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Electronic Supplementary Information

An efficient one-pot access to *N*-(pyridin-2-ylmethyl) substituent biphenyl-4-sulfonamides through water-promoted, palladium-catalyzed, microwave-assisted reactions

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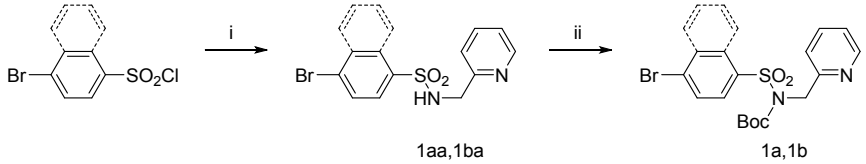
Table of Contents

1. General information

Solvents were commercially available and used without further purification. Other reagents were used as obtained from commercial providers except when otherwise noted. Thin-layer chromatography(TLC) analysis was used to monitor reaction which was carried out on silica plates. Flash column chromatography was performed using silica gel (200-300 mesh). ^{1}H spectra were recorded in $CDCl_3$ or DMSO-d_6 on 400 or 600 MHz NMR spectrometers and resonances (•) are given in parts per million relative to tetramethylsilane. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quarternary), coupling constants (Hz) and integration. ^{13}C spectra were recorded in $CDCl_3$ or DMSO-d_6 on 100 or 150 MHz NMR spectrometers and resonances (•) are given in ppm. High resolution mass spectra (HRMS) were obtained on an Agilent 6224 TOF LC/MS (USA). IR spectra were recorded on a Perkin-Elmer PE-983 infrared spectrometer as KBr pellets with absorption in cm^{-1}. The X-ray crystal-structure determinations of 3aw were obtained on a Bruker SMART APEX CCD system. Melting points were taken on a Buchi B-545 melting point apparatus without correcting. Microwave irradiation reactions were carried out on a Smith synthesizer^{TM} instrument.

2. General procedure for the synthesis of compounds 1aa, 1ba, 1a, 1b.



1aa,1ba 1a,1b

Sulfonyl chloride (2.0 mmol) were added to an ice-cold CH_2Cl_2(8 mL)solution of DIEA (6.0 mmol) and pyridin-2-ylmethanamine (2.1 mmol) and the resulting mixture was refluxed for 6 h. After the reaction mixture was cooled to ambient temperature, the product was concentrated, and the crude mixture was purified by column chromatography on silica gel (petroleum ether/acetone = 20:7) to the desired product as a while solid (1aa and 1ab).

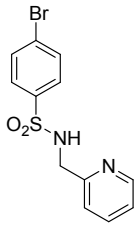
Di-tert-butyl dicarbonate (4 mmol) was slowly added to an ice-cold THF(8 mL) solution of 1aa or 1ba (2 mmol). DMAP (0.2 mmol) was then added and the reaction stirred overnight at room temperature. The product was concentrated, and the crude mixture was purified by column chromatography on silica gel (petroleum ether/acetone = 20:4) to the desired product(1a and 1b).[1]

3. General procedure for the synthesis of compounds 3.

1a or 1b (0.5 mmol) and 2 (0.5 mmol) were dissolved in dioxane (4 mL) and H_2O (1 mL) in a microwave tube under a nitrogen atmosphere. $Pd(PPh_3)_4$ (2 mmol% , 11.6 mg) and sodium bicarbonate (1.0 mmol) were added, the reaction mixture was irradiated in a microwave apparatus at 85 ℃ for 10-25 min. Then, the temperature was increased to 130 ℃ for another 8 min. After the reaction mixture was cooled to ambient temperature, the product was concentrated, and the crude mixture was purified by column chromatography on silica gel (petroleum ether/acetone = 20:6) to the desired product.

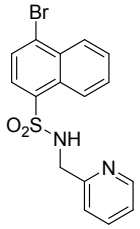
4. Analytical data of the products

4-bromo-*N*-(pyridin-2-ylmethyl)benzenesulfonamide(1aa)



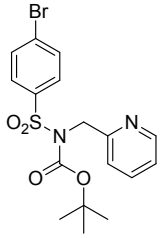
White solid; 596 mg; yield 91%; m.p. 104.5-104.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.44 (d, *J* = 4.2 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.17 (dd, *J* = 12.0, 7.8 Hz, 2H), 6.26 (s, 1H), 4.27 (d, *J* = 4.8 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 154.65, 148.80, 138.81, 136.89, 132.02, 128.50, 127.20, 122.63, 122.14, 77.21, 77.00, 76.79, 47.36. IR (neat): υ max = 3063, 2857, 1573, 1465, 1439, 1326, 1162, 1090, 1064, 1006, 818, 743, 623, 591, 557, 521 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{12}H_{12}BrN_2O_2S$: 326.9803; found: 326.9813.

4-bromo-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(1ba)



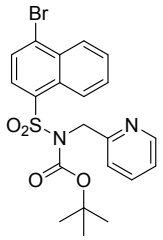
White solid; 694 mg; yield 92%; m.p. 86.0-86.6 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.70 (d, *J* = 9.0 Hz, 1H), 8.30 (d, *J* = 8.4 Hz, 1H), 8.21 (d, *J* = 4.8 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.73 – 7.63 (m, 2H), 7.51 – 7.43 (m, 1H), 7.02 (dd, *J* = 7.2, 5.4 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.48 (s, 1H), 4.23 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.43, 148.58, 136.44, 134.70, 132.32, 129.47, 129.27, 129.00, 128.81, 128.19, 128.06, 125.02, 122.32, 121.83, 77.32, 77.00, 76.68, 47.44. IR (neat): υ max = 3439, 3070, 2850, 1592, 1500, 1441, 1327, 1262, 1202, 1136, 1080, 1002, 880, 832, 757, 674, 619, 512, 409 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{14}BrN_2O_2S$: 376.9959; found: 376.9954.

tert-butyl (4-bromophenyl)sulfonyl(pyridin-2-ylmethyl)carbamate(1a)



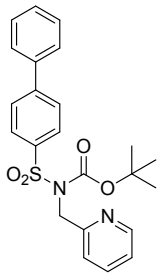
White solid; 786 mg; yield 92%; m.p. 124.3-125.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.53 (d, *J* = 4.8 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.68 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.23 – 7.17 (m, 1H), 5.14 (s, 2H), 1.30 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 156.45, 150.59, 149.05, 138.69, 136.60, 131.60, 130.05, 128.29, 122.21, 120.82, 84.69, 77.21, 77.00, 76.79, 51.16, 27.69. IR (neat): υ max = 3423, 3061, 2978, 1722, 1596, 1573, 1476, 1364, 1326, 1285, 1156, 1072, 842, 743, 606, 563 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{20}BrN_2O_4S$: 427.0327; found: 427.0330.

tert-butyl (4-bromonaphthalen-1-yl)sulfonyl(pyridin-2-ylmethyl)carbamate(1b)



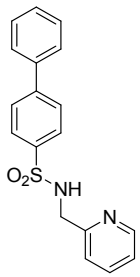
White solid; 888 mg; yield 93%; m.p. 168.4-169.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.53 (d, *J* = 4.2 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.22 – 7.17 (m, 1H), 5.14 (s, 2H), 1.30 (s, 9H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 156.67, 150.46, 149.10, 136.78, 134.43, 132.22, 132.04, 130.57, 129.18, 128.85, 128.36, 128.18, 128.12, 124.08, 122.16, 120.34, 84.79, 77.21, 77.00, 76.79, 51.43, 27.55. IR (neat): υ max = 3435, 3052, 2977, 2878, 1725, 1588, 1497, 1423, 1339, 1253, 1163, 989, 879, 758, 597, 530 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{21}H_{22}BrN_2O_4S$: 477.0484; found: 477.0482.

tert-butyl [1,1'-biphenyl]-4-ylsulfonyl(pyridin-2-ylmethyl)carba mate(3a)



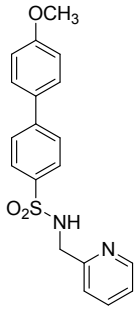
White solid; 183 mg; yield 86%; m.p. 116.7-116.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.56 (d, *J* = 4.2 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 2H), 7.71 (t, *J* = 9.0 Hz, 3H), 7.63 (d, *J* = 7.2 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 2H), 7.44 (d, *J* = 7.2 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.20 (d, *J* = 6.6 Hz, 1H), 5.19 (s, 2H), 1.31 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 156.83, 150.78, 149.08, 146.02, 139.00, 138.22, 136.62, 128.95, 128.79, 128.50, 127.22, 126.96, 122.11, 120.65, 84.50, 77.32, 77.00, 76.68, 51.33, 27.68. IR (neat): υ max = 3441, 3070, 2986, 2941, 1729, 1591, 1479, 1433, 1395, 1353, 1314, 1252, 1152, 1092, 1002, 929, 851, 813, 765, 730, 670, 607, 571, 538, 466 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{25}N_2O_4S$: 425.1535; found: 425.1541.

***N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3aa)**



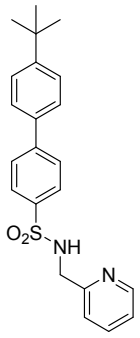
White solid; 152 mg; yield 94%; m.p. 90.4-91.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.2 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.68 – 7.59 (m, 3H), 7.56 (d, *J* = 7.2 Hz, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.42 (d, *J* = 7.2 Hz, 1H), 7.26 – 7.14 (m, 2H), 6.14 (s, 1H), 4.33 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.88, 148.76, 145.30, 139.22, 138.23, 136.92, 128.94, 128.34, 127.56, 127.49, 127.17, 122.59, 122.13, 77.32, 77.00, 76.68, 47.44. IR (neat): υ max = 3462, 3291, 3056, 2997, 1592, 1569, 1479, 1423, 1328, 1160, 1096, 1049, 1000, 872, 836, 770, 686, 588, 522 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_2S$: 325.1011; found: 325.1000.

4'-methoxy-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ab)



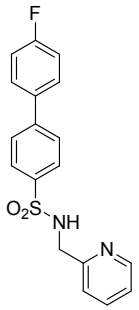
White solid; 166 mg; yield 94%; m.p. 160.5-161.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (d, *J* = 4.8 Hz, 1H), 7.88 (d, *J* = 8.4 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 3H), 7.51 (d, *J* = 9.0 Hz, 2H), 7.21 – 7.10 (m, 2H), 6.99 (d, *J* = 9.0 Hz, 2H), 6.03 (t, *J* = 5.4 Hz, 1H), 4.29 (d, *J* = 5.4 Hz, 2H), 3.86 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 159.91, 154.76, 148.92, 144.94, 137.28, 136.77, 131.57, 128.32, 127.62, 126.93, 122.57, 122.01, 114.38, 77.32, 77.00, 76.68, 55.34, 47.44. IR (neat): υ max = 3444, 3286, 2843, 1595, 1526, 1481, 1435, 1324, 1259, 1152, 1094, 1029, 998, 859, 820, 772, 639, 531 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{19}N_2O_3S$: 355.1116; found: 355.1112.

4'-(tert-butyl)-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ac)



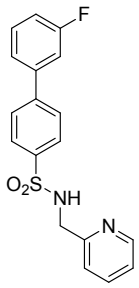
White solid; 181 mg; yield 95%; m.p. 165.5-166.4 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (d, *J* = 4.2 Hz, 1H), 7.89 (d, *J* = 7.8 Hz, 2H), 7.63 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 5.4 Hz, 4H), 7.18 (d, *J* = 7.8 Hz, 1H), 7.16 – 7.12 (m, 1H), 6.10 (s, 1H), 4.31 (d, *J* = 5.4 Hz, 2H), 1.36 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.87, 151.54, 148.90, 145.11, 137.80, 136.79, 136.27, 127.52, 127.27, 126.84, 125.93, 122.56, 122.10, 77.32, 77.00, 76.68, 47.50, 34.57, 31.21. IR (neat): υ max = 3445, 3035, 2956, 2832, 1596, 1481, 1389, 1356, 1326, 1152, 1114, 1052, 1004, 819, 772, 617, 562, 538 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{25}N_2O_2S$: 381.1637; found: 381.1633.

4'-fluoro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ad)



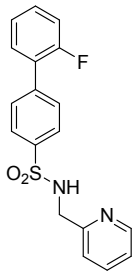
White solid; 161 mg; yield 94%; m.p. 126.4-127.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.8 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.61 (dd, *J* = 12.0, 8.4 Hz, 3H), 7.53 (dd, *J* = 8.4, 5.4 Hz, 2H), 7.23 – 7.11 (m, 4H), 6.05 (s, 1H), 4.31 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 164.16, 161.70, 154.80, 148.88, 144.23, 138.17, 136.83, 135.31, 128.91, 128.83, 127.63, 127.35, 122.58, 122.10, 116.03, 115.82, 77.32, 77.00, 76.68, 47.45. IR (neat): υ max = 3430, 3059, 2851, 1598, 1483, 1439, 1391, 1324, 1226, 1156, 1096, 1070, 1006, 820, 633, 572, 517 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}FN_2O_2S$: 343.0917 ; found: 343.0901.

3'-fluoro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ae)



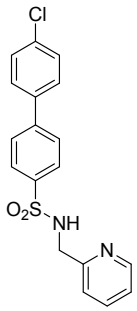
White solid; 159 mg; yield 93%; m.p. 100.9-101.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (d, *J* = 4.8 Hz, 1H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.66 – 7.56 (m, 3H), 7.44 (d, *J* = 6.0 Hz, 1H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.24 (s, 1H), 7.21 – 7.12 (m, 2H), 7.11 (s, 1H), 6.14 (s, 1H), 4.31 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 164.20, 161.75, 154.89, 148.81, 143.79, 141.30, 138.83, 136.87, 130.46, 127.60, 127.45, 122.82, 122.57, 122.18, 115.24, 115.03, 114.15, 113.93, 77.32, 77.00, 76.68, 47.47. IR (neat): υ max = 3424, 3065, 2950, 2854, 1590, 1565, 1473, 1438, 1394, 1325, 1155, 1065, 1005, 875, 836, 778, 664, 584, 514 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}FN_2O_2S$: 343.0917 ; found: 343.0909.

2'-fluoro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3af)



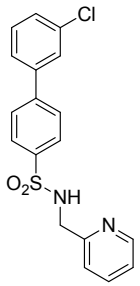
White solid; 154 mg; yield 90%; m.p. 90.2-91.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (s, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 3H), 7.40 (t, *J* = 7.8 Hz, 2H), 7.24 (s, 1H), 7.21 – 7.14 (m, 3H), 6.05 (s, 1H), 4.33 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 160.70, 158.23, 154.80, 148.89, 139.92, 138.66, 136.82, 130.48, 130.02, 129.38, 127.09, 124.57, 124.55, 122.60, 122.16, 116.31, 116.09, 77.32, 77.00, 76.68, 47.51. IR (neat): υ max = 3442, 3053, 2843, 1596, 1478, 1444, 1393, 1314, 1151, 1100, 1007, 842, 759, 656, 585, 521 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}FN_2O_2S$: 343.0917 ; found: 343.0893.

4'-chloro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ag)



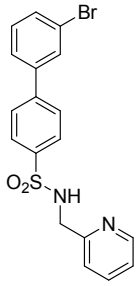
White solid; 167 mg; yield 93%; m.p. 134.6-135.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (d, *J* = 4.8 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.60 (d, *J* = 8.4 Hz, 3H), 7.49 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.21 – 7.05 (m, 2H), 6.14 (d, *J* = 5.4 Hz, 1H), 4.30 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.79, 148.93, 144.04, 138.62, 137.68, 136.80, 134.62, 129.16, 128.45, 127.72, 127.37, 122.59, 122.04, 77.32, 77.00, 76.68, 47.45. IR (neat): υ max = 3075, 2928, 2861, 1593, 1472, 1442, 1330, 1157, 1089, 1003, 812, 774, 602, 562, 523 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}ClN_2O_2S$: 359.0621 ; found: 359.0591.

3'-chloro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ah)



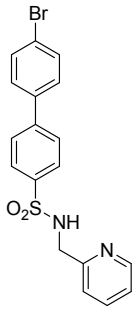
White solid; 165 mg; yield 92%; m.p. 101.9-102.6 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.8 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.62 (d, *J* = 8.4 Hz, 3H), 7.54 (s, 1H), 7.46 – 7.35 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.04 (s, 1H), 4.32 (d、, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.71, 148.88, 143.77, 140.99, 138.81, 136.85, 134.82, 130.23, 128.33, 127.67, 127.52, 127.27, 125.36, 122.61, 122.10, 77.32, 77.00, 76.68, 47.41. IR (neat): υ max = 3072, 2859, 1594, 1557, 1465, 1439, 1389, 1326, 1157, 1095, 1005, 842, 778, 718, 586, 520 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}ClN_2O_2S$: 359.0621 ; found: 359.0606.

3'-bromo-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ai)



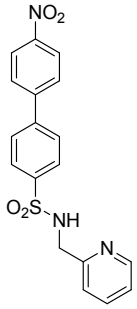
White solid; 107 mg; yield 53%; m.p. 107.1-107.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (s, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 7.63 – 7.57 (m, 5H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.17 (dd, *J* = 18.0, 7.2 Hz, 2H), 6.07 (s, 1H), 4.30 (d, *J* = 4.8 Hz, 2H). ^{13}C NMR (100 MHz, DMSO) (δ ppm): 154.74, 148.79, 143.66, 141.25, 138.83, 136.93, 131.24, 130.47, 130.15, 127.65, 127.51, 125.81, 123.00, 122.62, 122.14, 77.32, 77.00, 76.68, 47.39. IR (neat): υ max = 3029, 2848, 2872, 2681, 1590, 1472, 1436, 1334, 1161, 1095, 1053, 996, 811, 762, 696, 584, 539 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}BrN_2O_2S$: 403.0116 ; found: 403.0098.

4'-bromo-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3aj)



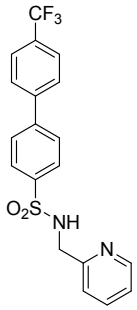
White solid; 103 mg; yield 51%; m.p. 127.4-128.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (s, 1H), 7.92 (d, *J* = 7.8 Hz, 2H), 7.63 – 7.57 (m, 5H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.27 (s, 1H), 7.21 – 7.13 (m, 2H), 6.07 (s, 1H), 4.30 (d, *J* = 4.2 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.61, 148.92, 144.13, 138.49, 138.14, 136.84, 132.14, 128.78, 127.76, 127.38, 122.86, 122.64, 122.03, 77.32, 77.00, 76.68, 47.37. IR (neat): υ max = 3069, 2861, 1593, 1470, 1443, 1331, 1157, 1096, 1071, 1002, 809, 830, 772, 716, 596, 520 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}BrN_2O_2S$: 403.0116 ; found: 403.0074.

4'-nitro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ak)



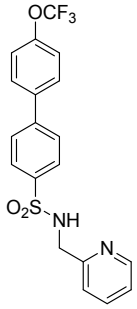
Yellow solid; 108 mg; yield 58%; m.p. 183.5-184.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.48 (d, *J* = 4.2 Hz, 1H), 8.34 (d, *J* = 8.4 Hz, 2H), 7.99 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 8.4 Hz, 2H), 7.69 (d, *J* = 8.4 Hz, 2H), 7.67 (d, *J* = 7.8 Hz, 1H), 7.25 (s, 1H), 7.24 – 7.20 (m, 1H), 6.20 (s, 1H), 4.35 (d, *J* = 4.8 Hz, 2H).. ^{13}C NMR (100 MHz, DMSO) (δ ppm): 156.97, 148.77, 147.28, 144.93, 141.46, 140.79, 136.71, 128.41, 128.08, 127.36, 124.20, 122.39, 121.72, 48.01, 40.13, 39.92, 39.71, 39.50, 39.29, 39.08, 38.88. IR (neat): υ max = 3091, 2870, 1597, 1516, 1468, 1337, 1159, 1098, 832, 759, 699, 601, 565, 513 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{16}N_3O_4S$: 370.0862 ; found: 370.0836.

***N*-(pyridin-2-ylmethyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-sulfonamide(3al)**



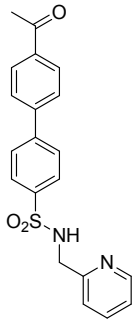
White solid; 179 mg; yield 91%; m.p. 162.8-163.5 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.8 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 2H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.69 – 7.65 (m, 4H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.18 (dd, *J* = 15.6, 7.8 Hz, 2H), 6.03 (s, 1H), 4.32 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.66, 148.89, 143.76, 142.73, 142.67, 139.18, 136.89, 132.12, 128.59, 127.77, 127.58, 125.93, 125.90, 122.66, 122.12, 77.32, 77.00, 76.68, 47.42. IR (neat): υ max = 3436, 3078, 2941, 2865, 1597, 1469, 1443, 1388, 1326, 1163, 1111, 1068, 1007, 827, 751, 596, 515 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{16}F_3N_2O_2S$: 393.0885 ; found: 393.0871.

***N*-(pyridin-2-ylmethyl)-4'-(trifluoromethoxy)-[1,1'-biphenyl]-4-sulfonamide(3am)**



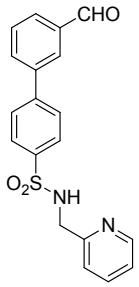
White solid; 190 mg; yield 93%; m.p. 121.0-121.8 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.8 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.62 (t, *J* = 7.8 Hz, 3H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.4 Hz, 2H), 7.19 (dd, *J* = 16.8, 7.2 Hz, 2H), 6.02 (s, 1H), 4.32 (d, *J* = 5.4 Hz, 2H) ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.69, 149.32, 148.92, 143.87, 138.62, 137.94, 136.84, 128.65, 127.73, 127.53, 122.62, 122.07, 121.38, 77.32, 77.00, 76.68, 47.43. IR (neat): υ max = 3114, 2870, 1596, 1516, 1483, 1436, 1391, 1325, 1258, 1155, 1108, 1004, 843, 811, 765, 592, 540 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{16}F_3N_2O_3S$: 409.0834 ; found: 409.0828.

4'-acetyl-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3an)



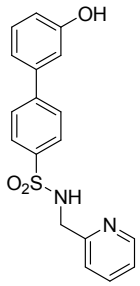
White solid; 190 mg; yield 90%; m.p. 168.9-169.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (s, 1H), 8.06 (d, *J* = 8.4 Hz, 2H), 7.95 (d, *J* = 8.4 Hz, 2H), 7.67 (dd, *J* = 132.2, 8.4 Hz, 4H), 7.61 (t, *J* = 7.8 Hz, 1H), 7.24 – 7.09 (m, 2H), 6.09 (s, 1H), 4.32 (d, *J* = 4.8 Hz, 2H), 2.66 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 197.57, 154.71, 143.93, 143.65, 139.13, 136.83, 136.59, 129.00, 127.73, 127.40, 122.62, 122.04, 109.93, 77.21, 77.00, 76.79, 47.41, 26.70. IR (neat): υ max = 3311, 3079, 2997, 1678, 1591, 1468, 1388, 1327, 1265, 1165, 1096, 1071, 996, 827, 722, 584, 515 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{19}N_2O_3S$: 367.1116 ; found: 367.1108.

3'-formyl-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ao)



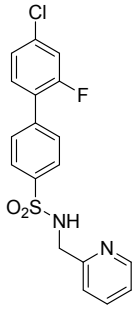
White solid; 164 mg; yield 93%; m.p. 119.3-120.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 10.10 (s, 1H), 8.48 (d, *J* = 4.8 Hz, 1H), 8.08 (s, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.93 (d, *J* = 7.8 Hz, 1H), 7.84 (d, *J* = 7.2 Hz, 1H), 7.72 – 7.65 (m, 4H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.21 (m, 1H), 6.28 (s, 1H), 4.37 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (600 MHz, $CDCl_3$) (δ ppm): 192.03, 154.73, 148.89, 148.79, 143.69, 140.15, 139.03, 136.88, 132.99, 129.81, 129.74, 127.87, 127.76, 127.57, 122.61, 122.08, 77.21, 77.00, 76.79, 47.40. IR (neat): υ max = 3439, 3065, 2852, 1699, 1594, 1471, 1438, 1383, 1320, 1153, 1095, 1006, 845, 795, 693, 584, 520 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{17}N_2O_3S$: 353.0960 ; found: 353.0941.

3'-hydroxy-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ap)



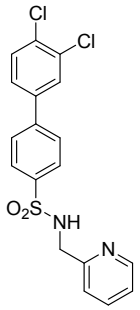
White solid; 148 mg; yield 87%; m.p. 140.4-141.1 °C; ^{1}H NMR (600 MHz, DMSO) (δ ppm): 9.68 (s, 1H), 8.43 (d, *J* = 4.8 Hz, 1H), 8.35 (t, *J* = 6.6 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 2H), 7.80 – 7.68 (m, 3H), 7.37 (d, *J* = 7.8 Hz, 1H), 7.31 (t, *J* = 7.8 Hz, 1H), 7.28 – 7.21 (m, 1H), 7.13 (d, *J* = 7.8 Hz, 1H), 7.07 (s, 1H), 6.84 (d, *J* = 8.4 Hz, 1H), 4.12 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) (δ ppm): 157.98, 157.11, 148.82, 144.08, 140.06, 139.28, 136.72, 130.23, 127.27, 127.22, 122.40, 121.73, 117.84, 115.49, 113.82, 48.04, 39.92, 39.78, 39.64, 39.50, 39.36, 39.22, 39.08. IR (neat): υ max = 3413, 3291, 3071, 1591, 1474, 1434, 1326, 1212, 1154, 1091, 1070, 1002, 822, 756, 686, 594, 531 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{17}N_2O_3S$: 341.0960 ; found: 341.0942.

4'-chloro-2'-fluoro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3aq)



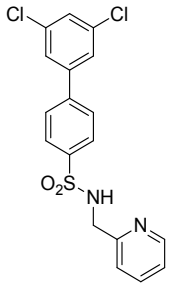
White solid; 172 mg; yield 91%; m.p. 151.4-152.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (d, *J* = 4.2 Hz, 1H), 7.91 (d, *J* = 8.4 Hz, 2H), 7.61 – 7.53 (m, 3H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.23 (dd, *J* = 13.2, 9.6 Hz, 2H), 7.17 (d, *J* = 7.2 Hz, 2H), 6.06 (s, 1H), 4.31 (d, *J* = 5.4 Hz, 2H) ^{13}C NMR (150 MHz, DMSO) (δ ppm): 159.76, 158.10, 156.99, 148.70, 140.17, 137.78, 136.67, 134.04, 133.97, 132.08, 129.49, 126.92, 125.83, 125.39, 122.38, 121.70, 116.97, 116.80, 109.58, 48.02, 39.92, 39.78, 39.64, 39.50, 39.36, 39.22, 39.08. IR (neat): υ max = 3446, 3080, 2863, 1596, 1473, 1441, 1388, 1331, 1161, 1095, 1073, 1049, 1004, 818, 766, 611, 578, 527 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{15}ClFN_2O_2S$: 377.0527 ; found: 377.0518.

3',4'-dichloro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3ar)



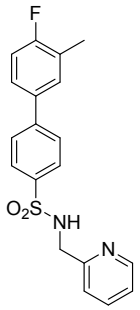
White solid; 181 mg; yield 92%; m.p. 126.5-127.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.8 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.67 – 7.57 (m, 4H), 7.54 (d, *J* = 8.4 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.17 (dd, *J* = 14.4, 7.2 Hz, 2H), 6.09 (s, 1H), 4.31 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.67, 148.89, 142.71, 139.08, 136.86, 133.10, 132.66, 130.91, 128.97, 127.79, 127.39, 126.39, 122.63, 122.09, 77.32, 77.00, 76.68, 47.39. IR (neat): υ max = 3444, 3285, 3055, 1592, 1468, 1433, 1374, 1320, 1158, 1095, 1055, 855, 814, 761, 661, 606 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{15}Cl_2N_2O_2S$: 393.0231 ; found: 393.0216.

3',5'-dichloro-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3as)



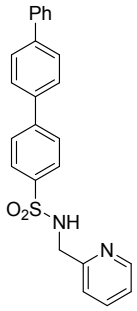
White solid; 181 mg; yield 92%; m.p. 150.3-151.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (s, 1H), 7.94 (d, *J* = 8.4 Hz, 2H), 7.61 (t, *J* = 10.8 Hz, 3H), 7.42 (d, *J* = 13.2 Hz, 3H), 7.18 (d, *J* = 7.8 Hz, 2H), 6.06 (s, 1H), 4.31 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.62, 148.91, 142.45, 142.14, 139.49, 136.87, 135.52, 128.19, 127.81, 127.55, 125.70, 122.65, 122.08, 77.32, 77.00, 76.68, 47.37. IR (neat): υ max = 3436, 3064, 2845, 1586, 1555, 1433, 1387, 1325, 1154, 1097, 1069, 838, 795, 705, 585, 518 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{18}H_{15}Cl_2N_2O_2S$: 393.0231 ; found: 393.0205.

4'-fluoro-3'-methyl-*N*-(pyridin-2-ylmethyl)-[1,1'-biphenyl]-4-sulfonamide(3at)



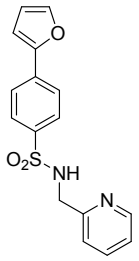
White solid; 162 mg; yield 91%; m.p. 106.5-107.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.46 (d, *J* = 4.2 Hz, 1H), 7.90 (d, *J* = 8.4 Hz, 2H), 7.60 (t, *J* = 9.0 Hz, 3H), 7.41 – 7.29 (m, 2H), 7.17 (dd, *J* = 13.8, 7.8 Hz, 2H), 7.09 (t, *J* = 9.0 Hz, 1H), 5.97 (s, 1H), 4.30 (d, *J* = 5.4 Hz, 2H), 2.35 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 162.41, 160.77, 154.73, 148.98, 144.58, 137.98, 136.80, 135.07, 130.38, 130.34, 127.63, 127.36, 126.19, 126.13, 125.55, 125.44, 122.60, 122.02, 115.62, 115.47, 77.21, 77.00, 76.79, 47.42, 14.67. IR (neat): υ max = 3440, 3067, 2860, 1596, 1483, 1438, 1385, 1323, 1230, 1154, 1119, 1095, 1006, 889, 818, 755, 716, 641, 577, 522 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{19}H_{18}FN_2O_2S$: 357.1073 ; found: 357.1054.

***N*-(pyridin-2-ylmethyl)-[1,1':4',1''-terphenyl]-4-sulfonamide(3au)**



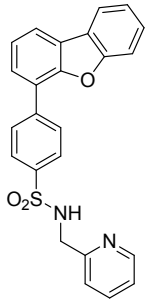
White solid; 185 mg; yield 92%; m.p. 191.4-192.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.47 (d, *J* = 4.2 Hz, 1H), 7.93 (d, *J* = 8.4 Hz, 2H), 7.70 (t, *J* = 6.6 Hz, 4H), 7.68 – 7.60 (m, 5H), 7.48 (t, *J* = 7.8 Hz, 2H), 7.40 (d, *J* = 7.2 Hz, 1H), 7.25 – 7.14 (m, 2H), 6.03 (s, 1H), 4.33 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, DMSO) (δ ppm): 157.09, 148.73, 143.29, 140.14, 139.34, 137.48, 136.70, 129.05, 127.78, 127.61, 127.36, 127.28, 127.19, 126.68, 122.38, 121.70, 48.04, 39.92, 39.78, 39.64, 39.50, 39.36, 39.22, 39.08. IR (neat): υ max = 3439, 3290, 3056, 1593, 1479, 1431, 1394, 1328, 1160, 1095, 1050, 870, 796, 729, 591, 511 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{21}N_2O_2S$: 401.1324 ; found: 401.1302.

4-(furan-2-yl)-*N*-(pyridin-2-ylmethyl)benzenesulfonamide(3av)



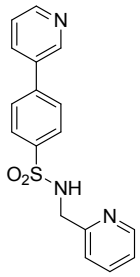
White solid; 146 mg; yield 93%; m.p. 131.4-132.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.45 (d, *J* = 4.2 Hz, 1H), 7.86 (d, *J* = 8.4 Hz, 2H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.59 (d, *J* = 7.8 Hz, 1H), 7.52 (s, 1H), 7.16 (t, *J* = 9.0 Hz, 2H), 6.78 (d, *J* = 3.6 Hz, 1H), 6.52 (s, 1H), 5.98 (s, 1H), 4.28 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.74, 152.02, 148.88, 143.36, 137.55, 136.83, 134.40, 127.62, 123.74, 122.62, 122.04, 112.06, 107.64, 77.32, 77.00, 76.68, 47.38. IR (neat): υ max = 3446, 3027, 2823, 2701, 1598, 1474, 1440, 1325, 1112, 1087, 1007, 837, 739, 603, 566, 533 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{16}H_{15}N_2O_3S$: 315.0803 ; found: 315.0793.

4-(dibenzo[b,d]furan-4-yl)-*N*-(pyridin-2-ylmethyl)benzenesulfonamide(3aw)



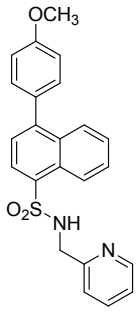
White solid; 197 mg; yield 95%; m.p. 148.4-149.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.48 (s, 1H), 8.00 (s, 6H), 7.60 (d, *J* = 7.8 Hz, 2H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 1H), 7.45 (t, *J* = 7.2 Hz, 1H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 7.16 (s, 1H), 6.10 (s, 1H), 4.36 (d, *J* = 4.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 156.02, 153.12, 148.94, 140.69, 138.56, 136.83, 129.16, 127.50, 127.43, 126.69, 125.15, 123.82, 123.31, 123.01, 122.62, 122.07, 120.81, 120.75, 111.73, 77.32, 77.00, 76.68, 47.53. IR (neat): υ max = 3445, 3144, 2858, 1594, 1474, 1449, 1426, 1390, 1327, 1165, 1095, 1070, 999, 837, 795, 754, 683, 593, 525 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{19}N_2O_3S$: 415.1116 ; found: 415.1100.

***N*-(pyridin-2-ylmethyl)-4-(pyridin-3-yl)benzenesulfonamide(3ax)**



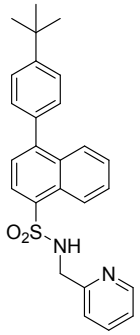
White solid; 145 mg; yield 89%; m.p. 143.4-144.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.84 (s, 1H), 8.67 (d, *J* = 4.2 Hz, 1H), 8.48 (d, *J* = 4.8 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 7.8 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.46 (dd, *J* = 7.8, 4.8 Hz, 1H), 7.28 (d, *J* = 7.8 Hz, 1H), 7.25 – 7.20 (m, 1H), 6.33 (s, 1H), 4.37 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 155.01, 149.14, 148.71, 147.89, 141.60, 139.31, 136.79, 134.79, 134.52, 127.70, 127.46, 123.69, 122.49, 122.07, 77.21, 77.00, 76.79, 47.51, 30.81. IR (neat): υ max = 3070, 2859, 1589, 1467, 1430, 1332, 1164, 1095, 1048, 1000, 849, 797, 690, 594, 569, 527 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{17}H_{16}N_3O_2S$: 326.0963 ; found: 326.0949.

4-(4-methoxyphenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3bb)



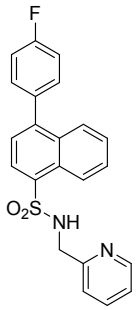
White solid; 189 mg; yield 93%; m.p. 151.4-152.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.76 (d, *J* = 8.4 Hz, 1H), 8.27 (d, *J* = 7.8 Hz, 2H), 7.94 (d, *J* = 8.4 Hz, 1H), 7.66 (t, *J* = 7.8 Hz, 1H), 7.53 – 7.43 (m, 2H), 7.37 (dd, *J* = 24.0, 7.8 Hz, 3H), 7.04 (t, *J* = 9.6 Hz, 4H), 6.28 (s, 1H), 4.26 (d, *J* = 5.4 Hz, 2H), 3.91 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 159.42, 154.74, 148.59, 145.92, 136.33, 133.27, 132.48, 131.60, 130.84, 129.00, 128.55, 127.78, 127.14, 126.54, 124.92, 122.23, 121.80, 113.82, 77.21, 77.00, 76.79, 55.32, 47.58. IR (neat): υ max = 3439, 3094, 2986, 2836, 1605, 1504, 1441, 1379, 1325, 1245, 1155, 1135, 1065, 1030, 900, 824, 761, 692, 640, 574, 518 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{21}N_2O_3S$: 405.1273 ; found: 405.1251.

4-(4-(tert-butyl)phenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3bc)



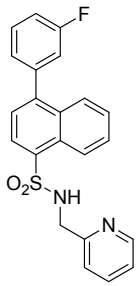
White solid; 205 mg; yield 95%; m.p. 146.3-146.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.75 (d, *J* = 9.0 Hz, 1H), 8.28 (d, *J* = 7.8 Hz, 1H), 8.25 (s, 1H), 7.95 (d, *J* = 8.4 Hz, 1H), 7.66 (t, *J* = 7.2 Hz, 1H), 7.57 – 7.43 (m, 4H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 8.4 Hz, 2H), 7.02 (d, *J* = 7.2 Hz, 2H), 6.26 (s, 1H), 4.27 (d, *J* = 5.4 Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.68, 151.01, 148.64, 146.27, 136.33, 133.33, 132.42, 129.40, 129.04, 128.51, 127.83, 127.30, 126.55, 125.32, 124.96, 124.61, 122.25, 121.81, 77.32, 77.00, 76.68, 47.61, 34.65, 31.33. IR (neat): υ max = 3081, 2960, 2862, 1592, 1504, 1442, 1324, 1132, 1152, 1074, 902, 833, 761,676, 626, 531 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{26}H_{27}N_2O_2S$: 431.1793 ; found: 431.1777.

4-(4-fluorophenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3bd)



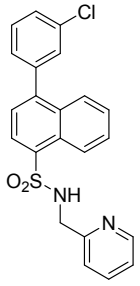
White solid; 179 mg; yield 91%; m.p. 144.5-145.2 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.77 (d, *J* = 8.4 Hz, 1H), 8.27 (t, *J* = 7.2 Hz, 2H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.67 (t, *J* = 7.8 Hz, 1H), 7.61 – 7.41 (m, 3H), 7.41 – 7.33 (m, 3H), 7.20 (t, *J* = 8.4 Hz, 2H), 7.04 (d, *J* = 7.8 Hz, 2H), 6.28 (s, 1H), 4.27 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 163.32, 161.68, 154.77, 148.63, 144.95, 136.36, 135.24, 133.99, 132.32, 131.30, 131.25, 128.78, 128.46, 127.88, 126.79, 125.04, 122.25, 121.85, 115.46, 115.32, 77.21, 77.00, 76.79, 47.57. IR (neat): υ max = 3083, 2854, 1597, 1504, 1440, 1380, 1219, 1156, 1134, 1095, 1068, 1005, 901, 832, 762, 688, 640, 570, 514 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{18}FN_2O_2S$: 393.1073 ; found: 393.1062.

4-(3-fluorophenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3be)



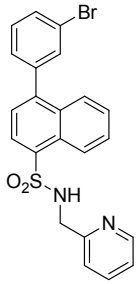
White solid; 181 mg; yield 92%; m.p. 156.6-157.3 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.78 (d, *J* = 9.0 Hz, 1H), 8.28 (dd, *J* = 17.4, 6.0 Hz, 2H), 7.86 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.56 – 7.42 (m, 3H), 7.41 (d, *J* = 7.8 Hz, 1H), 7.19 (t, *J* = 9.6 Hz, 2H), 7.13 (d, *J* = 9.0 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 2H), 6.26 (s, 1H), 4.28 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 163.34, 161.70, 154.61, 148.67, 144.68, 141.50, 141.45, 136.39, 134.26, 132.14, 130.05, 130.00, 128.81, 128.51, 128.05, 126.96, 126.79, 125.49, 124.96, 122.32, 121.80, 116.80, 116.65, 115.04, 114.90, 77.21, 77.00, 76.79, 47.57. IR (neat): υ max = 3440, 3069, 2986, 2834, 1581, 1479, 1434, 1378, 1324, 1260, 1197, 1148, 1074, 1001, 940, 829, 790, 755, 663, 512 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{18}FN_2O_2S$: 393.1073 ; found: 393.1053.

4-(3-chlorophenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3bh)



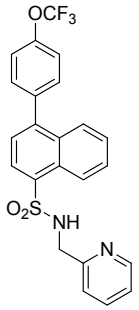
White solid; 191 mg; yield 93%; m.p. 81.1-82.0 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.78 (d, *J* = 8.4 Hz, 1H), 8.28 (dd, *J* = 14.4, 6.0 Hz, 2H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 7.2 Hz, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.51 – 7.43 (m, 3H), 7.42 – 7.37 (m, 2H), 7.30 (d, *J* = 6.6 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 2H), 6.33 (s, 1H), 4.28 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.66, 148.66, 144.43, 141.07, 136.39, 134.25, 132.07, 129.68, 129.59, 128.73, 128.43, 128.01, 127.88, 126.96, 126.70, 124.98, 124.79, 122.29, 121.84, 77.32, 77.00, 76.68, 47.54. IR (neat): υ max = 3090, 2854, 1587, 1473, 1440, 1373, 1325, 1197, 1155, 1074, 994, 918, 844, 799, 754, 665, 617, 581, 512, 434 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{18}ClN_2O_2S$: 409.0778 ; found: 409.0750.

4-(3-bromophenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3bj)



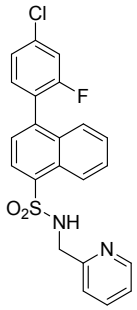
White solid; 119 mg; yield 52%; m.p. 148.1-148.9 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.78 (d, *J* = 8.4 Hz, 1H), 8.34 – 8.20 (m, 2H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.69 (t, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 7.56 (s, 1H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.42 – 7.37 (m, 2H), 7.34 (d, *J* = 7.8 Hz, 1H), 7.04 (s, 2H), 6.33 (s, 1H), 4.27 (d, *J* = 4.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.60, 148.69, 144.37, 141.38, 136.39, 134.31, 132.47, 132.11, 131.06, 129.95, 128.77, 128.47, 128.35, 128.06, 127.01, 126.73, 125.03, 124.81, 122.45, 122.31, 121.81, 77.32, 77.00, 76.68, 47.54. IR (neat): υ max = 3075, 2848, 1590, 1559, 1511, 1473, 1441, 1326, 1203, 1156, 1072, 995, 914, 830, 798, 760, 674, 618, 586, 513 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{18}BrN_2O_2S$: 453.0272 ; found: 453.0257.

***N*-(pyridin-2-ylmethyl)-4-(4-(trifluoromethoxy)phenyl)naphthalene-1-sulfonamide(3bm)**



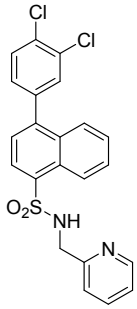
White solid; 209 mg; yield 91%; m.p. 138.6-139.4 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.79 (d, *J* = 8.4 Hz, 1H), 8.32 – 8.19 (m, 2H), 7.83 (d, *J* = 8.4 Hz, 1H), 7.70 (t, *J* = 7.8 Hz, 1H), 7.53 (dd, *J* = 13.8, 7.2 Hz, 2H), 7.45 (d, *J* = 8.4 Hz, 2H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 7.8 Hz, 2H), 7.07 (t, *J* = 7.2 Hz, 2H), 6.33 (s, 1H), 4.30 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) (δ ppm): 154.69, 149.06, 144.62, 138.06, 136.46, 134.35, 132.30, 131.14, 128.81, 128.61, 128.09, 127.00, 126.77, 125.13, 124.91, 122.36, 121.83, 120.90, 77.32, 77.00, 76.68, 47.58. IR (neat): υ max = 3086, 2850, 1595, 1503, 1443, 1381, 1329, 1252, 1159, 1070, 1015, 900, 84l, 762, 671, 617, 593, 531, 510 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{18}F_3N_2O_3S$: 459.0990 ; found: 459.0971.

4-(4-chloro-2-fluorophenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3bq)



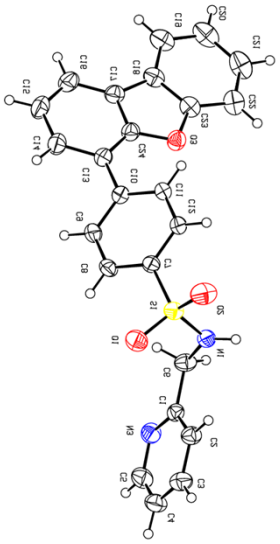
White solid; 193 mg; yield 90%; m.p. 168.2-169.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.76 (d, *J* = 9.0 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 1H), 8.23 (d, *J* = 4.8 Hz, 1H), 7.68 (t, *J* = 7.8 Hz, 1H), 7.62 (d, *J* = 8.4 Hz, 1H), 7.53 (d, *J* = 7.8 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 1H), 7.40 (d, *J* = 7.8 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.00 (dd, *J* = 12.0, 7.2 Hz, 2H), 6.33 (s, 1H), 4.29 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 160.27, 158.61, 154.52, 148.68, 138.73, 136.41, 135.28, 135.21, 135.10, 132.51, 132.37, 128.62, 128.27, 128.12, 127.09, 126.47, 125.86, 125.41, 125.30, 124.77, 124.75, 122.36, 121.76, 116.76, 116.59, 77.21, 77.00, 76.79, 47.60. IR (neat): υ max = 3086, 2853, 1601, 1569, 1484, 1441, 1403, 1325, 1212, 1130, 1067, 911, 852, 680,65, 510 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{17}ClFN_2O_2S$: 427.0683 ; found: 427.0657.

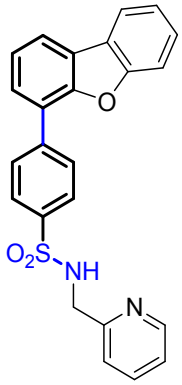
4-(3,4-dichlorophenyl)-*N*-(pyridin-2-ylmethyl)naphthalene-1-sulfonamide(3br)



White solid; 202 mg; yield 91%; m.p. 145.7-146.4 °C; ^{1}H NMR (600 MHz, $CDCl_3$) (δ ppm): 8.80 (d, *J* = 8.4 Hz, 1H), 8.29 (d, *J* = 7.8 Hz, 2H), 7.81 (d, *J* = 8.4 Hz, 1H), 7.71 (t, *J* = 7.8 Hz, 1H), 7.62 – 7.49 (m, 4H), 7.39 (d, *J* = 7.8 Hz, 1H), 7.06 (d, *J* = 7.2 Hz, 2H), 6.28 (s, 1H), 4.28 (d, *J* = 5.4 Hz, 2H). ^{13}C NMR (150 MHz, $CDCl_3$) (δ ppm): 154.55, 148.67, 143.36, 139.29, 136.47, 134.63, 132.66, 132.42, 132.01, 131.43, 130.44, 129.03, 128.72, 128.53, 128.20, 127.20, 126.49, 125.05, 122.36, 121.80, 77.21, 77.00, 76.79, 47.50. IR (neat): υ max = 3081, 2852, 1592, 1471, 1439, 1378, 1325, 1157, 1134, 1072, 1031, 921, 826, 759, 679, 622, 534 cm^{-1}**.** HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{17}Cl_2N_2O_2S$: 443.0388 ; found: 443.0360.

5. Crystallographic data and molecular structure of compounds 3aw

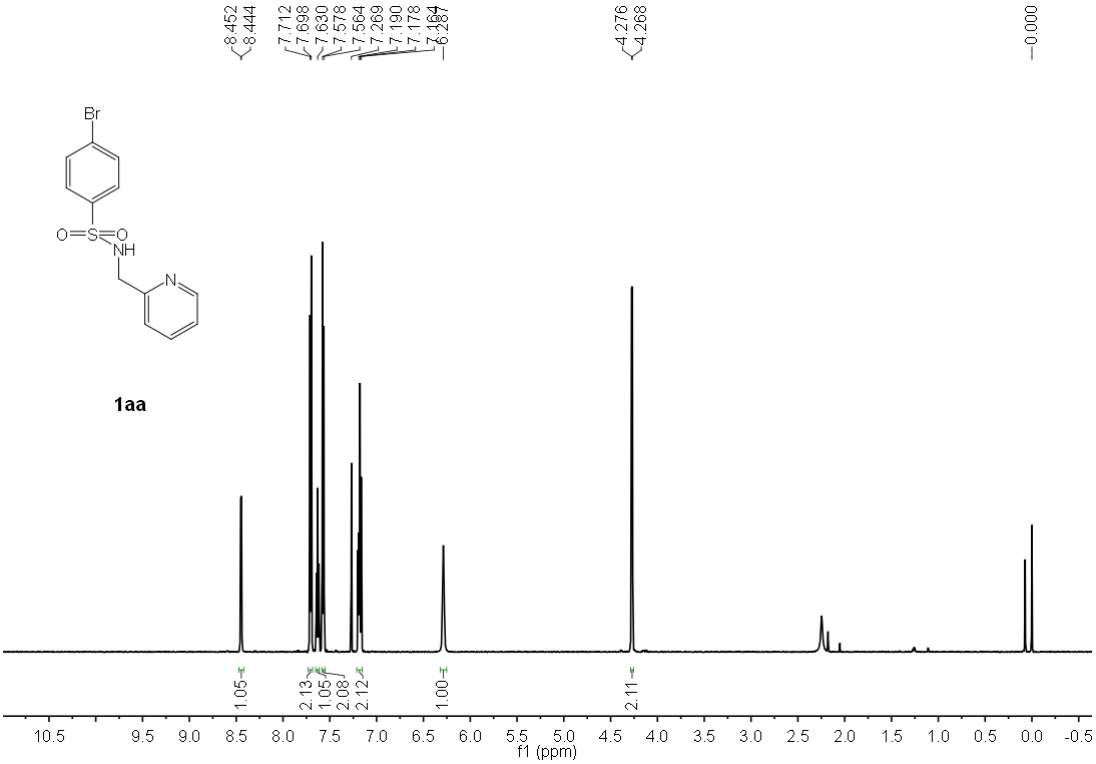


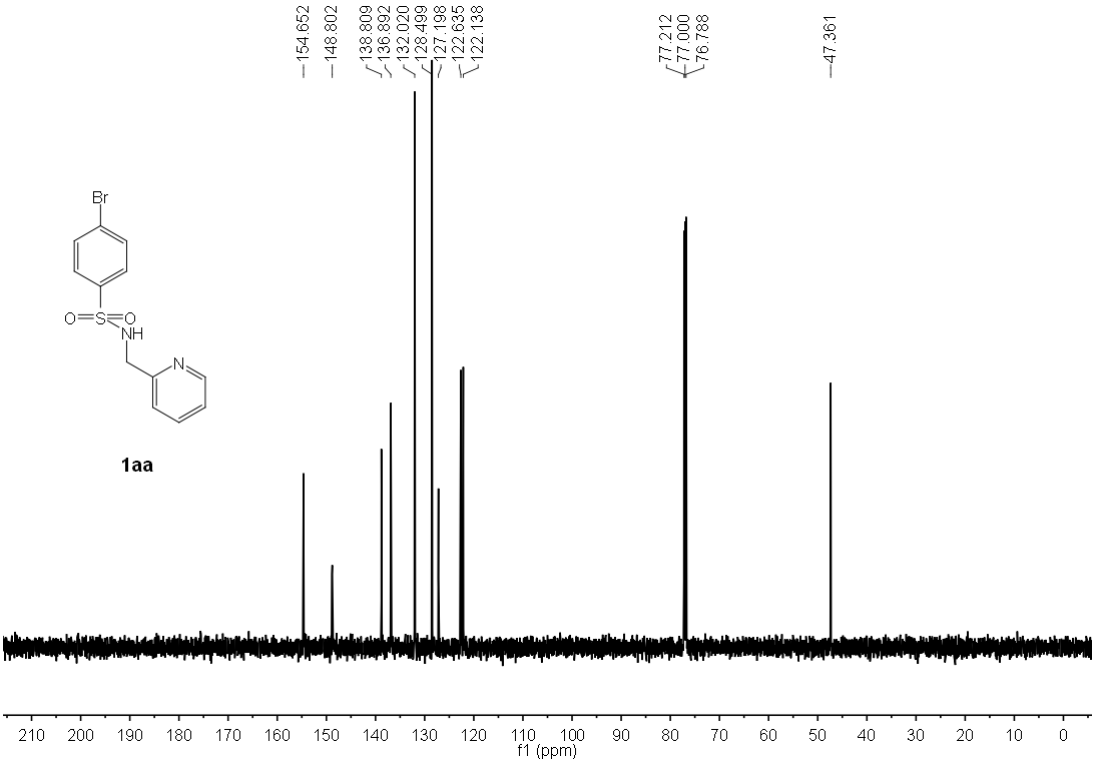


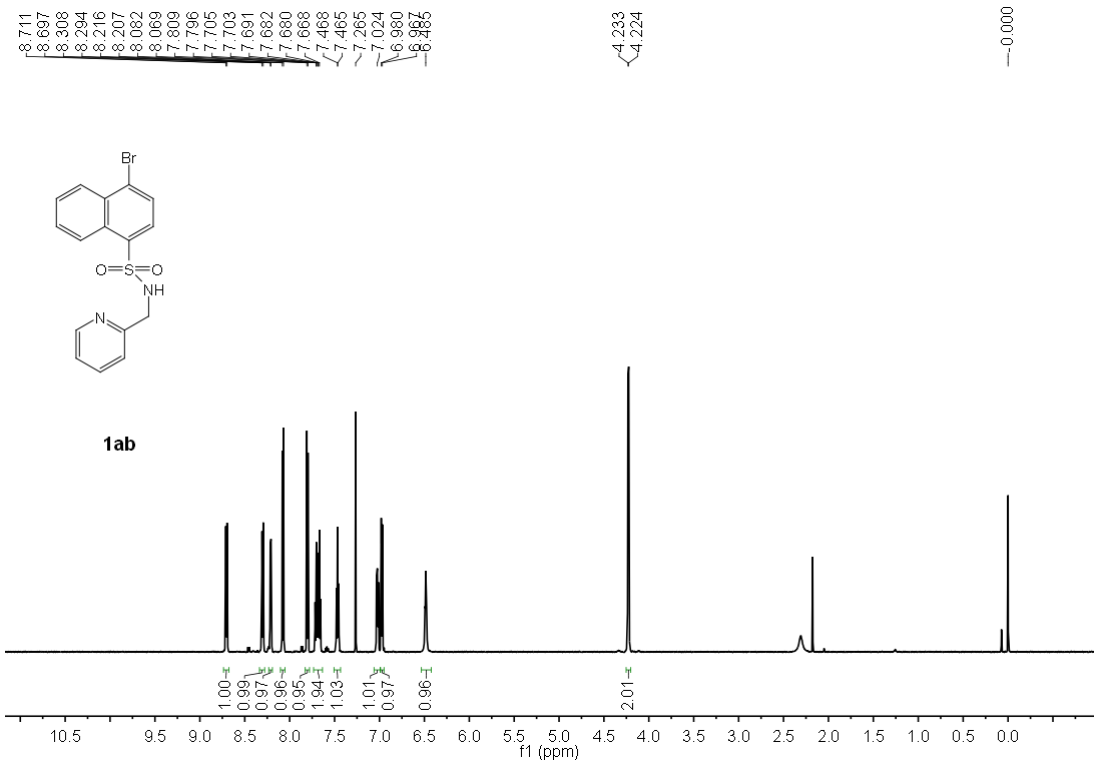
3 aw

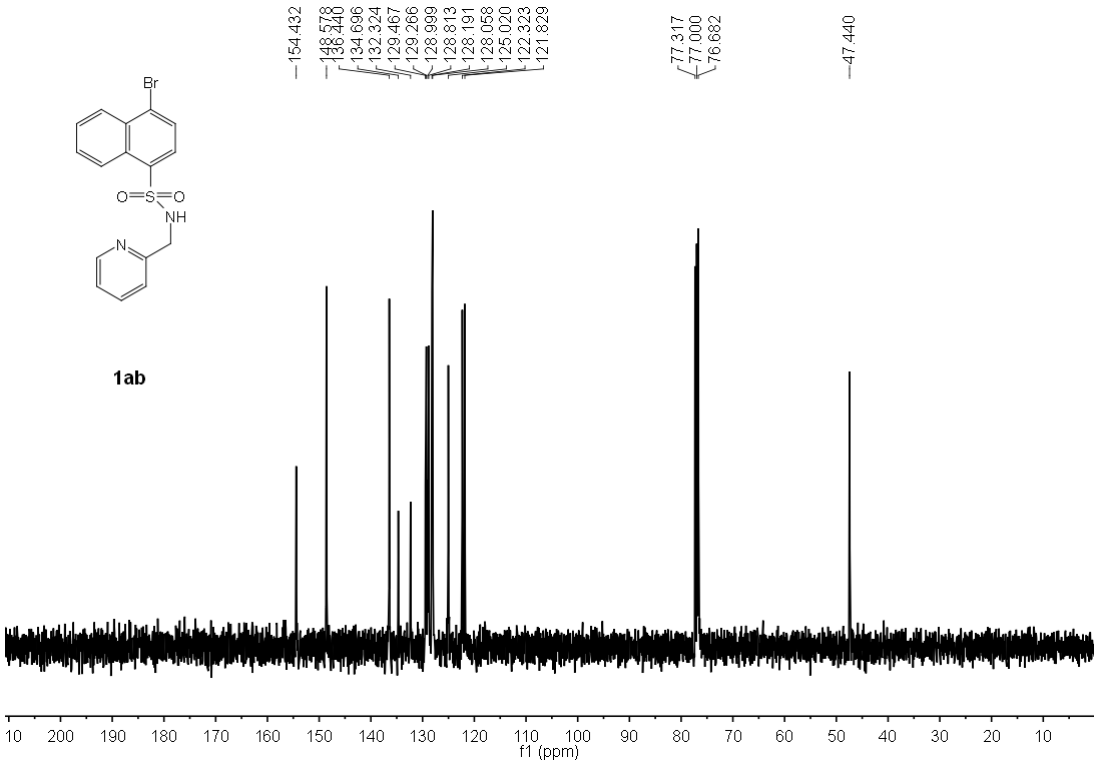
Crystal Data for Compound 3aw: $C_{24}H_{18}N_2O_3S$, MW = 414.46, Orthorhombic, a = 11.3834(14) Å, b = 12.9542(16) Å, c = 26.397(3) Å, α= 90°, β= 90°, γ = 90°, V = 3892.5(8) Å3, T = 298(2) K , space group Pbca, Z = 8, m(Mo–Ka) = 0.196 mm^{-1}, 39995 Reflections collected, 5669 unique [R(int) = 0.0298] which were used in all calculations. The final wR2 (F2) was 0.1213. CCDC 1057970 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.

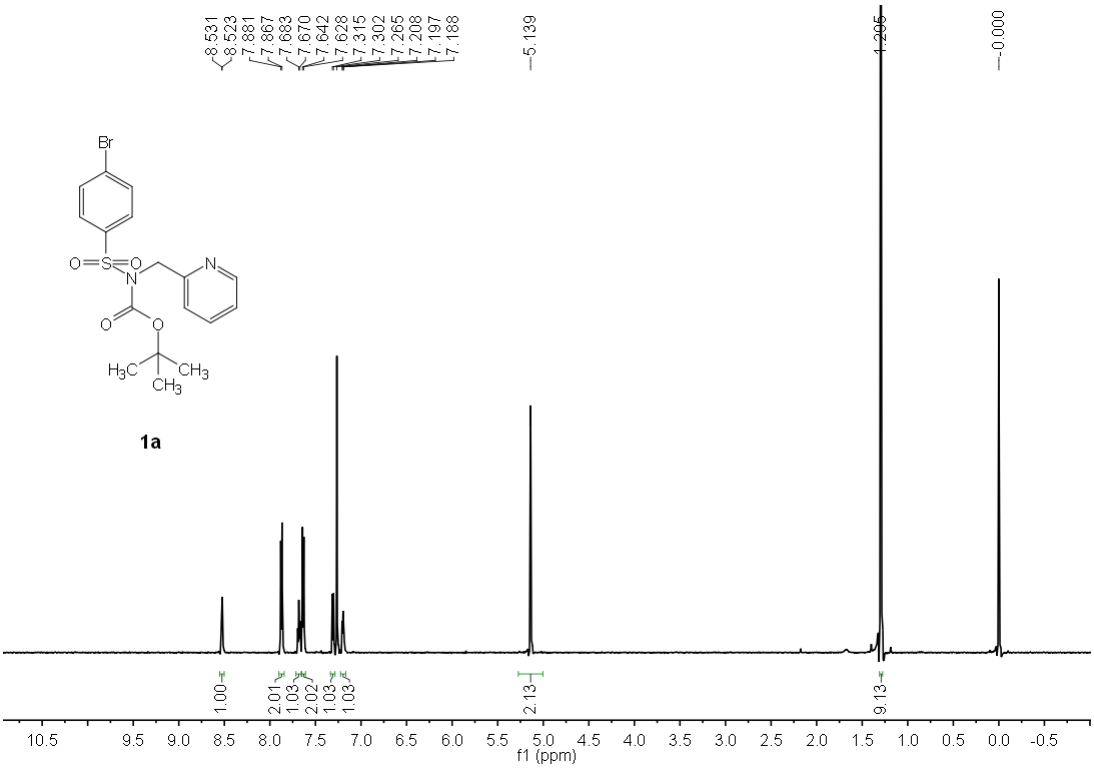
5. Copies of NMR Spectra

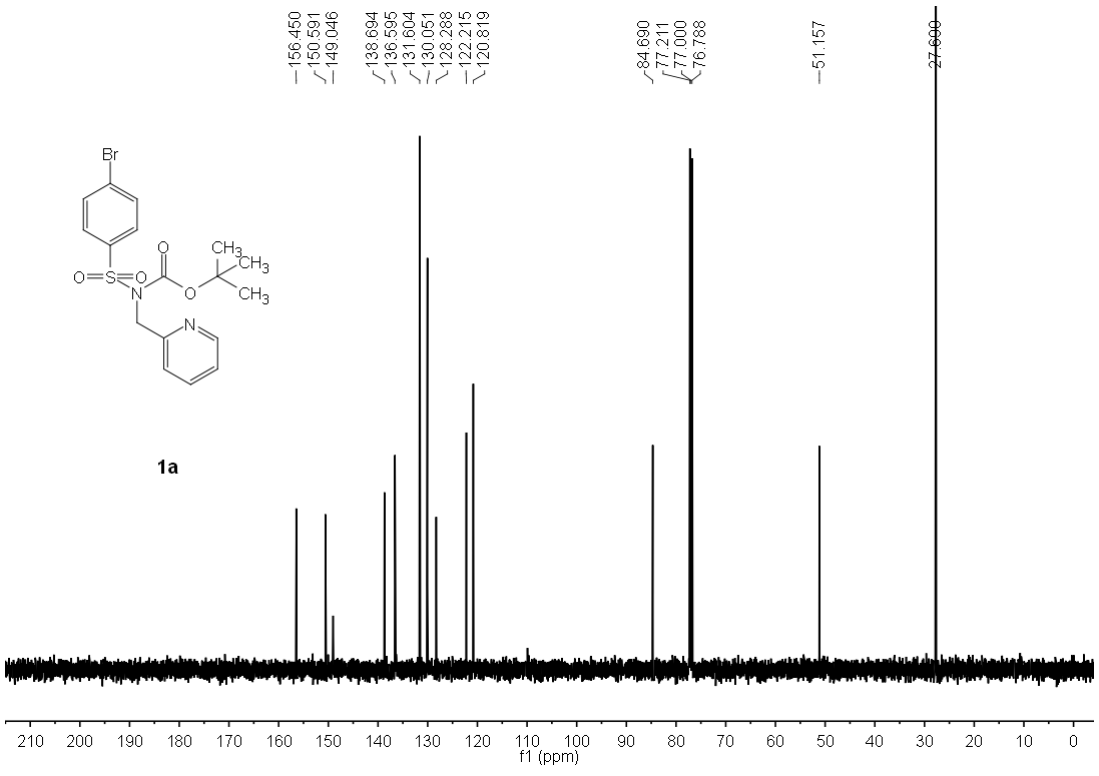


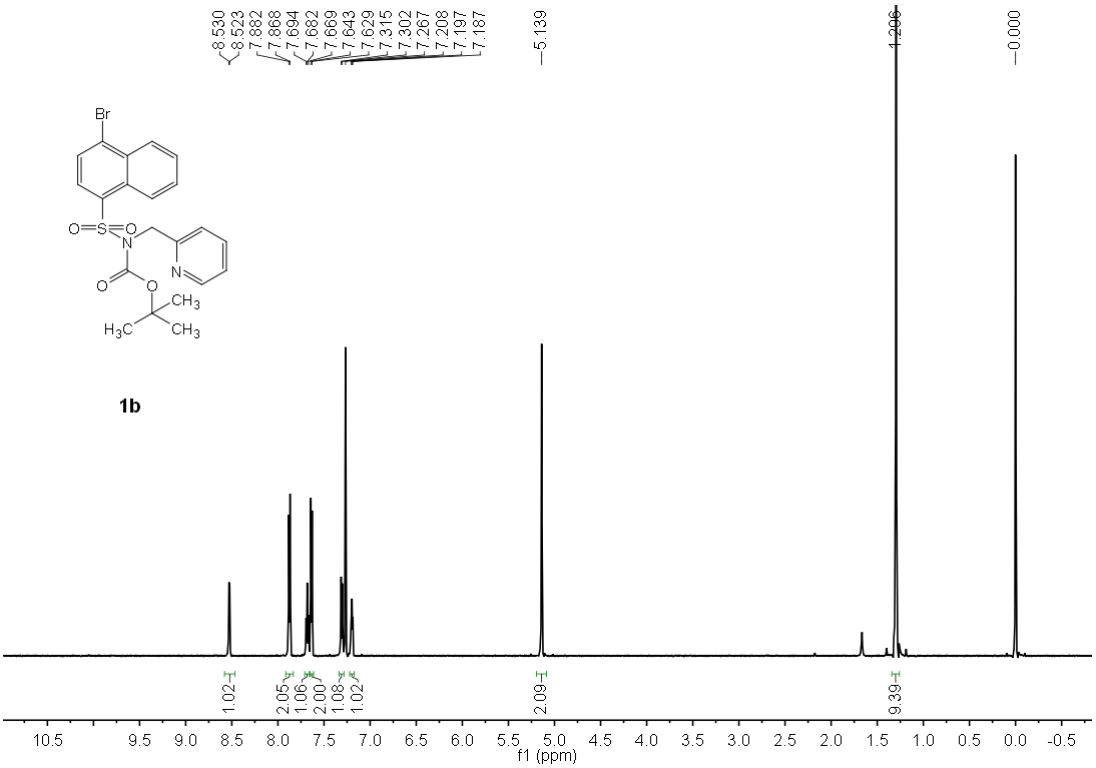



8.711
8.697
8.308
8.294
8.216
8.207
8.082
8.069
7.809
7.796
7.705
7.703
7.691
7.682
7.680
7.668
7.468
7.465
7.265
7.024
6.980
6.967
6.485
4.233
4.224
0.000
Br
O=S=O
NH
N
1ab
1.00
0.99
0.97
0.96
0.95
1.94
1.03
1.01
0.97
0.96
2.01
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


154.432
148.578
138.440
134.696
132.324
129.467
129.266
128.999
128.813
128.191
128.058
125.020
122.323
121.829
77.317
77.000
76.682
47.440
Br
O=S=O
NH
N
1ab
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)


8.531
8.523
7.881
7.867
7.683
7.670
7.642
7.628
7.315
7.302
7.265
7.208
7.197
7.188
5.139
1.205
0.000
Br
O=S=O
N
O
O
H3C
CH3
CH3
1a
1.00
2.01
1.03
2.02
1.03
1.03
2.13
9.13
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


156.450
150.591
149.046
138.694
136.595
131.604
130.051
128.288
122.215
120.819
84.690
77.211
77.000
76.788
51.157
27.600
Br
O=S=O
N
O
O
CH3
CH3
CH3
1a
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)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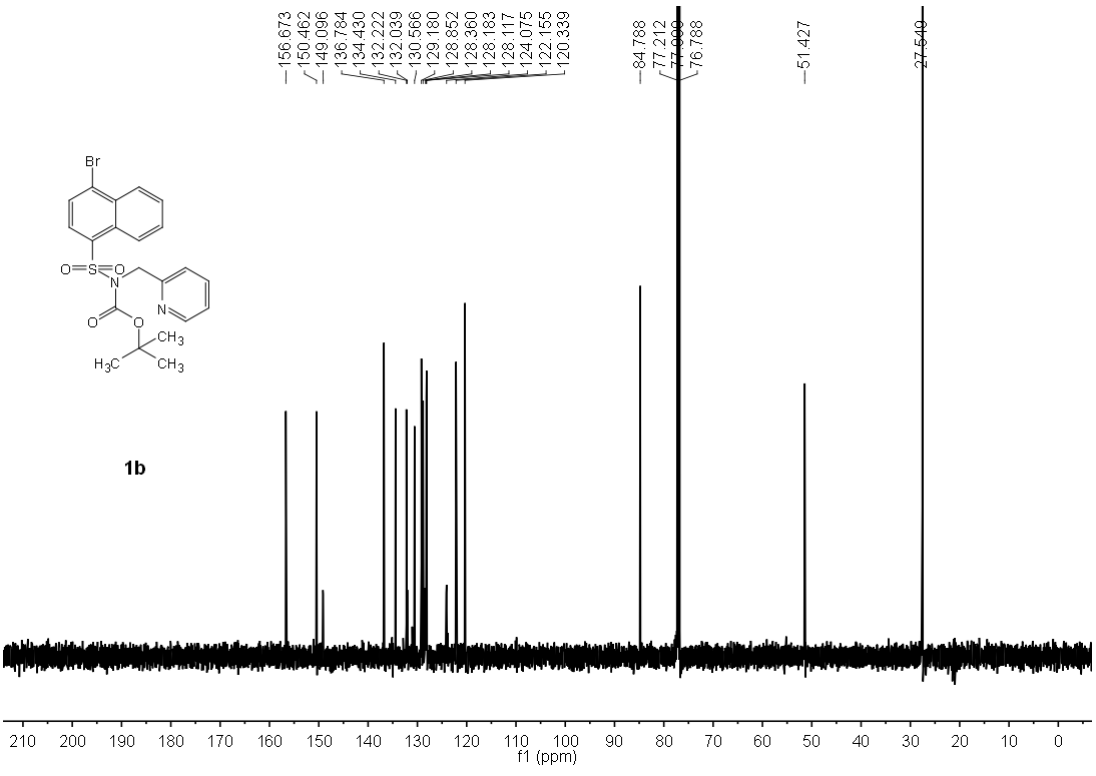
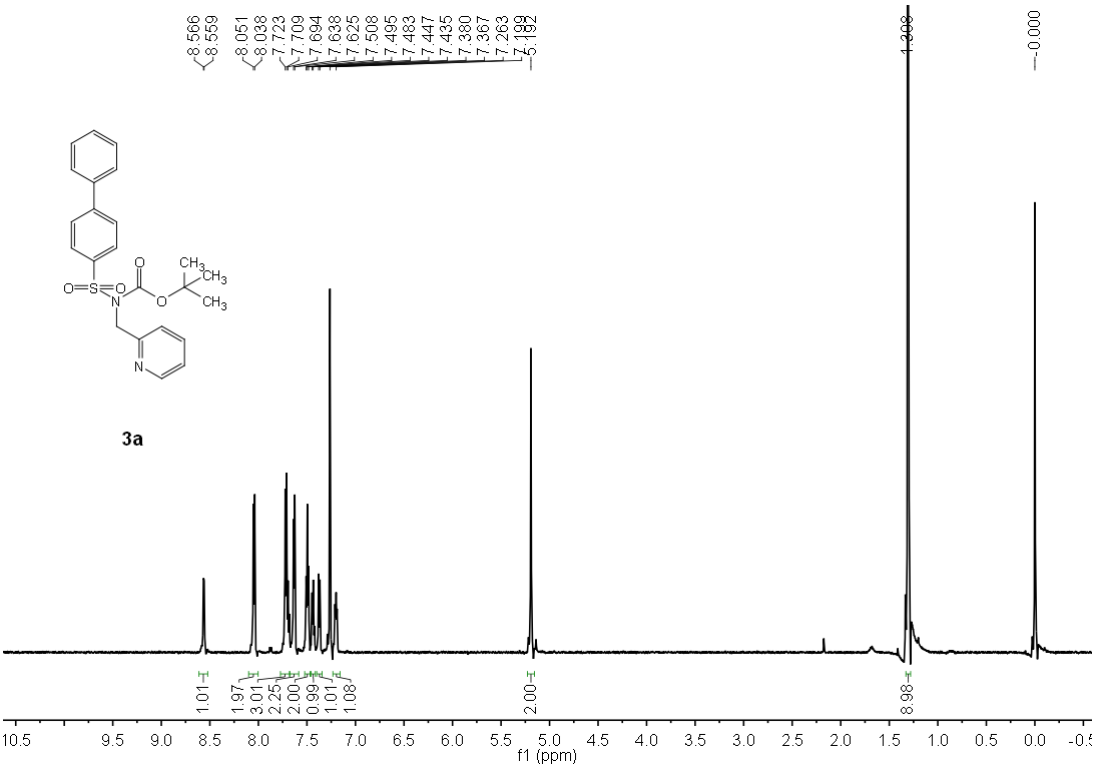
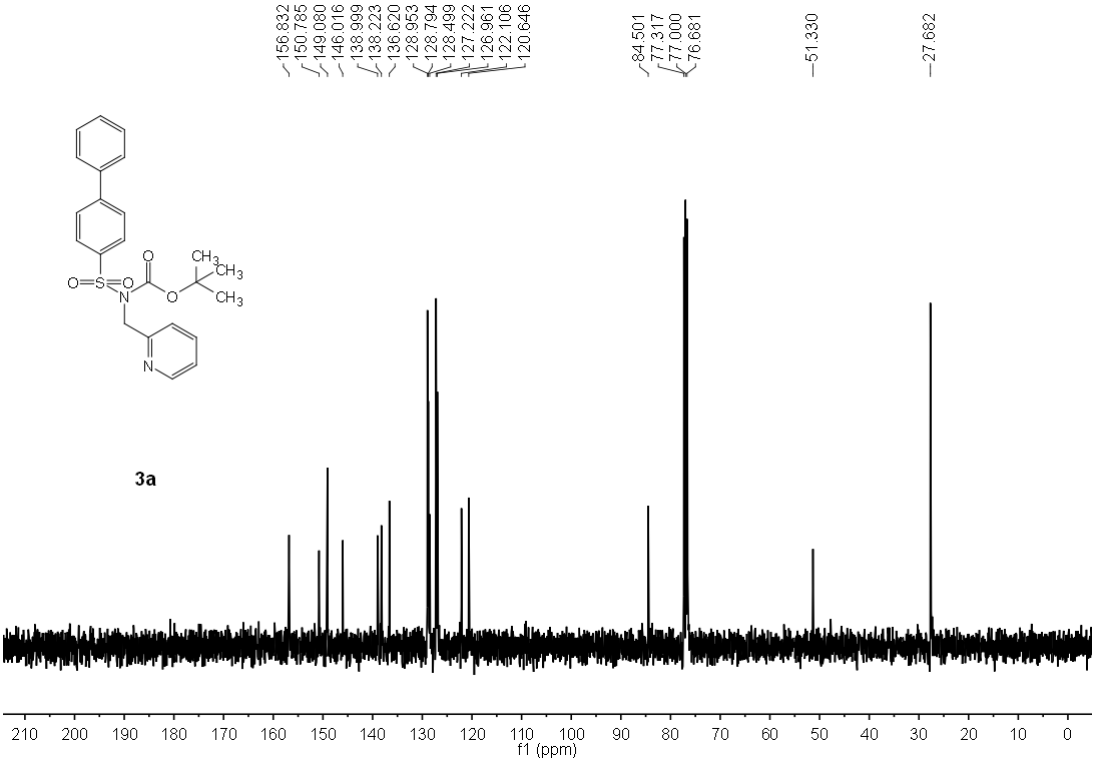
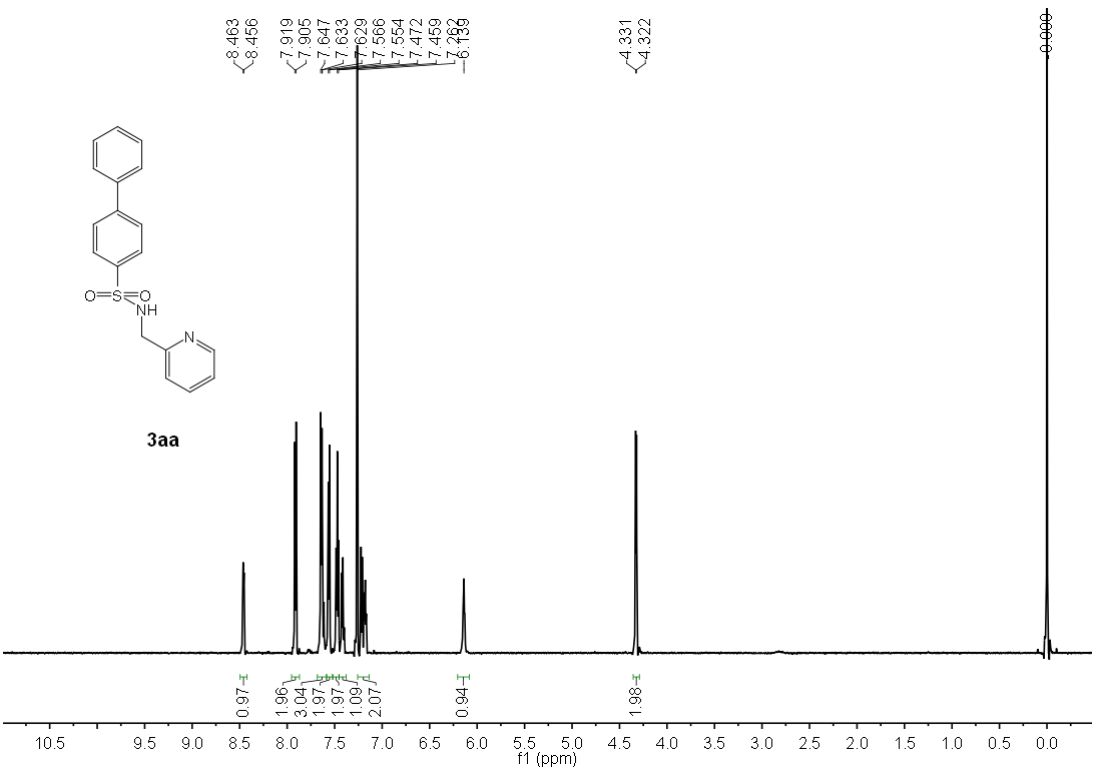
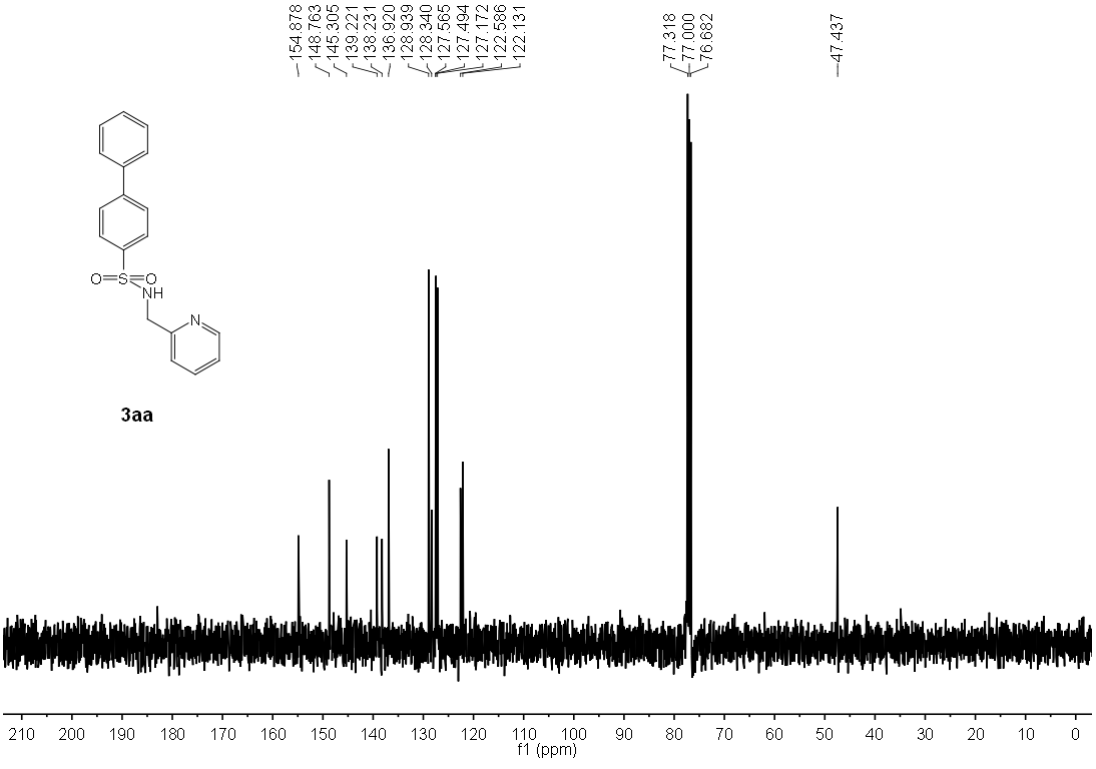
8.523
7.882
7.868
7.694
7.682
7.669
7.643
7.629
7.315
7.302
7.267
7.208
7.197
7.187
5.139
1.296
0.000
Br
O=S=O
N
O
O
N
CH3
H3C
CH3
1b
1.02
2.05
1.06
2.00
1.08
1.02
2.09
9.39
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


156.673
150.462
149.096
136.784
134.430
132.222
132.039
130.566
129.180
128.852
128.360
128.183
128.117
124.075
122.155
120.339
84.788
77.212
77.000
76.788
51.427
27.649
Br
O=S=O
N
O
O
N
CH3
H3C
CH3
1b
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.566
8.559
8.051
8.038
7.723
7.709
7.694
7.638
7.625
7.508
7.495
7.483
7.447
7.435
7.380
7.367
7.263
1.308
0.000
3a
1.01
1.97
3.01
2.25
2.00
0.99
1.01
1.08
2.00
8.98
f1 (ppm)


156.832
150.785
149.080
146.016
138.999
138.223
136.620
128.953
128.794
128.499
127.222
126.961
122.106
120.646
84.501
77.317
77.000
76.681
51.330
27.682
3a
f1 (ppm)


8.463
8.456
7.919
7.905
7.647
7.633
7.629
7.566
7.554
7.472
7.459
4.331
4.322
0.000
O=S=O
NH
N
3aa
0.97
1.96
3.04
1.97
1.97
1.09
2.07
0.94
1.98
f1 (ppm)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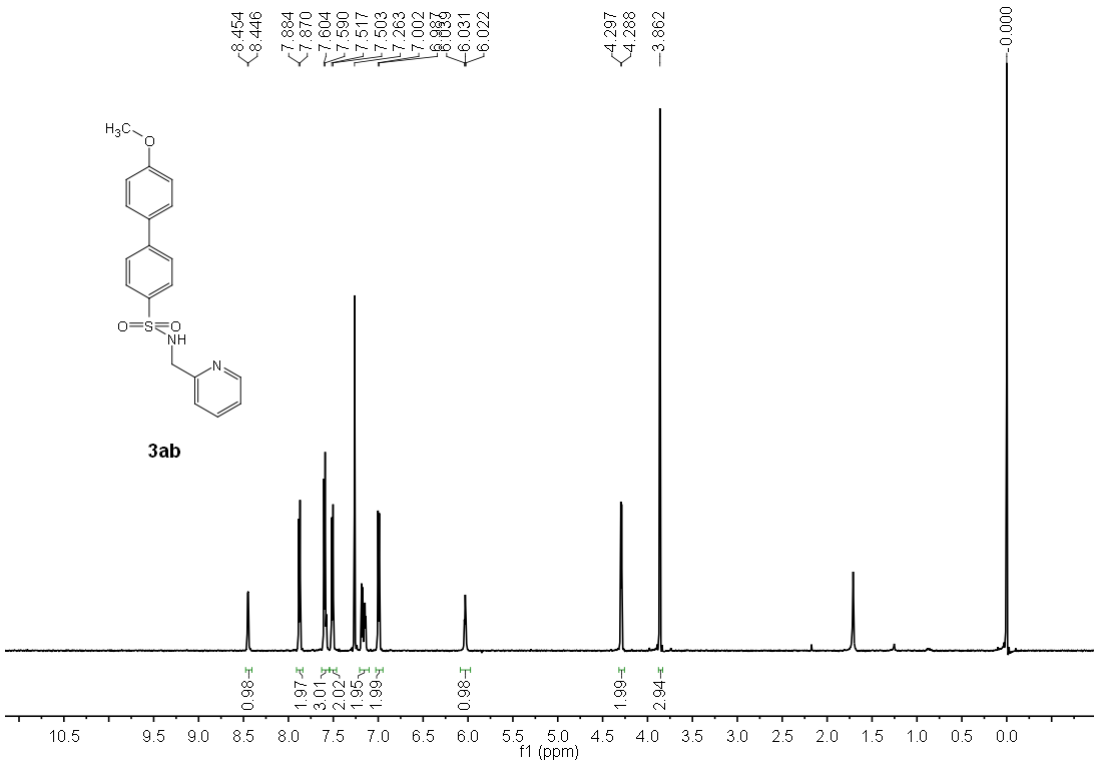
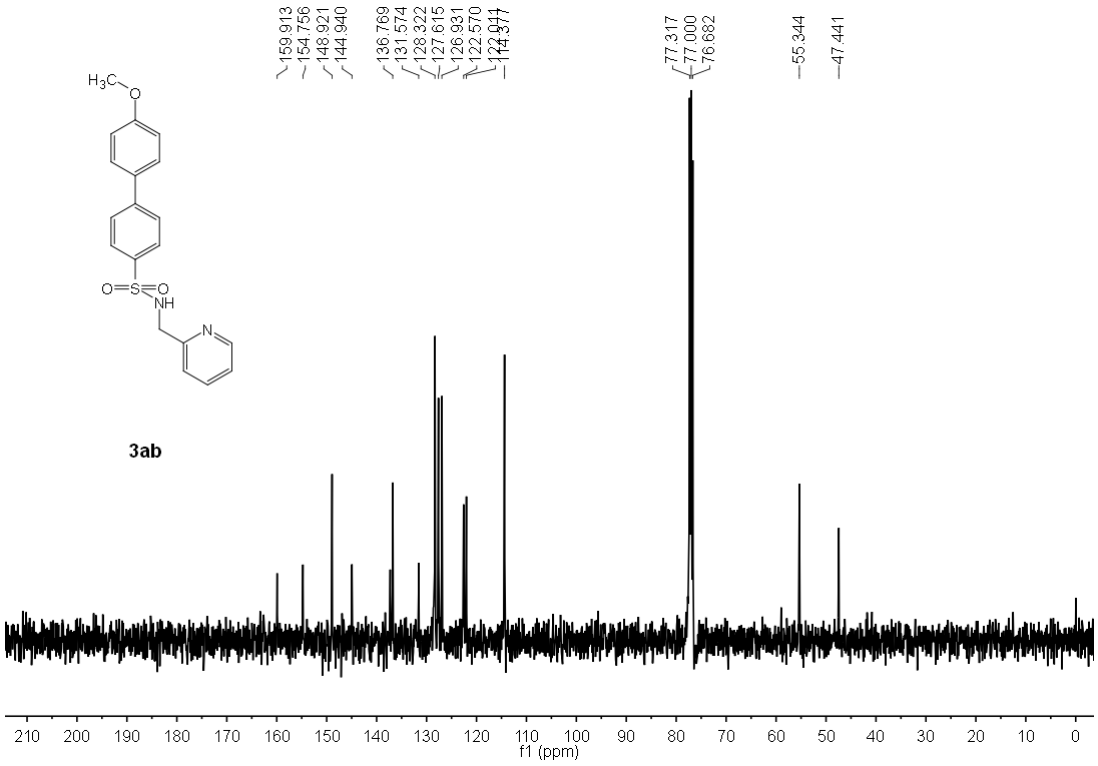
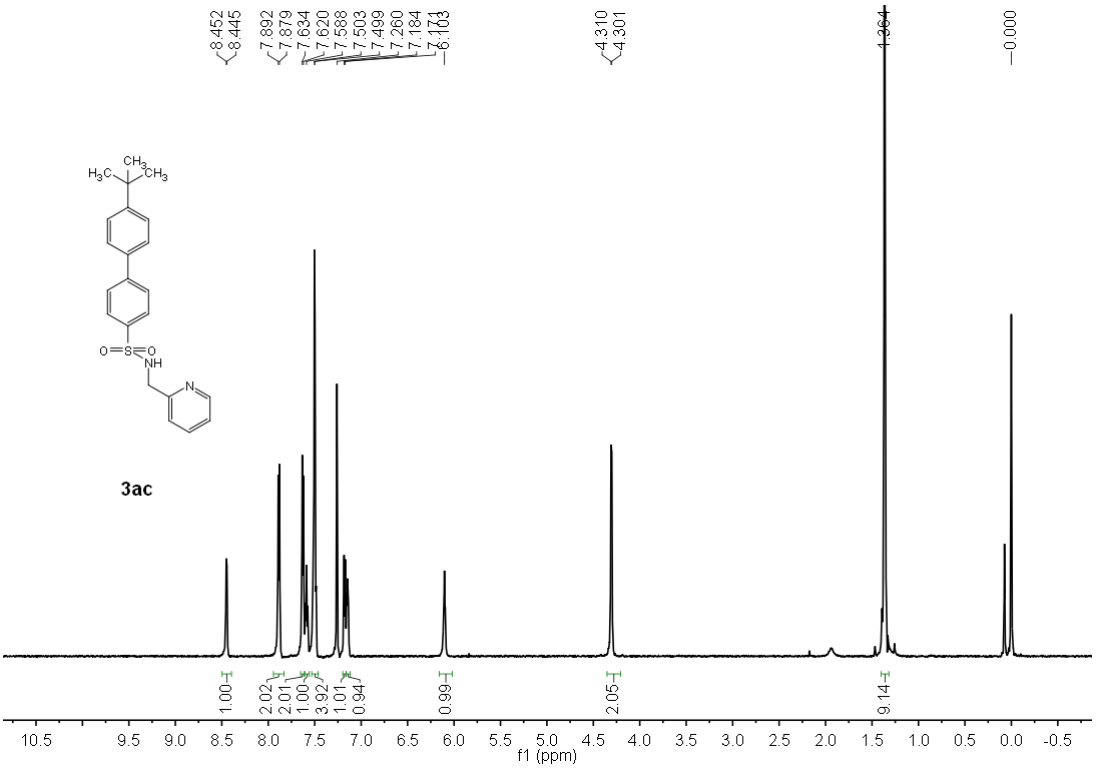
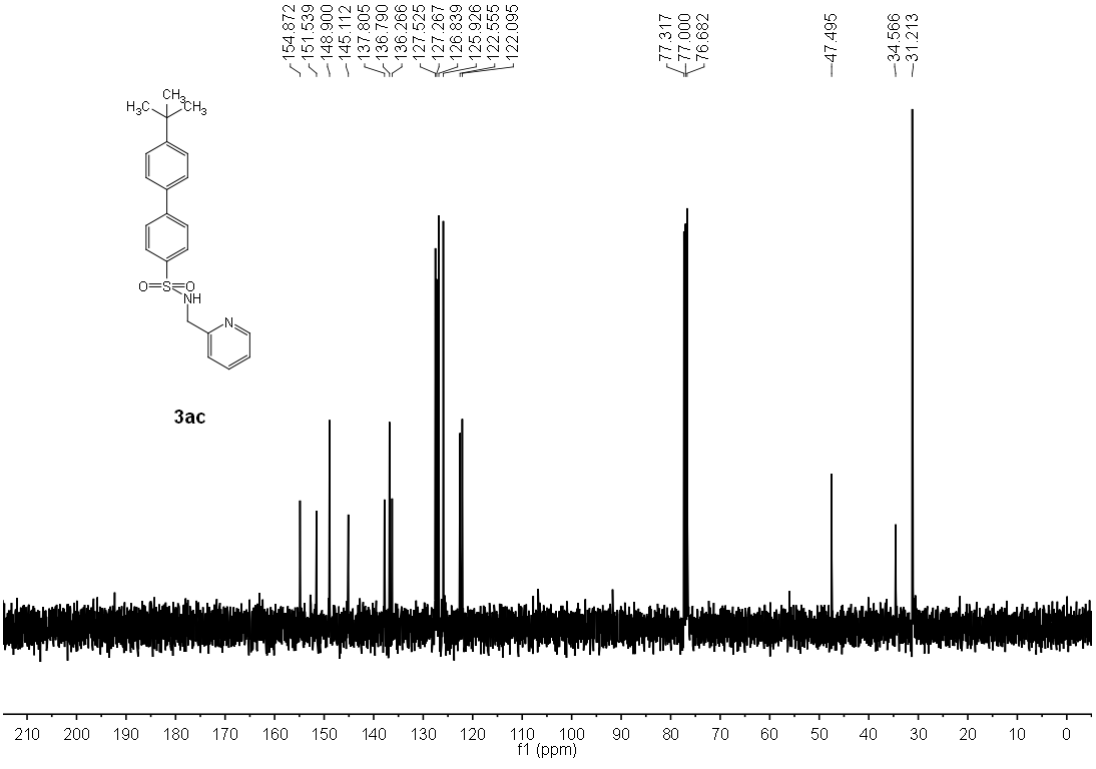
148.763
145.305
139.221
138.231
136.920
128.939
128.340
127.565
127.494
127.172
122.586
122.131
77.318
77.000
76.682
47.437
O=S=O
NH
N
3aa
f1 (ppm)


8.454
8.446
7.884
7.870
7.604
7.590
7.517
7.503
7.263
7.002
6.987
6.039
6.031
6.022
4.297
4.288
3.862
0.000
3ab
0.98
1.97
3.01
2.02
1.95
1.99
0.98
1.99
2.94
f1 (ppm)


159.913
154.756
148.921
144.940
136.769
131.574
128.322
127.615
126.931
122.570
122.011
77.317
77.000
76.682
55.344
47.441
3ab
f1 (ppm)


8.452
8.445
7.892
7.879
7.634
7.620
7.588
7.503
7.499
7.260
7.184
7.171
6.103
4.310
4.301
1.364
0.000
3ac
1.00
2.02
2.01
1.00
3.92
1.01
0.94
0.99
2.05
9.14
f1 (ppm)


154.872
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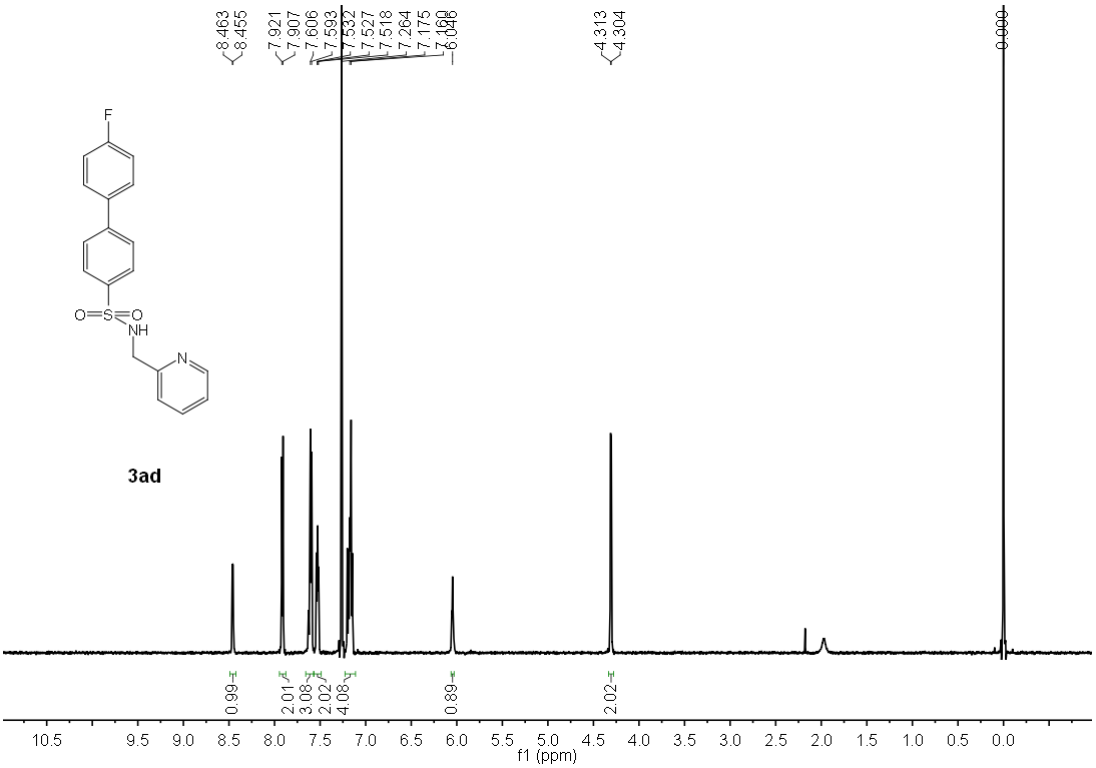
148.900
145.112
137.805
136.790
136.266
127.525
127.267
126.839
125.926
122.555
122.095
77.317
77.000
76.682
47.495
34.566
31.213
3ac
f1 (ppm)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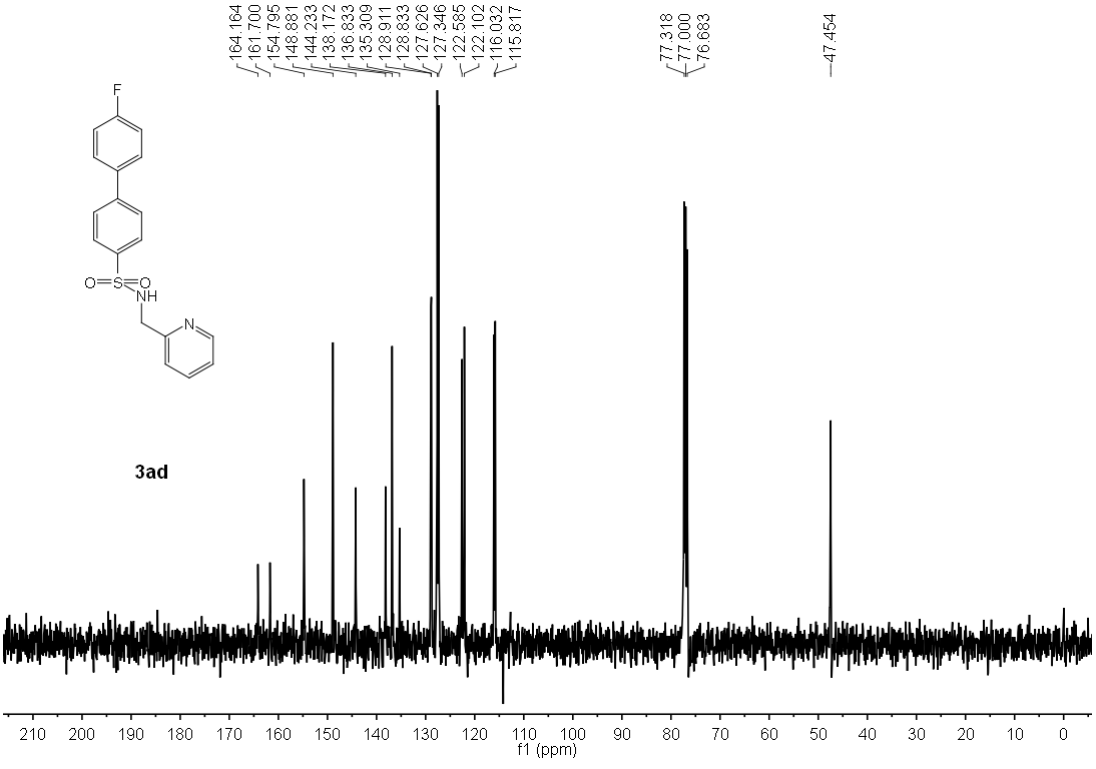
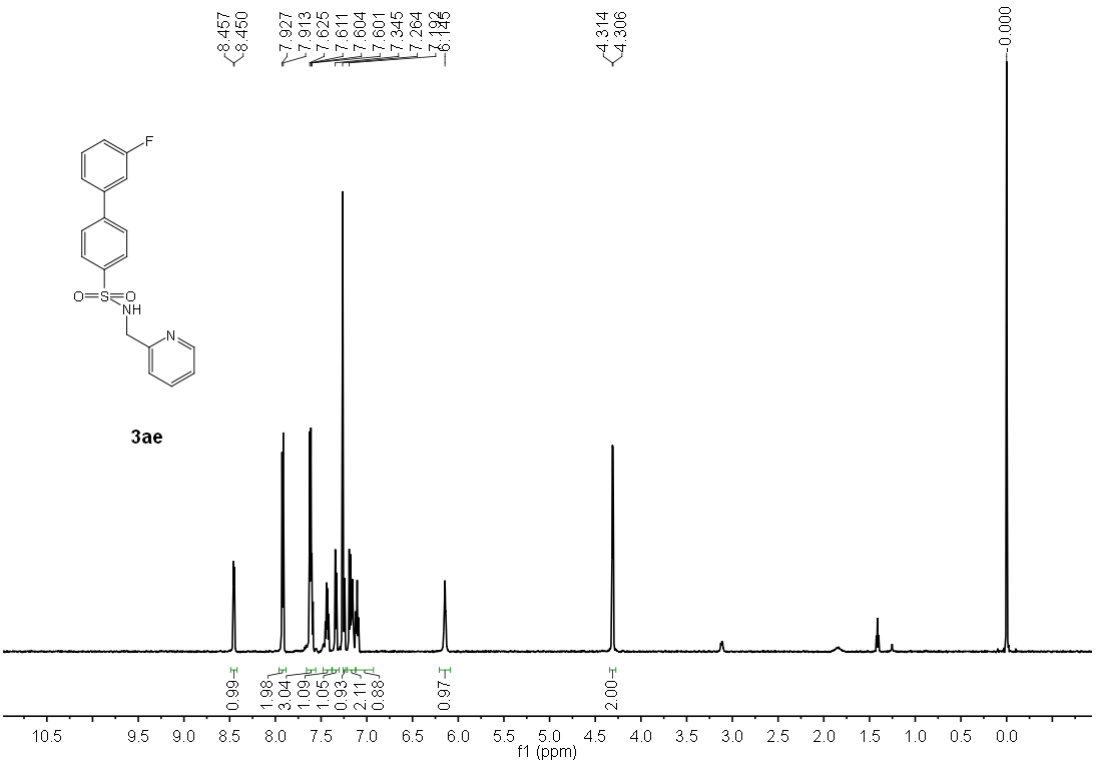
8.455
7.921
7.907
7.606
7.593
7.532
7.527
7.518
7.264
7.175
7.160
6.046
4.313
4.304
0.000
F
O=S=O
NH
N
3ad
0.99
2.01
3.08
2.02
4.08
0.89
2.02
f1 (ppm)


164.164
161.700
154.795
148.881
144.233
138.172
136.833
135.309
128.911
128.833
127.626
127.346
122.585
122.102
116.032
115.817
77.318
77.000
76.683
47.454
F
O=S=O
NH
N
3ad
f1 (ppm)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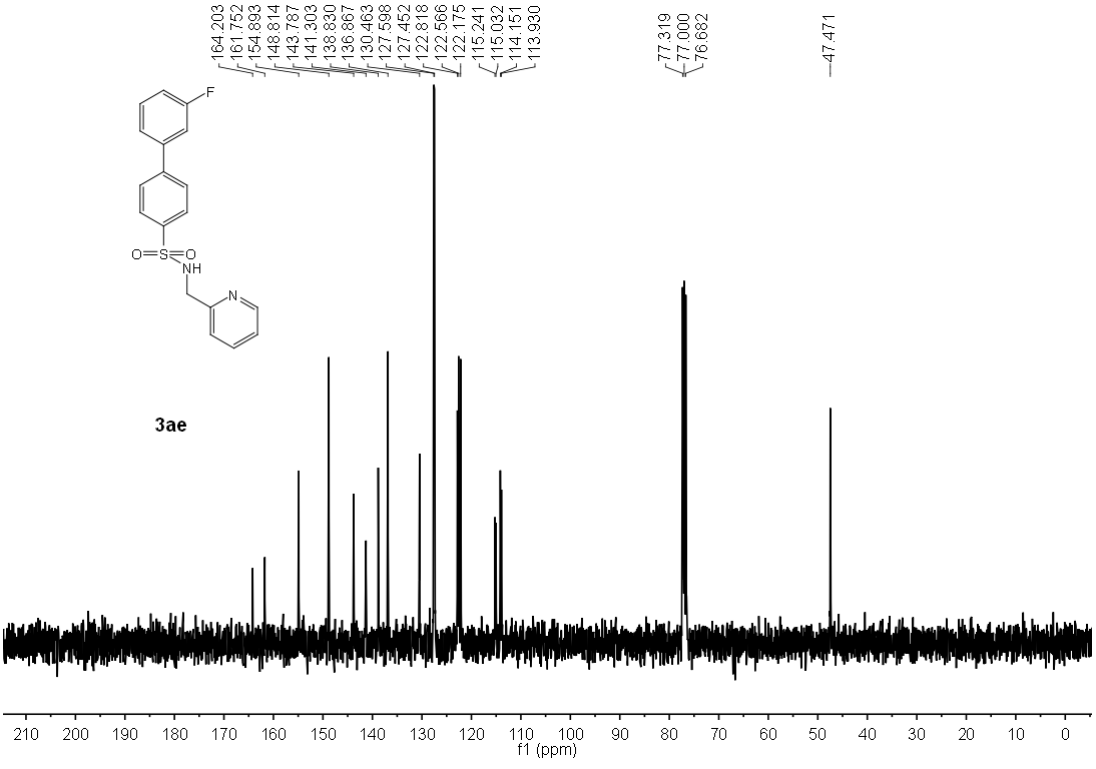
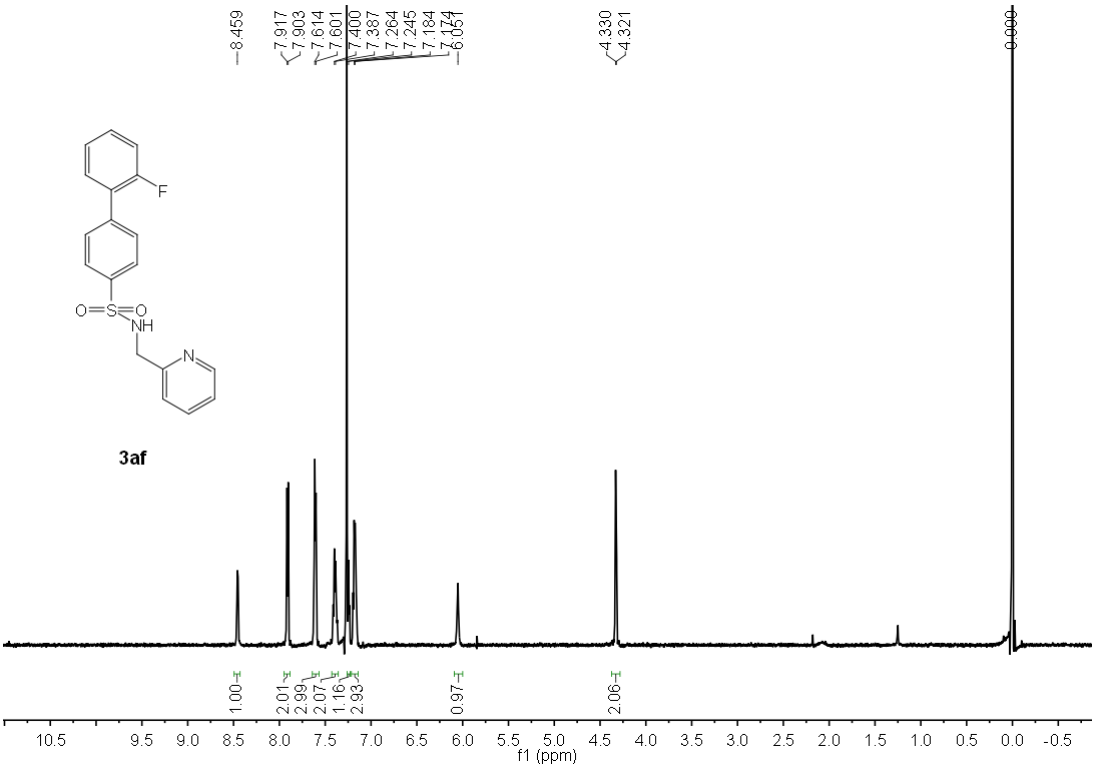
8.450
7.927
7.913
7.625
7.611
7.604
7.601
7.345
7.264
7.192
6.145
4.314
4.306
0.000
F
O=S=O
NH
N
3ae
0.99
1.98
3.04
1.09
1.05
0.93
2.11
0.88
0.97
2.00
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


164.203
161.752
154.893
148.814
143.787
141.303
138.830
136.867
130.463
127.598
127.452
122.818
122.566
122.175
115.241
115.032
114.151
113.930
77.319
77.000
76.682
47.471
F
O=S=O
NH
N
3ae
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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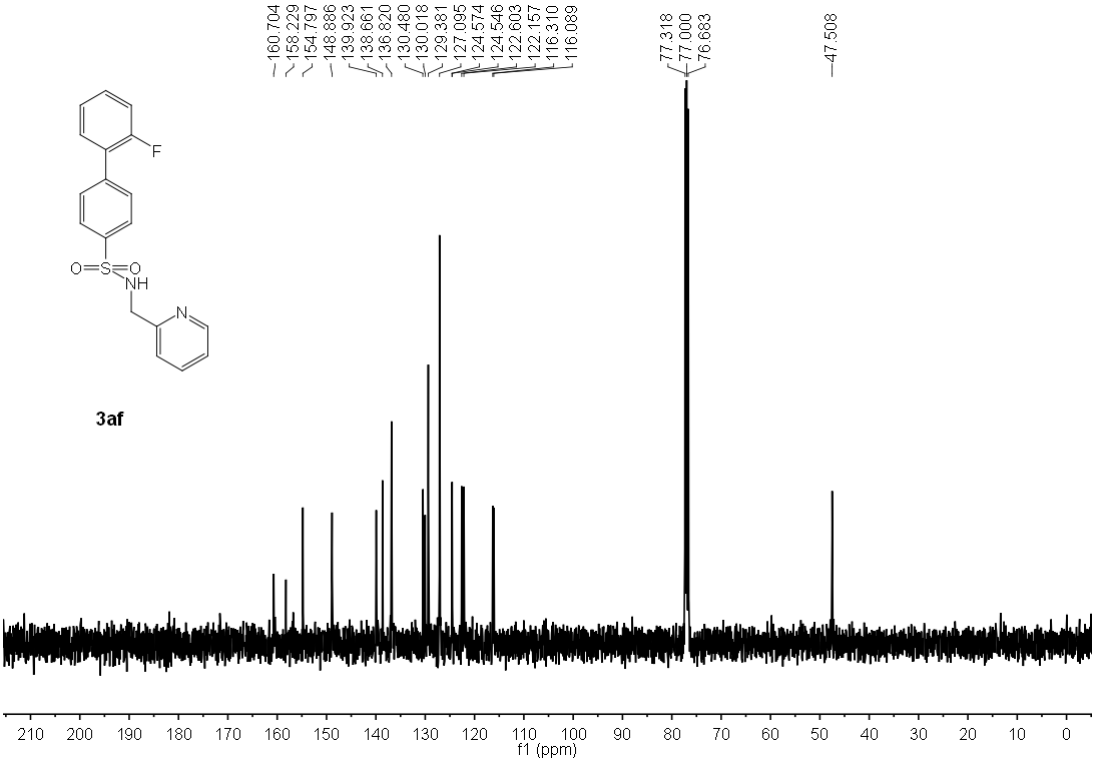
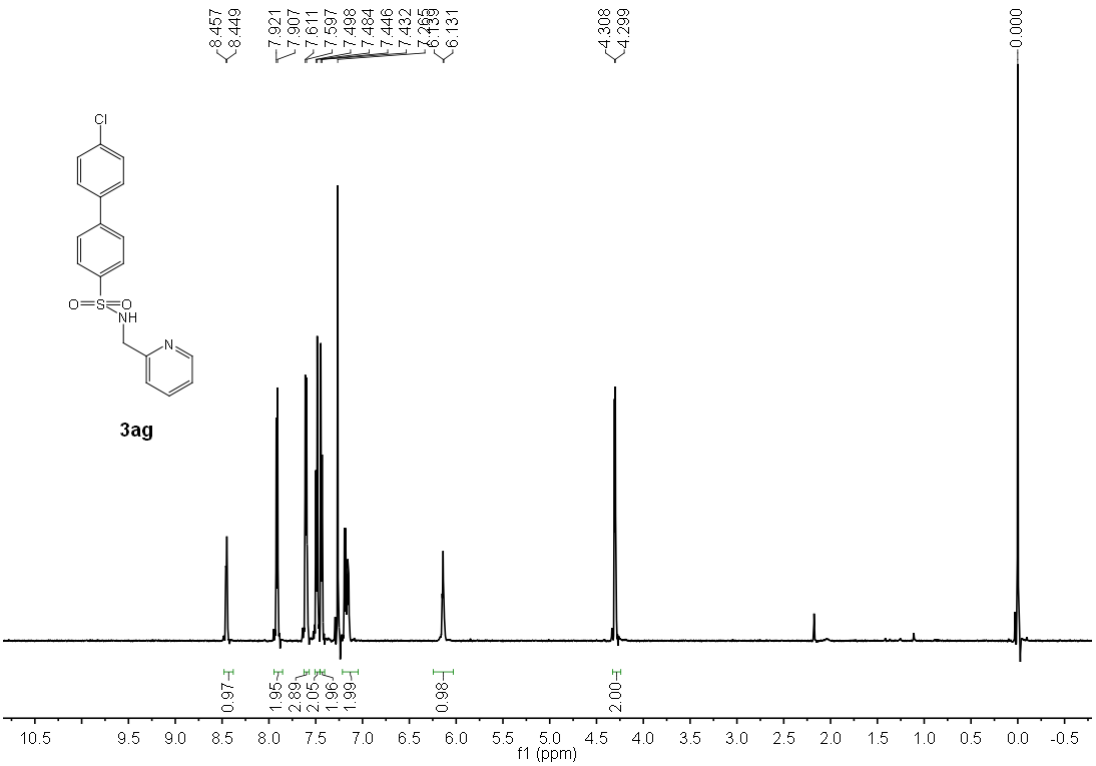
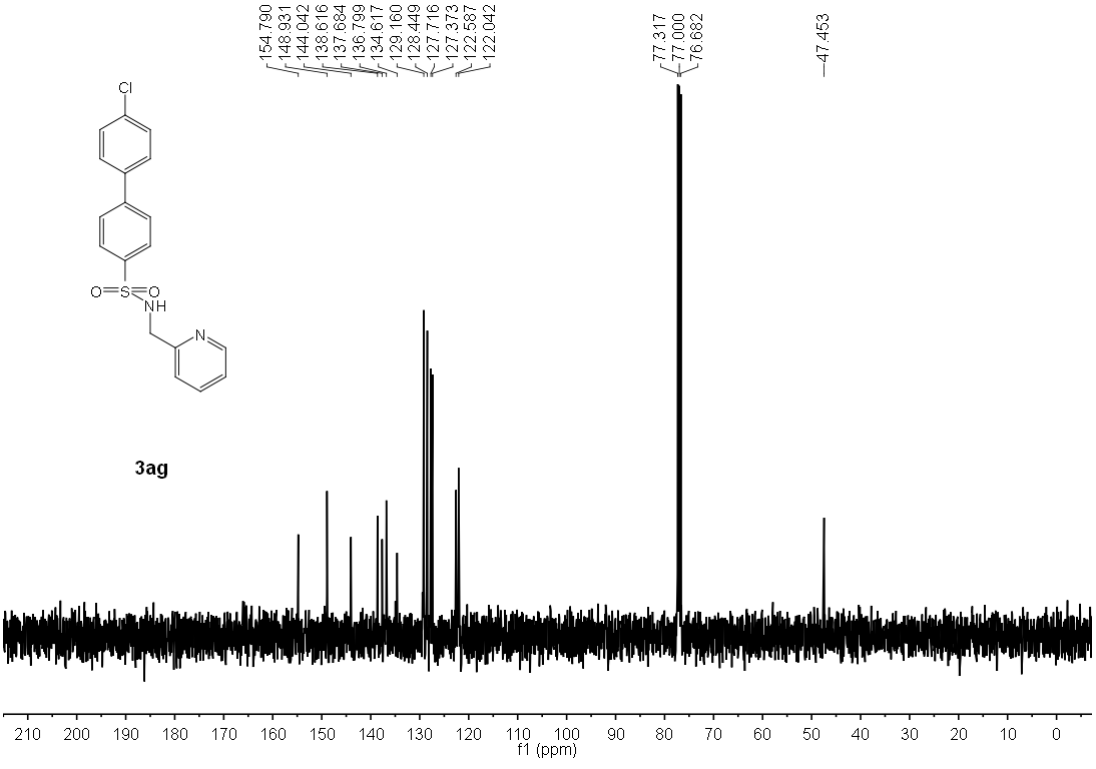
7.917
7.903
7.614
7.601
7.400
7.387
7.264
7.245
7.184
7.174
6.051
4.330
4.321
0.000
F
O=S=O
NH
N
3af
1.00
2.01
2.99
2.07
1.16
2.93
0.97
2.06
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


160.704
158.229
154.797
148.886
139.923
138.661
136.820
130.480
130.018
129.381
127.095
124.574
124.546
122.603
122.157
116.310
116.089
77.318
77.000
76.683
47.508
F
O=S=O
NH
N
3af
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.457
8.449
7.921
7.907
7.611
7.597
7.498
7.484
7.446
7.432
6.131
4.308
4.299
0.000
Cl
O=S=O
NH
N
3ag
0.97
1.95
2.89
2.05
1.96
1.99
0.98
2.00
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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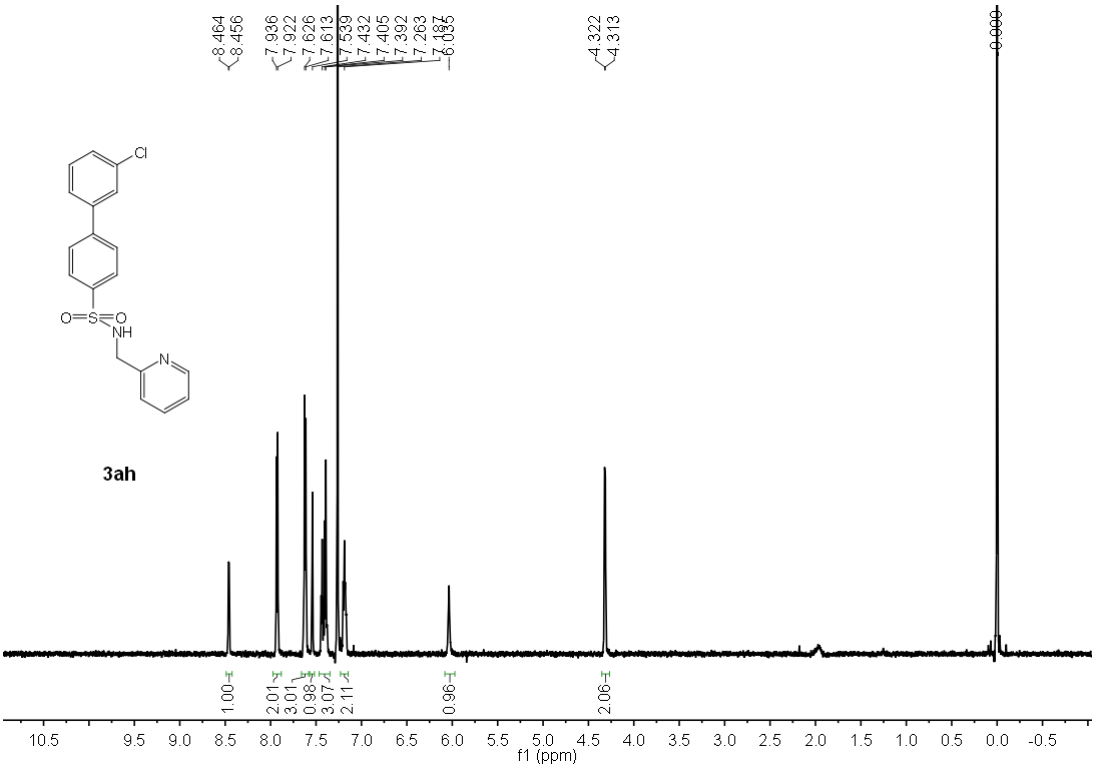
148.931
144.042
138.616
137.684
136.799
134.617
129.160
128.449
127.716
127.373
122.587
122.042
77.317
77.000
76.682
47.453
Cl
O=S=O
NH
N
3ag
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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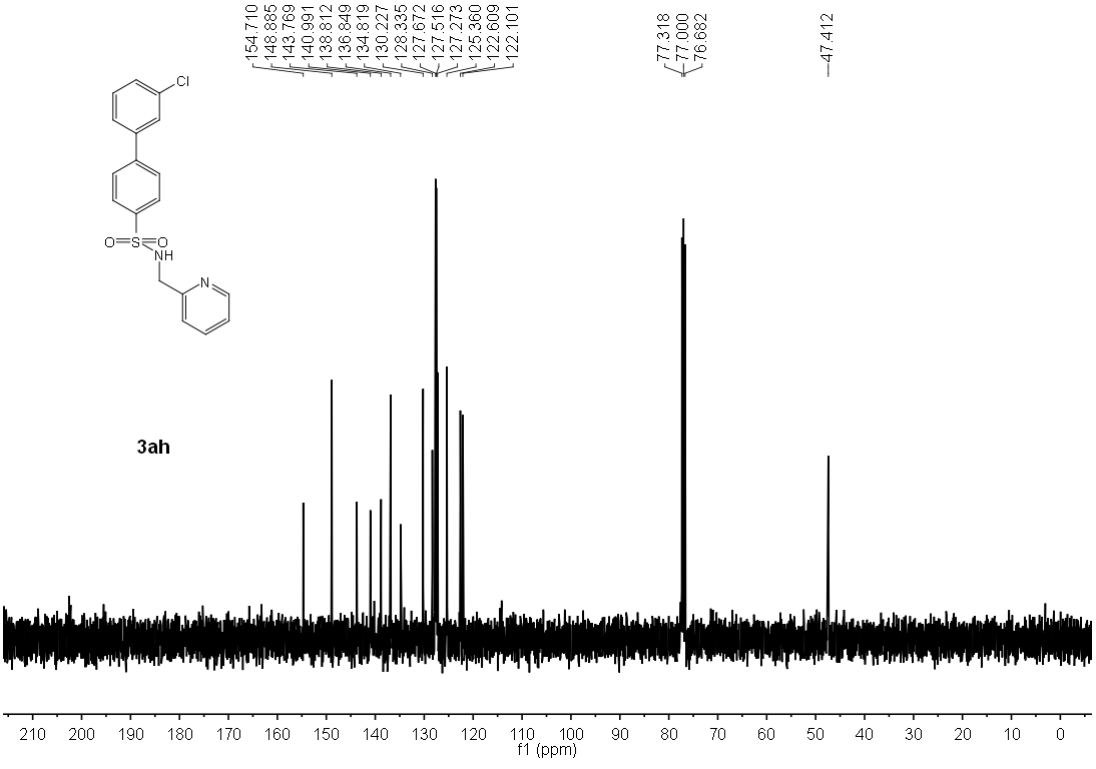
8.456
7.936
7.922
7.626
7.613
7.539
7.432
7.405
7.392
7.263
4.322
4.313
0.000
Cl
O=S=O
NH
N
3ah
1.00
2.01
3.01
0.98
3.07
2.11
0.96
2.06
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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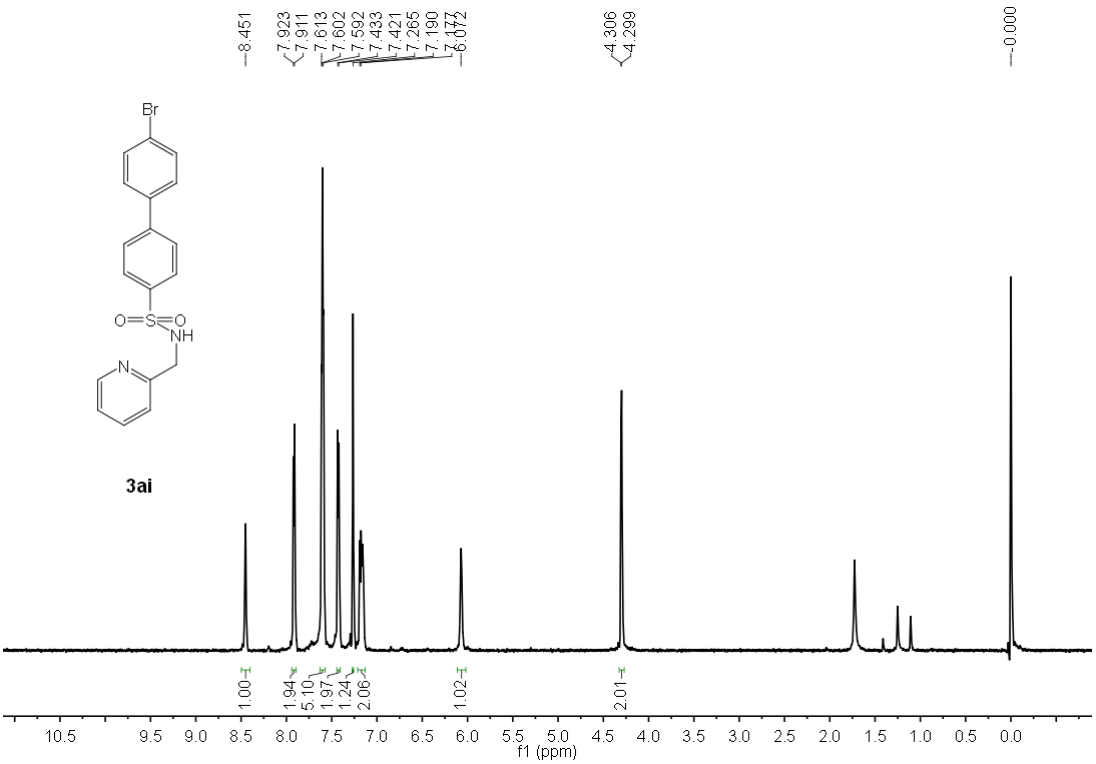
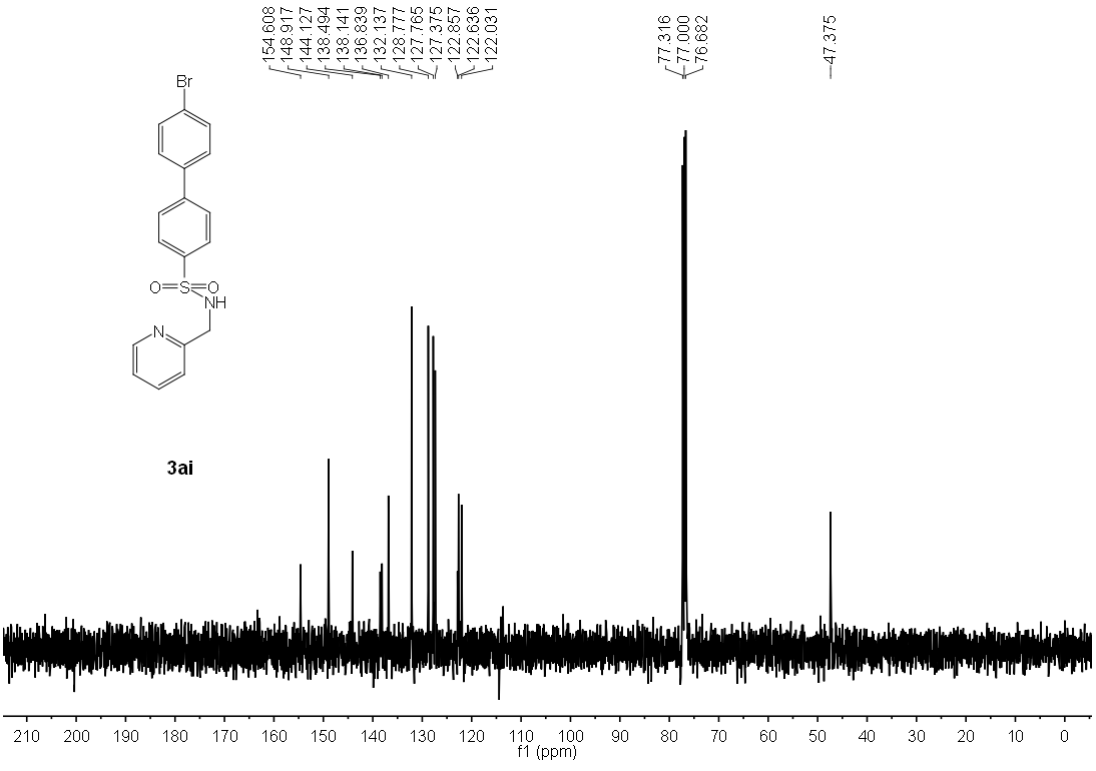
140.991
138.812
136.849
134.819
130.227
128.335
127.672
127.516
127.273
125.360
122.609
122.101
77.318
77.000
76.682
47.412
Cl
O=S=O
NH
N
3ah
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.451
7.923
7.911
7.613
7.602
7.592
7.433
7.421
7.265
7.190
7.177
6.072
4.306
4.299
0.000
Br
O=S=O
NH
N
3ai
1.00
1.94
5.10
1.97
1.24
2.06
1.02
2.01
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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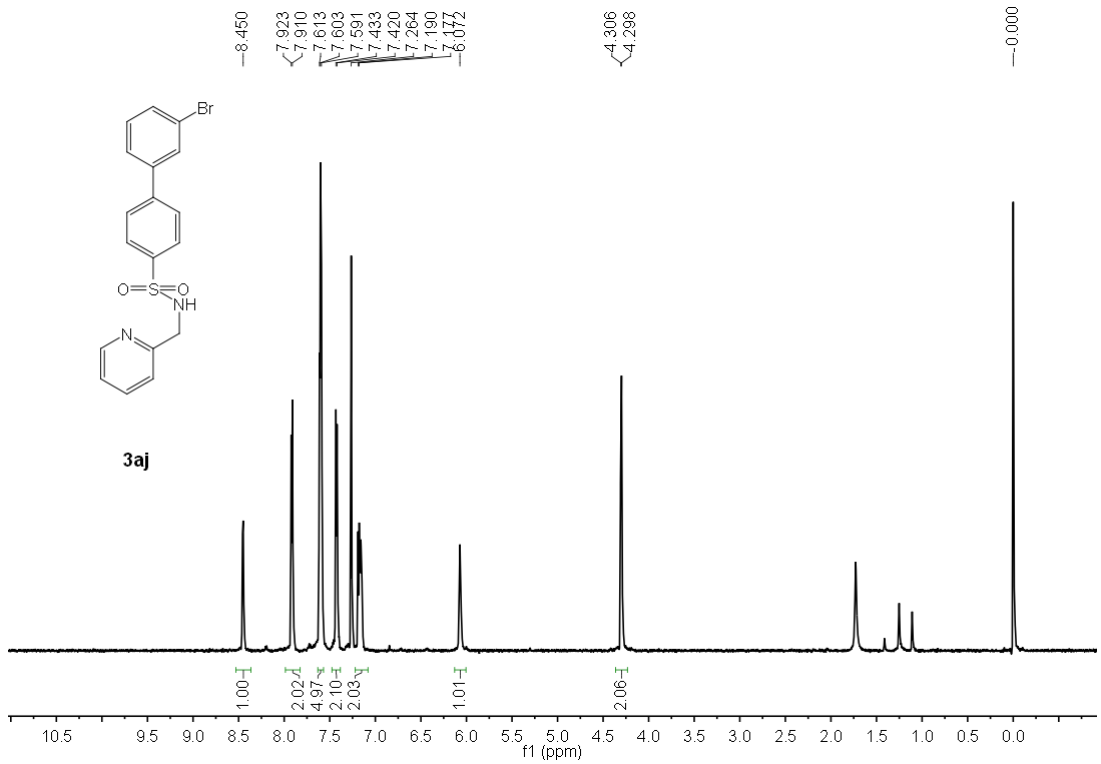
138.494
138.141
136.839
132.137
128.777
127.765
127.375
122.857
122.636
122.031
77.316
77.000
76.682
47.375
Br
O=S=O
NH
N
3ai
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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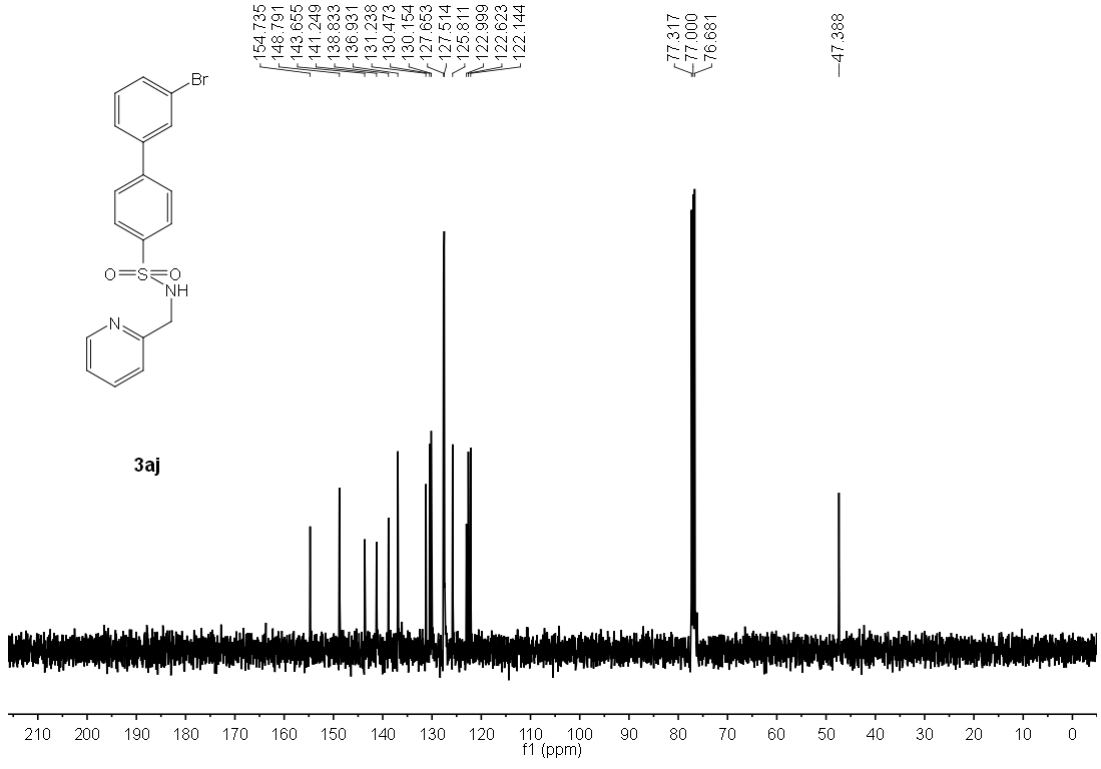
7.923
7.910
7.613
7.603
7.591
7.433
7.420
7.264
7.190
7.177
6.072
4.306
4.298
0.000
Br
O=S=O
NH
N
3aj
1.00
2.02
4.97
2.10
2.03
1.01
2.06
f1 (ppm)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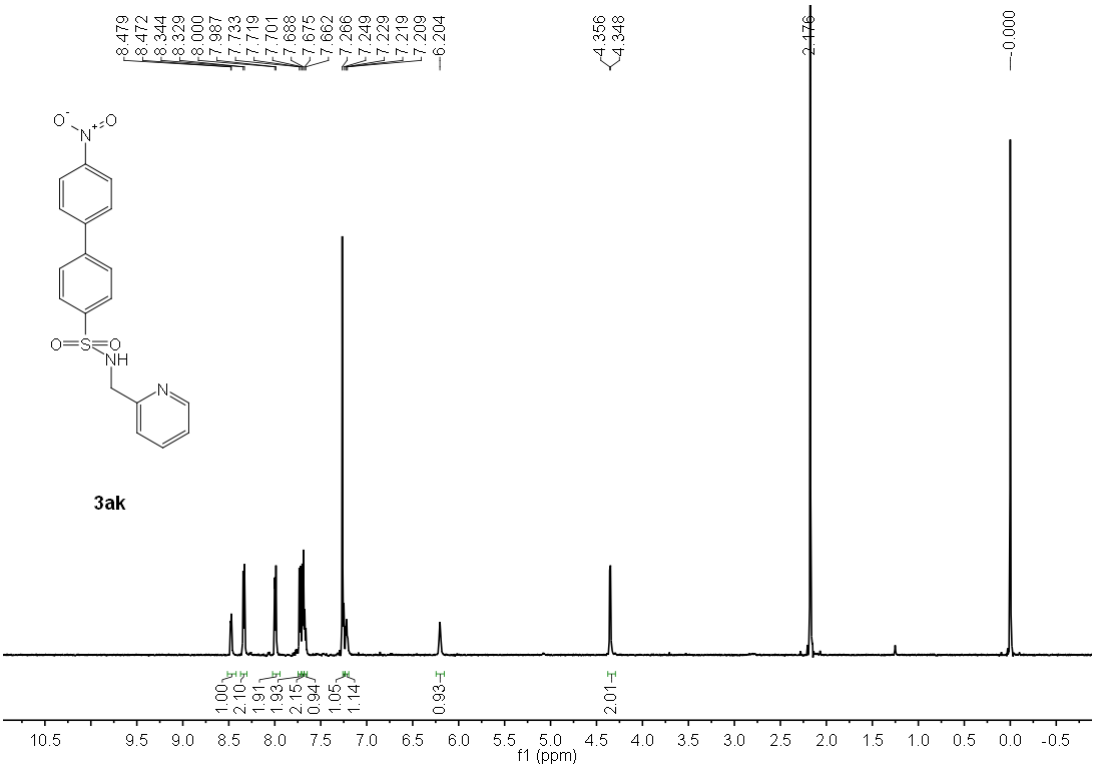
148.791
143.655
141.249
138.833
136.931
131.238
130.473
130.154
127.653
127.514
125.811
122.999
122.623
122.144
77.317
77.000
76.681
47.388
Br
O=S=O
NH
N
3aj
f1 (ppm)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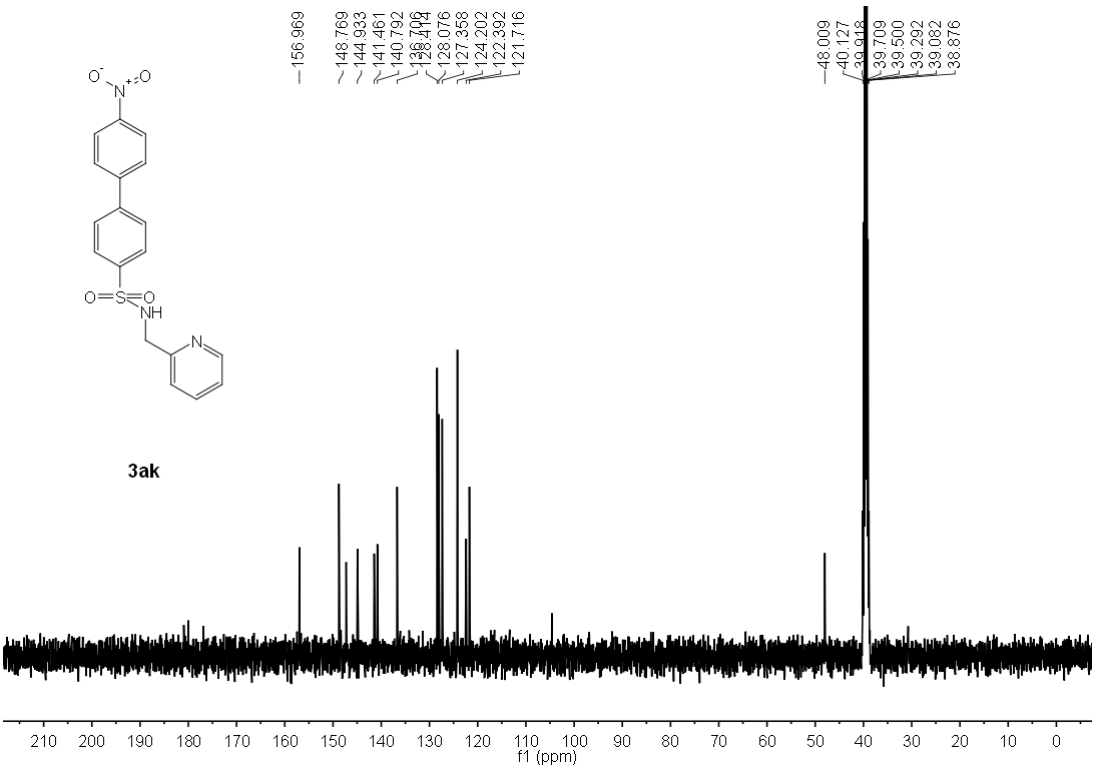
8.472
8.344
8.329
8.000
7.987
7.733
7.719
7.701
7.688
7.675
7.662
7.266
7.249
7.229
7.219
7.209
6.204
4.356
4.348
2.476
0.000
3ak
1.00
2.10
1.91
1.93
2.15
0.94
1.05
1.14
0.93
2.01
f1 (ppm)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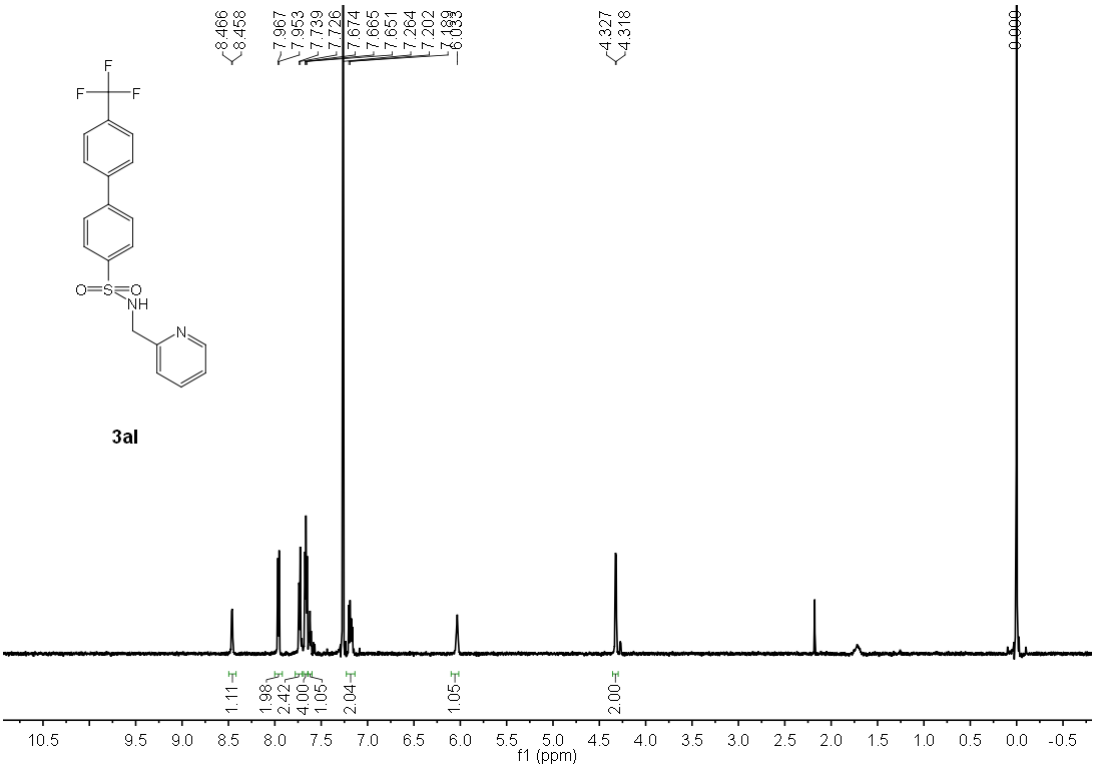
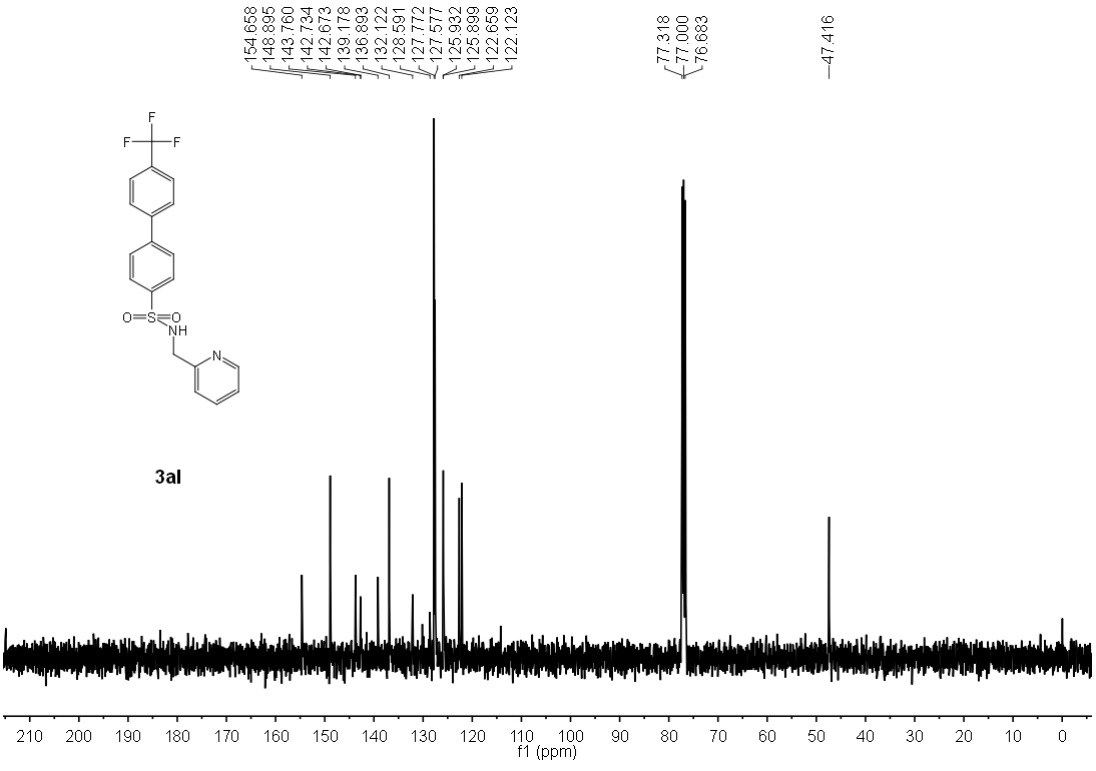
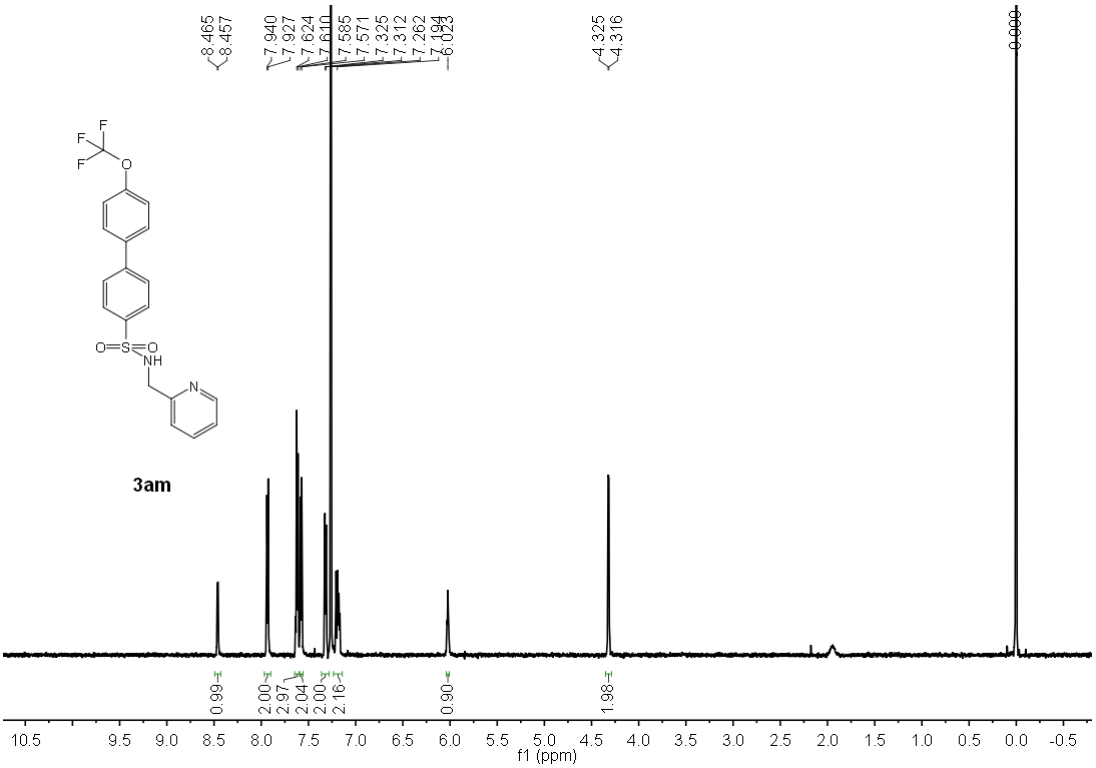
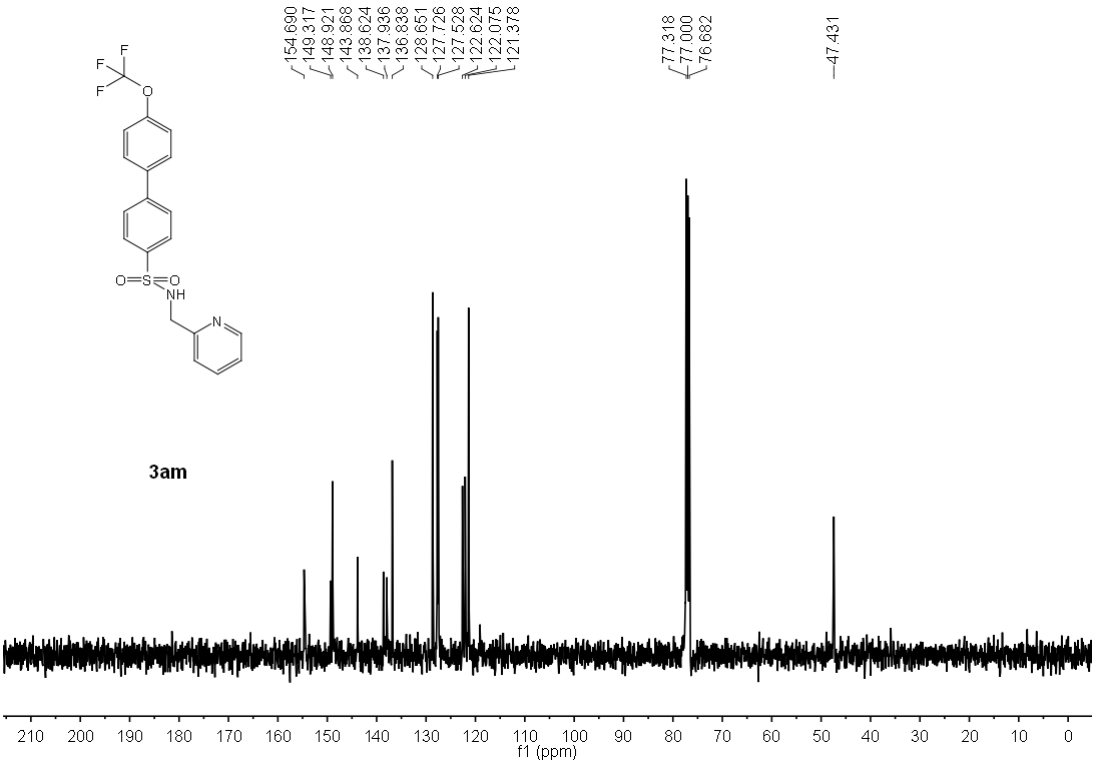
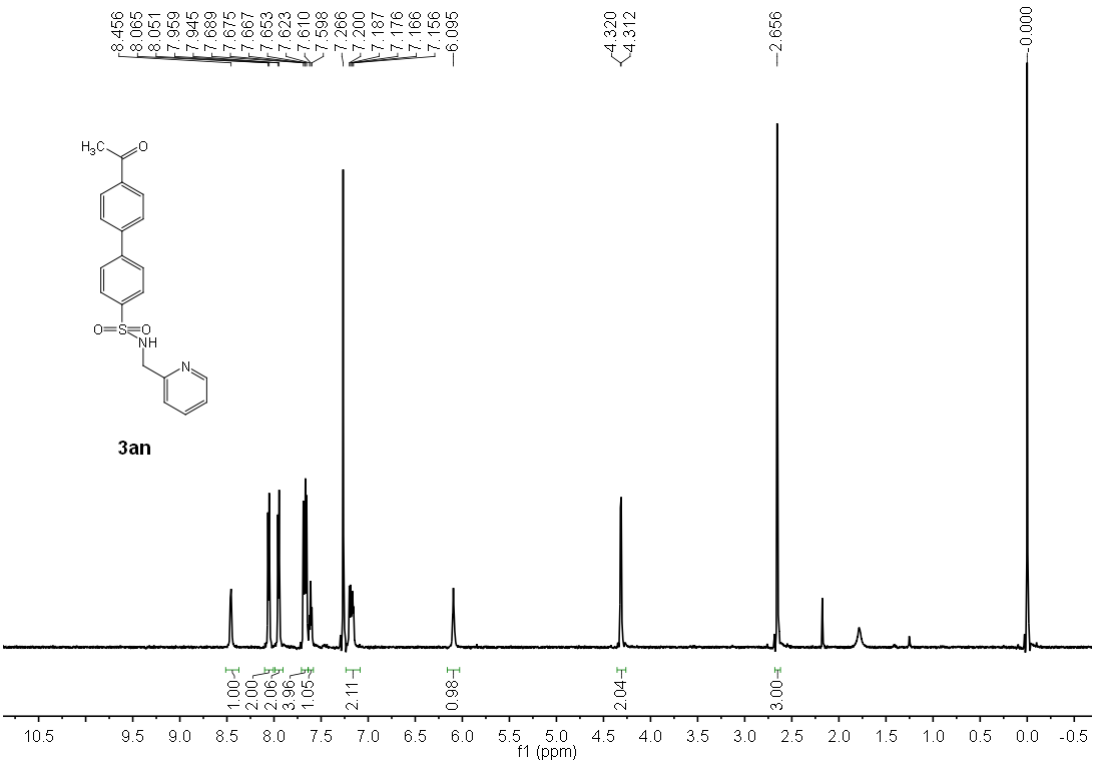
148.769
144.933
141.461
140.792
136.706
128.414
128.076
127.358
124.202
122.392
121.716
48.009
40.127
39.918
39.709
39.500
39.292
39.082
38.876
3ak
f1 (ppm)

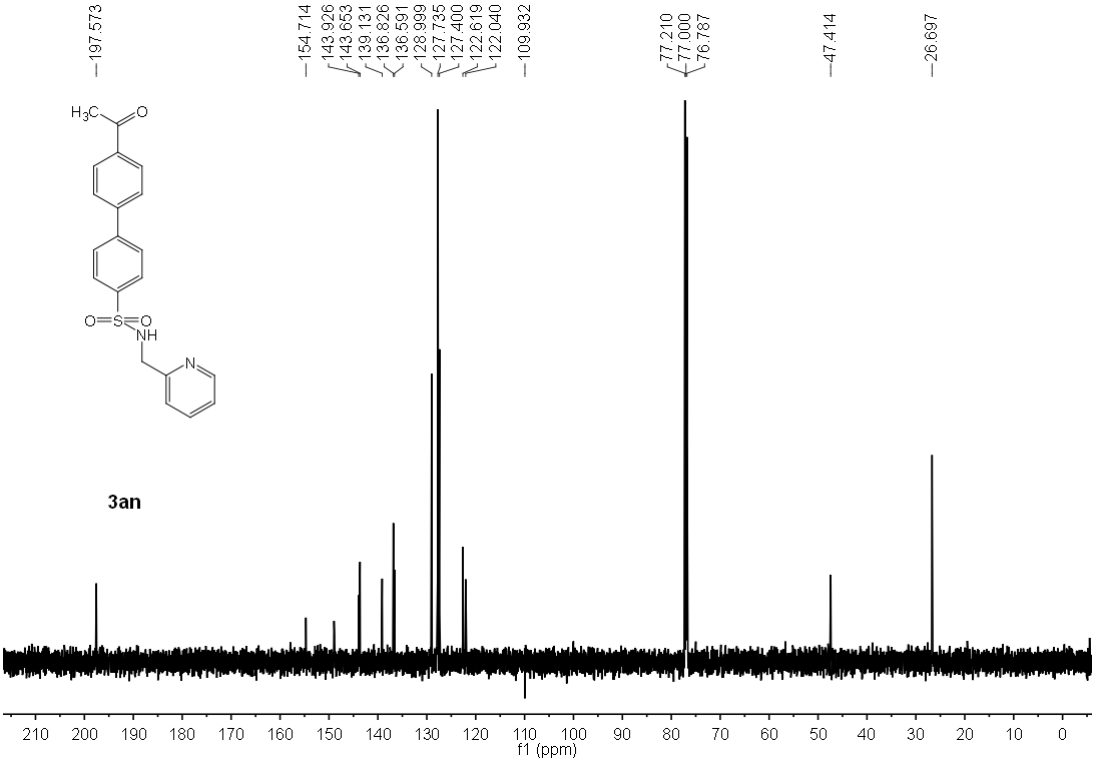

8.466
8.458
7.967
7.953
7.739
7.726
7.674
7.665
7.651
7.264
7.202
7.189
6.033
4.327
4.318
0.000
1.11
1.98
2.42
4.00
1.05
2.04
1.05
2.00
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)
F
F F
O=S=O
NH
N
3al


154.658
148.895
143.760
142.734
142.673
139.178
136.893
132.122
128.591
127.772
127.577
125.932
125.899
122.659
122.123
77.318
77.000
76.683
47.416
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
F
F F
O=S=O
NH
N
3al


8.465
8.457
7.940
7.927
7.624
7.610
7.585
7.571
7.325
7.312
7.262
7.194
6.023
4.325
4.316
0.000
3am
0.99
2.00
2.97
2.04
2.00
2.16
0.90
1.98
f1 (ppm)


154.690
149.317
148.921
143.868
138.624
137.936
136.838
128.651
127.726
127.528
122.624
122.075
121.378
77.318
77.000
76.682
47.431
3am
f1 (ppm)


8.456
8.065
8.051
7.959
7.945
7.689
7.675
7.667
7.653
7.623
7.610
7.598
7.266
7.200
7.187
7.176
7.166
7.156
6.095
4.320
4.312
2.656
0.000
3an
1.00
2.00
2.06
3.96
1.05
2.11
0.98
2.04
3.00
f1 (ppm)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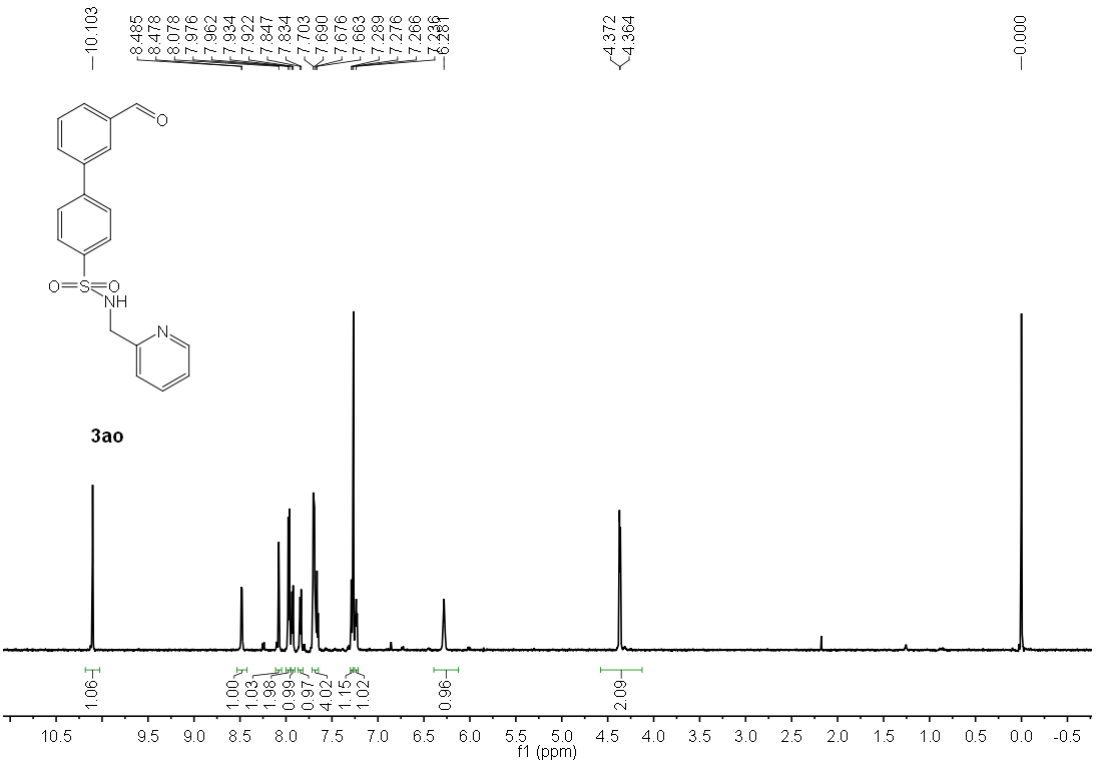
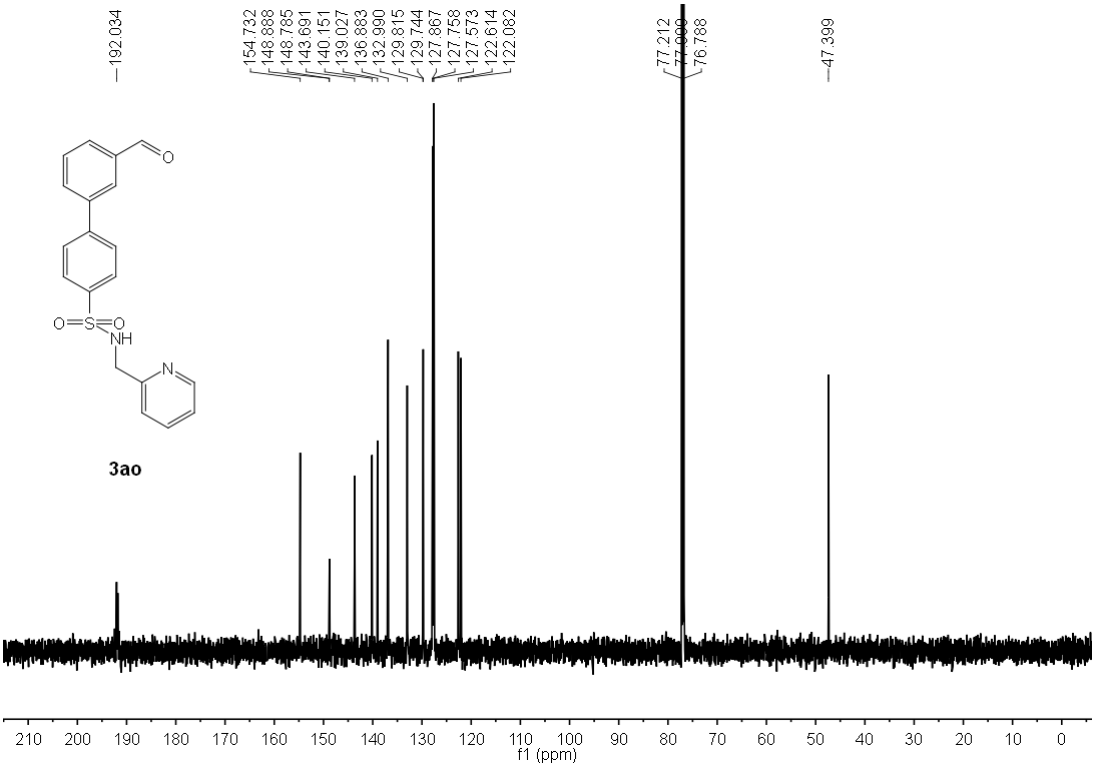
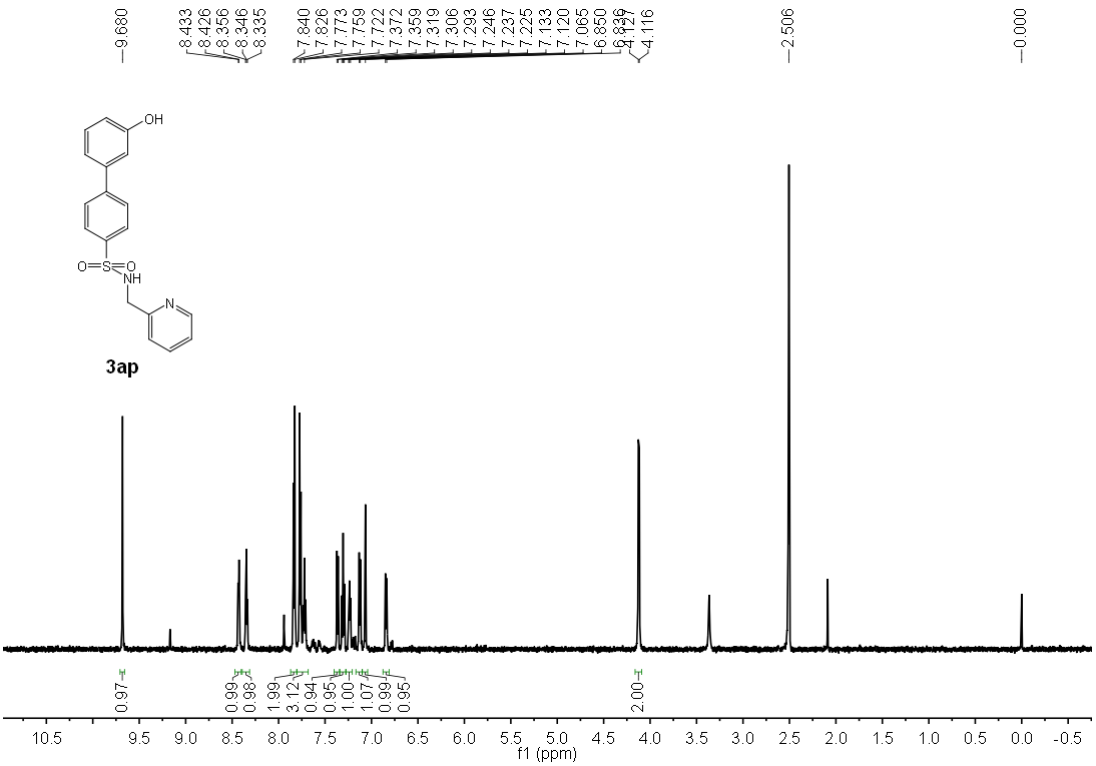
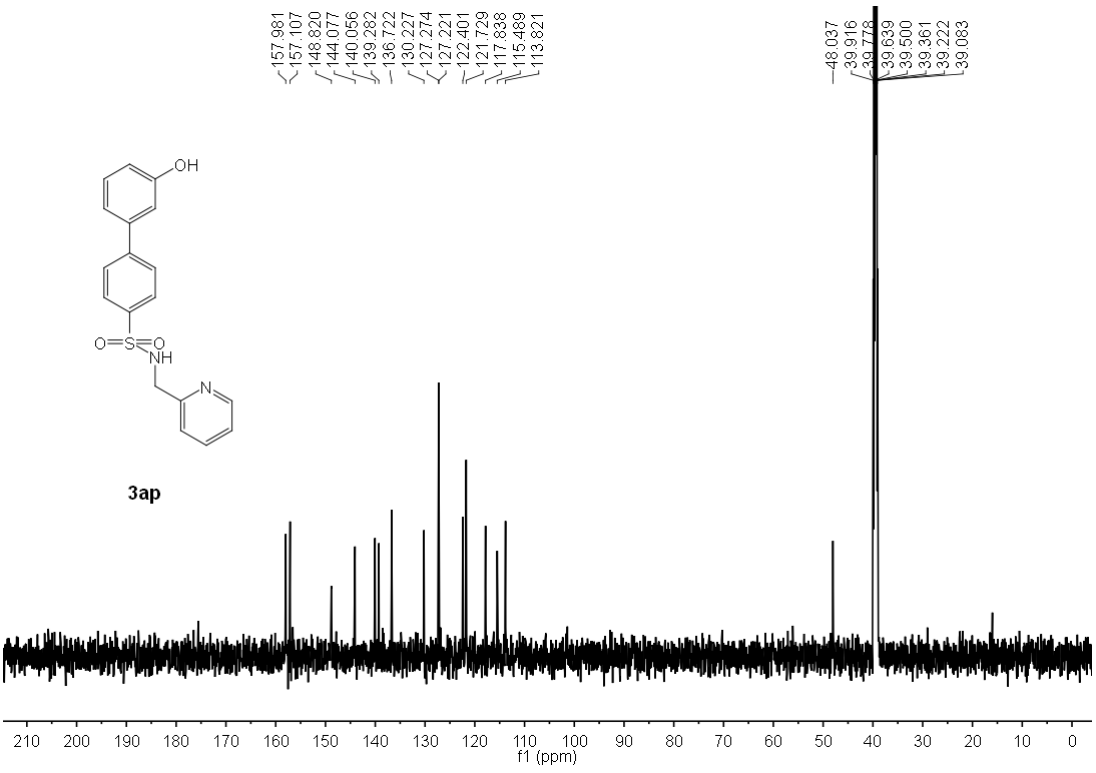
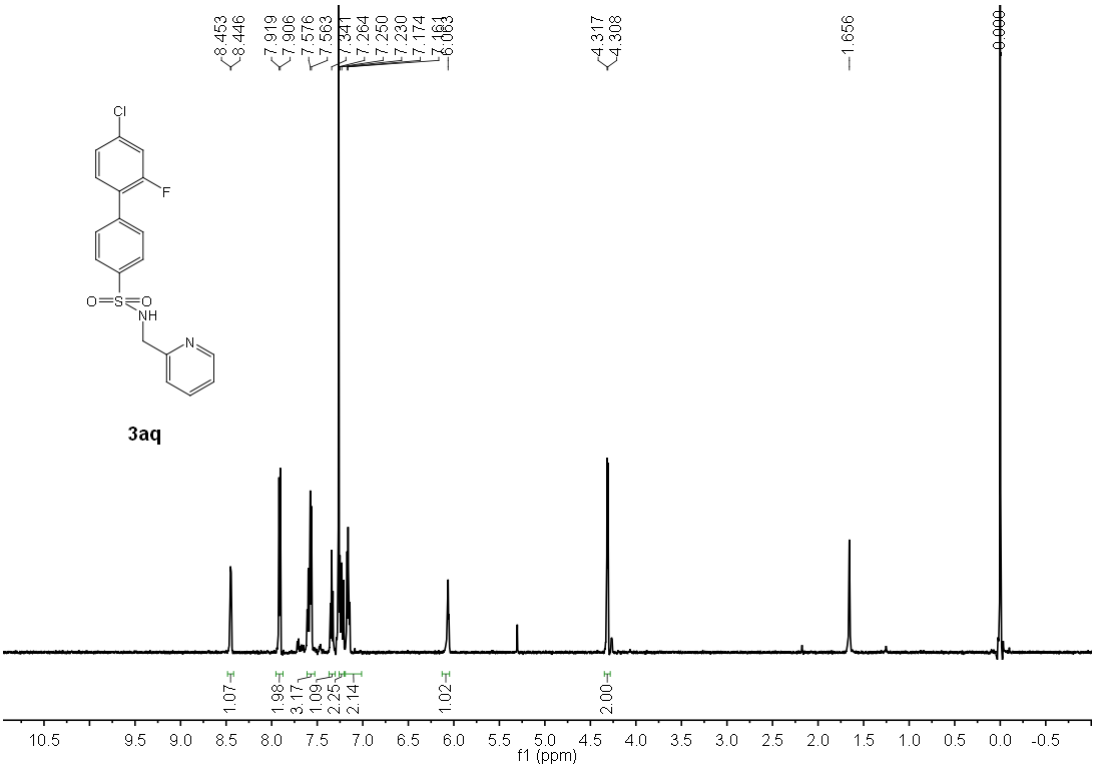
154.714
143.926
143.653
139.131
136.826
136.591
128.999
127.735
127.400
122.619
122.040
109.932
77.210
77.000
76.787
47.414
26.697
3an
f1 (ppm)

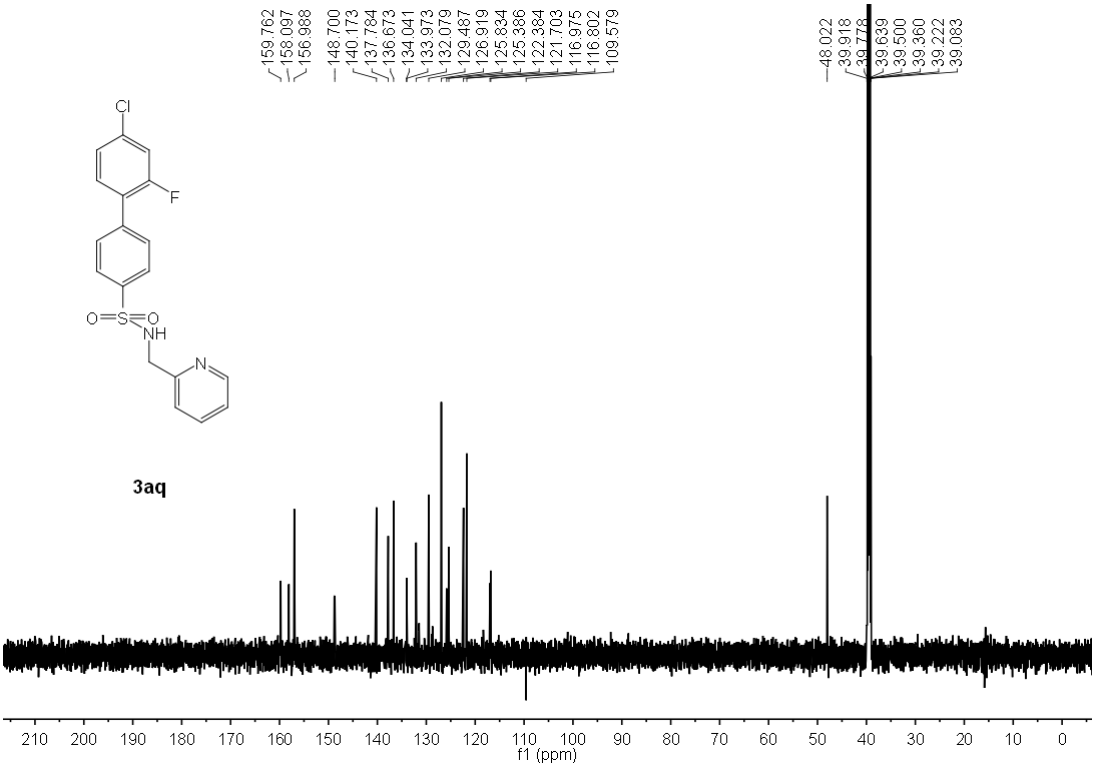

10.103
8.485
8.478
8.078
7.976
7.962
7.934
7.922
7.847
7.834
7.703
7.690
7.676
7.663
7.289
7.276
7.266
7.236
6.261
4.372
4.364
0.000
3ao
1.06
1.00
1.03
1.98
0.99
0.97
4.02
1.15
1.02
0.96
2.09
f1 (ppm)

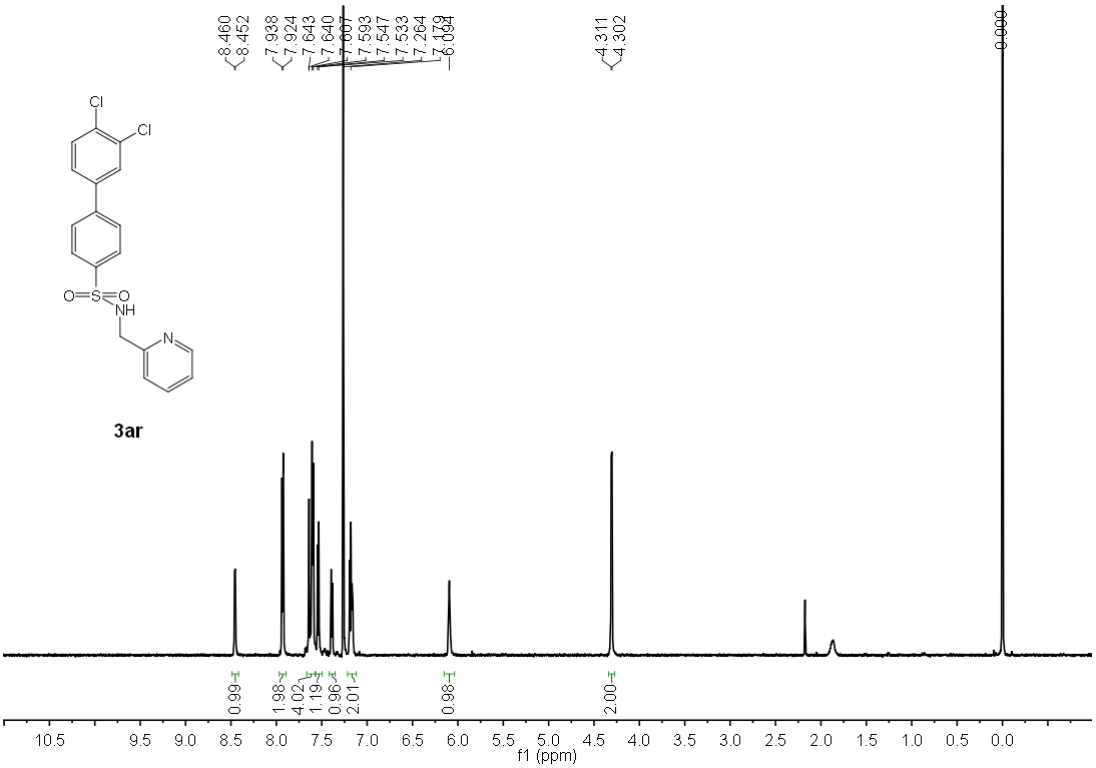

192.034
154.732
148.888
148.785
143.691
140.151
139.027
136.883
132.990
129.815
129.744
127.867
127.758
127.573
122.614
122.082
77.212
77.000
76.788
47.399
3ao
f1 (ppm)

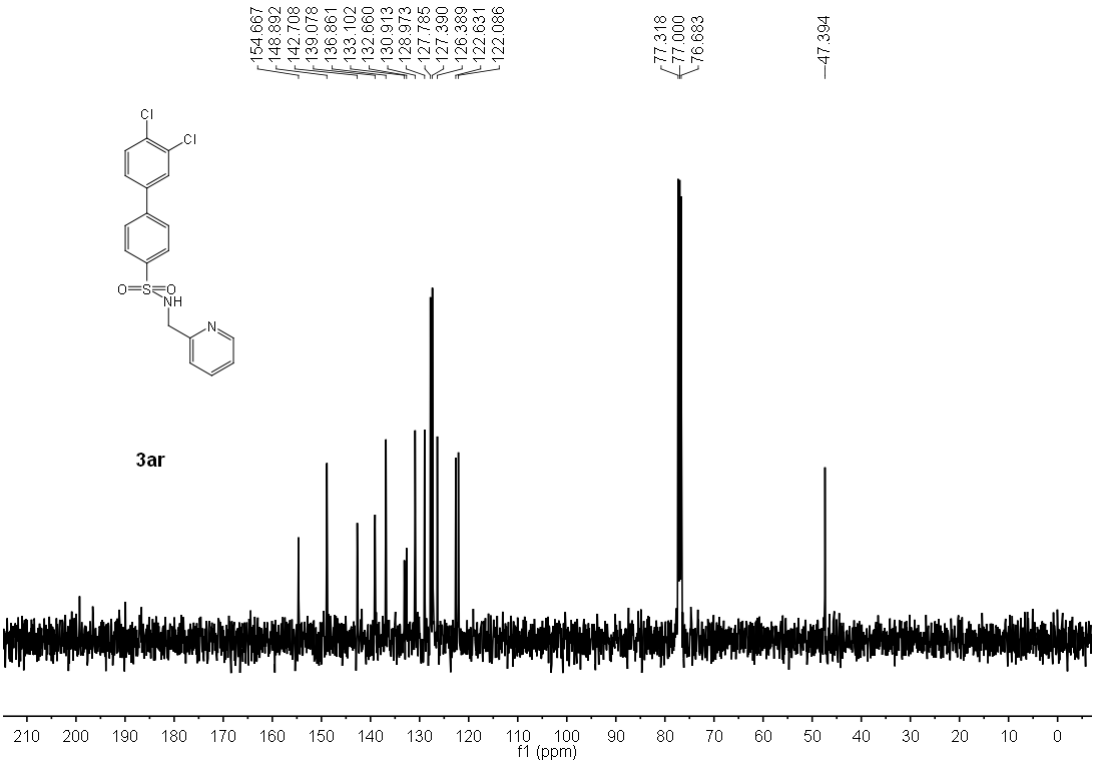

9.680
8.433
8.426
8.356
8.346
8.335
7.840
7.826
7.773
7.759
7.722
7.372
7.359
7.319
7.306
7.293
7.246
7.237
7.225
7.133
7.120
7.065
6.850
6.836
4.116
2.506
0.000
OH
O=S=O
NH
N
3ap
0.97
0.99
0.98
1.99
3.12
0.94
0.95
1.00
1.07
0.99
0.95
2.00
f1 (ppm)


157.981
157.107
148.820
144.077
140.056
139.282
136.722
130.227
127.274
127.221
122.401
121.729
117.838
115.489
113.821
48.037
39.916
39.778
39.639
39.500
39.361
39.222
39.083
OH
O=S=O
NH
N
3ap
f1 (ppm)


8.453
8.446
7.919
7.906
7.576
7.563
7.341
7.264
7.250
7.230
7.174
7.161
6.083
4.317
4.308
1.656
0.000
Cl
F
O=S=O
NH
N
3aq
1.07
1.98
3.17
1.09
2.25
2.14
1.02
2.00
f1 (ppm)


159.762
158.097
156.988
148.700
140.173
137.784
136.673
134.041
133.973
132.079
129.487
126.919
125.834
125.386
122.384
121.703
116.975
116.802
109.579
48.022
39.918
39.778
39.639
39.500
39.360
39.222
39.083
Cl
F
O=S=O
NH
N
3aq
f1 (ppm)


8.460
8.452
7.938
7.924
7.643
7.640
7.607
7.593
7.547
7.533
7.264
4.311
4.302
0.000
Cl
Cl
O=S=O
NH
N
3ar
0.99
1.98
4.02
1.19
0.96
2.01
0.98
2.00
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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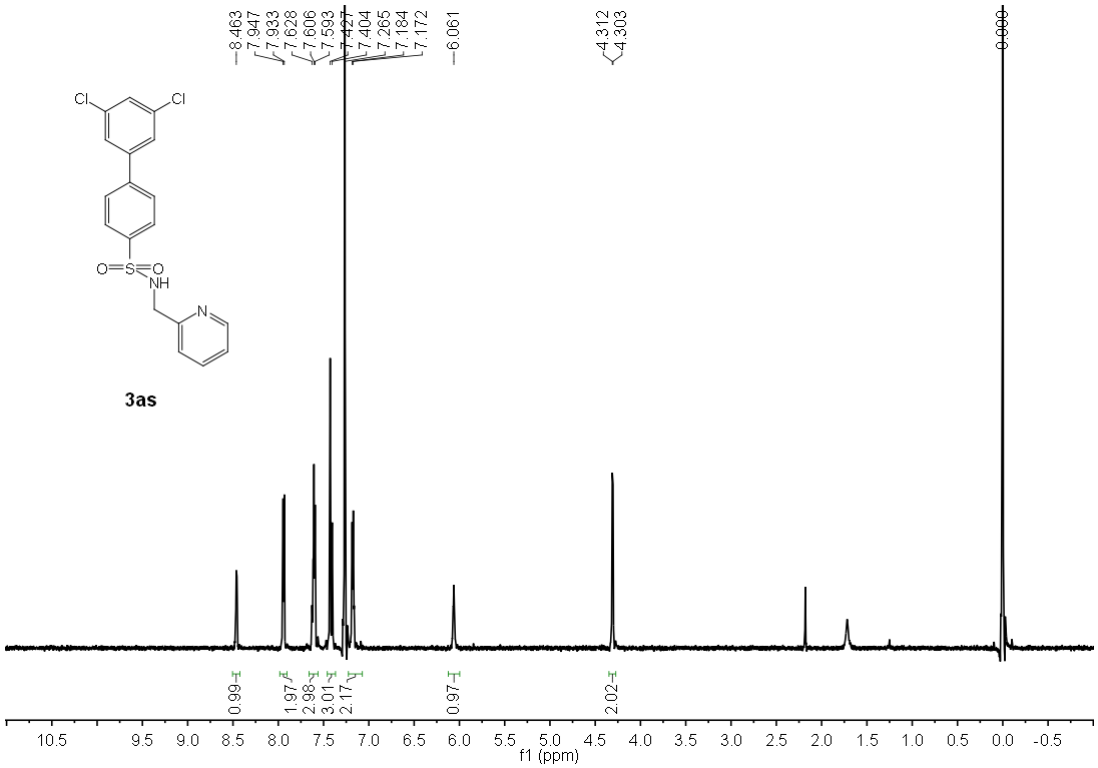
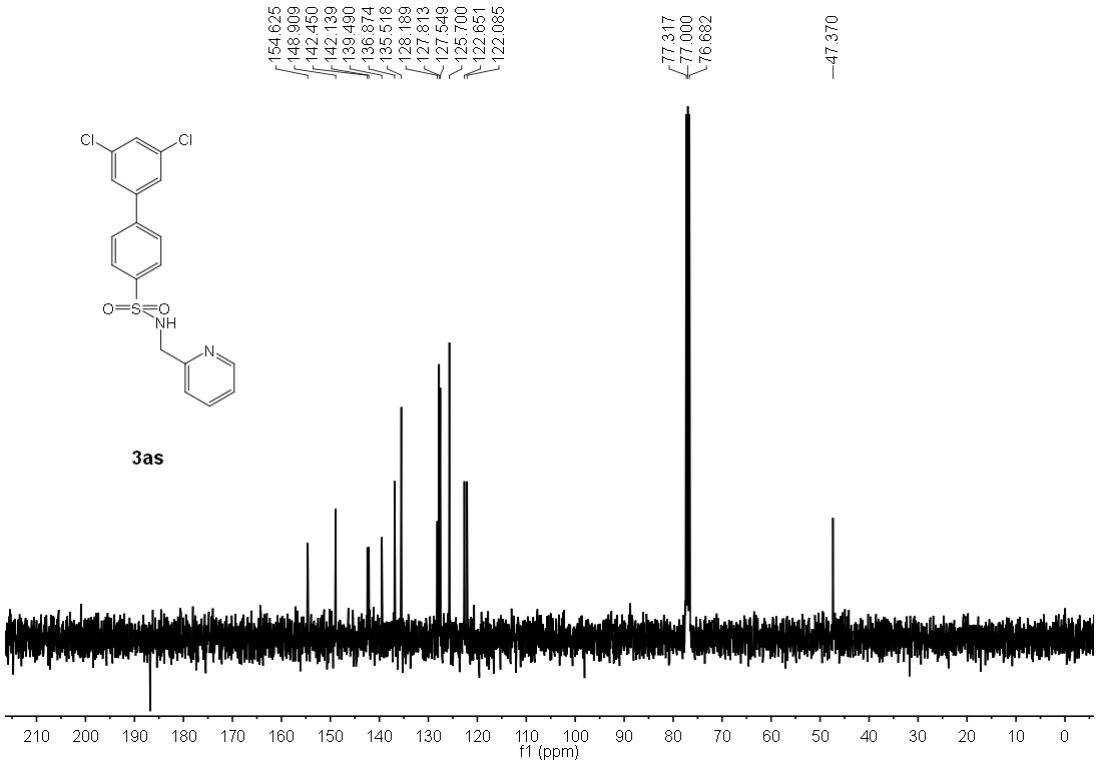
142.708
139.078
136.861
133.102
132.660
130.913
128.973
127.785
127.390
126.389
122.631
122.086
77.318
77.000
76.683
47.394
Cl
Cl
O=S=O
NH
N
3ar
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.463
7.947
7.933
7.628
7.606
7.593
7.427
7.404
7.265
7.184
7.172
6.061
4.312
4.303
0.000
Cl
Cl
O=S=O
NH
N
3as
0.99
1.97
2.98
3.01
2.17
0.97
2.02
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)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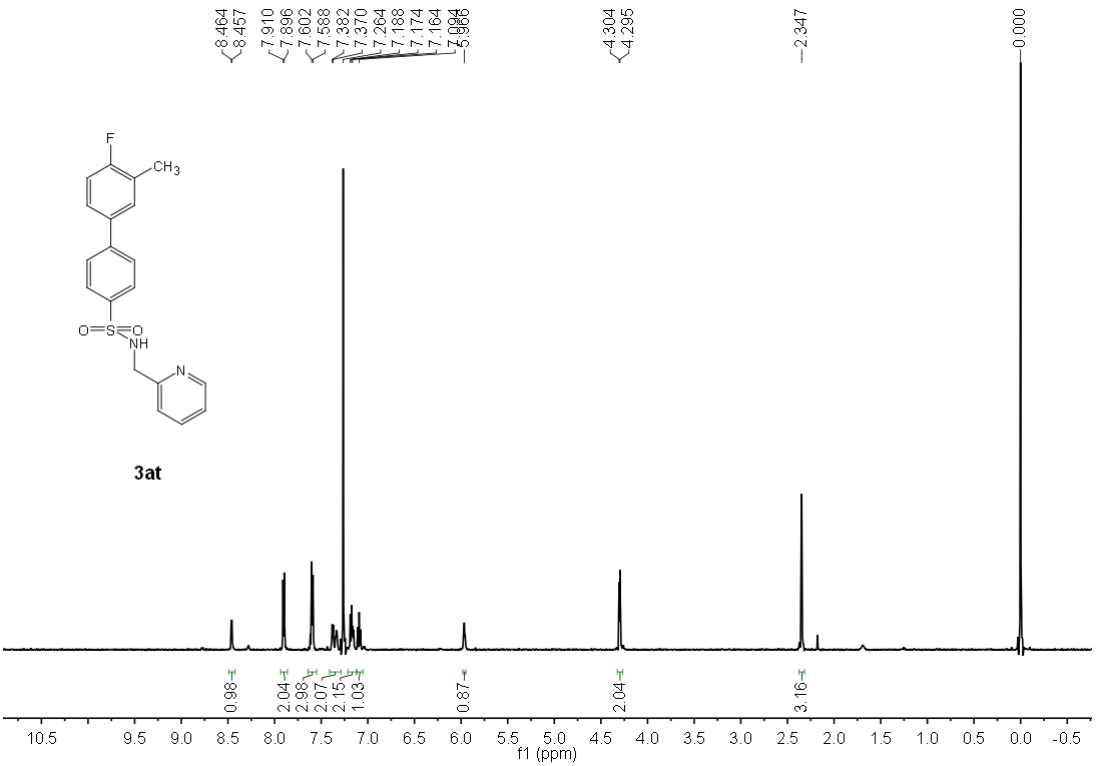
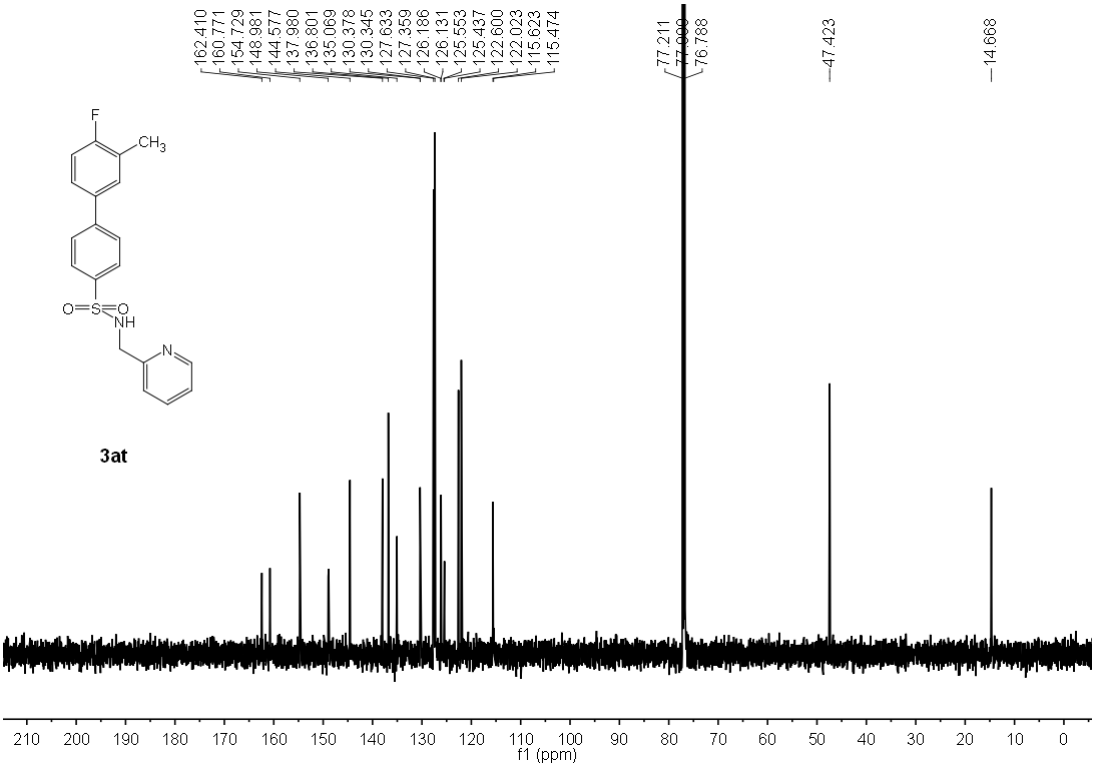
142.450
142.139
139.490
136.874
135.518
128.189
127.813
127.549
125.700
122.651
122.085
77.317
77.000
76.682
47.370
Cl
Cl
O=S=O
NH
N
3as
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.464
8.457
7.910
7.896
7.602
7.588
7.382
7.370
7.264
7.188
7.174
7.164
4.304
4.295
2.347
0.000
F
CH3
O=S=O
NH
N
3at
0.98
2.04
2.98
2.07
2.15
1.03
0.87
2.04
3.16
f1 (ppm)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160.771
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148.981
144.577
137.980
136.801
135.069
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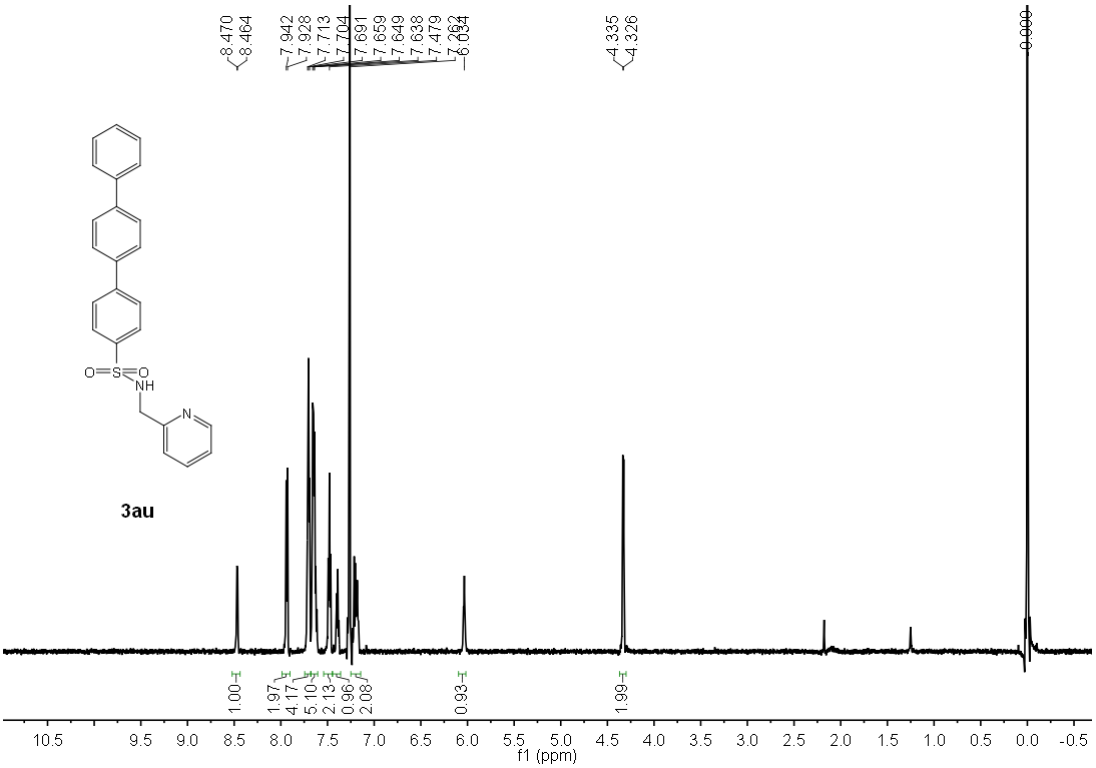
130.345
127.633
127.359
126.186
126.131
125.553
125.437
122.600
122.023
115.623
115.474
77.211
77.000
76.788
47.423
14.668
F
CH3
O=S=O
NH
N
3at
f1 (ppm)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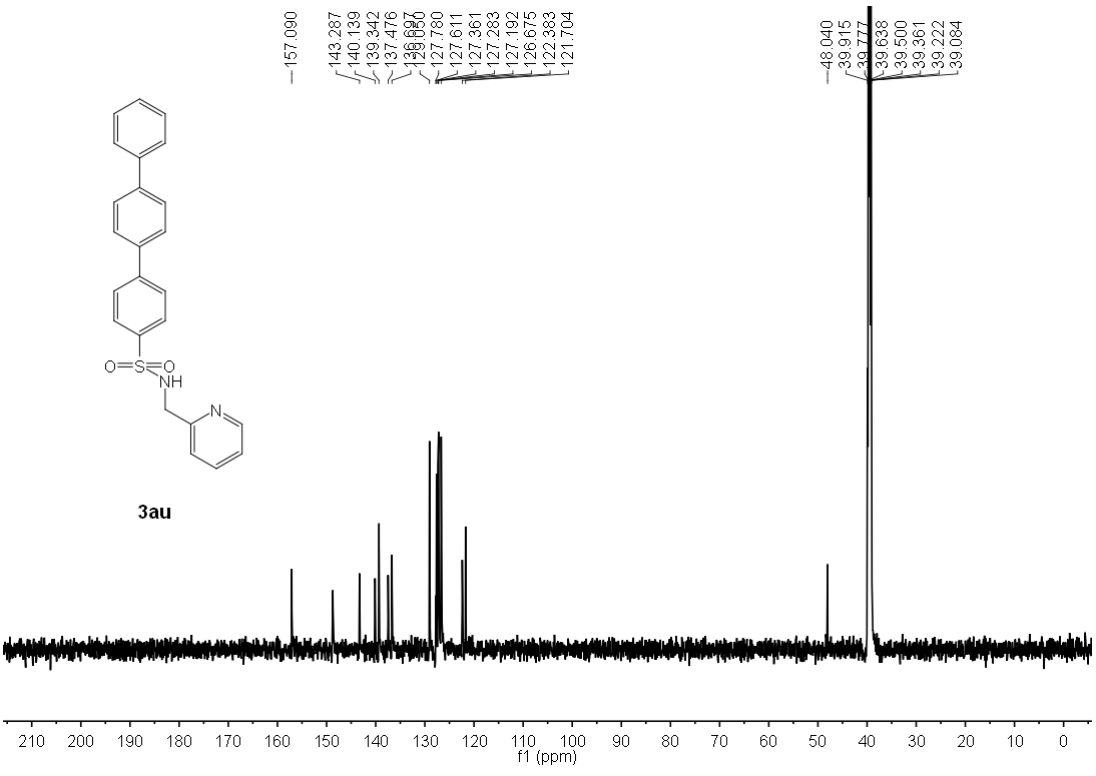
7.691
7.659
7.649
7.638
7.479
6.034
4.335
4.326
0.000
1.00
1.97
4.17
5.10
2.13
0.96
2.08
0.93
1.99
f1 (ppm)
3au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137.476
127.780
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127.283
127.192
126.675
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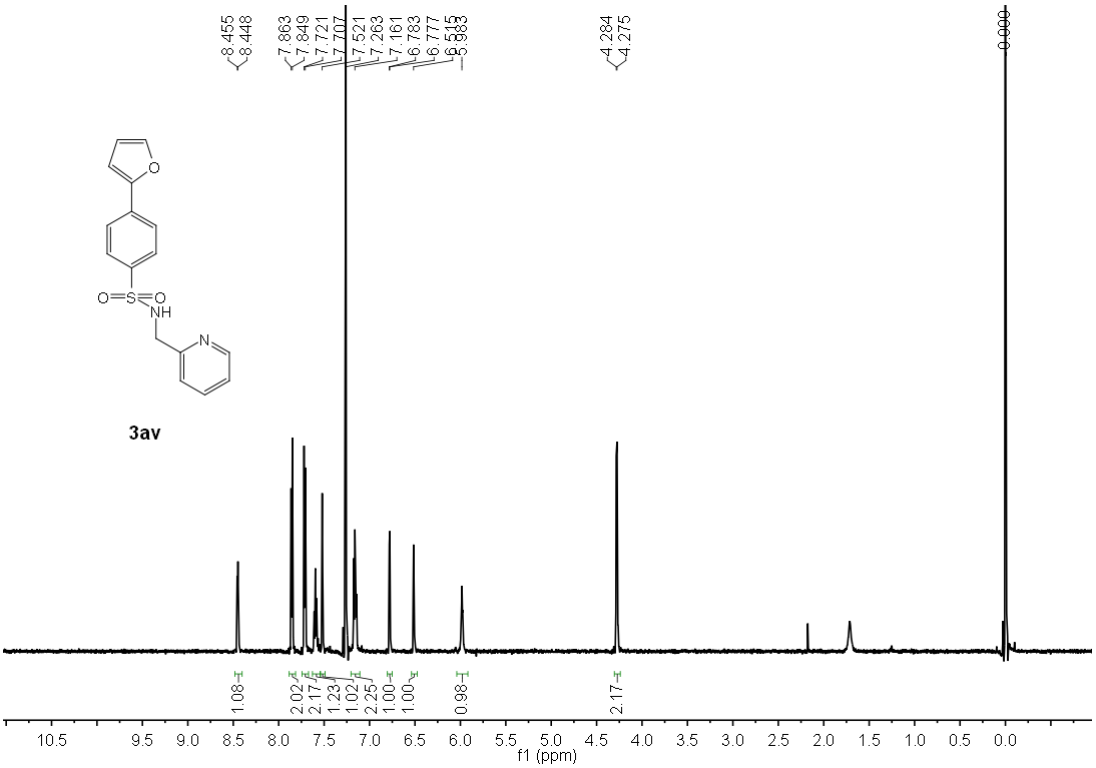
48.040
39.915
39.777
39.638
39.500
39.361
39.222
39.084
f1 (ppm)
3au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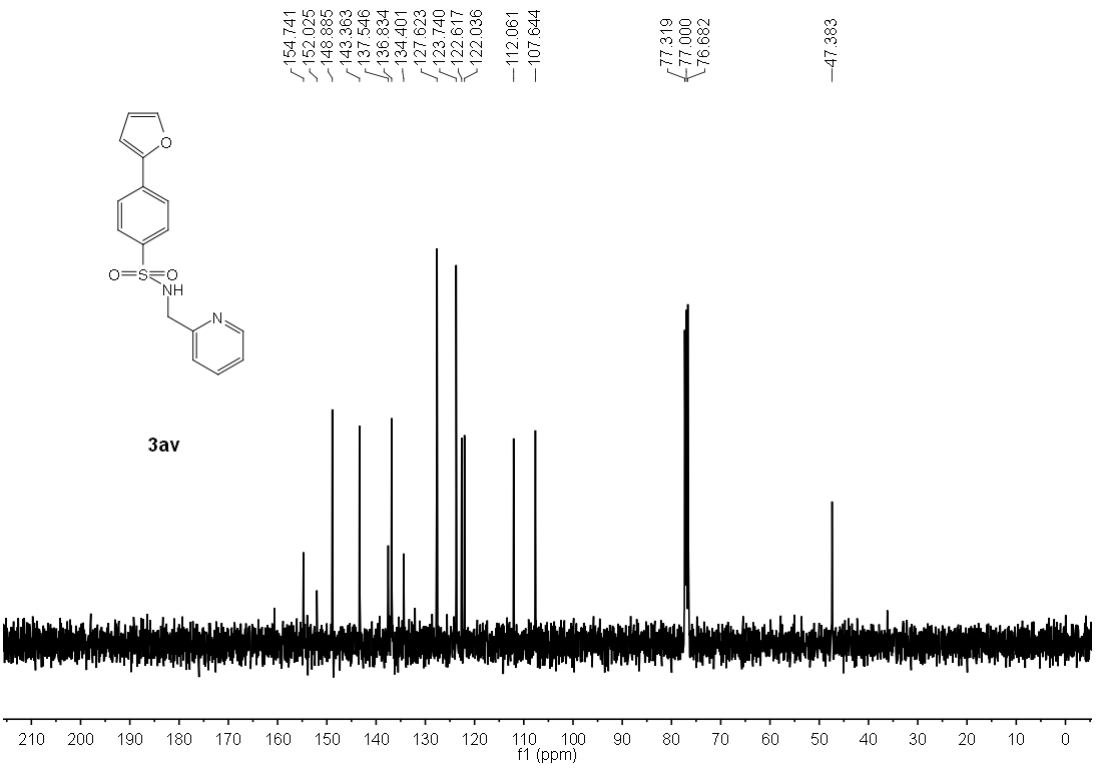
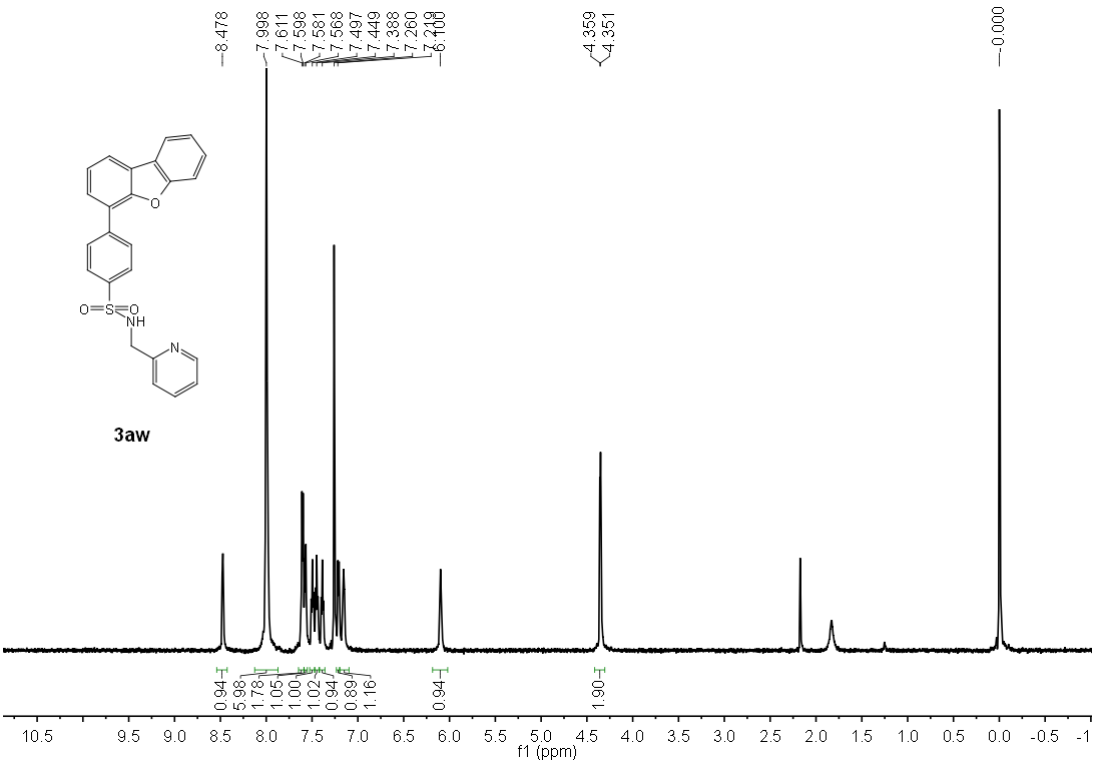
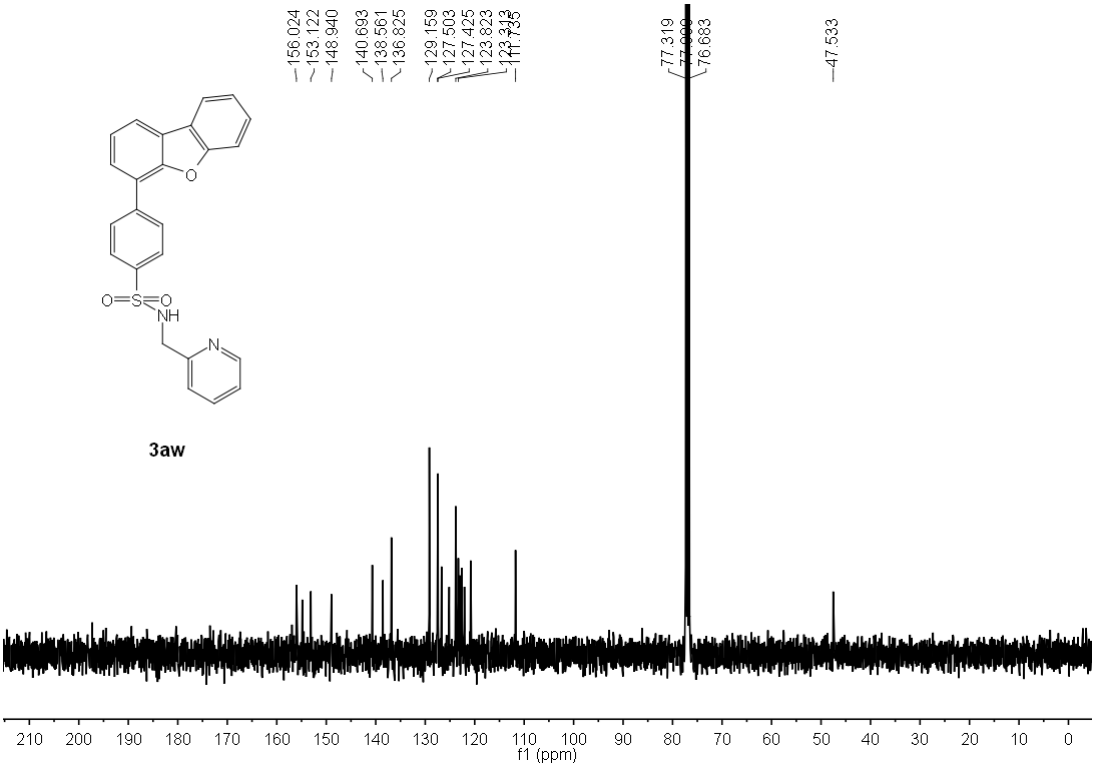
7.721
7.707
7.521
7.263
7.161
6.783
6.777
5.515
5.383
4.284
4.275
0.000
O
O=S=O
NH
N
3av
1.08
2.02
2.17
1.23
1.02
2.25
1.00
1.00
0.98
2.17
10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


154.741
152.025
148.885
143.363
137.546
136.834
134.401
127.623
123.740
122.617
122.036
112.061
107.644
77.319
77.000
76.682
47.383
O
O=S=O
NH
N
3av
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.478
7.998
7.611
7.598
7.581
7.568
7.497
7.449
7.388
7.260
7.219
6.100
4.359
4.351
0.000
O
O=S=O
NH
N
3aw
0.94
5.98
1.78
1.05
1.00
1.02
0.94
0.89
1.16
0.94
1.90
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1
f1 (ppm)


156.024
153.122
148.940
140.693
138.561
136.825
129.159
127.503
127.425
123.823
123.313
111.735
77.319
77.000
76.683
47.533
O
O=S=O
NH
N
3aw
210
200
190
180
170
160
150
140
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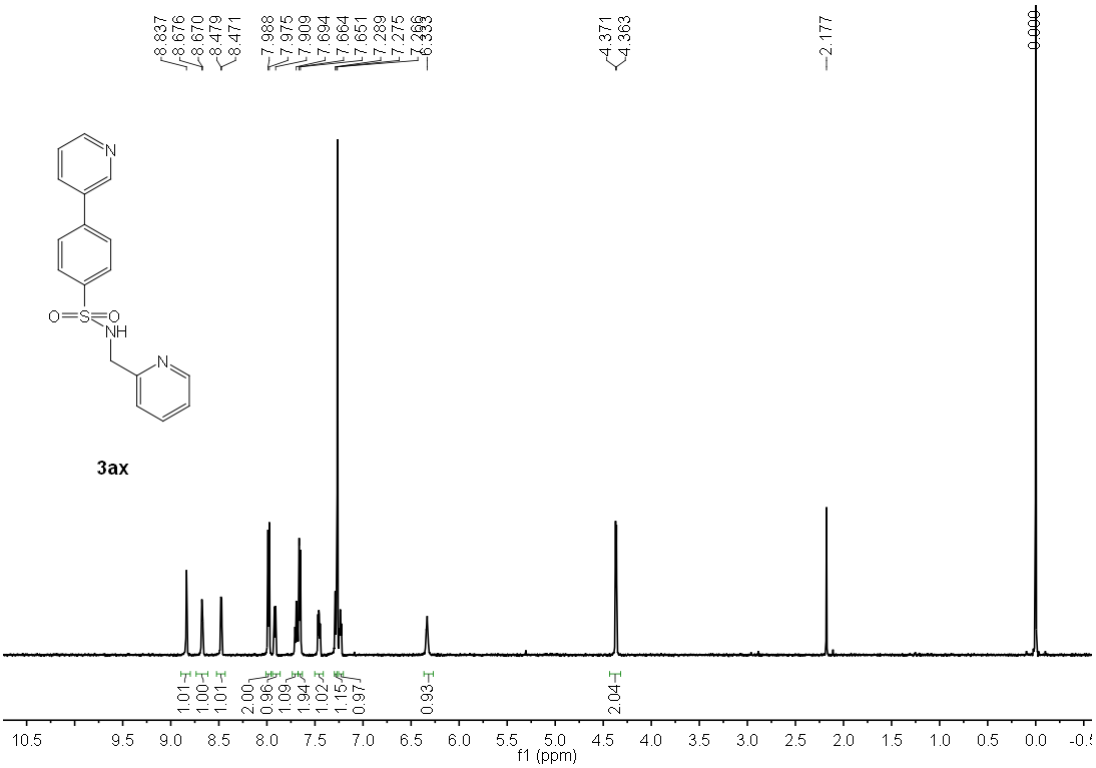
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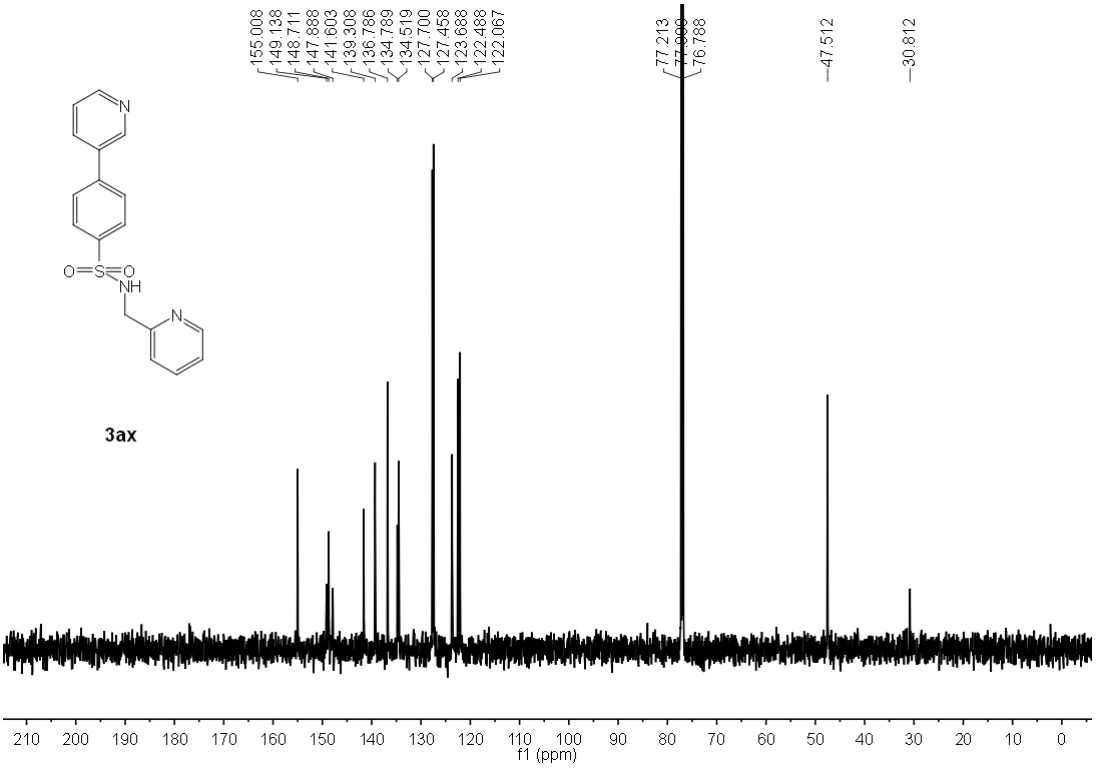
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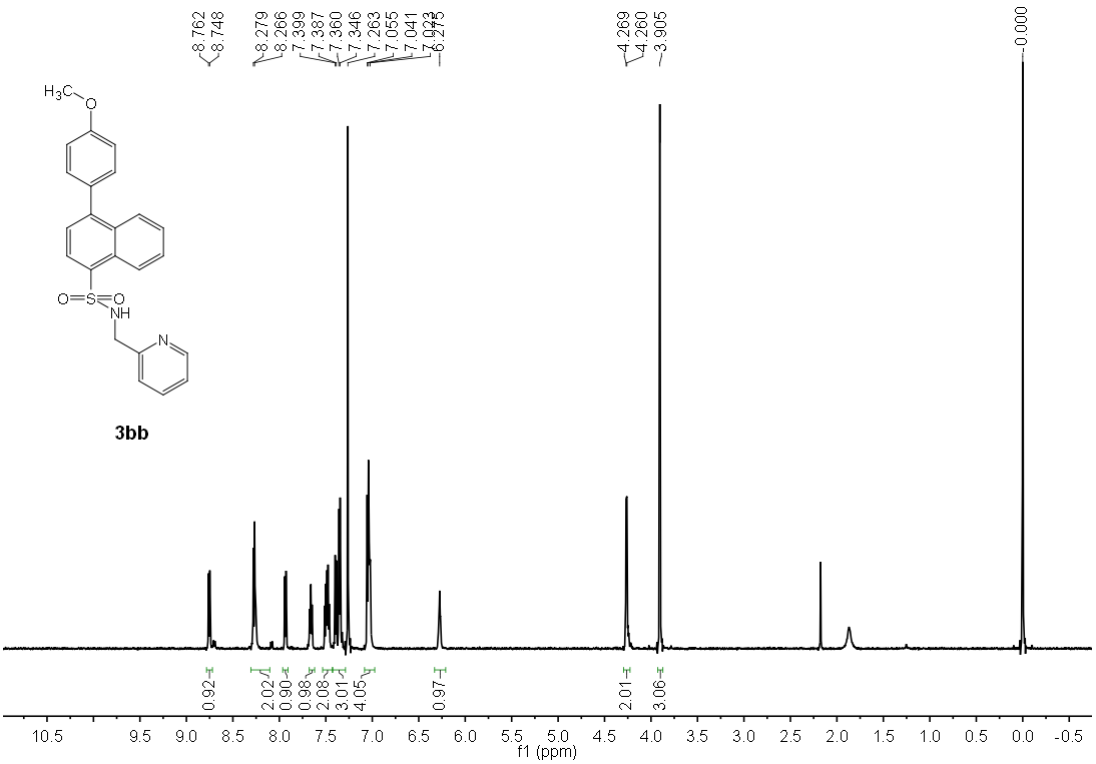
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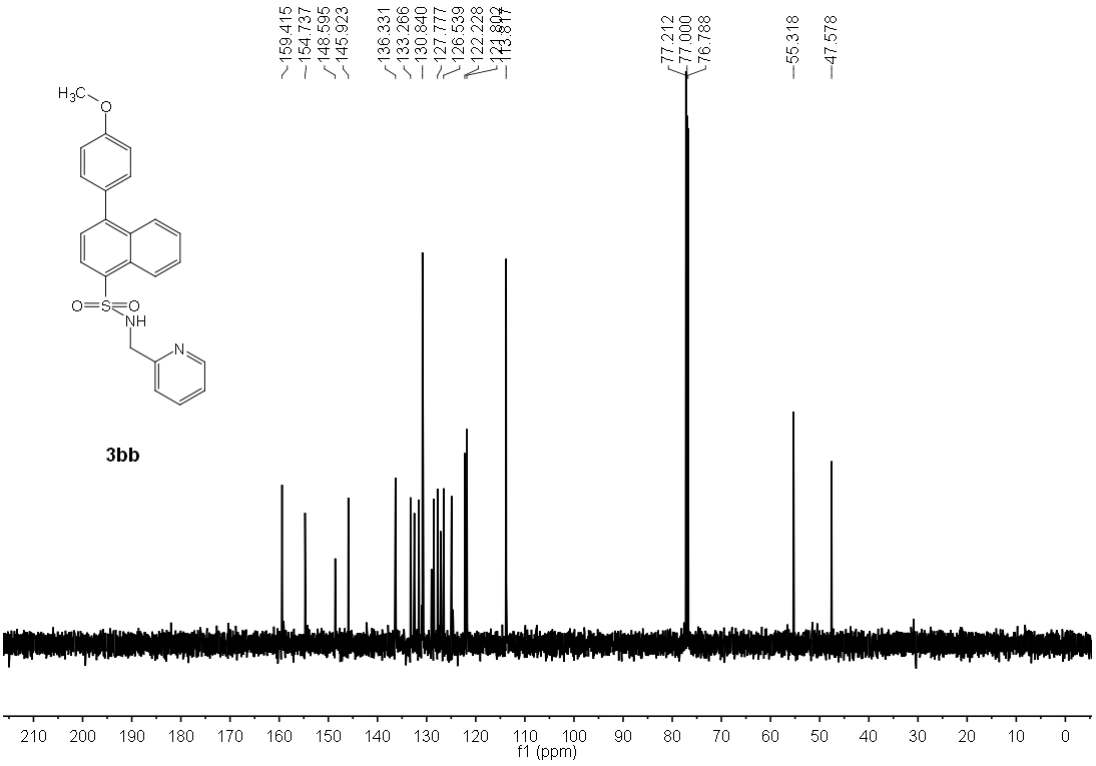
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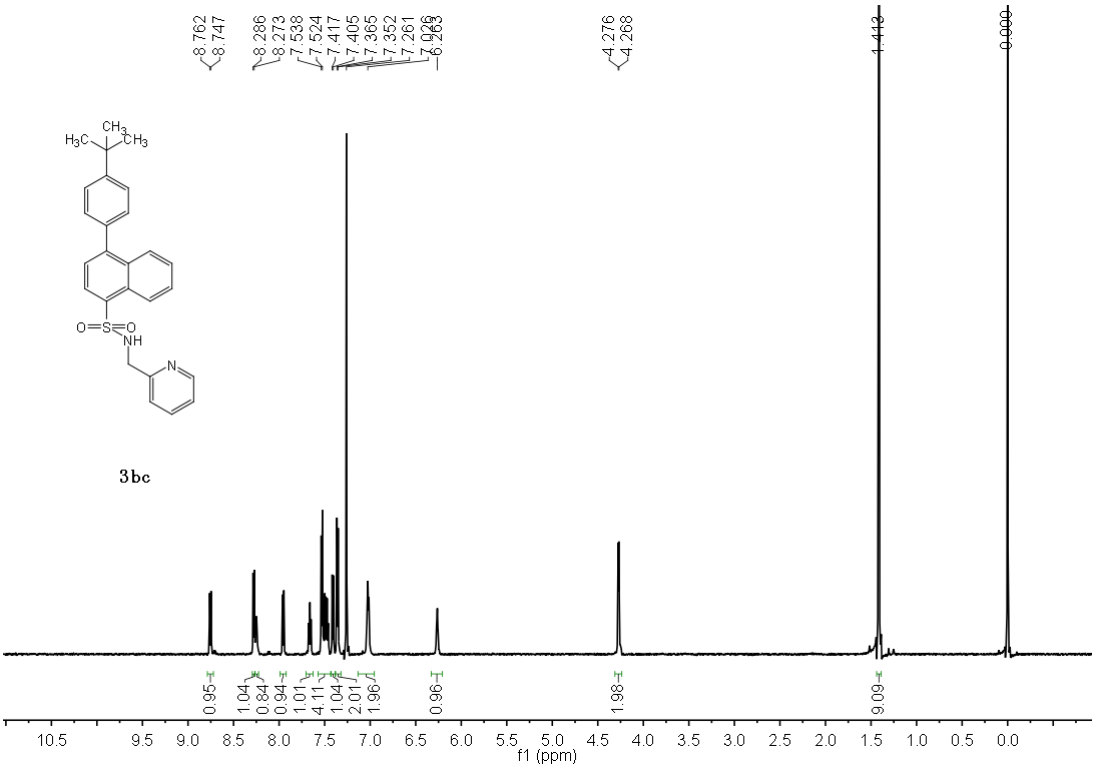
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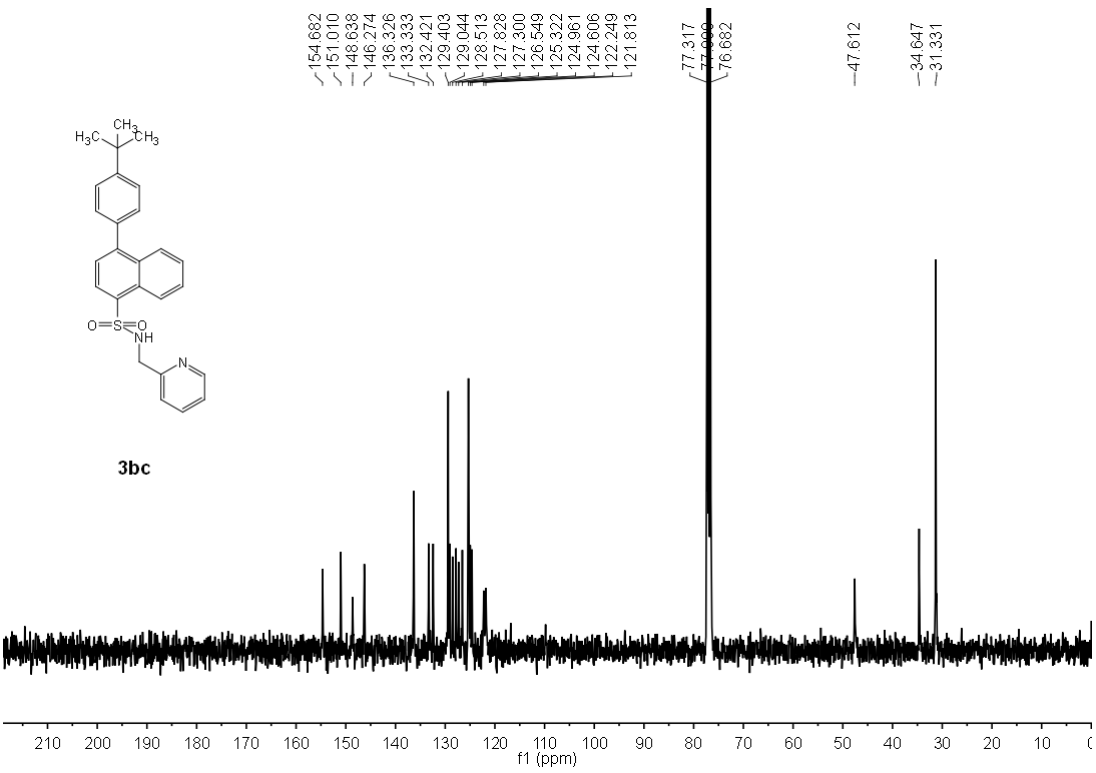
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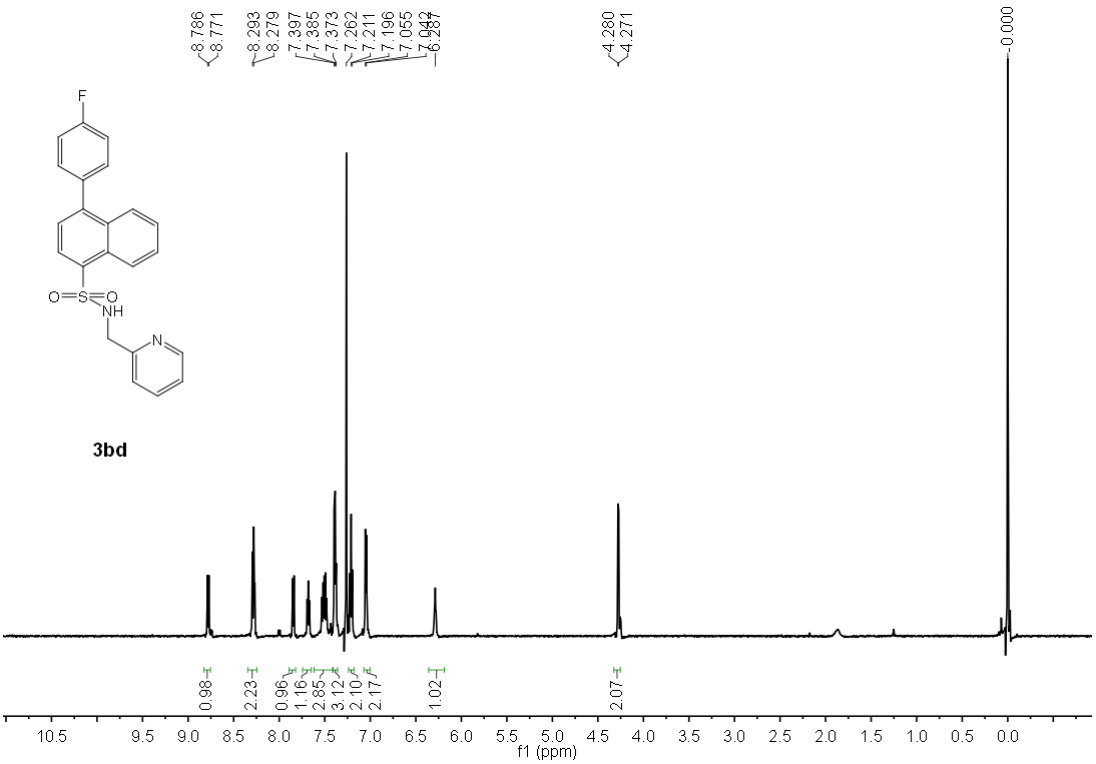
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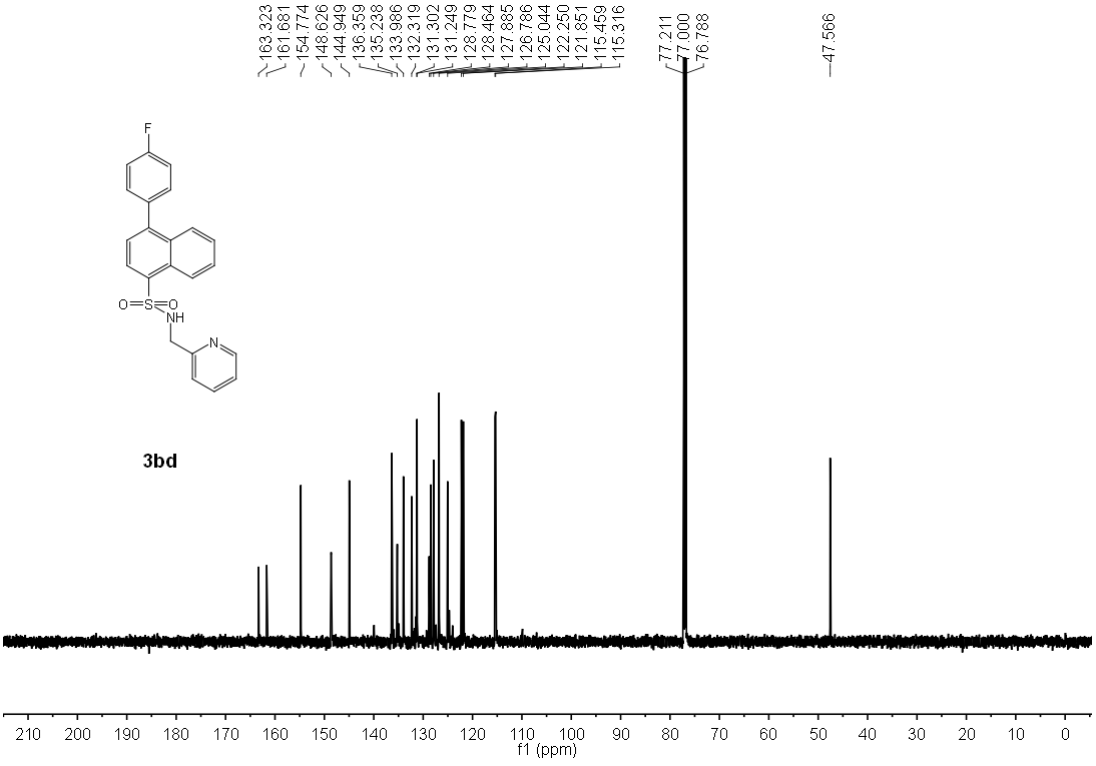
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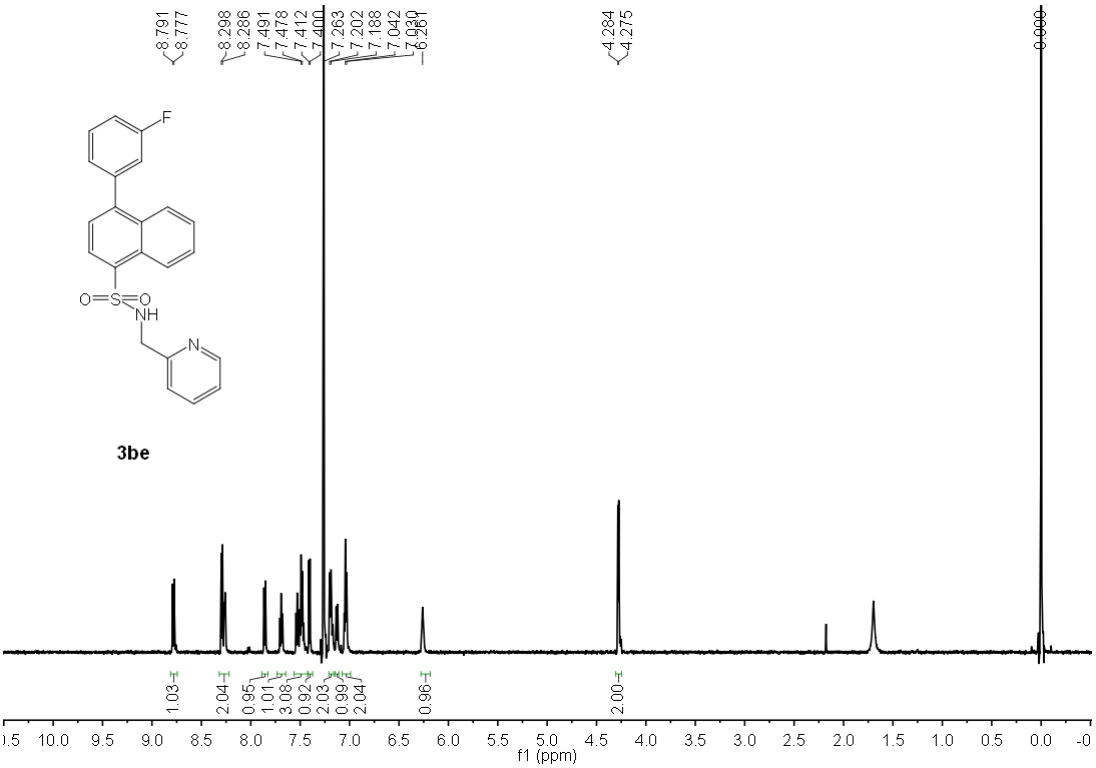
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4.275
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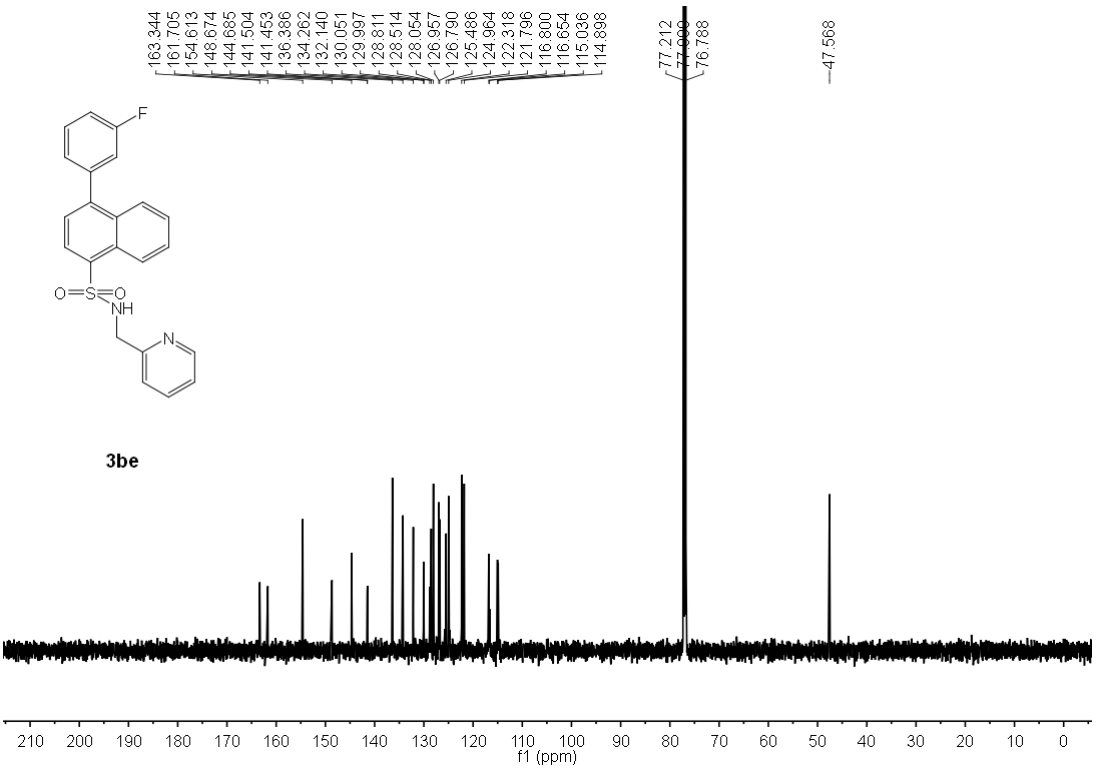
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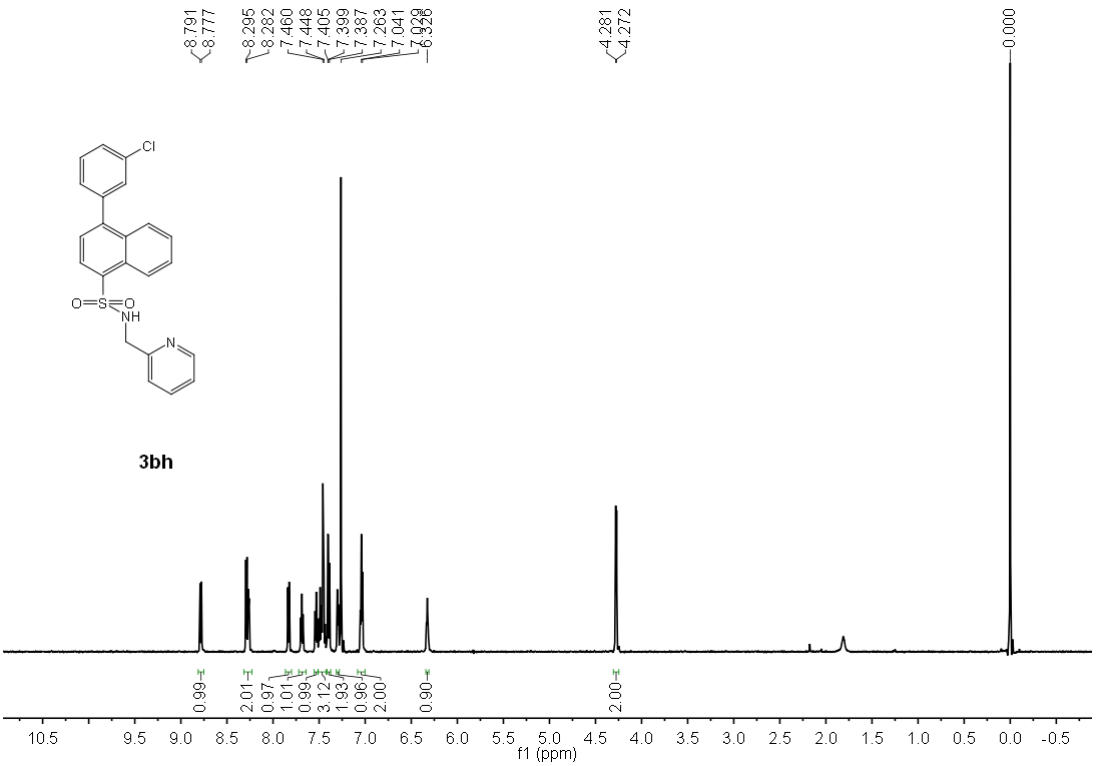
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2.01
0.97
1.01
0.99
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1.93
0.96
2.00
0.90
2.00
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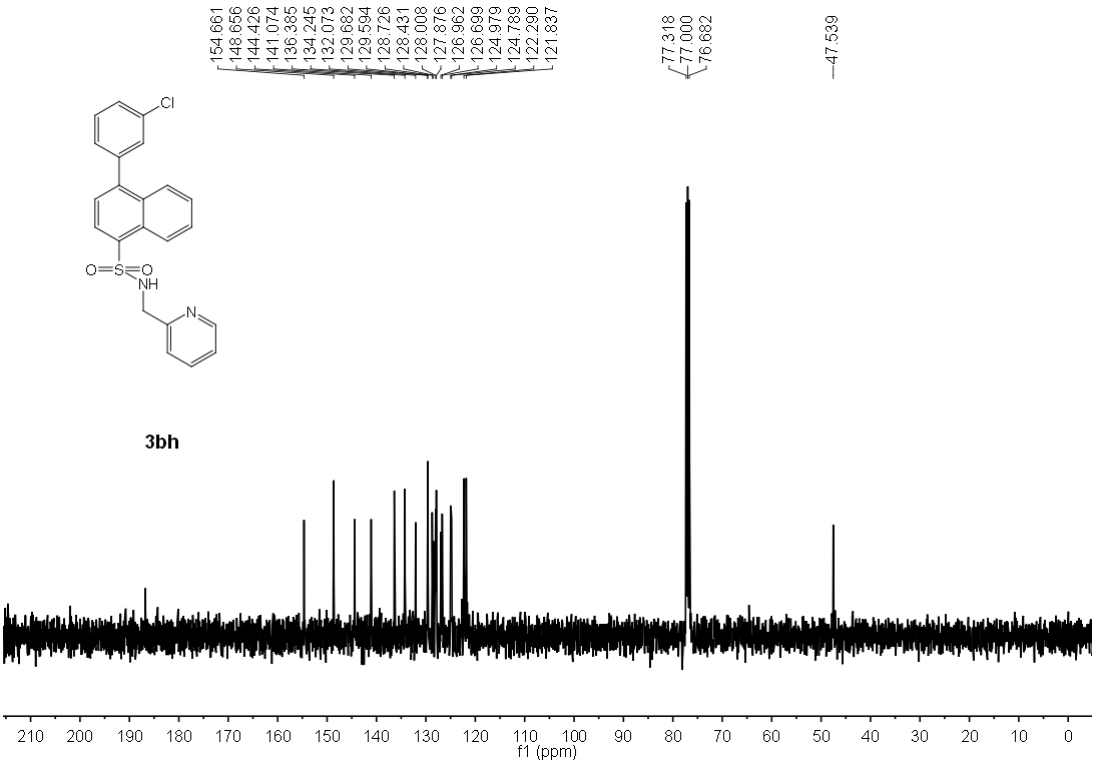
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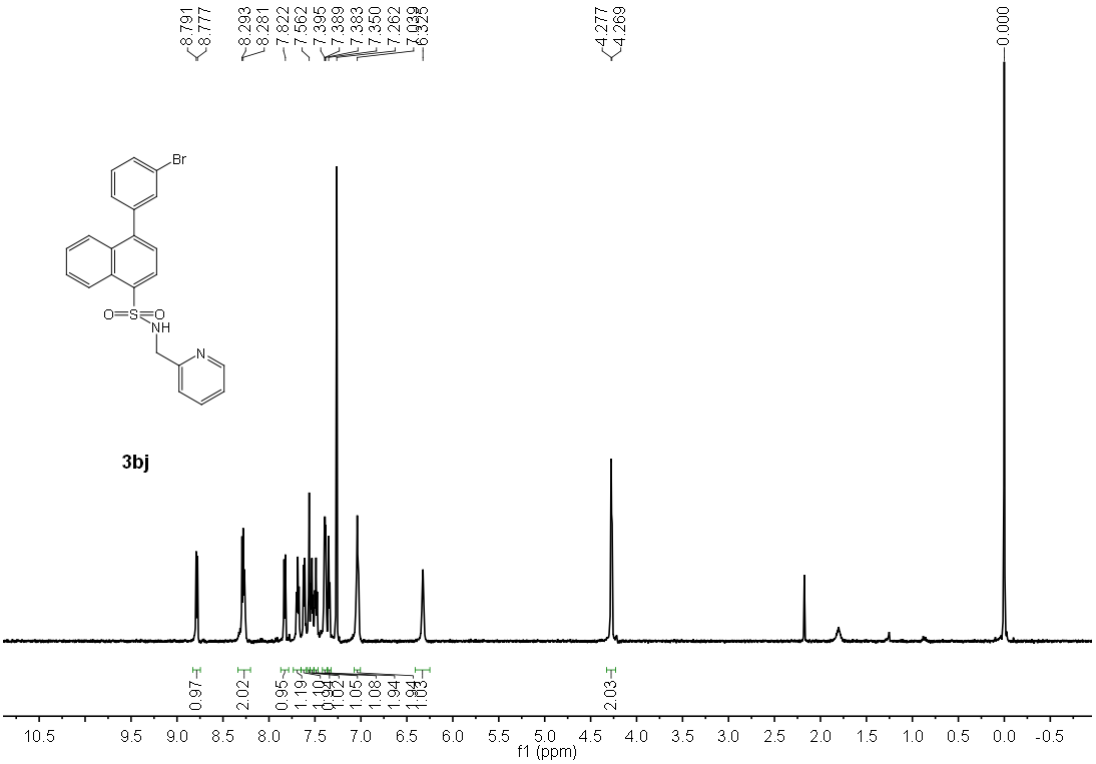
f1 (ppm)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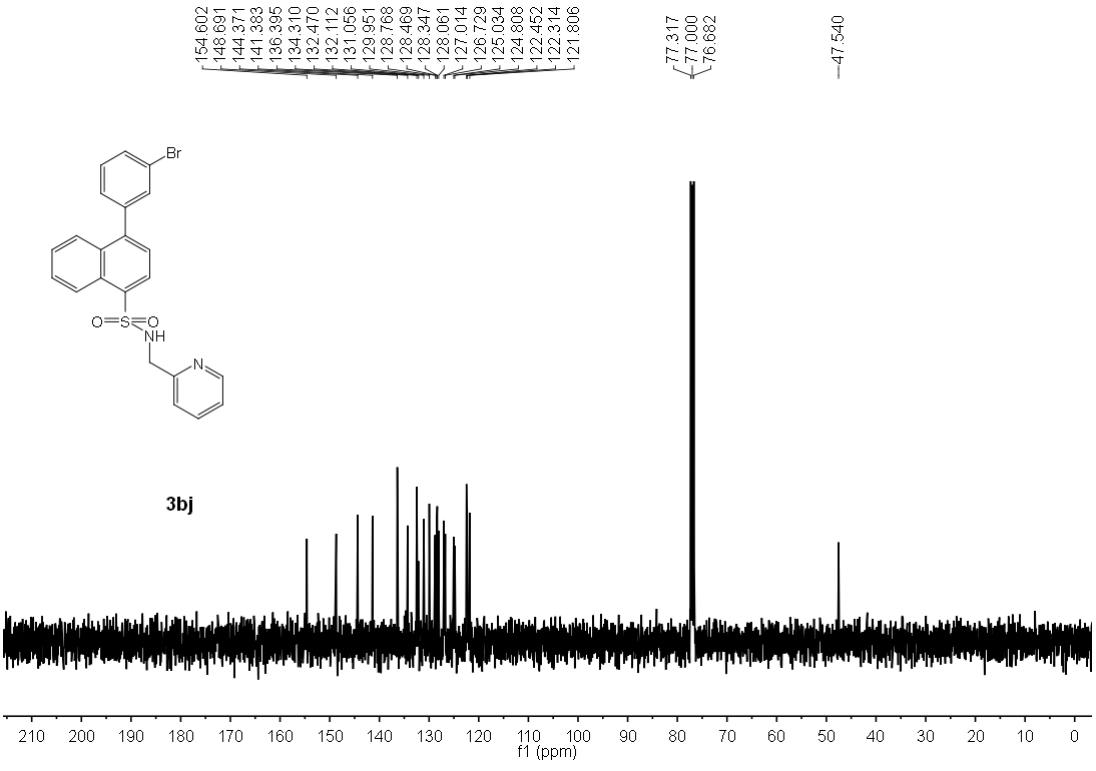
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O=S=O
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180
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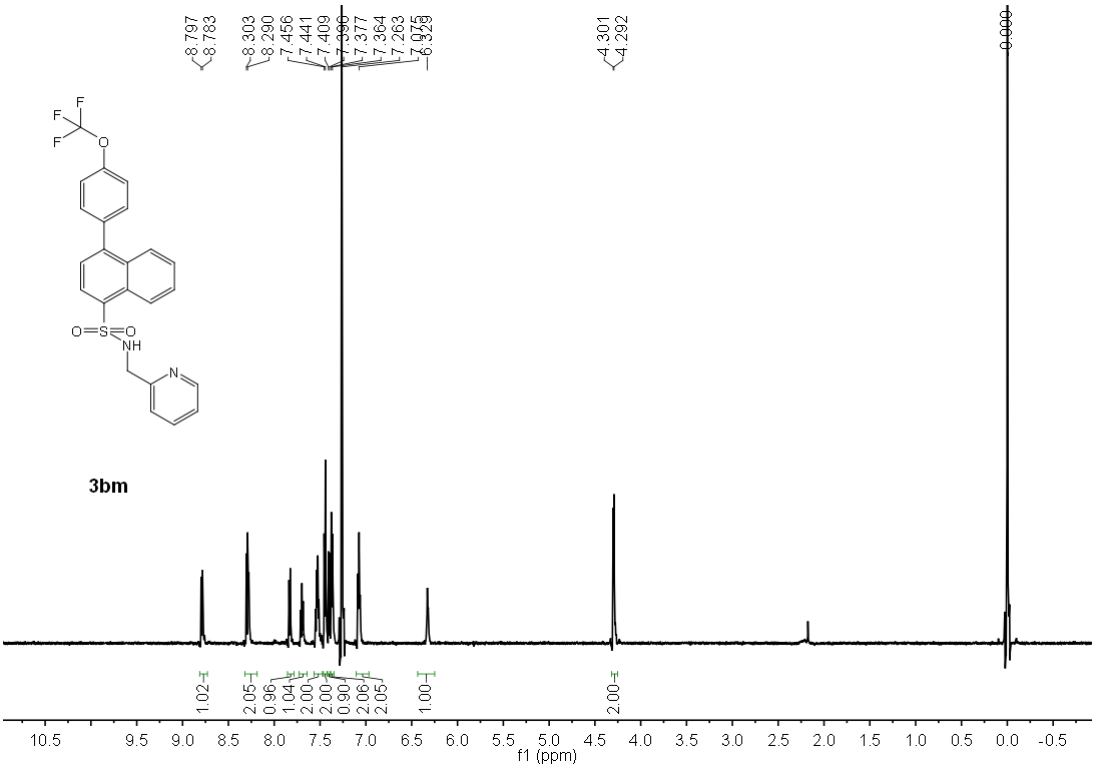
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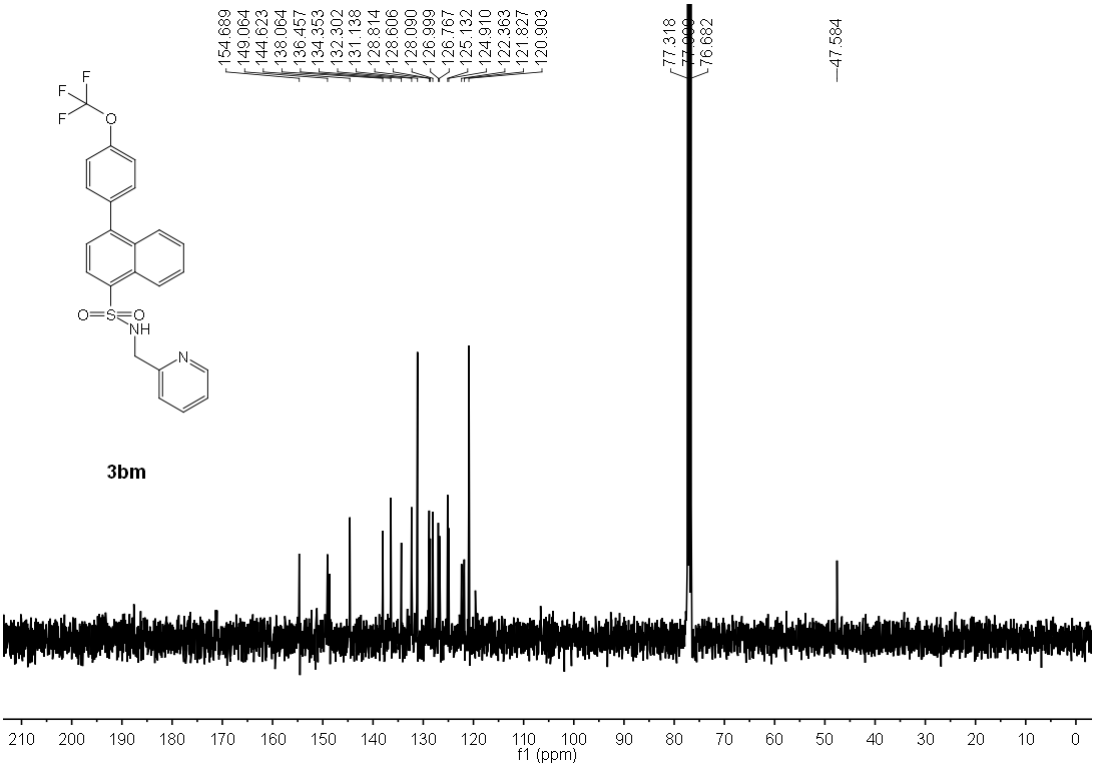
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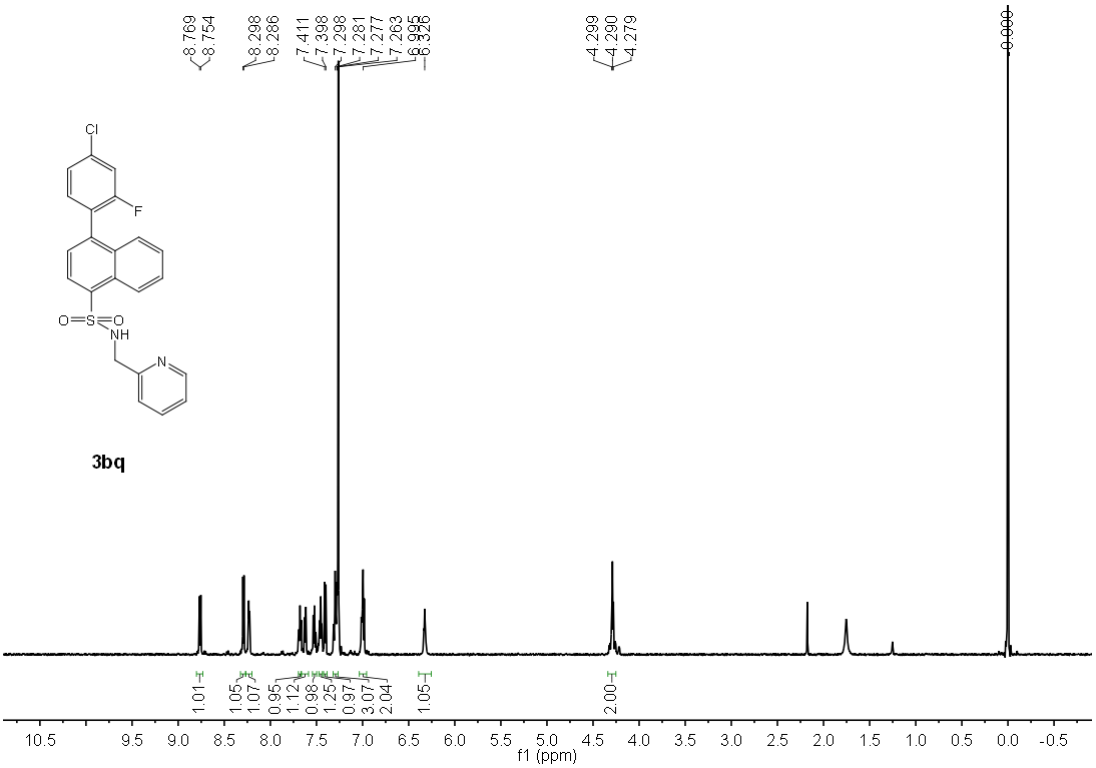
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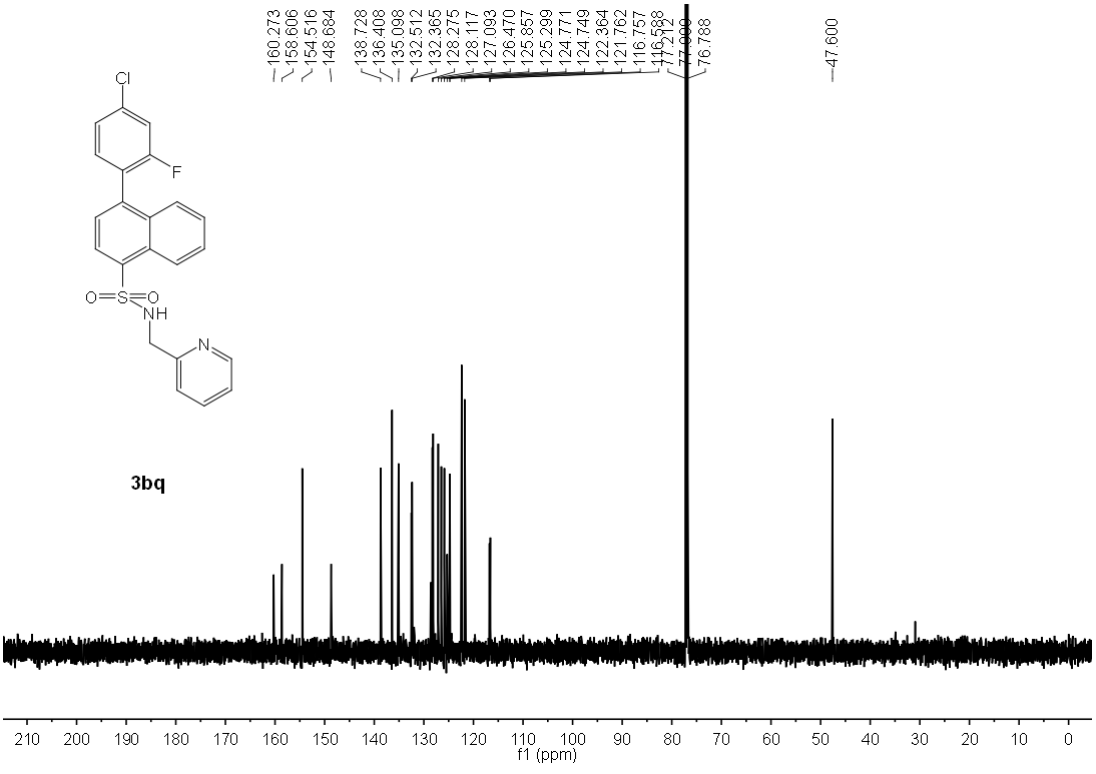
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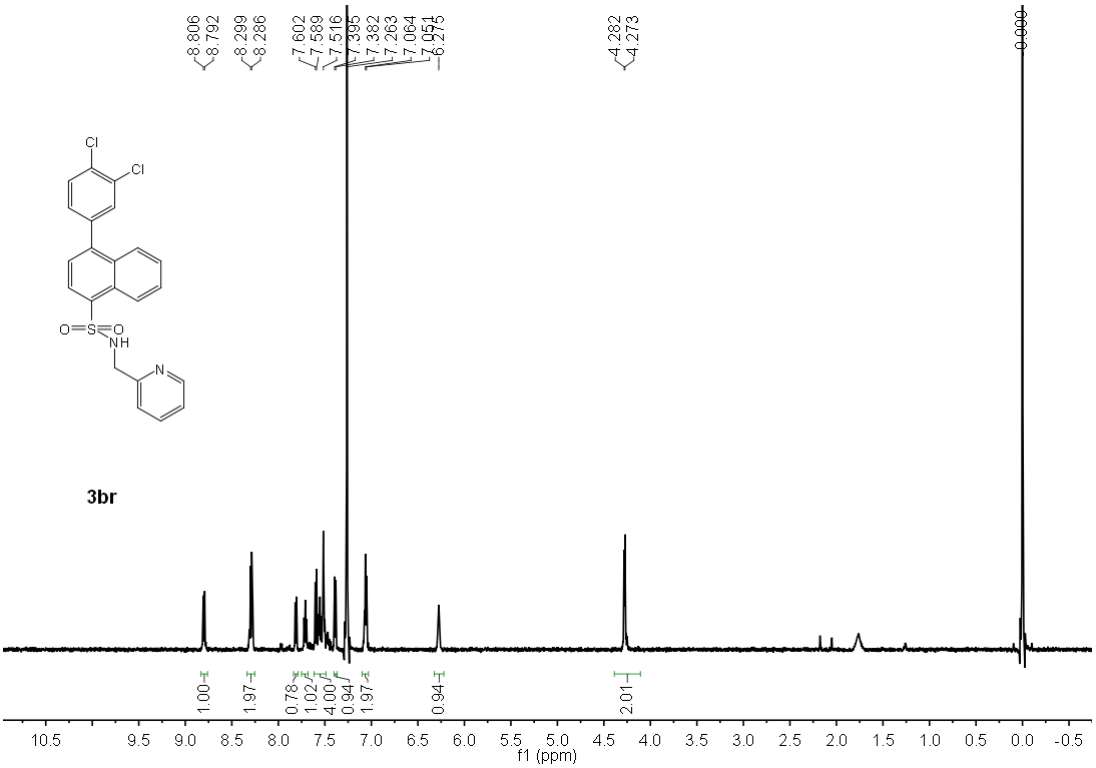
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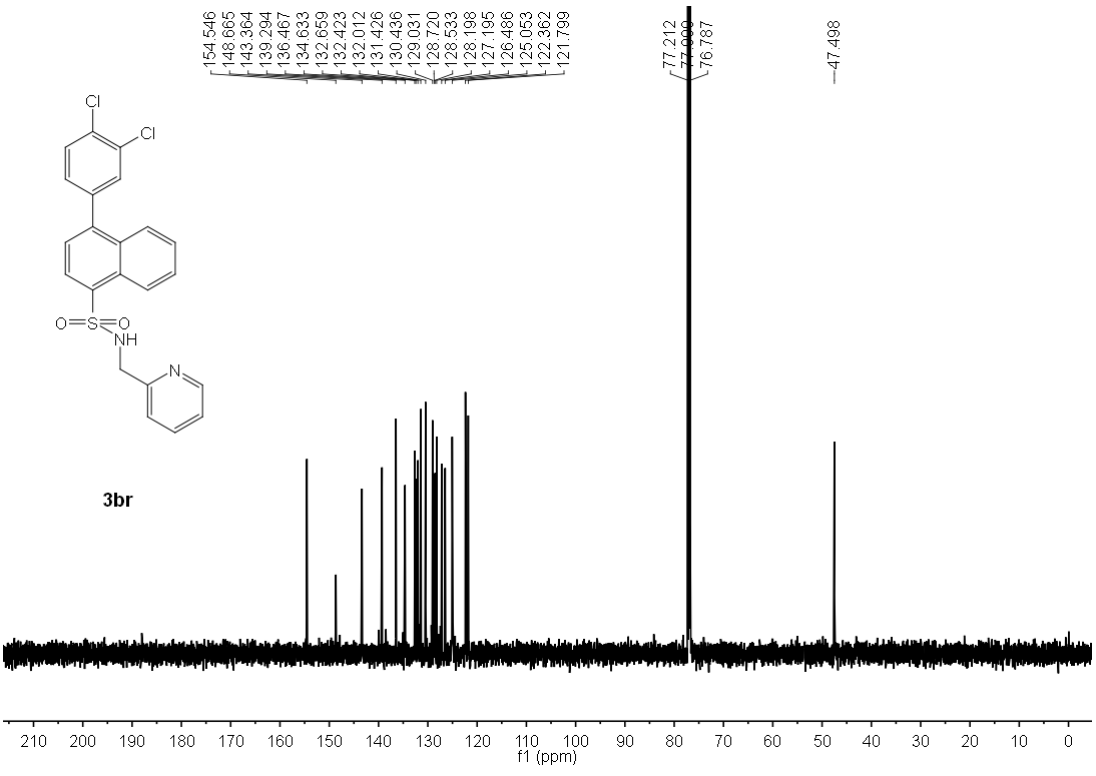
f1 (ppm)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125.053
122.362
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77.000
76.787
47.498
Cl
Cl
O=S=O
NH
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3br
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200
190
180
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160
150
140
130
120
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100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

7. PYL1 Computational Modeling

High-throughout screening was used to get compounds with potential bioactivity. Molecular docking studies were performed to simulate the binding of compounds to PYL1. Conformational optimizations were performed to obtain a total of 34 compounds (**3aa-3ax**, **3bb-3be**, **3bh**, **3bj**, **3bm**, **3bq**, **3br** and **pyrabactin**), all of which were used as starting structures for docking. The PYL1 crystal structure (PDB: 3NEG) was prepared as follows: 1) All waters and ligand were removed; 2) The polar hydrogen atoms were added; 3) A grid box for the binding site was created (center x = -58.325, center y = 41.754, center z = -20.937/ size x = 18, size y = 18, size z = 18). Docking calculations were performed on these compounds with AutoDock4.0.[2] The protein and ligand structures were prepared with AutoDock Tools.[3] The atomic Gasteiger-Huckel charges were assigned to the ligand and receptor. A total of 50 runs were launched for each compound. Most of the parameters for the docking calculation were set to the default values recommended by the software. Each docked structure was scored by the built-in scoring function and was clustered by 2 Å of RMSD criterions. Potency is an important criteria for assessing leads (or 'hits') discovered in virtual screening, however, potency alone is often a false prophet. Ligand efficiency is a way of normalizing the potency and molecular weight (MW) of a compound to provide a useful comparison between compounds with a range of MWs and activities. Comparison of lead compounds on the basis of ligand efficiency (binding energy per heavy atom) rather than the potency alone could be useful in deciding the potential for further optimization for particular 'hits' and chemical scaffolds.[4] Hence, in this study we use LE as a criteria for "lead" selection. According to the LE, compounds **3aa** and **3ai** should be the most feasible lead compounds (As shown in the following Table S1).

Table S1. Calculated Binding Free Energy and Ligand Efficiency of compounds

Rank	Compounds	Autodock4 binding energy(kcal/mol)	LE(kcal/mol/non-hydrogen atom)[a]
1	**3ai**	-8.89	0.3704
2	**pyrabactin**	-7.98	0.3627
3	**3aa**	-8.20	0.3565
4	**3ag**	-8.48	0.3533
5	**3ax**	-8.12	0.3530
6	**3bj**	-9.84	0.3514
7	**3av**	-7.72	0.3509
8	**3af**	-8.42	0.3508

9	**3ae**	-8.41	0.3504
10	**3at**	-8.76	0.3504
11	**3ar**	-8.75	0.3500
12	**3aj**	-8.39	0.3496
13	**3ad**	-8.38	0.3492
14	**3ao**	-8.71	0.3484
15	**3be**	-9.68	0.3457
16	**3ap**	-8.27	0.3446
17	**3bc**	-9.61	0.3432
18	**3aq**	-8.58	0.3432
19	**3bh**	-9.57	0.3418
20	**3ah**	-8.09	0.3371
21	**3ak**	-8.73	0.3358
22	**3br**	-9.67	0.3334
23	**3ab**	-8.32	0.3328
24	**3bd**	-9.27	0.3311
25	**3an**	-8.60	0.3308
26	**3as**	-8.22	0.3288
27	**3bb**	-9.24	0.3186
28	**3aw**	-9.05	0.3017
29	**3au**	-8.70	0.3000
30	**3bq**	-8.58	0.2959
31	**3al**	-7.89	0.2922
32	**3am**	-7.89	0.2818
33	**3ac**	-7.57	0.2804
34	**3bm**	-8.61	0.2691

[a] $LE == \Delta G/N_{non\text{-}hydrogen\ atoms}$

8. The experiment of chemical mediated root growth inhibition

The experimental procedure of root growth inhibition was the same as previous works.[5]

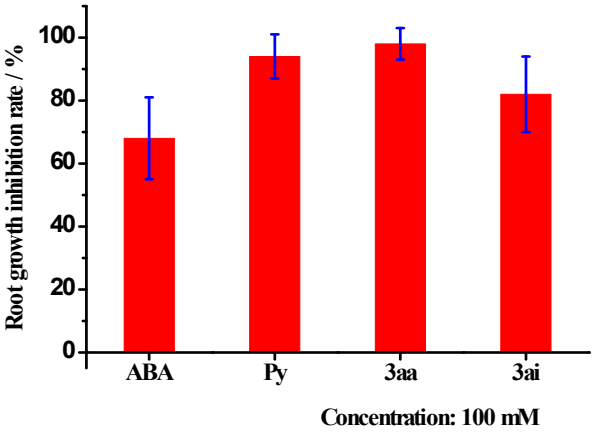

Fig. S1 The experiment of chemical mediated root growth inhibition

Compounds	ABA	Py	3aa	3ai
Root growth inhibition ratio (%)	68 ± 13	94 ± 7	98 ± 5	82 ± 12

References:

(1) D. C. Johnson and T. S. Widlanski, *Tetrahedron Lett*., 2004, **45**, 8483-8487.

(2) R. Huey, G. M. Morris, A. J. Olson and D. S. Goodsell, *J. Comput. Chem*., 2007, **28**, 1145–1152.

(3) M. F. Sanner, *Structure*, 2005, **13**, 447–462.

(4) (a) M. M. Hann, A. R. Leach and G. Harper, *J. Chem. Inf. Comput. Sci*., 2001, **41**, 856–864; (b) S. J. Teague, A. M. Davis, P. D. Leeson and T. *Oprea*, *Int. Ed. Engl*., 1999, **24**, 3743–3748; (c) T. I. Oprea, A. M. Davis, S. J. Teague and P.D. Leeson, *J. Chem. Inf. Comput. Sci*., 2001, **41**, 1308–1315; (d) A. L. Hopkins, C. R. Groom and A. Alex, *Drug. Discov. Today*., 2004, **10**, 430-431.

(5) (a) H. Fujii and J. K. Zhu *Proc. Natl. Acad. Sci. U.S.A.*, 2009, **106**, 8380-8385; (b) Y. Z. Du, M. X. Chen, Q. F. Chen, S. Xiao and M. L. Chye, *Plant. Cell. Environ.,* 2013, **36**, 300-314.