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Electronic Supplementary Information

Palladium-Catalyzed Remote *para*-C−H Activation of Arenes Assisted by a Recyclable Pyridine-Based Template

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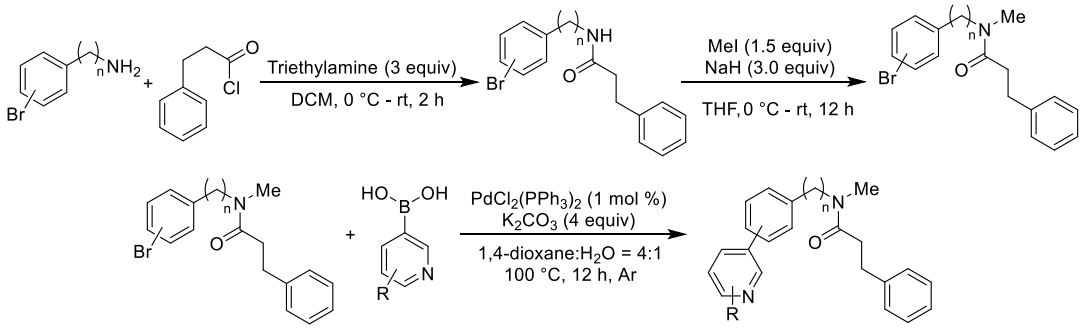
1 General Information

Unless otherwise noted, commercial available reagents were purchased from commercial suppliers (such as Strem, Alfa Aesar, J&K Chemical Co., Energy Chemical, Sinocompound and Adamas) and used as received. Solvents were generally dried over 4 Å molecular sieves. Hexafluoroisopropanol (HFIP) was dried over 4 Å molecular sieves and distilled before use. The reaction vessels used for C–H functionalization were 15 mL sealed tube or 50 mL Schlenk tube (Synthware). Purification of products was performed by flashchromatography (FC) using silica gel or preparative thin layer chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AVANCE III spectrometer (400 MHz and 101 MHz, respectively).Chemical shifts are reported parts per million (ppm) referenced to $CDCl_3$ (δ 7.26 ppm) or DMSO-d_6 (δ 2.50 ppm), tetramethylsilane (TMS, δ 0.00 ppm) for ^{1}H NMR; $CDCl_3$ (δ 77.16 ppm) or DMSO-d_6 (δ 39.52 ppm) for ^{13}C NMR. The following abbreviations (or combinations thereof) were used to explain multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, hept = heptaplet, m = multiplet, and br = broad. To distinguish, some ^{13}C NMR chemical shifts retain two decimal places. High-resolution mass spectra (HRMS) were obtained on an Impact II UHR-TOF mass spectrometry equipped with an ESI source from Bruker at Fujian Institute of Research on the Structure of Matter.

2 Experimental Section

2.1 Synthesis of Different Scaffolds.

General Procedure I



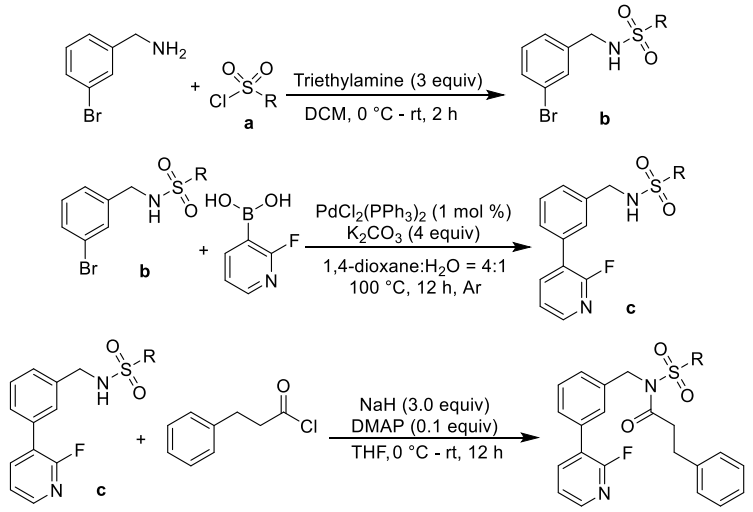
To a solution of (3-bromophenyl)methanamine (3.0 mmol), hydrocinnamoyl chloride (3.6 mmol) and triethylamine (9.0 mmol) in DCM (10 mL) at room temperature stirred for 6 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-2:1) as the eluent to give *N*-(3-bromobenzyl)-3-phenylpropanamide.

To a dry round bottom flask under nitrogen atmosphere was charged with *N*-(3-bromobenzyl)-3-phenylpropanamide (3.0 mmol) and NaH (60% dispersion in mineral oil, 9.0 mmol). The bottom was placed into an ice bath for 10 minutes followed by addition of anhydrous THF (15 mL). After stirred for 0.5 h at 0 °C, MeI (4.5 mmol) was added dropwise to the mixture. The reaction was allowed to warm to room temperate and stirred for 12 h. H_2O was slowly added (be careful!!) to quench the reaction. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give N-(3-bromobenzyl)-N-methyl-3-phenylpropanamide.

To a solution of *N*-(3-bromobenzyl)-*N*-methyl-3-phenylpropanamide (1.0 mmol), $PdCl_2(PPh_3)_2$ (0.01 mmol), pyridin-3-ylboronic acid (1.1 mmol) and K_2CO_3 (4.0 mmol) in 1,4-dioxane:H_2O = 4 mL: 1 mL under nitrogen atmosphere at 100 °C stirred for 12

h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (3:1-2:1) as the eluent to give the desired compound.

General Procedure II

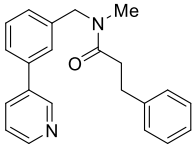


To a solution of (3-bromophenyl)methanamine (3.0 mmol), **a** (3.6 mmol) and triethylamine (9.0 mmol) in DCM (10 mL) at room temperature stirred for 6 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-2:1) as the eluent to give **b**.

To a solution of **b** (1.0 mmol), $PdCl_2(PPh_3)_2$ (0.01 mmol), (2-fluoropyridin-3-yl)boronic acid (1.1 mmol) and K_2CO_3 (4.0 mmol) in 1,4-dioxane : H_2O = 4 mL : 1 mL under nitrogen atmosphere at 100 °C stirred for 12 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (3:1-2:1) as the eluent to give **c**.

To a dry round bottom flask under nitrogen atmosphere was charged with **c** (1.0 mmol) and NaH (60% dispersion in mineral oil, 3.0 mmol). The bottom was placed into an ice bath for 10 minutes followed by addition of anhydrous THF (5 mL). After stirred for 0.5 h at 0 °C, hydrocinnamoyl chloride (1.2 mmol) was added dropwise to the mixture. The reaction was allowed to warm to room temperate and stirred for 12 h. H_2O

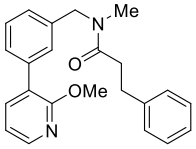
was slowly added (be careful!!) to quench the reaction. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give the desired compound.



***N*-methyl-3-phenyl-*N*-(3-(pyridin-3-yl)benzyl)propanamide (1a$_1$)**

The general procedure **I** was followed. Yield: 231 mg, (70 %).Two rotamers can be observed on the NMR spectrum and the ratio is about 65:35.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.88 (s, 0.61H), 8.85 (s, 0.38H), 8.65 – 8.62 (m, 1H), 7.89 (d, *J* = 8.0 Hz, 0.65H), 7.85 (d, *J* = 7.6 Hz, 0.37H), 7.56 – 7.43 (m, 3H), 7.41 – 7.37 (m, 1H), 7.35 – 7.27 (m, 4H), 7.25 – 7.14 (m, 2H), 4.71 (s, 1.29H), 4.58 (s, 0.69H), 3.11 – 3.05 (m, 2H), 3.03 (s, 1.22H), 2.93 (s, 1. 91H), 2.75 (td, *J* = 7.8, 2.3 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.4, 172.2, 148.5, 148.3, 148.03, 148.00, 141.1, 141.0, 138.4, 138.3, 138.0, 137.5, 136.2, 136.0, 134.4, 134.3, 129.6, 129.2, 128.31, 128.29, 128.26, 127.6, 126.6, 126.3, 126.01, 125.98, 125.7, 124.8, 123.50, 123.46, 53.0, 50.7, 35.1, 34.8, 34.7, 33.9, 31.3, 31.1. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{22}N_2ONa^+$ [M+Na$^+$] 353.1624, found 353.1625.

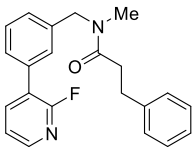


***N*-(3-(2-methoxypyridin-3-yl)benzyl)-*N*-methyl-3-phenylpropanamide (1a$_2$)**

The general procedure **I** was followed. Yield: 180 mg, (50 %). Two rotamers can be observed on the NMR spectrum and the ratio is about 58:42.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (td, *J* = 4.7, 1.9 Hz, 1H), 7.62 (dd, *J* = 7.3, 1.9 Hz, 0.62H), 7.58 (dd, *J* = 7.3, 1.9 Hz, 0.48H), 7.53 – 7.47 (m, 1H), 7.44 – 7.38 (m, 1.67H), 7.33 (s, 0.45H), 7.30 – 7.16 (m, 5.57H), 7.10 (d, *J* = 7.6 Hz, 0.43H), 6.99 (dd, *J* = 7.3, 5.0 Hz, 1H), 4.68 (s, 1.16H), 4.54 (s, 0.83H), 3.99 (s, 1.59H), 3.98 (s, 1.29H), 3.10 – 3.03 (m, 2H), 3.02 (s, 1.40H), 2.91 (s, 1.73H), 2.73 (q, *J* = 7.7 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.6, 172.2, 160.8, 160.7, 146.0, 145.8, 141.3, 141.2,

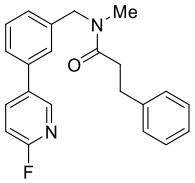
138.6, 138.5, 137.5, 137.3, 137.0, 136.5, 128.83, 128.80, 128.44, 128.41, 128.39, 128.37, 128.2, 127.2, 126.9, 126.10, 126.08, 125.3, 124.3, 124.0, 117.13, 117.12, 53.51, 53.49, 53.2, 50.8, 35.4, 34.9, 34.8, 34.1, 31.5, 31.3. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{24}N_2O_2Na^+$ [M+Na^+] 383.1730, found 383.1731.



***N*-(3-(2-fluoropyridin-3-yl)benzyl)-*N*-methyl-3-phenylpropanamide (1a$_3$)**

The general procedure **I** was followed. Yield: 296 mg, (85 %). Two rotamers can be observed on the NMR spectrum and the ratio is about 65:35.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 – 8.17 (m, 1H), 7.89 – 7.79 (m, 1H), 7.52 – 7.40 (m, 3H), 7.31 – 7.24 (m, 5H), 7.22 – 7.12 (m, 2H), 4.67 (s, 1.37H), 4.55 (s, 0.73H), 3.08 – 3.01 (m, 2H), 3.00 (s, 1H), 2.92 (s, 2H), 2.72 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.7, 172.4, 160.41 (d, J_{C-F} = 240.1 Hz), 160.36 (d, J_{C-F} = 239.9 Hz), 146.7 (d, J_{C-F} = 14.6 Hz), 146.4 (d, J_{C-F} = 14.7 Hz), 141.33, 141.26, 140.8 (d, J_{C-F} = 4.4 Hz), 140.7 (d, J_{C-F} = 4.3 Hz), 138.1, 137.3, 134.7 (d, J_{C-F} = 4.8 Hz), 134.3 (d, J_{C-F} = 5.0 Hz), 129.4, 129.0, 128.51, 128.49, 128.4 (d, J_{C-F} = 2.9 Hz), 128.2, 128.1, 127. 9 (d, J_{C-F} = 3.0 Hz), 126.6 (d, J_{C-F} = 3.0 Hz), 126.3, 126.2, 123. 9, 123.6, 123.3, 121.98, 121.95, 121.9, 53.2, 50. 9, 35.4, 35.02, 34.96, 34.1, 31.5, 31.4. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{21}FN_2ONa^+$ [M+Na^+] 371.1530, found 371.1531.

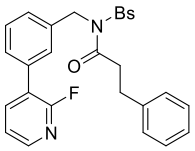


***N*-(3-(6-fluoropyridin-3-yl)benzyl)-*N*-methyl-3-phenylpropanamide (1a$_4$)**

The general procedure **I** was followed. Two rotamers can be observed on the NMR spectrum and the ratio is about 66:34.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 2.6 Hz, 0.57H), 8.27 (d, *J* = 2.6 Hz, 0.35H), 7.82 (dtd, *J* = 19.6, 8.0, 2.6 Hz, 2H), 7.38 – 7.28 (m, 2.64H), 7.21 – 7.01 (m, 6.54H), 6.90 (dd, *J* = 8.5, 2.9 Hz, 1H), 4.57 (s, 1.31H), 4.45 (s, 0.65H), 2.97 – 2.91 (m, 2H), 2.90 (s, 1.10H), 2.81 (s, 1.87H), 2.62 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.6, 172.4, 163.3 (d, J_{C-F} = 239.6 Hz), 163.2 (d, J_{C-F} = 239.4 Hz),

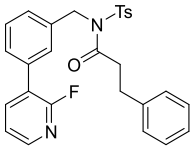
145. 9 (d, J_{C-F} = 14.7 Hz), 141.3, 141.2, 139.9 (d, J_{C-F} = 8.0 Hz), 139.8 (d, J_{C-F} = 7.9 Hz), 138.6, 137.8, 137.5, 137.1, 134.6 (d, J_{C-F} = 4.5 Hz), 134.4 (d, J_{C-F} = 4.5 Hz), 129. 9, 129.4, 128.51, 128.48, 128.46, 127.8, 126.7, 126.4, 126.2, 126.1, 126.0, 124. 9, 109.6 (d, J_{C-F} = 37.5 Hz), 109.5 (d, J_{C-F} = 37.5 Hz), 53.2, 50.9, 35.3, 35.01, 34.98, 34.2, 31.5, 31.3. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{21}FN_2ONa^+$ [M+Na^+] 371.1530, found 371.1531.



***N*-(3-(2-fluoropyridin-3-yl)benzyl)-3-phenyl-*N*-(phenylsulfonyl)propanamide (1a$_5$)**

The general procedure **II** was followed. Yield: 380 mg, (80 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (d, *J* = 4.2 Hz, 1H), 7.79 (t, *J* = 8.2 Hz, 1H), 7.72 (d, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.51 – 7.35 (m, 6H), 7.28 (d, *J* = 5.8 Hz, 1H), 7.18 – 7.10 (m, 3H), 6.99 (d, *J* = 7.0 Hz, 2H), 5.13 (s, 2H), 2.98 – 2.91 (m, 2H), 2.90 – 2.83 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.5, 160.4 (d, J_{C-F} = 240.6 Hz), 146.6 (d, J_{C-F} = 14.8 Hz), 140. 9 (d, J_{C-F} = 4.5 Hz), 140.2, 139.6, 137.3, 134.4 (d, J_{C-F} = 4.9 Hz), 133.9, 129.3, 129.2, 128.5, 128.4 (d, J_{C-F} = 3.4 Hz), 128.34, 128.27 (d, J_{C-F} = 2.5 Hz), 128.1, 127.7, 126.3, 123.6 (d, J_{C-F} = 28.1 Hz), 122.0 (d, J_{C-F} = 4.4 Hz), 49.3, 38.1, 30.7. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{23}FN_2O_3SNa^+$ [M+Na^+] 497.1306, found 497.1306.

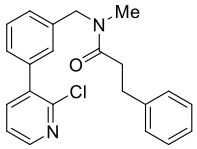


***N*-(3-(2-fluoropyridin-3-yl)benzyl)-3-phenyl-*N*-tosylpropanamide (1a$_6$)**

The general procedure **II** was followed. Yield: 342 mg, (70 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.20 (dt, *J* = 4.9, 1.6 Hz, 1H), 7.82 – 7.77 (m, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.53 – 7.45 (m, 2H), 7.44 – 7.36 (m, 2H), 7.29 – 7.22 (m, 3H), 7.19 – 7.11 (m, 3H), 7.03 – 6.96 (m, 2H), 5.12 (s, 2H), 2.97 – 2.93 (m, 2H), 2.89 – 2.85 (m, 2H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.5, 160.4 (d, J_{C-F} = 240.1 Hz), 146.5 (d, J_{C-F} = 14.7 Hz), 145.1, 140.8 (d, J_{C-F} = 4.4 Hz), 140.2, 137.4, 136.6, 134.3 (d, J_{C-F} = 5.0 Hz), 129. 9, 129.1, 128.5, 128.32, 128.28, 128.2 (d, J_{C-F} = 2.4 Hz), 128.1, 127.7, 126.2, 123.6 (d, J_{C-F} = 28.2 Hz), 121.9 (d, J_{C-F} = 4.4 Hz), 49.3,

38.0, 30.7, 21.7. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{25}FN_2O_3S$ Na^+ [M+Na^+] 511.1462, found 511.1463.

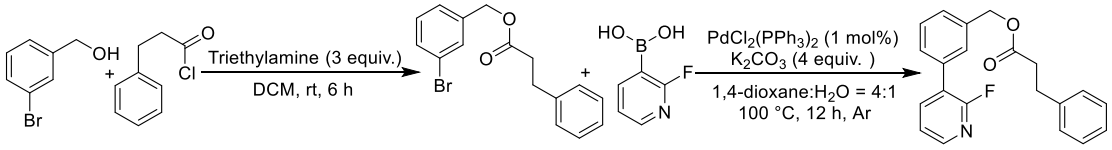


***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-methyl-3-phenylpropanamide (1a7)**

The general procedure **I** was followed. Yield: 218 mg, (60 %). Two rotamers can be observed on the NMR spectrum and the ratio is about 64:36.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (td, *J* = 5.1, 1.9 Hz, 1H), 7.58 (dd, *J* = 7.6, 2.0 Hz, 0.69H), 7.53 (dd, *J* = 7.5, 2.0 Hz, 0.42H), 7.33 (t, *J* = 7.8 Hz, 1H), 7.29 – 7.12 (m, 7H), 7.11 – 7.05 (m, 2H), 4.58 (s, 1.29H), 4.45 (s, 0.69H), 2.97 – 2.91 (m, 2H), 2.91 (s, 1.32H), 2.82 (s, 1. 92H), 2.62 (td, *J* = 7.8, 7.4, 2.5 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.7, 172.5, 149.70, 149.67, 148.7, 148.5, 141.34, 141.29, 139.8, 139.6, 138.2, 137.8, 137.7, 137.0, 136.8, 136.5, 129.1, 128.8, 128.7, 128.6, 128.53, 128.51, 128.49, 128.3, 128.1, 127.1, 126.3, 126.2, 122.7, 53.2, 50.8, 35.4, 35.1, 35.0, 34.2, 31.6, 31.4. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{21}ClN_2ONa^+$ [M+Na^+] 387.1235, found 387.1235.

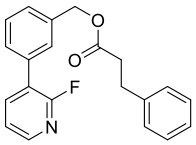
Preparation of 3-(2-fluoropyridin-3-yl)benzyl 3-phenylpropanoate:



To a solution of (3-bromophenyl)methanol (2.0 mmol), hydrocinnamoyl chloride (2.4 mmol) and triethylamine (6.0 mmol) in DCM (10 mL) at room temperature stirred for 6 h . Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-2:1) as the eluent to give 3-bromobenzyl 3-phenylpropanoate.

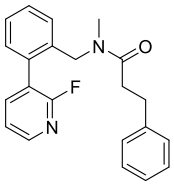
To a solution of 3-bromobenzyl 3-phenylpropanoate (1.0 mmol), $PdCl_2(PPh_3)_2$ (0.01 mmol), (2-fluoropyridin-3-yl)boronic acid (1.1 mmol) and K_2CO_3 (4.0 mmol) in 1,4-dioxane:H_2O = 4 mL: 1 mL under nitrogen atmosphere at 100 ℃ stirred for 12 h . Then the crude reaction mixture was extracted with EtOAc and water, the combined

organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give 3-(2-fluoropyridin-3-yl)benzyl 3-phenylpropanoate.



3-(2-fluoropyridin-3-yl)benzyl 3-phenylpropanoate (**1a**[9])

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.24 (d, *J* = 3.8 Hz, 1H), 7. 90 – 7.85 (m, 1H), 7.59 – 7.51 (m, 2H), 7.48 (t, *J* = 7.6 Hz, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.32 – 7.27 (m, 3H), 7.24 – 7.16 (m, 3H), 5.20 (s, 2H), 3.02 (t, *J* = 7.7 Hz, 2H), 2.74 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.7, 160.4 (d, J_{C-F} = 240.3 Hz), 146.6 (d, J_{C-F} = 14.7 Hz), 140.8, 140.3, 136.6, 134.2 (d, J_{C-F} = 4.9 Hz), 129.0, 128.7 (d, J_{C-F} = 3.1 Hz), 128.6 (d, J_{C-F} = 2.9 Hz), 128.5, 128.31, 128.27, 126.3, 123.5 (d, J_{C-F} = 28.3 Hz), 121.9 (d, J_{C-F} = 4.4 Hz), 66.0, 35.8, 30.9. HRMS (m/z, ESI-TOF): Calcd for $C_{21}H_{18}FNO_2Na^+$ [M+Na^+] 358.1214, found 358.1215.

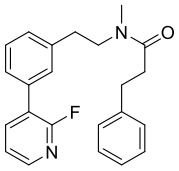


***N*-(2-(2-fluoropyridin-3-yl)benzyl)-*N*-methyl-3-phenylpropanamide** (**1a**[10])

The general procedure **I** was followed. Yield: 244 mg, (70 %). Two rotamers can be observed on the NMR spectrum and the ratio is about 61:39.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.25 (dd, *J* = 13.5, 4.8 Hz, 1H), 7.73 – 7.59 (m, 1H), 7.43 – 7.08 (m, 10H), 4.52 (s, 1.23H), 4.27 (br, 0.72H), 2.93 (t, *J* = 7.9 Hz, 2H), 2.88 (s, 1.12H), 2.72 (s, 1.72H), 2.80 – 2.56 (m, 1.18H), 2.54 – 2.47 (m, 0.85H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.8, 172.2, 160.3(d, J_{C-F} = 237.7 Hz), 160.1 (d, J_{C-F} = 237.9 Hz), 147.5 (d, J_{C-F} = 14.4 Hz), 147.0 (d, J_{C-F} = 14.3 Hz), 142.0 (d, J_{C-F} = 4.4 Hz), 141.8 (d, J_{C-F} = 4.4 Hz), 141.3, 141.1, 135.6, 135.0, 133.3 (d, J_{C-F} = 3.5 Hz), 132.7 (d, J_{C-F} = 3.3 Hz), 130.8, 130.5, 129.4, 129.1, 128.50, 128.49, 128.45, 128.1, 127.8, 127.4, 126.2, 126.1, 125.9, 122.8 (d, J_{C-F} = 32.2 Hz), 122.3 (d, J_{C-F} = 32.5 Hz), 121.9 (d, J_{C-F} = 4.3 Hz), 121.6 (d, J_{C-F} = 4.4 Hz), 51.1 (d, J_{C-F} = 4.1 Hz), 48.4 (d, J_{C-F}

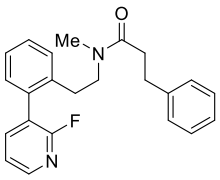
= 2.4 Hz), 35.1, 34.8, 34.6, 34.1, 31.5, 31.2. HRMS (m/z, ESI-TOF): Calcd for $C_{22}H_{21}FN_2ONa^+$ [M+Na^+] 371.1530, found 371.1530.



***N*-(3-(2-fluoropyridin-3-yl)phenethyl)-*N*-methyl-3-phenylpropanamide (1a$_{11}$)**

The general procedure **I** was followed. Yield: 272 mg, (75 %).Two rotamers can be observed on the NMR spectrum and the ratio is about 57:43.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.27 – 8.25 (m, 1H), 7.97 – 7.92 (m, 0.57H), 7.89 – 7.84 (m, 0.44H), 7.55 – 7.42 (m, 3H), 7.39 – 7.27 (m, 5H), 7.20 (dd, *J* = 27.2, 7.5 Hz, 2H), 3.77 – 3.66 (m, 1.14H), 3.58 (t, *J* = 7.0 Hz, 0.85H), 3.07 – 2.95 (m, 3.69H), 2.93 – 2.87 (m, 3.40H), 2.67 (t, *J* = 7.9 Hz, 1.14H), 2.45 – 2.36 (m, 0.87H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 172.1, 160.4 (d, J_{C-F} = 240.1 Hz), 160.3 (d, J_{C-F} = 240.3 Hz), 146.5, 146.4, 146.2, 141.4 (d, J_{C-F} = 2.9 Hz), 140.8 (d, J_{C-F} = 4.5 Hz), 139.8, 138. 9, 134.4 (d, J_{C-F} = 5.1 Hz), 134.1 (d, J_{C-F} = 4.8 Hz), 129.3 (d, J_{C-F} = 2.9 Hz), 129.22 (d, J_{C-F} = 2.9 Hz), 129.17, 129.0, 128.94, 128.90, 128.47, 128.45, 128.42, 128.36, 127.3 (d, J_{C-F} = 3.0 Hz), 126. 9 (d, J_{C-F} = 3.0 Hz), 126.1, 126.0, 124.0, 123.7, 123.4, 121.94 (d, J_{C-F} = 4.4 Hz), 121.88 (d, J_{C-F} = 4.5 Hz), 51.4, 49.9, 36.0, 35.5, 34.71, 34.70, 33.6, 31.4, 31.2. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{23}FN_2O$ Na^+ [M+Na^+] 385.1687, found 385.1686.

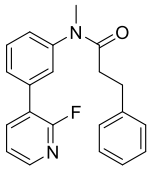


***N*-(2-(2-fluoropyridin-3-yl)phenethyl)-*N*-methyl-3-phenylpropanamide (1a$_{12}$)**

The general procedure **I** was followed. Yield: 236 mg, (65 %).Two rotamers can be observed on the NMR spectrum and the ratio is about 52:48.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (d, *J* = 4.7 Hz, 0.52H), 8.16 (d, *J* = 4.7 Hz, 0.48H), 7.79 (t, *J* = 9.1 Hz, 0.53H), 7.60 (t, *J* = 7.7 Hz, 0.51H), 7.45 – 7.27 (m, 6H), 7.24 – 7.17 (m, 3H), 7.14 (d, *J* = 7.5 Hz, 1H), 3.46 (t, *J* = 8.0 Hz, 1H), 3.27 (t, *J* = 7.2 Hz, 1H), 2.94 (t, *J* = 8.0 Hz, 1H), 2.82 (t, *J* = 8.0 Hz, 1H), 2.77 – 2.72 (m, 3.54H), 2.67

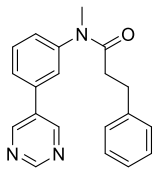
(s, 1.56H), 2.55 (t, *J* = 7.6 Hz, 1H), 2.16 (t, *J* = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 171.8, 160.5 (d, *J* = 238.8 Hz), 160.2 (d, *J* = 238.7 Hz),147.2 (d, *J* = 14.3 Hz), 147.0 (d, *J* = 14.2 Hz), 142.4 (d, *J* = 4.6 Hz), 142.0 (d, *J* = 4.4 Hz), 141.41, 141.37, 137.5, 136.7, 133.8 (d, *J* = 3.7 Hz), 133.6 (d, *J* = 3.6 Hz), 130.7, 130.4, 129.97, 129.95, 129.2, 128.9, 128.52, 128.48, 128.45, 128.4, 127.2, 126.6, 126.12, 126.09, 123.5 (d, *J* = 32.2 Hz), 123.2 (d, *J* = 32.3 Hz), 121.7 (d, *J* = 4.3 Hz), 121.6 (d, *J* = 4.3 Hz), 50.7, 49.0, 35.6, 35.4, 34.3, 33.4, 32.1, 31.3, 31.2, 30.8. HRMS (m/z, ESI-TOF): Calcd for $C_{23}H_{23}FN_2ONa^+$ [M+Na^+] 385.1687, found 385.1687.



***N*-(3-(2-fluoropyridin-3-yl)phenyl)-*N*-methyl-3-phenylpropanamide (1a$_{13}$)**

The general procedure **I** was followed. Yield: 234 mg, (70 %).

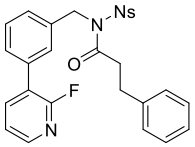
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.21 (s, 1H), 7.81 (t, *J* = 8.5 Hz, 1H), 7.54 – 7.42 (m, 2H), 7.31 – 7.28 (m, 1H), 7.22 – 7.01 (m, 7H), 3.28 (s, 3H), 2.93 (t, *J* = 7.6 Hz, 2H), 2.43 (t, *J* = 7.7 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 160.1 (d, J_{C-F} = 240.1 Hz), 146.8 (d, J_{C-F} = 14.9 Hz), 144.3, 141.0, 140.6 (d, J_{C-F} = 4.1 Hz), 135.5, 130.1, 128.4, 128.3, 128.0, 127.7, 127.2, 126.0, 122.6 (d, J_{C-F} = 28.3 Hz), 121.9 (d, J_{C-F} = 4.5 Hz), 37.3, 35.9, 31.7. HRMS (m/z, ESI-TOF): Calcd for $C_{21}H_{19}FN_2ONa^+$ [M+Na^+] 357.1374, found 357.1373.



***N*-methyl-3-phenyl-*N*-(3-(pyrimidin-5-yl)phenyl)propanamide (1a$_{14}$)**

The general procedure **I** was followed. Yield: 160 mg, (50 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.18 (s, 1H), 8.84 (s, 21H), 7.48 (d, *J* = 4.7 Hz, 2H), 7.16 – 7.01 (m, 7H), 3.26 (s, 3H), 2.89 (t, *J* = 7.5 Hz, 2H), 2.37 (t, *J* = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 157.8, 154.8, 145.0, 141.0, 136.0, 133.1, 130.8, 128.40, 128.3, 127.8, 126.2, 126.1, 125.8, 37.4, 35.9, 31.7. HRMS (m/z, ESI-TOF): Calcd for $C_{20}H_{19}N_3ONa^+$ [M+Na^+] 340.1420, found 340.1420.

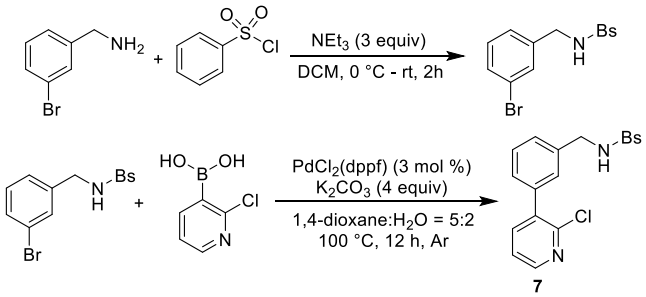


***N*-(3-(2-fluoropyridin-3-yl)benzyl)-*N*-((4-nitrophenyl)sulfonyl)-3-phenylpropanamide (1a$_{15}$)**

The general procedure **II** was followed. Yield: 468 mg, (90 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.26 – 8.17 (m, 3H), 7.89 (d, *J* = 8.8 Hz, 2H), 7.82 – 7.77 (m, 1H), 7.52 (d, *J* = 7.8 Hz, 1H), 7.46 – 7.41 (m, 2H), 7.32 – 7.27 (m, 2H), 7.17 – 7.11 (m, 3H), 7.01 – 6.94 (m, 2H), 5.14 (s, 2H), 2.93 – 2.78 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.4, 160.3 (d, J_{C-F} = 239.9 Hz), 150.5, 146.8 (d, J_{C-F} = 14.9 Hz), 144.8, 140.8 (d, J_{C-F} = 4.3 Hz), 139.8, 136.5, 134.7 (d, J_{C-F} = 5.0 Hz), 129.5, 128.7 (d, *J* = 3.0 Hz), 128.6, 128.4, 127.9 (d, J_{C-F} = 3.1 Hz), 127.6, 126.5, 124.2, 123.2 (d, J_{C-F} = 28.2 Hz), 122.1 (d, J_{C-F} = 4.4 Hz), 49.5, 38.1, 30.5. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{22}FN_3O_5S$ Na^+ [M+Na^+] 542.1156, found 542.1157.

2.2 Synthesis of Directing Template.



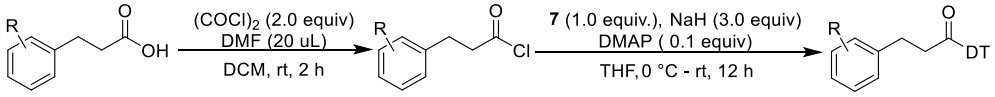
To a stirred solution of (3-bromophenyl)methanamine (10.0 mmol) in anhydrous DCM (20 mL) at , The mixture was cooled to 0 °C and benzenesulfonyl chloride (11.0 mmol) was added dropwise. The mixture was allowed to warm to room temperate and stirred for 2 h. The crude reaction mixture was diluted with EtOAc (40 mL) and filtered through a short pad of Celite. The filtrate was concentrated in vacuo and purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give *N*-(3-bromobenzyl)benzenesulfonamide (99%).

To a solution of *N*-(3-bromobenzyl)benzenesulfonamide (5.0 mmol), $PdCl_2$(dppf) (0.15 mmol), (2-chloropyridin-3-yl)boronic acid (5.5 mmol) and K_2CO_3 (20.0 mmol) in 1,4-dioxane:H_2O = 25 mL:10 mL under nitrogen atmosphere at 100 °C stirred for 12

h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (3:1-2:1) as the eluent to give ***N*-(3-(2-chloropyridin-3-yl) -benzyl)benzenesulfonamide** (**7**) (70%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.33 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.82 (d, *J* = 7.5 Hz, 2H), 7.56 – 7.47 (m, 2H), 7.44 – 7.41 (m, 2H), 7.32 – 7. 29 (m, 2H), 7.25 – 7.18 (m, 3H), 5.37 (t, *J* = 6.3 Hz, 1H), 4.18 (d, *J* = 6.3 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 149.5, 148.6, 140.0, 139.8, 137. 9, 136.8, 136.5, 132.8, 129.2, 128. 9, 128.8, 128.7, 127. 9, 127.1, 122.7, 47.1. HRMS (m/z, ESI-TOF): Calcd for $C_{18}H_{15}ClN_2O_2SNa^+$ [M+Na^+] 381.0435, found 381.0434.

2.3 Synthesis of Substrates.

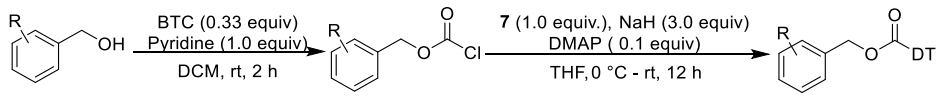
General Procedure i



To a stirred solution of substituted phenylpropionic acid (1.2 mmol) in anhydrous DCM (5 mL) under nitrogen atmosphere was added DMF (20 uL). The mixture was cooled to 0 °C and oxalyl chloride (203 uL, 2.4 mmol) was added dropwise. The mixture was allowed to warm to room temperate and stirred for 2 h. Then volatile matter was removed under reduced pressure. The residue was re-dissolved with anhydrous THF (5 mL) and kept under N_2 atmosphere, which was used in following operation without further purification.

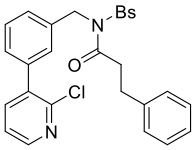
To a dry round bottom flask under N_2 atmosphere was charged with **7** (1.0 mmol) , DMAP (0.1 mmol) and NaH (60% dispersion in mineral oil, 3 mmol). The bottom was placed into an ice bath for 10 minutes followed by addition of anhydrous THF (5 mL). After stirred for 0.5 h at 0 °C, the acyl chloride prepared above was added dropwise to the mixture. The reaction was allowed to warm to room temperate and stirred for 12 h. H_2O was slowly added (be careful!!) to quench the reaction. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give desired compound. (60 % - 95 %)

General Procedure ii



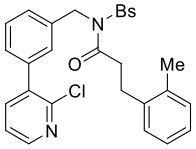
To a stirred solution of substituted benzyl alcohol (1.0 mmol) in anhydrous DCM (5 mL) under nitrogen atmosphere was added BTC (Triphosgene) (0.33 mmol). The mixture was cooled to 0 °C and pyridine (1.0 mmol) was added dropwise. The mixture was allowed to warm to room temperate and stirred for 2 h. Then volatile matter was removed under reduced pressure. The residue was re-dissolved with anhydrous THF (5 mL) and kept under N_2 atmosphere, which was used in following operation without further purification.

To a dry round bottom flask under N_2 atmosphere was charged with **7** (1.0 mmol) , DMAP (0.1 mmol) and NaH (60% dispersion in mineral oil, 3 mmol). The bottom was placed into an ice bath for 10 minutes followed by addition of anhydrous THF (5 mL). After stirred for 0.5 h at 0 °C, the acyl chloride prepared above was added dropwise to the mixture. The reaction was allowed to warm to room temperate and stirred for 12 h. H_2O was slowly added (be careful!!) to quench the reaction. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give desired compound. (20 % - 70 %)



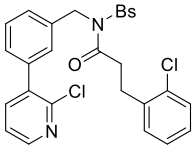
***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-phenyl-*N*-(phenylsulfonyl)propanamide** (**1a$_8$**). The general procedure **i** was followed. Yield: 466 mg, (95 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.74 – 7.66 (m, 2H), 7.62-7.57 (m, 2H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.41-7.37 (m, 4H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.20 – 7.09 (m, 3H), 7.03 – 6.94 (m, 2H), 5.13 (s, 2H), 2.97 – 2.90 (m, 2H), 2.88 – 2.84 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.5, 149.7, 148.6, 140.1, 139.8, 139.6, 137.9, 137.0, 136.6, 133.9, 129.3, 128.90, 128.88, 128.8, 128.6, 128.3, 128.1, 127.7, 126.3, 122.7, 49.2, 38.1, 30.7. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{23}ClN_2O_3SNa^+$ [M+Na^+] 513.1010, found 513.1011.



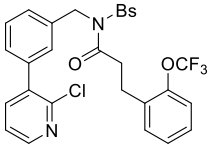
***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(o-tolyl)propanamide (1b).** The general procedure **i** was followed. Yield: 403 mg, (80 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.77 – 7.71 (m, 2H), 7.64 – 7.56 (m, 2H), 7.50 – 7.38 (m, 6H), 7.30 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.06 (d, *J* = 4.4 Hz, 2H), 7.02 – 6.98 (m, 1H), 6.89 (d, *J* = 7.4 Hz, 1H), 5.17 (s, 2H), 2.87 (s, 4H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.5, 149.5, 148.5, 139.7, 139.5, 138.1, 137.8, 136.9, 136.5, 135. 9, 133.8, 130.3, 129.2, 128.8, 128.7, 128.7, 128.4, 127.9, 127.6, 126.4, 126.0, 122.6, 49.2, 36.6, 28.0, 19.1. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{25}ClN_2O_3SNa^+$ [M+Na^+] 527.1167, found 527.1165.



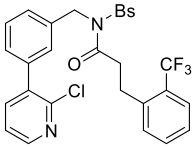
3-(2-chlorophenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N* (phenylsulfonyl)-propanamida (1c). The general procedure **i** was followed. Yield: 471 mg, (90 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.62 – 7.54 (m, 2H), 7.47 – 7.35 (m, 6H), 7.29 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.22 (d, *J* = 7.4 Hz, 1H), 7.09 – 7.03 (m, 3H), 5.15 (s, 2H), 3.02 – 2.88 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.3, 149.6, 148.6, 139.8, 139.5, 137.9, 137.6, 136.9, 136.6, 133.9, 133.8, 130.7, 129.5, 129.3, 128.9, 128.8, 128.0, 127.94, 127.7, 126.9, 122.7, 49.3, 36.2, 28.7. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{22}Cl_2N_2O_3SNa^+$ [M+Na^+] 547.0620, found 547.0621.



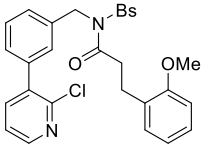
***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(2-(trifluoromethoxy) -phenyl)propanamide (1d)**. The general procedure **i** was followed. Yield: 430 mg, (75 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.73 – 7.68 (m, 2H), 7.62 – 7.57 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.41 – 7.38 (m, 4H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.20 – 7.10 (m, 2H), 7.08 (d, *J* = 4.1 Hz, 2H), 5.15 (s, 2H), 2.92 (s, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 149.7, 148.6, 147.6 (d, J_{C-F} = 1.6 Hz), 139.8, 139.5, 137.9, 137.0, 136.6, 134.0, 132.5, 131.0, 129.4, 128.9, 128.9, 128.8, 128.1, 128.0, 127.6, 126.9, 122.7, 120.6 (q, J_{C-F} = 257.5 Hz), 120.4 (d, J_{C-F} = 1.8 Hz), 49.4, 36.6, 25.1. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{22}ClF_3N_2O_4SNa^+$ [M+Na^+] 597.0833, found 597.0833.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(2-(trifluoromethyl) -phenyl)propanamide (1e$_1$).** The general procedure **i** was followed. Yield: 390 mg, (70 %).

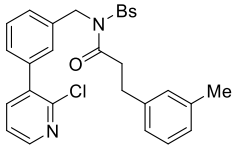
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.75 – 7.68 (m, 2H), 7.64 – 7.52 (m, 3H), 7.48 – 7.38 (m, 6H), 7.37 – 7.28 (m, 2H), 7.25 – 7.23 (m, 1H), 7.13 (d, *J* = 7.6 Hz, 1H), 5.16 (s, 2H), 3.05 (t, *J* = 7.6 Hz, 2H), 2.91 (t, *J* = 7.6 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 149.7, 148.6, 139.8, 139.5, 138.9 (d, J_{C-F} = 1.8 Hz), 137.9, 136.9, 136.6, 134.0, 132.0, 131.2, 129.3, 128.92, 128.86, 128.8, 128.5 (d, J_{C-F} = 29.9 Hz), 128.1, 127.7, 126.6, 126.2 (q, J_{C-F} = 5.8 Hz), 124.5 (q, J_{C-F} = 273.8 Hz), 122.7, 49.4, 38.2, 27.6 (d, J_{C-F} = 2.0 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{22}ClF_3N_2O_3SNa^+$ [M+Na^+] 581.0884, found 581.0884.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(2-methoxyphenyl)-*N*-(phenylsulfonyl)-propanamide (1e$_2$).** The general procedure **i** was followed. Yield: 416 mg, (80 %).

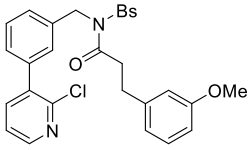
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.36 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.75 (d, *J* = 7.2 Hz, 2H), 7.61 – 7.53 (m, 2H), 7.46 – 7.36 (m, 6H), 7.28 (dd, *J* = 7.6, 4.9 Hz, 1H), 7.12 (td, *J* = 7.8, 1.8 Hz, 1H), 6.96 (dd, *J* = 7.4, 1.7 Hz, 1H), 6.79 – 6.71 (m, 2H), 5.15 (s, 2H), 3.63 (s, 3H), 2.95 – 2.81 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.8,

157.2, 148.4, 139.6, 139.4, 137.6, 136.9, 133.6, 129.9, 128.9, 128.59, 128.56, 128.4, 128.0, 127.63, 127.59, 127.57, 122.6, 120.3, 110.0, 54.9, 49.1, 36.0, 25.8. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{25}ClN_2O_4SNa^+$ [M+Na^+] 543.1116, found 543.1114.



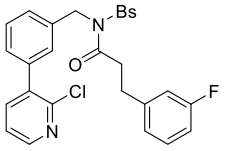
***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(m-tolyl)propanamide (1f).** The general procedure **i** was followed. Yield: 403 mg, (80 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.76 – 7.69 (m, 2H), 7.64 – 7.56 (m, 2H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.37 (m, 4H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.95 (d, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 5.15 (s, 2H), 2.97 – 2.88 (m, 2H), 2.88 – 2.79 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.5, 149.6, 148.6, 140.0, 139.7, 139.6, 138.0, 137.8, 137.0, 133.8, 129.2, 129.1, 128.82, 128.78, 128.76, 128.4, 128.0, 127.7, 127.0, 125.2, 122.7, 49.2, 38.1, 30.5, 21.4. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{25}ClN_2O_3SNa^+$ [M+Na^+] 527.1167, found 527.1164.

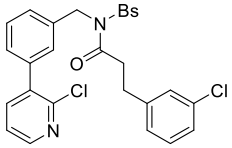


***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-methoxyphenyl)-*N*-(phenylsulfonyl)-propanamide (1g).** The general procedure **i** was followed. Yield: 443 mg, (85 %).

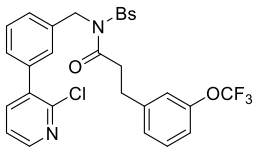
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.75 – 7.69 (m, 2H), 7.62 – 7.54 (m, 2H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.40 – 7.38 (m, 4H), 7.29 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.07 (t, *J* = 8.1 Hz, 1H), 6.71 – 6.65 (m, 1H), 6.60 – 6.54 (m, 2H), 5.14 (s, 2H), 3.71 (s, 3H), 2.94 – 2.90 (m, 2H), 2.86 – 2.82 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.4, 159.6, 149.5, 148.5, 141.7, 139.7, 139.5, 137.8, 136.9, 136.5, 133.8, 129.4, 129.2, 128.8, 128.71, 128.70, 127.9, 127.6, 122.6, 120.5, 114.0, 111.6, 55.1, 49.2, 37.9, 30.6. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{25}ClN_2O_4SNa^+$ [M+Na^+] 543.1116, found 543.1114.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluorophenyl)-*N*-(phenylsulfonyl)-propanamide (1h).** The general procedure **i** was followed. Yield: 460 mg, (91 %). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.60 (td, *J* = 7.6, 1.6 Hz, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.42 – 7.37 (m, 4H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.10 (td, *J* = 7.9, 6.0 Hz, 1H), 6.81 (td, *J* = 8.5, 2.6 Hz, 1H), 6.76 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.64 (dt, *J* = 9.9, 2.1 Hz, 1H), 5.14 (s, 2H), 2.96 – 2.89 (m, 2H), 2.88 – 2.84(m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 162.9 (d, J_{C-F} = 246Hz), 149.7, 148.7, 142.7 (d, J_{C-F} = 7 Hz), 139.8, 139.6, 138.0, 137.0, 136.7, 134.0, 123.0 (d, J_{C-F} = 8 Hz), 129.4, 129.02, 129.00, 128.9, 128.2, 127.7, 124.1 (d, J_{C-F} = 3 Hz), 122.7, 115.2 (d, J_{C-F} = 21 Hz), 113.3 (d, J_{C-F} = 21 Hz), 49.3, 37.9, 30.4 (d, J_{C-F} = 1.8 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{22}ClFN_2O_3SNa^+$ [M+Na$^+$] 531.0916, found 531.0916.



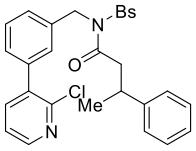
3-(3-chlorophenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-propanamide (1i). The general procedure **i** was followed. Yield: 315 mg, (60 %). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.64 – 7.58 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.43 – 7.35 (m, 4H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.12 – 7.04 (m, 2H), 6.94 (s, 1H), 6.87 (dt, *J* = 6.8, 1.9 Hz, 1H), 5.14 (s, 2H), 2.94 – 2.90 (m, 2H), 2.86 – 2.82 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 149.7, 148.7, 142.3, 139.8, 139.6, 137.9, 137.0, 136.7, 134.2, 134.1, 129.8, 129.4, 129.01, 129.00, 128.9, 128.5, 128.2, 127.6, 126.7, 126.6, 122.7, 49.3, 37.9, 30.3. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{22}Cl_2N_2O_3SNa^+$ [M+Na$^+$] 547.0620, found 547.0620.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(3-(trifluoromethoxy)-**

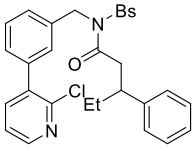
phenyl)propanamide (1j). The general procedure **i** was followed. Yield: 460 mg, (80 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.65 – 7.56 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.42 – 7.37 (m, 4H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.18 (t, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 6.92 (d, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 5.15 (s, 2H), 3.03 – 2.79 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 149.7, 149.4, 148.7, 142.6, 139.8, 139.6, 138.0, 137.0, 136.6, 134.1, 129.9, 129.4, 129.1, 129.0, 128.9, 128.2, 127.6, 126.9, 122.7, 120.9, 120.5 (d, $J_{C\text{-}F}$ = 256.8 Hz), 118.8, 49.3, 37.8, 30.3. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{22}ClF_3N_2O4SNa^+$ [M+Na^+] 597.0833, found 597.0834.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-phenyl-*N*-(phenylsulfonyl)butanamide (1k).** The general procedure **i** was followed. Yield: 428 mg, (85 %).

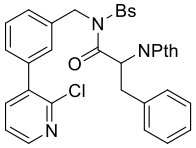
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.69 – 7.63 (m, 2H), 7.63 – 7.56 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.40 – 7.35 (m, 2H), 7.34 – 7.27 (m, 3H), 7.16 – 7.05 (m, 3H), 6.94 (d, *J* = 6.9 Hz, 2H), 5.16 – 5.02 (m, 2H), 3.32 (h, *J* = 7.0 Hz, 1H), 2.96 (dd, *J* = 16.6, 7.3 Hz, 1H), 2.83 (dd, *J* = 16.6, 7.0 Hz, 1H), 1.12 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 149.7, 148.6, 145.4, 139.80, 139.77, 137.9, 137.1, 136.7, 133.9, 129.3, 128.91, 128.87, 128.8, 128.5, 128.2, 127.7, 126.7, 126.4, 122.7, 49.0, 44.7, 36.1, 21.8. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{25}ClN_2O_3SNa^+$ [M+Na^+] 527.1167, found 527.1168.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-phenyl-*N*-(phenylsulfonyl)pentanamide (1l).** The general procedure **i** was followed. Yield: 440 mg, (85 %).

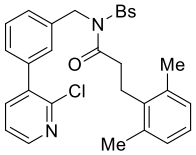
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.65 – 7.55 (m, 4H), 7.49 – 7.43 (m, 2H), 7.40 – 7.33 (m, 2H), 7.31 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.27 – 7.26 (m, 1H), 7.22 (dt, *J* = 7.1, 1.8 Hz, 1H), 7.13 – 7.01 (m, 3H), 6.90 – 6.83 (m, 2H), 5.20 – 4.95 (m, 2H), 3.11 – 2.82 (m, 3H), 1.60 – 1.49 (m, 1H), 1.46 – 1.35 (m, 1H),

0.67 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 149.7, 148.6, 143.7, 139.84, 139.83, 137.9, 137.2, 136.7, 133.8, 129.3, 128.92, 128.88, 128.8, 128.4, 128.2, 127.7, 127.5, 126.4, 122.7, 48.9, 43.5, 43.3, 29.0, 12.0. HRMS (m/z, ESI-TOF): Calcd for $C_{29}H_{27}ClN_2O_3SNa^+$ [M+Na$^+$] 541.1323, found 541.1323.



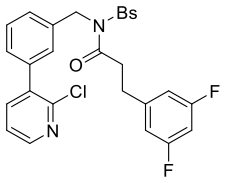
***N*-(3-(2-chloropyridin-3-yl)benzyl)-2-(1,3-dioxoisoindolin-2-yl)-3-phenyl-*N*-(phenylsulfonyl)propanamide (1m).** The general procedure **i** was followed. Yield: 381 mg, (60 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.91 (dd, *J* = 7.4, 1.8 Hz, 2H), 7.63 – 7.49 (m, 6H), 7.43 (t, *J* = 7.6, Hz, 2H), 7.27 – 7.17 (m, 5H), 7.14 – 7.09 (m, 2H), 7.08 – 6.99 (m, 3H), 5.90 (dd, *J* = 10.9, 4.8 Hz, 1H), 4.89 (q, *J* = 16.0 Hz, 2H), 3.63 (dd, *J* = 13.9, 10.9 Hz, 1H), 3.48 (dd, *J* = 13.9, 4.8 Hz, 1H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.1, 167.8, 149.6, 148.6, 139.8, 138.6, 137.6, 136.5, 136.4, 136.0, 134.19, 134.15, 131.4, 129.4, 129.1, 128.8, 128.61, 128.59, 128.4, 128.1, 127.5, 127.0, 123.4, 122.7, 56.6, 50.0, 34.9. HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{26}ClN_3O_5SNa^+$ [M+Na$^+$] 658.1174, found 658.1174.

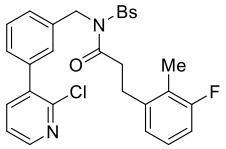


***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(2,6-dimethylphenyl)-*N*-(phenylsulfonyl)-propanamide (1n)** . The general procedure **i** was followed. Yield: 466 mg, (90 %).

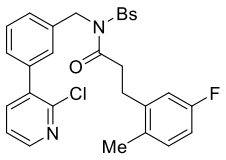
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.79 – 7.72 (m, 2H), 7.66 – 7.58 (m, 2H), 7.50 – 7.41 (m, 6H), 7.32 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.03 – 6.90 (m, 3H), 5.18 (s, 2H), 2.91 – 2.84 (m, 2H), 2.73 – 2.64 (m, 2H), 2.10 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.9, 149.7, 148.7, 139.8, 139.6, 138.0, 137.0, 136.8, 136.6, 136.3, 134.0, 129.4, 128.97, 128.95, 128.7, 128.4, 127.9, 127.8, 126.4, 122.7, 49.5, 35.5, 24.9, 19.7. HRMS (m/z, ESI-TOF): Calcd for $C_{29}H_{27}ClN_2O_3SNa^+$ [M+Na$^+$] 541.1323, found 541.1322.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3,5-difluorophenyl)-*N*-(phenylsulfonyl)-propanamide (1o).** The general procedure **i** was followed. Yield: 447 mg, (85 %).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.64 – 7.57 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.41 – 7.36 (m, 4H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.54 (tt, *J* = 9.0, 2.4 Hz, 1H), 6.46 (h, *J* = 4.3 Hz, 2H), 5.15 (s, 2H), 2.93 – 2.89 (m, 2H), 2.85 – 2.82 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 162.9 (dd, J_{C-F} = 248.3, 12.9 Hz), 149.6, 148.6, 144.0 (t, J_{C-F} = 9.1 Hz), 139.8, 139.5, 137.9, 136.9, 136.5, 134.1, 129.4, 129.0, 128.8, 128.2, 127.5, 122.7, 111.2 (dd, J_{C-F} = 24.7, 11.5 Hz), 101.8 (t, J_{C-F} = 25.2 Hz), 49.2, 37.4, 30.2. HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{21}ClF_2N_2O_3SNa^+$ [M+Na$^+$] 549.0822, found 549.0819.

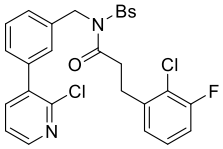


***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluoro-2-methylphenyl)-*N*-(phenylsulfonyl)-propanamide (1p).** The general procedure **i** was followed. Yield: 418 mg, (80 %).
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.73 – 7.65 (m, 2H), 7.64 – 7.57 (m, 2H), 7.51 – 7.38 (m, 6H), 7.32 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.93 (td, *J* = 7.9, 5.8 Hz, 1H), 6.85 – 6.78 (m, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 5.16 (s, 2H), 2.89 – 2.81 (m, 4H), 2.00 (d, *J* = 2.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.4, 161.4 (d, J_{C-F} = 243.5 Hz), 149.7, 148.7, 140.8 (d, J_{C-F} = 4.1 Hz), 139.8, 139.6, 138.0, 137.0, 136.6, 134.0, 129.4, 129.00, 128.98, 128.9, 128.2, 127.6, 126.7 (d, J_{C-F} = 9.1 Hz), 124.2 (d, J_{C-F} = 3.1 Hz), 123.2 (d, J_{C-F} = 16.0 Hz), 122.7, 113.2 (d, J_{C-F} = 23.3 Hz), 49.4, 36.8, 27.9 (d, J_{C-F} = 2.8 Hz), 10.3 (d, J_{C-F} = 5.8 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{24}ClFN_2O_3SNa^+$ [M+Na$^+$] 545.1072, found 545.1071.



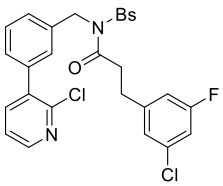
***N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(5-fluoro-2-methylphenyl)-*N*-(phenylsulfonyl)-propanamide (1q).** The general procedure **i** was followed. Yield: 444 mg, (85 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 – 7.69 (m, 2H), 7.65 – 7.57 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.44 – 7.39 (m, 4H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.99 (dd, *J* = 8.4, 5.9 Hz, 1H), 6.74 (td, *J* = 8.4, 2.8 Hz, 1H), 6.56 (dd, *J* = 9.8, 2.8 Hz, 1H), 5.17 (s, 2H), 2.92 – 2.75 (m, 4H), 2.09 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.3, 161.2 (d, J_{C-F} = 243.5 Hz), 149.7, 148.6, 140.3 (d, J_{C-F} = 7.0 Hz), 139.8, 139.6, 138.0, 137.0, 136.6, 134.0, 131.55 (d, J_{C-F} = 2.8 Hz), 131.51 (d, J_{C-F} = 7.6 Hz), 129.4, 129.01, 128.97, 128.9, 128.2, 127.6, 122.7, 115.1 (d, J_{C-F} = 21.1 Hz), 113.0 (d, J_{C-F} = 20.5 Hz), 49.4, 36.5, 28.0 (d, J_{C-F} = 1.6 Hz), 18.5. HRMS (m/z, ESI-TOF): Calcd for $C_{28}H_{24}ClFN_2O_3SNa^+$ [M+Na$^+$] 545.1072, found 545.1071.



3-(2-chloro-3-fluorophenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-propanamide (1r). The general procedure **i** was followed. Yield: 434 mg, (80 %).

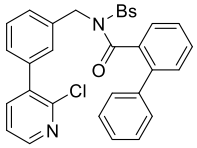
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.65 – 7.55 (m, 2H), 7.48 – 7.36 (m, 6H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.00 (td, *J* = 7.9, 5.4 Hz, 1H), 6.93 (td, *J* = 8.5, 1.6 Hz, 1H), 6.86 (d, *J* = 7.5 Hz, 1H), 5.16 (s, 2H), 3.02 – 3.00 (m, 2H), 2.96 – 2.90 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 158.3 (d, J_{C-F} = 247.9 Hz), 149.7, 148.6, 140.2, 139.8, 139.5, 137.9, 136.9, 136.6, 134.0, 129.4, 128.9, 128.82, 128.15, 127.6, 127.5, 127.4, 125.7 (d, J_{C-F} = 3.3 Hz), 122.7, 120.8 (d, J_{C-F} = 17.3 Hz), 114.6 (d, J_{C-F} = 21.4 Hz), 49.3, 36.0, 28.4 (d, J_{C-F} = 2.6 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{21}Cl_2FN_2O_3SNa^+$ [M+Na$^+$] 565.0526, found 565.0524.



3-(3-chloro-5-fluorophenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-

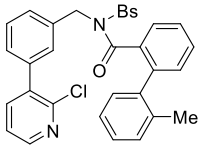
(phenylsulfonyl)-propanamide (1s). The general procedure **i** was followed. Yield: 325 mg, (60 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.61 (td, *J* = 7.0, 6.2, 1.6 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.2 – 7.36 (m, 4H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.84 (dt, *J* = 8.5, 2.1 Hz, 1H), 6.75 (s, 1H), 6.56 (d, *J* = 9.3 Hz, 1H), 5.15 (s, 2H), 2.91 (t, *J* = 7.3 Hz, 2H), 2.83 (t, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 162.6 (d, J_{C-F} = 249.4 Hz), 149. 7, 148.6, 143.9 (d, J_{C-F} = 8.2 Hz), 139.8, 139.5, 137.9, 136.8, 136.6, 134.8 (d, J_{C-F} = 10.9 Hz), 134.1, 129.4, 129.04, 129.01, 128. 9, 128.2, 127.5, 124.4 (d, J_{C-F} = 3.1 Hz), 122.7, 114.2 (d, J_{C-F} = 24.8 Hz), 113. 9 (d, J_{C-F} = 21.2 Hz), 49.3, 37.5, 30.1 (d, J_{C-F} = 1.8 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{27}H_{21}Cl_2FN_2O_3SNa^+$ [M+Na$^+$] 565.0526, found 565.0529.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (5a).** The general procedure **i** was followed. Yield: 350 mg, (65 %).

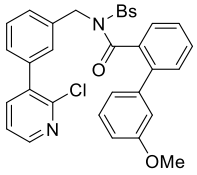
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.43 – 8.41 (m, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.62 (t, *J* = 7.5 Hz, 1H), 7.54 – 7.50 (m, 1H), 7.48 – 7.41 (m, 3H), 7.40 – 7.21 (m, 10H), 7.16 (d, *J* = 7.7 Hz, 1H), 7.02 (d, *J* = 7.5 Hz, 1H), 6.97 (s, 1H), 4.62 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.1, 149.6, 148.6, 139.7, 139.0, 138.9, 138.8, 137.7, 136.7, 136.5, 134.0, 133.7, 130.7, 129.9, 129.1, 128.9, 128.84, 128.75, 128.7, 128.6, 128.5, 128.4, 128.1, 127.7, 127.4, 122.7, 50.5. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{23}ClN_2O_3SNa^+$ [M+Na$^+$] 561.1010, found 561.1010.



***N*-(3-(2-chloropyridin-3-yl)benzyl)-2'-methyl-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (5b).** The general procedure **i** was followed. Yield: 386 mg, (70 %).

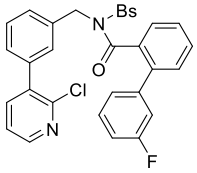
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.65 – 7.53 (m, 4H), 7.45 (td, *J* = 7.5, 1.5 Hz, 1H), 7.40 (t, *J* = 7.9 Hz, 2H), 7.36 – 7.27 (m, 4H), 7.26 – 7.21 (m, 3H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.12 – 7. 06 (m, 4H), 4.73 (br, 2H), 2.07 (br, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.7, 149.6, 148.6, 139.8, 138.79, 138.78,

138.3, 137.7, 136.7, 136.5, 134.9, 133.6, 130.7, 130.6, 130.2, 128.80, 128.75, 128.7, 128.4, 128.20, 128.17, 127. 9, 127.6, 127.3, 125.6, 122.7, 50.8, 20.1. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{25}ClN_2O_3SNa^+$ [M+Na^+] 575.1166, found 575.1167.



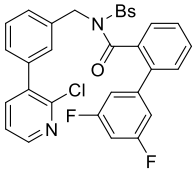
***N*-(3-(2-chloropyridin-3-yl)benzyl)-3'-methoxy-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (5c).** The general procedure **i** was followed. Yield: 370 mg, (65 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.66 (d, *J* = 7.1 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.50 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.45 – 7.34 (m, 4H), 7.33 – 7.26 (m, 3H), 7.24 – 7.14 (m, 2H), 7.11 (dd, *J* = 7.7, 1.4 Hz, 1H), 6.99 (d, *J* = 7.2 Hz, 1H), 6.96 (s, 1H), 6.92 – 6.83 (m, 3H), 4.65 (br, 2H), 3.71 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.1, 159.6, 149.6, 148.6, 140.3, 139.7, 139.0, 138.9, 137.6, 136.7, 136.5, 134.0, 133.7, 130.6, 129.94, 129.86, 128.85, 128.72, 128.70, 128.5, 128.39, 128.36, 127.6, 127.5, 122. 7, 121.1, 114.4, 114.0, 55.3, 50.6. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{25}ClN_2O_4SNa^+$ [M+Na^+] 591.1116, found 591.1113.



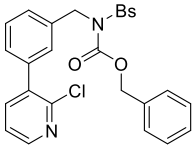
***N*-(3-(2-chloropyridin-3-yl)benzyl)-3'-fluoro-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (5d).** The general procedure **i** was followed. Yield: 333 mg, (60 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.66 (d, *J* = 7.4 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.51 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.34 – 7.28 (m, 4H), 7.25 – 7.21 (m, 1H), 7.18 (dd, *J* = 7.9, 5.9 Hz, 1H), 7.13 (d, *J* = 7.7 Hz, 1H), 7.08 – 6.95 (m, 5H), 4.68 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.7, 162.6 (d, J_{C-F} = 247.4 Hz), 149.6, 148.7, 141.0 (d, J_{C-F} = 7.5 Hz), 139.7, 138.8, 137.9 (d, J_{C-F} = 1.9 Hz), 137.7, 136.6, 136.5, 134.1, 133. 9, 130.7, 130.4 (d, J_{C-F} = 8.1 Hz), 130. 0, 128.8, 128.6, 128.5, 128.3, 127.8, 127.7, 124.8 (d, J_{C-F} = 2.9 Hz), 122.7, 115.9 (d, J_{C-F} = 22.1 Hz), 115.1 (d, J_{C-F} = 20.9 Hz), 50.6. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{22}ClFN_2O_3SNa^+$ [M+Na^+] 579.0916, found 579.0915.



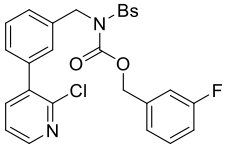
***N*-(3-(2-chloropyridin-3-yl)benzyl)-3',5'-difluoro-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (5e).** The general procedure **i** was followed. Yield: 403 mg, (70 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.66 (d, *J* = 8.4 Hz, 2H), 7.59 (t, *J* = 7.5 Hz, 1H), 7.54 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.48 – 7.39 (m, 3H), 7.37 – 7.27 (m, 4H), 7.25 (d, *J* = 6.5 Hz, 1H), 7.15 – 7.05 (m, 3H), 6.82 – 6.69 (m, 3H), 4.77 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.3, 162.7 (dd, J_{C-F} = 249.8, 12.9 Hz), 149.6, 148.7, 142.1 (t, J_{C-F} = 9.6 Hz), 139.7, 138.8, 137.8, 137.2 (t, J_{C-F} = 2.2 Hz), 136.5, 136.4, 134.1, 134.0, 130.8, 129.8, 128.94, 128.93, 128.7, 128.64, 128.63, 128.2, 128.1, 127.8, 122.7, 112.2 (dd, J_{C-F} = 25.9, 11.0 Hz), 103.5 (t, J_{C-F} = 25.0 Hz), 50.5. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{21}ClF_2N_2O_3SNa^+$ [M+Na$^+$] 597.0822, found 597.0821.



benzyl (3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamate (5f). The general procedure **ii** was followed. Yield: 394 mg, (80 %).

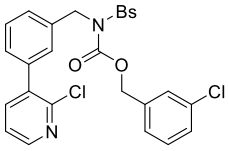
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.42 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 2H), 7.59 (dd, *J* = 7.4, 1.9 Hz, 1H), 7.56 – 7.47 (m, 2H), 7.45 – 7.43 (m, 3H), 7.37 – 7.24 (m, 6H), 7.13 (d, *J* = 6.4 Hz, 2H), 5.16 (s, 2H), 5.11 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.4, 149.7, 148.6, 139.8, 139.2, 137.8, 137.2, 136.7, 134.3, 133.6, 129.3, 129.0, 128.8, 128.7, 128.64, 128.62, 128.6, 128.5, 122.7, 69.5, 49.9. HRMS (m/z, ESI-TOF): Calcd for $C_{26}H_{21}ClN_2O_4SNa^+$ [M+Na$^+$] 515.0803, found 515.0803.



3-fluorobenzyl (3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamate[1] **(5g).**

The general procedure **ii** was followed. Yield: 357 mg, (70 %).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 3.8 Hz, 1H), 7.65 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.53 (t, *J* = 7.4 Hz, 1H), 7.50 – 7.39 (m, 4H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.20 (td, *J* = 7.9, 5.8 Hz, 1H), 6.95 (td, *J* = 8.5, 2.5 Hz, 1H), 6.89 (d, *J* = 7.5 Hz, 1H), 6.71 (d, *J* = 9.1 Hz, 1H), 5.15 (s, 3H), 5.07 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.7 (d, J_{C-F} = 246.9 Hz), 152.3, 149.7, 148.6, 139.8, 139.2, 137.9, 137.1, 136.8 (d, J_{C-F} = 7.4 Hz), 136.6, 133.7, 130.3 (d, J_{C-F} = 8.1 Hz), 129.2, 129.1, 128.80, 128.76, 128.5, 128.4, 123. 9 (d, J_{C-F} = 3.0 Hz), 122.7, 115.6 (d, J_{C-F} = 21.1 Hz), 115.1 (d, J_{C-F} = 21.9 Hz), 68.4 (d, J_{C-F} = 2.0 Hz), 50.0. HRMS (m/z, ESI-TOF): Calcd for $C_{26}H_{20}ClFN_2O_4SNa^+$ [M+Na$^+$] 533.0709, found 533.0709.

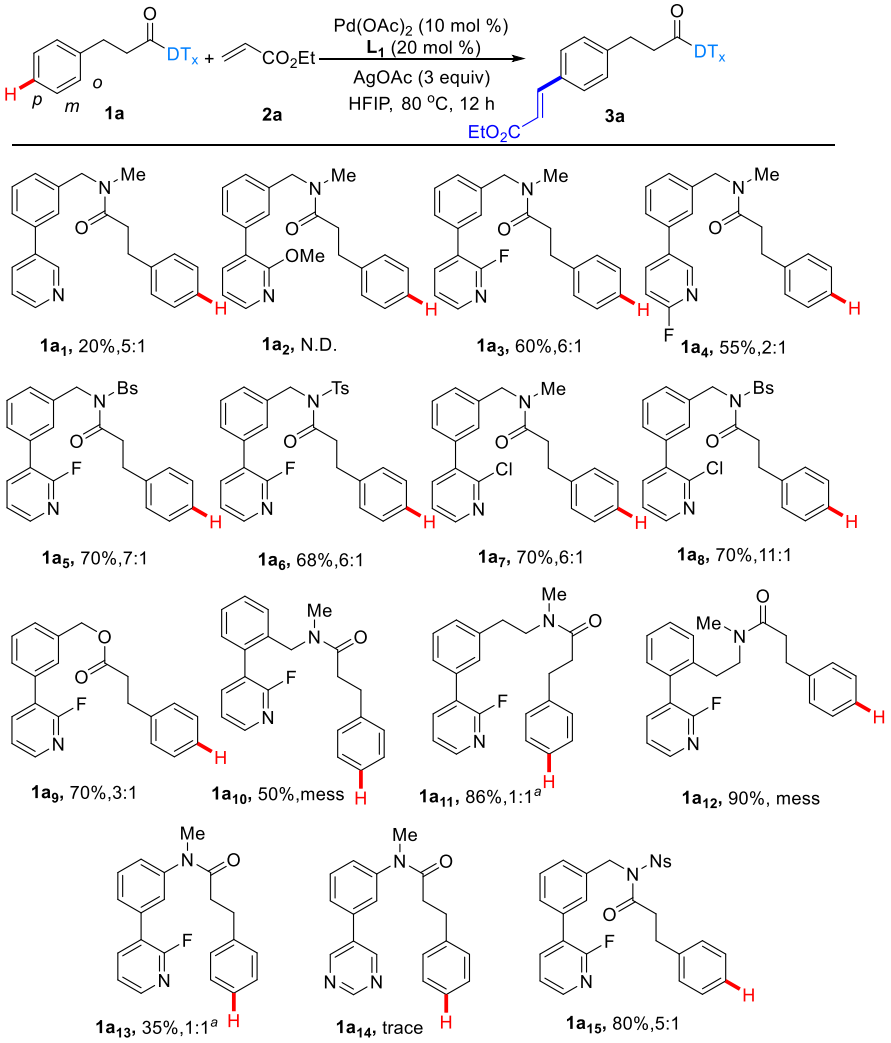


3-chlorobenzyl (3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamate (5h). The general procedure **ii** was followed. Yield: 105 mg, (20 %).

^{1}H NMR (400 MHz, Chloroform-d) δ 8.40 (dd, J = 4.8, 1.9 Hz, 1H), 7.64 (d, J = 7.2 Hz, 2H), 7.59 (dd, J = 7.5, 2.0 Hz, 1H), 7.54 (t, J = 7.5 Hz, 1H), 7.51 – 7.39 (m, 4H), 7.35 (t, J = 7.9 Hz, 2H), 7.30 (dd, J = 7.6, 4.7 Hz, 1H), 7.28 – 7.21 (m, 1H), 7.17 (t, J = 8.0 Hz, 1H), 7.01 – 6.99 (m, 2H), 5.14 (s, 2H), 5.05 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-d) δ 152.3, 149.7, 148.6, 139.8, 139.2, 137.9, 137.1, 136.7, 136.4, 134.5, 133.8, 130.0, 129.3, 129.1, 128.9, 128.83, 128.80, 128.6, 128.40, 128.36, 126.5, 122.7, 68.4, 50.0. HRMS (m/z, ESI-TOF): Calcd for $C_{26}H_{21}Cl_2N_2O_4S^+$ [M+H$^+$] 527.0594, found 527.0596.

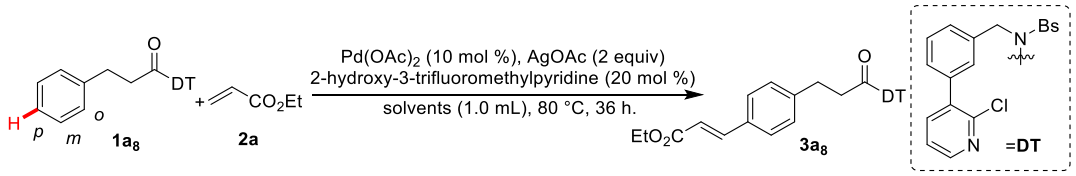
2.4 Optimization of Reaction Conditions

Table S1: Optimization by Varying Different Templates.



Reaction condition: **1a** (0.1 mmol), **2a** (2 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2 equiv), 2-hydroxy-3-trifluoromethylpyridine(**L1**) (20 mol %), HFIP (1.0 mL), 80 °C, 12 h. Yield and selectivity are based on ^1H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^1H NMR and products of others were mainly *m*- and *o*-isomers. N.D.= no detected. [a]Ratios of two major products, C-H olefination sites not determined.

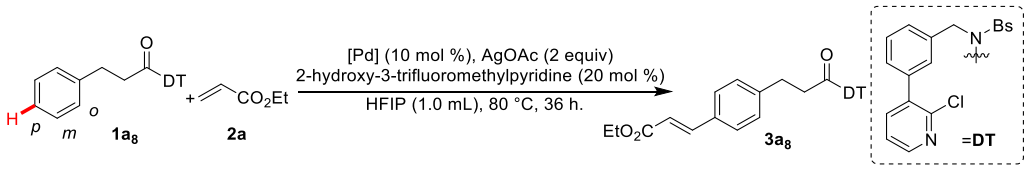
Table S2: Optimization by Varying Different Solvents



entry	solvents (1 mL)	**3a8** yield (%)[a]	Ratio (*p*:others)[a]
1	HFIP	75	10:1
2	TFE	60	7:1
3	AcOH	trace	-
4	TFA	0	-

Reaction condition: **1a8** (0.1 mmol), **2a** (2 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (2 equiv), 2-hydroxy-3-trifluoromethylpyridine (20 mol %), solvents (1.0 mL), 80 °C, 36 h. [a]Yield and selectivity are based on ^1H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^1H NMR and products of others were mainly *m*- and *o*-isomers.

Table S3: Optimization of Palladium Catalyst

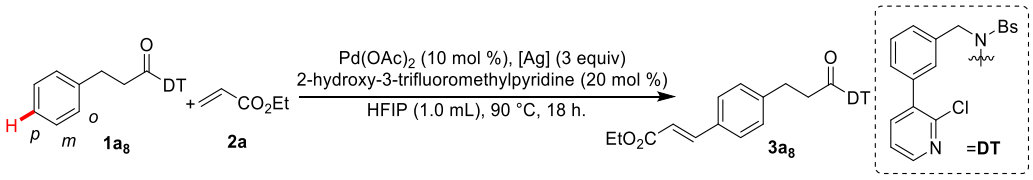


1a$_8$ **2a** **3a$_8$**

entry	[Pd]	**3a$_8$** yield (%)[a]	Ratio (*p*:others)[a]
1	$Pd(OAc)_2$	75	11:1
2	$Pd(OTFA)_2$	61	9:1
3	$PdCl_2$	46	9:1
4	$Pd(MeCN)_2Cl_2$	50	11:1

Reaction condition: **1a$_8$** (0.1 mmol), **2a** (2 equiv), [Pd] (10 mol %), AgOAc (2 equiv), 2-hydroxy-3-trifluoromethylpyridine (20 mol %), HFIP (1.0 mL), 80 °C, 36 h. [a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^{1}H NMR and products of others were mainly *m*- and *o*-isomers.

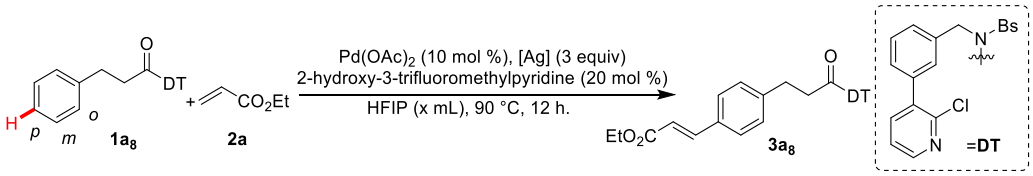
Table S4: Optimization by Varying Different Ag Salts



entry	[Ag]	**3a8** yield (%)[a]	Ratio (*p*:others)[a]
1	AgF_2	11	5:1
2	Ag_2SO_4	33	mess
3	Ag_2O	0	-
4	AgTFA	40	8:1
5	AgOBz	0	-
6	AgOPiv	30	6:1
7	Ag_2CO_3	69	10:1
8	$AgSbF_6$	0	-
9	$AgNO_3$	63	10:1
10	$AgBF_4$	0	-
11	Ag_3PO_4	20	4:1
12	$AgPF_6$	0	-
13	Ag_2WO_4	14	6:1
14	AgOTf	trace	10:1

Reaction condition: **1a8** (0.1 mmol), **2a** (2 equiv), $Pd(OAc)_2$ (10 mol%), [Ag] (3 equiv), 2-hydroxy-3-trifluoromethylpyridine (20 mol %), HFIP (1.0 mL), 90 °C, 18 h. [a]Yield and selectivity are based on ^1H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^1H NMR and products of others were mainly *m*- and *o*-isomers.

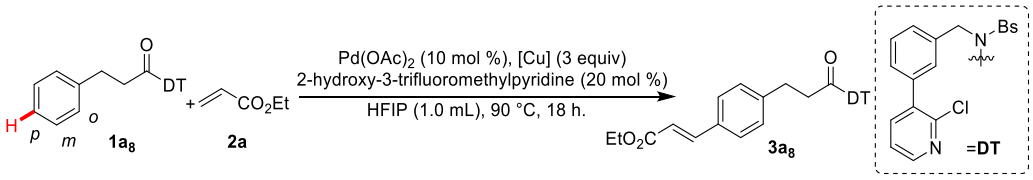
Table S5: Optimization of Reaction Concentration



entry	[x mL]	**3a8** yield (%)[a]	Ratio (*p*:others)[a]
1	0.5	65	7:1
2	1.0	70	10:1
3	1.5	90 (79)[b]	15:1

Reaction condition: **1a8** (0.1 mmol), **2a** (2 equiv), $Pd(OAc)_2$ (10 mol %), AgOAc (3 equiv), 2-hydroxy-3-trifluoromethylpyridine (20 mol %), HFIP (x mL), 90 °C, 12 h. [a]Yield and selectivity are based on ^1H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^1H NMR and products of others were mainly *m*- and *o*-isomers. [b]Isolated yield.

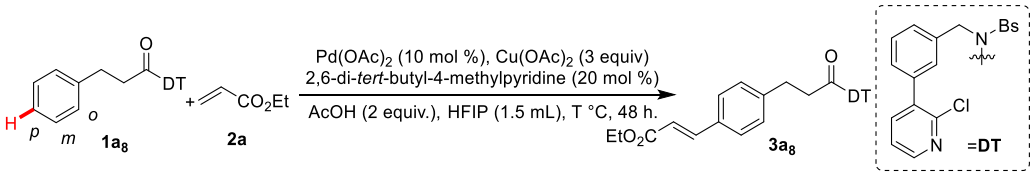
Table S6: Optimization by Varying Different Cu Salts



entry	[Cu]	**3a8** yield (%)[a]	Ratio (*p*:others)[a]
1	$Cu(TFA)_2$	21	7:1
2	$CuCl_2$	-	-
3	CuI	11	5:1
4	$Cu(OAc)_2$	40	8:1

Reaction condition: **1a8** (0.1 mmol), **2a** (2 equiv), $Pd(OAc)_2$ (10 mol %), [Cu] (3 equiv), 2-hydroxy-3-trifluoromethylpyridine (20 mol %), HFIP (1.0 mL), 90 °C, 18 h. [a]Yield and selectivity are based on ^1H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^1H NMR and products of others were mainly *m*- and *o*-isomers.

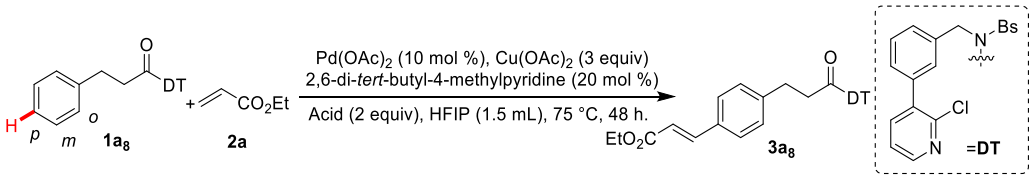
Table S7: Optimization of Reaction Temperature

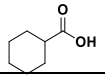


entry	Temperature (°C)	**3a8** yield (%)[a]	Ratio (*p*:others)[a]
1	70	72	12:1
2	80	53	12:1
3	90	29	13:1
4	60	68	12:1
5	65	72	11:1
6	75	80 (72)[b]	12:1

Reaction condition: **1a8** (0.1 mmol), **2a** (3 equiv), $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (0.5 equiv), 2,6-di-tert-butyl-4-methylpyridine (20 mol %), AcOH (2 equiv), HFIP (1.5 mL), T °C, 48 h. [a]Yield and selectivity are based on ^{1}H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^{1}H NMR and products of others were mainly *m*- and *o*-isomers. [b]Isolated yield.

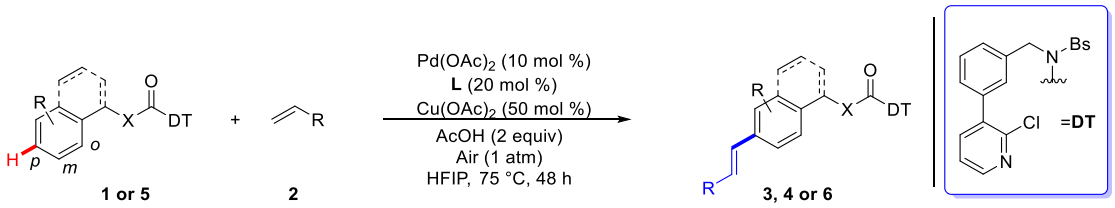
Table S8: Optimization by Varying Different Acids



entry	Acid (2 equiv.)	**3a8** yield (%)[a]	Ratio (*p*:others)[a]
1	TFA	-	-
2		-	-
3		-	-
4		74	11:1
5	HCOOH	70	10:1
6		63	12:1
7		68	12:1
8		64	12:1

Reaction condition: **1a8** (0.1 mmol), **2a** (3 equiv), $Pd(OAc)_2$ (10 mol %), $Cu(OAc)_2$ (0.5 equiv), 2,6-di-tert-butyl-4-methylpyridine (20 mol %), Acid (2 equiv), HFIP (1.5 mL), T °C, 48 h. [a]Yield and selectivity are based on ^1H NMR of the crude reaction mixture using CH_2Br_2 as internal standard; products ratios were determined from crude ^1H NMR and products of others were mainly *m*- and *o*-isomers.

2.5 General Procedures and Characterizations of Products



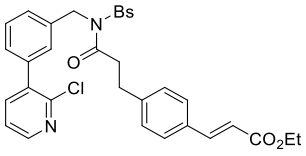
General Procedure A

An oven-dried Schlenk tube (50 mL) was charged with a magnetic stir bar, under air or O_2 atmosphere, **1** (0.1 mmol, 1.0 equiv), **2** (0.3 mmol, 3.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 10 mol %), $Cu(OAc)_2$ (9.1 mg, 0.05 mmol, 0.5 equiv), 2,6-di-tert-butyl-4-methylpyridine (4.1 mg, 0.02 mmol, 20 mol %), AcOH (0.2 mmol, 2.0 equiv), HFIP (1.5 mL) were added. The reaction mixture was stirred vigorously on a preheated hotplate (70 or 75 °C) for 48 h and then cooled down to room temperature. After removal of HFIP under reduced pressure, then diluted with EtOAc (10 mL) and filtered through a short pad of Celite and neutral alumina. The sealed tube and Celite and neutral alumina pad were washed with an additional 50 mL EtOAc. The filtrate was concentrated in vacuo, and crude ^{1}H NMR spectrum was taken using CH_2Br_2 as internal standard. Products ratios were determined from crude ^{1}H NMR and products of others were mainly *m*- and *o*-isomers. The resulting residue was purified by flash silica gel chromatography or preparative thin layer chromatography using petroleum ether/EtOAc (3:1-2:1) as the eluent to give the desired products. Isolated yield of pure desired *para*-isomer was reported herein.

General Procedure B

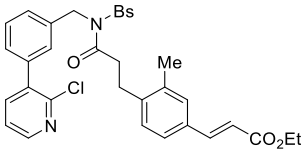
An oven-dried 15 mL sealed tube (with a Teflon cap) equipped with a magnetic stir bar was charged with compound **1** (0.1 mmol, 1.0 equiv), **2** (0.2 mmol, 2.0 equiv or 0.3 mmol, 3.0 equiv), $Pd(OAc)_2$ (2.2 mg, 0.01 mmol, 10 mol %), AgOAc (50.1 mg, 0.3 mmol, 3.0 equiv), 3-(trifluoromethyl)pyridin-2-ol (3.2 mg, 0.02 mmol, 20 mol %). HFIP (1.0 mL or 1.5 mL) were added. The reaction mixture was stirred vigorously on a preheated hotplate (80, 90 or 100 °C) for 24 h and then cooled down to room temperature. After removal of HFIP under reduced pressure, then diluted with EtOAc (10 mL) and filtered through a short pad of Celite and neutral alumina. The sealed tube and Celite and neutral alumina pad were washed with an additional 50 mL EtOAc. The filtrate was concentrated in vacuo, and crude ^{1}H NMR spectrum was taken using

CH_2Br_2 as internal standard. The resulting residue was purified by flash silica gel chromatography or preparative thin layer chromatography using petroleum ether/EtOAc (3:1-2:1) as the eluent to give the desired products. Isolated yield of pure desired *para*-isomer was reported herein.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)phenyl)acrylate (3a)

The general procedure **A** was followed. (75 °C under air) Conversion: 81 %. Yield: 42.3 mg (72%), *p*: others = 12:1. When the general procedure **B** was followed. [**2** (2.0 equiv), HFIP (1.5 mL), 90 °C], Conversion: 87 %. Yield: 47.0 mg (79%), *p*: others = 15:1. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 – 7.65 (m, 2H), 7.64 – 7.57 (m, 3H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.40 – 7.36 (m, 4H), 7.34 – 7.27 (m, 3H), 7.00 (d, *J* = 7.9 Hz, 2H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.13 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.95 – 2.92 (m, 2H), 2.90 – 2.86 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 167.2, 149.7, 148.7, 144.3, 142.8, 139.8, 139.6, 137.9, 136.9, 136.6, 134.0, 132.6, 129.4, 129.0, 128.9, 128.8, 128.3, 128.1, 127.8, 122.7, 117.8, 60.6, 49.3, 37.8, 30.5, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{29}ClN_2O_5SNa^+$ [M+Na^+] 611.1378, found 611.1378.

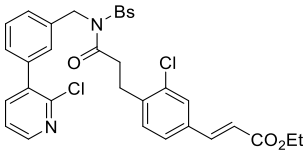


Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-3-methylphenyl)acrylate (3b)

The general procedure **A** was followed. (75 °C under air) Conversion: 80 %. Yield: 45.7 mg (76%), *p*: others = 15:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.75 – 7.67 (m, 2H), 7.65 – 7.54 (m, 3H), 7.49 – 7.35 (m, 6H), 7.30 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.22 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.15 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 2.86 (s, 4H), 2.14 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C

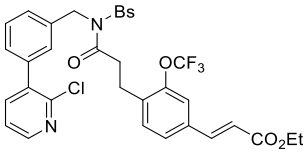
NMR (101 MHz, Chloroform-*d*) δ 172.4, 167.2, 149.6, 148.6, 144.4, 140.9, 139.8, 139.6, 137.9, 136.9, 136.7, 136.6, 134.0, 132.7, 130.0, 129.4, 129.1, 128.93, 128.91, 128.8, 128.1, 127.6, 125.9, 122.7, 117.6, 60.5, 49.4, 36.5, 27.9, 19.2, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{31}ClN_2O_5SNa^+$ [M+Na^+] 625.1534, found 625.1534.



Ethyl (*E*)-3-(3-chloro-4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido) -3-oxopropyl)phenyl)acrylate (3c)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 80 %. Yield: 37.3 mg (60%), *p*: others = 7.5:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.61 (td, *J* = 7.2, 2.0 Hz, 2H), 7.54 (d, *J* = 16.0 Hz, 1H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.40 (s, 5H), 7.31 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.21 (dd, *J* = 7.8, 1.8 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 1H), 6.37 (d, *J* = 16.0 Hz, 1H), 5.15 (s, 2H), 4.26 (q, *J* = 7.2 Hz, 2H), 3.00 – 2. 93 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 166.8, 149.8, 148.7, 142.8, 139. 9, 139.8, 139.6, 138. 0, 136.9, 136.6, 134.60, 134.58, 134. 0, 131.2, 129.4, 128.99, 128.97, 128. 9, 128.8, 128.2, 127.7, 126.5, 122.7, 119.4, 60.8, 49.4, 36.0, 28.7, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{28}Cl_2N_2O_5SNa^+$ [M+Na^+] 645.0988, found 645.0988.

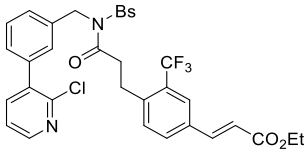


Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-3-(trifluoromethoxy)phenyl)acrylate (3d)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 69 %. Yield: 34.3 mg (51%), *p*: others = 13:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.32 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.63 (d, *J* = 7.4 Hz, 2H), 7.57 – 7.47 (m, 3H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.35 – 7.31 (m, 4H), 7.23 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.21 – 7.15 (m, 2H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.31 (d, *J* = 16.0 Hz, 1H), 5.07 (s, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 2.86 (s, 4H), 1.27 (t, *J* = 7.1 Hz, 3H). ^{13}C

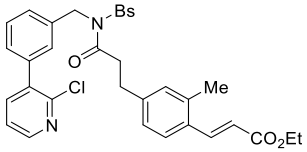
NMR (101 MHz, Chloroform-*d*) δ 172.0, 166.6, 149.7, 148.7, 147.9, 142.8, 139.8, 139.5, 137.9, 136.9, 136.6, 134.7, 134.0, 131.4, 129.4, 129.0, 128.9, 128.8, 128.1, 127.6, 126.4, 122.7, 120.5 (d, J_{C-F} = 258.2 Hz), 119.62, 119.58, 119.56, 60.8, 49.4, 36.3, 25.1, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{28}ClF_3N_2O_6SNa^+$ [M+Na^+] 695.1201, found 695.1200.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-3-(trifluoromethyl)phenyl)acrylate (3e)

The general procedure **B** was followed. (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 42 %. Yield: 25.0 mg (38%), *p*: others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.71 – 7.68 (m, 3H), 7.65 – 7.57 (m, 3H), 7.51 – 7.38 (m, 7H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 6.43 (d, *J* = 16.0 Hz, 1H), 5.15 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.06 (t, *J* = 7.5 Hz, 2H), 2.92 (t, *J* = 7.5 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 166.6, 149.7, 148.7, 142.6, 141.0 (d, J_{C-F} = 1.1 Hz), 139.8, 139.5, 138.0, 136.9, 136.6, 134.0, 133.2, 131.9, 131.1, 129.4, 129.3 (d, J_{C-F} = 30.1 Hz), 129.00, 128.99, 128.87, 128.2, 127.6, 125.8 (q, J_{C-F} = 5.8 Hz), 124.1 (q, J_{C-F} = 271.4 Hz), 122.7, 119.8, 60.9, 49.5, 37.9, 27.5, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{28}ClF_3N_2O_5SNa^+$ [M+Na^+] 679.1252, found 679.1248.

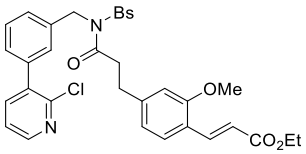


Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-methylphenyl)acrylate (3f)

The general procedure **A** was followed. (75 °C under air) Conversion: 60 %. Yield: 25.9 mg (43%), *p*: others = 7:1; (75 °C under O_2) Yield: 30.8 mg (51%), *p*: others = 8:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.90 (d, *J* = 15.9 Hz, 1H), 7.74 – 7.66 (m, 2H), 7.64 – 7.56 (m, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.36 (m, 5H), 7.30 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.84 – 6.81 (m, 2H), 6.30 (d, *J* = 15.9 Hz, 1H),

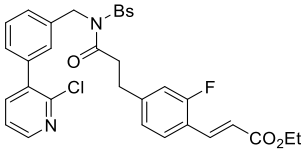
5.14 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.92 (t, *J* = 7.5 Hz, 2H), 2.84 (t, *J* = 7.5 Hz, 2H), 2.33 (s, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.3, 167.2, 149.7, 148.7, 142.4, 142.0, 139.8, 139.6, 137.92, 137.89, 137.0, 136.6, 133.9, 131.6, 130.9, 129.4, 129.0, 128.9, 128.8, 128.1, 127.7, 126.7, 126.4, 122.7, 118.8, 60.6, 49.3, 37.8, 30.4, 19.9, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{31}ClN_2O_5SNa^+$ [M+Na$^+$] 625.1534, found 625.1533.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-methoxyphenyl)acrylate (3g)

The general procedure **A** was followed. (75 °C under air) Conversion: 72 %. Yield: 37.1 mg (60%), *p*: others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.91 (d, *J* = 16.2 Hz, 1H), 7.75 – 7.66 (m, 2H), 7.64 – 7.56 (m, 2H), 7.51 – 7.34 (m, 6H), 7.30 (m, 2H), 6.61 (s, 1H), 6.56 (d, *J* = 7.9 Hz, 1H), 6.47 (d, *J* = 16.1 Hz, 1H), 5.14 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.77 (s, 3H), 2.97 – 2.93 (m, 2H), 2.92 – 2.86 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 167.7, 158.4, 149.6, 148.6, 144.4, 139.8, 139.7, 139.6, 137.9, 136.9, 136.5, 133.9, 129.3, 129.2, 128.9, 128.8, 128.0, 127.6, 122.7, 121.6, 120.5, 118.3, 111.4, 60.4, 55.5, 49.3, 37.8, 30.9, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{31}ClN_2O_6SNa^+$ [M+Na$^+$] 641.1484, found 641.1484.

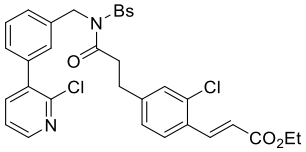


Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluorophenyl)acrylate (3h)

The general procedure **A** was followed (75 °C under air). Conversion: 85 %. Yield: 48.5 mg (80%), *p:* others > 20:1. The general procedure **B** was followed. (2 (2.0 equiv), HFIP (1.5 mL), 90 °C). Yield: 43.6 mg (72%), *p:* others = 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.75 – 7.65 (m, 3H), 7.60 (td, *J* = 7.6, 1.7 Hz, 2H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.34 (m, 4H), 7.34

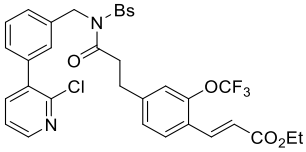
– 7.27 (m, 2H), 6.78 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.68 (dd, *J* = 11.5, 1.7 Hz, 1H), 6.45 (d, *J* = 16.1 Hz, 1H), 5.13 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.95 – 2.90 (m, 2H), 2.88 – 2.84 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 167.0, 161.2 (d, J_{C-F} = 254.3 Hz), 149.6, 148.6, 145.0 (d, J_{C-F} = 8.2 Hz), 139.7, 139.5, 137.9, 137.0 (d, J_{C-F} = 2.6 Hz), 136.8, 136.6, 134.0, 129.4, 129.1 (d, J_{C-F} = 3.6 Hz), 129.01, 128.96, 128.8, 128.1, 127.6, 124.6 (d, J_{C-F} = 3.1 Hz), 122.7, 120.5 (d, J_{C-F} = 11.9 Hz), 120.3 (d, J_{C-F} = 6.6 Hz), 116.0 (d, J_{C-F} = 21.9 Hz), 60.7, 49.3, 37.4, 30.2, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{28}ClFN_2O_5SNa^+$ [M+Na$^+$] 629.1284, found 629.1280.



Ethyl (*E*)-3-(2-chloro-4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamid -o)-3-oxopropyl)phenyl)acrylate (3i)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 75 %. Yield: 37.3 mg (60%), *p*: others > 20:1.

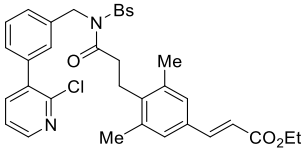
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 8.00 (d, *J* = 16.0 Hz, 1H), 7.68 (d, *J* = 7.5 Hz, 2H), 7.64 – 7.57 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.37 (m, 5H), 7.34 – 7.28 (m, 1H), 7.02 (s, 1H), 6.90 (d, *J* = 8.0 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.14 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.93 (t, *J* = 6.9 Hz, 2H), 2.85 (t, *J* = 6.9 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 166.7, 149.7, 148.7, 144.0, 140.1, 139.8, 139.5, 137.9, 136.9, 136.6, 135.0, 134.1, 130.7, 129.9, 129.4, 129.1, 129.0, 128.9, 128.2, 127.7, 127.6, 127.4, 122.7, 120.5, 60.8, 49.3, 37.5, 30.1, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{28}Cl_2N_2O_5SNa^+$ [M+Na$^+$] 645.0988, found 645.0988.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-(trifluoromethoxy)phenyl)acrylate (3j)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 60 %. Yield: 33.6 mg (50%), *p*: others > 20:1.

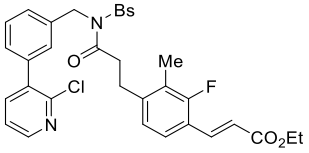
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 3.6 Hz, 1H), 7.83 (d, *J* = 16.1 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.65 – 7.56 (m, 2H), 7.51 – 7.37 (m, 7H), 7.31 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.00 – 6.88 (m, 2H), 6.41 (d, *J* = 16.1 Hz, 1H), 5.14 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 2.96 – 2.87 (m, 4H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 166.6, 149.7, 148.7, 147.5 (d, *J* = 1.5 Hz), 144.6, 139.8, 139.5, 138.0, 137.1, 136.9, 136.6, 134.1, 129.4, 129.1, 129.0, 128.9, 128.2, 128.1, 127.6, 127.3, 125.9, 122.7, 121.4, 120.8, 120.5 (q, *J* = 258.7 Hz), 60.8, 49.4, 37.6, 30.3, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{28}ClF_3N_2O_6SNa^+$ [M+Na^+] 695.1201, found 695.1201.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-3,5-dimethylphenyl)acrylate (3k)

The general procedure **A** was followed (75 °C under O_2). Conversion: 65 %. Yield: 35.1 mg (57%), *p*: others = 8:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.73 (dd, *J* = 7.3, 1.7 Hz, 2H), 7.65 – 7.59 (m, 2H), 7.56 (d, *J* = 16.0 Hz, 1H), 7.49 – 7.40 (m, 6H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.10 (s, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.18 (s, 2H), 4.24 (q, *J* = 7.1 Hz, 2H), 2.91 – 2.82 (m, 2H), 2.69 – 2.65 (m, 2H), 2.11 (s, 6H), 1.32 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.6, 167.3, 149.7, 148.7, 144.5, 139.8, 139.6, 139.5, 138.0, 137.0, 136.9, 136.6, 134.0, 132.4, 129.4, 129.00, 128.96, 128.8, 128.0, 127.7, 122.7, 117.6, 60.5, 49.5, 35.3, 25.0, 19.7, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{34}H_{33}ClN_2O_5SNa^+$ [M+Na^+] 639.1691, found 639.1688.

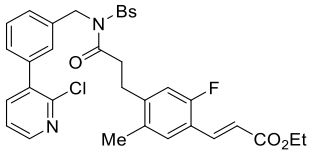


Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluoro-3-methylphenyl)acrylate (3l)

The general procedure **A** was followed (75 °C under air). Conversion: 85 %. Yield: 43.4

mg (70%), *p:* others > 20:1.

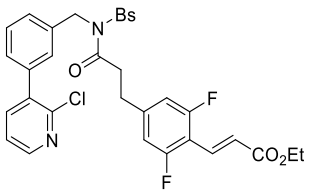
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 (d, *J* = 16.2 Hz, 1H), 7.70 – 7.66 (m, 2H), 7.64 – 7.56 (m, 2H), 7.47 – 7.39 (m, 6H), 7.31 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.15 (t, *J* = 7.7 Hz, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.44 (d, *J* = 16.1 Hz, 1H), 5.15 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.86 (s, 4H), 2.02 (d, *J* = 2.4 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 167.1, 159.7 (d, J_{C-F} = 252.0 Hz), 149.6, 148.7, 143.1 (d, J_{C-F} = 4.6 Hz), 139.8, 139.5, 137.9, 137.6 (d, J_{C-F} = 3.6 Hz), 136.9, 136.5, 134.0, 129.4, 128.98, 128.97, 128.9, 128.1, 127.5, 125.8 (d, J_{C-F} = Hz), 124.4 (d, J_{C-F} =3.7 Hz), 124.0 (d, J_{C-F} = 16.6 Hz), 122.7, 120.4 (d, J_{C-F} = 13.5 Hz), 120.0 (d, J_{C-F} = 6.4 Hz), 60.7, 49.4, 36.5, 28.0 (d, J_{C-F} = 2.6 Hz), 14.4, 10.4 (d, J_{C-F} = 7.0 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{30}ClFN_2O_5SNa^+$ [M+Na$^+$] 643.1440, found 643.1440.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluoro-5-methylphenyl)acrylate (3m)

The general procedure **A** was followed (75 °C under air). Conversion: 80 %. Yield: 43.4 mg (70%), *p:* others > 20:1.

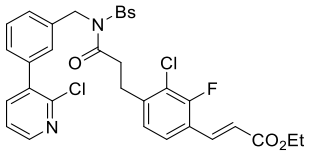
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.74 – 7.65 (m, 3H), 7.65 – 7.57 (m, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.40 (m, 4H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.19 (d, *J* = 7.4 Hz, 1H), 6.57 (d, *J* = 11.4 Hz, 1H), 6.45 (d, *J* = 16.2 Hz, 1H), 5.16 (s, 2H), 4.25 (q, *J* = 7.1 Hz, 2H), 2.89 – 2.79 (m, 4H), 2.10 (s, 3H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 167.0, 159.7 (d, J_{C-F} = 252.0 Hz), 149.6, 148.6, 142.8 (d, J_{C-F} = 7.5 Hz), 139.7, 139.5, 137.9, 137.2 (d, J_{C-F} = 2.2 Hz), 136. 9, 136.5, 134.1, 132.2 (d, J_{C-F} = 3.2 Hz), 130.5 (d, J_{C-F} = 3.2 Hz), 129.4, 129. 0, 128. 9, 128.1, 127.6, 122.7, 120.2 (d, J_{C-F} = 11.8 Hz), 120.1 (d, J_{C-F} = 6.8 Hz), 115.8 (d, J_{C-F} = 22.0 Hz), 60.6, 49.4, 36.1, 27.8, 18.6, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{30}ClFN_2O_5SNa^+$ [M+Na$^+$] 643.1440, found 643.1439.



Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2,6-difluorophenyl)acrylate (3n)

The general procedure **A** was followed (75 °C under air). Conversion: 84 %. Yield: 45.6 mg (73%), *p*: others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.72 – 7.64 (m, 3H), 7.64 – 7.57 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.43 – 7.37 (m, 4H), 7.30 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.65 (d, *J* = 16.5 Hz, 1H), 6.53 (d, *J* = 9.6 Hz, 2H), 5.14 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 2.97 – 2.89 (m, 2H), 2.86 – 2.83 (m, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 167.1, 161.5 (dd, J_{C-F} = 255.5, 7.7 Hz), 149.6, 148.7, 145.0 (t, J_{C-F}= 10.2 Hz), 139.7, 139.5, 137.9, 136.8, 136.5, 134.2, 130.6, 129.5, 129.1, 129.0, 128.9, 128.2, 127.5, 123.7 (t, J_{C-F} = 8.5 Hz), 122.7, 111.8 (dd, J_{C-F}= 25.4, 14.2 Hz), 110.4 (t, J_{C-F}= 15.2 Hz), 60.8, 49.4, 37.1, 30.2, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{27}ClF_2N_2O_5SNa^+$ [M+Na^+] 647.1189, found 647.1186.

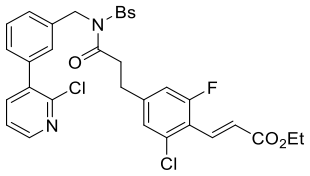


Ethyl (*E*)-3-(3-chloro-4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamid -o)-3-oxopropyl)-2-fluorophenyl)acrylate (3o)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 70 %. Yield: 35.2 mg (55%), *p:* others = 15:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 – 7.66 (m, 3H), 7.64 – 7.55 (m, 2H), 7.49 – 7.36 (m, 6H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.21 (t, *J* = 7.5 Hz, 1H), 6.89 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.47 (d, *J* = 16.2 Hz, 1H), 5.15 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.02 – 2.98 (m, 2H), 2.96 – 2.94 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 166.6, 156.7 (d, J_{C-F} = 255.6 Hz), 149.7, 148.7, 142.0, 139.8, 139.5, 137.9, 136. 9, 136.6, 136.2 (d, J_{C-F} = 2.3 Hz), 134.0, 129.4, 129.03, 128.97, 128.8, 128.2, 127.6, 126.4 (d, J_{C-F} = 3.3 Hz), 125.7 (d, J_{C-F} = 3.8 Hz), 122.7, 122.1 (d, J_{C-F} = 12.3 Hz), 121. 9 (d, J_{C-F} = 17.8 Hz), 121.6 (d, J_{C-F} = 6.4

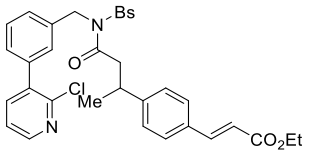
Hz), 60.9, 49.4, 35.8, 28.7 (d, $J_{C\text{-}F}$ = 2.4 Hz), 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{27}Cl_2FN_2O_5SNa^+$ [M+Na^+] 663.0894, found 663.0894.



Ethyl (*E*)-3-(2-chloro-4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamid -o)-3-oxopropyl)-6-fluorophenyl)acrylate (3p)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 68 %. Yield: 36.5 mg (57%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.82 (d, *J* = 16.4 Hz, 1H), 7.71 – 7.66 (m, 2H), 7.61 (td, *J* = 7.7, 1.8 Hz, 2H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.37 (m, 4H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.87 (s, 1H), 6.64 (d, *J* = 16.0 Hz, 1H), 6.64 (d, *J* = 10.6 Hz, 1H), 5.14 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 2.93 (t, *J* = 7.1 Hz, 2H), 2.84 (t, *J* = 6.6 Hz, 3H), 1.34 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 167.0, 161. 9 (d, $J_{C\text{-}F}$ = 256.7 Hz), 149.7, 148.7, 144.3 (d, $J_{C\text{-}F}$ = 9.8 Hz), 139.8, 139.5, 138. 0, 136.8, 136.6, 135.9 (d, $J_{C\text{-}F}$ = 6.0 Hz), 134.6 (d, $J_{C\text{-}F}$ = 2.2 Hz), 134.2, 129.5, 129.1, 129.1, 128.9, 128.2, 127.5, 125. 0 (d, $J_{C\text{-}F}$ = 2.9 Hz), 124.8 (d, $J_{C\text{-}F}$ = 14.6 Hz), 122.7, 119.6 (d, $J_{C\text{-}F}$ = 14.2 Hz), 114.9 (d, $J_{C\text{-}F}$ = 23.5 Hz), 60. 0, 49.4, 37.2, 29.9, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{27}Cl_2FN_2O_5SNa^+$ [M+Na^+] 663.0894, found 663.0888.

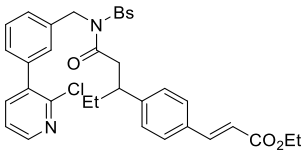


Ethyl (*E*)-3-(4-(4-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-4-oxo -butan-2-yl)phenyl)acrylate (3q)

The general procedure **A** was followed (75 °C under air). Conversion: 80 %. Yield: 42.1 mg (70%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.64 – 7.56 (m, 3H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.24 (m, 7H), 6.97 (d, *J* = 7.9 Hz, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.14 – 5.02 (m, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.34

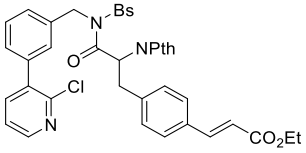
(h, *J* = 7.0 Hz, 1H), 2.98 (dd, *J* = 16.7, 7.5 Hz, 1H), 2.84 (dd, *J* = 16.7, 6.7 Hz, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.7, 167.2, 149.6, 148.6, 148.0, 144.3, 139.7, 139.7, 137.8, 137.0, 136.6, 133.9, 132.6, 129.4, 129.0, 128.9, 128.8, 128.3, 128.1, 127.6, 127.4, 122.7, 117.8, 60.6, 49.1, 44.4, 36.0, 21.7, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{31}ClN_2O_5SNa^+$ [M+Na^+] 625.1534, found 625.1534.



Ethyl (*E*)-3-(4-(1-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-1-oxo -pentan-3-yl)phenyl)acrylate (3r)

The general procedure **A** was followed (75 °C under air). Conversion: 75 %. Yield: 41.3 mg (67%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.68 – 7.55 (m, 5H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.38 – 7.25 (m, 6H), 7.20 (d, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 8.0 Hz, 2H), 6.36 (d, *J* = 16.0 Hz, 1H), 5.12 – 5.00 (m, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 3.11 – 3.04 (m, 1H), 2.98 (dd, *J* = 16.6, 8.4 Hz, 1H), 2.88 (dd, *J* = 16.6, 5.7 Hz, 1H), 1.59 – 1.52 (m, 1H), 1.48 – 1.37 (m, 1H), 1.34 (t, *J* = 7.1 Hz, 3H), 0.67 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 167.2, 149.7, 148.6, 146.4, 144.4, 139.74, 139.73, 137.8, 137.0, 136.6, 133.9, 132.6, 129.4, 129.0, 128.8, 128.7, 128.2, 128.08, 128.06, 127.6, 122.7, 117.7, 60.6, 49.0, 43.3, 43.0, 28.9, 14.4, 11.9. HRMS (m/z, ESI-TOF): Calcd for $C_{34}H_{33}ClN_2O_5SNa^+$ [M+Na^+] 639.1691, found 639.1692.

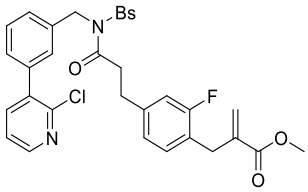


Ethyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido) -2-(1,3-di -oxoisoindolin-2-yl)-3-oxopropyl)phenyl)acrylate (3s)

The general procedure **A** was followed (75 °C under air). Conversion: 50 %. Yield: 30.8 mg (42%), *p:* others = 9:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.98 (dd, *J* = 7.4, 1.8 Hz, 2H), 7.70 – 7.58 (m, 6H), 7.57 – 7.48 (m, 3H), 7.38 – 7.27 (m, 7H), 7.23 (d, *J*

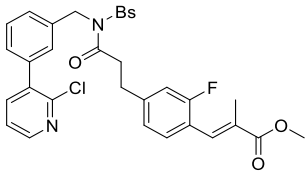
= 8.1 Hz, 2H), 6.31 (d, *J* = 16.0 Hz, 1H), 6.03 (dd, *J* = 11.0, 4.7 Hz, 1H), 5.02 – 4.88 (m, 2H), 4.22 (q, *J* = 7.1 Hz, 2H), 3.75 (dd, *J* = 13.9, 11.0 Hz, 1H), 3.58 (dd, *J* = 13.9, 4.7 Hz, 1H), 1.30 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.0, 167.9, 167.1, 149.7, 148.6, 144.2, 139.8, 139.0, 138.5, 137.7, 136.5, 135.9, 134.3, 133.2, 131.4, 129.7, 129.5, 128.8, 128.7, 128.6, 128.4, 128.1, 127.6, 123.6, 122.7, 118.1, 60.6, 56.5, 50.0, 34.8, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{40}H_{32}ClN_3O_7SNa^+$ [M+Na^+] 756.1542, found 756.1540.



Methyl 2-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluorobenzyl)acrylate (3ha$_1$)

The general procedure **A** was followed (75 °C under air). Conversion: 80 %. Yield: 30.9 mg (51%), *p:* others > 20:1.

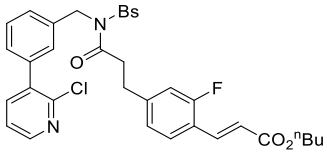
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.73 – 7.67 (m, 2H), 7.65 – 7.57 (m, 2H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.41 (dd, *J* = 8.8, 1.6 Hz, 4H), 7.31 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.00 (t, *J* = 7.8 Hz, 1H), 6.71 (dd, *J* = 7.7, 1.7 Hz, 1H), 6.63 (dd, *J* = 10.7, 1.7 Hz, 1H), 6.22 (s, 1H), 5.41 (s, 1H), 5.14 (s, 2H), 3.74 (s, 3H), 3.58 (s, 2H), 2.94 – 2.87 (m, 2H), 2.84 – 2.80 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 167.3, 161.0 (d, $J_{C\text{-}F}$ = 246.5 Hz), 149.7, 148.6, 141.0 (d, $J_{C\text{-}F}$ = 7.4 Hz), 139.8, 139.6, 138.5, 137.9, 137.0, 136.6, 134.0, 131.3 (d, $J_{C\text{-}F}$ = 4.9 Hz), 129.4, 129.01, 128.95, 128.8, 128.1, 127.6, 126.5, 124.0 (d, $J_{C\text{-}F}$ = 3.2 Hz), 123.5 (d, $J_{C\text{-}F}$ = 15.8 Hz), 122.7, 115.2 (d, $J_{C\text{-}F}$ = 22.1 Hz), 52.1, 49.3, 37.8, 30.9 (d, $J_{C\text{-}F}$ = 2.9 Hz), 30.1. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{28}ClFN_2O_5SNa^+$ [M+Na^+] 629.1284, found 629.1283.



Methyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluorophenyl)-2-methylacrylate (3ha$_2$)

The general procedure **A** was followed (75 °C under air). Conversion: 80 %. Yield: 13.3 mg (22%), *p:* others > 20:1.

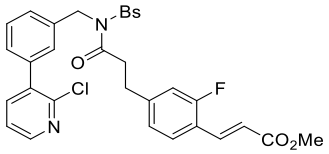
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.74 – 7.69 (m, 2H), 7.66 – 7.58 (m, 3H), 7.47 (t, *J* = 7.9 Hz, 2H), 7.43 – 7.37 (m, 4H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.81 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.69 (dd, *J* = 11.0, 1.7 Hz, 1H), 5.15 (s, 2H), 3.82 (s, 3H), 2.96 – 2.92 (m, 2H), 2.89 – 2.85 (m, 2H), 2.01 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 168.7, 160.3 (d, $J_{C\text{-}F}$ = 250.3 Hz), 149.7, 148.7, 143.3 (d, $J_{C\text{-}F}$ = 7.9 Hz), 139.8, 139.6, 138.0, 136.9, 136.6, 134.1, 131.5 (d, $J_{C\text{-}F}$ = 3.4 Hz), 130.5 (d, $J_{C\text{-}F}$ = 3.3 Hz), 130.4, 129.4, 129.1, 129.0, 128.9, 128.2, 127.7, 123.9 (d, $J_{C\text{-}F}$ = 3.1 Hz), 122.7, 121.7 (d, $J_{C\text{-}F}$ = 13.8 Hz), 115.5 (d, $J_{C\text{-}F}$ = 22.0 Hz), 52.3, 49.4, 37.6, 30.2, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{28}ClFN_2O_5SNa^+$ [M+Na$^+$] 629.1284, found 629.1280.



Butyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluorophenyl)acrylate (3hb)

The general procedure **A** was followed (75 °C under air). Conversion: 80 %. Yield: 43.1 mg (68%), *p:* others > 20:1.

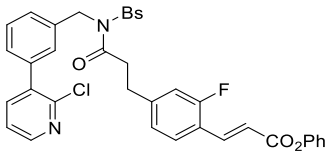
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 – 7.65 (m, 3H), 7.64 – 7.57 (m, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.40 – 7.35 (m, 4H), 7.34 – 7.27 (m, 2H), 6.79 (dd, *J* = 8.1, 1.7 Hz, 1H), 6.68 (dd, *J* = 11.5, 1.7 Hz, 1H), 6.46 (d, *J* = 16.2 Hz, 1H), 5.13 (s, 2H), 4.21 (t, *J* = 6.7 Hz, 2H), 2.95 – 2.91 (m, 2H), 2.88 – 2.84 (m, 2H), 1.74 – 1.63 (m, 2H), 1.50 – 1.37 (m, 2H), 0.96 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 167.1, 161.2 (d, $J_{C\text{-}F}$ = 254.3 Hz), 149.6, 148.6, 145.0 (d, $J_{C\text{-}F}$ = 8.2 Hz), 139.8, 139.5, 137.9, 137.0 (d, $J_{C\text{-}F}$ = 2.5 Hz), 136.8, 136.5, 134.0, 129.4, 129.1 (d, $J_{C\text{-}F}$ = 3.4 Hz), 129.02, 128.96, 128.8, 128.1, 127.6, 124.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 122.7, 120.5 (d, $J_{C\text{-}F}$ = 11.8 Hz), 120.3 (d, $J_{C\text{-}F}$ = 6.5 Hz), 116.0 (d, $J_{C\text{-}F}$ = 21.8 Hz), 64.6, 49.3, 37.4, 30.8, 30.2, 19.3, 13.8. HRMS (m/z, ESI-TOF): Calcd for $C_{34}H_{32}ClFN_2O_5SNa^+$ [M+Na$^+$] 657.1597, found 657.1599.



Methyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo-propyl)-2-fluorophenyl)acrylate (3hc)

The general procedure **A** was followed (75 °C under air). Conversion: 87 %. Yield: 43.2 mg (73%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.72 (d, *J* = 16.2 Hz, 1H), 7.70 – 7.65 (m, 2H), 7.60 (td, *J* = 7.7, 1.6 Hz, 2H), 7.45 (t, *J* = 7.8 Hz, 2H), 7.42 – 7.35 (m, 4H), 7.33 – 7.28 (m, 2H), 6.79 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.68 (dd, *J* = 11.5, 1.7 Hz, 1H), 6.46 (d, *J* = 16.2 Hz, 1H), 5.13 (s, 2H), 3.80 (s, 3H), 2.95 – 2.91 (m, 2H), 2.88 – 2.84 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 167.4, 161.2 (d, $J_{C\text{-}F}$ = 254.4 Hz), 149.6, 148.7, 145.1 (d, $J_{C\text{-}F}$ = 8.1 Hz), 139.7, 139.5, 137.9, 137.3 (d, $J_{C\text{-}F}$ = 2.5 Hz), 136.8, 136.5, 134.0, 129.4, 129.1 (d, $J_{C\text{-}F}$ = 3.4 Hz), 129.02, 128.97, 128.8, 128.1, 127.6, 124.6 (d, $J_{C\text{-}F}$ = 3.2 Hz), 122.7, 120.4 (d, $J_{C\text{-}F}$ = 11.7 Hz), 119.8 (d, $J_{C\text{-}F}$ = 6.6 Hz), 116.0 (d, $J_{C\text{-}F}$ = 21.9 Hz), 51.9, 49.3, 37.4, 30.2. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{26}ClFN_2O_5SNa^+$ [M+Na$^+$] 615.1127, found 615.1128.

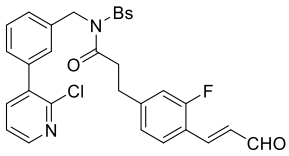


Phenyl (*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo-propyl)-2-fluorophenyl)acrylate (3hd)

The general procedure **A** was followed (75 °C under air). Conversion: 74 %. Yield: 39.2 mg (60%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.90 (d, *J* = 16.2 Hz, 1H), 7.74 – 7.68 (m, 2H), 7.65 – 7.58 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.44 – 7.35 (m, 7H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.28 – 7.22 (m, 1H), 7.20 – 7.15 (m, 2H), 6.84 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.73 (dd, *J* = 11.5, 1.6 Hz, 1H), 6.67 (d, *J* = 16.2 Hz, 1H), 5.15 (s, 2H), 2.98 – 2.94 (m, 2H), 2.91 – 2.98 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 165.4, 161.4 (d, $J_{C\text{-}F}$ = 254.9 Hz), 150.8, 149.6, 148.7, 145.6 (d, $J_{C\text{-}F}$ = 8.2 Hz), 139.8, 139.5, 139.0 (d, $J_{C\text{-}F}$ = 2.4 Hz), 137.9, 136.8, 136.6, 134.1, 129.6, 129.43, 129.41, 129.03, 128.99, 128.8, 128.1, 127.6, 125.9, 124.7 (d, $J_{C\text{-}F}$ = 3.1 Hz),

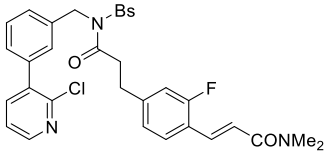
122.7, 121.7, 120.3 (d, $J_{C\text{-}F}$ = 11.7 Hz), 119.4 (d, $J_{C\text{-}F}$ = 6.8 Hz), 116.1 (d, $J_{C\text{-}F}$ = 21.9 Hz), 49.34, 37.40, 30.27. HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{28}ClFN_2O_5SNa^+$ [M+Na^+] 677.1284, found 677.1278.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluoro-4-(3-oxoprop-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (3he)

The general procedure **A** was followed (75 °C under air). Conversion: 72 %. Yield: 36.5 mg (65%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.69 (d, *J* = 7.7 Hz, 1H), 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.71 – 7.67 (m, 2H), 7.64 – 7.58 (m, 2H), 7.56 (d, *J* = 16.2 Hz, 1H), 7.46 (t, *J* = 7.9 Hz, 2H), 7.42 – 7.34 (m, 5H), 7.31 (dd, *J* = 7.5, 4.8 Hz, 1H), 6.85 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.77 – 6.67 (m, 2H), 5.14 (s, 2H), 2.98 – 2.93 (m, 2H), 2.91 – 2.87 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 193.9, 171.8, 161.2 (d, $J_{C\text{-}F}$ = 255.5 Hz), 149.7, 148.7, 146.5 (d, $J_{C\text{-}F}$ = 8.3 Hz), 144.7 (d, $J_{C\text{-}F}$ = 3.3 Hz), 139.8, 139.5, 138.0, 136.8, 136.6, 134.1, 130.1 (d, $J_{C\text{-}F}$ = 5.4 Hz), 129.4, 129.1, 129.0, 128.93 (d, $J_{C\text{-}F}$ = 3.0 Hz), 128.86, 128.2, 127.6, 124.8 (d, $J_{C\text{-}F}$ = 3.0 Hz), 122.7, 120.2 (d, $J_{C\text{-}F}$ = 11.7 Hz), 116.2 (d, $J_{C\text{-}F}$ = 21.7 Hz), 49.4, 37.4, 30.4 (d, $J_{C\text{-}F}$ = 1.5 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{30}H_{24}ClFN_2O_4SNa^+$ [M+Na^+] 585.1022, found 585.1019.

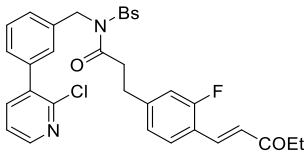


(*E*)-3-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxopropyl)-2-fluorophenyl)-*N*,*N*-dimethylacrylamide (3hf)

The general procedure **A** was followed (75 °C under air). Conversion: 80 %. Yield: 42.3 mg (70%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 – 7.55 (m, 5H), 7.44 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.34 (m, 4H), 7.32 – 7.27 (m, 2H), 6.95 (d, *J* = 15.6 Hz, 1H), 6.77 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.66 (dd, *J* = 11.7, 1.7 Hz, 1H), 5.13 (s, 2H), 3.15 (s, 3H), 3.06 (s, 3H), 2.94 – 2.90 (m, 2H), 2.87 – 2.83 (m, 2H). ^{13}C NMR

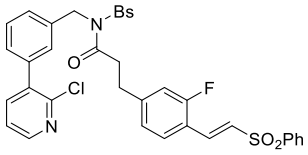
(101 MHz, Chloroform-*d*) δ 172.0, 166.8, 161.2 (d, J_{C-F} = 253.5 Hz), 149.6, 148.6, 144.0 (d, J_{C-F} = 8.1 Hz), 139.8, 139.5, 137.9, 136.9, 136.6, 135.2, 134.0, 129.8 (d, J_{C-F} = 3.9 Hz), 129.4, 129.01, 128.96, 128.8, 128.1, 127.6, 124.4 (d, J_{C-F} = 3.2 Hz), 122.7, 121.4 (d, J_{C-F} = 11.8 Hz), 120.0 (d, J_{C-F} = 7.9 Hz), 116.0 (d, J_{C-F} = 22.1 Hz), 49.3, 37.5, 36.0, 30.2. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{29}ClFN_3O_4SNa^+$ [M+Na^+] 628.1444, found 628.1444.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluoro-4-(3-oxopent-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (3hg)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 76 %. Yield: 36.6 mg (62%), *p:* others > 20:1.

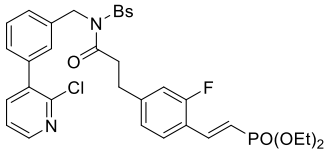
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.65 – 7.56 (m, 3H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.41 – 7.37 (m, 4H), 7.36 – 7.28 (m, 2H), 6.79 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.74 (d, *J* = 16.4 Hz, 1H), 6.69 (dd, *J* = 11.5, 1.7 Hz, 1H), 5.13 (s, 2H), 2.95 – 2.91 (m, 2H), 2.89 – 2.85 (m, 2H), 2.70 (q, *J* = 7.3 Hz, 2H), 1.16 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 201.1, 171.9, 161.4 (d, J_{C-F} = 254.1 Hz), 149.6, 148.7, 145.2 (d, J_{C-F} = 8.1 Hz), 139.8, 139.5, 137.9, 136.9, 136.6, 134.5 (d, J_{C-F} = 2.7 Hz), 134.7, 129.4, 129.0, 129.0, 128.9, 128.8, 128.2, 127.8 (d, J_{C-F} = 5.8 Hz), 127.6, 124.6 (d, J_{C-F} = 3.1 Hz), 122.7, 120.7 (d, J_{C-F} = 11.8 Hz), 116.0 (d, J_{C-F} = 22.0 Hz), 49.3, 37.4, 34.1, 30.2, 8.3. HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{28}ClFN_2O_4SNa^+$ [M+Na^+] 613.1335, found 613.1340.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluoro-4-(2-(phenylsulfonyl)vinyl)phenyl)-*N*-(phenylsulfonyl)propanamide (3hh)

The general procedure **A** was followed (75 °C under air). Conversion: 55 %. Yield: 30.3 mg (45%), *p:* others > 20:1.

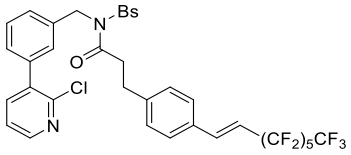
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.38 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.97 – 7.91 (m, 2H), 7.71 – 7.63 (m, 3H), 7.63 – 7.51 (m, 5H), 7.45 (t, *J* = 7.7 Hz, 2H), 7.38 (d, *J* = 5.5 Hz, 4H), 7.30 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 6.94 (d, *J* = 15.5 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.70 (d, *J* = 11.6 Hz, 1H), 5.12 (s, 2H), 2.94 – 2.90 (m, 2H), 2.89 – 2.84 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 161.5 (d, J_{C-F} = 255.8 Hz), 149.6, 148.7, 146.4 (d, J_{C-F} = 8.4 Hz), 140.6, 139.7, 139.5, 137.9, 136.8, 136.5, 135.4 (d, J_{C-F} = 1.8 Hz), 134.1, 133.6, 130.4 (d, J_{C-F} = 3.1 Hz), 129.6 (d, J_{C-F} = 8.9 Hz), 129.5, 129.4, 129.01, 128.97, 128.8, 128.2, 127.8, 127.6, 124.8 (d, J_{C-F}= 3.2 Hz), 122.8, 118.6 (d, J_{C-F} = 11.6 Hz), 116.2 (d, J_{C-F} = 21.7 Hz), 49.3, 37.3, 30.2. HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{28}ClFN_2O_5S_2Na^+$ [M+Na$^+$] 697.1004, found 697.1005.



Diethyl (*E*)-(4-(3-(*N*-(3-(2-chloropyridin-3-yl)benzyl)phenylsulfonamido)-3-oxo -propyl)-2-fluorostyryl)phosphonate (3hi)

The general procedure **A** was followed (75 °C under air). Conversion: 77 %. Yield: 38.2 mg (57%), *p:* others > 20:1.

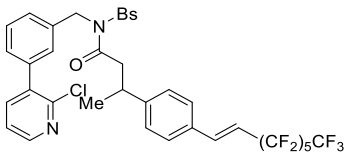
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.72 – 7.65 (m, 2H), 7.64 – 7.49 (m, 3H), 7.50 – 7.41 (m, 2H), 7.41 – 7.36 (m, 4H), 7.34 – 7.25 (m, 2H), 6.79 (dd, *J* = 8.0, 1.7 Hz, 1H), 6.68 (dd, *J* = 11.5, 1.7 Hz, 1H), 6.30 (t, *J* = 17.9 Hz, 1H), 5.13 (s, 2H), 4.17 – 4.09 (m, 4H), 2.96 – 2.90 (m, 2H), 2.90 – 2.83 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 161.0 (d, J_{C-F} = 254.1 Hz), 149.6, 148.7, 145.0 (d, J_{C-F} = 8.3 Hz), 141.0 (dd, J_{C-P} = 7.4, J_{C-F} = 2.8 Hz), 139.7, 139.5, 137.9, 136.8, 136.6, 134.2, 129.4, 129.4, 129.0, 128.9, 128.8, 128.1, 127.6, 124.5 (d, J_{C-F} = 3.1 Hz), 122.7, 120.9 (dd, J_{C-P} = 23.9, J_{C-F} = 11.5 Hz), 116.5 (dd, J_{C-P} = 190.7, J_{C-F} = 6.3 Hz), 116.0 (d, J_{C-F} = 21.9 Hz), 62.0 (d, J_{C-P} = 5.5 Hz), 49.3, 37.4, 30.2, 16.5 (d, J_{C-P} = 6.4 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{33}ClFN_2O_6PSNa^+$ [M+Na$^+$] 693.1362, found 693.1362.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)propanamide (4a)

The general procedure **A** was followed (70 °C under air). Conversion: 77 %. Yield: 54.2 mg (65%), *p:* others > 20:1; The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.5 mL), 80 °C). Conversion: 85 %. Yield: 60.9 mg (73%), *p:* others > 20:1.

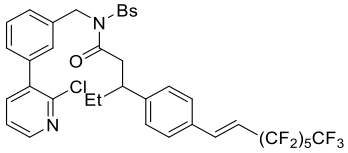
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 – 7.66 (m, 2H), 7.64 – 7.56 (m, 2H), 7.45 (t, *J* = 7.9 Hz, 2H), 7.39 (td, *J* = 4.8, 4.0, 1.7 Hz, 4H), 7.33 – 7.27 (m, 3H), 7.10 (dt, *J* = 16.3, 2.5 Hz, 1H), 7.03 (d, *J* = 8.1 Hz, 2H), 6.14 (dt, *J* = 16.2, 12.2 Hz, 1H), 5.14 (s, 2H), 2. 97 – 2. 93 (m, 2H), 2. 91 – 2.87 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.2, 149.7, 148.7, 142.8, 139.8, 139.6, 139.5 (t, J_{C-F} = 9.7 Hz), 137.9, 136.9, 136.6, 134. 0, 131.7, 129.4, 129.0, 128.9, 128.8, 128.3, 127.9, 127.7, 122.7, 113. 9 (t, J_{C-F} = 23.0 Hz), 49.3, 37.8, 30.5. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111. 0 (q, *J* = 12.3, 11.5 Hz), -121.5 – -121.7 (m), -122.7 – -123.0 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{24}ClF_{13}N_2O_3SNa^+$ [M+Na$^+$] 857.0881, found 857.0876.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)butanamide (4b)

The general procedure **A** was followed (70 °C under air). Conversion: 80 %. Yield: 61.9 mg (73%), *p:* others > 20:1.

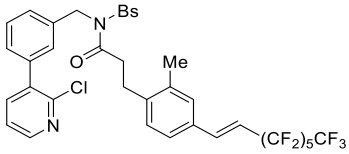
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 2H), 7.61 (dd, *J* = 7.7, 2.6 Hz, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.41 – 7.34 (m, 3H), 7.33 – 7.26 (m, 4H), 7.11 (dt, *J* = 16.1, 2.3 Hz, 1H), 7.03 (d, *J* = 8.0 Hz, 2H), 6.14 (dt, *J* = 16.0, 12.1 Hz, 1H), 5.15 – 5. 06 (m, 2H), 3.36 (h, *J* = 6.9 Hz, 1H), 3.01 (dd, *J* = 16.7, 7.6 Hz, 1H), 2.87 (dd, *J* = 16.7, 6.7 Hz, 1H), 1.14 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.7, 149.7, 148.7, 148.1, 139.8, 139.7, 139.5 (t, J_{C-F} = 9.3 Hz), 137.9, 137.0, 136.6, 133.9, 131.7, 129.4, 129.1, 128. 9, 128.8, 128.2, 127.9, 127.6, 127.5, 122.7, 113.8 (t, J_{C-F} = 23.0 Hz), 49.1, 44.4, 36.0, 21.7. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -110.9 (q, *J* = 12.7, 12.3 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{26}ClF_{13}N_2O_3SNa^+$ [M+Na$^+$] 871.1031, found 871.1032.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-3-(4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)pentanamide (4c)

The general procedure **A** was followed (70 °C under air). Conversion: 82 %. Yield: 64.7 mg (75%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 4.7 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.64 – 7.56 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.39 – 7.36 (m, 2H), 7.34 – 7.20 (m, 5H), 7.10 (d, *J* = 16.1 Hz, 1H), 6.97 (d, *J* = 7.8 Hz, 2H), 6.14 (dt, *J* = 16.2, 12.1 Hz, 1H), 5.30 – 4.98 (m, 2H), 3.21 – 2.80 (m, 3H), 1.63 – 1.53 (m, 1H), 1.49 – 1.39 (m, 1H), 0.68 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 149.7, 148.6, 146.4, 139. 79, 139.75, 139.6 (t, J_{C-F} = 9.2 Hz), 137. 9, 137.0, 136.6, 133.9, 131.7, 129.4, 129.0, 128.8, 128.7, 128.2, 128.1, 127.8, 127.6, 122.7, 113.7 (t, J_{C-F} = 22.9 Hz), 49.1, 43.3, 43.0, 29.0, 11. 9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.8 Hz), -110.9 (q, *J* = 12.9, 12.3 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.1 – -123.2 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{28}ClF_{13}N_2O_3SNa^+$ [M+Na^+] 885.1194, found 885.1189.

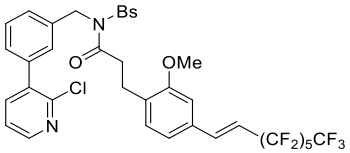


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(2-methyl-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (4d)

The general procedure **A** was followed (70 °C under air). Conversion: 70 %. Yield: 51.7 mg (61%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 2H), 7.65 – 7.57 (m, 2H), 7.50 – 7.38 (m, 6H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.18 (s, 1H), 7.15 – 7.04 (m, 2H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.13 (dt, *J* = 16.4, 12.2 Hz, 1H), 5.16 (s, 2H), 2.88 (s, 4H), 2.16 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.4, 149.7, 148.7, 140.9, 139.8, 139.6, 139.6 (t, J_{C-F} = 8.9 Hz), 138. 0, 137. 0, 136.9, 136.6, 134. 0, 131.8, 129.6, 129.4, 129.2, 129. 0, 128. 9, 128.2, 127.7, 125.5, 122.7, 113.6 (t, J_{C-F} = 22.9 Hz), 49.4, 36.5, 27.9, 19.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t,

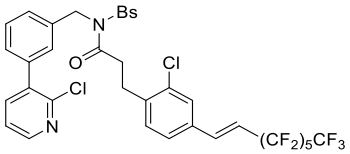
J = 10.0 Hz), -110.9 (q, *J* = 12.7, 12.3 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{26}ClF_{13}N_2O_3SNa^+$ [M+Na^+] 871.1037, found 871.1032.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(2-methoxy-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (4e)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.5 mL), 80 °C). Conversion: 70 %. Yield: 44.9 mg (52%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.73 (d, *J* = 7.8 Hz, 2H), 7.65 – 7.54 (m, 2H), 7.46 (d, *J* = 7.7 Hz, 2H), 7.40 (s, 4H), 7.30 (dd, *J* = 7.6, 4.7 Hz, 1H), 7.10 (dt, *J* = 16.0 Hz, 2.3 Hz, 1H), 7.00 (d, *J* = 7.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 6.82 (s, 1H), 6.13 (dt, *J* = 16.0, 12.1 Hz, 1H), 5.15 (s, 2H), 3.72 (s, 3H), 2. 92 – 2.85 (m, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.8, 157.8, 149.7, 148.7, 139.8 (t, J_{C-F} = 9.2 Hz), 139.8, 139.7, 137.9, 137.1, 136.6, 133.8, 133.2, 131.2, 130.7, 129.2, 128.88, 128.87, 128.8, 128.0, 127.8, 122.7, 120.4, 113.8 (t, J_{C-F} = 23.3 Hz), 108. 9, 55.3, 49.4, 36.0, 26.0. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 10.0 Hz), -110. 9 (t, *J* = 13.0 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.1 – -123.2 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{26}ClF_{13}N_2O_4SNa^+$ [M+Na^+] 887.0986, found 887.0978.

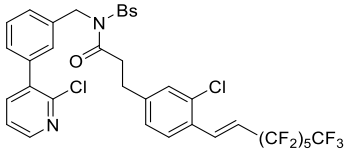


(*E*)-3-(2-chloro-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)propanamide (4f)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.5 mL), 80 °C). Conversion: 60 %. Yield: 46.0 mg (53%), *p:* others = 13:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.71 (d, *J* = 7.9 Hz, 2H), 7.65 – 7.56 (m, 2H), 7.48 – 7.35 (m, 7H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.17 (dd, *J* = 7.9, 1.6 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 1H), 7.05 (d, *J* = 16.1 Hz, 1H), 6.16 (dt, *J* = 16.3, 11.9 Hz, 1H), 5.15 (s, 2H), 3. 02 – 2. 94 (m, 4H). ^{13}C NMR (101 MHz,

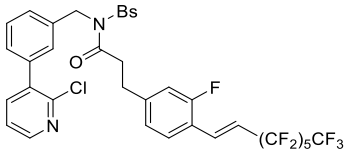
Chloroform-*d*) δ 172.1, 149.7, 148.7, 139.9, 139.8, 139.6, 138.2 (t, J_{C-F} = 9.3 Hz), 138.0, 136.9, 136.6, 134.7, 134. 0, 133.6, 131.3, 129.4, 128.99, 128.96, 128.9, 128.5, 128.2, 127.7, 126.2, 122.7, 115.4 (t, J_{C-F} = 23.2 Hz), 49.4, 36.0, 28.7. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 10.0 Hz), -111.3 (t, *J* = 12.5 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.1 – -123.2 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{23}Cl_2F_{13}N_2O_3SNa^+$ [M+Na$^+$] 891.0491, found 891.0484.



(*E*)-3-(3-chloro-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)propanamide (4g)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.5 mL), 80 °C). Conversion: 65 %. Yield: 48.6 mg (56%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.7, 1.7 Hz, 1H), 7.69 (d, *J* = 7.4 Hz, 2H), 7.66 – 7.56 (m, 2H), 7.52 (d, *J* = 16.2 Hz, 1H), 7.46 (t, *J* = 7.8 Hz, 2H), 7.43 – 7.34 (m, 5H), 7.31 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.04 (s, 1H), 6.96 (d, *J* = 8.9 Hz, 1H), 6.15 (dt, *J* = 16.3, 12.0 Hz, 1H), 5.14 (s, 2H), 2.94 (t, *J* = 6.5 Hz, 3H), 2.87 (t, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 149.7, 148.7, 144.2, 139.8, 139.5, 138.0, 136. 9, 136.6, 135.9 (t, J_{C-F} = 9.5 Hz), 134.5, 134.1, 129.9, 129.4, 129.1, 129.0, 128. 9, 128.2, 127.61, 127.58, 127.5, 122.7, 116.6 (t, J_{C-F} = 22.9 Hz), 49.4, 37.5, 30.0. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.2 – -111.3 (m), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.1 – -123.2 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{23}Cl_2F_{13}N_2O_3SNa^+$ [M+Na$^+$] 891.0491, found 891.0495.

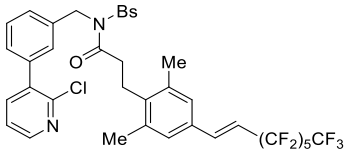


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluoro-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (4h)

The general procedure **A** was followed (70 °C under air). Conversion: 69 %. Yield: 51.1 mg (60%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 (d, *J* = 7.5 Hz, 2H), 7.66 – 7.57 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.44 – 7.37 (m, 4H), 7.35 – 7.25

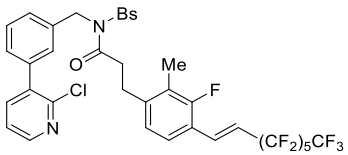
(m, 2H), 7.21 (dt, *J* = 16.4, 2.5 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 6.73 (d, *J* = 11.6 Hz, 1H), 6.28 (dt, *J* = 16.4, 12.1 Hz, 1H), 5.15 (s, 2H), 2. 98 – 2. 94 (m, 2H), 2. 91 – 2. 87 (m, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.9, 161.0 (d, J_{C-F} = 254.2 Hz), 149.7, 148.7, 145.1 (d, J_{C-F} = 8.2 Hz), 139.8, 139.6, 138.0, 136.9, 136.6, 134.1, 132.6 (td, J_{C-F} = 10.2, 2.2 Hz), 129.4, 129.1, 129.06 (d, J_{C-F} = 3.5 Hz), 129.00, 128.86, 128.2, 127.6, 124.7 (d, J_{C-F} = 3.2 Hz), 122.7, 119.6 (d, J_{C-F} = 11.7 Hz), 116.5 (td, J_{C-F} = 23.3, 22.8, 7.1 Hz), 116.1 (d, J_{C-F} = 22.0 Hz), 49.4, 37.5, 30.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.5 (q, *J* = 12.7, 12.3 Hz), -115.1 (dd, *J* = 11.5, 7.7 Hz), -121.5 – -121.6 (m), -122.8 – -122.9 (m), -123.1 – -123.2 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{23}ClF_{14}N_2O_3SNa^+$ [M+Na$^+$] 875.0787, found 875.0777.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(2,6-dimethyl-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (4i)

The general procedure **A** was followed (70 °C under air). Conversion: 60 %. Yield: 38.8 mg (45%), *p:* others = 13:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.74 (d, *J* = 7.4 Hz, 2H), 7.67 – 7.57 (m, 2H), 7.52 – 7.38 (m, 6H), 7.32 (dd, *J* = 7.5, 4.8 Hz, 1H), 7.06 – 7.02 (m, 3H), 6.13 (dt, *J* = 16.3, 12.2 Hz, 1H), 5.19 (s, 2H), 2.93 – 2.84 (m, 2H), 2.73 – 2.65 (m, 2H), 2.13 (s, 6H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.6, 149.7, 148.7, 139.8, 139.61, 139.60 (d, J_{C-F} = 9.4 Hz), 139.5, 138.1, 137.1, 137.0, 136.6, 134.0, 131.5, 129.4, 129.02, 128.97, 128. 9, 128.1, 127.7, 127.6, 122.7, 113.6 (t, J_{C-F} = 23.0 Hz), 49.5, 35.4, 24.9, 19.7. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 10.0 Hz), -110.9 (q, *J* = 13.0 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{28}ClF_{13}N_2O_3SNa^+$ [M+Na$^+$] 885.1194, found 885.1183.

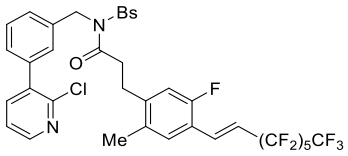


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3-fluoro-2-methyl-4-

(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)-propanamide (4j)

The general procedure **A** was followed (70 °C under air). Conversion: 56 %. Yield: 44.2 mg (51%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.69 (d, *J* = 7.2 Hz, 2H), 7.65 – 7.56 (m, 2H), 7.44 (dd, *J* = 16.2, 8.4 Hz, 6H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.22 (dt, *J* = 16.3, 2.5 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 6.26 (dt, *J* = 16.4, 12.1 Hz, 1H), 5.16 (s, 2H), 2.93 – 2.82 (m, 4H), 2.04 (d, *J* = 2.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.1, 159.5 (d, J_{C-F} = 251.2 Hz), 149.7, 148.7, 143.2 (d, J_{C-F} = 4.8 Hz), 139.8, 139.6, 138.0, 136.9, 136.6, 134.0, 133.3 – 132.9 (m), 129.4, 129.1, 129.0, 128.9, 128.2, 127.6, 125.8, 124.5 (d, J_{C-F} = 3.5 Hz), 124.2 (d, J_{C-F} = 16.6 Hz), 122.8, 119.5 (d, J_{C-F} = 13.9 Hz), 116.5 (td, J_{C-F} = 24.1, 23.7, 8.0 Hz), 49.4, 36.6, 28.0 (d, J_{C-F} = 2.6 Hz), 10.4 (d, J_{C-F} = 7.0 Hz). ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.4 (q, *J* = 12.7 Hz), -117.8 (d, *J* = 7.2 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{25}ClF_{14}N_2O_3SNa^+$ [M+Na^+] 889.0943, found 889.0931.

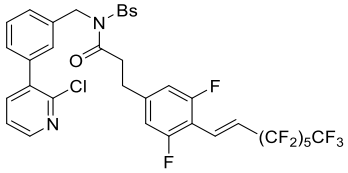


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(5-fluoro-2-methyl-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)-propanamide (4k)

The general procedure **A** was followed (70 °C under air). Conversion: 60 %. Yield: 50.2 mg (58%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 2H), 7.65 – 7.57 (m, 2H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.44 – 7.40 (m, 4H), 7.30 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.21 – 7.12 (m, 2H), 6.61 (d, *J* = 11.5 Hz, 1H), 6.26 (dt, *J* = 16.4, 12.1 Hz, 1H), 5.17 (s, 2H), 2.92 – 2.86 (m, 2H), 2.86 – 2.80 (m, 2H), 2.13 (s, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.0, 159.5 (d, J_{C-F} = 251.1 Hz), 149.7, 148.7, 142.9 (d, J_{C-F} = 7.7 Hz), 139.8, 139.6, 138.0, 136.9, 136.6, 134.1, 132.7 (t, J_{C-F} = 10.2 Hz), 132.4 (d, J_{C-F} = 3.3 Hz), 130.4, 129.5, 129.1, 129.0, 128.9, 128.2, 127.6, 122.7, 119.2 (d, J_{C-F} = 11.5 Hz), 116.6 – 115.9 (m), 115.9 (d, J_{C-F} = 21.9 Hz), 49.4, 36.2, 27. 9, 18.6. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.5 (q, *J* = 12.6, 12.1

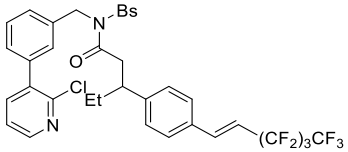
Hz), -119.5 (dd, *J* = 11.4, 7.6 Hz), -121.5 – -121.6 (m), -122.8 – -122.9 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{25}ClF_{14}N_2O_3SNa^+$ [M+Na^+] 889.0943, found 889.0937.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(3,5-difluoro-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)propanamide (4l)

The general procedure **A** was followed (70 °C under air). Conversion: 65 %. Yield: 53.1 mg (61%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.66 – 7.58 (m, 2H), 7.47 (t, *J* = 7.7 Hz, 2H), 7.43 (s, 1H), 7.40 (s, 3H), 7.31 (dd, *J* = 7.6, 4.8 Hz, 1H), 7.16 (dd, *J* = 16.5, 2.7 Hz, 1H), 6.57 (d, *J* = 9.7 Hz, 2H), 6.52 – 6.45 (m, 1H), 5.15 (s, 2H), 2.94 (t, *J* = 6.6 Hz, 2H), 2.87 (t, *J* = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.6, 161.2 (dd, J_{C-F} = 254.8, 7.4 Hz), 149.7, 148.7, 145.3 (t, J_{C-F} = 10.3 Hz), 139.8, 139.5, 138.0, 136.8, 136.6, 134.2, 129.5, 129.2, 129.0, 128. 9, 128.2, 127.6, 126.35 – 126.04 (m), 122.7, 120.4 – 119.4 (m), 111. 9 (dd, J_{C-F} = 24.4, 14.3 Hz), 109.4 (t, J_{C-F} = 14.8 Hz), 49.4, 37.2, 30.3. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.4 (d, *J* = 9.8 Hz), -112.3 (q, *J* = 12.8 Hz), -121.5 – -121.7 (m), -122.8 – -122.9 (m), -123.2 – -123.3 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{22}ClF_{15}N_2O_3SNa^+$ [M+Na^+] 893.0692, found 893.0688.

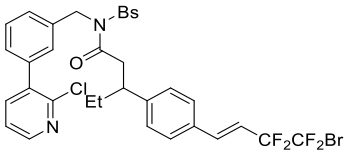


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(4-(3,3,4,4,5,5,6,6,6-nonafluorohex-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)pentanamide (4m)

The general procedure **A** was followed (70 °C under air). Conversion: 66 %. Yield: 38.1 mg (50%), *p:* others = 11:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.70 – 7.57 (m, 4H), 7.47 (t, *J* = 7.8 Hz, 2H), 7.40 – 7.35 (m, 2H), 7.34 – 7.28 (m, 2H), 7.27 – 7.22 (m, 3H), 7.10 (dt, *J* = 16.2, 2.5 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.13 (dt, *J* = 16.3, 12.3

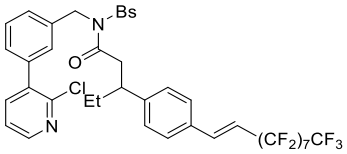
Hz, 1H), 5.15 – 5.01 (m, 2H), 3.13 – 3.06 (m, 1H), 3.05 – 2.85 (m, 2H), 1.61 – 1.52 (m, 1H), 1.47 – 1.40 (m, 1H), 0.68 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 149.7, 148.7, 146.4, 139.79, 139.77, 139.72 – 139.46 (m), 137. 9, 137.0, 136.6, 133.9, 131.7, 129.4, 129.1, 128. 9, 128.8, 128.2, 128.1, 127.8, 127.6, 122.7, 113.6 (t, $J_{C\text{-}F}$ = 23.1 Hz), 49.1, 43.3, 43.0, 29.0, 11. 9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -79.6 – -82.8 (m), -111.1 (q, *J* = 12.4 Hz), -124.0 – -124.1 (m), -125.6 – -125.7 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{28}ClF_9N_2O_3SNa^+$ [M+Na$^+$] 785.1258, found 785.1252.



(*E*)-3-(4-(4-bromo-3,3,4,4-tetrafluorobut-1-en-1-yl)phenyl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)pentanamide (4n)

The general procedure **A** was followed (70 °C under air). Conversion: 70 %. Yield: 35.4 mg (49%), *p:* others = 9:1.

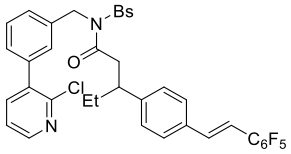
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 2.0 Hz, 1H), 7.72 – 7.56 (m, 4H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.42 – 7.28 (m, 4H), 7.29 – 7.21 (m, 3H), 7.10 (d, *J* = 16.2 Hz, 1H), 6.95 (d, *J* = 8.0 Hz, 2H), 6.16 (dt, *J* = 16.3, 11.8 Hz, 1H), 5.18 – 4.95 (m, 2H), 3.19 – 2.77 (m, 3H), 1.62 – 1.52 (m, 1H), 1.50 – 1.36 (m, 1H), 0.68 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 149.7, 148.7, 146.3, 139. 8, 139.6 (t, $J_{C\text{-}F}$ = 8.9 Hz), 137.8, 137.0, 136.6, 133.9, 131.8, 129.4, 129.0, 128. 9, 128.8, 128.2, 128.1, 127.8, 127.6, 122.7, 113.7 (t, $J_{C\text{-}F}$ = 23.8 Hz), 49.1, 43.3, 43.0, 29.0, 11.9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -65.6 (t, *J* = 6.5 Hz), -108.87 – -108. 9 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{33}H_{28}BrClF_4N_2O_3SNa^+$ [M+Na$^+$] 745.0521, found 745.0518.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(4-(3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-heptadecafluorodec-1-en-1-yl)phenyl)-*N*-(phenylsulfonyl)pentanamide (4o)

The general procedure **A** was followed (70 °C under air). Conversion: 70 %. Yield: 57.7 mg (60%), *p:* others > 20:1.

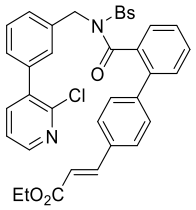
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.6, 1.9 Hz, 1H), 7.67 (d, *J* = 7.9 Hz, 2H), 7.64 – 7.57 (m, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.41 – 7.30 (m, 4H), 7.27 – 7.22 (m, 3H), 7.10 (d, *J* = 16.0 Hz, 1H), 6.96 (d, *J* = 7.9 Hz, 2H), 6.14 (dt, *J* = 16.2, 12.2 Hz, 1H), 5.18 – 5.02 (m, 2H), 3.18 – 2.86 (m, 3H), 1.61 – 1.53 (m, 1H), 1.51 – 1.37 (m, 1H), 0.68 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.8, 149.7, 148.7, 146.4, 139.80, 139.76, 139.7 – 139.4 (m), 137. 9, 137.0, 136.6, 133.9, 131.7, 129.4, 129.1, 128. 9, 128.8, 128.2, 128.1, 127.8, 127.6, 122.7, 113.7 (t, *J* = 23.1 Hz), 49.1, 43.3, 43.0, 29.0, 11. 9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 10.1 Hz), -110.9 (q, *J* = 12.9 Hz), -121.1 – -121.5 (m), -121.7 – -122.1 (m), -122.7 – -122.8 (m), -122.9 – -123.3 (m), -125.9 – -126.3 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{39}H_{28}ClF_{17}N_2O_3SNa^+$ [M+Na^+] 985.1130, found 985.1124.



(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3-(4-(2-(perfluorophenyl)vinyl)phenyl)-*N*-(phenylsulfonyl)pentanamide (4p)

The general procedure **A** was followed (70 °C under air). Conversion: 84 %. Yield: 49.0 mg (69%), *p:* others > 20:1.

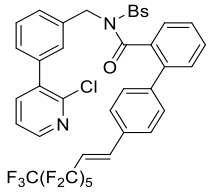
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.67 (t, *J* = 8.1 Hz, 2H), 7.64 – 7.58 (m, 2H), 7.48 (t, *J* = 7.7 Hz, 2H), 7.42 – 7.28 (m, 7H), 7.24 (d, *J* = 7.3 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 2H), 6.90 (d, *J* = 16.8 Hz, 1H), 5.15 – 5.01 (m, 2H), 3.19 – 2.79 (m, 3H), 1.63 – 1.52 (m, 1H), 1.51 – 1.37 (m, 1H), 0.70 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171. 9, 149.7, 148.6, 145.0, 139.80, 139.77, 137.8, 137.0, 136.6, 134.6, 133. 9, 129.4, 129.0, 128. 9, 128.8, 128.11, 128.09, 127.7, 127.0, 122.7, 112.6 (td, J_{C-F} = 13.8, 3.7 Hz), 112.2, 49.1, 43.3, 43.1, 29.0, 11.9. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -142.4 – -143.3 (m), -156.6 (t, *J* = 20.8 Hz), -162.9 (td, *J* = 21.5, 7.8 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{28}ClF_5N_2O_3SNa^+$ [M+Na^+] 733.1322, found 733.1321.



Ethyl (*E*)-3-(2'-((3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamoyl) -[1,1'-biphenyl]-4-yl)acrylate (6a)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 70 %. Yield: 33.7 mg (53%), *p:* others = 8:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.73 – 7.60 (m, 4H), 7.52 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.37 – 7.34 (m, 3H), 7.34 – 7.21 (m, 6H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.03 – 7.02 (m, 2H), 6.47 (d, *J* = 16.0 Hz, 1H), 4.65 (br, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 1.38 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 167.0, 149.6, 148.7, 143.8, 140.7, 139.71, 139.69, 138.8, 138.2, 137.7, 136.6, 136.4, 134.02, 134.00, 133.8, 129.7, 129.3, 129.0, 128.79, 128.78, 128.6, 128.5, 128.5, 128.3, 127.8, 127.7, 122.7, 119.0, 60.8, 50.6, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{36}H_{29}ClN_2O_5SNa^+$ [M+Na^+] 659.1378, found 659.1379.

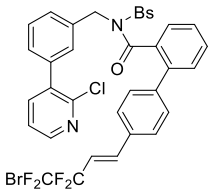


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-4'-(3,3,4,4,5,5,6,6,7,7, 8,8,8-tridecafluorooct-1-en-1-yl)-[1,1'-biphenyl]-2-carboxamide (6b)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 80 %. Yield: 52.9 mg (60%), *p:* others = 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.60 (t, *J* = 7.5 Hz, 1H), 7.52 (d, *J* = 7.1 Hz, 1H), 7.47 – 7.40 (m, 3H), 7.38 – 7.28 (m, 7H), 7.28 – 7.22 (m, 2H), 7.21 – 7.15 (m, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 7.05 – 7.03 (m, 2H), 6.24 (dt, *J* = 16.3, 12.1 Hz, 1H), 4.68 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 149.6, 148.7, 140.8, 139.7, 139.4 – 139.1 (m), 138.9, 138.2, 137.7, 136.6, 136.5, 134.1, 133.8, 133.0, 130.8, 129.8, 129.4, 129.0, 128.8, 128.66, 128.65, 128.3, 128.1, 127.8, 127.8, 122.7, 115.0 (t, J_{C-F} = 22.6 Hz), 50.6. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.7 (t, *J* = 9.8 Hz), -111.0 (q, *J* = 12.8 Hz), -121.5 – -121.6

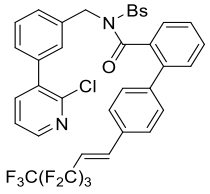
(m), -122.8 (br), -122. 9 – -123.0 (m), -126. 0 – -126.1 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{39}H_{24}ClF_{13}N_2O_3SNa^+$ [M+Na^+] 905.0881, found 905.0877.



(*E*)-4'-(4-bromo-3,3,4,4-tetrafluorobut-1-en-1-yl)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (6c)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 72 %. Yield: 33.4 mg (45%), *p:* others =10:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.70 (d, *J* = 7.8 Hz, 2H), 7.61 (t, *J* = 7.3 Hz, 1H), 7.52 (dd, *J* = 7.7, 1.9 Hz, 1H), 7.48 – 7.41 (m, 3H), 7.38 – 7.29 (m, 7H), 7.28 – 7.22 (m, 2H), 7.18 (dt, *J* = 16.2, 2.4 Hz, 1H), 7.12 (d, *J* = 7.7 Hz, 1H), 7.04 – 7.02 (m, 2H), 6.26 (dt, *J* = 16.1, 11.7 Hz, 1H), 4.67 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 149.6, 148.7, 140.6, 139.7, 139.2 (t, J_{C-F} = 8.7 Hz), 138.9, 138.2, 137.7, 136.6, 136.5, 134.1, 133.8, 133.1, 130.7, 129.8, 129.4, 129.0, 128.81, 128.79, 128.6, 128.2, 128.0, 127.79, 127.75, 122.7, 115.0 (t, J_{C-F} = 24.0 Hz), 50.6. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -65.6 (t, *J* = 6.4 Hz), -108. 9 – -109.0 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{35}H_{24}BrClF_4N_2O_3SNa^+$ [M+Na^+] 765.0208, found 765.0198.

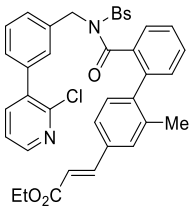


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-4'-(3,3,4,4,5,5,6,6,6-nonafluorohex-1-en-1-yl)-*N*-(phenylsulfonyl)-[1,1'-biphenyl]-2-carboxamide (6d)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 65 %. Yield: 39.1 mg (50%), *p:* others = 10:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (d, *J* = 3.9 Hz, 1H), 7.70 (d, *J* = 7.9 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 1H), 7.52 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.46 – 7.40 (m, 3H), 7.38 – 7.29 (m, 7H), 7.28 – 7.22 (m, 2H), 7.18 (dt, *J* = 16.1, 2.5 Hz, 1H), 7.12 (d, *J* = 7.6 Hz, 1H), 7.05 – 7.03 (m, 2H), 6.24 (dt, *J* = 16.2, 12.1 Hz, 1H), 4.66 (br, 2H). ^{13}C NMR (101

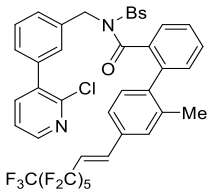
MHz, Chloroform-*d*) δ 170.8, 149.6, 148.7, 140.8, 139.7, 139.2 (t, J_{C-F} = 9.1 Hz), 138.9, 138.2, 137.7, 136.54, 136.46, 134.1, 133.8, 133.0, 130.8, 129.8, 129.4, 129.0, 128.8, 128.7, 128.6, 128.3, 128.1, 127.81, 127.77, 122.7, 114. 9 (t, J_{C-F} = 23.1 Hz), 50.6. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.9 (t, *J* = 9.5 Hz), -111.2 (q, *J* = 12.3 Hz), -122.97 – -124.86 (m), -125.6 – -125.7 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{24}ClF_9N_2O_3SNa^+$ [M+Na$^+$] 805.0945, found 805.0943.



Ethyl (*E*)-3-(2'-((3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamoyl)-2-methyl-[1,1'-biphenyl]-4-yl)acrylate (6e)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 65 %. Yield: 33.8 mg (52%), *p:* others = 8:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.7, 1.9 Hz, 1H), 7.70 – 7.52 (m, 5H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.41 – 7.26 (m, 7H), 7.21 (d, *J* = 7.7 Hz, 2H), 7.16 – 7.10 (m, 3H), 7.06 (d, *J* = 7.9 Hz, 1H), 6.47 (d, *J* = 16.0 Hz, 1H), 4.73 (br, 2H), 4.32 (q, *J* = 7.1 Hz, 2H), 2.07 (br, 3H), 1.39 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.4, 167.1, 149.6, 148.7, 144.3, 140.5, 139.78, 139.76, 138.7, 138.2, 137.7, 136.6, 136.5, 134. 9, 134.1, 133.7, 130.4, 130.3, 130.2, 128.83, 128.80, 128.76, 128.7, 128.6, 128.5, 127.7, 127.61, 127.59, 125.2, 122.7, 118.6, 60.7, 50.8, 20.2, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{31}ClN_2O_5SNa^+$ [M+Na$^+$] 673.1534, found 673.1533.

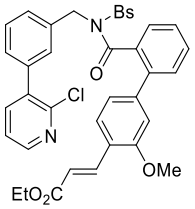


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-2'-methyl-*N*-(phenylsulfonyl)-4'-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)-[1,1'-biphenyl]-2-carboxamide (6f)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 73 %. Yield: 49.5 mg (55%), *p:* others = 10:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 3.7 Hz, 1H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.54 (d, *J* = 7.6 Hz, 2H), 7.44 (t, *J* = 7.4 Hz, 1H), 7.40 – 7.27 (m, 6H), 7.25 – 7.18 (m,

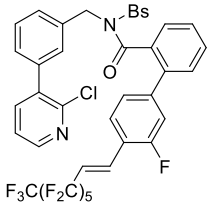
3H), 7.17 – 7.05 (m, 5H), 6.23 (dt, *J* = 16.2, 12.2 Hz, 1H), 4.75 (br, 2H), 2.10 (br, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.3, 149.6, 148.7, 140.5, 139.7, 139.7 – 139.4 (m), 138.8, 138.1, 137.7, 136.6, 136.5, 134.9, 133.6, 133.0, 130.4, 130.3, 129.84, 128.80, 128.78, 128.76, 128.7, 128.6, 127.62, 127.60, 124.8, 122.7, 114.6 (t, J_{C-F} = 22.9 Hz), 50.8, 20.2. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.7 (t, *J* = 9.7 Hz), -110.9 (q, *J* = 13.0 Hz), -121.4 – -121.6 (m), -122.80 (br), -122. 9 – -123.1 (m), -126. 0 – -126.1 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{40}H_{26}ClF_{13}N_2O_3SNa^+$ [M+Na$^+$] 919.1037, found 919.1027.



Ethyl (*E*)-3-(2'-((3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamoyl)-3-methoxy-[1,1'-biphenyl]-4-yl)acrylate (6g)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 60 %. Yield: 35.3 mg (53%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.99 (d, *J* = 16.2 Hz, 1H), 7.69 – 7.56 (m, 3H), 7.52 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.47 – 7.34 (m, 5H), 7.34 – 7.19 (m, 4H), 7.10 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.02 – 7.00 (m, 2H), 6.90 (dd, *J* = 7.8, 1.6 Hz, 1H), 6.84 (s, 1H), 6.59 (d, *J* = 16.1 Hz, 1H), 4.71 (br, 2H), 4.31 (q, *J* = 7.1 Hz, 2H), 3.69 (s, 3H), 1.38 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.8, 167.6, 158.1, 149.6, 148.7, 142.1, 139.7, 139.5, 138.8, 138.5, 137.6, 136.5, 136.4, 134.0, 133.8, 130.6, 129.7, 129.3, 128.8, 128.71, 128.66, 128.6, 128.4, 128.0, 127.8, 127.5, 123.0, 122.7, 120.8, 119.4, 60.6, 55.5, 50.7, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{37}H_{31}ClN_2O_6SNa^+$ [M+Na$^+$] 689.1484, found 689.1481.

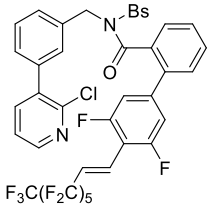


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3'-fluoro-*N*-(phenylsulfonyl)-4'-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)-[1,1'-biphenyl]-2-carboxamide (6h)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C).

Conversion: 70 %. Yield: 45.0 mg (50%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.41 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.69 (d, *J* = 7.8 Hz, 2H), 7.60 (t, *J* = 7.4 Hz, 1H), 7.54 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.50 – 7.39 (m, 3H), 7.37 – 7.24 (m, 7H), 7.14 – 7.01 (m, 5H), 6.38 (dt, *J* = 16.3, 11.9 Hz, 1H), 4.75 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.4, 160.7 (d, J_{C-F} = 254.6 Hz), 149.6, 148.7, 142.8 (d, J_{C-F} = 8.4 Hz), 139.7, 138.8, 137.8, 137.23, 137.22, 136.43, 136.39, 134.1, 133.9, 132.4 (t, J_{C-F} = 9.9 Hz), 130.8, 129.7, 129.2(d, J_{C-F} = 2.4 Hz), 128. 9, 128.80, 128.78, 128.7, 128.2, 128.1, 127.8, 125.2 (d, J_{C-F} = 3.1 Hz), 122.7, 120.9 (d, J_{C-F} = 11.4 Hz), 117.5 (td, J_{C-F} = 23.1, 7.1 Hz), 116.8 (d, J_{C-F} = 23.0 Hz), 50.6. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.6 (q, *J* = 12.8 Hz), -113.7 – -113.8 (m), -121.5 – -121.6 (m), -122.7 – -122.8 (m), -123.0 – -123.1 (m), -128.0 – -128.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{39}H_{23}ClF_{14}N_2O_3SNa^+$ [M+Na$^+$] 923.0787, found 923.0784.

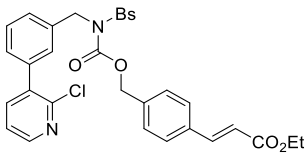


(*E*)-*N*-(3-(2-chloropyridin-3-yl)benzyl)-3',5'-difluoro-*N*-(phenylsulfonyl)-4'-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)-[1,1'-biphenyl]-2-carboxamide (6i)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 55 %. Yield: 45.9 mg (50%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.40 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.67 (d, *J* = 7.8 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.55 (dd, *J* = 7.5, 1.9 Hz, 1H), 7.47 (t, *J* = 7.7 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.37 – 7.27 (m, 5H), 7.22 (dt, *J* = 17.2, 2.6 Hz, 1H), 7.17 – 7.07 (m, 3H), 6.86 (d, *J* = 9.4 Hz, 2H), 6.60 (dt, *J* = 16.5, 11.9 Hz, 1H), 4.82 (br, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.1, 160.9 (dd, J_{C-F} = 255.6, 7.4 Hz), 149.6, 148.7, 142.8 (t, J_{C-F} = 10.9 Hz), 139.7, 138.8, 137.8, 136.6, 136.4, 136.2, 134.2, 134.1, 130.8, 129.6, 128.98, 128.96, 128.9, 128.7, 128.6, 128.4, 128.0, 127. 9, 126.1 (t, J_{C-F} = 10.8 Hz), 122.7, 112.7 (dd, J_{C-F} = 25.6, 14.1 Hz), 110.7 (t, J_{C-F} = 14.8 Hz), 50.5. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -109.9 (d, *J* = 9.9 Hz), -112.4 (q, *J* = 12.5 Hz), -121.37 – -121.74 (m), -122.7 – -122.9 (m), -123.0 – -123.1 (m), -

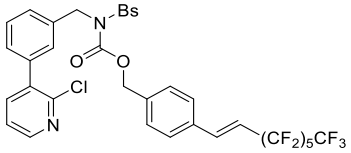
126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{39}H_{22}ClF_{15}N_2O_3SNa^+$ [M+Na^+] 941.0692, found 941.0689.



Ethyl (*E*)-3-(4-((((3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamoyl)oxy) -methyl)phenyl)acrylate (6j)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 75 %. Yield: 37.2 mg (63%), *p:* others = 8:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.31 (dd, *J* = 4.9, 1.9 Hz, 1H), 7.59 – 7.51 (m, 3H), 7.49 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 7.38 (dt, *J* = 5.9, 3.1 Hz, 1H), 7.36 – 7.32 (m, 3H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.25 – 7.17 (m, 3H), 7.02 (d, *J* = 7.9 Hz, 2H), 6.33 (d, *J* = 16.0 Hz, 1H), 5.05 (s, 2H), 5.01 (s, 2H), 4.19 (q, *J* = 7.1 Hz, 2H), 1.26 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 167.0, 152.4, 149.7, 148.7, 143.8, 139.8, 139.2, 137.9, 137.2, 136.7, 136.5, 134. 9, 133.7, 129.3, 129.1, 128.83, 128.80, 128.6, 128.4, 128.3, 122.7, 119.2, 68.8, 60.8, 50.0, 14.5. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{27}ClN_2O_6SNa^+$ [M+Na^+] 613.1171, found 613.1170.

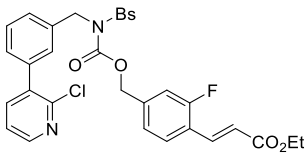


(*E*)-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)benzyl (3-(2-chloropyri -din-3-yl)benzyl)(phenylsulfonyl)carbamate (6k)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 90 %. Yield: 66.9 mg (80%), *p:* others = 10:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.66 (d, *J* = 7.9 Hz, 2H), 7.58 (dd, *J* = 7.6, 2.0 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.49 – 7.40 (m, 4H), 7.36 – 7.28 (m, 5H), 7.17 – 7.10 (m, 3H), 6.19 (dt, *J* = 16.3, 12.2 Hz, 1H), 5.14 (s, 2H), 5.10 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.3, 149.7, 148.6, 139.8, 139.2, 139.1 (t, J_{C-F} = 9.7 Hz), 137.9, 137.1, 136.7, 136.6, 133.8, 133.7, 129.3, 129.1, 128. 9, 128.80, 128.78, 128.6, 128.4, 127.9, 122.7, 115.2 (t, J_{C-F} = 23.0 Hz), 68.6, 50.0. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 9.9 Hz), -111.2 (q, *J* = 12.9, 12.3 Hz), -121.6 – -121.7 (m), -122.8 – -122.9 (m), -123.0 – -123.2 (m), -126.0 – -126.2 (m).

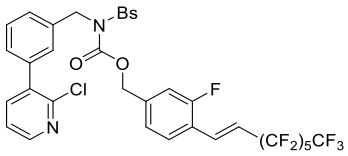
HRMS (m/z, ESI-TOF): Calcd for $C_{34}H_{22}ClF_{13}N_2O_4SNa^+$ [M+Na^+] 859.0673, found 859.0668.



Ethyl (*E*)-3-(4-((((3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamoyl)oxy)-methyl)-2-fluorophenyl)acrylate (6l)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 90 %. Yield: 45.6 mg (75%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.72 (d, *J* = 16.2 Hz, 1H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.59 (dd, *J* = 7.7, 2.0 Hz, 1H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.50 – 7.31 (m, 7H), 7.29 (dd, *J* = 7.6, 4.8 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 1H), 6.72 (d, *J* = 10.9 Hz, 1H), 6.50 (d, *J* = 16.2 Hz, 1H), 5.15 (s, 2H), 5.07 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 1.34 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.7, 161.1 (d, J_{C-F} = 254.8 Hz), 152.2, 149.7, 148.6, 139.7, 139.2, 138.6 (d, J_{C-F} = 8.4 Hz), 137.9, 137.0, 136.51 (d, J_{C-F} = 11.1 Hz), 136.48, 133.8, 129.3 (d, J_{C-F} = 3.2 Hz), 129.2, 129.1, 128. 9, 128.8, 128.5, 128.3, 123.9 (d, J_{C-F} = 3.4 Hz), 122.7 (d, J_{C-F} = 12.0 Hz), 122.7, 121.6 (d, J_{C-F} = 6.6 Hz), 115.6 (d, J_{C-F} = 23.1 Hz), 67.8, 60.8, 50.1, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{26}ClFN_2O_6SNa^+$ [M+Na^+] 631.1076, found 631.1075.

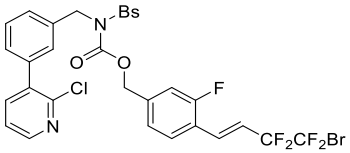


(*E*)-3-fluoro-4-(3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluorooct-1-en-1-yl)benzyl (3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamate (6m)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 90 %. Yield: 70.9 mg (83%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (d, *J* = 4.5 Hz, 1H), 7.68 (d, *J* = 7.8 Hz, 2H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.55 (t, *J* = 7.2 Hz, 1H), 7.51 – 7.41 (m, 4H), 7.40 – 7.34 (m, 3H), 7.29 (dd, *J* = 7.4, 4.8 Hz, 1H), 7.22 (d, *J* = 16.3 Hz, 1H), 6.94 (d, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 11.1 Hz, 1H), 6.33 (dt, *J* = 16.0, 12.0 Hz, 1H), 5.16 (s, 2H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160. 9 (d, J_{C-F} = 254.3 Hz), 152.2, 149.7, 148.7, 139.7, 139.2, 138. 9 (d, J_{C-F} = 8.2 Hz), 138.0, 137.1, 136.6, 133.8, 132.2 (t, J_{C-F} = 10.1

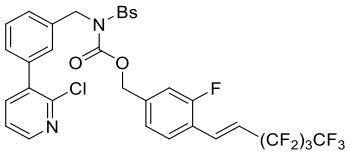
Hz), 129.3, 129.2, 129.1, 128.9, 128.8, 128.5, 128.4, 124.0 (d, J_{C-F} = 3.5 Hz), 122.7, 121.7 (d, J_{C-F} = 11.9 Hz), 117.8 (td, J_{C-F} = 23.2, 8.1 Hz), 115.7 (d, J_{C-F} = 23.0 Hz), 67.8 (d, J_{C-F} = 1.5 Hz), 50.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (t, *J* = 10.0 Hz), -111.7 (q, *J* = 12.5, 12.0 Hz), -114.3 (dd, *J* = 11.0, 7.4 Hz), -121.4 – -121.7 (m), -122.7 – -123.0 (m), -123.1 – -123.2 (m), -126.1 – -126.2 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{34}H_{21}ClF_{14}N_2O_4SNa^+$ [M+Na$^+$] 877.0579, found 877.0576.



(*E*)-4-(4-bromo-3,3,4,4-tetrafluorobut-1-en-1-yl)-3-fluorobenzyl (3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamate (6n)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 84 %. Yield: 53.6 mg (75%), *p:* others = 10:1.

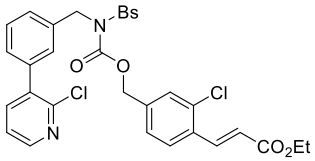
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.7, 2.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.61 – 7.52 (m, 2H), 7.49 – 7.41 (m, 4H), 7.41 – 7.34 (m, 3H), 7.29 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.23 (dt, *J* = 16.5, 2.5 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.75 (d, *J* = 10.9 Hz, 1H), 6.35 (dt, *J* = 16.2, 11.6 Hz, 1H), 5.15 (s, 2H), 5.08 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.8 (d, J_{C-F} = 254.2 Hz), 152.2, 149.7, 148.6, 139.7, 139.2, 138.7 (d, J_{C-F} = 8.2 Hz), 137.9, 137.0, 136.6, 133.8, 132.2 (td, J_{C-F} = 10.4, 9.9, 2.8 Hz), 129.20, 129.15, 129.1, 128. 9, 128.8, 128.5, 128.4, 123.9 (d, J_{C-F} = 3.5 Hz), 122.7, 121.8 (d, J_{C-F} = 11.5 Hz), 117.8 (td, J_{C-F} = 23.9, 7.2 Hz), 115.7 (d, J_{C-F} = 23.1 Hz), 67.8, 50.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -65.7 (t, *J* = 6.4 Hz), -109.5 (dt, *J* = 12.1, 6.7 Hz), -114.4 (dd, *J* = 11.1, 7.4 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{30}H_{21}BrClF_5N_2O_4SNa^+$ [M+Na$^+$] 736.9906, found 736.9905.



(*E*)-3-fluoro-4-(3,3,4,4,5,5,6,6,6-nonafluorohex-1-en-1-yl)benzyl (3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamate (6o)

The general procedure **B** was followed (**2** (3.0 equiv), HFIP (1.0 mL), 100 °C). Conversion: 84 %. Yield: 58.8 mg (78%), *p:* others = 10:1.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.39 (dd, *J* = 4.8, 1.9 Hz, 1H), 7.68 (d, *J* = 7.9 Hz, 2H), 7.60 (dd, *J* = 7.5, 2.0 Hz, 1H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.50 – 7.41 (m, 4H), 7.41 – 7.34 (m, 3H), 7.29 (dd, *J* = 7.5, 4.7 Hz, 1H), 7.22 (dt, *J* = 16.4, 2.6 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 1H), 6.76 (d, *J* = 11.0 Hz, 1H), 6.33 (dt, *J* = 16.3, 12.0 Hz, 1H), 5.15 (s, 2H), 5.09 (s, 2H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 160. 9 (d, J_{C-F} = 254.5 Hz), 152.2, 149.7, 148.7, 139.7, 139.2, 138. 9 (d, J_{C-F} = 8.2 Hz), 138.0, 137.0, 136.6, 133.8, 132.4 – 132.1 (m), 129.3(d, J_{C-F} = 2.9 Hz), 129.2, 129.1, 128.9, 128.8, 128.5, 128.4, 124.0 (d, J_{C-F} = 3.4 Hz), 122.7, 121.7 (d, J_{C-F} = 11.9 Hz), 117.7 (td, J_{C-F} = 23.1, 6.9 Hz), 115.7 (d, J_{C-F} = 23.0 Hz), 67.8, 50.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.5 – -81.5 (m), -112.0 (t, *J* = 12.1 Hz), -114.3 (dd, *J* = 11.1, 7.5 Hz), -124.0 (q, *J* = 9.4 Hz), -125.6 – -125.8 (m). HRMS (m/z, ESI-TOF): Calcd for $C_{32}H_{21}ClF_{10}N_2O_4SNa^+$ [M+Na$^+$] 777.0643, found 777.0635.

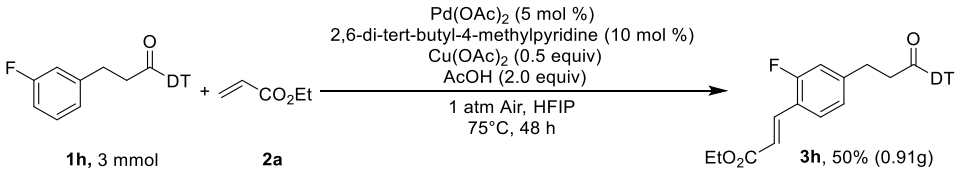


ethyl (*E*)-3-(2-chloro-4-((((3-(2-chloropyridin-3-yl)benzyl)(phenylsulfonyl)carbamoyl)oxy)methyl)phenyl)acrylate (6p)

The general procedure **B** was followed (**2** (2.0 equiv), HFIP (1.5 mL), 90 °C). Conversion: 60 %. Yield: 33.1 mg (53%), *p:* others > 20:1.

^{1}H NMR (400 MHz, Chloroform-d) δ 8.39 (dd, J = 4.8, 1.9 Hz, 1H), 8.00 (d, J = 16.0 Hz, 1H), 7.65 (d, J = 7.8 Hz, 2H), 7.59 (dd, J = 7.6, 1.9 Hz, 1H), 7.54 (t, J = 7.4 Hz, 1H), 7.50 – 7.40 (m, 5H), 7.36 (t, J = 7.7 Hz, 2H), 7.29 (dd, J = 7.5, 4.7 Hz, 1H), 7.06 (s, 1H), 7.00 (d, J = 8.0 Hz, 1H), 6.40 (d, J = 16.0 Hz, 1H), 5.14 (s, 2H), 5.05 (s, 2H), 4.28 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-d) δ 166.4, 152.2, 149.7, 148.7, 139.7, 139.6, 139.2, 137.9, 137.7, 137.0, 136.6, 135.0, 133.8, 133.0, 129.6, 129.2, 129.1, 128. 9, 128.8, 128.5, 128.3, 127.8, 126.8, 122.7, 121.7, 67.8, 60.9, 50.1, 14.4. HRMS (m/z, ESI-TOF): Calcd for $C_{31}H_{27}Cl_2N_2O_6S^+$ [M+H$^+$] 625.0961, found 625.0973.

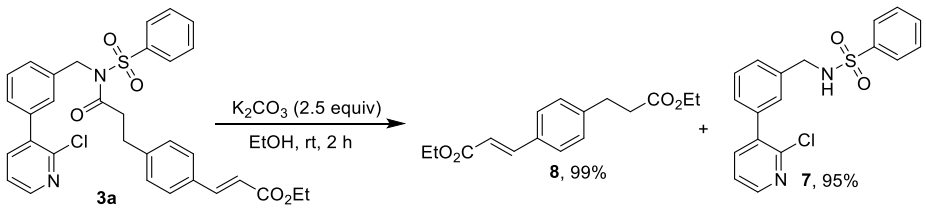
2.6 Scaled-up Reactions



An oven-dried Schlenk tube (1000 mL) was charged with a magnetic stir bar, under air atmosphere, **1h** (3.0 mmol, 1.0 equiv), **2a** (9.0 mmol, 3.0 equiv), $Pd(OAc)_2$ (0.15 mmol, 5 mol %), $Cu(OAc)_2$ (1.5 mmol, 0.5 equiv), 2,6-di-tert-butyl-4-methylpyridine (0.30 mmol, 10 mol %), AcOH (6.0 mmol, 2.0 equiv), HFIP (45 mL) were added. The reaction mixture was stirred vigorously on a preheated hotplate (75 °C) for 48 h and then cooled down to room temperature. After removal of HFIP under reduced pressure, then diluted with EtOAc (200 mL) and filtered through a short pad of Celite and neutral alumina. The sealed tube and Celite and neutral alumina pad were washed with an additional 150 mL EtOAc. The resulting residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (5:1-3:1) as the eluent to give **3h**. (50 %, 0.91g)

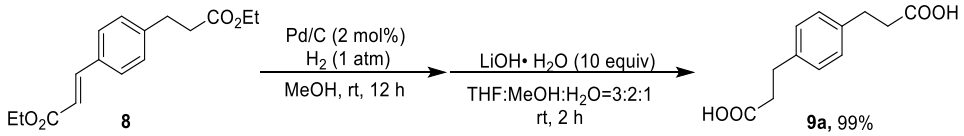
2.7 Synthetic Applications and Hydrolysis

Synthesis of 10a:



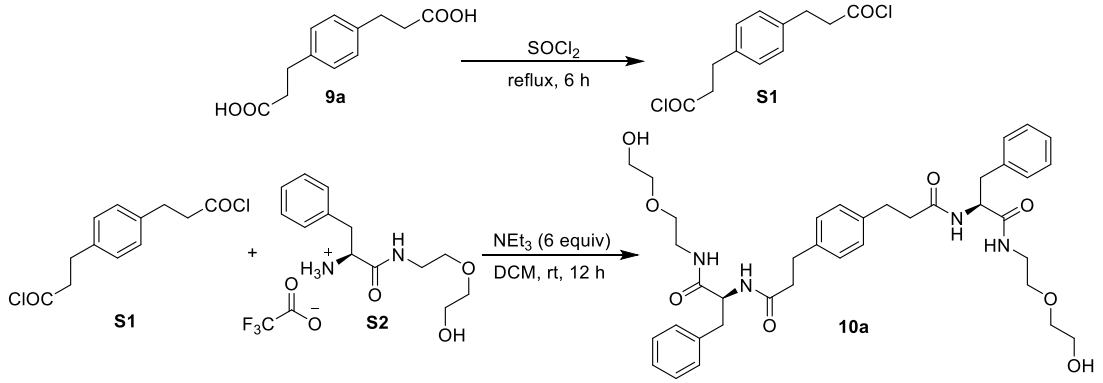
To a solution of **3a** (0.7 mmol, 1.0 equiv) and K_2CO_3 (1.75 mmol, 2.5 equiv) in EtOH (7 mL) at room temperature stirred for 2 h. Then volatile matter was removed under reduced pressure. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (10:1-2:1) as the eluent to give **7** (yield: 95%) and **ethyl (*E*)-3-(4-(3-ethoxy-3-oxopropyl)phenyl)acrylate (8)**. (yield: 99%) ^1H NMR (400 MHz, Chloroform-*d*) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.45 (d, *J* = 7.9 Hz, 2H),

7.22 (d, *J* = 7.9 Hz, 2H), 6.40 (d, *J* = 16.0 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.12 (q, *J* = 7.1 Hz, 2H), 2.96 (t, *J* = 7.7 Hz, 2H), 2.62 (t, *J* = 7.7 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.23 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.8, 167.3, 144.5, 143.3, 132.7, 129.0, 128.4, 117.8, 60.7, 60.6, 35.7, 30.9, 14.5, 14.3. HRMS (m/z, ESI-TOF): Calcd for $C_{16}H_{20}O_4Na^+$ [M+Na$^+$] 299.1254, found 299.1254.



To a solution of **8** (0.6mmol, 1.0 equiv), Pd/C (0.012 mmol, 2 mol %.), MeOH (10 mL) under H_2 atmosphere at room temperature stirred for 12 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was used in the next step without further purification.

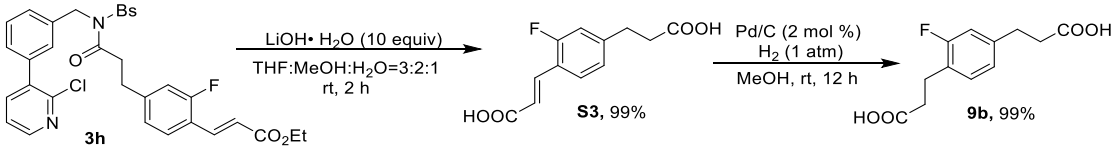
To a solution of the residue above and LiOH·H_2O (6.0 mmol, 10 equiv) in THF:MeOH:H_2O (6:4:2 mL) at room temperature stirred for 2 h. Then volatile matter was removed under reduced pressure. Then the crude reaction mixture was extracted with EtOAc and water, The combined water phase was added 1N HCl until pH ≈ 1, then filtered to give the **9a**.(yield: 99%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.12 (br, 2H), 7.12 (s, 4H), 2.77 (t, J = 7.6 Hz, 4H), 2.54 – 2.47 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173. 9, 138.5, 128.2, 35.1, 30.0. HRMS (m/z, ESI-TOF): Calcd for C12H13O4$^-$ [M-H$^-$] 221.0819, found 221.0819.



A suspension of **9a** (44.4 mg, 0.20 mmol) in freshly distilled thionyl chloride (3 mL) was gently refluxed to complete solution of the solid (6 h). After evaporation under vacuum the residue was pumped to dryness and without further purification.

To a solution of **S2** (0.6 mmol, 3.0 equiv), triethylamine (1.2 mmol, 6.0 equiv.), DCM (10 mL) under N_2 atmosphere at room temperature stirred for 0.5 h. Then **S1** was added and stirred for another 12 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by preparative thin layer chromatography using EtOAc/MeOH (20:1-5:1) as the eluent to give the **10a**[2]. (yield: 50%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.21 (d, J = 8.5 Hz, 2H), 8.09 (t, J = 5.6 Hz, 2H), 7.26 – 7.16 (m, 10H), 6.98 (s, 4H), 4.69 (t, J = 5.5 Hz, 2H), 4.48 (td, J = 9.0, 4.9 Hz, 2H), 3.49 (d, J = 5.2 Hz, 4H), 3.37 – 3.30 (m, 8H), 3.20 (p, J = 6.9 Hz, 4H), 2.95 (dd, J = 13.7, 5.0 Hz, 2H), 2.76 (dd, J = 13.6, 9.5 Hz, 2H), 2.62 (t, J = 7.9 Hz, 4H), 2.32 (t, J = 7.8 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.4, 171.3, 138.7, 138.0, 129.2, 128.02, 128.00, 126.2, 72.2, 68. 9, 60.2, 54.0, 38.6, 37.9, 36.9, 30.7. HRMS (m/z, ESI-TOF): Calcd for $C_{38}H_{50}N_4O_8Na^+$ [M+Na$^+$] 713.3521, found 713.3521.

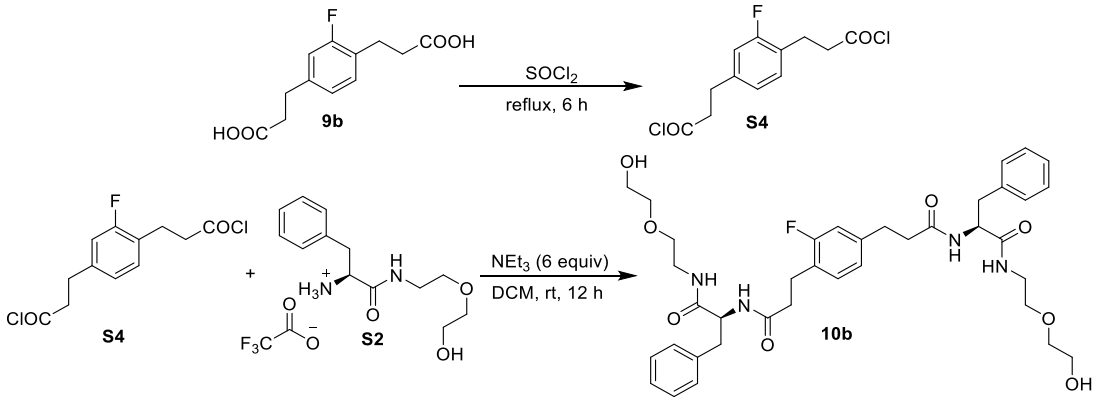
Synthesis of 10b:



To a solution of **3h** (1.5 mmol, 1.0 equiv) and LiOH·H_2O (15 mmol, 10 equiv) in THF:MeOH:H_2O (9:6:3 mL) at room temperature stirred for 2 h. Then volatile matter was removed under reduced pressure. Then the crude reaction mixture was extracted with EtOAc and water, The combined water phase was added 1N HCl until pH ≈ 1, then filtered to give **S3**. (yield: 99%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.74 (t, J = 8.0 Hz, 1H), 7.62 (d, J = 16.1 Hz, 1H), 7.18 (d, J = 12.1 Hz, 1H), 7.13 (d, J = 8.1 Hz, 1H), 6.55 (d, J = 16.1 Hz, 1H), 2.85 (t, J = 7.5 Hz, 2H), 2.57 (t, J = 7.5 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.6, 167.4, 160.5 (d, J_{C-F} = 250.7 Hz), 146.4 (d, J_{C-F} = 8.4 Hz), 135.8 (d, J_{C-F} = 3.2 Hz), 129.1 (d, J_{C-F} = 3.2 Hz), 125.1 (d, J_{C-F} = 2.9 Hz), 121.0 (d, J_{C-F} = 5.6 Hz), 119.6 (d, J_{C-F} = 11.5 Hz), 115.8 (d, J_{C-F} = 21.9 Hz), 34.5, 30.0. HRMS (m/z, ESI-TOF): Calcd for $C_{12}H_{10}FO_4^-$ [M-H$^-$] 237.0569, found 237.0569.

To a solution of **S3** (1.0 mmol, 1.0 equiv), Pd/C (0.02 mmol, 2 mol %), MeOH (10 mL) under H_2 atmosphere at room temperature stirred for 12 h. Then filtered and concentrated under reduced pressure to give **9b**. (yield: 99%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.19 (t, J = 8.0 Hz, 1H), 7.02 – 6. 96 (m, 2H), 2.85 – 2.73 (m, 4H), 2.54 –

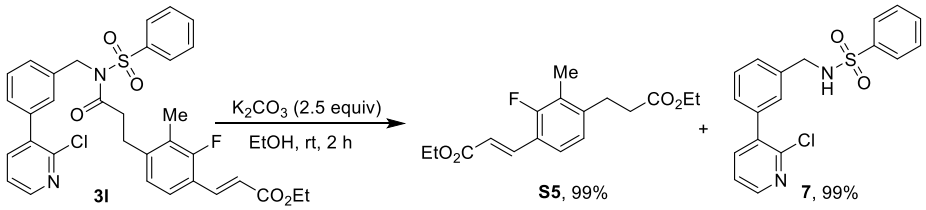
2.48 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.8, 173.6, 160.4 (d, J = 243.0 Hz), 141.6 (d, J = 7.6 Hz), 130.4 (d, J = 5.3 Hz), 124. 9 (d, J = 15.7 Hz), 124.2 (d, J = 2.9 Hz), 114.9 (d, J = 21.8 Hz), 35.0, 33.9, 29.8, 23.5. HRMS (m/z, ESI-TOF): Calcd for $C_{12}H_{12}FO_4^-$ [M-H$^-$] 239.0725, found 239.0595.



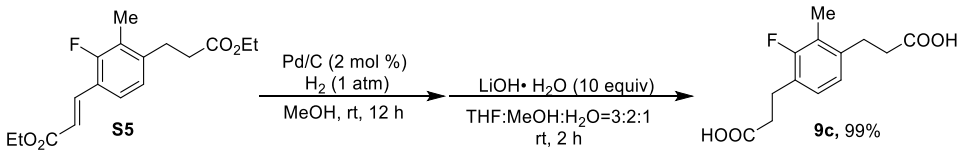
Asuspension of **9b** (48 mg, 0.20 mmol) in freshly distilled thionyl chloride (3 mL) was gently refluxed tocomplete solution of the solid (6 h). After evaporation under vacuum the residue was pumped to dryness and without further purification.

To a solution of **S2**[2] (0.6 mmol, 3.0 equiv), triethylamine (1.2 mmol, 6.0 equiv), DCM (10 mL) under N_2 atmosphere at room temperature stirred for 0.5 h. Then the **S4** was added and stirred for another 12 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by preparative thin layer chromatography using EtOAc/MeOH (20:1-5:1) as the eluent to give the **10b**. (yield: 40%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.16 (t, J = 9.2 Hz, 2H), 8.05 (t, J = 5.7 Hz, 2H), 7.26 – 7.16 (m, 10H), 7.01 (t, J = 8.0 Hz, 1H), 6.88 (d, J = 11.3 Hz, 1H), 6.82 (d, J = 7.7 Hz, 1H), 4.64 (t, J = 5.5 Hz, 2H), 4.55 – 4.50 (m, 2H), 3.52 – 3.45 (m, 8H), 3.41 (t, J = 5.3 Hz, 4H), 3.28 – 3.16 (m, 4H), 3.01 – 2.91 (m, 2H), 2.76 (dd, J = 13.6, 9.4 Hz, 2H), 2.66 (t, J = 7.9 Hz, 4H), 2.34 (q, J = 7.6 Hz, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.4, 171.2, 171.1, 160.3 (d, J_{C-F} = 242.8 Hz), 141.7 (d, J_{C-F} = 7.6 Hz), 138.00, 137.97, 130.2 (d, J_{C-F} = 5.3 Hz), 129.3, 128.1, 127.5, 126.3, 125.1 (d, J_{C-F} = 15.9 Hz), 124.1 (d, J_{C-F} = 3.0 Hz), 114.7 (d, J_{C-F} = 21.9 Hz), 114.0, 72.2, 69.0, 60.3, 56.2, 54.04, 54.00, 38.7, 38.0, 36.5, 35.3, 30.4, 24.0, 18.6. HRMS (m/z, ESI-TOF): Calcd for $C_{38}H_{49}FN_4O_8Na^+$ [M+Na$^+$] 731.3427, found 731.3426.

Synthesis of 10c:



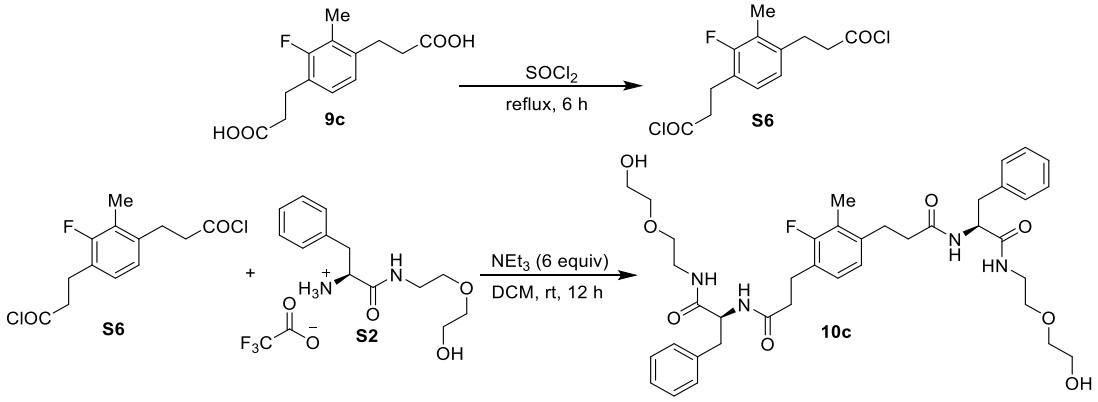
To **3l** (0.7 mmol, 1.0 equiv) and K_2CO_3 (1.75 mmol, 2.5 equiv) in EtOH (7 mL) at room temperature stirred for 2 h. Then volatile matter was removed under reduced pressure. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by flash silica gel chromatography using petroleum ether/EtOAc (10:1-2:1) as the eluent to give **7** (yield: 99%) and **S5** (yield: 99%). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.79 (d, *J* = 16.1 Hz, 1H), 7.30 (t, *J* = 7.7 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 1H), 6.47 (d, *J* = 16.2 Hz, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.13 (q, *J* = 7.1 Hz, 2H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.57 (t, *J* = 7.8 Hz, 2H), 2.24 (d, *J* = 2.4 Hz, 3H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 4H). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 172.6, 167.2, 159.9 (d, J_{C-F} = 251.7 Hz), 143.6 (d, J_{C-F} = 4.7 Hz), 137.7 (d, J_{C-F} = 3.7 Hz), 125.9 (d, J_{C-F} = 3.7 Hz), 124.4 (d, J_{C-F} = 3.6 Hz), 124.1 (d, J_{C-F} = 16.7 Hz), 120.4 (d, J_{C-F} = 13.6 Hz), 120.0 (d, J_{C-F} = 6.4 Hz), 60.8, 60.7, 34.4, 28.4 (d, J_{C-F} = 2.6 Hz), 14.4, 14.3, 10.6 (d, J_{C-F} = 7.0 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{17}H_{21}FO_4Na^+$ [M+Na^+] 331.1316, found 331.1317.



To a solution of ethyl **S5** (0.6 mmol, 1.0 equiv), Pd/C (0.012 mmol, 2 mol %), MeOH (10 mL) under H_2 atmosphere at room temperature stirred for 12 h . Then the crude reaction mixture was extracted with EtOAc and water, The combined organic phase was dried overanhydrous Na_2SO_4 and concentrated under reduced pressure. The residue without further purification.

To a solution of the residue above and $LiOH·H_2O$ (6.0 mmol, 10 equiv) in THF : MeOH : H_2O (6:4:2 mL) at room temperature stirred for 2 h. Then volatile matter was removed under reduced pressure. Then the crude reaction mixture was extracted with EtOAc and water, The combined water phase was added 1N HCl until pH ≈ 1, then filtered to give **9c**. (yield: 99%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (br, 2H), 7.03

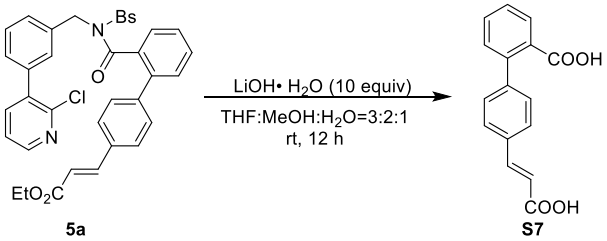
(t, J = 7.9 Hz, 1H), 6.92 (d, J = 7.8 Hz, 1H), 2.79 (td, J = 7.7, 4.5 Hz, 4H), 2.49 – 2.44 (m, 4H), 2.16 (d, J = 2.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.7, 173.6, 158. 9 (d, $J_{C\text{-}F}$ = 241.1 Hz), 139.5 (d, $J_{C\text{-}F}$ = 4.0 Hz), 127.1 (d, $J_{C\text{-}F}$ = 5.8 Hz), 124.7 (d, $J_{C\text{-}F}$ = 17.6 Hz), 123. 9 (d, $J_{C\text{-}F}$ = 3.4 Hz), 122.3 (d, $J_{C\text{-}F}$ = 16.5 Hz), 34.0, 33.8, 27.4 (d, $J_{C\text{-}F}$ = 2.6 Hz), 23.8 (d, $J_{C\text{-}F}$ = 3.2 Hz), 10.2 (d, $J_{C\text{-}F}$ = 6.3 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{13}H_{14}FO_4^-$ [M-H$^-$] 253.0882, found 253.0883.



A suspension of **9c** (50.8 mg, 0.20 mmol) in freshly distilled thionyl chloride (3 mL) was gently refluxed to complete solution of the solid (6 h). After evaporation under vacuum the residue was pumped to dryness and without further purification.

To a solution of **S2**[2] (0.6 mmol, 3.0 equiv), triethylamine (1.2 mmol, 6.0 equiv), DCM (10 mL) under N_2 atmosphere at room temperature stirred for 0.5 h. Then **S6** was added and stirred for another 12 h. Then the crude reaction mixture was extracted with EtOAc and water, the combined organic phase was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The resulting residue was purified by preparative thin layer chromatography using EtOAc/MeOH (20:1-5:1) as the eluent to give the **10c**. (yield: 40%) ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.25 (t, J = 8.9 Hz, 2H), 8.11 (q, J = 6.0 Hz, 2H), 7.30 – 7.12 (m, 10H), 6.84 (t, J = 7.9 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 4.71 (br, 2H), 4.52 – 4.45 (m, 2H), 3.42 – 3.34 (m, 12H), 3.25 – 3.16 (m, 4H), 2.95 (dd, J = 13.7, 5.0 Hz, 2H), 2.76 (dd, J = 13.6, 9.6 Hz, 2H), 2.62 (q, J = 7.7 Hz, 4H), 2.36 – 2.23 (m, 4H), 2.09 (d, J = 2.1 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.4, 171.2, 171.1, 158.8 (d, $J_{C\text{-}F}$ = 240.7 Hz), 139.7 (d, $J_{C\text{-}F}$ = 4.0 Hz), 138.0, 129.3, 129.2, 128.0, 127.0 (d, $J_{C\text{-}F}$ = 5.6 Hz), 126.3, 125.0, 124.8, 123.8 (d, $J_{C\text{-}F}$ = 3.1 Hz), 122.1 (d, $J_{C\text{-}F}$ = 16.6 Hz), 72.2, 68.8, 60.2, 54.12, 54.10, 38.0, 37.9, 35.7, 35.3, 28.3, 24.3, 10.2 (d, $J_{C\text{-}F}$ = 6.4 Hz). HRMS (m/z, ESI-TOF): Calcd for $C_{39}H_{51}FN_4O_8Na^+$ [M+Na$^+$] 745.3583, found 745.3583.

Hydrolysis of 5a:

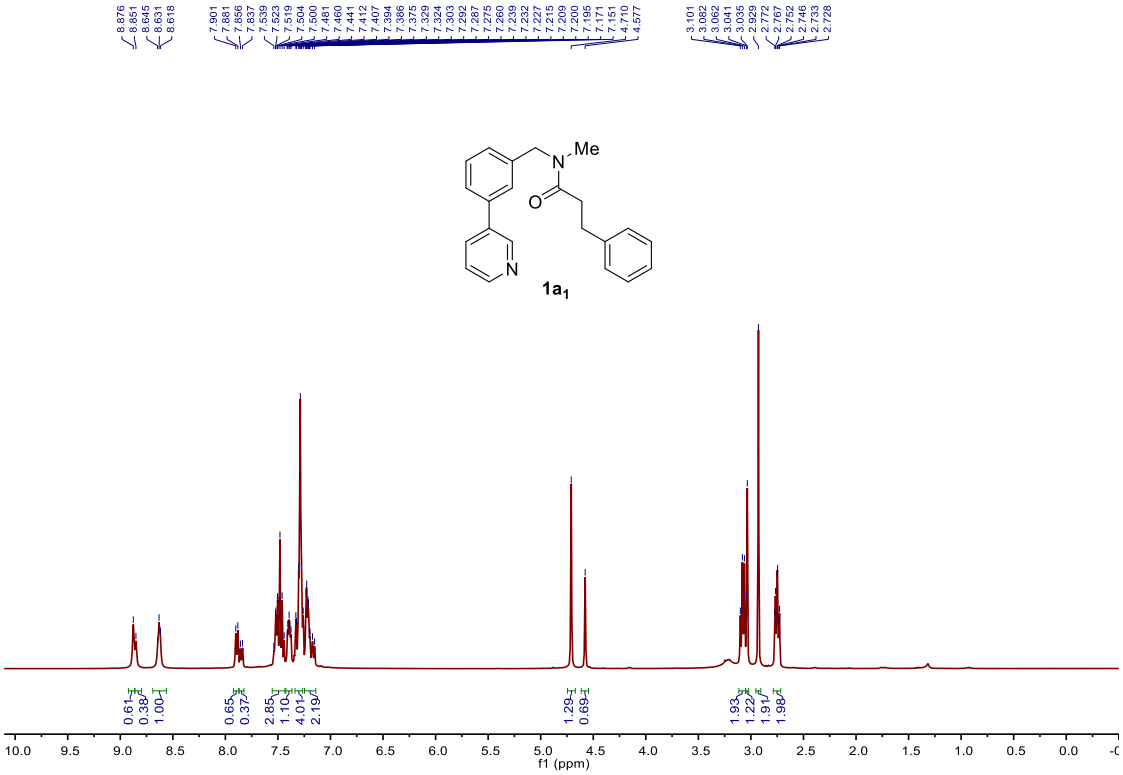


5a **S7**

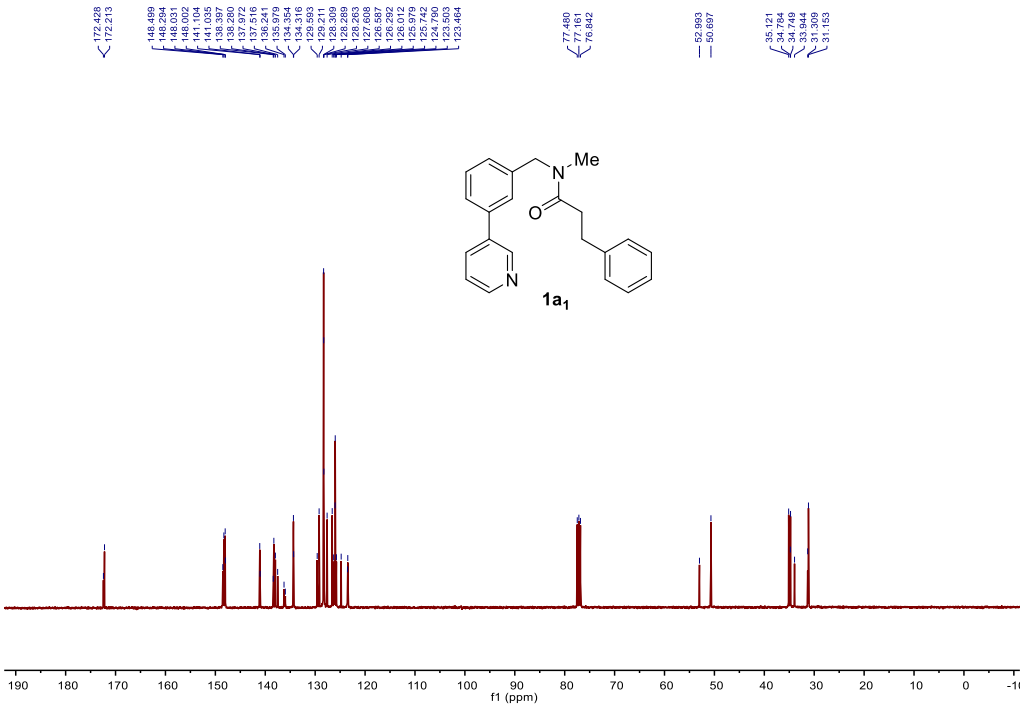
To a solution of **5a** (0.05 mmol) and LiOH·H_2O (0.5 mmol, 10 equiv) in THF : MeOH : H_2O (1.5:1.0:0.5 mL) at room temperature stirred for 12 h. Then volatile matter was removed under reduced pressure. Then the crude reaction mixture was extracted with EtOAc and water, The combined water phase was added 1N HCl until pH ≈ 1, then filtered to give **S7**. ^{1}H NMR (400 MHz, DMSO-d6) δ 7.75 (d, J = 7.6 Hz, 1H), 7.73 (d, J = 8.1 Hz, 2H), 7.66 – 7.57 (m, 2H), 7.48 (t, J = 7.5 Hz, 1H), 7.41 (d, J = 7.6 Hz, 1H), 7.37 (d, J = 8.0 Hz, 2H), 6.57 (d, J = 16.0 Hz, 1H). ^{13}C NMR (101 MHz, DMSO-d6) δ 169.5, 167.7, 143.6, 142.8, 140.4, 133.2, 132.3, 131.1, 130.4, 129.3, 128.9, 128.1, 127.7, 119.2. HRMS (m/z, ESI-TOF): Calcd for $C_{16}H_{12}O_4Na^+$ [M+Na^+] 291.0628, found 291.0631.

3 NMR Spectrc of Compounds

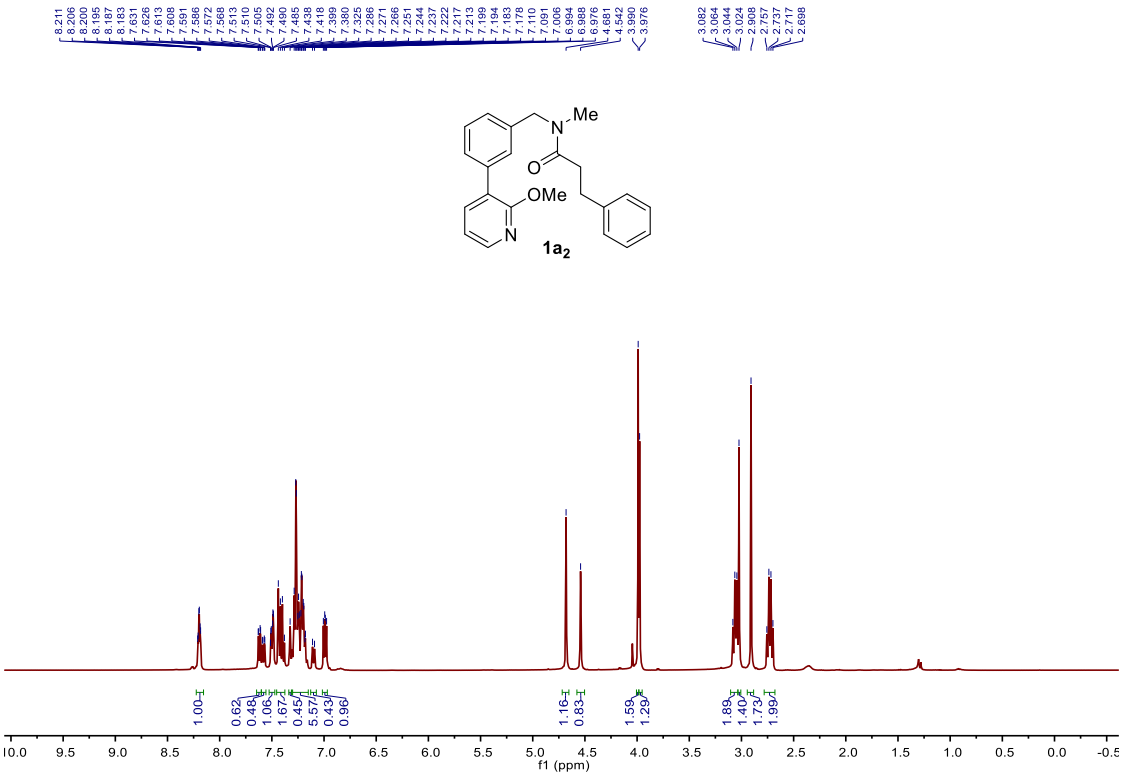
^{1}H NMR (400 MHz, Chloroform-*d*)



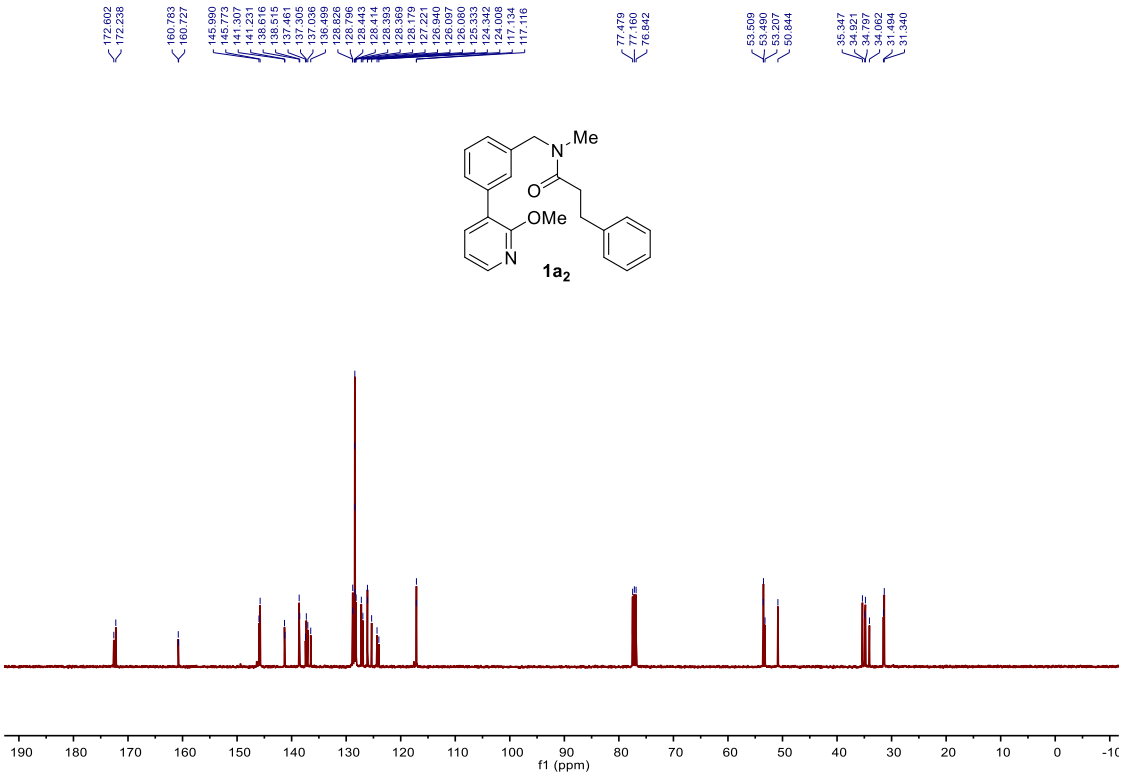
^{13}C NMR (101 MHz, Chloroform-*d*)



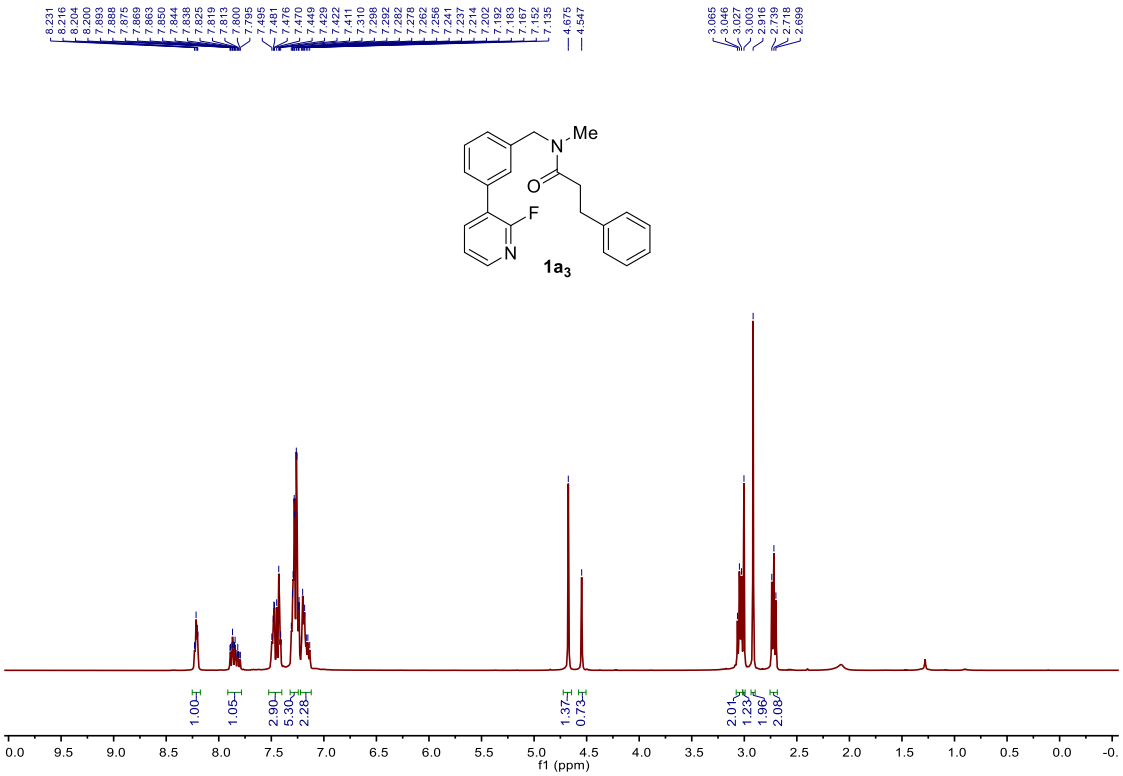
^{1}H NMR (400 MHz, Chloroform-*d*)



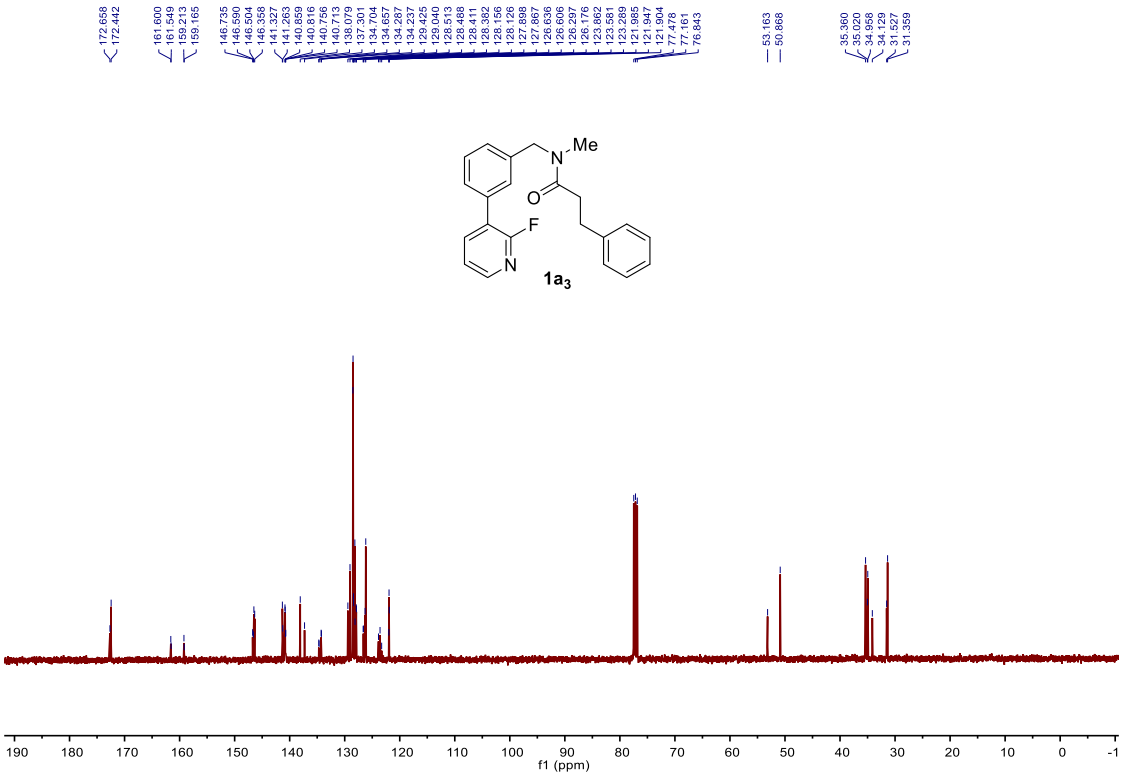
^{13}C NMR (101 MHz, Chloroform-*d*)



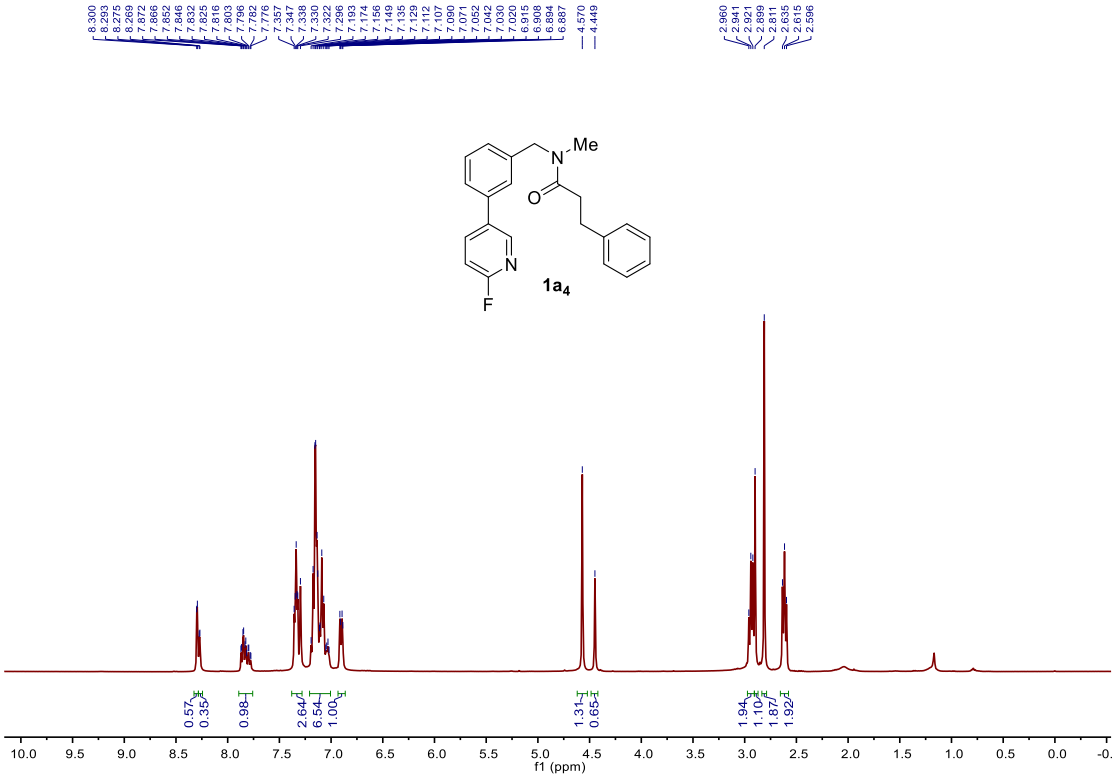
^{1}H NMR (400 MHz, Chloroform-*d*)



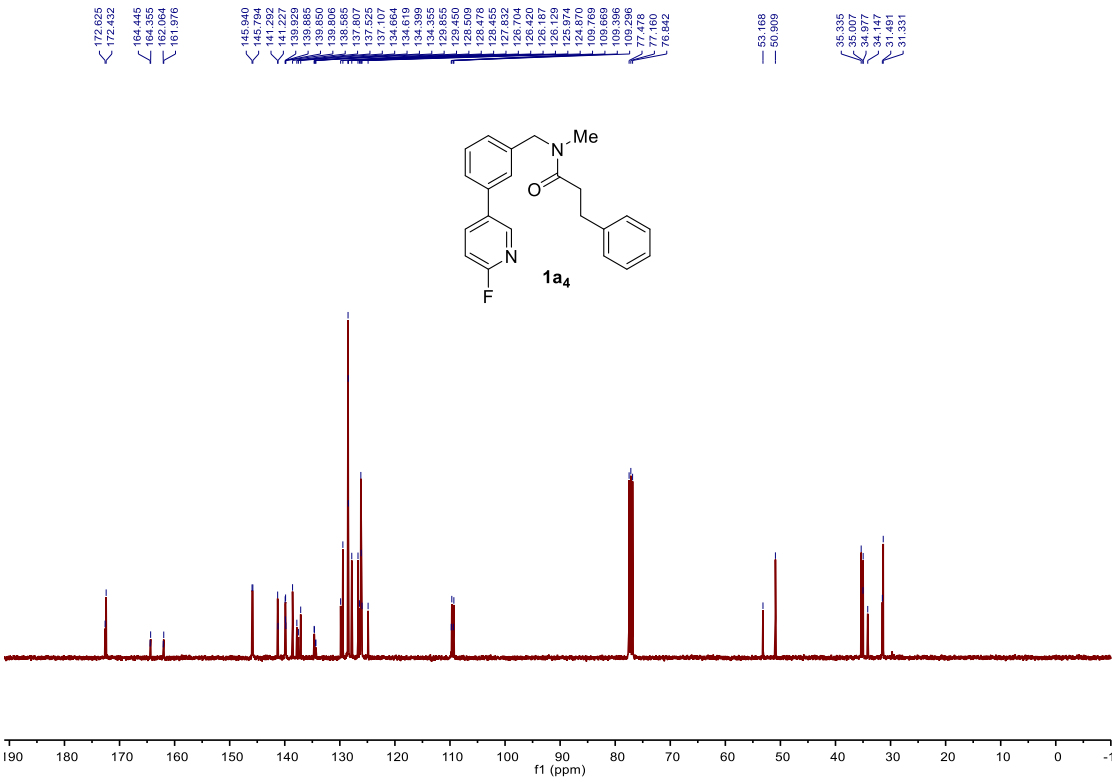
^{13}C NMR (101 MHz, Chloroform-*d*)



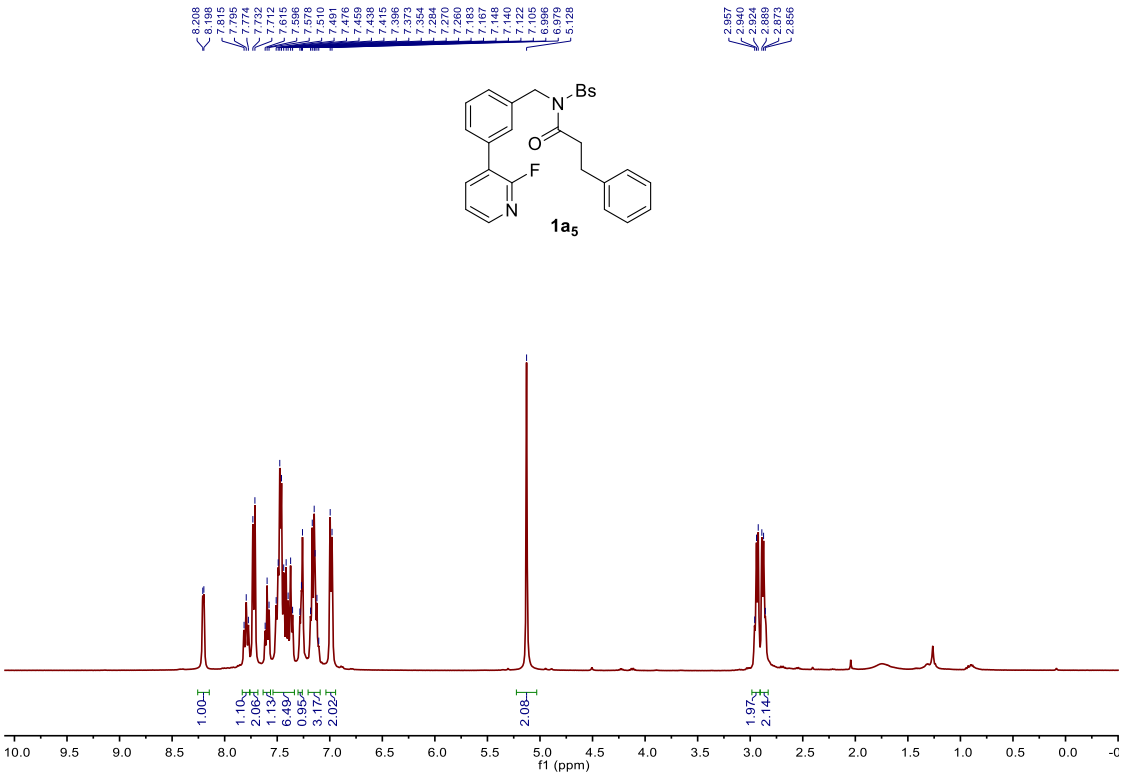
^{1}H NMR (400 MHz, Chloroform-*d*)



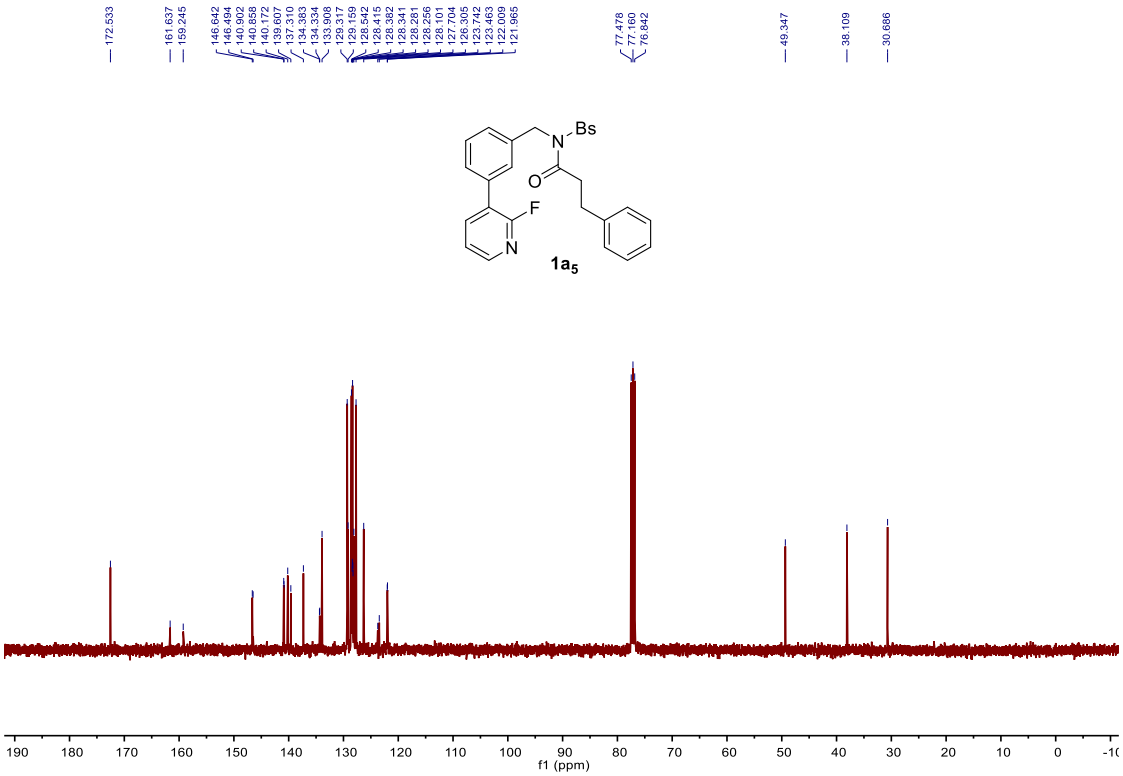
^{13}C NMR (101 MHz, Chloroform-*d*)



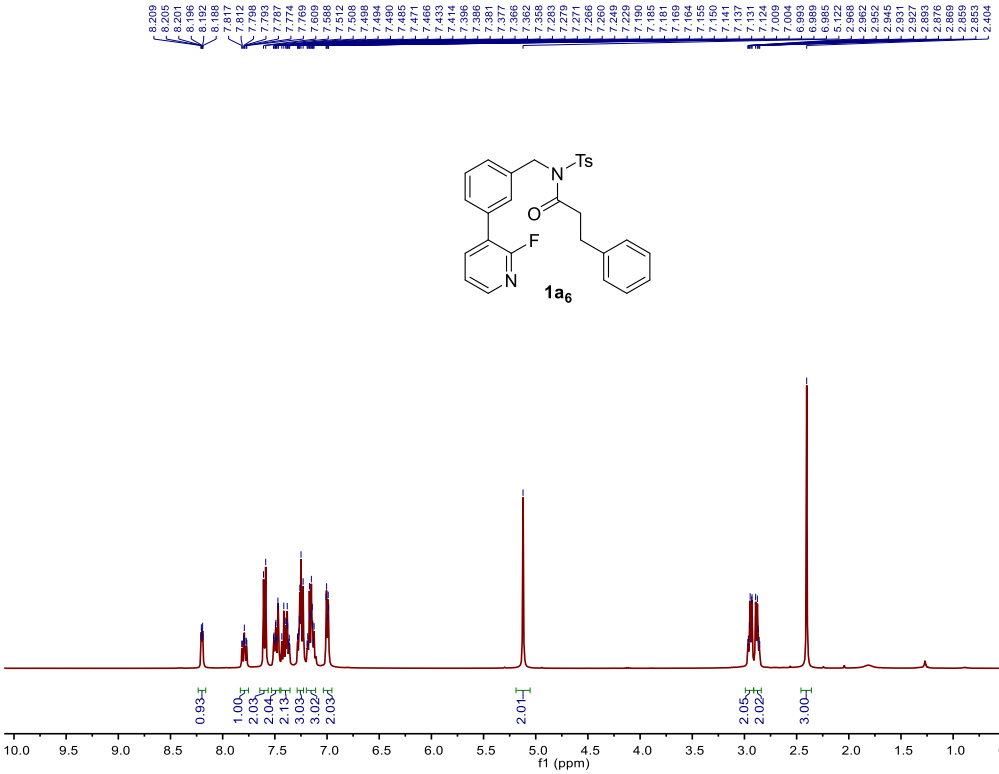
^{1}H NMR (400 MHz, Chloroform-*d*)



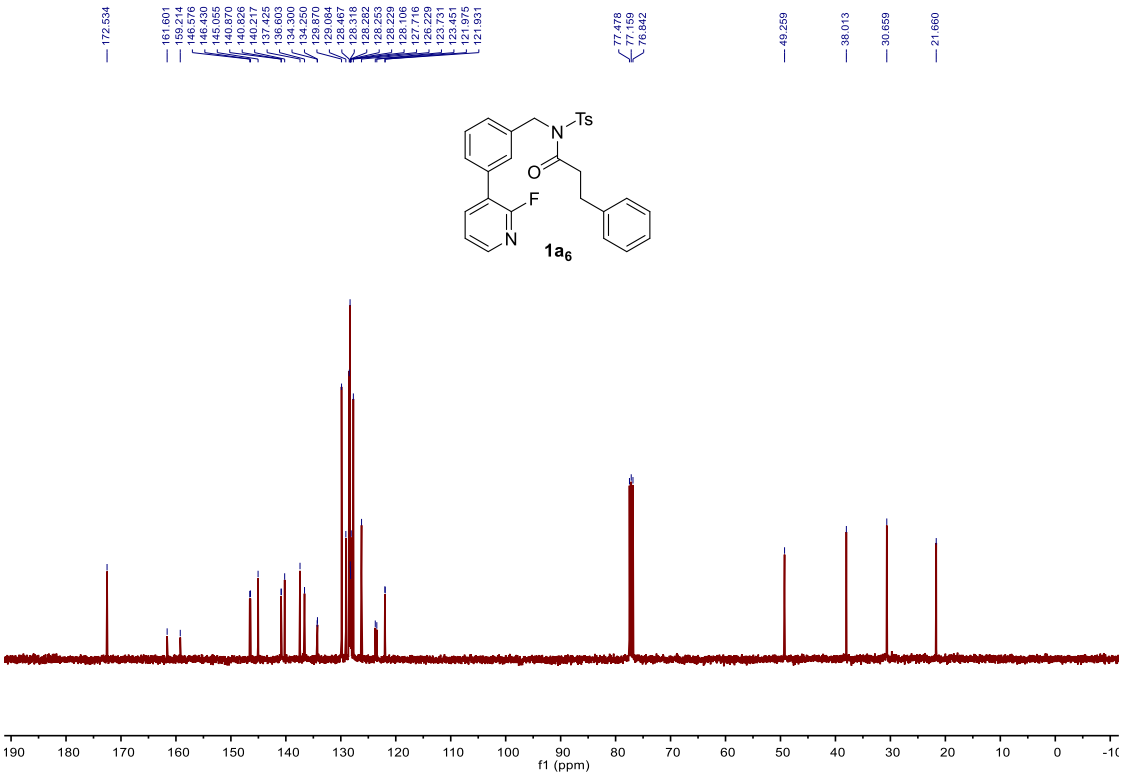
^{13}C NMR (101 MHz, Chloroform-*d*)



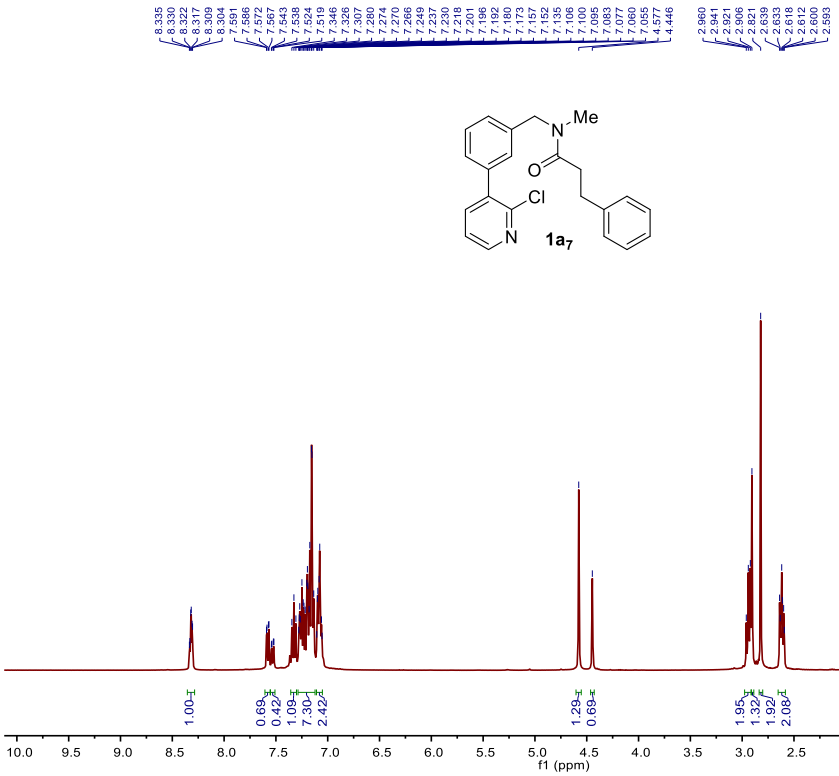
^{1}H NMR (400 MHz, Chloroform-*d*)



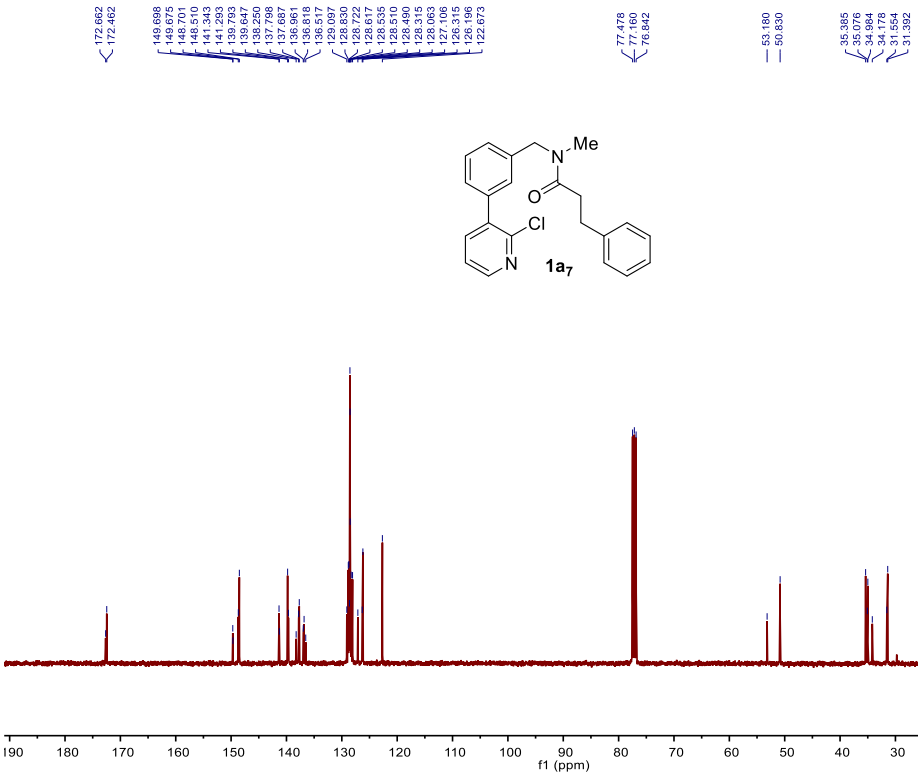
^{13}C NMR (101 MHz, Chloroform-*d*)



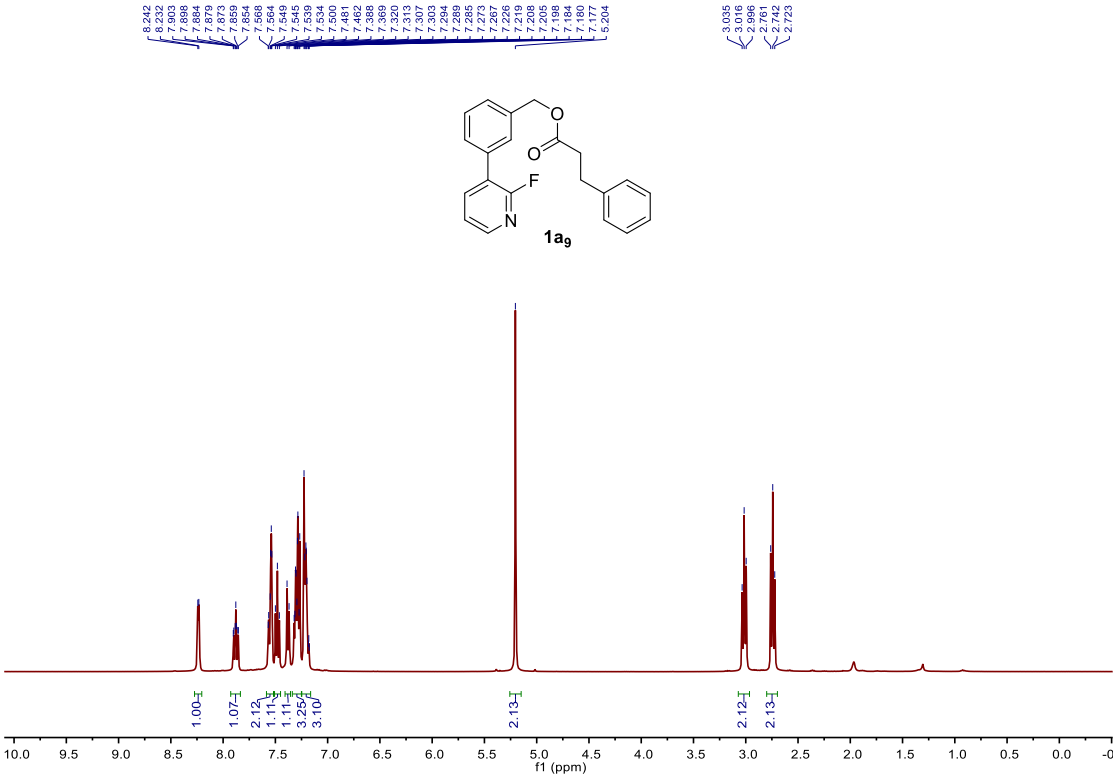
^{1}H NMR (400 MHz, Chloroform-*d*)



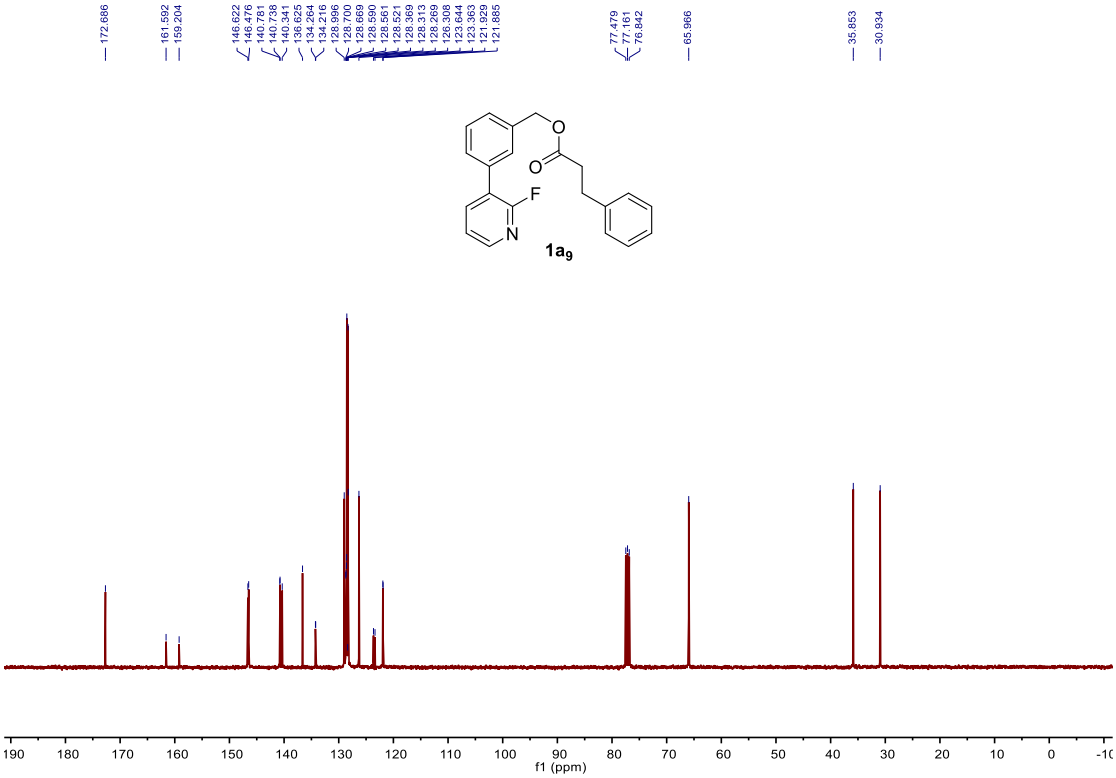
^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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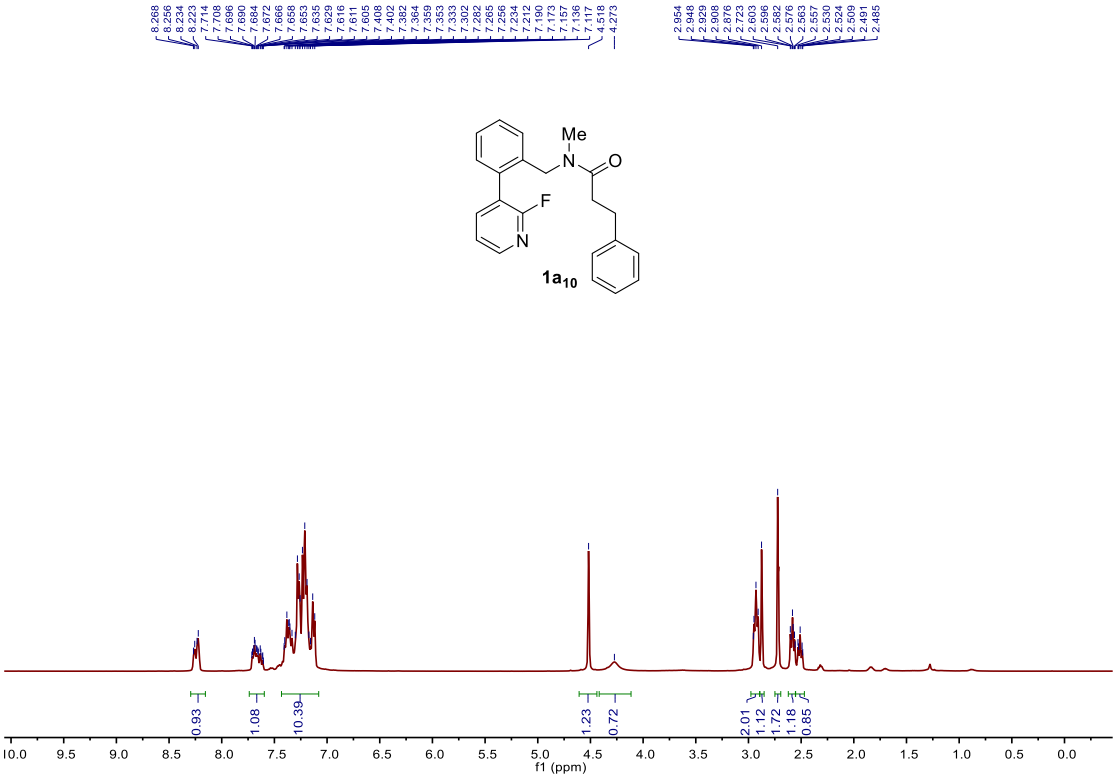

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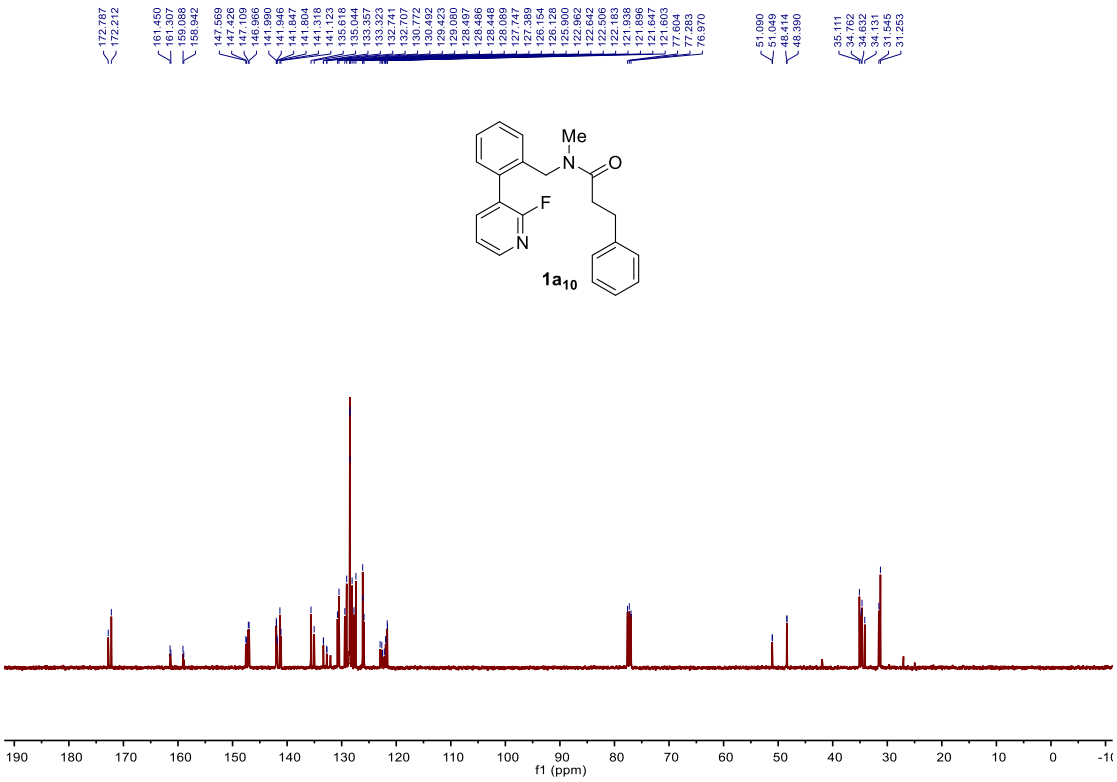
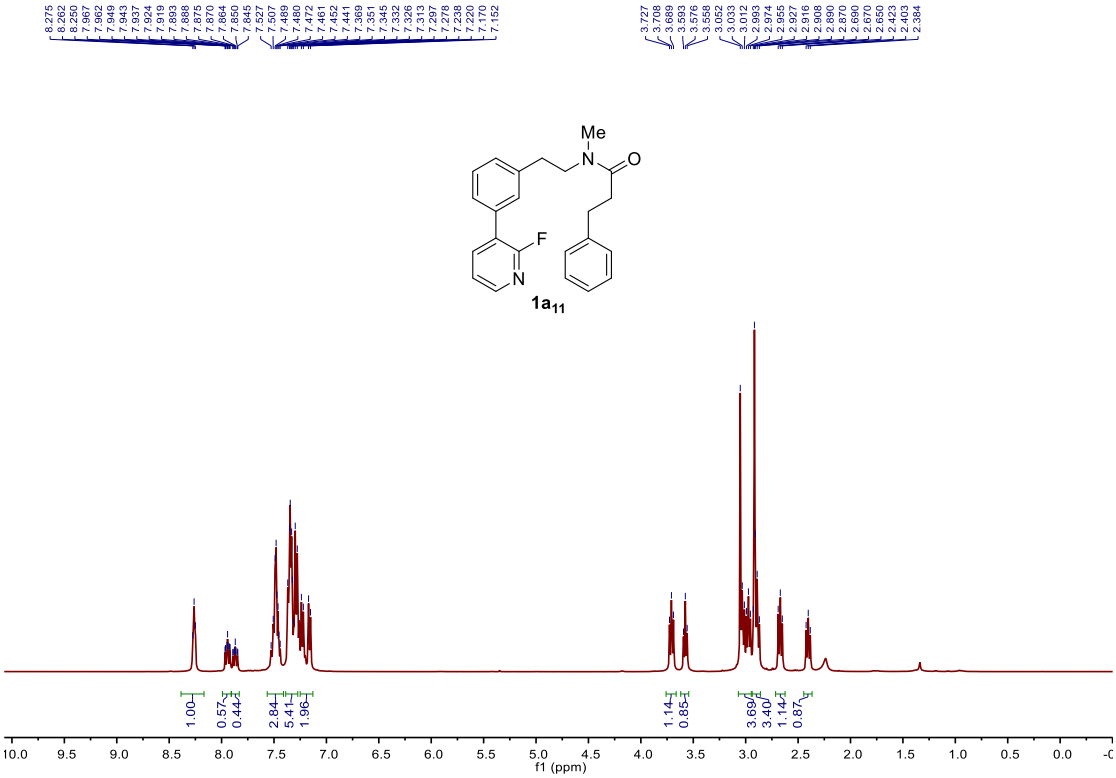
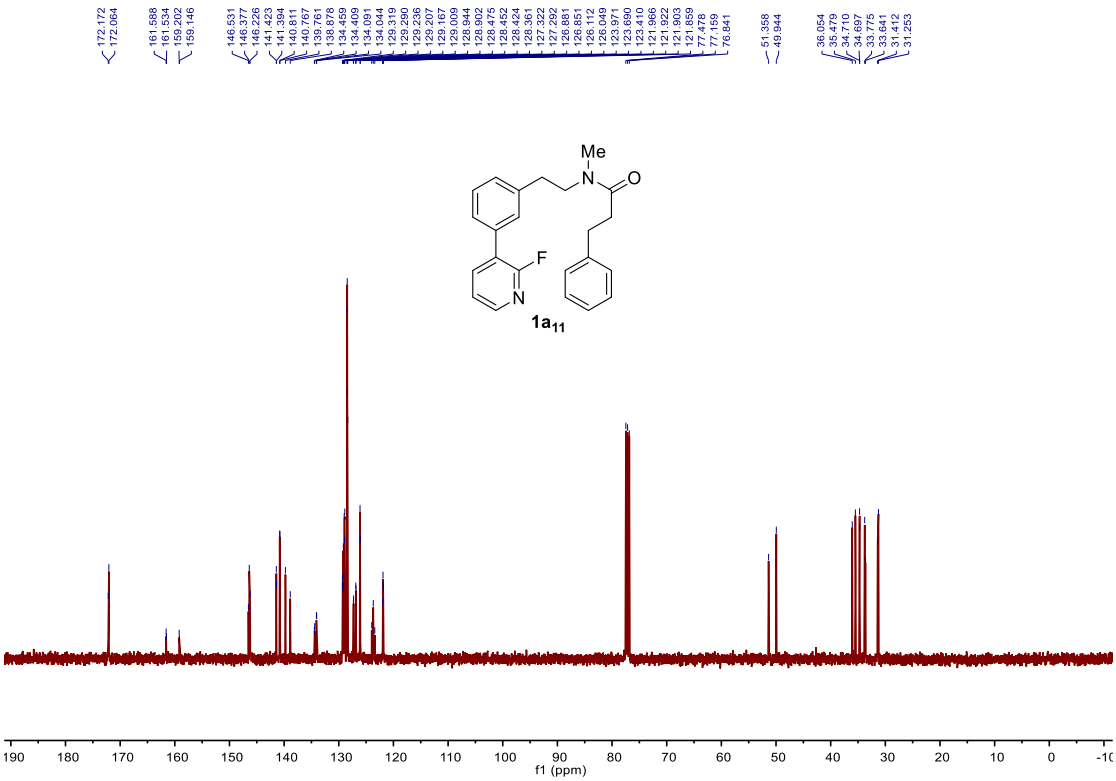


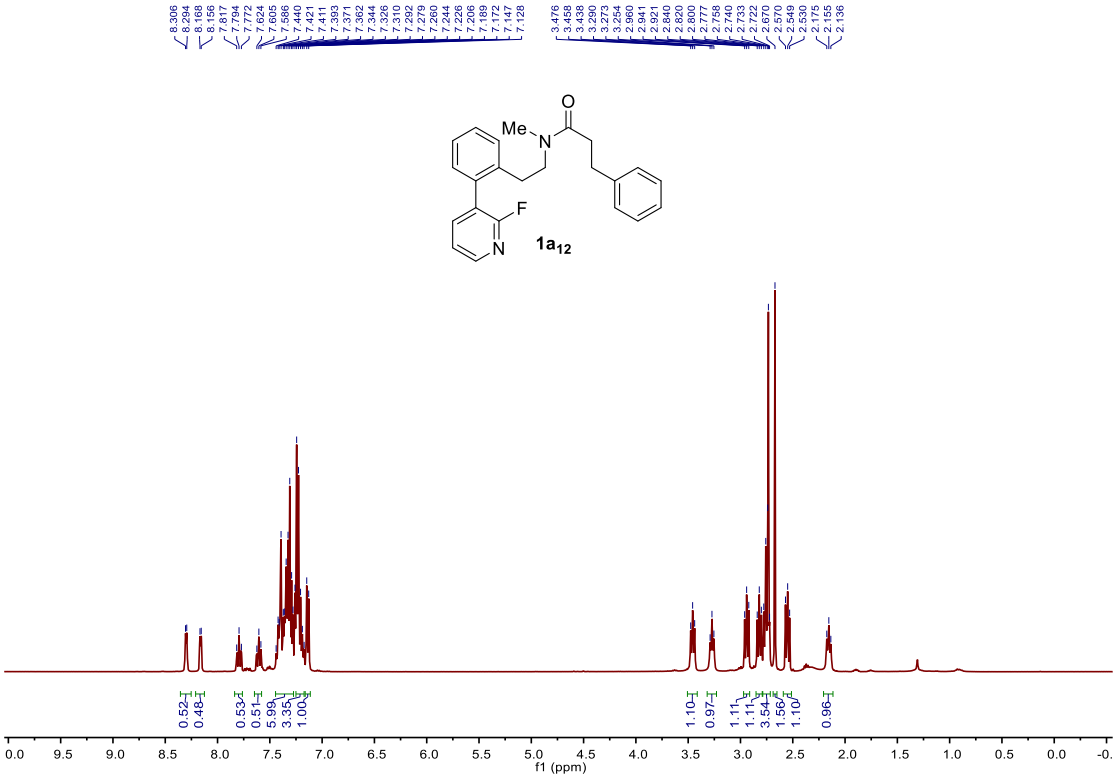
^{1}H NMR (400 MHz, Chloroform-*d*)



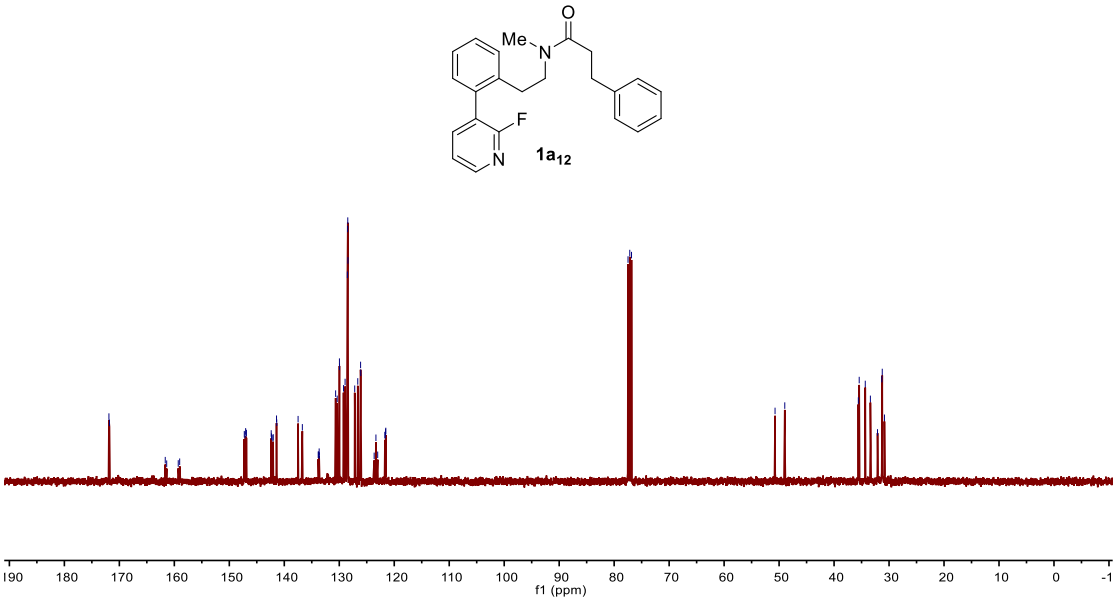
^{13}C NMR (101 MHz, Chloroform-*d*)



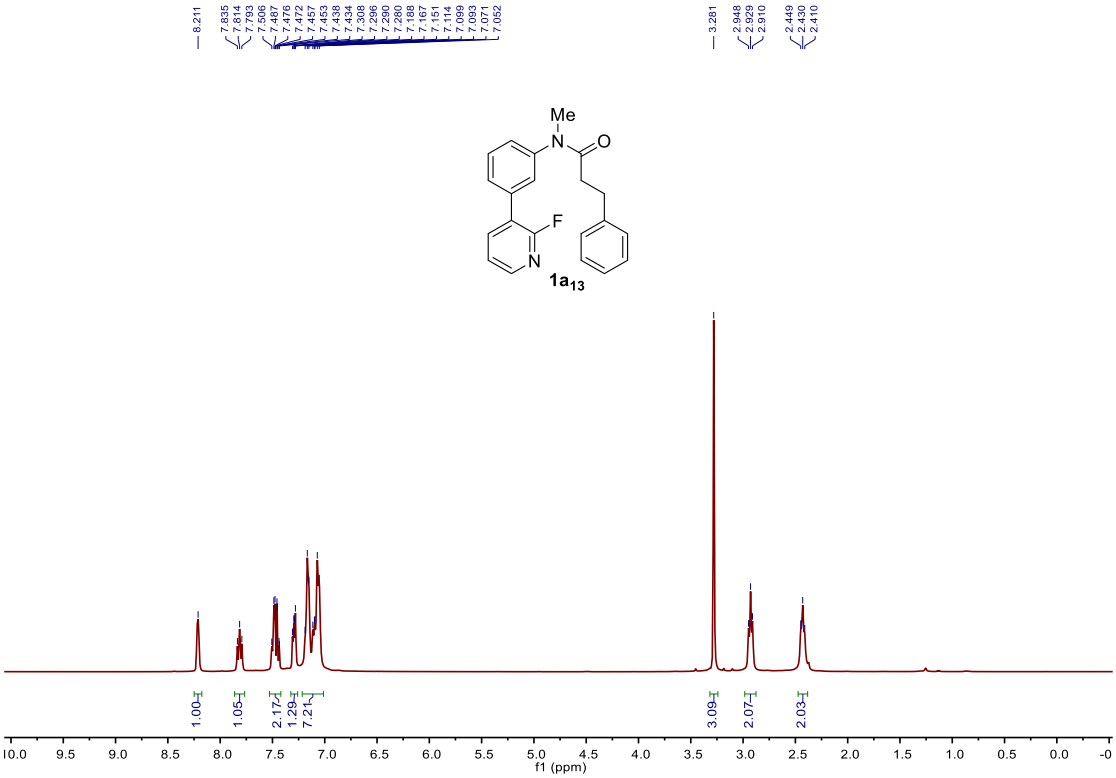
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



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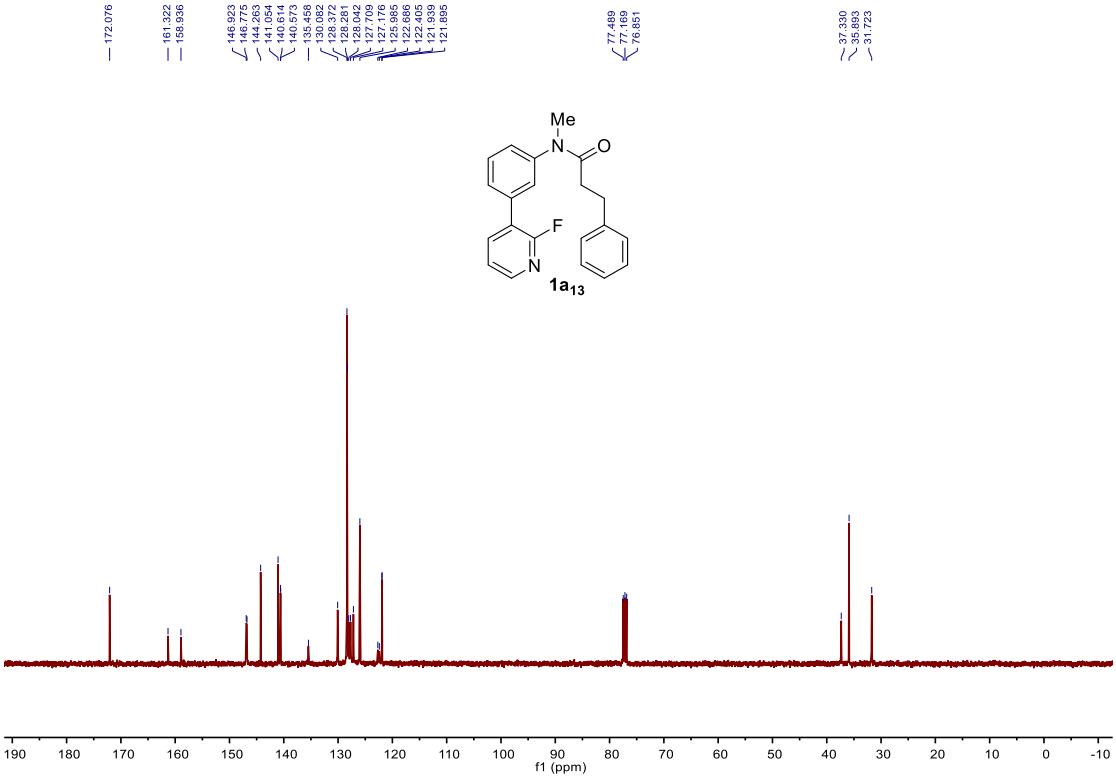

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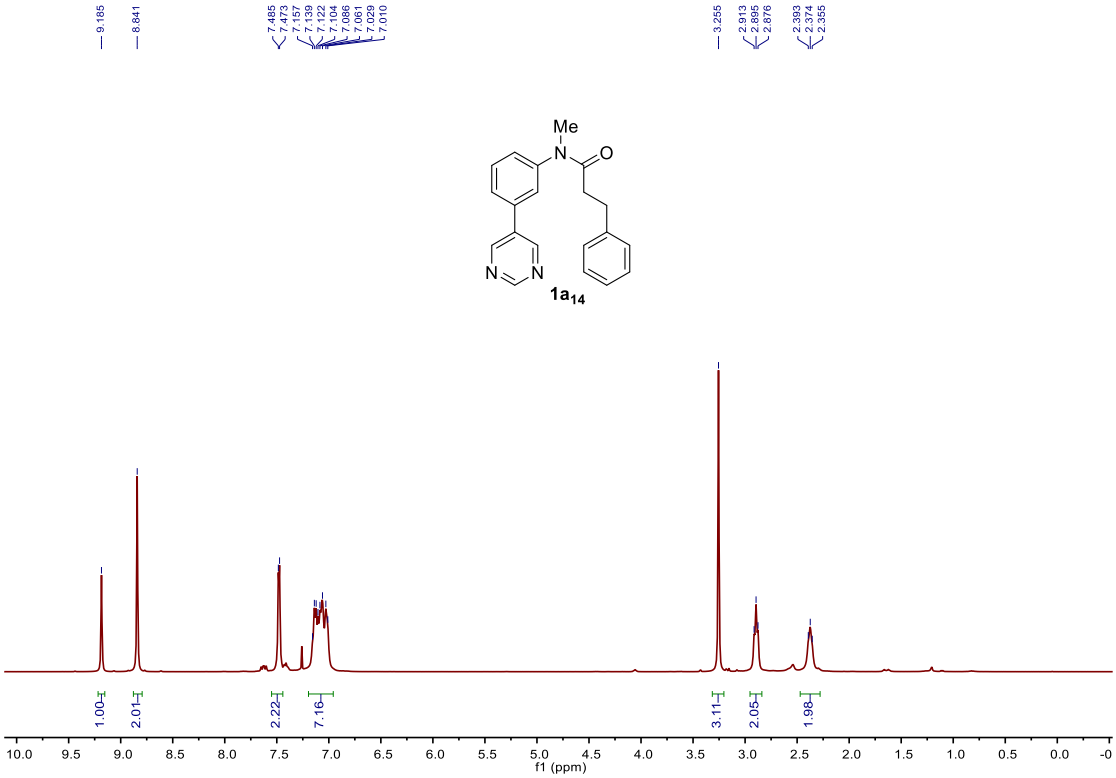
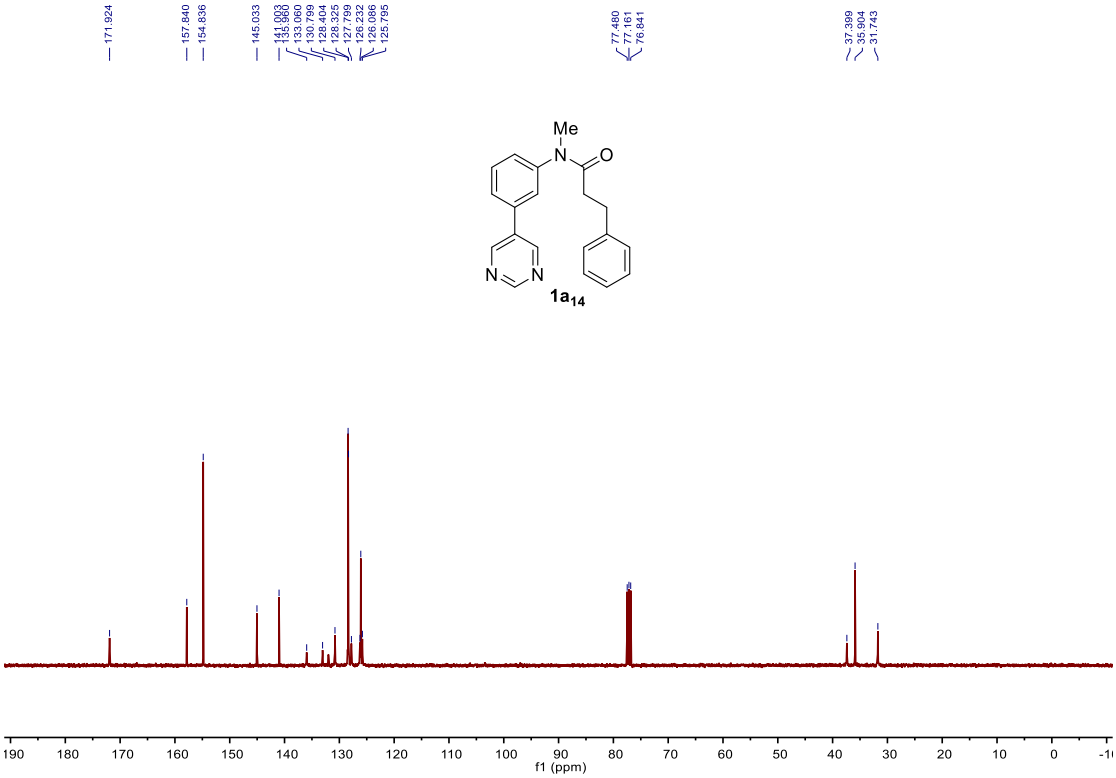
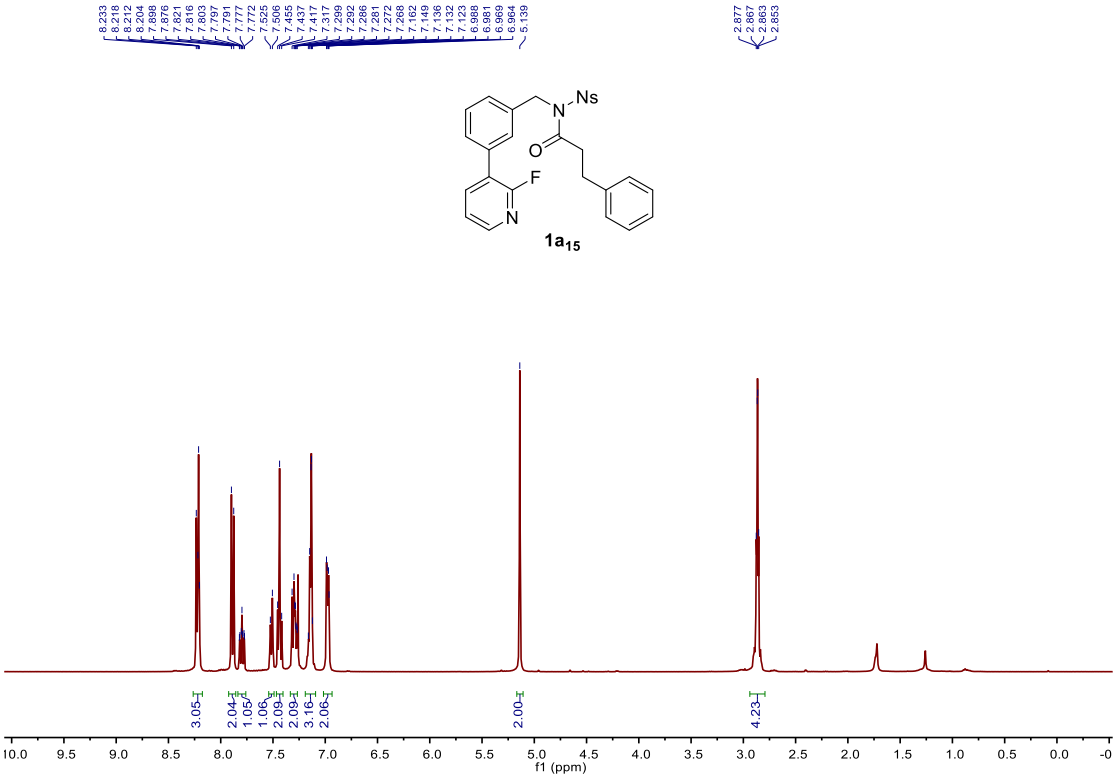


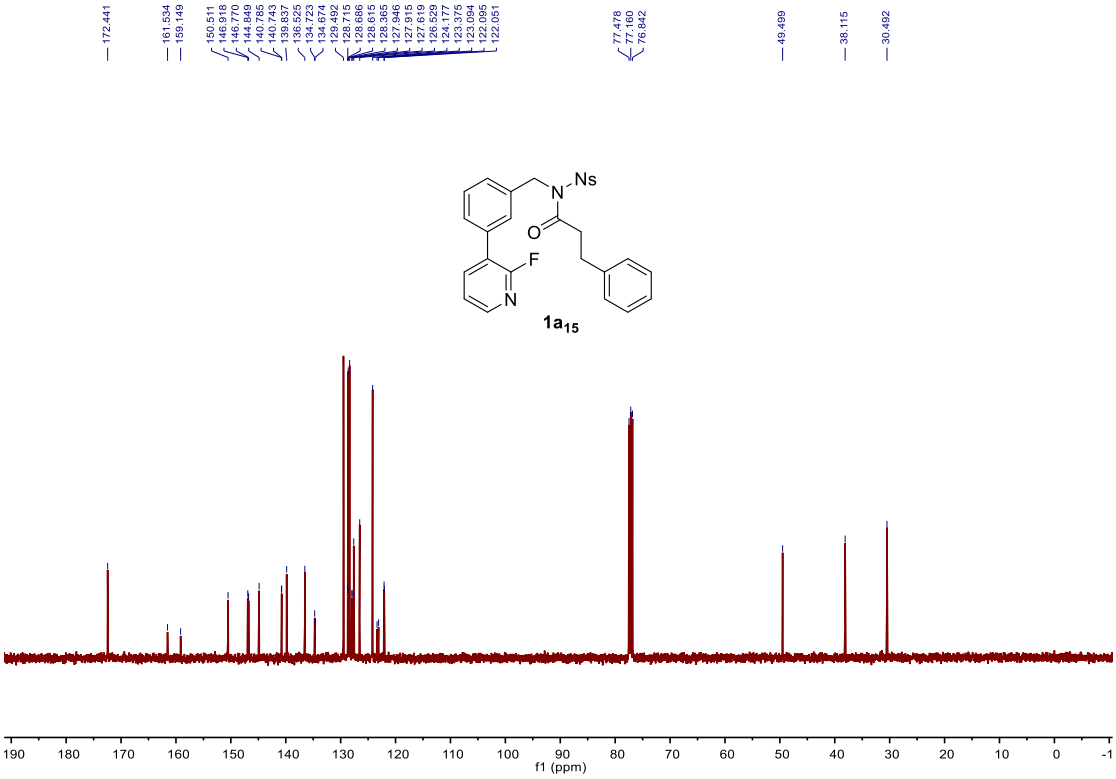
^{13}C NMR (101 MHz, Chloroform-*d*)



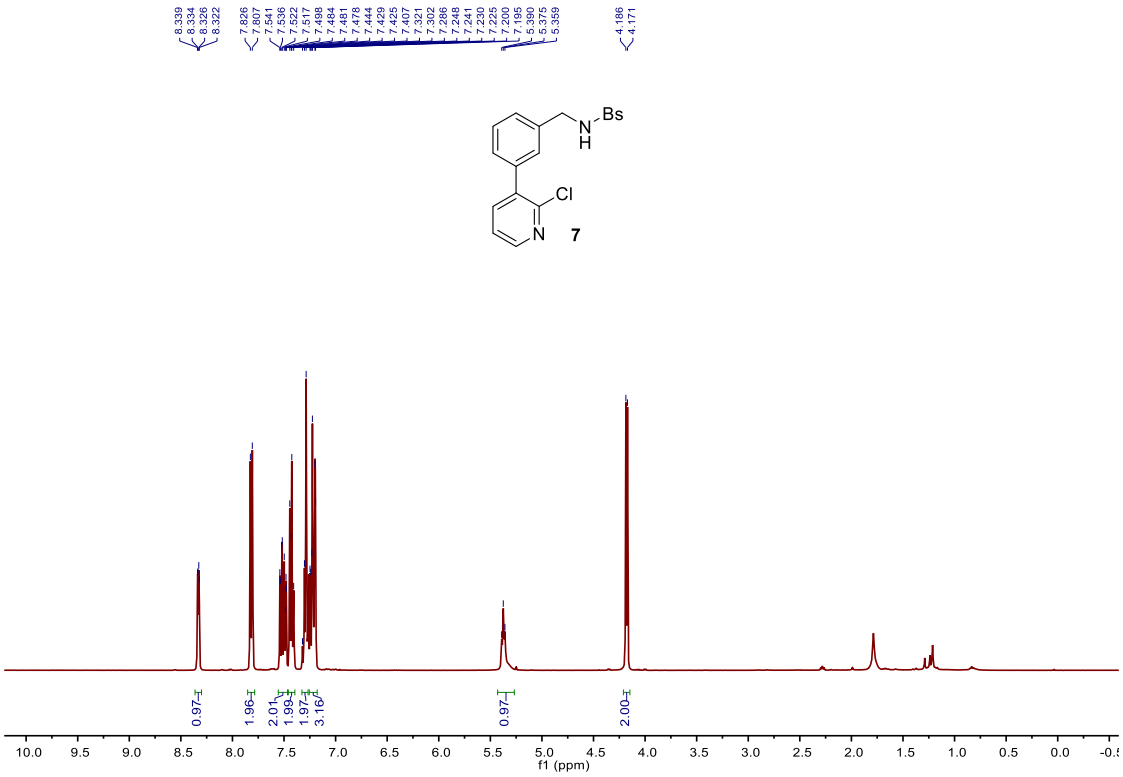
^{1}H NMR (400 MHz, Chloroform-*d*)



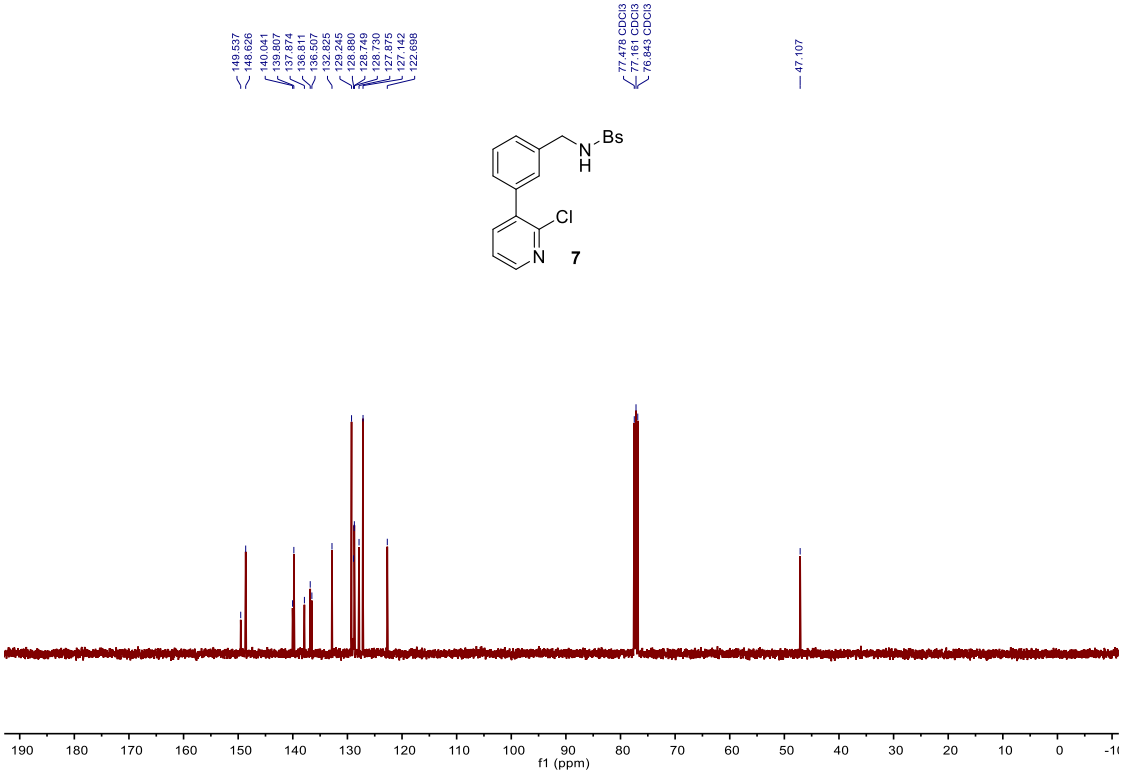
^{13}C NMR (101 MHz, Chloroform-*d*)



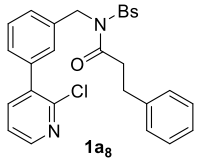
^{1}H NMR (400 MHz, Chloroform-*d*)



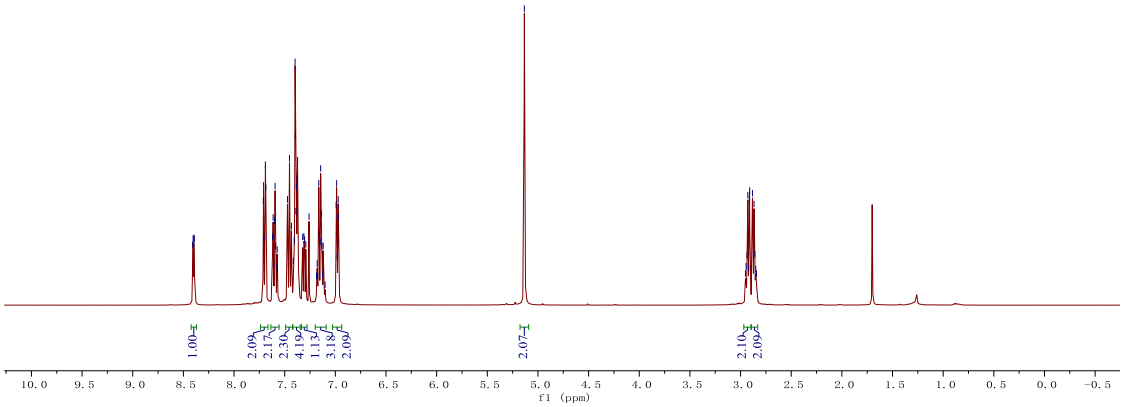
^{13}C NMR (101 MHz, Chloroform-*d*)



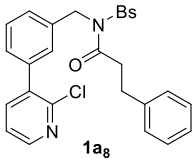
^{1}H NMR (400 MHz, Chloroform-*d*)



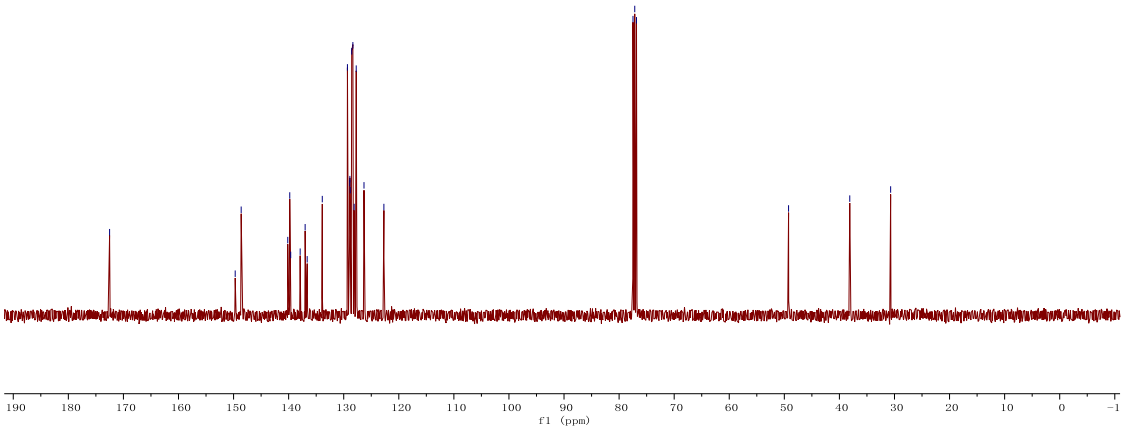
1a$_8$



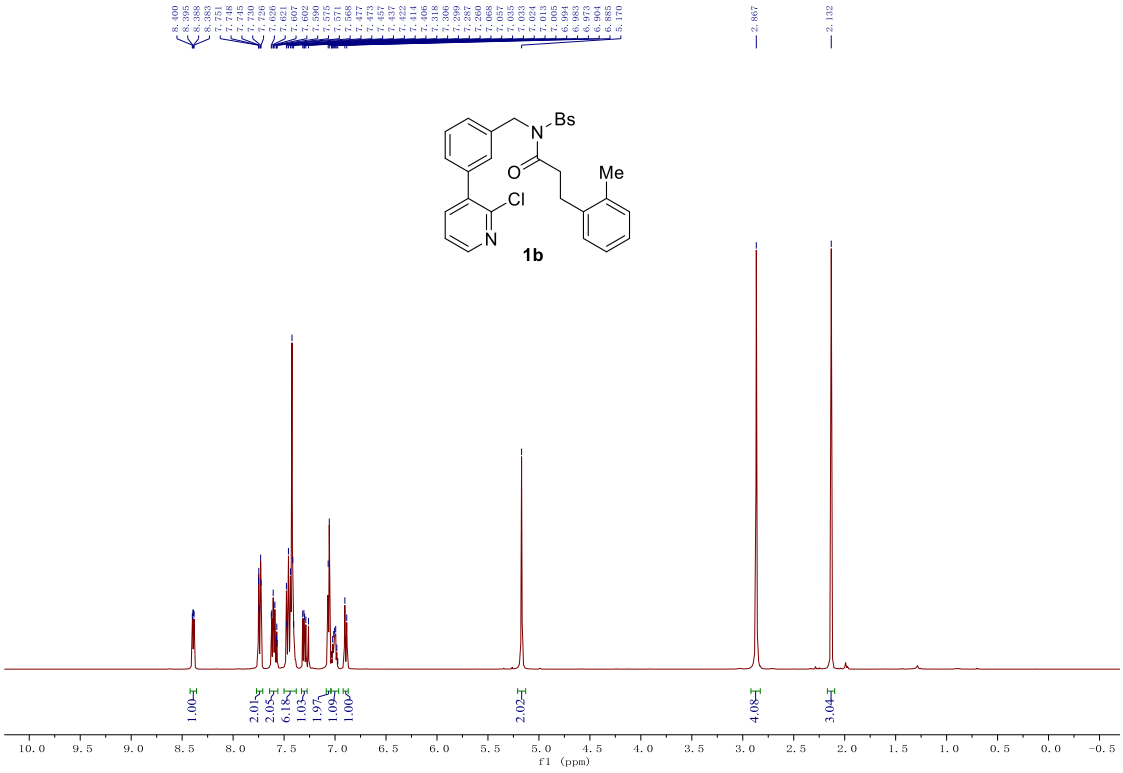
^{13}C NMR (101 MHz, Chloroform-*d*)



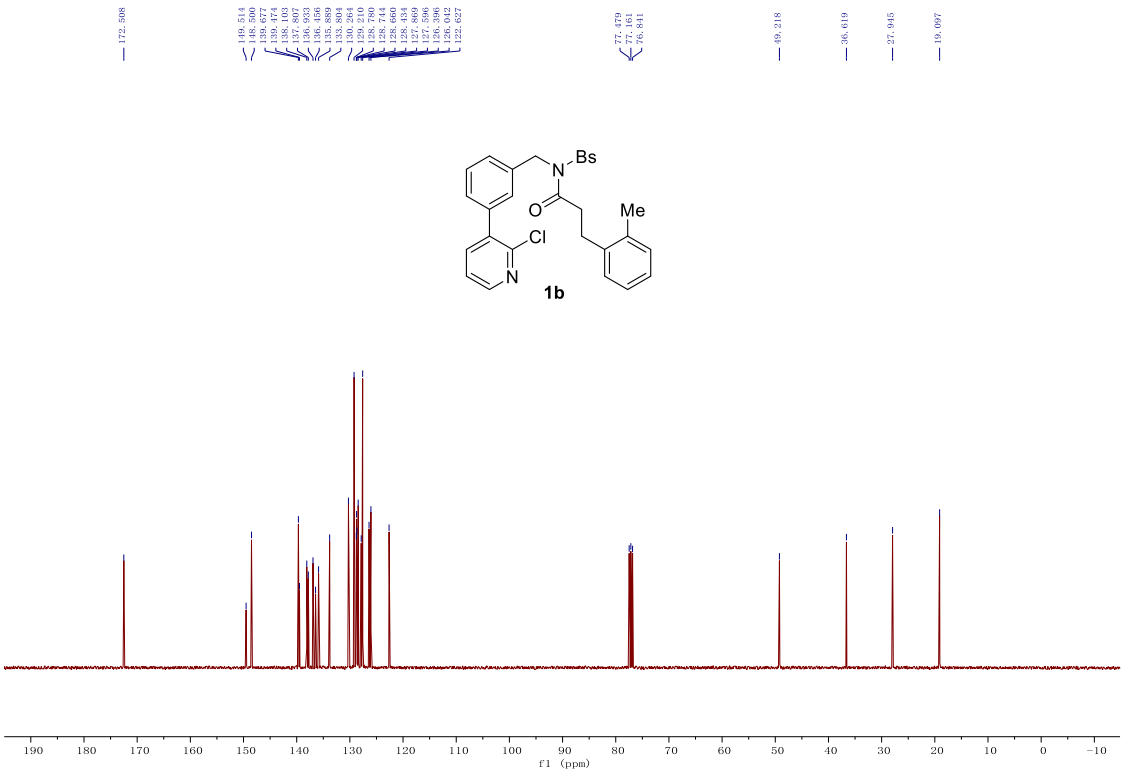
1a$_8$



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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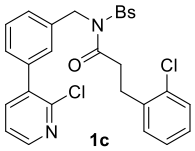
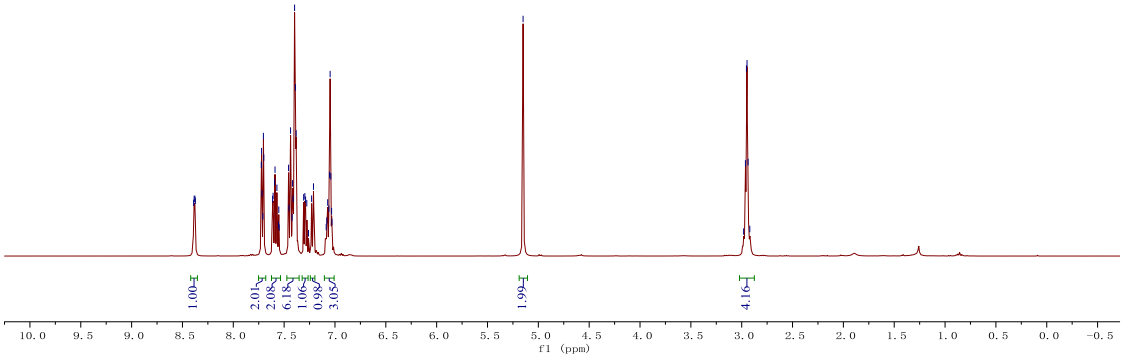
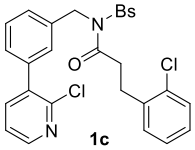
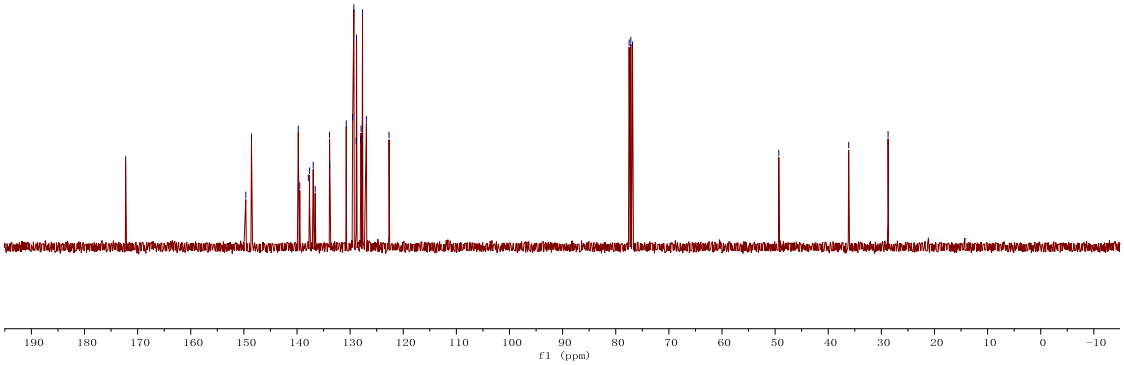




^{13}C NMR (101 MHz, Chloroform-*d*)





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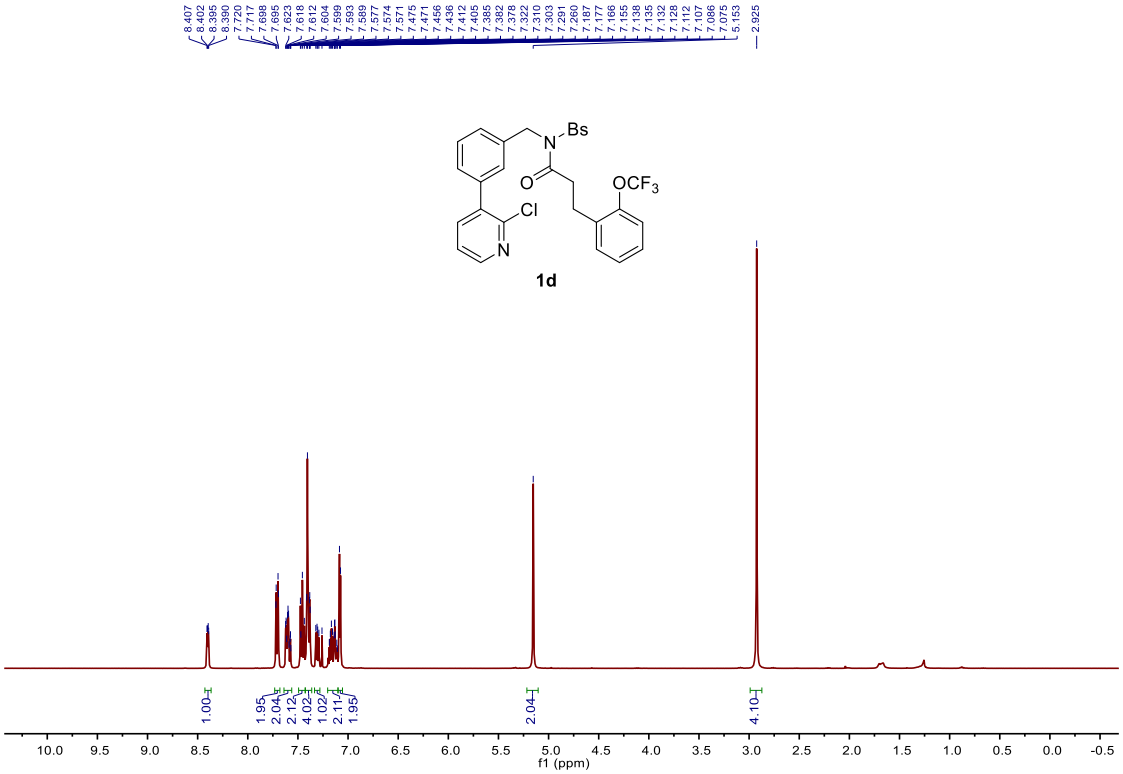
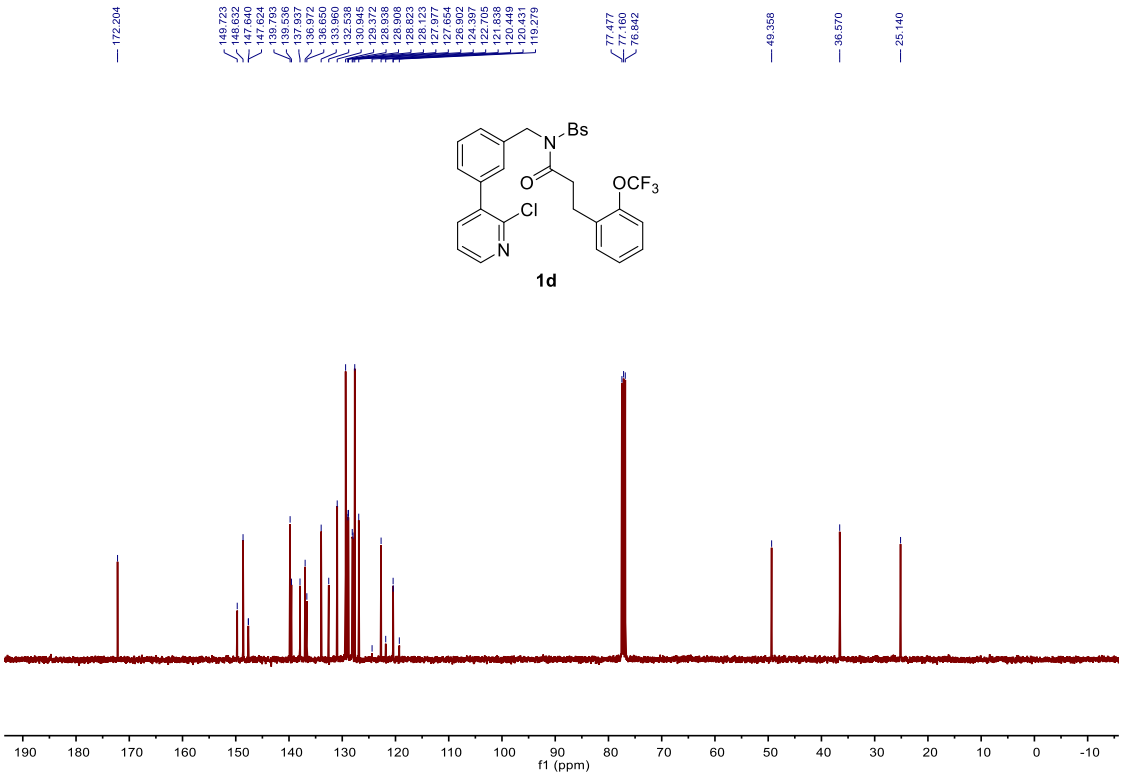
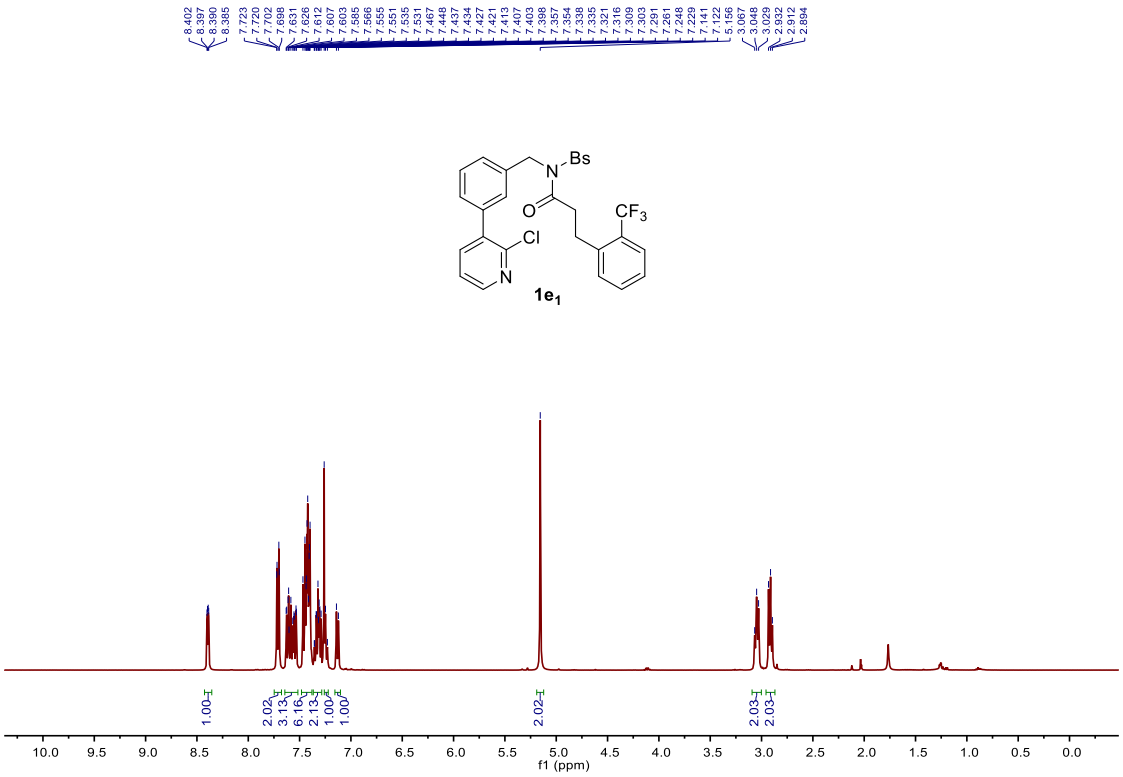


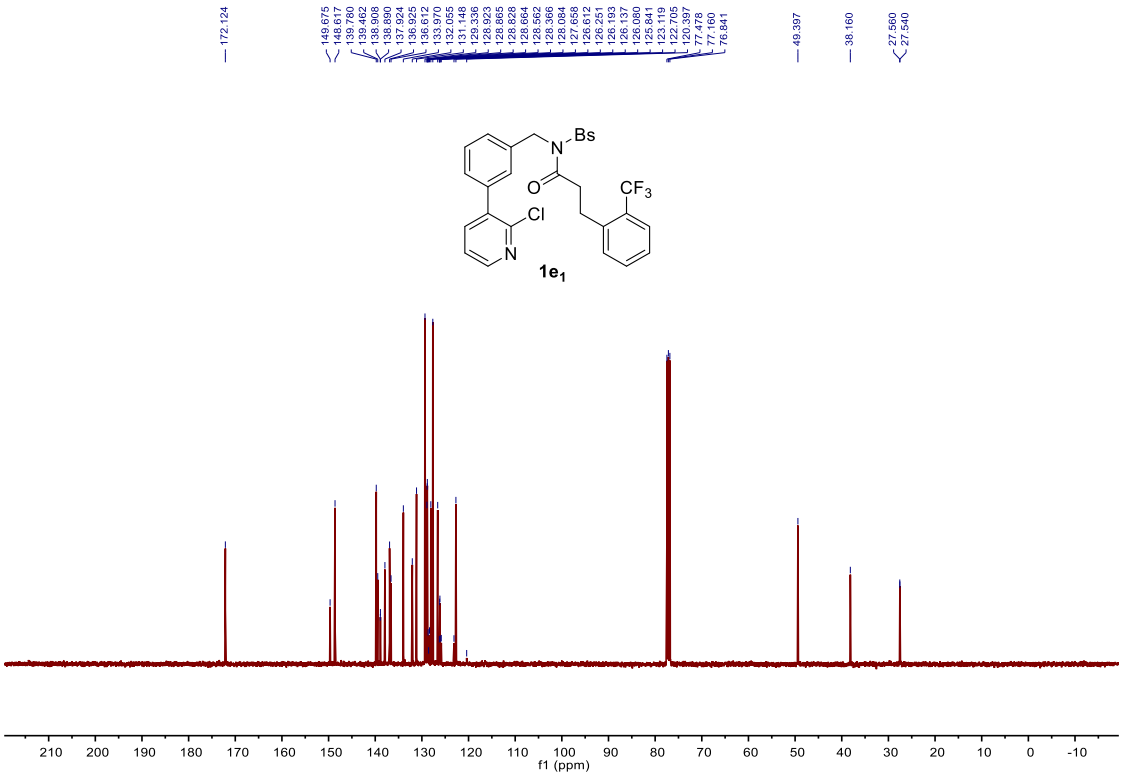
^{13}C NMR (101 MHz, Chloroform-*d*)



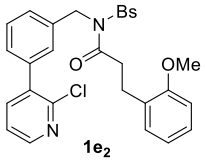
^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



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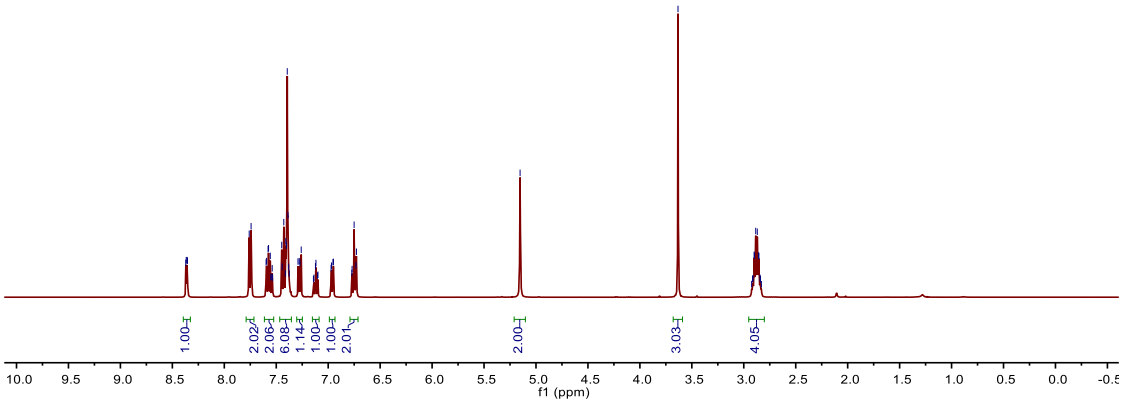
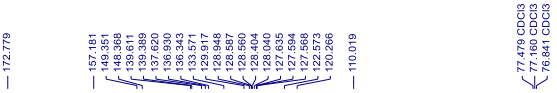
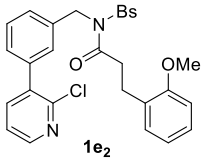


^{13}C NMR (101 MHz, Chloroform-*d*)





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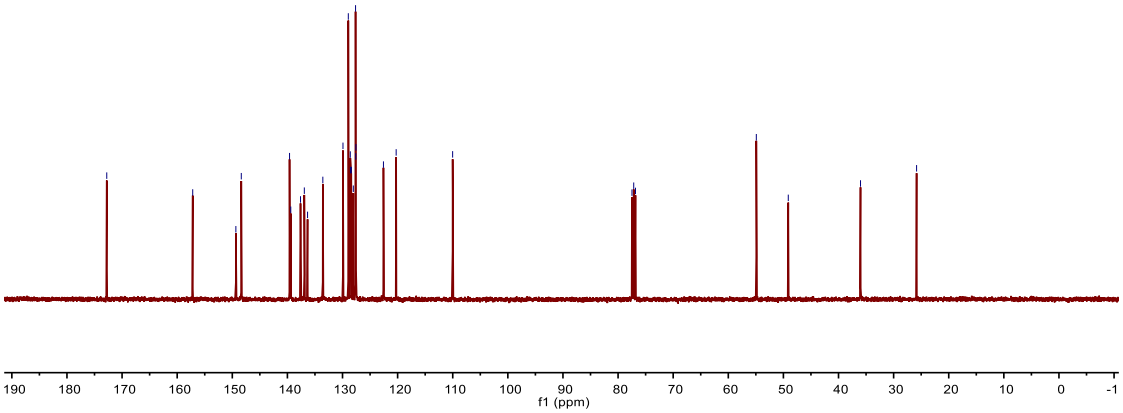
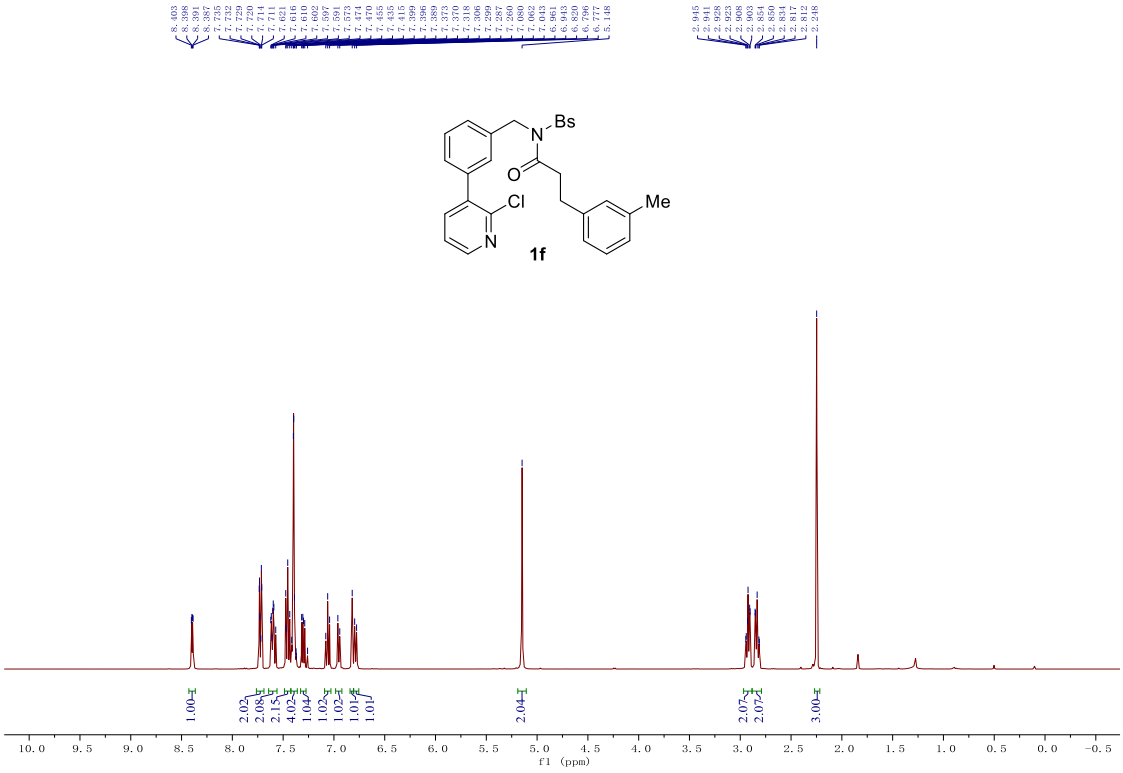
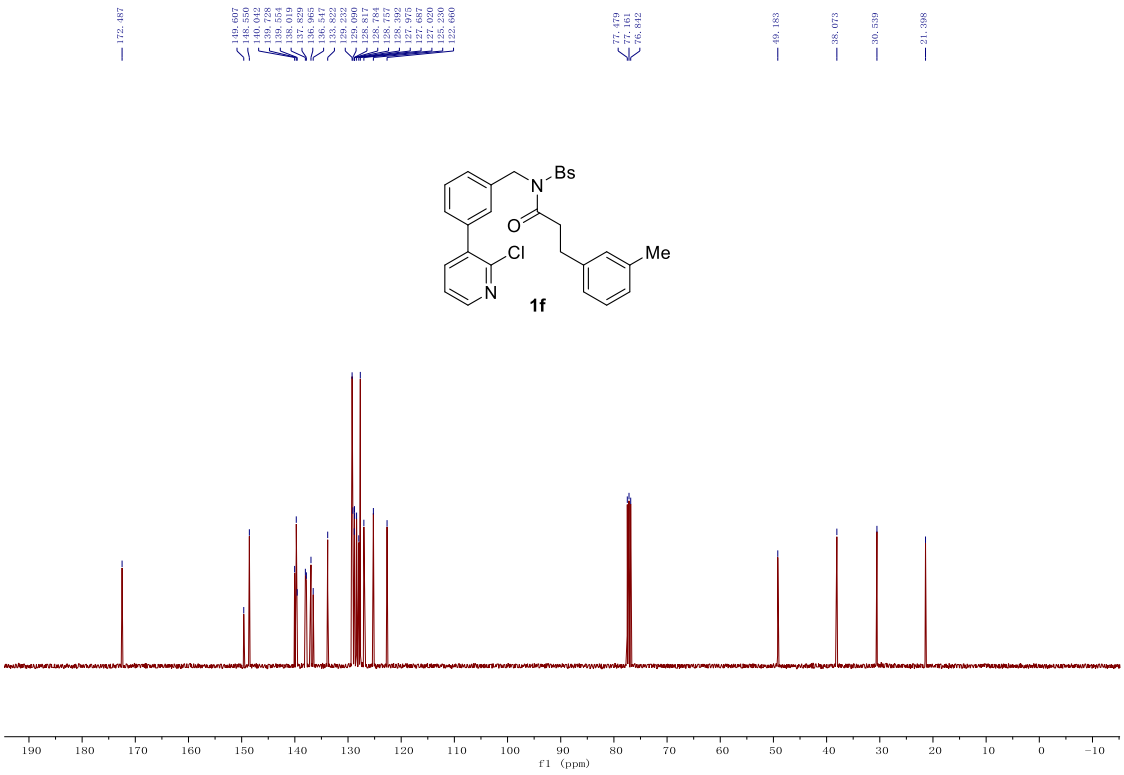


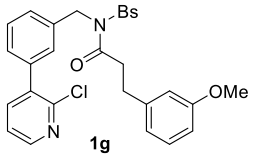
^{1}H NMR (400 MHz, Chloroform-*d*)

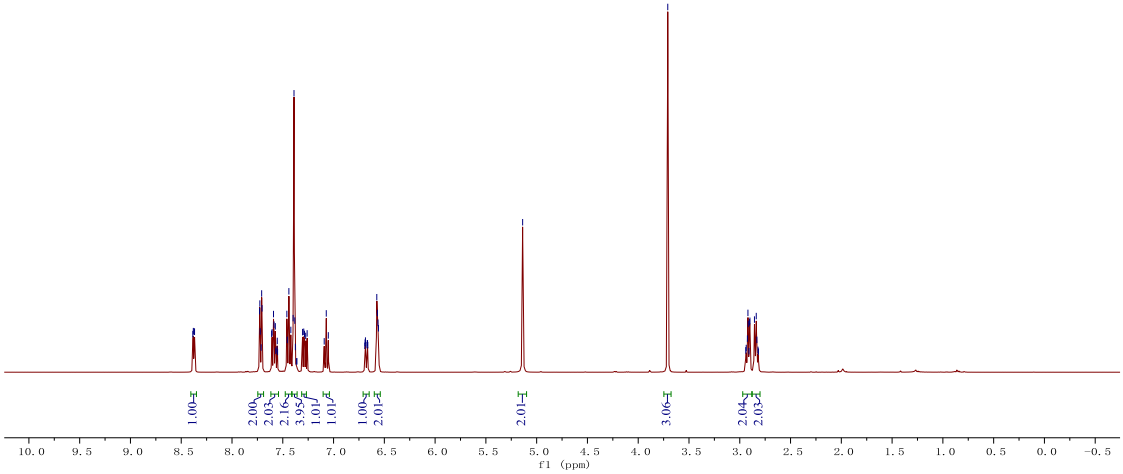


^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)





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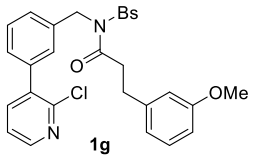

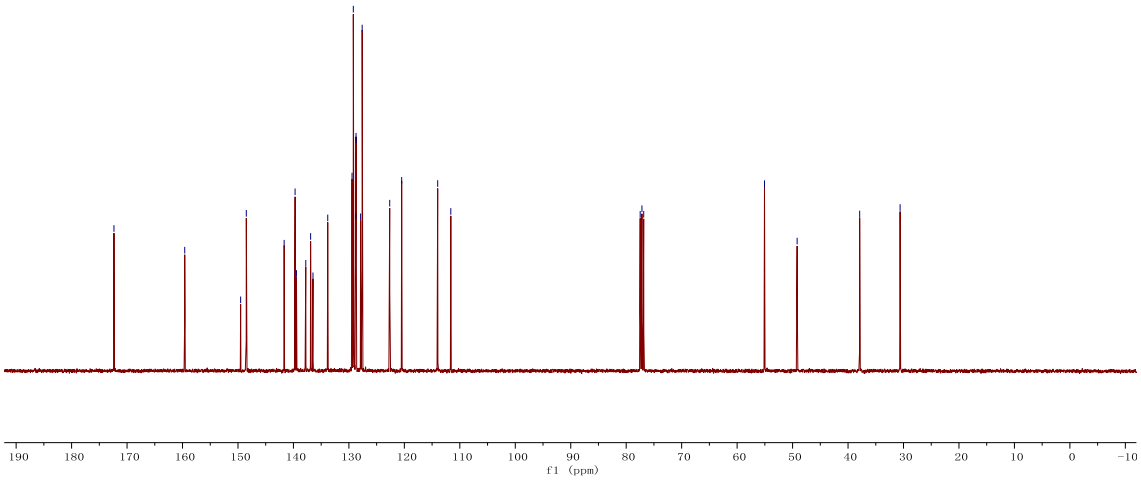

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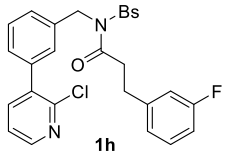

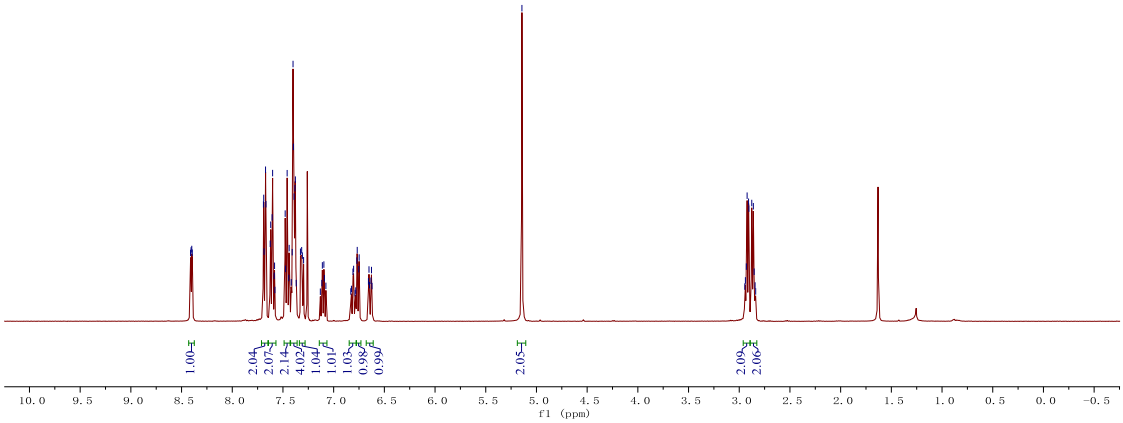

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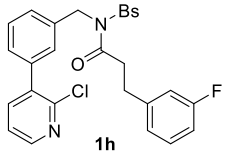

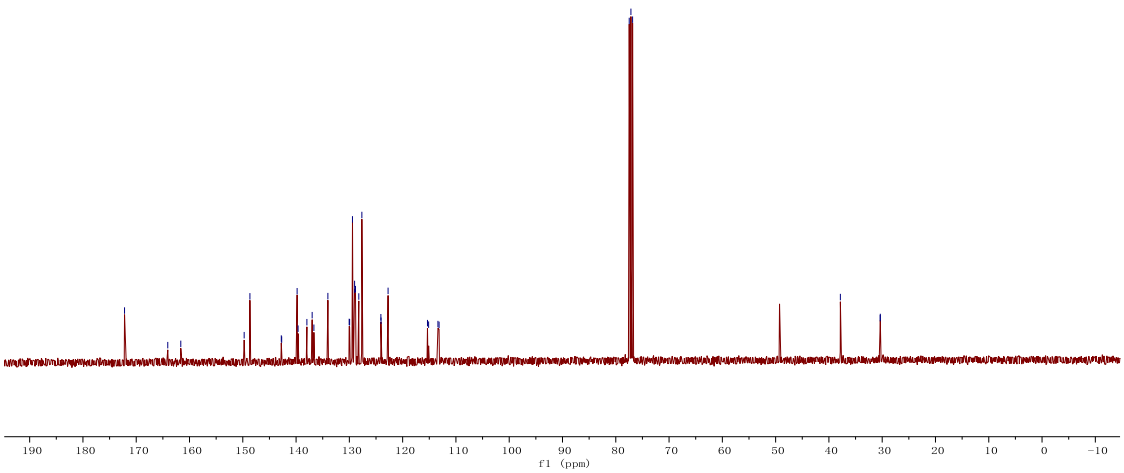

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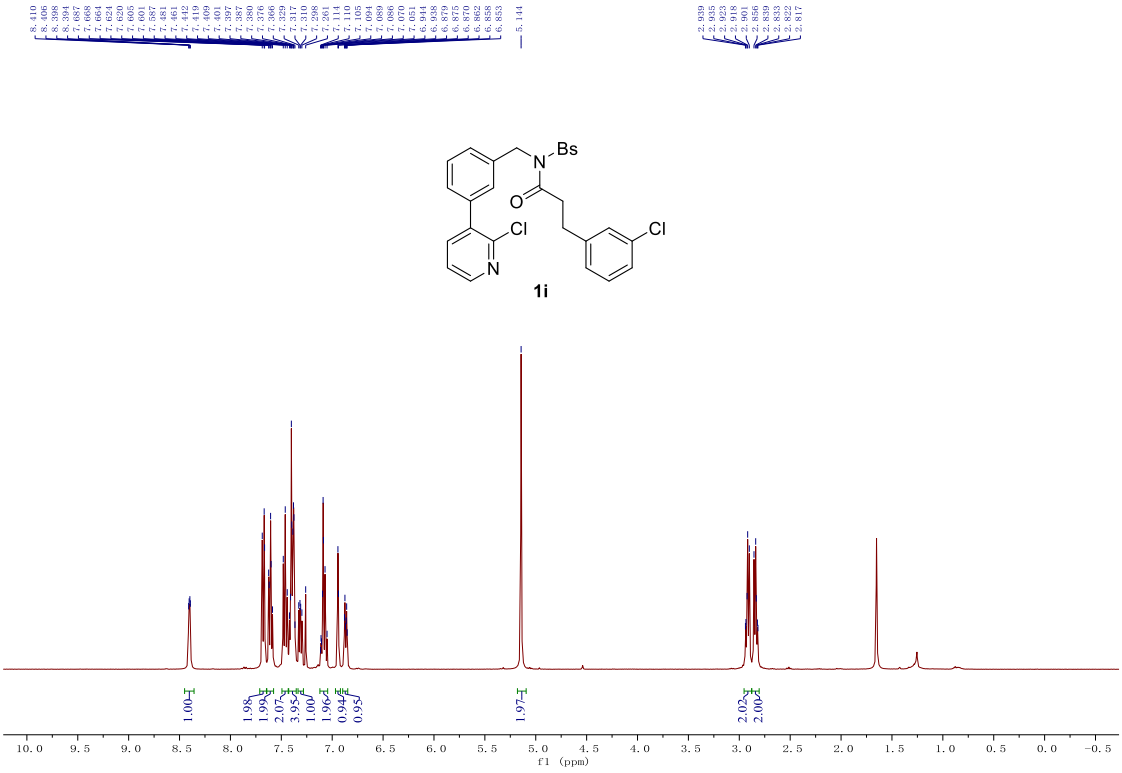

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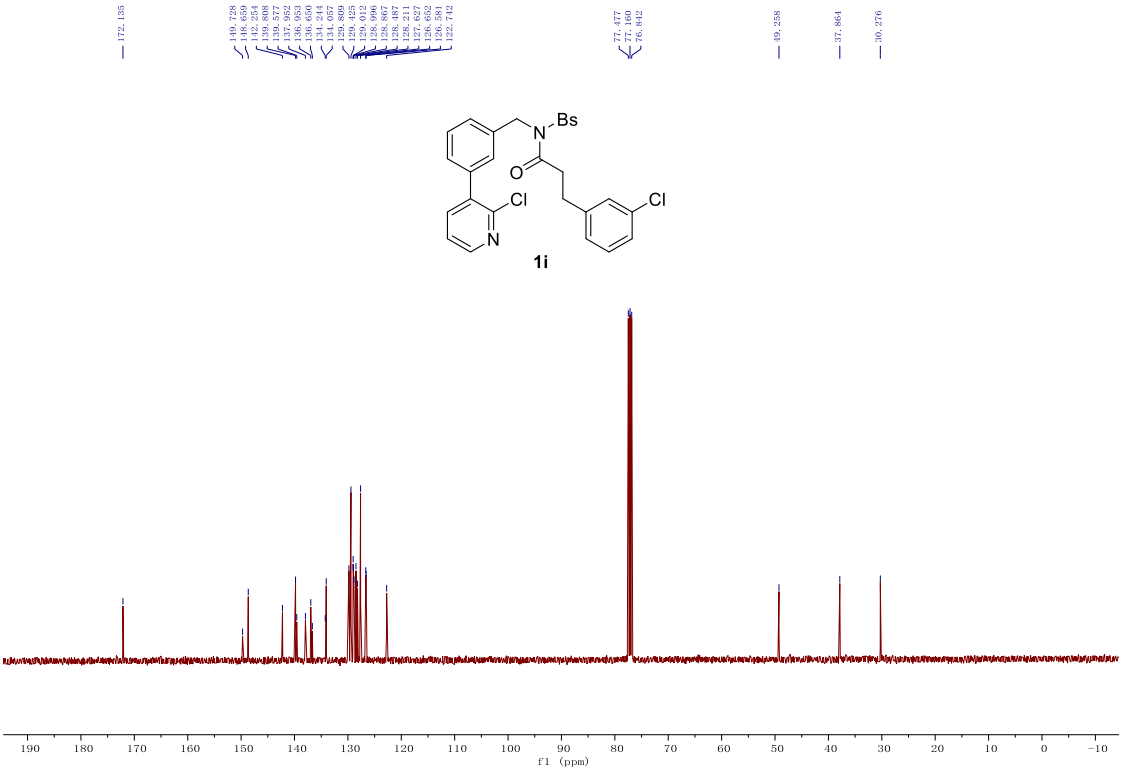

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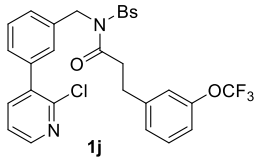

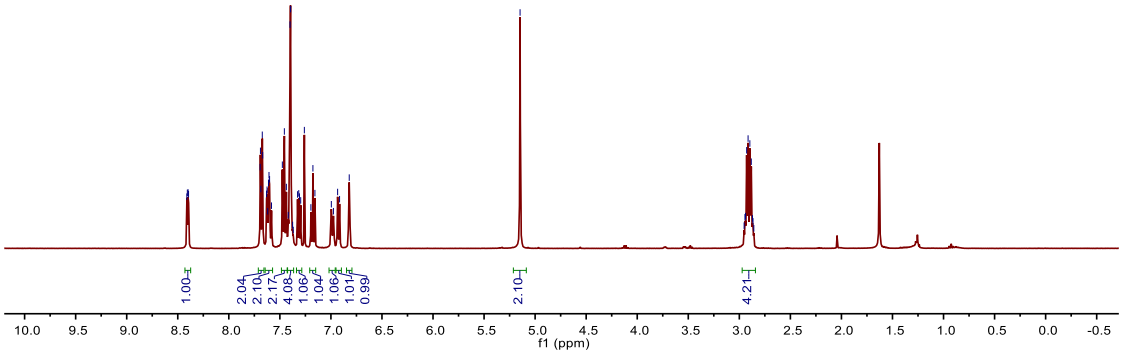

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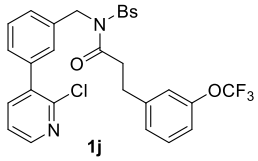

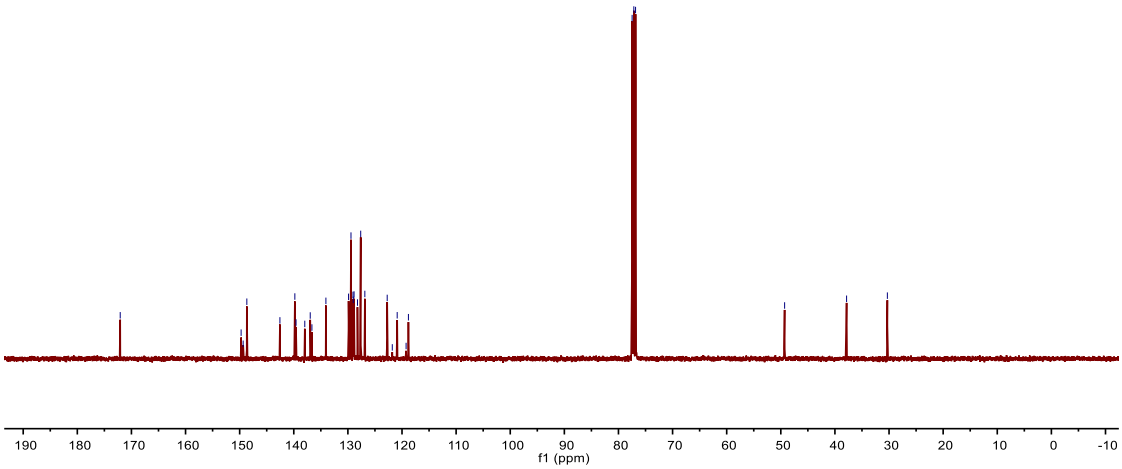

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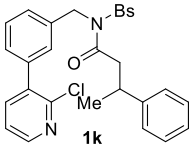

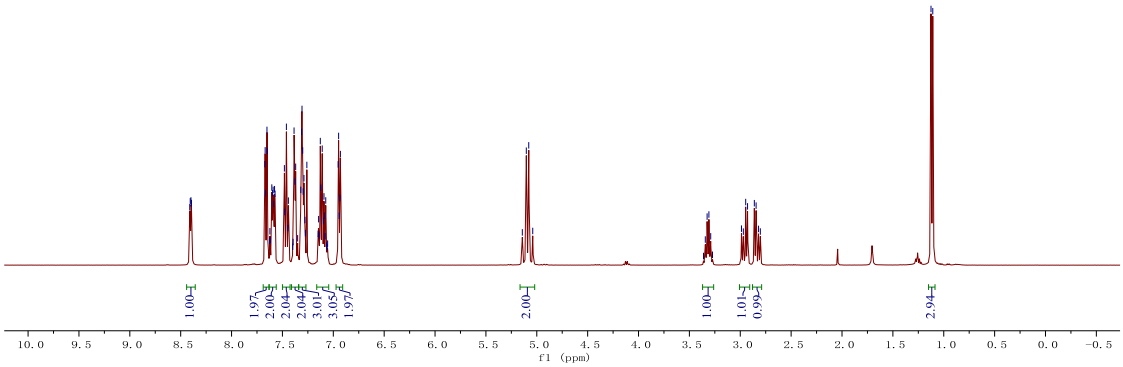

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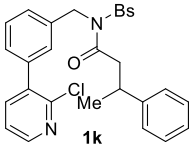

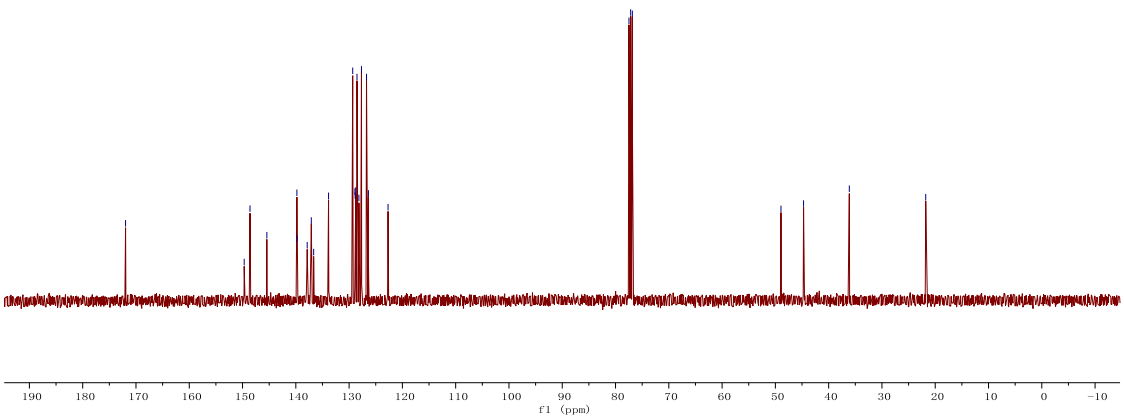

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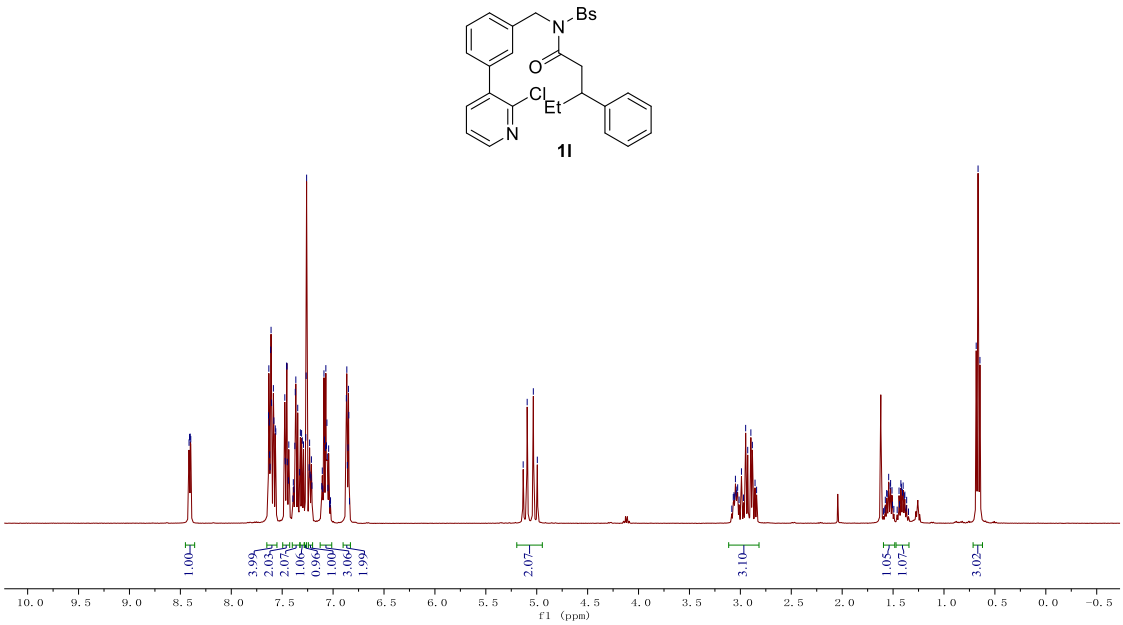

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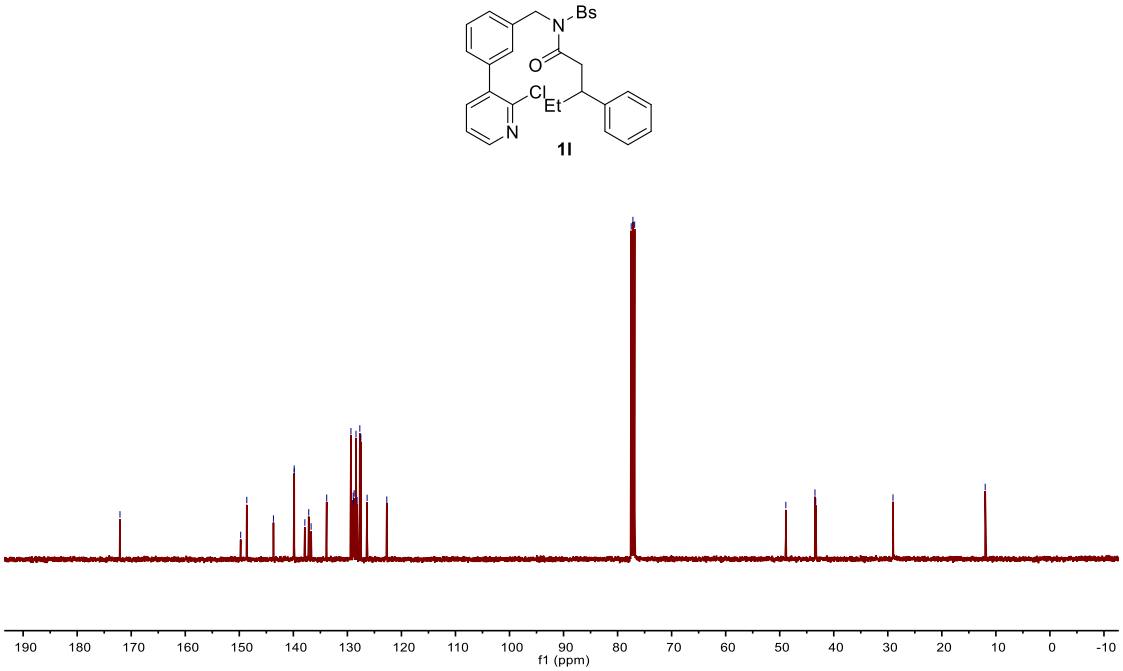

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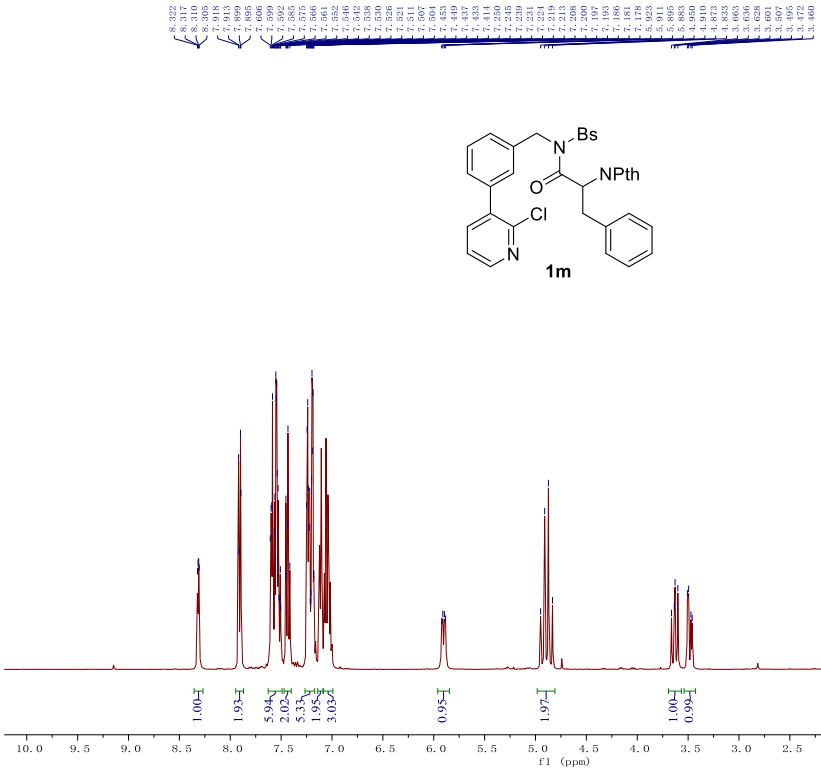

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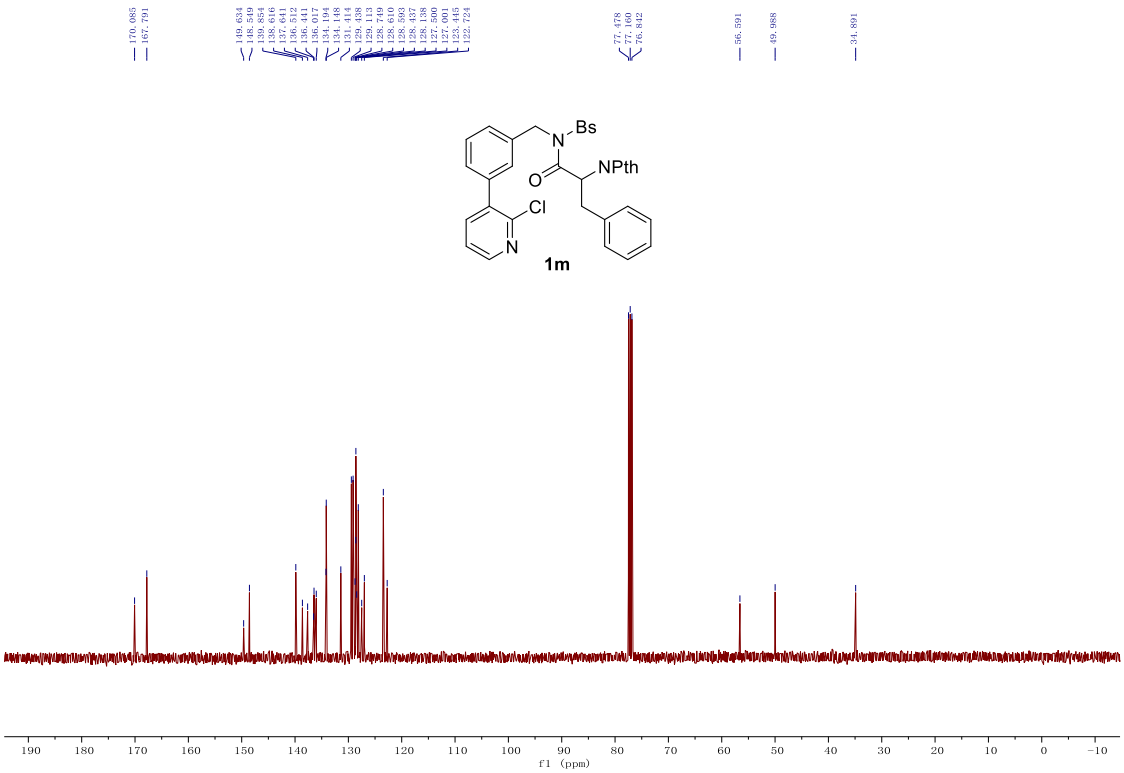

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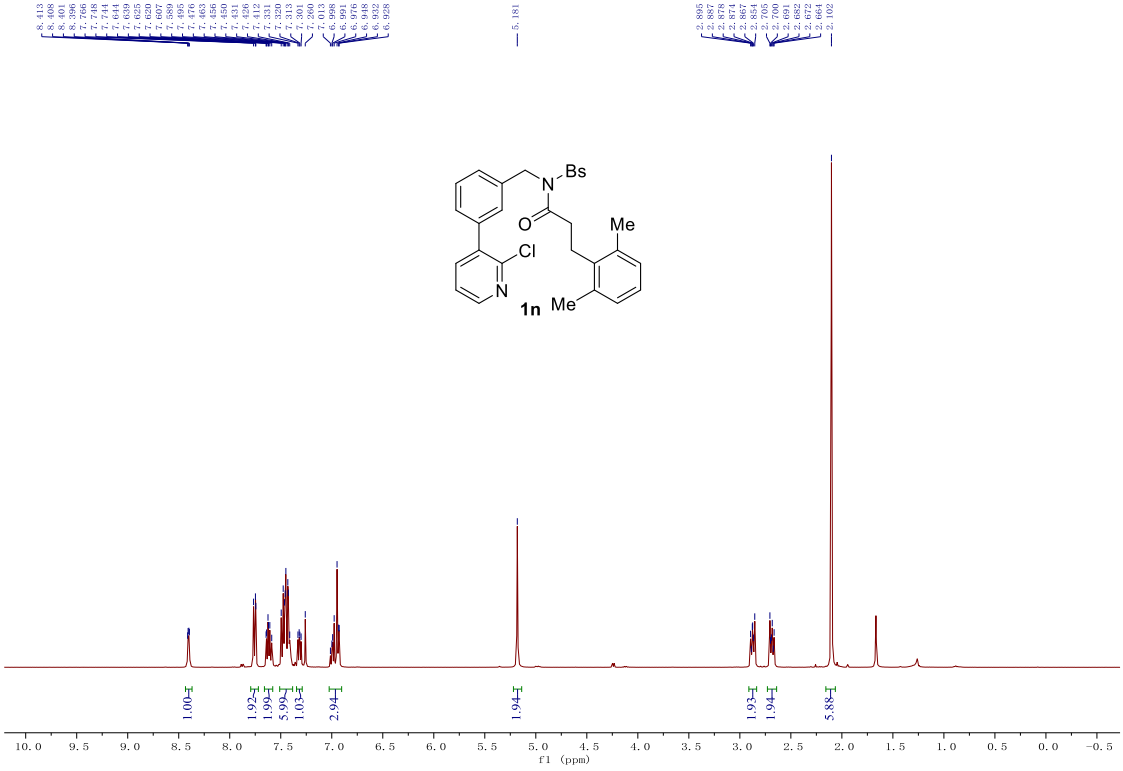

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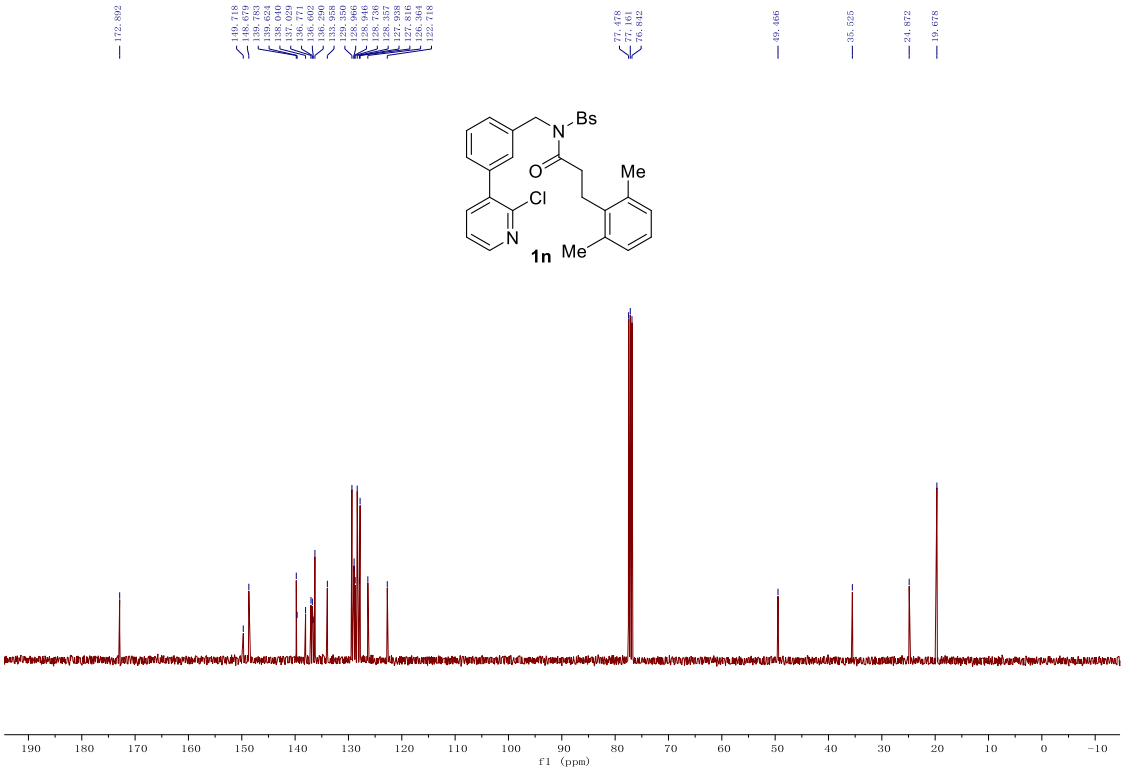

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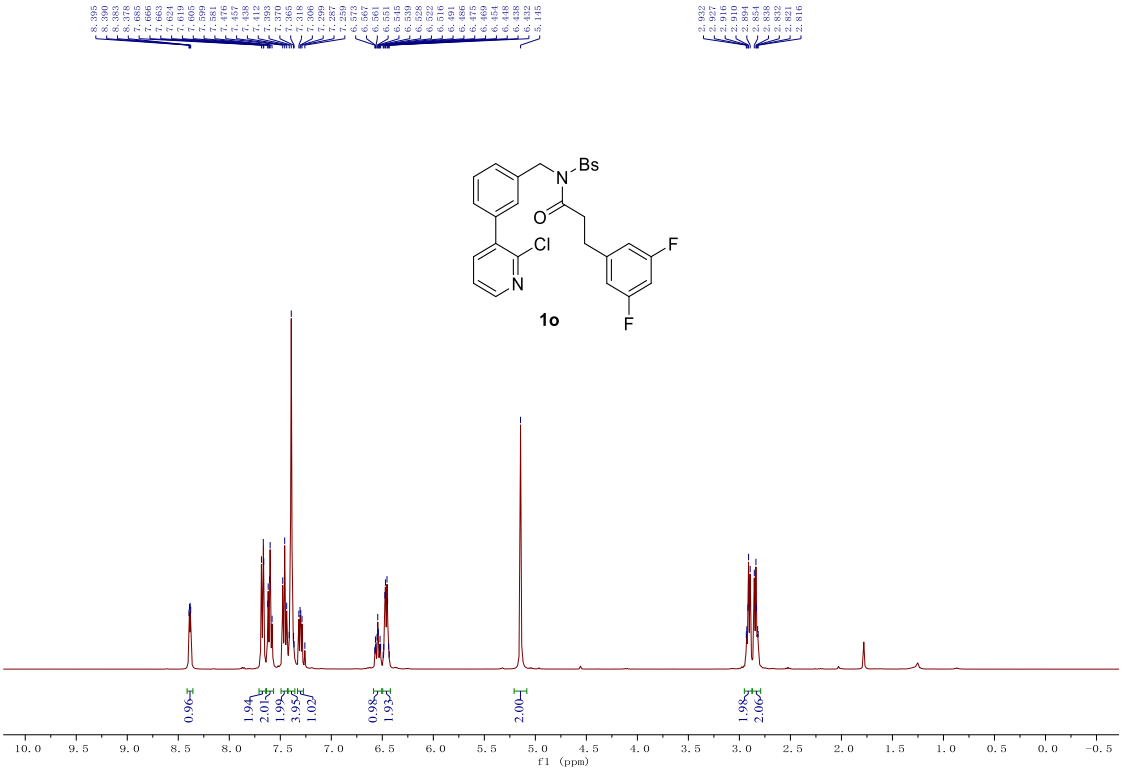

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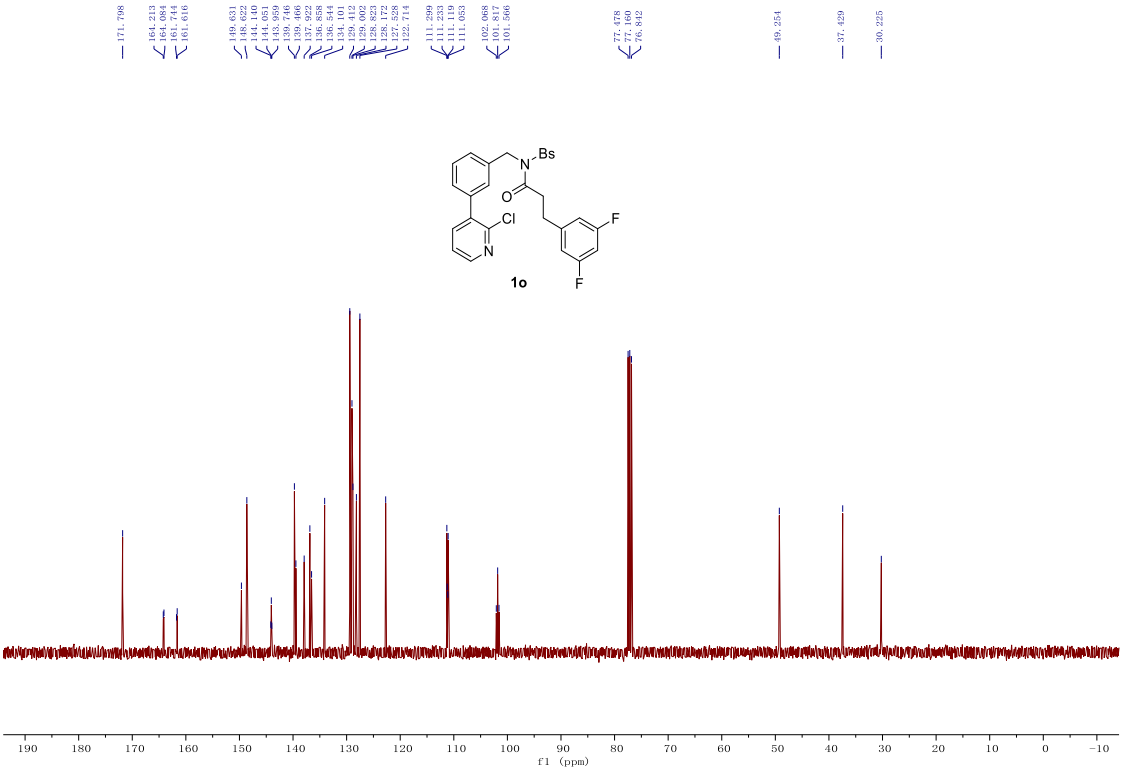

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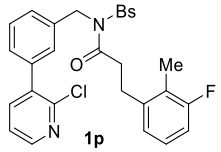

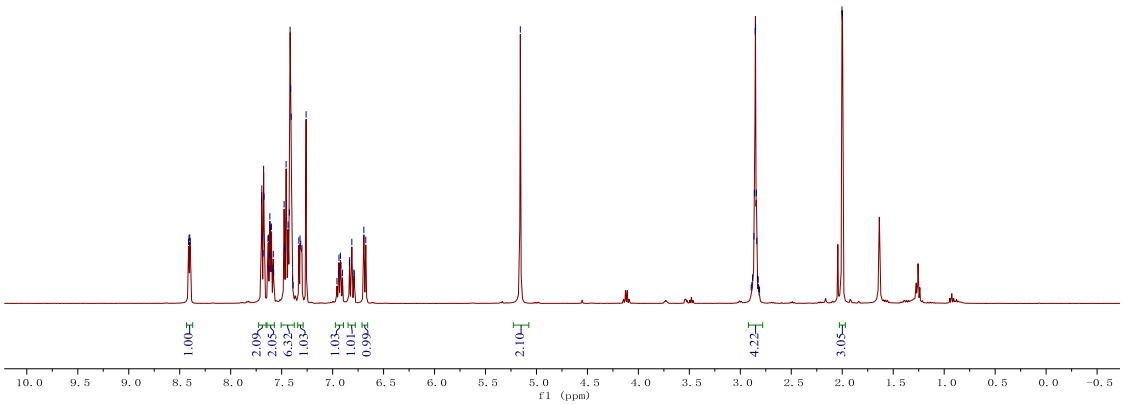

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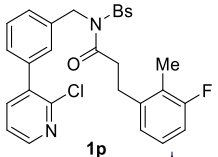

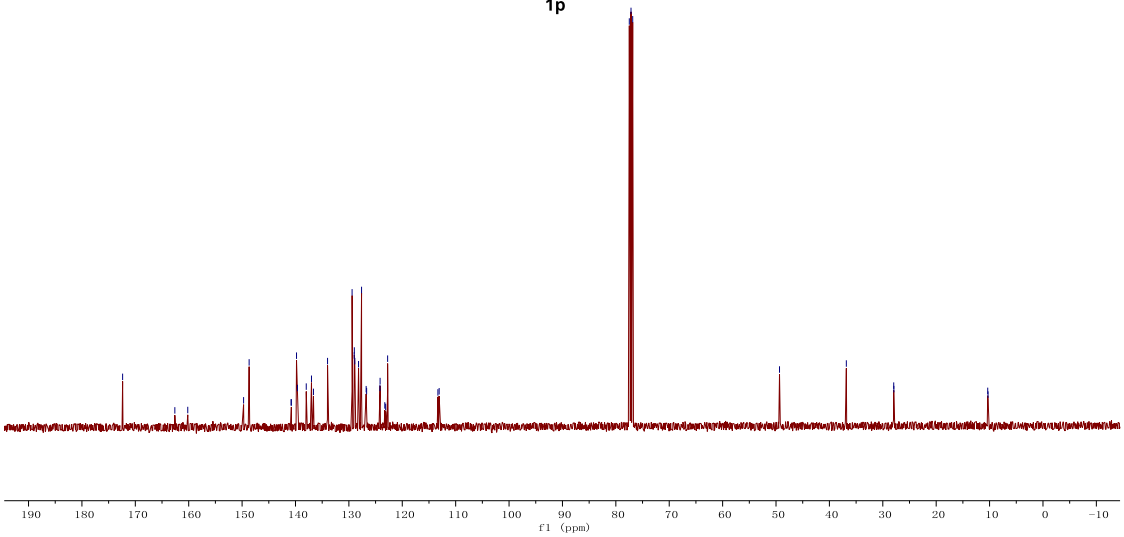

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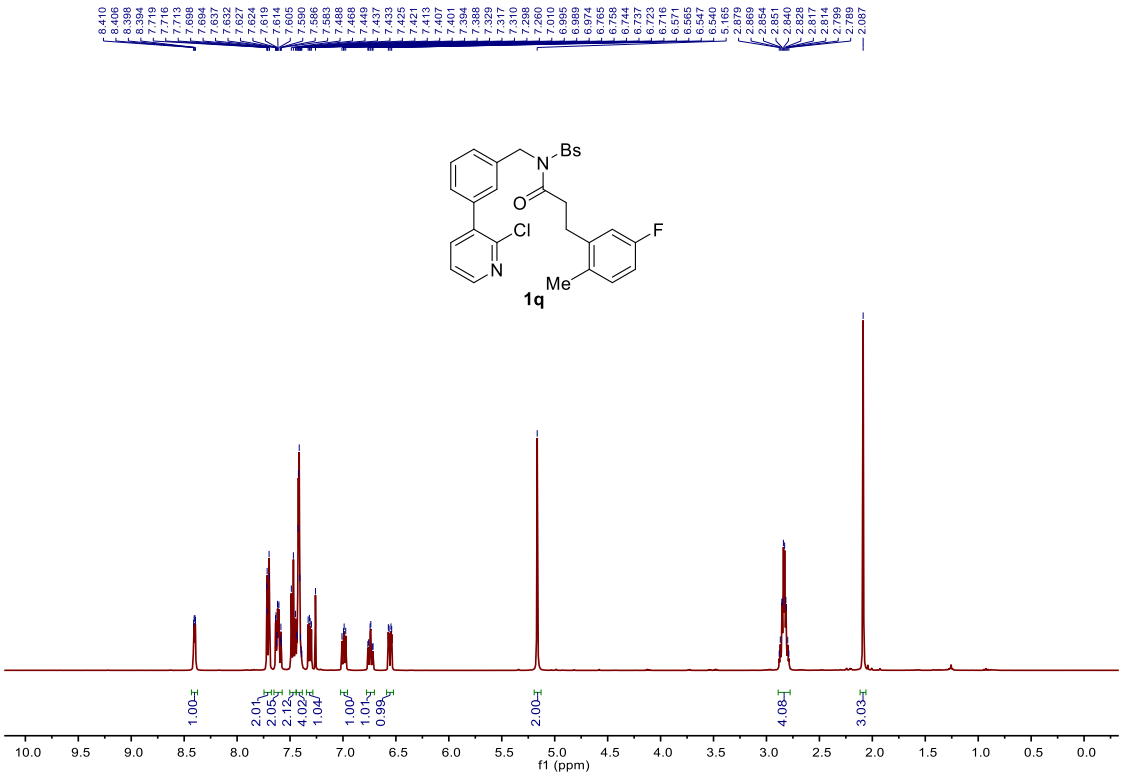

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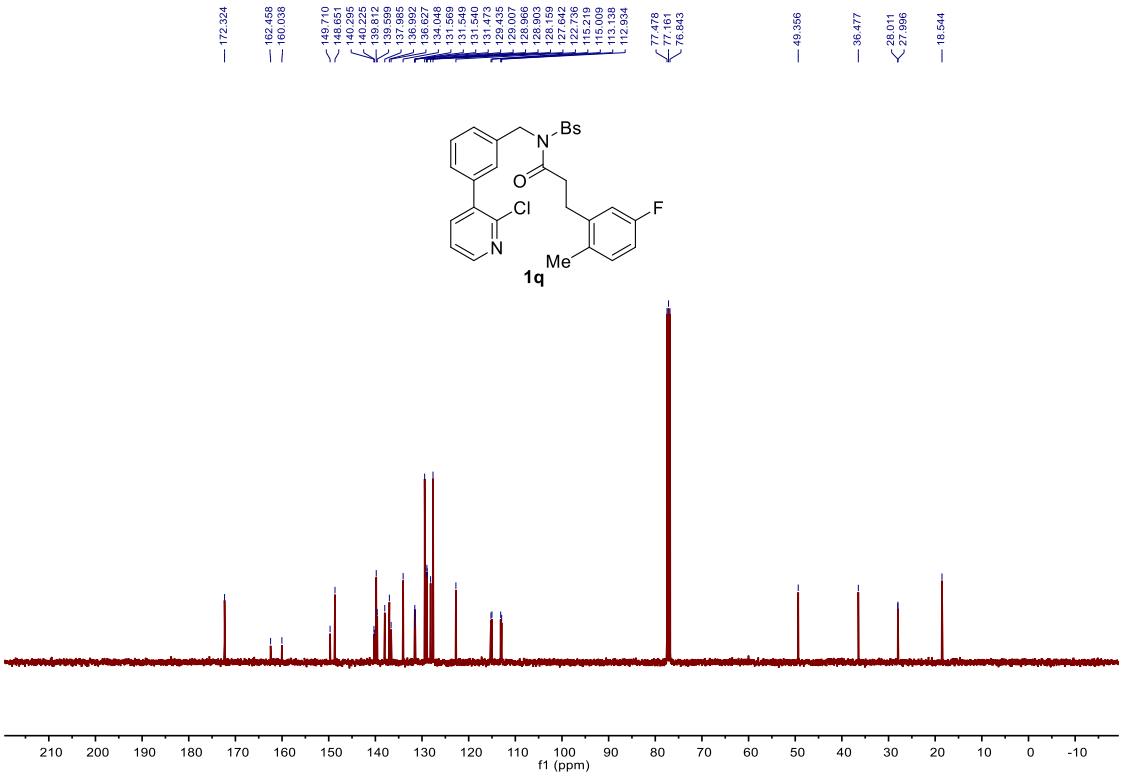

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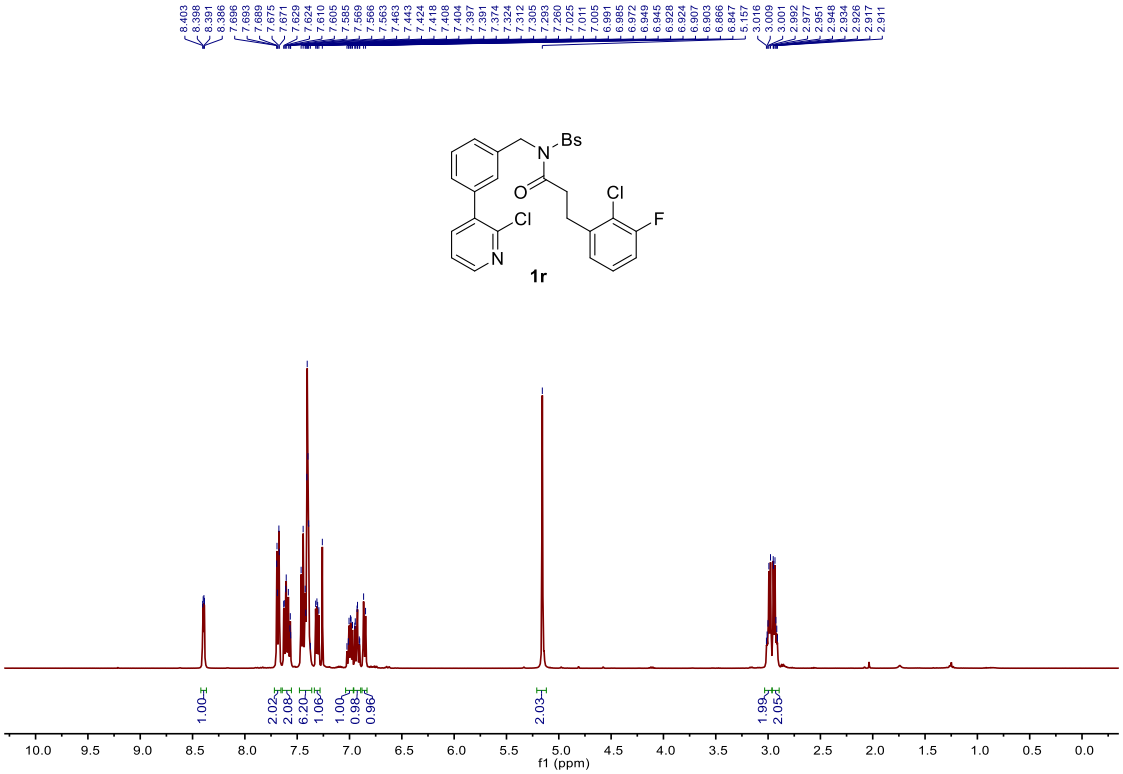

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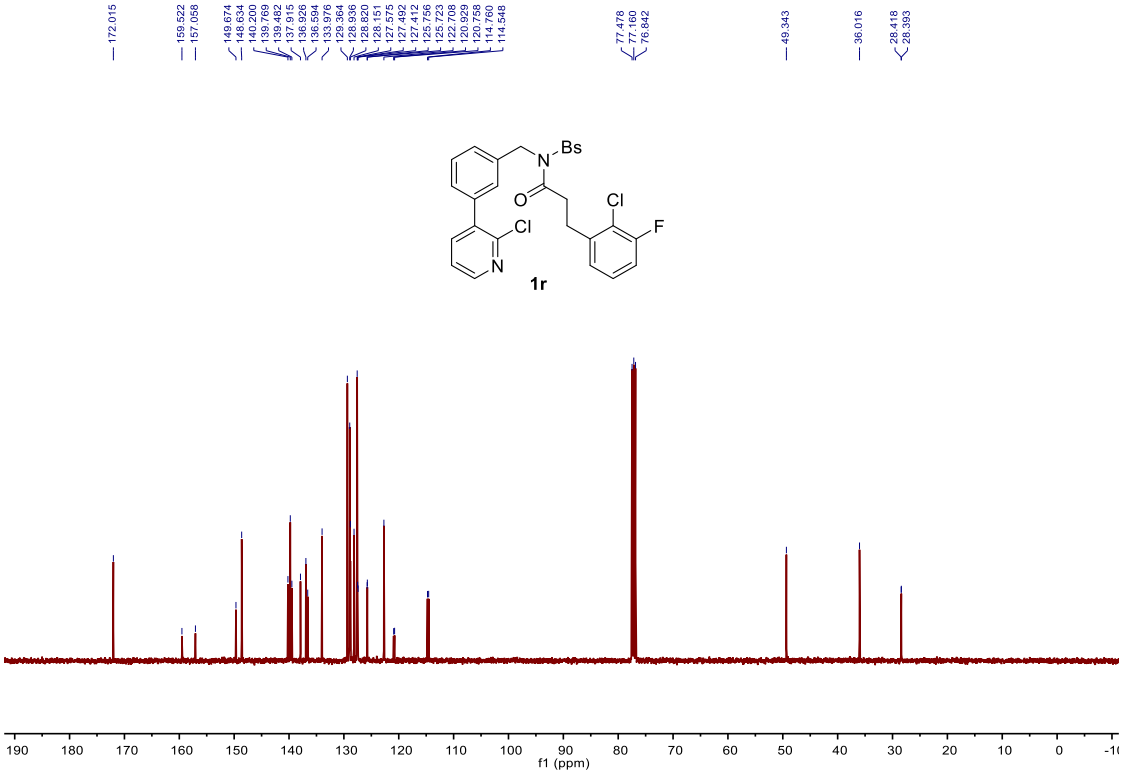

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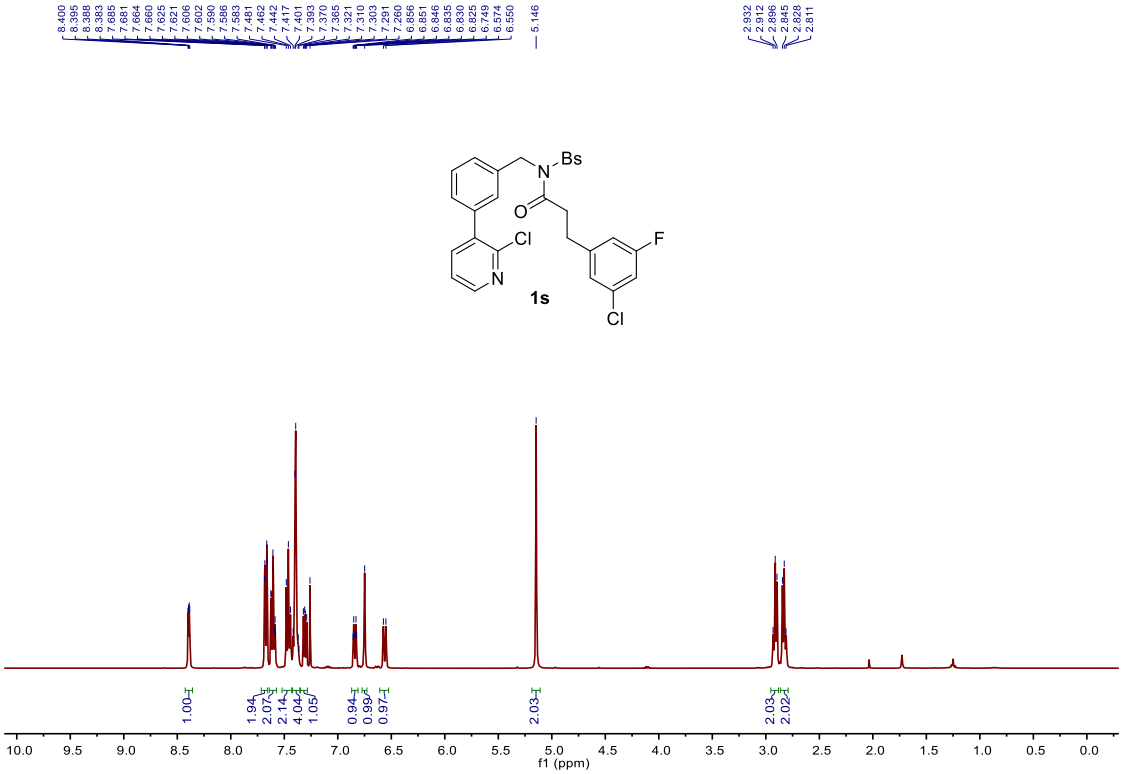

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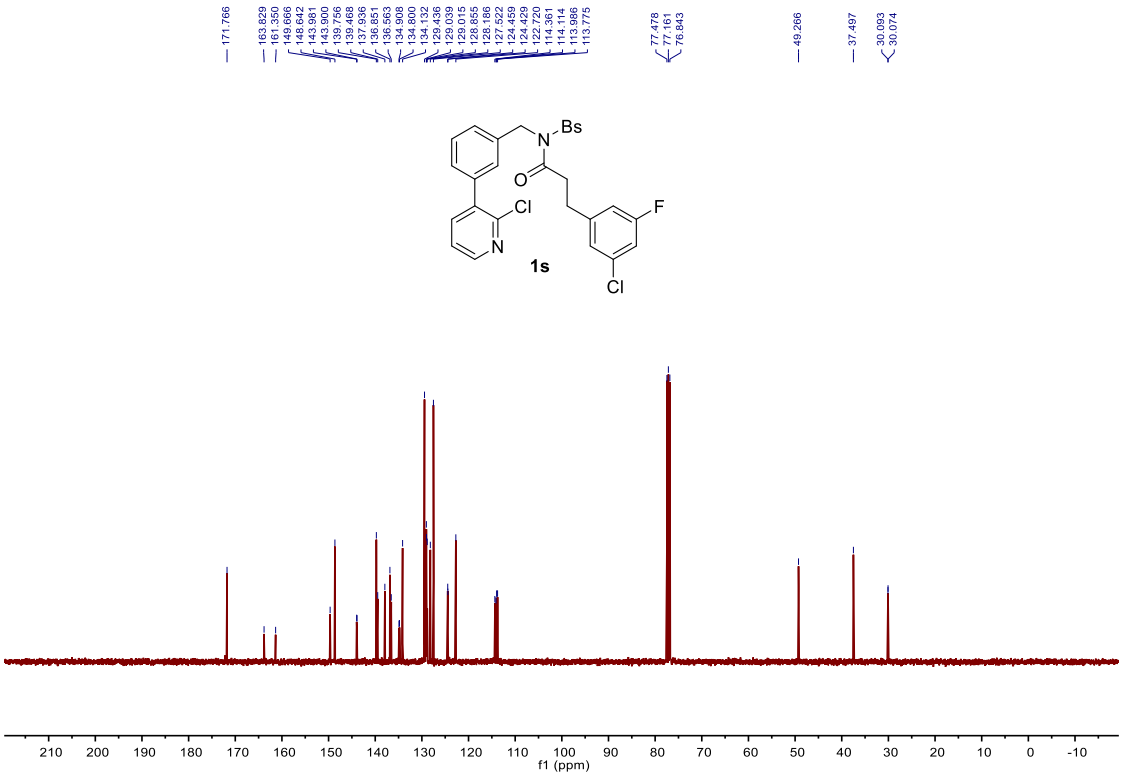

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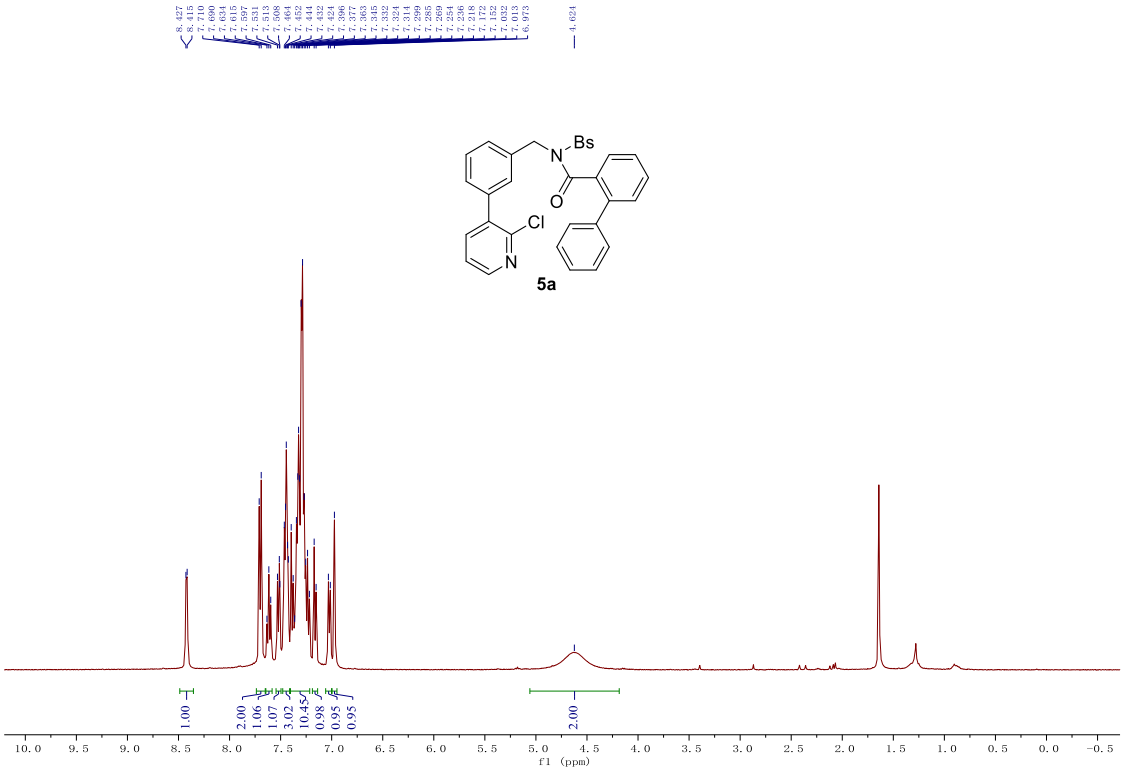

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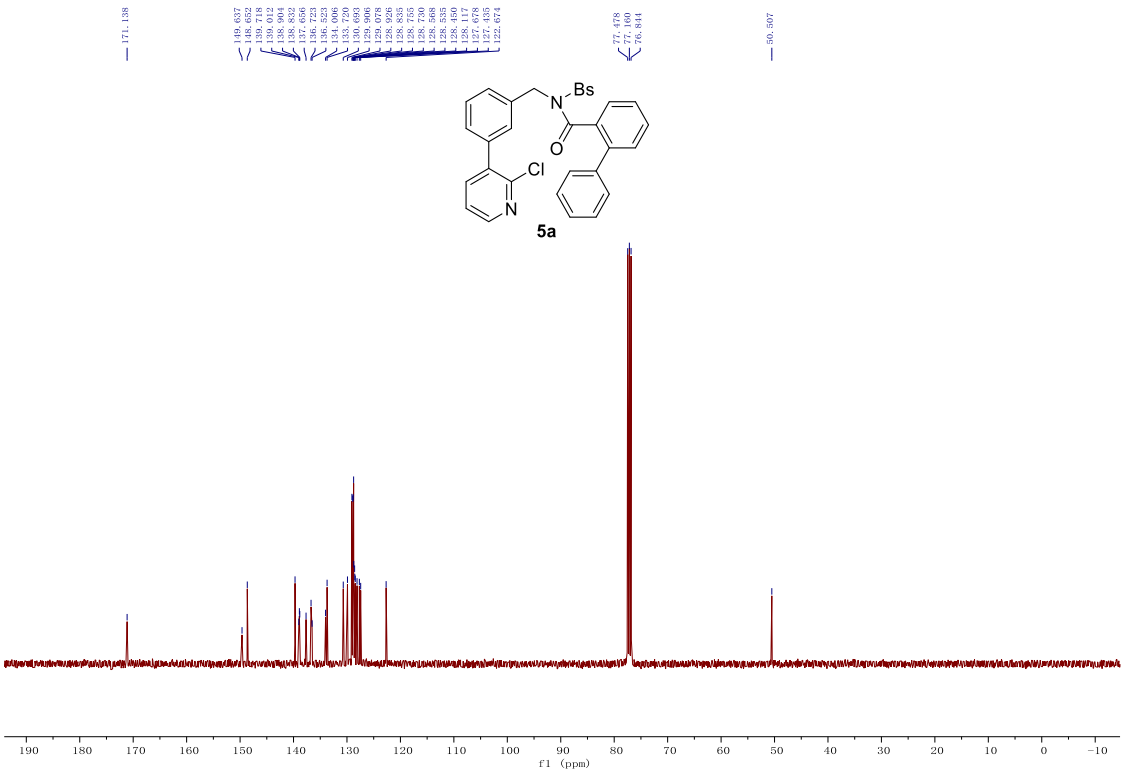

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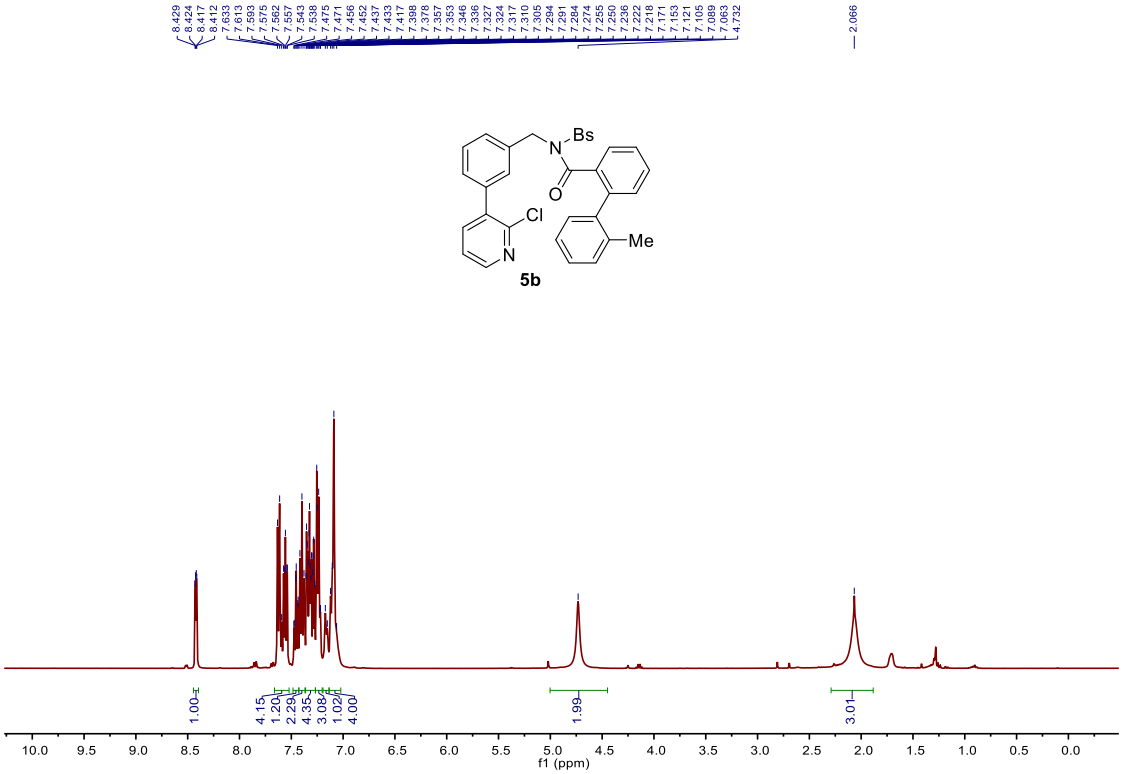

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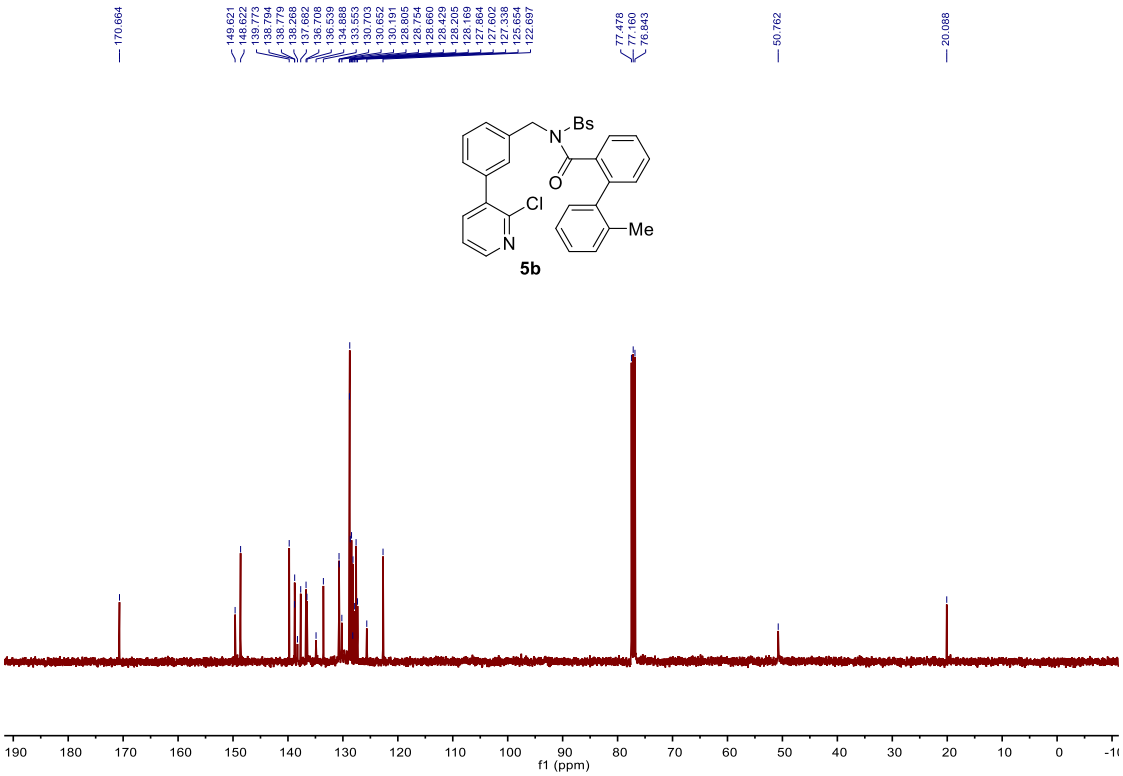

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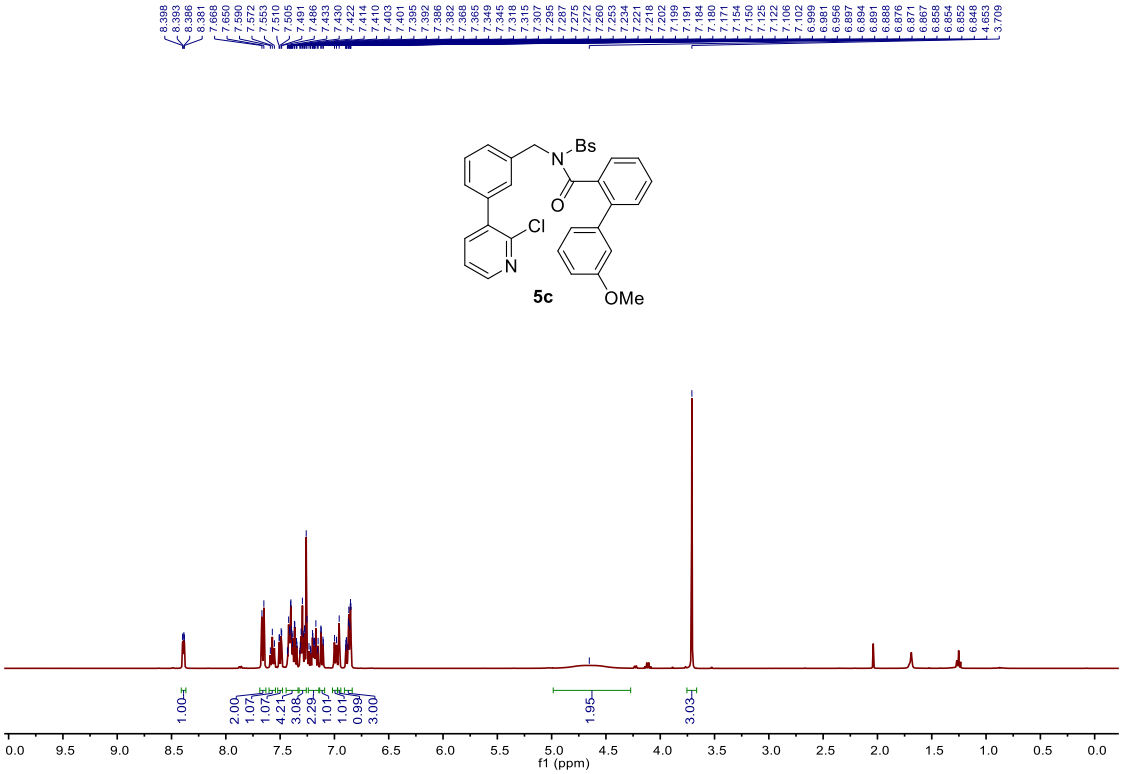

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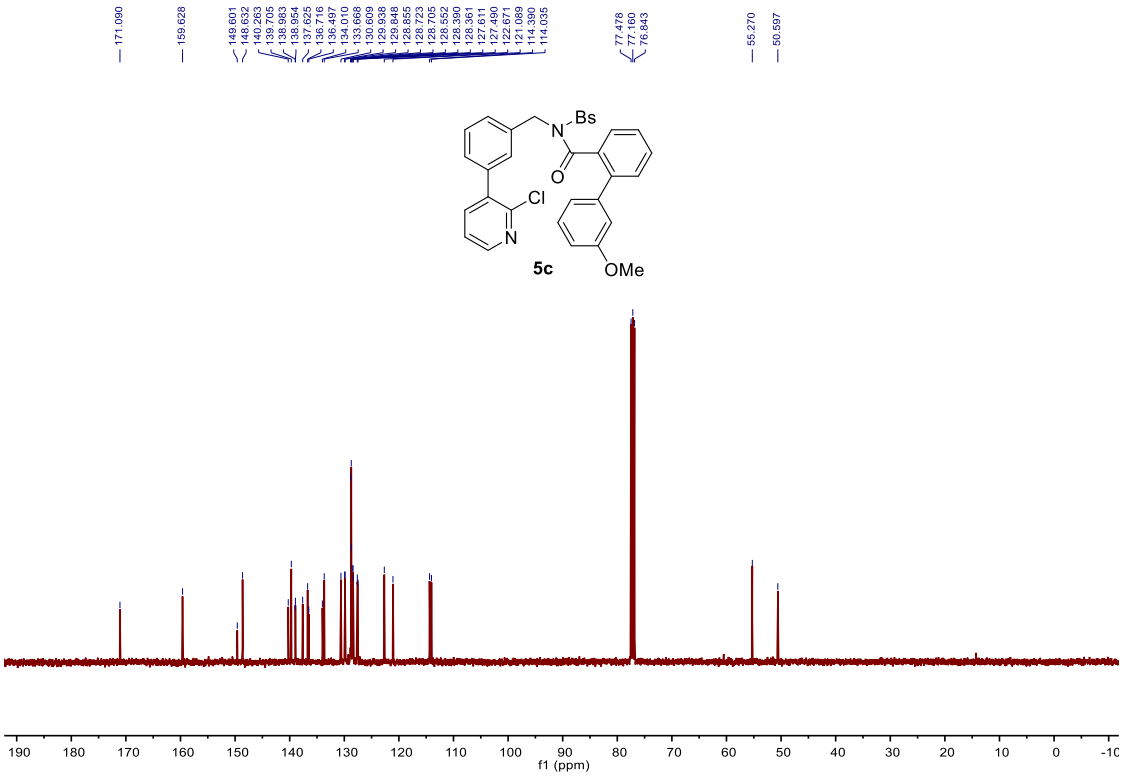

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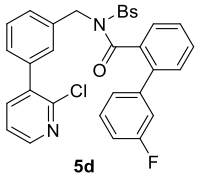

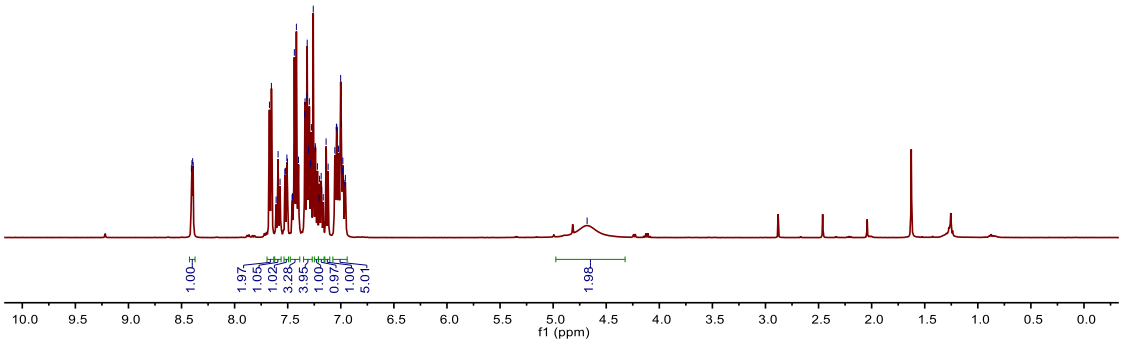

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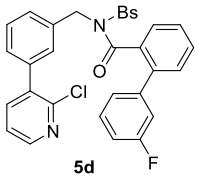

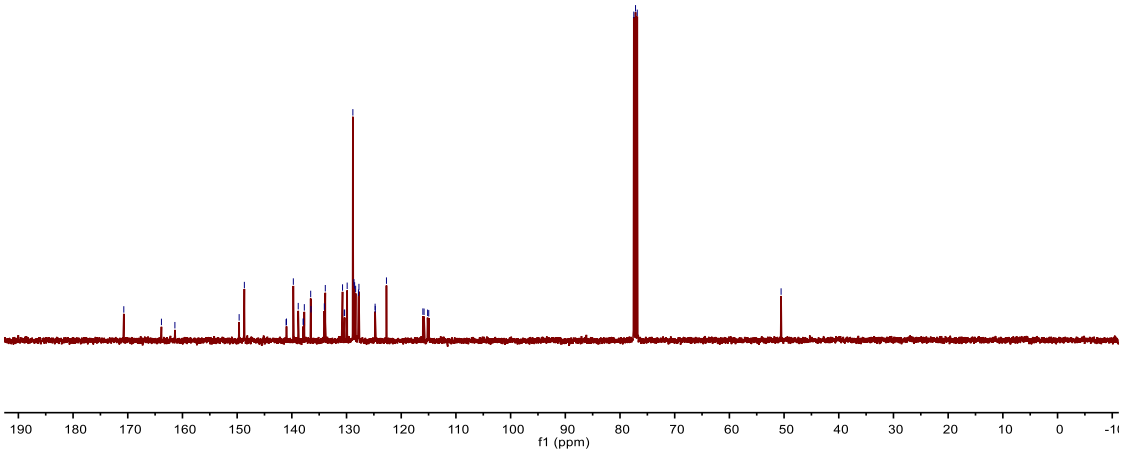

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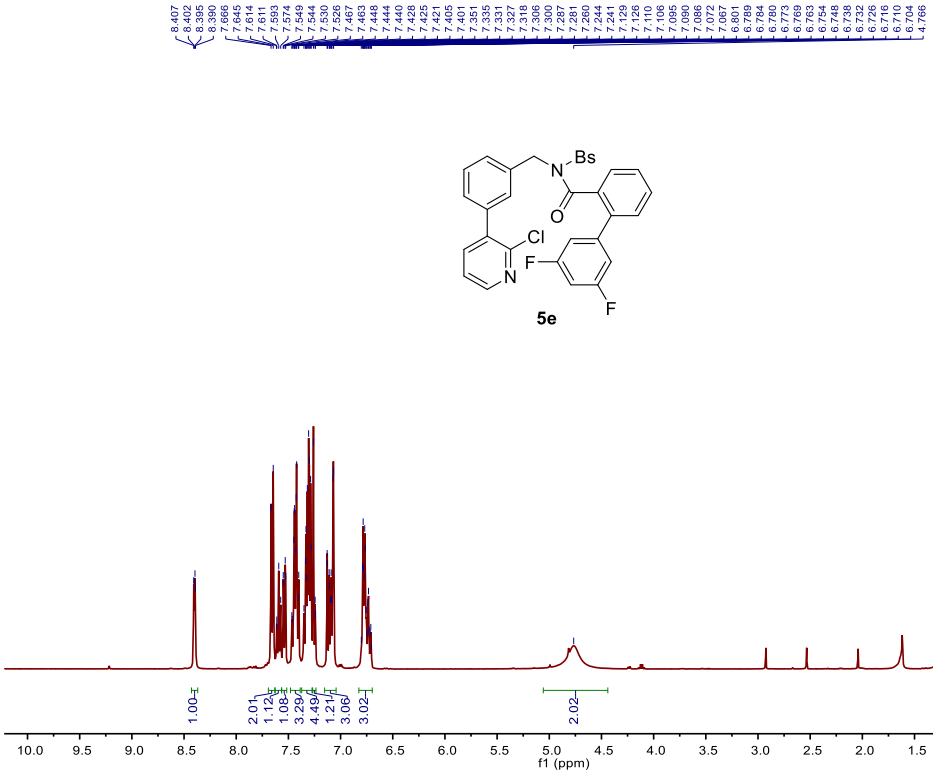

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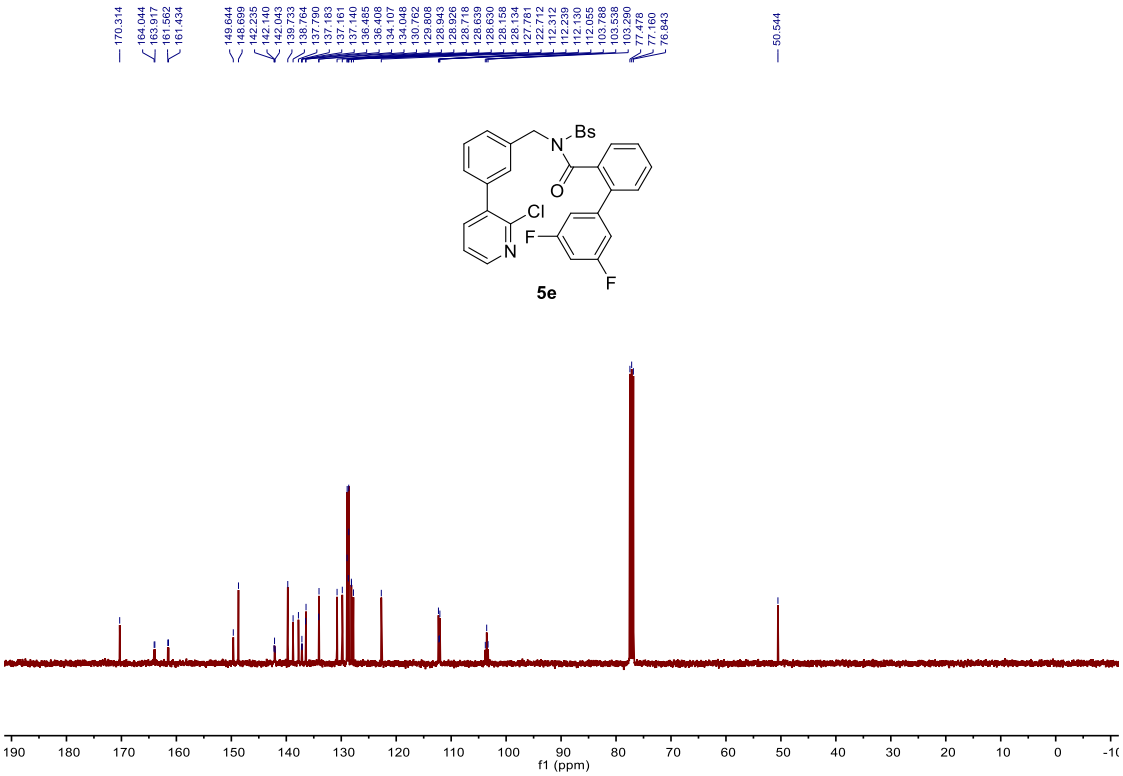
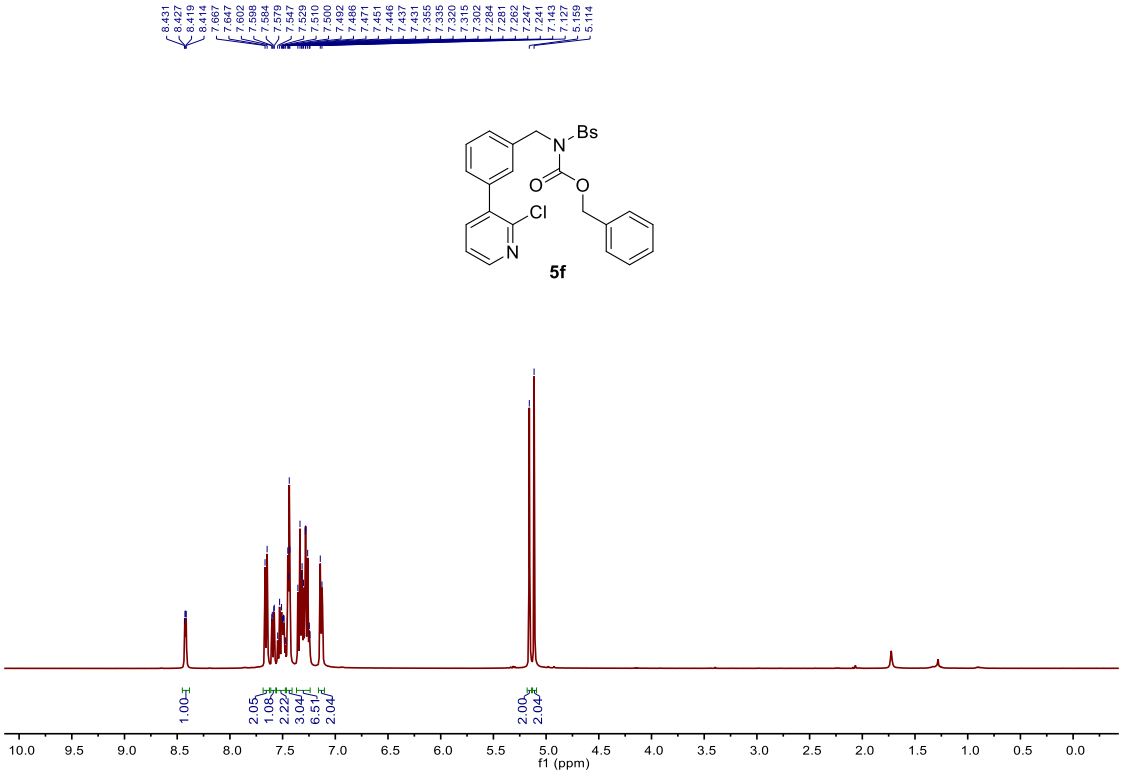
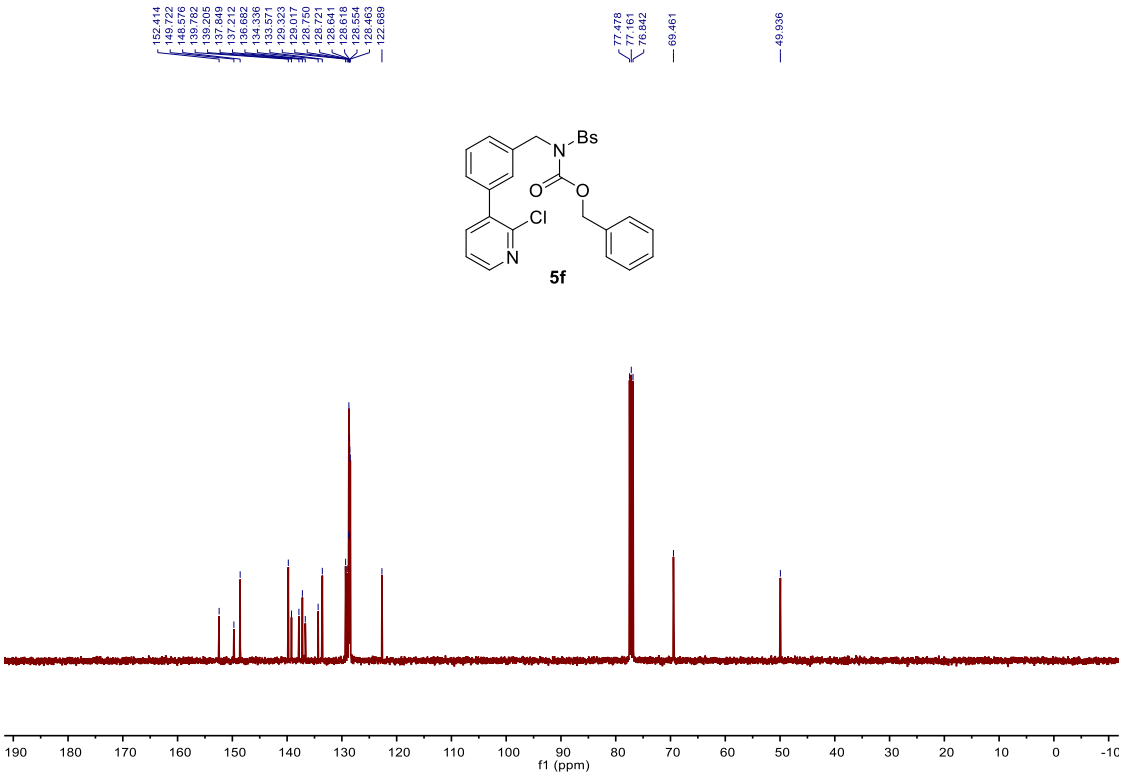


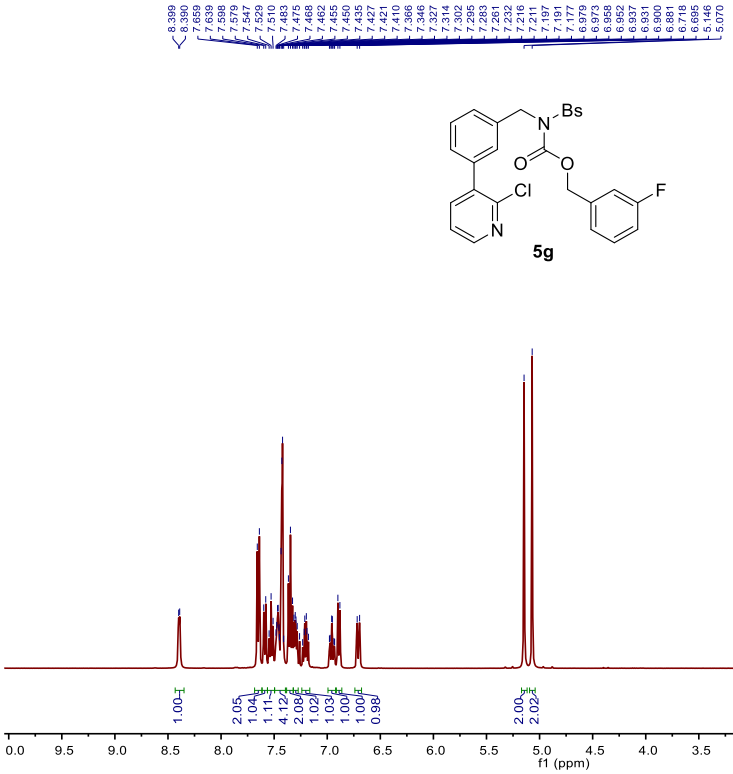
^{1}H NMR (400 MHz, Chloroform-*d*)



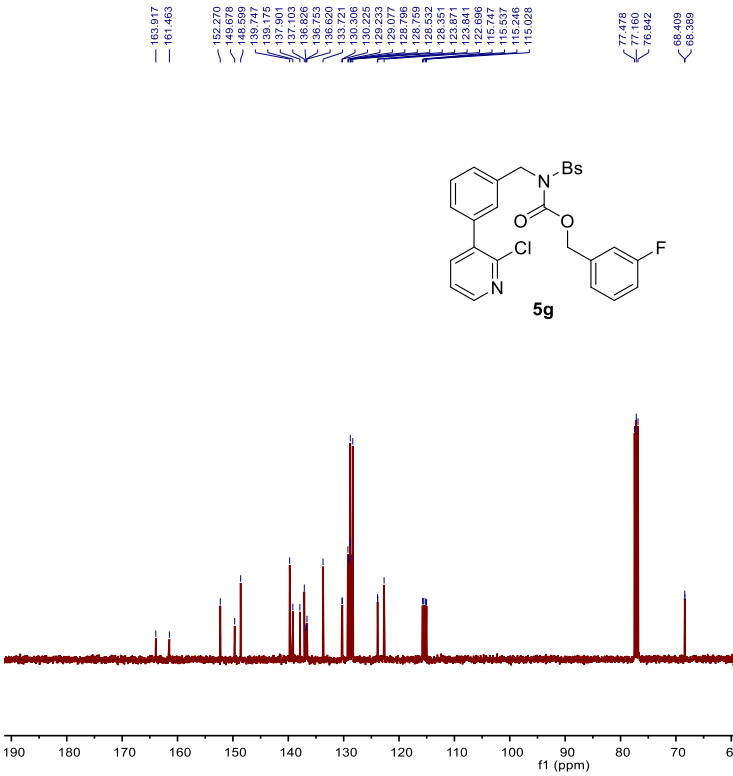
^{13}C NMR (101 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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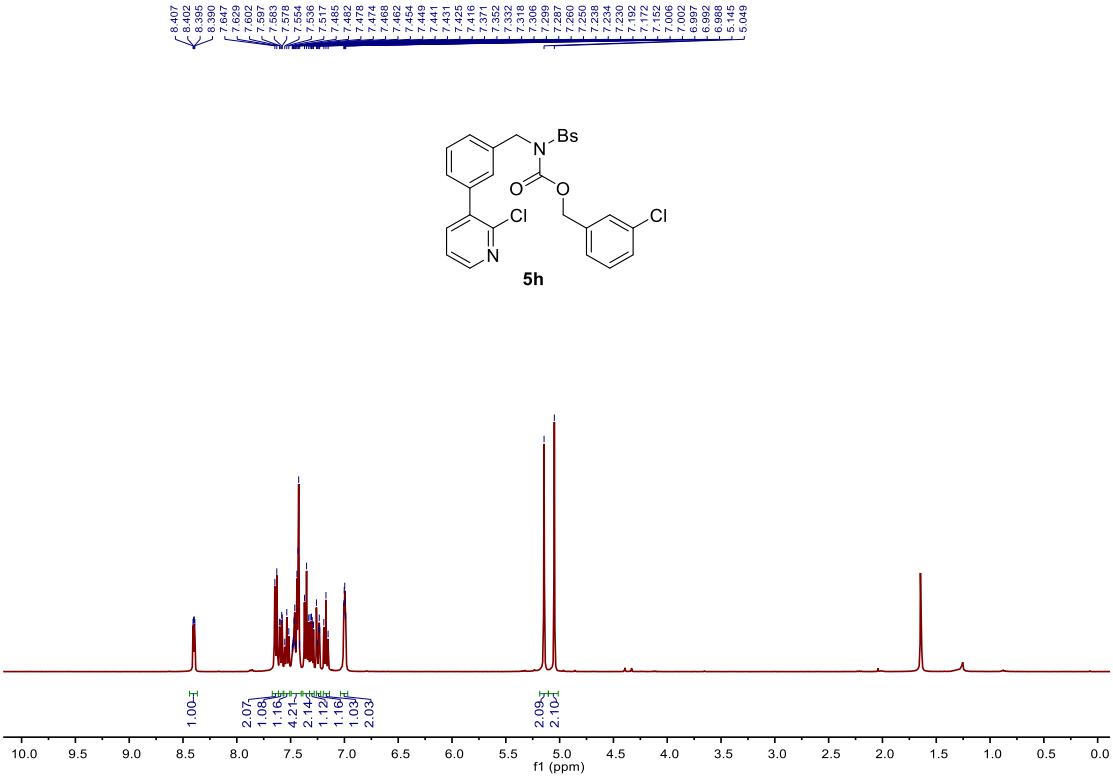

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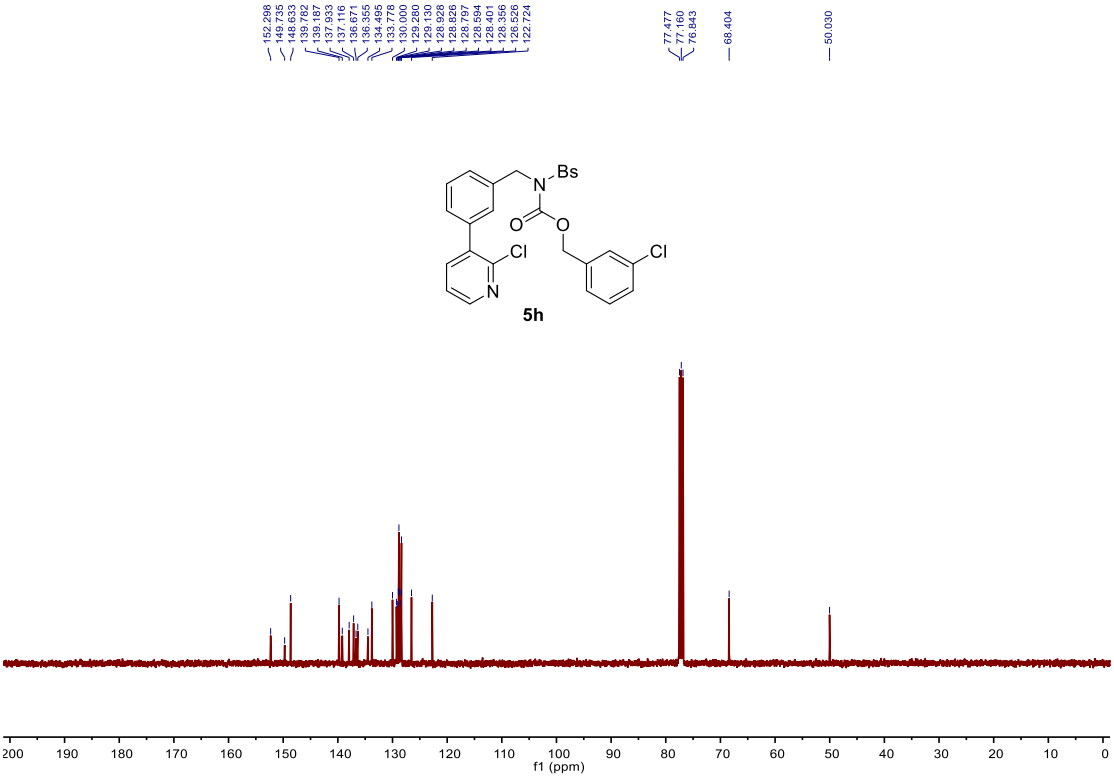

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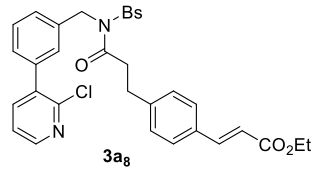
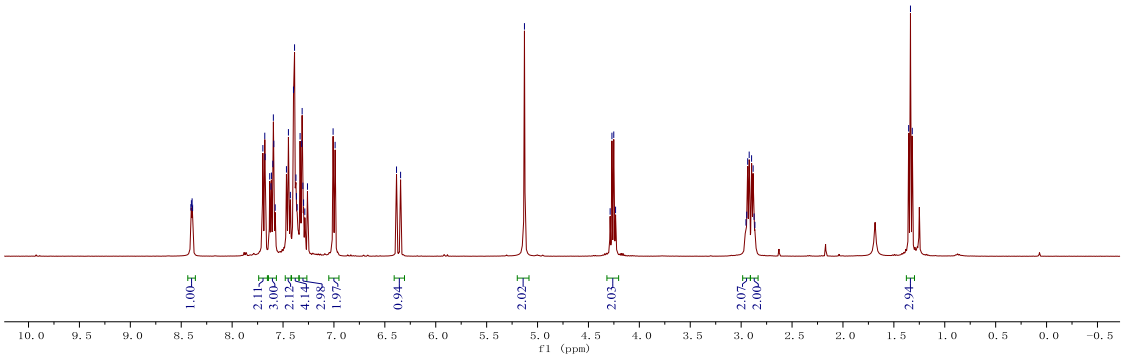


3a$_8$



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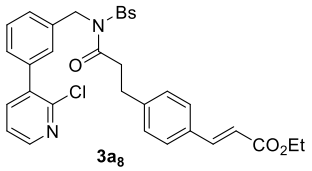

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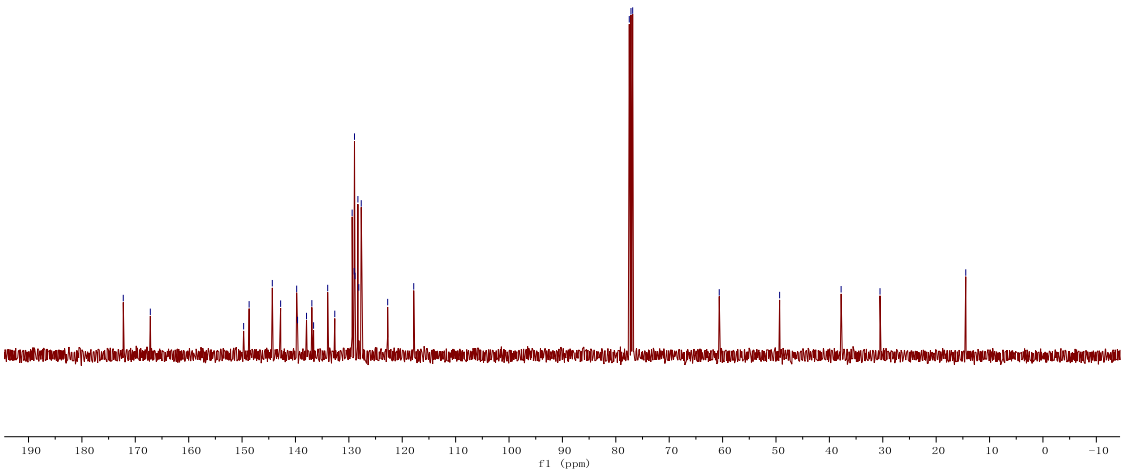

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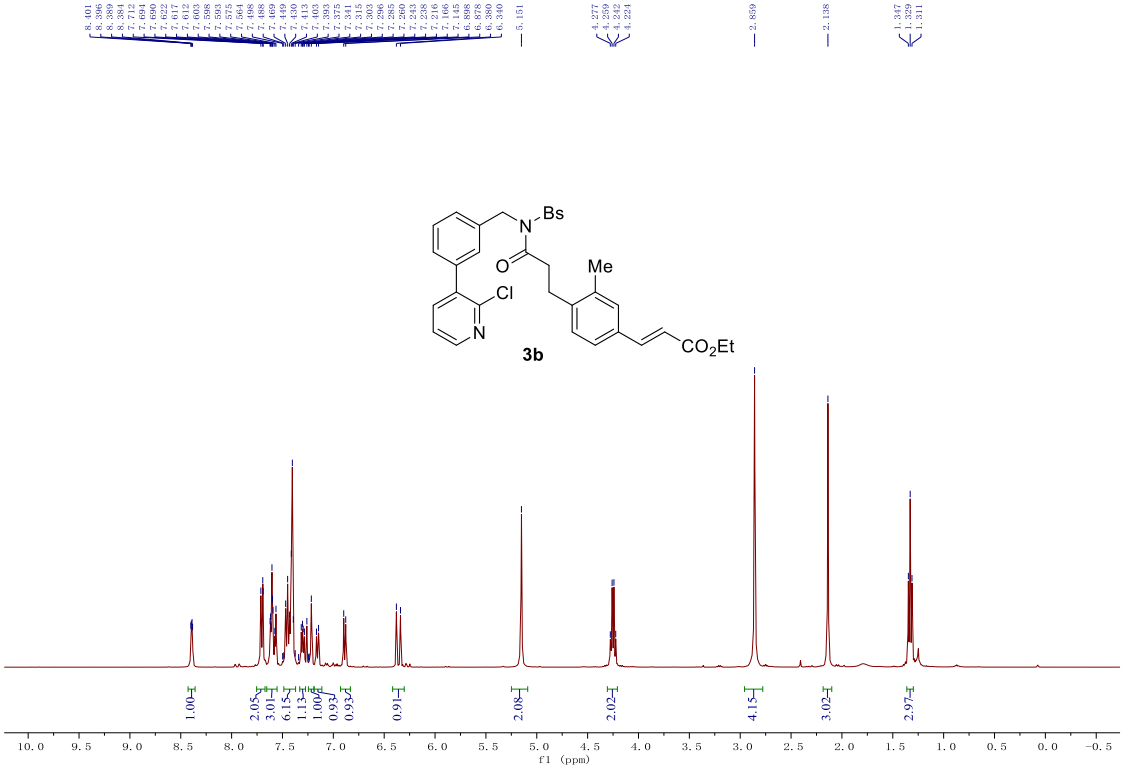

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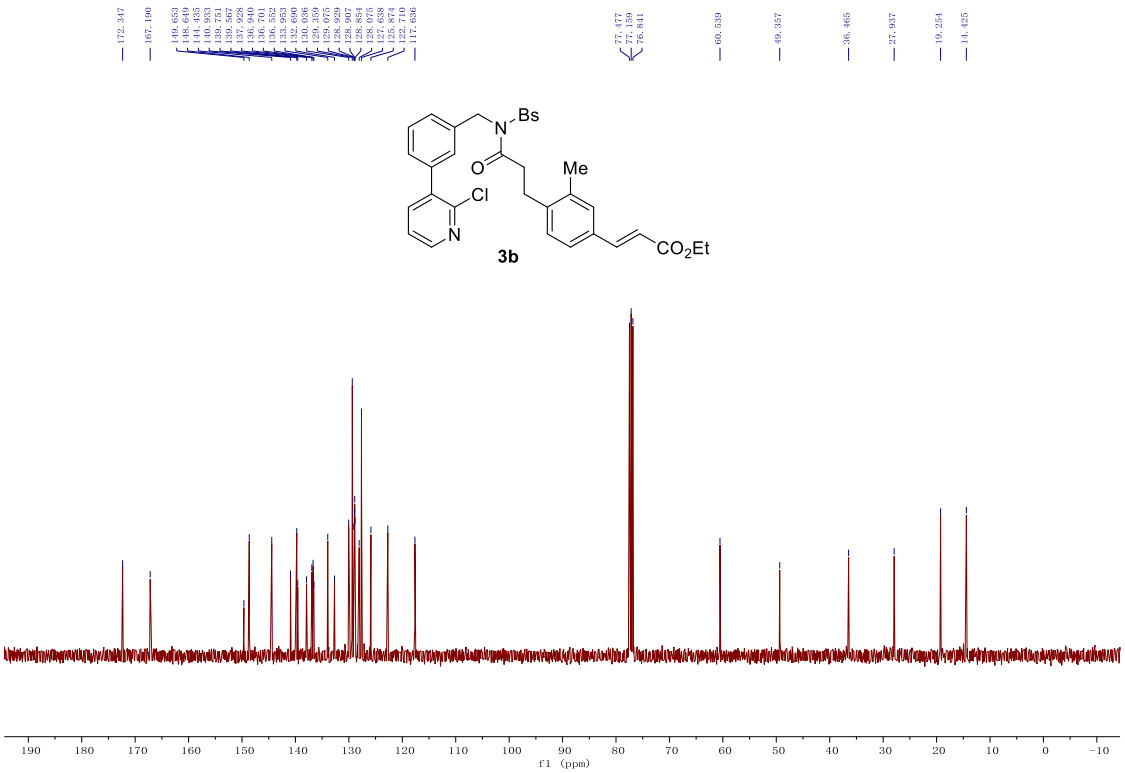

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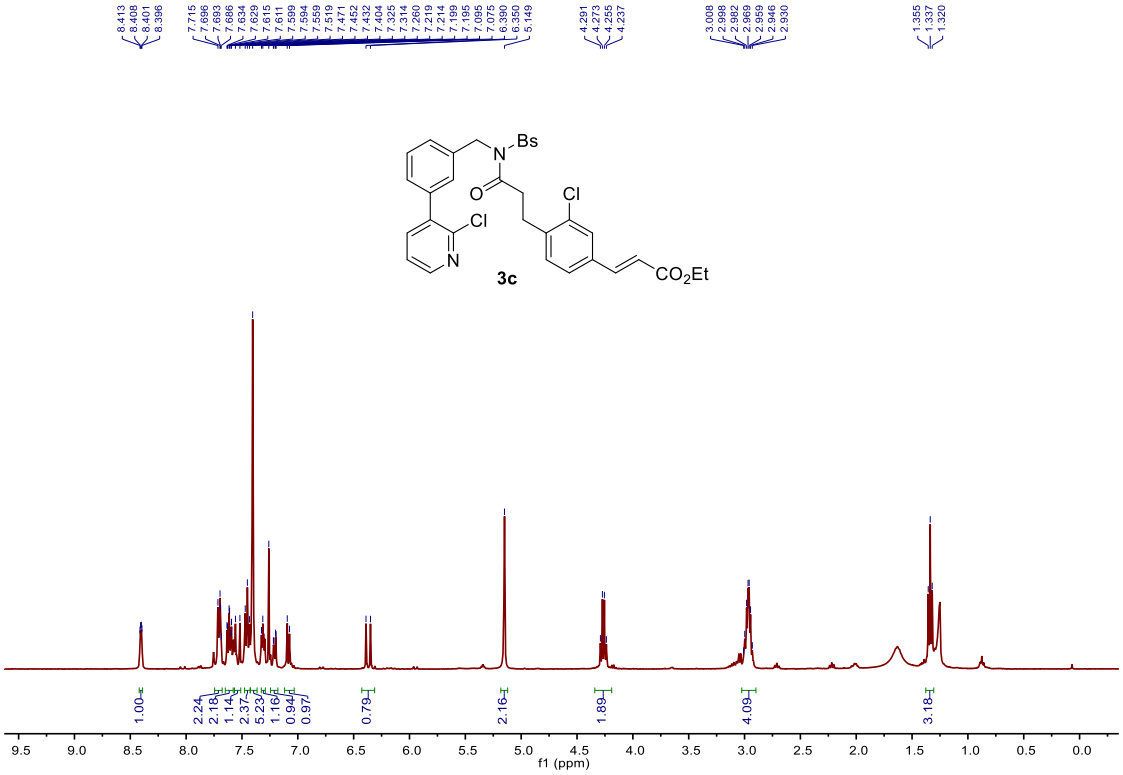

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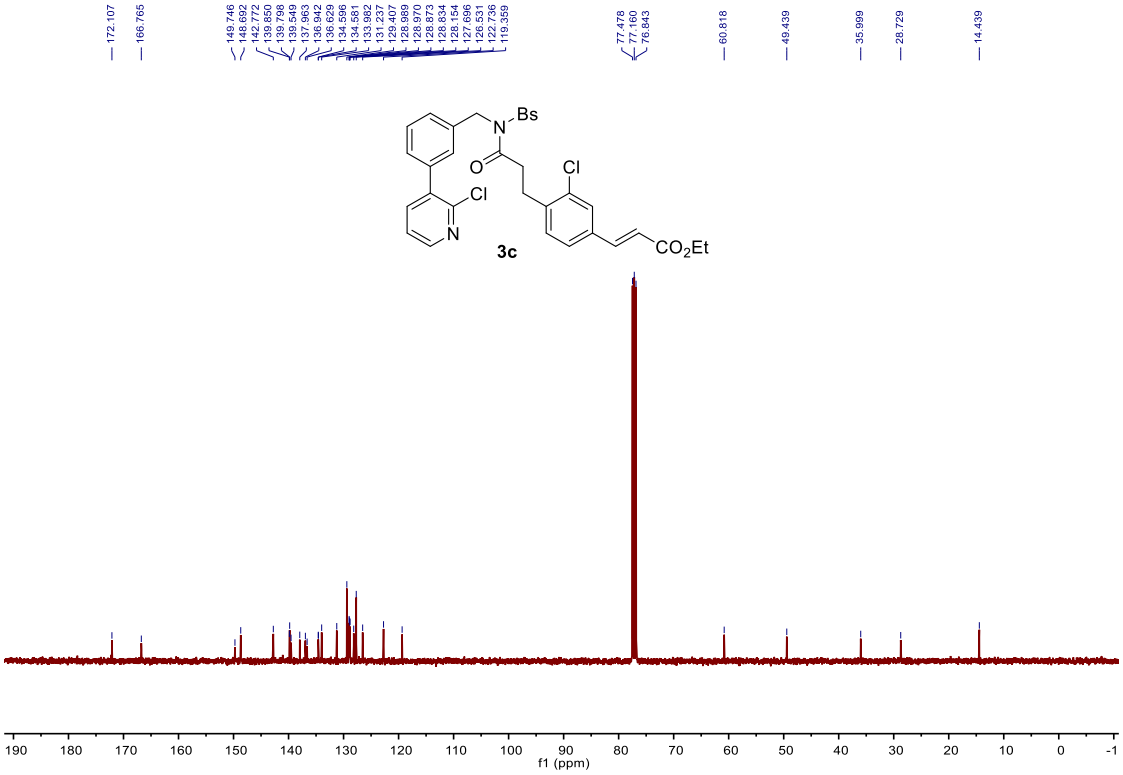

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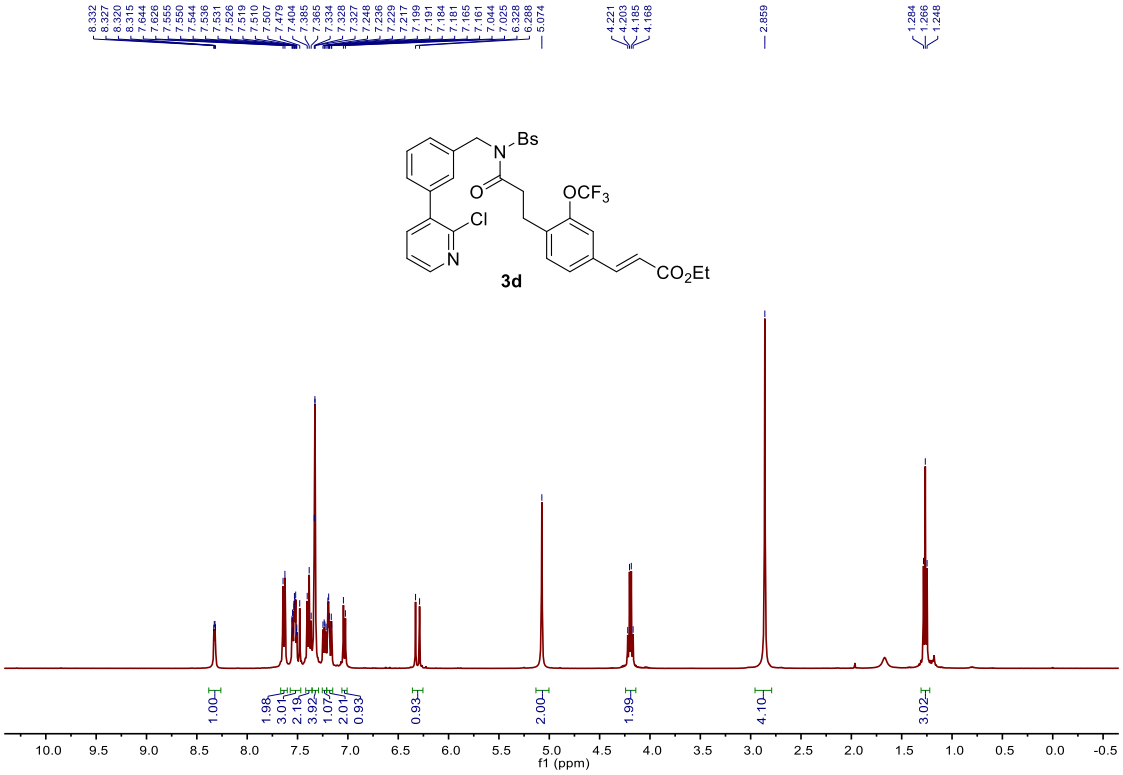

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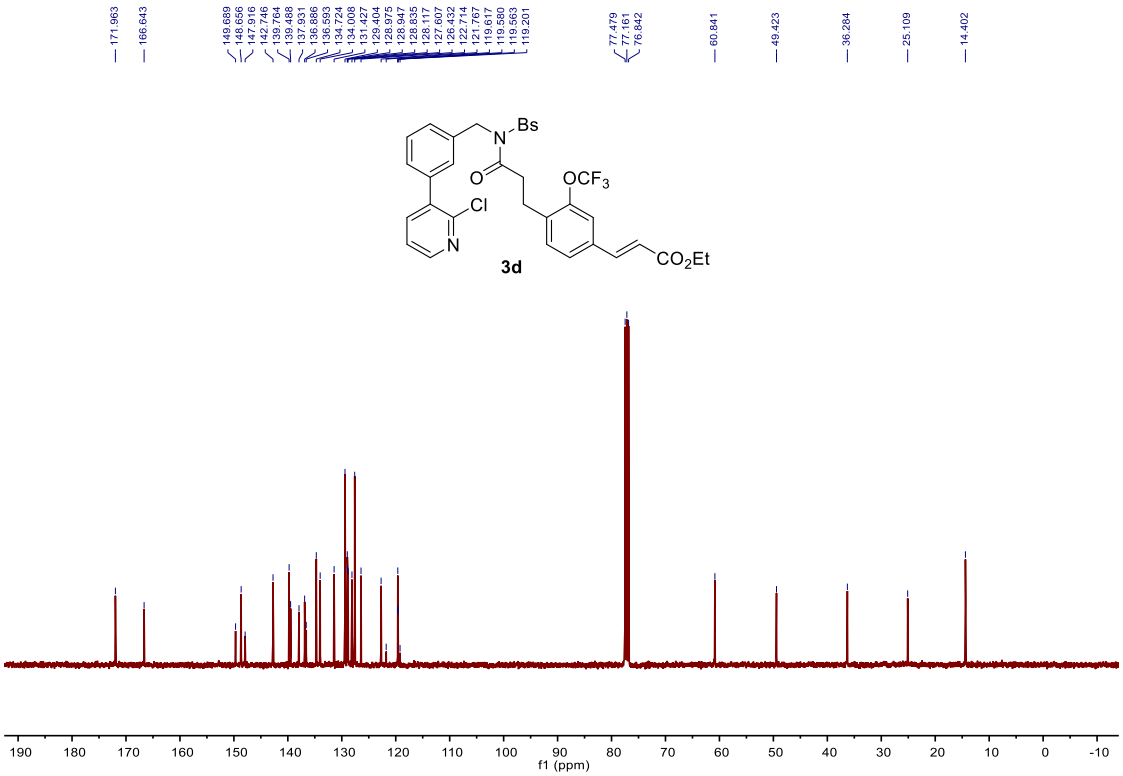

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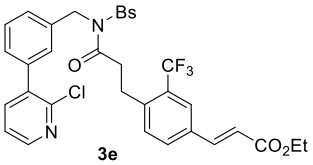

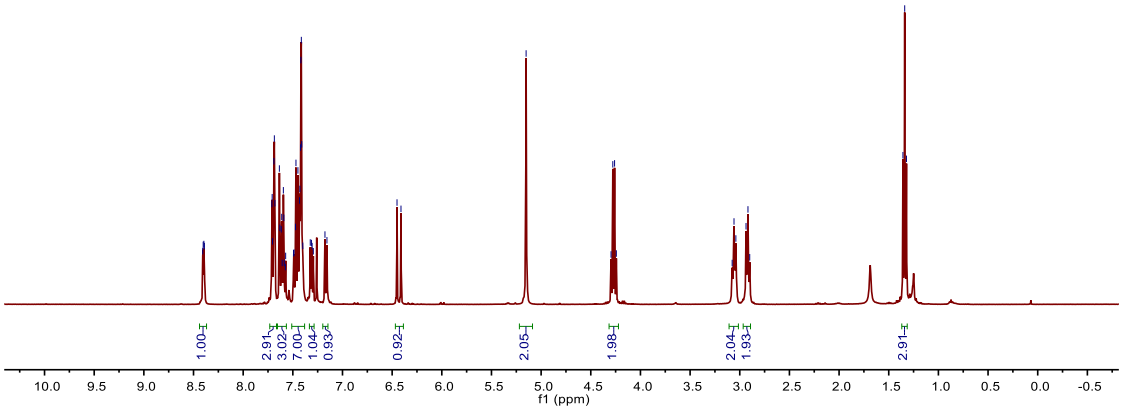

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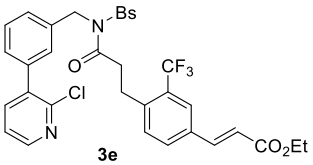

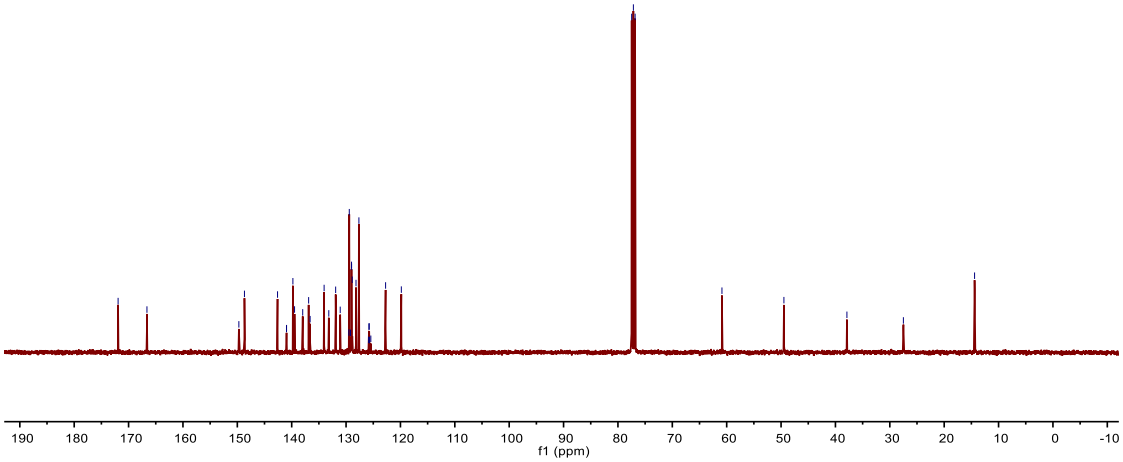

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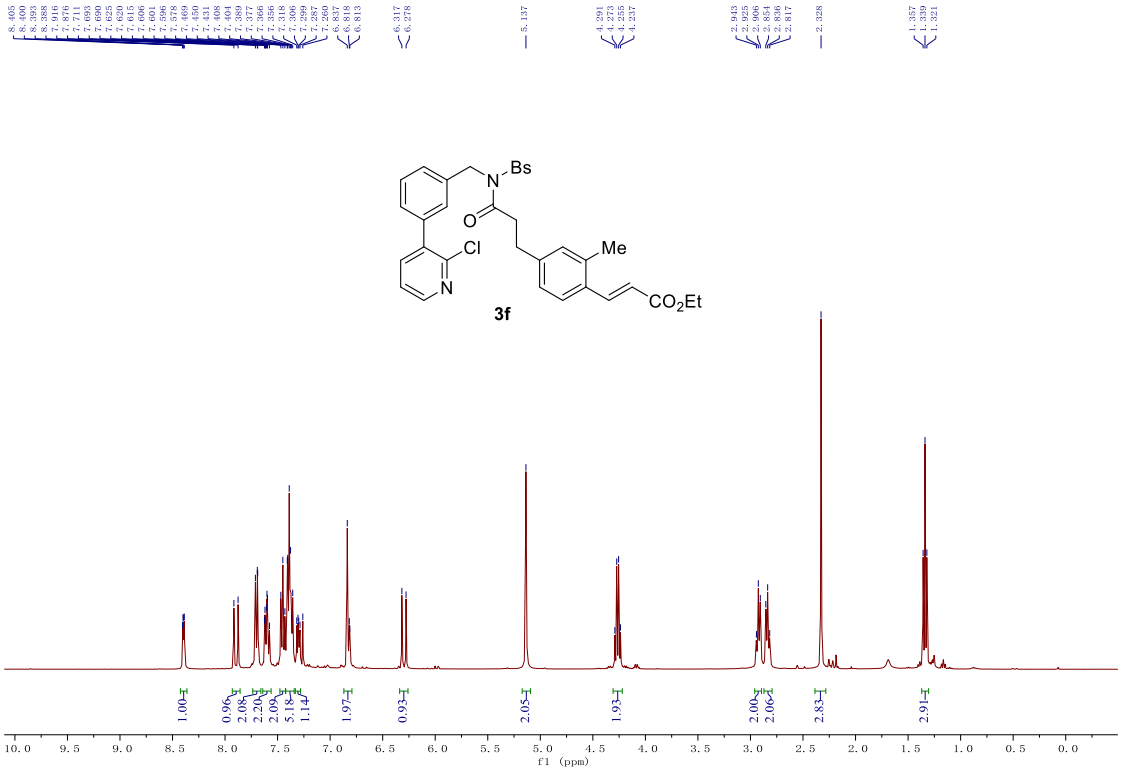

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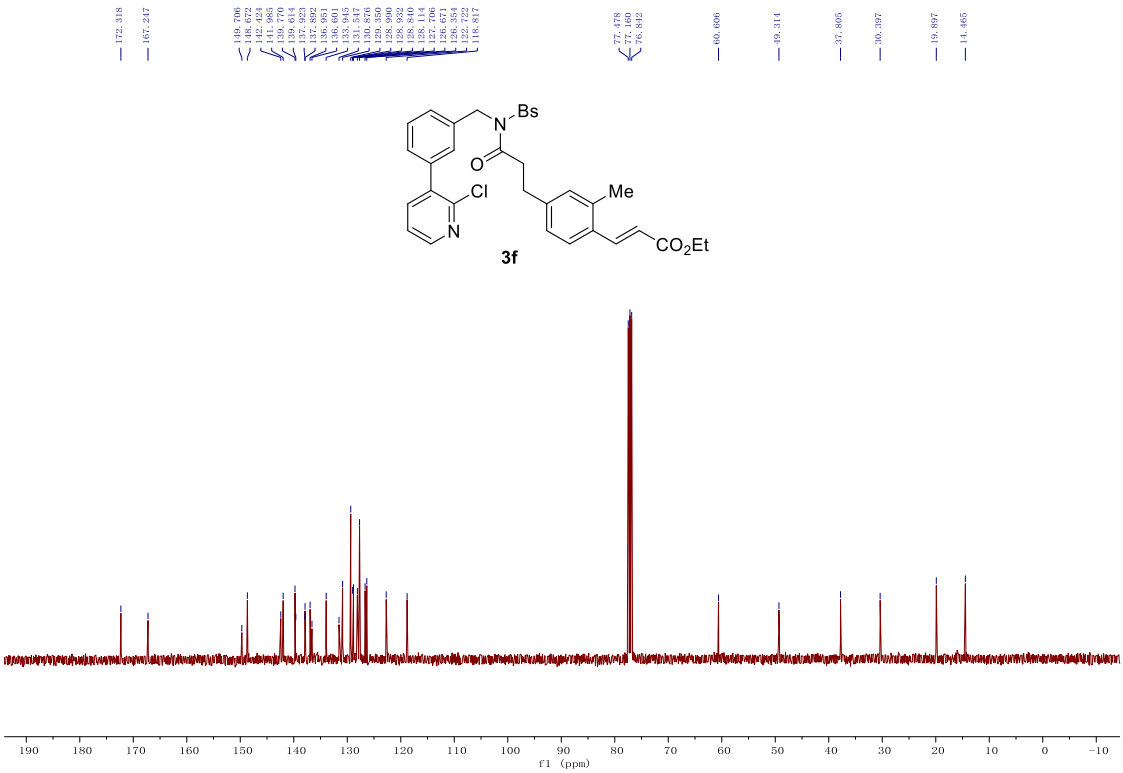

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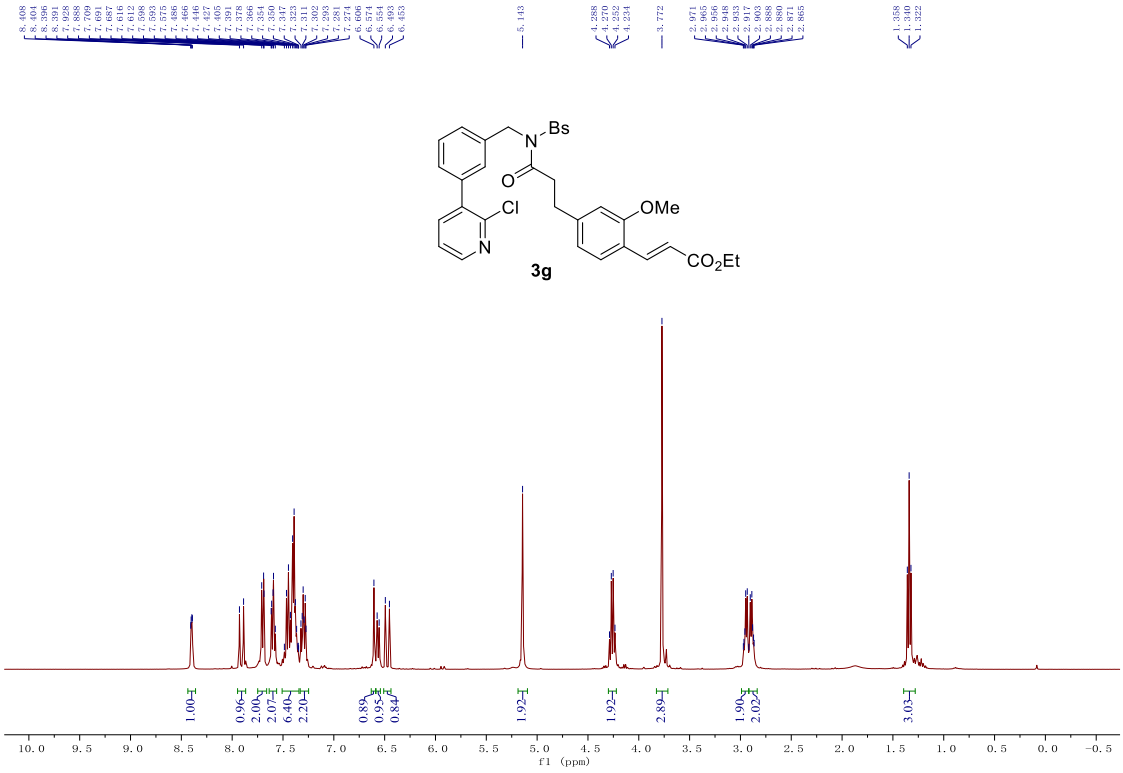

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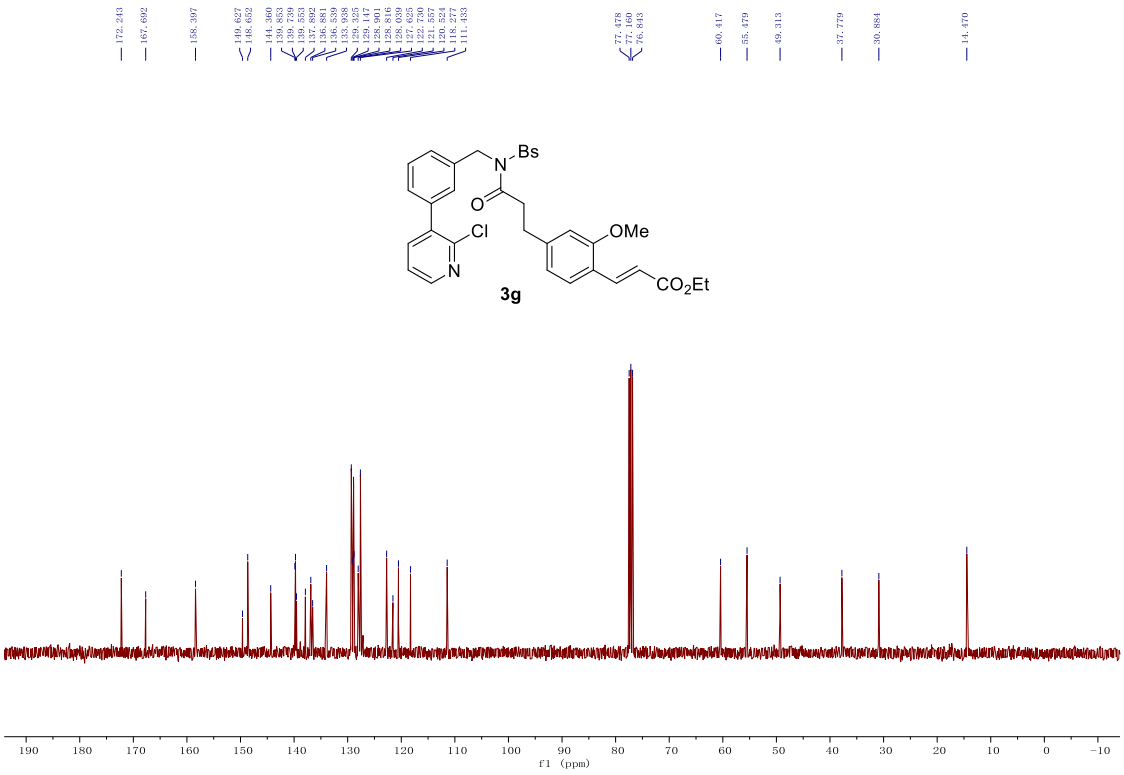

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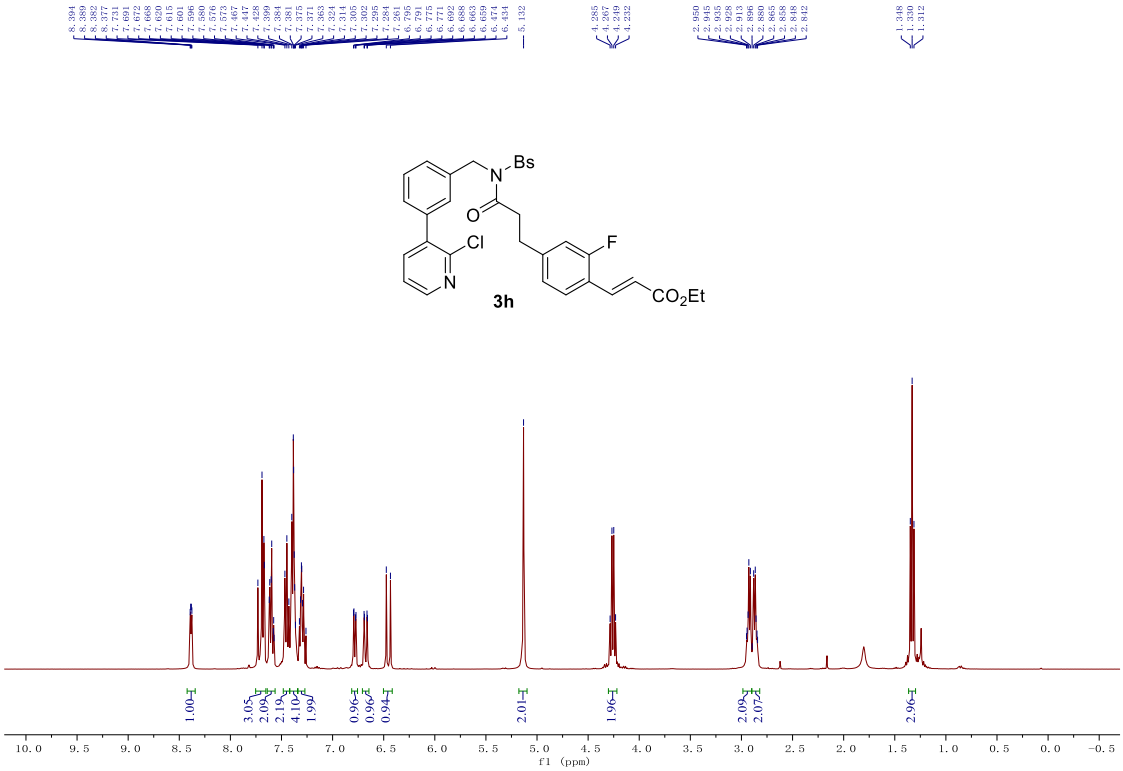

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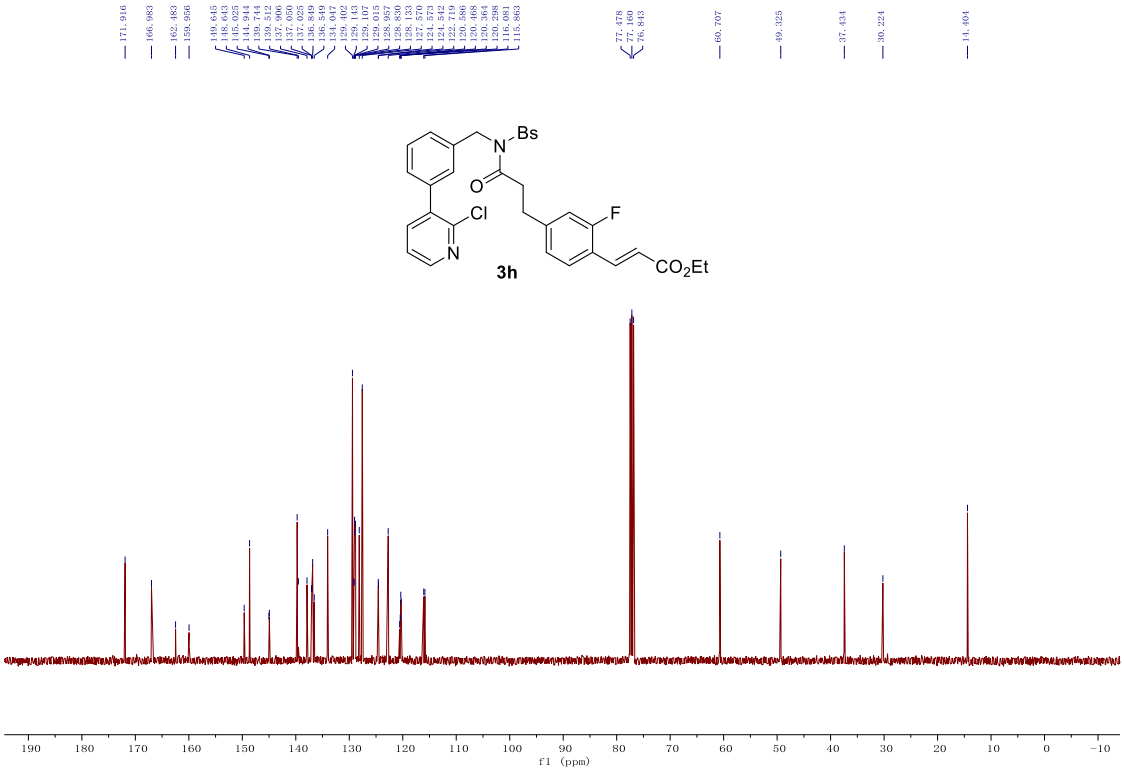

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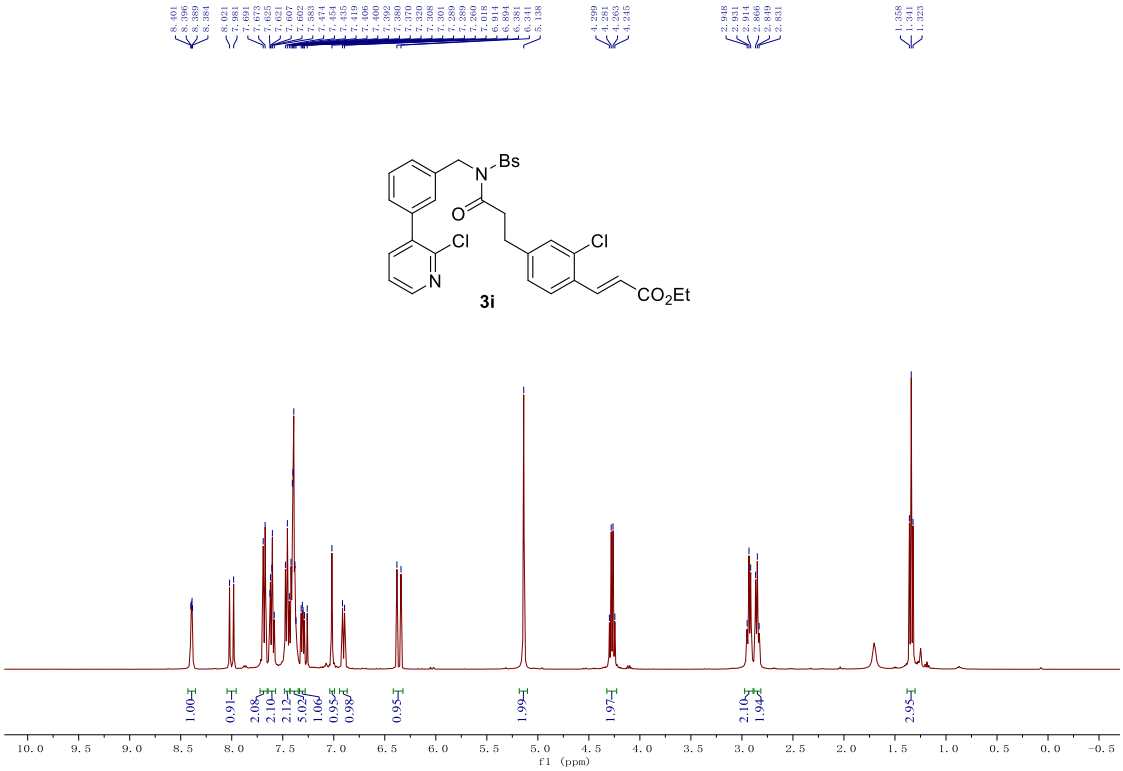

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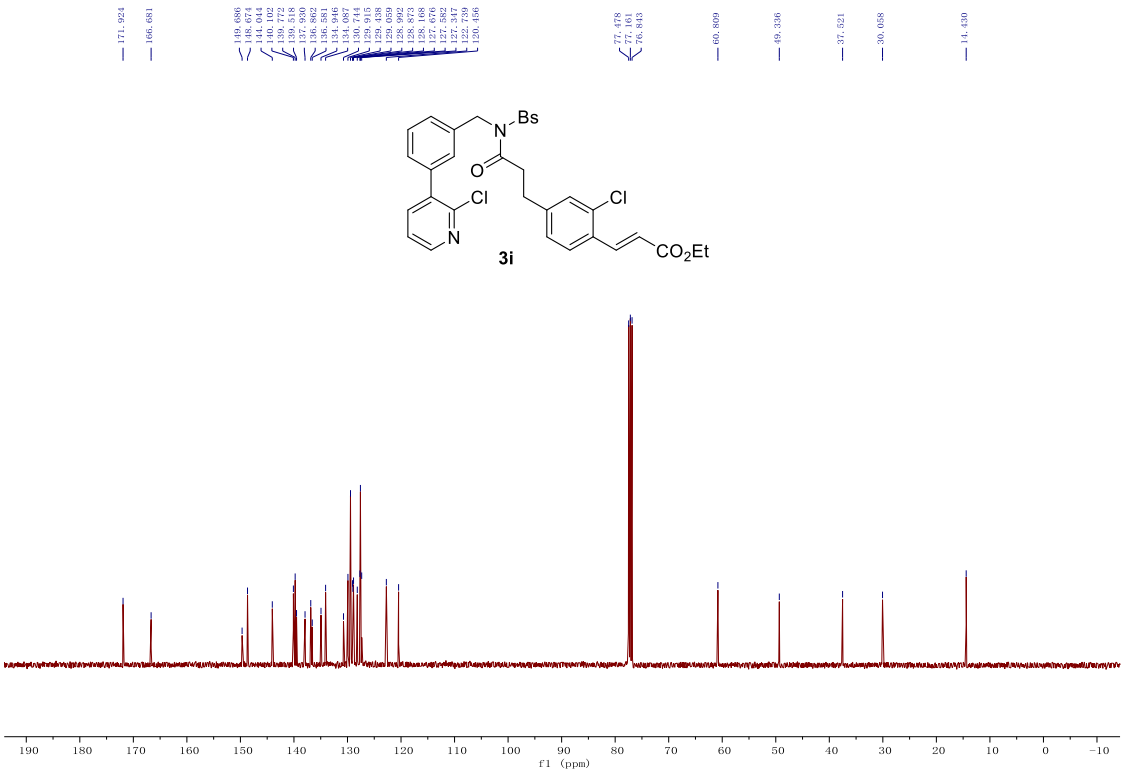

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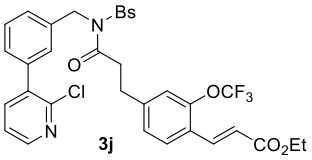

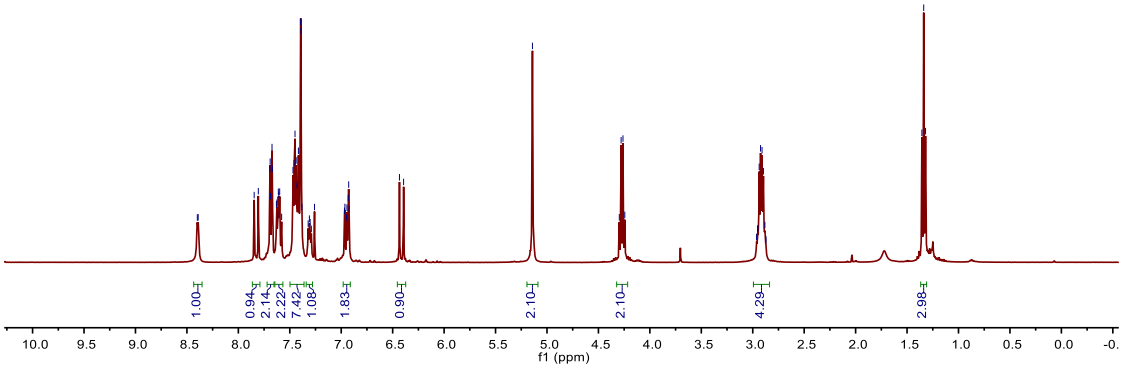

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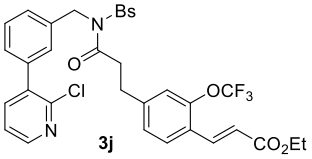

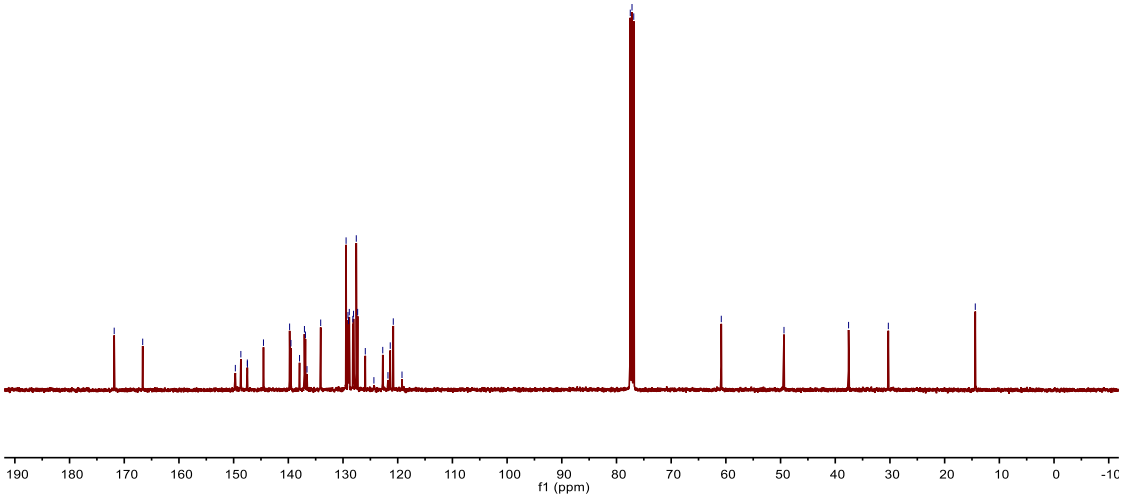

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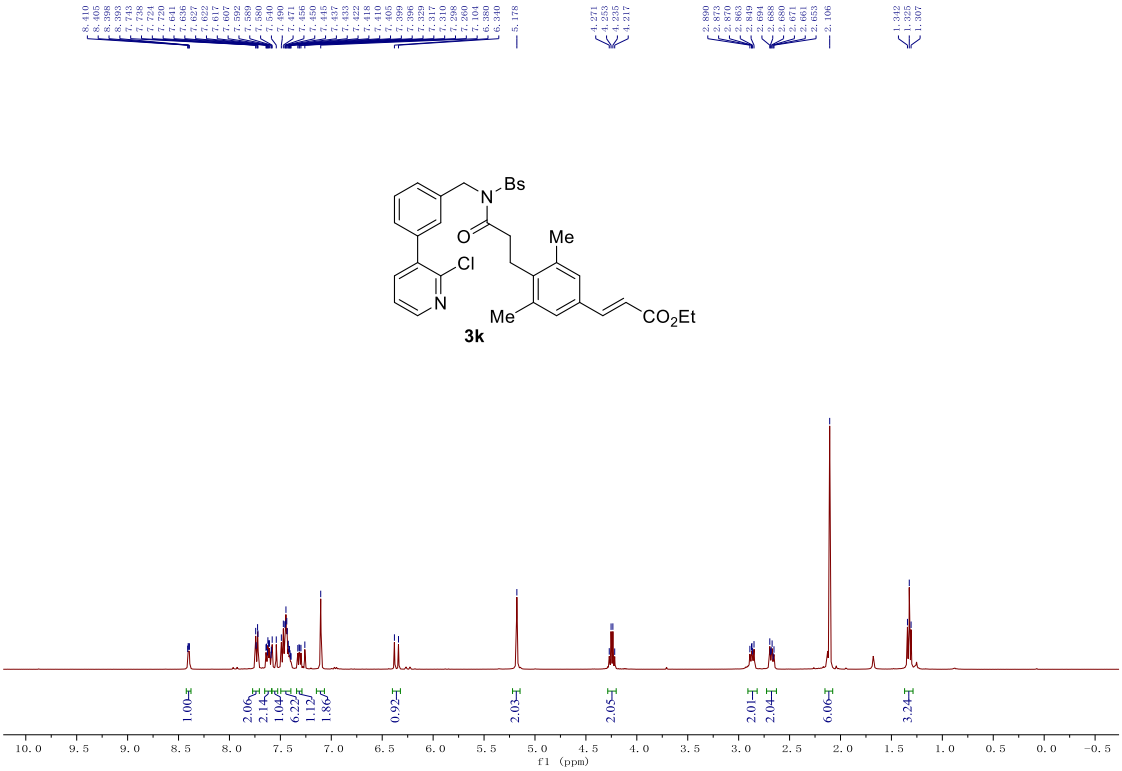

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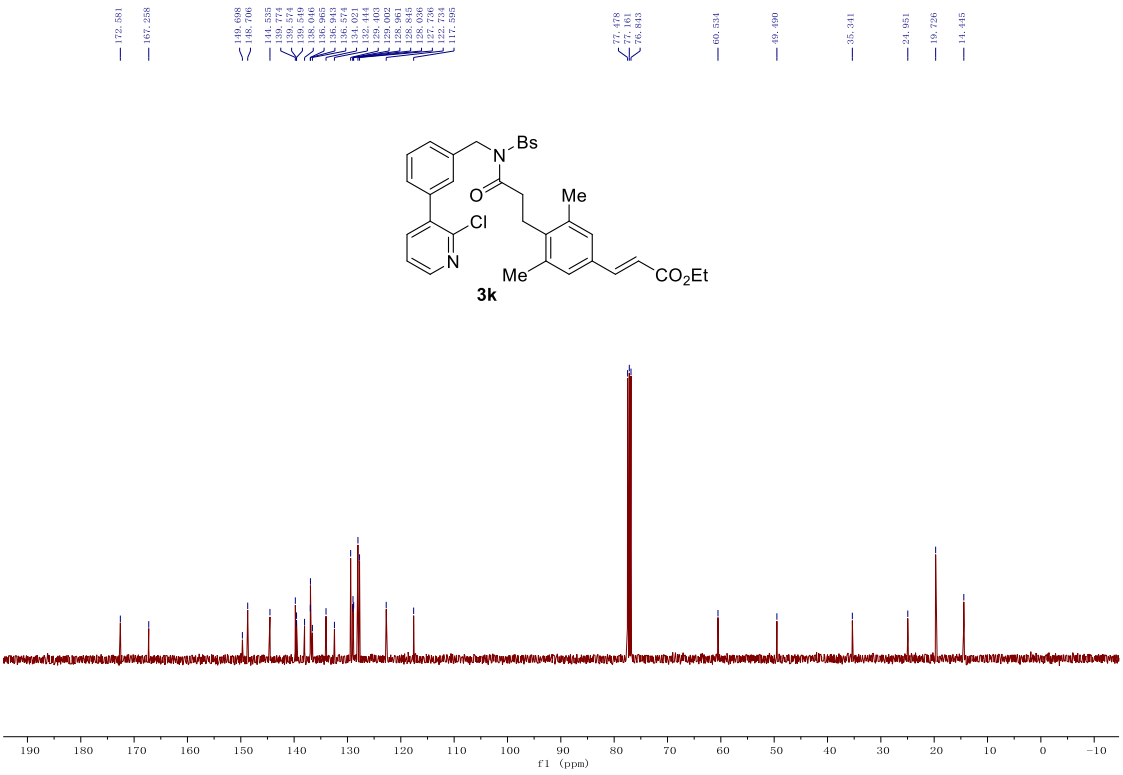

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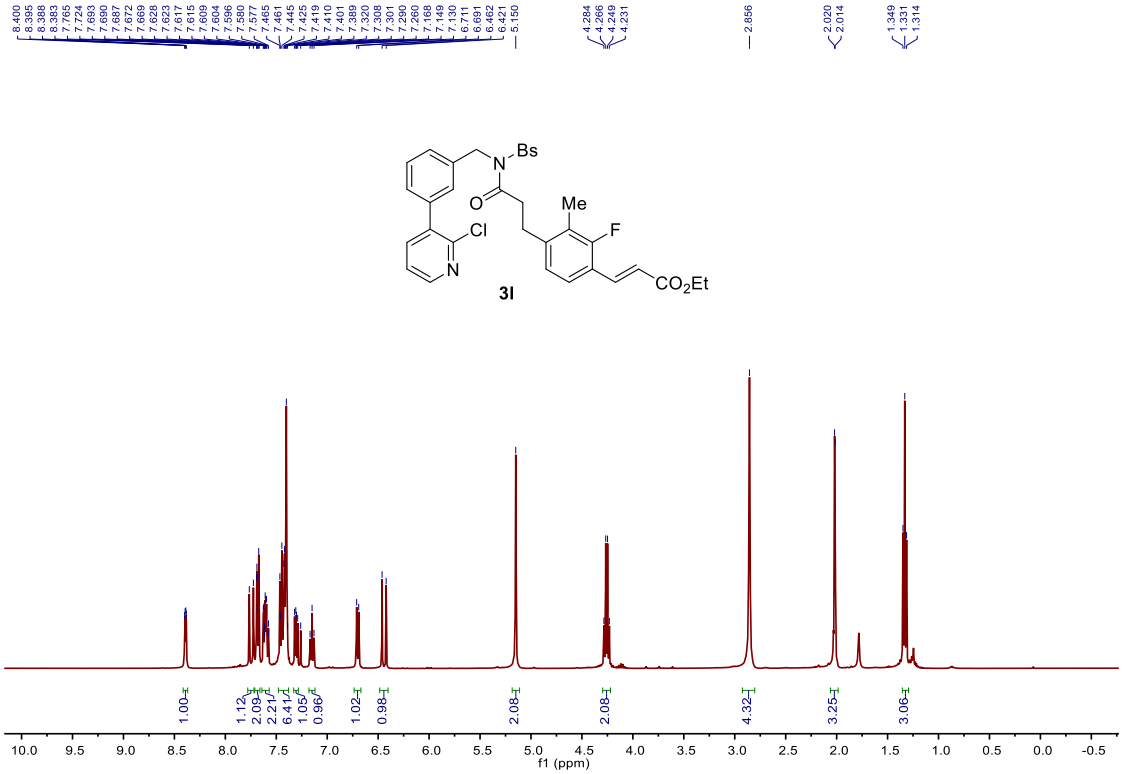

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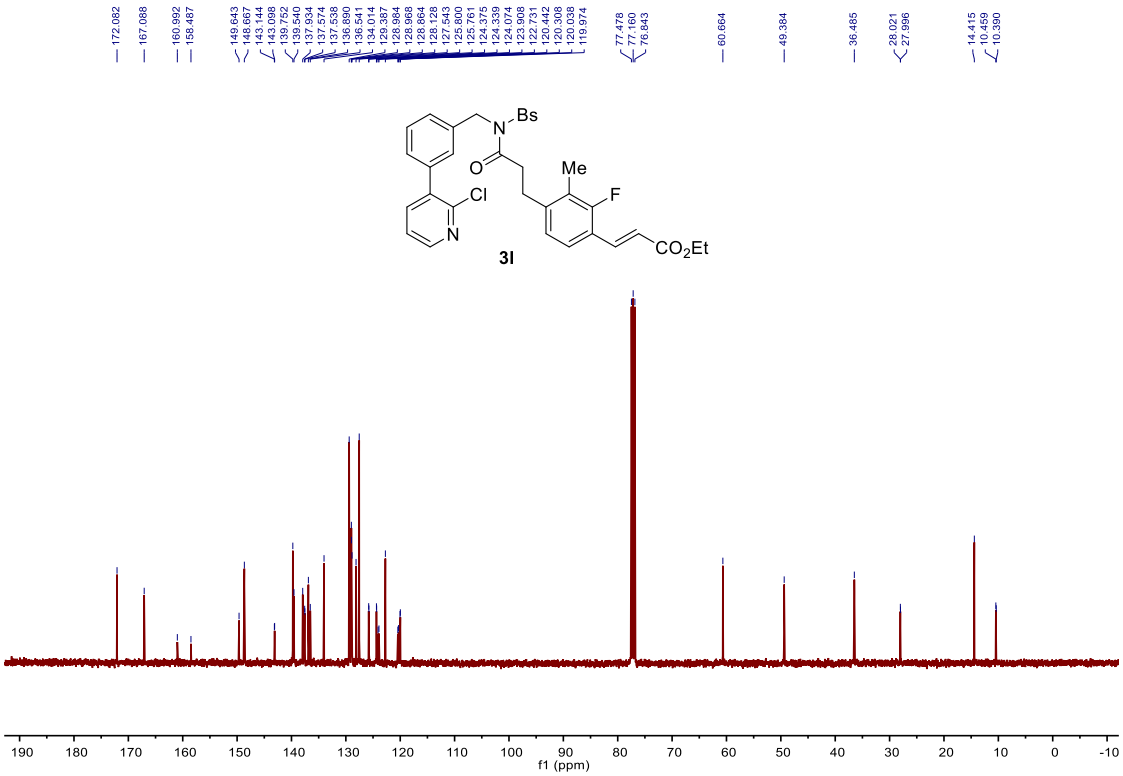

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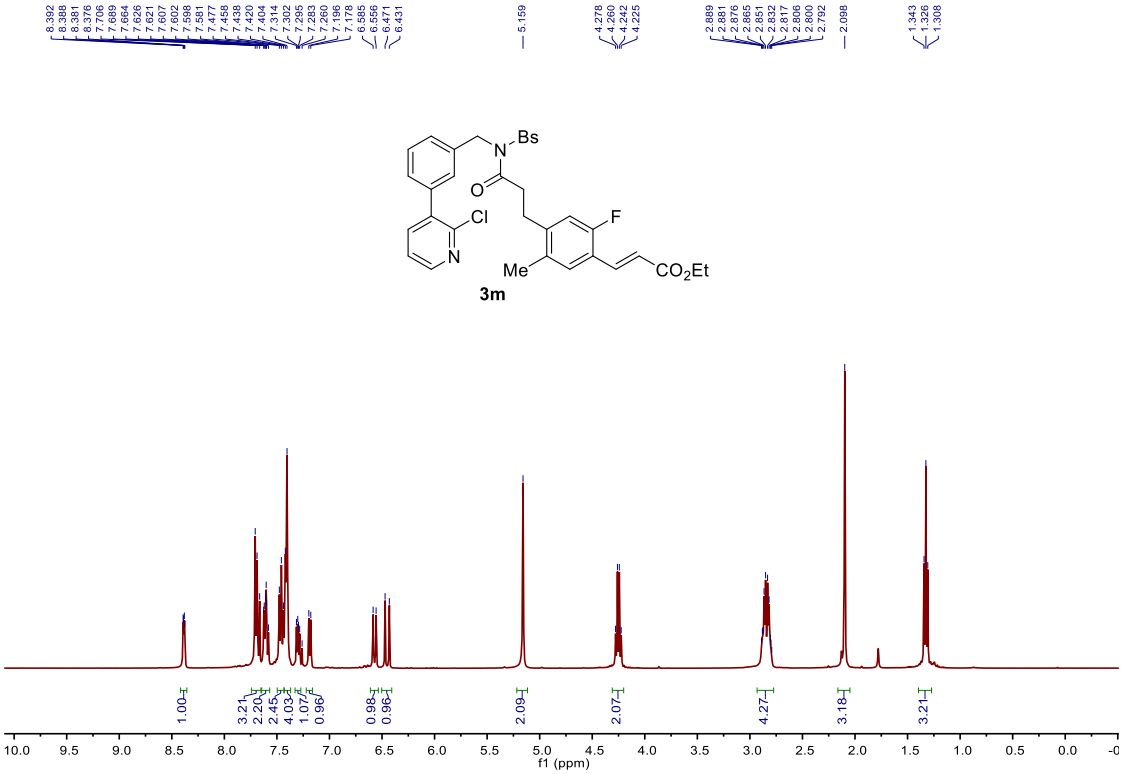

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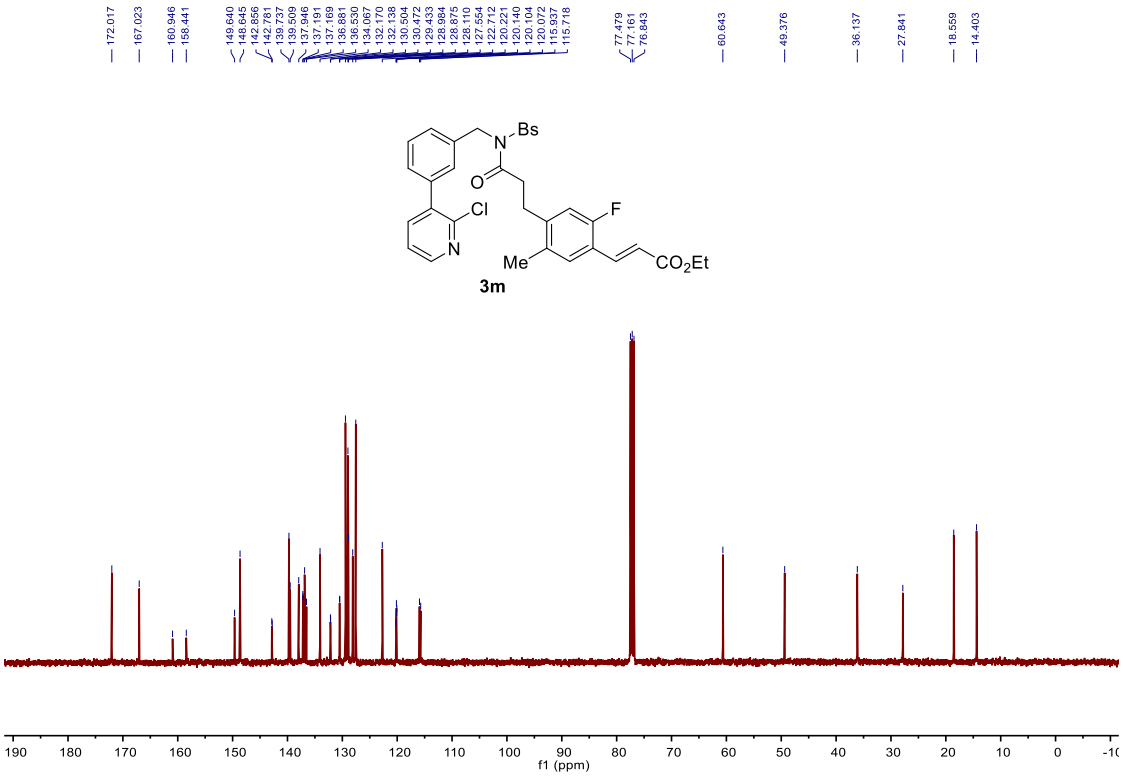

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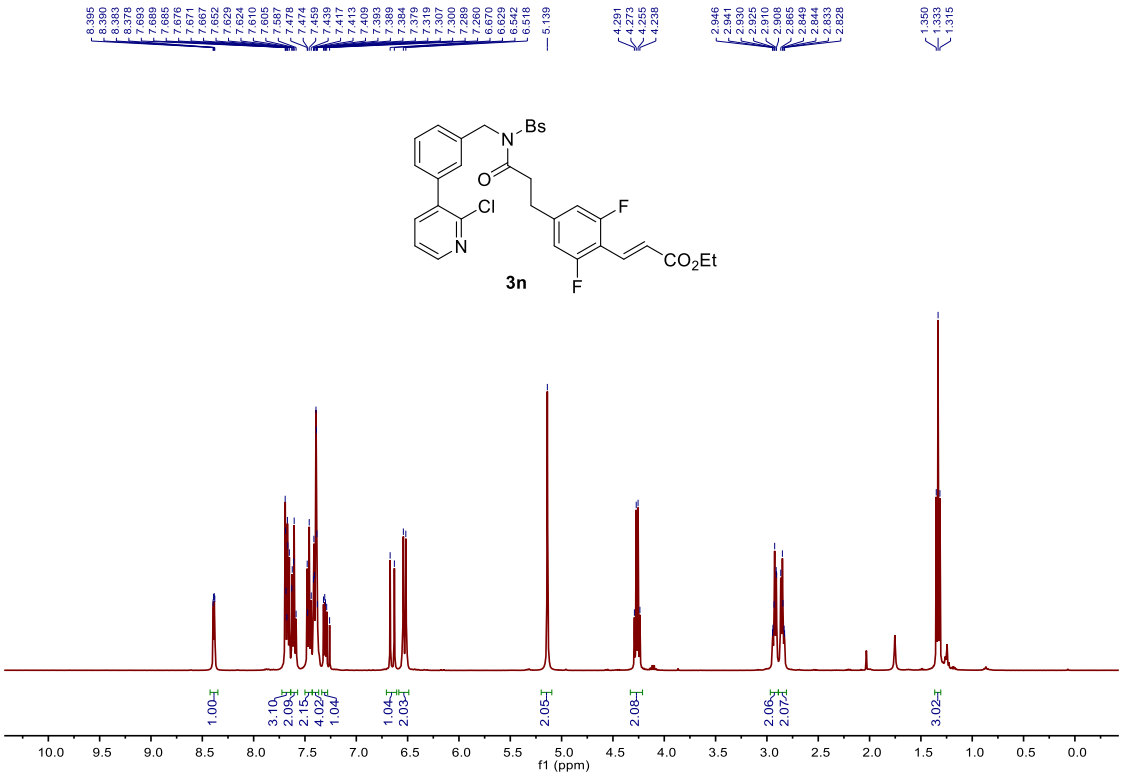

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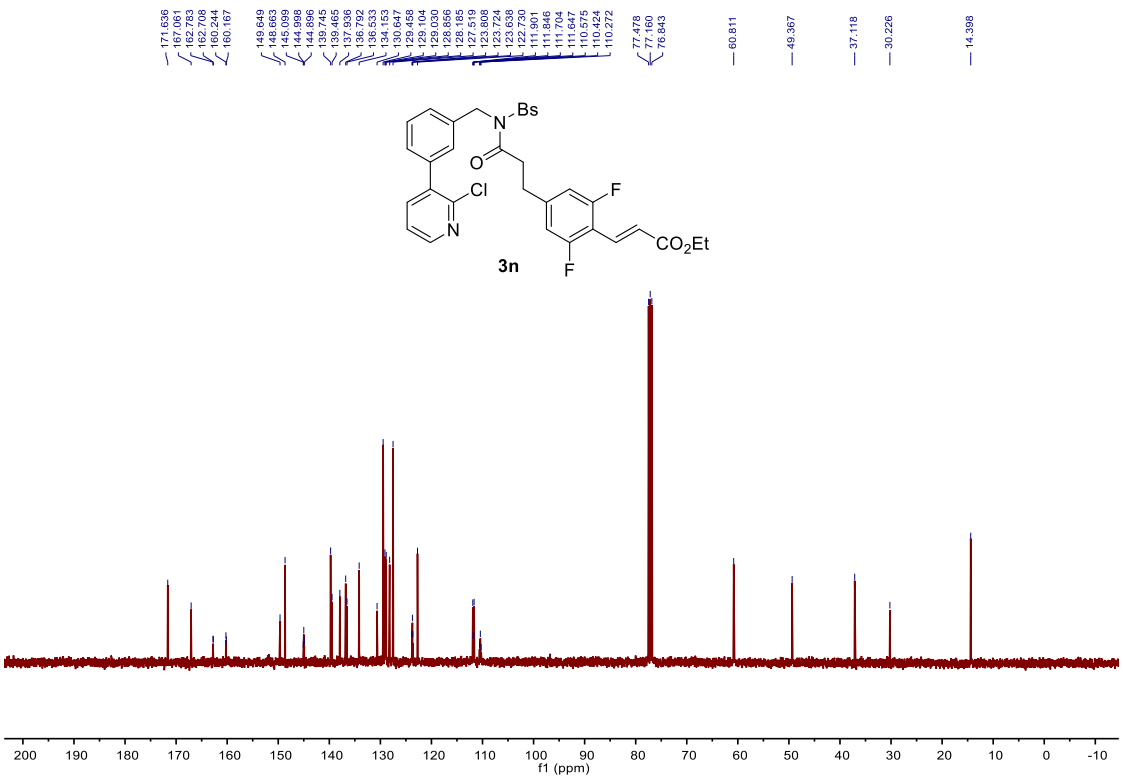

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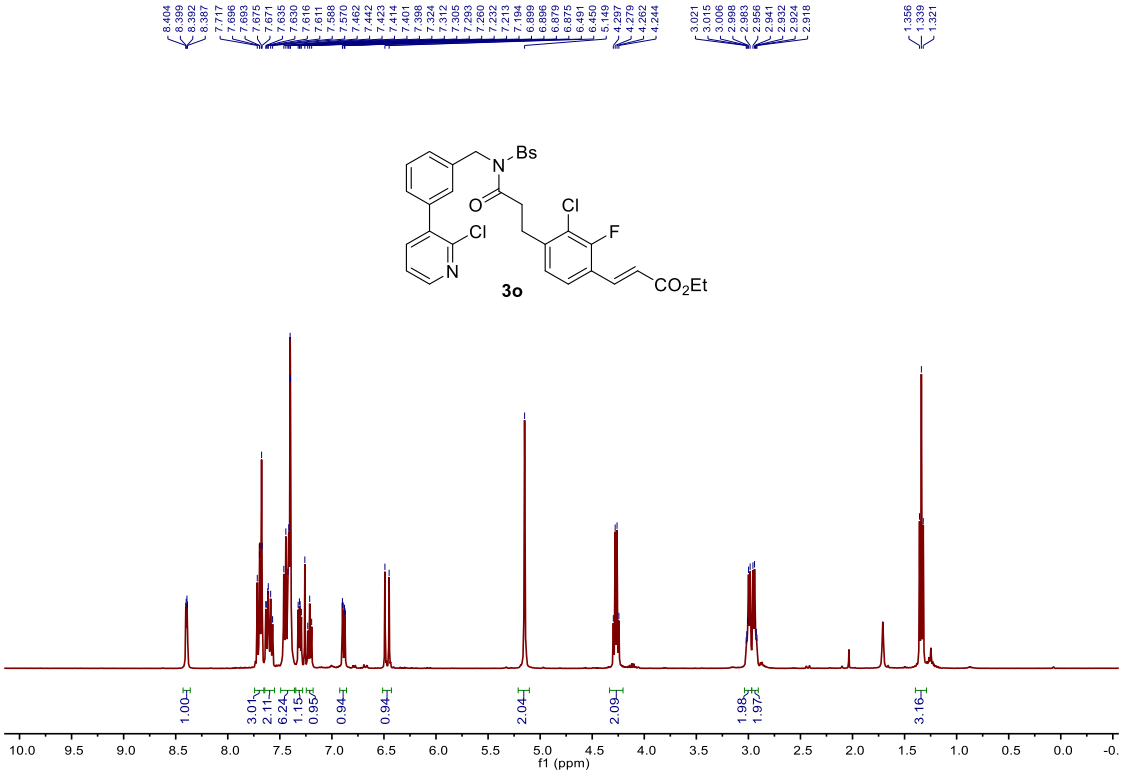

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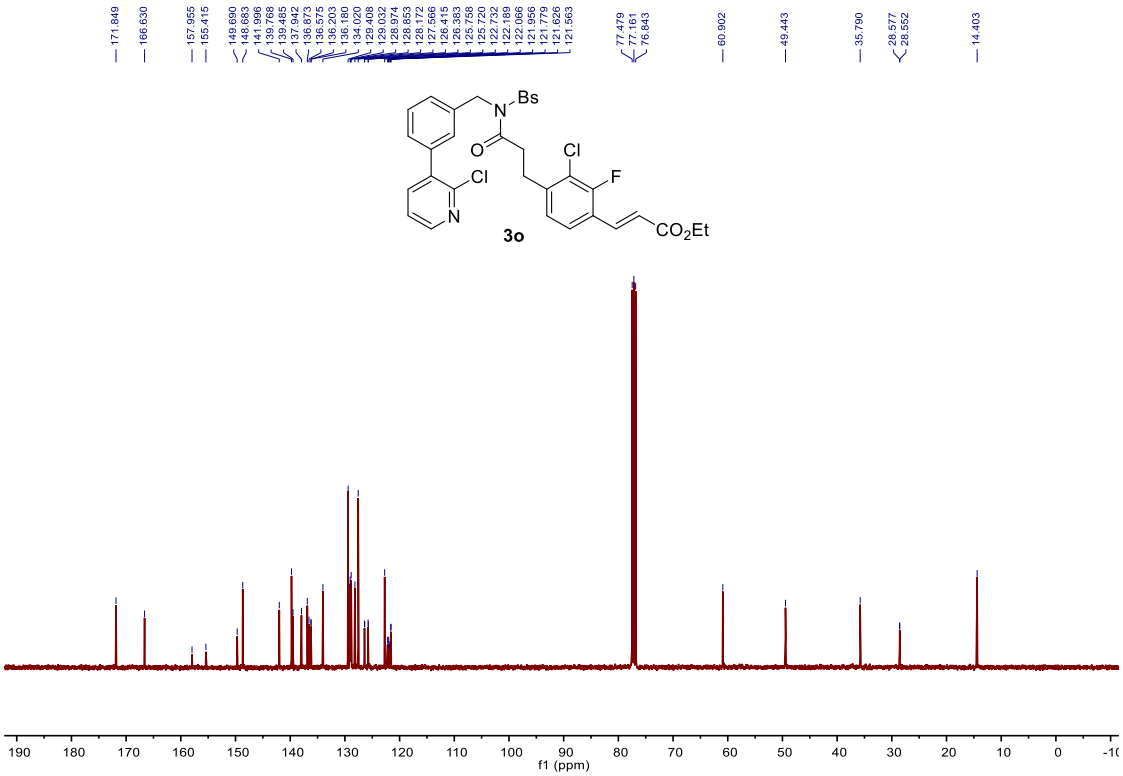

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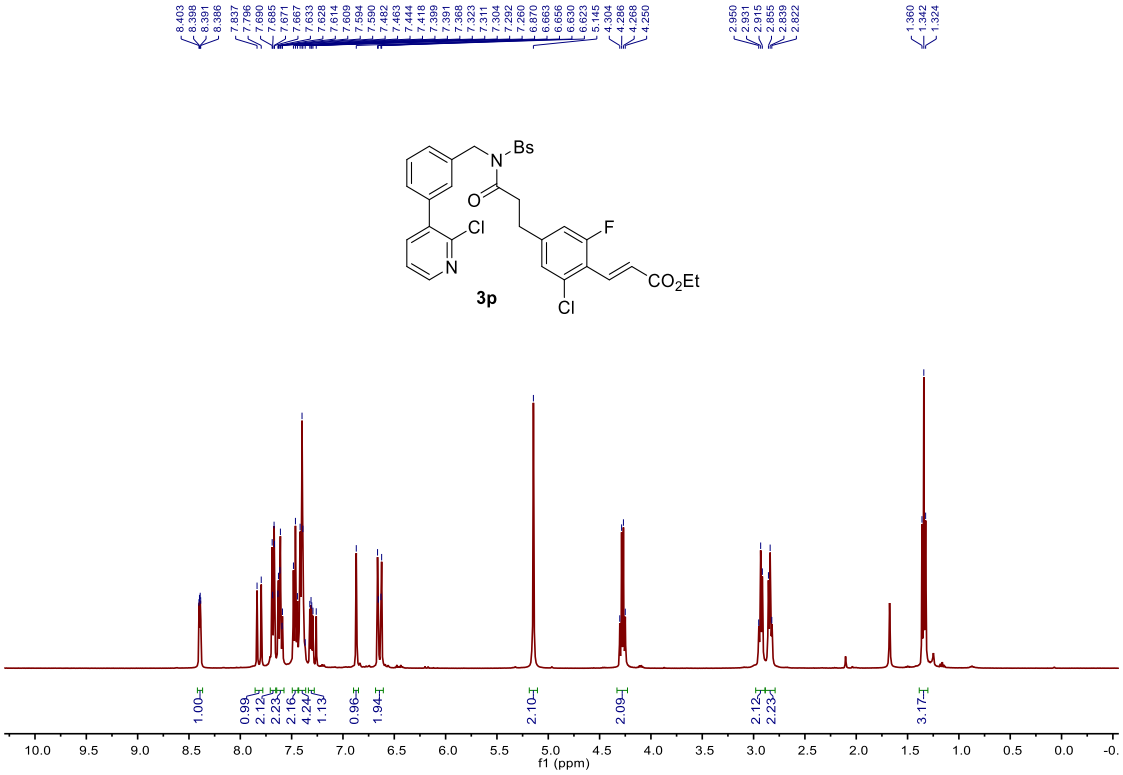

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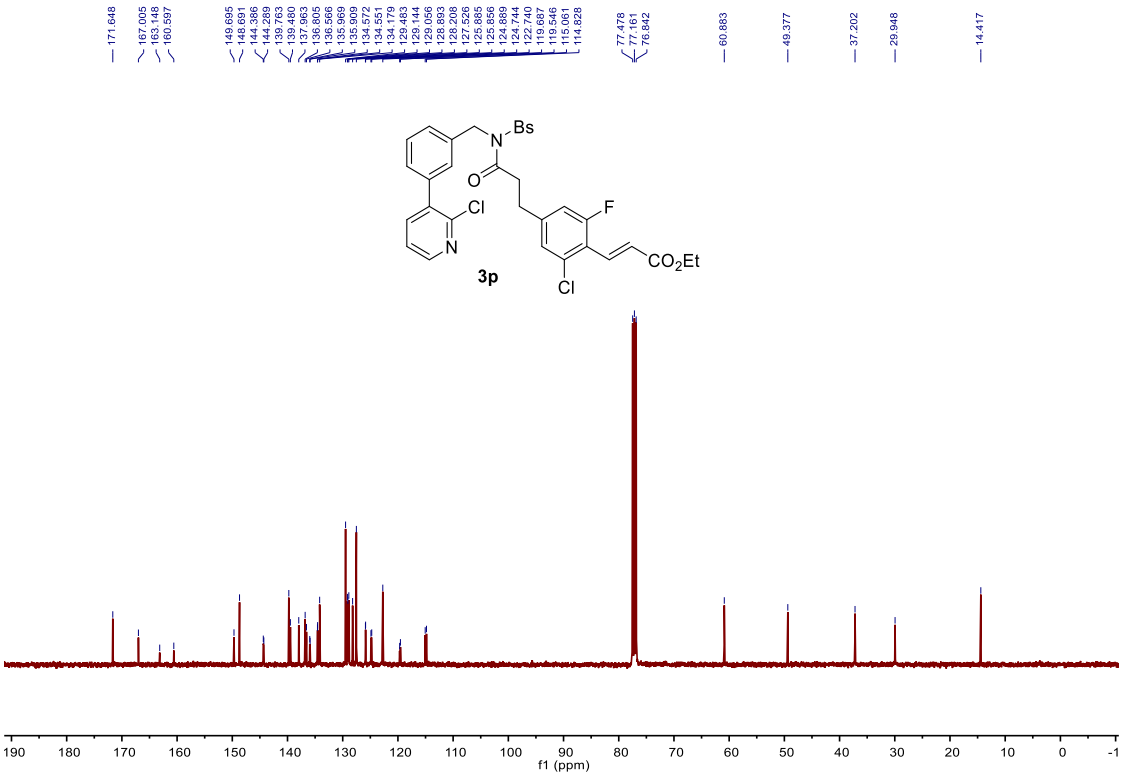

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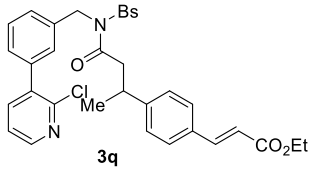

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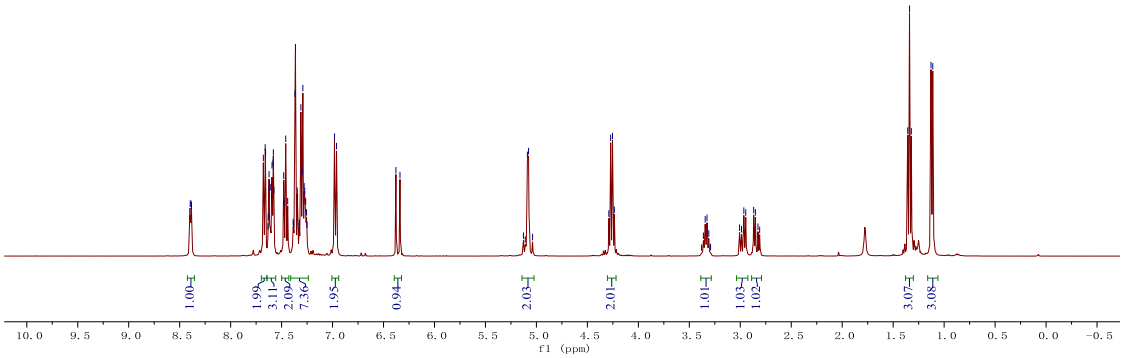

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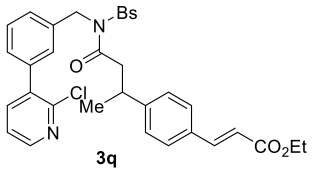

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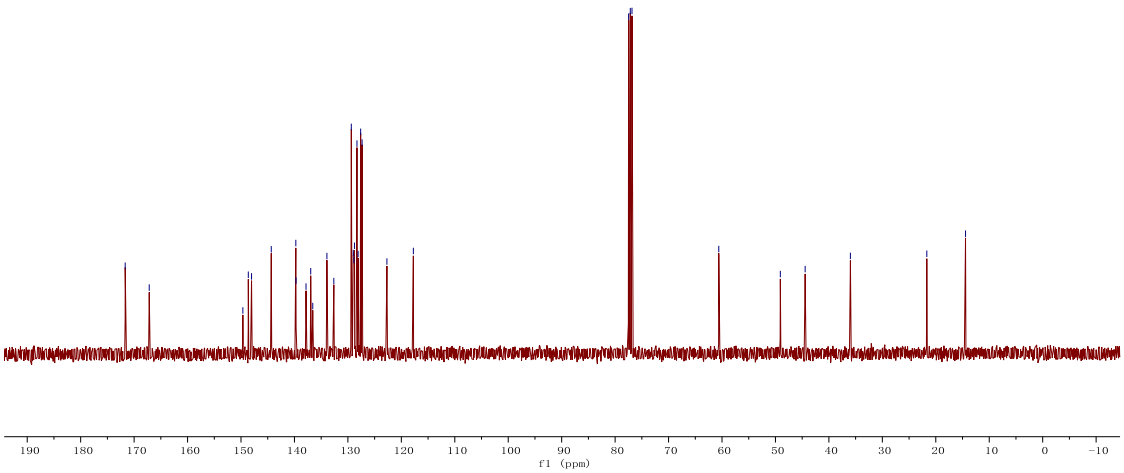

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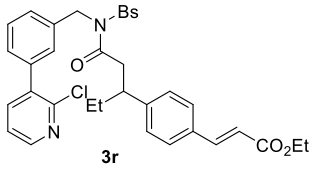

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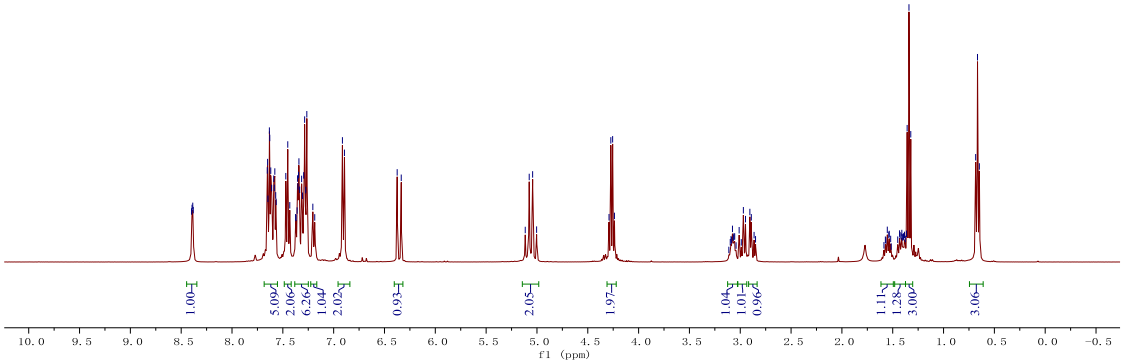

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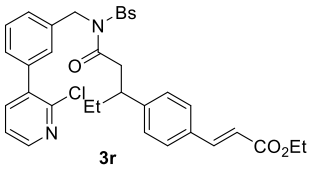

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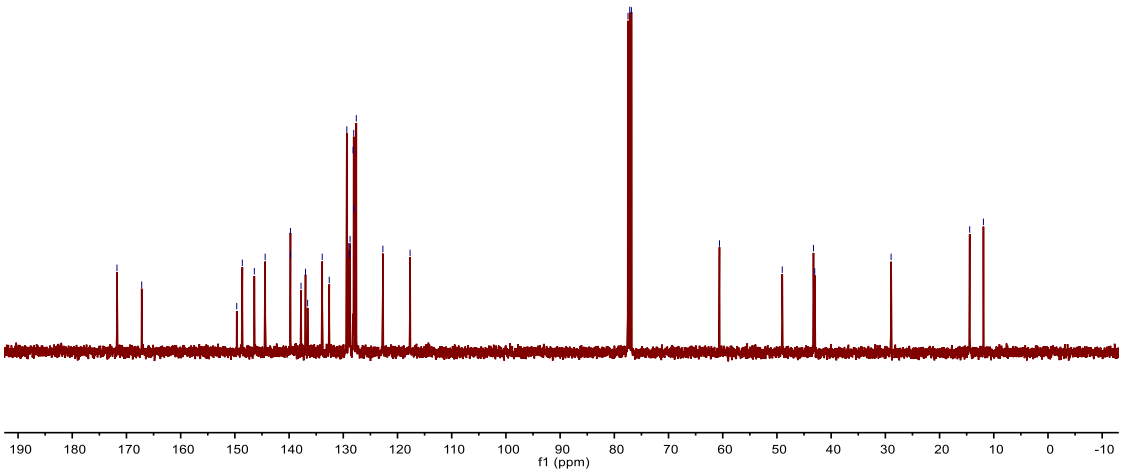

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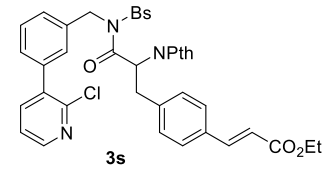

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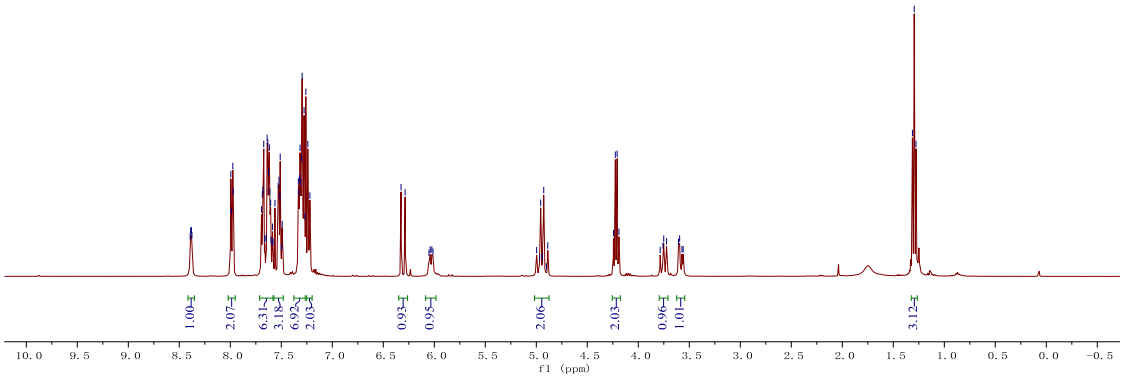

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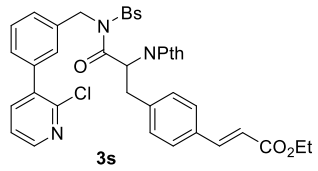

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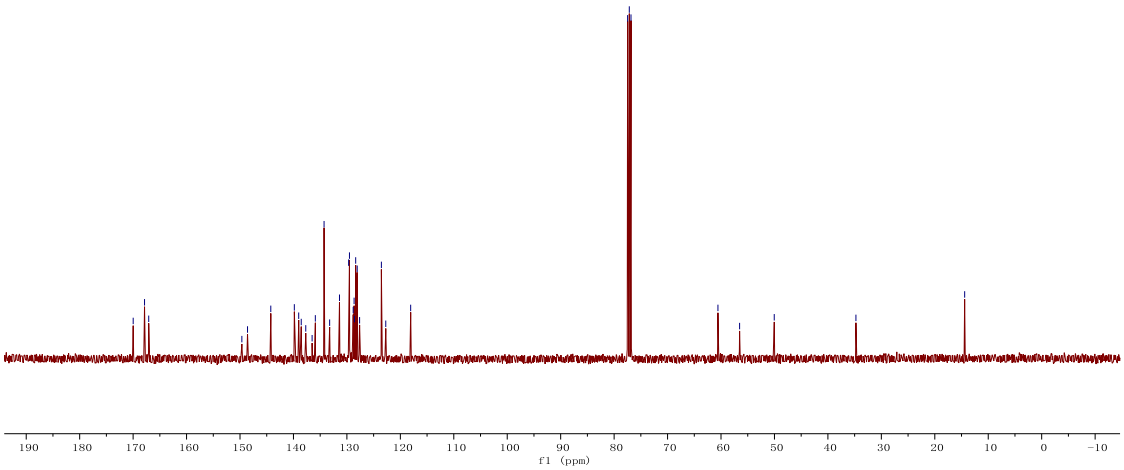
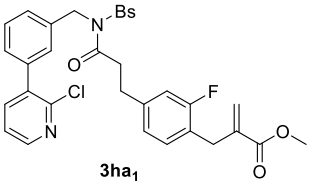


^{1}H NMR (400 MHz, Chloroform-*d*)



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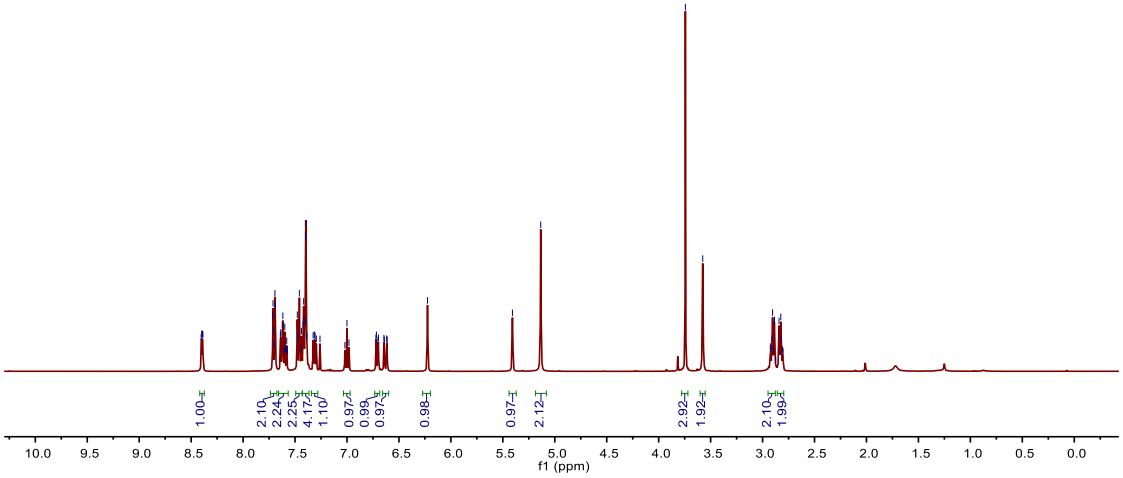
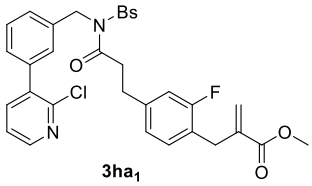


^{13}C NMR (101 MHz, Chloroform-*d*)



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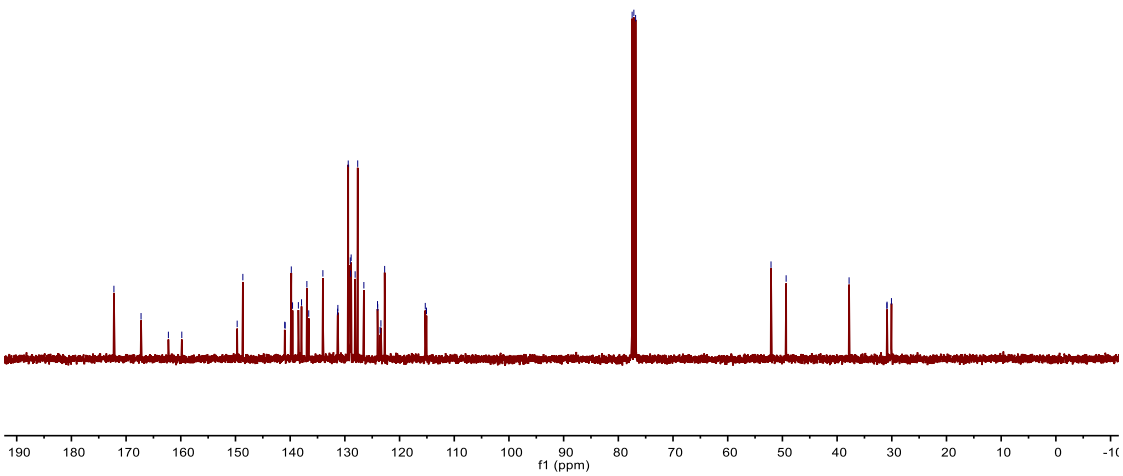
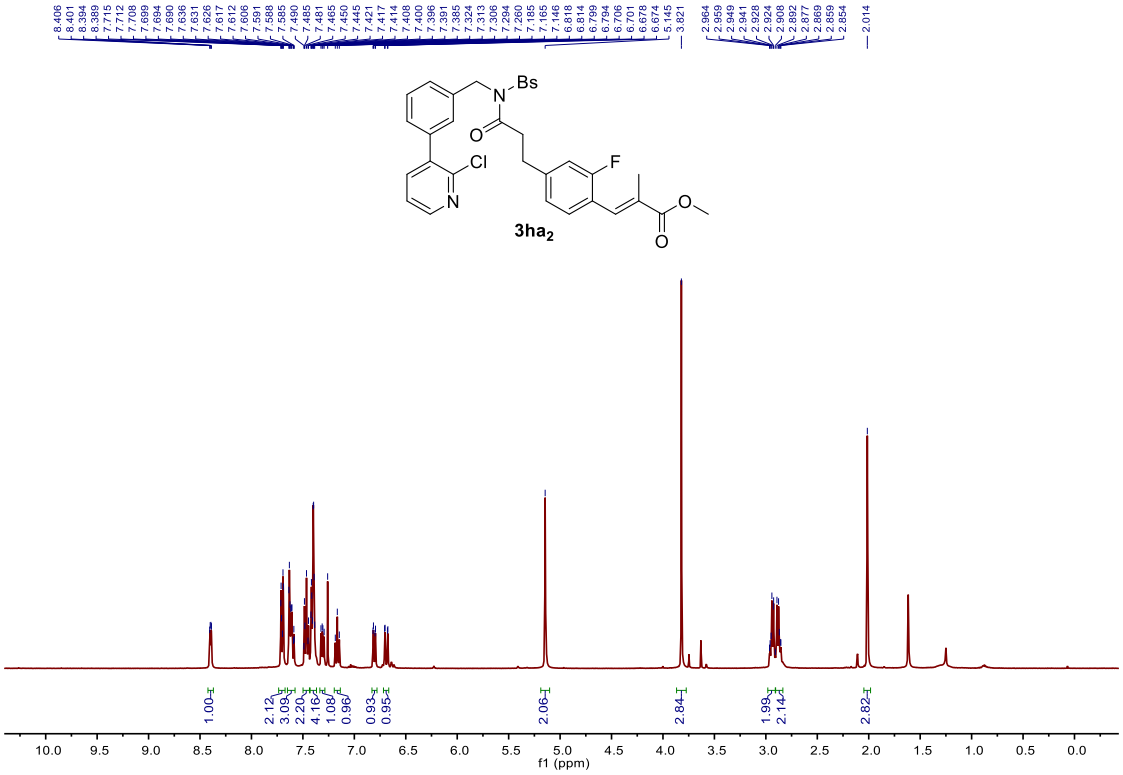


^{1}H NMR (400 MHz, Chloroform-*d*)



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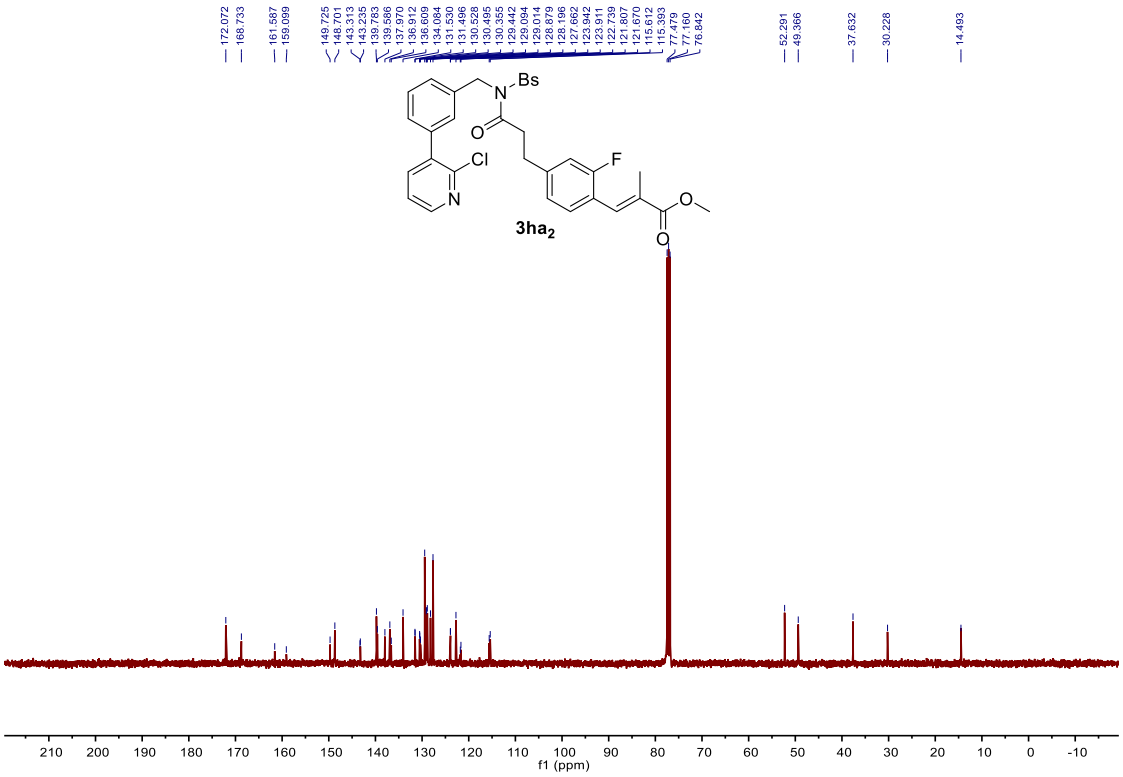

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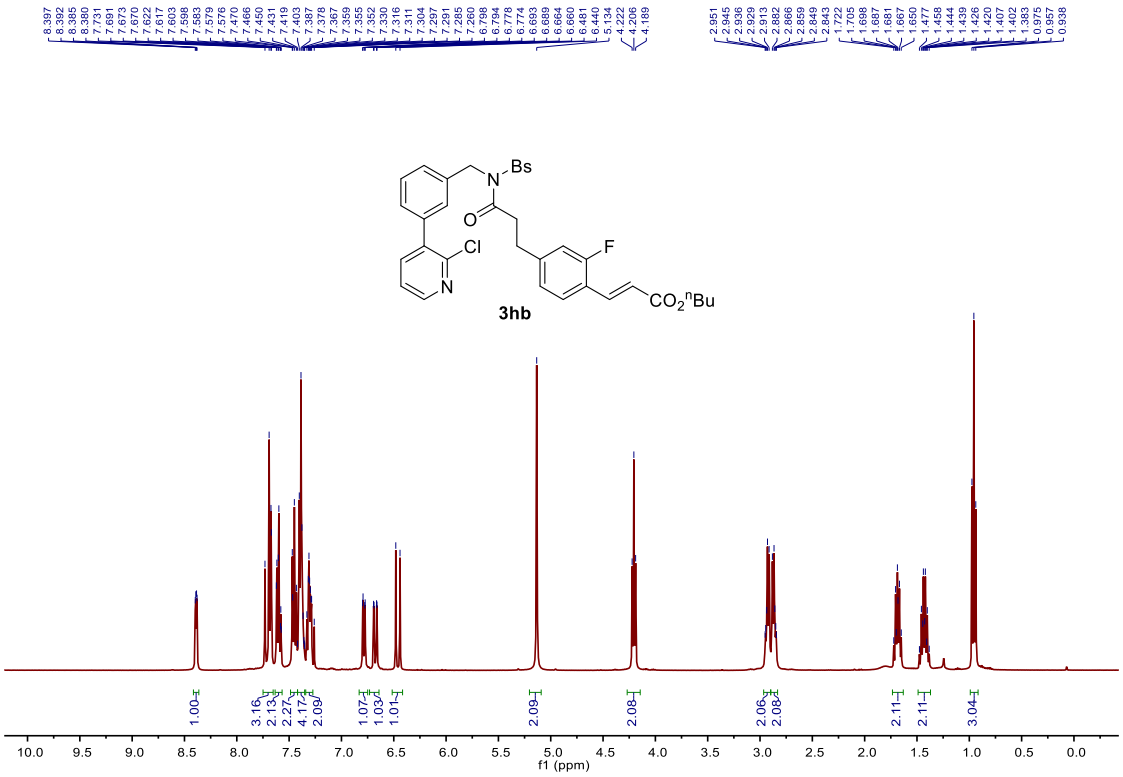

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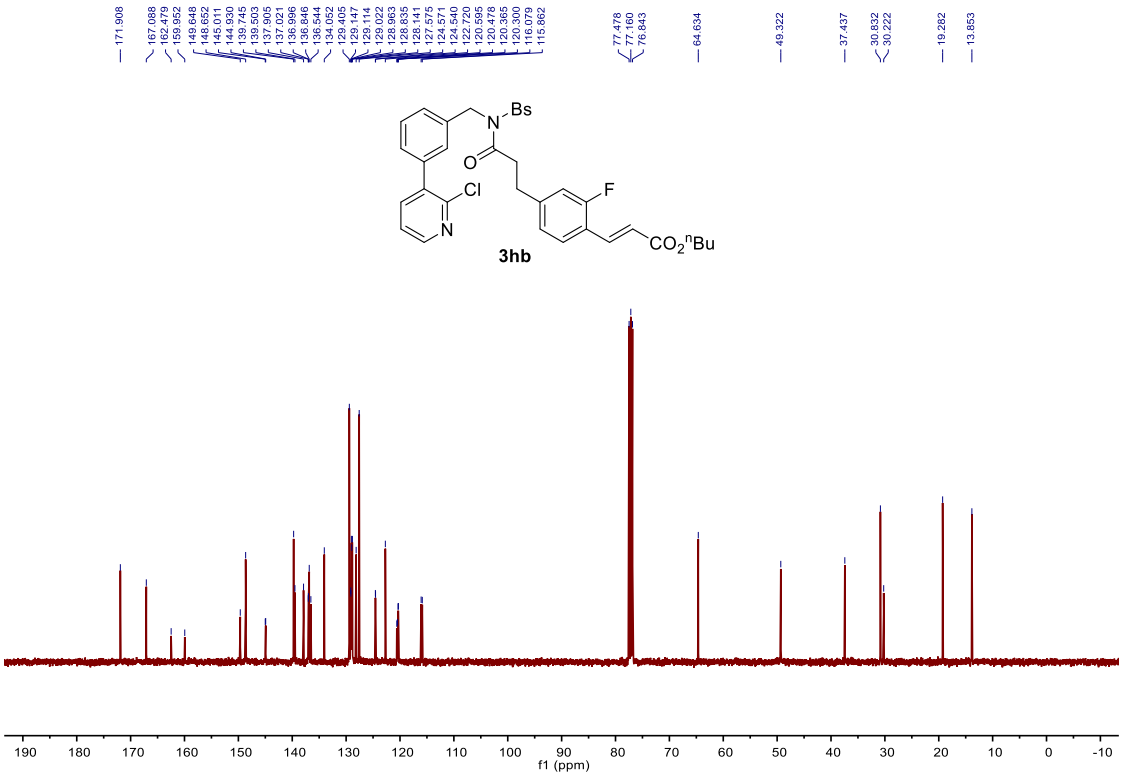

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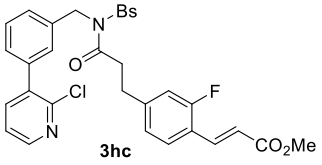

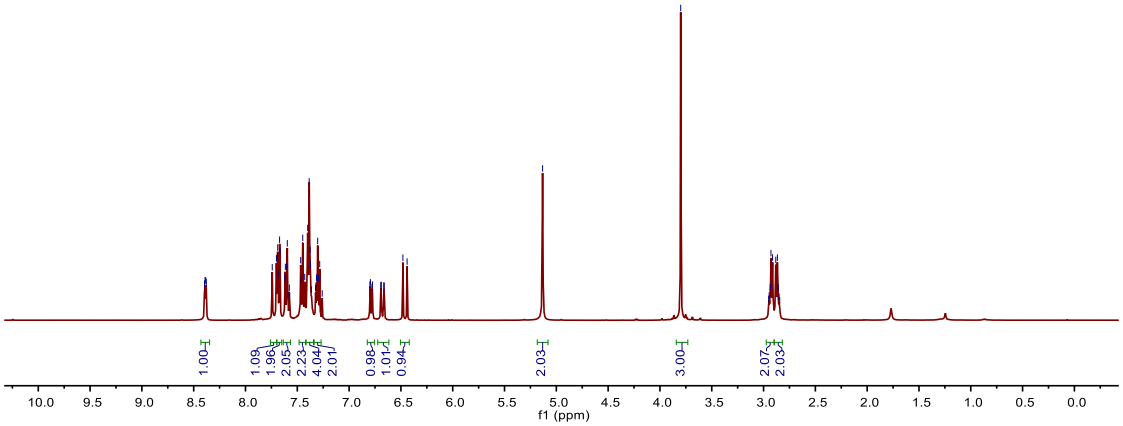

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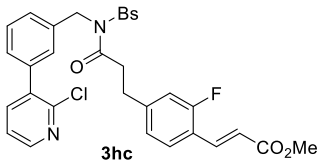

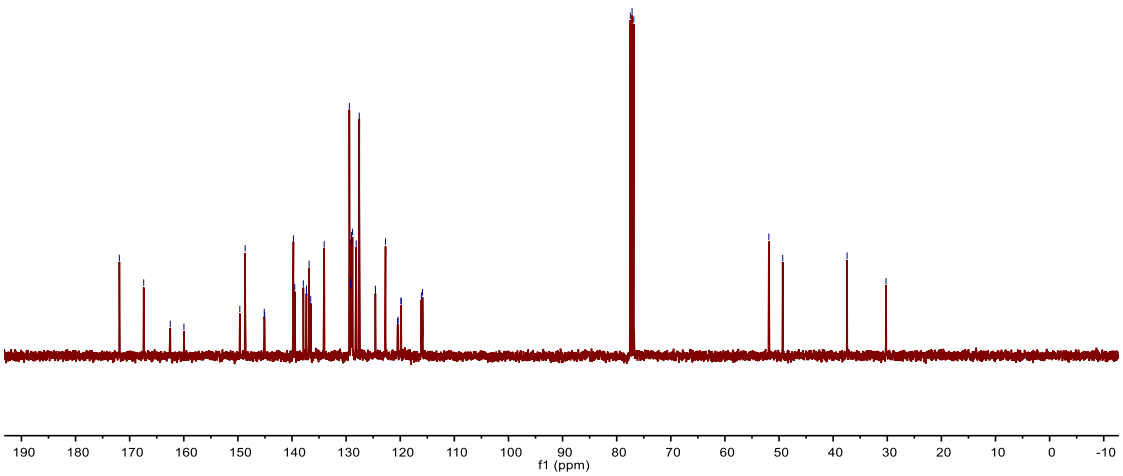

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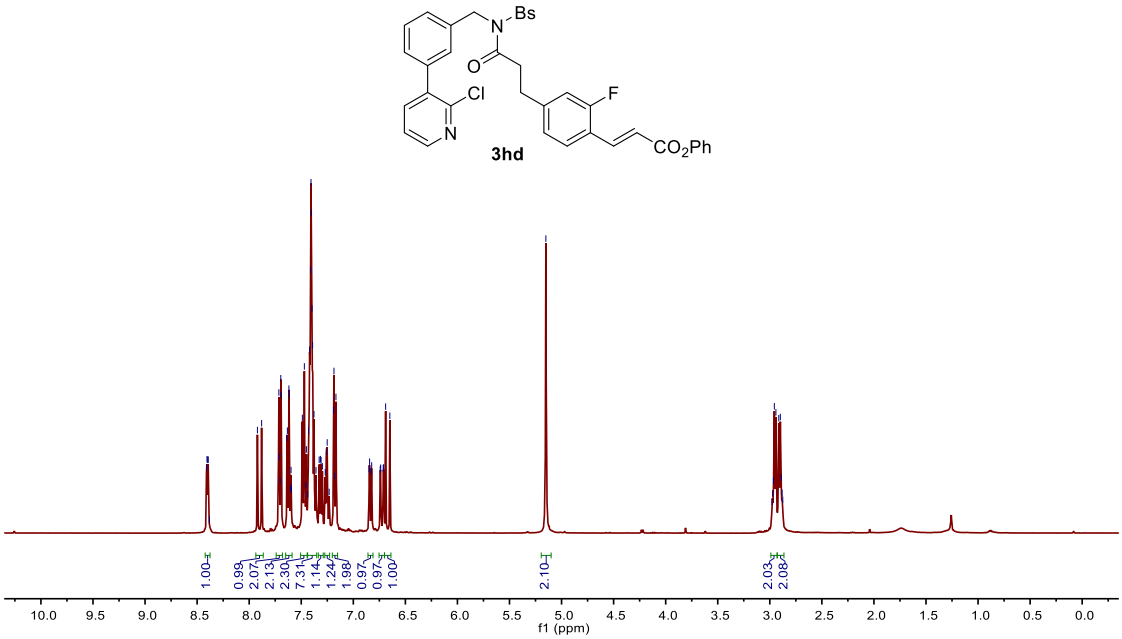

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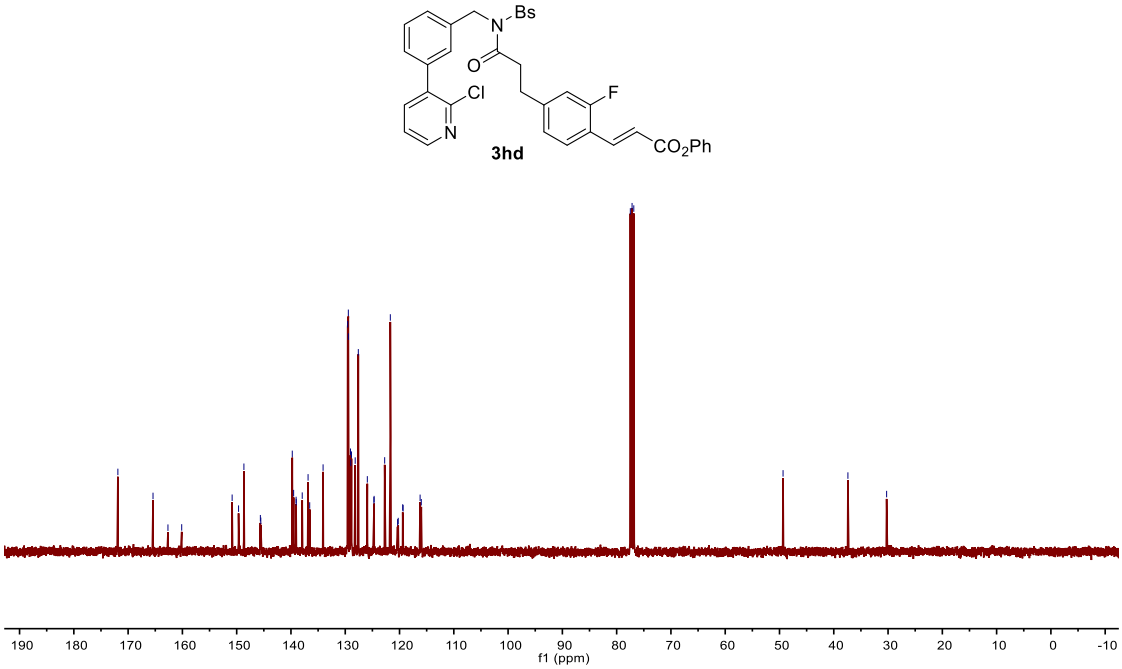

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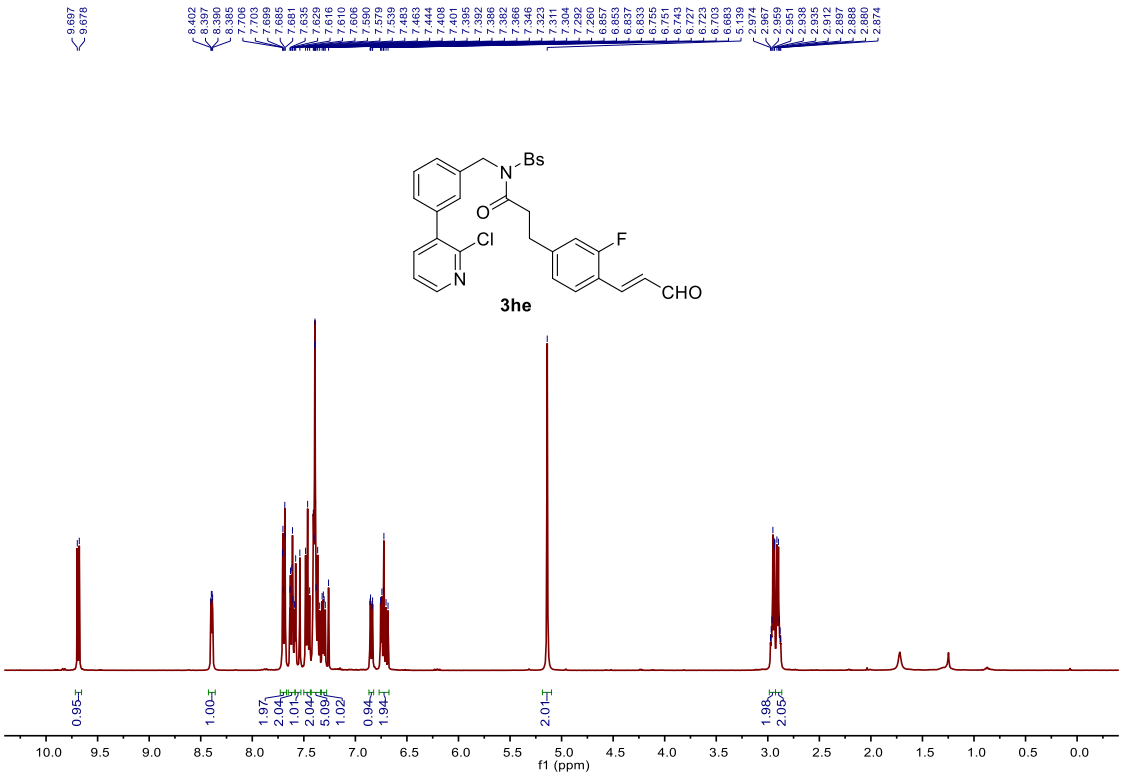

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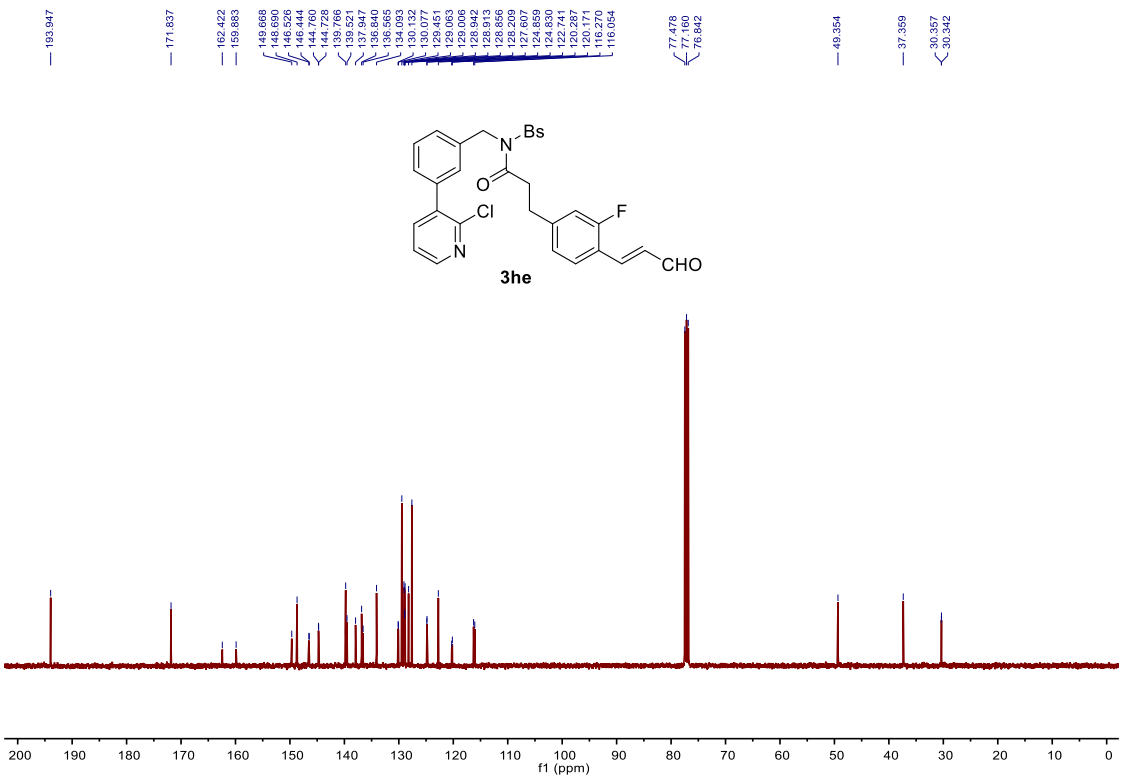

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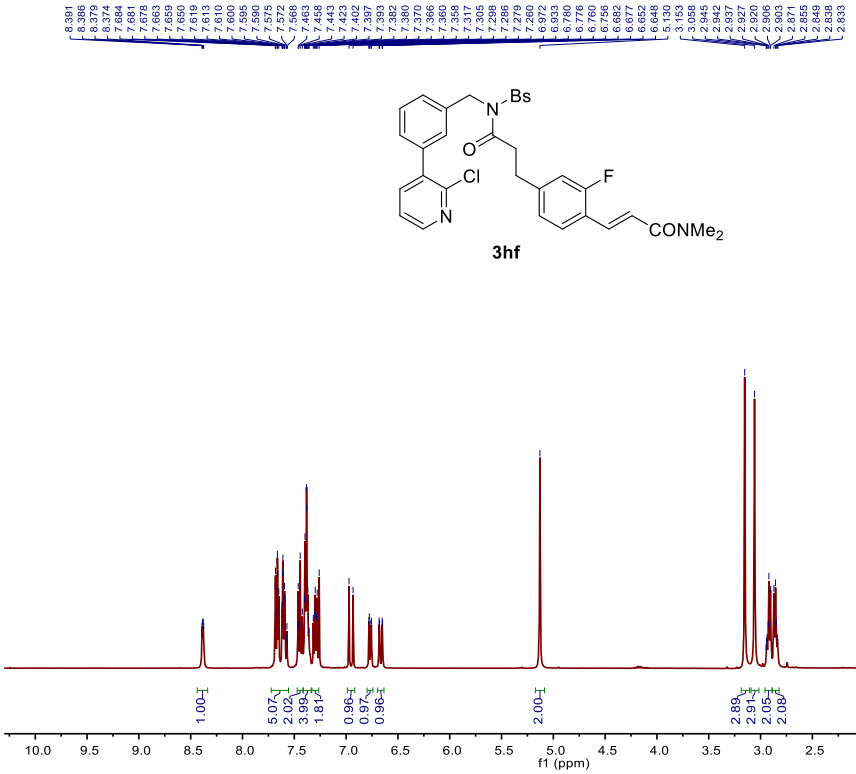

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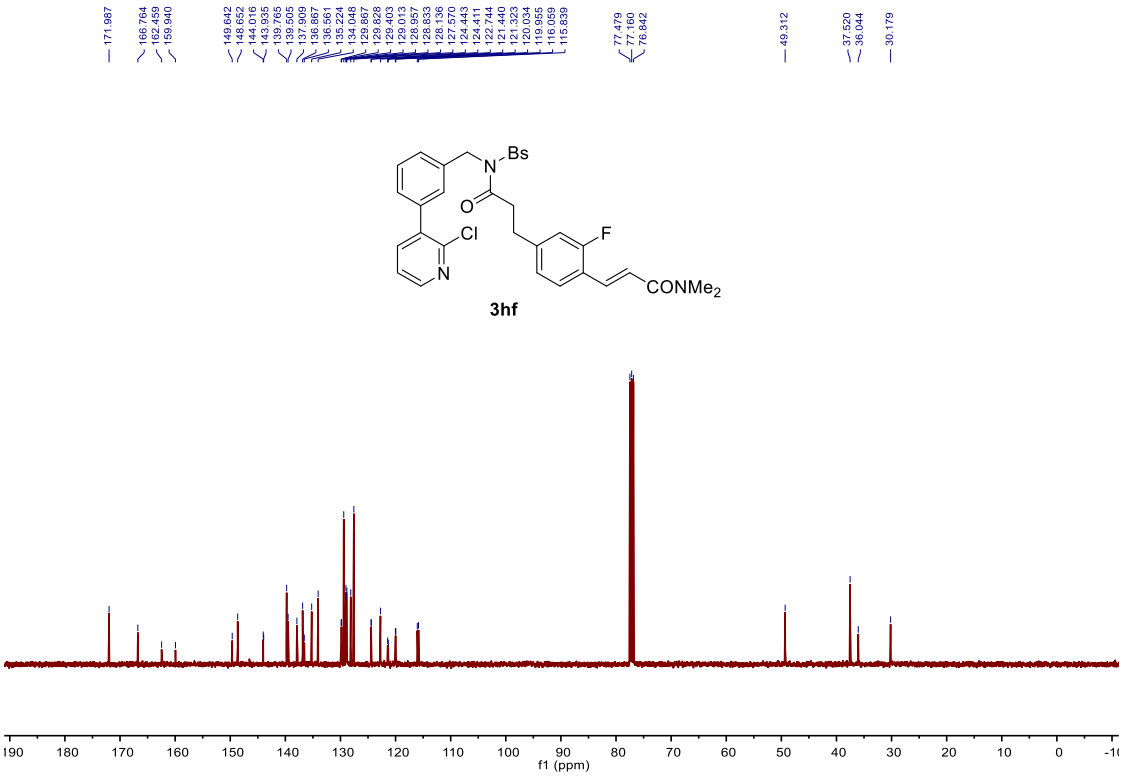

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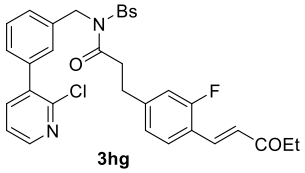

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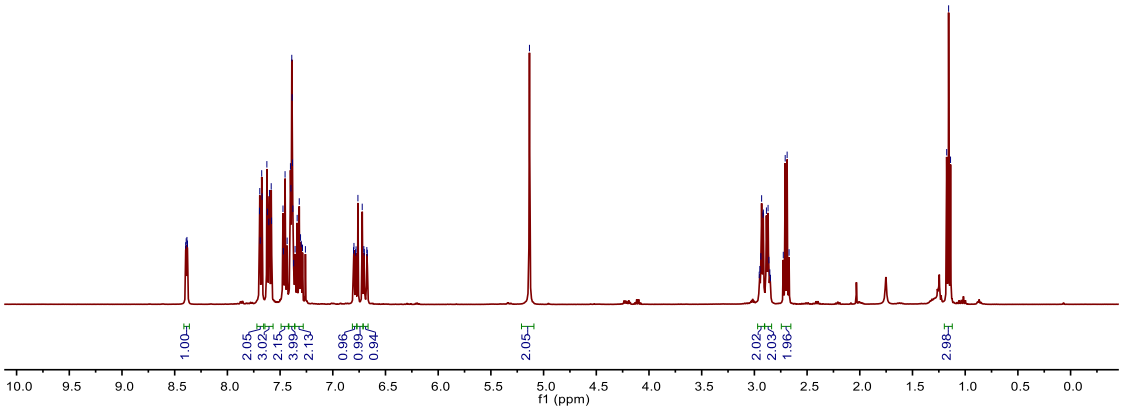

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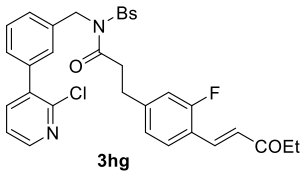

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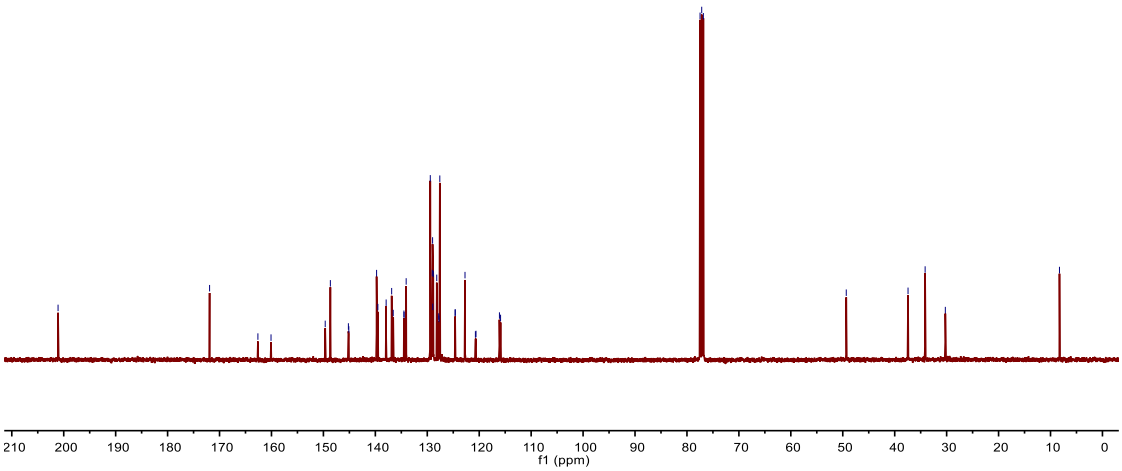

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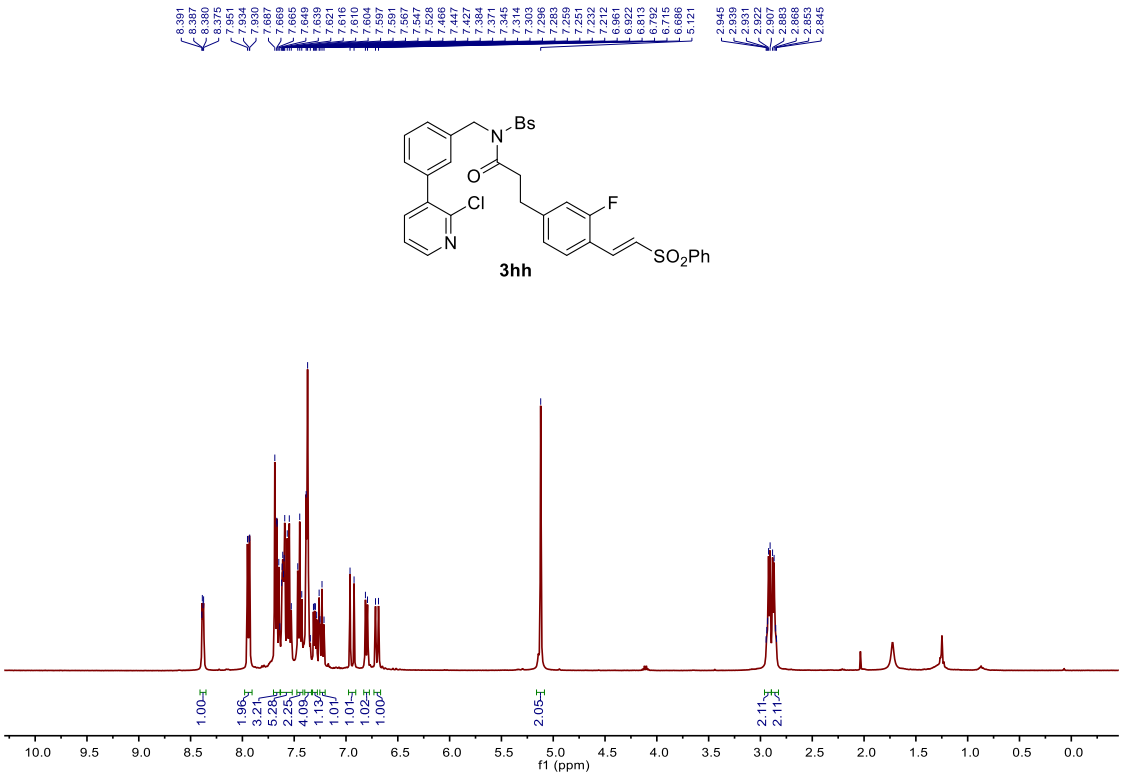

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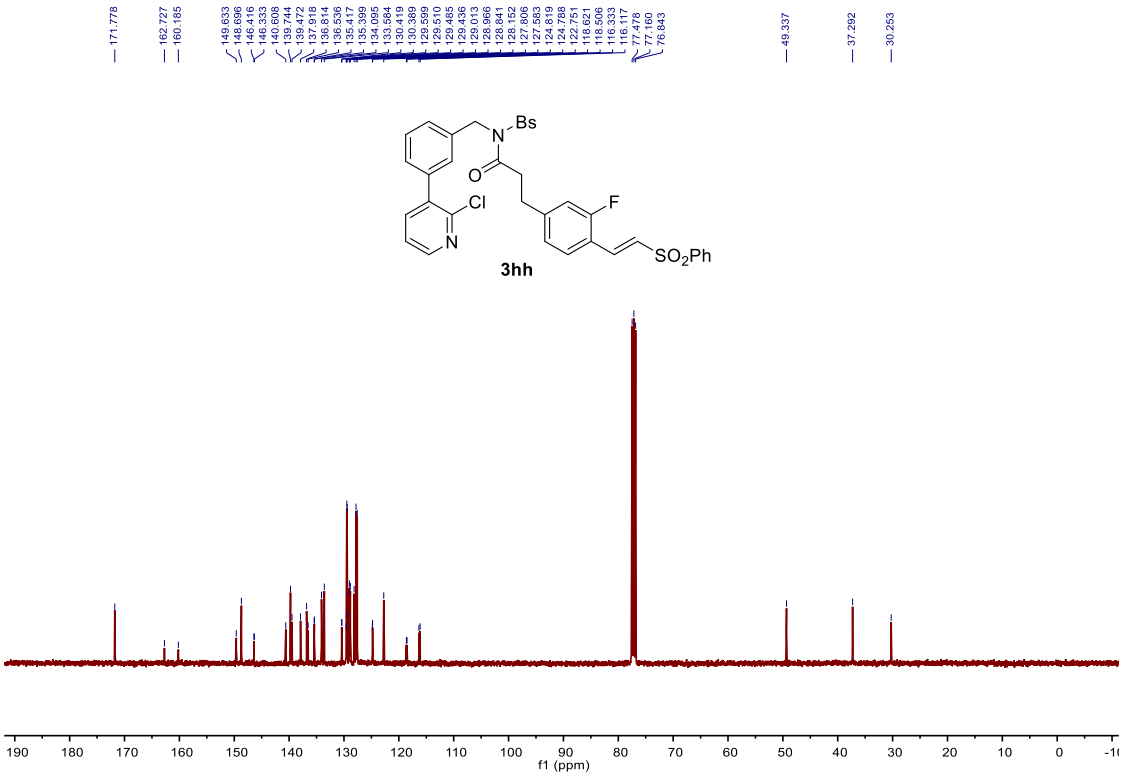

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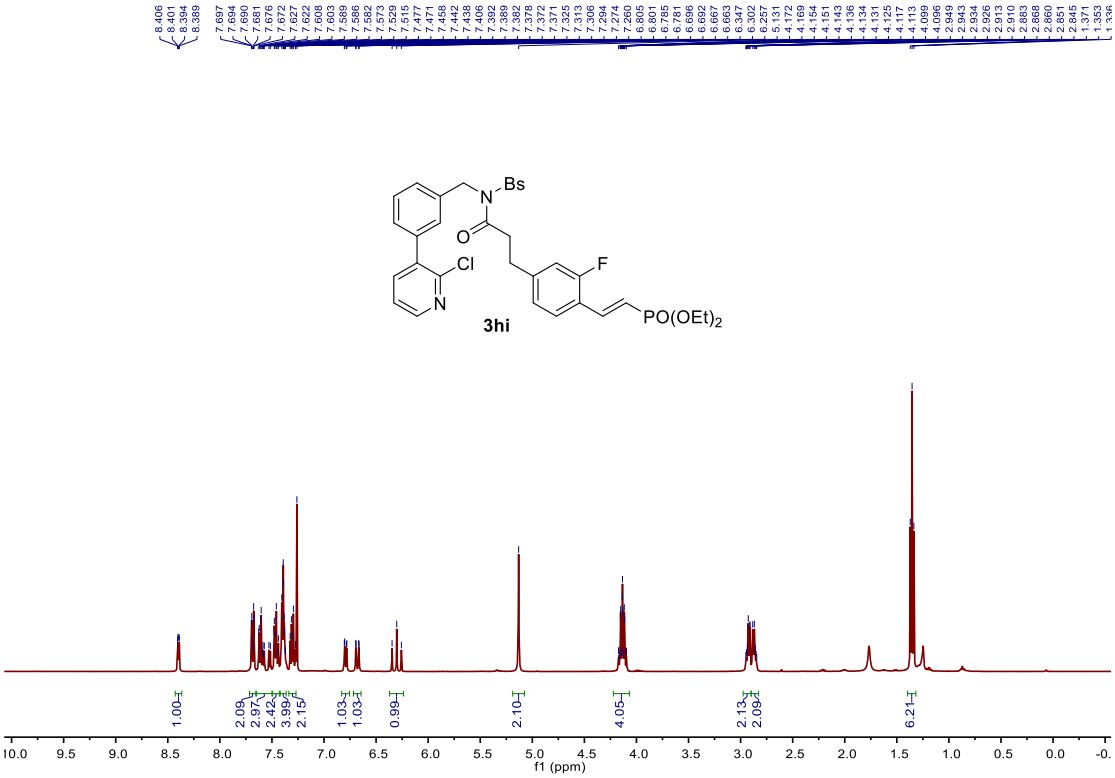

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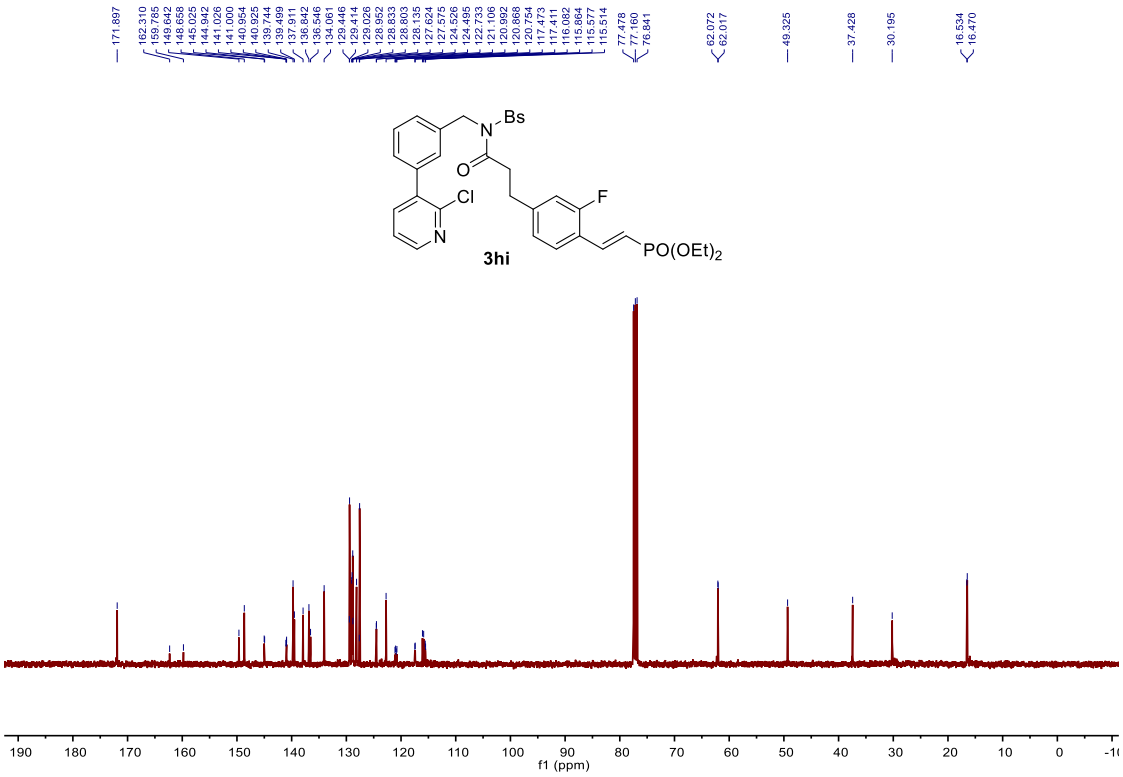

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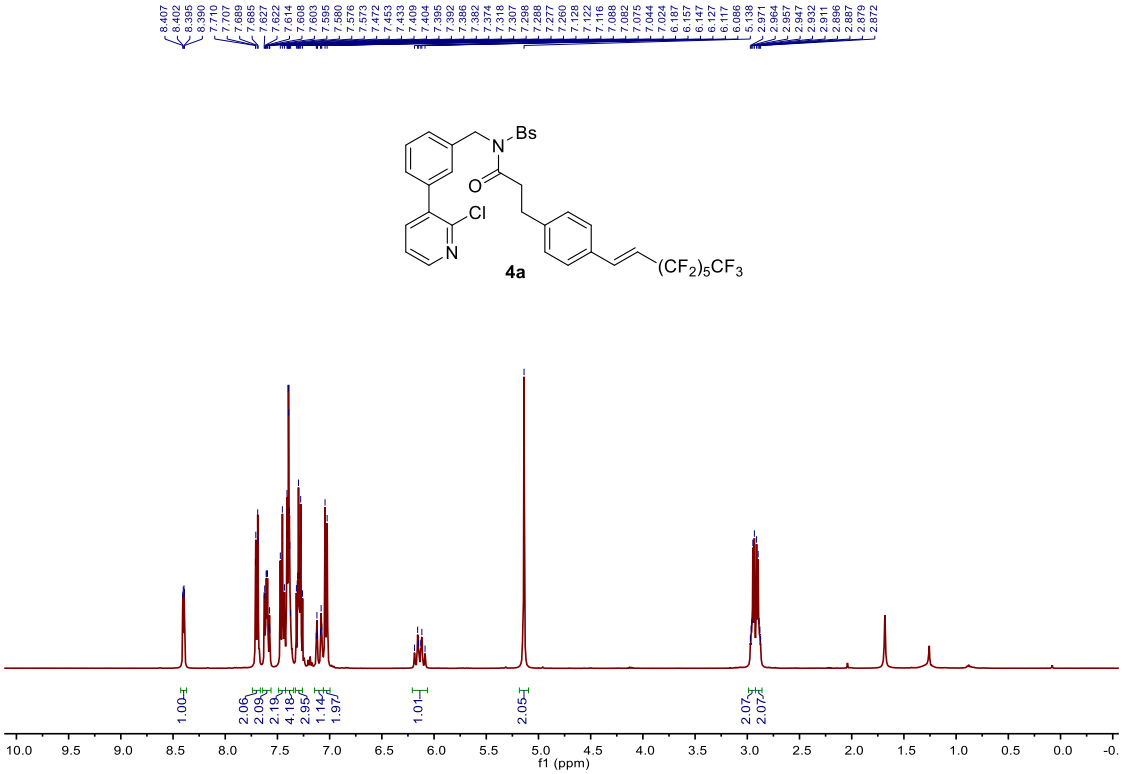

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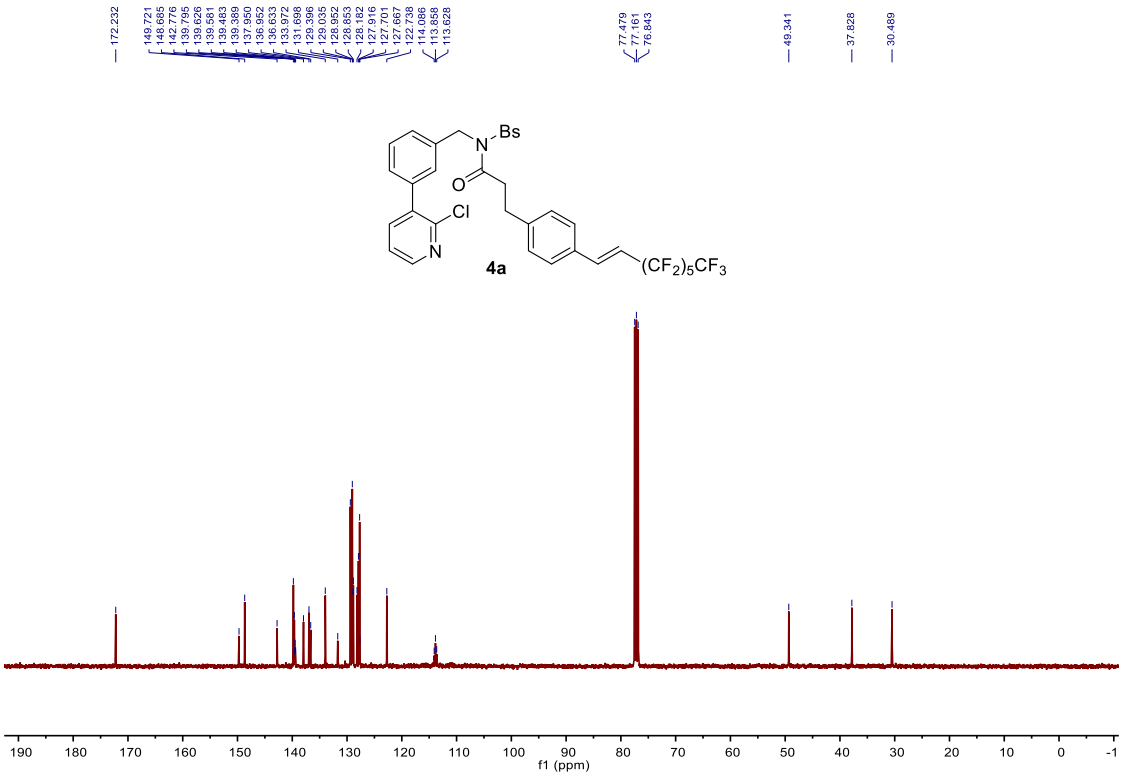
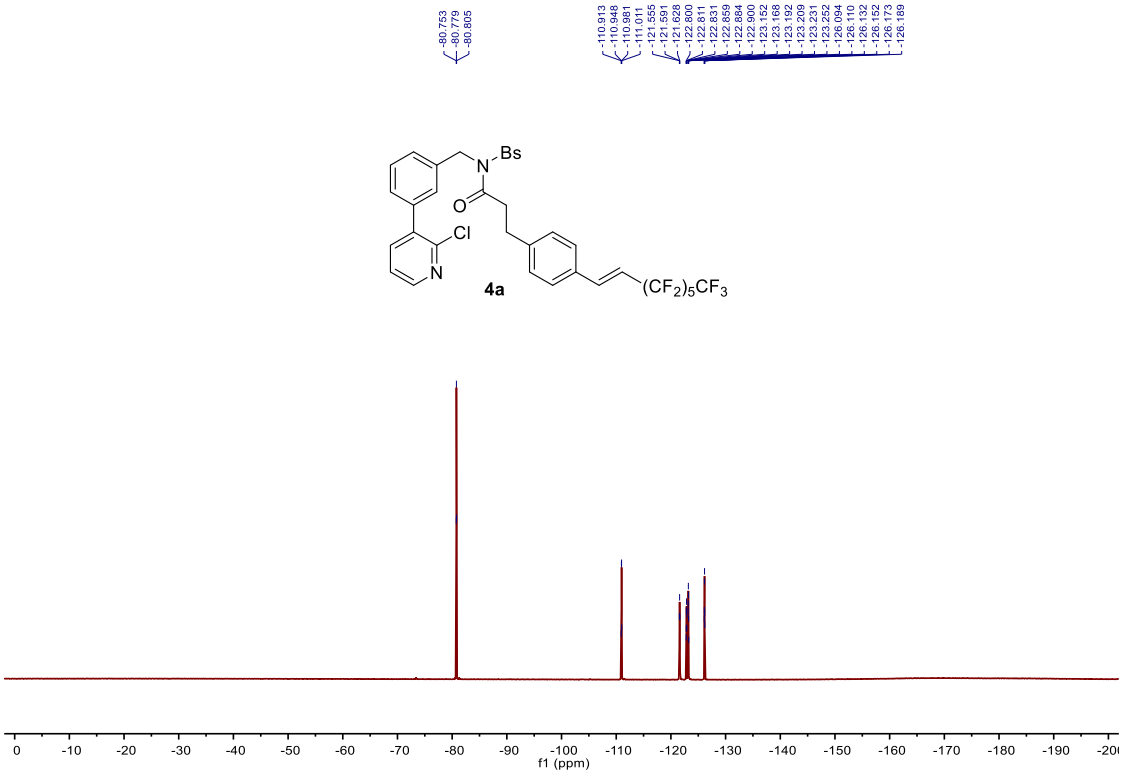
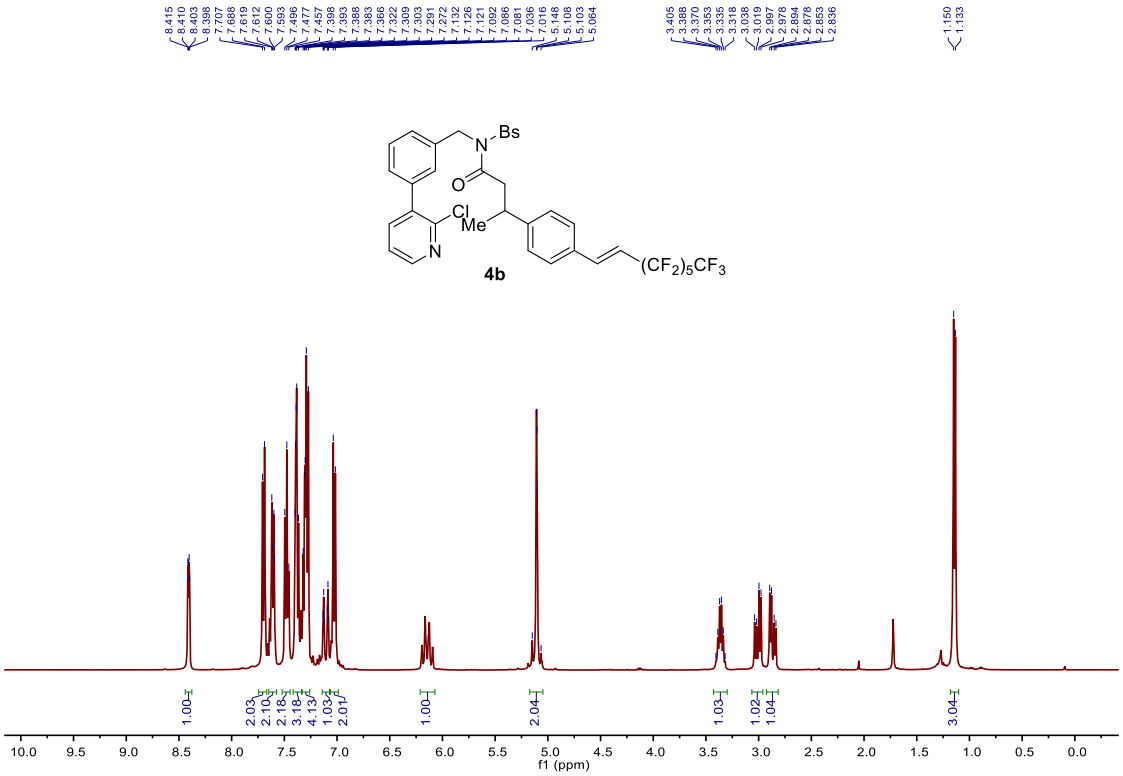


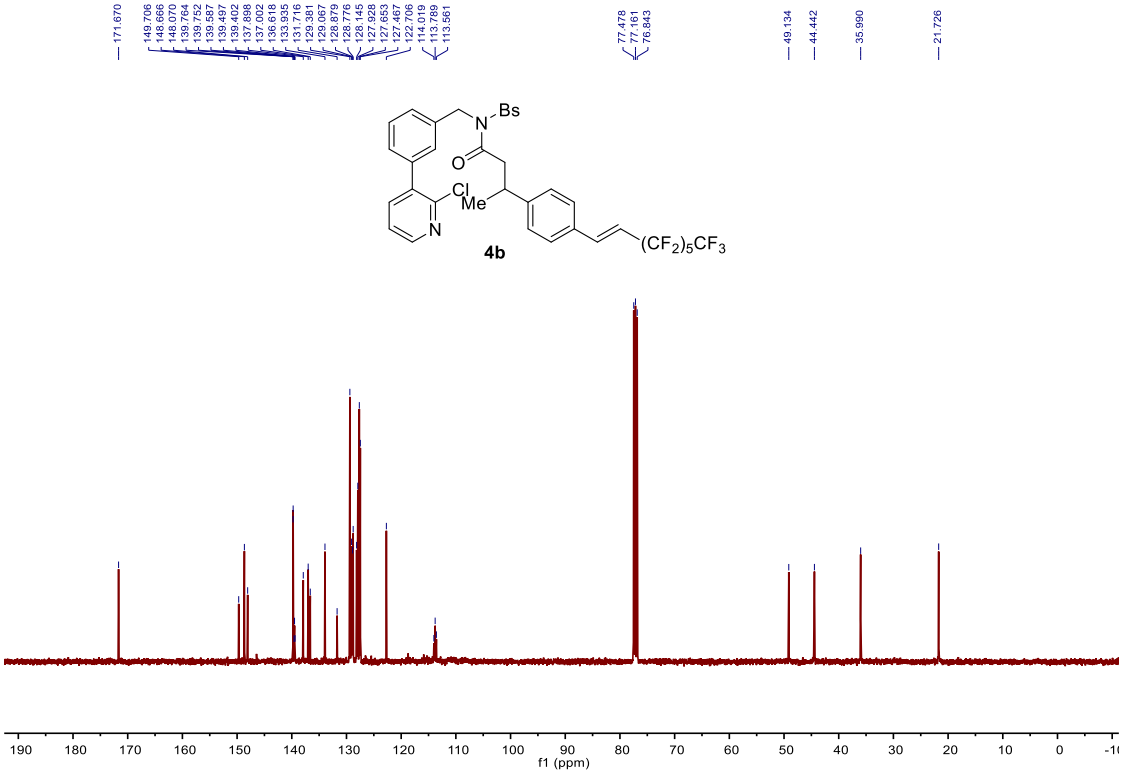
^{19}F NMR (376 MHz, Chloroform-*d*)



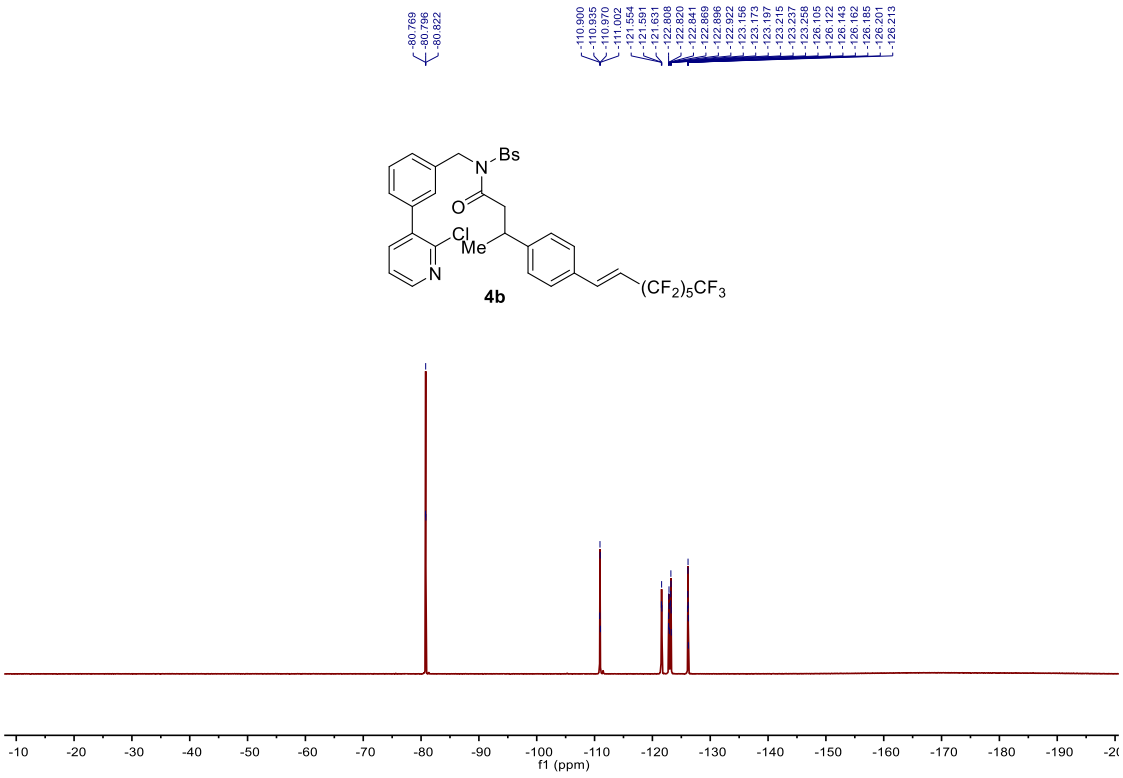
^{1}H NMR (400 MHz, Chloroform-*d*)



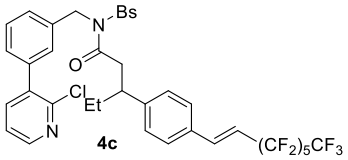
^{13}C NMR (101 MHz, Chloroform-*d*)

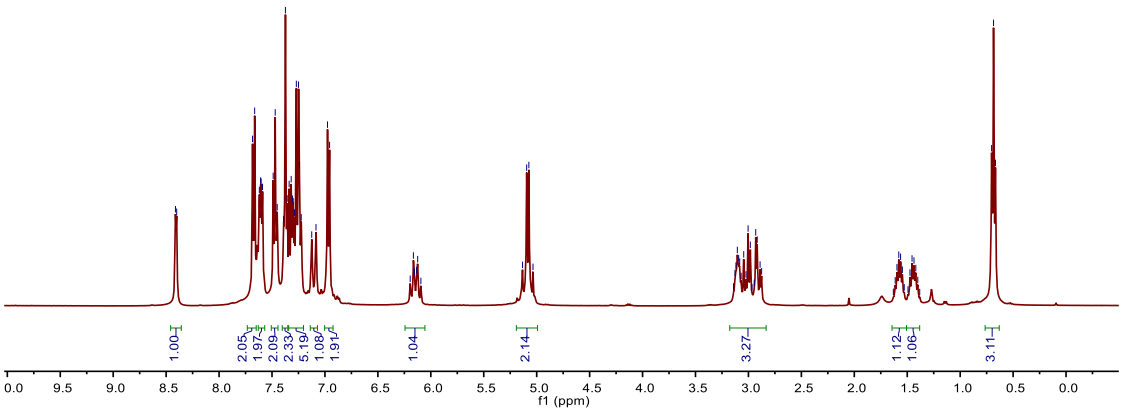


^{19}F NMR (376 MHz, Chloroform-*d*)

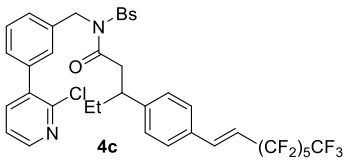


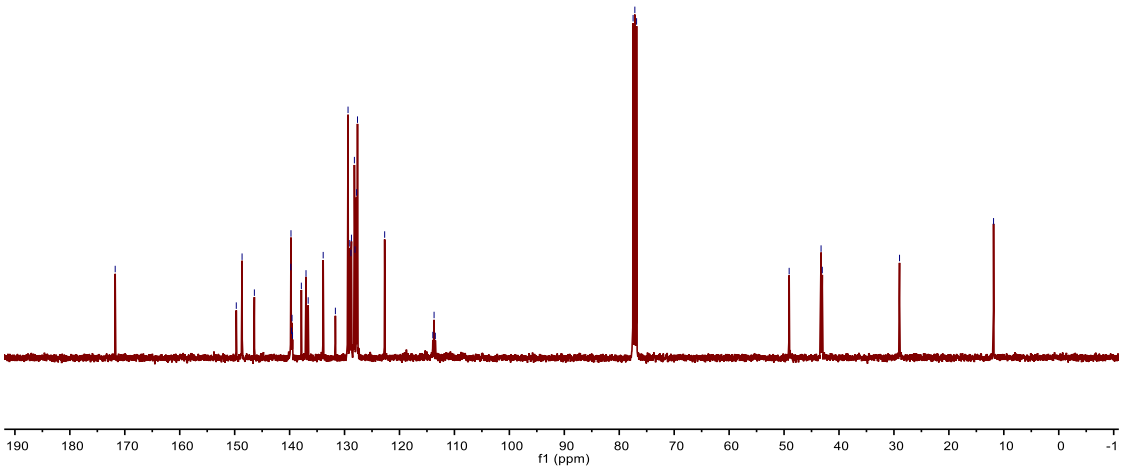
^{1}H NMR (400 MHz, Chloroform-*d*)





^{13}C NMR (101 MHz, Chloroform-*d*)





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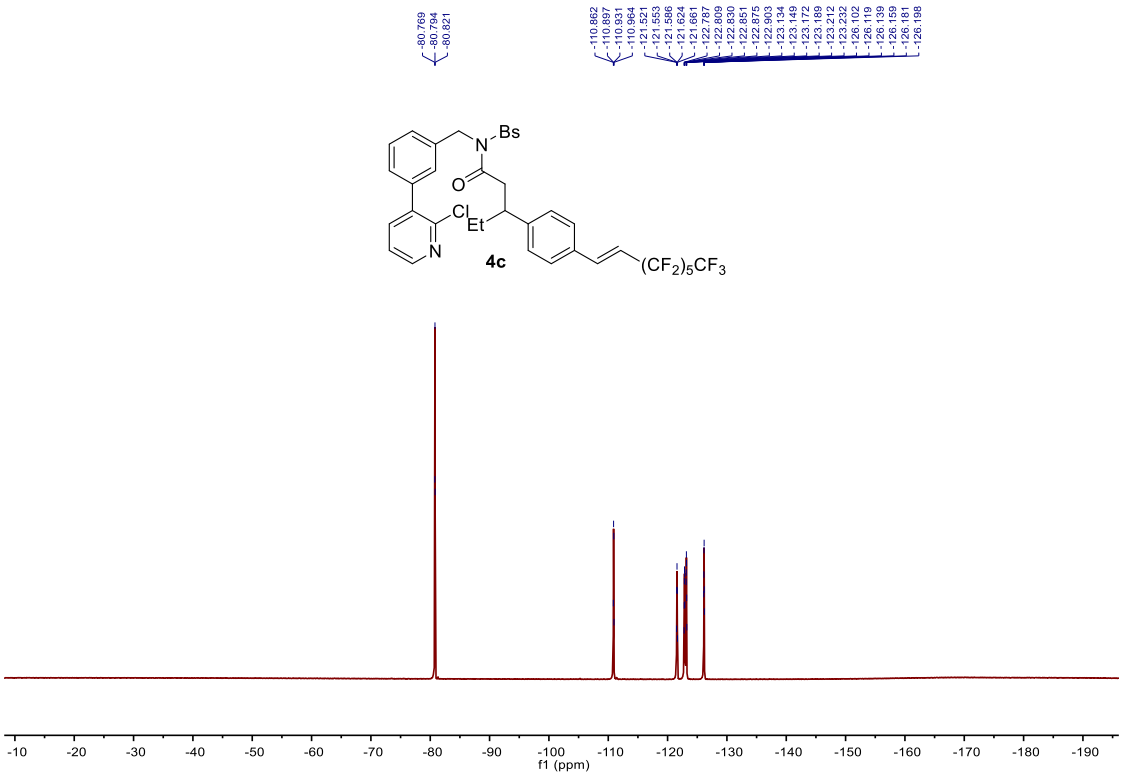

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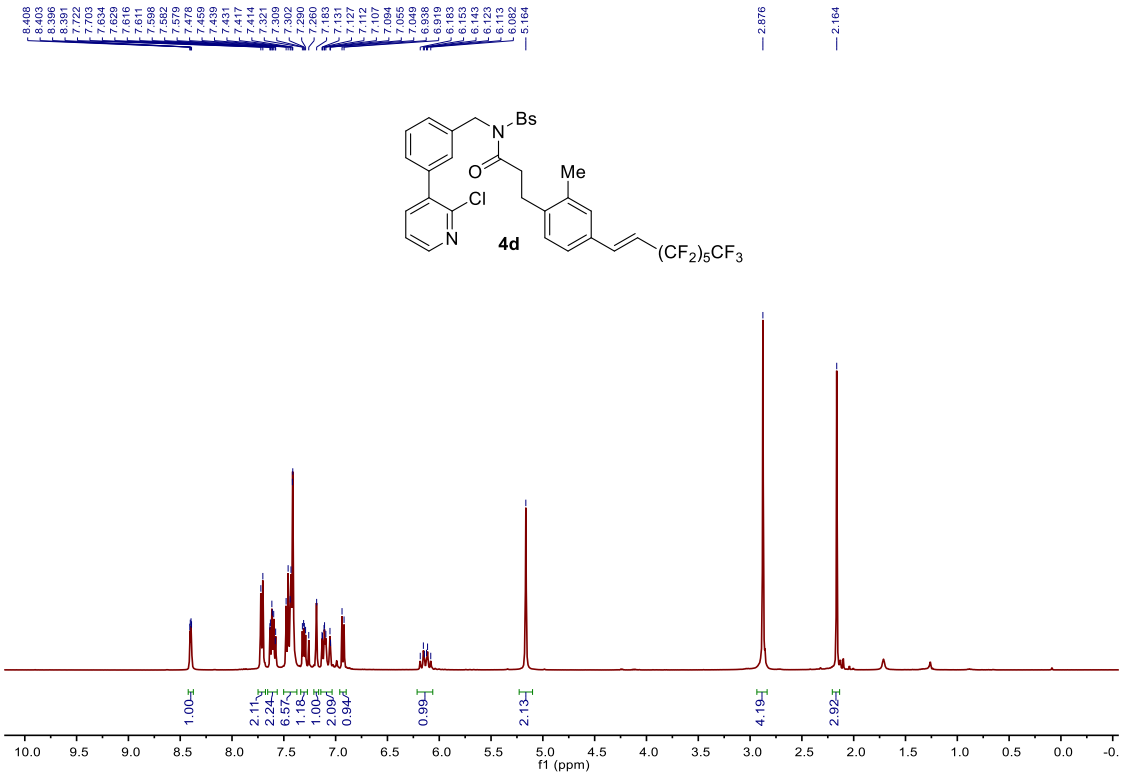

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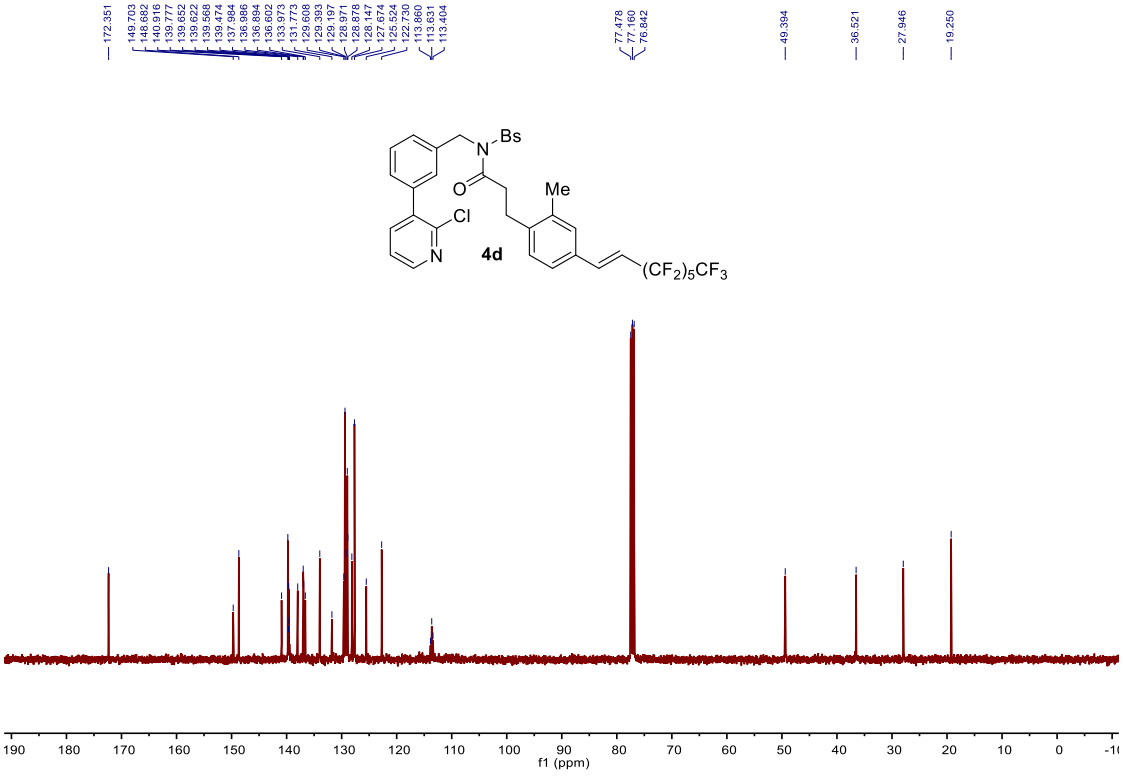

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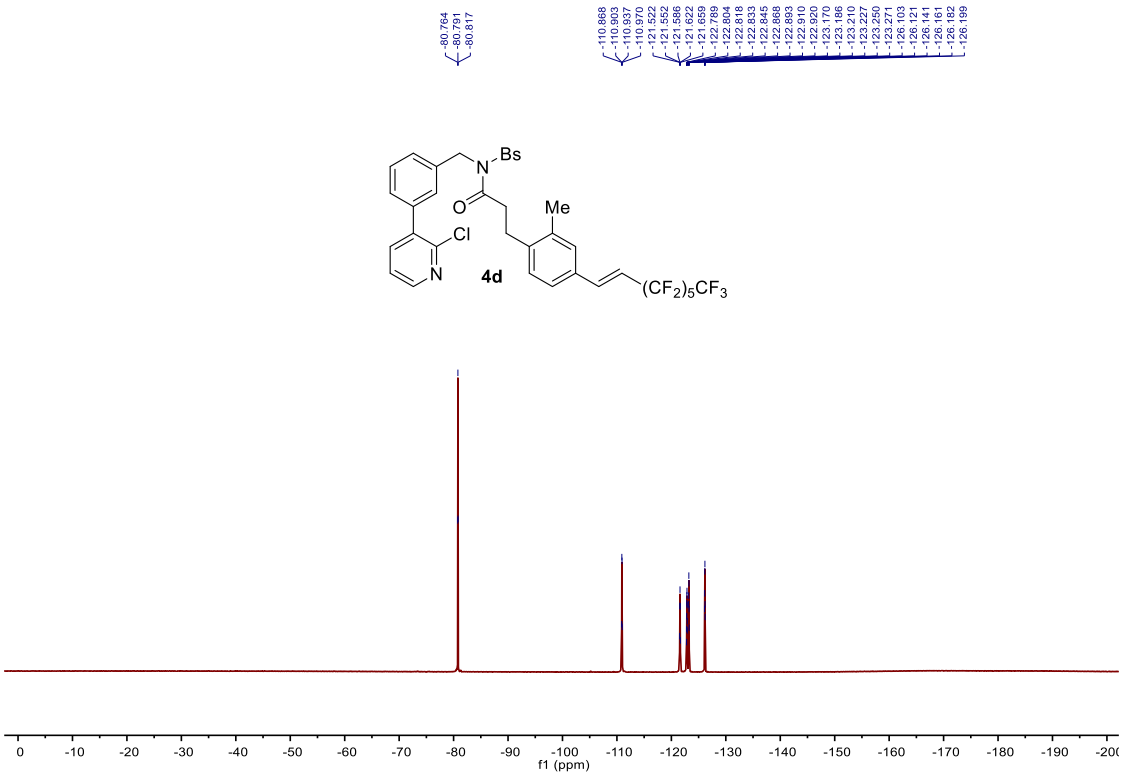

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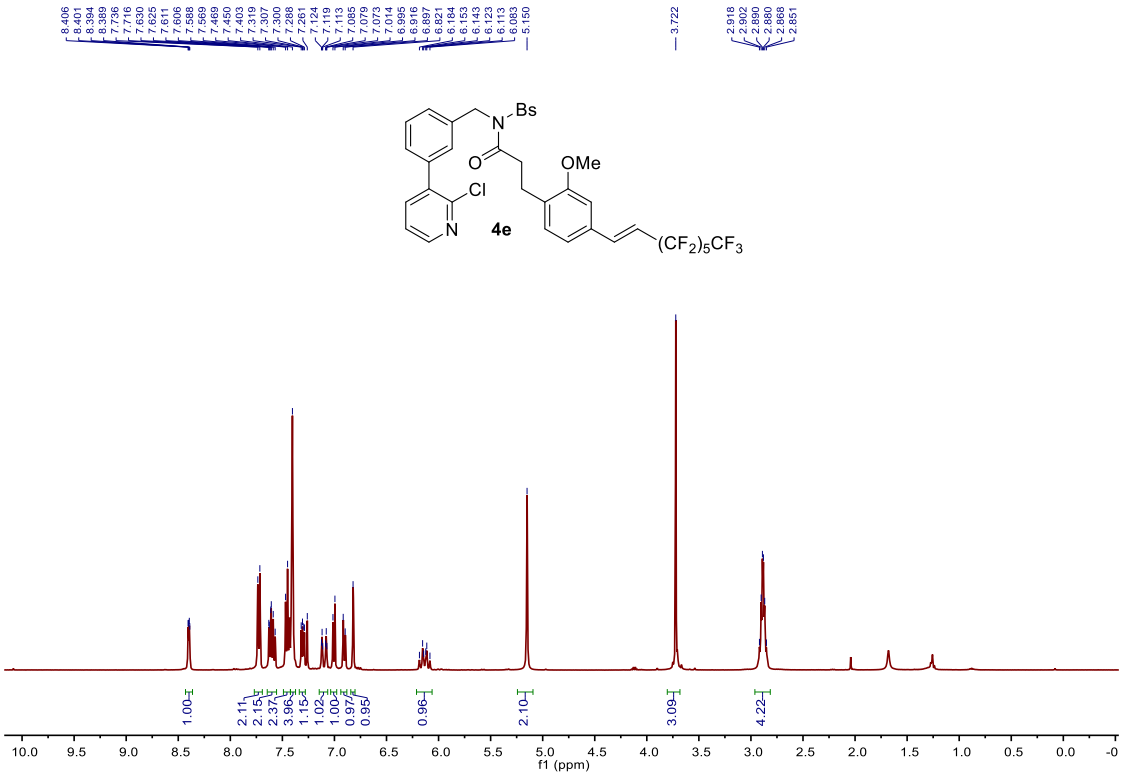

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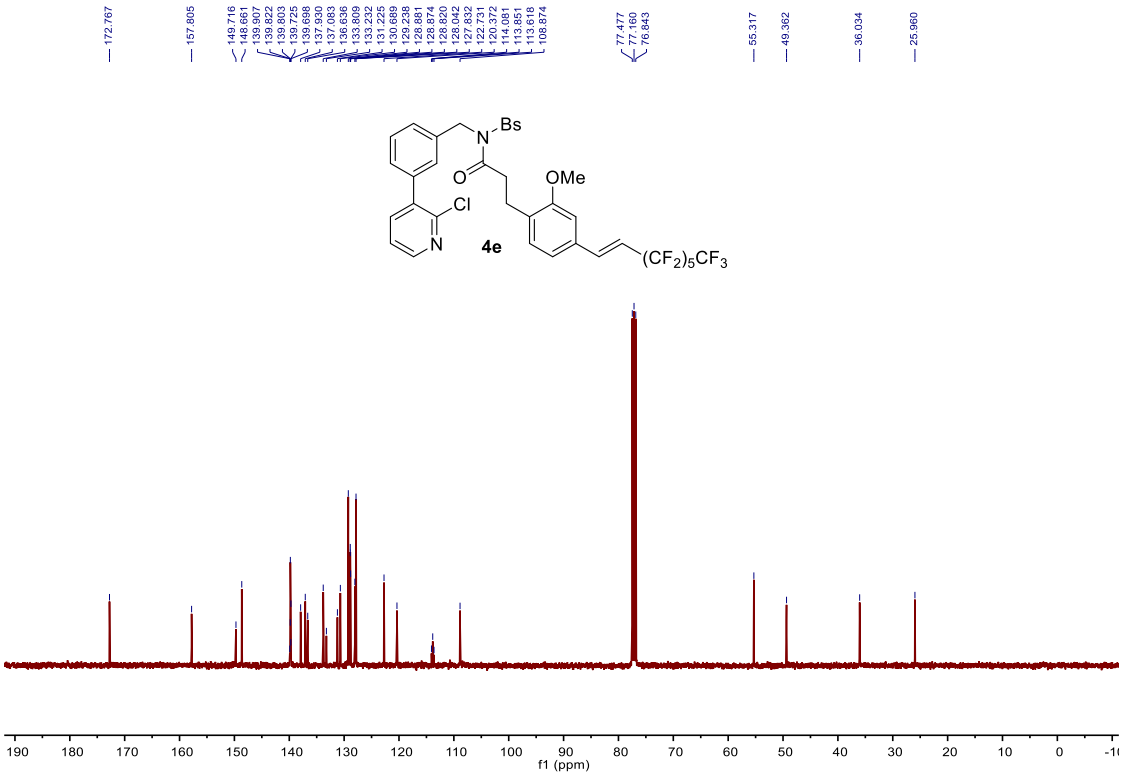

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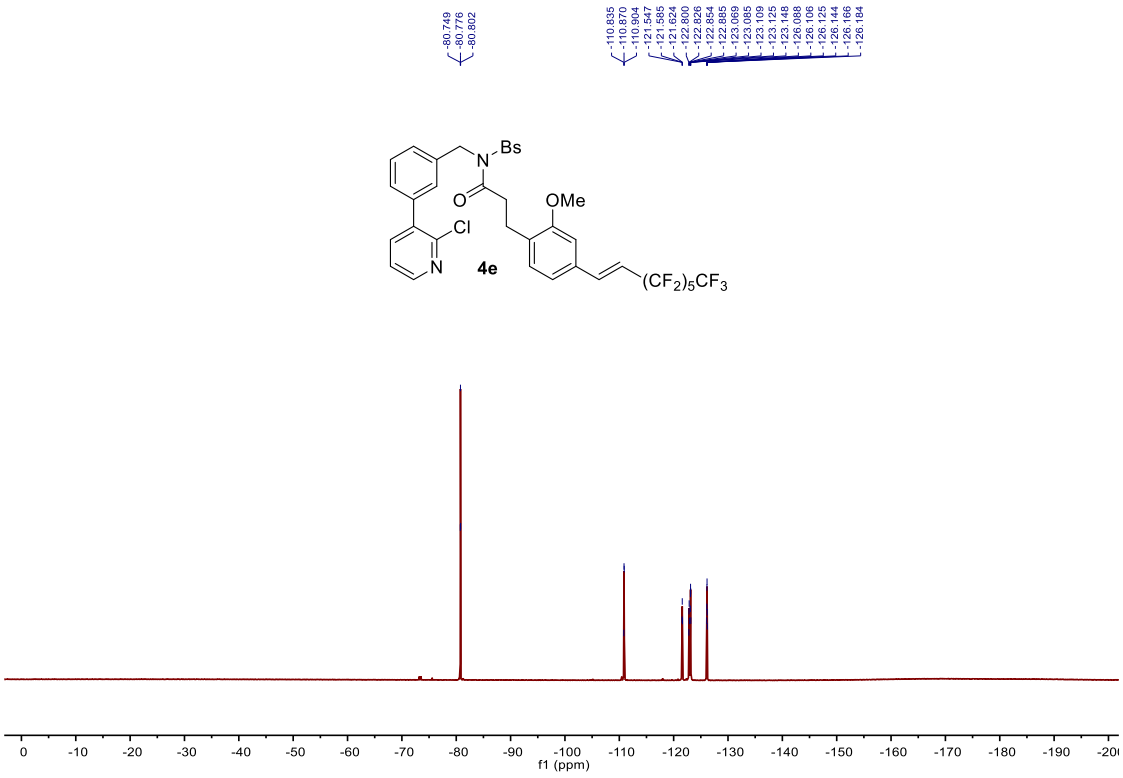

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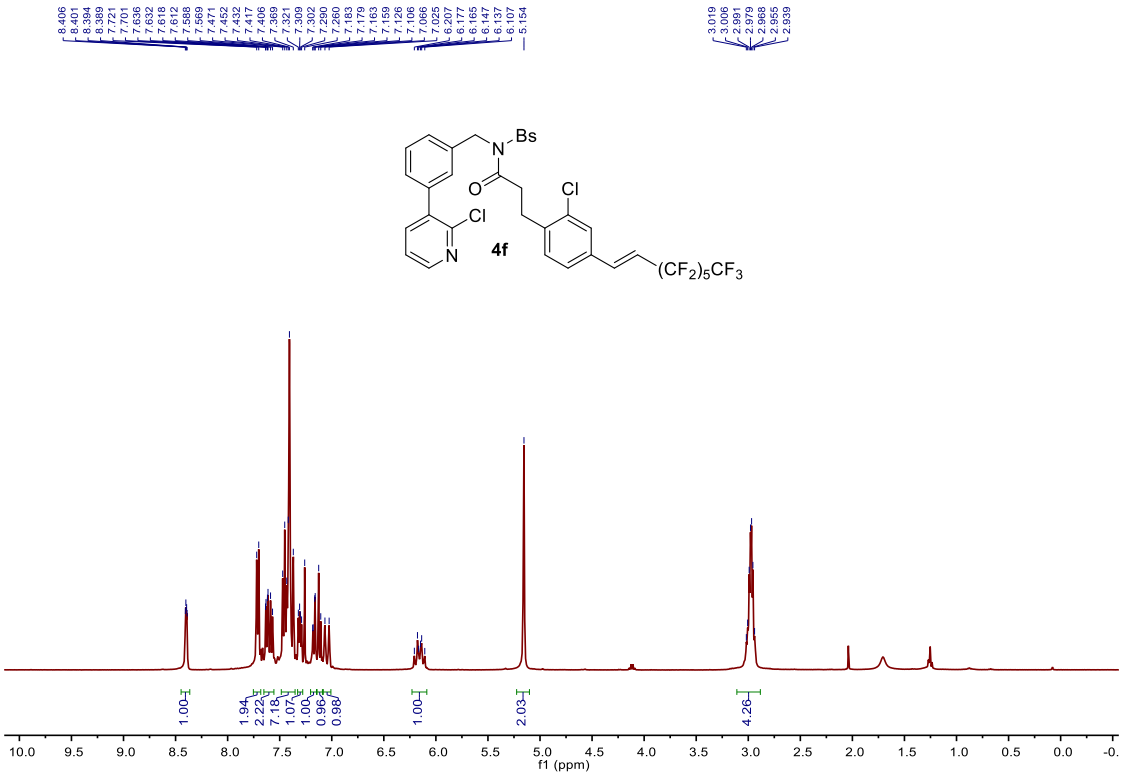

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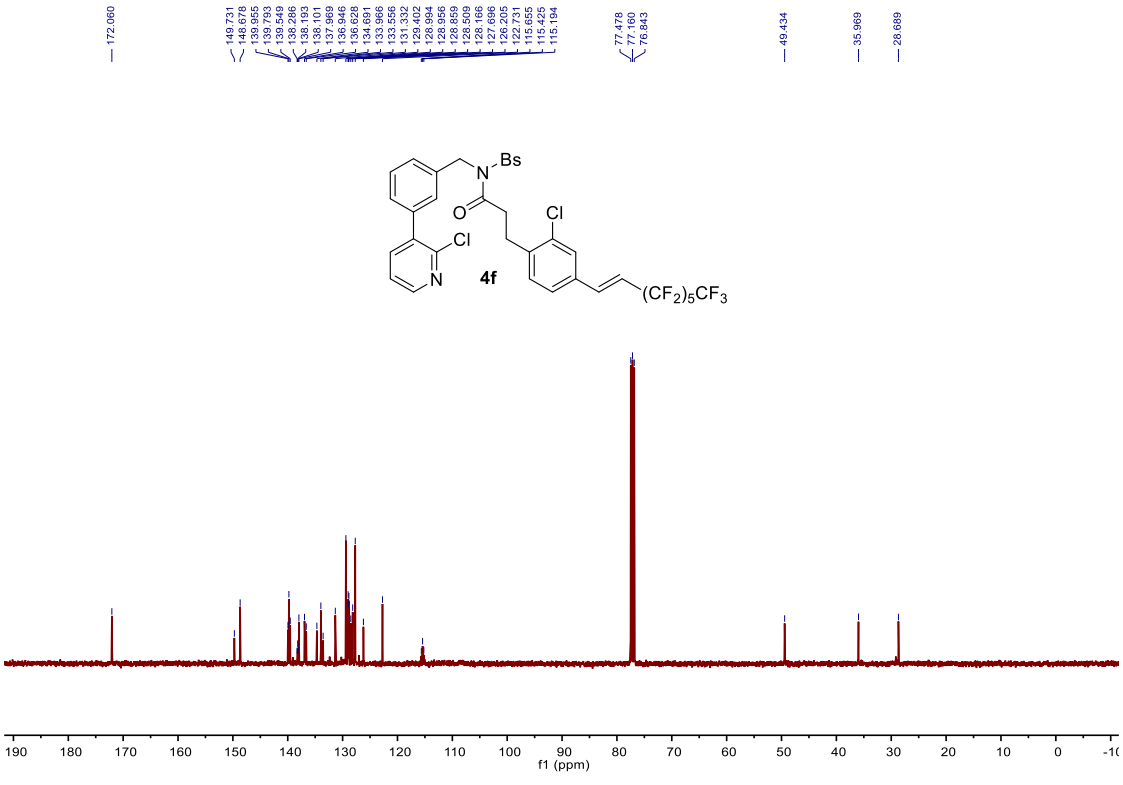

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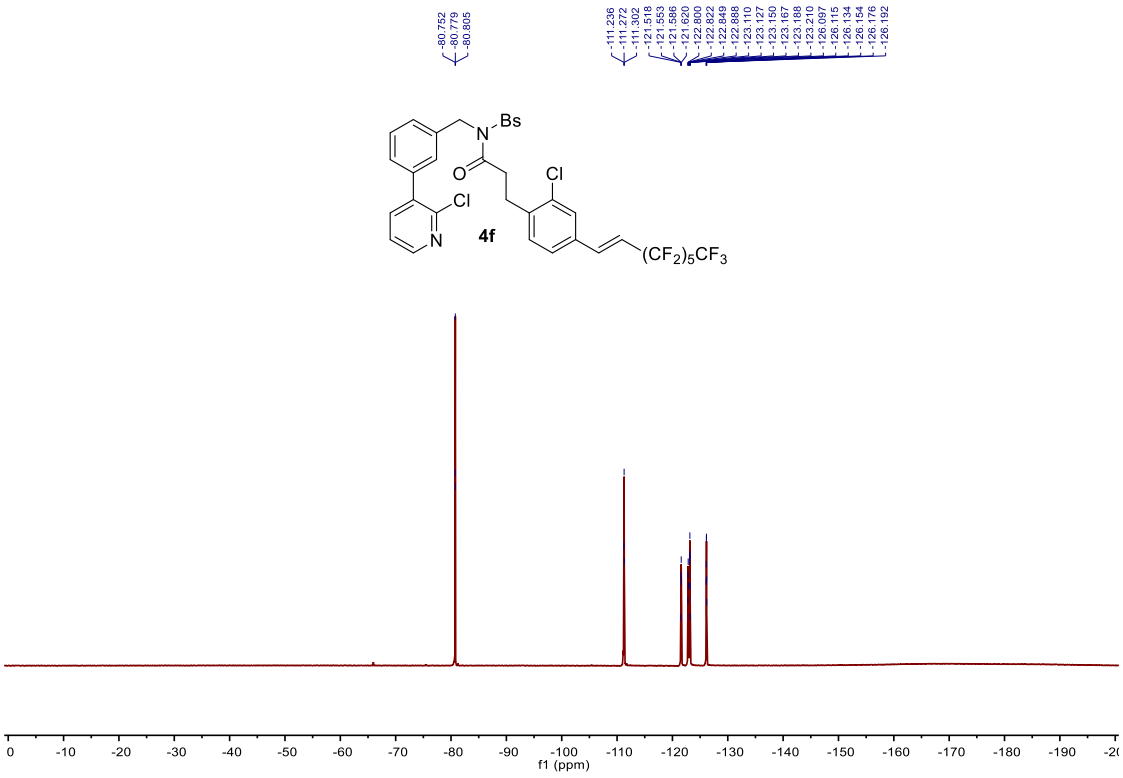

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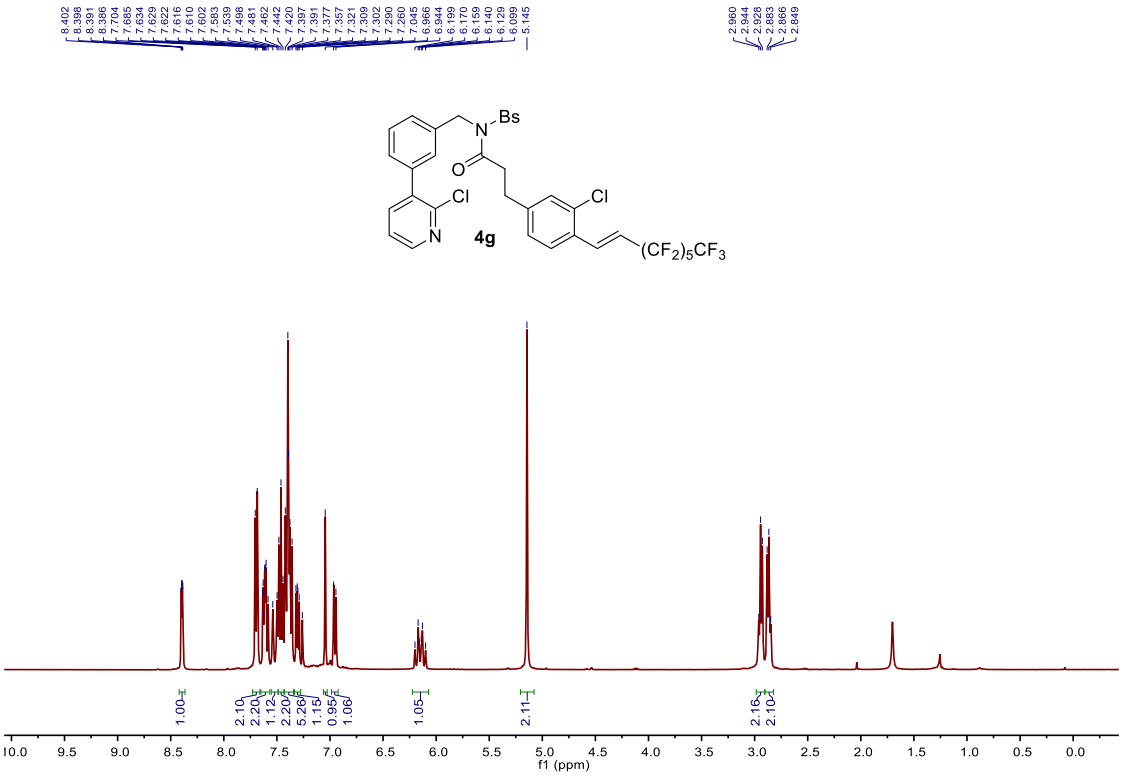

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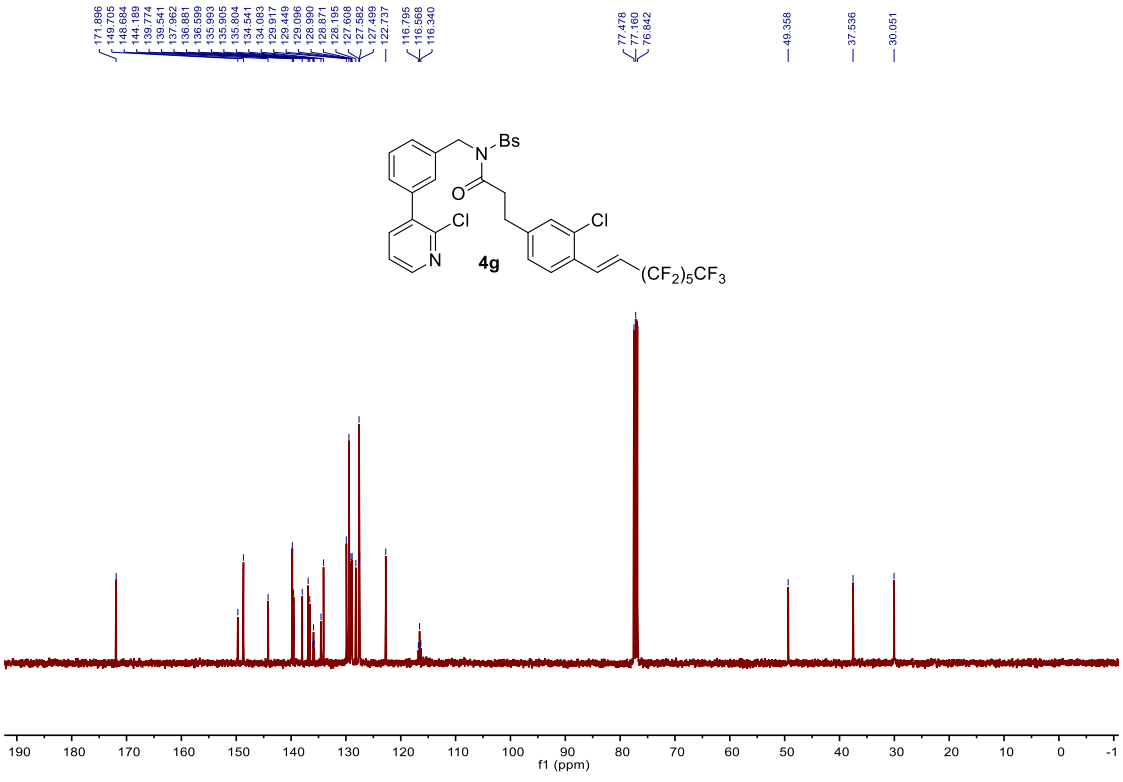

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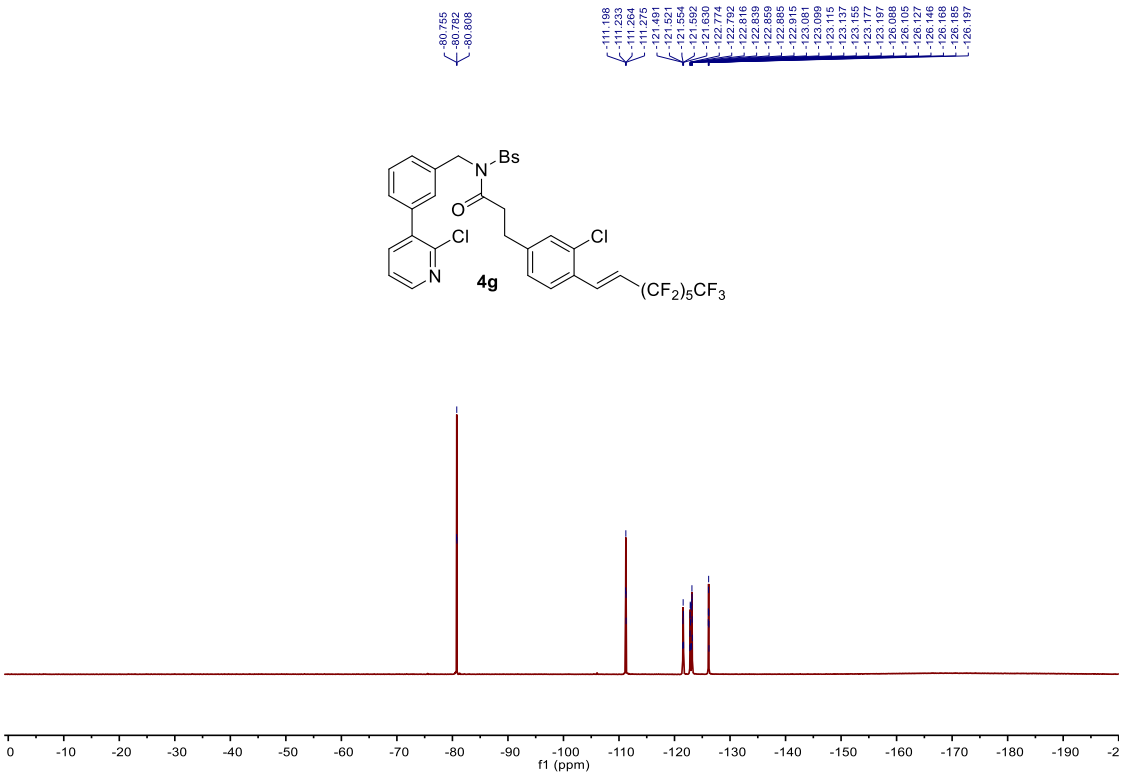

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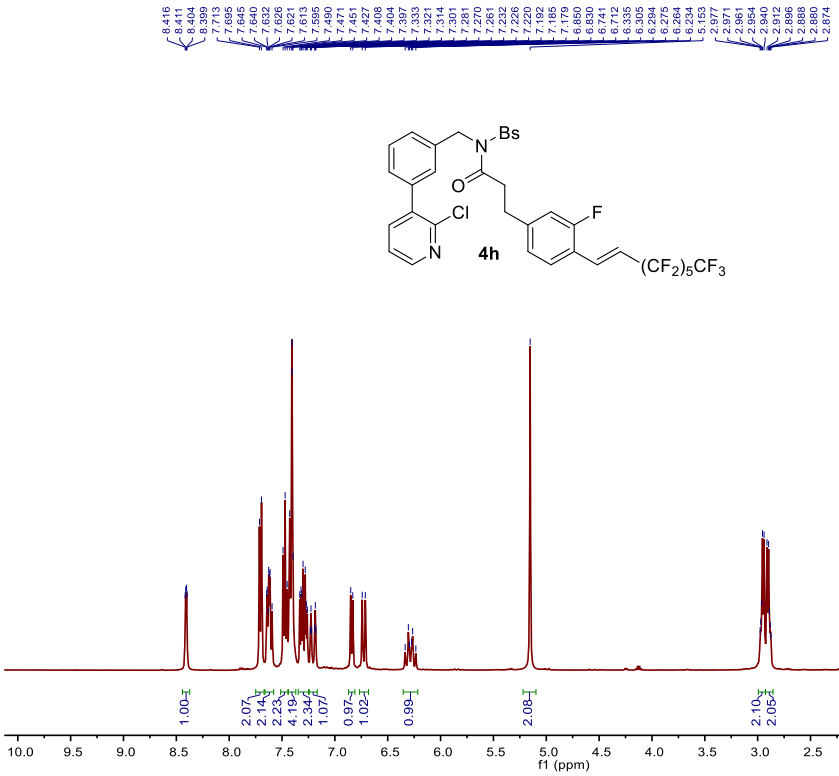

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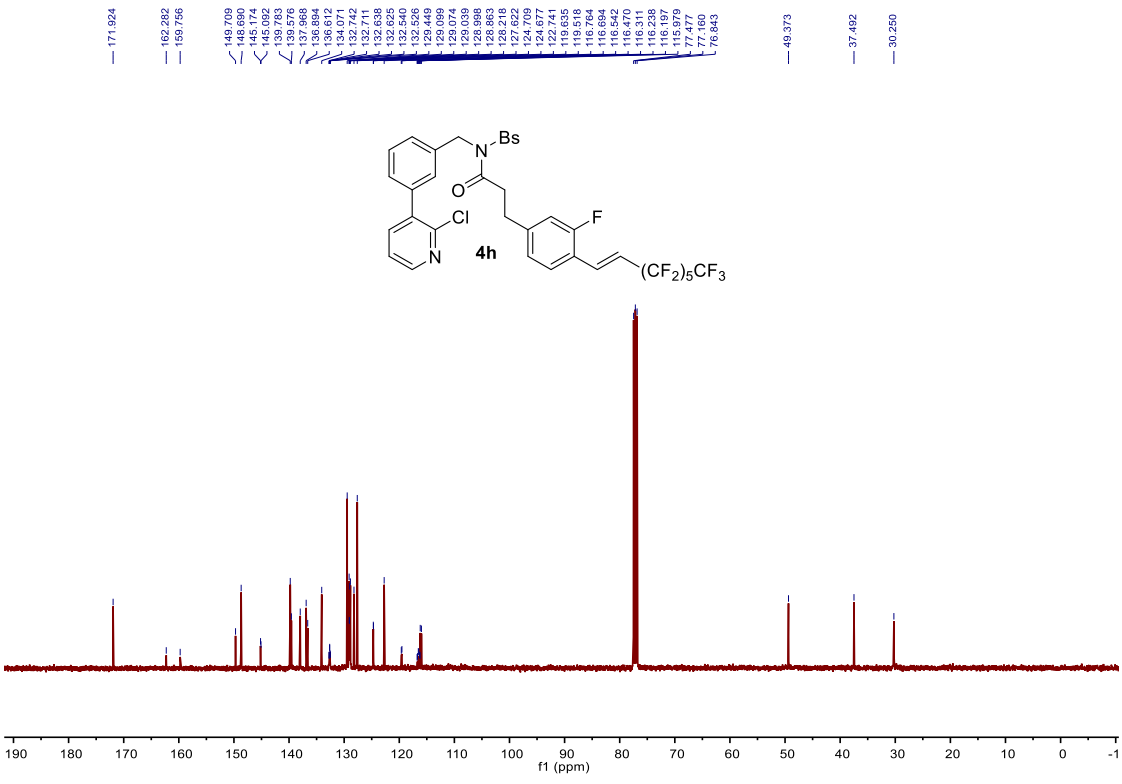

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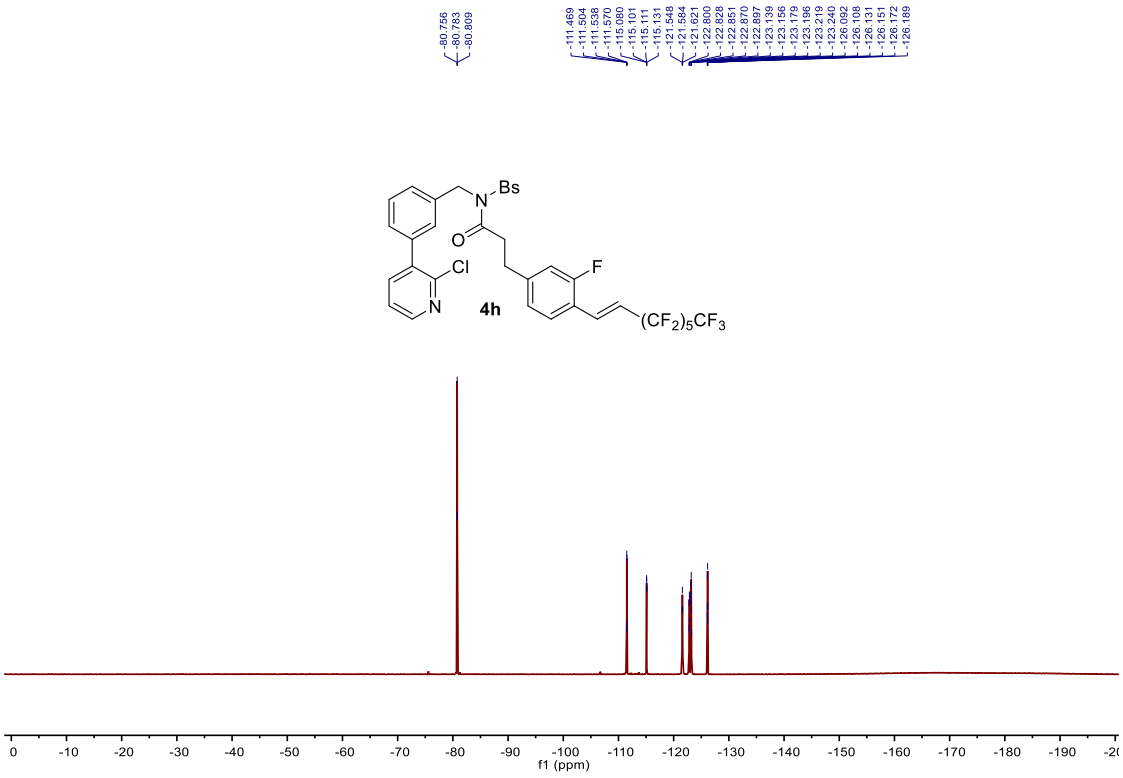

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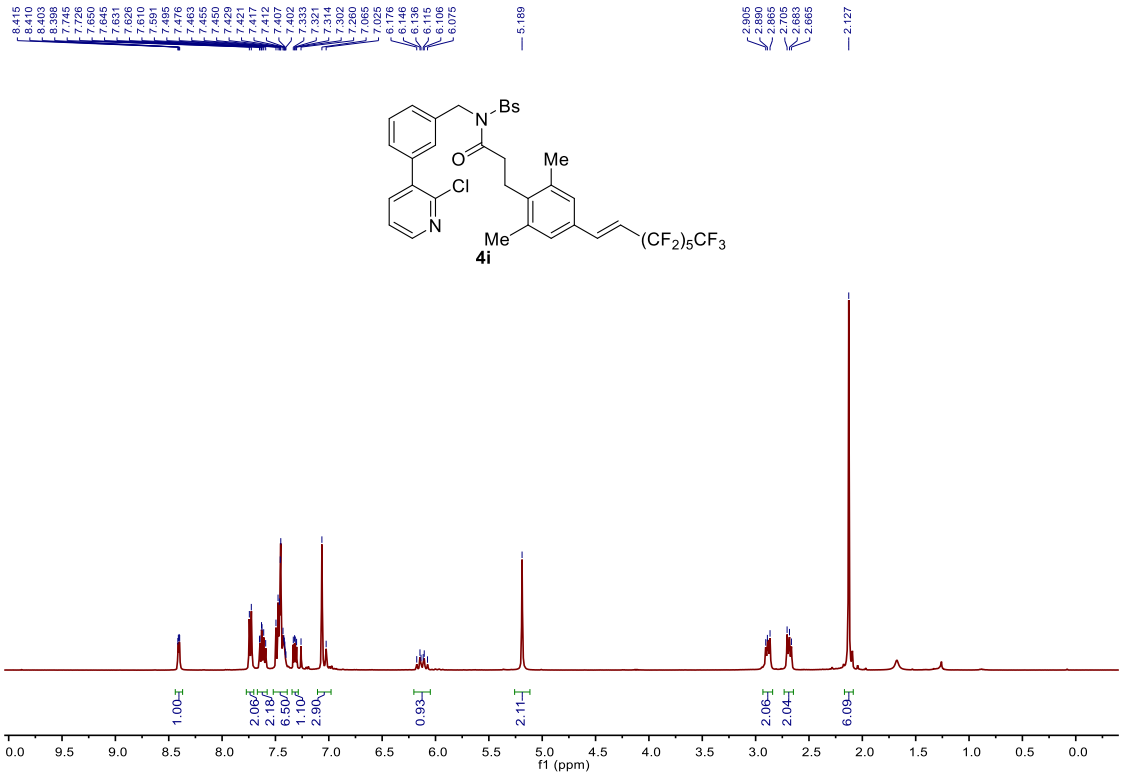

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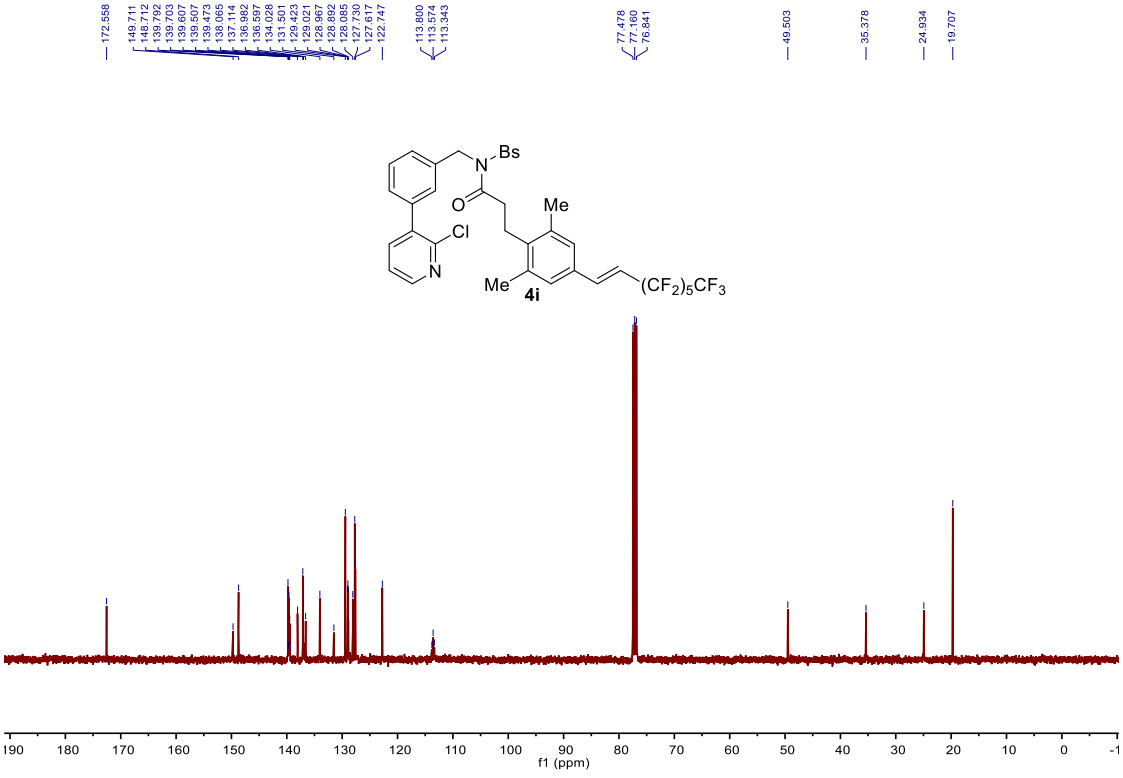
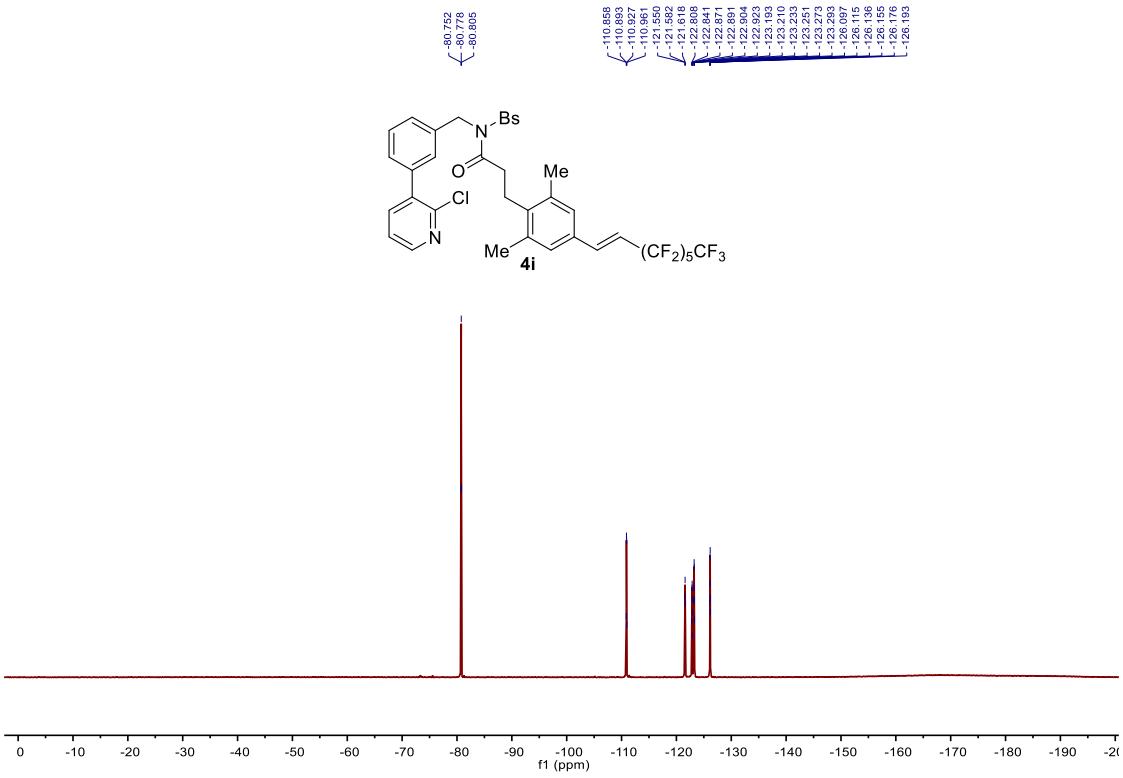
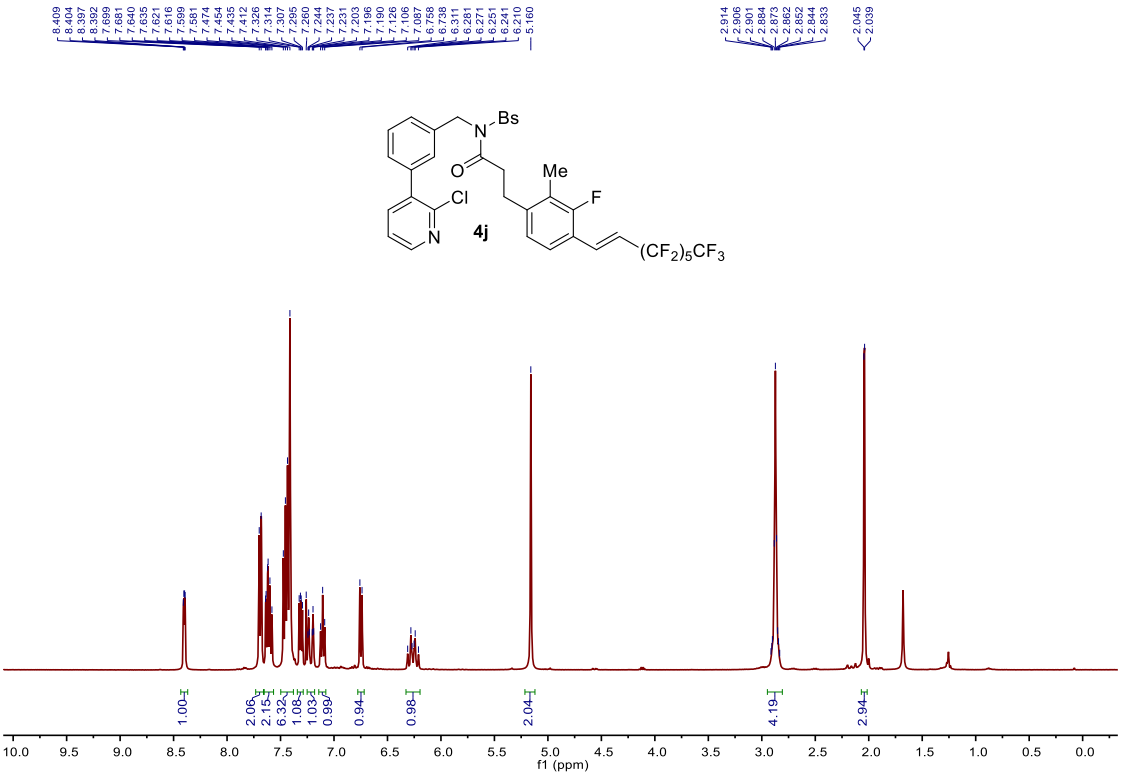


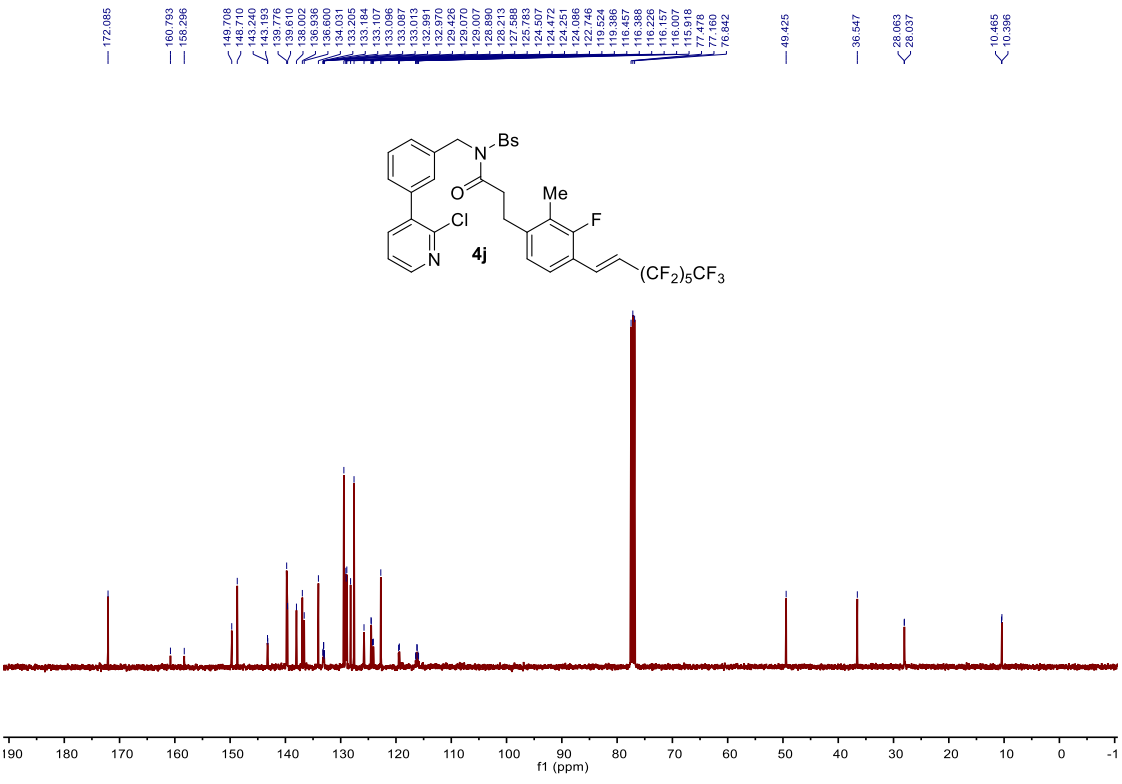
^{19}F NMR (376 MHz, Chloroform-*d*)



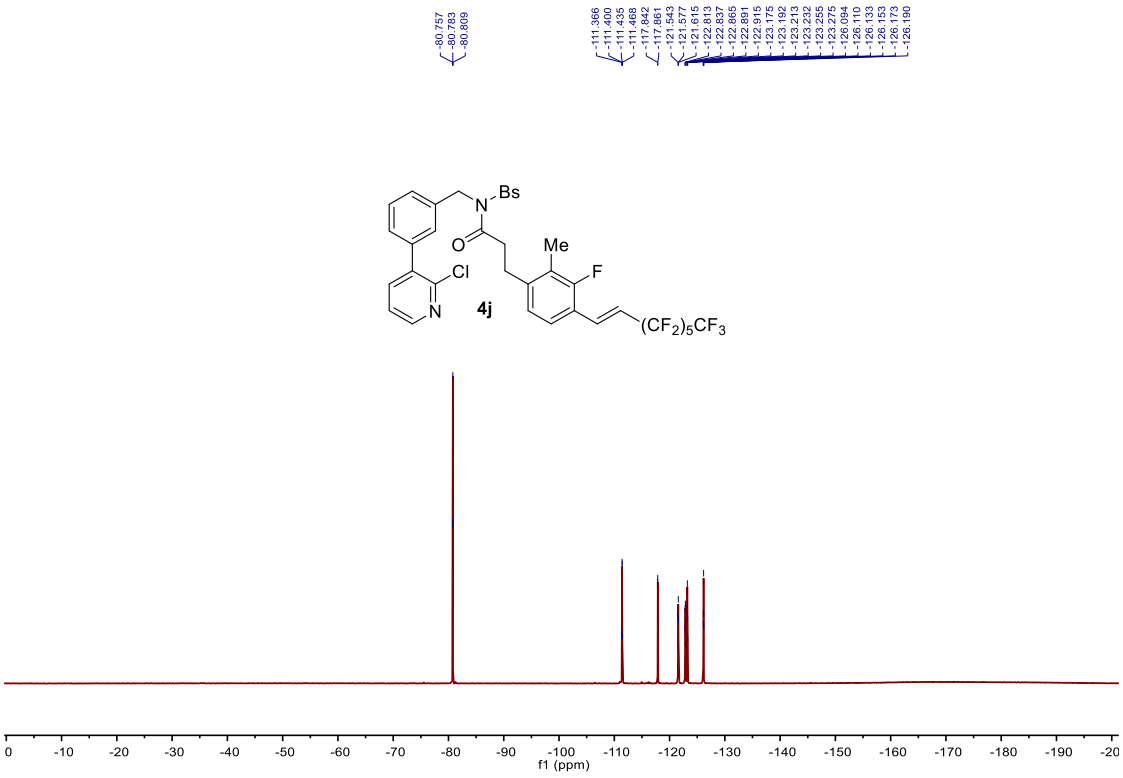
^{1}H NMR (400 MHz, Chloroform-*d*)



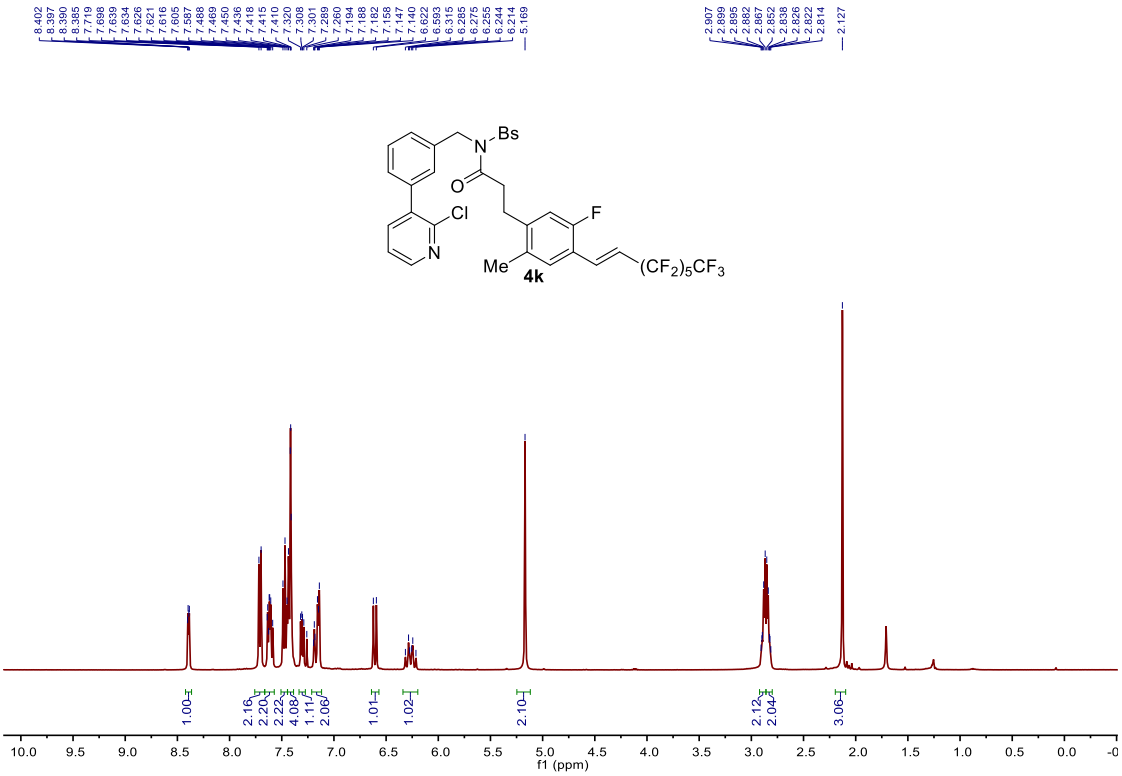
^{13}C NMR (101 MHz, Chloroform-*d*)



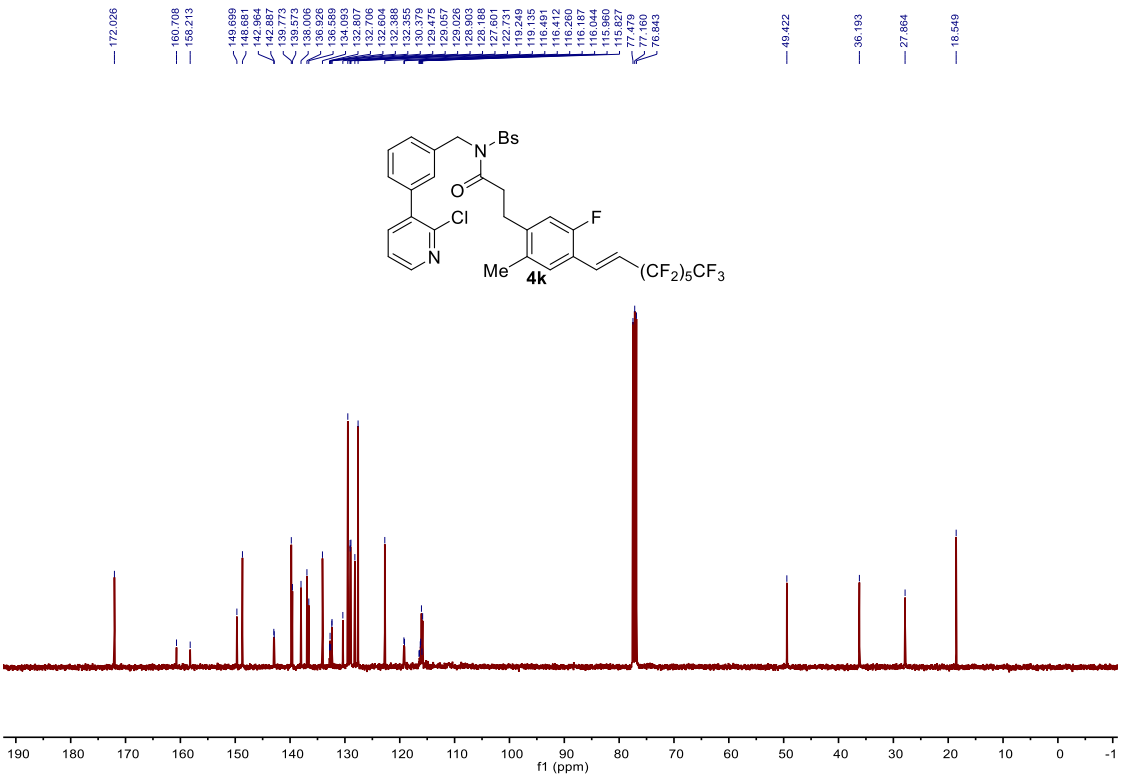
^{19}F NMR (376 MHz, Chloroform-*d*)



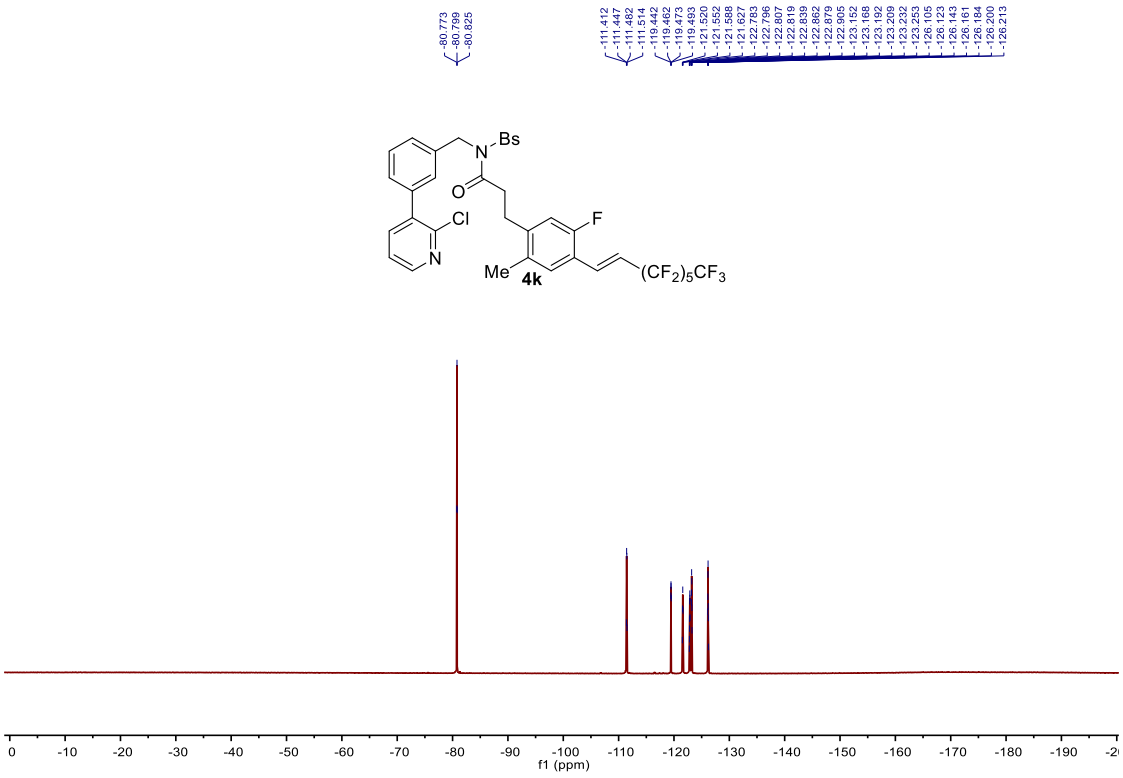
^{1}H NMR (400 MHz, Chloroform-*d*)



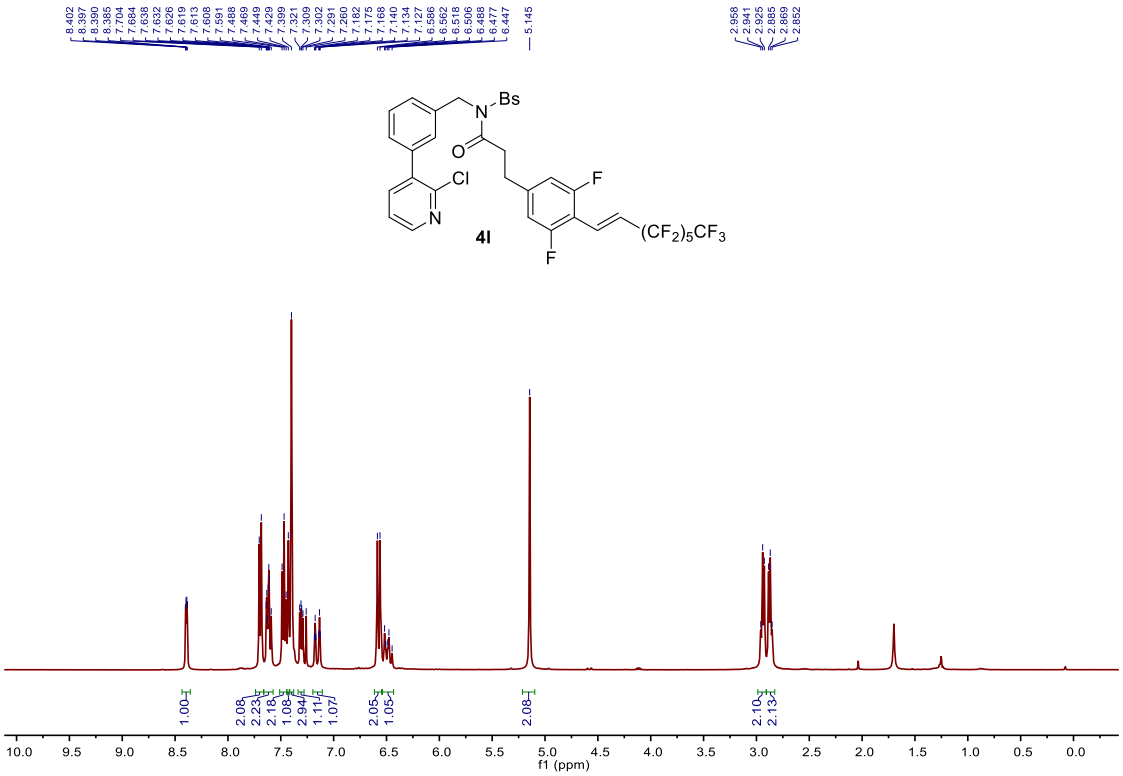
^{13}C NMR (101 MHz, Chloroform-*d*)



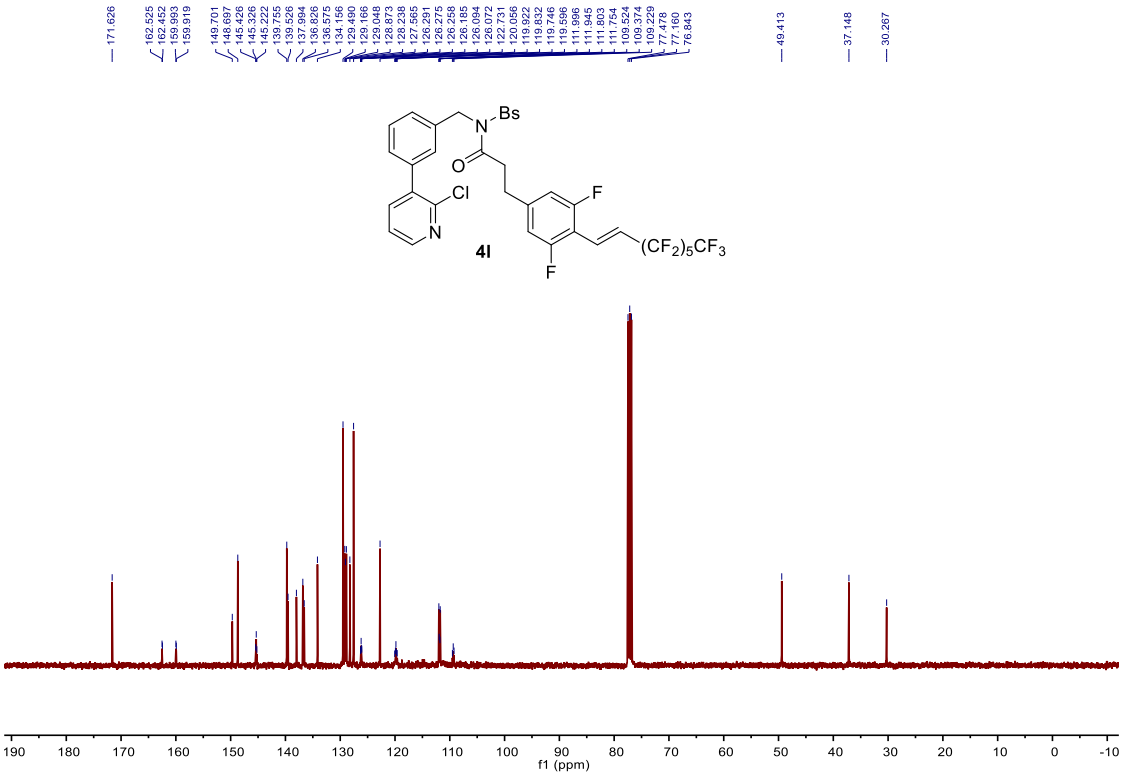
^{19}F NMR (376 MHz, Chloroform-*d*)



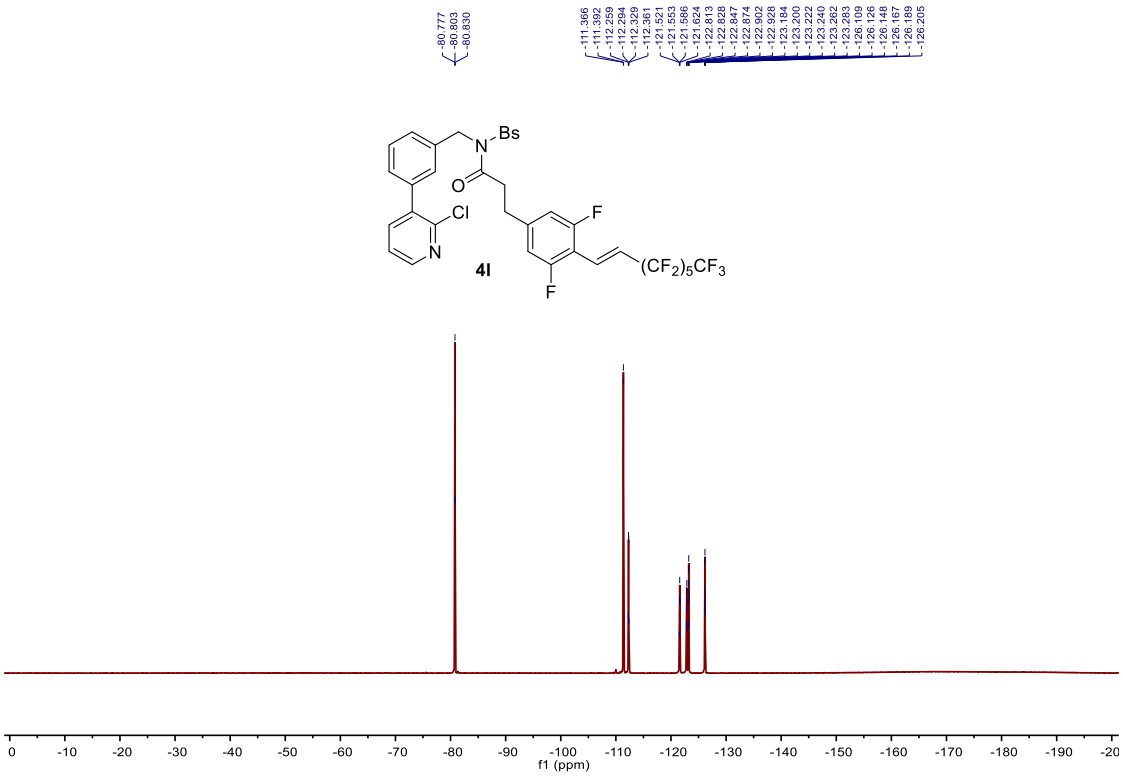
^{1}H NMR (400 MHz, Chloroform-*d*)



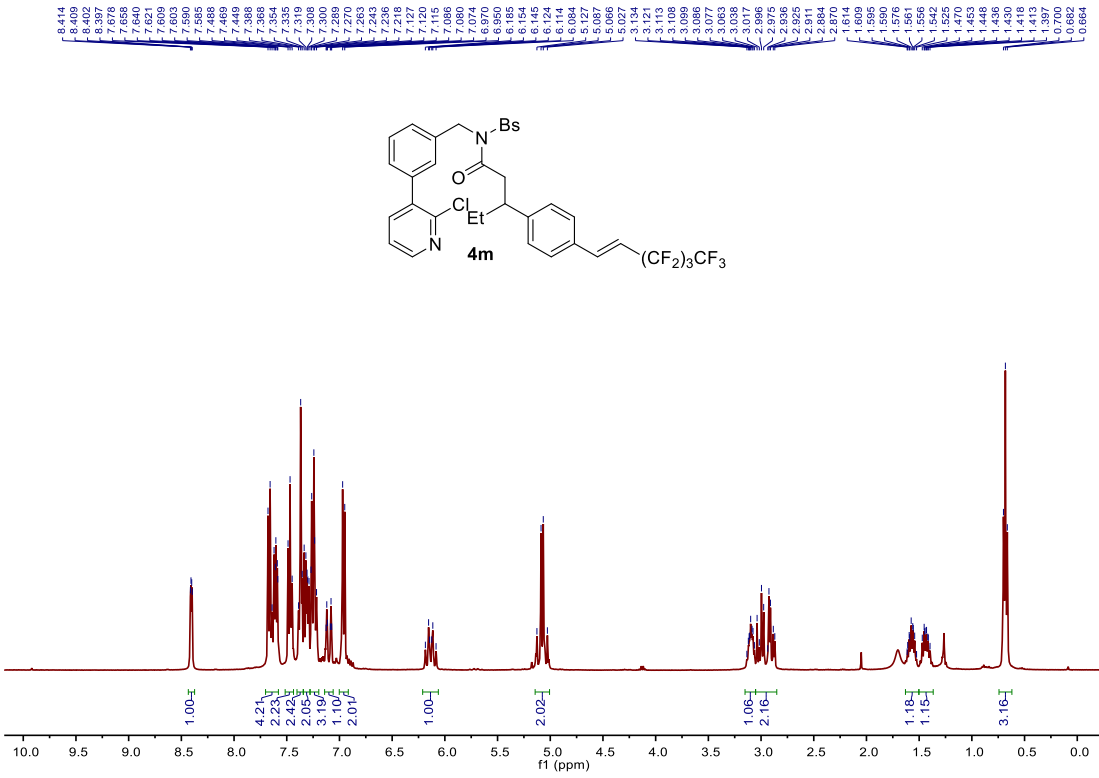
^{13}C NMR (101 MHz, Chloroform-*d*)



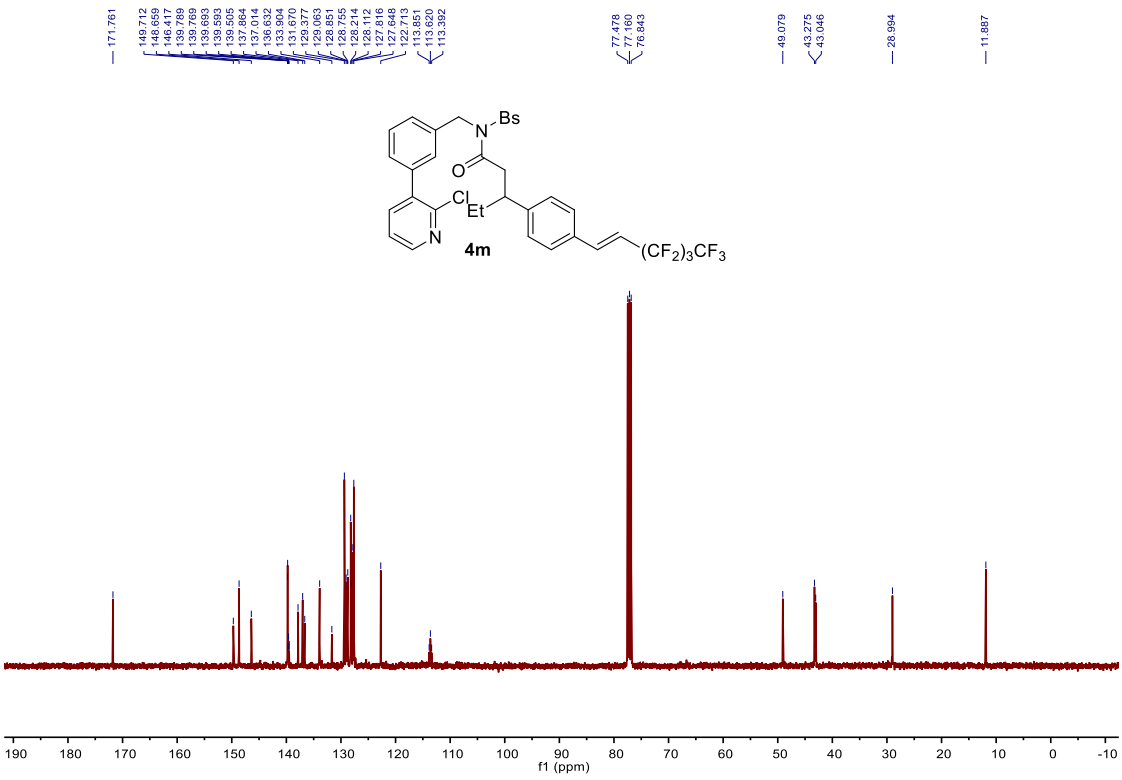
^{19}F NMR (376 MHz, Chloroform-*d*)



^{1}H NMR (400 MHz, Chloroform-*d*)



^{13}C NMR (101 MHz, Chloroform-*d*)



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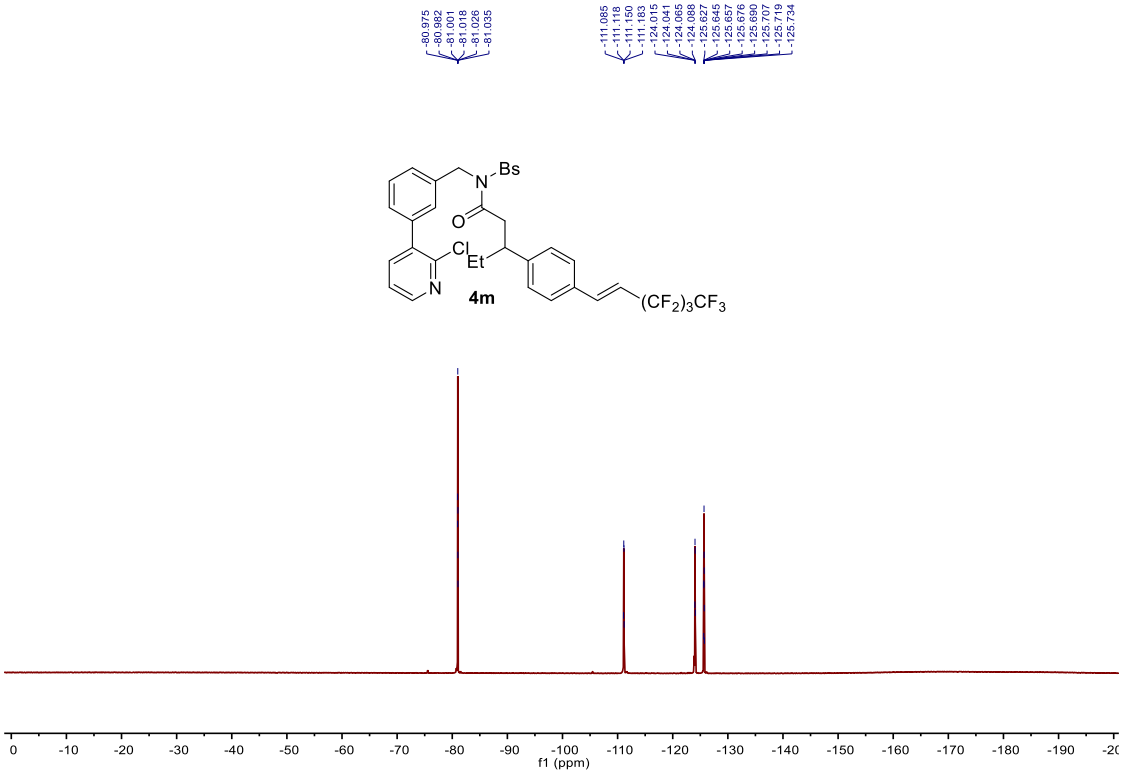
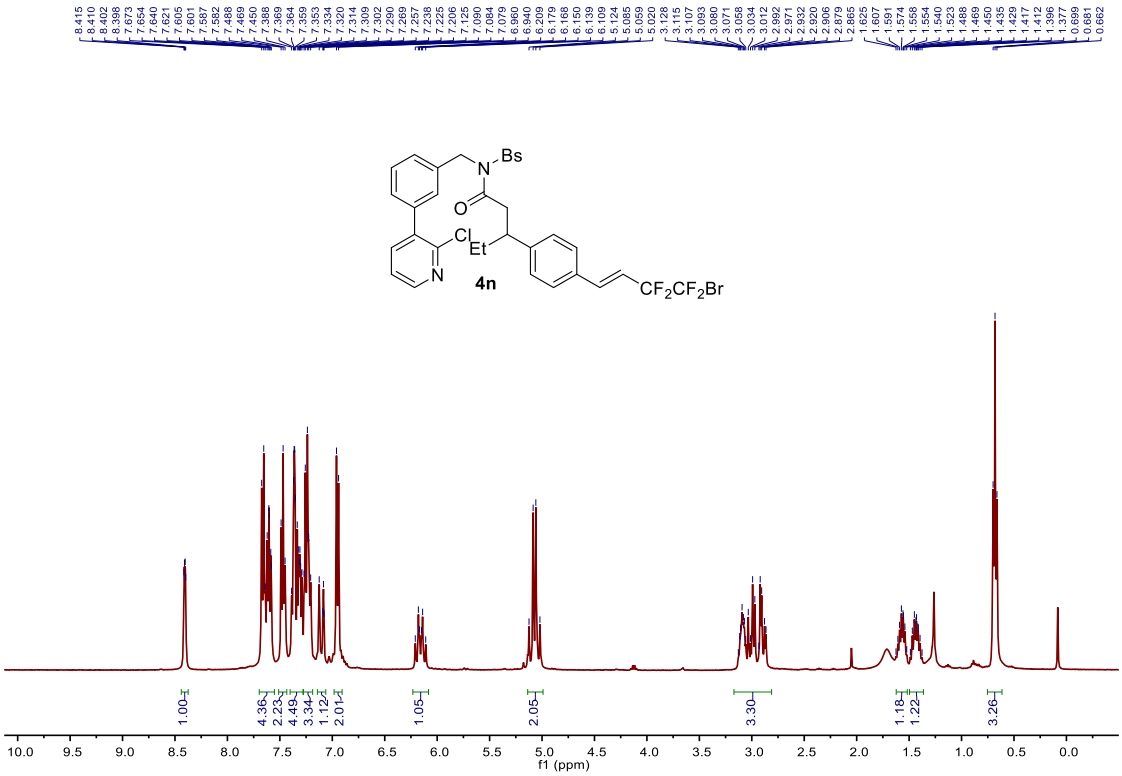


^{1}H NMR (400 MHz, Chloroform-*d*)



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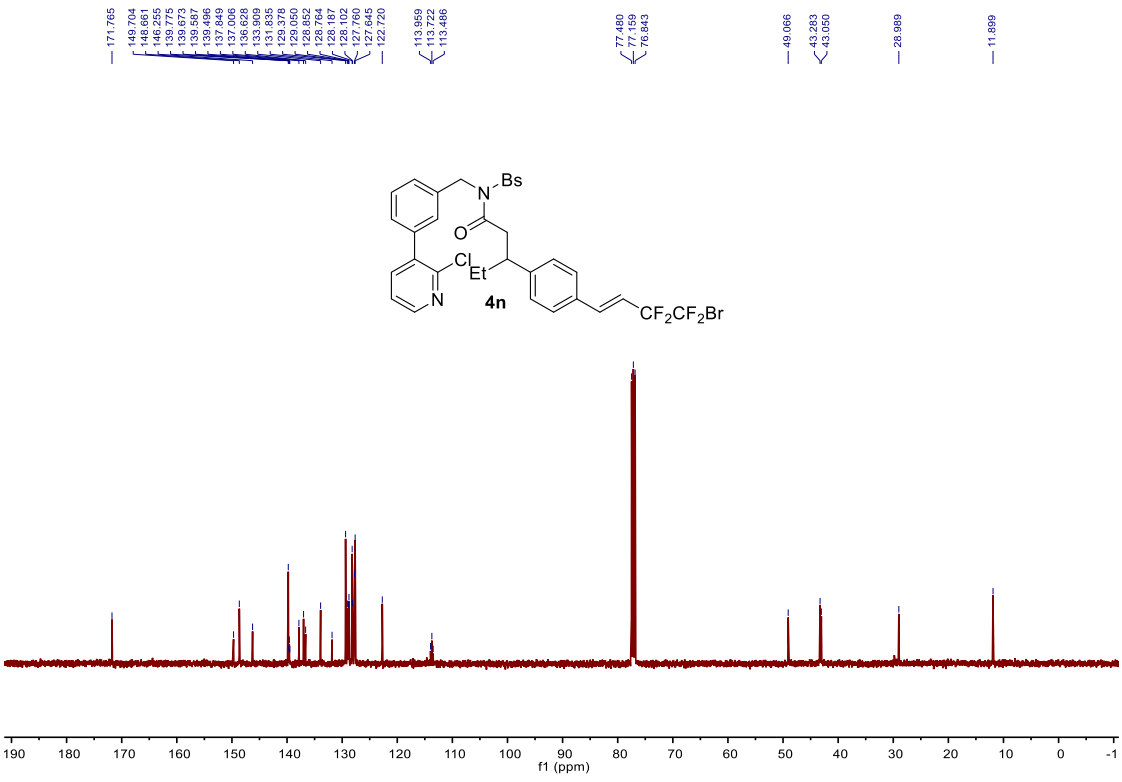
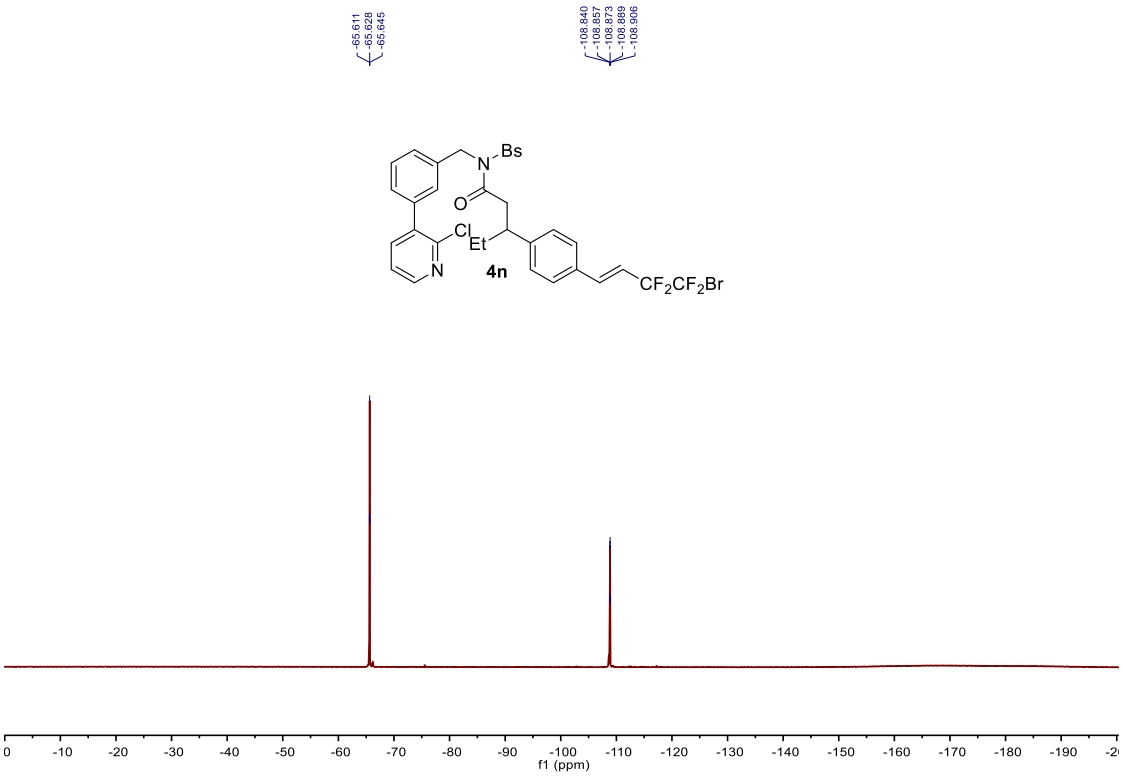


^{19}F NMR (376 MHz, Chloroform-*d*)



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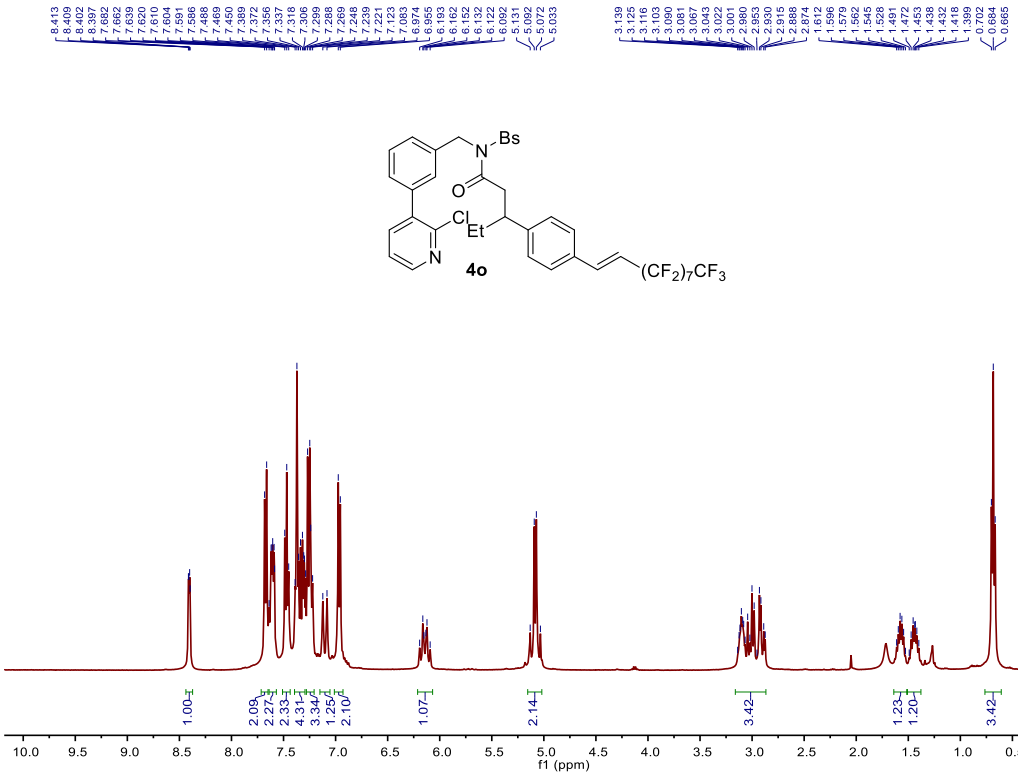
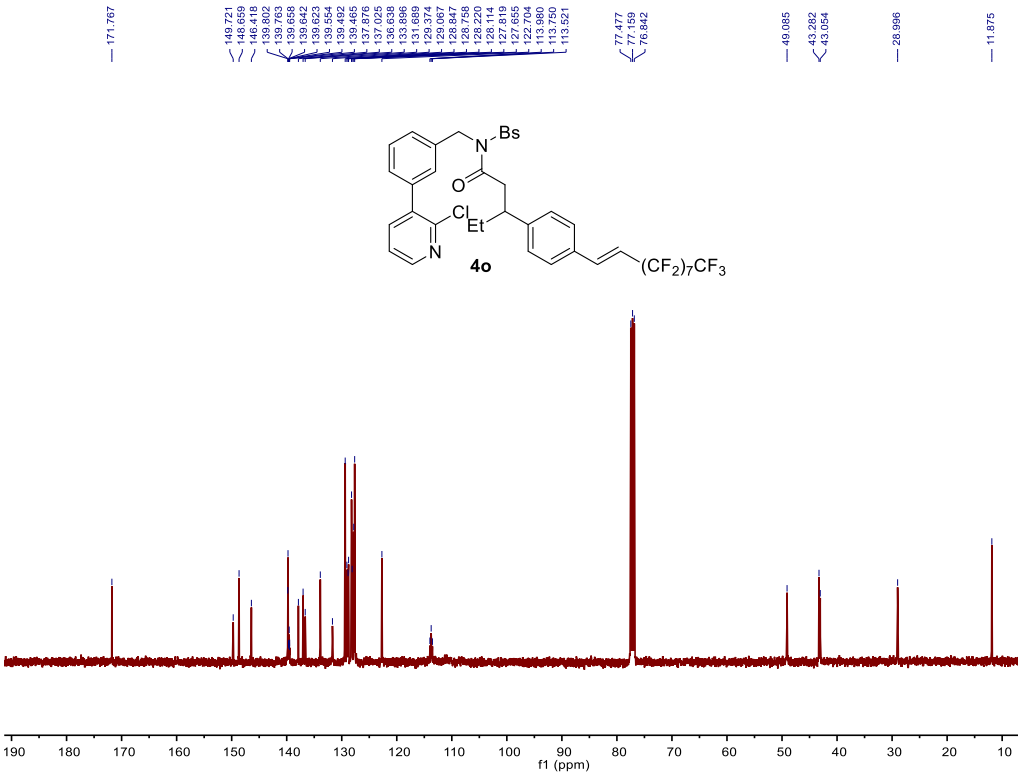
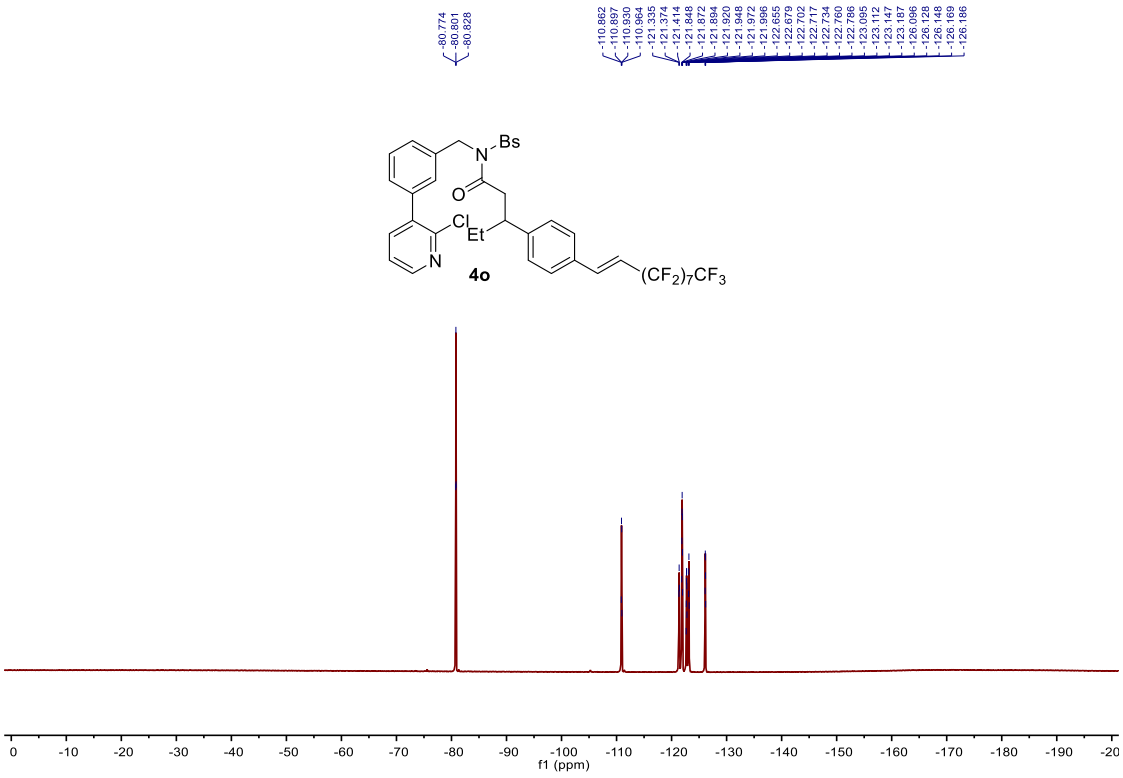


^{13}C NMR (101 MHz, Chloroform-*d*)



^{19}F NMR (376 MHz, Chloroform-*d*)



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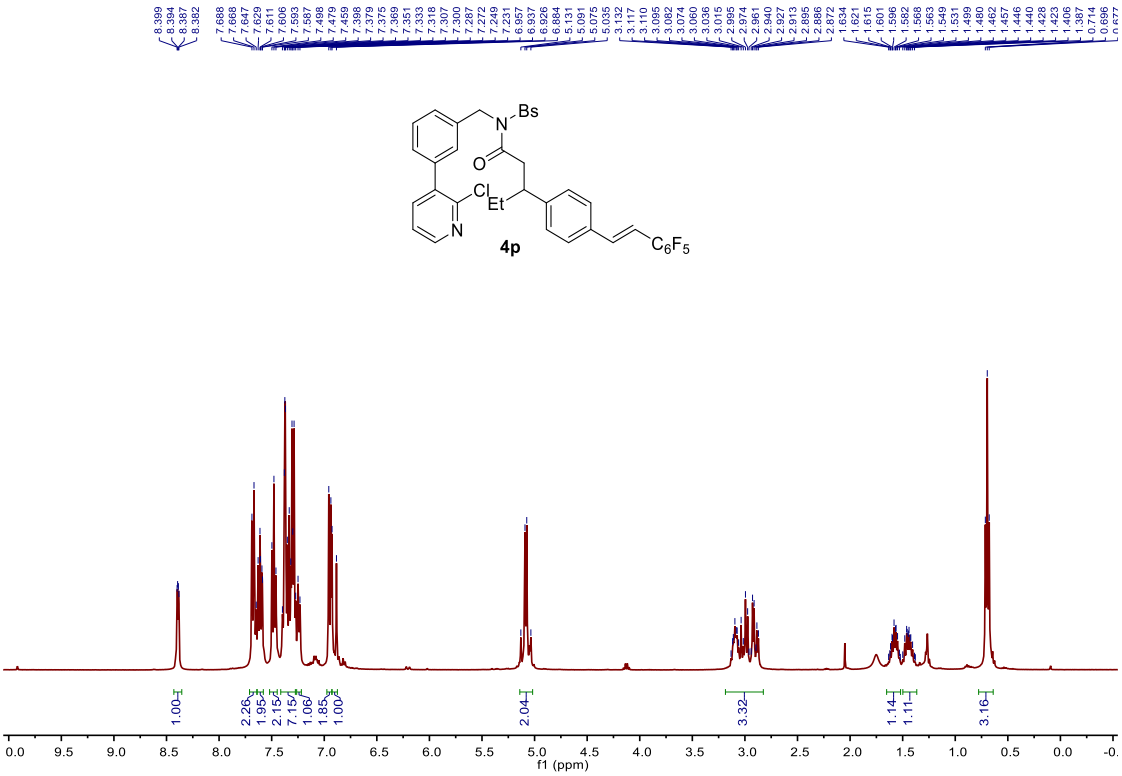

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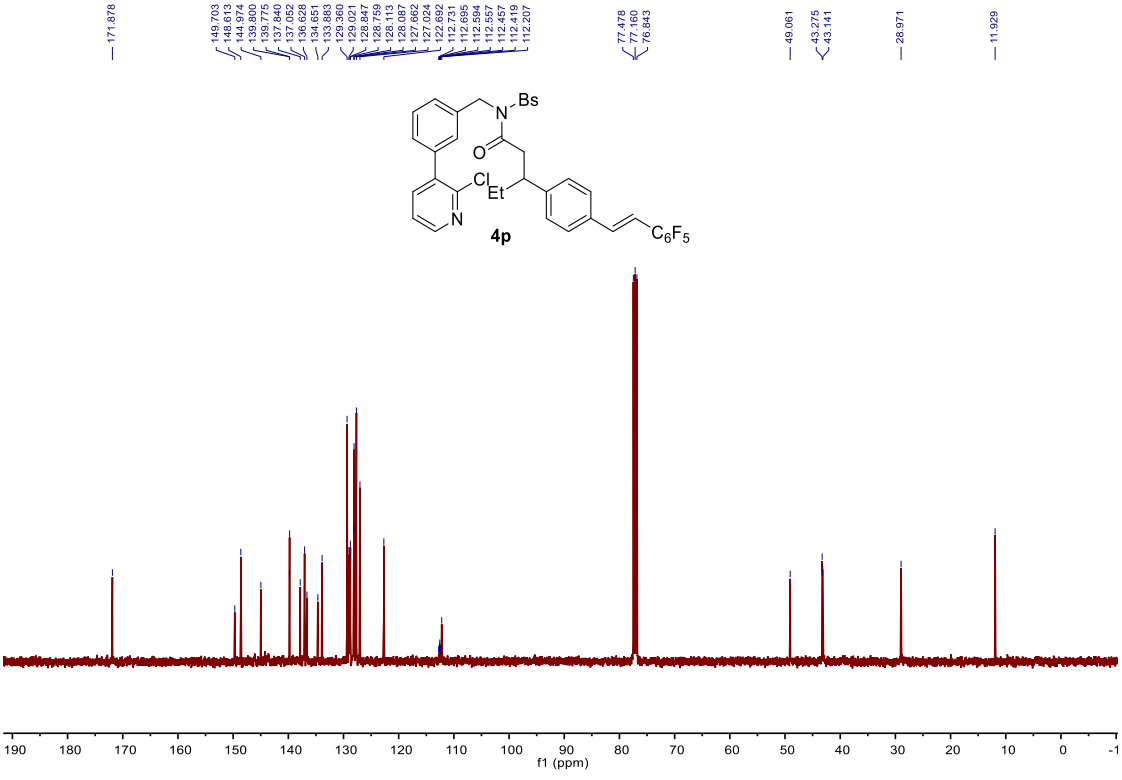

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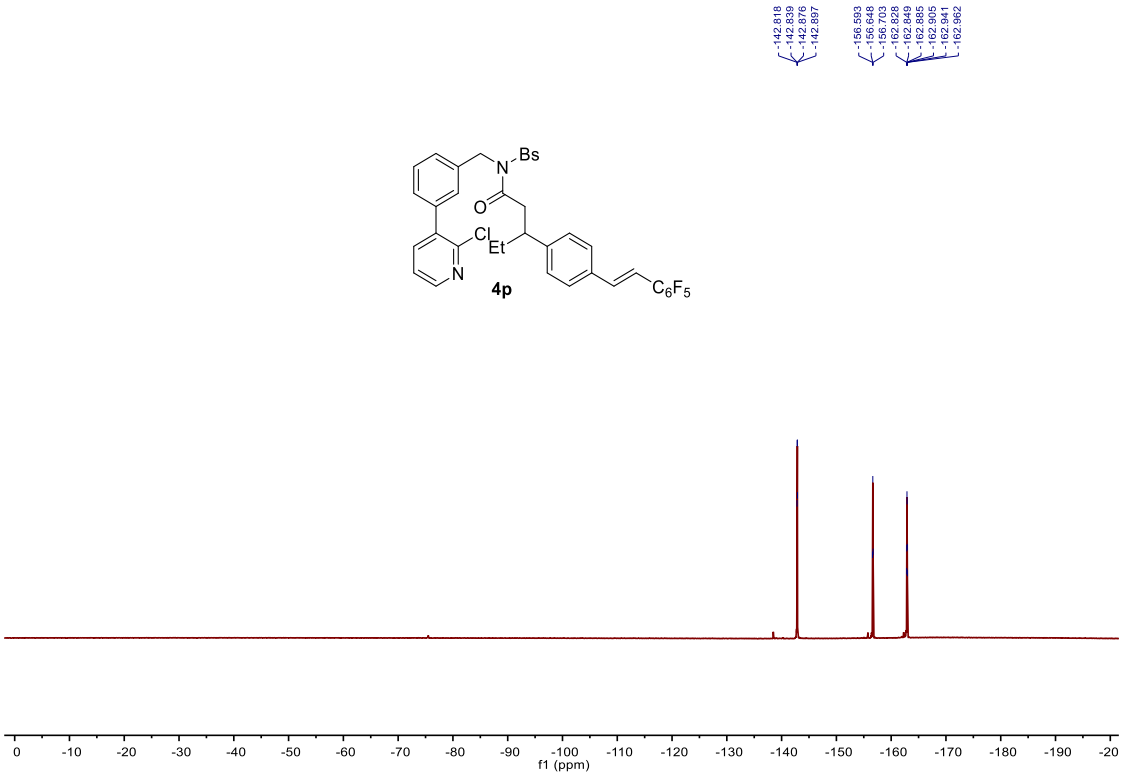

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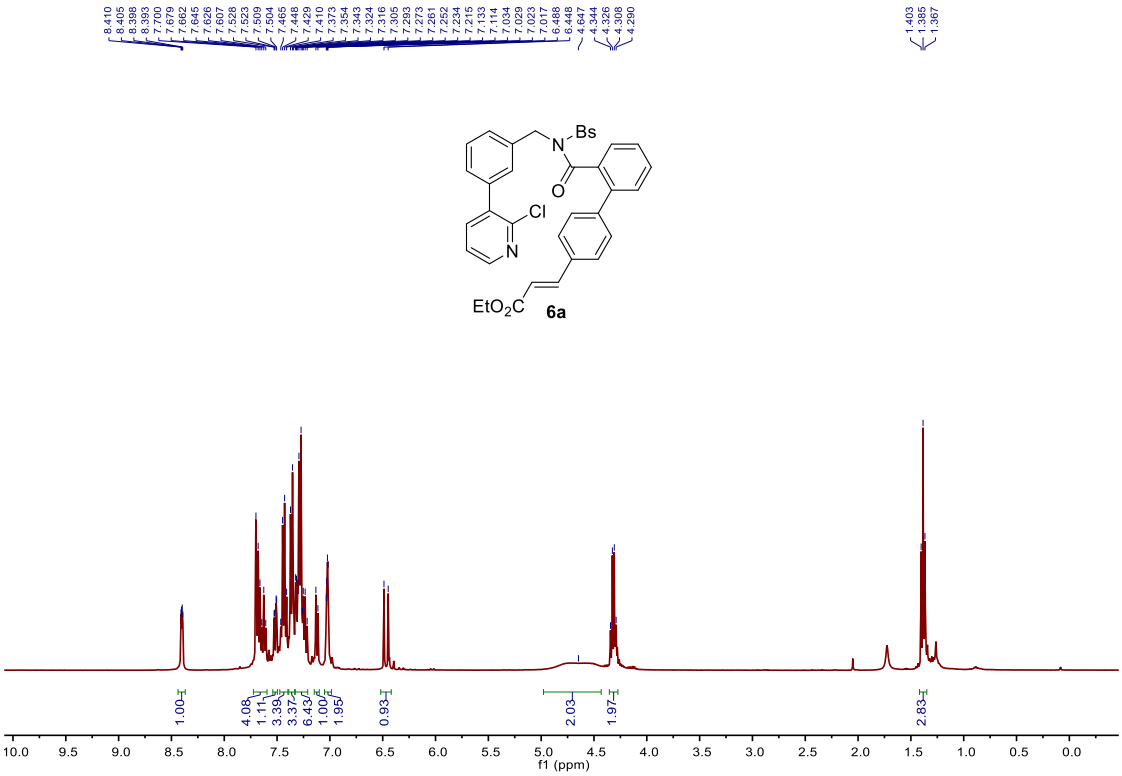

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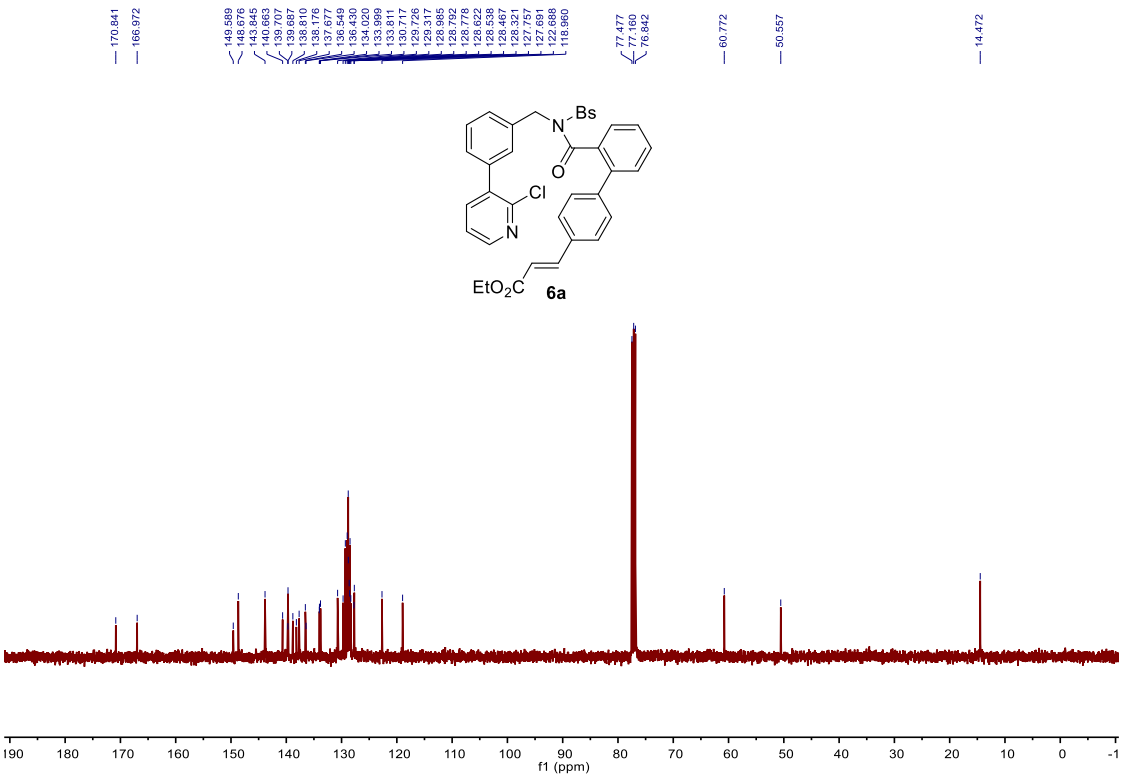

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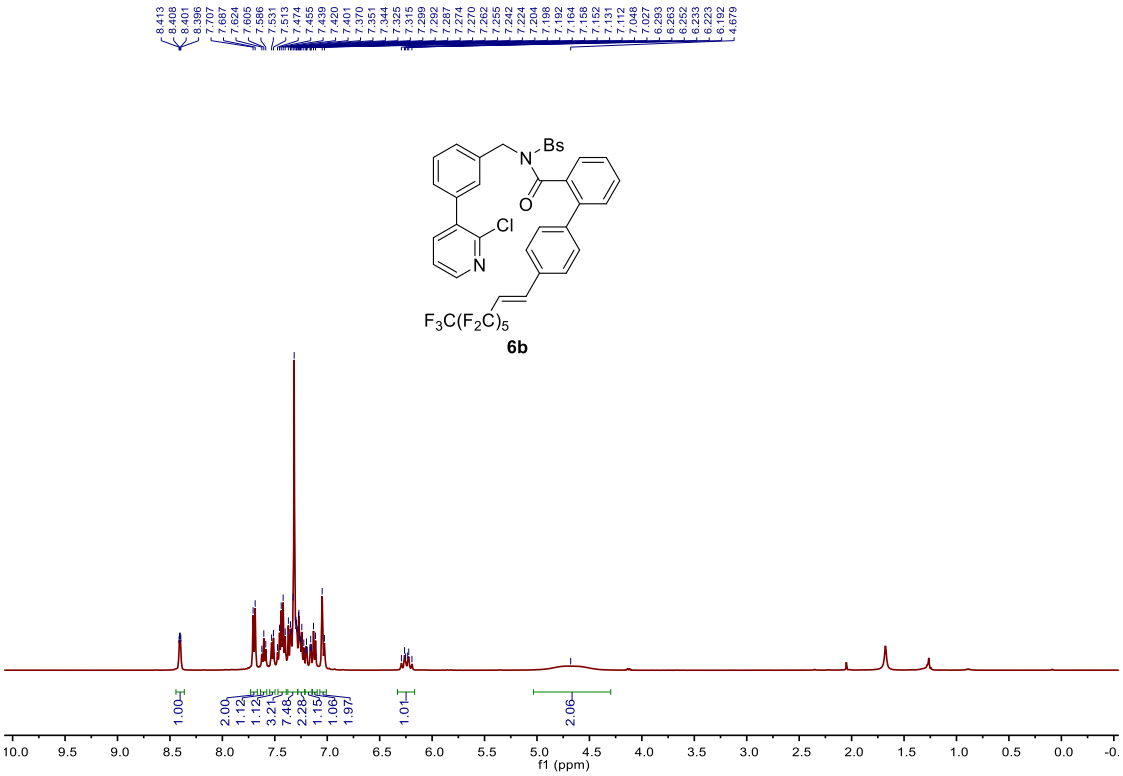

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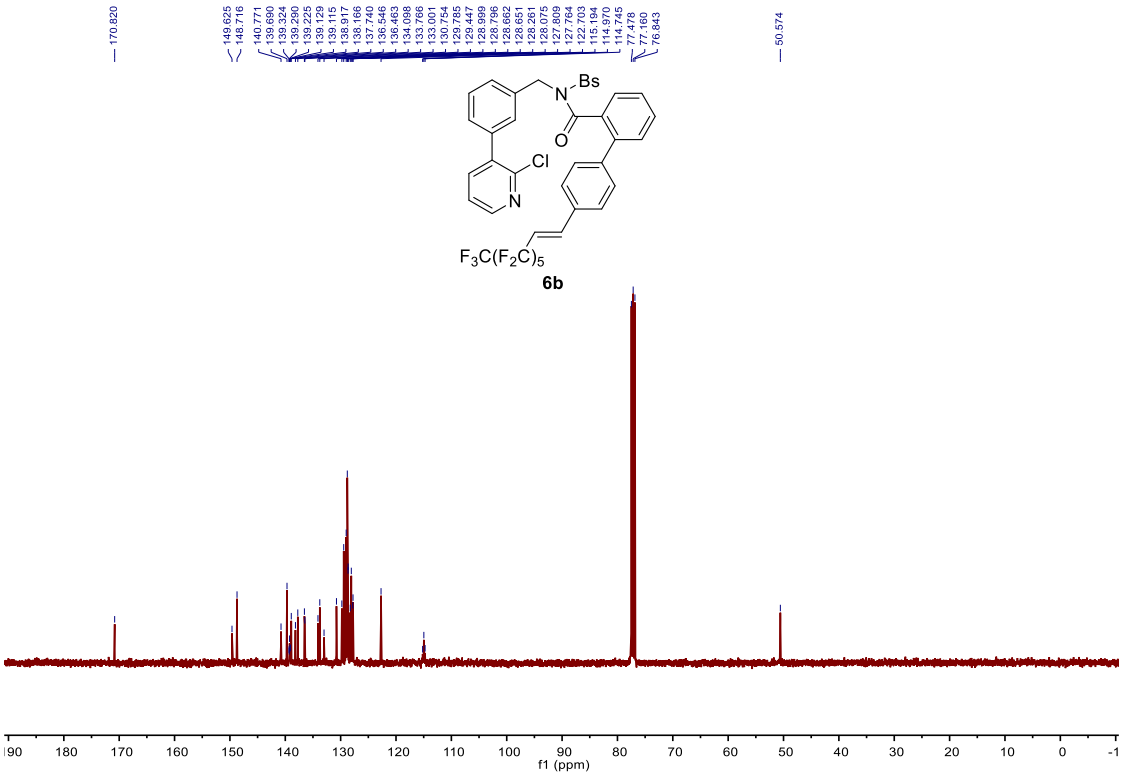

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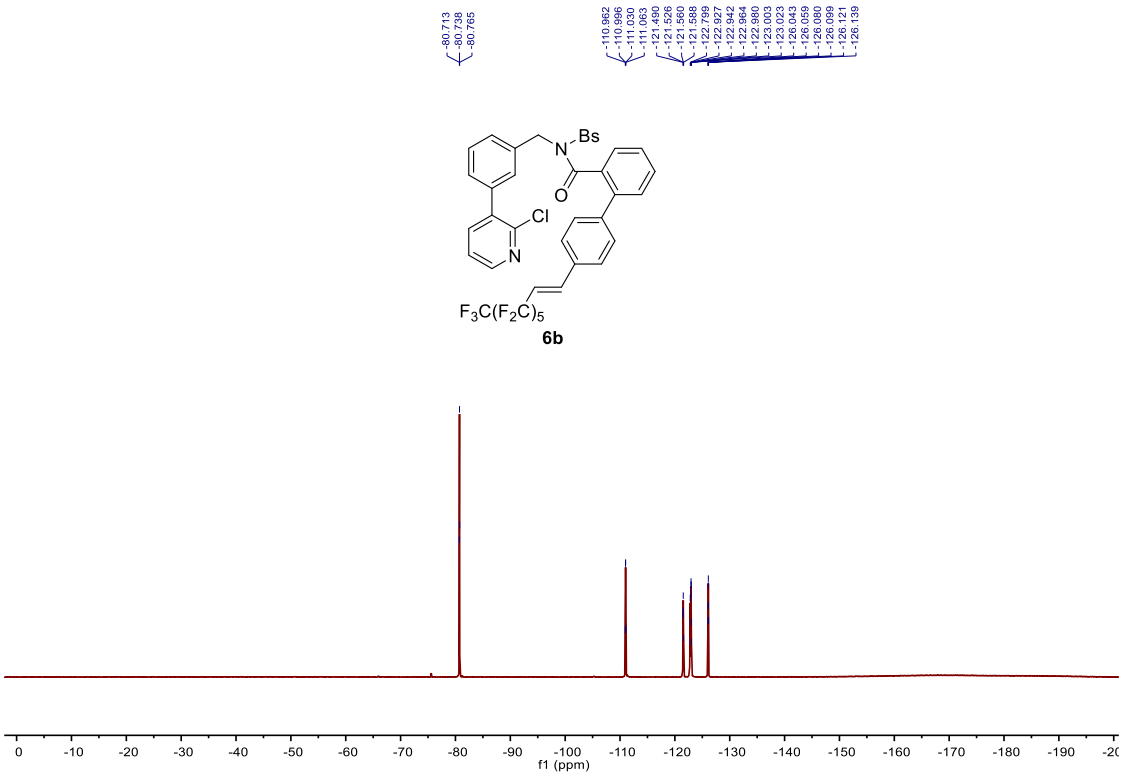

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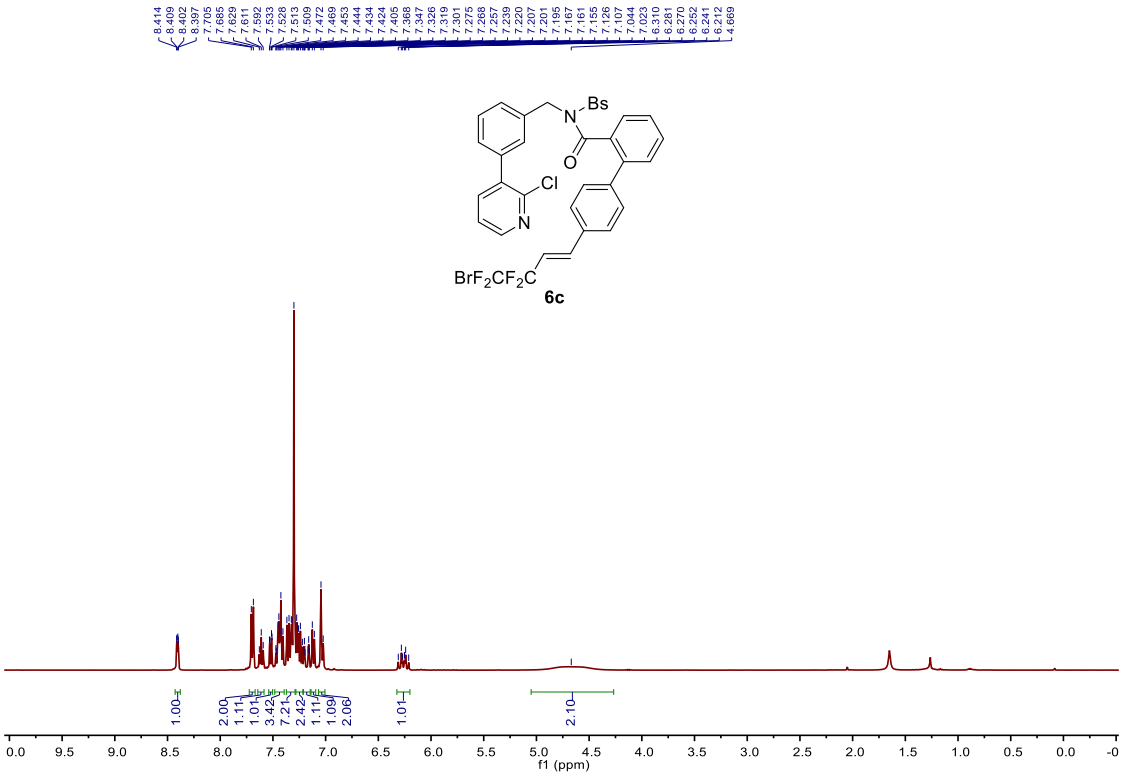

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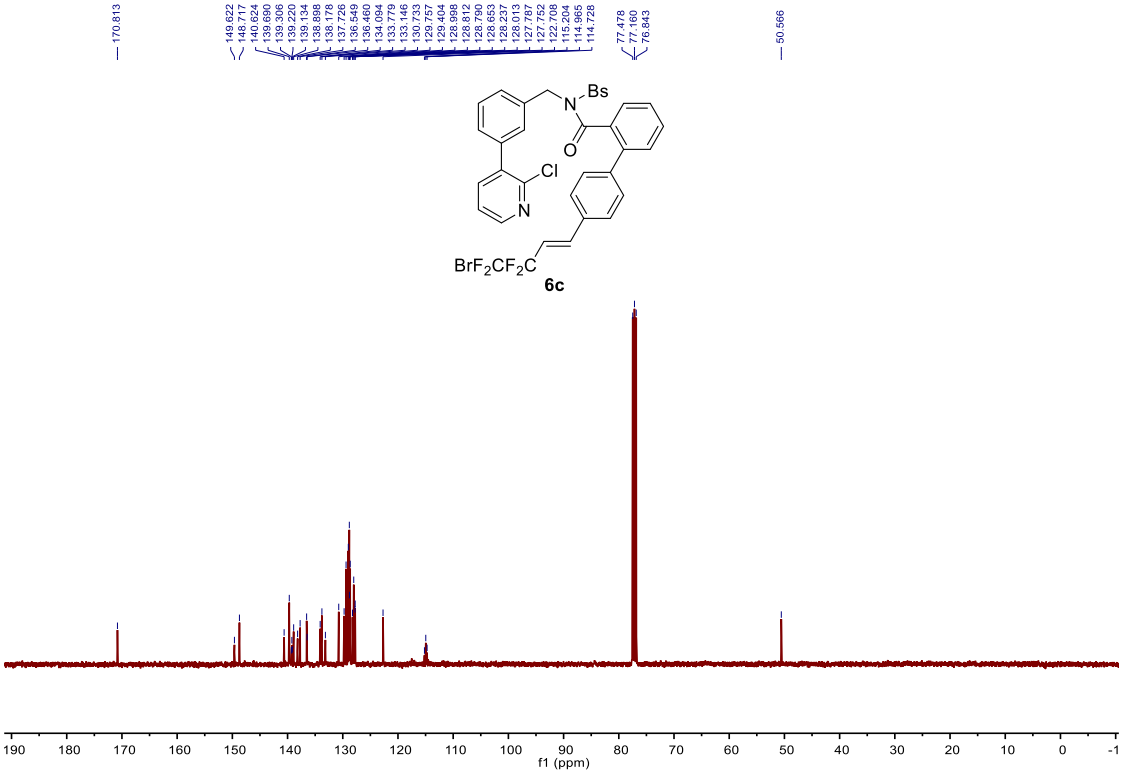

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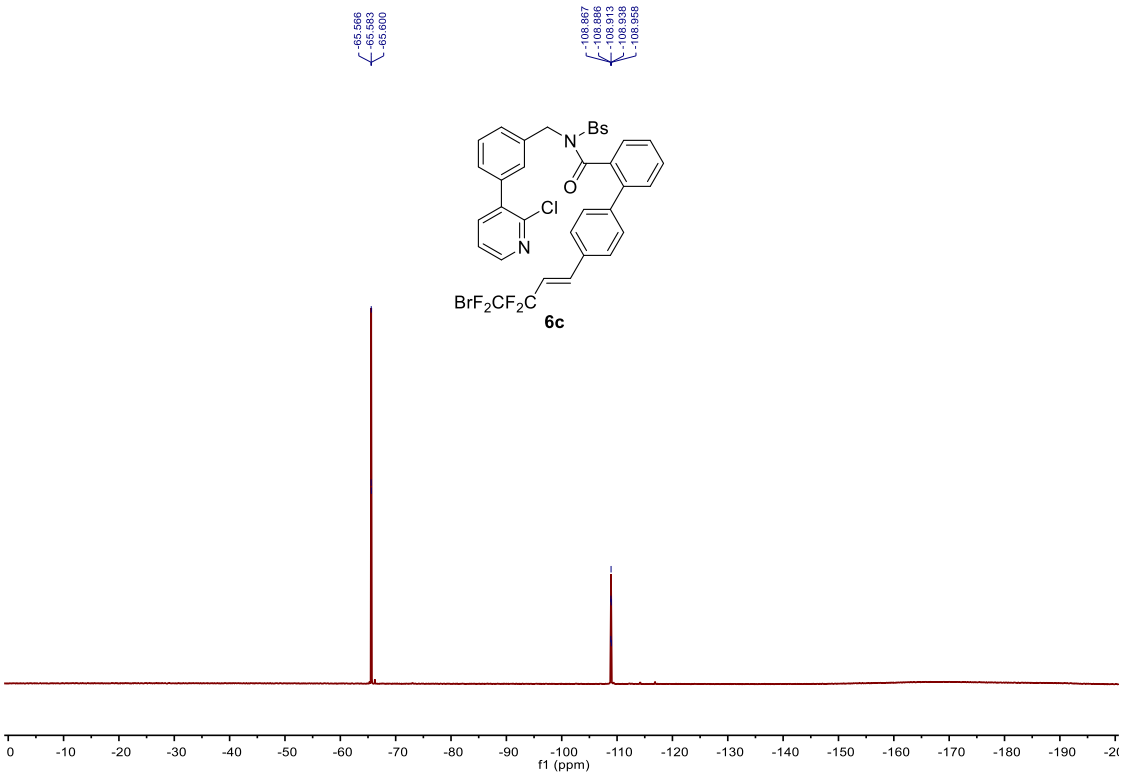

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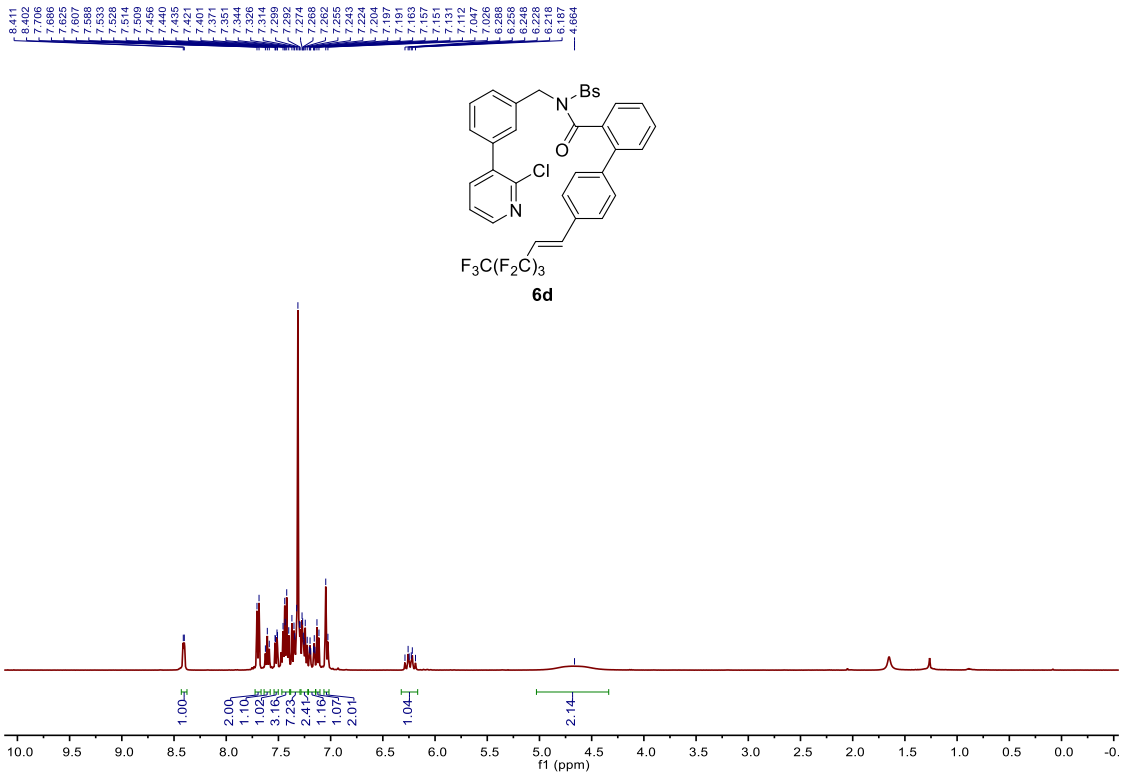

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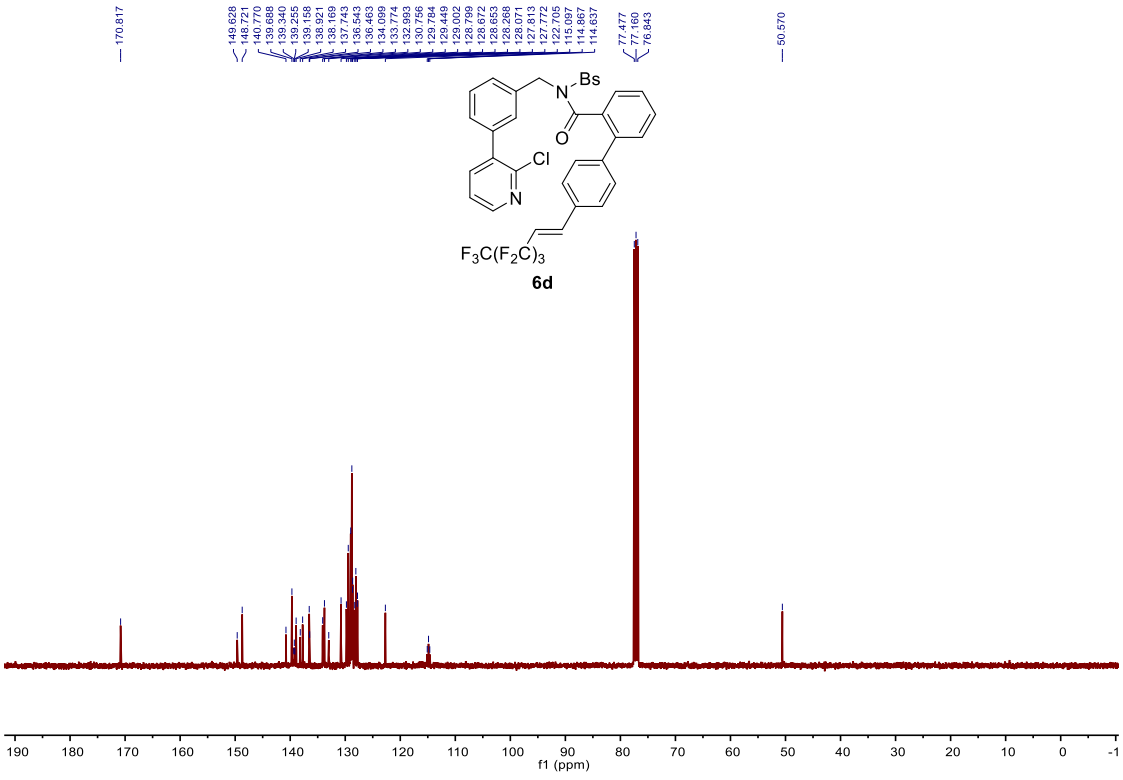

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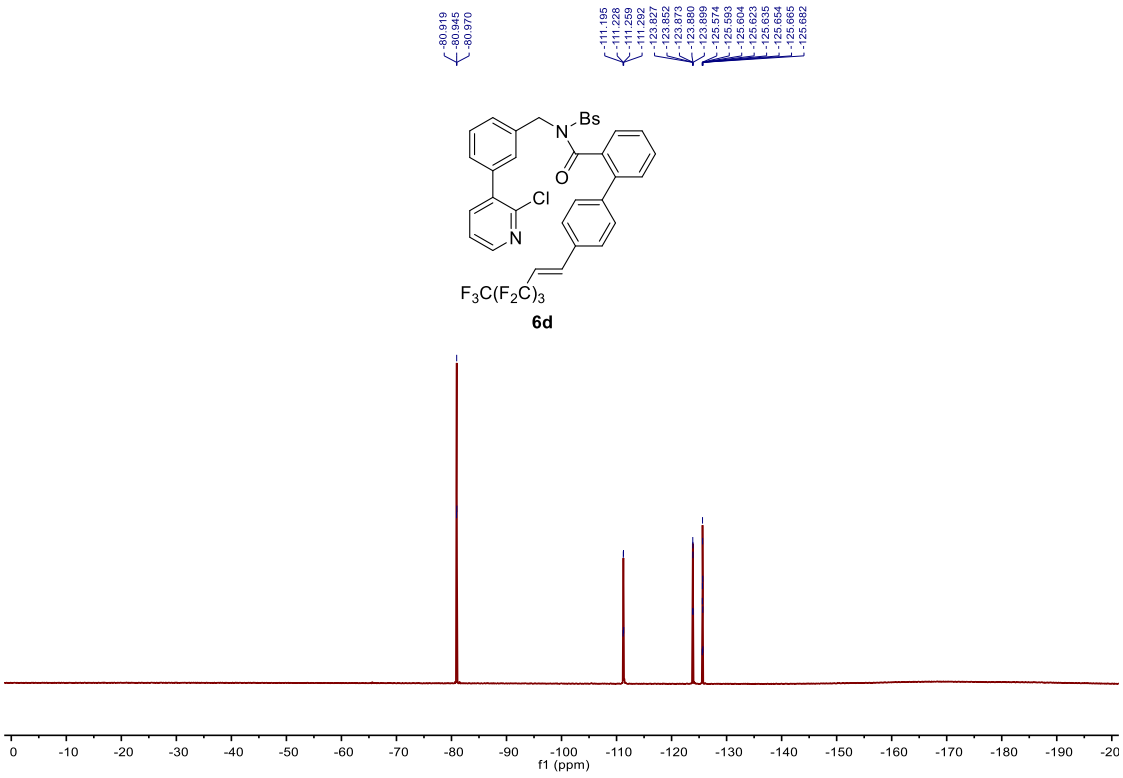

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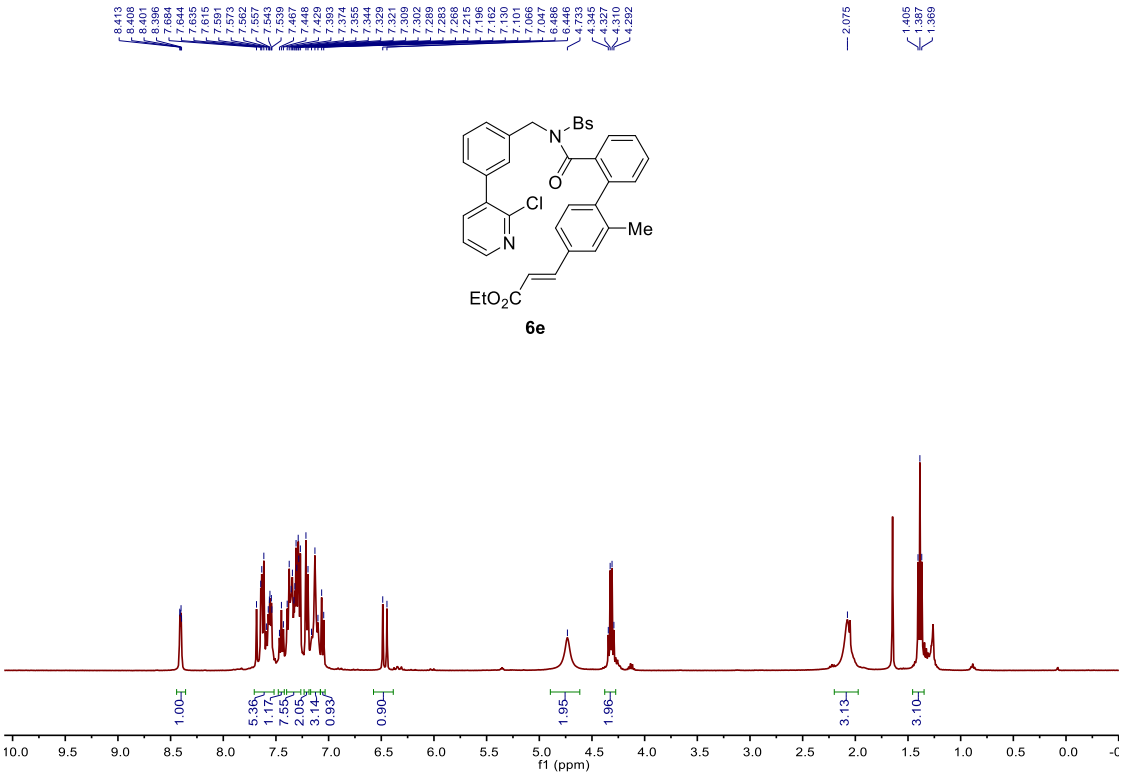

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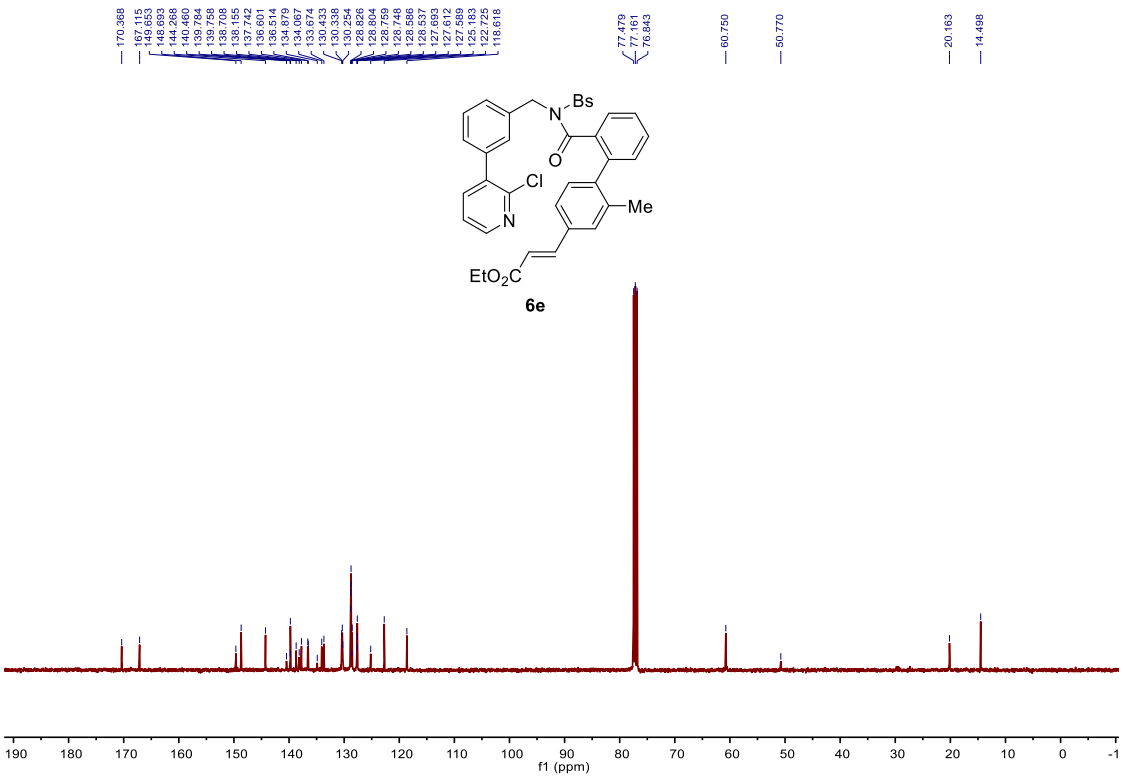

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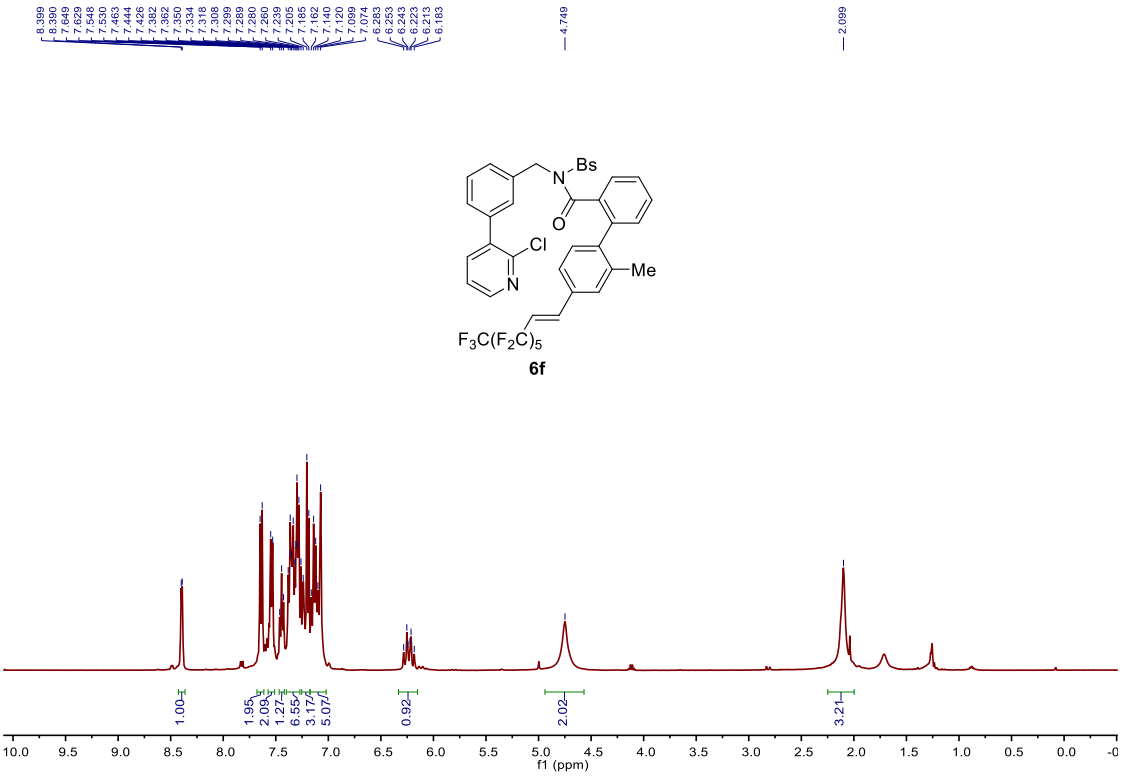

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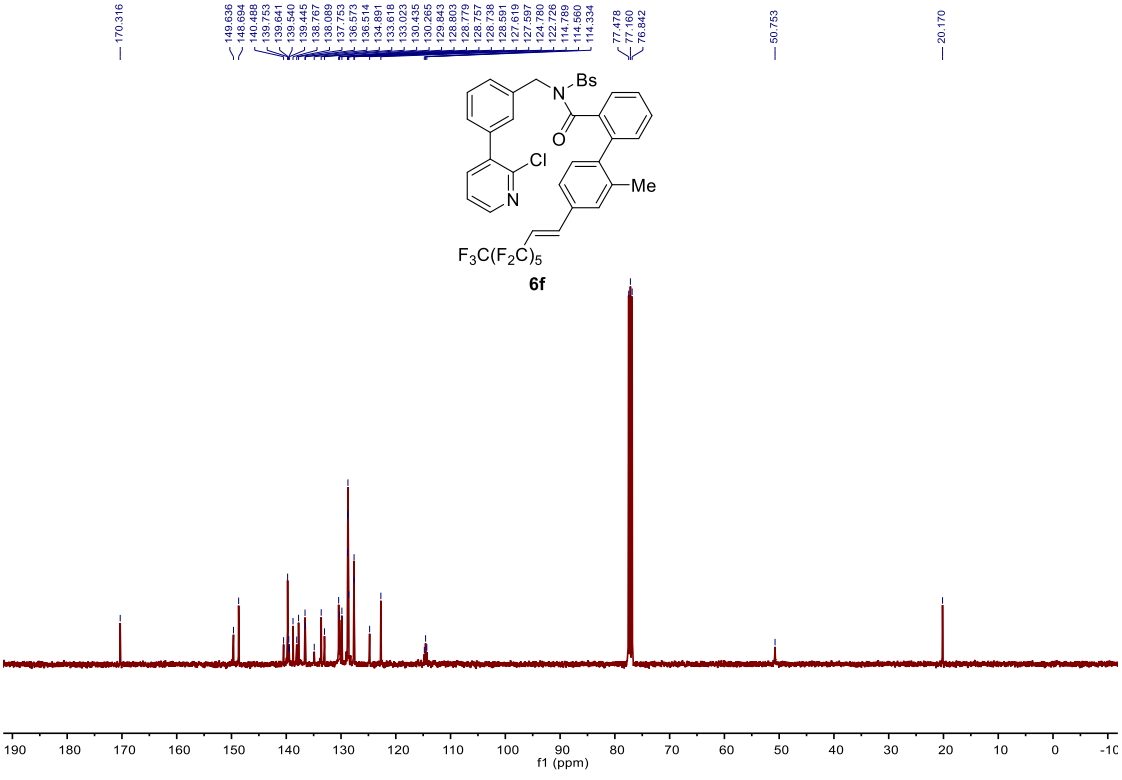

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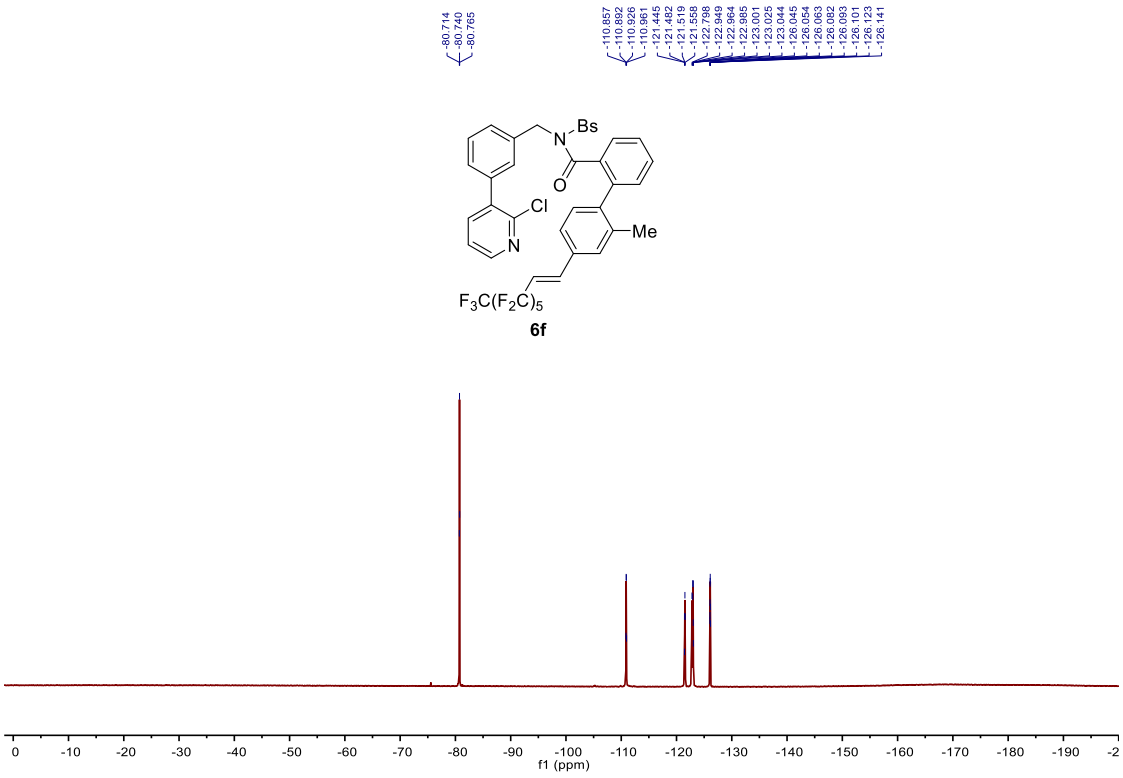

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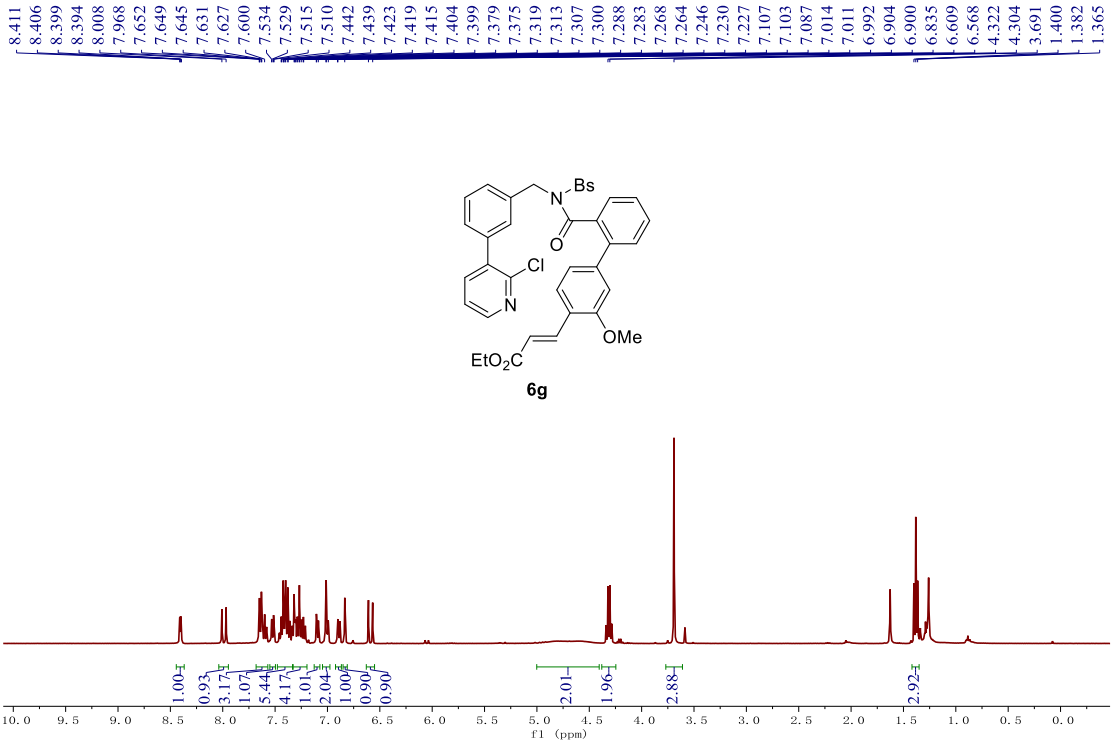
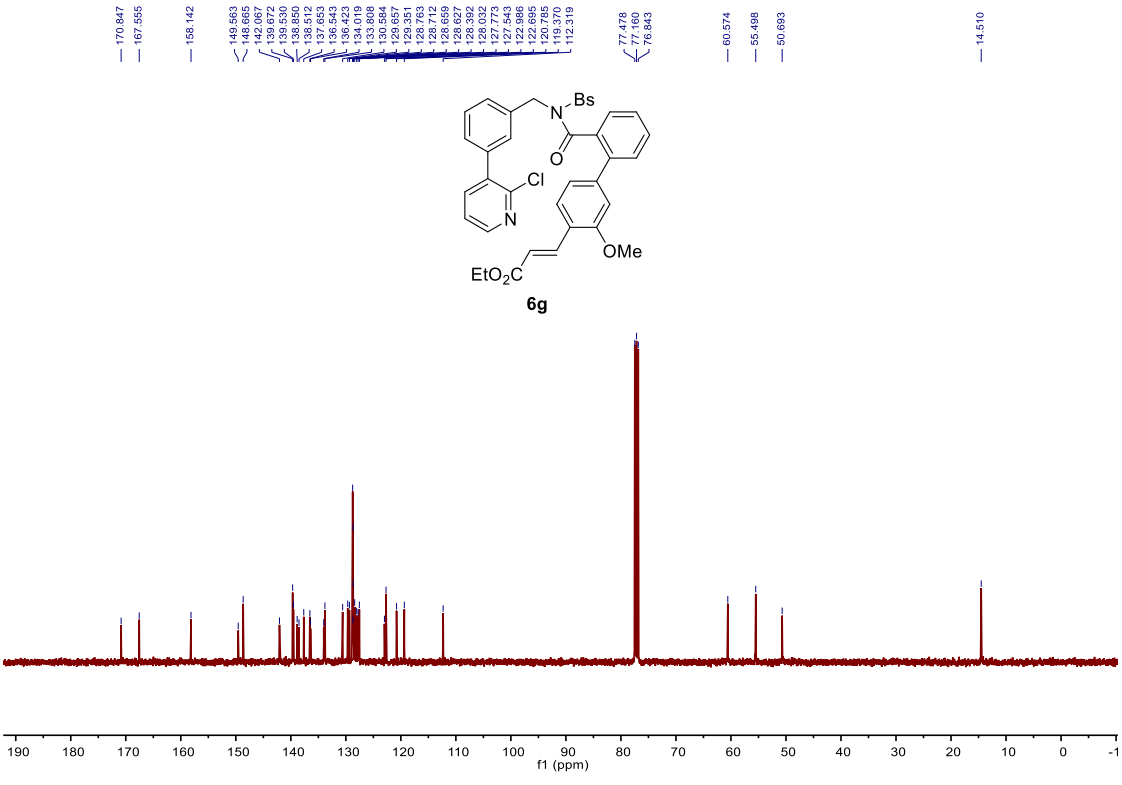
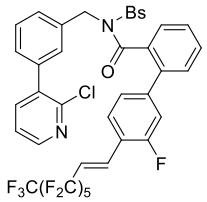


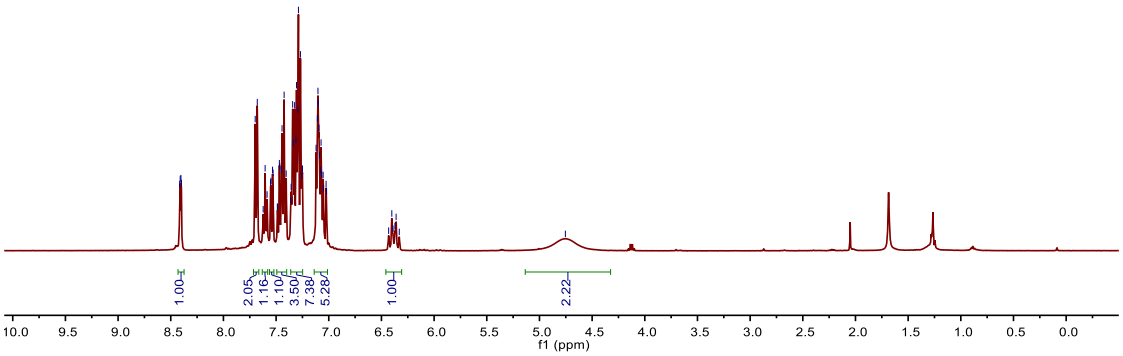
^{13}C NMR (101 MHz, Chloroform-*d*)



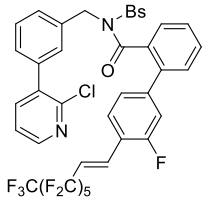
^{1}H NMR (400 MHz, Chloroform-*d*)



6h



^{13}C NMR (101 MHz, Chloroform-*d*)



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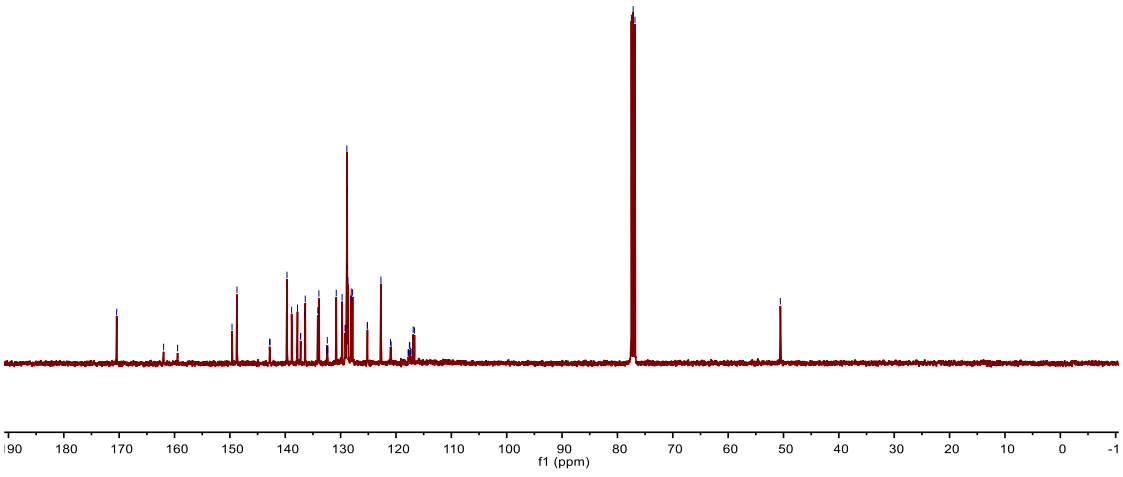
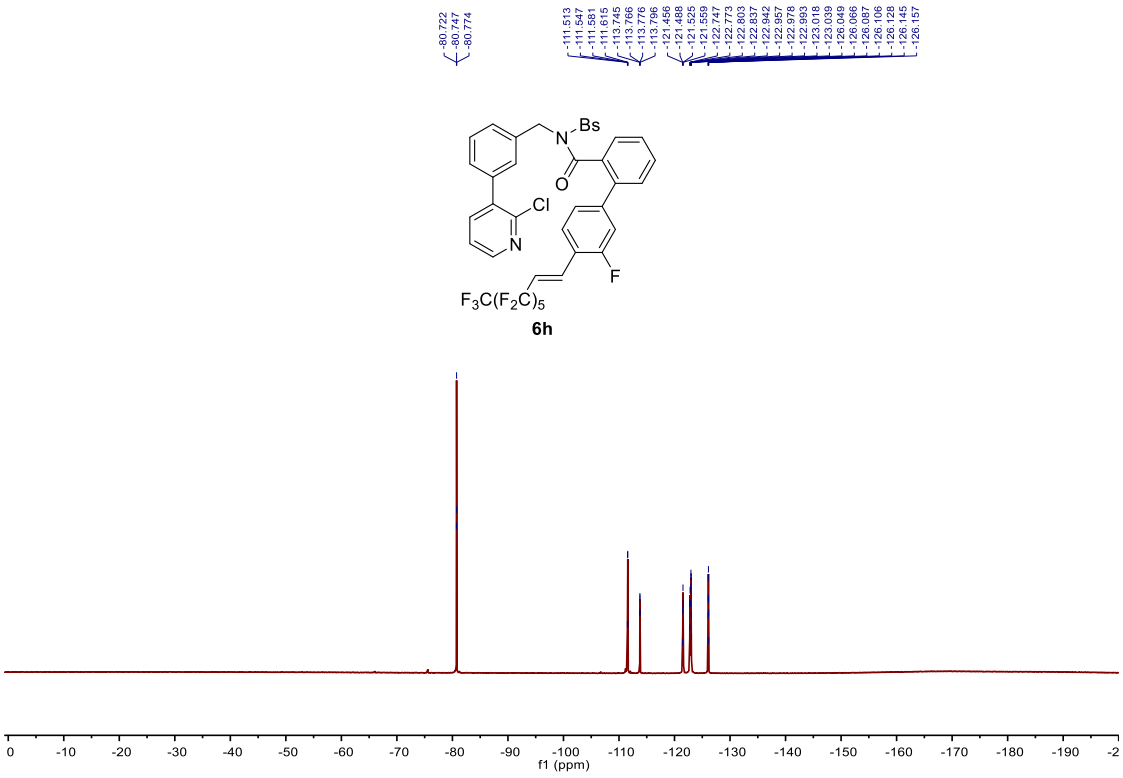


^{19}F NMR (376 MHz, Chloroform-*d*)



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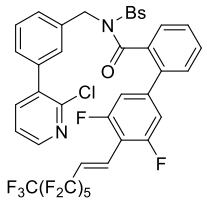

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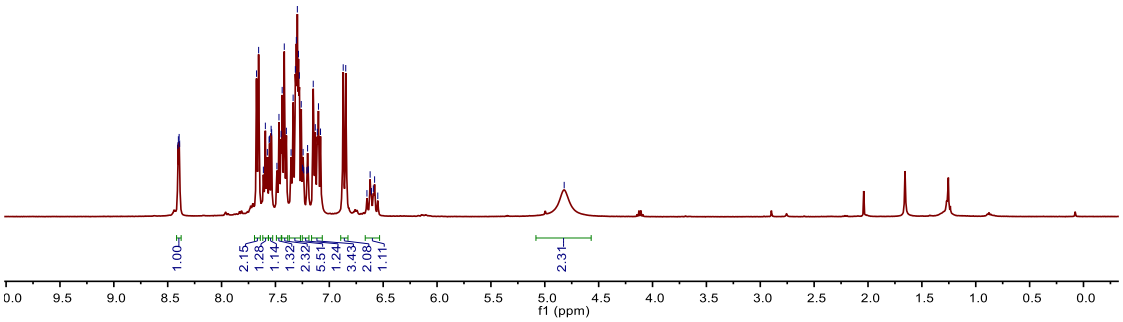
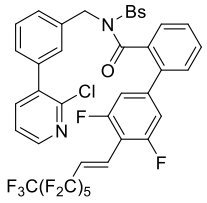


^{13}C NMR (101 MHz, Chloroform-*d*)



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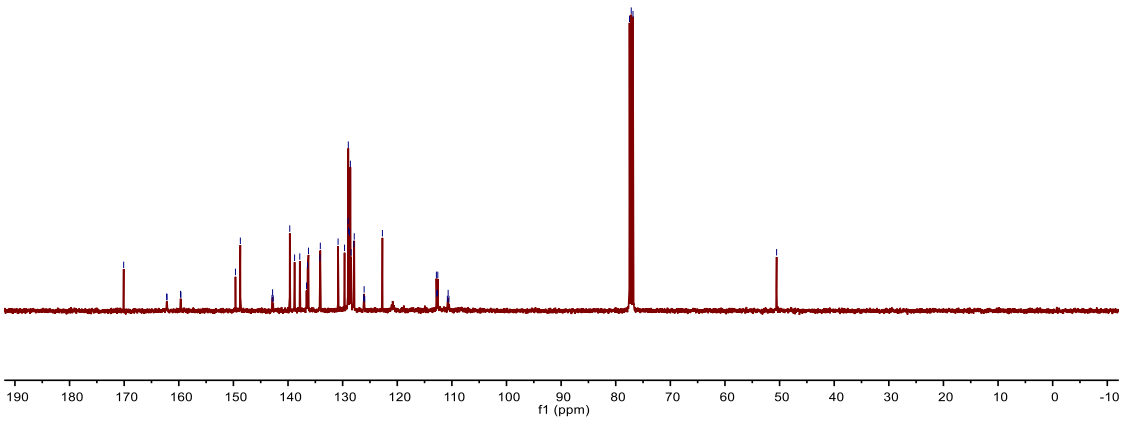
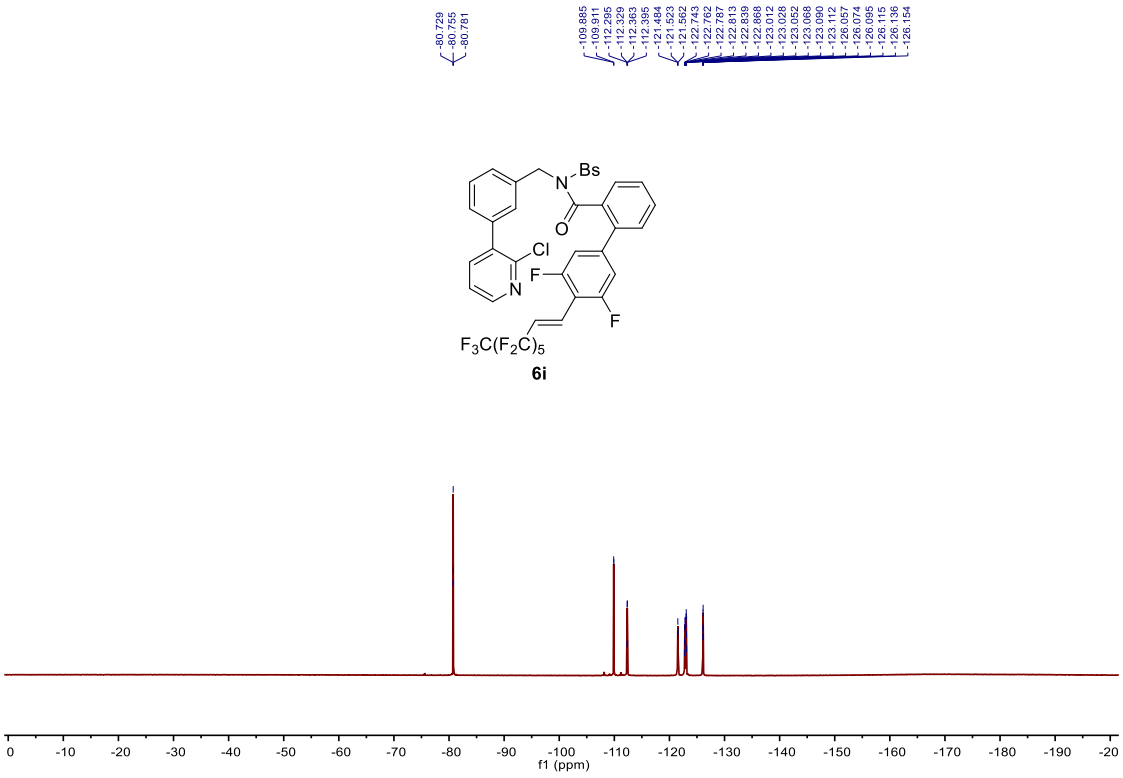


^{19}F NMR (376 MHz, Chloroform-*d*)



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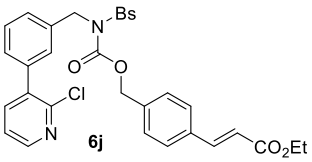
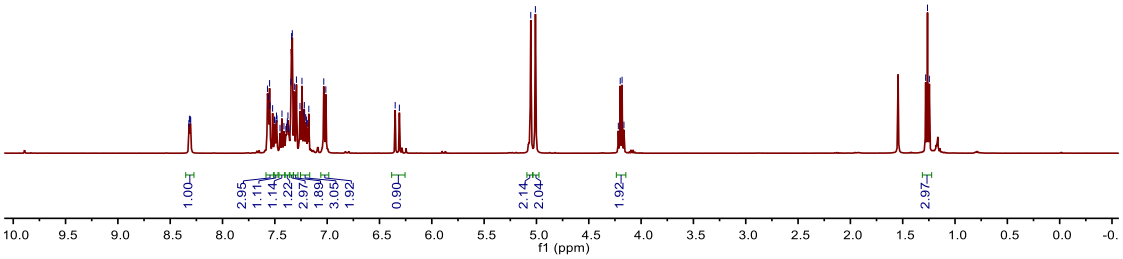
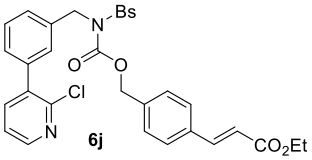
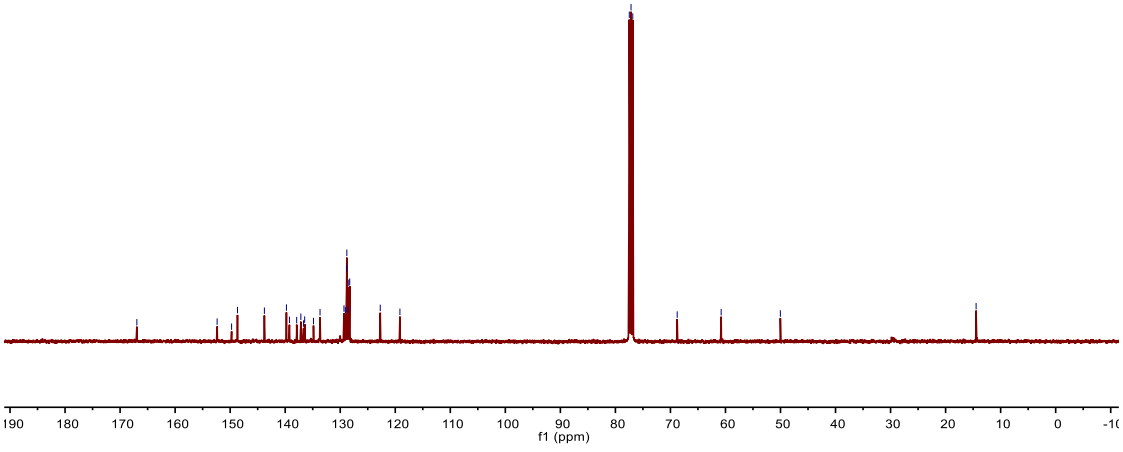




^{13}C NMR (101 MHz, Chloroform-*d*)





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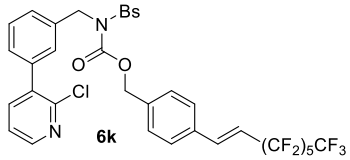
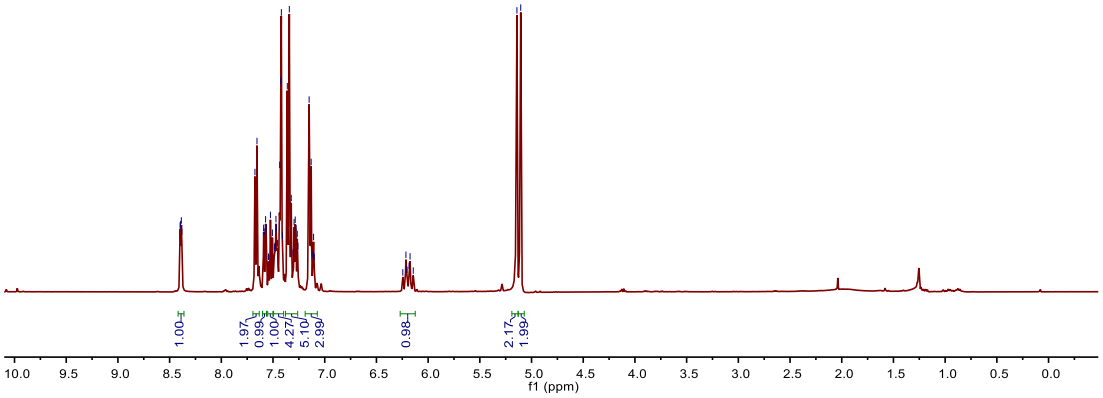
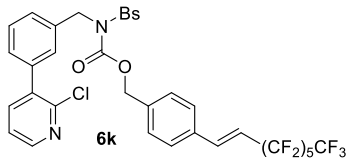
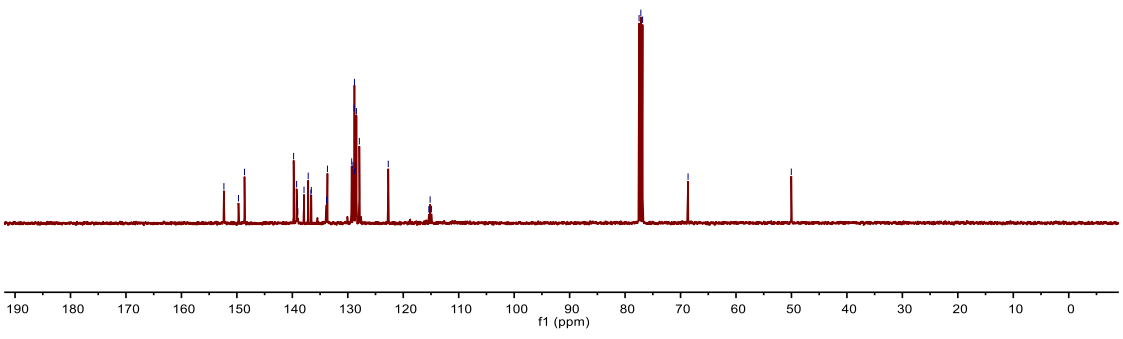


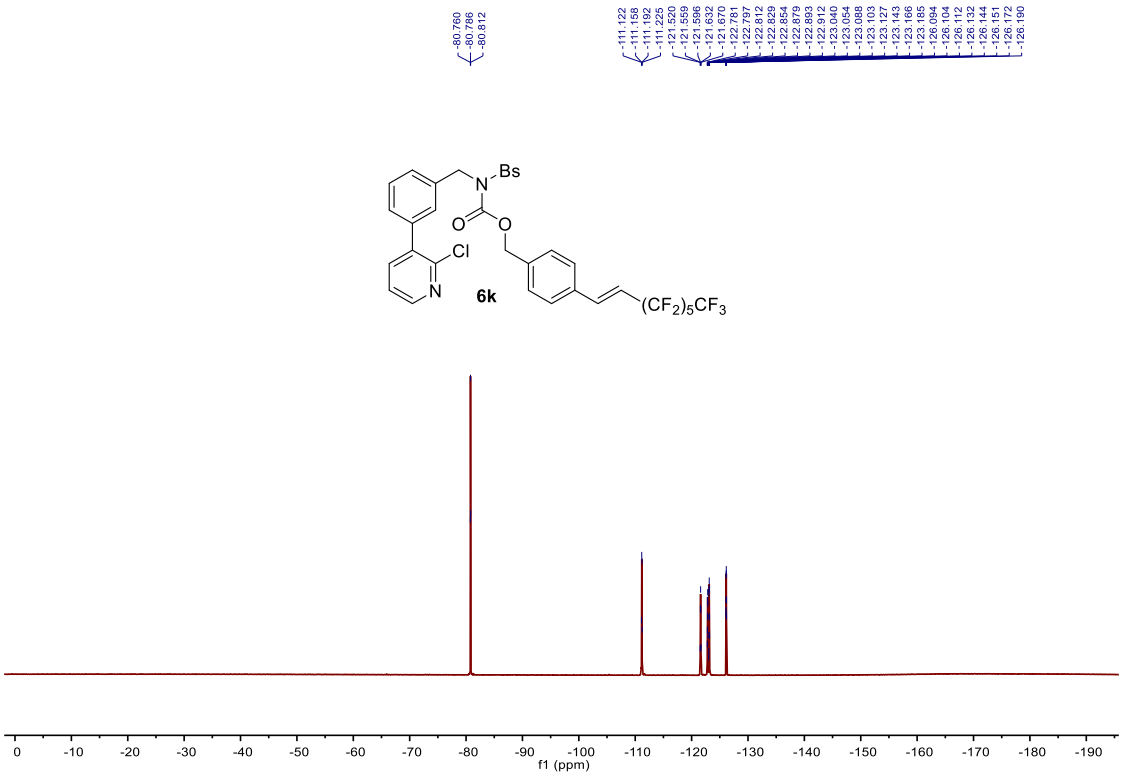


^{13}C NMR (101 MHz, Chloroform-*d*)





^{19}F NMR (376 MHz, Chloroform-*d*)



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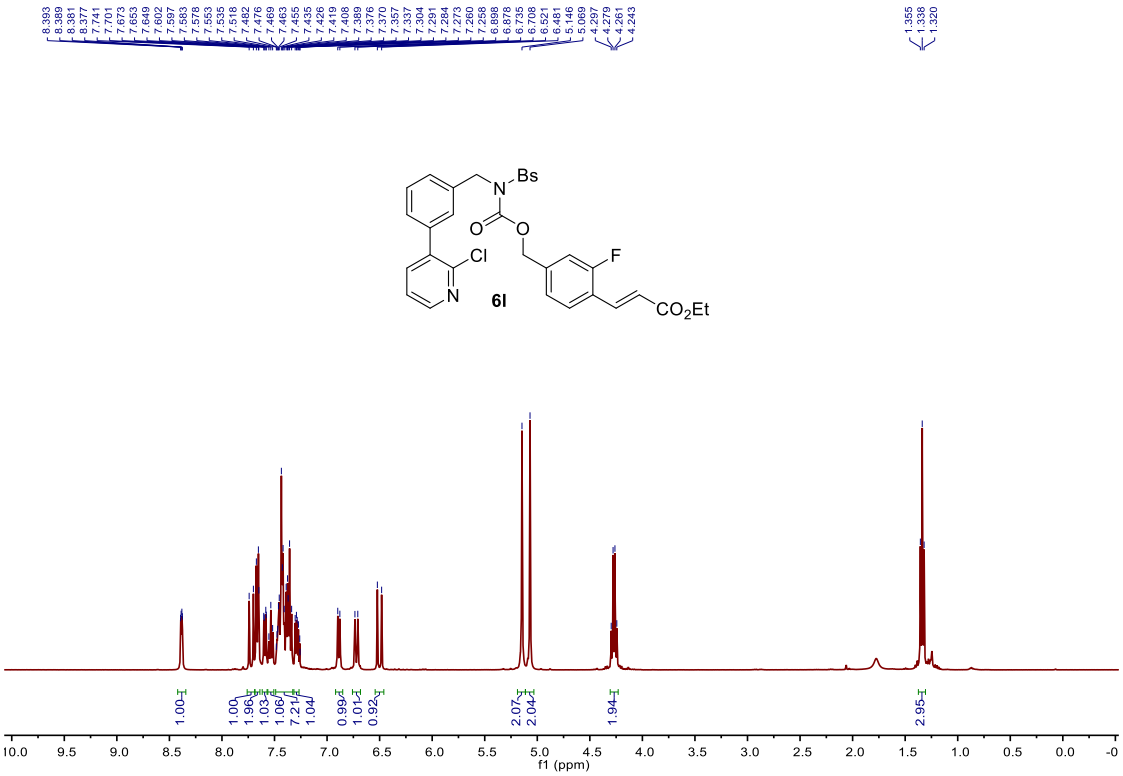

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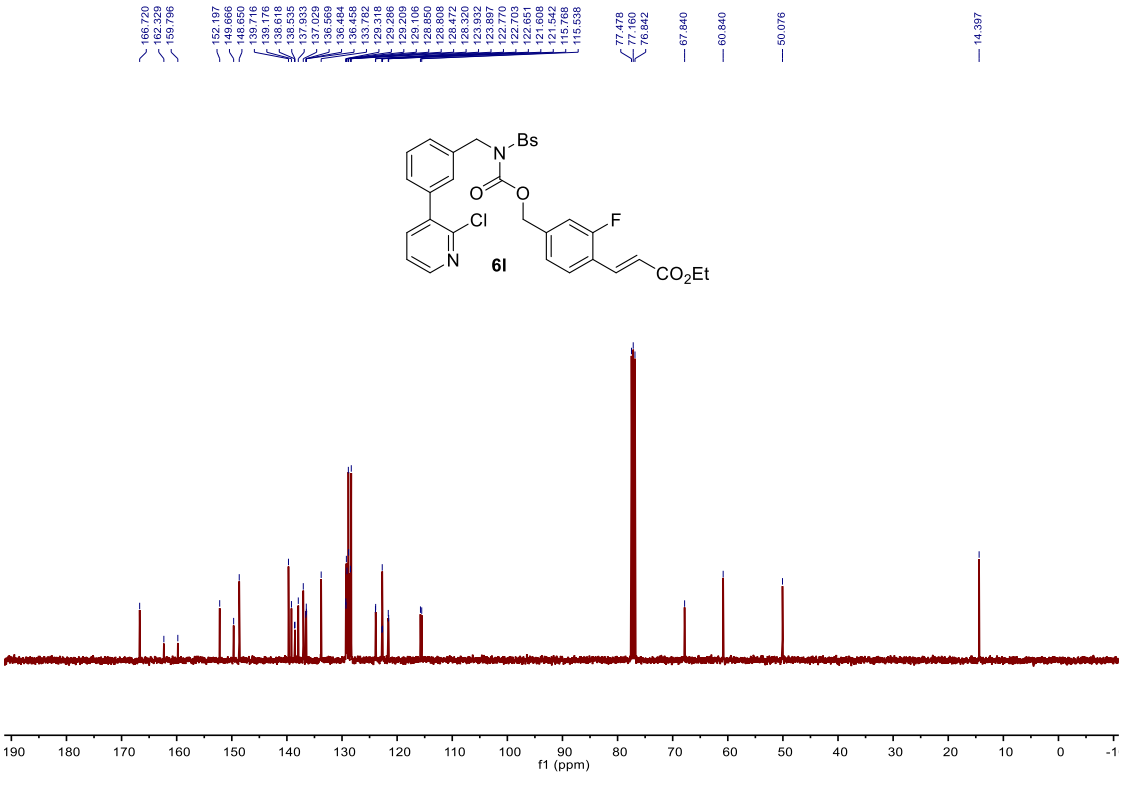

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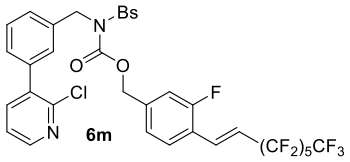

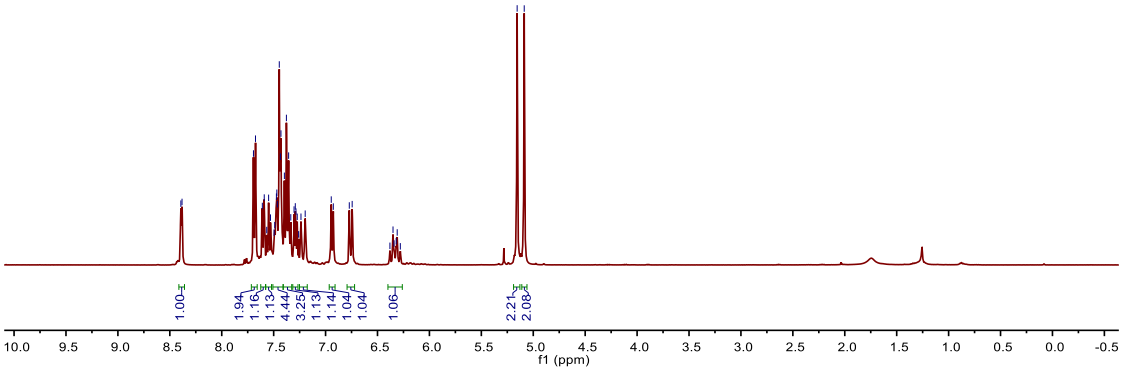

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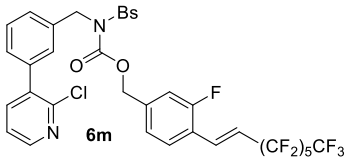
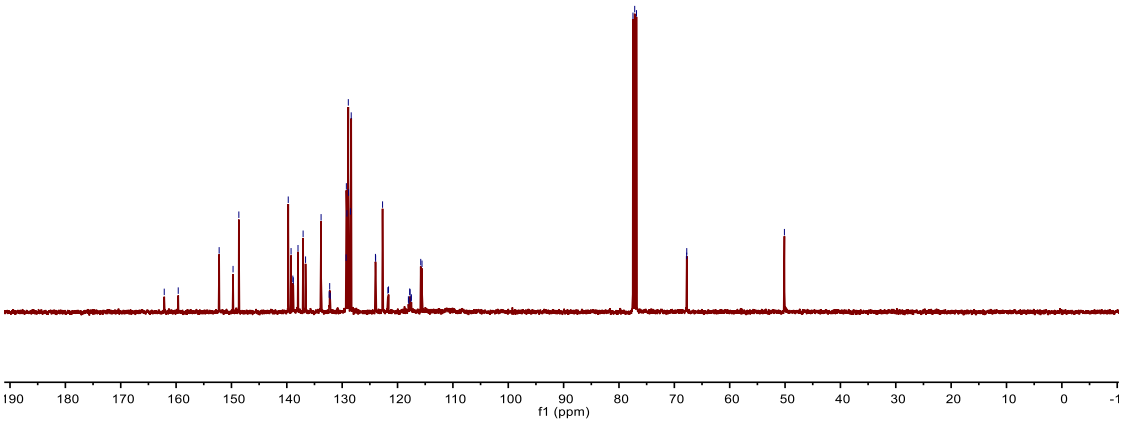
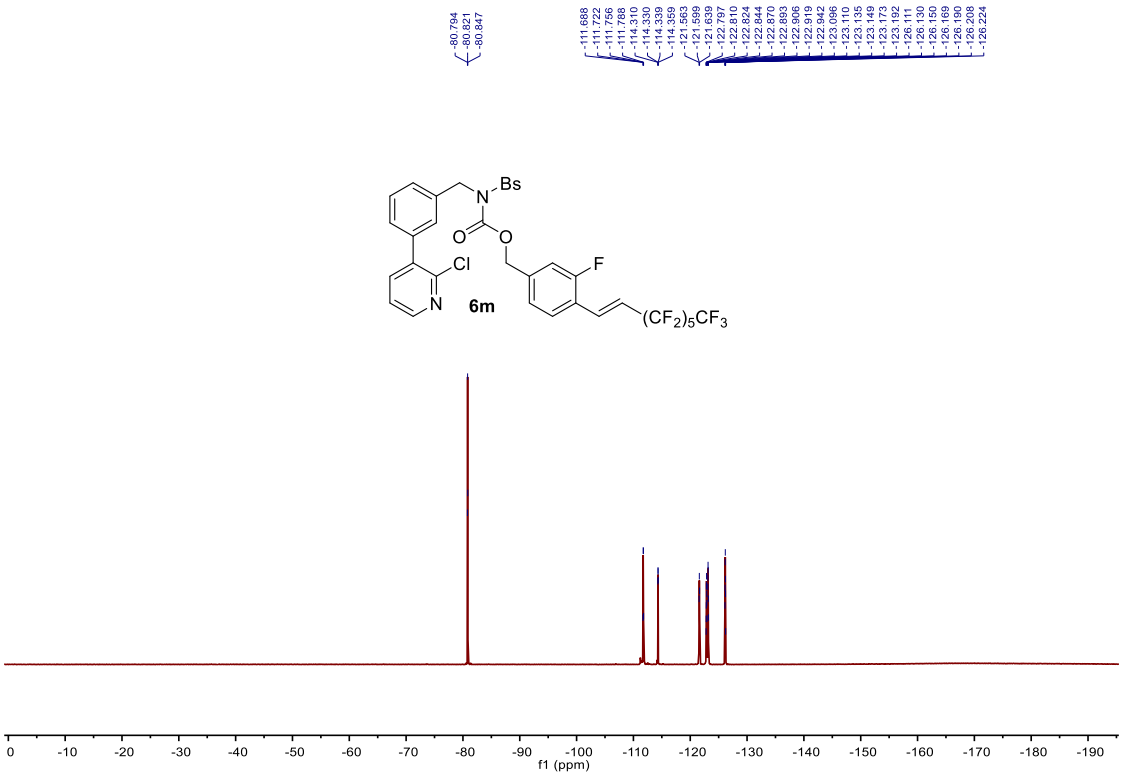




^{19}F NMR (376 MHz, Chloroform-*d*)



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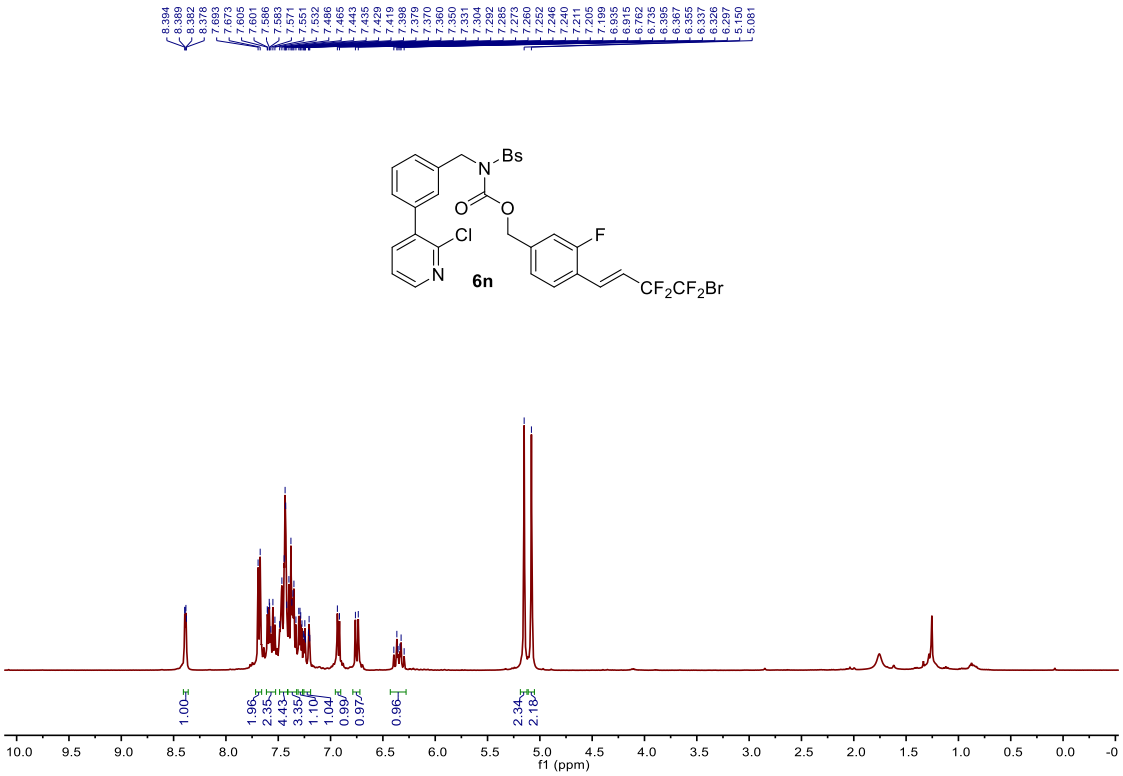

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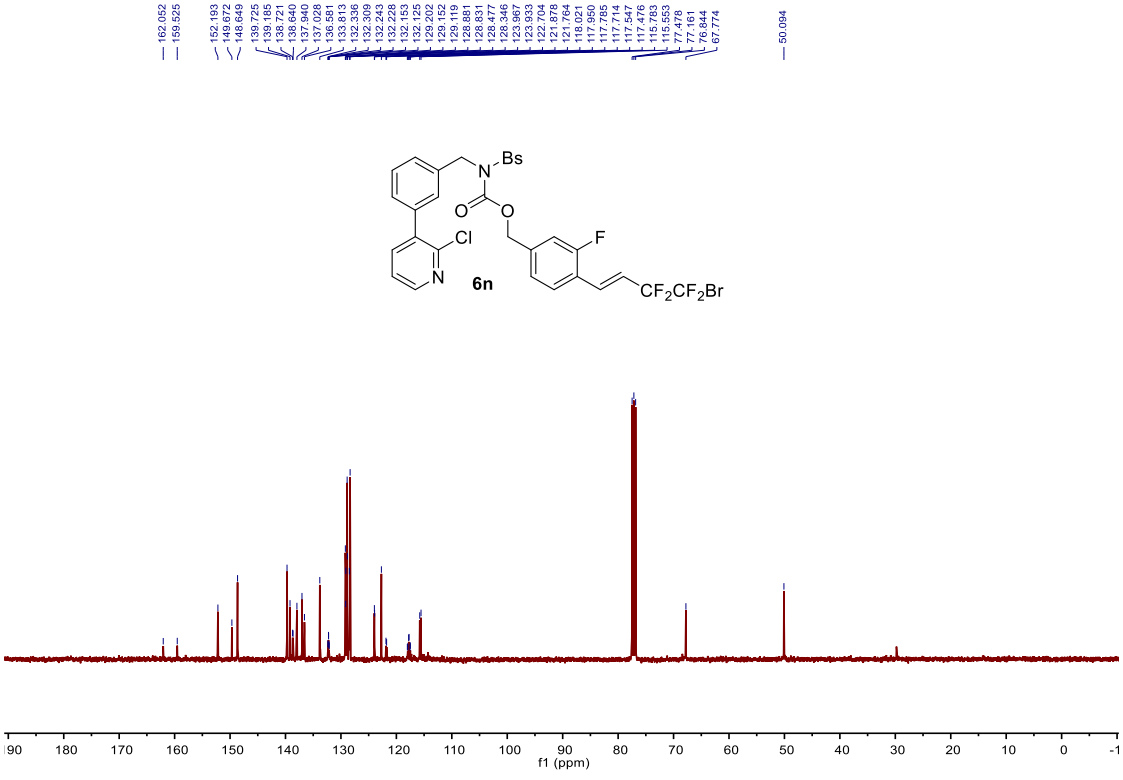

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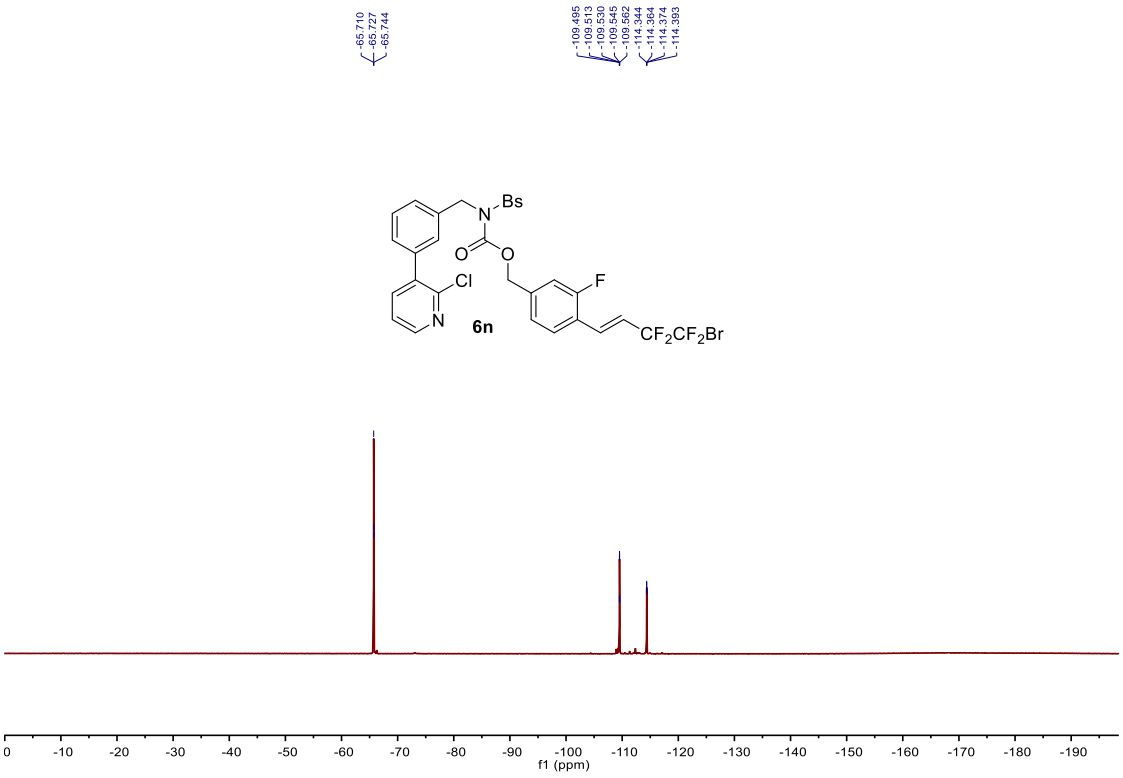

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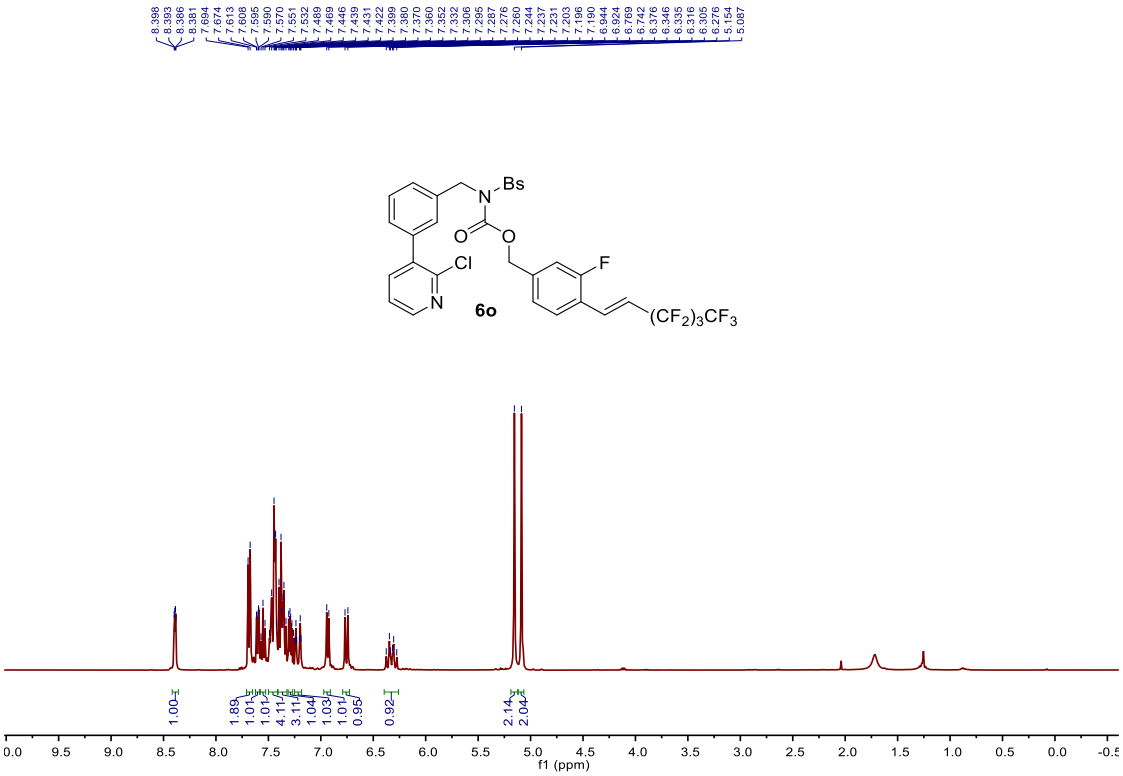

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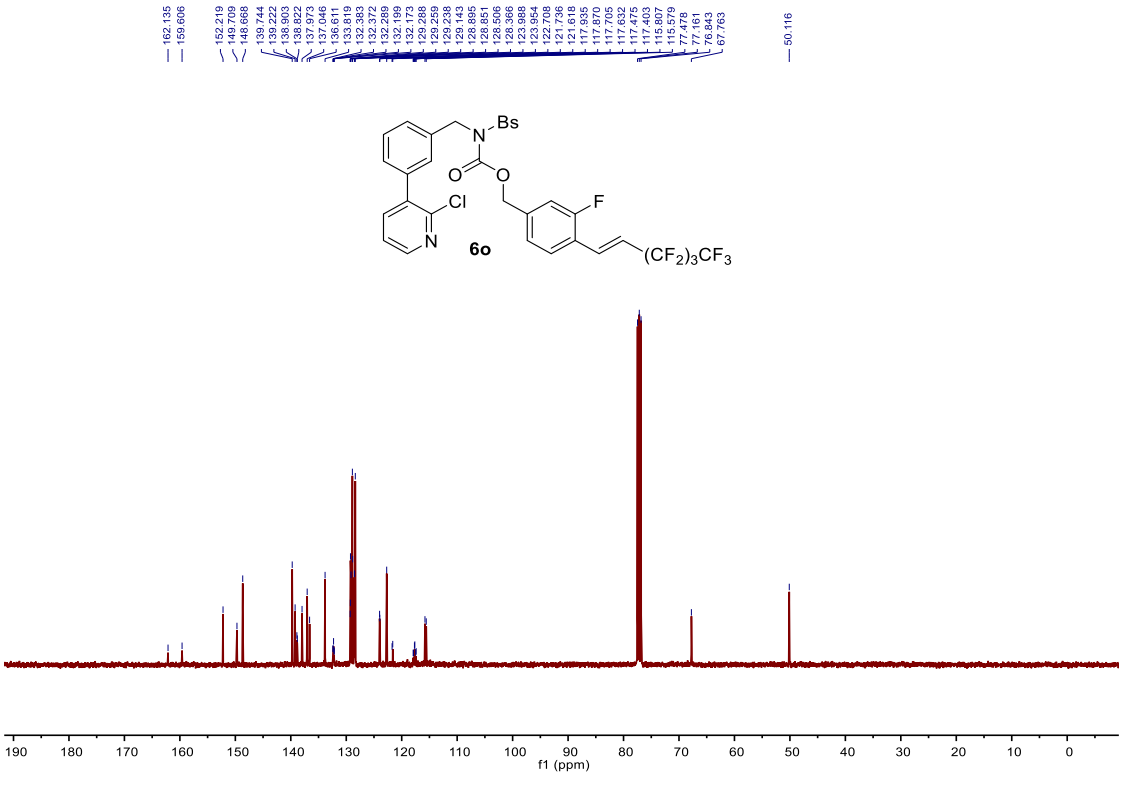

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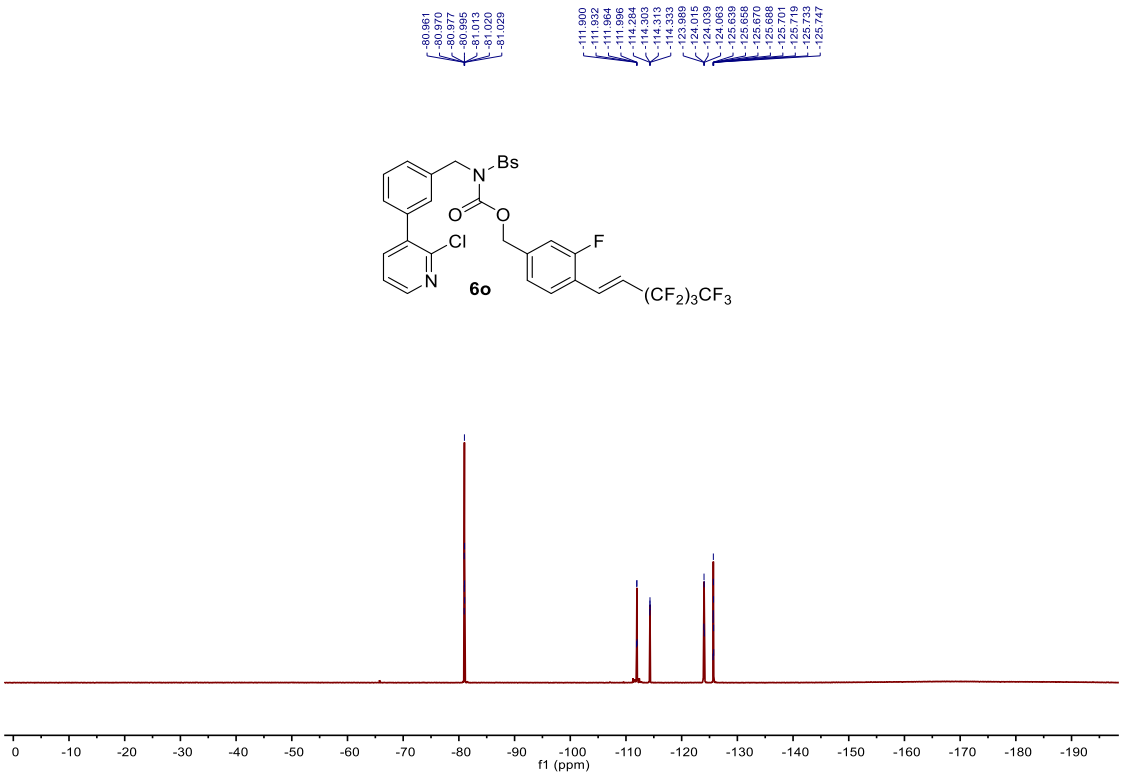

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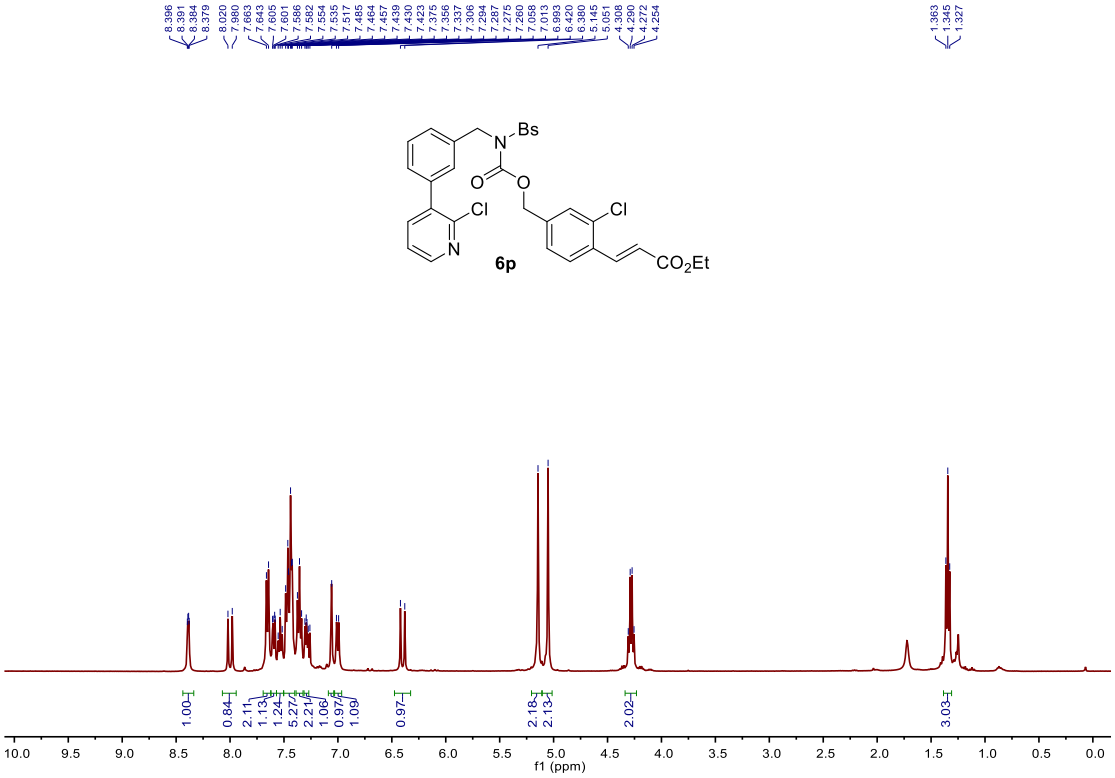

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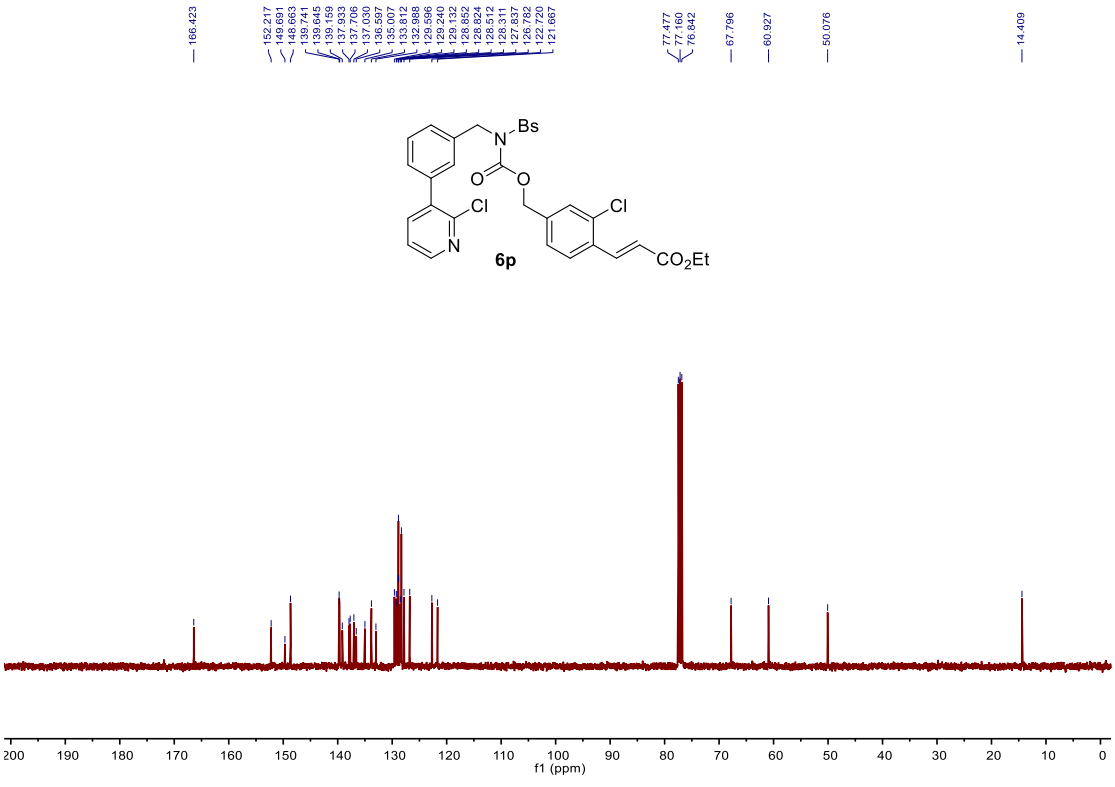

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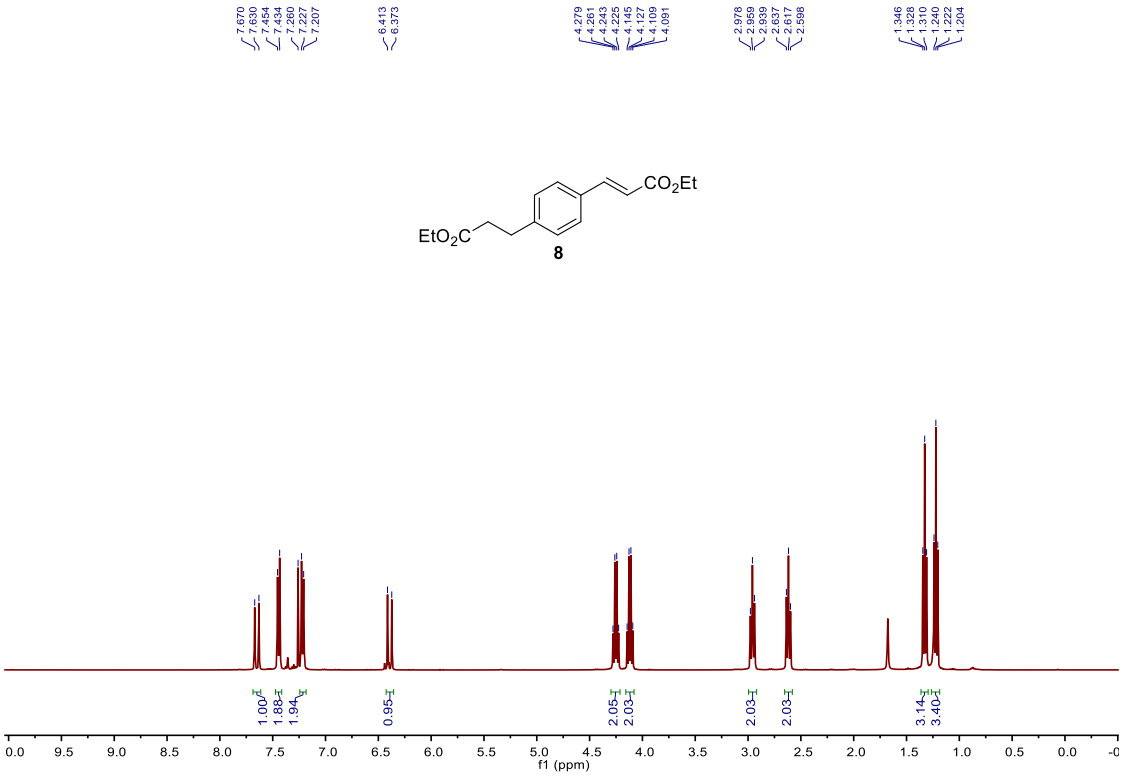

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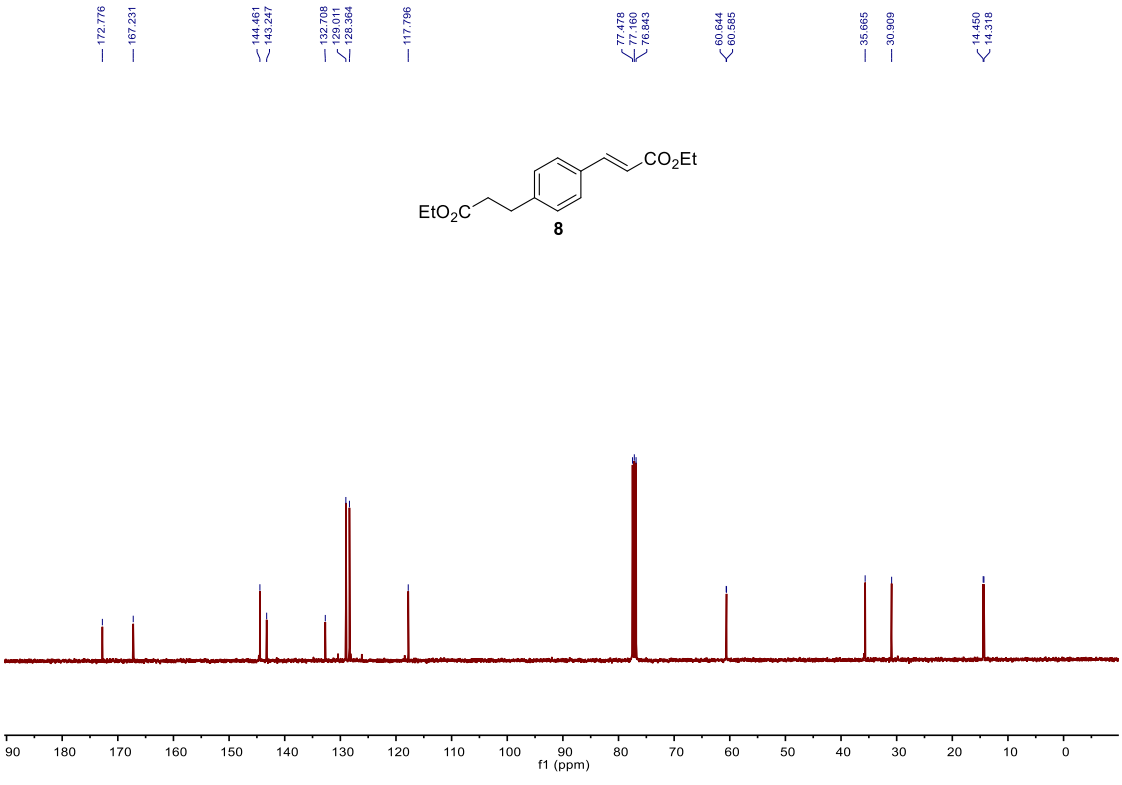

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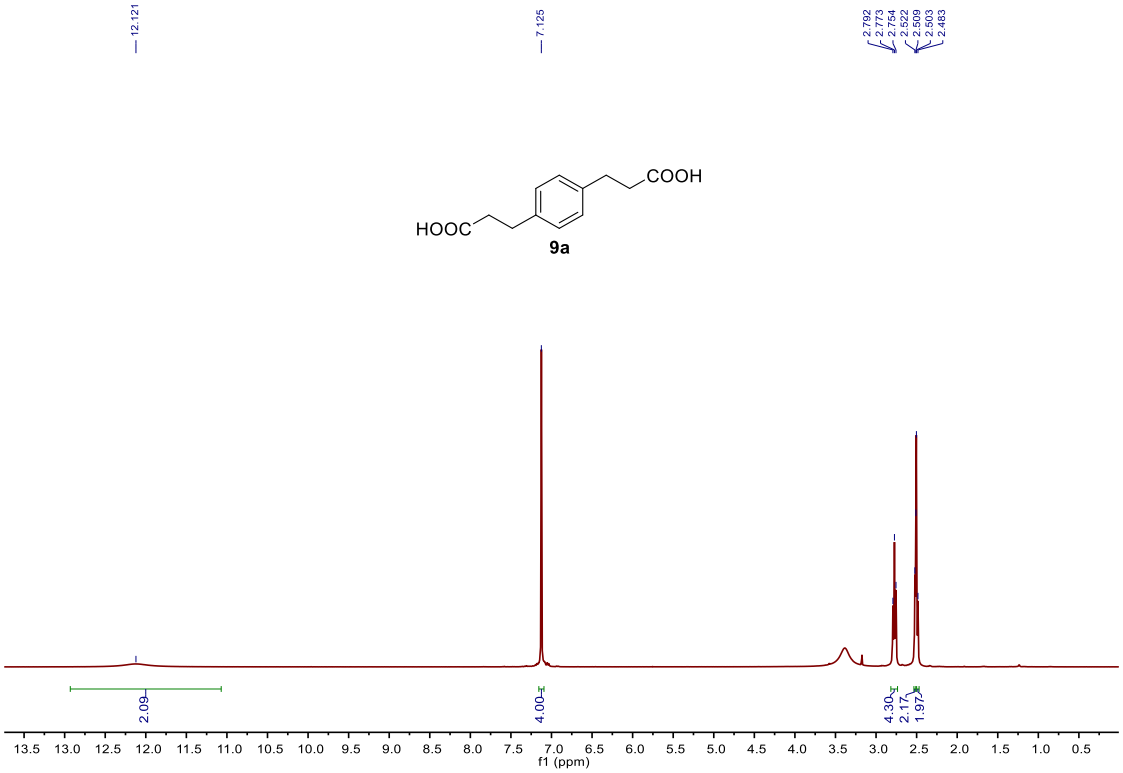

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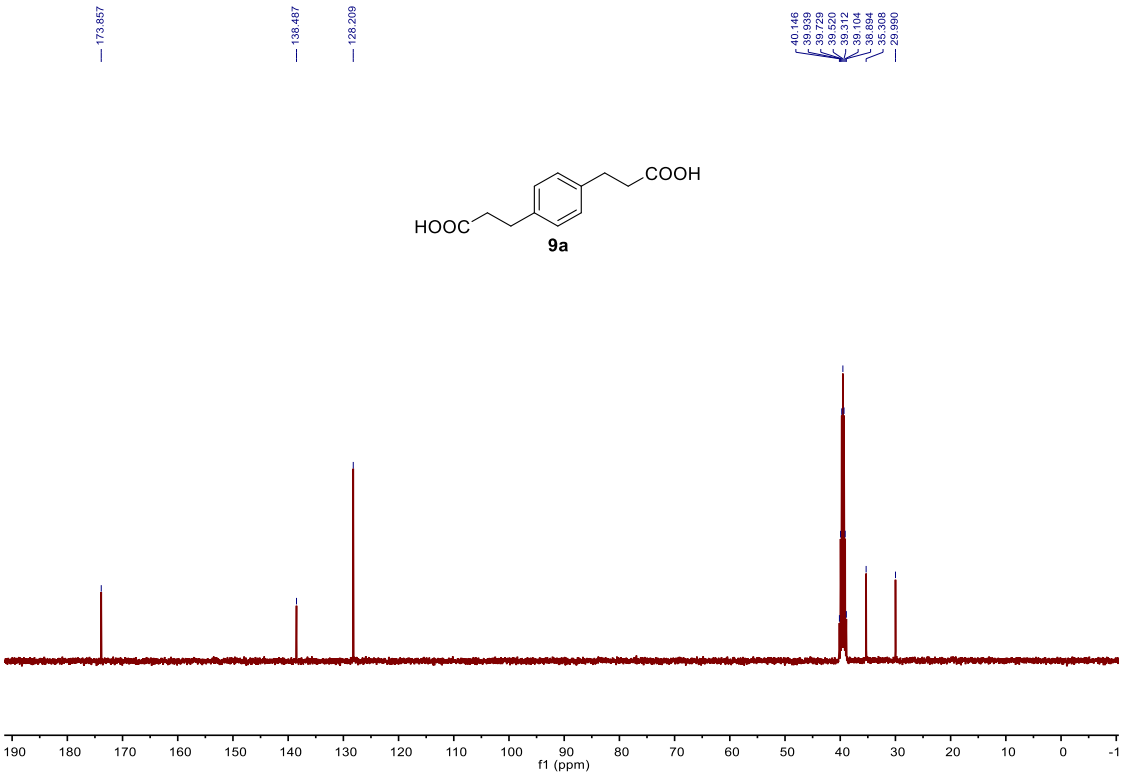

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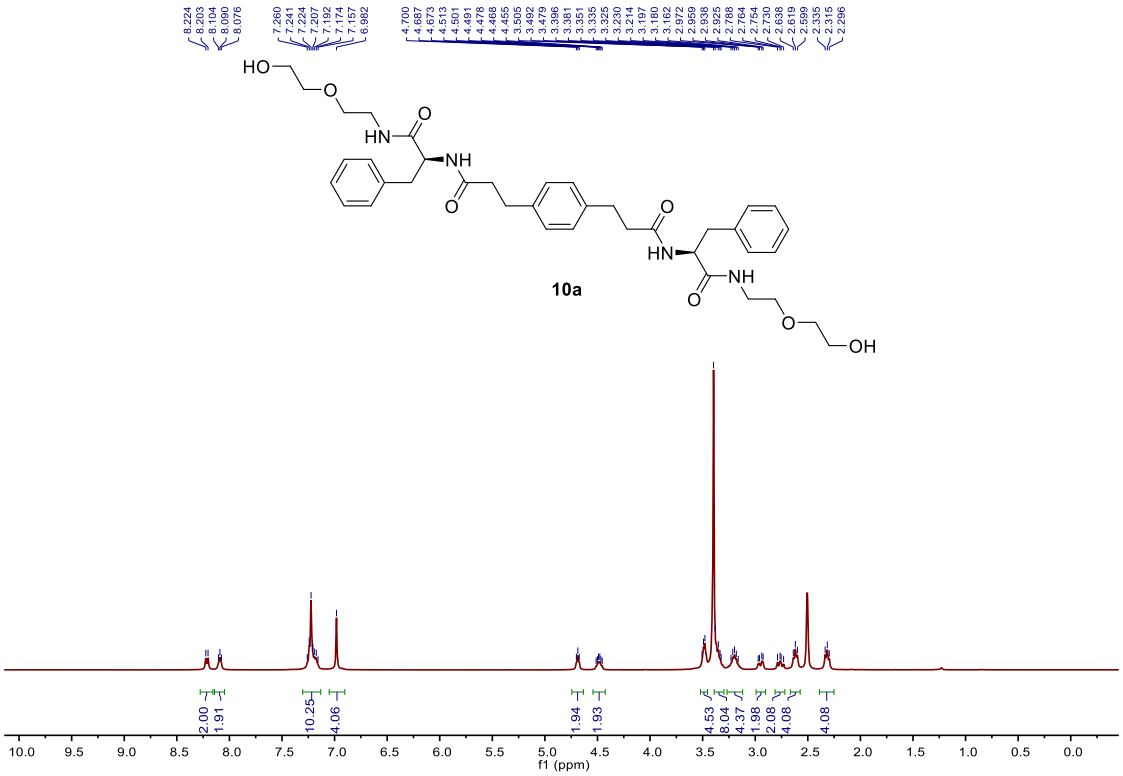

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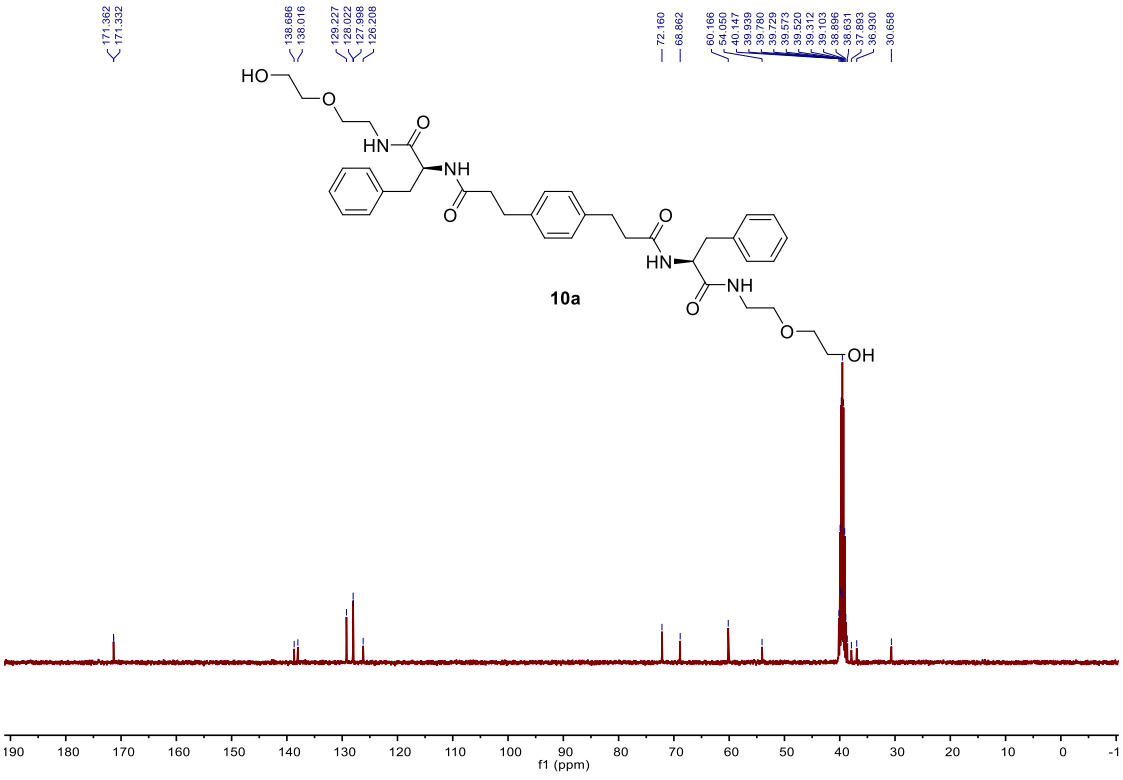

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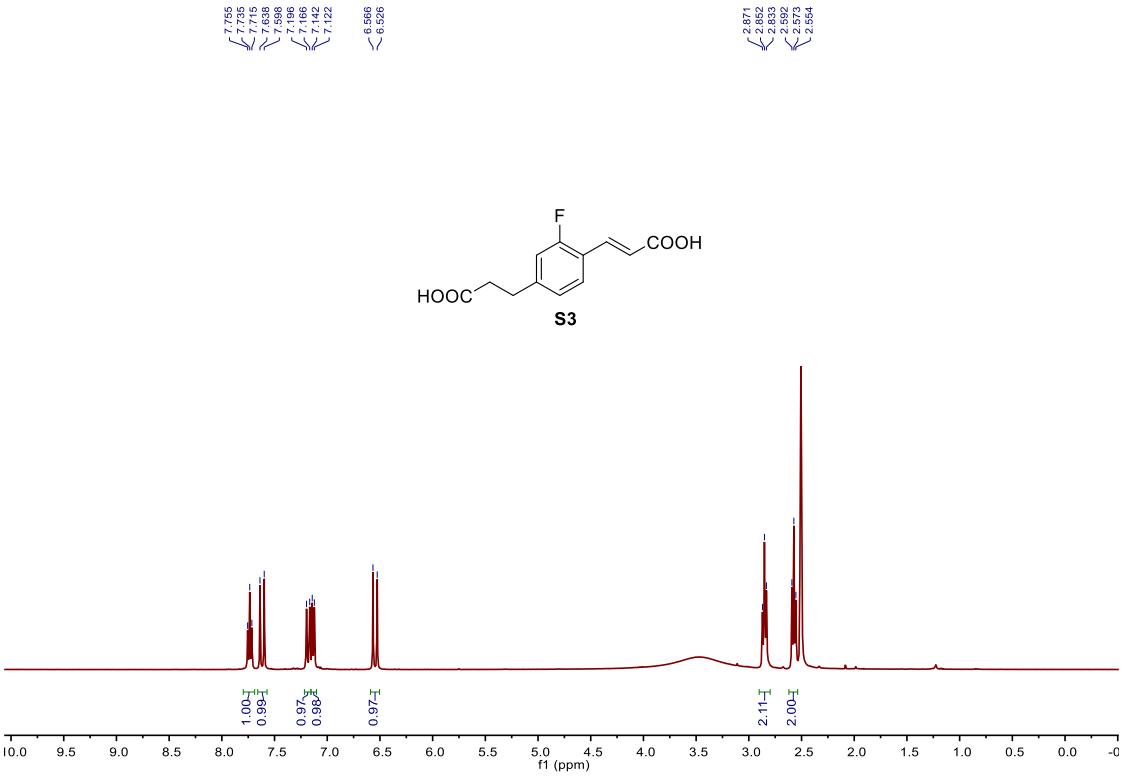

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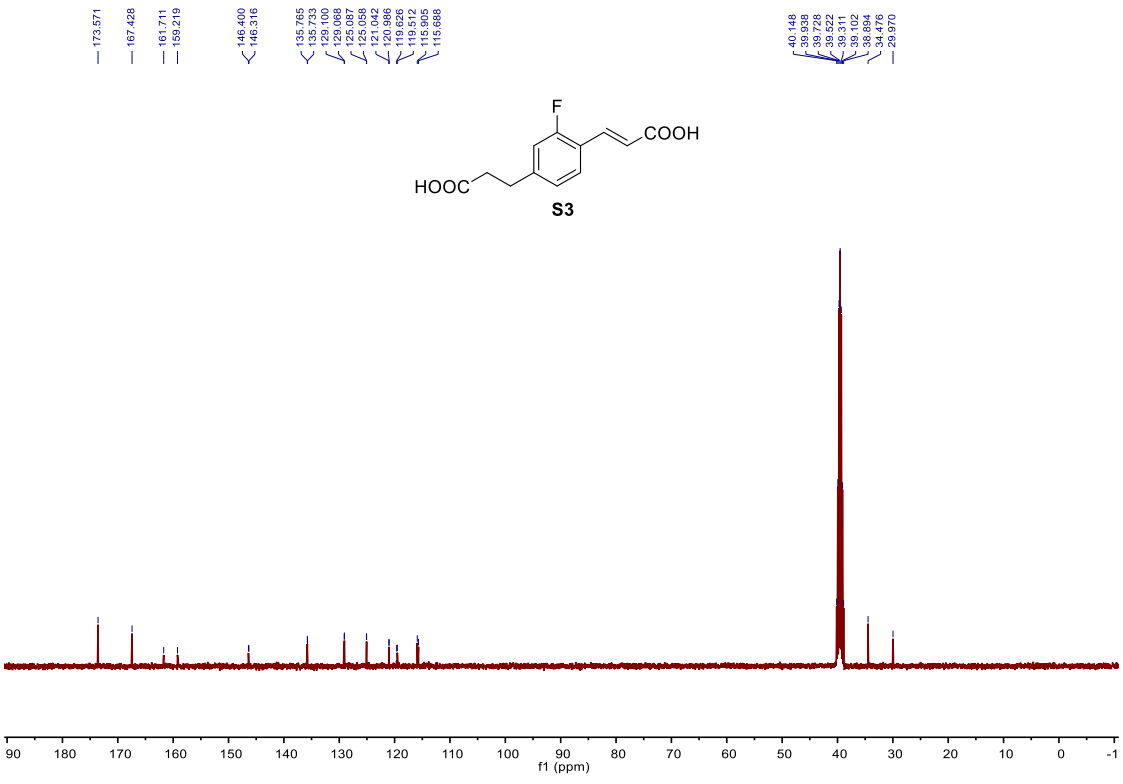

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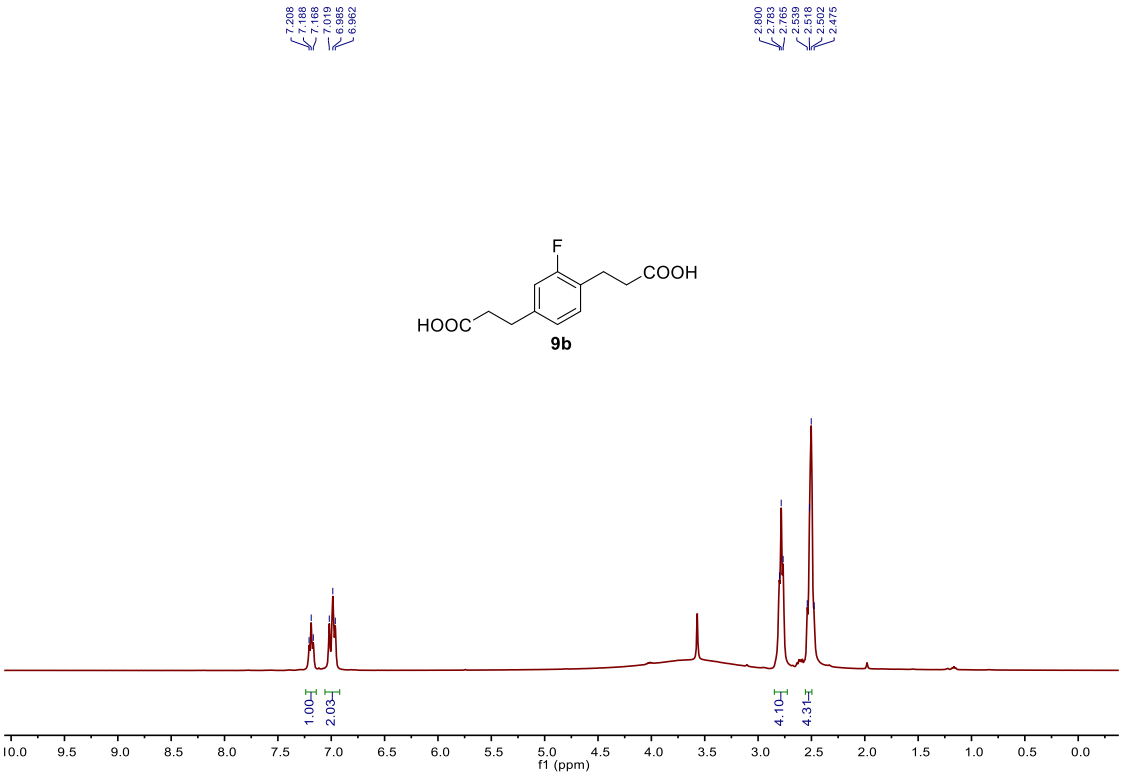

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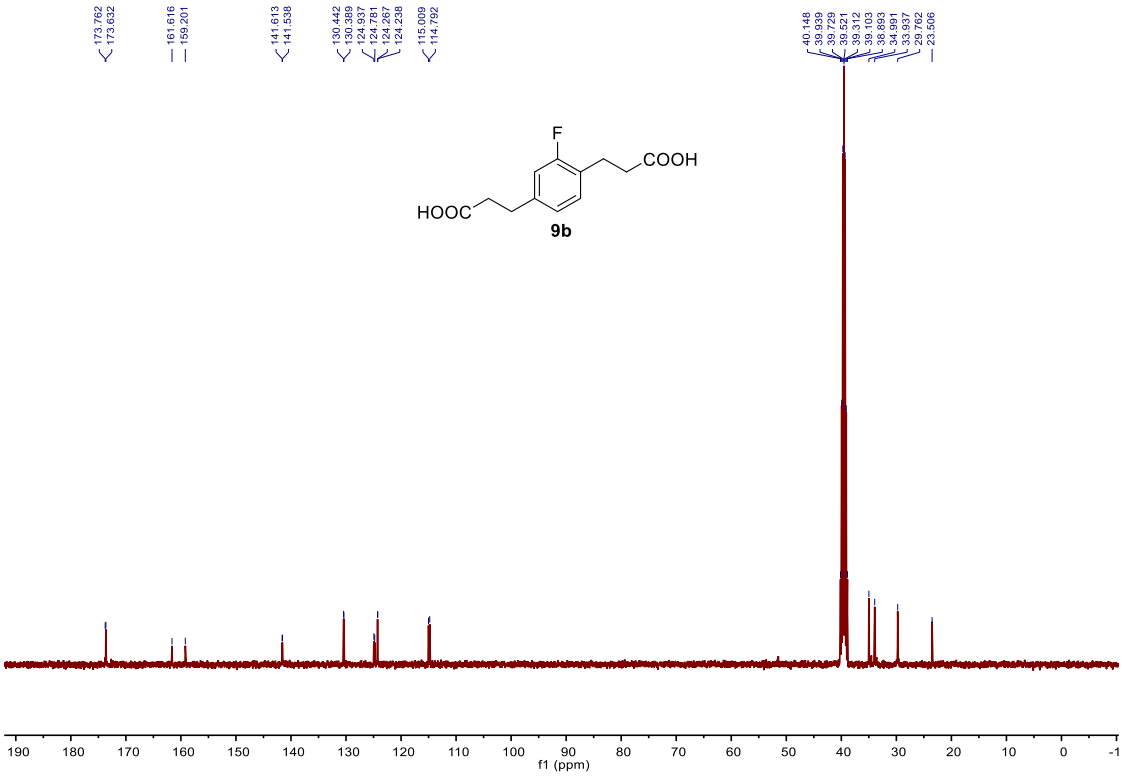

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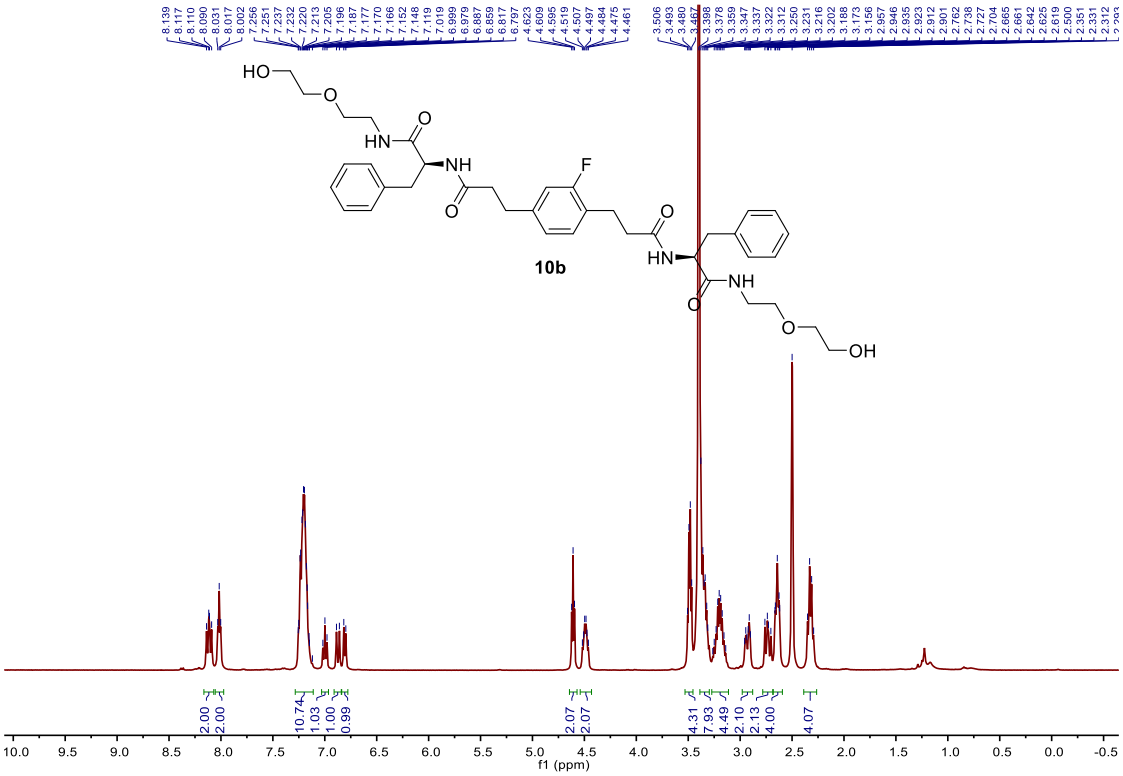

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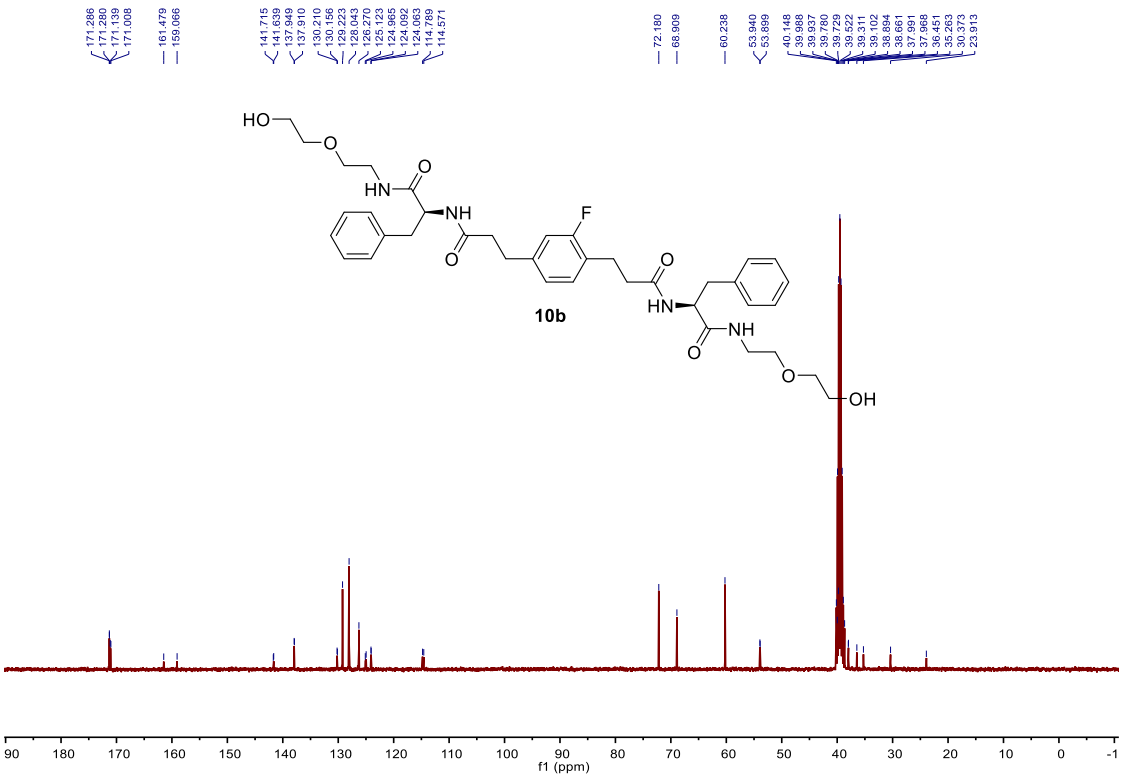

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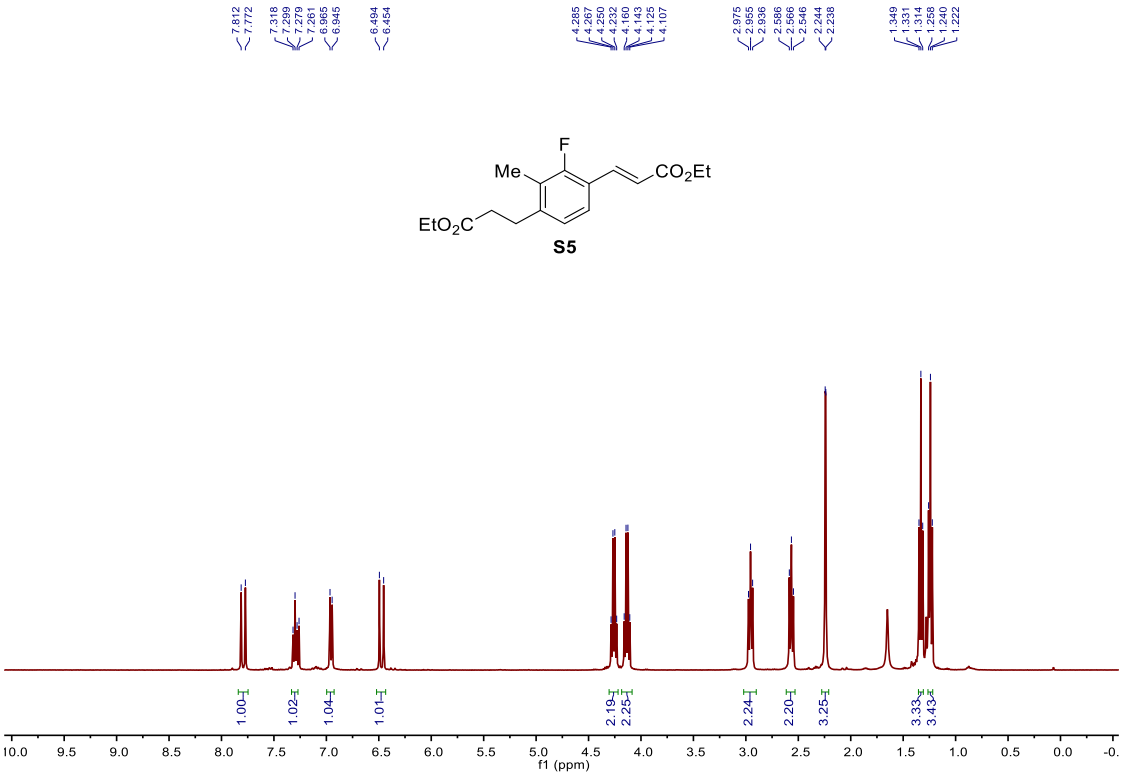

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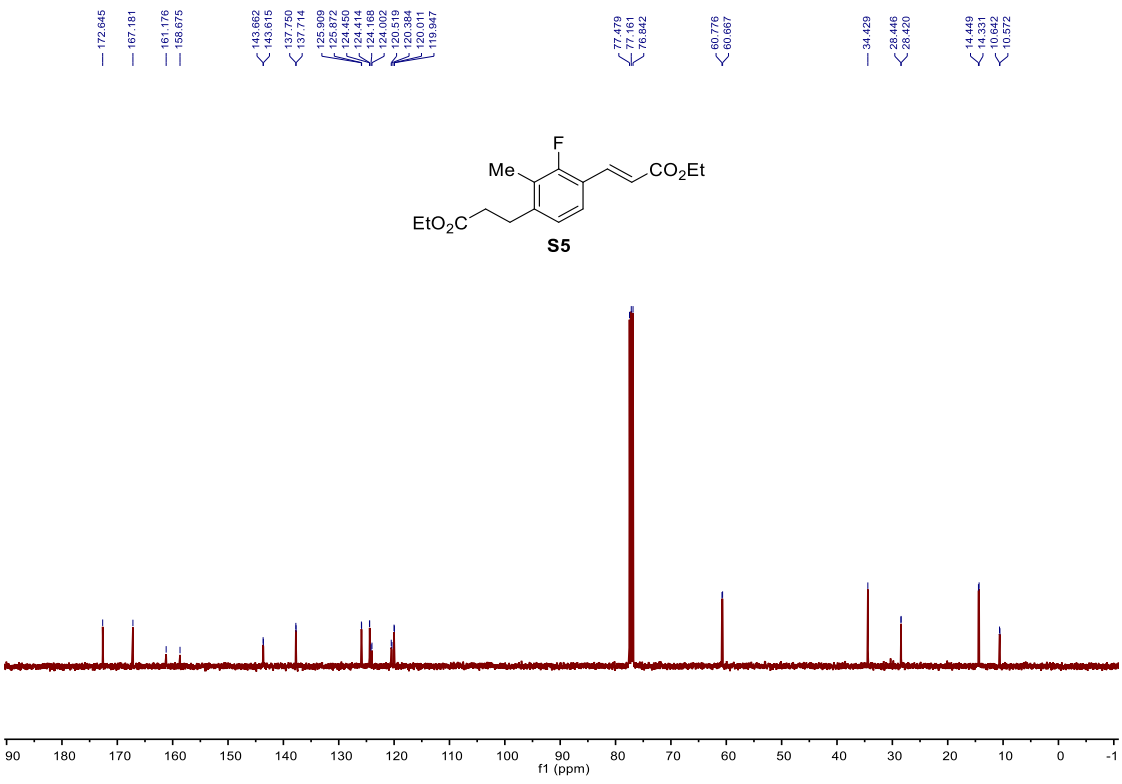

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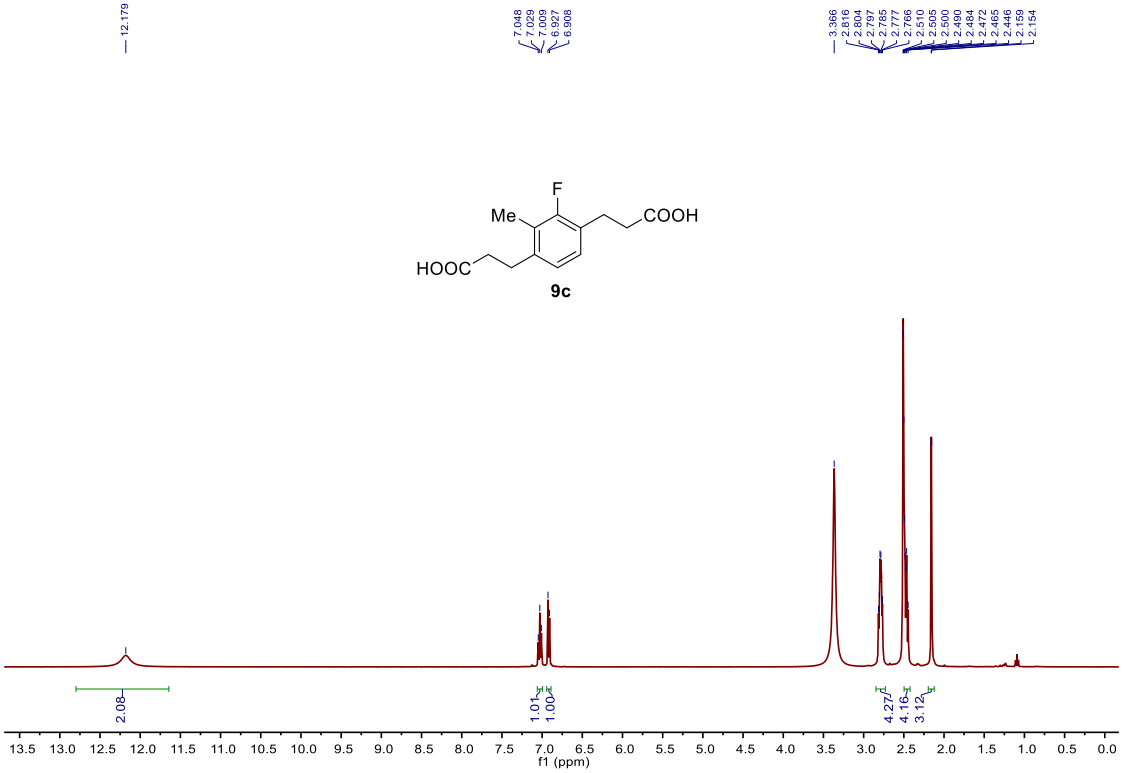

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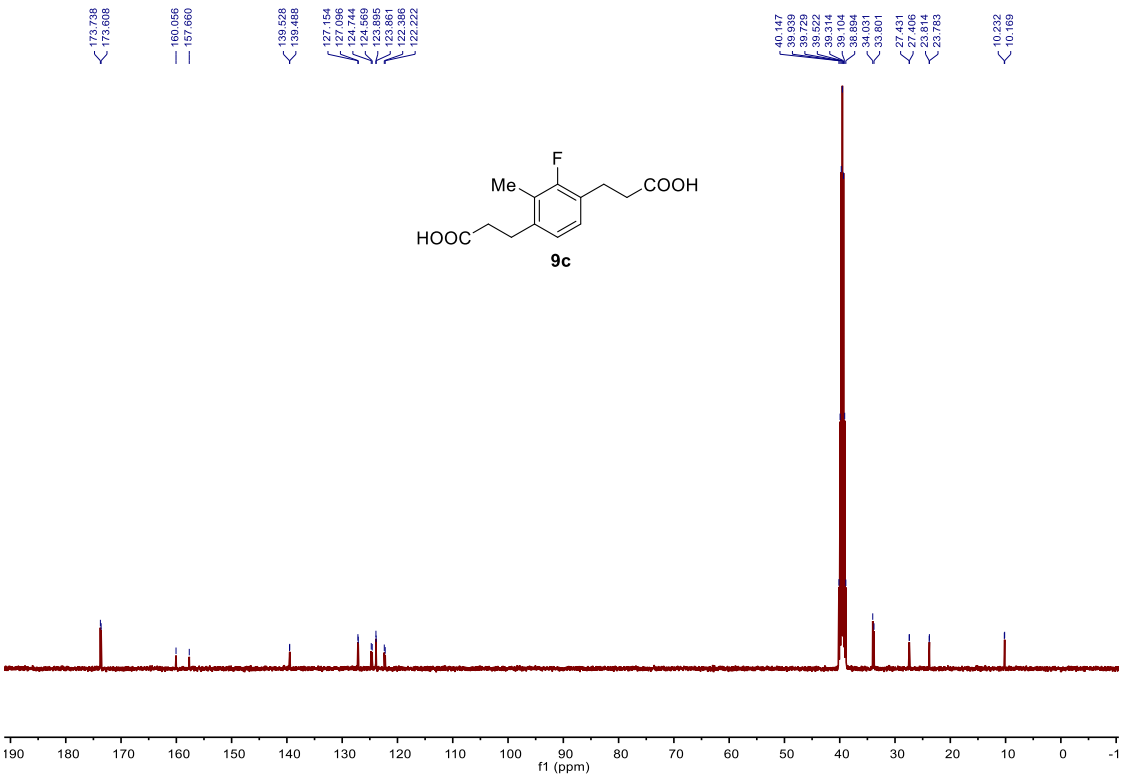

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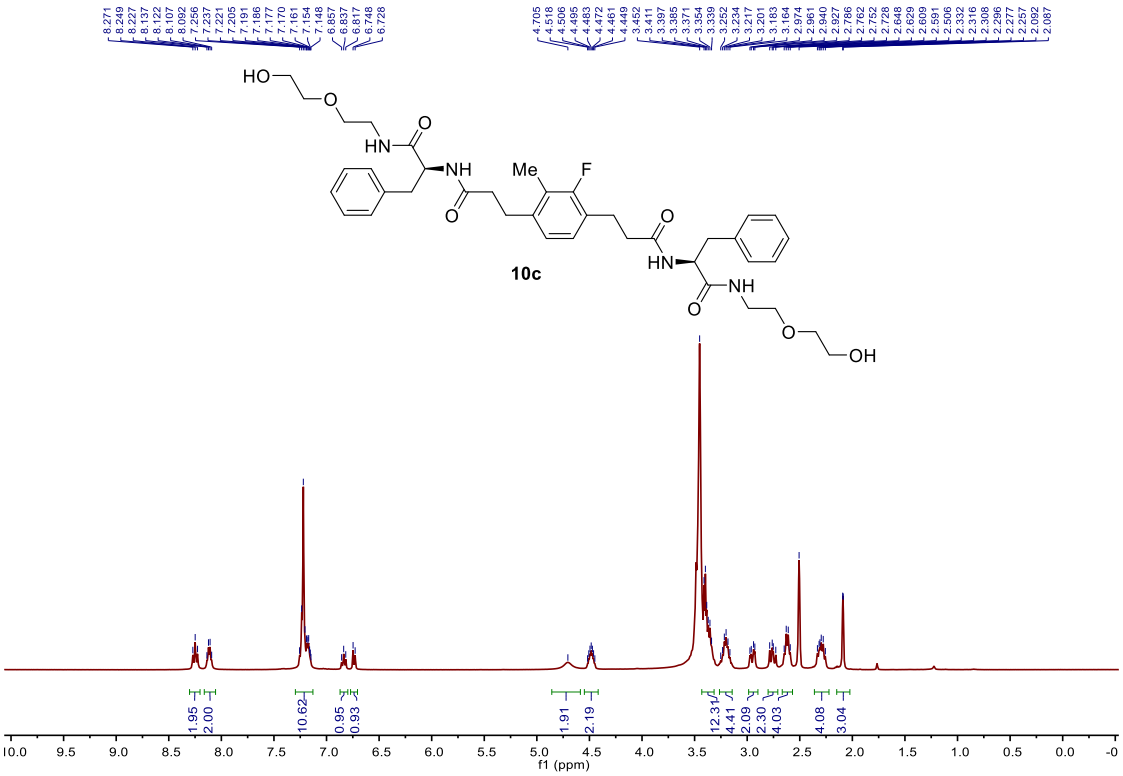

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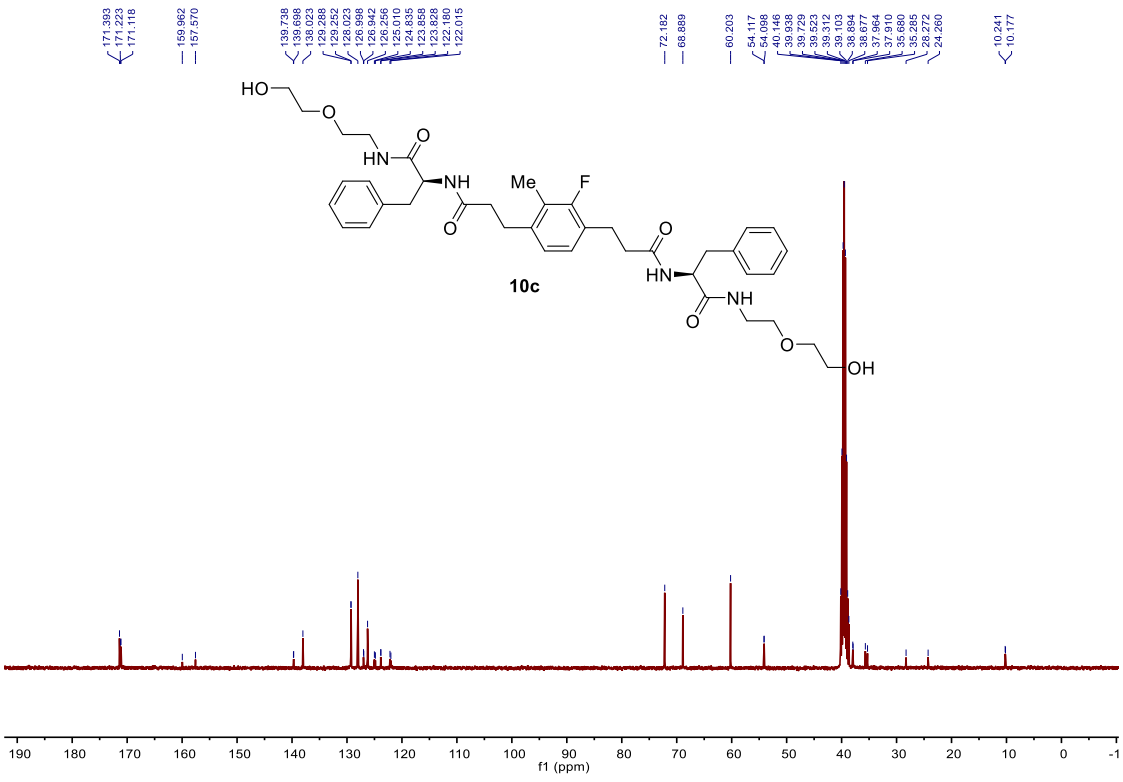

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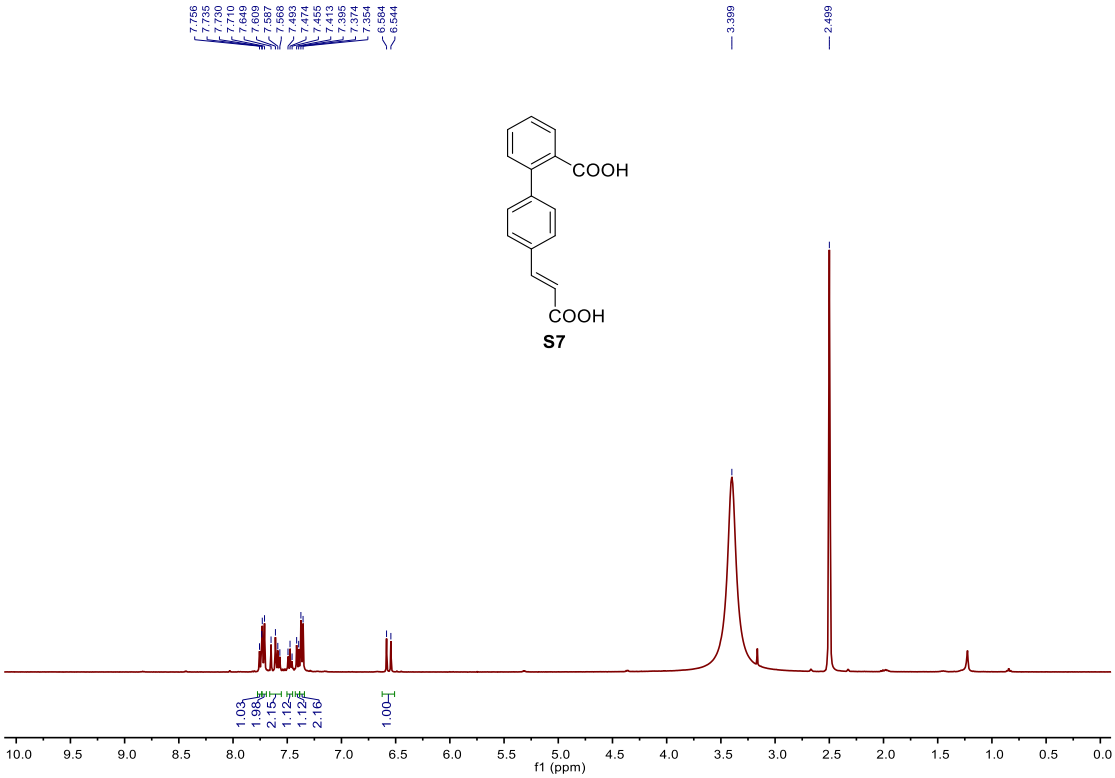

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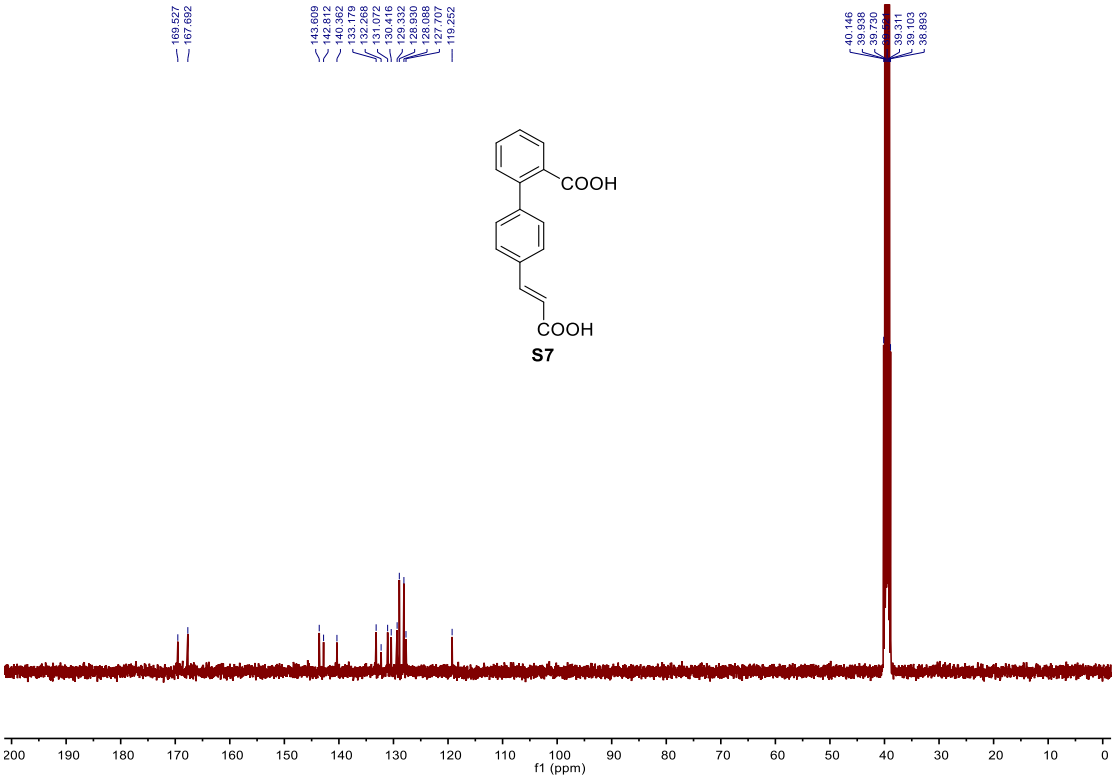

4 References

(1) Yamamoto, T.; Murakami, R.; Suginome. M. Single-Handed Helical Poly(quinoxaline-2,3-diyl)s Bearing Achiral 4‑Aminopyrid-3-yl Pendants as Highly Enantioselective, Reusable Chiral Nucleophilic Organocatalysts in the Steglich Reaction. *J. Am. Chem. Soc.* **2017**, *139*, 2557−2560.
(2) Liu, J.; Yuan, F.; Ma, X.; Auphedeous, D. Y.; Zhao, C.; Liu, C.; Shen, C.; Feng, C-L. The Cooperative Effect of both Molecular and Supramolecular Chirality on Cell Adhesion. *Angew. Chem., Int. Ed.* **2018**, *57*, 6475.