Electronic Supplementary Information

Substrate controlled regioselective C(sp^2)–H sulfonylation of *ortho*-aminophenols

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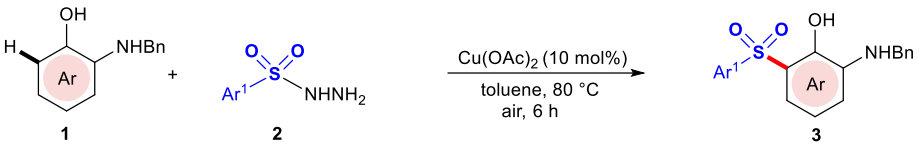
1. General Information

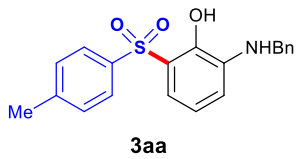
Reactions were performed under aerial conditions. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL-ECS400 spectrometer at 400 MHz and 100 MHz respectively. The ^{1}H NMR and ^{13}C NMR chemical shifts were assigned to tetramethylsilane (TMS) or residual solvent peak as an internal standard. High-resolution mass spectra (HRMS) were recorded on an Agilent–6545Q-TOF micro mass spectrometer. Fluorescence measurements were carried out using a Hitachi fluorimeter. Aldehydes, ketones, Sulfonyl Chloride, Sulfonyl hydrazide, amino phenol derivatives, copper compounds, and other chemicals were purchased from Sigma-Aldrich, Alfa-Aesar, and Acros Organics and used as received. Solvents used in the reactions were collected from the M-Braun Solvent Purification System. Sulfonyl hydrazide[1,2] and *N*-benzyl amino phenol[3,4] were prepared according to the standard procedure reported in the literature.

2. Cu(II)-catalyzed sulfonylation of *ortho*-aminophenols



General Procedure: Amino phenol **1** (0.25 mmol, 1.0 equiv) and aryl sulfonyl hydrazide **2** (0.75 mmol, 3.0 equiv.) were dissolved in 1 mL toluene in a 25 mL round bottom flask. Next, Cu(II)-catalyst (0.025 mmol, 10 mol%) was added to that solution at room temperature with continuous stirring for 10 minutes. The reaction mixture was heated at 80 °C for 6 h in an oil bath under aerial conditions. after completion of the reaction, the solvent was evaporated under reduced pressure. Pure compound was isolated with the aid of column chromatography using ethyl acetate/hexane as eluent to afford aryl sulfone **3**.

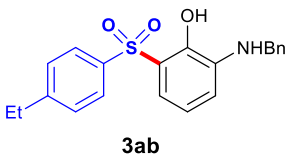
2-(Benzylamino)-6-tosylphenol (3aa): Analytical TLC in silica gel 1:4 ethyl acetate/hexane



3aa

R_f = 0.50; White Solid, Yield = 89% (79 mg, 0.22 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.47 (s, 1H), 7.82 (d, *J* = 8.4 Hz, 2H), 7.27-7.35 (m, 7H), 6.90-6.93 (m, 1H), , 6.78 (t, *J* = 8 Hz, 1H), 6.63-6.65 (m, 1H), 4.85 (s, 1H), 4.35 (d, *J* = 3.6 Hz, 2H), 2.41 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 144.6, 143.0, 138.9, 138.5, 138.4, 130.0, 128.7, 127.4, 127.3, 126.9, 122.2, 120.9, 115.1, 114.4 47.8, 21.6; HRMS [M+H$^+$] calcd for $C_{20}H_{20}NO_3S$: (m/z) = 354.1164, found = 354.1162.

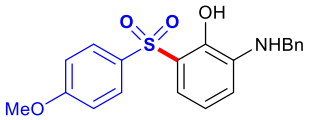
2-(Benzylamino)-6-((4-ethylphenyl)sulfonyl)phenol (3ab): Analytical TLC in silica gel 1:4



3ab

ethyl acetate/hexane R_f = 0.50; Yield = 81% (74.7 mg, 0.20 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.47 (s, 1H), 7.84 (d, *J* = 8.8 Hz, 2H), 7.27-7.35 (m, 7H), 6.92-6.94 (m, 1H), 6.78 (t, *J* = 8 Hz, 1H), 6.63-6.66 (m, 1H), 4.85 (s, 1H), 4.35 (s, 2H), 2.70 (q, *J* = 7.6 Hz, 2H), 1.23 (t, *J* =7.6 Hz, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 150.7, 143.0, 139.1, 138.6, 138.5, 128.8, 128.7, 127.4, 127.3, 127.0, 122.2, 120.9, 115.1, 114.5, 47.9, 28.9, 15.0; HRMS [M+H$^+$] calcd for $C_{21}H_{22}NO_3S$: (m/z) = 368.1320, 368.1320, found = 368.1325.

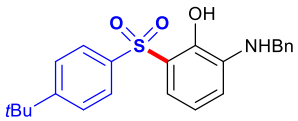
2-(Benzylamino)-6-((4-methoxyphenyl)sulfonyl)phenol (**3ac**): Analytical TLC in silica gel



3ac

1:4 ethyl acetate/hexane R_f = 0.50; Yield = 87% (80.8 mg, 0.22 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.47 (s, 1H), 7.87 (d, *J* =8.4 Hz, 2H), 7.28-7.35 (m, 5H), 6.97 (d, *J* =8.8 Hz, 2H), 6.89-6.91 (m, 1H), 6.78 (t, *J* =8 Hz, 1H), 6.62-6.64 (m, 1H), 4.85 (s, 1H), 4.35 (d, *J* = 4.4 Hz, 2H), 3.85 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 163.6, 142.8, 138.6, 138.4, 133.4, 129.1, 128.7, 127.4, 127.3, 122.6, 120.9, 115.0, 114.5, 114.3, 55.7, 47.8; HRMS [M+H$^+$] calcd for $C_{20}H_{20}NO_4S$: (m/z) =370.1113, found = 370.1127.

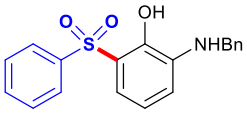
2-(Benzylamino)-6-((4-(tert-butyl)phenyl)sulfonyl)phenol (3ad): Analytical TLC in silica



3ad

gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 80% (79.5 mg, 0.20 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.48 (s, 1H), 7.85 (d, *J* = 8.8 Hz, 2H), 7.52(d, *J* =8.8 Hz, 2H), 7.27-7.35 (m, 7H), 6.94-6.97 (m, 1H), 6.79 (t, *J* = 8Hz, 1H), 6.65-6.67 (m, 1H), 4.36 (s, 2H), 1.31 (s, 9H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 157.5, 143.1, 138.8, 138.5, 128.7, 127.4, 127.35, 126.7, 126.4, 126.2, 122.2, 120.9, 115.3, 114.6, 47.9, 35.2, 31.0; HRMS [M+H$^+$] calcd for $C_{23}H_{26}NO_3S$: (m/z) = 396.1633, found =396.1644.

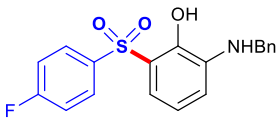
2-(Benzylamino)-6-(phenylsulfonyl)phenol (**3ae**): Analytical TLC in silica gel 1:4 ethyl



3ae

acetate/hexane R_f = 0.50; Yield = 79% (67.5 mg, 0.198 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.47 (s, 1H), 7.94-7.96 (m, 2H), 7.57-7.61 (m, 1H), 7.45-7.53 (m, 2H), 7.27-7.36 (m, 5H), 6.93-6.95 (m, 1H), 6.80 (t, *J* = 8 Hz, 1H), 6.65-6.68 (m, 1H), 4.89 (s, 1H), 4.36 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.2, 141.9, 138.6, 133.6, 129.4, 128.8, 127.5, 127.4, 126.9, 121.9, 121.1, 115.3, 114.8, 48.0; HRMS [M+H$^+$] calcd for $C_{19}H_{18}NO_3S$: (m/z) = 340.1007, found =340.1018.

2-(Benzylamino)-6-((4-fluorophenyl)sulfonyl)phenol (**3af**): Analytical TLC in silica gel 1:4

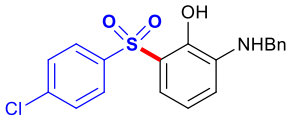


3af

ethyl acetate/hexane R_f = 0.50; Light Brown solid, Yield = 73% (65.7 mg, 0.18 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.37 (s, 1H), 7.94-7.97 (m, 2H), 7.27-7.35 (m, 5H), 7.17-7.21 (m, 2H), 6.90-6.92 (m, 1H), 6.80 (t, *J* = 8 Hz, 1H), 6.66-6.68 (m, 1H), 4.88(s, 1H), 4.36 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 142.9, 138.5, 138.4, 137.9, 129.7, 129.6, 128.7, 127.4, 127.3, 121.4 (C-F, *J* = 210.8 Hz), 116.65 (C-F, *J* = 92 Hz), 114.9, 114.7, 47.8; **^{19}F NMR (CDCl$_3$, 400 MHz):** δ [(-

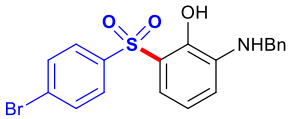
103.32)-(-103.38)] (m, 1F); HRMS [M+H$^+$] calcd for $C_{19}H_{17}FNO_3S$: (m/z) =358.0913, found = 358.0910.

2-(Benzylamino)-6-((4-chlorophenyl)sulfonyl)phenol (3ag): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 79% (73.8 mg, 0.197 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.34 (s, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.49 (d, *J* = 8.8 Hz, 2H), 7.28-7.35 (m, 5H), 6.89-6.91 (m, 1H), 6.80 (t, *J* = 8 Hz, 1H), 6.66-6.68 (m, 1H), 4.86 (s, 1H), 4.36 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.0, 140.3, 140.26, 138.6, 138.4, 129.7, 128.7, 128.3, 127.4, 127.3, 121.5, 121.2, 115.0, 114.8, 47.8; HRMS [M+H$^+$] calcd for $C_{19}H_{17}ClNO_3S$: (m/z) = 374.0618, found = 374.0623



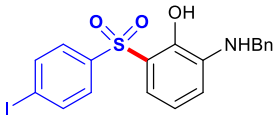
3ag

2-(Benzylamino)-6-((4-bromophenyl)sulfonyl)phenol (**3ah**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 75% (79 mg, 0.188 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.33 (s, 1H), 7.79 (d, *J* = 8.8 Hz, 2H), 7.65 (d, *J* = 8.8 Hz, 2H), 7.27-7.35 (m, 5H), 6.89-6.91 (m, 1H), 6.80 (t, *J* = 8 Hz, 1H), 6.66-6.68 (m, 1H), 4.88 (s, 1H), 4.36 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.0, 140.9, 138.6, 138.4, 132.7, 128.8, 128.7, 128.3, 127.4, 127.3, 121.4, 121.2, 115.0, 114.9, 47.8; HRMS [M+H$^+$] calcd for $C_{19}H_{17}{}^{81}BrNO_3S$: (m/z) = 420.0092, found = 420.0094.



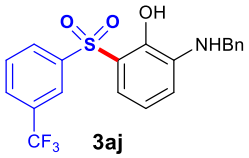
3ah

2-(Benzylamino)-6-((4-iodophenyl)sulfonyl)phenol (**3ai**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 72% (83.9 mg, 0.18 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.33 (s, 1H), 7.87 (d, *J* = 8.8 Hz, 2H), 7.63 (d, *J* =8.4 Hz), 7.27-7.35 (m, 5H), 6.89-6.91 (m, 1H), 6.80 (t, *J* = 8.0 Hz, 1H), 6.66-6.68 (m, 1H), 4.90 (s, 1H), 4.36 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.2, 141.6, 138.7, 138.66, 138.5, 128.8, 128.2, 127.5, 127.4, 121.5, 121.3, 115.1, 115.0, 101.5, 47.9; HRMS [M+H$^+$] calcd for $C_{19}H_{17}INO_3S$: (m/z) = 465.9974, found =465.9976.



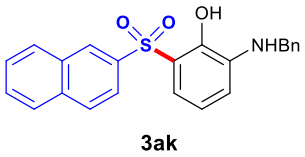
3ai

2-(Benzylamino)-6-((3-(trifluoromethyl)phenyl)sulfonyl)phenol (**3aj**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 52% (53.5 mg, 0.13 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.30 (s, 1H), 8.20 (s, 1H), 8.11 (d, *J* = 8 Hz, 1H), 7.85 (d, *J* =8.4 Hz, 1H), 7.68 (t, *J* = 8 Hz, 1H), 7.28-7.35 (m, 5H), 6.94-6.97 (m, 1H), 6.83 (t, *J* =8.4 Hz, 1H), 6.70-6.73 (m, 1H), 4.37 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.1-143.2 (C-F, J= 40 Hz), 138.7, 138.5, 131.9-132.2 (C-F, J=130.4 Hz), 130.2, 128.8, 127.4, 127.3, 124.4, 123.9, 121.7, 121.4, 120.9, 115. 1, 115.0, 47.8; **^{19}F NMR (CDCl$_3$, 400 MHz):** δ -63.12 (S, 3F); HRMS [M+H$^+$] calcd for $C_{20}H_{17}F_3NO_3S$: (m/z) = 408.0881, found = 408.0887.



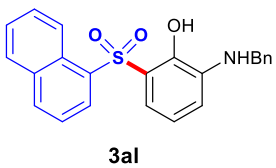
3aj

2-(Benzylamino)-6-(naphthalen-2-ylsulfonyl)phenol (3ak): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 75% (73.3 mg, 0.187 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.56 (s, 1H), 8.55 (s, 1H), 7.85-8.00 (m, 4H), 7.59-7.67 (m, 2H), 7.27-7.35 (m, 5H), 6.97-7.00 (m, 1H), 6.79 (t, *J* = 8 Hz, 1H), 6.64-6.66 (m, 1H), 4.88 (s, 1H), 4.35 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.1, 138.6, 138.5, 135.2, 132.1, 129.8, 129.5, 129.3, 128.7, 128.2, 127.9, 127.7, 127.4, 127.3, 121.9, 121.0, 115.3, 114.6, 47.9; HRMS [M+H$^+$] calcd for $C_{23}H_{20}NO_3S$: (m/z) = 390.1164, found = 390.1164.



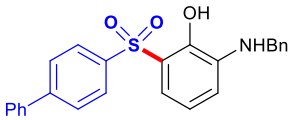
3ak

2-(Benzylamino)-6-(naphthalen-1-ylsulfonyl)phenol (**3al**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 80% (78.1 mg, 0.20 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.62 (s, 1H), 8.60 (d, *J* = 9.2 Hz, 1H), 8.32-8.34 (m, 1H), 8.10 (d, *J* = 8.4 Hz, 1H), 7.92 (d, *J* = 7.6 Hz, 1H), 7.63-7.67 (m, 1H), 7.56-7.60 (m, 2H), 7.27-7.36 (m, 5H), 6.80-6.83 (m, 1H), 6.73 (t, *J* = 8 Hz, 1H), 6.63-6.65 (m, 1H), 4.93 (s, 1H), 4.37 (s, 2H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.5, 138.5, 136.1, 135.3, 134.3, 129.1, 129.05, 128.7, 128.6, 128.3, 127.4, 127.3, 127.0, 124.2, 123.9, 121.5, 120.8, 115.3, 114.5, 47.9; HRMS [M+H$^+$] calcd for $C_{23}H_{20}NO_3S$: (m/z) =390.1164, found = 390.1175.



3al

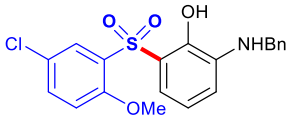
2-([1,1'-Biphenyl]-4-ylsulfonyl)-6-(benzylamino)phenol (3am): Analytical TLC in silica gel



3am

1:4 ethyl acetate/hexane R_f = 0.50; Yield = 83% (86.8 mg, 0.21 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.48 (s, 1H), 8.00 (d, *J* = 8.8 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.55-7.58 (m, 2H), 7.41-7.49 (m, 3H), 7.27- 7.36 (m, 5H), 6.96-6.99(m, 1H), 6.82 (t, *J* = 8 Hz, 1H), 6.66-6.68 (m, 1H), 4.88 (s, 1H), 4.36 (s, 2H);); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 146.6, 143.1, 140.3, 139.1, 138.5, 129.1, 128.7, 128.6, 128.0, 127.4, 127.35, 127.3, 122.0, 121.0, 115.2, 114.6, 47.9; HRMS [M+H$^+$] calcd for $C_{25}H_{22}NO_3S$: (m/z) = 416.1320, found = 416.1322.

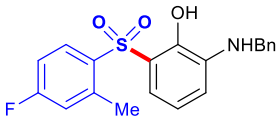
2-(Benzylamino)-6-((5-chloro-2-methoxyphenyl)sulfonyl)phenol (**3an**): Analytical TLC in



3an

silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 65% (65.5 mg, 0.16 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.50 (s, 1H), 8.06 (d, *J* =2.4 Hz, 1H), 7.47-7.50 (m, 1H), 7.28-7.36 (m, 5H), 6.88 (d, *J* = 8.8 Hz, 1H), 6.79-6.81 (m, 1H), 6.56 (t, *J* = 8 Hz, 1H), 6.66-6.68 (m, 1H), 4.88 (s, 1H), 4.39 (s, 2H), 3.80 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 156.2, 144.8, 138.7, 138.0, 135.1, 130.7, 128.8, 128.7, 127.4, 127.3, 125.9, 120.4, 120.1, 115.8, 114.4, 113.8, 56.3, 47.8; HRMS [M+H$^+$] calcd for $C_{20}H_{19}ClNO_4S$: (m/z) = 404.0723, found = 404.0720.

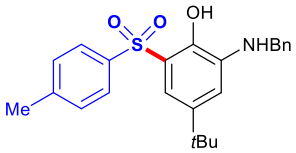
2-(Benzylamino)-6-((4-fluoro-2-methylphenyl)sulfonyl)phenol (**3ap**): Analytical TLC in



3ao

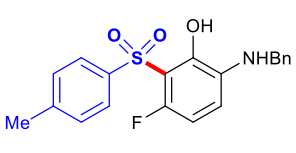
silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 62% (58 mg, 0.156 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.51 (s, 1H), 8.11-8.15 (m, 1H), 7.27-7.36 (m, 5H), 7.04-7.09 (m, 1H), 6.96-6.99 (m, 1H), 6.76 (t, *J* = 8 Hz, 1H), 6.65-6.67 (m, 1H), 6.62-6.64 (m, 1H), 4.90 (s, 1H), 4.38 (d, *J* = 3.2 Hz, 2H), 2.50 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 143.9, 141.7, 141.6, 138.4, 135.2,131.7 (C-F, J= 46 Hz), 128.7, 127.4, 127.3, 120.8, 120.6, 119.8 (C-F, J= 92 Hz), 115.1, 114.3, 113.5, 113.3, 47.8, 20.1; **^{19}F NMR (CDCl$_3$, 400 MHz):** δ [(-104.5)-(-104.6)] (m, 1F); HRMS [M+H$^+$] calcd for $C_{20}H_{19}FNO_3S$: (m/z) =372.1070, found = 372.1077.

2-(Benzylamino)-4-(tert-butyl)-6-tosylphenol (**3ba**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 85% (87 mg, 0.21 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.27 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.28-7.38 (m, 7H), 6.95 (d, *J* = 2 Hz, 1H), 6.76 (d, *J* = 2 Hz, 1H), 4.36 (s, 2H), 2.41 (s,3H), 1.15 (s, 9H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 144.5, 144.0, 141.6, 138.9, 130.2, 130.0, 128.7, 127.8, 127.6, 126.8, 121.6, 48.6, 34.5, 31.1, 21.6; HRMS [M+H$^+$] calcd for $C_{24}H_{28}NO_3S$: (m/z) =410.1790, found = 410.1809.



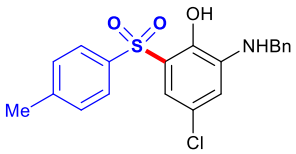
3ba

6-(Benzylamino)-3-fluoro-2-tosylphenol (**3ca**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 65% (60.8 mg, 0.16 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 10.41 (s, 1H) 7.88-7.90 (m,2H), 7.27-7.36 (m, 7H), 6.51-6.54 (m, 1H), 6.39- 6.44 (m, 1H), 4.69 (s, 1H), 4.33 (s, 2H), 2.43 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 149.3, 145.2, 138.5, 138.4, 134.8, 129.7, 128.7, 127.6, 127.4, 127.3, 113.7, 113.6, 106.4, 106.2, 48.0, 21.7; **^{19}F NMR (CDCl$_3$, 400 MHz):** δ -124. 07 (s, 1F); HRMS [M+H$^+$] calcd for $C_{20}H_{18}FNO_3S$: (m/z) =372.1070, found = 372.1069.



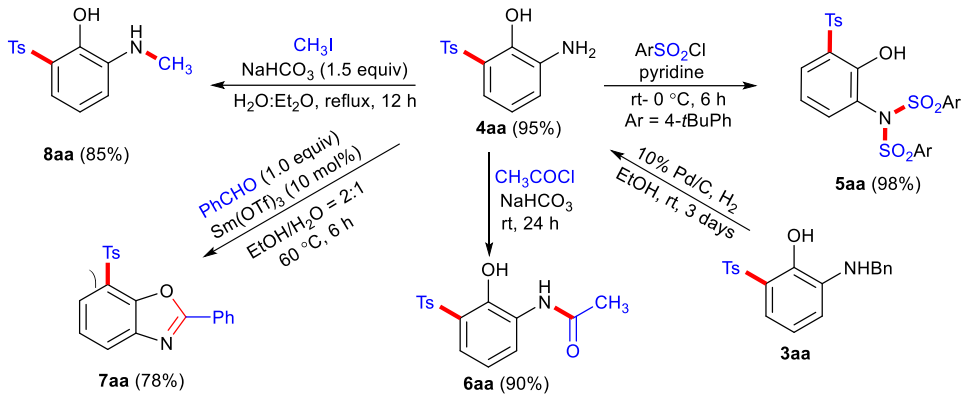
3ca

2-(Benzylamino)-4-chloro-6-tosylphenol (**3da**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 76% (74 mg, 0.19 mmol).**^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.45 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.28-7.38 (m, 7H) 6.85 (d, *J* = 2.0 Hz, 1H), 6.57 (d, *J* =2.0 Hz, 1H), 4.93 (s, 1H), 4.32 (d, J = 5.2 Hz, 2H), 2.43 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 145.1, 141.7, 139.6, 138.3, 137.7, 130.1, 128.8, 127.6, 127.4, 127.0, 126.2, 122.8, 113.9, 113.5, 47.7, 21.6; HRMS [M+H$^+$] calcd for $C_{20}H_{19}ClNO_3S$: (m/z) =388.0774, found =388.0777.



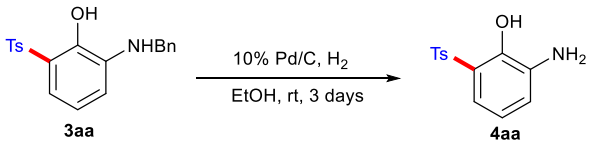
3da

3. Synthetic transformation of aryl sulfone

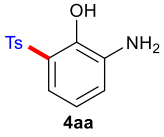


Scheme S1 Synthetic transformation of sulfonylated *ortho*-aminophenol 3aa.

3A. Benzyl group deprotection of aryl sulfone 3aa

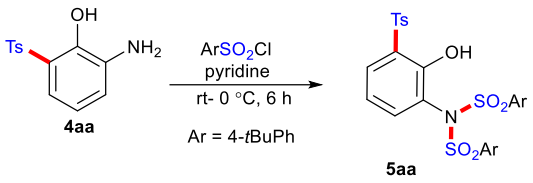


Experimental procedure[5]: Compound **3aa** (71.0 mg, 0.2 mmol, 1.0 equiv.) was taken in an autoclave by dissolving in 30 mL of EtOH under argon atmosphere. Next, 7.1 mg of 10% Pd/C (50% wet), was added. After that, the reaction chamber was degassed and purged with hydrogen gas. The reaction was allowed to proceed for 3 days at room temperature. After completion, the solvent was removed using a rotary evaporator, and the resulting reaction mixture was filtered through celite and extracted three times with ethyl acetate. The final wash of the crude reaction mixture with distilled hexane yielded a yellowish solid **4aa**.



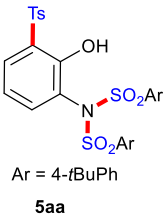
2-Amino-6-tosylphenol (**4aa**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 95% (50.2 mg, 0.1908 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.28 (bs, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.99-7.02 (m, 1H), 6.82-6.84 (m, 1H), 6.76 (t, *J* = 8.0 Hz, 1H), 3.80 (s, 2H), 2.39 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 144.6, 143.2, 138.7, 136.9, 129.9, 126.8, 123.2, 120.7, 119.7, 117.4, 21.6; HRMS [M+H$^+$] calcd for $C_{13}H_{14}NO_3S$: (m/z) =264.0694, found = 264.0698.

3B. Amine sulfonylation of aryl sulfone 4aa

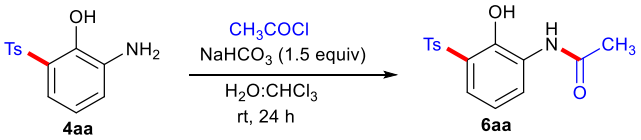


Experimental procedure[6]: was dissolved in 5ml of pyridine and kept at 0 °C for 15 minutes. Next, the 4-tert-butylbenzenesulfonyl chloride (17.83 µl, 0.25 mmol, 1.0 equiv.) was added dropwise, and the reaction mixture was stirred at room temperature for 6 h. The progress of the reaction was monitored by TLC. After completion, the reaction mixture was extracted with ethyl acetate and column chromatography was conducted by using 5% ethyl acetate in hexane to get pure **5aa** as white solid.

4-(Tert-butyl)-*N*-((4-(tert-butyl)phenyl)sulfonyl)-*N*-(2-hydroxy-3-tosylphenyl)benzene sulfonamide (**5aa**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; White Solid, Yield = 98% (160.2 mg, 0.24 mmol). **^{1}H NMR ($CDCl_3$, 400 MHz)**: δ 8.48 (s, 1H), 8.07 (d, *J* = 8.8 Hz, 2H), 7.84-7.87 (m, 1H), 7.79-7.81 (m, 3H), 7.69 (d, *J* = 8.8 Hz, 2H), 7.43 (d, *J* = 8.8 Hz, 2H), 7.34 (t, *J* = 8 Hz, 1H), 6.99-7.04 (m, 5H), 2.34 (s, 3H), 1.43 (s, 9H), 1.29 (s, 9H); **^{13}C NMR ($CDCl_3$, 100 MHz)**: δ 160.0, 157.5, 144.5, 137.8, 136.0, 133.3, 131.1, 129.8, 129.4, 127.9, 127.6, 127.4, 126.3, 126.1, 126.0, 125.6, 35.7, 35.3, 31.2, 31.1, 21.7; HRMS [M+H$^+$] calcd for $C_{33}H_{38}NO_7S_3$: (m/z) = 656.1810, found = 656.1822.

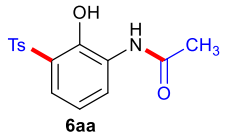


3C. Acylation of 4aa



Experimental procedure[7]: The compound **4aa** (88.52 mg, 0.25mmol, 1equiv.) was introduced into a solvent mixture of H_2O: $CHCl_3$ and subsequently treated with $NaHCO_3$ (31.50 mg, 0.375 mmol, 1.5 equiv.) by stirring at room temperature for 15 minutes. Now, acyl chloride (17.83

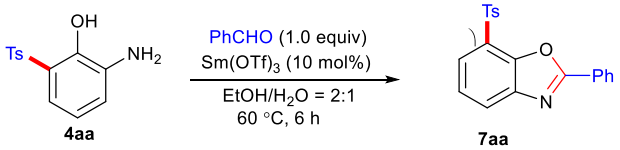
µl,0.25 mmol, 1equiv.) was added drop-wise, and the reaction was subjected to reflux for 24 h. The reaction mixture was then extracted with ethyl acetate, followed by column chromatography by using 50% ethyl acetate in hexane to get **6aa** as white solid.



6aa

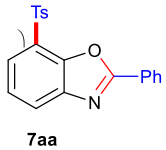
***N*-(2-Hydroxy-3-tosylphenyl)acetamide (6aa):** Analytical TLC in silica gel 1:1 ethyl acetate/hexane R_f = 0.50; Yield = 90% (69 mg, 0.22 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 9.73 (s, 1H), 8.47 (d, *J* = 8.0 Hz, 1H), 7.79-7.81 (m, 3H), 7.31-7.35(m, 3H), 6.95 (t, *J* = 8.0 Hz, 1H), 2.41 (s, 3H), 2.22 (s, 3H); **13C NMR (DMSO, 100 MHz): δ** 168.6, 145.1, 144.3, 138.3, 130.1, 129.5, 128.3, 127.0, 125.3, 123.5, 122.7, 120.9, 24.4, 21.7; HRMS [M+H$^+$] calcd for $C_{15}H_{16}NO_4S$: (m/z) =306.0800, found = 306.0802.

3D. Cyclization of sulfonylated aminophenol 4aa



4aa **7aa**

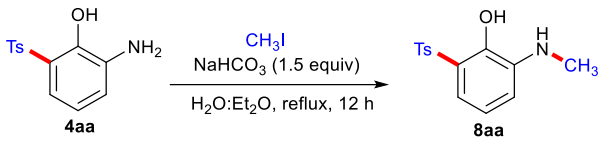
Experimental procedure[8]: In a 4 ml of solvent mixture of EtOH and H_2O (1:1), the substrate **4aa** (88.52 mg, 0.25 mmol, 1 eq.) and bezaldehyde (25 µl, 0.25 mmol, 1.0 equiv.) were added. Next, $Sm(OTf)_2$ (14.93 mg, 0.025mmol, 10 mol%) was added, and the reaction mixture was stirred at 80°C for 12 h. Upon completion of the reaction, which was monitored via TLC, the mixture was extracted with H_2O:EtOAc (1:1), filtered through sodium sulfate and then evaporated in rotary evaporator. The crude product was purified by recrystallization from MeOH to get colourless solid **7aa**.



7aa

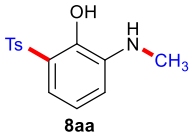
2-Phenyl-7-tosylbenzo[d]oxazole (7aa): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 78% (68.5 mg, 0.196 mmol). **^{1}H NMR (CDCl$_3$, 400 MHz)**: δ 8.25-8.27 (m, 2H), 8.07 (d, *J* = 8.4 Hz, 2H), 7.94-8.00 (m, 2H), 7.55-7.62 (m, 3H), 7.48 (t, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.0 Hz, 2H), 2.39 (s, 3H); **^{13}C NMR (CDCl$_3$, 100 MHz)**: δ 164.2, 146.2, 144.9, 143.9, 138.0, 132.3, 129.9, 129.1, 128.2, 128.0, 126.1, 125.7, 125.2, 124.7, 124.3, 21.6; HRMS [M+H$^+$] calcd for $C_{20}H_{16}NO_3S$: (m/z) =350.0851, found = 350.0850.

3E. Methylation of sulfonylated aminophenols 4aa



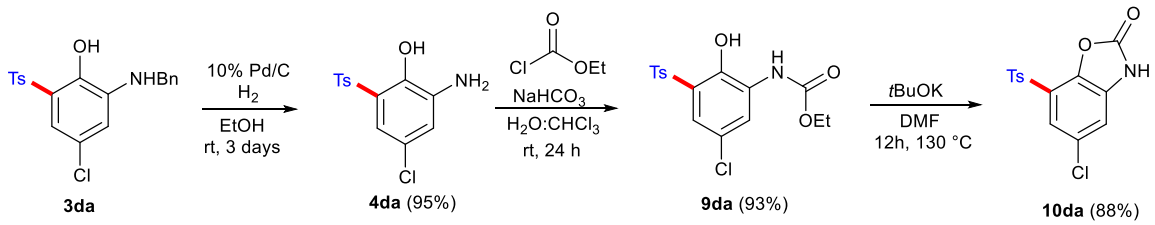
Experimental procedure[9]: The compound **4aa** (88.52 mg, 0.25mmol, 1.0 equiv.) was added to the solvent mixture of H_2O: Et_2O (1:1) and later charged with $NaHCO_3$ (31.50 mg, 0.375 mmol, 1.5 equiv.) at room temperature. After 15 minutes, drop-wise addition of methyl iodide (15 µL, 0.25 mmol, 1.0 equiv.) was performed and the solvent was refluxed for 12 h. Progress of the reaction was monitored by TLC. After completion, the reaction mixture was extracted with ethyl acetate, and further column chromatography was performed to purify **8aa**. The compound was isolated in 3% ethyl acetate in hexane.

2-(methylamino)-6-tosylphenol (8aa): Analytical TLC in silica gel 1:4 ethyl acetate/hexane



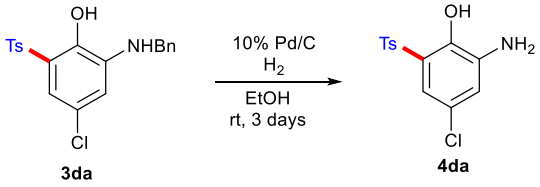
R_f = 0.50; Yield = 85% (59.2 mg, 0.21 mmol). **^{1}H NMR ($CDCl_3$, 400 MHz)**: δ 9.39 (s, 1H), 7.80 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 6.92-6.95 (m, 1H), 6.86 (t, *J* = 8.0 Hz, 1H), 6.69.6.72 (m, 1H), 2.87 (s, 3H), 2.39 (s, 3H); **^{13}C NMR ($CDCl_3$, 100 MHz)**: δ 144.6, 143.2, 139.1, 138.2, 129.9, 126.8, 122.1, 121.0, 115.2, 114.2, 30.5, 21.6; HRMS [M+H$^+$] calcd for $C_{14}H_{16}NO_3S$: (m/z) = 278.0851, found = 278.0862.

4. Late-stage modification of chlorzoxazone

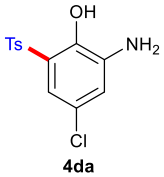


Scheme S2 Synthesis of sulfonylated chlorzoxazone.

4A. Debenzylation of 3da

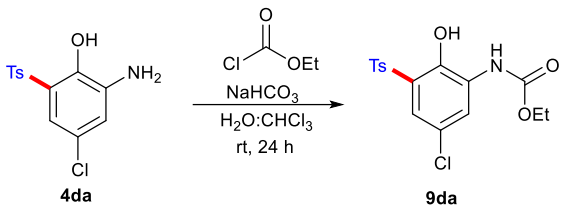


Experimental procedure[5]: Compound **3da** (193.9 mg, 0.5 mmol) was taken in an autoclave by dissolving in 70 mL of EtOH under argon atmosphere. Next, 19.4 mg of 10% Pd/C (50% wet), was added. After that, the reaction chamber was degassed and purged with hydrogen gas. The reaction was allowed to proceed for 3 days at room temperature. After completion, the solvent was removed using a rotary evaporator, and the resulting reaction mixture was filtered through celite and extracted three times with ethyl acetate. The final wash of the crude reaction mixture with distilled hexane yielded a yellowish solid **4da**.



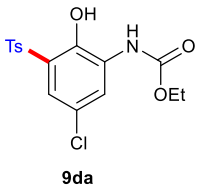
2-Amino-4-chloro-6-tosylphenol (**4da**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Yield = 95% (141.4 mg, 0.475 mmol). **^{1}H NMR ($CDCl_3$, 400 MHz)**: δ 9.28 (s, 1H), 7.81 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.4 Hz, 2H), 6.94-6.95 (m, 1H), 6.756-6.764 (m, 1H), 4.08 (s, 2H), 2.42 (s, 3H); **^{13}C NMR ($CDCl_3$, 100 MHz)**: δ 145.2, 141.9, 138.3, 138.1, 130.1, 127.0, 125.6, 123.9, 118.8, 115.8, 21.6; HRMS [M+H$^+$] calcd for $C_{13}H_{13}ClNO_3S$: (m/z) =298.0305, found =298.0315.

4B. Esterification of amine of 4da



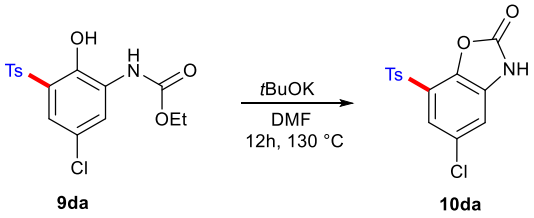
Experimental procedure[7]: The compound **4da** (72.26 mg, 0.25mmol, 1equiv) was introduced into a solvent mixture of H_2O:$CHCl_3$ and subsequently treated with $NaHCO_3$ (25.20 mg, 0.30 mmol, 1.2 equiv.) by stirring at room temperature for 15 minutes. Now, ethyl chloroformate (23.80 µl, 0.25 mmol, 1equiv.) was added drop-wise, and the reaction was subjected to reflux for 24 h. The reaction mixture was then extracted with ethyl acetate, followed by column chromatography by using 4% ethyl acetate in hexane to get **6aa** as a white solid.

Ethyl (5-chloro-2-hydroxy-3-tosylphenyl)carbamate (**9da**): Analytical TLC in silica gel 1:4



ethyl acetate/hexane R_f = 0.50; Yield = 93% (86.2 mg, 0.23 mmol). **^{1}H NMR ($CDCl_3$, 400 MHz)**: δ 9.56 (s, 1H), 8.31 (s, 1H), 7.79 (d, *J* = 10.4 Hz, 2H), 7.35 (d, *J* = 8.8 Hz, 2H), 7.23 (d, *J*= 2.4 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 2.43 (s, 3H), 1.32 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR ($CDCl_3$, 100 MHz)**: δ 153.0, 145.5, 137.7, 130.3, 129.8, 127.1, 126.2, 124.1, 123.3, 120.5, 61.9, 21.7, 14.3; HRMS [M+H^+] calcd for $C_{16}H_{17}ClNO_5S$: (m/z) =370.0516, found = 370.0508.

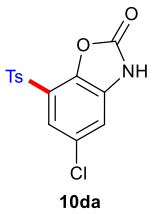
4B. Cyclization of 9da to form sulfonylated chloroxazone 10da



Experimental procedure[10]: A 25 mL round bottom flask was charged with compound **9da** (92.5 mg, 0.25 mmol, 1.0 equiv.) in 3 mL of DMF and *t*-BuOK (84.15 mg, 0.75 mmol 3.0 equiv.) was added to the reaction under inert atmosphere. The reaction mixture was stirred for 12 h at 130 °C. After completion, the DMF was evaporated in a high vacuum rotatory evaporator, and the remaining DMF of the reaction mixture was removed by extraction with

cold water and ethyl acetate. The compound **10da** was isolated by column chromatography as a light-yellow solid.

5-Chloro-7-tosylbenzo[d]oxazol-2(3*H*)-one (**10da**): Analytical TLC in silica gel 1:4 ethyl acetate/hexane R_f = 0.50; Light yellow solid, Yield = 88% (71.7 mg, 0.22 mmol).



10da

^{1}H NMR (DMSO-d$_6$, 400 MHz): δ 7.90 (d, *J* = 8.4 Hz, 2H), 7.52 (d, *J* = 2Hz, 1H), 7.47 (d, *J* = 8.4 Hz, 2H), 7.45 (d, *J* = 2Hz, 1H), 2.38 (s, 3H); **^{13}C NMR (DMSO-d$_6$, 100 MHz)**: δ 153.5, 145.3, 138.7, 136.9, 133.9, 130.3, 128.0, 127.7, 123.8, 118.9, 114.9, 21.1; HRMS [M+H$^+$] calcd for $C_{14}H_{11}ClNO_4S$: (m/z) =324.0097, found =324.0091.

5. Photophysical studies

5A. Preparation of Solutions

A 10 mM stock solution of the compound was prepared in DMSO. For fluorescence measurements, a working concentration of 10 μM was prepared by diluting the stock solution in the desired solvent system.

5B. Quantum Yield Measurements.

The quantum yield of the compound was determined using Coumarin153 as a standard in ethanol. The fluorescence quantum yield (Φ) was calculated using the comparative method, where the standard and sample were excited at the same wavelength, and their integrated emission intensities were recorded. The quantum yield of the synthesized compound was measured in THF and ACN to compare solvent-dependent variations.

$$\Phi_{(Un)} = [FLI_{(Un)}/Abs_{(Un)}]x[Abs_{(Std)}/FLI_{(Std)}]x[n_{(Un)}/n_{(Std)}2]x\Phi_{(Std)}$$

FLI = Fluorescence intensity (measured by area under the curve), excitation at 420 nm
Abs = Absorbance at 420 nm
UN = Unknown sample
Std = coumarin153 in Ethanol as standard. Quantum yield of Coumarin153 in Ethanol is 0.73.

6. Mechanistic investigations

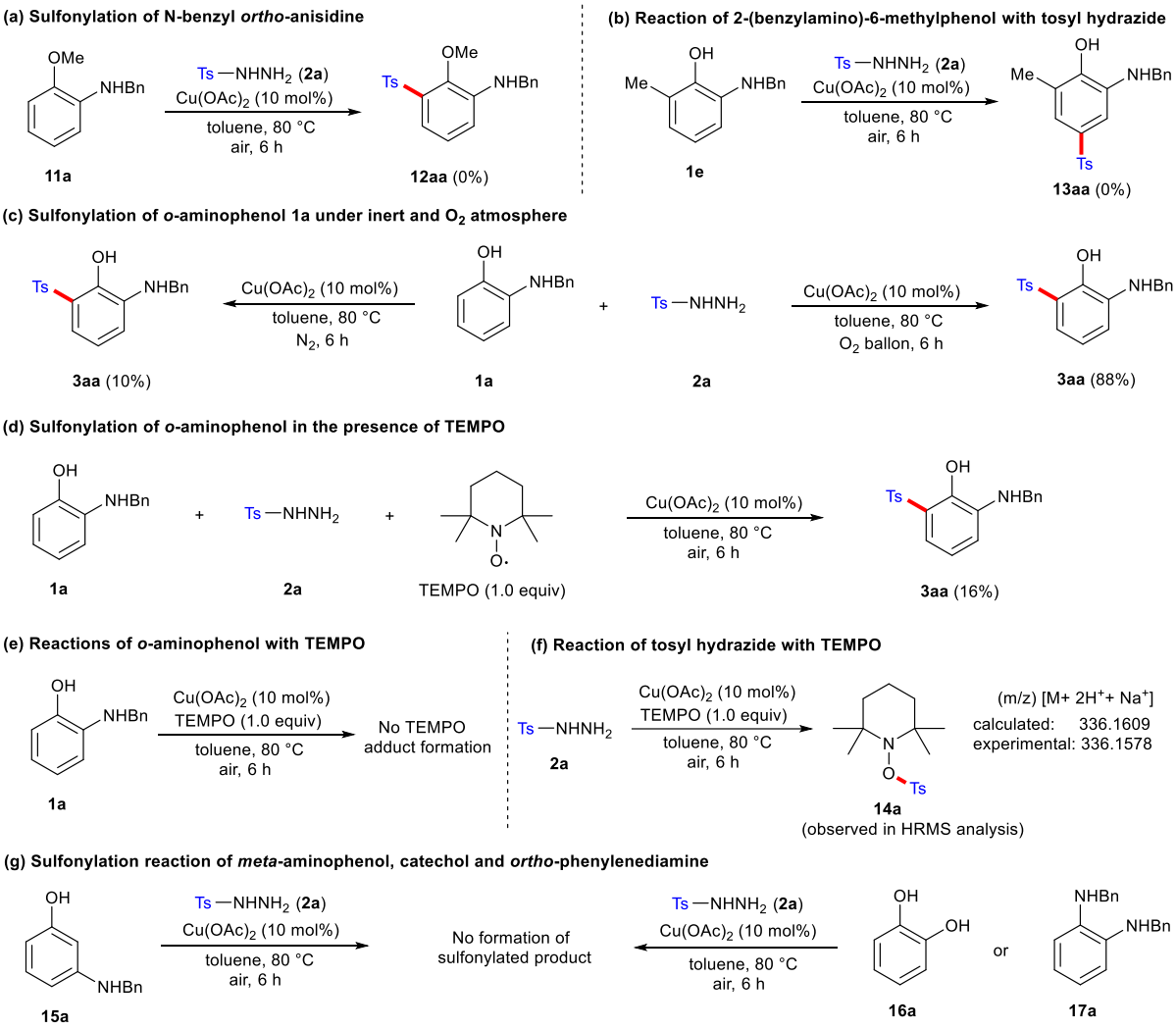
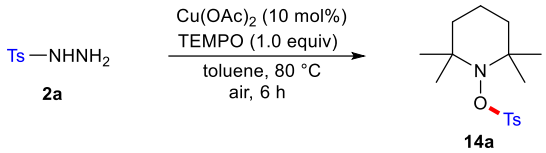
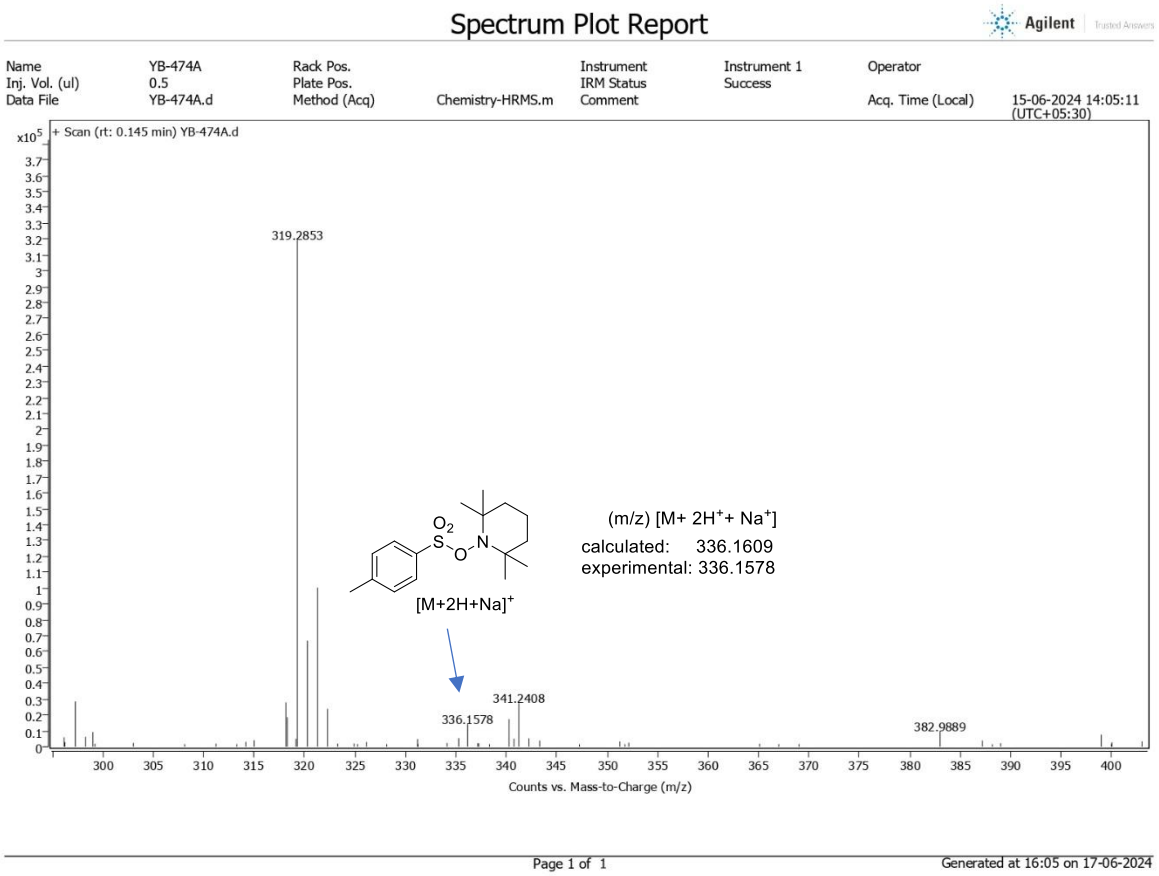


Fig.S1 Mechanistic investigations for the sulfonylation of *ortho*-aminophenol.

6A. Reaction of tosyl hydrazide with TEMPO



p-Tolyl sulfonyl hydrazide **2a** (46.55 mg, 0.25 mmol, 1.0 equiv) was dissolved in 1 mL of toluene in a 25 mL round bottom flask. Next, Cu $(OAc)_2$ catalyst (4.99 mg, 0.025 mmol, 10 mol%) and TEMPO (39.06 mg, 0.25 mmol, 1eq.) were added to that solution at room temperature with continuous stirring for 10 minutes. The reaction mixture was heated at 80 °C for 6 h in an oil bath. Next, the solvent was evaporated under reduced pressure and the crude reaction mixture was analyzed by HRMS as given below.



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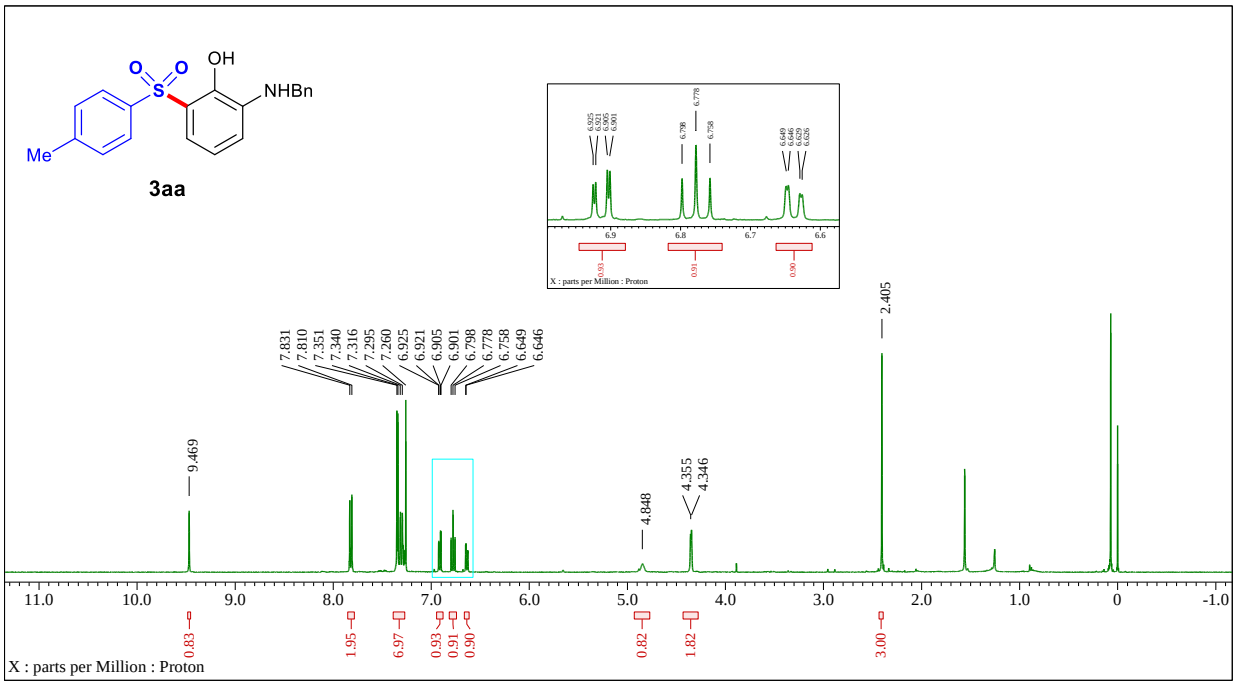
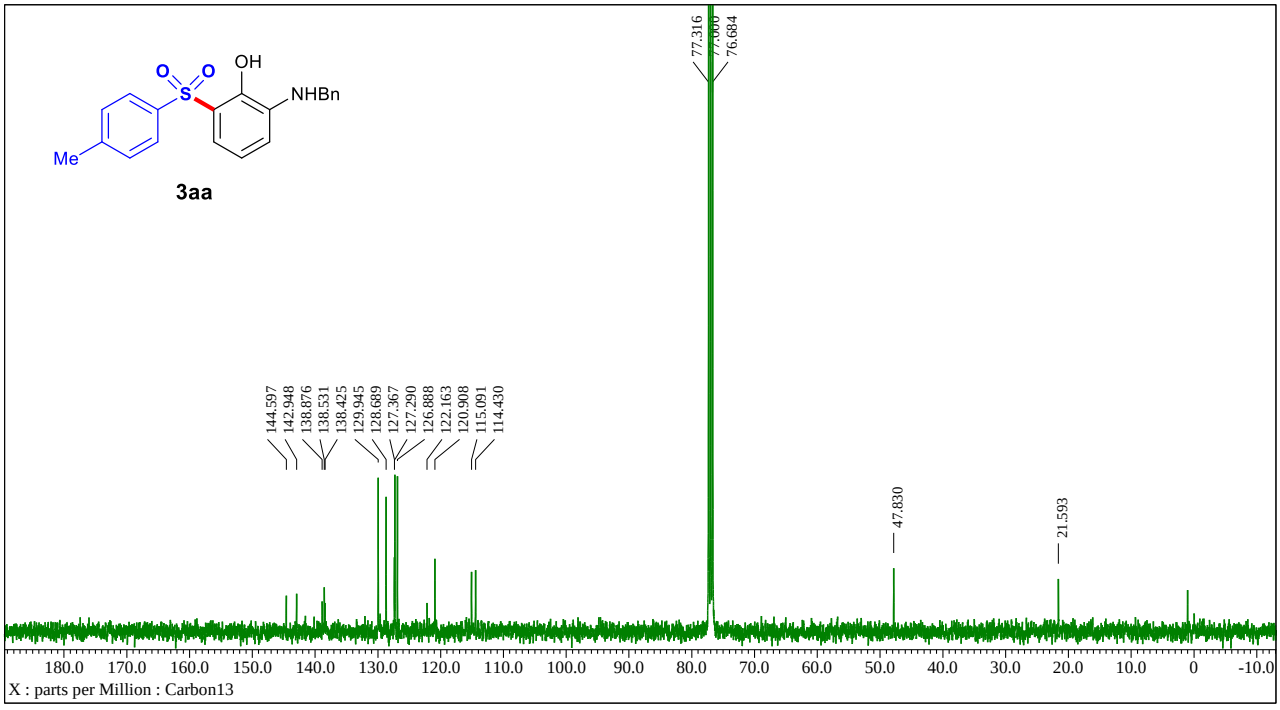
7. NMR Spectra

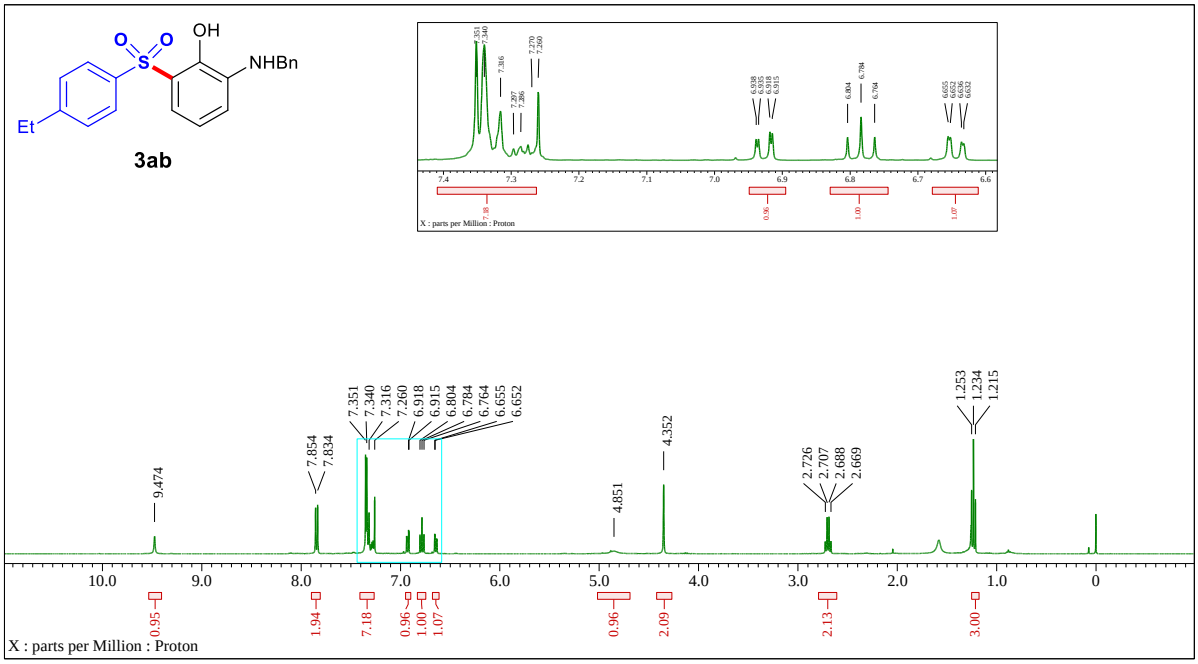
^{1}H NMR (400 MHz, Chloroform-*d*) for compound (3aa)



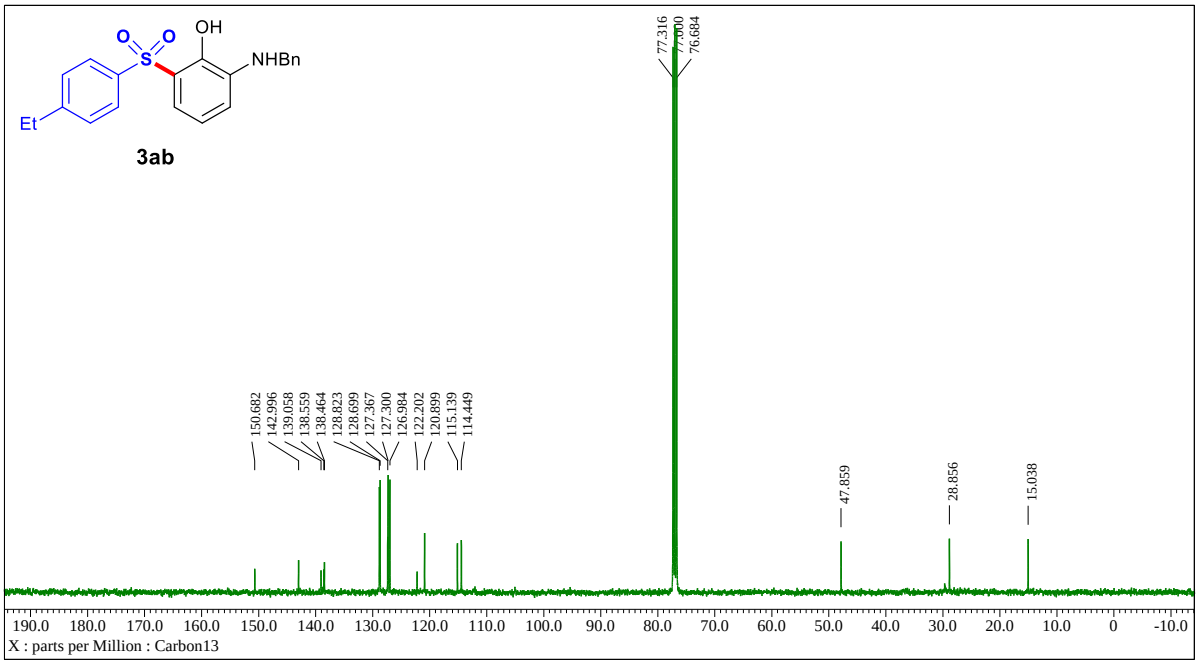
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3aa)



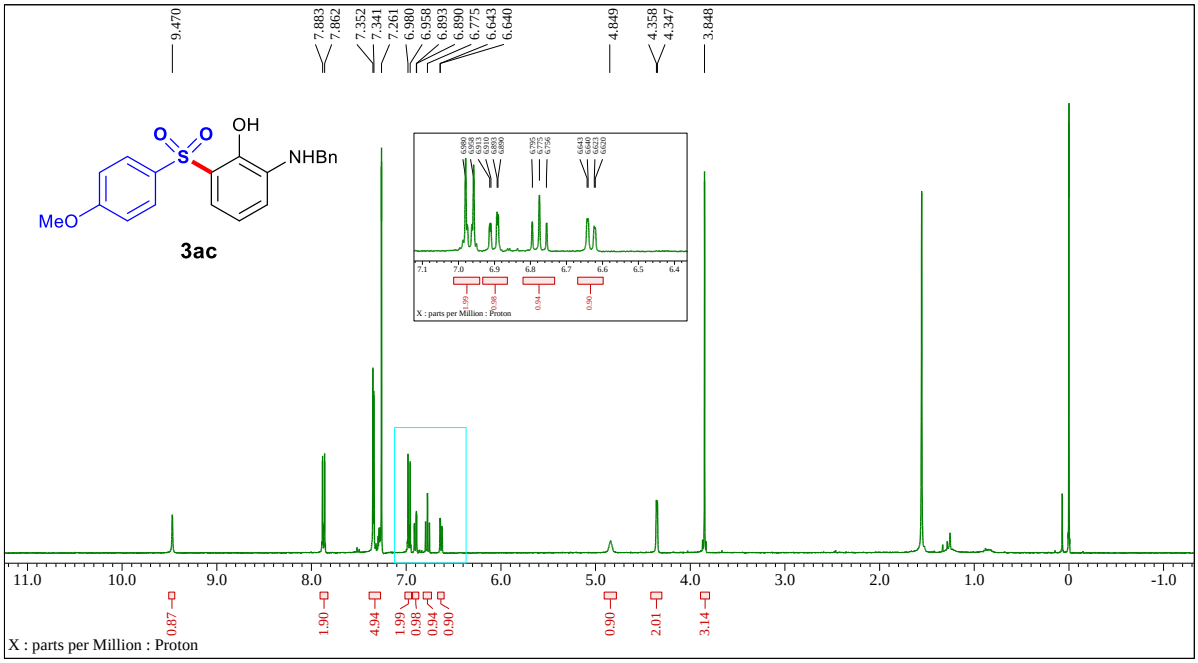
^{1}H NMR (400 MHz, Chloroform-*d*) for compound (3ab)



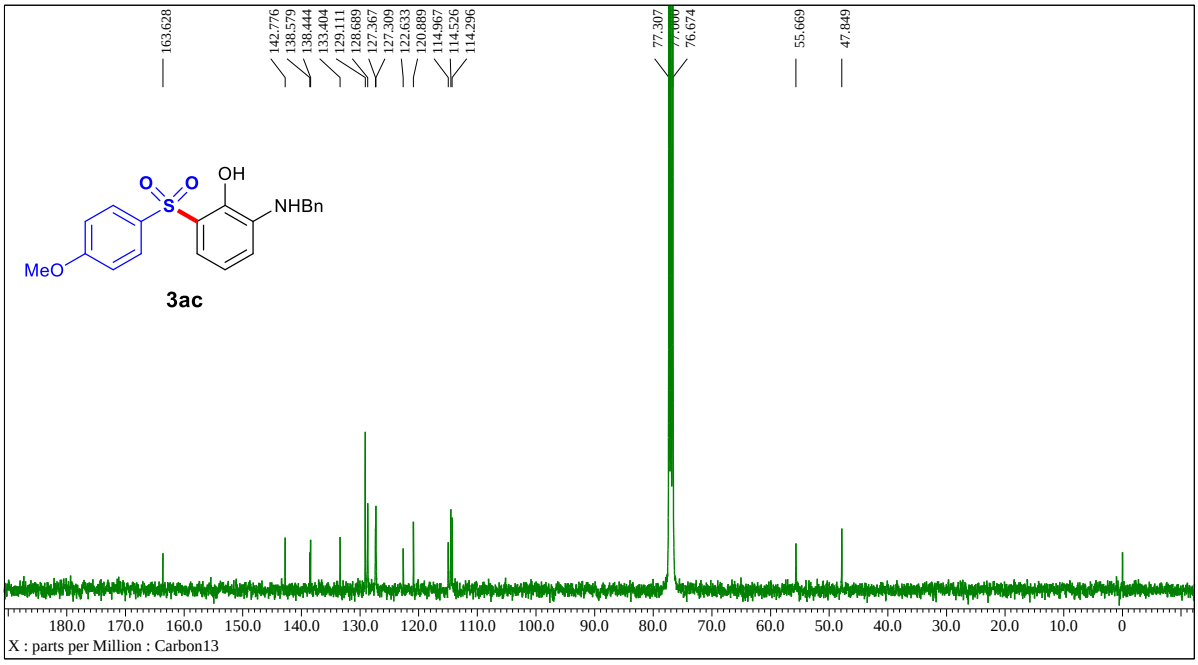
^{13}C NMR (100 MHz, Chloroform-d) for compound (3ab)



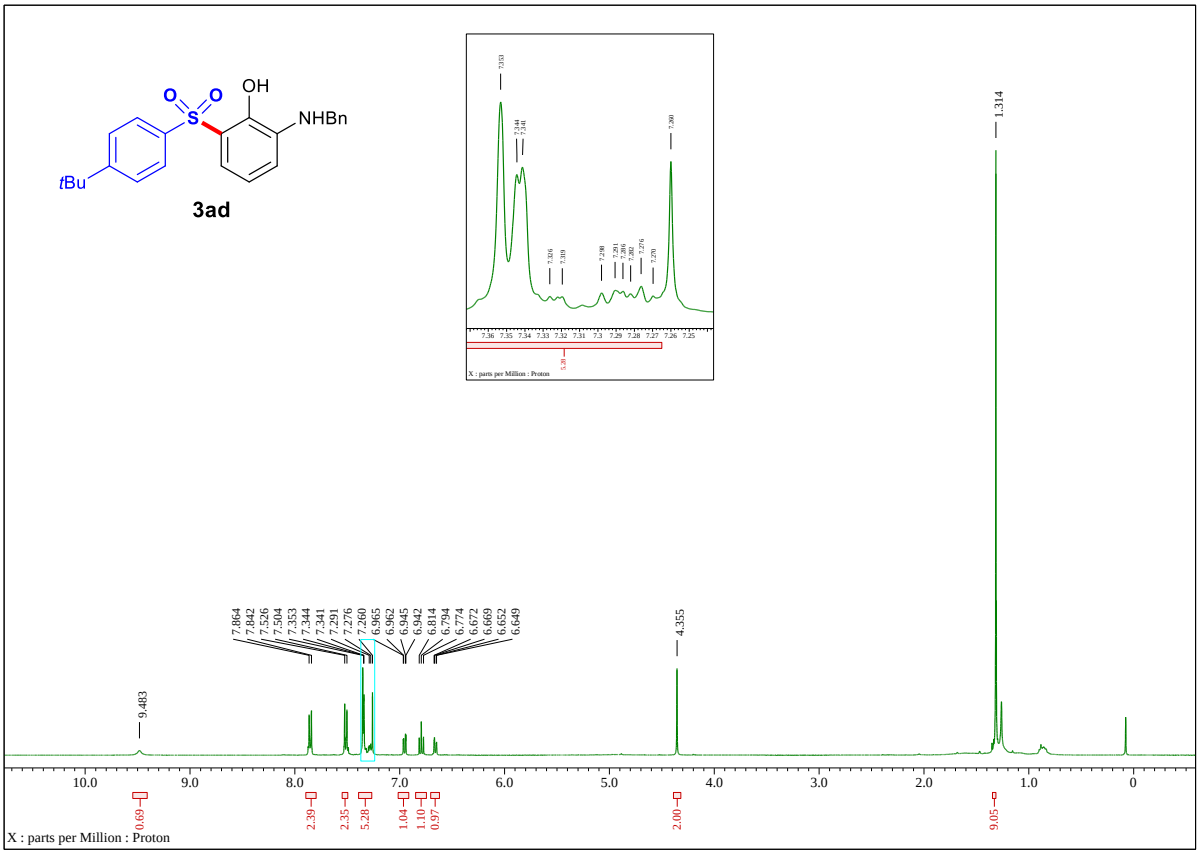
^{1}H NMR (400 MHz, Chloroform-*d*) for compound (3ac)



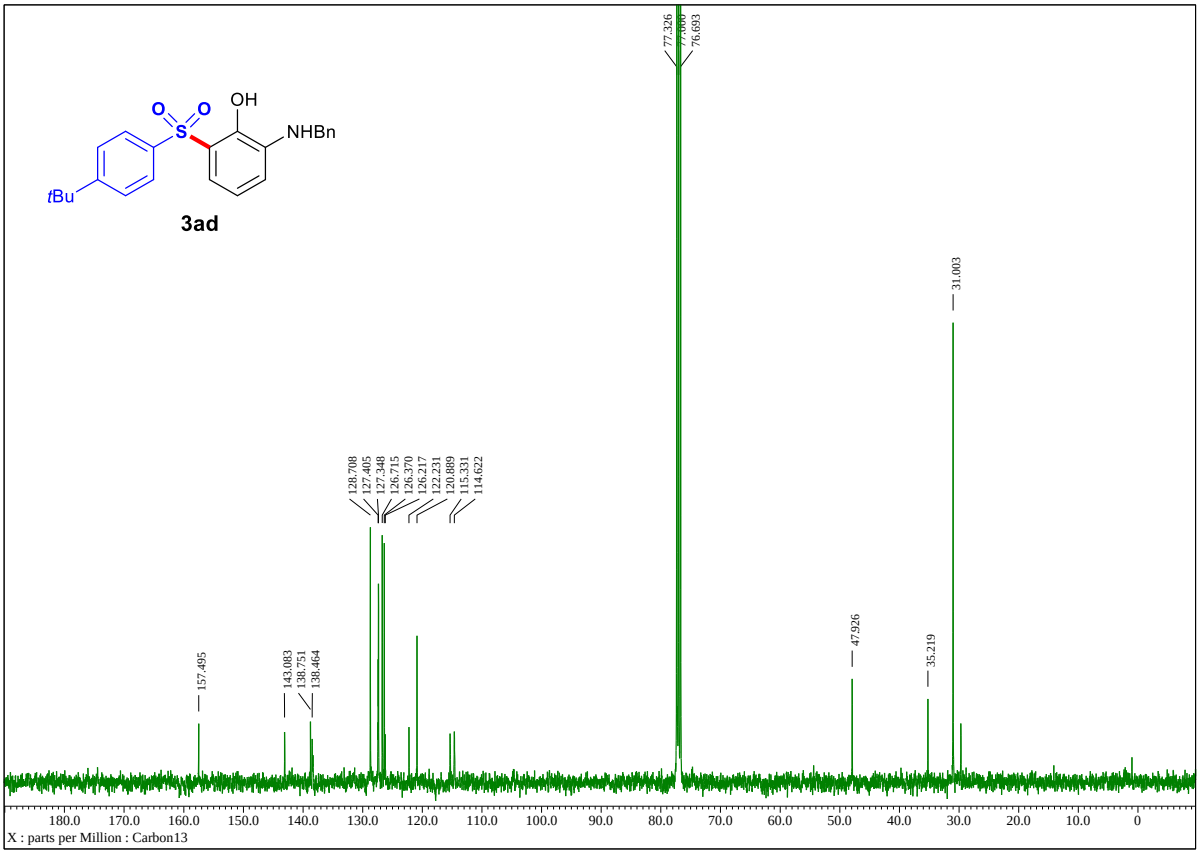
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ac)



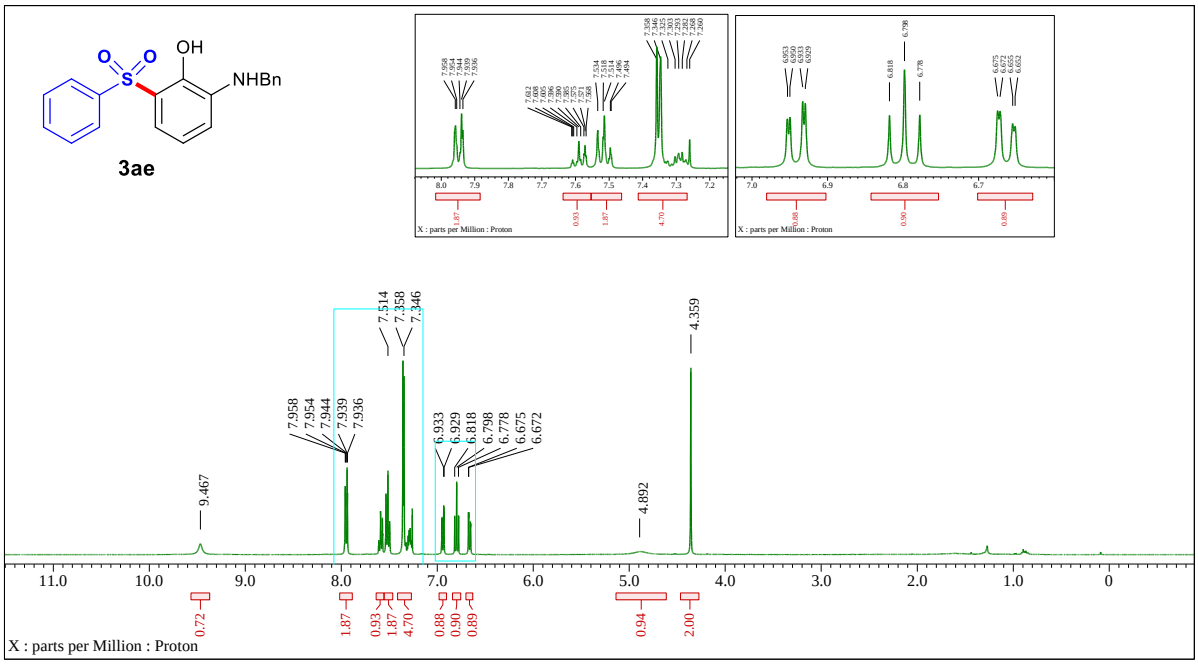
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ad)



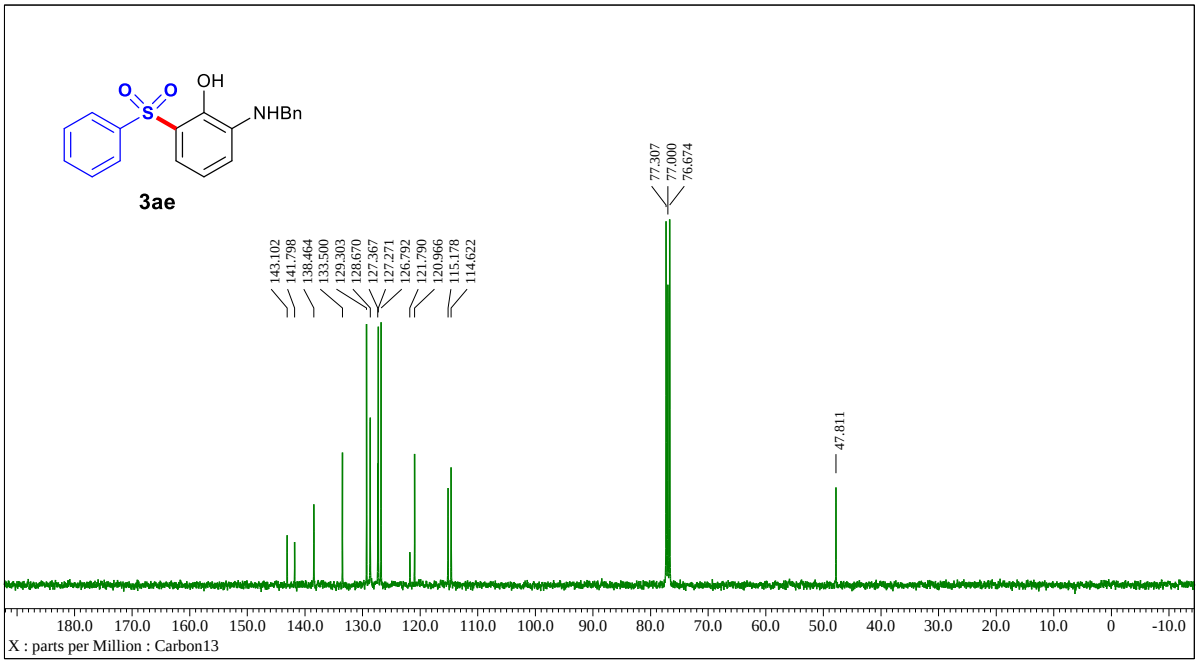
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ad)



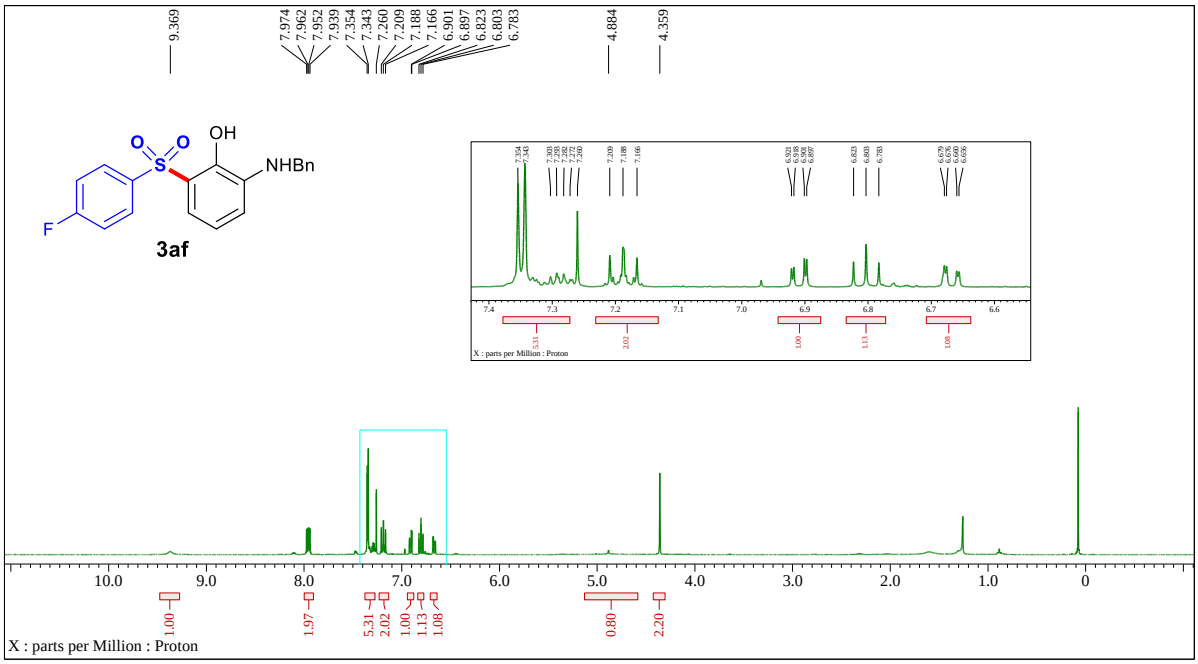
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ae)



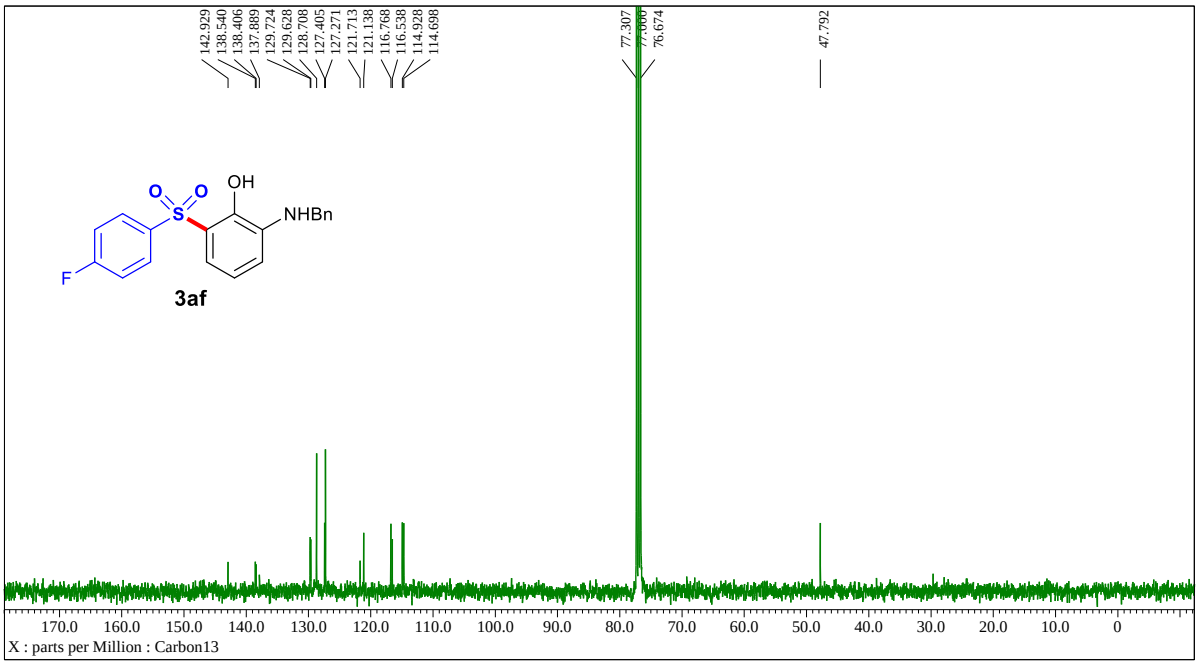
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ae)



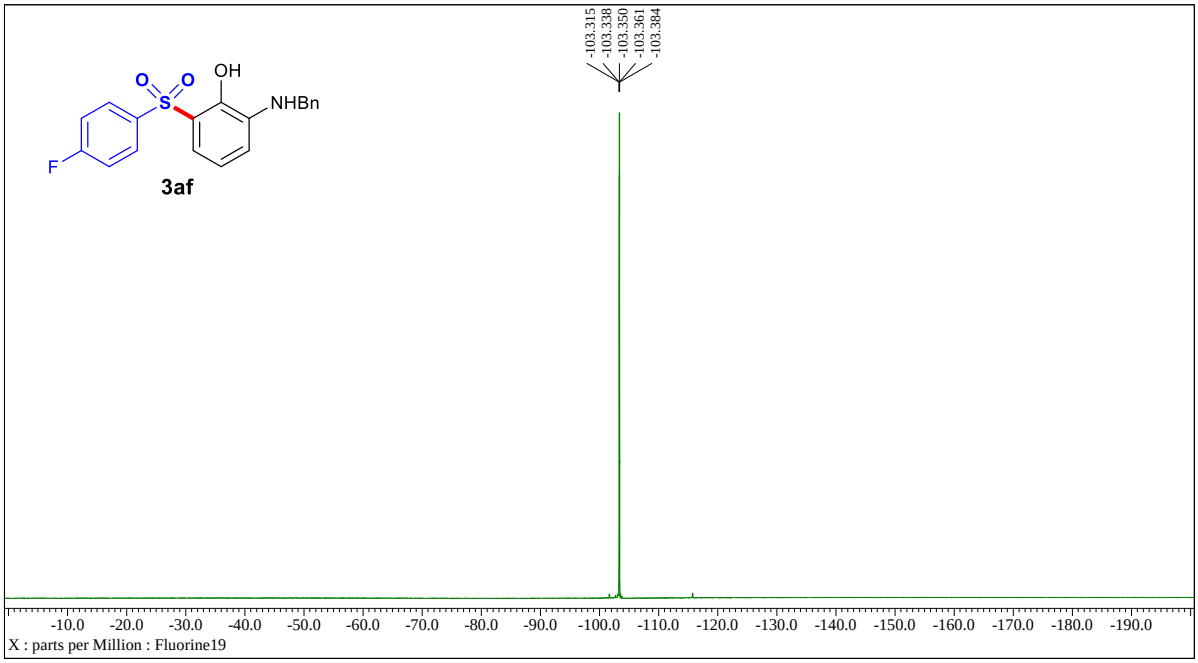
^{1}H NMR (400 MHz, Chloroform-d) for compound (3af)



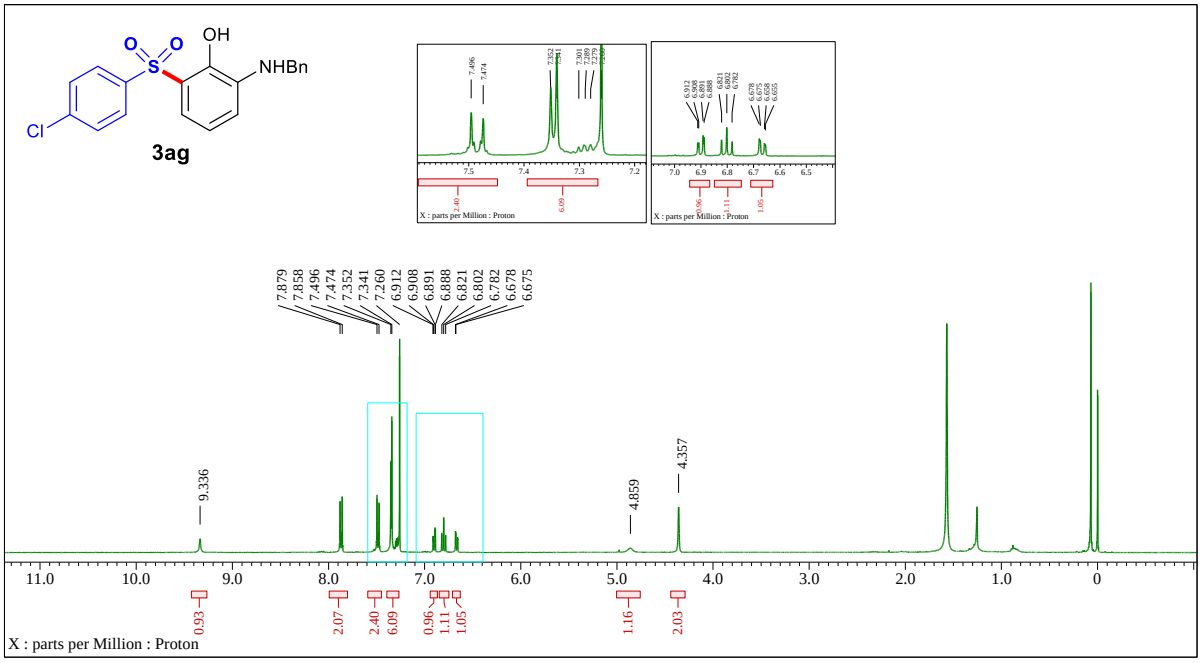
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3af)



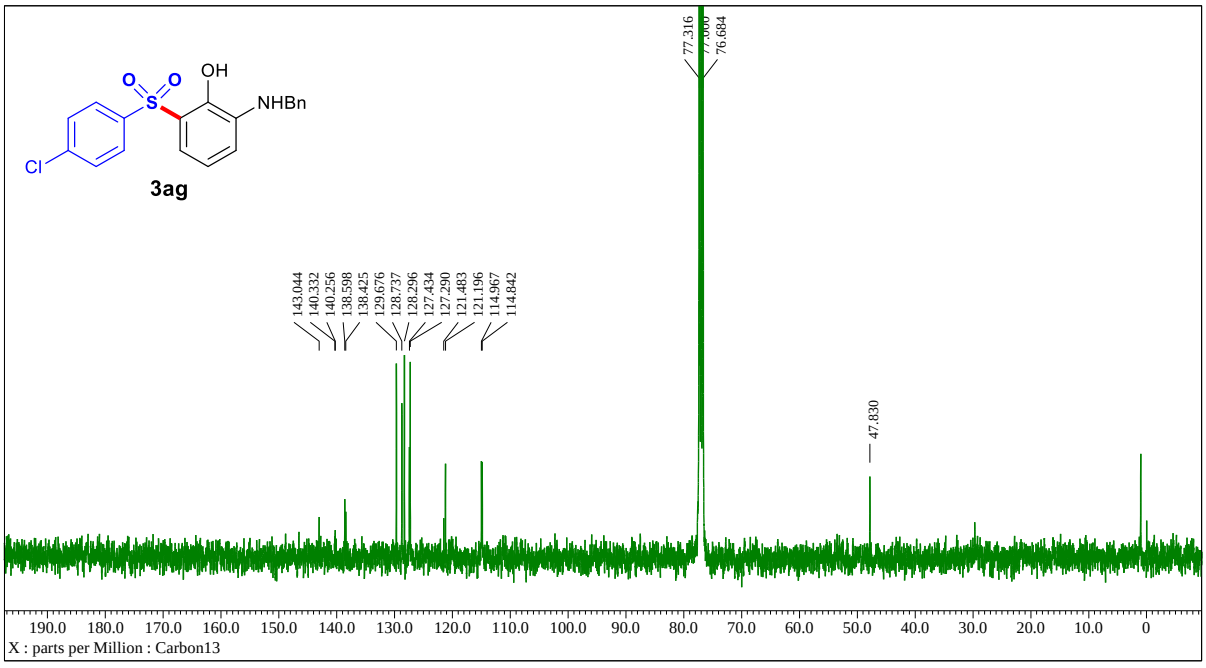
^{19}F NMR (100 MHz, Chloroform-*d*) for compound (3af)



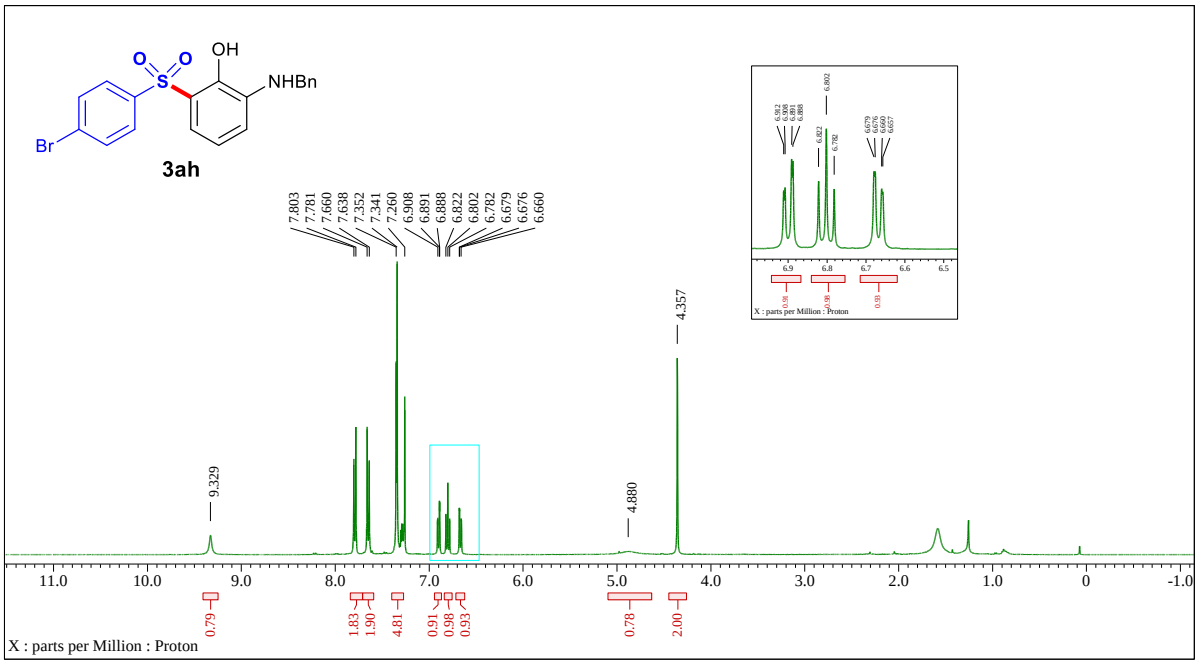
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ag)



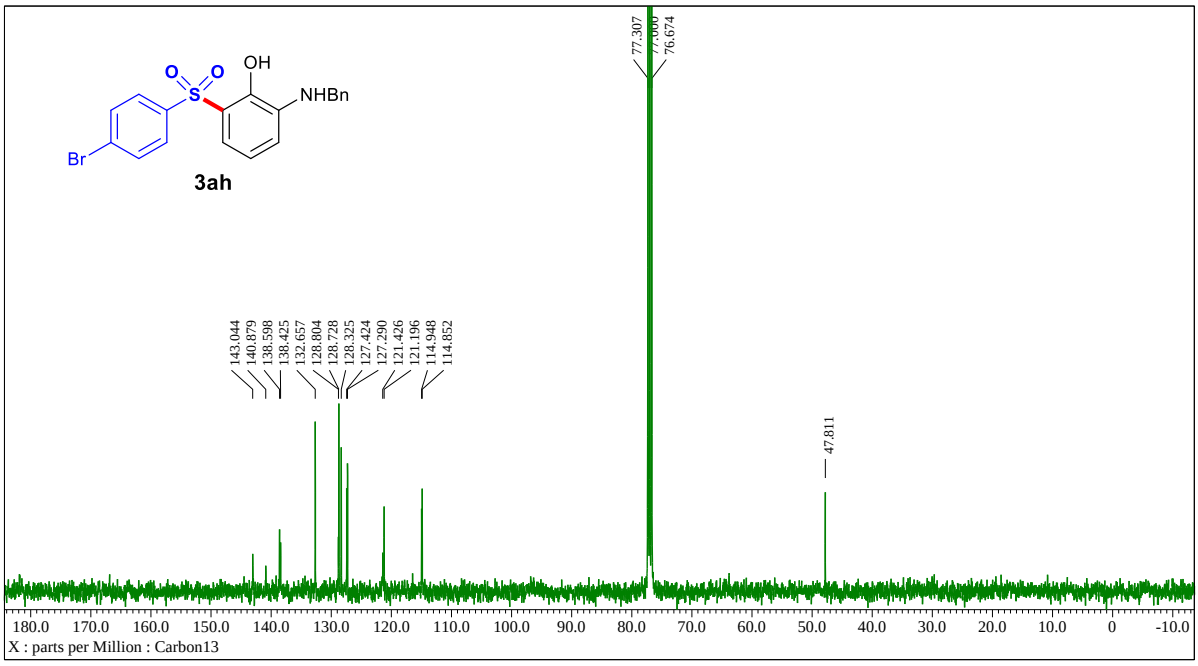
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ag)



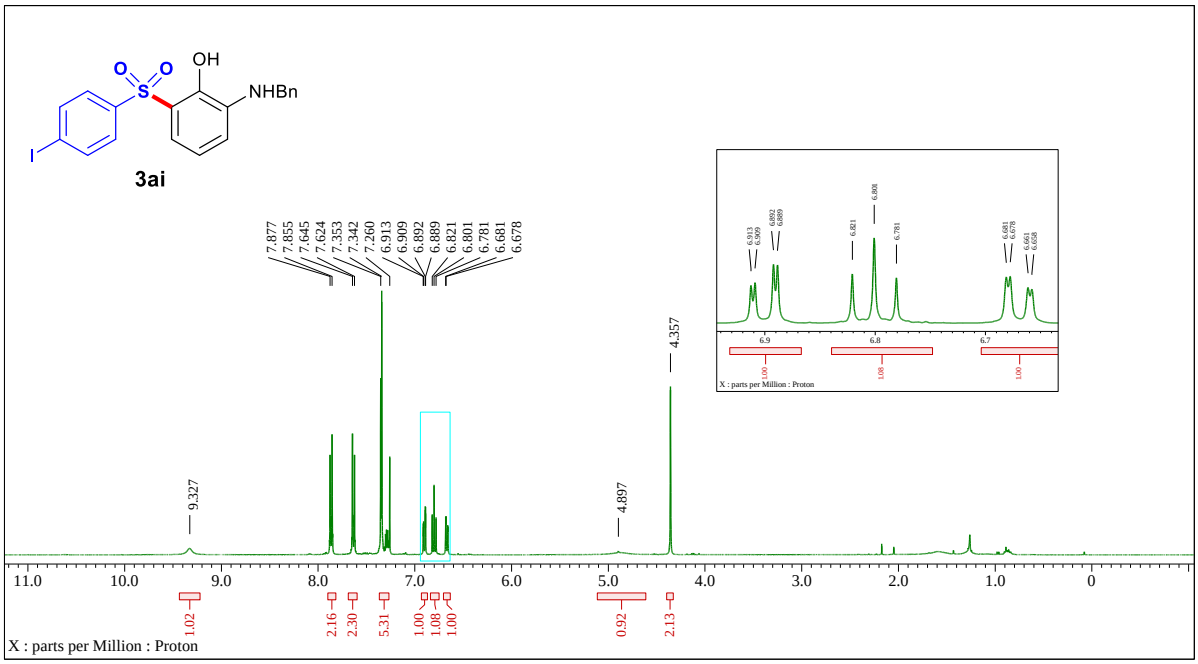
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ah)



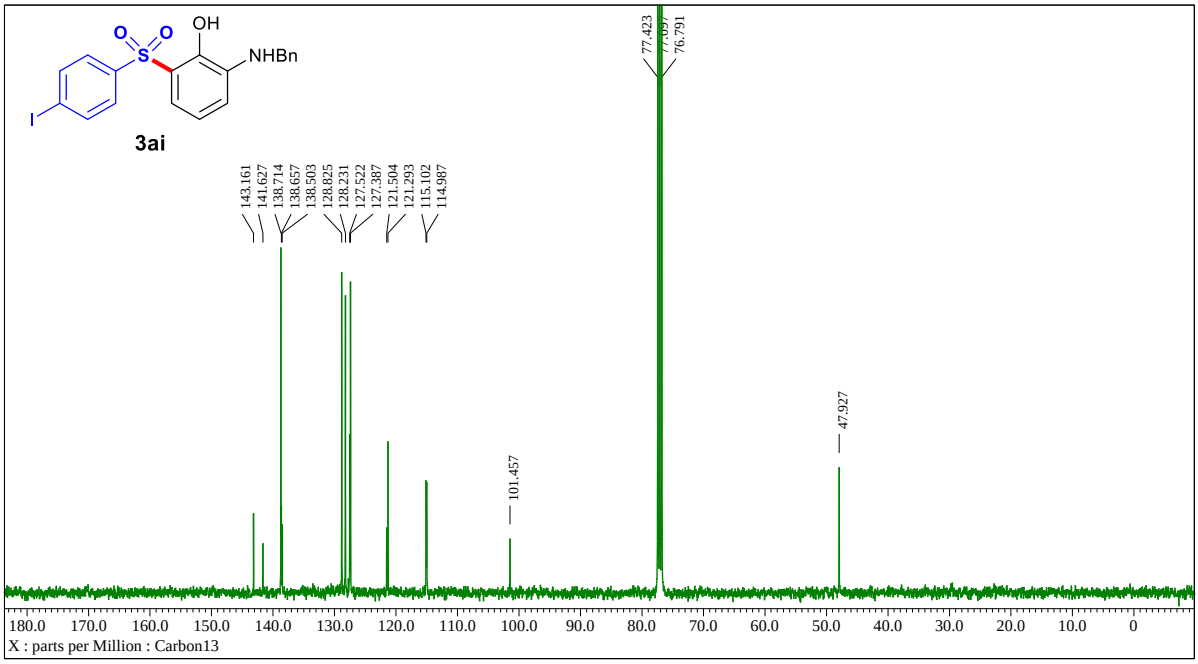
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ah)



^{1}H NMR (400 MHz, Chloroform-d) for compound (3ai)



^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ai)



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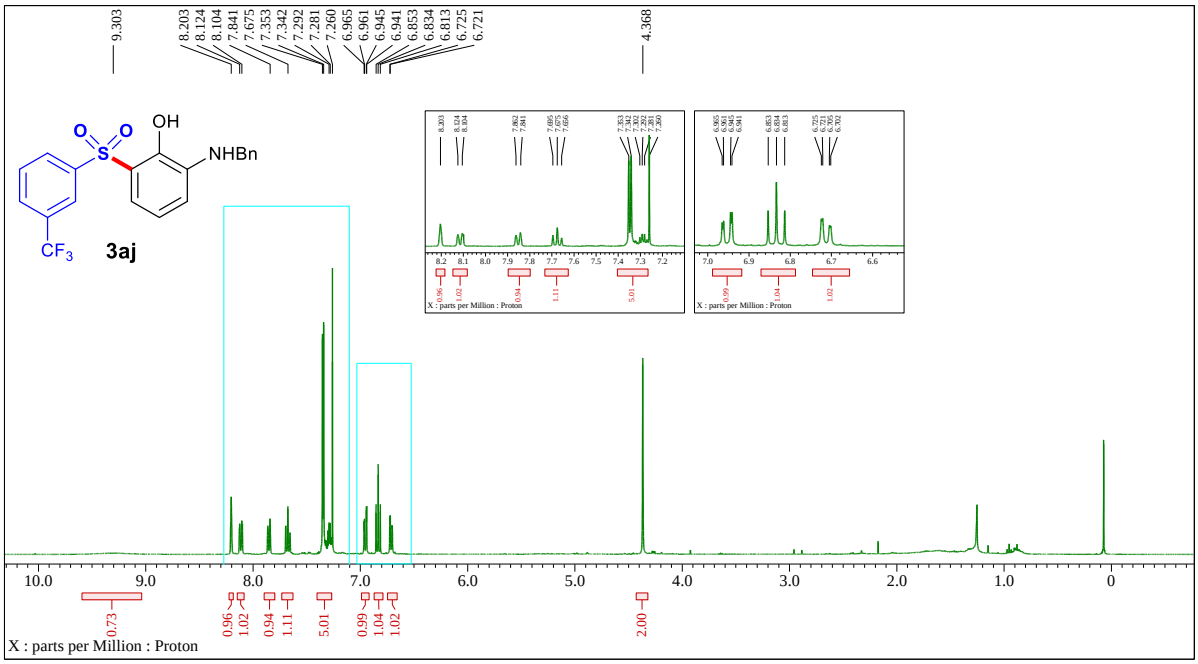
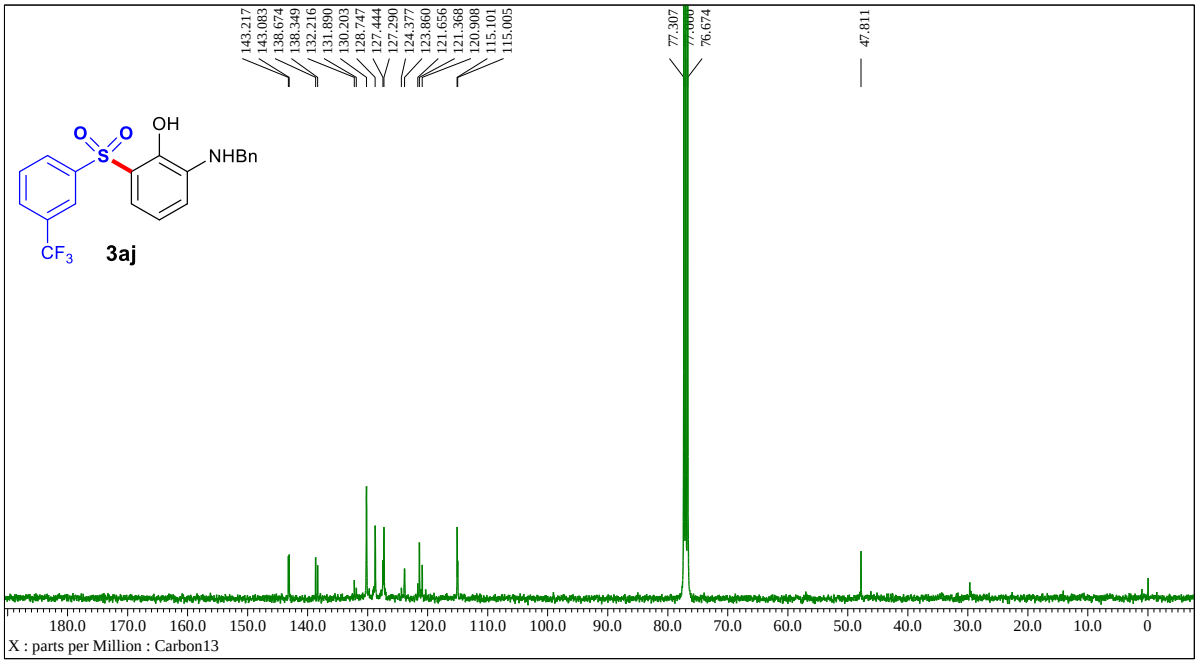
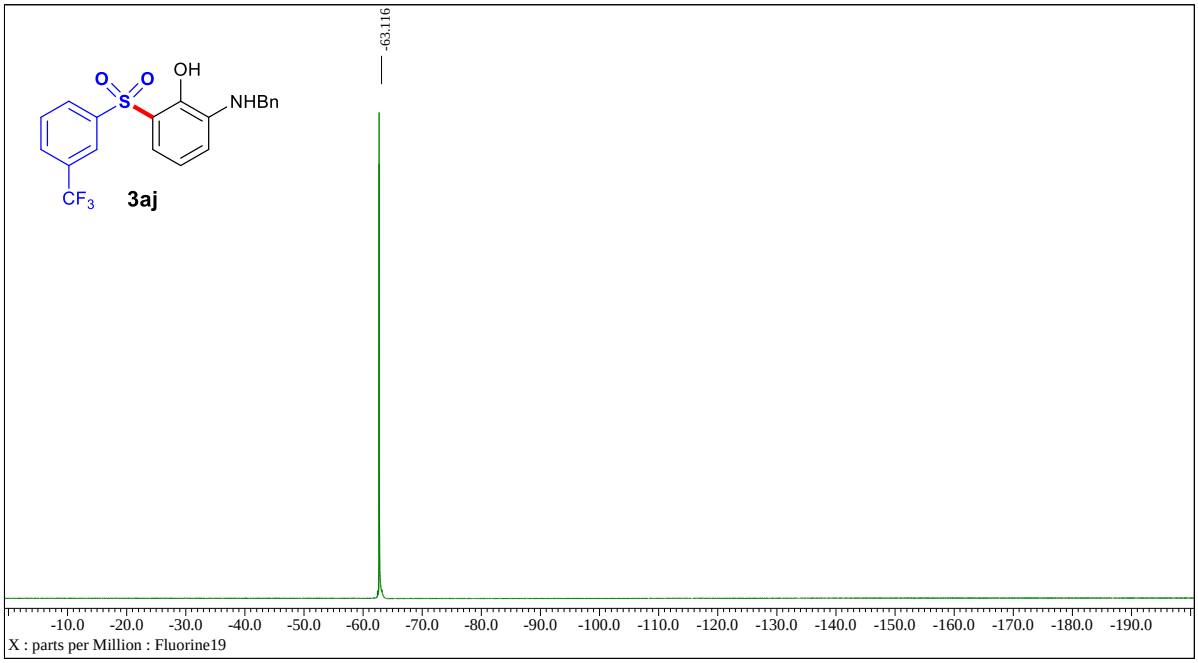


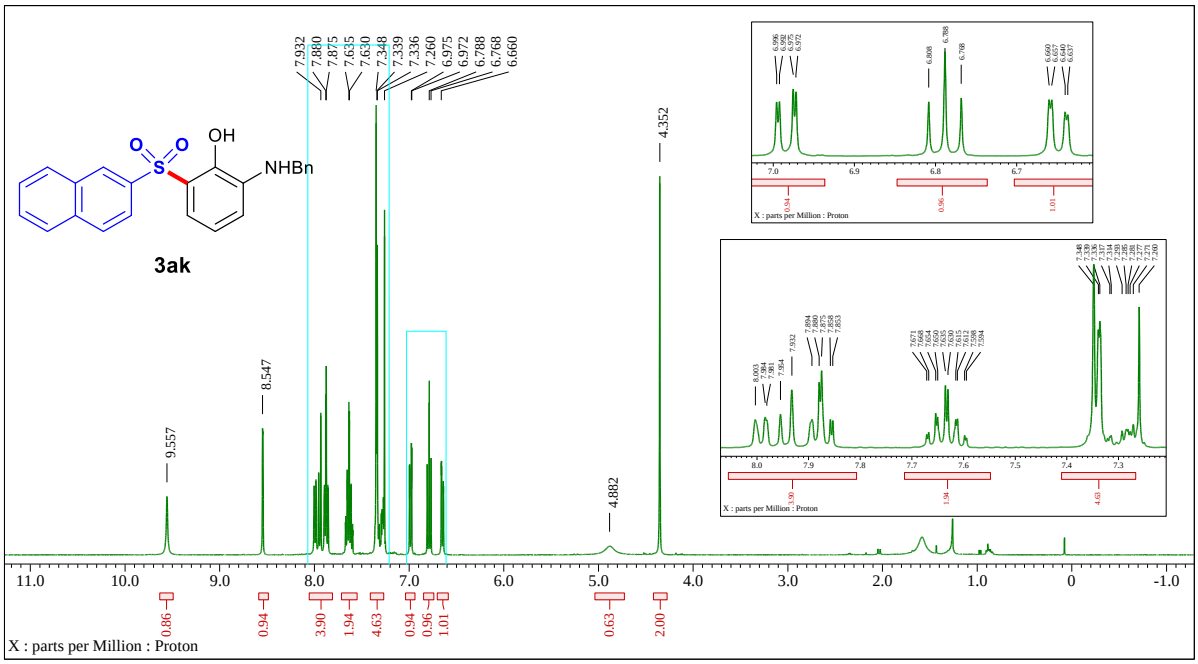
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3aj)



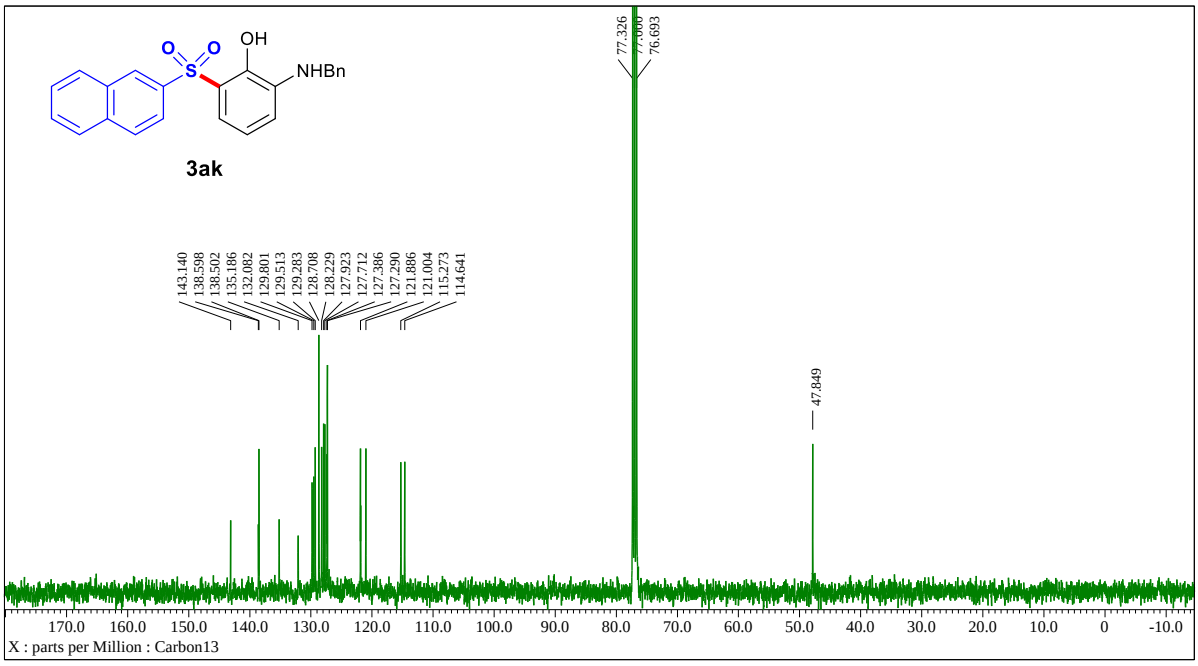
^{19}F NMR (100 MHz, Chloroform-*d*) for compound (3aj)



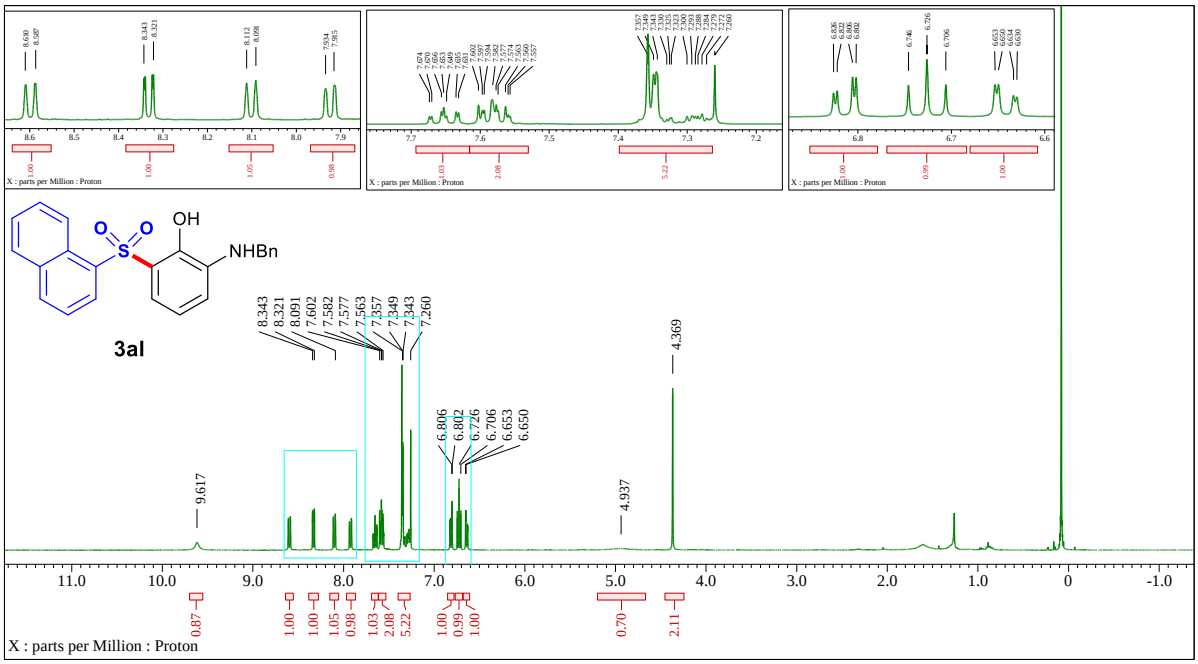
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ak)



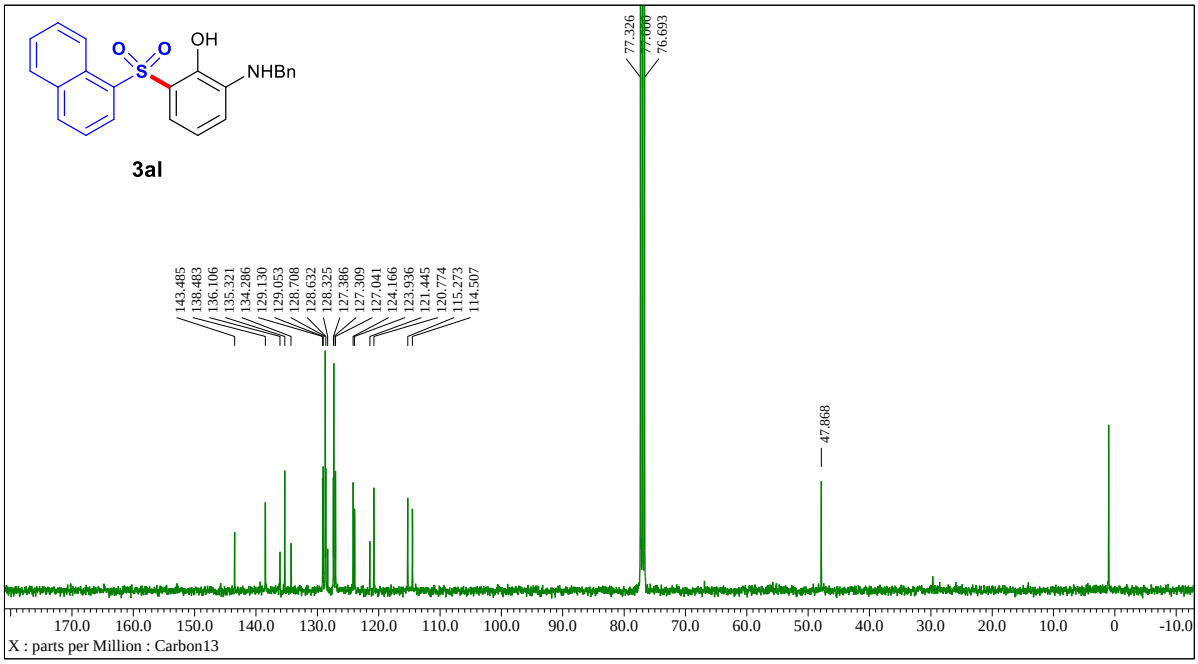
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ak)



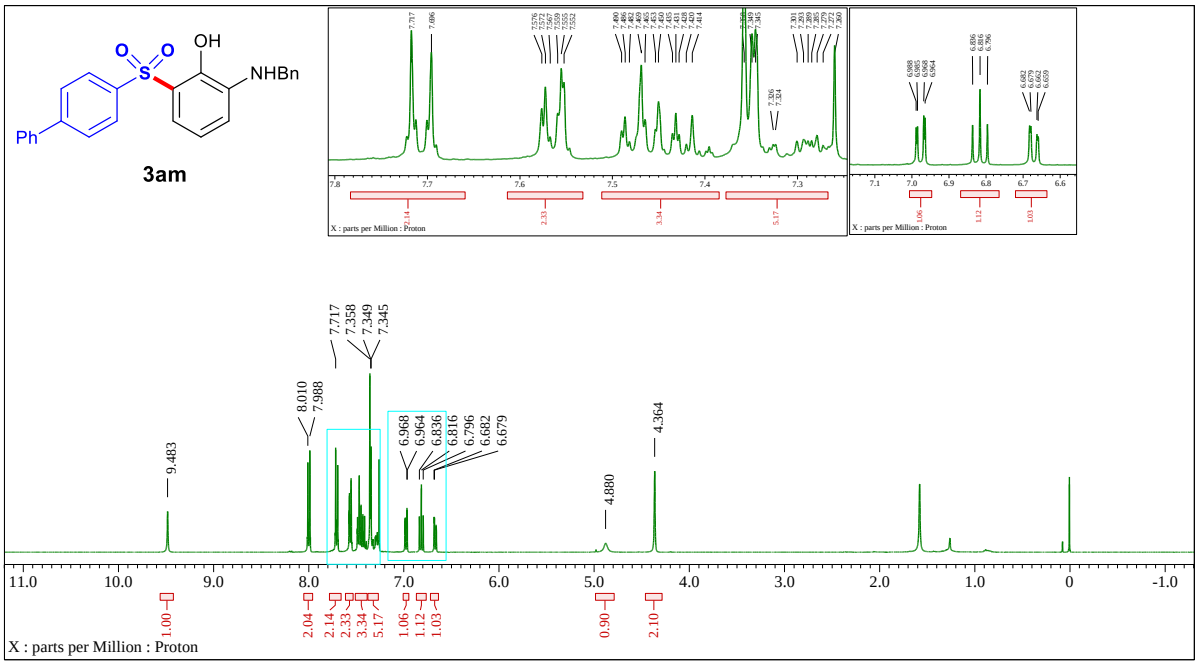
^{1}H NMR (400 MHz, Chloroform-d) for compound (3al)



^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3al)



^{1}H NMR (400 MHz, Chloroform-d) for compound (3am)



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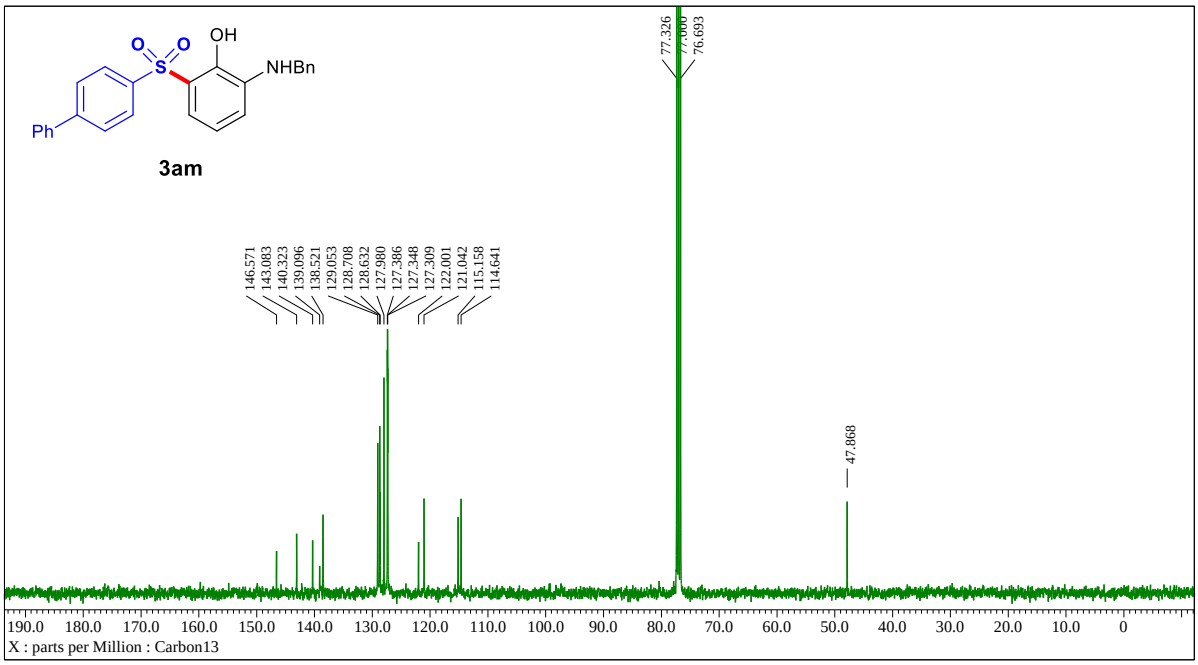
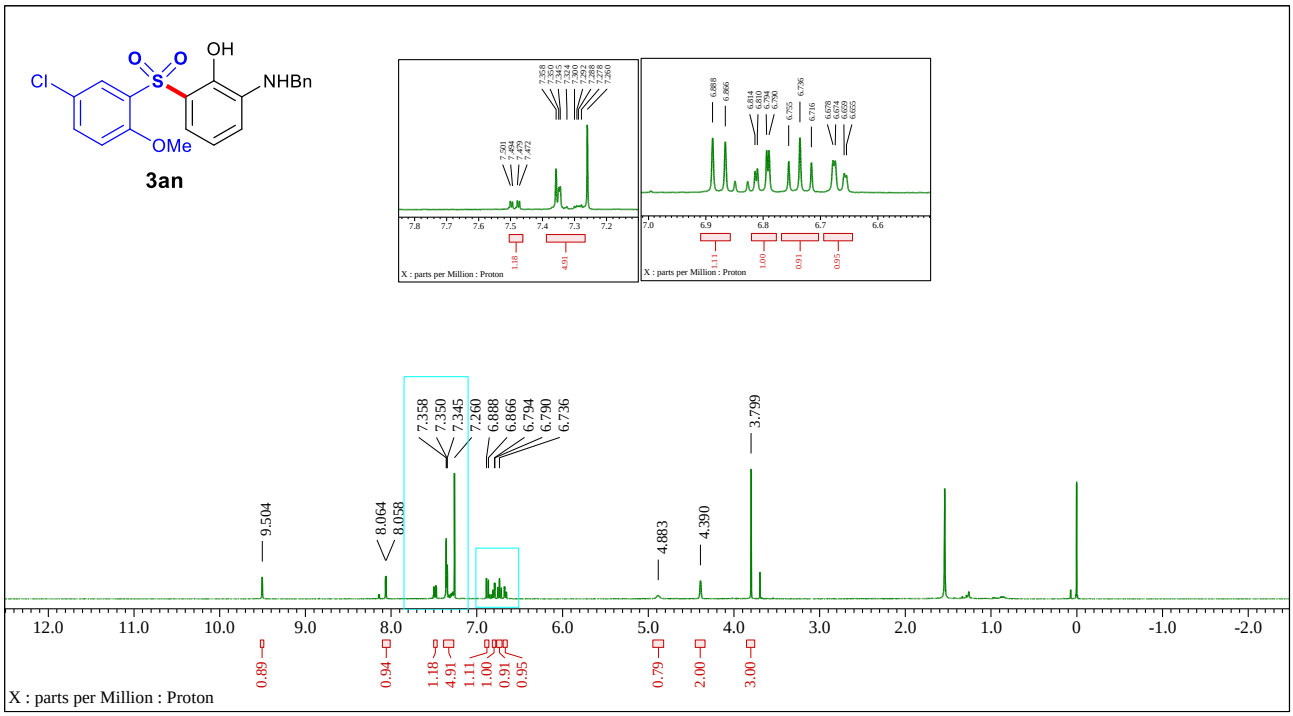
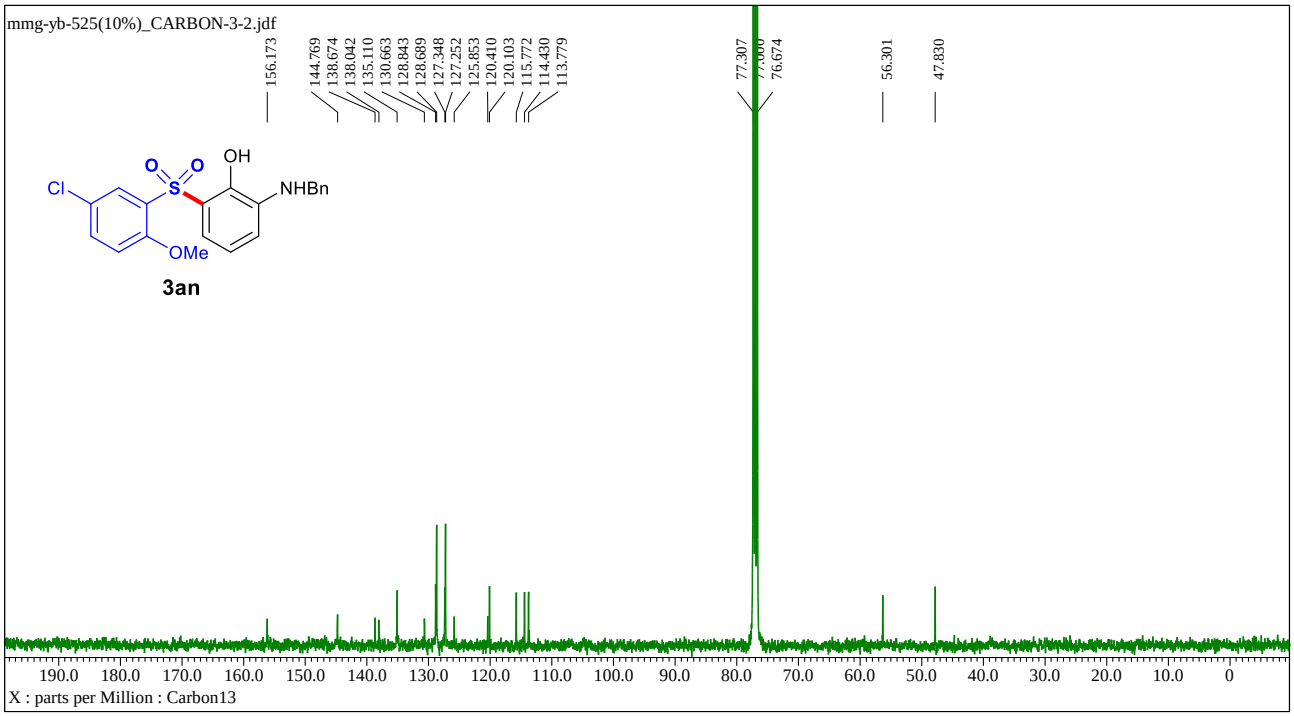


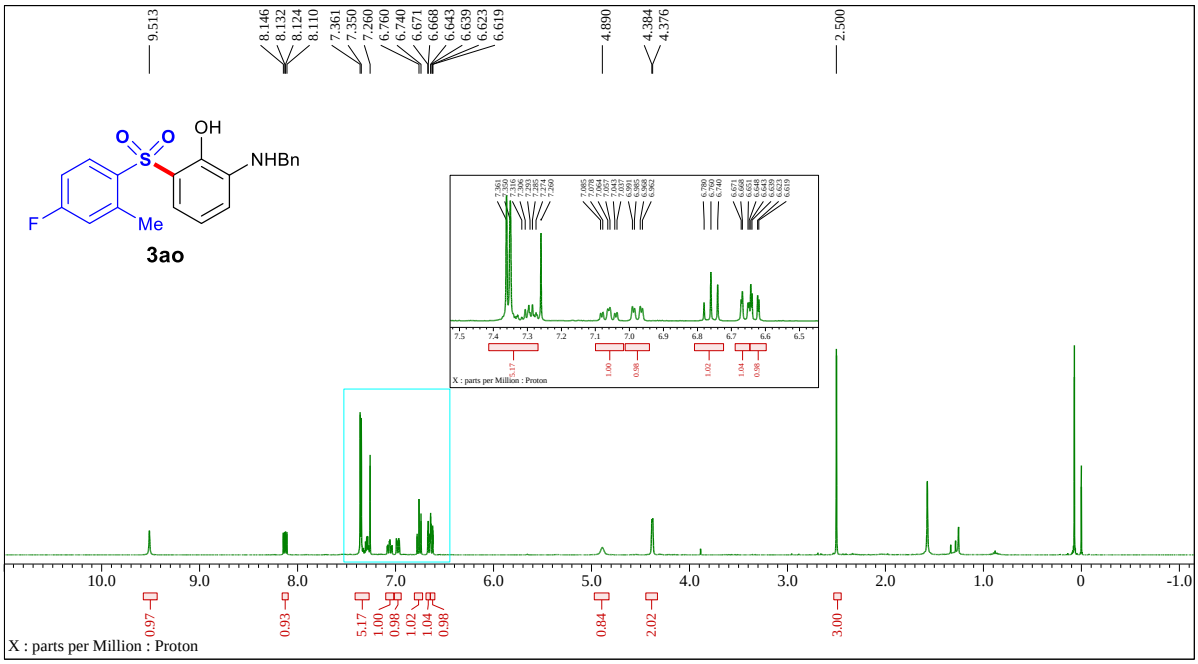
^{1}H NMR (400 MHz, Chloroform-d) for compound (3an)



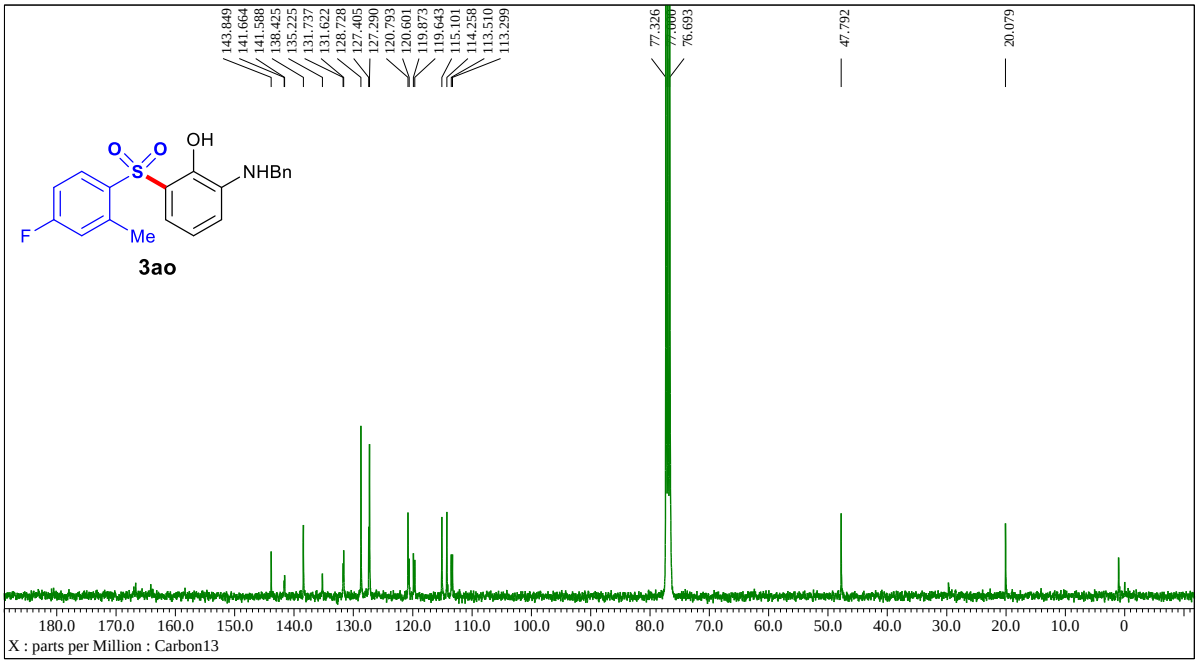
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3an)



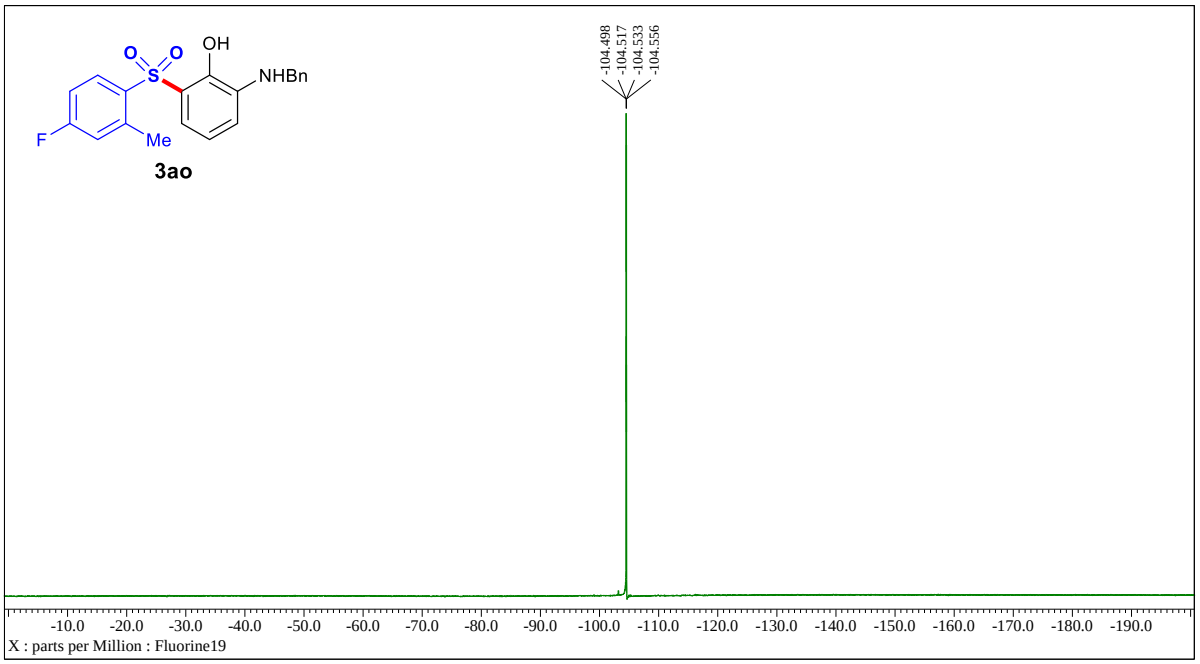
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ao)



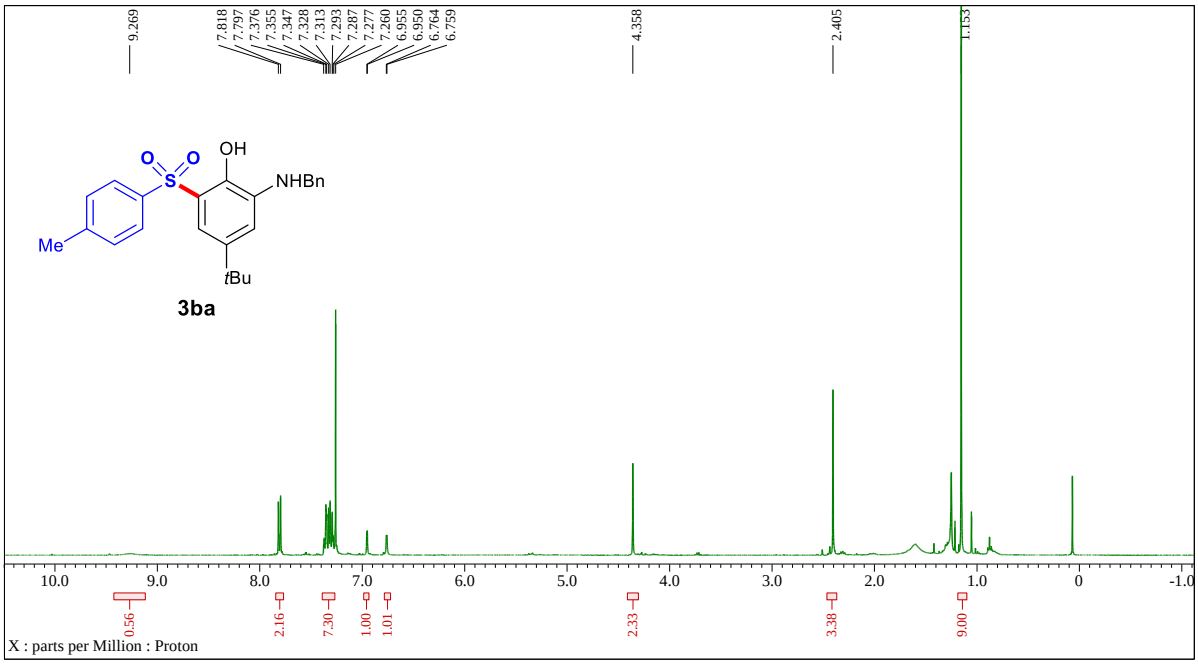
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ao)



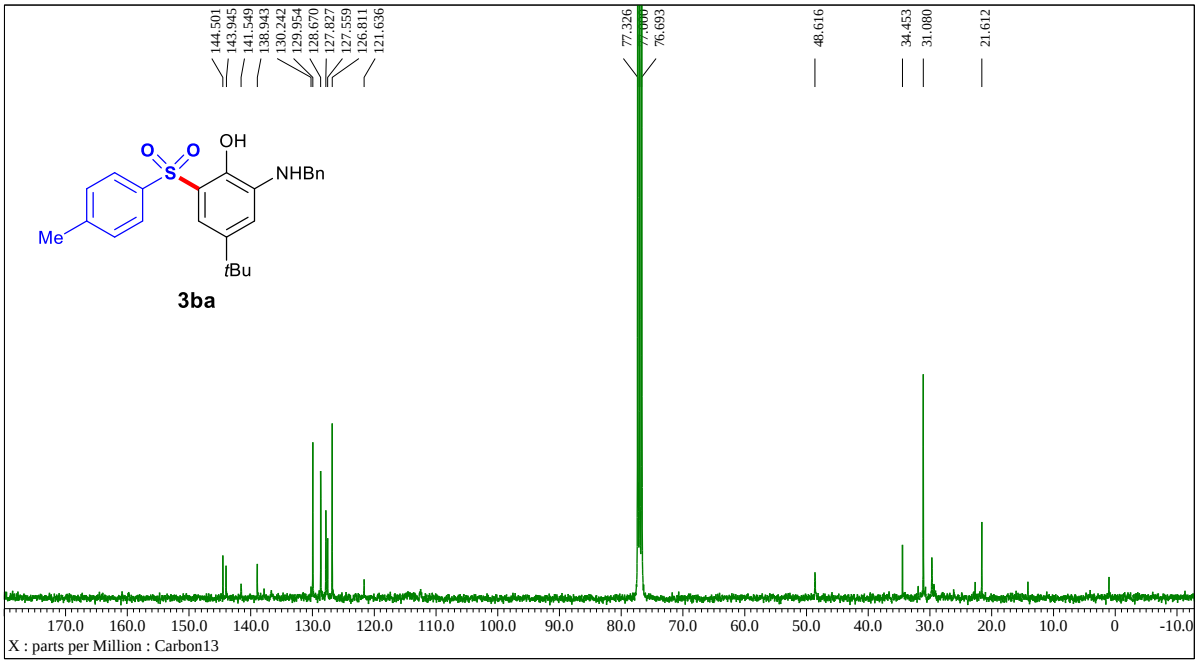
19F NMR (400 MHz, Chloroform-d) for compound (3ao)



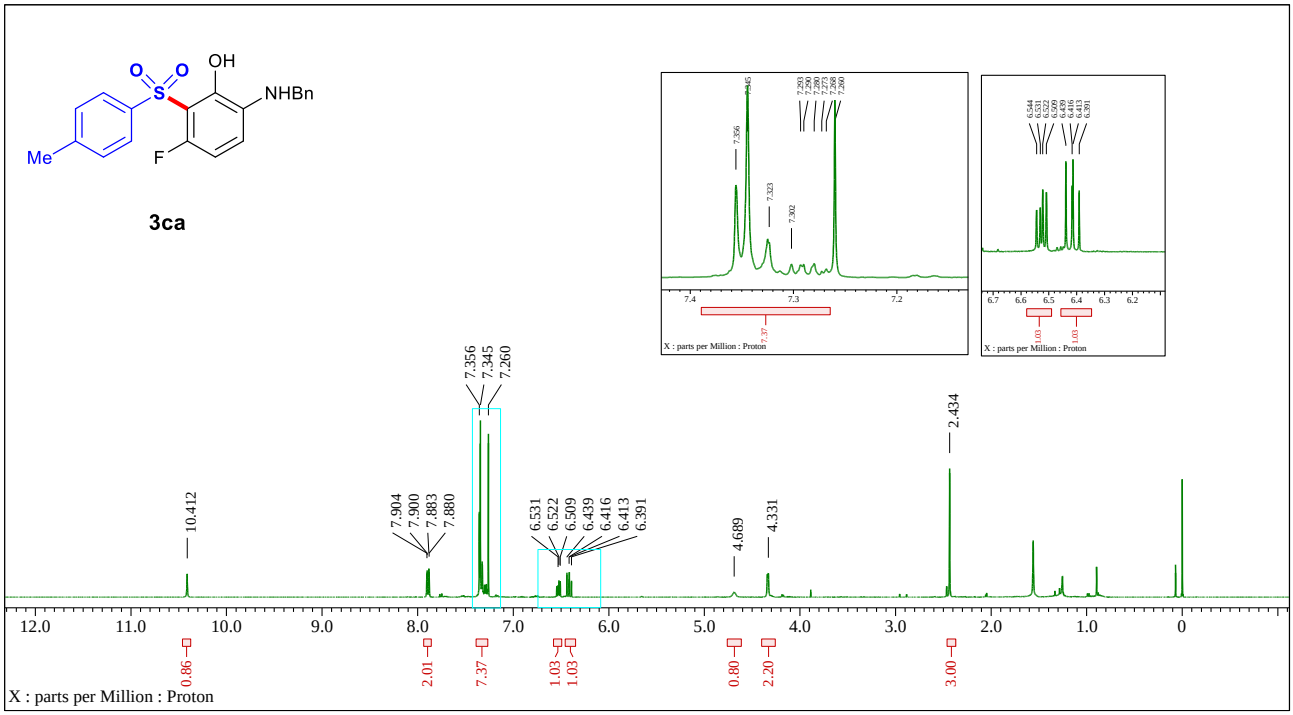
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ba)



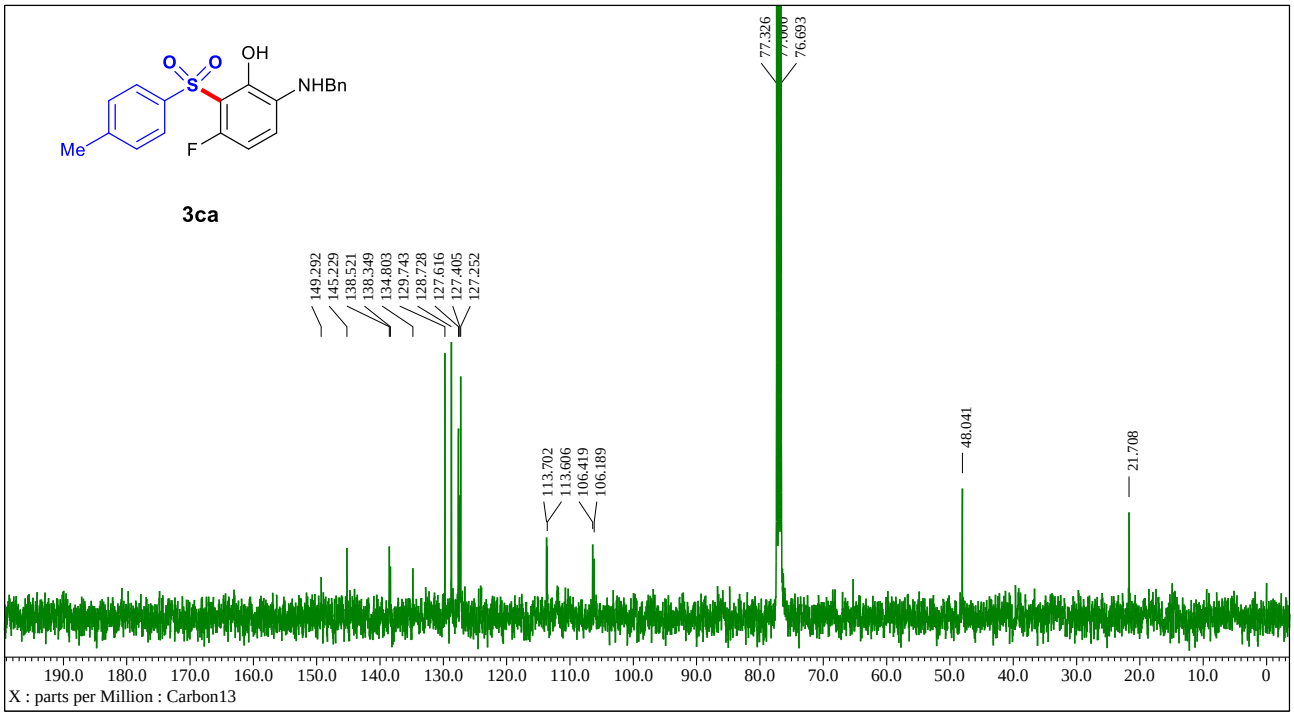
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ba)



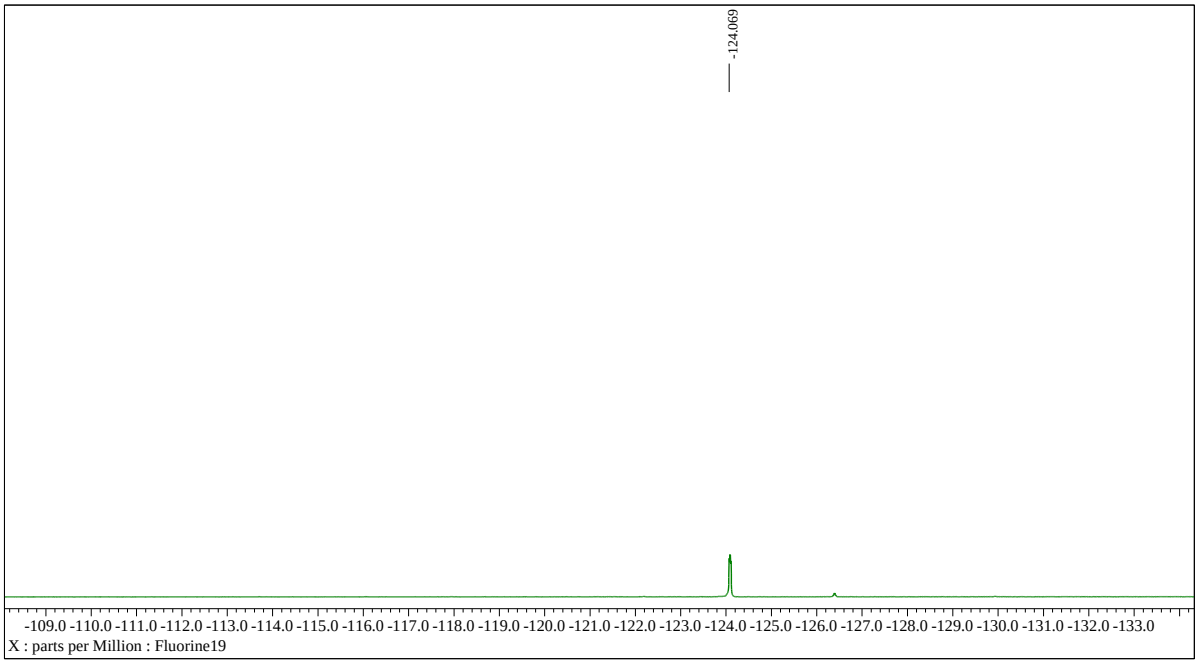
^{1}H NMR (400 MHz, Chloroform-d) for compound (3ca)



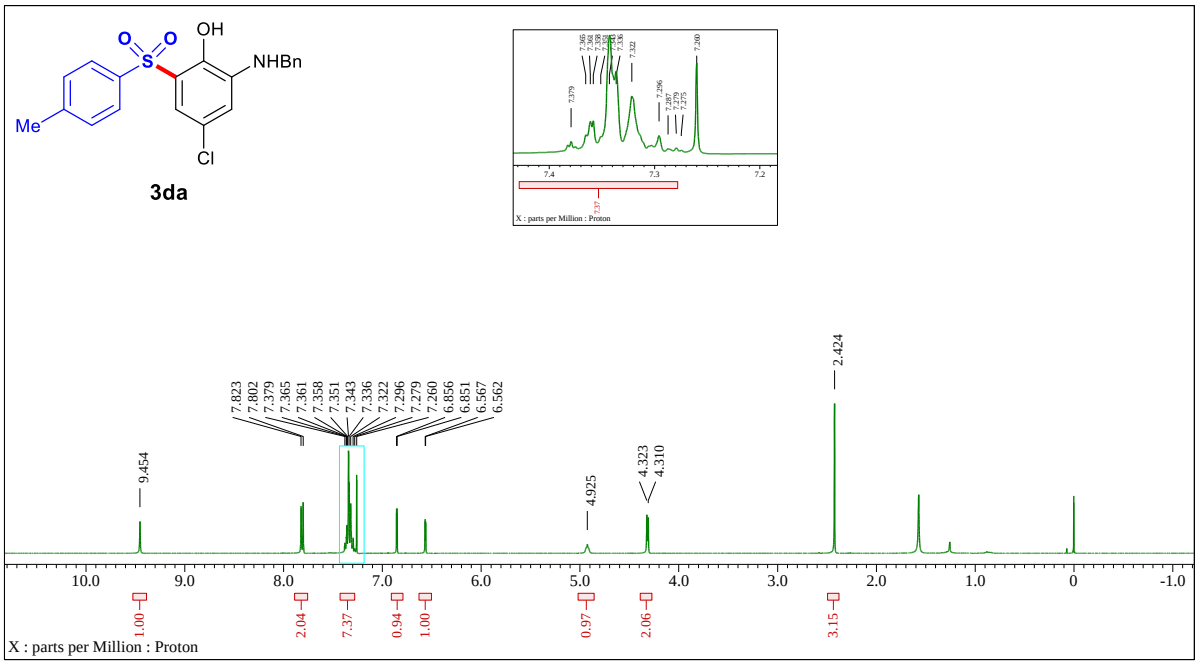
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3ca)



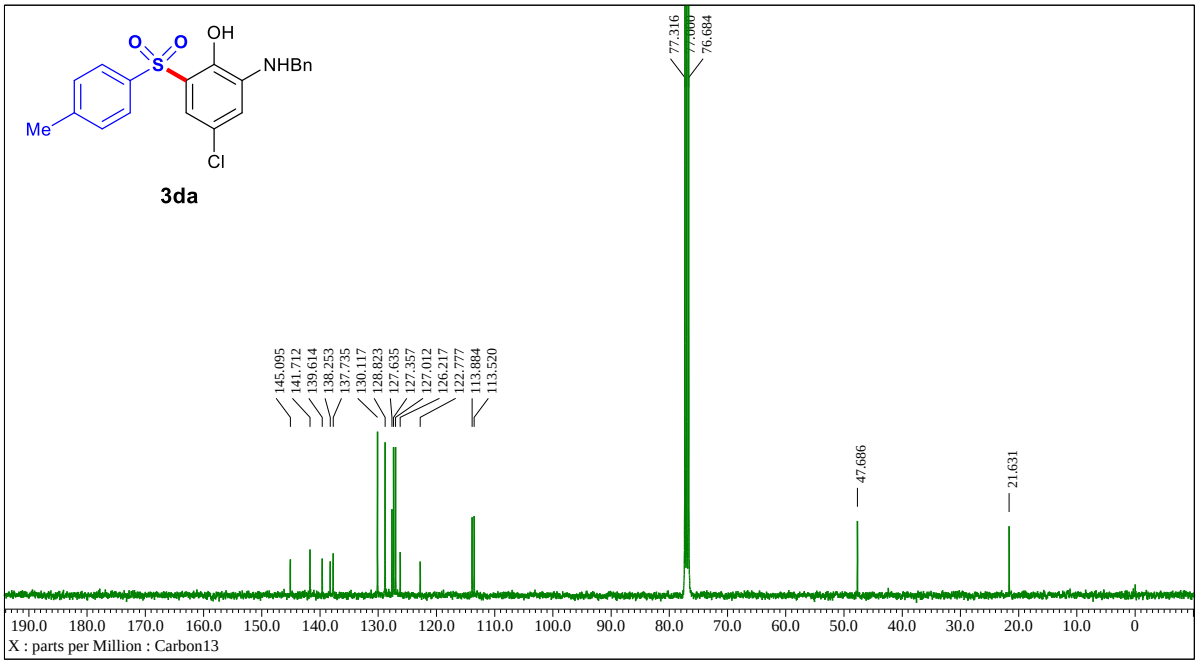
^{19}F NMR (100 MHz, Chloroform-*d*) for compound (3ca)



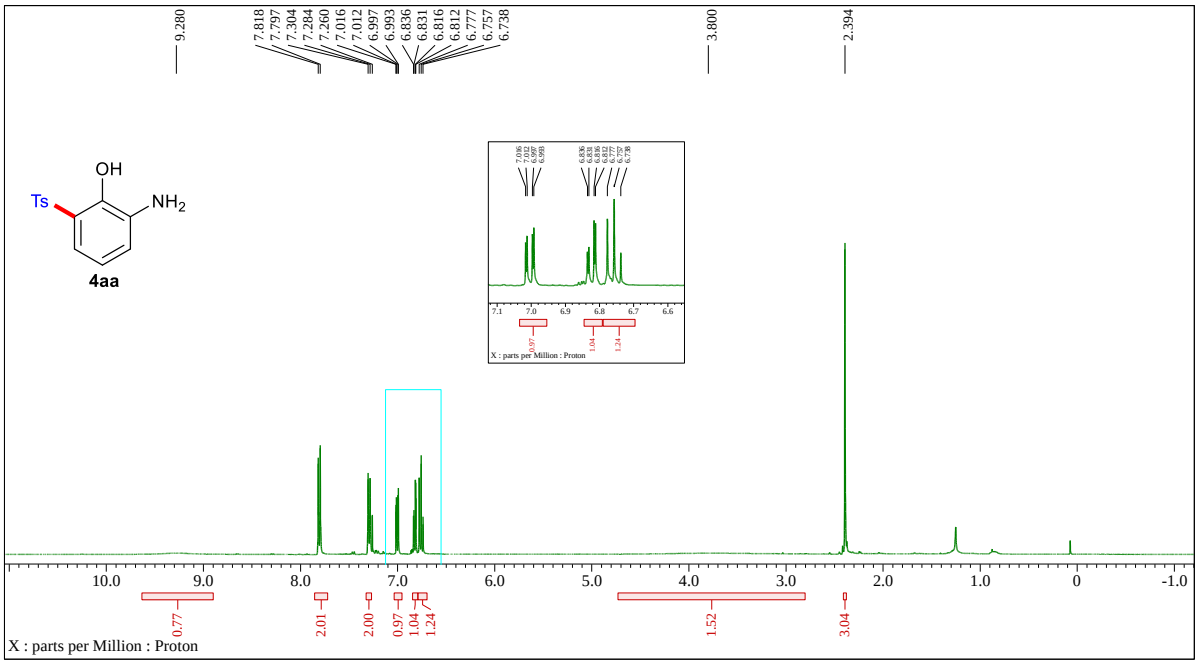
^{1}H NMR (400 MHz, Chloroform-d) for compound (3da)



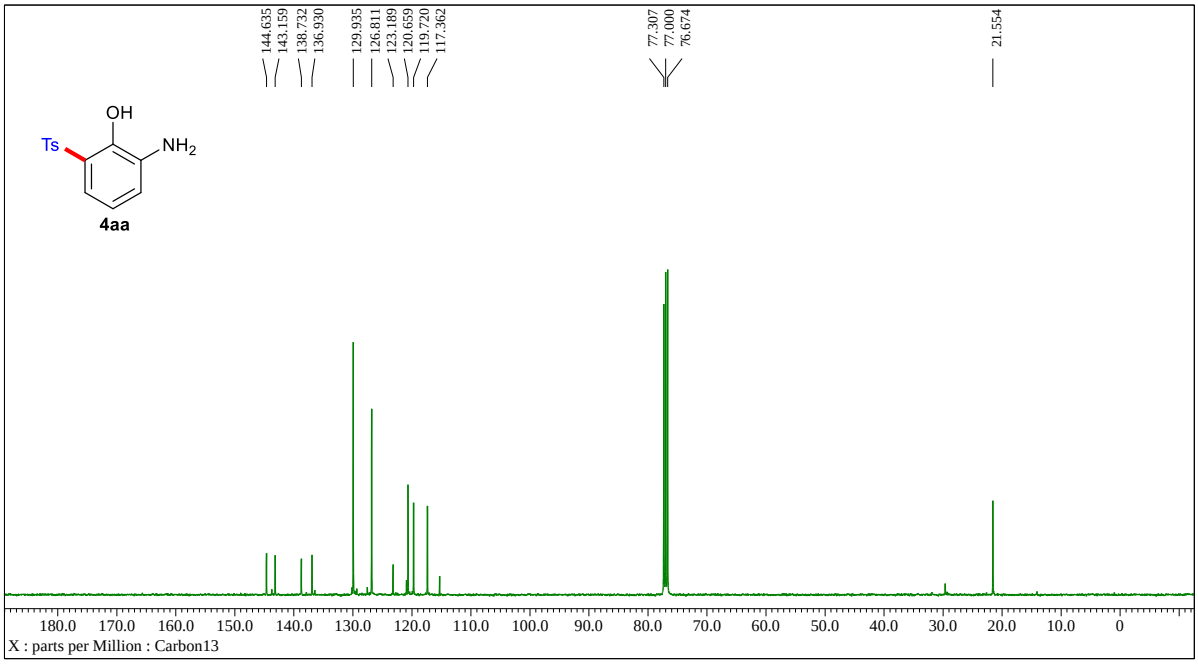
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (3da)



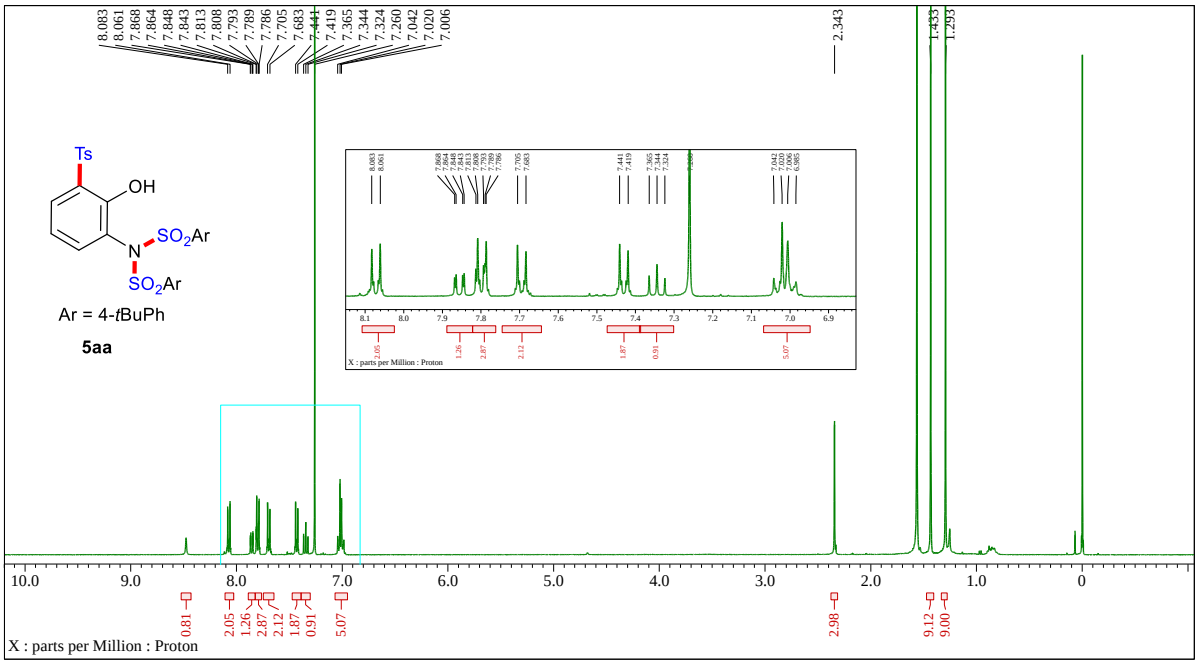
^{1}H NMR (400 MHz, Chloroform-d) for compound (4aa)



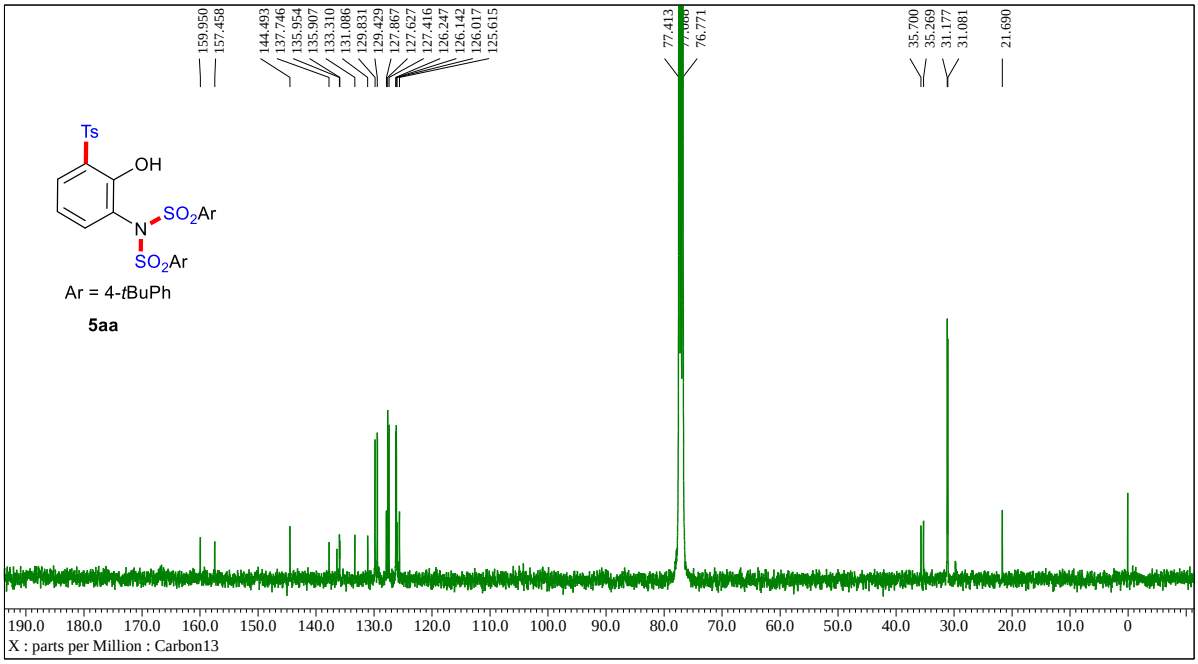
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (4aa)



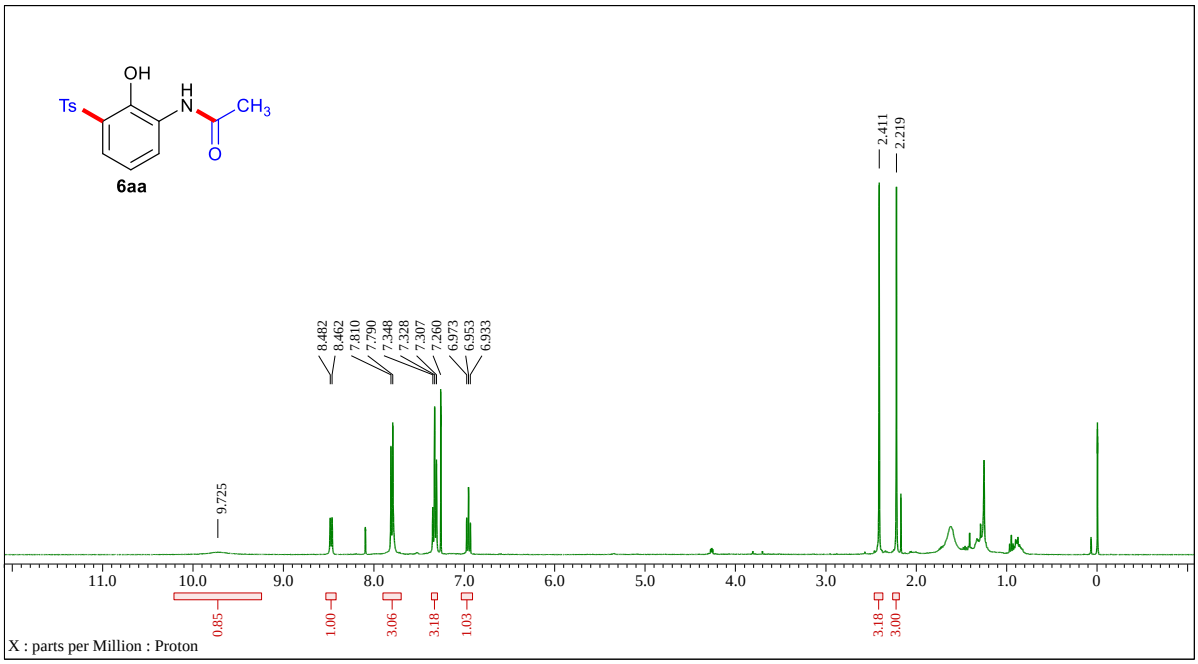
^{1}H NMR (400 MHz, Chloroform-d) for compound (5aa)



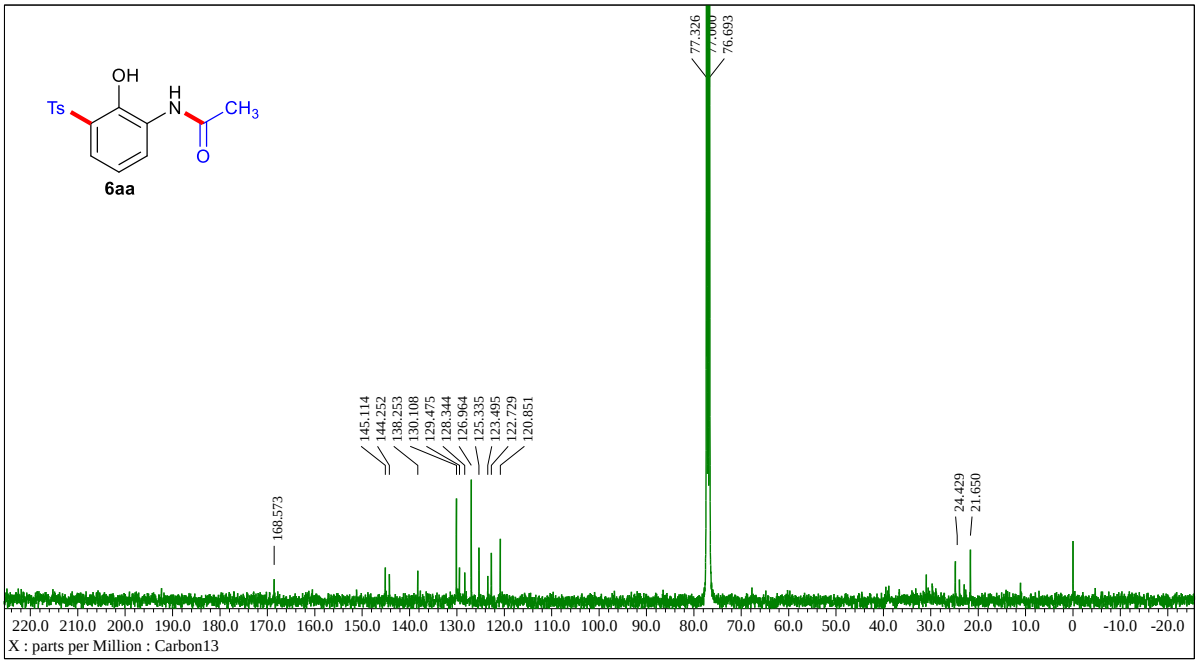
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (5aa)



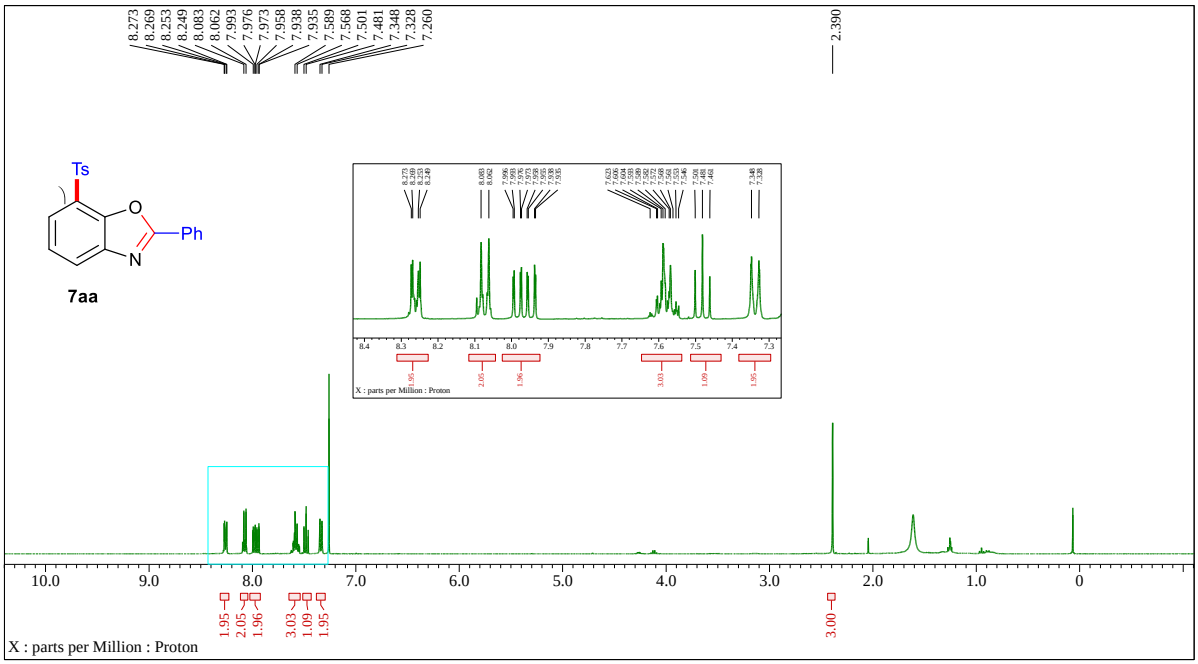
^{1}H NMR (400 MHz, Chloroform-d) for compound (6aa)



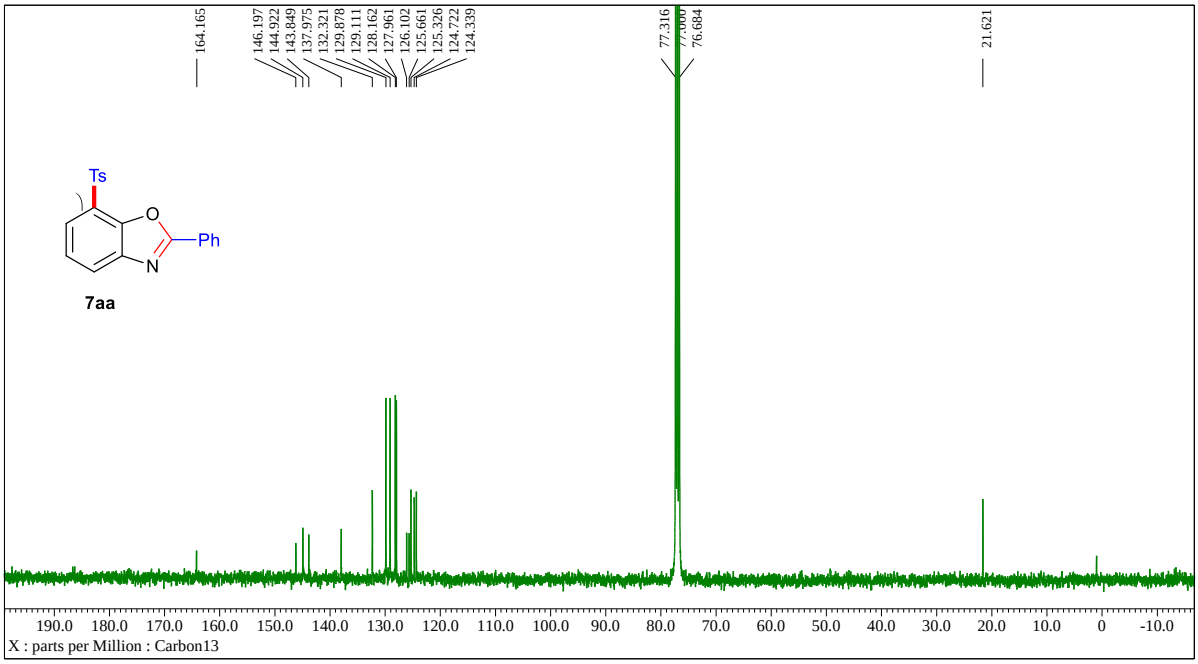
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (6aa)



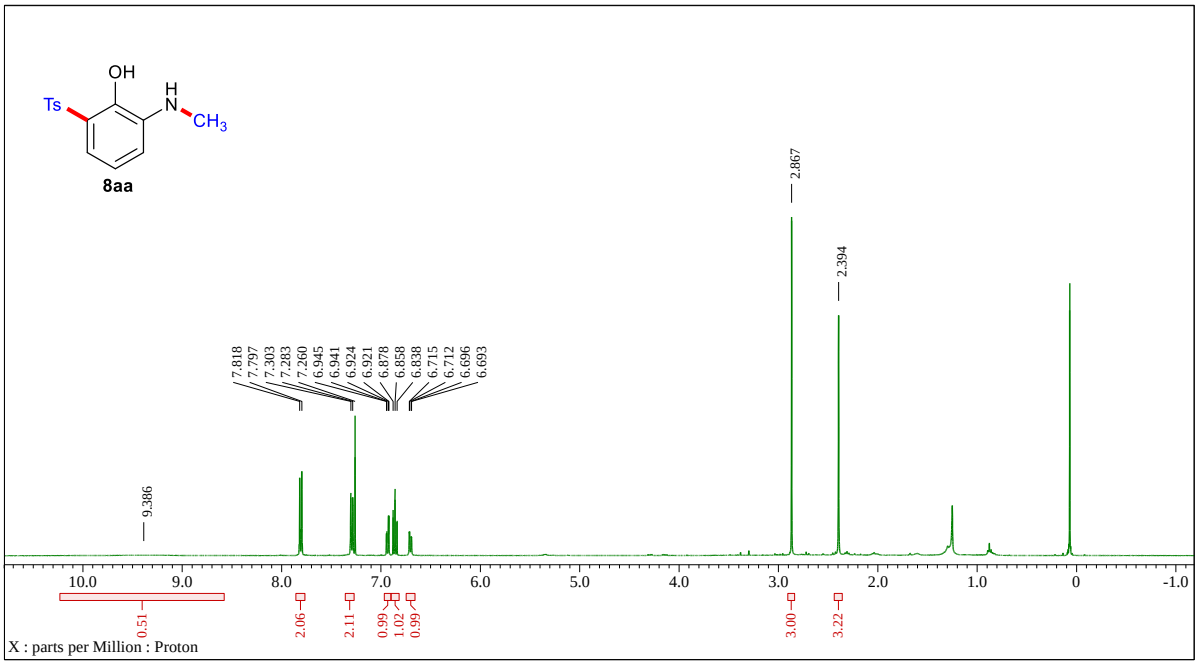
^{1}H NMR (400 MHz, Chloroform-d) for compound (7aa)



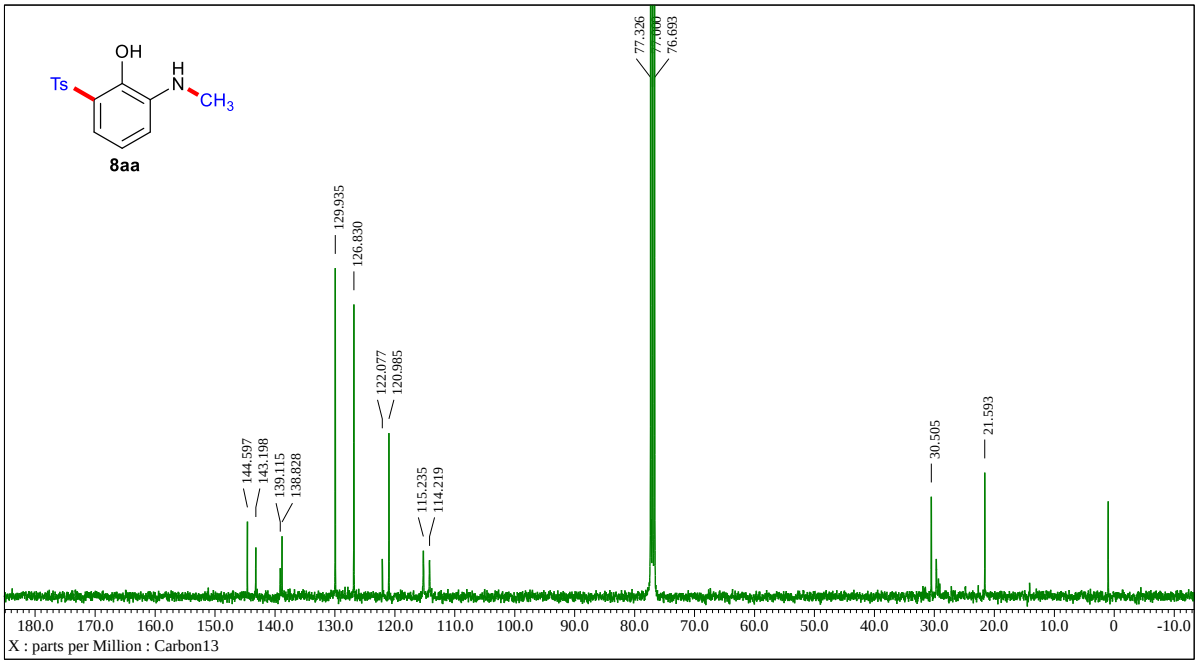
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (7aa)



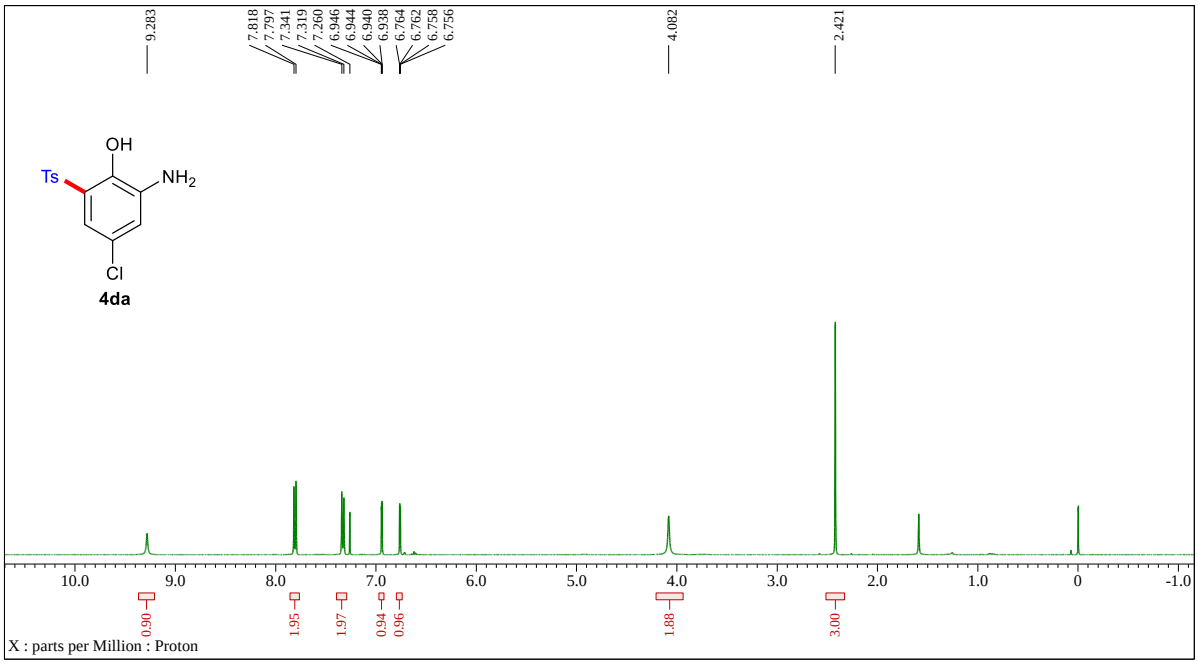
^{1}H NMR (400 MHz, Chloroform-d) for compound (8aa)



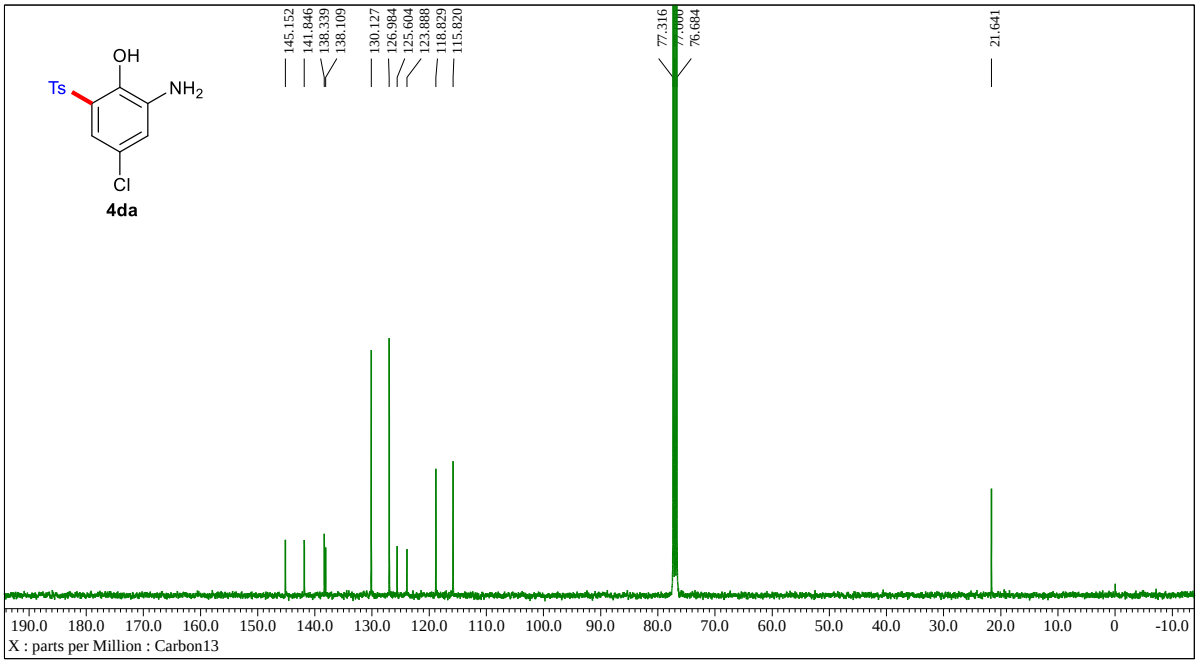
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (8aa)



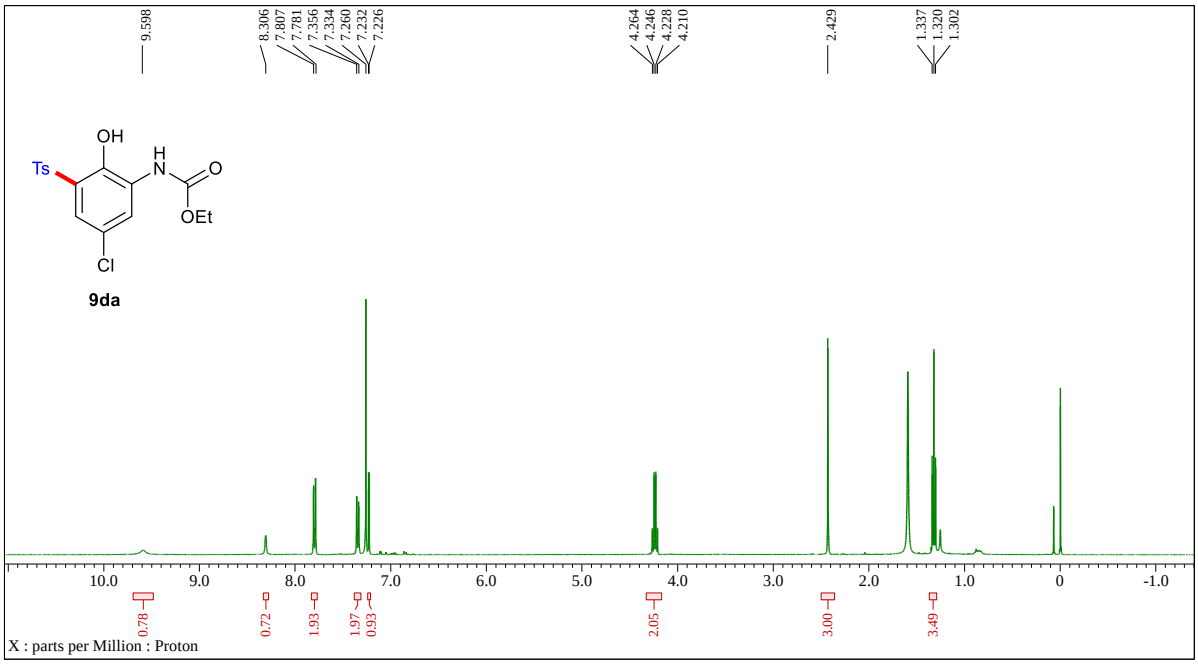
^{1}H NMR (400 MHz, Chloroform-d) for compound (4da)



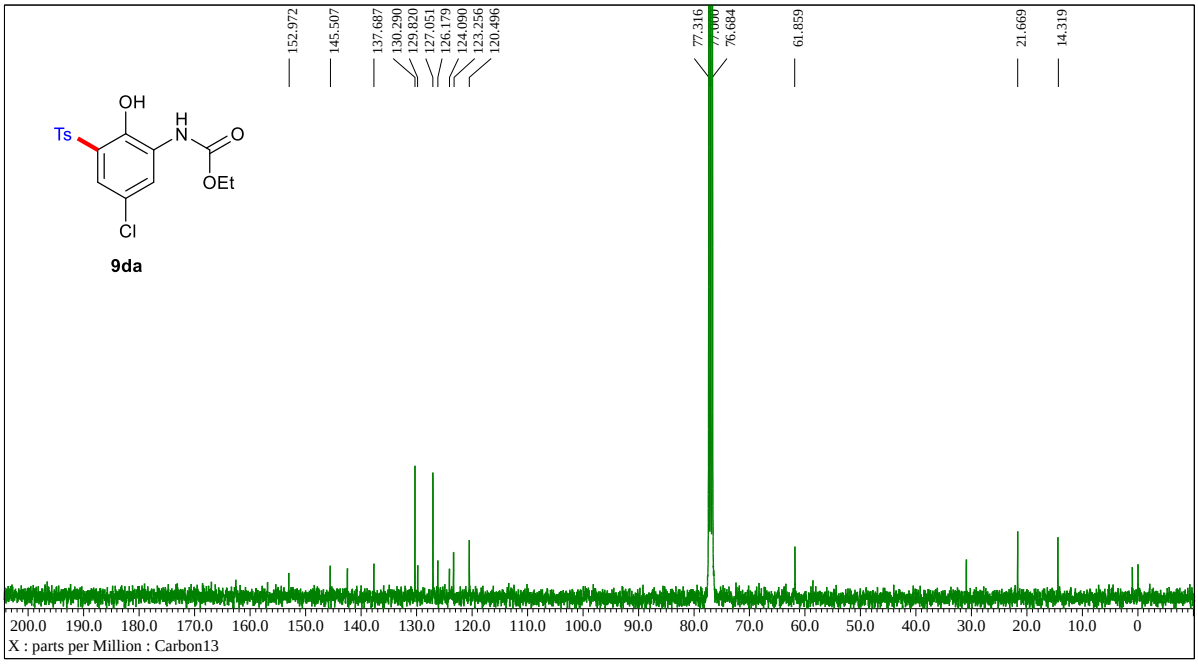
^{13}C NMR (100 MHz, Chloroform-*d*) for compound (4da)



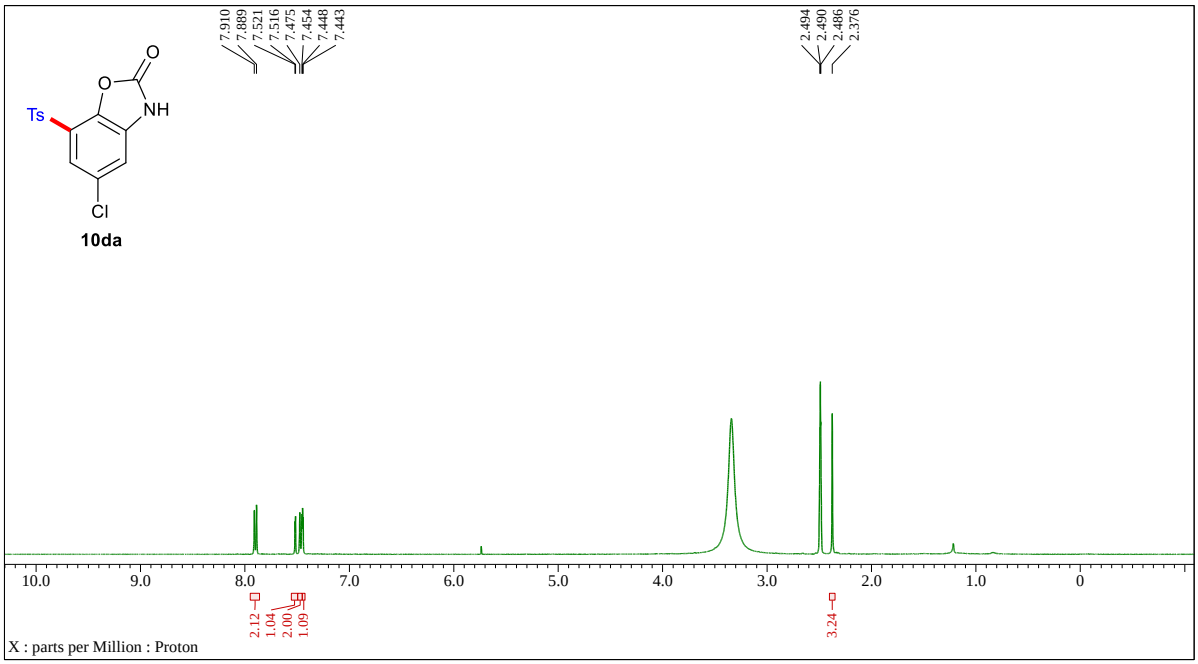
^{1}H NMR (400 MHz, Chloroform-d) for compound (9da)



^{13}C NMR (100 MHz, Chloroform-*d*) for compound (9da)



^{1}H NMR (400 MHz, DMSO-d_6) for compound (10da)



^{13}C NMR (100 MHz, DMSO-d_6) for compound (10da)