

Carbon Dioxide-Mediated C(*sp*²)-H Arylation of Primary and Secondary Benzylamines

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Supporting Information

Table of Contents

1. General Information	S-2
2. Safety Notes.....	S-2
3. Synthesis of 1° Benzylamine Substrates.....	S-4
4. Synthesis of 2° Benzylamine Substrates.....	S-14
5. Synthesis of Iodoarenes	S-19
6. Optimization and Synthesis of γ -Arylated 1° Amines	S-20
7. Optimization and Synthesis of γ -Arylated 2° Amines	S-37
8. Application Experiments	S-51
9. Scale-Up Experiments	S-54
10. Mechanism Experiments	S-55
11. ¹ H, ¹³ C, and Select IR Spectra of New Compounds	S-60
12. References	S-182

1. General Information

^1H , ^{13}C , and ^{19}F spectra were recorded on a Varian Inova 400 MHz NMR spectrometer or a Varian Inova 600 MHz NMR spectrometer, or an Avance 600 MHz spectrometer, and were processed using MestReNova by Mestrelab Research S.L. Proton (^1H) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane (TMS, $\delta=0$), and referenced internally with respect to the protio solvent impurity. Carbon (^{13}C) chemical shifts are reported in parts per million (δ) with respect to tetramethylsilane (TMS, $\delta=0$), and referenced internally with respect to the carbon signal of the solvent. Fluorine (^{19}F) chemical shifts are reported in parts per million (δ) and referenced internally with respect to hexafluorobenzene included in an insert tube (C_6F_6 , $\delta=-164.9$). Deuterated NMR solvents were obtained from Cambridge Isotope Laboratories, Inc., Andover, MA, and used without further purification. Mass spectra were recorded on an Agilent 6530 LC Q-TOF mass spectrometer using electrospray ionization with fragmentation voltage set at 115 V or lower for sensitive substrates, and processed with an Agilent MassHunter Operating System, or on a Waters SYNAPT G2-Si High Definition Mass Spectrometer. For limited cases where ESI data was not obtained, an Agilent 5975C Inert XL MSD with Triple-Axis Detector were used, and data processed using 5975C MSD Data Analysis software. All other materials were obtained from Sigma-Aldrich Chemical Company, St. Louis, MO, Combi-Blocks, San Diego, CA, Oakwood Chemical, Estill, SC, Alfa Aesar, Ward Hill, MA, Acros Organic, Geel, Belgium, or TCI, Tokyo, Japan, and were used as received.

2. Safety Notes

A. Notes on Pressure Reactions in 2 Dram Vials

During our work, we found that standard 2 dram vials from Qorpak could be set-up with the necessary reagents, 1 mL of solvent, and ~33 - 66 mg of dry ice, followed by immediately sealing. In our experience, the vials never failed, even upon heating to 100°C. Although we did not have any lab incidents, we advise that all reactions should be performed behind appropriate shielding, and should not be heated until such engineering controls (blast shield and/or hood sash) are in place. It is worth noting that a similar strategy has been used frequently to allow the use of *liquid CO₂* as a solvent for thin layer chromatography, which may provide additional guidelines for the safe handling of CO₂ pressure in non-standard sealed systems.¹ Alternatively, one may consider using a pressure tube for these reactions (*e.g.* Ace Glassware, 8648-03). When it is time to work-up the reactions, we first always cool the reactions to room temperature. The caps are slowly opened, and allowed to vent. Sometimes, depending on the level of precipitate at the bottom of the flask, the reaction mixtures bubble vigorously, which necessitates performing this operation multiple times to slowly bleed off the carbon dioxide. Although the pressures observed have never caused any incidents in our hands using the published conditions, we recommend this operation be performed in the fume hood, and that all appropriate PPE, especially goggles, are worn at all times. When using a pressure tube, we will treat the top much like a champagne cork, and as a precaution will secure a towel over the cap to ensure it does not go flying off and subsequently bouncing around the hood. Although this has never happened to us, we do recommend this precaution when using enough dry ice to generate the maximum recommended pressure for the pressure tubes. We have also published a visual demonstration to assist with the safe handling of this procedure.²

B. Notes on the Use of Azides

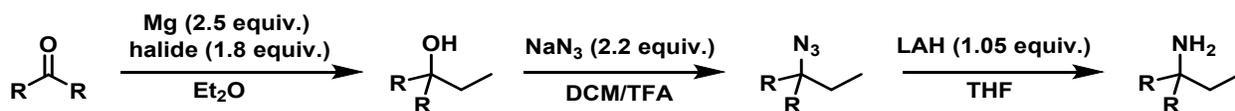
Many of the starting materials in this study were prepared by a well-established two step procedure where an alcohol is combined in dichloromethane with sodium azide, followed by addition of excess of trifluoroacetic acid in dichloromethane. This procedure produces hydrazoic acid *in situ*, and as a result should be given great care.³ Furthermore, use of dichloromethane can lead to explosive diazidomethane. Keeping the concentration *and* temperature low is critical to prevent formation of this compound. Although using chloroform may obviate some of these risks, we found that more reliable yields were obtained by using dichloromethane as the solvent.

- The reaction should always be run on relatively small scale, as HN_3 is a powerful explosive.
- The reaction should always be kept cold while HN_3 is present, as its exothermic decomposition can lead to explosions.
- The reaction should always be kept relatively dilute, and efforts should be made to prevent any concentration through solvent loss throughout the duration of the reaction.
- Because HN_3 is highly volatile, the reaction should be performed in a fume hood under a nitrogen atmosphere.
- It is important to fully neutralize *all* hydrazoic acid to ensure it is not present during the work-up, and to furthermore ensure that all waste is disposed of into containers that will not collect any acids or transition metals, as this can lead to explosions from formation of HN_3 as well as various metal-nitrides. These containers should be well labeled, and it is safest if their volume is small, and that they are not stored for long periods of time.

The organoazide products are expected to be stable at room temperature, but care should also be taken to not heat them excessively. In our hands, the reaction mixtures and purified products are always kept at room temperature or below, and once purified the organoazides are used immediately and are not stored.

3. Synthesis of 1° Benzylamine Substrates

A) General Procedure for Synthesis of Primary Amines Bearing an α -Tertiary Center

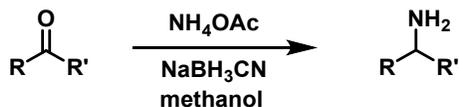


To an oven dried 50 mL round bottom flask was added freshly ground magnesium turnings (2.5 equiv.) and a single crystal of iodine. The flask was placed under N_2 , followed by addition of diethyl ether (10 mL). After stirring for 15 min at room temperature, the organohalide (1.8 equiv.) was added dropwise. The reaction mixture was refluxed for 1 h, followed by cooling to ~ 0 - 5°C . After cooling, the appropriate ketone (1.0 equiv.) was added as an ether solution in a dropwise manner, ensuring to maintain a low temperature. After stirring for 4-5 h at 0°C , the reaction mixture was quenched with saturated aqueous ammonium chloride (NH_4Cl) and extracted with diethyl ether (3 x 10 mL). The combined organic layer was washed with brine, dried over Na_2SO_4 (s), and concentrated *in vacuo* to give the crude alcohol product, which were used for the next step without any further purification.

To a solution of the alcohol (1.0 equiv.) in anhydrous CH_2Cl_2 (10 mL), NaN_3 (2.2 equiv.) was added at room temperature under a nitrogen atmosphere. The suspension was cooled to -5°C , followed by dropwise addition of a 1:2 mixture of TFA: DCM (8.4 equiv. of TFA) under vigorous stirring over a period of 15 min. The resulting suspension was stirred at 0°C for an additional 1-2 h. The reaction mixture was quenched with distilled H_2O , followed by the dropwise addition of a 1:1 mixture of 14% aqueous NH_4OH solution (5.0 mL). After 30 min, the reaction mixture was extracted with CH_2Cl_2 (20 mL), and the organic layer was washed with H_2O , brine, and dried over Na_2SO_4 . The filtrate was concentrated *in vacuo* and the crude azide were used in the next step without further purification.

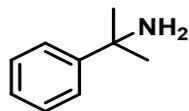
To a solution of the azide (1.0 equiv.) in anhydrous THF (10 mL) was added LiAlH_4 (1.05 equiv.) portion wise at 0°C under a nitrogen atmosphere. The reaction mixture was stirred at room temperature for 3-4 h, and then quenched by dropwise addition of 1.0 M aqueous NaOH . The reaction mixture was then portioned between Et_2O and 1.0 M aqueous HCl . The aqueous layer was treated with 28% aqueous NH_4OH solution, followed by extraction with CH_2Cl_2 (2 x 10 mL). The filtrate was concentrated *in vacuo* and the residual amine was purified on silica gel by flash column chromatography, if necessary.

B) General Procedure for Synthesis of α -Secondary Amines *via* Reductive Amination

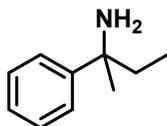


To a solution of the carbonyl compound (1.0 equiv.) in methanol (10 mL) was added ammonium acetate (10 equiv.) at room temperature under a nitrogen atmosphere. After the reaction mixture was stirred for 90 min at room temperature, NaBH_3CN (1.0 equiv) was added portion wise. The reaction mixture was stirred for 24-48 h at room temperature and concentrated under reduced pressure. The reaction mixture was then diluted with NaOH solution (1.0 M, 10 mL). After stirring for 30 min at room temperature, the reaction mixture was then portioned between Et_2O and 1.0 M HCl . The aqueous layer was basified with 28% aqueous NH_4OH solution (pH 8.0), and then extracted with

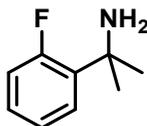
CH₂Cl₂ (2 x 10 mL). The filtrate was concentrated *in vacuo* and the residual amine was purified on silica gel by flash column chromatography.



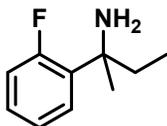
2-Phenylpropan-2-amine (S-1): Method A used. Acetophenone (500 mg) and iodomethane (1.8 equiv.) were used. Product was purified on silica gel by CH₂Cl₂/MeOH (98:2) and recovered as a yellow oil (0.51 g, 90% yield), which was found to match the data reported in the literature.⁴ ¹H NMR (400 MHz, CDCl₃) δ 7.51 (d, *J* = 7.6 Hz, 2H), 7.34 (t, *J* = 7.7 Hz, 2H), 7.22 (t, *J* = 7.3 Hz, 1H), 1.50 (s, 6H). LRMS (ESI - MS): calcd. 158.1 [M+Na]⁺ Found: 158.1.



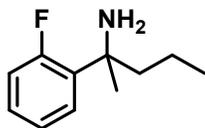
2-Phenylbutan-2-amine (S-2): Method A used. Acetophenone (500 mg) and iodoethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.54 g, 87% yield), which was found to match the data reported in the literature.⁵ ¹H NMR (400 MHz, CDCl₃) δ 7.44 (d, *J* = 8.0 Hz, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.21 (t, *J* = 7.3 Hz, 1H), 1.87 – 1.66 (m, 2H), 1.52 (brs, 2H), 1.45 (s, 3H), 0.74 (t, *J* = 7.4 Hz, 3H). LRMS (ESI - MS): calcd. 150.2 [M+H]⁺ Found: 150.1.



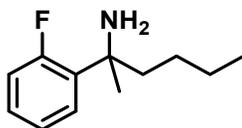
2-(2-Fluorophenyl)propan-2-amine (S-3): Method A used. *o*-Fluoroacetophenone (500 mg) and iodomethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a colorless oil (0.44 g, 79% yield), which was found to match the data in literature.⁶ ¹H NMR (400 MHz, CDCl₃) δ 7.47 – 7.39 (m, 1H), 7.21 (ddd, *J* = 9.8, 7.6, 3.3 Hz, 1H), 7.12 – 7.06 (m, 1H), 7.05 – 6.98 (m, 1H), 1.79 (s, 2H). ¹⁹F NMR (376 Hz, CDCl₃), -120.3. HRMS (ESI - MS): calcd. 154.1026 [M+H]⁺ Found: 154.1023.



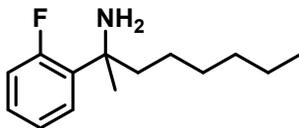
2-(2-Fluorophenyl)butan-2-amine (S-4): Method A used. *o*-Fluoroacetophenone (500 mg) and iodoethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.5 g, 84% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.41 (t, *J* = 8.2 Hz, 1H), 7.21 – 7.16 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 7.01 – 6.96 (m, 1H), 1.98 – 1.89 (m, 1H), 1.85 – 1.76 (m, 1H), 1.66 (br, 2H), 1.48 (s, 3H), 0.73 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.0 (d, *J* = 245.2 Hz), 135.2 (d, *J* = 11.4 Hz), 128.2 (d, *J* = 9.0 Hz), 127.7 (d, *J* = 5.1 Hz), 123.8 (d, *J* = 3.1 Hz), 116.2 (d, *J* = 24.7 Hz), 55.0, 35.5 (d, *J* = 3.5 Hz), 28.6 (d, *J* = 3.0 Hz), 9.0. ¹⁹F NMR (376 Hz, CDCl₃), -119.9. HRMS (ESI - MS): calcd. 168.1182 [M+H]⁺ Found: 168.1180.



2-(2-Fluorophenyl)pentan-2-amine (S-5): Method A used. *o*-fluoroacetophenone (500 mg) and iodopropane (1.8 equiv.) were used. Product was purified on silica gel in CH₂Cl₂/MeOH (98:2) and recovered as a yellow oil (0.61 g, 92% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.39 (t, *J* = 8.2 Hz, 1H), 7.20 – 7.17 (m, 1H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.98 (dd, *J* = 12.8, 8.1 Hz, 1H), 1.88 (td, *J* = 13.3, 4.9 Hz, 1H), 1.77 – 1.72 (m, 1H), 1.49 (s, 3H), 1.15 – 1.06 (m, 2H), 0.84 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.0 (d, *J* = 245.8 Hz), 135.4 (d, *J* = 11.3 Hz), 128.2 (d, *J* = 8.9 Hz), 127.4 (d, *J* = 5.1 Hz), 123.8 (d, *J* = 3.3 Hz), 116.2 (d, *J* = 24.5 Hz), 54.8 (d, *J* = 3.0 Hz), 45.3 (d, *J* = 3.6 Hz), 29.0 (d, *J* = 2.9 Hz), 18.0, 14.5. ¹⁹F NMR (376 Hz, CDCl₃), -119.8. HRMS (ESI - MS): calcd. 182.1346 [M+H]⁺ Found: 182.1344.



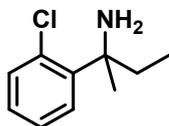
2-(2-Fluorophenyl)hexan-2-amine (S-6): Method A used. *o*-fluoroacetophenone (500 mg) and iodobutane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.51 g, 74% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.43 – 7.38 (m, 1H), 7.22 – 7.17 (m, 1H), 7.08 (td, *J* = 7.6, 1.3 Hz, 1H), 6.99 (ddd, *J* = 12.8, 8.1, 1.3 Hz, 1H), 1.95 – 1.87 (m, 1H), 1.81 – 1.73 (m, 3H), 1.50 (s, 3H), 1.28 – 1.20 (m, 2H), 1.12 – 1.01 (m, 2H), 0.83 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.9 (d, *J* = 245.8 Hz), 135.4 (d, *J* = 11.3 Hz), 128.0 (d, *J* = 8.8 Hz), 127.4 (d, *J* = 5.2 Hz), 123.7 (d, *J* = 3.3 Hz), 116.1 (d, *J* = 24.4 Hz), 54.6 (d, *J* = 2.9 Hz), 42.6 (d, *J* = 3.7 Hz), 29.0 (d, *J* = 3.0 Hz), 26.8, 23.0, 14.0. ¹⁹F NMR (376 Hz, CDCl₃), -109.6. HRMS (ESI - MS): calcd. 196.1502 [M+H]⁺ Found: 196.1457.



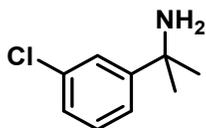
2-(2-Fluorophenyl)octan-2-amine (S-7): Method A used. *o*-fluoroacetophenone (500 mg) and iodoheptane (1.8 equiv.) were used. Product was purified on silica gel in CH₂Cl₂/MeOH (95:5) and recovered as a colorless oil (0.55 mg, 68% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.45 – 7.34 (m, 1H), 7.24 – 7.16 (m, 1H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.99 (dd, *J* = 12.8, 8.0 Hz, 1H), 1.96 – 1.83 (m, 1H), 1.80 – 1.72 (m, 3H), 1.49 (s, 3H), 1.20 (br, 6H), 1.13 – 1.01 (m, 2H), 0.83 (t, *J* = 6.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.0 (d, *J* = 245.8 Hz), 135.5 (dd, *J* = 10.8, 5.2 Hz), 128.1 (d, *J* = 8.8 Hz), 127.4 (d, *J* = 5.1 Hz), 123.8, 116.2 (d, *J* = 24.2 Hz), 60.4, 54.7, 42.9, 31.7, 29.7, 29.1, 24.6, 22.6, 14.1. ¹⁹F NMR (376 Hz, CDCl₃), -111.6. HRMS (ESI - MS): calcd. 224.1815 [M+H]⁺ Found: 224.1825.



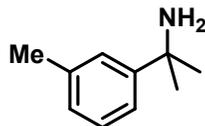
2-(3-Fluorophenyl)butan-2-amine (S-8): Method A used. *m*-Fluoroacetophenone (500 mg) and iodoethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.49 g, 81% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.31 – 7.27 (m, 1H), 7.23 – 7.17 (m, 2H), 6.93 – 6.88 (m, 1H), 1.83 – 1.77 (m, 1H), 1.74 – 1.68 (m, 1H), 1.55 (brs, 2H), 1.45 (s, 3H), 0.75 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 162.9 (d, *J* = 244.5 Hz), 151.8 (d, *J* = 6.2 Hz), 129.5 (d, *J* = 8.2 Hz), 121.0 (d, *J* = 2.7 Hz), 112.8 (d, *J* = 21.1 Hz), 112.7 (d, *J* = 22.1 Hz), 55.2 (d, *J* = 1.5 Hz), 37.7, 30.7, 8.6. . ¹⁹F NMR (376 Hz, CDCl₃), -109.6. HRMS (ESI - MS): calcd. 168.1182 [M+H]⁺ Found: 168.1188.



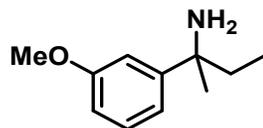
2-(2-Chlorophenyl)butan-2-amine (S-9): Method A used. *o*-Chloroacetophenone (500 mg) and iodoethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a colorless oil (0.49 g, 83% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.54 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.33 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.21 (td, *J* = 7.4, 1.0 Hz, 1H), 7.14 (td, *J* = 7.5, 1.1 Hz, 1H), 2.13 1.98 (m, 2H), 1.88 (br s, 2H), 1.56 (s, 3H), 0.70 (t, *J* = 7.5 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 144.6, 132.5, 131.8, 128.4, 127.8, 126.8, 56.7, 34.0, 28.4, 9.1. HRMS (ESI - MS): calcd. 184.0893 [M+H]⁺ Found: 184.0890.



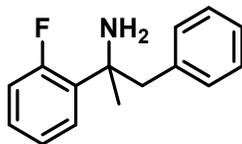
2-(3-Chlorophenyl)propan-2-amine (S-10): Method A used. *m*-Chloroacetophenone (500 mg) and iodomethane (1.8 equiv.) were used. Product was purified on silica gel in CH₂Cl₂/MeOH (97:3) and recovered as a yellow oil (0.44 g, 81% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.49 (t, *J* = 1.9 Hz, 1H), 7.36 (dt, *J* = 8.0, 0.8 Hz, 1H), 7.23 (t, *J* = 7.8 Hz, 1H), 7.17 (dt, *J* = 7.6, 1.2 Hz, 1H), 1.55 (s, 2H), 1.46 (s, 6H). ¹³C NMR (101 MHz, CDCl₃) 152.5, 134.1, 129.5, 126.3, 125.3, 123.0, 52.4, 32.8. HRMS (ESI - MS): calcd. 170.0730 [M+H]⁺ Found: 170.0737.



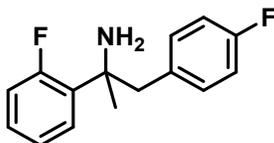
2-(*m*-tolyl)propan-2-amine (S-11): Method A used. *m*-Methylacetophenone (500 mg) and iodomethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a colorless oil (0.43 g, 77% yield), which was found to match the data reported in the literature.⁷ ¹H NMR (400 MHz, CDCl₃) δ 7.34 (s, 1H), 7.30 (d, *J* = 7.9 Hz, 1H), 7.23 (t, *J* = 7.7 Hz, 1H), 7.05 (d, *J* = 7.3 Hz, 1H), 2.38 (s, 3H), 1.49 (s, 6H). HRMS (ESI - MS): calcd. 150.1276 [M+H]⁺ Found: 150.1281.



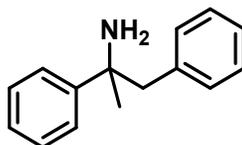
2-(3-methoxyphenyl)butan-2-amine (S-12): Method A used. *m*-Methoxyacetophenone (500 mg) and iodoethane (1.8 equiv.) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.40 g, 68% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.26 – 7.20 (m, 1H), 7.05 – 6.96 (m, 1H), 6.78 – 6.72 (m, 1H), 3.80 (s, 3H), 1.83 – 1.74 (m, 1H), 1.76 – 1.65 (m, 1H), 1.43 (s, 3H), 0.74 (t, *J* = 7.4 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 159.5, 150.7, 129.0, 117.8, 111.8, 110.8, 55.2, 55.2, 37.6, 30.6, 8.7. HRMS (ESI - MS): calcd. 180.1382 [M+H]⁺ Found: 180.1376.



2-(2-Fluorophenyl)-1-phenylpropan-2-amine (S-13): Method A used. *o*-Fluoroacetophenone (500 mg) and benzyl bromide (1.8 equiv.) were used. Product was purified on silica gel in CH₂Cl₂/MeOH (98:2) and recovered as a light yellow oil (0.71 g, 85% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.26 – 7.21 (m, 2H), 7.19 – 7.16 (m, 3H), 7.12 – 7.06 (m, 1H), 7.04 – 7.01 (m, 1H), 6.96 – 6.93 (m, 2H), 3.27 (d, *J* = 13.1 Hz, 1H), 3.08 (d, *J* = 13.1 Hz, 1H), 1.65 (br, 2H), 1.57 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.8 (d, *J* = 245.2 Hz), 137.6, 134.9 (d, *J* = 11.2 Hz), 130.4, 128.4 (d, *J* = 8.9 Hz), 127.8, 127.6 (d, *J* = 4.9 Hz), 126.3, 123.9 (d, *J* = 3.3 Hz), 116.1 (d, *J* = 24.2 Hz), 55.1 (d, *J* = 3.7 Hz), 48.8 (d, *J* = 4.0 Hz), 28.7 (d, *J* = 3.6 Hz). ¹⁹F NMR (376 Hz, CDCl₃), -120.1. HRMS (ESI - MS): calcd. 230.1340 [M+H]⁺ Found: 230.1342.

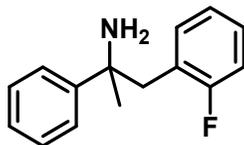


2-(2-Fluorophenyl)-1-(4-fluorophenyl)propan-2-amine (S-14): Method A used. *o*-Fluoroacetophenone (500 mg) and *p*-fluoro benzyl bromide (1.8 equiv.) were used. Product was purified on silica gel in CH₂Cl₂/MeOH (97:3) and recovered as a yellow oil (0.75 g, 82% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.25 – 7.14 (m, 2H), 7.10 – 6.99 (m, 2H), 6.86 – 6.83 (m, 3H), 3.21 (d, *J* = 13.3 Hz, 1H), 3.02 (d, *J* = 13.3 Hz, 1H), 1.64 (br, 2H), 1.54 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.3 (d, *J* = 157.2 Hz), 161.2 (d, *J* = 333.3 Hz), 134.7 (d, *J* = 11.1 Hz), 133.3 (d, *J* = 3.4 Hz), 131.7 (d, *J* = 7.8 Hz), 128.6 (d, *J* = 8.8 Hz), 127.6 (d, *J* = 4.9 Hz), 124.0 (d, *J* = 3.3 Hz), 116.2 (d, *J* = 24.2 Hz), 114.7 (d, *J* = 21.1 Hz), 55.2 (dd, *J* = 3.6, 1.1 Hz), 48.0 (d, *J* = 4.0 Hz), 28.7 (d, *J* = 3.6 Hz). ¹⁹F NMR (376 MHz, CDCl₃), -62.8, -105.3 (d). HRMS (ESI - MS): calcd. 248.1251 [M+H]⁺ Found: 248.1246.

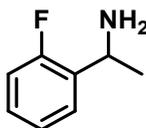


1,2-Diphenylpropan-2-amine (S-15): Method A used. Acetophenone (500 mg) and benzyl bromide (1.8 equiv.) were used. Product was purified on silica gel in hexanes/EtOAc (30:70) and recovered as a colorless oil (0.65 g, 75% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.43 (d, *J* = 7.8 Hz, 2H), 7.34 (t, *J* = 7.5 Hz, 2H), 7.28 – 7.23 (m, 1H), 7.20 – 7.19 (m, 3H), 6.97 – 6.87 (m, 3H), 3.01 (q, *J* = 13.0 Hz, 2H), 1.57 (s, 2H), 1.52 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 148.6,

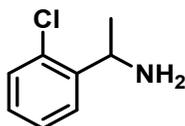
137.6, 130.6, 128.1, 127.9, 126.5, 126.4, 125.6, 55.6, 51.8, 30.7. LRMS (ESI - MS): calcd. 212.1 [M+H]⁺ Found: 212.9.



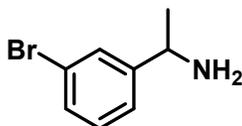
1-(2-Fluorophenyl)-2-phenylpropan-2-amine (S-16): Method A used. Acetophenone (500 mg) and *o*-fluoro benzyl bromide (1.8 equiv.) were used. Product was purified on silica gel in hexanes/EtOAc (30:70) and recovered as a colorless oil (0.81 g, 84% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.48 (d, *J* = 7.6 Hz, 2H), 7.35 (dd, *J* = 9.9, 4.4 Hz, 2H), 7.25 (t, *J* = 6.5 Hz, 1H), 7.20 – 7.14 (m, 1H), 7.07 – 6.92 (m, 2H), 6.85 (t, *J* = 7.3 Hz, 1H), 3.05 (dd, *J* = 55.0, 13.3 Hz, 1H), 1.60 (s, 2H), 1.51 (s, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.7 (d, *J* = 244.7 Hz), 148.4, 132.7 (d, *J* = 4.6 Hz), 128.2 (d, *J* = 8.2 Hz), 128.1, 126.4, 125.4, 124.7 (d, *J* = 15.8 Hz), 123.5 (d, *J* = 3.5 Hz), 115.2 (d, *J* = 23.2 Hz), 55.9, 44.1, 30.1. ¹⁹F NMR (376 Hz, CDCl₃), -109.6. LRMS (ESI - MS): calcd. 230.3 [M+H]⁺ Found: 230.5.



1-(2-fluorophenyl)ethan-1-amine (S-17): Method B used. *o*-Fluoroacetophenone (500 mg) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.34 g, 68% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.42 – 7.34 (m, 1H), 7.23 – 7.14 (m, 1H), 7.11 (t, *J* = 6.9 Hz, 1H), 7.04 – 6.94 (m, 1H), 4.37 (q, *J* = 6.6 Hz, 1H), 1.64 (s, 2H), 1.41 (d, *J* = 6.7 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 160.4 (d, *J* = 245.0 Hz), 134.5 (d, *J* = 13.6 Hz), 128.1 (d, *J* = 8.3 Hz), 126.7 (d, *J* = 5.0 Hz), 124.2 (d, *J* = 3.5 Hz), 115.4 (d, *J* = 22.3 Hz), 45.4 (d, *J* = 2.8 Hz), 24.1. ¹⁹F NMR (376 Hz, CDCl₃), -109.5. HRMS (ESI - MS): calcd. 140.0869 [M+H]⁺ Found: 140.0872.



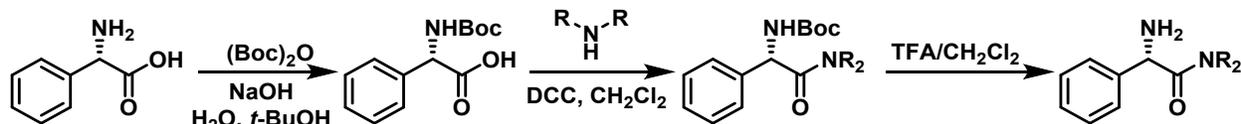
1-(2-chlorophenyl)ethan-1-amine (S-18): Method B used. *o*-Chloroacetophenone (500 mg) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.31 g, 62% yield), which was found to match the literature data.⁸ ¹H NMR (400 MHz, CDCl₃) δ 7.51 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.32 (dd, *J* = 7.9, 1.0 Hz, 1H), 7.28 – 7.23 (m, 1H), 7.15 (td, *J* = 7.7, 1.6 Hz, 1H), 4.53 (q, *J* = 6.6 Hz, 1H), 1.56 (s, 2H), 1.38 (d, *J* = 6.6 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 144.6, 132.7, 129.6, 127.8, 127.2, 126.3, 47.6, 23.7. LRMS (ESI - MS): calcd. 156.6 [M+H]⁺ Found: 157.1.



1-(3-bromoophenyl)ethan-1-amine (S-19): Method B used. *m*-Bromoacetophenone (500 mg) were used. Product was purified by acid/base workup and recovered as a yellow oil (0.29 g, 57% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.48 (s, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.24 (d, *J* = 7.4 Hz, 1H), 7.16 (t, *J* = 7.7 Hz, 1H), 4.05 (q, *J* = 6.4 Hz, 1H), 1.48

(s, 2H), 1.33 (d, $J = 6.4$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 150.1, 130.1, 129.8, 128.9, 124.4, 122.6, 50.9, 25.7. HRMS (ESI - MS): calcd. 200.0069 $[\text{M}+\text{H}]^+$ Found: 200.0060.

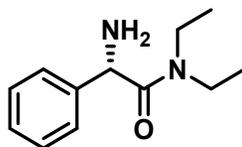
C) General Procedure for Synthesis of α -Secondary Amines Acetamide via Amide Coupling



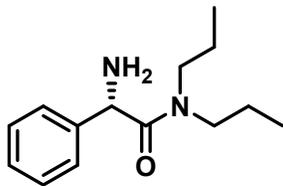
NaOH (330 mg, 1.1 equiv) in a mixture of $\text{H}_2\text{O}/t\text{-BuOH}$ (8.0 + 4.5 mL) was prepared in a 50 mL round bottom flask. Phenyl glycine (1.13 g, 1.0 equiv.) was added to the flask, and the reaction was stirred at room temperature. After 15 min, $(\text{Boc})_2\text{O}$ (1.1 equiv.) was added in a dropwise manner. The reaction mixture was stirred overnight followed by removal of volatiles *in vacuo*. The resulting oily residue was diluted with dichloromethane, washed with water, and concentrated to give Boc-protected phenyl glycine. The crude residue was subjected to column chromatography on silica gel and hexanes/EtOAc (40:60) as eluent to obtain purified Boc-protected phenyl glycine.

Boc-protected phenyl glycine (1.0 equiv.) was added to an oven dried round bottom flask and dry CH_2Cl_2 was added to it under an N_2 atmosphere. Dicyclohexylcarbodiimide (DCC, 1.0 equiv.) was added to the reaction mixture in one portion. The reaction mixture was cooled to 0°C and stirred for 15 minutes under N_2 atmosphere followed by the addition of appropriate amine (1.0 equiv.) as a solution in dry CH_2Cl_2 in a dropwise manner. The reaction mixture was stirred overnight at room temperature followed by concentrating *in vacuo* to give a white residue. The crude residue was treated with ethyl acetate (30 mL) and stirred for 30 min at room temperature. The solid was filtered off and washed with additional ethyl acetate. The combined filtrate was concentrated *in vacuo* to afford the crude amide as colorless oil.

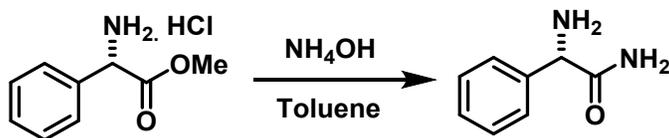
The Boc-protected crude amide was dissolved in dry CH_2Cl_2 and trifluoroacetic acid (5.0 equiv.) was added at room temperature under an N_2 atmosphere. After the reaction mixture was stirred for 2.0 hours at room temperature, the organic solvent was evaporated *in vacuo*. The reaction mixture was treated with aqueous sodium hydroxide (1.0 M, 20 mL) and stirred for 30 min. The reaction mixture was then extracted with CH_2Cl_2 (2×10 mL), dried over Na_2SO_4 , and concentrated to give the crude product as a colorless oil, which was subjected to column chromatography on silica gel to get pure amine.



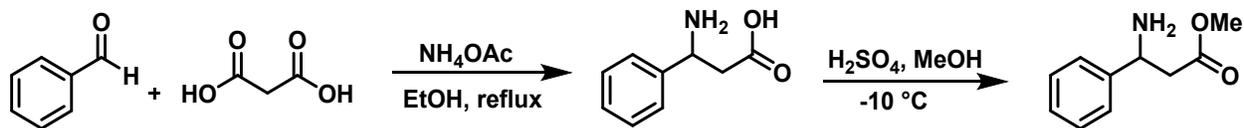
(S)-2-Amino-N,N-diethyl-2-phenylacetamide (S-20): Diethylamine were used. Product was purified on silica gel in hexanes/EtOAc (20:80) and recovered as a light yellow oil (0.98 g, 64% yield), which was found to match the literature data.⁹ ^1H NMR (400 MHz, CDCl_3) δ 7.33 – 7.28 (m, 5H), 4.63 (s, 1H), 3.57 – 3.47 (m, 1H), 3.30 – 3.21 (m, 2H), 3.10 – 3.03 (m, 1H), 1.10 (t, $J = 7.1$ Hz, 1H), 0.92 (t, $J = 7.1$ Hz, 1H). LRMS (ESI): calcd. 207.3 $[\text{M}+\text{H}]^+$ Found: 207.5. $[\alpha]_D^{21} = +95^\circ$ (c 0.044, EtOH)



(S)-2-Amino-2-phenyl-N,N-dipropylacetamide (S-21): Dipropylamine were used. Product was purified on silica gel in hexanes/EtOAc (20:80) and recovered as a yellow oil (1.0 g, 59% yield). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.37 – 7.27 (m, 5H), 4.65 (s, 1H), 3.54 – 3.45 (m, 1H), 3.17 – 3.05 (m, 2H), 2.93 – 2.86 (m, 1H), 2.01 (brs, 2H), 1.61 – 1.42 (m, 3H), 1.28 – 1.15 (m, 1H), 0.84 (t, $J = 7.4$ Hz, 3H), 0.76 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 172.4, 141.9, 129.1, 127.8, 127.1, 57.0, 48.7, 47.9, 21.9, 20.7, 11.4, 11.2. HRMS (EI): calcd. 235.1811 $[\text{M}+\text{H}]^+$ Found: 235.1818. $[\alpha]_D^{21} = +112^a$ (c 0.015, EtOH).



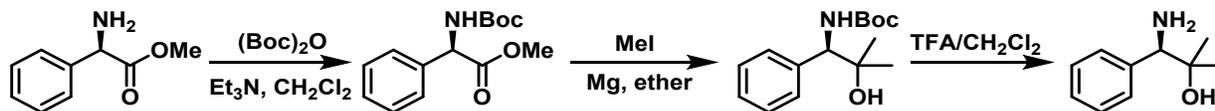
(S)-2-Amino-2-phenylacetamide (S-22): In a 50 mL round bottom flask was added methyl (R)-2-amino-2-phenylacetate hydrochloride (0.5 g, 1.0 equiv) in toluene (5.0 mL) and ammonium hydroxide (5.0 mL). The reaction was stirred overnight at room temperature, followed by quenching with water. The reaction mixture was extracted with ether (2×10 mL), dried over Na_2SO_4 and concentrated *in vacuo* to give the crude acetamide product as colorless oil. Crude residue was subjected to flash column chromatography on silica gel using $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (97:3) to give the pure product as colorless oil (0.35 g, 94% yield), which was found to match the literature data.¹⁰ $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.38 – 7.22 (m, 1H), 4.52 (s, 1H), 1.89 (s, 1H). LRMS (EI-MS): calcd. 151.0 $[\text{M}]^+$ Found: 151.1.



Synthesis of Methyl 3-amino-3-phenylpropanoate (S-23): In a 50 mL round bottom flask, benzaldehyde (0.5 g) was dissolved in ethanol (5.0 mL). Malonic acid (0.49 g, 1.0 equiv.) and ammonium acetate (0.73 g, 2.0 equiv.) were added to the reaction and the resulting mixture was refluxed for overnight. After stirring overnight, the reaction mixture was allowed to cool to room temperature and the resulting solid was filtered. The solid was washed with methanol and dried *in vacuo* to give the intermediate as a white solid (0.51 g, 66% yield).

The amino acid was added to a round bottom flask followed by addition of methanol. The reaction mixture was cooled to -10 °C followed by the addition of conc. sulfuric acid (0.4 mL) in one portion. The reaction mixture was stirred at room temperature for 6.0 h and concentrated *in vacuo*. The reaction mixture was treated with sodium hydroxide solution (2.0 M) and extracted with dichloromethane (2×10 mL). The combined organic phase was dried over Na_2SO_4 and concentrated *in vacuo* to give the product as colorless oil (0.39 g 69% yield), which was found to

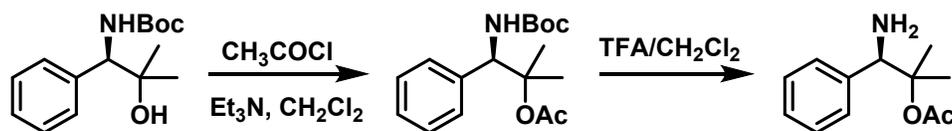
match the literature data.¹¹ ¹H NMR (400 MHz, CDCl₃) δ 7.34 – 7.26 (m, 4H), 7.24 – 7.18 (m, 1H), 4.37 (t, *J* = 6.9 Hz, 1H), 3.62 (s, 3H), 2.64 (d, *J* = 6.7 Hz, 2H), 2.15 (s, 2H). LRMS (ESI): calcd. 180.2 [M+H]⁺ Found: 180.3



Synthesis of (R)-1-Amino-2-methyl-1-phenylpropan-2-ol (S-24): In a 50 mL round bottom flask was added methyl (R)-2-amino-2-phenylacetate hydrochloride (2.0 g, 1.0 equiv) in dry CH₂Cl₂ (10 mL) under an N₂ atmosphere. Triethylamine (2.5 equiv.) was added to the flask and the reaction was cooled to 0°C. After 15 min of stirring, (Boc)₂O (1.1 equiv.) was added dropwise. The reaction was stirred overnight, followed by quenching with water. The reaction mixture was extracted with dichloromethane (2 × 10 mL), dried over Na₂SO₄ and concentrated *in vacuo* to give the crude Boc-protected product as colorless oil. Crude residue was subjected to column chromatography on silica gel using hexanes/EtOAc (80:20) to give the pure product as gummy solid.

To an oven dried 50 mL round bottom flask was added freshly ground magnesium turnings (3.0 equiv.) and a single crystal of iodine. The flask was placed under N₂, followed by addition of diethyl ether (10 mL). After stirring for 15 min at room temperature, methyl iodide (2.5 equiv.) was added dropwise. The reaction mixture was refluxed for 1 h, followed by cooling to ~0-5 °C. After cooling, the Boc-protected phenylglycine methylester (1.0 equiv.) was added as an ether solution in a dropwise manner, ensuring to maintain a low temperature. After stirring for 4-5 h at room temperature, the reaction mixture was quenched with saturated aqueous ammonium chloride (NH₄Cl) and extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ (s), and concentrated *in vacuo* to give the crude β-amino alcohol product, which was used for the next step without any further purification.

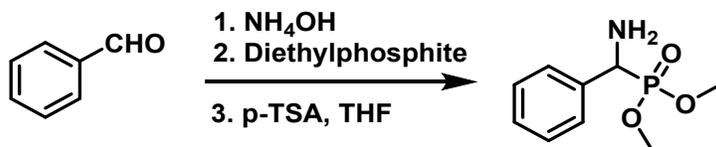
Crude Boc-protected β-amino alcohol was dissolved in dry CH₂Cl₂ and trifluoroacetic acid (5.0 equiv.) was added at room temperature under an N₂ atmosphere. After the reaction was stirred for 2.0 hours at room temperature, the volatiles were removed *in vacuo*. The reaction mixture was treated with sodium hydroxide (1.0 M, 20 mL) and stirred for 30 min. The reaction mixture was extracted with CH₂Cl₂ (2 × 10 mL), dried over Na₂SO₄, and concentrated *in vacuo* to give the crude product as a colorless oil, which was subjected to column chromatography on silica gel using CH₂Cl₂/MeOH (96:4) to give product as a colorless oil (0.52 g, 32%), which was found to match with literature data.¹² ¹H NMR (400 MHz, CDCl₃) δ 7.24 – 7.20 (m, 4H), 7.18 (dd, *J* = 8.0, 4.8 Hz, 1H), 3.69 (s, 1H), 1.11 (s, 3H), 0.95 (s, 3H). LRMS (ESI): calcd. 167.2 [M+H]⁺ Found: 167.2. [α]_D²¹ = +23.9^o (*c* 0.012, EtOH)



(R)-1-Amino-2-methyl-1-phenylpropan-2-yl acetate (S-25): The Boc-protected β -aminoalcohol (**S-23**) (1.0 equiv.) was taken in round bottom flask with pyridine under nitrogen. Acetic anhydride (1.5 equiv.) was added to the reaction followed by the addition of dimethyl amino pyridine (10 mol%). The reaction was stirred at room temperature overnight. Reaction mixture was concentrated *in vacuo*. Reaction was quenched with water and extracted with CH_2Cl_2 (2×10 mL). Organic layer was dried over Na_2SO_4 , and concentrated to get colorless oil as crude product, which was subjected to column chromatography on silica gel using hexanes/EtOAc (70:30) to get pure Boc-protected acylamine.

Boc-protected crude β -acylamine was dissolved in dry CH_2Cl_2 and trifluoroacetic acid (5.0 equiv.) was added to it at room temperature under N_2 atmosphere. After reaction mixture was stirred for 2.0 hours at room temperature, organic solvent was distilled off. Reaction mixture was diluted with sodium hydroxide (1.0 M, 20 mL) and stirred for 30 min. Reaction mixture was extracted with CH_2Cl_2 (2×10 mL), dried over Na_2SO_4 , and concentrated to get colorless oil as crude product, which was subjected to column chromatography on silica gel using $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (99:1) to give the pure β -acylamine (0.39g, 19%). ^1H NMR (400 MHz, CDCl_3) δ 7.33 (t, $J = 7.2$ Hz, 2H), 7.28 – 7.24 (m, 1H), 7.20 – 7.16 (m, 2H), 4.82 (s, 1H), 2.10 (s, 3H), 1.56 (s, 3H), 0.83 (s, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.3, 138.9, 128.3, 127.6, 127.1, 87.4, 78.0, 29.2, 24.0, 14.7. LRMS (ESI): calcd. 230.3 $[\text{M}+\text{Na}]^+$ Found: 230.4. $[\alpha]_D^{21} = +37.6^\circ$

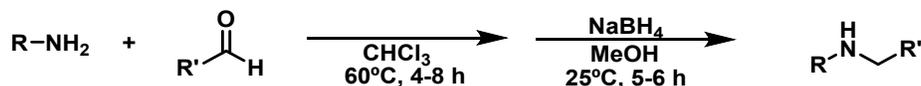
(c 0.003, EtOH)



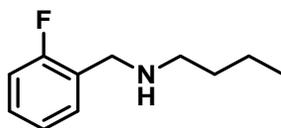
Diethyl (amino(phenyl)methyl)phosphonate (S-26): In a 100 mL round bottom flask was added benzaldehyde (1.6 g, 1.0 equiv.) and ammonium hydroxide (30%, 15 mL). The solution was refluxed for 8.0 h and cooled to room temperature. The white precipitate was removed by filtration and dried under air. Diethyl phosphite (2.1 g, 1.0 equiv.) was added to the solid and the resulting solution was stirred for 6.0 h at 70 °C. After 6.0 h of stirring, a solution of *p*-toluenesulfonic acid (1.0 equiv.) in tetrahydrofuran (THF, 50 mL) was added to the reaction mixture and the reaction was stirred for an additional 4.0 h at 0 °C. The resulting white precipitate was removed by filtration and washed with THF (2×10 mL). The precipitate was treated with aqueous ammonium hydroxide (20 mL, 10%) and stirred for 30 min at room temperature. The basic aqueous layer was extracted with ether (2×50 mL), dried over Na_2SO_4 , and concentrated *in vacuo* to give the product as a colorless oil (2.6 g, 72% yield), which was found to match with the literature data.¹³ ^1H NMR (400 MHz, CDCl_3) δ 7.42 (d, $J = 7.1$ Hz, 2H), 7.32 (t, $J = 7.5$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 1H), 4.23 (d, $J = 17.2$ Hz, 1H), 4.05 – 4.00 (m, 2H), 3.97 – 3.92 (m, 1H), 3.86 – 3.80 (m, 1H), 1.94 (br, 2H), 1.25 (t, $J = 7.1$ Hz, 3H), 1.15 (t, $J = 7.1$ Hz, 3H). LRMS (ESI): calcd. 244.2 $[\text{M}+\text{H}]^+$ Found: 244.9.

4. Synthesis of 2° Benzylamine Substrates

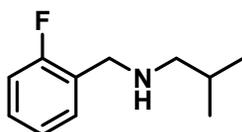
A) General Procedure for Synthesis of Secondary Amines *via* Reductive Amination From the Corresponding Aldehydes:



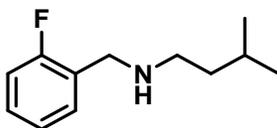
Typical procedure for a reductive amination: To a 50-mL round bottom flask charged with a stir bar was added the primary amine, the aldehyde, and 15 mL of chloroform. The reaction was stirred at 60 °C for 4-8 h, and filtered over Na₂SO₄. The filtrate was concentrated *in vacuo*, followed by dissolution in methanol (10 mL). Sodium borohydride (1.2 equiv) was added portion wise, followed by stirring for 5-6 h. After stirring the reaction was quenched with aq. NaOH solution. The aqueous layer was extracted with ether (2 x 25 mL), dried over Na₂SO₄, followed by concentration *in vacuo*. The residue was then acidified using 1.2 M hydrochloric acid, followed by subsequent washing with diethyl ether (2 x 50 mL). The aqueous layer was then made basic with ammonium hydroxide and extracted with DCM (2 x 50 mL). After drying over Na₂SO₄, the organic layer was concentrated *in vacuo* to give the secondary amine product.



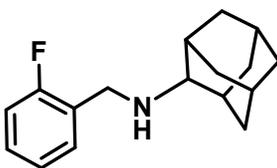
N-(2-Fluorobenzyl)butan-1-amine (S-27): *o*-Fluorobenzylamine (500 mg) and butyraldehyde (1.0 equiv.) were used. The amine product was obtained as a yellow oil (0.55 g, 79% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.32 (t, *J* = 7.5 Hz, 1H), 7.24 – 7.18 (m, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.03 – 6.99 (m, 1H), 3.83 (s, 2H), 2.61 (t, *J* = 7.2 Hz, 2H), 1.52 – 1.45 (m, 2H), 1.38 – 1.29 (m, 3H), 0.90 (t, *J* = 7.3 Hz, 3H). ¹³C NMR (101 MHz, CDCl₃) δ 161.2 (d, *J* = 245.2 Hz), 130.4 (d, *J* = 4.9 Hz), 128.5 (d, *J* = 8.2 Hz), 127.5 (d, *J* = 15.1 Hz), 124.0 (d, *J* = 3.5 Hz), 115.2 (d, *J* = 21.9 Hz), 49.1, 47.5 (d, *J* = 3.0 Hz), 32.2, 20.5, 14.0. ¹⁹F NMR (376 Hz, CDCl₃), -120.2. HRMS (ESI): calcd. 182.1345 [M+H]⁺ Found: 182.1348.



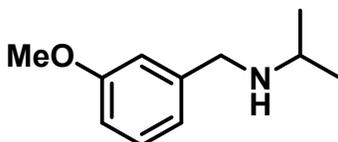
N-(2-Fluorobenzyl)-2-methylpropan-1-amine (S-28): *o*-Fluorobenzylamine (500 mg) and isobutyraldehyde (1.0 equiv.) were used. The amine product was obtained as a yellow oil (0.55 g, 78% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.34 (t, *J* = 7.4 Hz, 1H), 7.23 – 7.20 (m, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 7.05 – 7.00 (m, 1H), 3.83 (s, 2H), 2.43 (d, *J* = 6.8 Hz, 2H), 1.82 – 1.74 (m, 1H), 1.36 (br, 1H), 0.91 (d, *J* = 6.6 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 161.2 (d, *J* = 245.2 Hz), 130.3 (d, *J* = 4.9 Hz), 128.5 (d, *J* = 8.2 Hz), 127.62 (d, *J* = 15.1 Hz), 124.0 (d, *J* = 3.5 Hz), 115.2 (d, *J* = 21.9 Hz), 57.4, 47.5, 28.4, 20.7. ¹⁹F NMR (376 Hz, CDCl₃), -120.0. HRMS (ESI - MS): calcd. 182.1346 [M+H]⁺ Found: 182.1341.



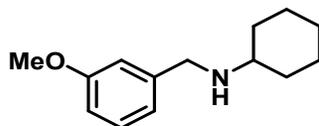
N-(2-Fluorobenzyl)-3-methylbutan-1-amine (S-29): *o*-Fluorobenzylamine (500 mg) and isovaleraldehyde (1.0 equiv.) were used. The amine product was obtained as a yellow oil (0.55 g, 73% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.33 (td, *J* = 7.5, 1.7 Hz, 1H), 7.23 – 7.20 (m, 1H), 7.09 (td, *J* = 7.4, 1.1 Hz, 1H), 7.06 – 6.98 (m, 1H), 3.83 (s, 1H), 2.65 – 2.60 (m, 1H), 1.6 – 1.59 (m, 1H), 1.40 (dd, *J* = 14.8, 7.2 Hz, 1H), 0.88 (d, *J* = 6.7 Hz, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 161.3 (d, *J* = 245.3 Hz), 130.4 (d, *J* = 4.9 Hz), 128.6 (d, *J* = 8.2 Hz), 127.5 (d, *J* = 15.1 Hz), 124.0 (d, *J* = 3.5 Hz), 115.3 (d, *J* = 21.9 Hz), 47.5, 39.2, 26.2, 22.7. ¹⁹F NMR (376 Hz, CDCl₃), -120.0 HRMS (ESI - MS): calcd. 196.1502 [M+H]⁺ Found: 196.1495.



(1R,2S,5S)-N-(2-fluorobenzyl)adamantan-2-amine (S-30): *o*-fluorobenzylamine (500 mg) and adamantan-2-one (1.0 equiv.) were used in the reaction. The amine product was obtained as a gummy solid (0.71 g, 69% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.42 (t, *J* = 7.2 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.12 (d, *J* = 7.3 Hz, 1H), 7.03 (dt, *J* = 12.4, 7.1 Hz, 1H), 4.59 (s, 2H), 3.23 (s, 1H), 2.64 (s, 1H), 2.09 (d, *J* = 10.3 Hz, 1H), 2.01 – 1.95 (m, 10H), 1.89 (s, 2H), 1.80 (d, *J* = 12.4 Hz, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 160.6 (d, *J* = 245.3 Hz), 129.8 (d, *J* = 4.7 Hz), 128.0 (d, *J* = 8.1 Hz), 127.6 (d, *J* = 14.9 Hz), 124.0 (d, *J* = 3.5 Hz), 115.0 (d, *J* = 21.6 Hz), 46.9, 46.7 (d, *J* = 2.8 Hz), 43.9, 39.2, 38.2, 36.5, 36.2, 33.3, 27.8, 27.4. ¹⁹F NMR (376 Hz, CDCl₃), -120.3. LRMS (ESI - MS): calcd. 260.3 [M+H]⁺ Found: 260.7.

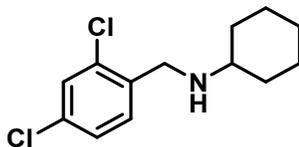


N-(3-Methoxybenzyl)propan-2-amine (S-31): *m*-Methoxybenzaldehyde (300 mg) and isopropyl amine (1.0 equiv.) were used. The amine product was obtained as a yellow oil (0.37 g, 94% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.23 (t, *J* = 7.8 Hz, 1H), 6.89 (dd, *J* = 9.5, 4.9 Hz, 2H), 6.78 (dd, *J* = 8.2, 2.5 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 2H), 2.87 – 2.83 (m, 1H), 1.09 (d, *J* = 6.3 Hz, 6H). ¹³C NMR (151 MHz, CDCl₃) δ 159.7, 142.4, 129.4, 120.4, 113.6, 112.3, 55.1, 51.6, 48.0, 22.9. HRMS (ESI - MS): calcd. 180.1382 [M+H]⁺ Found: 180.1375.

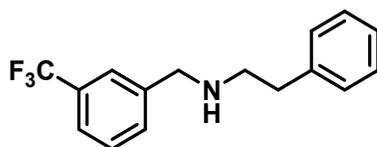


N-(3-Methoxybenzyl)cyclohexanamine (S-32): *m*-Methoxybenzaldehyde (300 mg) and cyclohexyl amine (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.42 g, 87% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.21 (t, *J* = 8.0 Hz, 1H), 6.89 – 6.87 (m, 2H), 6.76 (dd, *J* = 7.1, 2.0 Hz, 1H), 3.77 (s, 5H), 2.51 – 2.41

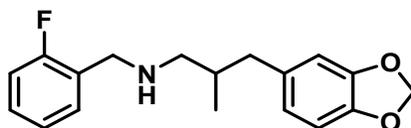
(m, 1H), 1.90 (d, $J = 11.6$ Hz, 2H), 1.72 (dd, $J = 9.1, 3.4$ Hz, 2H), 1.60 (d, $J = 10.9$ Hz, 1H), 1.30 – 1.04 (m, 5H). ^{13}C NMR (101 MHz, CDCl_3) δ 159.6, 142.6, 129.2, 120.2, 113.4, 112.1, 56.0, 55.0, 50.9, 33.5, 26.1, 24.9. LRMS (ESI - MS): calcd. 220.3 $[\text{M}+\text{H}]^+$ Found: 220.5.



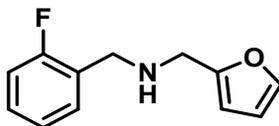
***N*-(2,4-dichlorobenzyl)cyclohexanamine (S-33):** 2,4-Dichlorobenzaldehyde (500 mg), cyclohexylamine (1.0 equiv.) were used. The amine product was obtained as a colorless oil (0.5 g, 71% yield). ^1H NMR (600 MHz, CDCl_3) δ 7.35 – 7.34 (m, 2H), 7.20 (dd, $J = 8.2, 2.1$ Hz, 1H), 3.85 (s, 2H), 2.45 – 2.40 (m, 1H), 1.90 (dd, $J = 12.7, 2.8$ Hz, 2H), 1.76 – 1.70 (m, 2H), 1.64 – 1.58 (m, 1H), 1.49 (br, 1H), 1.29 – 1.06 (m, 5H). ^{13}C NMR (151 MHz, CDCl_3) δ 137.0, 134.3, 133.1, 130.9, 129.3, 127.1, 56.2, 47.9, 33.6, 26.2, 25.0. HRMS (ESI - MS): calcd. 258.0810 $[\text{M}+\text{H}]^+$ Found: 258.0824.



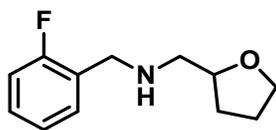
2-phenyl-*N*-(3-(trifluoromethyl)benzyl)ethan-1-amine (S-34): *m*-Trifluoromethylbenzaldehyde (500 mg) and 2-phenylethan-1-amine (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.53 g, 66% yield). ^1H NMR (600 MHz, CDCl_3) δ 7.57 (s, 1H), 7.51 (d, $J = 7.6$ Hz, 1H), 7.48 (d, $J = 7.6$ Hz, 1H), 7.42 (t, $J = 7.7$ Hz, 1H), 7.31 (t, $J = 7.6$ Hz, 2H), 7.23 (t, $J = 7.3$ Hz, 3H), 3.86 (s, 2H), 2.92 (t, $J = 7.4$ Hz, 2H), 2.85 (t, $J = 7.0$ Hz, 2H), 1.48 (s, 1H). ^{13}C NMR (151 MHz, CDCl_3) δ 141.4, 139.9, 131.5, 130.8 (q, $J = 32.0$ Hz), 128.9, 128.8, 128.6, 126.3, 124.8 (t, $J = 5.6$ Hz), 124.3 (d, $J = 273.3$ Hz), 123.8 (t, $J = 5.7$ Hz), 53.4, 50.6, 36.4. ^{19}F NMR (376 Hz, CDCl_3), -62.9. HRMS (ESI - MS): calcd. 280.1307 $[\text{M}+\text{H}]^+$ Found: 280.1310.



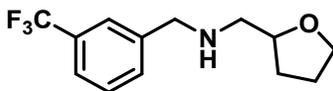
3-(benzo[*d*][1,3]dioxol-5-yl)-*N*-(2-fluorobenzyl)-2-methylpropan-1-amine (S-35): *o*-fluorobenzylamine (500 mg) and 3-(1,3-Benzodioxol-5-yl)-2-methylpropanal (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.84 g, 70% yield). ^1H NMR (600 MHz, CDCl_3) δ 7.32 (td, $J = 7.5, 1.5$ Hz, 1H), 7.23 (dt, $J = 7.8, 5.5$ Hz, 1H), 7.12 – 7.08 (m, 1H), 7.05 – 7.01 (m, 1H), 6.71 (d, $J = 7.9$ Hz, 1H), 6.64 (d, $J = 1.5$ Hz, 1H), 6.58 (dd, $J = 7.9, 1.6$ Hz, 1H), 5.91 (s, 2H), 3.82 (d, $J = 3.0$ Hz, 1H), 2.65 (dd, $J = 13.5, 6.0$ Hz, 1H), 2.55 (dd, $J = 11.6, 6.0$ Hz, 1H), 2.45 (dd, $J = 11.6, 6.9$ Hz, 1H), 2.31 (dd, $J = 13.5, 8.2$ Hz, 1H), 1.91 – 1.85 (m, 1H), 1.50 (br, 1H), 0.88 (d, $J = 6.7$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.2 (d, $J = 245.3$ Hz), 147.4, 145.5, 134.7, 130.3 (d, $J = 4.9$ Hz), 128.5 (d, $J = 8.1$ Hz), 124.0 (d, $J = 3.6$ Hz), 121.9, 115.2 (d, $J = 21.9$ Hz), 109.5, 107.9, 100.7, 55.1, 47.4, 41.1, 35.5, 17.9. ^{19}F NMR (376 Hz, CDCl_3), -119.9. HRMS (ESI): calcd. 302.1556 $[\text{M}+\text{H}]^+$ Found: 302.1554.



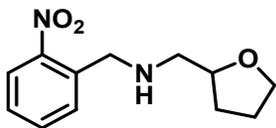
***N*-(2-Fluorobenzyl)-1-(furan-2-yl)methanamine (S-36):** *o*-fluorobenzylamine (500 mg) and furfuralaldehyde (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.47 g, 58% yield). ¹H NMR (600 MHz, CDCl₃) δ 7.35 (s, 1H), 7.32 (t, *J* = 7.8 Hz, 1H), 7.25 – 7.18 (m, 1H), 7.08 (t, *J* = 7.4 Hz, 1H), 7.04 – 6.98 (m, 1H), 6.31 – 6.29 (m, 1H), 6.18 (d, *J* = 3.1 Hz, 1H), 3.82 (s, 2H), 3.77 (s, 2H). ¹³C NMR (101 MHz, CDCl₃) δ 161.2 (d, *J* = 245.6 Hz), 153.6, 141.9 (d, *J* = 8.0 Hz), 131.2 – 129.8 (m), 128.8 (d, *J* = 8.0 Hz), 126.8 (d, *J* = 14.9 Hz), 124.1, 115.3 (d, *J* = 21.8 Hz), 110.1 (d, *J* = 9.9 Hz), 107.1 (d, *J* = 10.8 Hz), 46.3 (d, *J* = 7.9 Hz), 45.4. ¹⁹F NMR (376 Hz, CDCl₃), -119.3. HRMS (ESI - MS): calcd. 206.0975 [M+H]⁺ Found: 206.0978.



***N*-(2-fluorobenzyl)-1-(tetrahydrofuran-2-yl)methanamine (S-37):** *o*-Fluorobenzaldehyde (500 mg) and tetrahydrofurfurylamine (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.67 g, 79% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.24 – 7.21 (m, 1H), 7.07 – 7.02 (m, 1H), 6.91 – 6.87 (m, 1H), 4.03 – 3.96 (m, 1H), 3.84 – 3.79 (m, 3H), 3.74 – 3.69 (m, 1H), 2.69 – 2.58 (m, 2H), 1.97 – 1.82 (m, 3H), 1.58 – 1.51 (m, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 163.0 (d, *J* = 245.5 Hz), 143.2 (d, *J* = 6.9 Hz), 129.7 (d, *J* = 8.2 Hz), 123.5 (d, *J* = 2.8 Hz), 114.8 (d, *J* = 21.2 Hz), 113.6 (d, *J* = 21.1 Hz), 78.3, 68.0, 53.5 (d, *J* = 22.5 Hz), 29.2, 25.8. ¹⁹F NMR (376 Hz, CDCl₃), -114.1. LRMS (ESI - MS): calcd. 210.3 [M+H]⁺ Found: 210.7.

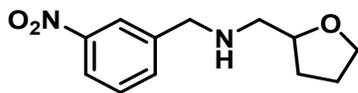


1-(Tetrahydrofuran-2-yl)-N-(3-(trifluoromethyl)benzyl)methanamine (S-38): *m*-Trifluoromethylbenzaldehyde (500 mg) and tetrahydrofurfurylamine (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.71 mg, 96% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.60 (s, 1H), 7.50 (dd, *J* = 12.8, 7.7 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 1H), 4.06 – 3.99 (m, 1H), 3.87 (s, 2H), 3.84 – 3.81 (m, 1H), 3.77 – 3.71 (m, 1H), 2.67 (ddd, *J* = 19.6, 12.0, 5.7 Hz, 2H), 1.98 – 1.83 (m, 3H), 1.81 (br, 1H), 1.60 – 1.50 (m, 1H). ¹³C NMR (151 MHz, CDCl₃) δ 141.5, 131.5, 130.6 (q, *J* = 32.0 Hz), 128.8, 124.8 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 272.1 Hz), 123.8 (q, *J* = 3.7 Hz), 78.3, 68.0, 53.8, 53.5, 29.3, 25.8. ¹⁹F NMR (376 Hz, CDCl₃), -62.8. HRMS (ESI - MS): calcd. 260.1256 [M+H]⁺ Found: 260.1252.



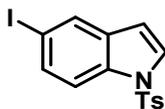
***N*-(2-Nitrobenzyl)-1-(tetrahydrofuran-2-yl)methanamine (S-39):** *o*-Nitrobenzaldehyde (500 mg) and tetrahydrofurfurylamine (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.64 g, 82% yield). ¹H NMR (400 MHz, CDCl₃) δ 7.92 (d, *J* = 8.0 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 1H), 7.56 (t, *J* = 8.0 Hz,

1H), 7.38 (t, $J = 8.0$ Hz, 1H), 4.08 (s, 2H), 4.01 – 3.99 (m, 1H), 3.86 – 3.80 (m, 1H), 3.75 – 3.70 (m, 1H), 2.73 – 2.63 (m, 2H), 1.99 – 1.85 (m, 3H), 1.60 – 1.50 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 135.8, 133.1, 130.8, 127.8, 124.7, 78.3, 68.0, 53.8, 50.7, 29.2, 25.8. HRMS (ESI - MS): calcd. 237.1233 $[\text{M}+\text{H}]^+$ Found: 237.1230.

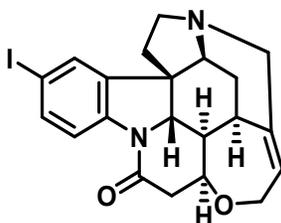


***N*-(3-Nitrobenzyl)-1-(tetrahydrofuran-2-yl)methanamine (S-40):** *m*-Nitrobenzaldehyde (500 mg) and tetrahydrofurfurylamine (1.0 equiv.) were used in the reaction. The amine product was obtained as a yellow oil (0.62 g, 80% yield). ^1H NMR (600 MHz, CDCl_3) δ 8.20 (s, 1H), 8.07 (d, $J = 8.0$ Hz, 1H), 7.68 (d, $J = 7.6$ Hz, 1H), 7.48 – 7.45 (m, 1H), 4.04 – 4.00 (m, 1H), 3.92 – 3.91 (m, 2H), 3.85 – 3.81 (m, 1H), 3.75 – 3.71 (m, 1H), 2.73 – 2.69 (m, 1H), 2.65 – 2.61 (m, 1H), 1.98 – 1.93 (m, 1H), 1.89 – 1.86 (m, 2H), 1.79 (s, 1H), 1.59 – 1.53 (m, 1H). ^{13}C NMR (101 MHz, CDCl_3) δ 142.7, 134.2, 129.2, 122.8, 121.9, 78.2, 68.0, 53.6, 53.0, 29.2, 25.8. HRMS (ESI - MS): calcd. 237.1233 $[\text{M}+\text{H}]^+$ Found: 237.1233.

5. Synthesis of Iodoarenes



5-Iodo-1-tosyl-1H-indole (S-41): Based on a modification to a known procedure,¹⁴ 5-iodoindole (500 mg, 2.05 mmol, 1.0 equiv.) was added to a stirred solution of sodium hydride (123 mg, 3.08 mmol, 1.5 equiv.) in DMF (5.0 mL) at room temperature under a nitrogen atmosphere. After the reaction mixture was stirred for 30 minutes, a tosyl chloride (470 mg, 2.67 mmol, 1.3 equiv.) solution in DMF (3.0 mL) was added via syringe. The reaction mixture was stirred overnight at 0–25 °C, and was afterwards quenched with water. The reaction mixture was then extracted with ethyl acetate, dried over Na₂SO₄, and concentrated *in vacuo* to give the desired product as a brown solid (702 mg, 86%). $R_f = 0.4$ (Hex/EA/DCM = 5:1:2). ¹H NMR (400 MHz, CDCl₃) δ 7.84 (d, $J = 1.6$ Hz, 1H), 7.78 (s, 1H), 7.74 (d, $J = 8.0$ Hz, 2H), 7.57 – 7.52 (m, 2H), 7.18 (d, $J = 8.0$ Hz, 2H), 6.56 (s, 1H), 2.31 (s, 3H). HRMS (ESI-MS): calcd. 419.9533 [M+Na]⁺ Found: 419.9510.

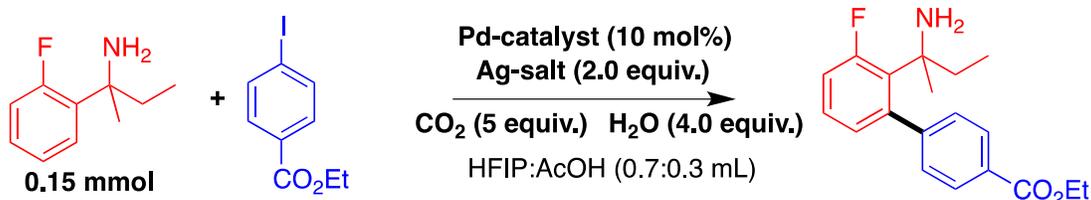


2-Iodostrychnine (S-42): Based on a modification to a known procedure,¹⁵ strychnine (1.00 g, 3.00 mmols) was dissolved in anhydrous dichloromethane (48 mL), followed by cooling to 0 °C. Trifluoroacetic acid (16 mL) was then added slowly. Subsequently, a solution/suspension of *N*-iodosuccinimide (675 mg, 3.00 mmols) was prepared in a 1:1 mixture of dichloromethane and trifluoroacetic acid, followed by cooling to 0 °C. This solution was added dropwise to the initial strychnine solution over a period of 30 minutes, followed by stirring the reaction mixture at 0 °C for a period of 4 h, after which point the reaction was warmed to room temperature and stirred for an additional 1 h. The reaction mixture was recooled to 0 °C, followed by dropwise addition of concentrated ammonium hydroxide until the acid had been quenched. The reaction mixture was then treated with saturated sodium thiosulfate_(aq), followed by extraction with dichloromethane (4 x 25 mL). This was dried over MgSO₄, then evaporated *in vacuo*. The resulting residue was chromatographed over silica gel (20% MeOH/DCM), giving the desired product as a white solid (760 mg, 55%). $R_f = 0.26$ (20% MeOH/DCM). ¹H NMR (600 MHz, CDCl₃) δ 7.82 (d, $J = 8.5$ Hz, 1H), 7.53 (d, $J = 8.5$ Hz, 1H), 7.45 (s, 1H), 6.01 (t, $J = 7.0$ Hz, 1H), 4.27 (dt, $J = 7.9, 3.0$ Hz, 1H), 4.14 (dd, $J = 13.9, 7.0$ Hz, 1H), 4.06 - 4.01 (m, 2H), 3.86 (d, $J = 10.6$ Hz, 1H), 3.79 (d, $J = 14.6$ Hz, 1H), 3.38 (dd, $J = 8.5, 5.2$ Hz, 1H), 3.19 (br s, 1H), 3.10 (dd, $J = 17.5, 8.4$ Hz, 1H), 2.94 – 2.88 (m, 1H), 2.85 (d, $J = 14.6$ Hz, 1H), 2.61 (dd, $J = 17.5, 3.0$ Hz, 1H), 2.39 (dt, $J = 14.7, 4.0$ Hz, 1H), 1.94 – 1.90 (m, 2H), 1.49 (d, $J = 14.7$ Hz, 1H), 1.26 (dt, $J = 10.3, 2.7$ Hz, 1H). ¹³C NMR (101 MHz, CDCl₃) δ 169.3, 142.0, 138.1, 137.9, 134.2, 131.4, 129.9, 87.2, 77.4, 64.5, 60.4, 60.0, 52.5, 51.8, 50.3, 47.8, 42.4, 42.3, 31.3, 26.5. HRMS (ESI-MS): calcd. 461.0720 [M+Na]⁺ Found: 461.0727.

6. Optimization and Synthesis of γ -Arylated 1° Amines

Catalytic C(sp²)-H Arylation of Free Primary Amines

A. Typical procedure for optimization experiments for the γ -arylation of 1° amines:



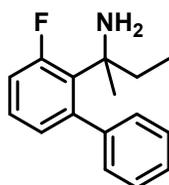
Solvent	Halide (equiv)	Pd-catalyst	Ag-salt	CO ₂ (equiv)	Yield (%)	Temperature (°C)	Time (h)
AcOH	1.5	Pd(OAc) ₂	AgTFA	3.0	22	100	12
AcOH	1.5	Pd(OAc) ₂	AgTFA	3.0	18	110	12
AcOH	1.5	Pd(OAc) ₂	AgTFA	3.0	15	90	12
AcOH	1.5	Pd(OAc) ₂	AgCO ₃	5.0	5	100	12
AcOH	1.5	Pd(OAc) ₂	AgOCOCH ₃	5.0	17	100	12
AcOH	2.0	Pd(OAc) ₂	AgTFA	5.0	27	100	12
AcOH	3.0	Pd(OAc) ₂	AgTFA	5.0	34	100	12
AcOH	3.0	Pd(OAc) ₂	AgTFA	5.0	38	100	24
HFIP	3.0	Pd(OAc) ₂	AgTFA	5.0	71	100	12
HFIP	3.0	Pd(OAc) ₂	AgTFA	5.0	66	110	12
HFIP	3.0	Pd(OAc) ₂	AgTFA	5.0	59	90	12
HFIP	3.0	Pd(OAc) ₂	AgOAc	5.0	28	100	12
HFIP	3.0	Pd(OAc) ₂	AgCO ₃	5.0	10	100	12
HFIP	3.0	Pd(OAc) ₂	AgOTf	5.0	44	100	12
HFIP/AcOH(1:1)	3.0	Pd(OAc) ₂	AgTFA	5.0	52	100	12
HFIP/AcOH(6:4)	3.0	Pd(OAc) ₂	AgTFA	5.0	63	100	12
HFIP/AcOH(7:3)	3.0	Pd(OAc) ₂	AgTFA	5.0	78	100	12
HFIP/AcOH (8:2)	3.0	Pd(OAc) ₂	AgTFA	5.0	77	100	12
HFIP/AcOH (9:1)	3.0	Pd(OAc) ₂	AgTFA	5.0	75	100	12
HFIP/AcOH (7:3)	3.0	Pd(OAc) ₂	--	5.0	5	100	12
HFIP/AcOH (7:3)	3.0	Pd(OAc) ₂	AgTFA	--	9	100	12
HFIP/AcOH (7:3)	3.0	PdCl ₂	AgTFA	5.0	22	100	12
HFIP/AcOH (7:3)	3.0	Pd(TFA) ₂	AgTFA	5.0	29	100	12
HFIP/AcOH (7:3)	3.0	--	AgTFA	5.0	0	100	12
HFIP/AcOH (7:3)	3.0	Pd(OAc) ₂	AgTFA (1.0 eq.)	5.0	43	100	12
HFIP/AcOH (7:3)	3.0	Pd(OAc) ₂	AgTFA (1.5 eq.)	5.0	57	100	12

Table S-1. Optimization of γ -Arylated of 1° Amines.

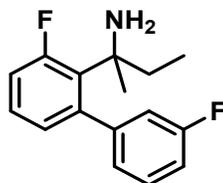
“Standard conditions”: A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.10 equiv), silver trifluoroacetate (66.2 mg, 0.30 mmol, 2.0 equiv), organohalide (0.45 mmol, 3.0 equiv), amine (0.15 mmol, 1.0 equiv), HFIP:acetic acid (0.7:0.3, 1.0 mL), and water (10.8 μ L, 0.6 mmol, 4.0 equiv), followed by the addition of dry ice (~33 mg, 0.75 mmol, 5.0 equiv) as CO₂ source. The vial was sealed with a PTFE lined cap and stirred at room temperature

for 15 min. After 15 min of stirring, the reaction mixture was heated in a pie-block at 100 °C under stirring for 12-15 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (2 ×10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The organic layer was concentrated *in vacuo* and further purified by flash column chromatography over silica (DCM/MeOH/ NH₄OH or hexanes/EtOAc) to give the C–H arylation product. All reactions were performed at least in duplicate, and the average isolated yield reported.

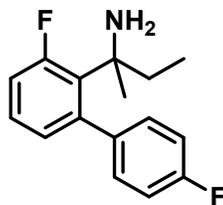
B. Characterization Data



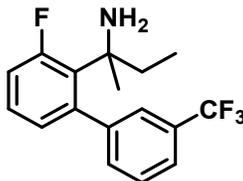
2-(3-Fluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1a): Reaction time 14 h, purified by hexanes:EtOAc (40:60). Product recovered as a colorless oil (25.9 mg, 71% yield). $R_f = 0.3$ (hexanes/EtOAc = 1:1). ¹H NMR (600 MHz, CDCl₃) δ 7.47 – 7.40 (m, 3H), 7.35 – 7.31 (m, 2H), 7.24 (td, $J = 7.8, 5.3$ Hz, 1H), 7.13 (ddd, $J = 13.4, 8.1, 1.5$ Hz, 1H), 6.94 – 6.91 (m, 1H), 2.16 (m, 1H), 1.83 – 1.77 (m, 1H), 1.47 (d, $J = 1.7$ Hz, 3H), 0.86 (t, $J = 7.5$ Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 161.3 (d, $J = 245.5$ Hz), 144.2 (d, $J = 3.1$ Hz), 143.2 (d, $J = 4.7$ Hz), 133.3 (d, $J = 11.5$ Hz), 128.7, 128.5, 127.9 (d, $J = 12.4$ Hz), 126.9, 126.5 (d, $J = 11.0$ Hz), 115.8 (d, $J = 27.6$ Hz), 58.2 (d, $J = 3.7$ Hz), 36.2 (d, $J = 6.1$ Hz), 30.6 (d, $J = 5.4$ Hz), 9.3. ¹⁹F NMR (376 MHz, CDCl₃) δ -105.5. HRMS (ESI-MS): calcd. 244.1495 [M+H]⁺ Found: 244.1497.



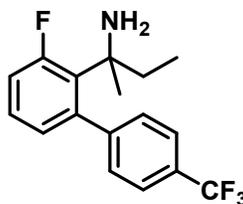
2-(3,3'-Difluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1b): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (25.1 mg, 64% yield). $R_f = 0.2$ (hexanes/EtOAc = 1:1). ¹H NMR (600 MHz, CDCl₃) δ 7.34 – 7.28 (m, 1H), 7.17 – 7.12 (m, 1H), 7.07 – 6.99 (m, 3H), 6.98 – 6.94 (m, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 2.09 – 2.01 (m, 1H), 1.74 – 1.64 (m, 1H), 1.36 (d, $J = 1.4$ Hz, 3H), 1.31 (br, 2H), 0.76 (td, $J = 7.5, 2.8$ Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 162.0 (dd, $J = 247.6, 13.9$ Hz), 161.2 (d, $J = 246.1$ Hz), 146.5 (dd, $J = 7.6, 2.4$ Hz), 141.8 – 141.4 (m), 133.6 (d, $J = 14.0$ Hz), 129.2 (dd, $J = 13.1, 8.5$ Hz), 128.1 (d, $J = 2.6$ Hz), 126.5 (d, $J = 10.9$ Hz), 124.5 (dd, $J = 40.4, 2.9$ Hz), 116.0 (d, $J = 28.7$ Hz), 115.8 (dd, $J = 33.2, 21.1$ Hz), 113.7 (dd, $J = 20.9, 4.1$ Hz), 57.9 (d, $J = 3.8$ Hz), 36.3 (d, $J = 6.4$ Hz), 30.6 (dd, $J = 7.6, 5.5$ Hz), 9.2 (d, $J = 3.8$ Hz). ¹⁹F NMR (376 MHz, CDCl₃), -62.9, -106.1 (d). HRMS (ESI-MS): calcd. 262.1401 [M+H]⁺ Found: 262.1405.



2-(3,4'-Difluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1c): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (24.7 mg, 63% yield). $R_f = 0.2$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.20 – 7.17 (m, 2H), 7.14 (td, $J = 7.8, 5.4$ Hz, 1H), 7.06 – 7.02 (m, 3H), 6.79 (d, $J = 7.6$ Hz, 1H), 2.05 – 1.99 (m, 1H), 1.72 – 1.66 (m, 1H), 1.33 (brs, 5H), 0.75 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.7 (d, $J = 311.0$ Hz), 161.6 (d, $J = 181.5$ Hz), 142.1 (d, $J = 4.9$ Hz), 140.2 (t, $J = 3.4$ Hz), 133.8 (d, $J = 11.4$ Hz), 130.2 (dd, $J = 40.0, 7.8$ Hz), 128.7 (d, $J = 1.7$ Hz), 126.5 (d, $J = 11.0$ Hz), 116.0 (d, $J = 27.6$ Hz), 114.8 (dd, $J = 21.3, 5.7$ Hz), 58.1 (d, $J = 3.7$ Hz), 36.6 (d, $J = 6.0$ Hz), 30.9 (d, $J = 5.4$ Hz), 9.4. $^{19}\text{F NMR}$ (376 MHz, CDCl_3), -62.8, -105.1 (d). HRMS (ESI-MS): calcd. 262.1401 $[\text{M}+\text{H}]^+$ Found: 262.1400.

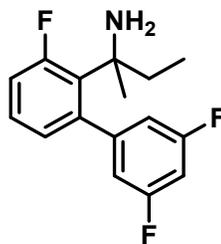


2-(3-Fluoro-3'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)butan-2-amine (1d): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (32.2 mg, 69% yield). $R_f = 0.34$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.59 (d, $J = 7.4$ Hz, 1H), 7.50 – 7.43 (m, 3H), 7.17 (td, $J = 7.8, 5.4$ Hz, 1H), 7.10 – 7.04 (m, 1H), 6.79 (d, $J = 7.5$ Hz, 1H), 2.05 – 1.94 (m, 1H), 1.77 – 1.64 (m, 1H), 1.31 (dd, $J = 5.9, 1.4$ Hz, 3H), 1.24 (s, 2H), 0.77 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 162.3 (d, $J = 5.5$ Hz), 160.7 (d, $J = 5.6$ Hz), 145.3, 141.6 (d, $J = 4.9$ Hz), 133.7 (t, $J = 11.4$ Hz), 132.1 (d, $J = 40.3$ Hz), 130.1 (dd, $J = 32.3, 10.1$ Hz), 128.4 (d, $J = 2.5$ Hz), 128.2 (d, $J = 16.4$ Hz), 126.7 (d, $J = 11.0$ Hz), 125.4 (dd, $J = 42.5, 3.7$ Hz), 123.7 (d, $J = 3.5$ Hz), 116.4 (d, $J = 27.5$ Hz), 58.0 (dd, $J = 3.3, 1.5$ Hz), 36.7 (dd, $J = 12.6, 5.9$ Hz), 31.0 (dd, $J = 14.3, 5.2$ Hz), 9.4 (d, $J = 9.5$ Hz). $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -62.8, -105.3. HRMS (ESI-MS): calcd. 312.1375 $[\text{M}+\text{H}]^+$ Found: 312.1386.

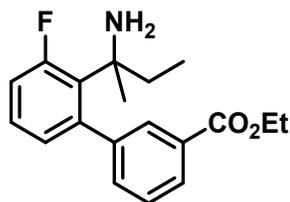


2-(3-Fluoro-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)butan-2-amine (1e): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (28.5 mg, 61% yield). $R_f = 0.32$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.61 (d, $J = 7.5$ Hz, 2H), 7.36 (d, $J = 7.4$ Hz, 2H), 7.17 (td, $J = 7.7, 5.5$ Hz, 1H), 7.07 (dd, $J = 13.3, 8.1$ Hz, 1H), 6.77 (d, $J = 7.5$ Hz, 1H), 2.12 – 1.96 (m, 1H), 1.73 – 1.64 (m, 1H), 1.34 (brs, 5H), 0.77 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.4 (d, $J = 246.1$ Hz), 148.4, 141.7 (d, $J = 4.9$ Hz), 133.5 (d, $J = 11.7$ Hz), 129.2, 128.9, 128.2, 126.8 (d, $J = 11.0$ Hz), 124.7 (dq, $J = 14.6, 3.6$ Hz), 124.2 (d, $J = 271.8$ Hz), 116.3 (d,

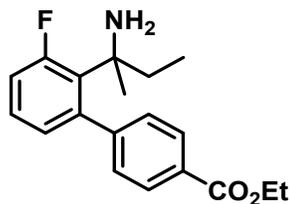
$J = 27.5$ Hz), 58.1 (d, $J = 3.5$ Hz), 36.6 (d, $J = 6.0$ Hz), 31.0 (d, $J = 5.2$ Hz), 9.3. ^{19}F NMR (376 MHz, CDCl_3) δ -62.8, -105.4. HRMS (ESI-MS): calcd. 312.1375 $[\text{M}+\text{H}]^+$ Found: 312.1382.



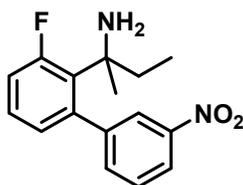
2-(3,3',5'-Trifluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1f): Reaction time 14 h, purified by hexanes:EtOAc (60:40). Product recovered as a yellow oil (23.1 mg, 55% yield). $R_f = 0.3$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) δ 7.16 (td, $J = 7.8, 5.3$ Hz, 1H), 7.06 (ddd, $J = 13.3, 8.1, 1.4$ Hz, 1H), 6.80 – 6.77 (m, 4H), 2.09 – 2.00 (m, 1H), 1.76 – 1.67 (m, 1H), 1.53 (br, 2H), 1.37 (d, $J = 1.5$ Hz, 3H), 0.77 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 163.1 (t, $J = 13.5$ Hz), 161.4 (t, $J = 13.6$ Hz), 161.3 (d, $J = 246.1$ Hz), 147.7 (td, $J = 9.7, 3.3$ Hz), 140.9 – 140.4 (m), 128.0 (d, $J = 2.7$ Hz), 126.9 (d, $J = 11.0$ Hz), 116.5 (d, $J = 27.5$ Hz), 112.3 (dd, $J = 21.4, 3.4$ Hz), 112.1 (dd, $J = 21.4, 3.5$ Hz), 102.4 (t, $J = 25.1$ Hz), 58.1 (d, $J = 3.6$ Hz), 36.5 (d, $J = 6.1$ Hz), 30.7 (d, $J = 5.2$ Hz), 9.4. ^{19}F NMR (376 MHz, CDCl_3) δ -120.2, -139.6. HRMS (ESI): calcd. 280.1314 $[\text{M}+\text{H}]^+$ Found: 280.1326.



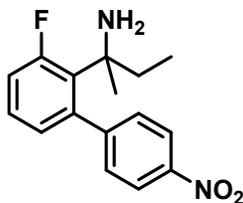
Ethyl 2'-(2-aminobutan-2-yl)-3'-fluoro-[1,1'-biphenyl]-3-carboxylate (1g): Reaction time 15 h, purified by hexanes:EtOAc (40:60). Product recovered as a colorless oil (34.5 mg, 73% yield). $R_f = 0.22$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) δ 8.04 – 7.98 (m, 1H), 7.92 (d, $J = 6.2$ Hz, 1H), 7.43 – 7.42 (m, 2H), 7.16 (td, $J = 7.8, 5.5$ Hz, 1H), 7.05 (ddd, $J = 13.3, 8.1, 1.3$ Hz, 1H), 6.79 (d, $J = 7.5$ Hz, 1H), 4.38 (q, $J = 7.1$ Hz, 2H), 2.07 – 1.98 (m, 1H), 1.72 – 1.65 (m, 1H), 1.52 (s, 2H), 1.38 (t, $J = 7.1$ Hz, 3H), 0.77 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) 166.5 (d, $J = 1.0$ Hz), 161.4 (dd, $J = 245.9, 2.8$ Hz), 144.6 (d, $J = 3.0$ Hz), 142.1 (d, $J = 4.8$ Hz), 133.6 (d, $J = 11.4$ Hz), 132.9 (d, $J = 44.1$ Hz), 130.1 (d, $J = 7.9$ Hz), 129.5 (d, $J = 35.4$ Hz), 128.5, 128.1 (d, $J = 1.3$ Hz), 127.9 (d, $J = 13.5$ Hz), 126.7 (d, $J = 11.0$ Hz), 116.1 (d, $J = 27.5$ Hz), 61.2, 58.1 (t, $J = 3.4$ Hz), 36.5 (dd, $J = 18.4, 6.0$ Hz), 31.0 (dd, $J = 17.3, 5.2$ Hz), 14.4, 9.4 (d, $J = 6.8$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -120.1. HRMS (ESI-MS): calcd. 316.1714 $[\text{M}+\text{H}]^+$ Found: 316.1723.



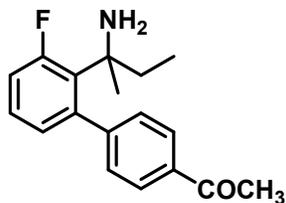
Ethyl 2'-(2-aminobutan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (1h): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (36.4 mg, 77% yield). $R_f = 0.21$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.03 (dd, $J = 7.2, 1.0$ Hz, 2H), 7.32 (d, $J = 6.9$ Hz, 2H), 7.19 – 7.13 (m, 1H), 7.09 – 7.02 (m, 1H), 6.77 (d, $J = 7.5$ Hz, 1H), 4.47 – 4.34 (m, 2H), 2.09 – 2.00 (m, 1H), 1.74 – 1.61 (m, 1H), 1.41 (t, $J = 7.5$ Hz, 3H), 1.34 (s, 3H), 0.76 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 161.4 (d, $J = 245.9$ Hz), 149.3, 142.3, 129.1, 129.0, 128.9, 128.7, 128.1 (d, $J = 2.5$ Hz), 126.8 (d, $J = 11.0$ Hz), 116.2 (d, $J = 27.4$ Hz), 61.2, 58.2, 36.4, 30.7, 14.5, 9.3. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -120.2. HRMS (ESI-MS): calcd. 316.1714 $[\text{M}+\text{H}]^+$ Found: 316.1711.



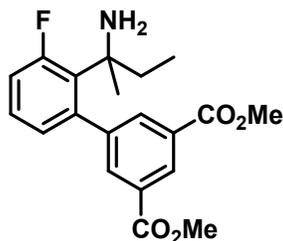
2-(3-Fluoro-3'-nitro-[1,1'-biphenyl]-2-yl)butan-2-amine (1i): Reaction time 15 h, purified by hexanes:EtOAc (30:70). Product recovered as a light yellow oil (24.6 mg, 57% yield). $R_f = 0.24$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.19 (d, $J = 8.1$ Hz, 1H), 8.11 (d, $J = 1.5$ Hz, 1H), 7.58 (d, $J = 6.5$ Hz, 1H), 7.55 – 7.48 (m, 1H), 7.20 (td, $J = 7.8, 5.4$ Hz, 1H), 7.10 (ddd, $J = 13.2, 8.1, 1.3$ Hz, 1H), 6.78 (d, $J = 7.5$ Hz, 1H), 2.11 – 1.96 (m, 1H), 1.76 – 1.64 (m, 1H), 1.52 (s, 2H), 1.38 – 1.31 (m, 3H), 0.78 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.5 (dd, $J = 246.5, 3.7$ Hz), 147.5 (d, $J = 13.8$ Hz), 146.3 (dd, $J = 6.0, 3.4$ Hz), 140.7, 135.0, 134.6, 128.4 (d, $J = 19.0$ Hz), 128.3 (d, $J = 2.7$ Hz), 127.1 (dd, $J = 11.0, 3.1$ Hz), 123.5 (d, $J = 65.0$ Hz), 121.8 (d, $J = 3.2$ Hz), 116.8 (d, $J = 27.4$ Hz), 58.1 (dd, $J = 6.3, 3.4$ Hz), 36.8 (t, $J = 6.7$ Hz), 31.3 (t, $J = 4.6$ Hz), 9.4 (d, $J = 6.7$ Hz). $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -120.3. HRMS (ESI-MS): calcd. 289.1352 $[\text{M}+\text{H}]^+$ Found: 289.1348.



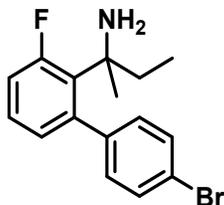
2-(3-Fluoro-4'-nitro-[1,1'-biphenyl]-2-yl)butan-2-amine (1j): Reaction time 15 h, purified by hexanes:EtOAc (20:80). Product recovered as a yellow oil (22.0 mg, 51% yield). $R_f = 0.18$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.23 – 8.21 (m, 2H), 7.41 (d, $J = 8.4$ Hz, 2H), 7.21 – 7.18 (m, 1H), 7.10 (dd, $J = 13.3, 8.1$ Hz, 1H), 6.75 (d, $J = 7.6$ Hz, 1H), 2.08 – 2.03 (m, 3H), 1.73 – 1.67 (m, 1H), 1.35 (s, 3H), 0.77 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.4 (d, $J = 246.6$ Hz), 152.0 (d, $J = 3.1$ Hz), 146.7, 141.0 (d, $J = 5.0$ Hz), 129.8, 129.4, 127.7 (d, $J = 2.7$ Hz), 127.0 (d, $J = 11.0$ Hz), 122.9 (d, $J = 21.3$ Hz), 116.7 (d, $J = 27.3$ Hz), 58.1 (d, $J = 3.4$ Hz), 36.7 (d, $J = 6.1$ Hz), 31.1 (d, $J = 5.2$ Hz), 9.3. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -120.2. HRMS (ESI-MS): calcd. 289.1352 $[\text{M}+\text{H}]^+$ Found: 289.1361.



1-(2'-(2-Aminobutan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-yl)ethan-1-one (1k): Reaction time 15 h, purified by hexanes:EtOAc (20:80). Product recovered as a colorless oil (27.4 mg, 64% yield). $R_f = 0.33$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.94 (d, $J = 7.2$ Hz, 2H), 7.34 (d, $J = 5.7$ Hz, 2H), 7.16 (td, $J = 7.7, 5.6$ Hz, 1H), 7.05 (dd, $J = 12.6, 8.1$ Hz, 1H), 6.75 (d, $J = 7.4$ Hz, 1H), 2.63 (s, 3H), 2.12 – 1.97 (m, 1H), 1.75 – 1.60 (m, 1H), 1.50 (s, 2H), 1.34 (s, 3H), 0.75 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 197.7, 161.4 (d, $J = 246.0$ Hz), 149.8 (d, $J = 3.1$ Hz), 142.1 (d, $J = 4.9$ Hz), 135.6, 133.4 (d, $J = 11.8$ Hz), 129.0 (d, $J = 46.9$ Hz), 127.9, 127.8, 126.7 (d, $J = 11.0$ Hz), 116.2 (d, $J = 27.4$ Hz), 58.1 (d, $J = 3.6$ Hz), 36.5 (d, $J = 6.1$ Hz), 30.9 (d, $J = 5.3$ Hz), 26.7, 9.3. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -119.2. HRMS (ESI-MS): calcd. 286.1608 $[\text{M}+\text{H}]^+$ Found: 286.1618.

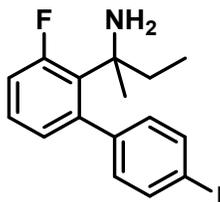


Dimethyl 2'-(2-aminobutan-2-yl)-3'-fluoro-[1,1'-biphenyl]-3,5-dicarboxylate (1l): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (34.5 mg, 64% yield). $R_f = 0.21$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.64 (d, $J = 1.0$ Hz, 1H), 8.10 (d, $J = 1.4$ Hz, 2H), 7.19 – 7.15 (m, 1H), 7.07 (dd, $J = 13.3, 8.1$ Hz, 1H), 6.76 (d, $J = 7.5$ Hz, 1H), 3.94 (s, 2H), 2.07 – 1.98 (m, 1H), 1.72 – 1.65 (m, 1H), 1.31 (s, 3H), 1.22 (br, 2H), 0.77 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.2, 161.5 (d, $J = 246.3$ Hz), 145.4 (d, $J = 3.2$ Hz), 141.1 (d, $J = 5.0$ Hz), 133.7 (d, $J = 60.4$ Hz), 133.6 (d, $J = 11.5$ Hz), 130.0 (d, $J = 14.0$ Hz), 129.1, 128.5 (d, $J = 2.6$ Hz), 126.9 (d, $J = 11.0$ Hz), 116.5 (d, $J = 27.4$ Hz), 58.1 (d, $J = 3.4$ Hz), 52.6, 36.8 (d, $J = 6.1$ Hz), 31.4 (d, $J = 5.1$ Hz), 9.4. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) δ -119.7. HRMS (ESI-MS): calcd. 360.1611 $[\text{M}+\text{H}]^+$ Found: 360.1599.

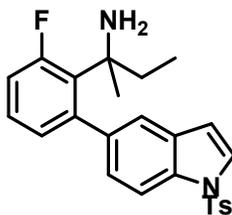


2-(4'-Bromo-3-fluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1m): Reaction time 13 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (34.7 mg, 72% yield). $R_f = 0.35$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.48 (d, $J = 7.6$ Hz, 2H), 7.17 – 7.08 (m, 3H), 7.07 – 7.01 (m, 1H), 6.77 (d, $J = 7.1$ Hz, 1H), 2.07 – 1.97 (m, 1H), 1.73 – 1.65 (m, 1H), 1.44 (s, 2H), 1.33 (s, 3H), 0.75 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.3 (d, $J = 245.9$ Hz), 142.5 (d, $J = 223.9$ Hz), 133.5 (d, $J = 11.4$ Hz), 130.8 (d, $J = 11.1$ Hz), 130.4, 130.1, 128.2

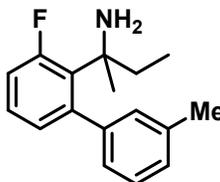
(d, $J = 2.6$ Hz), 126.5 (d, $J = 11.0$ Hz), 116.0 (d, $J = 27.5$ Hz), 58.0 (d, $J = 3.6$ Hz), 36.5 (d, $J = 6.0$ Hz), 30.8 (d, $J = 5.3$ Hz), 9.2. ^{19}F NMR (376 MHz, CDCl_3) δ -120.3. HRMS (ESI-MS): calcd. 322.0607 $[\text{M}+\text{H}]^+$ Found: 322.0613.



2-(3-Fluoro-4'-iodo-[1,1'-biphenyl]-2-yl)butan-2-amine (1n): Reaction time 14 h, purified by hexanes:EtOAc (65:35). Product recovered as a colorless oil (38.7 mg, 70% yield). $R_f = 0.4$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 7.67 (d, $J = 7.2$ Hz, 2H), 7.14 (td, $J = 7.8, 5.5$ Hz, 1H), 7.04 (dd, $J = 7.2, 6.1$ Hz, 1H), 7.01 – 6.98 (m, 2H), 6.76 (d, $J = 7.5$ Hz, 1H), 2.07 – 1.98 (m, 1H), 1.73 – 1.64 (m, 1H), 1.36 (br, 2H), 1.34 (s, 3H), 0.75 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.4 (d, $J = 245.9$ Hz), 144.0 (d, $J = 3.2$ Hz), 141.9 (d, $J = 4.9$ Hz), 136.9 (d, $J = 12.5$ Hz), 133.6 (d, $J = 11.5$ Hz), 130.8, 130.5, 128.3 (d, $J = 2.6$ Hz), 126.6 (d, $J = 11.0$ Hz), 116.1 (d, $J = 27.5$ Hz), 92.3, 58.1 (d, $J = 3.7$ Hz), 36.6 (d, $J = 6.0$ Hz), 31.0 (d, $J = 5.4$ Hz), 9.4. ^{19}F NMR (376 MHz, CDCl_3) δ -119.6. HRMS (ESI-MS): calcd. 370.0468 $[\text{M}+\text{H}]^+$ Found: 370.0464.

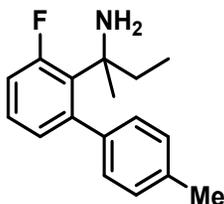


2-(2-Fluoro-6-(1-tosyl-1H-indol-5-yl)phenyl)butan-2-amine (1o): Reaction time 14 h, purified by hexanes:EtOAc (30:70). Product recovered as a yellow oil (32.0 mg, 49% yield). $R_f = 0.22$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 7.94 (d, $J = 8.4$ Hz, 1H), 7.80 (d, $J = 8.1$ Hz, 2H), 7.60 (d, $J = 3.6$ Hz, 1H), 7.37 (d, $J = 16.6$ Hz, 1H), 7.28 – 7.23 (m, 2H), 7.22 – 7.15 (m, 1H), 7.15 – 7.07 (m, 1H), 7.01 (dd, $J = 13.2, 8.1$ Hz, 1H), 6.78 (d, $J = 7.5$ Hz, 1H), 6.63 (d, $J = 3.4$ Hz, 1H), 2.36 (s, 3H), 2.08 – 1.96 (m, 1H), 1.78 – 1.68 (m, 1H), 1.31 (d, $J = 7.0$ Hz, 3H), 0.75 (q, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.3 (dd, $J = 245.7, 1.8$ Hz), 145.2, 143.3 – 142.9 (m), 139.2, 135.3 (d, $J = 2.3$ Hz), 133.7 (d, $J = 4.0$ Hz), 130.3 (d, $J = 8.2$ Hz), 130.1, 129.1, 127.2 (d, $J = 4.3$ Hz), 126.9, 126.6, 125.6, 121.2, 115.9 (d, $J = 27.5$ Hz), 112.7 (d, $J = 8.4$ Hz), 108.9 (d, $J = 5.2$ Hz), 58.6, 36.1, 30.3, 21.7, 9.3 (d, $J = 5.5$ Hz). ^{19}F NMR (376 MHz, CDCl_3) δ -105.5. HRMS (ESI-MS): calcd. 437.1693 $[\text{M}+\text{H}]^+$ Found: 437.1696

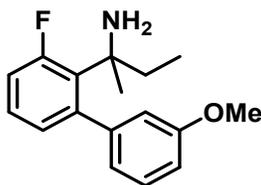


2-(3-Fluoro-3'-methyl-[1,1'-biphenyl]-2-yl)butan-2-amine (1p): Reaction time 15 h, purified by hexanes:EtOAc (45:55). Product recovered as a yellow oil (28.9 mg, 75% yield). $R_f = 0.31$ (hexanes/EtOAc = 1:1). ^1H NMR (400

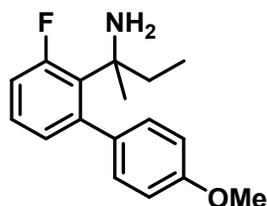
MHz, CDCl₃) δ 7.26 – 7.19 (m, 1H), 7.15 – 7.10 (m, 2H), 7.04 – 6.99 (m, 3H), 6.81 (d, J = 7.5 Hz, 1H), 2.37 (s, 3H), 2.10 – 2.03 (m, 1H), 1.72 – 1.65 (m, 1H), 1.38 (dd, J = 4.8, 1.8 Hz, 3H), 1.28 (br, 2H), 0.76 (t, J = 7.5 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 161.3 (dd, J = 245.4, 3.5 Hz), 144.6 – 144.1 (m), 143.4 (dd, J = 4.8, 1.3 Hz), 137.6 (d, J = 9.0 Hz), 133.7 (dd, J = 11.8, 7.5 Hz), 129.3 (d, J = 31.0 Hz), 128.5 (d, J = 2.5 Hz), 127.8 (d, J = 13.8 Hz), 127.6 (d, J = 3.1 Hz), 126.3 (d, J = 10.9 Hz), 125.7 (d, J = 41.0 Hz), 115.6 (d, J = 27.6 Hz), 58.1, 36.3 (dd, J = 11.1, 6.3 Hz), 30.9 – 30.4 (m), 21.5, 9.4 (d, J = 3.0 Hz). ¹⁹F NMR (376 MHz, CDCl₃) δ -120.0. HRMS (ESI-MS): calcd. 258.1658 [M+H]⁺ Found: 258.1660.



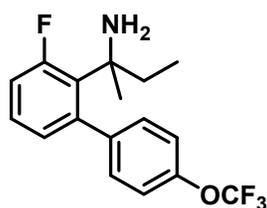
2-(3-Fluoro-4'-methyl-[1,1'-biphenyl]-2-yl)butan-2-amine (1q): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (31.2 mg, 81% yield). R_f = 0.31 (hexanes/EtOAc = 1:1). ¹H NMR (400 MHz, CDCl₃) δ 7.17 – 7.10 (m, 5H), 7.01 (dd, J = 13.3, 9.5 Hz), 6.81 (d, J = 7.5 Hz), 2.39 (s, 3H), 2.11 – 2.03 (m, 1H), 1.72 – 1.63 (m, 1H), 1.37 (d, J = 1.8 Hz), 1.26 (br, 2H), 0.76 (t, J = 8.0 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 161.3 (d, J = 245.4 Hz), 143.3 (d, J = 4.9 Hz), 141.3 (d, J = 3.2 Hz), 136.5, 128.7 (d, J = 2.6 Hz), 128.6 (d, J = 9.1 Hz), 128.6, 128.3, 126.3 (d, J = 11.0 Hz), 115.6 (d, J = 27.6 Hz), 58.1 (d, J = 3.9 Hz), 36.4 (d, J = 6.2 Hz), 30.8 (d, J = 5.6 Hz), 21.2, 9.3. ¹⁹F NMR (376 MHz, CDCl₃) δ -120.1. HRMS (ESI-MS): calcd. 258.1658 [M+H]⁺ Found: 258.1660.



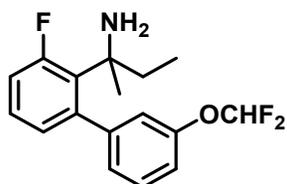
2-(3-Fluoro-3'-methoxy-[1,1'-biphenyl]-2-yl)butan-2-amine (1r): Reaction time 15 h, purified by pure EtOAc. Product recovered as a yellow oil (25.0 mg, 61% yield). R_f = 0.18 (hexanes/EtOAc = 1:1). ¹H NMR (600 MHz, CDCl₃) δ 7.27 – 7.24 (m, 1H), 7.16 – 7.11 (m, 1H), 7.05 – 6.99 (m, 1H), 6.85 (d, J = 5.8 Hz, 1H), 6.82 – 6.80 (m, 2H), 6.77 (d, J = 9.2 Hz, 1H), 3.80 (s, 3H), 1.68 (brs, 2H), 1.61 (brs, 2H), 1.39 (s, 3H), 0.76 (t, J = 7.2 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 161.2 (d, J = 245.5 Hz), 159.1 (d, J = 9.0 Hz), 145.4, 143.0 (t, J = 4.8 Hz), 129.0 (d, J = 13.9 Hz), 128.4 (d, J = 2.5 Hz), 126.7 (dd, J = 10.9, 2.4 Hz), 121.4 (d, J = 19.4 Hz), 115.8 (d, J = 27.5 Hz), 114.7 (d, J = 25.8 Hz), 112.4 (d, J = 8.0 Hz), 58.4, 55.3, 36.0 (t, J = 6.1 Hz), 30.5 – 30.1 (m), 9.4 (d, J = 1.7 Hz). ¹⁹F NMR (376 MHz, CDCl₃) -120.3. HRMS (ESI-MS): calcd. 274.1607 [M+H]⁺ Found: 274.1612.



2-(3-Fluoro-4'-methoxy-[1,1'-biphenyl]-2-yl)butan-2-amine (1s): Reaction time 15 h, purified by pure EtOAc. Product recovered as a yellow oil (24.2 mg, 59% yield). $R_f = 0.18$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.16 – 7.10 (m, 3H), 7.01 (ddd, $J = 13.5, 8.1, 1.4$ Hz, 1H), 6.89 (d, $J = 8.6$ Hz, 2H), 6.82 (dd, $J = 7.5, 0.8$ Hz, 1H), 3.84 (s, 3H), 2.07 – 2.02 (m, 1H), 1.72 – 1.67 (m, 1H), 1.36 (d, $J = 1.8$ Hz, 3H), 0.76 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.4 (d, $J = 245.4$ Hz), 158.6, 142.9 (d, $J = 4.9$ Hz), 136.5 (d, $J = 3.2$ Hz), 133.8 (d, $J = 11.2$ Hz), 129.6 (d, $J = 38.4$ Hz), 129.0 (d, $J = 2.5$ Hz), 126.4 (d, $J = 11.1$ Hz), 115.7 (d, $J = 27.7$ Hz), 113.3, 58.1 (d, $J = 3.8$ Hz), 55.4, 36.5 (d, $J = 6.1$ Hz), 30.8 (d, $J = 5.6$ Hz), 9.4. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -120.1. LRMS (ESI-MS): calcd. 274.3 $[\text{M}+\text{H}]^+$ Found: 274.9.

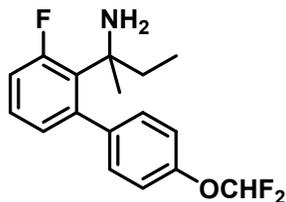


2-(3-Fluoro-4'-(trifluoromethoxy)-[1,1'-biphenyl]-2-yl)butan-2-amine (1t): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (29.9 mg, 61% yield). $R_f = 0.34$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.29 (d, $J = 7.7$ Hz, 1H), 7.25 (dd, $J = 9.2, 1.8$ Hz, 1H), 7.22 – 7.18 (m, 2H), 7.16 (dd, $J = 7.6, 5.5$ Hz, 1H), 7.04 (dd, $J = 14.1, 7.4$ Hz, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 2.06 – 1.97 (m, 1H), 1.80 – 1.71 (m, 1H), 1.33 (s, 3H), 0.76 (t, $J = 7.4$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.4 (d, $J = 246$ Hz), 148.2 (d, $J = 1.6$ Hz), 142.9 (d, $J = 2.7$ Hz), 141.8 (d, $J = 4.8$ Hz), 130.1, 128.6 (d, $J = 2.5$ Hz), 126.9 (d, $J = 11.0$ Hz), 120.6 (d, $J = 773$ Hz), 120.6 (d, $J = 256$ Hz), 120.3 (d, $J = 10.4$ Hz), 116.2 (d, $J = 27.4$ Hz), 58.5, 36.3 (d, $J = 4.5$ Hz), 9.3. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -105.3 (d), -58.2. LRMS (ESI-MS): calcd. 328.3 $[\text{M}+\text{H}]^+$ Found: 328.0.

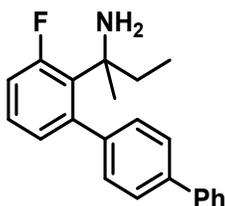


2-(3'-(Difluoromethoxy)-3-fluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1u): Reaction time 15 h, purified by hexanes:EtOAc (45:55). Product recovered as a colorless oil (26.4 mg, 57% yield). $R_f = 0.29$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.36 – 7.32 (m, 1H), 7.19 – 7.11 (m, 1H), 7.08 (dd, $J = 13.2, 5.0$ Hz, 2H), 7.04 – 6.99 (m, 1H), 6.80 (d, $J = 7.5$ Hz, 1H), 6.55 (td, $J = 73.7, 4.6$ Hz, 1H), 2.03 (dt, $J = 15.3, 7.7$ Hz, 1H), 1.80 – 1.65 (m, 1H), 1.38 – 1.30 (m, 2H), 0.76 (t, $J = 7.4$ Hz, 2H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 161.4 (dd, $J = 245.9, 5.4$ Hz), 150.5 (dt, $J = 14.7, 2.7$ Hz), 146.2, 141.8 (dd, $J = 4.8, 1.5$ Hz), 129.2 (d, $J = 12.8$ Hz), 128.3 (d, $J = 2.5$ Hz), 126.8 (d, $J = 10.8$ Hz), 125.9 (d, $J = 17.3$ Hz), 120.1 (d, $J = 35.6$ Hz), 117.9 (d, $J = 5.1$ Hz), 116.26 (d, $J = 27.5$ Hz), 115.8 (t, $J = 261.2$ Hz).

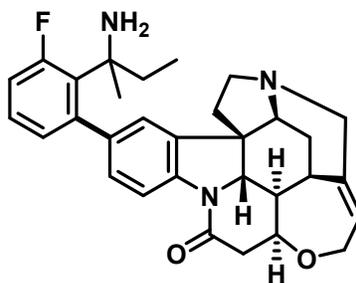
Hz), 58.2, 36.3 (d, $J = 4.7$ Hz), 30.6 (d, $J = 4.6$ Hz), 9.3 (d, $J = 6.5$ Hz). ^{19}F NMR (376 MHz, CDCl_3) -105.3 (d), -58.2. HRMS (ESI-MS): calcd. 310.1412 $[\text{M}+\text{H}]^+$ Found: 310.1409.



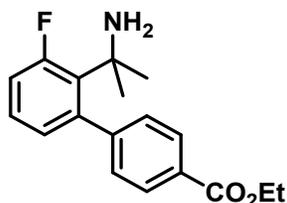
2-(4'-(Difluoromethoxy)-3-fluoro-[1,1'-biphenyl]-2-yl)butan-2-amine (1v): Reaction time 14 h, purified by hexanes:EtOAc (45:55). Product recovered as a colorless oil (26.7 mg, 57% yield). $R_f = 0.26$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 7.23 (d, $J = 8.3$ Hz, 2H), 7.15 (t, $J = 8.4$ Hz, 1H), 7.11 (d, $J = 7.9$ Hz, 2H), 7.04 (dd, $J = 13.3, 8.1$ Hz, 1H), 6.79 (d, $J = 7.5$ Hz, 1H), 6.55 (t, $J = 7.6$ Hz, 1H), 2.07 – 1.98 (m, 1H), 1.73 – 1.64 (m, 1H), 1.34 (s, 3H), 1.31 (br, 2H), 0.76 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.4 (d, $J = 245.8$ Hz), 150.1 (t, $J = 2.8$ Hz), 141.8 (dd, $J = 51.2, 4.1$ Hz), 133.7 (d, $J = 11.5$ Hz), 130.2, 129.9, 128.6 (d, $J = 2.6$ Hz), 126.6 (d, $J = 11.0$ Hz), 118.9 (d, $J = 6.9$ Hz), 116.2 (t, $J = 22.5$ Hz), 116.0 (d, $J = 7.7$ Hz), 58.1 (d, $J = 3.7$ Hz), 36.6 (d, $J = 6.0$ Hz), 30.9 (d, $J = 5.4$ Hz), 9.4. ^{19}F NMR (376 MHz, CDCl_3) -104.2 (d), -58.4. HRMS (ESI-MS): calcd. 309.1340 $[\text{M}+\text{H}]^+$ Found: 310.1419.



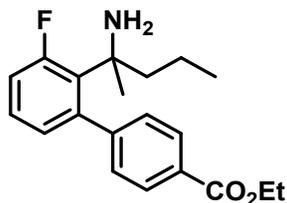
2-(3-Fluoro-[1,1':4',1''-terphenyl]-2-yl)butan-2-amine (1w): Reaction time 14 h, purified by hexanes:EtOAc (60:40). Product recovered as a yellow oil (31.6 mg, 66% yield). $R_f = 0.38$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 7.63 (d, $J = 7.2$ Hz, 2H), 7.59 (d, $J = 7.6$ Hz, 2H), 7.46 (t, $J = 7.6$ Hz, 2H), 7.37 (d, $J = 6.3$ Hz, 1H), 7.32 – 7.26 (m, 2H), 7.18 – 7.14 (m, 1H), 7.08 – 7.02 (m, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 2.11 – 2.05 (m, 1H), 1.81 (br, 2H), 1.77 – 1.65 (m, 1H), 1.40 (s, 3H), 0.79 (t, $J = 8.0$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 161.4 (d, $J = 245.6$ Hz), 143.3 (d, $J = 2.9$ Hz), 142.9 (d, $J = 4.8$ Hz), 140.6, 139.8, 129.2, 128.9, 128.6 (d, $J = 2.4$ Hz), 127.5, 127.1, 126.6 (d, $J = 12.1$ Hz), 126.5 (d, $J = 10.5$ Hz), 115.9 (d, $J = 27.6$ Hz), 58.2 (d, $J = 3.4$ Hz), 36.4 (d, $J = 6.1$ Hz), 30.8 (d, $J = 5.4$ Hz), 9.4. ^{19}F NMR (376 MHz, CDCl_3) δ -105.6. HRMS (ESI-MS): calcd. 320.1815 $[\text{M}+\text{H}]^+$ Found: 320.1818.



2-(2-Fluoro-3-strychninephenyl)butan-2-amine (1x): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a light yellow gummy oil (25.4 mg, 34% yield). $R_f = 0.22$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.83 (d, $J = 8.5$ Hz, 1H), 7.51 (dd, $J = 8.5, 1.7$ Hz, 1H), 7.42 (s, 1H), 7.22 – 7.16 (m, 1H), 7.07 (t, $J = 5.8$ Hz, 1H), 7.01 – 6.94 (m, 1H), 5.91 (s, 1H), 4.27 – 4.23 (m, 1H), 4.12 (dd, $J = 13.8, 7.0$ Hz, 1H), 4.02 (dd, $J = 13.8, 6.1$ Hz, 1H), 3.89 (s, 1H), 3.83 (d, $J = 10.5$ Hz, 1H), 3.69 (d, $J = 14.7$ Hz, 1H), 3.26 – 3.20 (m, 1H), 3.17 – 3.05 (m, 3H), 2.90 – 2.78 (m, 1H), 2.73 (d, $J = 14.7$ Hz, 1H), 2.61 (dd, $J = 17.4, 3.1$ Hz, 1H), 2.36 – 2.32 (m, 1H), 1.98 – 1.90 (m, 1H), 1.90 – 1.80 (m, 3H), 1.51 (s, 3H), 1.44 (d, $J = 14.6$ Hz, 1H), 1.25 – 1.20 (m, 1H), 0.72 (t, $J = 7.5$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 169.3, 160.9 (d, $J = 246.0$ Hz), 142.0, 139.6, 137.6, 135.1, 131.4, 128.4 (d, $J = 8.9$ Hz), 128.2, 127.7 (d, $J = 5.0$ Hz), 123.9 (d, $J = 3.2$ Hz), 118.2, 116.9 (d, $J = 199.3$ Hz), 116.2 (d, $J = 24.1$ Hz), 87.0, 64.6, 60.2 (d, $J = 7.1$ Hz), 52.6, 51.8, 50.3, 48.0, 42.7, 42.4, 35.2, 31.4, 28.1, 26.7, 8.9. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -120.3. LRMS (ESI-MS): calcd. 499.6 $[\text{M}+\text{H}]^+$ Found: 499.7.

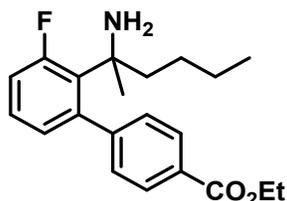


Ethyl 2'-(2-aminopropan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2a): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (32.5 mg, 72% yield). $R_f = 0.22$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.04 (d, $J = 8.3$ Hz, 2H), 7.32 (d, $J = 8.3$ Hz, 2H), 7.16 (td, $J = 7.8, 5.4$ Hz, 1H), 7.07 (ddd, $J = 13.3, 8.1, 1.4$ Hz, 1H), 6.79 (d, $J = 7.5$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 1.55 (s, 2H), 1.45 – 1.36 (m, 9H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 161.8 (d, $J = 245.9$ Hz), 149.2 (d, $J = 3.1$ Hz), 141.2 (d, $J = 4.7$ Hz), 135.1 (d, $J = 11.0$ Hz), 129.2, 129.2, 128.9, 127.9 (d, $J = 2.6$ Hz), 126.7 (d, $J = 11.0$ Hz), 116.2 (d, $J = 27.2$ Hz), 61.2, 54.6 (d, $J = 2.4$ Hz), 32.8, 14.5. $^{19}\text{F NMR}$ (376 Hz, CDCl_3), -109.5. HRMS (ESI-MS): calcd. 302.1550 $[\text{M}+\text{H}]^+$ Found: 302.1553.

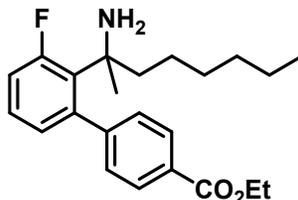


Ethyl 2'-(2-aminopentan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2b): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (34.5 mg, 70% yield). $R_f = 0.27$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.02 – 7.99 (m, 2H), 7.29 – 7.24 (m, 2H), 7.12 (td, $J = 7.8, 5.2$ Hz, 1H), 7.03 – 7.00 (m, 1H), 6.73 (d, $J = 7.5$ Hz, 1H), 4.36 (q, $J = 7.1$ Hz, 2H), 1.98 – 1.94 (m, 1H), 1.58 – 1.56 (m, 1H), 1.37 (t, $J = 7.1$ Hz, 3H), 1.32 (s, 1H), 1.26 (br, 2H), 1.19 – 1.12 (m, 1H), 1.09 – 1.03 (m, 1H), 0.81 (t, $J = 7.3$ Hz, 2H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 161.3 (d, $J = 245.9$ Hz), 149.4 (d, $J = 3.0$ Hz), 142.0 (d, $J = 4.9$ Hz), 129.1 (d, $J = 15.1$ Hz), 129.0, 128.8, 128.6, 128.0 (d, $J = 2.5$ Hz), 126.6 (d, $J = 10.9$ Hz), 116.1 (d, $J = 27.4$ Hz), 61.1, 57.8 (d, $J = 3.5$ Hz),

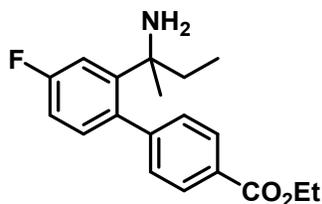
46.4 (d, $J = 5.8$ Hz), 31.4 (d, $J = 5.2$ Hz), 18.3, 14.5, 14.4. ^{19}F NMR (376 MHz, CDCl_3) -120.1. HRMS (ESI-MS): calcd. 330.1863 $[\text{M}+\text{H}]^+$ Found: 330.1880.



Ethyl 2'-(2-aminohexan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2c): Reaction time 12 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (32.4 mg, 63% yield). $R_f = 0.31$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) δ 8.06 – 8.02 (m, 2H), 7.33 – 7.29 (m, 2H), 7.16 (td, $J = 7.8, 5.3$ Hz, 1H), 7.05 (ddd, $J = 13.3, 8.1, 1.5$ Hz, 1H), 6.76 (d, $J = 7.5$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.06 – 1.98 (m, 1H), 1.66 – 1.62 (m, 1H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.35 (d, $J = 1.5$ Hz, 3H), 1.32 – 1.20 (m, 3H), 1.17 – 0.99 (m, 1H), 0.84 (t, $J = 7.2$ Hz, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.4, 161.3 (d, $J = 245.9$ Hz), 149.5 (d, $J = 3.0$ Hz), 142.0 (d, $J = 4.9$ Hz), 129.1 (d, $J = 16.6$ Hz), 129.0, 128.8, 128.6, 128.0 (d, $J = 2.5$ Hz), 126.6 (d, $J = 10.9$ Hz), 116.2 (d, $J = 27.5$ Hz), 61.1, 57.7 (d, $J = 3.3$ Hz), 43.8, 31.4, 27.2, 23.1, 14.4, 14.1. ^{19}F NMR (376 MHz, CDCl_3) δ -119.6. HRMS (ESI-MS): calcd. 344.2027 $[\text{M}+\text{H}]^+$ Found: 344.2024.

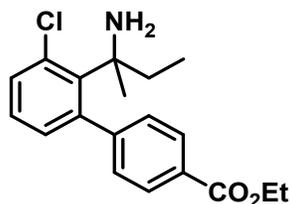


Ethyl 2'-(2-aminooctan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2d): Reaction time 14 h, purified by hexanes:EtOAc (40:60). Product recovered as a colorless oil (32.8 mg, 59% yield). $R_f = 0.28$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) δ 8.01 (t, $J = 6.5$ Hz, 2H), 7.28 (t, $J = 6.5$ Hz, 2H), 7.13 (td, $J = 7.8, 3.9$ Hz, 1H), 7.02 (dd, $J = 12.7, 7.6$ Hz, 1H), 6.74 (d, $J = 7.5$ Hz, 1H), 4.37 (q, $J = 7.1$ Hz, 2H), 2.00 – 1.92 (m, 1H), 1.63 – 1.57 (m, 1H), 1.38 (t, $J = 7.1$ Hz, 3H), 1.32 (s, 4H), 1.22 – 1.18 (m, 7H), 1.13 – 1.11 (m, 1H), 1.05 – 1.02 (m, 1H), 0.82 (t, $J = 6.9$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.4, 161.3 (d, $J = 245.9$ Hz), 149.4, 142.0, 134.0 (d, $J = 11.8$ Hz), 129.1 (d, $J = 16.6$ Hz), 128.9, 128.6, 128.0 (d, $J = 2.5$ Hz), 126.6 (d, $J = 10.9$ Hz), 116.2 (d, $J = 27.4$ Hz), 61.1, 57.7 (d, $J = 3.7$ Hz), 44.0 (d, $J = 5.9$ Hz), 31.9, 31.4 (d, $J = 5.1$ Hz), 29.7, 25.0, 22.7, 14.5, 14.2. ^{19}F NMR (376 MHz, CDCl_3) δ -119.8. HRMS (ESI-MS): calcd. 372.2333 $[\text{M}+\text{H}]^+$ Found: 372.2324.

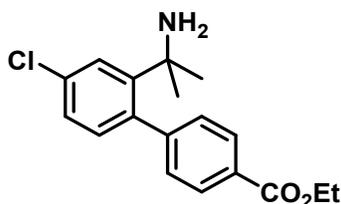


Ethyl 2'-(2-aminobutan-2-yl)-4'-fluoro-[1,1'-biphenyl]-4-carboxylate (2e): Reaction time 14 h, purified by hexanes:EtOAc (60:40). Product recovered as a yellow oil (31.2 mg, 66% yield). $R_f = 0.26$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 8.04 (d, $J = 8.5$ Hz, 2H), 7.38 – 7.32 (m, 3H), 6.96 – 6.88 (m, 2H), 4.40 (q, $J = 7.1$ Hz,

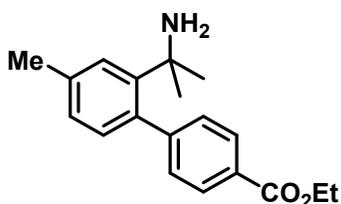
2H), 1.66 – 1.56 (m, 1H), 1.54 – 1.43 (m, 1H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.34 (s, 2H), 1.32 (s, 3H), 0.70 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 162.2 (d, $J = 245.4$ Hz), 148.7, 148.3 (d, $J = 6.1$ Hz), 136.0 (d, $J = 3.0$ Hz), 133.4 (d, $J = 7.8$ Hz), 130.1 – 129.6 (m), 129.3, 129.0, 114.5 (d, $J = 22.8$ Hz), 112.4 (d, $J = 20.9$ Hz), 61.2, 57.1, 37.3, 31.6, 14.5, 9.0. ^{19}F NMR (376 MHz, CDCl_3) δ -119.9. HRMS (ESI-MS): calcd. 316.1713 $[\text{M}+\text{H}]^+$ Found: 316.1702.



Ethyl 2'-(2-aminobutan-2-yl)-3'-chloro-[1,1'-biphenyl]-4-carboxylate (2f): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (30.2 mg, 61% yield). $R_f = 0.32$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 8.05 – 8.01 (m, 2H), 7.42 (dd, $J = 7.9, 1.5$ Hz, 1H), 7.33 – 7.26 (m, 2H), 7.09 (t, $J = 7.7$ Hz, 1H), 6.89 (dd, $J = 7.6, 1.5$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.40 – 2.31 (m, 1H), 1.89 – 1.80 (m, 1H), 1.43 – 1.41 (m, 5H), 0.75 (t, $J = 7.5$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.4, 151.0, 143.7, 143.0, 134.1, 132.2, 131.5, 129.2, 129.1, 128.8, 128.6, 128.3, 126.1, 61.2, 59.6, 34.8, 30.6, 14.5, 9.2. HRMS (ESI-MS): calcd. 332.1411 $[\text{M}+\text{H}]^+$ Found: 332.1418.

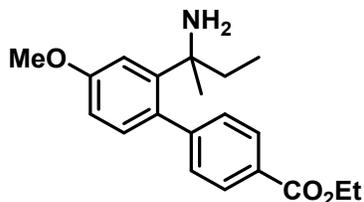


Ethyl 2'-(2-aminopropan-2-yl)-4'-chloro-[1,1'-biphenyl]-4-carboxylate (2g): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (35.7 mg, 75% yield). $R_f = 0.31$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) δ 8.06 (d, $J = 8.4$ Hz, 2H), 7.70 (d, $J = 2.2$ Hz, 1H), 7.36 (d, $J = 8.5$ Hz, 2H), 7.20 (dd, $J = 8.1, 2.2$ Hz, 1H), 6.93 (d, $J = 8.1$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.35 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.4, 149.3, 148.4, 138.5, 133.7, 133.2, 129.9, 129.5, 129.1, 126.7, 125.8, 61.2, 54.1, 33.7, 14.5. HRMS (ESI-MS): calcd. 318.1261 $[\text{M}+\text{H}]^+$ Found: 318.1262.

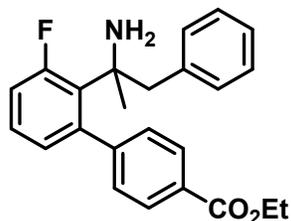


Ethyl 2'-(2-aminopropan-2-yl)-4'-methyl-[1,1'-biphenyl]-4-carboxylate (2h): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (36.5 mg, 82% yield). $R_f = 0.36$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 8.05 (d, $J = 8.3$ Hz, 2H), 7.48 (s, 1H), 7.37 (d, $J = 8.3$ Hz, 2H), 7.04 (d, $J = 7.7$ Hz,

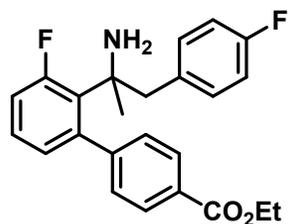
1H), 6.89 (d, $J = 7.6$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 2.40 (s, 3H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.37 (s, 6H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.6, 149.9, 147.1, 137.4, 137.2, 132.0, 130.0, 129.1, 129.0, 127.0, 126.4, 61.1, 54.1, 33.9, 21.5, 14.5. HRMS (ESI-MS): calcd. 298.1807 $[\text{M}+\text{H}]^+$ Found: 298.1803.



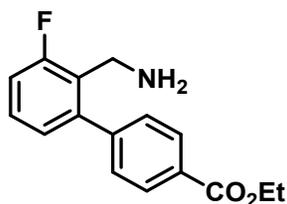
Ethyl 2'-(2-aminobutan-2-yl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (2i): Reaction time 15 h, purified by hexanes:EtOAc (20:80). Product recovered as a yellow oil (37.7 mg, 77% yield). $R_f = 0.18$ (DCM/MeOH = 4.5:0.5). ^1H NMR (400 MHz, CDCl_3) 8.02 (d, $J = 7.5$ Hz, 2H), 7.34 (d, $J = 7.7$ Hz, 2H), 7.17 (s, 1H), 6.91 (d, $J = 8.3$ Hz, 1H), 6.75 (d, $J = 8.3$ Hz, 1H), 4.40 (q, $J = 7.0$ Hz, 2H), 3.84 (s, 3H), 1.67 – 1.59 (m, 1H), 1.56 – 1.50 (m, 1H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.34 (s, 3H), 0.71 (t, $J = 7.3$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.6, 158.9, 149.6, 133.0, 132.7, 130.1, 129.0, 128.9, 113.9, 110.1, 61.1, 55.4, 53.5, 37.1, 31.4, 14.5, 9.0. HRMS (ESI-MS): calcd. 328.1913 $[\text{M}+\text{H}]^+$ Found: 328.1909.



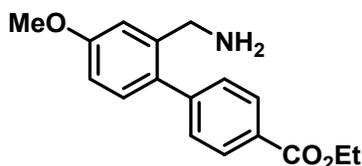
Ethyl 2'-(2-amino-1-phenylpropan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2j): Reaction time 13 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (38.4 mg, 68% yield). $R_f = 0.30$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 7.86 (dd, $J = 8.0, 1.8$ Hz, 1H), 7.65 (dd, $J = 8.0, 1.8$ Hz, 1H), 7.28 – 7.12 (m, 5H), 6.87 (dd, $J = 8.0, 1.7$ Hz, 1H), 6.82 (d, $J = 6.9$ Hz, 2H), 6.61 – 6.59 (m, 1H), 5.80 (dd, $J = 8.0, 1.6$ Hz, 1H), 4.41 – 4.31 (q, $J = 7.6$ Hz, 2H), 3.45 (d, $J = 13.0$ Hz, 1H), 2.83 (d, $J = 13.0$ Hz, 1H), 1.49 (d, $J = 1.4$ Hz, 3H), 1.39 (t, $J = 7.1$ Hz, 3H), 1.15 (br, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.4, 161.1 (d, $J = 245.0$ Hz), 148.9 (d, $J = 3.1$ Hz), 142.4 (d, $J = 4.8$ Hz), 138.2, 132.8 (d, $J = 11.6$ Hz), 130.7, 128.7 (d, $J = 5.0$ Hz), 128.5 (d, $J = 26.2$ Hz), 128.2 (s), 128.0 (d, $J = 2.5$ Hz), 127.9, 126.9 (d, $J = 11.0$ Hz), 126.6, 116.0 (d, $J = 27.2$ Hz), 61.1, 58.5 (d, $J = 4.2$ Hz), 49.2 (d, $J = 5.2$ Hz), 31.2 (d, $J = 6.7$ Hz), 14.4. ^{19}F NMR (376 MHz, CDCl_3), -105.8. HRMS (ESI-MS): calcd. 378.1869 $[\text{M}+\text{H}]^+$ Found: 378.1879.



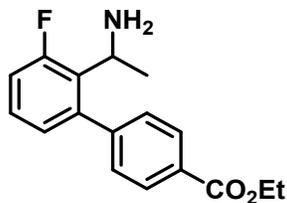
Ethyl 2'-(2-amino-1-(4-fluorophenyl)propan-2-yl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2k): Reaction time 14 h, purified by hexanes:EtOAc (40:60). Product recovered as a colorless oil (42.1 mg, 71% yield). $R_f = 0.34$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 7.89 (dd, $J = 8.0, 1.7$ Hz, 1H), 7.72 (dd, $J = 8.0, 1.7$ Hz, 1H), 7.20 – 7.11 (m, 2H), 6.93 – 6.88 (m, 3H), 6.79 – 6.76 (m, 2H), 6.62 (dd, $J = 6.6, 2.3$ Hz, 1H), 6.00 (dd, $J = 8.0, 1.6$ Hz, 1H), 4.37 (q, $J = 7.4$ Hz, 2H), 3.41 (d, $J = 13.2$ Hz, 1H), 2.80 (d, $J = 13.2$ Hz, 1H), 1.47 (s, 3H), 1.39 (t, $J = 7.1$ Hz, 3H), 1.05 (s, 2H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 161.9 (d, $J = 244.6$ Hz), 161.1 (d, $J = 244.6$ Hz), 148.8 (d, $J = 3.1$ Hz), 142.3 (d, $J = 4.8$ Hz), 133.9 (d, $J = 3.2$ Hz), 132.6 (d, $J = 11.6$ Hz), 132.0 (d, $J = 7.7$ Hz), 128.9, 128.8 (d, $J = 26.4$ Hz), 128.1 (d, $J = 98.1$ Hz), 128.0 (d, $J = 2.5$ Hz), 127.0 (d, $J = 10.9$ Hz), 116.1 (d, $J = 27.1$ Hz), 114.9 (d, $J = 20.9$ Hz), 61.1, 58.4 (d, $J = 3.6$ Hz), 48.3 (d, $J = 5.5$ Hz), 31.1 (d, $J = 6.6$ Hz), 14.4. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -104.9, -116.8. HRMS (ESI-MS): calcd. 396.1770 $[\text{M}+\text{H}]^+$ Found: 396.1787.



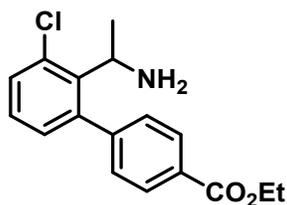
Ethyl 2'-(aminomethyl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2l): Reaction time 14 h, purified by hexanes:EtOAc (30:70). Product recovered as a yellow oil (28.6 mg, 70% yield). $R_f = 0.24$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.11 (d, $J = 7.9$ Hz, 2H), 7.45 (d, $J = 7.9$ Hz, 2H), 7.28 (d, $J = 5.9$ Hz, 1H), 7.12 – 7.04 (m, 1H), 4.41 (q, $J = 6.9$ Hz, 2H), 3.79 (s, 2H), 1.42 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 162.0 (d, $J = 245.5$ Hz), 144.6 (d, $J = 2.6$ Hz), 142.8 (d, $J = 4.6$ Hz), 129.7, 129.7, 129.3, 128.3 (d, $J = 9.4$ Hz), 125.7 (d, $J = 3.0$ Hz), 115.1 (d, $J = 22.8$ Hz), 61.2, 37.7 (d, $J = 4.3$ Hz), 14.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3), -105.8. HRMS (ESI-MS): calcd. 274.1243 $[\text{M}+\text{H}]^+$ Found: 274.1246.



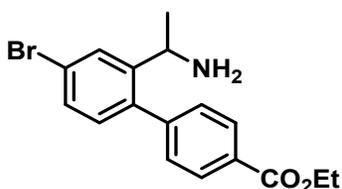
Ethyl 2'-(aminomethyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (2m): Reaction time 13 h, purified by CH_2Cl_2 :MeOH (98:2). Product recovered as a colorless oil (29.1 mg, 68% yield). $R_f = 0.27$ (DCM/MeOH = 4.5:0.5). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.07 (d, $J = 7.9$ Hz, 2H), 7.39 (d, $J = 7.9$ Hz, 2H), 7.16 (d, $J = 8.4$ Hz, 1H), 7.05 (d, $J = 2.4$ Hz, 1H), 6.85 (dd, $J = 8.4, 2.3$ Hz, 1H), 4.40 (q, $J = 6.8$ Hz, 2H), 3.86 (s, 3H), 3.78 (s, 2H), 1.41 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.6, 159.7, 145.8, 141.9, 132.8, 131.2, 129.6, 129.4, 129.0, 113.6, 112.3, 61.1, 55.5, 44.3, 14.5. HRMS (ESI-MS): calcd. 286.1444 $[\text{M}+\text{H}]^+$ Found: 286.1451.



Ethyl 2'-(1-aminoethyl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (2n): Reaction time 15 h, purified by hexanes:EtOAc (30:70). Product recovered as a colorless oil (34.8 mg, 81% yield). $R_f = 0.23$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.13 – 8.06 (m, 2H), 7.35 (d, $J = 6.3$ Hz, 2H), 7.25 – 7.21 (m, 1H), 7.09 – 7.06 (m, 1H), 6.97 (d, $J = 7.6$ Hz, 1H), 4.40 (q, $J = 6.1$ Hz, 2H), 4.00 – 3.97 (m, 1H), 1.71 (s, 2H), 1.47 (d, $J = 6.8$ Hz, 3H), 1.41 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.3, 162.4 (d, $J = 246.2$ Hz), 145.1 (d, $J = 2.4$ Hz), 141.5 (d, $J = 6.0$ Hz), 132.2 (d, $J = 11.7$ Hz), 129.5, 129.4, 129.1, 127.5 (d, $J = 9.9$ Hz), 125.6 (d, $J = 2.8$ Hz), 116.0 (d, $J = 23.0$ Hz), 61.1, 47.1, 23.8 (d, $J = 3.2$ Hz), 14.3. $^{19}\text{F NMR}$ (376 MHz, CDCl_3), -62.8. HRMS (ESI-MS): calcd. 288.1395 $[\text{M}+\text{H}]^+$ Found: 288.1402.

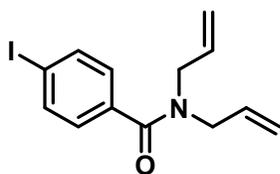


Ethyl 2'-(1-aminoethyl)-3'-chloro-[1,1'-biphenyl]-4-carboxylate (2o): Reaction time 14 h, purified by hexanes:EtOAc (30:70). Product recovered as a yellow oil (38.3 mg, 84% yield). $R_f = 0.25$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.09 (d, $J = 8.6$ Hz, 2H), 7.38 (dd, $J = 8.0, 1.3$ Hz, 1H), 7.35 – 7.30 (m, 1H), 7.19 (t, $J = 7.8$ Hz, 1H), 7.06 (dd, $J = 7.6, 1.3$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 4.21 (d, $J = 6.4$ Hz, 1H), 1.50 (d, $J = 7.0$ Hz, 3H), 1.41 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 146.0, 142.5, 133.6, 131.2, 129.7, 129.6, 129.2, 129.0, 127.3, 61.2, 49.0, 22.4, 14.4. HRMS (ESI-MS): calcd. 304.1105 $[\text{M}+\text{H}]^+$ Found: 304.1105.

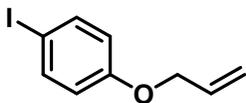


Ethyl 2'-(1-aminoethyl)-4'-bromo-[1,1'-biphenyl]-4-carboxylate (2p): Reaction time 15 h, purified by hexanes:EtOAc (30:70). Product recovered as a colorless oil (41.6 mg, 80% yield). $R_f = 0.31$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.09 (d, $J = 8.4$ Hz, 2H), 7.82 (d, $J = 2.0$ Hz, 1H), 7.42 (dd, $J = 8.1, 2.1$ Hz, 1H), 7.36 – 7.33 (m, 2H), 7.04 (d, $J = 8.2$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 4.16 (q, $J = 6.5$ Hz, 1H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.28 (d, $J = 6.6$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 144.8, 138.6, 131.4, 131.0, 130.0, 129.7, 129.5, 129.3, 129.0, 122.8, 61.2, 47.0, 25.1, 14.4. HRMS (ESI-MS): calcd. 348.0600 $[\text{M}+\text{H}]^+$ Found: 348.0611.

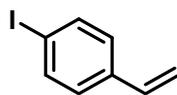
Unsuccessful Halide Substrates:



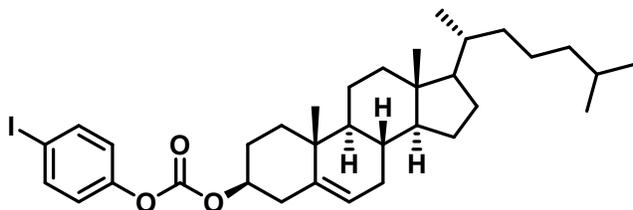
N,N-Diallyl-3-iodobenzamide



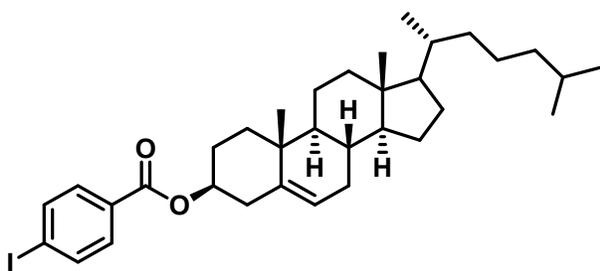
1-(Allyloxy)-4-iodobenzene



4-Iodostyrene



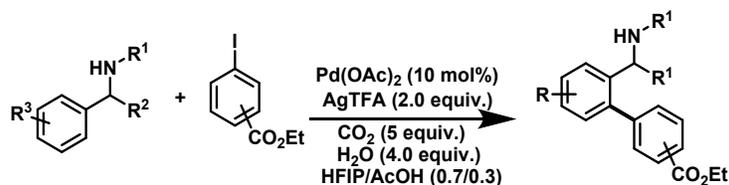
4-Iodophenyl Cholesterol Carbonate



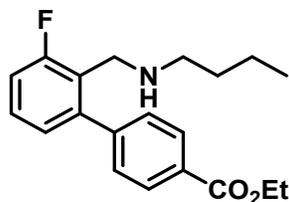
Cholesterol 4-Iodobenzoate

7. Optimization and Synthesis of γ -Arylated 2° Amines

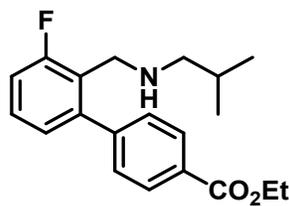
Catalytic C(sp³)-H Arylation of Secondary Amines



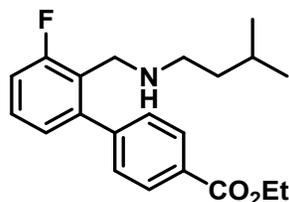
“Standard conditions”: A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.10 equiv), silver trifluoroacetate (66.2 mg, 0.30 mmol, 2.0 equiv), organohalide (0.45 mmol, 3.0 equiv), amine (0.15 mmol, 1.0 equiv), HFIP:acetic acid (0.7:0.3, 1.0 mL), and water (10.8 μ L, 0.6 mmol, 4.0 equiv), followed by the addition of dry ice (~33 mg, 0.75 mmol, 5.0 equiv) as CO₂ source. The vial was sealed with a PTFE lined cap and stirred at room temperature for 15 min. After 15 min of stirring, the reaction mixture was heated in a pie-block at 100 °C under stirring for 12-15 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (2 \times 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The filtrate was concentrated under *vacuo* and further purified by flash column chromatography over silica (DCM/MeOH/ NH₄OH or hexanes/EtOAc) to give the C-H arylation product.



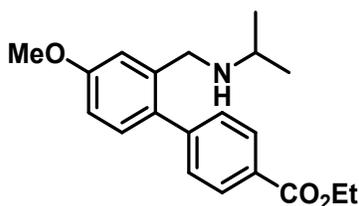
Ethyl 2'-((butylamino)methyl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (3a): Reaction time 13 h, purified by hexanes:EtOAc (55:45). Product recovered as a colorless oil (35.0 mg, 71% yield). R_f = 0.33 (hexanes/EtOAc = 1:1). ¹H NMR (600 MHz, CDCl₃) δ 8.10 (d, J = 8.4 Hz, 2H), 7.52 (d, J = 8.5 Hz, 2H), 7.30 – 7.27 (m, 1H), 7.10 – 7.05 (m, 2H), 4.41 (q, J = 7.1 Hz, 2H), 3.72 (s, 2H), 2.48 (t, J = 7.1 Hz, 1H), 1.42 (t, J = 7.1 Hz, 3H), 1.38 – 1.33 (m, 3H), 1.29 – 1.24 (m, 3H), 0.85 (t, J = 7.3 Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 166.5, 162.0 (d, J = 245.4 Hz), 144.7 (d, J = 2.5 Hz), 143.5 (d, J = 4.4 Hz), 129.7, 129.5, 129.3, 128.5 (d, J = 9.4 Hz), 125.6 (d, J = 2.9 Hz), 125.2 (d, J = 15.7 Hz), 114.9 (d, J = 23.0 Hz), 61.2, 49.1, 44.4 (d, J = 3.8 Hz), 31.9, 20.4, 14.4, 14.0. ¹⁹F NMR (376 MHz, CDCl₃) -119.5. HRMS (ESI-MS): calcd. 330.1864 [M+H]⁺ Found: 330.1876.



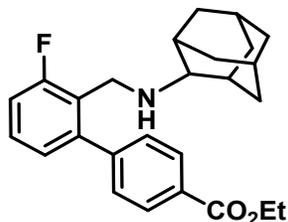
Ethyl 3'-fluoro-2'-((isobutylamino)methyl)-[1,1'-biphenyl]-4-carboxylate (3b): Reaction time 13 h, purified by hexanes:EtOAc (60:40). Product recovered as a colorless oil (33.1 mg, 67% yield). $R_f = 0.31$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.11 – 8.09 (m, 2H), 7.57 – 7.55 (m, 2H), 7.31 – 7.27 (m, 1H), 7.10 – 7.07 (m, 2H), 4.41 (q, $J = 7.1$ Hz, 2H), 3.69 (s, 2H), 2.31 (d, $J = 6.8$ Hz, 2H), 1.67 – 1.60 (m, 1H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.36 (br, 1H), 0.84 (d, $J = 6.7$ Hz, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 162.0 (d, $J = 245.1$ Hz), 144.8 (d, $J = 2.5$ Hz), 143.5 (d, $J = 4.5$ Hz), 129.6, 129.5, 129.4, 128.4 (d, $J = 9.4$ Hz), 125.7 (d, $J = 2.7$ Hz), 125.6, 114.92 (d, $J = 23.1$ Hz), 61.2, 57.7, 44.7 (d, $J = 3.9$ Hz), 28.2, 20.7, 14.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -119.3. HRMS (ESI-MS): calcd. 330.1869 $[\text{M}+\text{H}]^+$ Found: 330.1878.



Ethyl 3'-fluoro-2'-((isopentylamino)methyl)-[1,1'-biphenyl]-4-carboxylate (3c): Reaction time 14 h, purified by hexanes:EtOAc (60:40). Product recovered as a colorless oil (36.5 mg, 71% yield). $R_f = 0.34$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.11 – 8.09 (m, 2H), 7.54 – 7.52 (m, 2H), 7.30 – 7.27 (m, 1H), 7.10 – 7.06 (m, 2H), 4.41 (q, $J = 7.1$ Hz, 2H), 3.70 (s, 2H), 2.50 – 2.48 (m, 2H), 1.58 – 1.51 (m, 1H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.28 – 1.25 (m, 3H), 0.83 (d, $J = 6.6$ Hz, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 162.0 (d, $J = 245.2$ Hz), 144.8 (d, $J = 2.6$ Hz), 143.5 (d, $J = 4.5$ Hz), 129.7, 129.5, 129.4, 128.4 (d, $J = 9.4$ Hz), 125.6 (d, $J = 2.7$ Hz), 125.5, 114.9 (d, $J = 23.1$ Hz), 61.2, 47.6, 44.6 (d, $J = 3.9$ Hz), 39.0, 26.0, 22.7, 14.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -120.1. HRMS (ESI-MS): calcd. 344.2020 $[\text{M}+\text{H}]^+$ Found: 344.2028.

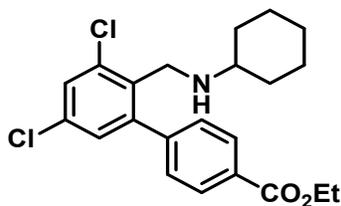


Ethyl 2'-((isopropylamino)methyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3d): Reaction time 15 h, purified by hexanes:EtOAc (20:80). Product recovered as a colorless oil (25.1 mg, 51% yield). $R_f = 0.21$ (DCM/MeOH = 4.5:0.5). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.07 (d, $J = 8.3$ Hz, 2H), 7.46 (d, $J = 8.3$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 1H), 7.03 (d, $J = 2.4$ Hz, 1H), 6.86 (dd, $J = 8.4, 2.6$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 3.86 (s, 1H), 3.69 (s, 1H), 2.68 – 2.62 (m, 1H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.25 (s, 1H), 0.94 (d, $J = 6.2$ Hz, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.7, 159.5, 145.9, 133.4, 131.1, 130.1, 129.5, 129.4, 129.0, 114.9, 112.6, 61.1, 55.5, 48.3, 29.8, 24.1, 22.8, 14.5. HRMS (HRMS-MS): calcd. 328.1913 $[\text{M}+\text{H}]^+$ Found: 328.1919.

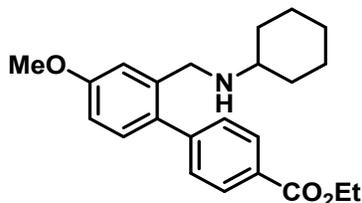


Ethyl 2'-((((1R,3S,5r,7r)-adamantan-2-yl)methyl)amino)methyl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (3e):

Reaction time 14 h, purified by hexanes:EtOAc (80:20). Product recovered as a colorless oil (34.8 mg, 57% yield). $R_f = 0.51$ (hexanes/EtOAc = 4:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.09 (d, $J = 8.2$ Hz, 2H), 7.60 (d, $J = 8.2$ Hz, 2H), 7.35 – 7.28 (m, 1H), 7.09 (t, $J = 8.8$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 3.70 (s, 2H), 2.68 (s, 1H), 1.91 (d, $J = 12.4$ Hz, 2H), 1.85 – 1.71 (m, 6H), 1.70 – 1.59 (m, 5H), 1.42 (dt, $J = 16.9, 8.4$ Hz, 5H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.6, 162.1 (d, $J = 245.3$ Hz), 144.7, 143.5 (d, $J = 4.4$ Hz), 129.7, 129.5, 129.5, 129.5, 128.5 (d, $J = 12.2$ Hz), 125.7, 115.0 (d, $J = 23.0$ Hz), 62.4, 61.2, 52.3, 42.5 (d, $J = 2.9$ Hz), 39.4, 37.9, 37.5, 32.1, 31.4, 29.8, 27.8, 27.7, 14.53 (s). $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -118.3. LRMS (ESI): calcd. 408.5 $[\text{M}+\text{H}]^+$ Found: 408.8.

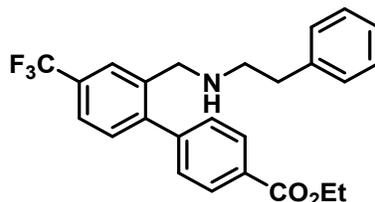


Ethyl 3',5'-dichloro-2'-((cyclohexylamino)methyl)-[1,1'-biphenyl]-4-carboxylate (3f): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (43.8 mg, 72% yield). $R_f = 0.26$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.11 – 8.09 (m, 2H), 7.60 – 7.57 (m, 2H), 7.42 (d, $J = 2.2$ Hz, 1H), 7.19 (d, $J = 2.2$ Hz, 1H), 4.42 (q, $J = 7.1$ Hz, 2H), 3.71 (s, 2H), 2.32 – 2.28 (m, 1H), 1.67 (t, $J = 13.2$ Hz, 5H), 1.43 (t, $J = 7.1$ Hz, 3H), 1.16 (dd, $J = 19.0, 9.9$ Hz, 3H), 1.07 – 0.99 (m, 2H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.4, 144.7, 144.0, 136.2, 130.1, 129.5, 129.4, 129.0, 128.8, 61.3, 56.8, 45.6, 33.4, 26.1, 25.0, 14.5. HRMS (ESI-MS): calcd. 406.1341 $[\text{M}+\text{H}]^+$ Found: 406.1349.

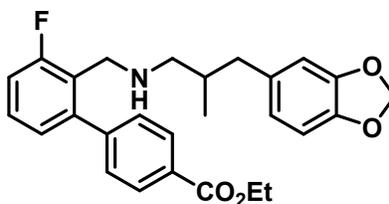


Ethyl 2'-((cyclohexylamino)methyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (3g): Reaction time 14 h, purified by hexanes:EtOAc (30:70). Product recovered as a colorless oil (46.2 mg, 84% yield). $R_f = 0.24$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.07 (d, $J = 8.3$ Hz, 2H), 7.45 (d, $J = 8.3$ Hz, 2H), 7.17 (d, $J = 8.4$ Hz, 1H), 7.06 (d, $J = 2.2$ Hz, 1H), 6.86 (dd, $J = 8.4, 2.7$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 3.86 (s, 3H), 3.73 (s, 2H), 2.36 – 2.24 (m, 1H), 1.71 – 1.63 (m, 5H), 1.42 (t, $J = 7.1$ Hz, 3H), 1.20 – 0.9 (m, 5H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.7, 159.5,

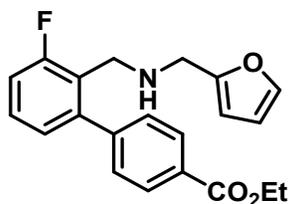
145.9, 133.4, 131.1, 129.5, 129.4, 128.9, 114.8, 112.6, 61.1, 56.4, 55.5, 48.6, 33.3, 26.1, 25.0, 14.5. LRMS (ESI-MS): calcd. 368.4 [M+H]⁺ Found: 368.4.



Ethyl 2'-((phenethylamino)methyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate (3h): Reaction time 13 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (36.5 mg, 57% yield). $R_f = 0.33$ (hexanes/EtOAc = 1:1). ¹H NMR (400 MHz, CDCl₃) δ 8.05 (d, $J = 8.3$ Hz, 2H), 7.75 (s, 1H), 7.56 (d, $J = 7.9$ Hz, 1H), 7.33 (d, $J = 8.1$ Hz, 2H), 7.30 (d, $J = 5.1$ Hz, 1H), 7.26 (d, $J = 7.3$ Hz, 2H), 7.21 (dd, $J = 8.2, 6.3$ Hz, 1H), 7.11 (d, $J = 6.9$ Hz, 2H), 4.42 (q, $J = 7.1$ Hz, 2H), 3.71 (s, 2H), 2.75 (dd, $J = 12.0, 5.2$ Hz, 4H), 1.43 (brt, $J = 7.1$ Hz, 5H). ¹³C NMR (151 MHz, CDCl₃) δ 166.4, 144.5, 144.3, 139.8, 138.7, 130.3, 130.2 (d, $J = 33.2$ Hz), 129.9, 129.7, 128.9, 128.7, 128.6, 126.3, 126.0 (q, $J = 3.6$ Hz), 124.2 (d, $J = 273.3$ Hz), 123.8 (q, $J = 3.6$ Hz), 61.2, 51.1, 50.5, 36.3, 14.5. ¹⁹F NMR (376 MHz, CDCl₃) δ -63.2. HRMS (ESI-MS): calcd. 428.1838 [M+H]⁺ Found: 428.1833.

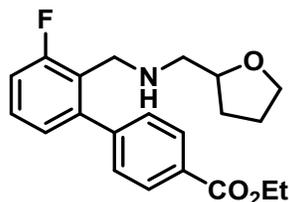


Ethyl 2'-(((3-(benzo[d][1,3]dioxol-5-yl)-2-methylpropyl)amino)methyl)-3'-fluoro-[1,1'-biphenyl]-4-carboxylate (3i): Reaction time 15 h, purified by hexanes:EtOAc (60:40). Product recovered as a colorless oil (44.5 mg, 66% yield). $R_f = 0.23$ (hexanes/EtOAc = 1:1). ¹H NMR (600 MHz, CDCl₃) δ 8.12 (d, $J = 8.2$ Hz, 2H), 7.56 (d, $J = 8.3$ Hz, 2H), 7.34 – 7.30 (m, 1H), 7.13 – 7.09 (m, 2H), 6.72 (d, $J = 7.9$ Hz, 1H), 6.61 (s, 1H), 6.55 (d, $J = 9.2$ Hz, 1H), 5.94 (s, 2H), 4.44 (q, $J = 7.1$ Hz, 2H), 3.75 – 3.66 (m, 2H), 2.60 (dd, $J = 13.5, 5.9$ Hz, 1H), 2.45 (dd, $J = 11.6, 6.0$ Hz, 1H), 2.34 (dd, $J = 11.6, 6.9$ Hz, 1H), 2.26 (dd, $J = 13.5, 8.2$ Hz, 1H), 1.80 – 1.75 (m, 1H), 1.45 (t, $J = 7.1$ Hz, 3H), 1.28 (s, 2H), 0.83 (d, $J = 6.7$ Hz, 3H). ¹³C NMR (151 MHz, CDCl₃) δ 166.5, 162.0 (d, $J = 245.3$ Hz), 147.5 (s), 145.6, 144.8 (d, $J = 2.4$ Hz), 143.6 (d, $J = 4.5$ Hz), 134.8, 129.7, 129.6, 129.4, 128.5 (d, $J = 9.3$ Hz), 125.7 (d, $J = 2.8$ Hz), 122.0, 114.9 (d, $J = 23.1$ Hz), 109.5, 108.0, 100.8, 61.2, 55.4, 44.7, 41.0, 35.4, 17.9, 14.5. ¹⁹F NMR (376 MHz, CDCl₃) -118.1. HRMS (ESI-MS): calcd. 450.2081 [M+H]⁺ Found: 450.2093.

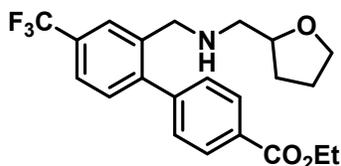


Ethyl 3'-fluoro-2'-(((furan-2-ylmethyl)amino)methyl)-[1,1'-biphenyl]-4-carboxylate (3j): Reaction time 14 h, purified by hexanes:EtOAc (45:55). Product recovered as a colorless oil (22.7 mg, 43% yield). $R_f = 0.32$ (hexanes/EtOAc = 1:1). ¹H NMR (600 MHz, CDCl₃) δ 8.03 (d, $J = 8.5$ Hz, 2H), 7.69 (d, $J = 8.4$ Hz, 2H), 7.51 (d, $J =$

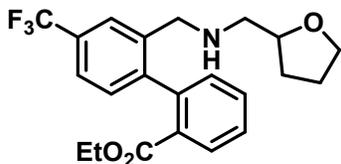
8.3 Hz, 1H), 7.39 (t, $J = 7.0$ Hz, 1H), 7.11 (t, $J = 7.5$ Hz, 1H), 7.08 – 7.01 (m, 1H), 6.71 (d, $J = 3.3$ Hz, 1H), 6.36 (d, $J = 3.3$ Hz, 1H), 4.38 (q, $J = 7.1$ Hz, 2H), 3.96 – 3.81 (m, 4H), 1.40 (t, $J = 7.1$ Hz, 4H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 161.3 (d, $J = 245.9$ Hz), 152.5, 139.0, 137.0, 134.7, 130.7 (d, $J = 4.6$ Hz), 130.1, 129.2 (d, $J = 8.2$ Hz), 128.8, 125.5, 124.3 (d, $J = 3.6$ Hz), 123.3, 115.5 (d, $J = 21.7$ Hz), 110.2, 108.0, 61.0, 46.2 (d, $J = 2.9$ Hz), 45.3, 14.4. ^{19}F NMR (376 MHz, CDCl_3) -119.3. HRMS (ESI-MS): calcd. 354.1506 $[\text{M}+\text{H}]^+$ Found: 354.1518.



Ethyl 3'-fluoro-2'-((((tetrahydrofuran-2-yl)methyl)amino)methyl)-[1,1'-biphenyl]-4-carboxylate (3k): Reaction time 15 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (34.2 mg, 64% yield). $R_f = 0.35$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) 8.12 – 8.05 (m, 2H), 7.57 – 7.50 (m, 2H), 7.31 – 7.24 (m, 1H), 7.07 (dd, $J = 16.9, 8.5$ Hz, 2H), 4.40 (q, $J = 7.1$ Hz, 2H), 3.91 – 3.85 (m, 1H), 3.80 – 3.74 (m, 1H), 3.73 (dd, $J = 4.7, 1.4$ Hz, 2H), 3.70 – 3.66 (m, 1H), 2.55 (qd, $J = 11.9, 5.7$ Hz, 2H), 1.93 – 1.86 (m, 2H), 1.82 (dt, $J = 12.5, 6.1$ Hz, 2H), 1.53 – 1.45 (m, 1H), 1.41 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 162.0 (d, $J = 245.6$ Hz), 144.7 (d, $J = 2.6$ Hz), 143.6 (d, $J = 4.4$ Hz), 129.6, 129.5, 129.4, 128.4 (d, $J = 9.4$ Hz), 125.6 (d, $J = 3.0$ Hz), 125.3 (d, $J = 15.8$ Hz), 114.9 (d, $J = 23.1$ Hz), 78.2, 67.9, 61.1, 53.6, 44.6 (d, $J = 3.8$ Hz), 29.3, 25.8, 14.4. ^{19}F NMR (376 MHz, CDCl_3) -118.1. HRMS (ESI-MS): calcd. 358.1818 $[\text{M}+\text{H}]^+$ Found: 358.1827.

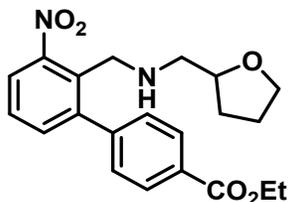


Ethyl 2'-((((tetrahydrofuran-2-yl)methyl)amino)methyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxylate (3l): Reaction time 13 h, purified by hexanes:EtOAc (50:50). Product recovered as a colorless oil (52.5 mg, 86% yield). $R_f = 0.31$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.2$ Hz, 2H), 7.83 (s, 1H), 7.55 (d, $J = 7.9$ Hz, 1H), 7.44 (d, $J = 8.2$ Hz, 2H), 7.33 (d, $J = 7.9$ Hz, 1H), 4.40 (q, $J = 7.1$ Hz, 2H), 3.94 – 3.92 (m, 1H), 3.80 – 3.67 (m, 4H), 2.61 – 2.57 (m, 1H), 2.54 – 2.49 (m, 1H), 1.93 – 1.80 (m, 3H), 1.68 (s, 1H), 1.54 – 1.47 (m, 1H), 1.41 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (101 MHz, CDCl_3) δ 166.4, 144.5, 144.2, 138.8, 130.2, 130.1 (d, $J = 32.3$ Hz), 129.8, 129.6, 129.0, 125.8 (q, $J = 3.7$ Hz), 124.2 (d, $J = 273.7$ Hz), 123.7 (q, $J = 3.7$ Hz), 78.1, 68.0, 61.2, 53.8, 51.1, 29.2, 25.8, 14.4. ^{19}F NMR (376 MHz, CDCl_3) δ -62.9. LRMS (ESI-MS): calcd. 408.4 $[\text{M}+\text{H}]^+$ Found: 408.2.

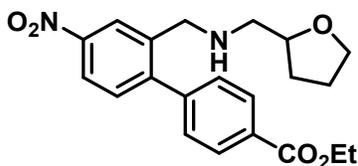


Ethyl 2'-((((tetrahydrofuran-2-yl)methyl)amino)methyl)-4'-(trifluoromethyl)-[1,1'-biphenyl]-2-carboxylate (3m): Reaction time 14 h, purified by hexanes:EtOAc (50:50). Product recovered as a yellow oil (53.8 mg, 88% yield).

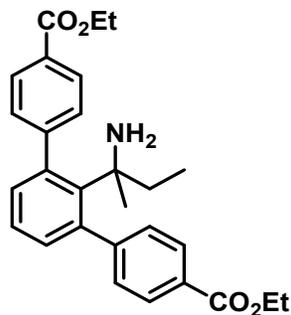
$R_f = 0.32$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.02 (dd, $J = 7.7, 1.1$ Hz, 1H), 7.81 (s, 1H), 7.54 (td, $J = 7.5, 1.4$ Hz, 1H), 7.50 – 7.44 (m, 2H), 7.21 (d, $J = 7.6$ Hz, 1H), 7.18 (dd, $J = 8.0, 2.7$ Hz, 1H), 4.07 – 3.98 (m, 2H), 3.91 – 3.85 (m, 1H), 3.78 – 3.72 (m, 1H), 3.70 – 3.64 (m, 1H), 3.58 – 3.56 (m, 2H), 2.54 – 2.44 (m, 2H), 1.90 – 1.78 (m, 3H), 1.51 – 1.42 (m, 2H), 0.94 (td, $J = 7.1, 1.4$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.0, 145.1 (d, $J = 2.6$ Hz), 140.7, 138.9 (d, $J = 6.2$ Hz), 131.7 (d, $J = 2.1$ Hz), 130.5 (d, $J = 1.6$ Hz), 130.5 (d, $J = 2.7$ Hz), 130.4 (d, $J = 9.2$ Hz), 129.6 (dd, $J = 32.2, 1.7$ Hz), 129.2, 127.9, 124.8 – 124.7 (m), 124.4 (d, $J = 816.9$ Hz), 124.4 (d, $J = 279$ Hz), 123.0 – 122.9 (m), 78.2 (d, $J = 2.5$ Hz), 67.9, 60.9, 53.8, 51.1, 29.2 (d, $J = 6.2$ Hz), 25.8 (d, $J = 3.8$ Hz), 13.6. $^{19}\text{F NMR}$ (376 Hz, CDCl_3), -62.5. HRMS (ESI-MS): calcd. 407.1787 $[\text{M}+\text{H}]^+$ Found: 407.1790.



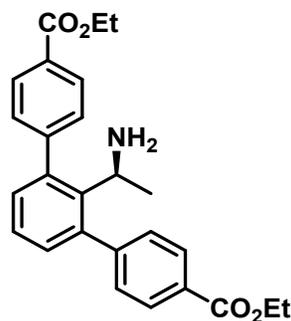
Ethyl 3'-nitro-2'-((tetrahydrofuran-2-yl)methyl)amino)methyl-[1,1'-biphenyl]-4-carboxylate (3n): Reaction time 15 h, purified by hexanes:EtOAc (25:75). Product recovered as a colorless oil (28.8 mg, 52% yield). $R_f = 0.24$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) 8.13 – 8.09 (m, 2H), 7.78 (dd, $J = 7.8, 1.6$ Hz, 1H), 7.58 – 7.54 (m, 2H), 7.47 (dd, $J = 7.7, 1.6$ Hz, 1H), 7.44 (t, $J = 7.8$ Hz, 1H), 4.42 (q, $J = 7.1$ Hz, 2H), 3.88 – 3.84 (m, 1H), 3.70 – 3.77 (m, 1H), 3.73 (s, 2H), 3.70 – 3.66 (m, 1H), 2.51 (qd, $J = 11.8, 5.5$ Hz, 2H), 1.93 – 1.86 (m, 1H), 1.85 – 1.80 (m, 2H), 1.55 – 1.51 (m, 1H), 1.42 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.4, 151.7, 144.1, 144.0, 134.0, 132.4, 130.1, 129.7, 129.5, 127.8, 123.9, 78.2, 68.1, 61.3, 53.8, 47.3, 29.2, 25.9, 14.5. HRMS (ESI-MS): calcd. 385.1757 $[\text{M}+\text{H}]^+$ Found: 385.1757.



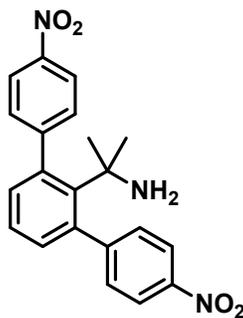
Ethyl 4'-nitro-2'-((tetrahydrofuran-2-yl)methyl)amino)methyl-[1,1'-biphenyl]-4-carboxylate (3o): Reaction time 15 h, purified by hexanes:EtOAc (30:70). Product recovered as a colorless oil (34.6 mg, 60% yield). $R_f = 0.23$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.47 (d, $J = 2.3$ Hz, 1H), 8.15 (dd, $J = 8.4, 2.4$ Hz, 1H), 8.12 (d, $J = 8.4$ Hz, 2H), 7.45 (d, $J = 8.4$ Hz, 2H), 7.39 (d, $J = 8.4$ Hz, 1H), 4.42 (q, $J = 7.1$ Hz, 2H), 3.97 – 3.93 (m, 1H), 3.81 – 3.78 (m, 1H), 3.76 (s, 2H), 3.73 – 3.69 (m, 1H), 2.62 (dd, $J = 11.9, 3.7$ Hz, 1H), 2.54 (dd, $J = 11.9, 7.5$ Hz, 1H), 1.95 – 1.90 (m, 1H), 1.88 – 1.83 (m, 2H), 1.68 (s, 1H), 1.56 – 1.50 (m, 1H), 1.42 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.3, 147.7, 147.2, 143.7, 140.1, 130.8, 130.3, 129.7, 128.9, 124.0, 121.9, 78.1, 68.1, 61.3, 53.8, 50.9, 29.2, 25.9, 14.4. HRMS (ESI-MS): calcd. 385.1757 $[\text{M}+\text{H}]^+$ Found: 385.1750.



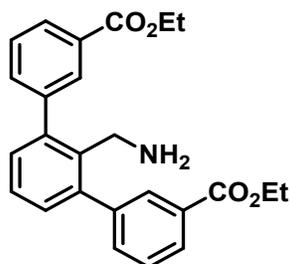
Diethyl 2'-(2-aminobutan-2-yl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4a): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 15 h, purified by hexanes:EtOAc (65:35). Product recovered as a yellow oil (45.4 mg, 68% yield). $R_f = 0.41$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) 8.06 (d, $J = 8.4$ Hz, 1H), 7.43 (t, $J = 8.8$ Hz, 1H), 7.18 (t, $J = 7.5$ Hz, 1H), 7.02 (d, $J = 7.5$ Hz, 1H), 4.41 (q, $J = 7.2$ Hz, 1H), 1.61 (dt, $J = 14.2, 7.3$ Hz, 1H), 1.42 (t, $J = 7.1$ Hz, 2H), 1.21 (s, 1H), 0.63 (t, $J = 7.4$ Hz, 1H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.5, 151.4, 144.8, 142.0, 132.5, 129.3, 129.1, 128.8, 124.5, 61.1, 59.2, 37.7, 33.5, 14.5, 8.8. HRMS (ESI-MS): calcd. 446.2332 $[\text{M}+\text{H}]^+$ Found: 446.2324.



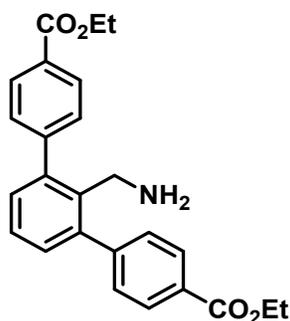
Diethyl (S)-2'-(1-aminoethyl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4b): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (60:40). Product recovered as a yellow oil (43.8 mg, 70% yield). $R_f = 0.42$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) 8.10 (d, $J = 8.2$ Hz, 4H), 7.46 (d, $J = 8.2$ Hz, 4H), 7.29 – 7.26 (m, 1H), 7.14 (d, $J = 7.6$ Hz, 2H), 4.41 (q, $J = 7.1$ Hz, 4H), 4.12 (q, $J = 7.0$ Hz, 1H), 1.42 (t, $J = 7.1$ Hz, 6H), 1.10 (d, $J = 7.0$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 147.5, 141.2, 130.7, 129.8, 129.4, 129.3, 125.7, 61.2, 53.5, 25.6, 14.5. HRMS (ESI-MS): calcd. 418.2019 $[\text{M}+\text{H}]^+$ Found: 418.2019.0 $[\alpha]_D^{21} = -7.33^\circ$ (c 0.003, EtOH). $ee > 96\%$ (Mosher Amide Method).



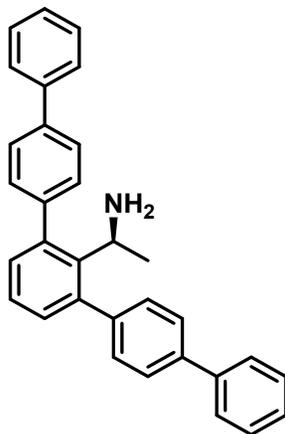
2-(4,4''-Dinitro-[1,1':3',1''-terphenyl]-2'-yl)propan-2-amine (4c): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (60:40). Product recovered as a yellow solid (26.6 mg, 47% yield). $R_f = 0.32$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) 8.29 (d, $J = 8.7$ Hz, 4H), 7.64 – 7.43 (m, 4H), 7.29 (t, $J = 3.9$ Hz, 1H), 7.08 (d, $J = 7.6$ Hz, 2H), 1.28 (s, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 153.4, 146.7, 145.6, 140.9, 132.5, 130.1, 125.1, 123.2, 55.9, 36.1. LRMS (ESI-MS): calcd. 378.1 $[\text{M}+\text{H}]^+$ Found: 378.5.



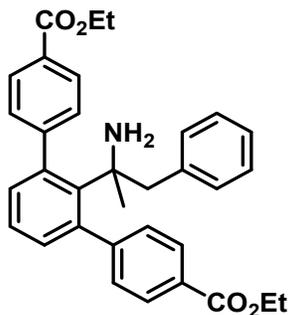
Diethyl 2'-(aminomethyl)-[1,1':3',1''-terphenyl]-3,3''-dicarboxylate (4d): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (65:35). Product recovered as a colorless oil (36.8 mg, 61% yield). $R_f = 0.36$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) 8.11 (s, 2H), 8.07 (d, $J = 8.5$ Hz, 2H), 7.63 (d, $J = 7.5$ Hz, 2H), 7.52 (t, $J = 7.7$ Hz, 2H), 7.39 – 7.34 (m, 1H), 7.28 (s, 2H), 4.39 (q, $J = 7.1$ Hz, 4H), 3.67 (s, 2H), 1.40 (t, $J = 7.1$ Hz, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 141.8, 141.8, 133.7, 130.7, 130.3, 130.2, 128.5, 128.5, 126.8, 61.2, 40.6, 14.4. LRMS (ESI-MS): calcd. 404.1 $[\text{M}+\text{H}]^+$ Found: 404.9.



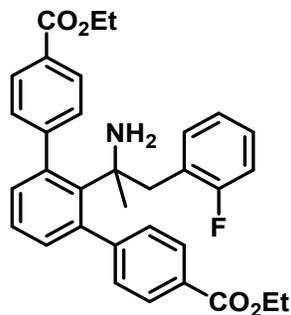
Diethyl 2'-(aminomethyl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4e): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (65:35). Product recovered as a colorless oil (43.5 mg, 72% yield). $R_f = 0.37$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) 8.12 (d, $J = 8.3$ Hz, 4H), 7.50 (d, $J = 8.3$ Hz, 4H), 7.38 (t, $J = 7.6$ Hz, 1H), 7.27 (d, $J = 7.6$ Hz, 2H), 4.41 (q, $J = 7.1$ Hz, 4H), 3.69 (s, 2H), 1.42 (t, $J = 7.1$ Hz, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 146.1, 141.9, 137.2, 130.0, 129.7, 129.6, 129.3, 127.0, 61.2, 40.4, 14.4. LRMS (ESI-MS): calcd. 404.1 $[\text{M}+\text{H}]^+$ Found: 404.5.



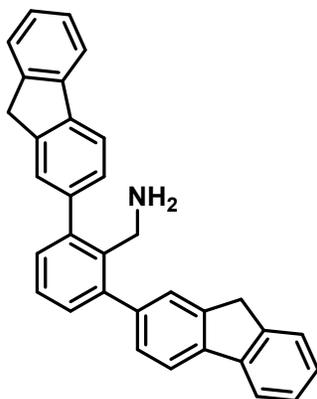
(S)-1-((1,1':4',1'':3'',1''':4''',1''''-Quinquephenyl]-2''-yl)ethan-1-amine (4f): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (70:30). Product recovered as a white solid (51.6 mg, 81% yield). $R_f = 0.45$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) 7.70 – 7.64 (m, 9H), 7.48 (t, $J = 7.7$ Hz, 9H), 7.41 – 7.36 (m, 2H), 7.30 (dd, $J = 8.4, 6.6$ Hz, 1H), 7.24 – 7.20 (m, 2H), 4.30 (q, $J = 7.0$ Hz, 1H), 1.24 (d, $J = 7.0$ Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 142.7, 141.8, 141.6, 140.7, 140.0, 130.8, 130.2, 128.9, 127.5, 127.2, 126.7, 125.549.2, 25.7. HRMS (ESI-MS): calcd. 426.2222 $[\text{M}+\text{H}]^+$ Found: 426.2229. $[\alpha]_D^{21} = -7.7^\circ$ (c 0.0013, EtOH). $ee >96\%$ (Mosher Amide Method).



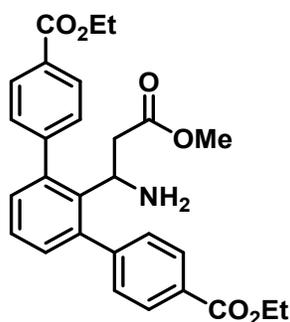
Diethyl 2'-(2-amino-1-phenylpropan-2-yl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4g): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (60:40). Product recovered as a light yellow oil (53.9 mg, 71% yield). $R_f = 0.39$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.03 (dd, $J = 8.0, 1.5$ Hz, 2H), 7.99 (dd, $J = 8.0, 1.4$ Hz, 2H), 7.36 (dd, $J = 7.9, 1.2$ Hz, 2H), 7.24 – 7.16 (m, 4H), 7.08 (d, $J = 6.9$ Hz, 2H), 7.00 (d, $J = 7.5$ Hz, 2H), 6.76 (d, $J = 6.9$ Hz, 2H), 4.41 (q, $J = 7.1$ Hz, 4H), 3.18 (d, $J = 13.3$ Hz, 1H), 2.90 (d, $J = 13.3$ Hz, 1H), 1.43 (t, $J = 7.1$ Hz, 6H), 1.04 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 151.3, 143.9, 141.7, 137.7, 132.5, 130.7, 129.5, 129.4, 128.9, 128.9, 128.2, 126.6, 124.7, 61.2, 59.5, 51.7, 33.1, 14.5. LRMS (ESI-MS): calcd. 530.2 $[\text{M}+\text{Na}]^+$ Found: 530.9.



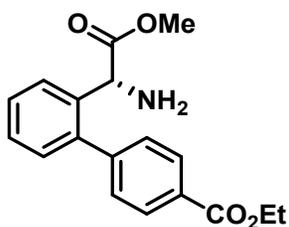
Diethyl 2'-(2-amino-1-(2-fluorophenyl)propan-2-yl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4h): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 14 h, purified by hexanes:EtOAc (60:40). Product recovered as a colorless oil (48.8 mg, 62% yield). $R_f = 0.38$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.07 – 8.02 (m, 4H), 7.40 (d, $J = 7.9$ Hz, 2H), 7.27 (d, $J = 8.0$ Hz, 2H), 7.21 (t, $J = 7.5$ Hz, 1H), 7.17 (dd, $J = 14.3, 6.5$ Hz, 1H), 7.03 (d, $J = 7.5$ Hz, 2H), 6.94 (dt, $J = 13.5, 7.9$ Hz, 2H), 6.73 (td, $J = 7.4, 1.4$ Hz, 1H), 4.42 (q, $J = 7.1$ Hz, 4H), 3.20 (d, $J = 13.5$ Hz, 1H), 3.09 (d, $J = 13.5$ Hz, 1H), 1.43 (t, $J = 7.1$ Hz, 6H), 0.99 (s, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 166.5, 161.7 (d, $J = 245.5$ Hz), 151.1, 144.2, 141.8, 132.8 (d, $J = 4.7$ Hz), 132.5, 129.5 (d, $J = 7.7$ Hz), 129.0, 128.9, 128.5 – 128.2 (m), 124.8, 124.6 (d, $J = 15.7$ Hz), 123.7 (d, $J = 3.3$ Hz), 115.4 (d, $J = 23.1$ Hz), 61.1, 59.6, 44.8, 32.4, 14.5. $^{19}\text{F NMR}$ (376 MHz, CDCl_3) -105.5. LRMS (ESI-MS): calcd. 526.2 $[\text{M}+\text{Na}]^+$ Found: 526.9.



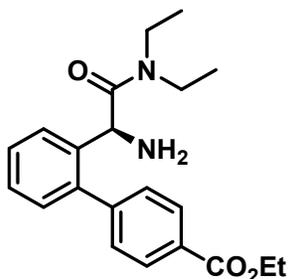
Diethyl 2'-(2-amino-1-phenylpropan-2-yl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4i): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 13 h, purified by hexanes:EtOAc (70:30). Product recovered as a yellow solid (43.0 mg, 66% yield). $R_f = 0.44$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) 7.86 (d, $J = 7.8$ Hz, 2H), 7.83 (d, $J = 7.5$ Hz, 2H), 7.62 (s, 2H), 7.58 (d, $J = 7.5$ Hz, 2H), 7.45 (d, $J = 7.8$ Hz, 2H), 7.41 (t, $J = 7.4$ Hz, 2H), 7.37 – 7.32 (m, 5H), 3.97 (s, 4H), 3.84 (s, 2H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 143.3, 142.9, 141.4, 140.8, 140.4, 138.8, 129.9, 128.0, 126.9, 126.9, 126.5, 126.0, 125.2, 120.0, 119.7, 40.9, 37.1. HRMS (ESI-MS): calcd. 436.2066 $[\text{M}-\text{NH}_2]$ Found: 436.2079.



Diethyl 2'-(1-amino-3-methoxy-3-oxopropyl)-[1,1':3',1''-terphenyl]-4,4''-dicarboxylate (4j): Procedure modified by using 6 equivalents of aryl halide instead of 3. Reaction time 15 h, purified by hexanes:EtOAc (60:40). Product recovered as a yellow oil (48.4 mg, 68% yield). $R_f = 0.29$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.11 (d, $J = 8.2$ Hz, 4H), 7.48 (d, $J = 8.2$ Hz, 4H), 7.31 (t, $J = 7.6$ Hz, 1H), 7.16 (d, $J = 7.6$ Hz, 2H), 4.47 – 4.45 (m, 1H), 4.41 (q, $J = 7.1$ Hz, 4H), 3.48 (s, 3H), 2.39 (dd, $J = 16.0, 4.5$ Hz, 1H), 2.28 – 2.16 (m, 1H), 1.54 (br, 2H), 1.42 (t, $J = 7.1$ Hz, 6H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 171.9, 166.5, 147.0, 141.7, 138.8, 130.8, 129.8, 129.6, 129.4, 126.4, 61.2, 51.6, 50.1, 42.9, 14.5. HRMS (ESI-MS): calcd. 476.2067 $[\text{M}+\text{H}]^+$ Found: 476.2056.

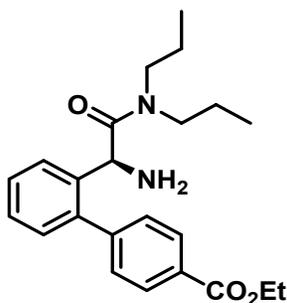


Ethyl (R)-2'-(1-amino-2-methoxy-2-oxoethyl)-[1,1'-biphenyl]-4-carboxylate (5a): Reaction time 13 h, purified by hexanes:EtOAc (20:80). Product recovered as a colorless oil (32.4 mg, 69% yield). $R_f = 0.22$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.11 (d, $J = 8.1$ Hz, 2H), 7.53 (d, $J = 8.2$ Hz, 2H), 7.41 – 7.34 (m, 3H), 7.28 (d, $J = 7.5$ Hz, 1H), 4.66 (s, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 3.66 (s, 3H), 1.85 (s, 2H), 1.41 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C NMR}$ (151 MHz, CDCl_3) δ 175.1, 166.5, 145.3, 140.9, 130.3, 129.7, 129.6, 128.8, 128.0, 126.5, 61.1, 54.9, 14.5. HRMS (ESI-MS): calcd. 315.1472 $[\text{M}+\text{H}]^+$ Found: 315.1442. $[\alpha]_D^{21} = -41.9^\circ$ (c 0.002, EtOH). $ee = 15\%$ (Mosher Amide Method).

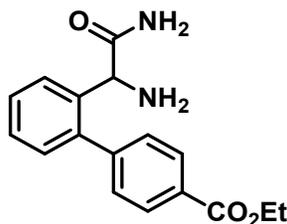


Ethyl (S)-2'-(1-amino-2-(diethylamino)-2-oxoethyl)-[1,1'-biphenyl]-4-carboxylate (5b): Reaction time 15 h, purified by hexanes:EtOAc (20:80). Product recovered as a colorless oil (34.5 mg, 65% yield). $R_f = 0.19$ (hexanes/EtOAc = 1:1). $^1\text{H NMR}$ (600 MHz, CDCl_3) δ 8.17 (d, $J = 8.5$ Hz, 2H), 7.64 (d, $J = 7.9$ Hz, 2H), 7.43 – 7.37

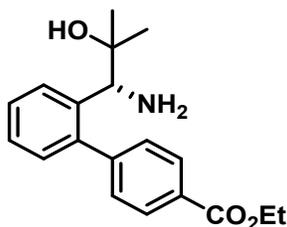
(m, 3H), 7.35 – 7.33 (m, 1H), 4.52 (s, 1H), 4.48 – 4.39 (m, 2H), 3.38 – 3.30 (m, 1H), 3.29 – 3.23 (m, 1H), 2.77 – 2.71 (m, 1H), 2.68 – 2.62 (m, 1H), 1.95 (br, 2H), 1.45 (t, $J = 7.4$ Hz, 3H), 1.04 (t, $J = 7.1$ Hz, 3H), 0.50 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 172.7, 166.5, 145.1, 140.1, 139.0, 130.3, 129.7, 129.5, 129.2, 128.0, 126.8, 61.2, 53.4, 40.7, 40.6, 14.5, 13.1, 12.7. LRMS (ESI-MS): calcd. 355.2 $[\text{M}+\text{H}]^+$ Found: 355.5. $[\alpha]_D^{21} = +26.2^\circ$ (c 0.0024, EtOH). $ee = 50\%$ (Mosher Amide Method).



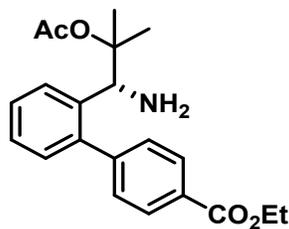
Ethyl (S)-2'-(1-amino-2-(dipropylamino)-2-oxoethyl)-[1,1'-biphenyl]-4-carboxylate (5c): Reaction time 13 h, purified by hexanes:EtOAc (20:80). Product recovered as a colorless oil (32.7 mg, 57% yield). $R_f = 0.19$ (hexanes/EtOAc = 1:1). ^1H NMR (600 MHz, CDCl_3) δ 8.15 (d, $J = 8.6$ Hz, 2H), 7.68 (d, $J = 7.2$ Hz, 2H), 7.41 (dd, $J = 6.3, 2.8$ Hz, 1H), 7.39 – 7.35 (m, 2H), 7.33 (dd, $J = 6.2, 2.9$ Hz, 1H), 4.52 (s, 1H), 4.44 – 4.38 (m, 2H), 3.48 – 3.40 (m, 1H), 2.98 – 2.94 (m, 1H), 2.64 – 2.58 (m, 1H), 2.50 – 2.44 (m, 1H), 1.48 – 1.38 (m, 5H), 1.06 – 1.02 (m, 1H), 1.00 – 0.95 (m, 1H), 0.80 (t, $J = 7.4$ Hz, 3H), 0.40 (t, $J = 7.4$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 173.2, 166.5, 145.0, 140.0, 138.9, 130.4, 129.7, 129.7, 129.1, 128.1, 126.8, 61.2, 53.4, 48.1, 47.8, 21.5, 20.6, 14.5, 11.4, 10.8. LRMS (ESI-MS): calcd. 383.2 $[\text{M}+\text{H}]^+$ Found: 384.1. $[\alpha]_D^{21} = +47.7^\circ$ (c 0.0013, EtOH). $ee = 60\%$ (Mosher Amide Method).



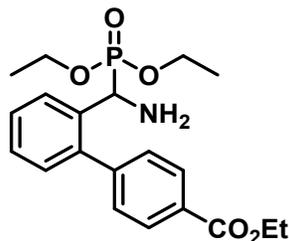
Ethyl 2'-(1,2-diamino-2-oxoethyl)-[1,1'-biphenyl]-4-carboxylate (5d): Reaction time 15 h, purified by CH_2Cl_2 :MeOH (95:5). Product recovered as a colorless oil (18.3 mg, 41% yield). $R_f = 0.11$ (hexanes/EtOAc = 1:1). ^1H NMR (400 MHz, CDCl_3) δ 8.06 (d, $J = 7.6$ Hz, 1H), 7.54 (d, $J = 7.4$ Hz, 2H), 7.34 (s, 1H), 7.30 (s, 1H), 4.69 (s, 1H), 4.38 (dd, $J = 14.1, 7.1$ Hz, 1H), 1.40 (t, $J = 7.1$ Hz, 2H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 166.4, 144.9, 141.1, 130.3, 129.8, 129.8, 129.7, 129.1, 128.8, 128.5, 127.0, 126.9, 61.2, 55.0, 14.4. LRMS (ESI-MS): calcd. 299.1 $[\text{M}+\text{H}]^+$ Found: 299.2.



Ethyl (R)-2'-(1-amino-2-hydroxy-2-methylpropyl)-[1,1'-biphenyl]-4-carboxylate (5e): Reaction time 14 h, purified by EtOAc. Product recovered as a colorless oil (28.6 mg, 61% yield). $R_f = 0.21$ (DCM/MeOH = 4.5:0.5). ^1H NMR (600 MHz, CDCl_3) δ 8.11 (d, $J = 8.3$ Hz, 2H), 7.77 (d, $J = 7.9$ Hz, 1H), 7.43 – 7.39 (m, 3H), 7.35 (td, $J = 7.5, 1.0$ Hz, 1H), 7.21 (dd, $J = 7.6, 1.0$ Hz, 1H), 4.43 (q, $J = 7.1$ Hz, 2H), 4.06 (s, 1H), 1.44 (t, $J = 7.1$ Hz, 3H), 1.00 (s, 3H), 0.91 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 146.6, 141.4, 129.9, 129.6, 129.3, 128.2, 127.4, 127.3, 72.6, 61.2, 58.3, 28.4, 25.5, 14.5. HRMS (ESI-MS): calcd. 314.1750 $[\text{M}+\text{H}]^+$ Found: 314.1745. $[\alpha]_D^{21} = +29.2^\circ$ (c 0.0013, EtOH). $ee = 88\%$ (Mosher Amide Method).



Ethyl (R)-2'-(2-acetoxy-1-amino-2-methylpropyl)-[1,1'-biphenyl]-4-carboxylate (5f): Reaction time 15 h, purified by EtOAc. Product recovered as a colorless oil (25.0 mg, 47% yield). $R_f = 0.22$ (DCM/MeOH = 4.5:0.5). ^1H NMR (600 MHz, CDCl_3) δ 8.12 (d, $J = 8.6$ Hz, 2H), 7.42 – 7.39 (m, 2H), 7.36 – 7.32 (m, 2H), 7.20 (dd, $J = 7.5, 0.9$ Hz, 2H), 5.15 (s, 1H), 4.43 (q, $J = 7.1$ Hz, 2H), 2.08 (d, $J = 1.3$ Hz, 3H), 1.44 (t, $J = 7.1$ Hz, 3H), 0.93 (s, 3H), 0.85 (s, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 164.9, 146.2, 140.5, 136.5, 129.7, 129.6, 128.2, 128.0, 127.8, 127.3, 127.1, 86.9, 73.9, 61.2, 28.9, 24.6, 14.5, 14.4. LRMS (ESI-MS): calcd. 355.2 $[\text{M}+\text{H}]^+$ Found: 355.5. $[\alpha]_D^{21} = +35.1^\circ$ (c 0.002, EtOH). $ee = 86\%$ (Mosher Amide Method).

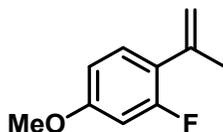


Ethyl 2'-(amino(diethoxyphosphoryl)methyl)-[1,1'-biphenyl]-4-carboxylate (5g): Reaction time 14 h, purified by hexanes:toluene:EtOAc (10:10:80). Product recovered as a colorless oil (30.4 mg, 52% yield). $R_f = 0.22$ (DCM/MeOH = 4.5:0.5). ^1H NMR (400 MHz, CDCl_3) δ 8.10 (d, $J = 8.4$ Hz, 2H), 7.82 (d, $J = 7.9$ Hz, 2H), 7.47 (d, $J = 8.1$ Hz, 1H), 7.42 (d, $J = 11.6$ Hz, 1H), 7.35 (t, $J = 5.8$ Hz, 1H), 7.23 (d, $J = 7.7$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 4.29 (d, $J = 17.0$ Hz, 1H), 4.10 – 4.02 (m, 1H), 3.98 – 3.92 (m, 1H), 3.85 – 3.78 (m, 1H), 1.78 (s, 2H), 1.41 (t, $J = 7.1$ Hz, 3H), 1.28 (t, $J = 7.1$ Hz, 3H), 1.10 (t, $J = 7.1$ Hz, 3H). ^{13}C NMR (151 MHz, CDCl_3) δ 166.5, 145.4, 141.1 (d, $J = 9.5$ Hz), 135.9, 130.1, 129.6, 129.6, 128.7 (d, $J = 1.7$ Hz), 128.5 (d, $J = 2.4$ Hz), 128.2 (d, $J = 4.3$ Hz), 127.8 (d, $J = 2.3$ Hz), 62.9, 62.6, 61.1, 31.0, 16.5, 16.3, 14.5. LRMS (ESI-MS): calcd. 414.0 $[\text{M}+\text{Na}]^+$ Found: 414.0

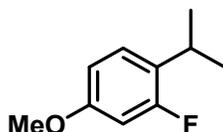
General Procedure for Preparation of Mosher Amides to Determine ee of Chiral Amines

Amine (1 equiv.) and potassium carbonate (2 equiv.) were combined in a 2 dram reaction vial under N₂. Anhydrous MeCN (1 mL) was added, followed by addition of (S)-(+)- α -Methoxy- α -(trifluoromethyl)phenylacetyl chloride (1.3 equiv.). The reaction were stirred at RT for 16 h. The reaction mixtures were then treated with sat. NaHCO_{3(aq)} (6 mL), and stirred for 30 min. Afterwards, the reaction were diluted with additional water and extracted with dichloromethane (3 x 5 mL), followed by drying over MgSO₄ and evaporating *in vacuo*. The ¹H NMR spectrum was acquired in CDCl₃, and the relative integration of fully resolved diastereomer peaks used to ascertain the level of *ee*.¹⁶

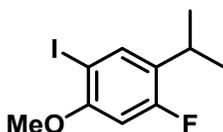
8. Application Experiments



2-Fluoro-4-methoxy-1-(prop-1-en-2-yl)benzene (S-43): Potassium *tert*-Butoxide (1.40 g, 12.5 mmol) and methyltriphenylphosphonium bromide (4.14 g, 11.6 mmol) were combined in a 50 mL round bottom flask with a stir bar, followed by placing under an N₂ atmosphere. Anhydrous toluene (20 mL) was added, and the reaction was purged and backfilled with nitrogen over three additional cycles, followed by stirring at room temperature for 30 minutes. 2-Fluoro-4-methoxyacetophenone (1.50 g, 8.92 mmol) was then added, and the reaction was allowed to stir for an additional 4h at room temperature. The reaction was then evaporated *in vacuo*, and the resulting residue was triturated in hexanes (50 mL), followed by filtering through a short silica plug, and evaporation *in vacuo* to give the product as a colorless oil (1.31 g, 88% yield) that matched data in the literature.¹⁷ $R_f = 0.76$ (Hex/Et₂O = 4:1). ¹H NMR (400 MHz, CDCl₃) δ 7.31 – 7.17 (m, 1H), 6.71 – 6.61 (m, 2H), 5.25 (d, $J = 0.8$ Hz, 1H), 5.20 (d, $J = 1.1$ Hz, 1H), 3.81 (s, 3H), 2.16 (s, 3H). ¹⁹F NMR (376 MHz, CDCl₃) δ -110.2 (dd, $J = 12.1, 8.9$ Hz). HRMS (ESI-MS): calcd. 167.0867 [M+H]⁺ Found: 167.0864.

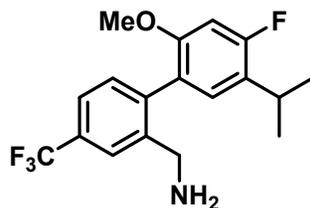


2-Fluoro-1-isopropyl-4-methoxybenzene (S-44): 2-Fluoro-4-methoxy-1-(prop-1-en-2-yl)benzene (3.69 g, 22.2 mmol) was added to 95% ethanol (60 mL), followed by addition of ammonium formate (7.00 g, 111.0 mmol). Pd/C (10 wt%, 400 mg) was then added, and the reaction was heated under reflux for 8 h. Afterwards the reaction was cooled, followed by filtration. The solution was diluted with 0.1 M KOH_(aq) (100 mL), followed by extraction with dichloromethane (4 x 25 mL). The combined organic fractions were dried over MgSO₄, then evaporated *in vacuo* to give the desired product as a colorless oil (3.22 g, 86% yield) that matched the literature data.¹⁸ $R_f = 0.76$ (Hex/Et₂O = 4:1). ¹H NMR (400 MHz, CDCl₃) δ 7.14 (t, $J = 8.7$ Hz, 1H), 6.66 (dd, $J = 8.5, 2.5$ Hz, 1H), 6.59 (dd, $J = 12.2, 2.6$ Hz, 1H), 3.78 (s, 3H), 3.17 (sep, $J = 6.9$ Hz, 1H), 1.24 (d, $J = 6.9$ Hz, 6). ¹³C NMR (101 MHz, CDCl₃) δ 161.1 (d, $J = 244.5$ Hz), 158.9 (d, $J = 11.1$ Hz), 127.5 (d, $J = 7.2$ Hz), 127.3 (d, $J = 15.2$ Hz), 109.6 (d, $J = 3.0$ Hz), 101.6 (d, $J = 26.6$ Hz), 55.4, 26.8 (d, $J = 1.8$ Hz), 22.9. ¹⁹F NMR (376 MHz, CDCl₃) δ -115.7 (dd, $J = 12.1, 8.9$ Hz). HRMS (ESI-MS): calcd. 169.1023 [M+H]⁺ Found: 169.1024.



1-Fluoro-4-iodo-2-isopropyl-5-methoxybenzene (S-45): 2-Fluoro-1-isopropyl-4-methoxybenzene (445 mg, 2.65 mmol) was dissolved in MeOH (10 mL), followed by simultaneous addition of silver sulfate (826 mg, 2.65 mmol) and iodine (673 mg, 2.65 mmol). The reaction was stirred in the dark for 8 h, at which point in time the residual solid was filtered. The reaction was then evaporated *in vacuo*. The residue was treated with NaS₂O_{3(aq)}, followed by extracting with dichloromethane (3 x 15 mL), drying over MgSO₄, and finally evaporating *in vacuo* to give the desired

product as a light yellow-orange oil (689 mg, 88%) that matched the literature data.¹⁷ $R_f = 0.65$ (Hex/Et₂O = 4:1). ¹H NMR (400 MHz, CDCl₃) δ 7.59 (d, $J = 8.3$ Hz, 1H), 6.53 (d, $J = 12.0$ Hz, 1H), 3.83 (s, 3H), 3.11 (sep, $J = 6.9$ Hz, 1H), 1.22 (d, $J = 6.9$ Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 161.3 (d, $J = 246.0$ Hz), 157.0 (d, $J = 10.1$ Hz), 137.1 (d, $J = 6.8$ Hz), 129.3 (d, $J = 15.9$ Hz), 99.6 (d, $J = 28.3$ Hz), 78.9 (d, $J = 3.5$ Hz), 56.6, 26.7, 22.8. ¹⁹F NMR (376 MHz, CDCl₃) δ -114.6 (dd, $J = 11.9, 8.4$ Hz). HRMS (ESI-MS): calcd. 294.9990 [M+H]⁺ Found: 294.9703.

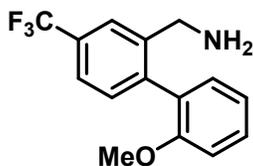


(4'-Fluoro-5'-isopropyl-2'-methoxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)methanamine (6): A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.10 equiv), silver triflate (77.1 mg, 0.30 mmol, 2.0 equiv), organohalide (132.3 mg, 0.45 mmol, 3.0 equiv), amine (26.1 mg, 0.15 mmol, 1.0 equiv), HFIP (1.0 mL), and water (10.8 μ L, 0.6 mmol, 4.0 equiv), followed by the addition of dry ice (~33 mg, 0.75 mmol, 5.0 equiv) as CO₂ source. The vial was sealed with a PTFE lined cap and stirred at room temperature for 15 min. After 15 min of stirring, the reaction mixture was heated in a pie-block at 100 °C under stirring for 14 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (2 \times 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The organic layer was concentrated *in vacuo* and further purified by flash column chromatography over silica (DCM/MeOH/ NH₄OH, 96/3/1) to give the C–H arylation product (21.5 mg, 42% yield) as light-yellow oil. $R_f = 0.37$ (5 % MeOH/DCM). ¹H NMR (600 MHz, CDCl₃) δ 7.79 (s, 1H), 7.57 (d, $J = 9.1$ Hz, 1H), 7.30 (d, $J = 7.9$ Hz, 1H), 7.00 (d, $J = 8.6$ Hz, 1H), 6.69 (d, $J = 12.1$ Hz, 1H), 3.77 – 3.68 (m, 5H), 3.27 – 3.20 (m, 1H), 1.78 (br, 2H), 1.26 (brs, 7H). ¹³C NMR (151 MHz, CDCl₃) δ 160.9 (d, $J = 246.0$ Hz), 155.2 (d, $J = 10.0$ Hz), 142.7, 140.9, 131.1, 130.1 (q, $J = 32.2$ Hz), 129.0 (d, $J = 7.2$ Hz), 127.2 (d, $J = 15.3$ Hz), 125.3, 124.3 (q, $J = 3.6$ Hz), 124.1 (d, $J = 3.5$ Hz), 123.5 (dd, $J = 8.0, 4.2$ Hz), 99.3 (d, $J = 27.6$ Hz), 56.2 – 56.1 (m), 43.9 (s), 26.76 (s), 22.9. HRMS (ESI-MS): calcd. 342.1476 [M+H]⁺ Found: 342.1469.



(2'-Fluoro-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)methanamine (S-46): A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.10 equiv), silver triflate (77.1 mg, 0.30 mmol, 2.0 equiv), organohalide (99.9 mg, 0.45 mmol, 3.0 equiv), amine (26.1 mg, 0.15 mmol, 1.0 equiv), HFIP (1.0 mL), and water (10.8 μ L, 0.6 mmol, 4.0 equiv), followed by the addition of dry ice (~33 mg, 0.75 mmol, 5.0 equiv) as CO₂ source. The vial was sealed with a PTFE lined cap and stirred at room temperature for 15 min. After 15 min of stirring, the reaction mixture was heated

in a pie-block at 100 °C under stirring for 14 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (2 × 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The organic layer was concentrated *in vacuo* and further purified by flash column chromatography over silica (DCM/MeOH (99/1)) to give the C–H arylation product (19.8 mg, 17% yield) as light-yellow oil. $R_f = 0.28$ (1 % MeOH/DCM). ¹H NMR (600 MHz, CDCl₃) δ 7.83 (s, 1H), 7.57 (d, $J = 7.9$ Hz, 1H), 7.44 – 7.39 (m, 1H), 7.34 (d, $J = 7.9$ Hz, 1H), 7.25 – 7.23 (m, 1H), 7.17 (t, $J = 9.0$ Hz, 1H) 3.78 (s, 2H), 1.59 (br s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 159.5 (d, $J = 245.9$ Hz), 142.7, 138.3, 131.3 (d, $J = 2.9$ Hz), 131.0, 130.8 (q, $J = 32.4$ Hz), 130.2 (d, $J = 8.0$ Hz), 127.3 (d, $J = 16.7$ Hz), 124.7 (q, $J = 3.6$ Hz), 124.5 (d, $J = 3.5$ Hz), 124.3 (q, $J = 272.2$ Hz), 123.6 (q, $J = 3.5$ Hz), 115.9 (d, $J = 22.2$ Hz), 43.8. LRMS (EI-MS): calcd. 269.1 [M]⁺ Found: 269.1.



(2'-Methoxy-4-(trifluoromethyl)-[1,1'-biphenyl]-2-yl)methanamine (S-47): A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.10 equiv), silver triflate (77.1 mg, 0.30 mmol, 2.0 equiv), organohalide (105.3 mg, 0.45 mmol, 3.0 equiv), amine (26.1 mg, 0.15 mmol, 1.0 equiv), HFIP (1.0 mL), and water (10.8 μL, 0.6 mmol, 4.0 equiv), followed by the addition of dry ice (~33 mg, 0.75 mmol, 5.0 equiv) as CO₂ source. The vial was sealed with a PTFE lined cap and stirred at room temperature for 15 min. After 15 min of stirring, the reaction mixture was heated in a pie-block at 100 °C under stirring for 14 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (2 × 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The organic layer was concentrated *in vacuo* and further purified by flash column chromatography over silica (DCM/MeOH, 99/1) to give the C–H arylation product (32.6 mg, 26% yield) as light-yellow oil. $R_f = 0.23$ (1 % MeOH/DCM). ¹H NMR (600 MHz, CDCl₃) δ 7.76 (s, 1H), 7.54 (d, $J = 7.1$ Hz, 1H), 7.39 (td, $J = 8.3, 1.8$ Hz, 1H), 7.29 (d, $J = 7.9$ Hz, 1H), 7.13 (dd, $J = 7.4, 1.7$ Hz, 1H), 7.04 (td, $J = 7.4, 0.8$ Hz, 1H), 6.98 (d, $J = 8.2$ Hz, 1H), 3.76 (s, 3H), 3.70 (d, $J = 11.3$ Hz, 2H), 1.56 (br s, 2H). ¹³C NMR (151 MHz, CDCl₃) δ 156.4, 142.9, 141.4, 130.9, 130.0 (q, $J = 32.2$ Hz), 129.6, 128.8, 124.5 (q, $J = 272.1$ Hz), 124.3 (q, $J = 3.7$ Hz), 123.5 (q, $J = 8.5$ Hz), 120.9, 110.9, 55.6, 44.1. LRMS (EI-MS): calcd. 281.1 [M]⁺ Found: 281.1.

9. Scale-Up Experiments

a. Performing Reaction in a Sealed Tube

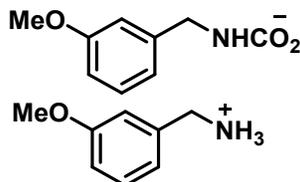
A 40 mL sealed tube (Ace Glassware) was charged with Pd(OAc)₂ (336 mg, 1.5 mmol, 0.10 equiv), silver trifluoroacetate (6.62 g, 30.0 mmol, 2.0 equiv), ethyl 4-iodobenzoate (45.0 mmol, 3.0 equiv), 2-fluorobenzylamine (15.0 mmol, 1.0 equiv), HFIP:acetic acid (0.7:0.3, 15.0 mL), and water (1.10 mL), followed by the addition of dry ice (~3.3 g, 75.0 mmol, 5.0 equiv) as CO₂ source. The tube was sealed and stirred at room temperature for 15 min. After 15 min of stirring, the reaction mixture was heated in an oil bath at 100 °C under stirring for 12 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (3 x 16.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (4 x 20 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The organic layer was concentrated *in vacuo* and further purified by flash column chromatography over silica (DCM/MeOH/NH₄OH or hexanes/EtOAc) to give the C–H arylation product **21** (2.94 g, 71%).

b. Performing Reaction Using Schlenk Line

A 50 mL round bottom flask was charged with Pd(OAc)₂ (336 mg, 1.5 mmol, 0.10 equiv), silver trifluoroacetate (6.62 g, 30.0 mmol, 2.0 equiv), ethyl 4-iodobenzoate (45.0 mmol, 3.0 equiv), 2-fluorobenzylamine (15.0 mmol, 1.0 equiv), HFIP:acetic acid (0.7:0.3, 15.0 mL), and water (1.10 mL), followed by attachment of a reflux condenser and placing the system under a CO₂ atmosphere. The reaction mixture was stirred at room temperature for 15 min, followed by heating in an oil bath at 100 °C under stirring for 12 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (3 x 16.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution up to pH=8, followed by extraction with dichloromethane (4 x 20 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The organic layer was concentrated *in vacuo* and further purified by flash column chromatography over silica (DCM/MeOH/ NH₄OH or hexanes/EtOAc) to give the C–H arylation product **21** (1.21 g, 30%).

10. Mechanism Experiments

a. Substoichiometric CO₂ Experiments:



Synthesis of *m*-methoxy benzylamine carbamate salt (7): A 20 mL tube was charged with *m*-methoxy benzylamine (500 mg, 3.6 mmol) and carbon dioxide as CO₂ source. After stirring at room temperature for 5.0 min, a white solid had formed. Excess free amine and CO₂ were removed *in vacuo* to give the *m*-methoxy benzylamine carbamate product as a white solid (620 mg, 94% yield). ¹H NMR (600 MHz, DMSO-*d*₆) δ 7.22 (s, 1H), 6.93 (d, *J* = 30.6 Hz, 1H), 6.87 – 6.73 (m, 1H), 4.12 (s, 1H), 3.74 (s, 4H). ¹³C NMR (151 MHz, DMSO) δ 159.3, 158.4, 129.2, 119.4, 119.1, 112.7, 112.5, 112.0, 111.8, 54.9, 45.1, 43.8. IR (ATR): 3317, 2837, 1609, 1596, 1485, 1460, 1431, 1374, 1281, 1268, 1251 cm⁻¹.

Synthesis of Ethyl 2'-(aminomethyl)-4'-methoxy-[1,1'-biphenyl]-4-carboxylate (2m) using 7: A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.10 equiv), silver trifluoroacetate (66.2 mg, 2.0 equiv), ethyl-4-iodobenzoate (120 mg, 3.0 equiv), HFIP:acetic acid (1.0 mL, 7:3), and water (11.1 μL, 4.0 equiv). The ammonium carbamate **7** (47.7 mg, 1.0 equiv) was added to the vial, which was *immediately* sealed with a PTFE lined cap and stirred at room temperature for 15 min. After 15 min of stirring, the reaction vial was heated in a pre-heated pie-block at 100 °C under stirring for 13 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution, followed by extraction with dichloromethane (2 × 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The filtrate was concentrated *in vacuo* to give the C–H arylation product **1a** (24.3 mg) in 57% yield as a yellow oil.

b. Performing Reactions in Deuterated AcOD

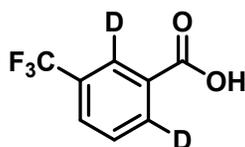
Reaction in Trifluoroacetic acid-*d*: A 7.5 mL vial was charged with Pd(OAc)₂ (1.68 mg, 0.0075 mmol, 0.05 equiv), silver acetate (50.1 mg, 0.3 mmol, 2.0 equiv), and TFA-*d* (1.0 mL). *o*-fluorobenzylamine (18.8 mg, 0.15 mmol, 1.0 equiv) was added to the vial, which was *immediately* sealed with a PTFE lined cap and the reaction vial was heated in a pre-heated pie-block at 130 °C under stirring for 2.5 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution, followed by extraction with dichloromethane (2 × 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The filtrate was concentrated *in*

vacuo to give *o*-fluorobenzylamine in 98% yield. ¹H NMR analysis suggested no appreciable incorporation of deuterium.

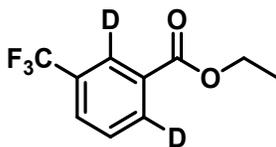
Reaction in Acetic acid-*d*: A 7.5 mL vial was charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.1 equiv), silver trifluoroacetate (66.2 mg, 0.3 mmol, 2.0 equiv), and AcOD (1.0 mL). *o*-fluorobenzylamine (18.8 mg, 0.15 mmol, 1.0 equiv) was added to the vial, followed by dry ice (~ 33 mg). The vial was then *immediately* sealed with a PTFE lined cap and the reaction was heated in a pre-heated pie-block at 100 °C under stirring for 12 h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution, followed by extraction with dichloromethane (2 × 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. The filtrate was concentrated *in vacuo* to give *o*-fluorobenzylamine in 96% yield. ¹H NMR analysis suggested no appreciable incorporation of deuterium.

c. Kinetic Isotope Experiments

Part 1: Synthesis of Deuterated Substrate

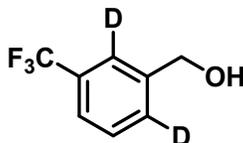


3-(Trifluoromethyl)benzoic-2,6-*d*₂ Acid (S-48): 3-(Trifluoromethyl)benzoic Acid (3.80 g, 20.0 mmol), anhydrous sodium acetate (1.66 g, 40.4 mmol), and [Rh(cp*)(MeCN)₃](SbF₆)₂ (16.6 mg, 0.02 mmol) were combined in a 40 mL vial with a PTFE lined cap that had been previously blanketed with N₂. Freshly procured D₂O (30 mL, 135.0 mmol) was added, followed by sealing and heating at 90 °C. After 16 h the reaction was cooled, followed by diluting with ~100 mL of 1.2 HCl_(aq), then extracting with dichloromethane (6 x 25 mL). The organic layer was dried over Na₂SO₄, followed by evaporating *in vacuo*, giving the desired product as a tan solid (3.31 g, 86%), with 97% deuteration observed at C6, and 67% deuteration observed at C2. *R_f* = 0.17 (Hex/EA = 1:1). ¹H NMR (400 MHz, CDCl₃) δ 8.39 (s, 0.33H), 8.31 (d, *J* = 7.4 Hz, 0.03H), 7.89 (d, *J* = 7.8 Hz, 1H), 7.64 (d, *J* = 7.8 Hz, 1H). HRMS (ESI-MS): calcd. 191.0294 [M-H]⁻ Found: 191.0368 (for monodeuteration, calcd. 190.0232 [M-H]⁻ Found: 190.0227).

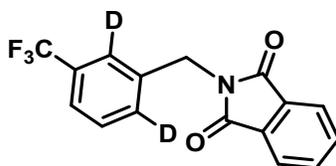


Ethyl 3-(Trifluoromethyl)benzoate-2,6-*d*₂ (S-49): 3-(Trifluoromethyl)benzoic-2,6-*d*₂ Acid (3.30 g, 17.2 mmol) was added to anhydrous ethanol (70 mL), followed by dropwise addition of acetyl chloride (613 μL, 5.60 mmol), followed by heating the reaction under reflux under N₂. The reaction was cooled after 18h, followed by evaporation of volatiles *in vacuo*. The residue was treated with 1M KOH_(aq) (75 mL), followed by extraction with dichloromethane (4 x 20 mL). The combined organic phase was dried over MgSO₄, followed by evaporation *in vacuo* to give the product as an

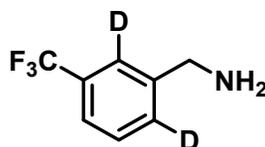
orange oil (3.23 g, 85%), with 97% deuteration observed at C6, and 67% deuteration observed at C2. $R_f = 0.61$ (Hex/Et₂O = 4:1). ¹H NMR (400 MHz, CDCl₃) δ 8.30 (s, 0.33H), 8.22 (d, $J = 7.8$ Hz, 0.03 H), 7.79 (d, $J = 7.8$ Hz, 1H), 7.57 (d, $J = 7.8$ Hz, 1H), 4.41 (q, $J = 7.1$ Hz, 2H), 1.41 (t, $J = 7.1$ Hz, 3H). LRMS (EI-MS): calcd. 220.18 [M]⁺ Found: 220.4.



(3-(Trifluoromethyl)phenyl-2,6-d₂)methanol (S-50): Ethyl 3-(Trifluoromethyl)benzoate-2,6-d₂ (3.10 g, 14.1 mmol) was placed under N₂, followed by addition of anhydrous tetrahydrofuran (75 mL). The reaction mixture was cooled to 0 °C, followed by portionwise addition of lithium aluminum hydride (321 mg, 8.46 mmol) over 10 min. The reaction was stirred at 0 °C for 2 h, followed by slowly warming to RT over 1 h. The Reaction was then recooled to 0 °C, followed by carefully quenching with saturated NH₄Cl_(aq) (~10 mL), followed by diluting with additional deionized water, then extracting the reaction mixture with diethyl ether (4 x 20 mL). The combined organic phase was washed with saturated brine solution (3 x 50 mL), followed by drying over MgSO₄, then evaporating *in vacuo* to a colorless oil (2.25 g, 90%). Level of deuteration could not be readily assessed from the ¹H NMR spectrum, but was expected to retain the 97% deuteration previously observed at C6 and 67% deuteration observed at C2. $R_f = 0.13$ (Hex/Et₂O = 4:1). ¹H NMR (400 MHz, CDCl₃) δ 7.56 (s, 0.35H), 7.51 (d, $J = 7.8$ Hz, 1 H), 7.40 (d, $J = 7.8$ Hz, 1H), 4.61 (d, $J = 4.5$ Hz, 2H), 3.78 (t, $J = 4.9$ Hz, 1H). LRMS (ESI): calcd. 179.1 [M+H]⁺ Found: 179.5.

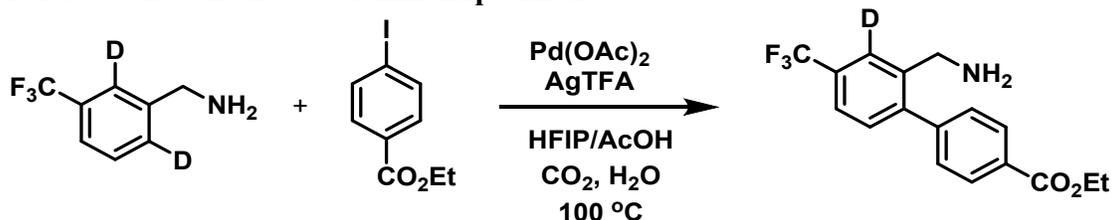


2-(3-(Trifluoromethyl)benzyl-2,6-d₂)isoindoline-1,3-dione (S-51): (3-(Trifluoromethyl)phenyl-2,6-d₂)methanol (2.00 g, 11.2 mmol) was combined with triphenylphosphine (3.83 g, 14.6 mmol) and phthalimide (2.15 g, 14.6 mmol), followed by dissolution in anhydrous tetrahydrofuran (50 mL). Diisopropylazodicarboxylate (DIAD, 2.87 mL, 14.6 mmol) was then added dropwise over 10 min. The reaction was stirred for 4 h, followed by addition of deionized water (150 mL). The reaction was extracted with dichloromethane (6 x 25 mL). The combined organic phase was dried over MgSO₄, followed by evaporating *in vacuo* to a yellow sludge. This was dissolved in a minimum amount of dichloromethane, followed by diluting with hexanes (200 mL) to give a turbid solution that was then filtered through celite. The filtrate was again evaporated *in vacuo*, followed by chromatography over silica (4:1 hexanes/Et₂O) to give the desired product as a white solid (2.05 g, 60%). $R_f = 0.27$ (Hex/Et₂O = 4:1). ¹H NMR (400 MHz, CDCl₃) δ 7.86 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.73 (dd, $J = 5.4, 3.0$ Hz, 2H), 7.69 (s, 0.35H), 7.62 (d, $J = 7.8$ Hz, 0.05H), 7.54 (d, $J = 7.8$ Hz, 1H), 7.44 (d, $J = 7.8$ Hz, 1H), 4.89 (s, 2H). LRMS (ESI): calcd. 353.2 [M+2Na]⁺ Found: 353.1.



(3-(Trifluoromethyl)phenyl-2,6- d_2)methanamine (8): 2-(3-(Trifluoromethyl)benzyl-2,6- d_2)isoindoline-1,3-dione (315 mg, 1.03 mmol) was suspended in methanol (50 mL), followed by addition of hydrazine monohydrate (500 μ L, 10.3 mmol). The reaction was stirred at RT for 12 h, followed by addition of 1.2M HCl_(aq) and stirring for an additional 2 h. The reaction was then filtered, and the filtrate washed with 1:1 Et₂O/hexanes (3 x 10 mL) which was discarded. The aqueous phase was then made basic with 6.0 M KOH_(aq), followed by extraction with Et₂O (4 x 15 mL). The combined Et₂O layers were washed with brine (3x) followed by drying over Na₂SO₄, followed by evaporation *in vacuo* to give the desired product as a faint tan oil (122 mg, 67%). R_f = 0.16 (Hex/Et₂O = 1:1). ¹H NMR (400 MHz, CDCl₃) δ 7.57 (s, 0.33H), 7.48 (m, 1.03H), 7.42 (d, J = 7.8Hz, 1H), 3.92 (s, 2H), 1.78 (br s, 2H). LRMS (EI-MS): calcd. 161.1 [M-NH₂]⁺ Found: 161.1.

Part 2: Procedure and Data for KIE Experiments



Multiple 7.5 mL vials were charged with Pd(OAc)₂ (6.7 mg, 0.03 mmol, 0.10 equiv), silver trifluoroacetate (132.3 mg, 0.6 mmol, 2.0 equiv), ethyl 4-iodobenzoate (248.4 mg, 0.9 mmol, 3.0 equiv), amine **8** (0.30 mmol, 1.0 equiv), HFIP (0.7 mL), acetic acid (0.3 mL), and water (21.4 μ L, 1.2 mmol, 4.0 equiv). Dry ice (66 mg, 1.5 mmol, 5.0 equiv.) was added to the vials, which were *immediately* sealed with a PTFE lined cap and stirred at room temperature for 15 min. After 15 min of stirring, the reaction vials was heated in a pre-heated pie-block at 100 °C under stirring. The reactions were cooled at predetermined time points, followed by evaporating solvent *in vacuo*. The crude reaction mixtures were then analyzed by ¹H NMR analysis in CDCl₃ in the presence of 1,1,2,2-tetrachloroethane as an internal standard, and reaction yields were determined by integration of well-resolved aromatic protons on the products. Reactions were run in triplicate for each data point, and the average value plotted.

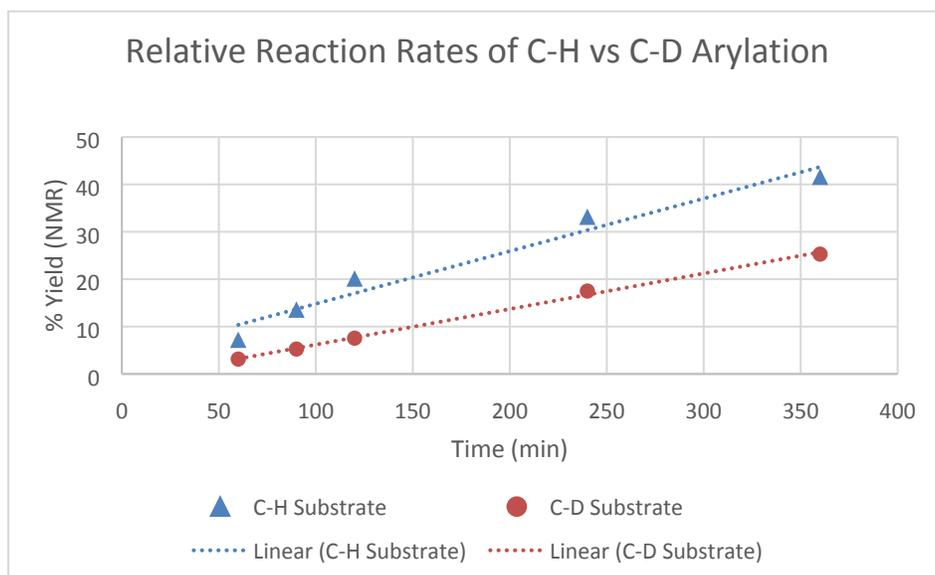


Figure S-2. KIE Experiment Determined by ¹H NMR (1,1,2,2-Tetrachloroethane).

d. Pd Dimer Experiment

Synthesis of 10: Based on a slight modification of a literature procedure,¹⁹ palladium acetate (273 mg, 0.407 mmol) was added to a 50 mL round bottom flask, followed by 20 mL of anhydrous MeCN. The reaction was placed under N₂, followed by addition of benzylamine (133 μ L, 0.407 mmol). The reaction was stirred at RT for 15 min, followed by heating under reflux for 12 h. The reaction was then cooled, followed by filtration through MgSO₄. The reaction mixture was then evaporated *in vacuo*. The resulting residue was treated with Me₂CO (2 mL), followed by Et₂O (100 mL). The crude mixture was cooled to -20 °C, and the resulting solid was filtered, rinsed with additional Et₂O, then dried *in vacuo* to give the desired product as a yellow solid (118 mg, 39%). The spectral data matched that in the literature.²⁰

Procedure: Complex **10** (40.7, 0.075 mmol) was added to a 7.5 mL vial along with silver trifluoroacetate (66.2 mg, 0.3 mmol), ethyl 4-iodobenzoate (248.5 mg, 0.9 mmol), and a 7:3 mixture of HFIP/AcOH (1.0 mL), then deionized water (10.8 μ L). Dry ice (33 mg, 0.75 mmol) was added, and the vial was then *immediately* sealed with a PTFE lined cap and stirred at RT for 15 min. The reaction was then heated in a pre-heated pie-block at 100 °C under stirring for 14h. After cooling to room temperature, the reaction mixture was added to 1M NaOH_(aq) (100 mL), followed by extraction with dichloromethane (3 \times 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. ¹H NMR analysis of the crude mixture was then performed, and only ethyl 4-iodobenzoate and diethyl 4,4'-biphenyldicarboxylate were recovered.

e. CO₂ Deinsertion Experiment

Procedure: 7.5 mL vials were charged with Pd(OAc)₂ (3.36 mg, 0.015 mmol, 0.1 equiv), silver trifluoroacetate (66.2 mg, 0.3 mmol, 2.0 equiv), ethyl 4-iodobenzoate (124.2 mg, 0.45 mmol, 3 eq), and a 7:3 mixture of HFIP/AcOH (1.0 mL). *o*-Carboxybenzylamine²¹ (22.7 mg, 0.15 mmol, 1.0 equiv) was added to the vial, followed by dry ice (between 17 – 172 mg). The vial was then *immediately* sealed with a PTFE lined cap and the reaction was heated in a pre-heated pie-block at 100 °C under stirring for 12h. After cooling to room temperature, the reaction mixture was concentrated *in vacuo*. Aq. HCl (10 mL, 1.2 M) was added to the residual reaction mixture and stirred for 15 min. The mixture was extracted with ether (8.0 mL) and the organic layer was discarded. The aqueous layer was made basic with ammonium hydroxide solution, followed by extraction with dichloromethane (2 \times 10 mL). The organic layer was washed with water (5.0 mL), followed by brine, and dried over Na₂SO₄. ¹H NMR analysis of the crude mixture was then performed, with 1,1,2,2-tetrachloroethane used as an internal standard to calculate the percent yield, which was determined to be 71% of free benzylamine. Notably, no sign of the *o*-carboxybenzylamine starting material, or any arylated versions thereof, were observed from the various washes.

11. ^1H , ^{13}C , and Select IR Spectra of New Compounds

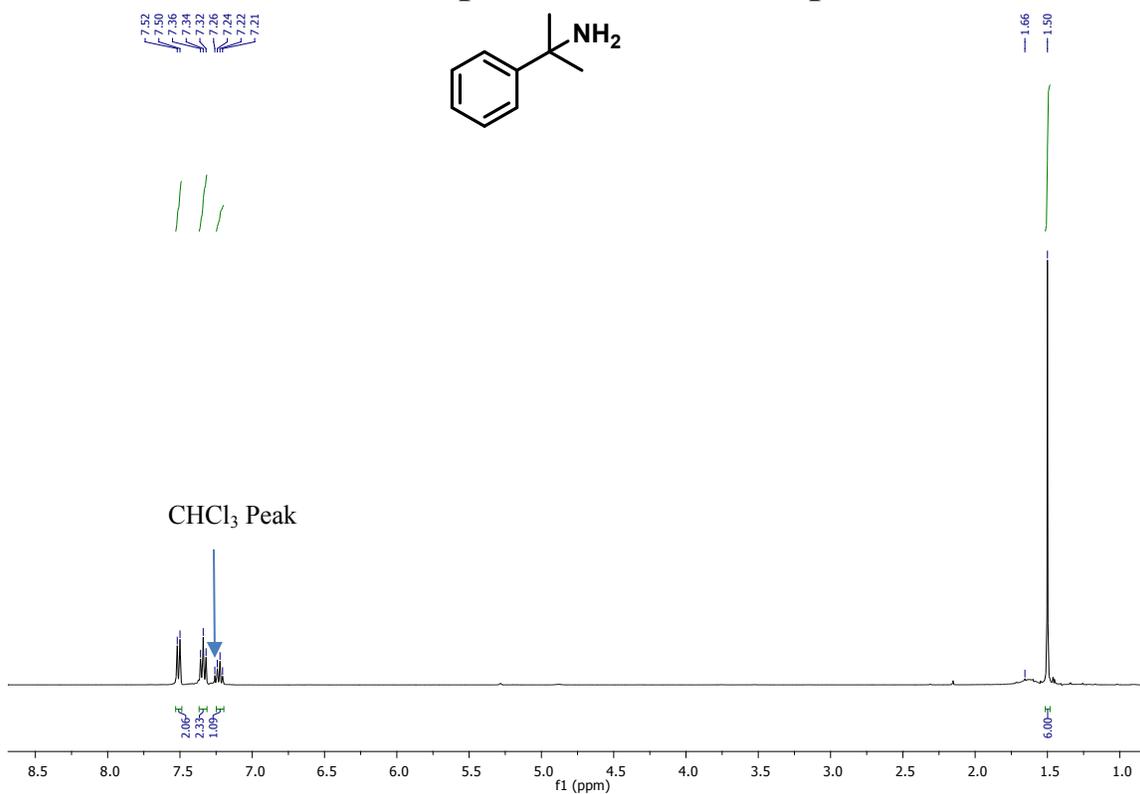


Figure S-3. ^1H NMR spectrum of S-1 (CDCl_3 , 400 MHz, 298 K)

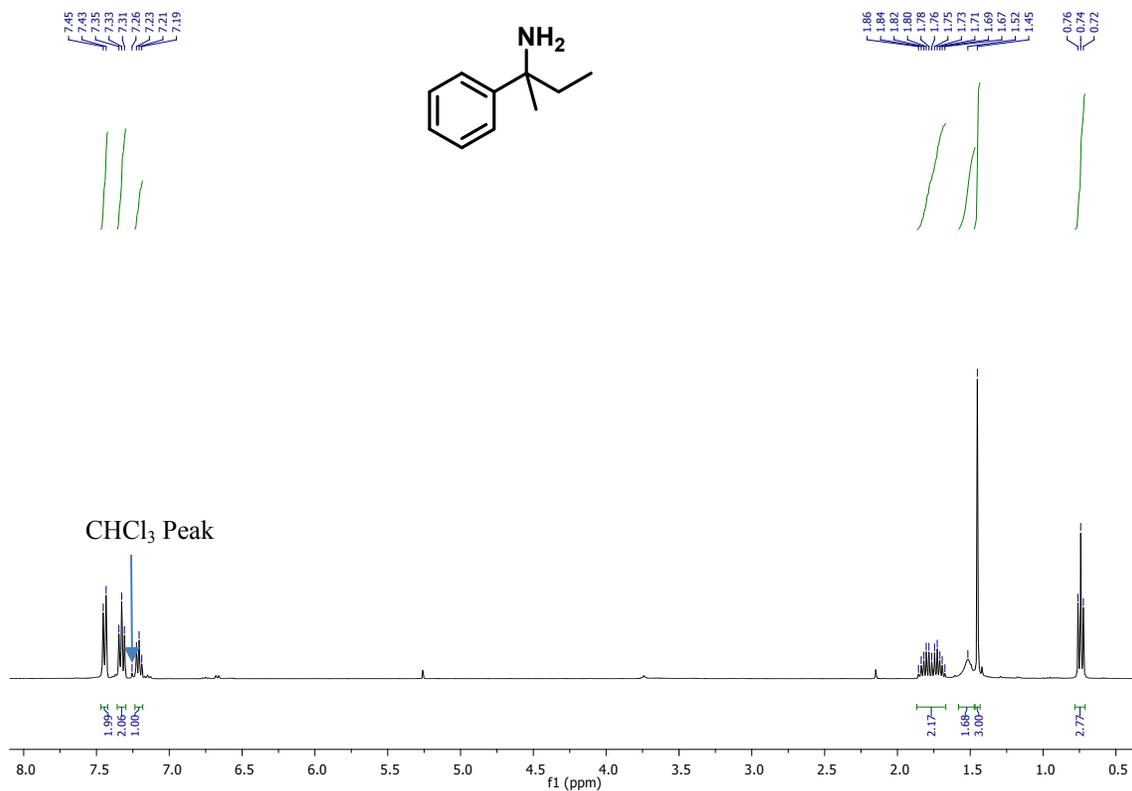


Figure S-4. ^1H NMR spectrum of S-2 (CDCl_3 , 400 MHz, 298 K)

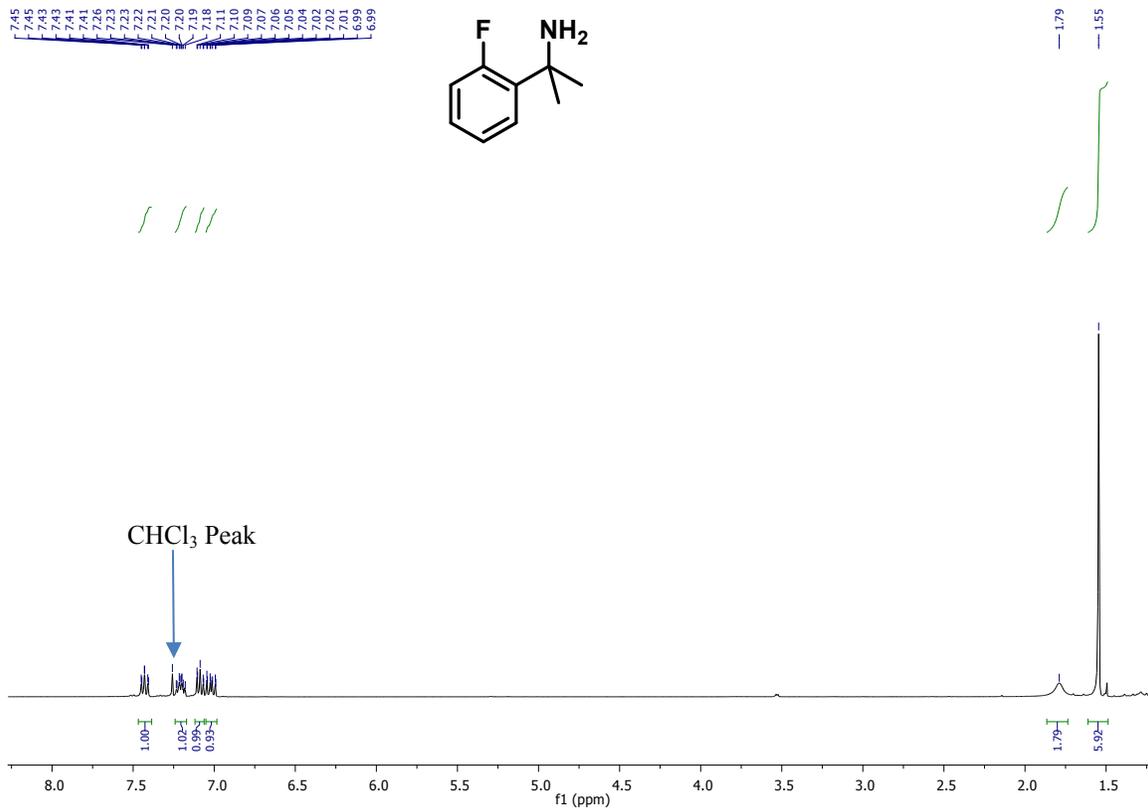


Figure S-5. ¹H NMR spectrum of S-3 (CDCl₃, 400 MHz, 298 K)

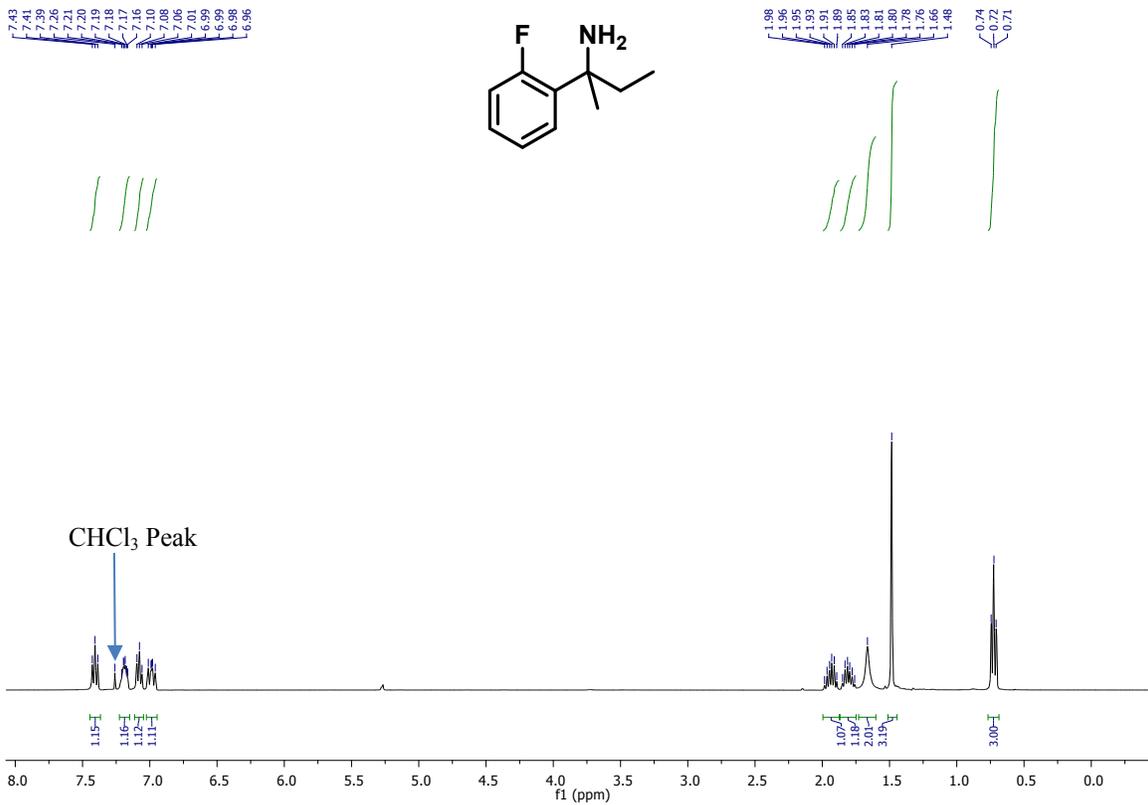


Figure S-6. ¹H NMR spectrum of S-4 (CDCl₃, 400 MHz, 298 K)

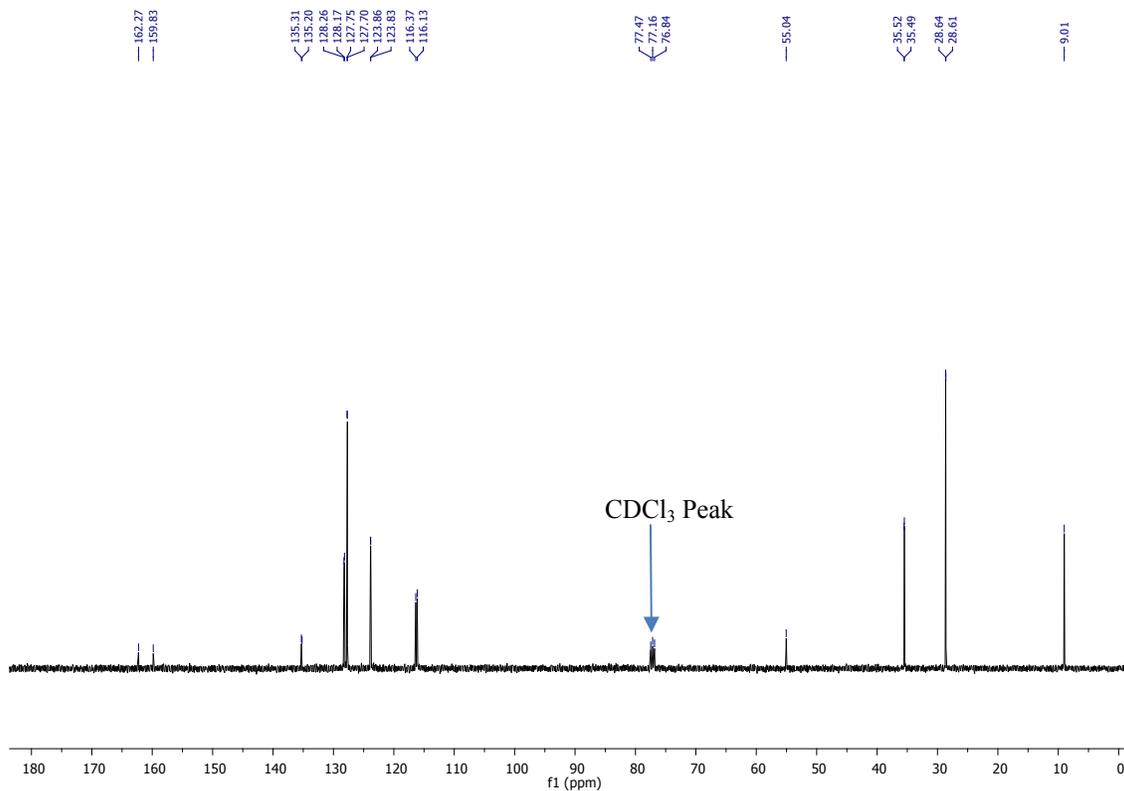


Figure S-7. ¹³C NMR spectrum of S-4 (CDCl₃, 101 MHz, 298 K)

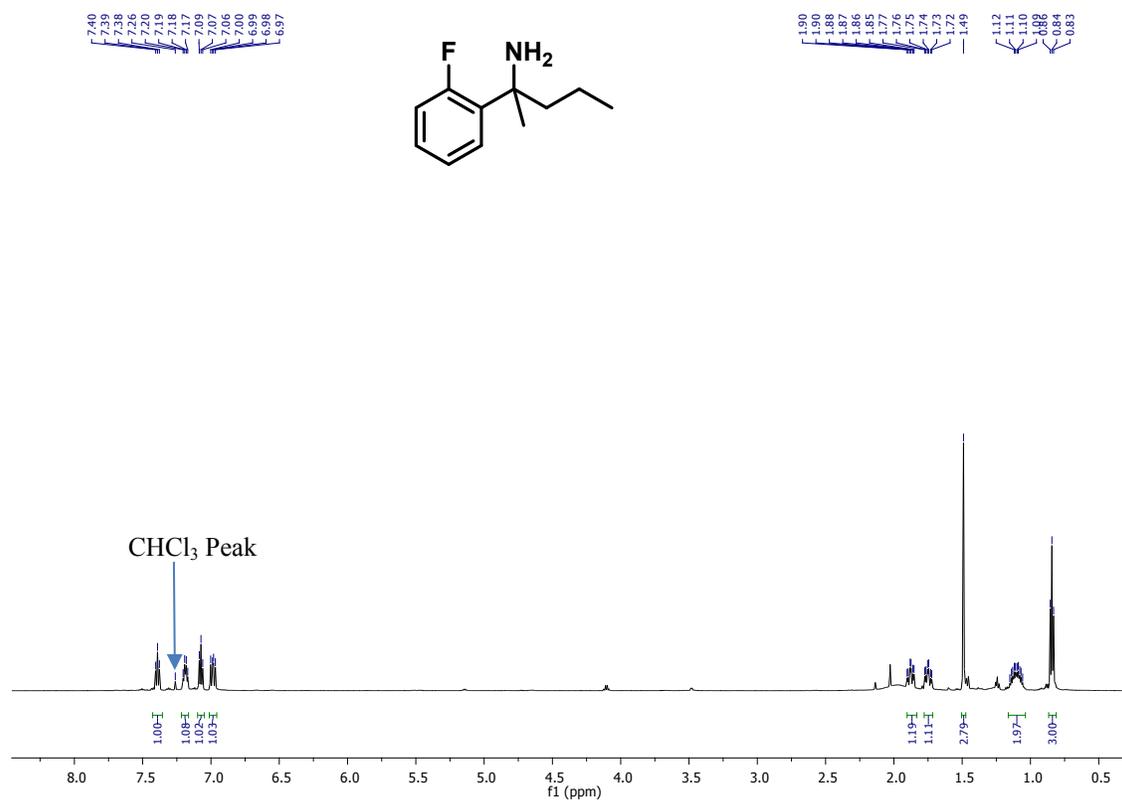


Figure S-8. ¹H NMR spectrum of S-5 (CDCl₃, 600 MHz, 298 K)

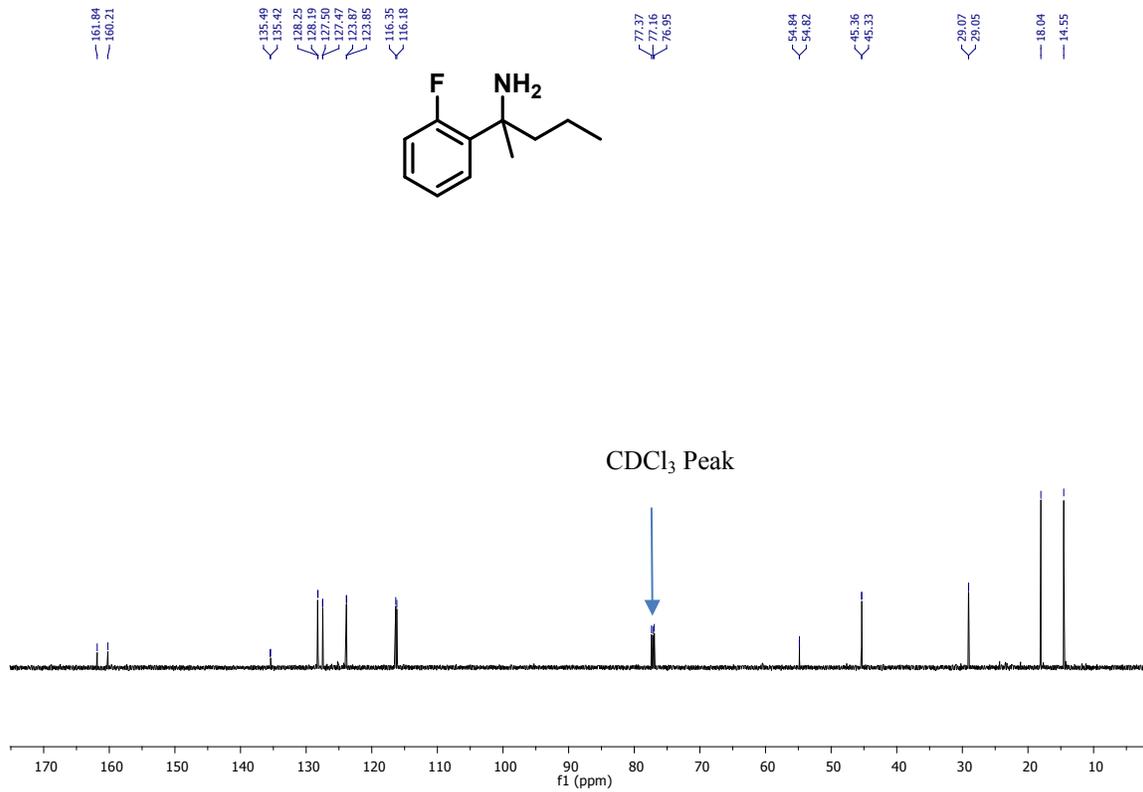


Figure S-9. ¹³C NMR spectrum of S-5 (CDCl₃, 101 MHz, 298 K)

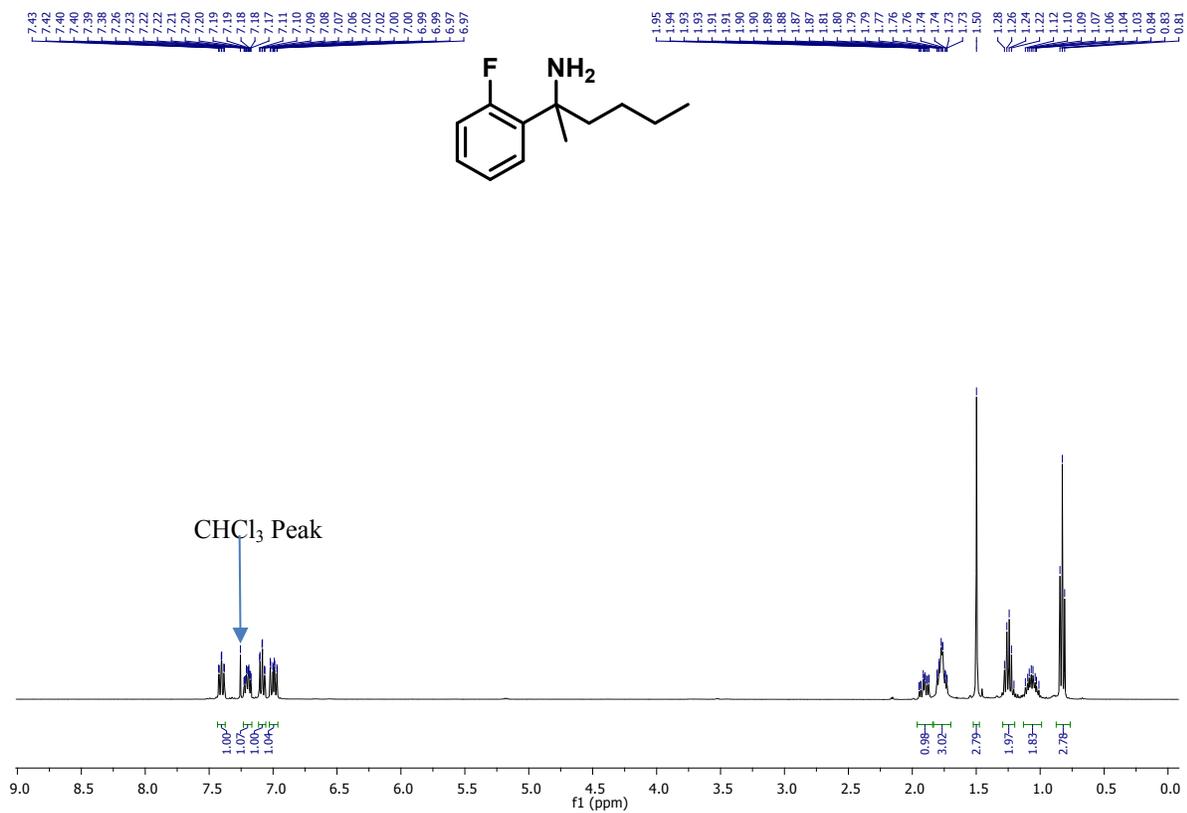


Figure S-10. ¹H NMR spectrum of S-6 (CDCl₃, 400 MHz, 298 K)

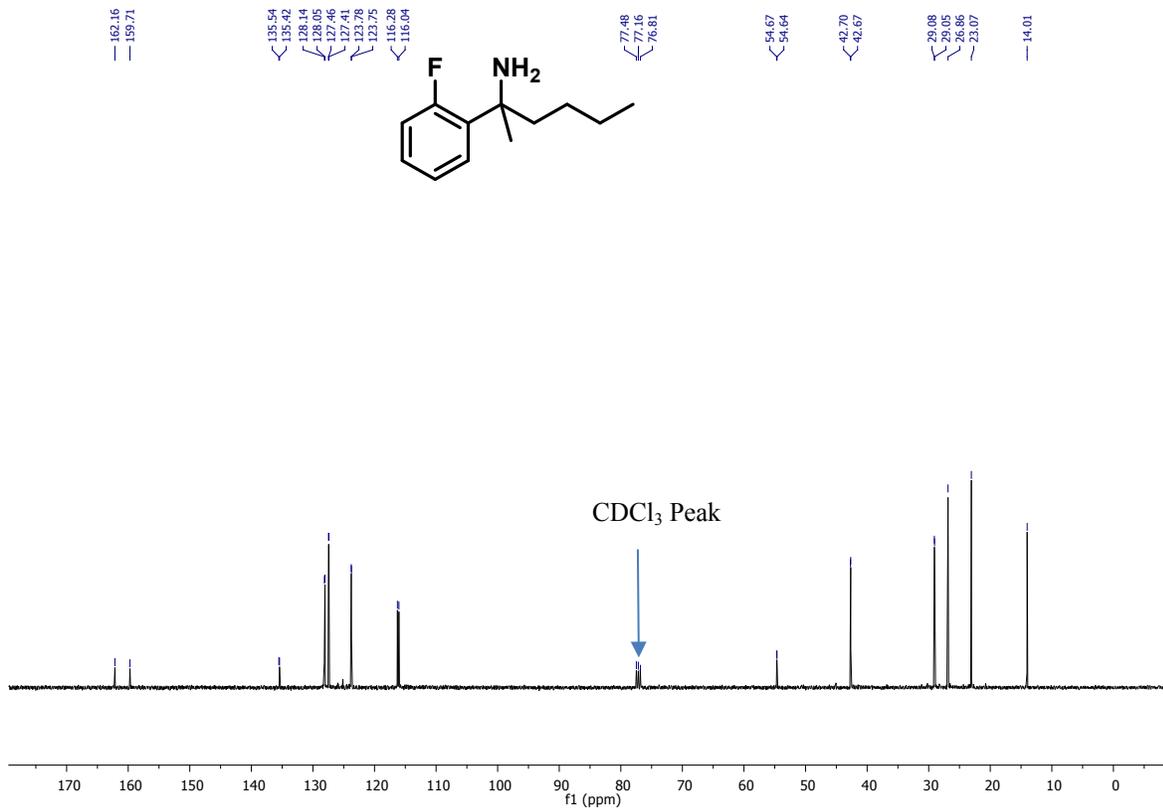


Figure S-11. ^{13}C NMR spectrum of S-6 (CDCl₃, 101 MHz, 298 K)

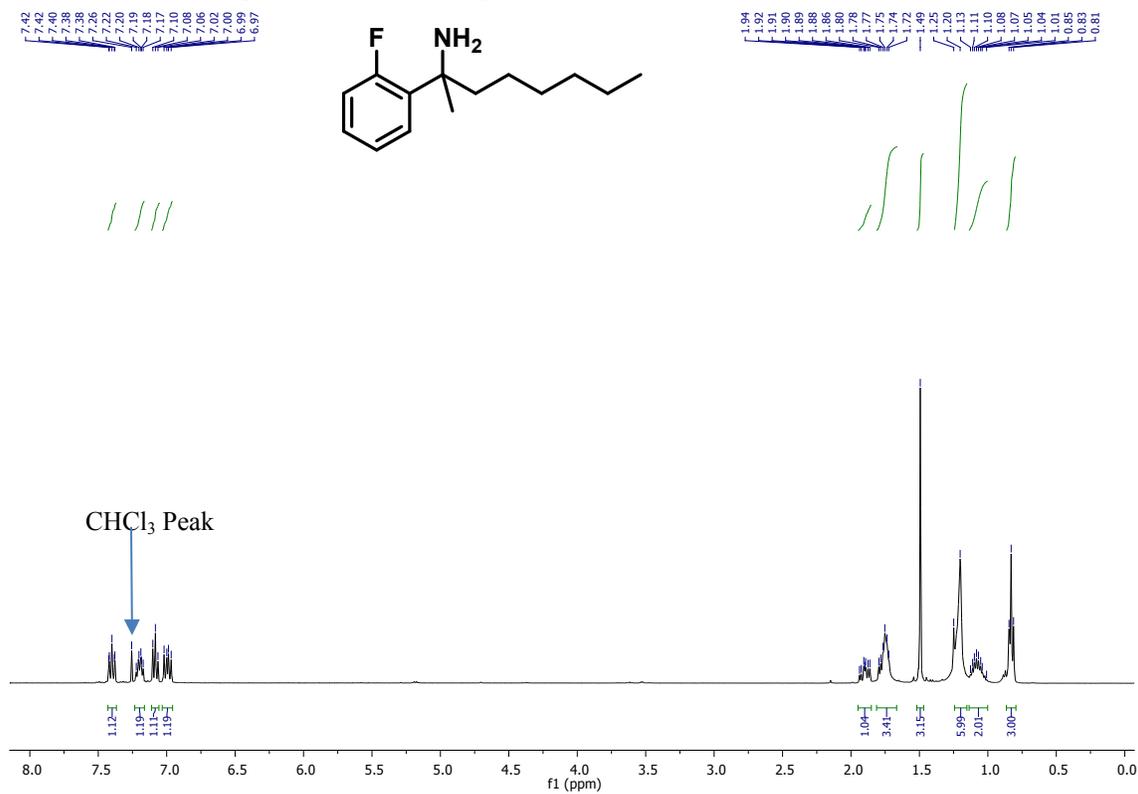


Figure S-12. ^1H NMR spectrum of S-7 (CDCl₃, 400 MHz, 298 K)

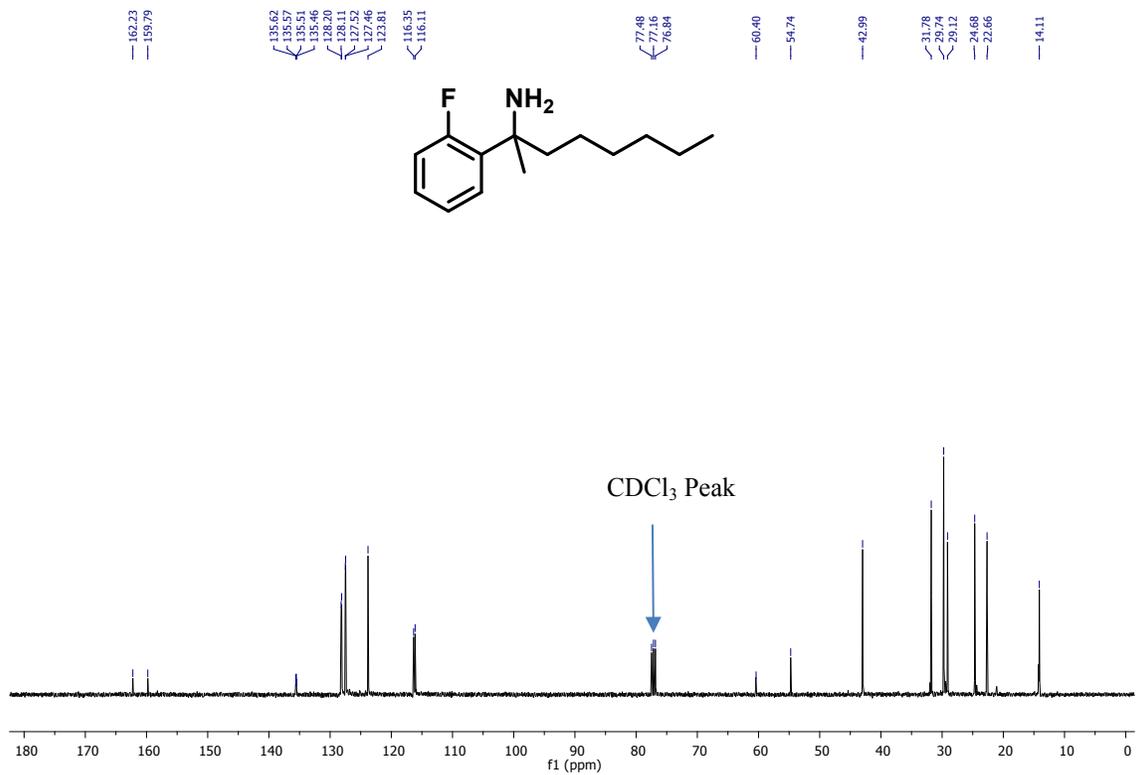


Figure S-13. ^{13}C NMR spectrum of S-7 (CDCl₃, 101 MHz, 298 K)

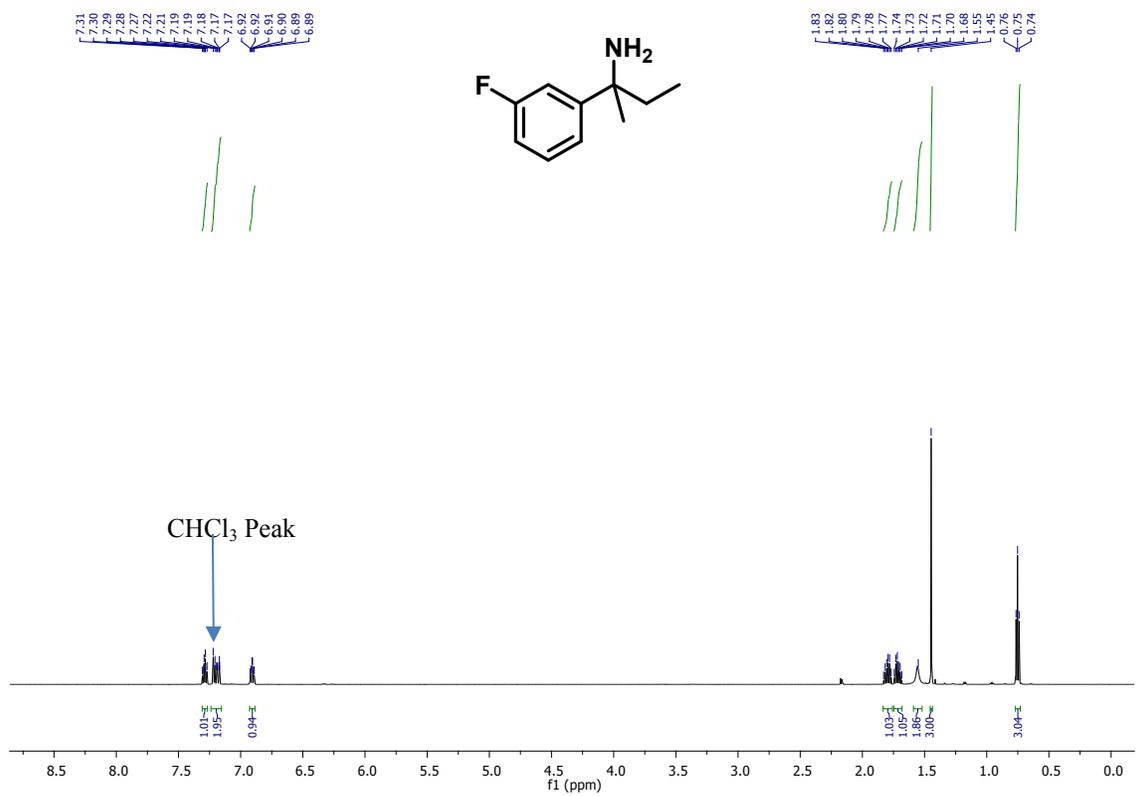


Figure S-14. ^1H NMR spectrum of S-8 (CDCl₃, 600 MHz, 298 K)

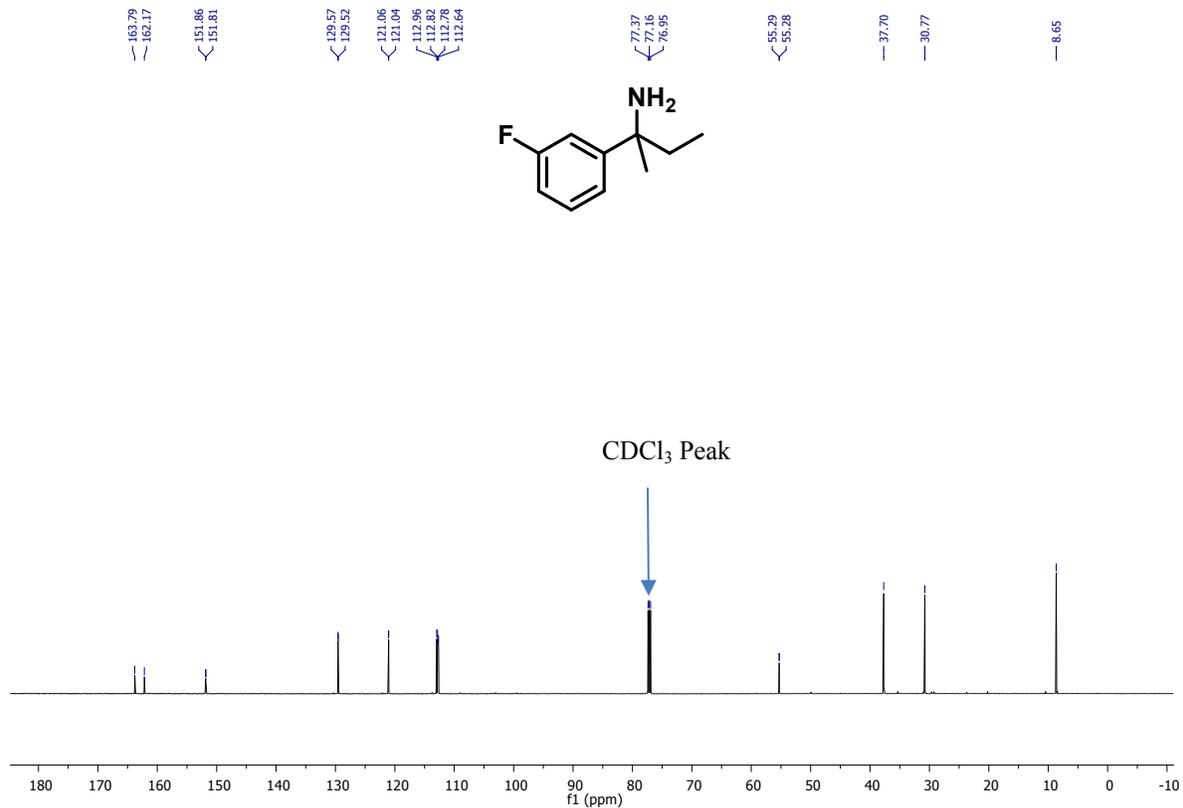


Figure S-15. ^{13}C NMR spectrum of S-8 (CDCl₃, 151 MHz, 298 K)

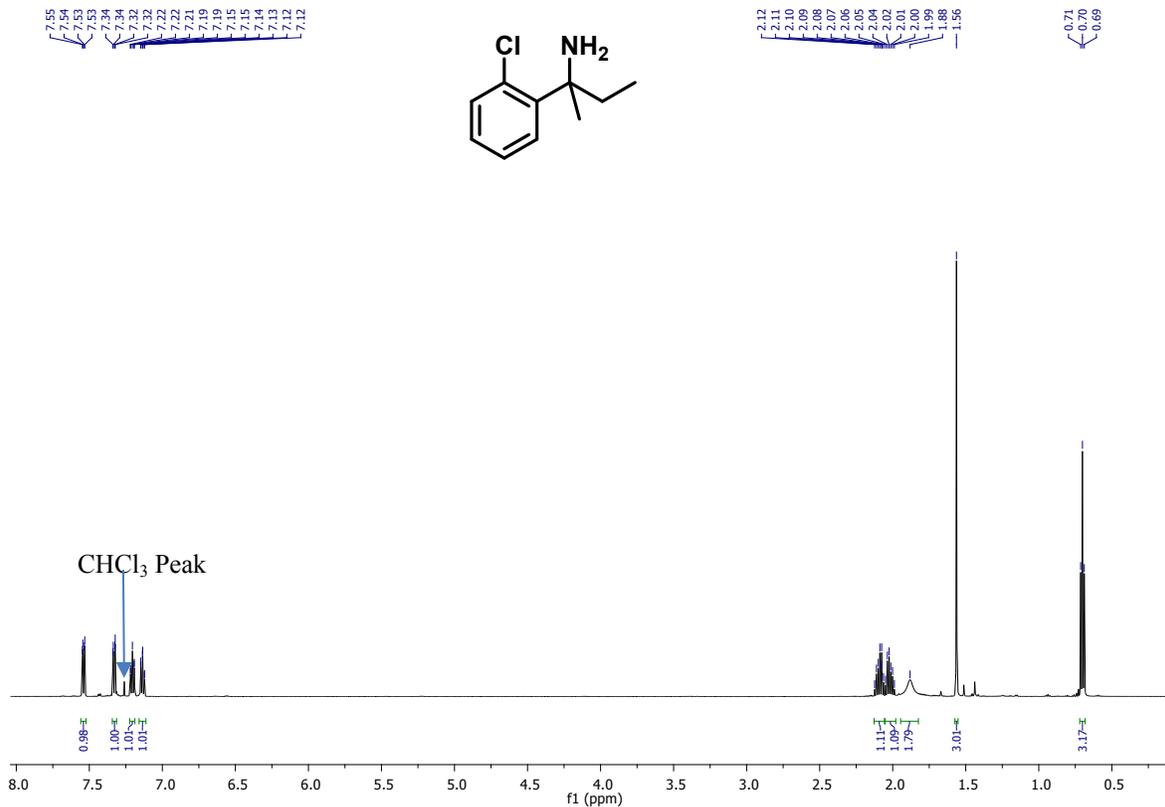


Figure S-16. ^1H NMR spectrum of S-9 (CDCl₃, 600 MHz, 298 K)

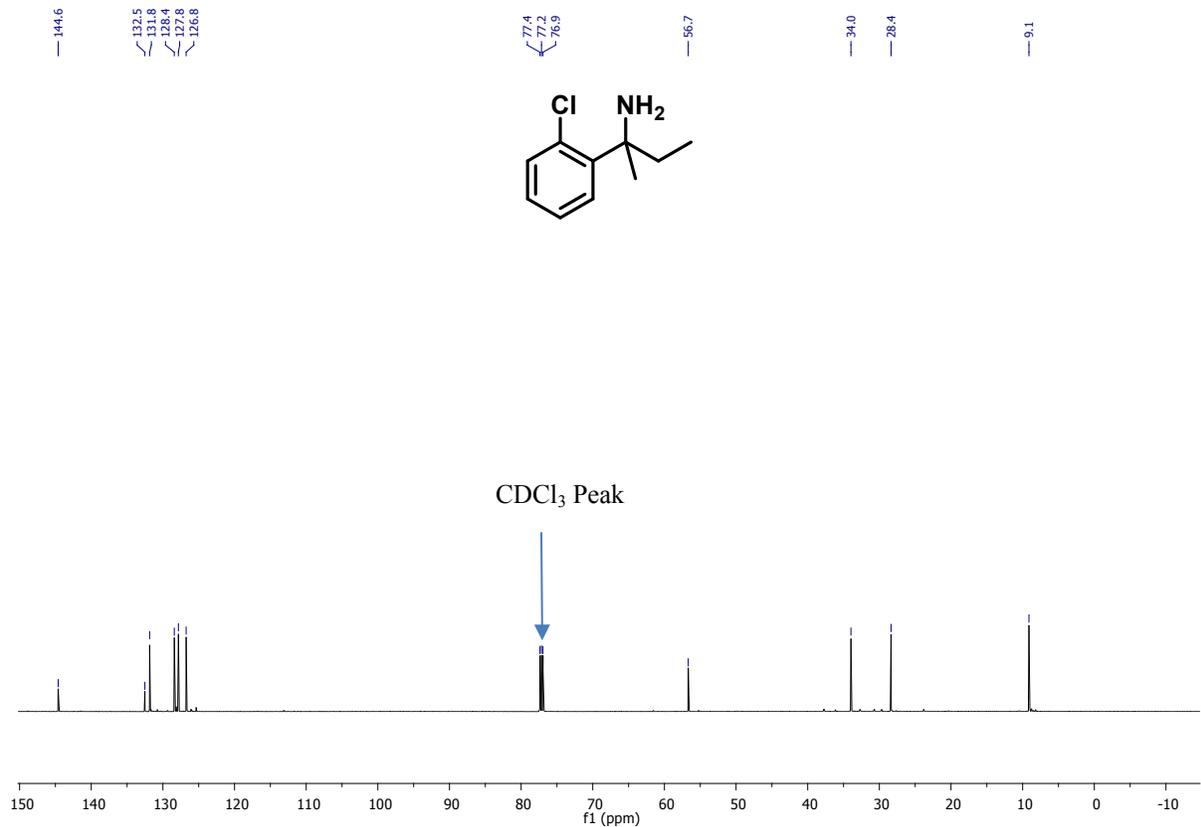


Figure S-17. ^{13}C NMR spectrum of S-9 (CDCl₃, 151 MHz, 298 K)

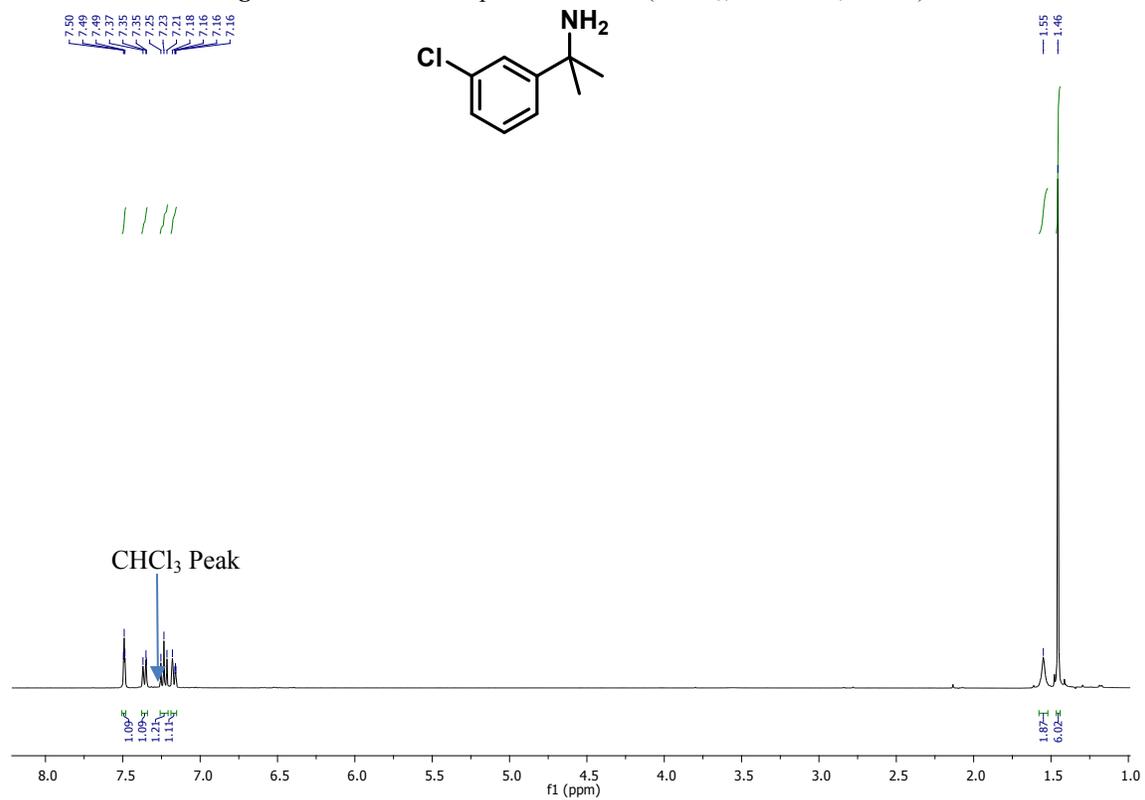


Figure S-18. ^1H NMR spectrum of S-10 (CDCl₃, 400 MHz, 298 K)

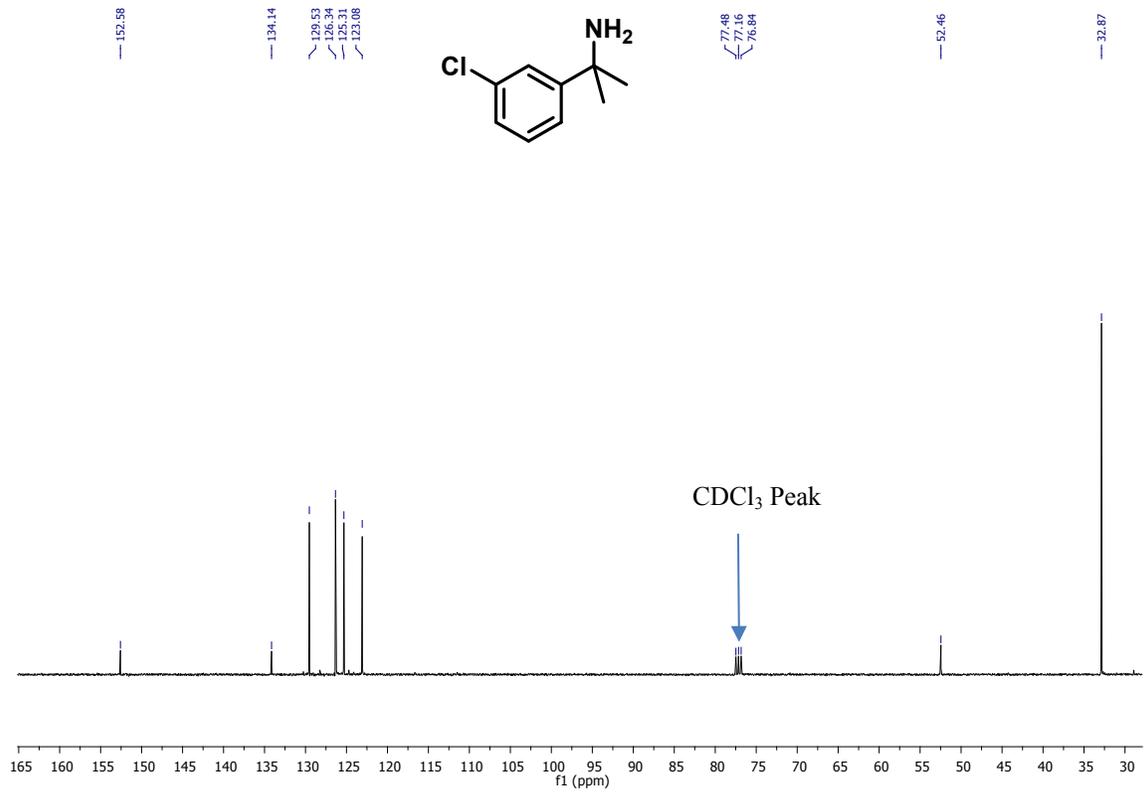


Figure S-19. ^{13}C NMR spectrum of S-10 (CDCl₃, 101 MHz, 298 K)

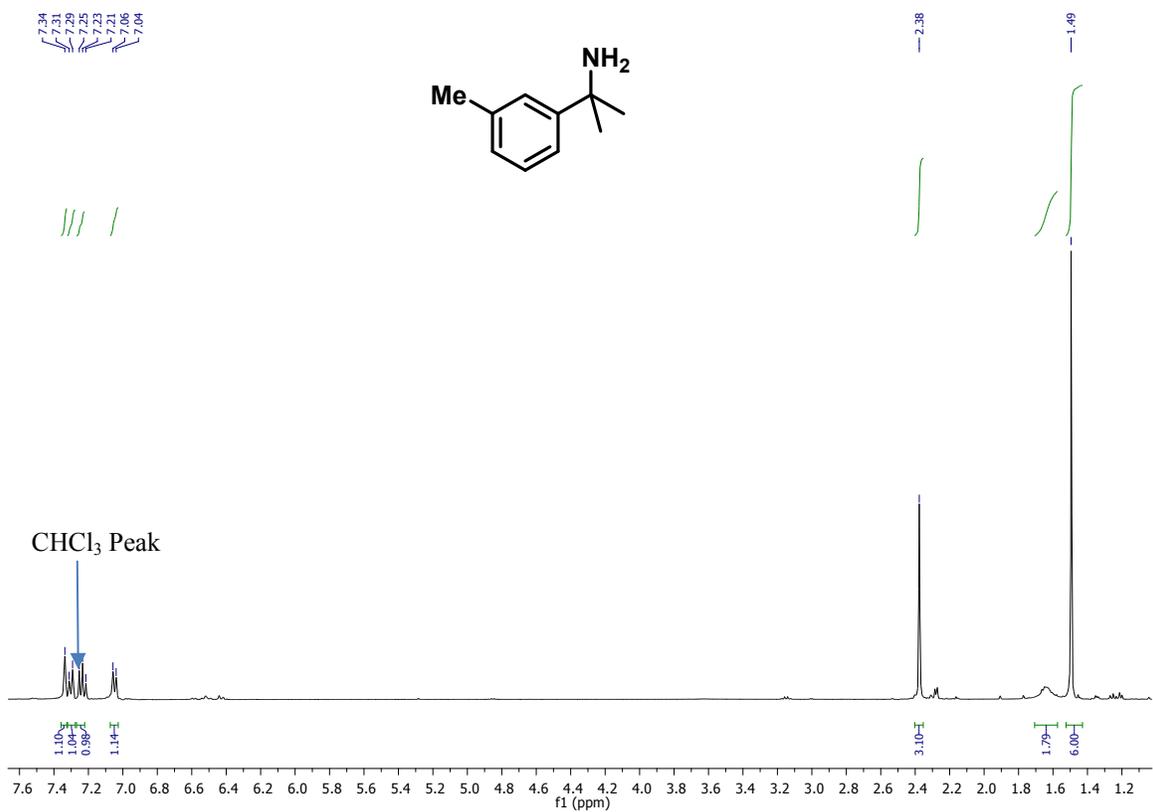


Figure S-20. ^1H NMR spectrum of S-11 (CDCl₃, 400 MHz, 298 K)

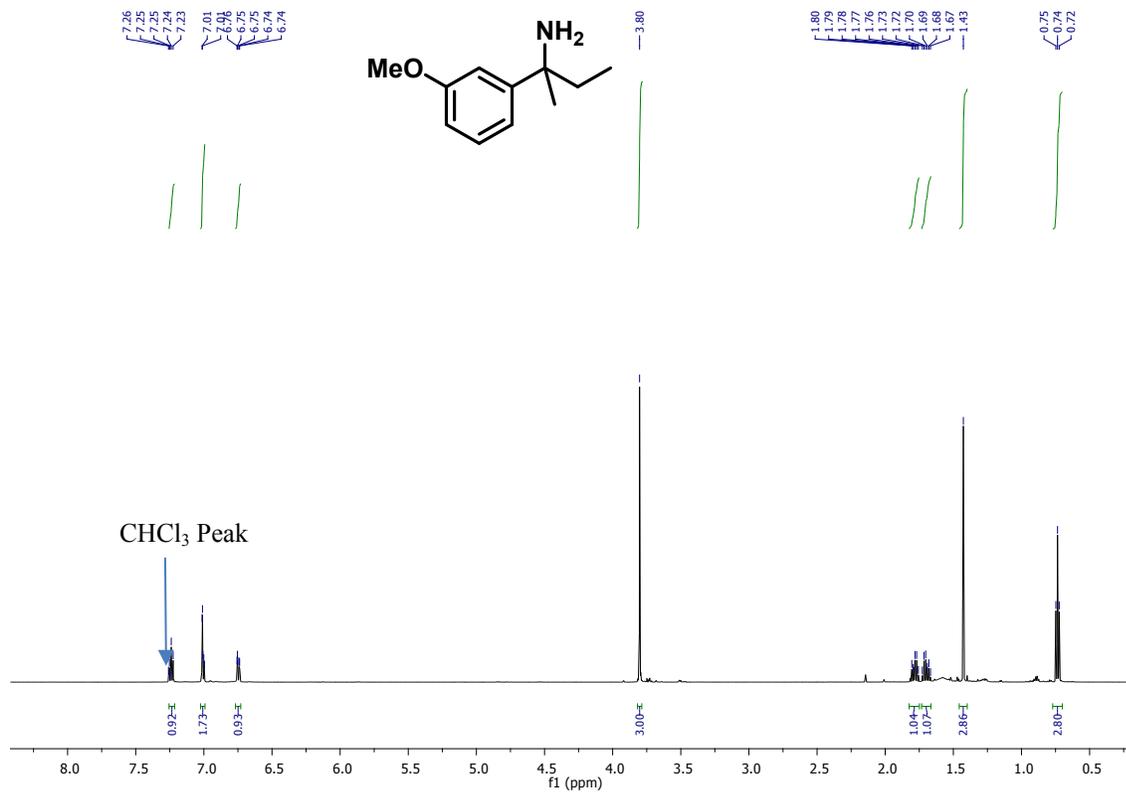


Figure S-21. ¹H NMR spectrum of S-12 (CDCl₃, 600 MHz, 298 K)

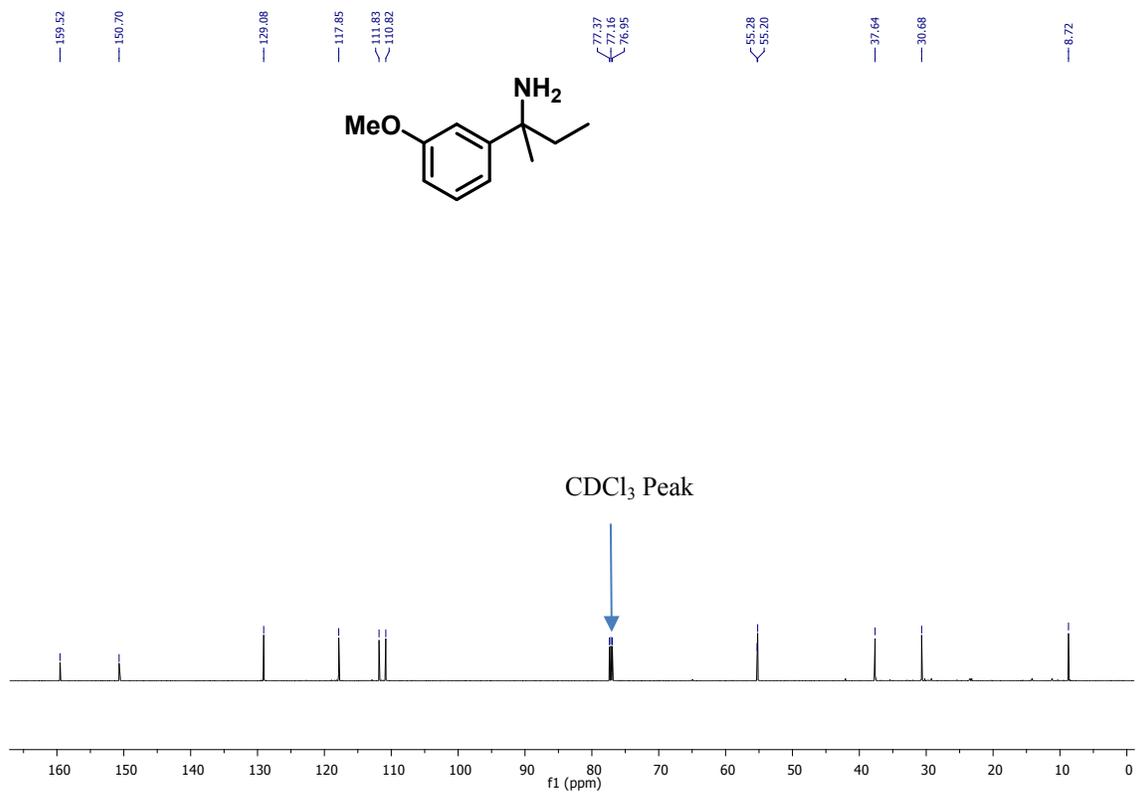
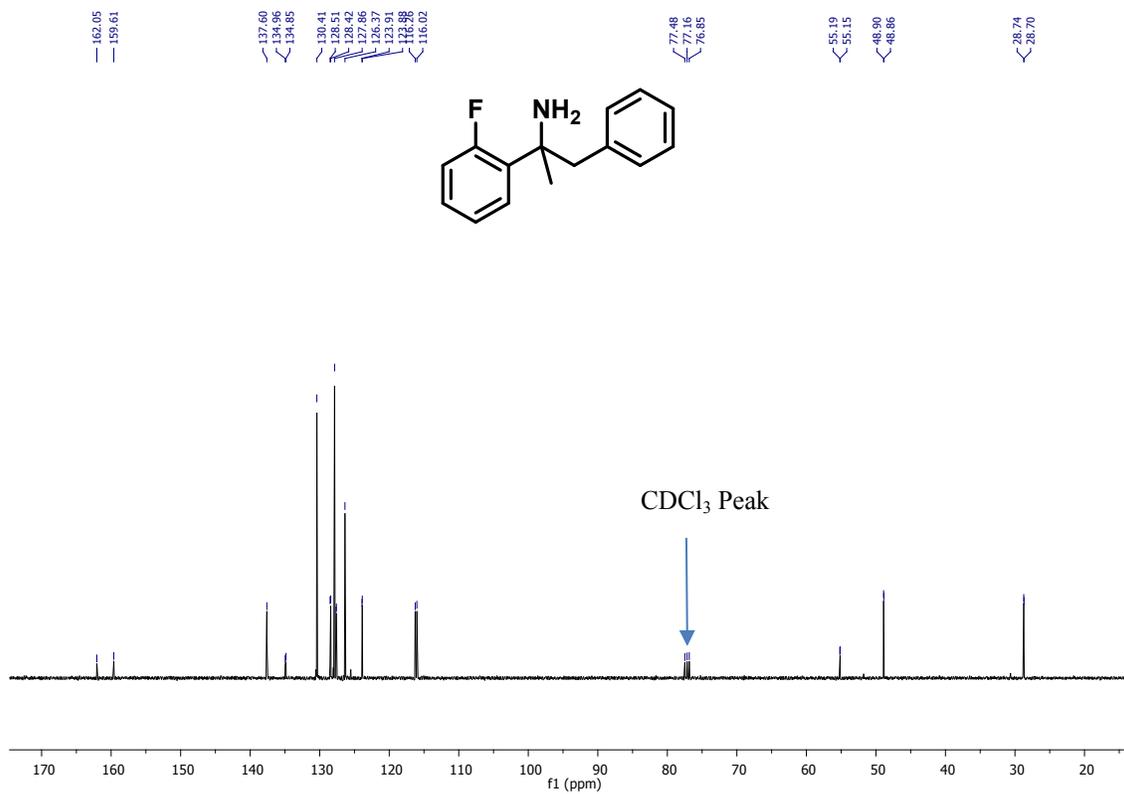
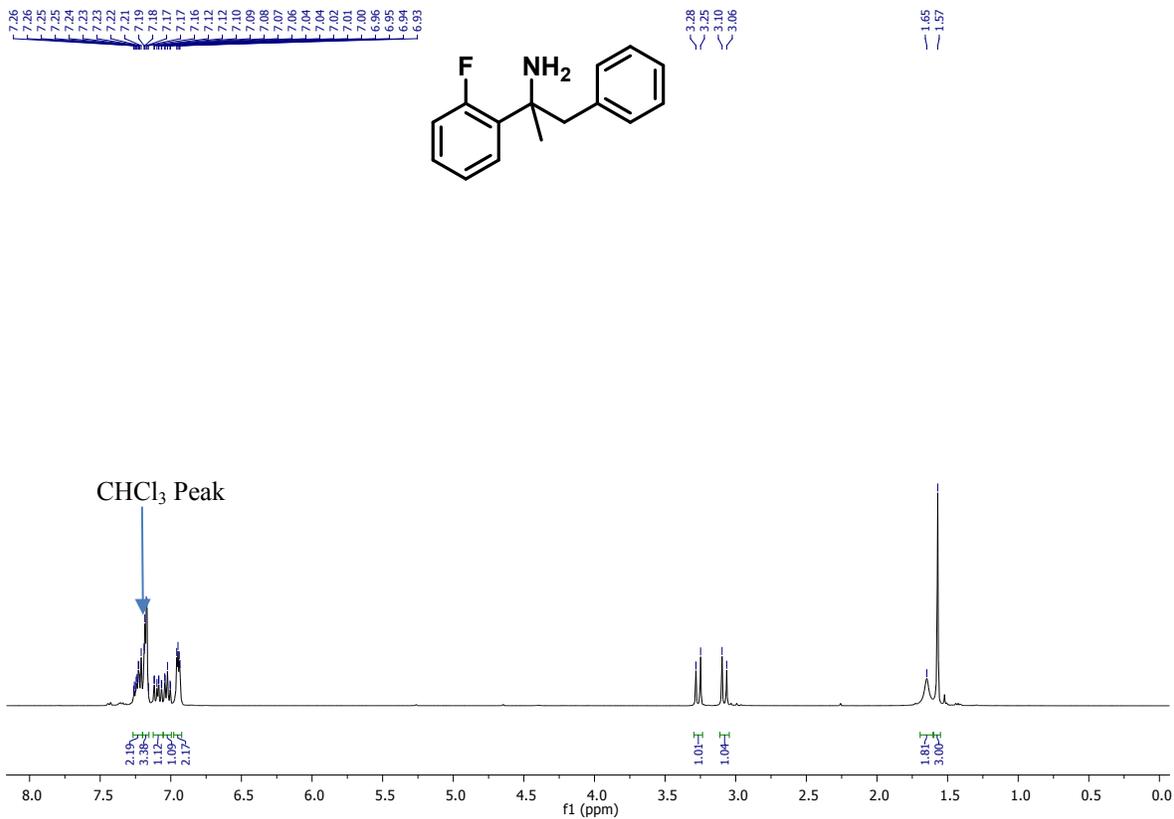


Figure S-22. ¹³C NMR spectrum of S-12 (CDCl₃, 151 MHz, 298 K)



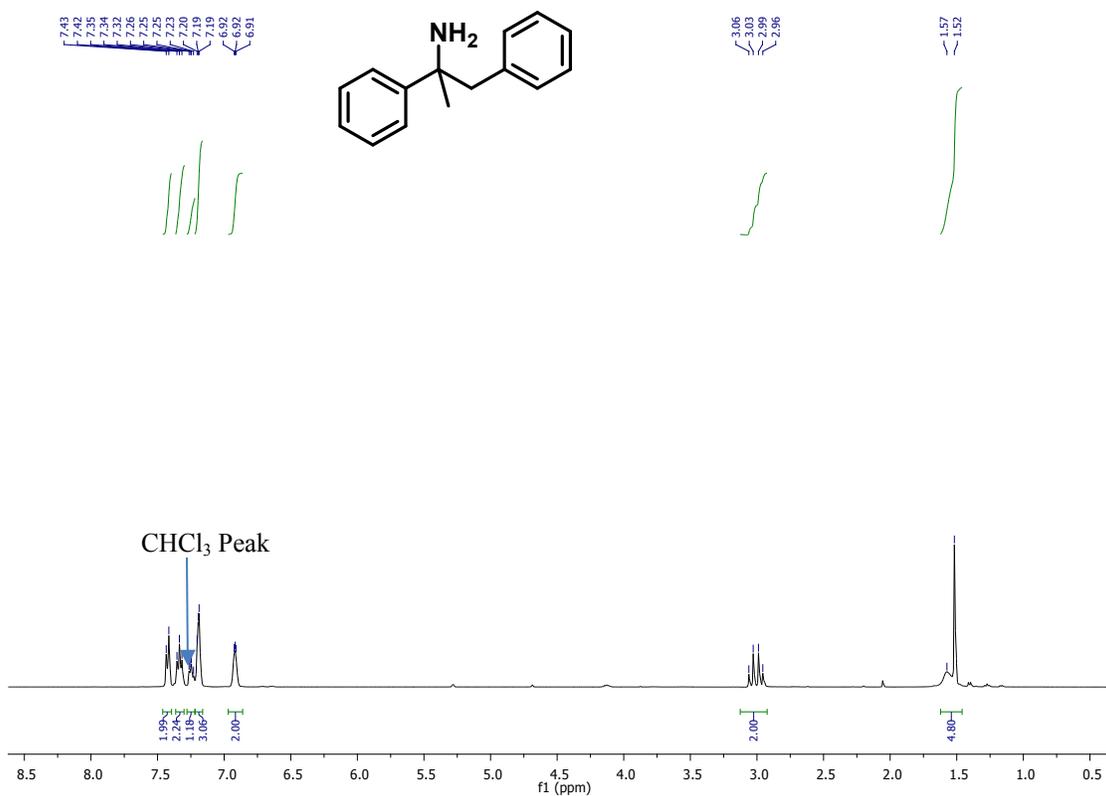


Figure S-27. ¹H NMR spectrum of S-15 (CDCl₃, 400 MHz, 298 K)

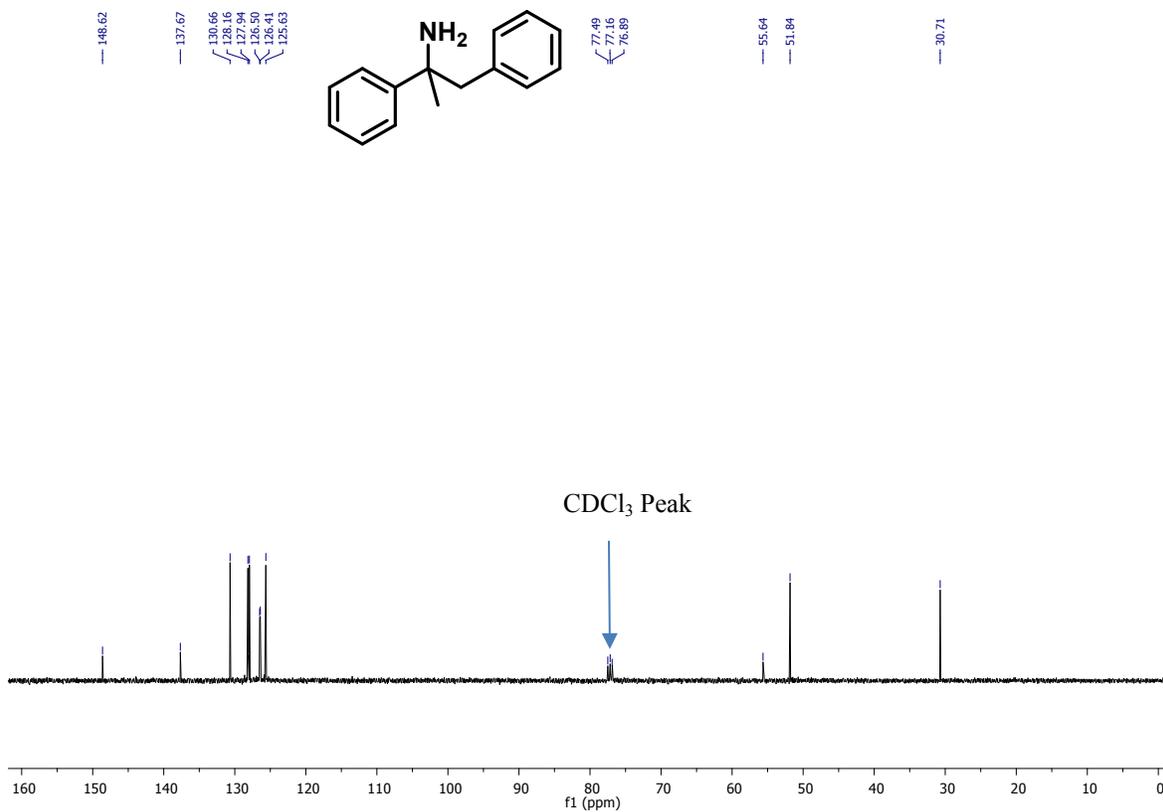


Figure S-28. ¹³C NMR spectrum of S-15 (CDCl₃, 101 MHz, 298 K)

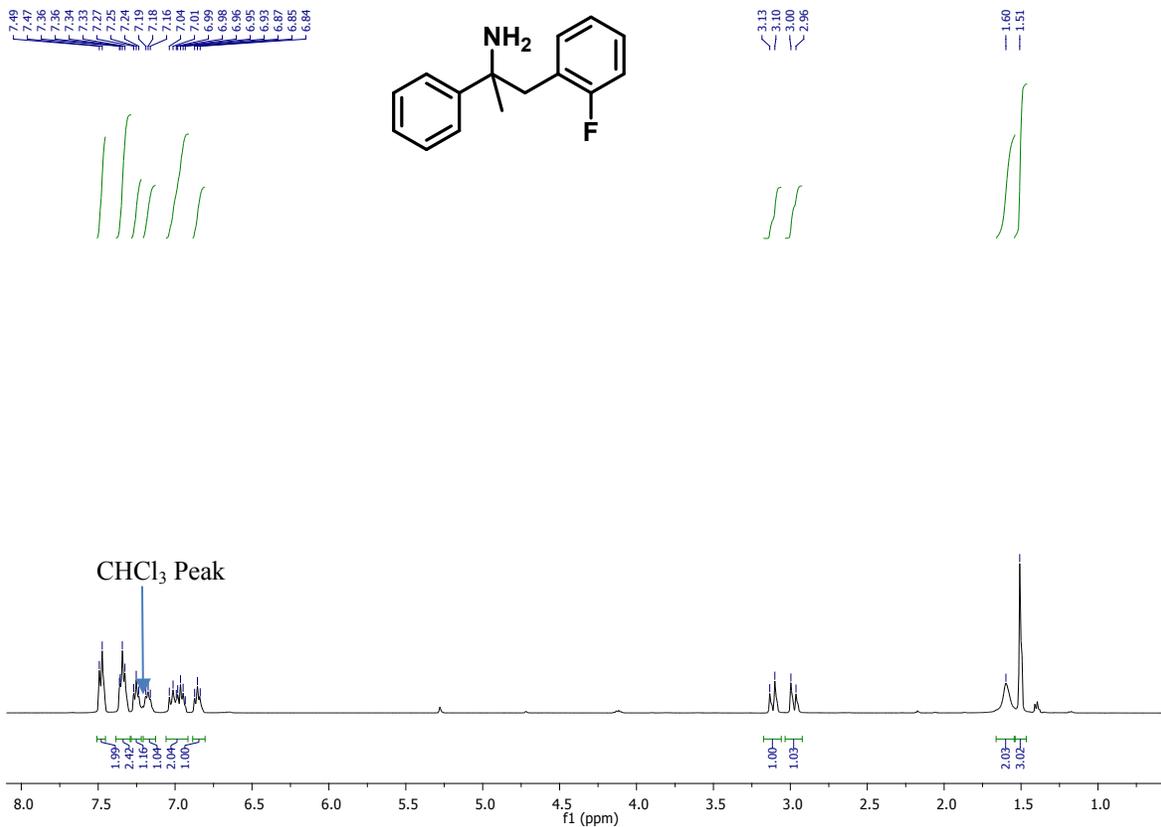


Figure S-29. ¹H NMR spectrum of S-16 (CDCl₃, 400 MHz, 298 K)

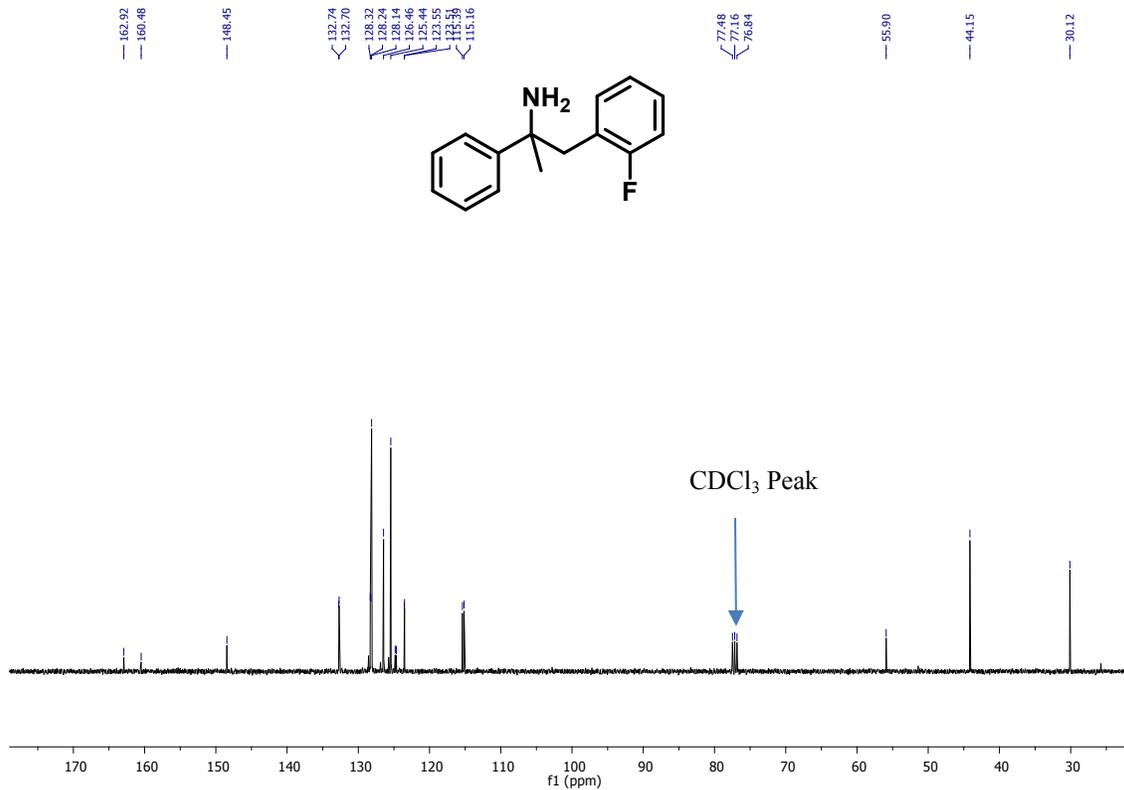


Figure S-30. ¹³C NMR spectrum of S-16 (CDCl₃, 400 MHz, 298 K)

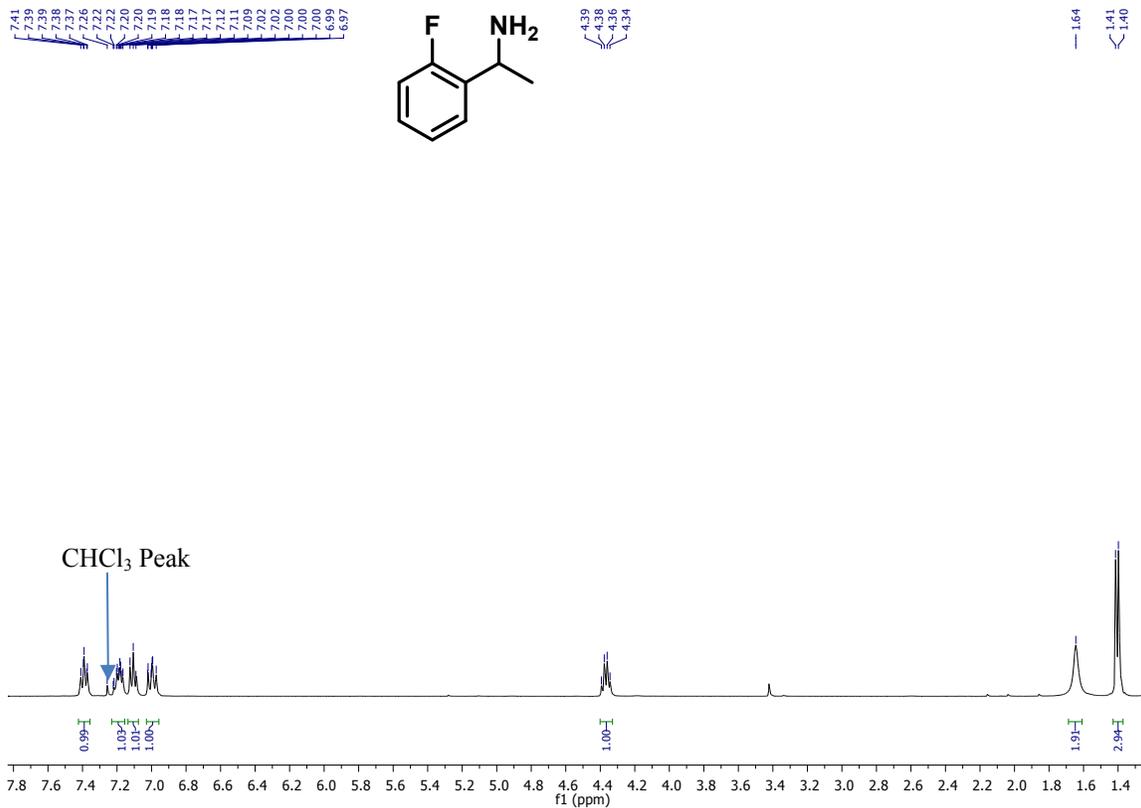


Figure S-31. ¹H NMR spectrum of S-17 (CDCl₃, 400 MHz, 298 K)

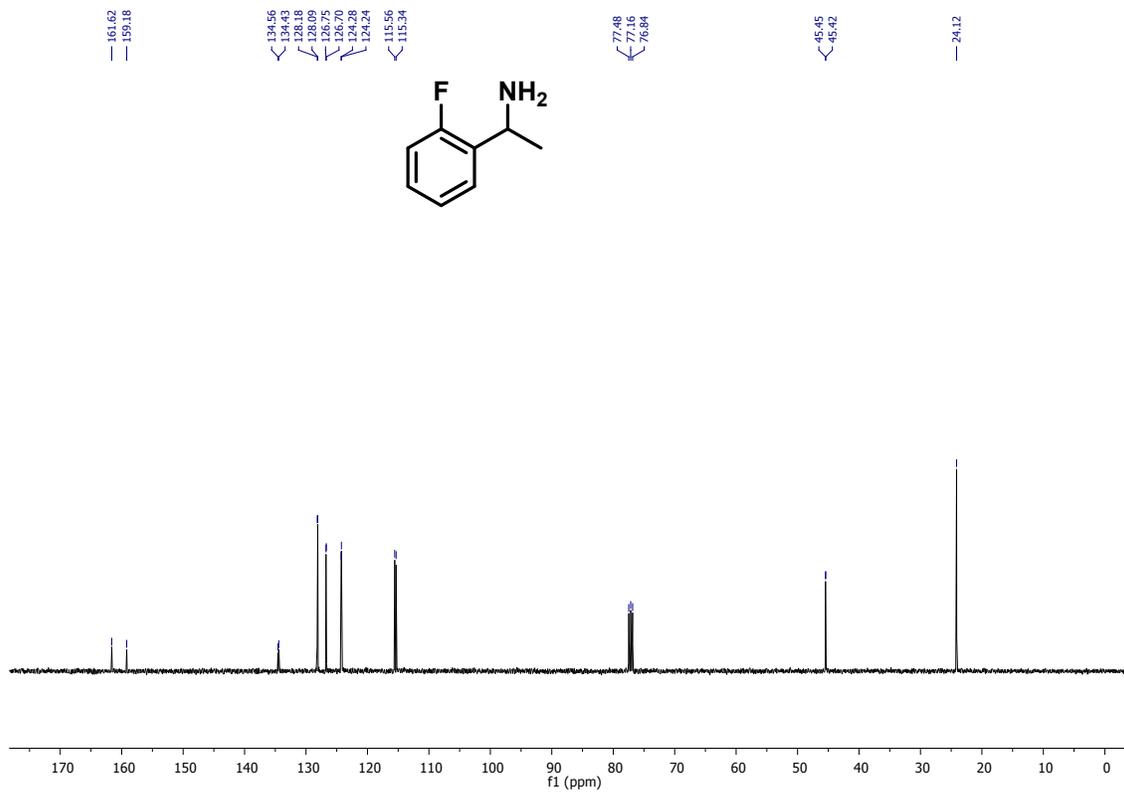


Figure S-32. ¹³C NMR spectrum of S-17 (CDCl₃, 101 MHz, 298 K)

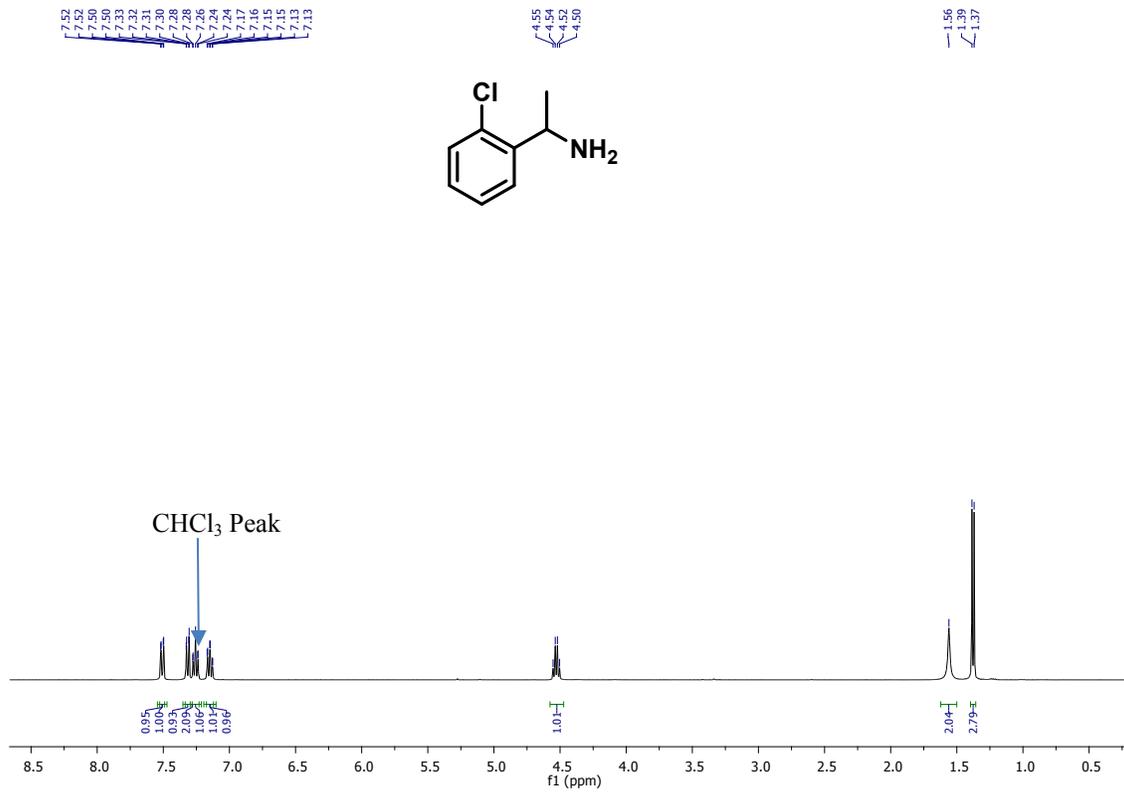


Figure S-33. ¹H NMR spectrum of S-18 (CDCl₃, 400 MHz, 298 K)

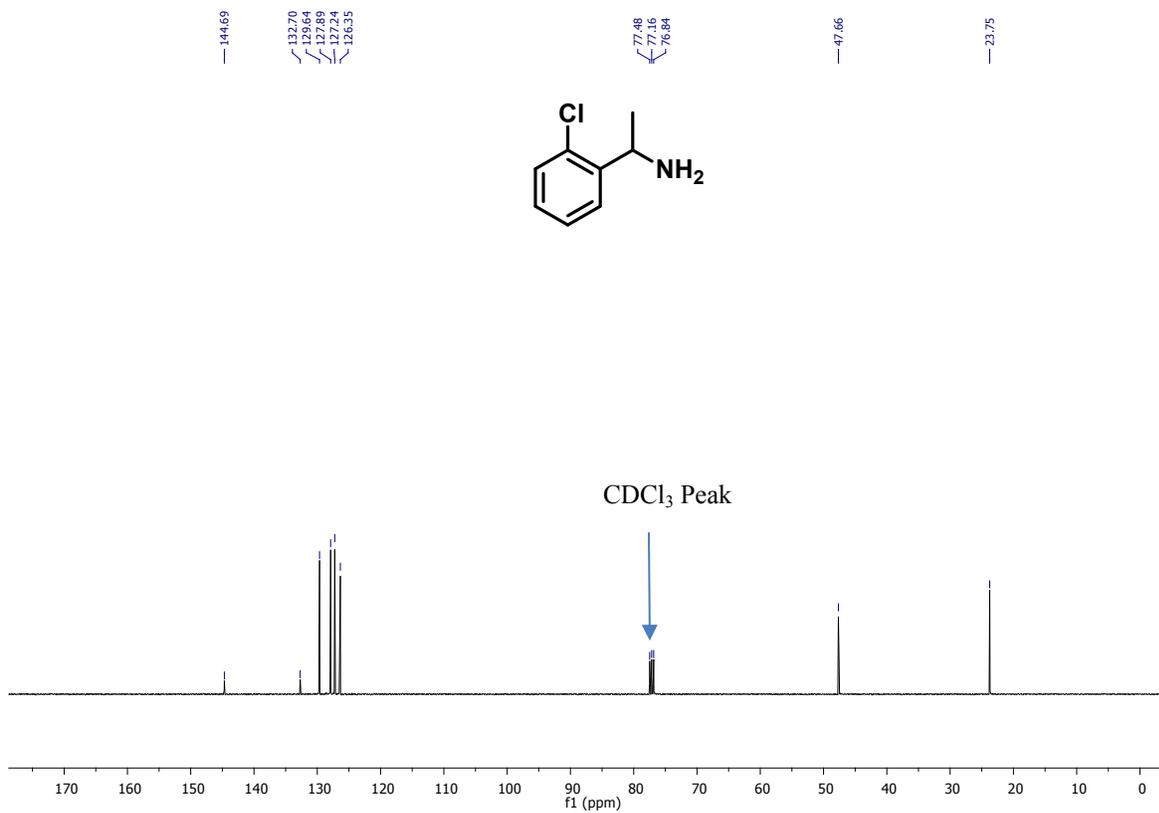


Figure S-34. ¹³C NMR spectrum of S-18 (CDCl₃, 101 MHz, 298 K)

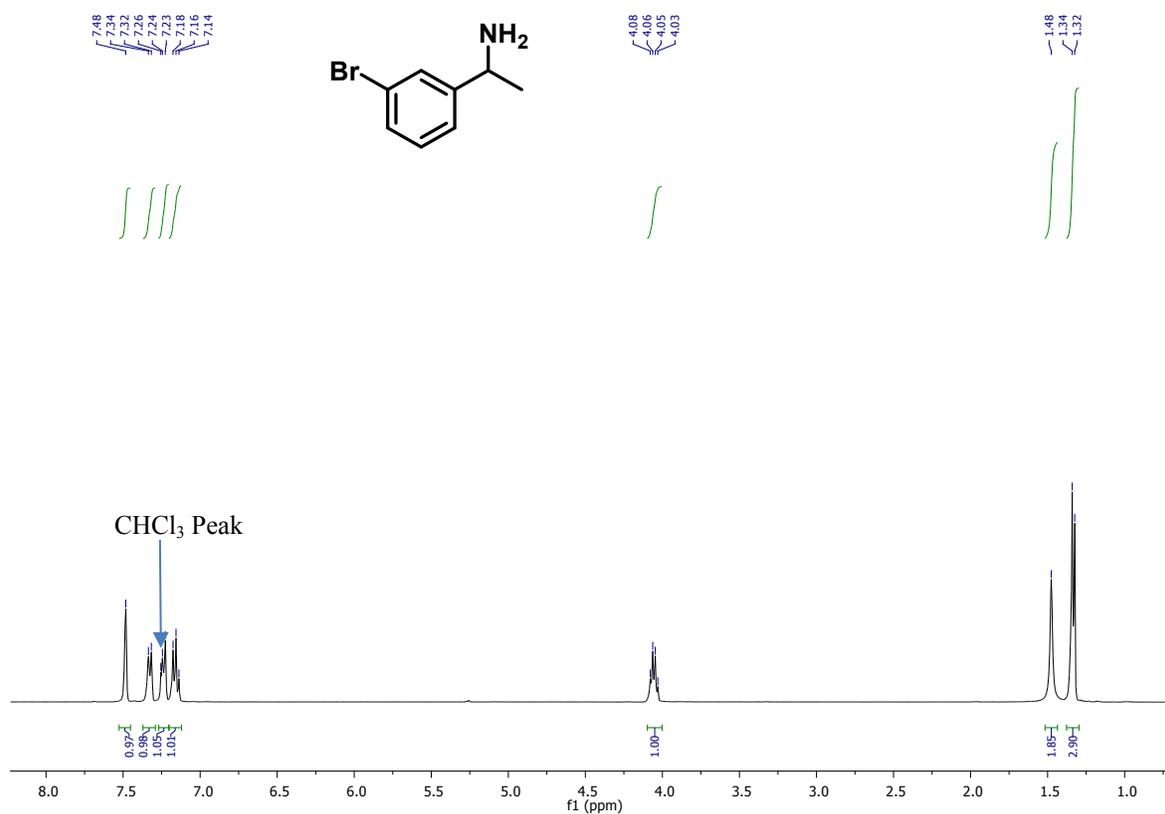


Figure S-35. ¹H NMR spectrum of S-19 (CDCl₃, 400 MHz, 298 K)

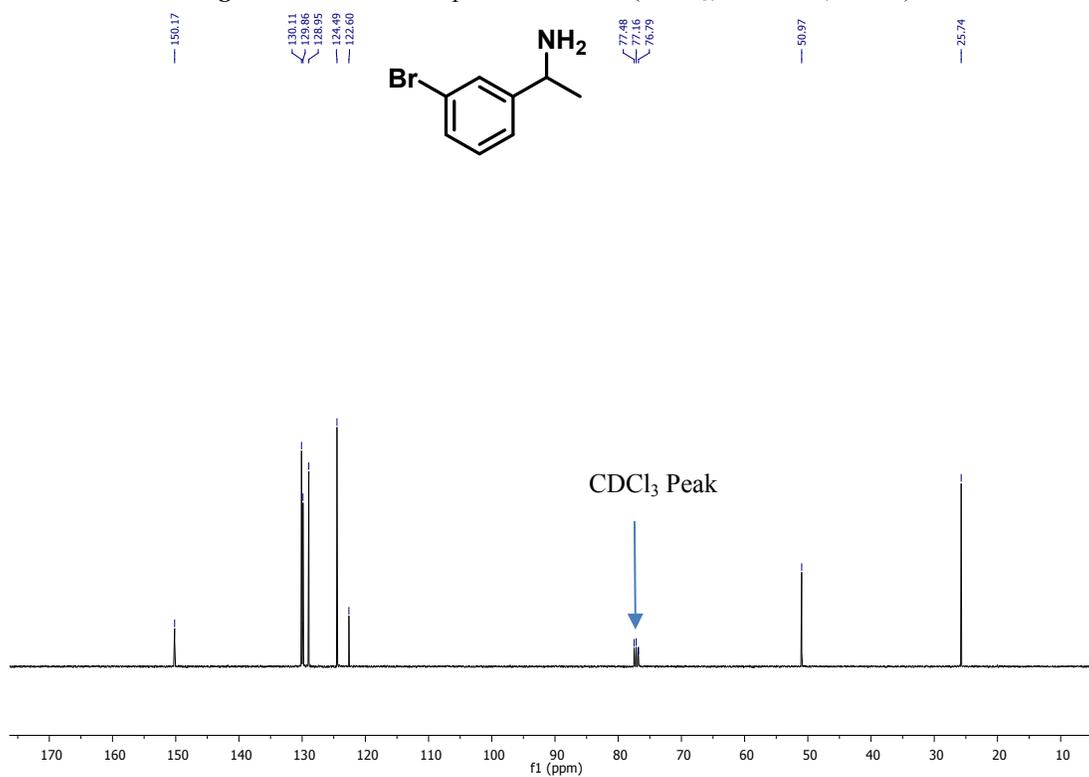


Figure S-36. ¹³C NMR spectrum of S-19 (CDCl₃, 101 MHz, 298 K)

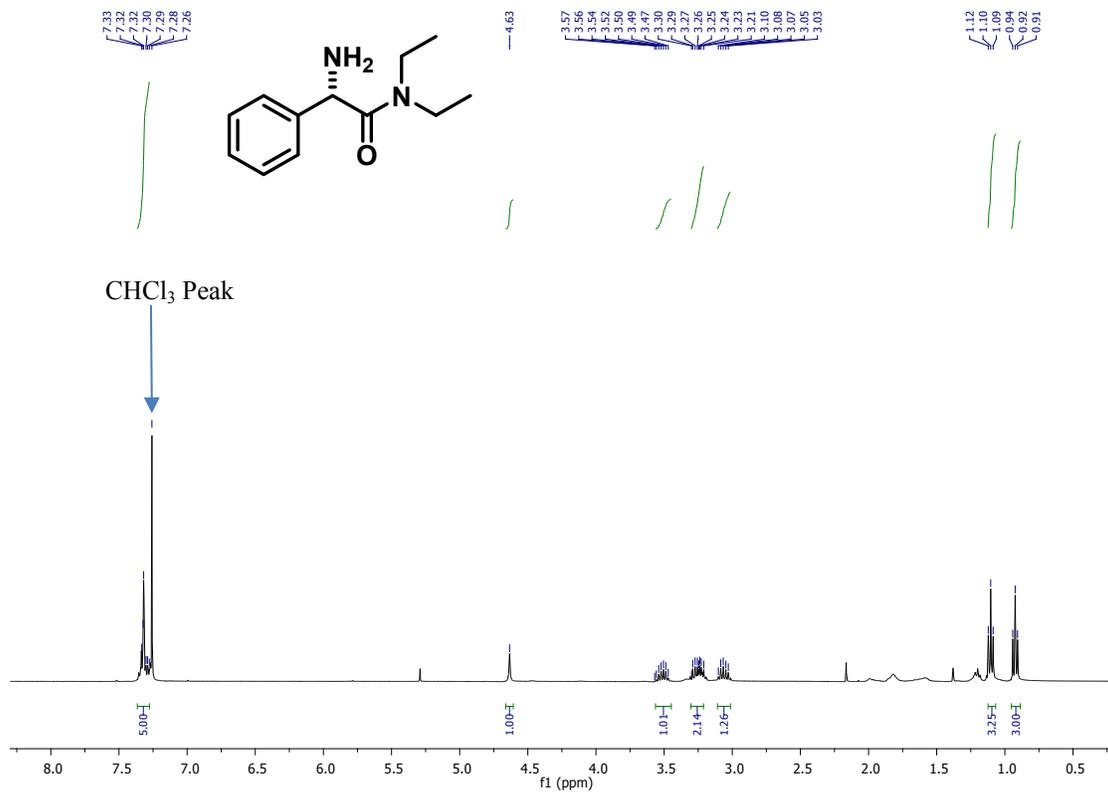


Figure S-37. ^1H NMR spectrum of S-20 (CDCl_3 , 400 MHz, 298 K)

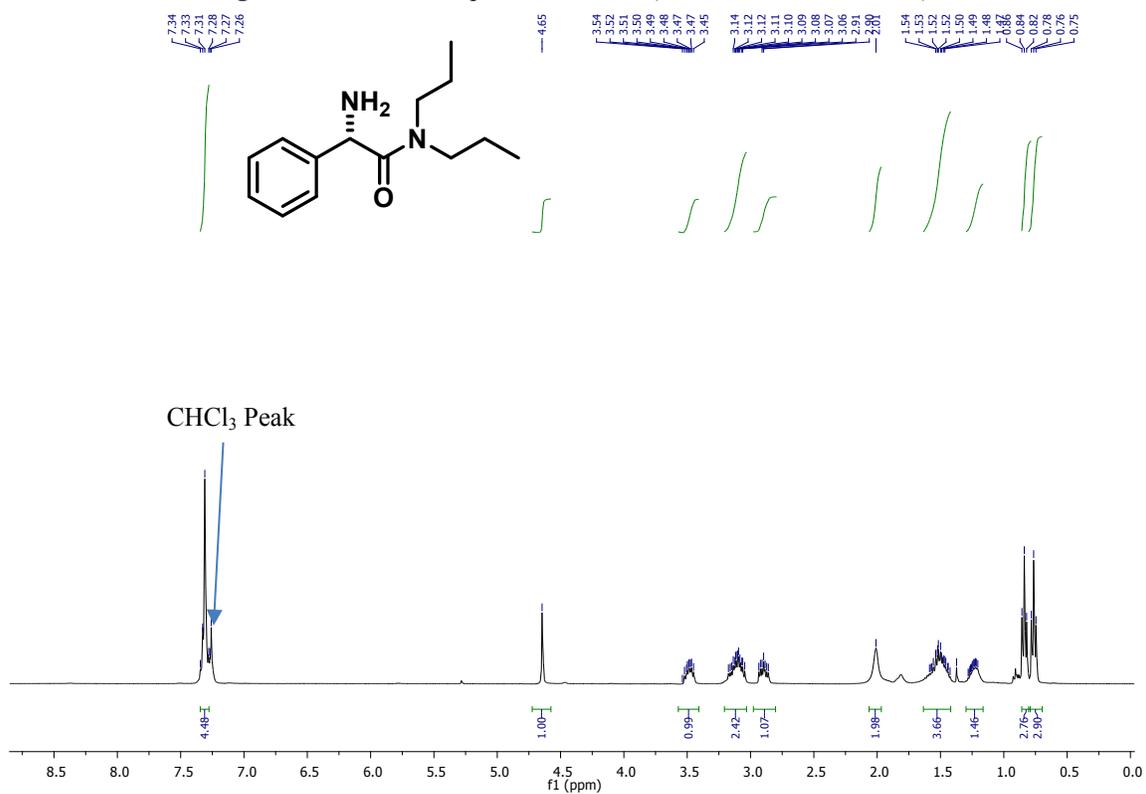


Figure S-38. ^1H NMR spectrum of S-21 (CDCl_3 , 400 MHz, 298 K)

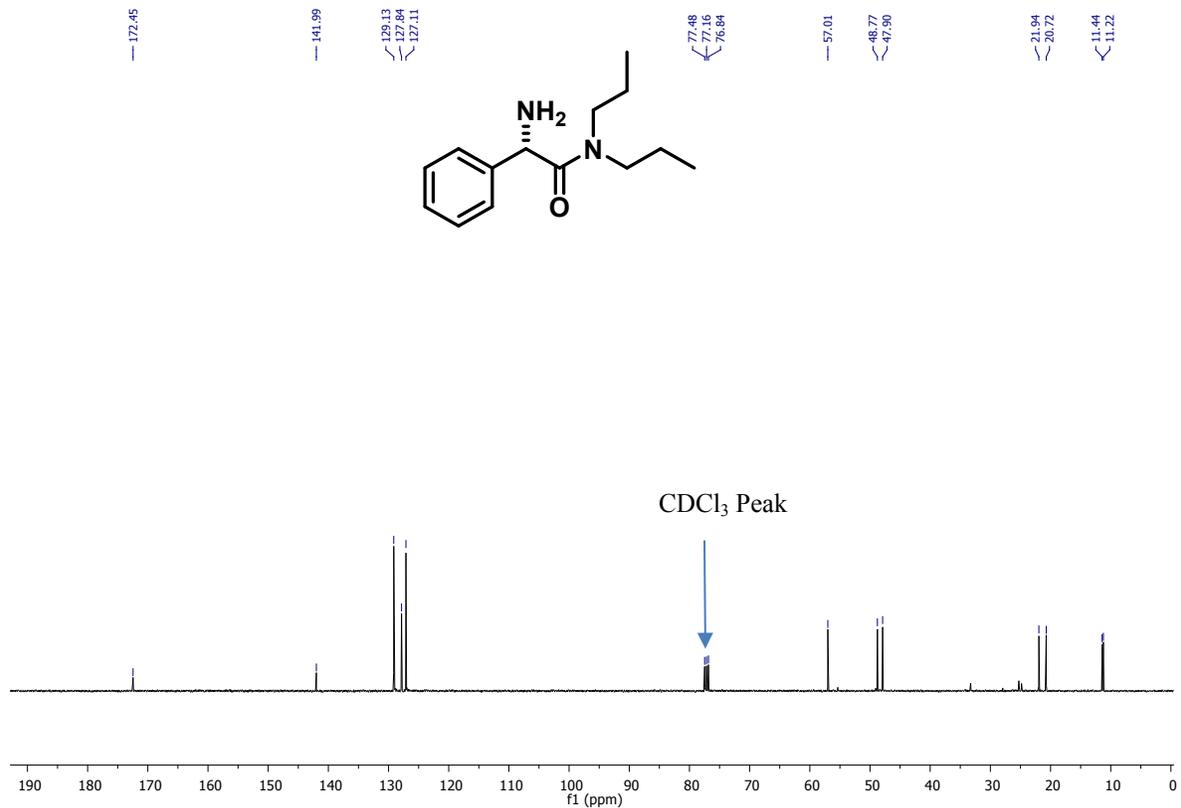


Figure S-39. ^{13}C NMR spectrum of S-21 (CDCl₃, 400 MHz, 298 K)

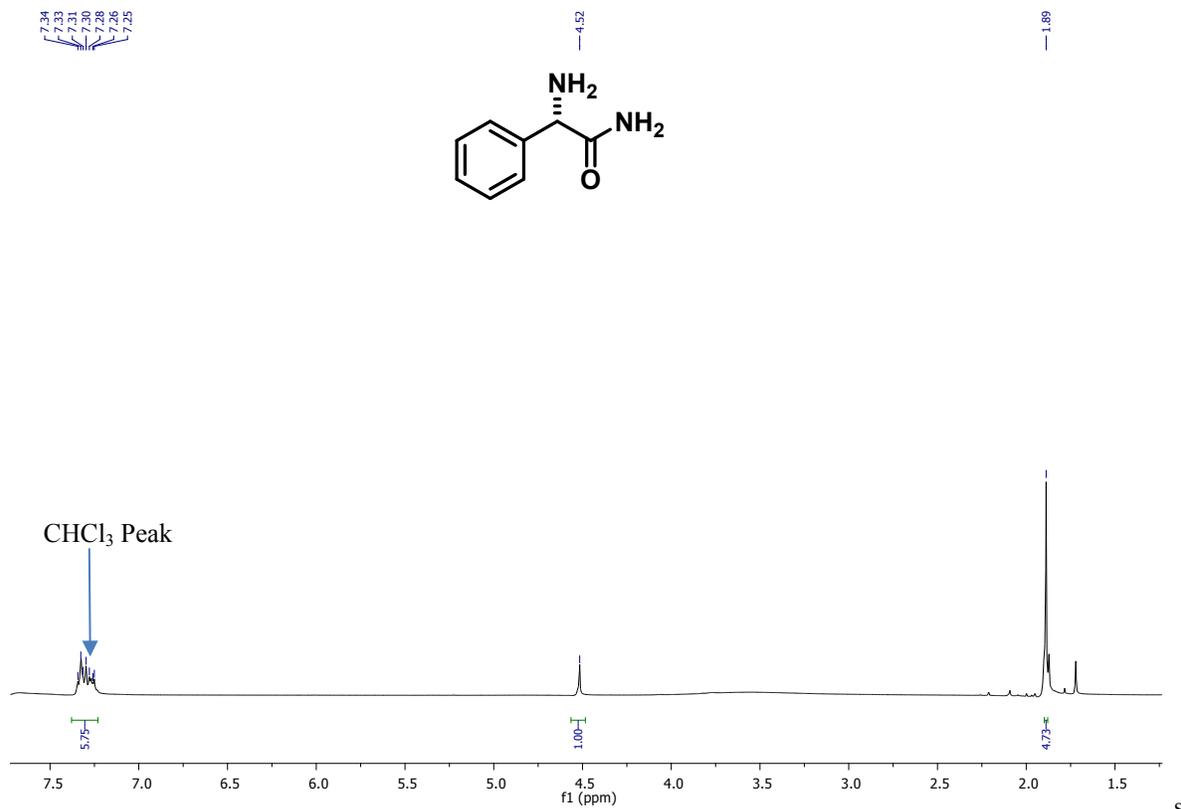


Figure S-40. ^1H NMR spectrum of S-22 (CDCl₃, 400 MHz, 298 K)

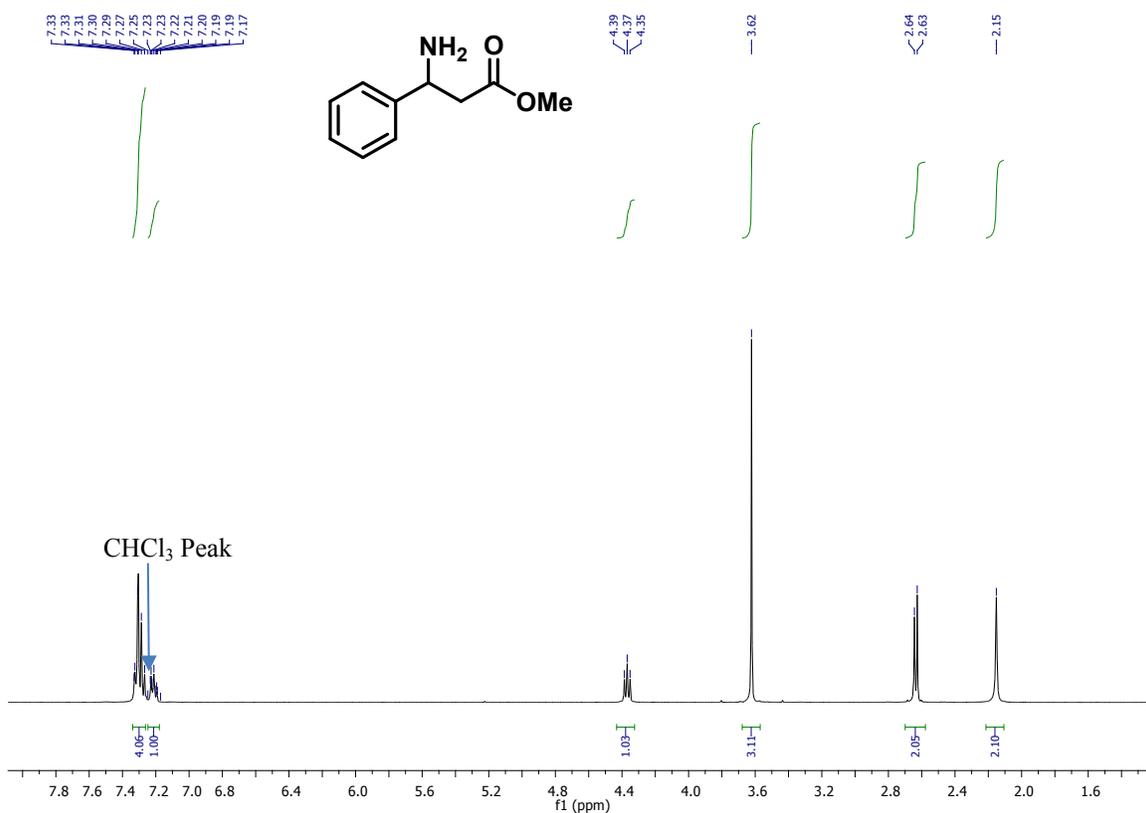


Figure S-41. ¹H NMR spectrum of S-23 (CDCl₃, 400 MHz, 298 K)

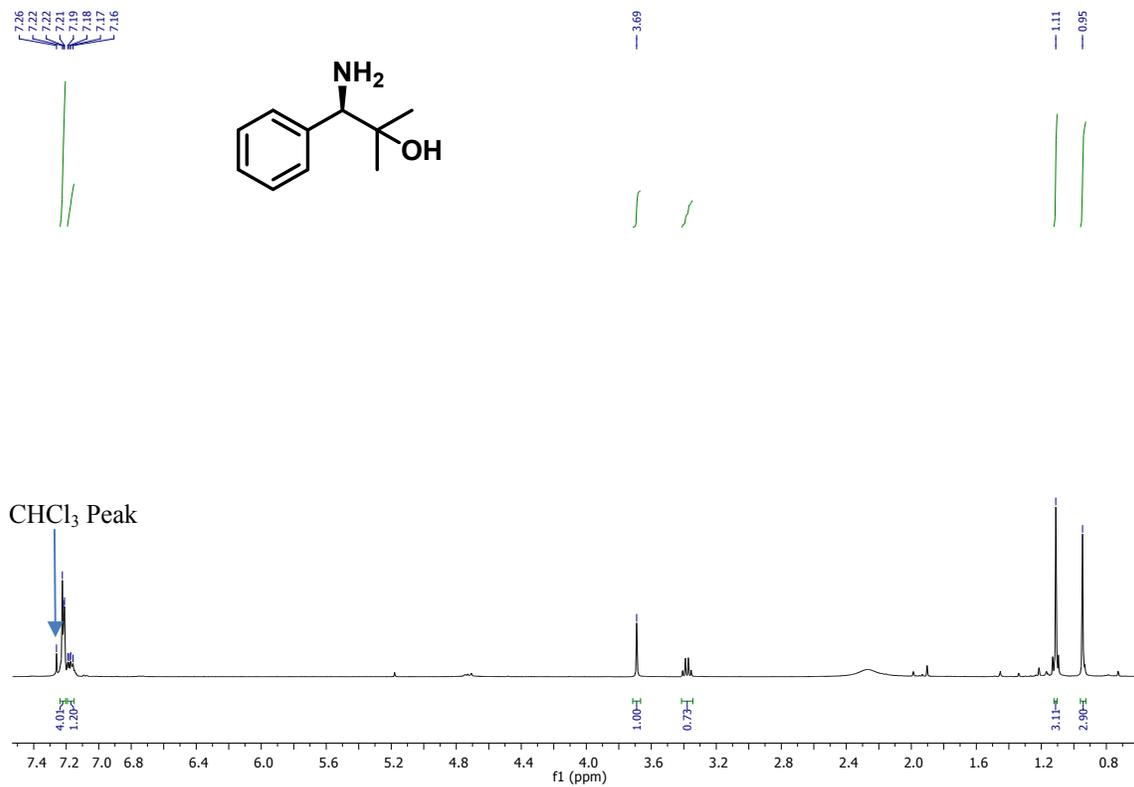
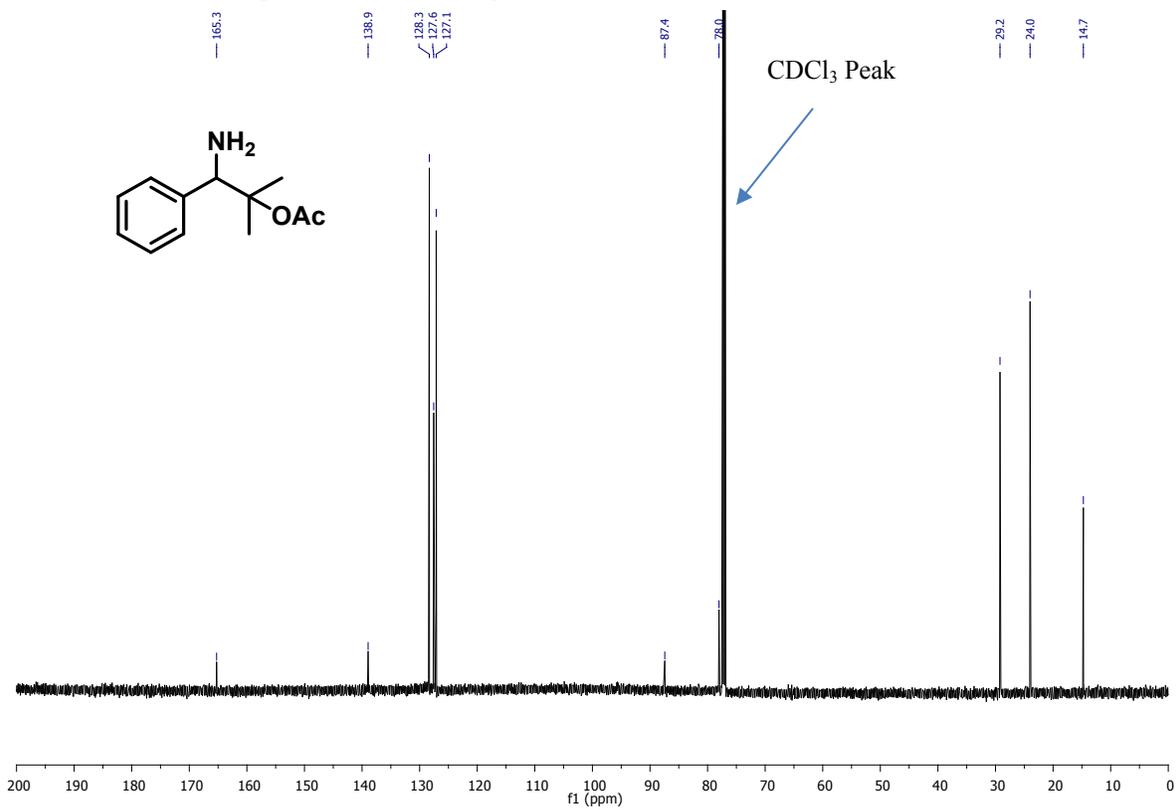
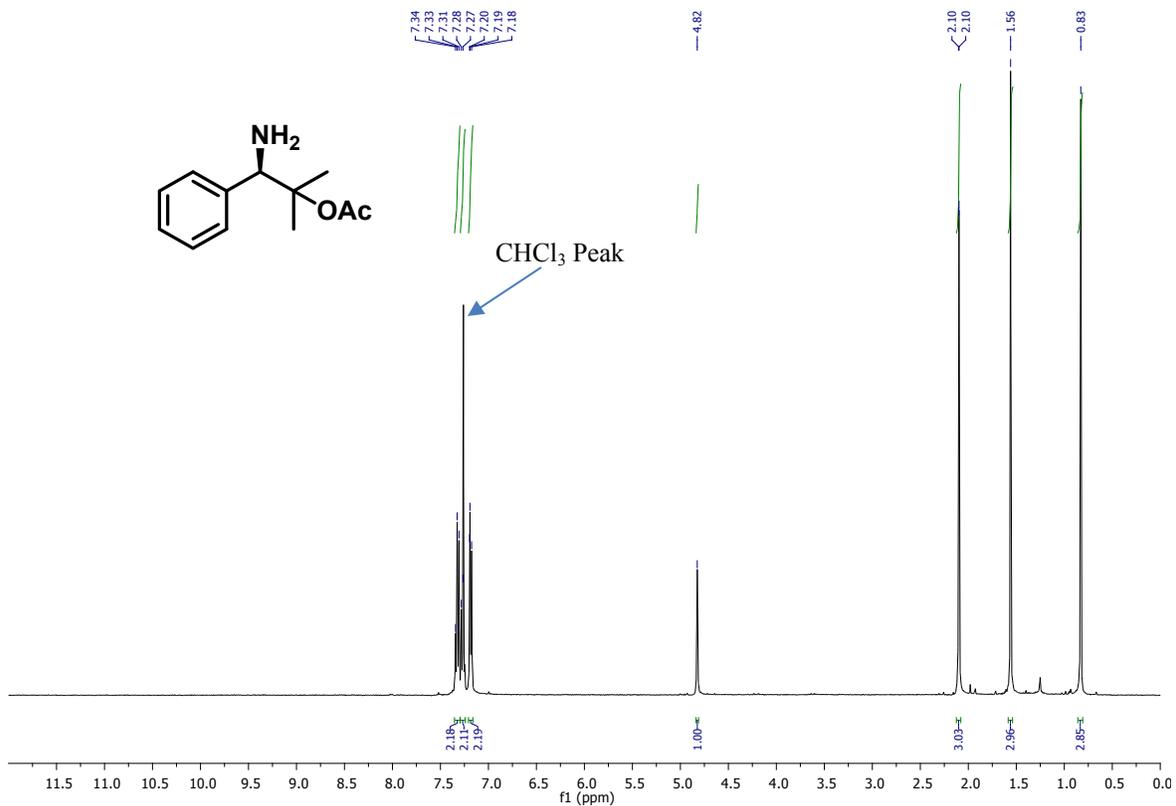


Figure S-42. ¹H NMR spectrum of S-24 (CDCl₃, 400 MHz, 298 K)



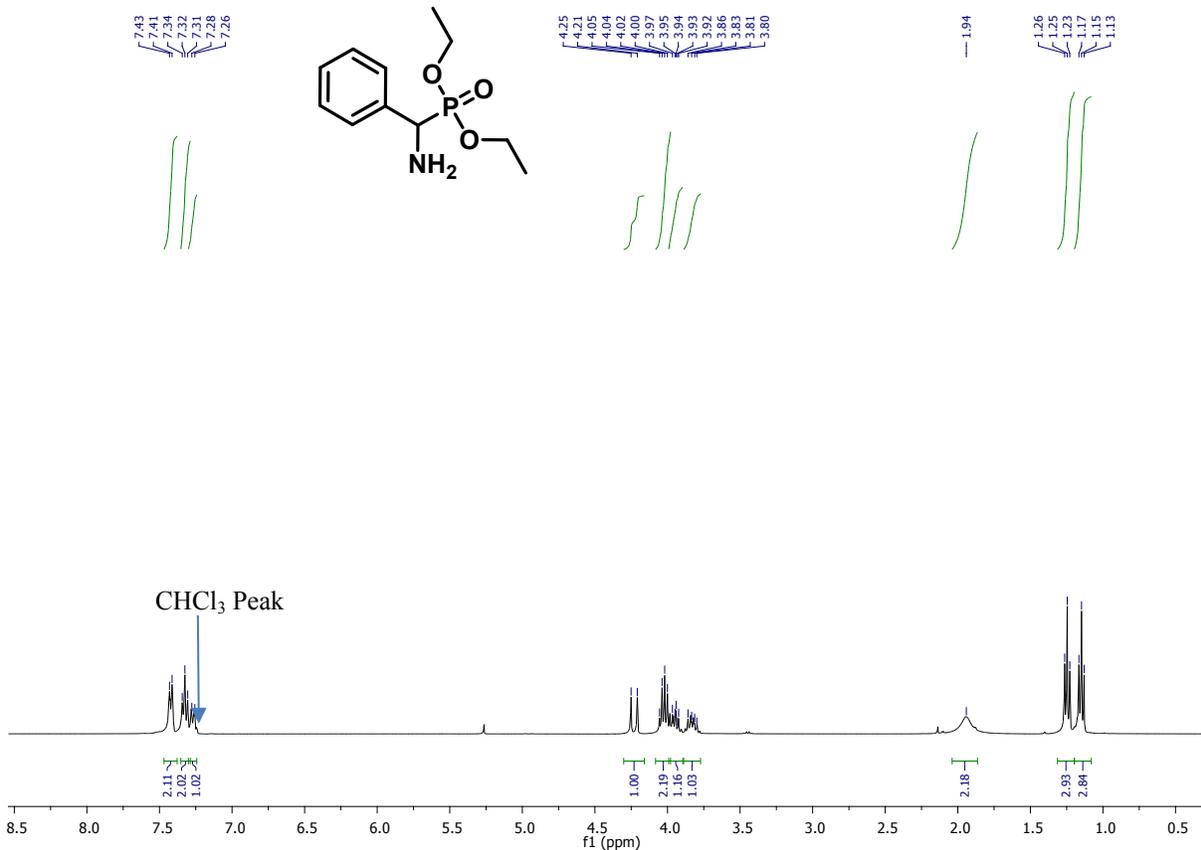


Figure S-45. ^1H NMR spectrum of S-26 (CDCl_3 , 400 MHz, 298 K)

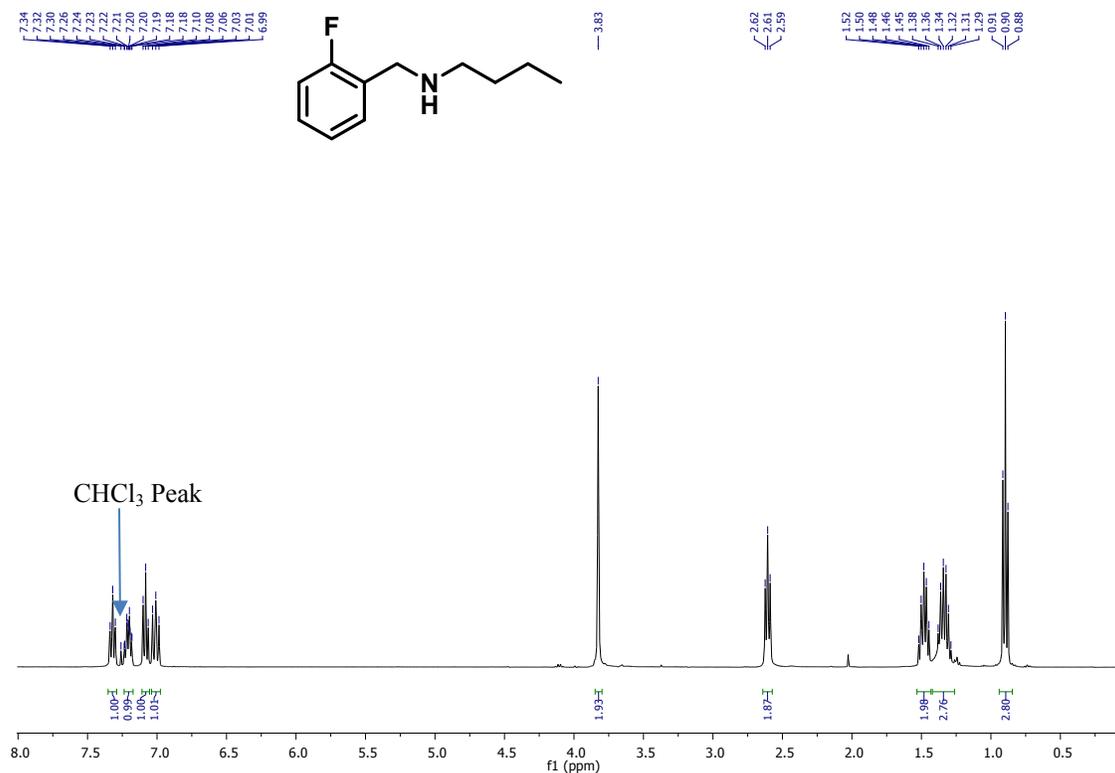


Figure S-46. ^1H NMR spectrum of S-27 (CDCl_3 , 400 MHz, 298 K)

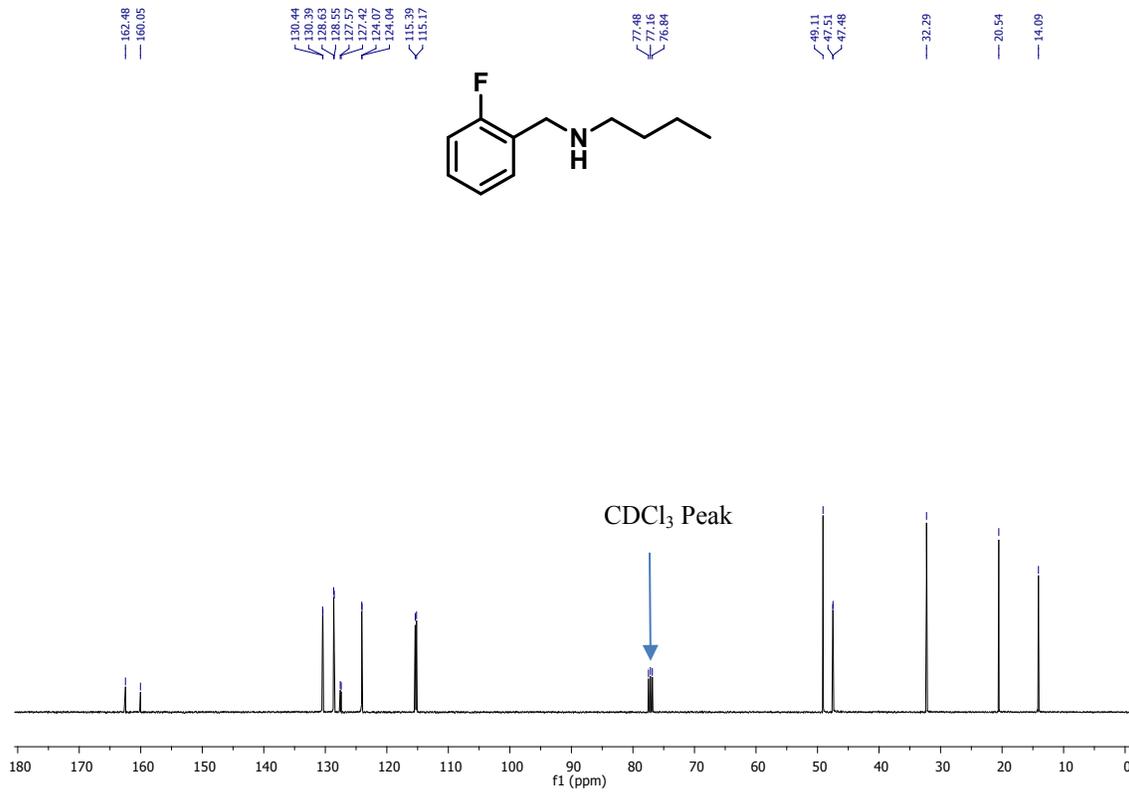


Figure S-47. ^{13}C NMR spectrum of S-27 (CDCl₃, 101 MHz, 298 K)

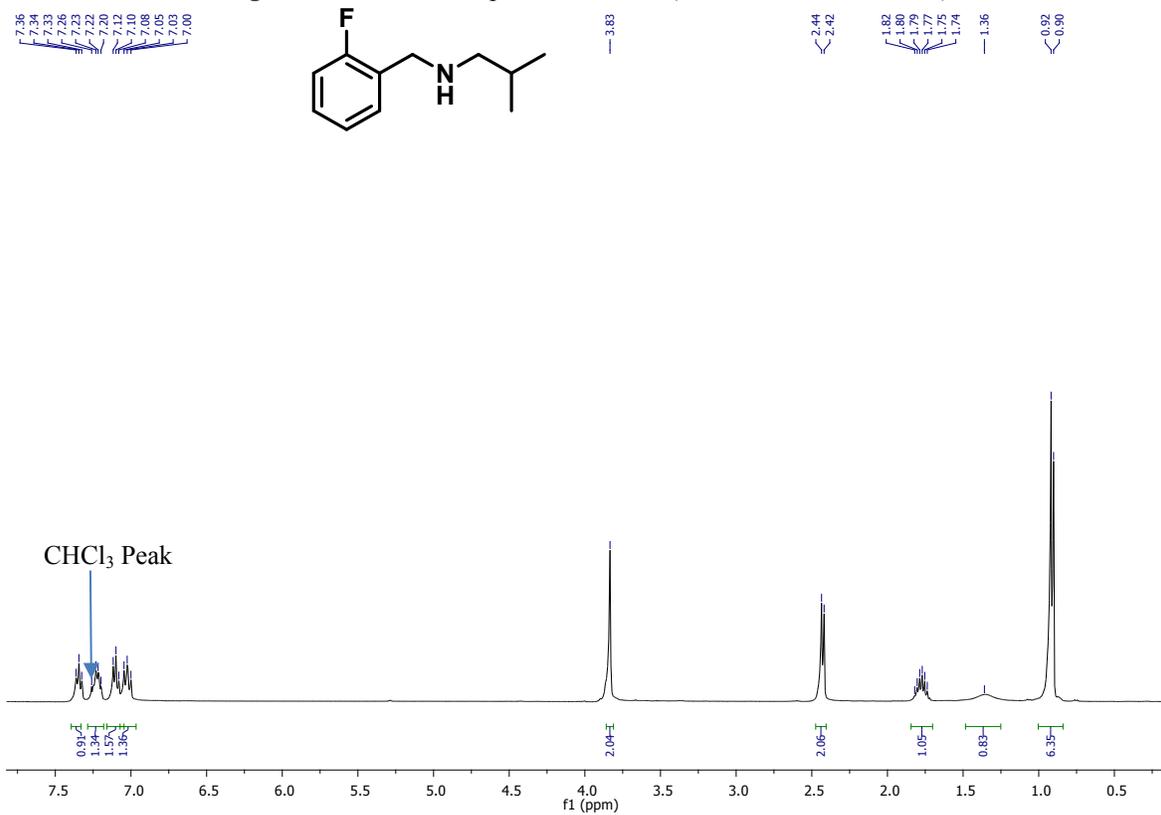
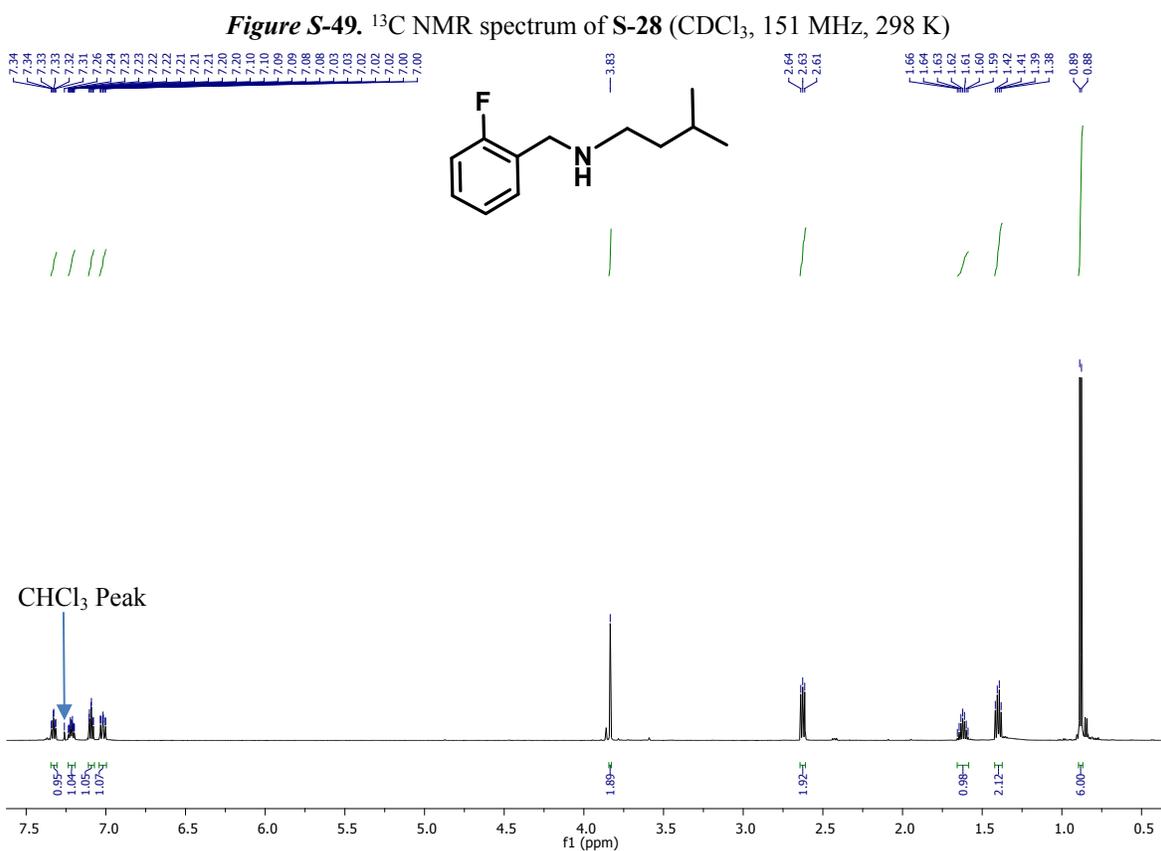
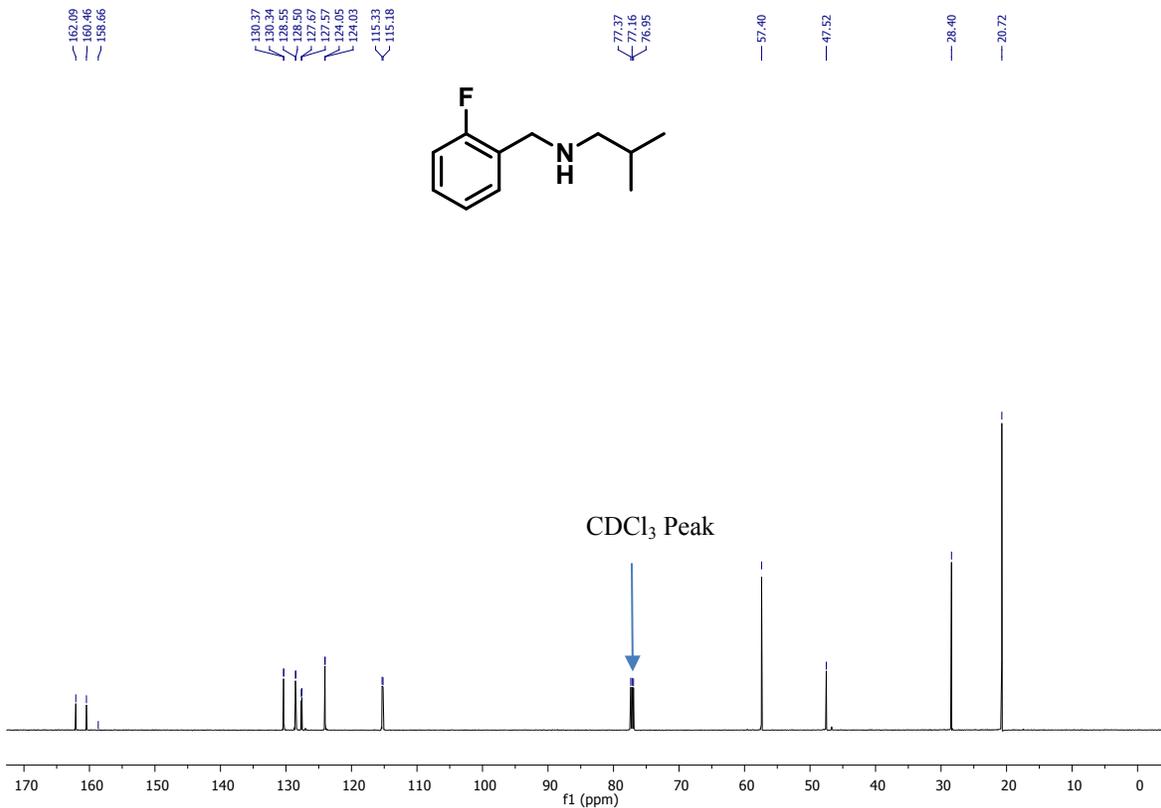


Figure S-48. ^1H NMR spectrum of S-28 (CDCl₃, 400 MHz, 298 K)



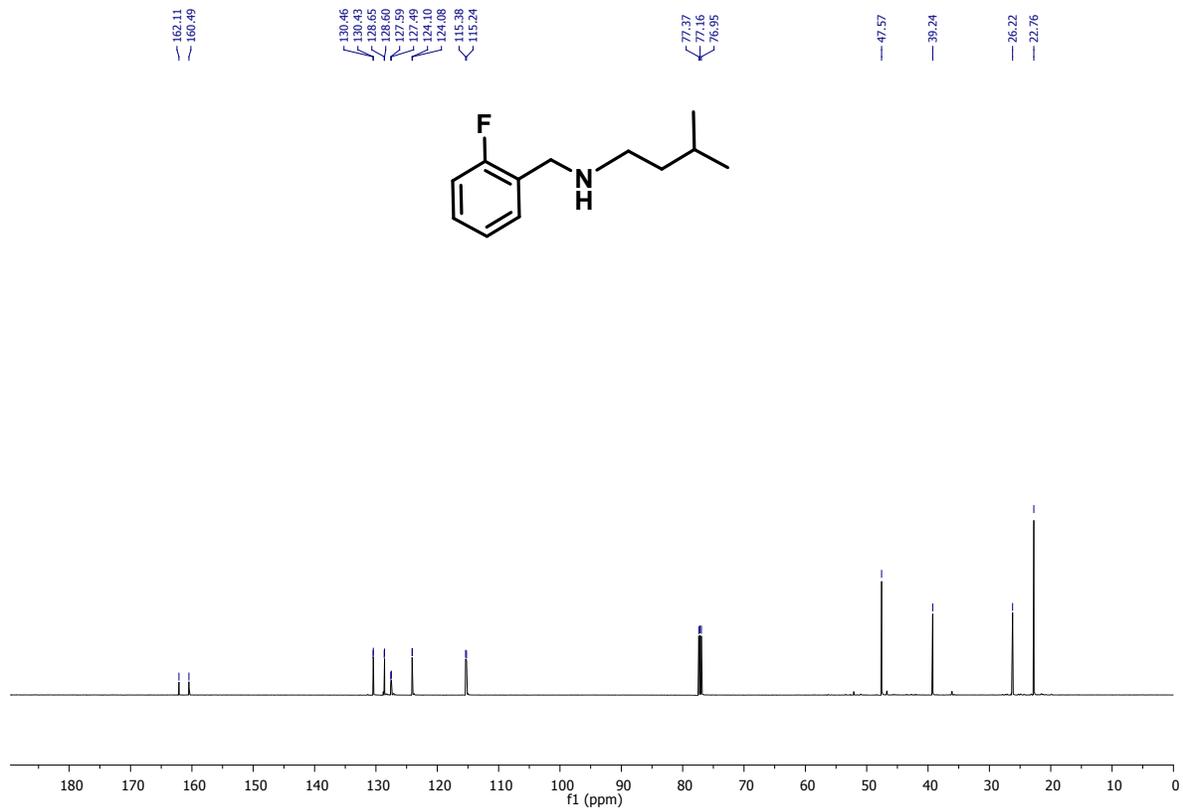


Figure S-51. ^{13}C NMR spectrum of S-29 (CDCl₃, 151 MHz, 298 K)

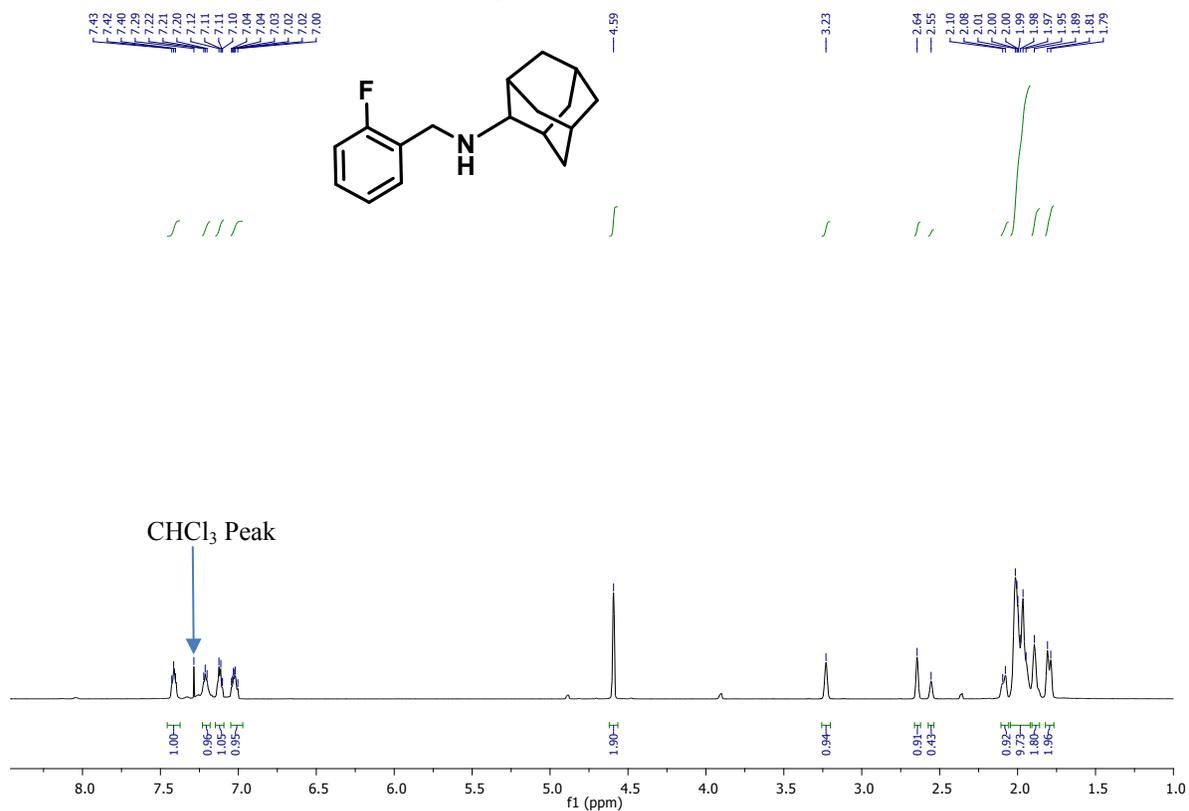


Figure S-52. ^1H NMR spectrum of S-30 (CDCl₃, 600 MHz, 298 K)

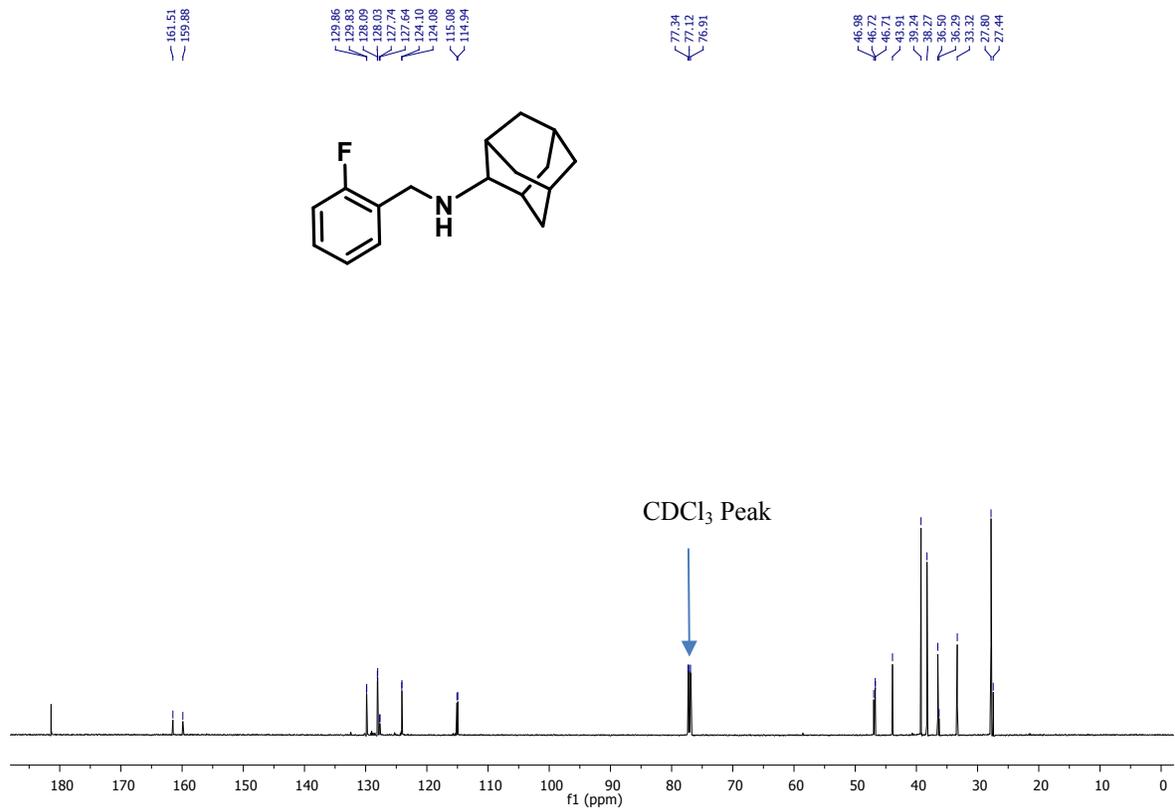


Figure S-53. ^{13}C NMR spectrum of S-30 (CDCl₃, 151 MHz, 298 K)

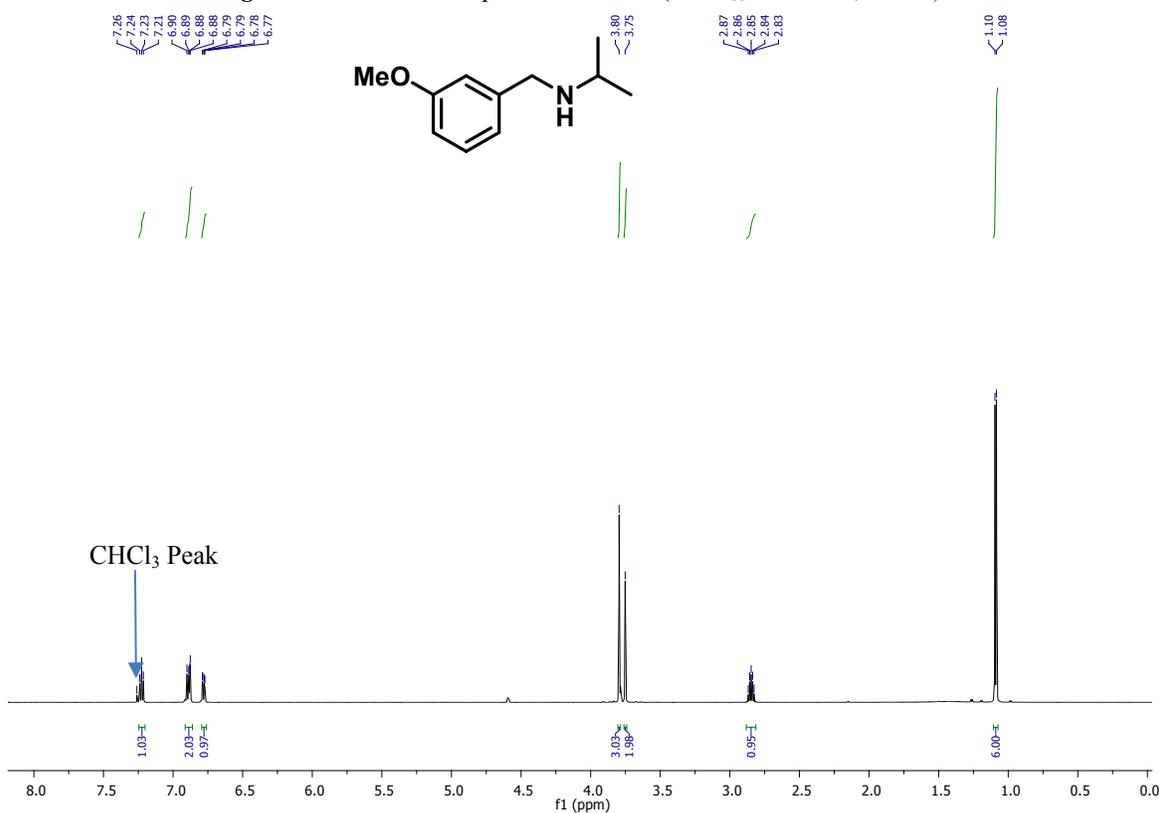


Figure S-54. ^1H NMR spectrum of S-31 (CDCl₃, 600 MHz, 298 K)

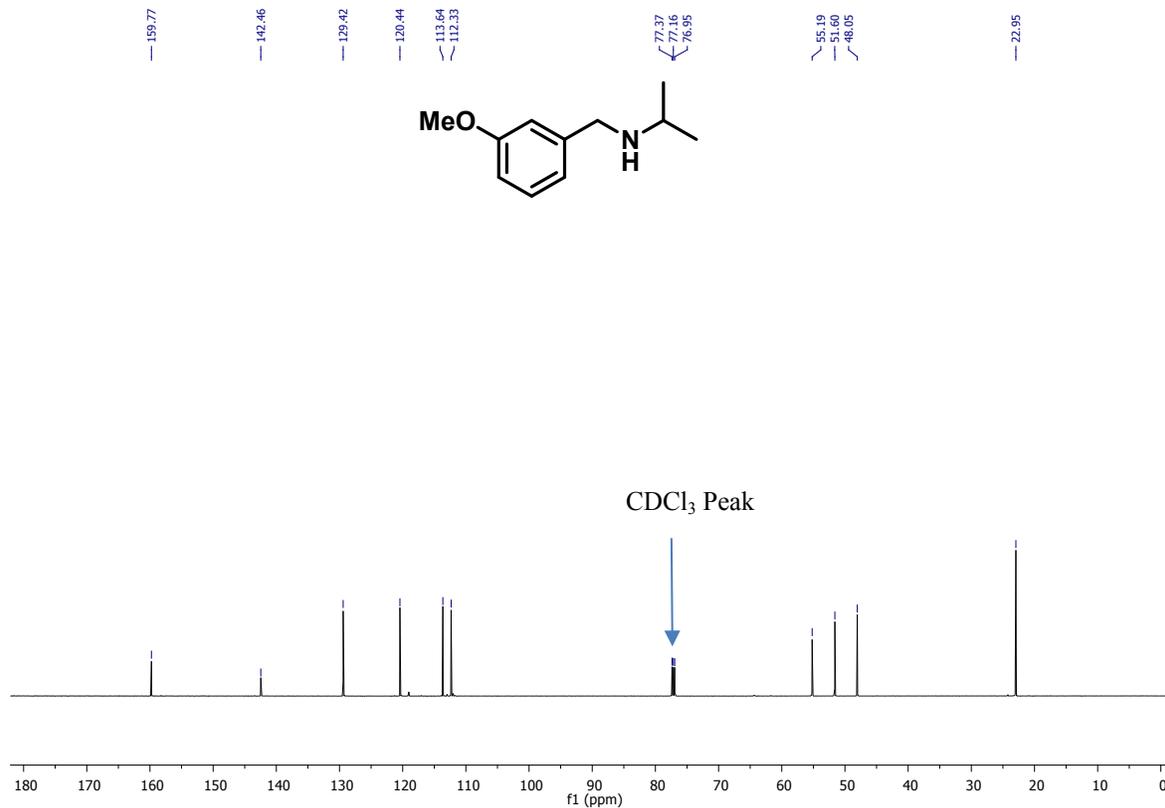


Figure S-55. ¹³C NMR spectrum of S-31 (CDCl₃, 151 MHz, 298 K)

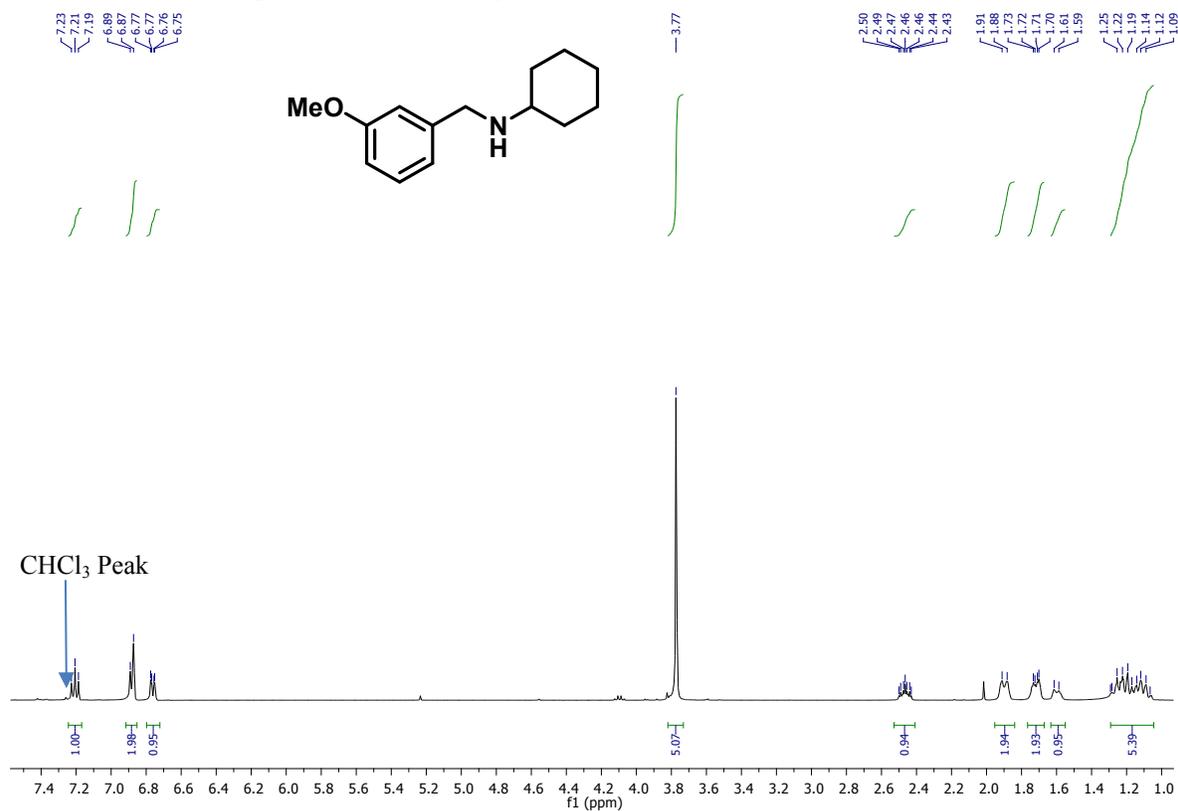


Figure S-56. ¹H NMR spectrum of S-32 (CDCl₃, 400 MHz, 298 K)

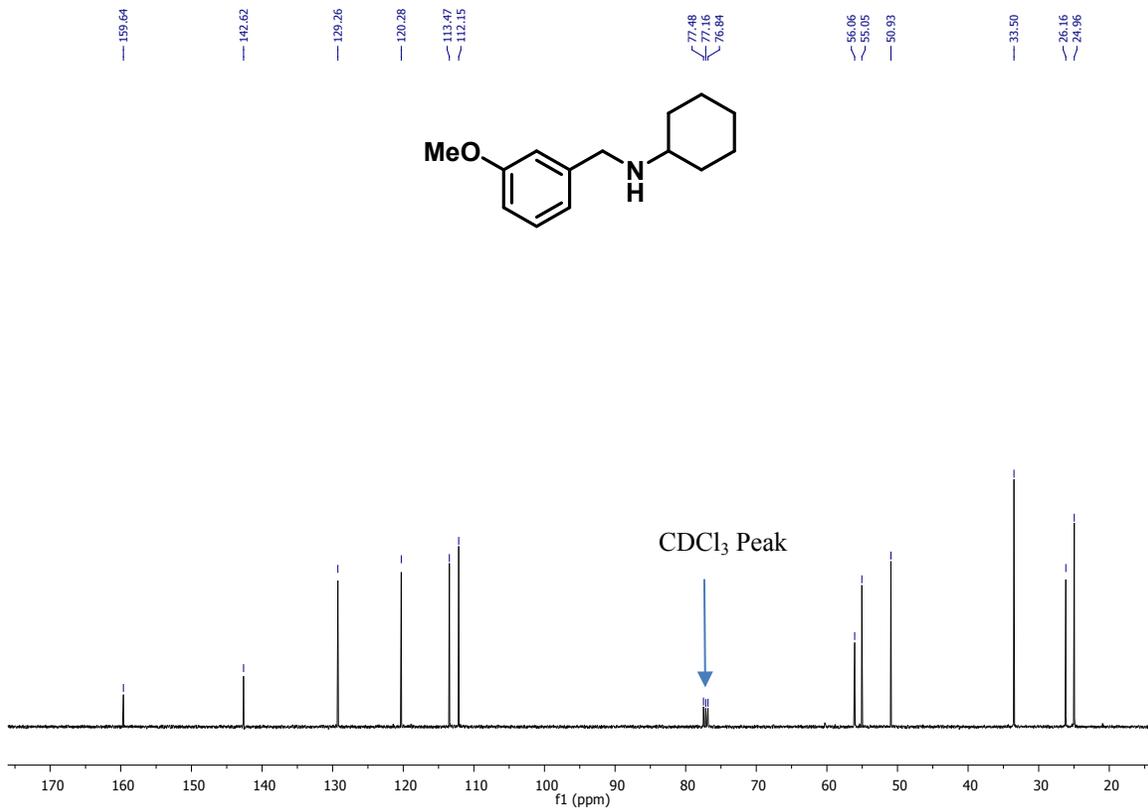


Figure S-57. ^{13}C NMR spectrum of S-32 (CDCl₃, 101 MHz, 298 K)

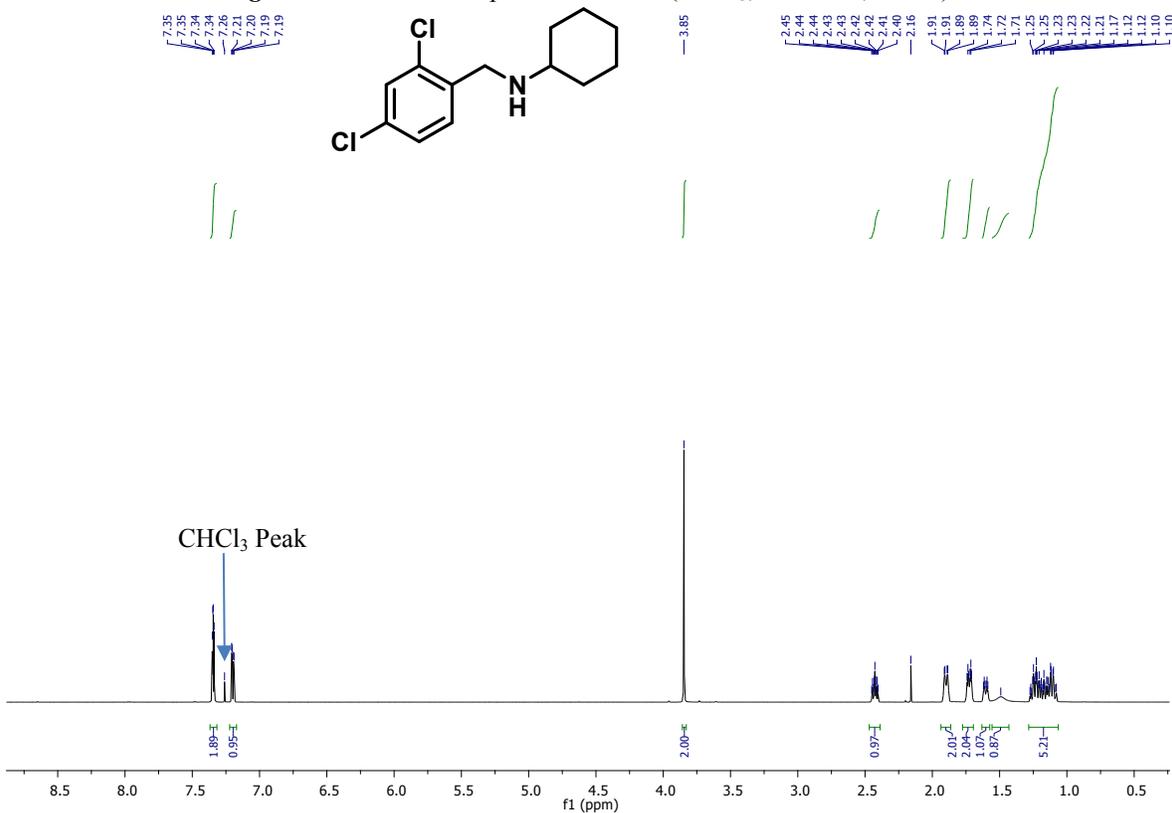


Figure S-58. ^1H NMR spectrum of S-33 (CDCl₃, 600 MHz, 298 K)

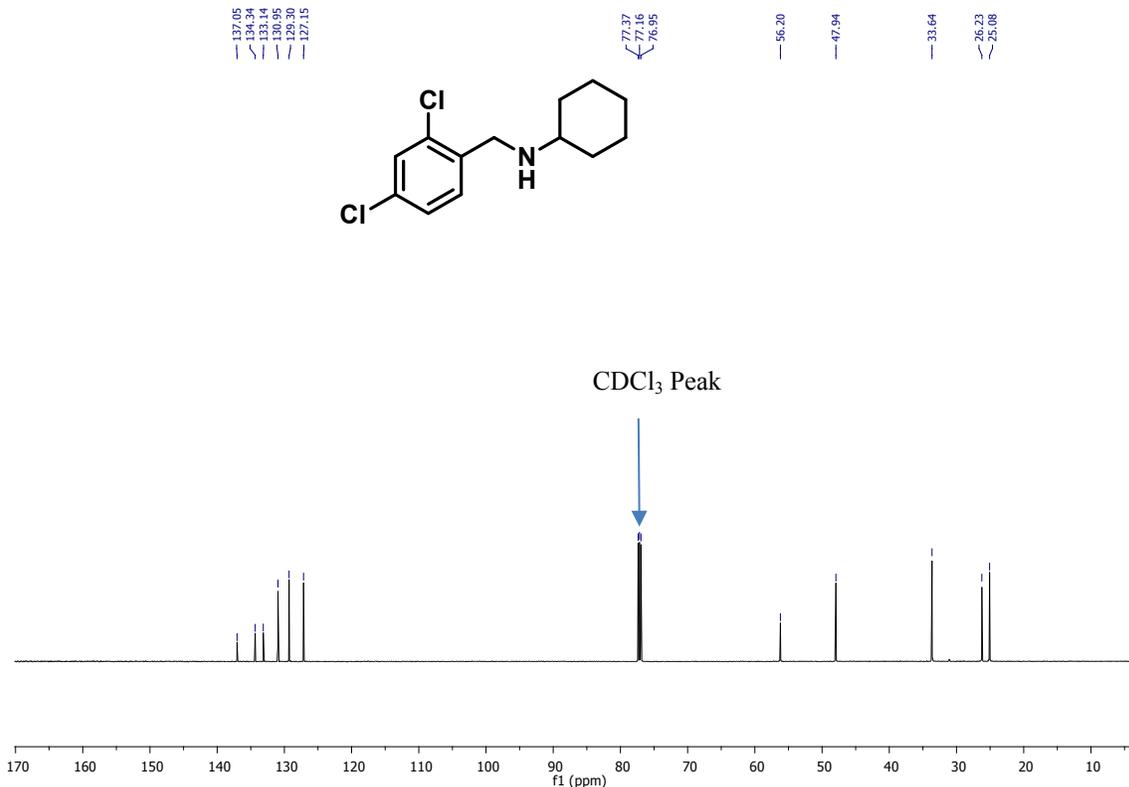


Figure S-59. ^{13}C NMR spectrum of S-33 (CDCl₃, 151 MHz, 298 K)

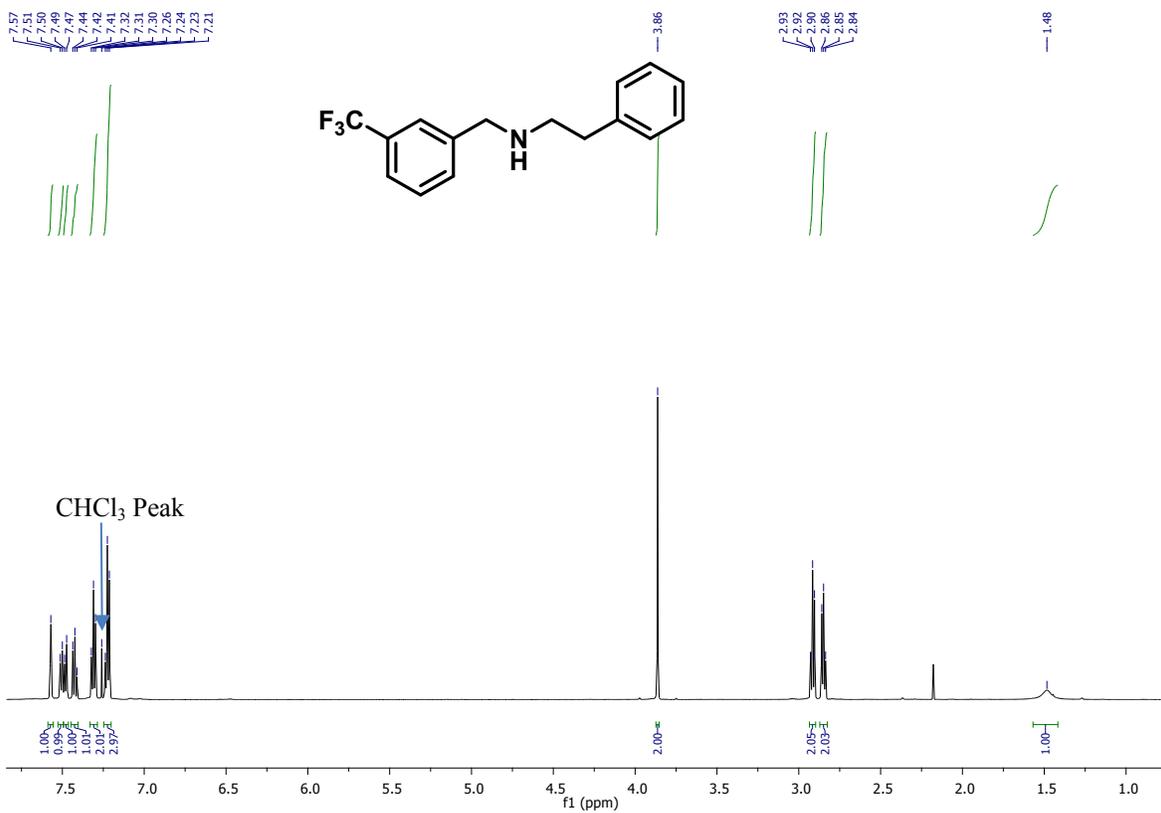


Figure S-60. ^1H NMR spectrum of S-34 (CDCl₃, 600 MHz, 298 K)

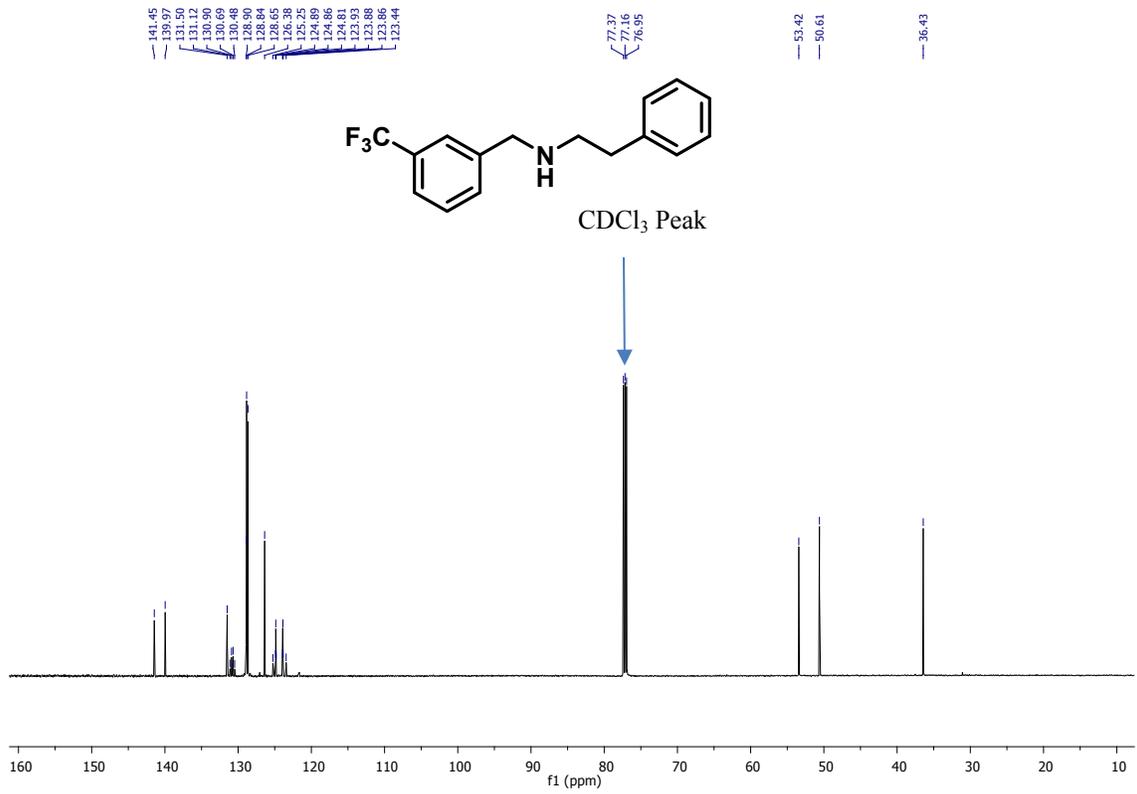


Figure S-61. ^{13}C NMR spectrum of S-34 (CDCl₃, 151 MHz, 298 K)

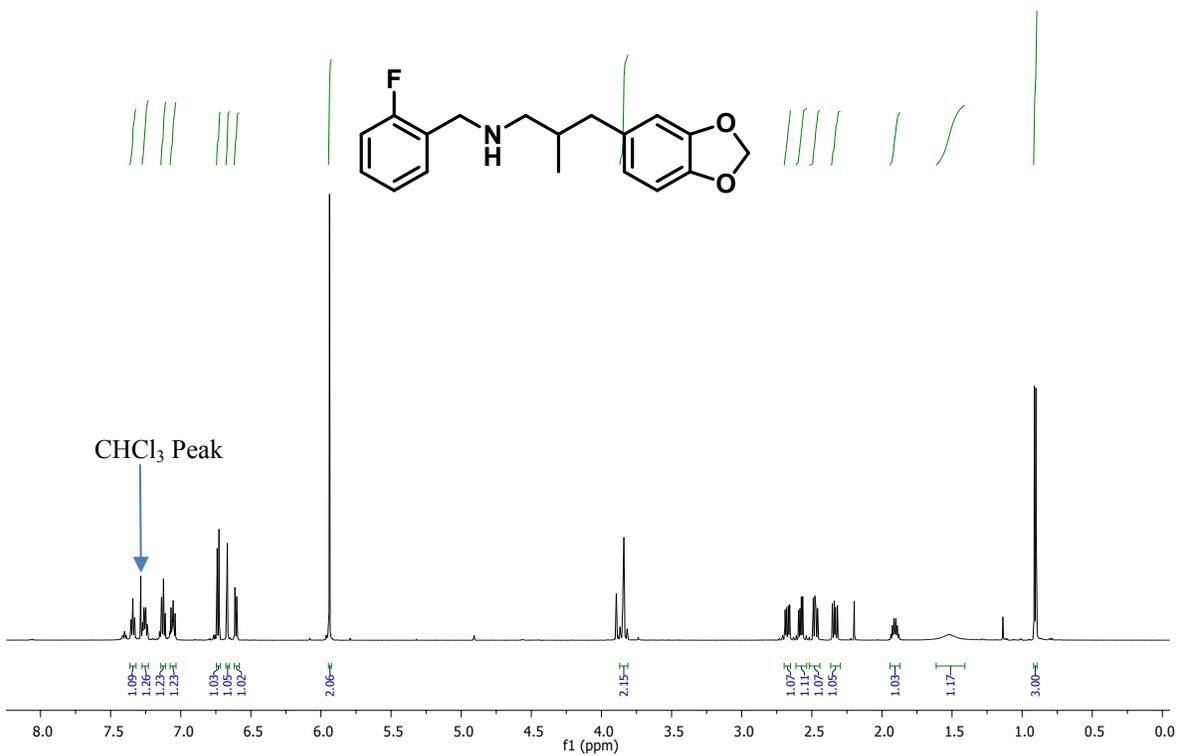


Figure S-62. ^1H NMR spectrum of S-35 (CDCl₃, 600 MHz, 298 K)

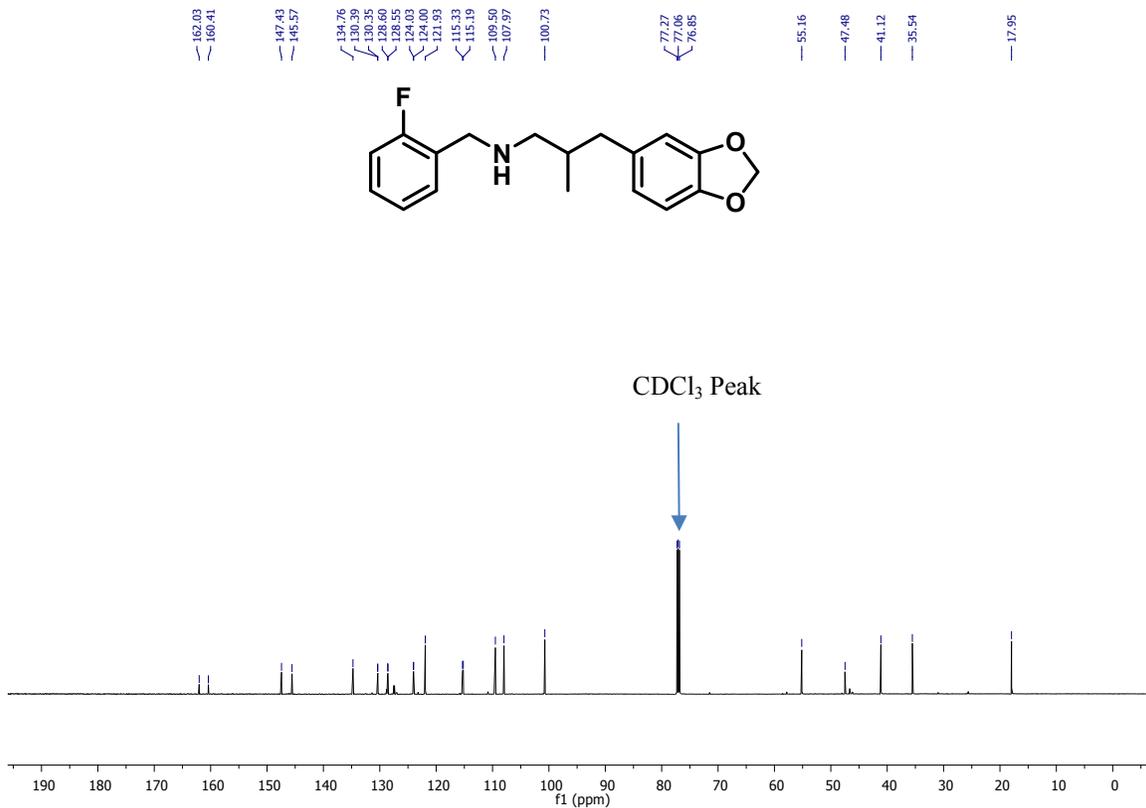


Figure S-63. ^{13}C NMR spectrum of S-35 (CDCl₃, 151 MHz, 298 K)

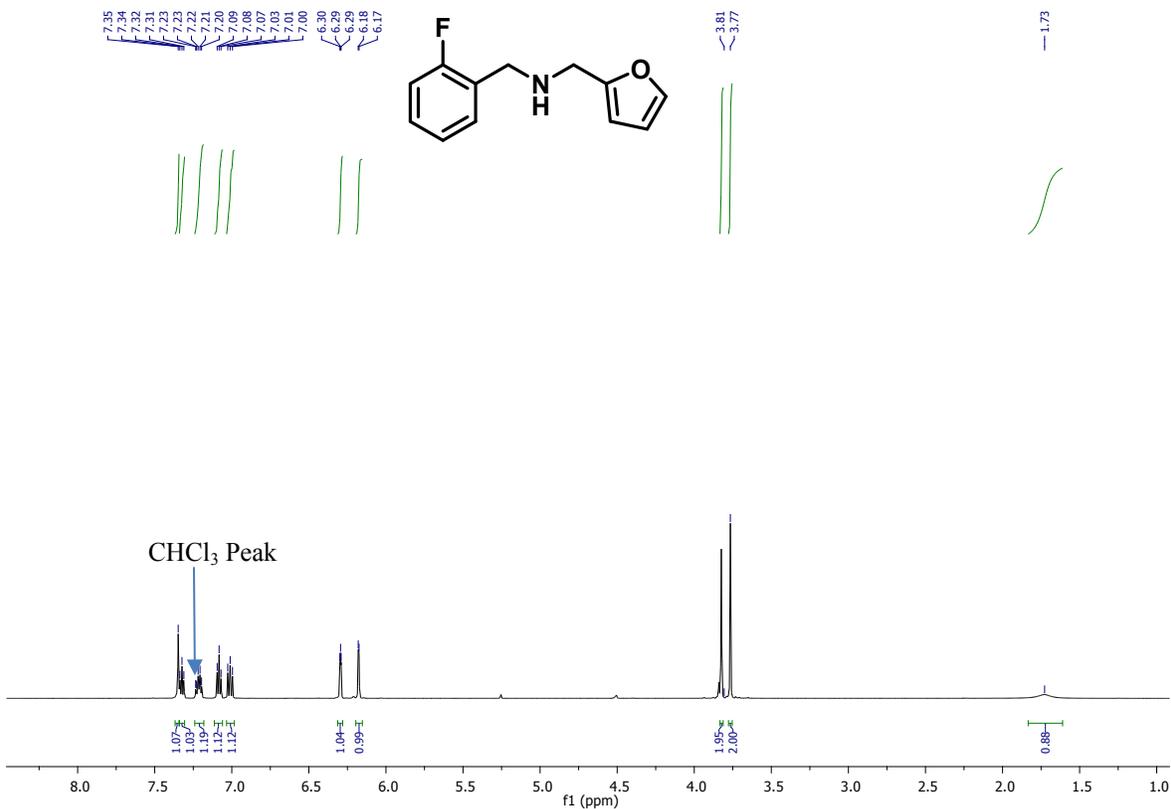


Figure S-64. ^1H NMR spectrum of S-36 (CDCl₃, 600 MHz, 298 K)

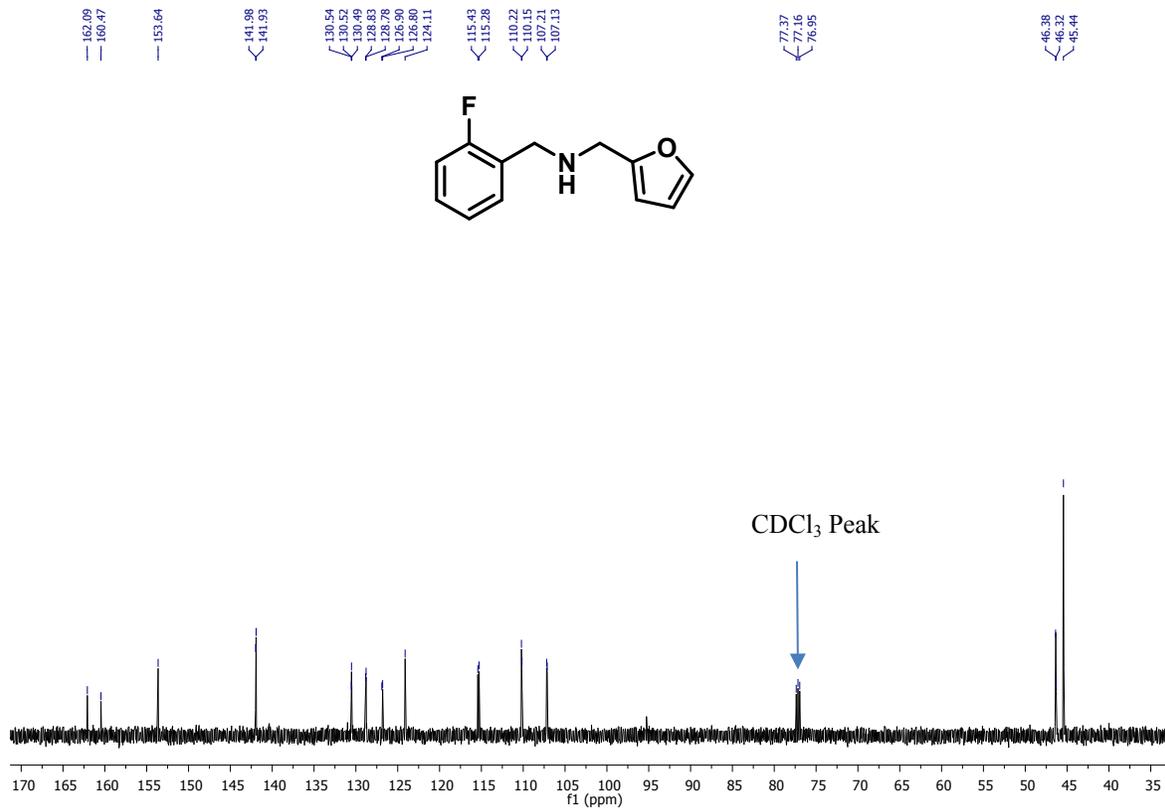


Figure S-65. ^{13}C NMR spectrum of S-36 (CDCl₃, 101 MHz, 298 K)

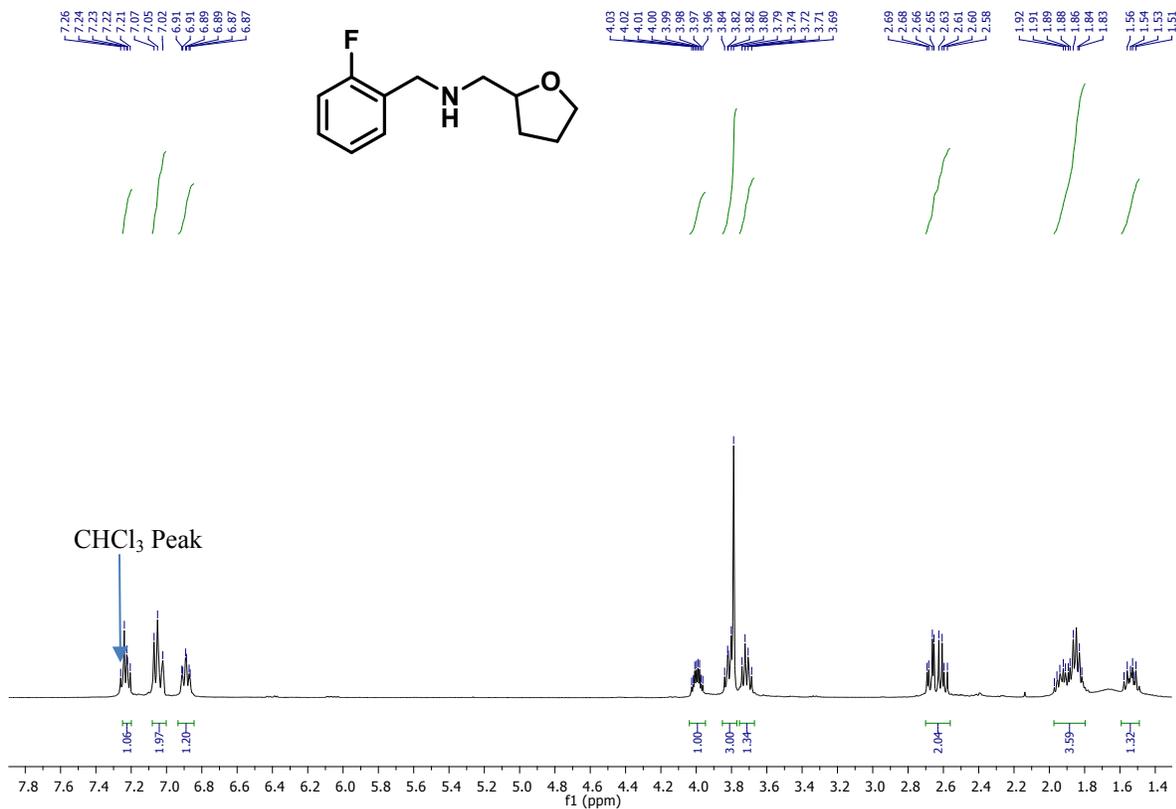


Figure S-66. ^1H NMR spectrum of S-37 (CDCl₃, 400 MHz, 298 K)

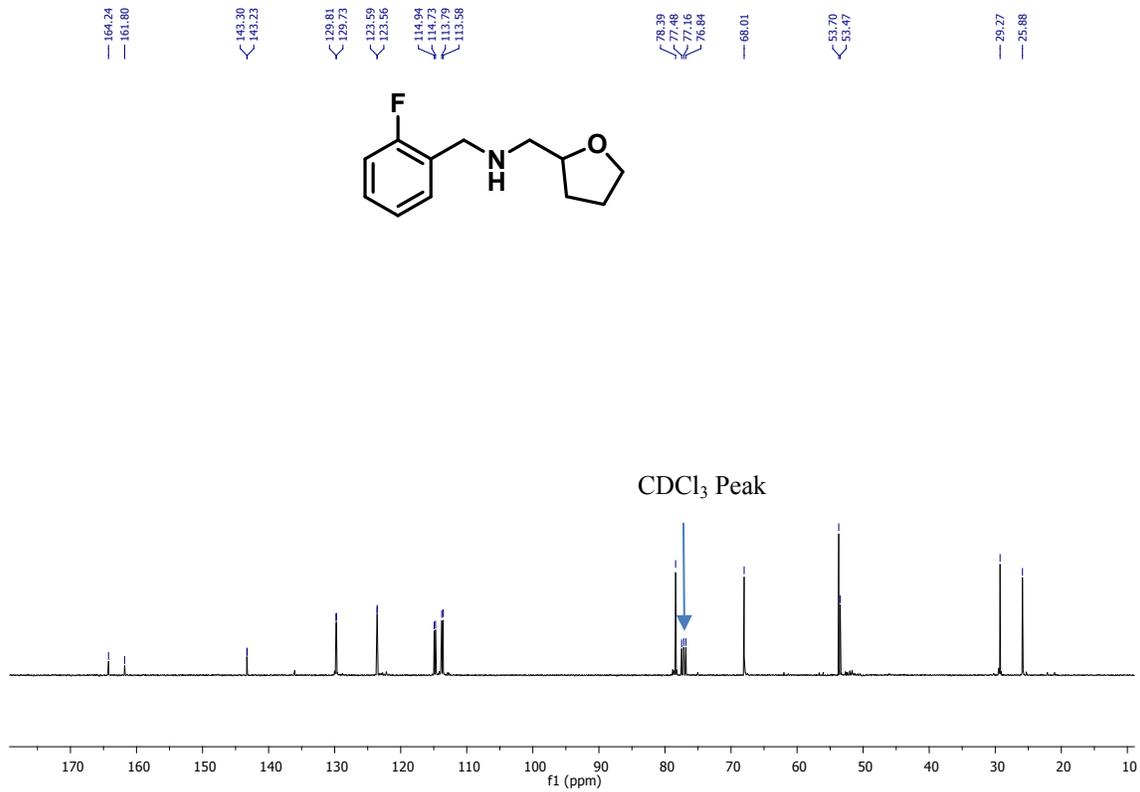


Figure S-67. ^{13}C NMR spectrum of S-37 (CDCl₃, 151 MHz, 298 K)

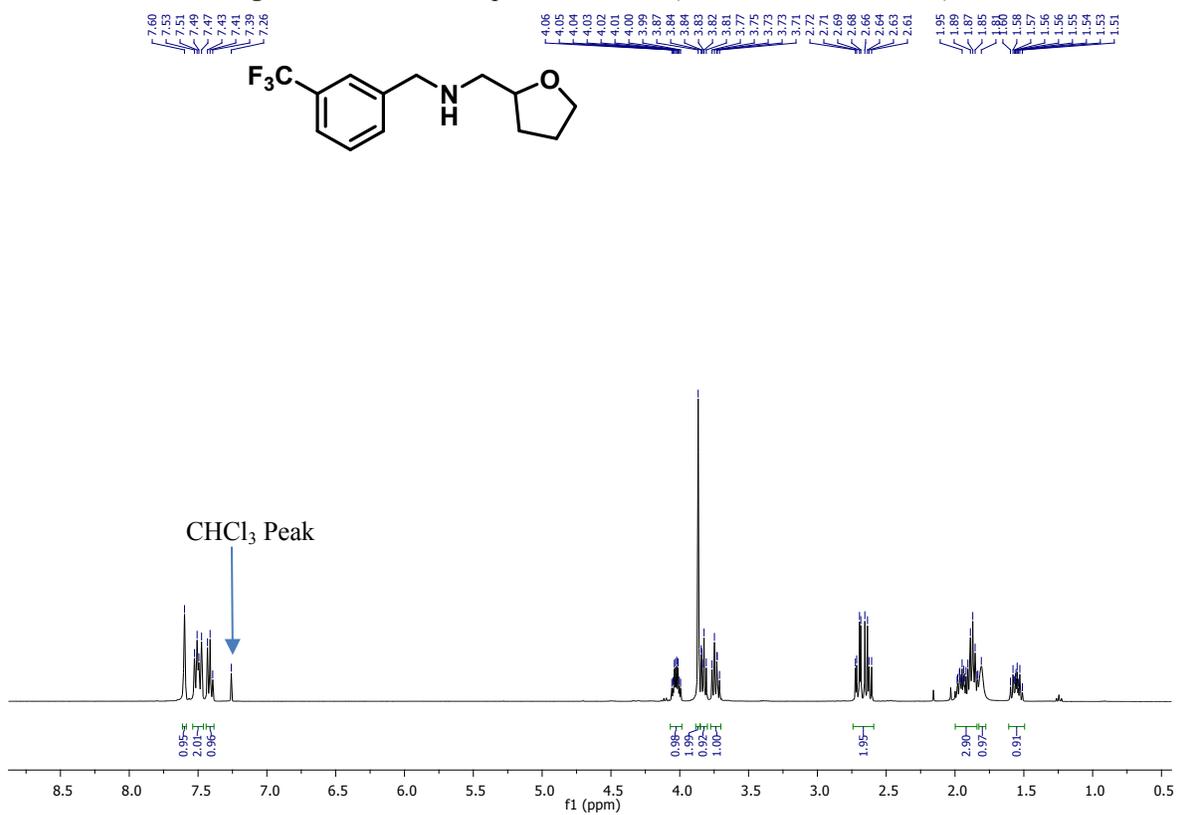


Figure S-68. ^1H NMR spectrum of S-38 (CDCl₃, 400 MHz, 298 K)

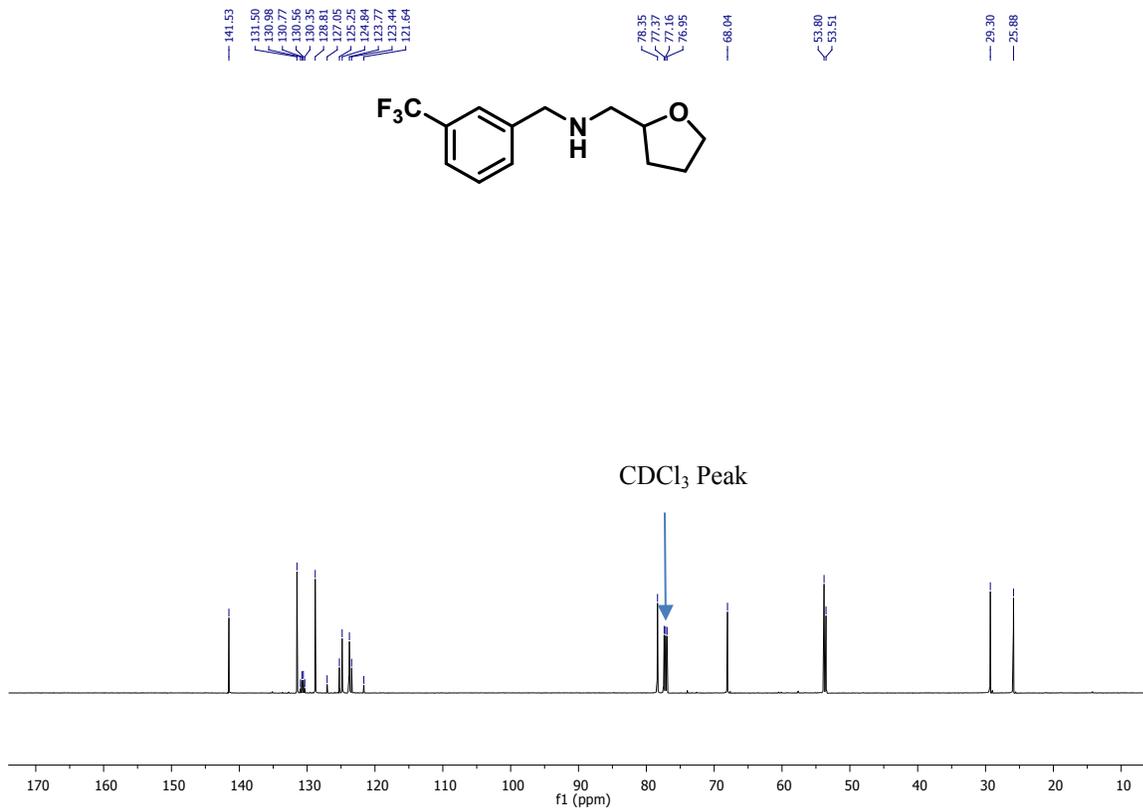


Figure S-69. ^{13}C NMR spectrum of S-38 (CDCl₃, 151 MHz, 298 K)

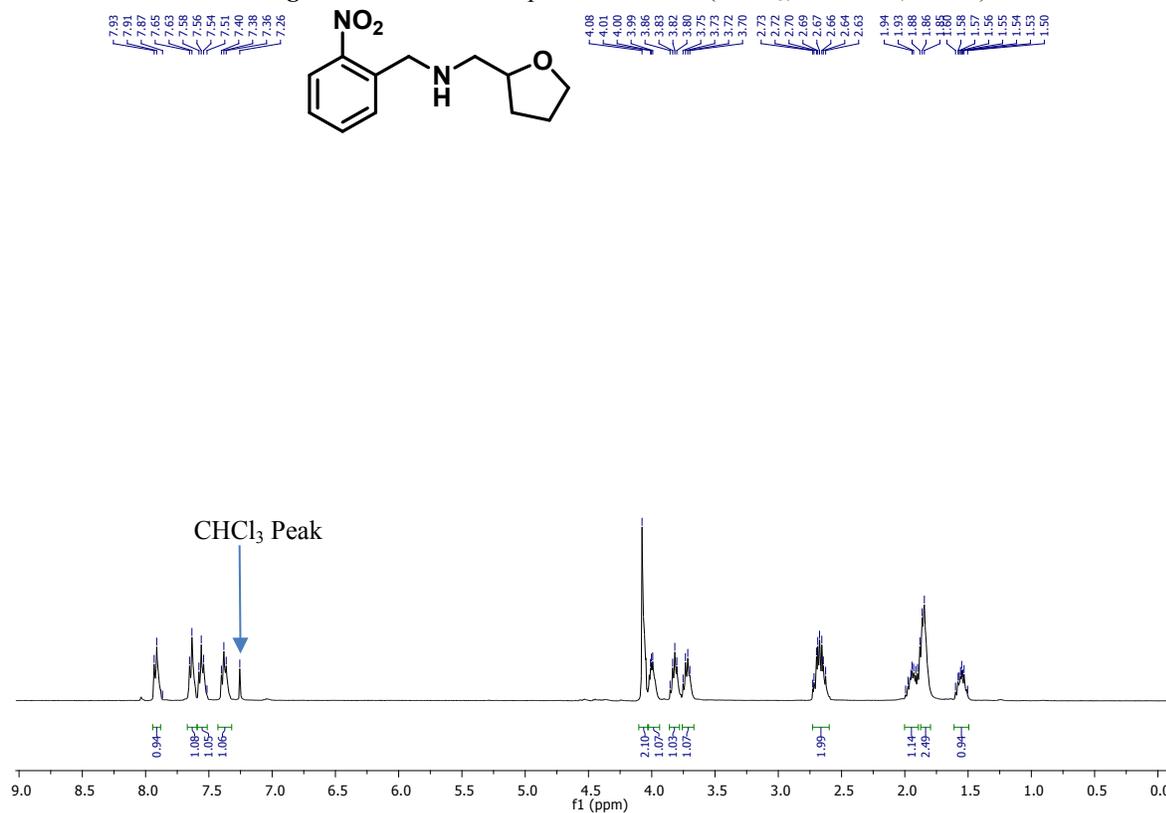


Figure S-70. ^1H NMR spectrum of S-39 (CDCl₃, 400 MHz, 298 K)

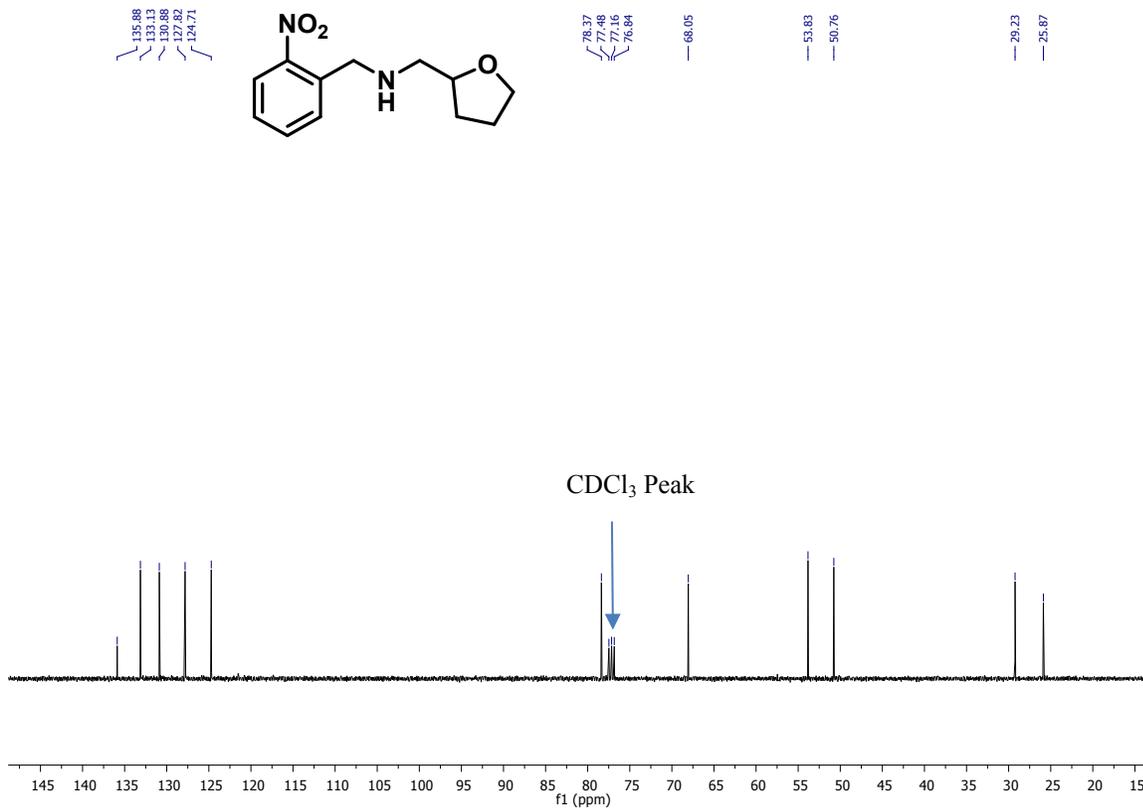


Figure S-71. ^{13}C NMR spectrum of S-39 (CDCl₃, 101 MHz, 298 K)

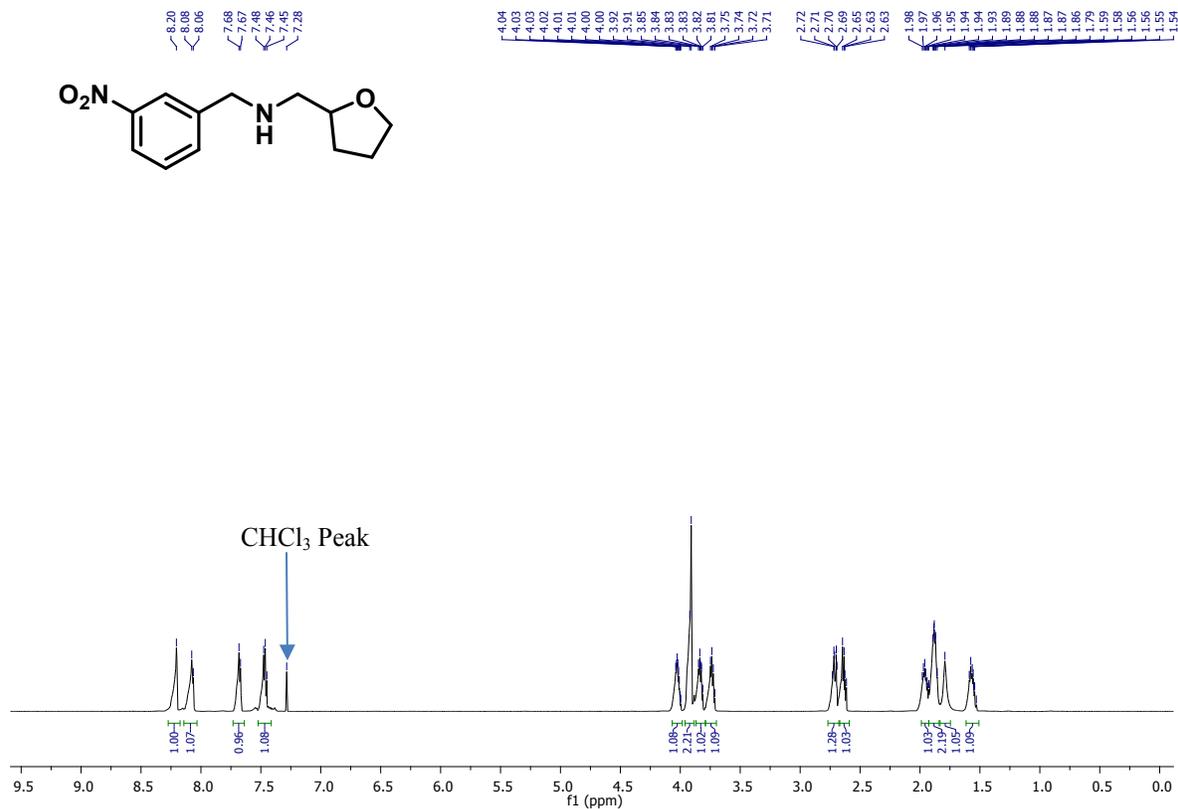


Figure S-72. ^1H NMR spectrum of S-40 (CDCl₃, 600 MHz, 298 K)

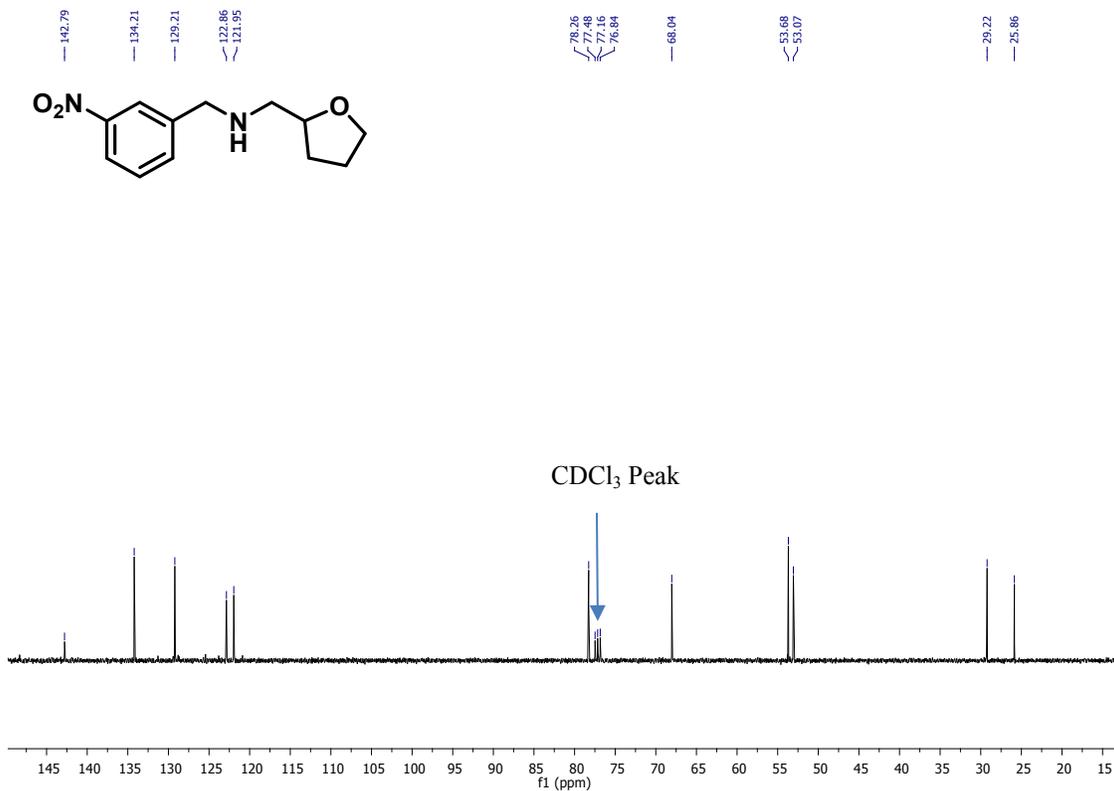


Figure S-73. ^{13}C NMR spectrum of S-40 (CDCl₃, 101 MHz, 298 K)

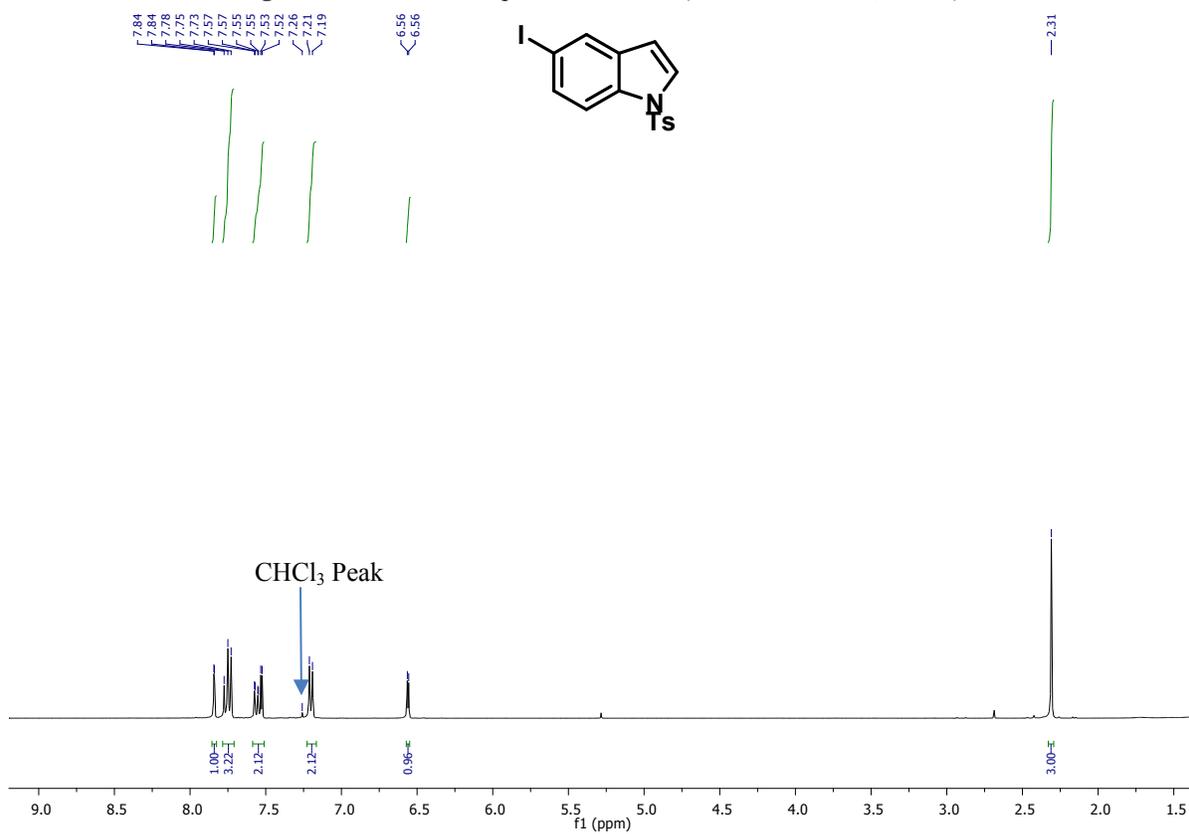


Figure S-74. ^1H NMR spectrum of S-41 (CDCl₃, 400 MHz, 298 K)

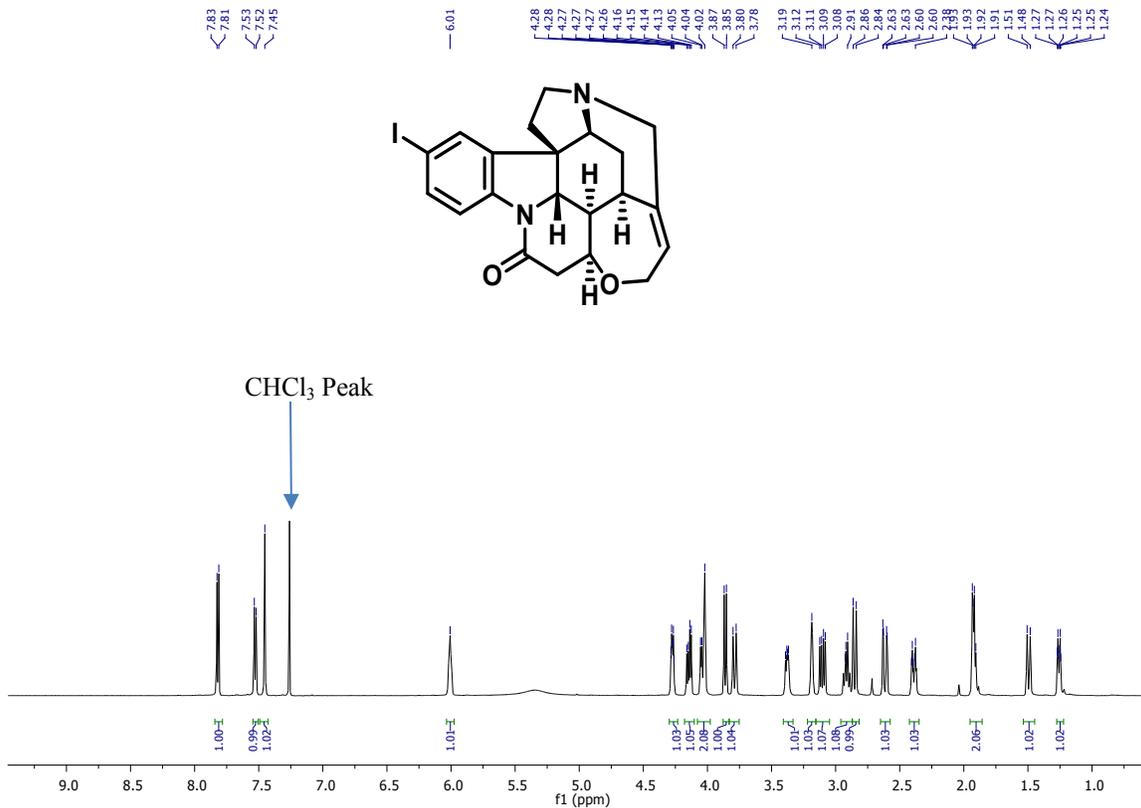


Figure S-75. ¹H NMR spectrum of S-42 (CDCl₃, 400 MHz, 298 K)

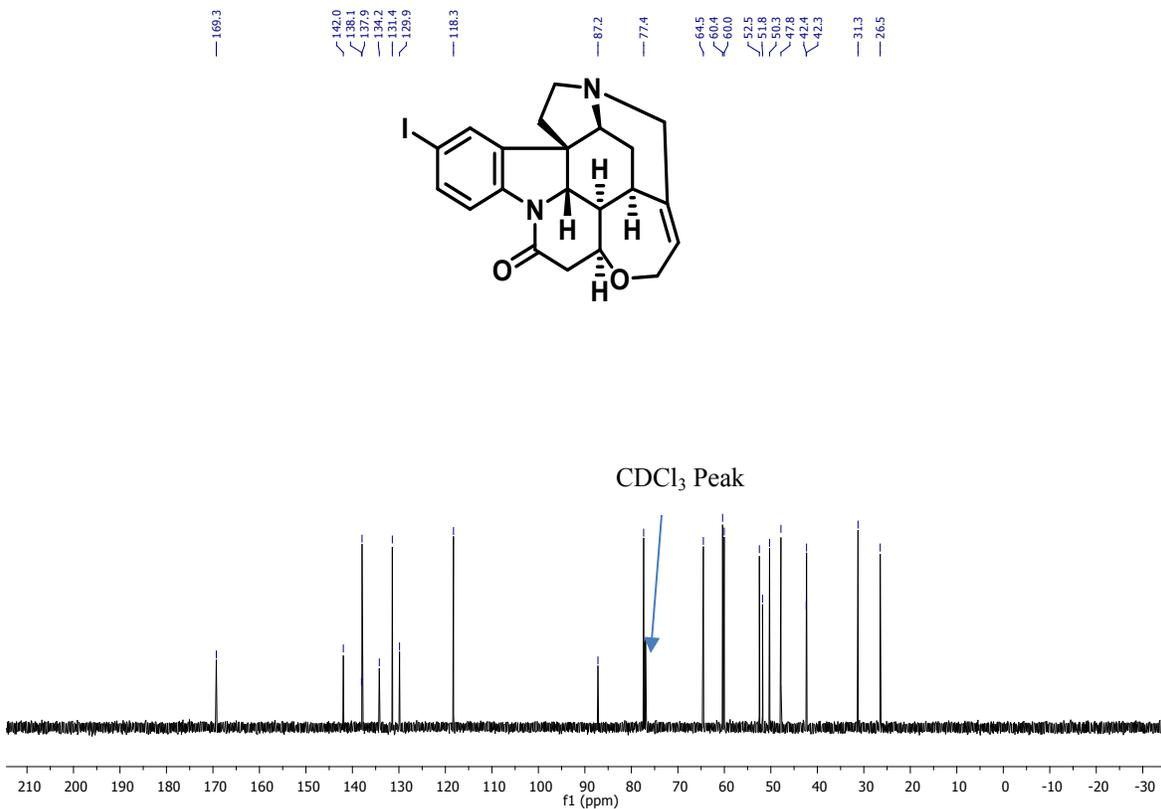


Figure S-76. ¹³C NMR spectrum of S-42 (CDCl₃, 101 MHz, 298 K)

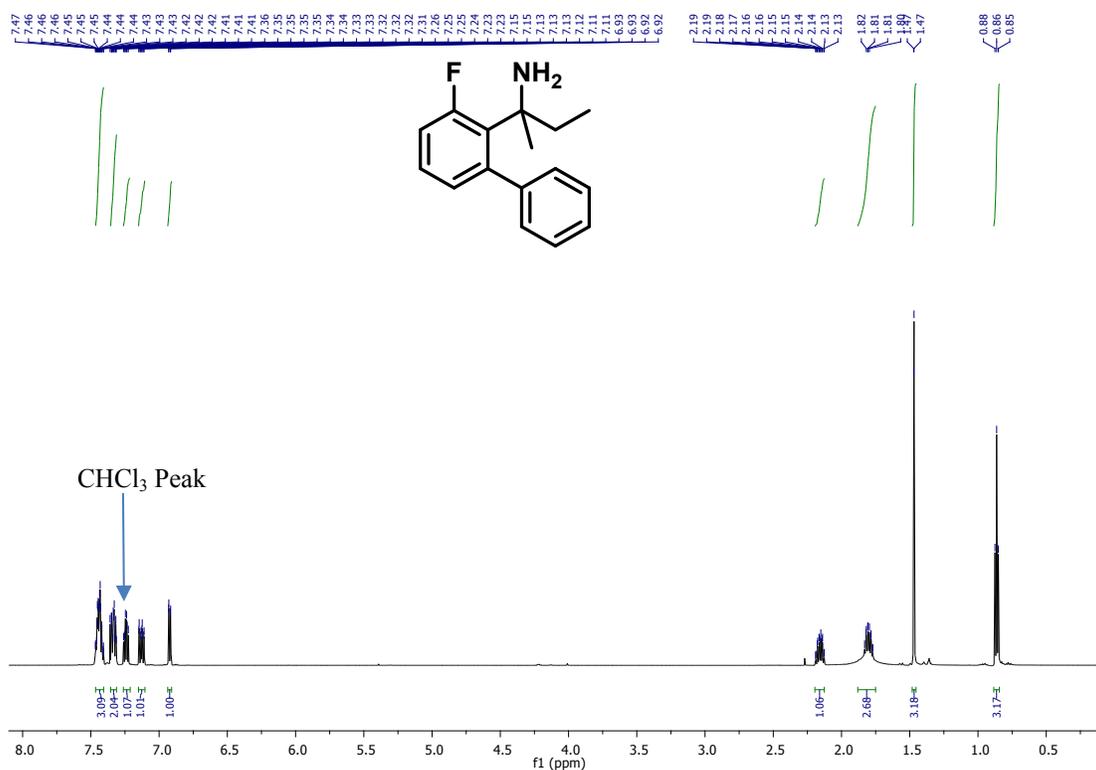


Figure S-77. ¹H NMR spectrum of 1a (CDCl₃, 600 MHz, 298 K)

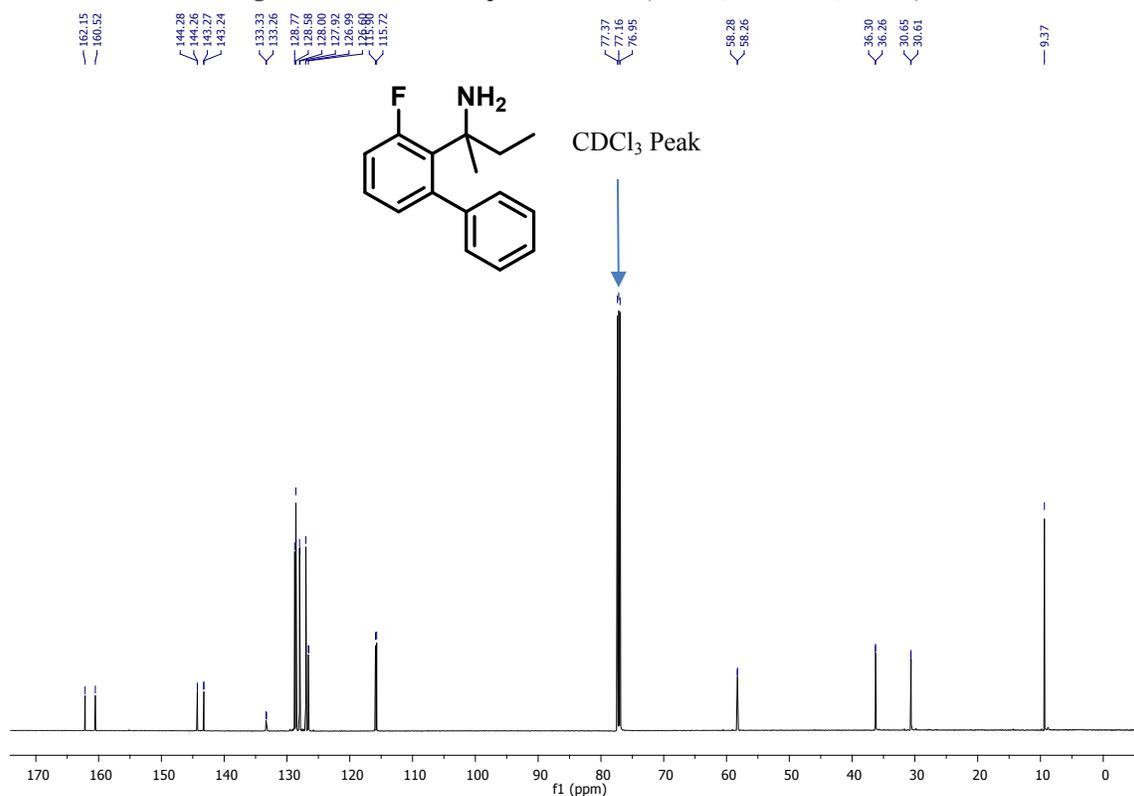
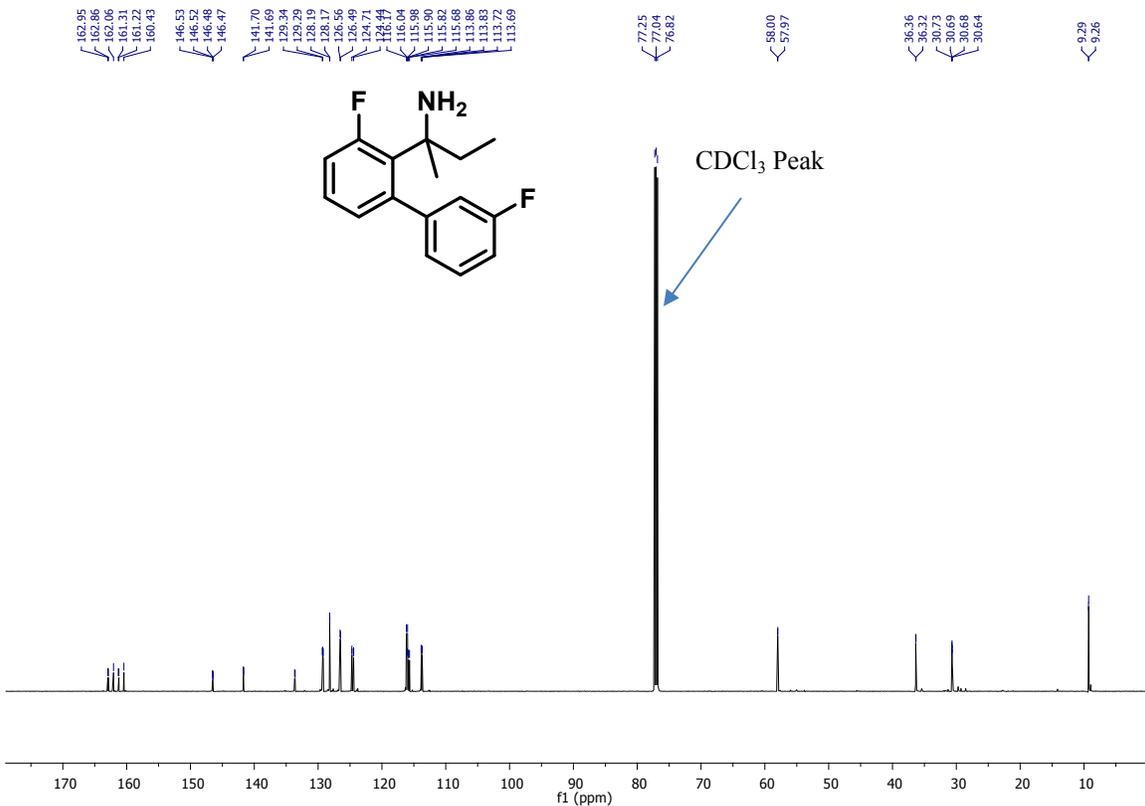
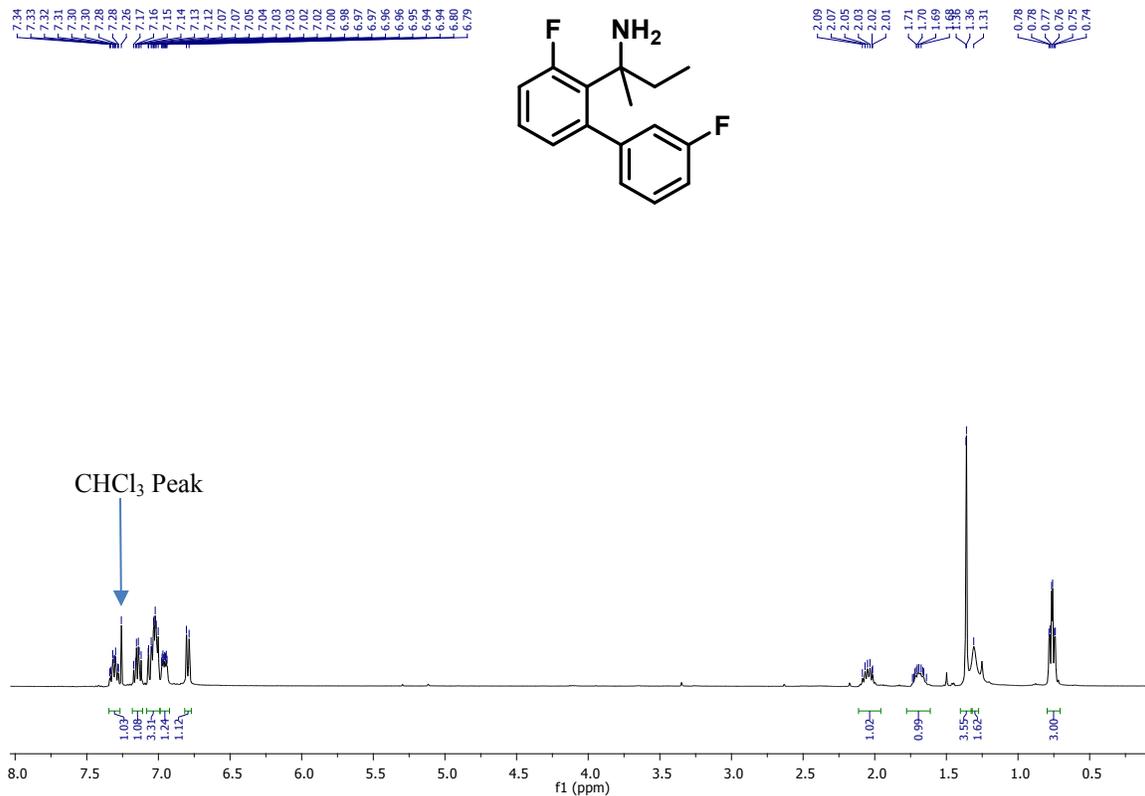


Figure S-78. ¹³C NMR spectrum of 1a (CDCl₃, 151 MHz, 298 K)



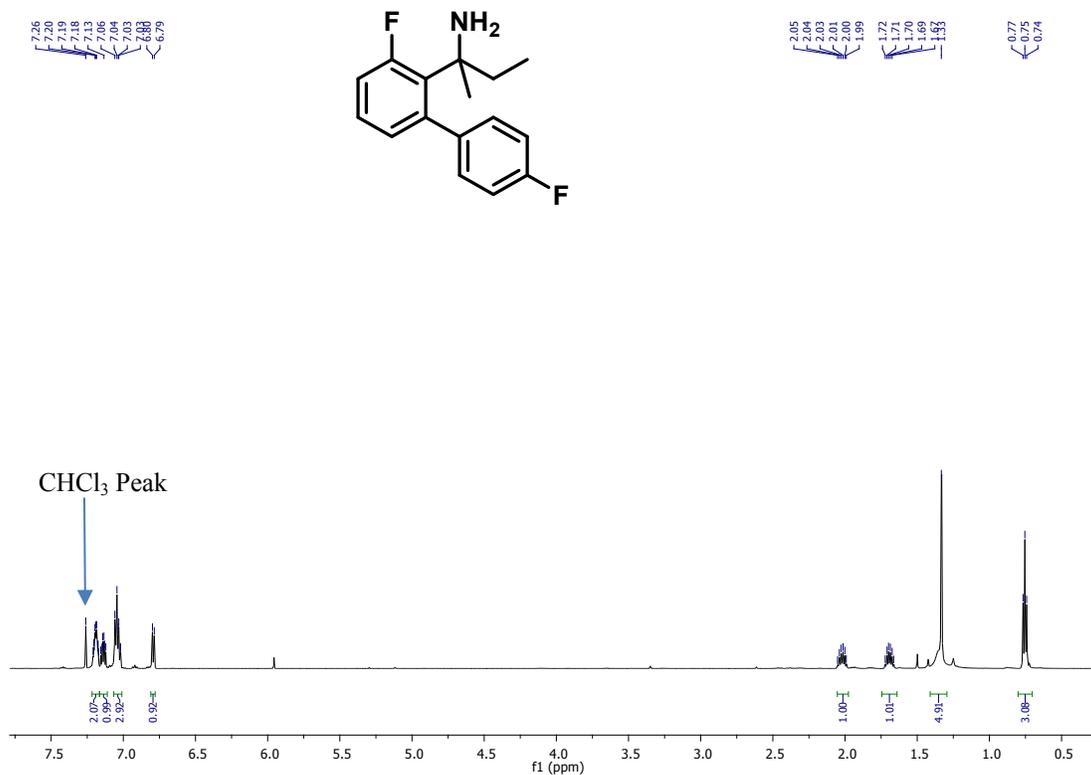


Figure S-81. ¹H NMR spectrum of **1c** (CDCl₃, 600 MHz, 298 K)

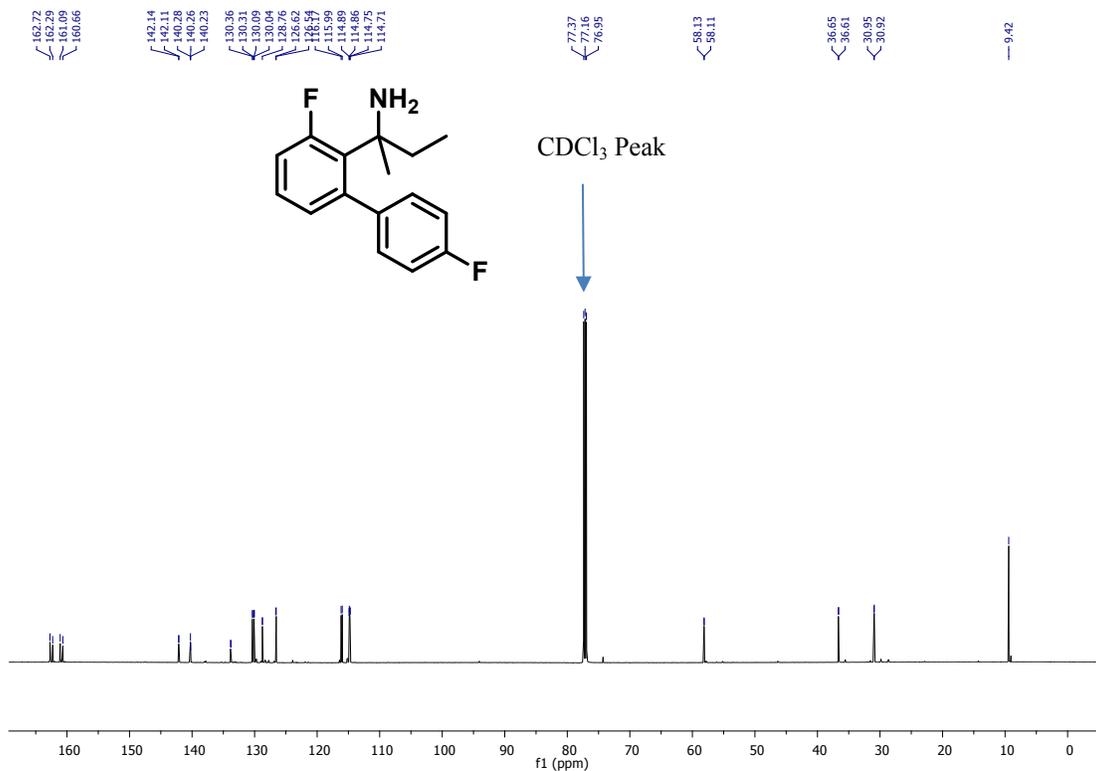


Figure S-82. ¹³C NMR spectrum of **1c** (CDCl₃, 151 MHz, 298 K)

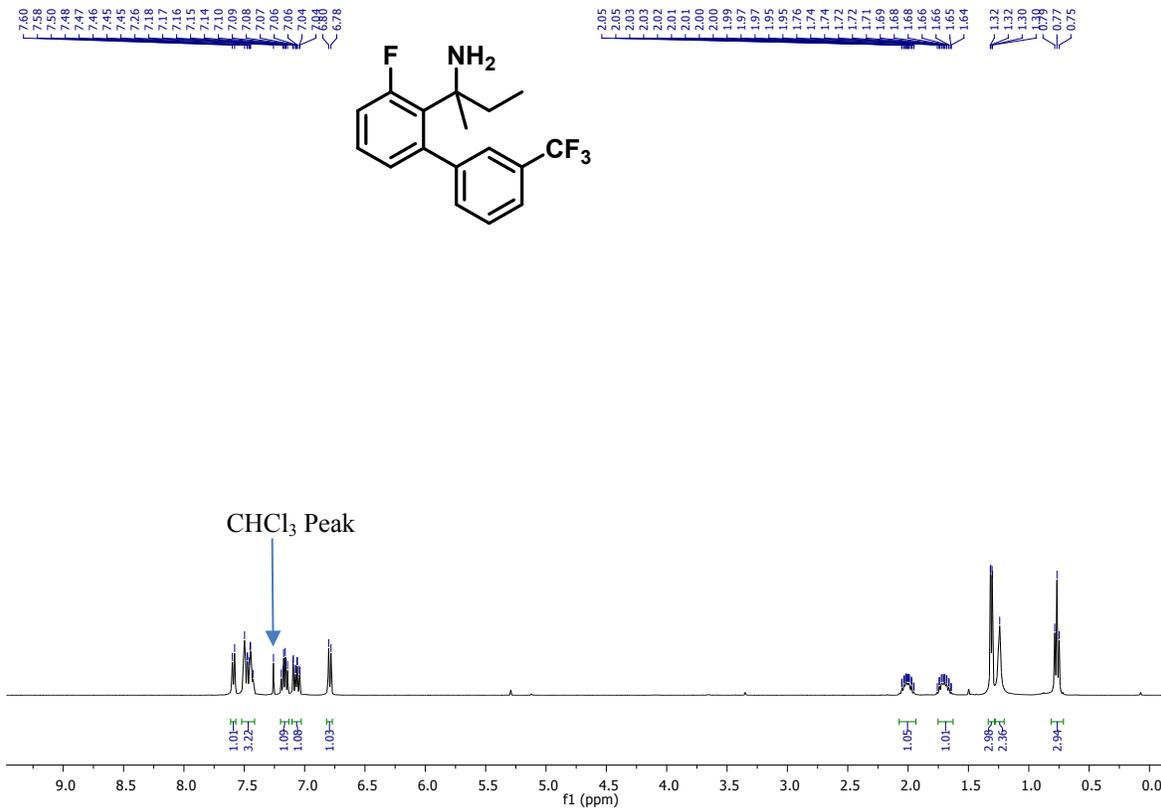


Figure S-83. ¹H NMR spectrum of **1d** (CDCl₃, 400 MHz, 298 K)

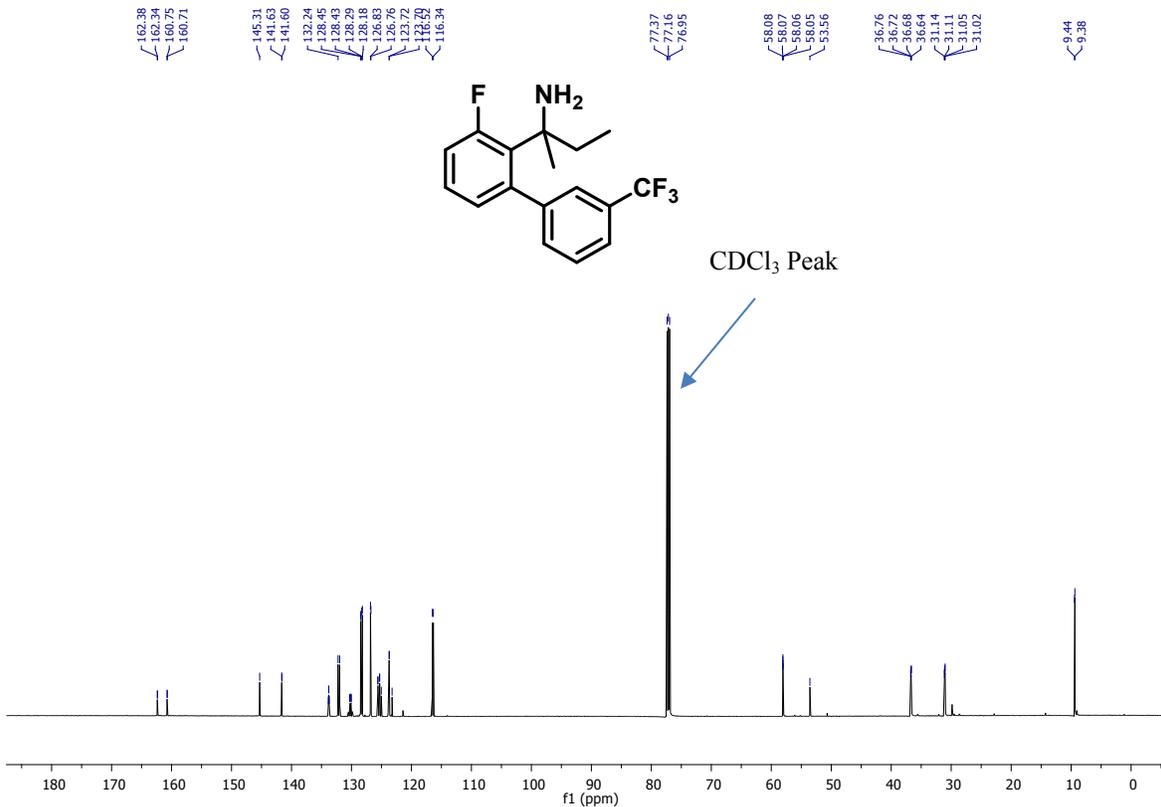


Figure S-84. ¹³C NMR spectrum of **1d** (CDCl₃, 151 MHz, 298 K)

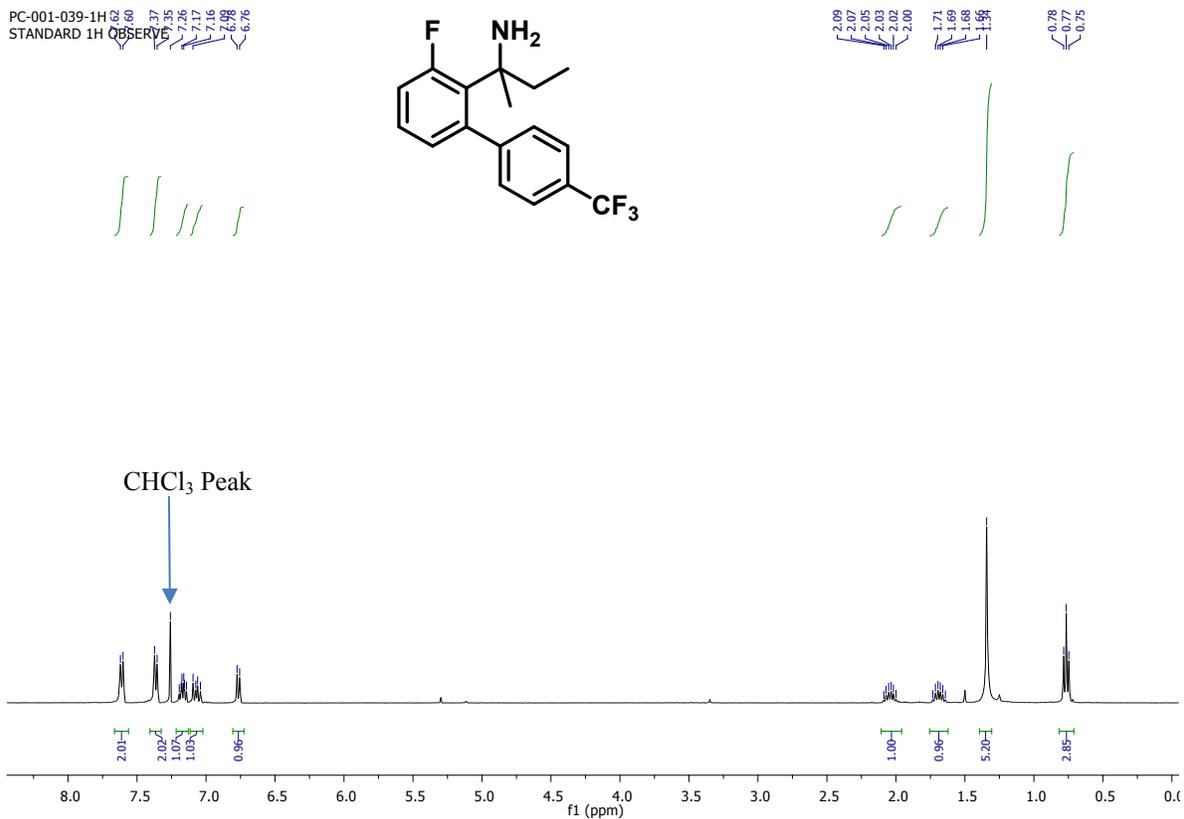


Figure S-85. ¹H NMR spectrum of **1e** (CDCl₃, 400 MHz, 298 K)

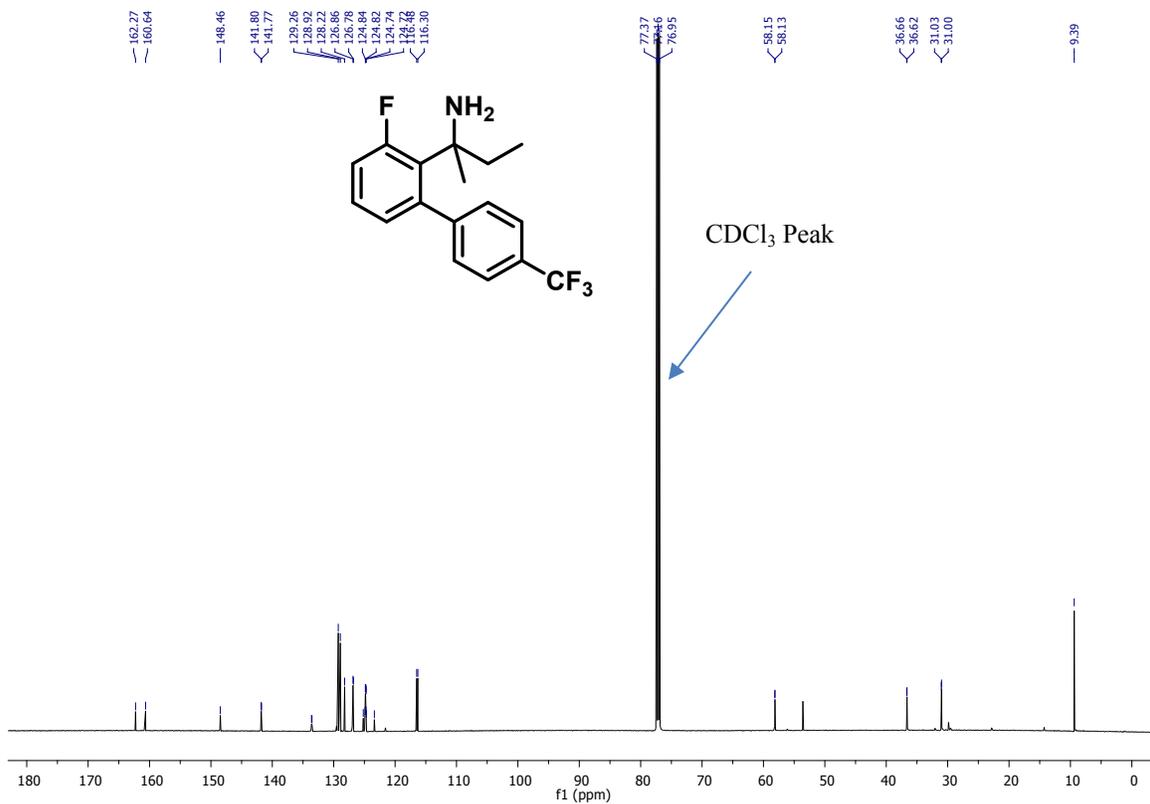


Figure S-86. ¹³C NMR spectrum of **1e** (CDCl₃, 151 MHz, 298 K)

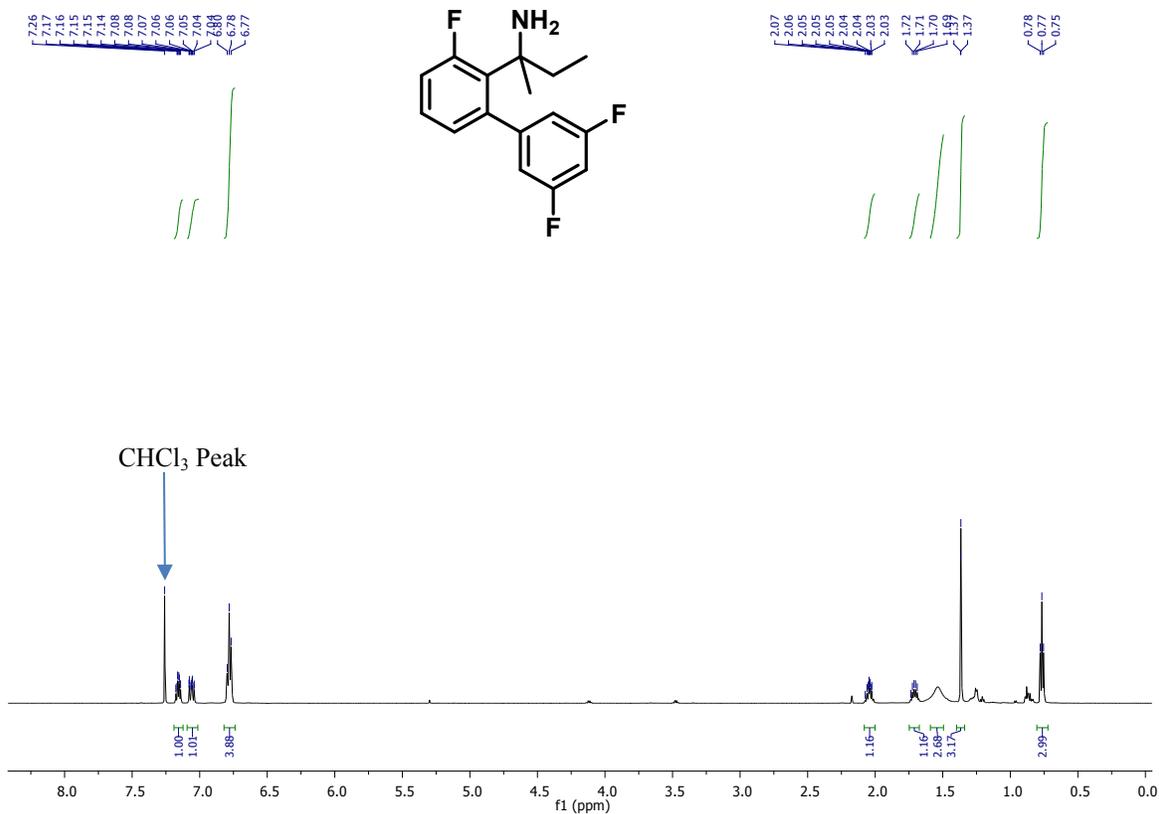


Figure S-87. ¹H NMR spectrum of **1f** (CDCl₃, 600 MHz, 298 K)

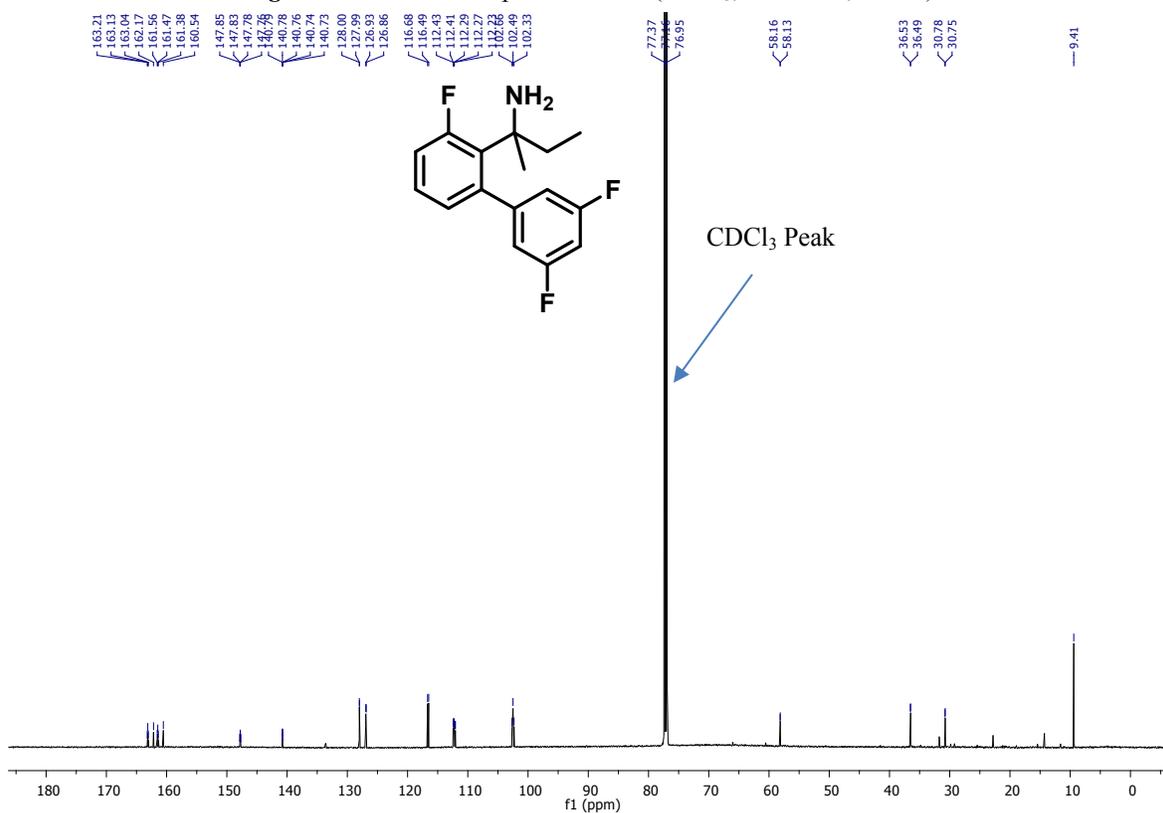


Figure S-88. ¹³C NMR spectrum of **1f** (CDCl₃, 151 MHz, 298 K)

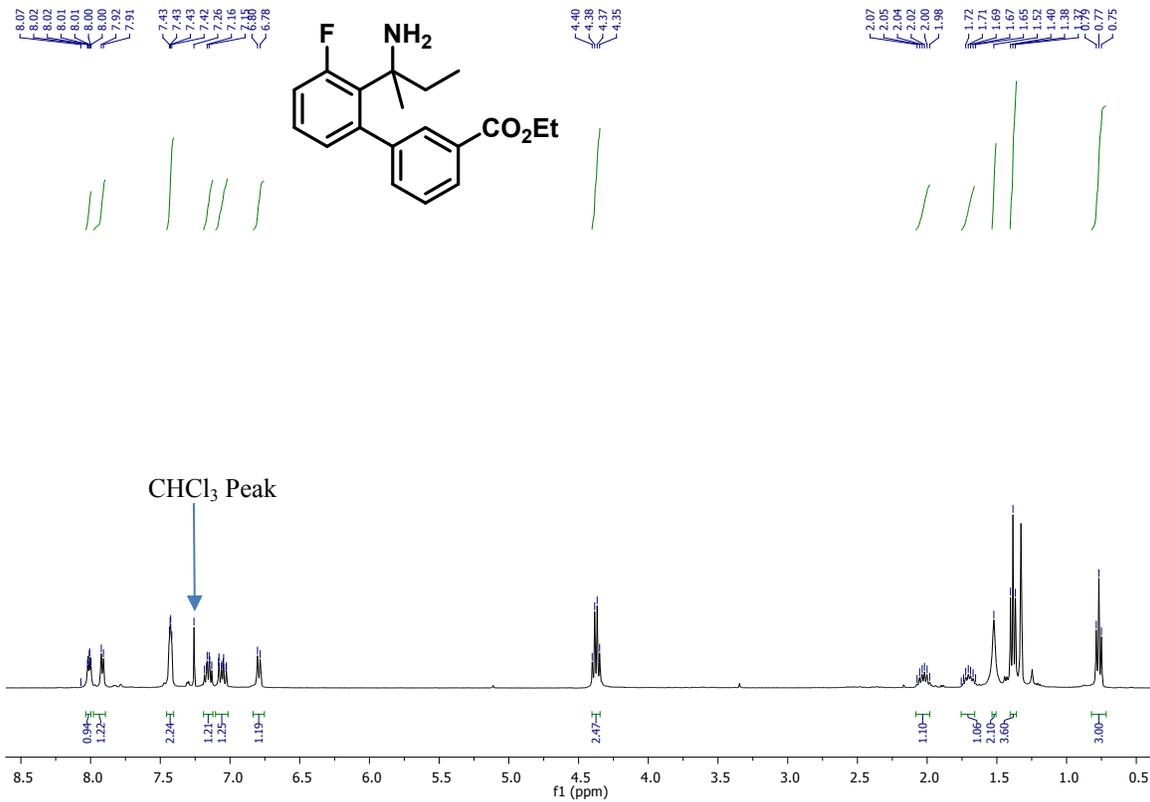


Figure S-89. ¹H NMR spectrum of **1g** (CDCl₃, 400 MHz, 298 K)

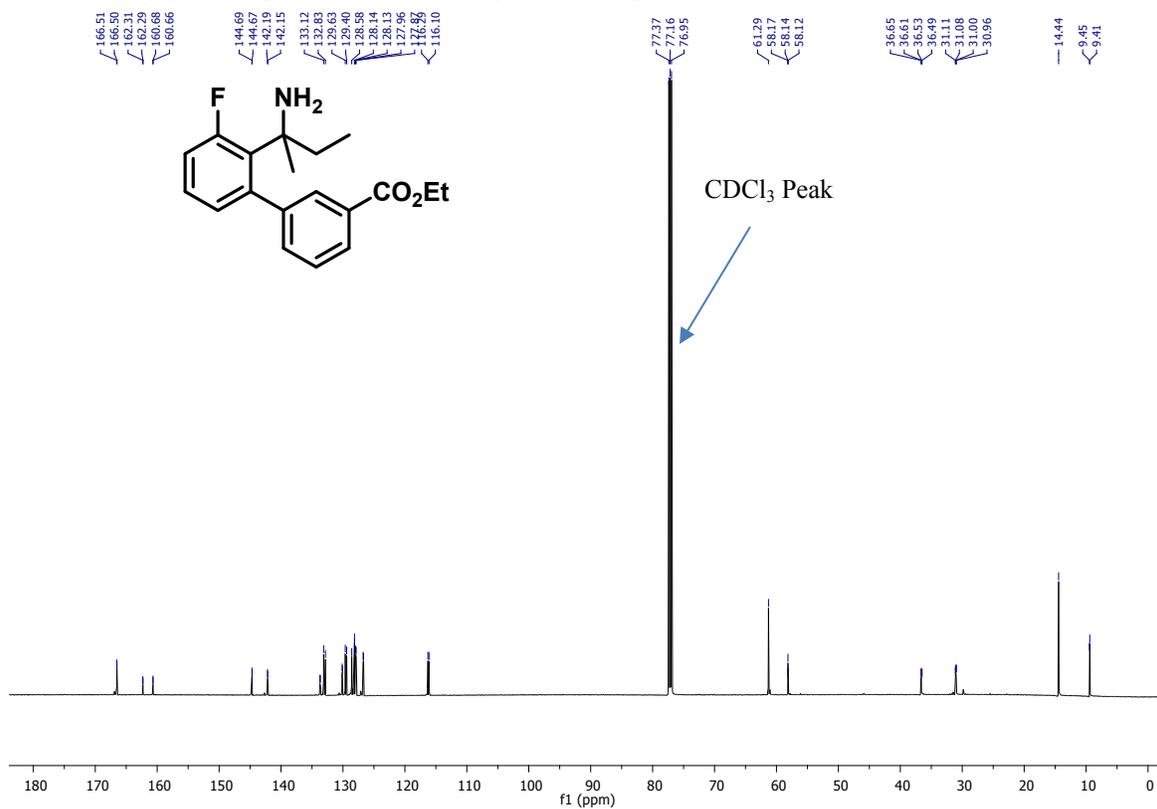


Figure S-90. ¹³C NMR spectrum of **1g** (CDCl₃, 151 MHz, 298 K)

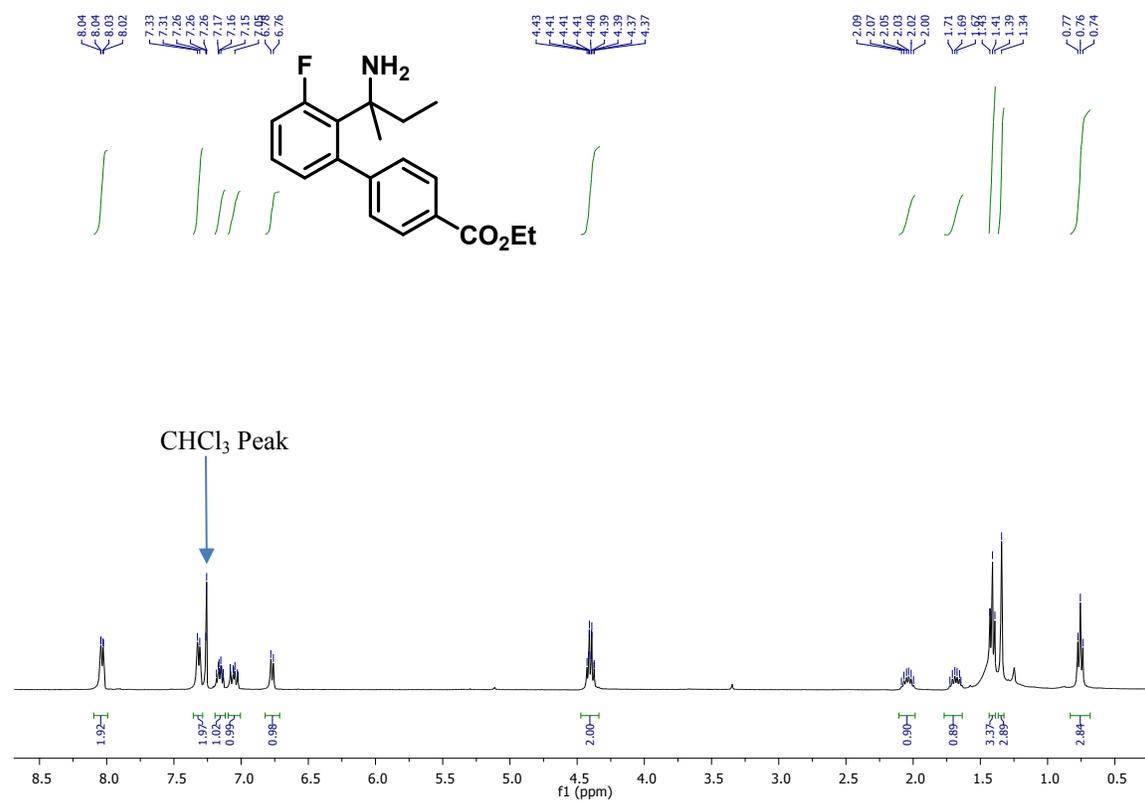


Figure S-91. ¹H NMR spectrum of **1h** (CDCl₃, 400 MHz, 298 K)

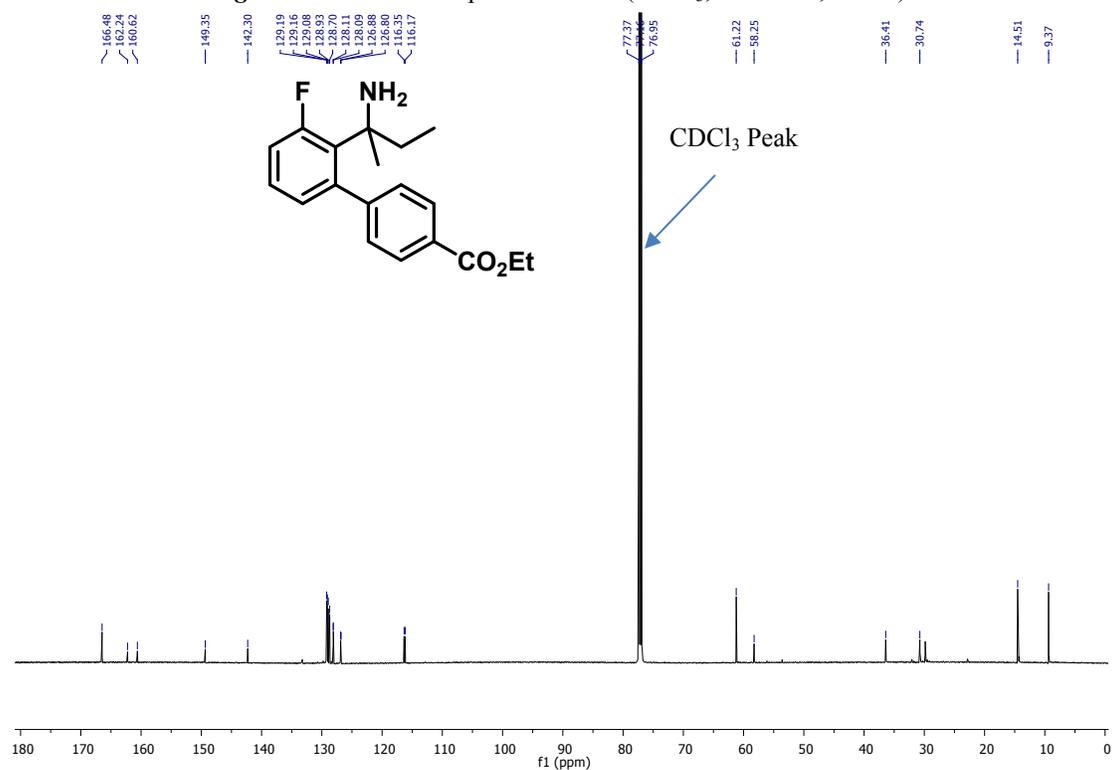
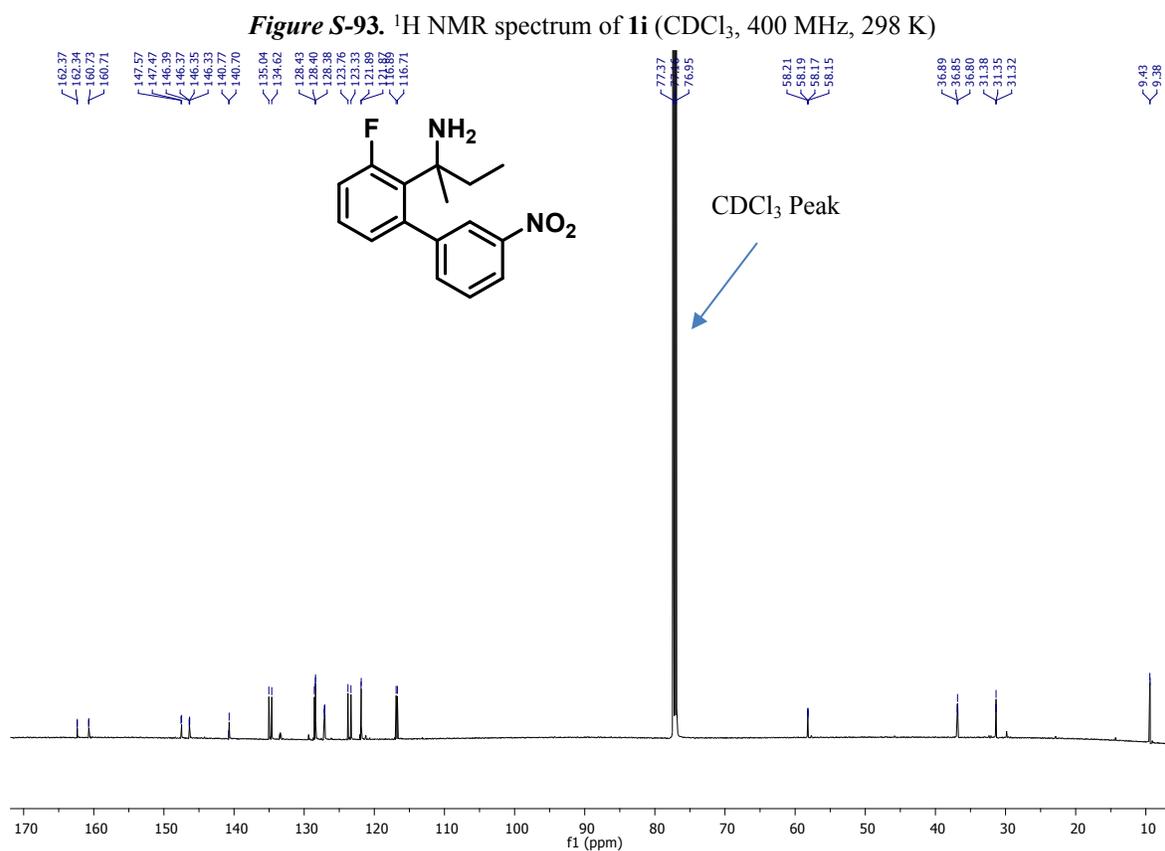
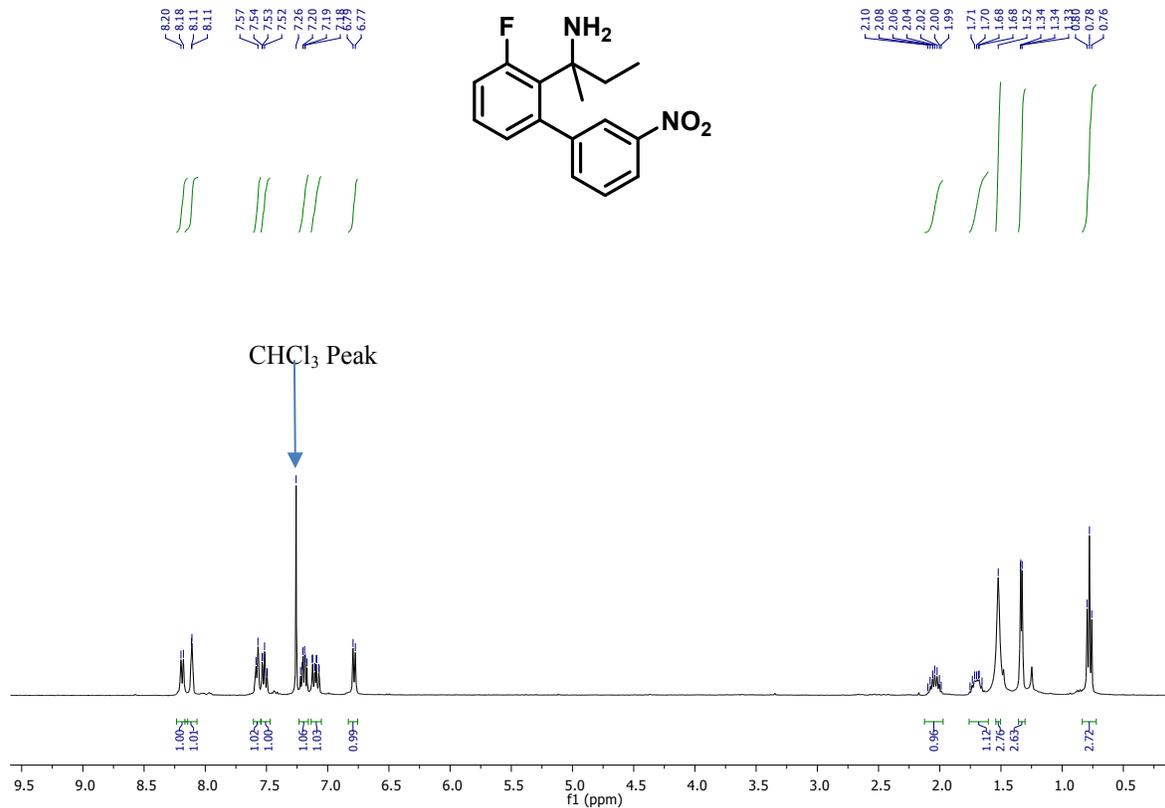


Figure S-92. ¹³C NMR spectrum of **1h** (CDCl₃, 151 MHz, 298 K)



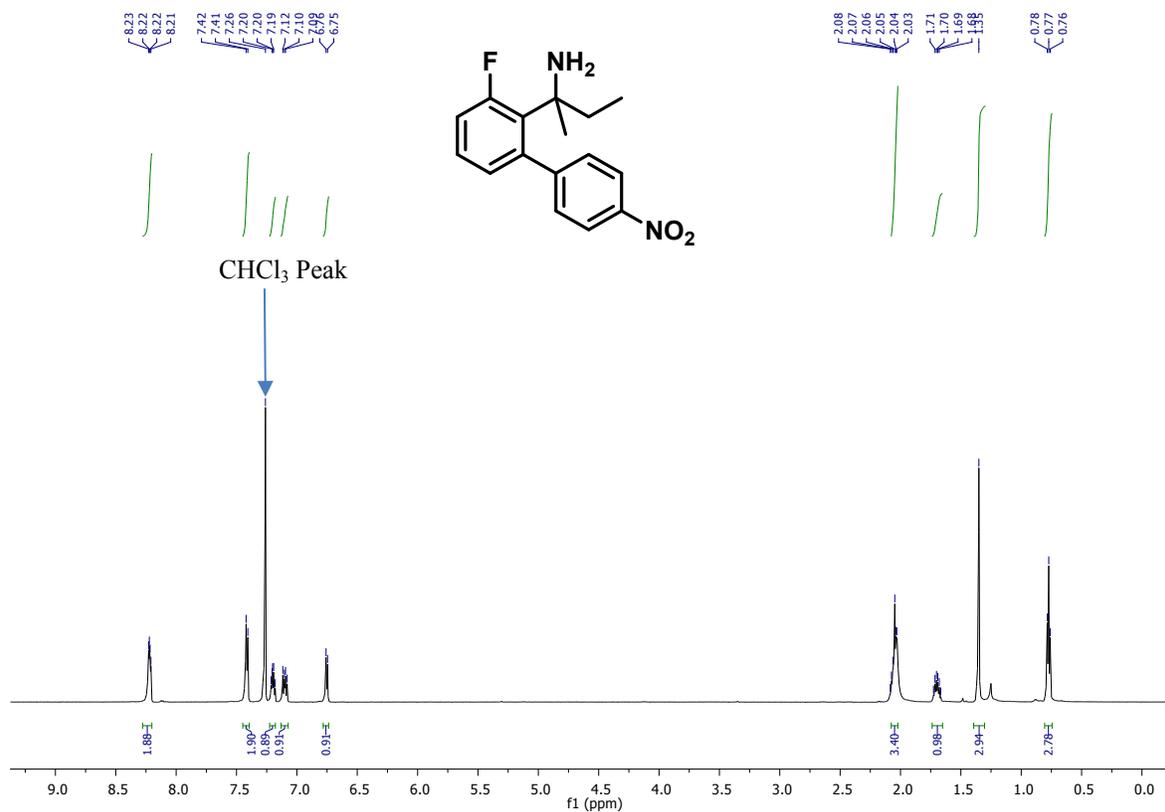


Figure S-95. ¹H NMR spectrum of **1j** (CDCl₃, 600 MHz, 298 K)

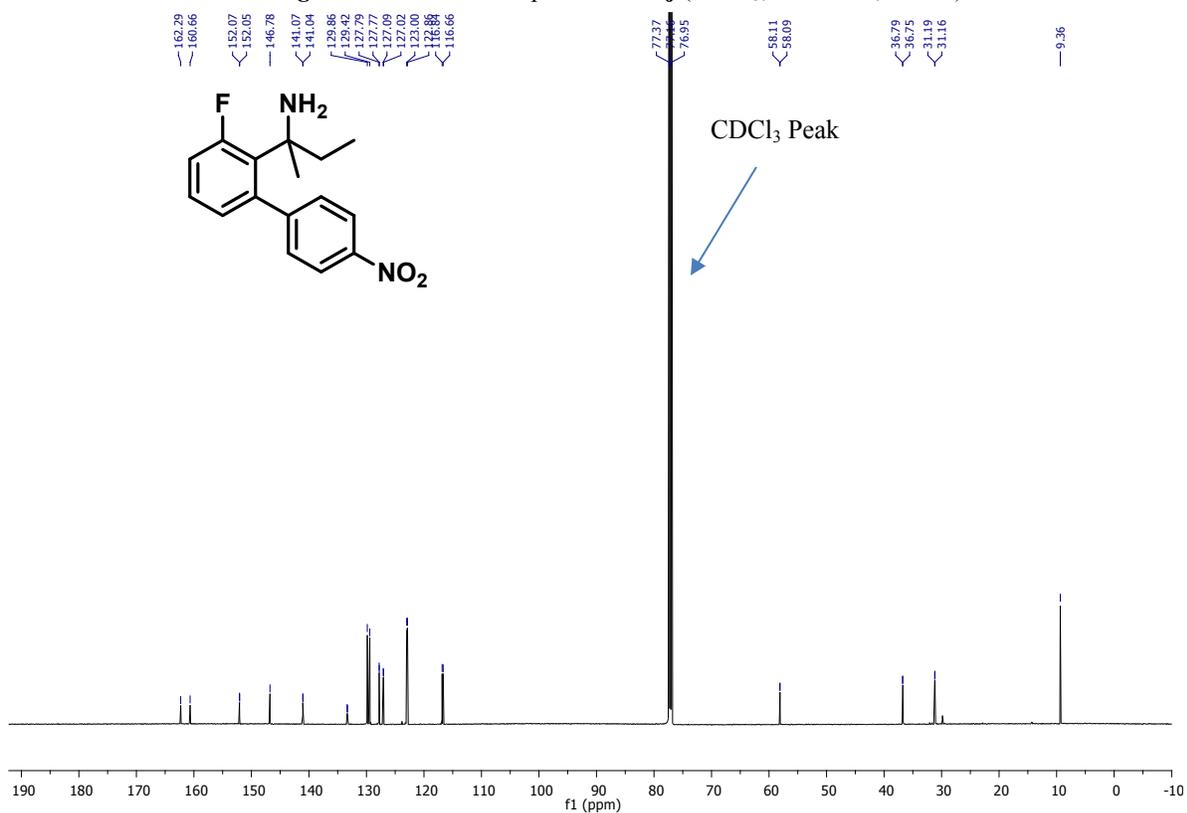


Figure S-96. ¹³C NMR spectrum of **1j** (CDCl₃, 151 MHz, 298 K)

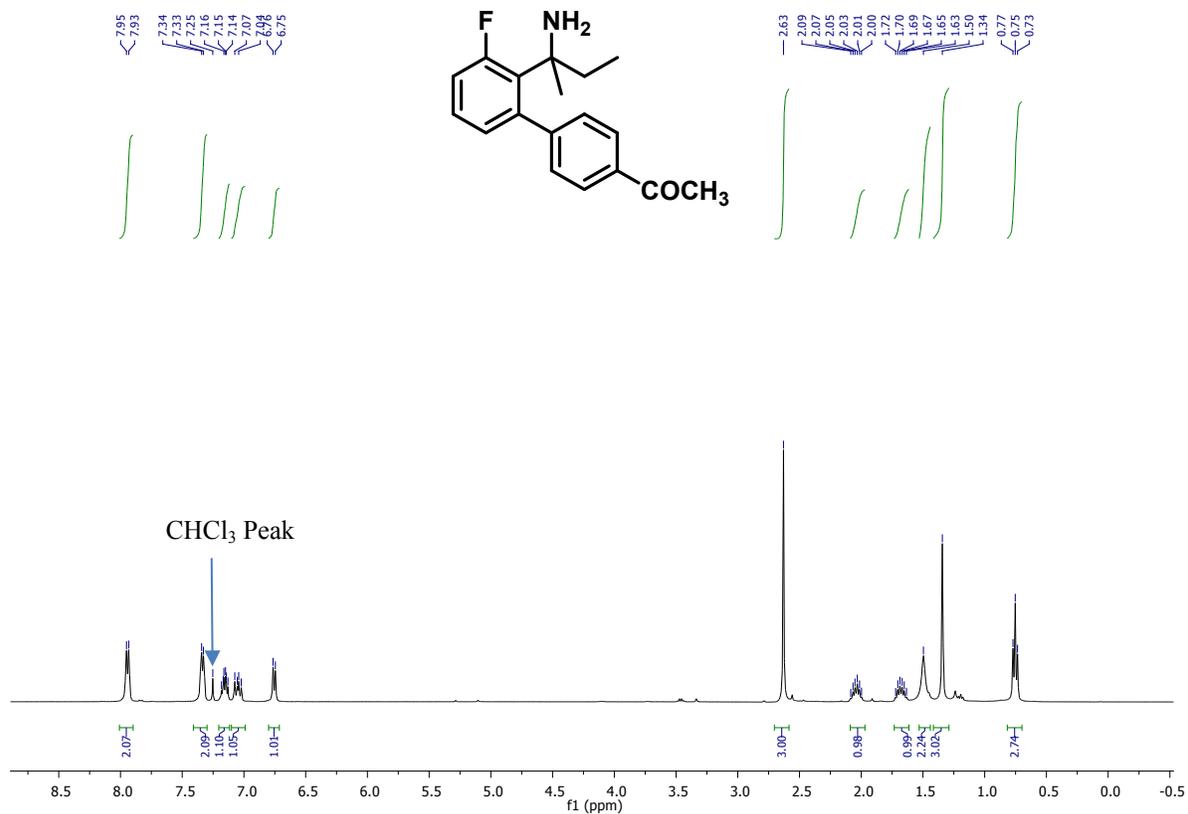


Figure S-97. ¹H NMR spectrum of **1k** (CDCl₃, 400 MHz, 298 K)

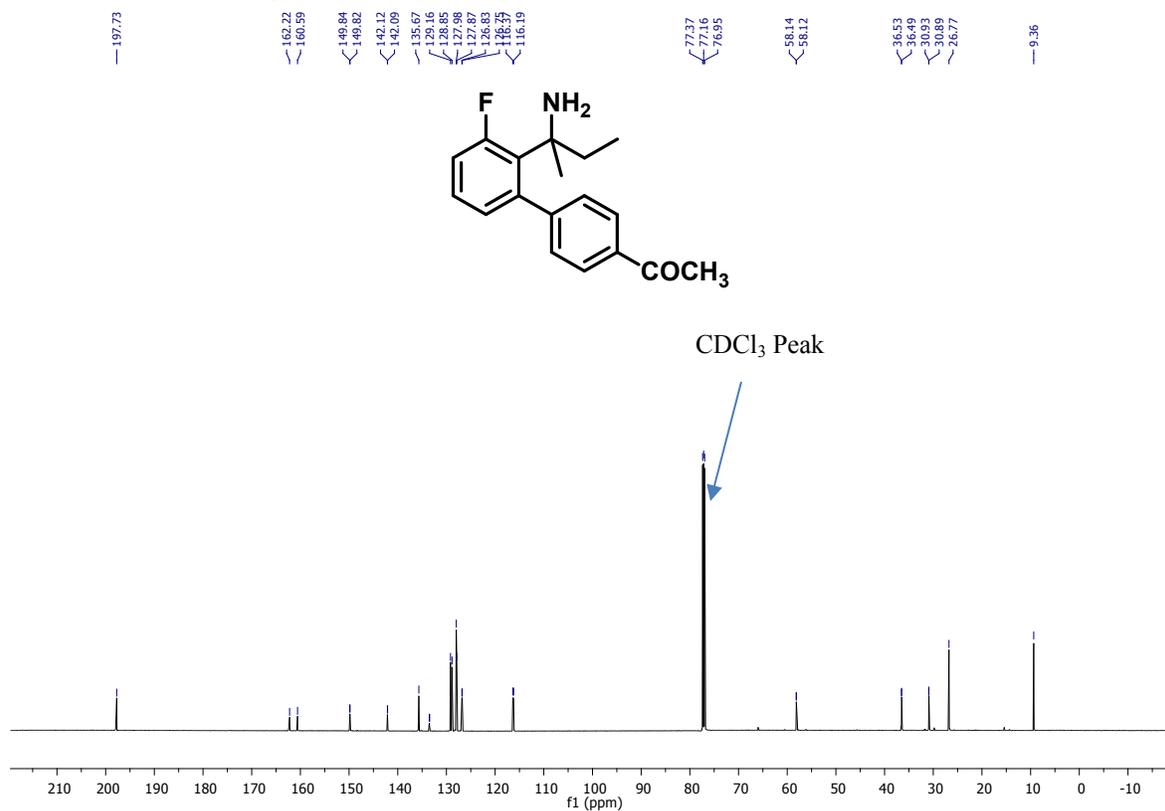


Figure S-98. ¹³C NMR spectrum of **1k** (CDCl₃, 151 MHz, 298 K)

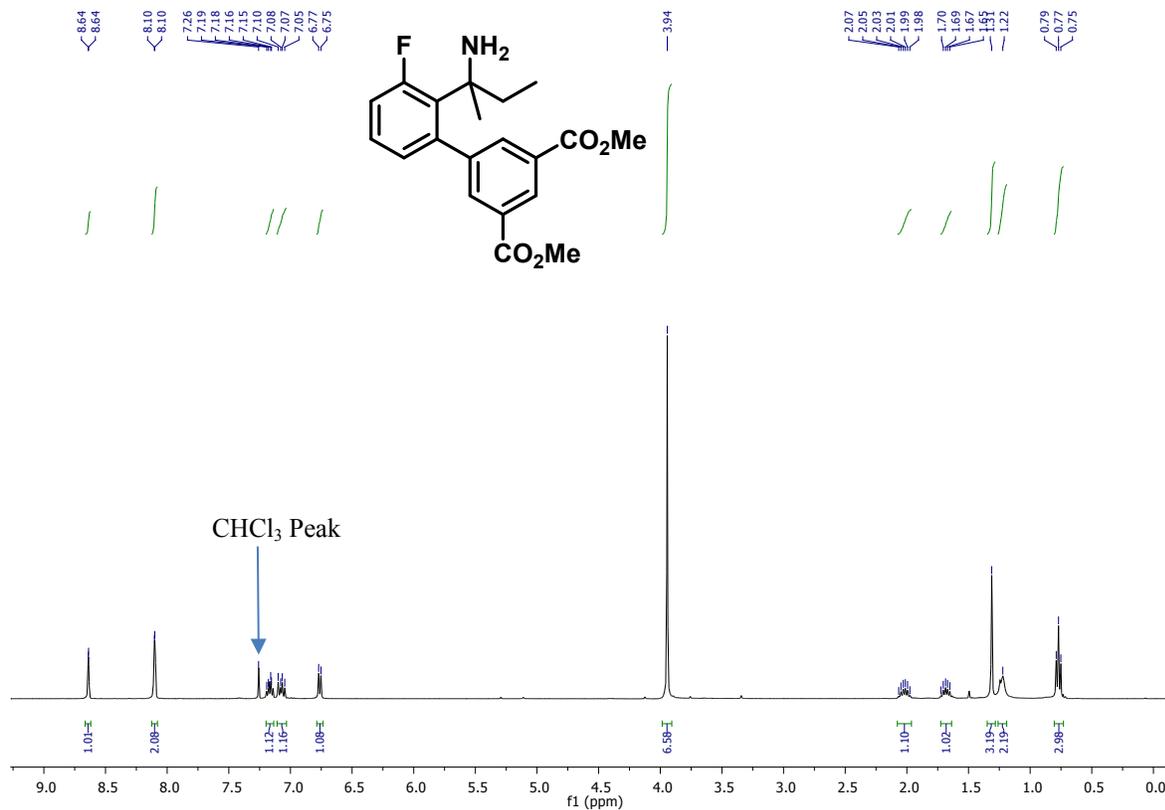


Figure S-99. ¹H NMR spectrum of **11** (CDCl₃, 400 MHz, 298 K)

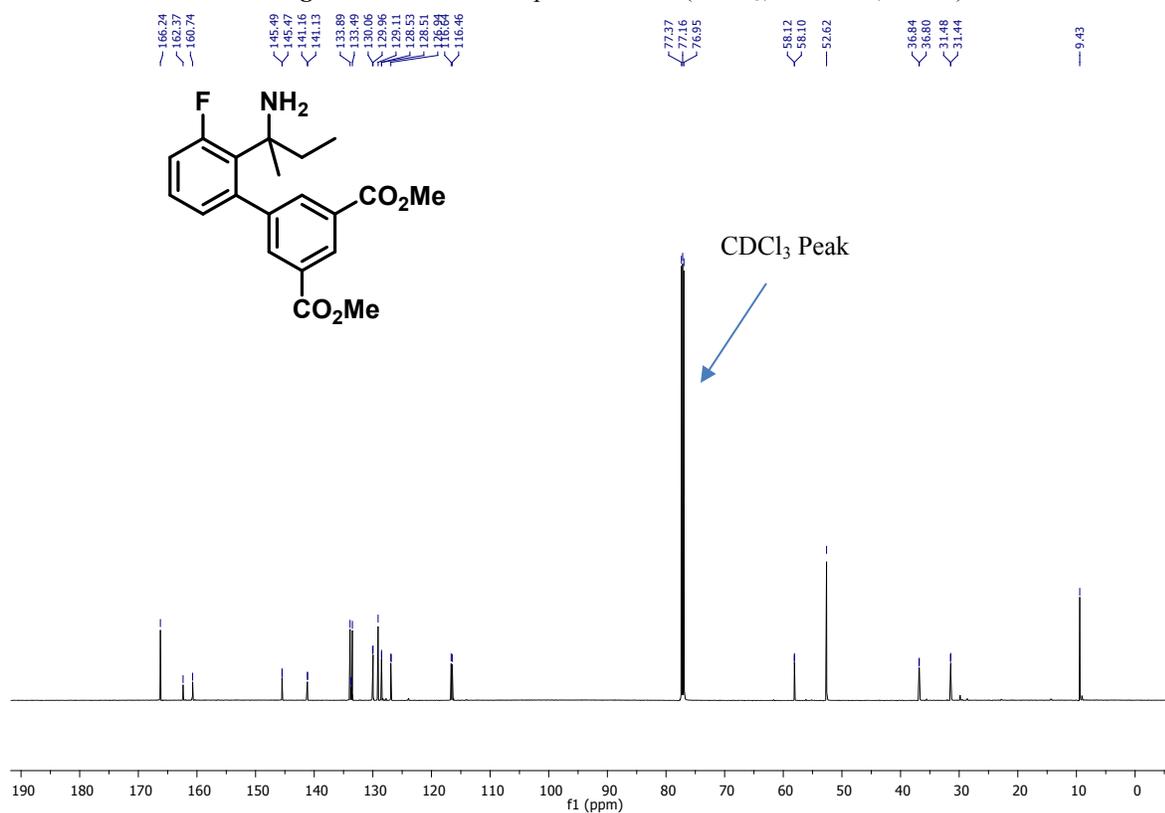


Figure S-100. ¹³C NMR spectrum of **11** (CDCl₃, 151 MHz, 298 K)

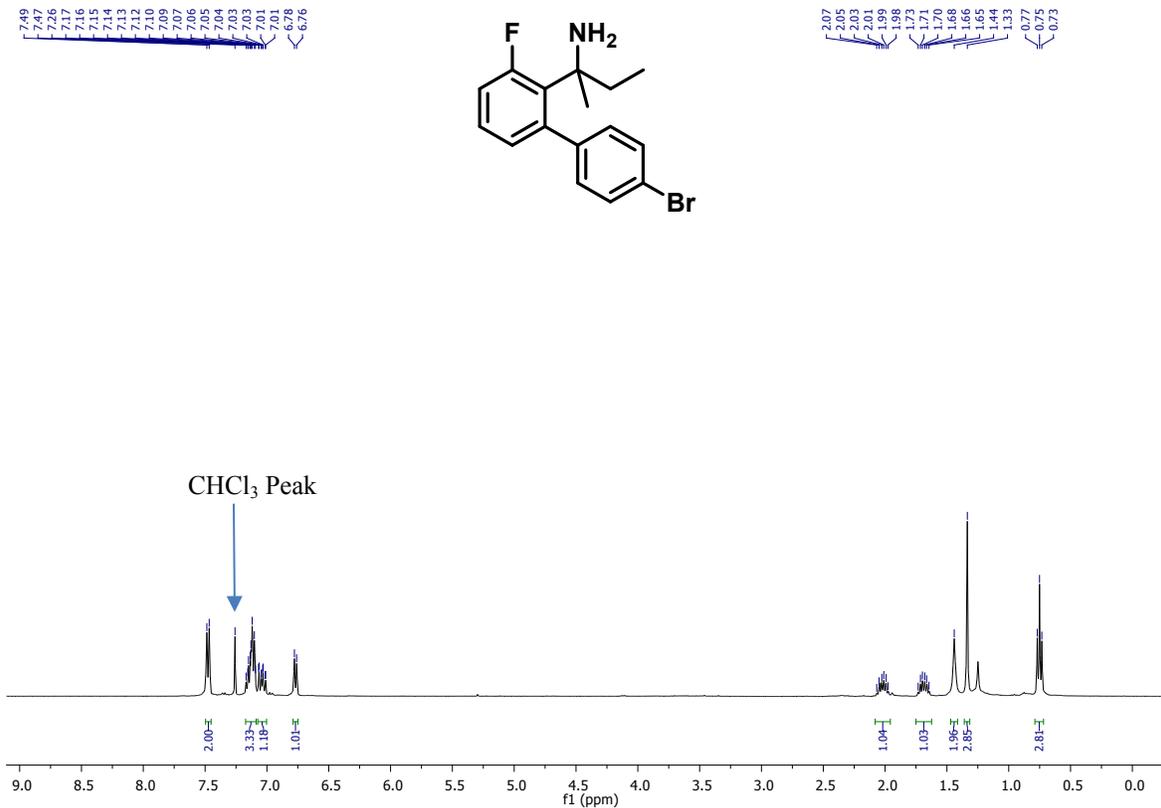


Figure S-101. ¹H NMR spectrum of **1m** (CDCl₃, 400 MHz, 298 K)

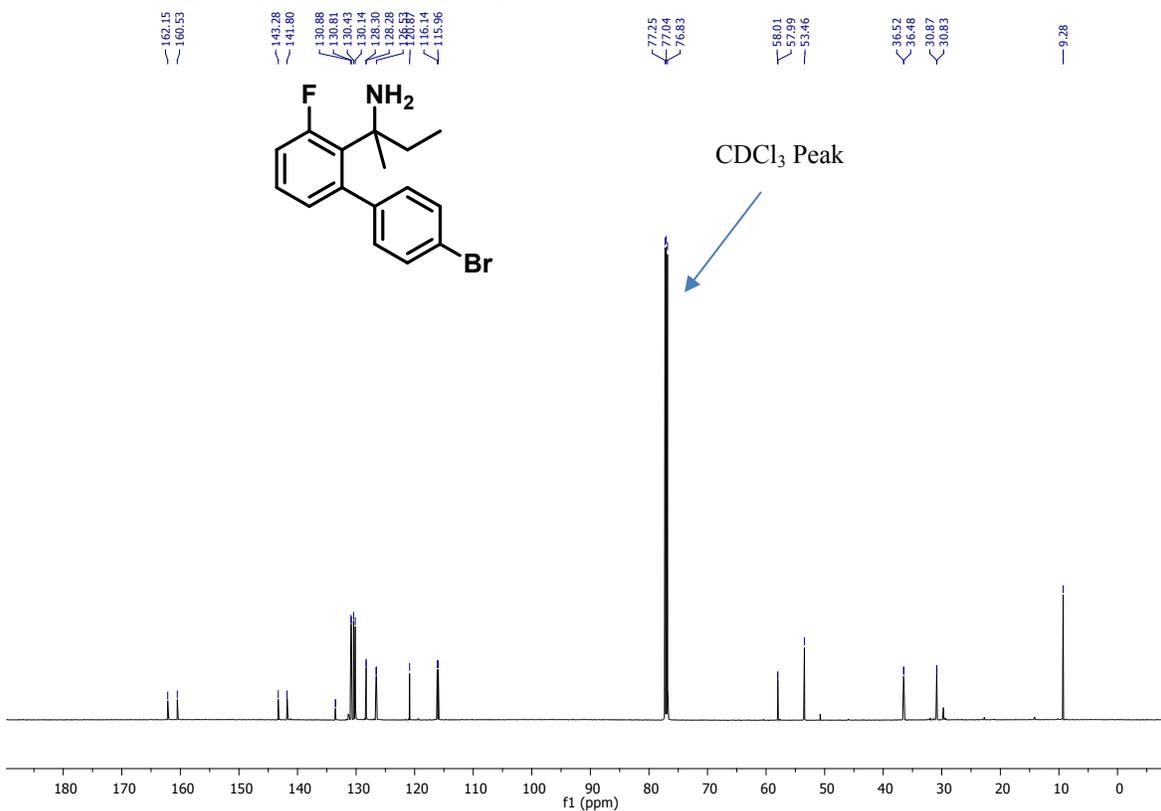


Figure S-102. ¹³C NMR spectrum of **1m** (CDCl₃, 151 MHz, 298 K)

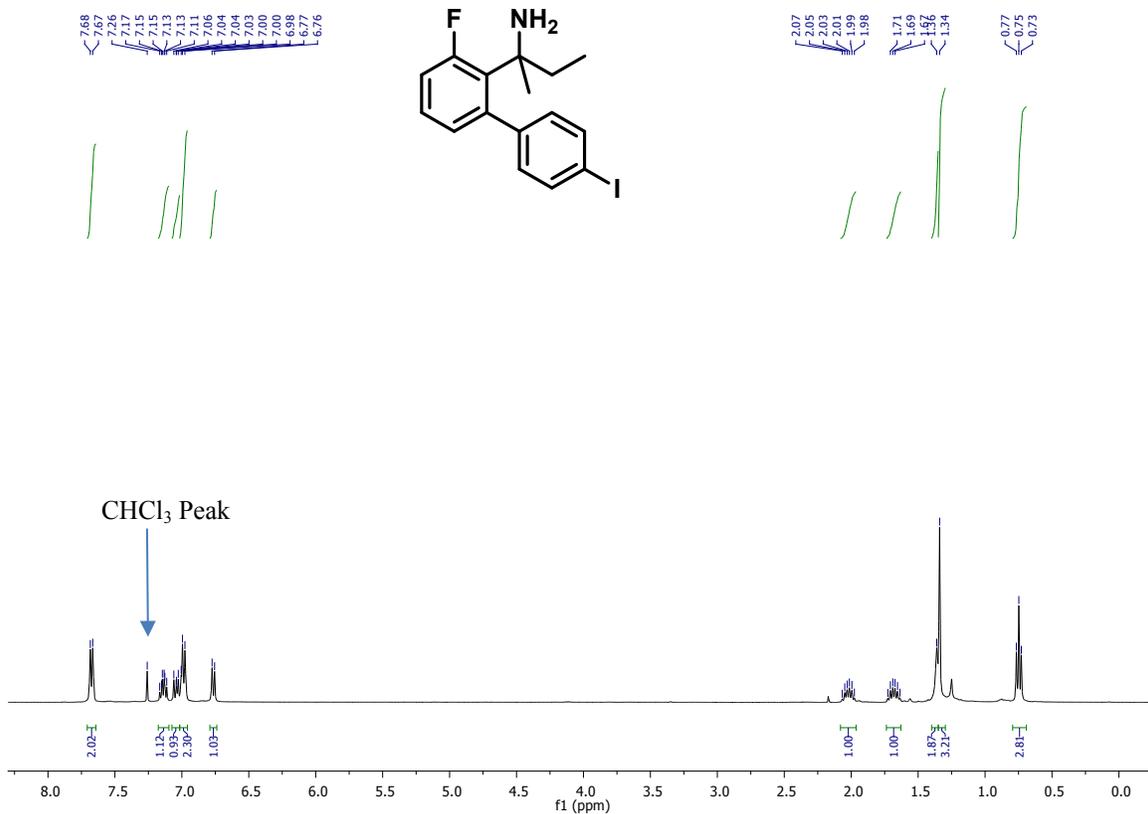


Figure S-103. ¹H NMR spectrum of **1n** (CDCl₃, 400 MHz, 298 K)

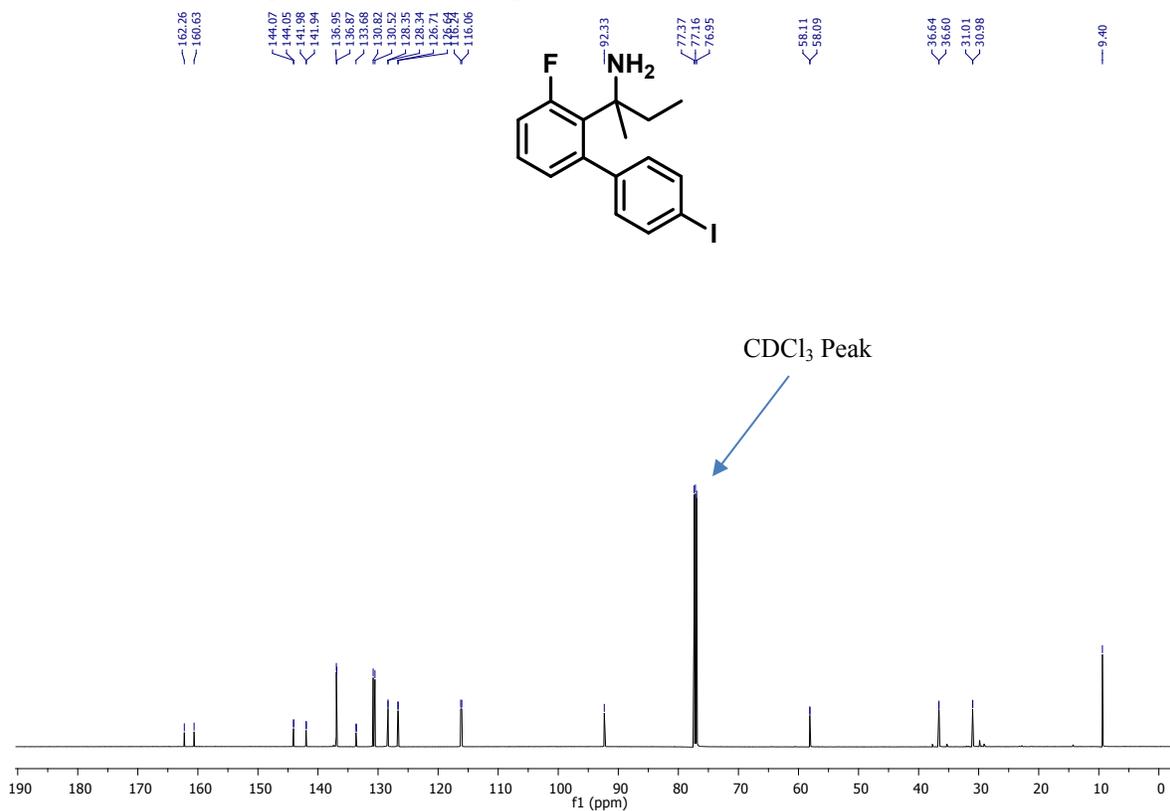


Figure S-104. ¹³C NMR spectrum of **1n** (CDCl₃, 151 MHz, 298 K)

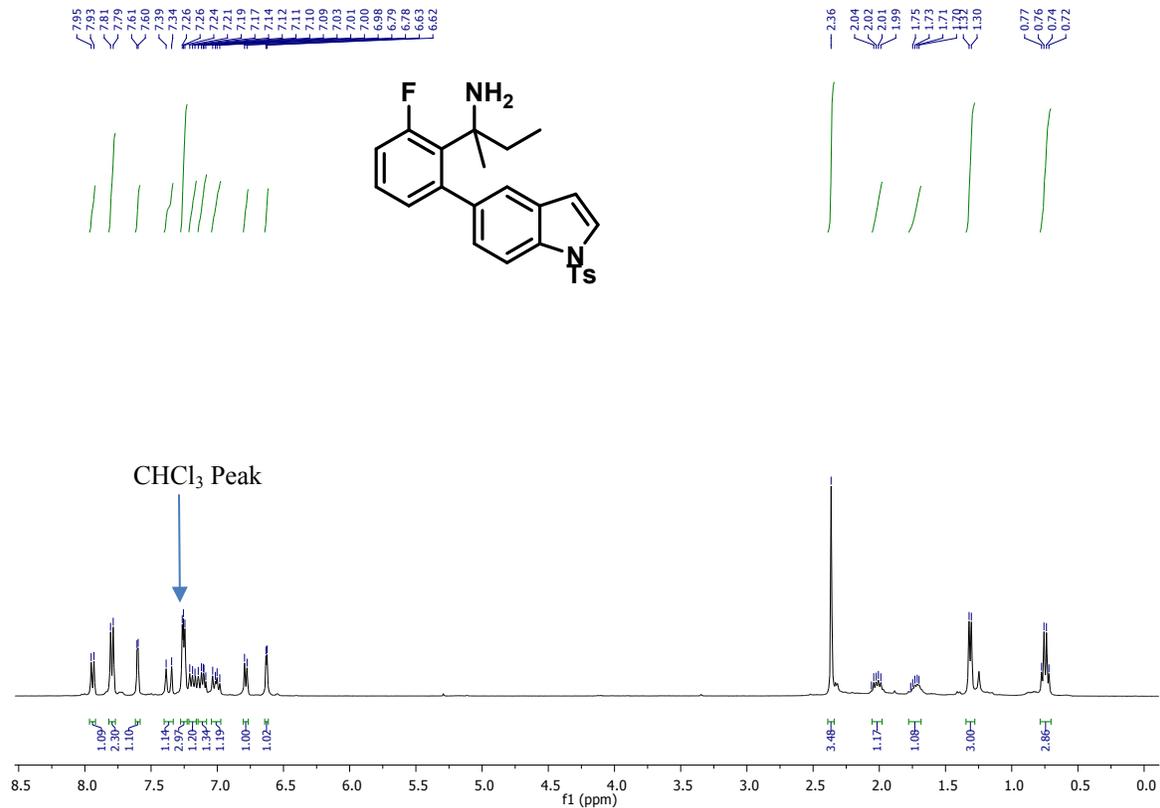


Figure S-105. ¹H NMR spectrum of **1o** (CDCl₃, 400 MHz, 298 K)

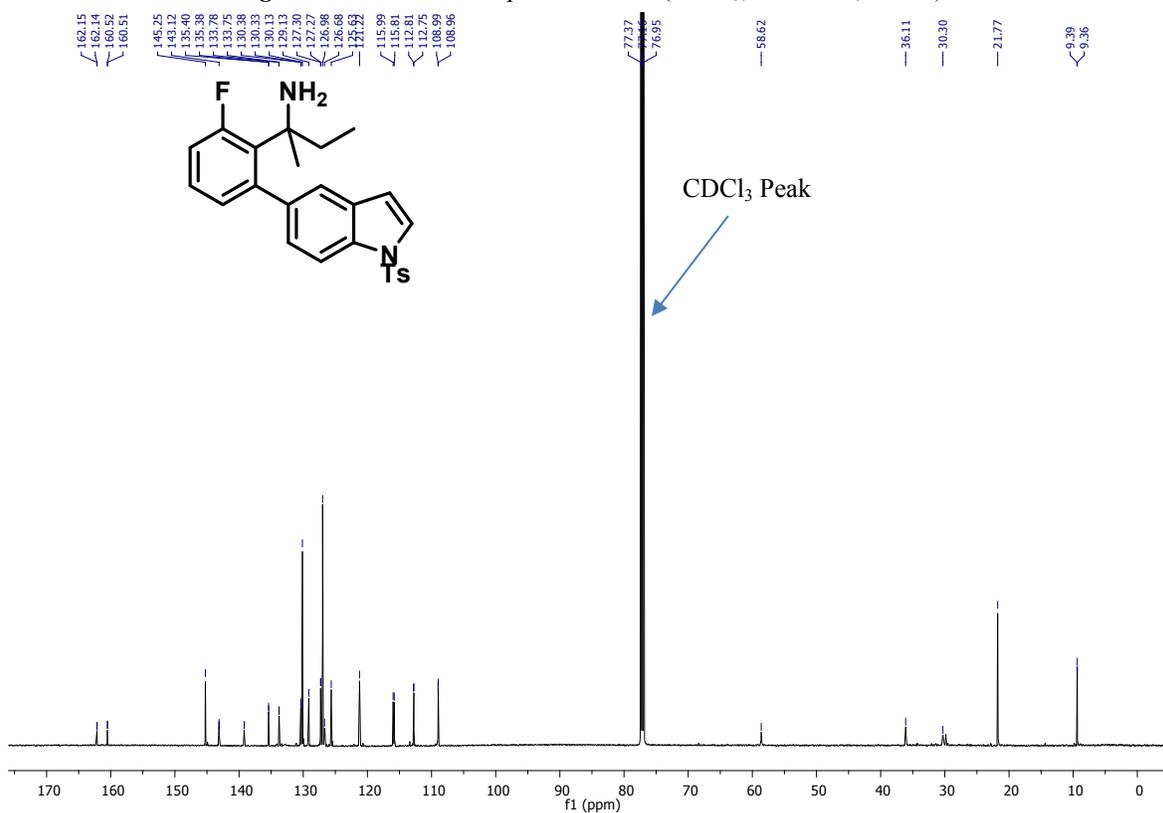


Figure S-106. ¹³C NMR spectrum of **1o** (CDCl₃, 151 MHz, 298 K)

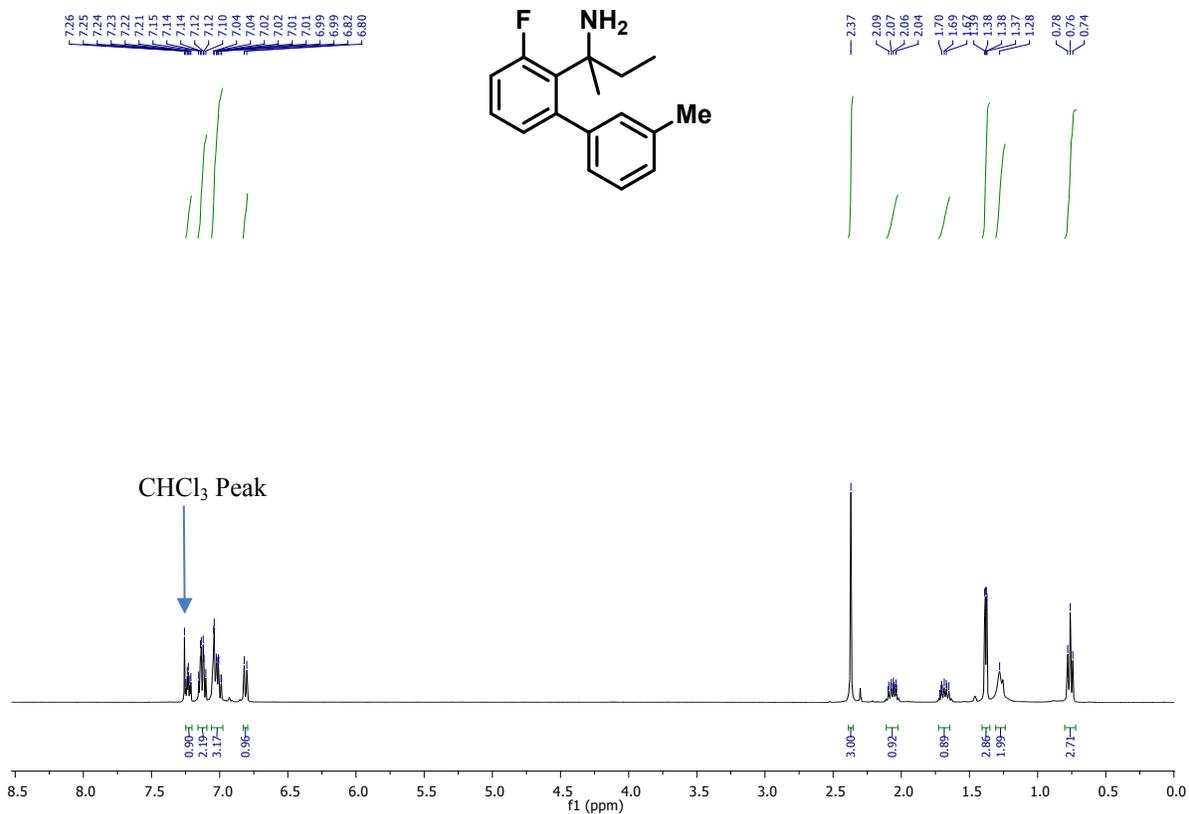


Figure S-107. ¹H NMR spectrum of **1p** (CDCl₃, 400 MHz, 298 K)

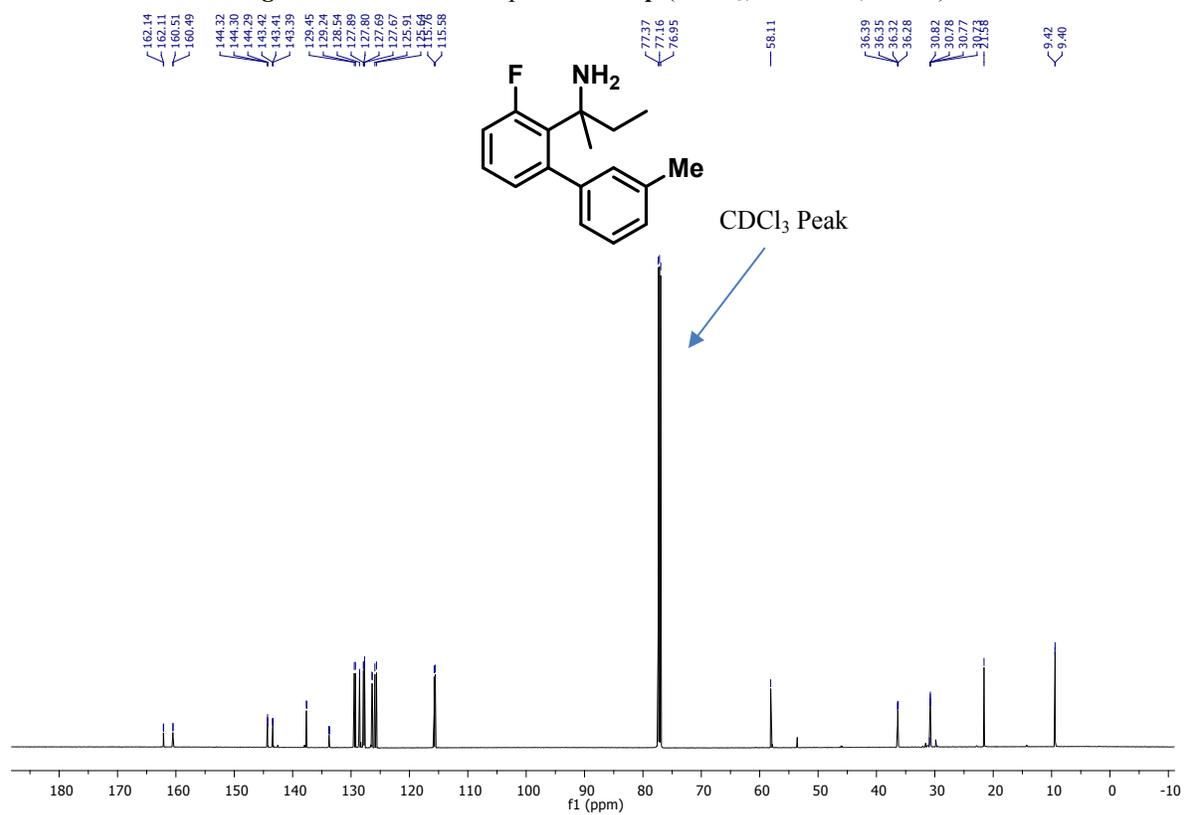


Figure S-108. ¹³C NMR spectrum of **1p** (CDCl₃, 151 MHz, 298 K)

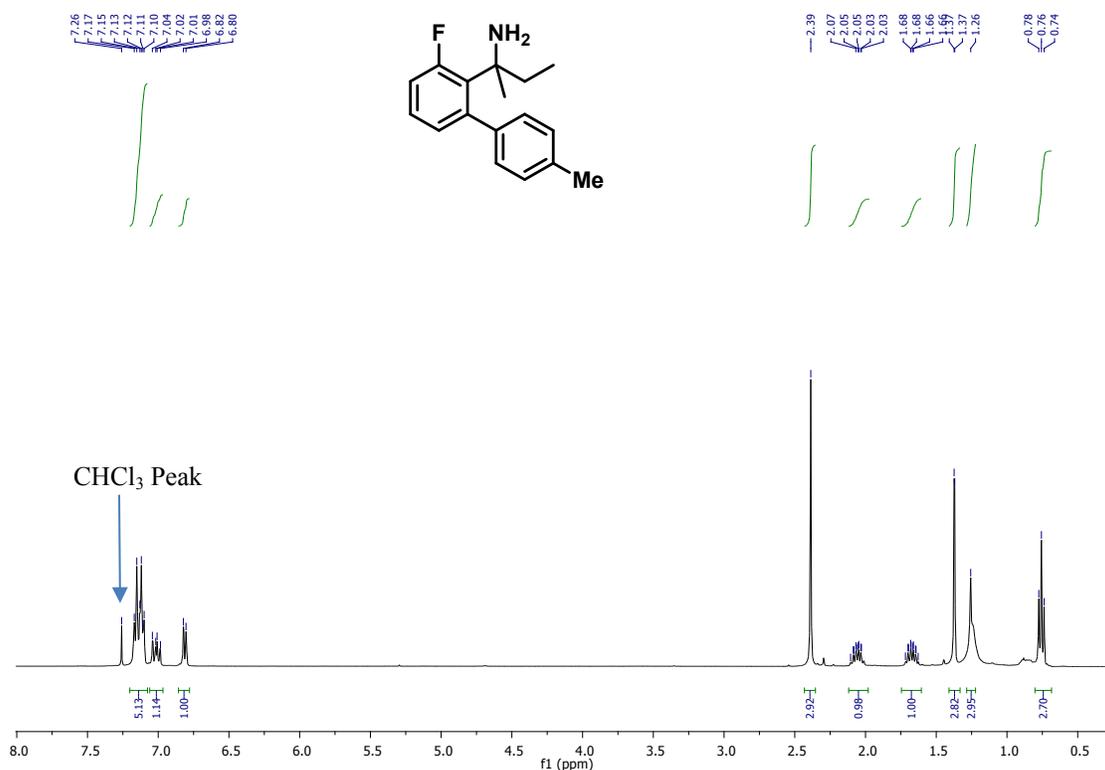


Figure S-109. ¹H NMR spectrum of **1q** (CDCl₃, 400 MHz, 298 K)

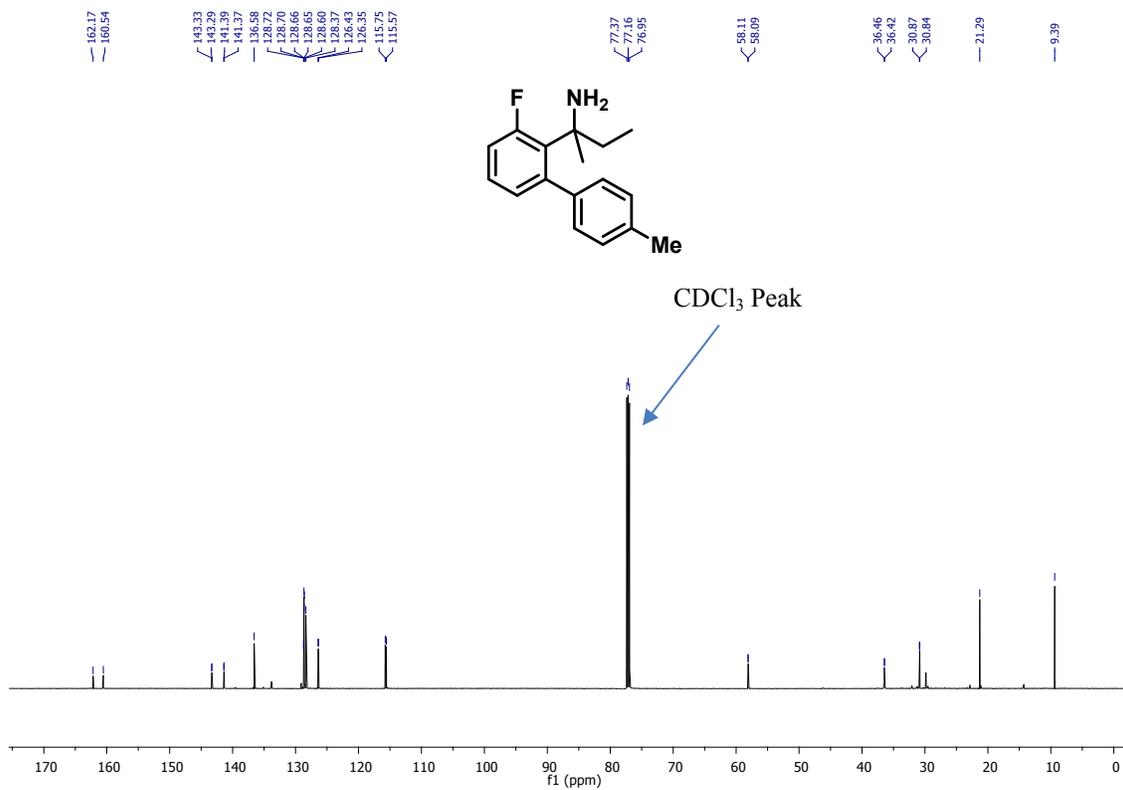


Figure S-110. ¹³C NMR spectrum of **1q** (CDCl₃, 151 MHz, 298 K)

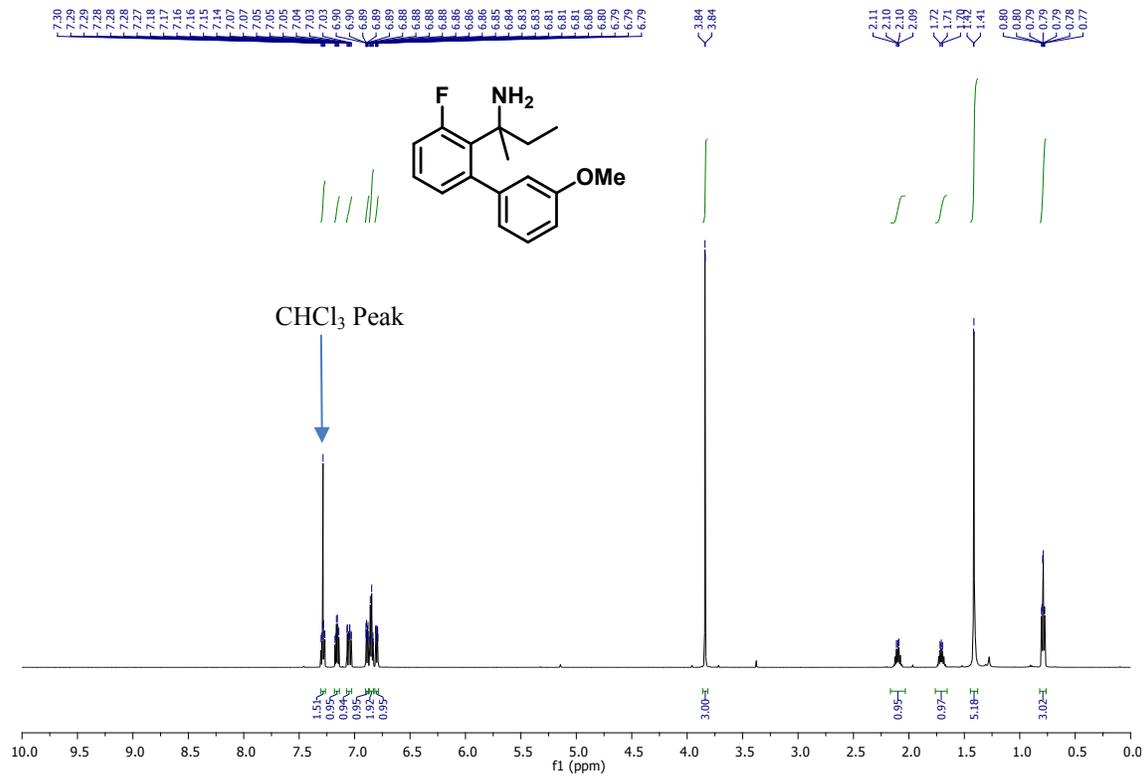


Figure S-111. $^1\text{H NMR}$ spectrum of **1r** (CDCl_3 , 400 MHz, 298 K)

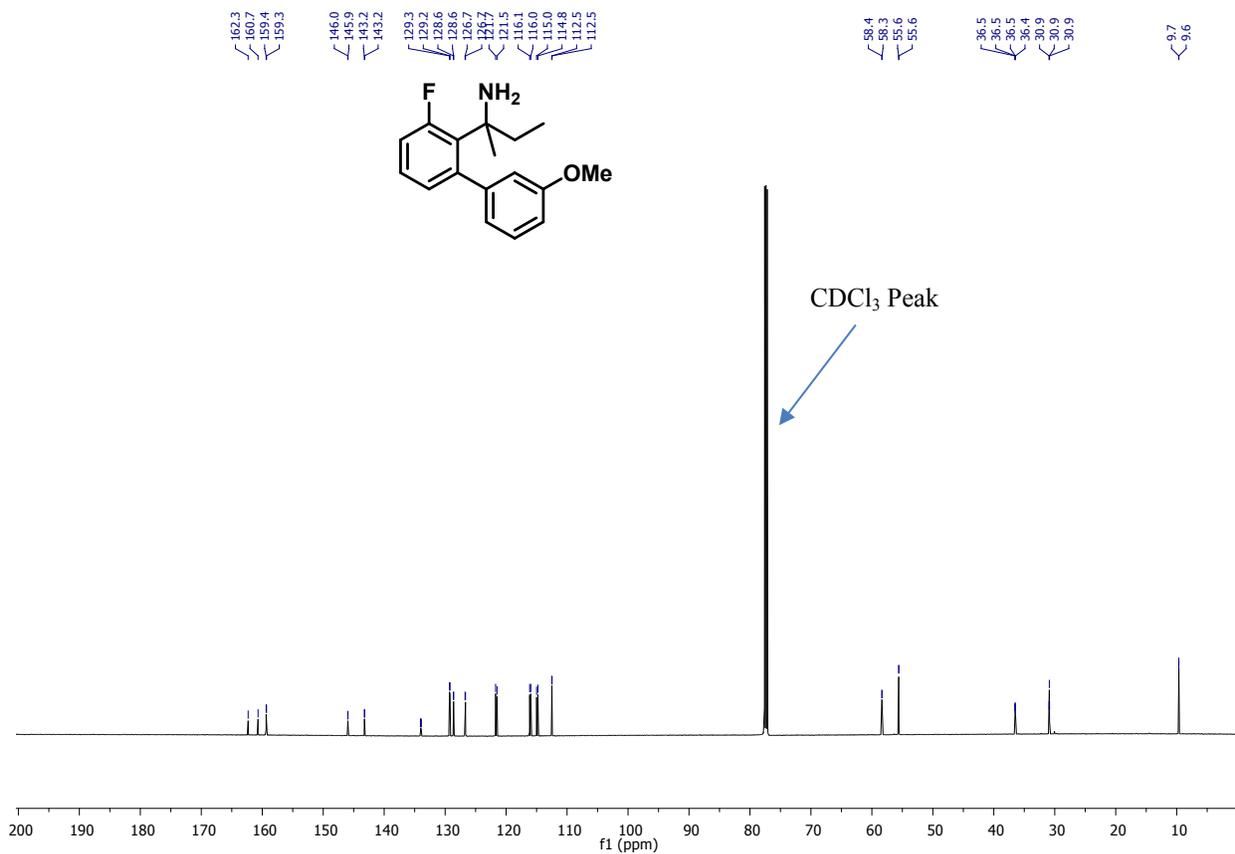


Figure S-112. $^{13}\text{C NMR}$ spectrum of **1r** (CDCl_3 , 151 MHz, 298 K)

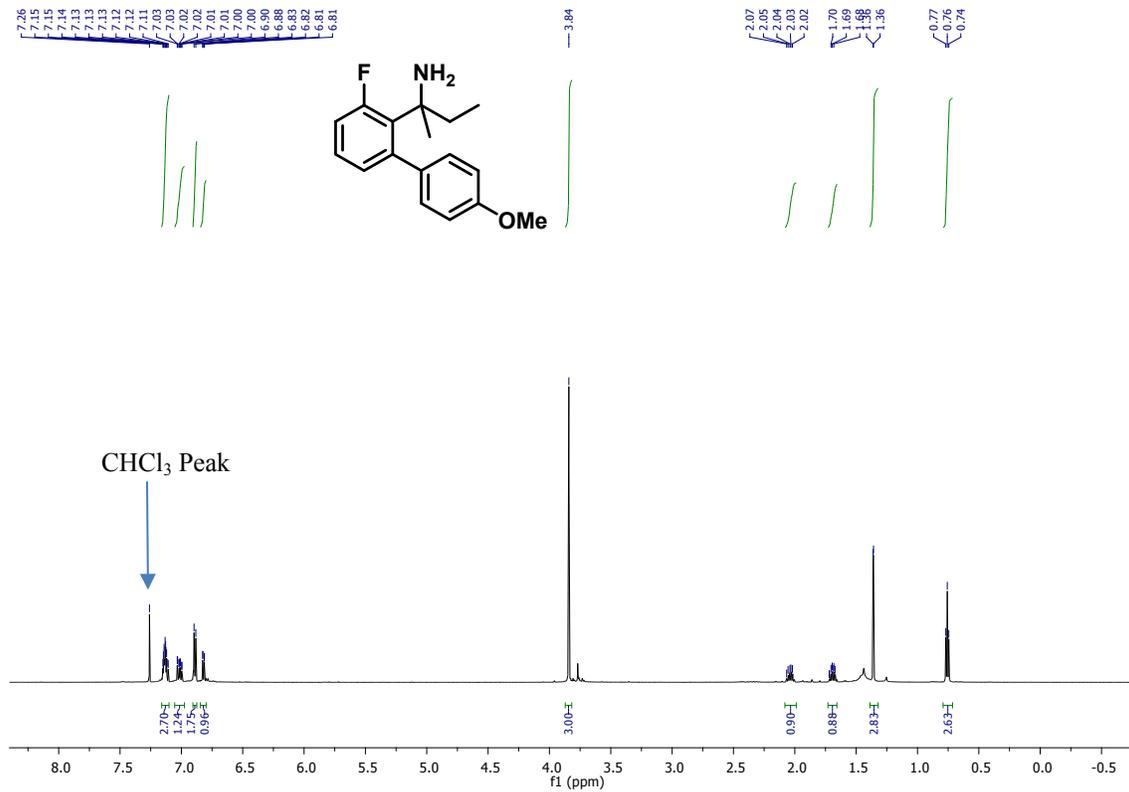


Figure S-113. ¹H NMR spectrum of **1s** (CDCl₃, 400 MHz, 298 K)

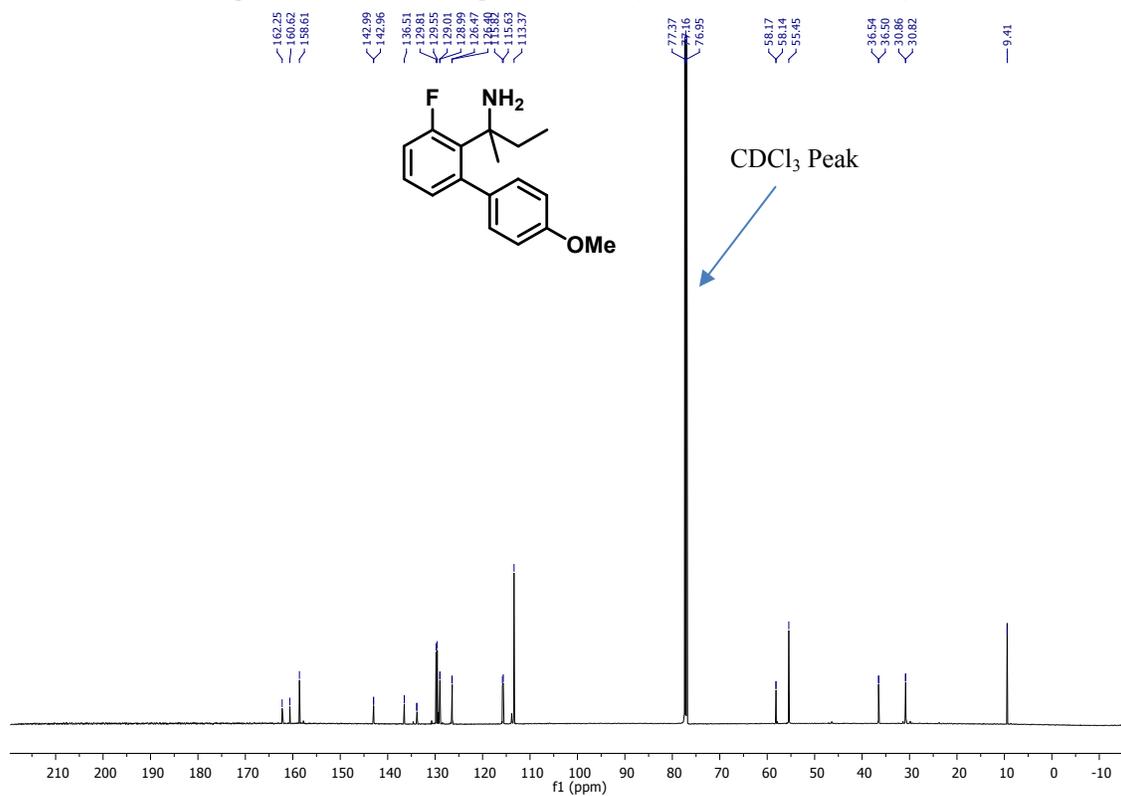


Figure S-114. ¹³C NMR spectrum of **1s** (CDCl₃, 151 MHz, 298 K)

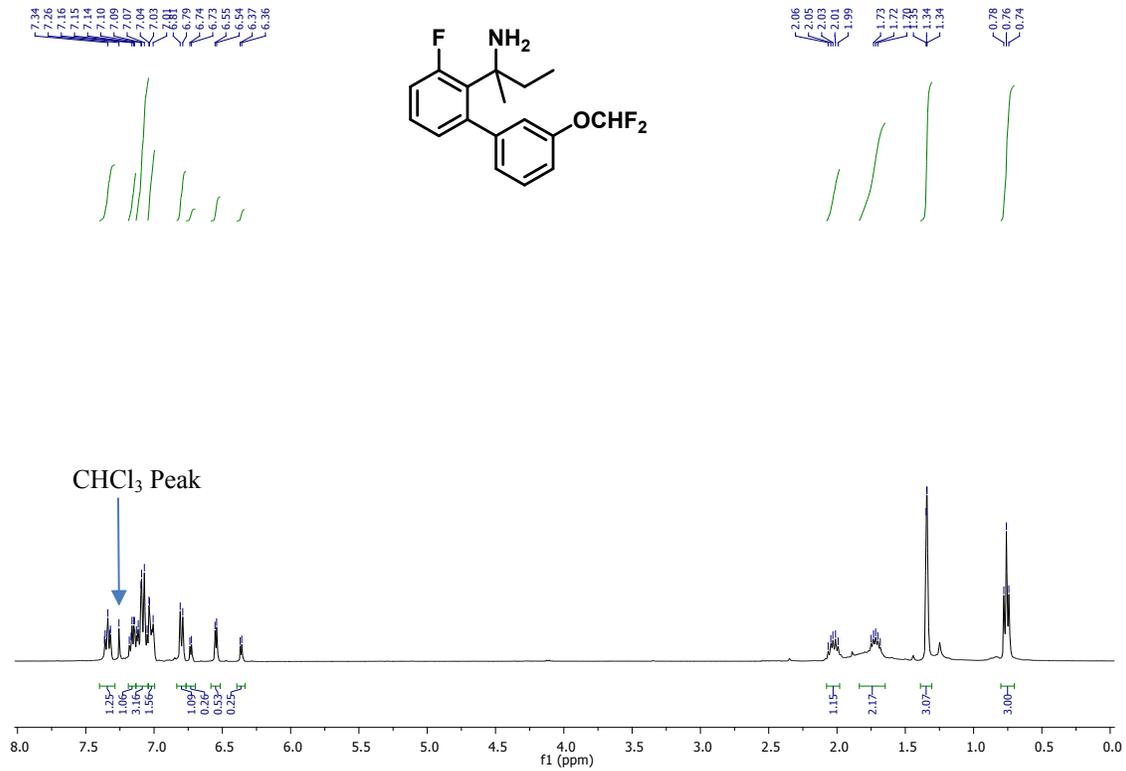


Figure S-115. ¹H NMR spectrum of **1t** (CDCl₃, 400 MHz, 298 K)

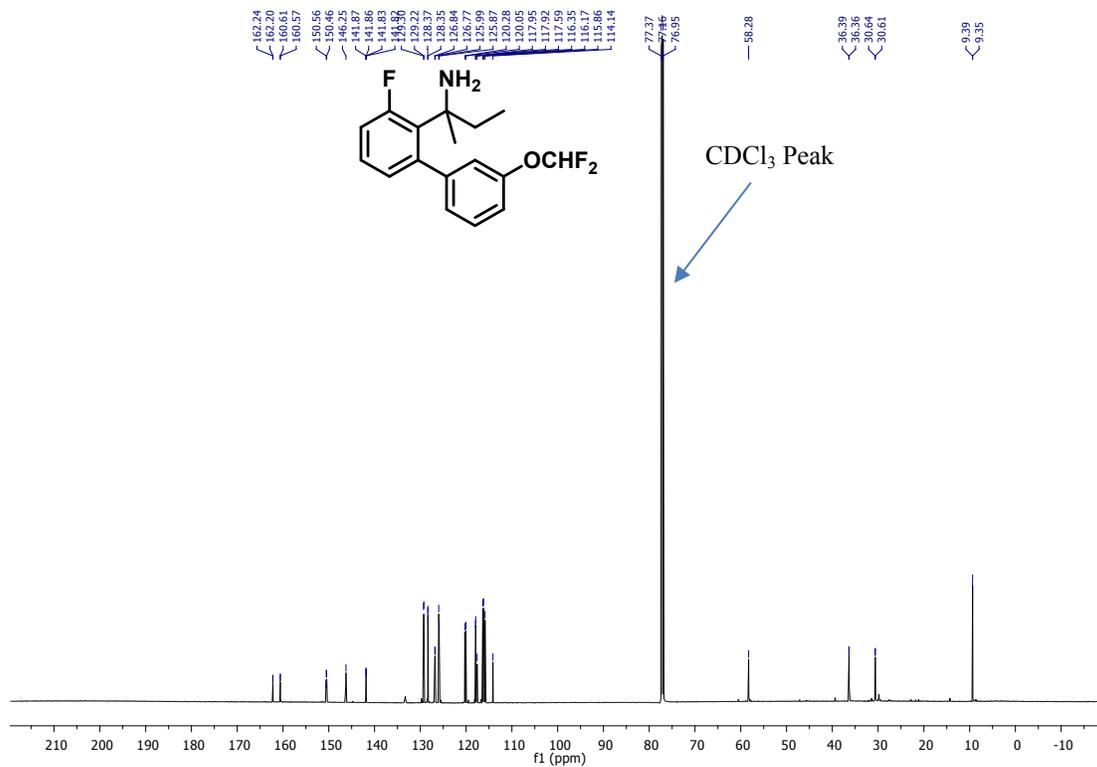


Figure S-116. ¹³C NMR spectrum of **1t** (CDCl₃, 151 MHz, 298 K)

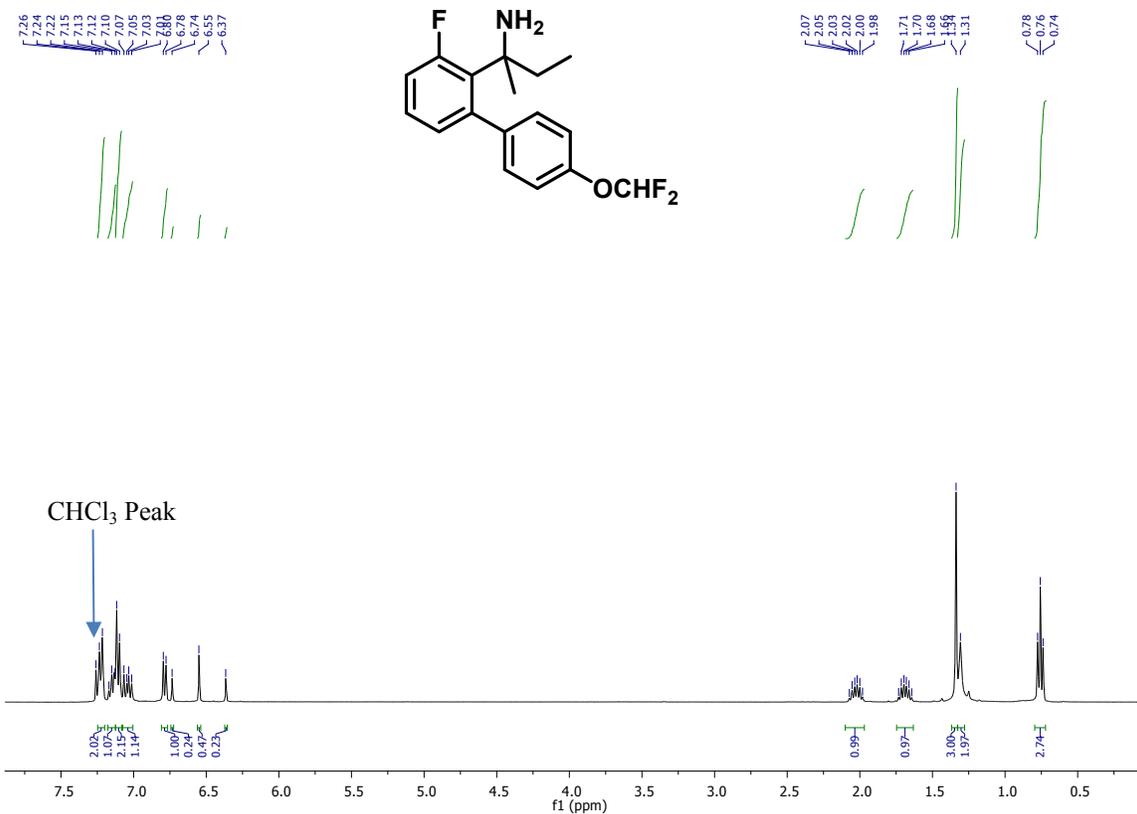


Figure S-117. ¹H NMR spectrum of **1u** (CDCl₃, 400 MHz, 298 K)

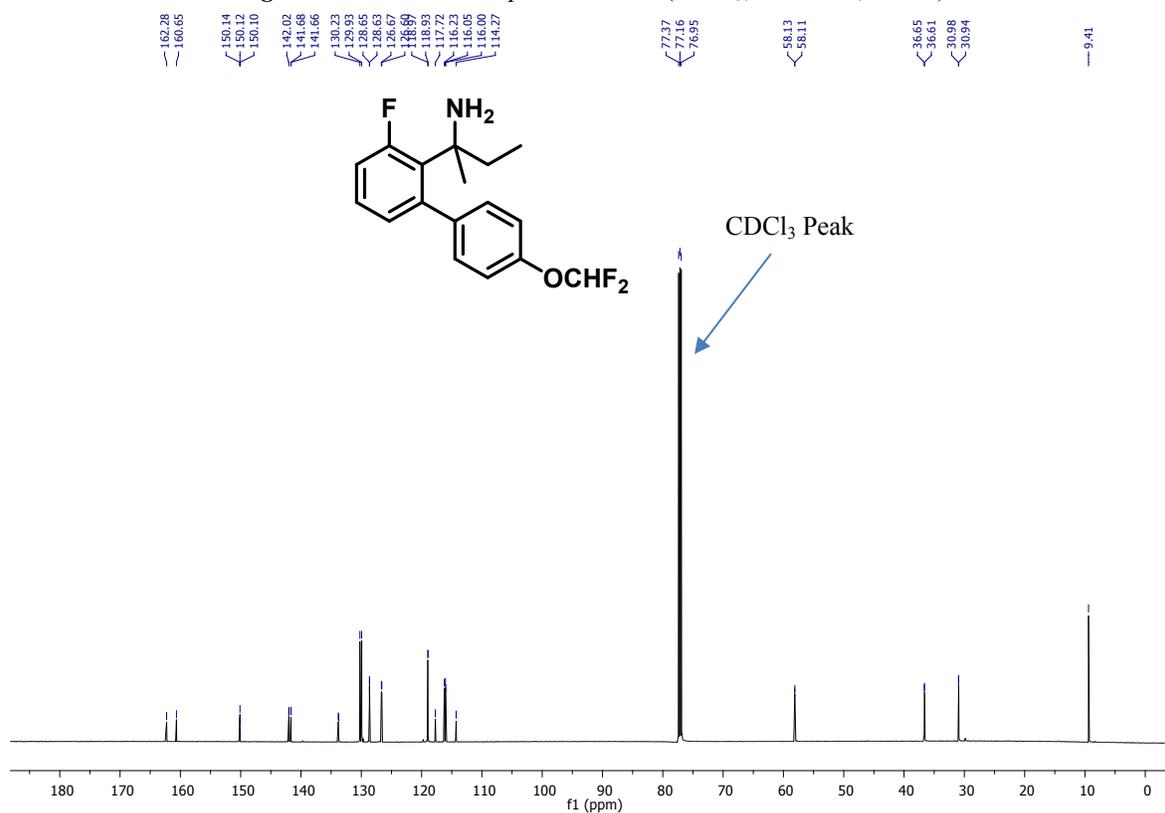


Figure S-118. ¹³C NMR spectrum of **1u** (CDCl₃, 151 MHz, 298 K)

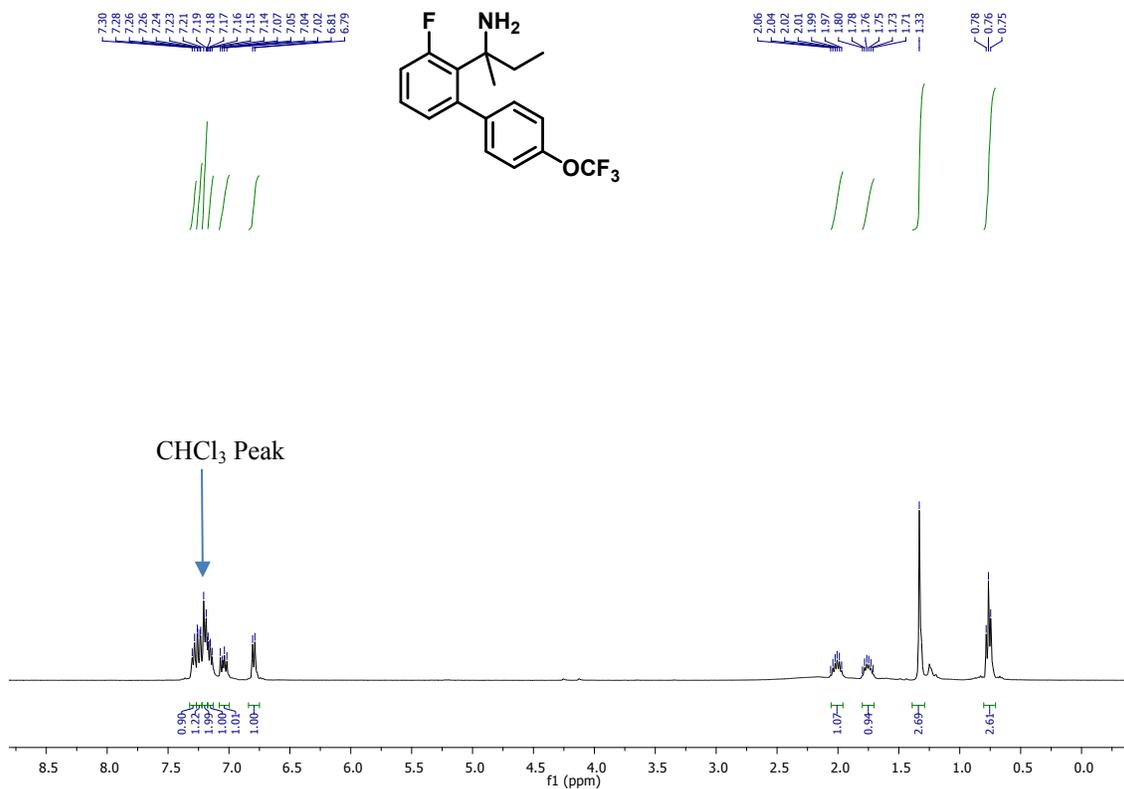


Figure S-119. ¹H NMR spectrum of **1v** (CDCl₃, 400 MHz, 298 K)

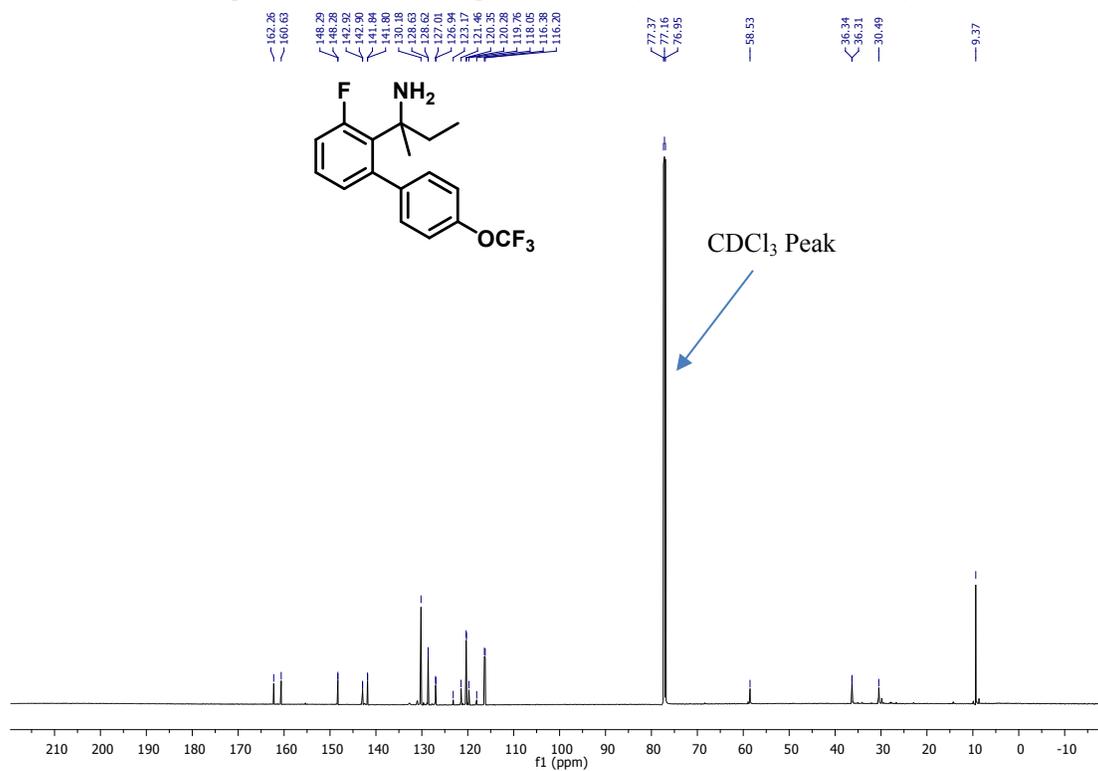


Figure S-120. ¹³C NMR spectrum of **1v** (CDCl₃, 151 MHz, 298 K)

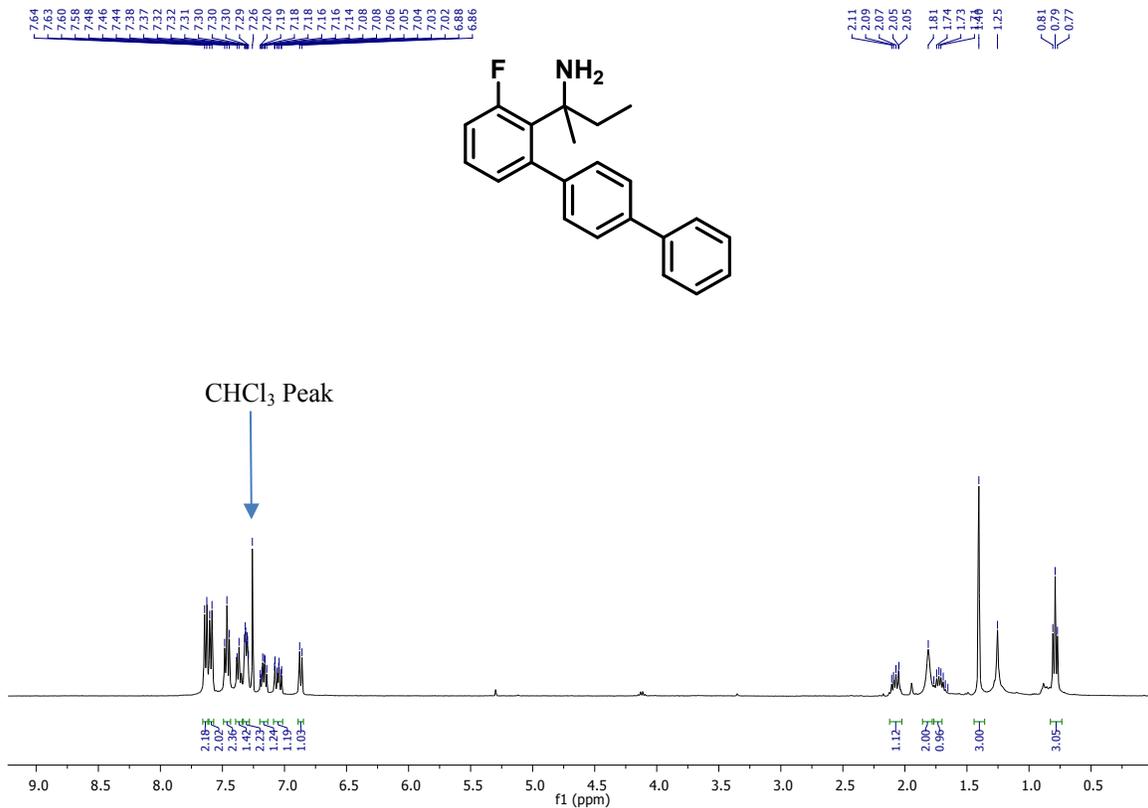


Figure S-121. ¹H NMR spectrum of **1w** (CDCl₃, 400 MHz, 298 K)

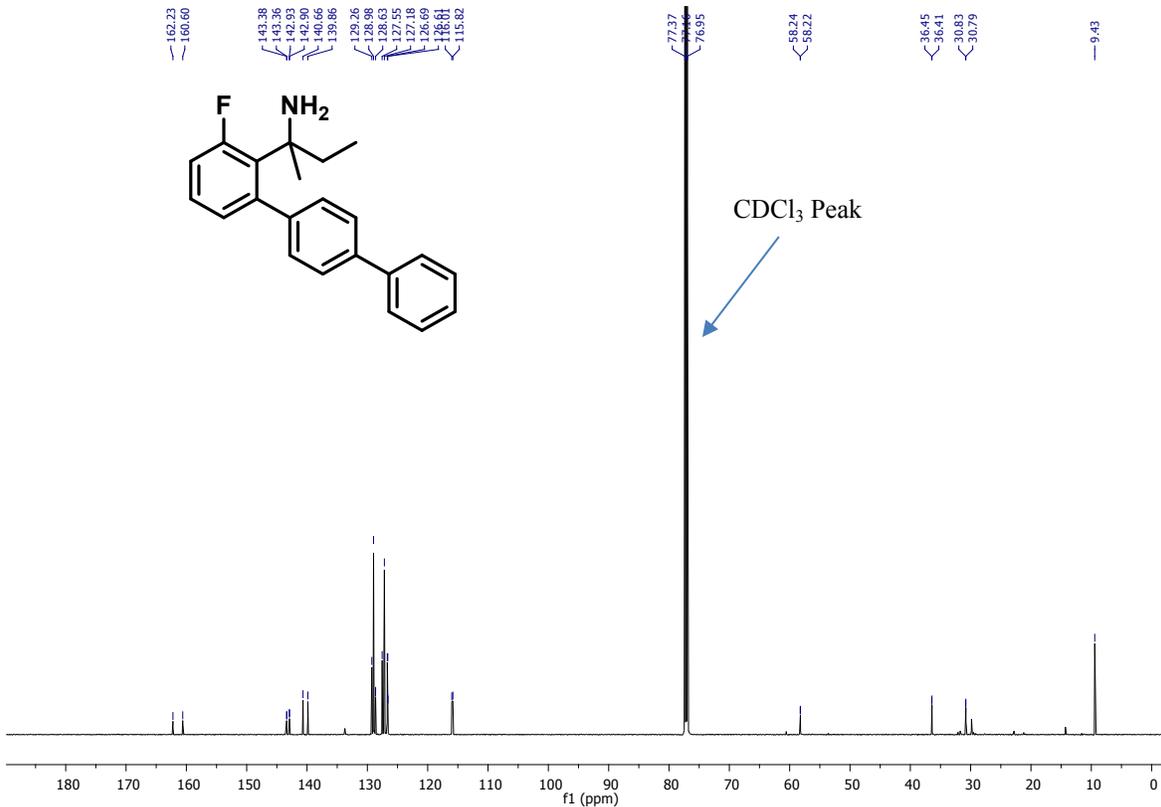


Figure S-122. ¹³C NMR spectrum of **1w** (CDCl₃, 151 MHz, 298 K)

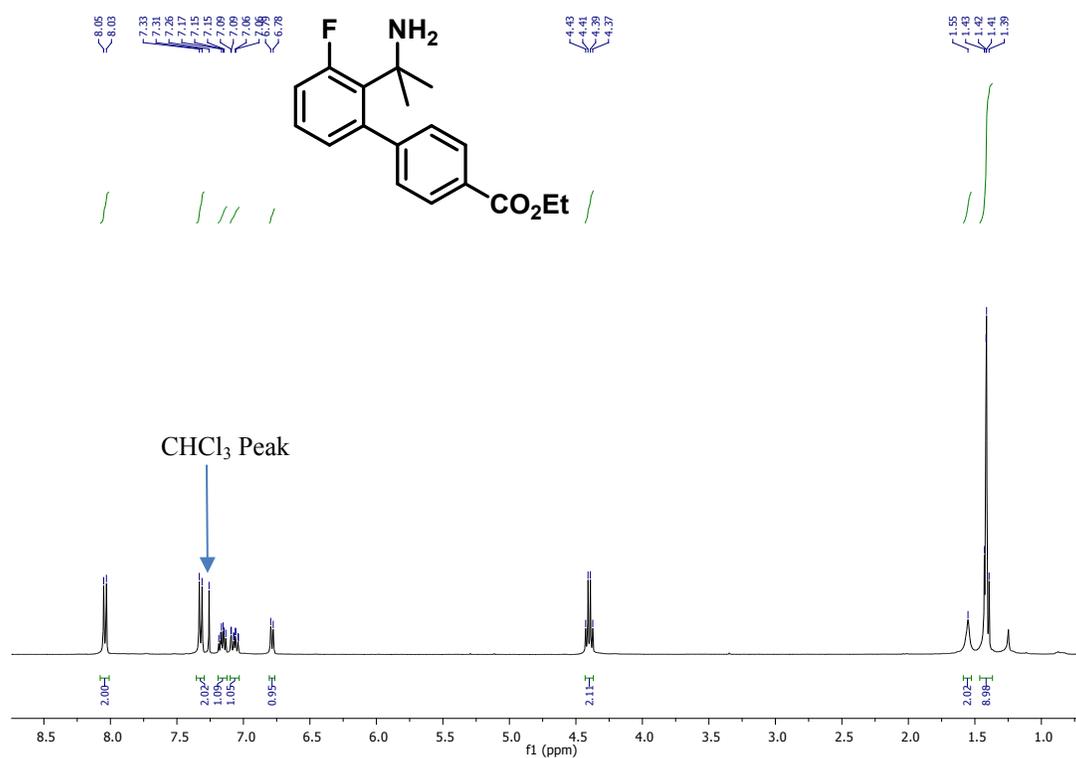


Figure S-125. ¹H NMR spectrum of **2a** (CDCl₃, 400 MHz, 298 K)

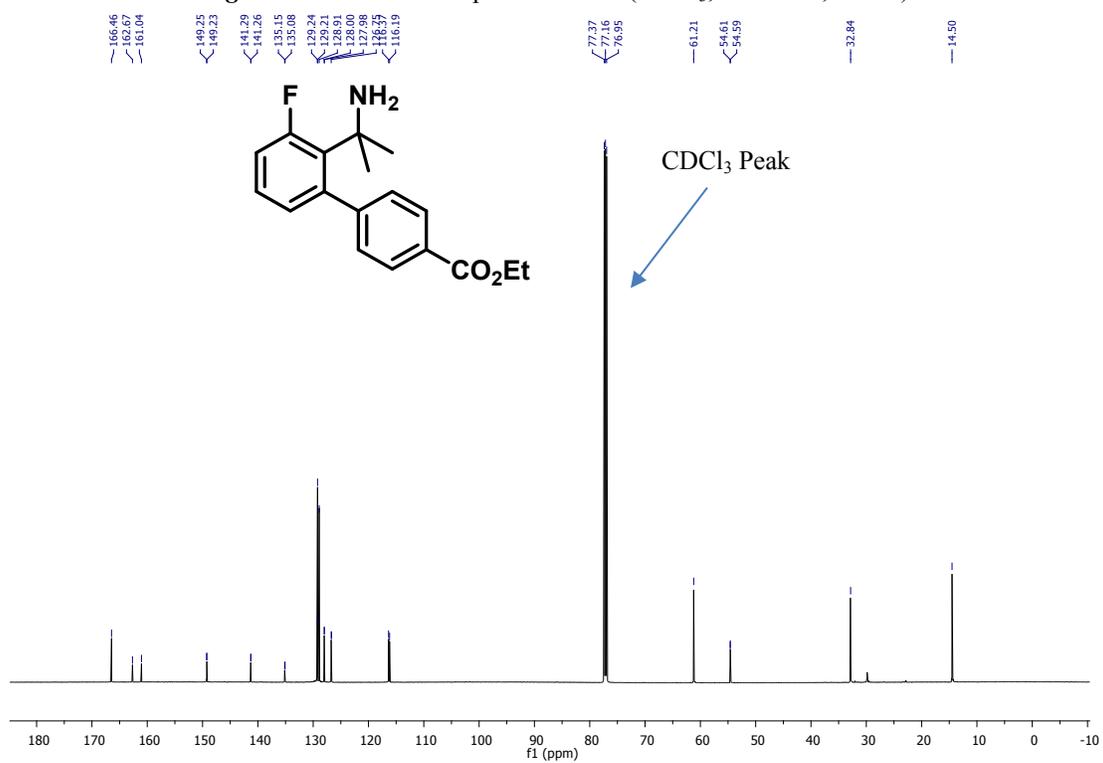


Figure S-126. ¹³C NMR spectrum of **2a** (CDCl₃, 151 MHz, 298 K)

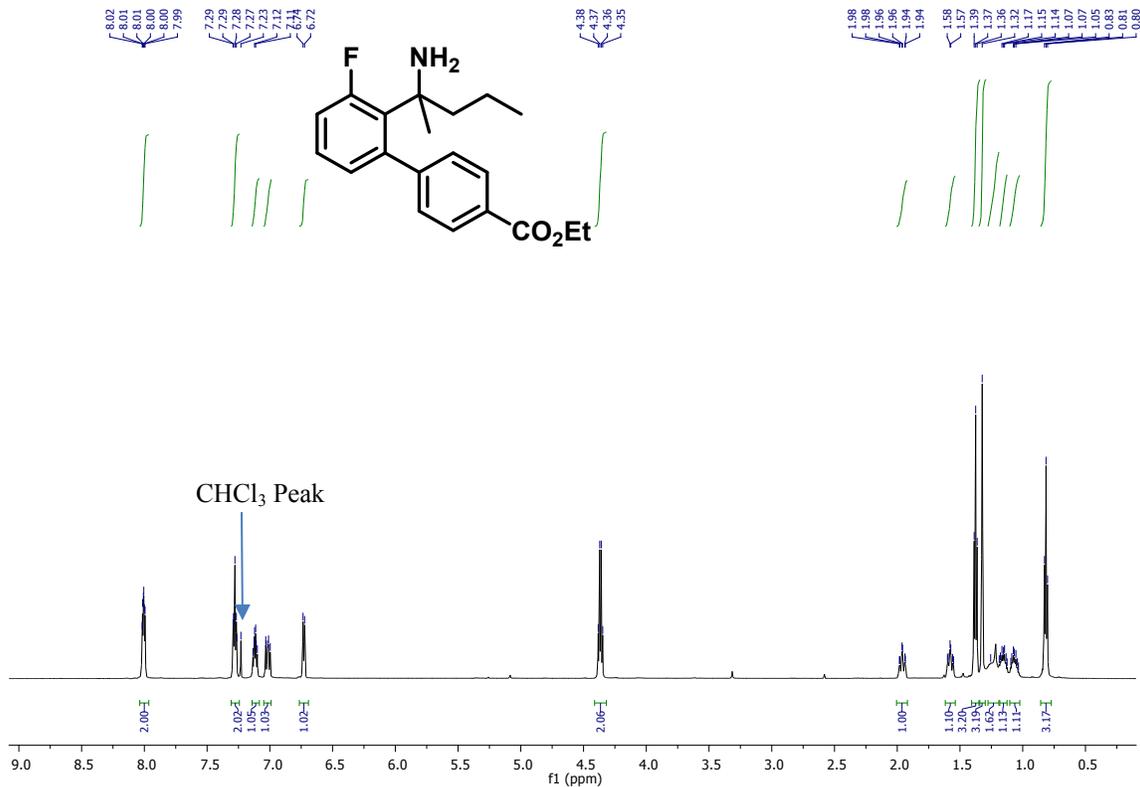


Figure S-127. ¹H NMR spectrum of **2b** (CDCl₃, 600 MHz, 298 K)

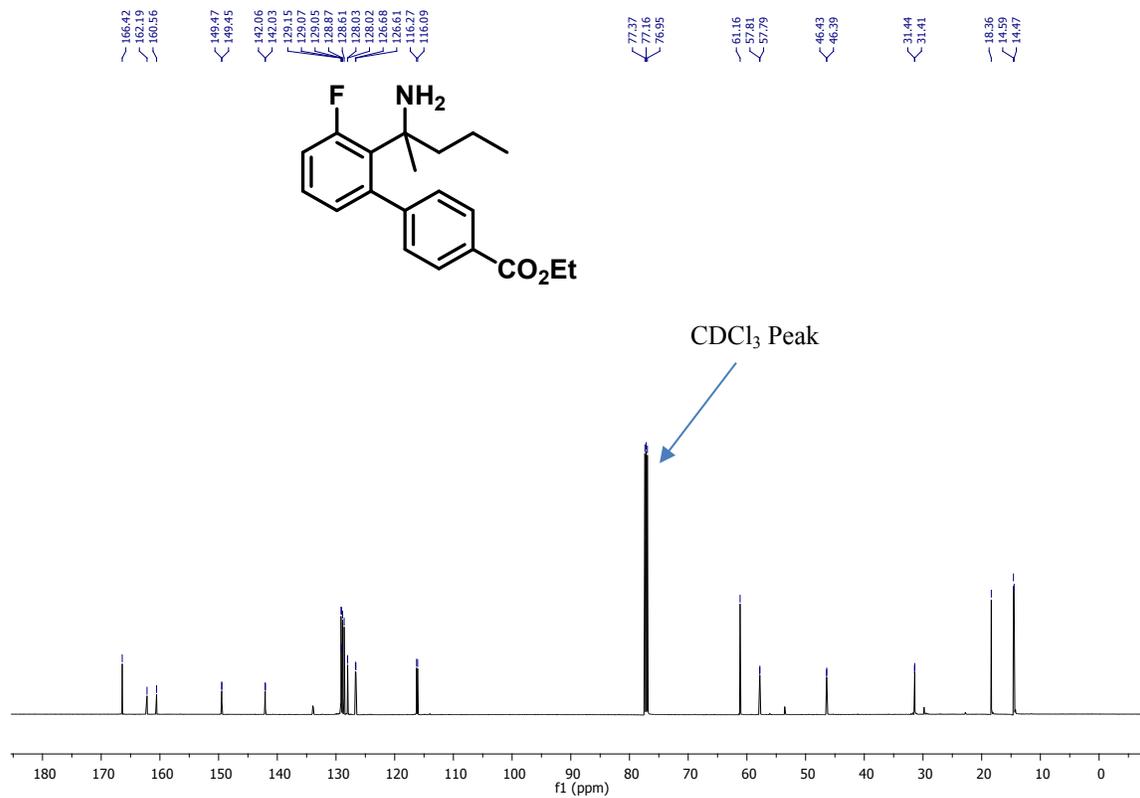


Figure S-128. ¹³C NMR spectrum of **2b** (CDCl₃, 151 MHz, 298 K)

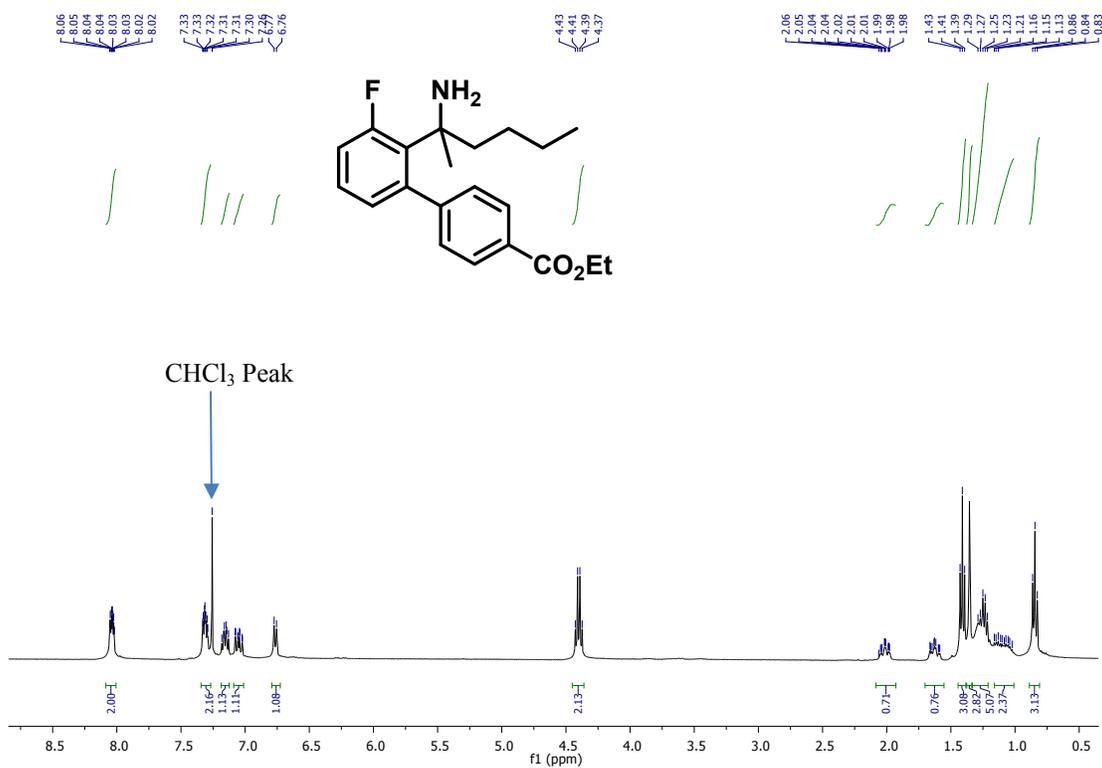


Figure S-129. ¹H NMR spectrum of **2c** (CDCl₃, 400 MHz, 298 K)

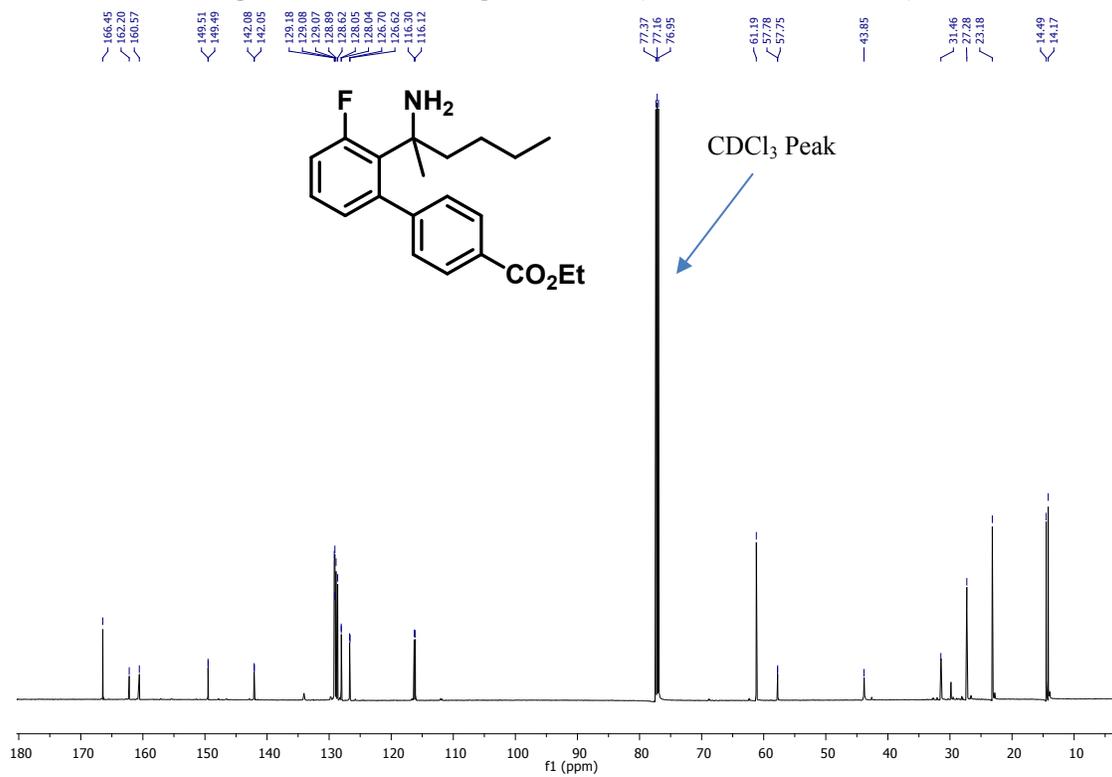


Figure S-130. ¹³C NMR spectrum of **2c** (CDCl₃, 151 MHz, 298 K)

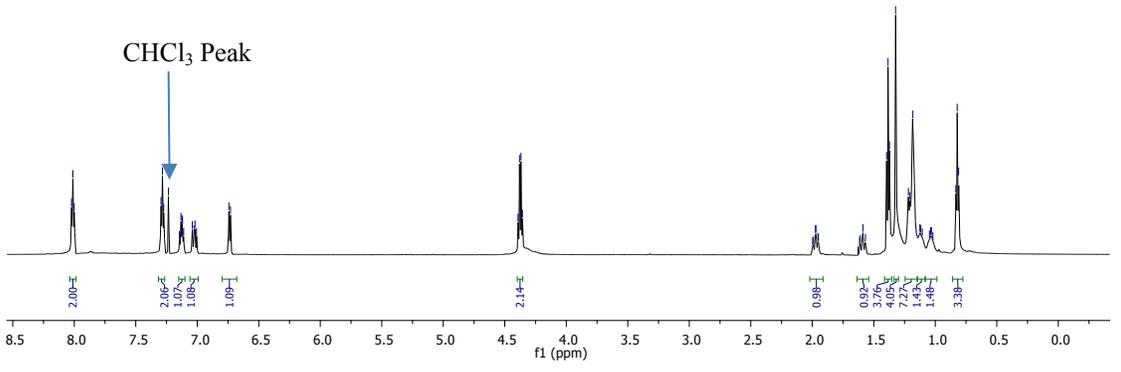
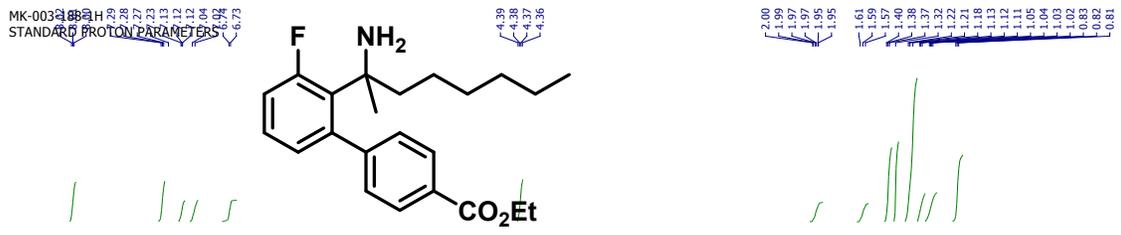


Figure S-131. ¹H NMR spectrum of **2d** (CDCl₃, 600 MHz, 298 K)

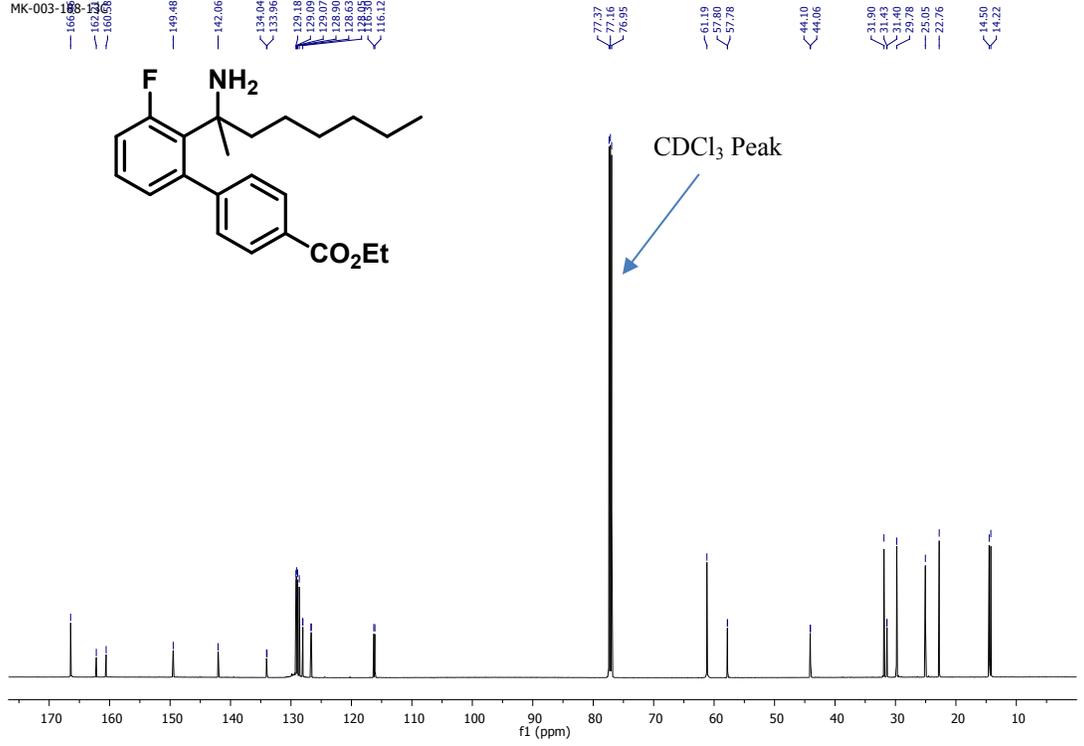


Figure S-132. ¹³C NMR spectrum of **2d** (CDCl₃, 151 MHz, 298 K)

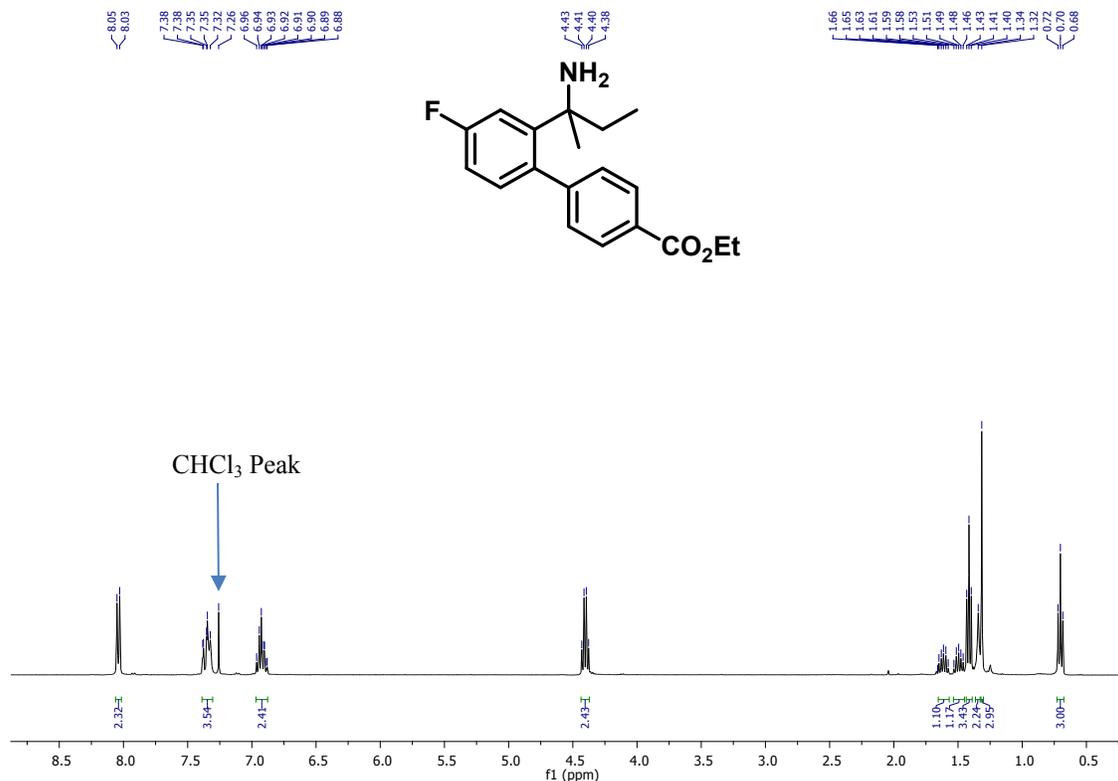


Figure S-133. ¹H NMR spectrum of **2e** (CDCl₃, 400 MHz, 298 K)

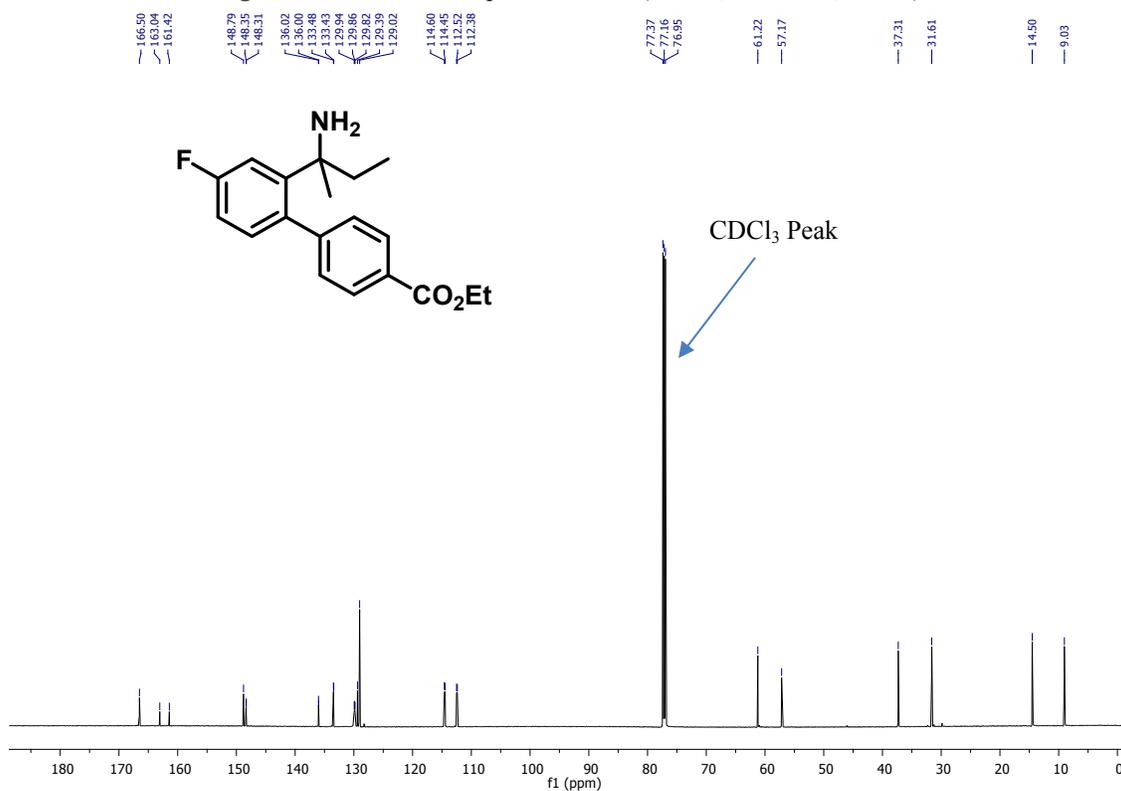


Figure S-134. ¹³C NMR spectrum of **2e** (CDCl₃, 151 MHz, 298 K)

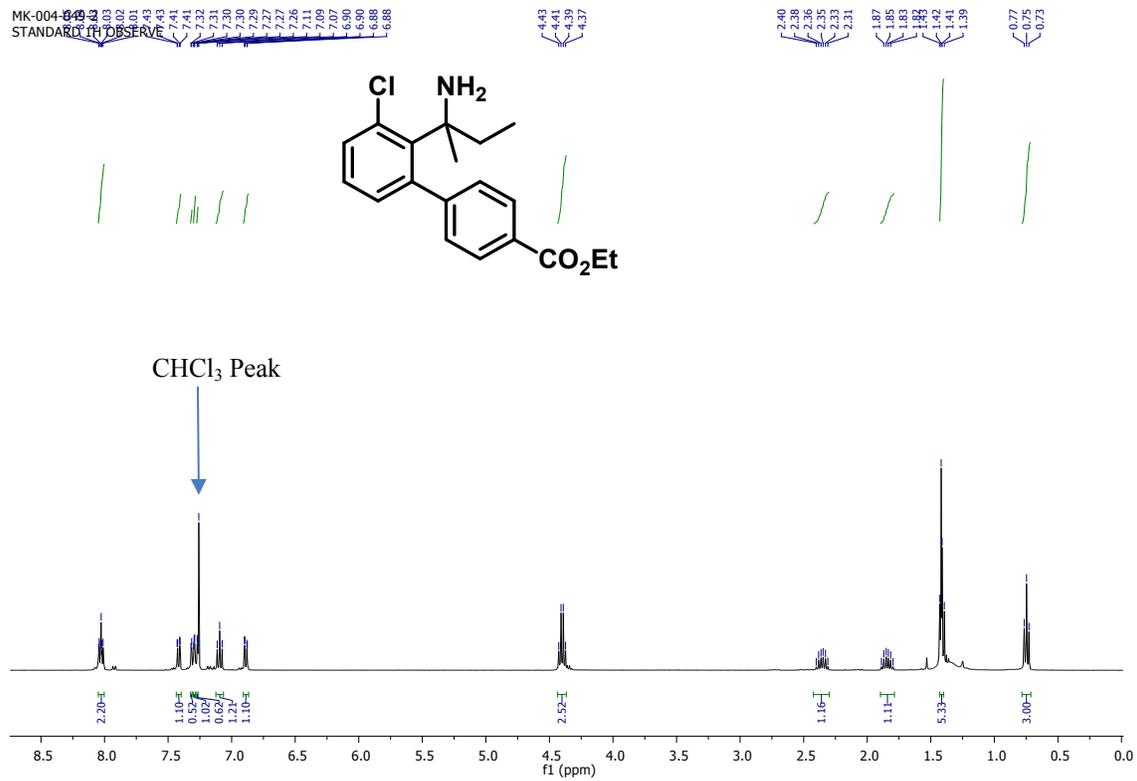


Figure S-135. ¹H NMR spectrum of **2f** (CDCl₃, 400 MHz, 298 K)

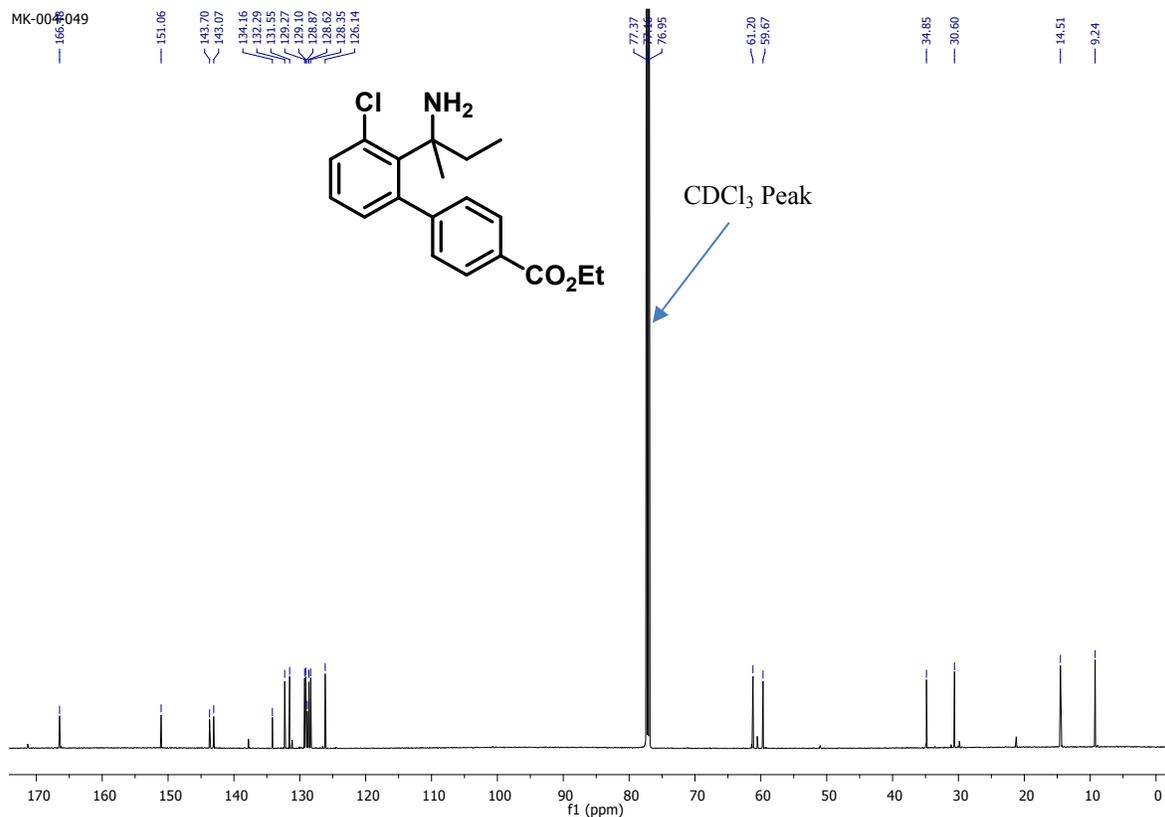


Figure S-136. ¹³C NMR spectrum of **2f** (CDCl₃, 151 MHz, 298 K)

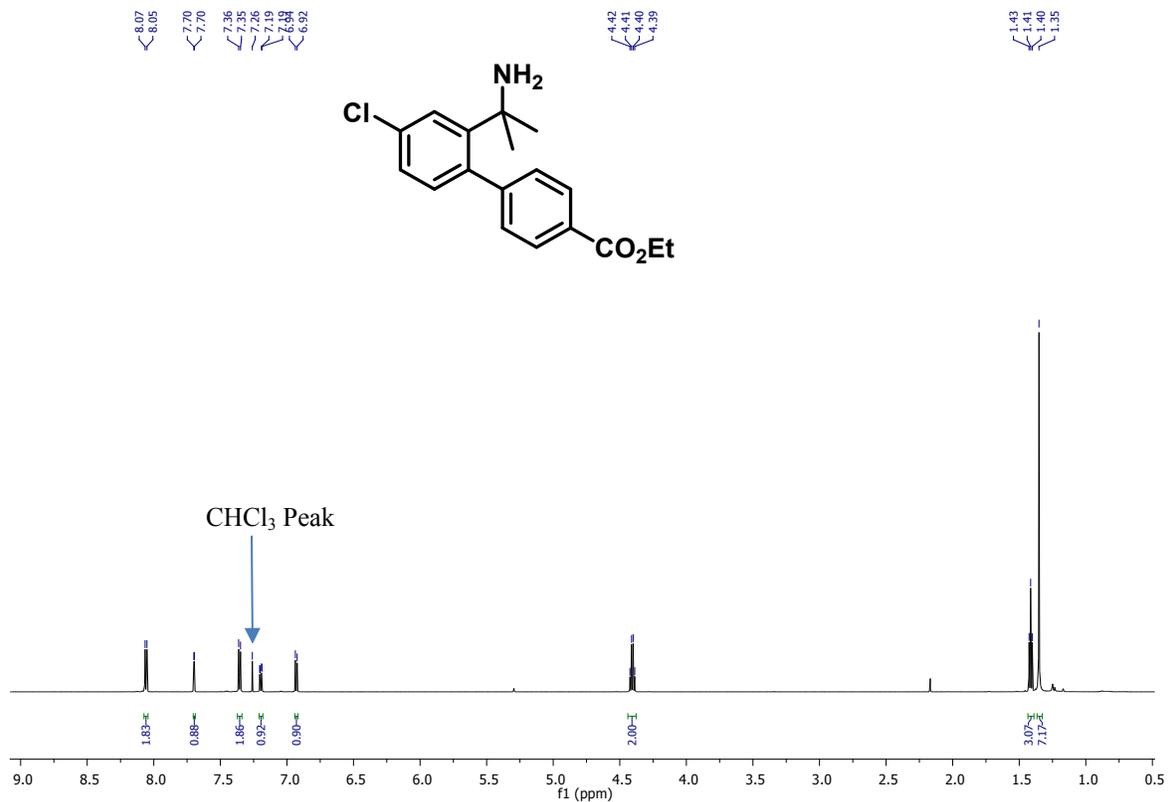


Figure S-137. ^1H NMR spectrum of **2g** (CDCl_3 , 400 MHz, 298 K)

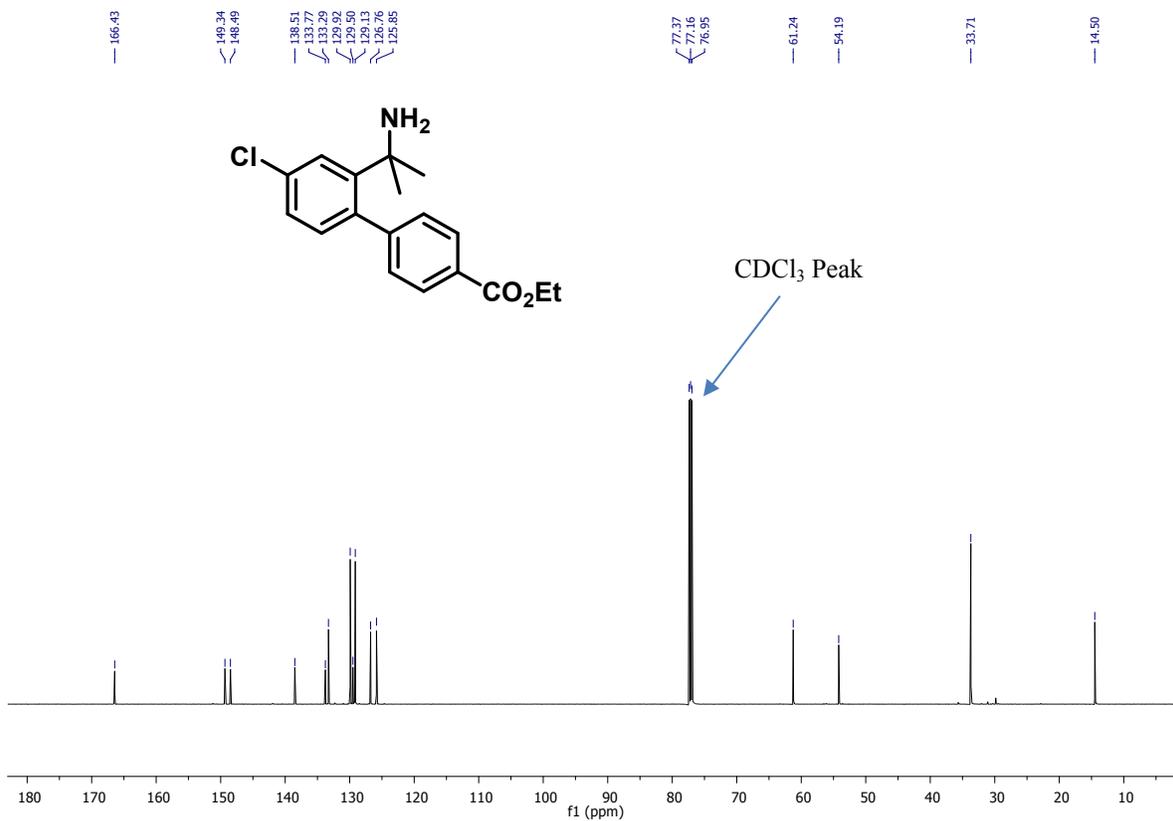


Figure S-138. ^{13}C NMR spectrum of **2g** (CDCl_3 , 151 MHz, 298 K)

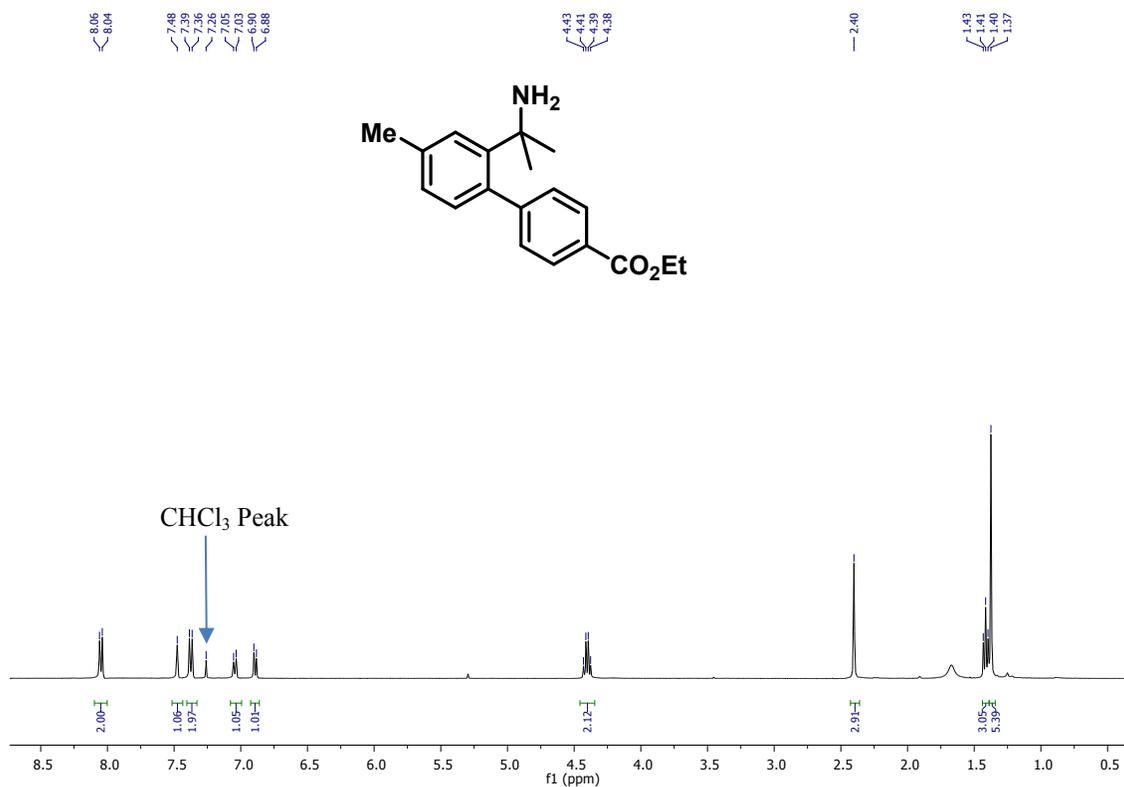


Figure S-139. ¹H NMR spectrum of **2h** (CDCl₃, 400 MHz, 298 K)

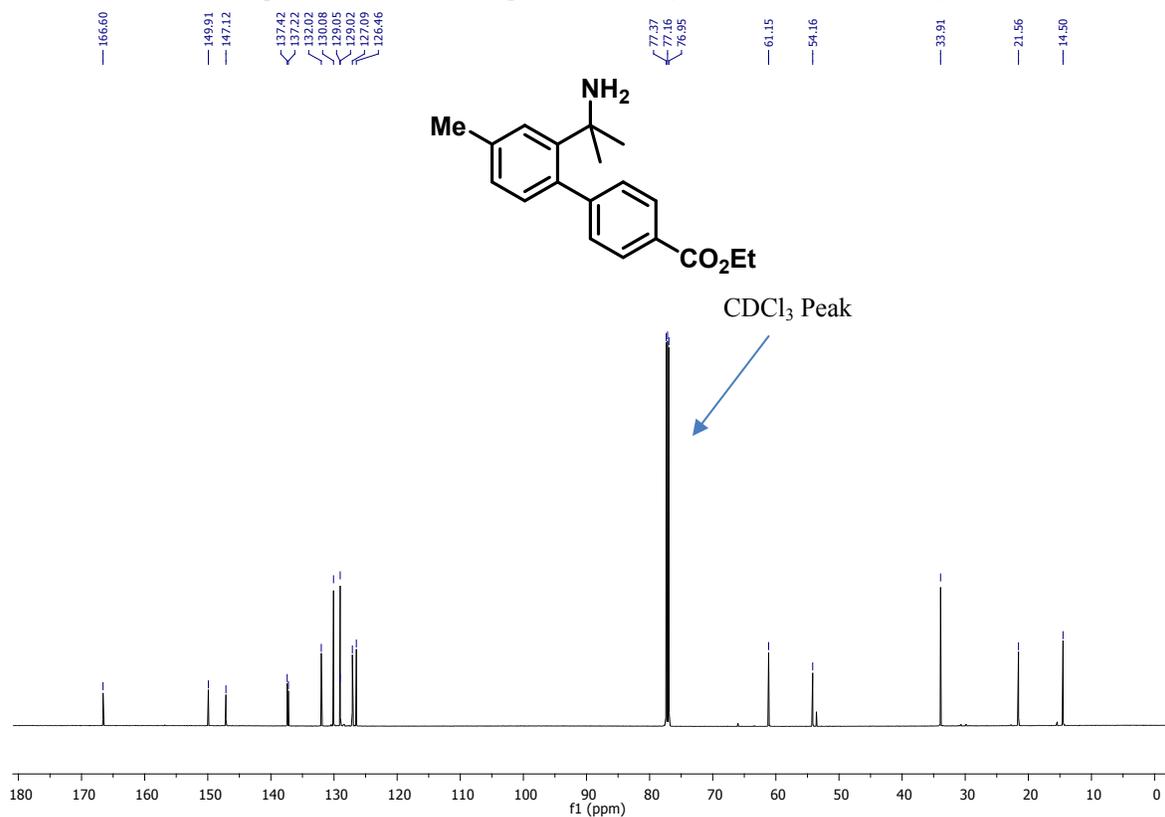


Figure S-140. ¹³C NMR spectrum of **2h** (CDCl₃, 151 MHz, 298 K)

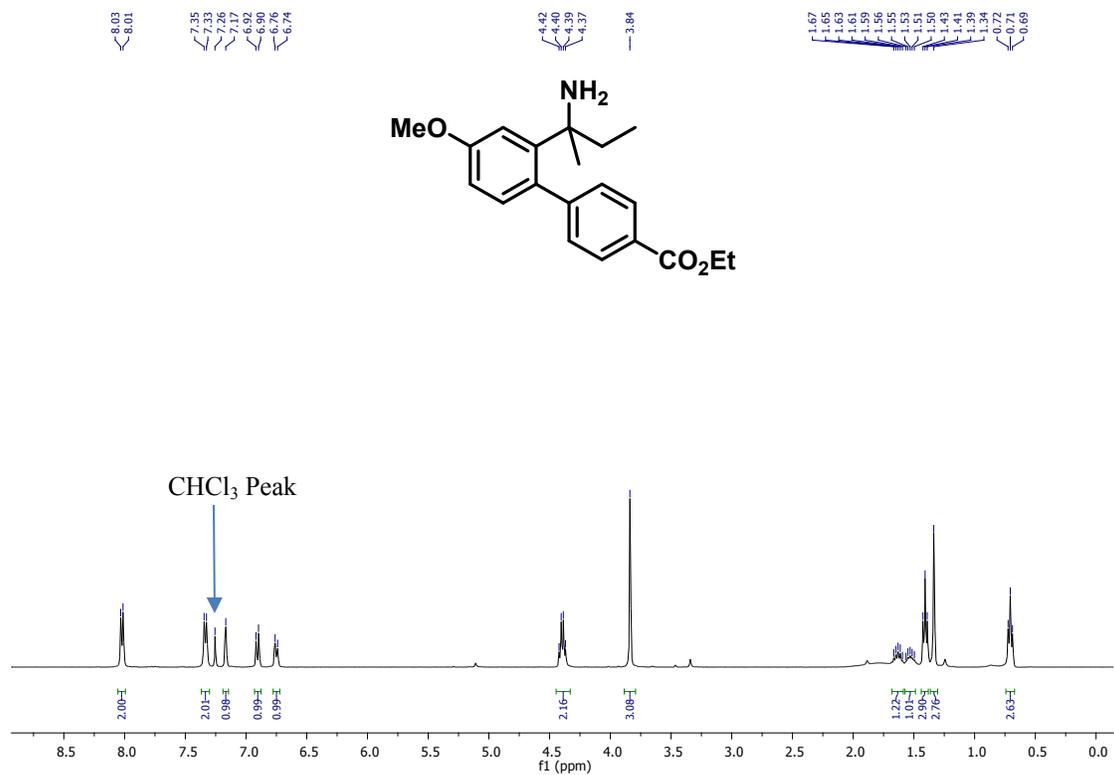


Figure S-141. ¹H NMR spectrum of **2i** (CDCl₃, 400 MHz, 298 K)

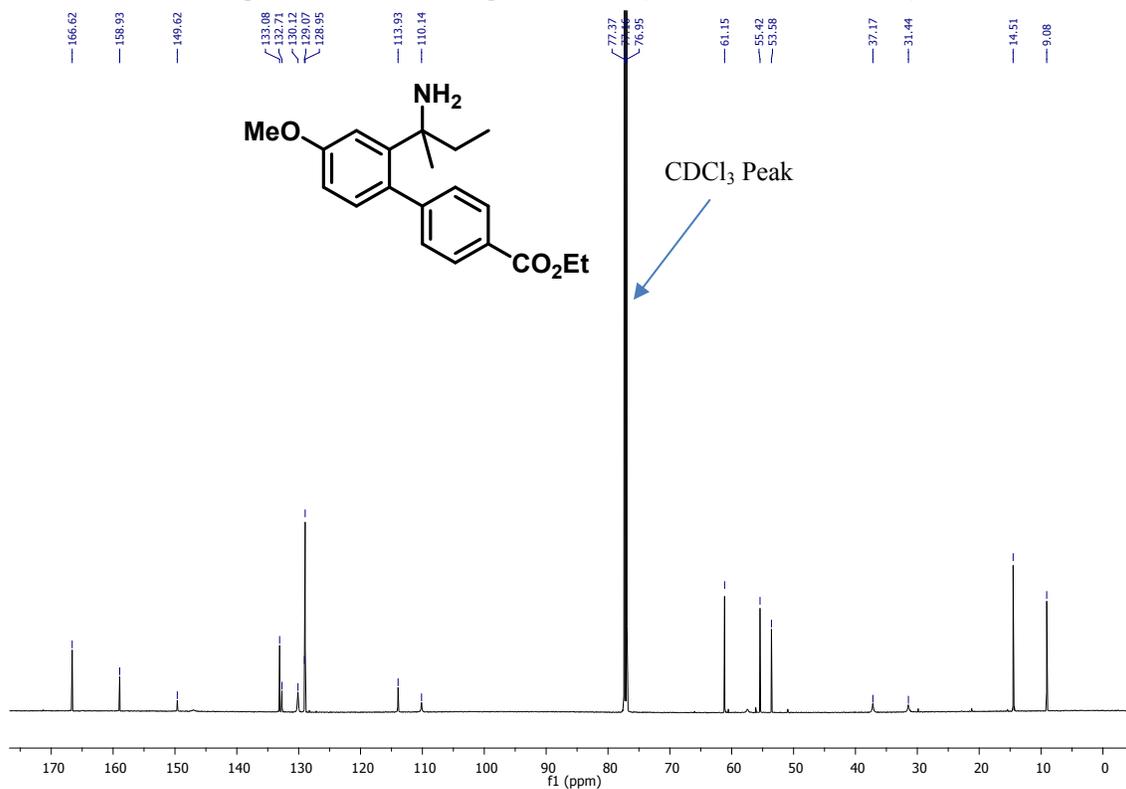


Figure S-142. ¹³C NMR spectrum of **2i** (CDCl₃, 151 MHz, 298 K)

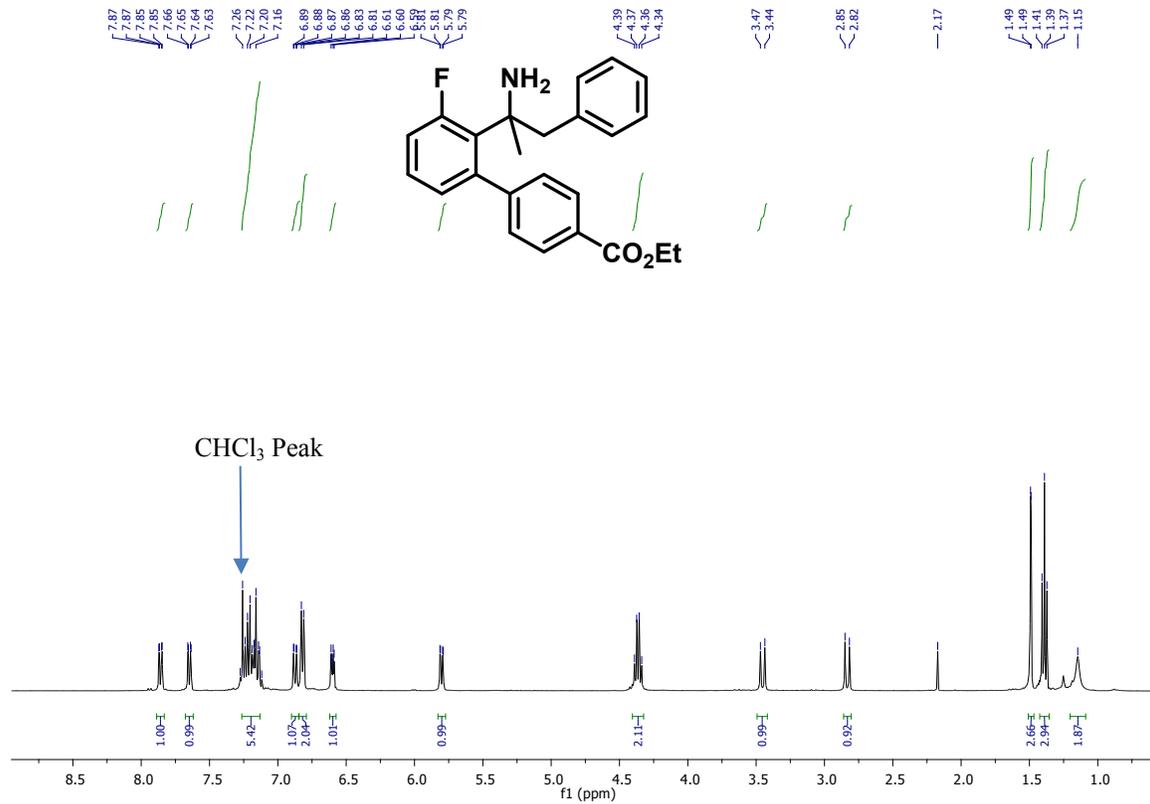


Figure S-143. ¹H NMR spectrum of **2j** (CDCl₃, 400 MHz, 298 K)

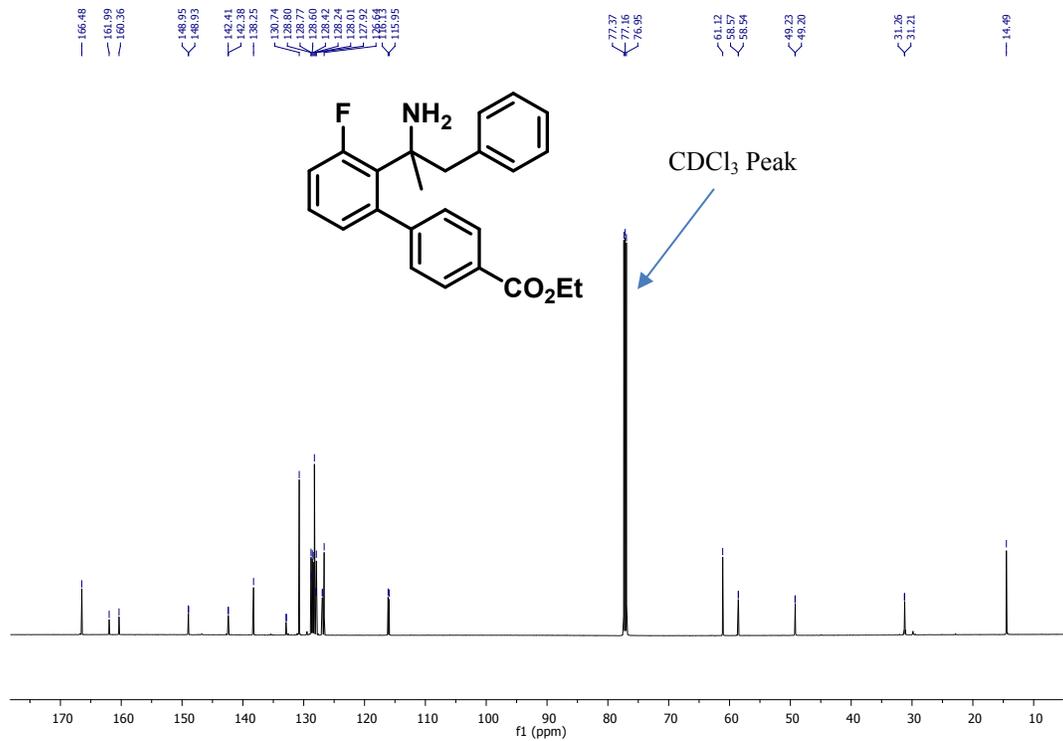


Figure S-144. ¹³C NMR spectrum of **2j** (CDCl₃, 151 MHz, 298 K)

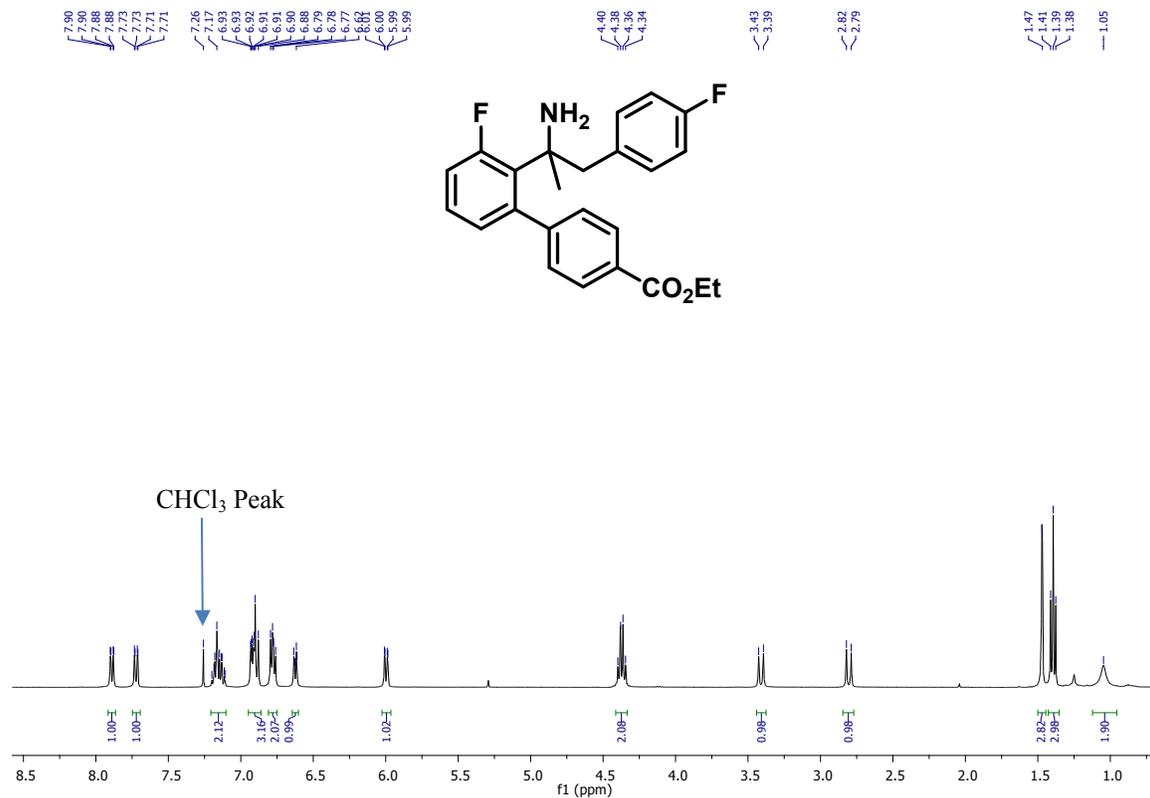


Figure S-145. ¹H NMR spectrum of **2k** (CDCl₃, 400 MHz, 298 K)

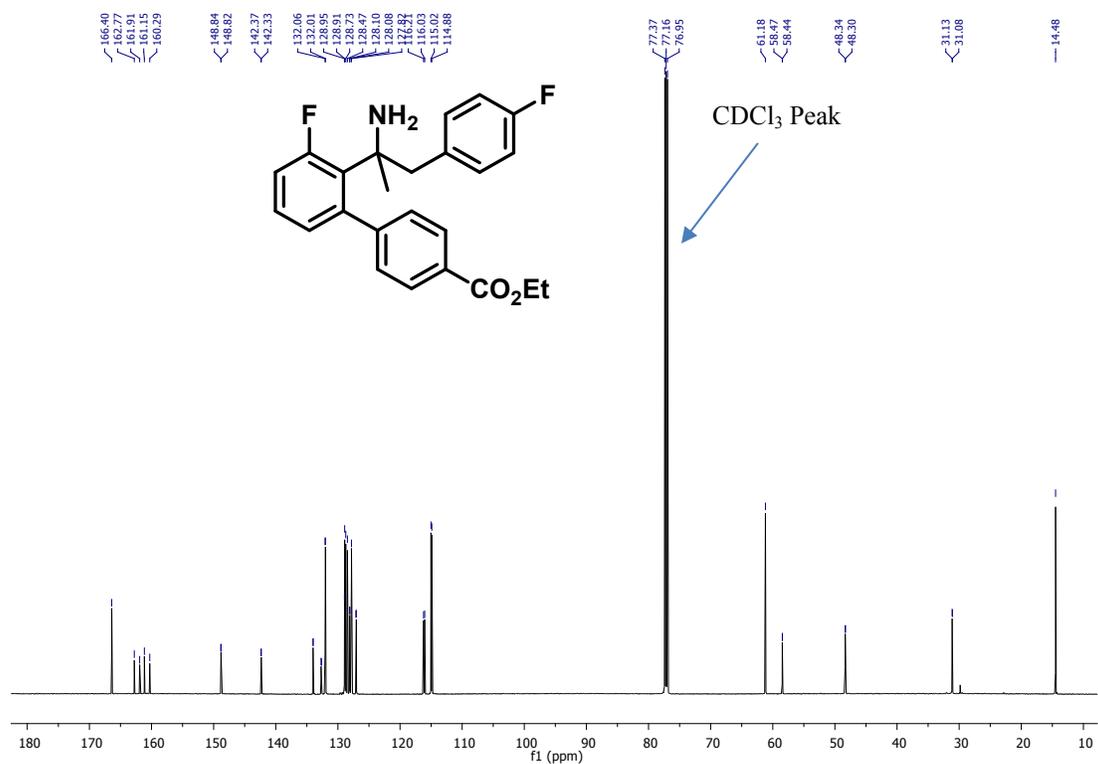


Figure S-146. ¹³C NMR spectrum of **2k** (CDCl₃, 151 MHz, 298 K)

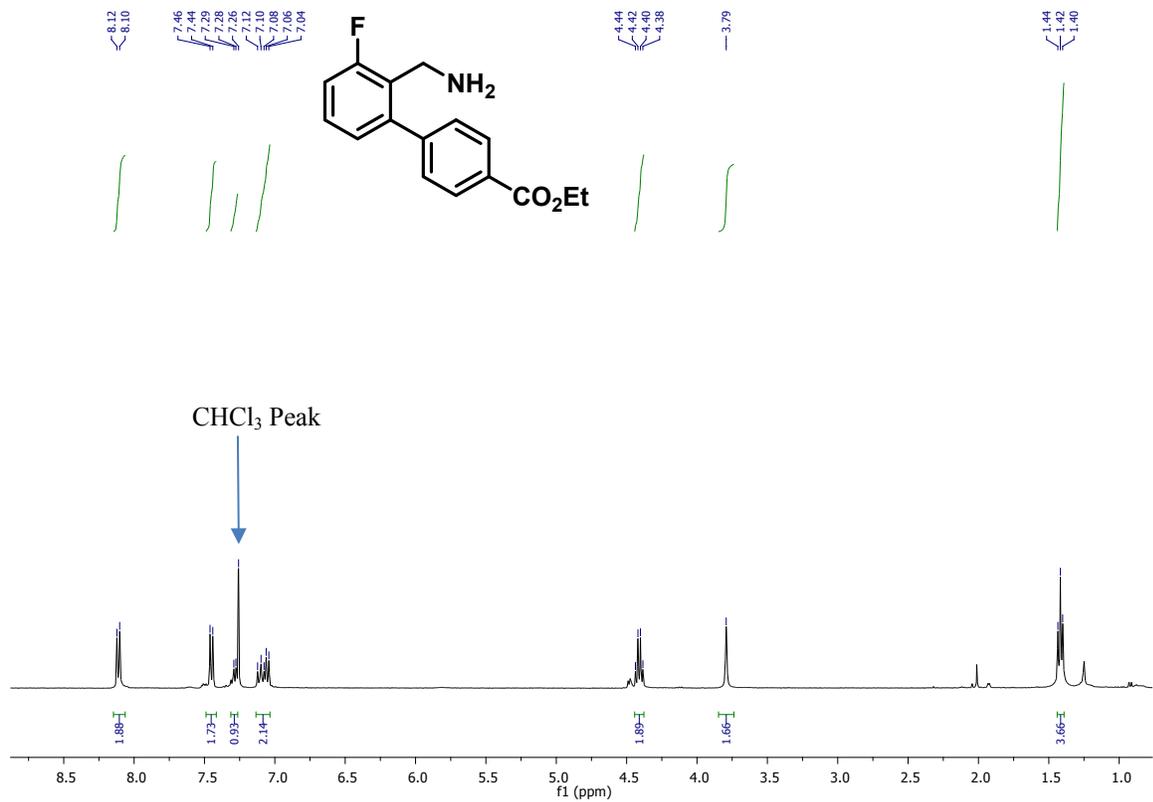


Figure S-147. ¹H NMR spectrum of **21** (CDCl₃, 400 MHz, 298 K)

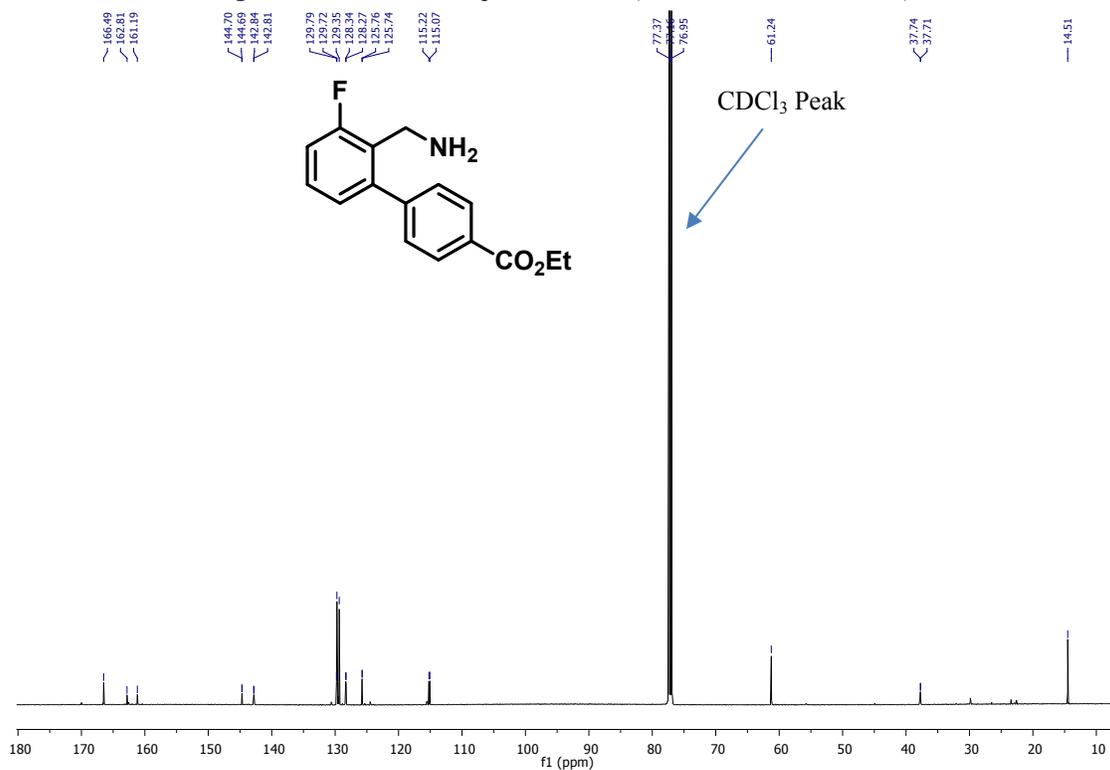


Figure S-148. ¹³C NMR spectrum of **21** (CDCl₃, 151 MHz, 298 K)

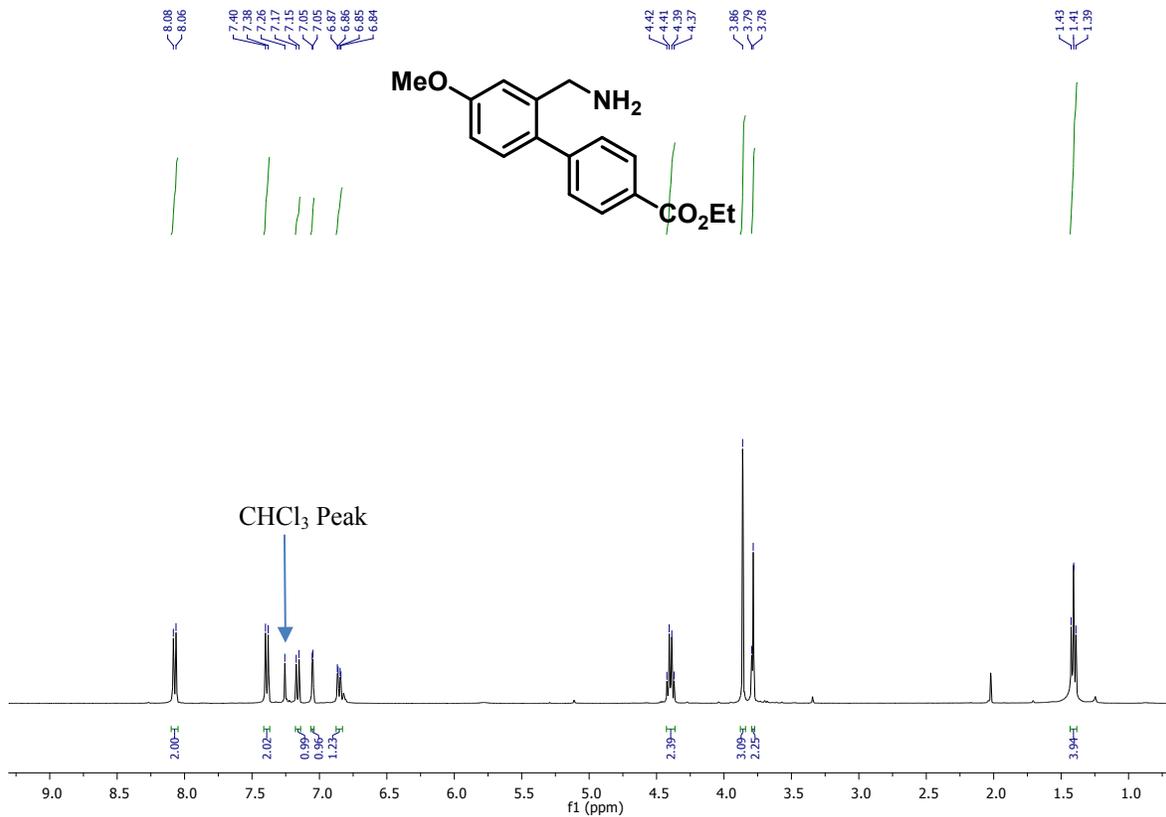


Figure S-149. ¹H NMR spectrum of **2m** (CDCl₃, 400 MHz, 298 K)

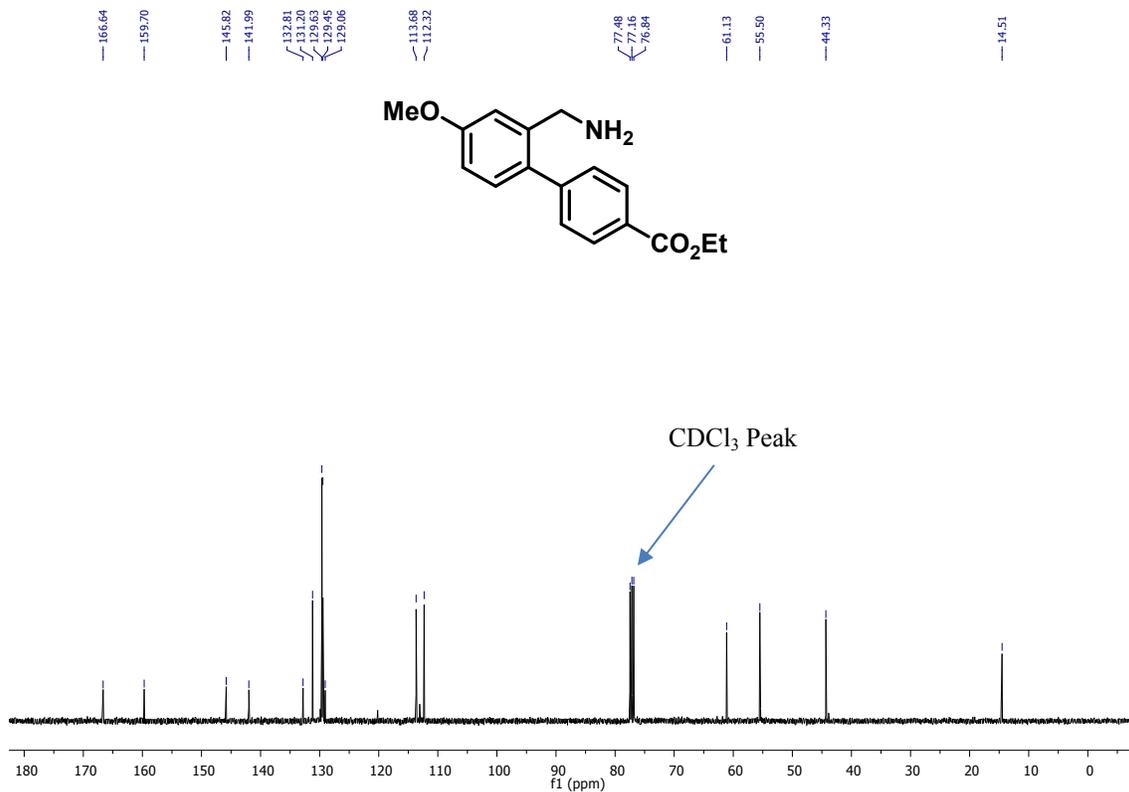


Figure S-150. ¹³C NMR spectrum of **2m** (CDCl₃, 151 MHz, 298 K)

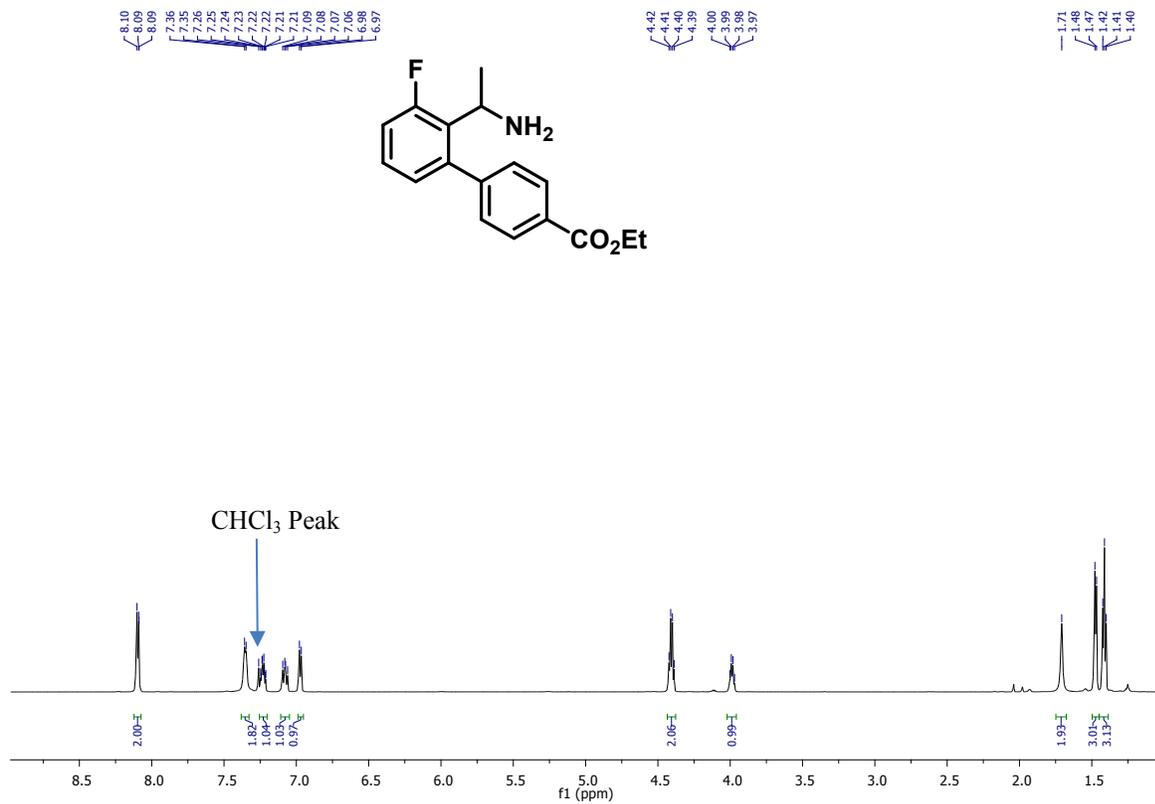


Figure S-151. ¹H NMR spectrum of **2n** (CDCl₃, 600 MHz, 298 K)

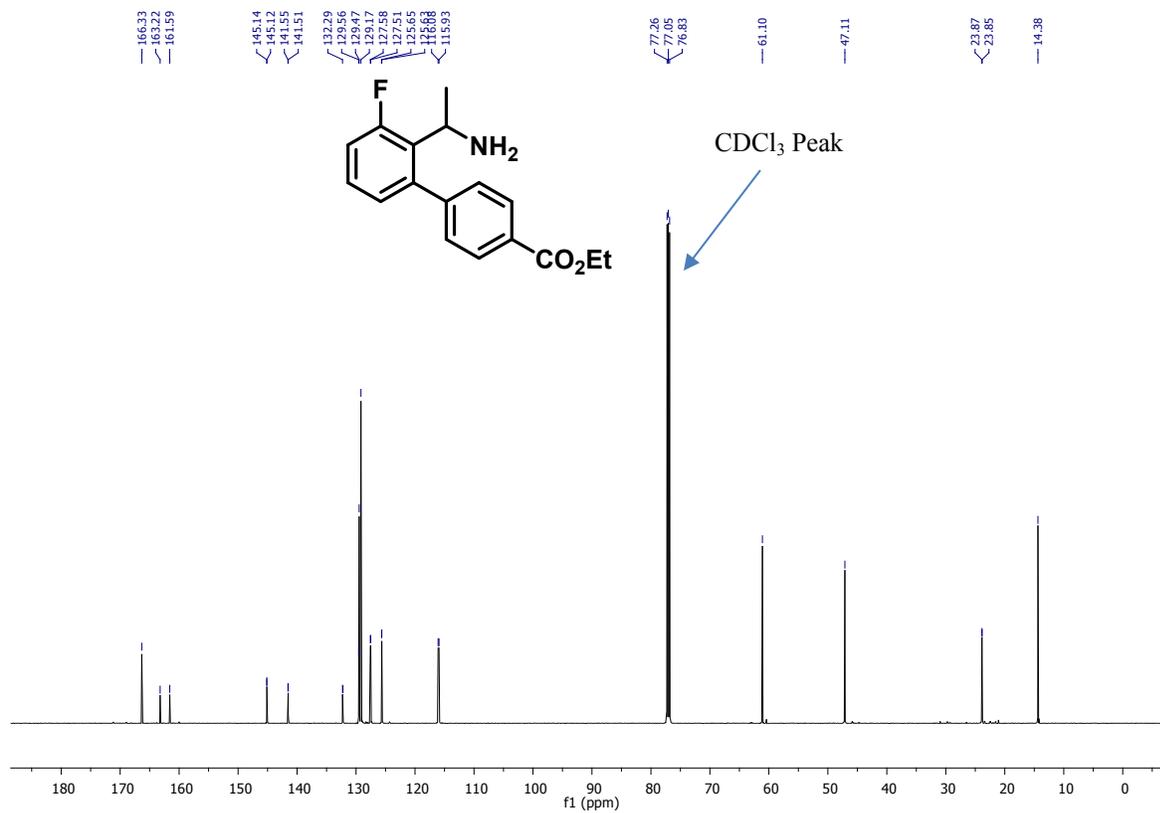


Figure S-152. ¹³C NMR spectrum of **2n** (CDCl₃, 151 MHz, 298 K)

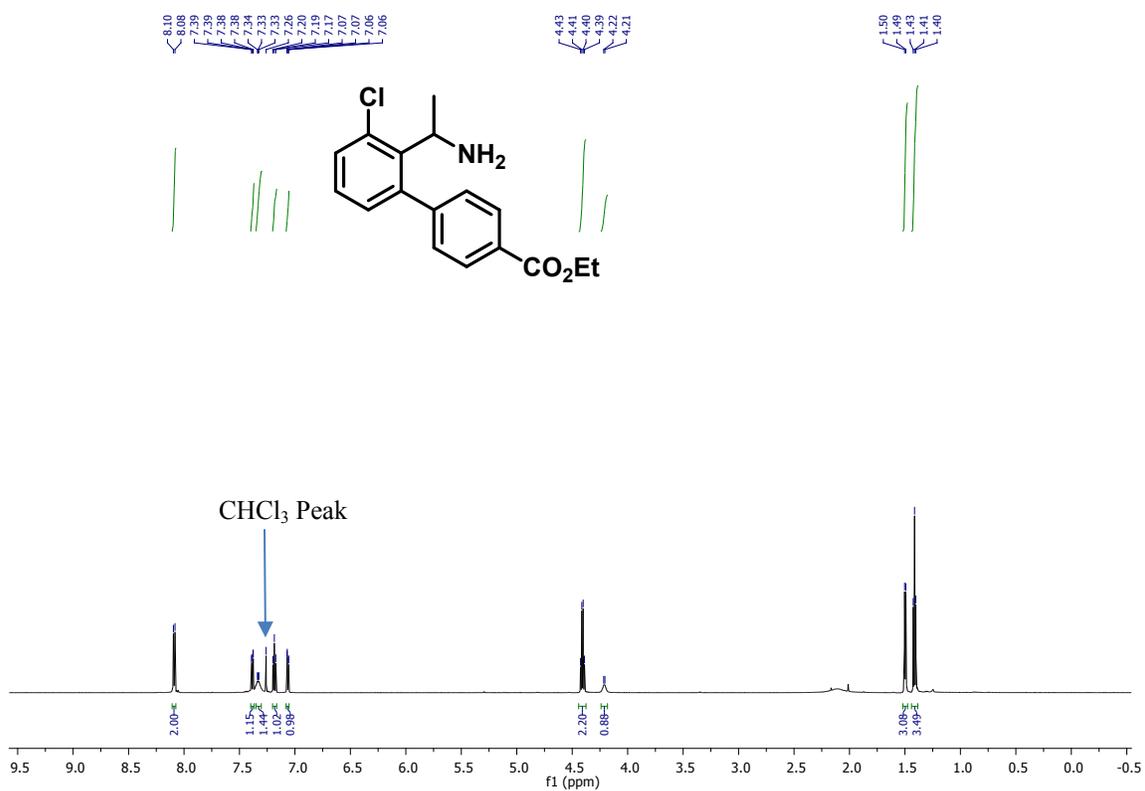


Figure S-153. ¹H NMR spectrum of **2o** (CDCl₃, 600 MHz, 298 K)

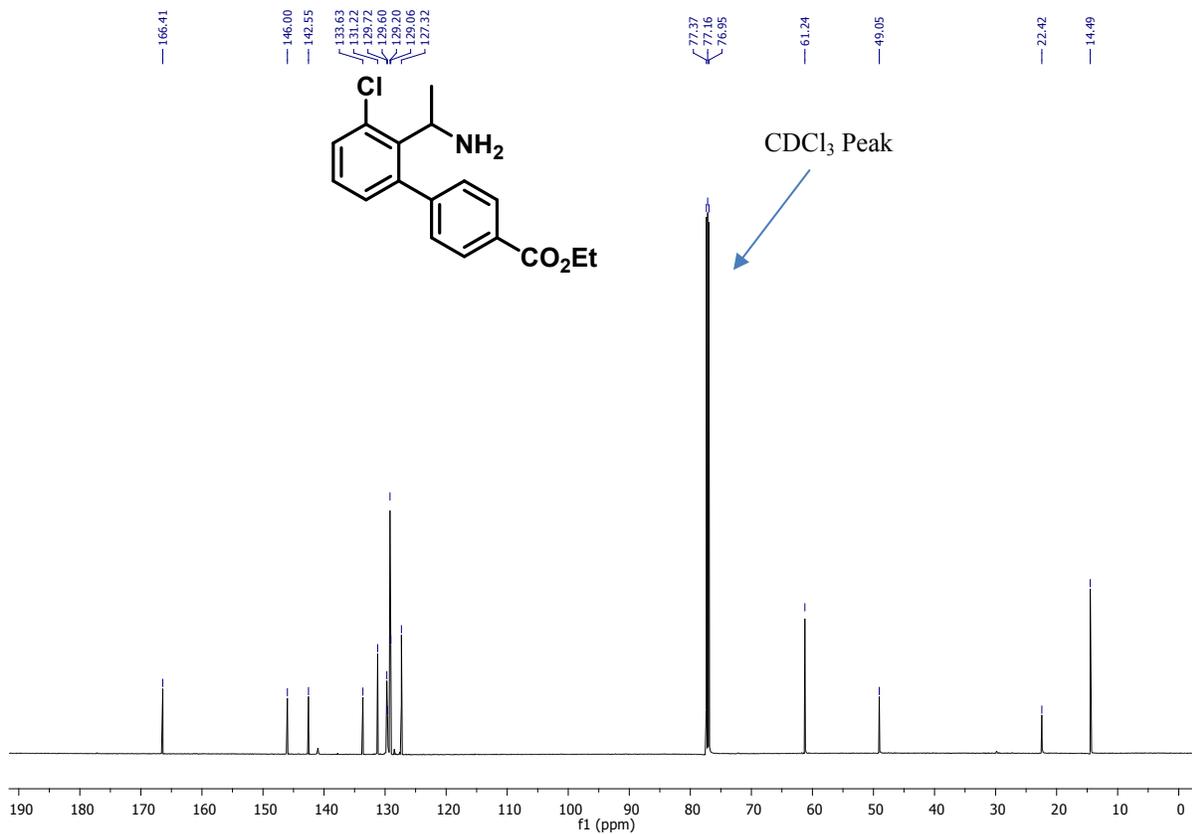


Figure S-154. ¹³C NMR spectrum of **2o** (CDCl₃, 151 MHz, 298 K)

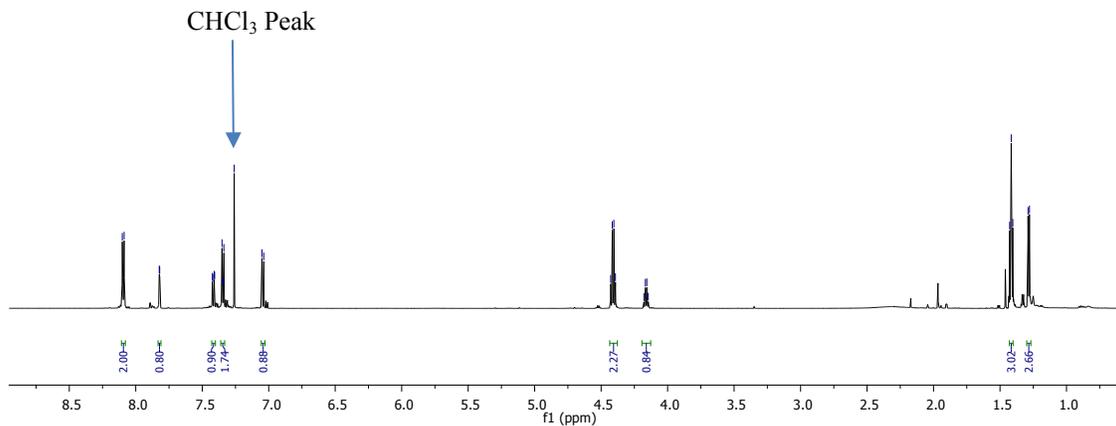
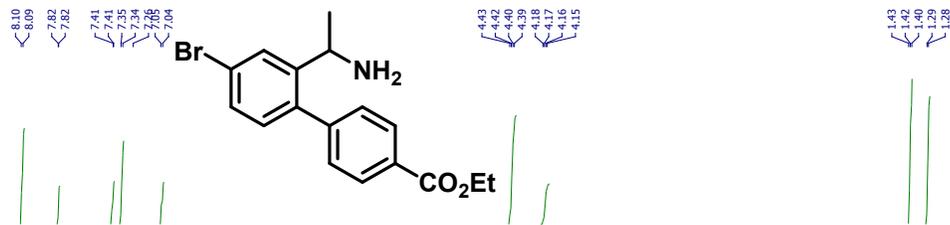


Figure S-155. ¹H NMR spectrum of **2p** (CDCl₃, 600 MHz, 298 K)

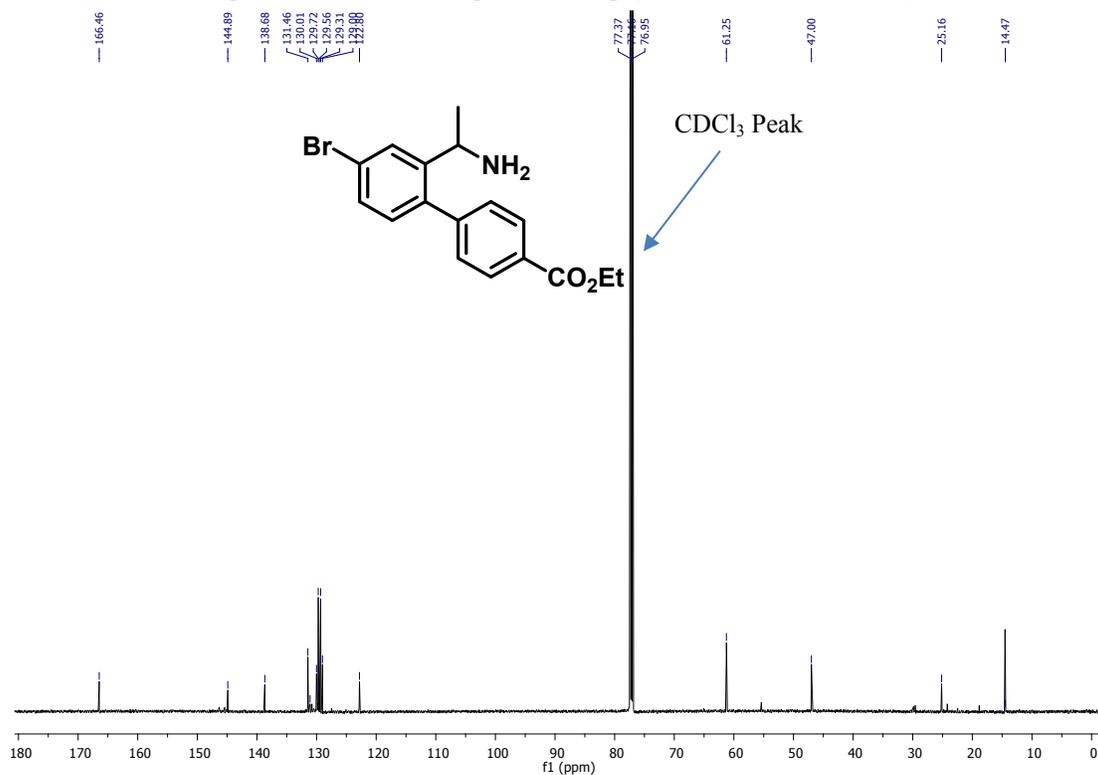


Figure S-156. ¹³C NMR spectrum of **2p** (CDCl₃, 151 MHz, 298 K)

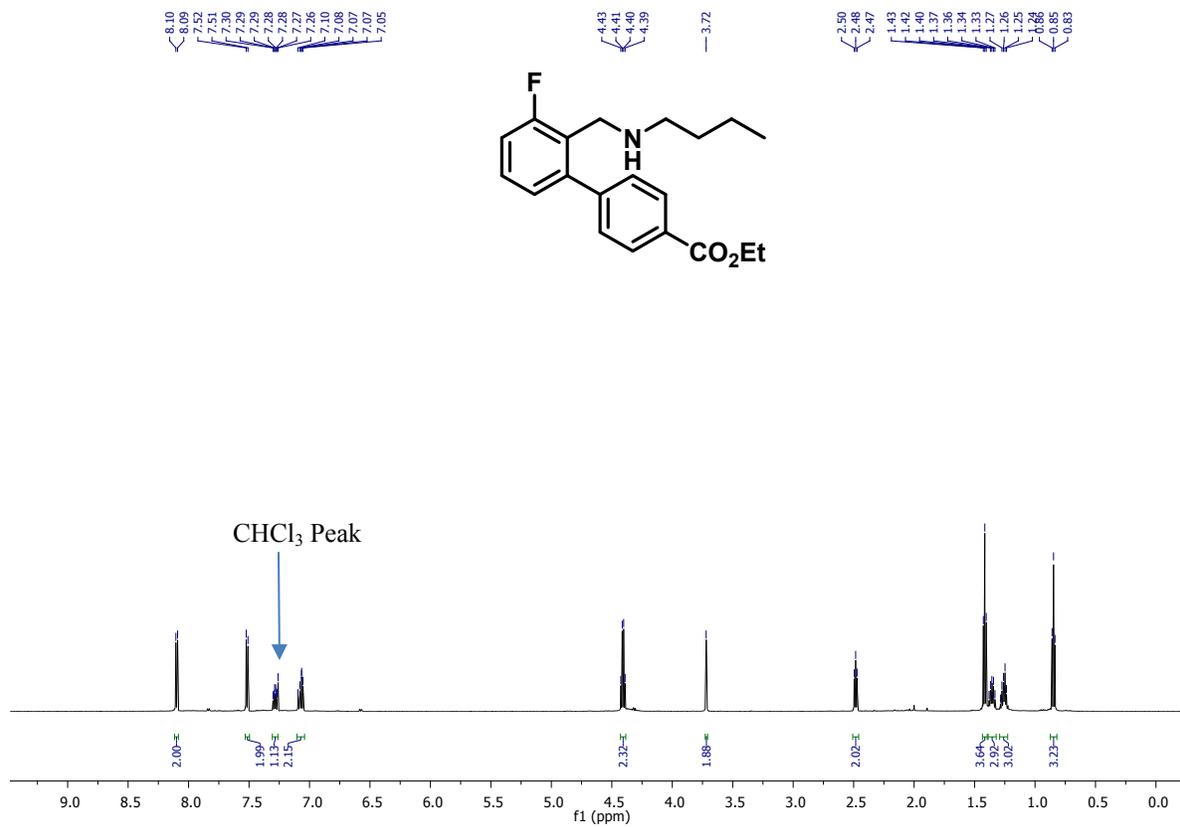


Figure S-157. ¹H NMR spectrum of **3a** (CDCl₃, 600 MHz, 298 K)

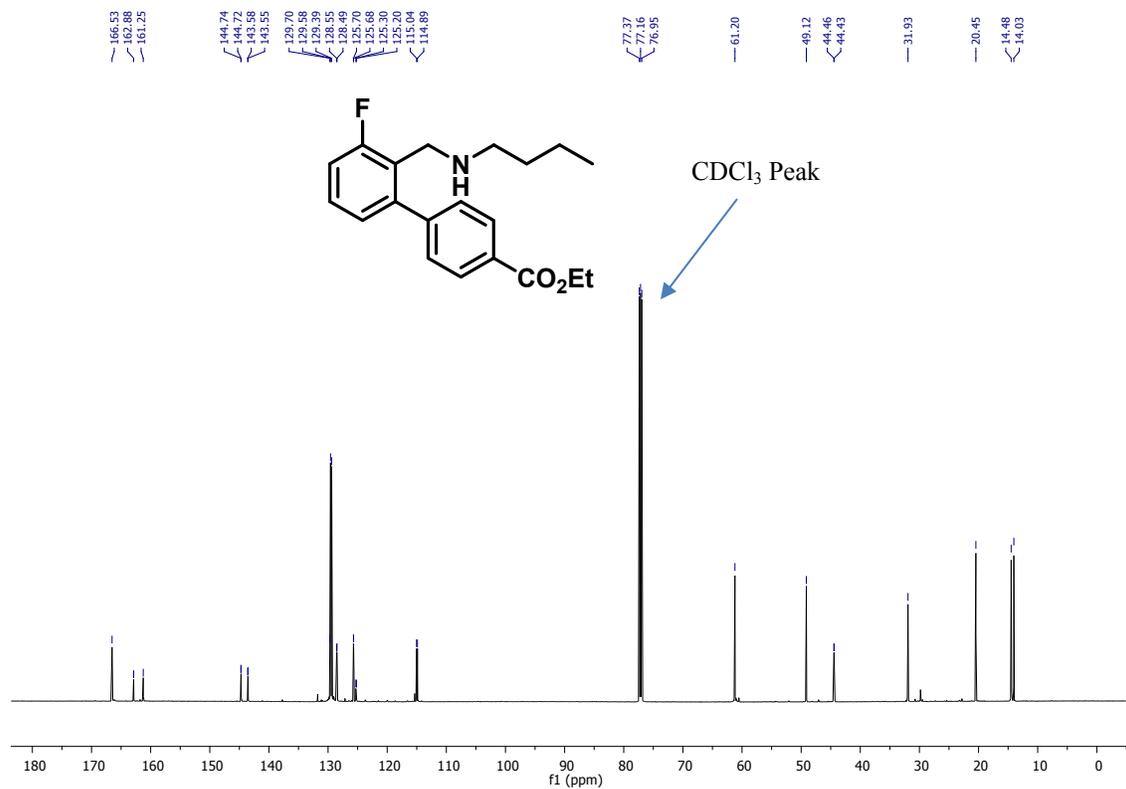


Figure S-158. ¹³C NMR spectrum of **3a** (CDCl₃, 151 MHz, 298 K)

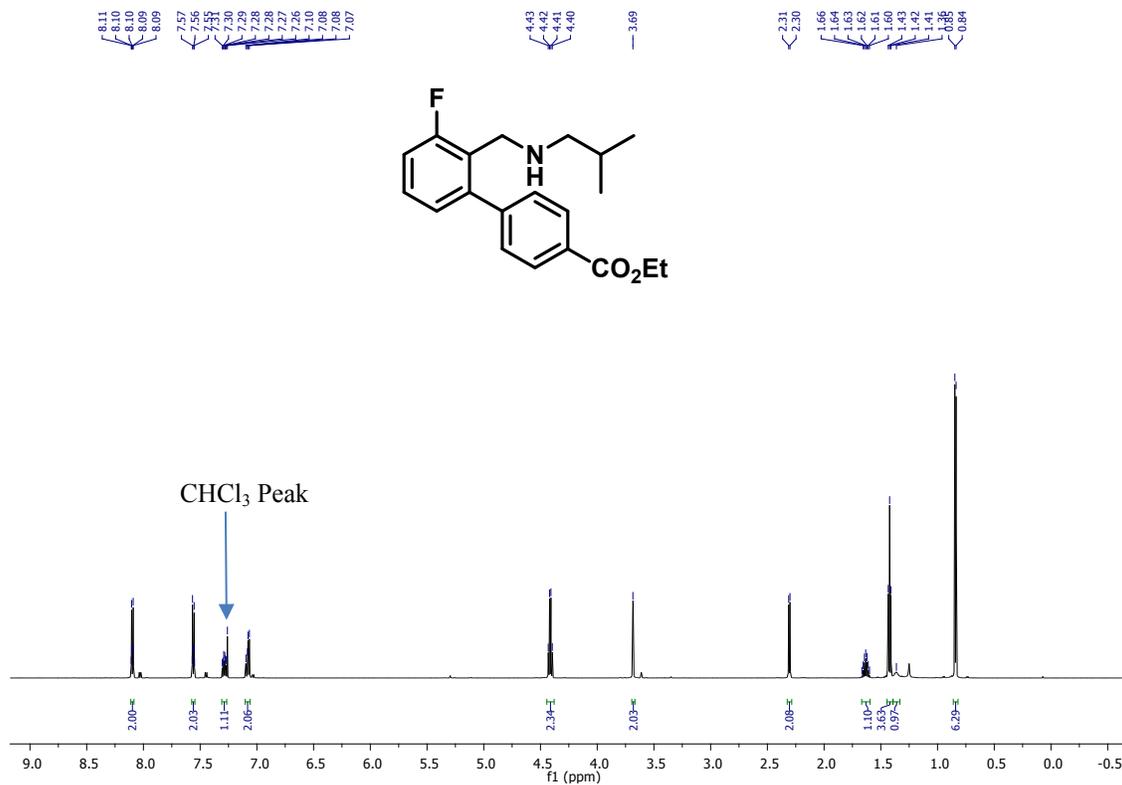


Figure S-159. ¹H NMR spectrum of **3b** (CDCl₃, 600 MHz, 298 K)

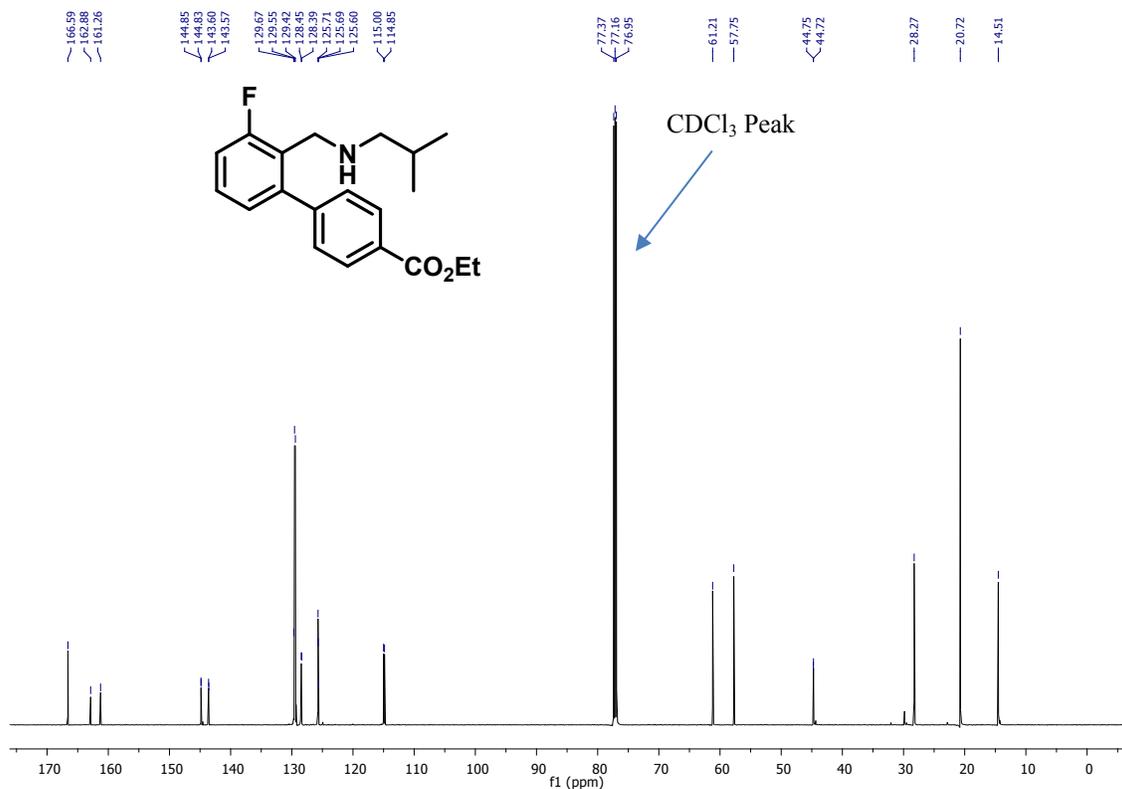


Figure S-160. ¹³C NMR spectrum of **3b** (CDCl₃, 151 MHz, 298 K)

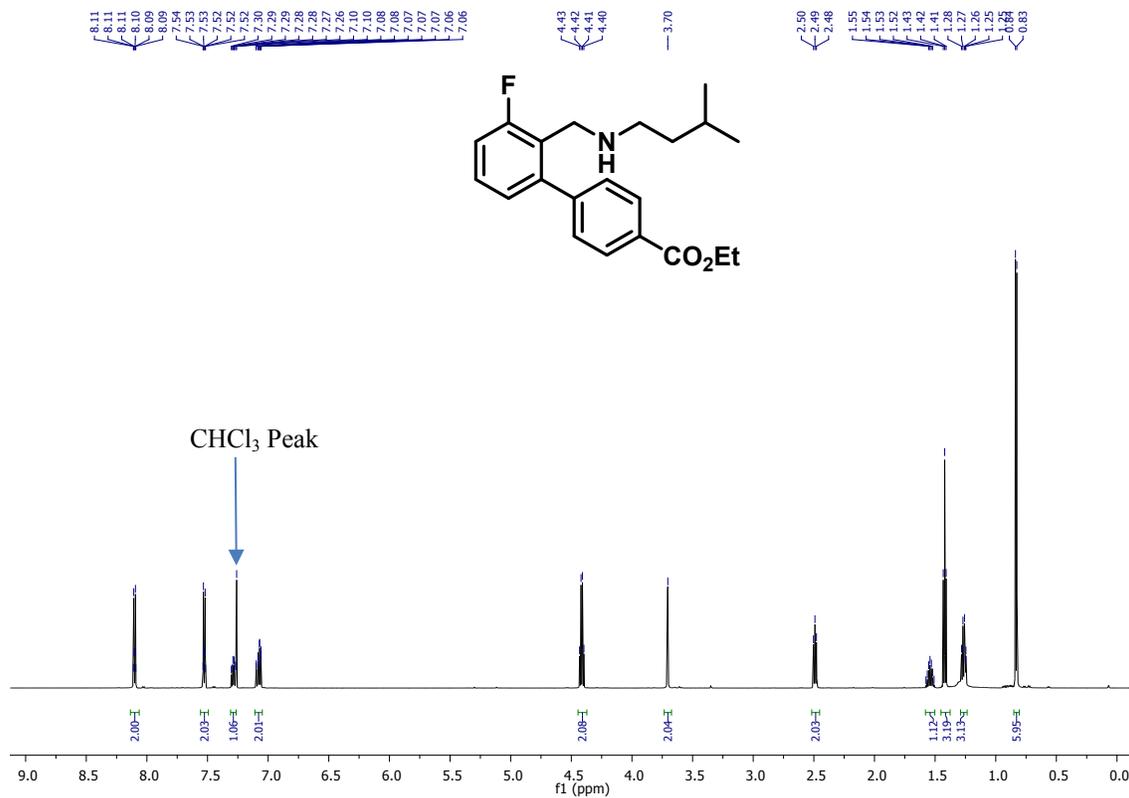


Figure S-161. ¹H NMR spectrum of 3c (CDCl₃, 600 MHz, 298 K)

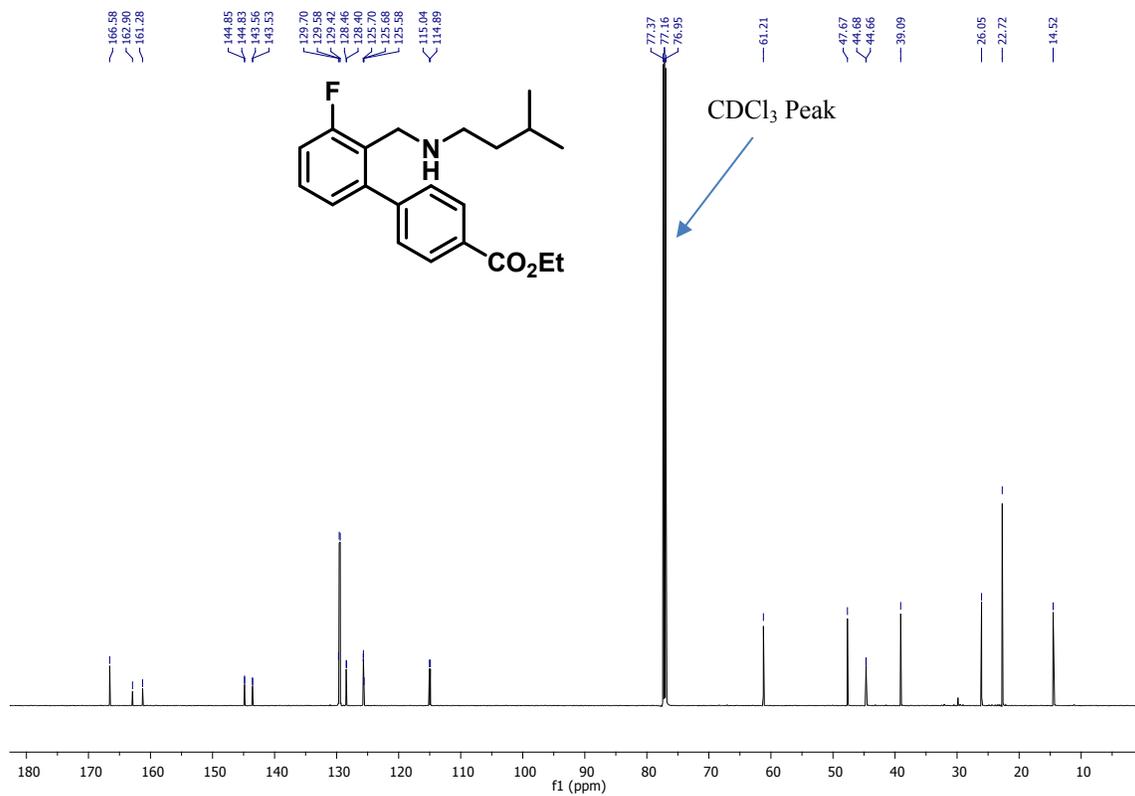


Figure S-162. ¹³C NMR spectrum of 3c (CDCl₃, 151 MHz, 298 K)

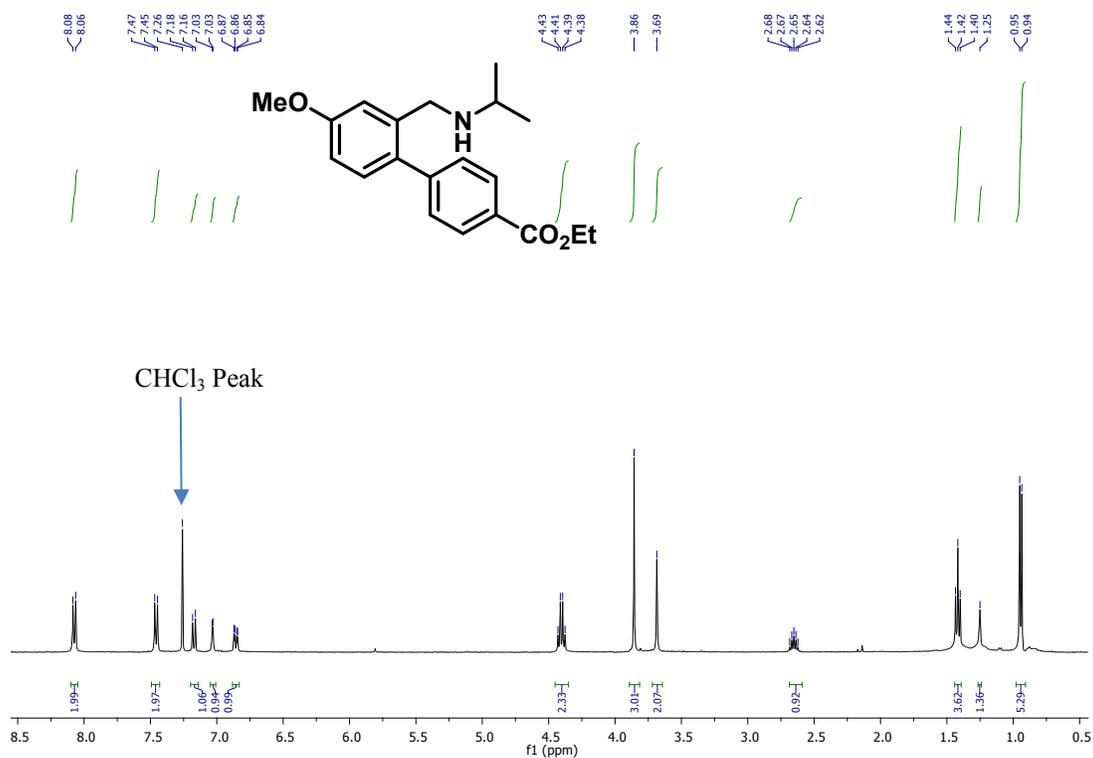


Figure S-163. ¹H NMR spectrum of **3d** (CDCl₃, 400 MHz, 298 K)

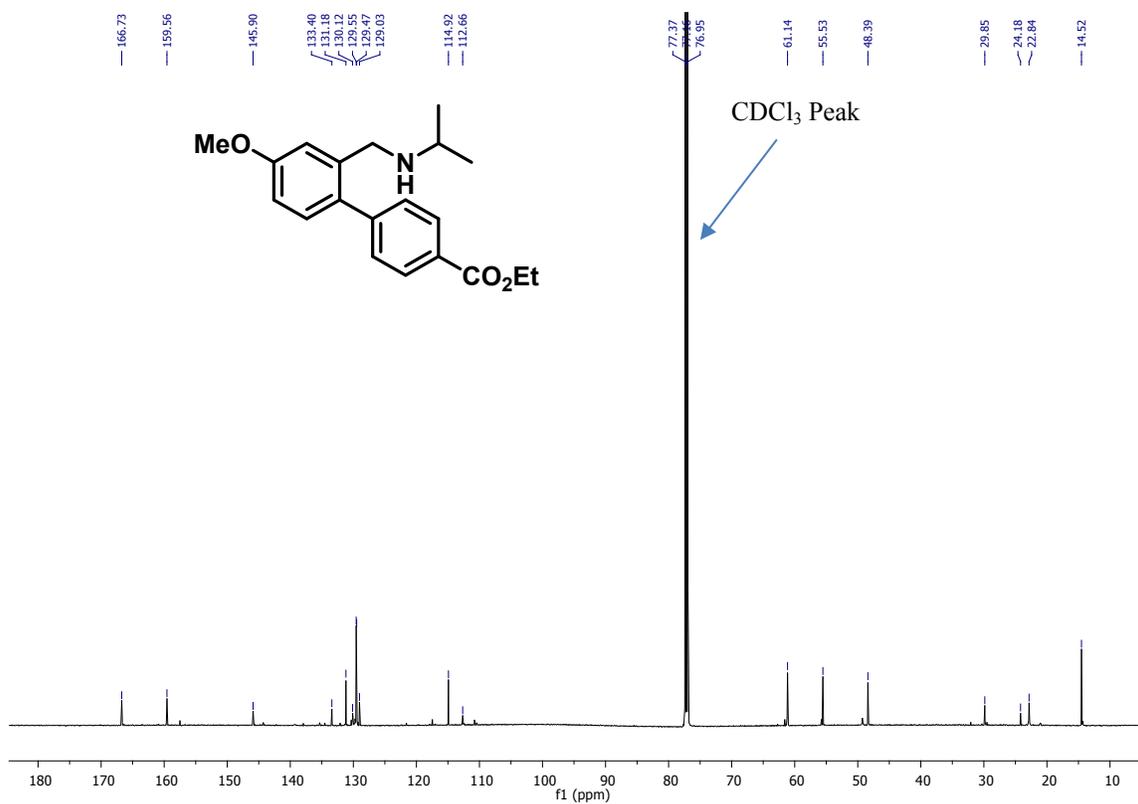


Figure S-164. ¹³C NMR spectrum of **3d** (CDCl₃, 151 MHz, 298 K)

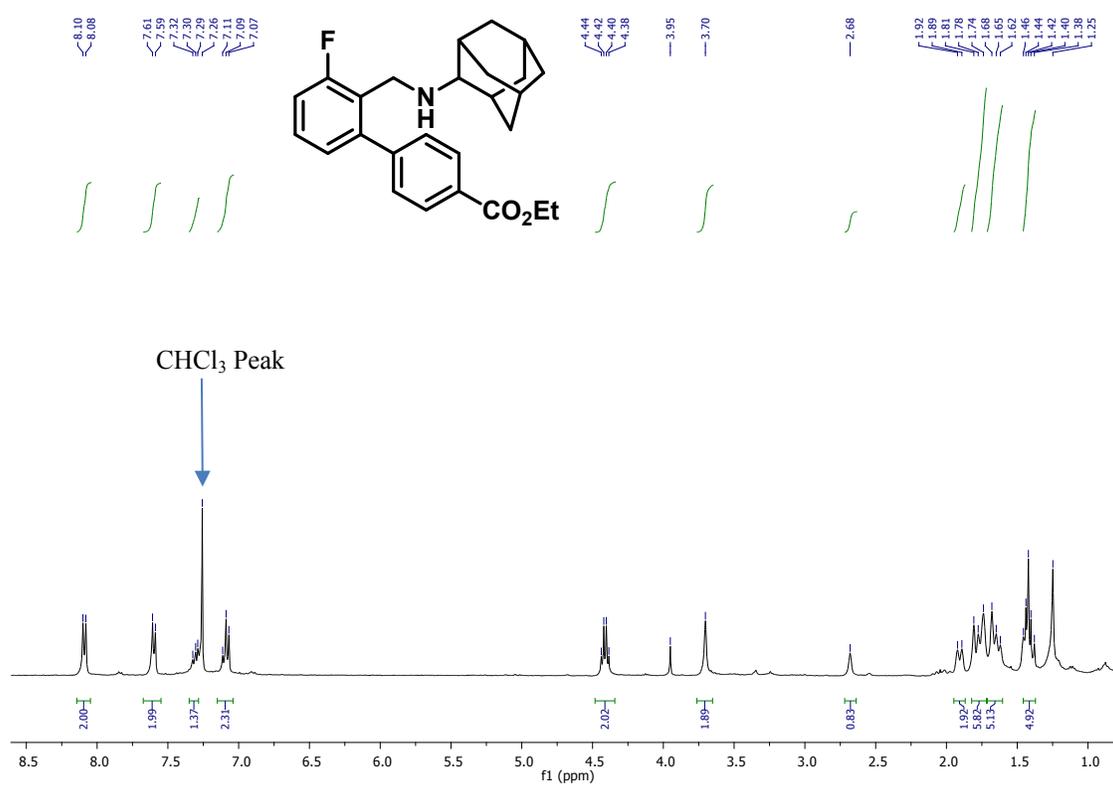


Figure S-165. ¹H NMR spectrum of **3e** (CDCl₃, 400 MHz, 298 K)

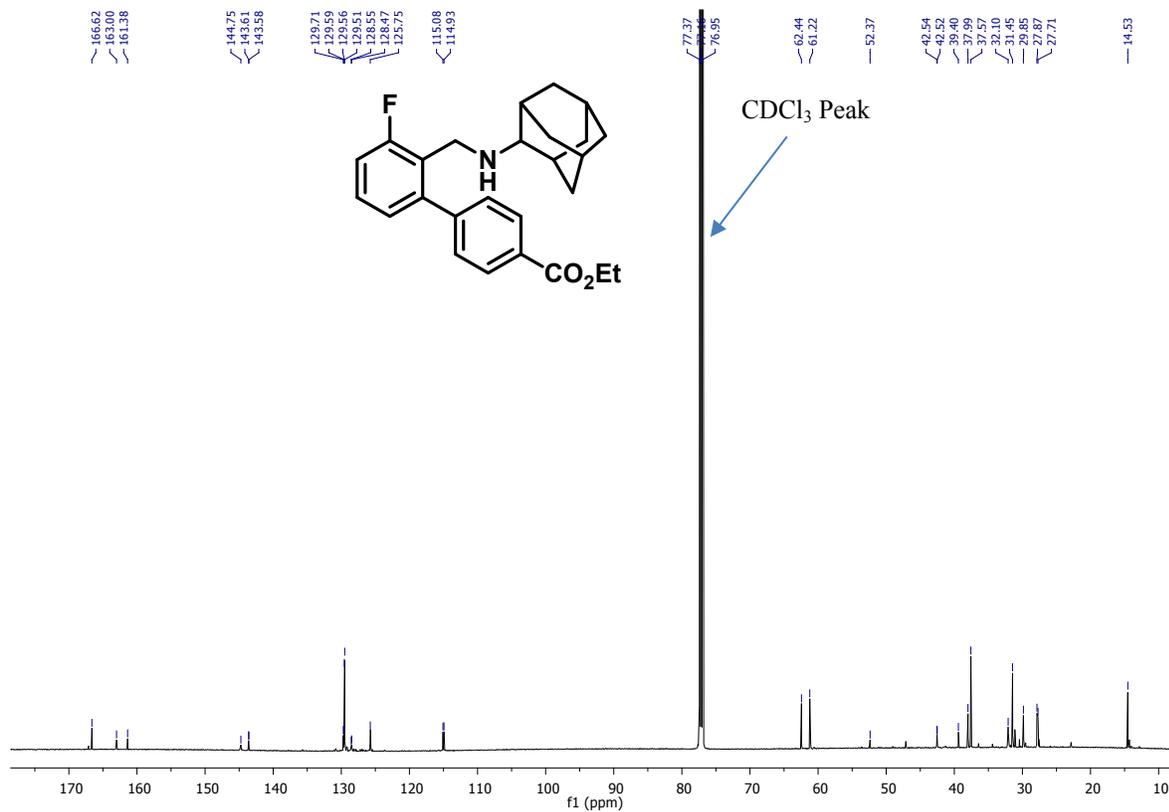


Figure S-166. ¹³C NMR spectrum of **3e** (CDCl₃, 151 MHz, 298 K)

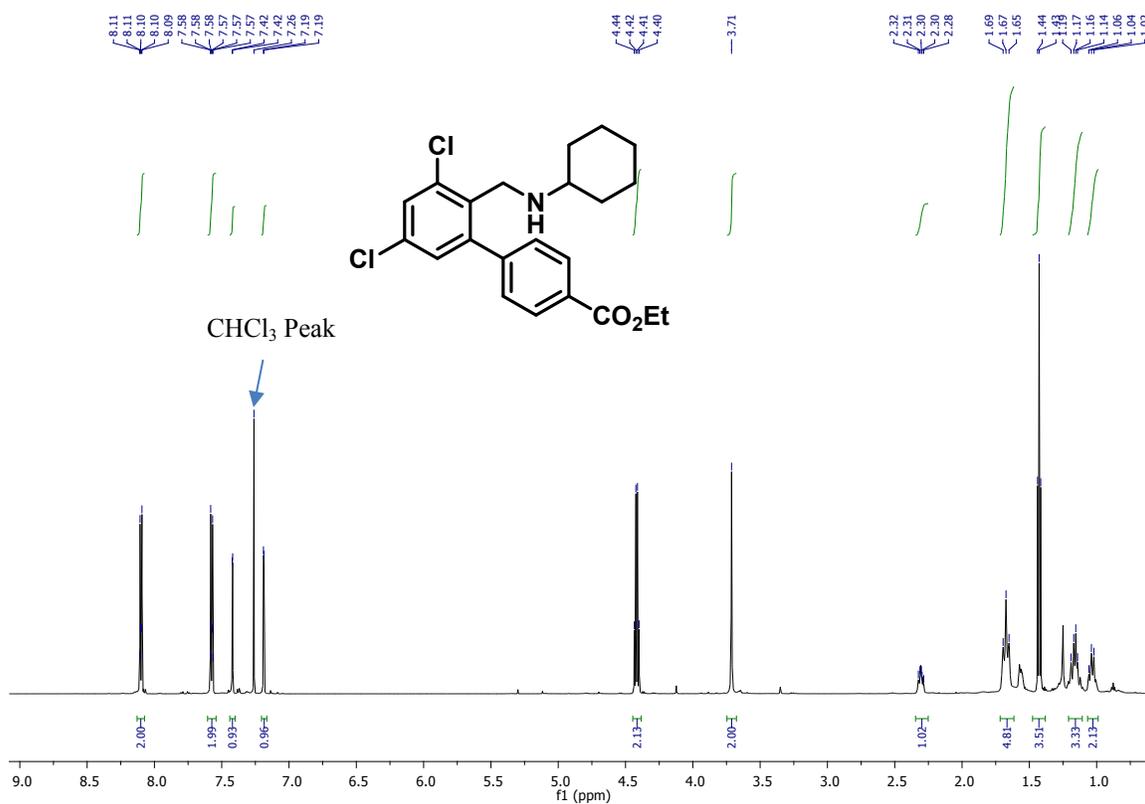


Figure S-167. ¹H NMR spectrum of **3f** (CDCl₃, 400 MHz, 298 K)

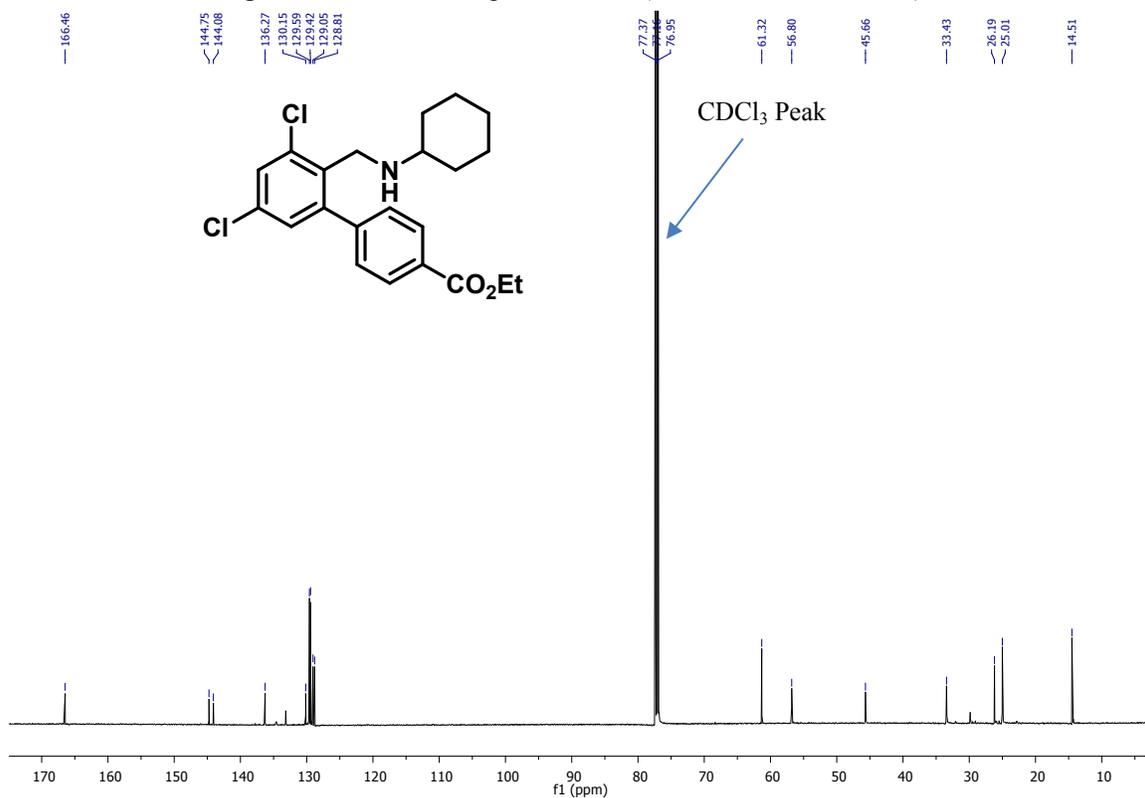


Figure S-168. ¹³C NMR spectrum of **3f** (CDCl₃, 151 MHz, 298 K)

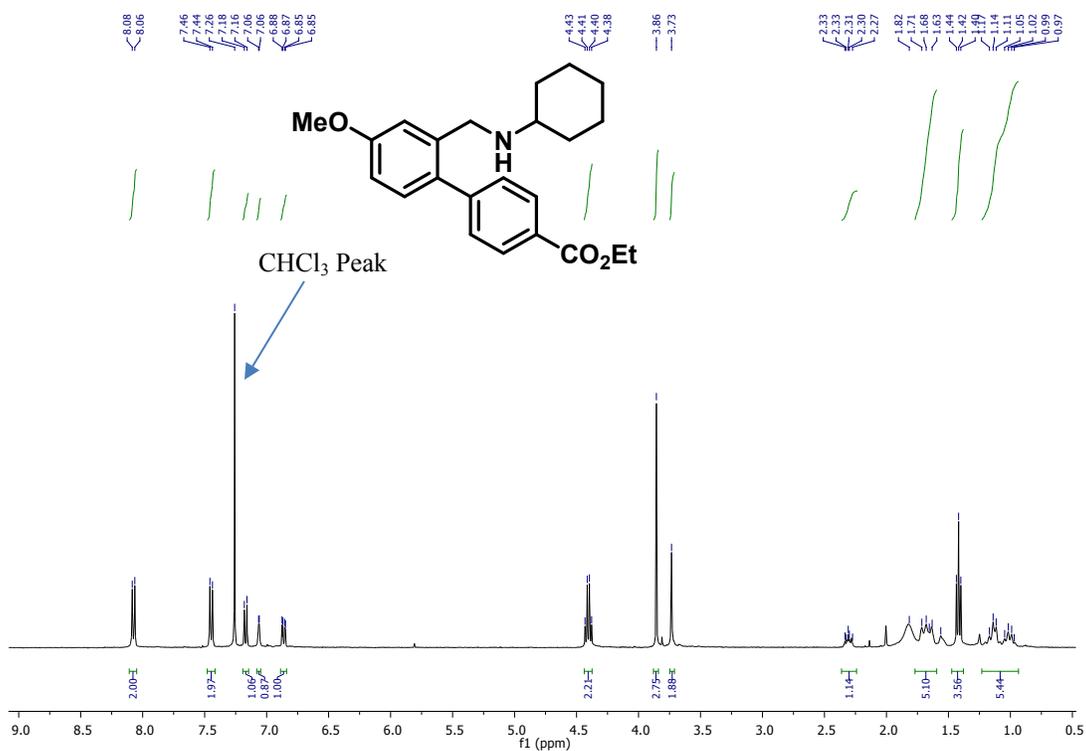


Figure S-169. ¹H NMR spectrum of **3g** (CDCl₃, 400 MHz, 298 K)

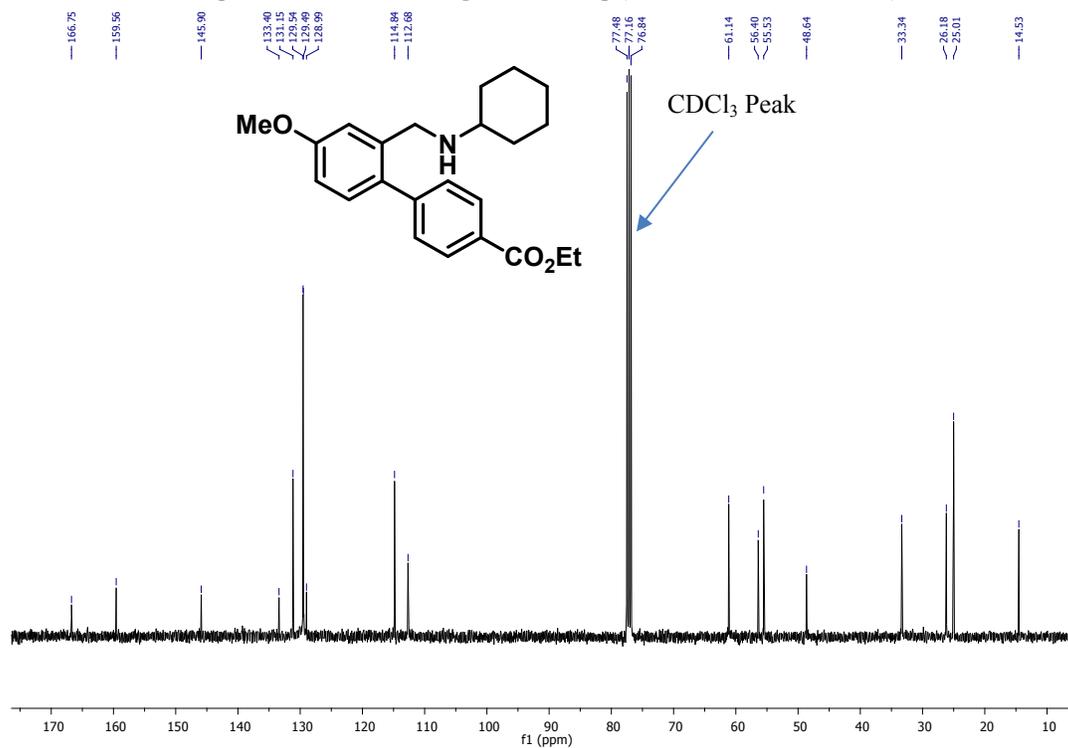


Figure S-170. ¹³C NMR spectrum of **3g** (CDCl₃, 101 MHz, 298 K)

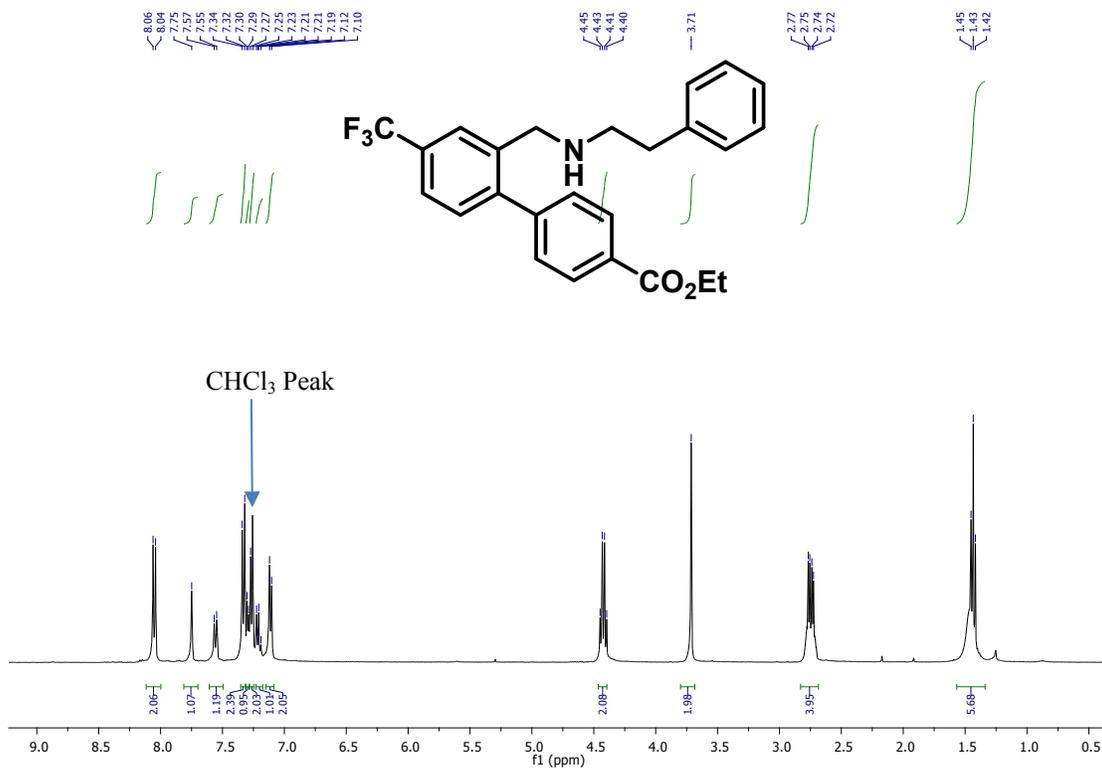


Figure S-171. ¹H NMR spectrum of **3h** (CDCl₃, 400 MHz, 298 K)

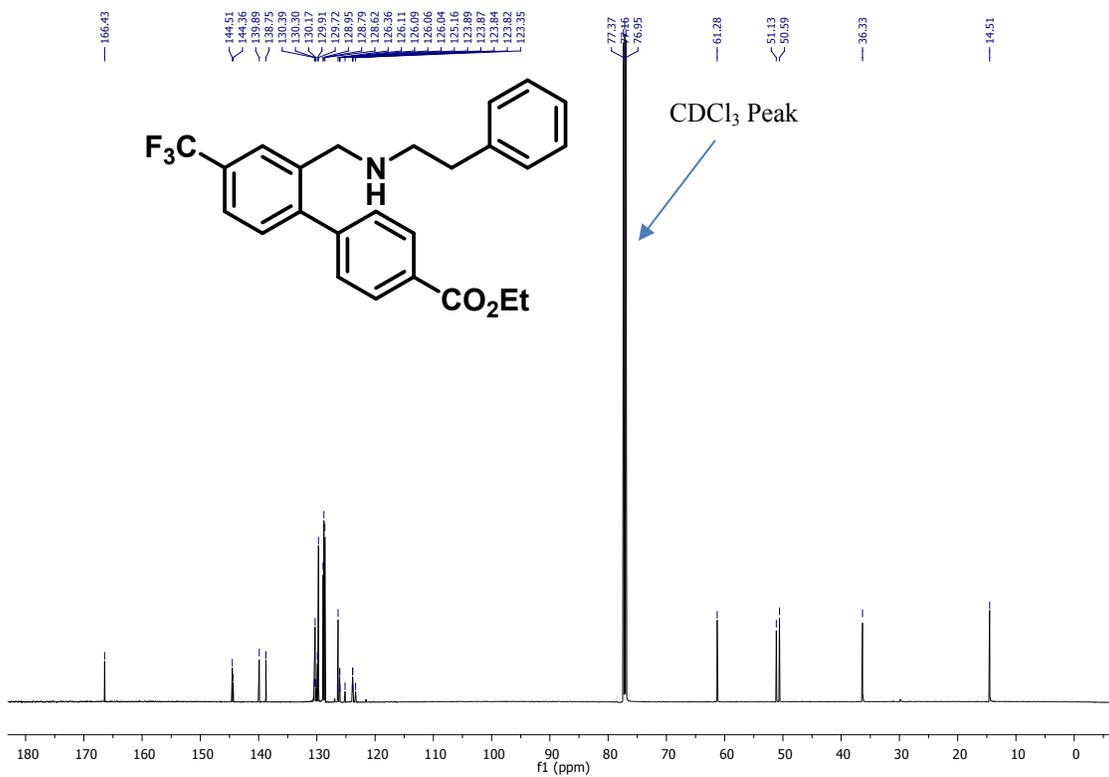


Figure S-172. ¹³C NMR spectrum of **3h** (CDCl₃, 151 MHz, 298 K)

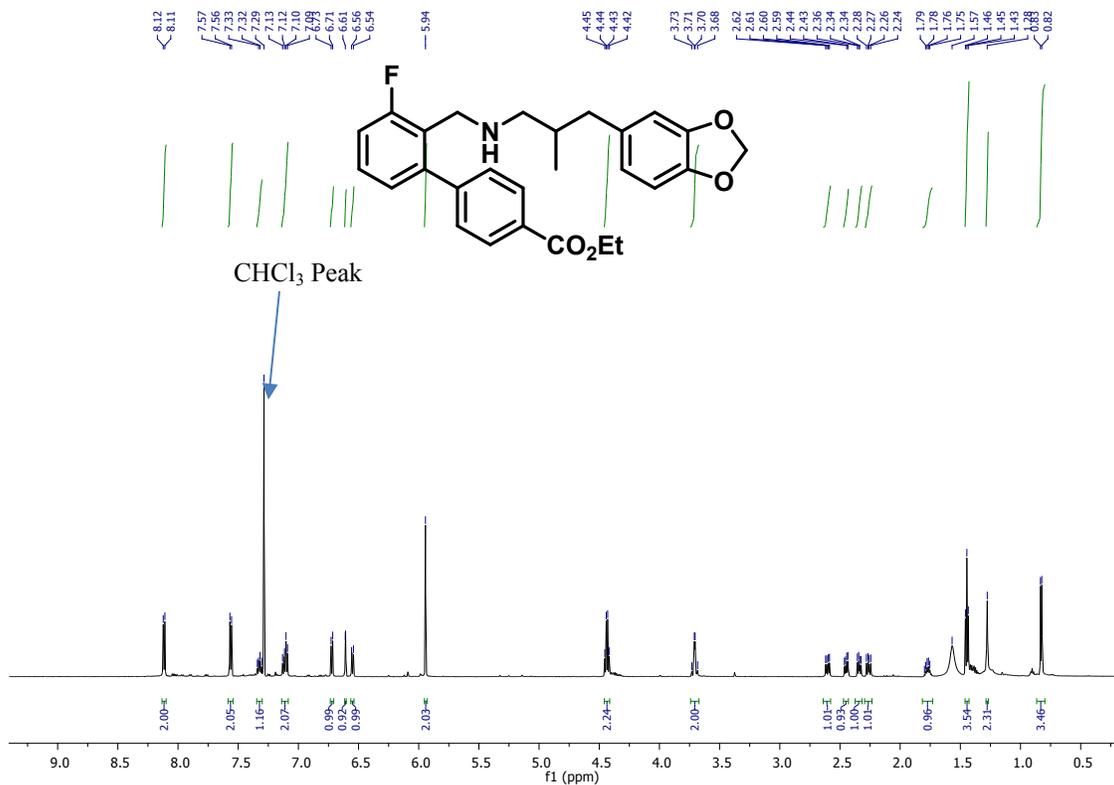


Figure S-173. ¹H NMR spectrum of **3i** (CDCl₃, 400 MHz, 298 K)

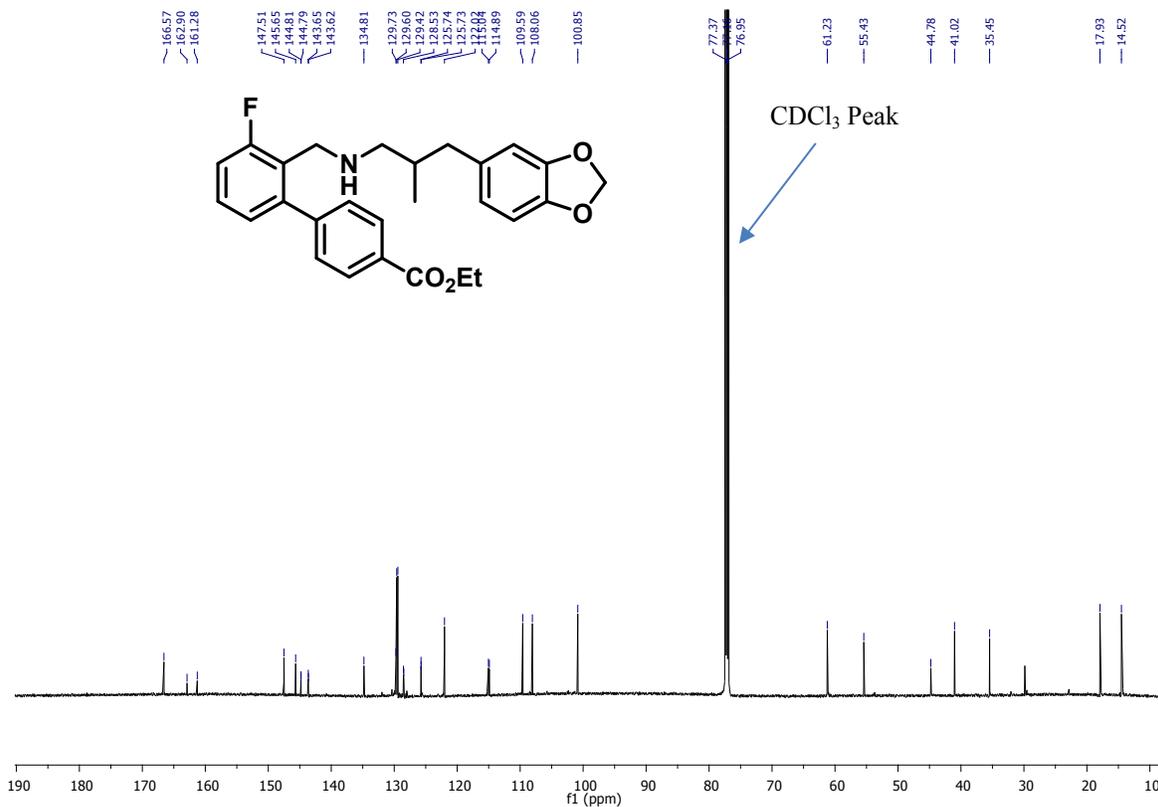


Figure S-174. ¹³C NMR spectrum of **3i** (CDCl₃, 151 MHz, 298 K)

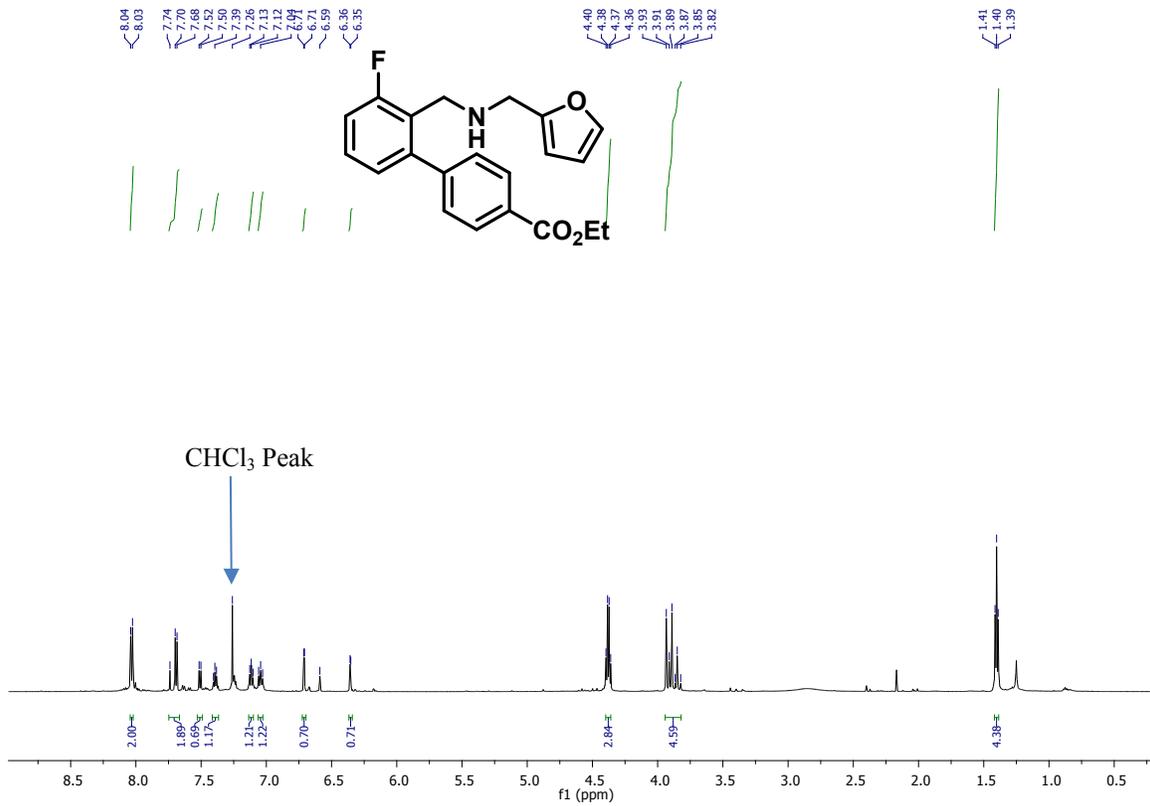


Figure S-175. ¹H NMR spectrum of **3j** (CDCl₃, 400 MHz, 298 K)

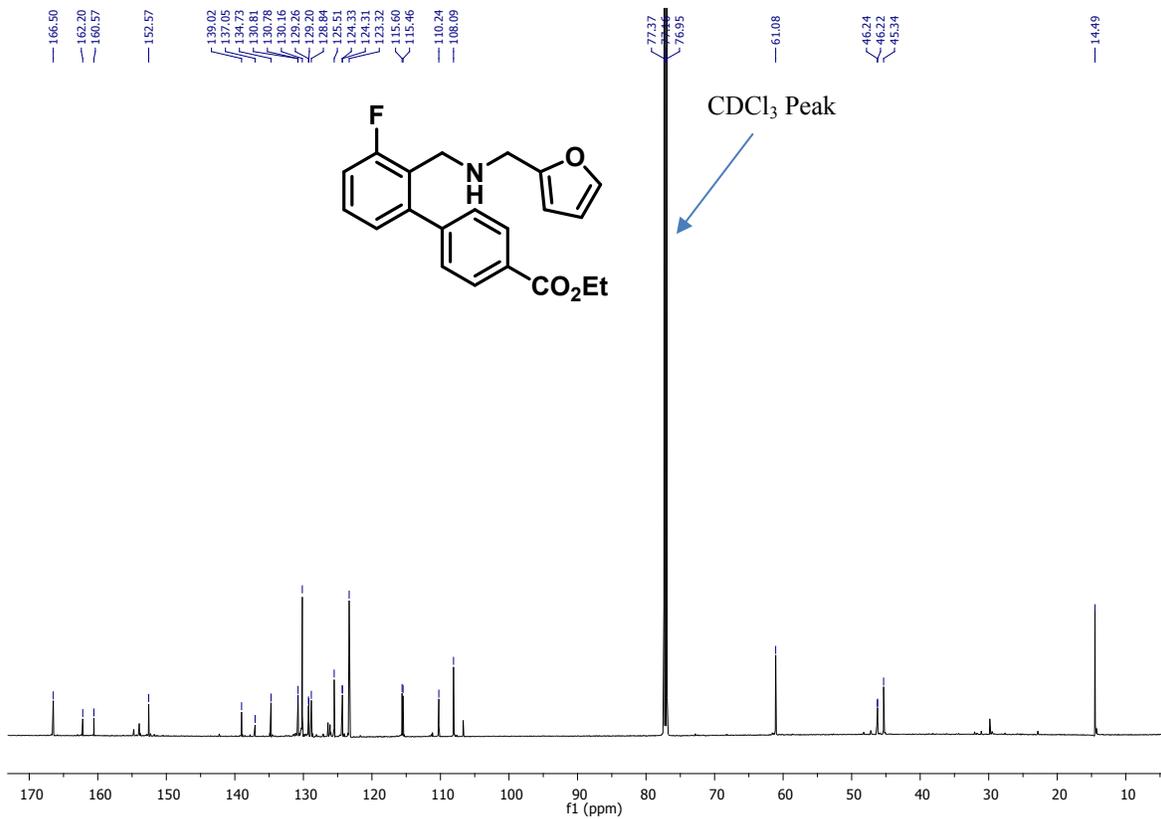


Figure S-176. ¹³C NMR spectrum of **3j** (CDCl₃, 151 MHz, 298 K)

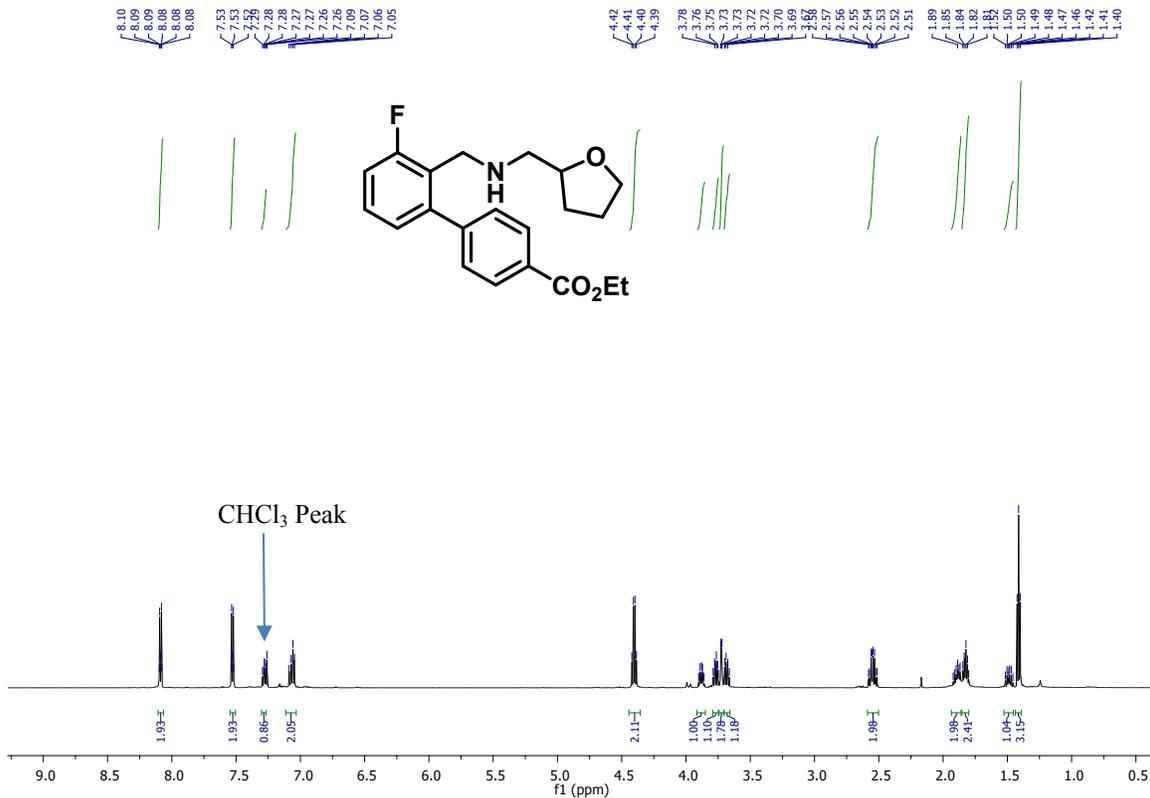


Figure S-177. ¹H NMR spectrum of **3k** (CDCl₃, 600 MHz, 298 K)

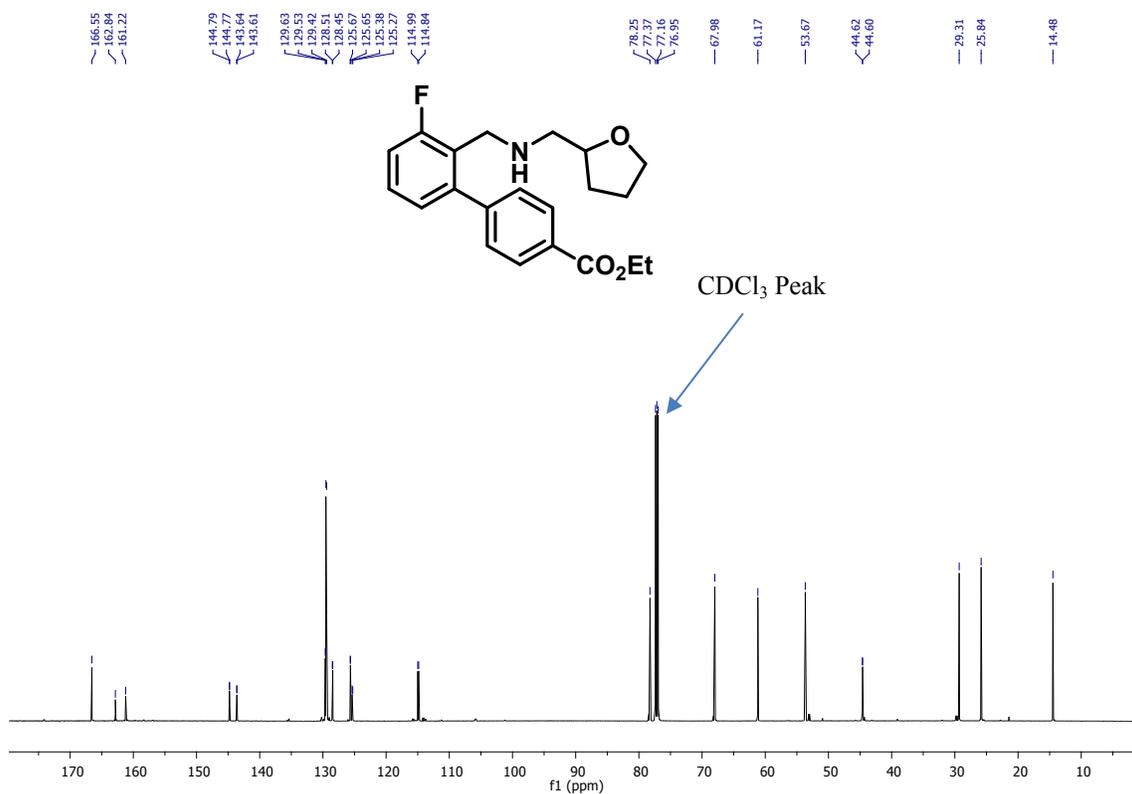


Figure S-178. ¹³C NMR spectrum of **3k** (CDCl₃, 151 MHz, 298 K)

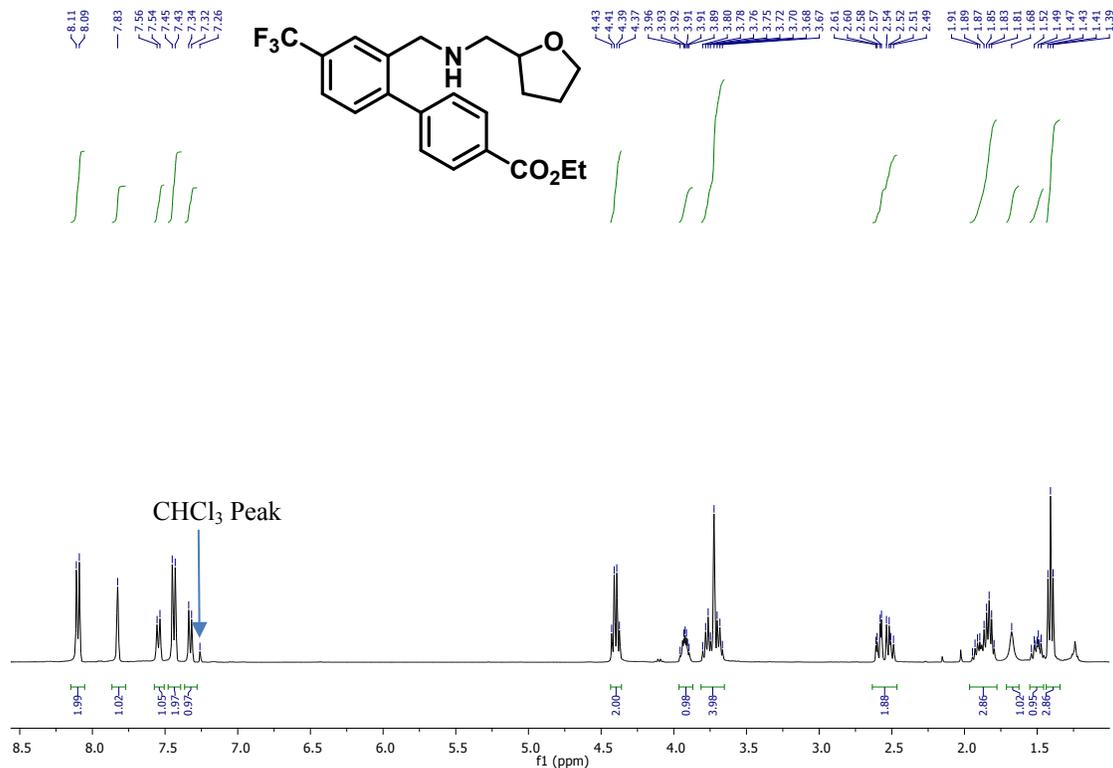


Figure S-179. $^1\text{H NMR}$ spectrum of **31** (CDCl_3 , 400 MHz, 298 K)

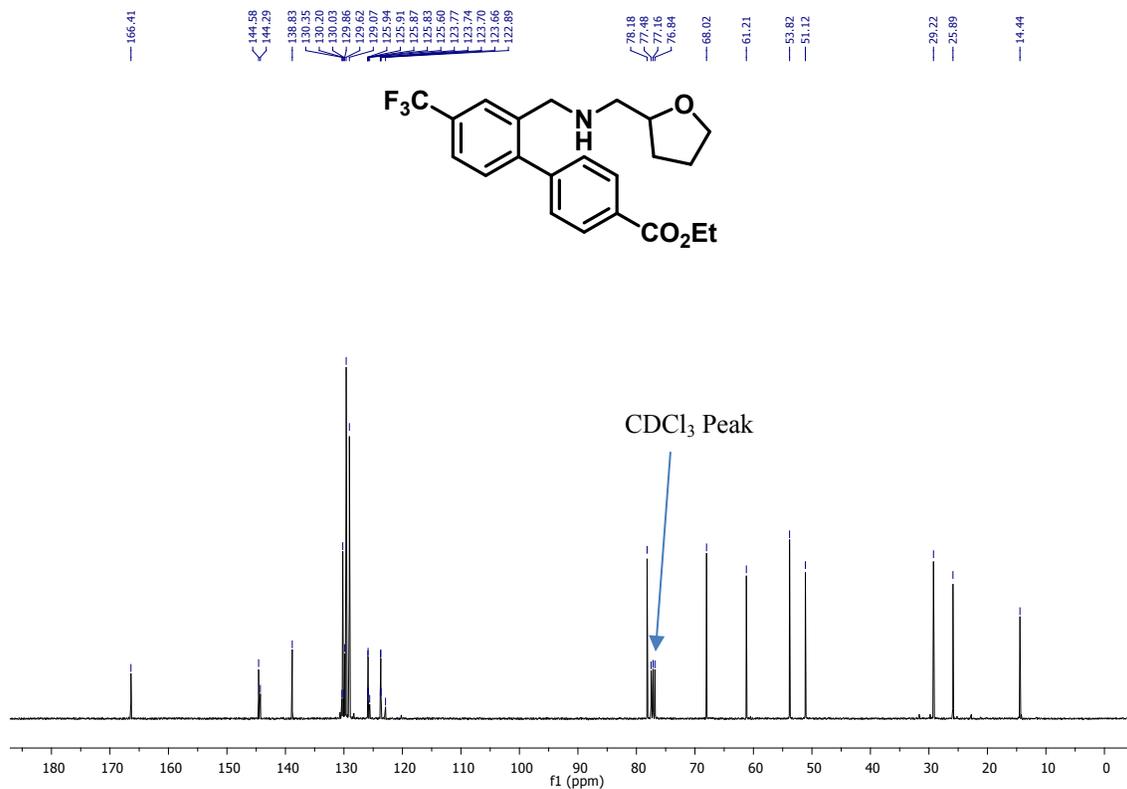


Figure S-180. $^{13}\text{C NMR}$ spectrum of **31** (CDCl_3 , 151 MHz, 298 K)

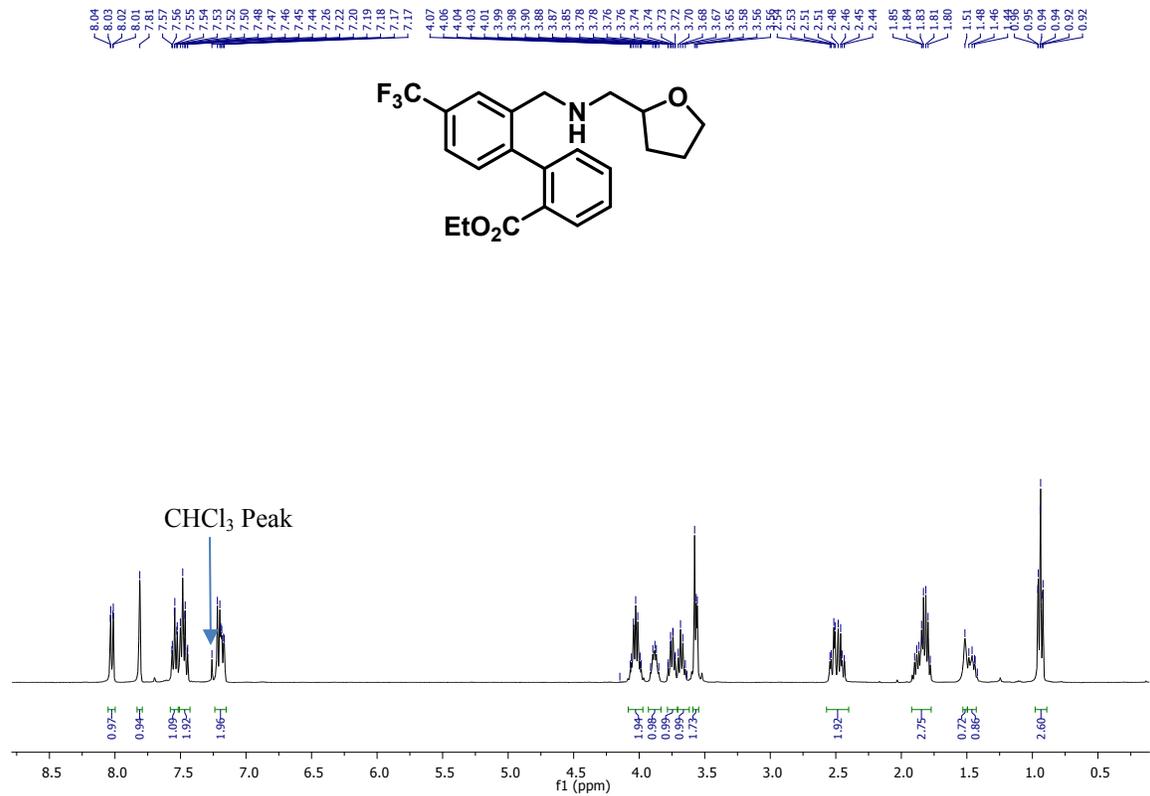


Figure S-181. ¹H NMR spectrum of **3m** (CDCl₃, 600 MHz, 298 K)

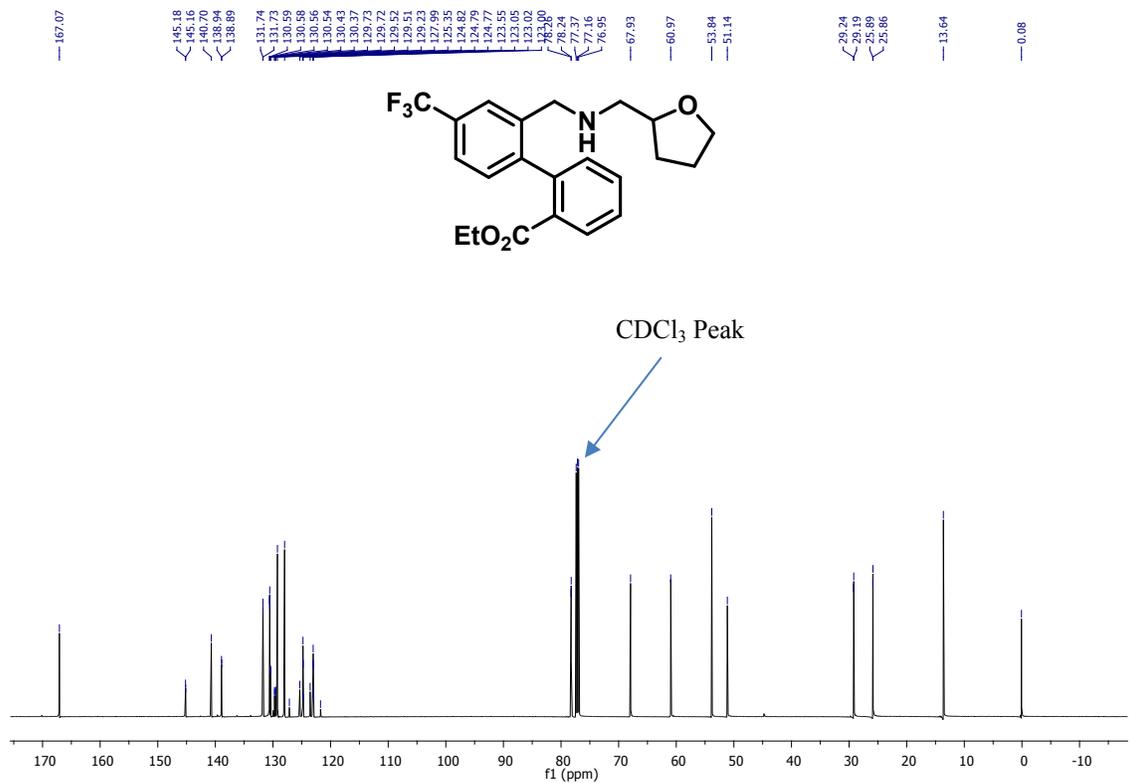


Figure S-182. ¹³C NMR spectrum of **3m** (CDCl₃, 151 MHz, 298 K)

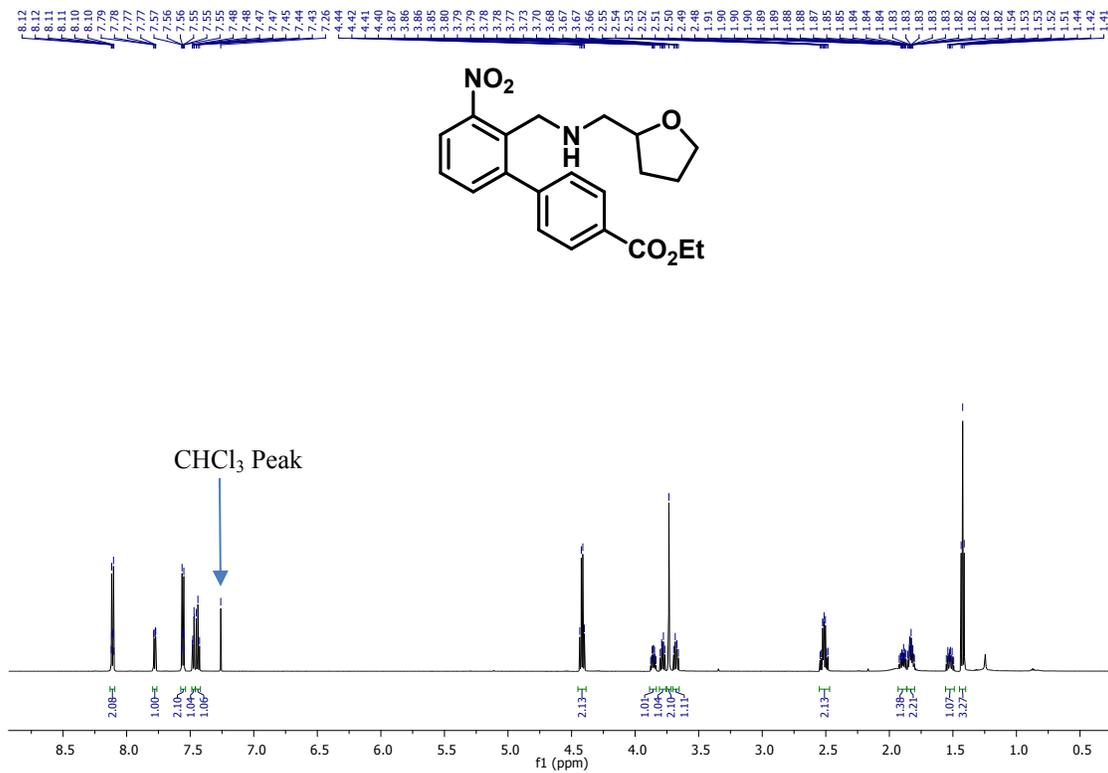


Figure S-183. ¹H NMR spectrum of **3n** (CDCl₃, 400 MHz, 298 K)

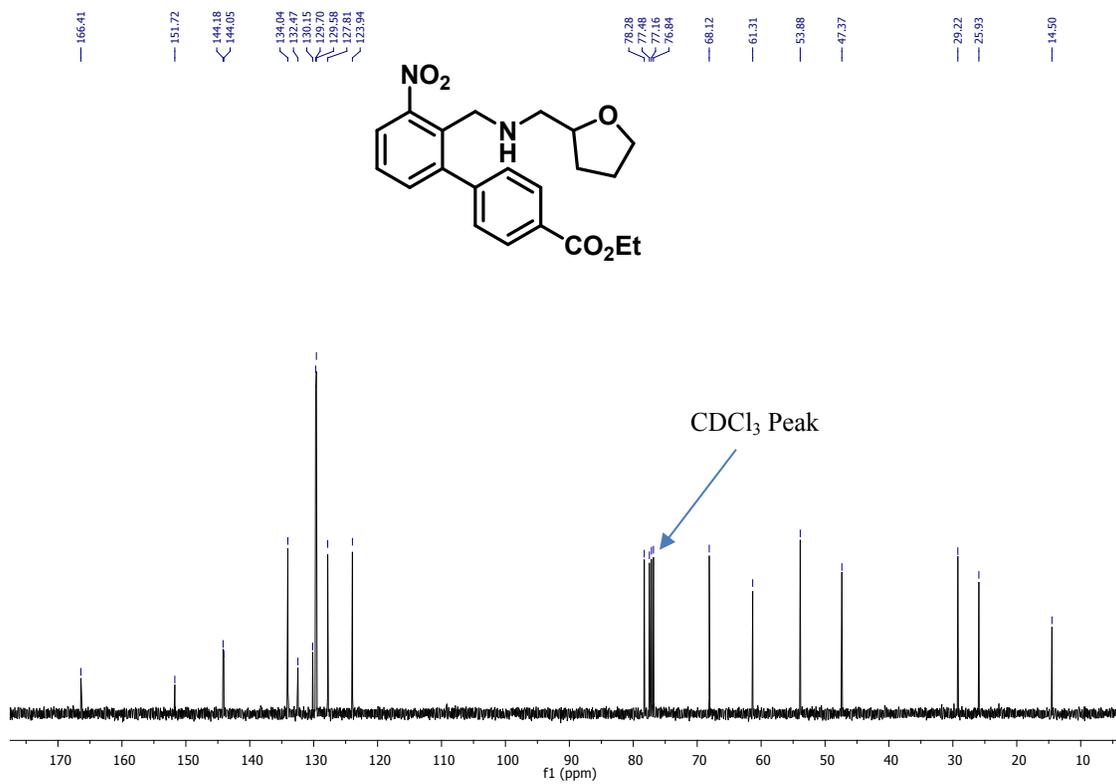


Figure S-184. ¹³C NMR spectrum of **3n** (CDCl₃, 101 MHz, 298 K)

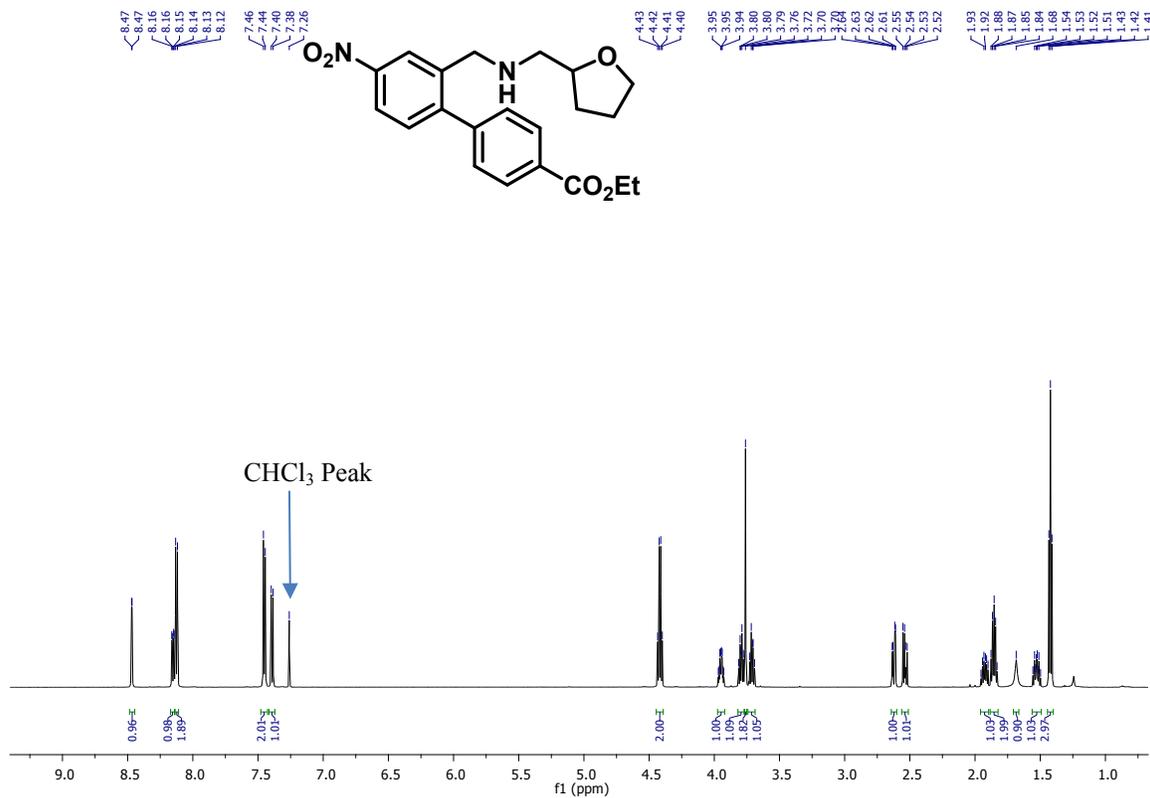


Figure S-185. ¹H NMR spectrum of **3o** (CDCl₃, 400 MHz, 298 K)

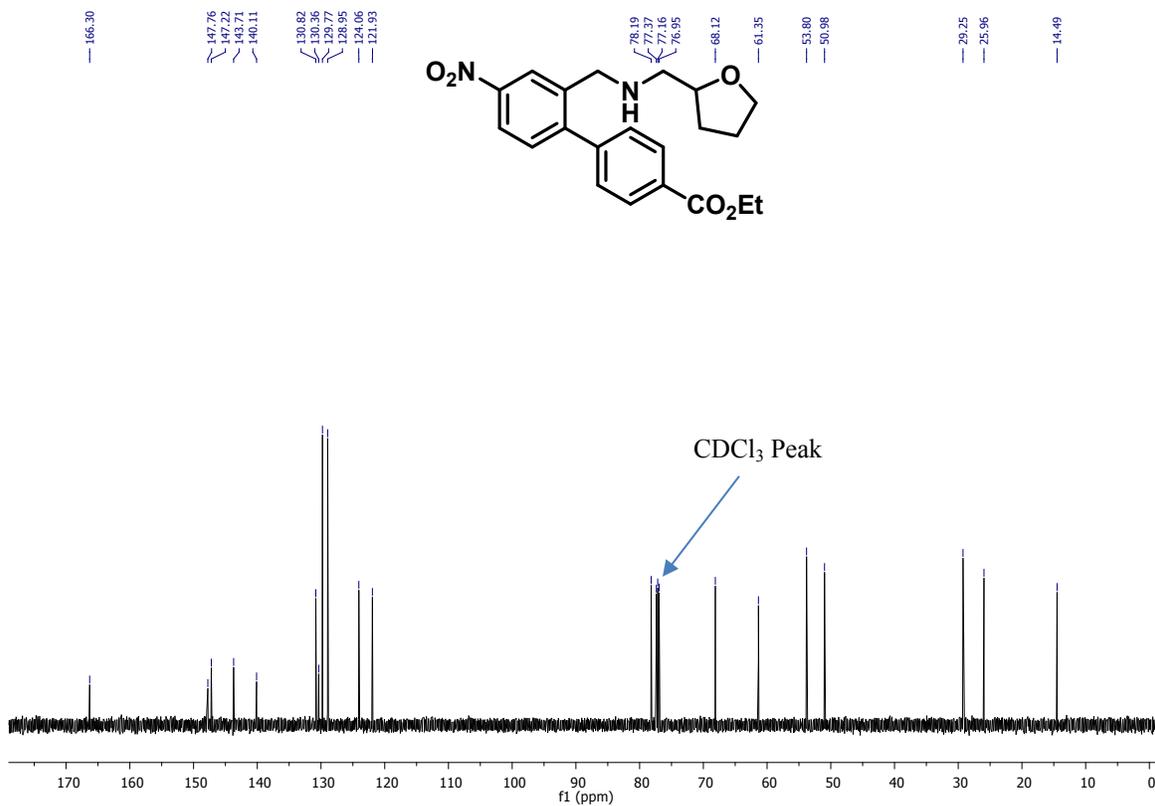


Figure S-186. ¹³C NMR spectrum of **3o** (CDCl₃, 101 MHz, 298 K)

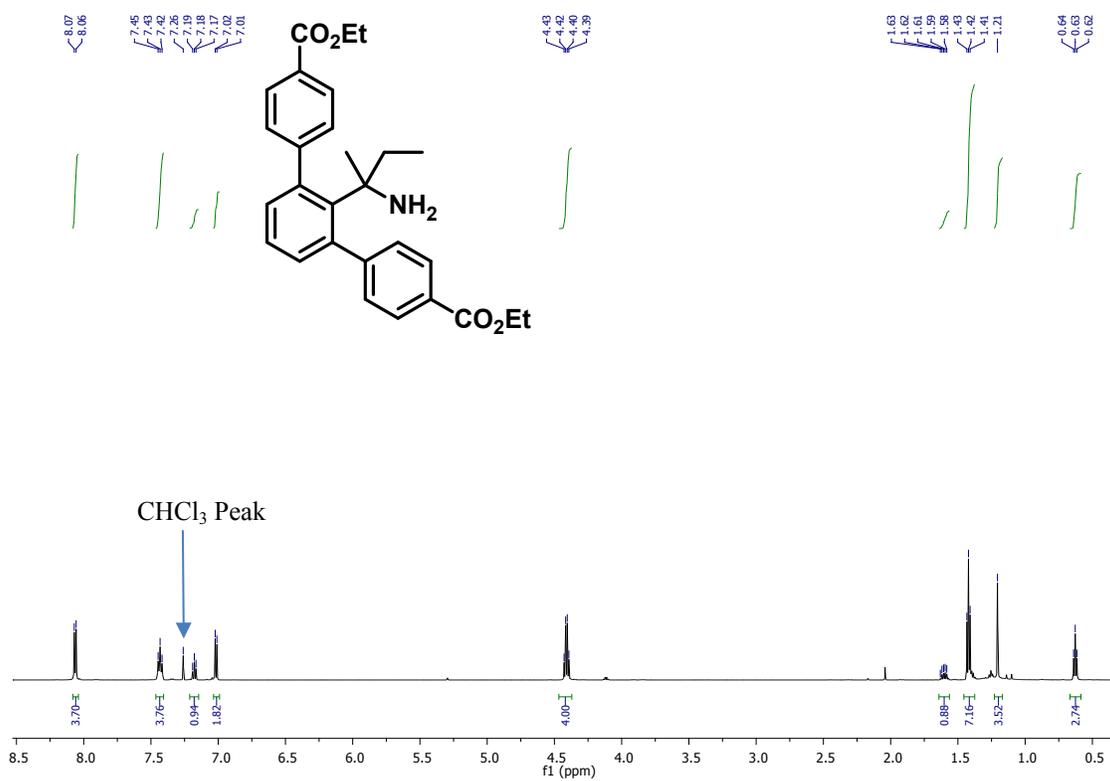


Figure S-187. ¹H NMR spectrum of **4a** (CDCl₃, 400 MHz, 298 K)

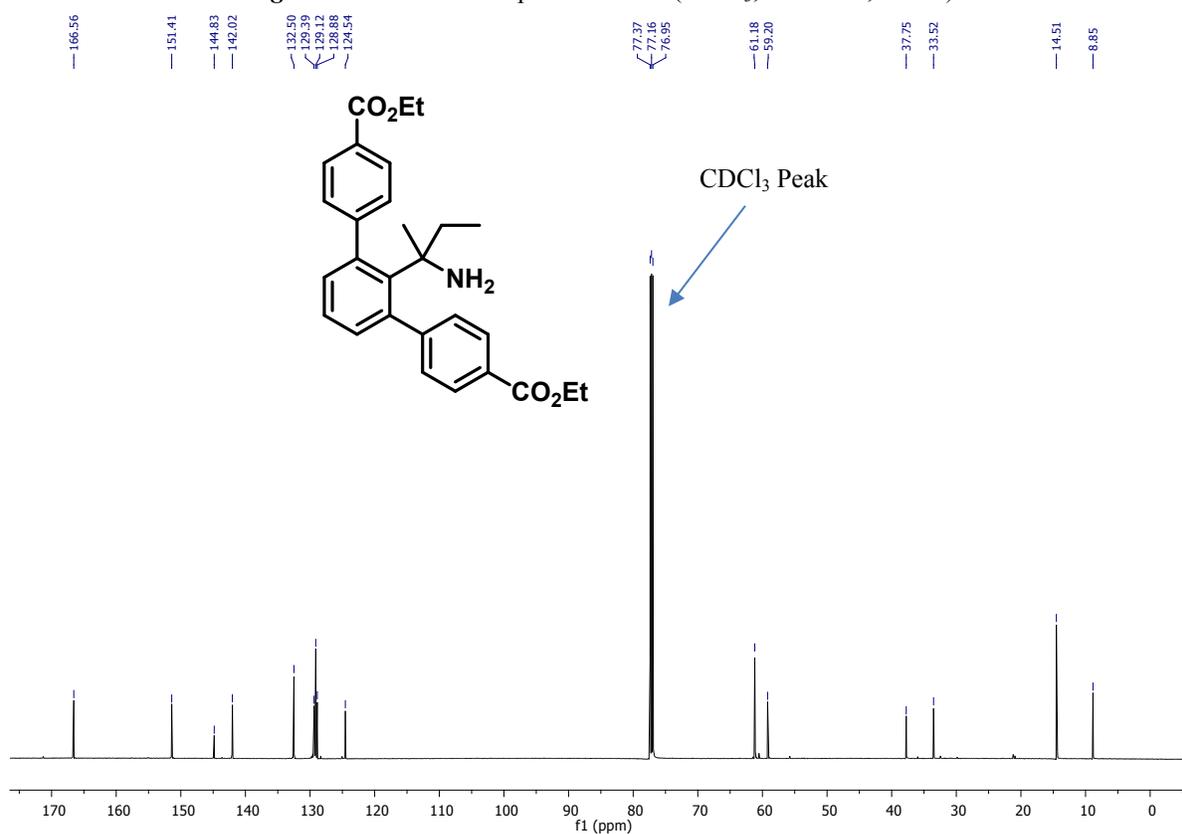


Figure S-188. ¹³C NMR spectrum of **4a** (CDCl₃, 151 MHz, 298 K)

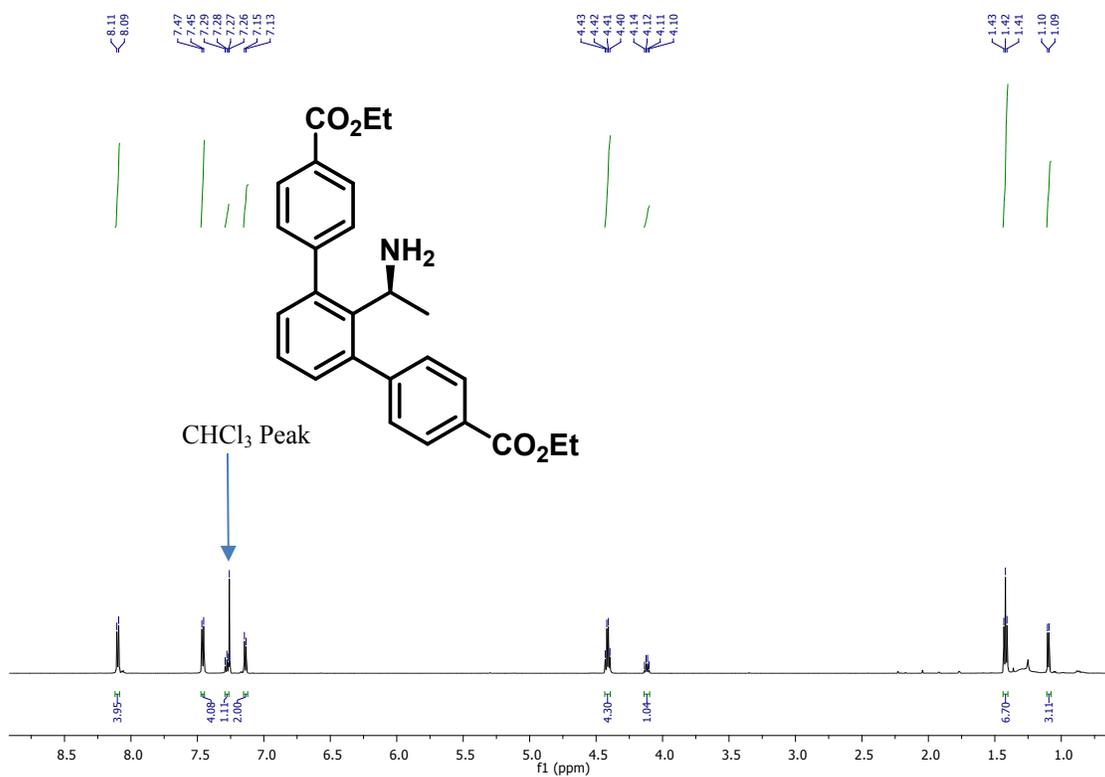


Figure S-189. ¹H NMR spectrum of **4b** (CDCl₃, 600 MHz, 298 K)

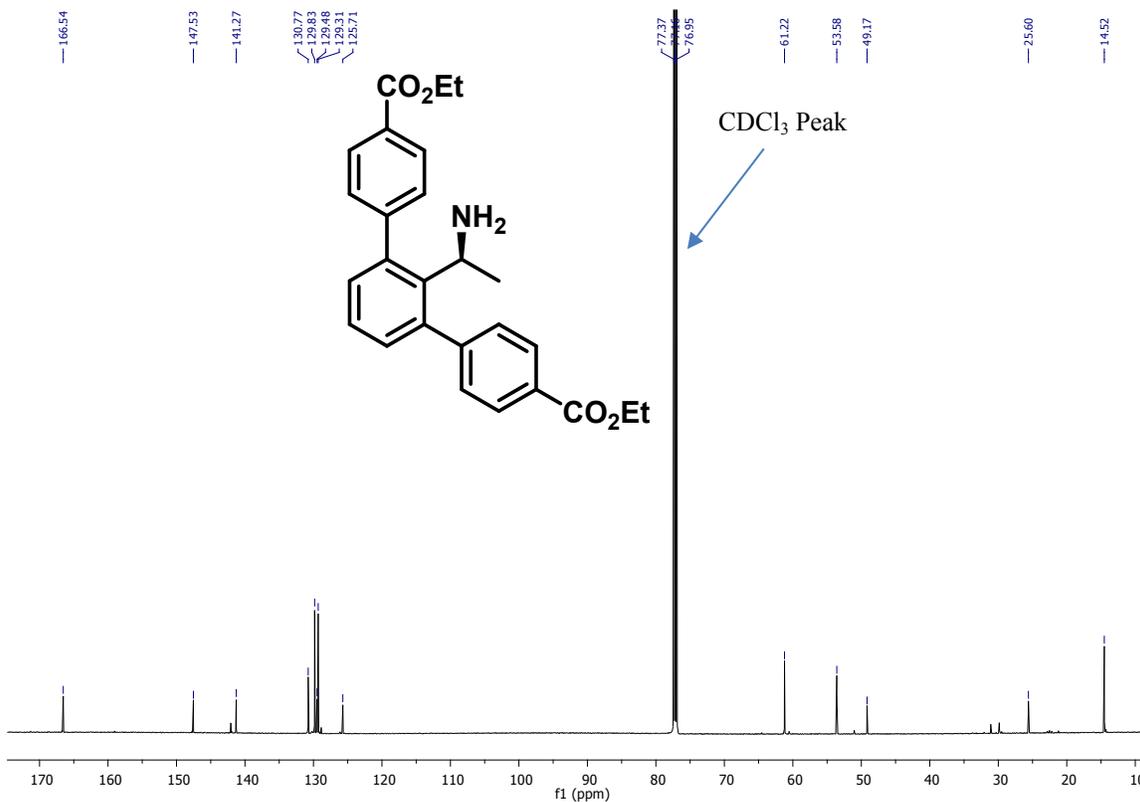


Figure S-190. ¹³C NMR spectrum of **4b** (CDCl₃, 151 MHz, 298 K)

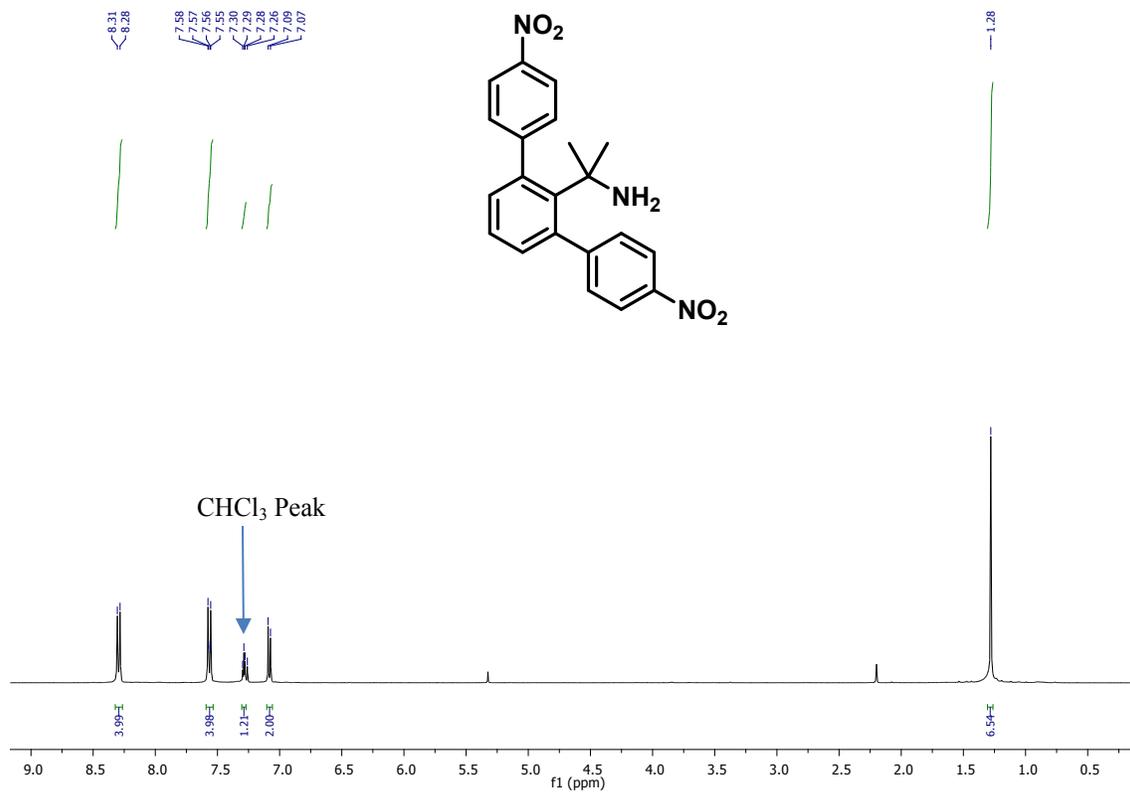


Figure S-191. ¹H NMR spectrum of 4c (CDCl₃, 400 MHz, 298 K)

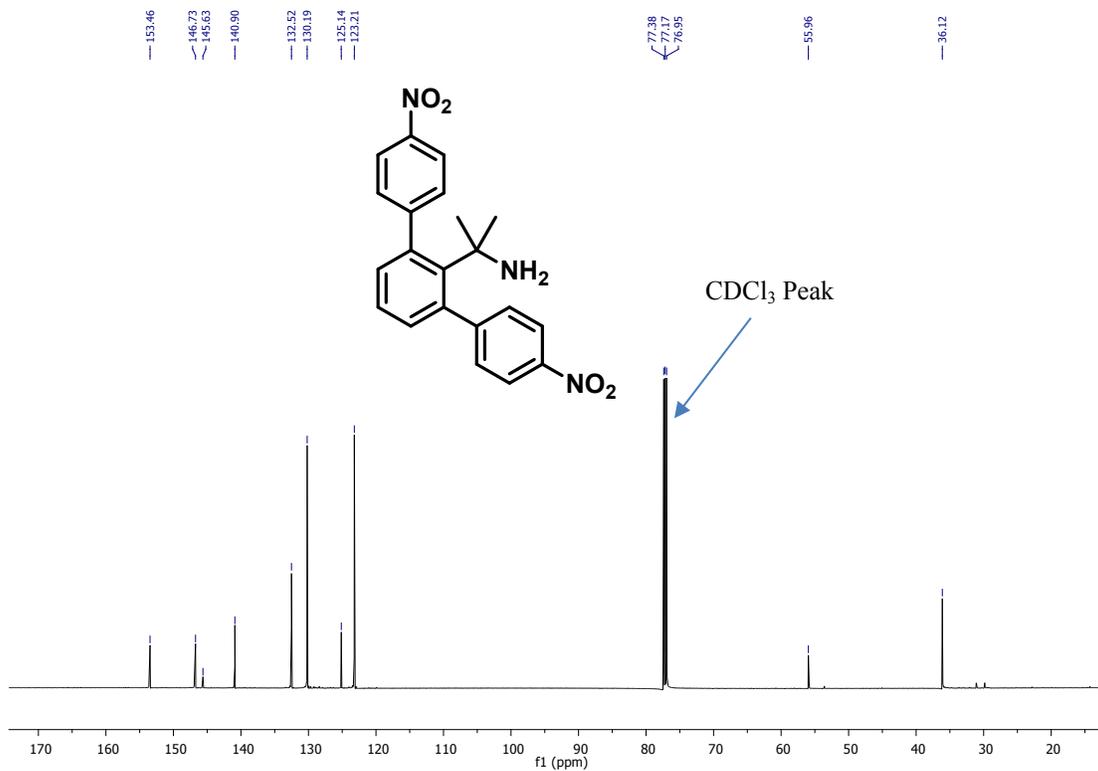


Figure S-192. ¹³C NMR spectrum of 4c (CDCl₃, 151 MHz, 298 K)

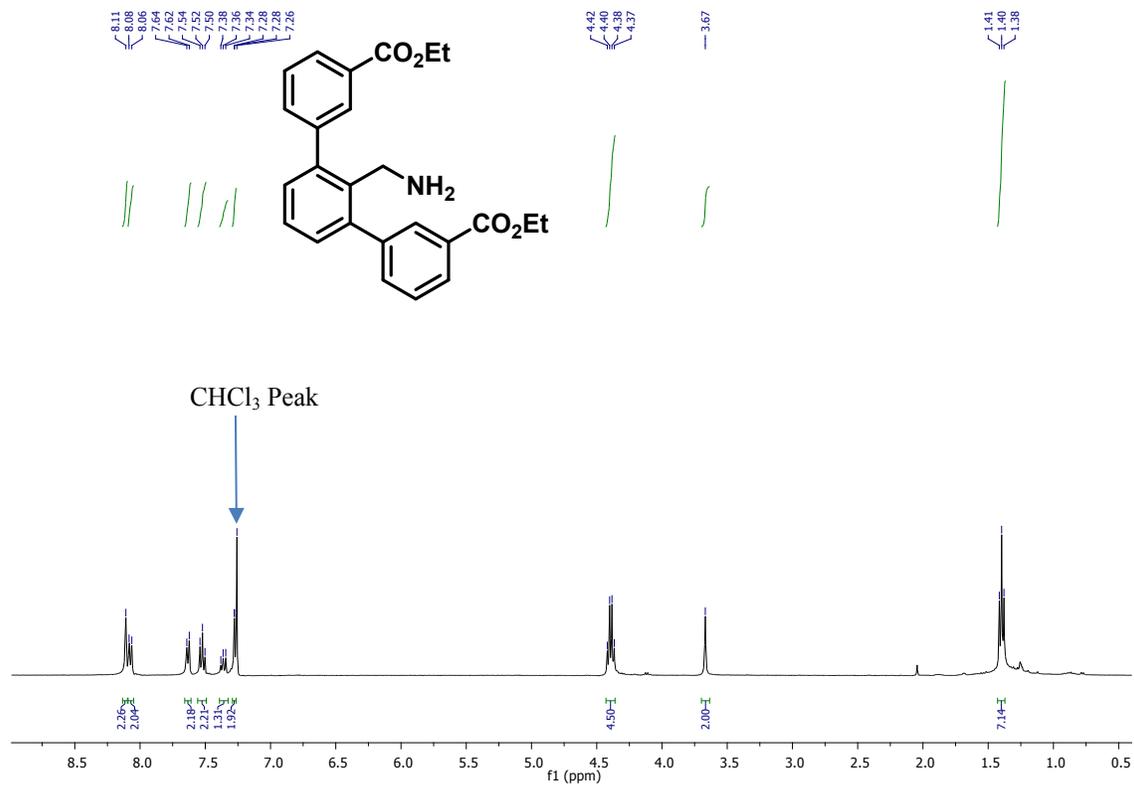


Figure S-193. ¹H NMR spectrum of **4d** (CDCl₃, 600 MHz, 298 K)

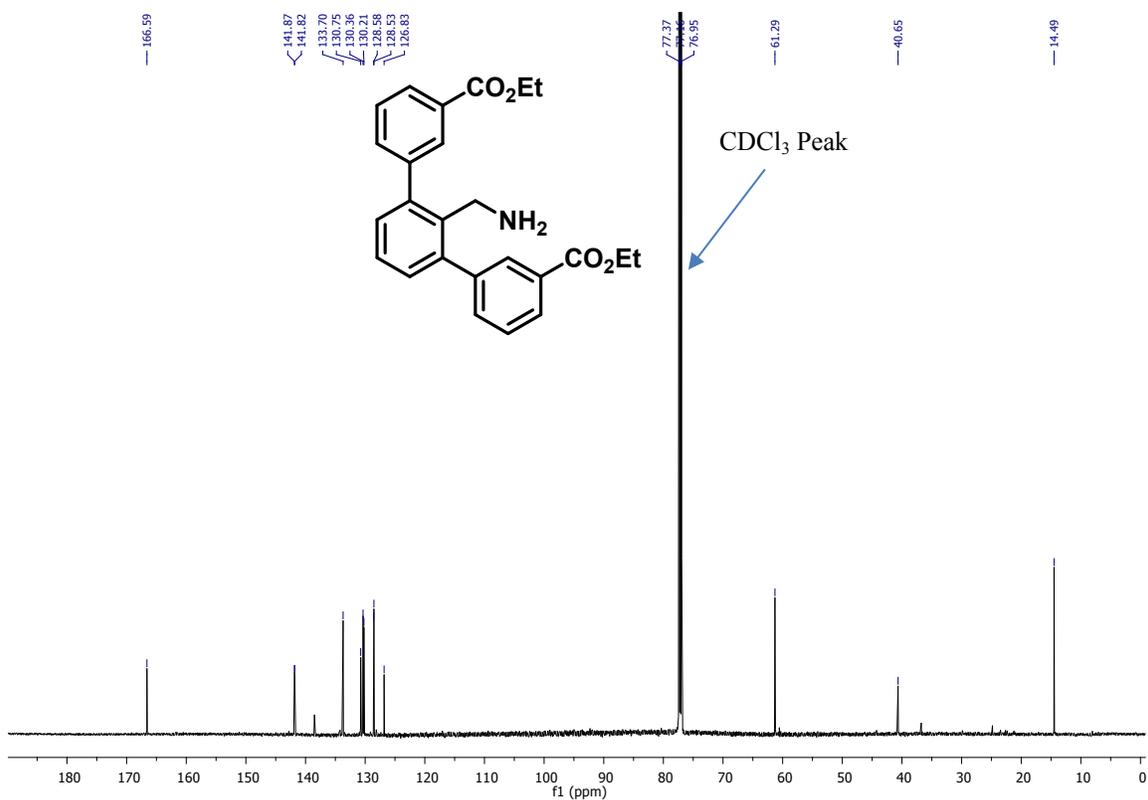


Figure S-194. ¹³C NMR spectrum of **4d** (CDCl₃, 151 MHz, 298 K)

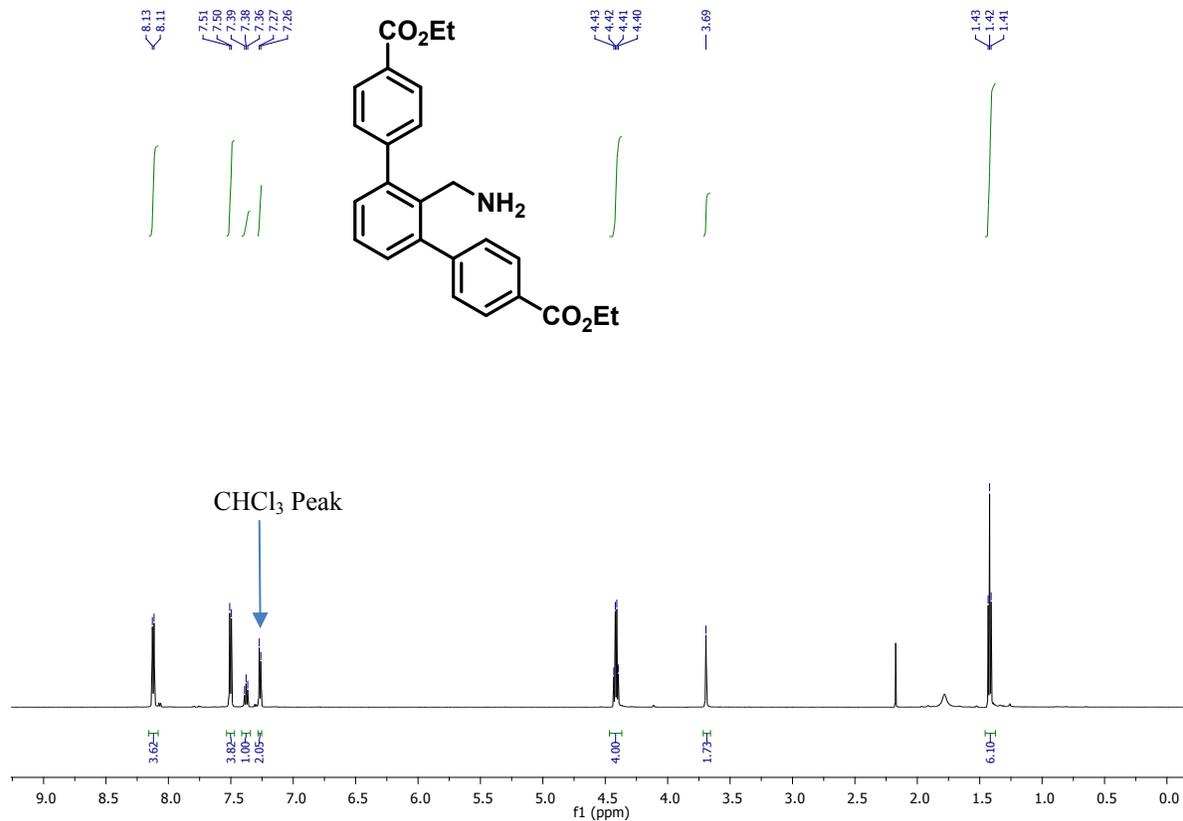


Figure S-195. ¹H NMR spectrum of 4e (CDCl₃, 600 MHz, 298 K)

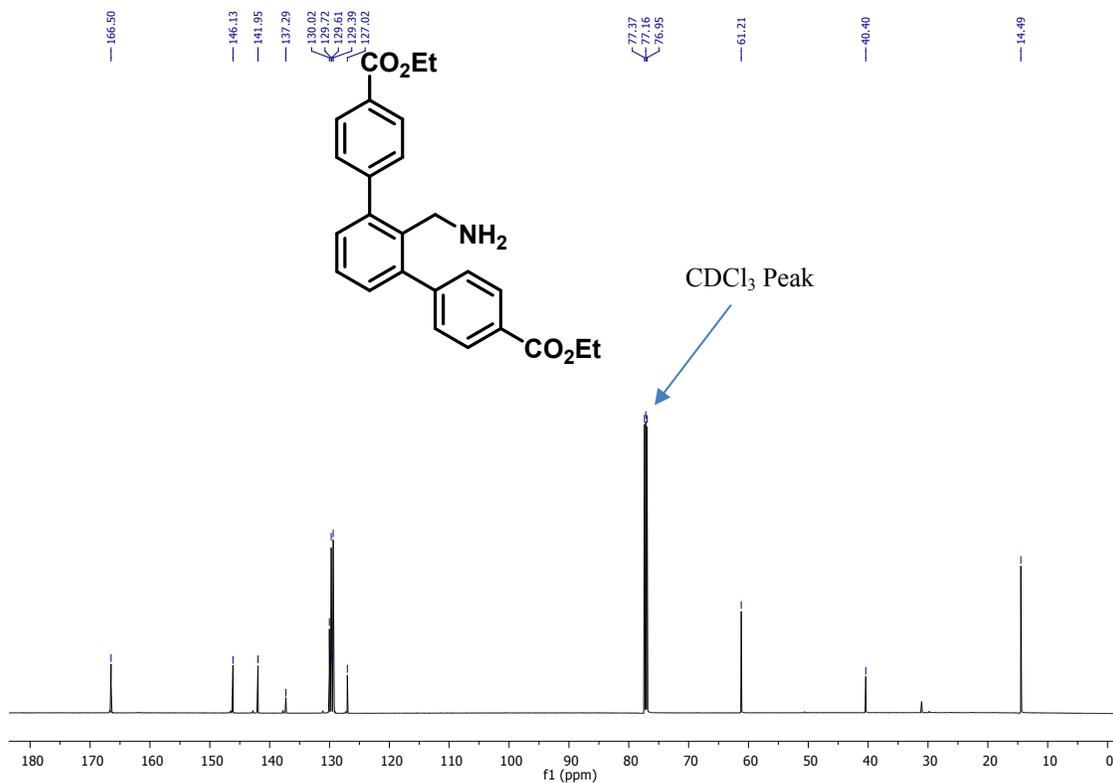


Figure S-196. ¹³C NMR spectrum of 4e (CDCl₃, 151 MHz, 298 K)

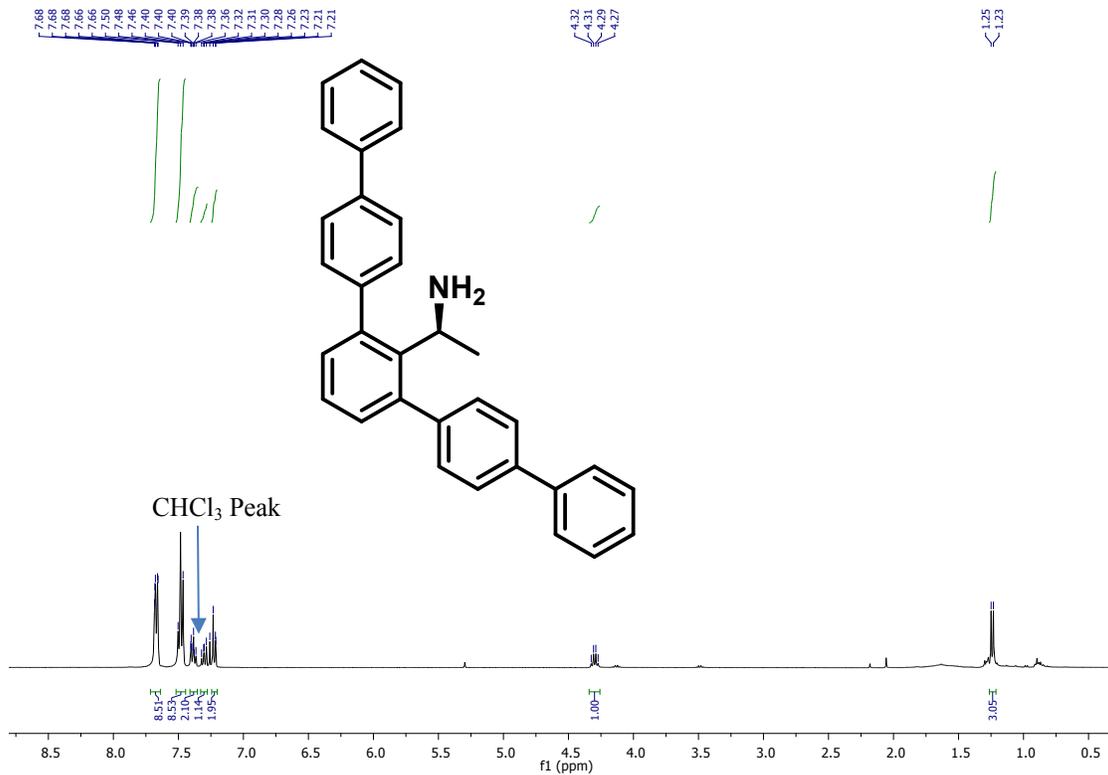


Figure S-197. $^1\text{H NMR}$ spectrum of 4f (CDCl_3 , 400 MHz, 298 K)

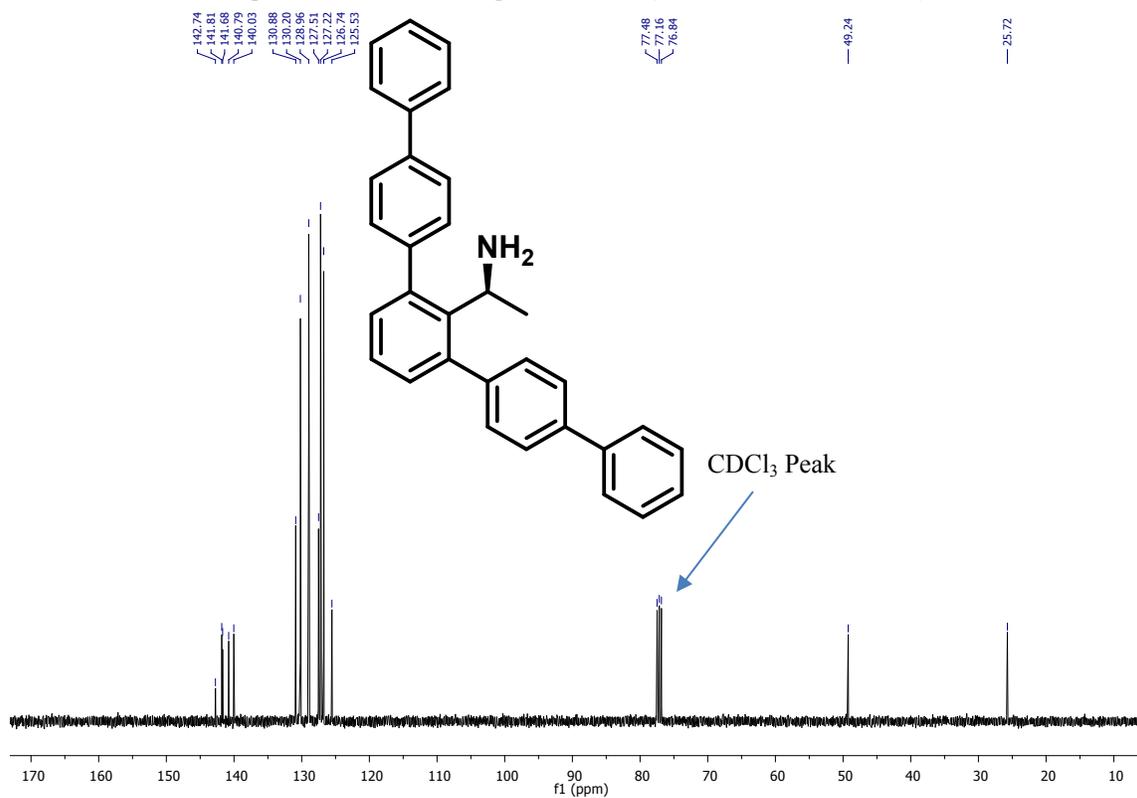


Figure S-198. $^{13}\text{C NMR}$ spectrum of 4f (CDCl_3 , 101 MHz, 298 K)

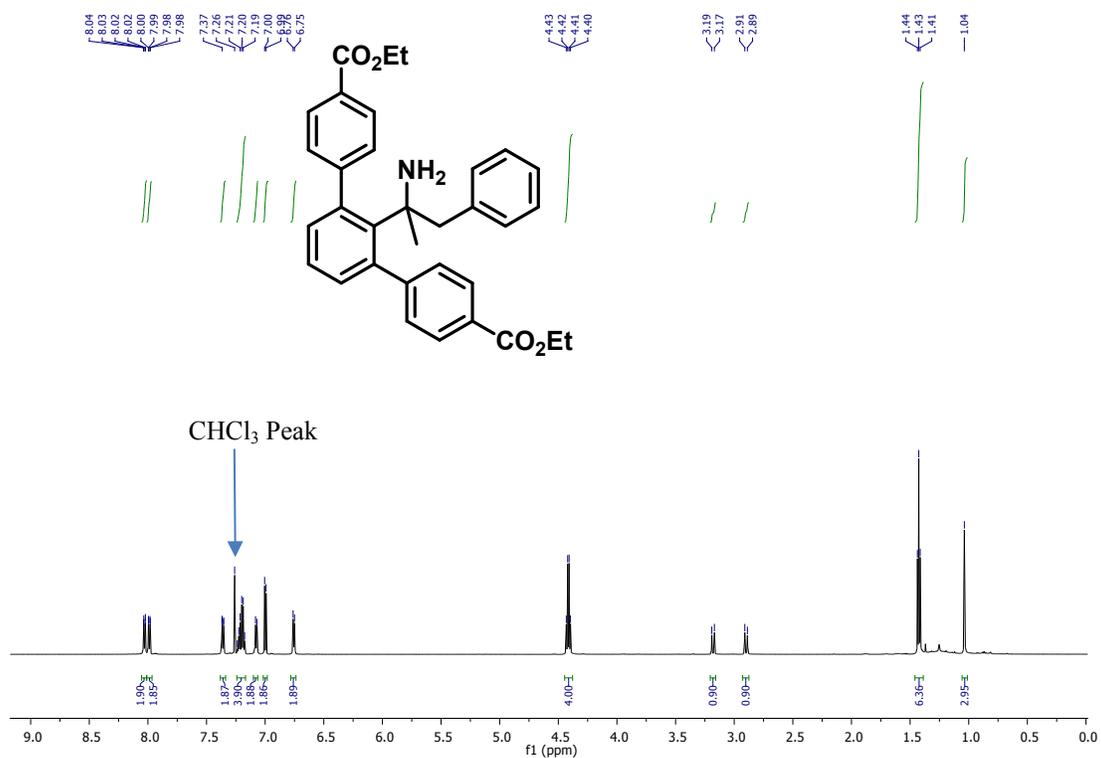


Figure S-199. ¹H NMR spectrum of **4g** (CDCl₃, 600 MHz, 298 K)

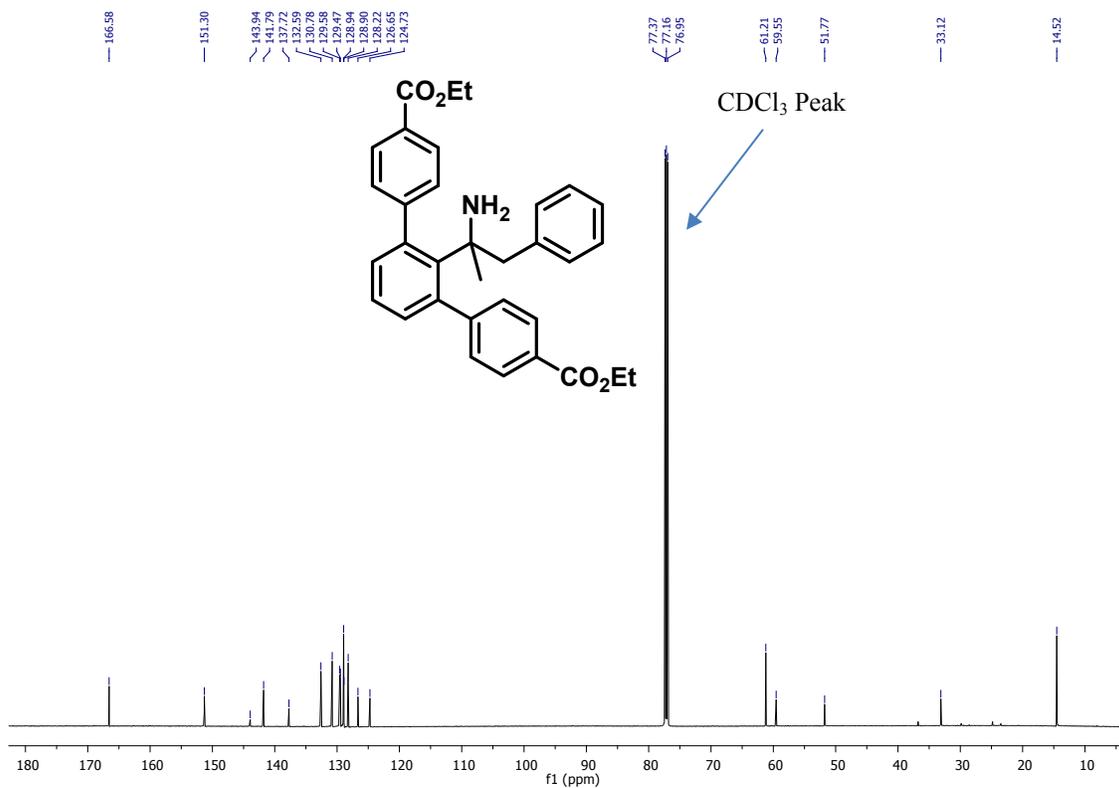


Figure S-200. ¹³C NMR spectrum of **4g** (CDCl₃, 151 MHz, 298 K)

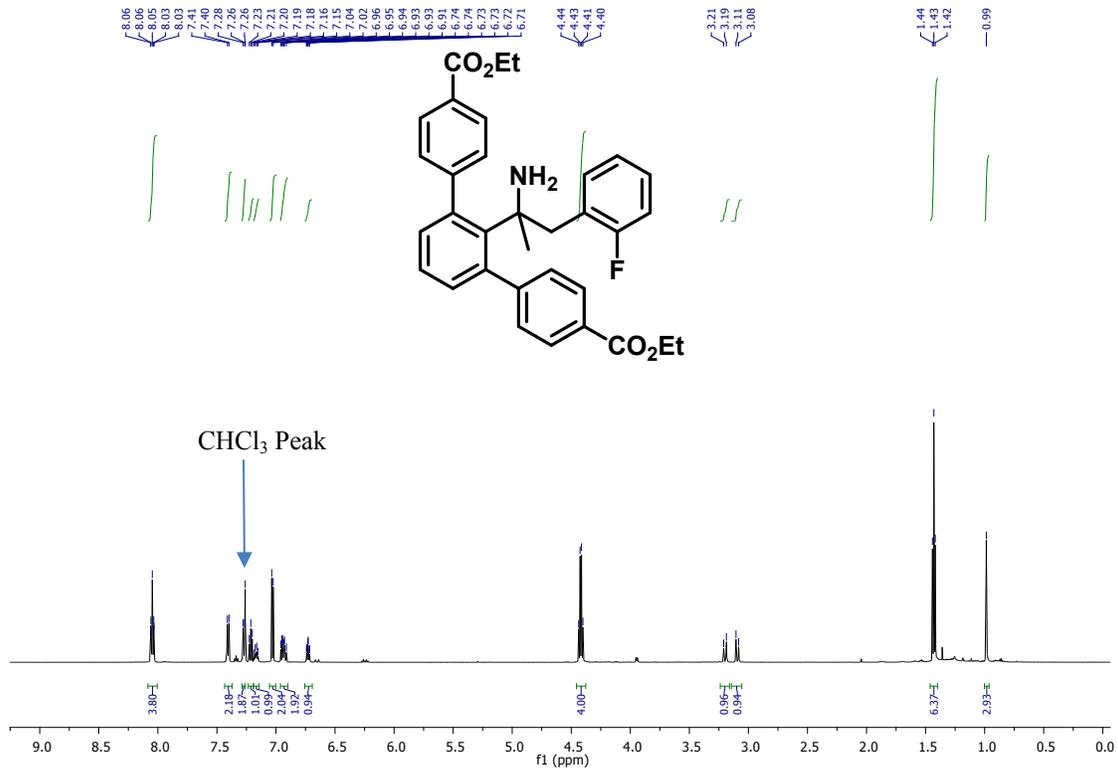


Figure S-201. ^1H NMR spectrum of **4h** (CDCl₃, 600 MHz, 298 K)

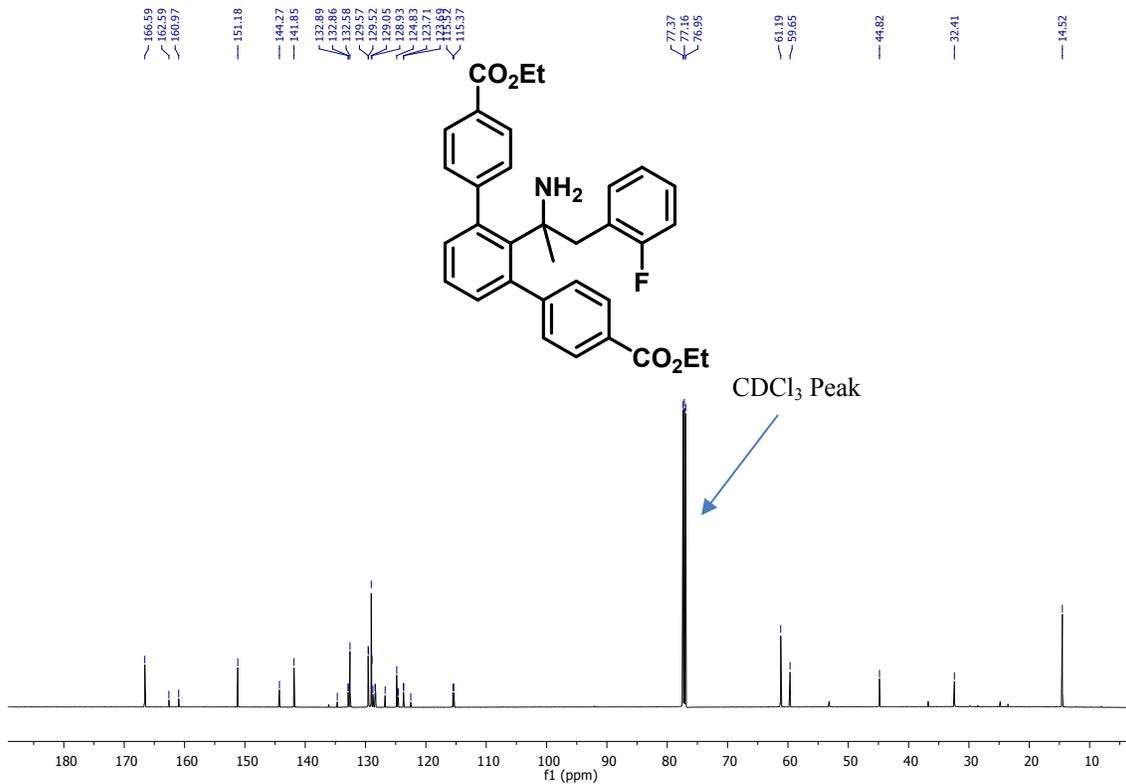


Figure S-202. ^{13}C NMR spectrum of **4h** (CDCl₃, 151 MHz, 298 K)

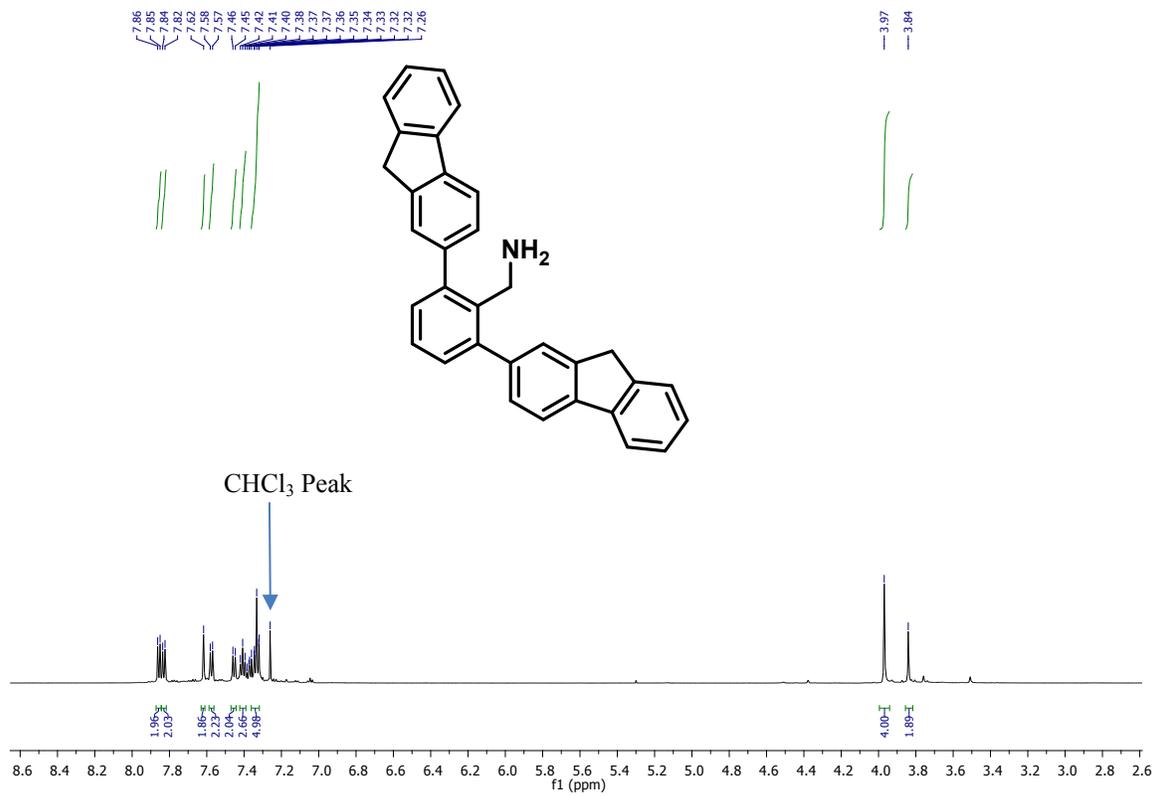


Figure S-203. $^1\text{H NMR}$ spectrum of **4i** (CDCl_3 , 600 MHz, 298 K)

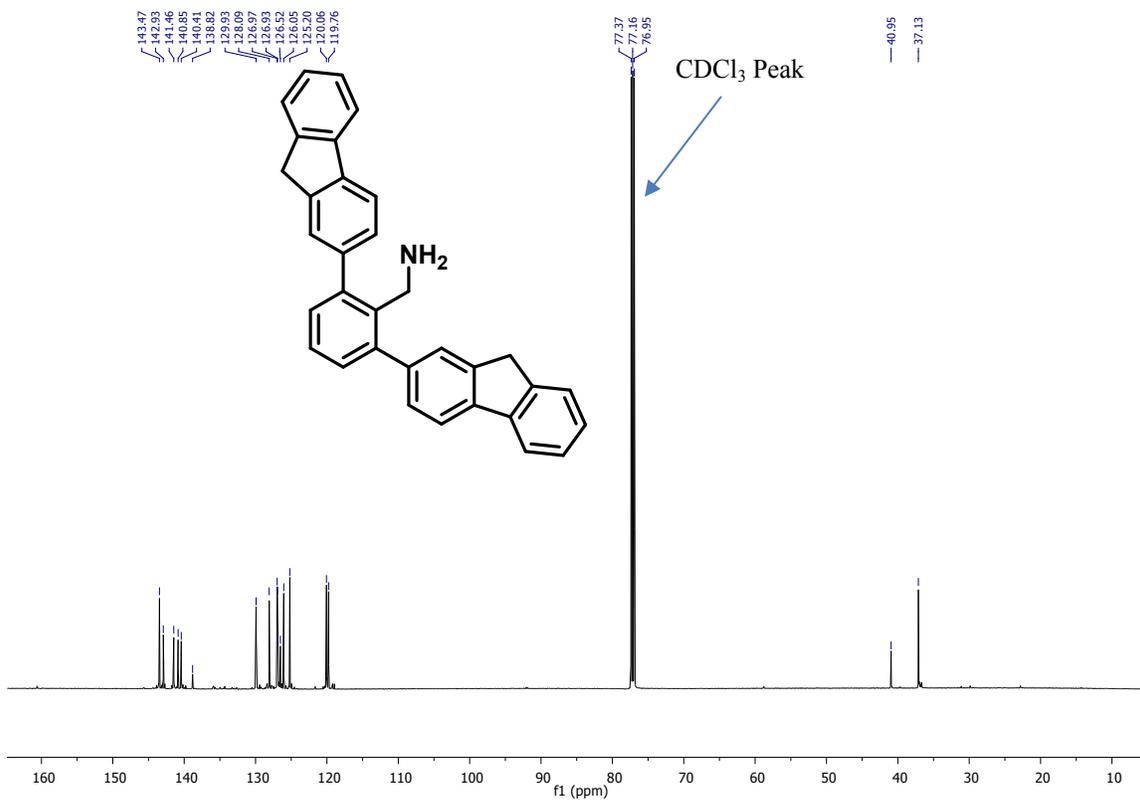


Figure S-204. $^{13}\text{C NMR}$ spectrum of **4i** (CDCl_3 , 151 MHz, 298 K)

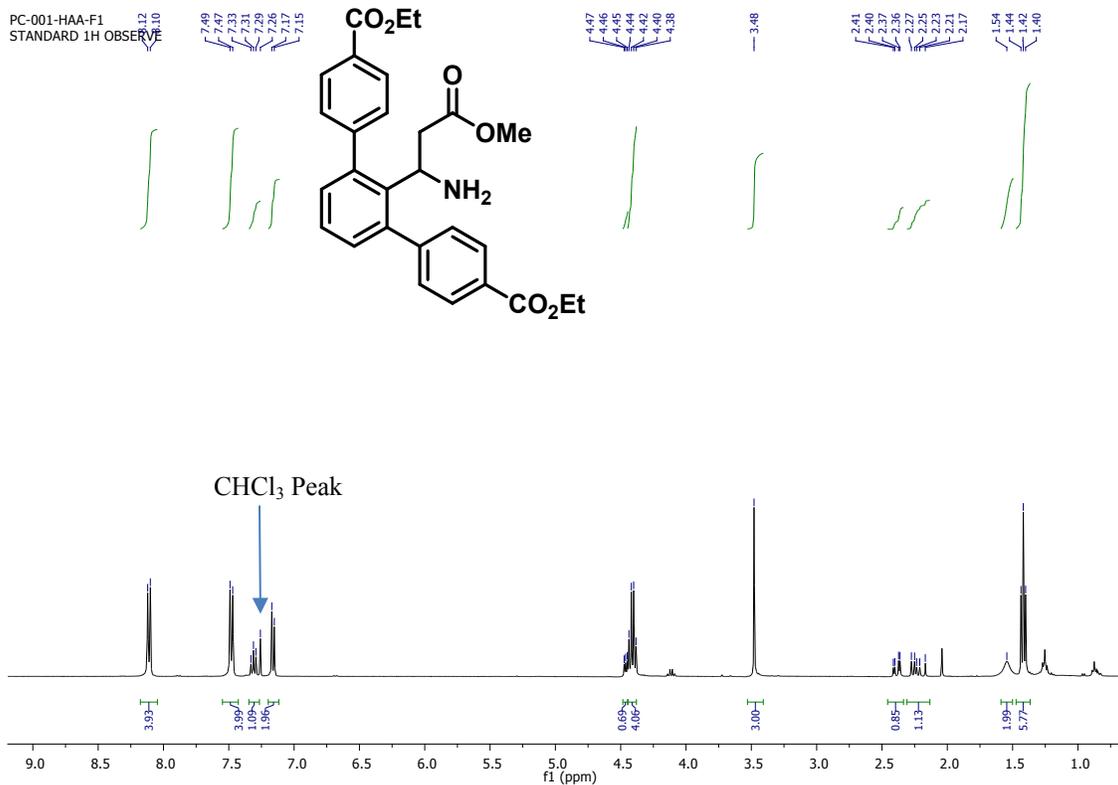


Figure S-205. ^1H NMR spectrum of 4j (CDCl₃, 400 MHz, 298 K)

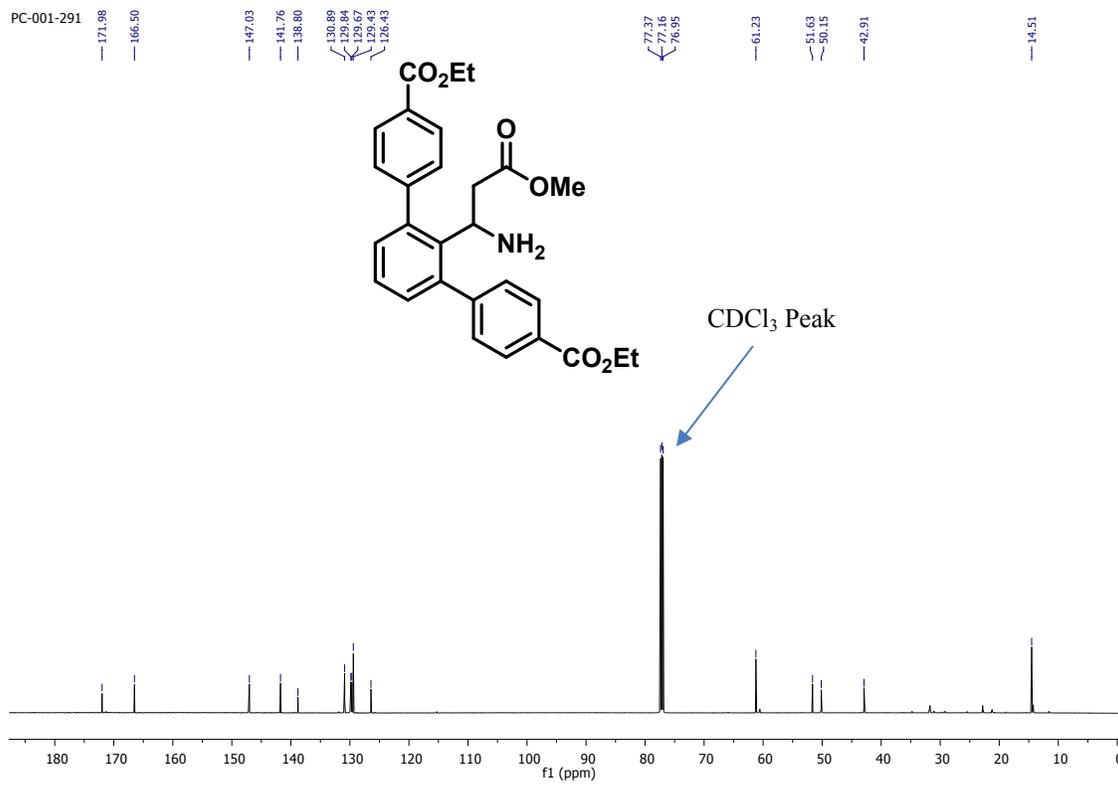


Figure S-206. ^{13}C NMR spectrum of 4j (CDCl₃, 151 MHz, 298 K)

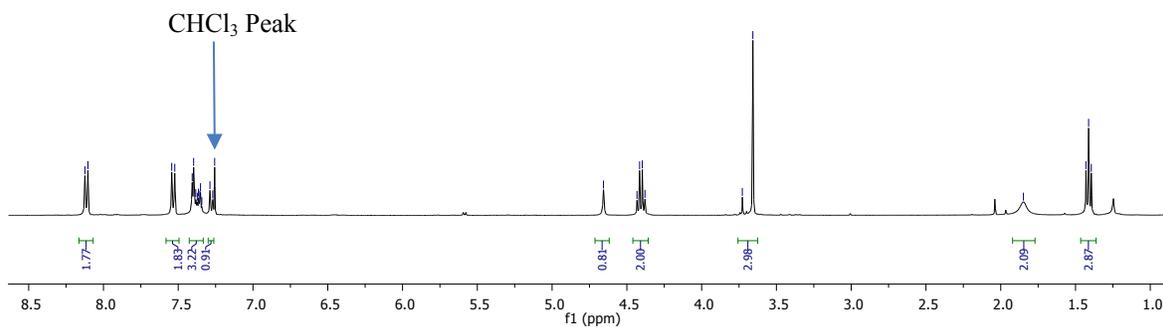
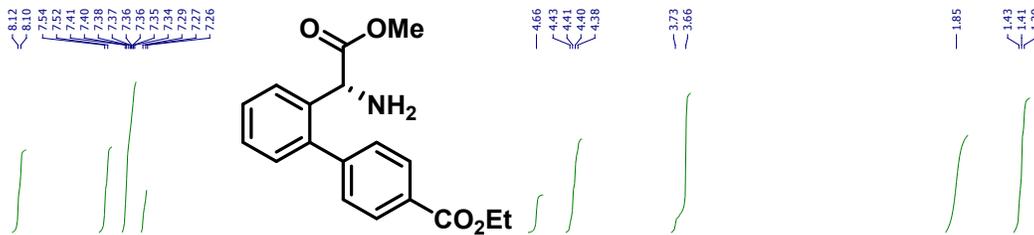


Figure S-207. ^1H NMR spectrum of **5a** (CDCl_3 , 400 MHz, 298 K)

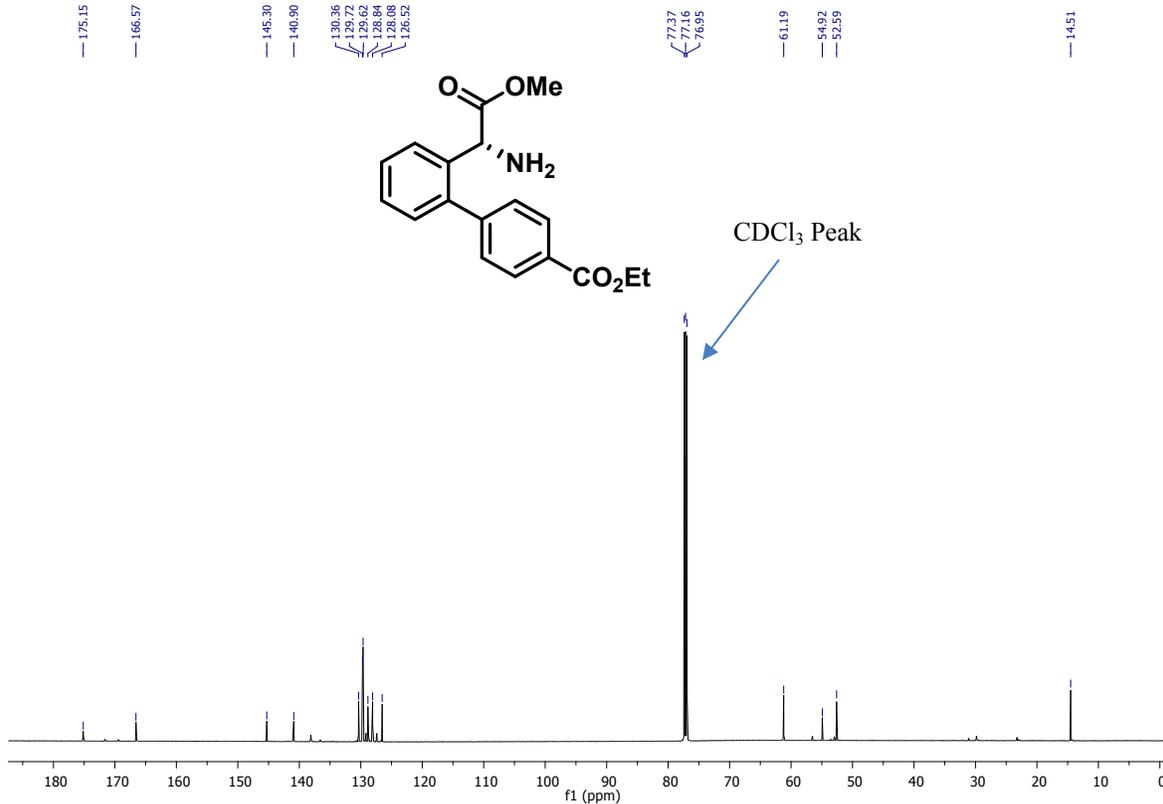
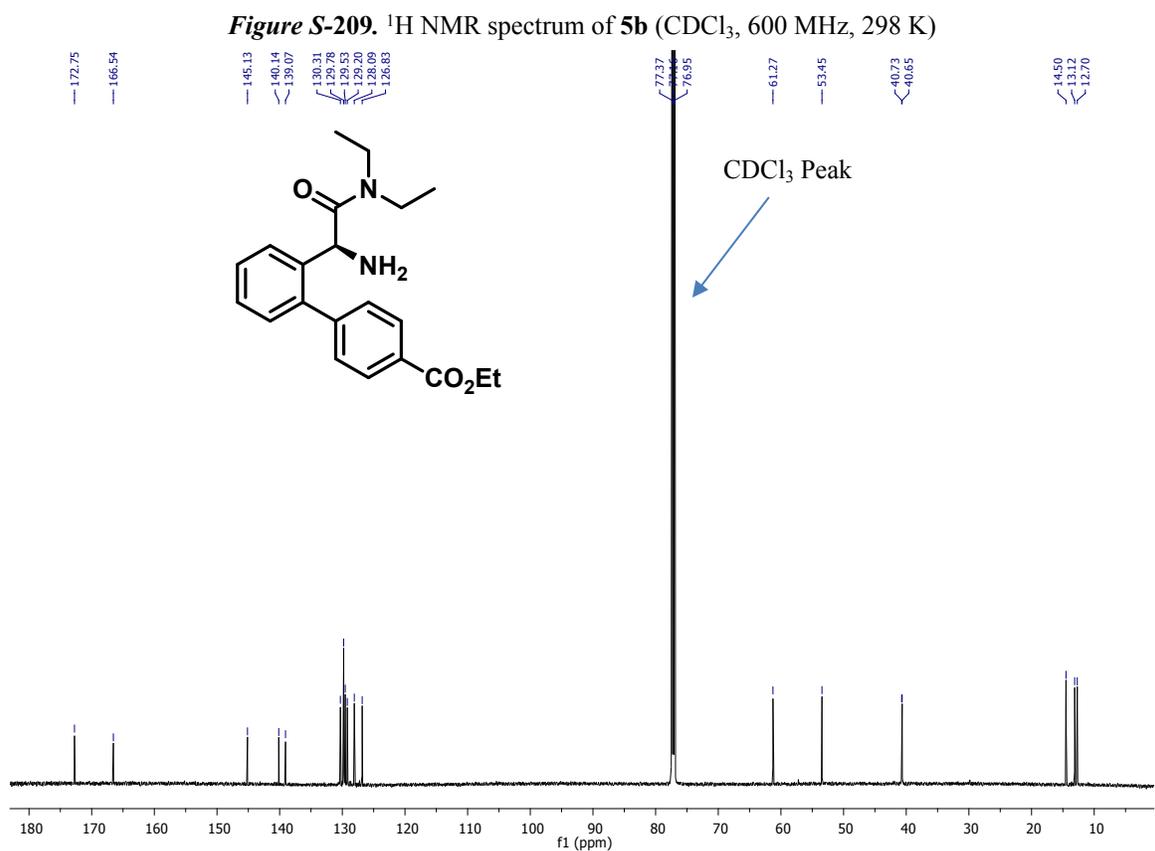
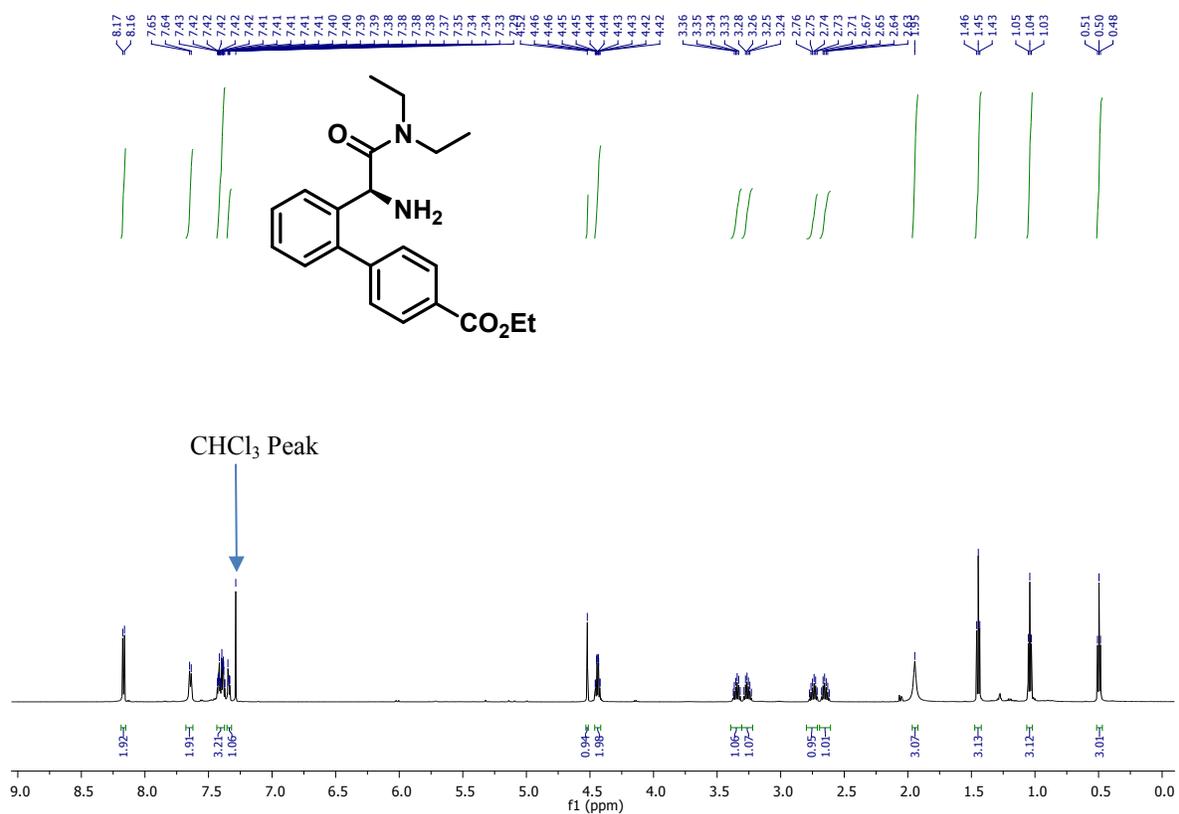


Figure S-208. ^{13}C NMR spectrum of **5a** (CDCl_3 , 151 MHz, 298 K)



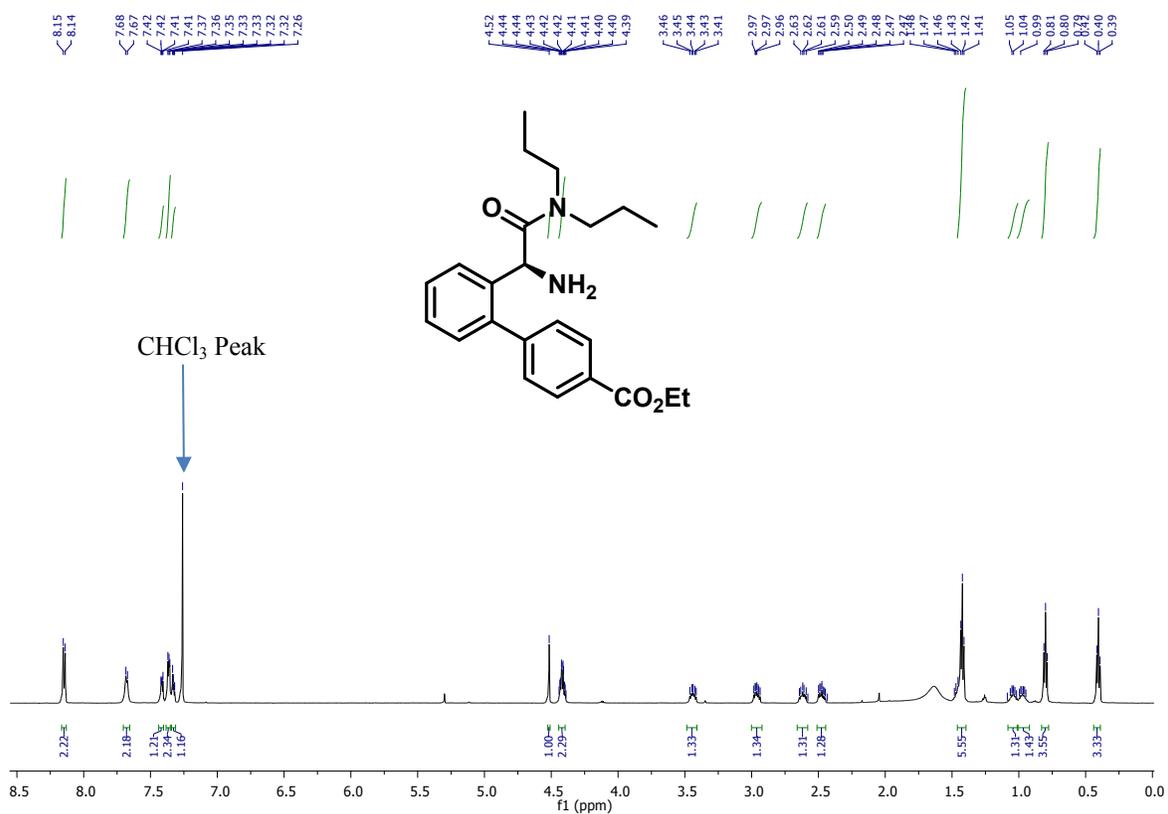


Figure S-211. ^1H NMR spectrum of 5c (CDCl_3 , 600 MHz, 298 K)

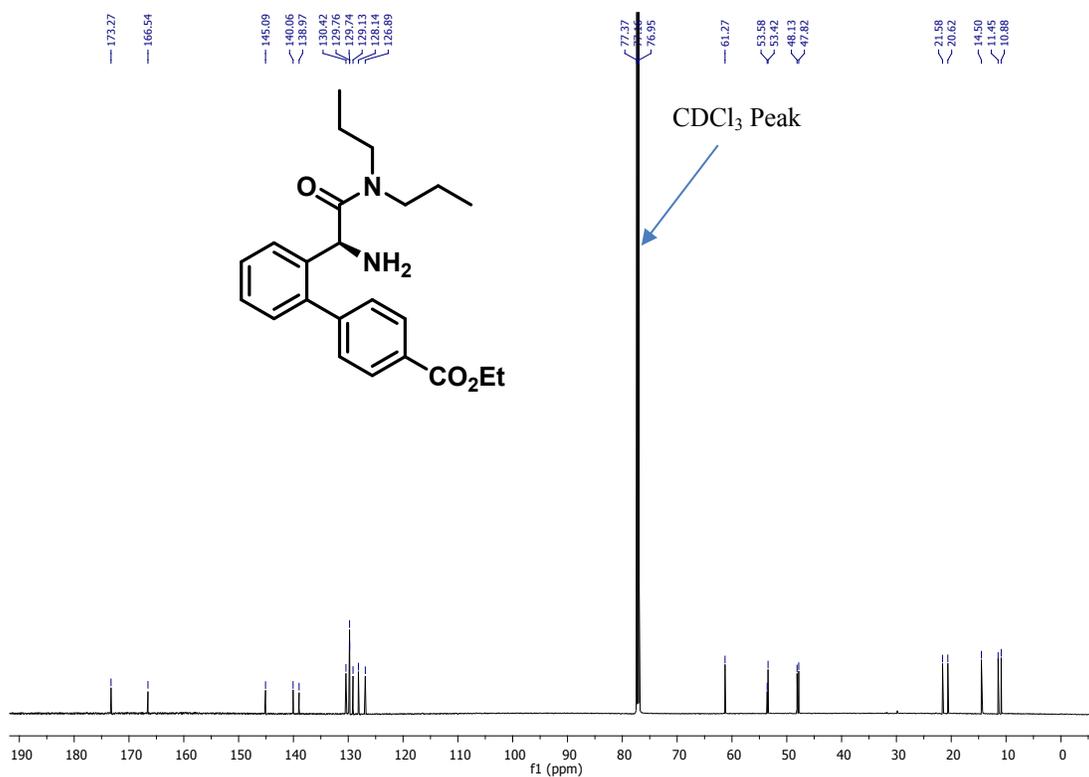


Figure S-212. ^{13}C NMR spectrum of 5c (CDCl_3 , 151 MHz, 298 K)

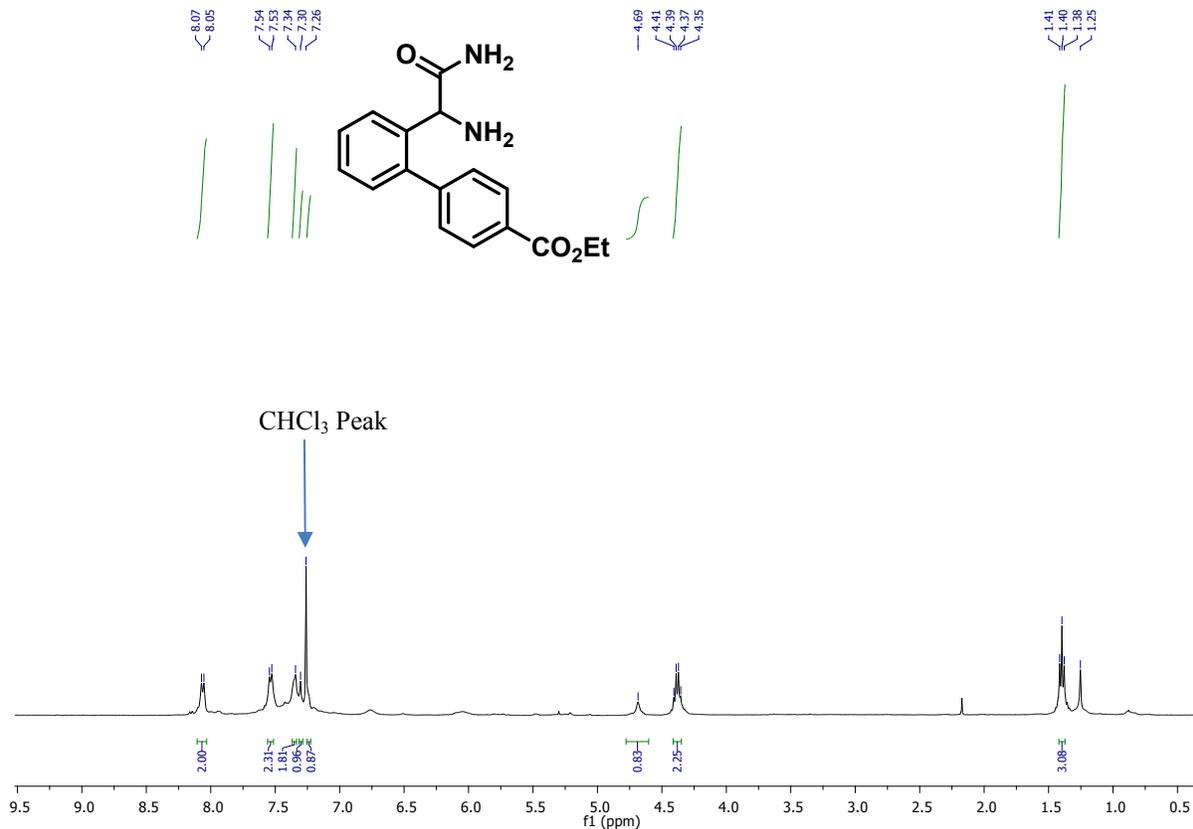


Figure S-213. ¹H NMR spectrum of **5d** (CDCl₃, 400 MHz, 298 K)

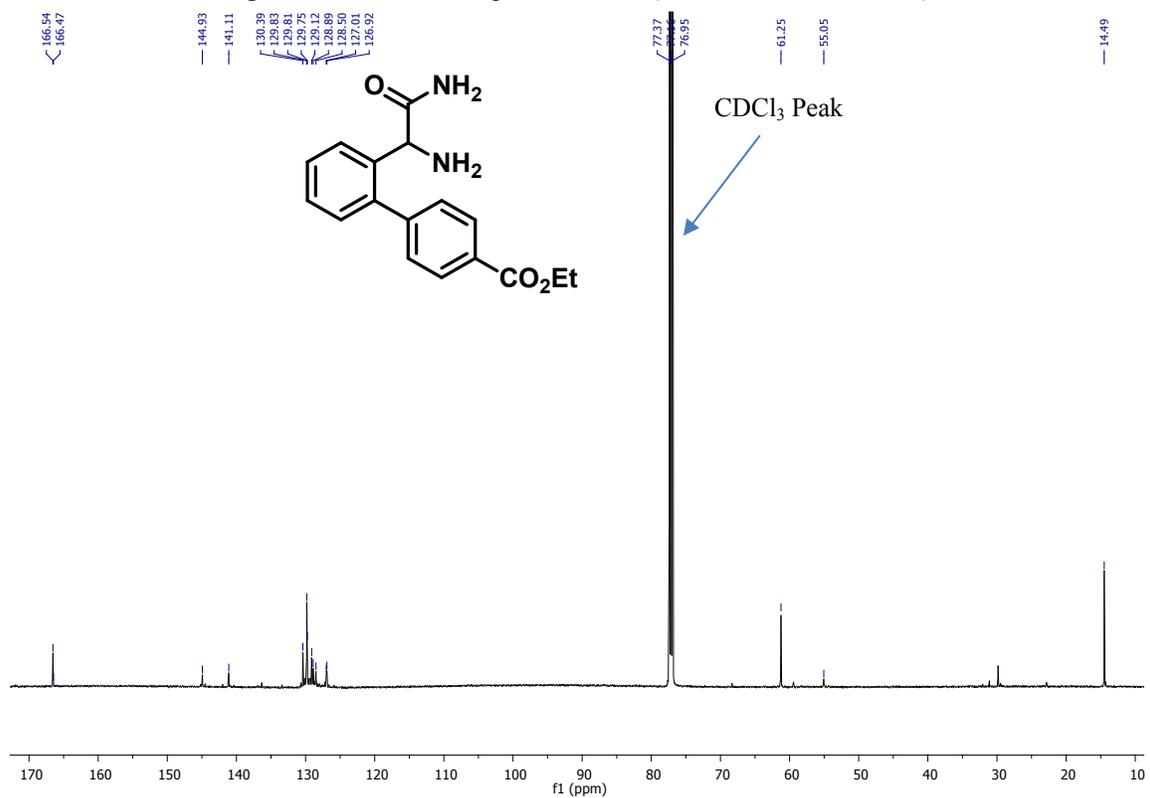


Figure S-214. ¹³C NMR spectrum of **5d** (CDCl₃, 151 MHz, 298 K)

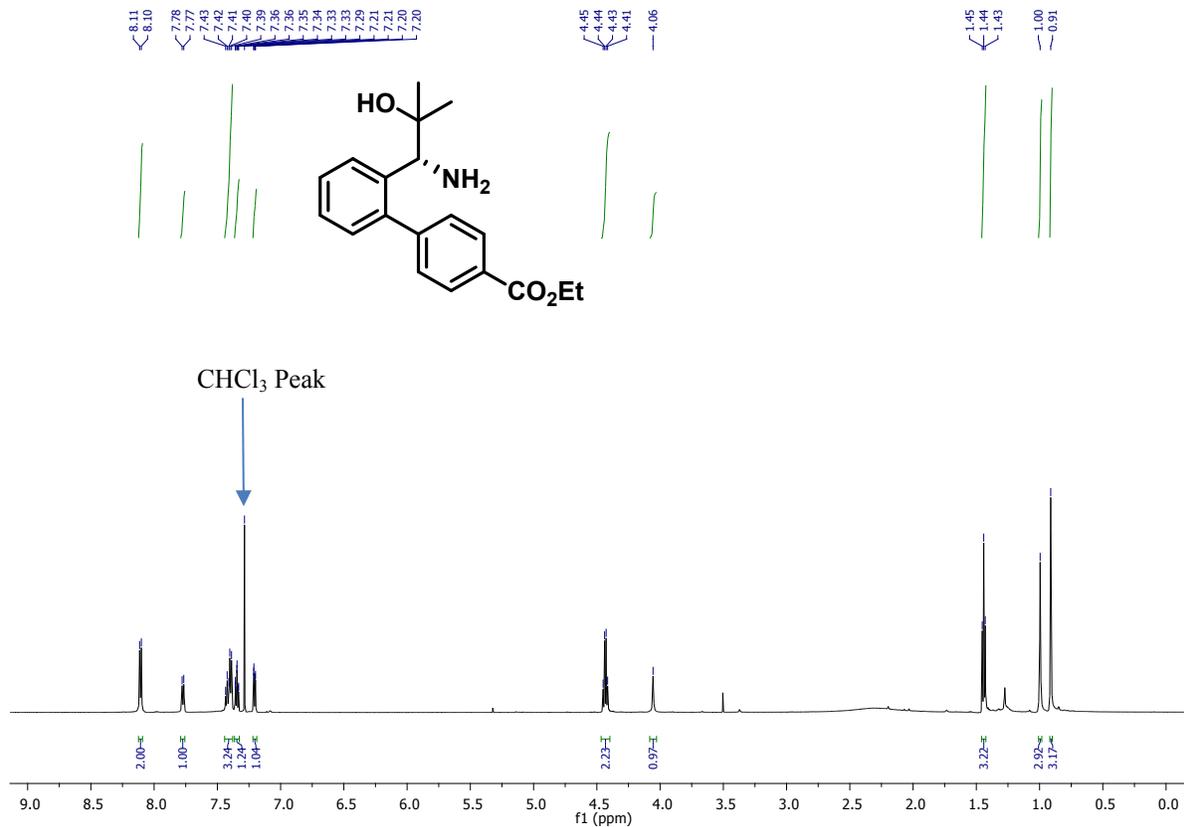


Figure S-215. ¹H NMR spectrum of **5e** (CDCl₃, 600 MHz, 298 K)

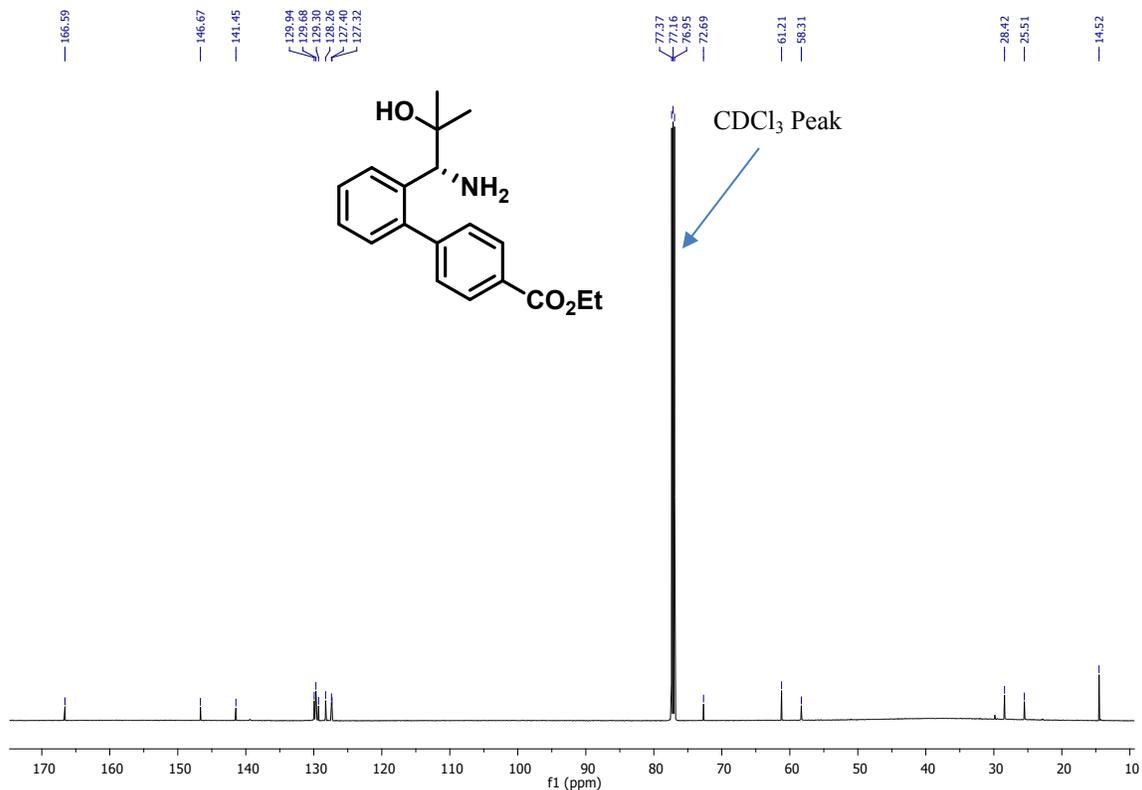


Figure S-216. ¹³C NMR spectrum of **5e** (CDCl₃, 151 MHz, 298 K)

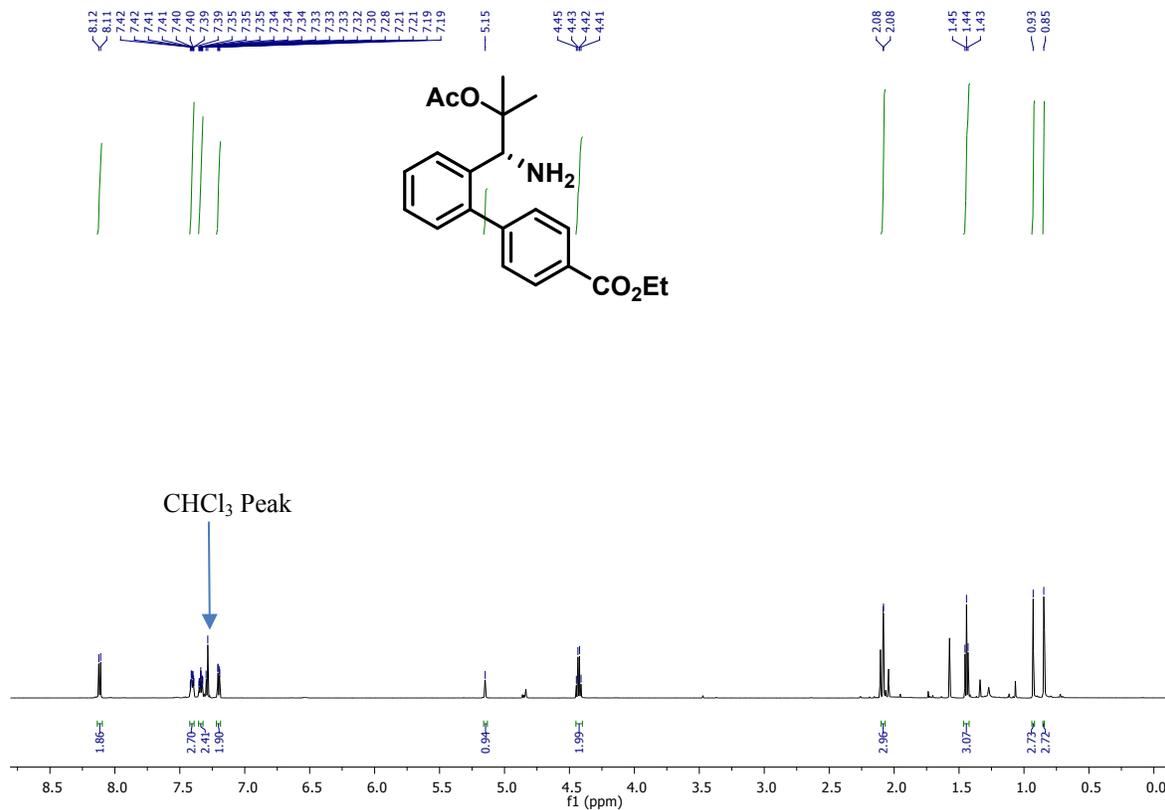


Figure S-217. ¹H NMR spectrum of **5f** (CDCl₃, 600 MHz, 298 K)

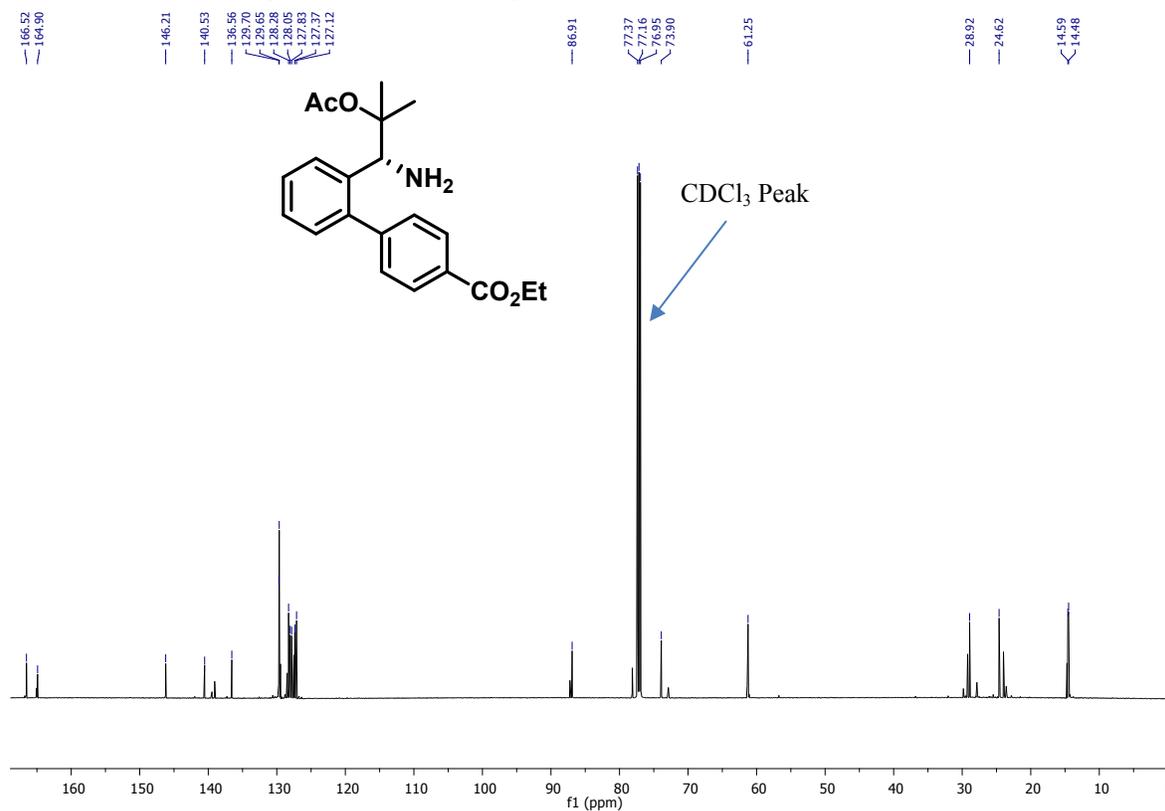


Figure S-218. ¹³C NMR spectrum of **5f** (CDCl₃, 151 MHz, 298 K)

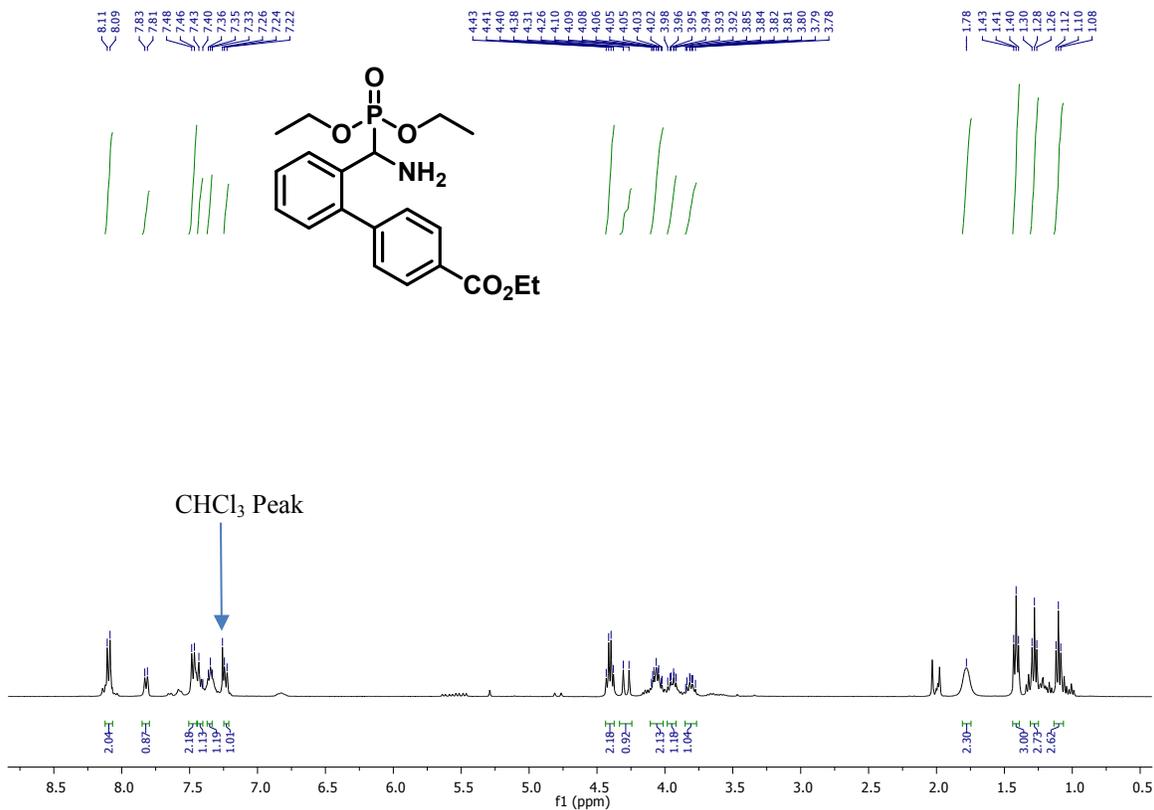


Figure S-219. ¹H NMR spectrum of **5g** (CDCl₃, 600 MHz, 298 K)

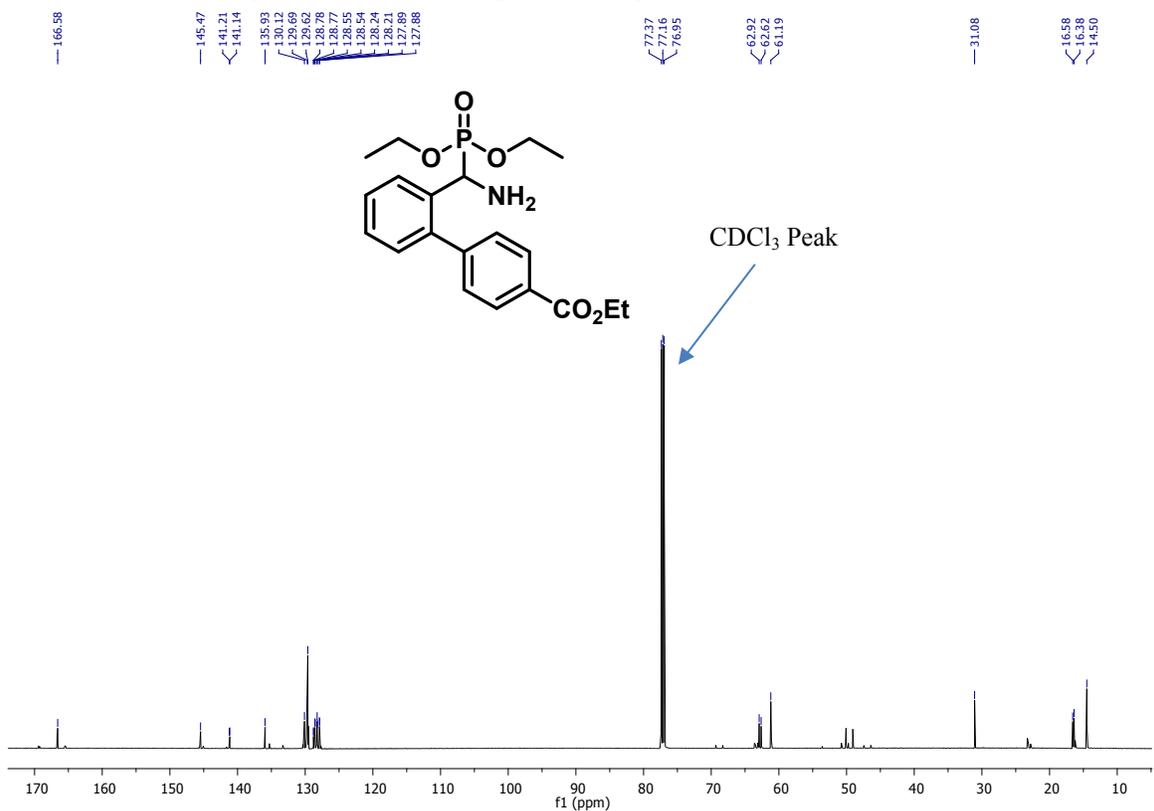


Figure S-220. ¹³C NMR spectrum of **5g** (CDCl₃, 151 MHz, 298 K)

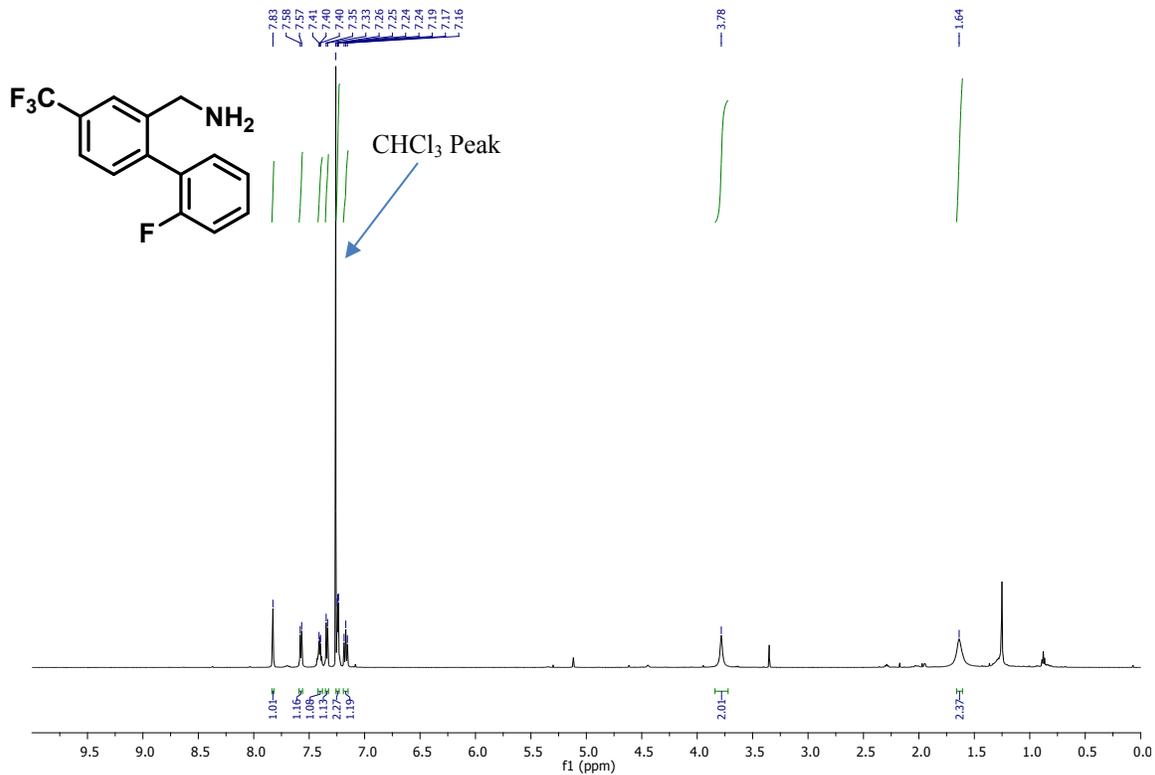


Figure S-221. ¹H NMR spectrum of S-46 (CDCl₃, 600 MHz, 298 K)

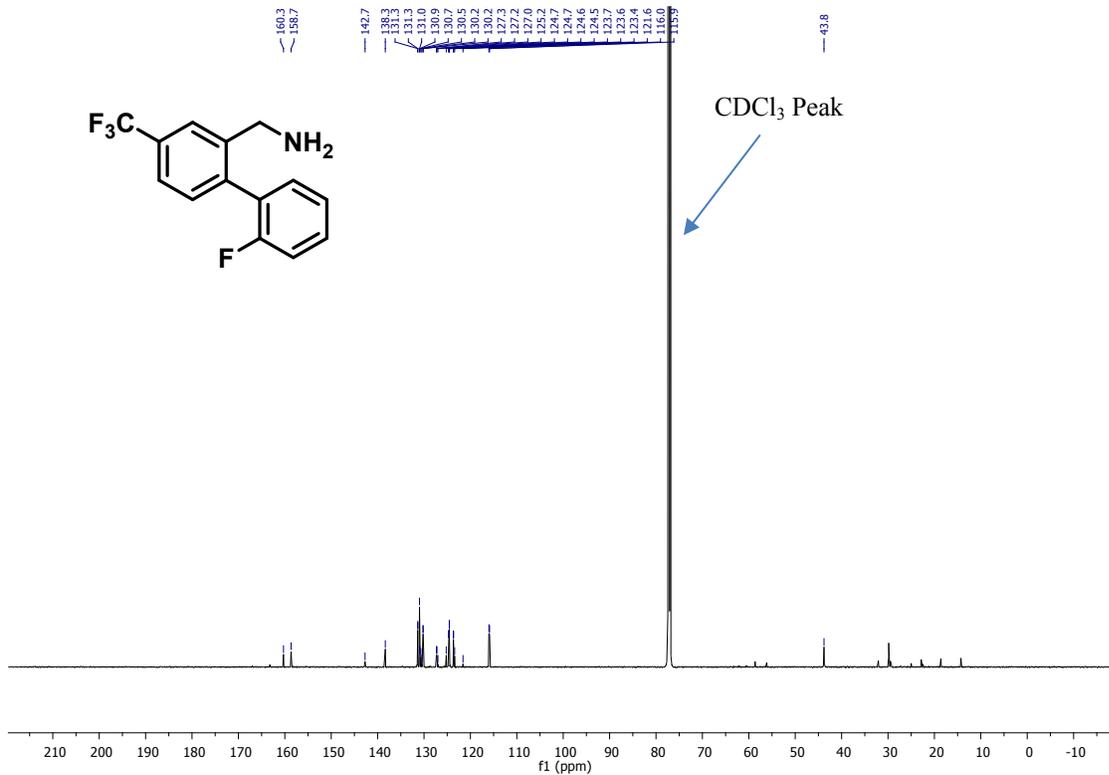


Figure S-222. ¹³C NMR spectrum of S-46 (CDCl₃, 151 MHz, 298 K)

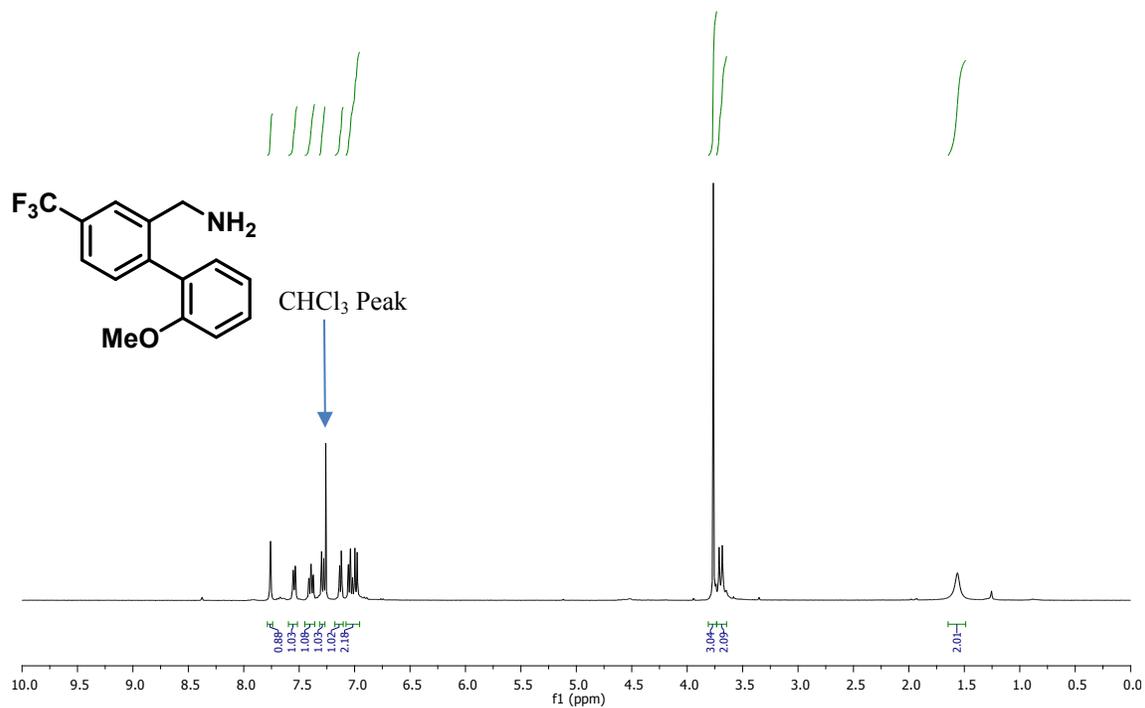


Figure S-223. $^1\text{H NMR}$ spectrum of S-47 (CDCl_3 , 600 MHz, 298 K)

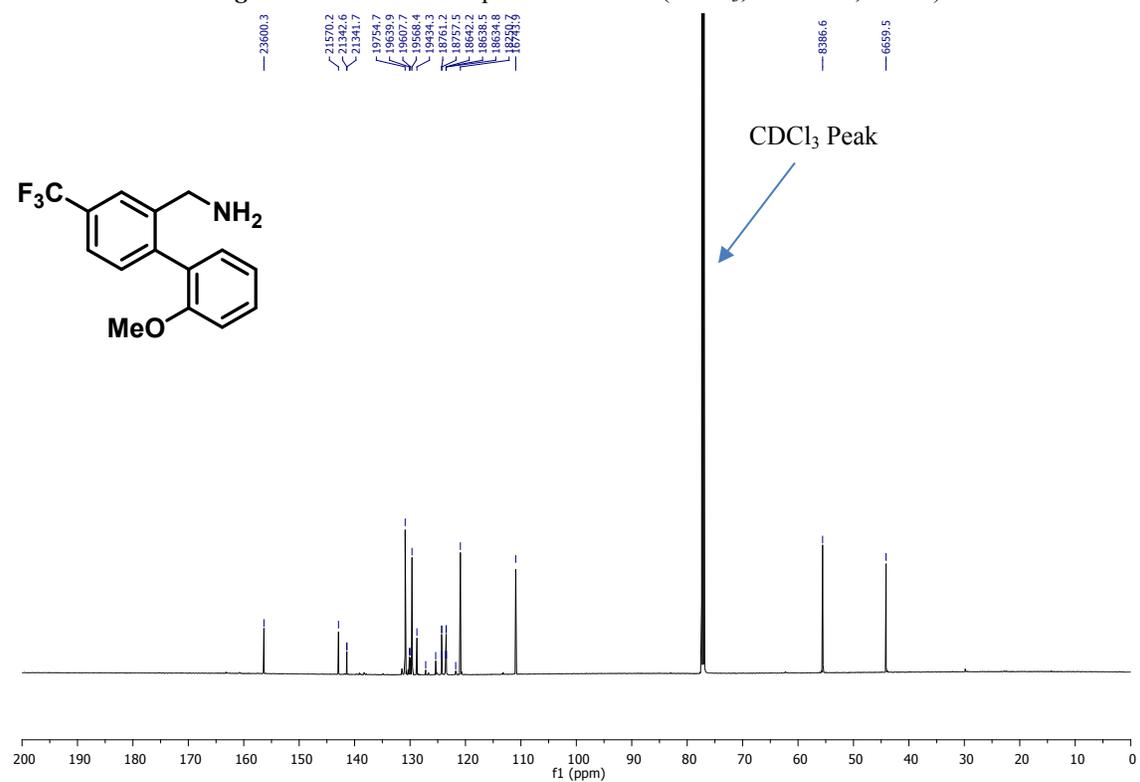


Figure S-224. $^{13}\text{C NMR}$ spectrum of S-47 (CDCl_3 , 151 MHz, 298 K)

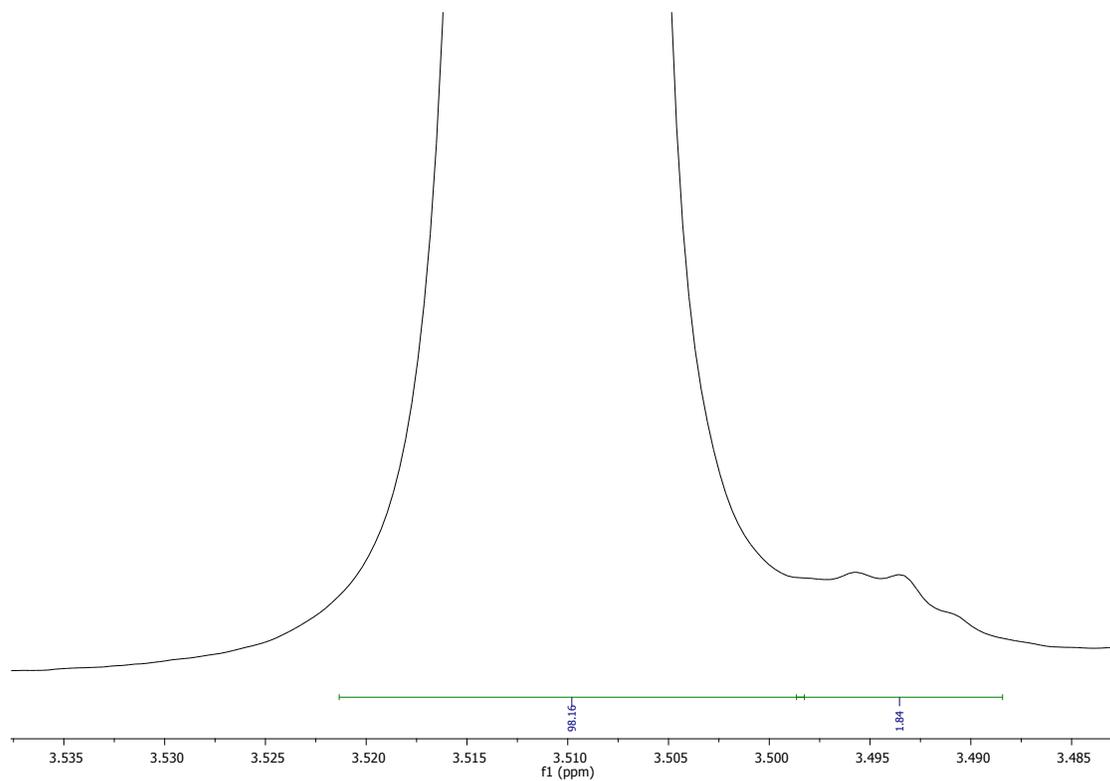


Figure S-225. ¹H NMR spectrum of *S*-24-Mosher Amide (Area of interest blown up) (CDCl₃, 600 MHz, 298 K)

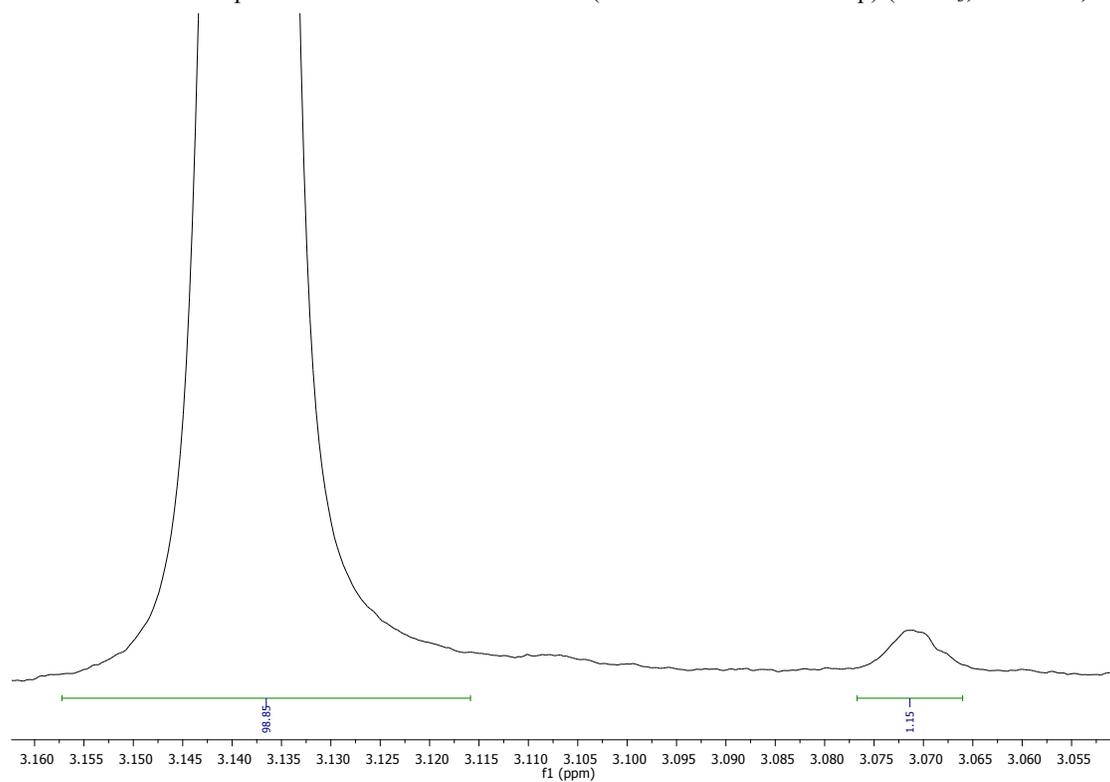


Figure S-226. ¹H NMR spectrum of 4b-Mosher Amide (Area of interest blown up) (CDCl₃, 600 MHz, 298 K)

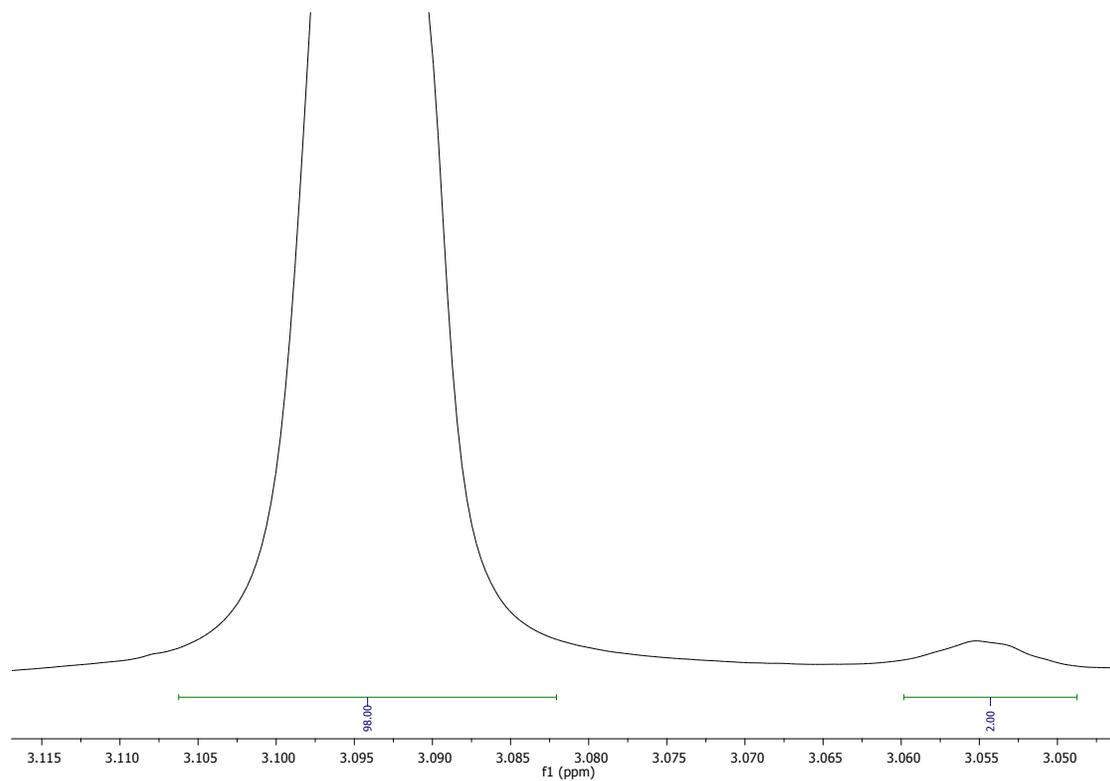


Figure S-227. ^1H NMR spectrum of **4f-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

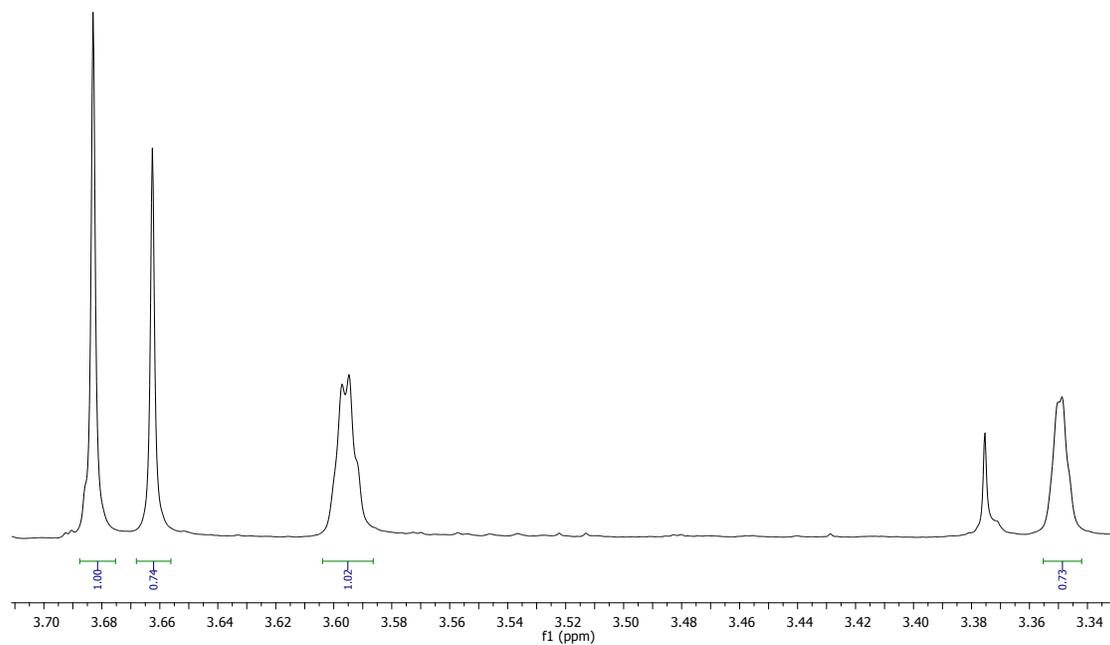


Figure S-228. ^1H NMR spectrum of **5a-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

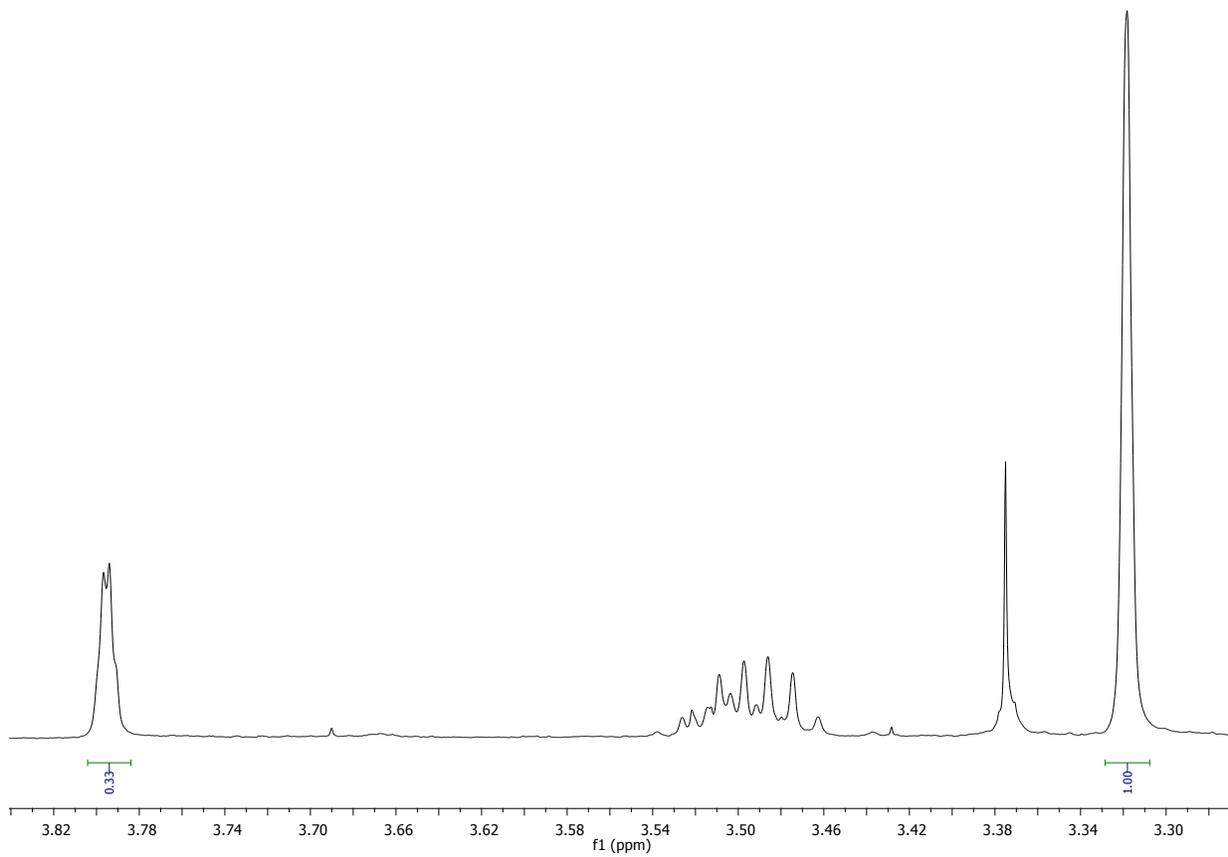


Figure S-229. ^1H NMR spectrum of **5b-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

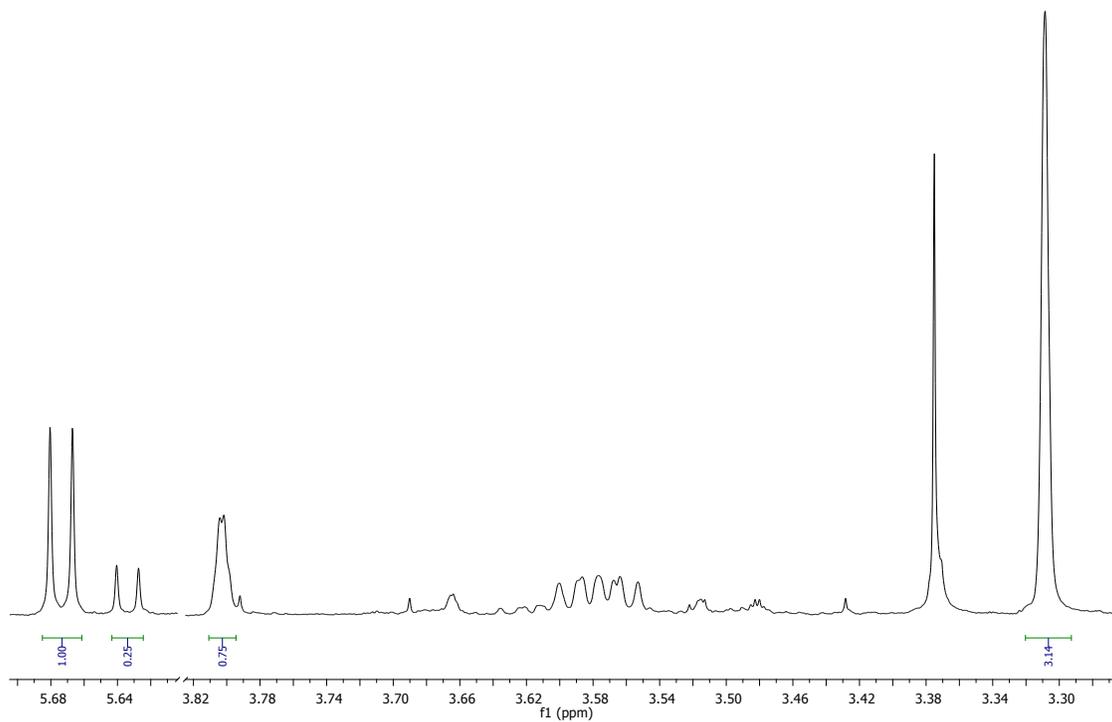


Figure S-230. ^1H NMR spectrum of **5c-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

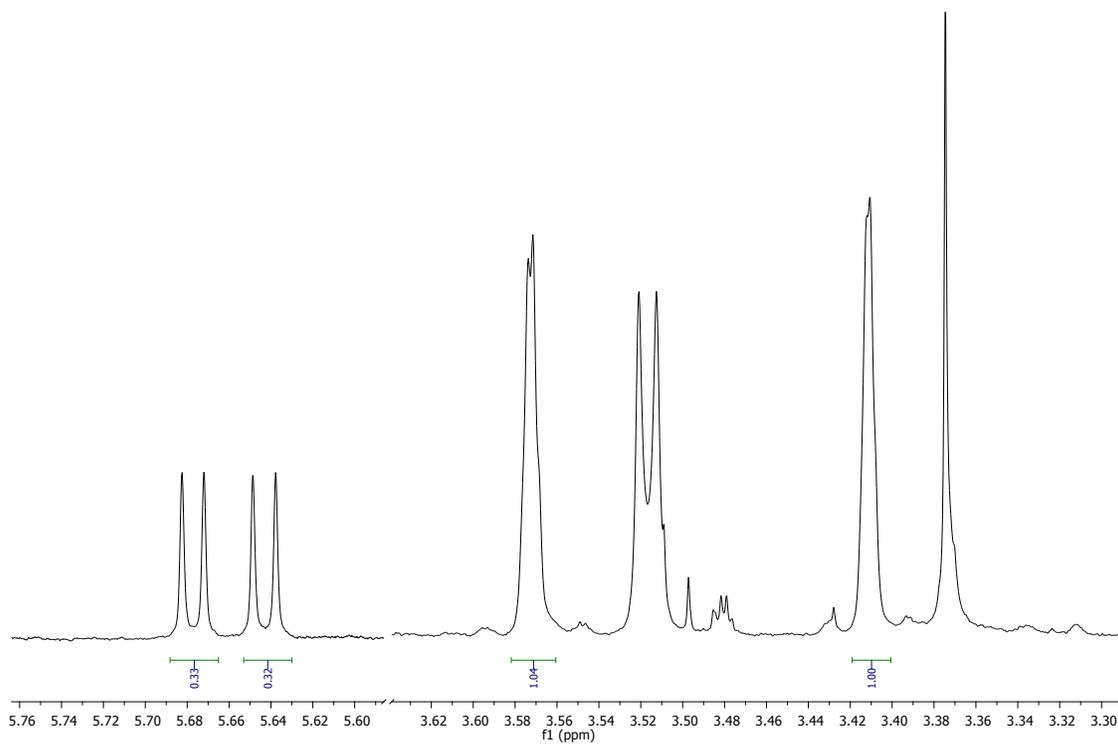


Figure S-231. ^1H NMR spectrum of **5d-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

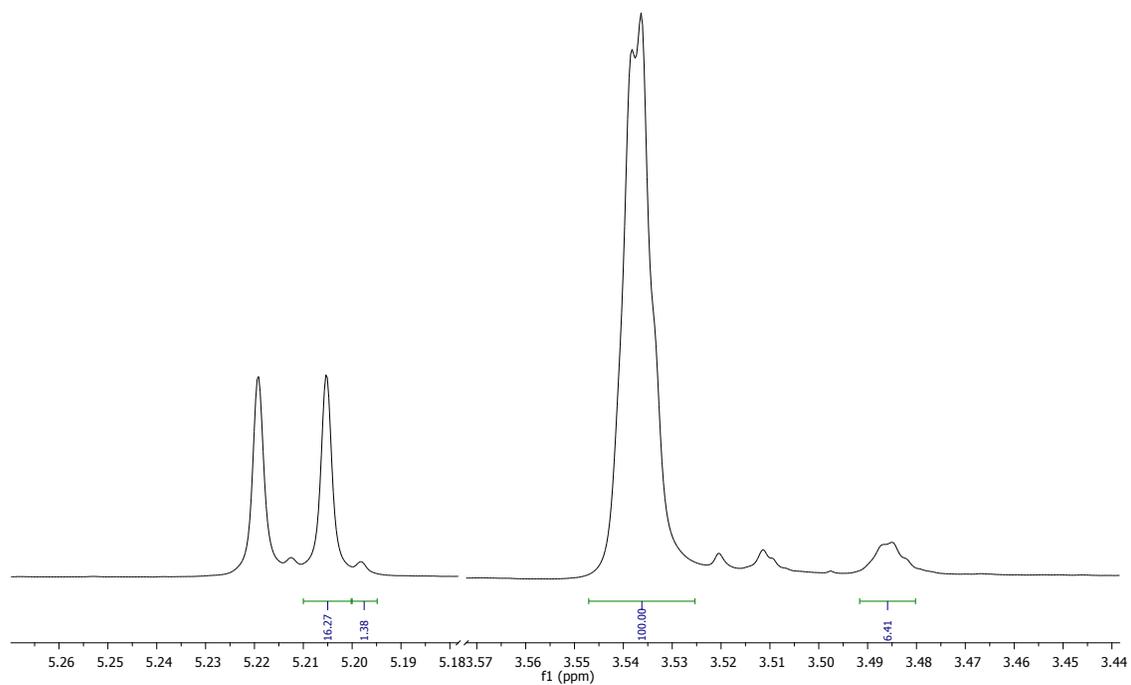


Figure S-232. ^1H NMR spectrum of **5e-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

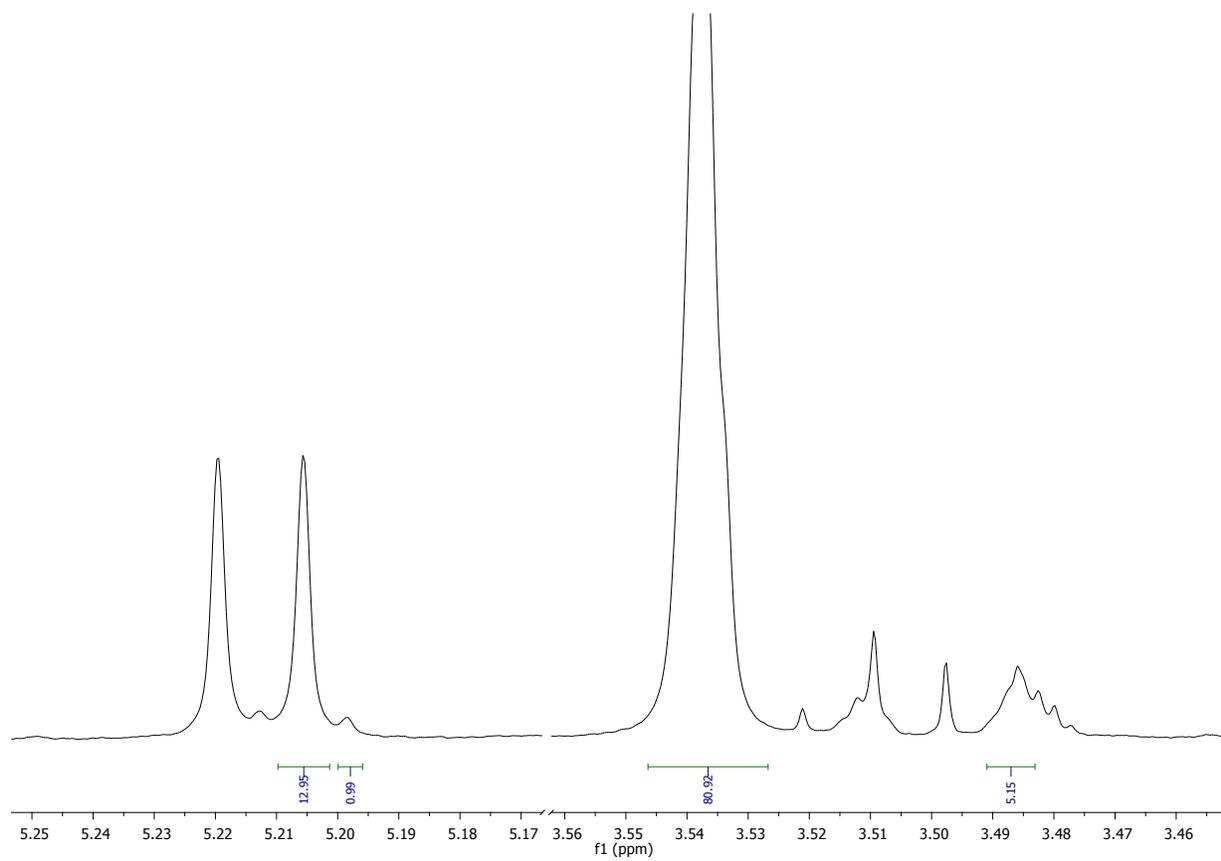


Figure S-233. ^1H NMR spectrum of **5f-Mosher Amide** (Area of interest blown up) (CDCl_3 , 600 MHz, 298 K)

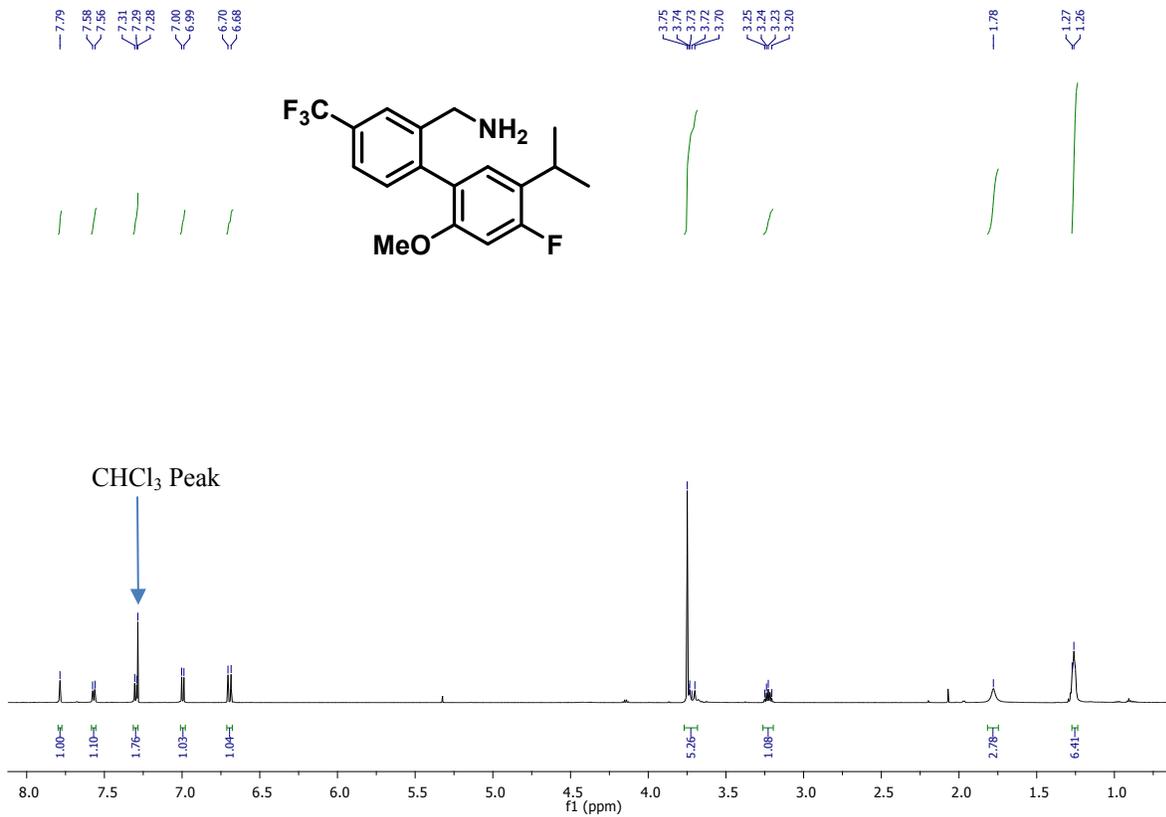


Figure S-234. ¹H NMR spectrum of **6** (CDCl₃, 600 MHz, 298 K)

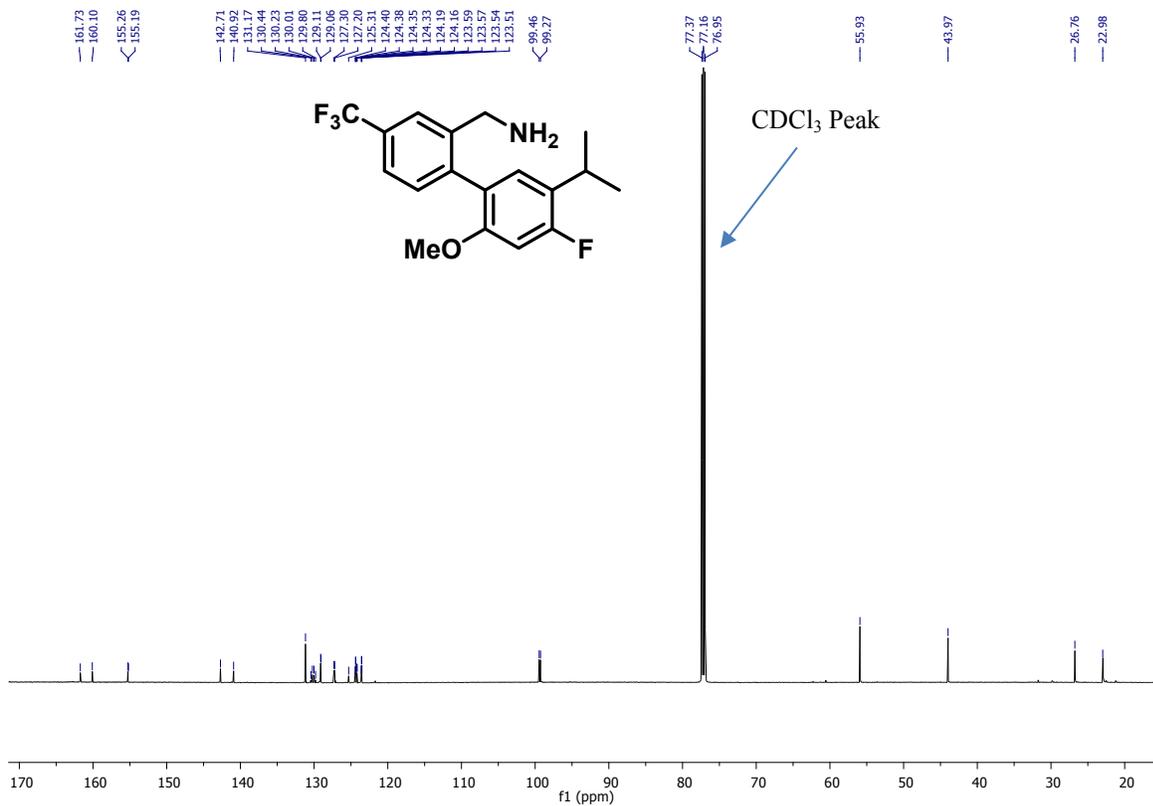


Figure S-235. ¹³C NMR spectrum of **6** (CDCl₃, 151 MHz, 298 K)

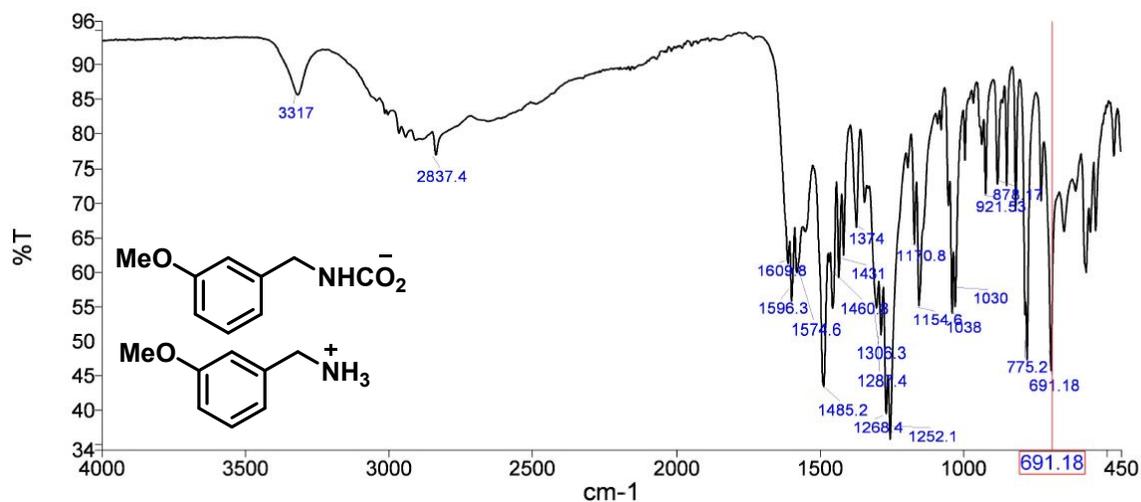


Figure S-236. IR spectrum of 7

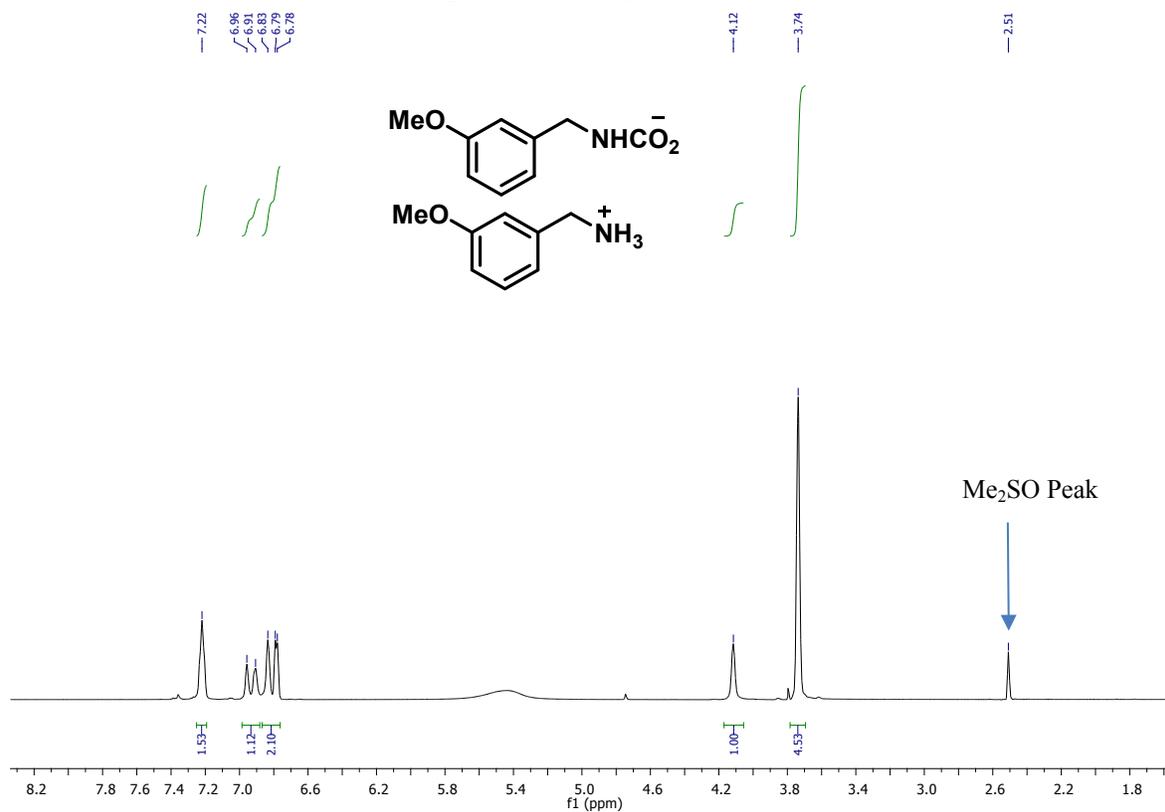


Figure S-237. ^1H NMR spectrum of 7 (DMSO- d_6 , 600 MHz, 298 K)

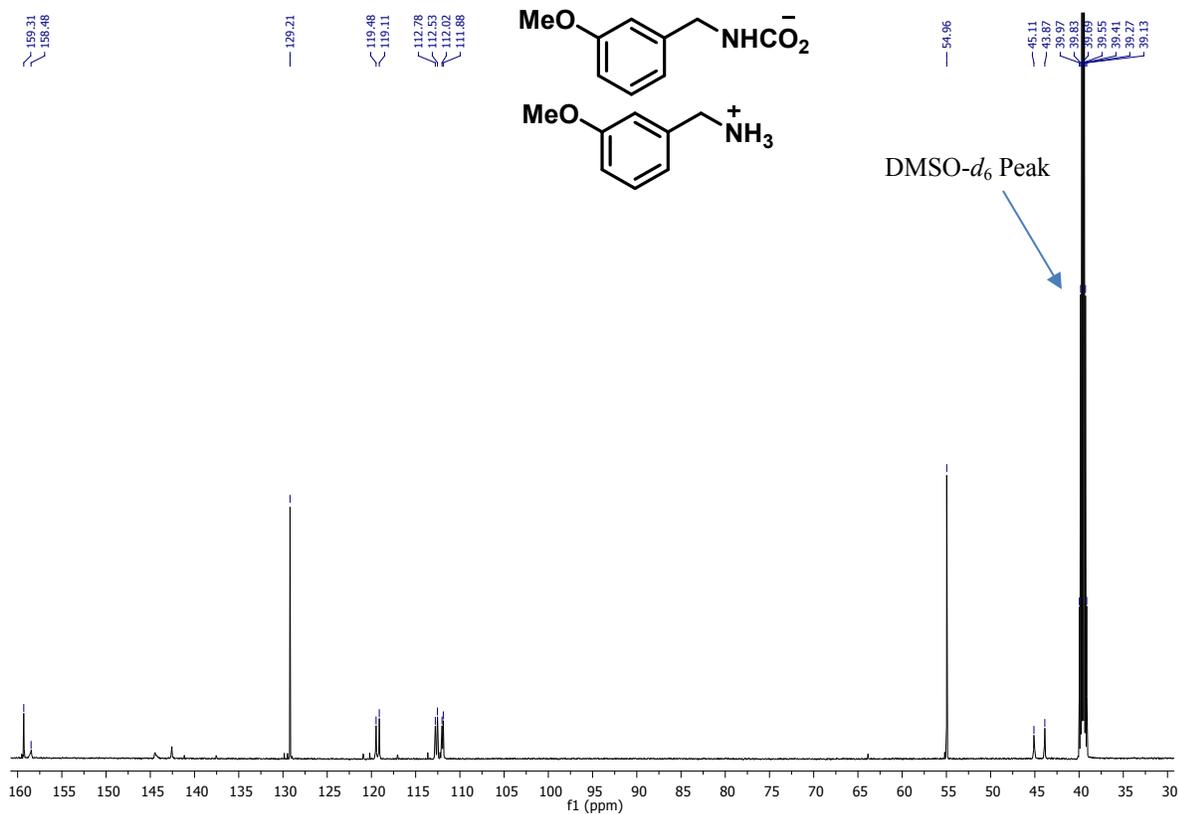


Figure S-238. ^{13}C NMR spectrum of **7** (DMSO- d_6 , 151 MHz, 298 K)

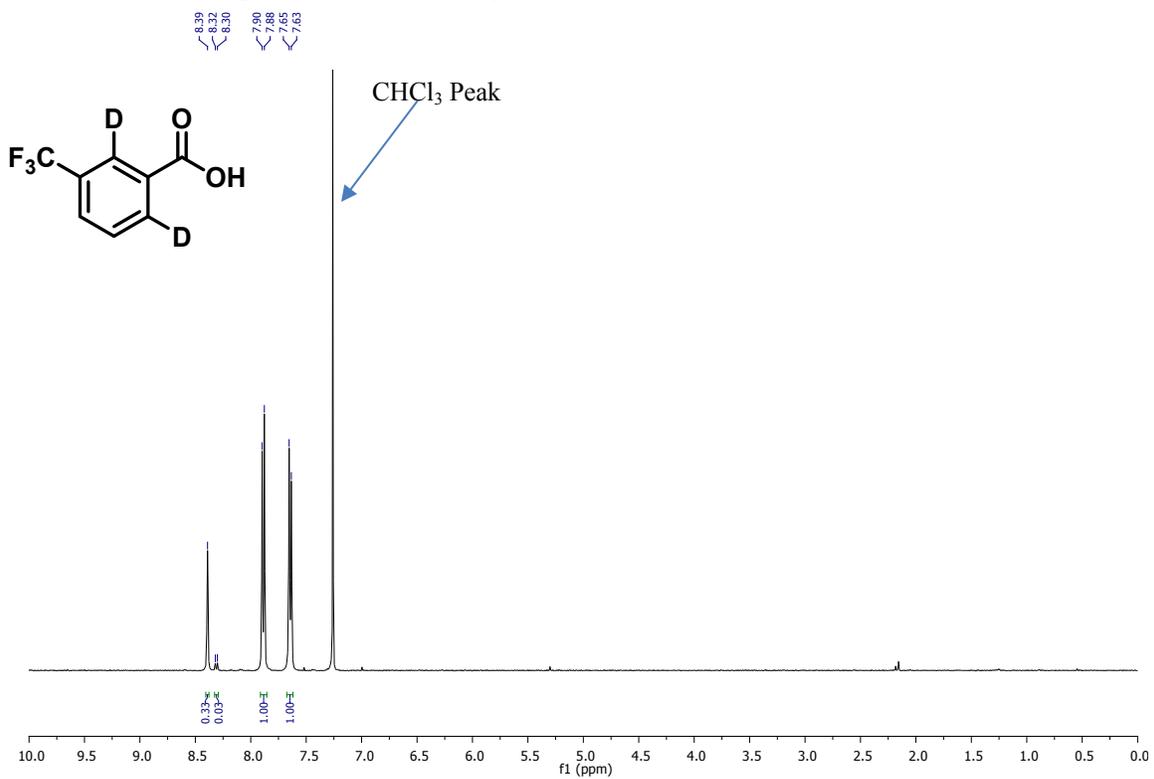


Figure S-239. ^{13}C NMR spectrum of **S-48** (CDCl₃, 400 MHz, 298 K)

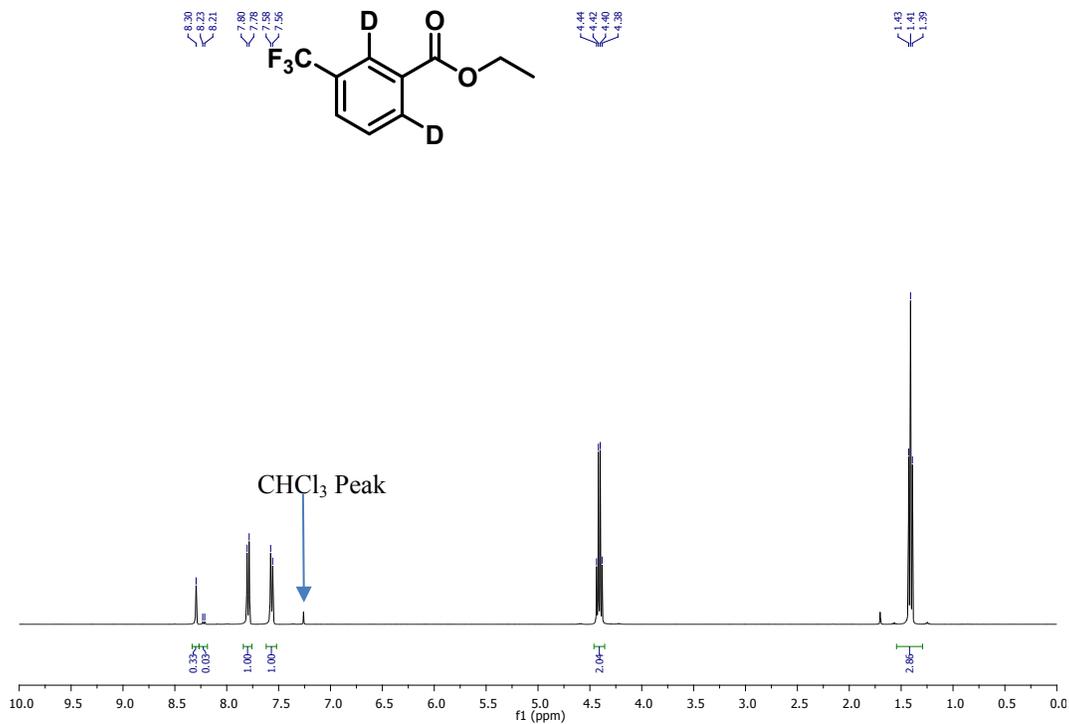


Figure S-240. ^1H NMR spectrum of **S-49** (CDCl₃, 400 MHz, 298 K)

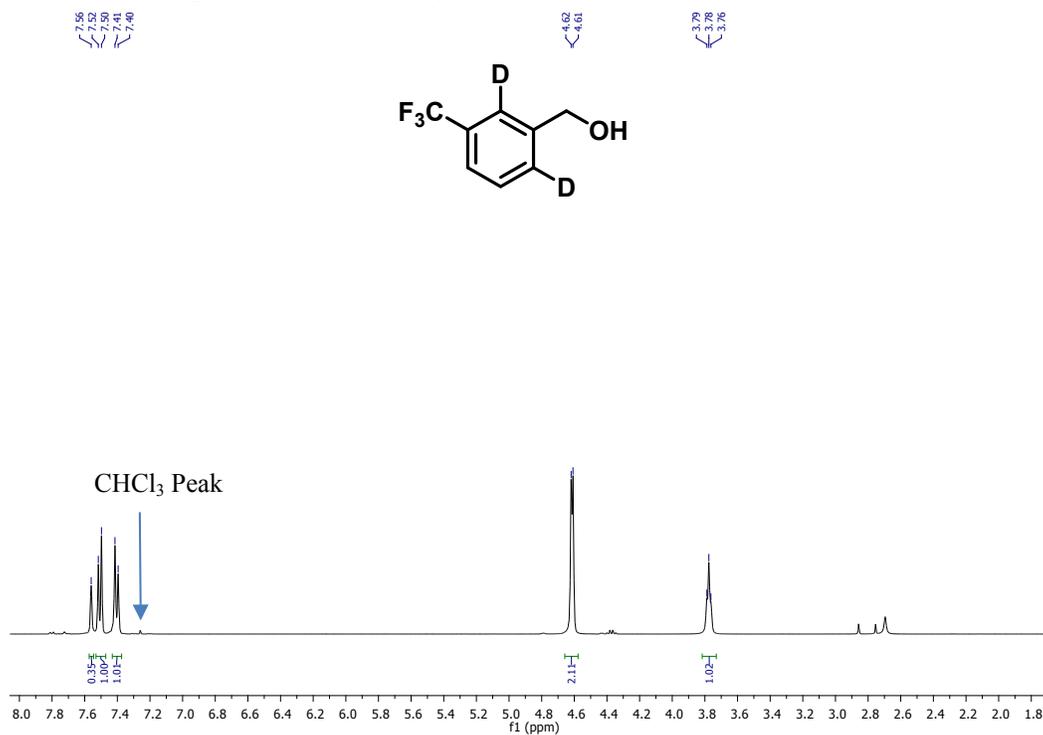


Figure S-241. ^1H NMR spectrum of **S-50** (CDCl₃, 400 MHz, 298 K)

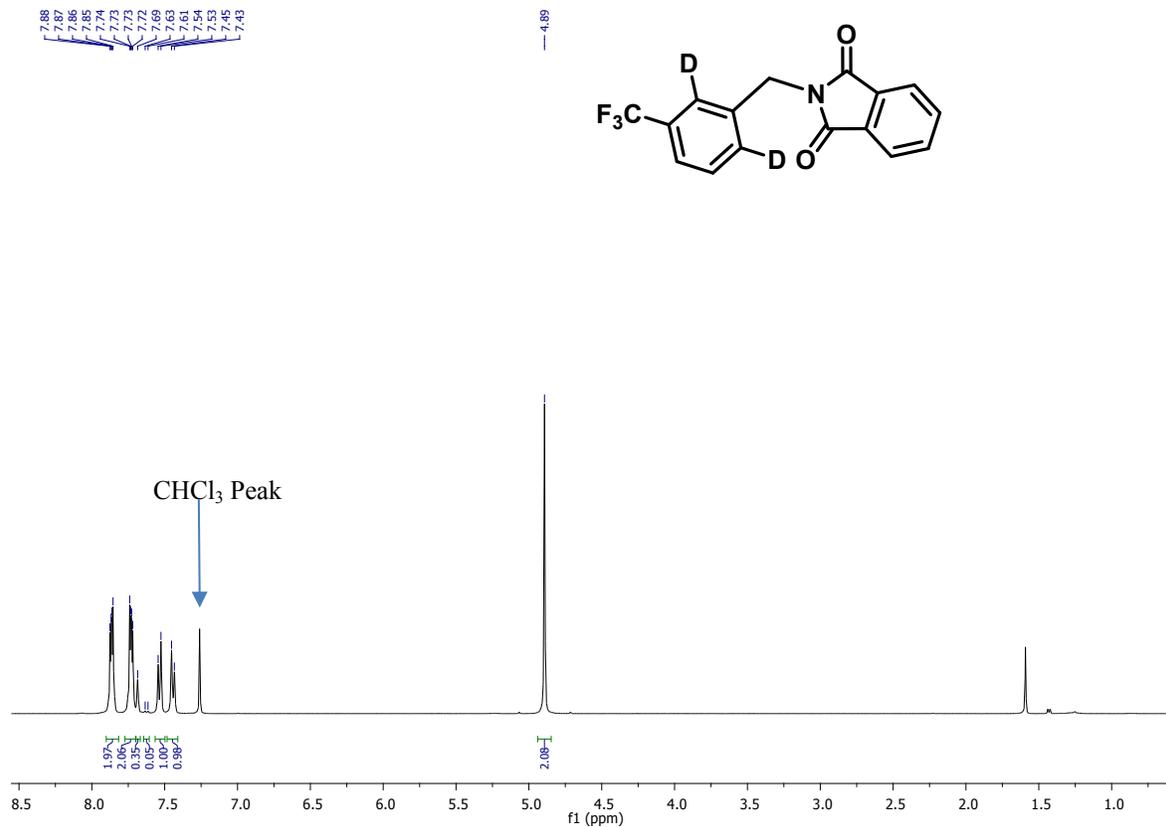


Figure S-242. ¹H NMR spectrum of S-51 (CDCl₃, 400 MHz, 298 K)

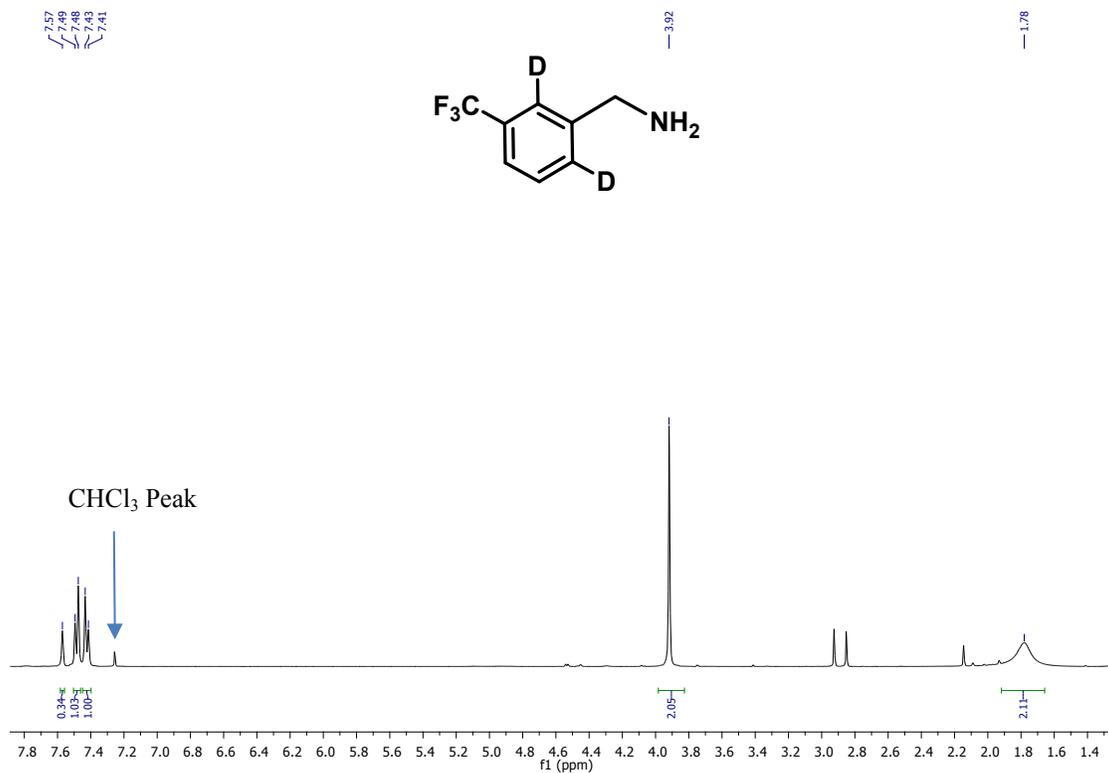


Figure S-243. ¹H NMR spectrum of 8 (CDCl₃, 400 MHz, 298 K)

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