Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

of

Nickel(0)-Catalyzed Linear-Selective Hydroarylation of 2-Aminostyrenes with Arylboronic Acids by a Bifunctional Temporary Directing Group Strategy

Qiang Wang, Zilong Yan and Dong Xing*

Shanghai Engineering Research Center of Molecular Therapeutics and New Drug Development, School of Chemistry and Molecular Engineering, East China Normal University, Shanghai 200062, China

E-mail: dxing@sat.ecnu.edu.cn

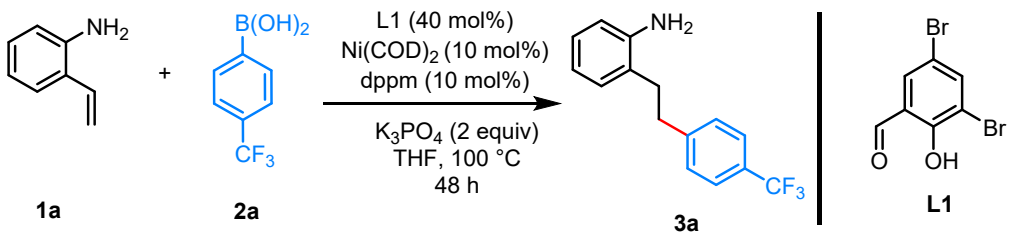
Table of Contents

1. General Information

Unless noted otherwise, all ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded on Brucker spectrometers in $CDCl_3$. Tetramethylsilane (TMS) served n internal standard ($\delta = 0$) for ^{1}H NMR, and $CDCl_3$ was used as internal standard ($\delta = 77.0$) for ^{13}C NMR. Chemical shifts are reported in parts per million as follows: chemical shift, multiplicity (s =singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad). Infrared (IR) spectra were obtained using a Bruker tensor 27 infrared spectrometer. High-resolution mass spectrometry (HRMS) was performed on IonSpec FT-ICR or Waters Micromass Q-TOF micro Synapt High-Definition Mass Spectrometer. Unless otherwise noted, solvents used for the key reactions were freshly distilled over calcium hydride or sodium. THF (Extra Dry, stabilized) used for the key reactions was purchased from Energy Chemical and degassed with nitrogen before use. All the key reactions were carried out under nitrogen atmosphere with a stir bar in a sealed vial and heated in a pie-block. Reaction temperatures were reported as the temperatures of the bather surrounding the vials. Sensitive ligands and metal catalysts and solvents were transferred under nitrogen into a nitrogen-filled glove box with standard techniques. $Ni(COD)_2$ and ligands were purchased from commercial source. Salicylaldehydes used for the key reactions was purified by vacuum distillation, column isolation (liquid aldehyde) or recrystallization (solid aldehyde). 2-vinylaniline were prepared by following literature procedures.[1] Aryl boric acid used for the key reactions were purified by recrystallization. All other materials were obtained from commercial sources and were used as received.

2. Experimental Procedures

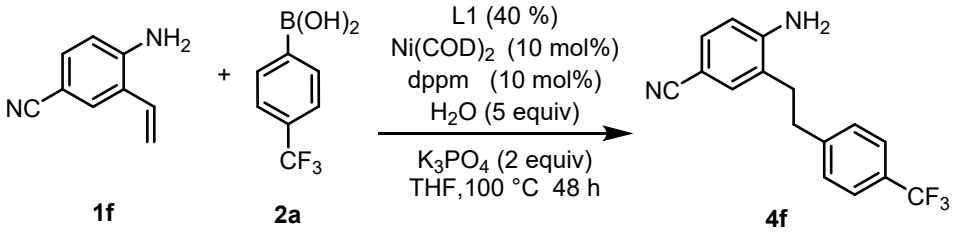
2.1 General procedure A (reaction between **1a** and **2a**):



1a **2a** **3a** **L1**

In glove box, a 4-mL vial charged with a stir bar was added $Ni(COD)_2$ (0.01 mmol, 2.75 mg) and dppm (0.01 mmol, 3.8 mg) in 0.3 mL of THF, the mixture was stirred for 5 minutes before **1a** (0.1 mmol, 11.9 mg), **L1** (0.04 mmol, 11.2 mg), **2a** (0.15 mmol, 27.5 mg), K_3PO_4 (0. 2 mmol, 42.5 mg) were subsequently added. The vial was tightly capped, removed from glove box and heated at 100 ℃ for 48 h. After completion, the reaction mixture was cooled to room temperature, subjected to flash column chromatography (eluent: PE/EA = 30:1) to get the pure product **3a**.

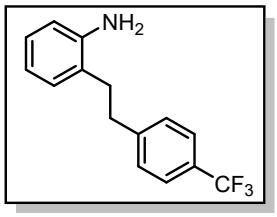
2.2 General procedure B (reaction between **1f** and **2a** with the addition of H_2O)**:**



1f **2a** **4f**

In glove box, a 4-mL vial charged with a stir bar was added $Ni(COD)_2$ (0.01 mmol, 2.75 mg) and dppm (0.01 mmol, 3.8 mg) in 0.3 mL of THF, the mixture was stirred for 5 minutes before **1f** (0.1 mmol, 14.4 mg), **L1** (0.04 mmol, 11.2 mg), **2a** (0.15 mmol, 27.5 mg) , K_3PO_4 (0.2 mmol, 42.5 mg), H_2O (0.5 mmol, 9.0 mg) were subsequently added. The vial was tightly capped, removed from glove box and heated at 100 ℃ for 48 h. After completion, the reaction mixture was cooled to room temperature, subjected to flash column chromatography (eluent: PE/EA = 10:1) to get the pure product **4f**.

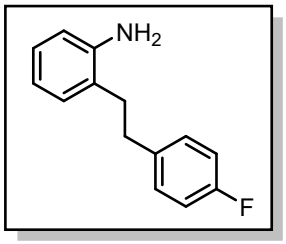
3. Characterization Data of the Products



2-(4-(trifluoromethyl)phenethyl)aniline (3a):

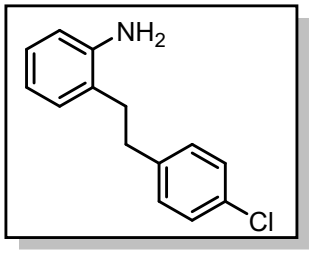
Synthesized from **1a** and **2a** by following general procedure A. 91% isolated yield (average value based on two parallel experiments on 0.1 mmol scale); or 83% isolated

yield on a 0.5 mmol scale. Yellow solid. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.7 Hz, 2H), 7.29 (d, *J* = 7.7 Hz, 2H), 7.06 (t, *J* = 7.6 Hz, 1H), 7.00 (d, *J* = 7.4 Hz, 1H), 6.72 (dd, *J* = 19.5, 7.6 Hz, 2H), 3.57 (s, 2H), 3.00 (t, *J* = 7.9 Hz, 2H), 2.80 (t, *J* = 7.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.90, 144.04, 129.44, 128.78, 127.42, 125.35 (q, *J* = 3.8 Hz), 119.03, 115.86, 34.89, 32.98. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.28. **IR (ν/cm^{-1}):** 1325, 1265, 1164, 1123, 1067, 735, 704, 594, 584, 573. **HRMS-ESI (m/z):** calcd. $C_{15}H_{15}NF_3$ $[M+H]^+$: 266.1157. Found: 266.1135.



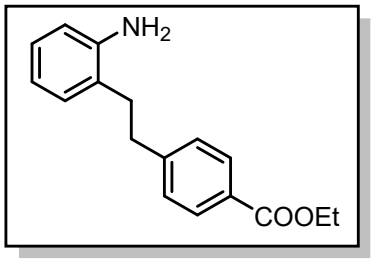
2-(4-fluorophenethyl)aniline(3b):

Synthesized from **1a** and (4-fluorophenyl) boronic acid by following general procedure A. 90% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (t, *J* = 6.3 Hz, 2H), 7.08 – 6.89 (m, 4H), 6.73 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.30 (d, *J* = 191.0 Hz, 2H), 2.91 (t, *J* = 7.8 Hz, 2H), 2.76 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.10, 129.80 (d, *J* = 7.8 Hz), 128.38 (d, *J* = 226.4 Hz), 125.70, 118.96, 115.78, 115.16 (d, *J* = 21.0 Hz), 34.39, 33.45. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -117.39. **IR (ν/cm^{-1}):** 1621, 1508, 1265, 1220, 1157, 823, 734,703, 614, 606. **HRMS-ESI (m/z):** calcd. $C_{14}H_{15}NF$ $[M+H]^+$: 216.1189. Found: 216.1205.



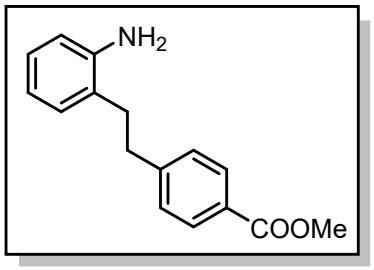
2-(4-chlorophenethyl)aniline(3c)：

Synthesized from **1a** and (4-chlorophenyl) boronic acid by following general procedure A. 87% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (s, 2H), 7.11 (d, *J* = 7.6 Hz, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.4 Hz, 1H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.53 (s, 2H), 2.90 (t, *J* = 7.8 Hz, 2H), 2.76 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.10, 140.22, 131.79, 129.81, 129.49, 128.51, 127.29, 125.53, 118.95, 115.78, 34.51, 33.20. **IR (ν/cm^{-1}):** 2034, 1964, 1497, 661, 637, 625, 615, 583. **HRMS-ESI (m/z):** calcd. $C_{14}H_{15}NCl$ $[M+H]^+$: 232.0893. Found: 232.0878.



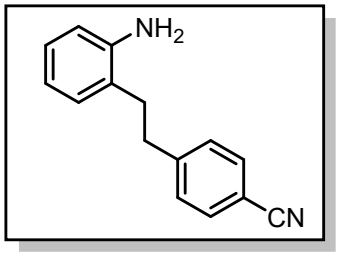
ethyl 4-(2-aminophenethyl)benzoate(3d):

Synthesized from **1a** and (4-(ethoxycarbonyl) phenyl)boronic acid by following general procedure A. 82% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f= 0.3 (PE: EA = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 7.6 Hz, 2H), 7.24 (s, 2H), 7.05 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 7.3 Hz, 1H), 6.77 – 6.61 (m, 2H), 4.37 (q, *J* = 6.8 Hz, 2H), 3.53 (s, 2H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.80 (t, *J* = 7.8 Hz, 2H), 1.39 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.65, 147.16, 144.10, 129.75, 129.49, 128.46, 128.41, 127.33, 125.42, 118.96, 115.80, 60.85, 35.20, 32.96, 14.36. **IR (ν/cm^{-1}):** 1985, 1264, 733, 704, 661, 636, 618, 606, 595. **HRMS-ESI (m/z):** calcd. $C_{17}H_{20}NO_2$ $[M+H]^+$: 270.1494. Found: 270.1492.



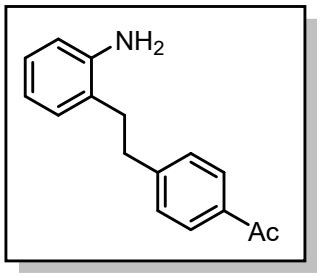
methyl 4-(2-aminophenethyl)benzoate(3e):

Synthesized from **1a** and (4-(methoxycarbonyl) phenyl)boronic acid by following general procedure A . 66% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). White oil. R_f = 0.3 (PE: EA = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 8.3 Hz, 2H), 7.27 – 7.22 (m, 2H), 7.05 (td, *J* = 7.7, 1.4 Hz, 1H), 7.02 – 6.96 (m, 1H), 6.72 (td, *J* = 7.4, 1.1 Hz, 1H), 6.70 – 6.64 (m, 1H), 3.90 (s, 3H), 3.53 (s, 2H), 2.98 (dd, *J* = 9.1, 6.8 Hz, 2H), 2.80 (dd, *J* = 9.1, 6.7 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 167.15, 147.31, 144.13, 129.80, 129.49, 128.54, 128.05, 127.36, 125.40, 118.96, 115.81, 52.05, 35.20, 32.95. **IR (v/cm^{-1}):** 1717, 1611, 1497, 1435, 1281, 1266, 1179, 1112, 736, 703. HRMS-ESI (m/z): calcd. $C_{16}H_{18}NO_2$ $[M+H]^+$: 256.1338. Found: 256.1334.



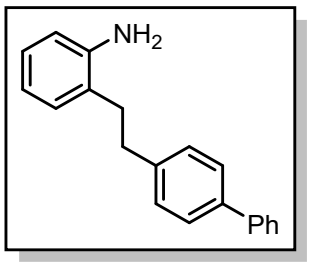
4-(2-aminophenethyl)benzonitrile(3f):

Synthesized from **1a** and (4-cyanophenyl)boronic acid by following general procedure A. 77% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). White solid. R_f = 0.3 (PE: EA = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.6 Hz, 2H), 7.27 (s, 2H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 7.5 Hz, 1H), 6.75 – 6.65 (m, 2H), 3.55 (s, 2H), 3.00 (t, *J* = 7.8 Hz, 2H), 2.79 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.36, 144.04, 132.23, 129.47, 129.31, 127.52, 124.83, 119.05, 119.00, 115.88, 109.97, 35.08, 32.73. **IR (v/cm^{-1}):** 3756, 3648, 2181, 1961, 1264, 734, 704, 635, 574. **HRMS-ESI (m/z):** calcd. $C_{15}H_{15}N_2$ $[M+H]^+$: 223.1235. Found: 223.1254.



1-(4-(2-aminophenethyl)phenyl)ethan-1-one(3g):

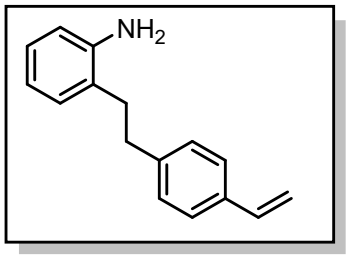
Synthesized from **1a** and (4-acetylphenyl)boronic acid by following general procedure B. 32% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f= 0.3 (PE: EA = 6:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.2 Hz, 2H), 7.06 (t, *J* = 7.4 Hz, 1H), 7.00 (d, *J* = 7.1 Hz, 1H), 6.76 – 6.67 (m, 2H), 3.55 (s, 2H), 3.04 – 2.96 (m, 2H), 2.85 – 2.77 (m, 2H), 2.59 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 197.99, 147.62, 135.24, 130.94, 128.72, 128.64, 115.32, 35.21, 32.80, 26.62, 26.36. **IR (ν/cm^{-1}):** 3649, 2034, 1606, 1678, 1264, 733, 704, 589, 572, 555. **HRMS-ESI (m/z):** calcd. $C_{16}H_{18}NO$ $[M+H]^+$: 240.1388. Found: 240.1366.



2-(2-([1,1'-biphenyl]-4-yl)ethyl)aniline(3h):

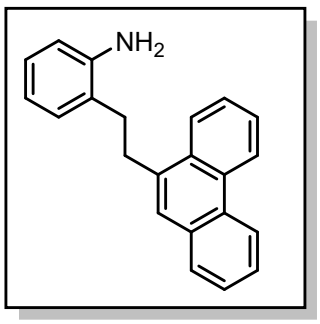
Synthesized from **1a** and [1,1'-biphenyl]-4-ylboronic acid by following general procedure A. 78% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). White solid. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 7.3 Hz, 2H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.43 (t, *J* = 7.4 Hz, 2H), 7.33 (t, *J* = 7.3 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 2H), 7.11 – 7.02 (m, 2H), 6.76 (t, *J* = 7.3 Hz, 1H), 6.69 (d, *J* = 7.8 Hz, 1H), 3.02 – 2.91 (m, 2H), 2.87 – 2.78 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.17, 141.00, 139.03, 129.44, 128.86, 128.76, 127.22, 127.19, 127.11, 127.01, 126.00, 118.97, 115.76, 34.90, 33.34. **IR (ν/cm^{-1}):** 3742, 3648, 1961, 1265,

736, 701, 607, 584, 569. **HRMS-ESI (m/z):** calcd. $C_{20}H_{20}N$ $[M+H]^+$: 274.1596. Found: 274.1605



2-(4-vinylphenethyl)aniline(3i):

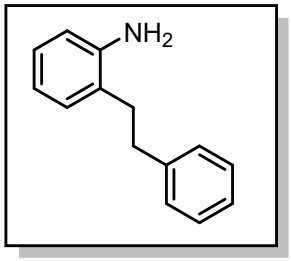
Synthesized from **1a** and (4-vinylphenyl)boronic acid by following general procedure A. 63% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). White solid. R_f= 0.3 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 7.4 Hz, 2H), 7.16 (d, *J* = 7.7 Hz, 2H), 7.04 (d, *J* = 6.7 Hz, 2H), 6.71 (dt, *J* = 21.8, 8.4 Hz, 3H), 5.72 (d, *J* = 17.7 Hz, 1H), 5.21 (d, *J* = 11.0 Hz, 1H), 3.49 (s, 2H), 2.98 – 2.88 (m, 2H), 2.83 – 2.73 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.58, 136.62, 129.45, 128.61, 127.18, 126.32, 118.92, 115.72, 113.15, 77.22, 35.01, 33.28. **IR (ν/cm^{-1}):** 3756, 3742, 3648, 2046, 1961, 1265, 738, 704, 617, 580, 571. **HRMS-ESI (m/z):** calcd. $C_{16}H_{18}N$ $[M+H]^+$: 224.1439. Found: 224.1431.



2-(2-(phenanthren-9-yl)ethyl)aniline(3j):

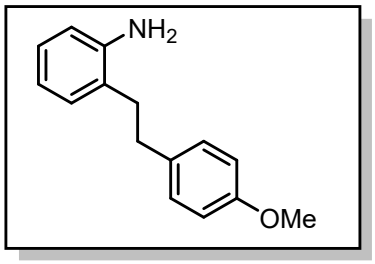
Synthesized from **1a** and phenanthren-9-ylboronic acid by following general procedure A. 77% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow Solid. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (d, *J* = 7.5 Hz, 1H), 8.67 (d, *J* = 7.9 Hz, 1H), 8.18 (d, *J* = 7.3 Hz, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.63 (dt, *J* = 29.9, 8.4 Hz, 5H), 7.18 (d, *J* = 7.3 Hz, 1H), 7.08 (t, *J* = 7.6 Hz, 1H),

6.79 (t, J = 7.4 Hz, 1H), 6.71 (d, J = 7.5 Hz, 1H), 3.59 (s, 2H), 3.50 – 3.37 (m, 2H), 3.04 – 2.94 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.23, 136.00, 131.87, 129.72, 129.32, 128.11, 127.28, 126.71, 126.68, 126.29, 126.23, 126.19, 126.11, 124.21, 123.35, 122.47, 119.01, 115.76, 32.61, 31.97. **IR (ν/cm^{-1}):** 3735, 3721, 2178, 2034, 1960, 1265, 739, 615, 593, 580, 575, 556. **HRMS-ESI (m/z):** calcd. $C_{22}H_{20}N$ $[M+H]^+$: 298.1596. Found: 298.1564.



2-phenethylaniline(3k):

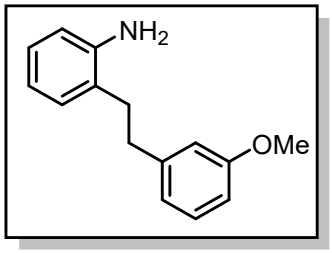
Synthesized from **1a** and phenylboronic acid by following general procedure A . 90% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). White solid. R_f = 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 – 7.27 (m, 2H), 7.25 – 7.17 (m, 3H), 7.05 (t, J = 7.0 Hz, 2H), 6.78 – 6.71 (m, 1H), 6.68 (dd, J = 8.3, 1.1 Hz, 1H), 3.52 (s, 2H), 2.94 (dd, J = 9.7, 6.3 Hz, 2H), 2.79 (dd, J = 9.7, 6.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.88, 129.42, 128.47, 128.44, 127.16, 126.07, 118.92, 115.72, 35.31, 33.39. **IR (ν/cm^{-1}):**3755, 3742, 1265, 737, 702, 636, 616, 607, 592, 572. **HRMS-ESI (m/z):** calcd. $C_{14}H_{16}N$ $[M+H]^+$: 198.1283. Found: 198.1299.



2-(4-methoxyphenethyl)aniline(3l):

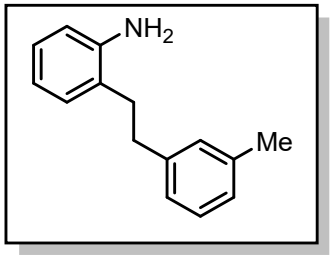
Synthesized from **1a** and (4-methoxyphenyl) boronic acid by following general procedure A. 65% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Brown solid. R_f = 0.2 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$)

δ 7.11 (d, *J* = 7.4 Hz, 2H), 7.08 – 7.00 (m, 2H), 6.83 (d, *J* = 7.3 Hz, 2H), 6.74 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.79 (s, 3H), 2.93 – 2.82 (m, 2H), 2.81 – 2.71 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.96, 144.08, 133.94, 129.49, 129.34, 127.11, 126.20, 118.97, 115.75, 113.87, 55.29, 34.44, 33.61. **IR (v/cm^{-1}):** 3869, 2181, 1986, 1265, 738, 703, 663, 606, 685, 576. **HRMS-ESI (m/z):** calcd. $C_{15}H_{18}NO$ $[M+H]^+$: 228.1388, Found: 228.1371.



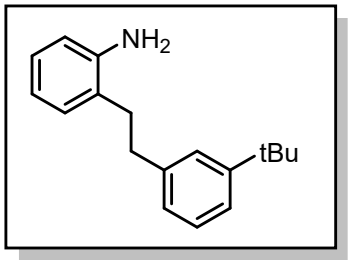
2-(3-methoxyphenethyl)aniline(3m):

Synthesized from **1a** and (3-methoxyphenyl)boronic acid by following general procedure A. 55% isolated yield (average value based on two parallel experiments on 0.1 mmol scale), or 53% isolated yield on a 0.5 mmol scale. Yellow oil. R_f= 0.2 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (t, *J* = 7.8 Hz, 1H), 7.05 (t, *J* = 7.3 Hz, 2H), 6.81 (d, *J* = 7.4 Hz, 1H), 6.79 – 6.70 (m, 3H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.77 (s, 3H), 3.52 (s, 2H), 2.95 – 2.87 (m, 2H), 2.82 – 2.74 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.68, 144.21, 143.51, 129.45, 129.43, 127.19, 125.99, 120.80, 118.92, 115.70, 114.16, 111.45, 55.18, 35.36, 33.27. **IR (v/cm^{-1}):** 3869, 3722, 2190, 1960, 1496, 1264, 1156, 734, 703, 585, 571. **HRMS-ESI(m/z):** calcd. $C_{15}H_{18}NO$ $[M+H]^+$: 228.1388. Found: 228.1371.



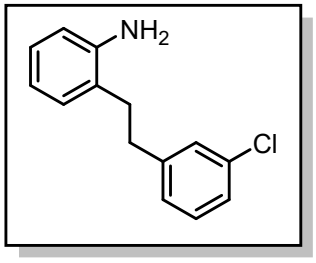
2-(3-methylphenethyl)aniline(3n):

Synthesized from **1a** and *m*-tolylboronic acid by following general procedure A. 83% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f= 0.3 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 7.7 Hz, 1H), 7.04 (q, *J* = 12.3, 10.3 Hz, 5H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 3.56 (s, 2H), 2.89 (dt, *J* = 8.8, 4.4 Hz, 2H), 2.78 (dt, *J* = 8.9, 4.1 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.16, 141.84, 138.04, 129.36, 129.22, 128.37, 127.13, 126.78, 126.16, 125.39, 118.89, 115.67, 35.24, 33.45, 21.40. **IR (ν/cm^{-1}):** 3869, 1960, 1264, 734, 703, 635, 626, 615, 606, 574. **HRMS-ESI (m/z):** calcd. $C_{15}H_{18}N$ $[M+H]^+$: 212.1439. Found: 212.1425.



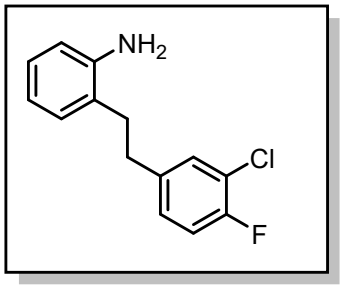
2-(3-(tert-butyl)phenethyl)aniline(3o):

Synthesized from **1a** and (3-(*tert*-butyl)phenyl)boronic acid by following general procedure A. 61% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, *J* = 3.3 Hz, 2H), 7.15 (s, 1H), 7.04 (t, *J* = 7.2 Hz, 3H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 7.8 Hz, 1H), 3.47 (s, 2H), 2.97 – 2.89 (m, 2H), 2.79 (t, *J* = 7.8 Hz, 2H), 1.32 – 1.25 (m, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.26, 144.21, 141.40, 129.49, 128.16, 127.09, 126.18, 125.58, 125.44, 123.00, 118.93, 115.72, 35.67, 34.59, 33.49, 31.35. **IR (ν/cm^{-1}):** 3649, 2182, 2036, 1961, 1264, 737, 704, 636, 623, 606, 585, 576. **HRMS-ESI (m/z):** calcd. $C_{18}H_{24}N$ $[M+H]^+$: 254.1909. Found: 254.1884.



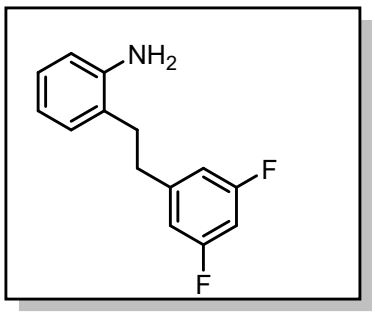
2-(3-chlorophenethyl)aniline(3p):

Synthesized from **1a** and *m*-chloroboronic acid by following general procedure A. 87% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 (s, 3H), 7.04 (dd, *J* = 19.2, 7.4 Hz, 3H), 6.78 – 6.66 (m, 2H), 3.63 (s, 2H), 2.95 – 2.87 (m, 2H), 2.81 – 2.74 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.08, 143.85, 134.16, 129.67, 129.40, 128.55, 127.34, 126.65, 126.24, 125.45, 118.96, 115.78, 34.81, 33.09. **IR (ν/cm^{-1}):** 3735, 1622, 1497, 1264, 894, 732, 703, 584, 572, 564. **HRMS-ESI (m/z):** calcd. $C_{14}H_{15}NCl$ $[M+H]^+$: 232.0893. Found: 232.0878



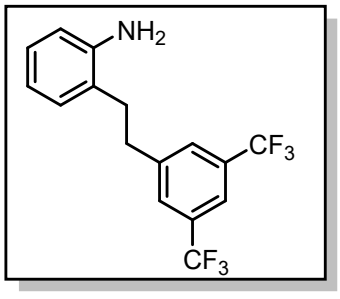
2-(3-chloro-4-fluorophenethyl)aniline(3q):

Synthesized from **1a** and (3-chloro-4-fluorophenyl)boronic acid by following general procedure A. 86% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f= 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (d, *J* = 7.0 Hz, 1H), 7.05 (dd, *J* = 15.6, 7.8 Hz, 3H), 6.98 (d, *J* = 7.6 Hz, 1H), 6.72 (dd, *J* = 19.1, 7.6 Hz, 2H), 3.55 (s, 2H), 2.93 – 2.85 (m, 2H), 2.80 – 2.70 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.05, 138.75, 130.39, 129.47, 128.06 (d, *J* = 6.9 Hz), 127.43, 125.17, 118.99, 116.37 (d, *J* = 20.8 Hz), 115.84, 34.05, 33.17. ^{19}F NMR (376 MHz, $CDCl_3$) δ -119.66. **IR (ν/cm^{-1}):** 3743, 2047, 1986, 1960, 1500, 1264, 735, 704, 616, 583, 573. **HRMS-ESI (m/z):** calcd. $C_{14}H_{14}NClF$ $[M+H]^+$: 250.0799. Found: 250.0822.



2-(3,5-difluorophenethyl)aniline(3r):

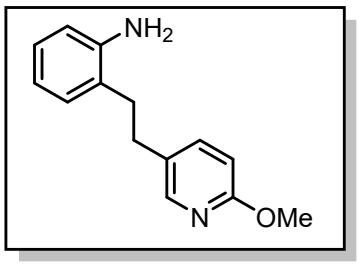
Synthesized from **1a** and (3,5-difluorophenyl) boronic acid by following general procedure A. 86% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow Solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (t, *J* = 7.5 Hz, 1H), 6.99 (d, *J* = 7.4 Hz, 1H), 6.69 (ddt, *J* = 25.4, 18.4, 8.2 Hz, 5H), 3.55 (s, 2H), 2.92 (t, *J* = 7.8 Hz, 2H), 2.77 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) 164.26 (d, *J* = 12.8 Hz), 161.80 (d, *J* = 13.0 Hz), 145.69 (t, *J* = 8.8 Hz), 144.03, 128.43 (d, *J* = 191.1 Hz),125.04, 119.03, 115.87, 111.21 (q, *J* = 24.5 Hz), 101.52 (t, *J* = 25.3 Hz), 34.78, 32.69. ^{19}F NMR (376 MHz, $CDCl_3$) δ -110.50. **IR (ν/cm^{-1}):** 3721, 1624, 1599, 1497, 1460, 1264, 1116, 996, 734, 703, 619, 580, 575. **HRMS-ESI (m/z):** calcd. $C_{14}H_{14}NF_2$ $[M+H]^+$: 234.1094. Found: 234.1096.



2-(3,5-bis(trifluoromethyl)phenethyl)aniline(3s):

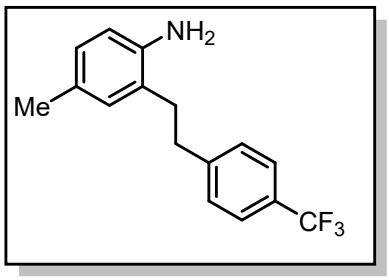
Synthesized from **1a** and (3,5-bis(trifluoromethyl)phenyl)boronic acid by following general procedure A. 63% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f = 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.58 (s, 2H), 7.07 (t, *J* = 7.6 Hz, 1H), 6.93 (d, *J* = 7.3 Hz, 1H), 6.72 (t, *J* = 7.9 Hz, 2H), 3.58 (s, 2H), 3.07 (t, *J* = 7.9 Hz, 2H), 2.82 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ144.00 (d, *J* = 3.1 Hz), 131.71, 131.38, 129.53, 128.73, 127.71, 124.75, 124.42, 120.15 (q, *J* = 3.8 Hz), 119.10, 116.01, 34.55, 32.92.

^{19}F NMR (376 MHz, $CDCl_3$) δ -62.83. **IR (ν/cm^{-1}):** 3743, 1379, 1279, 1264, 1174, 1134, 895, 733, 704, 683, 619. **HRMS-ESI (m/z):** calcd. $C_{16}H_{14}NF_6$ $[M+H]^+$: 334.1030. Found: 334.1016.



2-(2-(6-methoxypyridin-3-yl)ethyl)aniline(3t):

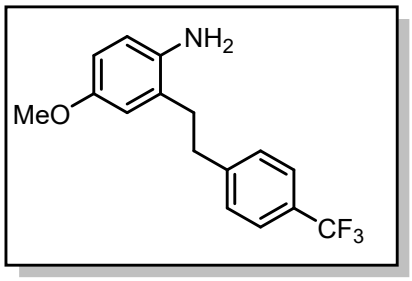
Synthesized from **1a** and (6-methoxypyridin-3-yl)boronic acid by following general procedure A. 36% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Brown solid. R_f= 0.2 (PE: EA = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1H), 7.36 (d, *J* = 8.4 Hz, 1H), 7.05 (t, *J* = 7.6 Hz, 1H), 6.99 (d, *J* = 7.5 Hz, 1H), 6.77 – 6.64 (m, 3H), 3.92 (s, 3H), 3.55 (s, 2H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.79 – 2.71 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.84, 146.09, 144.04, 139.01, 129.62, 129.51, 127.34, 125.36, 118.97, 115.81, 110.44, 53.35, 33.25, 31.24. **IR (ν/cm^{-1}):** 3743, 3649, 1493, 1264, 1028, 733, 704, 625, 616. **HRMS-ESI (m/z):** calcd. $C_{14}H_{17}N_2O$ $[M+H]^+$: 229.1341. Found: 229.1327.



4-methyl-2-(4-(trifluoromethyl)phenethyl)aniline(4a):

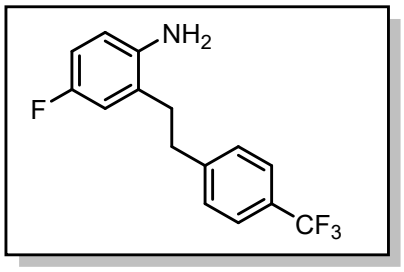
Synthesized from 4-methyl-2-vinylaniline and **2a** following general procedure A. 87% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f = 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.84 (s, 1H), 6.61 (d, *J* = 7.9 Hz, 1H), 3.42 (s, 2H), 3.02 – 2.92 (m, 2H), 2.80 – 2.70 (m, 2H), 2.22 (s, 3H). ^{13}C

NMR (101 MHz, $CDCl_3$) δ 146.01, 141.50, 130.07, 128.76, 128.23, 127.84, 125.50, 125.34 (q, *J* = 3.8 Hz), 116.02, 35.14, 33.10, 20.49. **IR (ν/cm^{-1}):** 3756, 1962, 1325, 1264, 1164, 1122, 1067, 896, 731, 703, 619, 606, 592, **HRMS-ESI (m/z):** calcd. $C_{16}H_{17}NF_3$ $[M+H]^+$: 280.1313. Found: 280.1313.



4-methoxy-2-(4-(trifluoromethyl)phenethyl)aniline(4b):

Synthesized from 4-methoxy-2-vinylaniline and **2a** following general procedure A. 77% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Brown solid. R_f = 0.2 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.29 (d, *J* = 7.7 Hz, 2H), 6.65 (s, 2H), 6.59 (s, 1H), 3.71 (s, 3H), 3.30 (s, 2H), 2.99 (t, *J* = 7.7 Hz, 2H), 2.79 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 152.99, 145.78, 137.67, 128.81, 127.08, 125.35 (q, *J* = 3.8 Hz), 117.06, 115.41, 112.60, 55.72, 35.01, 33.25. **IR (ν/cm^{-1}):** 3743, 1505, 1325, 1264, 1164, 1125, 1067, 735, 703, 661. **HRMS-ESI (m/z):** calcd. $C_{16}H_{17}NOF_3$ $[M+H]^+$: 296.1262. Found: 296.1273.

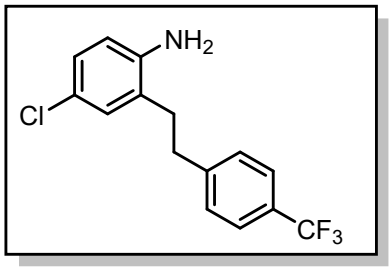


4-fluoro-2-(4-(trifluoromethyl)phenethyl)aniline(4c):

Synthesized from 4-fluoro-2-vinylaniline and **2a** following general procedure A. 88% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f = 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.6 Hz, 2H), 7.29 (d, *J* = 7.7 Hz, 2H), 6.76 (t, *J* = 11.2 Hz, 2H), 6.66 – 6.58 (m, 1H), 3.39 (s, 2H), 2.99 (t, *J* = 7.9 Hz, 2H), 2.77 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$)

δ 157.69, 145.39, 140.07, 128.75, 126.99 (d, J = 6.7 Hz), 125.43 (q, J = 3.8 Hz), 116.64 (d, J = 7.8 Hz), 115.70 (d, J = 22.3 Hz), 113.63 (d, J = 22.2 Hz).

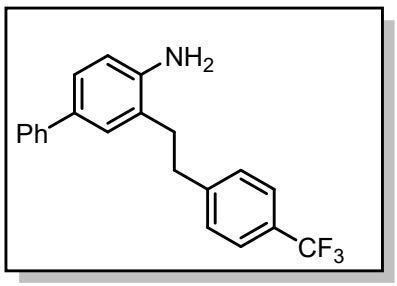
, 34.64, 32.91. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.28, -126.06. **IR (ν/cm^{-1}):** 1961, 1504, 1325, 1264, 1164, 1124, 1067, 730, 703, 580. **HRMS-ESI (m/z):** calcd. $C_{15}H_{14}NF_4$ $[M+H]^+$: 284.1062. Found: 284.1042.



4-chloro-2-(4-(trifluoromethyl)phenethyl)aniline(4d):

Synthesized from 4-chloro-2-vinylaniline and **2a** following general procedure A. 51% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f = 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 7.6 Hz, 2H), 7.34 – 7.24 (m, 2H), 7.01 (d, J = 9.6 Hz, 2H), 6.61 (d, J = 8.0 Hz, 1H), 3.51 (s, 2H), 3.05 – 2.90 (m, 2H), 2.75 (t, J = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.39, 142.69, 129.03, 128.74, 127.15, 126.92, 125.46 (q, J = 3.7 Hz)

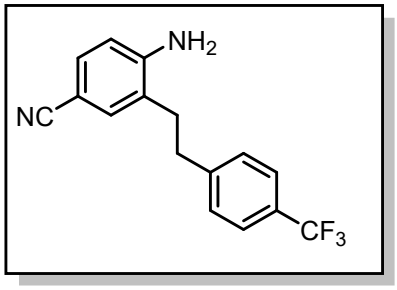
, 123.44, 116.87, 34.68, 32.79. **IR (ν/cm^{-1}):** 1960, 1326, 1264, 1164, 1124, 1067, 732, 704, 619, 582, 572. **HRMS-ESI (m/z):** calcd. $C_{15}H_{14}NF_3Cl$ $[M+H]^+$: 300.0767. Found: 300.0778.



3-(4-(trifluoromethyl)phenethyl)-[1,1'-biphenyl]-4-amine(4e):

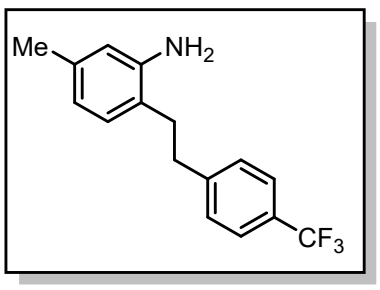
Synthesized from 3-vinyl-[1,1'-biphenyl]-4-amine and **2a** following general procedure A. 74% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f = 0.3 (PE: EA = 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d,

J = 8.0 Hz, 2H), 7.49 – 7.42 (m, 2H), 7.42 – 7.34 (m, 2H), 7.33 – 7.25 (m, 4H), 7.18 (d, *J* = 2.2 Hz, 1H), 6.76 (d, *J* = 8.2 Hz, 1H), 3.62 (s, 2H), 3.03 (dd, *J* = 9.2, 6.5 Hz, 2H), 2.85 (dd, *J* = 9.2, 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.54, 141.21, 131.98, 128.89, 128.66, 128.39, 126.46, 126.32, 126.12, 125.39 (q, *J* = 3.8 Hz), 116.17, 35.01, 33.21. **IR (ν/cm^{-1}):** 3740, 1621, 1486, 1325, 1246, 1164, 1123, 1067, 859, 734, 703, 581. **HRMS-ESI (m/z):** calcd. $C_{21}H_{19}NF_3$ $[M+H]^+$: 342.1470. Found: 342.1440.



4-amino-3-(4-(trifluoromethyl)phenethyl)benzonitrile(4f):

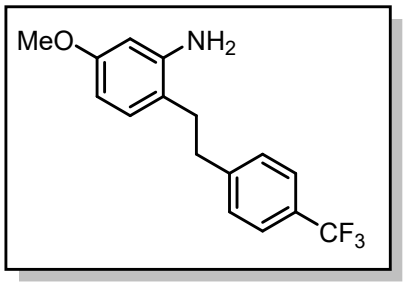
Synthesized from 4-amino-3-vinylbenzonitrile and **2a** following general procedure B. 35% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f = 0.3 (PE: EA =5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 7.9 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 1H), 7.31 – 7.27 (m, 3H), 6.66 (d, *J* = 8.3 Hz, 1H), 4.03 (s, 2H), 3.04 – 2.95 (m, 2H), 2.81 – 2.73 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.23, 144.87, 133.27, 131.87, 128.71, 125.58 (q, *J* = 3.7 Hz), 124.88, 120.10, 115.15, 100.74, 34.18, 32.33. **IR (ν/cm^{-1}):** 1961, 1326, 1264, 1165, 1125, 1067, 821, 734, 704, 572. **HRMS-ESI (m/z):** calcd. $C_{16}H_{14}N_2F_3$ $[M+H]^+$: 291.1109. Found: 291.1099.



5-methyl-2-(4-(trifluoromethyl)phenethyl)aniline(4g):

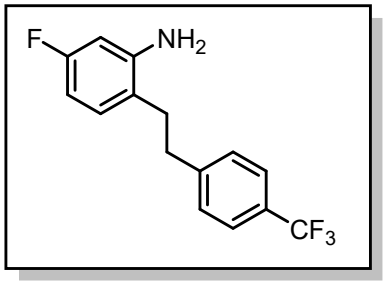
Synthesized from 5-methyl-2-vinylaniline and **2a** following general procedure A. 88% isolated yield (average value based on two parallel experiments on 0.1 mmol scale).

Yellow oil. R_f = 0.3 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 6.89 (d, *J* = 7.6 Hz, 1H), 6.56 (d, *J* = 7.6 Hz, 1H), 6.53 (s, 1H), 3.49 (s, 2H), 3.02 – 2.93 (m, 2H), 2.80 – 2.71 (m, 2H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.01, 143.91, 137.15, 129.34, 128.77, 125.33 (q, *J* = 3.8 Hz), 122.40, 119.81, 116.57, 35.11, 32.64, 21.07. **IR (ν/cm^{-1}):** 1325, 1264, 1165, 1122, 1067, 828, 734, 704, 580, 572. **HRMS-ESI (m/z):** calcd. $C_{16}H_{17}NF_3$ $[M+H]^+$: 280.1313. Found: 280.1313.



5-methoxy-2-(4-(trifluoromethyl)phenethyl)aniline(4h):

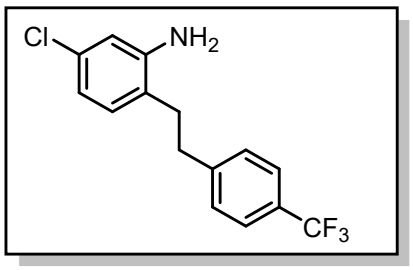
Synthesized from 5-methoxy-2-vinylaniline and **2a** following general procedure A . 75% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow solid. R_f = 0.2 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 7.7 Hz, 2H), 7.29 (s, 2H), 6.88 (d, *J* = 8.2 Hz, 1H), 6.33 – 6.24 (m, 2H), 3.76 (s, 3H), 3.55 (s, 2H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.74 (t, *J* = 7.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.20, 145.11, 130.26, 128.79, 125.31 (q, *J* = 3.7 Hz), 117.88, 104.11, 101.62, 55.17, 35.26, 32.34. **IR (ν/cm^{-1}):** 1621, 1510, 1325, 1264, 1210, 1165, 1123, 1066, 828, 733, 704. **HRMS-ESI (m/z):** calcd. $C_{16}H_{17}NOF_3$ $[M+H]^+$: 296.1262. Found: 296.1273.



5-fluoro-2-(4-(trifluoromethyl)phenethyl)aniline(4i):

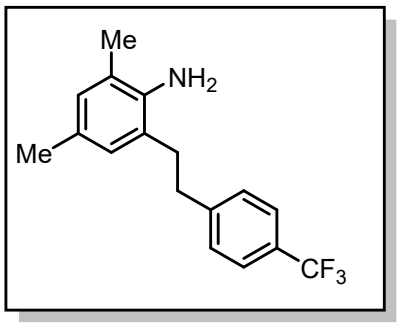
Synthesized from 5-fluoro-2-vinylaniline and **2a** following general procedure A. 66%

isolated yield (average value based on two parallel experiments on 0.1 mmol scale). solid. R_f = 0.3 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 7.8 Hz, 2H), 7.27 (d, *J* = 7.1 Hz, 2H), 6.88 (t, *J* = 7.2 Hz, 1H), 6.40 (t, *J* = 8.3 Hz, 2H), 3.63 (s, 2H), 2.96 (t, *J* = 7.8 Hz, 2H), 2.74 (t, *J* = 7.8 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 163.57, 145.57 (t, *J* = 2.2 Hz) , 145.45, 130.51 (d, *J* = 9.7 Hz), 128.79, 125.37 (q, *J* = 3.7 Hz), 120.66 (d, *J* = 2.8 Hz), 105.20 (d, *J* = 21.1 Hz), 102.40 (d, *J* = 24.5 Hz)., 34.92, 32.34. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.31, -116.14. **IR (v/cm^{-1}):** 1961, 1326, 1264, 1164, 1124, 1067, 734, 704, 581. **HRMS-ESI (m/z):** calcd. $C_{15}H_{14}NF_4$ $[M+H]^+$: 284.1062. Found: 284.1042.



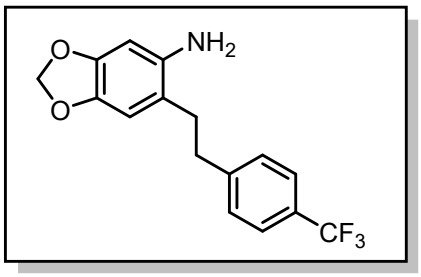
5-chloro-2-(4-(trifluoromethyl)phenethyl)aniline(4j):

Synthesized from 5-chloro-2-vinylaniline and **2a** following general procedure A. 73% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). White solid. R_f = 0.3 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.28 (s, 2H), 6.87 (d, *J* = 8.6 Hz, 1H), 6.72 – 6.60 (m, 2H), 3.59 (s, 2H), 2.99 – 2.92 (m, 2H), 2.81 – 2.70 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.21, 132.65, 130.52, 128.78, 125.40 (q, *J* = 3.7 Hz), 123.47, 118.71, 115.38, 34.71, 32.43. **IR (v/cm^{-1}):** 3648, 1961, 1325, 1276, 749, 636, 606, 581, 575. **HRMS-ESI (m/z):** calcd. $C_{15}H_{14}NF_3Cl$ $[M+H]^+$: 300.0767. Found: 300.0778.



2,4-dimethyl-6-(4-(trifluoromethyl)phenethyl)aniline(4k):

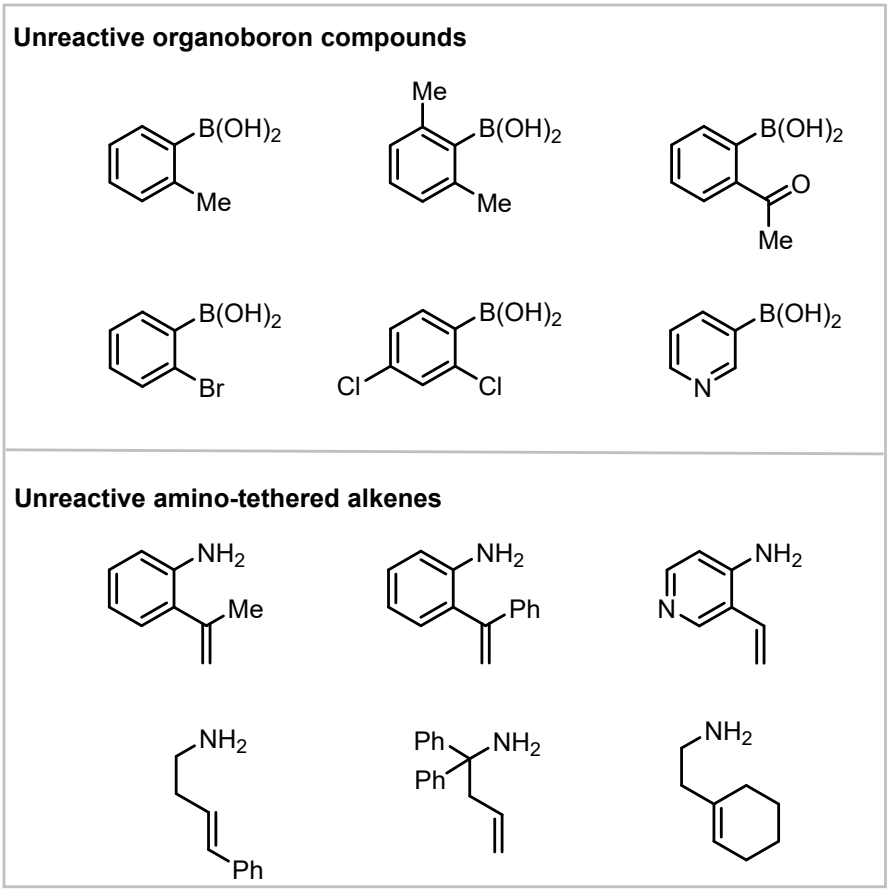
Synthesized from 2,4-dimethyl-6-vinylaniline and **2a** following general procedure A. 66% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Yellow oil. R_f = 0.3 (PE: EA =10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 7.8 Hz, 2H), 7.32 (d, *J* = 7.7 Hz, 2H), 6.81 (s, 1H), 6.74 (s, 1H), 3.44 (s, 2H), 3.02 – 2.94 (m, 2H), 2.81 – 2.73 (m, 2H), 2.21 (s, 3H), 2.17 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.10, 139.63, 129.37, 128.73, 127.70, 127.45, 125.34 (q, *J* = 3.8 Hz), 124.90, 122.58, 35.11, 33.36, 20.43, 17.74. **IR (ν/cm^{-1}):** 1721, 2156, 1962, 1326, 1264, 1067, 736, 704, 573. **HRMS-ESI (m/z):** calcd. $C_{17}H_{19}NF_3$ $[M+H]^+$: 294.1470. Found: 294.1492.



6-(4-(trifluoromethyl)phenethyl)benzo[d][1,3]dioxol-5-amine(4l):

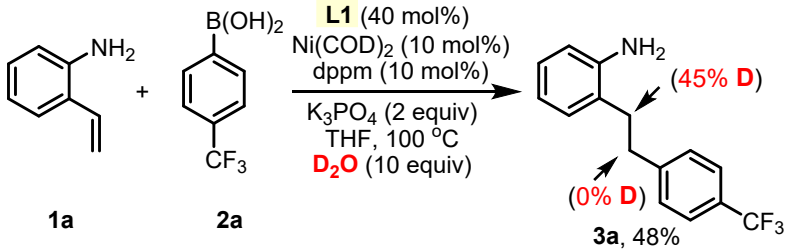
Synthesized from 6-vinylbenzo[d][1,3]dioxol-5-amine and **2a** following general procedure A. 73% isolated yield (average value based on two parallel experiments on 0.1 mmol scale). Brown solid. R_f = 0.2 (PE: EA = 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.1 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 6.51 (s, 1H), 6.29 (s, 1H), 5.84 (s, 2H), 3.30 (s, 2H), 2.97 – 2.89 (m, 2H), 2.72 (dd, *J* = 8.9, 6.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 146.52, 145.72, 140.57, 138.39, 128.79, 125.36 (q, *J* = 3.8 Hz), 117.49, 109.30, 100.58, 98.30, 35.32, 32.94. **IR (ν/cm^{-1}):** 1486, 1325, 1264, 1172, 1123, 1067, 736, 703, 615. **HRMS-ESI (m/z):** calcd. $C_{16}H_{15}NO_2F_3$ $[M+H]^+$: 310.1055. Found: 310.1074

Scheme S1: Unreacted substrates.



4. Deuterium Experiments & Control Experiment

4.1 Deuterium exchange experiment with the addition of D_2O

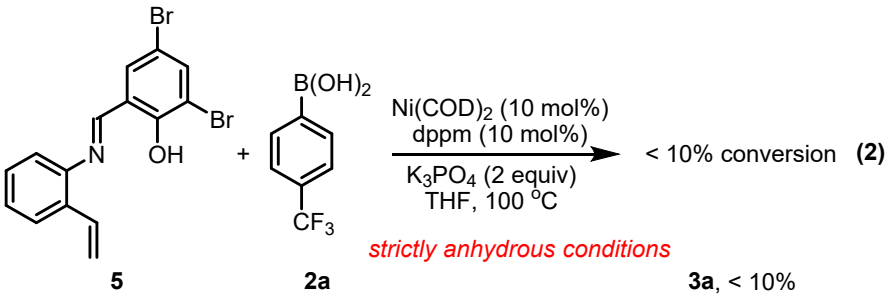


In glove box, a 4-mL vial charged with a stir bar was added $Ni(COD)_2$ (0.01 mmol, 2.75 mg) and dppm (0.01 mmol, 3.8 mg) in 0.3 mL of THF, the mixture was stirred for 5 minutes before **1a** (0.1 mmol, 19.5 mg), **L1**(0.04 mmol, 11.2 mg), **2a** (0.15 mmol, 27.5 mg), K_3PO_4 (0.2 mmol, 42.5 mg), D_2O (1 mmol, 18 mg) were subsequently added. The vial was tightly capped, removed from glove box and heated at 100 ℃ for 48 h. After

completion, the reaction mixture was cooled to room temperature, subjected to flash column chromatography (eluent: PE/EA = 30:1) to get the pure product *d*-**3a**.

d-**3a** (yield: 48%):^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.06 (td, *J* = 7.6, 1.6 Hz, 1H), 7.00 (dd, *J* = 7.5, 1.5 Hz, 1H), 6.80 – 6.63 (m, 2H), 3.55 (s, 2H), 3.00 (t, *J* = 7.8 Hz, 2H), 2.84 – 2.75 (m, 1.55H).

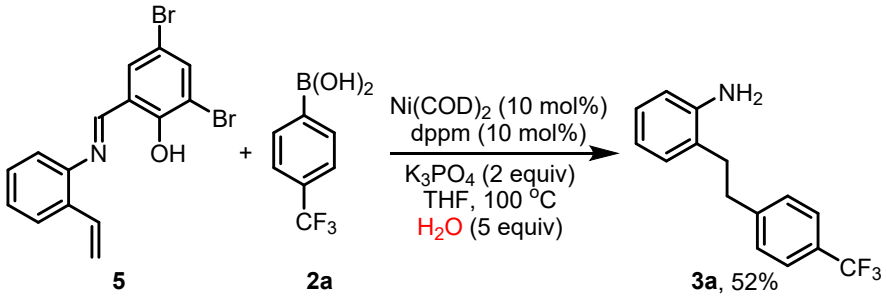
4.2 Reaction between compound 5 and 2a under anhydrous conditions



Note: The THF solvent being used (Extra dry) were further treated with 4 Å molecular sieve beads for overnight before use.

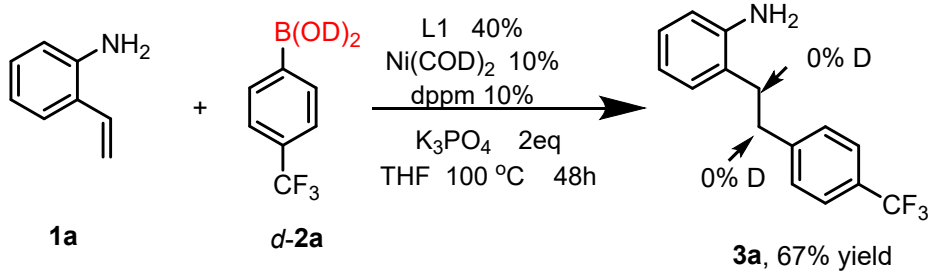
In glove box, a 4-mL vial charged with a stir bar was added $Ni(COD)_2$ (0.01 mmol, 2.75 mg) and dppm (0.01 mmol, 3.8 mg) in 0.3 mL of the pre-treated THF, the mixture was stirred for 5 minutes before **5** (0.1 mmol, 37.9 mg), **2a** (0.15 mmol, 27.5 mg), K_3PO_4 (0. 2 mmol, 42.5 mg) were subsequently added. The resulted reaction mixture was further treated with 4 Å molecular sieve beads for 6 h with stirring. The molecular sieve beads were then removed from the reaction system. The vial was tightly capped, removed from glove box and heated at 100 °C for 48 h. After completion, the reaction mixture was cooled to room temperature, The reaction was monitored by TLC plate and detected by ^{1}H NMR, only trace amount of **3a** was observed while **5** was retained.

4.3 Reaction between compound 5 and 2a with the addition of H_2O



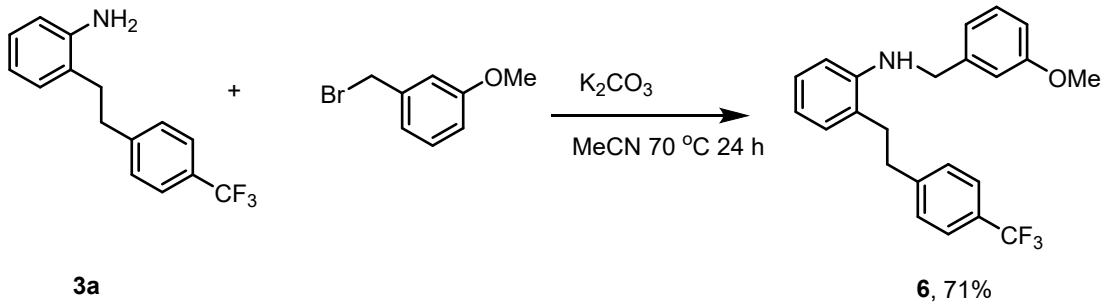
In glove box, a 4-mL vial charged with a stir bar was added $Ni(COD)_2$ (0.01 mmol, 2.7 mg) and dppm (0.01 mmol, 3.8 mg) in 0.3 mL of THF, the mixture was stirred for 5 minutes before **5** (0.1 mmol, 37.9 mg), **2a** (0.15 mmol, 27.5 mg), K_3PO_4 (0. 2 mmol, 42.5 mg), H_2O (0.5 mmol, 9 mg) were subsequently added. The vial was tightly capped, removed from glove box and heated at 100 ℃ for 48 h. After completion, the reaction mixture was cooled to room temperature, subjected to flash column chromatography (PE:EA =30:1) to get the pure product **3a** in 52 % yield.

4.4 Reaction between 1a and $ArB(OD)_2$ (*d*-2a)



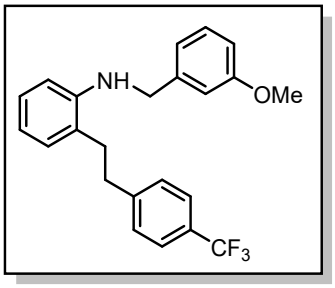
5. Experimental Procedure for the Synthetic Applications

5.1 Conversion of 3a into 6.[2]



To a flame-dried 10 mL vial charged with a stir bar was added **3a** (57 mg, 2.1 mmol, 1.2eq) and dry CH_3CN (1 mL), this mixture was cooled to 0 ℃ under a nitrogen

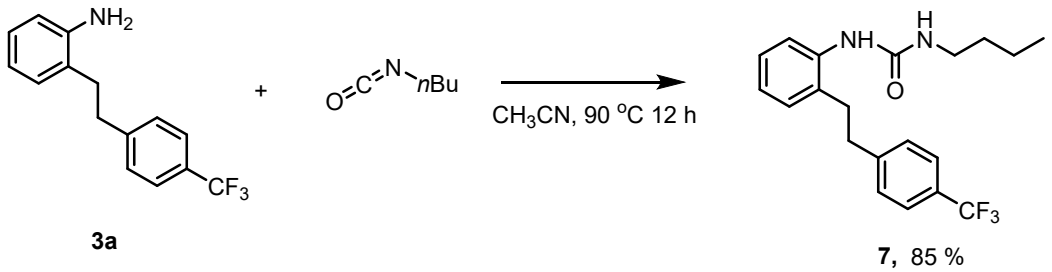
atmosphere. K_2CO_3 (55 mg, 4.0 mmol, 2 eq) and 1-(bromomethyl)-3-methoxybenzene (40 mg, 2.0 mmol, 1 eq) were then added. The reaction mixture was stirred for 24 h at room temperature. After completion of the reaction, the solvent was removed under vacuum. The crude mixture was then dissolved in 2 mL of H_2O and was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography (PE: EA=70:1) to give the desired product **6** (yield: 71%).



N-(3-methoxybenzyl)-2-(4-(trifluoromethyl)phenethyl)aniline (6):

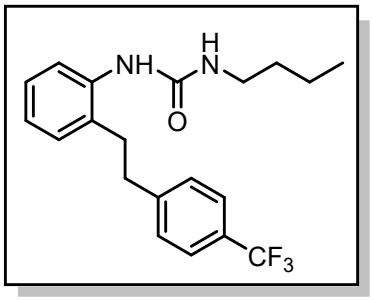
Yield: 71%. Colorless liquid. R_f = 0.4 (PE:EA=20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 7.7 Hz, 3H), 7.15 – 7.09 (m, 1H), 7.03 (d, *J* = 6.6 Hz, 1H), 6.97 – 6.90 (m, 2H), 6.83 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.74 – 6.67 (m, 1H), 6.64 (d, *J* = 8.0 Hz, 1H), 4.29 (s, 2H), 3.83 (s, 1H), 3.79 (s, 3H), 3.05 – 2.96 (m, 2H), 2.83 – 2.75 (m, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 159.95, 145.87, 145.53, 141.09, 129.75, 128.91, 128.79, 127.62, 125.36 (q, *J* = 3.7 Hz), 124.84, 119.72, 117.56, 113.25, 112.53, 110.81, 55.22, 48.41, 34.79, 32.90. **IR (ν/cm^{-1}):** 3649, 1325, 1264, 733, 704, 619, 606, 587, 578. **HRMS-ESI (m/z):** calcd. $C_{23}H_{23}NOF_3$ $[M+H]^+$: 386.1732. Found: 386.1731.

5.2 Conversion of 3a into 7.[3]



To a 4 mL vial was charged with **3a** (24 mg, 0.09 mmol,), 1-isocyanatobutane (13 mg, 1.2 mmol, 1.3 eq) and CH_3CN (0.3 mL), The reaction mixture was stirred for 12 h at

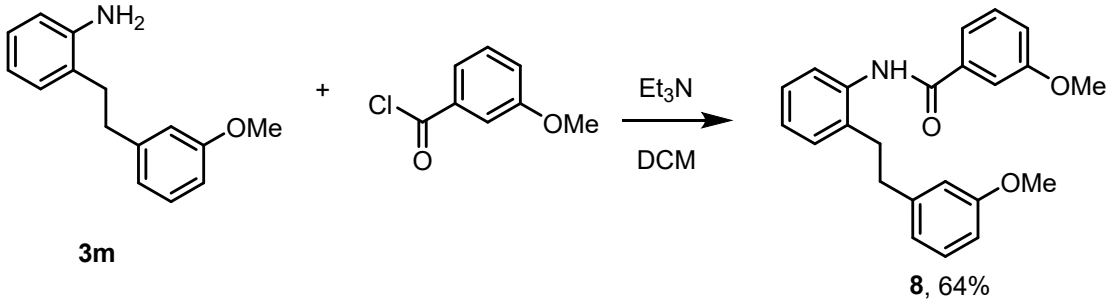
90 °C . After completion of the reaction, the solvent was removed under vacuum. The crude product was purified by flash chromatography (PE:EA=3:1) to give the desired product **7.**



1-butyl-3-(2-(4-(trifluoromethyl)phenethyl)phenyl)urea (7):

Yield: 85%. White solid. R_f = 0.3 (PE: EA= 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, *J* = 7.9 Hz, 2H), 7.32 – 7.21 (m, 6H), 5.84 (s, 1H), 4.47 – 4.37 (m, 1H), 3.18 (q, *J* = 6.8 Hz, 2H), 2.93 (s, 4H), 1.48 – 1.38 (m, 2H), 1.31 – 1.25 (m, 2H), 0.88 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.82, 145.37, 136.85, 135.63, 130.28, 128.84, 127.64, 127.14, 126.81, 125.34 (q, *J* = 3.7 Hz), 40.13, 36.39, 33.12, 32.27, 20.01, 13.77. **IR (ν/cm^{-1}):**1634, 1569, 1326, 1264, 1167, 1115, 1068, 736, 703, 579. **HRMS-ESI (m/z):** calcd. $C_{20}H_{24}F_3N_2O$ $[M+H]^+$: 365.1841. Found: 365.1845.

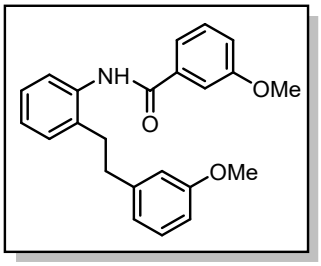
5.3 Conversion of 3l into 8. [4]



3m **8**, 64%

To a stirred solution of **3m** (25 mg, 0.11 mmol) in anhydrous dichloromethane (1.5 mL), were added triethylamine (22 mg, 0.22 mmol, 2 eq) and 3-methoxybenzoyl chloride (37 mg, 0.22 mmol, 2 eq) at 0 °C. The reaction mixture was stirred at room temperature overnight. After completion of the reaction, the solvent was removed under

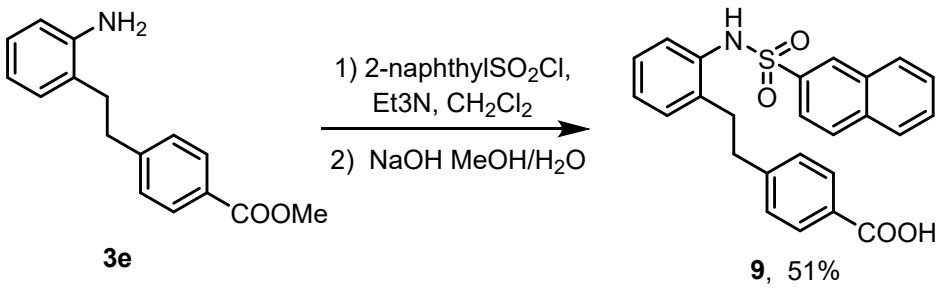
vacuum. The crude mixture was then dissolved in 2 mL of saturated aqueous $NaHCO_3$ (5 mL) and was extracted with DCM (3 × 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The crude product was purified by flash chromatography (PE: EA=10:1) to give the desired product **8** (yield: 64%).



3-methoxy-N-(2-(3-methoxyphenethyl)phenyl)benzamide (8):

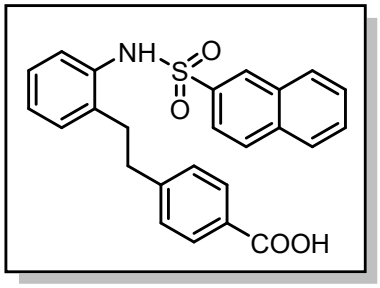
Yield: 64%, Colorless liquid. R_f = 0.2 (PE: EA=10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.7 Hz, 1H), 7.35 – 7.23 (m, 4H), 7.10 (td, *J* = 14.4, 13.7, 8.6 Hz, 4H), 6.74 (d, *J* = 8.1 Hz, 1H), 6.63 (d, *J* = 7.4 Hz, 1H), 6.55 (s, 1H), 3.85 (s, 3H), 3.65 (s, 3H), 2.92 (s, 4H).^{13}C NMR (101 MHz, CDCl3) δ 159.95, 159.77, 142.71, 136.15, 135.40, 134.06, 129.94, 129.75, 129.60, 127.04, 126.15, 124.98, 120.85, 118.68, 117.95, 113.95, 112.64, 112.15, 55.48, 55.04, 37.30, 33.65. **IR (ν/cm^{-1}):** 3315, 2942, 1961, 1026, 764, 621, 607, 595, 585. **HRMS-ESI (m/z):** calcd. $C_{23}H_{24}NO_3$ $[M+H]^+$: 362.1756. Found: 362.1750.

5.4 Conversion of 3e into 9. [5]



To a stirred solution of **3e** (44 mg 0.17 mmol, 1 eq) in anhydrous dichloromethane (2 mL) was added triethylamine (50 mg, 0.5 mmol, 3 eq), and the mixture was stirred at RT for 20 min. 2-Naphthoyl chloride (43 mg, 0.19 mmol, 1.1 eq) was then added in one

portion. The reaction mixture was stirred overnight at RT and then diluted with ethyl acetate and water. The layers were separated and the water layer was extracted two times with ethyl acetate. The combined organic layers were washed with saturated aqueous NaCl solution (10 mL), dried over Na_2SO_4 and concentrated under vacuum. The crude product was further dissolved in methanol (1 mL), and sodium hydroxide solution (NaOH 32 mg, 0.8 mmol, 10 eq) in 0.4 mL H_2O was added. The reaction was stirred at 50 °C for 12 h, and then HCl was added to adjust pH to 4. After dilution with water and ethyl acetate, the organic layer was washed with water and brine, dried over Na_2SO_4, filtered, and evaporated to dryness. The residue was purified by chromatography (DCM: MeOH=10:1) to give product **9** as a white foam (yield: 51% for 2 steps).



4-(2-(naphthalene-2-sulfonamido)phenethyl)benzoic acid (9):

Yield: 51%. White foam. R_f = 0.2 (DCM: MeOH= 4:1). ^{1}H NMR (400 MHz, DMSO-d6) δ 12.80 (s, 1H), 9.82 (s, 1H), 8.33 (s, 1H), 8.17 – 8.07 (m, 2H), 8.04 (d, *J* = 7.6 Hz, 1H), 7.87 – 7.75 (m, 3H), 7.68 (dt, *J* = 23.4, 7.0 Hz, 2H), 7.21 (d, *J* = 6.5 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 3H), 7.10 – 7.02 (m, 1H), 6.91 (d, *J* = 7.1 Hz, 1H), 2.77 (dd, *J* = 10.1, 4.5 Hz, 2H), 2.70 (dd, *J* = 11.0, 5.3 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 167.76, 147.32, 138.47, 138.17, 134.76, 134.68, 132.11, 130.23, 129.88, 129.73, 129.34, 128.79, 128.33, 128.13, 127.90, 127.35, 127.25, 127.09, 122.77, 35.80, 32.17. **IR (ν/cm^{-1}):**1962, 1264, 731, 702, 617, 606, 591, 580, 571, 556. **HRMS-ESI (m/z):** calcd. $C_{25}H_{22}NO_4S$ $[M+H]^+$: 432.1270. Found: 432.1242.

6. Reference:

[1] (a) L. Wang, J. Ferguson and F. Zeng, *Organic & Biomolecular Chemistry*, 2015, **13**, 11486-11491. (b) S. Ortgies and A. Breder, *Org. Lett.*, 2015, **17**, 2748-2751. (c) S. San Jang, Y. H. Kim and S. W. Youn, *Org. Lett.*, 2020, **22**, 9151-9157.

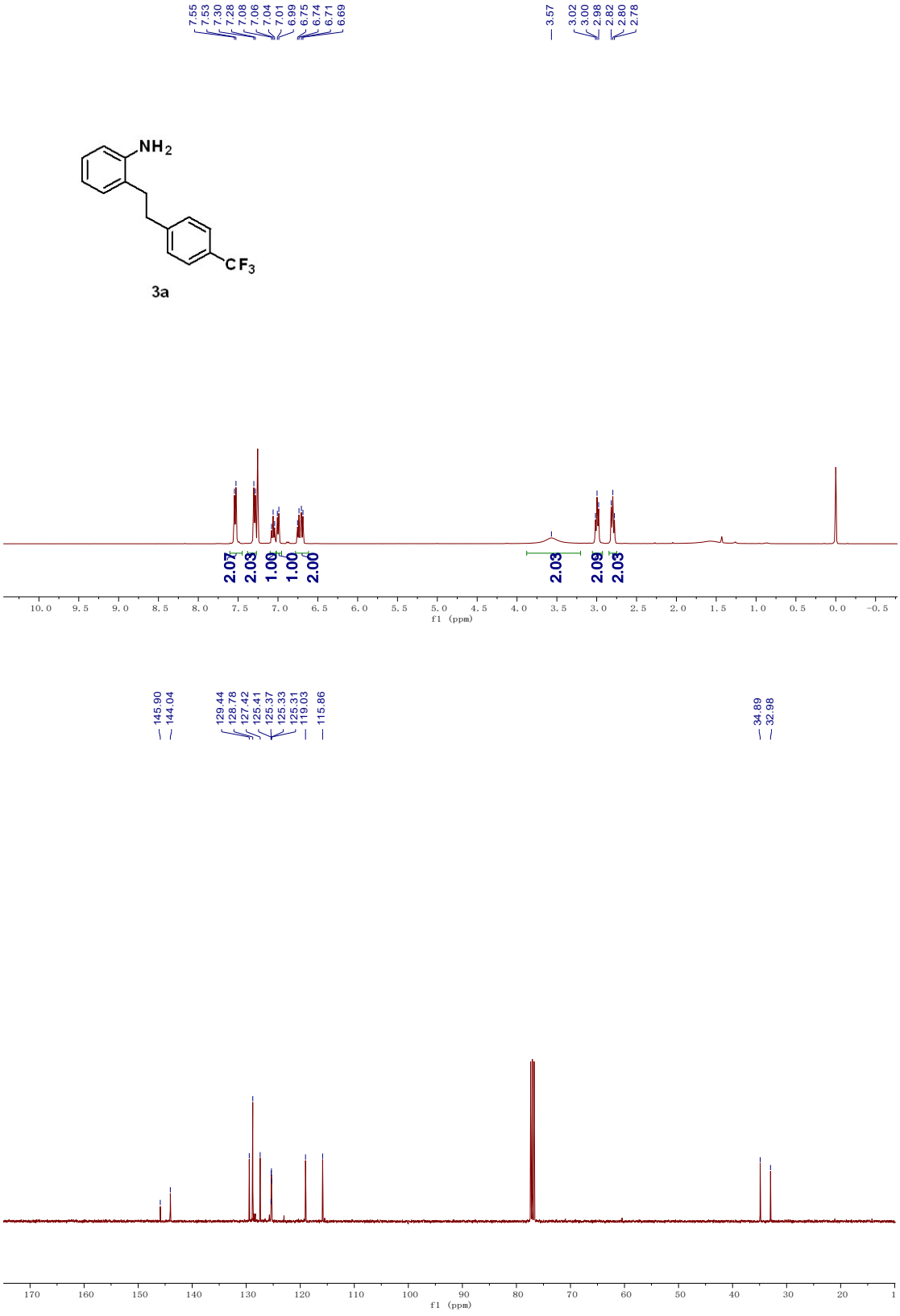
[2] N. A. Colabufo, F. Berardi, R. Perrone, S. Rapposelli, M. Digiacomo, M. Vanni and A. Balsamo, *J. Med. Chem.*, 2008, **51**, 1415-1422

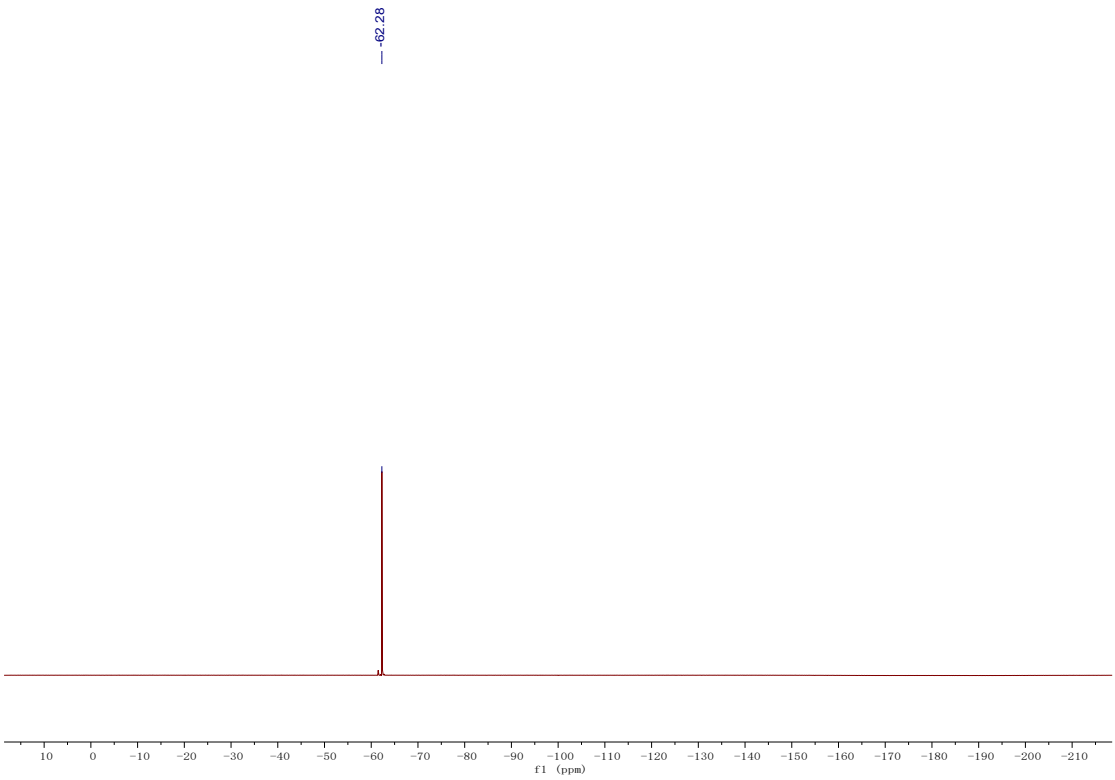
[3] M. Krátký, J. Stolaříková and J. Vinšová, *Molecules*, 2017, **22**, 535.

[4] G. Nesi, N. A. Colabufo, M. Contino, M. G. Perrone, M. Digiacomo, R. Perrone, A. Lapucci, M. Macchia and S. Rapposelli, *Eur. J. Med. Chem.*, 2014, **76**, 558-566.

[5] T. Heinrich, A. Sala-Hojman, R. Ferretti, C. Petersson, S. Minguzzi, A. Gondela, S. Ramaswamy, A. Bartosik, F. Czauderna, L. Crowley, P. Wahra, H. Schilke, P. Bopple, L. Dudek, M. Les, P. Niedziejko, K. Olech, H. Pawlik, L. Wloszczak, K. Zuchowicz, J. R. Suarez Alvarez, J. Martyka, E. Sitek, M. Mikulski, J. Szczesniak, S. Jackel, M. Krier, M. Krol, A. Wegener, M. Galezowski, M. Nowak, F. Becker and C. Herhaus, *J. Med. Chem.*, 2021, **64**, 11904-11933.

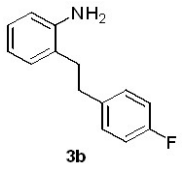
7. NMR Spectra



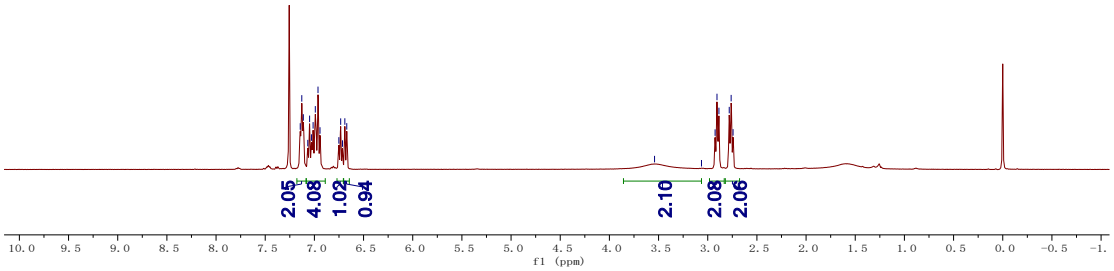

-62.28
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


7.14
7.13
7.11
7.07
7.05
7.03
7.01
6.99
6.96
6.94
6.75
6.73
6.71
6.69
6.67

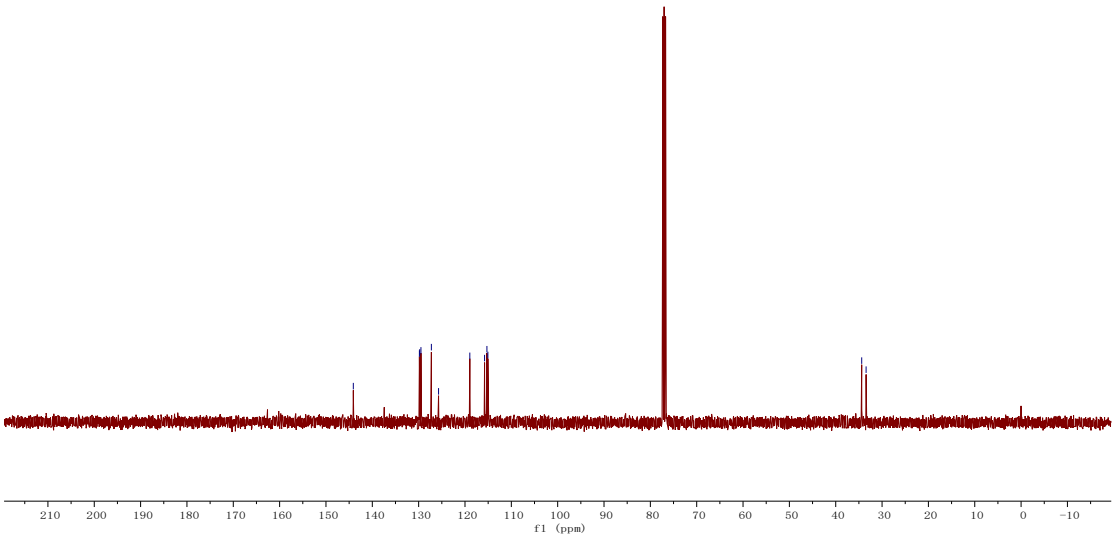

3.54
3.06
2.93
2.91
2.89
2.78
2.76
2.74

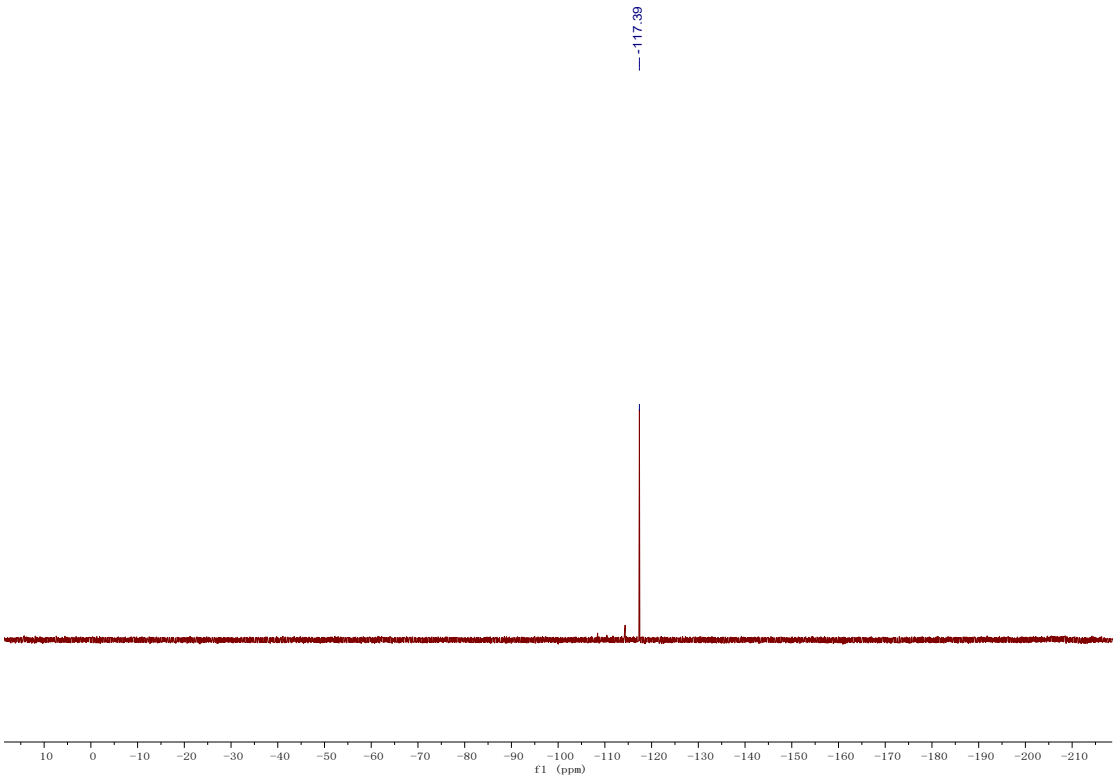

NH2
F

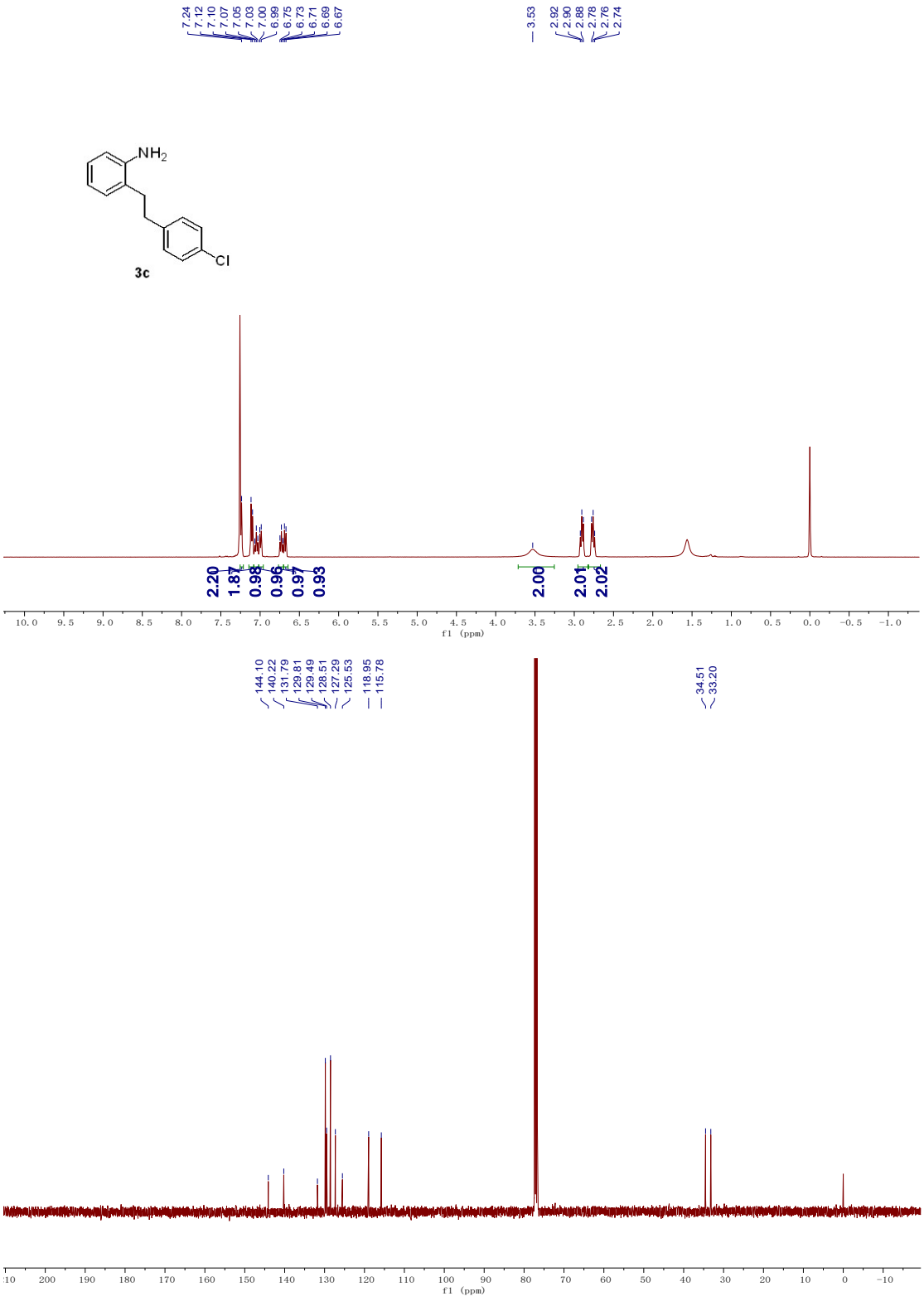
3b

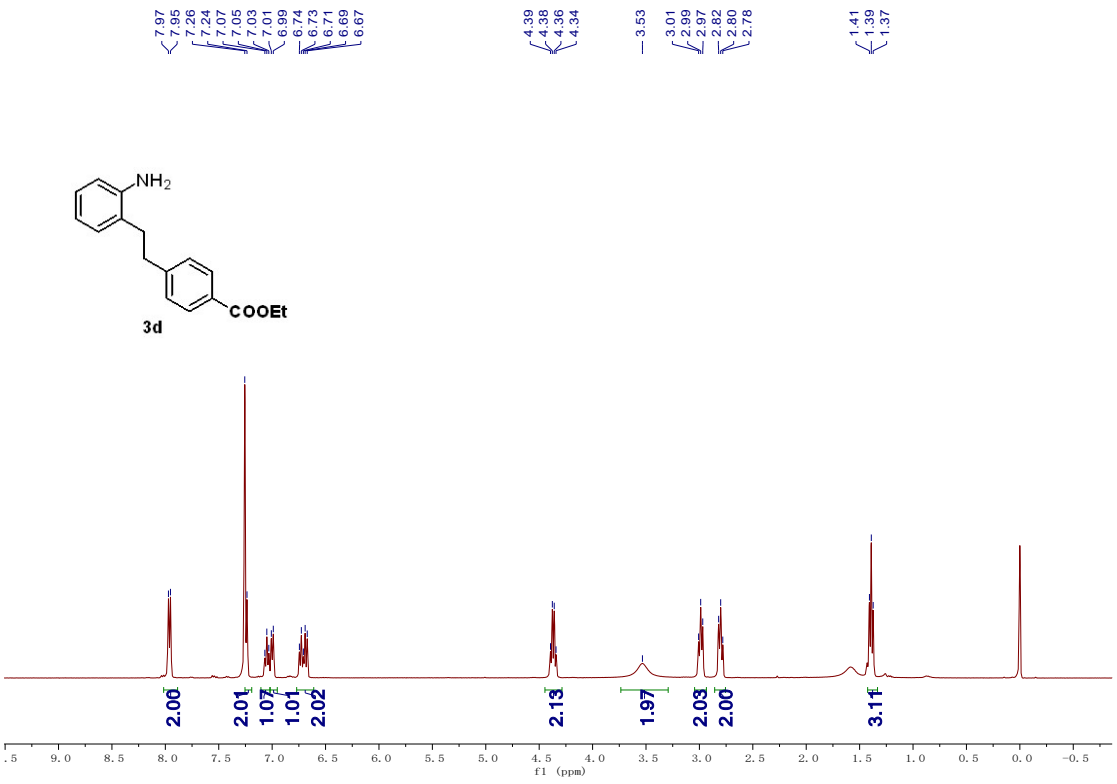

2.05
4.08
1.02
0.94
2.10
2.08
2.06
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 −0.5 −1.
f1 (ppm)

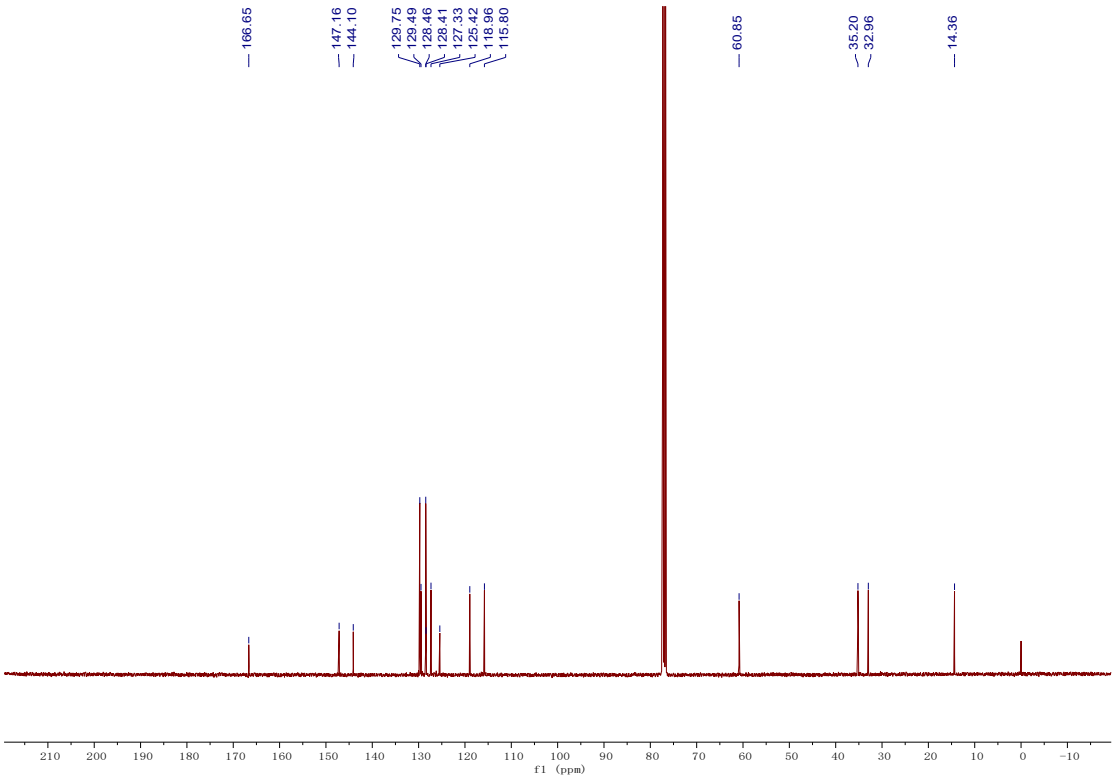

144.10
129.84
129.76
129.50
127.25
125.70
118.96
115.78
115.27
115.06
34.39
33.45

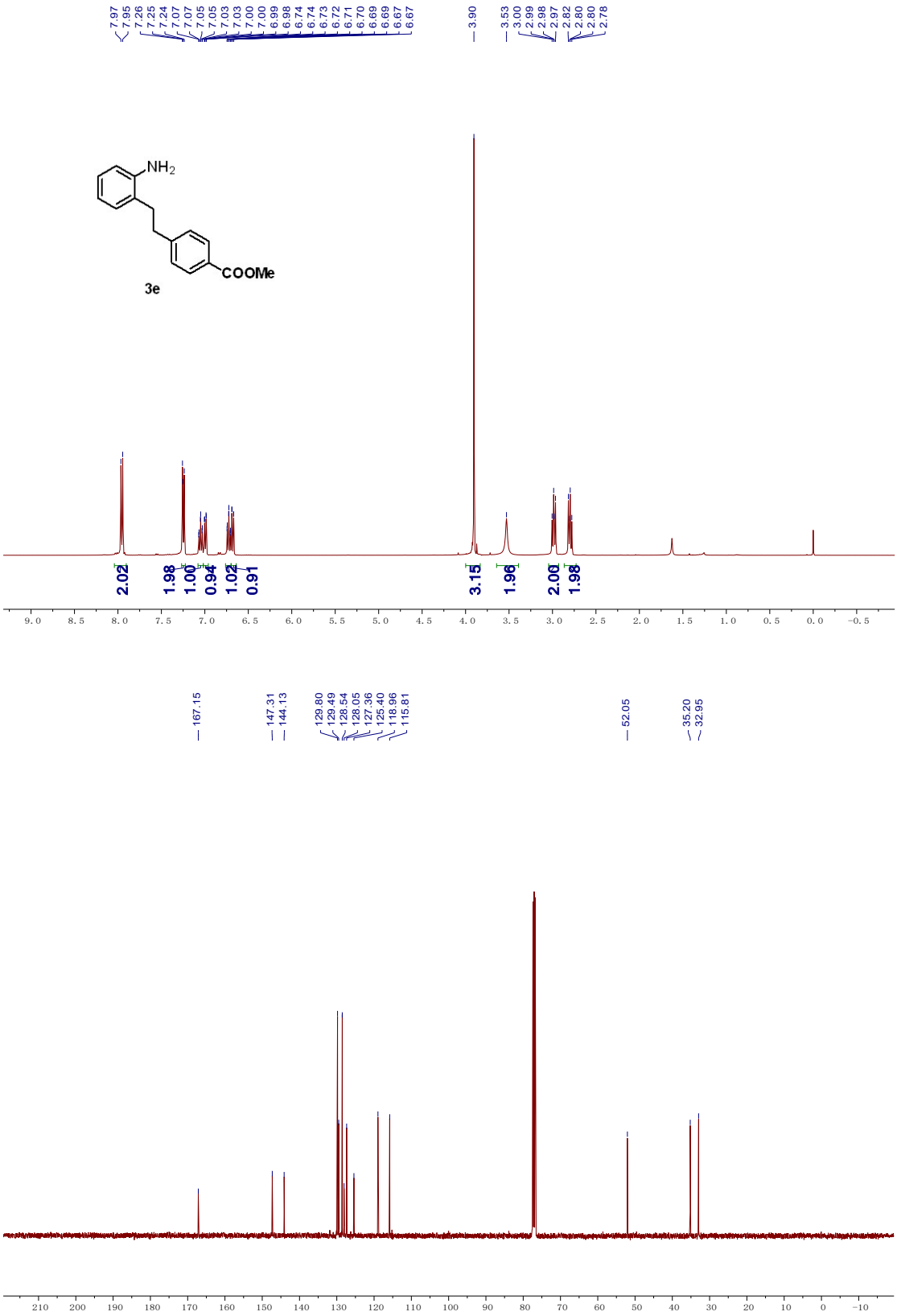

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)

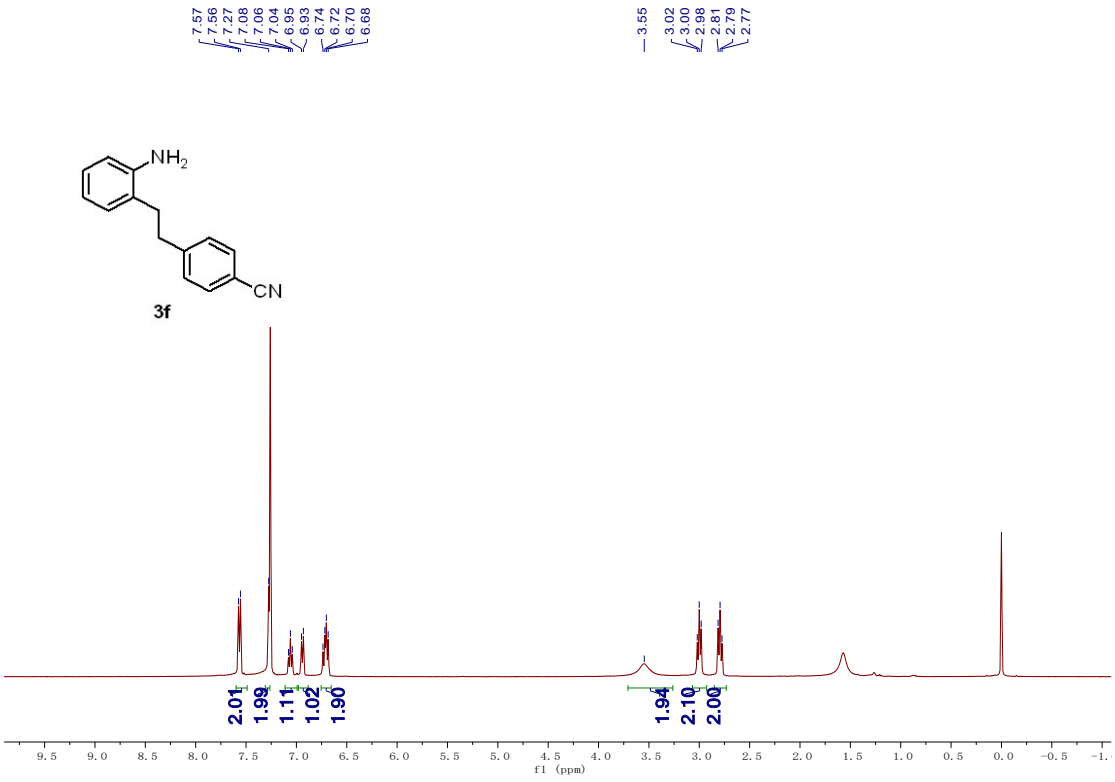

-117.39
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

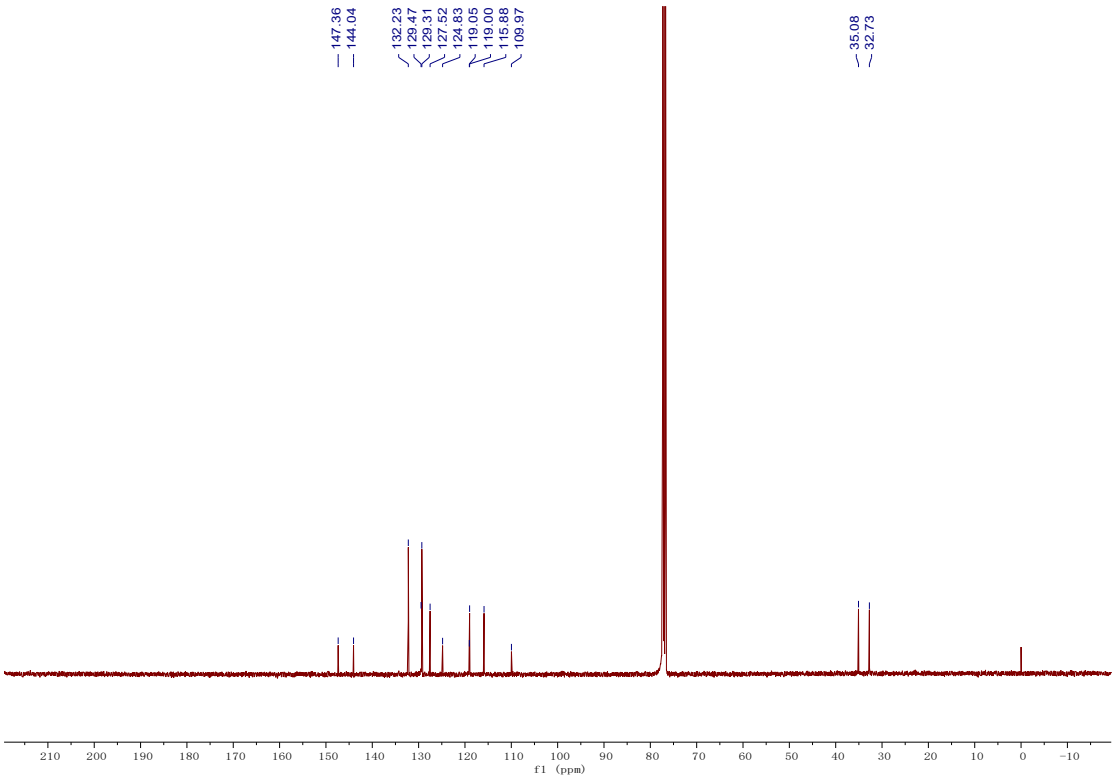

7.24
7.12
7.10
7.07
7.05
7.03
7.00
6.99
6.75
6.73
6.71
6.69
6.67
3.53
2.92
2.90
2.88
2.78
2.76
2.74
NH2
Cl
3c
2.20
1.87
0.98
0.96
0.97
0.93
2.00
2.01
2.02
f1 (ppm)
144.10
140.22
131.79
129.81
129.49
128.51
127.29
125.53
118.95
115.78
34.51
33.20
f1 (ppm)

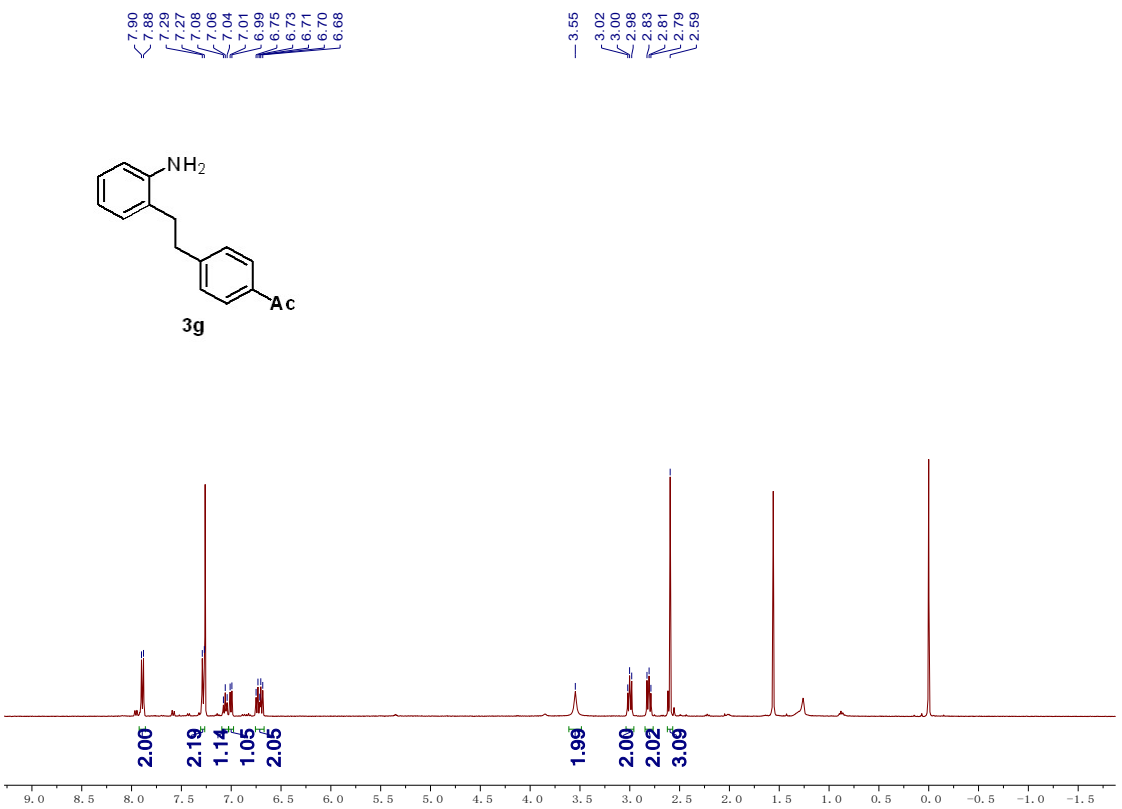

7.97
7.95
7.26
7.24
7.07
7.05
7.03
7.01
6.99
6.74
6.73
6.71
6.69
6.67
4.39
4.38
4.36
4.34
3.53
3.01
2.99
2.97
2.82
2.80
2.78
1.41
1.39
1.37
NH2
COOEt
3d
2.00
2.01
1.07
1.01
2.02
2.13
1.97
2.03
2.00
3.11
f1 (ppm)

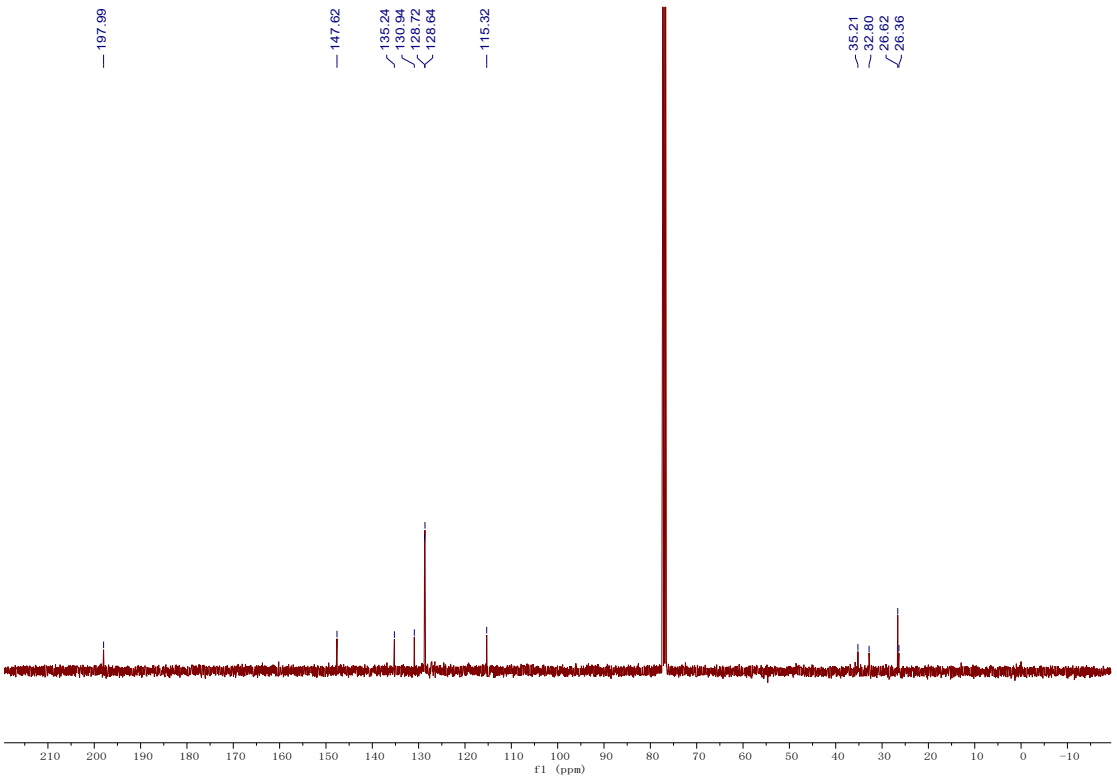

166.65
147.16
144.10
129.75
129.49
128.46
128.41
127.33
125.42
118.96
115.80
60.85
35.20
32.96
14.36
f1 (ppm)


7.97
7.95
7.26
7.25
7.24
7.07
7.07
7.05
7.05
7.03
7.03
7.00
7.00
6.99
6.98
6.74
6.74
6.73
6.72
6.71
6.70
6.69
6.69
6.67
6.67
3.90
3.53
3.00
2.99
2.98
2.97
2.82
2.80
2.80
2.78
NH2
COOMe
3e
2.02
1.98
1.00
0.94
1.02
0.91
3.15
1.96
2.00
1.98
167.15
147.31
144.13
129.80
129.49
128.54
128.05
127.36
125.40
118.96
115.81
52.05
35.20
32.95


7.57
7.56
7.27
7.08
7.06
7.04
6.95
6.93
6.74
6.72
6.70
6.68
3.55
3.02
3.00
2.98
2.81
2.79
2.77
NH2
CN
3f
2.01
1.99
1.11
1.02
1.90
1.94
2.10
2.00
f1 (ppm)

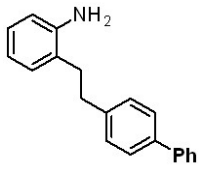

147.36
144.04
132.23
129.47
129.31
127.52
124.83
119.05
119.00
115.88
109.97
35.08
32.73
f1 (ppm)


7.90
7.88
7.29
7.27
7.08
7.06
7.04
7.01
6.99
6.75
6.73
6.71
6.70
6.68
3.55
3.02
3.00
2.98
2.83
2.81
2.79
2.59
NH2
Ac
3g
2.00
2.19
1.14
1.05
2.05
1.99
2.00
2.02
3.09
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5

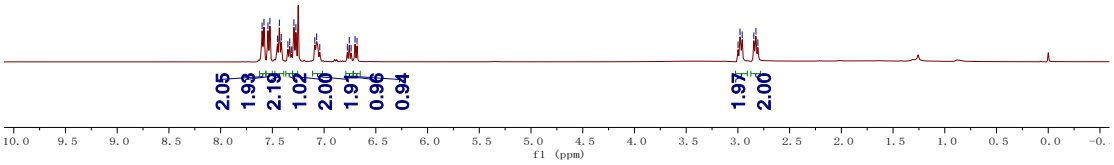

197.99
147.62
135.24
130.94
128.72
128.64
115.32
35.21
32.80
26.62
26.36
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

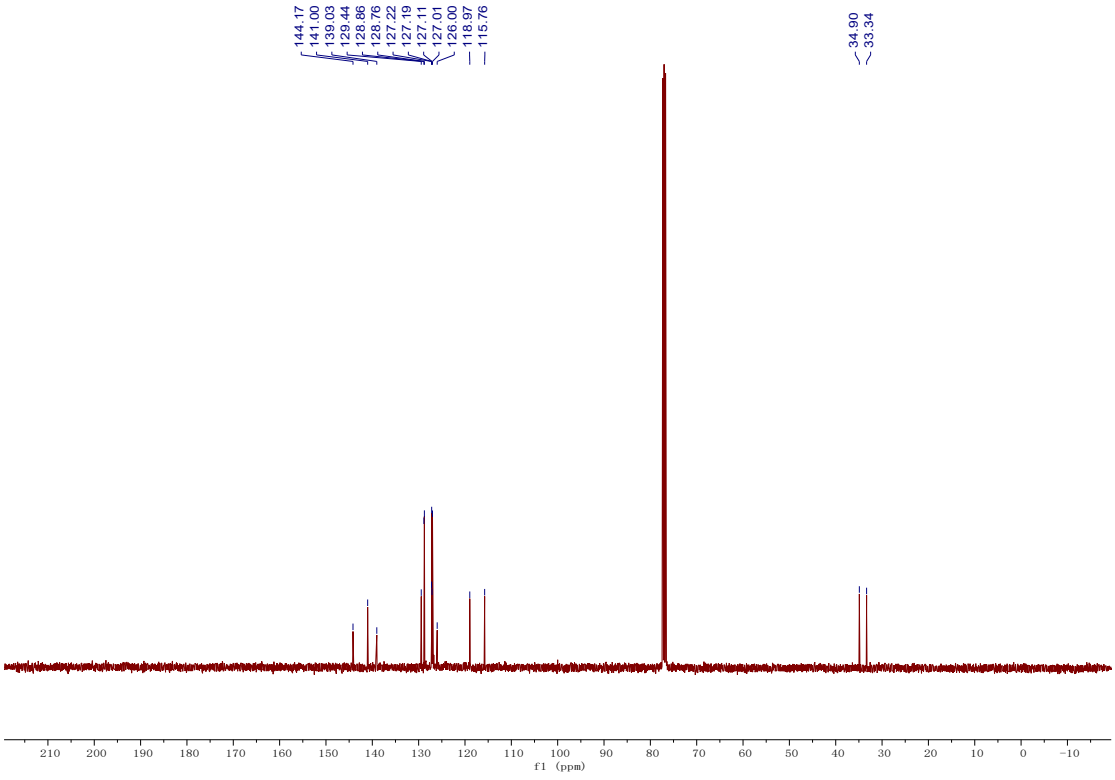

7.60
7.58
7.54
7.52
7.45
7.43
7.41
7.35
7.33
7.31
7.29
7.27
7.09
7.07
7.04
6.78
6.76
6.74
6.70
6.68

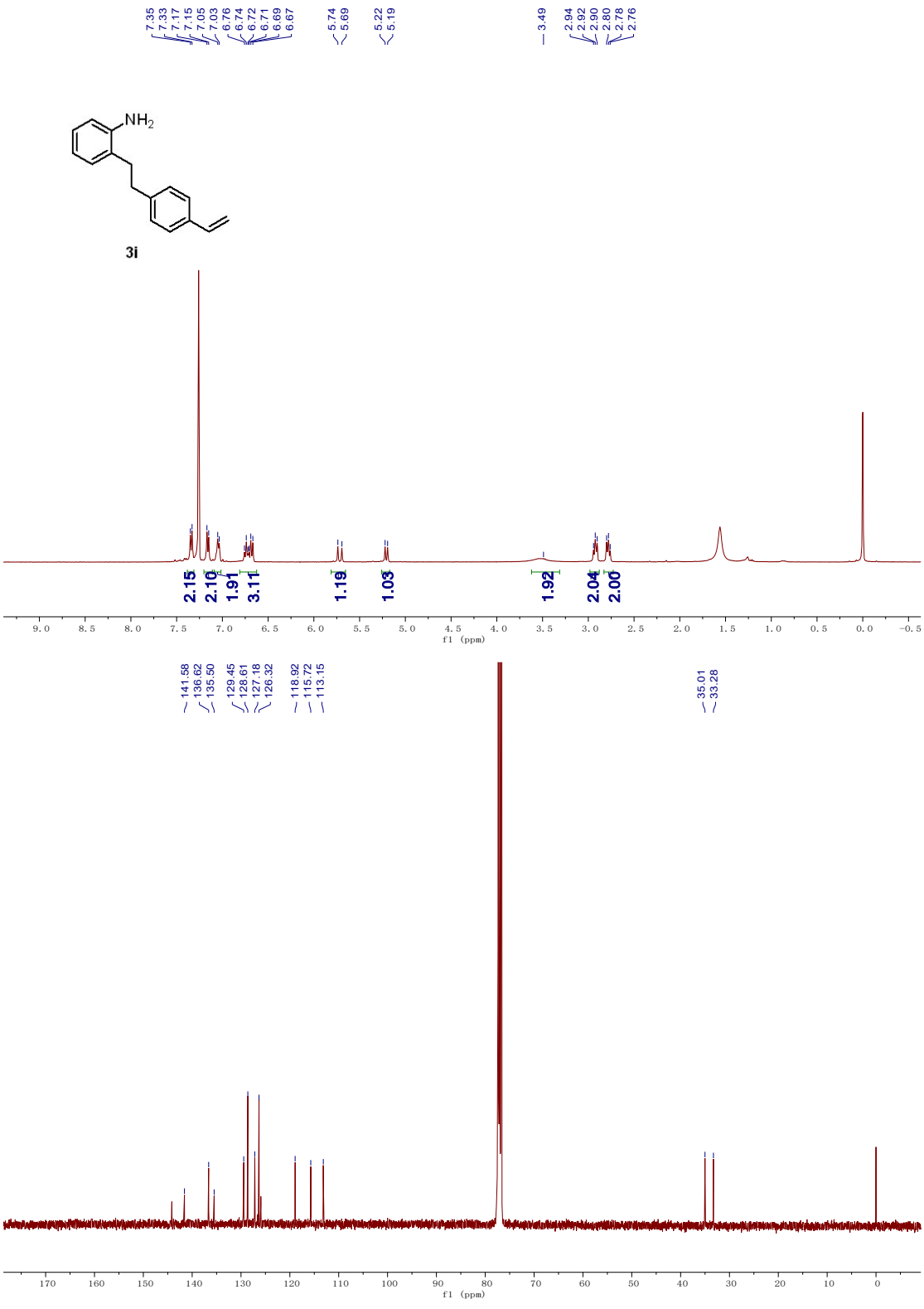

3.00
2.98
2.96
2.85
2.83
2.81

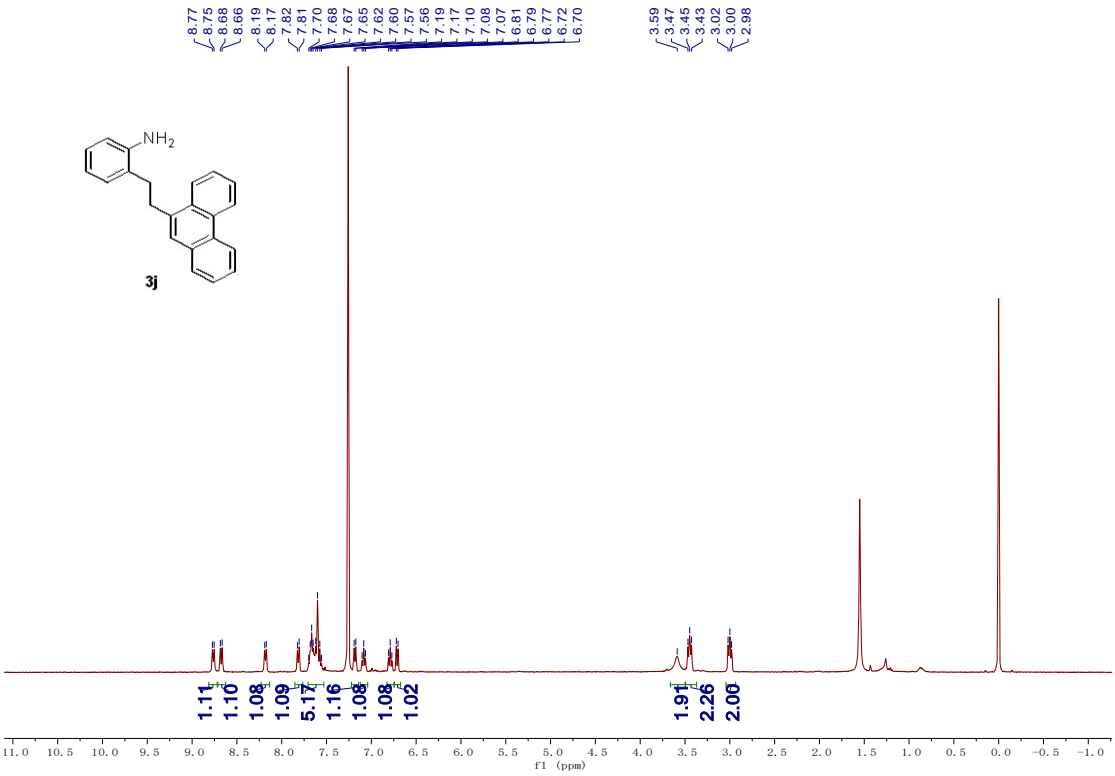

NH2
Ph

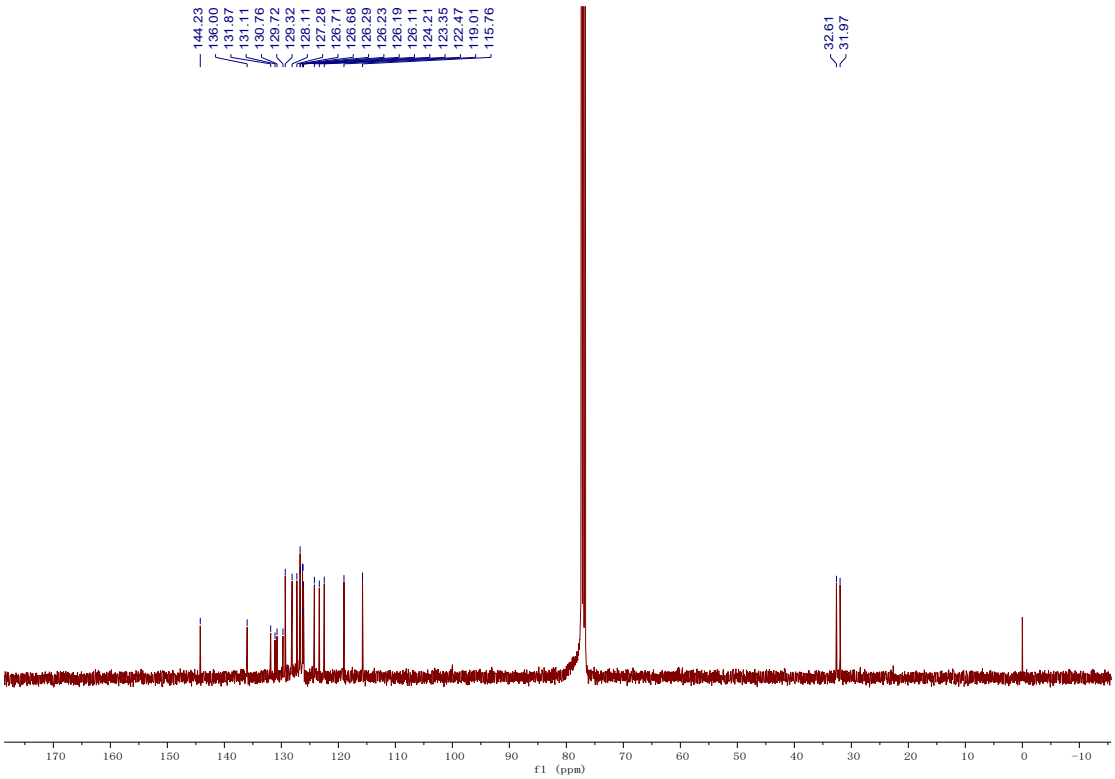
3h

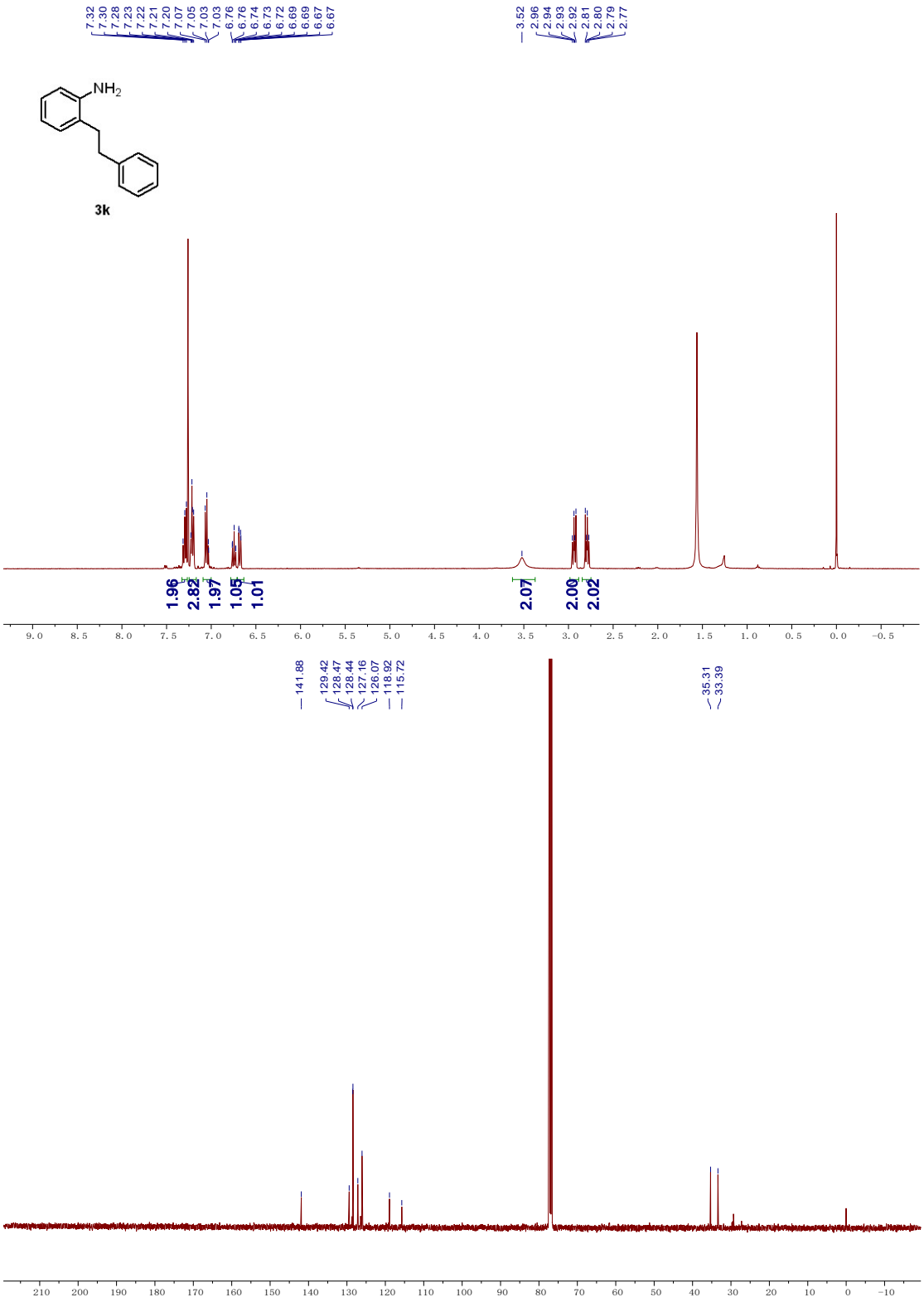

2.05
1.93
2.19
1.02
2.00
1.97
0.96
0.94
1.97
2.00
f1 (ppm)

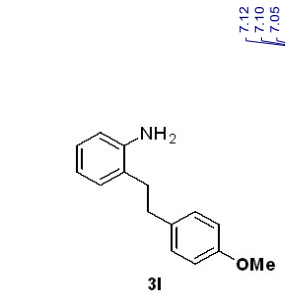

144.17
141.00
139.03
129.44
128.86
128.76
127.22
127.19
127.11
127.01
126.00
118.97
115.76
34.90
33.34
f1 (ppm)


7.35
7.33
7.17
7.15
7.05
7.03
6.76
6.74
6.72
6.71
6.69
6.67
5.74
5.69
5.22
5.19
3.49
2.94
2.92
2.90
2.80
2.78
2.76
NH2
3i
2.15
2.16
1.91
3.11
1.19
1.03
1.92
2.04
2.00
f1 (ppm)
141.58
136.62
135.50
129.45
128.61
127.18
126.32
118.92
115.72
113.15
35.01
33.28
f1 (ppm)


8.77
8.75
8.68
8.66
8.19
8.17
7.82
7.81
7.70
7.68
7.67
7.65
7.62
7.60
7.57
7.56
7.19
7.17
7.10
7.08
7.07
6.81
6.79
6.77
6.72
6.70
3.59
3.47
3.45
3.43
3.02
3.00
2.98
NH2
3j
1.11
1.10
1.08
1.09
5.17
1.16
1.08
1.08
1.02
1.91
2.26
2.00
f1 (ppm)

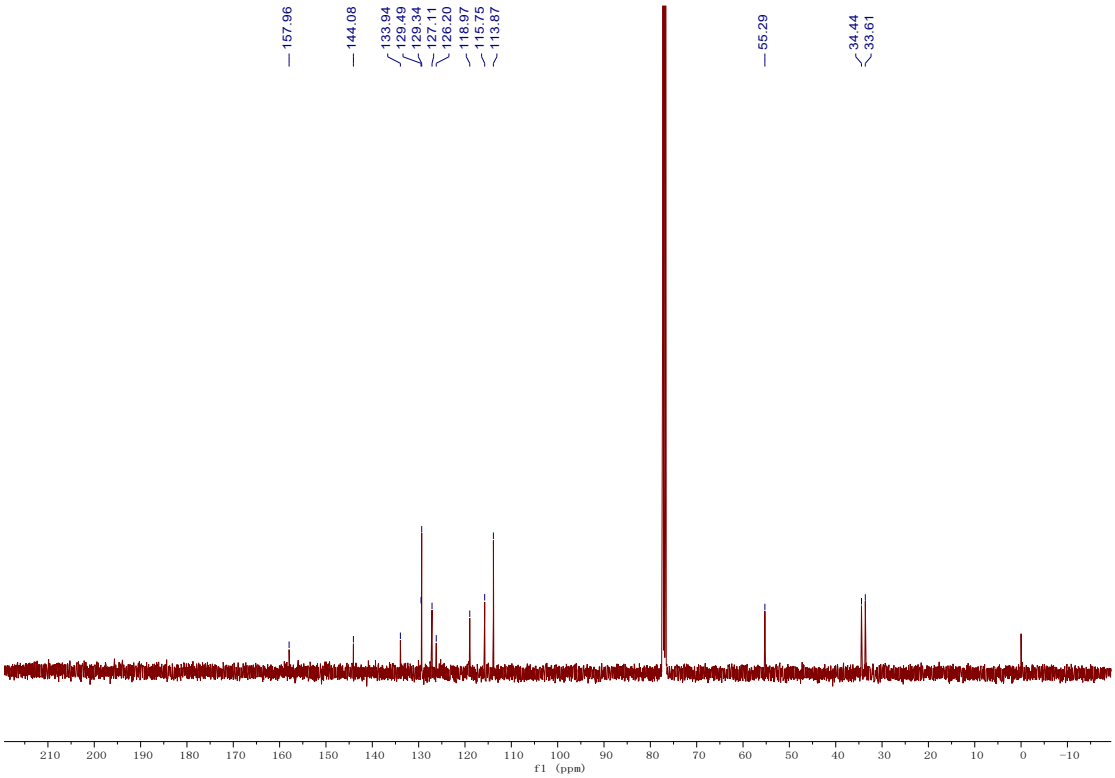

144.23
136.00
131.87
131.11
130.76
129.72
129.32
128.11
127.28
126.71
126.68
126.29
126.23
126.19
126.11
124.21
123.35
122.47
119.01
115.76
32.61
31.97
f1 (ppm)

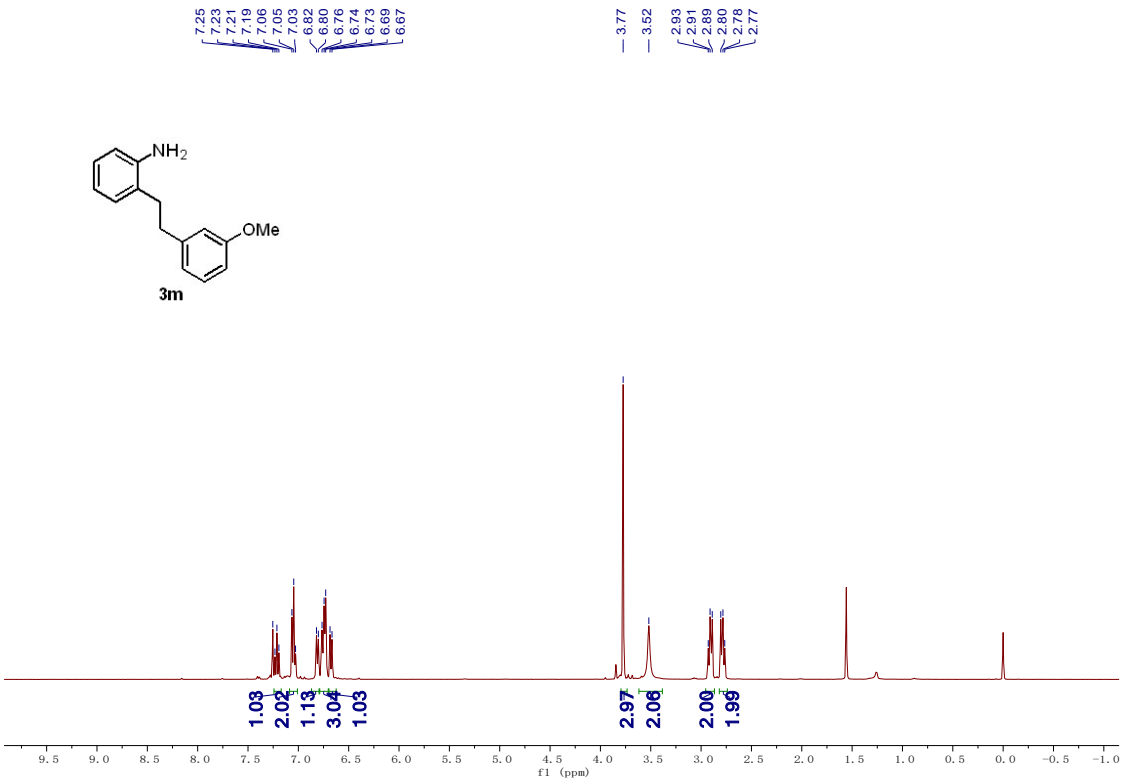

7.32
7.30
7.28
7.23
7.22
7.21
7.20
7.07
7.05
7.03
7.03
6.76
6.76
6.74
6.73
6.72
6.69
6.69
6.67
6.67
3.52
2.96
2.94
2.93
2.92
2.81
2.80
2.79
2.77
NH2
3k
1.96
2.82
1.97
1.05
1.01
2.07
2.00
2.02
141.88
129.42
128.47
128.44
127.16
126.07
118.92
115.72
35.31
33.39

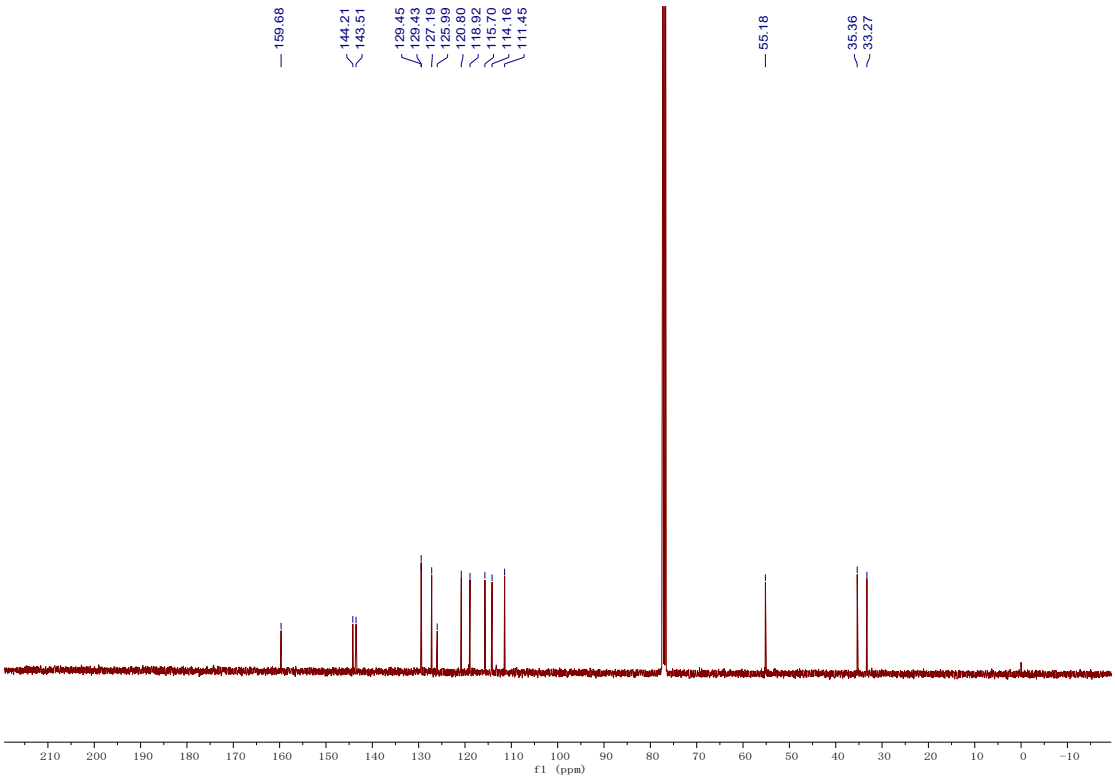

NH2
OMe

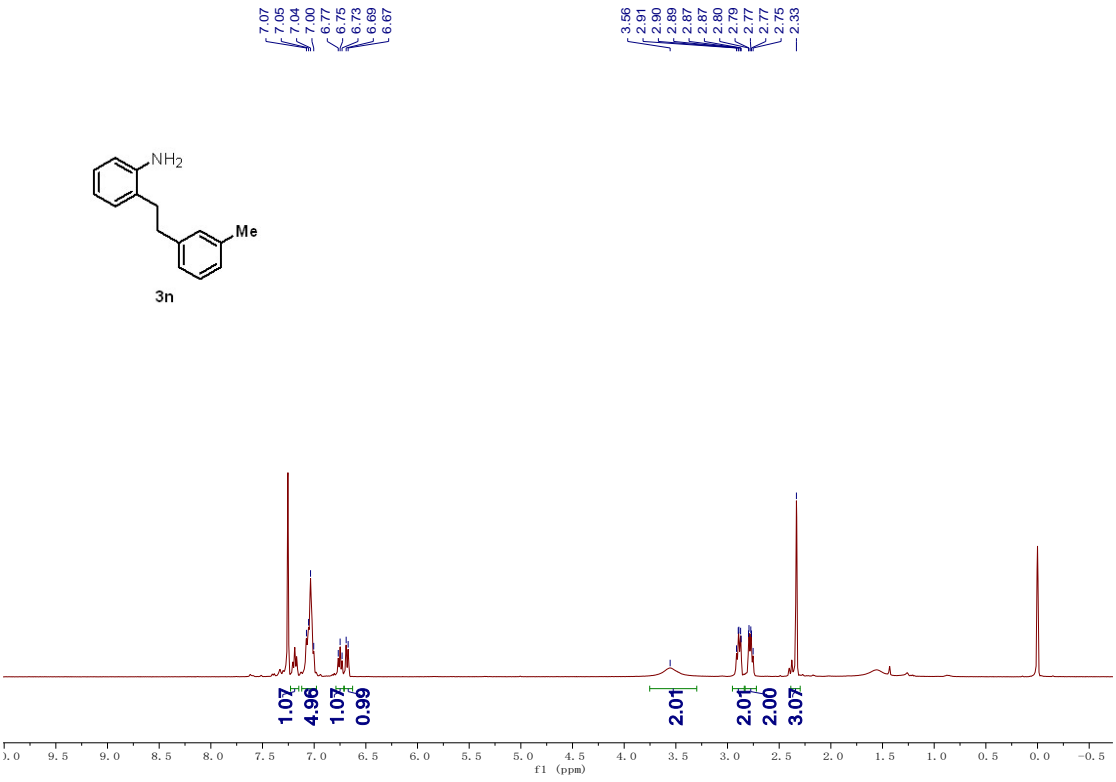
3l

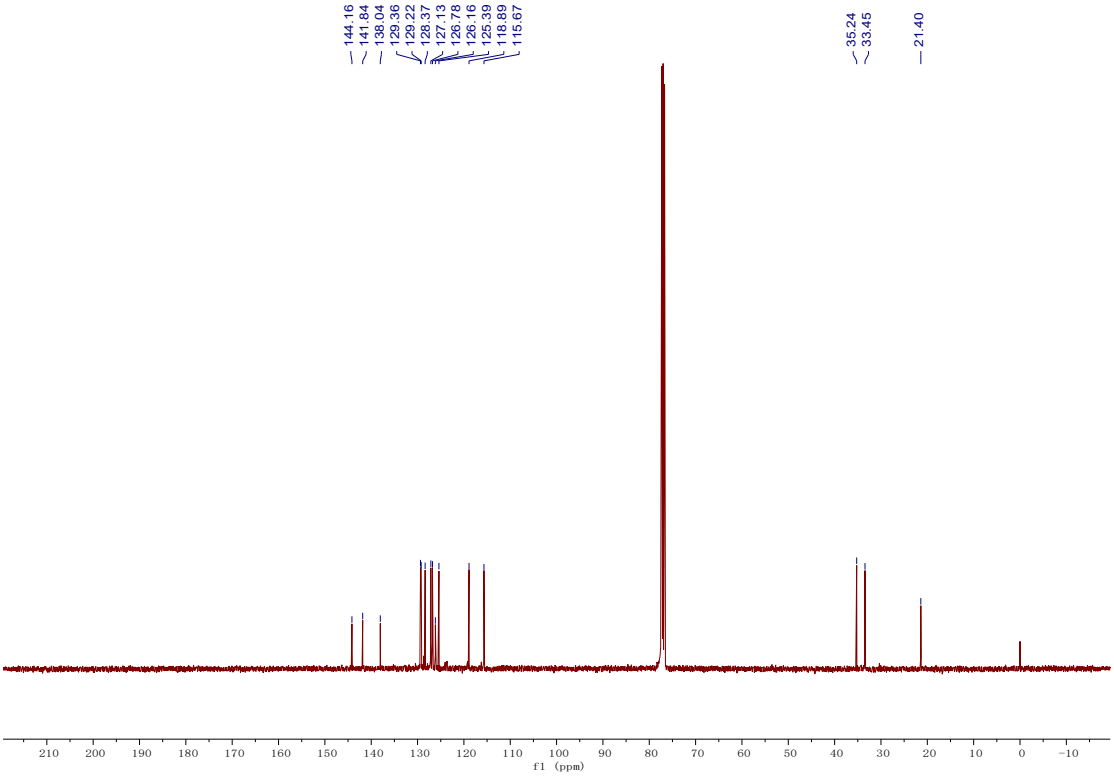
7.12
7.10
7.05
7.04
6.84
6.82
6.76
6.74
6.72
6.69
6.67
3.79
2.90
2.88
2.86
2.78
2.76
2.74
2.01
1.98
2.00
1.07
1.03
3.22
2.11
2.08
f1 (ppm)

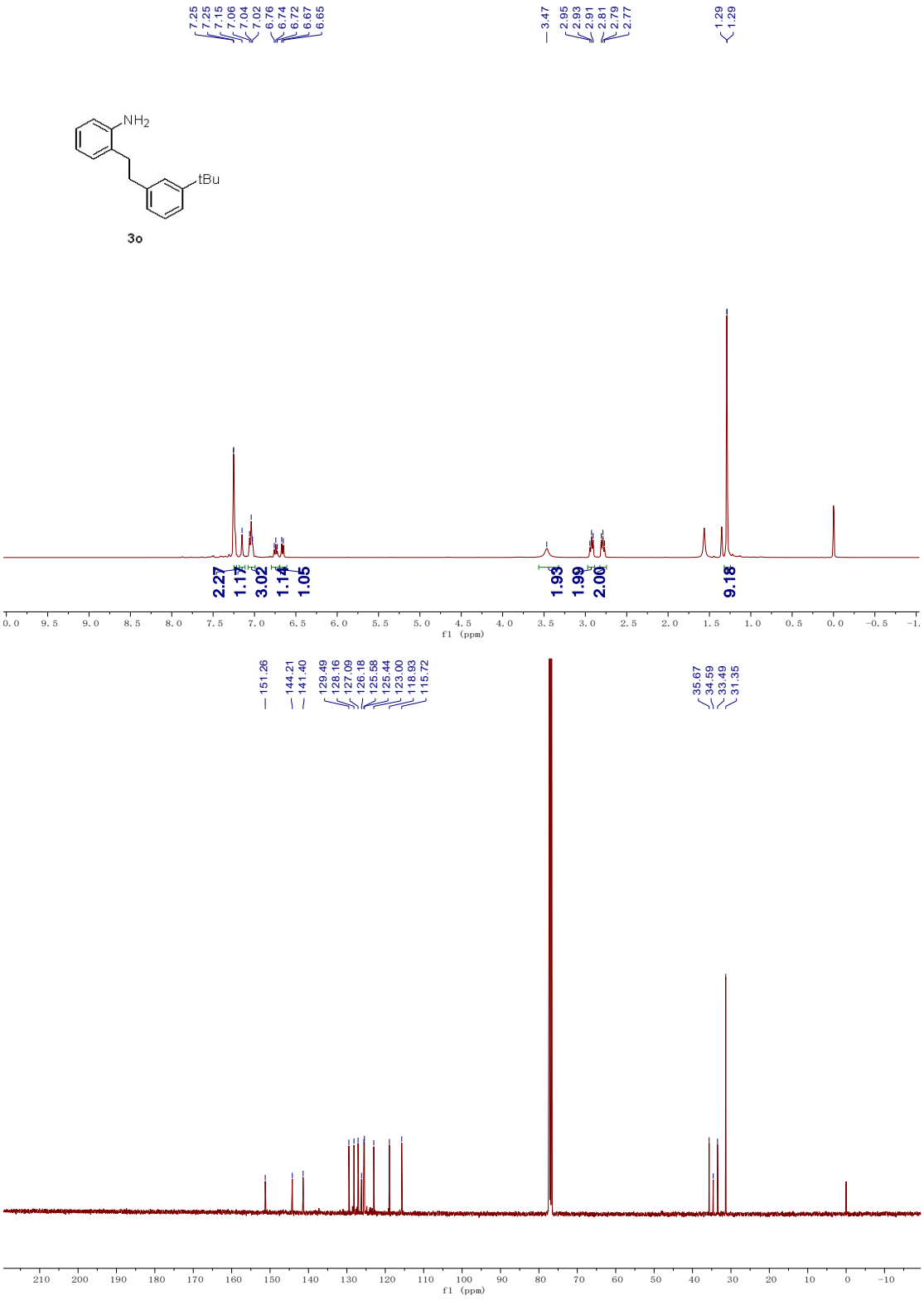

157.96
144.08
133.94
129.49
129.34
127.11
126.20
118.97
115.75
113.87
55.29
34.44
33.61
f1 (ppm)

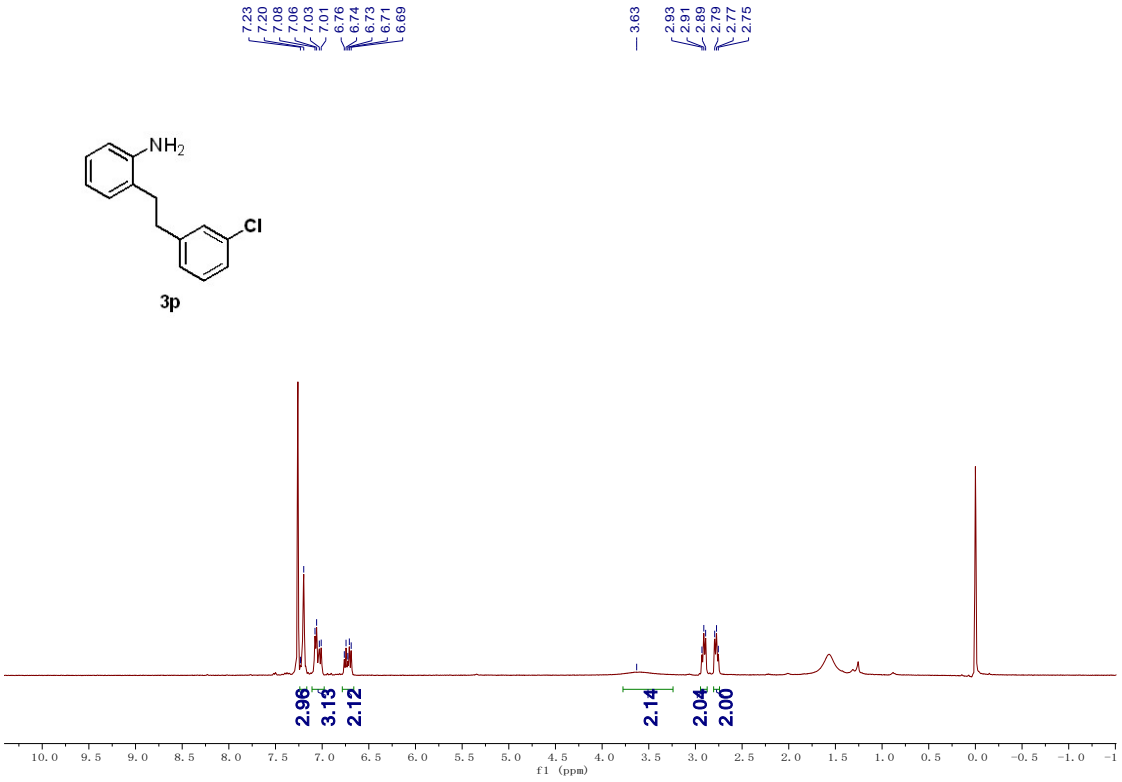

7.25
7.23
7.21
7.19
7.06
7.05
7.03
6.82
6.80
6.76
6.74
6.73
6.69
6.67
3.77
3.52
2.93
2.91
2.89
2.80
2.78
2.77
NH2
OMe
3m
1.03
2.02
1.13
3.04
1.03
2.97
2.06
2.00
1.99
f1 (ppm)

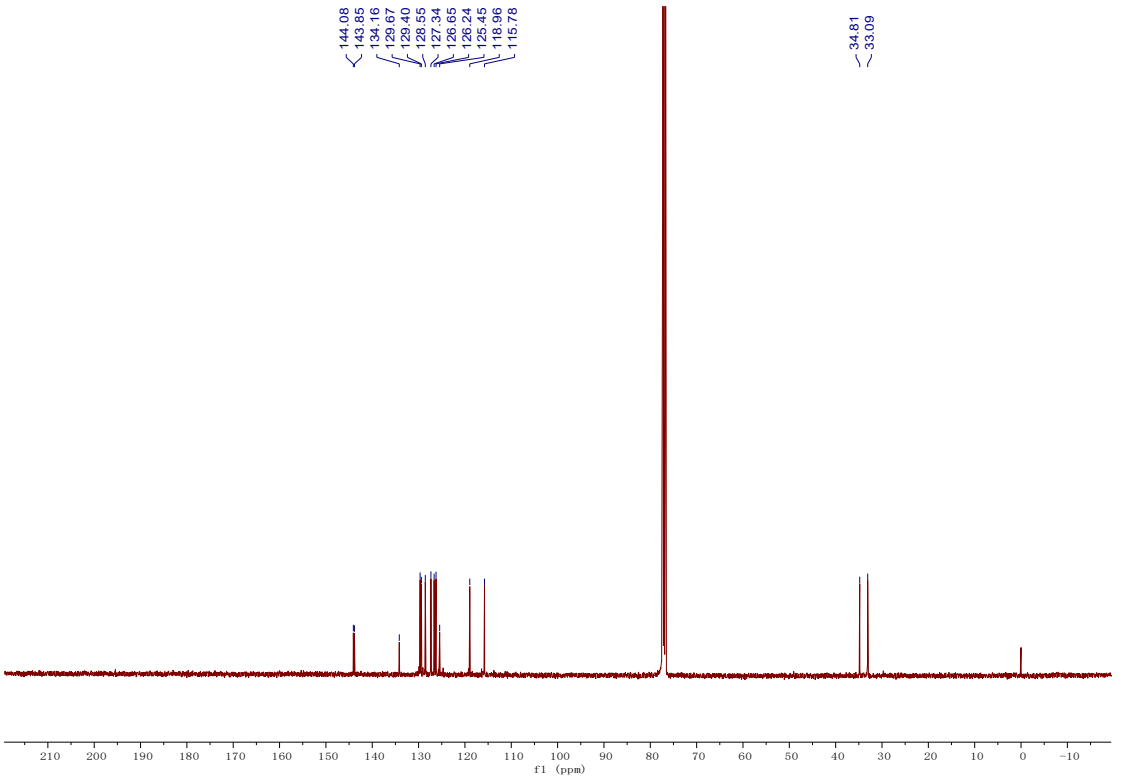

159.68
144.21
143.51
129.45
129.43
127.19
125.99
120.80
118.92
115.70
114.16
111.45
55.18
35.36
33.27
f1 (ppm)

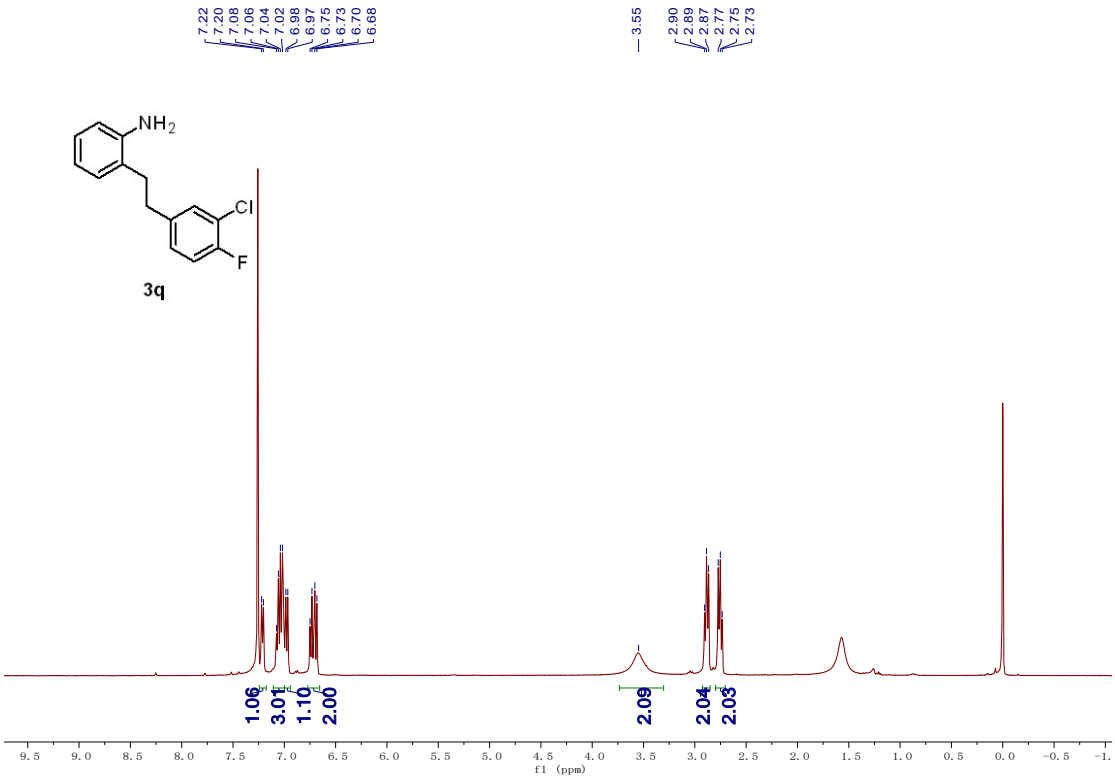

7.07
7.05
7.04
7.00
6.77
6.75
6.73
6.69
6.67
3.56
2.91
2.90
2.89
2.87
2.87
2.80
2.79
2.77
2.77
2.75
2.33
NH2
Me
3n
1.07
4.96
1.07
0.99
2.01
2.01
2.00
3.07
f1 (ppm)

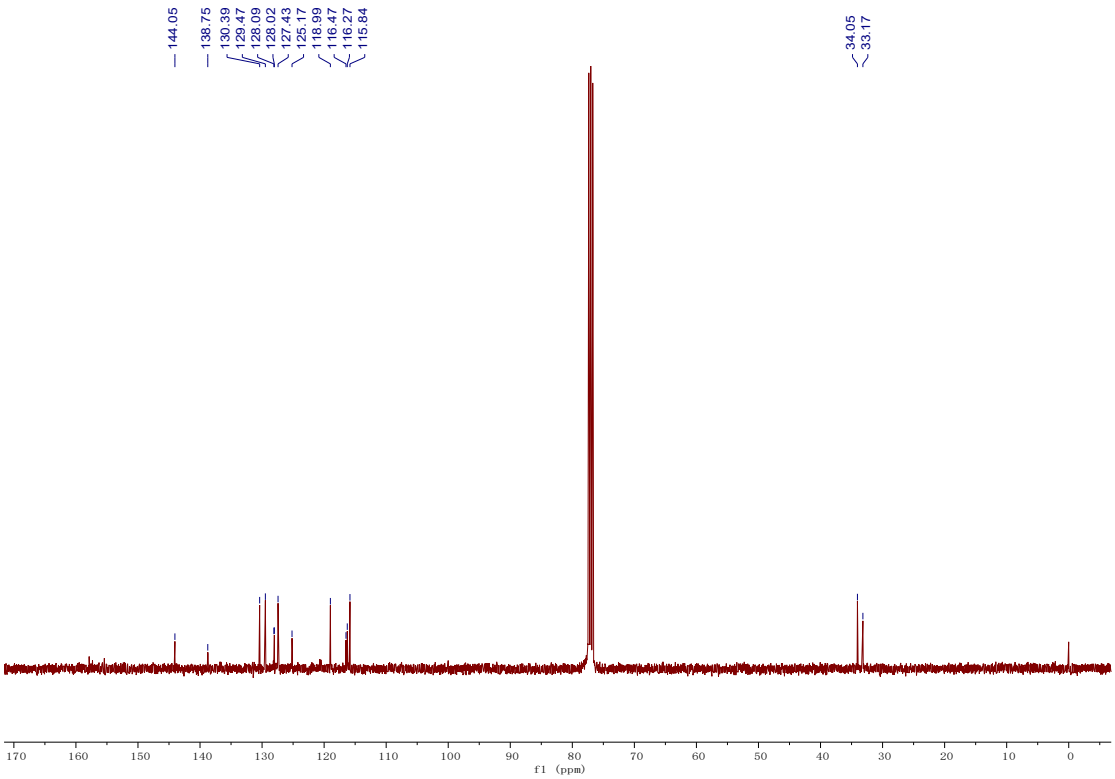

144.16
141.84
138.04
129.36
129.22
128.37
127.13
126.78
126.16
125.39
118.89
115.67
35.24
33.45
21.40
f1 (ppm)

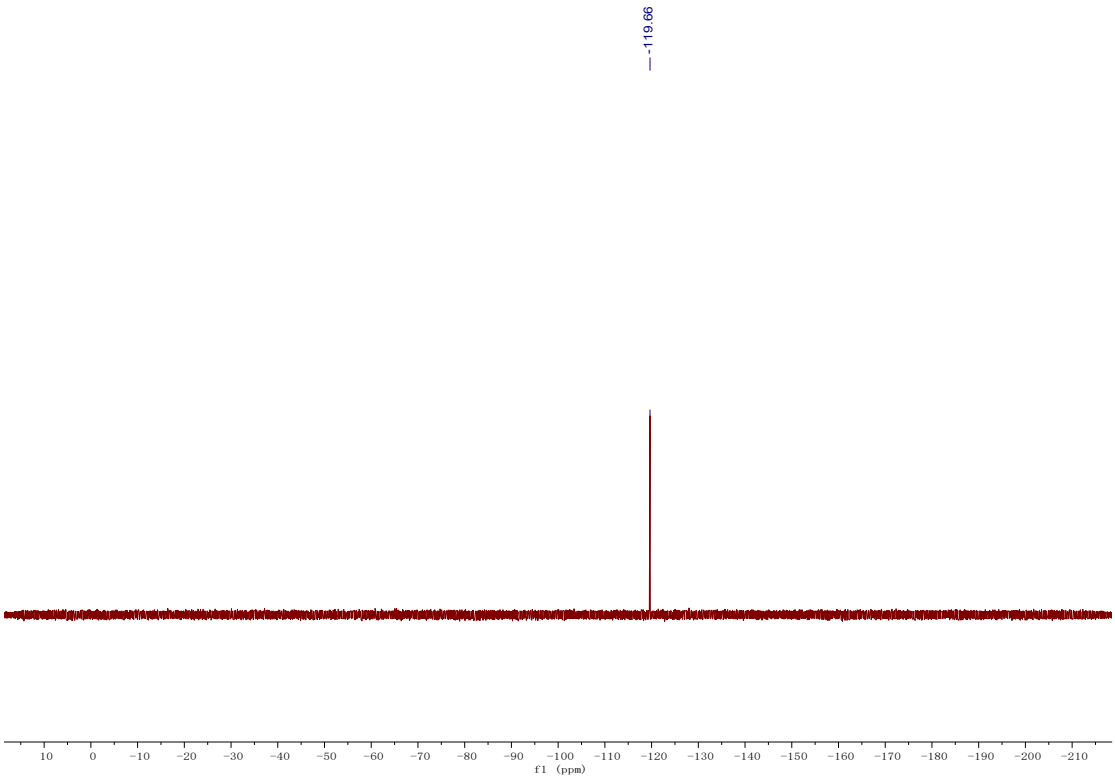

7.25
7.25
7.15
7.06
7.04
7.02
6.76
6.74
6.72
6.67
6.65
3.47
2.95
2.93
2.91
2.81
2.79
2.77
1.29
1.29
NH2
tBu
3o
2.27
1.17
3.02
1.14
1.05
1.93
1.99
2.00
9.18
f1 (ppm)
151.26
144.21
141.40
129.49
128.16
127.09
126.18
125.58
125.44
123.00
118.93
115.72
35.67
34.59
33.49
31.35
f1 (ppm)

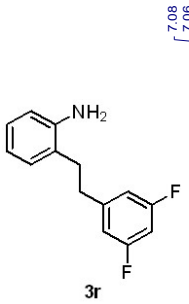

7.23
7.20
7.08
7.06
7.03
7.01
6.76
6.74
6.73
6.71
6.69
3.63
2.93
2.91
2.89
2.79
2.77
2.75
NH2
Cl
3p
2.96
3.13
2.12
2.14
2.04
2.00
f1 (ppm)


144.08
143.85
134.16
129.67
129.40
128.55
127.34
126.65
126.24
125.45
118.96
115.78
34.81
33.09
f1 (ppm)


7.22
7.20
7.08
7.06
7.04
7.02
6.98
6.97
6.75
6.73
6.70
6.68
3.55
2.90
2.89
2.87
2.77
2.75
2.73
NH2
Cl
F
3q
1.06
3.01
1.10
2.00
2.09
2.04
2.03
f1 (ppm)

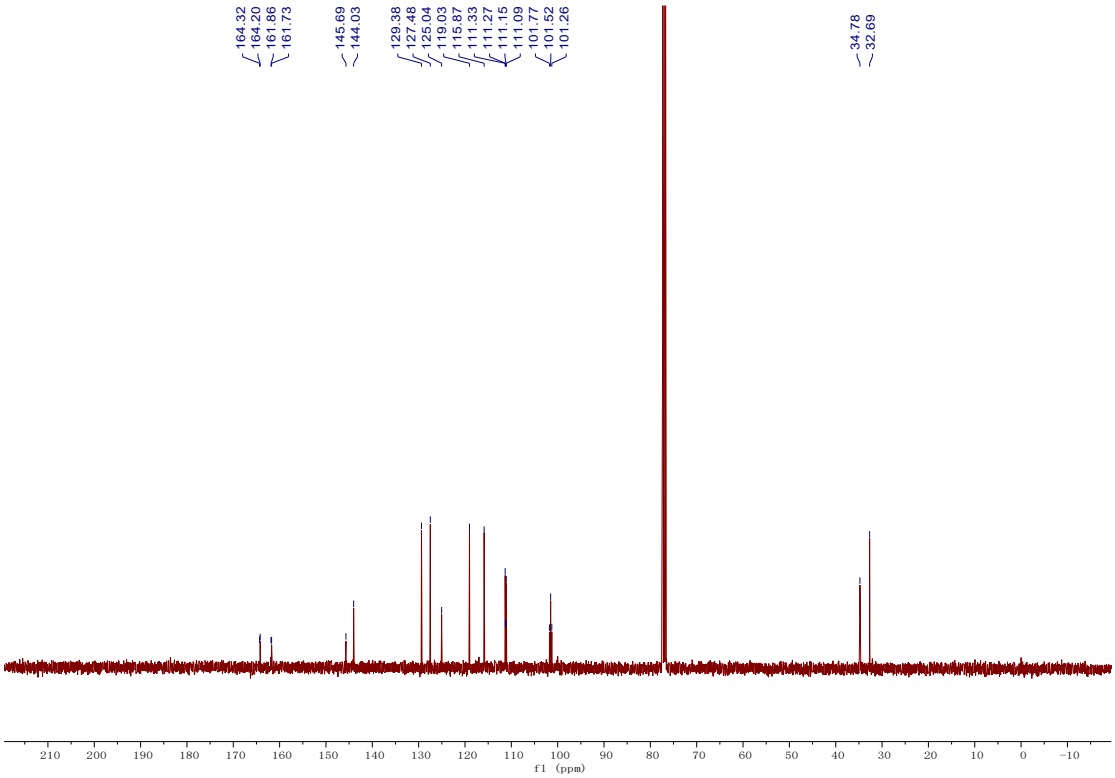

144.05
138.75
130.39
129.47
128.09
128.02
127.43
125.17
118.99
116.47
116.27
115.84
34.05
33.17
f1 (ppm)

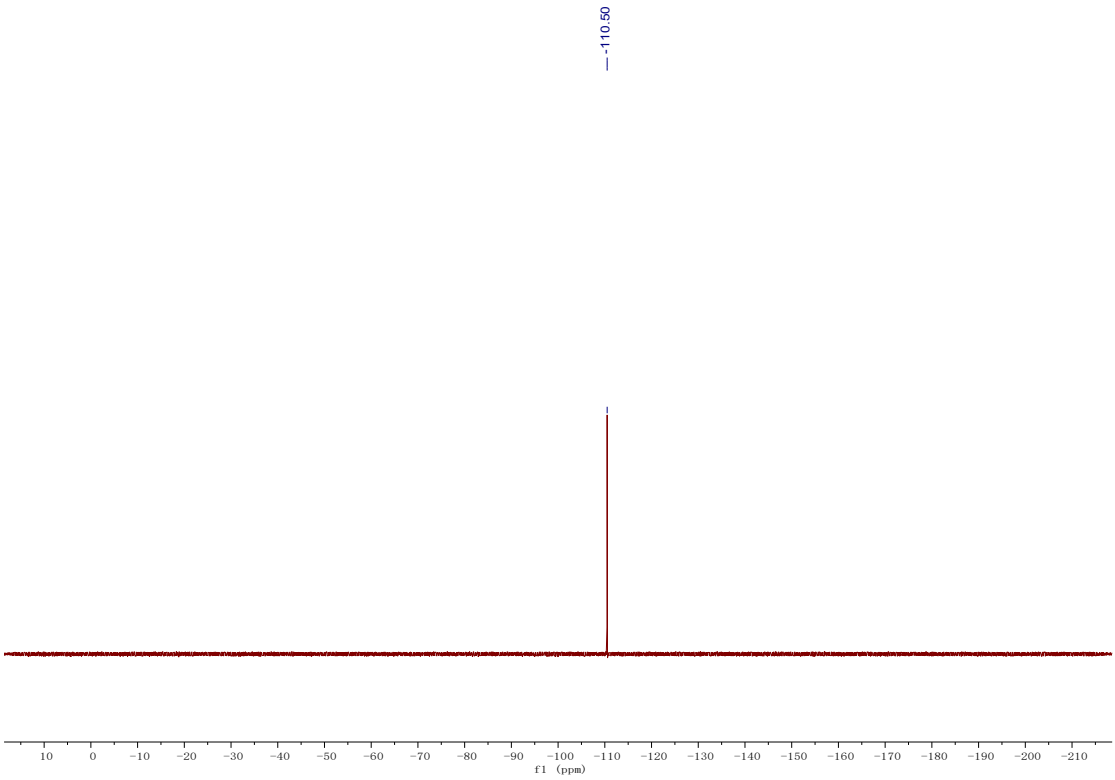

-119.66
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

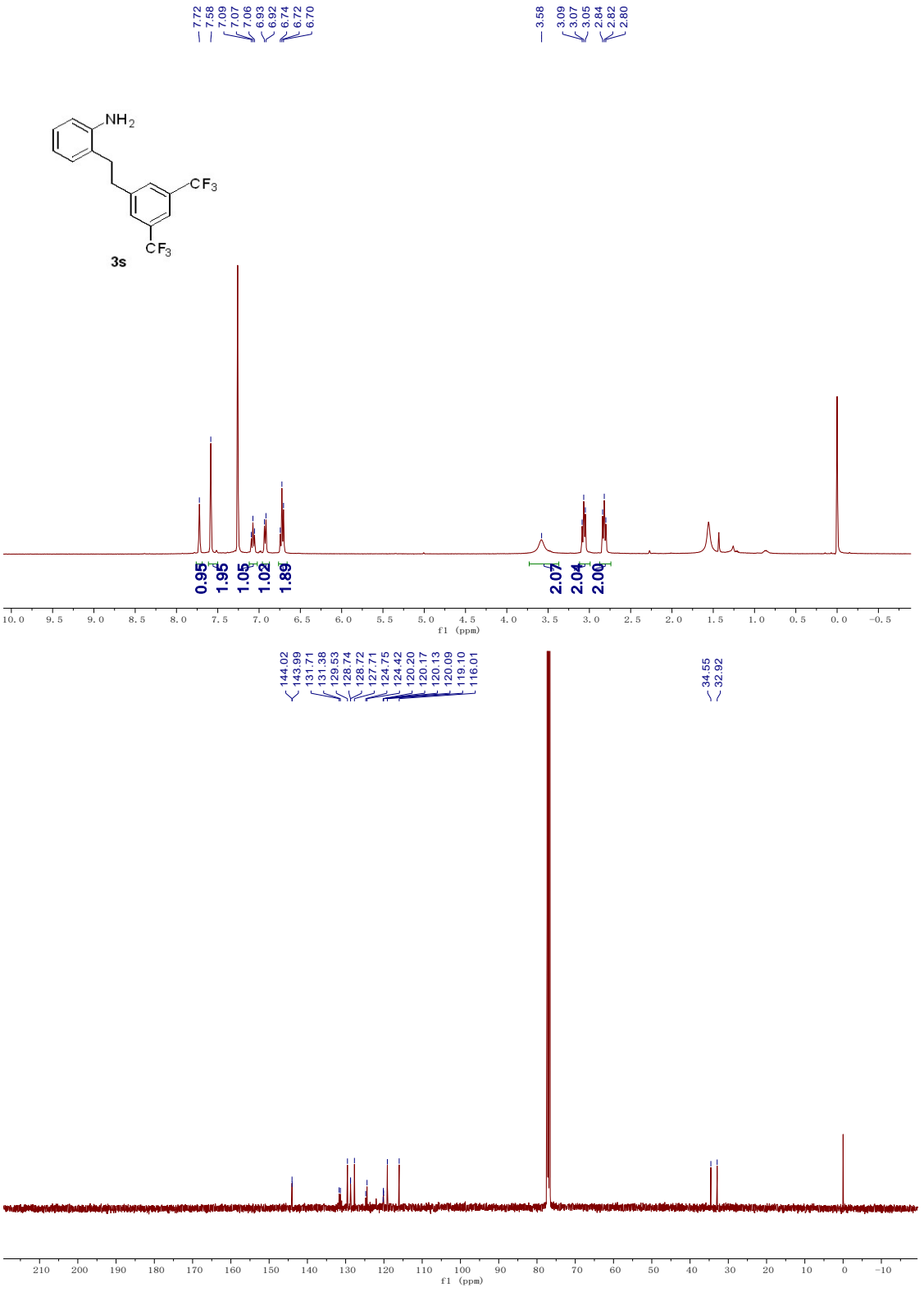

NH2
F
F

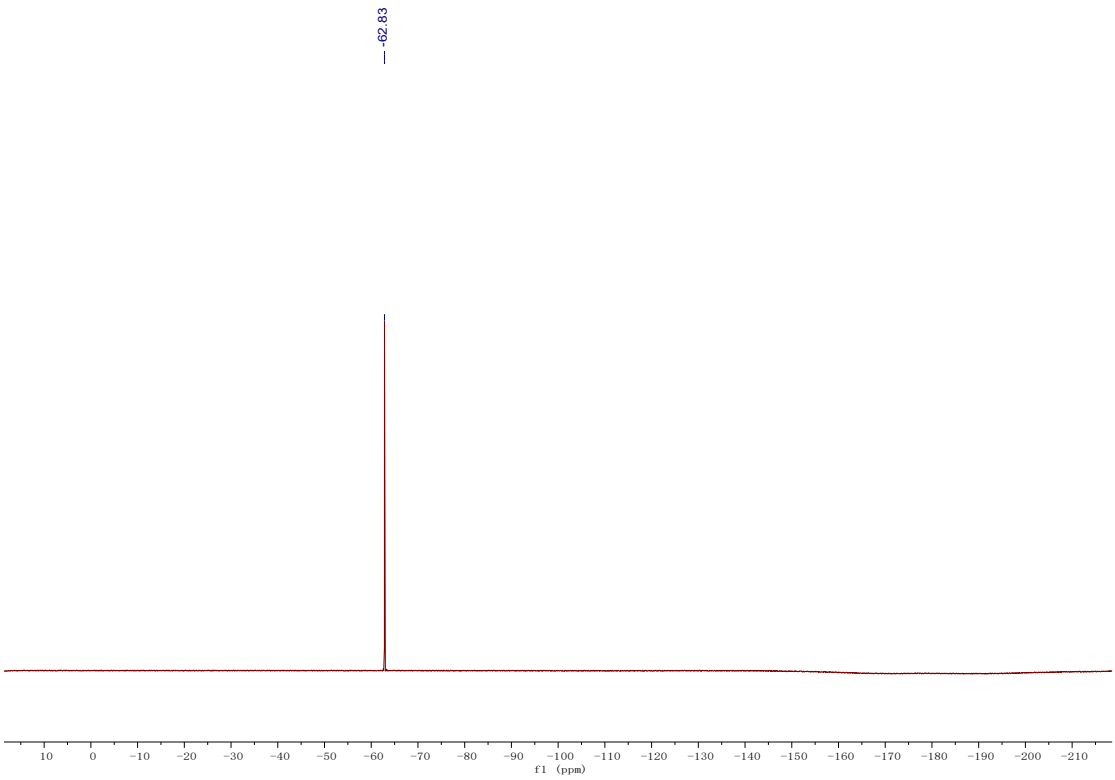
3r

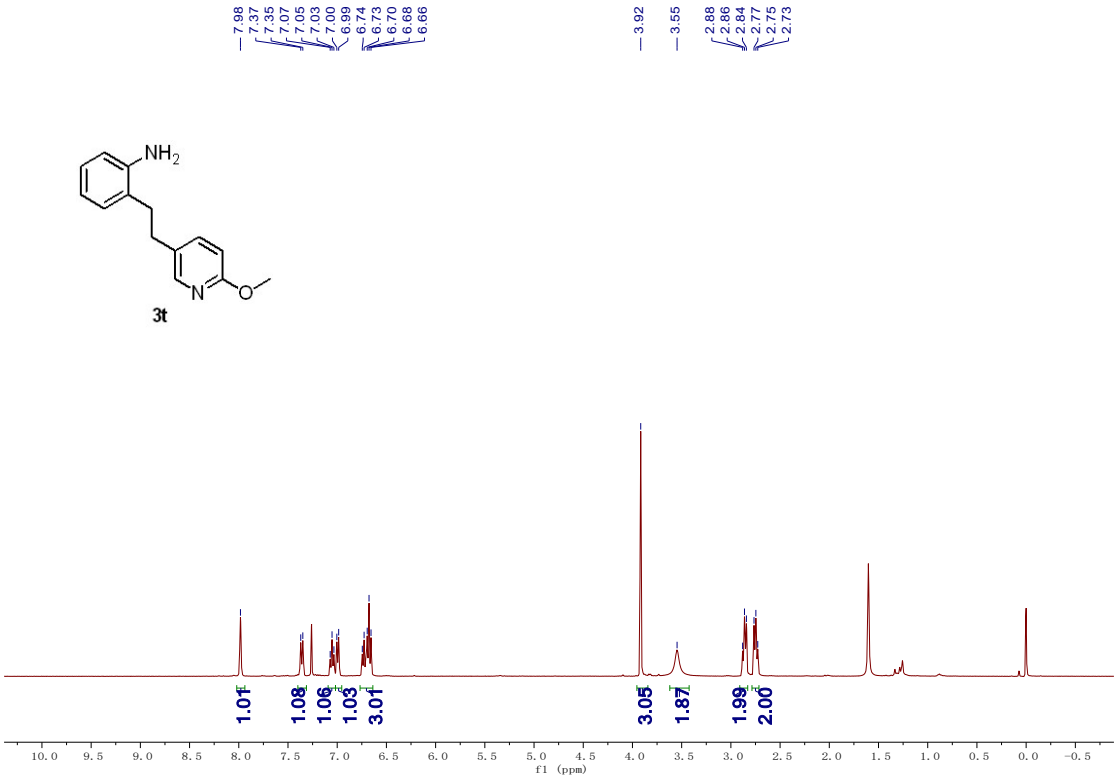
7.08
7.06
7.04
7.00
6.98
6.75
6.74
6.72
6.70
6.69
6.67
6.65
6.62
3.55
2.94
2.92
2.90
2.79
2.77
2.75
1.01
1.00
4.92
1.89
2.07
2.10
f1 (ppm)

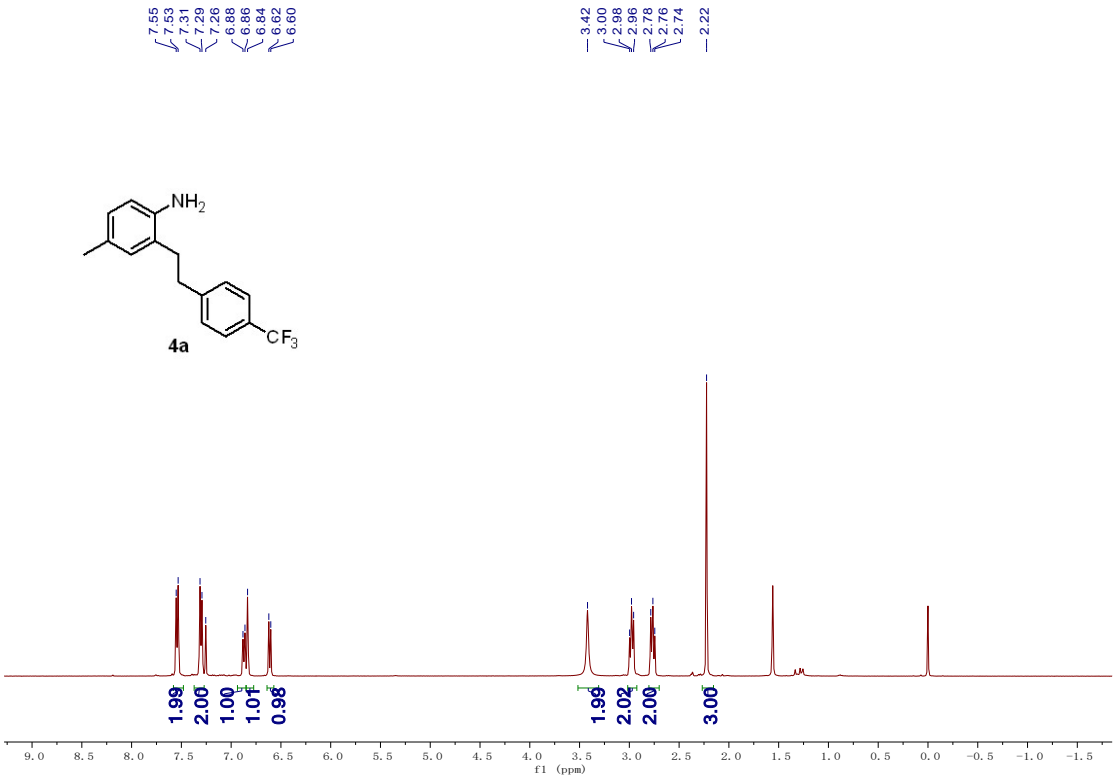

164.32
164.20
161.86
161.73
145.69
144.03
129.38
127.48
125.04
119.03
115.87
111.33
111.27
111.15
111.09
101.77
101.52
101.26
34.78
32.69
f1 (ppm)

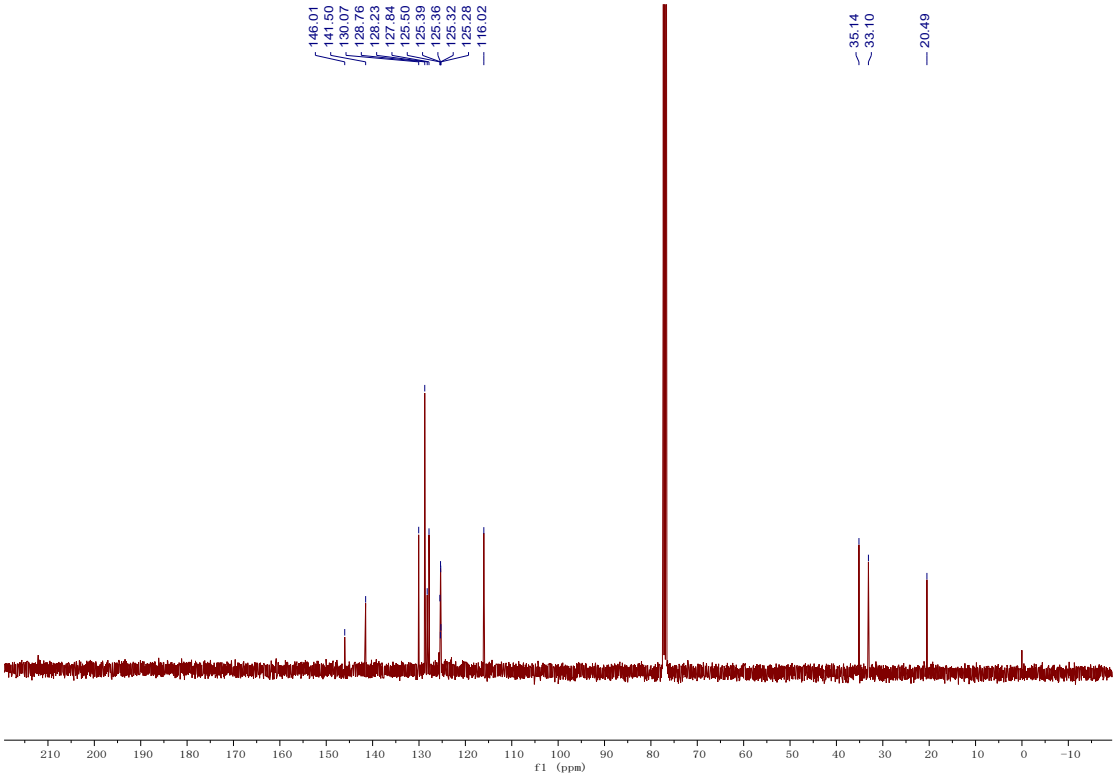

-110.50
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

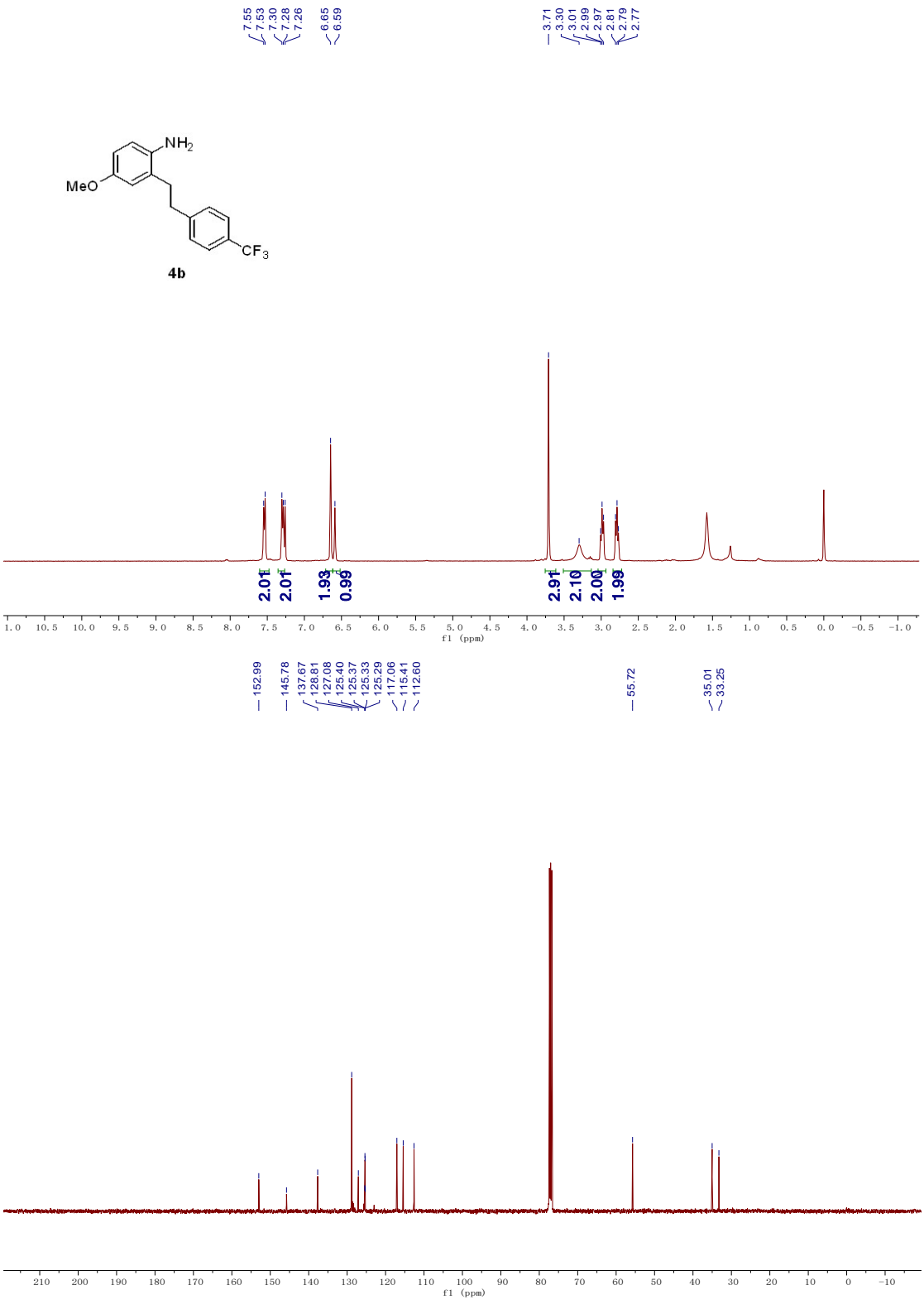

7.72
7.58
7.09
7.07
7.06
6.93
6.92
6.74
6.72
6.70
3.58
3.09
3.07
3.05
2.84
2.82
2.80
NH2
CF3
CF3
3s
0.95
1.95
1.05
1.02
1.89
2.07
2.04
2.00
f1 (ppm)
144.02
143.99
131.71
131.38
129.53
128.74
128.72
127.71
124.75
124.42
120.20
120.17
120.13
120.09
119.10
116.01
34.55
32.92
f1 (ppm)

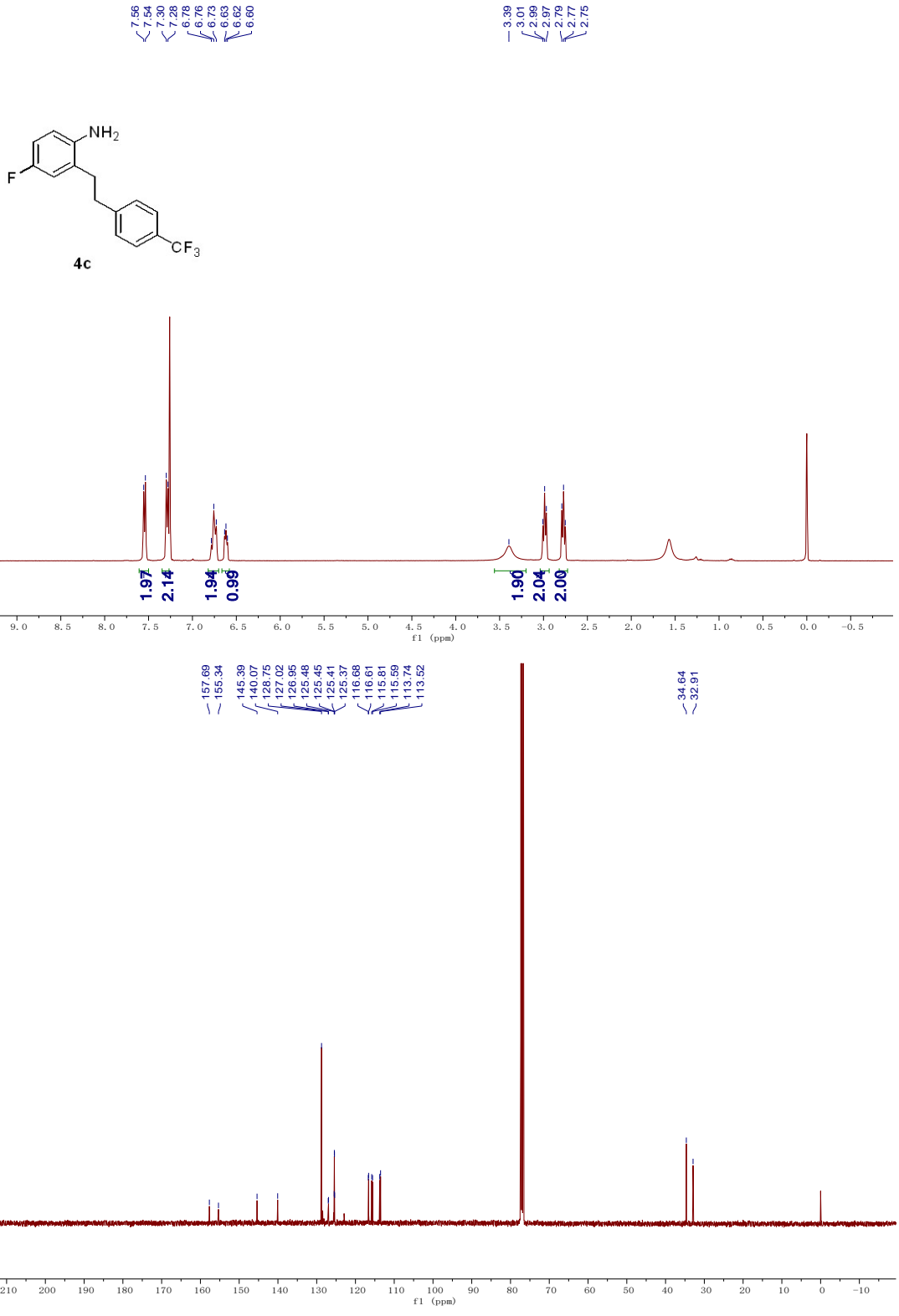

-62.83
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)

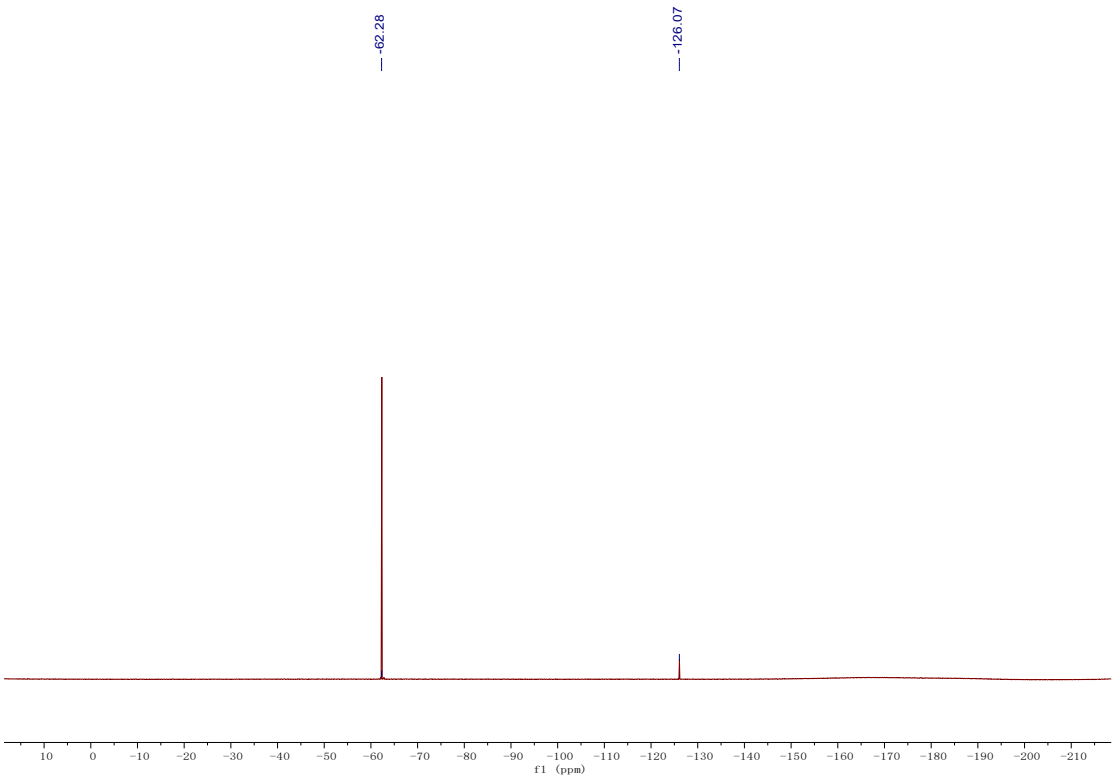

7.98
7.37
7.35
7.07
7.05
7.03
7.00
6.99
6.74
6.73
6.70
6.68
6.66
3.92
3.55
2.88
2.86
2.84
2.77
2.75
2.73
NH2
N
O
3t
1.01
1.08
1.06
1.03
3.01
3.05
1.87
1.99
2.00
f1 (ppm)
162.84
146.09
144.04
139.01
129.62
129.51
127.34
125.36
118.97
115.81
110.44
100.00
53.35
33.25
31.24
f1 (ppm)

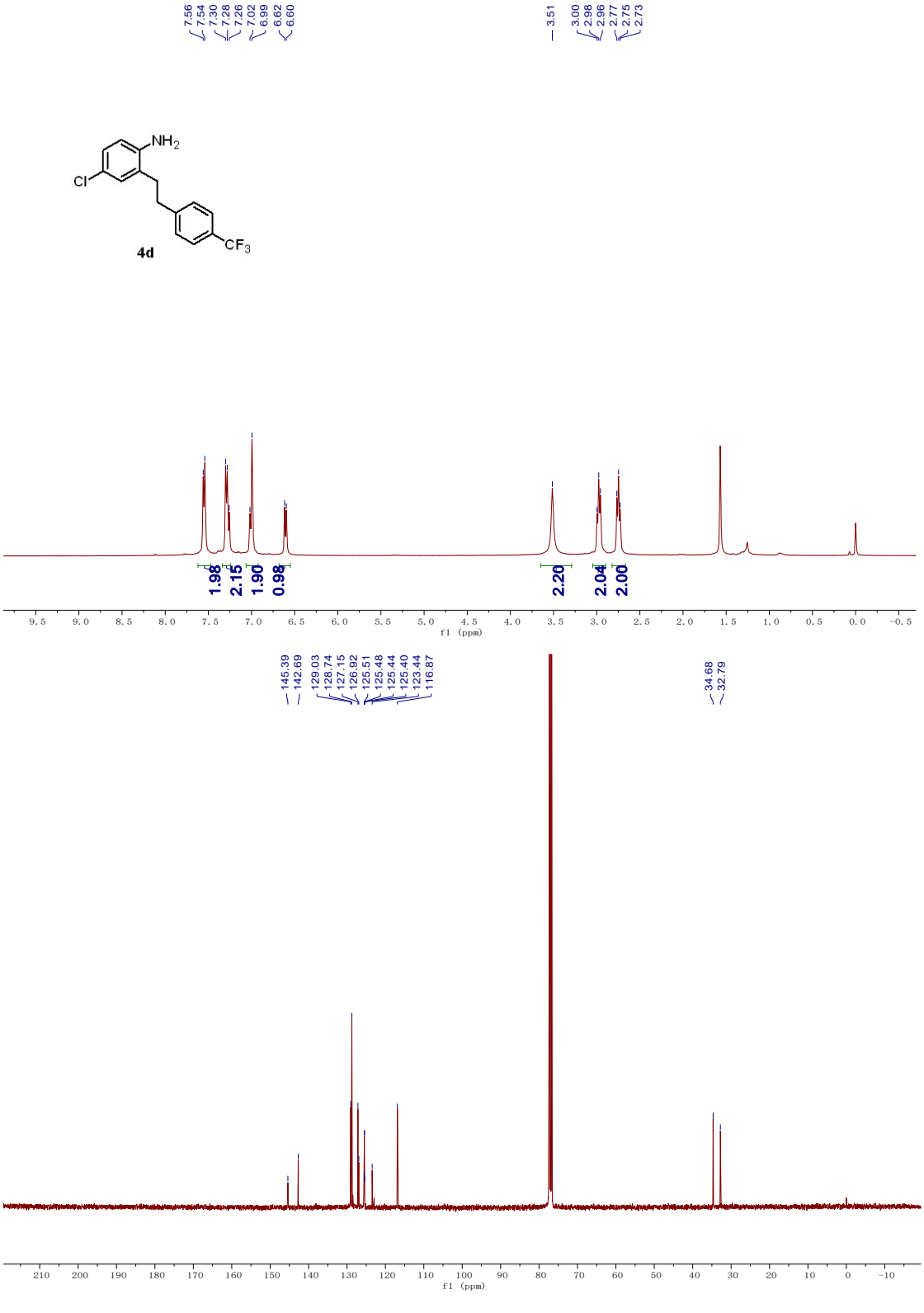

7.55
7.53
7.31
7.29
7.26
6.88
6.86
6.84
6.62
6.60
3.42
3.00
2.98
2.96
2.78
2.76
2.74
2.22
NH2
CF3
4a
1.99
2.00
1.00
1.01
0.98
1.99
2.02
2.00
3.00
f1 (ppm)


146.01
141.50
130.07
128.76
128.23
127.84
125.50
125.39
125.36
125.32
125.28
116.02
35.14
33.10
20.49
f1 (ppm)


7.55
7.53
7.30
7.28
7.26
6.65
6.59
3.71
3.30
3.01
2.99
2.97
2.81
2.79
2.77
NH2
MeO
CF3
4b
2.01
2.01
1.93
0.99
2.91
2.10
2.00
1.99
f1 (ppm)
152.99
145.78
137.67
128.81
127.08
125.40
125.37
125.33
125.29
117.06
115.41
112.60
55.72
35.01
33.25
f1 (ppm)

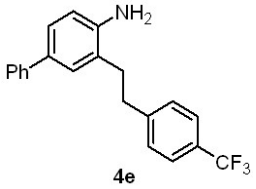

7.56
7.54
7.30
7.28
6.78
6.76
6.73
6.63
6.62
6.60
3.39
3.01
2.99
2.97
2.79
2.77
2.75
NH2
F
CF3
4c
1.97
2.14
1.94
0.99
1.90
2.04
2.00
f1 (ppm)
157.69
155.34
145.39
140.07
128.75
127.02
126.95
125.48
125.45
125.41
125.37
116.68
116.61
115.81
115.59
113.74
113.52
34.64
32.91
f1 (ppm)


-62.28
-126.07
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

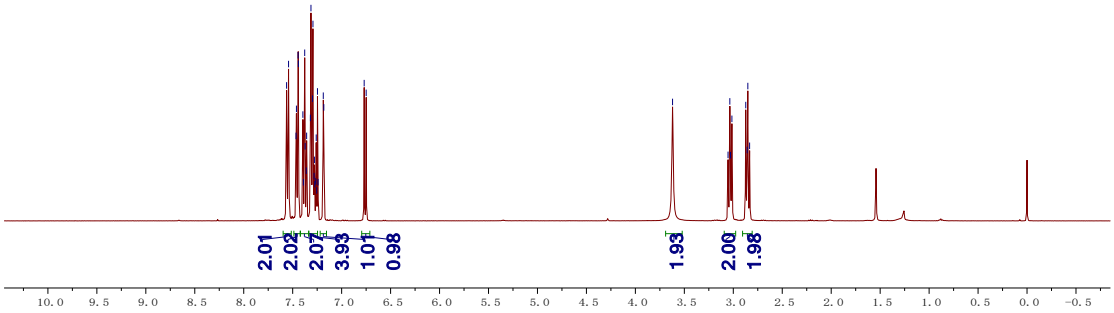

7.56
7.54
7.30
7.28
7.26
7.02
6.99
6.62
6.60
3.51
3.00
2.98
2.96
2.77
2.75
2.73
NH2
Cl
CF3
4d
1.98
2.15
1.90
0.98
2.20
2.04
2.00
f1 (ppm)
145.39
142.69
129.03
128.74
127.15
126.92
125.51
125.48
125.44
125.40
123.44
116.87
34.68
32.79
f1 (ppm)

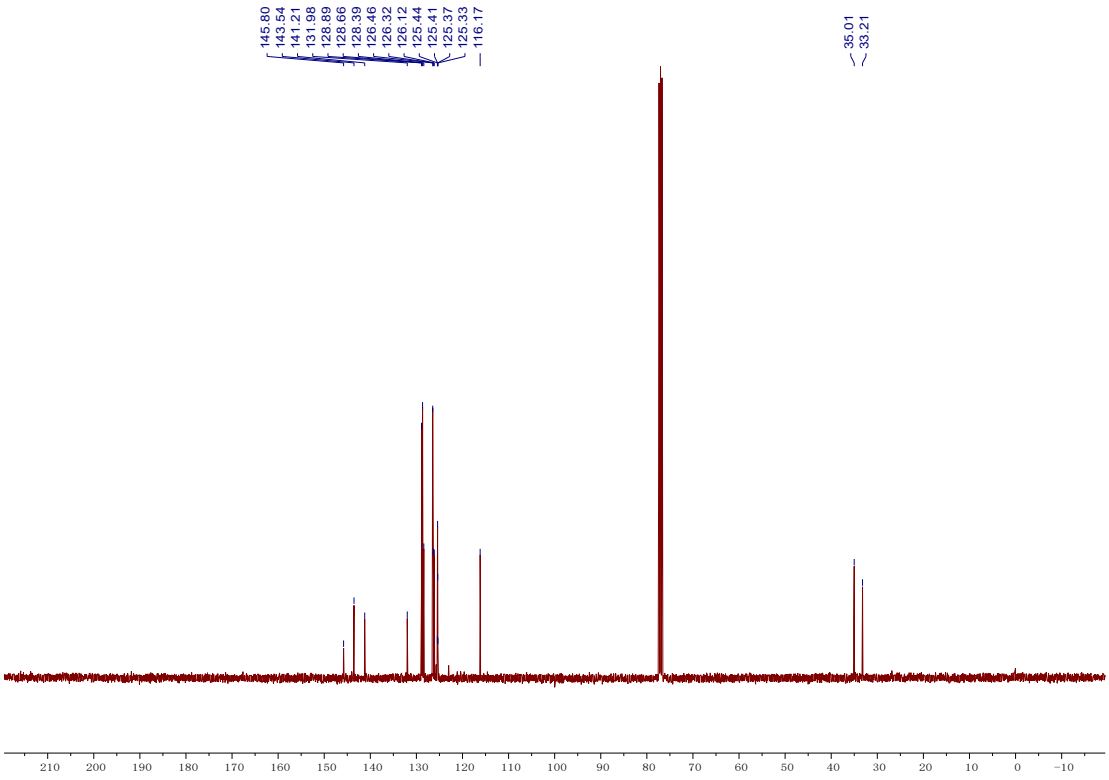

7.56
7.54
7.47
7.46
7.44
7.44
7.40
7.38
7.37
7.36
7.36
7.32
7.31
7.30
7.29
7.28
7.28
7.26
7.25
7.19
7.18
6.77
6.75

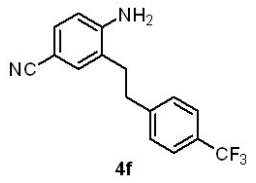

3.62
3.05
3.04
3.03
3.01
2.87
2.86
2.85
2.83


NH2
Ph
CF3

4e

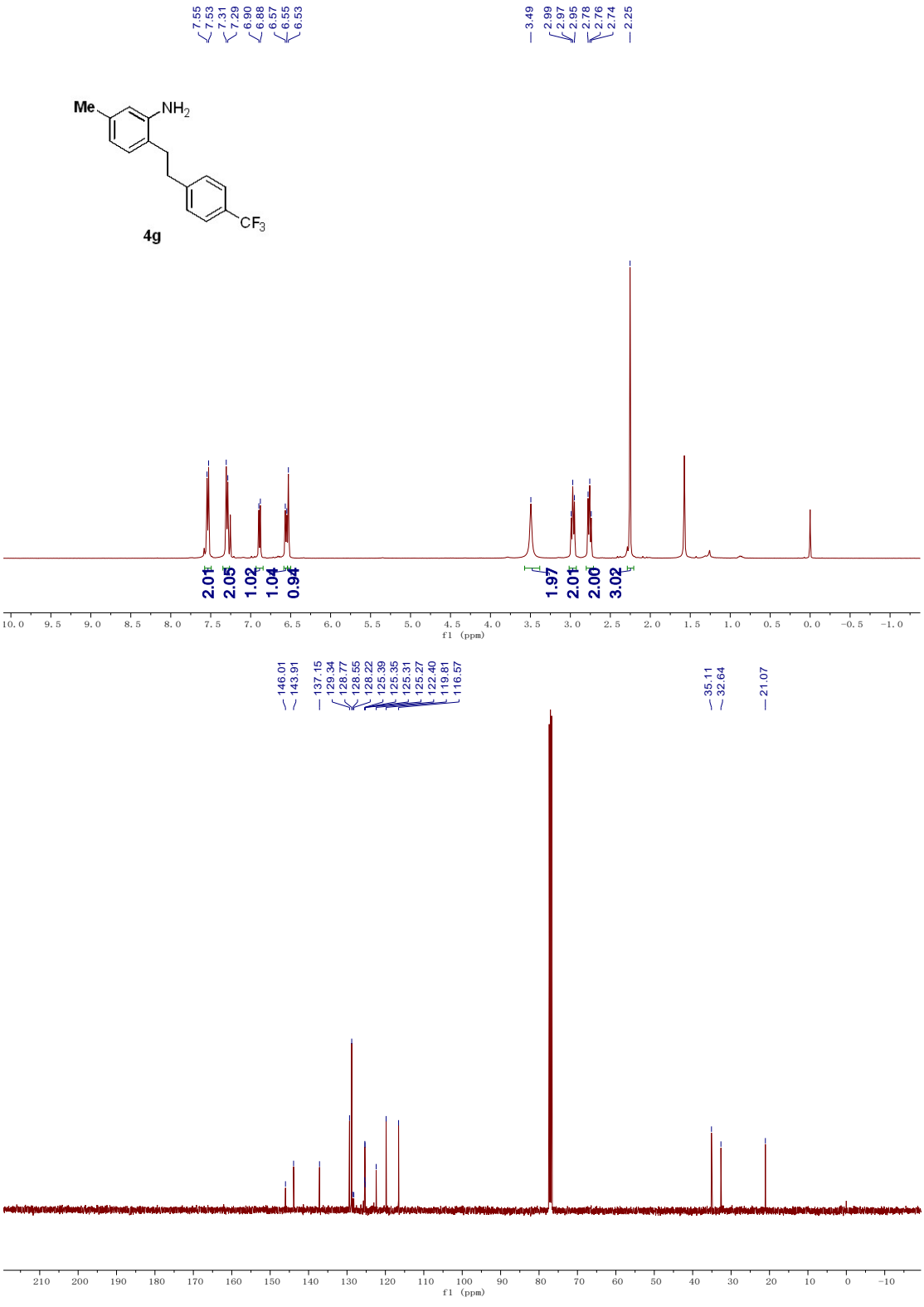

2.01
2.02
2.07
3.93
1.07
0.98
1.93
2.00
1.98
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5

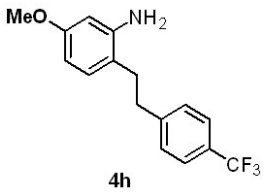

145.80
143.54
141.21
131.98
128.89
128.66
128.39
126.46
126.32
126.12
125.44
125.41
125.37
125.33
116.17
35.01
33.21
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10


NH2
NC
CF3

4f

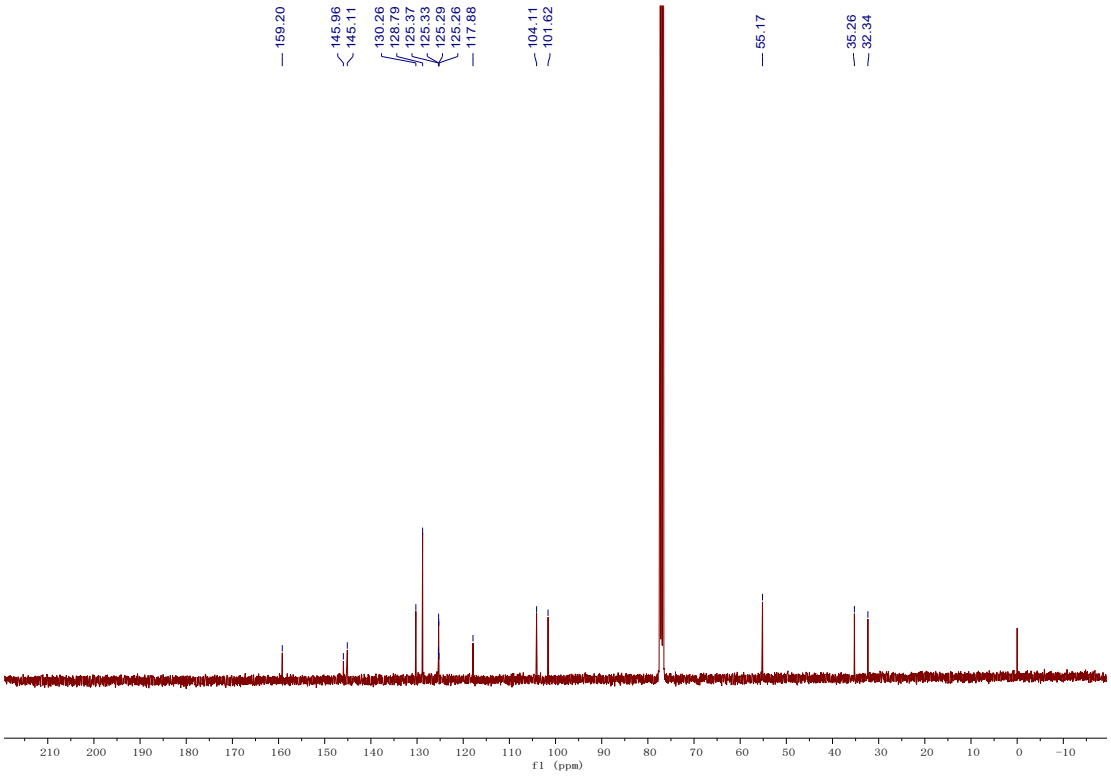
7.57
7.55
7.35
7.33
7.29
7.29
7.27
7.26
6.67
6.65
4.03
3.02
3.00
2.98
2.79
2.77
2.75
2.16
1.18
3.05
1.09
2.10
2.07
2.00
148.23
144.87
133.27
131.87
128.71
125.64
125.60
125.56
125.52
124.88
120.10
115.15
100.74
34.18
32.33

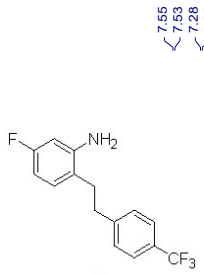

7.55
7.53
7.31
7.29
6.90
6.88
6.57
6.55
6.53
3.49
2.99
2.97
2.95
2.78
2.76
2.74
2.25
Me
NH2
CF3
4g
2.01
2.05
1.02
1.04
0.94
1.97
2.01
2.00
3.02
f1 (ppm)
146.01
143.91
137.15
129.34
128.77
128.55
128.22
125.39
125.35
125.31
125.27
122.40
119.81
116.57
35.11
32.64
21.07
f1 (ppm)


MeO
NH2
CF3

4h

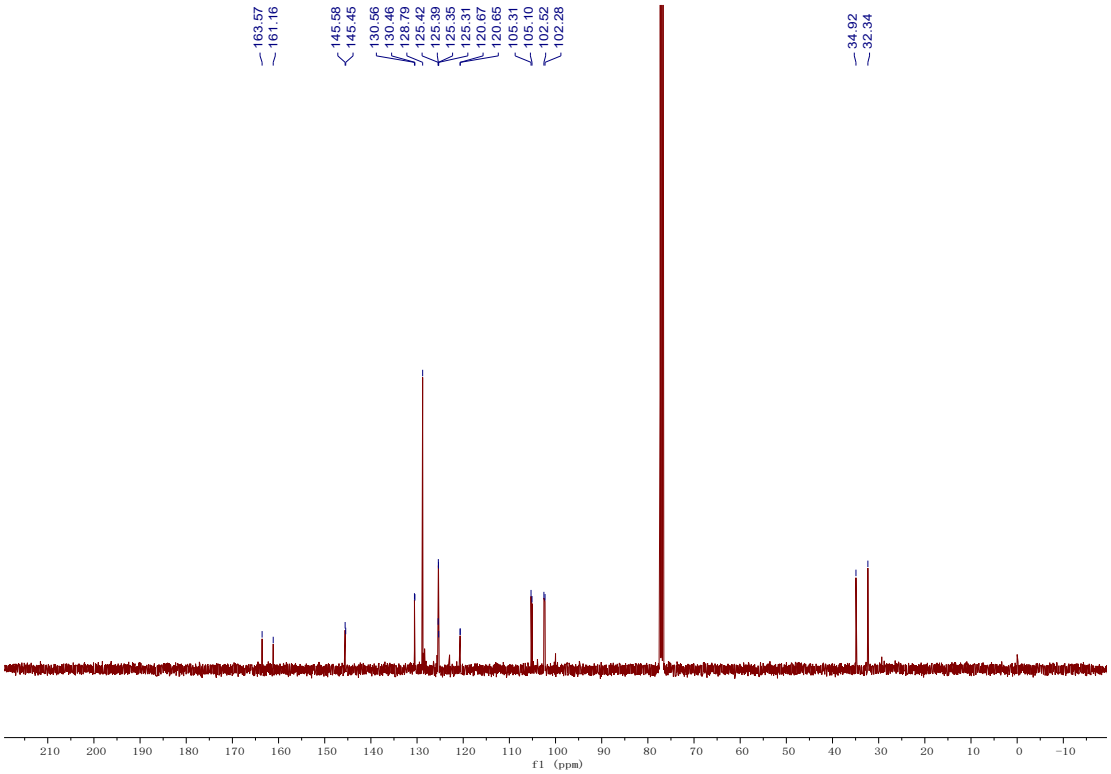
7.54
7.52
7.29
7.26
6.89
6.87
6.31
6.29
6.26
3.76
3.55
2.97
2.96
2.94
2.76
2.74
2.72
2.03
2.14
1.03
2.00
3.16
1.96
2.02
2.00
f1 (ppm)

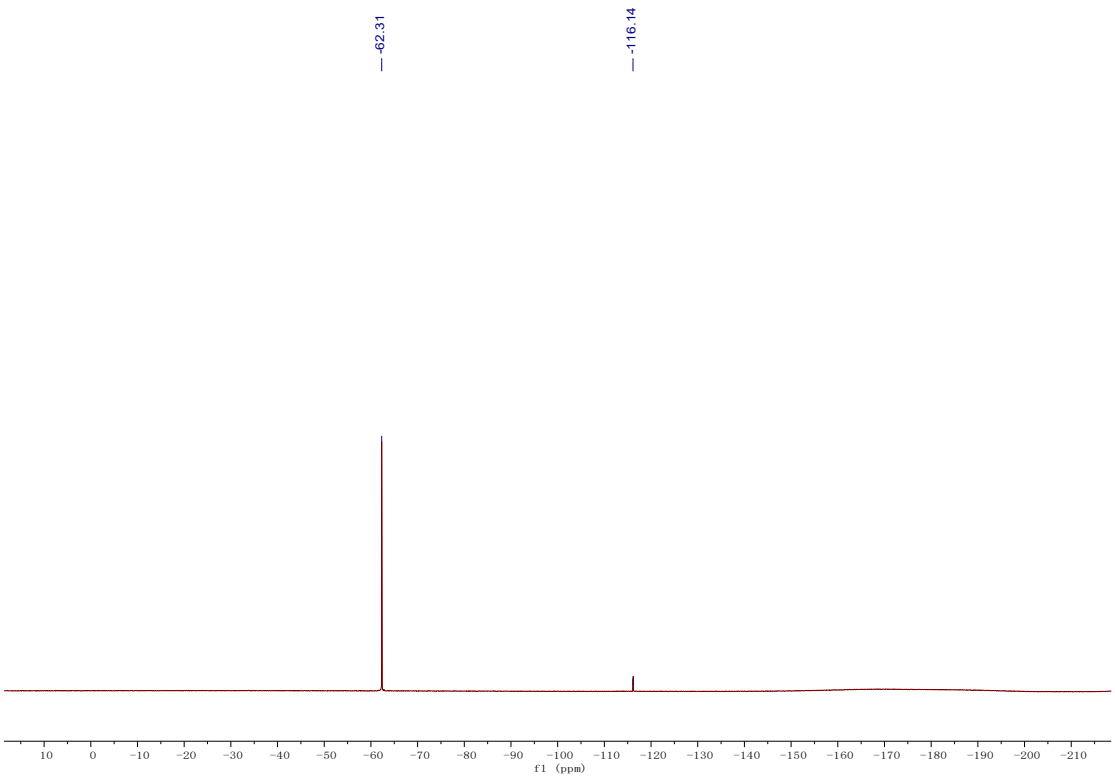

159.20
145.96
145.11
130.26
128.79
125.37
125.33
125.29
125.26
117.88
104.11
101.62
55.17
35.26
32.34
f1 (ppm)

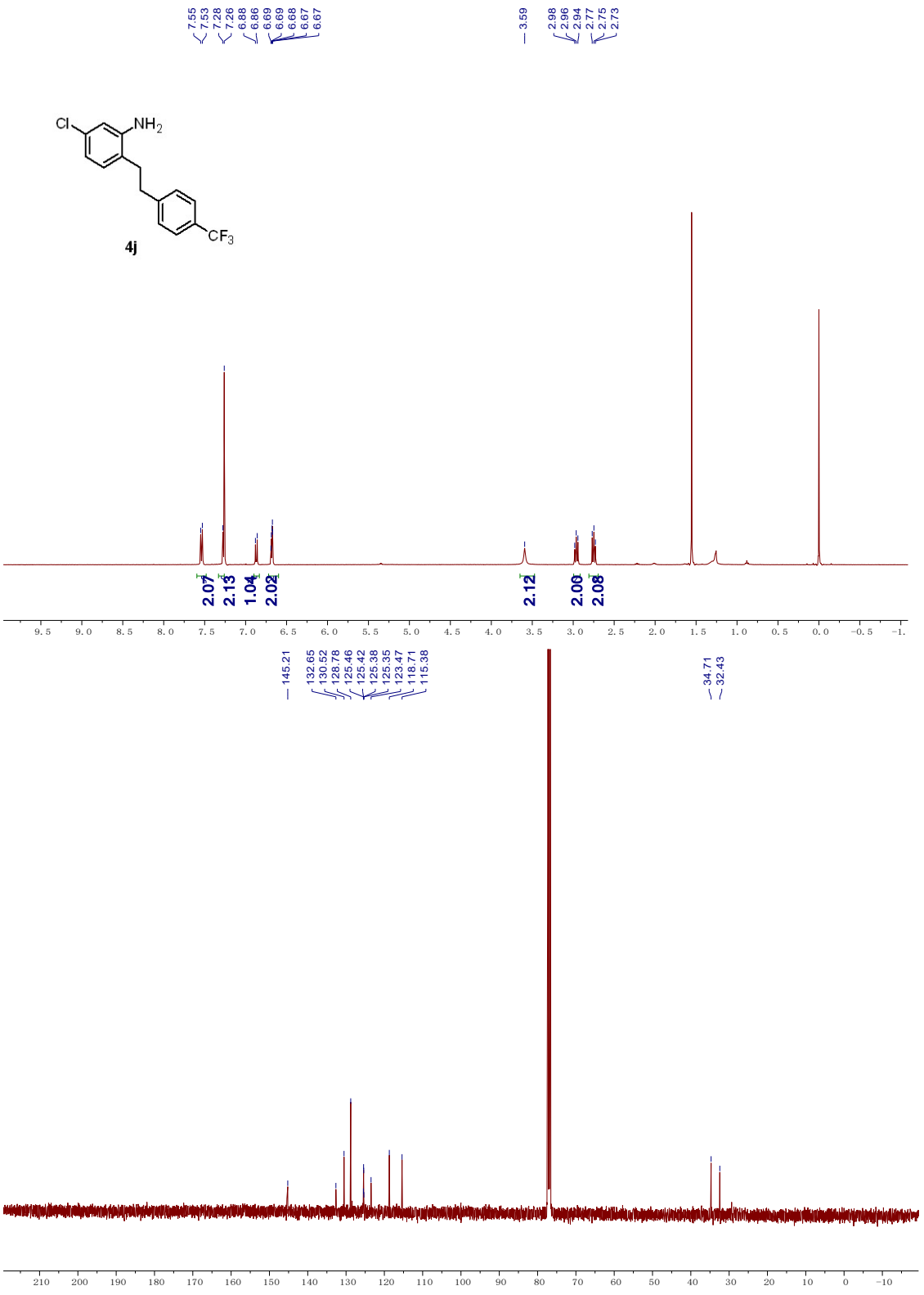

F
NH2
CF3

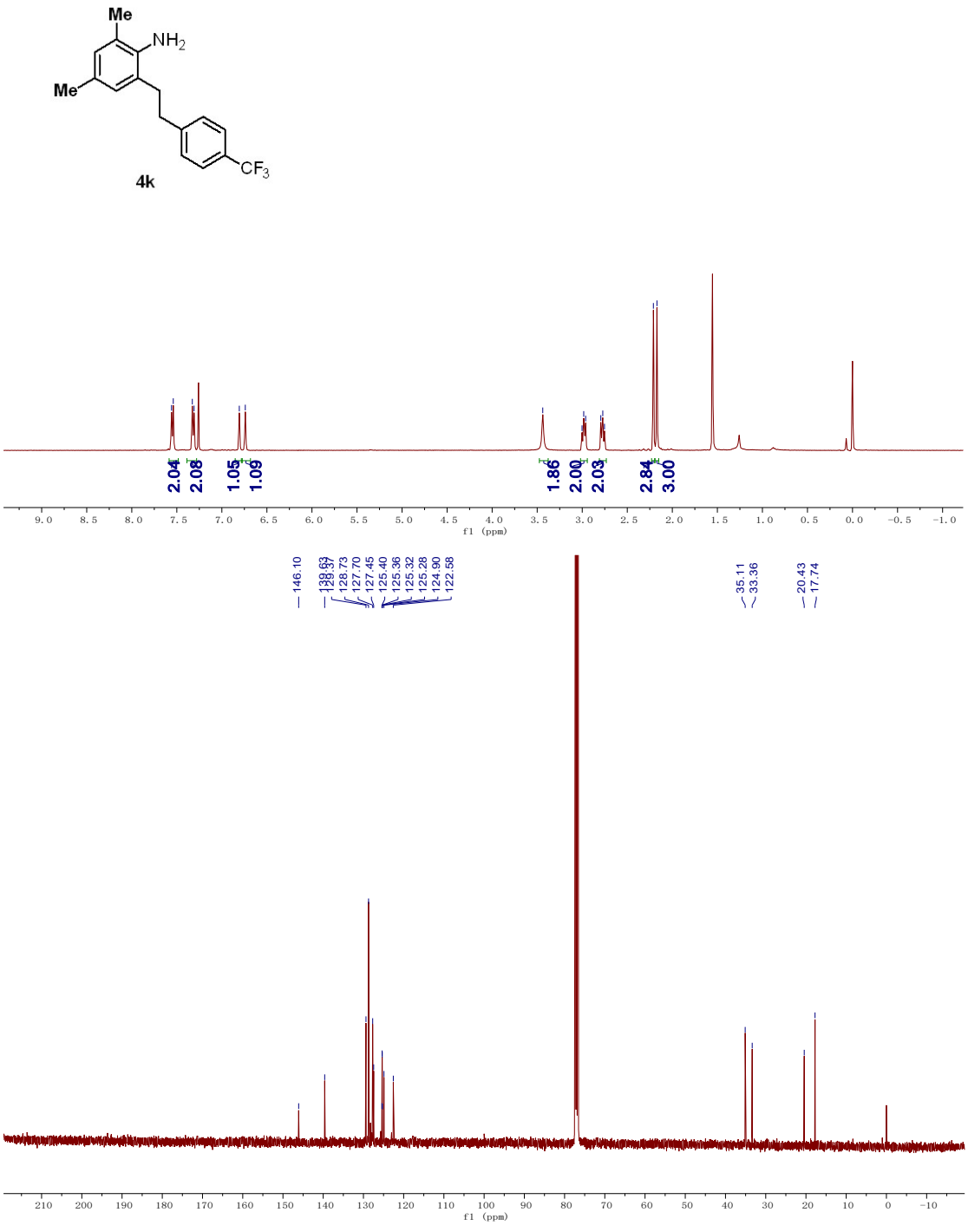
4i

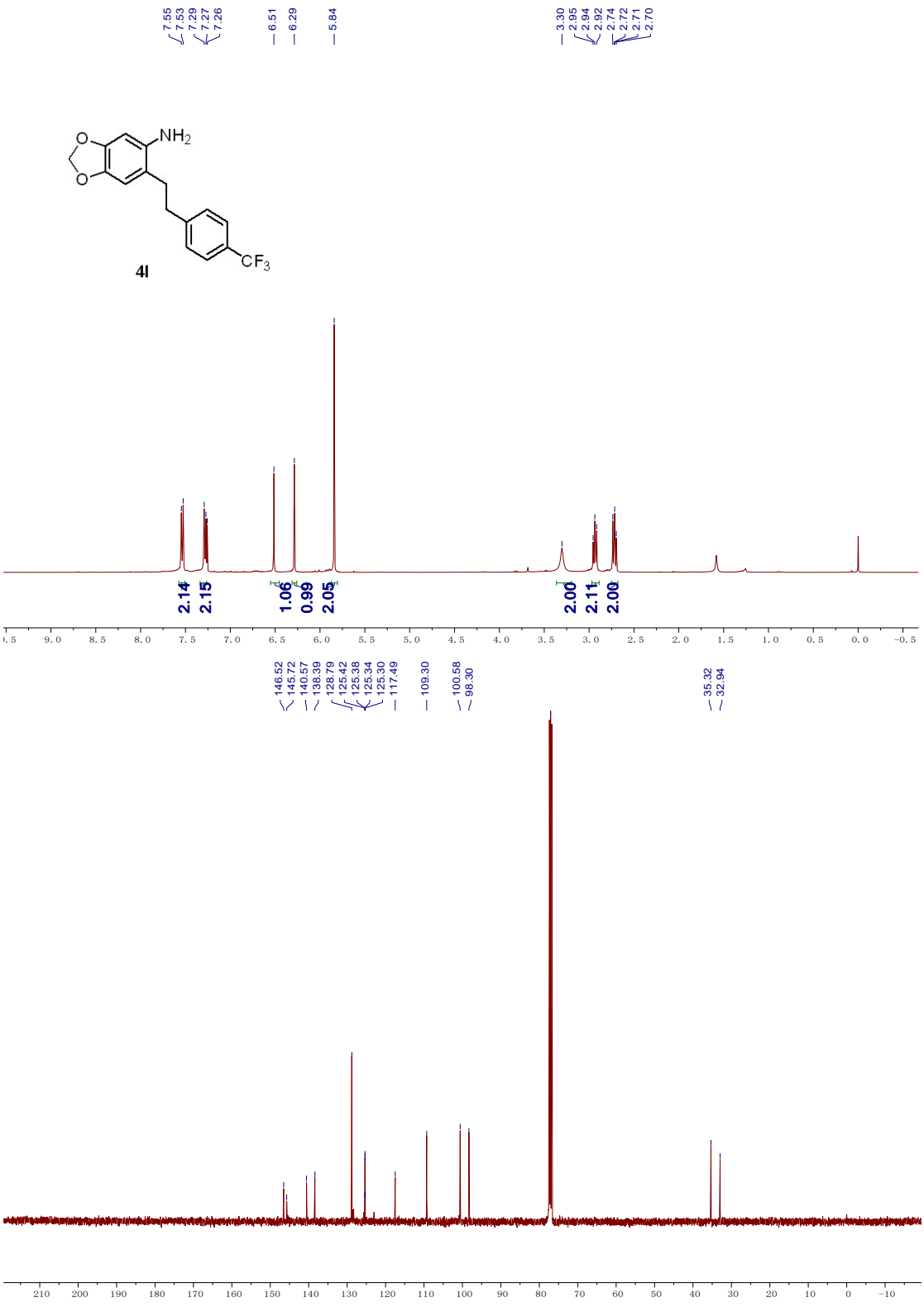
7.55
7.53
7.28
7.26
6.90
6.88
6.86
6.42
6.40
6.38
3.63
2.98
2.96
2.94
2.76
2.74
2.73
2.09
2.32
1.06
2.03
2.04
2.03
2.00
f1 (ppm)

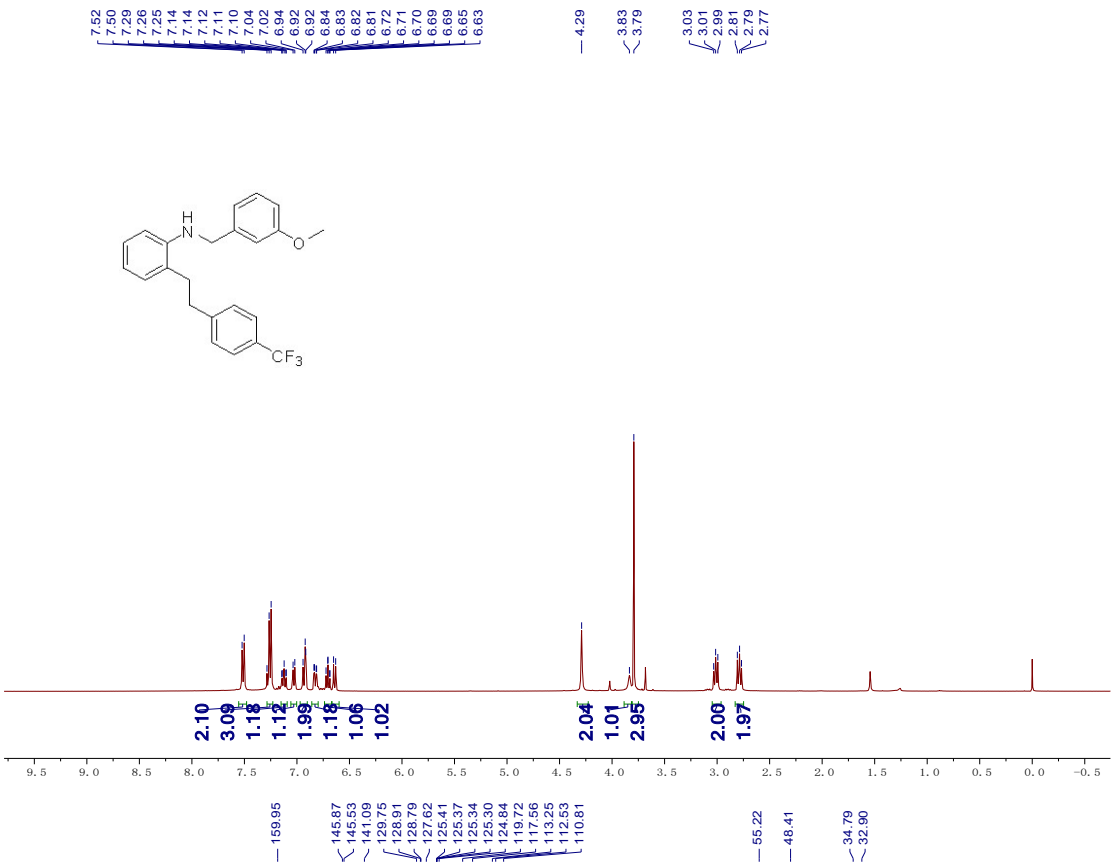

163.57
161.16
145.58
145.45
130.56
130.46
128.79
125.42
125.39
125.35
125.31
120.67
120.65
105.31
105.10
102.52
102.28
34.92
32.34
f1 (ppm)

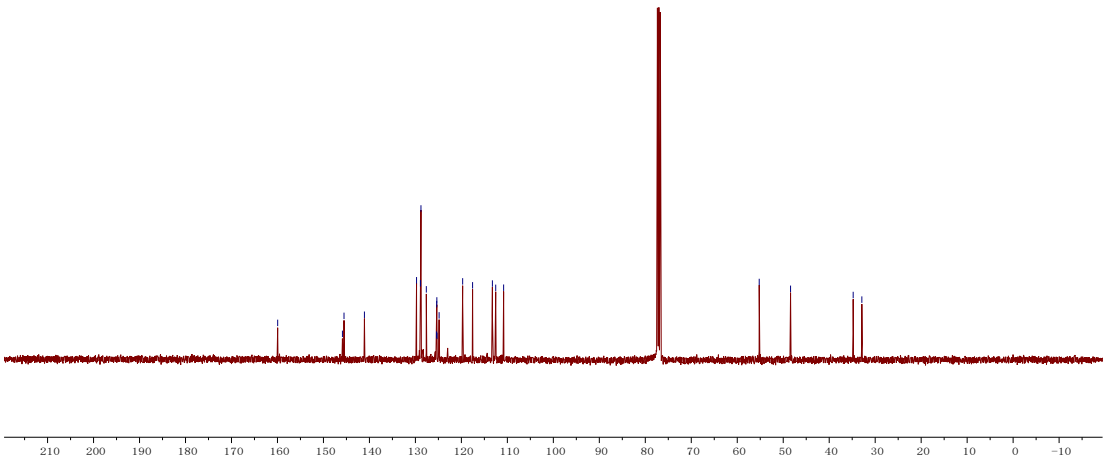

-62.31
-116.14
10
0
−10
−20
−30
−40
−50
−60
−70
−80
−90
−100
−110
−120
−130
−140
−150
−160
−170
−180
−190
−200
−210
f1 (ppm)

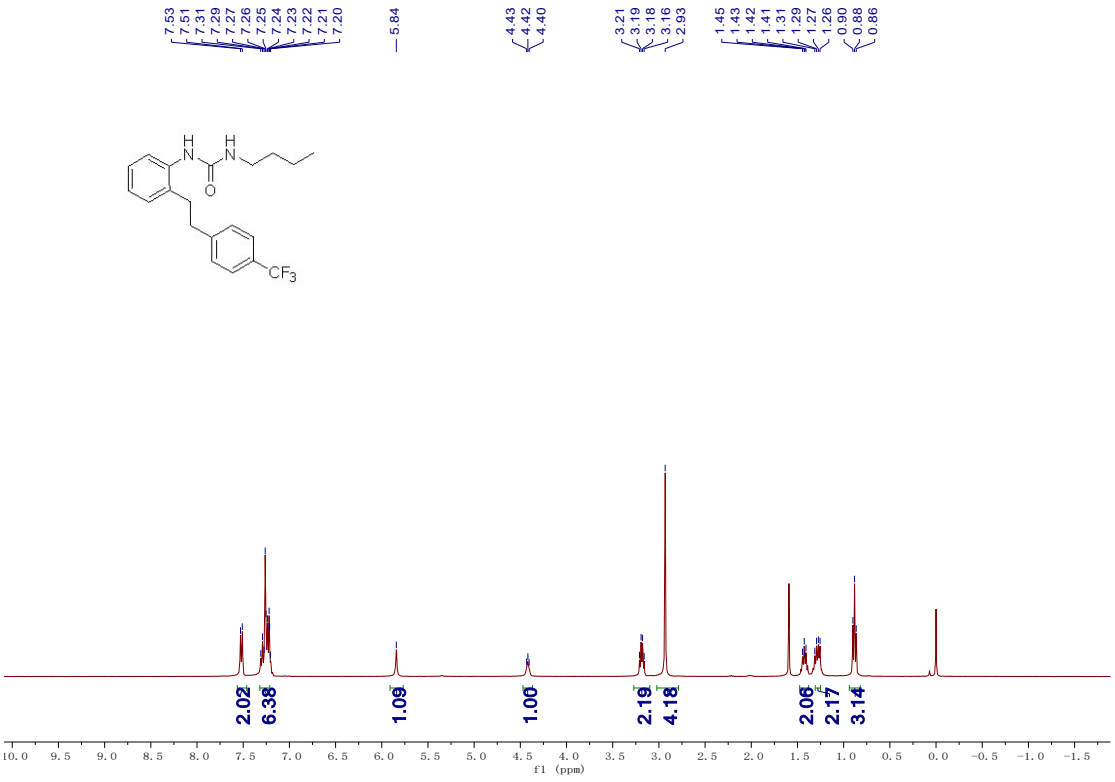

7.55
7.53
7.28
7.26
6.88
6.86
6.69
6.69
6.68
6.67
6.67
3.59
2.98
2.96
2.94
2.77
2.75
2.73
Cl
NH2
CF3
4j
2.07
2.13
1.04
2.02
2.12
2.00
2.08
145.21
132.65
130.52
128.78
125.46
125.42
125.38
125.35
123.47
118.71
115.38
34.71
32.43

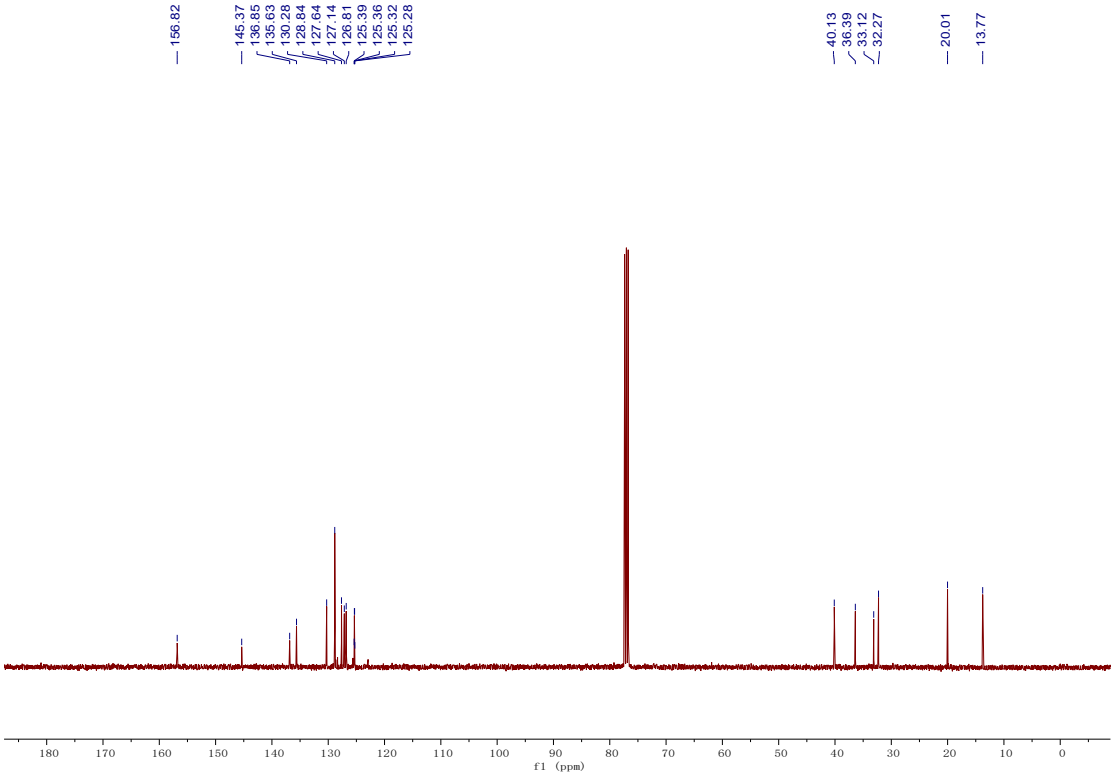

7.56
7.54
7.33
7.31
6.81
6.74
3.44
3.00
2.98
2.96
2.79
2.77
2.75
2.21
2.17
Me
NH2
Me
CF3
4k
2.04
2.08
1.05
1.09
1.86
2.00
2.03
2.84
3.00
f1 (ppm)
146.10
139.63
129.37
128.73
127.70
127.45
125.40
125.36
125.32
125.28
124.90
122.58
35.11
33.36
20.43
17.74
f1 (ppm)

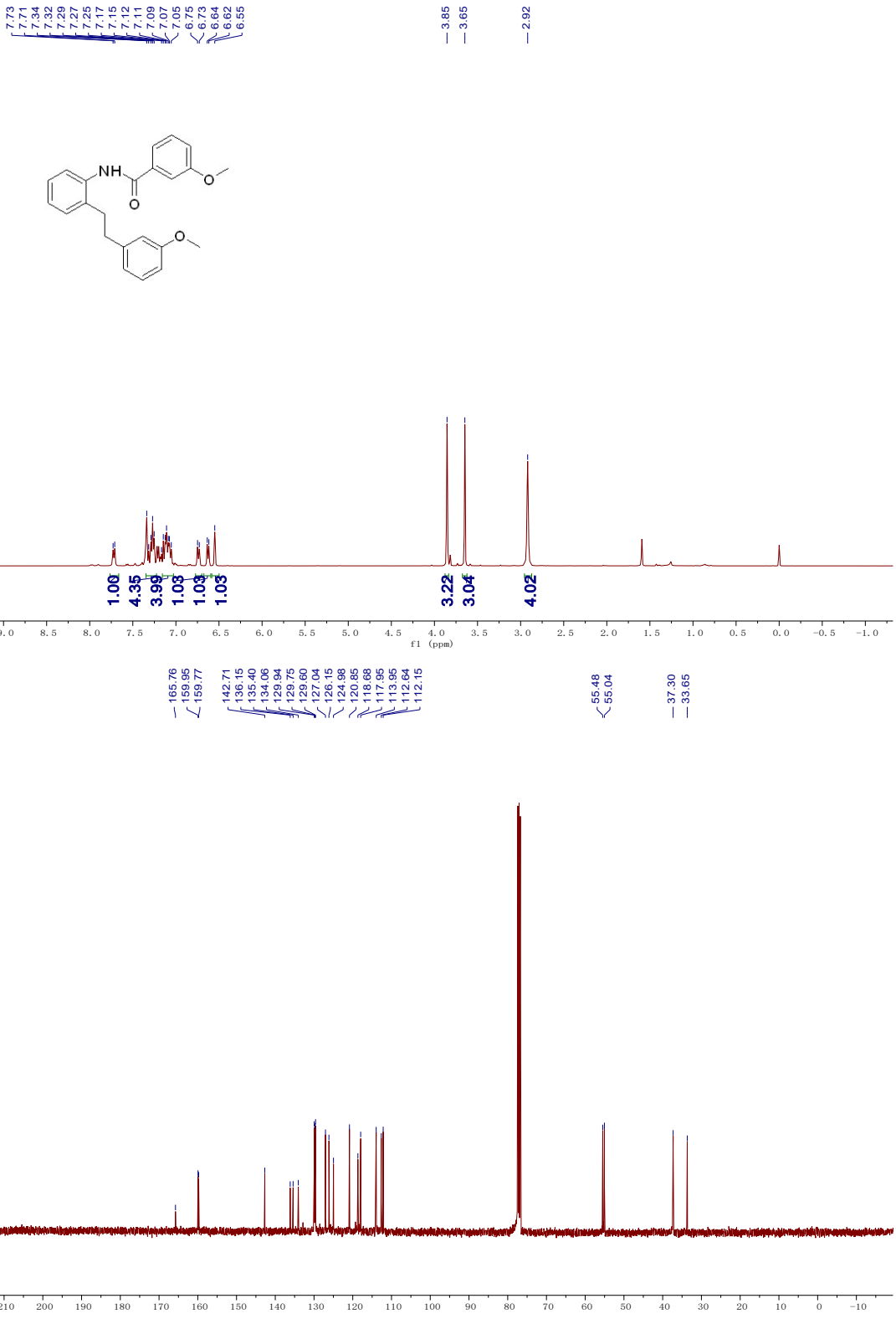

7.55
7.53
7.29
7.27
7.26
6.51
6.29
5.84
3.30
2.95
2.94
2.92
2.74
2.72
2.71
2.70
NH2
O
O
CF3
4l
2.14
2.15
1.06
0.99
2.05
2.00
2.11
2.00
146.52
145.72
140.57
138.39
128.79
125.42
125.38
125.34
125.30
117.49
109.30
100.58
98.30
35.32
32.94

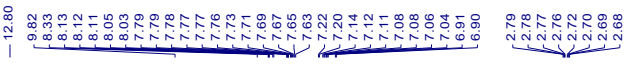

7.52
7.50
7.29
7.26
7.25
7.14
7.12
7.11
7.10
7.04
7.02
6.94
6.92
6.92
6.84
6.83
6.82
6.81
6.72
6.71
6.70
6.69
6.69
6.65
6.63
4.29
3.83
3.79
3.03
3.01
2.99
2.81
2.79
2.77
H
N
O
CF3
2.10
3.09
1.18
1.12
1.99
1.18
1.06
1.02
2.04
1.01
2.95
2.00
1.97
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5

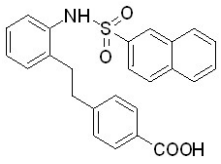

159.95
145.87
145.53
141.09
129.75
128.91
128.79
127.62
125.41
125.37
125.34
125.30
124.84
119.72
117.56
113.25
112.53
110.81
55.22
48.41
34.79
32.90
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10

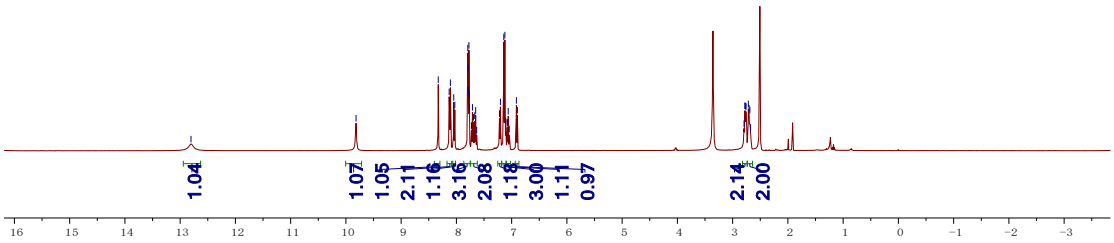

7.53
7.51
7.31
7.29
7.27
7.26
7.25
7.24
7.23
7.22
7.21
7.20
5.84
4.43
4.42
4.40
3.21
3.19
3.18
3.16
2.93
1.45
1.43
1.42
1.41
1.31
1.29
1.27
1.26
0.90
0.88
0.86
NH
NH
O
CF3
2.02
6.38
1.09
1.00
2.19
4.18
2.06
2.17
3.14
f1 (ppm)

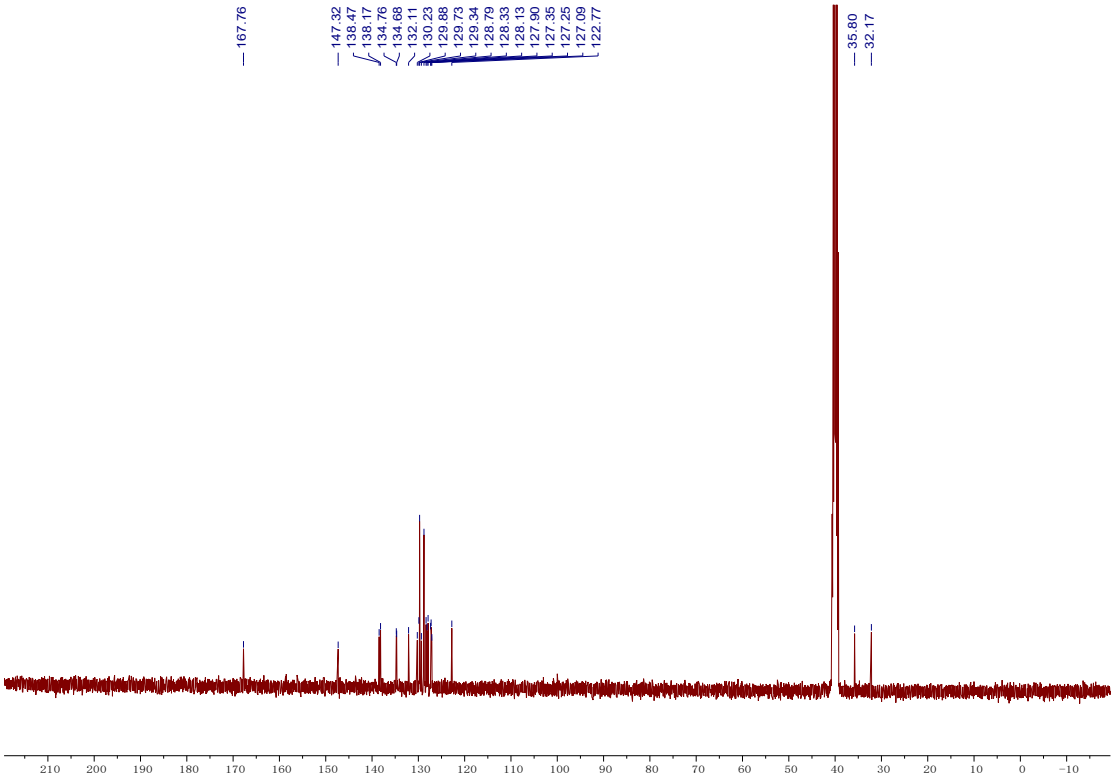

156.82
145.37
136.85
135.63
130.28
128.84
127.64
127.14
126.81
125.39
125.36
125.32
125.28
40.13
36.39
33.12
32.27
20.01
13.77
f1 (ppm)


7.73
7.71
7.34
7.32
7.29
7.27
7.25
7.17
7.15
7.12
7.11
7.09
7.07
7.05
6.75
6.73
6.64
6.62
6.55
3.85
3.65
2.92
NH
O
O
O
1.00
4.35
3.99
1.03
1.03
1.03
3.22
3.04
4.02
f1 (ppm)
165.76
159.95
159.77
142.71
136.15
135.40
134.06
129.94
129.75
129.60
127.04
126.15
124.98
120.85
118.68
117.95
113.95
112.64
112.15
55.48
55.04
37.30
33.65

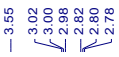

12.80
9.82
8.33
8.13
8.12
8.11
8.05
8.03
7.79
7.79
7.78
7.77
7.77
7.76
7.73
7.71
7.69
7.67
7.65
7.63
7.22
7.20
7.14
7.12
7.11
7.08
7.08
7.06
7.04
6.91
6.90
2.79
2.78
2.77
2.76
2.72
2.70
2.69
2.68

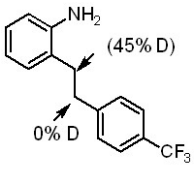

NH
S
O
O
COOH


1.04
1.07
1.05
2.11
1.16
3.16
2.08
1.18
3.00
1.11
0.97
2.14
2.00

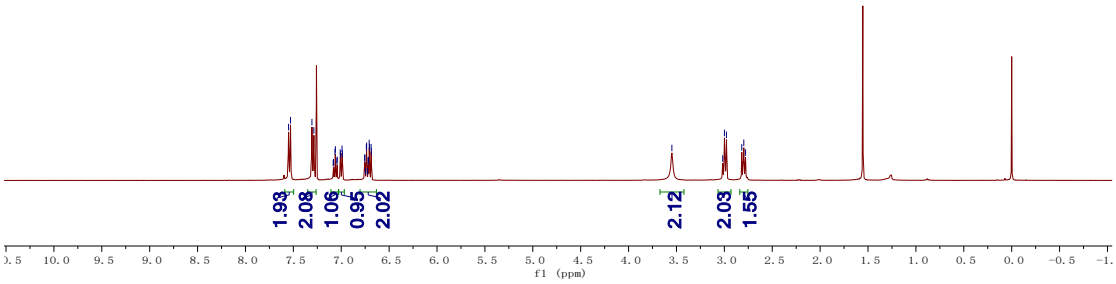

167.76
147.32
138.47
138.17
134.76
134.68
132.11
130.23
129.88
129.73
129.34
128.79
128.33
128.13
127.90
127.35
127.25
127.09
122.77
35.80
32.17


7.55
7.53
7.31
7.29
7.08
7.08
7.07
7.06
7.05
7.04
7.01
7.01
6.99
6.99
6.76
6.75
6.75
6.74
6.73
6.73
6.72
6.72
6.71
6.71
6.69
6.69


3.55
3.02
3.00
2.98
2.82
2.80
2.78


NH2
(45% D)
0% D
CF3

***d*-3a**


1.93
2.08
1.06
0.95
2.02
2.12
2.03
1.55
f1 (ppm)