.37–7.20 (m, 6H), 7.17 (d, *J* = 8.8 Hz, 1H), 4.15 (dd, *J* = 10.0, 5.2 Hz, 1H), 4.06 (d, *J* = 13.0 Hz, 1H), 3.09 (dd, *J* = 21.4, 12.3 Hz, 2H), 2.06 (m, 1H), 1.97–1.77 (m, 3H), 1.76–1.52 (m, 2H), 1.43 (m, 1H). ^{13}C NMR (101 MHz,

chloroform-*d*) δ: 154.7, 136.5, 131.9, 130.0, 130.0, 129.0, 129.0, 128.8, 128.4, 128.4, 127.4, 126.4, 122.5, 120.8, 119.5, 117.8, 62.6, 60.1, 52.5, 31.0, 25.5, 24.5. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{22}H_{24}NO$: 318.1852; found: 318.1859.



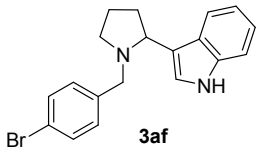
3ad

1-Benzyl-2-(phenylethynyl)piperidine (3ad). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 39.6 mg, 72%. Colorless oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.52–7.44 (m, 2H), 7.39 (d, *J* = 7.0 Hz, 2H), 7.31 (m, 5H), 7.25 (d, *J* = 1.5 Hz, 1H), 3.68 (m, 3H), 2.75–2.58 (m, 1H), 2.52 (m, 1H), 1.83 (m, 2H), 1.78–1.64 (m, 2H), 1.58 (m, 2H).



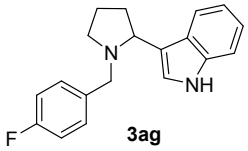
3ae

3-(1-(4-Methylbenzyl)pyrrolidin-2-yl)-1*H*-indole (3ae). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 38.8 mg, 67%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.16 (s, 1H), 7.94 (d, *J* = 7.8 Hz, 1H), 7.48–7.34 (m, 1H), 7.32–7.05 (m, 7H), 4.03 (d, *J* = 13.0 Hz, 1H), 3.88–3.59 (m, 1H), 3.34–2.93 (m, 2H), 2.37 (s, 3H), 2.29–2.21 (m, 2H), 2.14–1.96 (m, 2H), 1.84 (m, 1H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 136.8, 136.8, 136.1, 128.9, 128.9, 128.8, 128.8, 126.8, 122.1, 122.0, 120.1, 119.2, 118.0, 111.2, 62.2, 58.0, 53.4, 33.1, 22.2, 21.1. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{20}H_{23}N_2$: 291.1856; found: 291.1866.



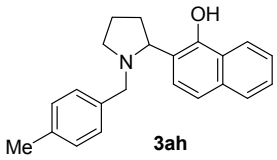
3af

3-(1-(4-Bromobenzyl)pyrrolidin-2-yl)-1*H*-indole (3af). The general method was followed. Purification by chromatography (25% EtOAc/PE) provided pure product. Yield: 51.1 mg, 72%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.02 (s, 1H), 7.88 (d, *J* = 7.9 Hz, 1H), 7.33 (m, 3H), 7.24–7.16 (m, 1H), 7.16–7.05 (m, 4H), 3.89 (m, 1H), 3.75–3.52 (m, 1H), 3.06 (m, 1H), 2.99 (d, *J* = 13.2 Hz, 1H), 2.23–2.09 (m, 2H), 2.08–1.97 (m, 1H), 1.97–1.85 (m, 1H), 1.80 (m, 1H).



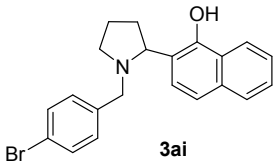
3ag

3-(1-(4-Fluorobenzyl)pyrrolidin-2-yl)-1*H*-indole (3ag). The general method was followed. Purification by chromatography (2% EtOAc/PE) provided pure product. Yield: 41.2 mg, 70%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.23 (s, 1H), 7.86 (s, 1H), 7.58–7.05 (m, 6H), 6.91 (m, 2H), 3.93 (d, *J* = 13.0 Hz, 1H), 3.71 (m, 1H), 3.06 (s, 2H), 2.39–1.71 (m, 5H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 163.1, 160.7, 136.8, 134.6, 130.5 (d, *J* = 36.0 Hz), 126.7, 122.5, 122.1, 122.1, 119.9, 119.3, 119.3, 115.0 (d, *J* = 88.0 Hz), 111.3, 62.2, 57.1, 53.0, 32.8, 22.1. ^{19}F NMR (376 MHz, chloroform-*d*) δ: -116.52 (s, 1F). ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{20}FN_2$: 295.1605; found: 295.1614.



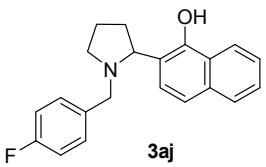
3ah

2-(1-(4-Methylbenzyl)pyrrolidin-2-yl)naphthalen-1-ol (3ah). The general method was followed. Purification by chromatography (1-2% EtOAc/PE) provided pure product. Yield: 58.3 mg, 92%. Colorless oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 12.46 (s, 1H), 8.54–7.92 (m, 1H), 7.84–7.50 (m, 1H), 7.34 (m, 2H), 7.20 (d, *J* = 8.2 Hz, 1H), 7.13–6.89 (m, 5H), 3.91 (d, *J* = 12.6 Hz, 1H), 3.55 (t, *J* = 8.4 Hz, 1H), 3.18–2.75 (m, 2H), 2.43–1.96 (m, 5H), 1.98–1.43 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 152.8, 137.1, 134.3, 134.0, 129.4, 129.4, 129.2, 129.2, 127.4, 127.0, 126.0, 125.6, 124.8, 122.4, 118.2, 117.6, 70.0, 57.9, 52.5, 32.84, 22.5, 21.2. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{22}H_{24}NO$: 318.1852; found:318.1866.



3ai

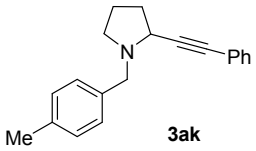
2-(1-(4-Bromobenzyl)pyrrolidin-2-yl)naphthalen-1-ol (3ai). The general method was followed. Purification by chromatography (1-2% EtOAc/PE) provided pure product. Yield: 66.3 mg, 87%. Yellow oil. ^{1}H NMR (500 MHz, chloroform-*d*) δ: 12.32 (s, 1H), 8.30 (d, *J* = 7.5 Hz, 1H), 7.76 (d, *J* = 7.2 Hz, 1H), 7.58–6.84 (m, 8H), 4.01 (m, 1H), 3.70 (s, 1H), 3.40–2.89 (m, 2H), 2.46–2.13 (m, 2H), 2.13–1.68 (m, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ: 152.5, 136.4, 133.9, 131.6, 131.6, 131.1, 131.1, 127.3, 126.8, 126.0, 125.4, 124.9, 122.2, 121.5, 118.3, 117.2, 70.2, 57.6, 52.5, 32.6, 22.4. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{21}H_{21}BrNO$: 382.0801; found: 382.0811.



3aj

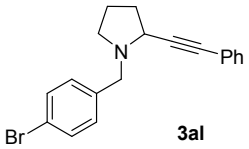
2-(1-(4-Fluorobenzyl)pyrrolidin-2-yl)naphthalen-1-ol (3aj). The general method was followed. Purification by chromatography (1-2% EtOAc/PE) provided pure product. Yield: 52 mg, 81%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 12.32 (s, 1H), 8.61–7.95 (m, 1H), 7.91–7.49 (m, 1H), 7.50–6.42 (m, 8H), 3.93 (d, *J* = 12.7 Hz, 1H), 3.59 (t, *J* = 8.4 Hz, 1H), 3.28–2.73 (m, 2H), 2.51–2.00 (m, 2H), 2.00–1.38 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 163.5, 161.0, 152.6, 133.9, 133.2 (d, *J* = 12.0 Hz), 131.0 (d, *J* = 32.0 Hz), 127.4, 126.9, 126.0, 125.4, 124.8, 122.3,

118.3, 117.4, 115.4, 115.2, 70.1, 57.5, 52.5, 32.7, 22.5. ^{19}F NMR (376 MHz, chloroform-*d*) δ: -115.13 (m, 1F). ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{21}H_{21}FNO$: 322.1602; found: 322.1618.



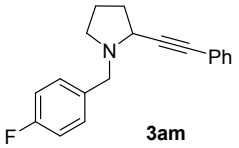
3ak

1-(4-Methylbenzyl)-2-(phenylethynyl)pyrrolidine (3ak). The general method was followed. Purification by chromatography (2% EtOAc/PE) provided pure product. Yield: 41.2 mg, 75%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.48 (m, 2H), 7.37–7.26 (m, 5H), 7.16 (d, *J* = 7.7 Hz, 2H), 4.04 (d, *J* = 12.8 Hz, 1H), 3.74–3.50 (m, 2H), 2.81 (m, 1H), 2.57 (m, 1H), 2.36 (s, 3H), 2.27–2.10 (m, 1H), 2.12–2.03 (m, 1H), 2.00–1.88 (m, 1H), 1.89–1.78 (m, 1H).



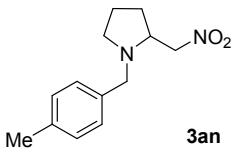
3al

1-(4-Bromobenzyl)-2-(phenylethynyl)pyrrolidine (3al). The general method was followed. Purification by chromatography (2% EtOAc/PE) provided pure product. Yield: 48.3 mg, 71%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.44 (d, *J* = 3.1 Hz, 4H), 7.35–6.87 (m, 5H), 3.98 (d, *J* = 13.0 Hz, 1H), 3.67–3.29 (m, 2H), 2.76 (m, 1H), 2.53 (m, 1H), 2.25–1.68 (m, 4H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 138.0, 131.7, 131.7, 131.3, 131.3, 130.8, 130.8, 128.2, 128.2, 128.0, 123.3, 120.8, 88.5, 85.1, 56.6, 54.4, 51.6, 31.7, 22.1. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{19}H_{19}BrN$: 340.0695; found: 340.0708.



3am

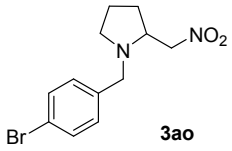
1-(4-Fluorobenzyl)-2-(phenylethynyl)pyrrolidine (3am). The general method was followed. Purification by chromatography (2% EtOAc/PE) provided pure product. Yield: 42 mg, 75%. Yellow oil. The compound has been reported.[3,4] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.37 (m, 2H), 7.32–7.19 (m, 5H), 6.92 (m, 2H), 3.92 (s, 1H), 3.61–3.36 (m, 2H), 2.68 (m, 1H), 2.46 (m, 1H), 2.08 (m, 1H), 1.94 (m, 1H), 1.85 (m, 1H), 1.79–1.72 (m, 1H).



3an

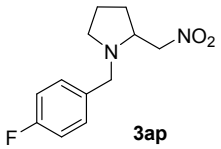
1-(4-Methylbenzyl)-2-(nitromethyl)pyrrolidine (3an). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 36.7 mg, 78%. Yellow oil. ^{1}H NMR (500 MHz, chloroform-*d*) δ: 7.23–6.86 (m, 4H), 4.19 (m, 2H), 3.76 (d, *J* =

13.3 Hz, 1H), 3.43 (d, *J* = 13.0 Hz, 1H), 3.23 (m, 1H), 2.87 (m, 1H), 2.42–2.10 (m, 4H), 2.06–1.84 (m, 1H), 1.79–1.39 (m, 3H). ^{13}C NMR (126 MHz, chloroform-*d*) δ: 135.8, 134.7, 128.0, 128.0, 127.7, 127.7, 78.3, 60.4, 58.0, 53.3, 28.3, 22.0, 20.1. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{13}H_{19}N_2O_2$: 235.1441; found: 235.1442.



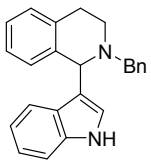
3ao

1-(4-Bromobenzyl)-2-(nitromethyl)pyrrolidine (3ao). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 42.3 mg, 71%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.34 (d, *J* = 8.2 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 4.53–3.96 (m, 2H), 3.77 (m, 1H), 3.37 (d, *J* = 13.3 Hz, 1H), 3.25 (m, 1H), 2.83 (m, 1H), 2.21 (m, 1H), 2.00 (m, 1H), 1.83–1.44 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 138.1, 131.5, 131.5, 130.3, 130.3, 120.9, 79.3, 61.6, 58.7, 54.2, 29.2, 23.1. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{12}H_{16}BrN_2O_2$: 299.0390; found: 299.0410.



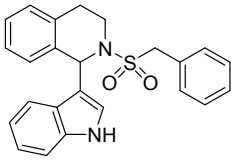
3ap

1-(4-Fluorobenzyl)-2-(nitromethyl)pyrrolidine (3ap). The general method was followed. Purification by chromatography (2-3% EtOAc/PE) provided pure product. Yield: 33.3 mg, 70%. Yellow oil. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 7.38–7.01 (m, 2H), 6.89 (t, *J* = 8.5 Hz, 2H), 4.23 (m, 2H), 3.78 (d, *J* = 13.0 Hz, 1H), 3.39 (d, *J* = 13.0 Hz, 1H), 3.25 (m, 1H), 2.82 (m, 1H), 2.22 (q, *J* = 8.5 Hz, 1H), 1.97 (m, 1H), 1.67 (m, 3H). ^{13}C NMR (101 MHz, chloroform-*d*) δ: 163.2, 160.8, 134.8, 130.2 (d, *J* = 32.0 Hz), 130.2, 115.2 (d, *J* = 72.0 Hz), 115.0, 79.3, 61.5, 58.6, 54.2, 29.2, 23.1. ^{19}F NMR (376 MHz, chloroform-*d*) δ: -115.64 (m, 1F). ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{12}H_{16}FN_2O_2$: 239.1190; found: 239.1180.



3aq

2-Benzyl-1-(1*H*-indol-3-yl)-1,2,3,4-tetrahydroiso quinoline (3aq). The general method was followed. Purification by chromatography (30% EtOAc/PE) provided pure product. Yield: 55.4 mg, 82%. Yellow oil. ^{1}H NMR (500 MHz, chloroform-*d*) δ: 7.88 (s, 1H), 7.69–7.48 (m, 1H), 7.36–7.15 (m, 6H), 7.10 (m, 3H), 7.02 (d, *J* = 8.4 Hz, 1H), 6.92 (d, *J* = 16.8 Hz, 3H), 4.95 (s, 1H), 3.88 (m, 1H), 3.31 (d, *J* = 3.0 Hz, 1H), 3.18–2.91 (m, 2H), 2.83 (m, 1H), 2.53 (m, 1H). ^{13}C NMR (126 MHz, chloroform-*d*) δ: 140.0, 138.7, 136.7, 134.8, 129.1, 129.1, 128.5, 128.5, 128.2, 128.2, 127.0, 126.8, 126.0, 125.7, 124.5, 122.1, 120.8, 119.5, 118.6, 111.1, 61.1, 59.0, 47.1, 28.8. ESI-HRMS: *m/z* $[M+H]^+$ calcd. for $C_{24}H_{23}N_2$: 339.1856; found: 339.1854.



4a

2-(Benzylsulfonyl)-1-(1*H*-indol-3-yl)-1,2,3,4-tetrahydro isoquinoline (4a). Yield: 68 mg, 70%. White solid. The compound has been reported.[5] NMR spectra match literature data. ^{1}H NMR (400 MHz, chloroform-*d*) δ: 8.19 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.31 (m, 1H), 7.24 (s, 1H), 7.14–6.99 (m, 7H), 6.92 (m, 1H), 6.75 (d, *J* = 6.6 Hz, 3H), 6.38 (s, 1H), 3.91 (m, 1H), 3.80 (m, 1H), 3.41 (m, 1H), 3.09 (m, 1H), 2.98–2.81 (m, 1H), 2.62 (m, 1H).

5. References

[1] Y. N. Belokon, V. I. Tararov, V. I. Maleev, T. F. Savel'eva, M. G. Ryzhov, *Tetrahedron: Asymmetry*, **1998**, *9*, 4249-4252.

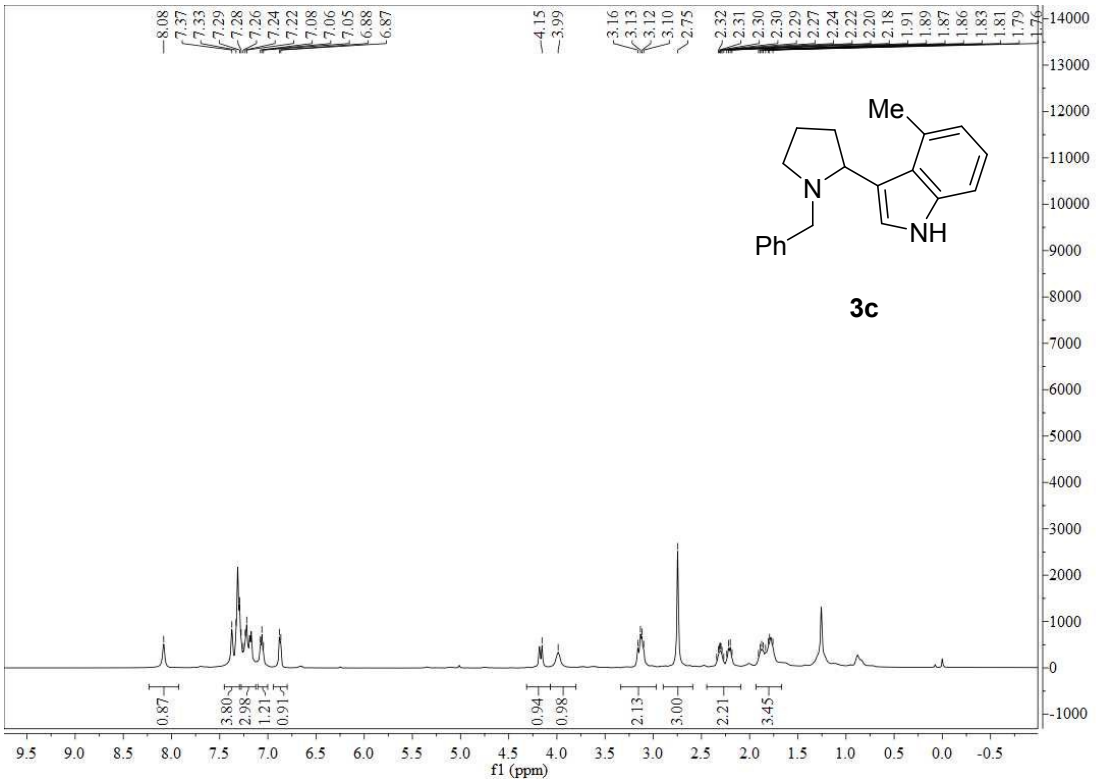
[2] a) D. Barbier, C. Marazano, C. Riche, B. C. Das, P. Potier, *J. Org. Chem.* **1998**, *63*, 1767-1772. b) S. K. Chakka, P. G. Andersson, G. E. M. Maguire, H. G. Kruger, T. Govender, *Eur. J. Org. Chem.* **2010**, 972-980. c) X.-L. Qiu, J. Zhu, G. Wu, W.-H. Lee, A. R. Chamberlin, *J. Org. Chem.* **2009**, *74*, 2018-2027. d) H. Chong, Y.-W. Chen, *Org. Lett.* **2013**, *15*, 5912-5915. e) L. Benmekhbi, F. Louafi, T. Roisnel, J.-P. Hurvois, *J. Org. Chem*. **2016**, *81*, 6721-6739.

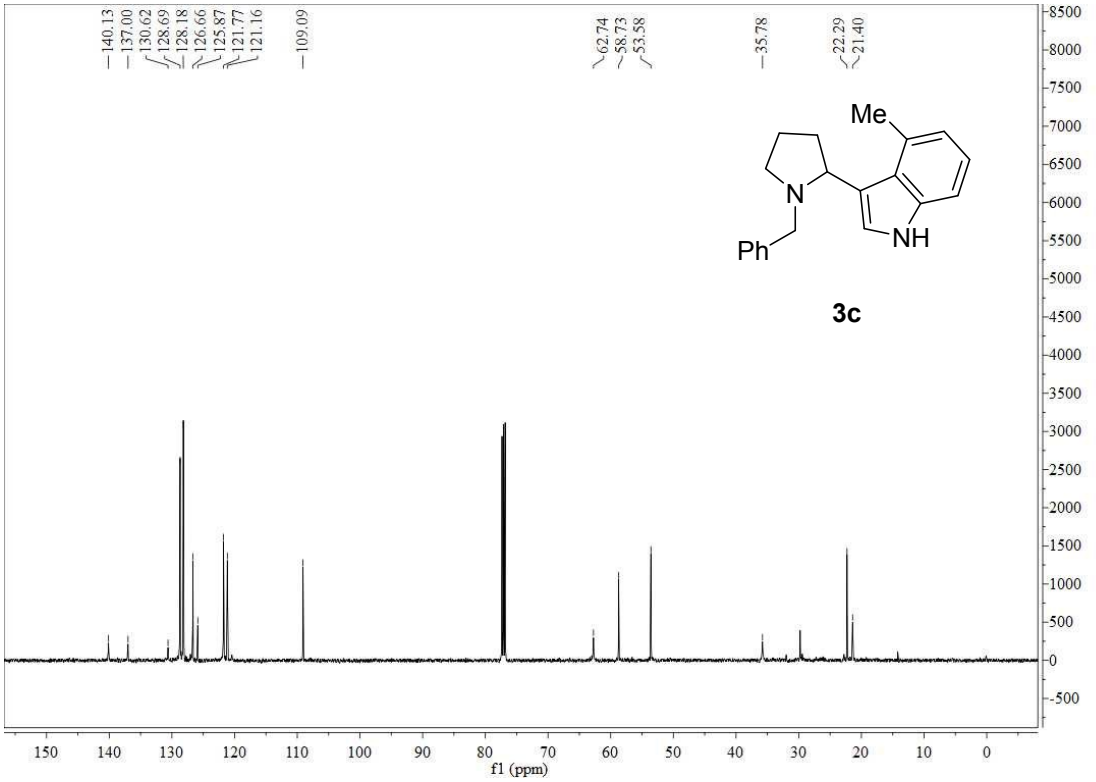
[3] a) H.-P. Bi, L. Zhao, Y.-M. Liang, C.-J. Li, *Angew. Chem., Int. Ed.* **2009**, *48*, 792-795; *Angew. Chem.* **2009**, *4*, 806-809. b) H.-P. Bi, W.-W. Chen, Y.-M. Liang, C.-J. Li, *Org. Lett.* **2009**, *11*, 3246-3249.

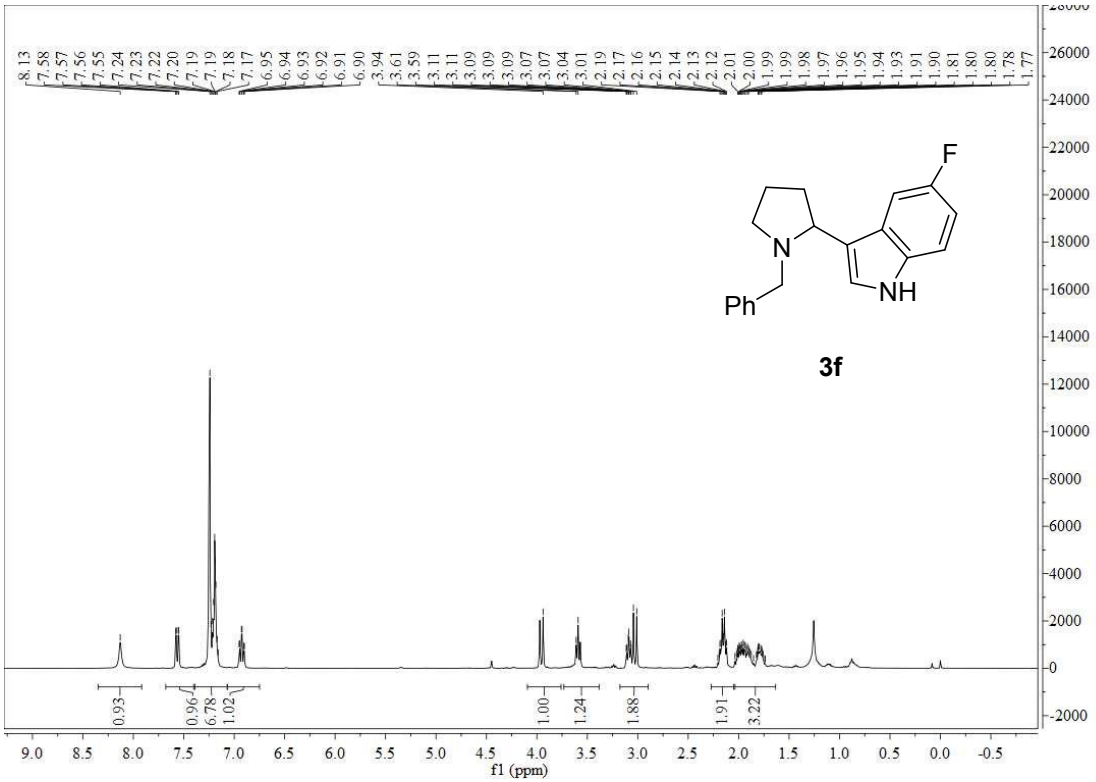
[4] C. Zhang, D. Seidel, *J. Am. Chem. Soc*. **2010**, *132*, 1798-1799.

[5] a) X.-L. Qiu, J. Zhu, G. Wu, W.-H. Lee, A. R. Chamberlin, *J. Org. Chem*. **2009**, *74*, 2018-2027. b) T.-W. Chung, Y.-T. Hung, T. Thikekar, V. V. Paike, F. Y. Lo, P.-H. Tsai, M.-C Liang, C.-M. Sun, *ACS Comb. Sci*. **2015**, *17*, 442-451. c) J. Zhu, H. Chen, X. E. Guo, X.-L. Qiu, C.-M. Hu, A. R. Chamberlin, W.-H. Lee. *Eur. J. Med. Chem*. **2015**, *96,* 196-208.

6. Copies of ^{1}H, and ^{13}C NMR Spectra of New Products



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NH
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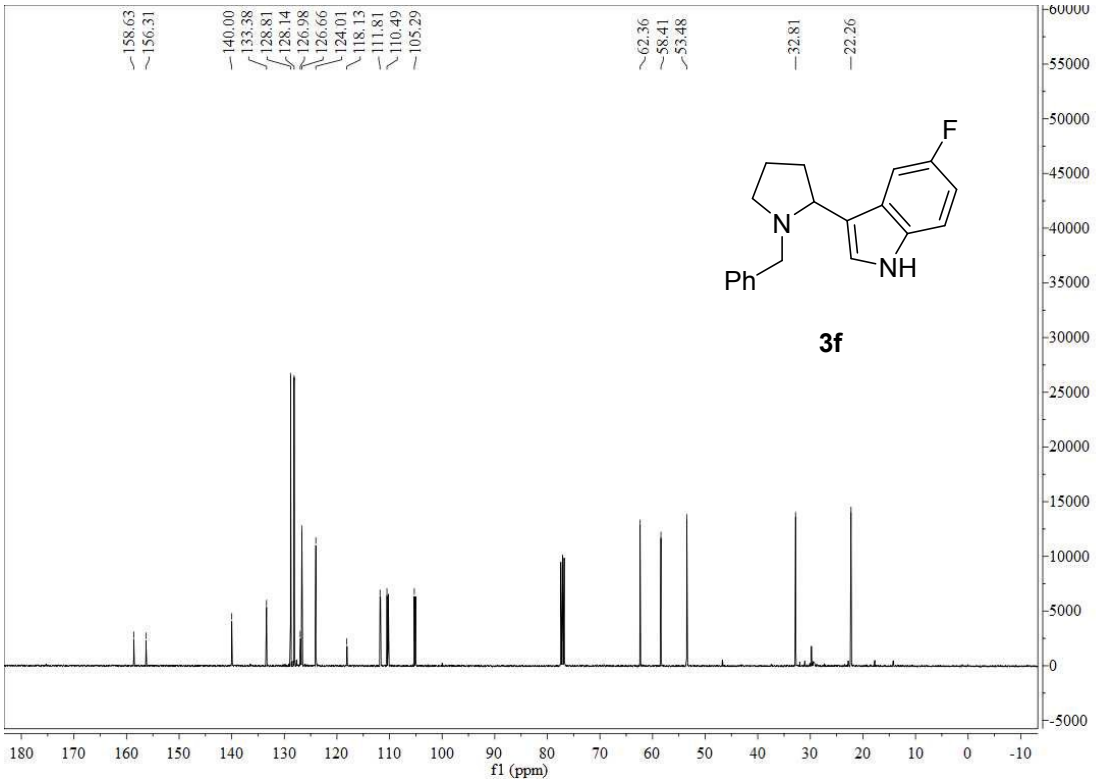
f1 (ppm)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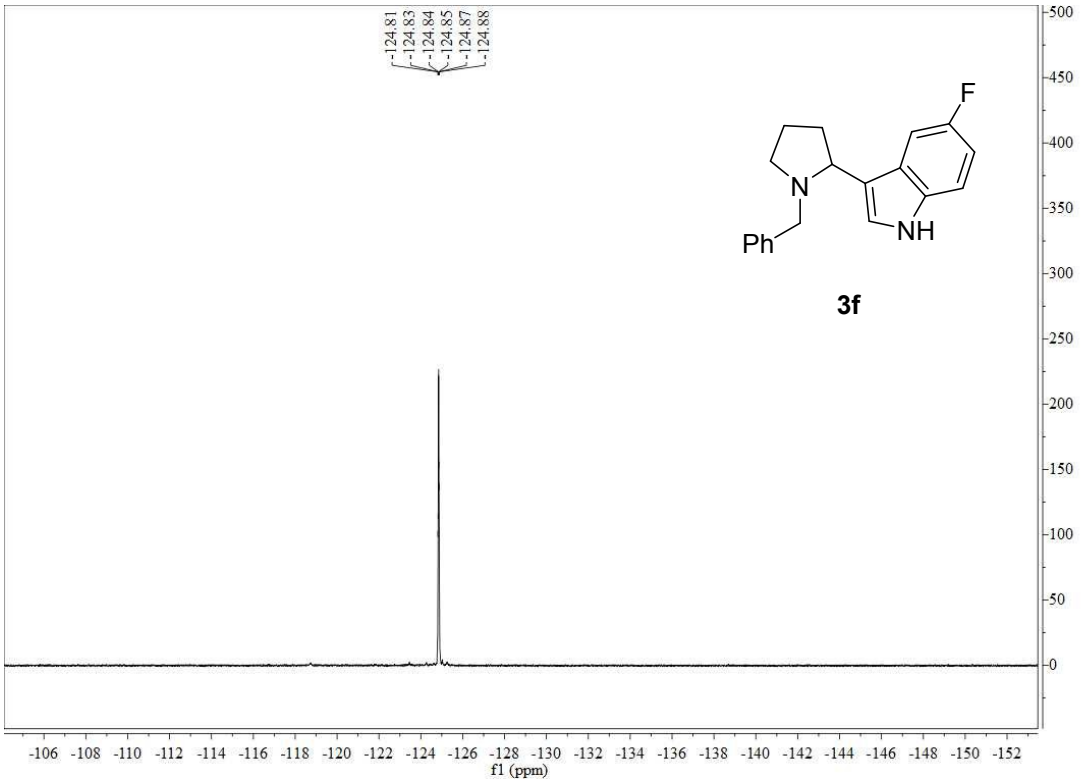
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N
Ph
NH
3f
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450
400
350
300
250
200
150
100
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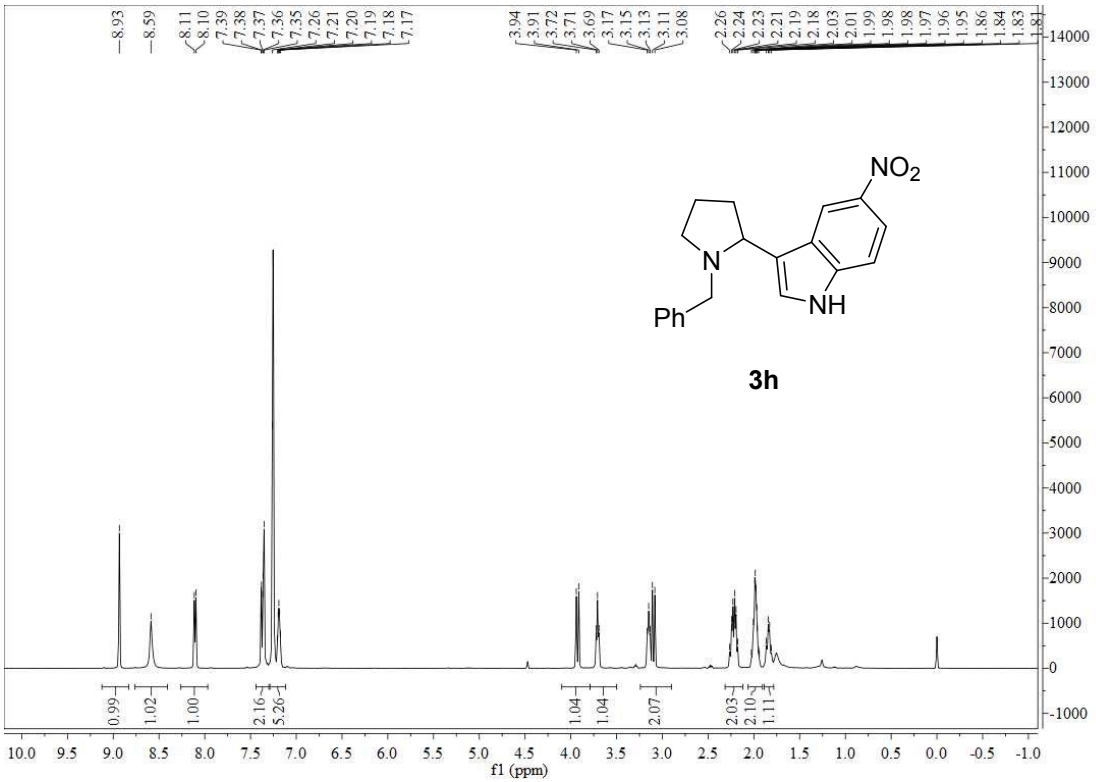
f1 (ppm)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7.18
7.17
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3.91
3.72
3.71
3.69
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3.13
3.11
3.08
2.26
2.24
2.23
2.21
2.19
2.18
2.03
2.01
1.99
1.98
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1.96
1.95
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1.83
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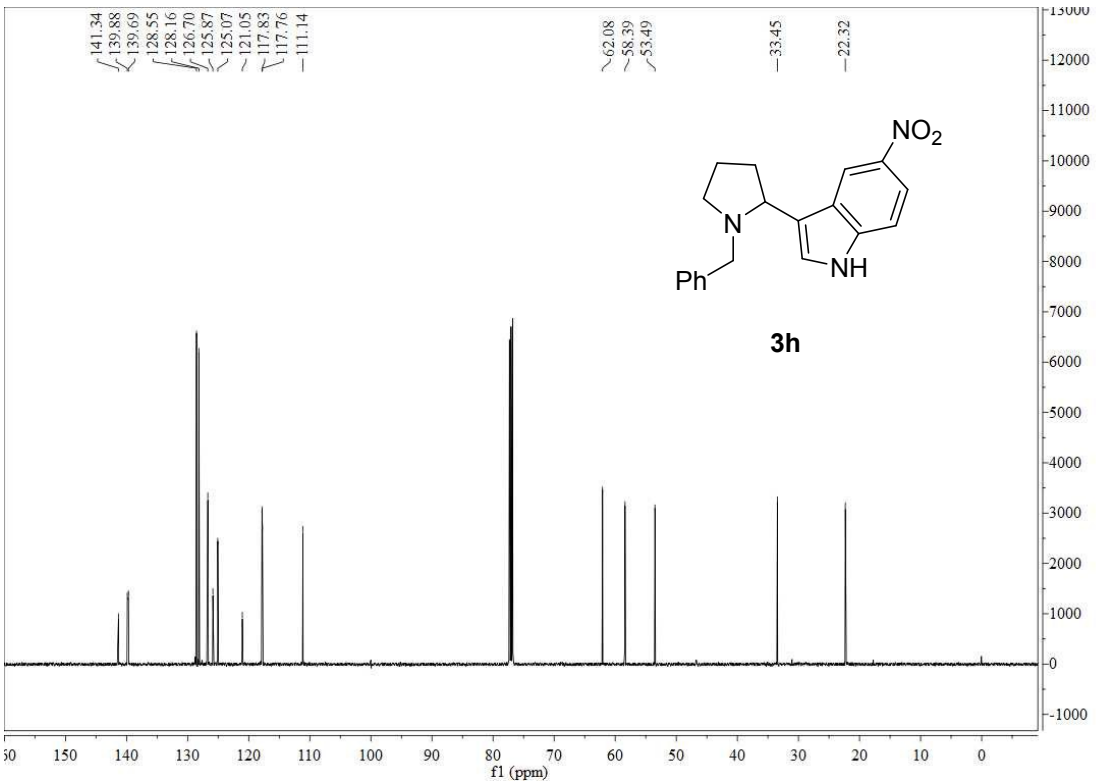
1.11
f1 (ppm)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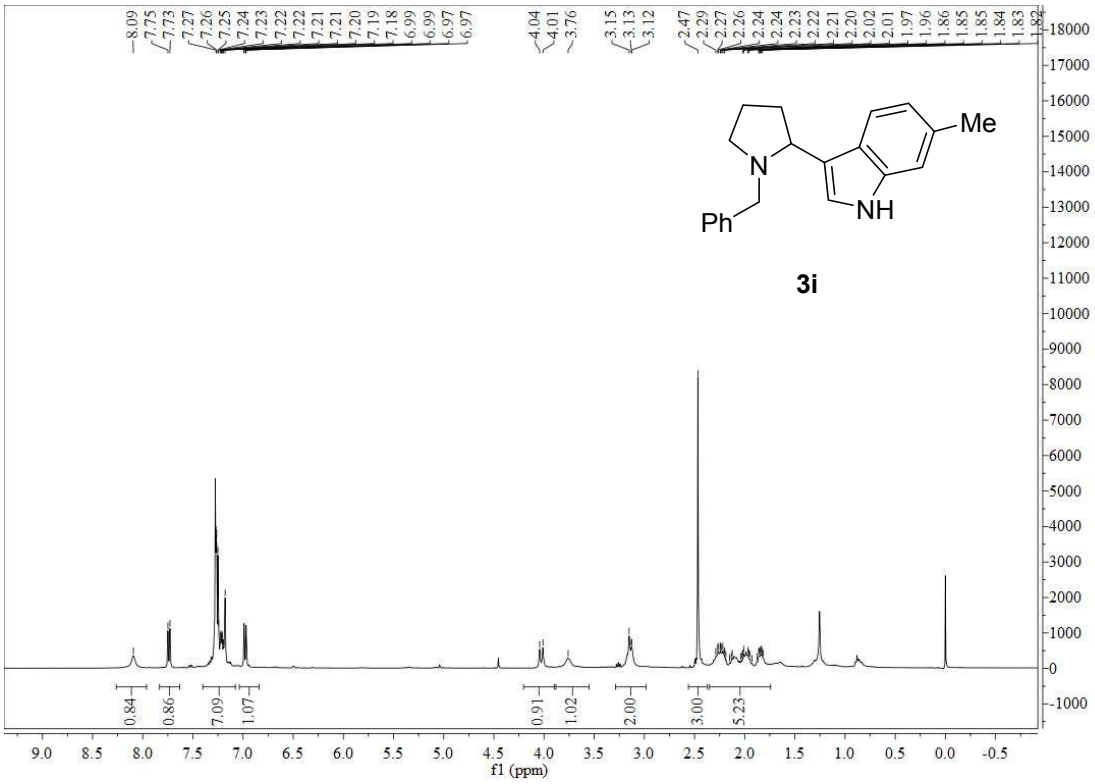
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7.19
7.18
6.99
6.99
6.97
6.97
4.04
4.01
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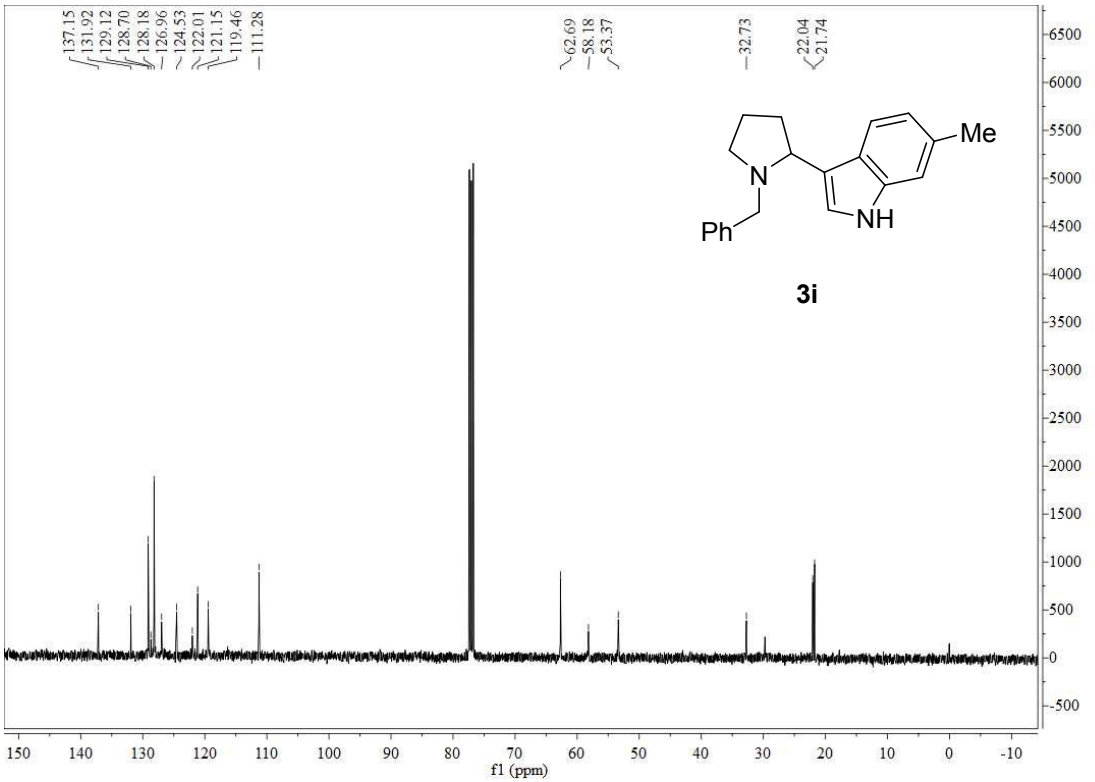
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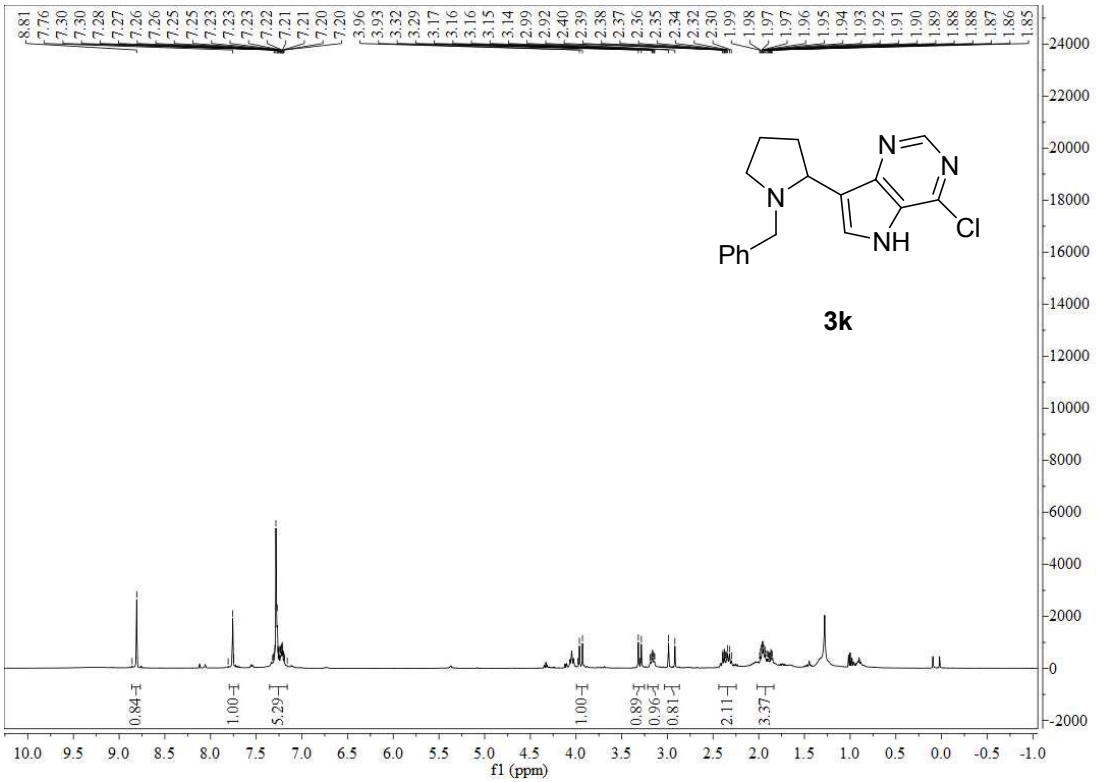
f1 (ppm)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3.96 3.93 3.32 3.29 3.17 3.16 3.16 3.15 3.14 2.99 2.92 2.40 2.39 2.38 2.37 2.36 2.35 2.34 2.32 2.30 1.99 1.98 1.97 1.97 1.96 1.95 1.94 1.93 1.92 1.91 1.90 1.89 1.88 1.88 1.87 1.86 1.85
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NH
Ph
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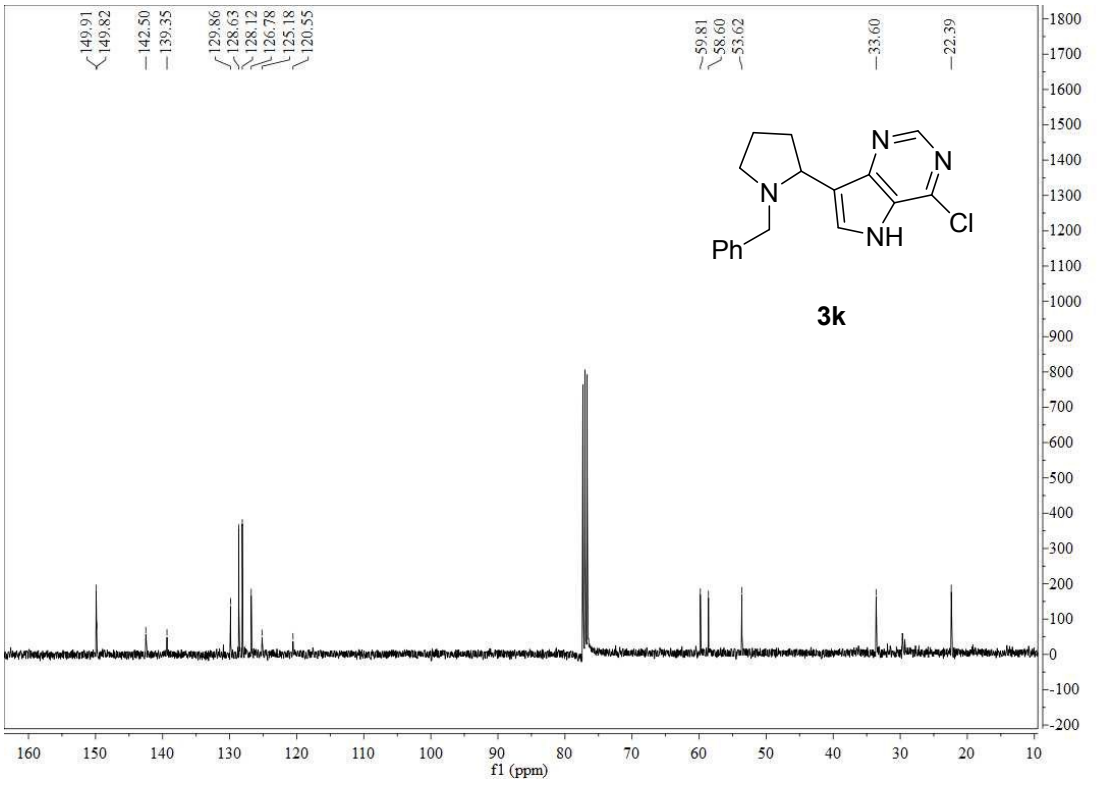
f1 (ppm)

3k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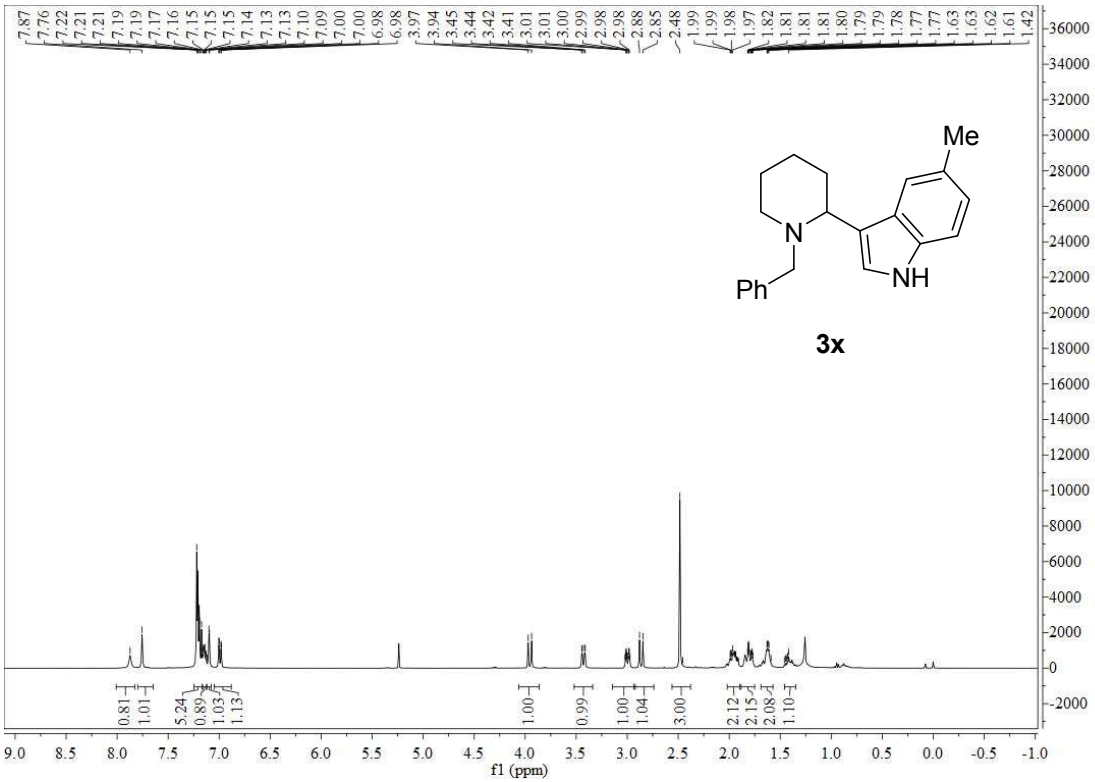
Cl
NH
Ph
f1 (ppm)

3k



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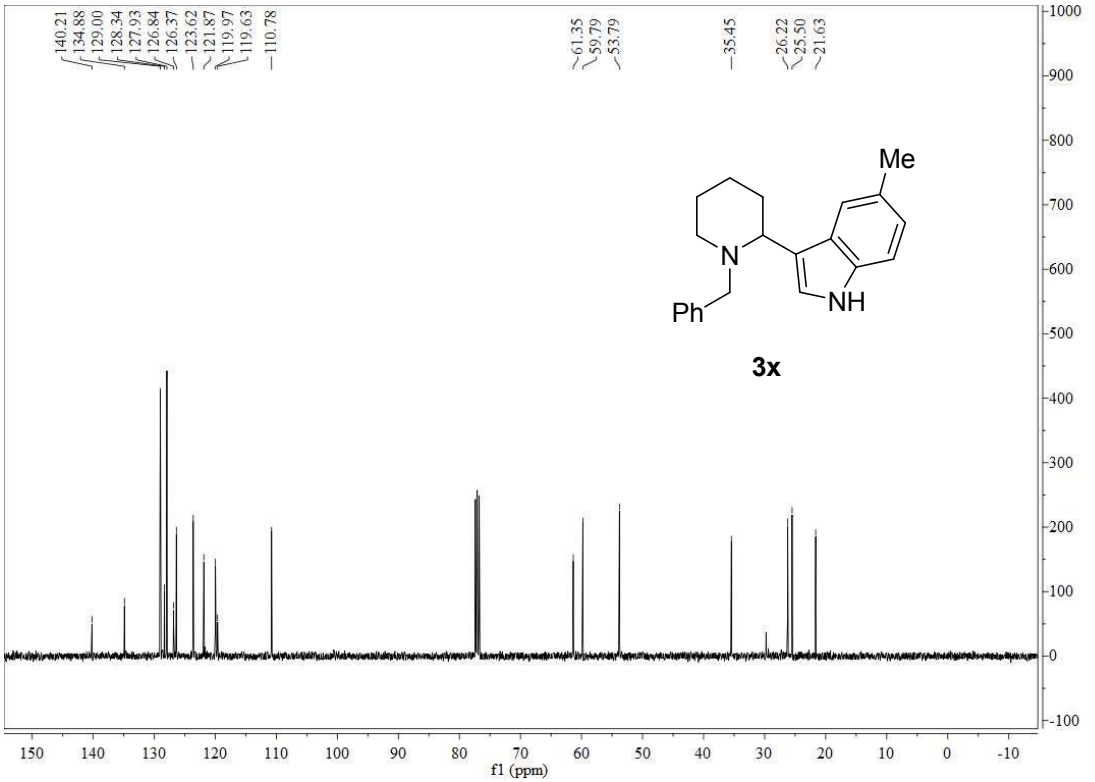

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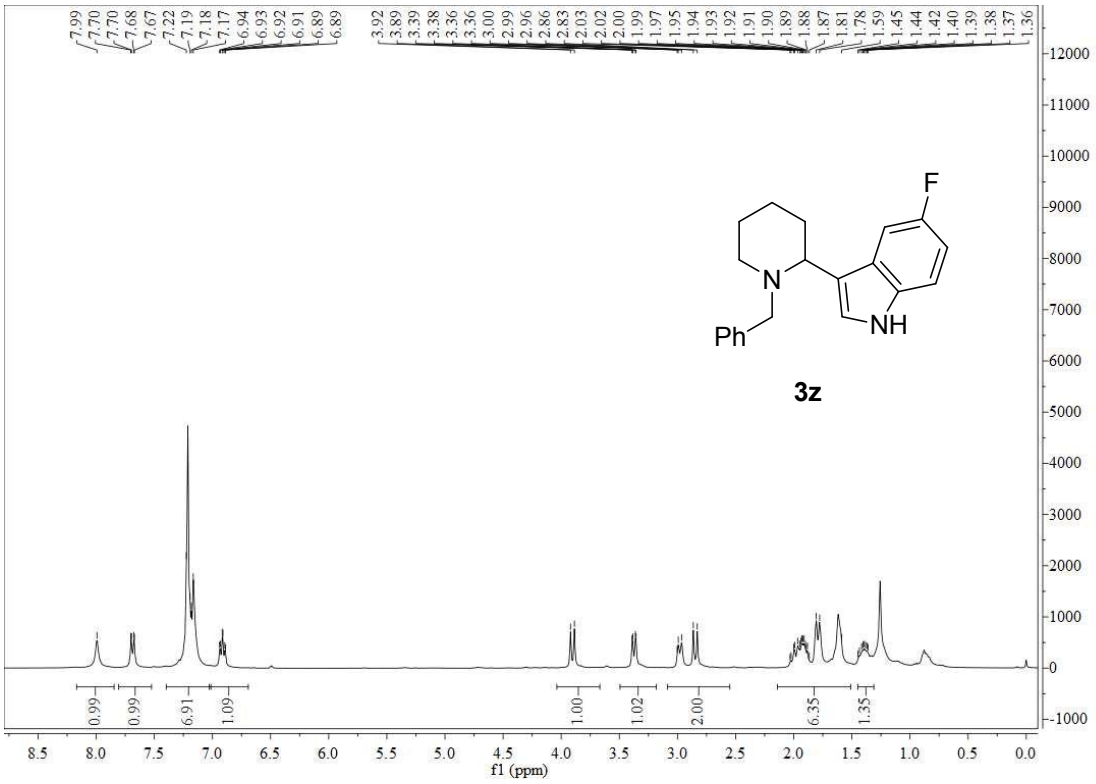
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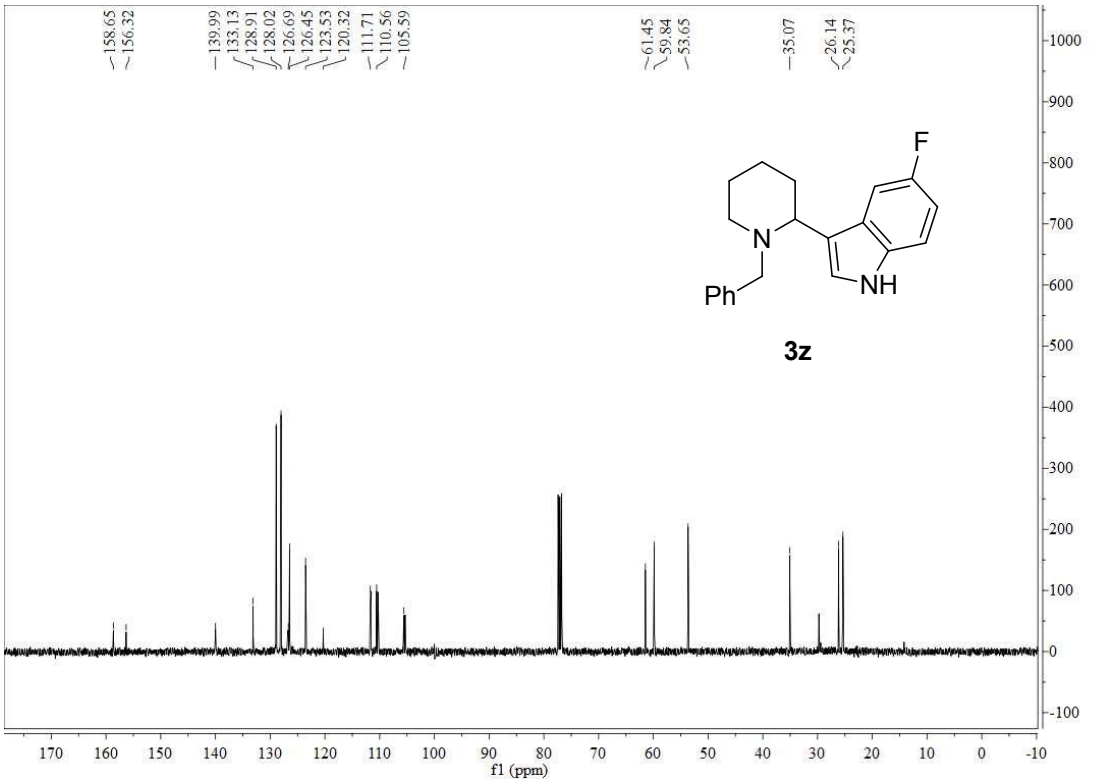
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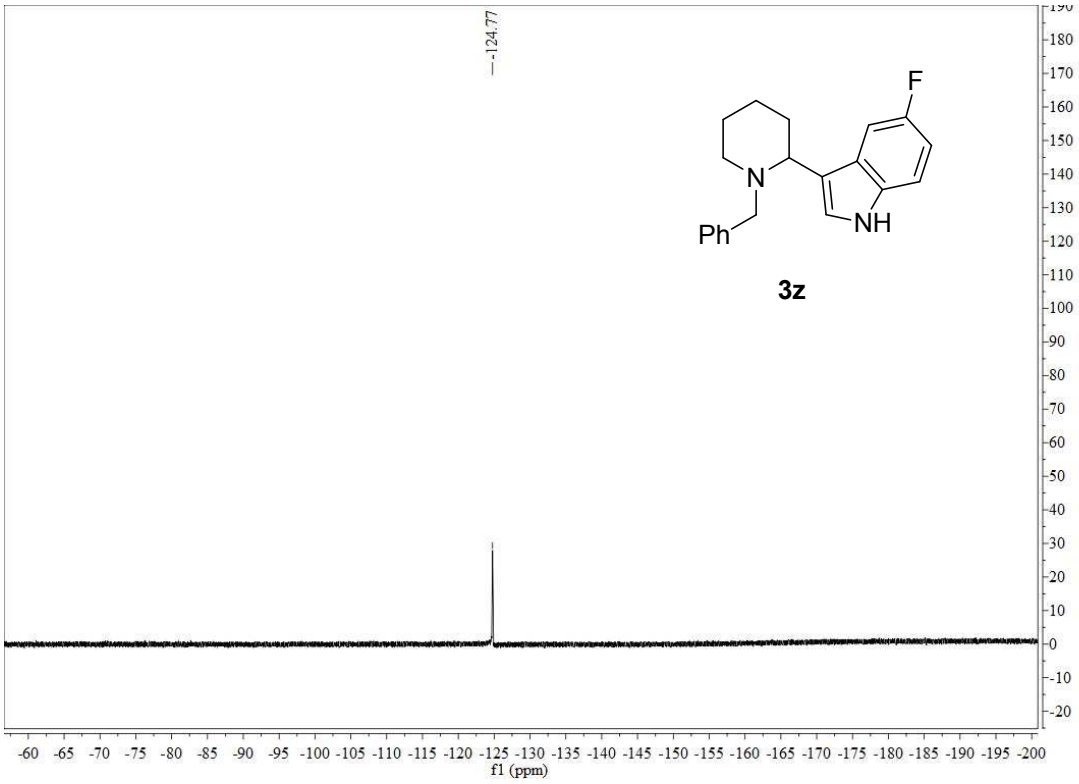
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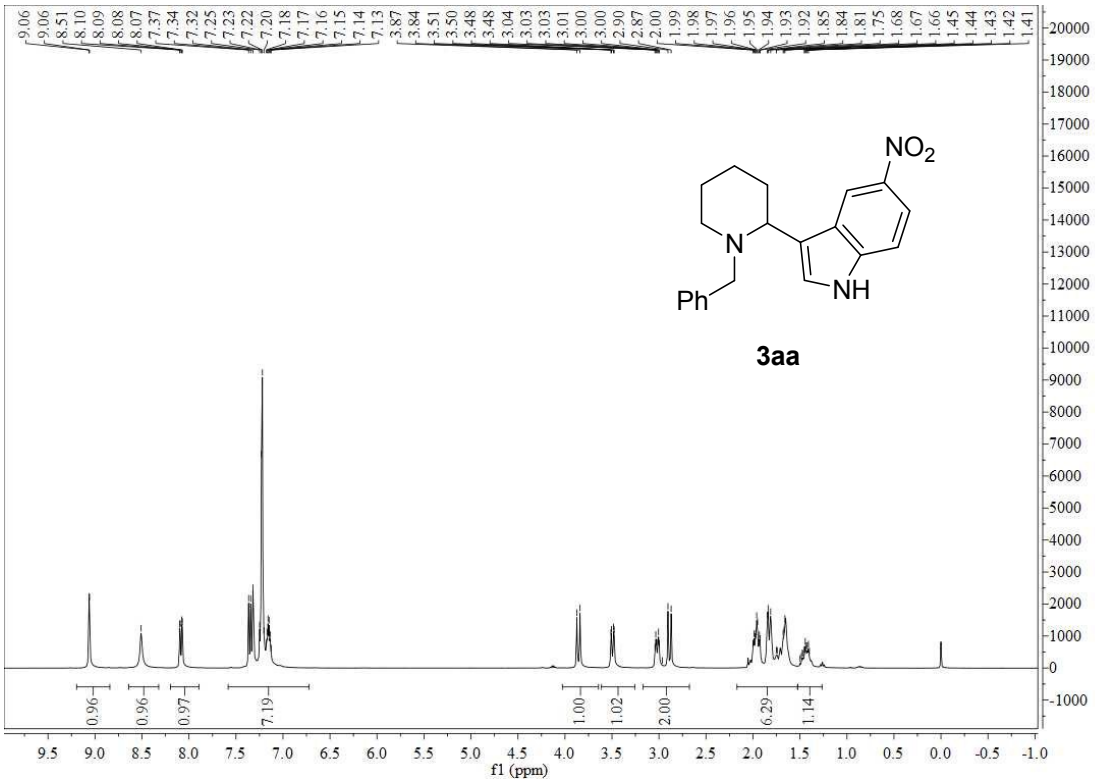

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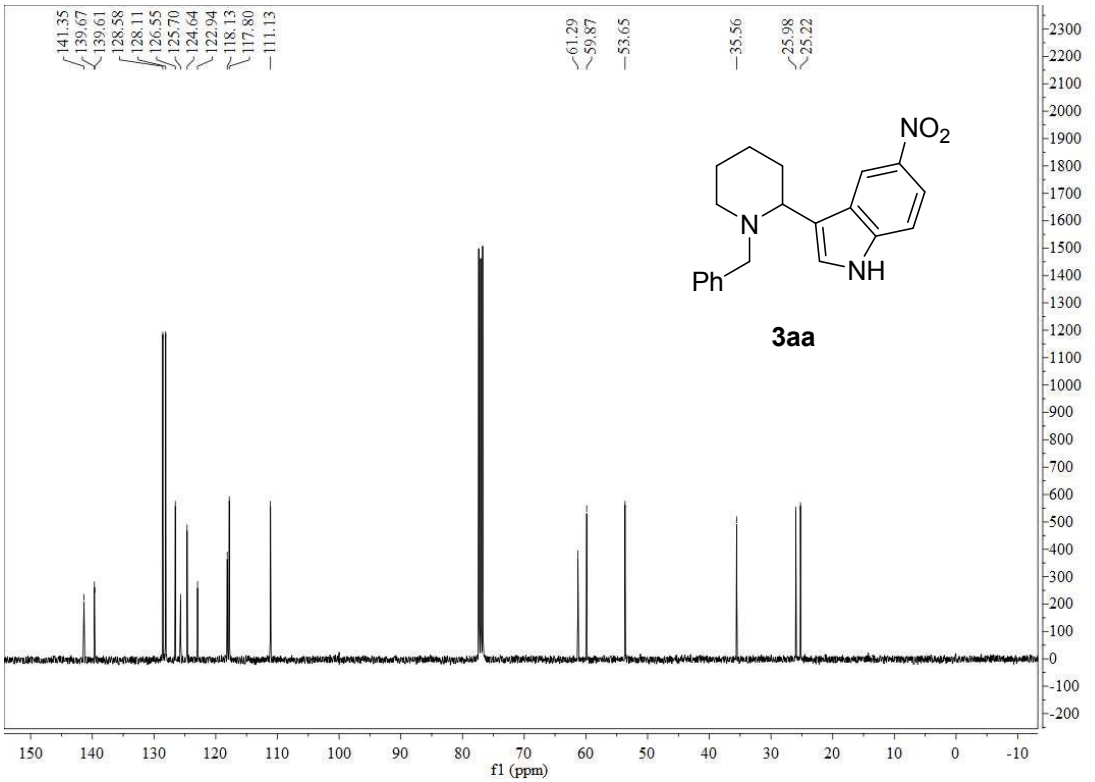

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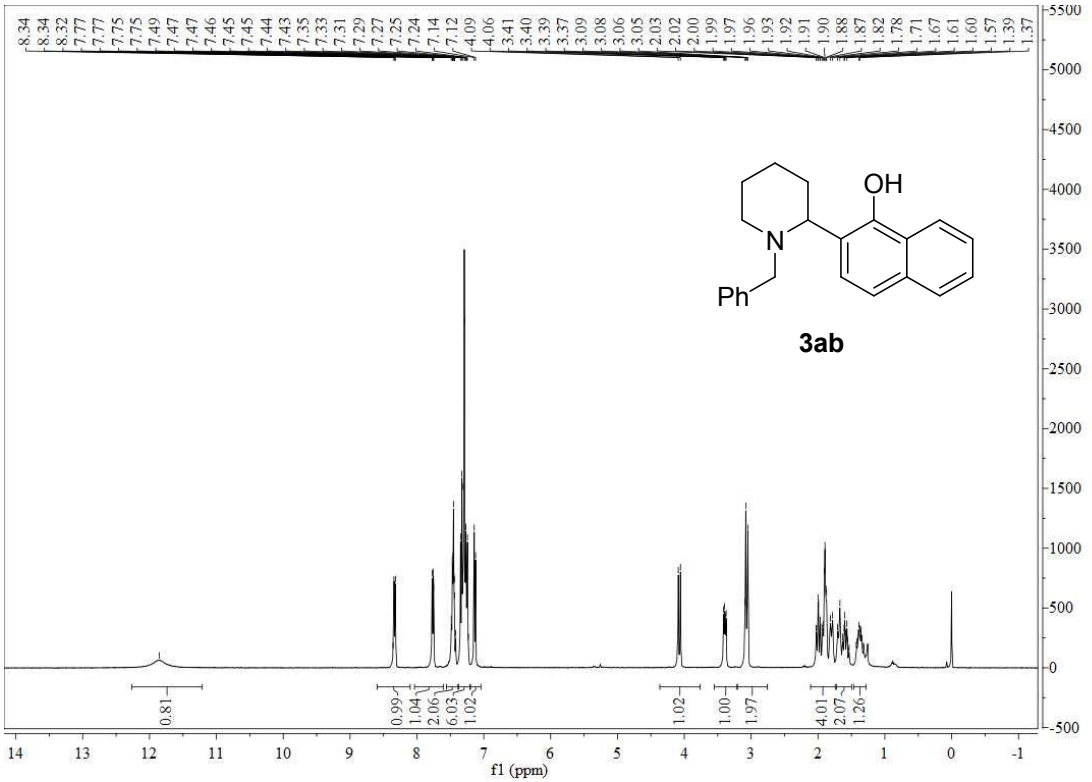

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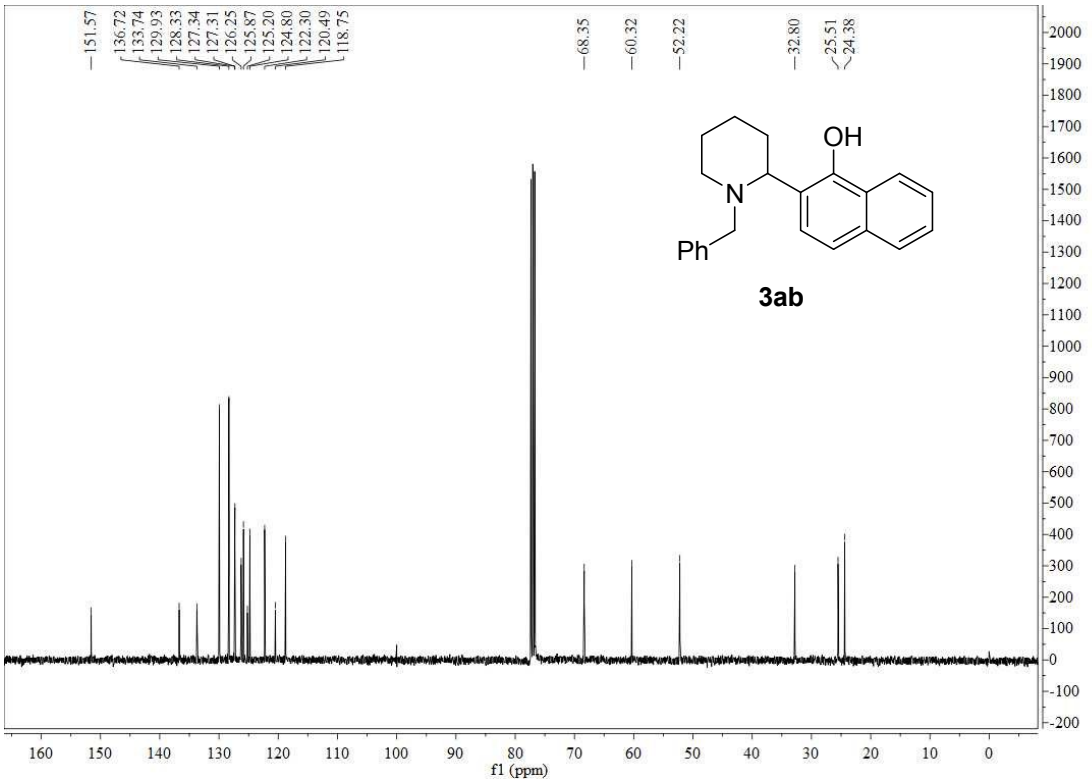

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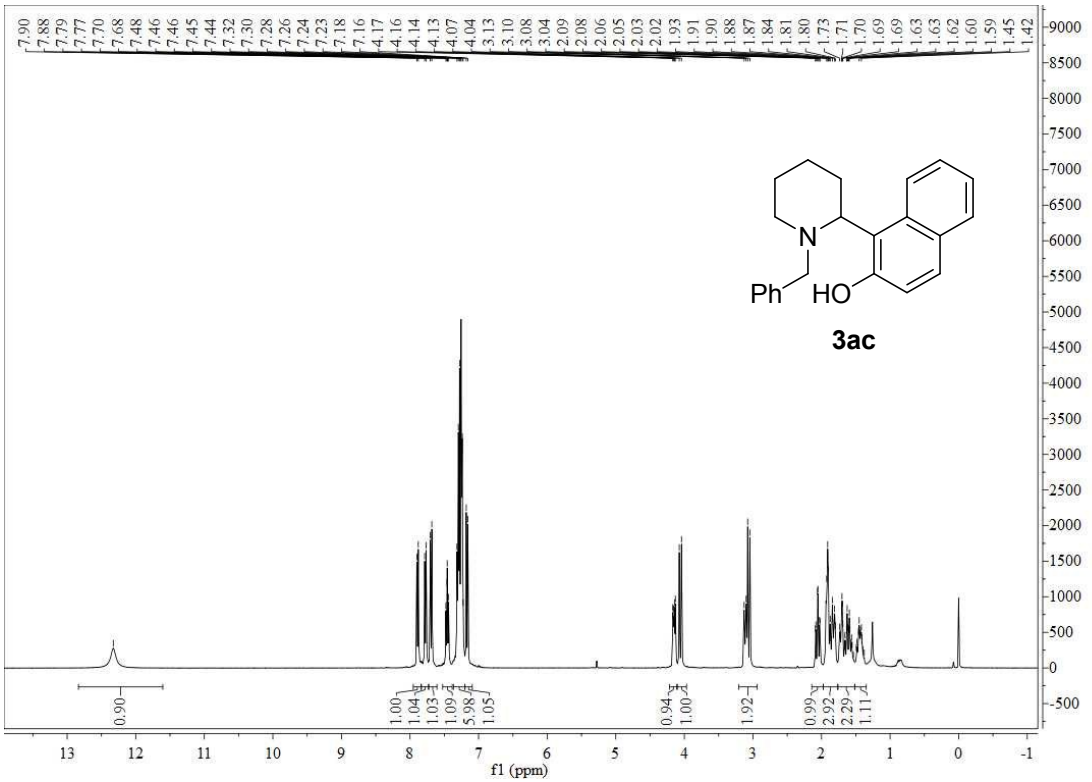
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Ph
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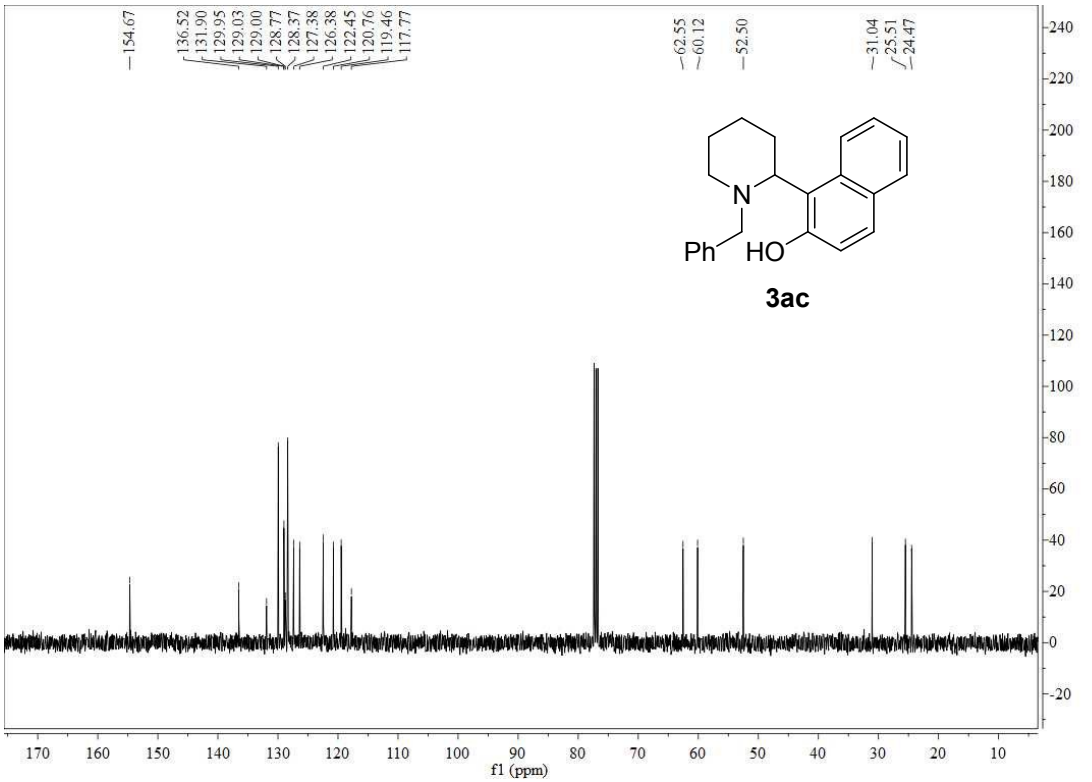
1.11
f1 (ppm)


154.67
136.52
131.90
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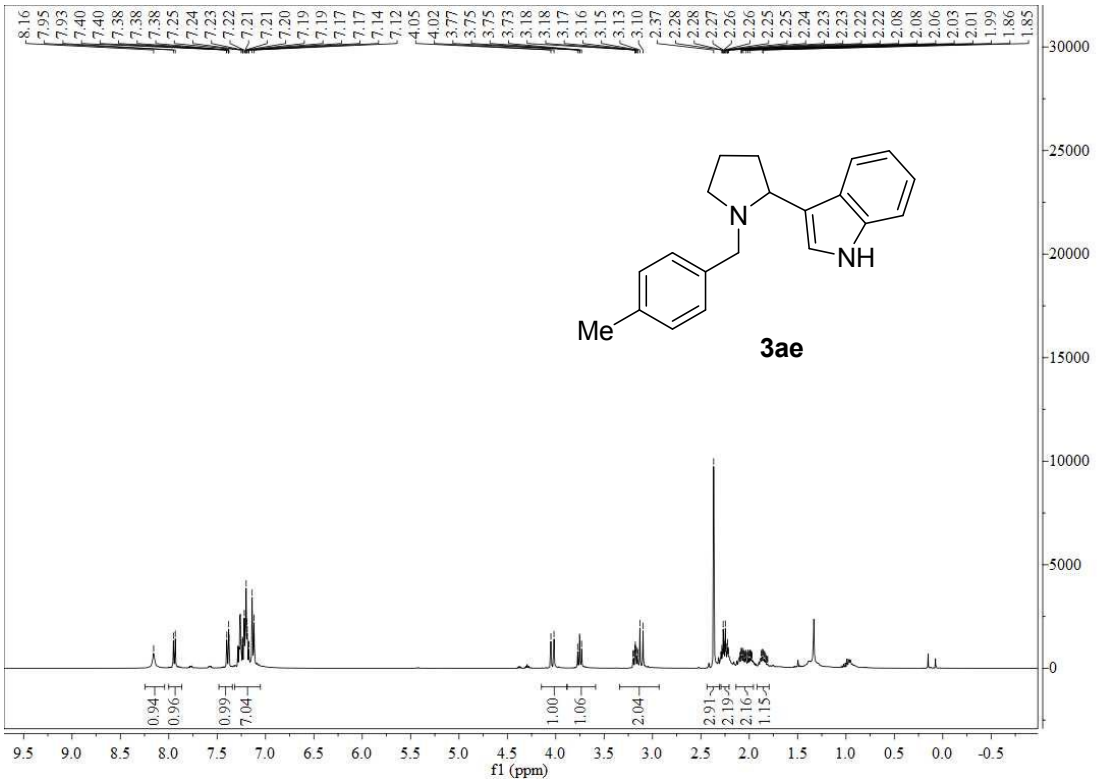
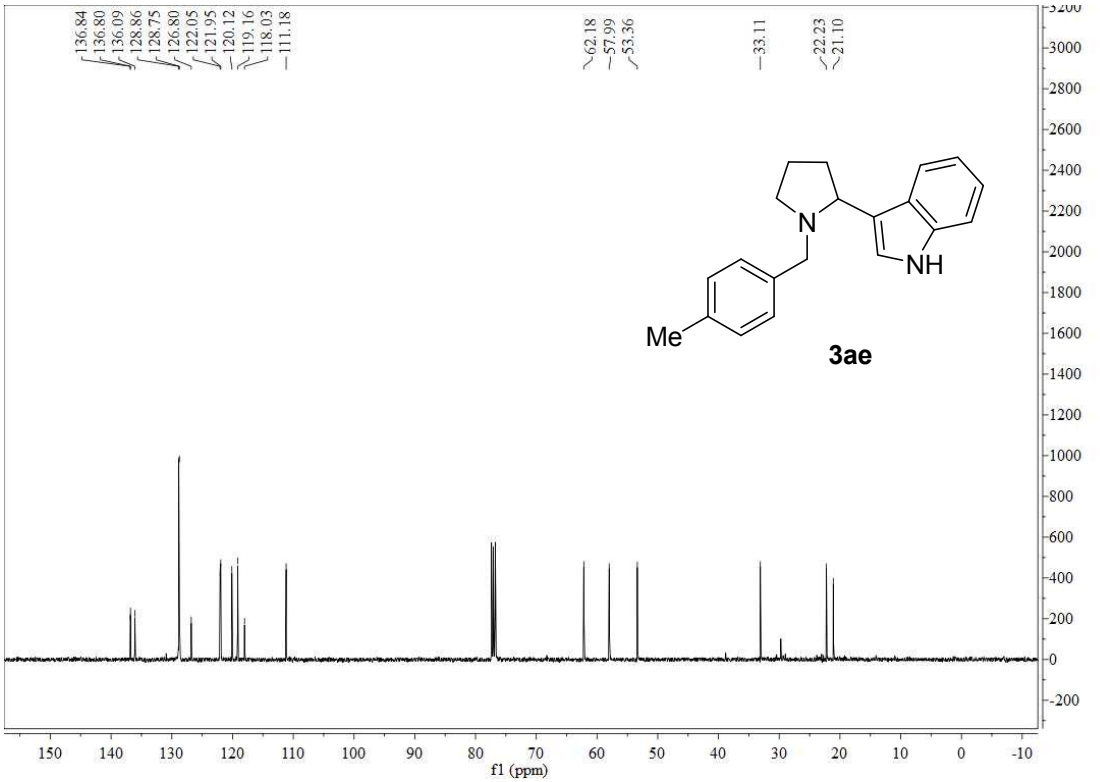
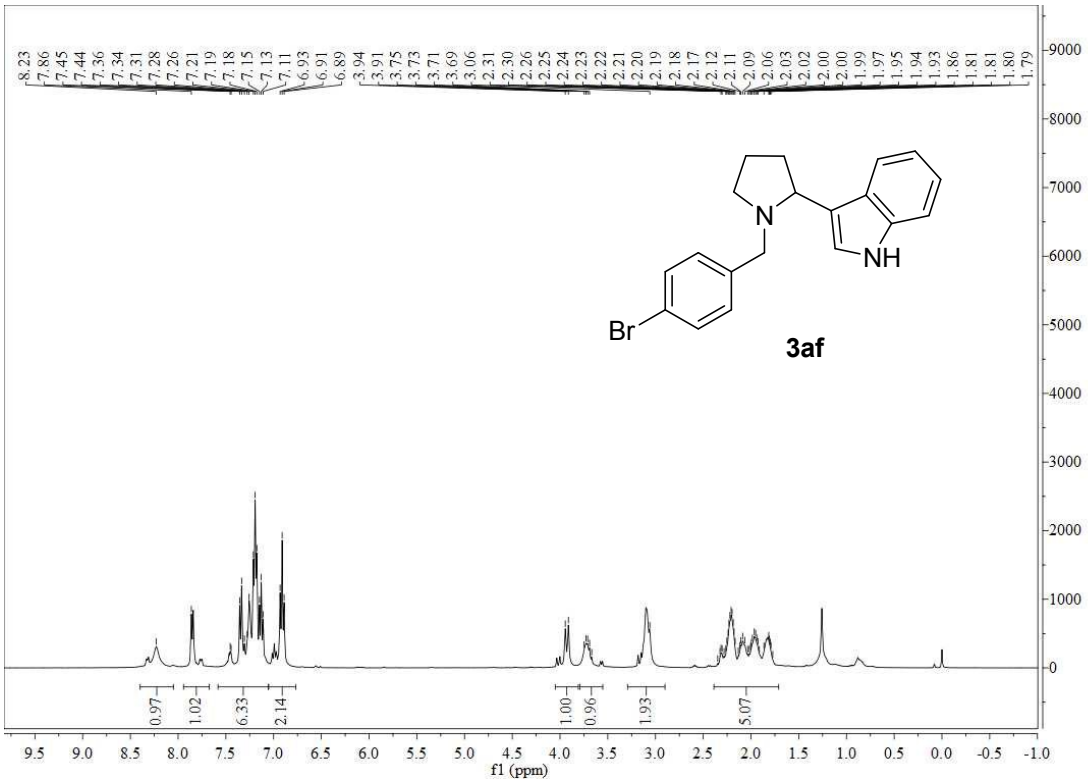
129.00
128.77
128.37
127.38
126.38
122.45
120.76
119.46
117.77
62.55
60.12
52.50
31.04
25.51
24.47
N
Ph
HO
3ac
f1 (ppm)


8.16 7.95 7.93 7.40 7.40 7.38 7.38 7.38 7.25 7.24 7.23 7.22 7.21 7.21 7.20 7.19 7.19 7.17 7.17 7.14 7.12 4.05 4.02 3.77 3.75 3.75 3.73 3.18 3.18 3.17 3.16 3.15 3.13 3.10 2.37 2.28 2.28 2.27 2.26 2.26 2.25 2.25 2.24 2.23 2.23 2.22 2.22 2.08 2.08 2.06 2.03 2.01 1.99 1.86 1.85
N
NH
Me
3ae
0.94 0.96 0.99 7.04 1.00 1.06 2.04 2.91 2.19 2.16 1.15
f1 (ppm)


136.84 136.80 136.09 128.86 128.75 126.80 122.05 121.95 120.12 119.16 118.03 111.18 62.18 57.99 53.36 33.11 22.23 21.10
N
NH
Me
3ae
f1 (ppm)


8.23
7.86
7.45
7.44
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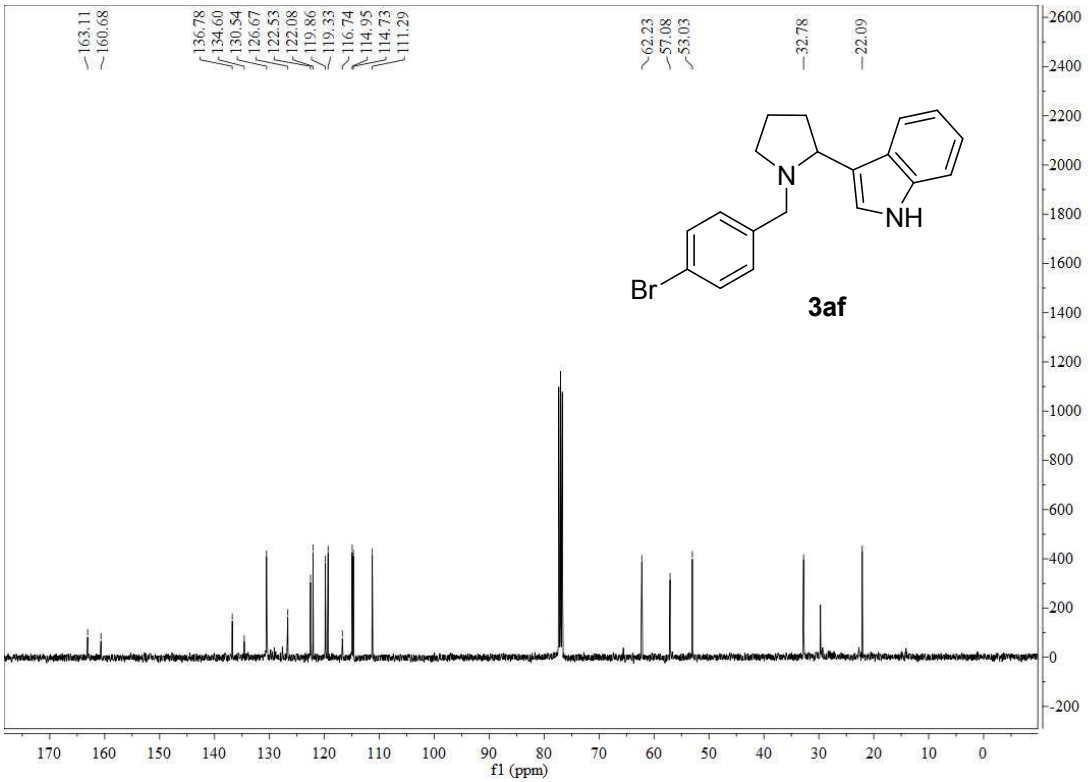
7.34
7.31
7.28
7.26
7.21
7.19
7.18
7.15
7.13
7.11
6.93
6.91
6.89
3.94
3.91
3.75
3.73
3.71
3.69
3.06
2.31
2.30
2.26
2.25
2.24
2.23
2.22
2.21
2.20
2.19
2.18
2.17
2.12
2.11
2.09
2.06
2.03
2.02
2.00
2.00
1.99
1.97
1.95
1.94
1.93
1.86
1.81
1.81
1.80
1.79
N
NH
Br
3af
0.97
1.02
6.33
2.14
1.00
0.96
1.93
5.07
f1 (ppm)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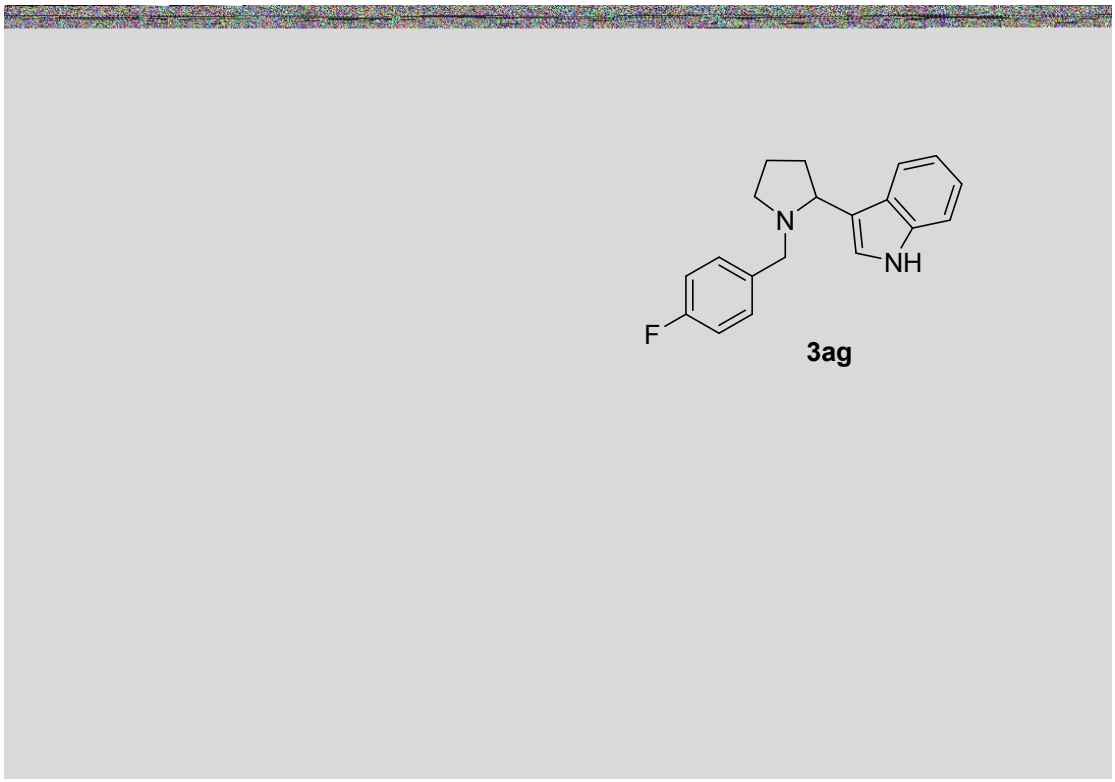
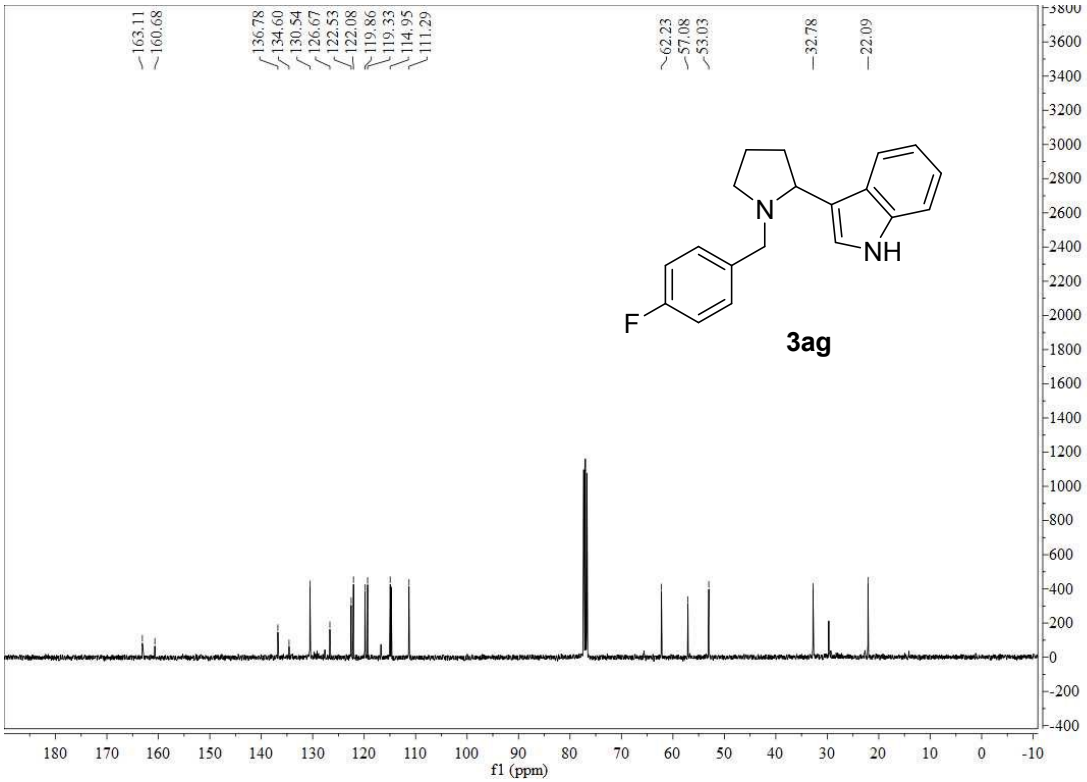
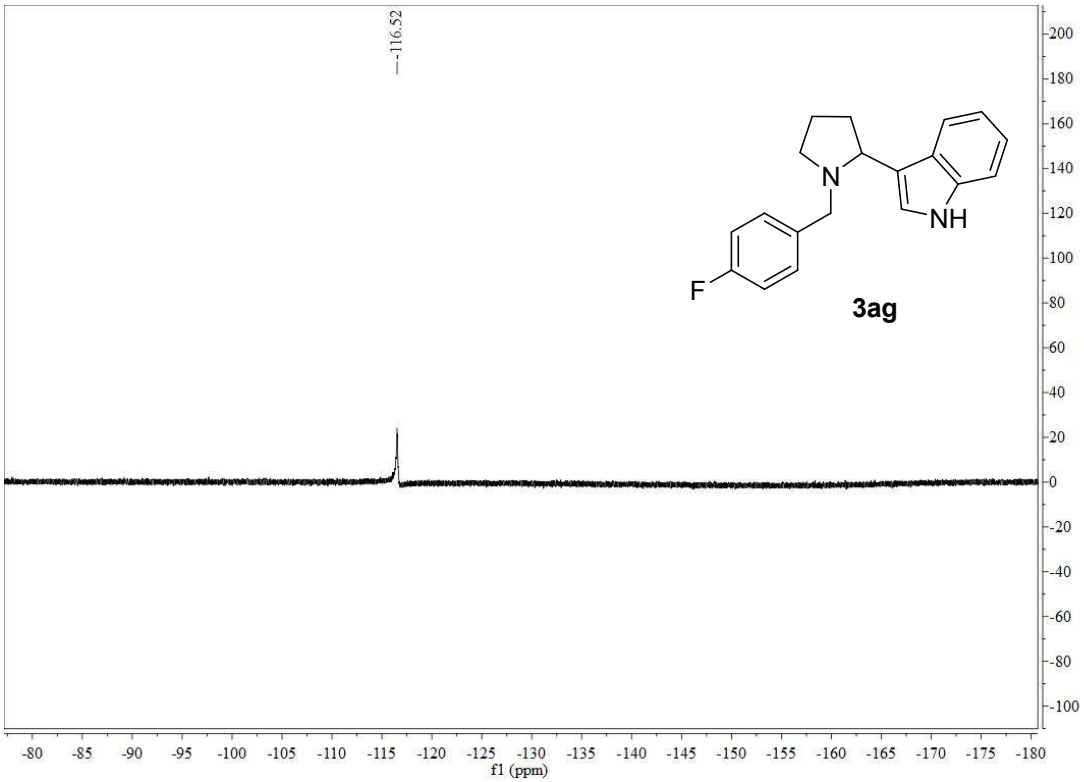
160.68
136.78
134.60
130.54
126.67
122.53
122.08
119.86
119.33
116.74
114.95
114.73
111.29
62.23
57.08
53.03
32.78
22.09
N
NH
Br
3af
f1 (ppm)


N
NH
F
3ag


163.11
160.68
136.78
134.60
130.54
126.67
122.53
122.08
119.86
119.33
114.95
111.29
62.23
57.08
53.03
32.78
22.09
N
NH
F
3ag
f1 (ppm)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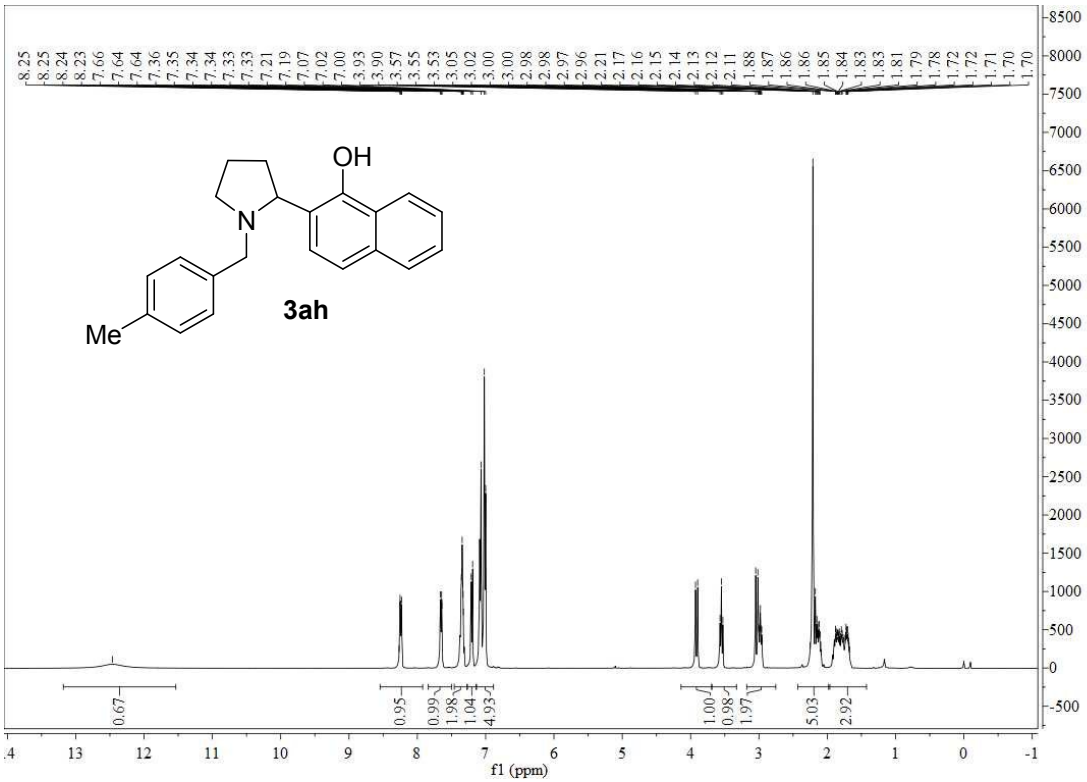
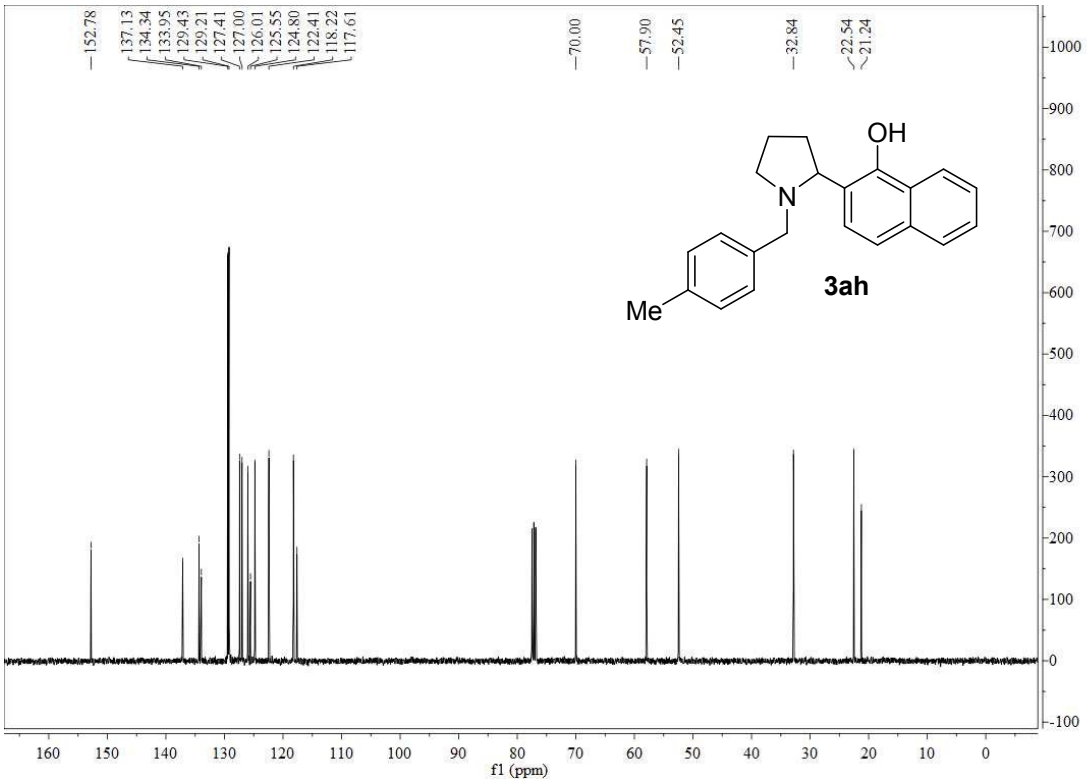
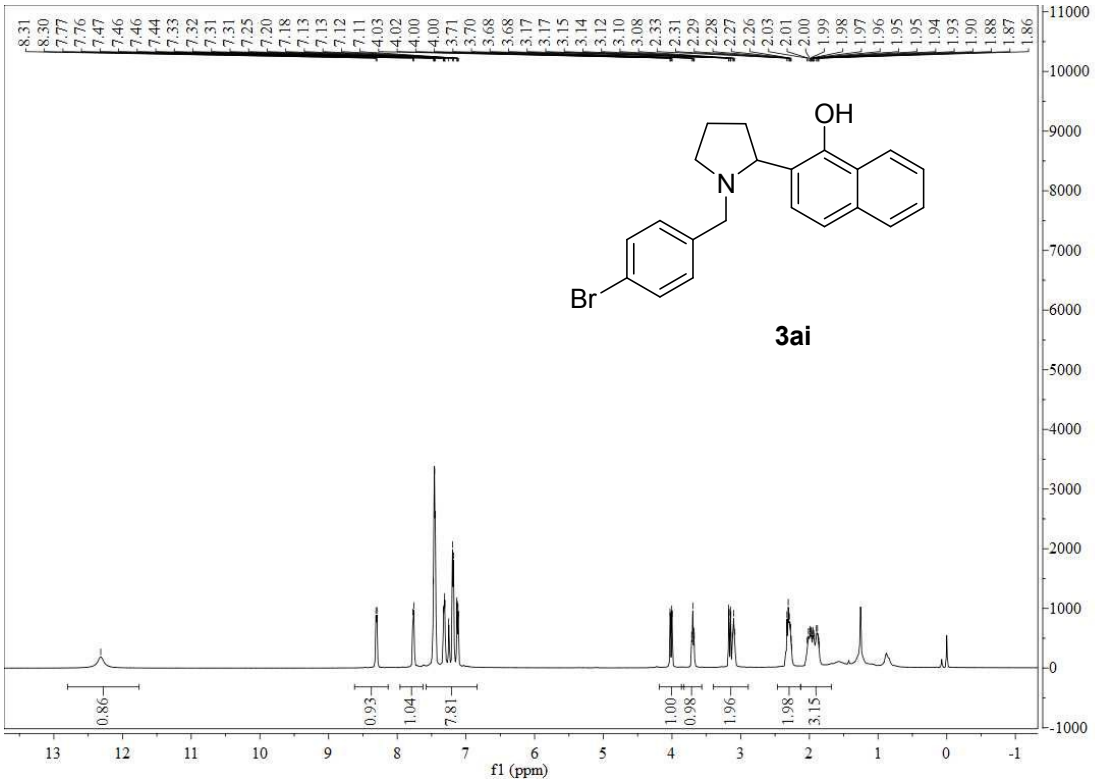
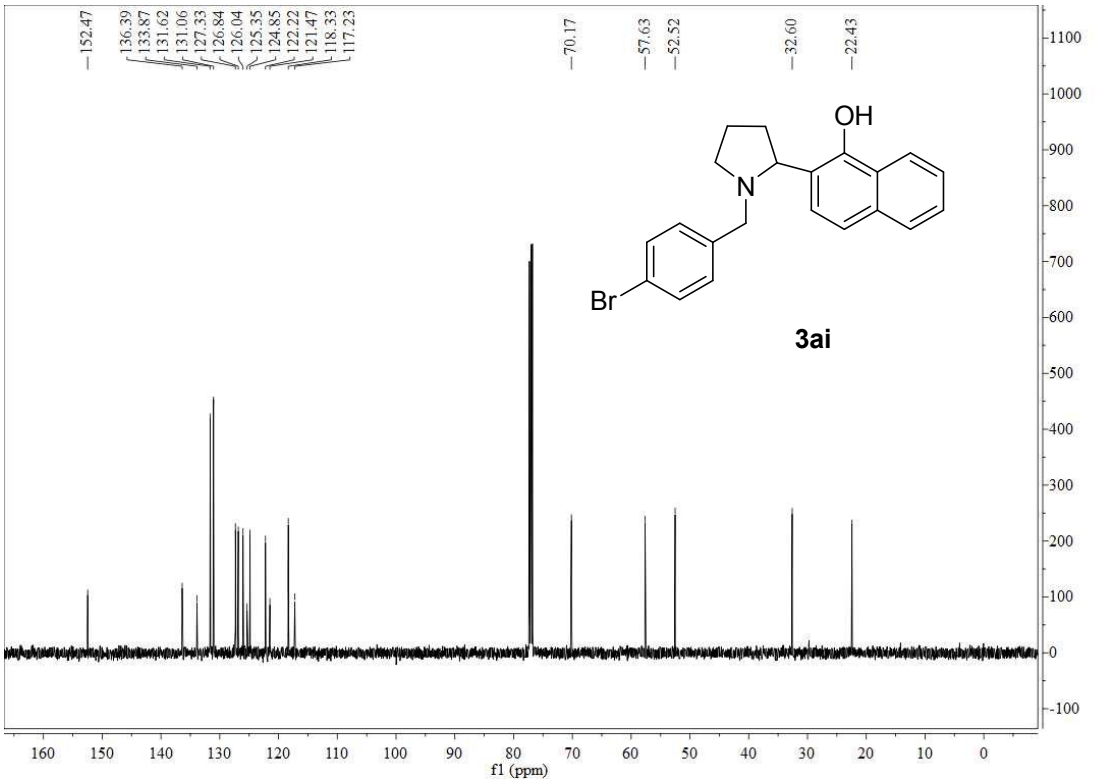
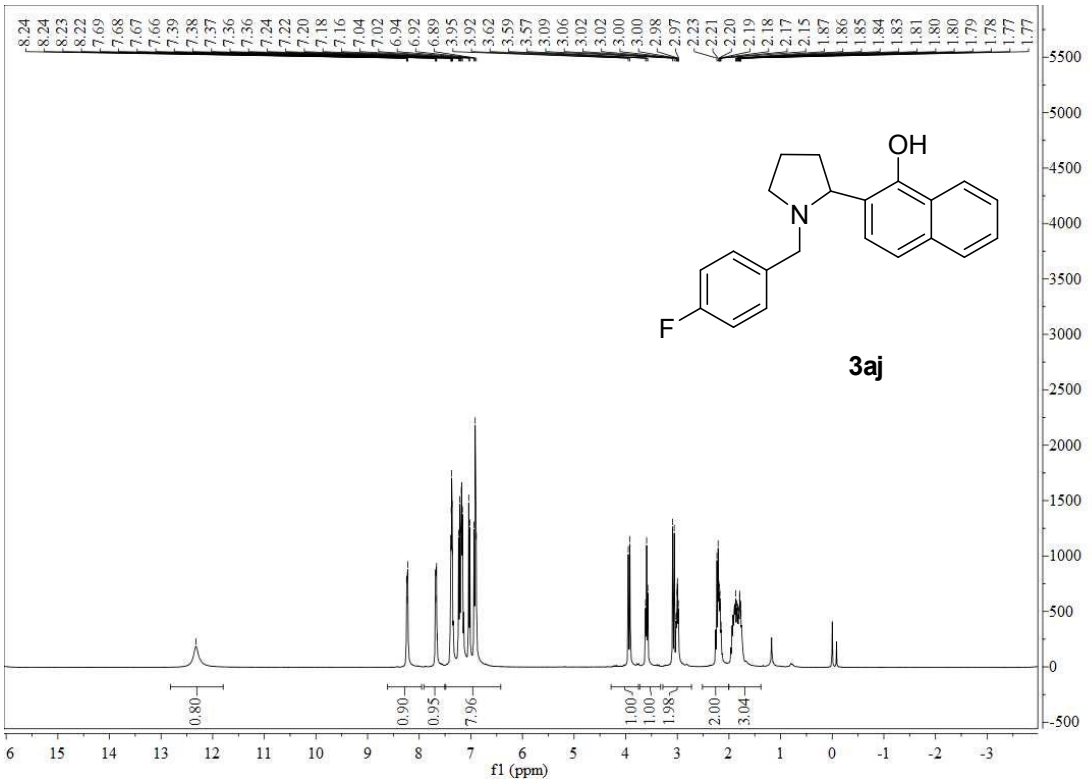
N
NH
F
3ag
f1 (ppm)

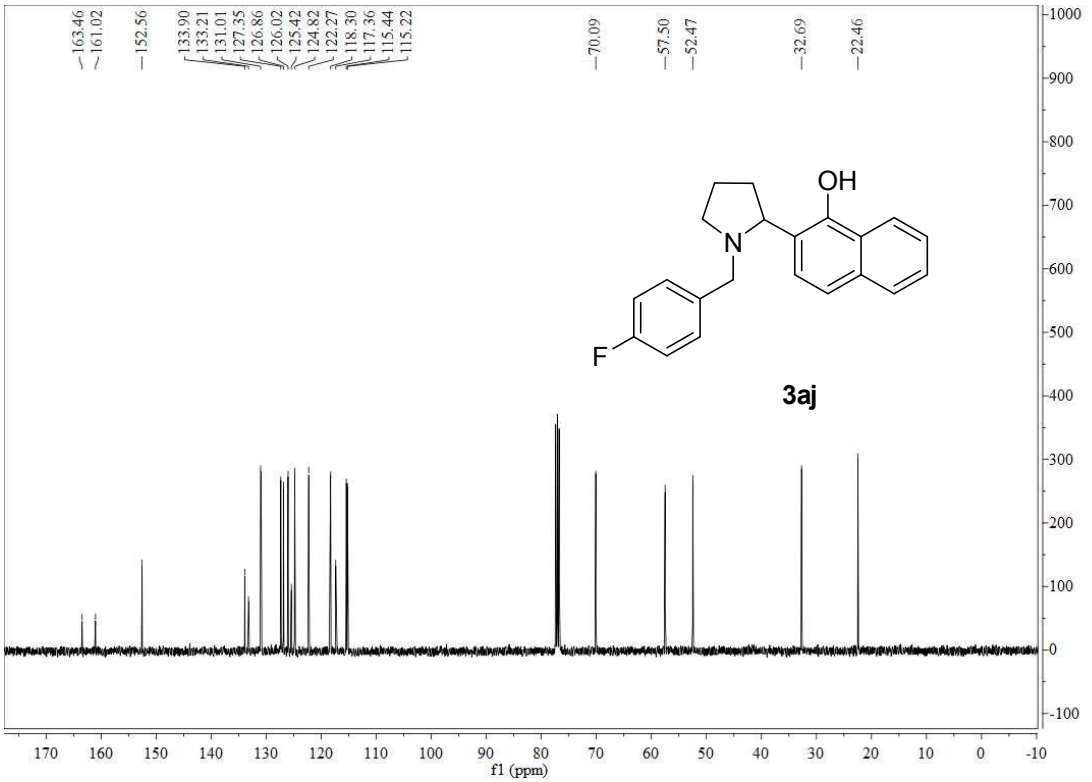

OH
N
Me
3ah
f1 (ppm)

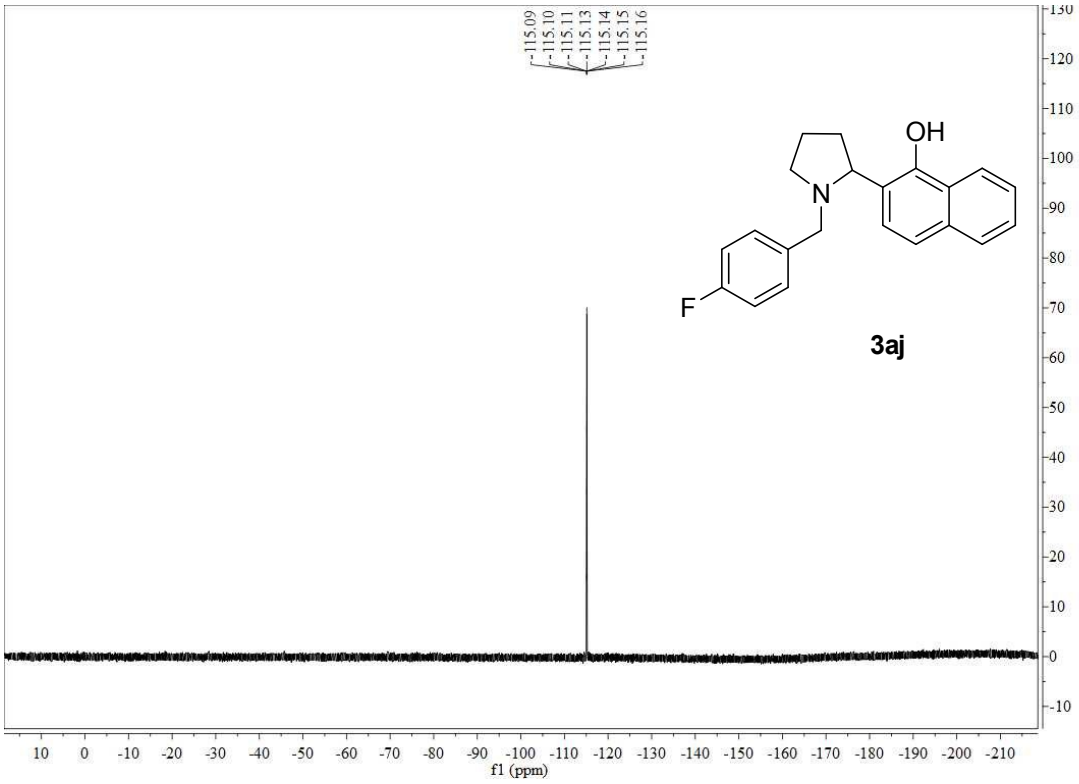

OH
N
Me
3ah
f1 (ppm)

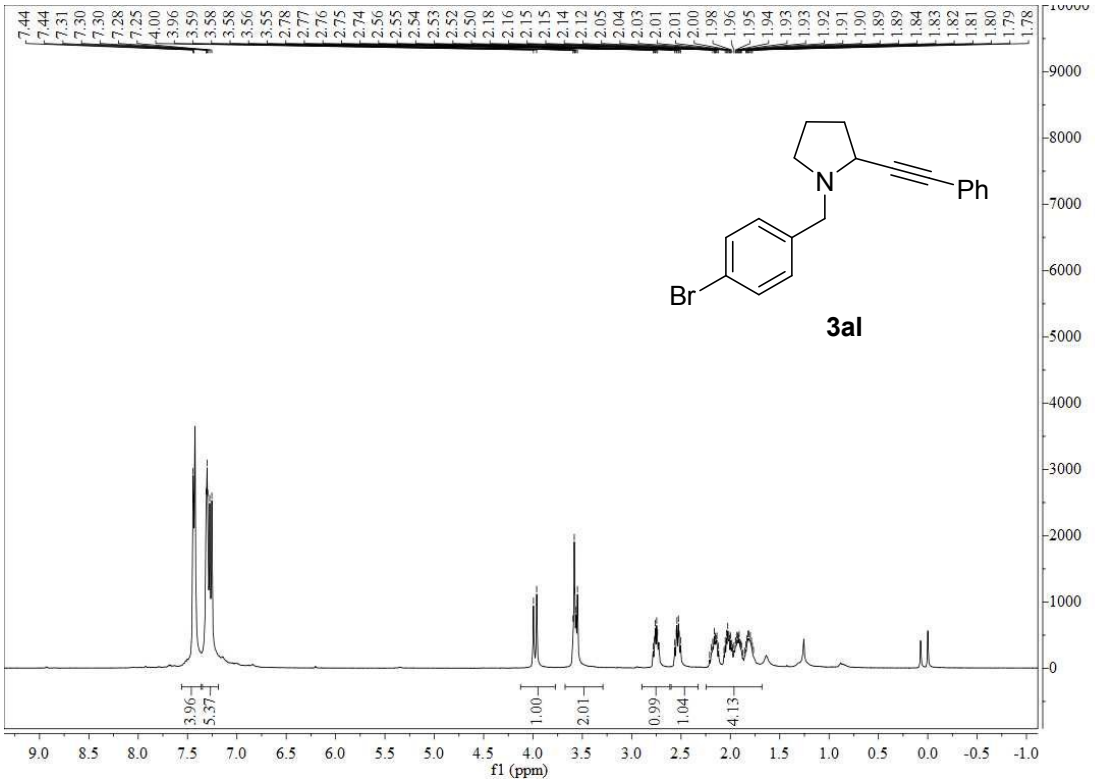

OH
N
Br
3ai
f1 (ppm)

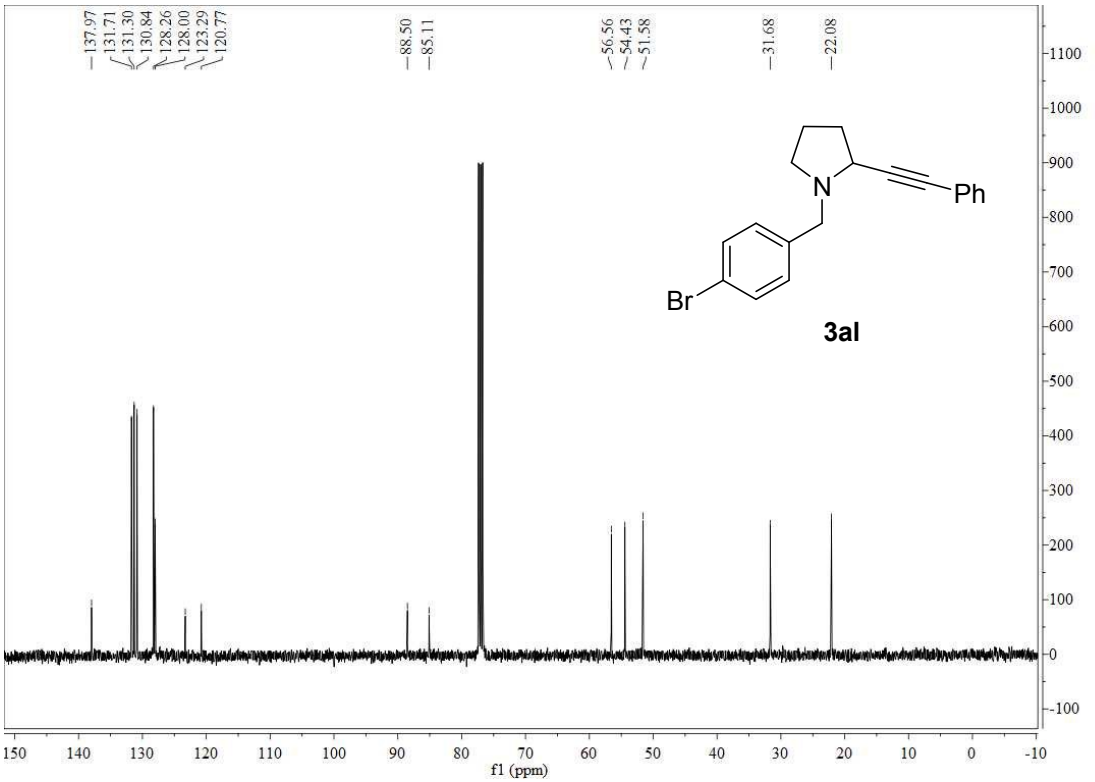

OH
N
Br
3ai
f1 (ppm)

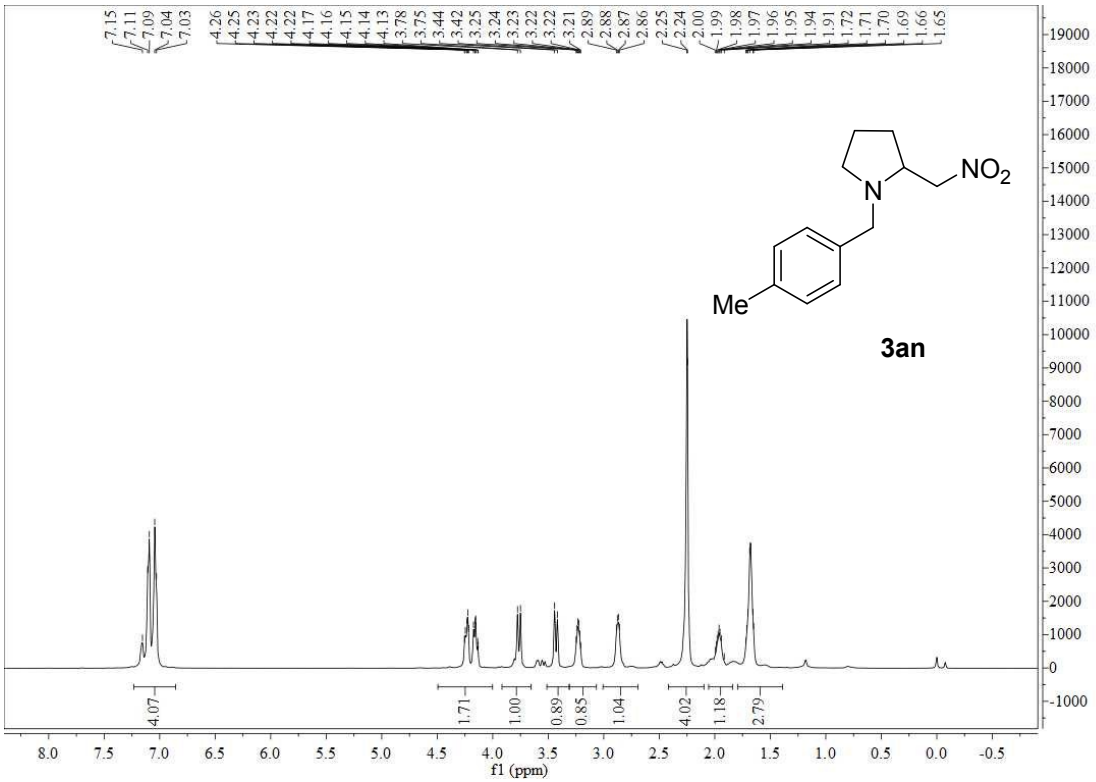

OH
N
F
3aj
f1 (ppm)


OH
N
F
3aj
f1 (ppm)


-115.09
-115.10
-115.11
-115.13
-115.14
-115.15
-115.16
OH
N
F
3aj
f1 (ppm)


7.44 7.44 7.31 7.30 7.30 7.28 7.25 4.00 3.96 3.59 3.58 3.58 3.56 3.55 2.78 2.77 2.76 2.75 2.74 2.56 2.55 2.54 2.53 2.52 2.50 2.18 2.16 2.15 2.15 2.14 2.12 2.05 2.04 2.03 2.01 2.01 2.00 1.98 1.96 1.95 1.94 1.93 1.93 1.92 1.91 1.90 1.89 1.89 1.84 1.83 1.82 1.81 1.80 1.79 1.78
N
Ph
Br
3al
3.96
5.37
1.00
2.01
0.99
1.04
4.13
f1 (ppm)


137.97 131.71 131.30 130.84 128.26 128.00 123.29 120.77
88.50 85.11
56.56 54.43 51.58
31.68
22.08
N
Ph
Br
3al
f1 (ppm)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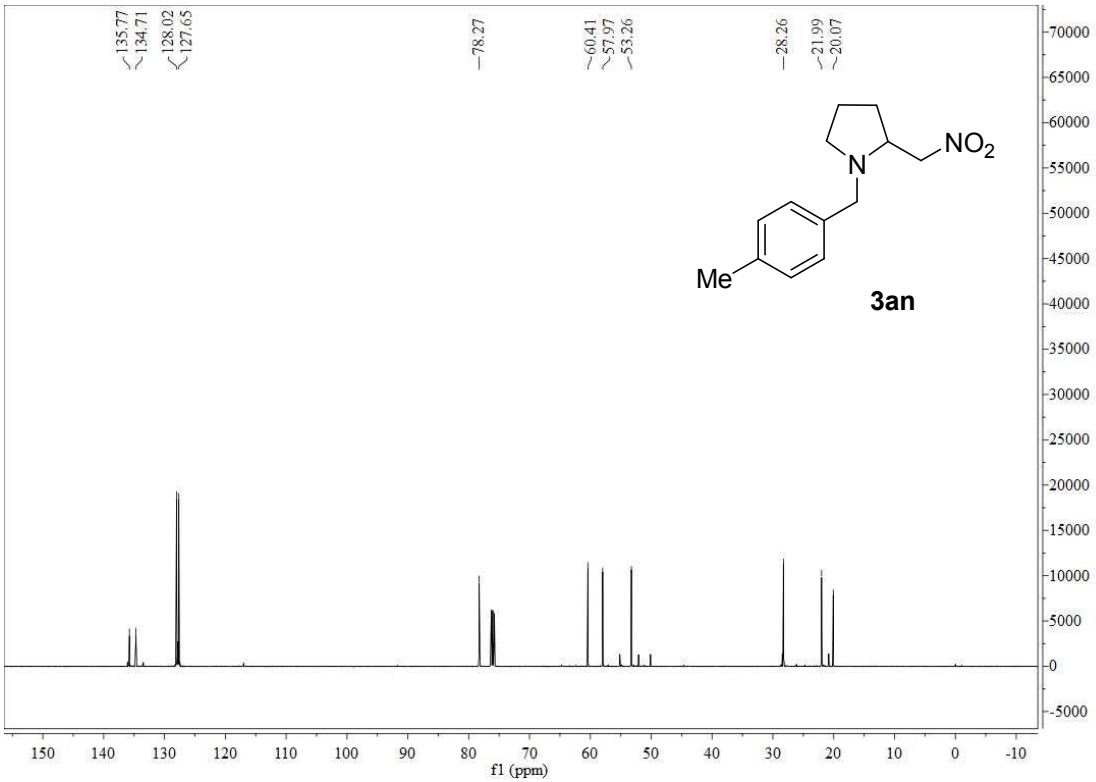
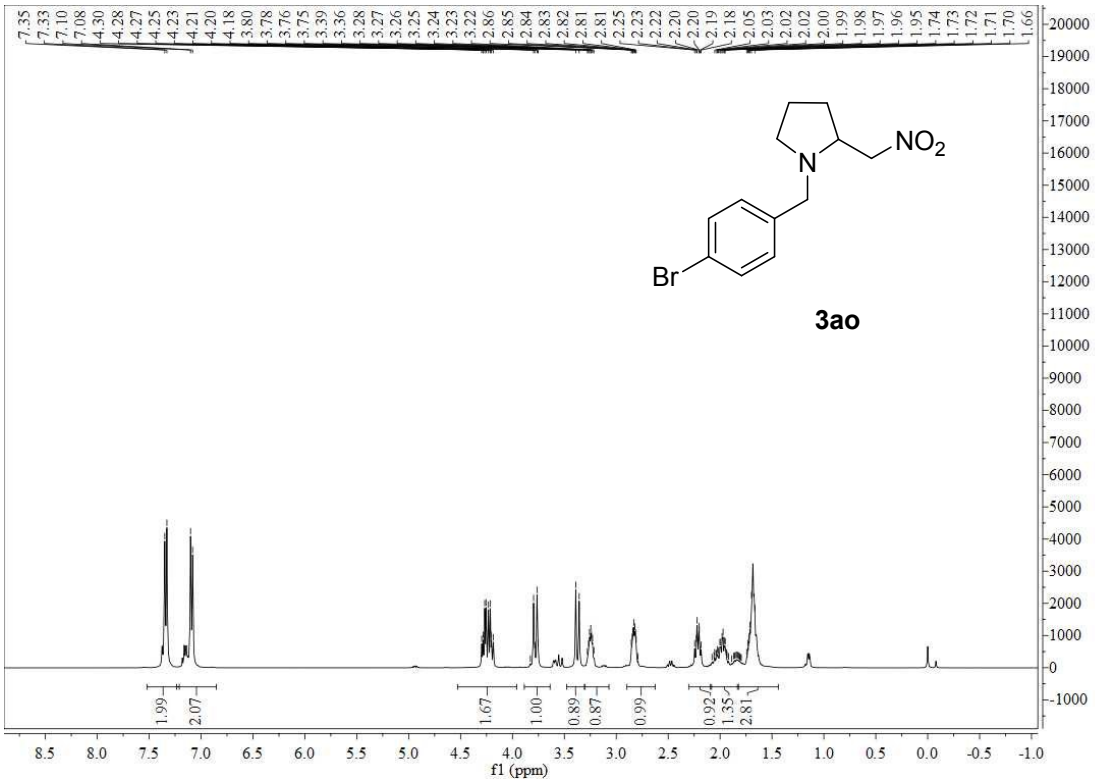
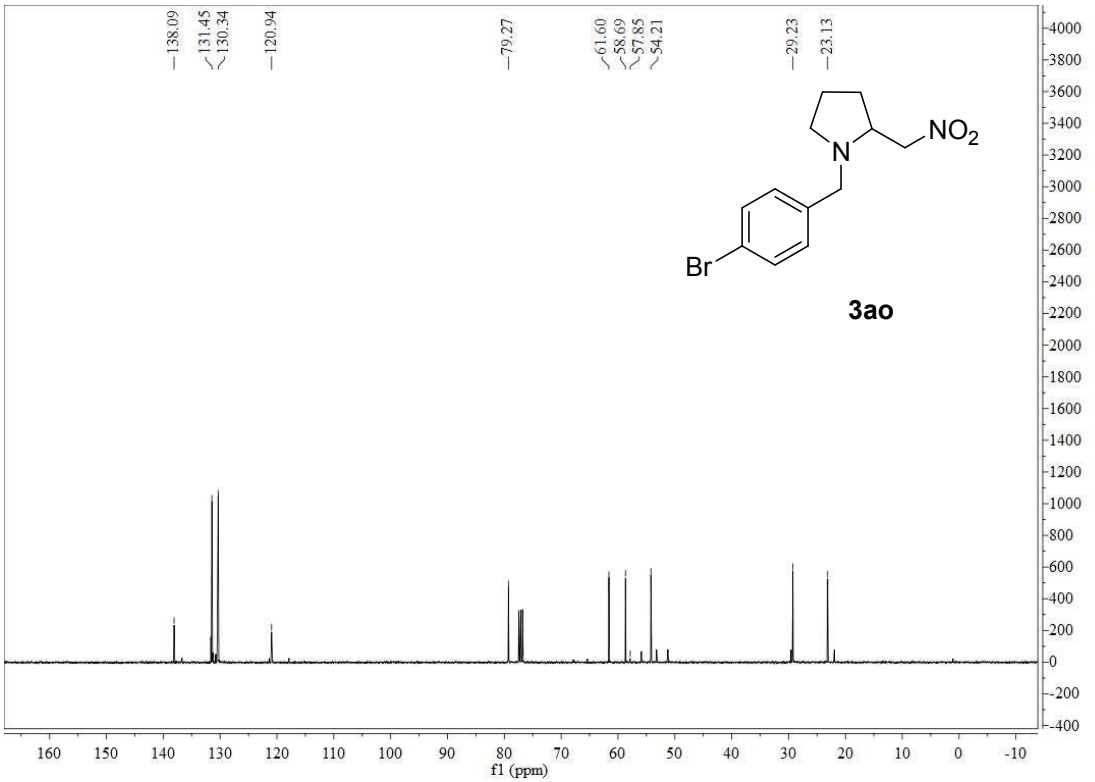
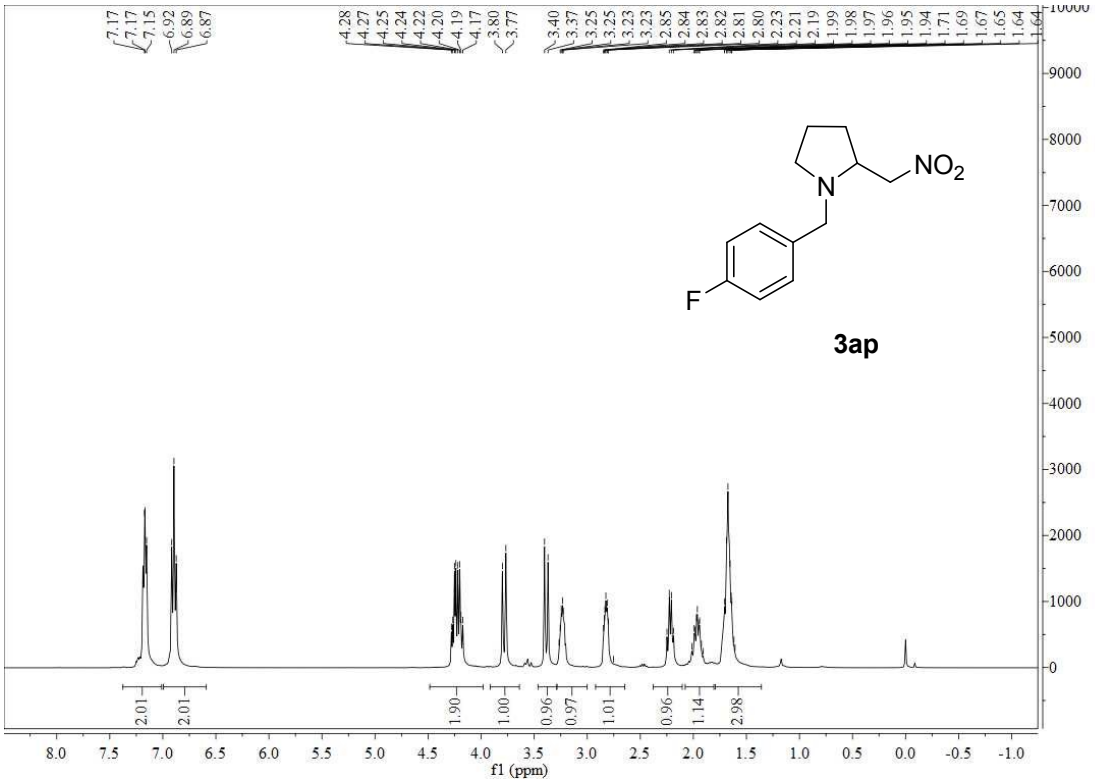
7.09
7.04
7.03
4.26
4.25
4.23
4.22
4.22
4.17
4.16
4.15
4.14
4.13
3.78
3.75
3.44
3.42
3.25
3.24
3.23
3.22
3.22
3.21
2.89
2.88
2.87
2.86
2.25
2.24
2.00
1.99
1.98
1.97
1.96
1.95
1.94
1.91
1.72
1.71
1.70
1.69
1.66
1.65
NO2
N
Me
3an
4.07
1.71
1.00
0.89
0.85
1.04
4.02
1.18
2.79
f1 (ppm)


135.77
134.71
128.02
127.65
78.27
60.41
57.97
53.26
28.26
21.99
20.07
NO2
N
Me
3an
f1 (ppm)


7.35 7.33 7.10 7.08 4.30 4.28 4.27 4.25 4.23 4.21 4.20 4.18 3.80 3.78 3.76 3.75 3.39 3.36 3.28 3.27 3.26 3.25 3.24 3.23 3.22 2.86 2.85 2.84 2.83 2.82 2.81 2.81 2.25 2.23 2.22 2.20 2.20 2.19 2.18 2.05 2.03 2.02 2.02 2.00 1.99 1.98 1.97 1.96 1.95 1.74 1.73 1.72 1.71 1.70 1.66
N
NO2
Br
3ao
1.99 2.07 1.67 1.00 0.89 0.87 0.99 0.92 1.35 2.81
f1 (ppm)


138.09 131.45 130.34 120.94 79.27 61.60 58.69 57.85 54.21 29.23 23.13
N
NO2
Br
3ao
f1 (ppm)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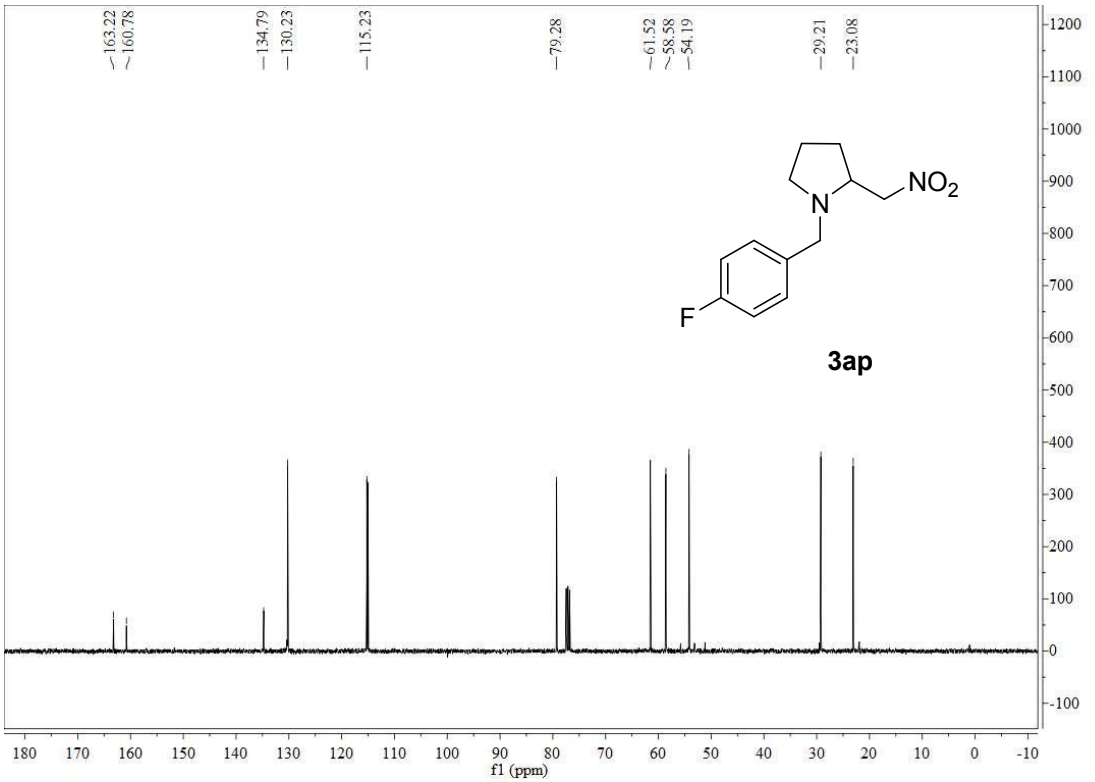
6.92
6.89
6.87
4.28
4.27
4.25
4.24
4.22
4.20
4.19
4.17
3.80
3.77
3.40
3.37
3.25
3.23
3.23
2.85
2.84
2.83
2.82
2.81
2.80
2.23
2.21
2.19
1.99
1.98
1.97
1.96
1.95
1.94
1.71
1.69
1.67
1.65
1.64
1.64
NO2
N
F
3ap
2.01
2.01
1.90
1.00
0.96
0.97
1.01
0.96
1.14
2.98
f1 (ppm)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160.78
134.79
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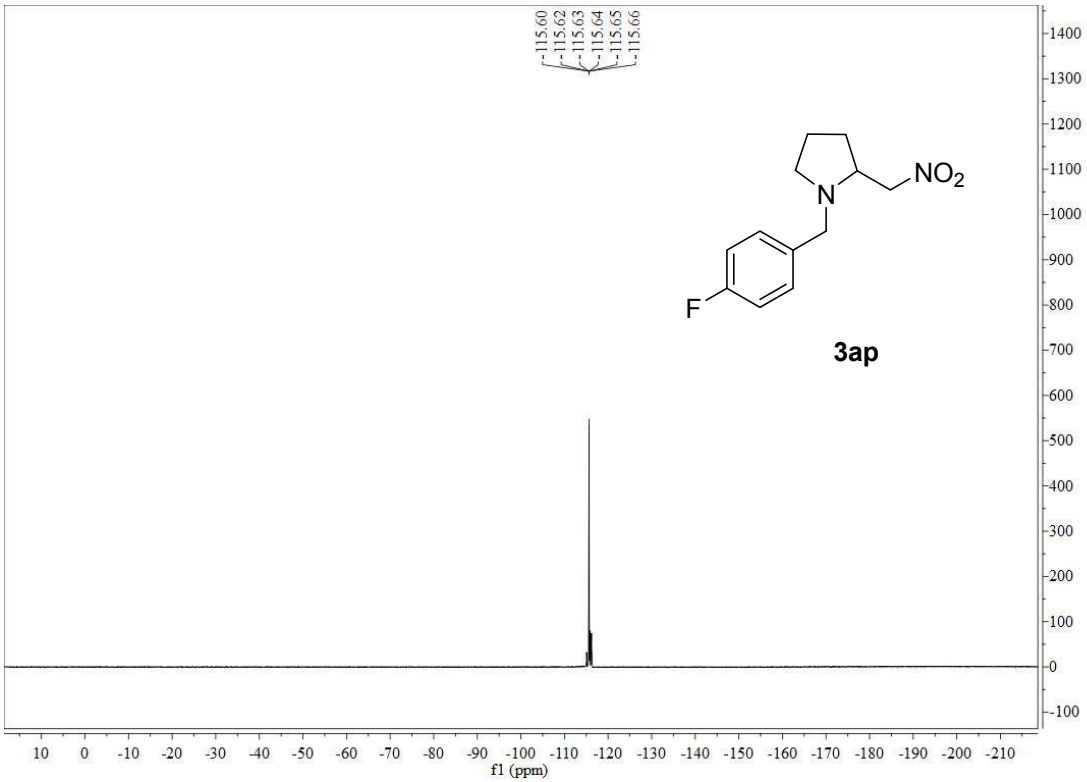
61.52
58.58
54.19
29.21
23.08
NO2
N
F
3ap
f1 (ppm)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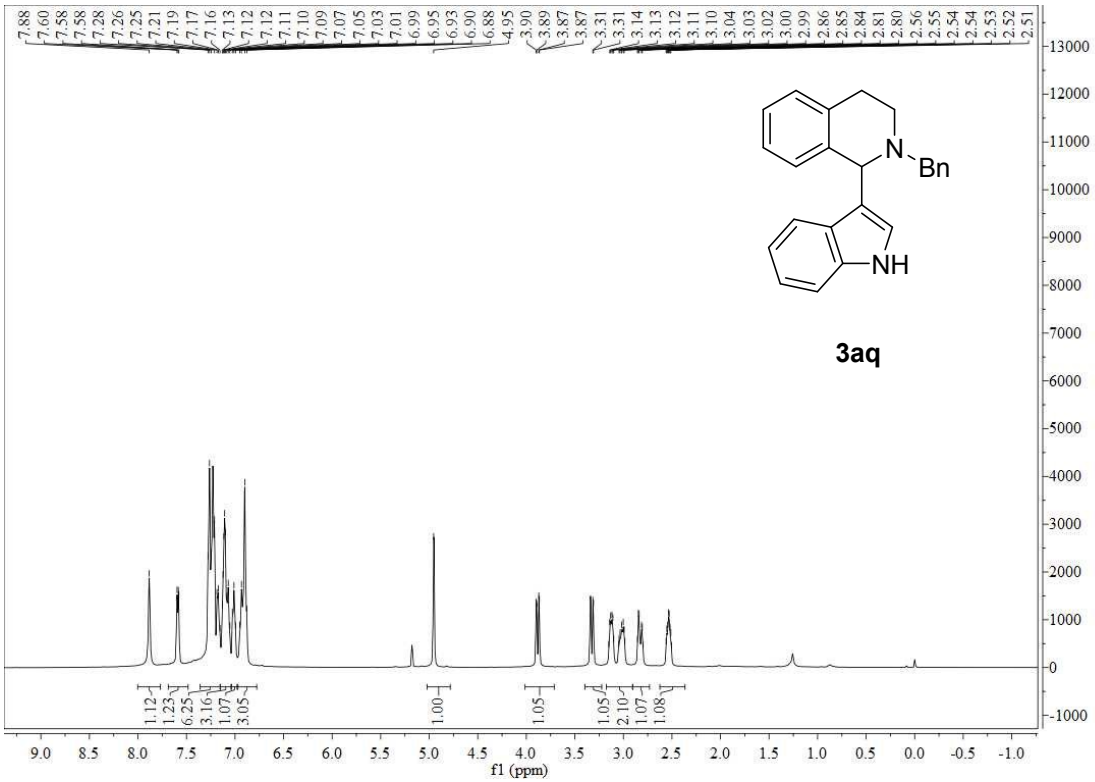
-115.63
-115.64
-115.65
-115.66
N
NO2
F
3ap
f1 (ppm)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7.58
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7.21
7.19
7.17
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7.13
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7.12
7.11
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7.09
7.07
7.05
7.03
7.01
6.99
6.95
6.93
6.90
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3.13
3.12
3.11
3.10
3.04
3.03
3.02
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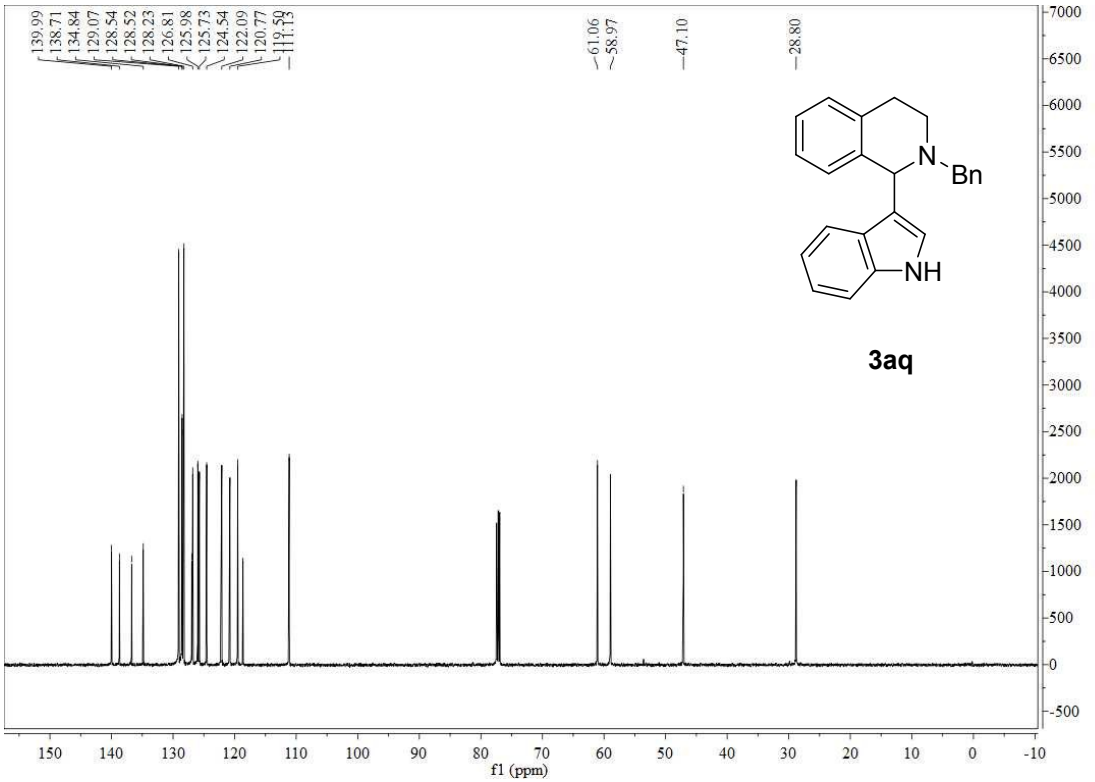
2.80
2.56
2.55
2.54
2.54
2.53
2.52
2.51
N
Bn
NH
3aq
1.12
1.23
6.25
3.16
1.07
3.05
1.00
1.05
1.05
2.10
1.07
1.08
f1 (ppm)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129.07
128.54
128.52
128.23
126.81
125.98
125.73
124.54
122.09
120.77
119.50
111.73
61.06
58.97
47.10
28.80
N
Bn
NH
3aq
f1 (ppm)