Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supplementary Information

Copper-Mediated Annulation of 2-(1-Arylvinyl)anilines and Aryl Nitrosos towards 2,3-Diaryl-2*H*-Indazoles

Weiming Hu, Jin-Tao Yu, Suqin Liu, Yan Jiang and Jiang Cheng*

School of Petrochemical Engineering, Jiangsu Key Laboratory of Advanced Catalytic Materials & Technology, Jiangsu Province Key Laboratory of Fine Petrochemical Engineering, Changzhou University, Changzhou 213164, P. R. China

Email: jiangcheng@cczu.edu.cn

Table of Contents

1. General Considerations

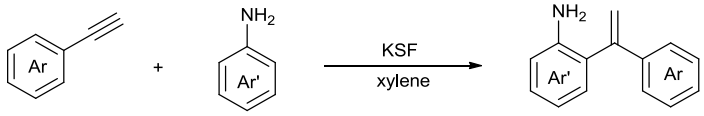
Unless otherwise noted, all chemicals were purchased from commercial suppliers and used without further purification. ^{1}H NMR、^{13}C NMR and ^{19}F spectra were recorded at ambient temperature on a 300 or 400 MHz NMR spectrometer (75 or 100 MHz for ^{13}C and 282 MHz for ^{19}F). NMR experiments are reported in δ units, parts per million (ppm), and were referenced to $CDCl_3$ (δ 7.26 or 77.0 ppm) as the internal standard. The coupling constants *J* are given in Hz. High-resolution mass spectra (HRMS) were obtained using a Bruker micro-TOF II focus spectrometer (ESI). IR spectra were recorded on a spectrometer using KBr discs. Column chromatography was performed using EM Silica gel 60 (300-400 mesh). All melting points were uncorrected.

2. Synthesis and Reaction

Synthesis of 2-(1-substituted vinyl) anilines were synthesized according to the literature methods.

Substrates 1a-1f, 1h, 1j-1m were synthesized according to Method A:[1]

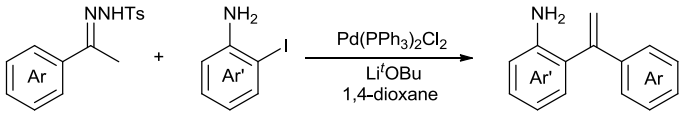
Method A :



Under air, anilines (9.0 mmol), phenylacetylenes (18.0 mmol) and 1.7 g of montmorillonite KSF were added to 150 mL of xylene in a round-bottomed flask. The flask was stirred and heated in an oil bath to 140 ℃, under a reflux condenser (running cold water as the coolant) that was connected at its top to a paraffin bubbler. After 18 h, the reaction mixture was cooled to room temperature and purified directly by flash chromatography with a gradient of hexane to hexane/ethyl acetate (V_1/V_2 = 60/1), followed by distillation under vacuum to afford corresponding 2-(1-arylvinyl) anilines.

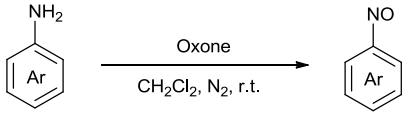
Substrates 1g, 1i, 1n and 1o-1r were synthesized according to Method B: [2]

Method B :



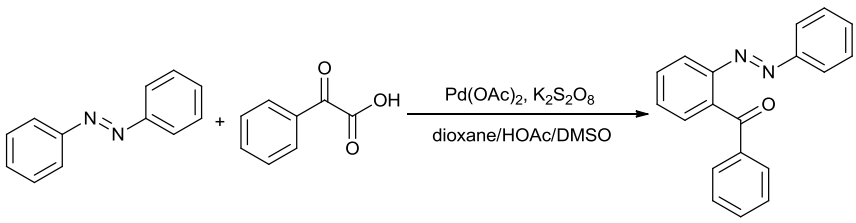
Under N_2, a well stirred mixture of tosylhydrazone (7.5 mmol), 2-iodoaniline (5 mmol), $Pd(PPh_3)_2Cl_2$ (2.5 mol%) in 1,4-dioxane (56 mL) was heated at 100℃. To this hot clear solution was added *t*-BuOLi (1.6 g, 20 mmol), and the reaction was stirred at 100℃ for 3 h. Then, the reaction mixture was cooled to room temperature and diluted with EtOAc (60 mL) and passed through a short Celite pad; the solvent was evaporated under reduced pressure, and purified on a silica gel column (hexane/EtOAc, 90:1) to obtain corresponding products.

Synthesis of nitrosobenzenes[3]



Under N_2, aniline (20 mmol) was dissolved in DCM (50 mL). Then the solution of oxone (22 mmol, 13.5 g) in 50 mL of water was added slowly. The reaction mixture was stirred at room temperature till full consumption of the starting material as monitored by TLC (about 30 min.). After that, the reaction mixture was separated and extracted with DCM (15 mL × 3). The combined organic layers were washed with HCl (1 M) then saturated Na_2CO_3 and brine. After dried by anhydrous Na_2SO_4, the solvent was evaporated, and the crude mixture was purified by flash column chromatography on silica gel with hexane to afford analytically pure aryl nitroso.

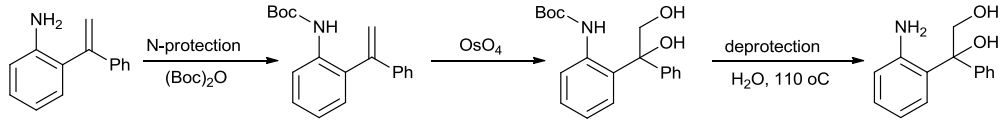
Synthesis of (*E*)-phenyl(2-(phenyldiazenyl)phenyl)methanone (5) [4]



A mixture of azobenzene (0.3 mmol), benzoylformic acid (0.33 mmol), $Pd(OAc)_2$ (6.8 mg, 0.03 mmol), $K_2S_2O_8$ (162.3 mg, 0.6 mmol) in 1,4-dioxane/AcOH/DMSO (7/2/1, V/V/V, 2 mL) was stirred at 80℃ for 10 h. The mixture was filtered by a silica gel plug with ethyl acetate as the eluent and evaporated in vacuum. The product was

purified by column chromatography over silica gel using petroleum ether and ethyl acetate (20:1) as the eluent. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 7.8 Hz, 1H), 7.78 (d, J = 8.5 Hz, 2H), 7.69-7.58 (m, 3H), 7.51-7.43 (m, 3H), 7.40-7.32 (m, 5H).

Synthesis of 1-(2-aminophenyl)-1-phenylethane-1,2-diol (6)



General procedure for *N*-protection[5]

To a magnetically stirred mixture of 2-(1-phenylvinyl)aniline (1 mmol) and $(Boc)_2O$ (1 mmol), a catalytic amount of iodine (10 mol %) was added under solvent-free conditions at room temperature. After stirring for 12 h, diethyl ether (10 mL) was added. The reaction mixture was washed with $Na_2S_2O_3$ (5%, 5 mL) and saturated $NaHCO_3$ and dried over Na_2SO_4, the solvent was rotavaped under reduced pressure, and the residue was purified by silica gel column chromatography (hexane/EtOAc, V_1/V_2 = 60:1) to afford the product *t*-butyl (2-(1-phenylvinyl)phenyl)carbamate in 89% yield as a yellowish oil.

General procedure for dihydroxylation[6]

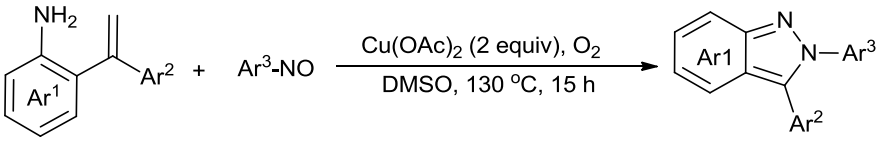
t-Butyl (2-(1-phenylvinyl)phenyl)carbamate (59 mg, 0.2 mmol), NMO (28 mg, 0.24 mmol), $[bmim]PF_6$ (0.1 mL), OsO_4 (1 mg, 2 mol %), DMAP (0.6 mg, 2.4 mol%), H_2O (0.1 mL), *t*-BuOH (0.2 mL) were added to a flask. Then the reaction mixture was stirred at rt for 16 h under air atmosphere. The ionic liquid layer was extracted with ethyl acetate (6 mL × 3). The combined extracts were concentrated and purified by flash silica gel column chromatography (hexane/EtOAc, v_1/v_2 = 3:1) to afford the product *t*-butyl (2-(1,2-dihydroxy-1-phenylethyl)phenyl)carbamate in 85% yield as a reddish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.82 (d, J = 8.0 Hz, 1H), 7.35-7.28 (m, 6H), 7.25-7.23 (m, 1H), 7.10-7.05 (m, 1H),4.33 (d, J = 11 Hz, 1H), 3.88 (d, J = 11 Hz, 1H), 2.07 (s, 1H), 1.60 (s, 1H), 1.29 (s, 9H).

General procedure for *N*-deprotection[7]

Under air, a 20 mL of Schlenk tube equipped with a stir bar was charged with

tert-butyl (2-(1,2-dihydroxy-1-phenylethyl)phenyl)carbamate (0.2 mmol) was added 4.0 mL of water. Then the reaction mixture was stirred for 6 h at 100 ^{o}C (monitored by TLC). After that, the reaction mixture was cooled down and extracted with ethyl acetate (6 mL×3). The extract was washed with brine, dried over anhydrous Na_2SO_4, and then concentrated in vacuum. The residue was purified by column chromatography (hexane/EtOAc, V_1/V_2 = 3:1) to afford the product 1-(2-aminophenyl)-1-phenylethane-1,2-diol in 75% yield as a white solid. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40-7.27 (m, 6H), 7.17-7.12 (m, 1H), 6.89-6.84 (m, 1H), 6.67-6.64 (m, 1H), 4.25 (d, J = 11 Hz, 1H), 3.84 (d, J = 11 Hz, 1H), 3.34 (br, 3H), 1.26 (s, 1H).

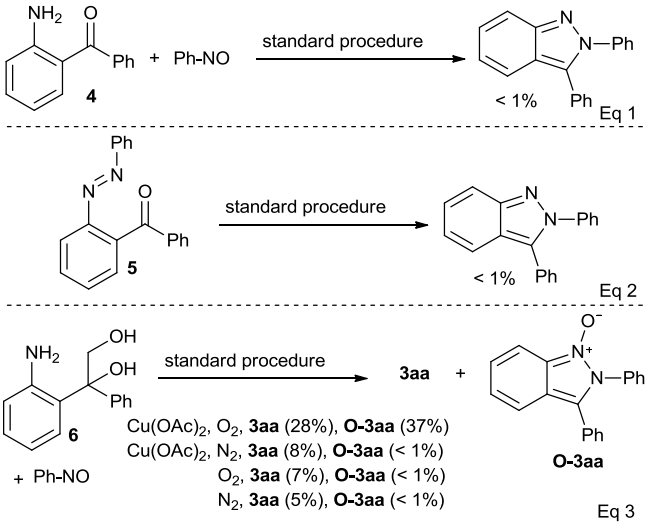
Annulation of 2-(1-Substituted vinyl) Anilines and Aryl Nitrosos



Scheme 1. Annulation of 2-(1-Substituted vinyl) Anilines and Aryl Nitrosos

Under O_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with 2-(1-arylvinyl) anilines (0.1 mmol), aryl nitrosos (0.25 mmol), $Cu(OAc)_2$ (0.2 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath. After the completion of the reaction, 6 mL of saturated brines was added to the mixture, and extracted with ethyl acetate (8 mL × 3) with ethyl acetate. The combined organic extracts were dried over anhydrous Na_2SO_4. Subsequently, the solvent was filtered and evaporated under reduced pressure, and the residue was purified by flash column chromatography on silica gel with petroleum ether-EtOAc (V_1/V_2, 30:1) as the eluent to give the desired products.

3. Research of Mechanism



Scheme S1. Mechanism Studies

General procedure for the reaction of 4 and 2 (Scheme S1, Eq 1)

Under O_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with **4** (0.1 mmol), aryl nitrosos **2** (0.25 mmol), $Cu(OAc)_2$ (0.2 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath.

General procedure for the reaction of 5 (Scheme S1, Eq 2)

Under O_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with **5** (0.1 mmol), $Cu(OAc)_2$ (0.2 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath.

General procedure for the reaction of 6 and 2 (Scheme S1, Eq 3)

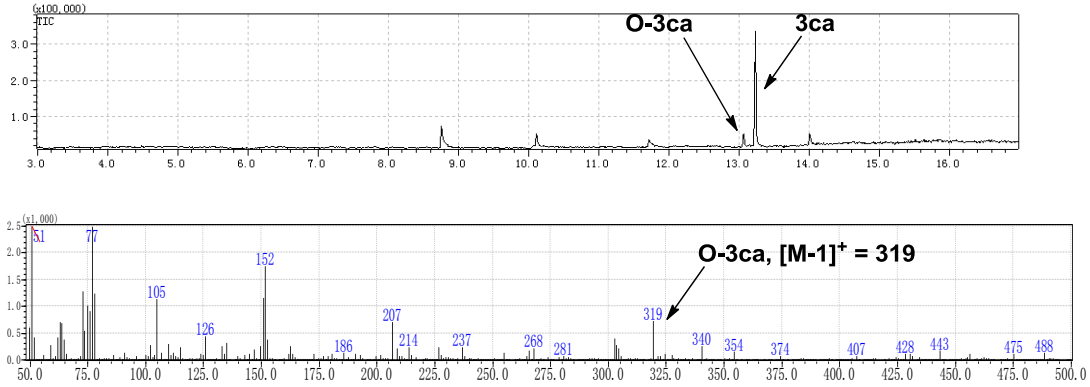
Under O_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with **6** (0.1 mmol), aryl nitrosos **2** (0.25 mmol), $Cu(OAc)_2$ (0.2 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath. Product **3aa** was formed in 28 yield, byproduct **O-3aa** was formed in 37 yield. ^{1}H NMR for **O-3aa** (300 MHz, $CDCl_3$) δ 8.19 (d, J = 8 Hz, 1H), 7.85-7.80 (m, 4H), 7.67-7.58 (m, 2H), 7.51-7.38 (m, 5H), 7.36-7.30 (m, 2H); ^{13}C NMR for **O-3aa** (300 MHz, $CDCl_3$) δ 142.1, 137.7, 137.3, 135.5, 135.3, 132.8, 131.9, 131.0, 129.8, 129.0, 128.60, 128.56, 128.3, 123.4, 122.2.

Under N_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with **6** (0.1 mmol), aryl nitrosos **2** (0.25 mmol), $Cu(OAc)_2$ (0.2 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath.

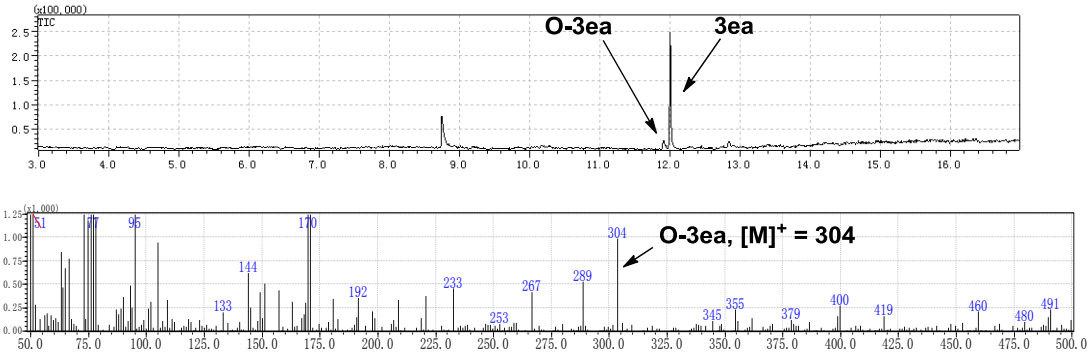
Under O_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with **6** (0.1 mmol), aryl nitrosos **2** (0.25 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath.

Under N_2, a 20 mL of Schlenk tube equipped with a stir bar was charged with **6** (0.1 mmol), aryl nitrosos **2** (0.25 mmol), DMSO (2.0 mL). The tube was sealed with a Teflon lined cap. The reaction mixture was stirred at 130 ℃ for 15 h in oil bath.

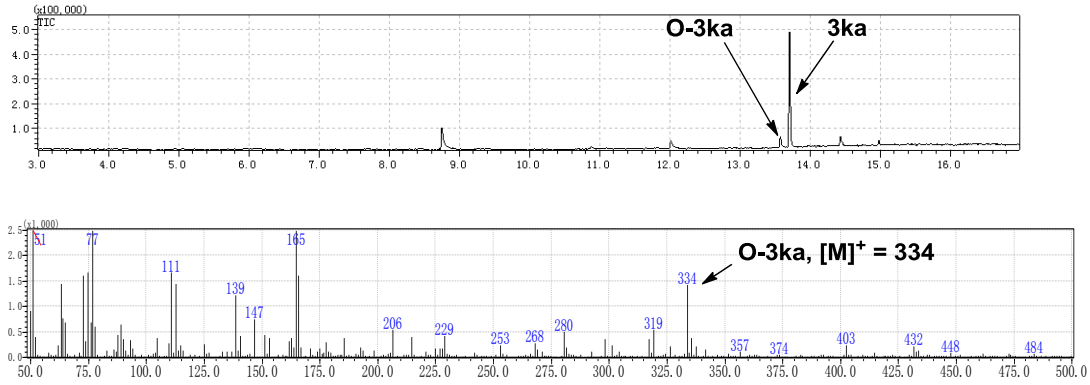
4. GC-MS Data of Compounds 3ca, 3ea, 3ka and 3 ma



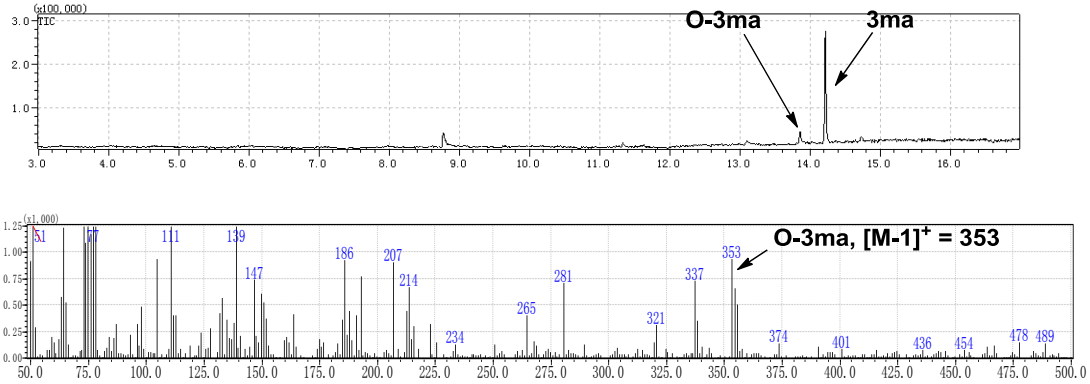
GC-MS data of 3ca and O-3ca



GC-MS data of 3ea and O-3ea



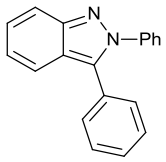
GC-MS data of 3ka and O-3ka



GC-MS data of 3ma and O-3ma

5. Characterization Data for the Products

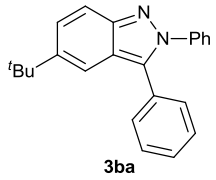
2,3-diphenyl-2*H*-indazole (3aa):[8]



3aa

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3aa** (20.3 mg, 75% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 8.8 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.47-7.43 (m, 2H), 7.41-7.36 (m, 9H), 7.17-7.13 (m, 1H), δ 148.9, 140.2, 135.4, 129.9, 129.6, 128.9, 128.7, 128.3, 128.2, 127.0, 126.0, 122.5, 121.7, 120.5, 117.7; IR (KBr) 3058, 1735, 1626, 1597, 1504, 1455, 1363 cm^{-1}.

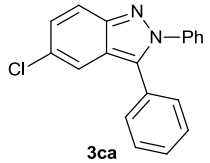
5-(*tert*-butyl)-2,3-diphenyl-2*H*-indazole (3ba):



3ba

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ba** (20.5 mg, 63% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, J = 9.1 Hz, 1H), 7.60 (s, 1H), 7.51 (d, J = 9.2 Hz, 1H), 7.42-7.36 (m, 10H), 1.39 (s, 9H),; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.9, 145.4, 140.4, 135.3, 130.3, 129.8, 129.0, 128.9, 128.23, 128.15, 126.9, 126.1, 121.6, 117.4, 114.4, 35.0, 31.3; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_2(M+H)^+$ 327.1856, found 327.1860; IR (KBr) 3061, 2960, 2926, 1596, 1538, 1502, 1457, 1365, 1311 cm^{-1}.

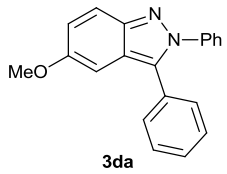
5-chloro-2,3-diphenyl-2*H*-indazole (3ca):



3ca

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ca** (21.6 mg, 71% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, J = 9.2 Hz, 1H), 7.69 (s, 1H), 7.44-7.38 (m, 8H), 7.34-7.28 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.3, 139.9, 135.2, 129.5, 129.3, 129.0, 128.9, 128.6, 128.5, 128.4, 128.1, 125.9, 122.1, 119.3, 119.2; HRMS (ESI) m/z calcd for $C_{19}H_{14}ClN_2$ $(M+H)^+$ 305.0840, found 305.0844; IR (KBr) 3063, 1597, 1499, 1454, 1340, 1321 cm^{-1}.

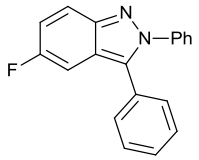
5-methoxy-2,3-diphenyl-2*H*-indazole (3da):[9]



3da

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3da** (19.5 mg, 65% yield) as a yellowish solid. m.p. 145-146 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, J = 9.3 Hz, 1H), 7.43-7.37 (m, 10H), 7.11 (d, J = 9.2 Hz, 1H), 6.93 (s, 1H), 3.86 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.9, 145.9, 140.3, 134.2, 130.3, 129.5, 128.9, 128.8, 128.0, 127.97, 125.8, 122.1, 121.6, 119.2, 96.2, 55.4; IR (KBr) 3060, 2998, 1634, 1596, 1505, 1457, 1325 cm^{-1}.

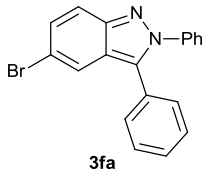
5-fluoro-2,3-diphenyl-2*H*-indazole (3ea):



3ea

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ea** (19.3 mg, 67% yield) as a white solid. m.p. 113-114 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.80-7.76 (m, 1H), 7.43-7.38 (m, 8H), 7.33-7.28 (m, 3H), 7.19- 7.15 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.0 (d, $J_{C\text{-}F}$ = 240 Hz), 146.4, 140.1, 135.6 (d, $J_{C\text{-}F}$ = 8.0 Hz), 129.6, 129.4, 129.0, 128.8, 128.41, 128.38, 125.9, 121.0 (d, $J_{C\text{-}F}$ = 12 Hz), 119.9 (d, $J_{C\text{-}F}$ = 10 Hz), 118.6 (d, $J_{C\text{-}F}$ = 29 Hz), 102.9 (d, $J_{C\text{-}F}$ = 24 Hz); ^{19}F NMR ($CDCl_3$, 282 MHz) δ -119.13; HRMS (ESI) m/z calcd for $C_{19}H_{14}FN_2$ $(M+H)^+$ 289.1136, found 289.1140; IR (KBr) 3064, 1635, 1597, 1528, 1505, 1456, 1344, 1326 cm^{-1}.

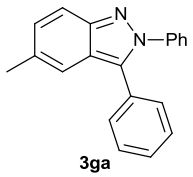
5-bromo-2,3-diphenyl-2*H*-indazole (3fa):



3fa

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3fa** (20.2 mg, 58% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (s, 1H), 7.69 (d, J = 9.1 Hz, 1H), 7.44-7.38 (m, 9H), 7.34-7.31 (m, 2H), ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.3, 139.9, 135.0, 130.6, 129.5, 129.3, 129.0, 128.9, 128.6, 128.5, 125.9, 122.9, 122.7, 119.5, 115.9; HRMS (ESI) m/z calcd for $C_{19}H_{14}BrN_2$ $(M+H)^+$ 349.0335, found 349.0338; IR (KBr) 3061, 1597, 1500, 1454, 1341, 1320 cm^{-1}.

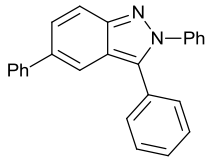
5-methyl-2,3-diphenyl-2*H*-indazole (3ga):



3ga

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ga** (19.9 mg, 70% yield) as yellowish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.44 (d, J = 8.8 Hz, 1H), 7.48-7.37 (m, 11H), 7.23 (d, J = 8.9 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.0, 140.3, 134.4, 131.9, 130.1, 129.9, 129.6, 128.9, 128.7, 128.10, 128.07, 125.9, 122.0, 118.4, 117.4, 21.8; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2$ $(M+H)^+$ 285.1386, found 285.1390; IR (KBr) 3057, 2958, 1597, 1535, 1504, 1455, 1398, 1345 cm^{-1}.

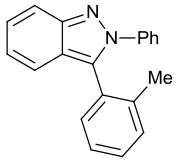
2,3,5-triphenyl-2*H*-indazole (3ha):



3ha

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ha** (24.9, 72% yield) as a reddish solid. m.p. 134-135 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.92-7.89 (m, 2H), 7.70-7.65 (m, 3H), 7.49-7.35 (m, 13H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5, 141.6, 140.1, 135.9, 135.8, 129.8, 129.7, 129.0, 128.8, 128.7, 128.4, 128.3, 127.7, 127.2, 126.9, 125.9, 122.2, 118.2, 118.1; HRMS (ESI) m/z calcd for $C_{25}H_{19}N_2$ $(M+H)^+$ 347.1543, found 347.1544; IR (KBr) 3057, 1597, 1497, 1485, 1343, 1307 cm^{-1}.

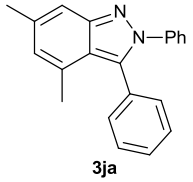
2-phenyl-3-(*o*-tolyl)-2*H*-indazole (3ia):[8a,10]



3ia

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ia** (15.1 mg, 53% yield) as a reddish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.85 (d, J = 8.8 Hz, 1H), 7.48-7.27 (m, 11H), 7.14-7.10 (m, 1H), 1.98 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.8, 140.4, 137.8, 135.2, 131.1, 130.6, 129.6, 129.2, 128.9, 127.9. 127.0, 126.0, 124.8, 122.6, 122.1, 120.7, 117.7, 19.9; IR (KBr) 3059, 2963, 1626, 1597, 1502, 1455, 1361, 1313 cm^{-1}.

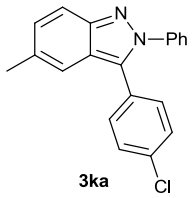
4,6-dimethyl-2,3-diphenyl-2*H*-indazole (3ja):



3ja

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give the product **3ja** (11.3 mg, 38% yield) as a reddish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.32-7.18 (m, 11H), 6.61 (s, 1H), 2.36 (s, 3H), 2.06 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.5, 140.2, 136.8, 136.0, 131.4, 131.3, 131.0, 128.63, 128.61, 128.0, 127.8, 125.9, 125.4, 120.2, 113.7, 22.1, 19.9; IR (KBr) 3058, 2958, 1625, 1596, 1504, 1443, 1363 cm^{-1}.

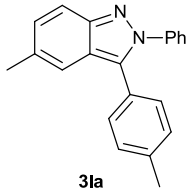
3-(4-chlorophenyl)-5-methyl-2-phenyl-2*H*-indazole (3ka):



3ka

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ka** (25.4 mg, 80% yield) as a reddish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.68 (d, J = 8.9 Hz, 1H), 7.38-7.31 (m, 8H), 7.26-7.17 (m, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.9, 140.0, 134.2, 133.1, 132.3, 130.8, 130.0, 129.1, 129.0, 128.5, 128.3, 125.9, 121.9, 118.0, 117.5, 21.8; HRMS (ESI) m/z calcd for $C_{20}H_{16}ClN_2$ $(M+H)^+$ 319.0997, found 319.0998; IR (KBr) 3047, 2919, 1597, 1503, 1455, 1406, 1345, 1322 cm^{-1}.

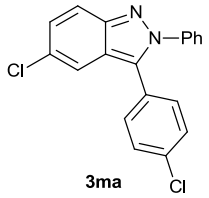
5-methyl-2-phenyl-3-(*p*-tolyl)-2*H*-indazole (3la):



3la

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3la** (23.2 mg, 78% yield) as a reddish solid. m.p. 125-126 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.69 (d, J = 8.9 Hz, 1H), 7.44-7.34 (m, 6H), 7.24-7.17 (m, 5H), 2.42 (s, 3H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 1147.9, 140.3, 138.1, 134.5, 131.7, 129.8, 129.5, 129.4, 128.9, 128.0, 127.1, 125.9, 121.9, 118.5, 117.3, 21.8, 21.3; HRMS (ESI) m/z calcd for $C_{21}H_{19}N_2$ $(M+H)^+$ 299.1543, found 299.1549; IR (KBr) 3056, 3019, 2960, 1597, 1539, 1509, 1497, 1455, 1345, 1324 cm^{-1}.

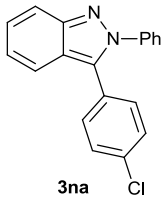
5-chloro-3-(4-chlorophenyl)-2-phenyl-2*H*-indazole (3ma):[11]



3ma

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ma** (20.6 mg, 61% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.74 (d, J = 9.2 Hz, 1H), 7.64 (d, J = 1.2 Hz, 1H), 7.41-7.36 (m, 7H), 7.32-7.23 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.0, 139.9, 134.1, 132.1, 131.1, 129.2, 128.8, 128.5, 127.1, 126.0, 122.9, 122.7, 121.6, 120.1, 117.9; IR (KBr) 3065, 1596, 1500, 1453, 1341, 1319 cm^{-1}.

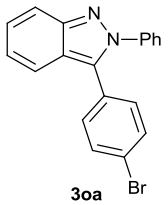
3-(4-chlorophenyl)-2-phenyl-2*H*-indazole (3na):[8,10,11]



3na

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3na** (19.2 mg, 63% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.79 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.5 Hz, 1H), 7.40-7.33 (m, 8H), 7.29-7.24 (m, 2H), 7.17-7.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 148.9, 139.9, 134.4, 134.1, 130.8, 129.13, 129.10, 128.5, 128.3, 127.1, 126.0, 122.8, 121.7, 120.1, 117.9; IR (KBr) 3059, 1596, 1502, 1454, 1363, 1297 cm^{-1}.

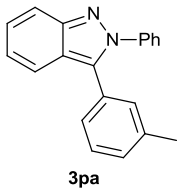
3-(4-bromophenyl)-2-phenyl-2*H*-indazole (3oa):[8,10,11,12]



3oa

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3oa** (19.2 mg, 45% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.81 (d, J = 8.8 Hz, 1H), 7.68 (d, J = 8.5 Hz, 1H), 7.54-7.51 (m, 2H), 7.41-7.35 (m, 6H), 7.24-7.14 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.0, 139.9, 134.1, 132.1, 131.1, 129.2, 128.8, 128.5, 127.1, 126.0, 122.9, 122.7, 121.6, 120.1, 117.9; IR (KBr) 3058, 1598, 1502, 1454, 1397, 1361 cm^{-1}.

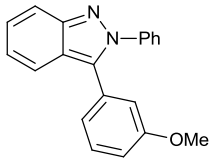
2-phenyl-3-(*m*-tolyl)-2*H*-indazole (3pa):[8a,10a,12]



3pa

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3pa** (21.6 mg, 76% yield) as a yellowish solid. m.p. 101-102 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 8.7 Hz, 1H), 7.73 (d, J = 8.5 Hz, 1H), 7.46-7.36 (m, 6H), 7.29-7.23 (m, 2H), 7.19-7.11 (m, 3H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 140.2, 138.4, 135.5, 130.2, 129.7, 129.1, 128.9, 128.6, 128.2, 126.9, 126.8, 125.9, 122.3, 121.7, 120.6, 117.7, 21.4; IR (KBr) 3057, 3022, 2966, 1593, 1551, 1455, 1355, 1329 cm^{-1}.

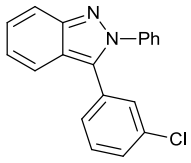
3-(3-methoxyphenyl)-2-phenyl-2*H*-indazole (3qa):[8a]



3qa

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3qa** (21.0 mg, 70% yield) as a yellowish solid. m.p. 148-149 ^{o}C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, J = 8.8 Hz, 1H), 7.75 (d, J = 8.5 Hz, 1H), 7.47-7.36 (m, 6H), 7.30 (t, J = 7.9 Hz, 1H), 7.15 (t, J = 7.5 Hz, 1H), 6.96-6.89 (m, 3H), 3.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.6, 148.9, 140.2, 135.2, 131.0, 129.8, 129.0, 128.3, 127.0, 126.0, 122.5, 122.1, 121.6, 120.5, 117.7, 114.9, 114.2, 55.2; IR (KBr) 3061, 2988, 1635, 1593, 1500, 1455, 1335 cm^{-1}.

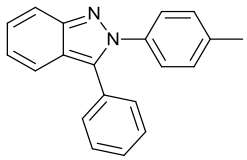
3-(3-chlorophenyl)-2-phenyl-2*H*-indazole (3ra):[12]



3ra

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ra** (20.7 mg, 68% yield) as a reddish oil. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 8.7 Hz, 1H), 7.71 (d, J = 8.5 Hz, 1H), 7.42-7.28 (m, 9H), 7.8 (t, J = 7.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.9, 139.8, 134.7, 133.7, 131.6, 130.0, 129.4, 129.1, 128.6, 128.4, 127.8, 127.1, 126.0, 123.0, 121.7, 120.1, 117.9; IR (KBr) 3064, 1588, 1512, 1455, 1368, 1290 cm^{-1}.

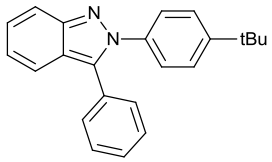
3-phenyl-2-(*p*-tolyl)-2*H*-indazole (3ab):



3ab

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ab** (12.8 mg, 45% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.80 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.41-7.29 (m, 8H), 7.19-7.11 (m, 3H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 1148.8, 138.2, 137.7, 135.3, 130.0, 129.7, 129.6, 128.7, 128.2, 126.9, 125.7, 122.4, 121.7, 120.5, 117.7, 21.2; HRMS (ESI) m/z calcd for $C_{20}H_{17}N_2$ $(M+H)^+$ 285.1386, found 285.1390; IR (KBr) 3058, 2960, 1625, 1601, 1351, 1461, 1363 cm^{-1}.

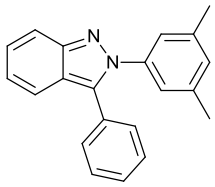
2-(4-(*tert*-butyl)phenyl)-3-phenyl-2*H*-indazole (3ac):



3ac

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ac** (20.5 mg, 63% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.80 (d, J = 8.8 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.41-7.34 (m, 10H), 7.16-7.11 (m, 1H), 1.33 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.4, 148.8, 137.6, 135.2, 130.0, 129.7, 128.7, 128.2, 126.8, 125.9, 125.4, 122.4, 121.7, 120.5, 117.7, 34.7, 31.3; HRMS (ESI) m/z calcd for $C_{23}H_{23}N_2$ $(M+H)^+$ 327.1856, found 327.1856; IR (KBr) 3059, 2961, 1625, 1601, 1517, 1497, 1461, 1363 cm^{-1}.

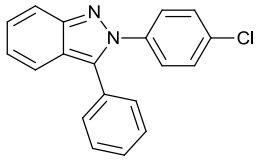
2-(3,5-dimethylphenyl)-3-phenyl-2*H*-indazole (3ad):[9,10a,12]



3ad

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ad** (17.6 mg, 59% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.80 (d, J = 8.7 Hz, 1H), 7.72 (d, J = 8.5 Hz, 1H), 7.40-7.34 (m, 6H), 7.16-7.11 (m, 1H), 7.04 (s, 2H), 7.00 (s, 1H), 2.27 (s, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.8, 140.0, 138.7, 135.3, 130.0, 129.9, 129.6, 128.6, 128.2, 126.8, 123.7, 122.3, 121.6, 120.5, 117.7, 21.2; IR (KBr) 3057, 2963, 1611, 1596, 1497, 1445, 1363 cm^{-1}.

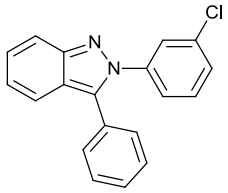
2-(4-chlorophenyl)-3-phenyl-2*H*-indazole (3ae):[13]



3ae

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ae** (17.3 mg, 57% yield) as a yellowish solid. m.p. 118-119 ^{o}C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.79 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.5 Hz, 1H), 7.43-7.34 (m, 10H), 7.17-7.12 (m, 1H),; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 138.7, 135.5, 134.1, 129.7, 129.6, 129.2, 128.9, 128.6, 127.3, 127.1, 122.7, 121.8, 120.4, 117.7; IR (KBr) 3059, 1626, 1599, 1501, 1445, 1364, 1301 cm^{-1}.

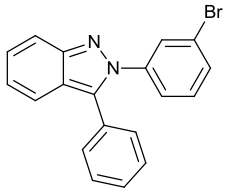
2-(3-chlorophenyl)-3-phenyl-2*H*-indazole (3af):



3af

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3af** (18.8 mg, 62% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.79 (d, J = 8.8 Hz, 1H), 7.70 (d, J = 8.6 Hz, 1H), 7.59-7.57 (m, 1H), 7.44-7.33 (m, 7H), 7.27-7.23 (m, 2H), 7.17-7.12 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 141.2, 134.7, 133.0, 131.9, 129.8, 129.6, 129.5, 128.9, 128.6, 128.4, 127.4, 126.2, 124.1, 127.8, 120.5, 117.7; HRMS (ESI) m/z calcd for $C_{19}H_{14}ClN_2$ $(M+H)^+$ 305.0840, found 305.0840; IR (KBr) 3059, 1664, 1626, 1592, 1499, 1482, 1362 cm^{-1}.

2-(3-bromophenyl)-3-phenyl-2H-indazole (3ag):



3ag

Flash column chromatography on a silica gel (ethyl acetate: petroleum ether, 1: 30) give **3ag** (21.9 mg, 63% yield) as a yellowish oil. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.77-7.75 (m, 2H), 7.70 (d, J = 8.5 Hz, 1H), 7.52-7.48 (m, 1H), 7.44-7.34 (m, 6H), 7.26-7.12 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.1, 141.2, 135.6, 134.9, 133.0, 131.3, 130.0, 129.7, 129.0, 128.9, 128.6, 127.4, 124.5, 122.8, 122.5, 120.5, 117.7; HRMS (ESI) m/z calcd for $C_{19}H_{14}BrN_2$ $(M+H)^+$ 349.0335, found 349.0339; IR (KBr) 3059, 1664, 1588, 1499, 1480, 1362 cm^{-1}.

6. Reference

(1) (*a*) Z. Zhang, L.-L. Liao, S.-S. Yan, L. Wang, Y.-Q. He, J.-H. Ye, J. Li, Y.-G. Zhi and D.-G. Yu, *Angew. Chem., Int. Ed*., 2016, **55**, 7068; (*b*) K. Sasano, J. Takaya and N. Iwasawa, *J. Am. Chem. Soc*., 2013, **135**, 10954; (*c*) L. Wang, J. Ferguson and F. Zeng, *Org. Biomol. Chem.*, 2015, **13**, 11486; (*d*) A. Arienti, F. Bigi, R. Maggi, E. Marzi, P. Moggi, M. Rastelli, G. Sartori and F. Tarantola, *Tetrahedron*, 1997, **53**, 3795; (*e*) J. Ferguson, F. L. Zeng, N. Alwis and H. Alper, *Org. Lett*., 2013, **15**, 1998.

(2) D. P. Ojha and K. R. Prabhu, *J. Org. Chem.*, 2012, **77**, 11027.

(3) (*a*) Q. Wang and X. Li, *Org. Lett*., 2016, **18**, 2102; (*b*) B. Priewisch and K. Ruck-Braun, *J. Org. Chem.*, 2005, **70**, 2350; (*c*) D. Zhao, M. Johansson and J.-E. Bäckvall, *Eur. J. Org. Chem*., 2007, 4431.

(4) Z.-Y. Li, D.-D. Li and G.-W. W, *J. Org. Chem*., 2013, **78**, 10414.

(5) R. Varala, S. Nuvula and S. R. Adapa, *J. Org. Chem*., 2006, **71**, 8283.

(6) Q. Yao, *Org. Lett*., 2002, 4, 2197.

(7) J. Wang, Y.-L. Liang and J. Qu, *Chem. Commun*., 2009, 5144.

(8) (*a*) H. Li, P. Li and L. Wang, *Org. Lett.* 2013, **15**, 620; (*b*) H. Li, P. Li, Q. Zhao and L. Wang, *Chem. Commun*., 2013, **49**, 9170; (*c*) H. Li, P. Li, H. Tan, L. Wang, *Chem. Eur. J*., 2013, **19**, 14432.

(9) Y. Lian, R. G. Bergman, L. D. Lavis and J. A. Ellman, *J. Am. Chem. Soc*., 2013, **135**, 7122.

(10) (*a*) X. Geng and C. Wang, *Org. Lett*., 2015, **17**, 2434; (*b*) K. Hattori, , K. Yamaguchi, J. Yamaguchi and K. Itami, *Tetrahedron Lett.*, 2012, **68**, 7605.

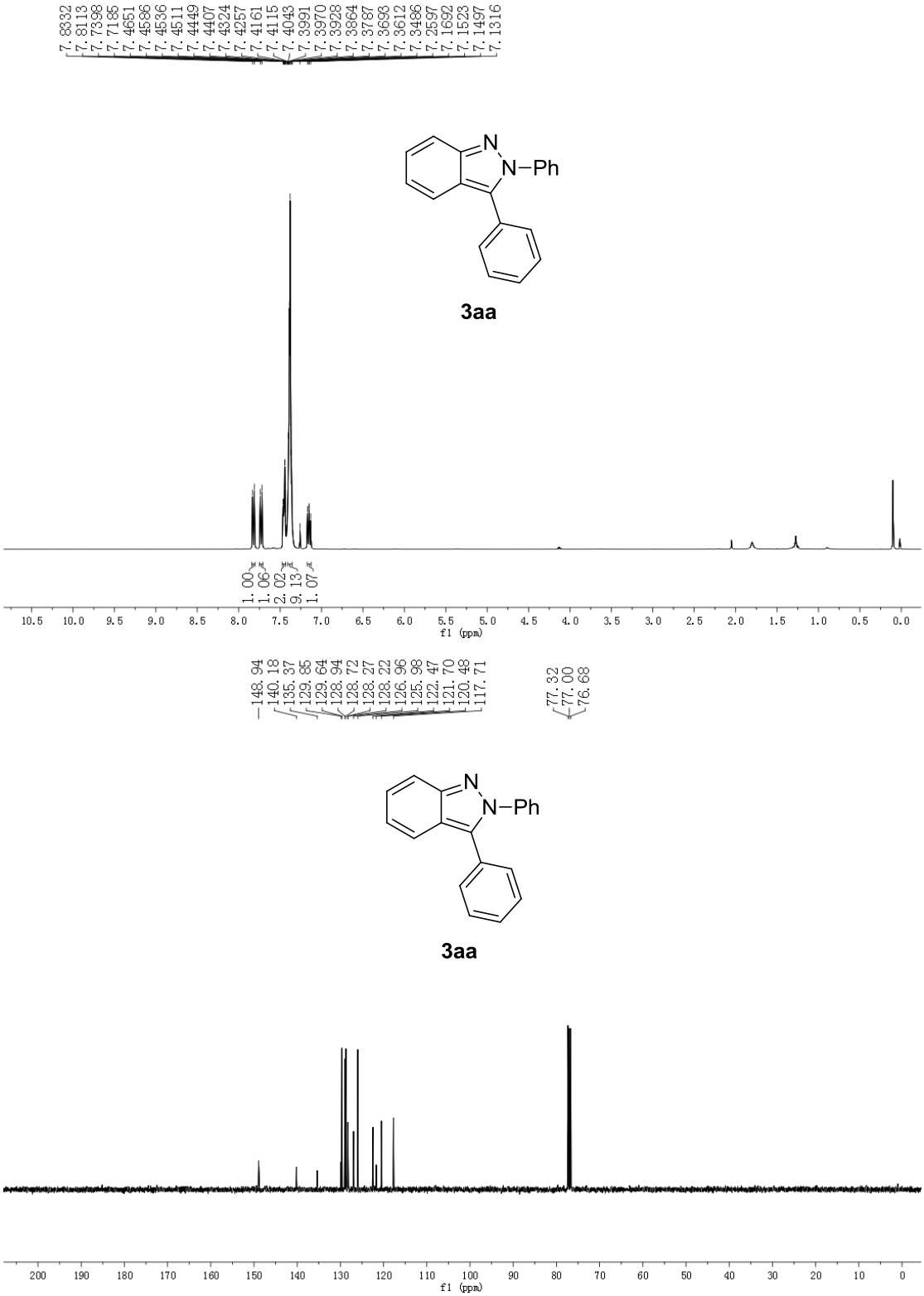
(11) S. A. Ohnmacht, A. J. Culshaw and M. F. Greaney, *Org. Lett*., 2010, **12**, 224.

(12) J. R. Hummel and J. A. Ellman, *J. Am. Chem. Soc*., 2015, **137**, 490.

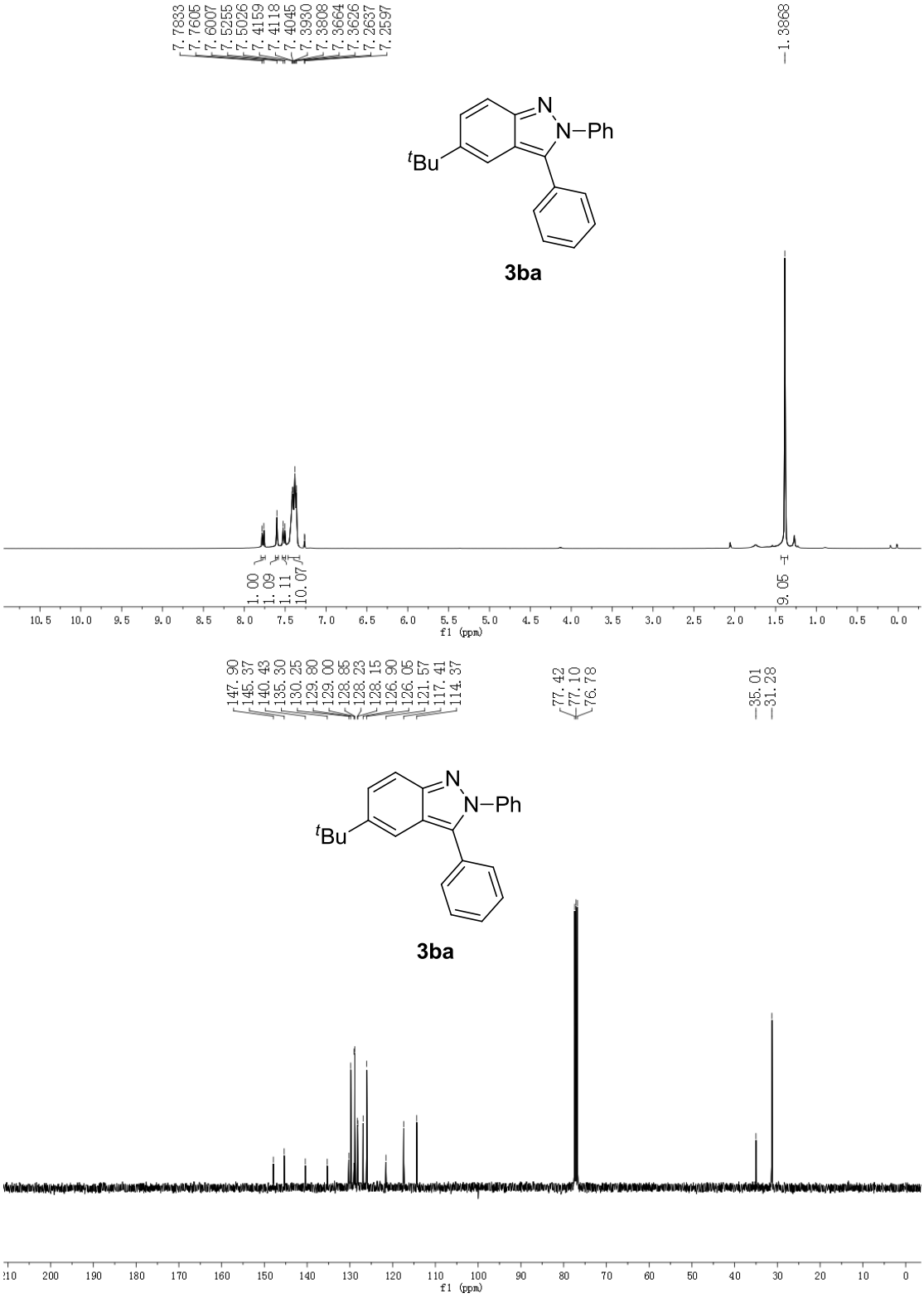
(13) J. H. Lee, A. Matsumoto, M. Yoshida and O. Simamur, *Chem. Lett*., 1974, **9**, 951.

7. Copies of the ^{1}H NMR, ^{13}C NMR Spectra

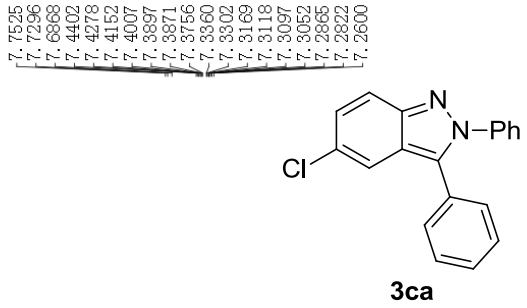
2,3-diphenyl-2*H*-indazole (3aa):



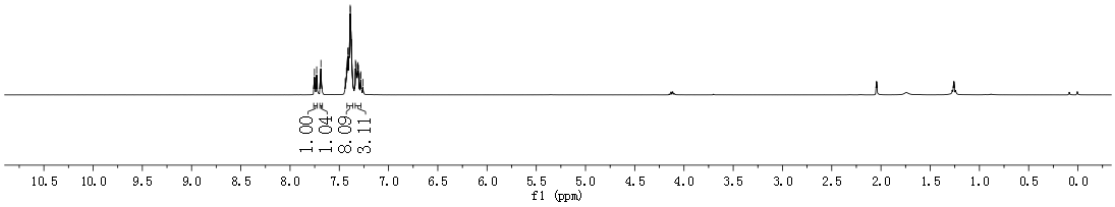
5-(*tert*-butyl)-2,3-diphenyl-2*H*-indazole (3ba):

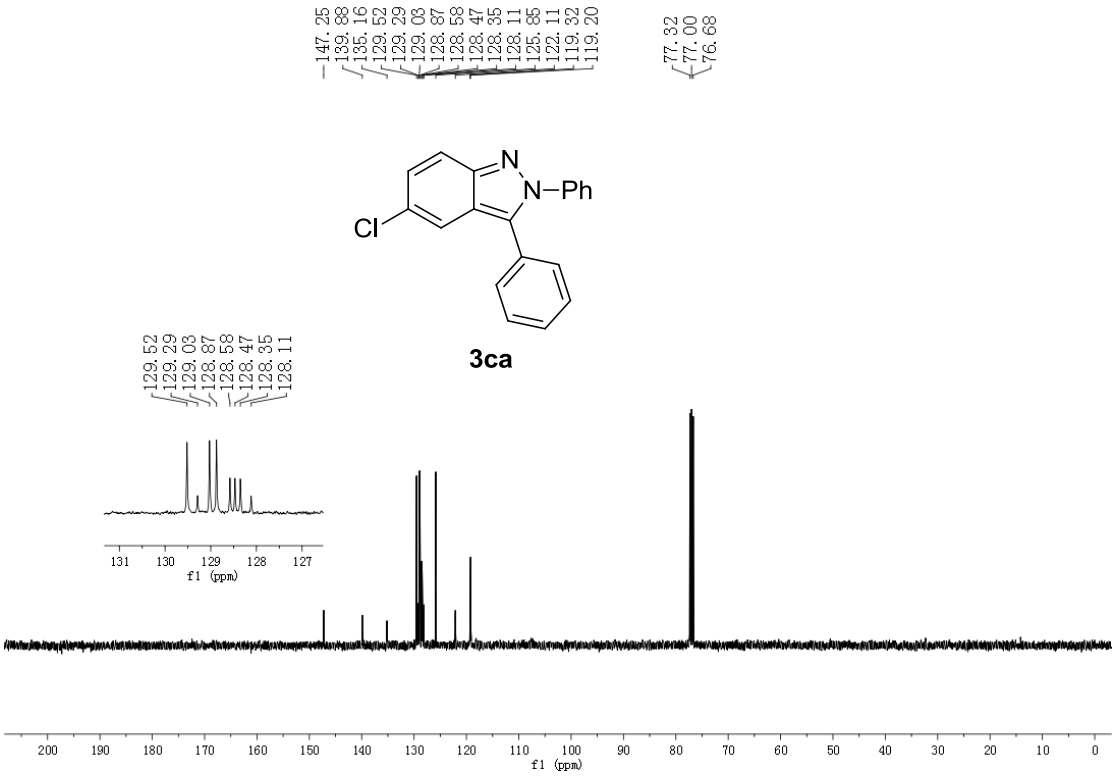


5-chloro-2,3-diphenyl-2*H*-indazole (3ca):



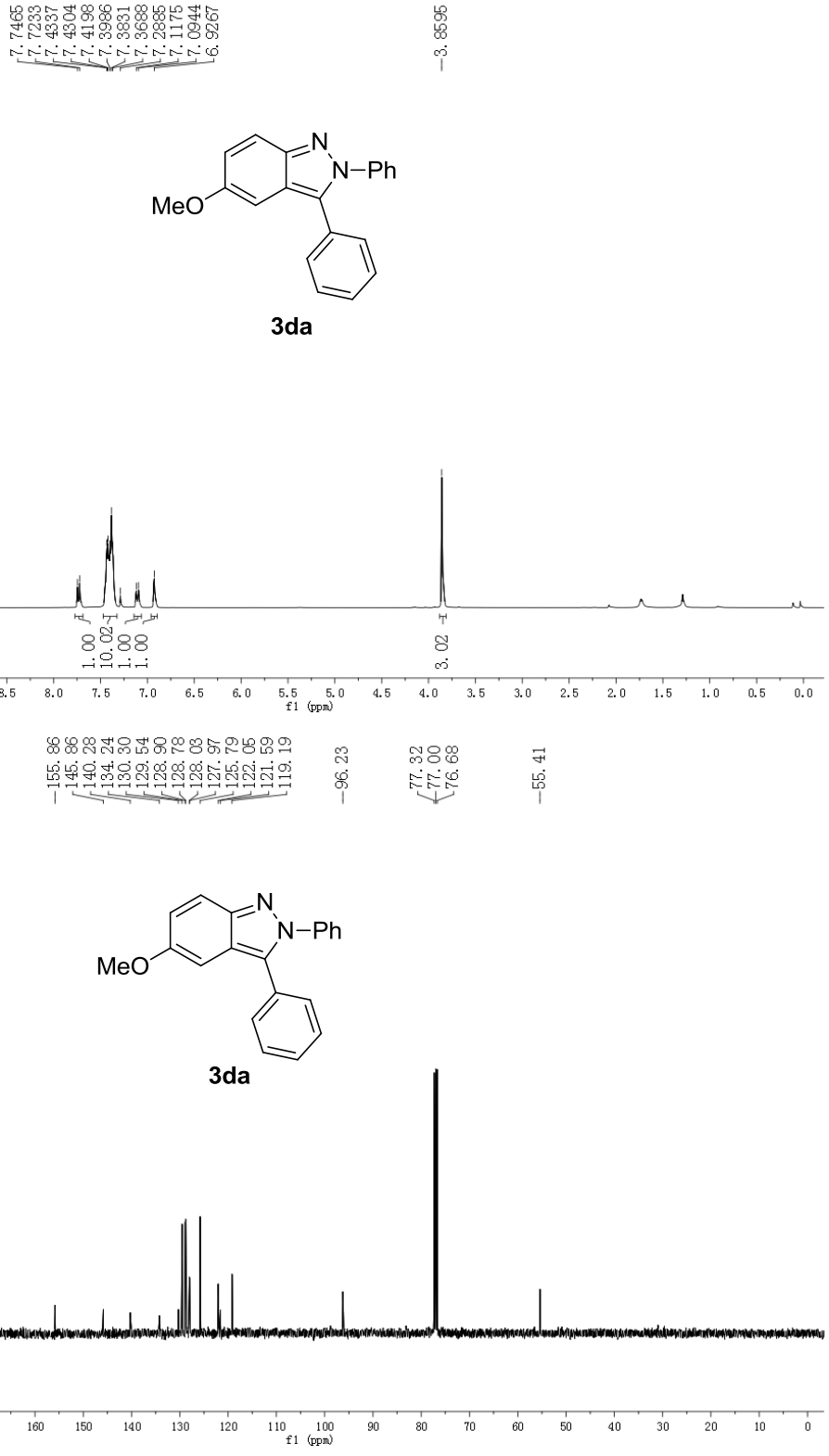
3ca



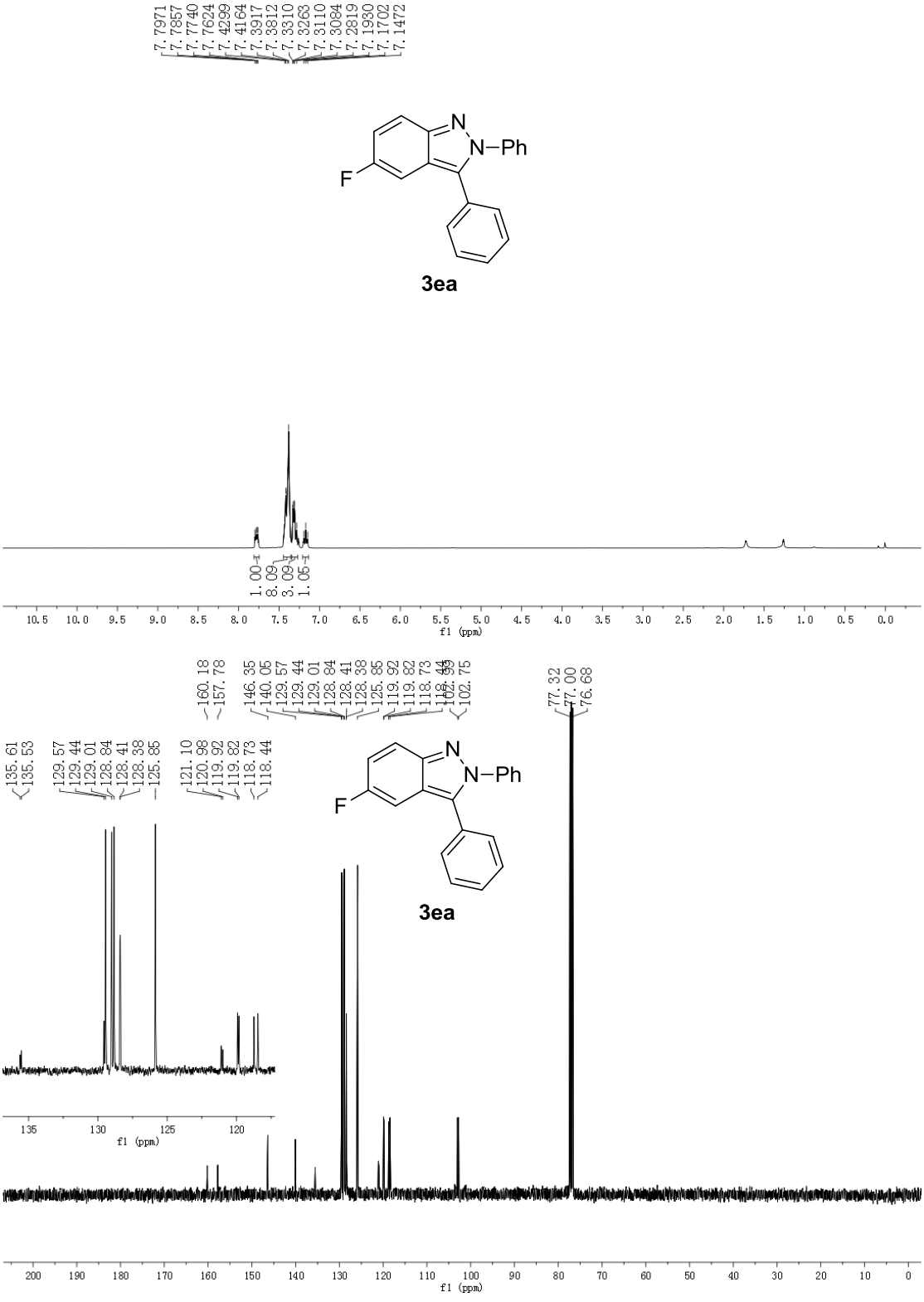


3ca

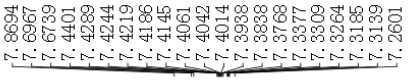
5-methoxy-2,3-diphenyl-2*H*-indazole (3da):

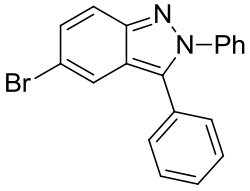


5-fluoro-2,3-diphenyl-2*H*-indazole (3ea):

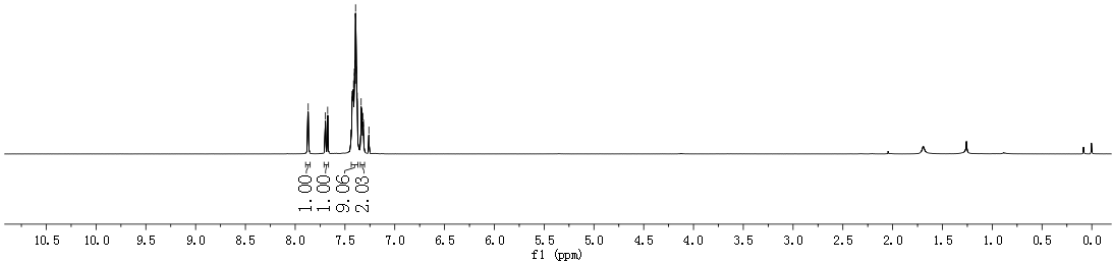


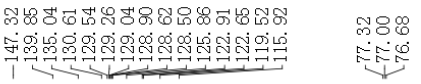
5-bromo-2,3-diphenyl-2*H*-indazole (3fa):

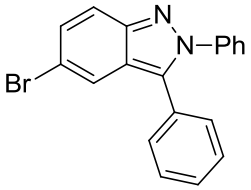




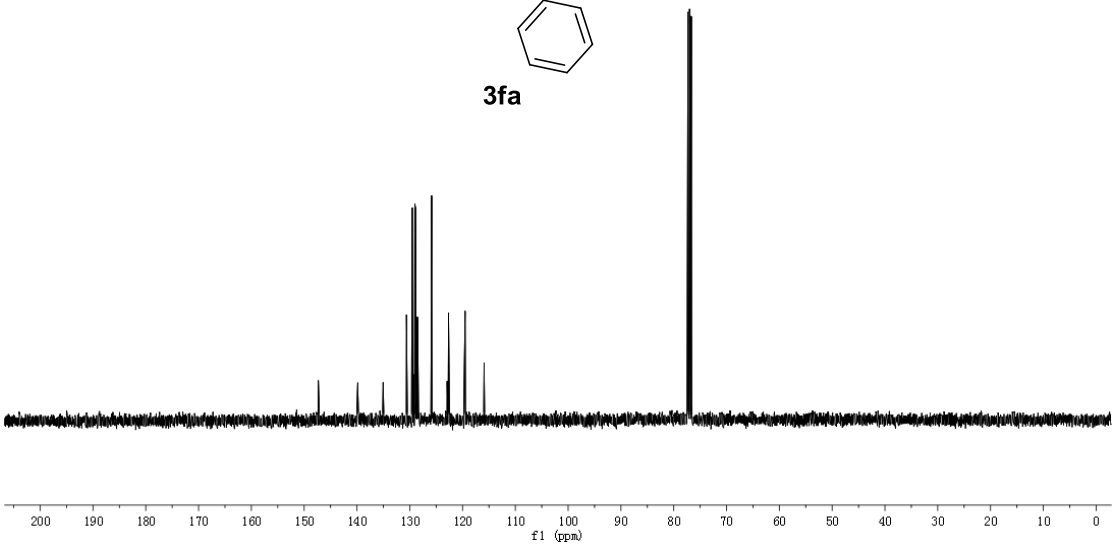
3fa



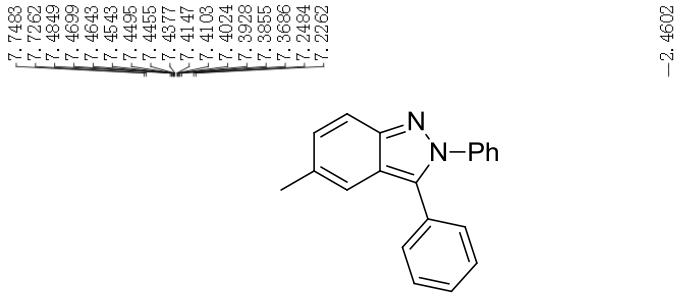




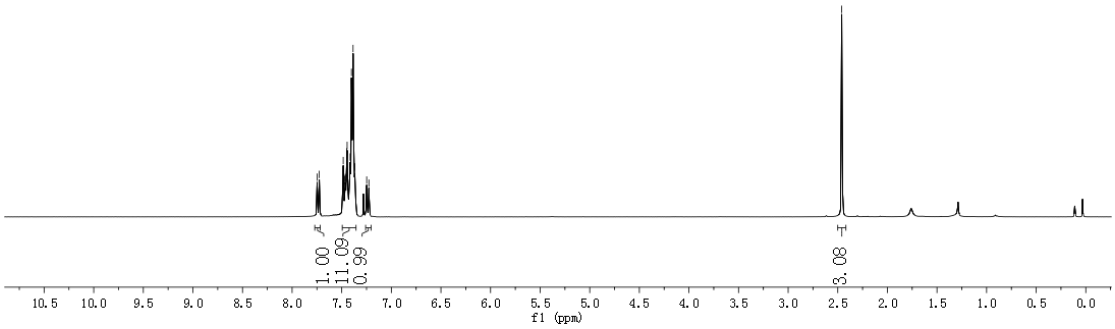
3fa

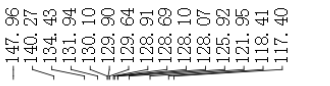


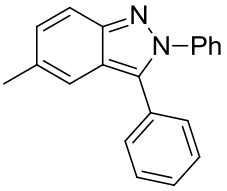
5-methyl-2,3-diphenyl-2*H*-indazole (3ga)



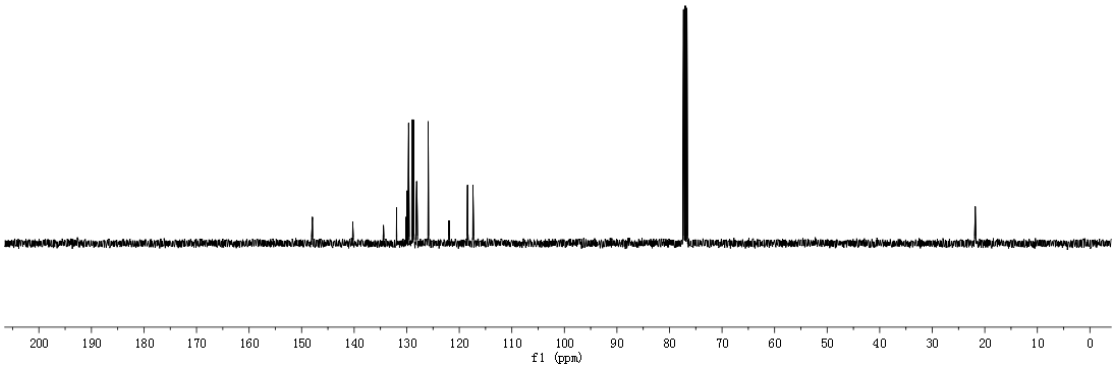
3ga



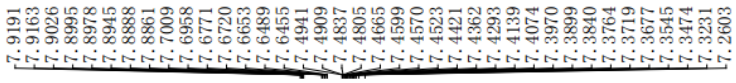


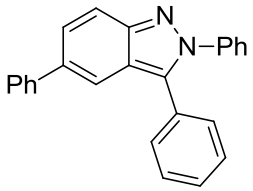


3ga

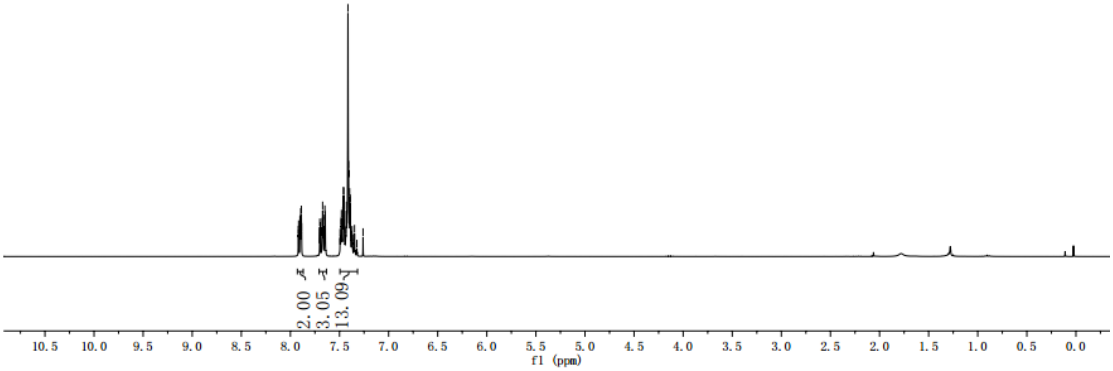


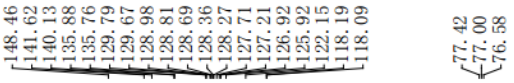
2,3,5-triphenyl-2*H*-indazole (3ha):

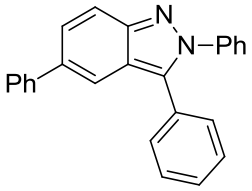




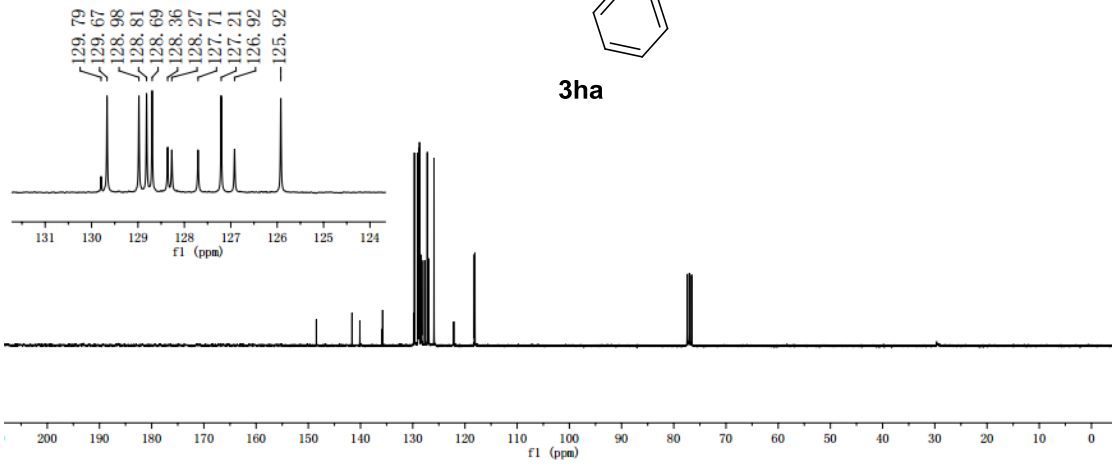
3ha



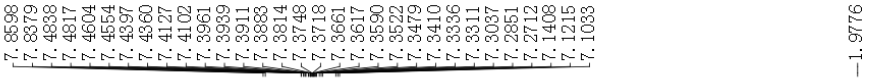


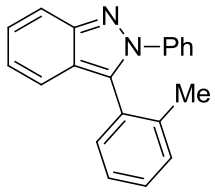


3ha

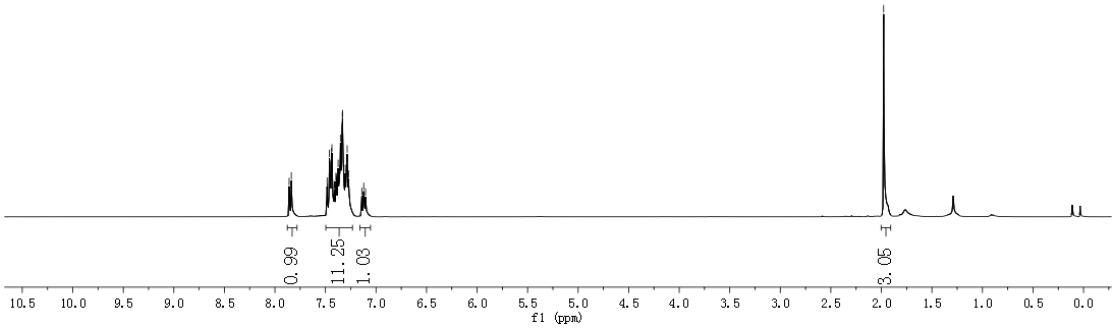


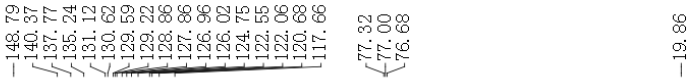
2-phenyl-3-(*o*-tolyl)-2*H*-indazole (3ia):

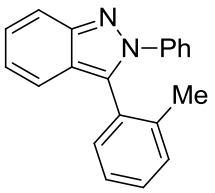




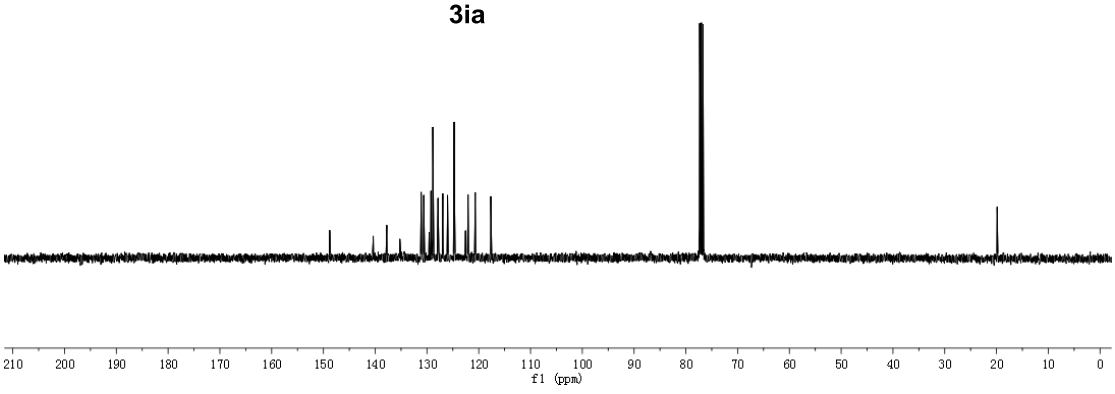
3ia



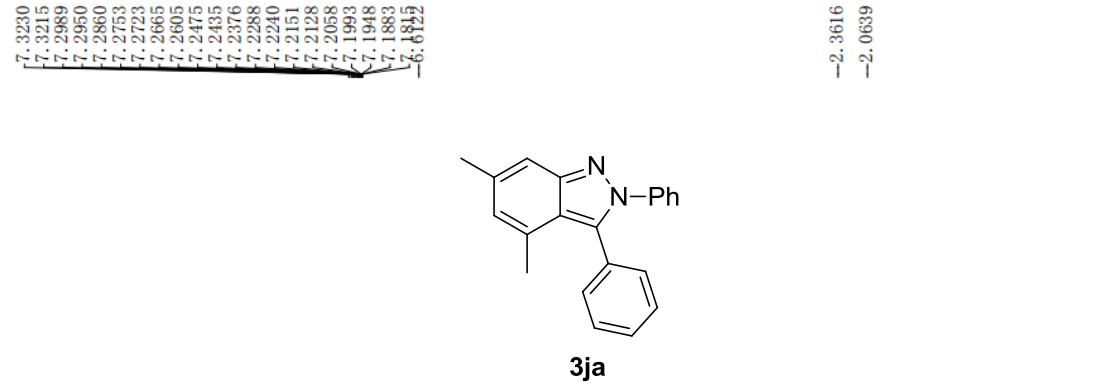




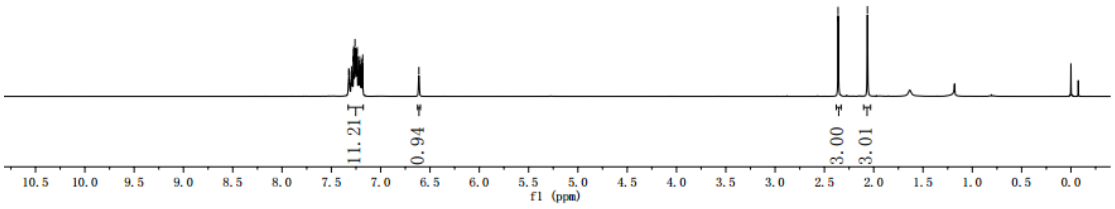
3ia

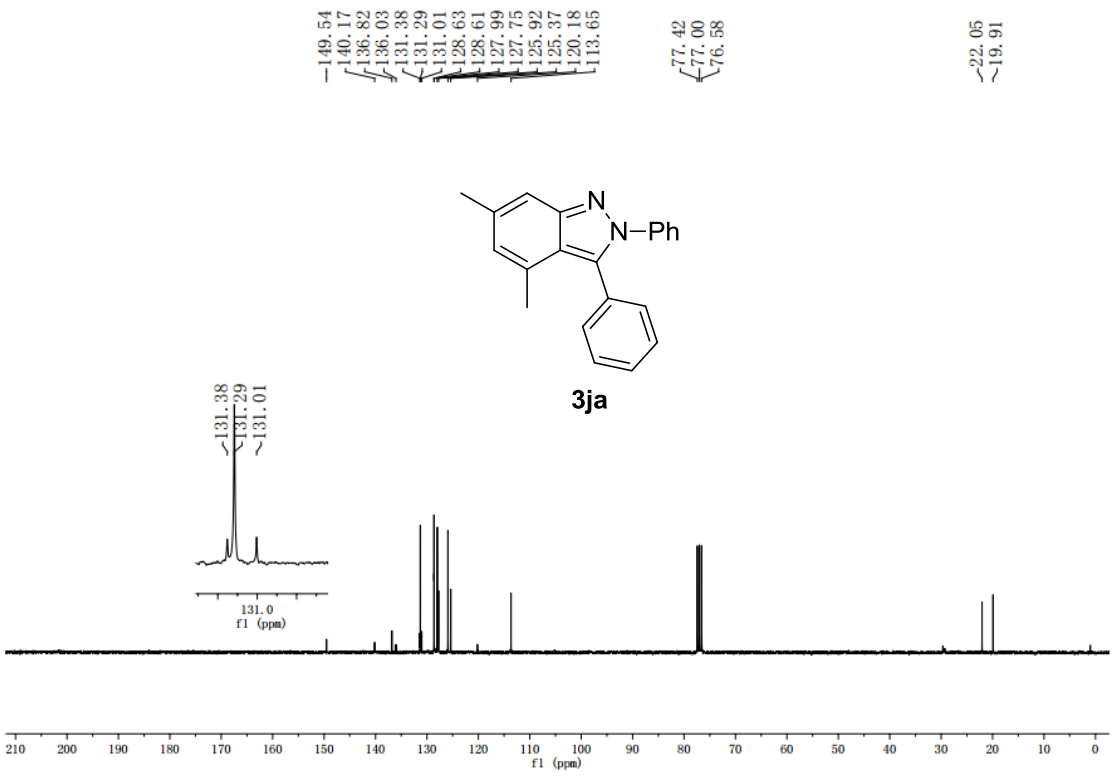


4,6-dimethyl-2,3-diphenyl-2*H*-indazole (3ja):



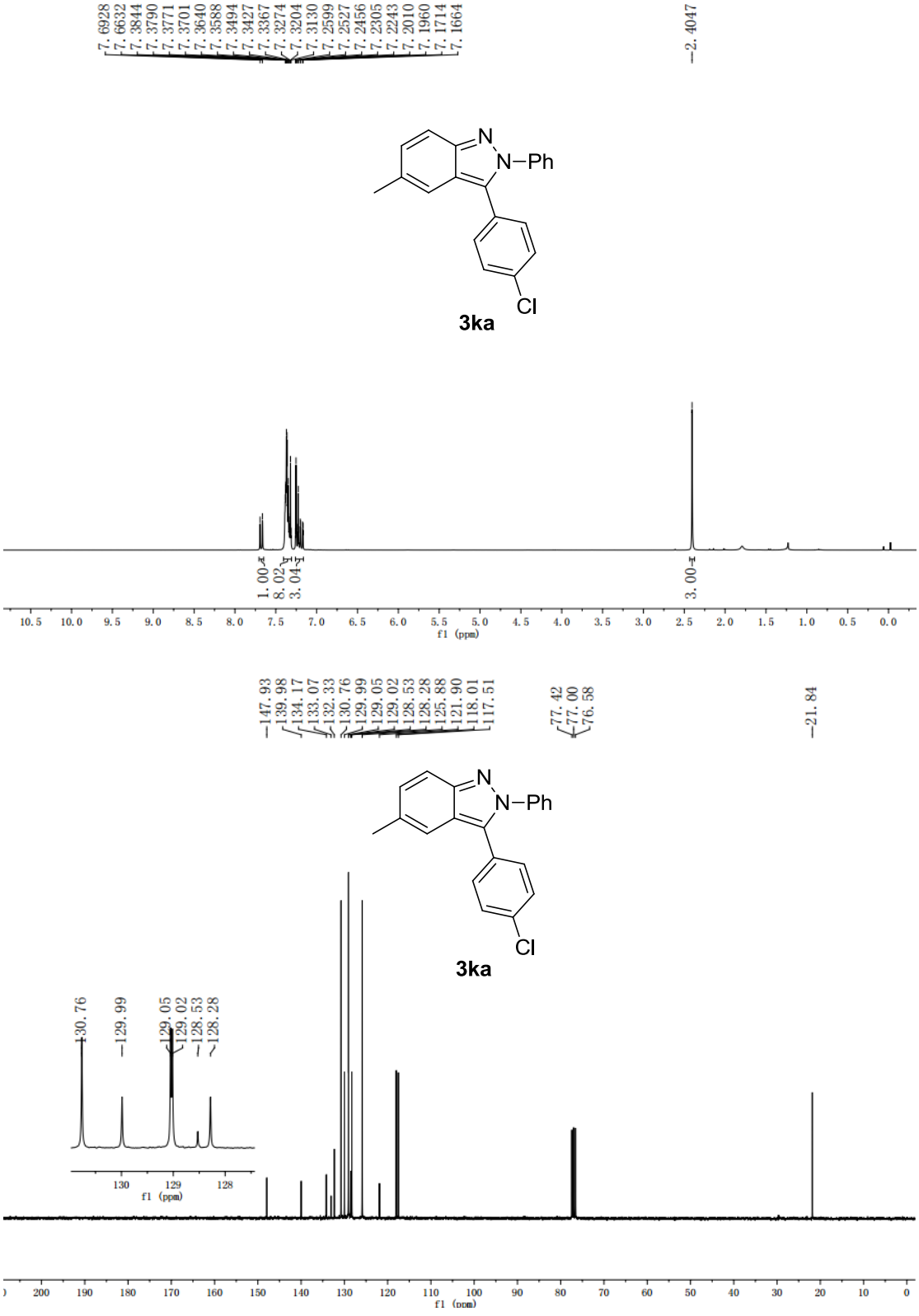
3ja



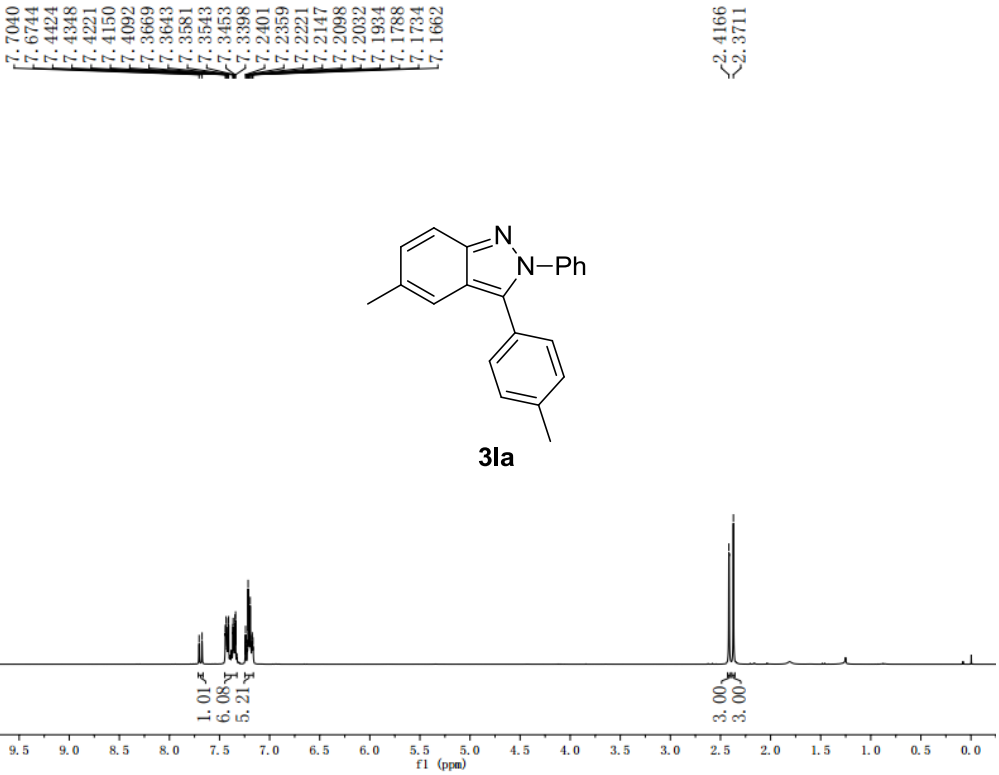


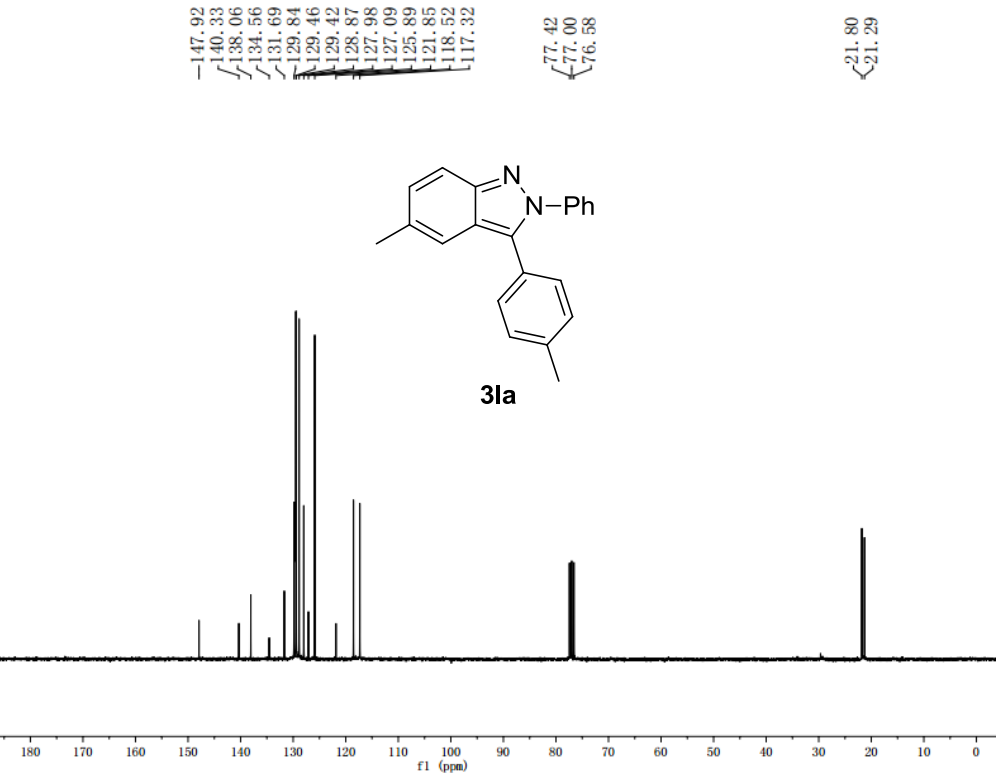
3ja

3-(4-chlorophenyl)-5-methyl-2-phenyl-2*H*-indazole (3ka):

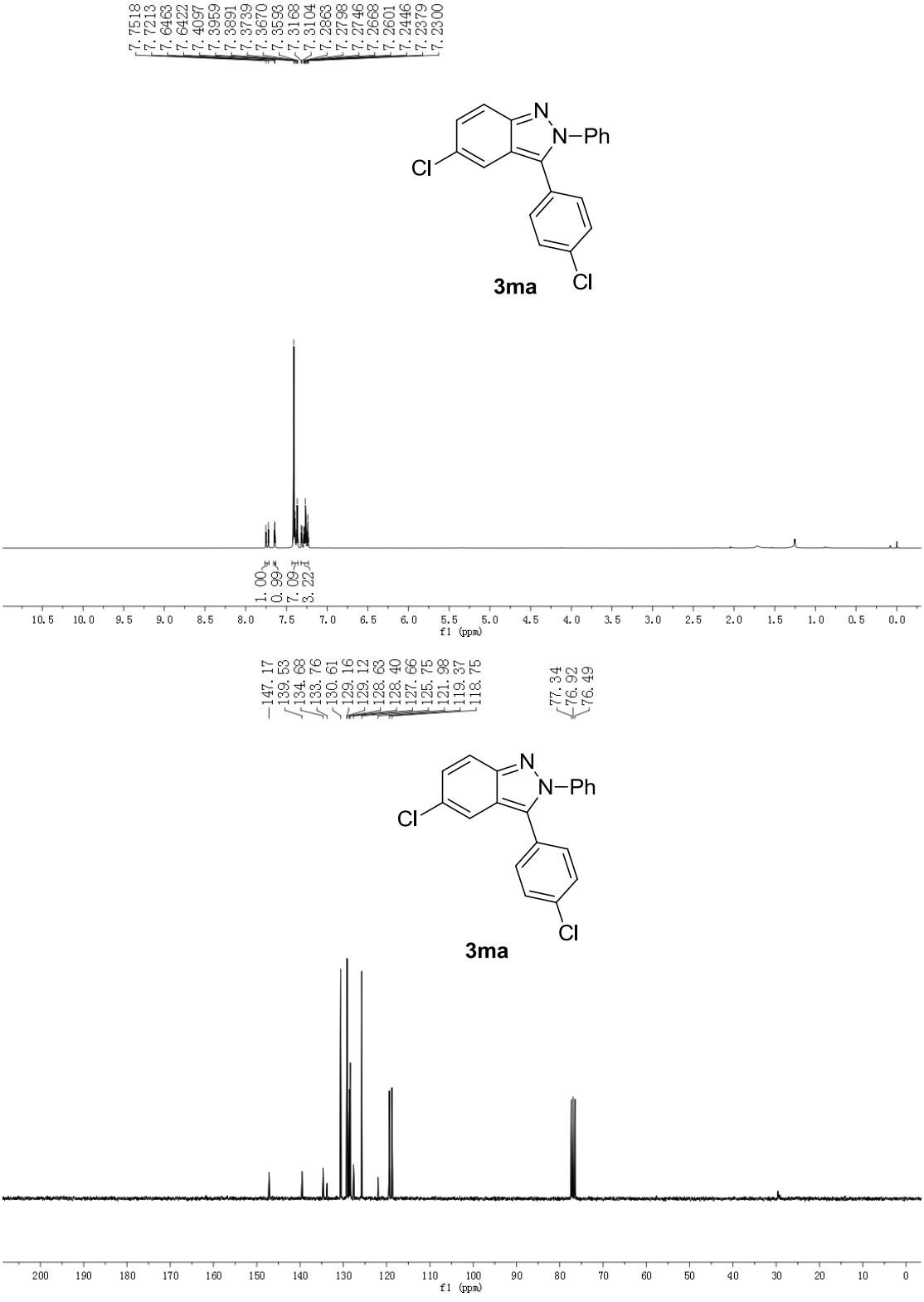


5-methyl-2-phenyl-3-(*p*-tolyl)-2*H*-indazole (3la):

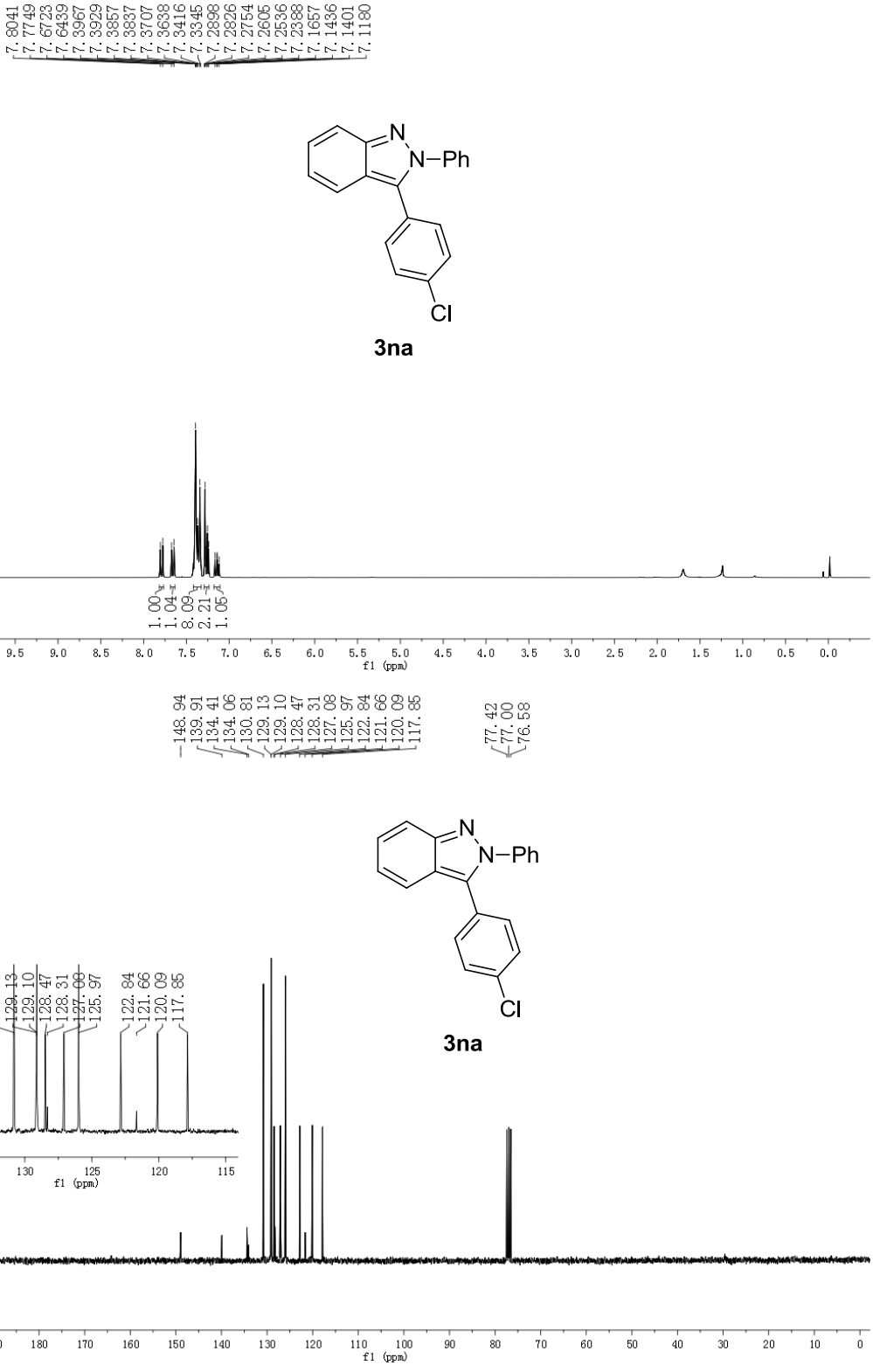




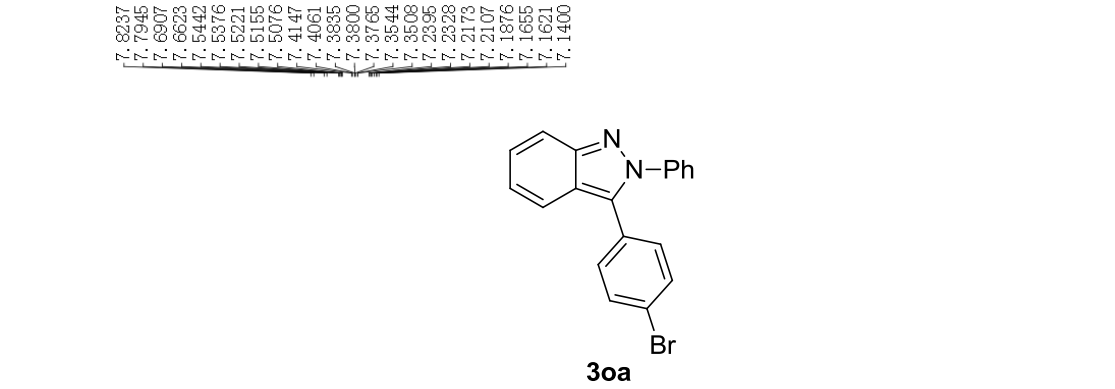
5-chloro-3-(4-chlorophenyl)-2-phenyl-2*H*-indazole (3ma):

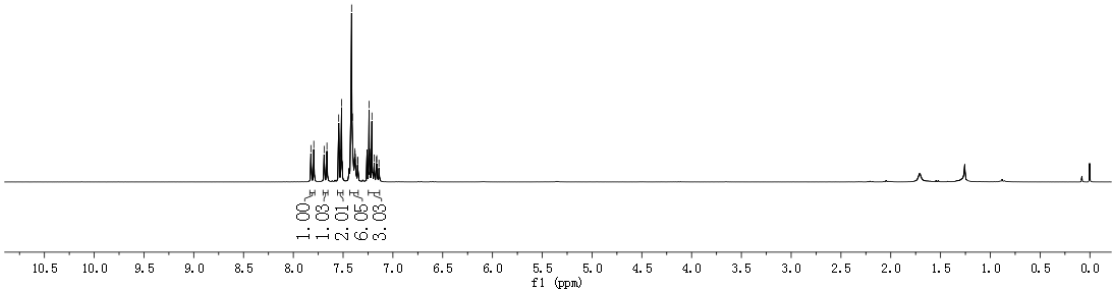


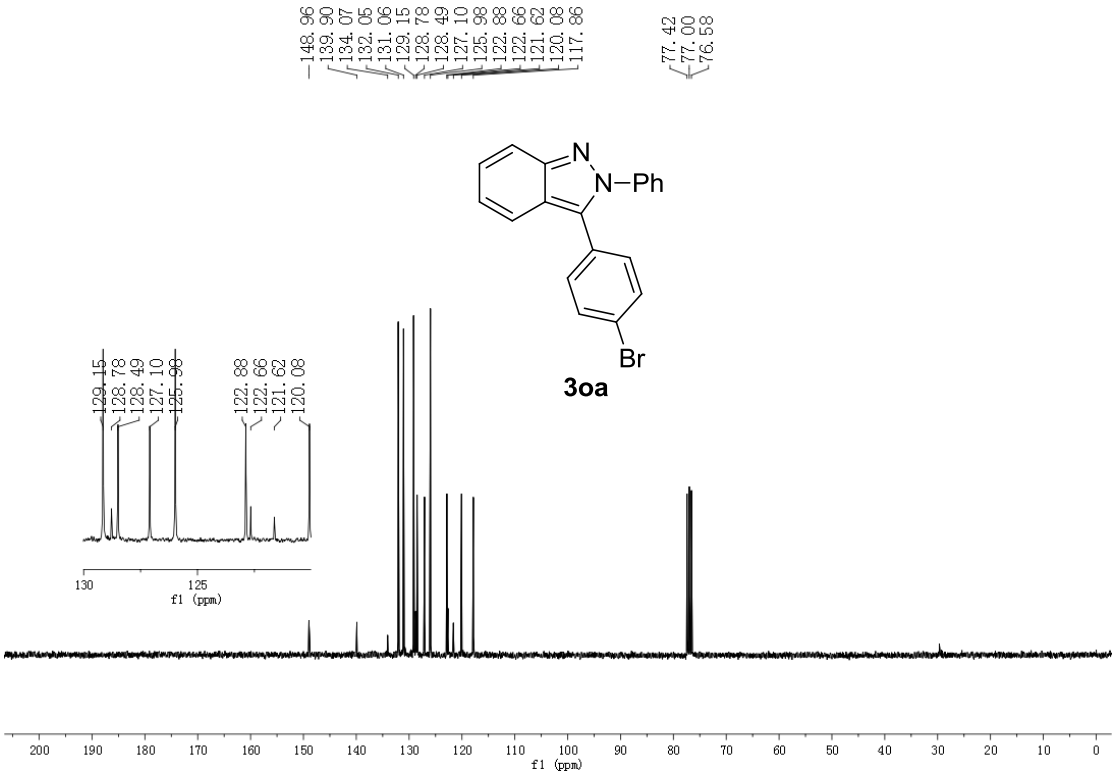
3-(4-chlorophenyl)-2-phenyl-2*H*-indazole (3na):



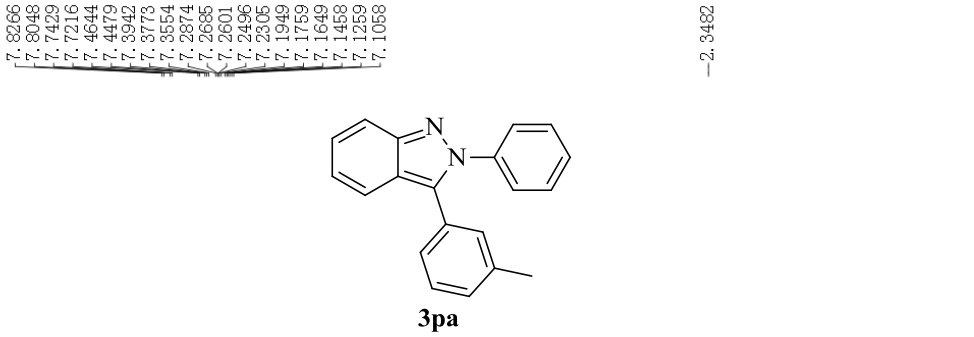
3-(4-bromophenyl)-2-phenyl-2*H*-indazole (3oa):



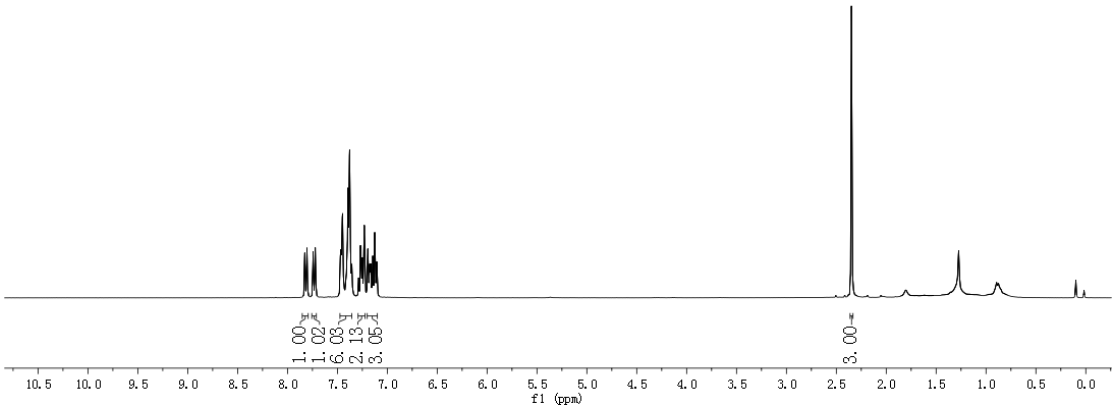


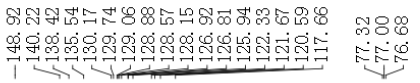


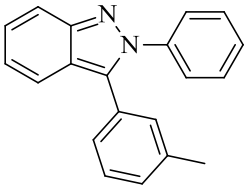
2-phenyl-3-(*m*-tolyl)-2*H*-indazole (3pa):



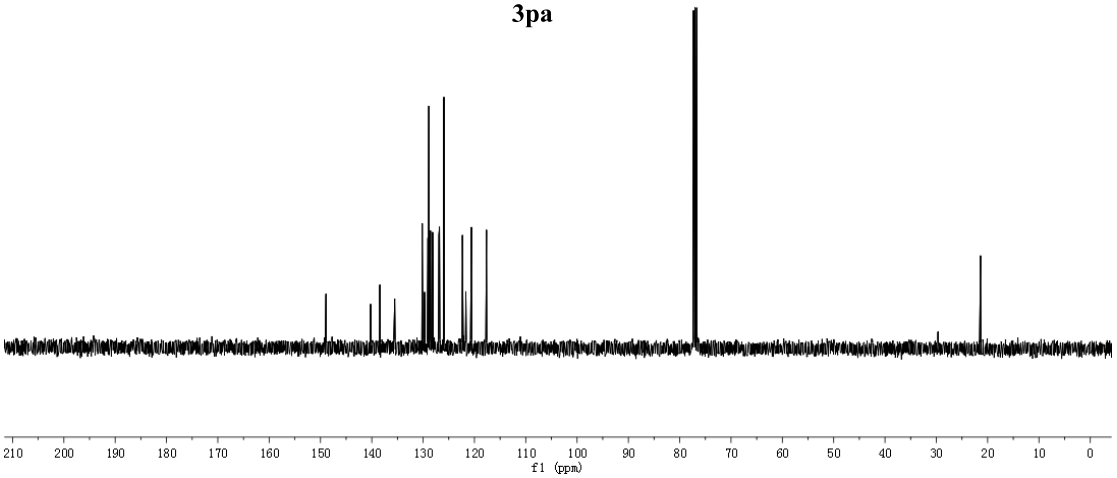
3pa



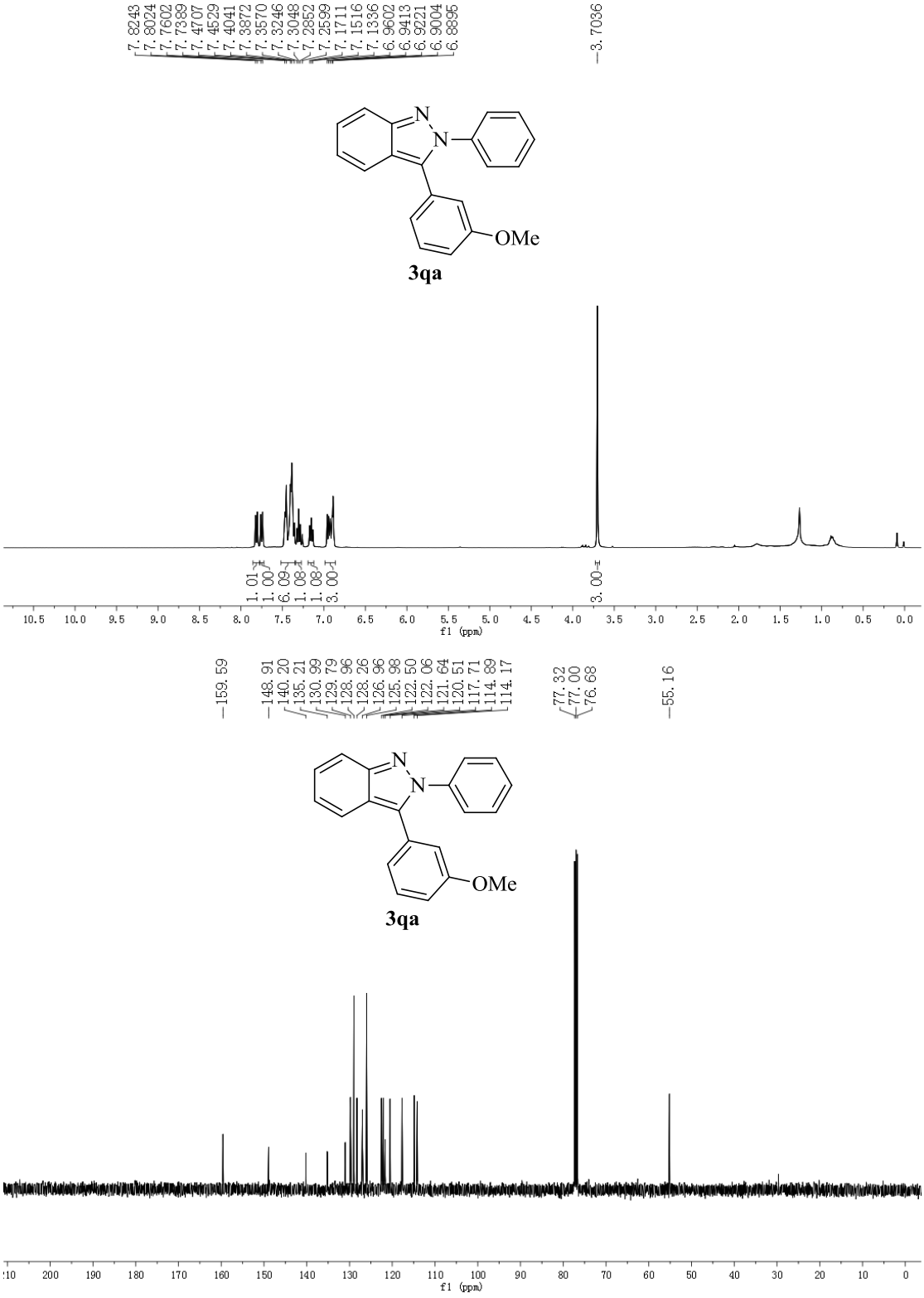




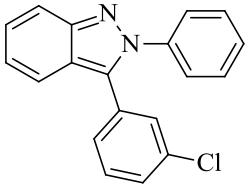
3pa



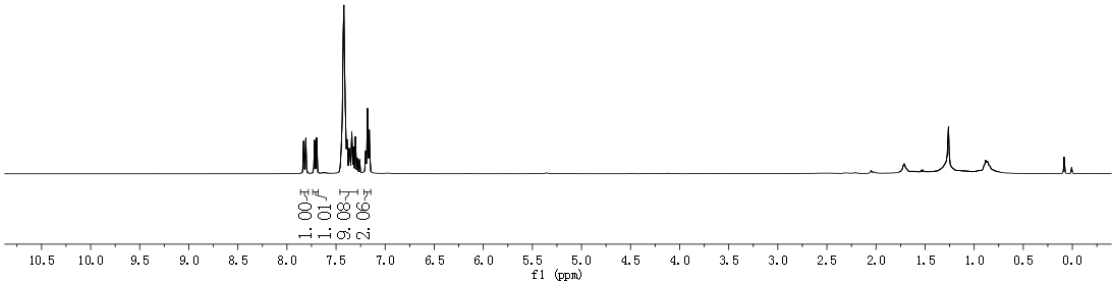
3-(3-methoxyphenyl)-2-phenyl-2*H*-indazole (3qa):

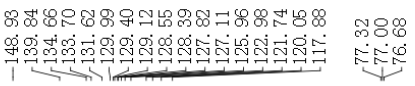


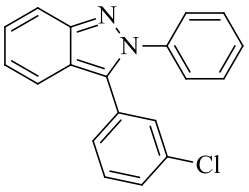
3-(3-chlorophenyl)-2-phenyl-2*H*-indazole (3ra):



3ra

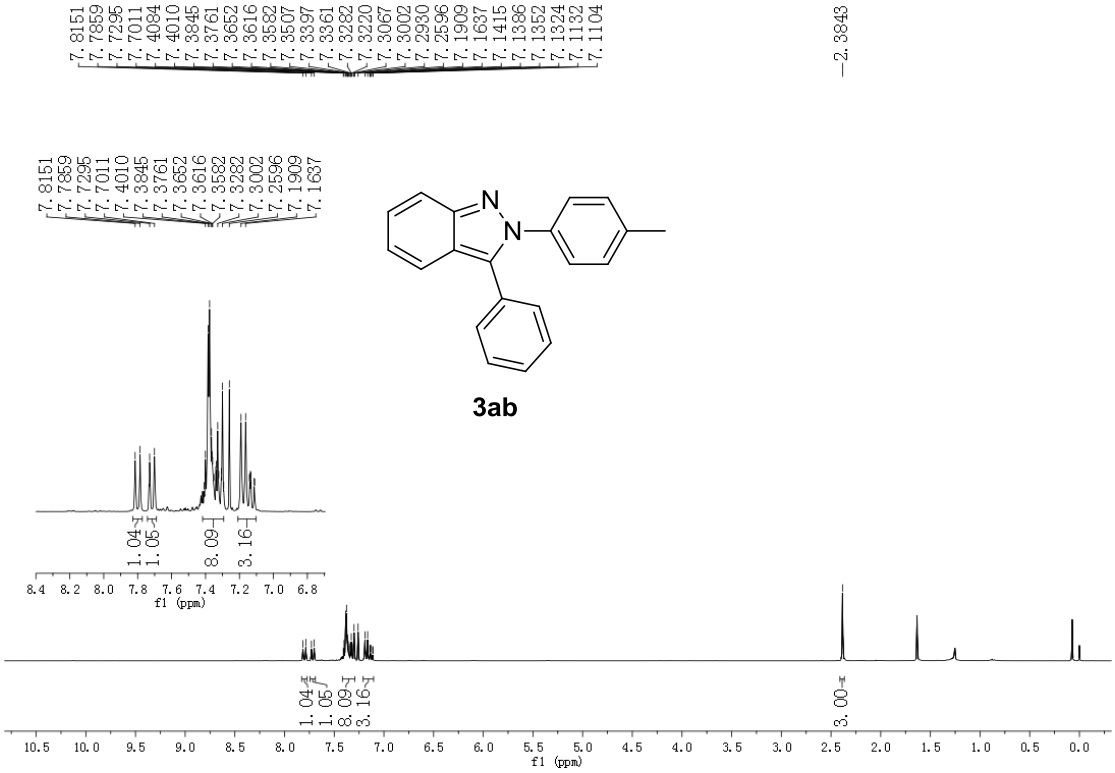




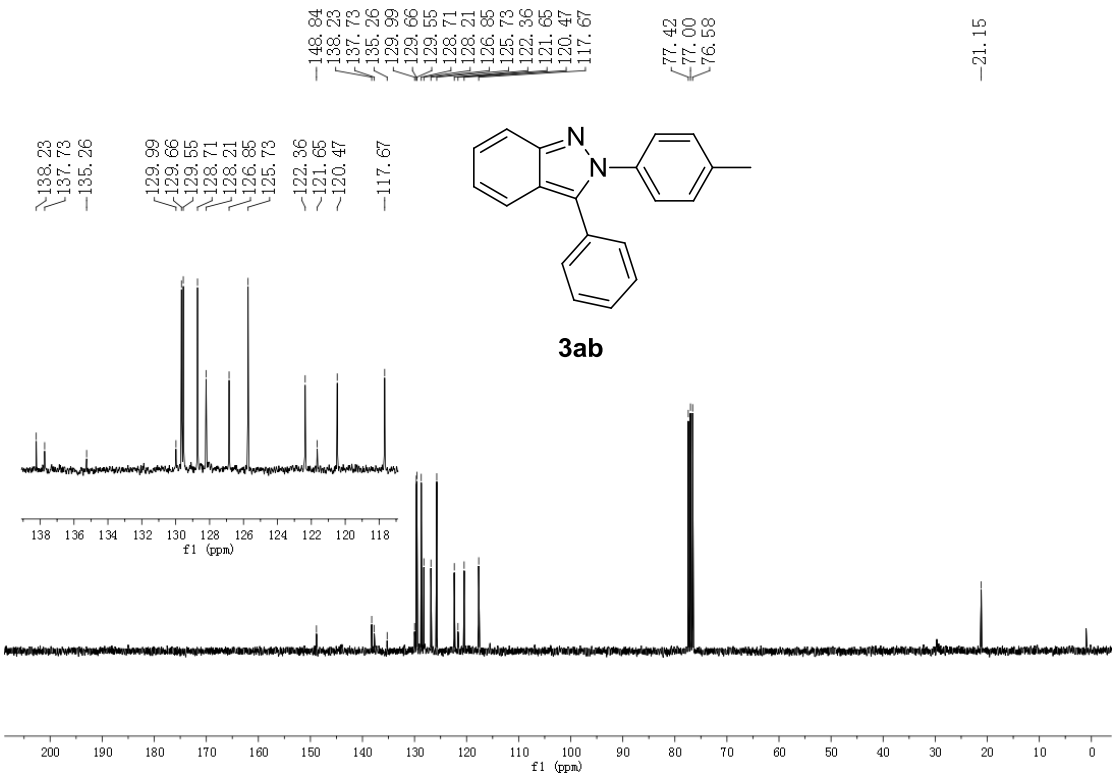


3ra

3-phenyl-2-(p-tolyl)-2*H*-indazole (3ab):

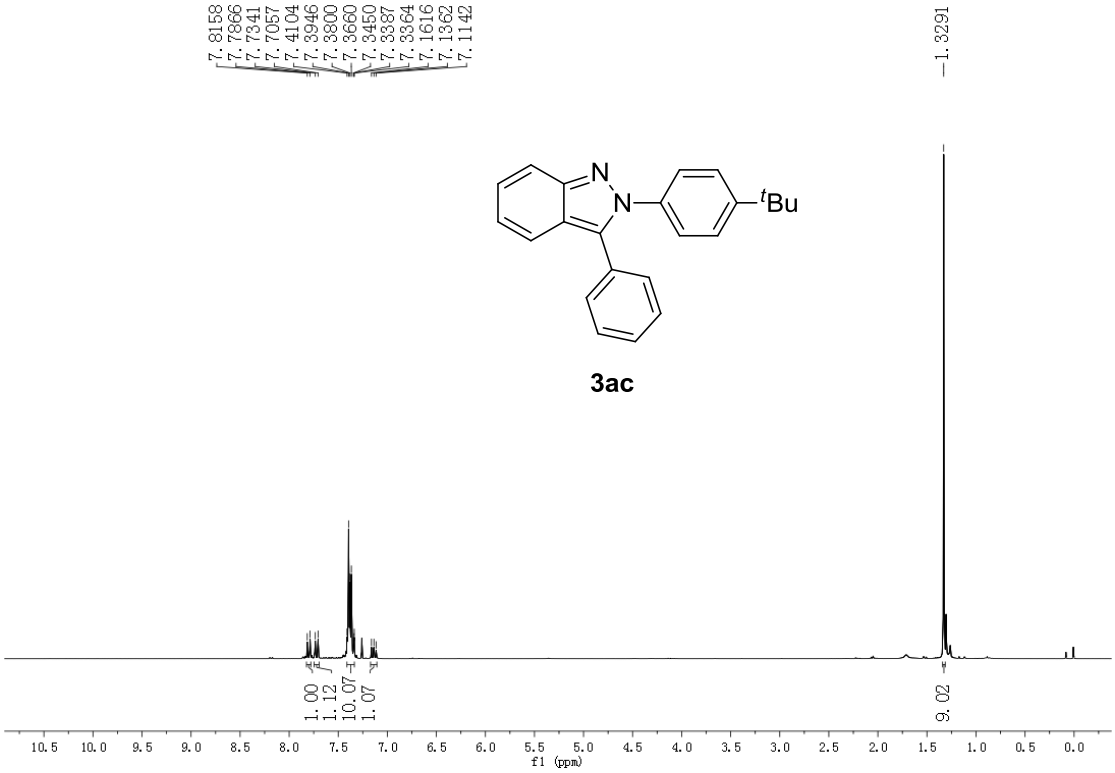


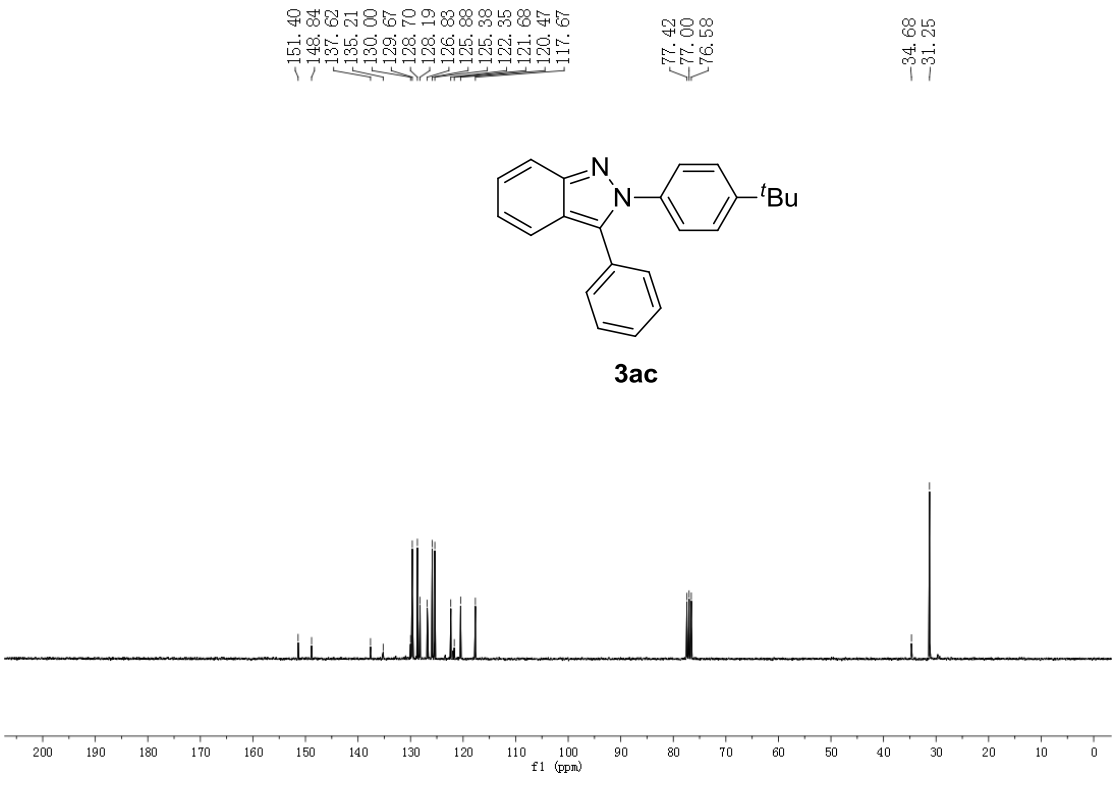
3ab



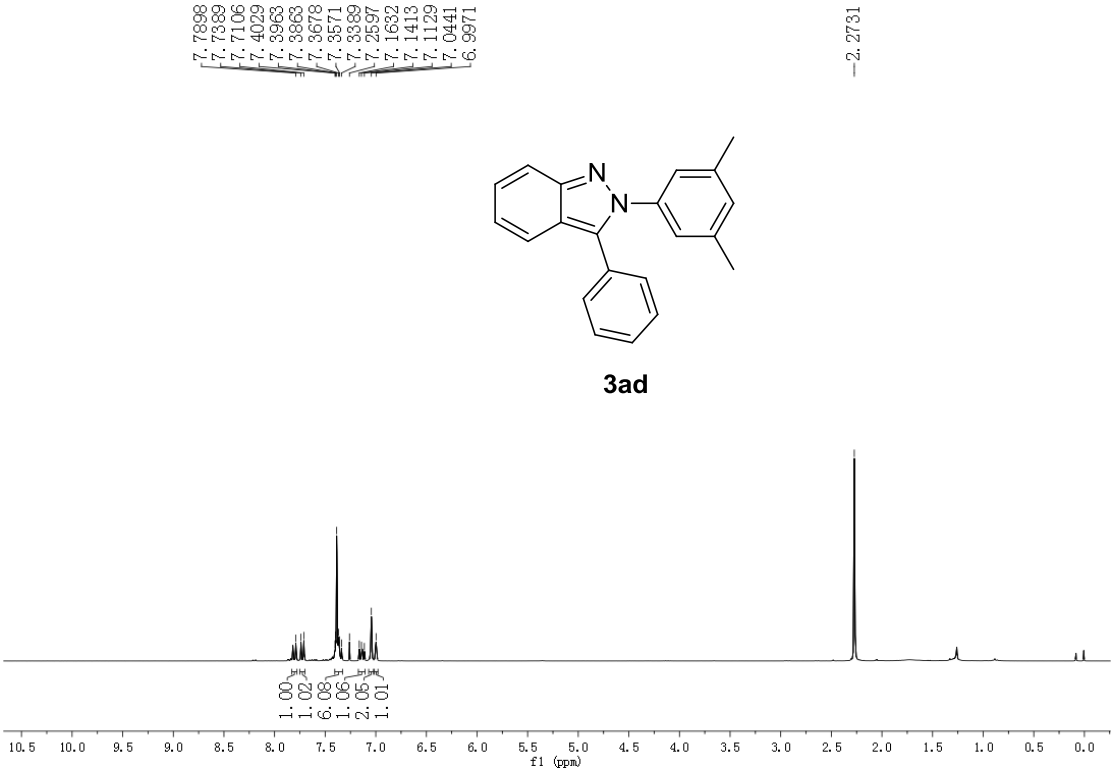
3ab

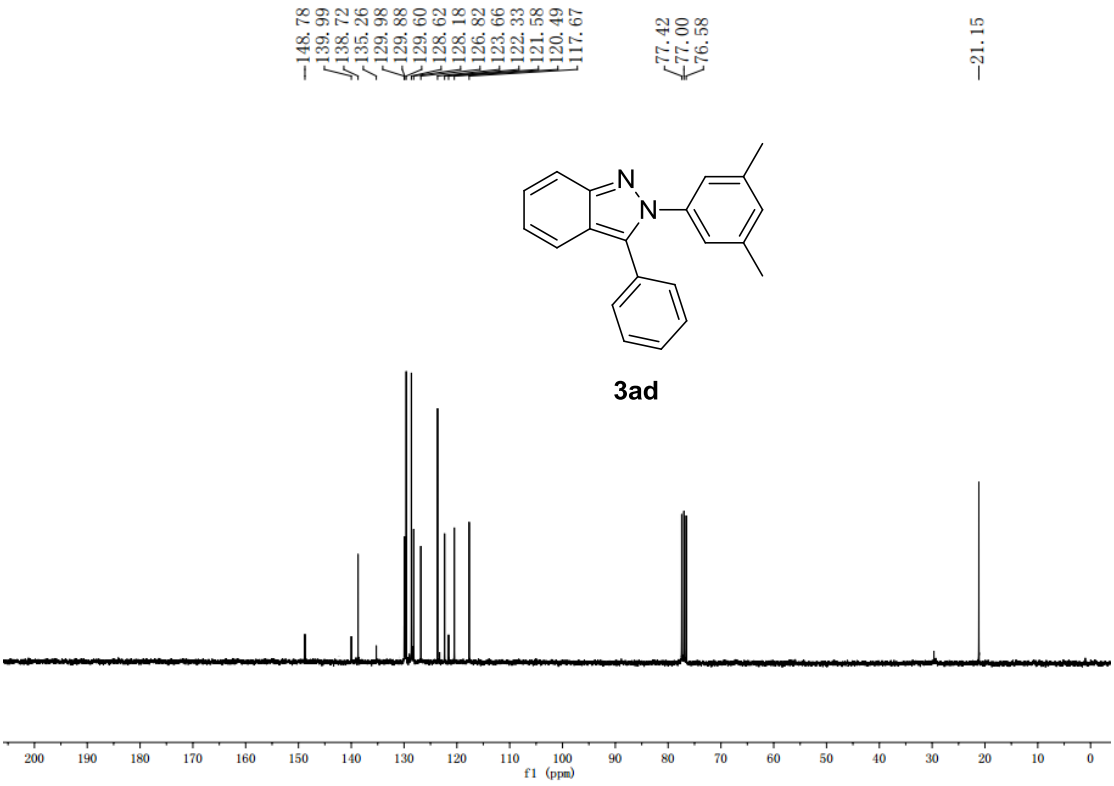
2-(4-(*tert*-butyl)phenyl)-3-phenyl-2*H*-indazole (3ac):



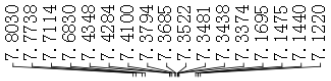


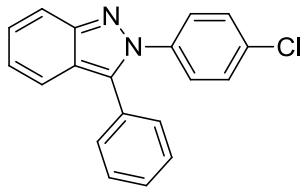
2-(3,5-dimethylphenyl)-3-phenyl-2*H*-indazole (3ad):



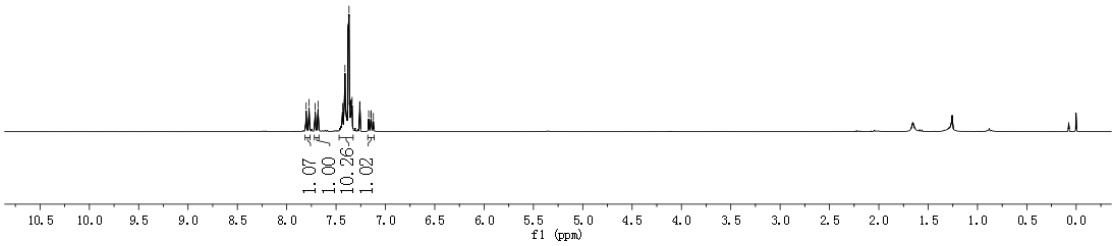


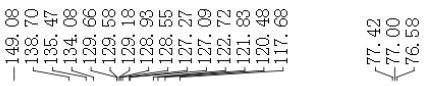
2-(4-chlorophenyl)-3-phenyl-2*H*-indazole (3ae):

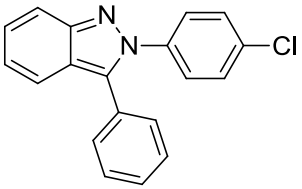




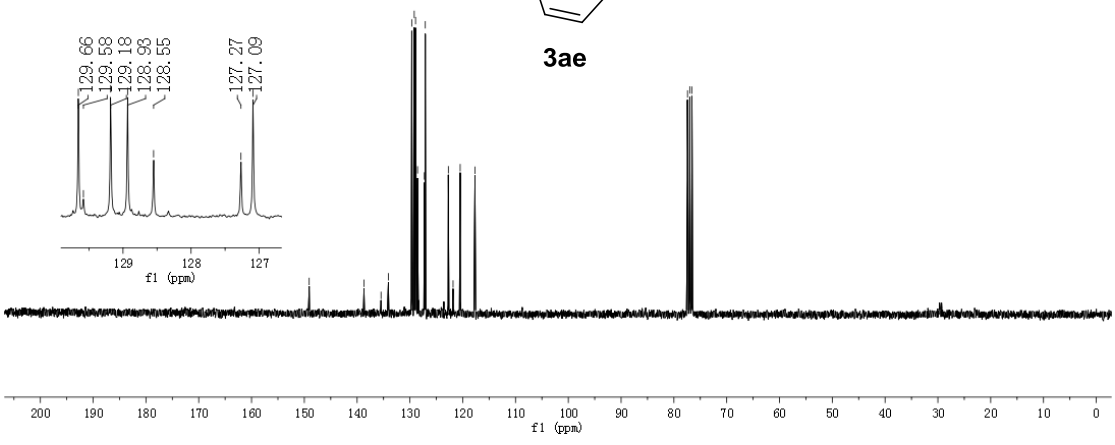
3ae



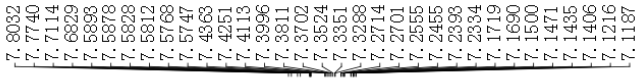


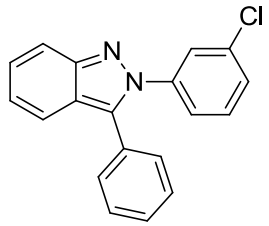


3ae

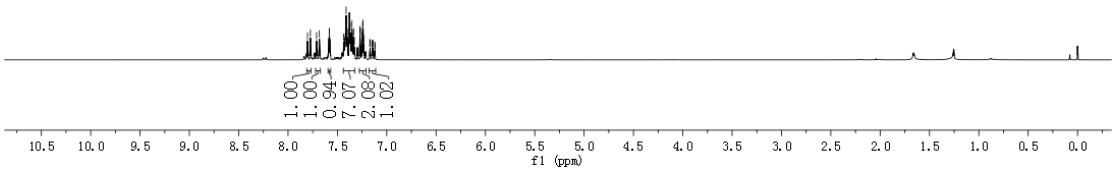


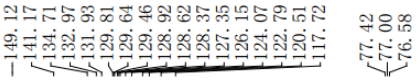
2-(3-chlorophenyl)-3-phenyl-2*H*-indazole (3af):

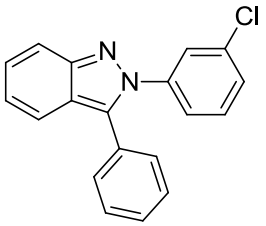




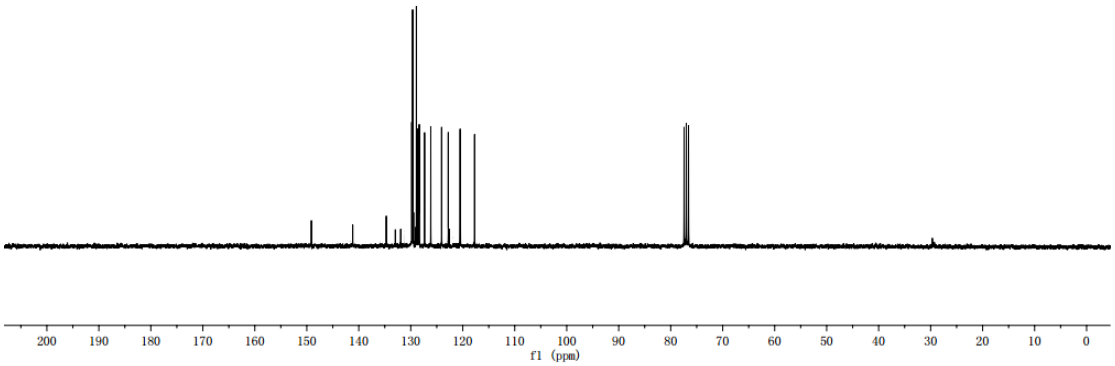
3af



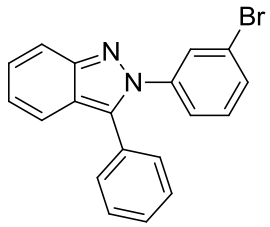




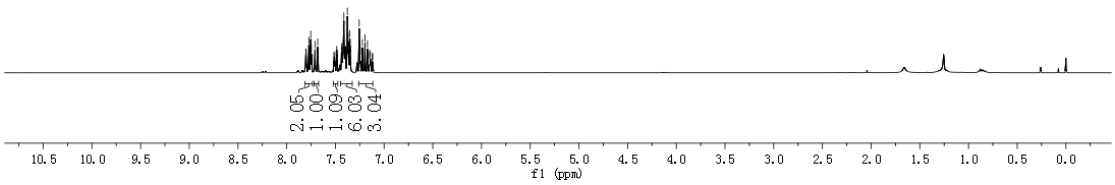
3af

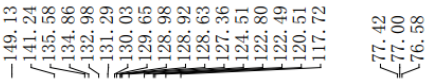


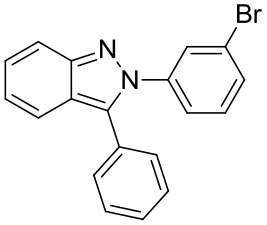
2-(3-bromophenyl)-3-phenyl-2*H*-indazole (3ag):



3ag







3ag