Supporting Information For:

Palladium-Catalyzed Nucleomethylation of Alkynes for Synthesis of Methylated Heteroaromatic Compounds

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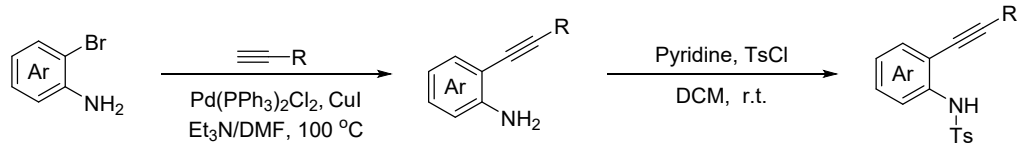
1. General

All reactions were carried out under an atmosphere of nitrogen using standard Schlenk techniques, unless otherwise noted. All solvents and reagents were used as obtained from commercial sources without further purification. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were recorded at room temperature on 400 MHz instrument with tetramethylsilane (TMS) as internal standard. Flash column chromatography was performed on silica gel (200-300 mesh). All reactions were monitored by TLC or NMR analysis.

2. General procedure for the synthesis of *ortho*-alkynylanilines

The *ortho*-alkynylanilines **1b-1k**, **1ai**, and **1aj** were synthesized according to the reported procedures. **1b**[1], **1c**[2], **1d-1f**[3], and **1g**[2] were known compounds and all data were in agreement with the reported literatures.

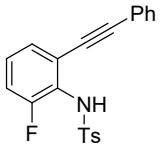


S1 **S2** **1b-1k, 1ai, 1aj**

Synthesis of compound S2:[4] Under nitrogen atmosphere, compound **S1** (1.0 equiv.) $Pd(PPh_3)_2Cl_2$ (2 mol%), and CuI (4 mol%) were dissolved in *N,N*-dimethylformamide, then triethylamine and alkyne compounds (1.5 equiv.) were added. The mixture was stirred overnight in 100 °C oil bath. After completion of the reaction (monitored by TLC), the reaction was cooled to room temperature and quenched by aqueous saturated solution of sodium chloride. The aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S2**.

Synthesis of compound 1:[5] Under nitrogen atmosphere, to a solution of **S2** (1.0 equiv.) in dichloromethane, the pyridine (2.0 equiv.) and sulfonyl chloride (1.2 equiv.) were added. The mixture was stirred at room temperature for 12 h. The mixture was quenched by aqueous dilute solution of hydrochloric acid, the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **1b-1k**, **1ai**, and **1aj**.

***N*-(2-fluoro-6-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (1h)**: the reaction was conducted at 3.5 mmol scale from **S1**, 377.1 mg, 29% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.64 (m, 2H), 7.45–7.39 (m, 2H), 7.39–7.31 (m, 3H), 7.26–7.24 (m, 1H), 7.21–7.16 (m, 1H), 7.15–7.06 (m, 3H), 6.53 (s, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9 (d, J_{C-F} = 250.6 Hz), 144.1, 137.2, 131.9, 129.7, 129.3, 128.6, 128.1 (d, J_{C-F} = 3.5 Hz), 128.0 (d, J_{C-F} = 8.7 Hz), 127.6, 125.5 (d, J_{C-F} = 13.5 Hz), 122.5 (d, J_{C-F} =



2.6 Hz), 122.2, 117.3 (d, J_{C-F} = 20.7 Hz), 96.2, 84.0 (d, J_{C-F} = 4.3 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.80. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{16}FNNaO_2S$ 388.0778; found 388.0773.

***N*-(4-chloro-2-fluoro-6-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (1i)**: the reaction was conducted at 3.5 mmol scale from **S1**, 381.8 mg, 27% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.64 (m, 2H), 7.40–7.33 (m, 5H), 7.24 (s, 1H), 7.19–7.05 (m, 3H), 6.54 (s, 1H), 2.29 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0 (d, J_{C-F} = 254.0 Hz), 144.2, 137.0, 133.1 (d, J_{C-F} = 10.9 Hz), 132.0, 129.8, 129.6, 128.6, 127.9 (d, J_{C-F} = 3.5 Hz), 127.6, 124.3 (d, J_{C-F} = 13.6 Hz), 123.9 (d, J_{C-F} = 3.4 Hz), 121.7, 117.9 (d, J_{C-F} = 23.9 Hz), 97.2, 83.0 (d, J_{C-F} = 4.1 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.89. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{15}ClFNNaO_2S$ 422.0388; found 422.0390.

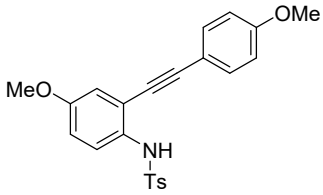
***N*-(3,5-difluoro-2-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (1j)**: the reaction was conducted at 3.5 mmol scale from **S1**, 389.8 mg, 29% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75–7.61 (m, 2H), 7.49–7.31 (m, 5H), 7.19–7.08 (m, 2H), 7.04–6.94 (m 1H), 6.93–6.82 (m, 1H), 6.36 (s, 1H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.9 (dd, J_{C-F} = 248.2, 12.5 Hz), 158.9 (dd, J_{C-F} = 253.4, 13.5 Hz), 144.2, 137.1, 132.0, 129.8, 129.6, 128.6, 127.6, 124.3 (dd, J_{C-F} = 12.1, 3.7 Hz), 121.9 (dd, J_{C-F} = 13.8, 4.2 Hz), 121.8, 114.9 (dd, J_{C-F} = 23.8, 3.7 Hz), 105.9 (dd, J_{C-F} = 24.9, 1.0 Hz), 97.0, 83.3 (dd, J_{C-F} = 4.4, 3.4 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.02 (d, *J* = 8.0 Hz), -111.86 (d, *J* = 7.9 Hz). HRMS (ESI-QEplus) *m/z* $[M+Na]^+$ Calcd for $C_{21}H_{15}F_2NNaO_2S$ 406.0684; found 406.0675.

***N*-(2-chloro-4-fluoro-6-(phenylethynyl)phenyl)-4-methylbenzenesulfonamide (1k)**: the reaction was conducted at 3.5 mmol scale from **S1**, 274.8 mg, 20% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77–7.61 (m, 2H), 7.47–7.39 (m, 2H), 7.38–7.29 (m, 3H), 7.21–7.03 (m, 4H), 6.43 (s, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6 (d, J_{C-F} = 249.9 Hz), 144.2, 137.6, 135.2 (d, J_{C-F} = 11.2 Hz), 132.0, 131.0 (d, J_{C-F} = 3.7 Hz), 129.8, 129.4, 128.5, 127.6, 126.4 (d, J_{C-F} = 11.2 Hz), 122.1, 118.5, 118.2, 118.0, 96.6, 84.6 (d, J_{C-F} = 3.2 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.48. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{15}ClFNNaO_2S$ 422.0388; found 422.0385.

***N*-(2-((3,4-dimethoxyphenyl)ethynyl)-4-methoxyphenyl)-4-methylbenzenesulfonamide (1ai)**: the reaction was conducted at 10.0 mmol scale from **S1**, 714.8 mg, 16% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62–7.57 (m, 2H), 7.57–7.53 (m, 1H), 7.17–7.10 (m, 2H), 7.07–7.01 (m, 1H), 6.95–6.83 (m, 5H), 3.94 (s, 3H), 3.93 (s, 3H), 3.77 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 150.3,

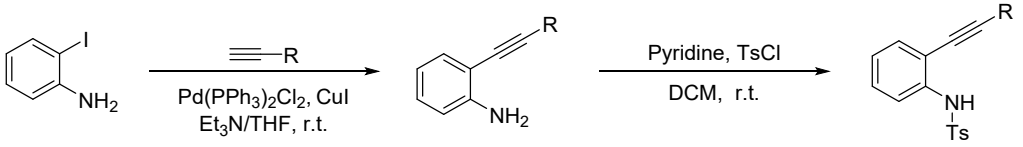
148.9, 144.0, 136.2, 130.6, 129.7, 127.5, 125.3, 124.2, 117.6, 116.2, 116.0, 114.2, 114.2, 111.2, 95.9, 82.8, 56.2, 56.2, 55.7, 21.8. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{23}NNaO_5S$ 460.1189; found 460.1183.

***N*-(4-methoxy-2-((4-methoxyphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (1aj)**: the



reaction was conducted at 15.0 mmol scale from **S1**, 1489.7 mg, 24% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.54 (m, 3H), 7.39–7.31 (m, 2H), 7.17–7.09 (m, 2H), 6.95–6.80 (m, 5H), 3.86 (s, 3H), 3.76 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 157.1, 143.9, 136.2, 133.3, 130.6, 129.7, 127.5, 124.2, 117.7, 116.2, 115.9, 114.4, 114.2, 95.8, 83.0, 55.7, 55.6, 21.7. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_4S$ 430.1083; found 430.1081.

The *ortho*-alkynylanilines **1a, 1l-1v, 1aa, 1ab,** and **1ad** were synthesized according to the reported procedures. **1a**[6]**, 1l-1m**[3]**, 1o**[6], **1p**[7]**, 1s-1t**[3]**, 1u**[7], **1v**[8], **1ab**[6]**, 1ac**[7]**,** and **1ad**[9] were known compounds and all data were in agreement with the reported literatures.

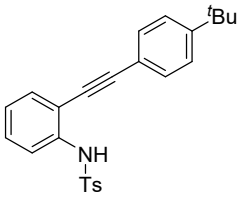


S3 **S4** **1a, 1l-1v, 1aa, 1ab, 1ad**

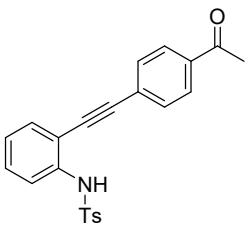
Synthesis of compound S4:[5] Under nitrogen atmosphere, to a solution of **S3** (1.0 equiv.) in tetrahydrofuran, $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), triethylamine (1.2 equiv.) and the alkyne compound (1.2 equiv.) were added. The mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S4**.

Synthesis of compound 1:[5] Under nitrogen atmosphere, to a solution of **S4** (1.0 equiv.) in dichloromethane, pyridine (2.0 equiv.) and sulfonyl chloride (1.2 equiv.) were added. The mixture was stirred at room temperature for 12 h. The mixture was quenched by aqueous dilute solution of hydrochloric acid, the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **1a**, **1l-1v**, **1ab**, **1ac**, and **1ad**.

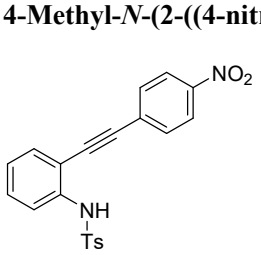
***N*-(2-((4-(*tert*-butyl)phenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (1n)**: the reaction was conducted at 4.0 mmol scale from **S3**, 1416.1 mg, 88% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.65 (m, 2H), 7.64–7.60 (m, 1H), 7.41 (s, 4H), 7.38–7.33 (m, 1H), 7.31–7.21 (m, 2H), 7.19–7.14 (m, 2H), 7.09–7.01 (m, 1H), 2.34 (s, 3H), 1.35 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.7, 144.2, 137.7, 136.3, 132.1, 131.6, 129.8, 129.6, 127.5, 125.8, 124.7, 120.3, 119.2, 115.0, 96.6, 83.3, 35.1, 31.4, 21.7. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{25}H_{26}NO_2S$ 404.1679; found 404.1676.



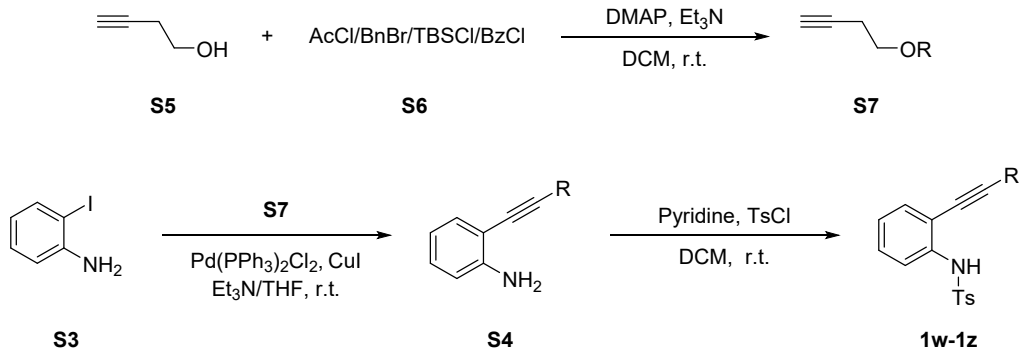
***N*-(2-((4-acetylphenyl)ethynyl)phenyl)-4-methylbenzenesulfonamide (1q)**: the reaction was conducted at 5.0 mmol scale from **S3**, 1837.2 mg, 94% yield, unknown compound, yellow solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02–7.94 (m, 2H), 7.71–7.65 (m, 2H), 7.64–7.60 (m, 1H), 7.58–7.51 (m, 2H), 7.43–7.37 (m, 1H), 7.36–7.30 (m, 1H), 7.22–7.14 (m, 3H), 7.13–7.06 (m, 1H), 2.64 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.4, 144.3, 137.9, 137.0, 136.2, 132.4, 131.9, 130.4, 129.9, 128.6, 127.4, 127.0, 124.9, 120.8, 114.3, 95.3, 87.1, 26.9, 21.7. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{23}H_{20}NO_3S$ 390.1158; found 390.1154.



4-Methyl-*N*-(2-((4-nitrophenyl)ethynyl)phenyl)benzenesulfonamide (1r): the reaction was conducted at 4.0 mmol scale from **S3**, 780.4 mg, 50% yield, unknown compound, yellow solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31–8.19 (m, 2H), 7.72–7.65 (m, 2H), 7.64–7.56 (m, 3H), 7.45–7.40 (m, 1H), 7.39–7.33 (m, 1H), 7.24–7.15 (m, 3H), 7.14–7.08 (m, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 144.5, 138.1, 136.3, 132.7, 132.5, 130.9, 129.9, 129.1, 127.4, 125.0, 124.0, 120.9, 113.8, 94.0, 89.1, 21.8. HRMS (ESI-QEplus) *m*/*z*: $[M-H]^-$ Calcd for $C_{21}H_{15}N_2O_4S$ 391.0758; found 391.0757.



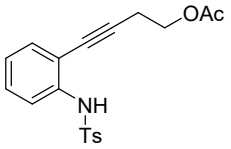
The *ortho*-alkynylanilines **1w-1z** were synthesized according to the reported procedures. **1w**[1] and **1y**[10] were known compounds and all data were in agreement with the reported literatures.



Synthesis of compound S7:[11] The mixture of **S6** (1.0 equiv.), 4-dimethylaminopyridine (0.1 equiv.), triethylamine (1.2 equiv.) in dry dichloromethane was stirred at room temperature, then **S5** was added into the system dropwise. The mixture was stirred at room temperature. After

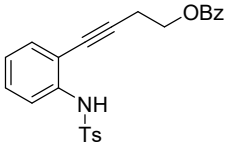
completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S7**. Then **S7** was used to synthesize **1w**-**1z** following the previous method.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl acetate (1x): the reaction was



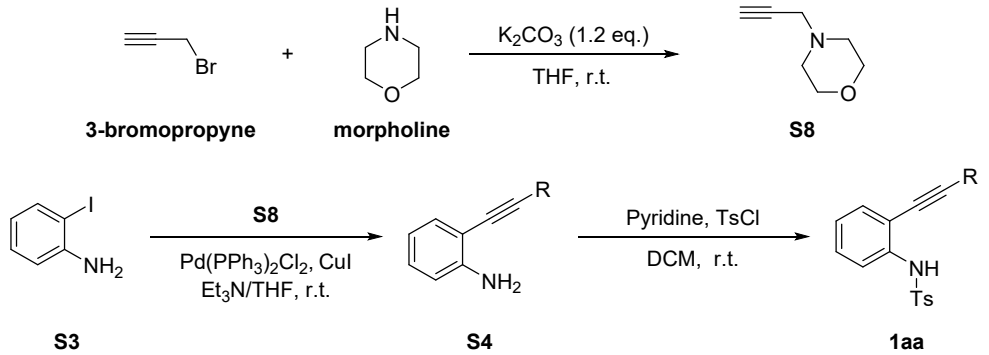
conducted at 3.1 mmol scale from **S4**, 842.1 mg, 76% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 7/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71–7.64 (m, 2H), 7.60–7.54 (m, 1H), 7.29–7.25 (m, 2H), 7.24–7.20 (m, 3H) 7.03–6.97 (m, 1H), 4.24 (t, *J* = 6.5 Hz, 2H), 2.75 (t, *J* = 6.5 Hz, 2H), 2.37 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 144.2, 138.1, 136.4, 132.1, 129.8, 129.5, 127.4, 124.4, 119.8, 114.4, 93.3, 77.0, 62.2, 21.7, 21.1, 20.3. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{19}H_{19}NNaO_4S$ 380.0927; found 380.0920.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl benzoate (1z): the reaction was



conducted at 4.8 mmol scale from **S4**, 865.8 mg, 43% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 6/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15–8.06 (m, 2H), 7.70–7.62 (m, 2H), 7.61–7.53 (m, 2H), 7.50–7.43 (m, 2H), 7.33–7.20 (m, 3H), 7.20–7.14 (m, 2H), 7.03–6.95 (m, 1H), 4.49 (t, *J* = 6.6 Hz, 2H), 2.89 (t, *J* = 6.6 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 144.1, 138.0, 136.4, 133.4, 132.4, 130.0, 129.9, 129.8, 129.4, 128.7, 127.4, 124.4, 120.0, 114.5, 93.1, 77.2, 62.7, 21.7, 20.5. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{24}H_{21}NNaO_4S$ 442.1083; found 442.1073.

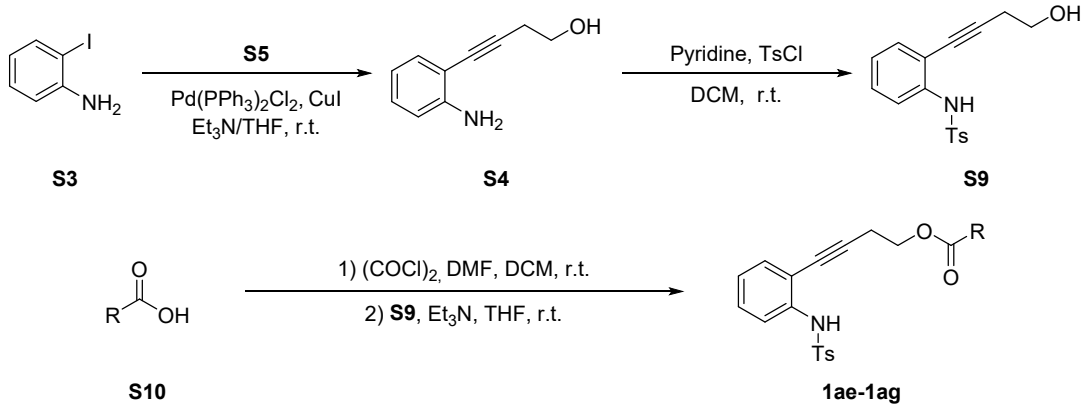
The *ortho*-alkynylanilines **1aa** were synthesized according to the reported procedures.



Synthesis of compound S8:[12] The mixture of 3-bromopropyne (1.2 equiv.), morpholine (1.0 equiv.), potassium carbonate (1.2 equiv.) in dry tetrahydrofuran was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (dichloromethane/ethyl acetate) to afford the desired compound **S8**. Then **S8** was used to synthesize **1aa** following the previous method.

4-Methyl-*N*-(2-(3-morpholinoprop-1-yn-1-yl)phenyl)benzenesulfonamide (1aa): the reaction was conducted at 5.9 mmol scale from **S4**, 1202.2 mg, 55% yield, unknown compound, yellow solid, R_f = 0.25 (dichloromethane/ethyl acetate 2/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.64 (m, 2H), 7.62–7.53 (m, 1H), 7.33–7.23 (m, 3H), 7.22–7.17 (m, 2H), 7.05–6.96 (m, 1H), 3.83–3.72 (m, 4H), 3.51 (s, 2H), 2.66–2.53 (m, 4H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 137.9, 136.4, 132.5, 129.7, 129.7, 127.4, 124.4, 119.6, 114.0, 91.6, 80.4, 66.9, 52.5, 48.1, 21.7. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{20}H_{23}N_2O_3S$ 371.1424; found 371.1416.

The *ortho*-alkynylanilines **1ae-1ag** were synthesized according to the reported procedures. The compound **S9** was synthesized following the previous method.



Synthesis of compound 1:[13] Under nitrogen atmosphere, to a solution of **S10** (1.0 equiv.) in dichloromethane was added oxalyl chloride (2.0 equiv.) and *N,N*-dimethylformamide (a few drops). The mixture was stirred at room temperature for 0.5 h. The mixture was concentrated under reduced pressure. The resulting crude material was dissolved in tetrahydrofuran at 0 °C, then **S9** (1.2 equiv.) and triethylamine (5.0 equiv.) were added into the system in the same temperature. The mixture was stirred at room temperature for 6 h. The mixture was quenched by aqueous dilute solution of hydrochloric acid, the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **1ae-1ag**.

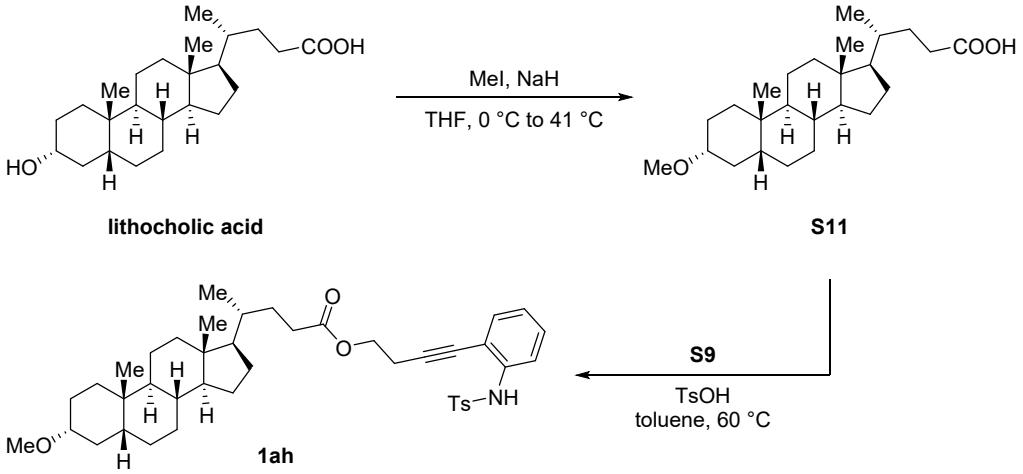
4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl 4-(*N,N*-dipropylsulfamoyl)benzoate (1ae): the reaction was conducted at 2.0 mmol scale from **S10**, 174.2 mg, 15% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28–8.17 (m, 2H), 7.96–7.84 (m, 2H), 7.69–7.61 (m, 2H), 7.57–7.48 (m, 1H), 7.29–7.23 (m, 3H), 7.22–7.18 (m, 2H), 7.03–6.93 (m, 1H), 4.53 (t, *J* = 6.5 Hz, 2H), 3.15–3.04 (m, 4H), 2.92 (t, *J* = 6.5 Hz, 2H), 2.36 (s, 3H), 1.63–1.47 (m, 4H), 0.86 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 144.8, 144.3, 138.1, 136.4, 133.2, 132.4, 130.6, 129.8, 129.6, 127.4, 127.4, 124.4, 119.6, 114.1, 92.8, 77.4, 63.3, 50.2, 22.2, 21.8, 20.5, 11.4. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{30}H_{34}N_2NaO_6S_2$

605.1750; found 605.1740.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl 2-(6-methoxynaphthalen-2-yl)propanoate (1af): the reaction was conducted at 1.5 mmol scale from **S10**, 348.2 mg, 44% yield, unknown compound, colorless oil, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73–7.65 (m, 2H), 7.65–7.60 (m, 3H), 7.56–7.49 (m, 1H), 7.45–7.37 (m, 1H), 7.24–7.19 (m, 1H), 7.19–7.14 (m, 3H), 7.12–7.03 (m, 3H), 6.96–6.87 (m, 1H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.96 (q, *J* = 7.1 Hz, 1H), 3.90 (s, 3H), 2.67 (t, *J* = 6.5 Hz, 2H), 2.32 (s, 3H), 1.60 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 157.8, 144.1, 138.0, 136.5, 135.6, 133.9, 132.2, 129.8, 129.5, 129.4, 129.1, 127.5, 127.4, 126.4, 126.2, 124.4, 119.9, 119.2, 114.5, 105.8, 93.0, 77.1, 62.4, 55.5, 45.5, 21.7, 20.3, 18.8. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{31}H_{29}NNaO_5S$ 550.1659; found 550.1653.

4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl 2-(4-isobutylphenyl)propanoate (1ag): the reaction was conducted at 2.0 mmol scale from **S10**, 886.4 mg, 88% yield, unknown compound, brown solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 8.2 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 1H), 7.26–7.17 (m, 7H), 7.05–7.03 (m, 2H), 7.00–6.96 (m, 1H), 4.27–4.18 (m, 2H), 3.80 (q, *J* = 7.0 Hz, 1H), 2.68 (t, *J* = 6.6 Hz, 2H), 2.40 (d, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.85–1.75 (m, 1H), 1.51 (d, *J* = 7.1 Hz, 3H), 0.87 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 144.2, 140.8, 138.0, 137.7, 136.5, 132.3, 129.8, 129.6, 129.4, 127.5, 127.4, 124.4, 120.0, 114.6, 93.0, 77.1, 62.3, 45.3, 45.2, 30.3, 22.6, 21.7, 20.3, 18.8. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{30}H_{33}NNaO_4S$ 526.2023; found 526.2019.

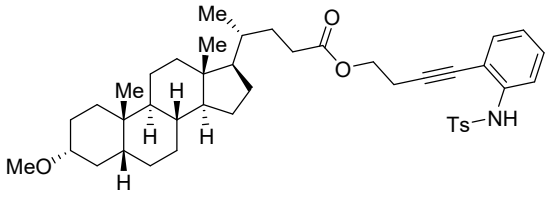
The *ortho*-alkynylanilines **1ah** were synthesized according to the reported procedures.



Synthesis of compound S11:[14] Under nitrogen atmosphere, to a solution of **lithocholic acid** (3.0 mmol, 1.0 equiv.) in tetrahydrofuran (30.0 mL) was added sodium hydride (18.0 mmol, 6.0 equiv.) at 0 °C. The mixture was stirred in the same temperature for 10 min. Then methyl iodide (30 mmol, 10.0 equiv.) was added slowly into the system in the same temperature. The mixture

was stirred at 41 °C for 24 h. The reaction was quenched by saturated ammonium chloride aqueous solution, the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S11**.

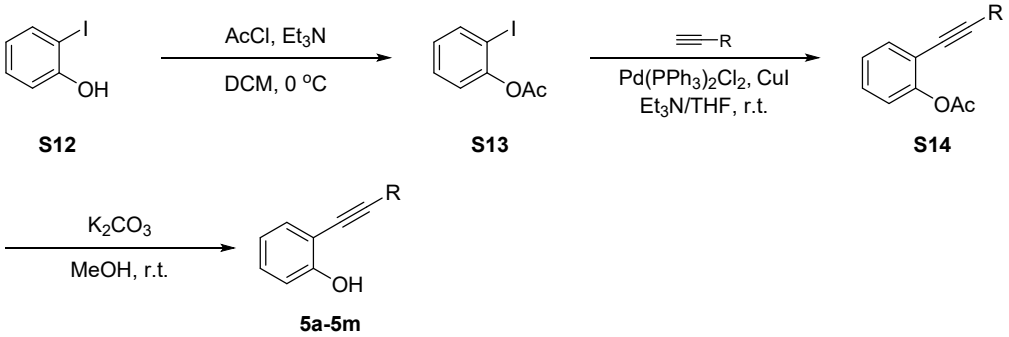
Synthesis of compound 1:[15] Under nitrogen atmosphere, the reaction tube was charged with **S11** (2.0 mmol, 1.0 equiv.), *p*-toluenesulfonic acid (0.2 mmol, 0.1 equiv.) and **S9** (2.4 mmol, 1.2 equiv.) in toluene (10.0 mL) at room temperature. The mixture was stirred at 60 °C. After completion of the reaction (monitored by TLC), the reaction was quenched by saturated sodium chloride aqueous solution, the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **1ah**.



4-(2-((4-Methylphenyl)sulfonamido)phenyl)but-3-yn-1-yl (*R*)-4-((3*R*,5*R*,8*S*,9*S*,10*R*,13*R*,17*R*) -3-methoxy-5,10,13-trimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (1ah): the reaction was conducted at 2.0 mmol scale from **S11**, 762.6 mg, 55% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 4/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 8.2 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 1H), 7.25–7.20 (m, 5H), 7.00–6.97 (m, 1H), 4.24 (t, *J* = 6.5 Hz, 2H), 3.35 (s, 3H), 3.21–3.10 (m, 1H), 2.74 (t, *J* = 6.5 Hz, 2H), 2.48–2.40 (m, 1H), 2.37 (s, 3H), 2.34–2.27 (m, 1H), 1.92 (d, *J* = 12.3 Hz, 1H), 1.86–1.71 (m, 5H), 1.68 (d, *J* = 12.3 Hz, 1H), 1.55–1.47 (m, 1H), 1.42–1.32 (m, 7H), 1.27–1.16 (m, 5H), 1.14–0.95 (m, 6H), 0.94–0.87 (m, 6H), 0.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.6, 144.2, 138.1, 136.5, 132.2, 129.8, 129.5, 127.5, 124.4, 119.9, 114.5, 93.3, 80.6, 77.4, 62.0, 56.6, 56.1, 55.8, 42.9, 42.3, 40.5, 40.3, 36.0, 35.6, 35.5, 35.1, 33.0, 31.4, 31.2, 28.4, 27.5, 27.0, 26.6, 24.4, 23.6, 21.8, 21.0, 20.4, 18.5, 12.2. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{42}H_{57}NNaO_5S$ 710.3850; found 710.3838.

3. General procedure for the synthesis of *ortho*-alkynylphenols

The *ortho*-alkynylanilines **5a-5m** were synthesized according to the reported procedures. **5a**[16], **5b**[17], **5c-5d**[16], **5e**[18], **5j-5l**[7] were known compounds and all data were in agreement with the reported literatures.



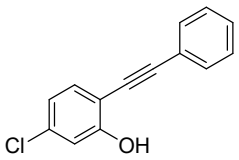
S12 **S13** **S14** **5a-5m**

Synthesis of compound S13:[11] The mixture of **S12** (1.0 equiv.) and, triethylamine (1.2 equiv.) in dry dichloromethane was stirred at 0 ºC. Then acetyl chloride (1.2 equiv.) was added dropwise, the mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S13**.

Synthesis of compound S14:[5] Under nitrogen atmosphere, to a solution of **S13** (1.0 equiv.) in tetrahydrofuran was added $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%), triethylamine (1.2 equiv.) and the alkyne compounds (1.2 equiv.). The mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S14**.

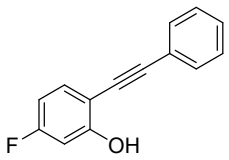
Synthesis of compound 5:[5] The mixture of **S14** (1.0 equiv.) and potassium carbonate (2.0 equiv.) in was methanol stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by water. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compound **5a-5m**.

5-Chloro-2-(phenylethynyl)phenol (5f): the reaction was conducted at 5.0 mmol scale from **S12**,



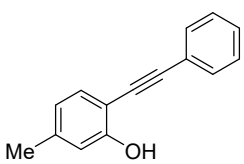
457.4 mg, 40% yield, unknown compound, yellow solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.15 (m, 6H), 7.11–6.67 (m, 2H), 5.88 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.5, 136.0, 132.6, 131.8, 129.2, 128.7, 122.3, 121.0, 115.7, 108.7, 97.1, 82.6. HRMS (ESI-QEplus) *m*/*z*: $[M-H]^-$ Calcd for $C_{14}H_8ClO$ 227.0269; found 227.0270.

5-Fluoro-2-(phenylethynyl)phenol (5g): the reaction was conducted at 5.0 mmol scale from **S12**,



350.9 mg, 33% yield, unknown compound, yellow solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.48 (m, 2H), 7.43–7.33 (m, 4H), 6.78–6.68 (m, 1H), 6.68–6.59 (m, 1H), 5.97 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.1 (d, J_{C-F} = 247.8 Hz), 158.2 (d, J_{C-F} = 13.0 Hz), 133.0 (d, J_{C-F} = 10.1 Hz), 131.8, 129.2, 128.8, 122.4, 108.3 (d, J_{C-F} = 22.6 Hz), 106.1 (d, J_{C-F} = 3.0 Hz), 102.9 (d, J_{C-F} = 25.4 Hz), 96.4, 82.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -107.63. HRMS (ESI-QEplus) *m*/*z*: $[M-H]^-$ Calcd for $C_{14}H_8FO$ 211.0565; found 211.0564.

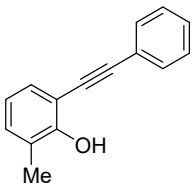
5-Methyl-2-(phenylethynyl)phenol (5h): the reaction was conducted at 5.0 mmol scale from **S12**,



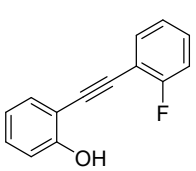
386.3 mg, 37% yield, unknown compound, white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66–7.45 (m, 2H), 7.42–7.23 (m, 4H), 6.90–6.64 (m, 2H), 5.79 (s, 1H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 141.4, 131.7, 131.6, 128.9, 128.7, 122.8,

121.7, 115.5, 106.8, 96.0, 83.5, 21.9. HRMS (ESI-QEplus) *m/z*: [M-H]$^-$ Calcd for $C_{15}H_{11}O$ 207.0815; found 207.0815.

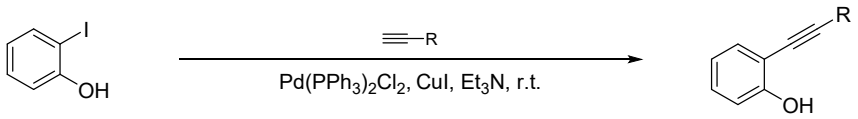
2-Methyl-6-(phenylethynyl)phenol (5i): the reaction was conducted at 5.0 mmol scale from **S12**, unknown compound, 300.2 mg, 29% yield, white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59–7.49 (m, 2H), 7.44–7.33 (m, 3H), 7.30–7.23 (m, 1H), 7.16–7.09 (m, 1H), 6.86–6.77 (m, 1H), 5.92 (s, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 132.0, 131.8, 129.3, 129.0, 128.7, 124.2, 122.7, 120.2, 109.1, 96.3, 83.6, 16.2. HRMS (ESI-QEplus) *m/z*: [M-H]$^-$ Calcd for $C_{15}H_{11}O$ 207.0815; found 207.0815.



2-((2-Fluorophenyl)ethynyl)phenol (5j): the reaction was conducted at 5.0 mmol scale from **S12**, 477.5 mg, 45% yield, unknown compound, yellow solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.48 (m, 1H), 7.47–7.40 (m, 1H), 7.39–7.23 (m, 2H), 7.21–7.07 (m, 2H), 7.05–6.96 (m, 1H), 6.95–6.84 (m, 1H), 5.96 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (d, $J_{C\text{-}F}$ = 249.8 Hz), 156.9, 133.1, 131.6, 131.1, 130.7 (d, $J_{C\text{-}F}$ = 8.0 Hz), 124.4 (d, $J_{C\text{-}F}$ = 3.6 Hz), 120.6, 115.8 (d, $J_{C\text{-}F}$ = 20.9 Hz), 115.1, 111.4 (d, $J_{C\text{-}F}$ = 15.3 Hz), 109.4, 89.9, 88.7 (d, $J_{C\text{-}F}$ = 3.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.84. HRMS (ESI-QEplus) *m/z*: [M-H]$^-$ Calcd for $C_{14}H_8FO$ 211.0565; found 211.0565.



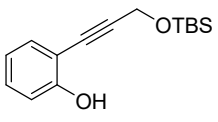
The *ortho*-alkynylanilines **5n**, **5o** were synthesized according to the reported procedures. **5o**[12] was known compound and all data were in agreement with reported literature.



S12 **5n, 5o**

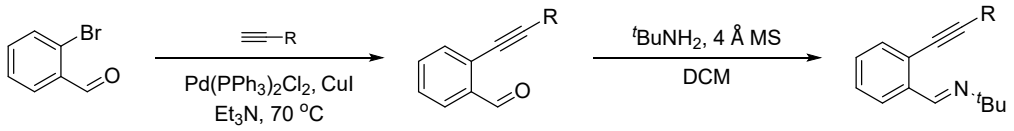
Synthesis of compound 5:[12] Under nitrogen atmosphere, to a solution of **S13** (1.0 equiv.) in triethylamine was added $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%) and the alkyne compound (1.2 equiv.). The mixture was stirred at room temperature. After completion of the reaction (monitored by TLC), the reaction was quenched by aqueous saturated solution of sodium chloride. Then the aqueous phase was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compound **5n** and **5o**.

2-(3-((*Tert*-butyldimethylsilyl)oxy)prop-1-yn-1-yl)phenol (5n): the reaction was conducted at 3.0 mmol scale from **S12**, 140.0 mg, 18% yield, unknown compound, yellow solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.30 (m, 1H), 7.27–7.21 (m, 1H), 6.96–6.92 (m, 1H), 6.89–6.83 (m, 1H), 5.81 (s, 1H), 4.59 (s, 2H), 0.94 (s, 9H), 0.17 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.0, 132.0, 130.7, 120.5, 114.9, 109.3, 95.4, 79.2, 52.4, 26.0, 18.5, -4.9. HRMS (ESI-QEplus) *m/z*: [M-H]$^-$ Calcd for $C_{15}H_{21}O_2Si$ 261.1316; found 261.1313.



4. General procedure for the synthesis of substrate alkynl-imines

The *ortho*-alkynylanilines **7a-7g** were synthesized according to the reported procedures. **7a-7d**[19] were known compounds and all data were in agreement with the reported literature.

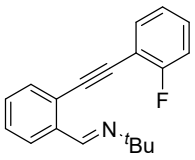


S15 **S16** **7a-7g**

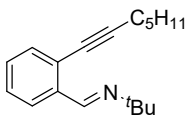
Synthesis of compound S16:[19] Under nitrogen atmosphere, to a solution of **S15** (1.0 equiv.), $Pd(PPh_3)_2Cl_2$ (2 mol%), and CuI (1 mol%) in triethylamine, the appropriate acetylene (1.5 equiv.) was added at room temperature. The mixture was stirred overnight in 70 °C oil bath. After completion of the reaction (monitored by TLC), the reaction was cooled to room temperature and quenched by water. The aqueous layer was extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **S16**.

Synthesis of compound 7:[19] To a suspension of *tert*-butylamine (2.0 equiv.) and 4Å MS in dichloromethane, compound **S16** (1.0 equiv.) was added at room temperature. The mixture was stirred overnight, then the mixture was filtered and the filtrate was concentrated to give **7a-7g**, which were used for the next step without purification.

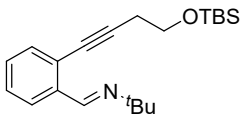
***N-tert*-butyl-1-(2-((2-fluorophenyl)ethynyl)phenyl)methanimine (7e):** the reaction was conducted at 3.0 mmol scale from **S15**, 536.4 mg, 64% yield, unknown compound, yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.96 (s, 1H), 8.12–8.06 (m, 1H), 7.60–7.55 (m, 1H), 7.54–7.50 (m, 1H), 7.40–7.36 (m, 2H), 7.35–7.30 (m, 1H), 7.18–7.09 (m, 2H), 1.34 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.9 (d, $J_{C\text{-}F}$ = 250.4 Hz), 154.5, 138.2, 133.4, 132.4, 130.4 (d, $J_{C\text{-}F}$ = 7.9 Hz), 129.9, 129.2, 126.2, 124.3 (d, $J_{C\text{-}F}$ = 3.5 Hz), 123.7, 115.8 (d, $J_{C\text{-}F}$ = 20.4 Hz), 112.0 (d, $J_{C\text{-}F}$ = 15.3 Hz), 92.1 (d, $J_{C\text{-}F}$ = 2.8 Hz), 88.3, 58.1, 30.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -109.53. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{19}H_{19}FN$ 280.1496; found 280.1490.



***N-tert*-butyl-1-(2-(hept-1-yn-1-yl)phenyl)methanimine (7f):** the reaction was conducted at 3.0 mmol scale from **S15**, 459.7 mg, 60% yield, unknown compound, brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.05–7.97 (m, 1H), 7.42–7.37 (m, 1H), 7.33–7.26 (m, 2H), 2.52–2.44 (m, 2H), 1.68–1.59 (m, 2H), 1.51–1.43 (m, 2H), 1.42–1.34 (m, 2H), 1.31 (s, 9H), 0.92 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.8, 137.9, 132.5, 129.8, 128.0, 126.0, 125.0, 96.4, 78.1, 57.8, 31.4, 30.0, 28.7, 22.5, 19.8, 14.2. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{18}H_{26}N$ 256.2060; found 256.2054.



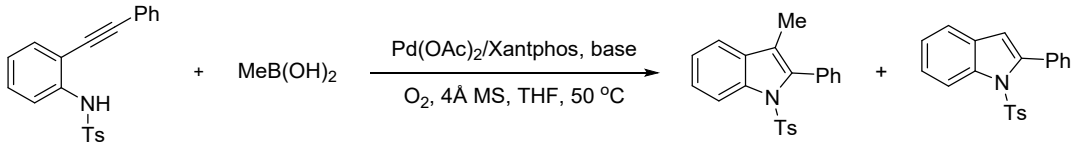
***N-tert*-butyl-1-(2-(4-((*tert*-butyldimethylsilyl)oxy)but-1-yn-1-yl)phenyl)methanimine (7g):** the



reaction was conducted at 3.0 mmol scale from **S15**, 927.7 mg, 90% yield, unknown compound, brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.77 (s, 1H), 8.04–7.97 (m, 1H), 7.43–7.37 (m, 1H), 7.33–7.27 (m, 2H), 3.85 (t, *J* = 7.2 Hz, 2H), 2.69 (t, *J* = 7.2 Hz, 2H), 1.31 (s, 9H), 0.91 (s, 9H), 0.09 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 138.0, 132.5, 129.8, 128.3, 126.0, 124.6, 92.9, 79.2, 62.3, 57.9, 30.0, 26.1, 24.2, 18.6, -5.1. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{21}H_{34}NOSi$ 344.2404; found 344.2397.

5. Optimization of the Conditions for synthesis of 3-methyl-1-tosyl-1*H*-indole

Table S1: Base screening

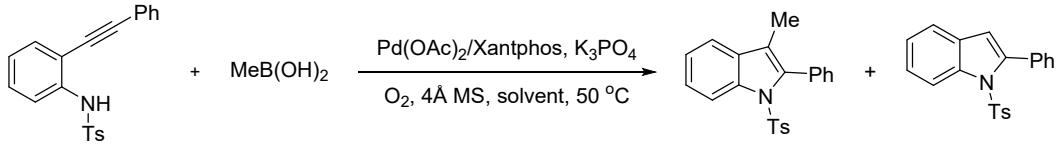


1a **2a** **3a** **4a**

Entry	Base	**3a** Yield (%)	**3a**:**4a**
1	DMAP	0	0:1
2	NaOEt	29	1:0.17
3	NaOMe	60	1:0.45
4	KOMe	32	1:0.09
5	KO^{t}Bu	36	1:0.06
6	NaO_2CH	70	1:0.42
7	KOAc	60	1:0.66
8	CsOAc	56	1:0.71
9	K_2CO_3	81	1:0.05
10	K_3PO_4	84	1:0.12

[a]**1a** (0.1 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol%), Xantphos (11 mol%), base (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h. Yields of **3a** and ratios of **3a**:**4a** were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as internal standard).

Table S2: Solvent screening

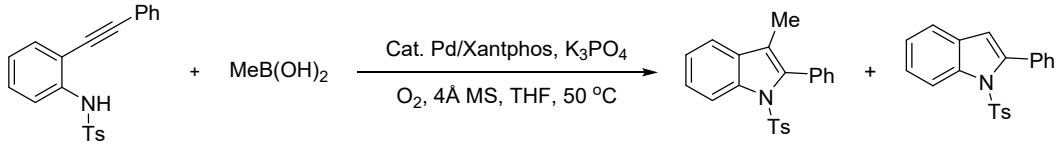


1a **2a** **3a** **4a**

Entry	Solvent	**3a** Yield (%)	**3a**:**4a**
1	THF	84	1:0.12
2	DCM	<5	N.D.
3	Ethyl ether	<5	N.D.
4	EA	69	1:0.13
5	MeOH	<5	N.D.
6	TFE	33	N.D.
7	NMP	<5	N.D.
8	DMSO	<5	N.D.
9	DMF	15	>20:1
10	PhMe	18	1:4.60
11	Benzene	24	1:2.60
12	Benzotrifluoride	39	1:0.89
13	1,4-dioxane	78	1:0.27

[a]**1a** (0.1 mmol), **2a** (0.3 mmol), $Pd(OAc)_2$ (10 mol%), Xantphos (11 mol%), K_3PO_4 (1.5 equiv.), solvent (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h. Yields of **3a** and ratios of **3a**:**4a** were determined by ^1H NMR (1,3,5-trimethoxybenzene as internal standard).

Table S3: Metal precursor screening

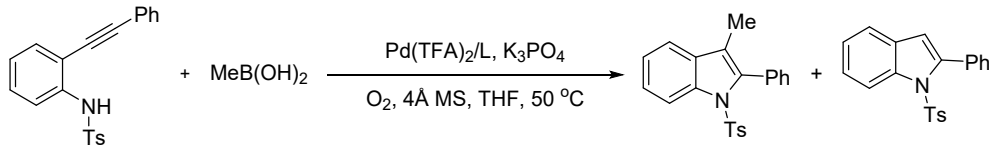


1a **2a** **3a** **4a**

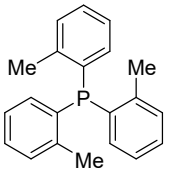
Entry	Cat. Pd	**3a** Yield (%)	**3a**:**4a**
1	$Pd(OAc)_2$	84	1:0.12
2[b]	$PdCl_2$	33	1:0.03
3	$PdBr_2$	<5	N.D.
4	$Pd(PPh_3)_2Cl_2$	8	N.D.
5	$Pd(TFA)_2$	97	1:0.03

[a]**1a** (0.1 mmol), **2a** (0.3 mmol), cat. Pd (10 mol%), Xantphos (11 mol%), K_3PO_4 (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h. Yields of **3a** and ratios of **3a**:**4a** were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as internal standard). [b]2.0 mg 2,2'-diphenyl-1,1'-ditosyl-1H,1'*H*- 3,3'-biindole was isolated, 6% yield, known compound[36]; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37–8.27 (m, 2H), 7.36–7.30 (m, 2H), 7.22–7.13 (m, 6H), 7.12–6.94 (m, 10H), 6.72 (s, 4H), 6.62–6.57 (m, 2H), 2.35 (s, 6H).^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 139.7, 137.9, 134.6, 132.0, 130.8, 129.3, 128.3, 127.2, 127.0, 125.4, 124.6, 119.8, 117.2, 117.2, 21.8.

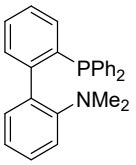
Table S4: Ligand screening



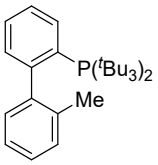
1a **2a** **3a** **4a**



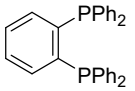
L_1 : Tri-*o*-tolylphosphine
5% yield **3a**
3a:**4a**=1:13.4



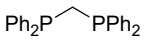
L_2 : PhDave-Phos
4% yield **3a**
3a:**4a**=1:19.0



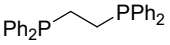
L_3 : ^{t}BuMePhos
10% yield **3a**
3a:**4a**=1:7.4



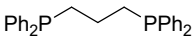
L_4 : dppbenz
20% yield **3a**
3a:**4a**=1:1.10



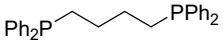
L_5: Dppm
23% yield **3a**
3a:**4a**=1:0.25



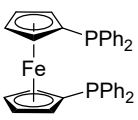
L_6 : Dppe
20% yield **3a**
3a:**4a**=1:0.60



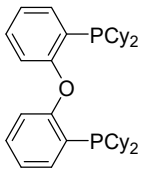
L_7 : Dppp
42% yield **3a**
3a:**4a**=1:0.26



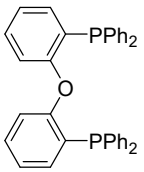
L_8 : Dppb
48% yield **3a**
3a:**4a**=1:0.10



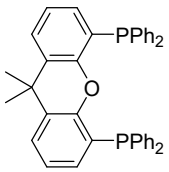
L_9 : DPPF
46% yield **3a**
3a:**4a**=1:0.37



L_{10}
12% yield **3a**
3a:**4a**=1:1.67



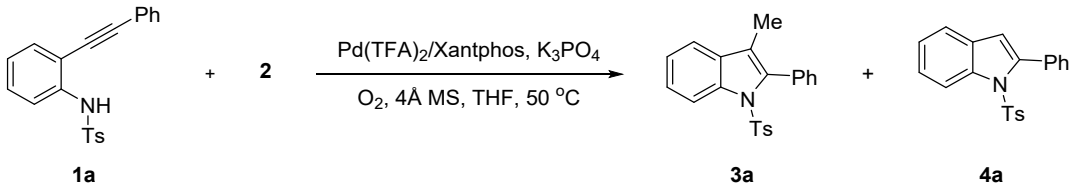
L_{11} : DPEPhos
92% yield **3a**
3a:**4a**=1:0.08



L_{12} : XantPhos
97% yield **3a**
3a:**4a**=1:0.03

[a] **1a** (0.1 mmol), **2a** (0.3 mmol), $Pd(TFA)_2$ (10 mol%), ligand (11 mol%), K_3PO_4 (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h. Yields of **3a** and ratios of **3a**:**4a** were determined by ^{1}H NMR (1,3,5-trimethoxybenzene as internal standard).

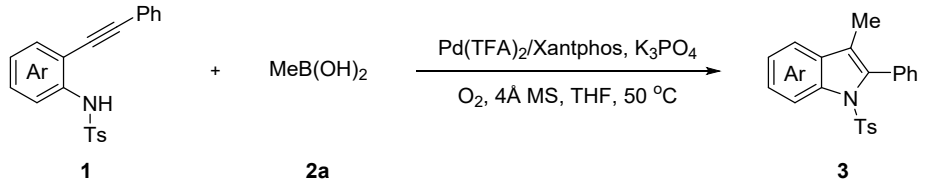
Table S5: The other reaction conditions screening



Entry	PG	$MeB(OR)_2$	T(°C)	**3a** Yield (%)	**3a**:**4a**
1	Ts	$MeB(OH)_2$ (3.0 eq)	50	95	1:0.03
2	Boc	$MeB(OH)_2$ (3.0 eq)	50	-	-
3	Ac	$MeB(OH)_2$ (3.0 eq)	50	-	-
4	Ts	$MeB(OH)_2$ (1.2 eq)	50	27	1:0.30
5	Ts	$MeB(OH)_2$ (2.0 eq)	50	59	1:0.10
6	Ts	Trimethylboroxine (3.0 eq)	50	60	1:0.04
7	Ts	$MeBF_3K$ (3.0 eq)	50	56	1:0.08
8	Ts	MeB(pin) (3.0 eq)	50	-	-
9[c]	Ts	$MeB(OH)_2$ (3.0 eq)	30	85	1:0.02
10[c]	Ts	$MeB(OH)_2$ (3.0 eq)	60	94	1:0.06
11[b,c]	Ts	$MeB(OH)_2$ (3.0 eq)	50	95	1:0.05

[a]**1a** (0.1 mmol), **2** (0.3 mmol), $Pd(TFA)_2$ (10 mol%), Xantphos (11 mol%), K_3PO_4 (1.5 equiv.), THF (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h. Yields of **3a** and ratios of **3a**:**4a** were determined by ^1H NMR (1,3,5-trimethoxybenzene as internal standard). [b]5 mol% cat Pd, 5.5 mol% ligand. [c]Isolated yields.

6. General procedure for synthesis of 3-methylindoles



In the glovebox, a Schlenk tube was charged with **1** (1.0 equiv.), **2a** (3.0 equiv.), $Pd(TFA)_2$ (5 mol%), Xantphos (5.5 mol%), potassium phosphate (1.5 equiv.), 4Å MS and tetrahydrofuran. Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compounds **3**.

3-Methyl-2-phenyl-1-tosyl-1*H*-indole (3a): the reaction was conducted at 0.1 mmol scale, 34.3 mg, 95% yield, known compound[20], white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40–8.26 (m, 1H), 7.53–7.40 (m, 4H), 7.39–7.25 (m, 6H), 7.12–6.96 (m, 2H), 2.29 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 137.4, 136.9, 135.3, 132.0, 131.8, 131.6, 129.4, 128.6, 127.6, 127.0, 125.2, 124.1, 120.0, 119.2, 116.4, 21.7, 9.7.

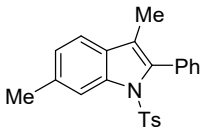
3,5-Dimethyl-2-phenyl-1-tosyl-1*H*-indole (3b): the reaction was conducted at 0.1 mmol scale, 36.0 mg, 96% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.14 (m, 1H), 7.47–7.38 (m, 3H), 7.38–7.31 (m, 2H), 7.30–7.25 (m, 2H), 7.22–7.15 (m, 2H), 7.08–6.99 (m, 2H), 2.44 (s, 3H), 2.28 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 137.0, 135.6, 135.2, 133.8, 132.3, 131.9, 131.5, 129.4, 128.5, 127.6, 127.0, 126.5, 120.0, 119.2, 116.2, 21.7, 21.6, 9.7. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_2S$ 398.1185; found 398.1184.

5-Methoxy-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3c): the reaction was conducted at 0.1 mmol scale, 37.5 mg, 96% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.16 (m, 1H), 7.47–7.40 (m, 3H), 7.39–7.31 (m, 2H), 7.29–7.23 (m, 2H), 7.09–7.01 (m, 2H), 7.00–6.93 (m, 1H), 6.88–6.80 (m, 1H), 3.85 (s, 3H), 2.28 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.2, 144.4, 137.9, 135.0, 133.3, 131.9, 131.8, 131.5, 129.3, 128.6, 127.6, 127.0, 120.2, 117.6, 113.5, 101.9, 55.8, 21.7, 9.8. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_3S$ 414.1134; found 414.1134.

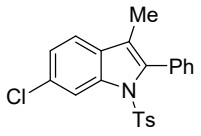
5-Chloro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3d): the reaction was conducted at 0.1 mmol scale, 19.7 mg, 50% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.29–8.20 (m, 1H), 7.48–7.41 (m, 3H), 7.40–7.37 (m, 1H), 7.36–7.29 (m, 3H), 7.28–7.24 (m, 2H), 7.11–7.02 (m, 2H), 2.31 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 137.7, 137.4, 135.2, 131.6, 131.2, 131.0, 130.4, 129.6, 128.8, 127.7, 127.1, 124.6, 119.9, 119.4, 116.5, 21.8, 9.6. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}ClNNaO_2S$ 418.0639; found 418.0633.

5-Fluoro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3e): the reaction was conducted at 0.1 mmol scale, 33.1 mg, 87% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–8.23 (m, 1H), 7.48–7.41 (m, 3H), 7.38–7.31 (m, 2H), 7.30–7.23 (m, 2H), 7.13–7.01 (m, 4H), 2.30 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3 (d, J_{C-F} = 239.8 Hz), 144.8, 138.7, 134.9, 133.6, 133.3 (d, J_{C-F} = 9.4 Hz), 131.5, 131.4, 129.5, 128.8, 127.7, 127.0, 119.8 (d, J_{C-F} = 4.0 Hz), 117.7 (d, J_{C-F} = 9.2 Hz), 112.8 (d, J_{C-F} = 25.1 Hz), 104.9 (d, J_{C-F} = 23.7 Hz), 21.8, 9.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -118.79. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}FNNaO_2S$ 402.0934; found 402.0930.

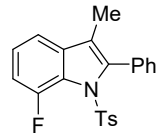
3,6-Dimethyl-2-phenyl-1-tosyl-1*H*-indole (3f): the reaction was conducted at 0.1 mmol scale, 34.5 mg, 92% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.47–7.38 (m, 3H), 7.36–7.31 (m, 2H), 7.30–7.26 (m, 3H), 7.15–7.11 (m, 1H), 7.09–7.02 (m, 2H), 2.54 (s, 3H), 2.30 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 137.8, 136.2, 135.4, 135.2, 131.9, 131.6, 129.8, 129.4, 128.4, 127.6, 127.0, 125.5, 120.0, 118.8, 116.6, 22.3, 21.7, 9.7. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_2S$ 398.1185; found 398.1184.



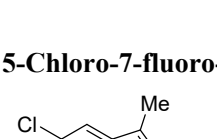
6-Chloro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3g): the reaction was conducted at 0.1 mmol scale, 19.3 mg, 49% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (s, 1H), 7.48–7.39 (m, 3H), 7.36–7.24 (m, 6H), 7.14–7.03 (m, 2H), 2.32 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.9, 137.7, 137.4, 135.2, 131.6, 131.2, 131.0, 130.4, 129.6, 128.8, 127.7, 127.1, 124.6, 119.9, 119.4, 116.5, 21.8, 9.6. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}ClNNaO_2S$ 418.0639; found 418.0642.



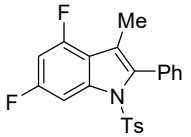
7-Fluoro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3h): the reaction was conducted at 0.1 mmol scale, 32.2 mg, 85% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.42 (m, 5H), 7.41–7.36 (m, 2H), 7.25–7.17 (m, 2H), 7.16–7.10 (m, 2H), 7.09–7.02 (m, 1H), 2.34 (s, 3H), 2.08 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5 (d, J_{C-F} = 251.6 Hz), 144.6, 139.8, 136.7 (d, J_{C-F} = 2.9 Hz), 135.4, 132.2, 130.7, 129.4, 128.5, 127.9, 127.5 (d, J_{C-F} = 1.5 Hz), 125.4 (d, J_{C-F} = 7.2 Hz), 120.3 (d, J_{C-F} = 1.8 Hz), 115.2 (d, J_{C-F} = 3.6 Hz), 112.7 (d, J_{C-F} = 21.7 Hz), 21.8, 10.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.45. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}FNNaO_2S$ 402.0934; found 402.0931.



5-Chloro-7-fluoro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3i): the reaction was conducted at 0.1 mmol scale, 29.0 mg, 70% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48–7.42 (m, 4H), 7.41 (s, 1H), 7.39–7.34 (m, 2H), 7.20–7.17 (m, 1H), 7.16–7.12 (m, 2H), 7.10–7.05 (m, 1H), 2.36 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9 (d, J_{C-F} = 256.3 Hz), 144.9, 141.3, 137.2 (d, J_{C-F} = 3.8 Hz), 135.2, 131.7, 130.7, 130.2 (d, J_{C-F} = 9.1 Hz), 129.5, 128.8, 128.0, 127.5 (d, J_{C-F} = 0.8 Hz), 123.9 (d, J_{C-F} = 9.5 Hz), 119.6 (d, J_{C-F} = 2.0 Hz), 115.2 (d, J_{C-F} = 3.9 Hz), 113.3 (d, J_{C-F} = 25.3 Hz), 21.8, 9.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.73. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{17}ClFNNaO_2S$ 436.0545; found 436.0552.



4,6-Difluoro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3j): the reaction was conducted at 0.1 mmol scale, 36.4 mg, 92% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.42 (m, 3H), 7.41 (s, 1H), 7.40–7.34 (m, 3H), 7.17–7.09 (m, 2H), 6.91–6.79 (m, 2H), 2.35 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (dd, J_{C-F} = 242.8, 10.2 Hz), 151.2 (dd, J_{C-F} = 255.2, 13.1 Hz), 144.9, 141.6, 137.0 (dd, J_{C-F} = 10.7, 4.4 Hz), 134.9, 131.8, 130.7, 129.5, 128.8, 128.0, 127.5 (d, J_{C-F} = 0.3 Hz), 121.9 (dd, J_{C-F} = 9.4, 2.3 Hz), 120.4 (dd, J_{C-F} = 3.8, 2.4 Hz), 101.9, 101.6, 101.6, 101.4, 101.4, 101.4, 101.2,



101.2,, 21.8, 9.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ = -112.06 (d, J = 6.5 Hz), -115.05 (d, J = 6.0 Hz). HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{17}F_2NNaO_2S$ 420.0840; found 420.0834.

7-Chloro-5-fluoro-3-methyl-2-phenyl-1-tosyl-1*H*-indole (3k): the reaction was conducted at 0.1 mmol scale, 37.9 mg, 92% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.35 (m, 3H), 7.34–7.27 (m, 2H), 7.18–7.10 (m, 3H), 7.07–7.00 (m, 2H), 6.98–6.92 (m, 1H), 2.35 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4 (d, J_{C-F} = 244.9 Hz), 144.7, 143.2, 138.4 (d, J_{C-F} = 10.0 Hz), 134.5, 133.9 (d, J_{C-F} = 2.1 Hz), 131.5, 130.6, 129.0, 128.7, 127.9, 127.6, 125.6 (d, J_{C-F} = 11.6 Hz), 121.7 (d, J_{C-F} = 4.1 Hz), 115.4 (d, J_{C-F} = 27.4 Hz), 104.3 (d, J_{C-F} = 23.2 Hz), 21.8, 10.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.73. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{17}ClFNNaO_2S$ 436.0545; found 436.0546.

2-(4-Methoxyphenyl)-3-methyl-1-tosyl-1*H*-indole (3l): the reaction was conducted at 0.1 mmol scale, 31.3 mg, 80% yield, known compound[34], white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35–8.27 (m, 1H), 7.43–7.34 (m, 2H), 7.32–7.23 (m, 5H), 7.09–7.01 (m, 2H), 7.00–6.92 (m, 2H), 3.89 (s, 3H), 2.29 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 144.5, 137.3, 136.8, 135.4, 132.9, 132.0, 129.4, 127.0, 125.0, 124.1, 123.9, 119.5, 119.1, 116.4, 113.1, 55.5, 21.7, 9.7.

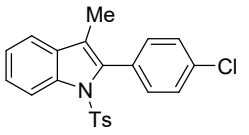
3-Methyl-2-(*p*-tolyl)-1-tosyl-1*H*-indole (3m): the reaction was conducted at 0.1 mmol scale, 33.2 mg, 88% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34–8.28 (m, 1H), 7.42–7.33 (m, 2H), 7.32–7.27 (m, 3H), 7.26–7.22 (m, 4H), 7.07–7.00 (m, 2H), 2.44 (s, 3H), 2.28 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 138.4, 137.3, 137.0, 135.2, 132.1, 131.4, 129.4, 128.8, 128.4, 127.0, 125.0, 124.1, 119.8, 119.1, 116.4, 21.7, 21.7, 9.7. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_2S$ 398.1185; found 398.1184.

2-(4-(*Tert*-butyl)phenyl)-3-methyl-1-tosyl-1*H*-indole (3n): the reaction was conducted at 0.1 mmol scale, 34.4 mg, 82% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34–8.28 (m, 1H), 7.43–7.40 (m, 3H), 7.38–7.33 (m, 1H), 7.30–7.25 (m, 5H), 7.07–6.99 (m, 2H), 2.29 (s, 3H), 2.04 (s, 3H), 1.40 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.4, 144.4, 137.4, 137.1, 135.3, 132.1, 131.2, 129.3, 128.6, 127.1, 125.0, 124.5, 124.0, 119.7, 119.1, 116.4, 34.9, 31.6, 21.7, 9.8. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{26}H_{27}NNaO_2S$ 440.1655; found 440.1652.

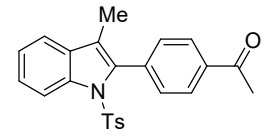
2-(4-Fluorophenyl)-3-methyl-1-tosyl-1*H*-indole (3o): the reaction was conducted at 0.1 mmol scale, 28.4 mg, 75% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36–8.27 (m, 1H), 7.45–7.36 (m, 2H), 7.34–7.24 (m, 5H), 7.17–7.09 (m, 2H), 7.08–7.02 (m, 2H), 2.30 (s, 3H), 2.02 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0 (d, J_{C-F} = 246.8 Hz), 144.7, 137.4, 135.7, 135.3, 133.3 (d, J_{C-F} = 38.1 Hz), 131.8, 129.5, 127.7 (d, J_{C-F} = 3.3 Hz), 126.9, 125.3, 124.2, 120.2, 119.2, 116.4, 114.8 (d, J_{C-F} = 21.6 Hz), 21.7,

9.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.83. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}FNNaO_2S$ 402.0934; found 402.0935.

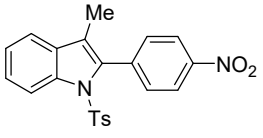
2-(4-Chlorophenyl)-3-methyl-1-tosyl-1*H*-indole (3p): the reaction was conducted at 0.1 mmol scale, 23.7 mg, 60% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.36–8.28 (m, 1H), 7.45–7.36 (m, 4H), 7.34–7.30 (m, 1H), 7.29–7.26 (m, 4H), 7.10–7.01 (m, 2H), 2.30 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 137.5, 135.6, 135.2, 134.7, 132.8, 131.9, 130.2, 129.5, 128.0, 127.0, 125.5, 124.3, 120.5, 119.3, 116.5, 21.8, 9.7. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}ClNNaO_2S$ 418.0639; found 418.0611.



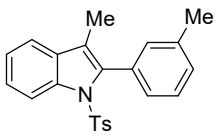
1-(4-(3-Methyl-1-tosyl-1*H*-indol-2-yl)phenyl)ethan-1-one (3q): the reaction was conducted at 0.1 mmol scale, 30.1 mg, 75% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 30/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35–8.29 (m, 1H), 8.08–8.02 (m, 2H), 7.53–7.47 (m, 2H), 7.46–7.37 (m, 2H), 7.35–7.27 (m, 3H), 7.09–7.03 (m, 2H), 2.69 (s, 3H), 2.30 (s, 3H), 2.06 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.0, 144.8, 137.7, 136.8, 136.7, 135.7, 134.8, 132.1, 131.6, 129.5, 127.7, 126.9, 125.7, 124.5, 121.5, 119.5, 116.6, 26.9, 21.8, 9.8. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{21}NNaO_3S$ 426.1134; found 426.1131.



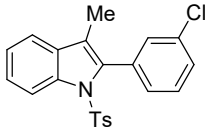
3-Methyl-2-(4-nitrophenyl)-1-tosyl-1*H*-indole (3r): the reaction was conducted at 0.1 mmol scale, 28.0 mg, 69% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 30/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35–8.29 (m, 3H), 7.62–7.54 (m, 2H), 7.48–7.41 (m, 2H), 7.37–7.31 (m, 1H), 7.30–7.24 (m, 2H), 7.10–7.05 (m, 2H), 2.31 (s, 3H), 2.09 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.7, 145.1, 138.7, 137.9, 134.6, 132.1, 131.9, 129.6, 126.9, 126.2, 124.7, 123.1, 122.9, 122.5, 119.7, 116.7, 21.8, 9.8. HRMS (ESI-QEplus) *m/z*: $[M-H]^-$ Calcd for $C_{22}H_{17}N_2O_4S$ 405.0915; found 405.0906.



3-Methyl-2-(*m*-tolyl)-1-tosyl-1*H*-indole (3s): the reaction was conducted at 0.1 mmol scale, 31.9 mg, 85% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35–8.27 (m, 1H), 7.45–7.39 (m, 1H), 7.39–7.22 (m, 6H), 7.17–7.08 (m, 2H), 7.08–7.01 (m, 2H), 2.40 (s, 3H), 2.29 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.5, 137.4, 137.1, 137.0, 135.4, 132.3, 132.0, 131.6, 129.4, 128.6, 127.5, 127.1, 125.1, 124.0, 119.7, 119.2, 116.4, 21.7, 21.7, 9.7. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_2S$ 398.1185; found 398.1183.



2-(3-Chlorophenyl)-3-methyl-1-tosyl-1*H*-indole (3t): the reaction was conducted at 0.1 mmol scale, 32.7 mg, 83% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.35–8.27 (m, 1H), 7.45–7.35 (m, 4H), 7.34–7.24 (m, 4H), 7.23–7.20 (m, 1H), 7.10–7.04 (m, 2H), 2.31 (s, 3H), 2.04 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 137.5, 135.2, 133.5, 131.7, 131.3, 129.9, 129.5, 128.9, 128.7, 127.0, 125.5, 124.2, 120.6,



119.4, 116.4, 21.8, 9.6. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}ClNNaO_2S$ 418.0639; found 418.0641.

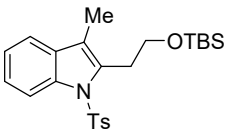
2-(2-Methoxyphenyl)-3-methyl-1-tosyl-1*H*-indole (3u): the reaction was conducted at 0.1 mmol scale, 36.8 mg, 94% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.29–8.22 (m, 1H), 7.45–7.42 (m, 2H), 7.40–7.36 (m, 2H), 7.35–7.30 (m, 1H), 7.29–7.24 (m, 1H), 7.15–7.13 (m, 1H), 7.09–6.98 (m, 3H), 6.97–6.93 (m, 1H), 3.72 (s, 3H), 2.29 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 144.2, 137.1, 136.1, 133.3, 133.1, 131.7, 130.6, 129.3, 127.1, 124.7, 123.5, 120.8, 119.8, 119.4, 119.1, 115.7, 110.8, 55.5, 21.7, 9.5. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{23}H_{21}NNaO_3S$ 414.1134; found 414.1130.

2-(2-Fluorophenyl)-3-methyl-1-tosyl-1*H*-indole (3v): the reaction was conducted at 0.1 mmol scale, 33.8 mg, 89% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.31–8.24 (m, 1H), 7.49–7.42 (m, 2H), 7.40–7.27 (m, 5H), 7.26–7.21 (m, 1H), 7.20–7.14 (m, 1H), 7.10–7.04 (m, 2H), 2.28 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8 (d, $J_{C\text{-}F}$ = 247.1 Hz), 144.7, 137.4, 135.3, 133.7 (d, $J_{C\text{-}F}$ = 2.7 Hz), 131.6, 131.0 (d, $J_{C\text{-}F}$ = 8.5 Hz), 130.2, 129.5, 127.0, 125.3, 124.0, 123.5 (d, $J_{C\text{-}F}$ = 3.6 Hz), 121.4, 119.9 (d, $J_{C\text{-}F}$ = 15.1 Hz), 119.3, 116.0, 115.7 (d, $J_{C\text{-}F}$ = 21.7 Hz), 21.7, 9.6 (d, $J_{C\text{-}F}$ = 0.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.42. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{22}H_{18}FNNaO_2S$ 402.0934; found 402.0928.

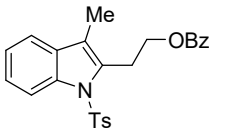
2-(2-(Benzyloxy)ethyl)-3-methyl-1-tosyl-1*H*-indole (3w): the reaction was conducted at 0.1 mmol scale, 39.9 mg, 95% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.21–8.14 (m, 1H), 7.59–7.52 (m, 2H), 7.41–7.35 (m, 1H), 7.33–7.21 (m, 7H), 7.16–7.09 (m, 2H), 4.52 (s, 2H), 3.79 (t, *J* = 6.9 Hz, 2H), 3.32 (t, *J* = 7.0 Hz, 2H), 2.30 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 138.8, 136.9, 136.3, 133.5, 131.6, 129.9, 128.5, 127.7, 127.7, 126.4, 124.5, 123.6, 118.9, 118.7, 115.3, 73.2, 70.1, 27.6, 21.7, 9.3. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{25}H_{25}NNaO_3S$ 442.1447; found 442.1445.

2-(3-Methyl-1-tosyl-1*H*-indol-2-yl)ethyl acetate (3x): the reaction was conducted at 0.1 mmol scale, 33.4 mg, 90% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^1H NMR (400 MHz, $CDCl_3$) δ 8.21–8.13 (m, 1H), 7.61–7.53 (m, 2H), 7.42–7.37 (m, 1H), 7.33–7.23 (m, 2H), 7.19–7.12 (m, 2H), 4.38 (t, *J* = 6.7 Hz, 2H), 3.34 (t, *J* = 6.7 Hz, 2H), 2.32 (s, 3H), 2.17 (s, 3H), 2.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 144.8, 136.8, 136.1, 132.4, 131.4, 130.0, 126.4, 124.8, 123.7, 119.4, 118.8, 115.3, 64.0, 26.3, 21.7, 21.2, 9.2. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{20}H_{21}NNaO_4S$ 394.1083; found 394.1078.

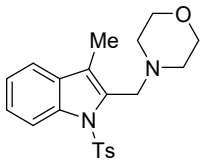
2-(2-((*Tert*-butyldimethylsilyl)oxy)ethyl)-3-methyl-1-tosyl-1*H*-indole (3y): the reaction was conducted at 0.1 mmol scale, 35.1 mg, 79% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20–8.14 (m, 1H), 7.59–7.52 (m, 2H), 7.40–7.34 (m, 1H), 7.30–7.20 (m, 2H), 7.17–7.10 (m, 2H), 3.92 (t, *J* = 6.7 Hz, 2H), 3.21 (t, *J* = 6.6 Hz, 2H), 2.31 (s, 3H), 2.17 (s, 3H), 0.85 (s, 9H), -0.03 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 136.8, 136.3, 133.8, 131.7, 129.9, 126.4, 124.4, 123.6, 119.1, 118.6, 115.3, 63.3, 30.5, 26.1, 21.7, 18.5, 9.5, -5.2. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{24}H_{33}NNaO_3SSi$ 466.1843; found 466.1834.



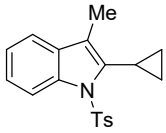
2-(3-Methyl-1-tosyl-1*H*-indol-2-yl)ethyl benzoate (3z): the reaction was conducted at 0.1 mmol scale, 36.8 mg, 85% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.16 (m, 1H), 8.03–7.95 (m, 2H), 7.63–7.57 (m, 2H), 7.56–7.50 (m, 1H), 7.45–7.35 (m, 3H), 7.34–7.28 (m, 1H), 7.27–7.22 (m, 1H), 7.19–7.12 (m, 2H), 4.65 (t, *J* = 6.6 Hz, 2H), 3.48 (t, *J* = 6.6 Hz, 2H), 2.31 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 144.8, 136.9, 136.2, 133.1, 132.4, 131.4, 130.4, 130.0, 129.8, 128.5, 126.4, 124.8, 123.7, 119.5, 118.9, 115.3, 64.4, 26.4, 21.7, 9.3. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{25}H_{23}NNaO_4S$ 456.1240; found 456.1234.



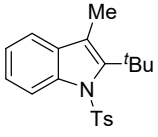
4-((3-Methyl-1-tosyl-1*H*-indol-2-yl)methyl)morpholine (3aa): the reaction was conducted at 0.1 mmol scale, 18.5 mg, 48% yield, unknown compound, white solid, R_f = 0.3 (dichloromethane/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.16–8.08 (m, 1H), 8.07–7.98 (m, 2H), 7.49–7.40 (m, 1H), 7.35–7.28 (m, 1H), 7.26–7.21 (m, 1H), 7.21–7.12 (m, 2H), 3.88 (s, 2H), 3.53 (br s, 4H), 2.50 (br s, 4H), 2.34 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 137.4, 136.6, 132.2, 130.3, 129.5, 127.3, 125.0, 123.2, 119.2, 119.1, 114.9, 66.9, 53.4, 52.1, 21.7, 9.5. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{21}H_{25}N_2O_3S$ 385.1580; found 385.1577.



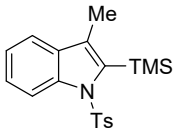
2-Cyclopropyl-3-methyl-1-tosyl-1*H*-indole (3ab): the reaction was conducted at 0.1 mmol scale, 27.7 mg, 85% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21–8.14 (m, 1H), 7.67–7.59 (m, 2H), 7.39–7.33 (m, 1H), 7.31–7.20 (m, 2H), 7.18–7.12 (m, 2H), 2.33 (s, 3H), 2.21 (s, 3H), 2.06–1.93 (m, 1H), 1.06–0.97 (m, 2H), 0.69–0.61 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 137.6, 136.9, 136.9, 131.5, 129.7, 126.6, 124.7, 123.4, 118.6, 118.4, 115.1, 21.7, 10.1, 8.5, 8.2. HRMS (ESI-QEplus) *m*/*z* Calcd for $C_{19}H_{19}NNaO_2S$ $[M+Na]^+$ 348.1029, found 348.1027.



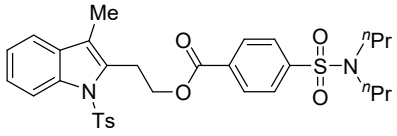
2-(*Tert*-butyl)-3-methyl-1-tosyl-1*H*-indole (3ac): the reaction was conducted at 0.1 mmol scale, 30.4 mg, 89% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03–7.96 (m, 1H), 7.27–7.23 (m, 2H), 7.21–7.16 (m, 1H), 7.14–7.08 (m, 2H), 6.97–6.90 (m, 2H), 2.22 (s, 6H), 1.66 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.6, 143.8, 139.9, 135.4, 132.7, 128.6, 127.0, 124.9, 124.7, 124.6, 118.5, 118.2, 36.1, 32.1, 21.7, 12.9. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{20}H_{23}NNaO_2S$ 364.1342; found 364.1340.



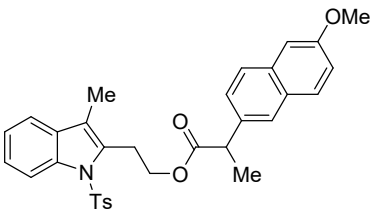
3-Methyl-1-tosyl-2-(trimethylsilyl)-1*H*-indole (3ad): the reaction was conducted at 0.1 mmol scale, 35.7 mg, 99% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97–7.92 (m, 1H), 7.46–7.41 (m, 2H), 7.38–7.34 (m, 1H), 7.26–7.21 (m, 1H), 7.19–7.13 (m, 1H), 7.08–7.02 (m, 2H), 2.32 (s, 3H), 2.24 (s, 3H), 0.52 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 139.5, 138.1, 135.2, 133.7, 133.4, 129.4, 126.7, 125.5, 123.6, 119.2, 115.6, 21.7, 12.1, 2.7. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{19}H_{23}NNaO_2SSi$ 380.1111; found 380.1108.



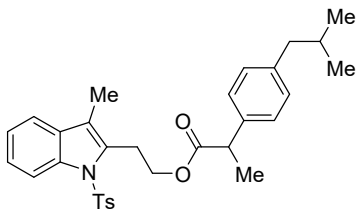
2-(3-Methyl-1-tosyl-1*H*-indol-2-yl)ethyl 3-(*N*,*N*-dipropylsulfamoyl)benzoate (3ae): the reaction was conducted at 0.1 mmol scale, 44.1 mg, 74% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22–8.16 (m, 1H), 8.14–8.05 (m, 2H), 7.88–7.81 (m, 2H), 7.62–7.54 (m, 2H), 7.39–7.37 (m 1H), 7.35–7.22 (m, 2H), 7.20–7.12 (m, 2H), 4.69 (t, *J* = 6.5 Hz, 2H), 3.50 (t, *J* = 6.5 Hz, 2H), 3.15–3.04 (m, 4H), 2.32 (s, 3H), 2.16 (s, 3H), 1.55–1.49 (m, 4H), 0.86 (t, *J* = 7.4 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 144.9, 144.4, 136.9, 136.0, 133.7, 132.1, 131.3, 130.4, 130.0, 127.2, 126.4, 124.9, 123.8, 119.6, 118.9, 115.3, 65.1, 50.1, 26.3, 22.1, 21.7, 11.3, 9.3. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{31}H_{36}N_2NaO_6S_2$ 619.1907; found 619.1908.



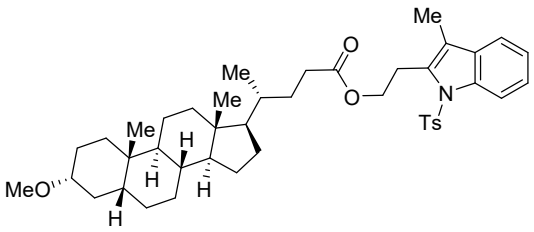
2-(3-Methyl-1-tosyl-1*H*-indol-2-yl)ethyl 2-(6-methoxynaphthalen-2-yl)propanoate (3af): the reaction was conducted at 0.1 mmol scale, 29.4 mg, 54% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17–8.11 (m, 1H), 7.60–7.58 (m, 2H), 7.55–7.53 (m, 1H), 7.52–7.46 (m, 2H), 7.32–7.18 (m, 4H), 7.13–7.03 (m, 4H), 4.40 (t, *J* = 6.5 Hz, 2H), 3.91 (s, 3H), 3.79 (q, *J* = 7.1 Hz, 1H), 3.33–3.21 (m, 2H), 2.27 (s, 3H), 1.94 (s, 3H), 1.53 (d, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.8, 157.8, 144.7, 136.9, 136.1, 135.8, 133.8, 132.3, 131.4, 129.9, 129.5, 129.1, 127.3, 126.4, 126.4, 126.1, 124.7, 123.6, 119.6, 119.1, 118.9, 115.3, 105.8, 64.4, 55.5, 45.7, 26.2, 21.7, 18.7, 9.0. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{32}H_{31}NNaO_5S$ 564.1815; found 564.1812.



2-(3-Methyl-1-tosyl-1*H*-indol-2-yl)ethyl 2-(4-isobutylphenyl)propanoate (3ag): the reaction was conducted at 0.1 mmol scale, 32.6 mg, 63% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18–8.12 (m, 1H), 7.56–7.49 (m, 2H), 7.36–7.27 (m, 2H), 7.25 – 7.21 (m, 1H), 7.16–7.08 (m, 4H), 7.02–6.96 (m, 2H), 4.44–4.32 (m, 2H), 3.63 (q, *J* = 7.0 Hz, 1H), 3.35–3.22 (m, 2H), 2.41 (d, *J* = 7.1 Hz, 2H), 2.30 (s, 3H), 2.02 (s, 3H), 1.88–1.76 (m, 1H), 1.44 (d, *J* = 7.2 Hz, 3H), 0.88 (d, *J* = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 144.7, 140.6, 137.9, 136.9, 136.1, 132.4, 131.4, 129.9, 129.5, 127.4, 126.4, 124.7, 123.7, 119.6, 118.9, 115.3, 64.3, 45.3, 45.2, 30.4, 29.9, 26.2, 22.6, 21.7, 18.8, 9.1. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{31}H_{35}NNaO_4S$ 540.2179; found 540.2174.



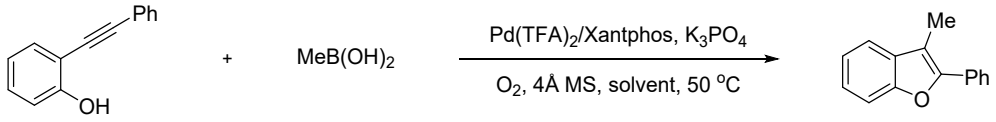
2-(3-Methyl-1-tosyl-1*H*-indol-2-yl)ethyl (*R*)-4-((3*R*,5*R*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-3-methoxy-10,13-dimethylhexadecahydro-1*H*-cyclopenta[*a*]phenanthren-17-yl)pentanoate (3ah): the



reaction was conducted at 0.1 mmol scale, 51.8 mg, 74% yield, unknown compound, white solid, R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21–8.14 (m, 1H), 7.61–7.52 (m, 2H), 7.40–7.38 (m, 1H), 7.31–7.27 (m, 1H), 7.26–7.21 (m, 1H), 7.18–7.10 (m, 2H), 4.38 (t, *J* = 6.6 Hz, 2H), 3.43–3.28 (m, 5H), 3.23–3.09 (m, 1H), 2.36–2.26 (m, 4H), 2.23–2.11 (m, 4H), 1.95–1.89 (m, 1H), 1.86–1.63 (m, 7H), 1.43–1.32 (m, 6H), 1.30–1.17 (m, 6H), 1.15–0.96 (m, 6H), 0.91 (s, 3H), 0.87 (d, *J* = 6.4 Hz, 3H), 0.61 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 144.8, 136.9, 136.2, 132.5, 131.4, 130.0, 126.4, 124.7, 123.7, 119.4, 118.8, 115.3, 80.6, 63.8, 56.6, 56.1, 55.7, 42.9, 42.2, 40.5, 40.3, 36.0, 35.5, 35.5, 35.1, 33.0, 31.5, 31.1, 28.3, 27.5, 27.0, 26.6, 26.3, 24.4, 23.6, 21.7, 21.0, 18.4, 12.2, 9.3. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{43}H_{60}NNaO_5S$ 702.4187; found 702.4173.

7. Optimization of the Conditions for synthesis of 3-methyl-2-phenylbenzofuran

Table S6: Solvent screening

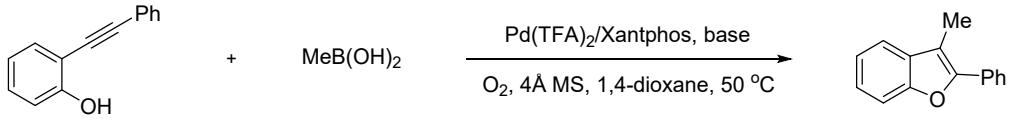


5a **2a** **6a**

Entry	Solvent	**6a** Yield(%)
1	1,4-Dioxane	64
2	2-Methyltetrahydrofuran	57
3	THF	48
4	1,2-Dimethoxyethane	39
5	EA	33
6	DCE	27
7	CH_3CN	15
8	DMF	15
9	Toluene	12
10	*o*-Xylene	12
11	Benzotrifluoride	12
12	CH_3OH	N.D.

[a]**5a** (0.1 mmol), **2a** (0.3 mmol), $Pd(TFA)_2$ (10 mol%), Xantphos (11 mol%), K_3PO_4 (1.5 equiv.), solvent (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h, isolated yields.

Table S7: Base screening

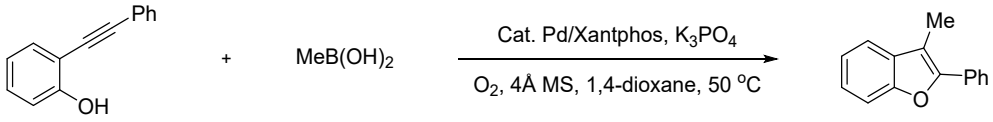


5a **2a** **6a**

Entry	Base	**6a** Yield(%)
1	K_3PO_3	64
2	K_2CO_3	63
3	Na_2CO_3	51
4	Cs_2CO_3	51
5	Li_2CO_3	9
6	$NaHCO_3$	9
7	KOAc	24
8	KO^{t}Bu	24
9	KOH	N.D.
10	DABCO	<5

[a]**5a** (0.1 mmol), **2a** (0.3 mmol), $Pd(TFA)_2$ (10 mol%), Xantphos (11 mol%), base (1.5 equiv.), 1,4-dioxane (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h, isolated yields.

Table S8: Metal precursor screening

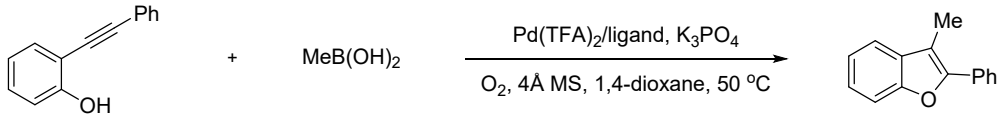


5a **2a** **6a**

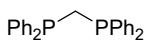
Entry	Pd-cat	**6a** Yield(%)
1	$Pd(TFA)_2$	64
2	$[PdCl(Allyl)]_2$	48
3	$Pd[(CH_3)_3CO_2]$	36
4	$PdCl_2(CN)_2$	33
5	$Pd(acac)_2$	15
6	$PdCl_2$(Amphos)	6
8	$Pd(PPh_3)_2Cl_2$	<5
9	$PdCl_2$	<5

[a]**5a** (0.1 mmol), **2a** (0.3 mmol), cat. Pd (10 mol%), Xantphos (11 mol%), K_3PO_4 (1.5 equiv.), 1,4-dioxane (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h, isolated yields.

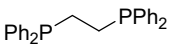
Table S9: Ligand screening



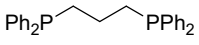
5a **2a** **6a**



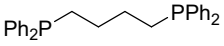
L_1: Dppm



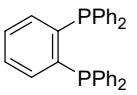
L_2 : Dppe



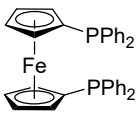
L_3 : Dppp



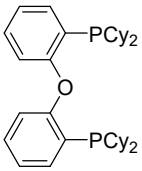
L_4 : Dppb



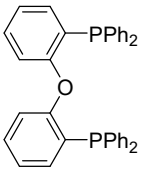
L_5 : dppbenz



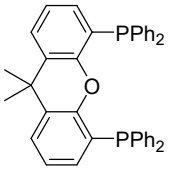
L_6 : DPPF



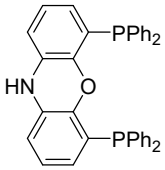
L_7



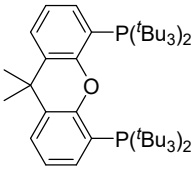
L_8 : DPEPhos



L_9 : XantPhos



L_{10} : N-XantPhos

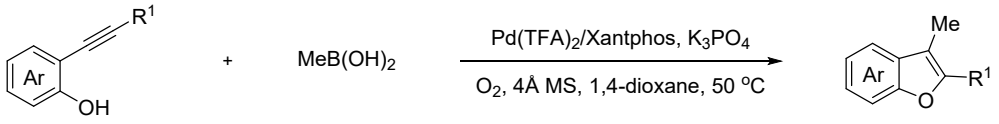


L_{11} : ^{t}BuXantPhos

Entry	Base	**6a** Yield(%)
1	**L1**	12
2	**L2**	15
3	**L3**	27
4	**L4**	33
5	**L5**	20
6	**L6**	39
7	**L7**	15
8	**L8**	42
9	**L9**	64
10	**L10**	30
11	**L11**	6

[a]**5a** (0.1 mmol), **2a** (0.3 mmol), $Pd(TFA)_2$ (10 mol%), ligand (11 mol%), K_3PO_4 (1.5 equiv.), 1,4-dioxane (2.0 mL), 4Å MS (100.0 mg), O_2 balloon, 50 °C, 10 h, isolated yields.

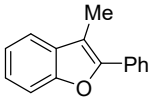
8. General procedure for synthesis of 3-methylbenzofurans



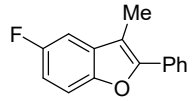
5 **2a** **6**

In the glovebox, a Schlenk tube was charged with **5** (1.0 equiv.), **2a** (3.0 equiv.), $Pd(TFA)_2$ (10 mmo%), Xantphos (11 mol%), potassium phosphate (1.5 equiv.), 4Å MS and 1,4-dioxane. Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compounds **6**.

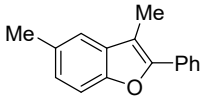
3-Methyl-2-phenylbenzofuran (6a): the reaction was conducted at 0.1 mmol scale, 13.3 mg, 64% yield, known compound[21], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89–7.77 (m, 2H), 7.58–7.52 (m, 1H), 7.52–7.43 (m, 3H), 7.40–7.33 (m, 1H), 7.32–7.24 (m, 2H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 150.9, 131.6, 131.4, 128.8, 128.1, 126.9, 124.5, 122.5, 119.5, 111.5, 111.2, 9.7.



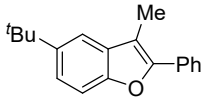
5-Fluoro-3-methyl-2-phenylbenzofuran (6b): the reaction was conducted at 0.1 mmol scale, 10.0 mg, 44% yield, known compound[21], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.76 (m, 2H), 7.52–7.44 (m, 2H), 7.42–7.34 (m, 2H), 7.21–7.15 (m, 1H), 7.05–6.95 (m, 1H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4 (d, $J_{C\text{-}F}$ = 236.4 Hz), 152.8, 150.2, 132.3 (d, $J_{C\text{-}F}$ = 10.1 Hz), 131.3, 128.9, 128.4, 127.0, 112.1 (d, $J_{C\text{-}F}$ = 26.0 Hz), 111.7 (d, $J_{C\text{-}F}$ = 9.5 Hz), 111.7 (d, $J_{C\text{-}F}$ = 3.8 Hz), 105.1 (d, $J_{C\text{-}F}$ = 24.6 Hz), 9.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -121.32.

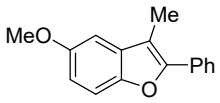


3,5-Dimethyl-2-phenylbenzofuran (6c): the reaction was conducted at 0.1 mmol scale, 12.9 mg, 58% yield, known compound[21], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.76 (m, 2H), 7.51–7.43 (m, 2H), 7.40–7.30 (m, 3H), 7.13–7.06 (m, 1H), 2.47 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 151.0, 132.0, 131.8, 131.5, 128.8, 128.0, 126.9, 125.8, 119.4, 111.3, 110.7, 21.6, 9.7.

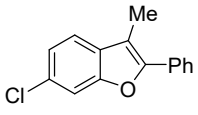


5-(*Tert*-butyl)-3-methyl-2-phenylbenzofuran (6d): the reaction was conducted at 0.1 mmol scale, 17.7 mg, 67% yield, known compound[22], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84–7.76 (m, 2H), 7.54–7.50 (m, 1H), 7.49–7.43 (m, 2H), 7.42–7.39 (m, 1H), 7.38–7.31 (m, 2H), 2.49 (s, 3H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.3, 151.1, 145.7, 131.9, 130.9, 128.8, 127.9, 126.9, 122.5, 115.5, 111.7, 110.5, 35.0, 32.1, 9.7.

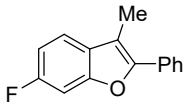


5-Methoxy-3-methyl-2-phenylbenzofuran (6e): the reaction was conducted at 0.1 mmol scale, 

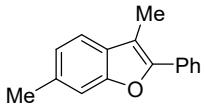
10.0 mg, 42% yield, known compound[21], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.76 (m, 2H), 7.52–7.44 (m, 2H), 7.41–7.31 (m, 2H), 7.01–6.96 (m, 1H), 6.93–6.87 (m, 1H), 3.89 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 151.8, 149.0, 131.9, 131.7, 128.8, 128.1, 126.9, 113.2, 111.6, 111.6, 102.1, 56.2, 9.8.

6-Chloro-3-methyl-2-phenylbenzofuran (6f): the reaction was conducted at 0.1 mmol scale, 6.3 

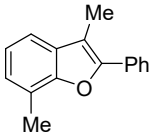
mg, 26% yield, known compound[22], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85–7.74 (m, 2H), 7.54–7.45 (m, 3H), 7.44–7.41 (m, 1H), 7.40–7.34 (m, 1H), 7.25–7.20 (m, 1H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.0, 151.7, 131.2, 130.2, 130.1, 128.9, 128.4, 126.9, 123.3, 120.0, 111.7, 111.3, 9.6.

6-Fluoro-3-methyl-2-phenylbenzofuran (6g): the reaction was conducted at 0.1 mmol scale, 7.2 

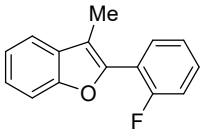
mg, 32% yield, known compound[21], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81–7.75 (m, 2H), 7.52–7.41 (m, 3H), 7.39–7.33 (m, 1H), 7.23–7.17 (m, 1H), 7.06–6.97 (m, 1H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.3 (d, $J_{C\text{-}F}$ = 270.1 Hz), 153.9 (d, $J_{C\text{-}F}$ = 13.1 Hz), 151.7 (d, $J_{C\text{-}F}$ = 4.0 Hz), 131.4, 128.9, 128.2, 127.7 (d, $J_{C\text{-}F}$ = 1.2 Hz), 126.8, 119.8 (d, $J_{C\text{-}F}$ = 10.0 Hz), 111.3, 110.8 (d, $J_{C\text{-}F}$ = 23.8 Hz), 99.0 (d, $J_{C\text{-}F}$ = 24.6 Hz), 9.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -117.45.

3,6-Dimethyl-2-phenylbenzofuran (6h): the reaction was conducted at 0.1 mmol scale, 15.9 mg, 

71% yield, unknown compound, white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83–7.76 (m, 2H), 7.51–7.43 (m, 2H), 7.42–7.38 (m, 1H), 7.37–7.31 (m, 1H), 7.30–7.27 (m, 1H), 7.11–7.04 (m, 1H), 2.49 (s, 3H), 2.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.4, 150.3, 134.8, 131.9, 129.0, 128.8, 127.8, 126.8, 124.0, 119.0, 111.4, 22.0, 9.8. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{15}O$ 223.1117; found 223.1116.

3,7-Dimethyl-2-phenylbenzofuran (6i): the reaction was conducted at 0.1 mmol scale, 15.8 mg, 

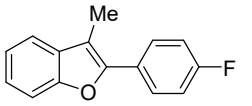
71% yield, unknown compound, white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87–7.79 (m, 2H), 7.53–7.44 (m, 2H), 7.40–7.32 (m, 2H), 7.20–7.13 (m, 1H), 7.12–7.05 (m, 1H), 2.57 (s, 3H), 2.47 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.0, 150.6, 131.9, 130.8, 128.8, 128.0, 126.9, 125.5, 122.6, 121.4, 117.0, 111.8, 15.2, 9.8. HRMS (ESI-QEplus) m/z: $[M+H]^+$ Calcd for $C_{16}H_{15}O$ 223.1117; found 223.1117.

2-(2-Fluorophenyl)-3-methylbenzofuran (6j): the reaction was conducted at 0.1 mmol scale, 

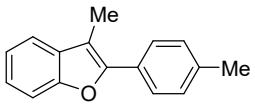
17.6 mg, 78% yield, unknown compound, white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69–7.61 (m, 1H), 7.60–7.53 (m, 1H), 7.52–7.46 (m, 1H), 7.43–7.36 (m, 1H), 7.35–7.23 (m, 3H), 7.22–7.15 (m, 1H), 2.32 (d, J = 2.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (d, $J_{C\text{-}F}$ = 249.6 Hz), 154.7, 146.5, 130.9 (d, $J_{C\text{-}F}$ = 3.3 Hz), 130.7, 130.6 (d, $J_{C\text{-}F}$ = 8.1 Hz), 124.7, 124.4 (d, $J_{C\text{-}F}$ =

3.4 Hz), 122.6, 119.8, 119.4 (d, J_{C-F} = 14.2 Hz), 116.5 (d, J_{C-F} = 22.0 Hz), 114.4, 111.3, 9.2 (d, J_{C-F} = 6.4 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -111.93. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{12}FO$ 227.0867; found 227.0866.

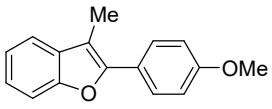
2-(4-Fluorophenyl)-3-methylbenzofuran (6k): the reaction was conducted at 0.1 mmol scale, 13.8 mg, 61% yield, known compound[23], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82–7.73 (m, 2H), 7.56–7.50 (m, 1H), 7.49–7.45 (m, 1H), 7.33–7.22 (m, 2H), 7.21–7.12 (m, 2H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, J_{C-F} = 246.9 Hz), 153.9, 150.1, 131.3, 128.7 (d, J_{C-F} = 8.2 Hz), 127.9 (d, J_{C-F} = 3.6 Hz), 124.6, 122.7, 119.5, 115.9 (d, J_{C-F} = 21.6 Hz), 111.1, 9.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -113.13.



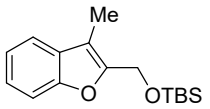
3-Methyl-2-(*p*-tolyl)benzofuran (6l): the reaction was conducted at 0.1 mmol scale, 13.8 mg, 62% yield, known compound[24], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74–7.67 (m, 2H), 7.56–7.50 (m, 1H), 7.49–7.44 (m, 1H), 7.32–7.20 (m, 4H), 2.46 (s, 3H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.9, 151.2, 138.1, 131.5, 129.6, 128.8, 126.9, 124.3, 122.5, 119.4, 111.1, 110.8, 21.6, 9.7.



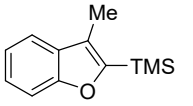
2-(4-Methoxyphenyl)-3-methylbenzofuran (6m): the reaction was conducted at 0.1 mmol scale, 16.0 mg, 67% yield, known compound[24], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79–7.70 (m, 2H), 7.55–7.49 (m, 1H), 7.48–7.43 (m, 1H), 7.31–7.20 (m, 2H), 7.06–6.98 (m, 2H), 3.87 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 153.8, 151.1, 131.5, 128.4, 124.4, 124.1, 122.5, 119.2, 114.3, 111.0, 109.9, 55.6, 9.6.



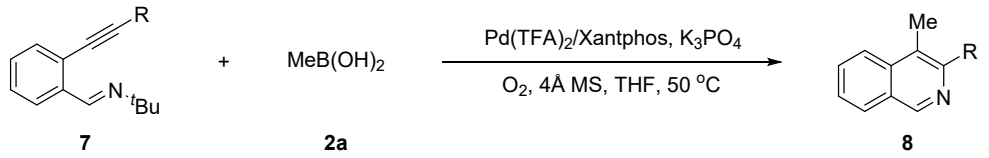
***Tert*-butyldimethyl((3-methylbenzofuran-2-yl)methoxy)silane (6n):** the reaction was conducted at 0.1 mmol scale, 13.3 mg, 48% yield, unknown compound, white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.46 (m, 1H), 7.44–7.41 (m, 1H), 7.29–7.24 (m, 1H), 7.23–7.19 (m, 1H), 4.78 (s, 2H), 2.25 (s, 3H), 0.92 (s, 9H), 0.12 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 151.7, 130.2, 124.4, 122.3, 119.6, 112.4, 111.3, 56.9, 26.1, 18.7, 8.2, -5.0. HRMS (ESI-QEplus) *m/z*: $[M-^tBu]^+$ Calcd for $C_{12}H_{15}O_2Si$ 219.0836; found 219.0833.



Trimethyl(3-methylbenzofuran-2-yl)silane (6o): the reaction was conducted at 0.1 mmol scale, 15.9 mg, 78% yield, known compound[25], white solid, R_f = 0.8 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.46 (m, 1H), 7.44–7.41 (m, 1H), 7.29–7.24 (m, 1H), 7.23–7.19 (m, 1H), 2.31 (s, 3H), 0.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 157.6, 130.1, 125.3, 124.4, 122.0, 119.4, 111.3, 9.1, -0.9.



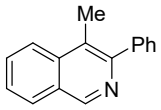
9. General procedure for synthesis of 4-methylisoquinolines



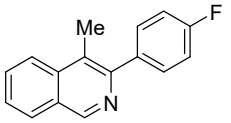
7 **2a** **8**

In the glovebox, a Schlenk tube was charged with **7** (1.0 equiv.), **2a** (3.0 equiv.), $Pd(TFA)_2$ (10 mol%), Xantphos (11 mol%), potassium phosphate (1.5 equiv.), 4Å MS and tetrahydrofuran. Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compounds **8**.

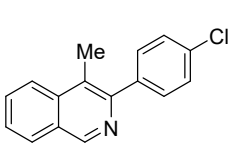
4-Methyl-3-phenylisoquinoline (8a): the reaction was conducted at 0.1 mmol scale, 12.1 mg, 55% yield, known compound[26], white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.10–8.05 (m, 1H), 8.03–7.97 (m, 1H), 7.81–7.73 (m, 1H), 7.66–7.56 (m, 3H), 7.53–7.45 (m, 2H), 7.44–7.37 (m, 1H), 2.66 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 150.4, 141.5, 136.5, 130.6, 130.1, 128.3, 127.8, 127.5, 126.9, 124.3, 123.8, 15.8.



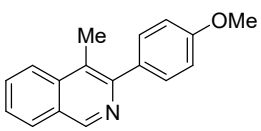
3-(4-Fluorophenyl)-4-methylisoquinoline (8b): the reaction was conducted at 0.1 mmol scale, 12.5 mg, 53% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.11–8.04 (m, 1H), 8.03–7.97 (m, 1H), 7.82–7.75 (m, 1H), 7.68–7.60 (m, 1H), 7.59–7.52 (m, 2H), 7.22–7.11 (m, 2H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.6 (d, $J_{C\text{-}F}$ = 245.0 Hz), 151.0, 150.4, 137.6 (d, $J_{C\text{-}F}$ = 3.5 Hz), 136.4, 131.8 (d, $J_{C\text{-}F}$ = 8.1 Hz), 130.8, 128.4, 127.5, 127.0, 124.3, 123.8, 115.3 (d, $J_{C\text{-}F}$ = 2.1 Hz), 15.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.77. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}FN$ 238.1027; found 238.1020.



3-(4-Chlorophenyl)-4-methylisoquinoline (8c): the reaction was conducted at 0.1 mmol scale, 11.2 mg, 44% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.12–8.05 (m, 1H), 8.03–7.98 (m, 1H), 7.83–7.74 (m, 1H), 7.69–7.60 (m, 1H), 7.58–7.51 (m, 2H), 7.49–7.42 (m, 2H), 2.65 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 150.5, 140.0, 136.4, 133.9, 131.5, 130.8, 128.5, 128.4, 127.6, 127.1, 124.4, 123.8, 15.7. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}ClN$ 254.0731; found 254.0725.

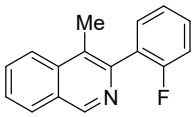


3-(4-Methoxyphenyl)-4-methylisoquinoline (8d): the reaction was conducted at 0.1 mmol scale, 14.7 mg, 59% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.19 (s, 1H), 8.09–8.02 (m, 1H), 8.01–7.95 (m, 1H), 7.80–7.72 (m, 1H), 7.66–

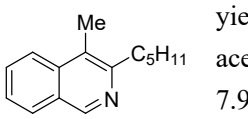


7.59 (m, 1H), 7.57–7.48 (m, 2H), 7.06–6.99 (m, 2H), 3.88 (s, 3H), 2.67 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 151.8, 150.3, 136.5, 134.0, 131.4, 130.6, 128.3, 127.3, 126.7, 123.9, 123.8, 113.8, 55.6, 15.9. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{16}NO$ 250.1226; found 250.1220.

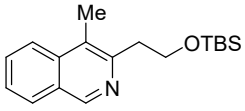
3-(2-Fluorophenyl)-4-methylisoquinoline (8e): the reaction was conducted at 0.1 mmol scale, 12.7 mg, 54% yield, unknown compound, white solid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 8.11–8.05 (m, 1H), 8.04–7.99 (m, 1H), 7.82–7.75 (m, 1H), 7.70–7.61 (m, 1H), 7.58–7.50 (m, 1H), 7.46–7.38 (m, 1H), 7.32–7.26 (m, 1H), 7.22–7.14 (m, 1H), 2.56 (d, J = 2.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.7 (d, $J_{C\text{-}F}$ = 245.5 Hz), 150.6, 146.7, 136.0, 132.2 (d, $J_{C\text{-}F}$ = 3.4 Hz), 130.7, 130.0 (d, $J_{C\text{-}F}$ = 8.4 Hz), 129.2 (d, $J_{C\text{-}F}$ = 16.0 Hz), 128.3, 127.8, 127.2, 126.5, 124.5 (d, $J_{C\text{-}F}$ = 3.6 Hz), 123.8, 115.8 (d, $J_{C\text{-}F}$ = 22.4 Hz), 15.3 (d, $J_{C\text{-}F}$ = 3.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.21. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{13}FN$ 238.1027; found 238.1020.



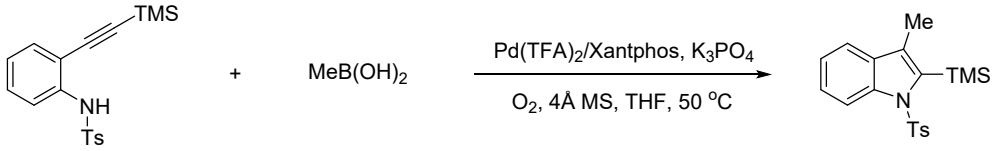
4-Methyl-3-pentylisoquinoline (8f): the reaction was conducted at 0.1 mmol scale, 15.0 mg, 70% yield, unknown compound, colorless oil, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.01–7.95 (m, 1H), 7.94–7.87 (m, 1H), 7.74–7.65 (m, 1H), 7.57–7.48 (m, 1H), 3.06–2.96 (m, 2H), 2.61 (s, 3H), 1.82–1.69 (m, 2H), 1.50–1.32 (m, 4H), 0.93 (t, J = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 150.1, 136.2, 130.2, 128.2, 127.1, 125.9, 123.5, 123.2, 36.2, 32.2, 29.9, 22.9, 14.3, 13.8. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{20}N$ 214.1590; found 214.1584.



3-(2-((*Tert*-butyldimethylsilyl)oxy)ethyl)-4-methylisoquinoline (8g): the reaction was conducted at 0.1 mmol scale, 10.3 mg, 34% yield, unknown compound, white liquid, R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.08 (s, 1H), 8.01–7.96 (m, 1H), 7.94–7.88 (m, 1H), 7.73–7.66 (m, 1H), 7.57–7.50 (m, 1H), 4.05 (t, J = 6.9 Hz, 2H), 3.25 (t, J = 6.9 Hz, 2H), 2.65 (s, 3H), 0.83 (s, 9H), -0.07 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.3, 150.2, 136.0, 130.2, 128.2, 127.2, 126.1, 125.0, 123.3, 63.5, 39.2, 26.1, 18.5, 14.1, -5.2. HRMS (ESI-QEplus) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{28}NOSi$ 302.1935; found 302.1928.



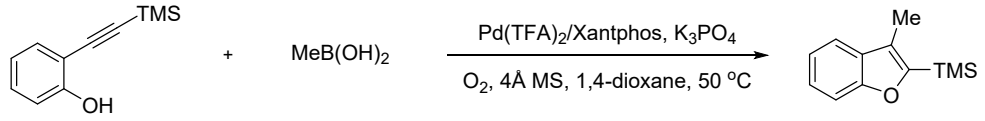
10. Scale-up experiment for synthesis of 3ad and 6o



1ad (1.0 mmol) **2a** (3.0 mmol) **3ad**: 98% yield

In the glovebox, a Schlenk tube was charged with **1ad** (343.5 mg, 1.0 mmol), **2a** (180.0 mg, 3.0 mmol), $Pd(TFA)_2$ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (318.0 mg, 1.5 mmol), and 4Å MS (1000.0 mg) in the tetrahydrofuran (20.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of

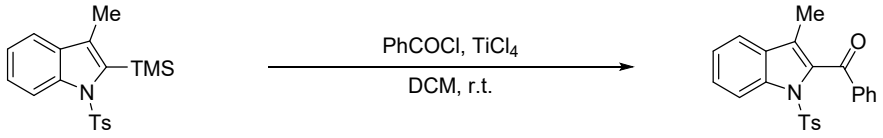
the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3ad** as white solid (350.0 mg, 98% yield).



5o (2.0 mmol) **2a** (6.0 mmol) **6o:** 77% yield

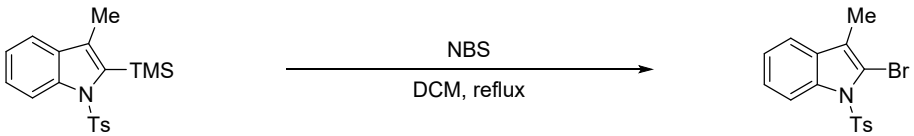
In the glovebox, a Schlenk tube was charged with **5o** (380.0 mg, 2 mmol), **2a** (360.0 mg, 6 mmol), $Pd(TFA)_2$ (66.0 mg, 0.2 mmol), Xantphos (127.3 mg, 0.22 mmol), potassium phosphate (636.0 mg, 3 mmol), and 4Å MS (2000.0 mg) in the 1,4-dioxane (40.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether) to afford the desired compound **6o** as white solid (319.4 mg, 77% yield).

11. Further synthetic transformations of product 3ad



3ad **9**

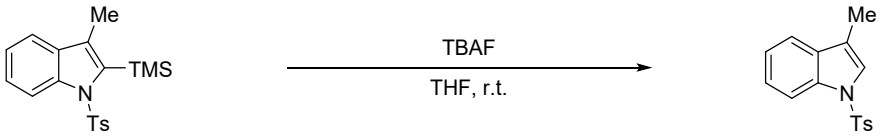
Synthesis of (3-methyl-1-tosyl-1*H*-indol-2-yl)(phenyl)methanone 9: In a nitrogen-filled Schlenk tube, to a solution of the **3ad** (35.7 mg, 0.1 mmol) and benzoyl chloride (15.5 mg, 1.1 mmol) in dichloromethane (2.0 mL) was added dropwise a solution of titanium tetrachloride in dichloromethane (3.0 M, 0.13 mL, 0.4 mmol) at 0 °C. The mixture was stirred for 0.5 h, the reaction was quenched by water, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **9** as white solid (22.2 mg, 57% yield), unknown compound, R_f = 0.25 (petroleum ether/ethyl acetate 30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14–8.06 (m, 1H), 7.96–7.88 (m, 2H), 7.74–7.67 (m, 2H), 7.62–7.56 (m, 1H), 7.52–7.40 (m, 4H), 7.34–7.28 (m, 1H), 7.19–7.13 (m, 2H), 2.31 (s, 3H), 2.18 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.8, 145.1, 138.6, 136.6, 134.0, 133.8, 133.6, 131.4, 129.8, 129.7, 128.8, 127.5, 126.9, 124.8, 124.5, 120.6, 115.5, 21.8, 9.6. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{23}H_{19}NNaO_3S$ 412.0975; found 412.0971.



3ad **10**

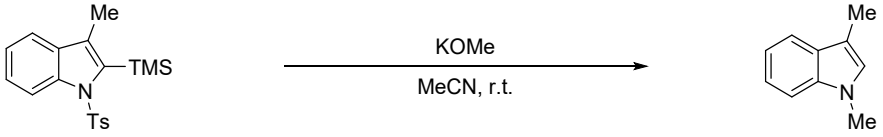
Synthesis of 2-bromo-3-methyl-1-tosyl-1*H*-indole 10: Under nitrogen atmosphere, the

mixture of **3ad** (35.7 mg, 0.1 mmol) and *N*-bromosuccinimide (35.6 mg, 0.2 mmol) in dichloromethane (2.0 mL) was stirred for 2h in 40 °C oil bath. Then the reaction was cooled to room temperature and quenched by water, the aqueous phase was extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **10** as white solid (24.4 mg, 67% yield), unknown compound, R_f = 0.25 (petroleum ether/ethyl acetate 30/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31–8.24 (m, 1H), 7.77–7.70 (m, 2H), 7.41–7.36 (m, 1H), 7.35–7.29 (m, 1H), 7.29–7.22 (m, 1H), 7.22–7.15 (m, 2H), 2.34 (s, 3H), 2.16 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 137.5, 135.5, 130.6, 129.9, 127.3, 125.2, 124.0, 121.9, 118.7, 115.7, 109.2, 21.8, 10.6. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{16}H_{14}BrNNaO_2S$ 385.9821; found 385.9816.



3ad **11**

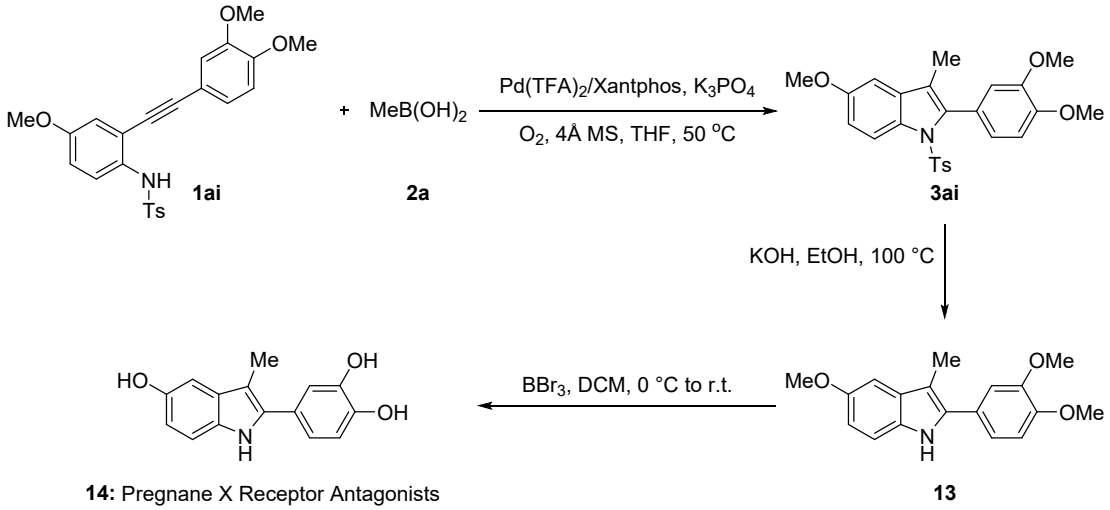
Synthesis of 3-methyl-1-tosyl-1*H*-indole 11: Under nitrogen atmosphere, to a solution of the **3ad** (35.7 mg, 0.1 mmol) in tetrahydrofuran (2.0 mL) was added dropwise a solution of tetrabutylammonium fluoride in tetrahydrofuran (1.0 M, 0.3 mL, 0.3 mmol). The mixture was stirred for 12 h. The reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **11** as white solid (22.5 mg, 79% yield), known compound[27], white solid, R_f = 0.25 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01–7.94 (m, 1H), 7.77–7.69 (m, 2H), 7.47–7.40 (m, 1H), 7.34–7.27 (m, 2H), 7.26–7.21 (m, 1H), 7.19–7.14 (m, 2H), 2.30 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 135.6, 135.5, 132.0, 130.0, 126.9, 124.8, 123.3, 123.2, 119.6, 118.8, 113.9, 21.7, 9.9.



3ad **12**

Synthesis of 1,3-dimethyl-1*H*-indole 12: Under nitrogen atmosphere, the mixture of **3ad** (35.7 mg, 0.1 mmol) and potassium methoxide (14.0 mg, 0.2 mmol) in acetonitrile (2.0 mL) was stirred overnight. After completion of the reaction (monitored by TLC), the reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **12** as white solid (12.1 mg, 83% yield), known compound[27], white solid, R_f = 0.25 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 –7.54 (m, 1H), 7.30–7.24 (m, 1H), 7.23–7.17 (m, 1H), 7.14–7.06 (m, 1H), 6.80 (s, 1H), 3.71 (s, 3H), 2.32 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 137.2, 128.8, 126.7, 121.6, 119.1, 118.7, 110.3, 109.2, 32.7, 9.7.

12. Synthesis of bioactive molecules and drugs



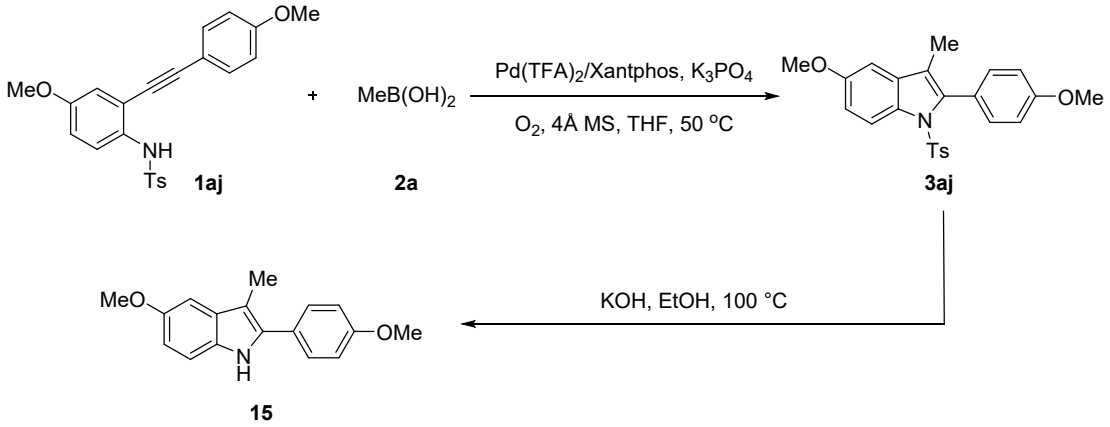
14: Pregnane X Receptor Antagonists

Synthesis of 2-(3,4-dimethoxyphenyl)-5-methoxy-3-methyl-1-tosyl-1*H*-indole 3ai: In the glovebox, a Schlenk tube was charged with **1ai** (438.0 mg, 1.0 mmol), **2a** (180.0 mg, 3.0 mmol), $Pd(TFA)_2$ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (318.0 mg, 1.5 mmol), and 4Å MS (1000.0 mg) in the tetrahydrofuran (20.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3ai** as white solid (375.0 mg, 83% yield), unknown compound, R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.18 (m, 1H), 7.29–7.24 (m, 2H), 7.07–7.01 (m, 2H), 7.00–6.95 (m, 1H), 6.94–6.90 (m, 1H), 6.89–6.82 (m, 3H), 3.96 (s, 3H), 3.87 (s, 3H), 3.86 (s, 3H), 2.30 (s, 3H), 2.01 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.1, 149.3, 148.0, 144.4, 137.7, 135.1, 133.2, 131.8, 129.3, 127.0, 124.0, 124.0, 119.7, 117.5, 115.1, 113.3, 110.0, 101.8, 56.1, 56.0, 55.8, 21.7, 9.9. HRMS (ESI-QEplus) *m*/*z*: $[M+Na]^+$ Calcd for $C_{25}H_{25}NNaO_5S$ 474.1346; found 474.1344.

Synthesis of 2-(3,4-dimethoxyphenyl)-5-methoxy-3-methyl-1*H*-indole 13: Under nitrogen atmosphere, the mixture of **3ai** (135.5 mg, 0.3 mmol) and potassium hydroxide (50.5 mg, 0.9 mmol) in ethanol (6.0 mL) was stirred overnight in 100 °C oil bath. The reaction was cooled to room temperature and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **13** as white solid (84.7 mg, 95% yield), known compound[28], R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (s, 1H), 7.28–7.25 (m, 1H), 7.14–7.10 (m, 1H), 7.09–7.06 (m, 1H), 7.04–7.01 (m, 1H), 6.99–6.95 (m, 1H), 6.88–6.82 (m, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.89 (s, 3H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.3, 149.3, 148.7, 135.3, 131.0, 130.7, 126.5, 120.5, 112.3, 111.6, 111.5, 111.2, 107.9, 100.9, 56.2, 9.9.

Synthesis of 4-(5-hydroxy-3-methyl-1*H*-indol-2-yl)benzene-1,2-diol 14: Under nitrogen atmosphere, to a solution of the **13** (29.7 mg, 0.1 mmol) in dichloromethane (2.0 mL) was added

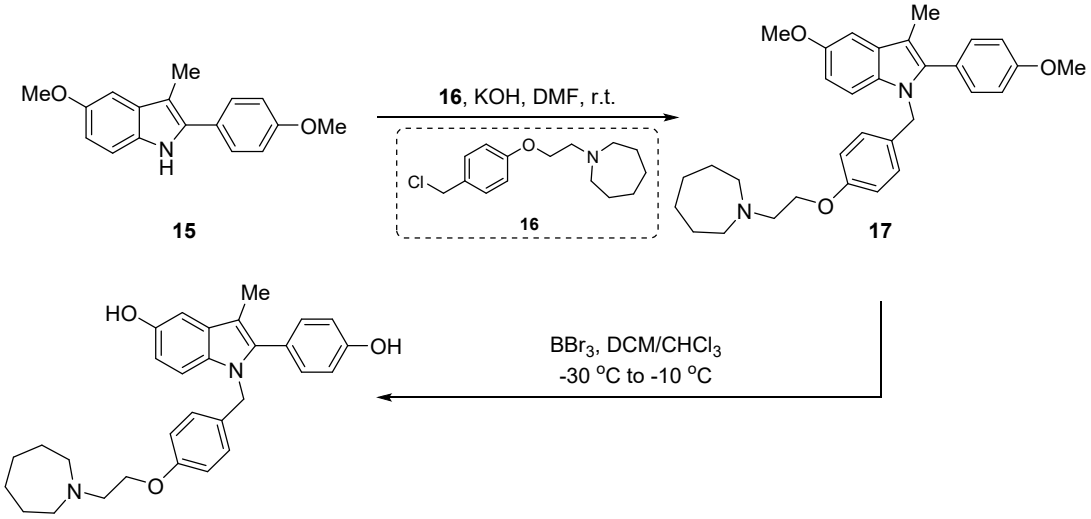
dropwise a solution of boron tribromide in dichloromethane (1 M, 0.9 mL, 0.9 mmol) in 0 °C. The mixture was stirred for 1.5 h at room temperature. The reaction was quenched by water, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **14** as yellow solid (20.4 mg, 80% yield), known compound[28], R_f = 0.25 (petroleum ether/ethyl acetate 4/1); ^{1}H NMR (400 MHz, CD_3OD) δ 7.17–7.14 (m, 1H), 7.09–7.08 (m, 1H), 6.98–6.95 (m, 1H), 6.90–6.85 (m, 2H), 6.66–6.64 (m, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 150.4, 145.7, 145.1, 136.2, 131.7, 131.4, 126.6, 119.9, 115.9, 115.4, 111.4, 111.3, 105.6, 102.8, 9.4.



Synthesis of 5-methoxy-2-(4-methoxyphenyl)-3-methyl-1-tosyl-1*H*-indole 3aj: In the glovebox, a Schlenk tube was charged with **1aj** (407.5 mg, 1.0 mmol), **2a** (180.0 mg, 3.0 mmol), $Pd(TFA)_2$ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (318.0 mg, 1.5 mmol), and 4Å MS (1000.0 mg) in the tetrahydrofuran (20.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath. After completion of the reaction (monitored by TLC), the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3aj** as white solid (384.0 mg, 91% yield), unknown compound, R_f = 0.3 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24–8.16 (m, 1H), 7.28–7.22 (m, 4H), 7.08–7.00 (m, 2H), 6.99–6.92 (m, 3H), 6.86–6.79 (m, 1H), 3.89 (s, 3H), 3.85 (s, 3H), 2.29 (s, 3H), 2.00 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.9, 157.1, 144.4, 137.8, 135.1, 133.3, 132.8, 131.8, 129.3, 127.0, 124.0, 119.7, 117.6, 113.3, 113.1, 101.9, 55.9, 55.5, 21.7, 9.8. HRMS (ESI-QEplus) *m/z*: $[M+Na]^+$ Calcd for $C_{24}H_{23}NNaO_4S$ 444.1240; found 444.1235.

Synthesis of 5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole 15: Under nitrogen atmosphere, the mixture of **3aj** (380.0 mg, 0.9 mmol) and potassium hydroxide (151.5 mg, 2.7 mmol) in ethanol (20.0 mL) was stirred overnight in 100 °C oil bath. The reaction was cooled to room temperature and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **15** as white solid (235.8 mg, 98% yield), known compound[29], R_f = 0.3 (petroleum ether/ethyl acetate 15/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.53–7.44 (m, 2H), 7.27–7.20 (m, 1H), 7.06–6.96 (m, 3H), 6.88–6.80 (m, 1H), 3.89 (s, 3H), 3.86 (s, 3H), 2.40 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 154.2, 135.2, 131.0, 130.6, 129.1,

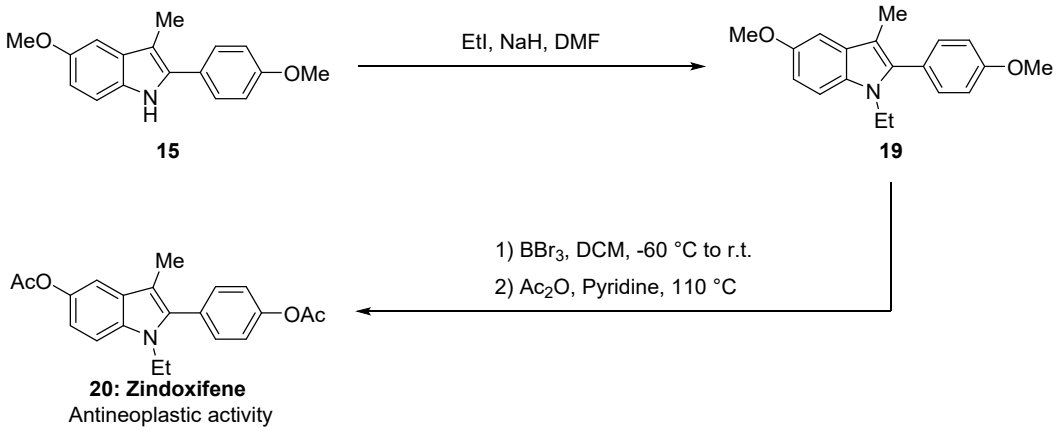
126.1, 114.4, 112.1, 111.5, 107.7, 100.9, 56.1, 55.6, 9.9.



18: Bazedoxifene
Estrogen receptor modulator

Synthesis of 1-(4-(2-(azepan-1-yl)ethoxy)benzyl)-5-methoxy-2-(4-methoxyphenyl)-3-methyl -1*H*-indole 17: Under nitrogen atmosphere, the mixture of **15** (26.7 mg, 0.1 mmol) and potassium hydroxide (50.5 mg, 0.3 mmol) in *N,N*-dimethylformamide (3.0 mL) was stirred for 1h. Then the compound **16** (32.1 mg, 0.12 mmol) was added into the mixture. The reaction was stirred for 24 h and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate/triethylamine) to afford the desired compound **17** as yellow oil (47.7 mg, 96% yield), known compound[10], R_f = 0.25 (petroleum ether/ethyl acetate/triethylamine 10/1/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27–7.20 (m, 2H), 7.09–7.03 (m, 2H), 6.96–6.90 (m, 2H), 6.87–6.83 (m, 2H), 6.82–6.78 (m, 1H), 6.78–6.71 (m, 2H), 5.11 (s, 2H), 4.00 (t, *J* = 6.2 Hz, 2H), 3.88 (s, 3H), 3.84 (s, 3H), 2.91 (t, *J* = 6.2 Hz, 2H), 2.80–2.71 (m, 4H), 2.25 (s, 3H), 1.70–1.54 (m, 8H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.5, 158.0, 154.2, 138.5, 132.1, 131.9, 131.0, 129.3, 127.4, 124.6, 114.8, 114.0, 111.8, 111.1, 108.5, 100.9, 66.4, 56.4, 56.2, 56.0, 55.5, 47.3, 27.8, 27.2, 9.7.

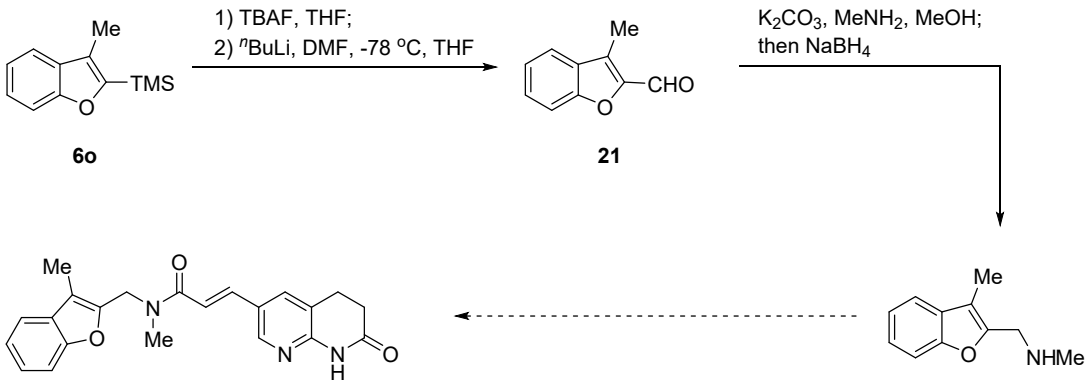
Synthesis of Bazedoxifene 18: Under nitrogen atmosphere, to a solution of the **17** (24.9 mg, 0.05 mmol) in chloroform (1.0 mL) was added dropwise a solution of boron tribromide in dichloromethane (1 M, 0.3 mL, 0.3 mmol) at -30 °C. The mixture was stirred for 16 h in at -10 °C. The reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (dichloromethane/methanol) to afford the desired compound **18** as yellow solid (8.0 mg, 34% yield), known compound[30], yellow solid, R_f = 0.25 (dichloromethane/methanol 10/1); ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.16–7.11 (m, 2H), 7.07–7.02 (m, 1H), 6.91–6.86 (m, 2H), 6.82–6.79 (m, 1H), 6.77–6.71 (m, 4H), 6.60–6.56 (m, 1H), 5.10 (s, 2H), 3.92 (t, *J* =6.2 Hz, 2H), 2.77 (t, *J* = 6.0 Hz, 2H), 2.67–2.60 (m, 4H), 2.10 (s, 3H), 1.58–1.45 (m, 8H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 157.9, 157.8, 151.4, 138.5, 131.8, 131.8, 131.1, 131.1, 131.1, 127.8, 127.8, 115.9, 114.8, 111.2, 106.9, 103.0, 66.6, 56.5, 55.6, 28.3, 27.0, 9.9.



Synthesis of 1-ethyl-5-methoxy-2-(4-methoxyphenyl)-3-methyl-1*H*-indole 19: Under nitrogen atmosphere, the mixture of **15** (80.0 mg, 0.3 mmol) and sodium hydride (10.8 mg, 0.45 mmol) in *N,N*-dimethylformamide (3.0 mL) was stirred for 15 min. Then a solution of iodoethane in *N,N*-dimethylformamide was added into the mixture. The reaction was stirred overnight and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **19** as white solid (75.0 mg, 85% yield), known compound[31], R_f = 0.3 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39–7.31 (m, 2H), 7.31–7.24 (m, 1H), 7.11–7.01 (m, 3H), 6.97–6.87 (m, 1H), 4.05 (q, *J* = 7.1 Hz, 2H), 3.93 (s, 3H), 3.92 (s, 3H), 2.24 (s, 3H), 1.22 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3, 153.9, 137.8, 131.7, 131.2, 128.9, 124.8, 113.9, 111.5, 110.2, 108.2, 100.8, 56.1, 55.4, 38.7, 15.5, 9.4.

Synthesis of Zindoxifene 20: Under nitrogen atmosphere, to a solution of the **19** (29.7 mg, 0.1 mmol) in dichloromethane (2.0 mL) was added dropwise a solution of boron tribromide in dichloromethane (1 M, 0.4 mL, 0.4 mmol) in -60 °C. After 30 min the cooling bath was removed and the mixture was stirred overnight. The reaction was quenched by an aqueous solution of sodium bicarbonate, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was used for next acetylation step without further purification.

Under nitrogen atmosphere, to a solution of the crude material in pyridine (1.0 mL) was added acetic anhydride (61.3 mg, 0.6 mmol). After refluxing in 110 °C oil bath for 2 h. The reaction was cooled to room temperature and quenched by aqueous dilute solution of hydrochloric acid, then extracted with dichloromethane. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **20** as white solid (32.3 mg, 92% yield), known compound[32], R_f = 0.25 (petroleum ether/ethyl acetate 10/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41–7.35 (m, 2H), 7.34–7.29 (m, 1H), 7.28–7.26 (m, 1H), 7.24–7.18 (m, 2H), 6.97–6.91 (m, 1H), 4.04 (q, *J* = 7.1 Hz, 2H), 2.34 (s, 3H), 2.33 (s, 3H), 2.18 (s, 3H), 1.20 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 169.6, 150.6, 144.2, 137.7, 134.1, 131.7, 129.9, 129.0, 121.8, 115.8, 111.2, 110.1, 109.5, 39.0, 21.4, 15.6, 9.4.



6o **21** **22**

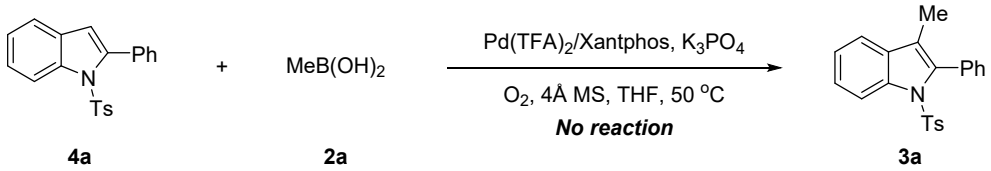
23: **AFN-1252**
FabI high-efficiency inhibitor

Synthesis of 3-methylbenzofuran-2-carbaldehyde 21: Under nitrogen atmosphere, to a solution of the **6o** (306.5 mg, 1.5 mmol) in tetrahydrofuran (2.0 mL) was added dropwise a solution of tetrabutylammonium fluoride in tetrahydrofuran (1.0 M, 0.3 mL, 0.3 mmol). The reaction was stirred overnight and quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The crude material was used for next acetylation step without further purification.

Under nitrogen atmosphere, to a solution of the crude material in tetrahydrofuran (10.0 mL) was added dropwise a solution of *n*-butyllithium (2.5 M, 0.4 mL, 1.6 mmol) in tetrahydrofuran at -78 °C. After 1 h the *N*,*N*-dimethylformamide (0.3 mL, 3.0 mmol) was added to the mixture and the reaction was stirred for 5h. The reaction was quenched by a saturated aqueous solution of ammonium chloride, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **21** as white solid (192.2 mg, 80% yield), known compound[33], R_f = 0.25 (petroleum ether); ^{1}H NMR (400 MHz, $CDCl_3$) ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.04 (s, 1H), 7.73–7.68 (m, 1H), 7.58–7.49 (m, 2H), 7.38–7.31 (m, 1H), 2.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.9, 155.6, 148.3, 129.6, 128.9, 123.8, 122.0, 112.8, 8.63.

Synthesis of *N*-methyl-1-(3-methylbenzofuran-2-yl)methanamine 22: Under nitrogen atmosphere, the reaction tube was charged with methylamine hydrochloride (20.3 mg, 0.3 mmol), potassium carbonate (20.7 mg, 0.15 mmol) and methanol (1 mL), and the reaction was stirred at 0 °C for 30 min. Then the compound **21** (32.2 mg, 0.2 mmol) was added to mixture, and the reaction was stirred at r.t. for 1 h. The reaction was cooled to 0 °C and sodium borohydride (11.4 mg, 0.3 mmol) was added. The reaction was stirred at room temperature for 4 h. The reaction was quenched by water, then extracted with ethyl acetate. The combined organic layers were dried over sodium sulfate, filtered and concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate/triethylamine) to afford the desired compound **22** as white solid (26.4 mg, 75% yield), unknown compound, R_f = 0.2 (petroleum ether/ethyl acetate/triethylamine 20/1/1); ^{1}H NMR (400 MHz, CD_3OD) δ 7.51–7.46 (m, 1H), 7.41–7.35 (m, 1H), 7.26–7.17 (m, 2H), 3.82 (s, 2H), 2.37 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 155.0, 151.0, 130.4, 124.6, 122.7, 119.7, 113.3, 111.0, 34.7, 7.2. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{14}NO$ 176.1070; found 176.1068.

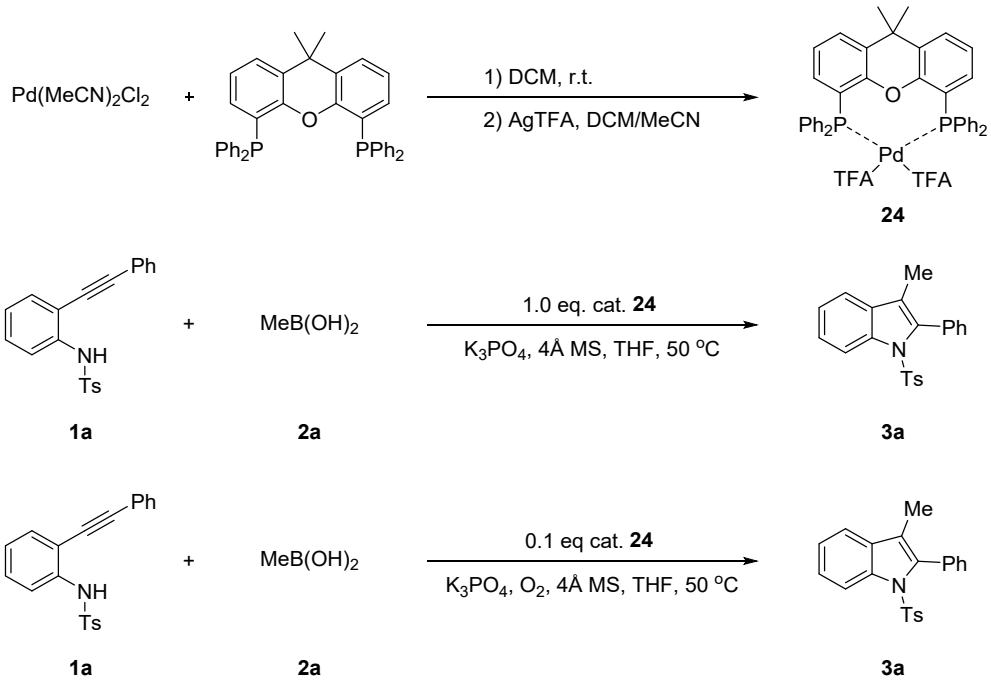
13. Mechanism studies



4a **2a** **3a**

In the glovebox, a Schlenk tube was charged with **4a** (24.5 mg, 0.07 mmol), **2a** (12.6 mg, 0.21 mmol), $Pd(TFA)_2$ (1.2 mg, 0.0035 mmol), Xantphos (2.2 mg, 0.00385 mmol), potassium phosphate (22.3 mg, 0.105 mmol), and 4Å MS (70.0 mg) in the tetrahydrofuran (1.4 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 5 h. After completion of the reaction, the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford 25.1 mg compound and confirmed as **4a** by ^{1}H NMR.

2-phenyl-1-tosyl-1H-indole 4a: known compound[34], white solid, R_f = 0.2 (petroleum ether/ethyl acetate 50/1); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35–8.28 (m, 1H), 7.54–7.47 (m, 2H), 7.47–7.39 (m, 4H), 7.39–7.32 (m, 1H), 7.31–7.22 (m, 3H), 7.08–6.99 (m, 2H), 6.54 (s, 1H), 2.28 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 142.3, 138.5, 134.9, 132.6, 130.8, 130.6, 129.4, 128.9, 127.7, 127.0, 125.0, 124.5, 120.9, 116.9, 113.8, 21.7.

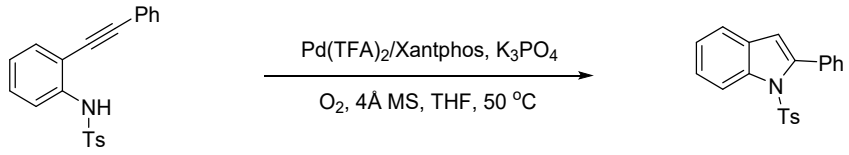


Preparation of (Xantphos)Pd(TFA)$_2$ 24 : In the glovebox, the reaction tube was charged with $Pd(CH_3CN)_2Cl_2$ (31.1 mg, 0.12 mmol), Xantphos (69.4 mg, 0.12 mmol) and dichloromethane (4.0 mL). Then the mixture was stirred in room temperature for 3 h. Filtration through Celite yielded a clear yellow solution, which was concentrated under reduced pressure. Then ethyl ether was added,

and the solution was cooled at -35 °C for 12 h. The resulting yellow crystals were washed two times with ethyl ether and dried in vacuo. Under nitrogen atmosphere, the reaction tube was charged with the resulting yellow crystals, silver trifluoroacetate (106.0 mg, 0.48 mmol), dichloromethane (5.0 mL) and acetonitrile (0.5 mL). Then the mixture was stirred in room temperature for 0.5 h. Filtration through Celite yielded a clear green solution, which was concentrated under reduced pressure. The resulting green crystals were washed two times with ethyl ether and dried in vacuo to afford **24** as yellow solid (79.0 mg, 75% yield), unknown compound, yellow solid; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.69–7.60 (m, 2H), 7.40–7.25 (m, 12H), 7.20–7.13 (m, 8H), 7.11–7.06 (m, 2H), 6.56–6.45 (m, 2H), 1.67 (s, 6H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 155.3, 155.3, 135.4, 135.4, 133.9, 133.8, 132.0, 132.0, 131.2, 131.2, 129.1, 128.5, 128.4, 125.8, 125.3, 125.3, 125.2, 117.2, 116.7, 36.8, 26.8. ^{19}F NMR (376 MHz, CD_2Cl_2) δ -74.80. ^{31}P NMR (161 MHz, CD_2Cl_2) δ 8.81. HRMS (ESI-QEplus) *m/z*: $[M\text{-}2TFA]^{2+}$ Calcd for $C_{39}H_{32}OP_2Pd$ 342.0476; found 342.0472.

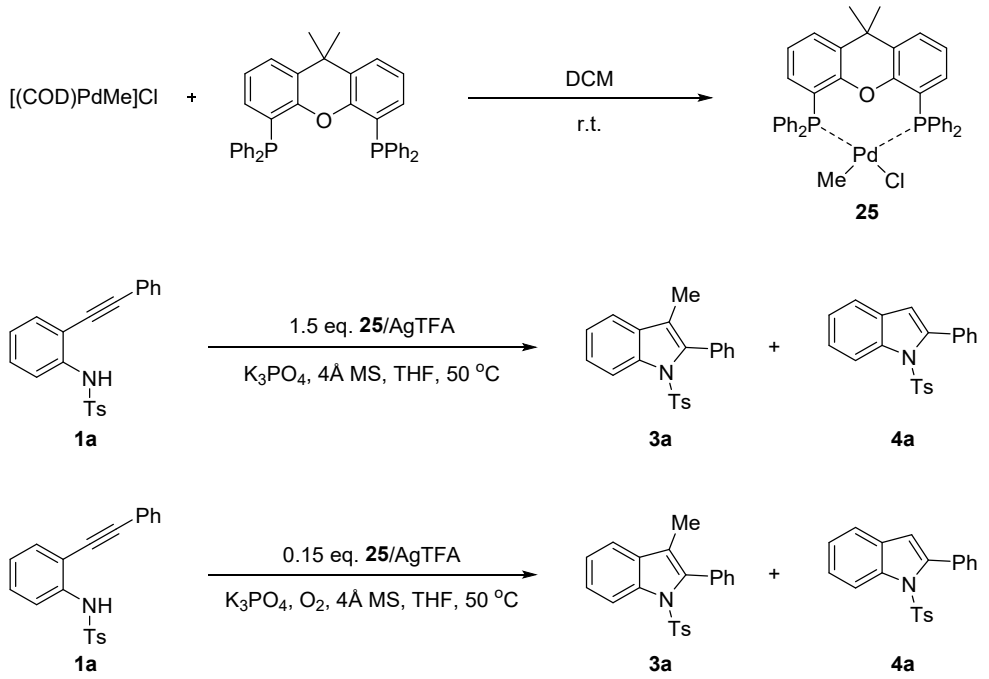
The reaction was conducted at 0.02 mmol scale using 1.0 equiv. (Xantphos)Pd(TFA)$_2$ 24: In the glovebox, a Schlenk tube was charged with **1a** (6.9 mg, 0.02 mmol), **2a** (3.6 mg, 0.06 mmol), **24** (17.6 mg, 0.02 mmol), potassium phosphate (6.4 mg, 0.03 mmol), 4Å MS (20.0 mg) and tetrahydrofuran (0.5 mL). Then the Schlenk tube was removed from glovebox and the mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the resulting mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3a** (7.1 mg, 98% yield).

The reaction was conducted at 0.1 mmol scale using 0.1 equiv. (Xantphos)Pd(TFA)$_2$ 24: In the glovebox, a Schlenk tube was charged with **1a** (34.7 mg, 0.1 mmol), **2a** (18.0 mg, 0.3 mmol), **24** (8.8 mg, 0.01 mmol), potassium phosphate (31.8 mg, 0.15 mmol), 4Å MS (100.0 mg) and tetrahydrofuran (2.0 mL). Then the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3a** (31.6 mg, 88% yield).



1a **4a**

In the glovebox, a Schlenk tube was charged with **1a** (34.7 mg, 0.1 mmol), $Pd(TFA)_2$ (1.7 mg, 0.005 mmol), Xantphos (3.2 mg, 0.0055 mmol), potassium phosphate (31.8 mg, 0.15 mmol), 4Å MS (100.0 mg) and tetrahydrofuran (2.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the resulting mixture was concentrated under reduced pressure. The resulting crude material was analyzed by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard and yield of **4a** is 6%.

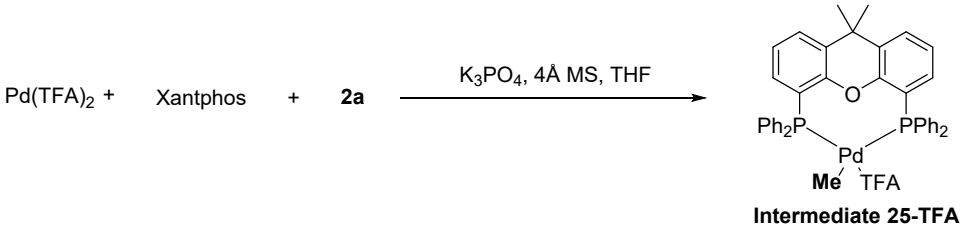


Preparation of (Xantphos)PdMeCl·25 : In the glovebox, the reaction tube was charged with (cod)PdMeCl (88.0 mg, 0.29 mmol), Xantphos (167.8 mg, 0.29 mmol) and dichloromethane (7.0 mL). Then the mixture was stirred in room temperature for 3 h. Filtration through Celite yielded a clear yellow solution, which was concentrated under reduced pressure. Then pentane was added, and the solution was cooled at -35 °C for 12 h. The resulting yellow crystals were washed two times with pentane and dried in vacuo to afford **25** as green solid, known compound[35]; ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.58–7.52 (m, 2H), 7.48–7.34 (m, 8H), 7.26–7.13 (m, 12H), 7.12–7.07 (m, 2H), 7.06–7.01 (m, 2H), 1.67 (s, 6H), 0.30 (s, 3H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 155.3, 155.2, 155.2, 134.8, 134.8, 134.8, 134.5, 134.4, 134.4, 131.8, 131.6, 131.4, 131.0, 129.8, 128.2, 128.2, 128.1, 127.0, 124.4, 124.4, 36.3, 27.6, 0.8. ^{31}P NMR (162 MHz, CD_2Cl_2) δ 15.21. HRMS (ESI-QEplus) *m/z*: $[M\text{-}Cl]^+$ Calcd for $C_{40}H_{35}OP_2Pd^+$ 699.1192; found 699.1197.

The reaction was conducted at 0.02 mmol scale using 1.5 equiv. (Xantphos)PdMeCl·25: Under nitrogen atmosphere, the reaction tube was charged with·**25** (22.1 mg, 0.03 mmol), silver trifluoroacetate (6.6 mg, 0.03 mmol), dichloromethane (1.0 mL). Then the mixture was stirred in room temperature for 0.5 h. Filtration through Celite yielded a clear brown solution, which was concentrated under reduced pressure. The resulting solid is dissolved in tetrahydrofuran (1.0 mL), then **1a** (6.9 mg, 0.02 mmol), potassium phosphate (6.4 mg, 0.03 mmol) and 4Å MS (20.0 mg) was added into the system. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3a** (5.9 mg, 82% yield) and **4a** (0.3 mg, 4% yield).

The reaction was conducted at 0.1 mmol scale using 0.15 equiv. (Xantphos)PdMeCl·25: Under nitrogen atmosphere, the reaction tube was charged with·**25** (11.0 mg, 0.015 mmol), silver trifluoroacetate (3.4 mg, 0.015 mmol), dichloromethane (1.0 mL). Then the mixture was stirred in room temperature for 0.5 h. Filtration through Celite yielded a clear brown solution, which was concentrated under reduced pressure. The resulting solid is dissolved in tetrahydrofuran (2.0 mL), then **1a** (34.7 mg, 0.1 mmol), potassium phosphate (31.8 mg, 0.15 mmol) and 4Å MS (100.0 mg)

was added into the system. Then the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 °C oil bath for 10 h. After completion of the reaction, the mixture was concentrated under reduced pressure. The resulting crude material was purified by flash column chromatography (petroleum ether/ethyl acetate) to afford the desired compound **3a** (4.9 mg, 14% yield) and **4a** (14.2 mg, 41% yield).



Intermediate 25-TFA

Determination of intermediate 25-TFA: In the glovebox, a seal tube was charged with **2a** (6.0 mg, 0.1 mmol), $Pd(TFA)_2$ (33.0 mg, 0.1 mmol), Xantphos (64.0 mg, 0.11 mmol), potassium phosphate (21.2 mg, 0.1 mmol), and 4Å MS (100.0 mg) in the tetrahydrofuran (2.0 mL). Then the seal tube was removed from glovebox and oscillated several times. The mixture was filtered and diluted with methanol, analyzed by HRMS immediately. HRMS (ESI-QEplus) *m*/*z*: $[M-X]^+$ Calcd for $C_{40}H_{35}OP_2Pd^+$ 699.1192; found 699.1209.

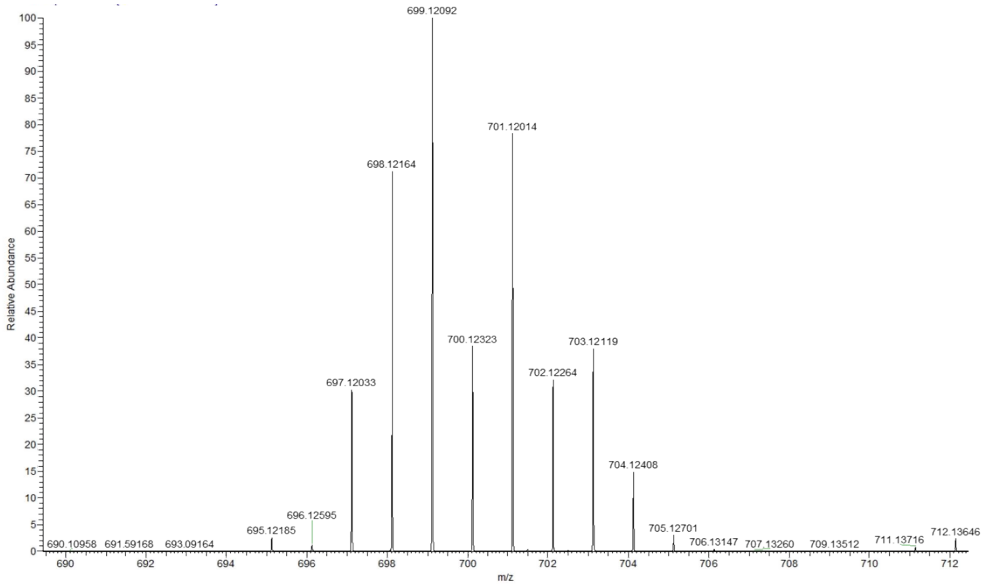
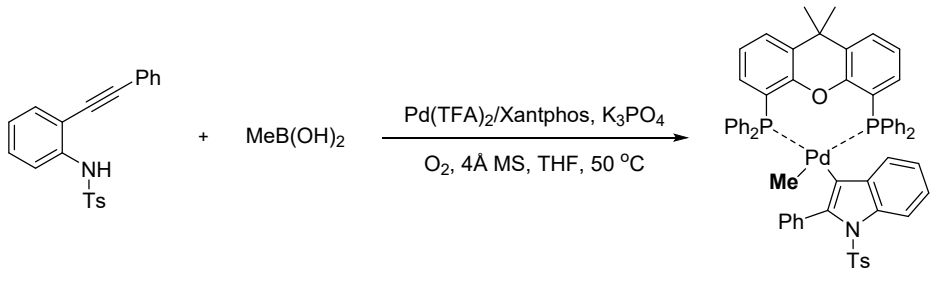


Fig.S1 HRMS analysis of intermediate 25-TFA



1a **2a** **26**

Determination of intermediate 26: In the glovebox, a seal tube was charged with **1a** (34.7 mg, 0.1 mmol), **2a** (18.0 mg, 0.3 mmol), $Pd(TFA)_2$ (3.3 mg, 0.01 mmol), Xantphos (6.4 mg, 0.011 mmol), potassium phosphate (31.8 mg, 0.15 mmol), and 4Å MS (100.0 mg) in the tetrahydrofuran (2.0 mL). Then the seal tube was removed from glovebox and oscillated several times. The

mixture was filtered and diluted with methanol, analyzed by HRMS immediately. HRMS (ESI-QEplus) *m*/*z*: $[M+H]^+$ Calcd for $C_{61}H_{52}NO_3P_2PdS$ 1046.2172; found 1046.1764.

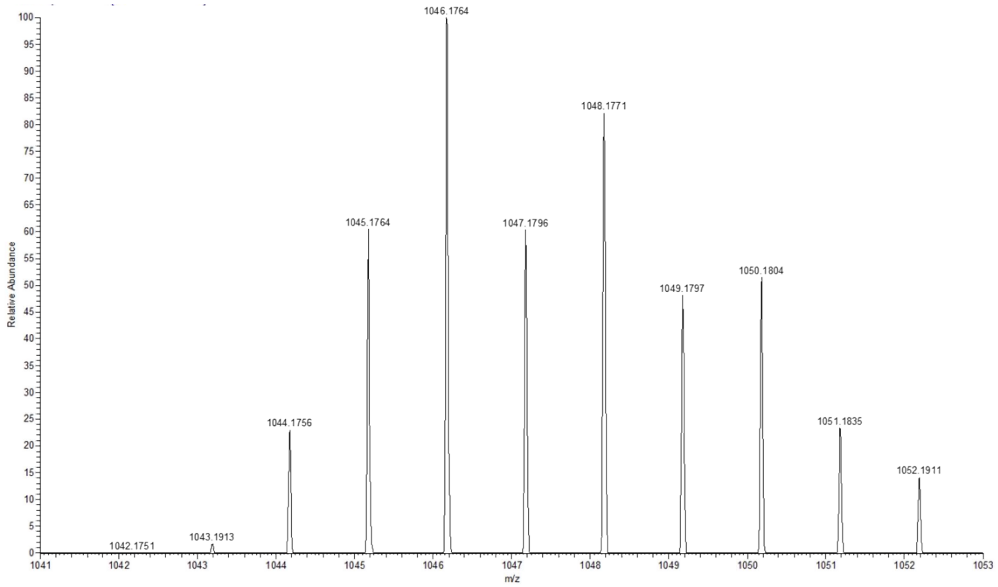


Fig.S2 HRMS analysis of intermediate 26

14. Kinetic studies

14.1 Kinetic order of catalyst

In the glovebox, a Schlenk tube was charged with **1a** (104.0 mg, 0.3 mmol), **2a** (53.9 mg, 0.9 mmol), trimethoxybenzene (50.5 mg, 0.3 mmol), $Pd(TFA)_2$, Xantphos, potassium phosphate (95.5 mg, 0.45 mmol), and 4Å MS (250.0 mg) in the tetrahydrofuran (6.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 ^{o}C oil bath and analyzed by ^{1}H NMR along time. The experimental details and results were shown in the tables below.

Table S10: The amount of materials used for kinetic order test of catalyst

Entry	Pd	Xantphos	**1a**	**2a**	K_3PO_4	Trimethoxybenzene	THF
	mg	mg	mg	mg	mg	mg	mL
1	6	11.5	104	53.9	95.5	50.5	6
2	5	9.5	104	53.9	95.5	50.5	6
3	4	7.6	104	53.9	95.5	50.5	6
4	3	5.7	104	53.9	95.5	50.5	6

Table S11: Concentration of 3a over time with reactions performed with varying concentration of catalyst

3 mol% **cat**	Time/min	3	5	8	10	12	15
	3a/M	0.00162	0.00236	0.003575	0.005095	0.0061	0.00741

4 mol% **cat**	Time/min	2	5	8	10	13
	3a/M	0.002065	0.0045	0.006225	0.00804	0.009885

5 mol% **cat**	Time/min	5	8	10	13	15
	3a/M	0.003495	0.005615	0.00768	0.01074	0.01262

6 mol% **cat**	Time/min	3	5	8	10	13	15
	3a/M	0.003435	0.00619	0.01027	0.013165	0.015565	0.0187

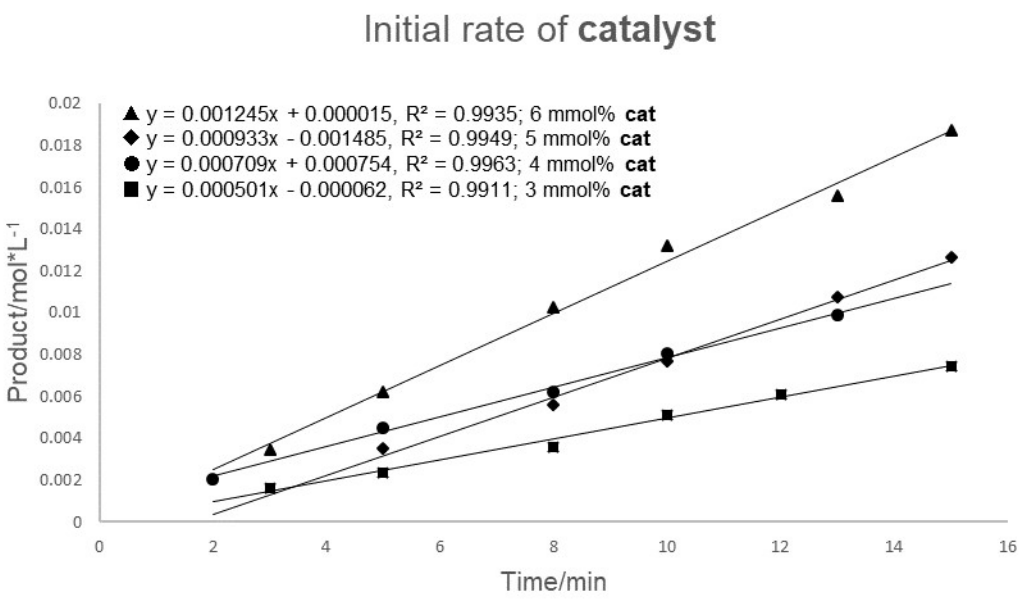


Fig.S3 Plot of concentration of 3a over time with reactions performed with varying concentration of catalyst

Table S12: Relationship between initial rate and concentration of catalyst

Cat/M	0.0015	0.002	0.0025	0.003
Initial rate/M·min^{-1}	0.000501	0.000709	0.000933	0.001245

-Ln(**cat**)	5.809143	5.991465	6.214608	6.50229
-Ln(v)	6.68862	6.977105	7.251655	7.598904

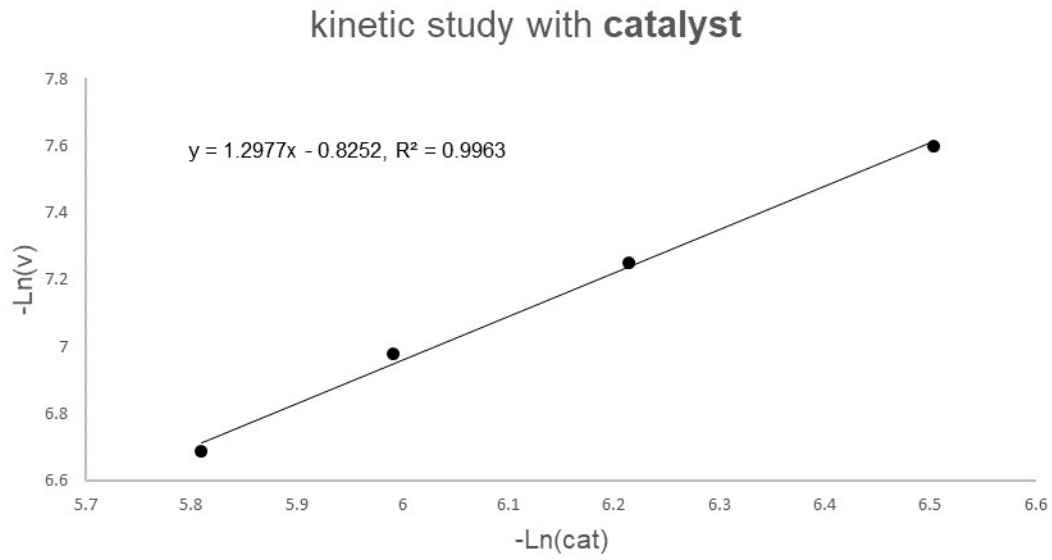


Fig.S4 Plot of -ln(v) vs. -ln(cat) for reaction

14.2 Kinetic order of 1a

In the glovebox, a Schlenk tube was charged with **1a**, **2a** (53.9 mg, 0.9 mmol), trimethoxybenzene (50.5 mg, 0.3 mmol), $Pd(TFA)_2$ (4.0 mg, 0.012 mmol), Xantphos (7.6 mg, 0.013 mmol), potassium phosphate (95.5 mg, 0.45 mmol), and 4Å MS (250.0 mg) in the tetrahydrofuran (6.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 ^{o}C oil bath and analyzed by ^{1}H NMR along time. The detailed amount of each substrate was shown in the table below.

Table S13: The amount of materials used for kinetic order test of 1a

Entry	Pd	Xantphos	**1a**	**2a**	K_3PO_4	Trimethoxybenzene	THF
	mg	mg	mg	mg	mg	mg	mL
1	4	7.6	86.8	53.9	95.5	50.5	6
2	4	7.6	104	53.9	95.5	50.5	6
3	4	7.6	121.5	53.9	95.5	50.5	6
4	4	7.6	138.8	53.9	95.5	50.5	6

Table S14: Concentration of 3a over time with reactions performed with varying concentration of 1a

0.0417 M **1a**	Time/min	3	5	8	11	13
	3a/M	0.00185	0.00329	0.005235	0.007255	0.009045

0.05 M **1a**	Time/min	2	5	8	10	13
	3a/M	0.002065	0.0045	0.006225	0.00804	0.009885

0.0583 M **1a**	Time/min	3	5	8	10	13
	3a/M	0.00224	0.003585	0.00566	0.00723	0.009235

0.0677 M **1a**	Time/min	3	5	8	10	13
	3a/M	0.002835	0.00449	0.006635	0.00801	0.009945

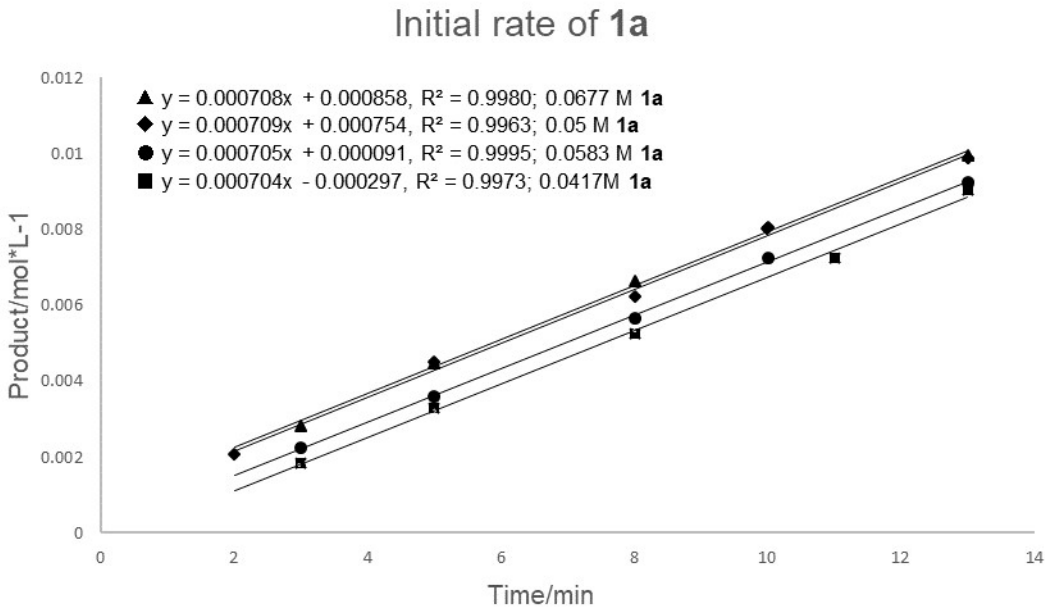


Fig.S5 Plot of concentration of 3a over time with reactions performed with varying concentration of 1a

Table S15: Relationship between initial rate and concentration of 1a

1a/M	0.0417	0.05	0.0583	0.0677
Initial rate/M·min^{-1}	0.000704	0.000709	0.000705	0.00708

-Ln(**1a**)	3.17725	2.99573	2.84215	2.69267
-Ln(v)	7.25873	7.25166	7.25731	7.25307

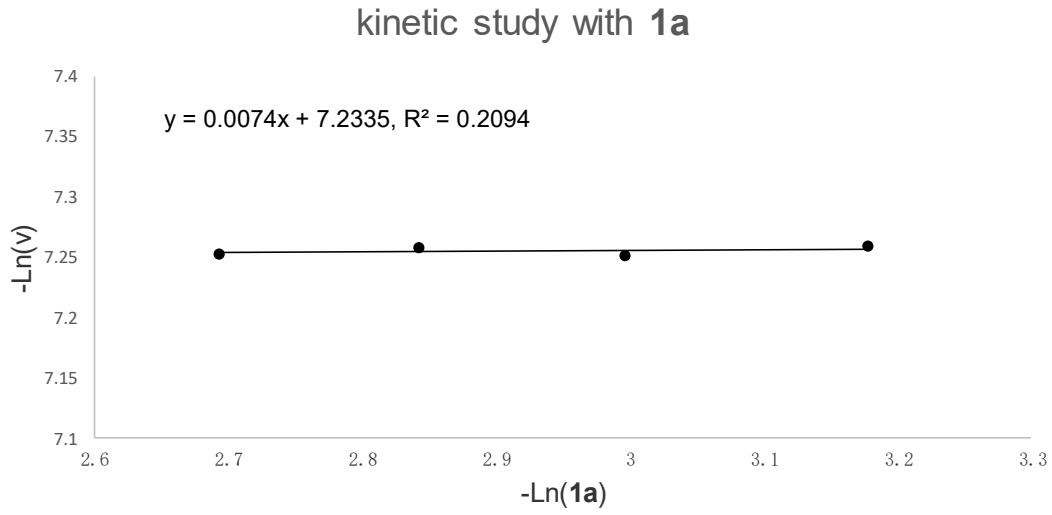


Fig.S6 Plot of -ln(v) vs. -ln(1a) for reaction

14.3 Kinetic order of 2a

In the glovebox, a Schlenk tube was charged with **1a** (104.0 mg, 0.3 mmol), **2a**, trimethoxybenzene (50.5 mg, 0.3 mmol), $Pd(TFA)_2$ (4.0 mg, 0.012 mmol), Xantphos (7.6 mg, 0.013 mmol), potassium phosphate (95.5 mg, 0.45 mmol), and 4Å MS (250.0 mg) in the tetrahydrofuran (6.0 mL). Then the Schlenk tube was removed from glovebox and the nitrogen atmosphere was replaced with the oxygen using an oxygen balloon. The mixture was stirred in 50 ^{o}C oil bath and analyzed by ^{1}H NMR along time. The detailed amount of each substrate was shown in the table below.

Table S16: The amount of materials used for kinetic order test of 2a

Entry	Pd	Xantphos	**1a**	**2a**	K_3PO_4	Trimethoxybenzene	THF
	mg	mg	mg	mg	mg	mg	mL
1	4	7.6	104	35.9	95.5	50.5	6
2	4	7.6	104	53.9	95.5	50.5	6
3	4	7.6	104	71.8	95.5	50.5	6

Table S17: Concentration of 3a over time with reactions performed with varying concentration of 2a

0.1 M **2a**	Time/min	2	5	7	10	12	15
	3a/M	0.00238	0.00358	0.005665	0.007095	0.00906	0.010955

0.15 M **2a**	Time/min	2	5	8	10	13
	3a/M	0.002065	0.0045	0.006225	0.00804	0.009884

0.2 M **2a**	Time/min	3	5	7	9	13
	3a/M	0.002185	0.00317	0.005285	0.0066	0.00926

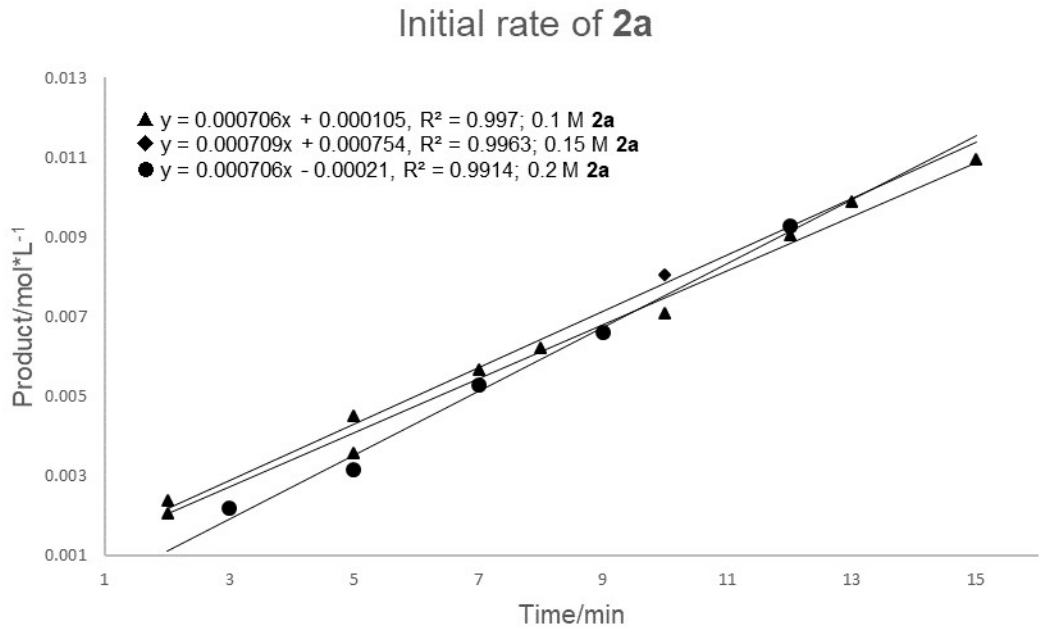


Fig.S7 Plot of concentration of 3a over time with reactions performed with varying concentration of 2a

Table S18: Relationship between initial rate and concentration of 2a

2a/M	0.1	0.15	0.2
Initial rate/M·min^{-1}	0.000709	0.000706	0.000706

-Ln(**2a**)	2.302585093	1.897119985	1.609437912
-Ln(v)	7.251655031	7.25589532	7.25589532

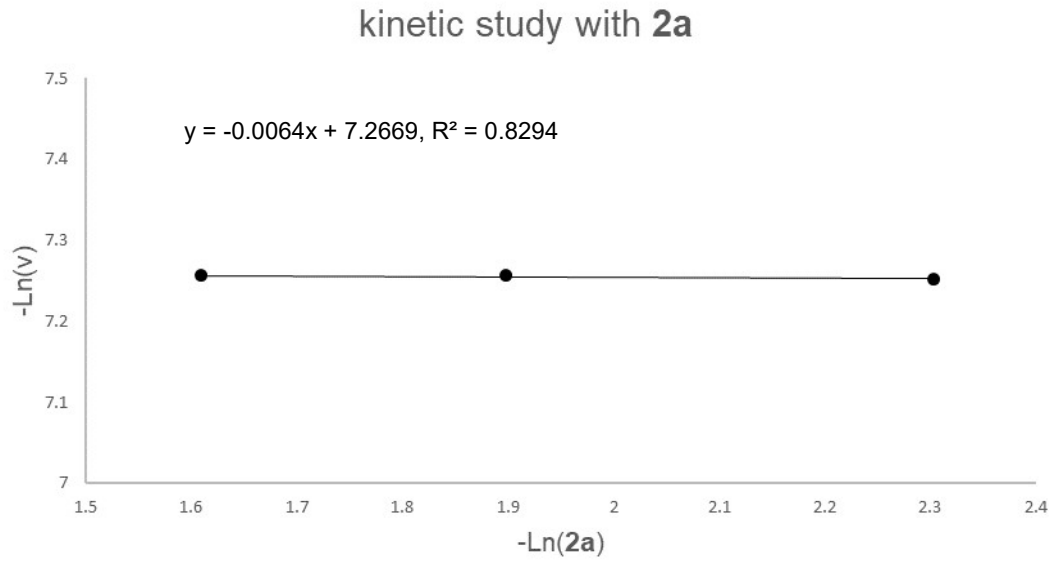


Fig.S8 Plot of -ln(v) vs. -ln(2a) for reaction

15. References

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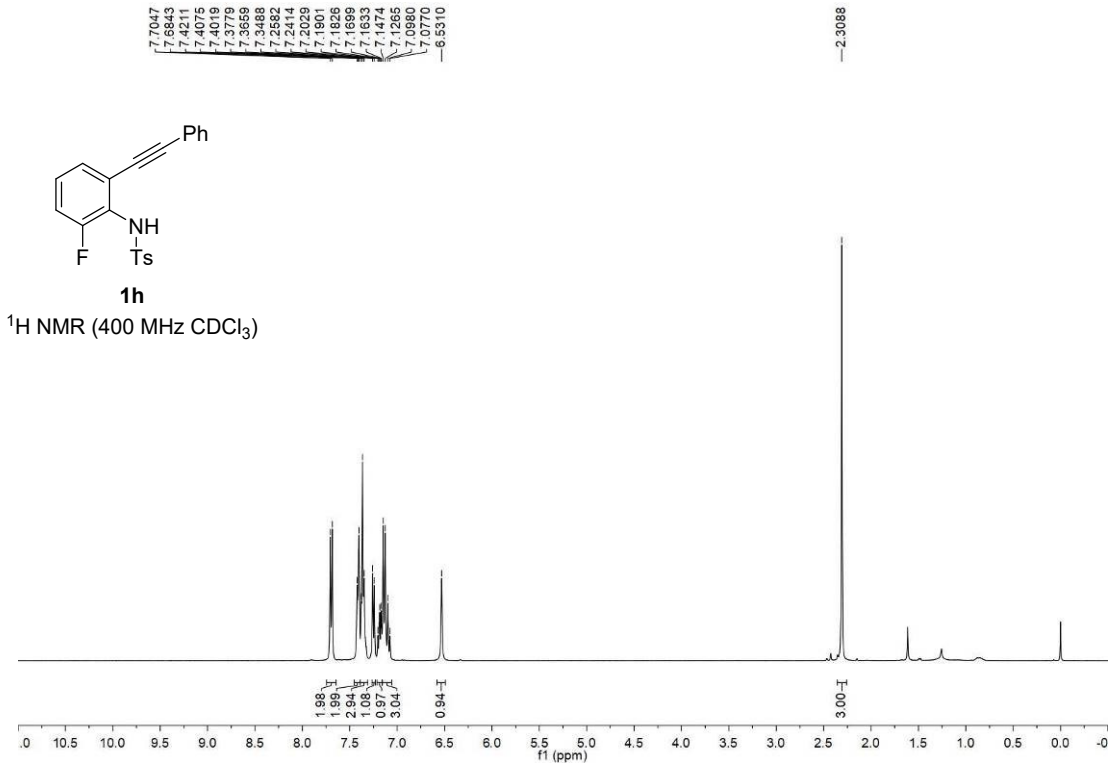
16. Copy of NMR for compounds



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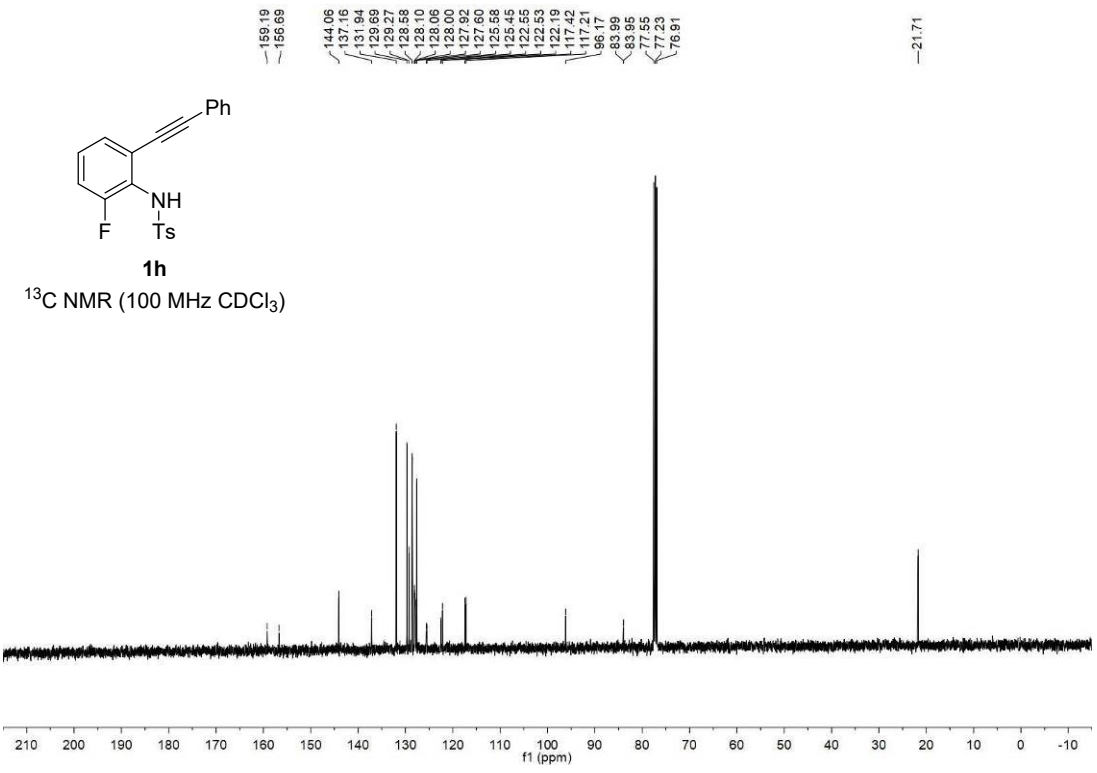

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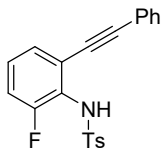

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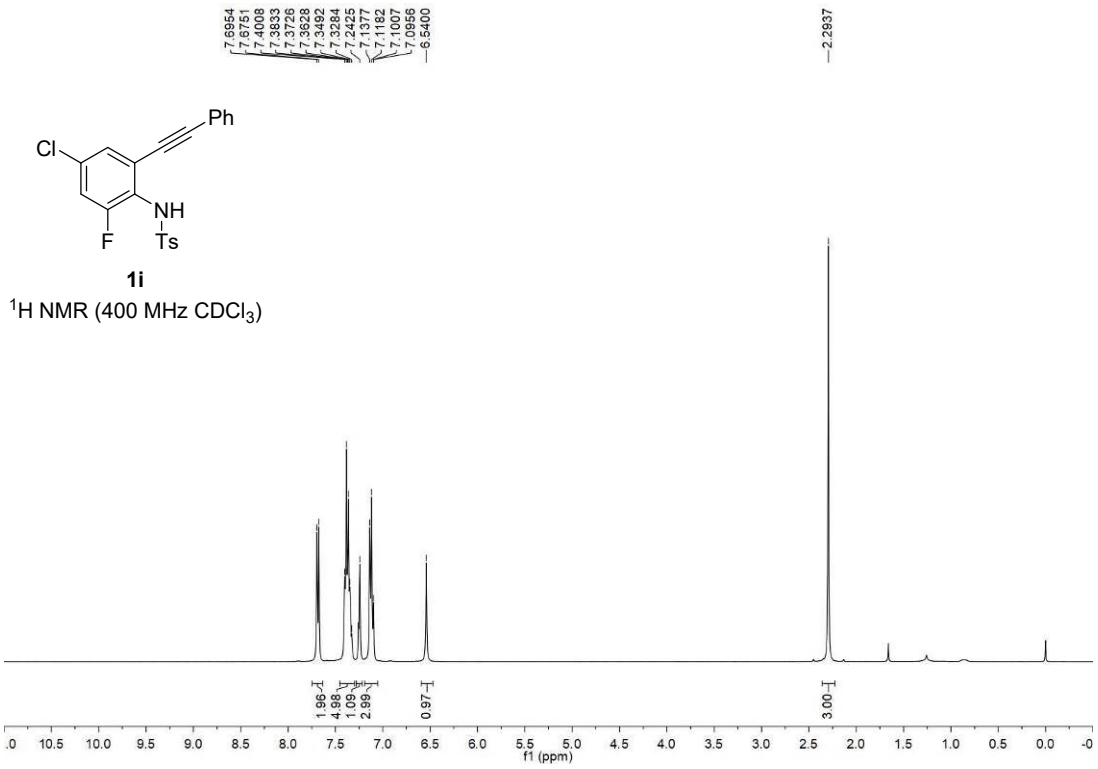

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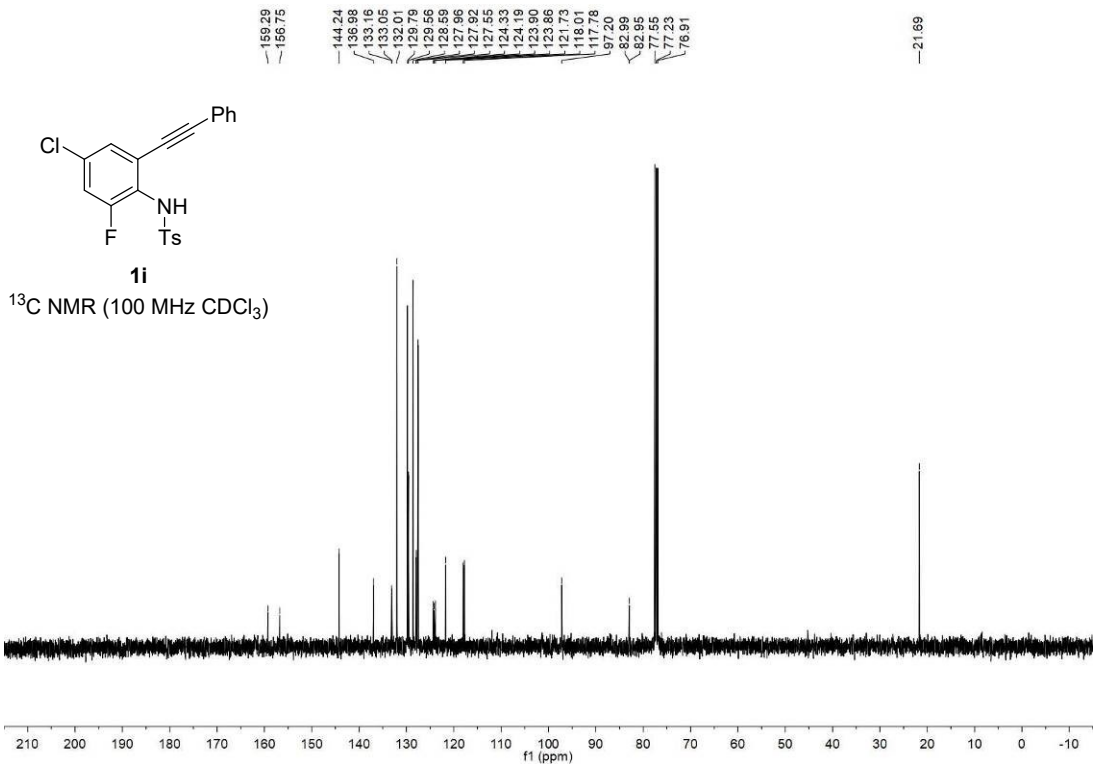

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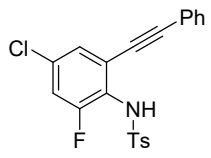

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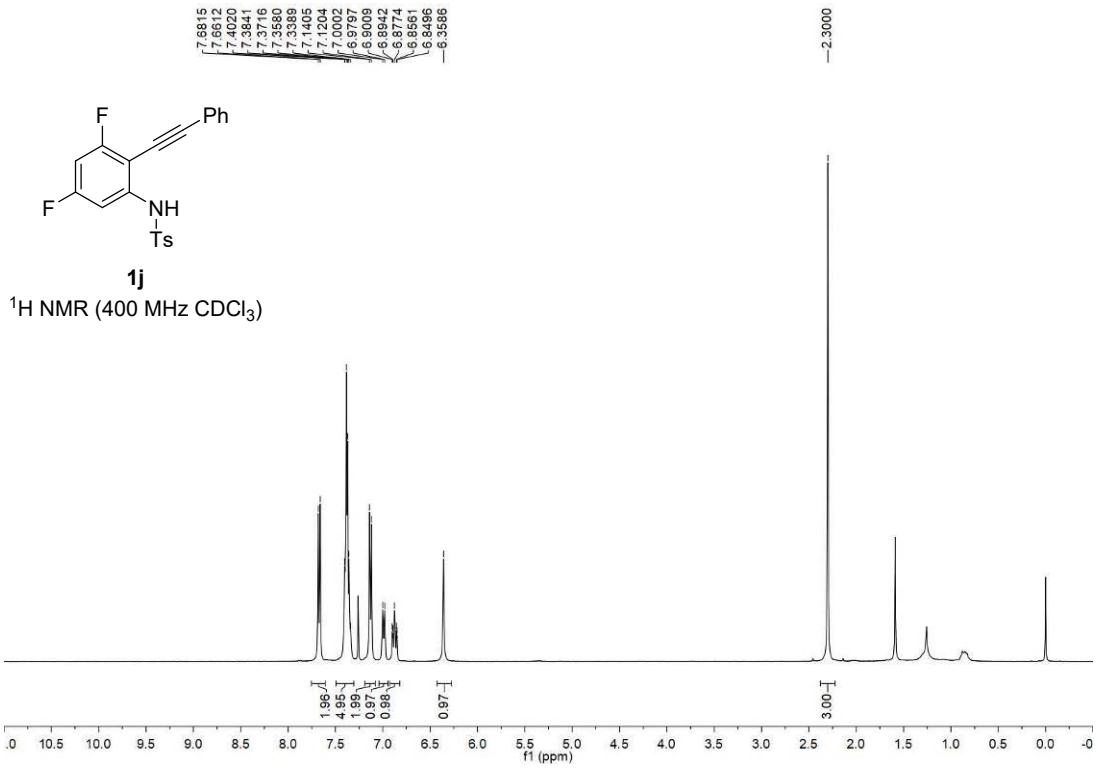

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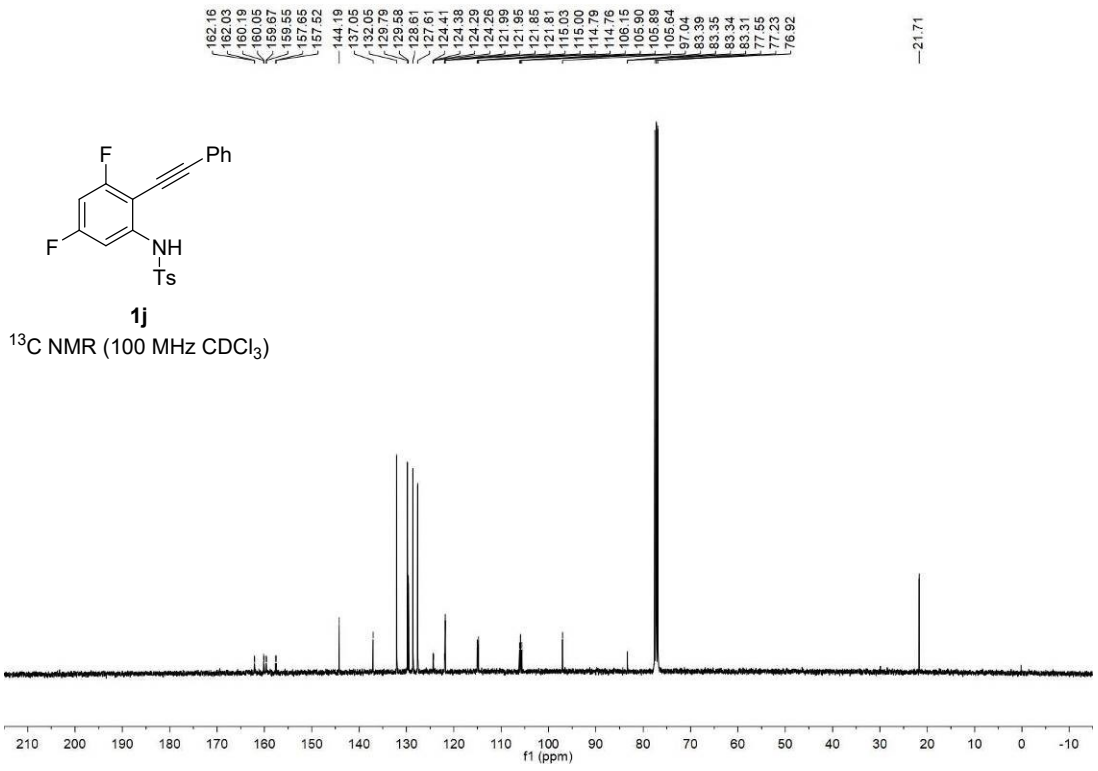

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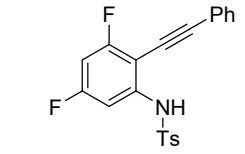

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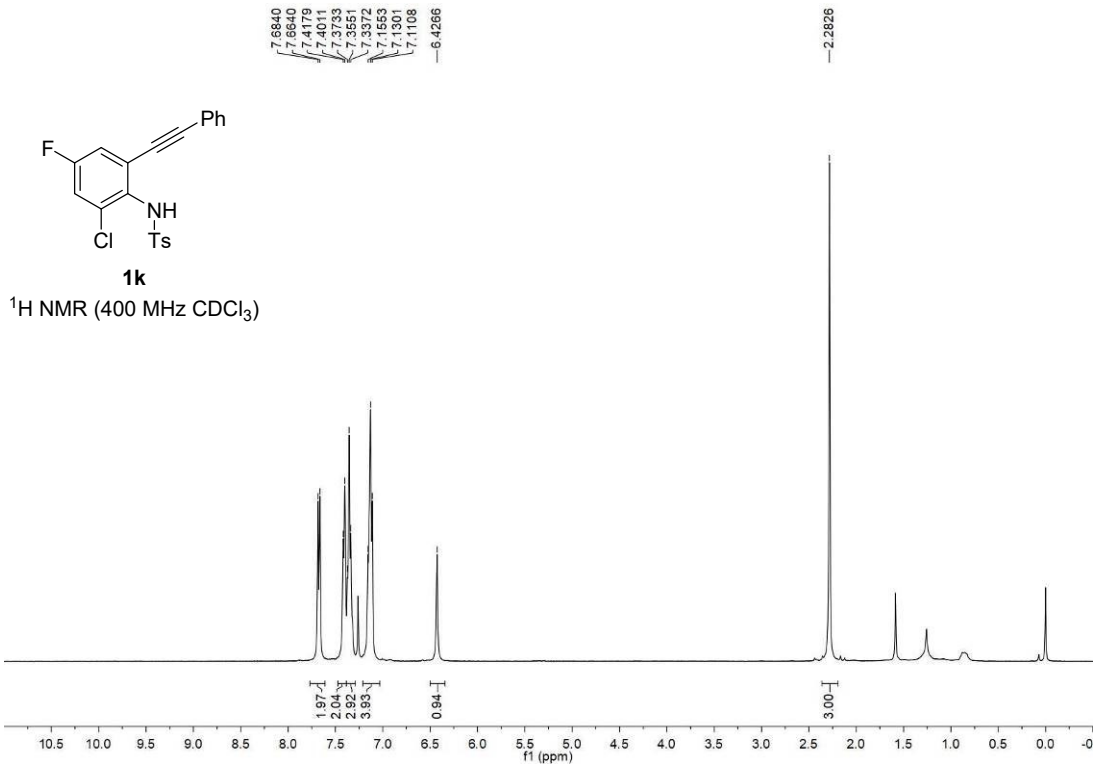

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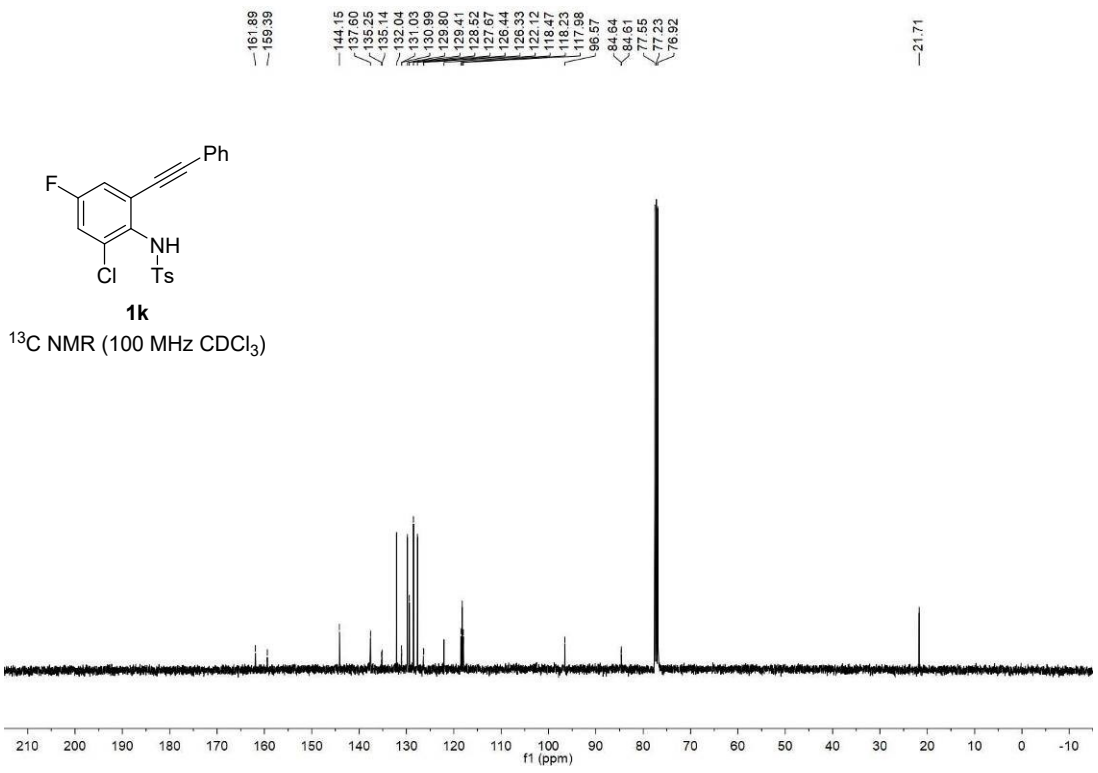

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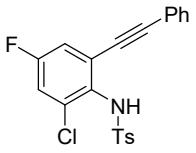
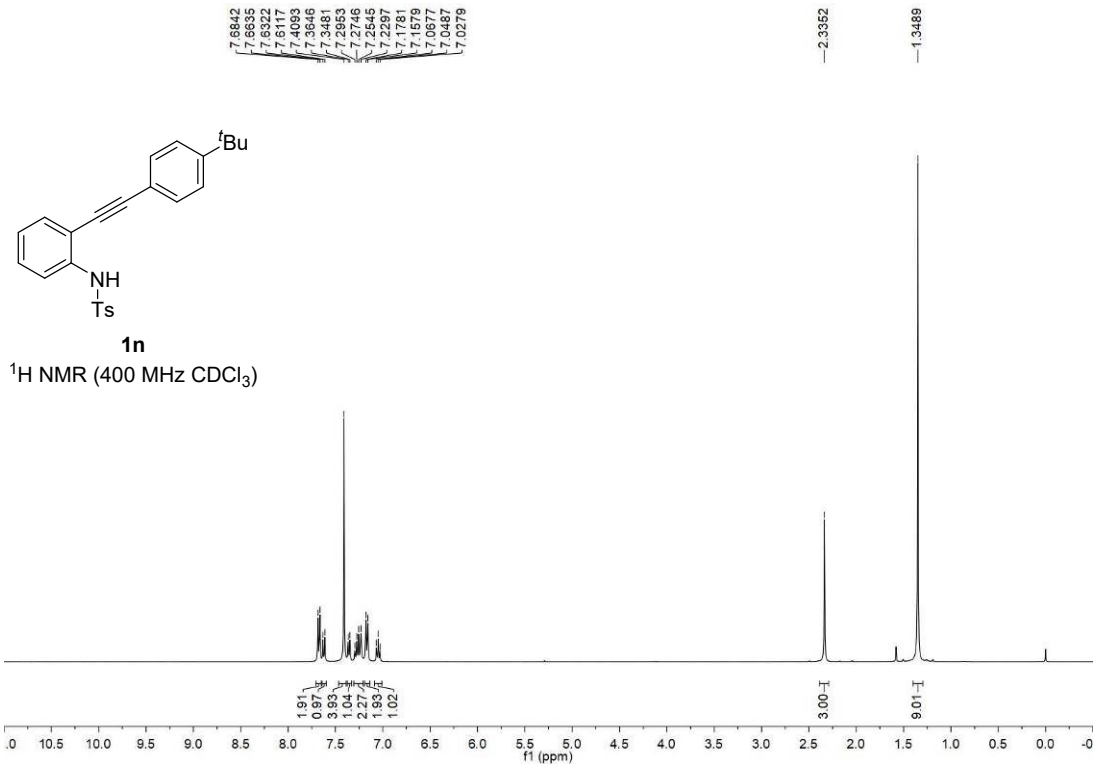
^{13}C NMR (100 MHz $CDCl_3$)



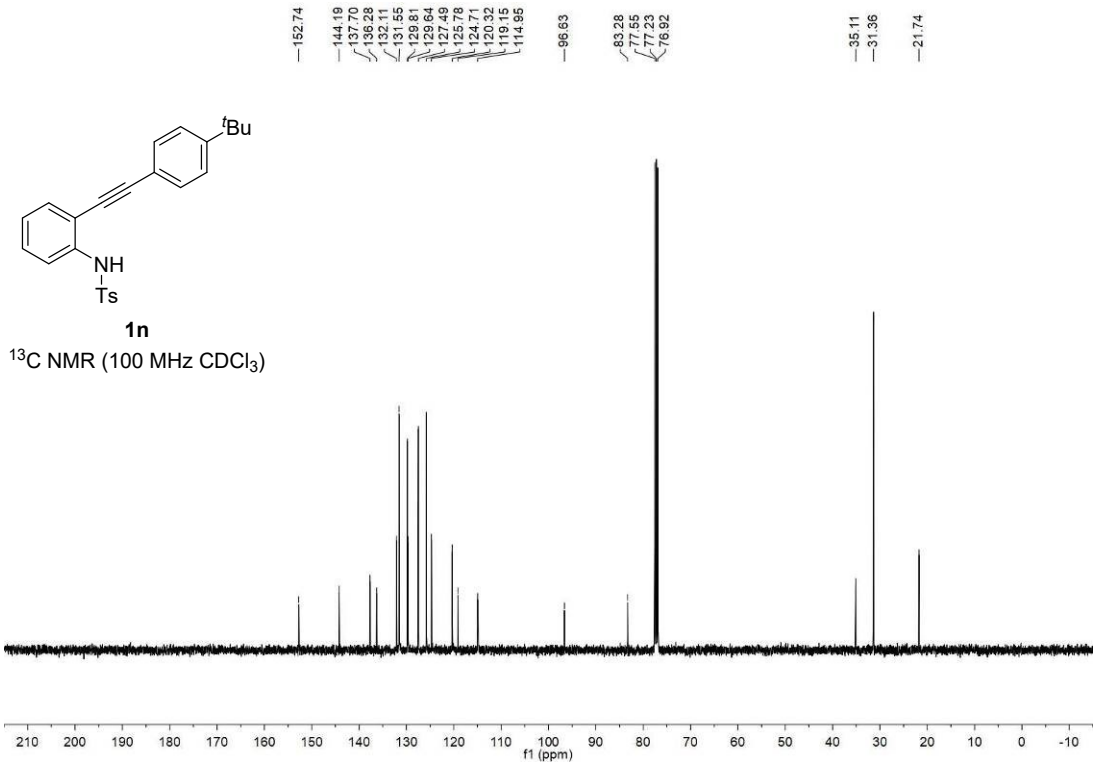
1k

^{19}F NMR (376 MHz $CDCl_3$))



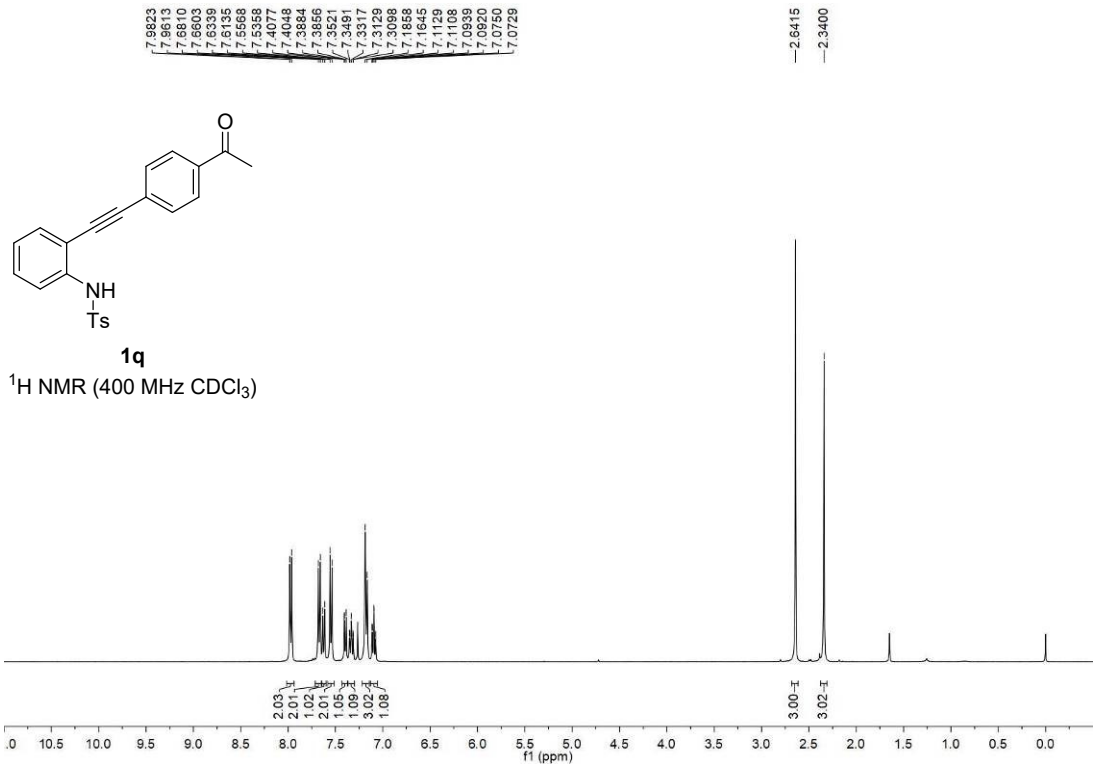
1n

^{1}H NMR (400 MHz $CDCl_3$)



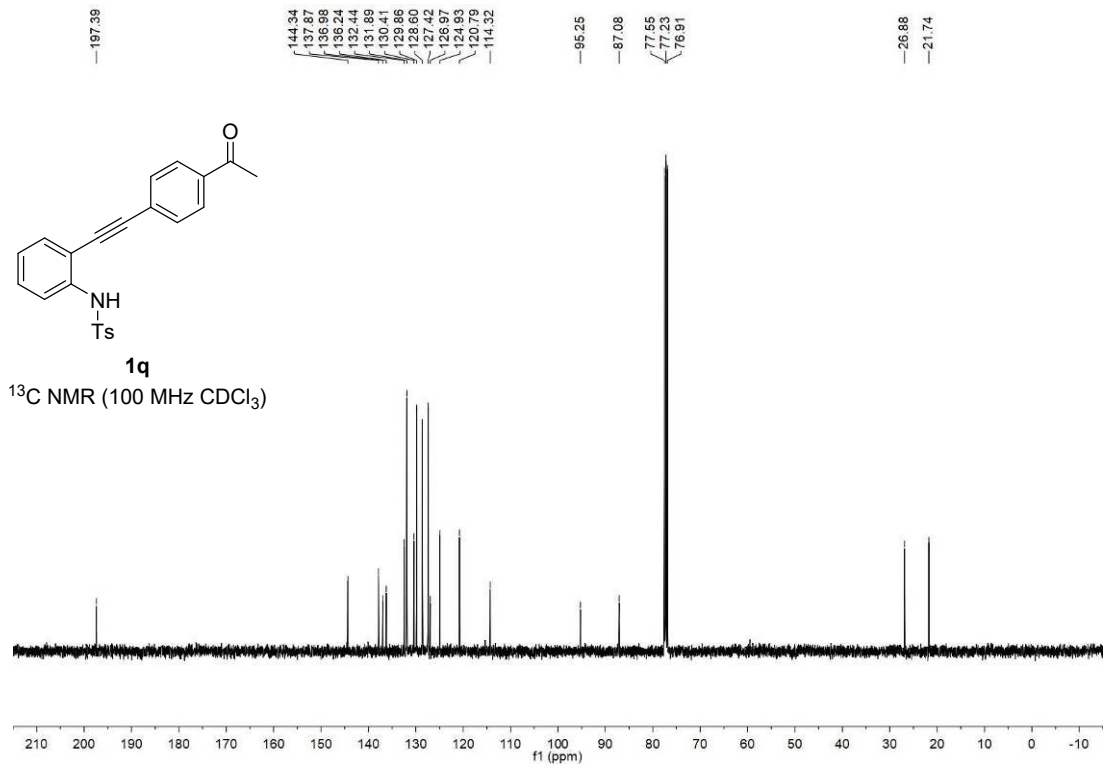
1n

^{13}C NMR (100 MHz $CDCl_3$)



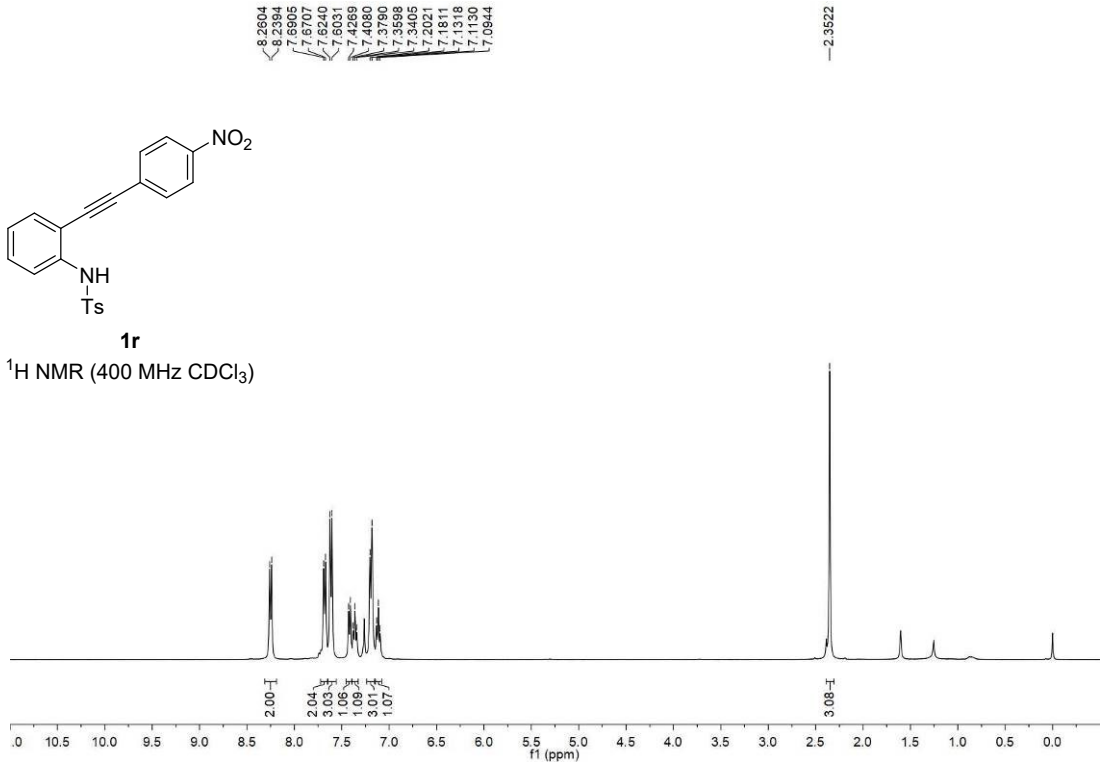
1q

^{1}H NMR (400 MHz $CDCl_3$)



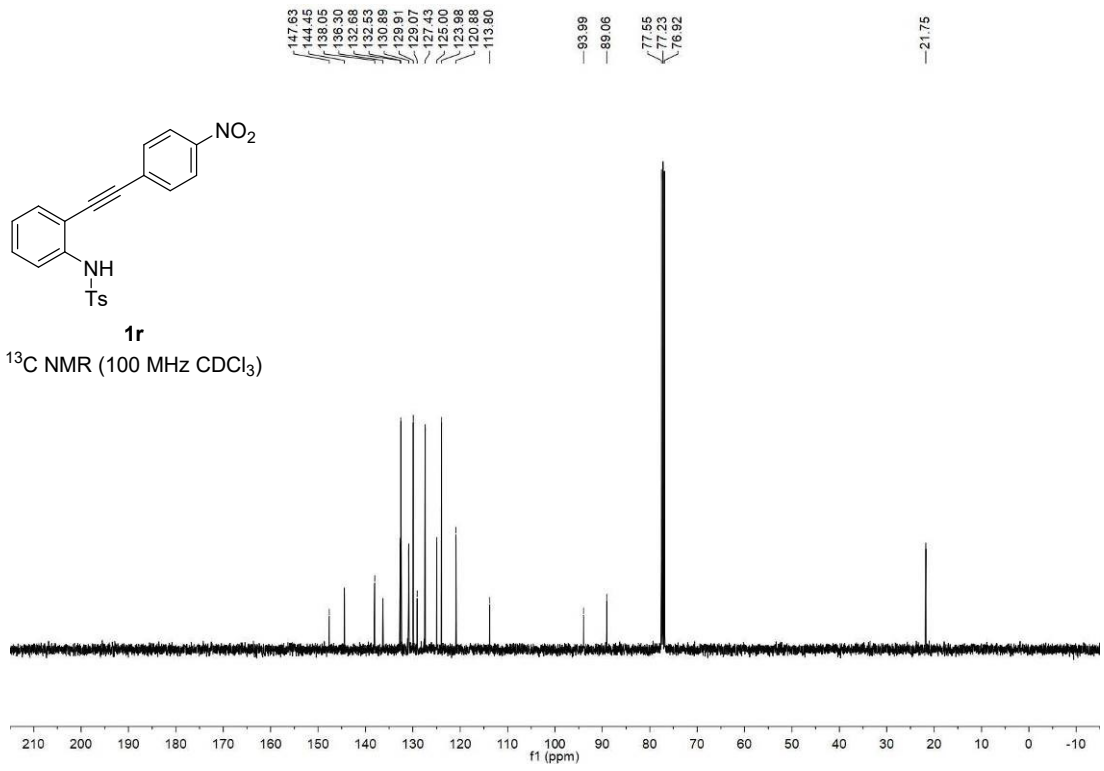
1q

^{13}C NMR (100 MHz $CDCl_3$)



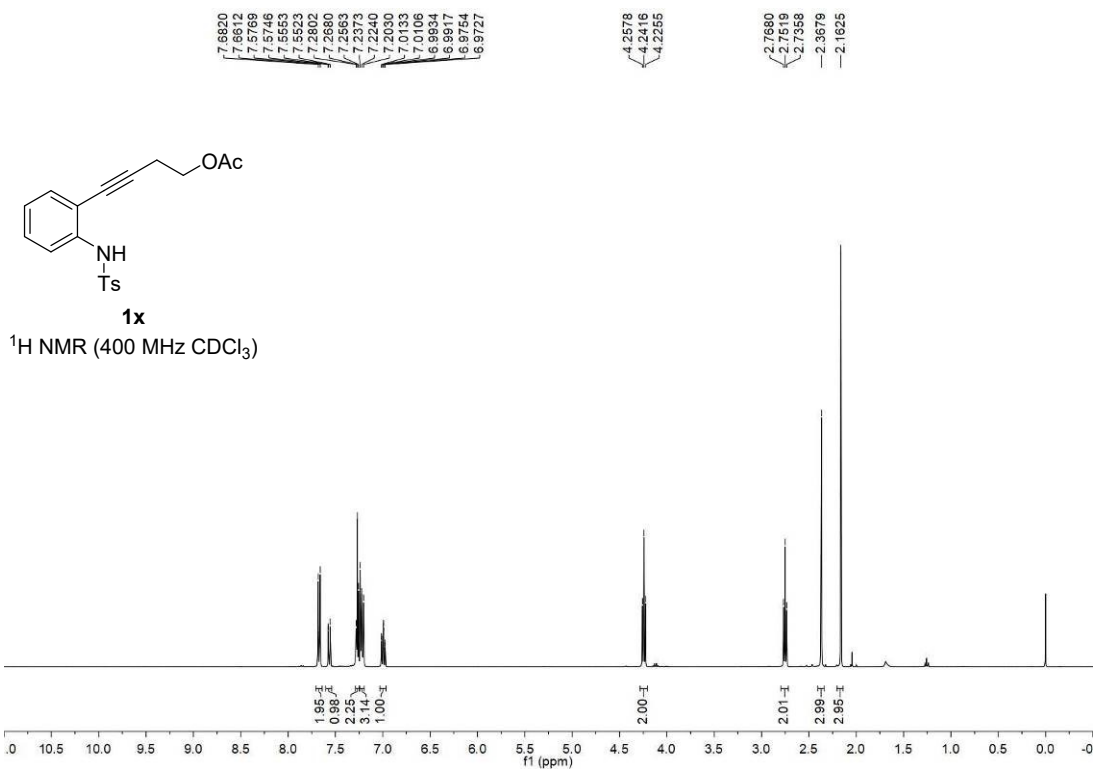
1r

^{1}H NMR (400 MHz $CDCl_3$)



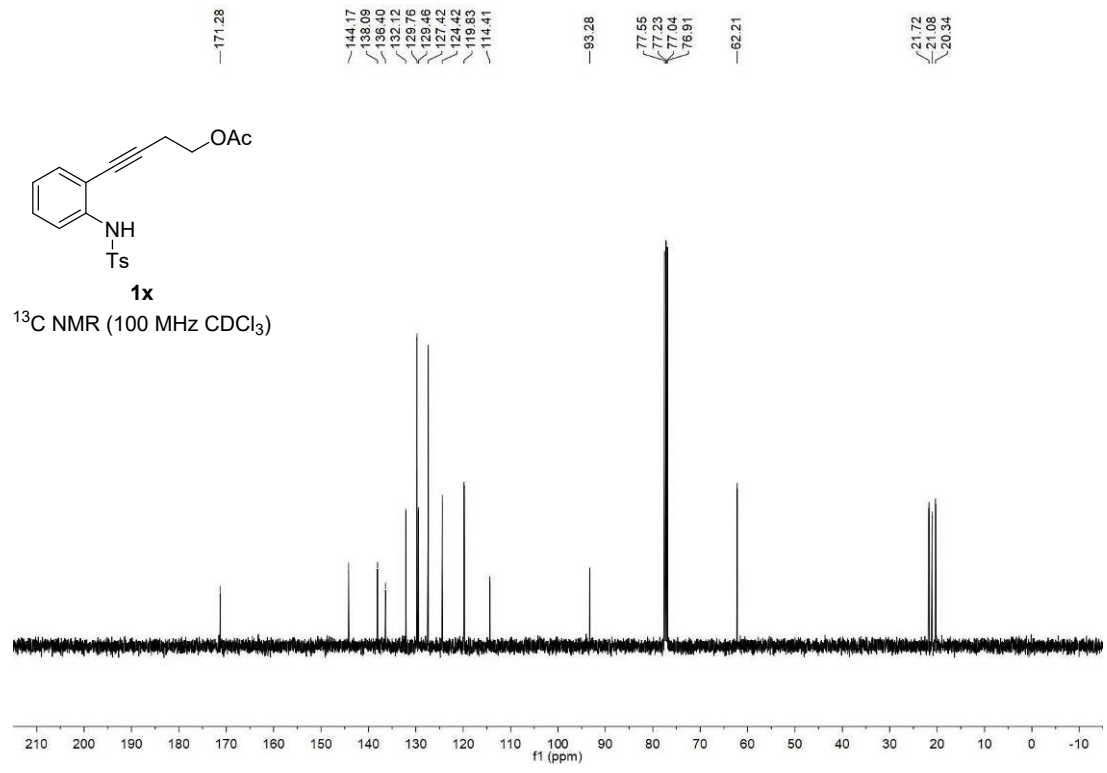
1r

^{13}C NMR (100 MHz $CDCl_3$)



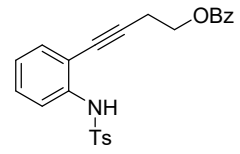
1x

^{1}H NMR (400 MHz $CDCl_3$)



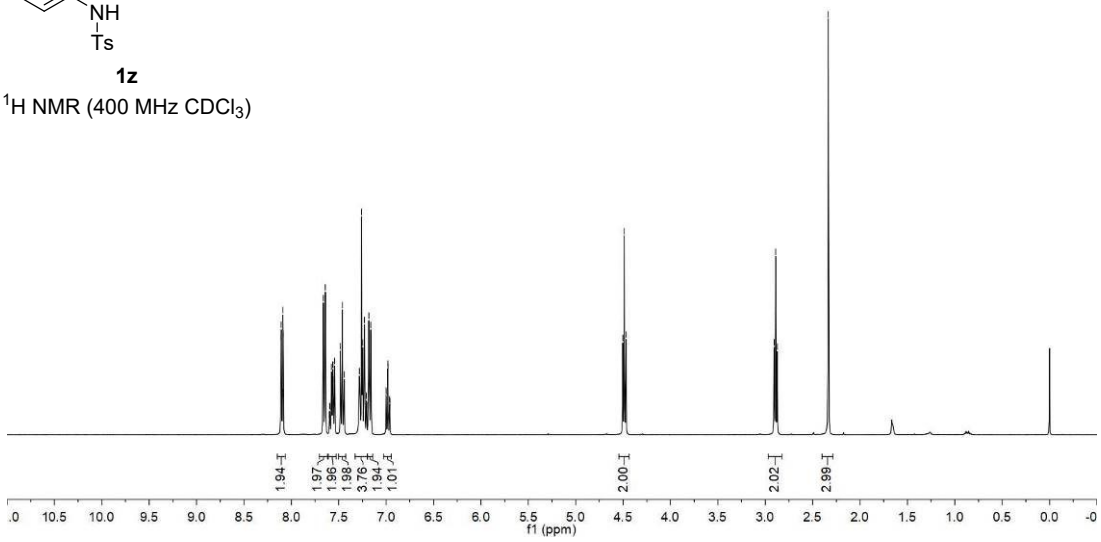
1x

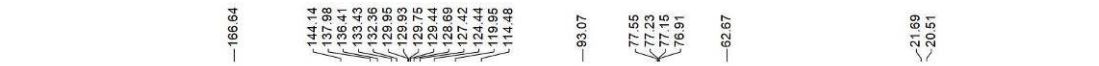
^{13}C NMR (100 MHz $CDCl_3$)

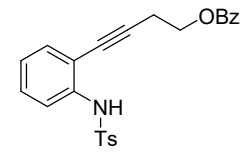


1z

^{1}H NMR (400 MHz $CDCl_3$)

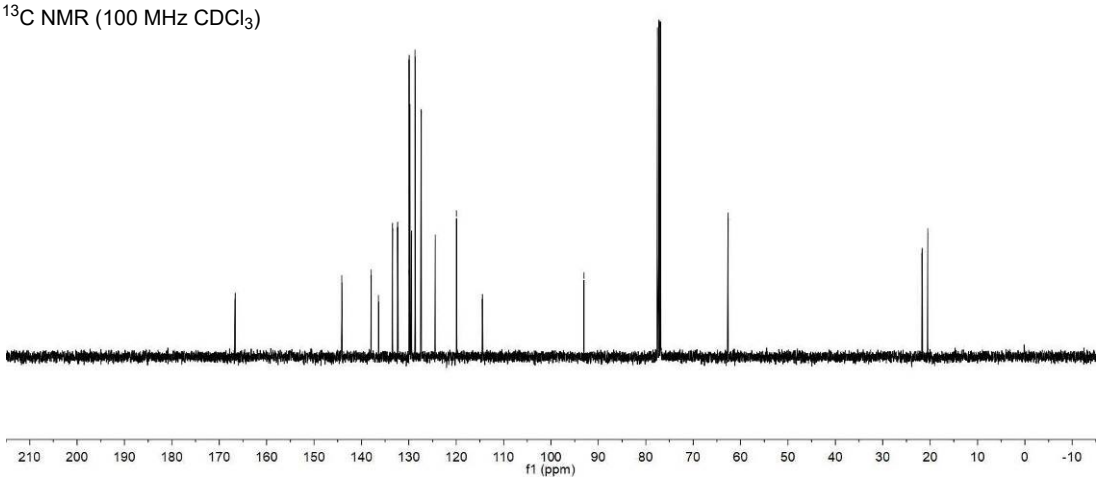


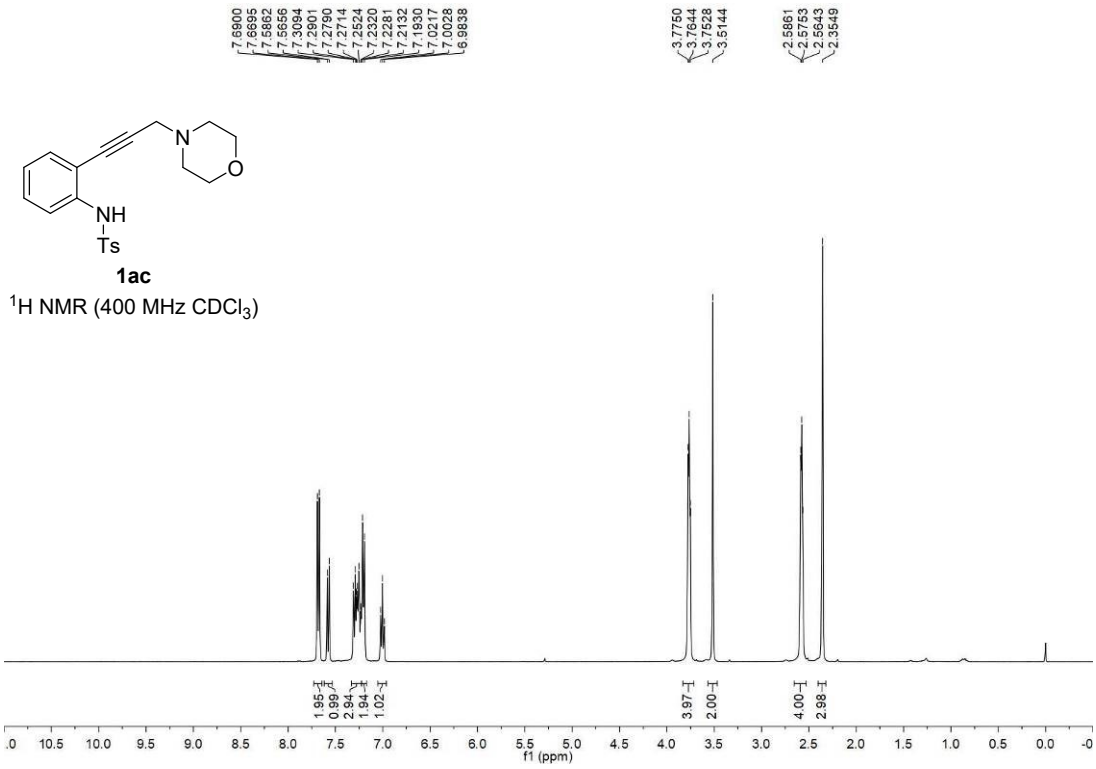




1z

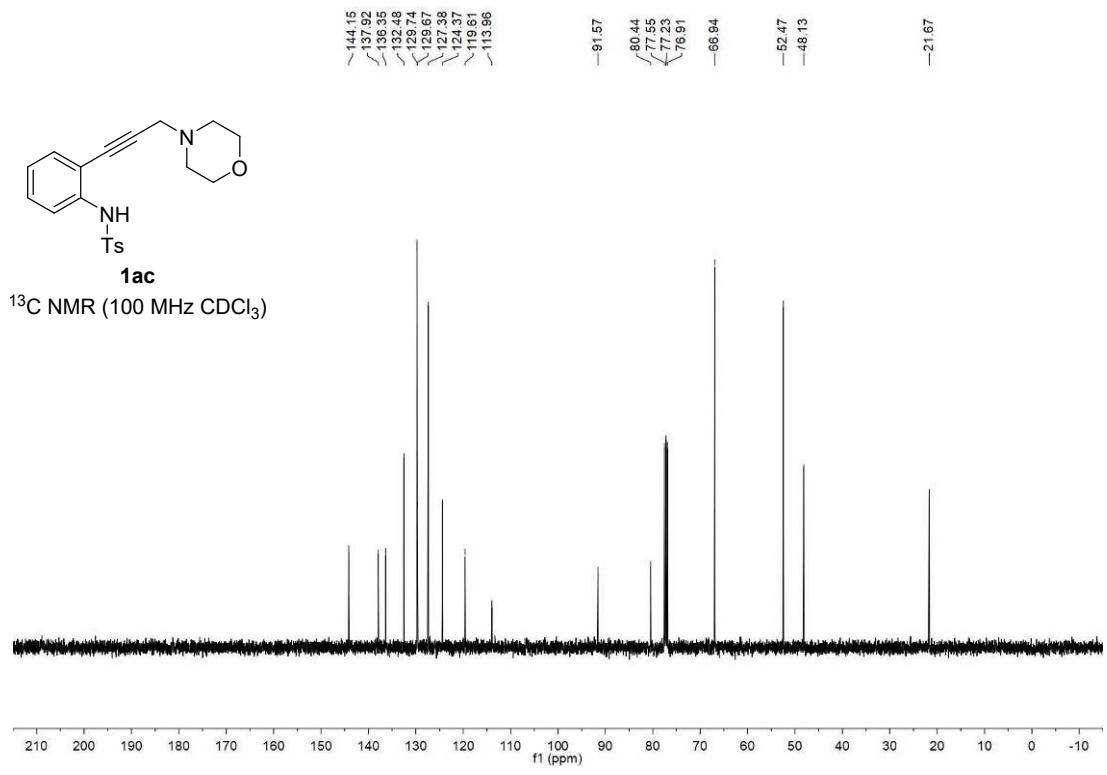
^{13}C NMR (100 MHz $CDCl_3$)





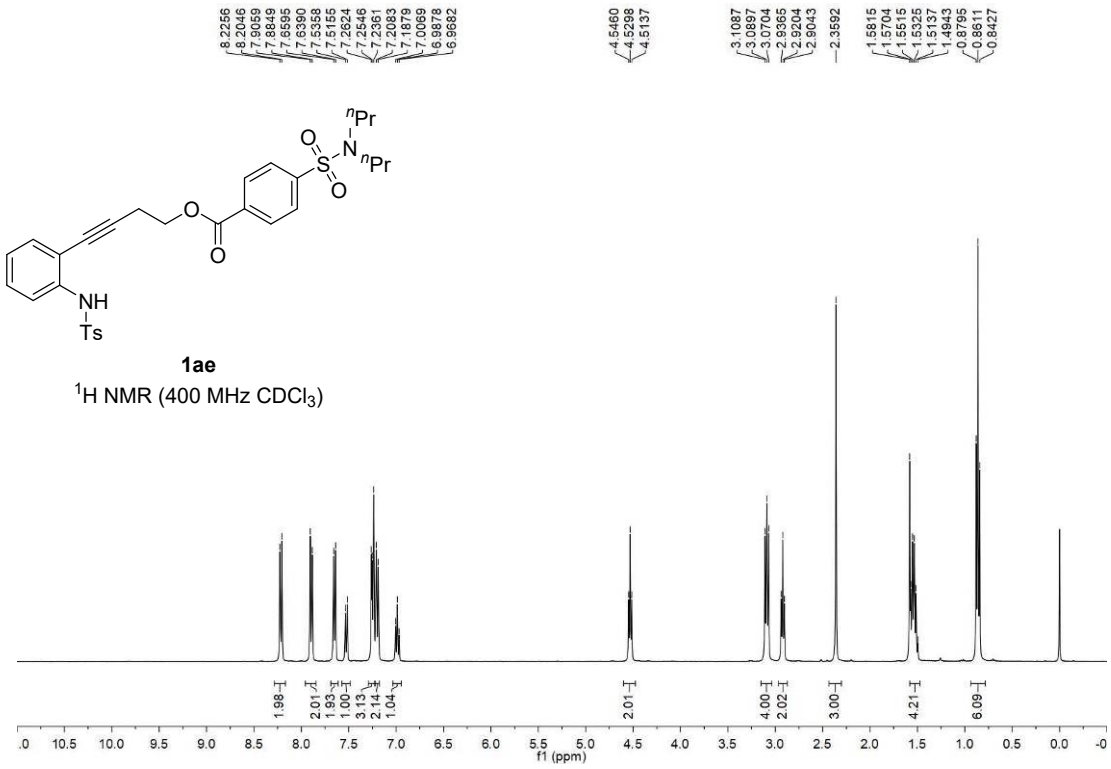
1ac

^{1}H NMR (400 MHz $CDCl_3$)



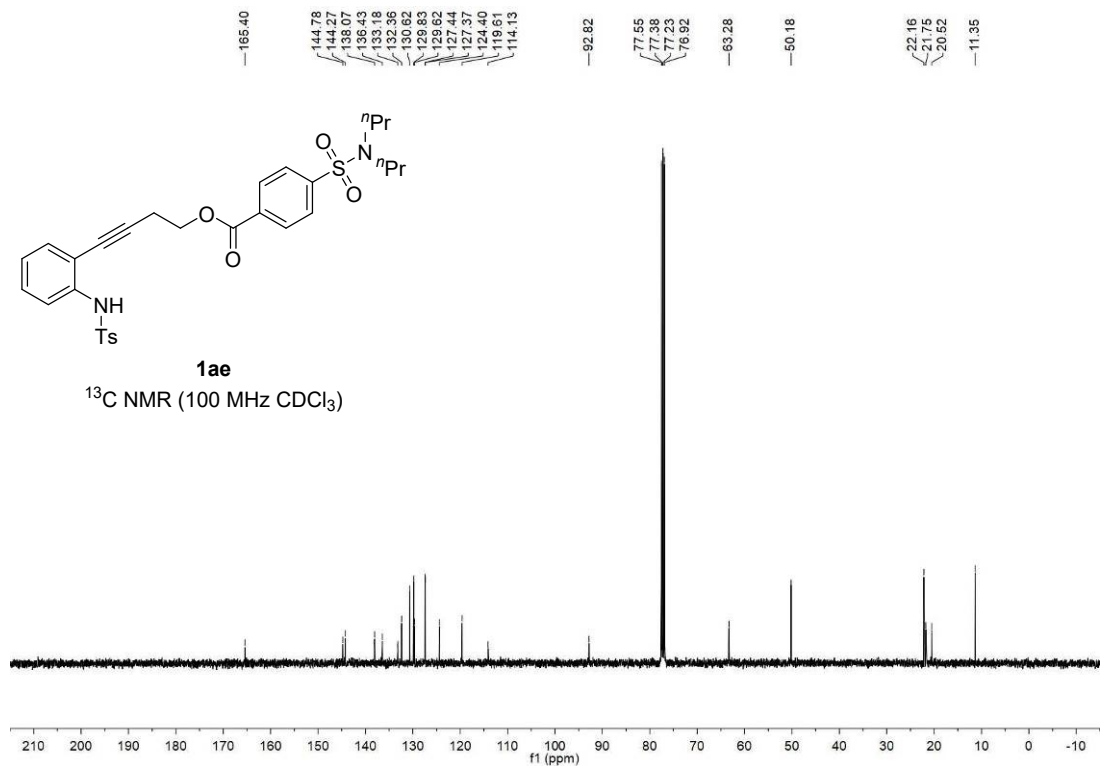
1ac

^{13}C NMR (100 MHz $CDCl_3$)



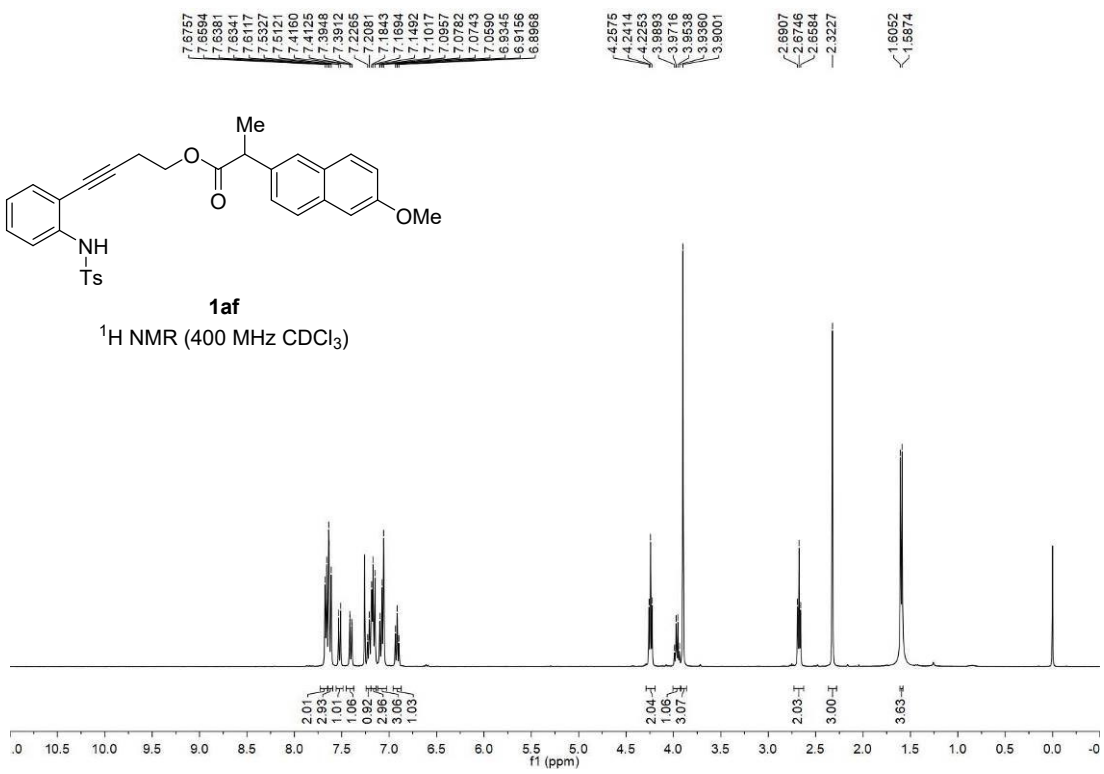
1ae

^{1}H NMR (400 MHz $CDCl_3$)



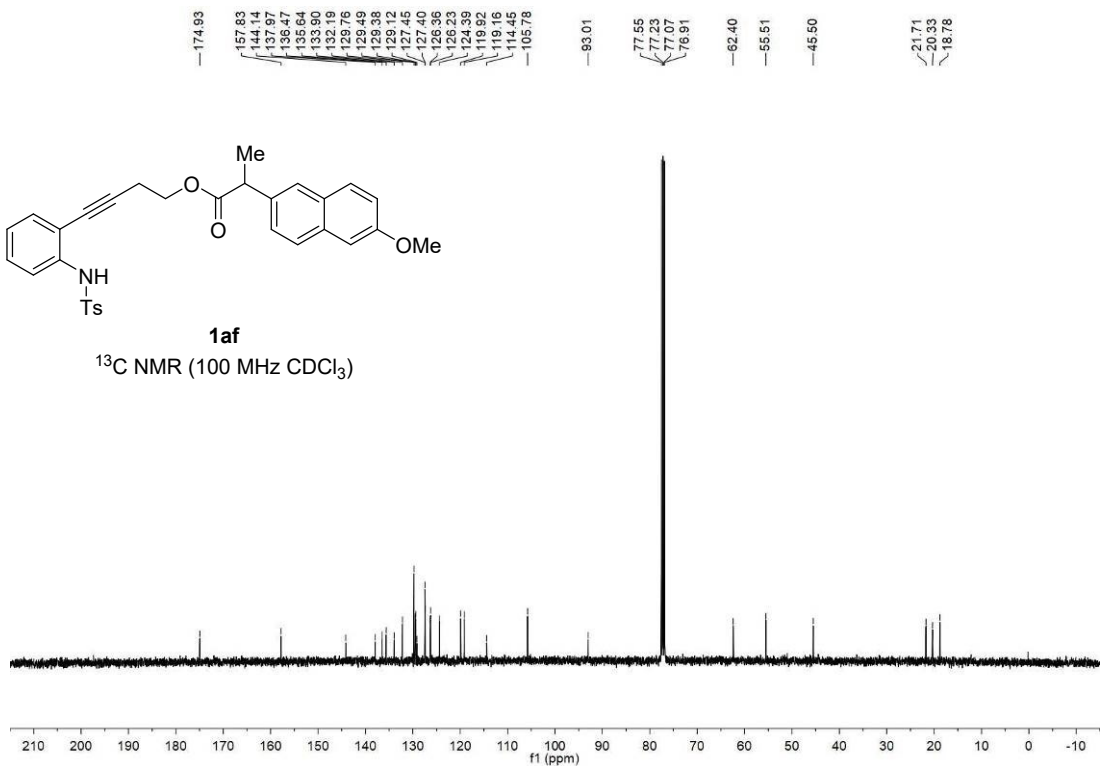
1ae

^{13}C NMR (100 MHz $CDCl_3$)



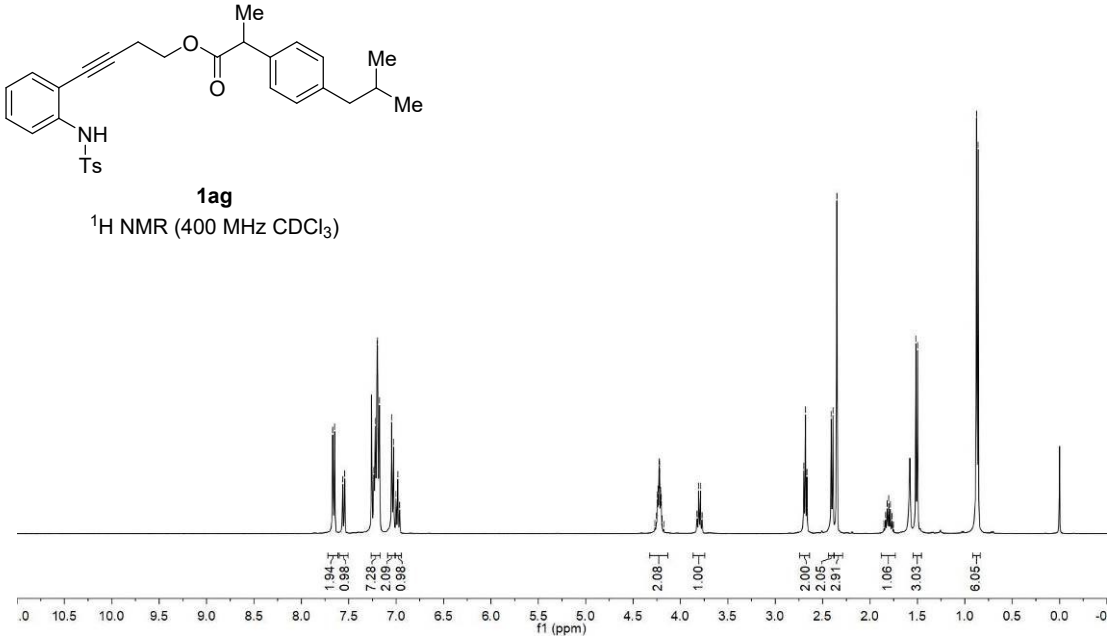
1af

^{1}H NMR (400 MHz $CDCl_3$)



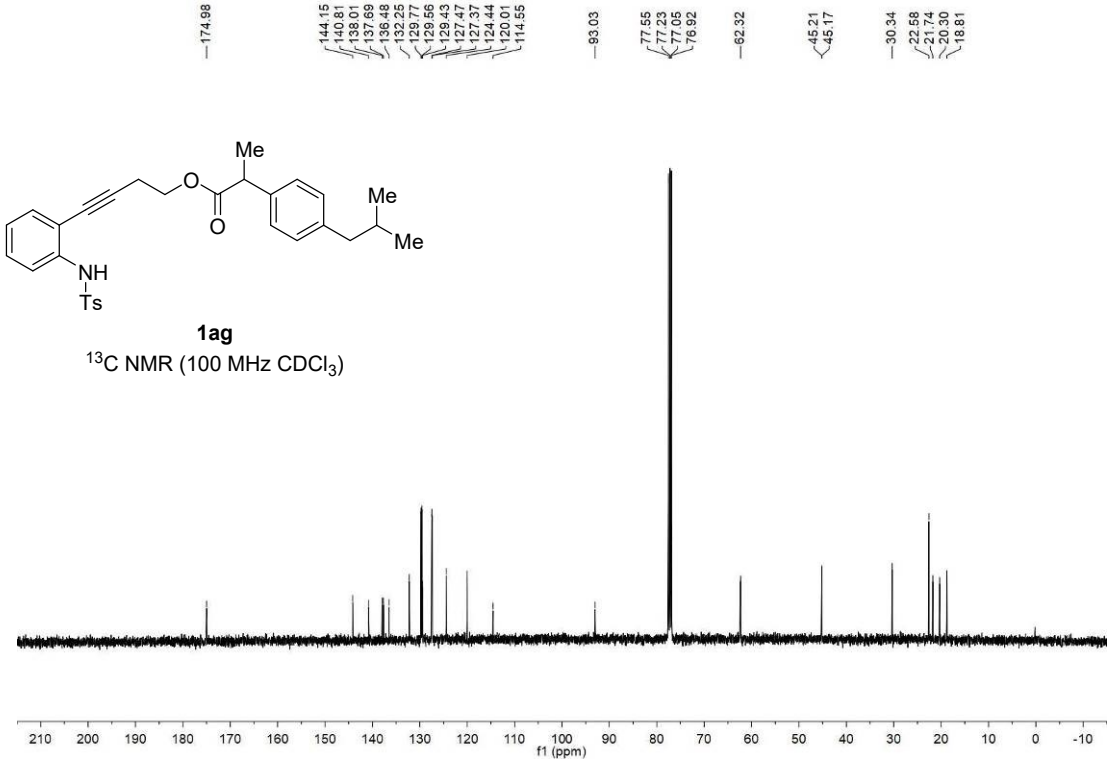
1af

^{13}C NMR (100 MHz $CDCl_3$)



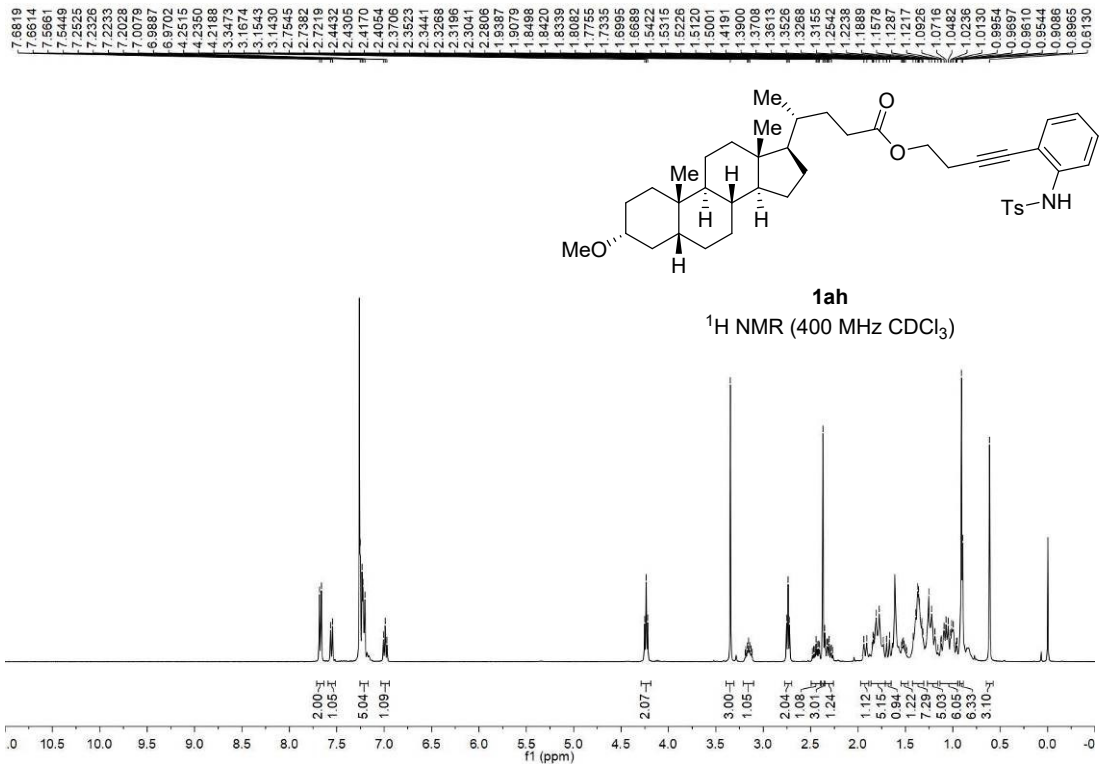
1ag

^{1}H NMR (400 MHz $CDCl_3$)



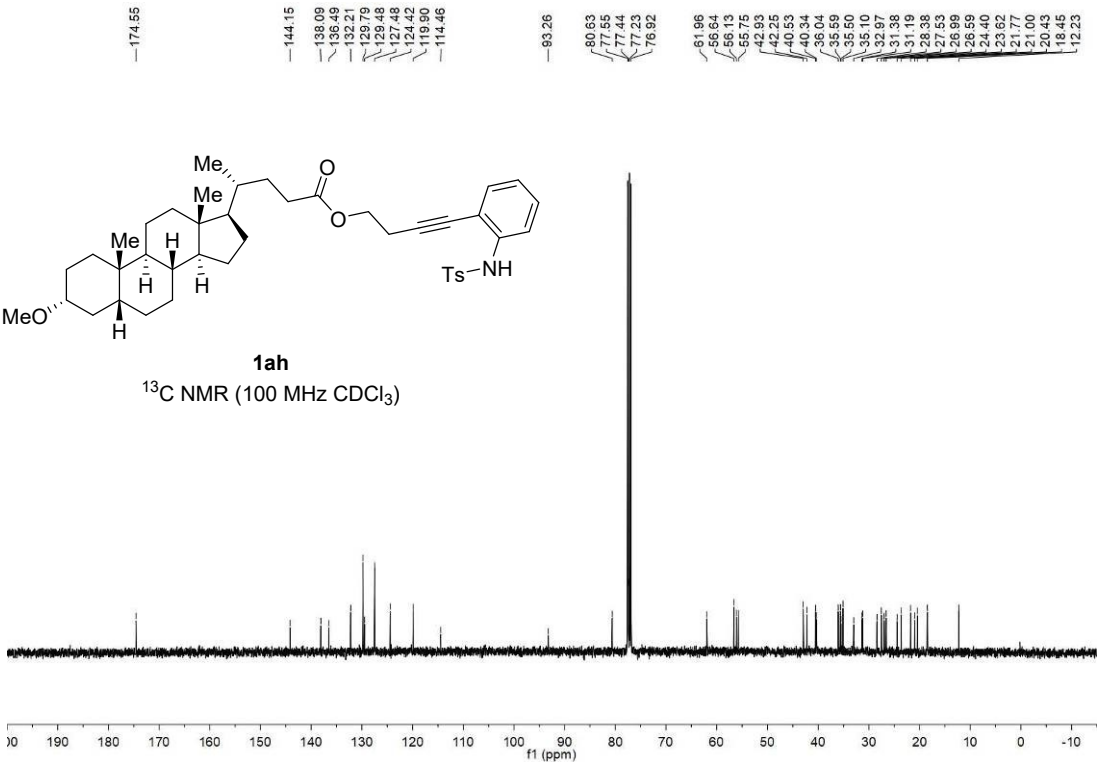
1ag

^{13}C NMR (100 MHz $CDCl_3$)



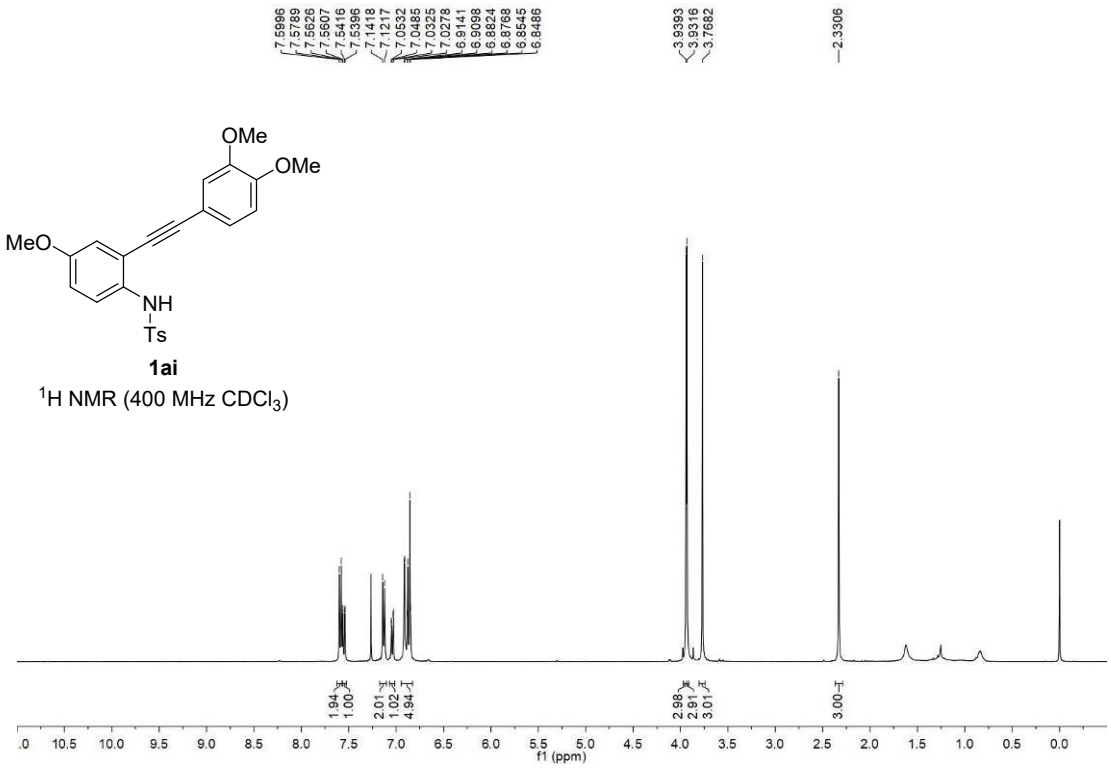
1ah

^{1}H NMR (400 MHz $CDCl_3$)



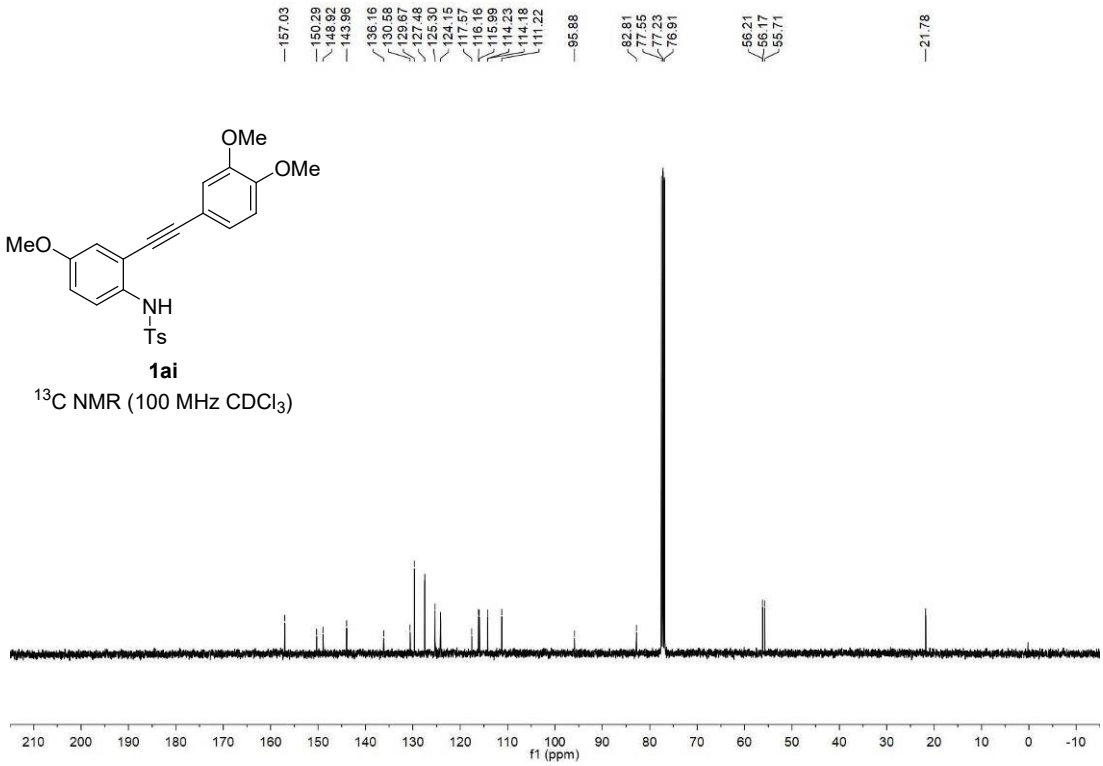
1ah

^{13}C NMR (100 MHz $CDCl_3$)



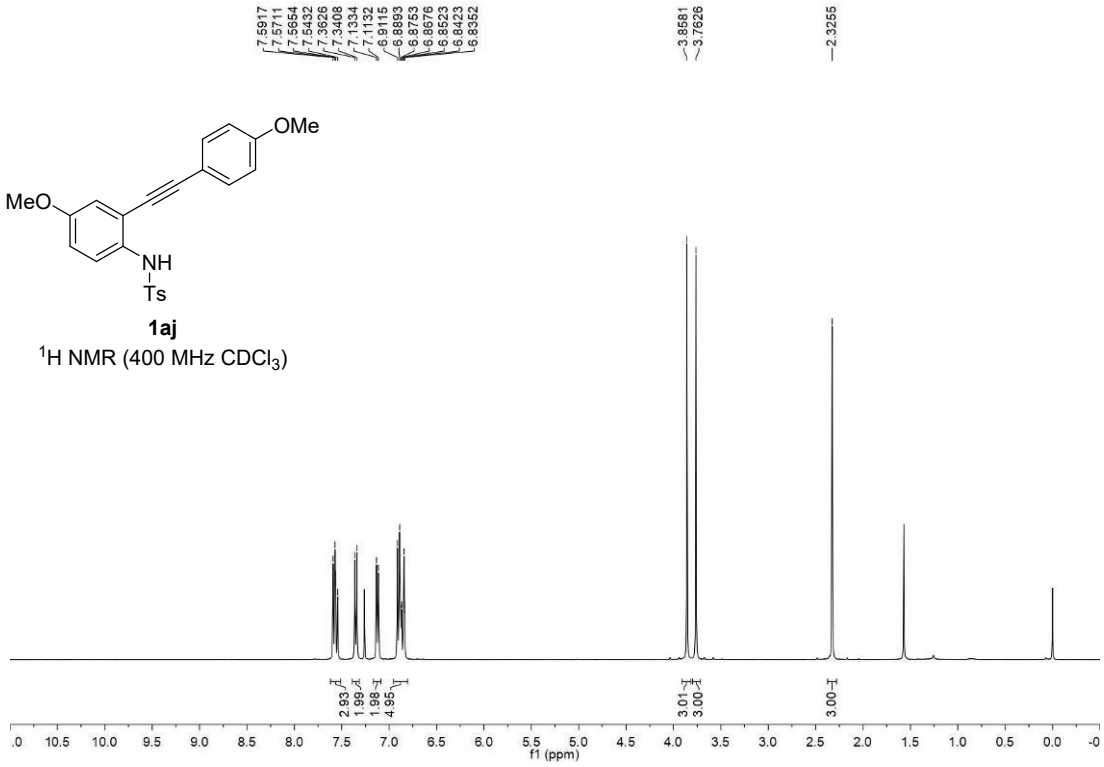
1ai

^{1}H NMR (400 MHz $CDCl_3$)



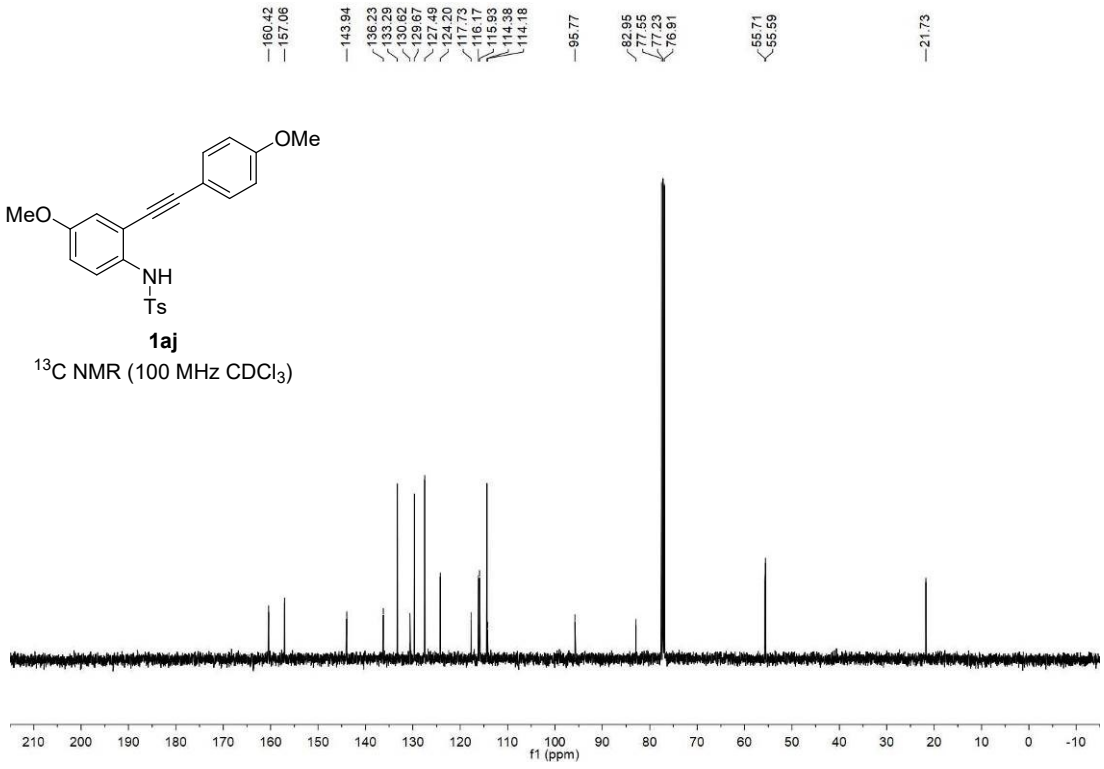
1ai

^{13}C NMR (100 MHz $CDCl_3$)



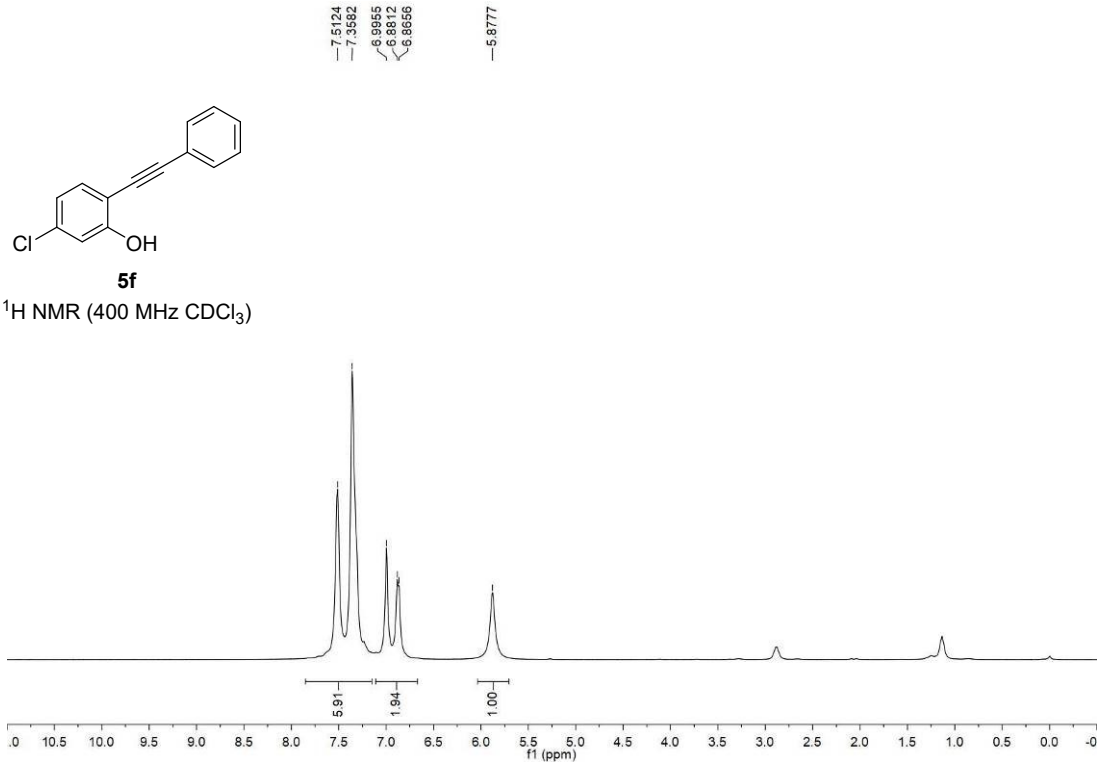
1aj

^{1}H NMR (400 MHz $CDCl_3$)



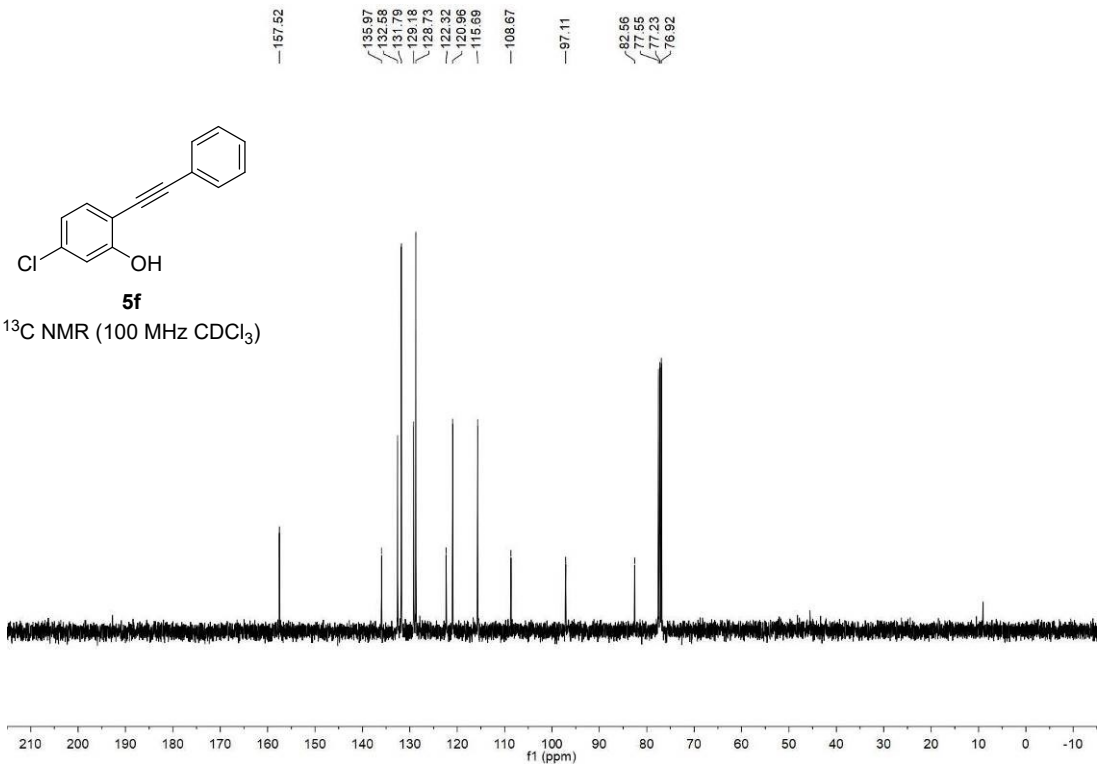
1aj

^{13}C NMR (100 MHz $CDCl_3$)



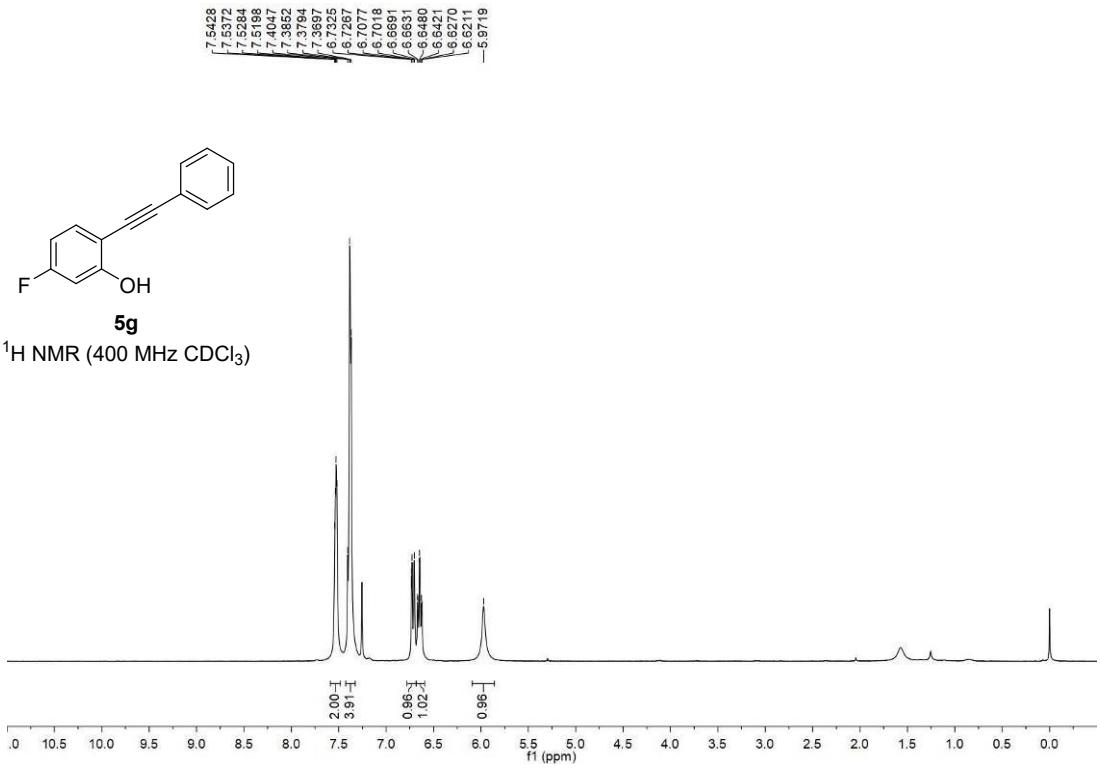
5f

^{1}H NMR (400 MHz $CDCl_3$)



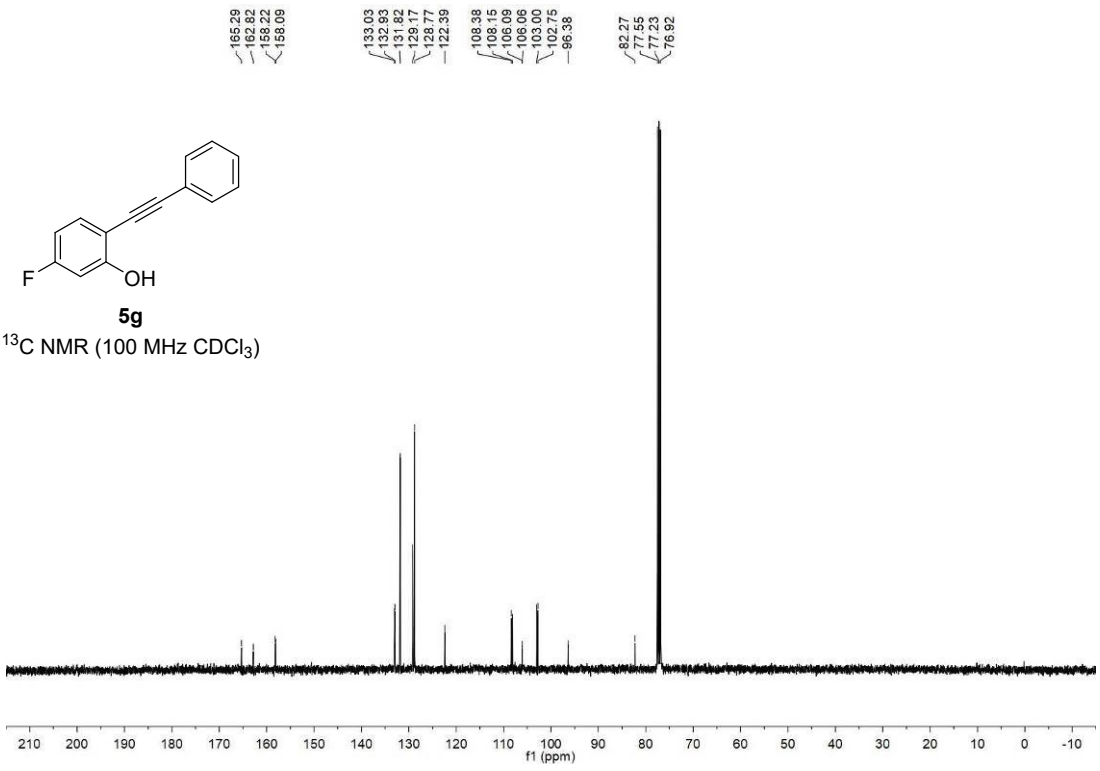
5f

^{13}C NMR (100 MHz $CDCl_3$)



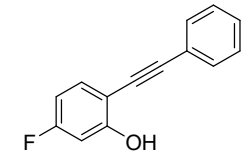
5g

^{1}H NMR (400 MHz $CDCl_3$)



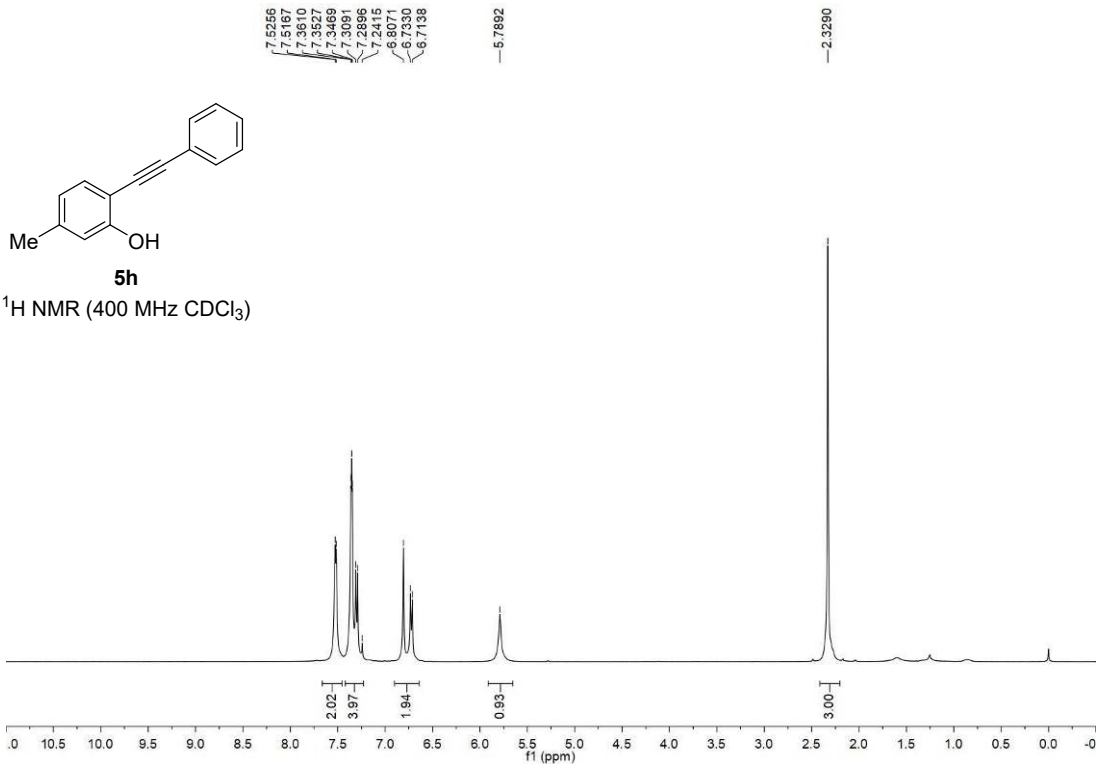
5g

^{13}C NMR (100 MHz $CDCl_3$)



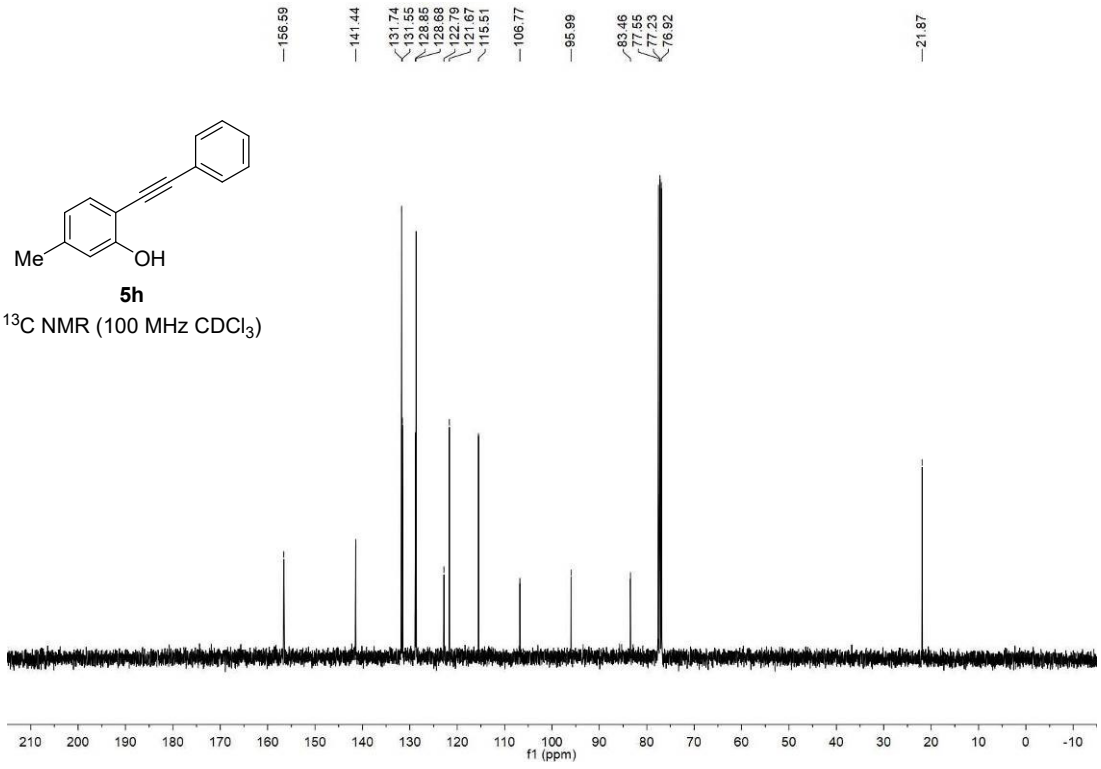
5g

^{19}F NMR (376 MHz $CDCl_3$))



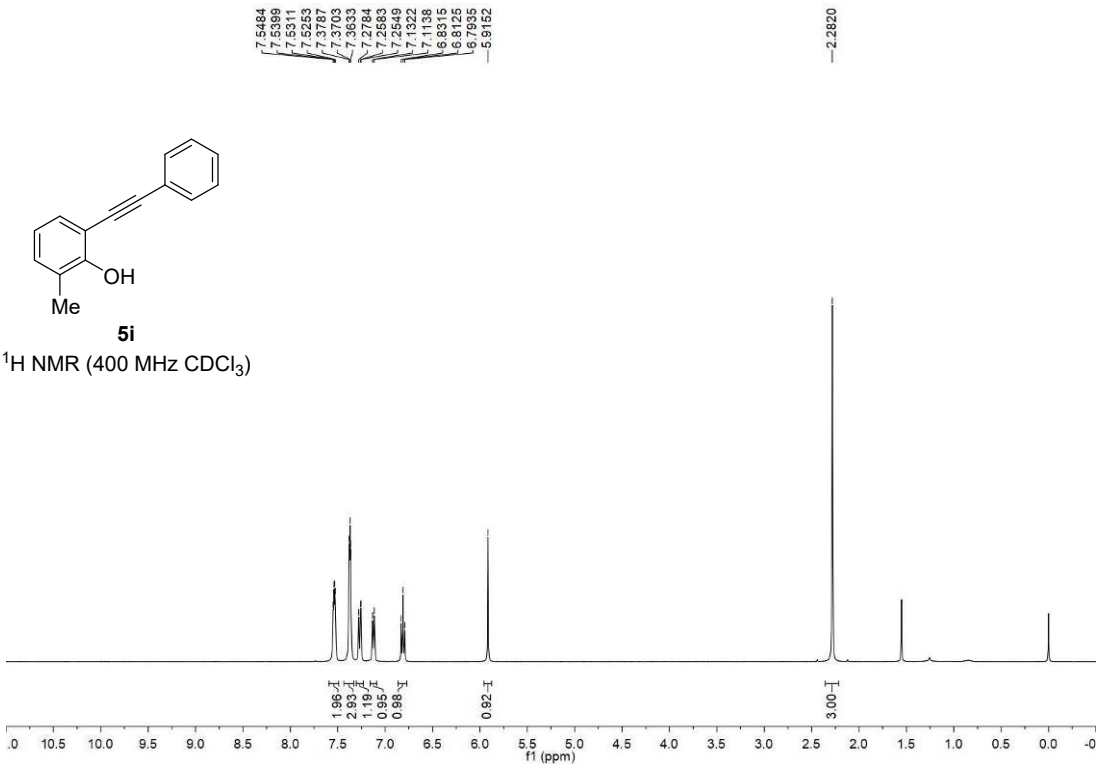
5h

^{1}H NMR (400 MHz $CDCl_3$)



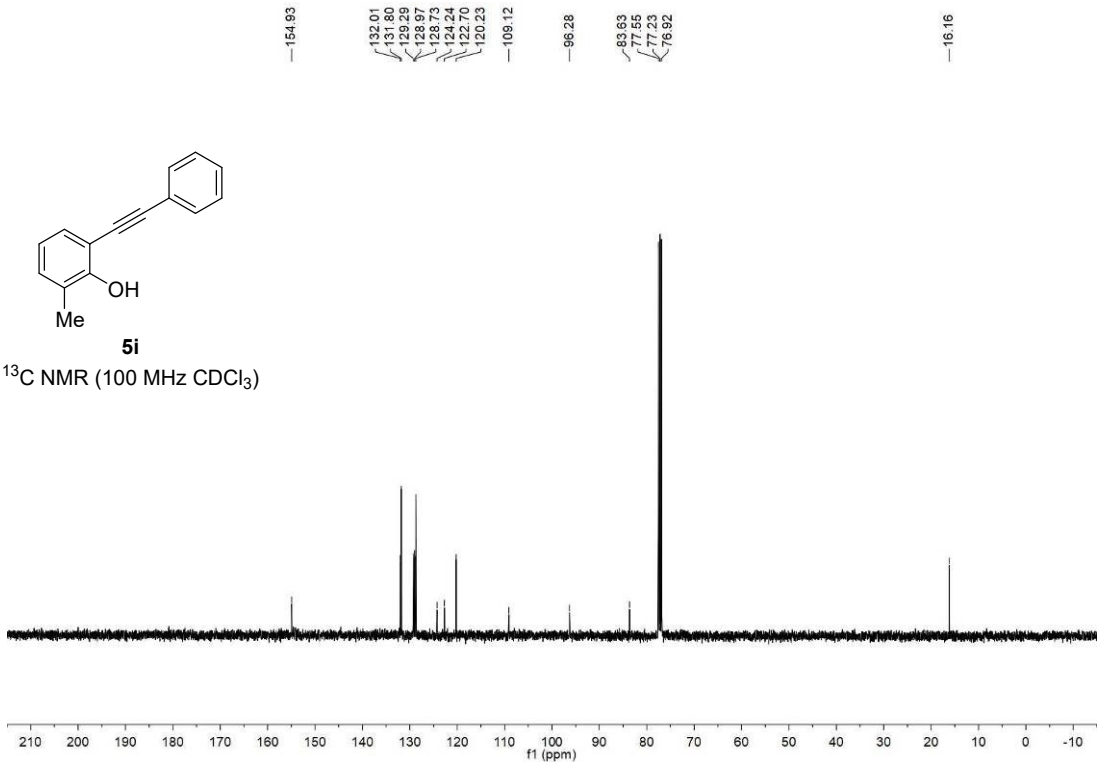
5h

^{13}C NMR (100 MHz $CDCl_3$)



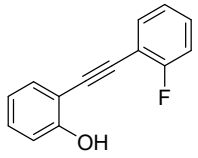
5i

^{1}H NMR (400 MHz $CDCl_3$)



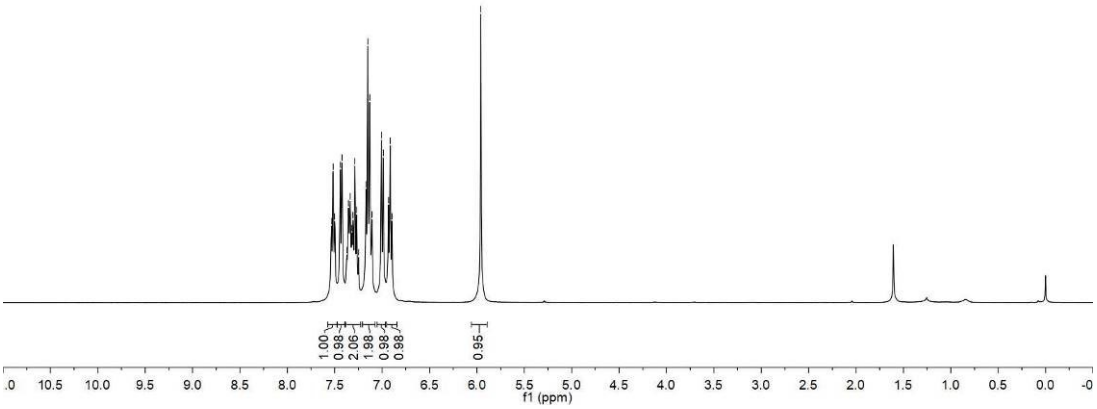
5i

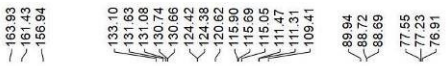
^{13}C NMR (100 MHz $CDCl_3$)

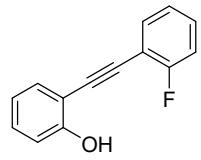


5j

^{1}H NMR (400 MHz $CDCl_3$)

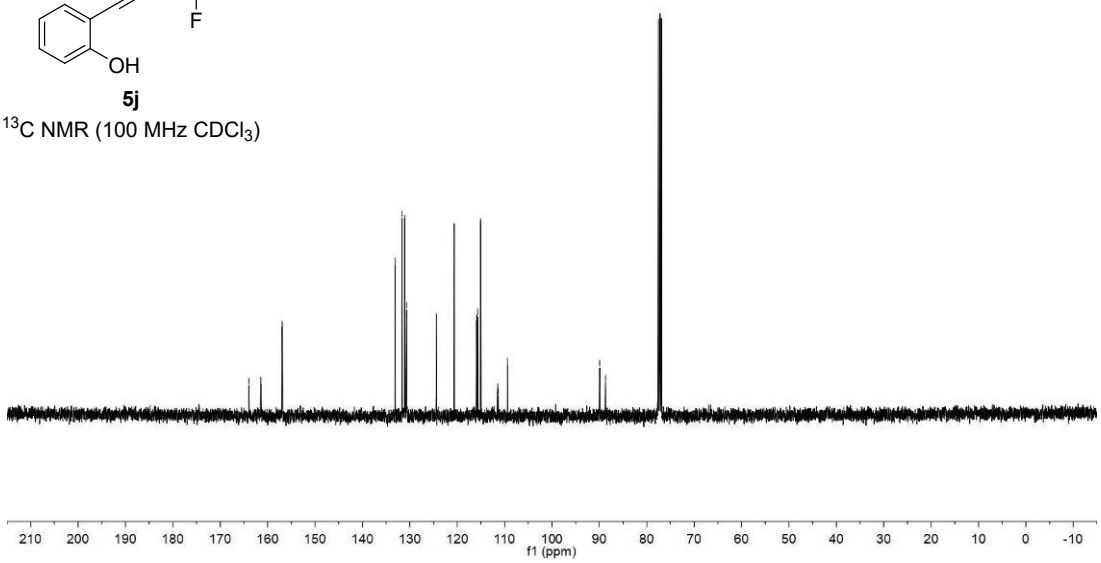


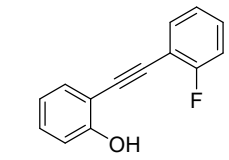




5j

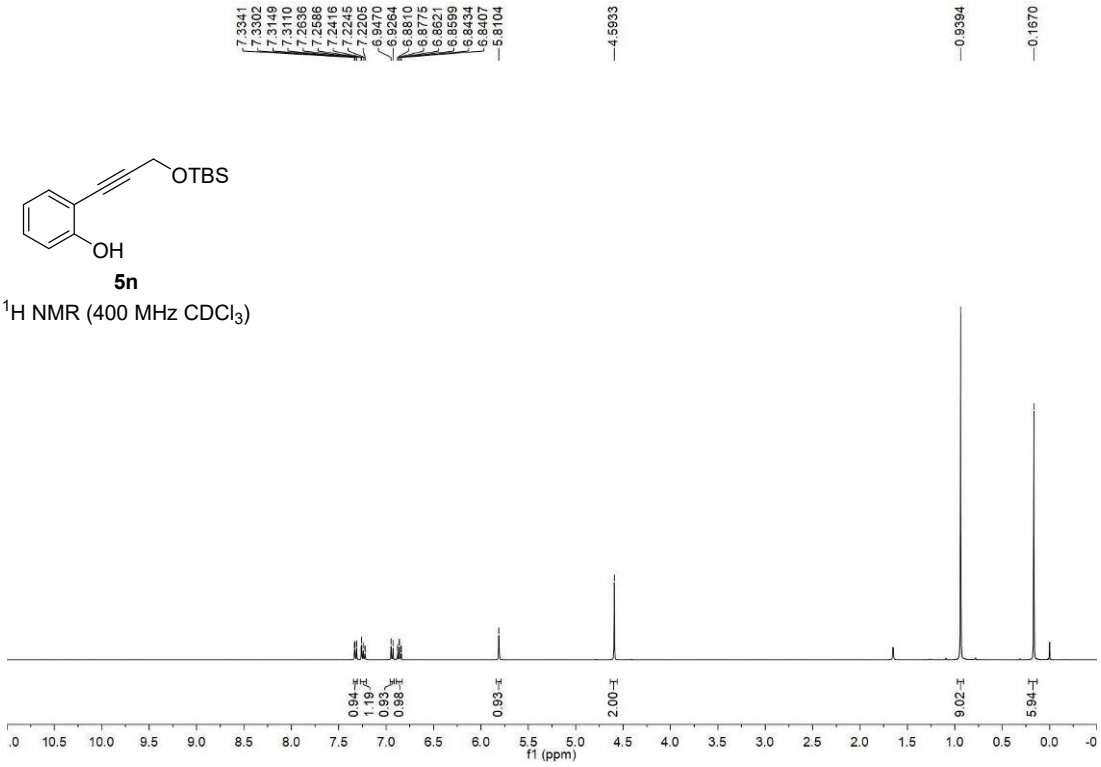
^{13}C NMR (100 MHz $CDCl_3$)





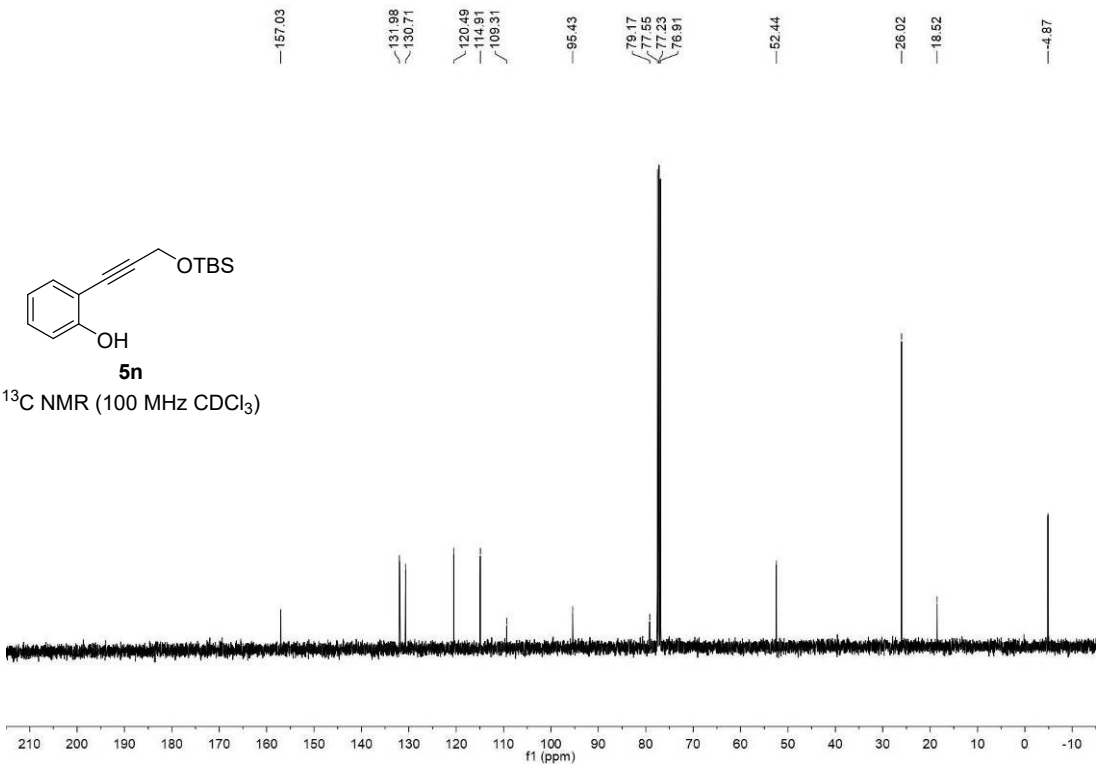
5j

^{19}F NMR (376 MHz $CDCl_3$))



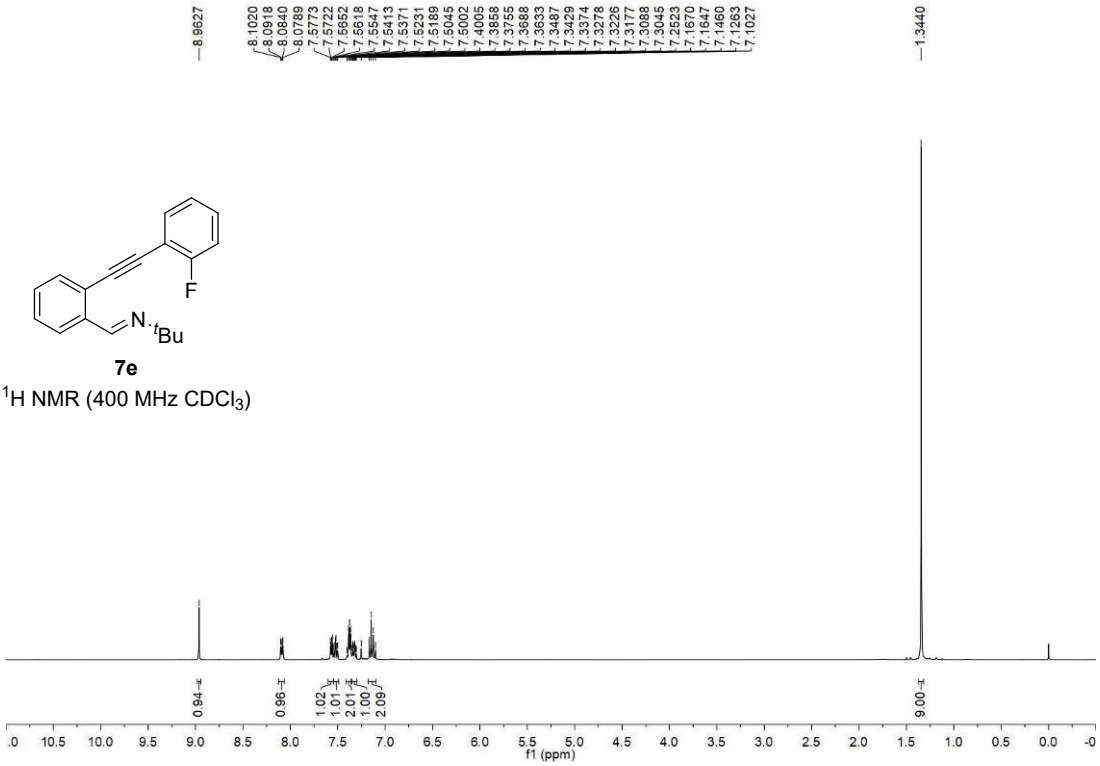
5n

^{1}H NMR (400 MHz $CDCl_3$)



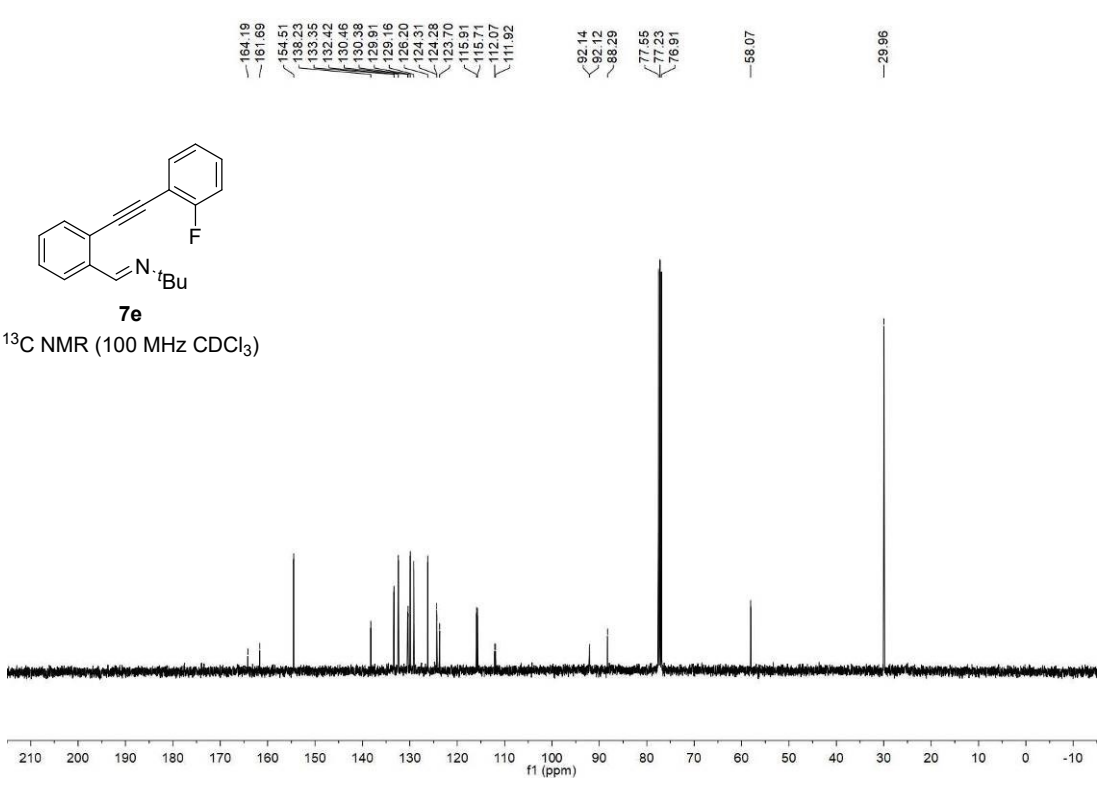
5n

^{13}C NMR (100 MHz $CDCl_3$)



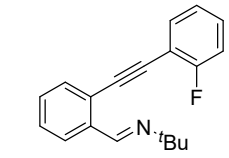
7e

^{1}H NMR (400 MHz $CDCl_3$)



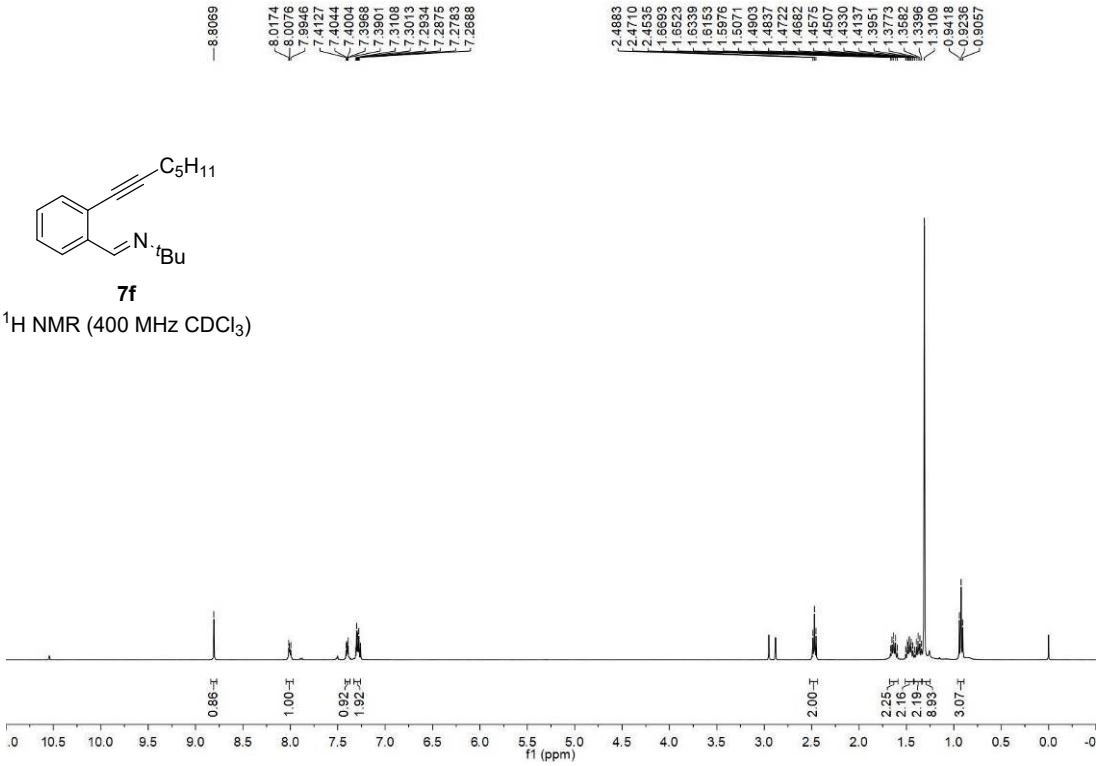
7e

^{13}C NMR (100 MHz $CDCl_3$)



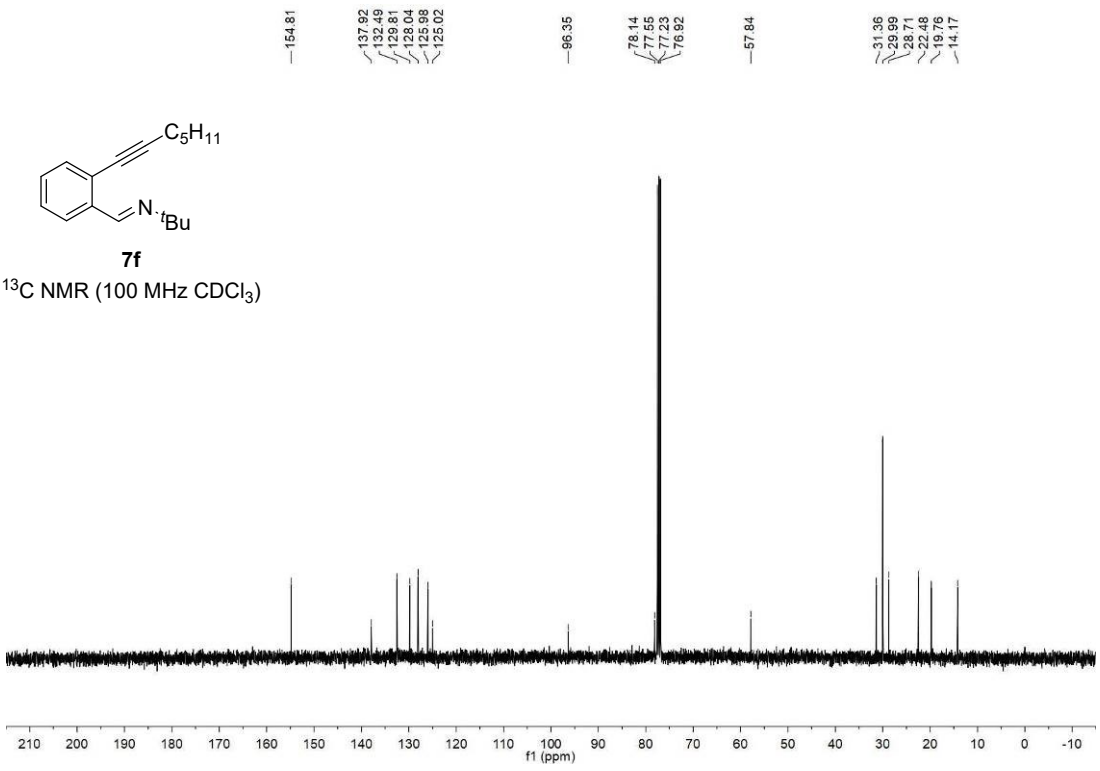
7e

^{19}F NMR (376 MHz $CDCl_3$))



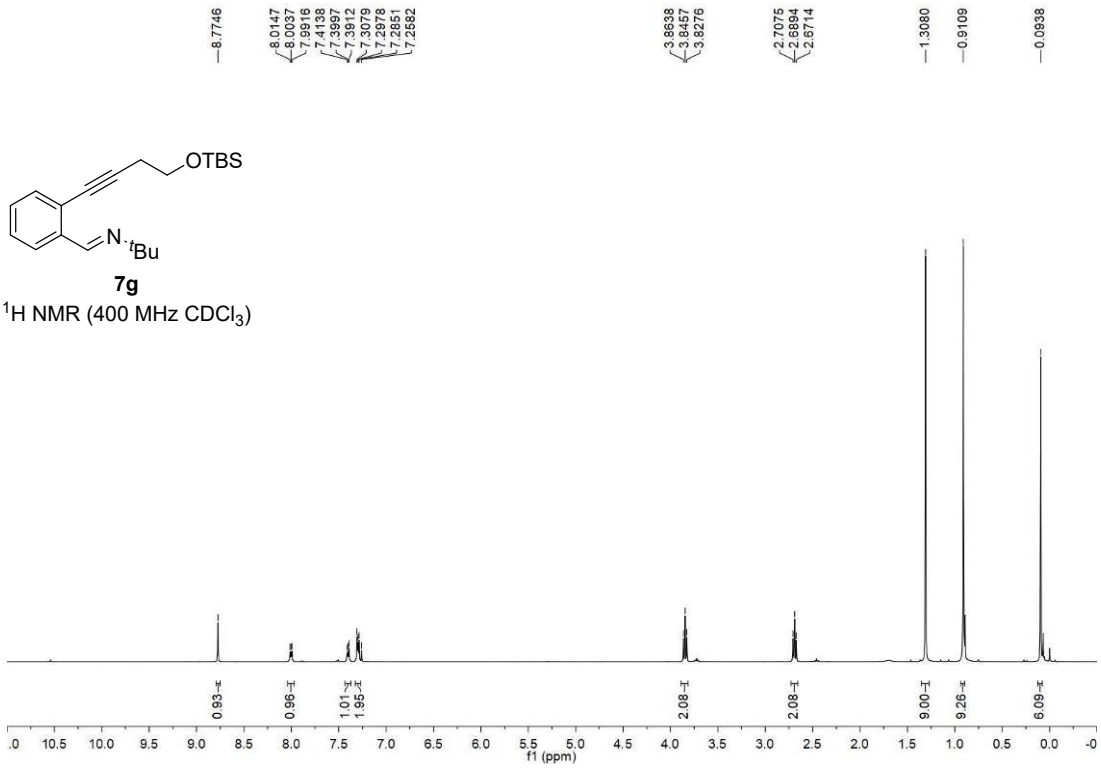
7f

^{1}H NMR (400 MHz $CDCl_3$)



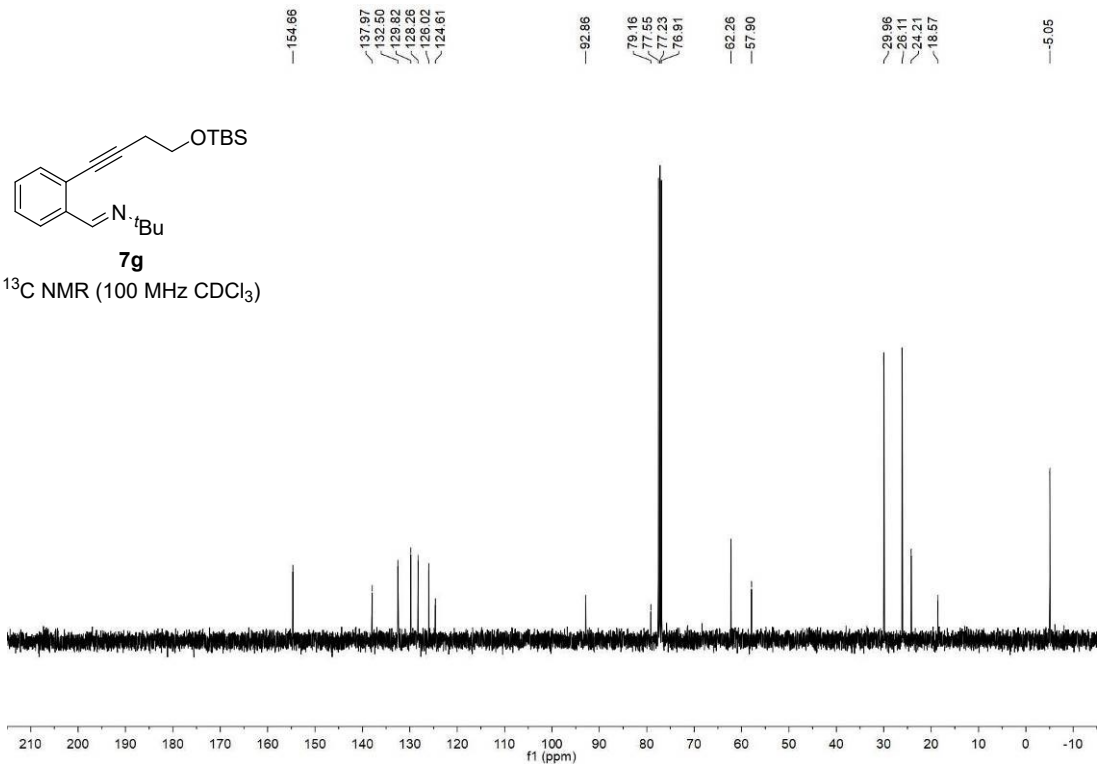
7f

^{13}C NMR (100 MHz $CDCl_3$)



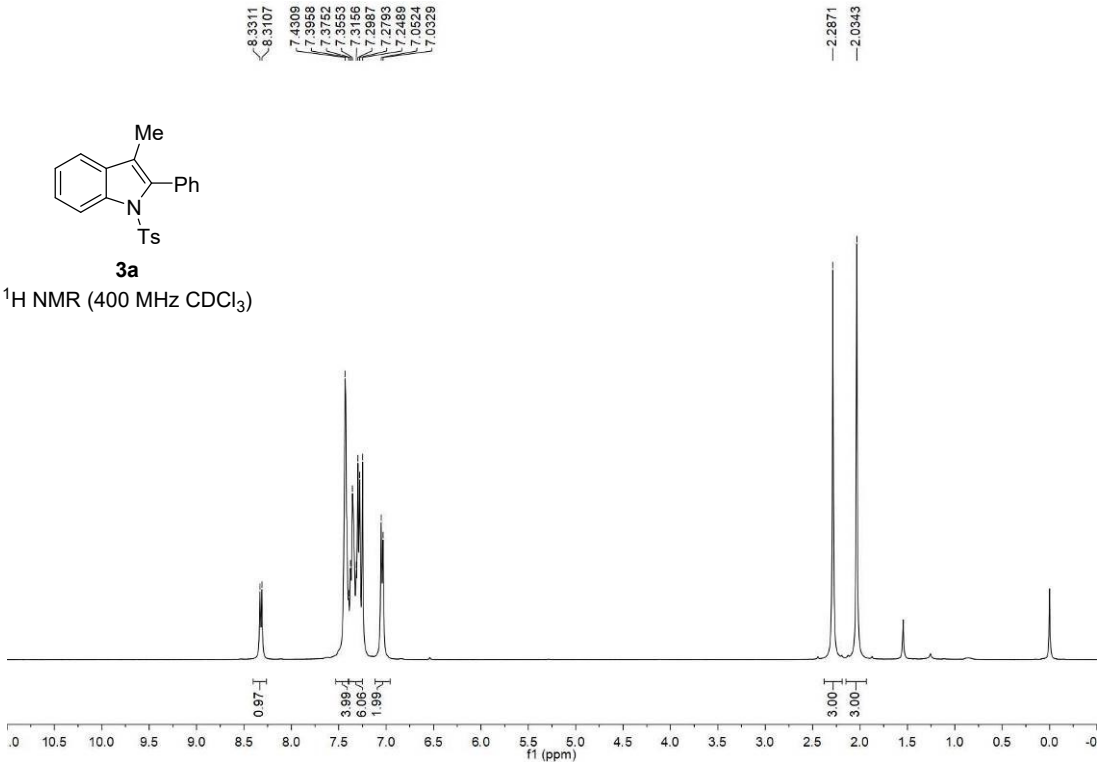
7g

^{1}H NMR (400 MHz $CDCl_3$)



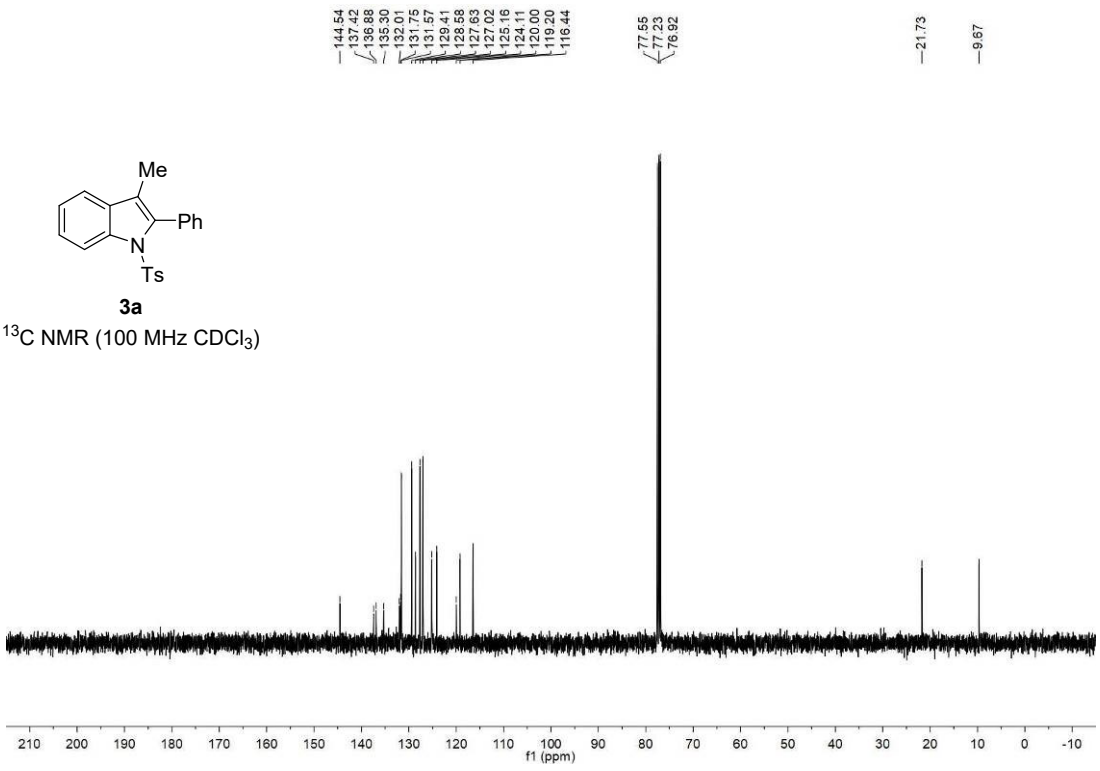
7g

^{13}C NMR (100 MHz $CDCl_3$)



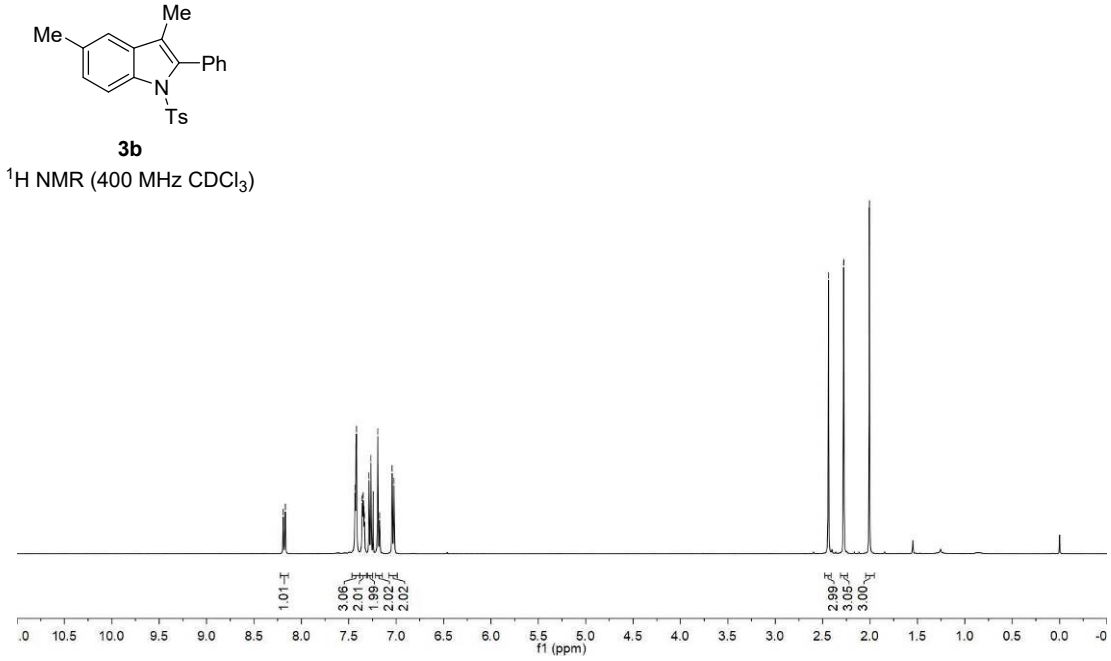
3a

^{1}H NMR (400 MHz $CDCl_3$)



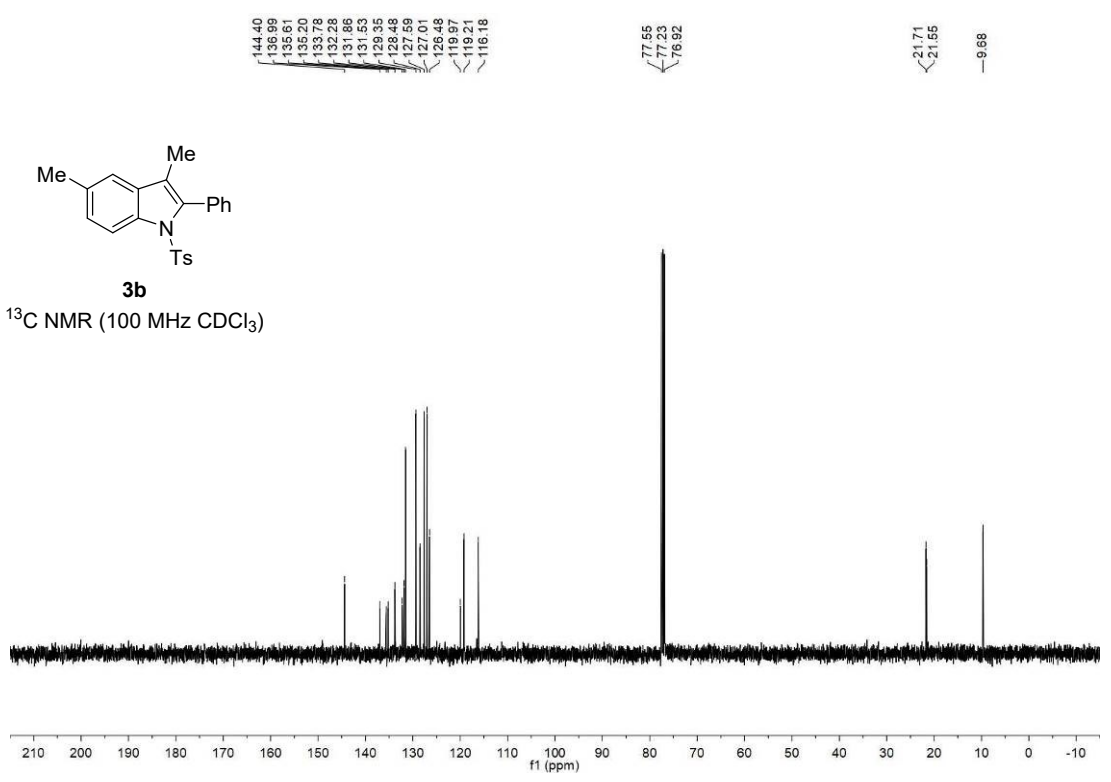
3a

^{13}C NMR (100 MHz $CDCl_3$)



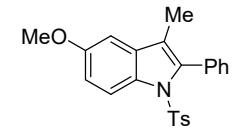
3b

^{1}H NMR (400 MHz $CDCl_3$)



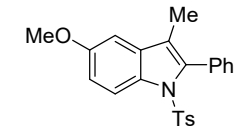
3b

^{13}C NMR (100 MHz $CDCl_3$)



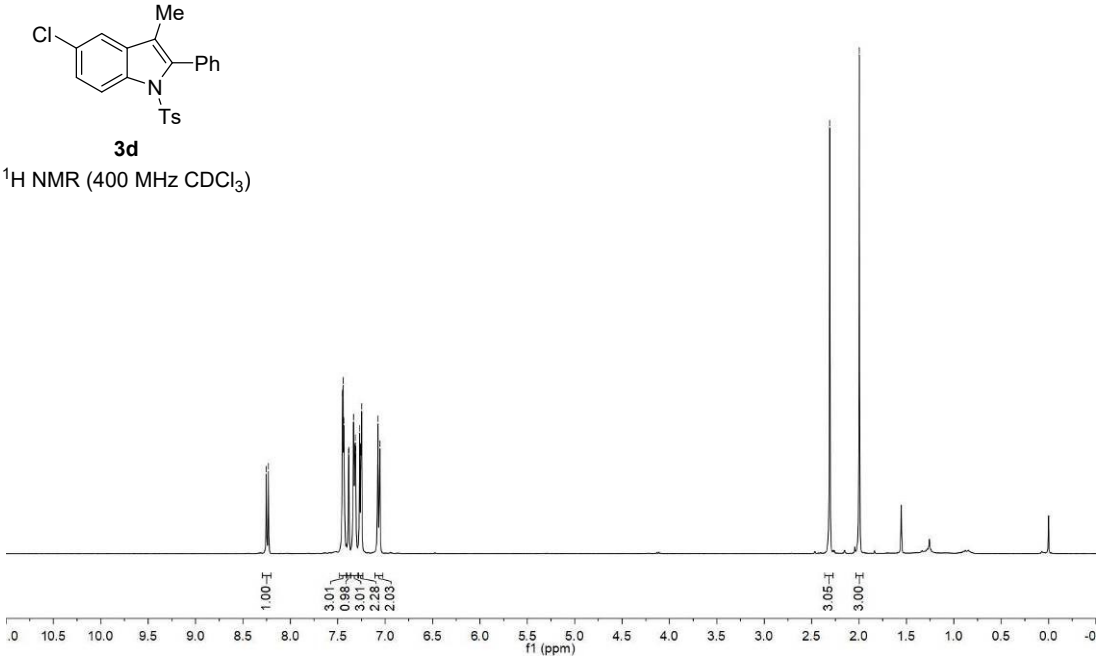
3c

^{1}H NMR (400 MHz $CDCl_3$)



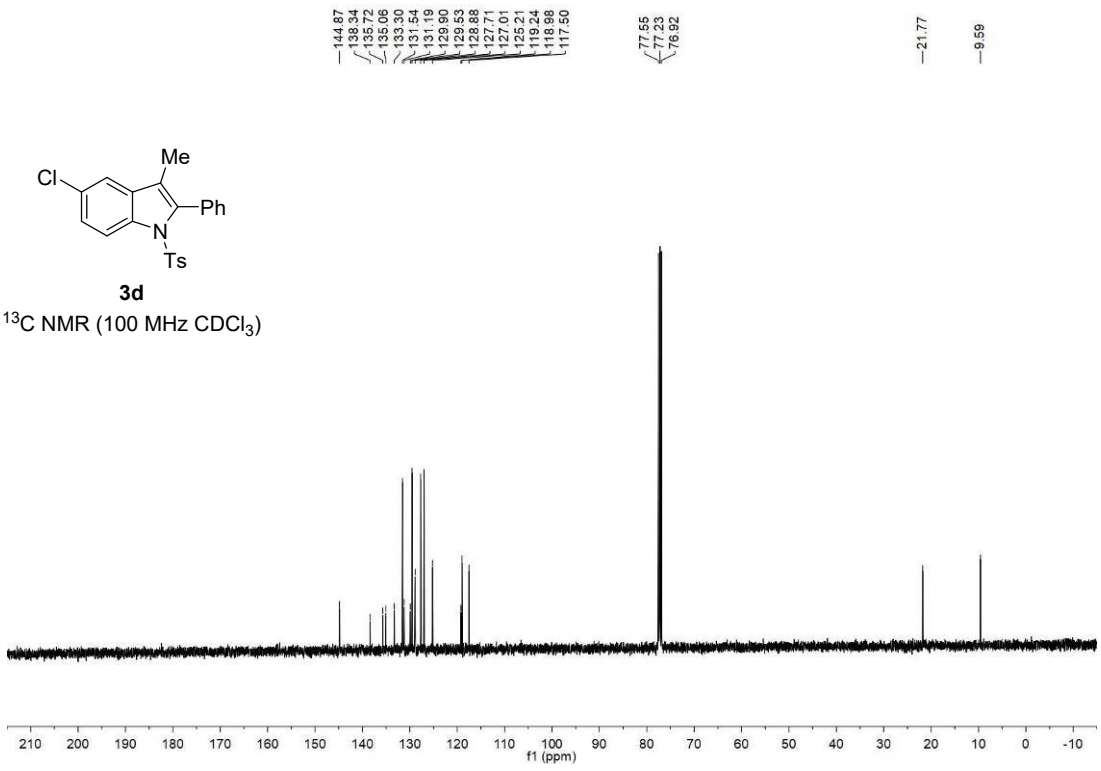
3c

^{13}C NMR (100 MHz $CDCl_3$)



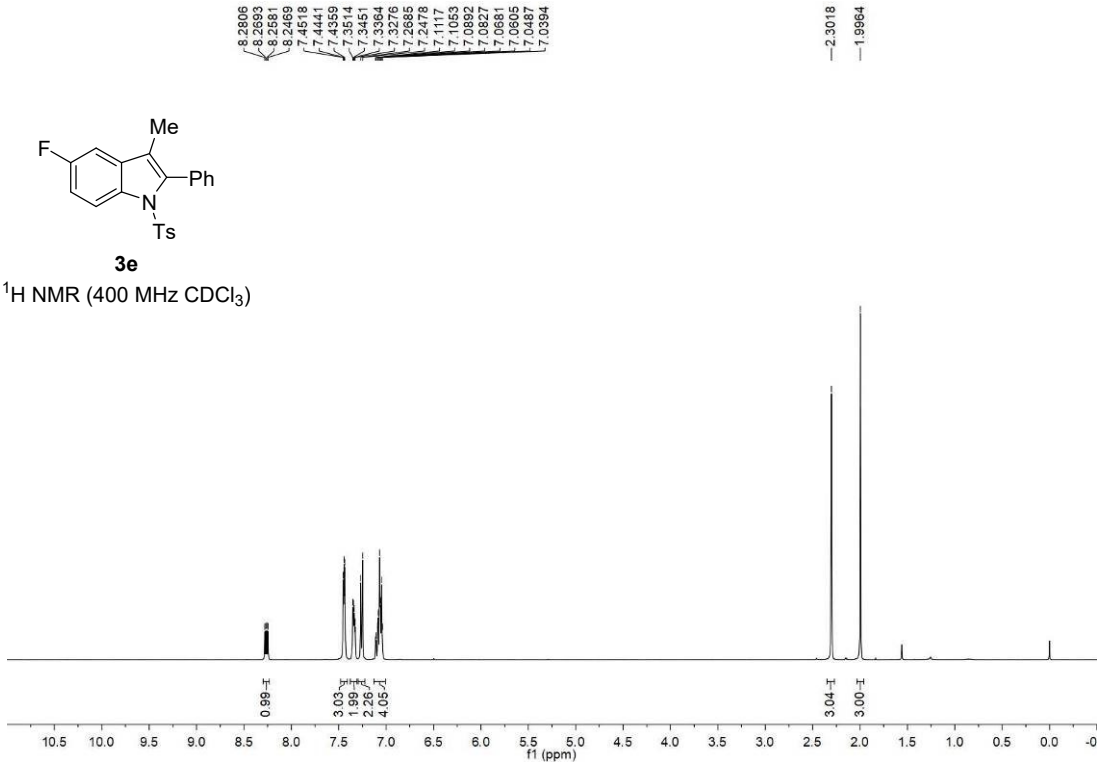
3d

^{1}H NMR (400 MHz $CDCl_3$)



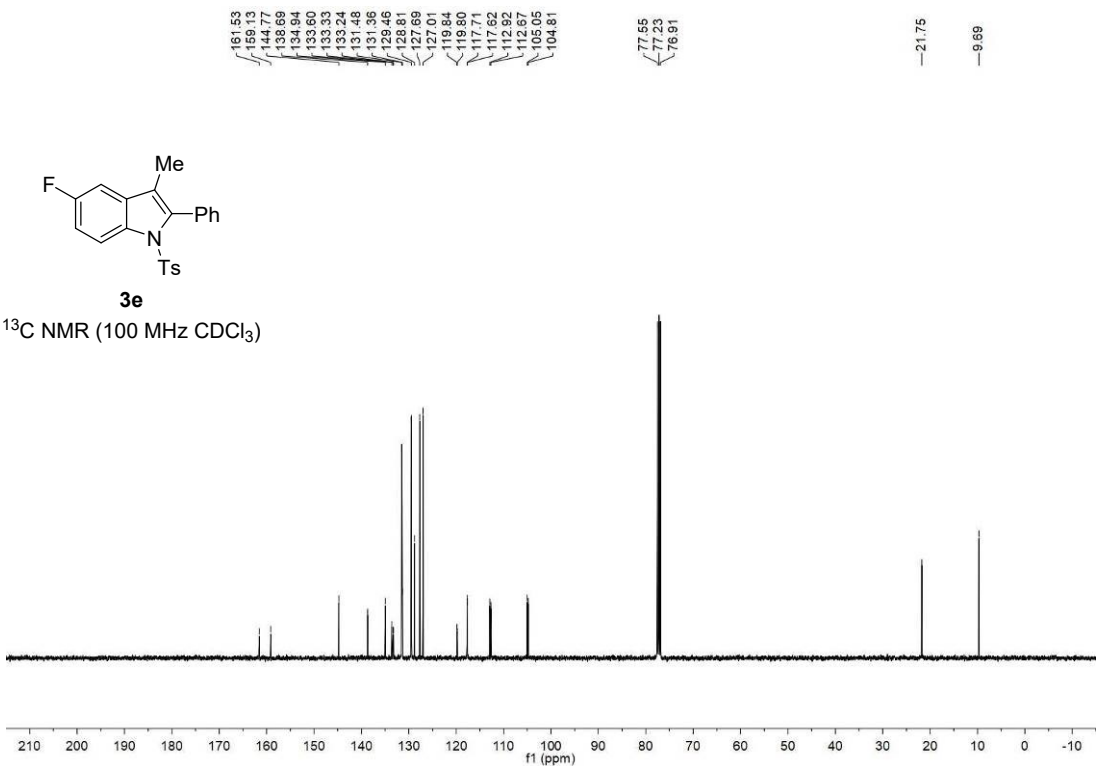
3d

^{13}C NMR (100 MHz $CDCl_3$)



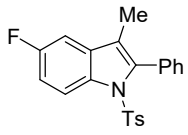
3e

^{1}H NMR (400 MHz $CDCl_3$)



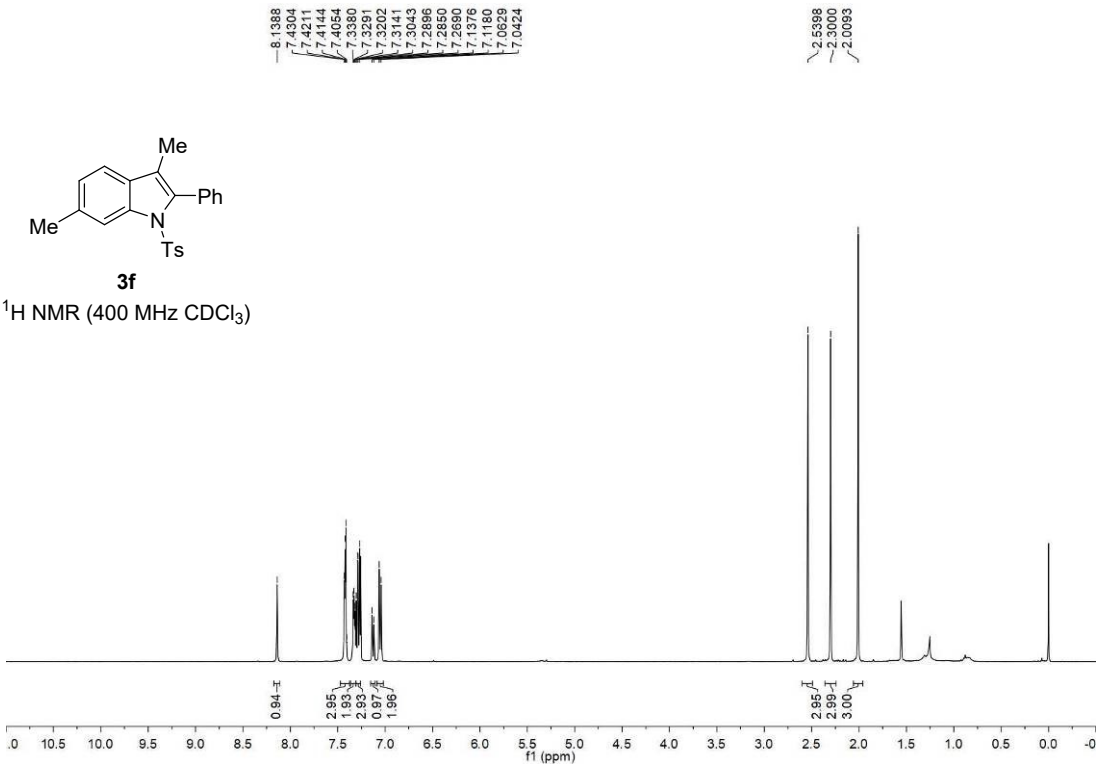
3e

^{13}C NMR (100 MHz $CDCl_3$)



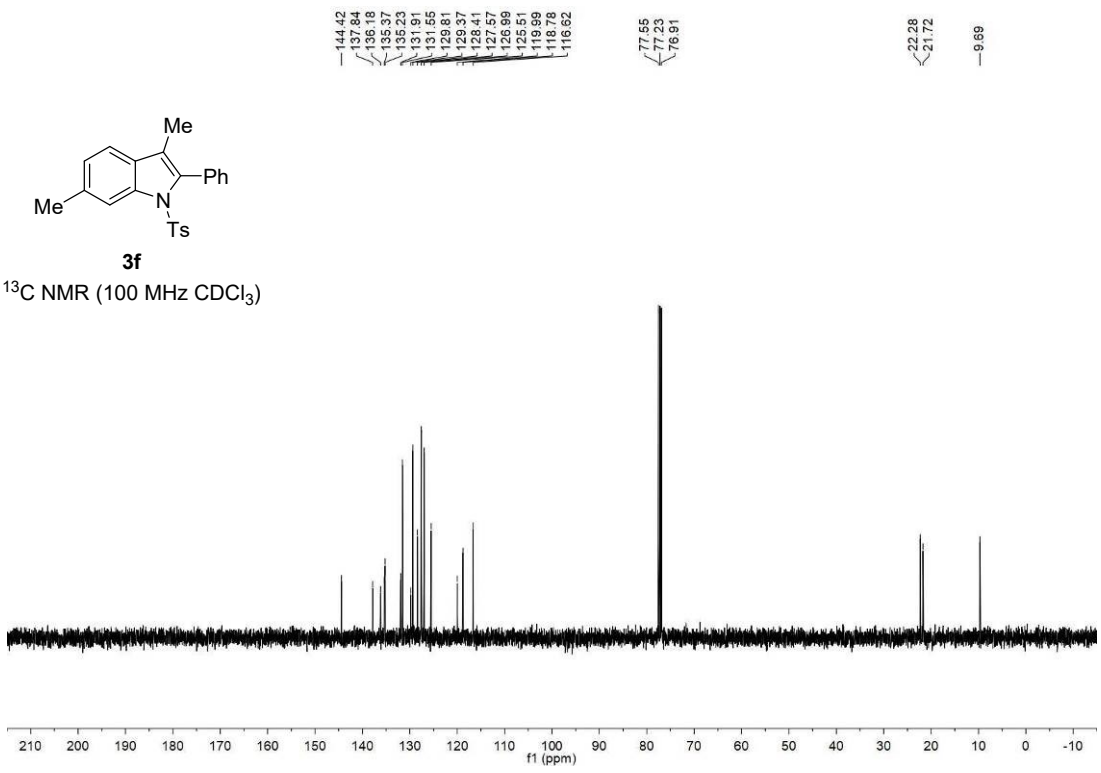
3e

^{19}F NMR (376 MHz $CDCl_3$)



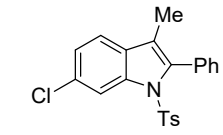
3f

^{1}H NMR (400 MHz $CDCl_3$)



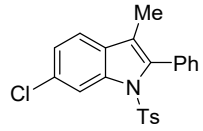
3f

^{13}C NMR (100 MHz $CDCl_3$)



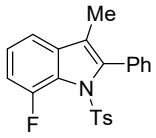
3g

^{1}H NMR (400 MHz $CDCl_3$)



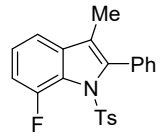
3g

^{13}C NMR (100 MHz $CDCl_3$)



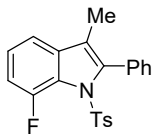
3h

^{1}H NMR (400 MHz $CDCl_3$)



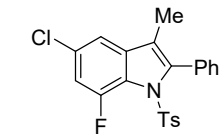
3h

^{13}C NMR (100 MHz $CDCl_3$)



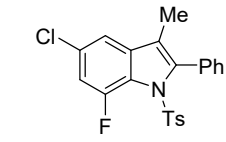
3h

^{19}F NMR (376 MHz $CDCl_3$)



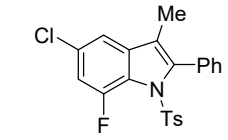
3i

^{1}H NMR (400 MHz $CDCl_3$)



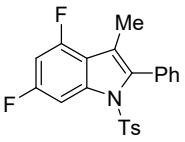
3i

^{13}C NMR (100 MHz $CDCl_3$)



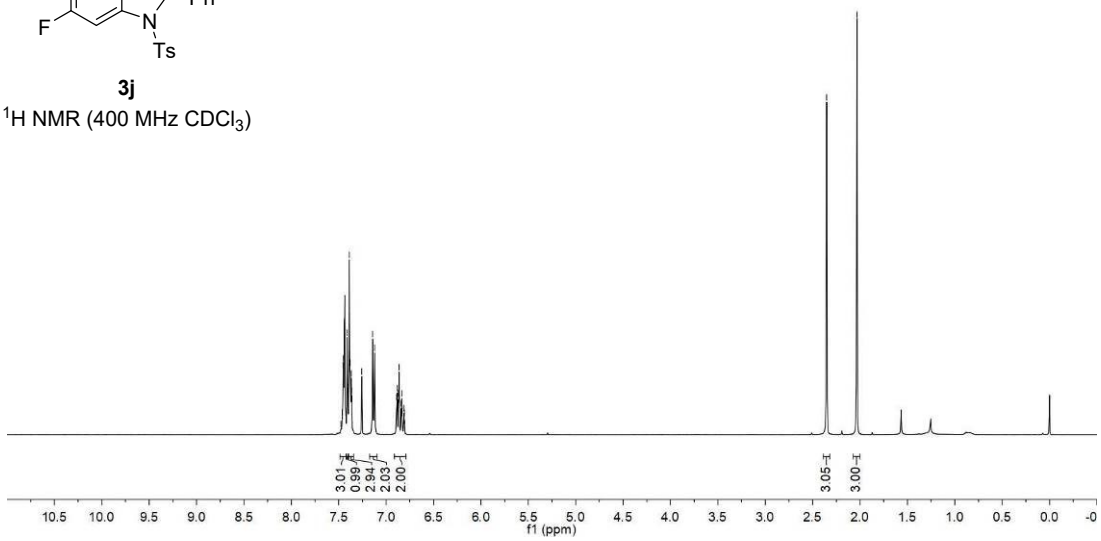
3i

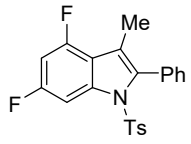
^{19}F NMR (376 MHz $CDCl_3$)



3j

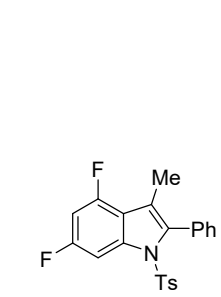
^{1}H NMR (400 MHz $CDCl_3$)





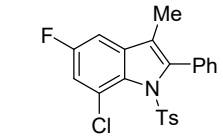
3j

^{13}C NMR (100 MHz $CDCl_3$)



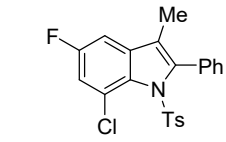
3j

^{19}F NMR (376 MHz $CDCl_3$)



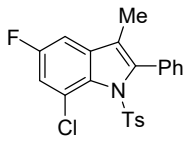
3k

^{1}H NMR (400 MHz $CDCl_3$)



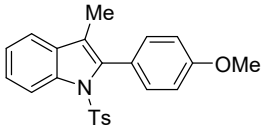
3k

^{13}C NMR (100 MHz $CDCl_3$)



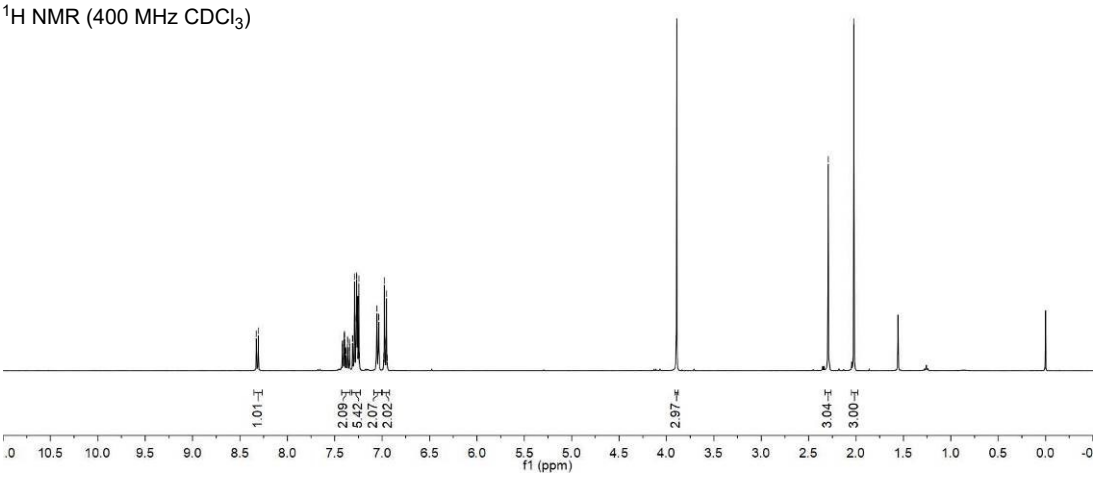
3k

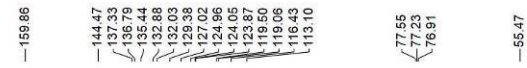
^{19}F NMR (376 MHz $CDCl_3$)

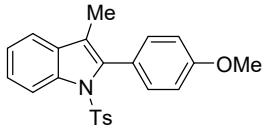


3l

^{1}H NMR (400 MHz $CDCl_3$)

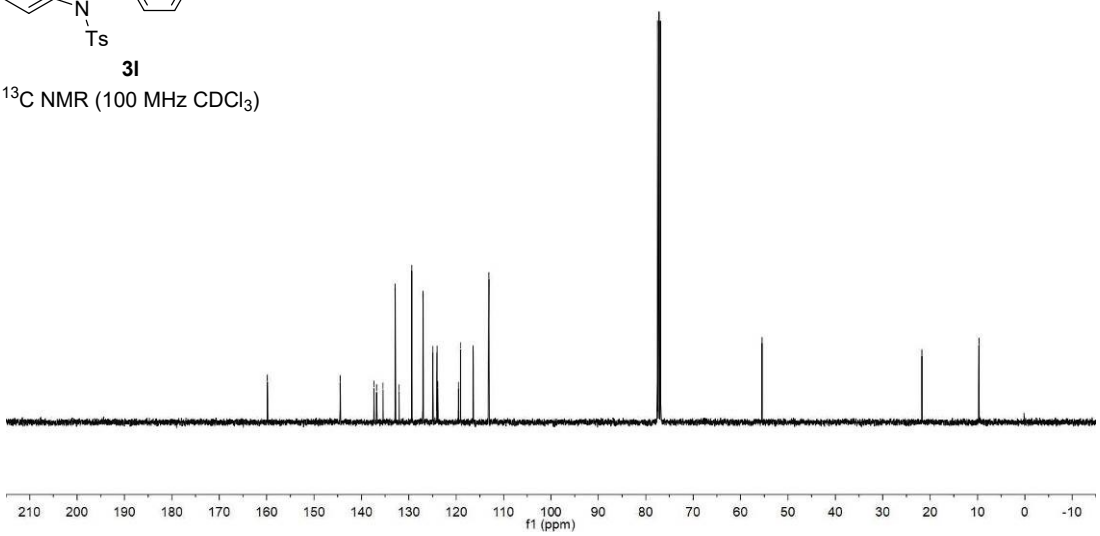


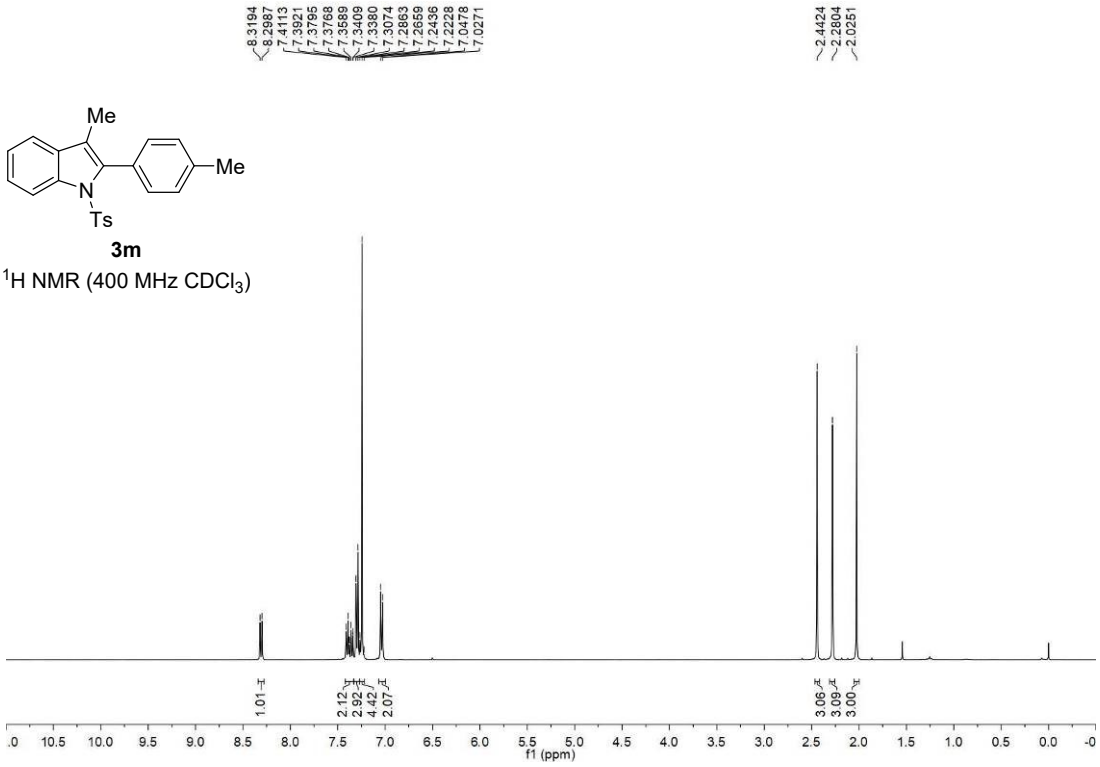




3l

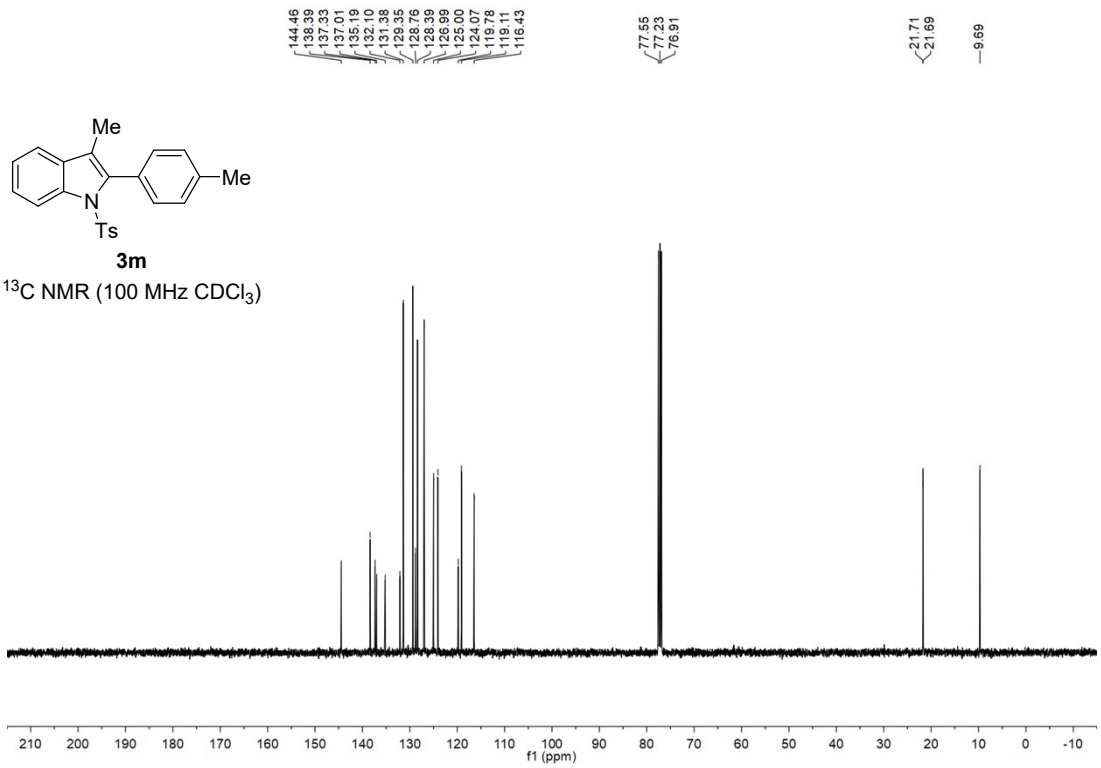
^{13}C NMR (100 MHz $CDCl_3$)





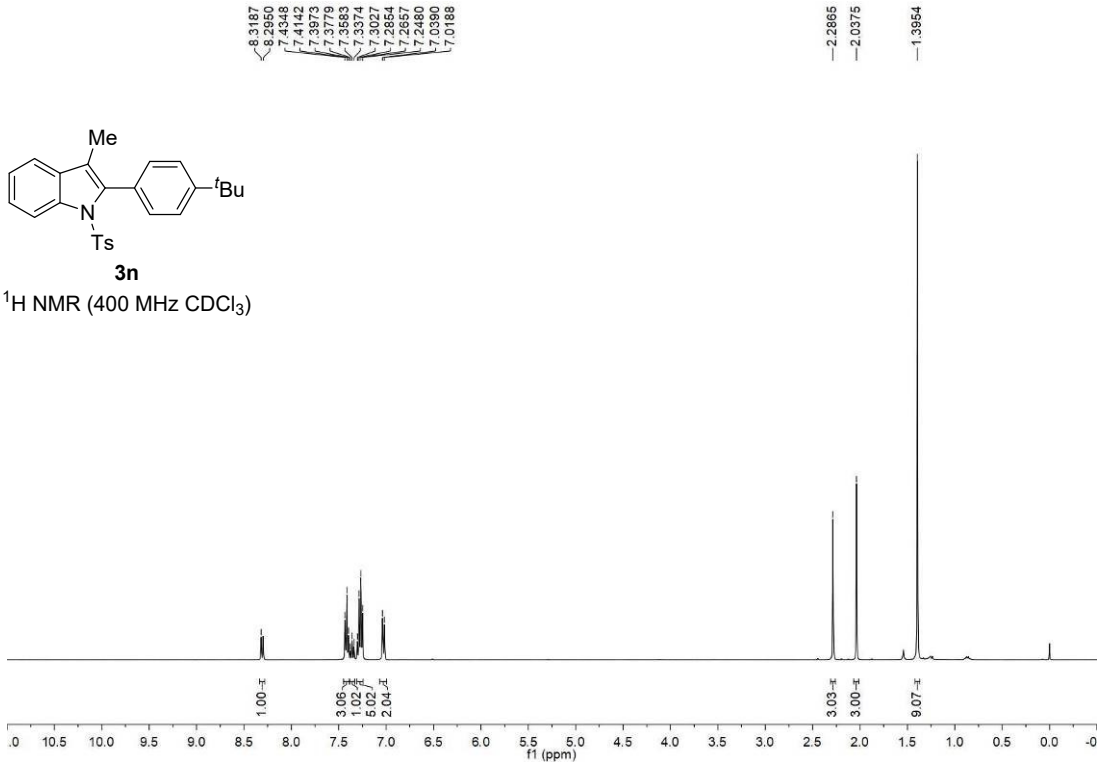
3m

^{1}H NMR (400 MHz $CDCl_3$)



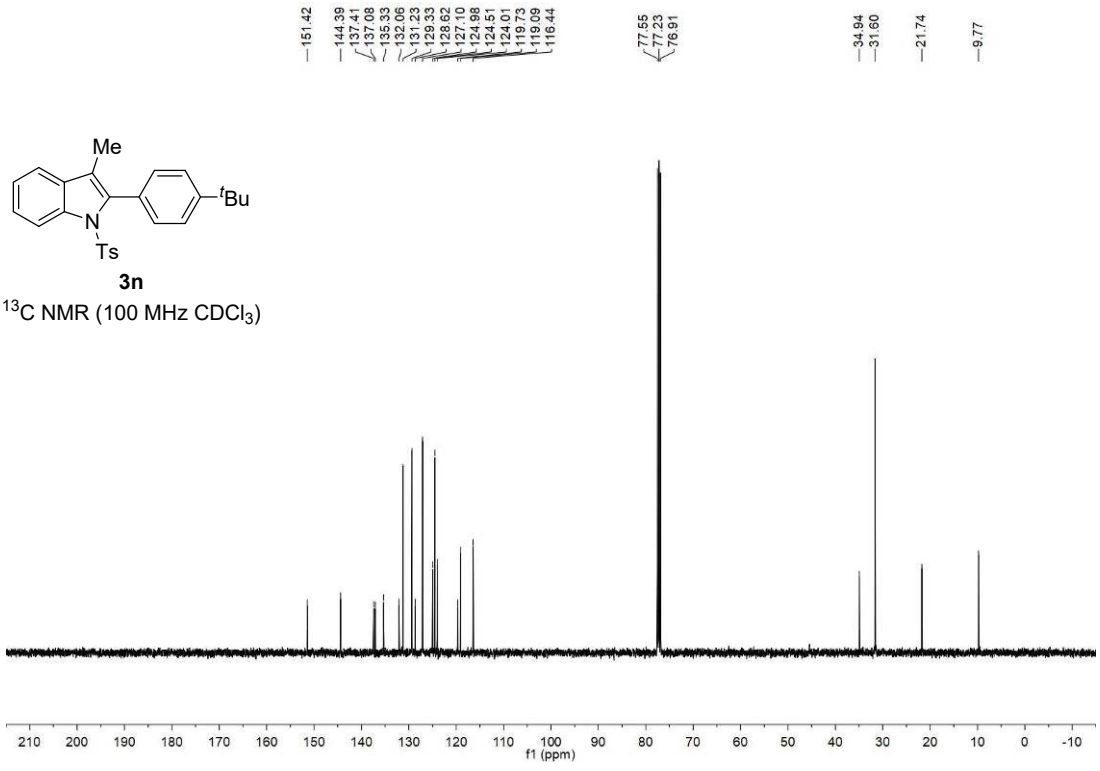
3m

^{13}C NMR (100 MHz $CDCl_3$)



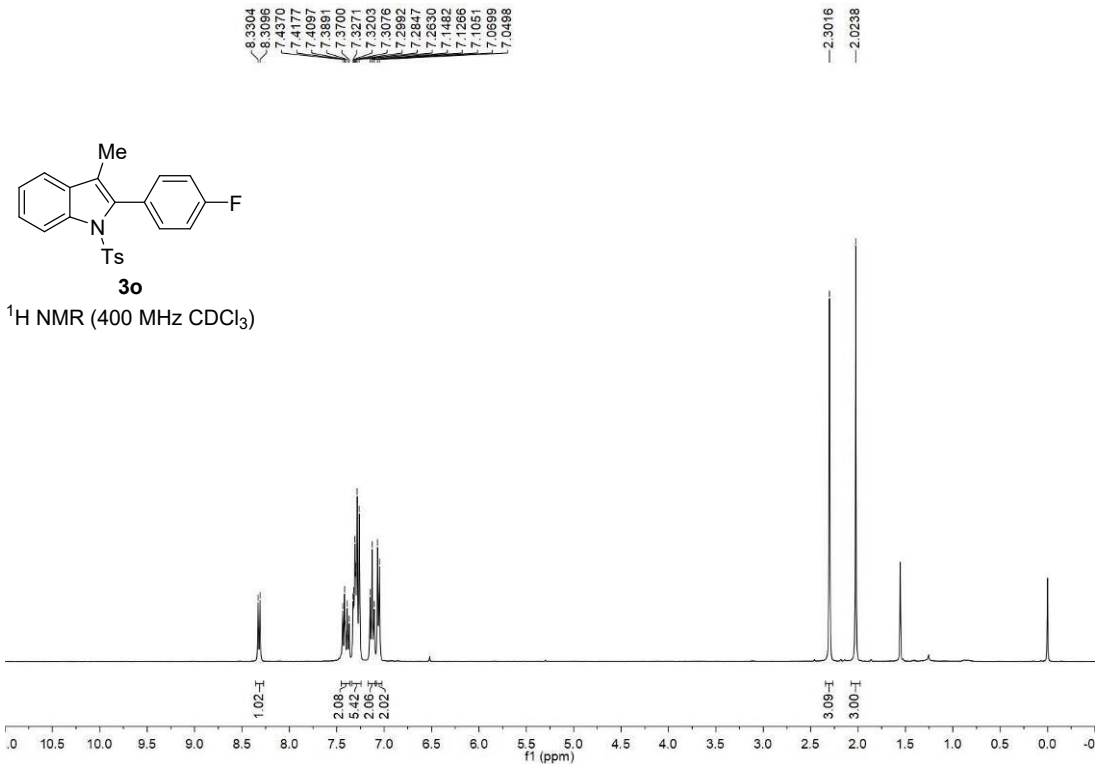
3n

^{1}H NMR (400 MHz $CDCl_3$)



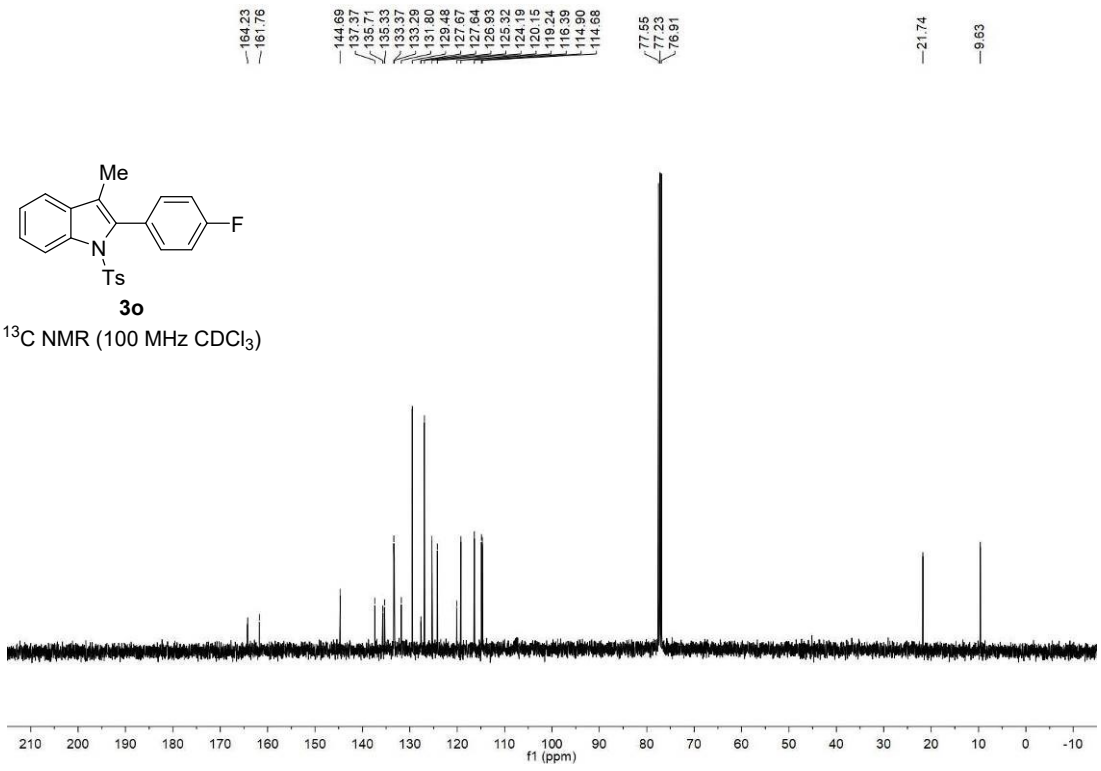
3n

^{13}C NMR (100 MHz $CDCl_3$)



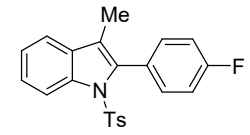
3o

^{1}H NMR (400 MHz $CDCl_3$)



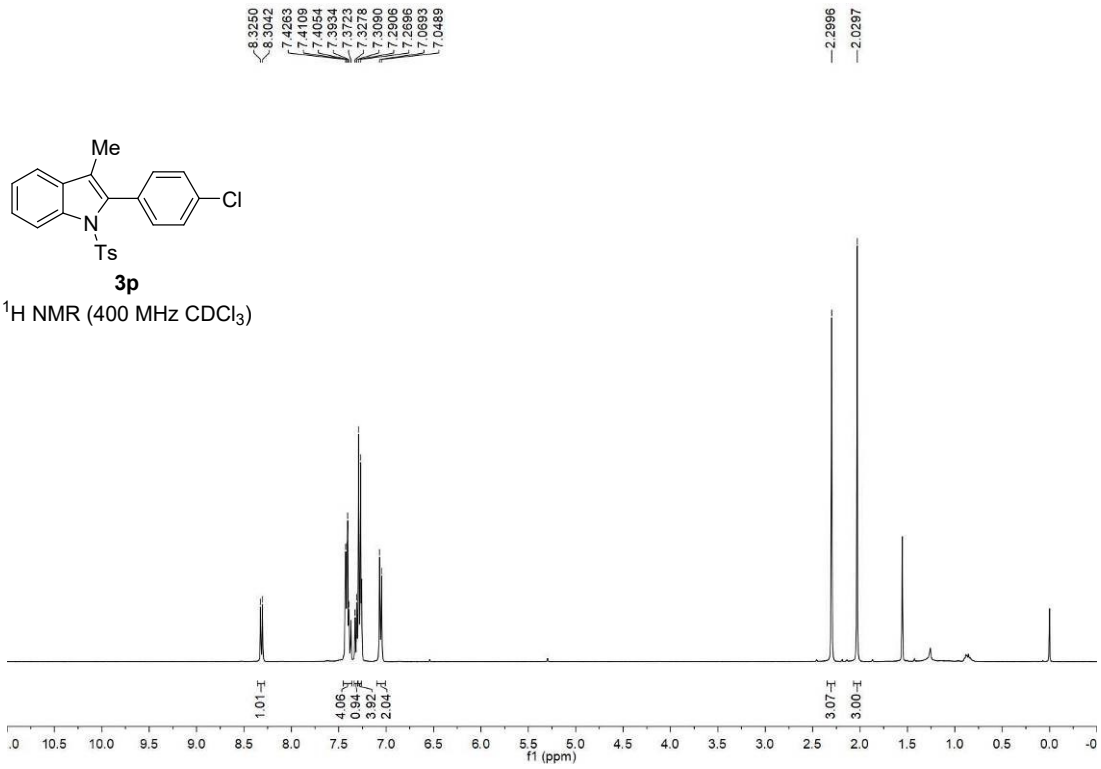
3o

^{13}C NMR (100 MHz $CDCl_3$)



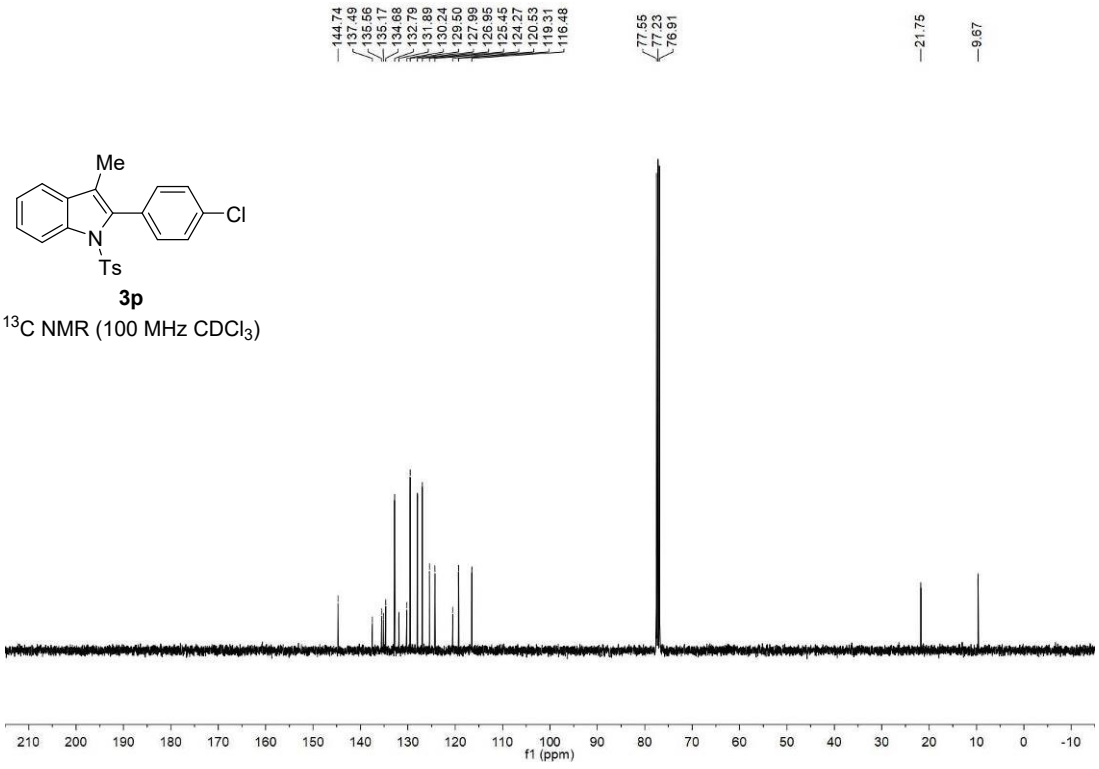
3o

^{19}F NMR (376 MHz $CDCl_3$)



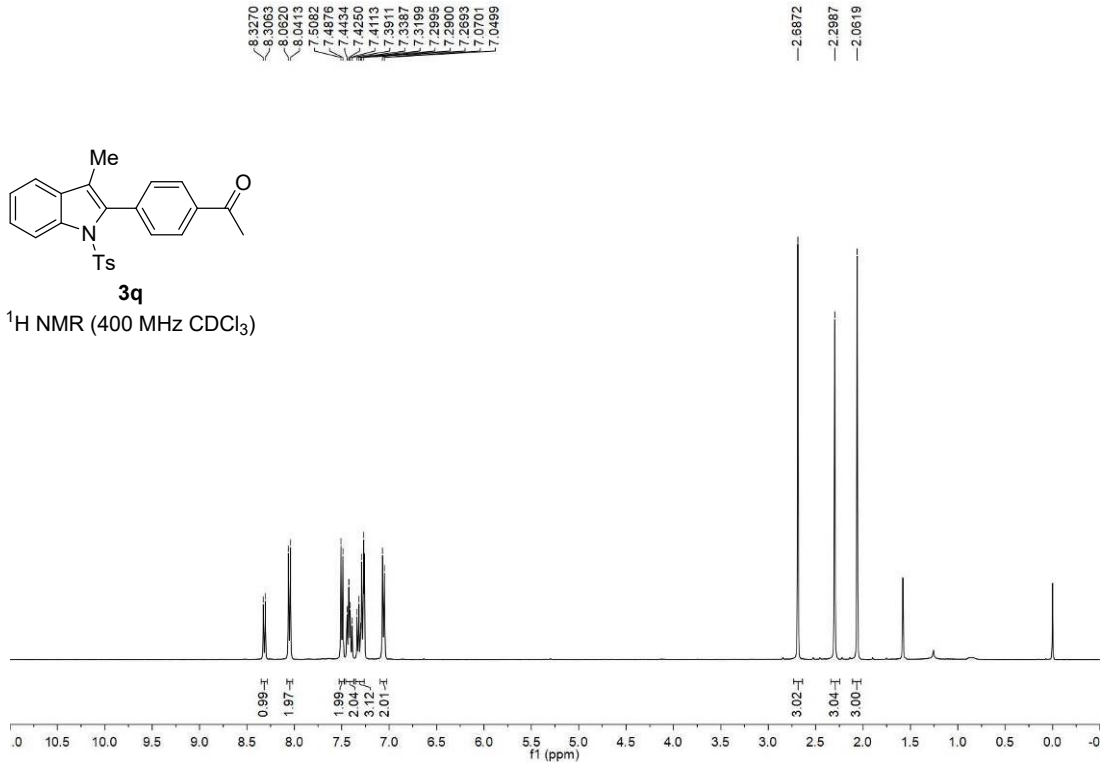
3p

^{1}H NMR (400 MHz $CDCl_3$)



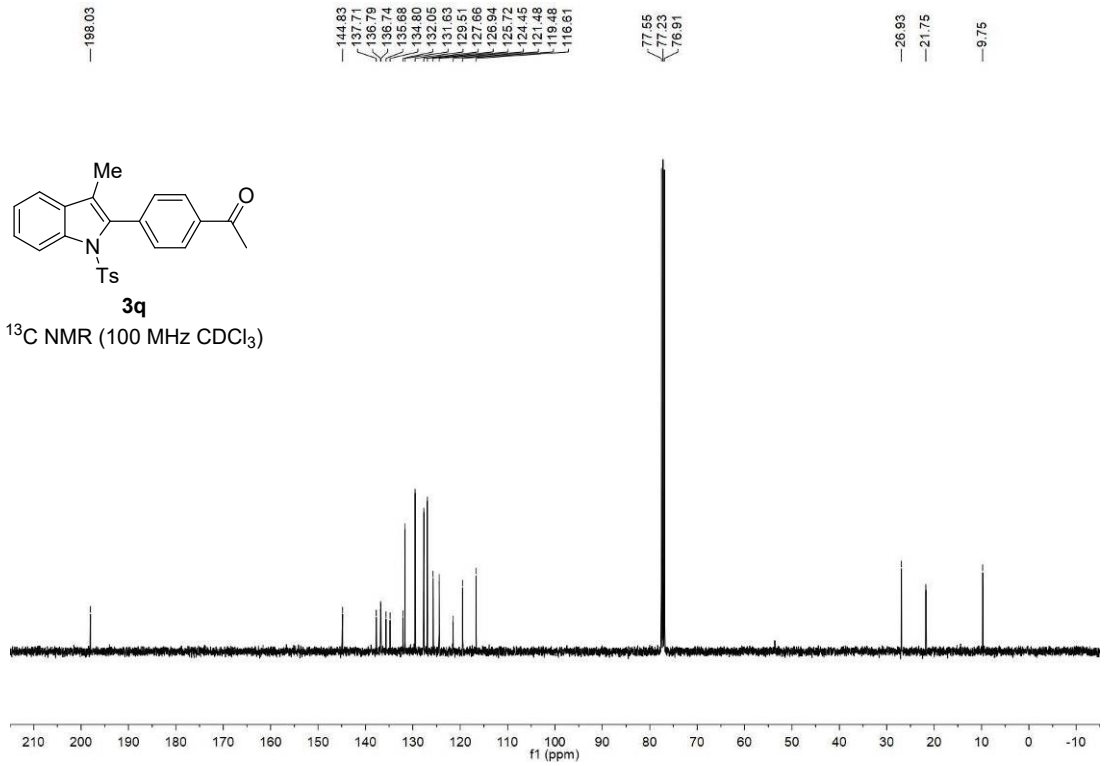
3p

^{13}C NMR (100 MHz $CDCl_3$)



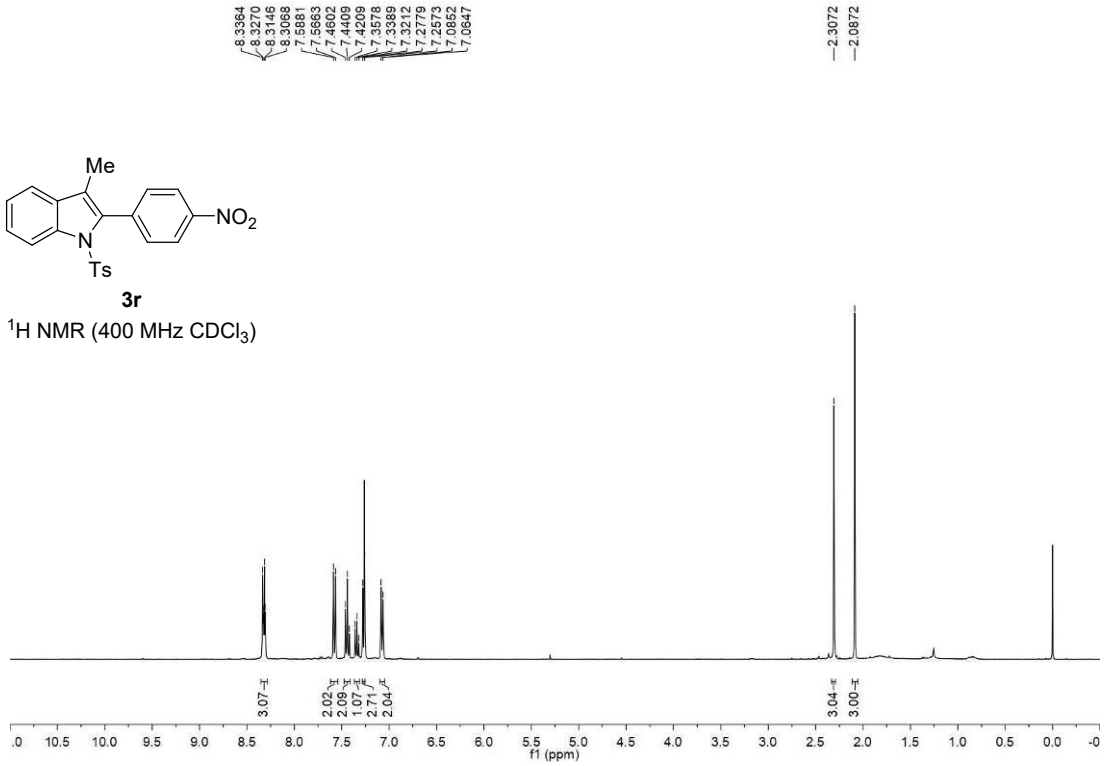
3q

^{1}H NMR (400 MHz $CDCl_3$)



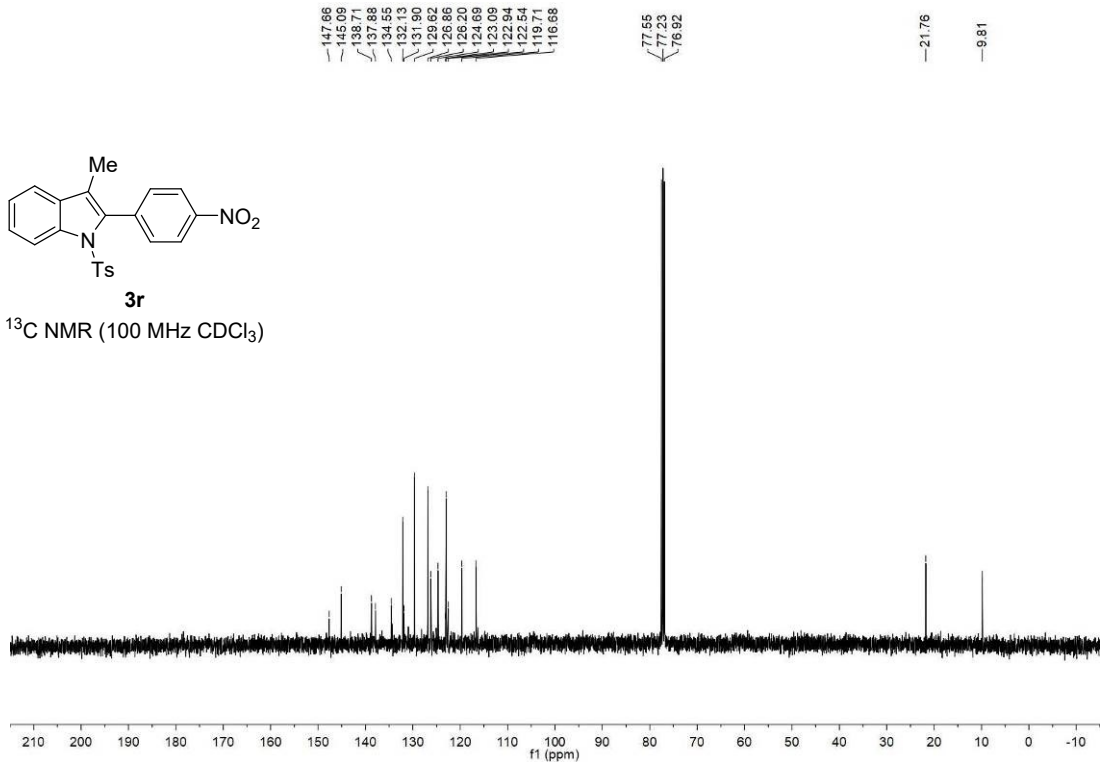
3q

^{13}C NMR (100 MHz $CDCl_3$)



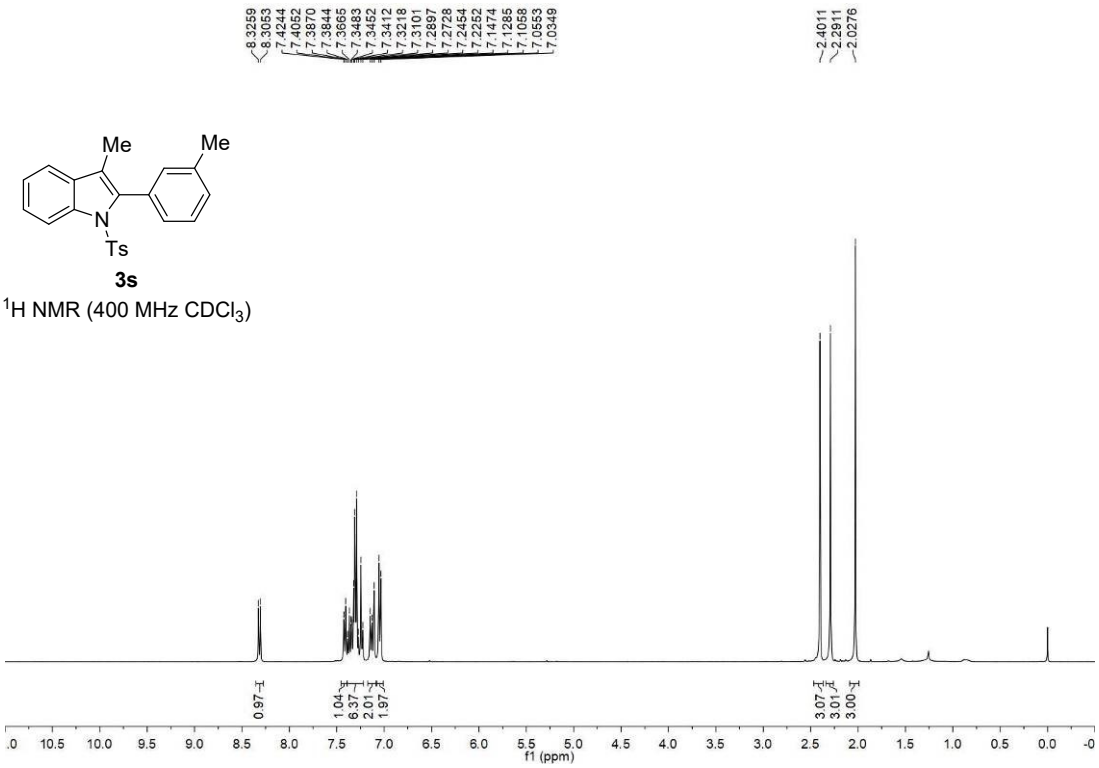
3r

^{1}H NMR (400 MHz $CDCl_3$)



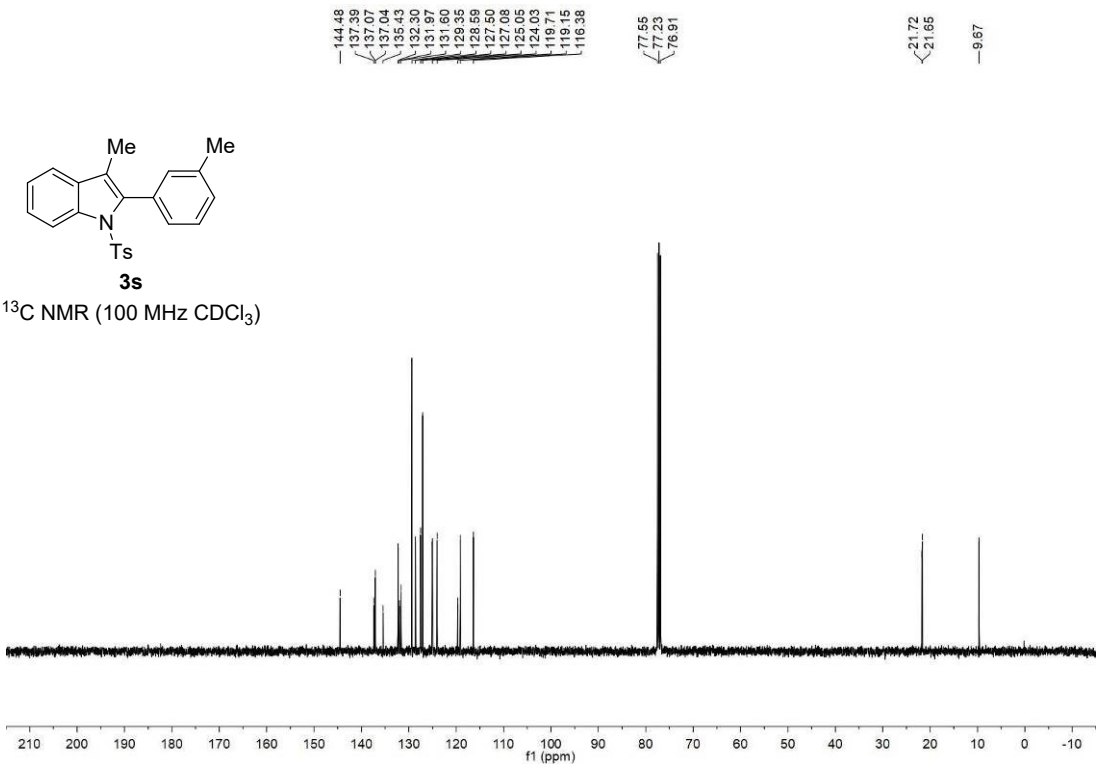
3r

^{13}C NMR (100 MHz $CDCl_3$)



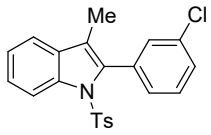
3s

^{1}H NMR (400 MHz $CDCl_3$)



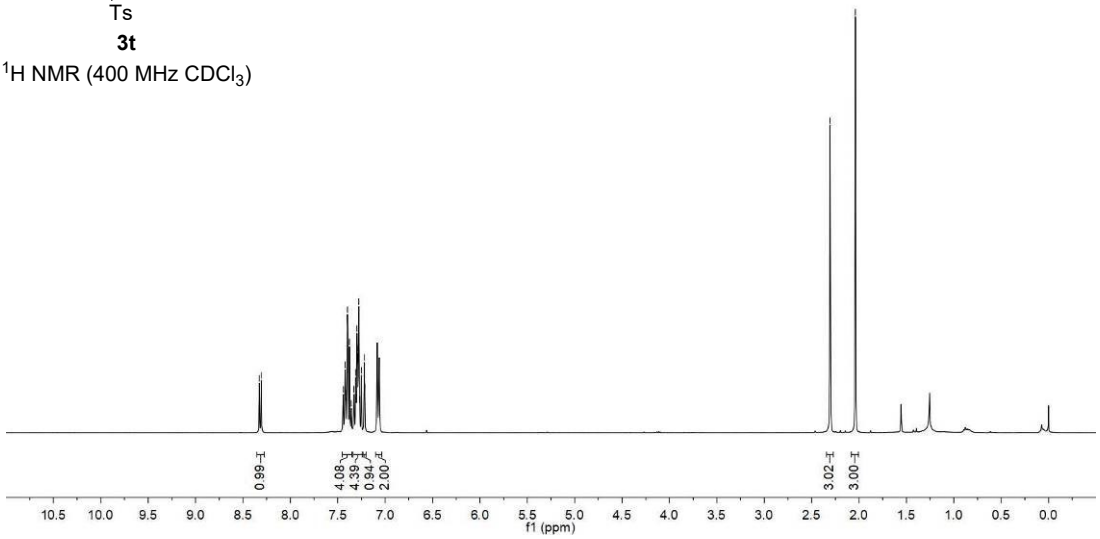
3s

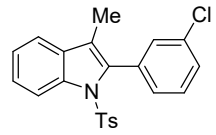
^{13}C NMR (100 MHz $CDCl_3$)



3t

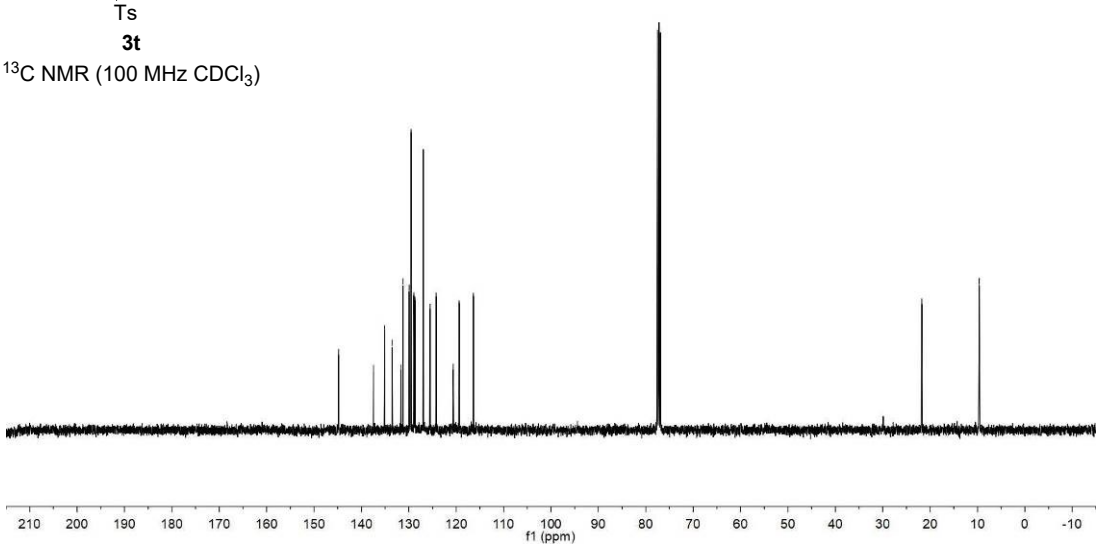
^{1}H NMR (400 MHz $CDCl_3$)

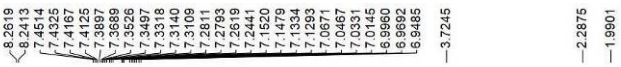


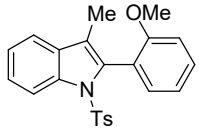


3t

^{13}C NMR (100 MHz $CDCl_3$)

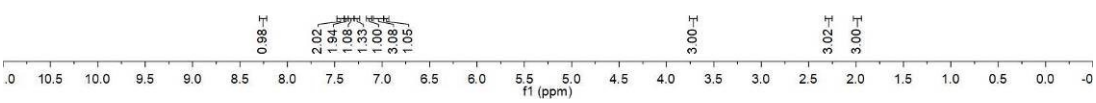


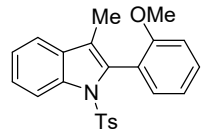




3u

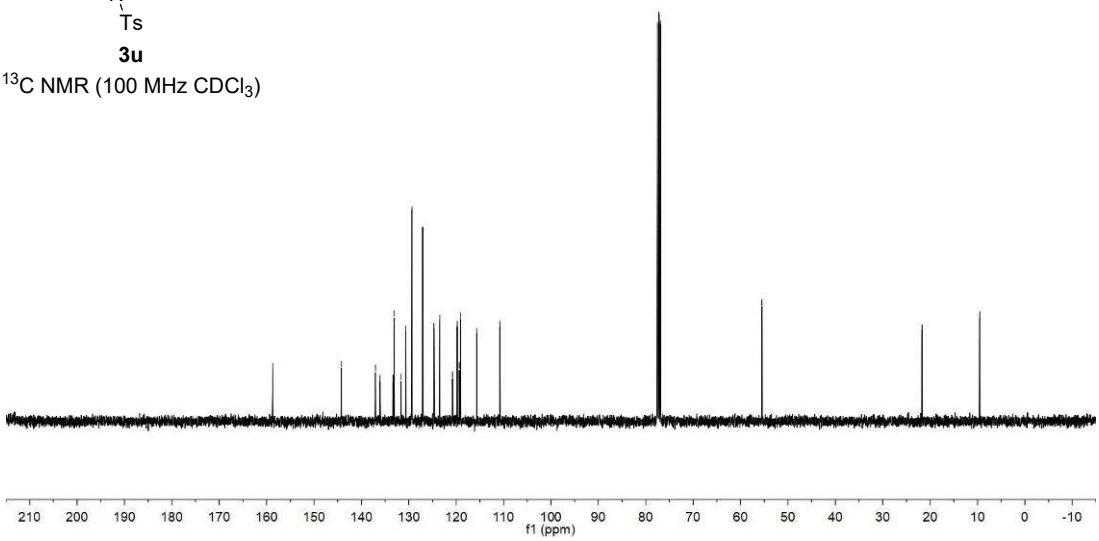
^{1}H NMR (400 MHz $CDCl_3$)

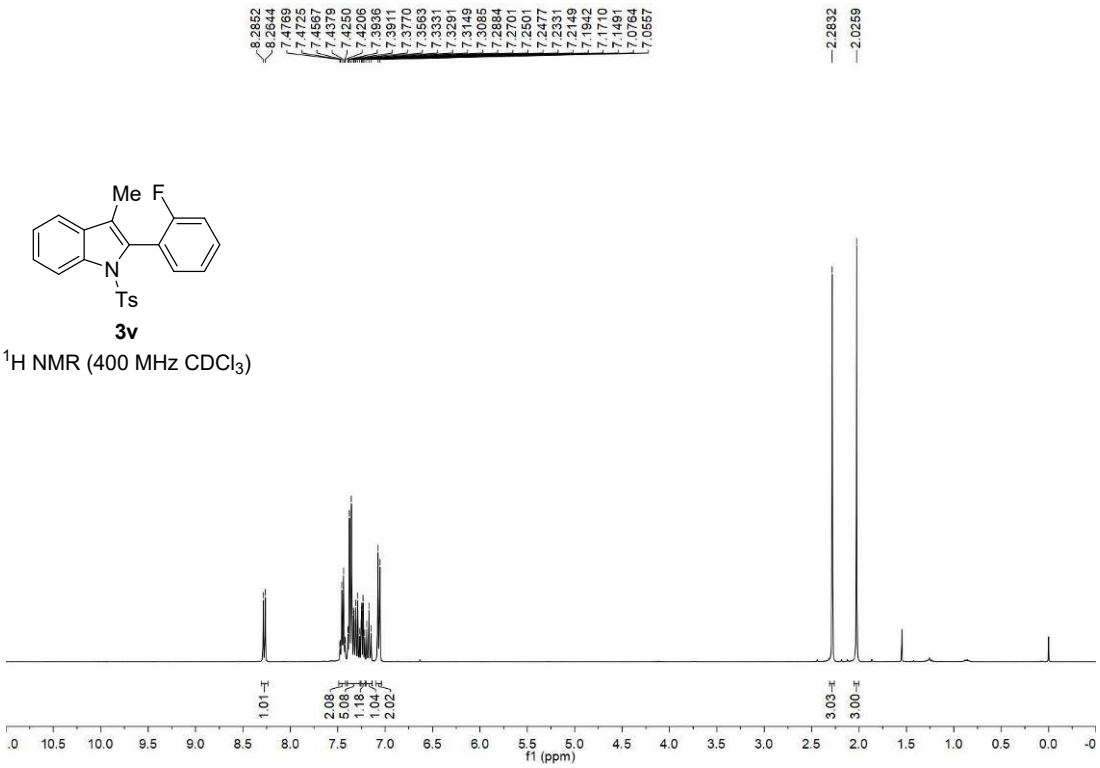




3u

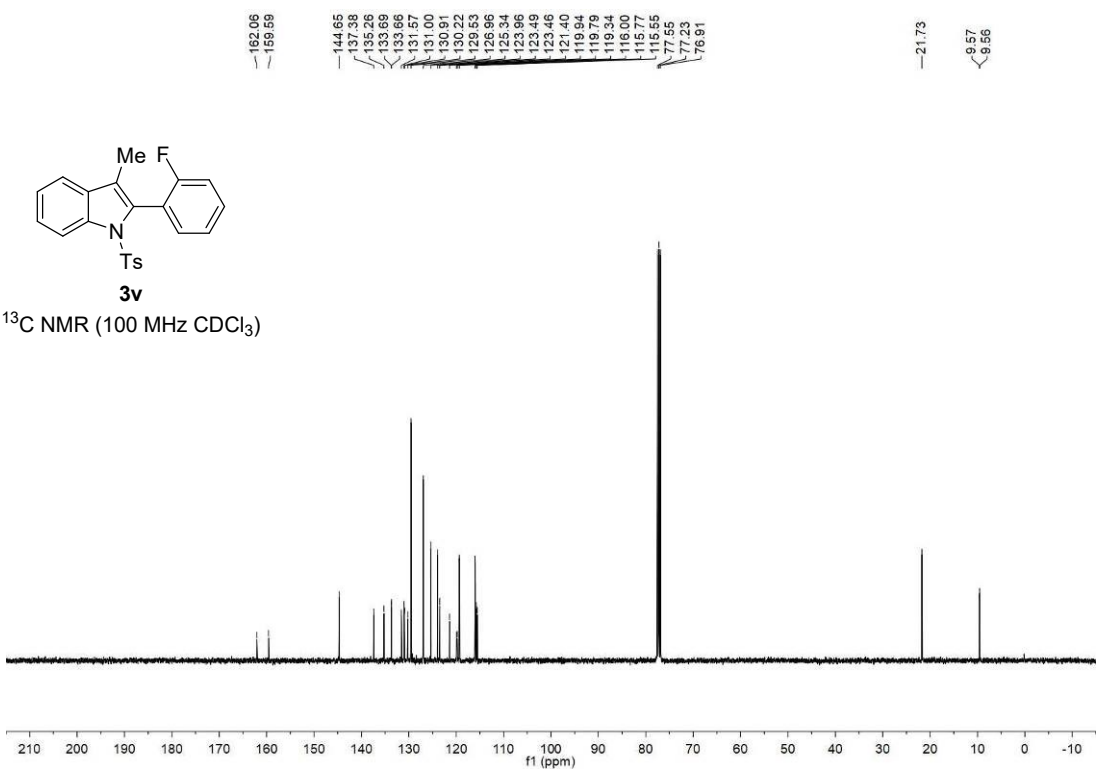
^{13}C NMR (100 MHz $CDCl_3$)





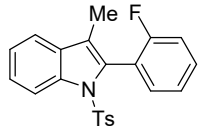
3v

^{1}H NMR (400 MHz $CDCl_3$)



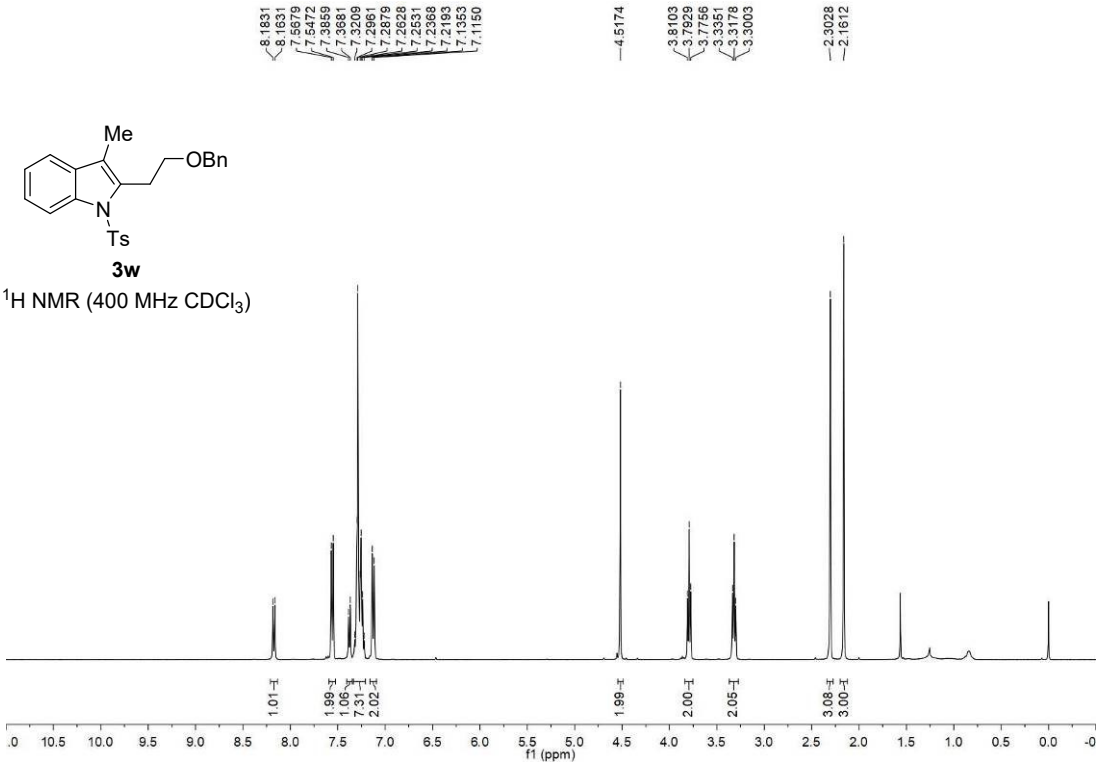
3v

^{13}C NMR (100 MHz $CDCl_3$)



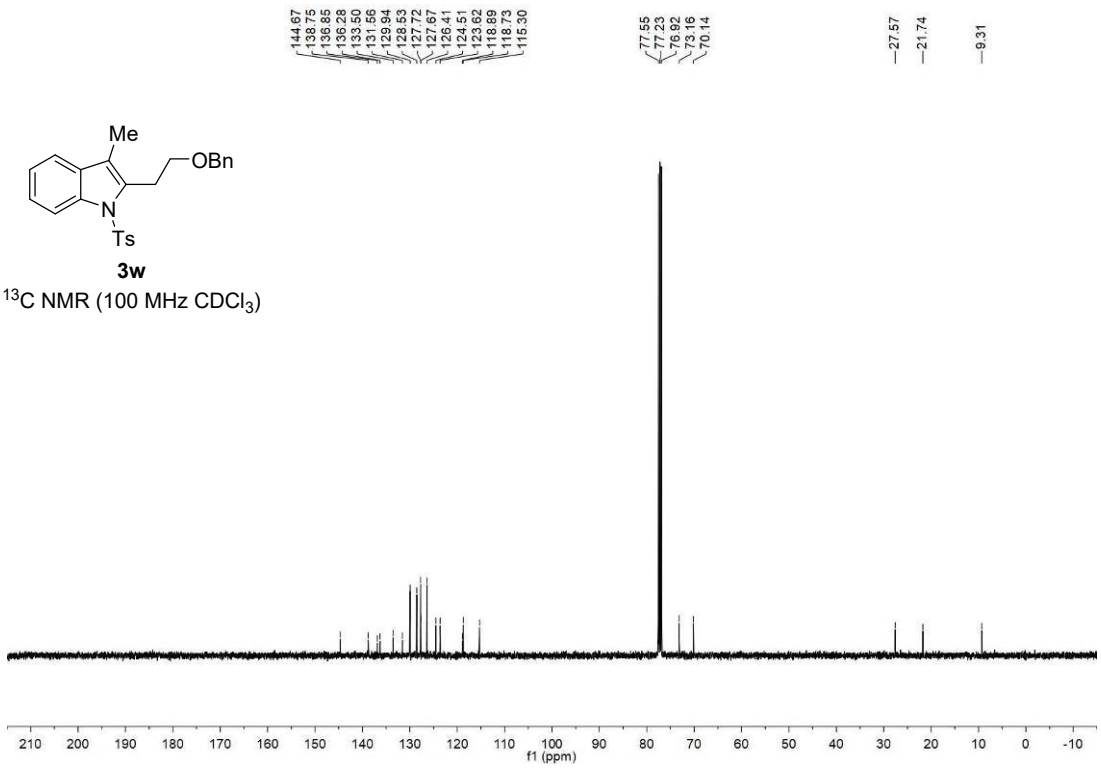
3v

^{19}F NMR (376 MHz $CDCl_3$)



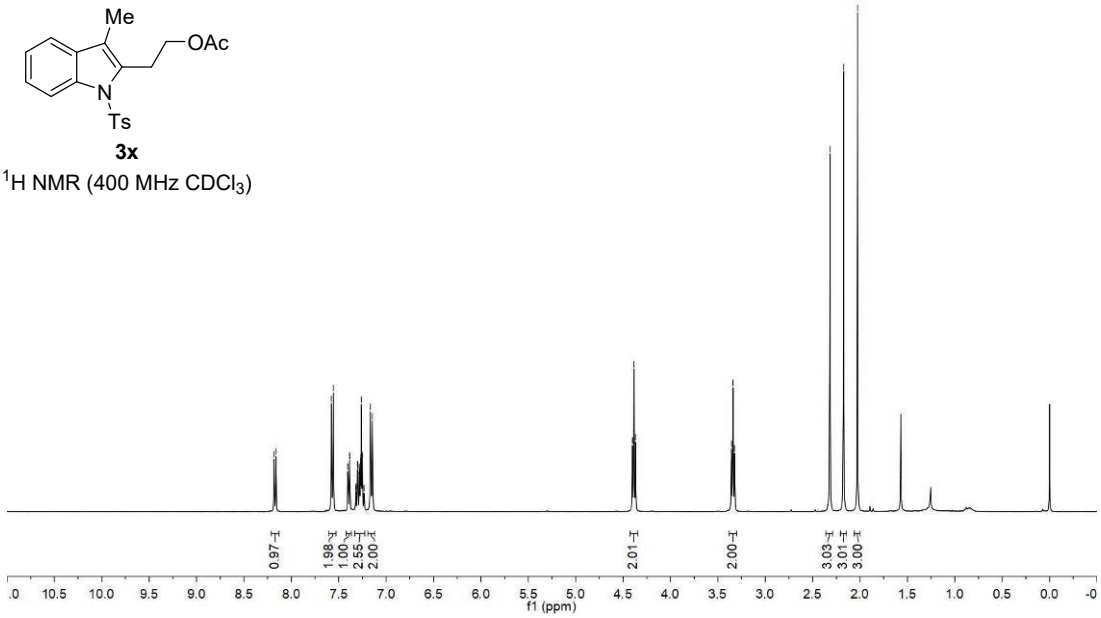
3w

^{1}H NMR (400 MHz $CDCl_3$)



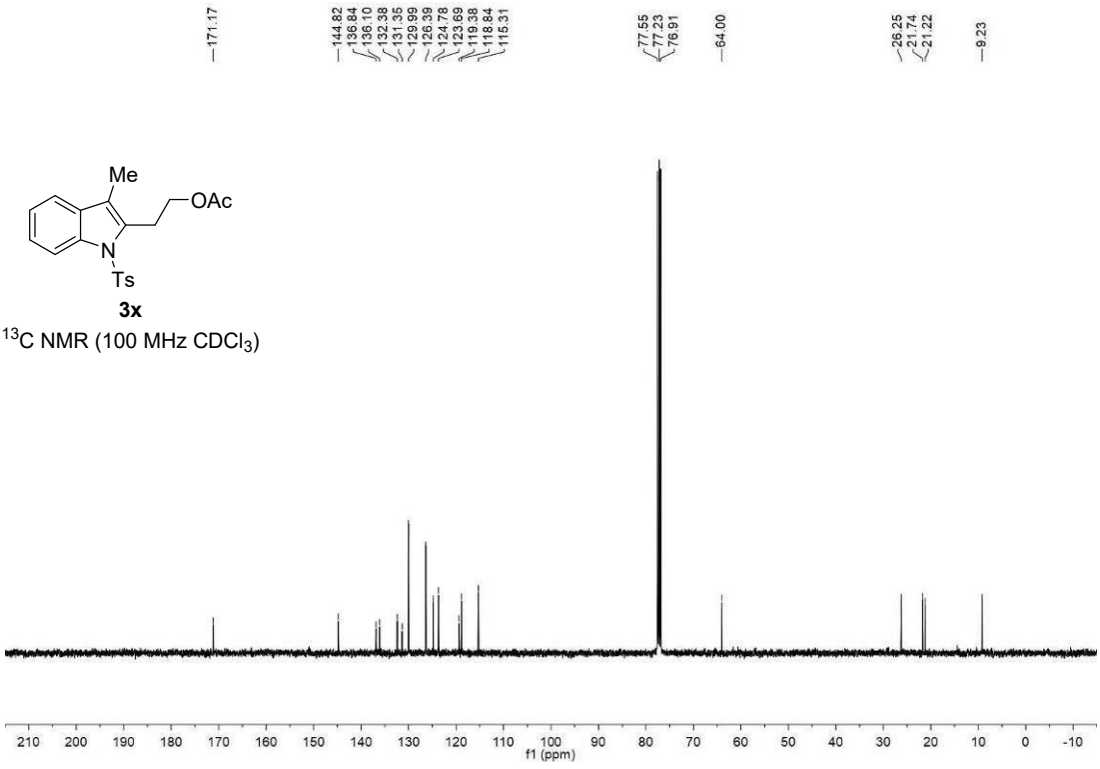
3w

^{13}C NMR (100 MHz $CDCl_3$)



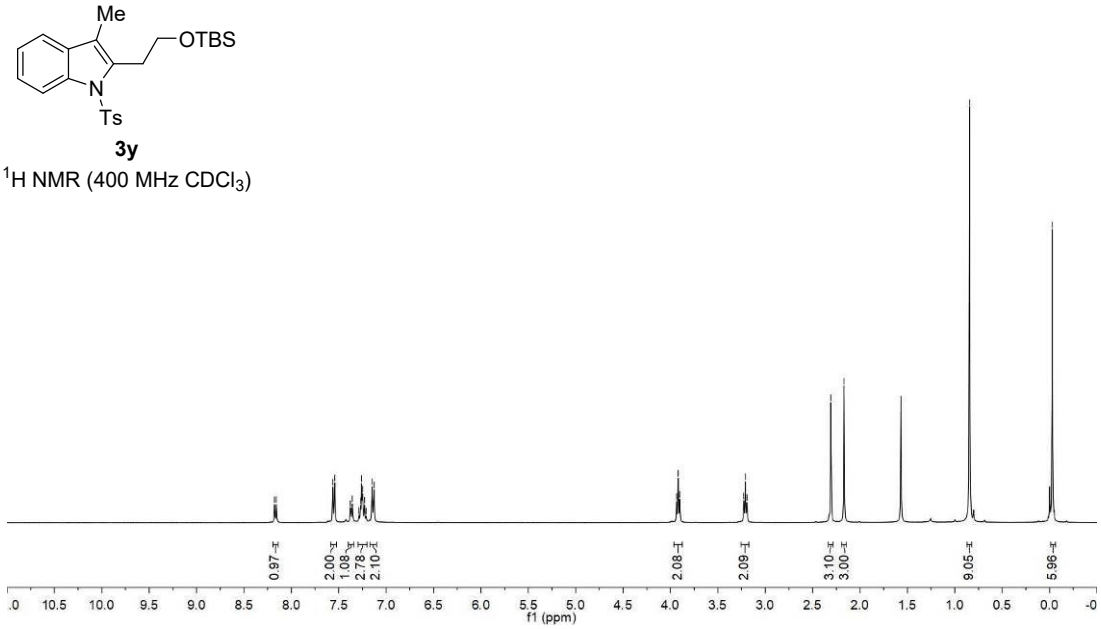
3x

^{1}H NMR (400 MHz $CDCl_3$)



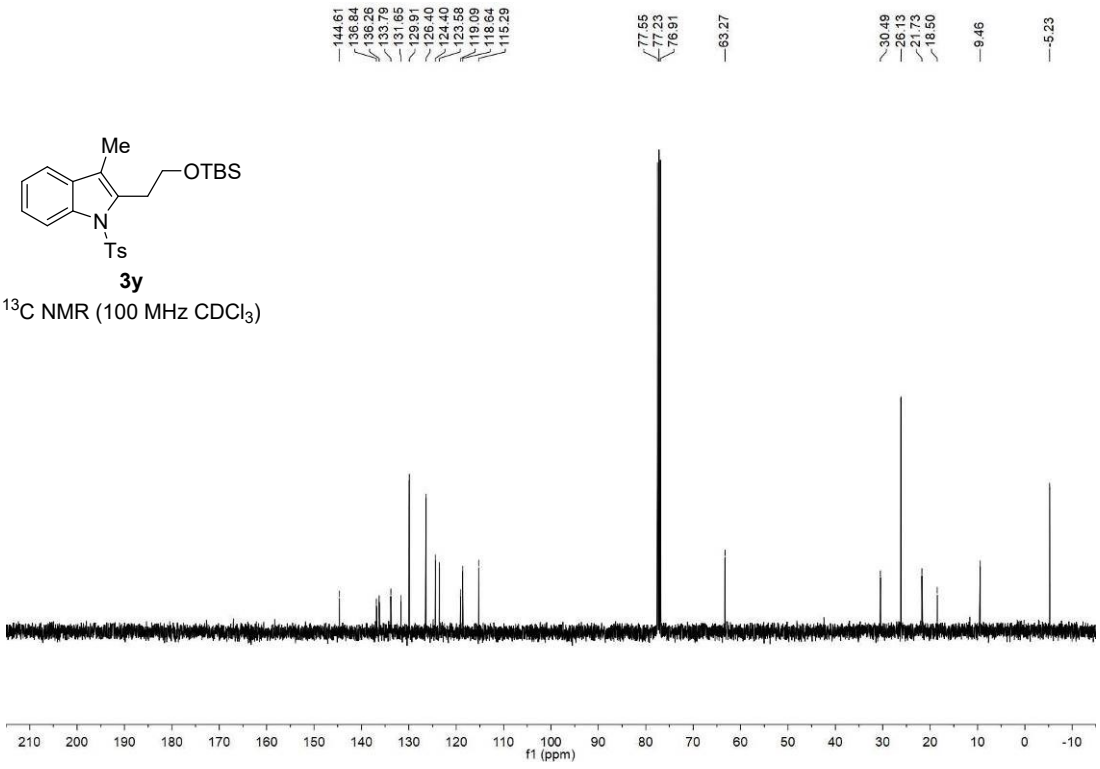
3x

^{13}C NMR (100 MHz $CDCl_3$)



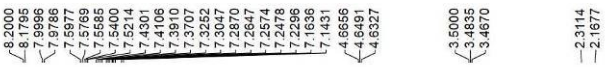
3y

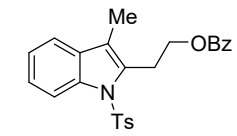
^{1}H NMR (400 MHz $CDCl_3$)



3y

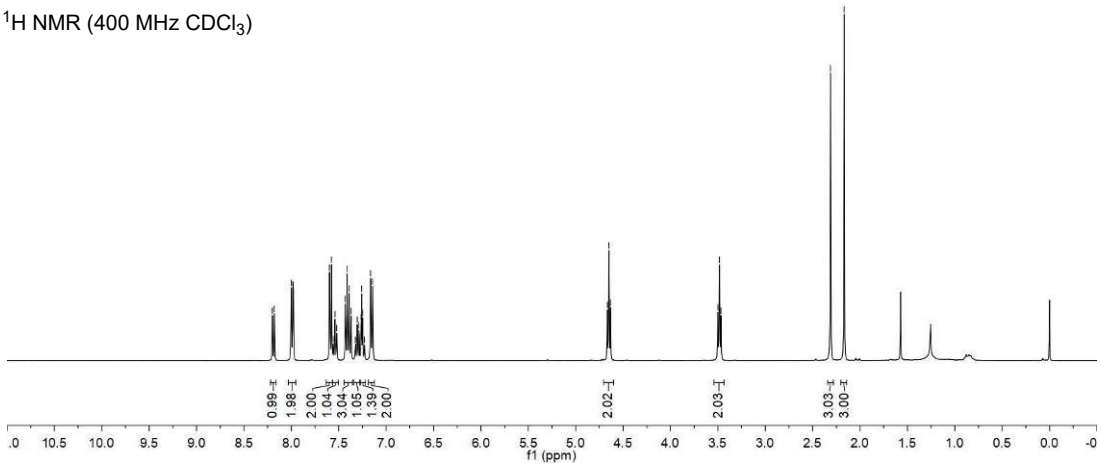
^{13}C NMR (100 MHz $CDCl_3$)

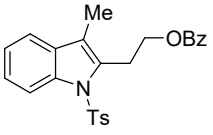




3z

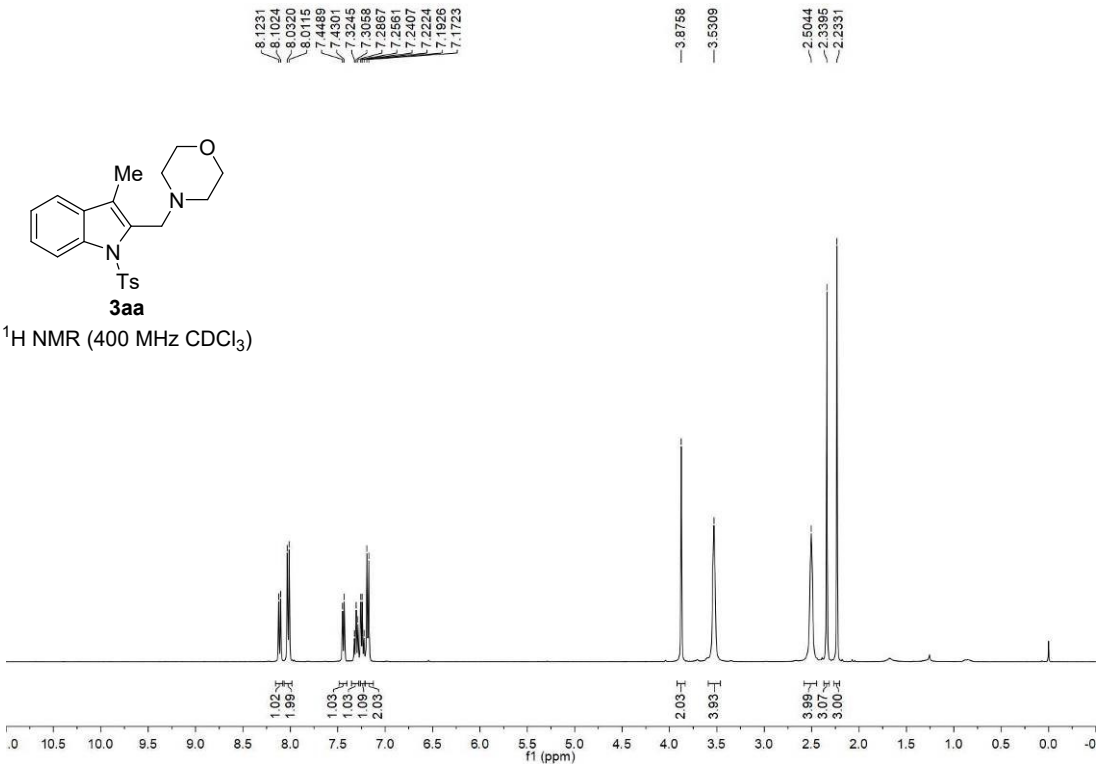
^{1}H NMR (400 MHz $CDCl_3$)





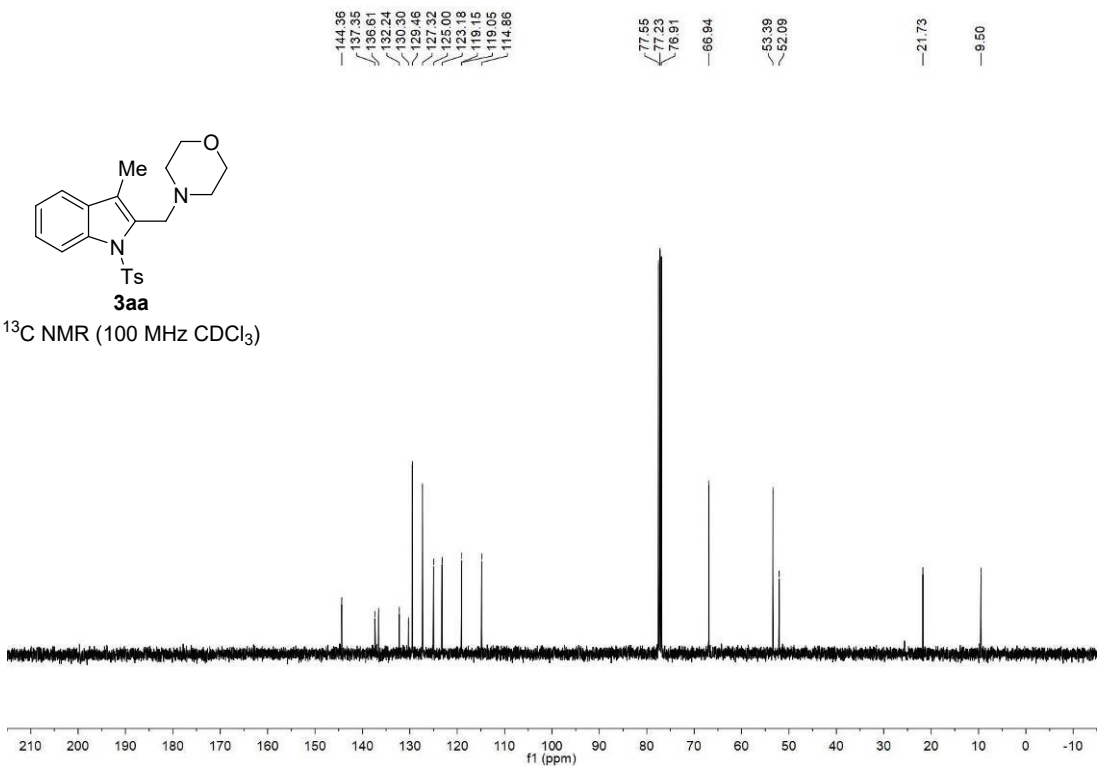
3z

^{13}C NMR (100 MHz $CDCl_3$)



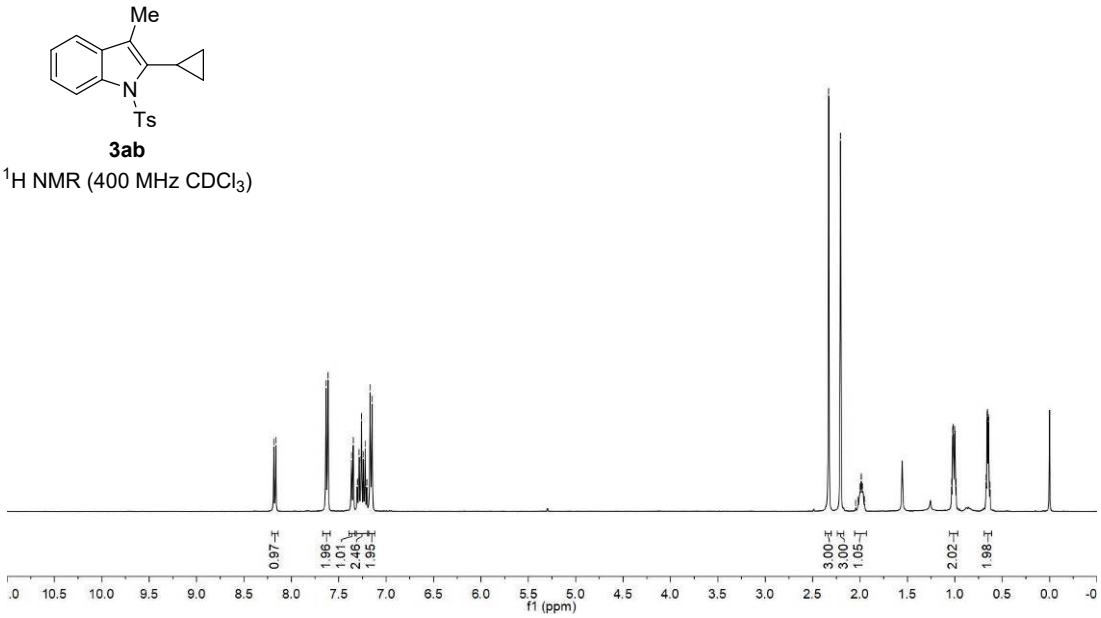
3aa

^{1}H NMR (400 MHz $CDCl_3$)



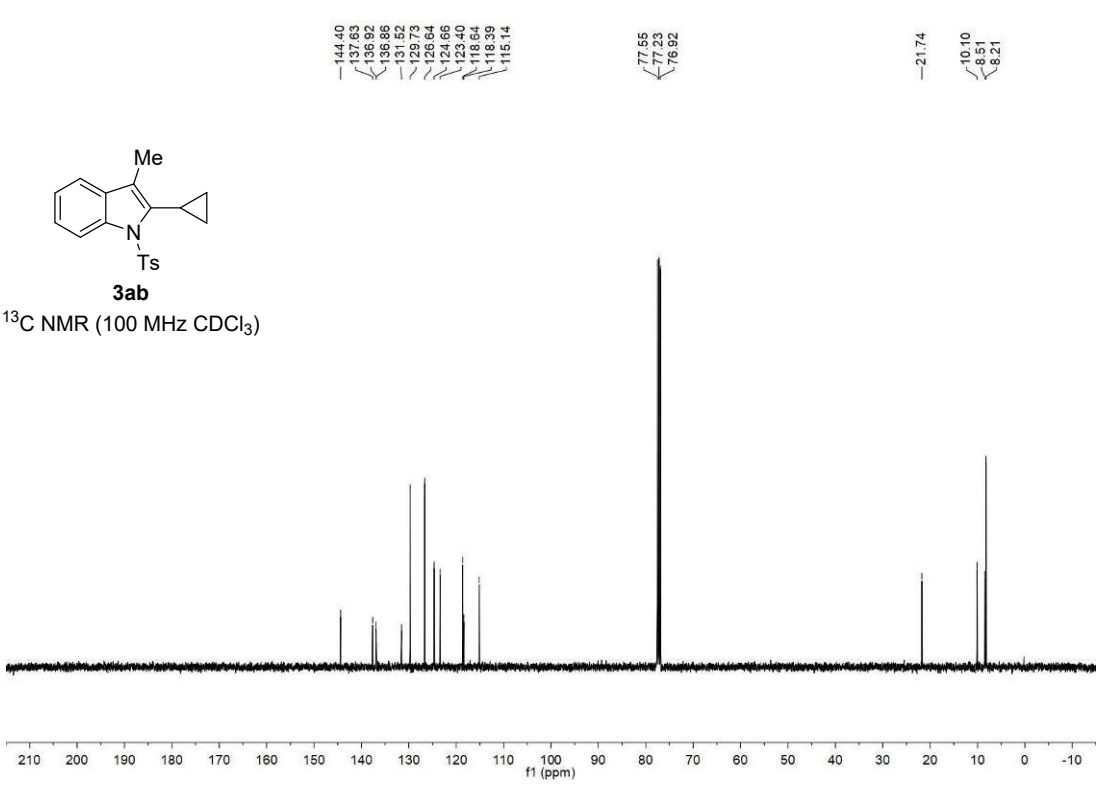
3aa

^{13}C NMR (100 MHz $CDCl_3$)



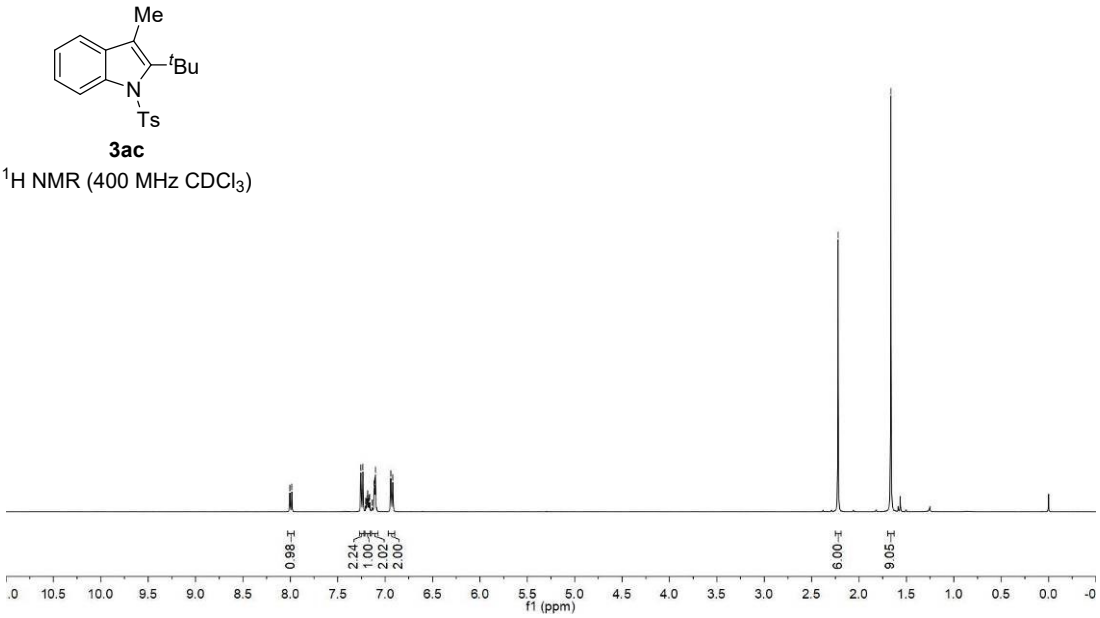
3ab

^{1}H NMR (400 MHz $CDCl_3$)



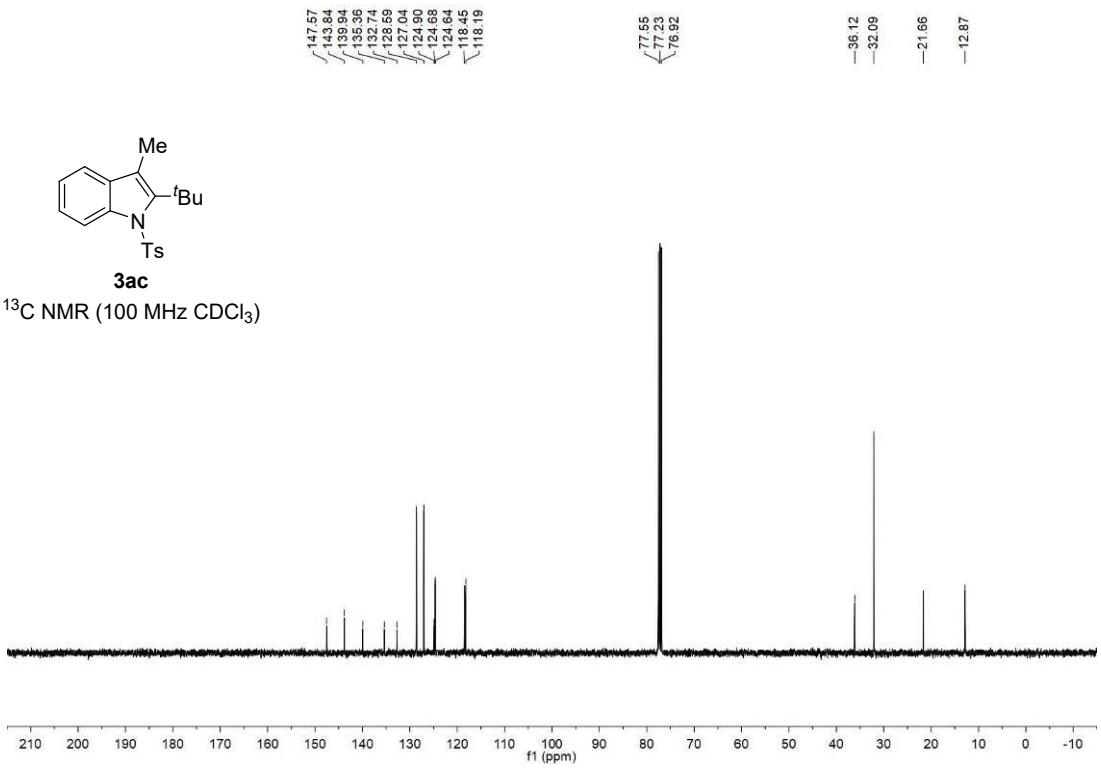
3ab

^{13}C NMR (100 MHz $CDCl_3$)



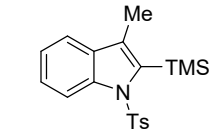
3ac

^{1}H NMR (400 MHz $CDCl_3$)



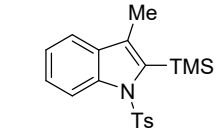
3ac

^{13}C NMR (100 MHz $CDCl_3$)



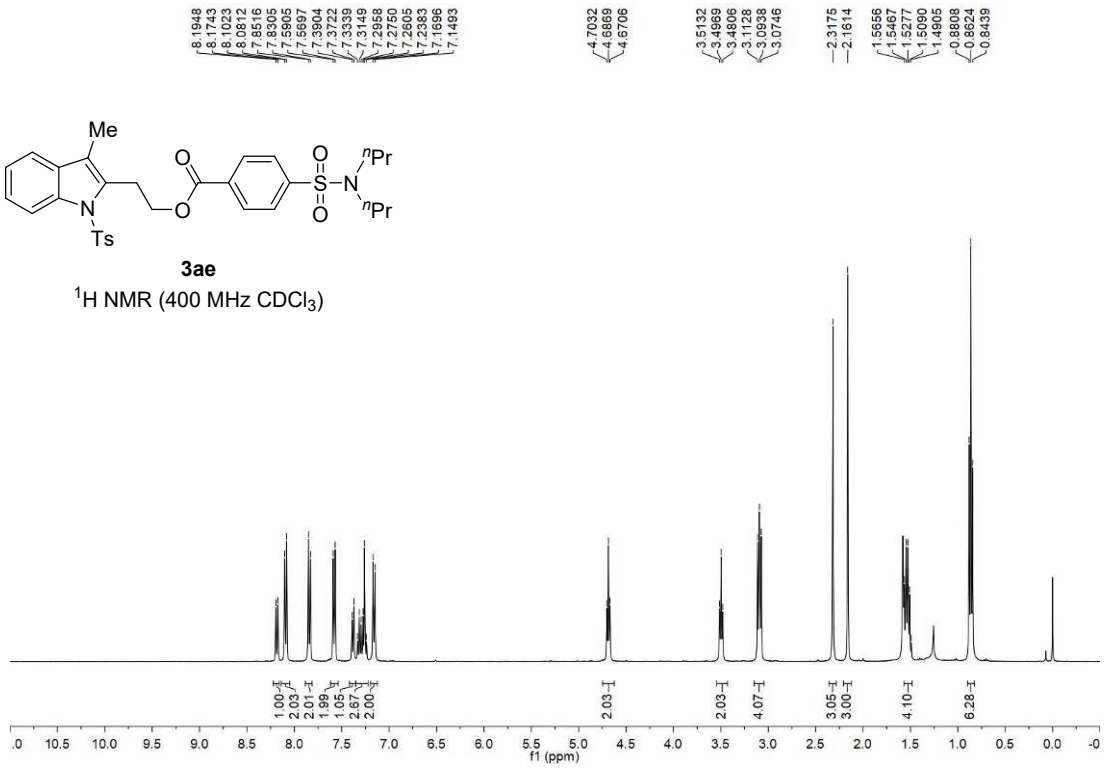
3ad

^{1}H NMR (400 MHz $CDCl_3$)



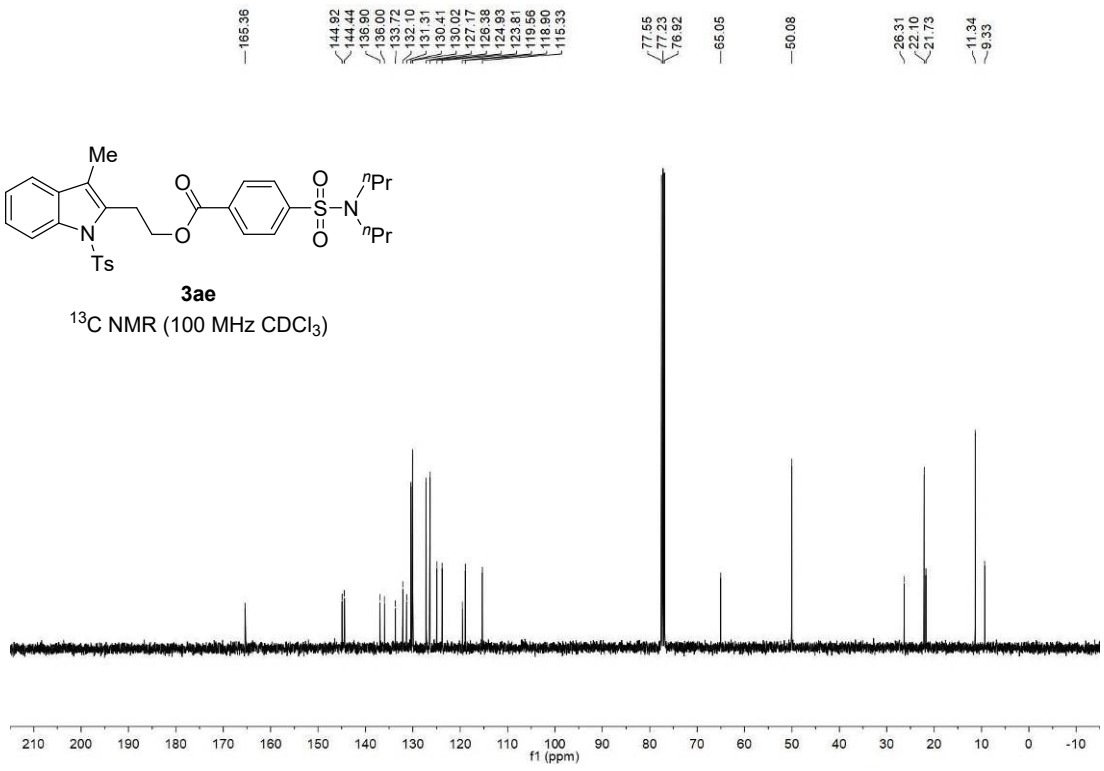
3ad

^{13}C NMR (100 MHz $CDCl_3$)



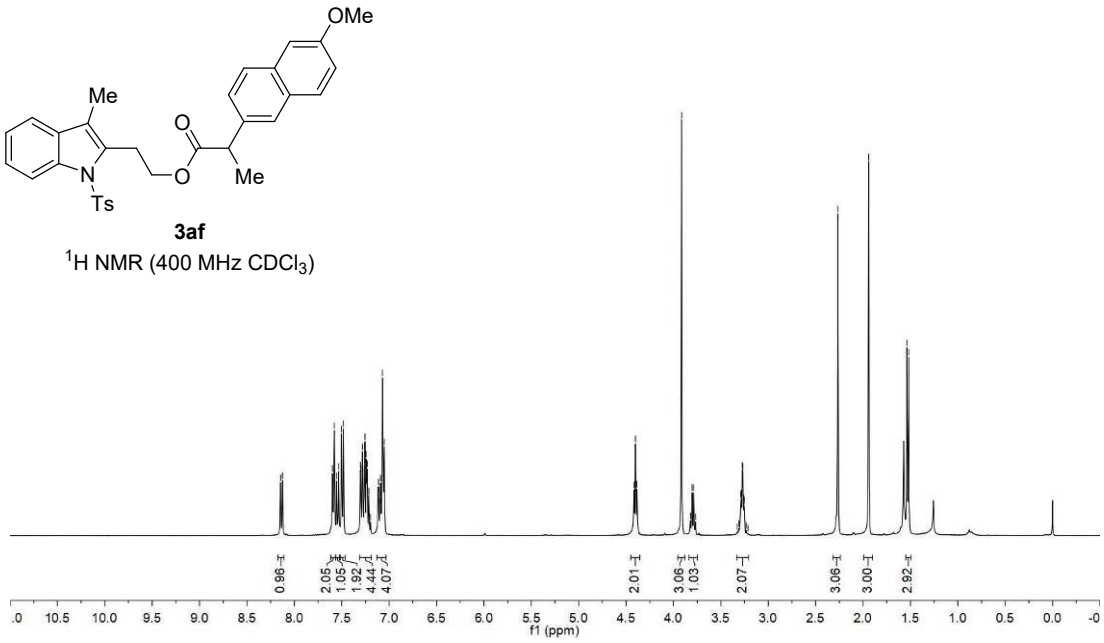
3ae

^{1}H NMR (400 MHz $CDCl_3$)



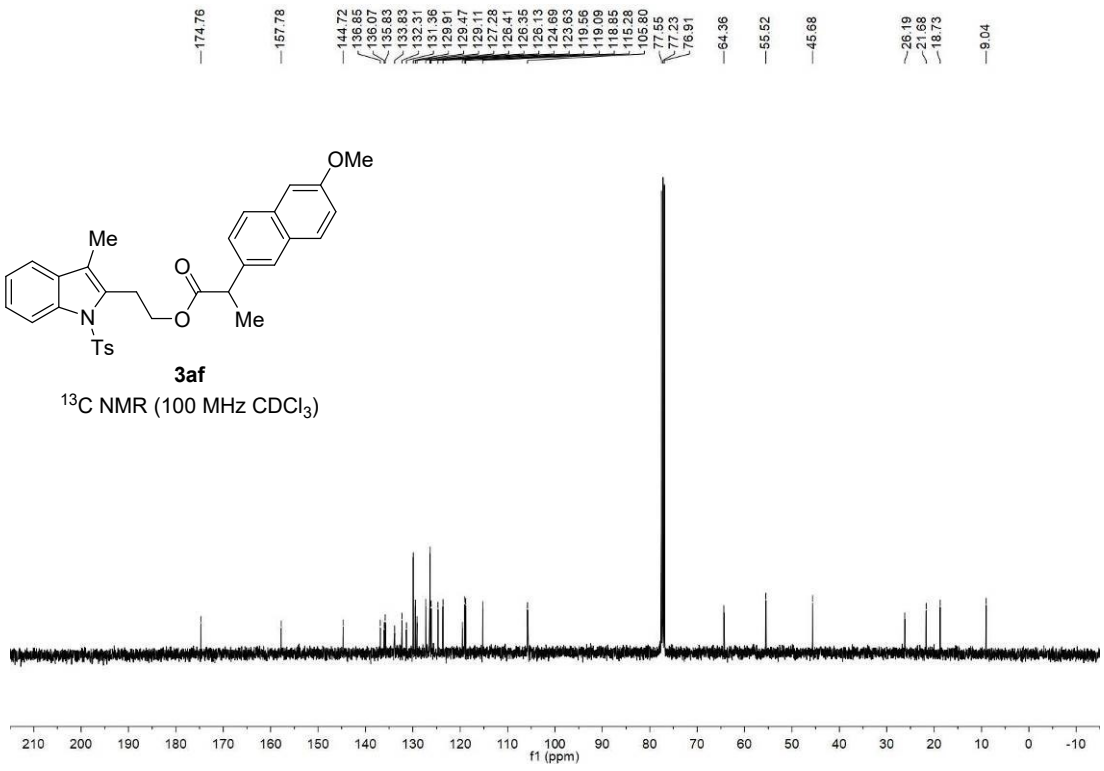
3ae

^{13}C NMR (100 MHz $CDCl_3$)



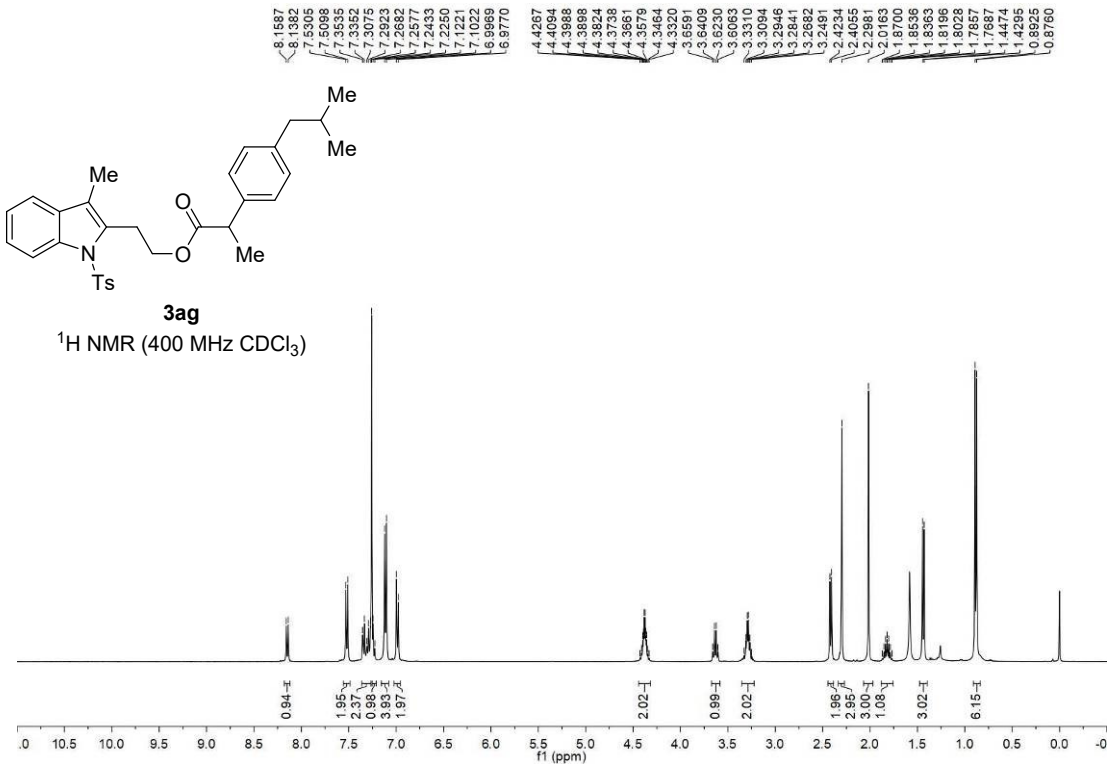
3af

^{1}H NMR (400 MHz $CDCl_3$)



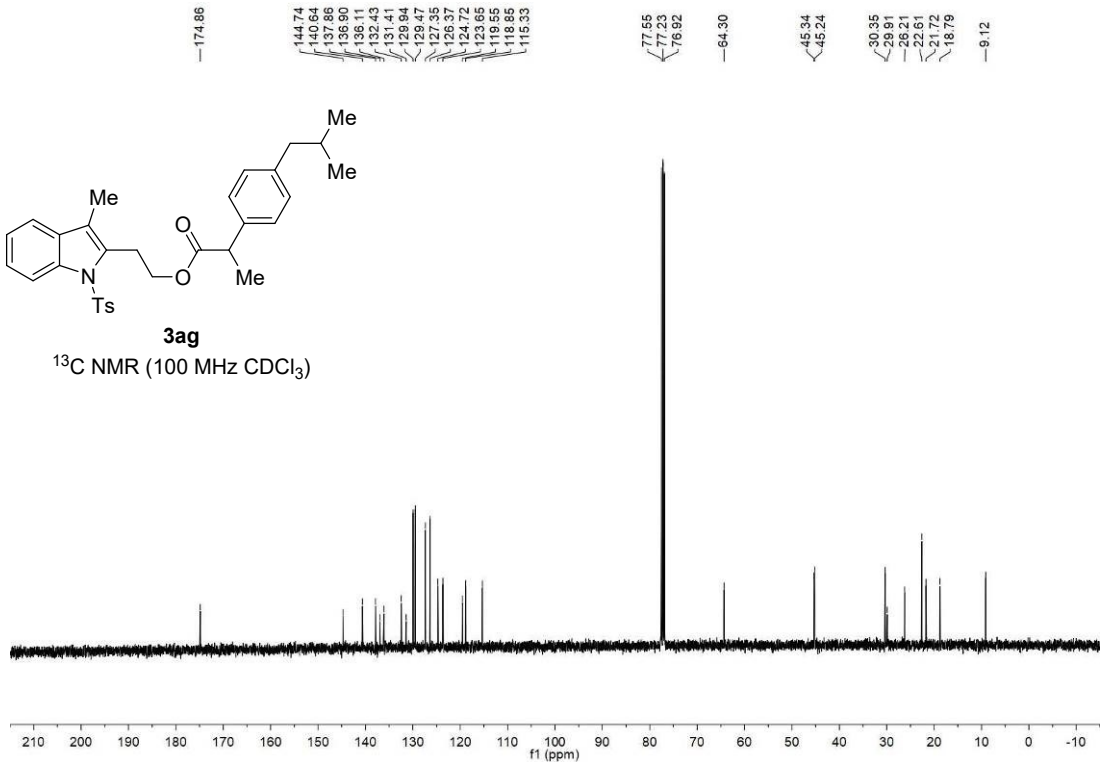
3af

^{13}C NMR (100 MHz $CDCl_3$)



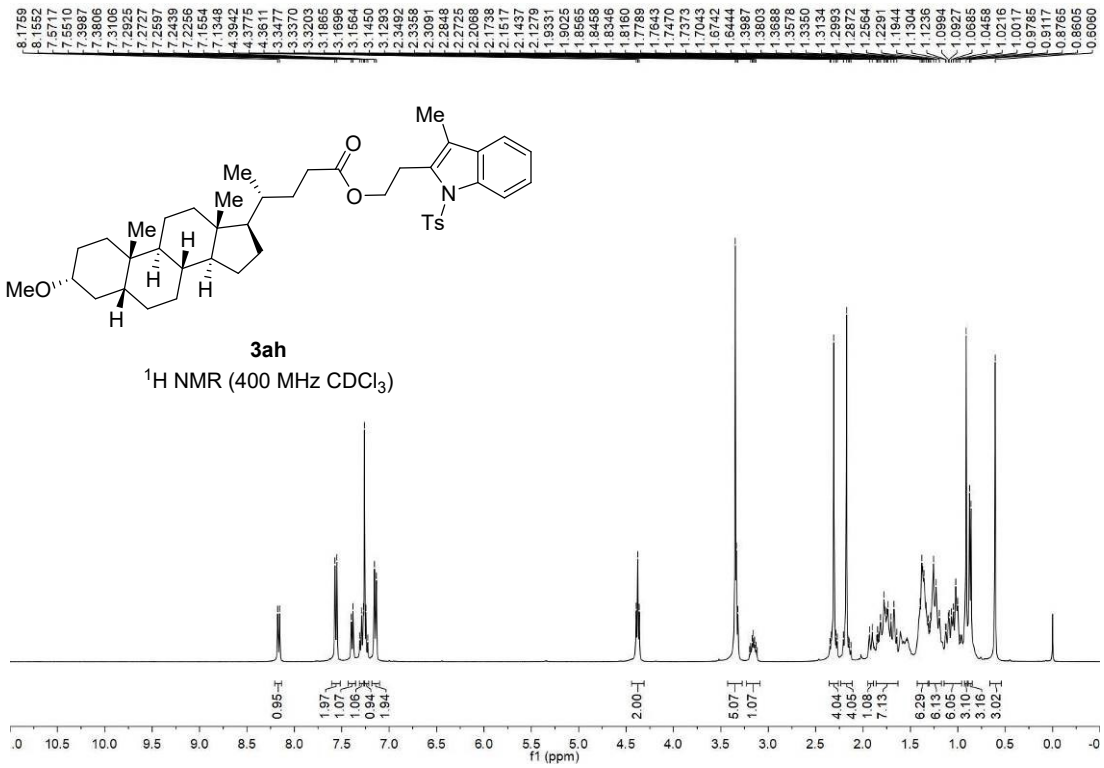
3ag

^{1}H NMR (400 MHz $CDCl_3$)



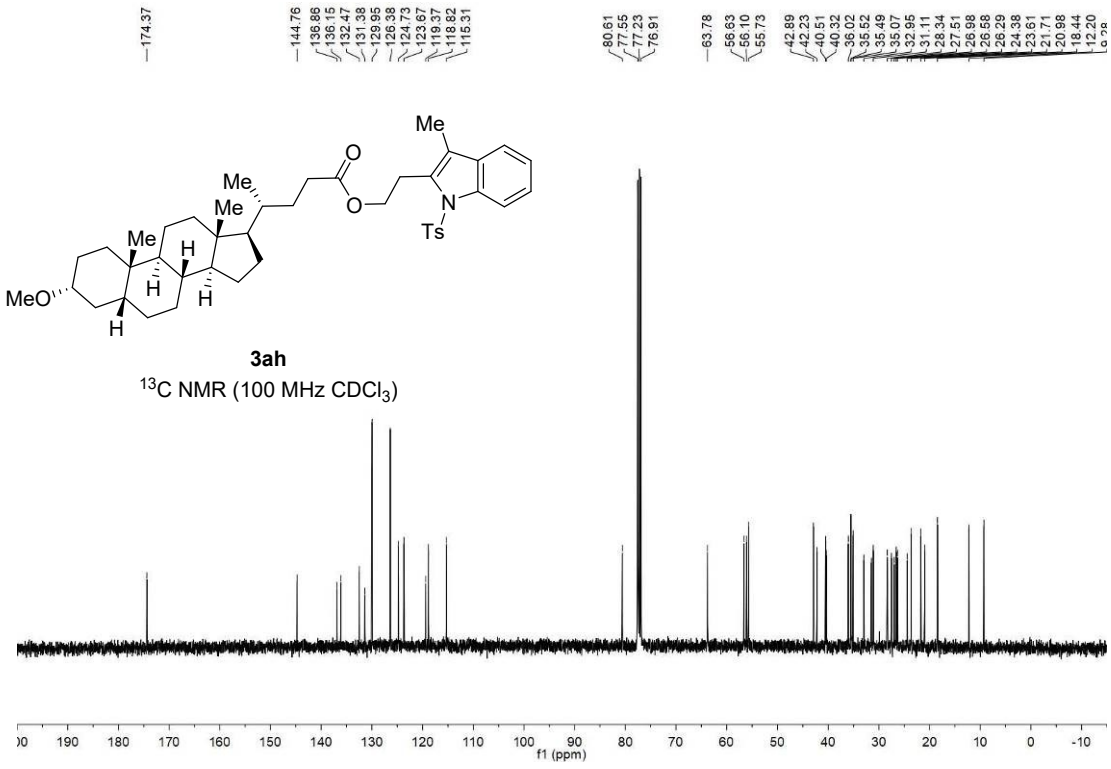
3ag

^{13}C NMR (100 MHz $CDCl_3$)



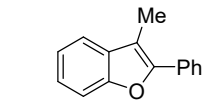
3ah

^{1}H NMR (400 MHz $CDCl_3$)



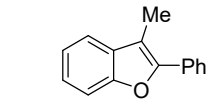
3ah

^{13}C NMR (100 MHz $CDCl_3$)



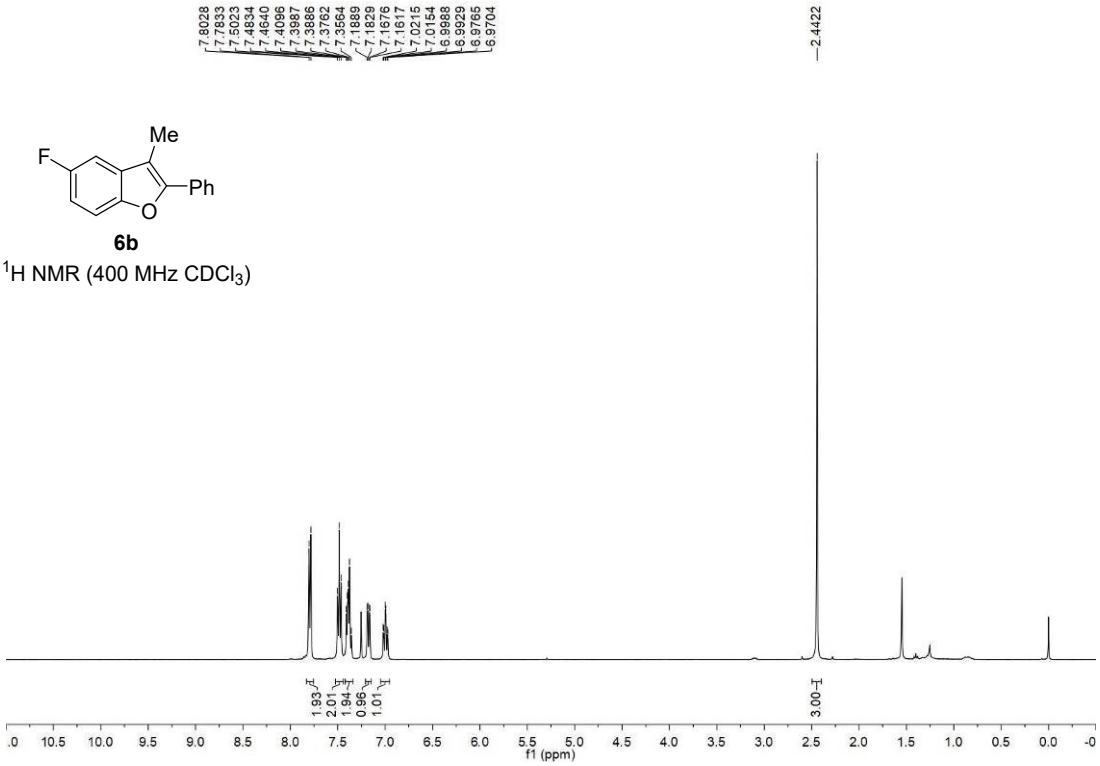
6a

^{1}H NMR (400 MHz $CDCl_3$)



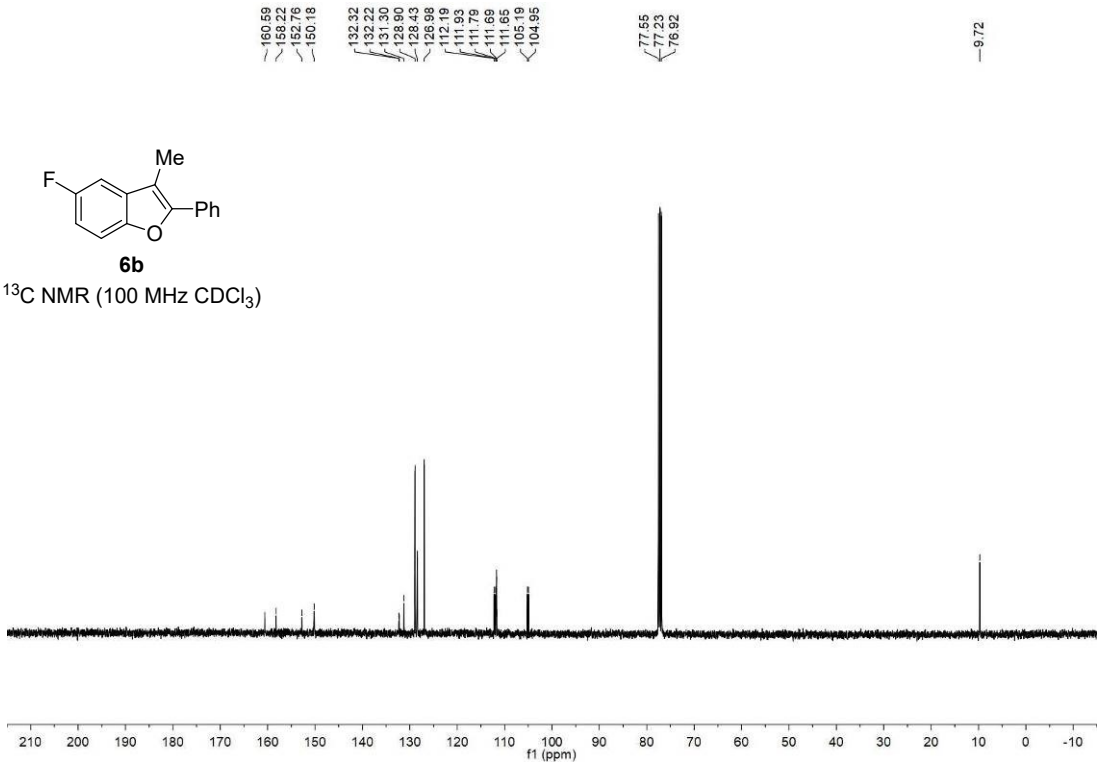
6a

^{13}C NMR (100 MHz $CDCl_3$)



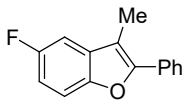
6b

^{1}H NMR (400 MHz $CDCl_3$)



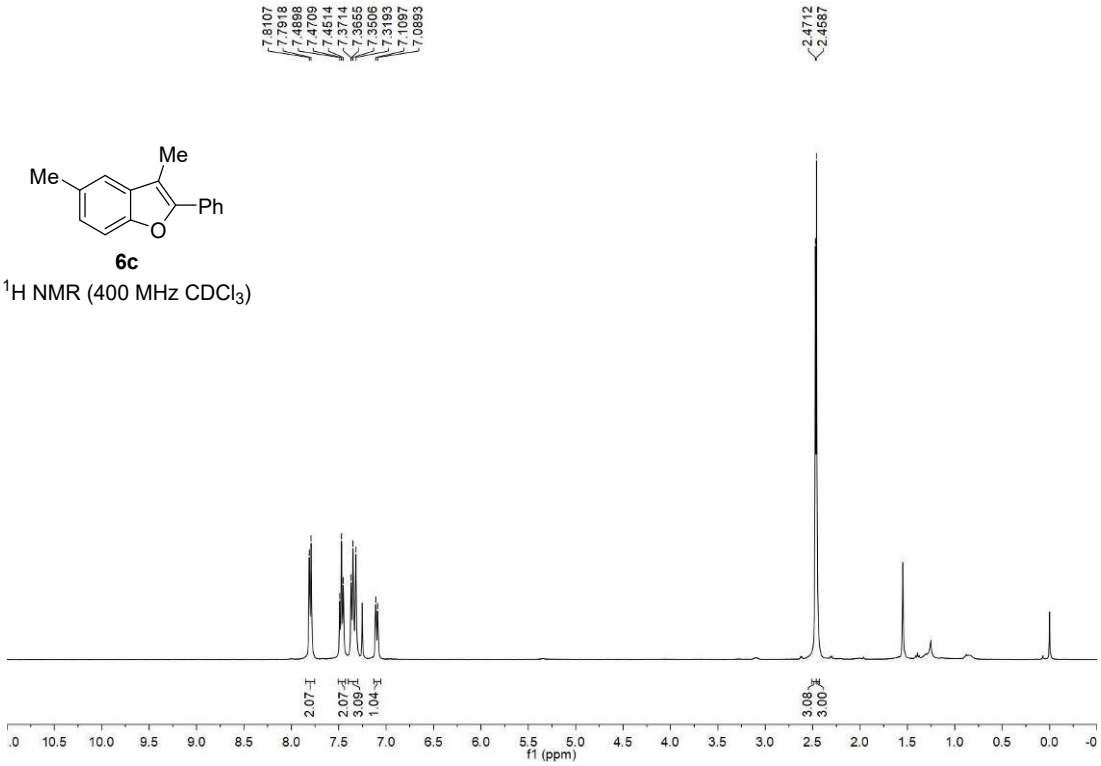
6b

^{13}C NMR (100 MHz $CDCl_3$)



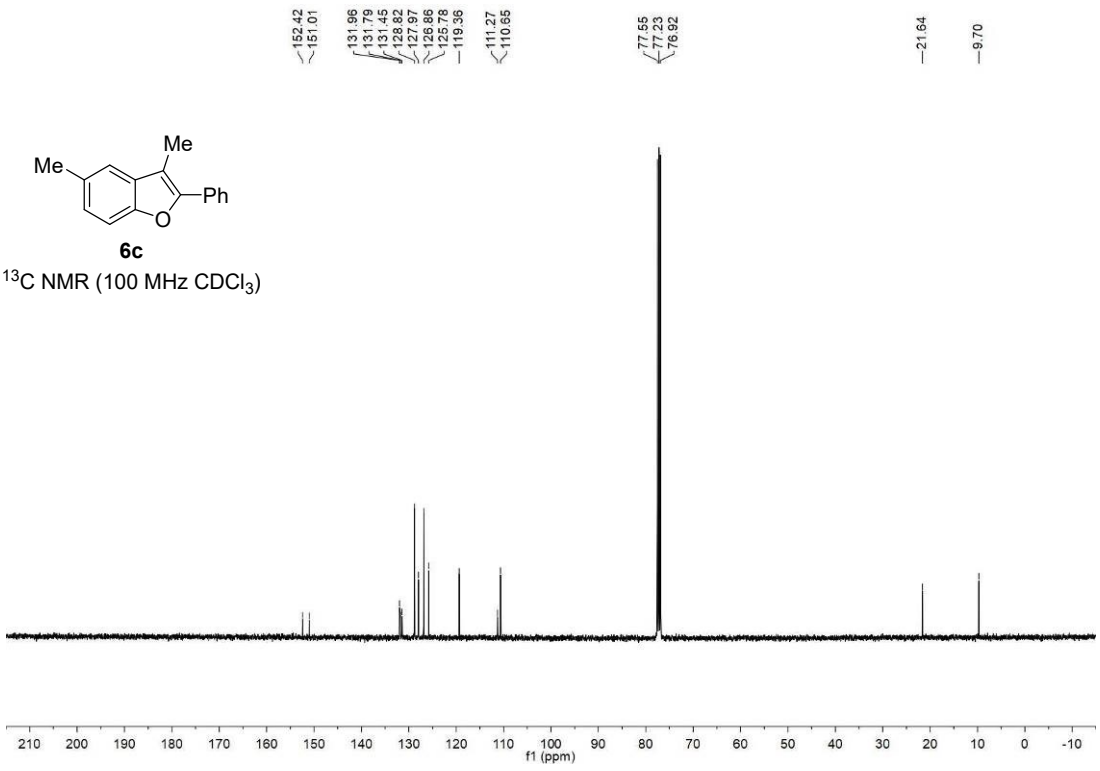
6b

^{19}F NMR (376 MHz $CDCl_3$)



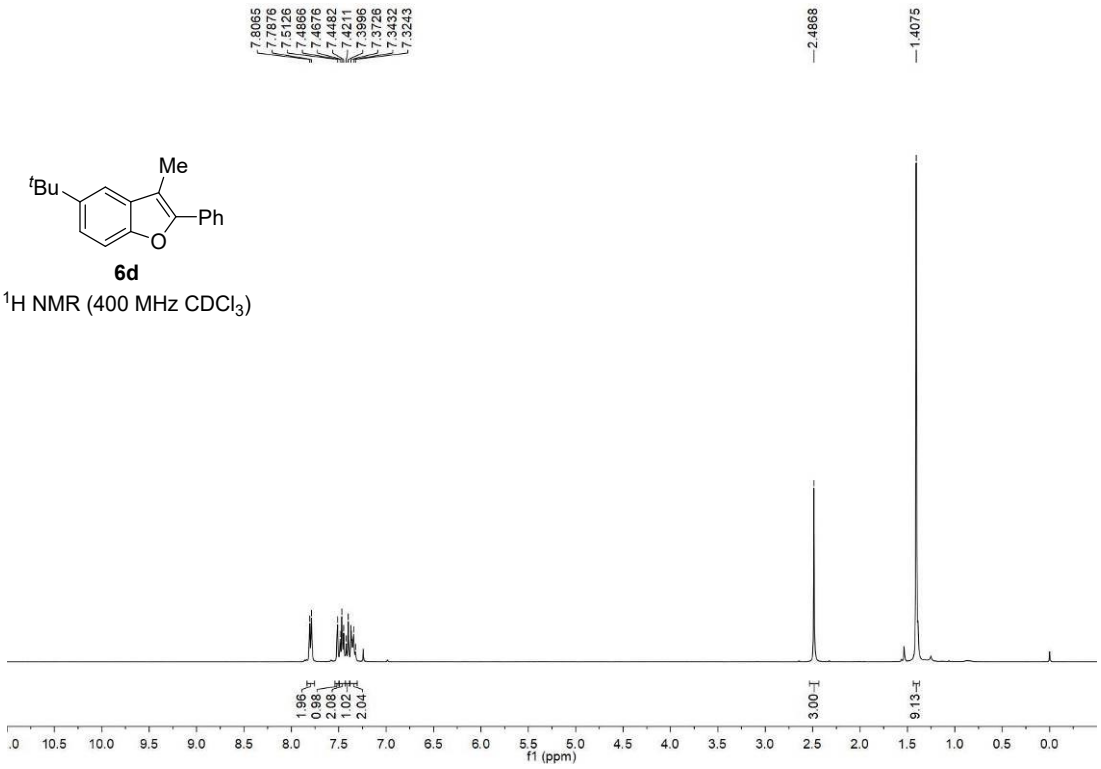
6c

^{1}H NMR (400 MHz $CDCl_3$)



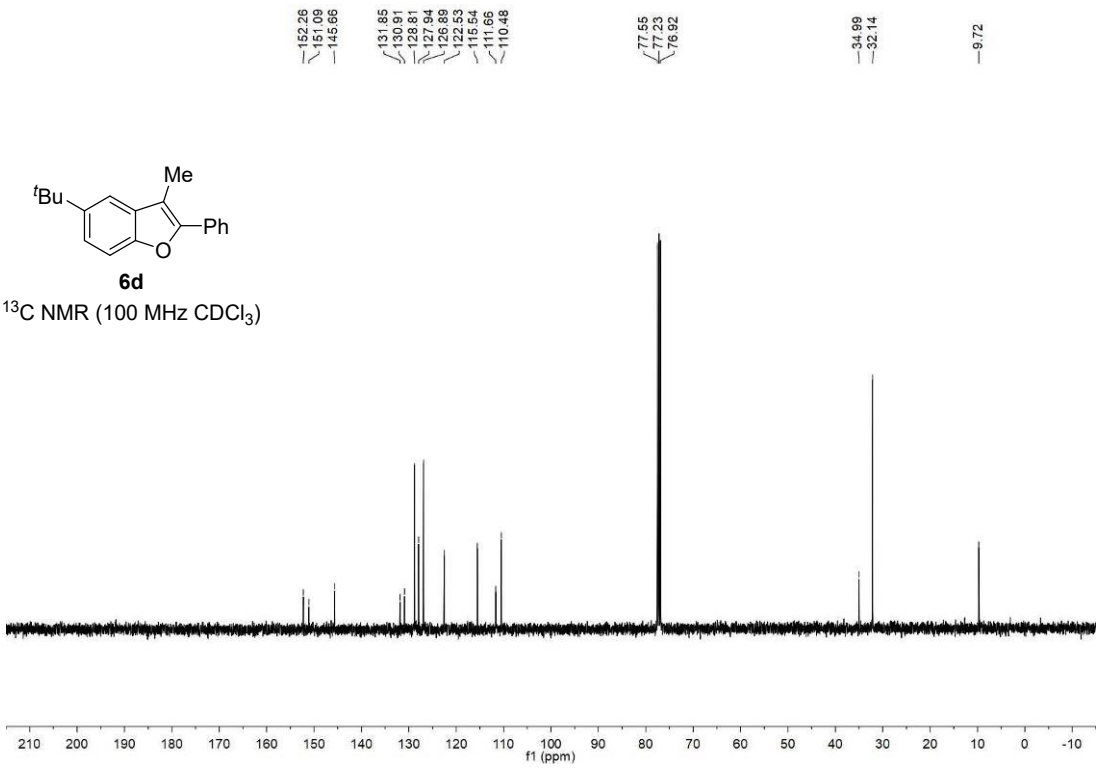
6c

^{13}C NMR (100 MHz $CDCl_3$)



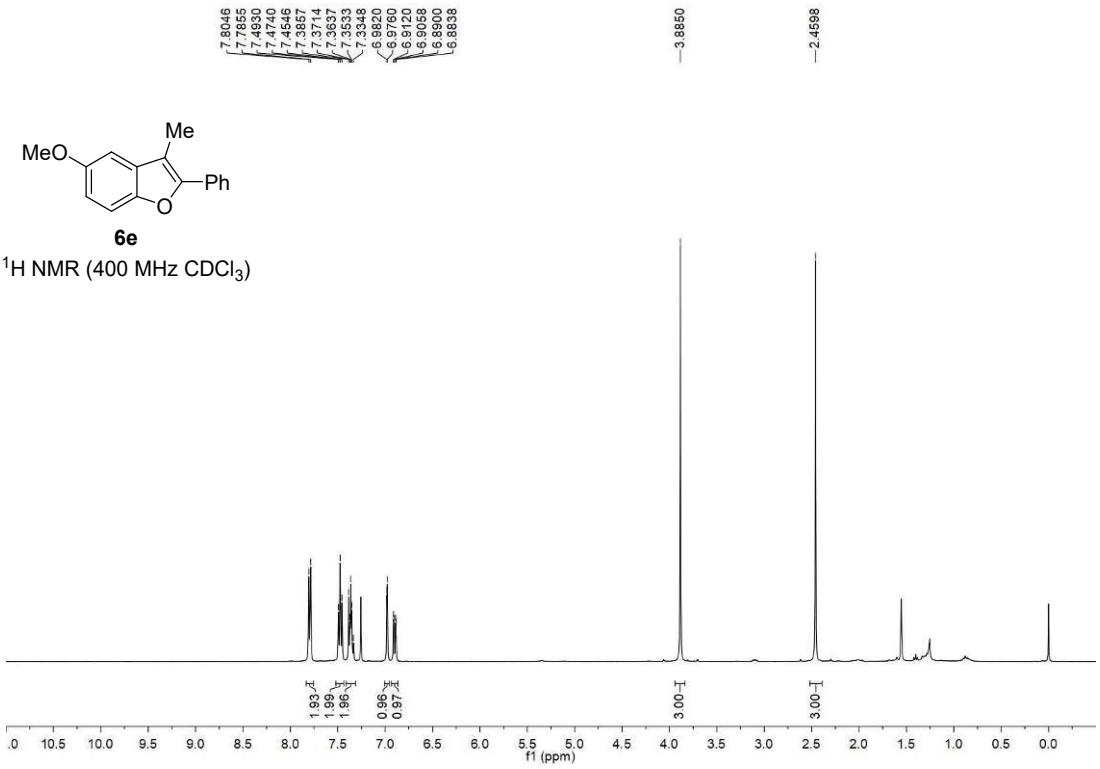
6d

^{1}H NMR (400 MHz $CDCl_3$)



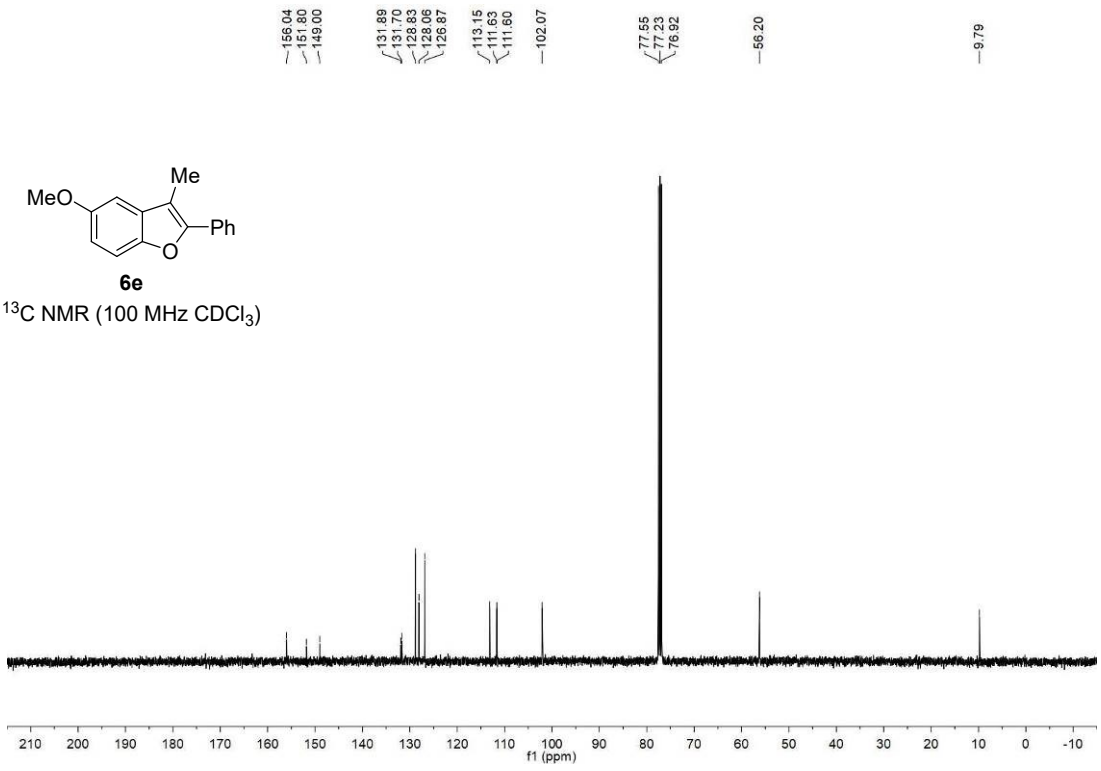
6d

^{13}C NMR (100 MHz $CDCl_3$)



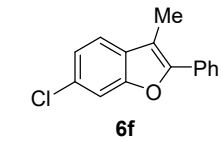
6e

^{1}H NMR (400 MHz $CDCl_3$)



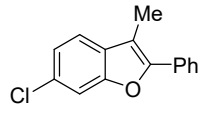
6e

^{13}C NMR (100 MHz $CDCl_3$)



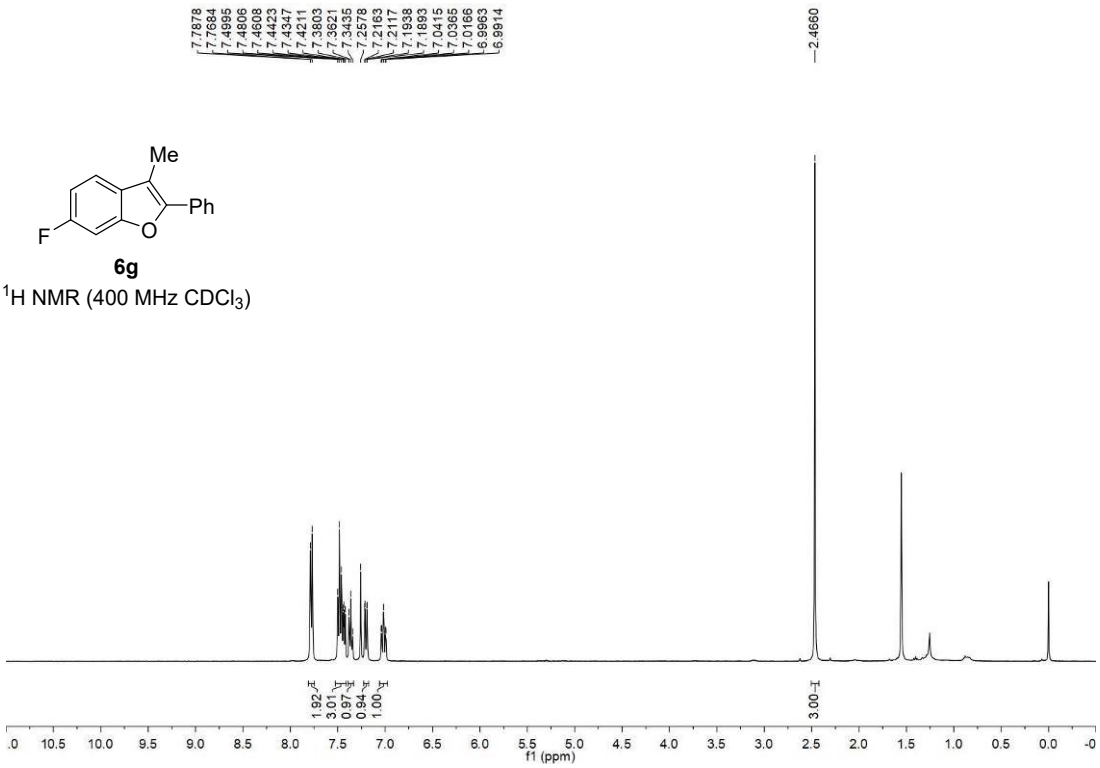
6f

^{1}H NMR (400 MHz $CDCl_3$)



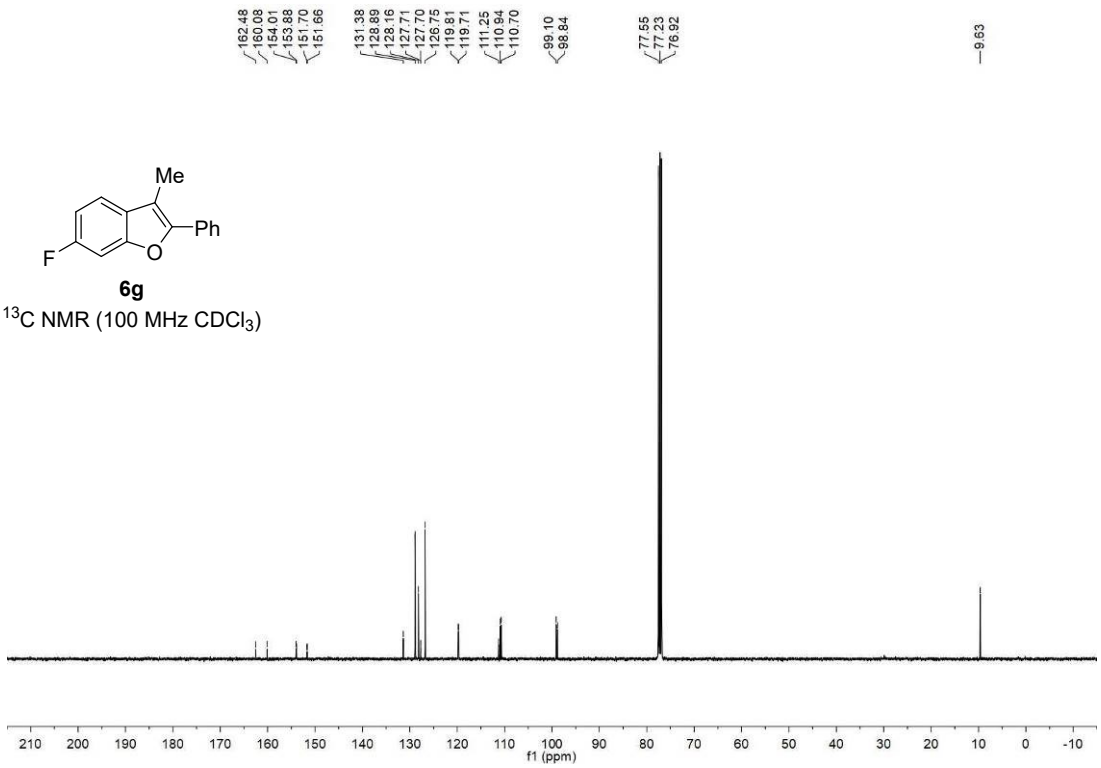
6f

^{13}C NMR (100 MHz $CDCl_3$)



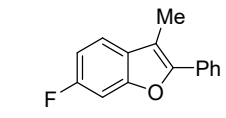
6g

^{1}H NMR (400 MHz $CDCl_3$)



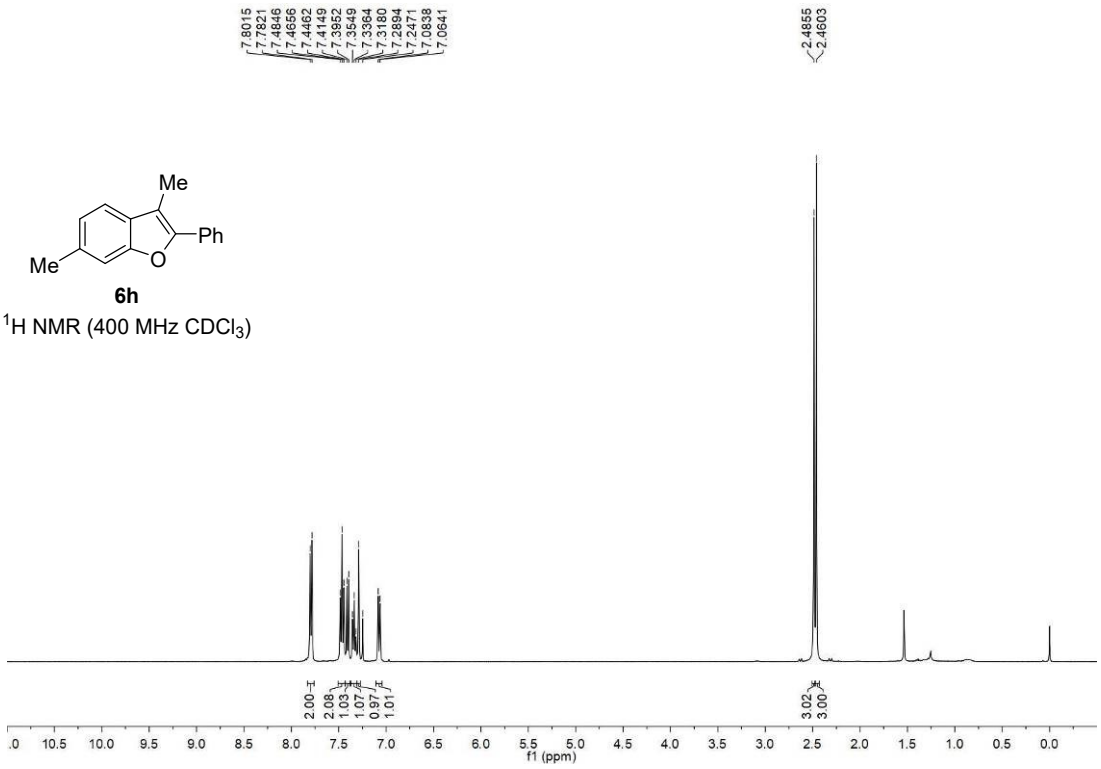
6g

^{13}C NMR (100 MHz $CDCl_3$)



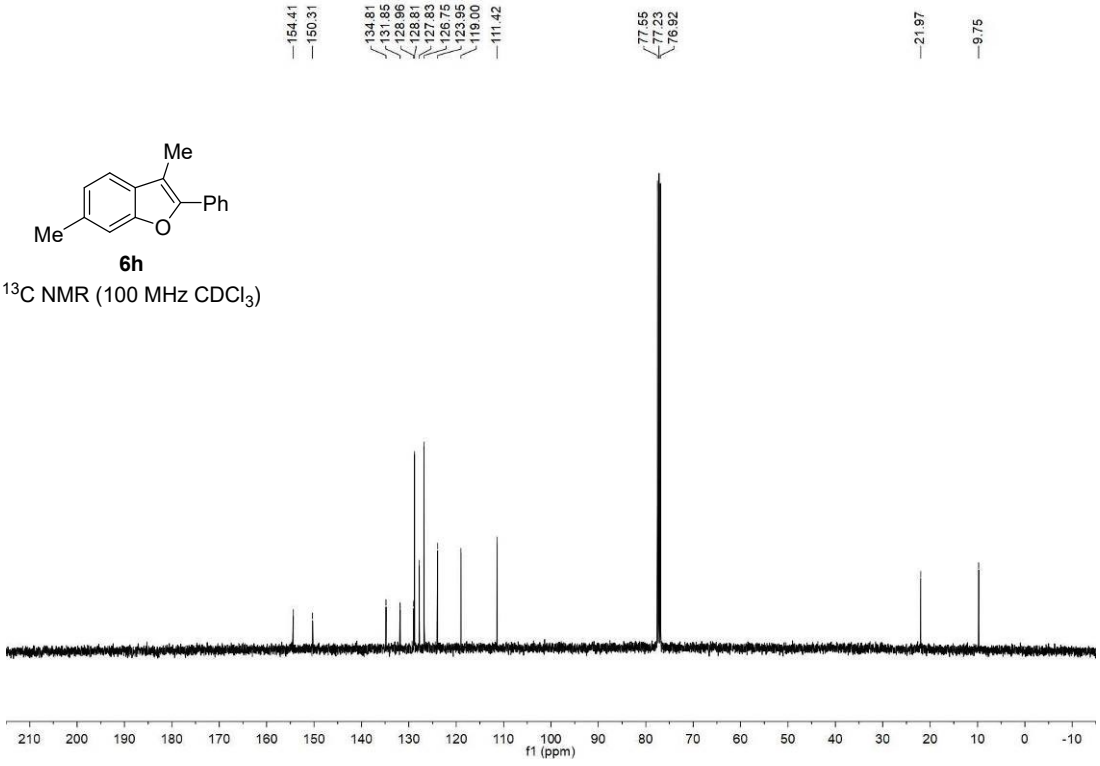
6g

^{19}F NMR (376 MHz $CDCl_3$)



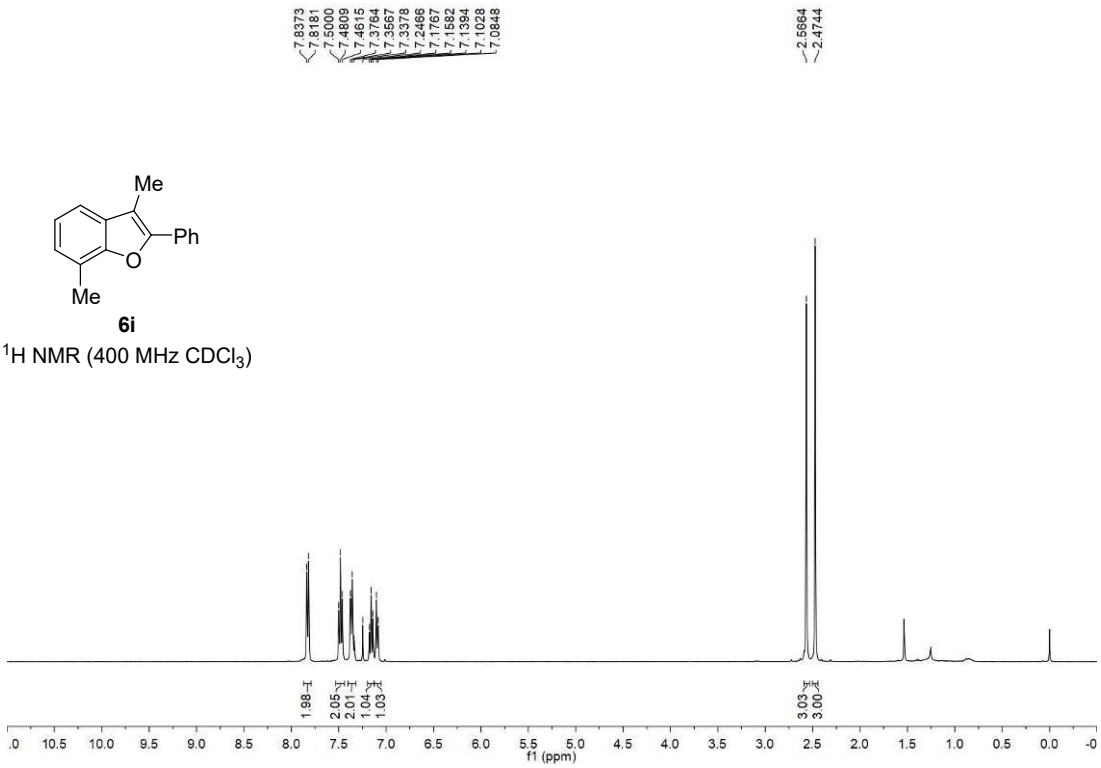
6h

^{1}H NMR (400 MHz $CDCl_3$)



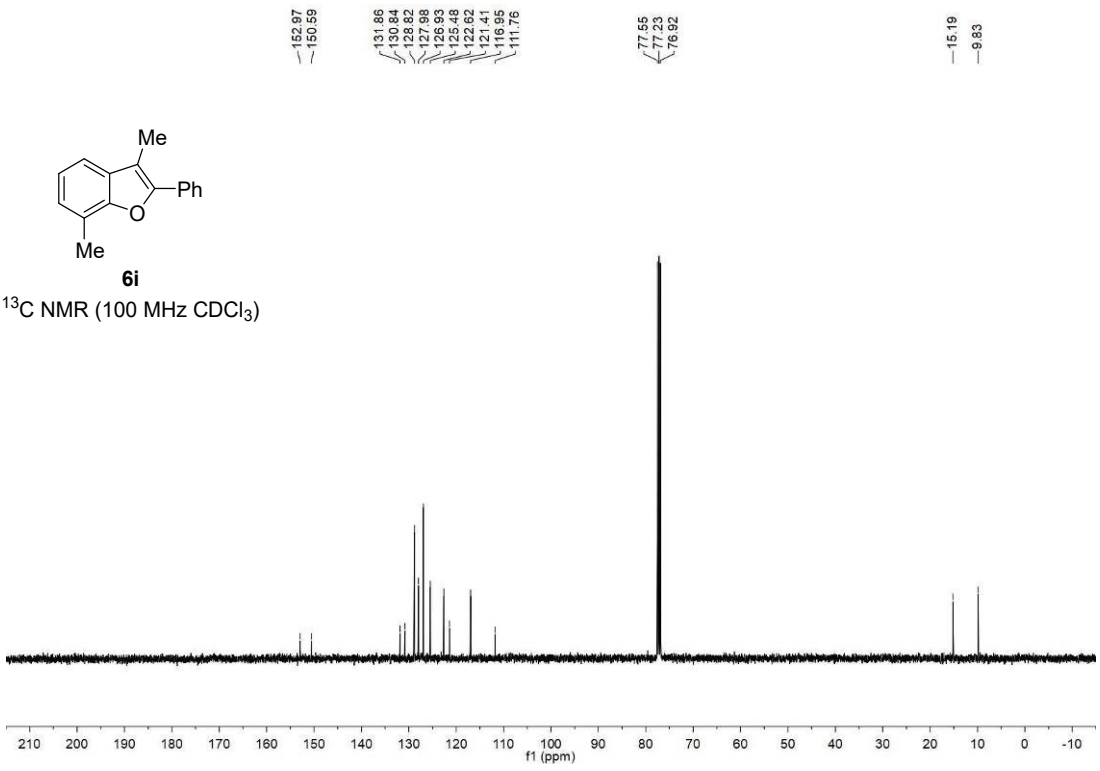
6h

^{13}C NMR (100 MHz $CDCl_3$)



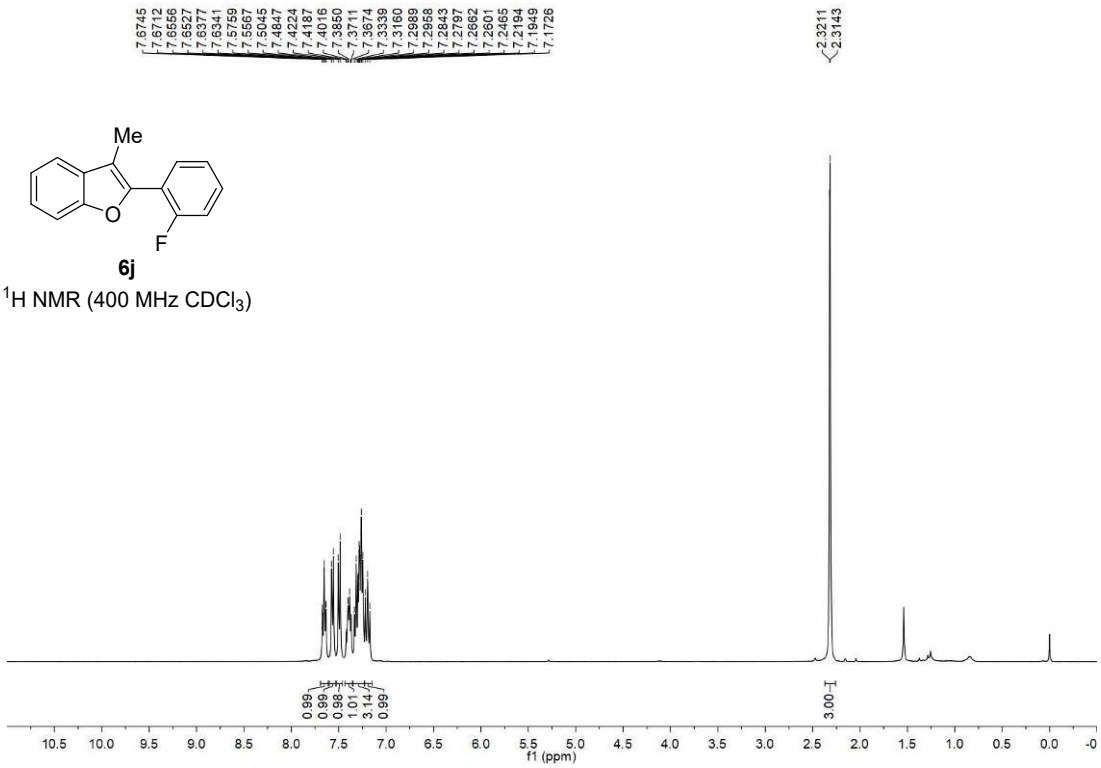
6i

^{1}H NMR (400 MHz $CDCl_3$)



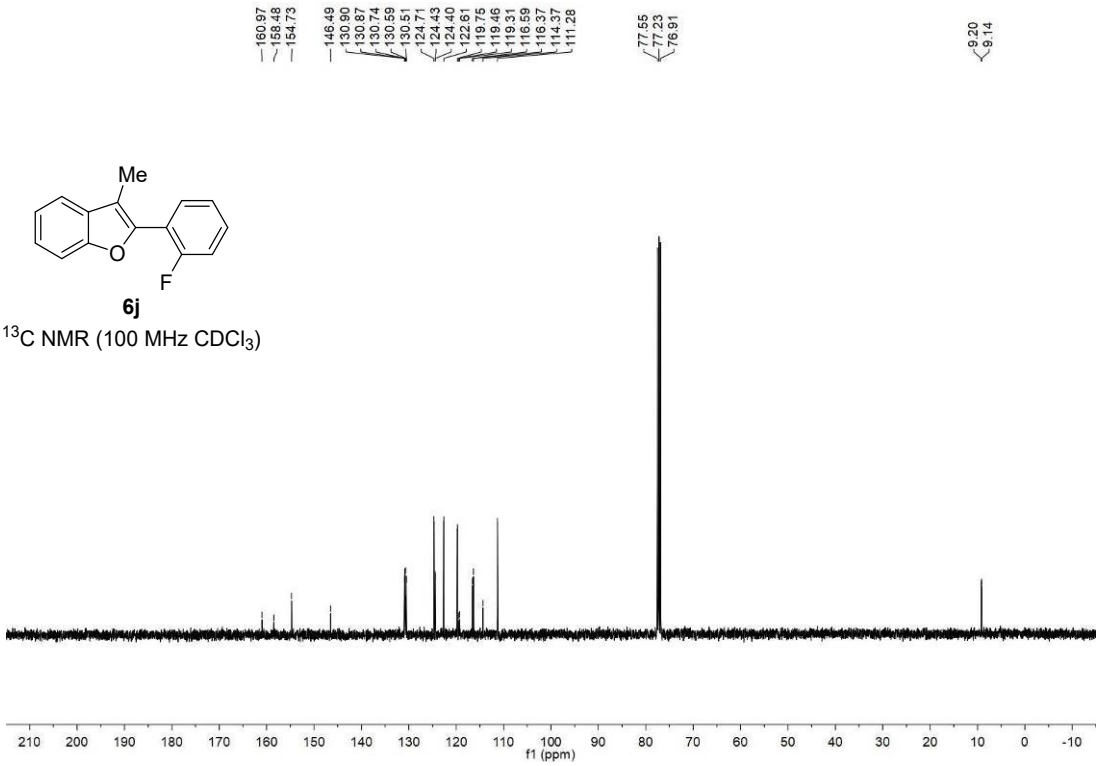
6i

^{13}C NMR (100 MHz $CDCl_3$)



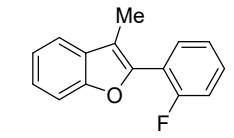
6j

^{1}H NMR (400 MHz $CDCl_3$)



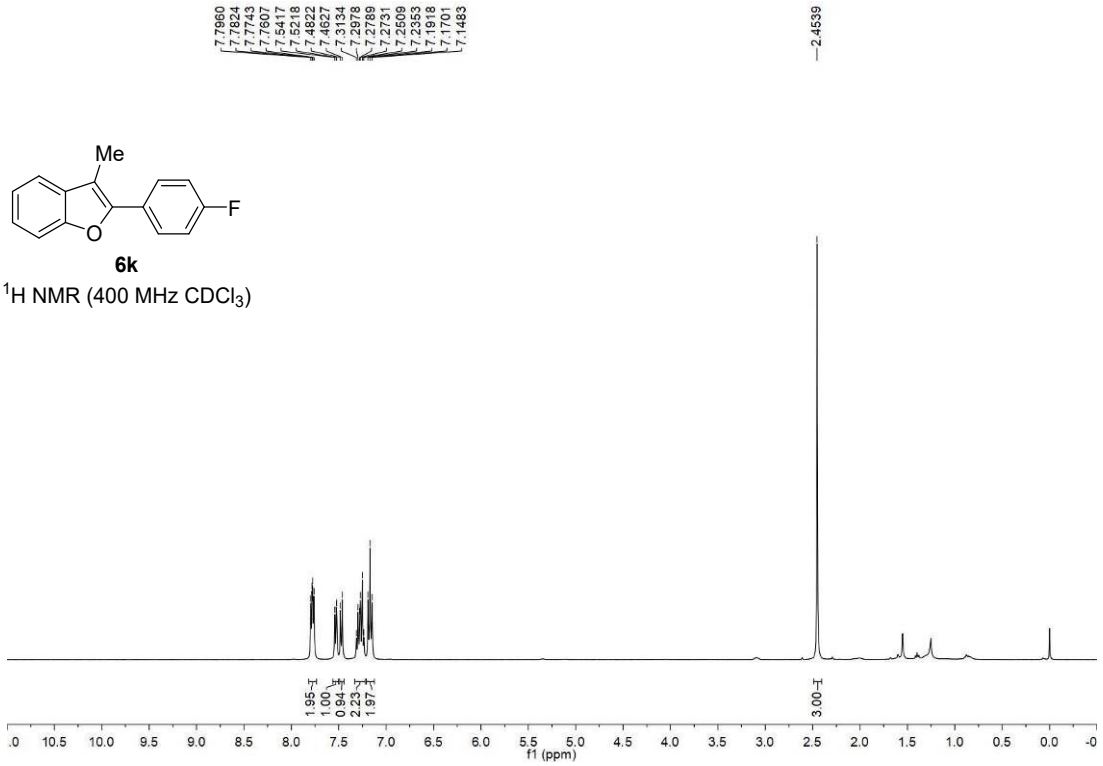
6j

^{13}C NMR (100 MHz $CDCl_3$)



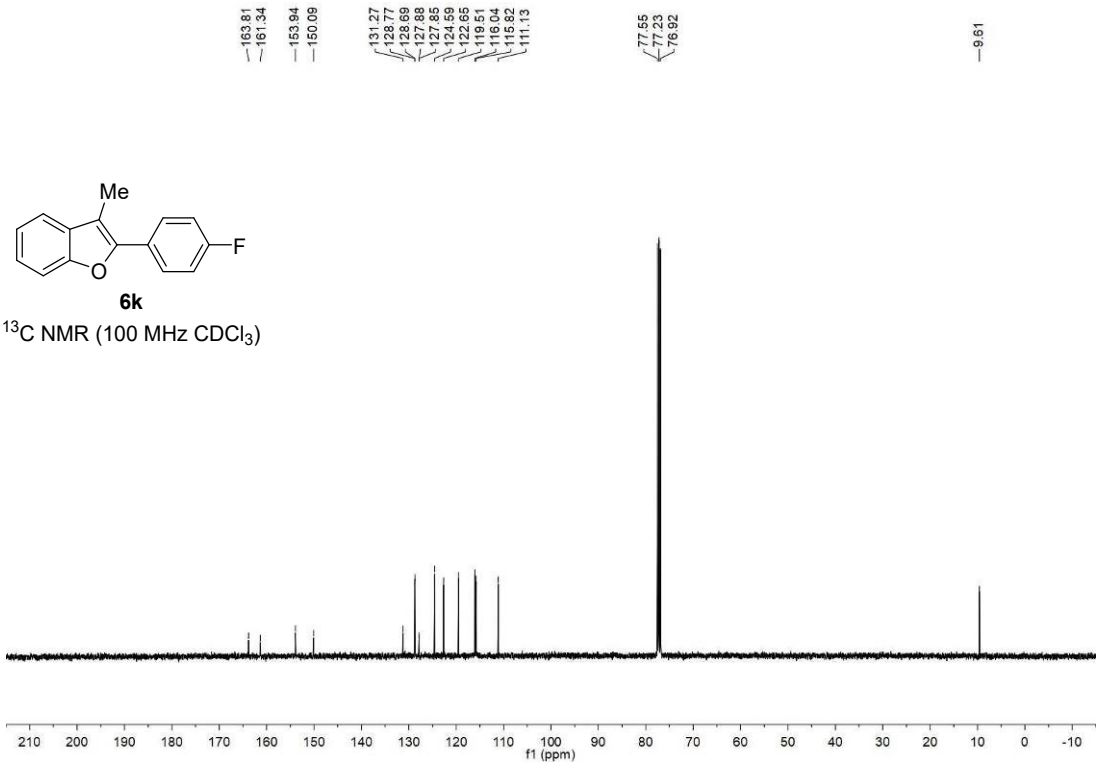
6j

^{19}F NMR (376 MHz $CDCl_3$)



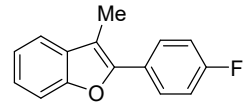
6k

^{1}H NMR (400 MHz $CDCl_3$)



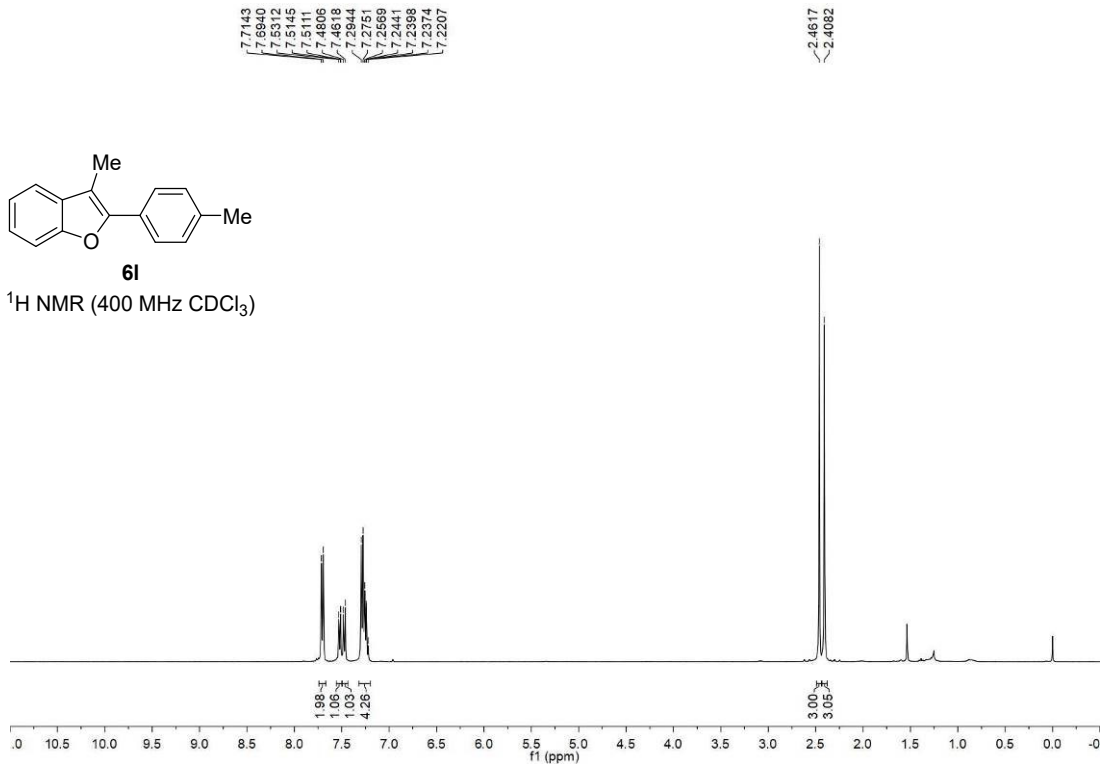
6k

^{13}C NMR (100 MHz $CDCl_3$)



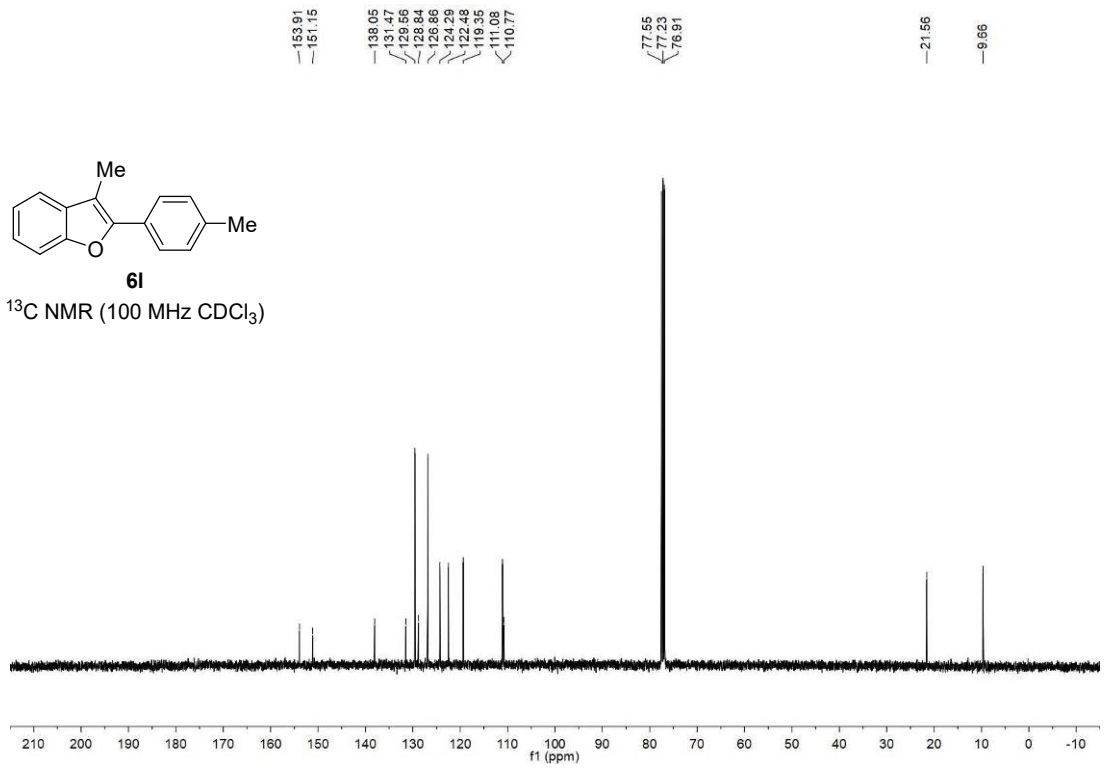
6k

^{19}F NMR (376 MHz $CDCl_3$)



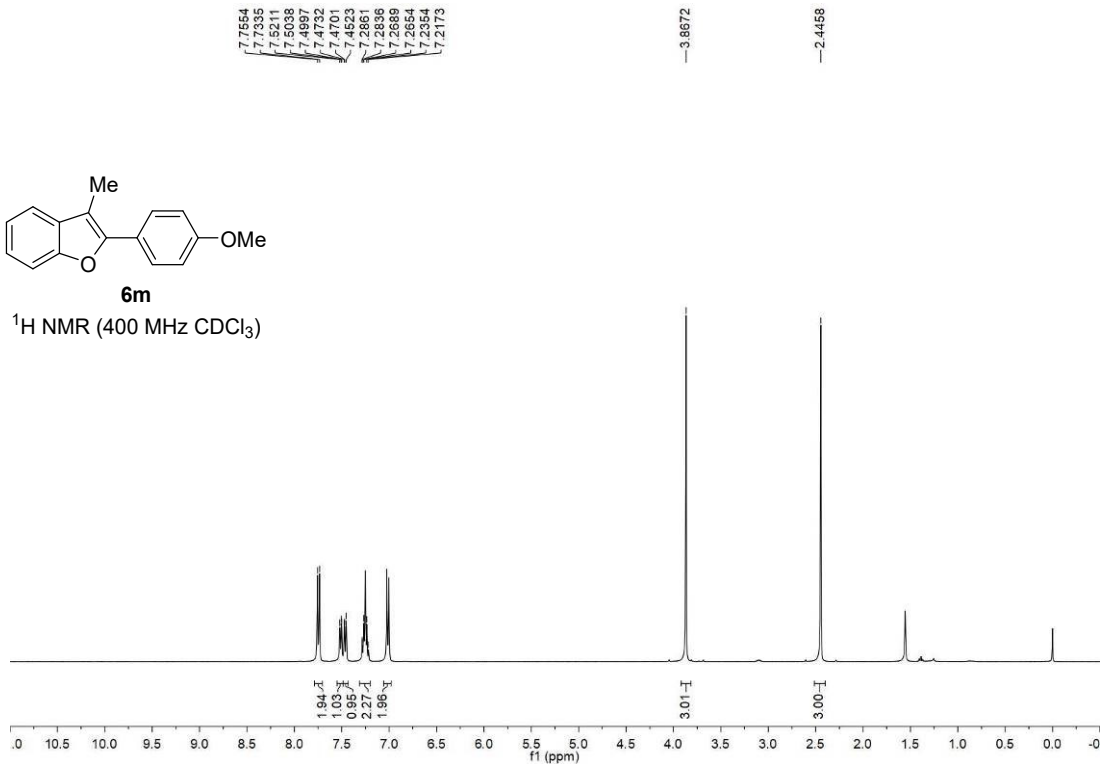
6l

^{1}H NMR (400 MHz $CDCl_3$)



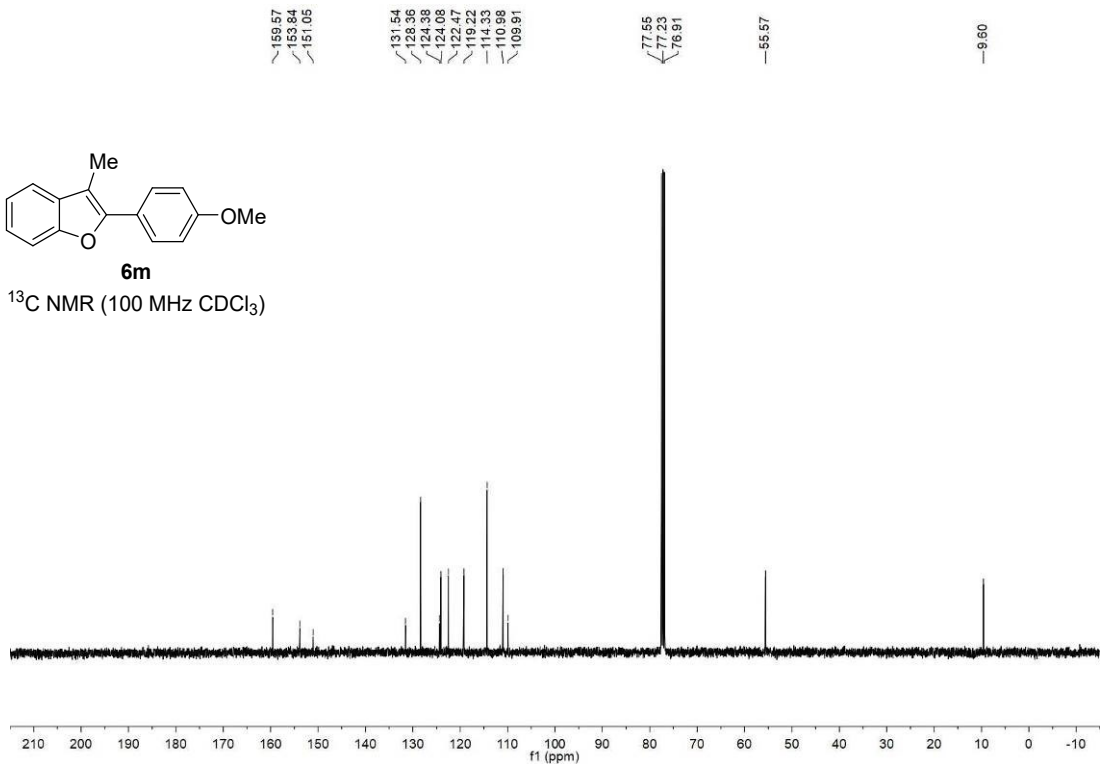
6l

^{13}C NMR (100 MHz $CDCl_3$)



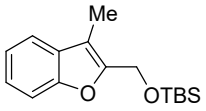
6m

^{1}H NMR (400 MHz $CDCl_3$)



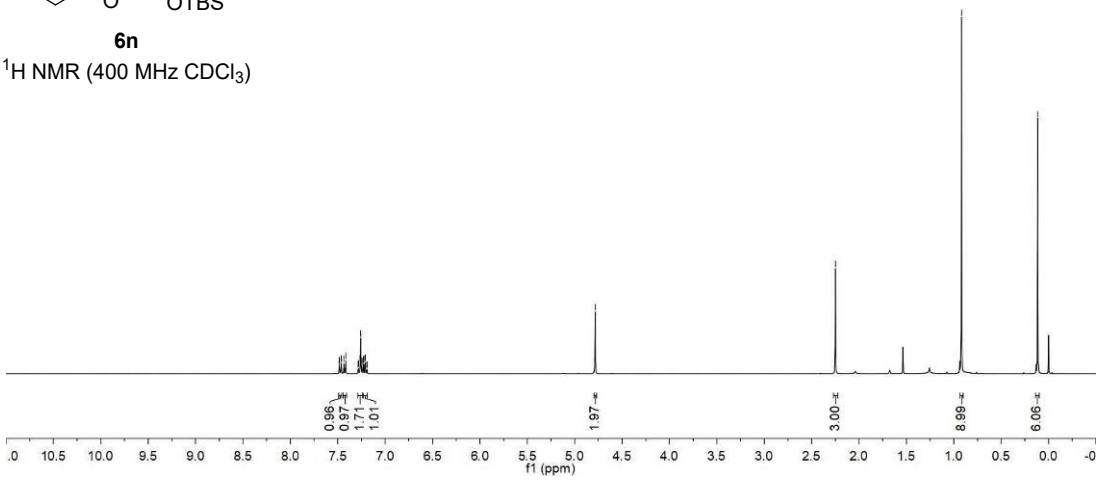
6m

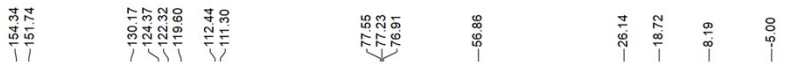
^{13}C NMR (100 MHz $CDCl_3$)

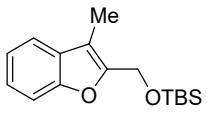


6n

^{1}H NMR (400 MHz $CDCl_3$)

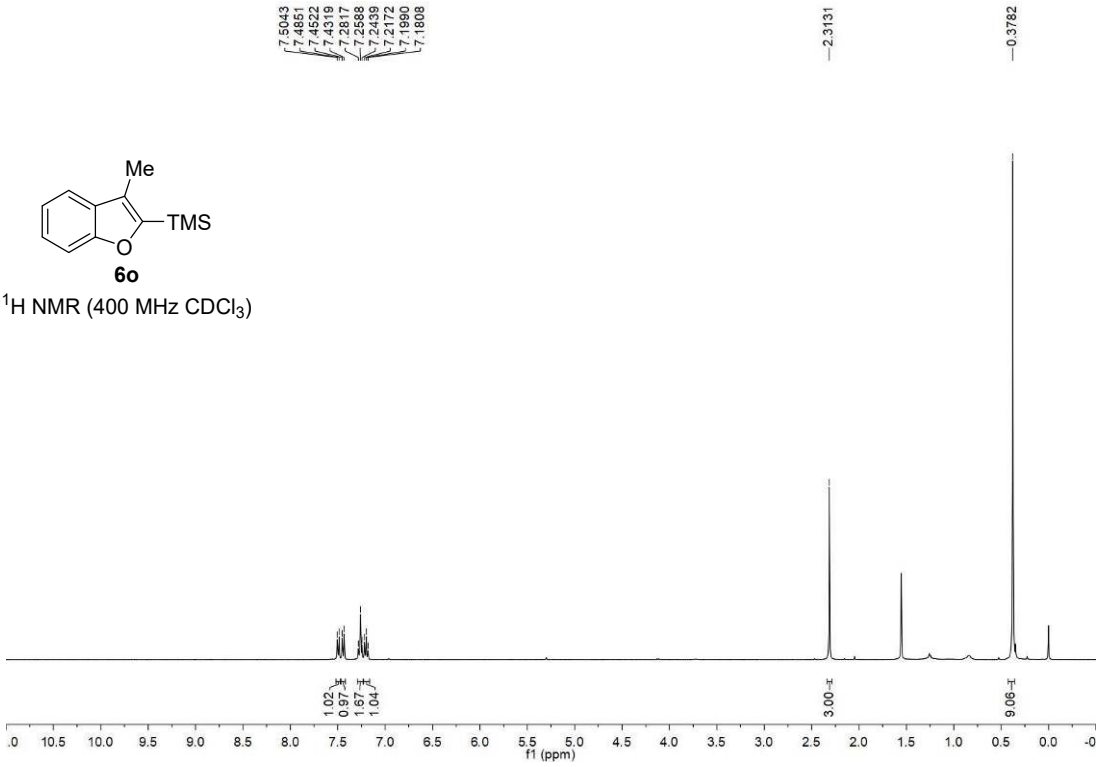






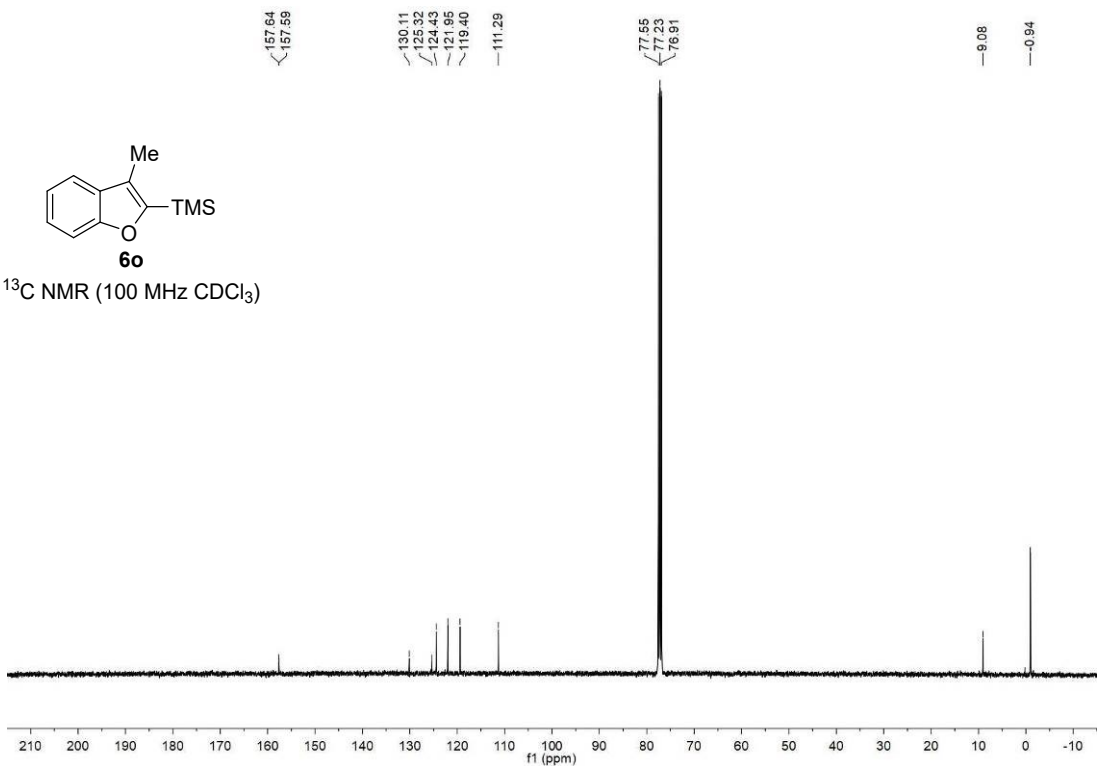
6n

^{13}C NMR (100 MHz $CDCl_3$)



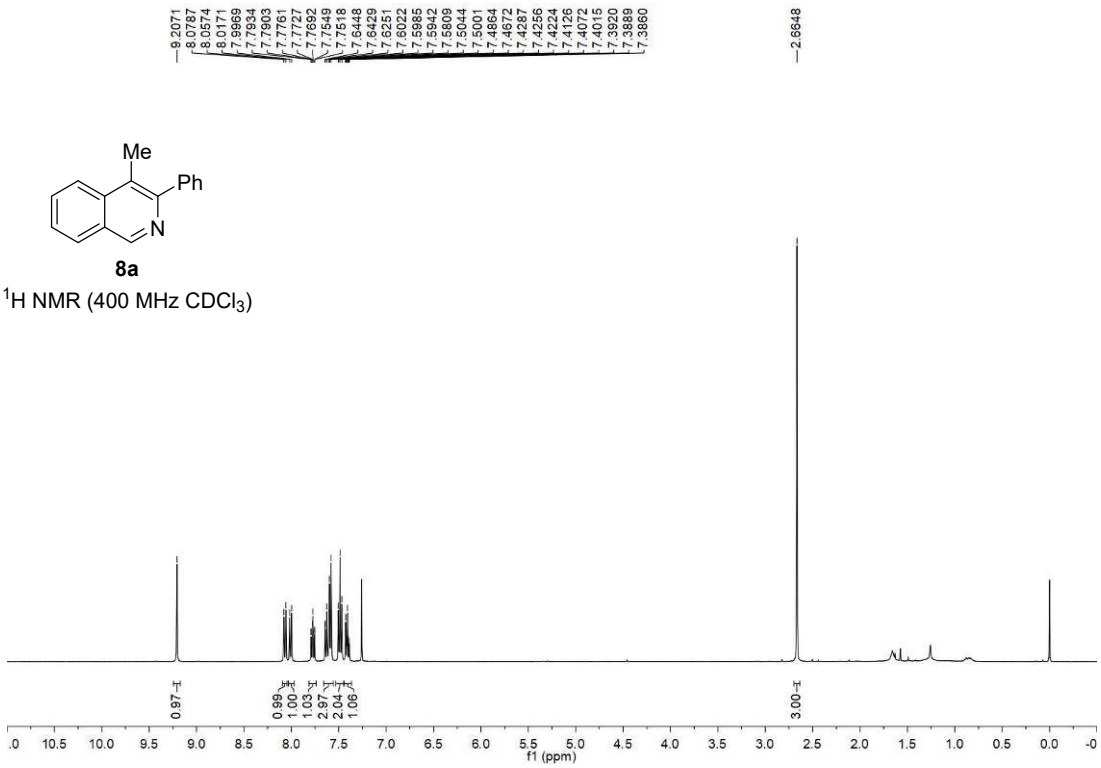
6o

^{1}H NMR (400 MHz $CDCl_3$)



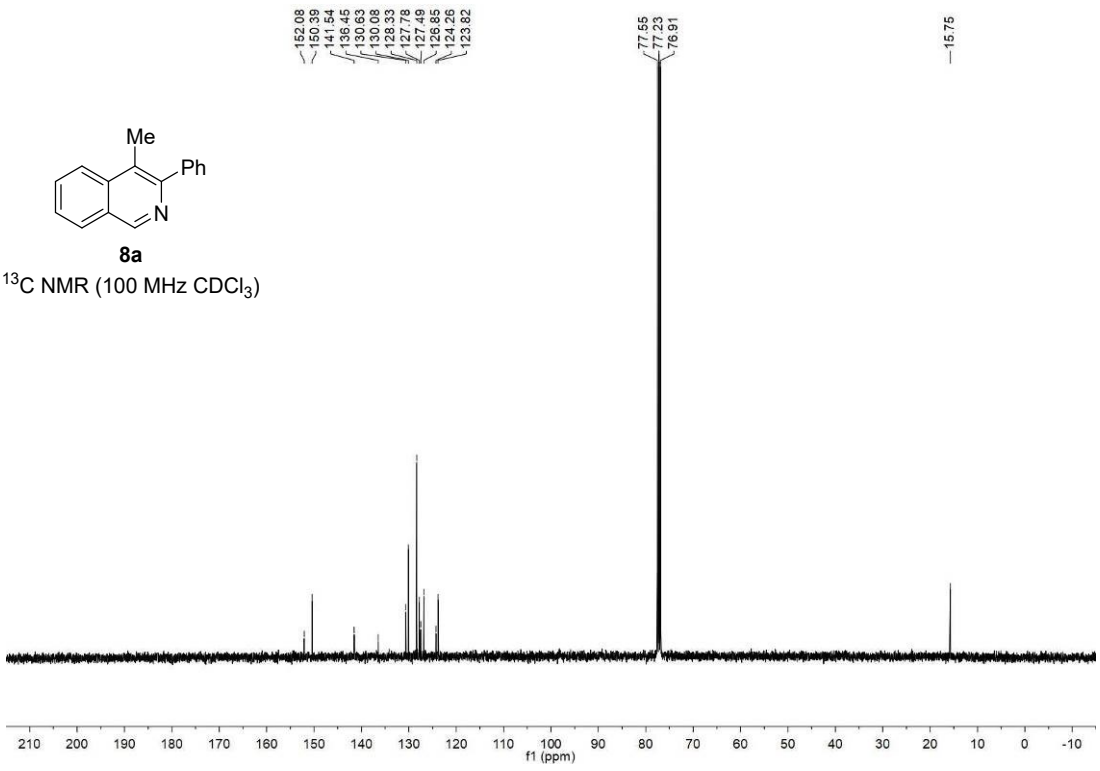
6o

^{13}C NMR (100 MHz $CDCl_3$)



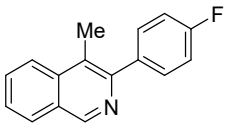
8a

^{1}H NMR (400 MHz $CDCl_3$)



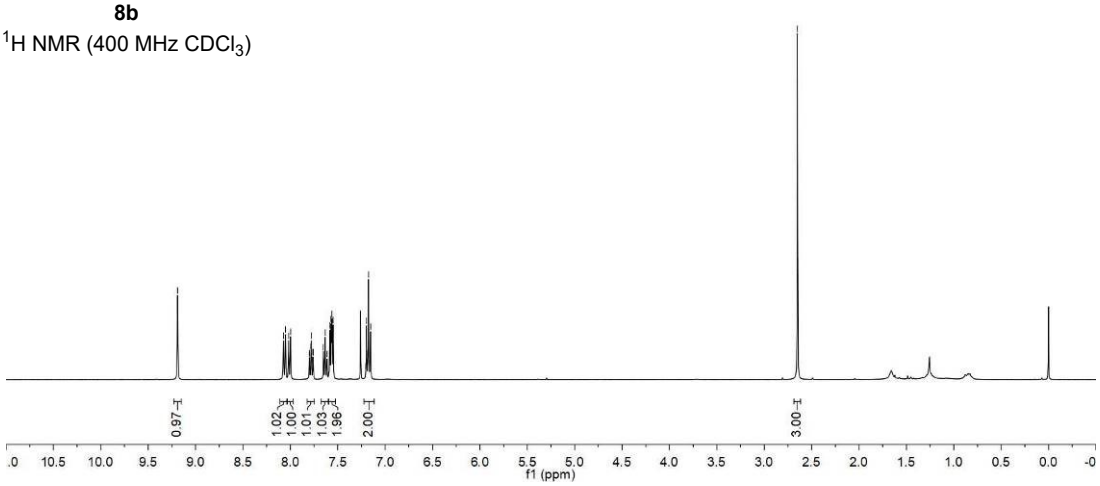
8a

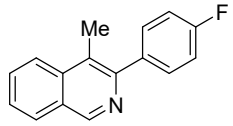
^{13}C NMR (100 MHz $CDCl_3$)



8b

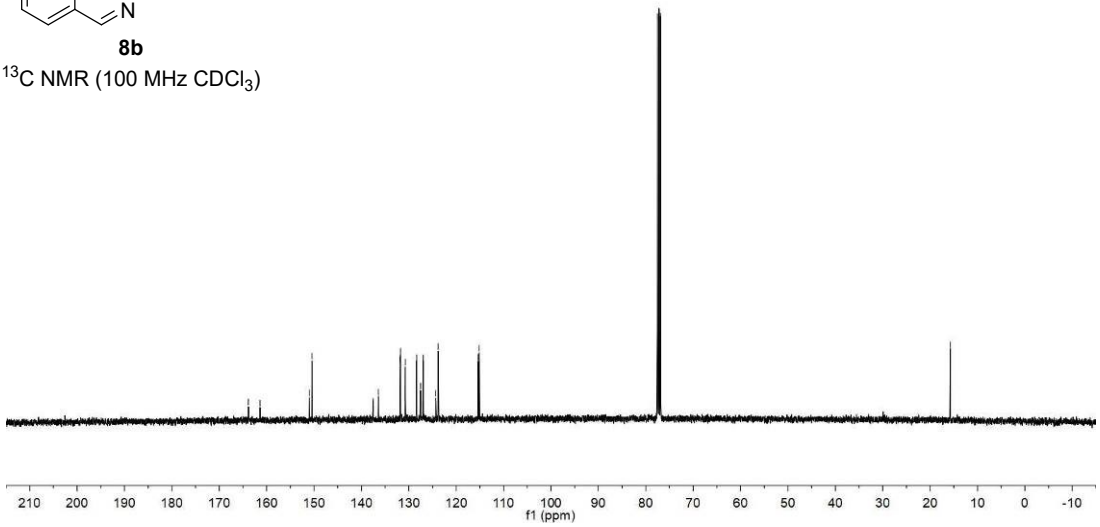
^{1}H NMR (400 MHz $CDCl_3$)

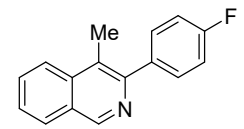




8b

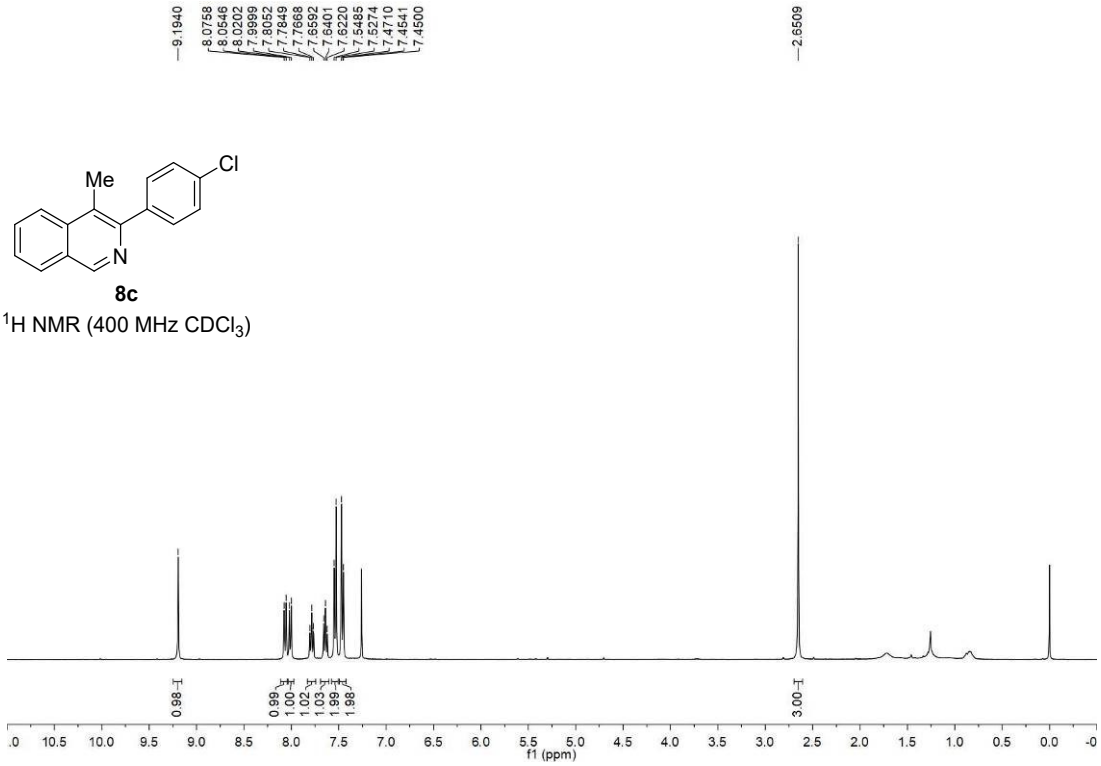
^{13}C NMR (100 MHz $CDCl_3$)





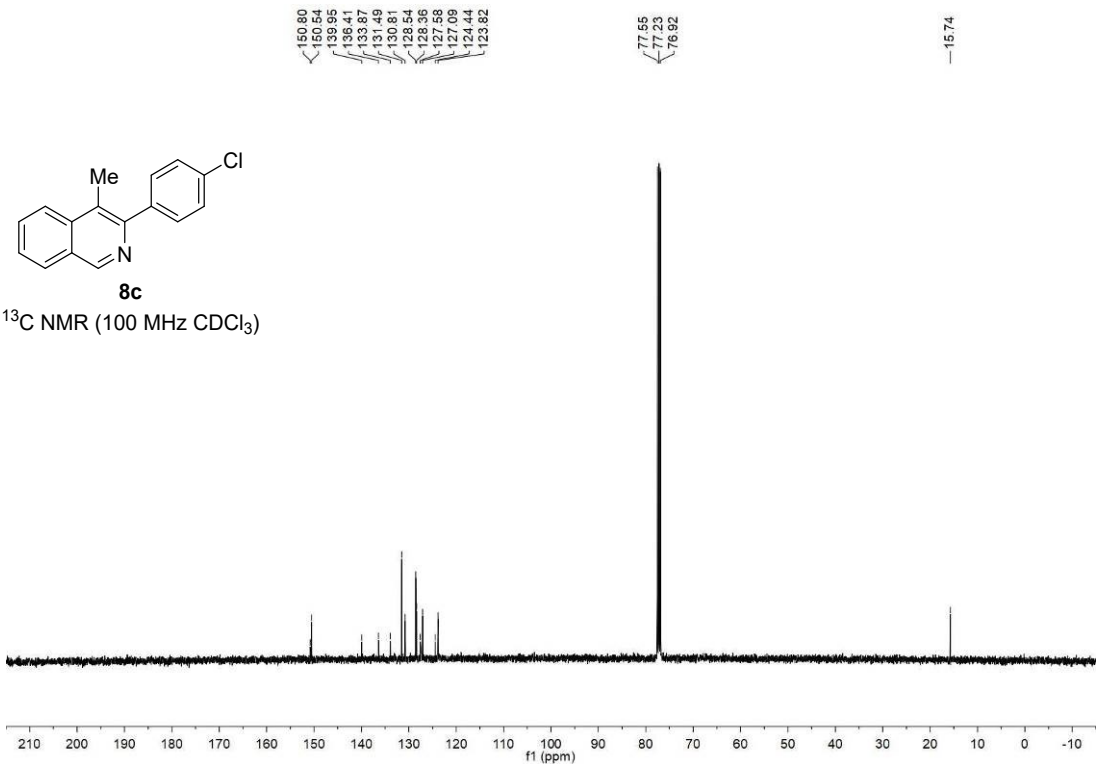
8b

^{19}F NMR (376 MHz $CDCl_3$)



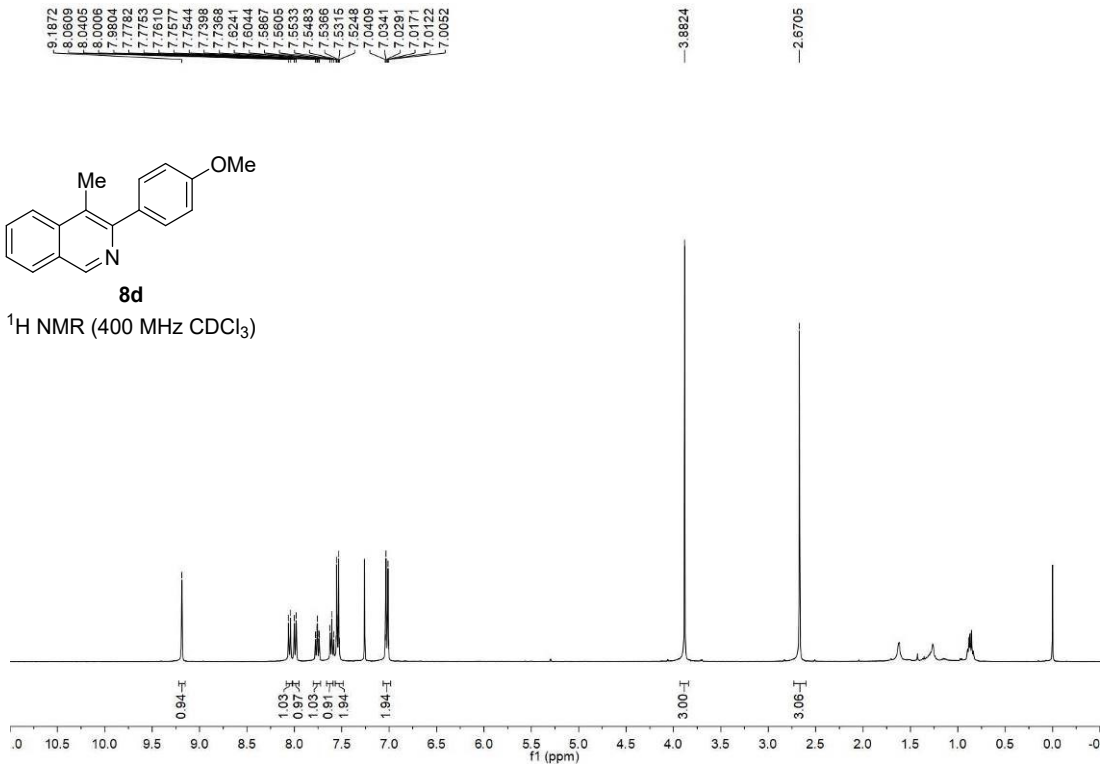
8c

^{1}H NMR (400 MHz $CDCl_3$)



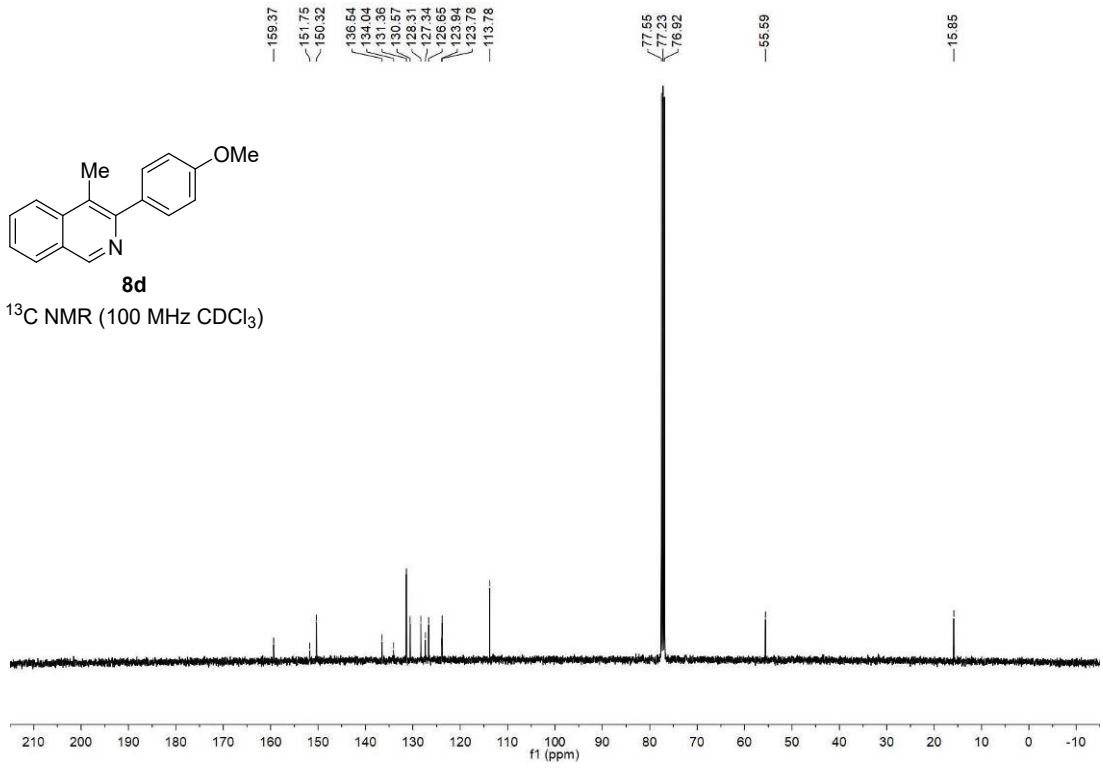
8c

^{13}C NMR (100 MHz $CDCl_3$)



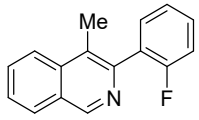
8d

^{1}H NMR (400 MHz $CDCl_3$)



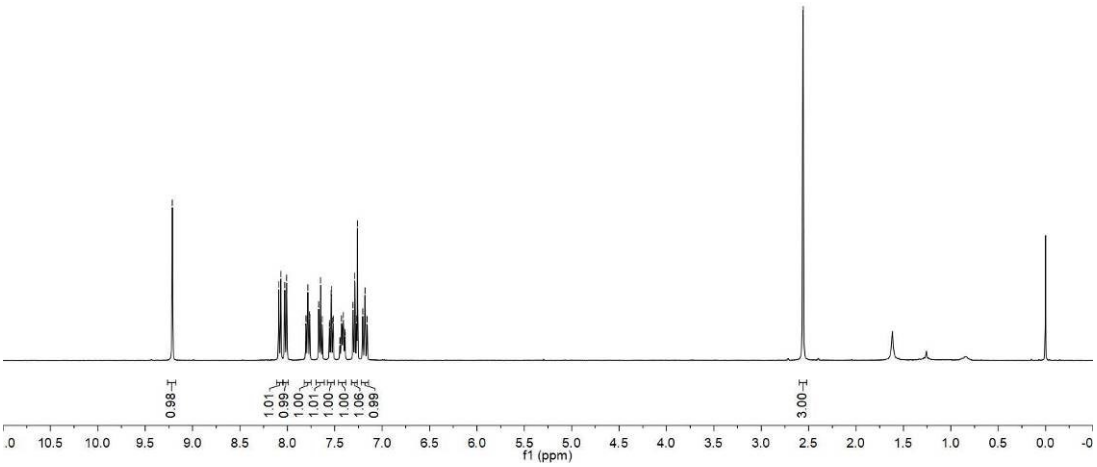
8d

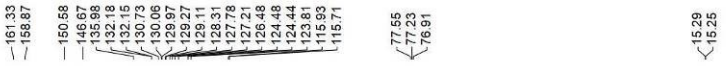
^{13}C NMR (100 MHz $CDCl_3$)

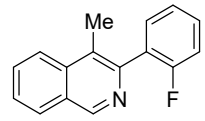


8e

^{1}H NMR (400 MHz $CDCl_3$)

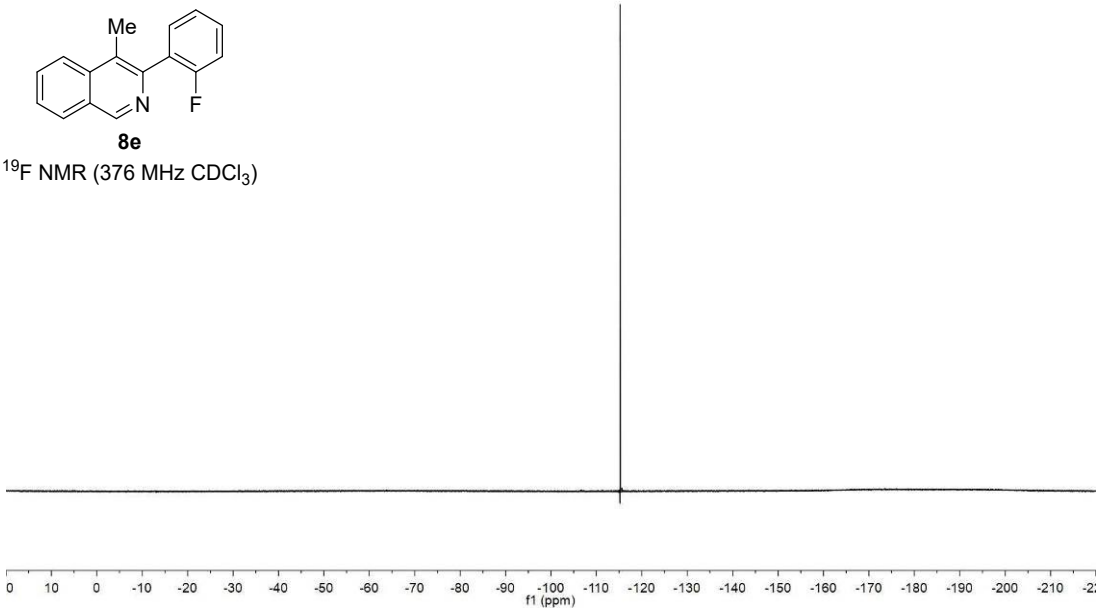






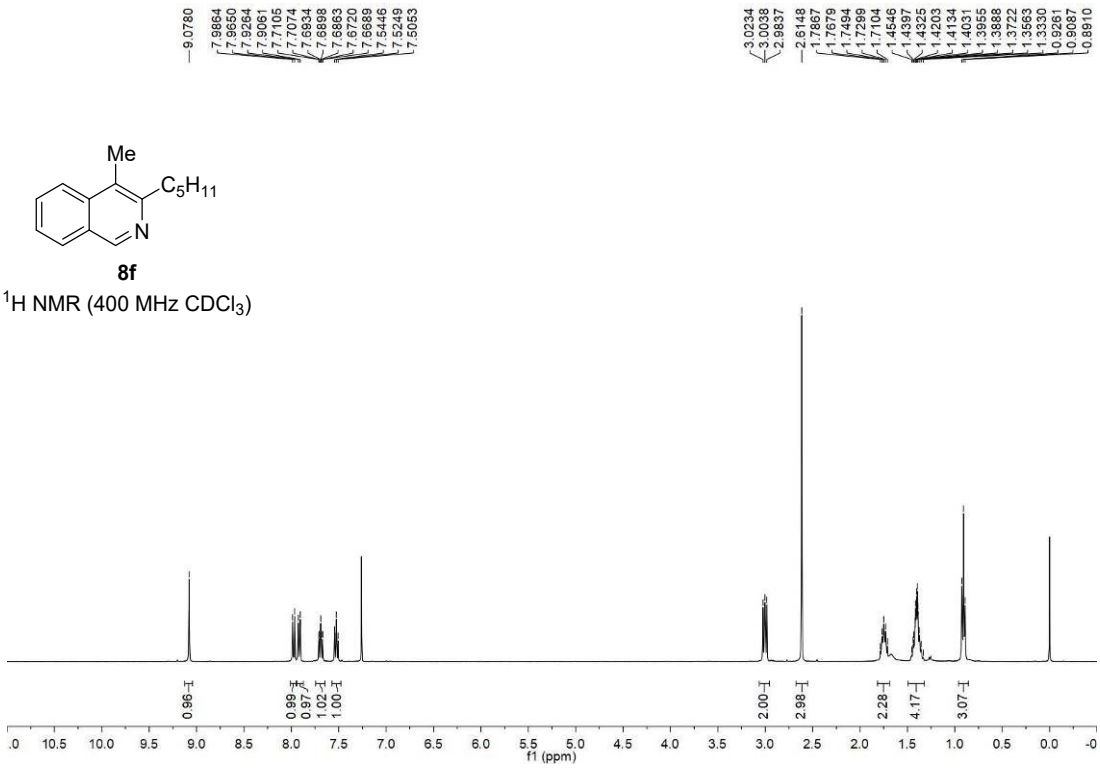
8e

^{13}C NMR (100 MHz $CDCl_3$)



8e

^{19}F NMR (376 MHz $CDCl_3$)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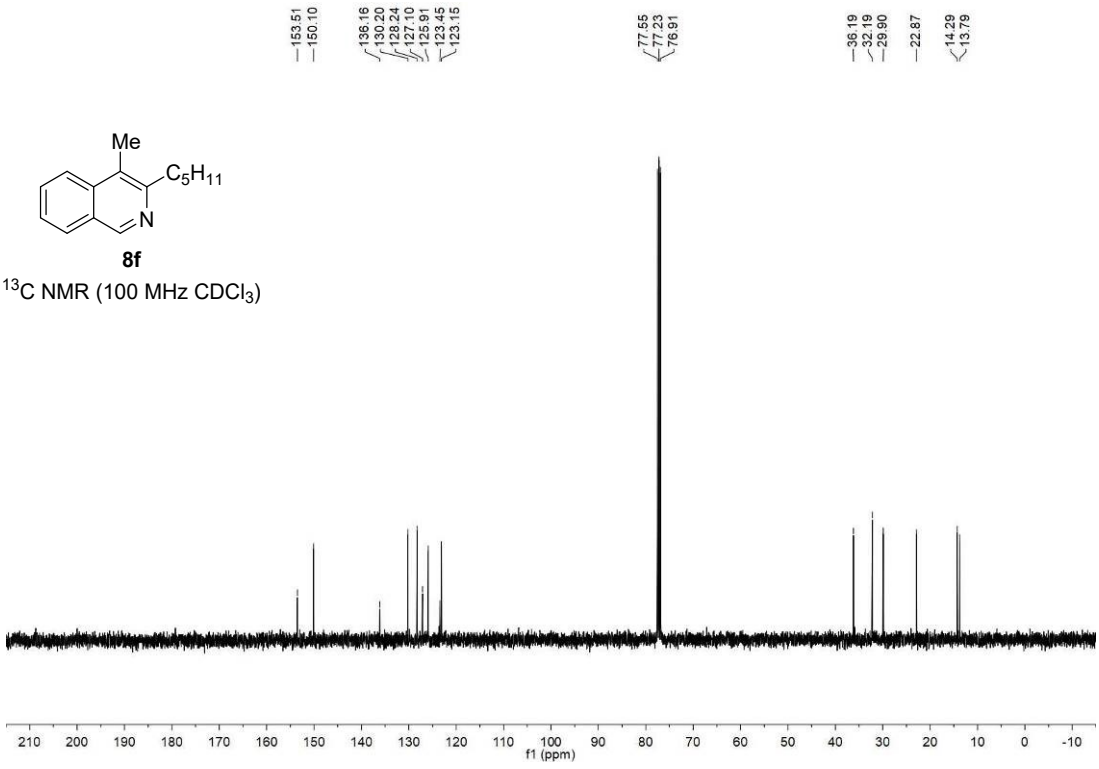
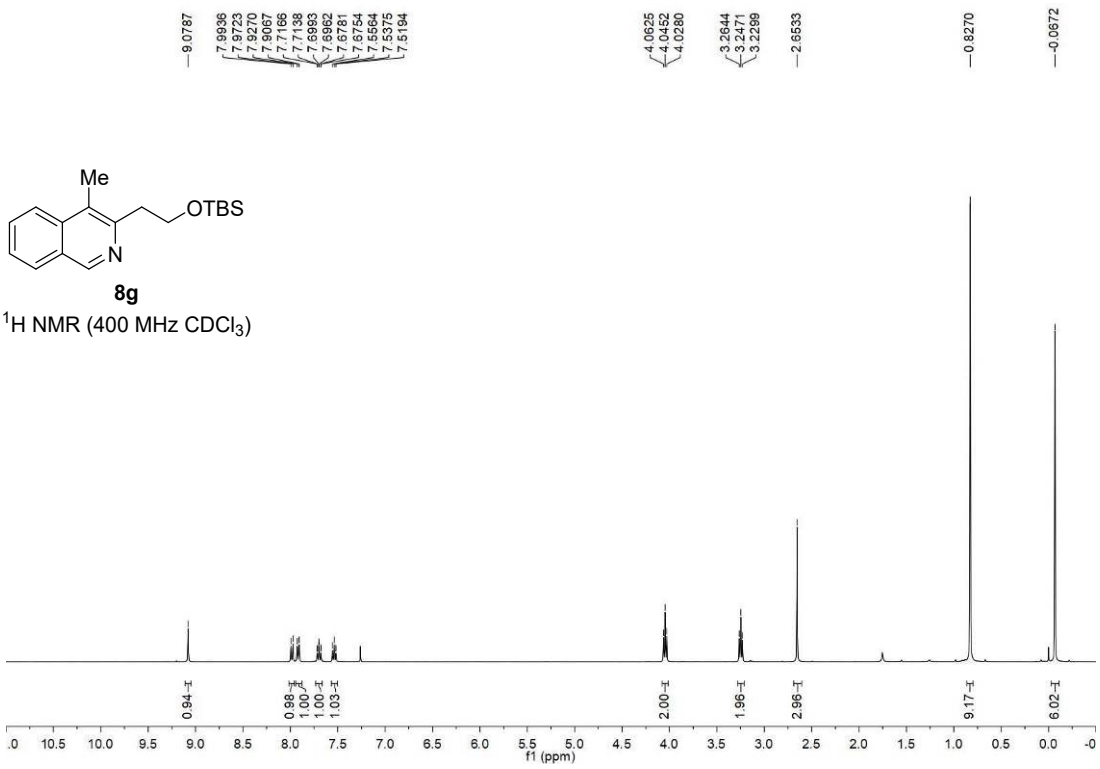
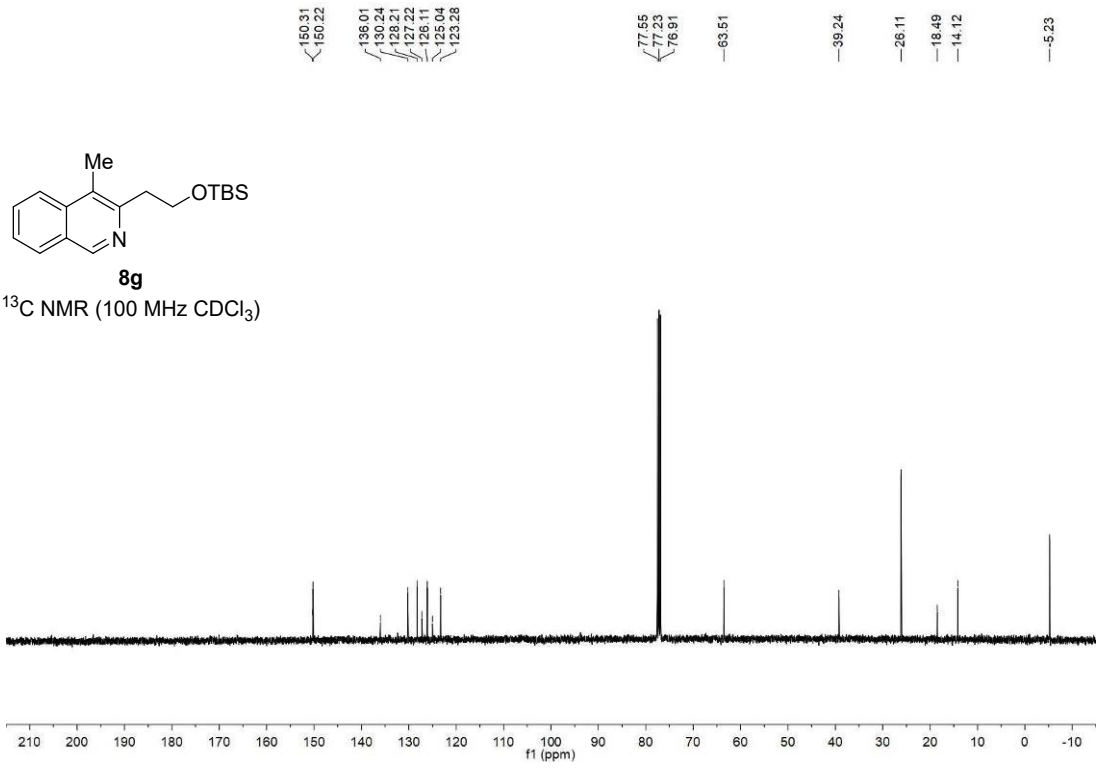
7.9864
7.9650
7.9264
7.9061
7.7105
7.7074
7.6934
7.6898
7.6863
7.6720
7.6689
7.5446
7.5249
7.5053
3.0234
3.0038
2.9837
2.6148
1.7867
1.7679
1.7494
1.7299
1.7104
1.4546
1.4397
1.4325
1.4203
1.4134
1.4031
1.3955
1.3888
1.3722
1.3563
1.3330
0.9261
0.9087
0.8910
Me
C5H11
N
8f
1H NMR (400 MHz CDCl3)
0.96
0.99
0.97
1.02
1.00
2.00
2.98
2.28
4.17
3.07
f1 (ppm)


153.51
150.10
136.16
130.20
128.24
127.10
125.91
123.45
123.15
77.55
77.23
76.91
36.19
32.19
29.90
22.87
14.29
13.79
Me
C5H11
N
8f
13C NMR (100 MHz CDCl3)
f1 (ppm)



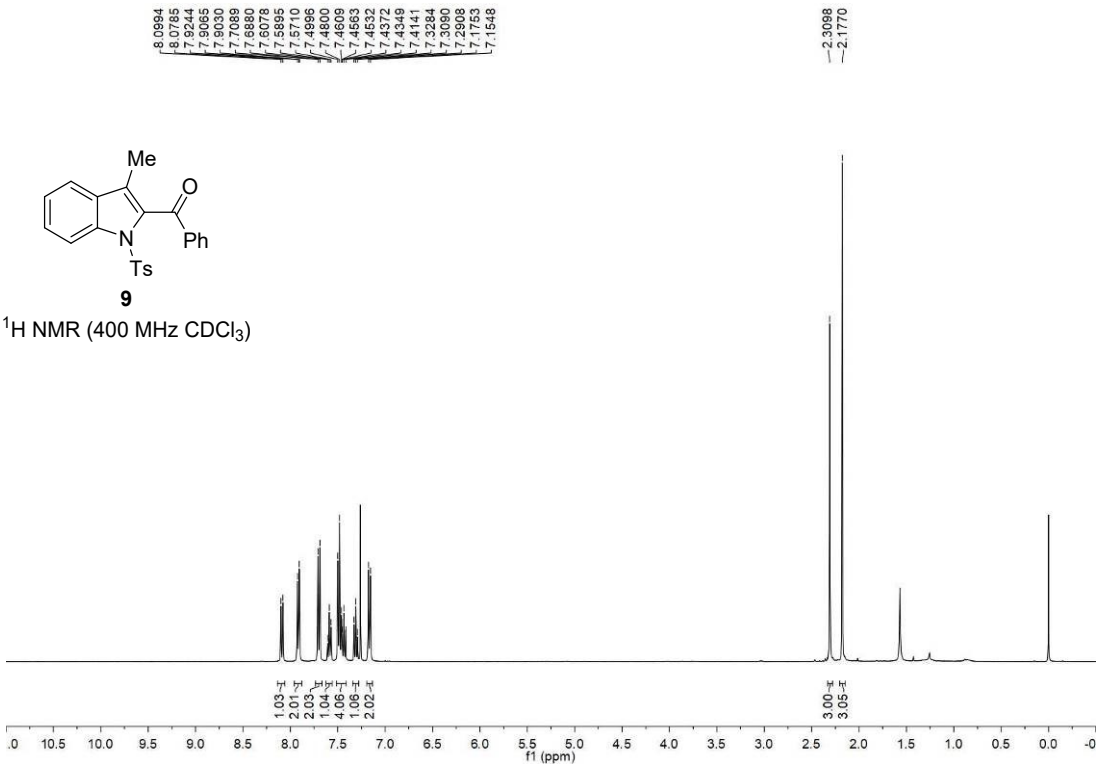
8g

^{1}H NMR (400 MHz $CDCl_3$)



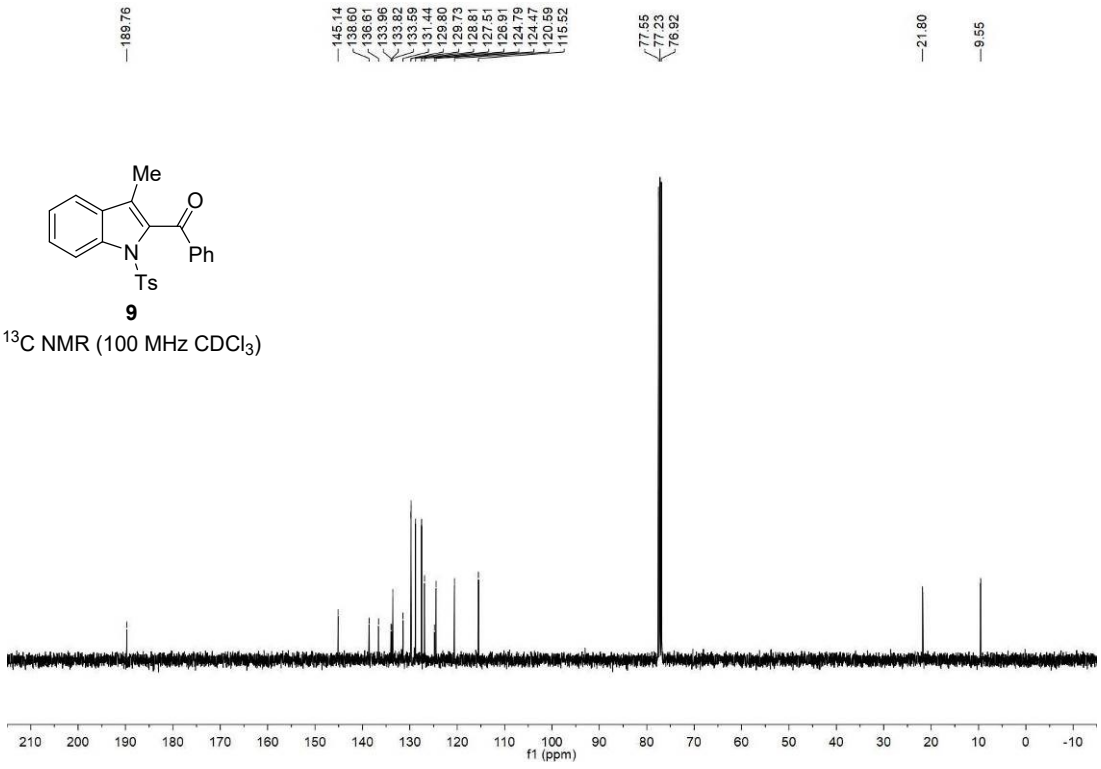
8g

^{13}C NMR (100 MHz $CDCl_3$)



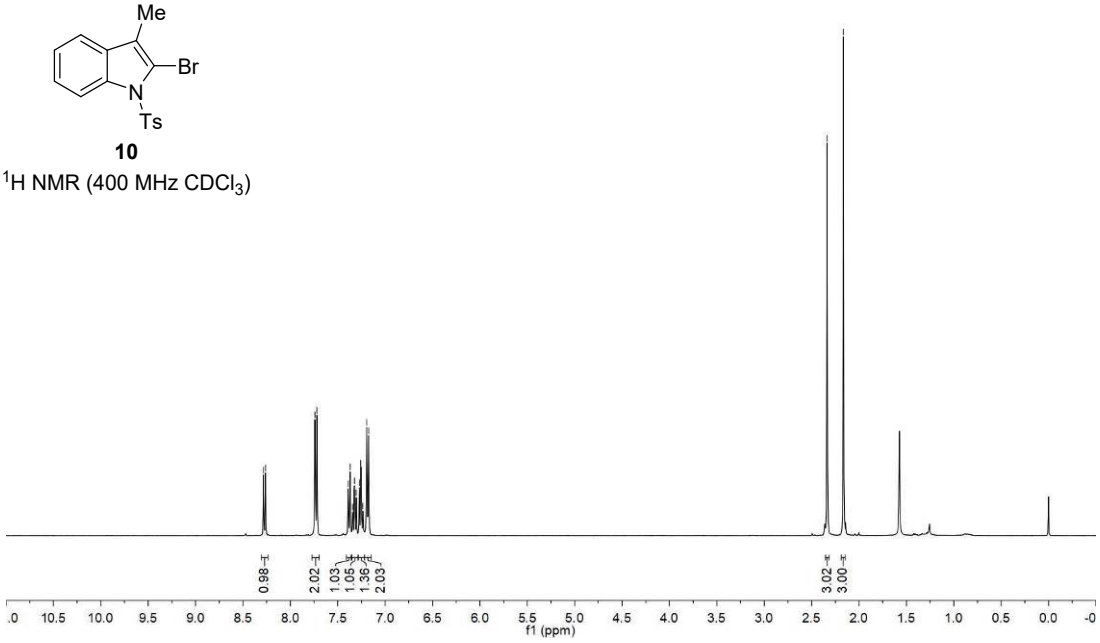
9

^{1}H NMR (400 MHz $CDCl_3$)



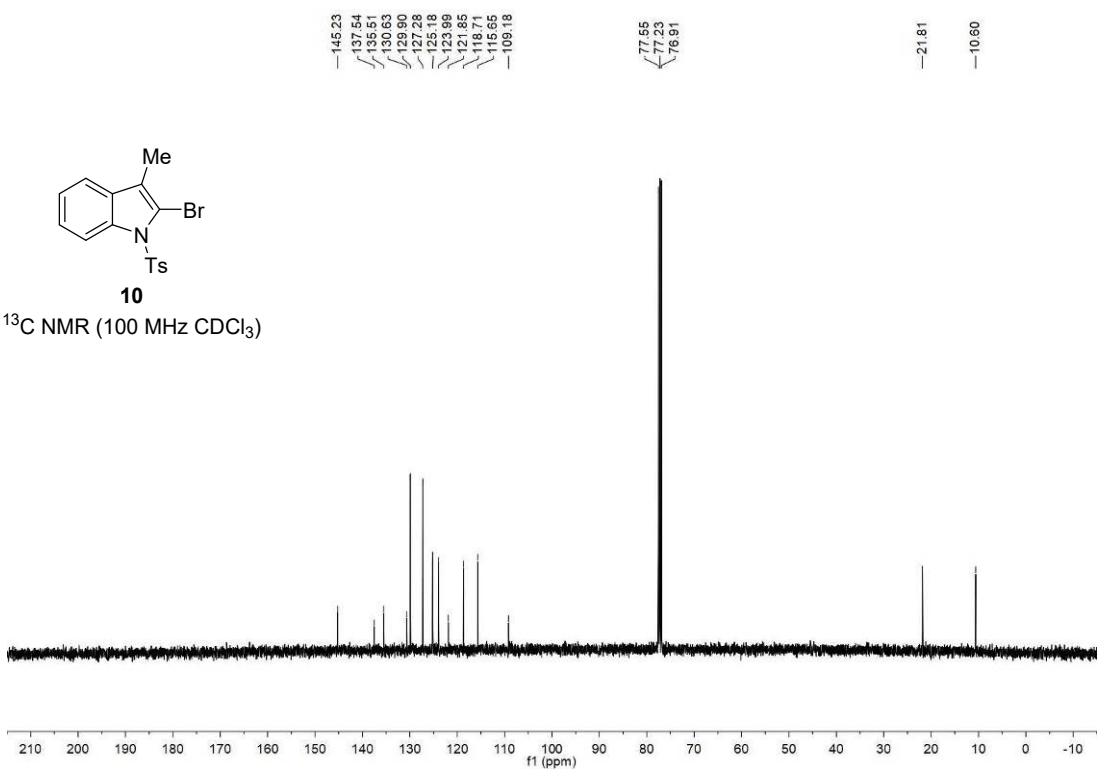
9

^{13}C NMR (100 MHz $CDCl_3$)



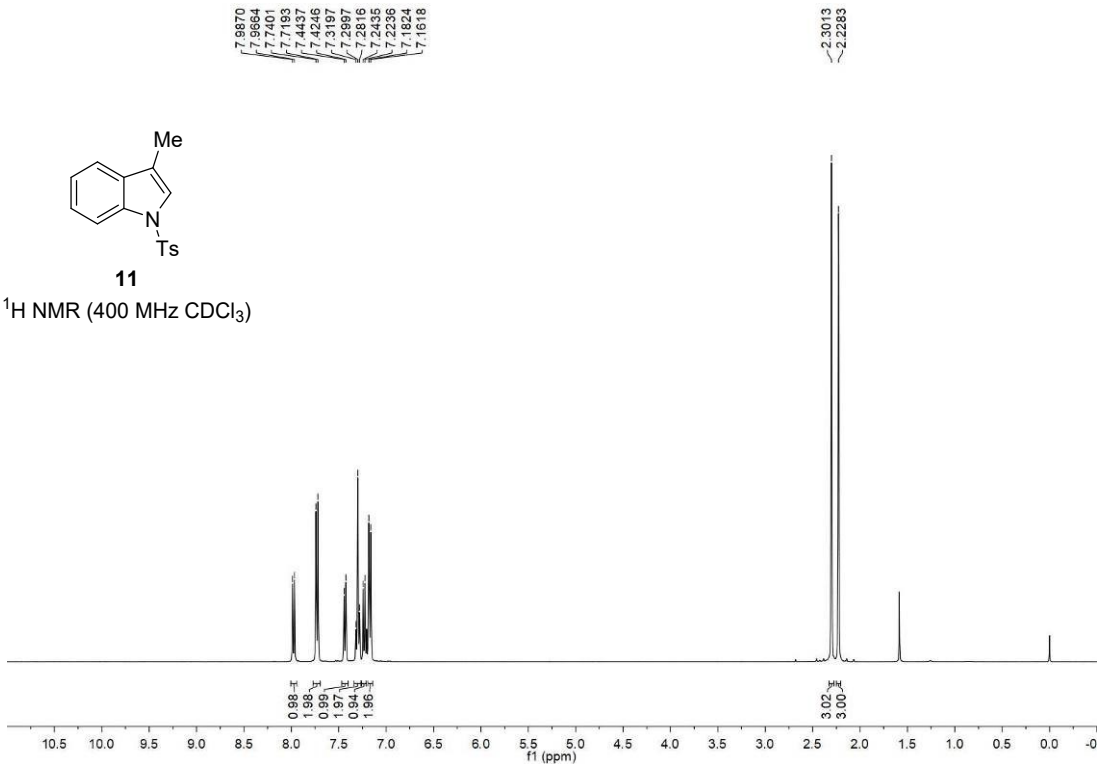
10

^{1}H NMR (400 MHz $CDCl_3$)



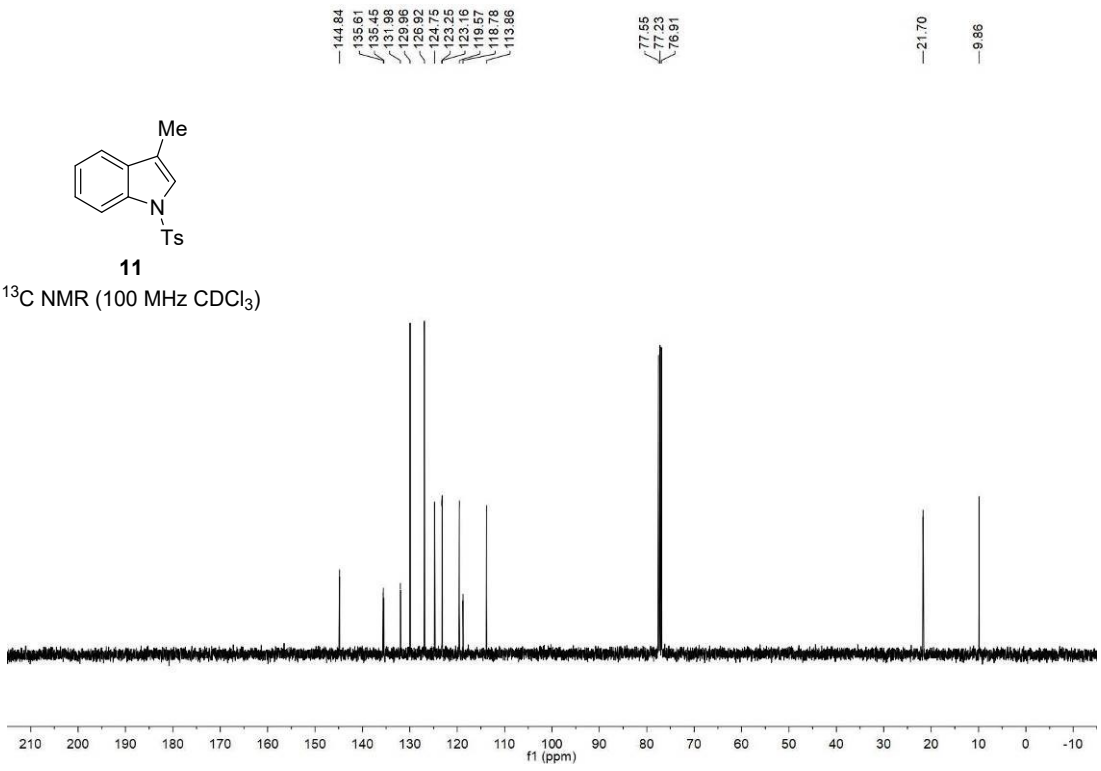
10

^{13}C NMR (100 MHz $CDCl_3$)



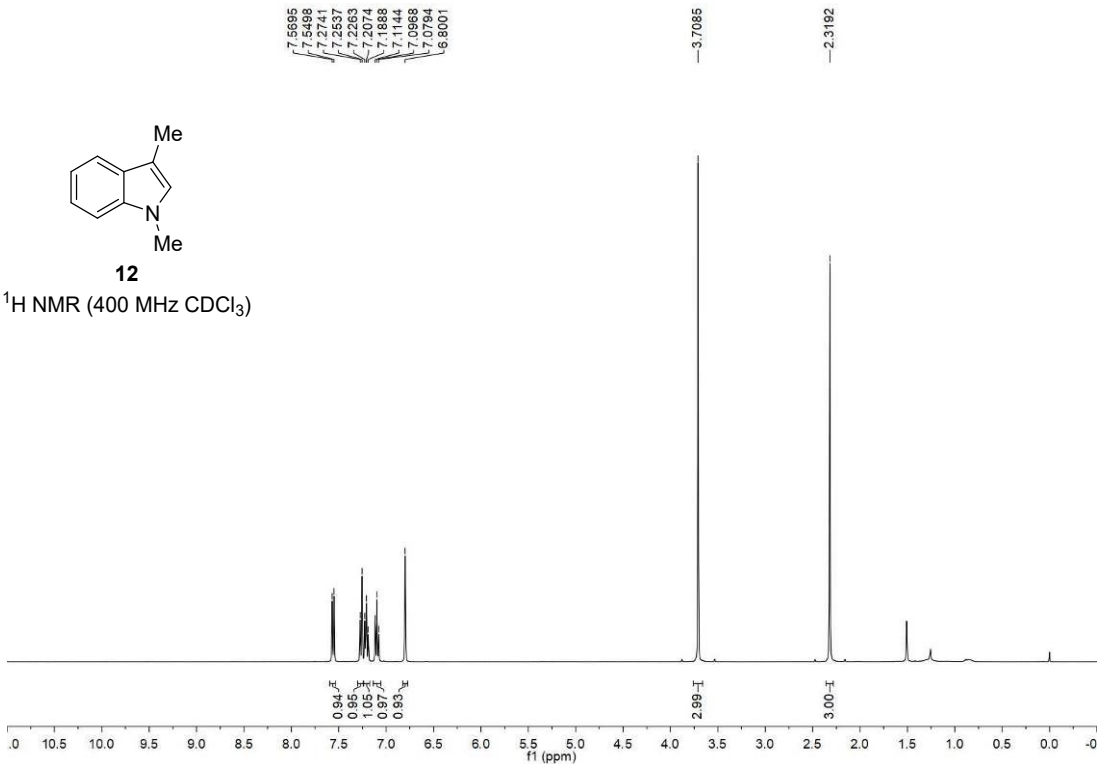
11

^{1}H NMR (400 MHz $CDCl_3$)



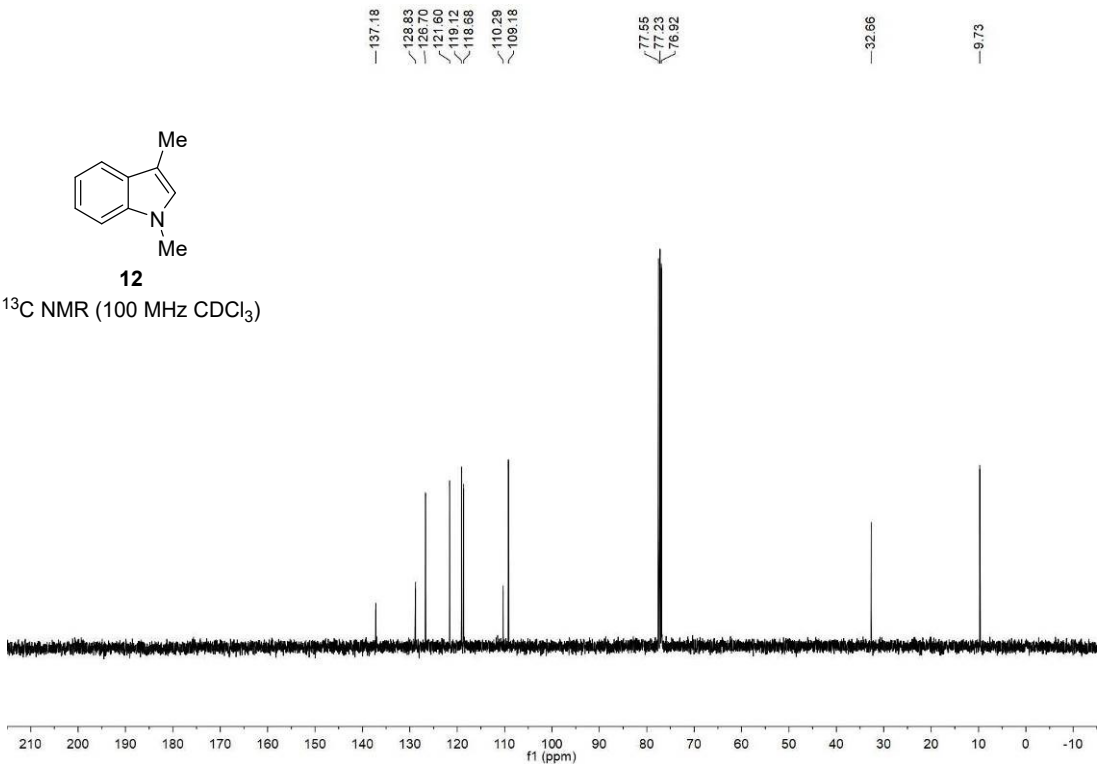
11

^{13}C NMR (100 MHz $CDCl_3$)



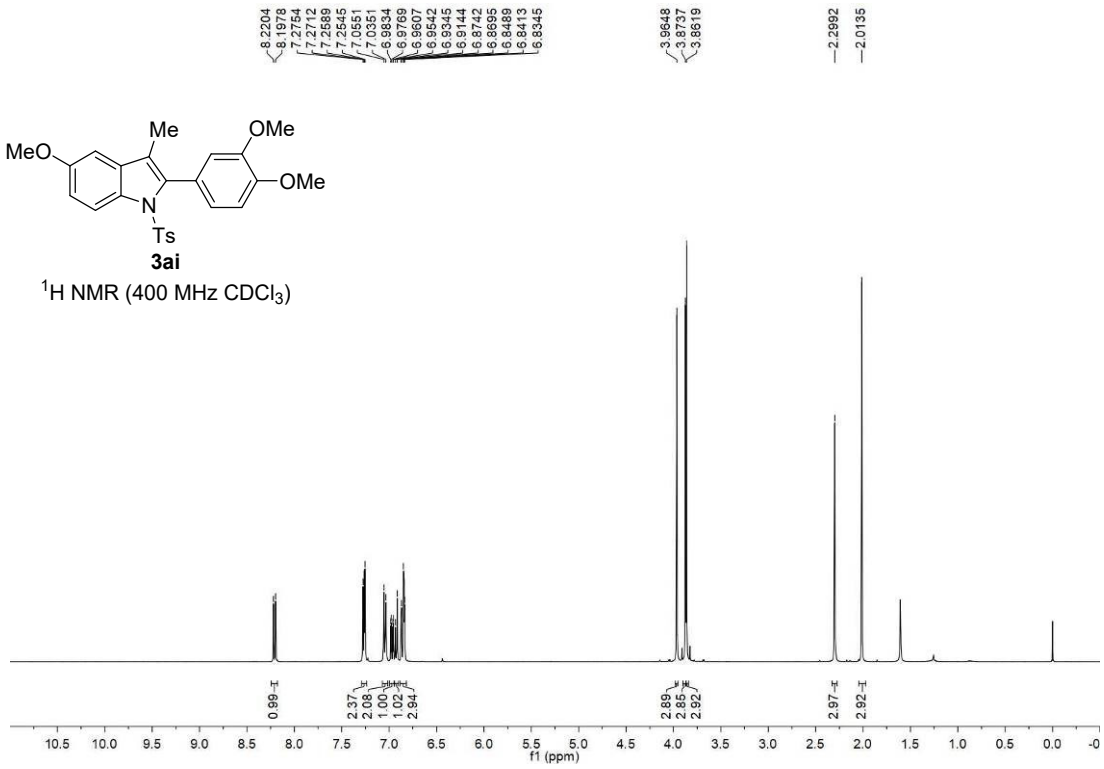
12

^{1}H NMR (400 MHz $CDCl_3$)



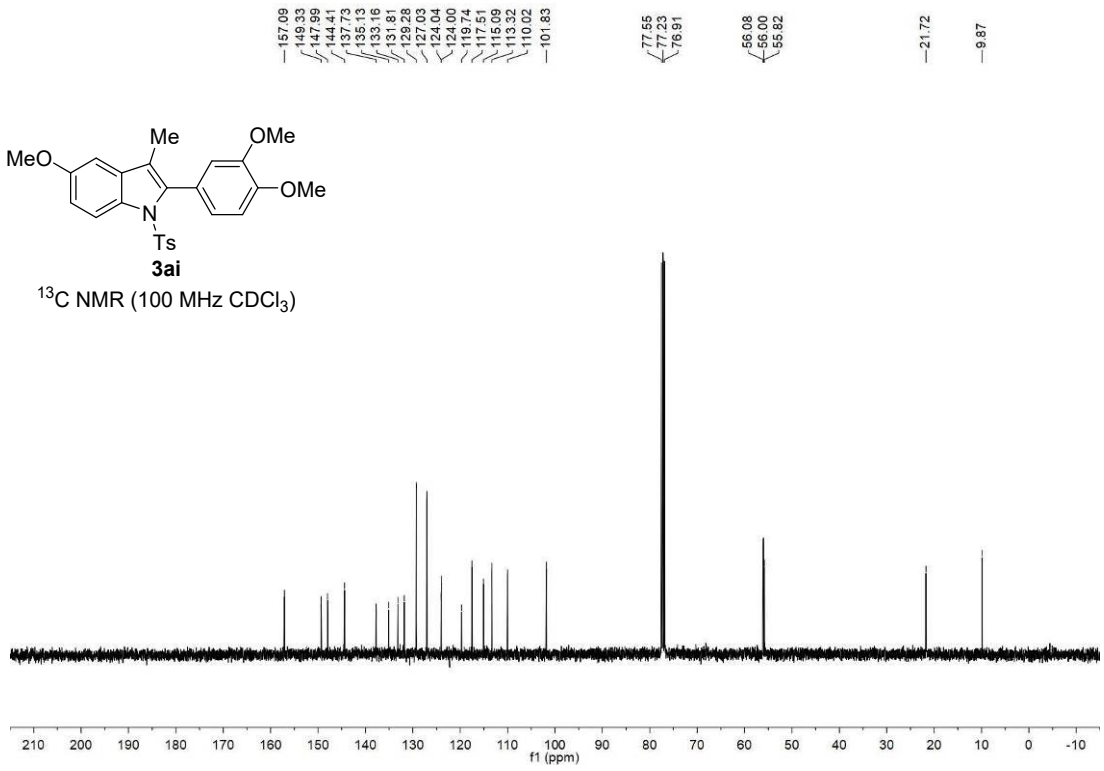
12

^{13}C NMR (100 MHz $CDCl_3$)



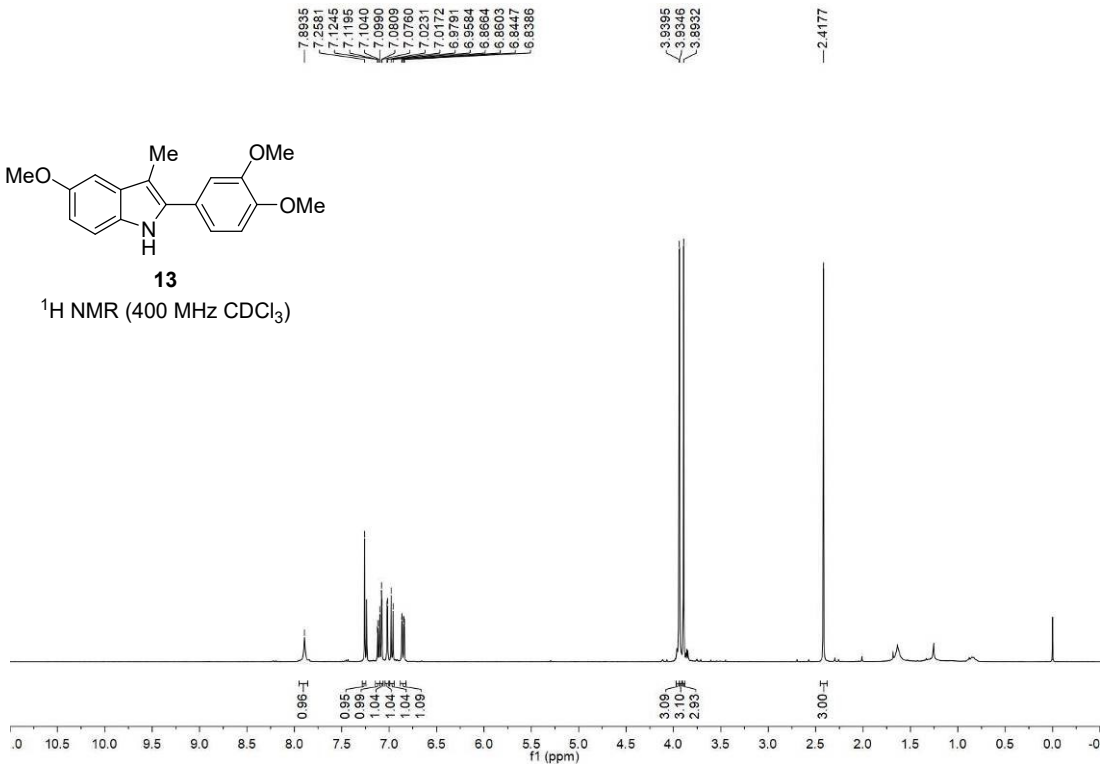
3ai

^{1}H NMR (400 MHz $CDCl_3$)



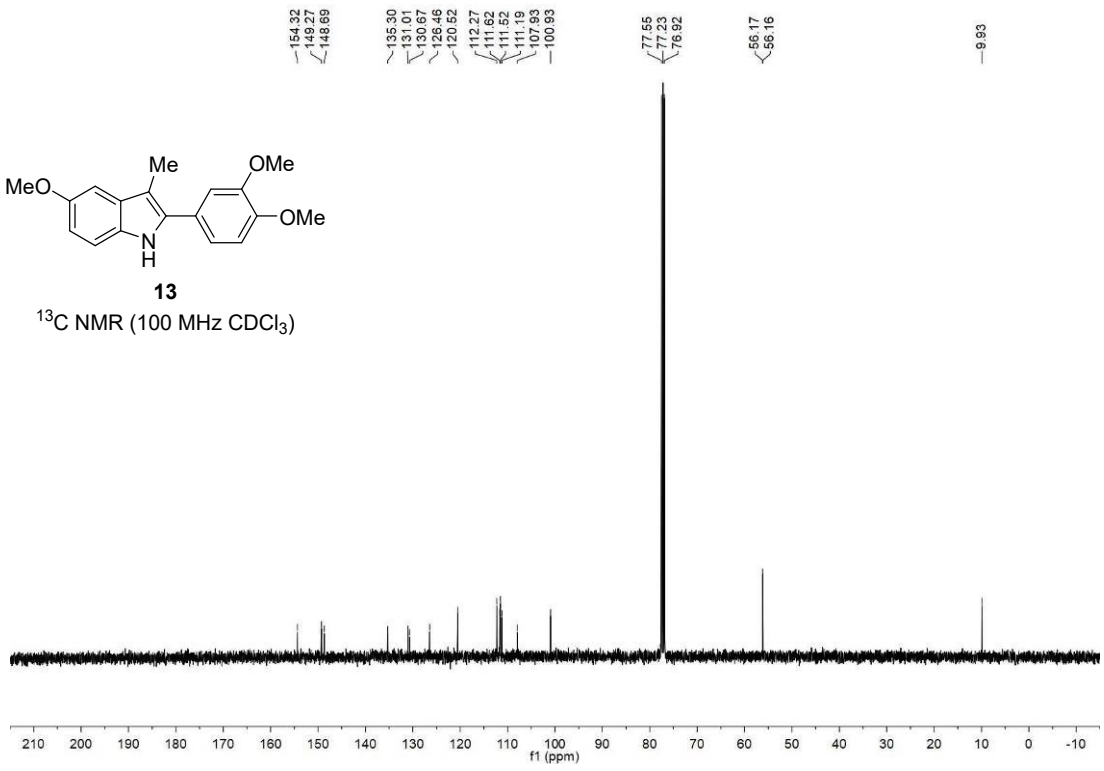
3ai

^{13}C NMR (100 MHz $CDCl_3$)



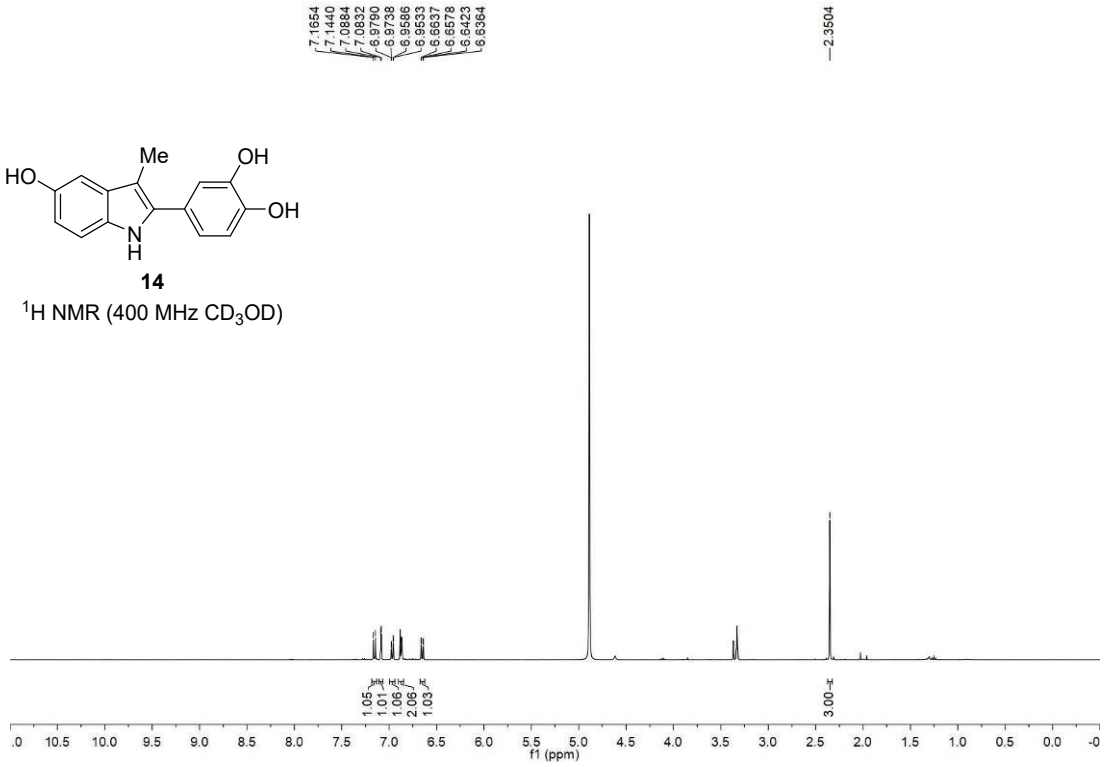
13

^{1}H NMR (400 MHz $CDCl_3$)



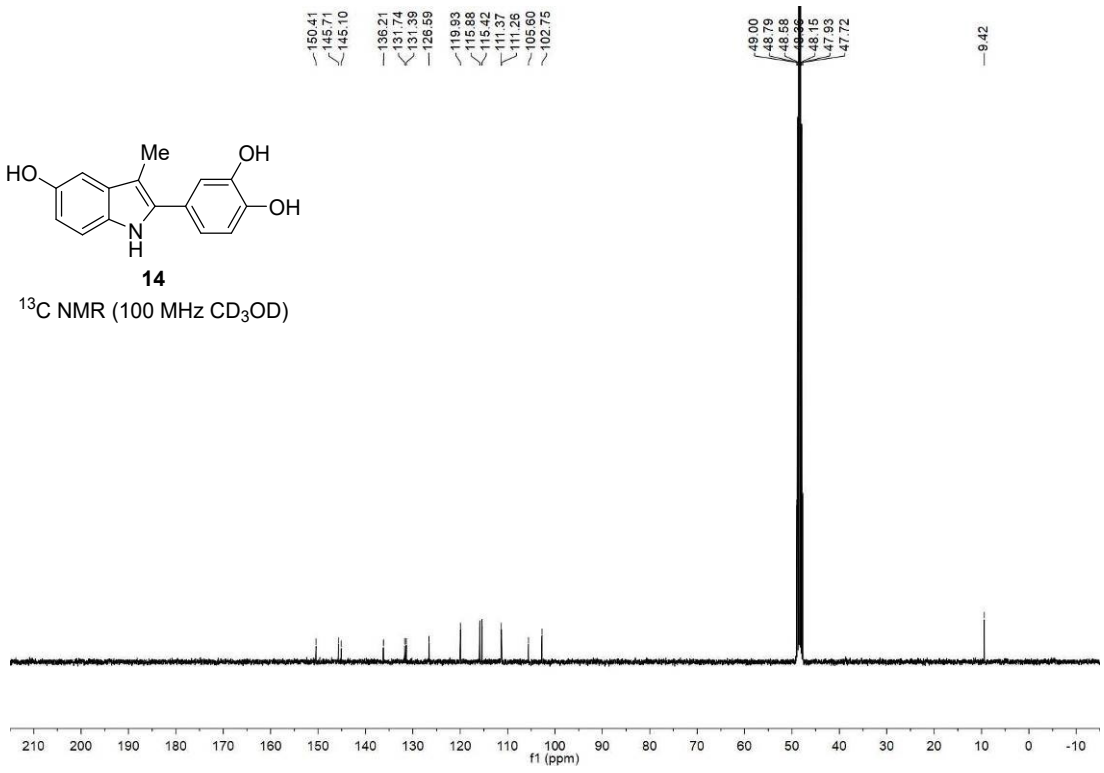
13

^{13}C NMR (100 MHz $CDCl_3$)



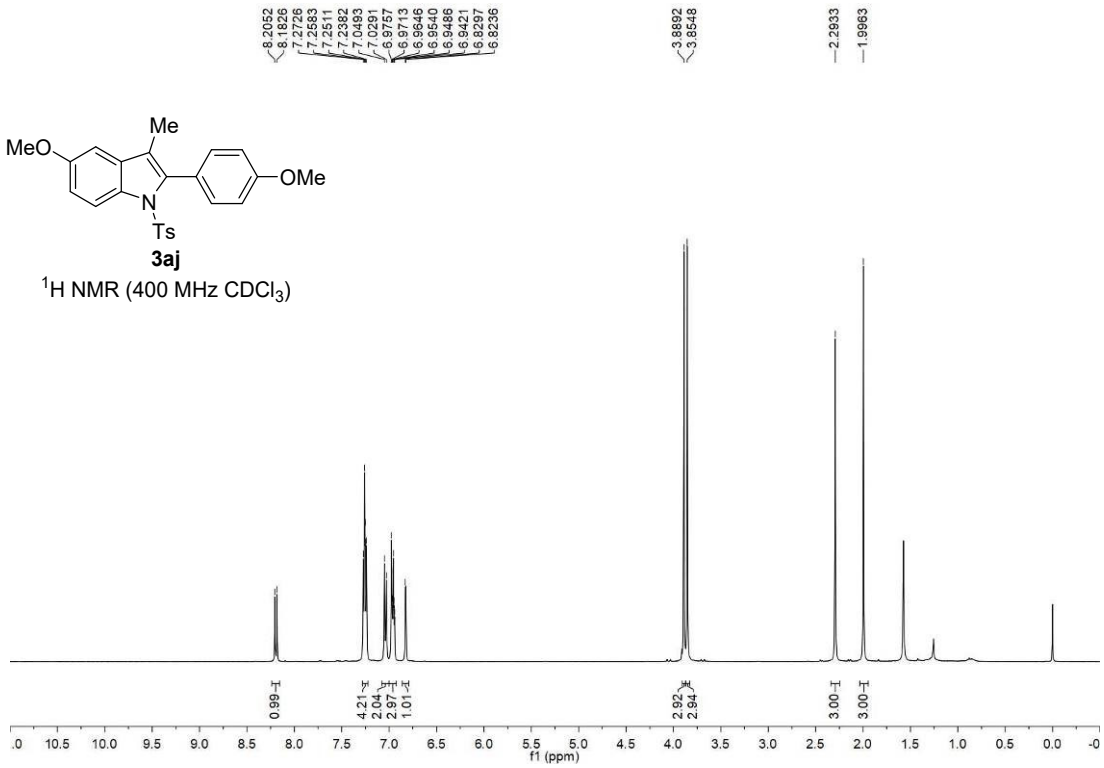
14

^{1}H NMR (400 MHz CD_3OD)



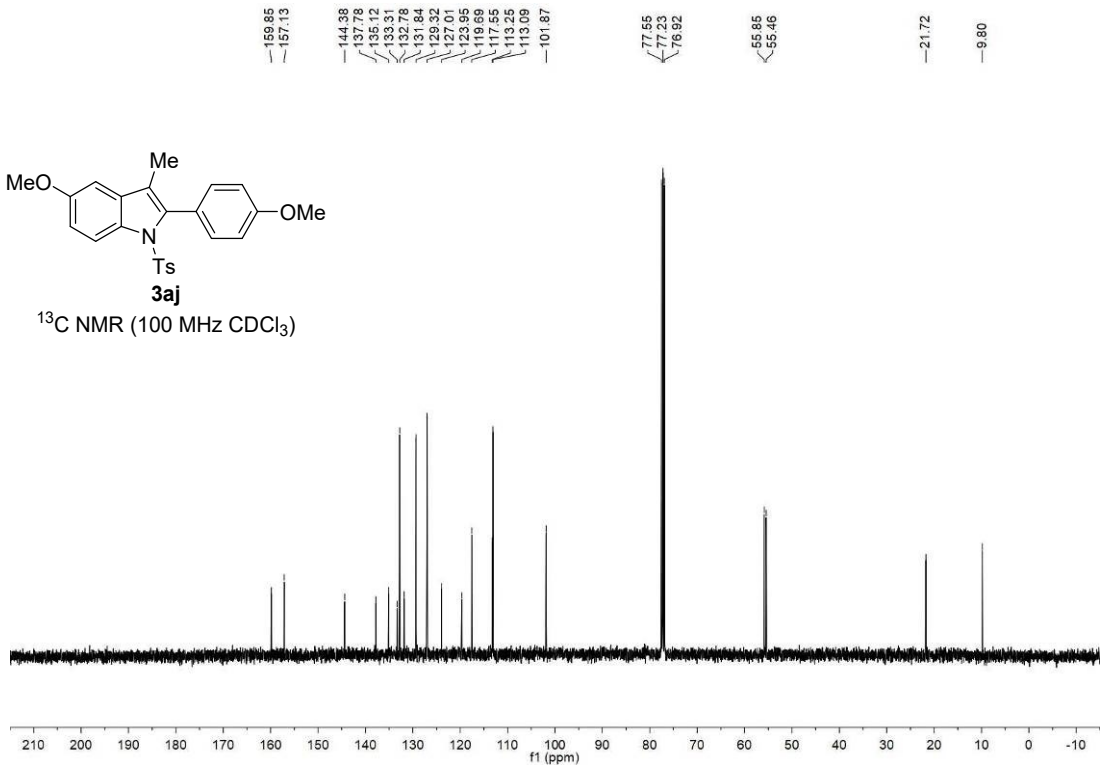
14

^{13}C NMR (100 MHz CD_3OD)



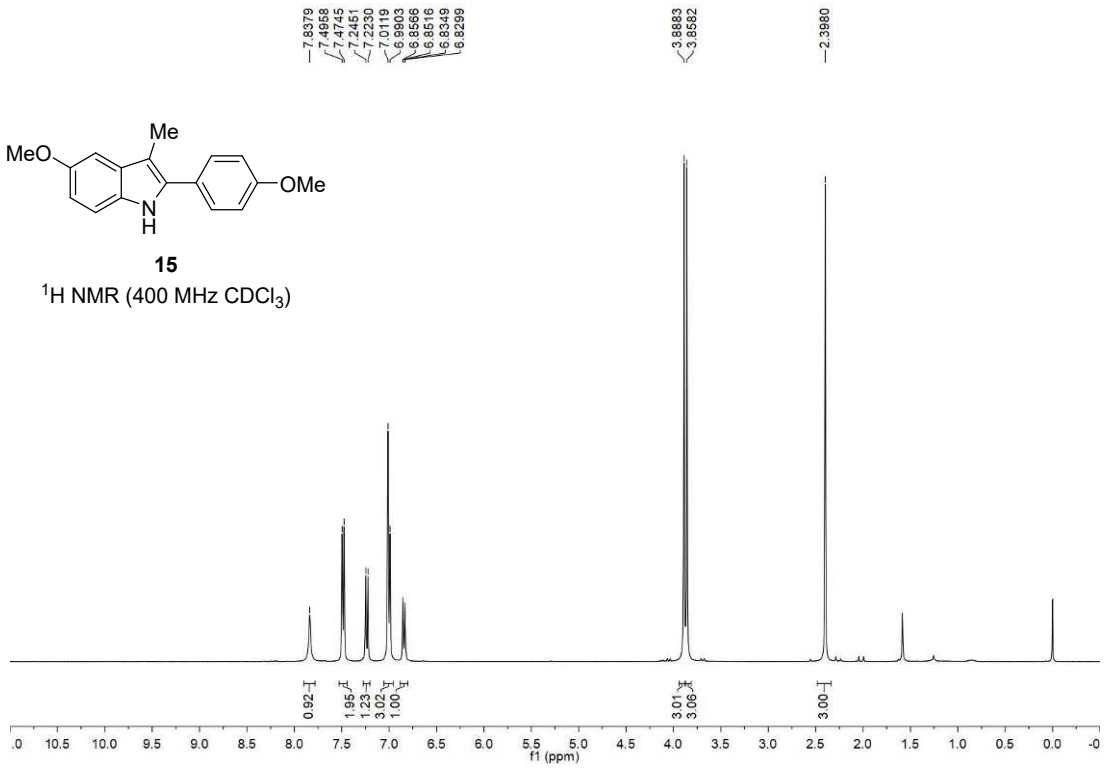
3aj

^{1}H NMR (400 MHz $CDCl_3$)



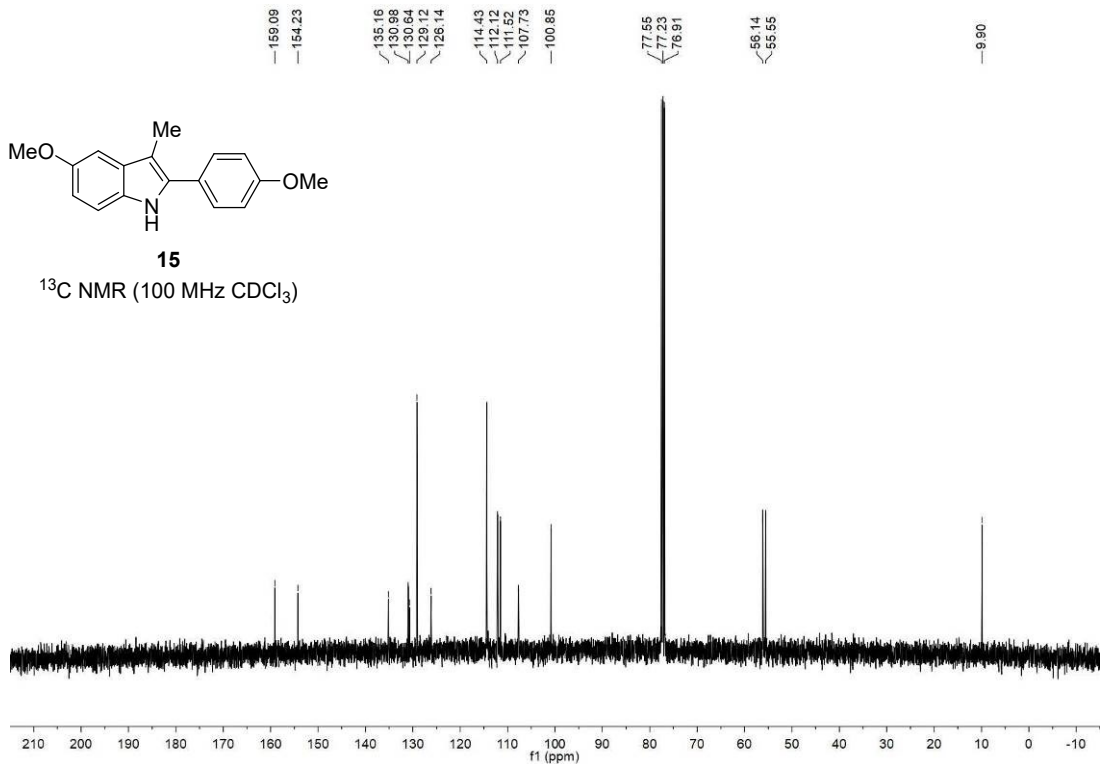
3aj

^{13}C NMR (100 MHz $CDCl_3$)



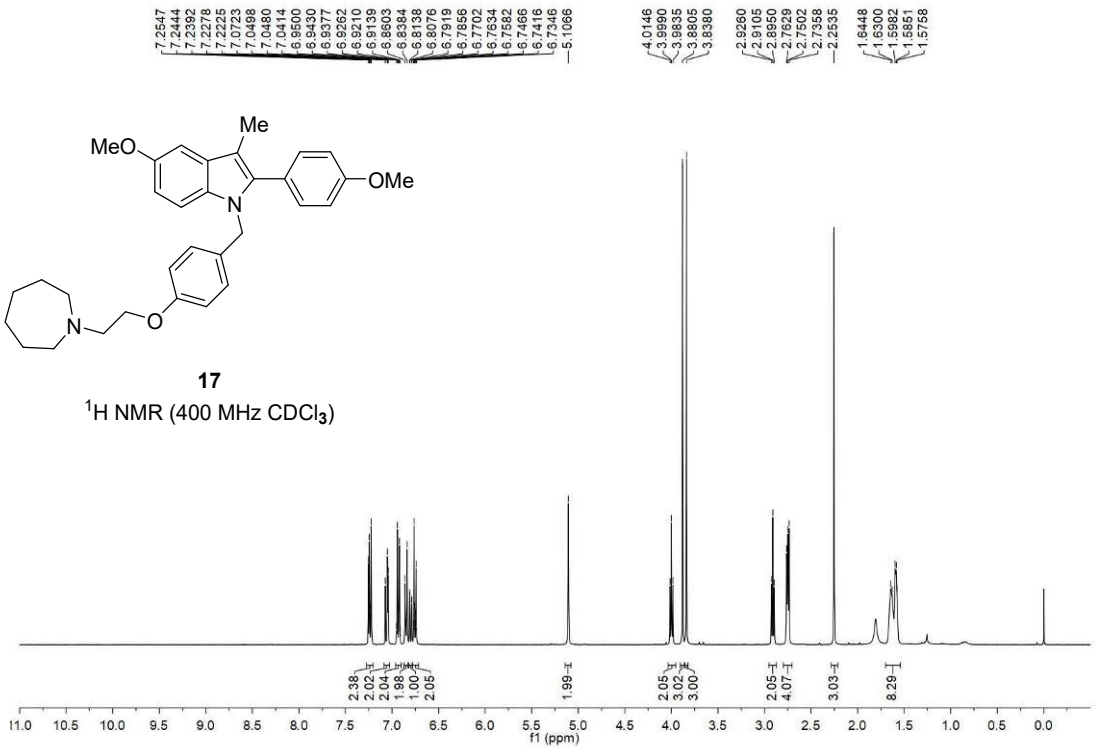
15

^{1}H NMR (400 MHz $CDCl_3$)



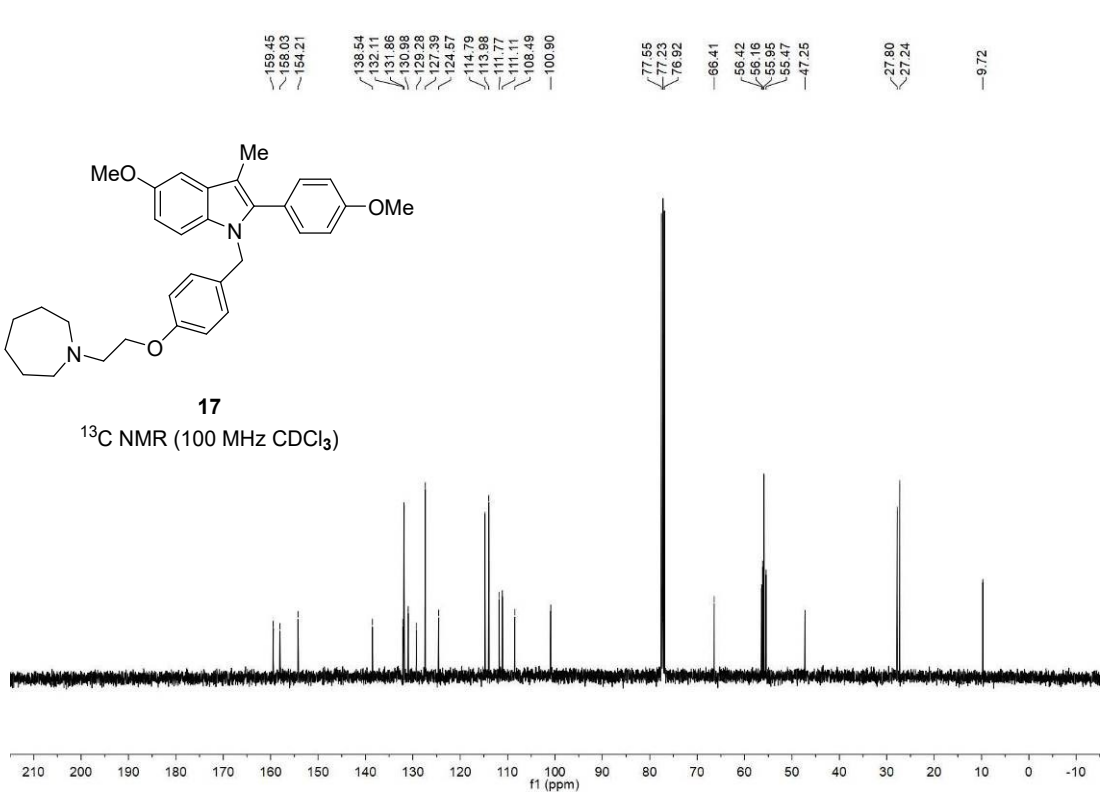
15

^{13}C NMR (100 MHz $CDCl_3$)



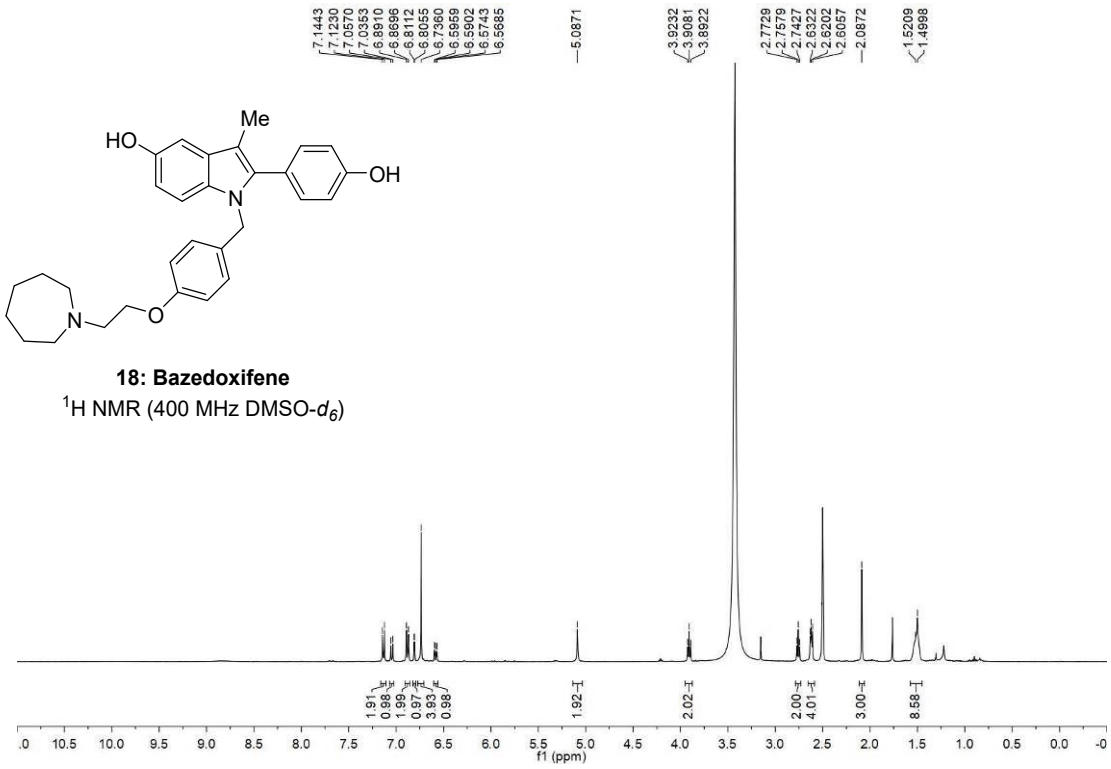
17

^{1}H NMR (400 MHz $CDCl_3$)



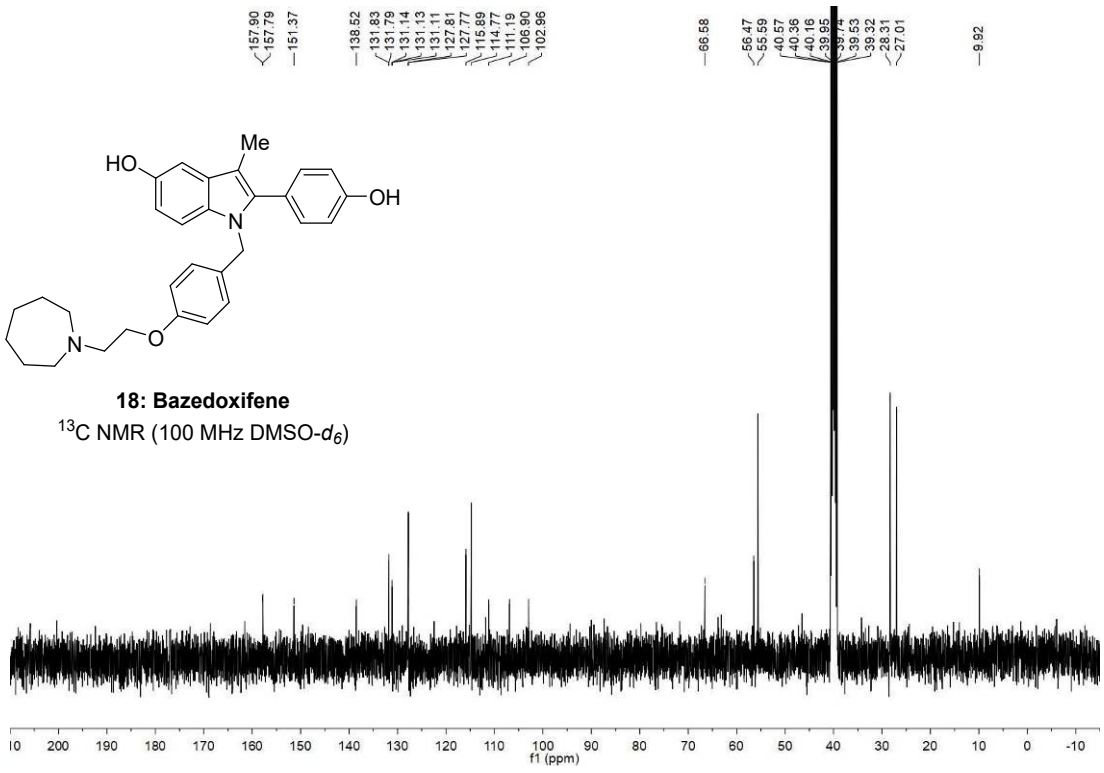
17

^{13}C NMR (100 MHz $CDCl_3$)



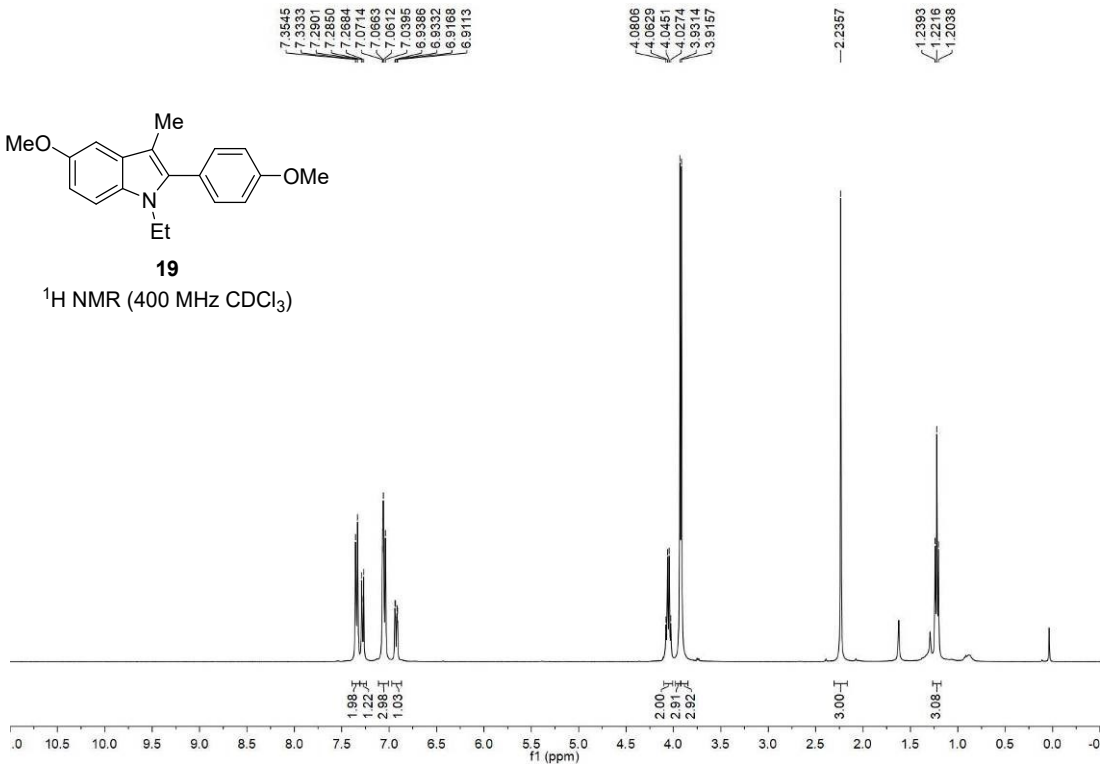
18: Bazedoxifene

^{1}H NMR (400 MHz DMSO-d_6)



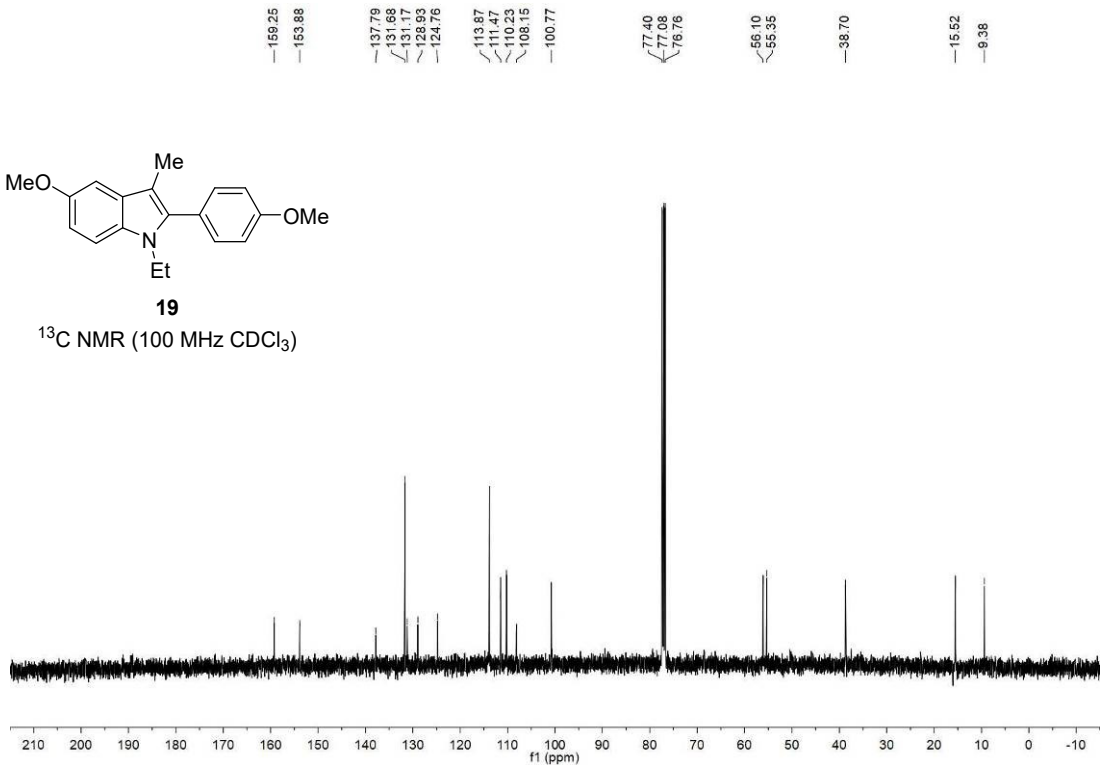
18: Bazedoxifene

^{13}C NMR (100 MHz DMSO-d_6)



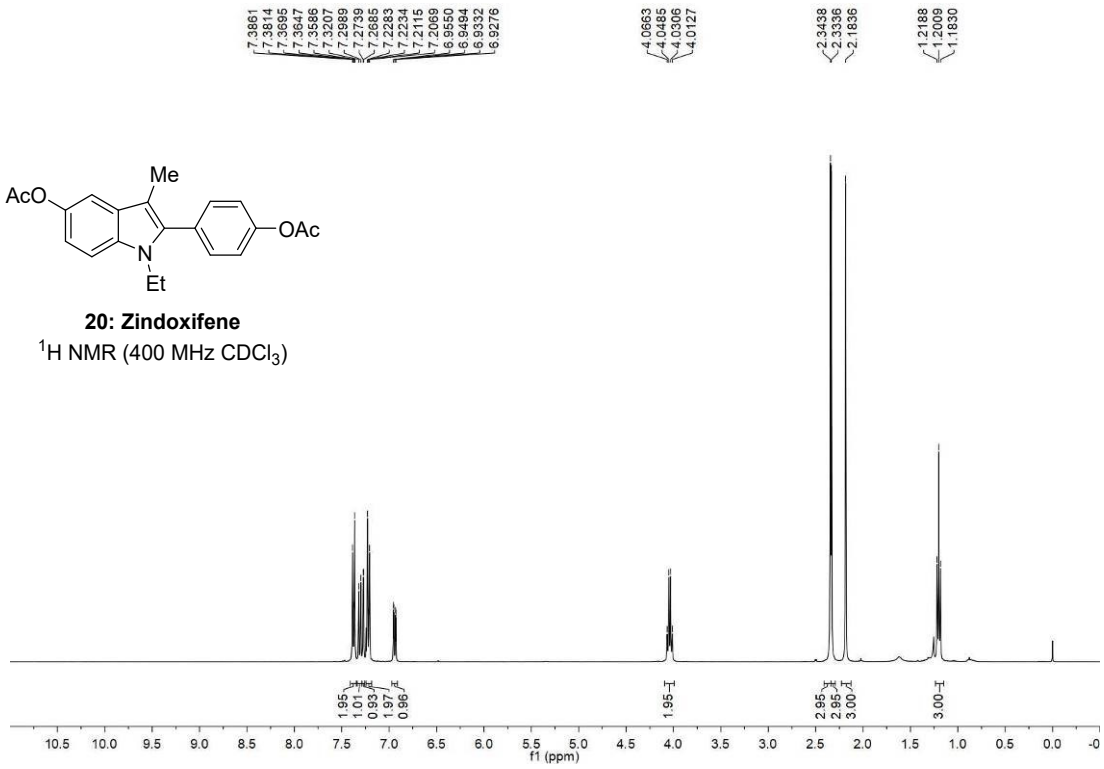
19

^{1}H NMR (400 MHz $CDCl_3$)



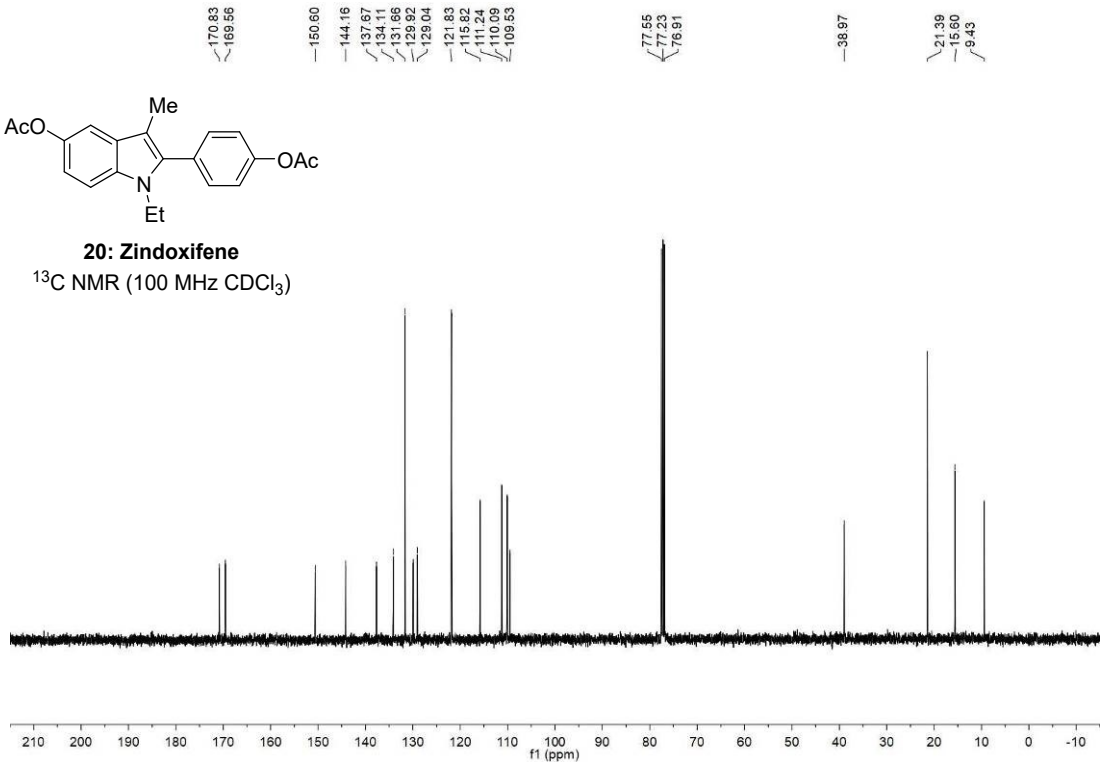
19

^{13}C NMR (100 MHz $CDCl_3$)



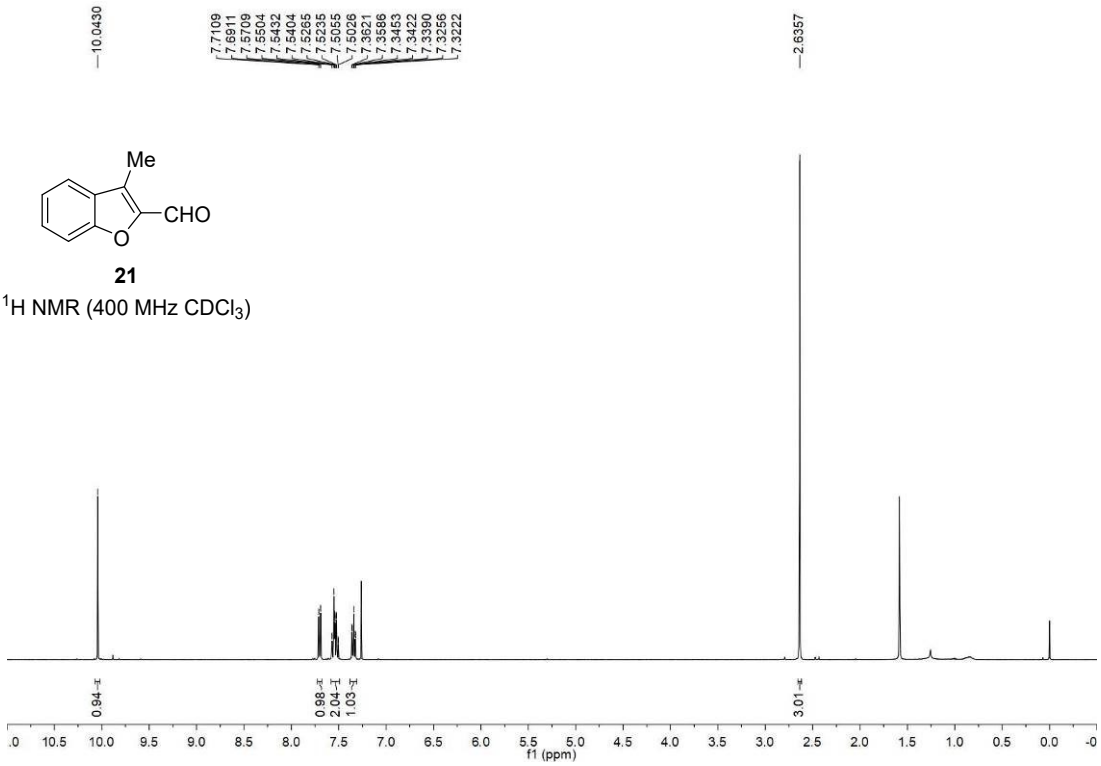
20: Zindoxifene

^{1}H NMR (400 MHz $CDCl_3$)



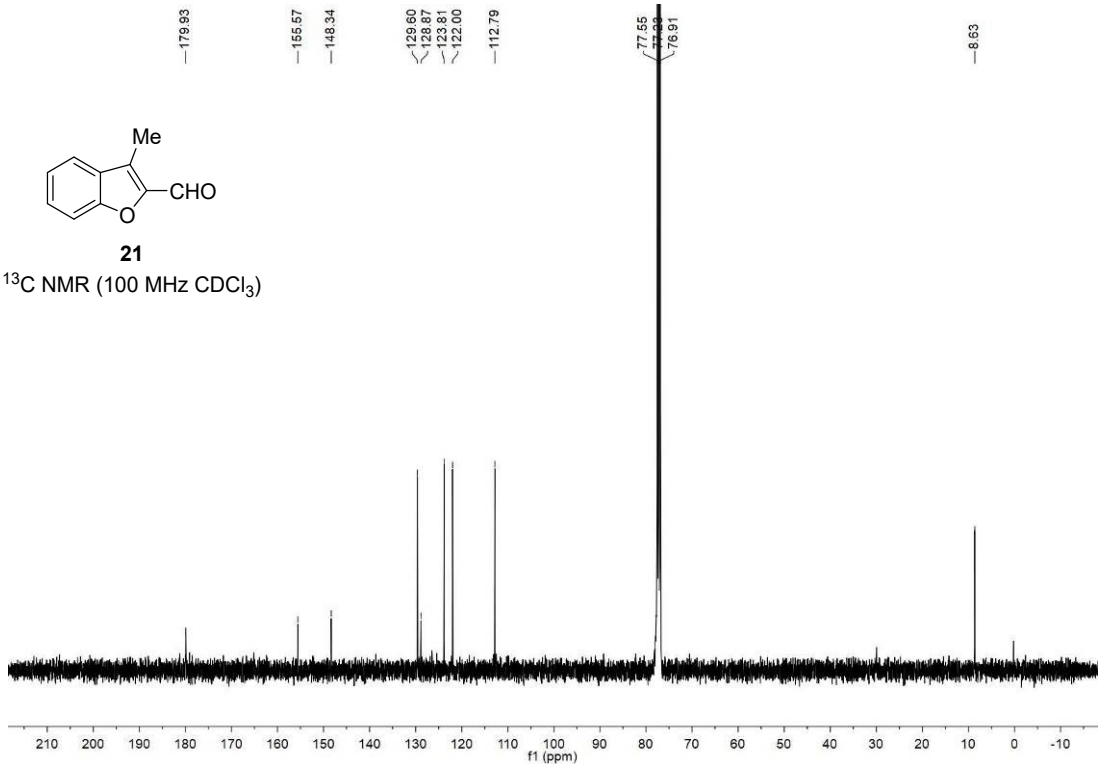
20: Zindoxifene

^{13}C NMR (100 MHz $CDCl_3$)



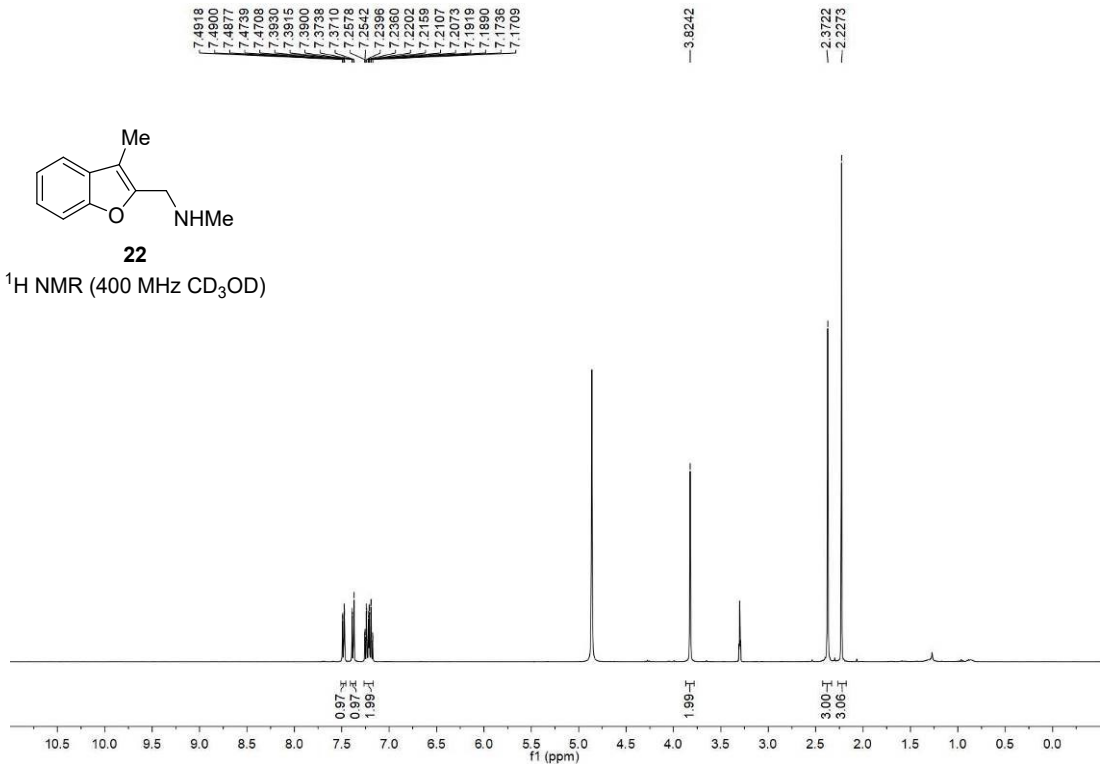
21

^{1}H NMR (400 MHz $CDCl_3$)



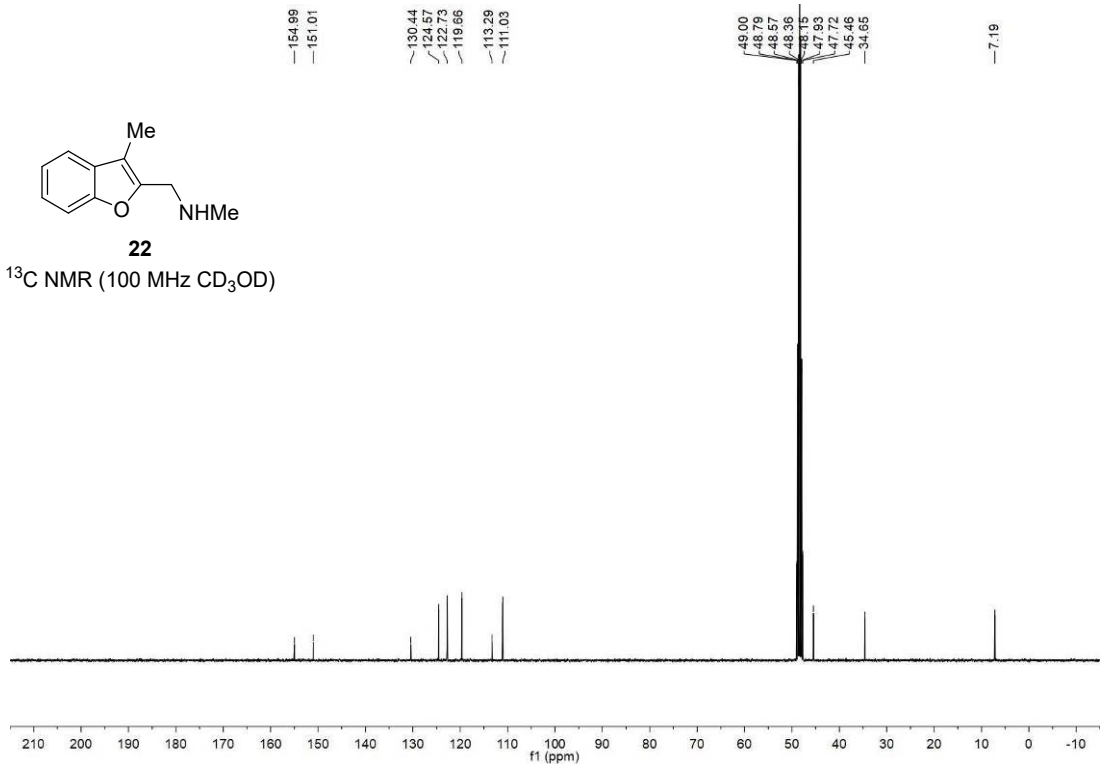
21

^{13}C NMR (100 MHz $CDCl_3$)



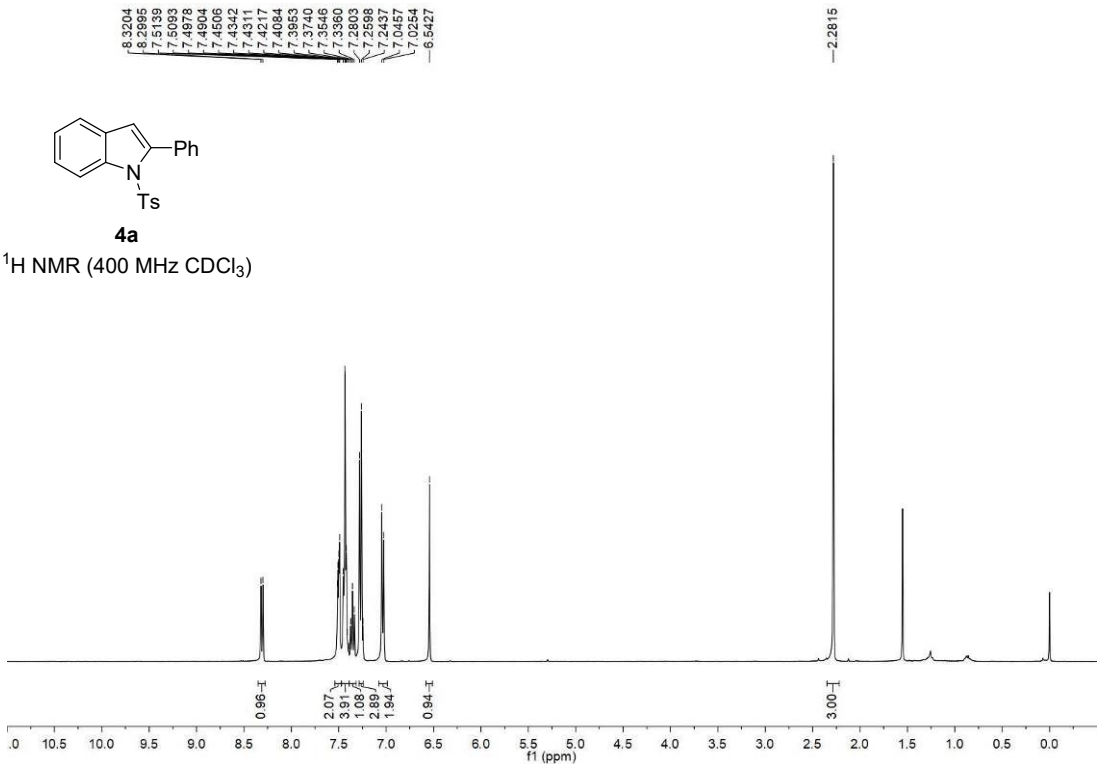
22

^{1}H NMR (400 MHz CD_3OD)



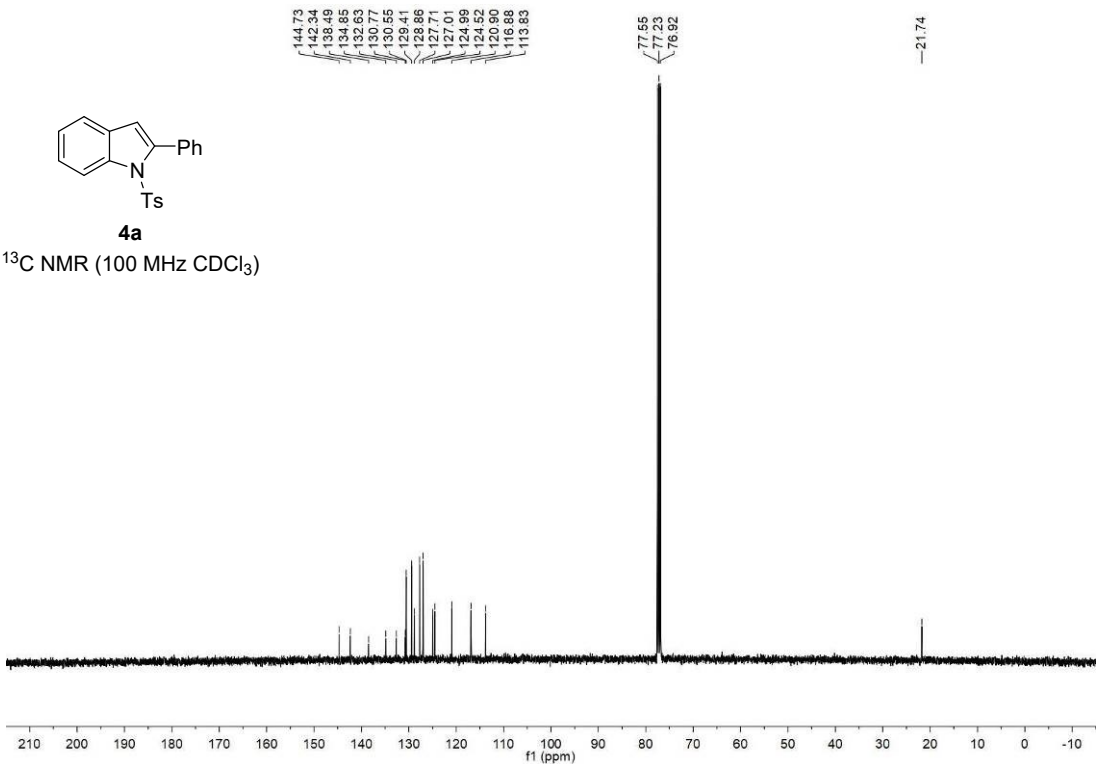
22

^{13}C NMR (100 MHz CD_3OD)



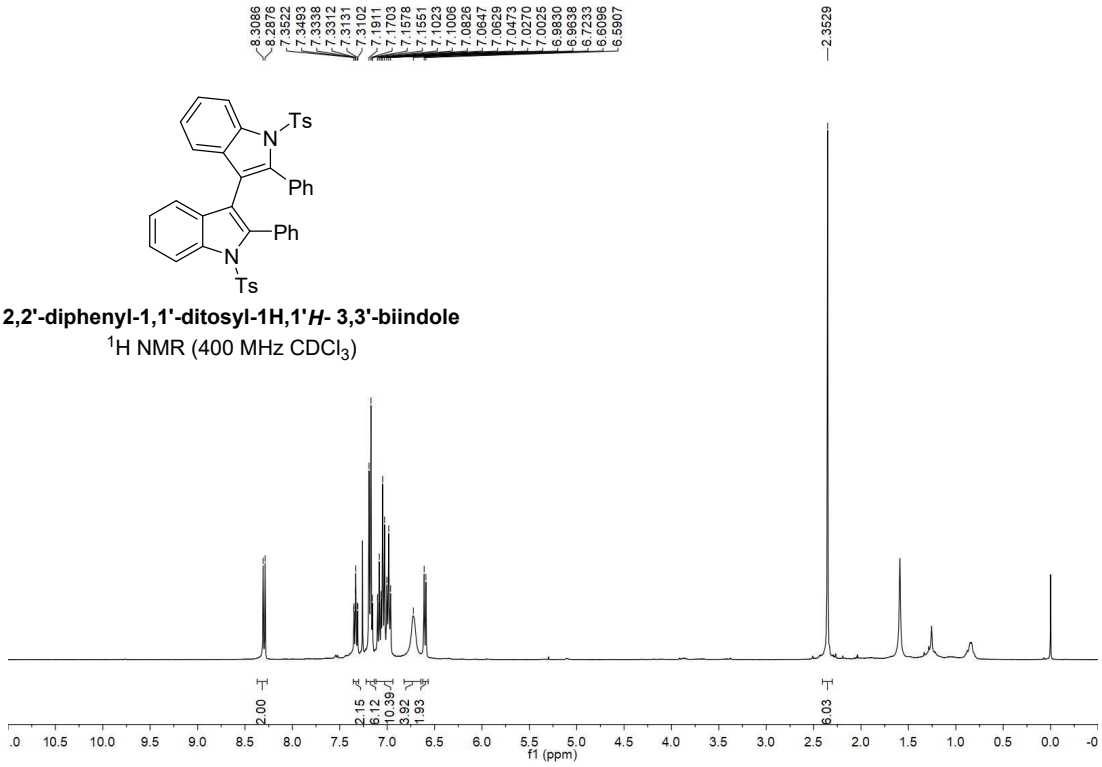
4a

^{1}H NMR (400 MHz $CDCl_3$)



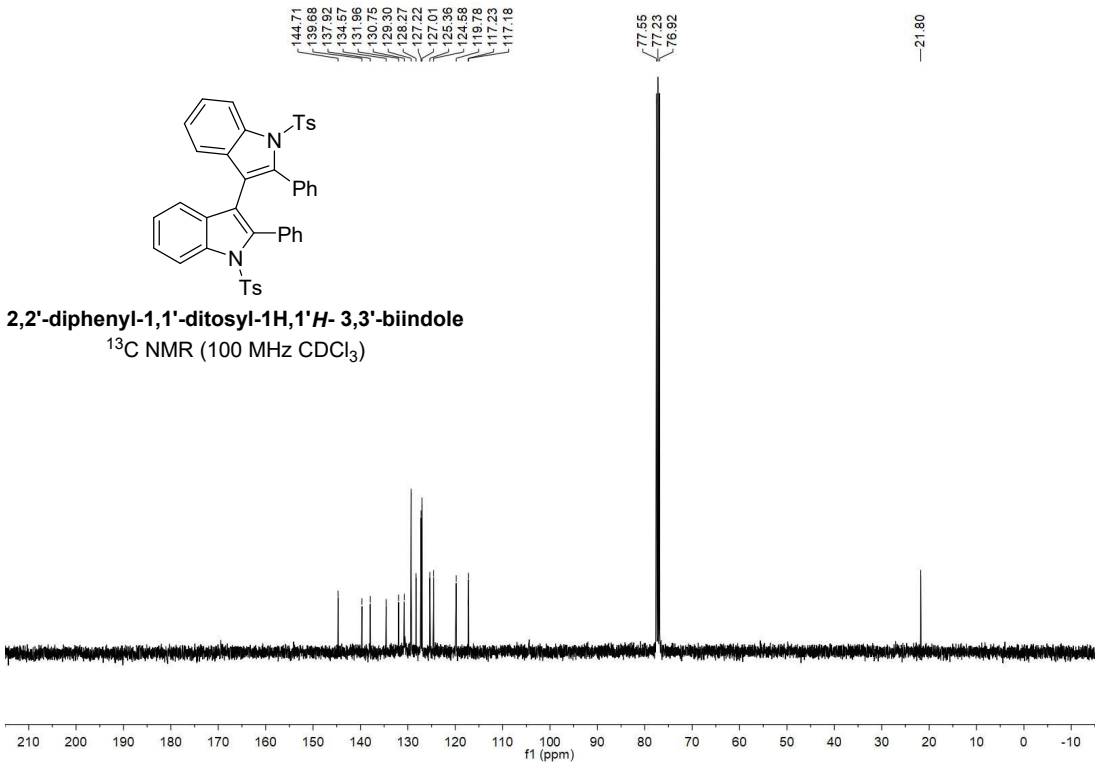
4a

^{13}C NMR (100 MHz $CDCl_3$)



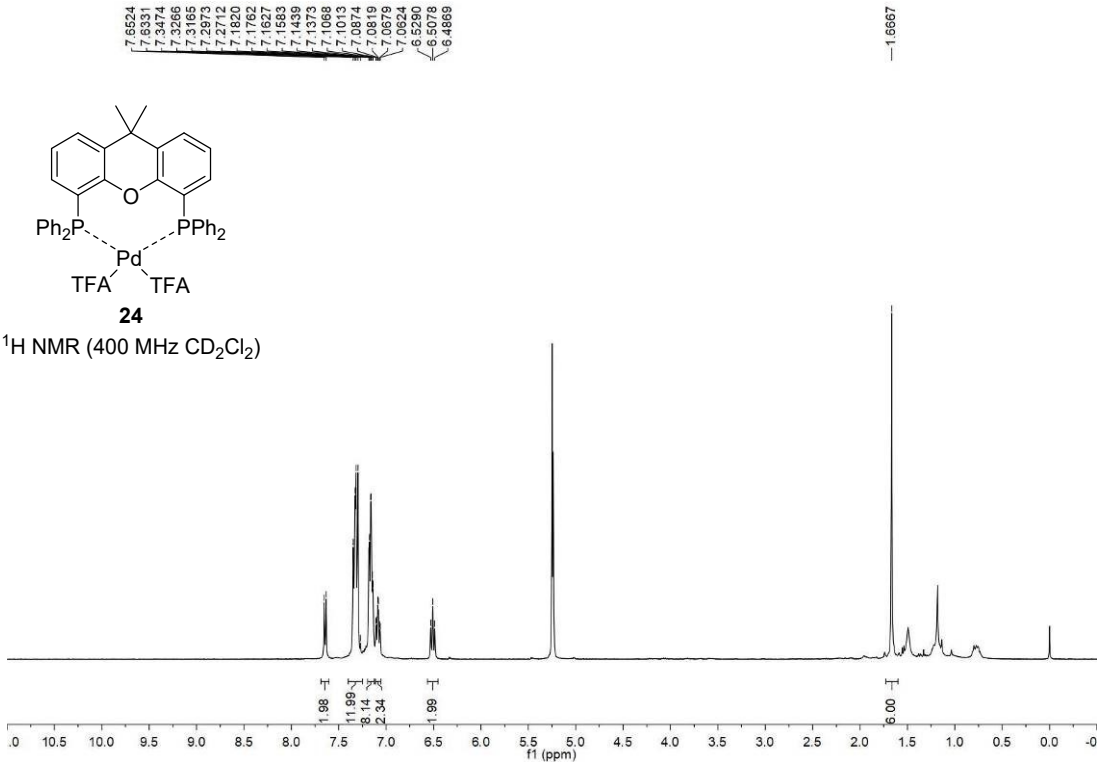
2,2'-diphenyl-1,1'-ditosyl-1H,1'*H*- 3,3'-biindole

^{1}H NMR (400 MHz $CDCl_3$)



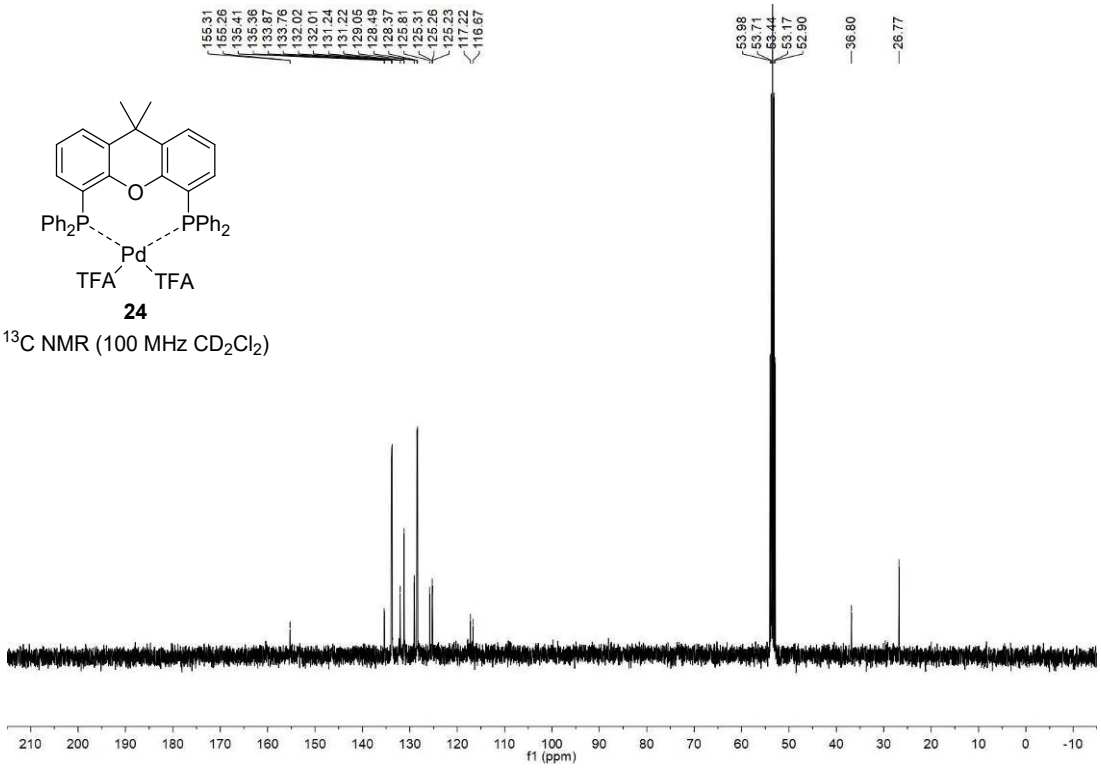
2,2'-diphenyl-1,1'-ditosyl-1H,1'*H*- 3,3'-biindole

^{13}C NMR (100 MHz $CDCl_3$)



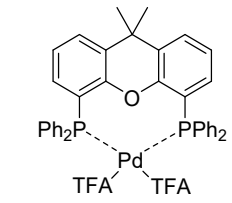
24

^{1}H NMR (400 MHz CD_2Cl_2)



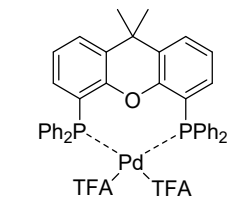
24

^{13}C NMR (100 MHz CD_2Cl_2)



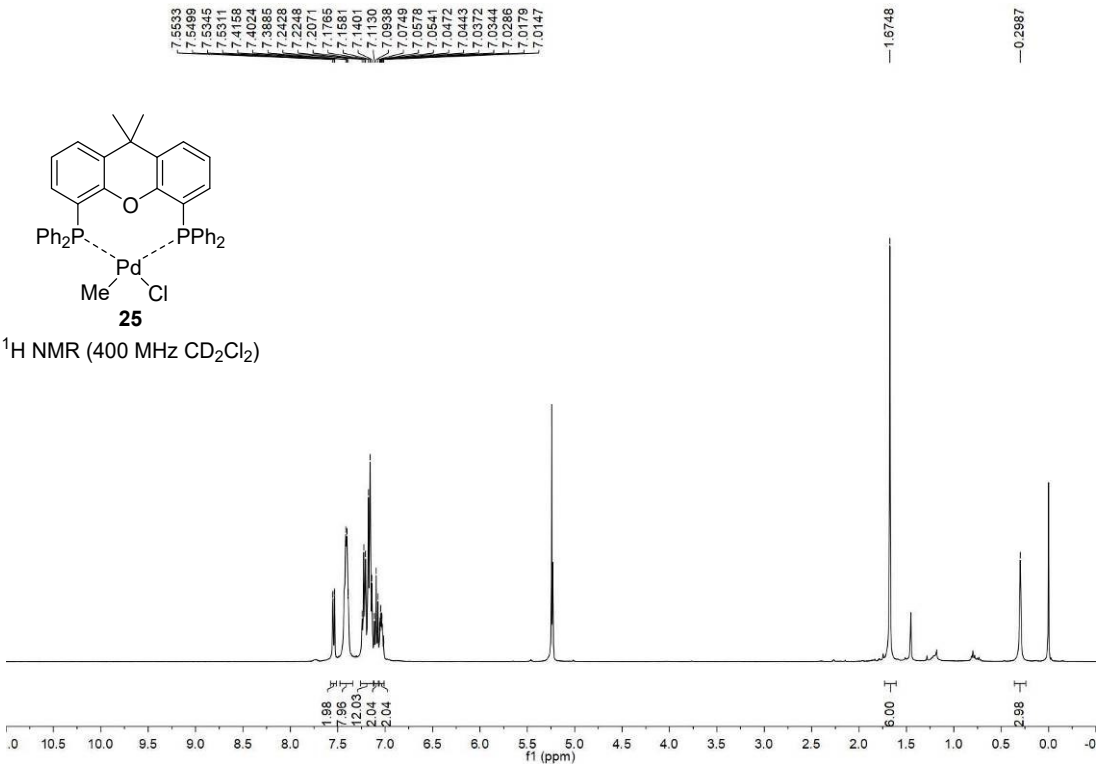
24

^{19}F NMR (376 MHz CD_2Cl_2)



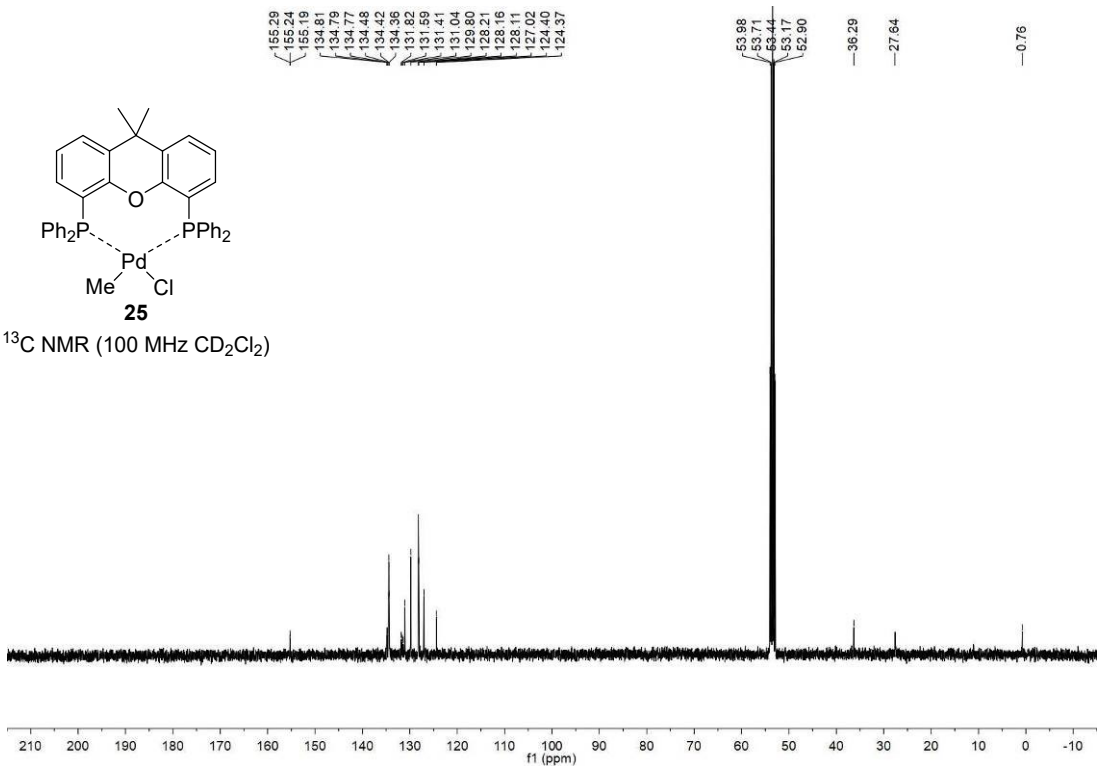
24

^{31}P NMR (162 MHz CD_2Cl_2)



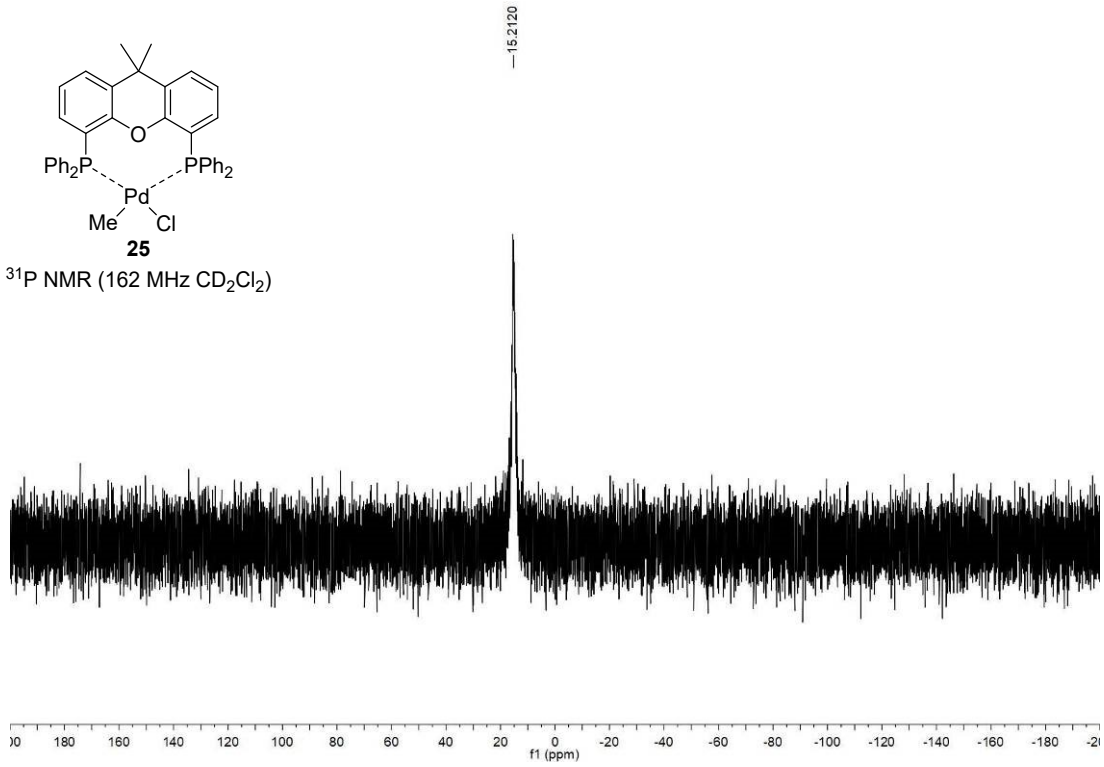
25

^{1}H NMR (400 MHz CD_2Cl_2)



25

^{13}C NMR (100 MHz CD_2Cl_2)



25

^{31}P NMR (162 MHz CD_2Cl_2)