Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Decarboxylative Umpolung of Conjugated Enal to β-Carbanion for Intramolecular Nucleophilic Addition to Aldehyde

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Supporting Information

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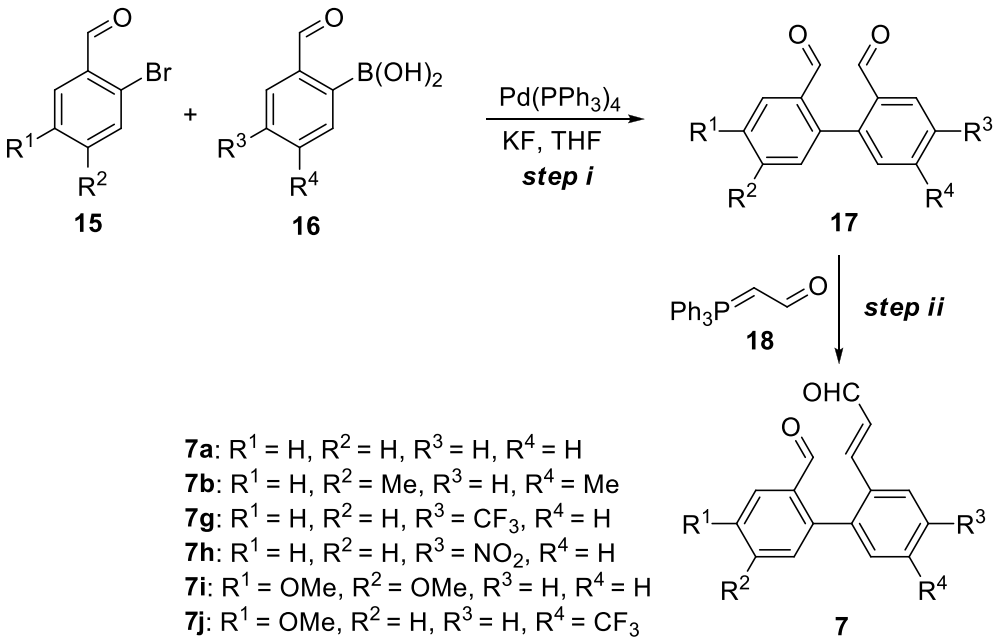
General Methods. All commercially available reagents were used without further purification unless otherwise stated. Column chromatography was performed on silica gel (200-300 mesh). ^{1}H NMR spectra were recorded on a 400 or 600 MHz NMR spectrometer and ^{13}C NMR spectra were recorded on a 100 MHz NMR spectrometer. IR spectra were recorded on a FT-IR spectrometer. Melting points were uncorrected.

Procedures for the Synthesis of Compounds 7a-b and 7g-j Using 7a as the Representative Example (Table 2)



***Step i.* Synthesis of compound 17a**[1]

A mixture of 2-bromobenzaldehyde **15a** (10.0 g, 54.1 mmol), (2-formylphenyl)boronic acid **16a** (9.84 g, 65.6 mmol), $KF{\cdot}2H_2O$ (17.0 g, 180.3 mmol), and $Pd(PPh_3)_4$ (1.89 g, 1.64 mmol) in THF (250 mL) was vigorously stirred under N_2 atmosphere at room temperature for 20 min and then at 60 ^{o}C for 24 hours. The reaction mixture was cooled to room temperature and concentrated under reduced pressure to remove most of the solvent. Water (30 mL) was added. The resulting suspend was extracted with EtOAc (50 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by

column chromatography (petroleum ether / ethyl acetate = 30:1) to give the product **17a** (9.3 g, 82%) as a white solid.

17a: White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.84 (s, 2H), 8.07 (dd, *J* = 7.6, 1.2 Hz, 2H), 7.68 (td, *J* = 7.6, 1.6 Hz, 2H), 7.60 (dd, *J* = 7.6, 7.2 Hz, 2H), 7.36 (d, *J* = 7.6 Hz, 2H).

Reference 1: K. Yasamut, J. Jongcharoenkamol, S. Ruchirawat and P. Ploypradith, *Tetrahedron*, 2016, **72**, 5994-6000.

Step ii. **Synthesis of compound 7a**

A mixture of compound **17a** (2.0 g, 9.51 mmol) and Wittig reagent **18** (4.4 g, 14.4 mmol) in toluene (30 mL) was stirred at 60 ^{o}C for 24 h. The reaction mixture was cooled to room temperature, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate = 10:1) to give the product **7a** (0.80 g, 36%) as a yellow oil.

7a: Yellow oil; IR (KBr) 2747, 1678, 1621, 1594, 1468, 1393, 1161, 1128 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.76 (s, 1H), 9.43 (d, *J* = 7.2 Hz, 1H), 8.08 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.83-7.76 (m, 1H), 7.69 (ddd, *J* = 7.8, 7.2, 1.2 Hz, 1H), 7.60 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.55-7.50 (m, 2H), 7.37-7.32 (m, 2H), 7.21 (d, *J* = 15.6 Hz, 1H), 6.63 (dd, *J* = 15.6, 7.2 Hz, 1H); HRMS *m/z* Calcd. For $C_{16}H_{12}O_2$ (M + Na^+): 259.0735; Found: 259.0735.

Compounds **7b** and **7g-j** were prepared respectively in 27%, 22%, 38%, 22%, and 17% yields for two steps by following a similar procedure.

7b: Yellow solid; IR (KBr) 2847, 1686, 1665, 1600, 1389, 1206, 1123 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.42 (d, *J* = 7.8 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 1H), 7.38 (d, *J* = 7.8 Hz, 1H), 7.31 (d, *J* = 7.8 Hz, 1H), 7.17 (d, *J* = 15.6 Hz, 1H), 7.14 (s, 1H), 7.12 (s, 1H), 6.59 (dd, *J* = 16.2, 7.8 Hz, 1H), 2.48 (s, 3H), 2.43 (s, 3H); HRMS *m/z* Calcd. For $C_{18}H_{16}O_2$ (M + Na^+): 287.1048; Found: 287.1050.

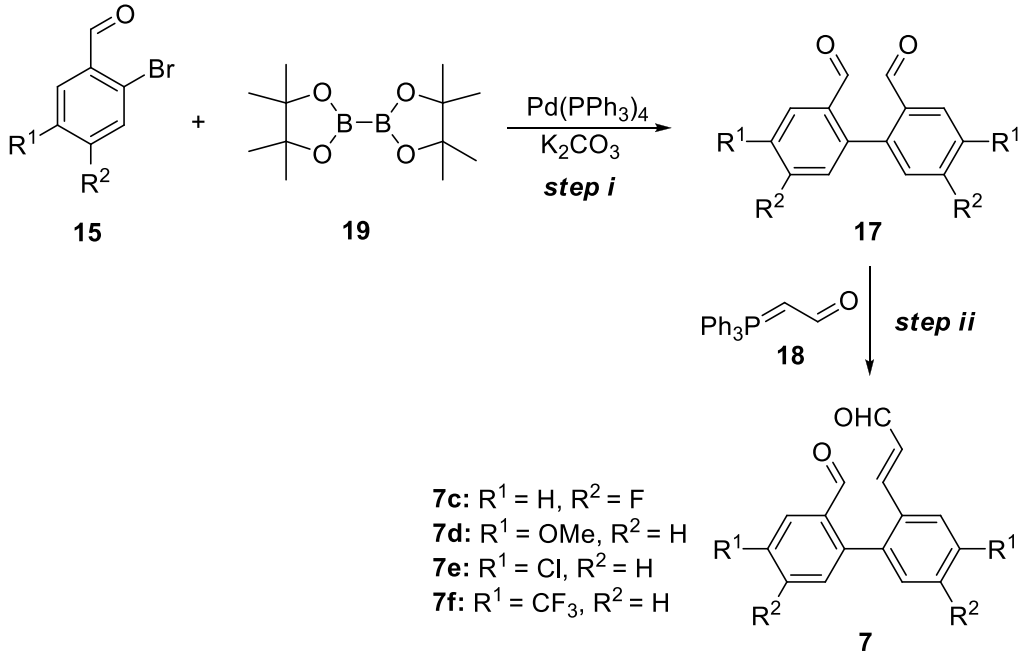
7g: Yellow solid; IR (KBr) 2741, 1682, 1615, 1597, 1332, 1772, 1128 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.77 (s, 1H), 9.46 (d, *J* = 7.6 Hz, 1H), 8.09 (d, *J* = 7.6 Hz, 1H), 8.01 (s, 1H), 7.80-7.70 (m, 2H), 7.66 (dd, *J* = 7.6, 7.2 Hz, 1H), 7.48 (d, *J* = 8.0 Hz, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 7.18 (d, *J* = 16.0 Hz, 1H), 6.67 (dd, *J* = 16.0, 7.2 Hz, 1H); HRMS *m/z* Calcd. For $C_{17}H_{11}F_3O_2$ ($M + Na^+$): 327.0609; Found: 327.0608.

7h: Yellow solid; IR (KBr) 2851, 1691, 1676, 1592, 1515, 1346, 1114 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 9.81 (s, 1H), 9.48 (d, *J* = 7.2 Hz, 1H), 8.62 (d, *J* = 2.4 Hz, 1H), 8.34 (dd, *J* = 8.4, 2.4 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.76 (dd, *J* = 7.8, 6.6 Hz, 1H), 7.71 (dd, *J* = 7.8, 7.2 Hz, 1H), 7.51 (d, *J* = 8.4 Hz, 1H), 7.31 (d, *J* = 7.2 Hz, 1H), 7.15 (d, *J* = 16.2 Hz, 1H), 6.73 (dd, *J* = 16.2, 7.8 Hz, 1H); HRMS *m/z* Calcd. For $C_{16}H_{11}NO_4$ ($M + Na^+$): 304.0586; Found: 304.0582.

7i: White solid; IR (KBr) 2843, 1676, 1593, 1511, 1352, 1280, 1139 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.56 (s, 1H), 9.47 (d, *J* = 7.6 Hz, 1H), 7.83-7.75 (m, 1H), 7.56 (s, 1H), 7.55-7.49 (m, 2H), 7.40-7.36 (m, 1H), 7.22 (s, 1H), 6.73 (s, 1H), 6.65 (dd, *J* = 16.0, 7.6 Hz, 1H), 4.02 (s, 3H), 3.95 (s, 3H); HRMS *m/z* Calcd. For $C_{18}H_{16}O_4$ ($M + Na^+$): 319.0946; Found: 319.0938.

7j: Yellow solid; IR (KBr) 2740, 1683, 1604, 1416, 1336, 1132 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.68 (s, 1H), 9.48 (d, *J* = 7.6 Hz, 1H), 7.88 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 8.0 Hz, 1H), 7.60 (s, 1H), 7.57 (d, *J* = 1.6 Hz, 1H), 7.29-7.24 (m, 2H), 7.21 (d, *J* = 16.0 Hz, 1H), 6.68 (dd, *J* = 16.0, 7.6 Hz, 1H), 3.95 (s, 3H); HRMS *m/z* Calcd. For $C_{18}H_{13}F_3O_3$ ($M + Na^+$): 357.0714; Found: 357.0713.

Procedures for Synthesis of Compounds 7c-f Using 7d as the Representative Example (Table 2)



***Step i.* Synthesis of compound 17d**[1]

A mixture of 2-bromo-5-methoxybenzaldehyde (**15d**) (0.86 g, 4.0 mmol), 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) (**19**) (0.51 g, 2.0 mmol), K_2CO_3 (0.83 g, 6.0 mmol) and $Pd(PPh_3)_4$(0.070 g, 0.060 mmol) in dioxane (20 mL) was vigorously stirred under N_2 atmosphere at room temperature for 20 min and then at 80 ^oC for 12 hours. The reaction mixture was cooled to room temperature, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate=10:1) to give the product **17d** (0.184 g, 34%) as a white solid.

17d: White solid; ^1H NMR (600 MHz, $CDCl_3$) δ 9.80 (s, 2H), 7.54 (d, *J* = 2.4 Hz, 2H), 7.26 (d, *J* = 8.4 Hz, 2H), 7.20 (dd, *J* = 8.4, 2.4 Hz, 2H), 3.93 (s, 6H).

Reference 1: K. Yasamut, J. Jongcharoenkamol, S. Ruchirawat and P. Ploypradith, *Tetrahedron*, 2016, **72**, 5994-6000.

***Step ii.* Synthesis of compound 7d**

A mixture of dialdehyde **17d** (0.184 g, 0.68 mmol) and Wittig reagent **18** (0.42 g,

1.37 mmol) in toluene (10 mL) was stirred at 80 ^{o}C for 3 d. The reaction mixture was cooled to room temperature, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate = 5:1) to give the product **7d** (0.081 g, 40%) as a red solid.

7d: Red solid; IR (KBr) 2840, 1670, 1602, 1476, 1423, 1392, 1126 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.71 (s, 1H), 9.46 (d, *J* = 7.8 Hz, 1H), 7.54 (s, 1H), 7.26-7.17 (m, 5H), 7.06 (dd, *J* = 7.8, 1.8 Hz, 1H), 6.62 (dd, *J* = 16.2, 7.8 Hz, 1H), 3.93 (s, 3H), 3.91 (s, 3H); HRMS *m/z* Calcd. For $C_{18}H_{16}O_4$(M + Na^+): 319.0946; Found: 319.0944.

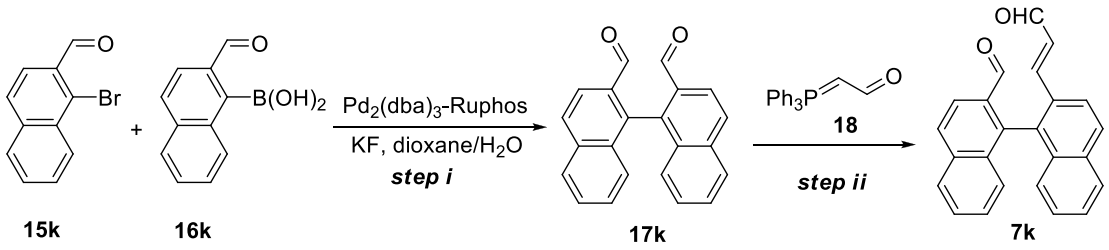
Compounds **7c** and **7e-f** were prepared respectively in 22%, 11%, and 25% yields for two steps by following a similar procedure.

7c: Red solid; IR (KBr) 2754, 1702, 1670, 1574, 1484, 1123 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.67 (s, 1H), 9.44 (d, *J* = 7.6 Hz, 1H), 8.12 (dd, *J* = 8.8, 5.6 Hz, 1H), 7.80 (dd, *J* = 8.8, 5.2 Hz, 1H), 7.33 (ddd, *J* = 8.8, 8.0, 2.4 Hz, 1H), 7.29-7.23 (m, 1H), 7.13-7.01 (m, 3H), 6.58 (dd, *J* = 16.0, 7.6 Hz, 1H); HRMS *m/z* Calcd. For $C_{16}H_{10}F_2O_2$(M + Na^+): 295.0547; Found: 295.0545.

7e: Yellow solid; IR (KBr) 2853, 1676, 1584, 1459, 1385, 1206, 1112 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ 9.70 (s, 1H), 9.47 (d, *J* = 7.2 Hz, 1H), 8.03 (s, 1H), 7.76 (s, 1H), 7.67 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.55-7.44 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 1H), 7.09 (d, *J* = 15.6 Hz, 1H), 6.63 (dd, *J* = 15.6, 7.8 Hz, 1H); HRMS *m/z* Calcd. For $C_{16}H_{10}Cl_2O_2$(M + Na^+): 326.9956; Found: 326.9951.

7f: Yellow solid; IR (KBr) 2854, 1676, 1614, 1571, 1330, 1119 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.79 (s, 1H), 9.50 (d, *J* = 7.2 Hz, 1H), 8.36 (s, 1H), 8.04 (s, 1H), 7.98 (d, *J* = 8.0 Hz, 1H), 7.80 (d, *J* = 7.8 Hz, 1H), 7.54-7.42 (m, 2H), 7.13 (d, *J* = 16.0 Hz, 1H), 6.72 (dd, *J* = 16.0, 7.6 Hz, 1H); HRMS *m/z* Calcd. For $C_{18}H_{10}F_6O_2$(M + Na^+): 395.0483; Found: 395.0476.

Procedure for Synthesis of Compound 7k



***Step i.* Synthesis of compound 17k**[2]

A mixture of 1-bromo-2-naphthaldehyde (**15k**) (1.0 g, 4.26 mmol), (2-formylnaphthalen-1-yl)boronic acid (**16k**) (1.28 g, 6.38 mmol), $Pd_2(dba)_3$ (0.10 g, 0.109 mmol) and dicyclohexyl(2',6'-diisopropoxy-[1,1'-biphenyl]-2-yl)phosphine **(**RuPhos) (0.10 g, 0.215 mmol) in dioxane (5.0 mL) and H_2O (40 mL) was vigorously stirred under N_2 atmosphere at room temperature for 20 min and then at 100 ^oC for 21 hours. The reaction mixture was cooled to room temperature and extracted with EtOAc (10 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressureand, and purified by column chromatography (petroleum ether / ethyl acetate=30:1) to give the product **17k** (0.687 g, 52%) as a yellow solid.

17k: Yellow solid; ^1H NMR (600 MHz, $CDCl_3$) δ 9.62 (s, 2H), 8.21 (d, *J* = 8.4 Hz, 2H), 8.13 (d, *J* = 8.4 Hz, 2H), 8.02 (d, *J* = 8.4 Hz, 2H), 7.64 (dd, *J* = 8.4, 6.6 Hz, 2H), 7.38 (t, *J* = 7.8 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H).

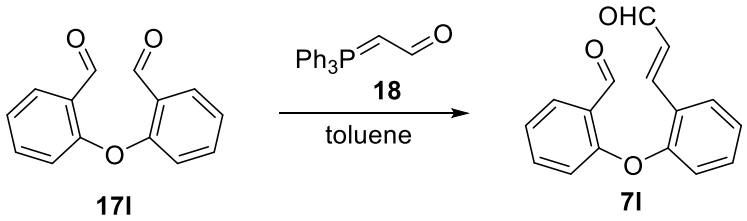
Reference 2: C. Zhu, Y. Shi, M.-H. Xu and G.-Q. Lin, *Org. Lett.*, 2008, **10**, 1243-1246.

***Step ii.* Synthesis of compound 7k**

A mixture of dicarbaldehyde **17k** (0.68 g, 2.19 mmol) and 2-(triphenylphosphoranylidene)acetaldehyde (**18**) (1.33 g, 4.39 mmol) in toluene (15.0 mL) was stirred at 60 ^oC for 24 h. The reaction mixture was cooled to room temperature, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate = 10:1) to give the product **7k** (0.183 g, 25%) as a yellow solid.

7k: Yellow solid; IR (KBr) 2923, 2852, 1630, 1612, 1577, 1402, 1384, 1119 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 9.57 (s, 1H), 9.25 (d, *J* = 7.6 Hz, 1H), 8.21 (d, *J* = 8.8 Hz, 1H), 8.14 (d, *J* = 8.8 Hz, 1H), 8.09 (d, *J* = 8.8 Hz, 1H), 8.04 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 7.66 (dd, *J* = 8.0, 7.2 Hz, 1H), 7.56 (dd, *J* = 8.0, 6.8 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.32 (dd, *J* = 8.0, 7.2 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.07 (d, *J* = 8.4 Hz, 1H), 7.00 (d, *J* = 16.0 Hz, 1H), 6.75 (dd, *J* = 16.0, 7.6 Hz, 1H); HRMS *m/z* Calcd. For $C_{24}H_{16}O_2$(M + Na^+): 359.1048; Found: 359.1042.

Procedure for Synthesis of Compound 7l

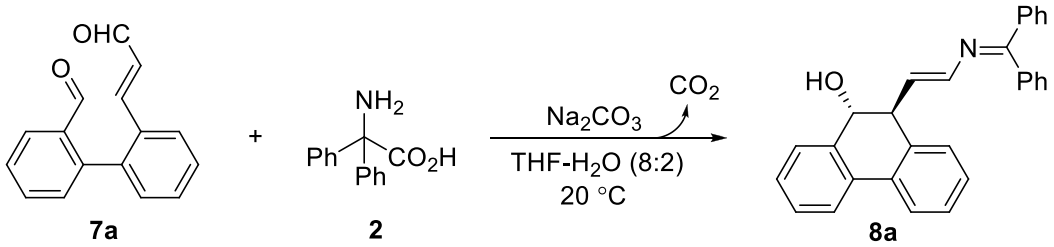


A mixture of dicarbaldehyde **17l**[3] (1.50 g, 6.64 mmol) and 2-(triphenylphosphoranylidene)acetaldehyde (**18**) (4.00 g, 13.27 mmol) in toluene (25.0 mL) was stirred at 60 ^oC for 24 h. The reaction mixture was cooled to room temperature, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate = 10:1) to give the product **7l** (0.367 g, 22%) as a yellow solid.

7l: Yellow oil; IR (KBr) 2831, 1672, 1626, 1601, 1472, 1450, 1405, 1237, 1130 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.50 (s, 1H), 9.69 (d, *J* = 7.6 Hz, 1H), 7.99 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.86 (d, *J* = 16.0 Hz, 1H), 7.74 (d, *J* = 8.0 Hz, 1H), 7.60-7.54 (m, 1H), 7.42 (dd, *J* = 8.0, 7.6 Hz, 1H), 7.28 (d, *J* = 7.6 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 6.92 (d, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.6 Hz, 1H), 6.82 (dd, *J* = 16.0, 8.0 Hz, 1H); HRMS *m/z* Calcd. For $C_{16}H_{12}O_3$(M + Na^+): 275.0684; Found: 275.0687.

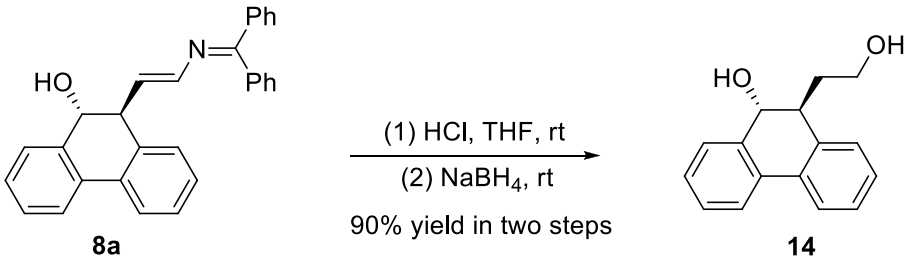
Reference 3: Y. Xia, Z. Liu, Q. Xiao, P. Qu, R. Ge, Y. Zhang and J. Wang, *Angew. Chem.; Int. Ed.*, 2012, **51**, 5714.

Representative Procedure for Cyclization of Compounds 7 (Table 2， entry1)



A mixture of compound **7a** (0.60 g, 2.54 mmol), 2,2-diphenylglycine **2** (0.577 g, 2.54 mmol) and Na_2CO_3 (0.0543 g, 0.512 mmol) in THF (12.0 mL) and H_2O (3.0 mL) was stirred at 20 ^oC for 12 h. The reaction mixture was concentrated under reduced pressure to remove most of the THF. The resulting suspend was extracted with EtOAc (5 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate = 10:1) to give the product **8a** (0.862 g, 85%) as a yellow solid.

Procedure for Synthesis of Compound 14

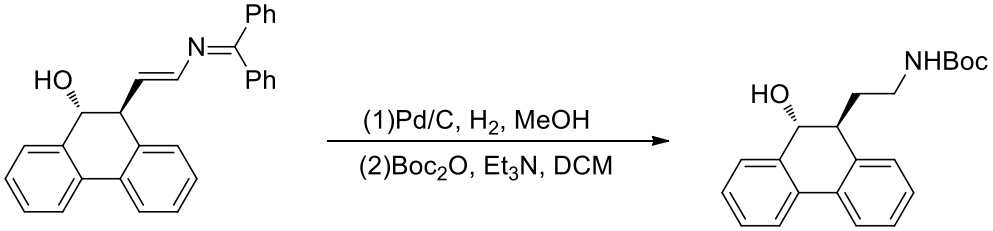


A mixture of compound **8a** (0.40 g, 0.996 mmol), 0.1 M HCl (10.0 mL) and THF (10.0 mL) was stirred at room temperature overnight. The reaction is completed as judged by TLC analysis. The reaction was neutralized with saturated aqueous $NaHCO_3$ solution until the pH = 7-8. The THF solvent was removed by concentration under reduced pressure. The resulting stuff was extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl

acetate = 5:1) to give the hydrolysis product as a yellow oil. The oil was dissolved in MeOH (4.0 mL). To the solution was added a solution of $NaBH_4$ (0.080 g, 2.1 mmol) of MeOH (4.0 mL) at 0 ^oC over 5 min. After being stirred at 0 ℃ for 2 h, the reaction was quenched with saturated aqueous NH_4Cl solution. The resulting mixture was concentrated under reduced pressure to remove most of the solvent and then extracted with ethyl acetate (5 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered, concentrated under reduced pressure, and purified by column chromatography (petroleum ether / ethyl acetate = 4:3) to give the product **14** (0.216 g, 90% for two steps) as a white solid.

14: White solid; m.p. 178-181 ^oC; IR (KBr) 3406, 1572, 1439, 1246, 1233, 1051 cm^{-1}; ^1H NMR (400 MHz, DMSO) δ 7.86 (d, *J* = 7.6 Hz, 1H), 7.85 (d, *J* = 7.2 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.2, 2.0 Hz, 1H), 7.36-7.26 (m, 3H), 7.26-7.20 (m, 2H), 5.00 (d, *J* = 3.2 Hz, 1H), 4.60-4.46 (m, 2H), 3.36-3.28 (m, 2H), 3.12 (ddd, *J* = 8.8, 5.6, 2.4 Hz, 1H), 1.50-1.38 (m, 1H), 1.14-1.01 (m, 1H); ^{13}C NMR (100 MHz, DMSO) δ 138.7, 136.7, 132.7, 132.0, 130.00, 129.96, 128.6, 127.7, 127.4, 126.8, 123.7, 123.5, 71.1, 58.4, 42.6, 35.6; HRMS *m/z* Calcd. For $C_{16}H_{16}O_2Na$ ($M + Na^+$): 263.1048; Found: 263.1055.

Procedure for Synthesis of Compound 15



8a **15**

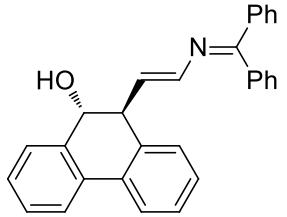
A mixture of compound **8a** (0.40 g, 1.0 mmol), Pd/C (0.40 g) and anhydrous MeOH (8.0 mL) was stirred at 50 ^oC in an autoclave under 50 atm of H_2 for 24 h. After cooling to room temperature, the reaction mixture was submitted to filtration and then concentrated under reduced pressure to give the reduced free amino alcohol as a yellow oil. The residue was dissolved in dry CH_2Cl_2 (2.0 mL). To the solution

was added Et_3N (0.152 g, 1.50 mmol) and Boc_2O (0.328 g, 1.50 mmol) at 0 ℃. After stirring at room temperature for 12 h, the reaction mixture was concentrated and purified via column chromatography (petroleum ether / ethyl acetate=3:1) to give the product **15** as a white solid (0.129 g, 38% in two steps)

15: White solid; m.p. 47-48 ^oC; IR (KBr) 3427, 3068, 2974, 2926, 1681, 1384 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.84-7.77 (m, 2H), 7.42 (ddd, *J* = 7.8, 7.2, 1.6 Hz, 1H), 7.38-7.22 (m, 5H), 4.61 (s, 1H), 4.50 (s, 1H), 3.20-2.90 (m, 3H), 2.14 (s, 1H), 1.63-1.49 (m, 1H), 1.41 (s, 9H), 1.32-1.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 136.6, 135.6, 132.7, 132.0, 130.5, 129.8, 129.5, 128.3, 128.2, 127.7, 124.3, 124.1, 72.78, 72.77, 44.4, 38.6, 33.0, 28.5; HRMS *m/z* Calcd. For $C_{21}H_{25}NO_3Na$ ($M + Na^+$): 362.1732; Found: 362.1729.

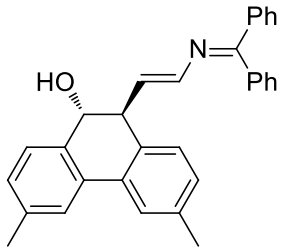
Characterization Data

Compound 8a



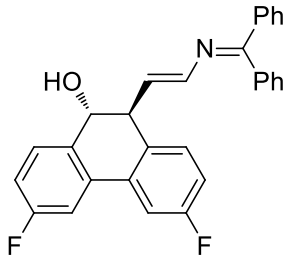
Yellow solid; m.p. 147-150 ^oC; IR (KBr) 3420, 1656, 1548, 1445, 1277 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 7.78 (t, *J* = 6.6 Hz, 2H), 7.68 (d, *J* = 7.8 Hz, 2H), 7.52 (d, *J* = 7.6 Hz, 1H), 7.49-7.44 (m, 3H), 7.41 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.35-7.315 (m, 4H), 7.30-7.26 (m, 2H), 7.20-7.15 (m, 2H), 6.90 (d, *J* = 13.2 Hz, 1H), 6.12 (dd, *J* = 13.2, 9.6 Hz, 1H), 4.69 (d, *J* = 7.2 Hz, 1H), 3.68 (dd, *J* = 9.6, 7.2 Hz, 1H), 2.41 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 141.2, 139.3, 136.6, 136.1, 135.7, 132.9, 132.7, 131.0, 130.5, 129.1, 129.0, 128.9, 128.8, 128.7, 128.6, 128.22, 128.20, 127.8, 127.2, 123.9, 123.8, 71.8, 49.2. HRMS *m/z* Calcd. For $C_{29}H_{24}NO$ ($M + H^+$): 402.1858; Found: 402.1857.

Compound 8b



Yellow solid; m.p. 80-82 ^{o}C; IR (KBr) 3424, 1617, 1560, 1444, 1384, 1318 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.6 Hz, 2H), 7.60 (s, 1H), 7.59 (s, 1H), 7.49-7.43 (m, 3H), 7.41-7.37 (m, 2H), 7.33 (dd, *J* = 7.6, 7.2 Hz, 2H), 7.19-7.10 (m, 4H), 7.08 (d, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 13.2 Hz, 1H), 6.07 (dd, *J* = 13.2, 9.2 Hz, 1H), 4.65 (d, *J* = 6.8 Hz, 1H), 3.63 (dd, *J* = 9.2, 6.8 Hz, 1H), 2.44 (s, 3H), 2.41 (s, 3H), 2.08 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.9, 141.0, 139.5, 138.2, 137.3, 136.2, 133.9, 132.9, 132.8, 132.7, 131.5, 130.5, 129.2, 129.0, 128.91, 128.90, 128.8, 128.6, 128.2, 127.4, 124.55, 124.52, 72.0, 49.1, 21.6, 21.5. HRMS *m/z* Calcd. For $C_{31}H_{28}NO$ ($M + H^+$): 430.2171; Found: 430.2152.

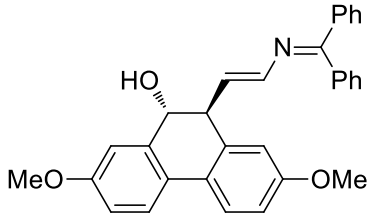
Compound 8c



Yellow solid; m.p. 69-72 ^{o}C; IR (KBr) 3428, 1613, 1578, 1450, 1428, 1171 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.6 Hz, 2H), 7.48-7.42 (m, 4H), 7.40 (t, *J* = 7.2 Hz, 1H), 7.37-7.27 (m, 4H), 7.20 (dd, *J* = 8.4, 6.0 Hz, 1H), 7.14-7.08 (m, 2H), 7.01 (td, *J* = 8.4, 2.4 Hz, 1H), 6.96 (td, *J* = 8.4, 2.4 Hz, 1H), 6.78 (d, *J* = 13.2 Hz, 1H), 6.02 (dd, *J* = 13.2, 9.2 Hz, 1H), 4.63 (d, *J* = 6.8 Hz, 1H), 3.62 (dd, *J* = 9.2, 6.8 Hz, 1H), 2.43 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.7, 164.5, 163.9, 162.0, 161.5, 141.5, 139.2, 136.0, 134.13, 134.10, 134.05, 134.03, 133.98, 133.96, 133.91, 133.88, 132.51, 132.48, 131.64, 131.61, 130.9, 130.8, 130.7, 130.1, 129.4, 129.3, 129.0, 128.7,

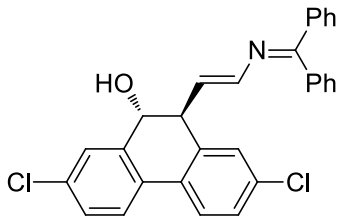
128.6, 128.3, 115.6, 115.5, 115.4, 115.3, 111.1, 111.0, 110.8, 110.76, 71.3, 48.5; HRMS *m/z* Calcd. For $C_{29}H_{22}NOF_2$ ($M + H^+$): 438.1669; Found: 438.1663.

Compound 8d



Yellow solid; m.p. 69-72 ^oC; IR (KBr) 3431, 1610, 1485, 1248 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 7.6 Hz, 2H), 7.61 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 7.50-7.30 (m, 6H), 7.18-7.12 (m, 2H), 7.05 (d, *J* = 2.4 Hz, 1H), 6.93-6.79 (m, 4H), 6.10 (dd, *J* = 13.2, 9.2 Hz, 1H), 4.62 (d, *J* = 7.2 Hz, 1H), 3.84 (s, 3H), 3.81 (s, 3H), 3.61 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.32 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 159.1, 159.0, 141.3, 139.4, 137.4, 136.5, 136.1, 130.9, 130.5, 129.0, 128.9, 128.8, 128.6, 128.2, 125.9, 125.6, 124.6, 124.5, 114.65, 114.56, 113.2, 112.0, 72.2, 55.4, 49.6. HRMS *m/z* Calcd. For $C_{31}H_{28}NO_3$ ($M + H^+$): 462.2069; Found: 462.2044.

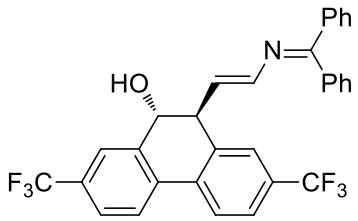
Compound 8e



Yellow solid; m.p. 94-96 ^oC; IR (KBr) 3424, 1578, 1553, 1468, 1444, 1095 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.0 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.52-7.44 (m, 4H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.37-7.29 (m, 3H), 7.28-7.20 (m, 2H), 7.19-7.12 (m, 2H), 6.84 (d, *J* = 13.2 Hz, 1H), 5.99 (dd, *J* = 12.8, 9.2 Hz, 1H), 4.55 (d, *J* = 8.0 Hz, 1H), 3.52 (dd, *J* = 9.2, 8.0 Hz, 1H), 2.98 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 142.5, 139.2, 138.5, 137.7, 136.0, 134.3, 134.2, 130.9, 130.8, 130.5, 129.2, 129.1, 129.0, 128.9, 128.74, 128.70, 128.3, 128.1, 127.0,

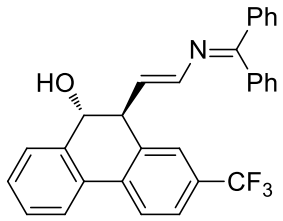
125.2, 125.1, 71.1, 49.0. HRMS *m/z* Calcd. For $C_{29}H_{22}Cl_2NO$ ($M + H^+$): 470.1078; Found: 470.1019.

Compound 8f



Yellow solid; m.p. 76-78 ^oC; IR (KBr) 3412, 1621, 1557, 1446, 1327, 1121 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90-7.80 (m, 3H), 7.70-7.64 (m, 3H), 7.61 (d, *J* = 8.0 Hz, 1H), 7.56 (s, 1H), 7.50-7.38 (m, 4H), 7.34 (dd, *J* = 8.0, 7.2 Hz, 2H), 7.20-7.13 (m, 2H), 6.90 (d, *J* = 13.2 Hz, 1H), 6.06 (dd, *J* = 13.2, 9.2 Hz, 1H), 4.72 (d, *J* = 8.4 Hz, 1H), 3.67 (dd, *J* = 9.2, 8.4 Hz, 1H), 2.77 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 142.9, 139.1, 138.2, 137.4, 136.0, 135.3, 135.0, 131.2, 131.0, 130.9, 129.23, 129.17, 128.71, 128.69, 128.4, 128.3, 125.9 (q, *J* = 3.7 Hz), 125.6 (q, *J* = 3.7 Hz), 124.9 (q, *J* = 3.6 Hz), 124.7, 124.2 (q, *J* = 3.8 Hz), 70.9, 48.9; HRMS *m/z* Calcd. For $C_{31}H_{22}NOF_6$ ($M + H^+$): 538.1606; Found: 538.1604.

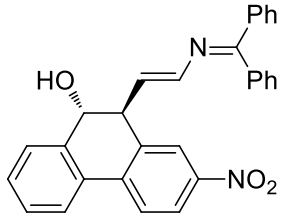
Compound 8g



Yellow solid; m.p. 74-77 ^oC; IR (KBr) 3424, 1618, 1556, 1331, 1120 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.0 Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.57 (d, *J* = 8.4 Hz, 1H), 7.52-7.28 (m, 10H), 7.17-7.11 (m, 2H), 6.84 (d, *J* = 12.8 Hz, 1H), 6.02 (dd, *J* = 12.8, 8.8 Hz, 1H), 4.67 (d, *J* = 6.8 Hz, 1H), 3.68 (dd, *J* = 8.8, 6.8 Hz, 1H), 2.72 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 141.9, 139.3, 137.0, 136.7, 136.4, 136.1, 131.6, 130.7, 129.4, 129.1, 129.0, 128.8, 128.6, 128.3,

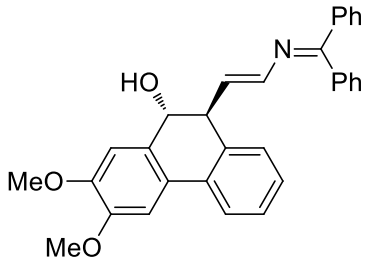
127.7, 126.1 (q, *J* = 3.7 Hz), 124.7 (q, *J* = 3.8 Hz), 124.4, 124.2, 71.6, 49.0; HRMS *m/z* Calcd. For $C_{30}H_{23}NOF_3$ (M + H^+): 470.1732; Found: 470.1721.

Compound 8h



Yellow solid; m.p. 82-85 ^oC; IR (KBr) 3424, 1519, 1446 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 9.0, 2.4 Hz, 1H), 8.09 (d, *J* = 2.4 Hz, 1H), 7.87 (d, *J* = 9.0 Hz, 1H), 7.78 (d, *J* = 7.2 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 2H), 7.51 (d, *J* = 7.2 Hz, 1H), 7.50-7.36 (m, 6H), 7.31 (dd, *J* = 7.8, 7.2 Hz, 2H), 7.15-7.10 (m, 2H), 6.83 (d, *J* = 13.2 Hz, 1H), 5.98 (dd, *J* = 13.2, 9.0 Hz, 1H), 4.71 (d, *J* = 6.6 Hz, 1H), 3.72 (dd, *J* = 9.0, 6.6 Hz, 1H), 2.55 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 147.3, 142.2, 139.3, 139.1, 137.7, 137.4, 136.0, 130.9, 130.8, 130.2, 129.2, 129.14, 129.12, 128.8, 128.7, 128.4, 128.3, 127.8, 125.0, 124.6, 124.4, 123.0, 71.4, 49.0; HRMS *m/z* Calcd. For $C_{29}H_{23}N_2O_3$ (M + H^+): 447.1709; Found: 447.1704.

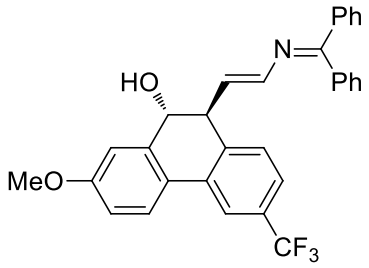
Compound 8i



Yellow solid; m.p. 65-68 ^oC; IR (KBr) 3432, 1516, 1489, 1444, 1277, 1145 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.69-7.60 (m, 3H), 7.47-7.41 (m, 3H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.35-7.18 (m, 6H), 7.17-7.11 (m, 2H), 7.02 (s, 1H), 6.87 (d, *J* = 13.2 Hz, 1H), 6.10 (dd, *J* = 13.2, 9.2 Hz, 1H), 4.61 (d, *J* = 6.8 Hz, 1H), 3.97 (s, 3H), 3.91 (s, 3H), 3.64 (dd, *J* = 9.2, 6.8 Hz, 1H), 2.43 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 149.2, 149.1, 140.9, 139.3, 136.1, 135.1, 132.8, 131.2, 130.5, 129.6, 129.2, 128.91,

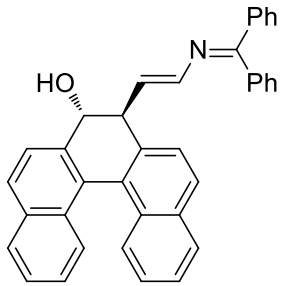
128.86, 128.7, 128.5, 128.2, 127.7, 127.4, 125.4, 123.0, 110.3, 107.2, 71.7, 56.2, 56.0, 49.4; HRMS *m/z* Calcd. For $C_{31}H_{28}NO_3$ (M + H^+): 462.2069; Found: 462.2069.

Compound 8j



Yellow solid; m.p. 69-72 ^oC; IR (KBr) 3419, 1610, 1419, 1336, 1267, 1119 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.90 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.64 (d, *J* = 7.2 Hz, 2H), 7.48-7.36 (m, 5H), 7.36-7.28 (m, 3H), 7.15-7.08 (m, 2H), 7.06 (d, *J* = 2.4 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.4 Hz, 1H), 6.82 (d, *J* = 13.2 Hz, 1H), 6.06 (dd, *J* = 13.2, 9.2 Hz, 1H), 4.64 (d, *J* = 7.2 Hz, 1H), 3.84 (s, 3H), 3.67 (dd, *J* = 9.2, 7.2 Hz, 1H), 2.63 (brs, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 160.4, 141.8, 141.7, 139.2, 138.9, 138.4, 136.0, 133.8, 130.7, 129.6, 129.5, 129.0, 128.7, 128.6, 128.3, 125.6, 124.3, 123.6 (q, *J* = 3.7 Hz), 119.9 (q, *J* = 3.7 Hz), 114.8, 112.3, 71.7, 55.4, 49.1; HRMS *m/z* Calcd. For $C_{31}H_{25}NO_2F_3$ (M + H^+): 500.1837; Found: 500.1835.

Compound 8k



Yellow solid; m.p. 146-148 ^oC; IR (KBr) 3432, 1583, 1552, 1505, 1443, 1318, 1090 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.4 Hz, 1H), 7.98 (d, *J* = 8.4 Hz, 1H), 7.94-7.88 (m, 3H), 7.78 (d, *J* = 7.6 Hz, 2H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.52-7.35 (m, 9H), 7.30-7.19 (m, 4H), 7.14 (d, *J* = 12.8 Hz, 1H), 6.41 (dd, *J* = 12.8, 10.4 Hz, 1H), 4.72 (d, *J* = 12.0 Hz, 1H), 3.56 (dd, *J* = 12.0, 10.4 Hz, 1H), 2.50

(s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.9, 144.2, 139.4, 139.3, 136.1, 136.0, 133.51, 133.50, 130.9, 130.43, 130.36, 130.2, 130.0, 129.2, 129.1, 128.8, 128.73, 128.69, 128.5, 128.41, 128.37, 128.34, 128.2, 127.8, 127.3, 125.4, 125.3, 125.2, 125.1, 125.0, 121.5, 72.0, 51.2. HRMS *m/z* Calcd. For $C_{37}H_{28}NO$ ($M + H^+$): 502.2171; Found: 502.2145.

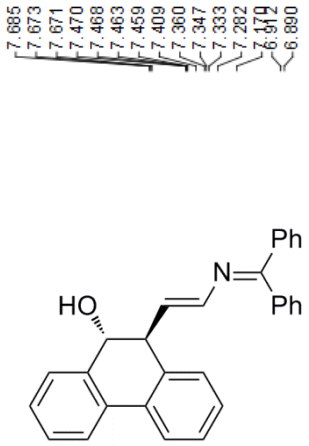
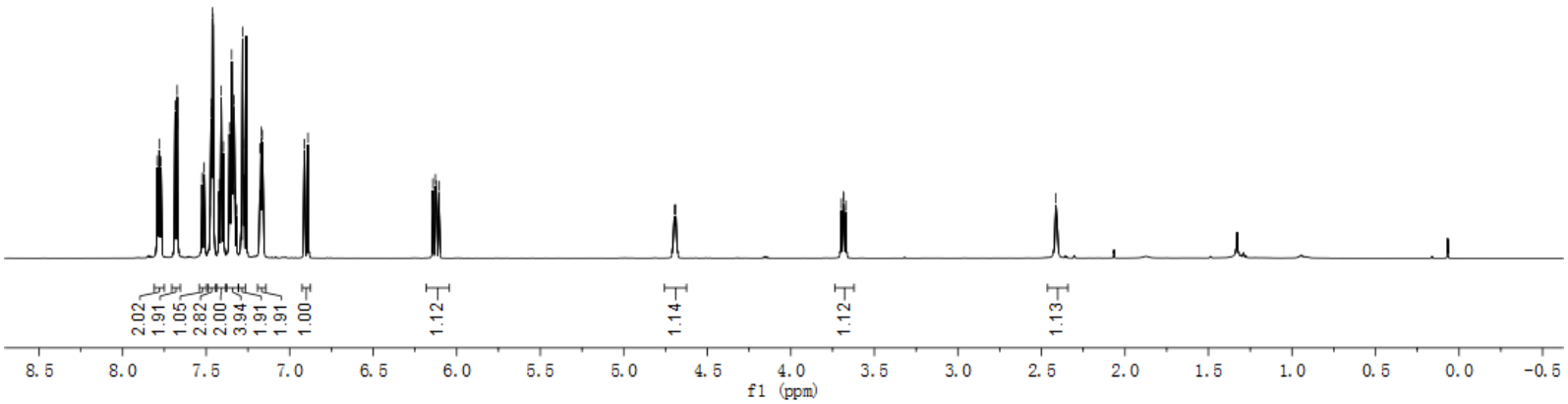


Table 2, entry 1, 8a



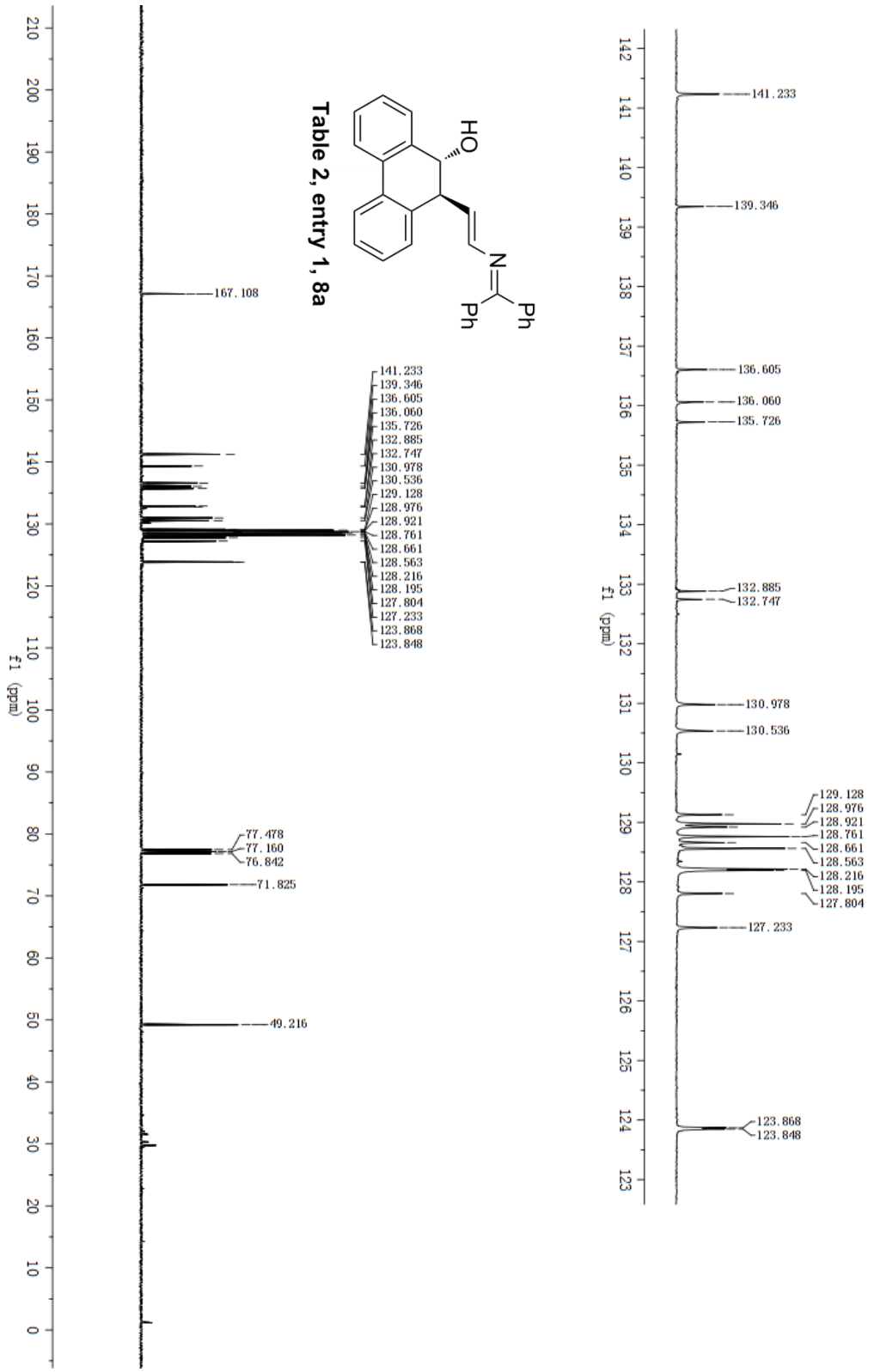


Table 2, entry 1, 8a
HO
N
Ph
Ph
f1 (ppm)
167.108
141.233
139.346
136.605
136.060
135.726
132.885
132.747
130.978
130.536
129.128
128.976
128.921
128.761
128.661
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77.478
77.160
76.842
71.825
49.216

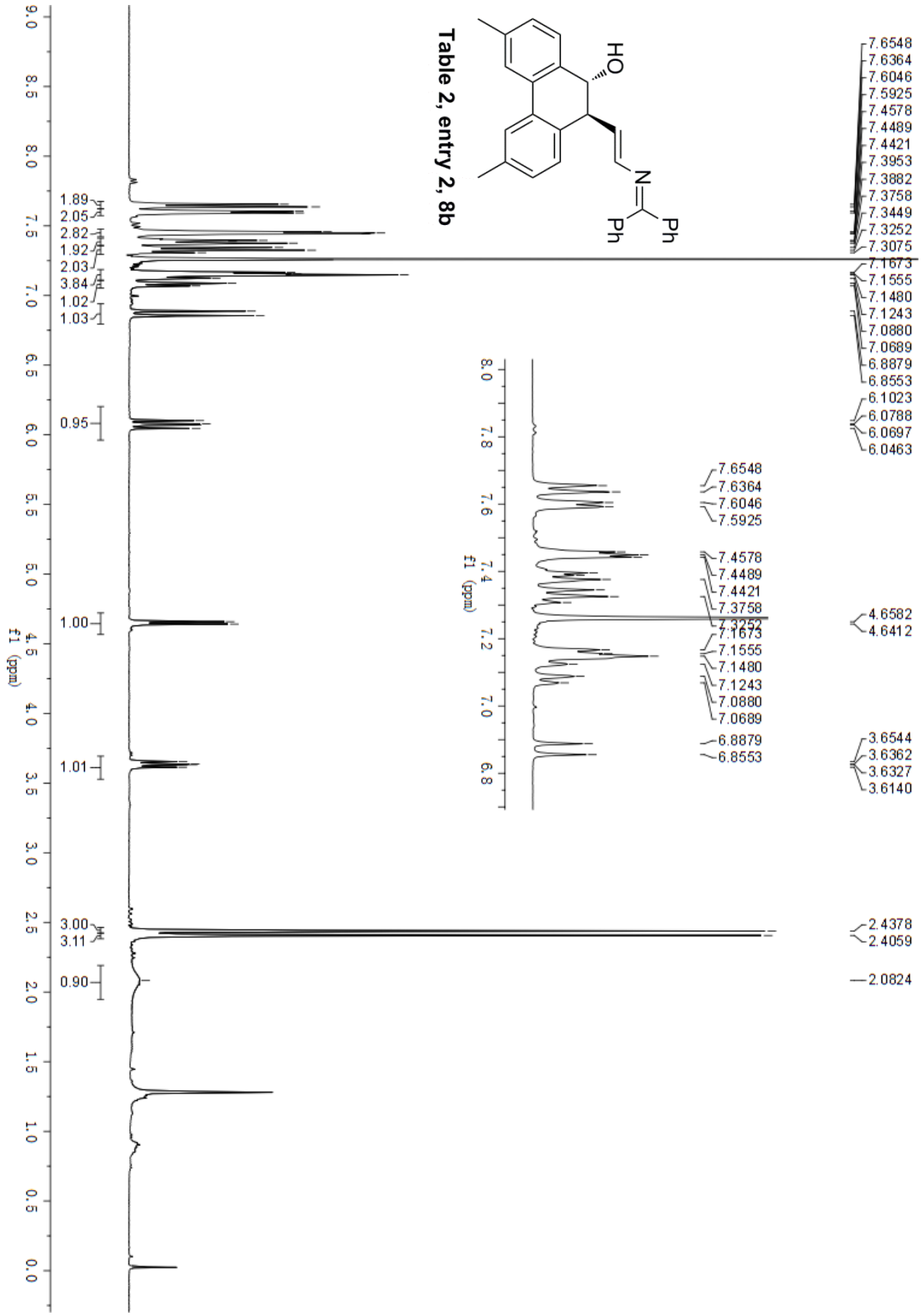
Table 2, entry 2, 8b
HO
N
Ph
Ph
f1 (ppm)
1.89
2.05
2.82
1.92
2.03
3.84
1.02
1.03
0.95
1.00
1.01
3.00
3.11
0.90
7.6548
7.6364
7.6046
7.5925
7.4578
7.4489
7.4421
7.3953
7.3882
7.3758
7.3449
7.3252
7.3075
7.1673
7.1555
7.1480
7.1243
7.0880
7.0689
6.8879
6.8553
6.1023
6.0788
6.0697
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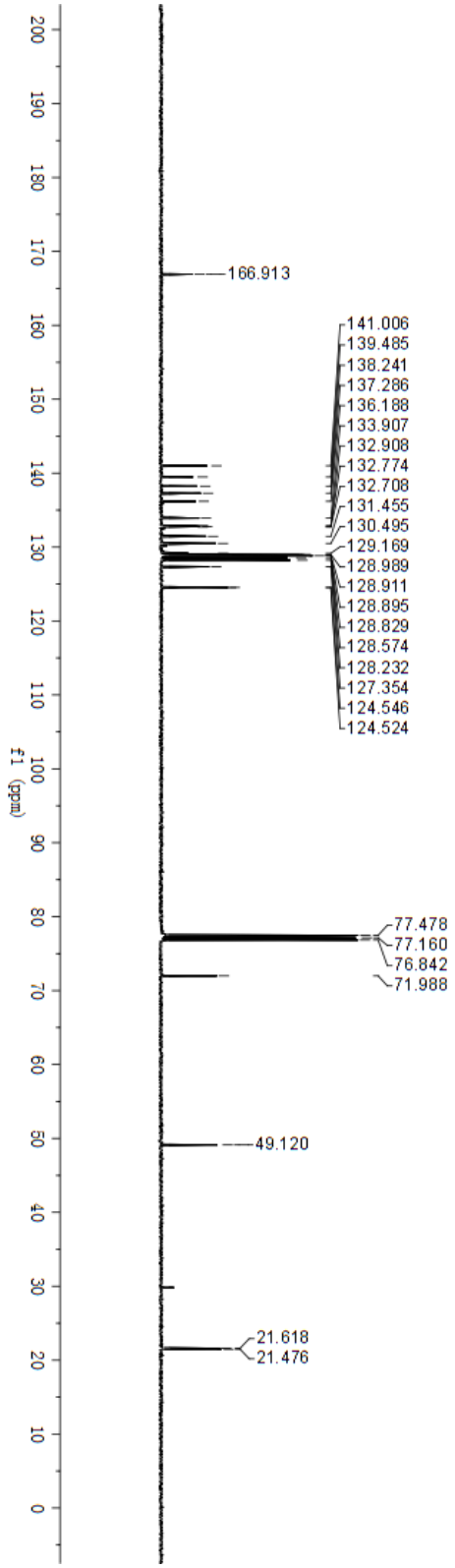
3.6327
3.6140
2.4378
2.4059
2.0824



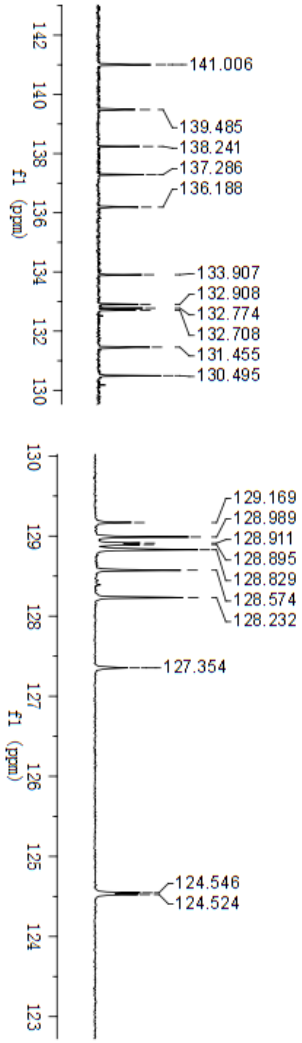
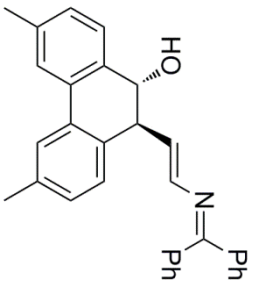


Table 2, entry 2, 8b



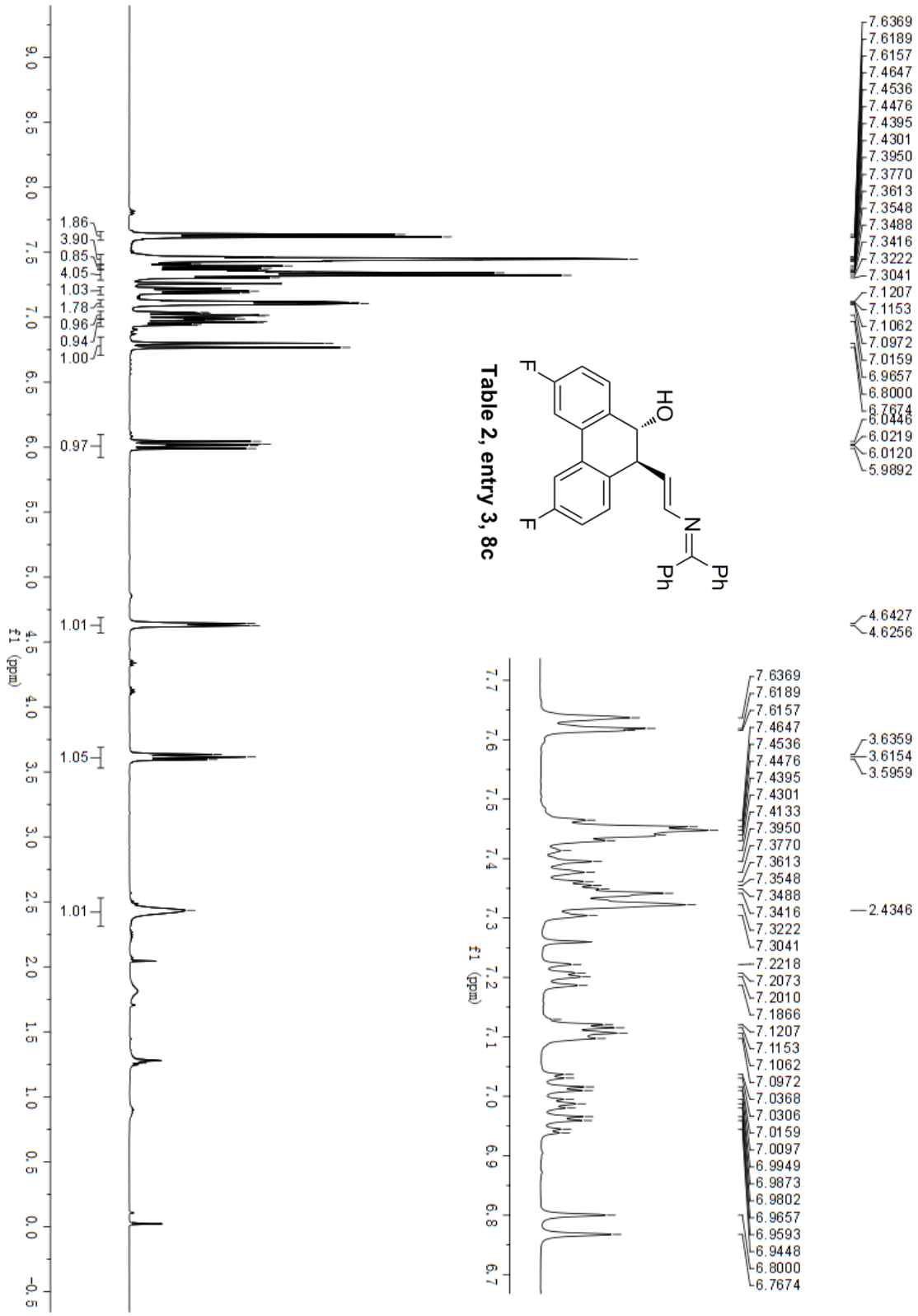
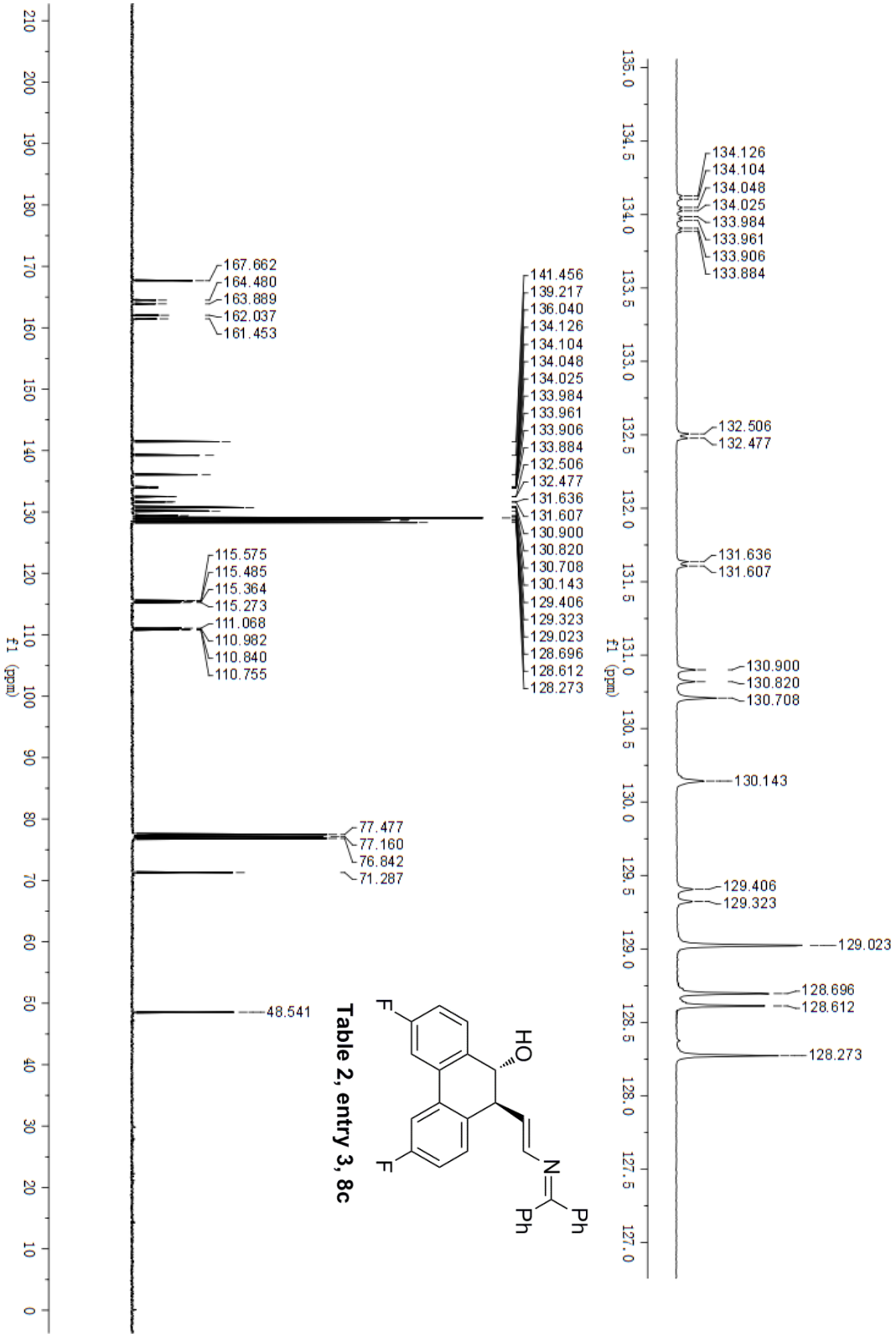


Table 2, entry 3, 8c
F
HO
F
N
Ph
Ph
f1 (ppm)
1.86
3.90
0.85
4.05
1.03
1.78
0.96
0.94
1.00
0.97
1.01
1.05
1.01
7.6369
7.6189
7.6157
7.4647
7.4536
7.4476
7.4395
7.4301
7.3950
7.3770
7.3613
7.3548
7.3488
7.3416
7.3222
7.3041
7.1207
7.1153
7.1062
7.0972
7.0159
6.9657
6.8000
6.7674
6.0446
6.0219
6.0120
5.9892
4.6427
4.6256
3.6359
3.6154
3.5959
2.4346
7.2218
7.2073
7.2010
7.1866
7.0368
7.0306
7.0097
6.9949
6.9873
6.9802
6.9593
6.9448


167.662
164.480
163.889
162.037
161.453
141.456
139.217
136.040
134.126
134.104
134.048
134.025
133.984
133.961
133.906
133.884
132.506
132.477
131.636
131.607
130.900
130.820
130.708
130.143
129.406
129.323
129.023
128.696
128.612
128.273
115.575
115.485
115.364
115.273
111.068
110.982
110.840
110.755
77.477
77.160
76.842
71.287
48.541
f1 (ppm)
Table 2, entry 3, 8c
F
HO
F
N
Ph
Ph

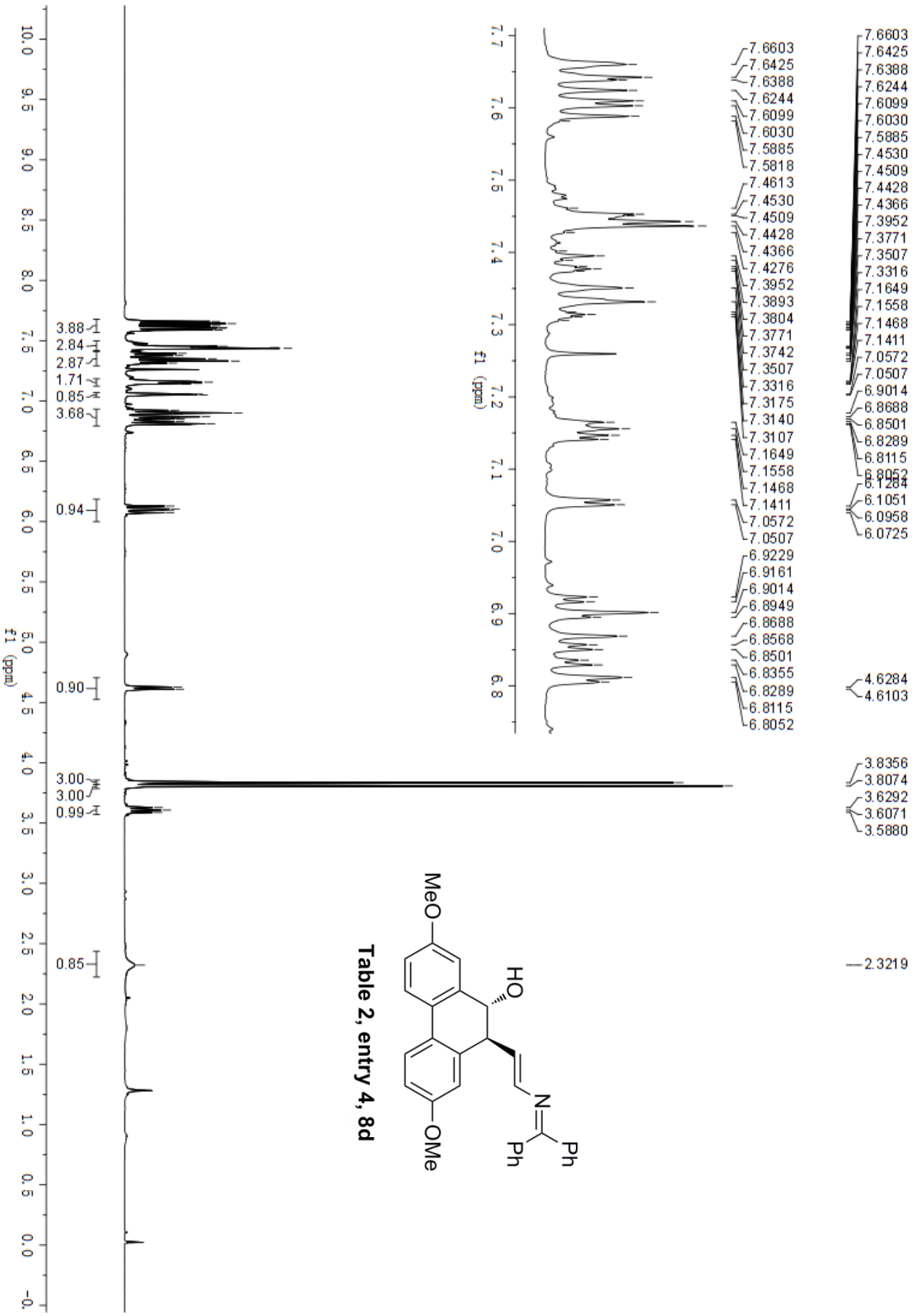


Table 2, entry 4, 8d

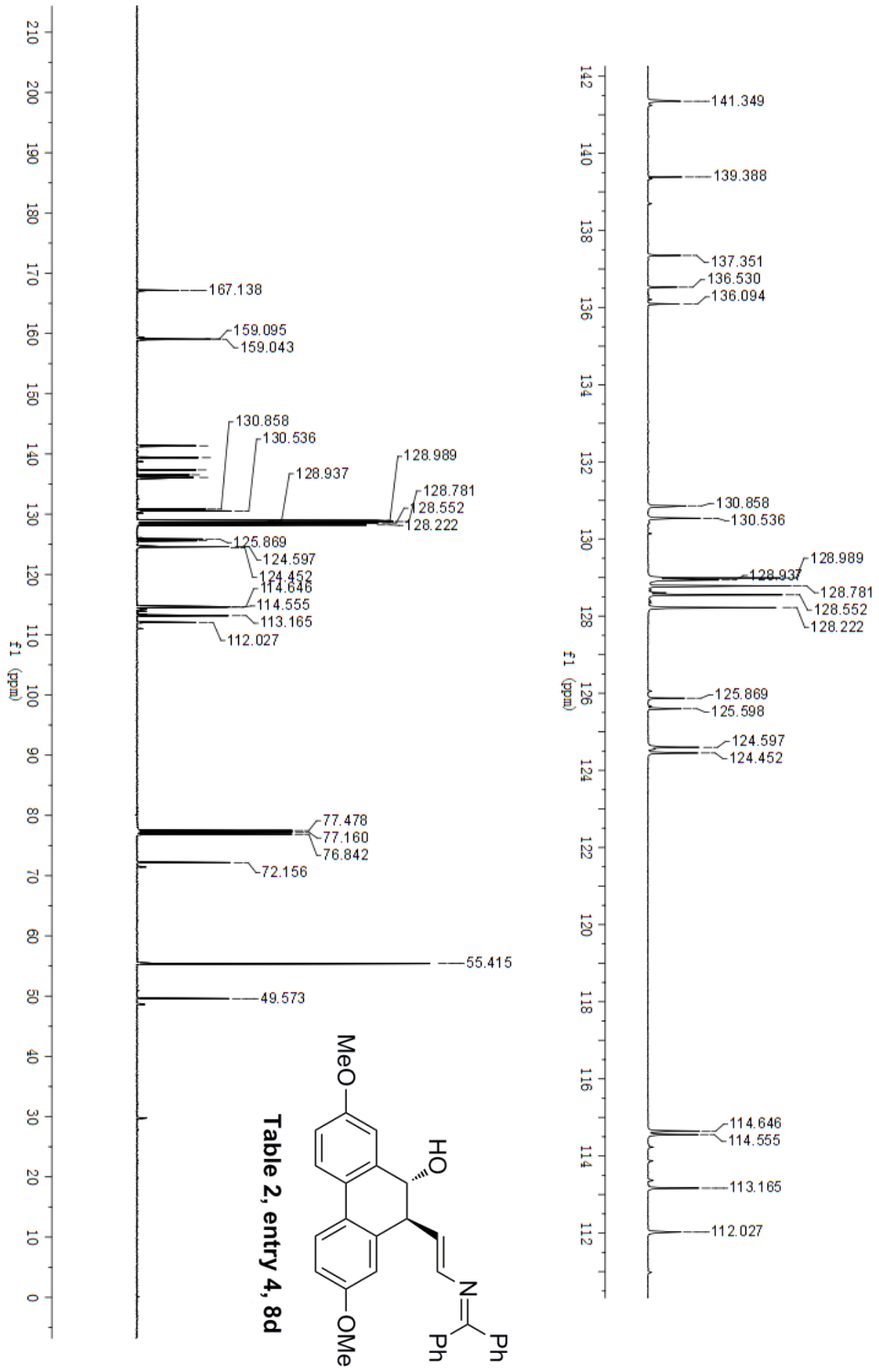


Table 2, entry 4, 8d

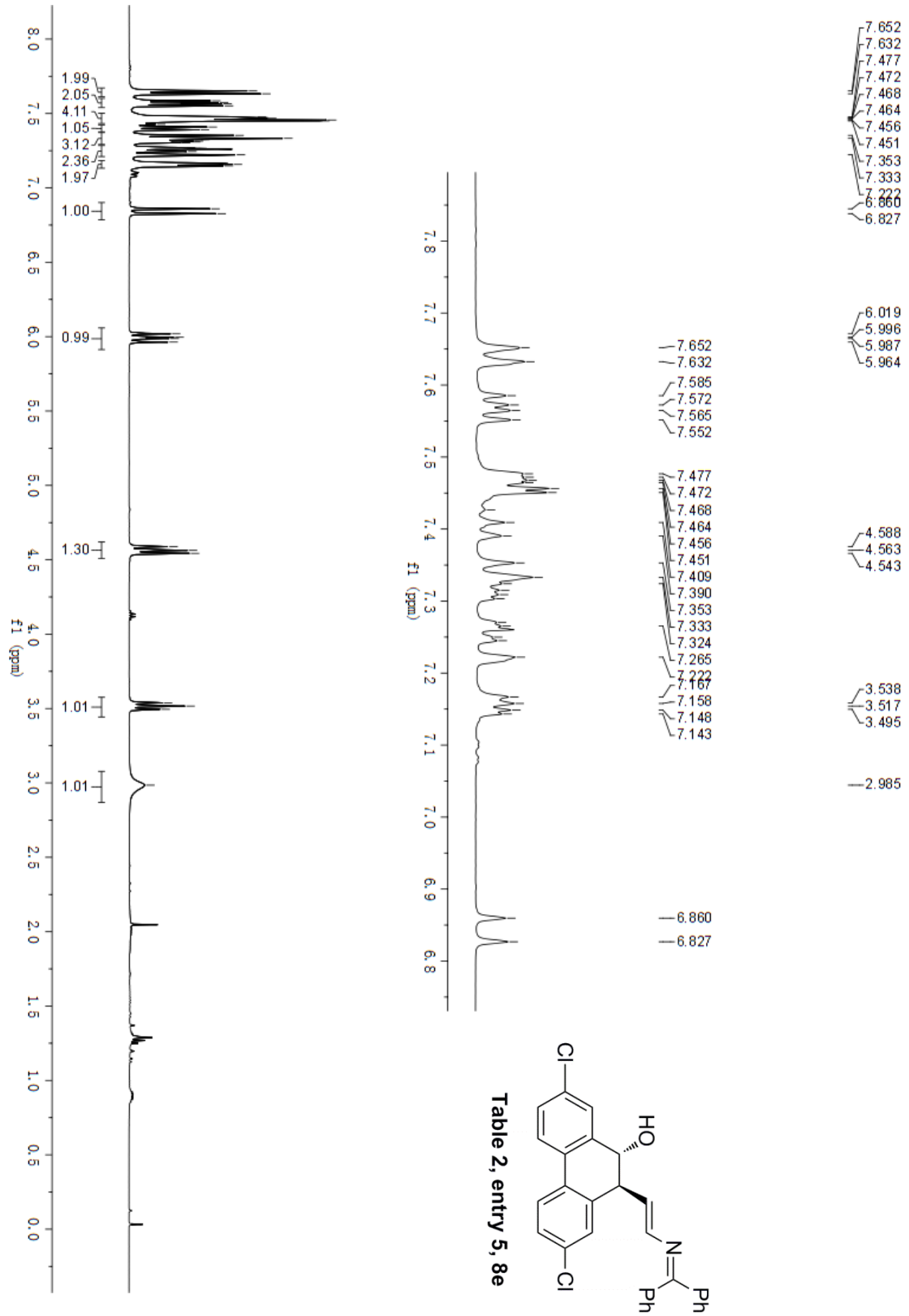


Table 2, entry 5, 8e

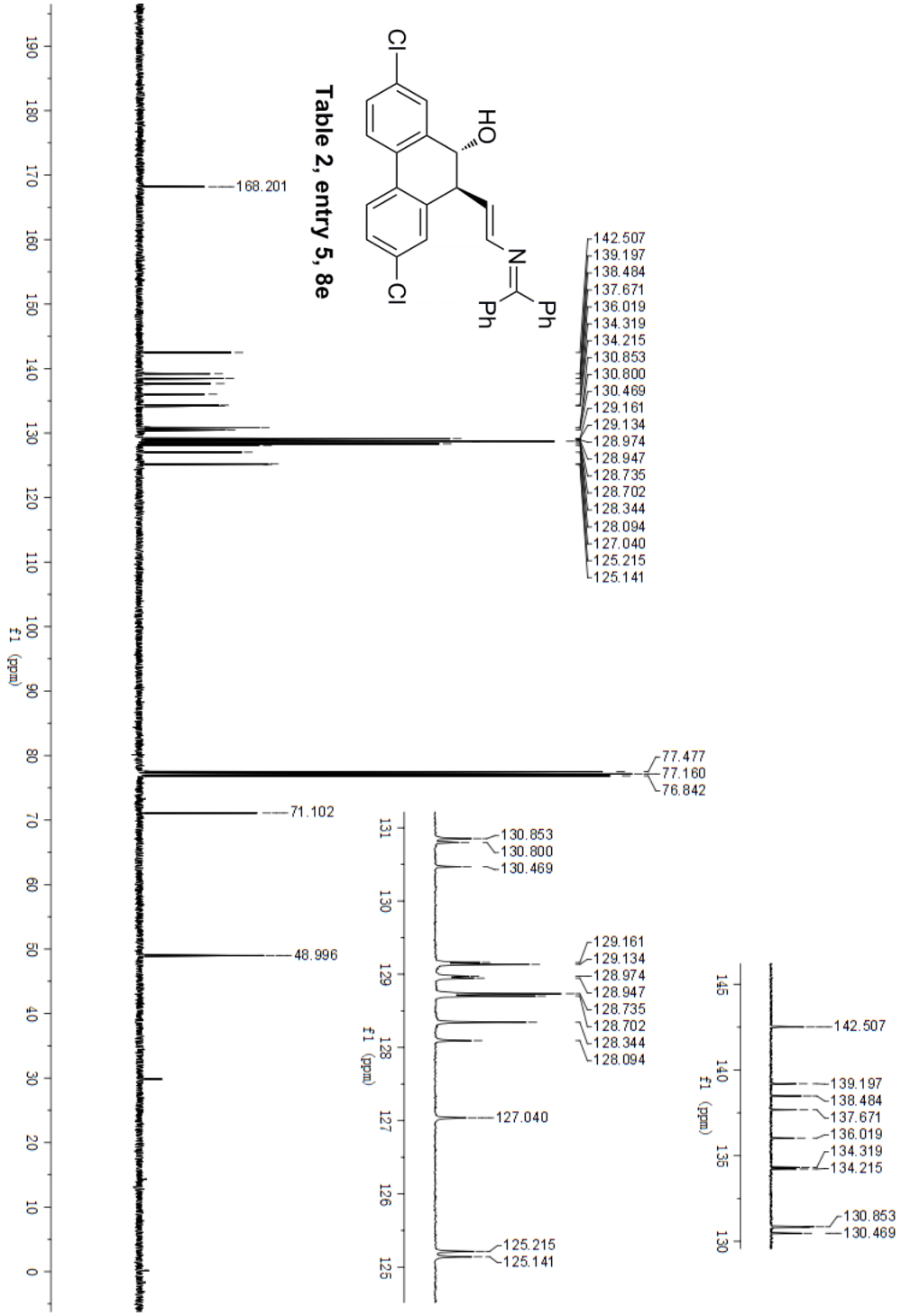


Table 2, entry 5, 8e
Cl
HO
N
Ph
Ph
Cl
168.201
142.507
139.197
138.484
137.671
136.019
134.319
134.215
130.853
130.800
130.469
129.161
129.134
128.974
128.947
128.735
128.702
128.344
128.094
127.040
125.215
125.141
77.477
77.160
76.842
71.102
48.996
f1 (ppm)

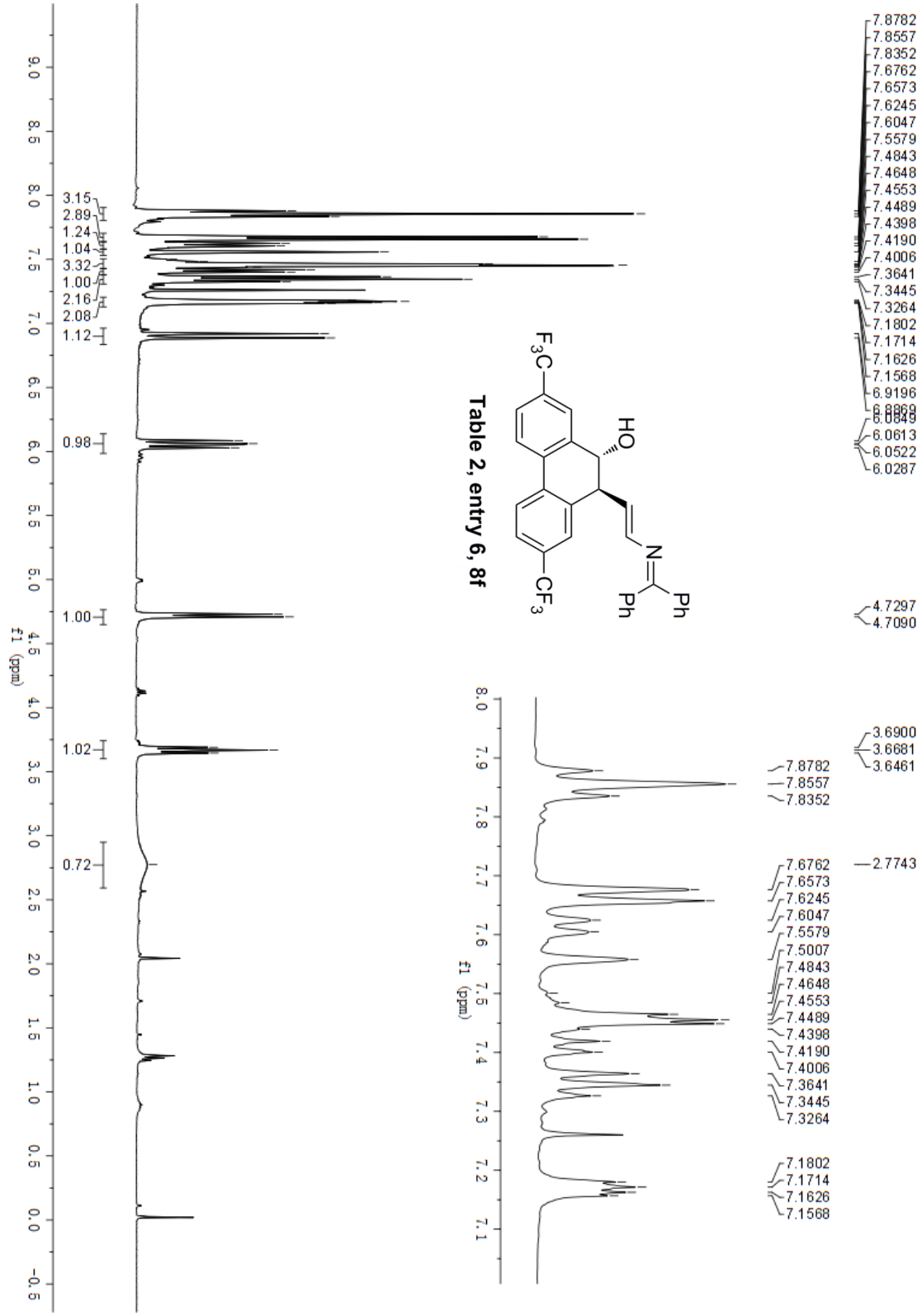
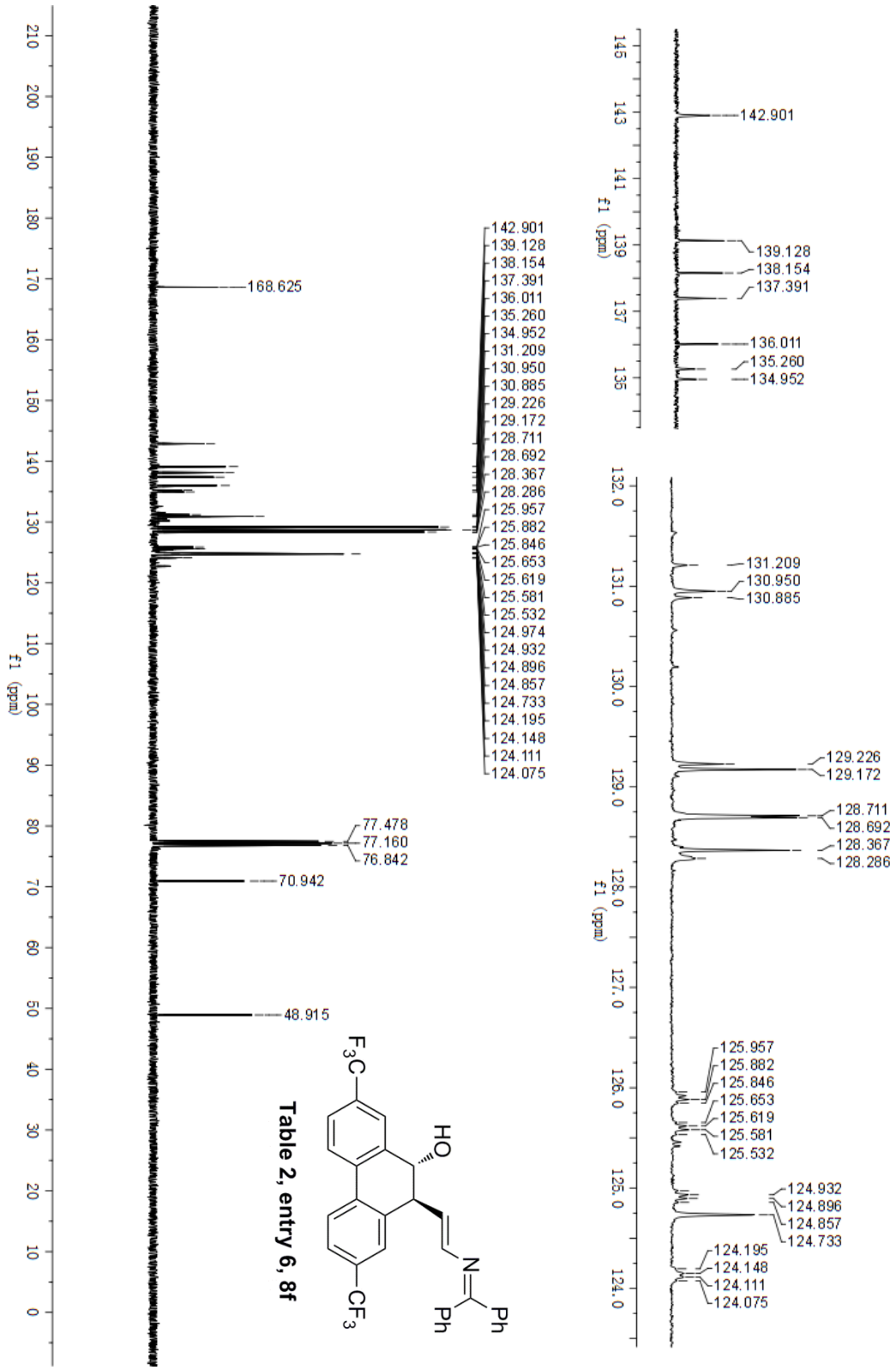
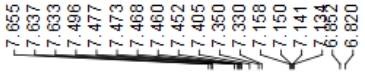


Table 2, entry 6, 8f
F3C
CF3
HO
N
Ph
Ph
7.8782
7.8557
7.8352
7.6762
7.6573
7.6245
7.6047
7.5579
7.4843
7.4648
7.4553
7.4489
7.4398
7.4190
7.4006
7.3641
7.3445
7.3264
7.1802
7.1714
7.1626
7.1568
6.9196
6.0613
6.0522
6.0287
4.7297
4.7090
3.6900
3.6681
3.6461
2.7743
3.15
2.89
1.24
1.04
3.32
1.00
2.16
2.08
1.12
0.98
1.00
1.02
0.72
f1 (ppm)


168.625
142.901
139.128
138.154
137.391
136.011
135.260
134.952
131.209
130.950
130.885
129.226
129.172
128.711
128.692
128.367
128.286
125.957
125.882
125.846
125.653
125.619
125.581
125.532
124.974
124.932
124.896
124.857
124.733
124.195
124.148
124.111
124.075
77.478
77.160
76.842
70.942
48.915
f1 (ppm)
F3C
CF3
HO
N
Ph
Ph
Table 2, entry 6, 8f



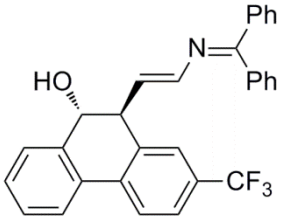
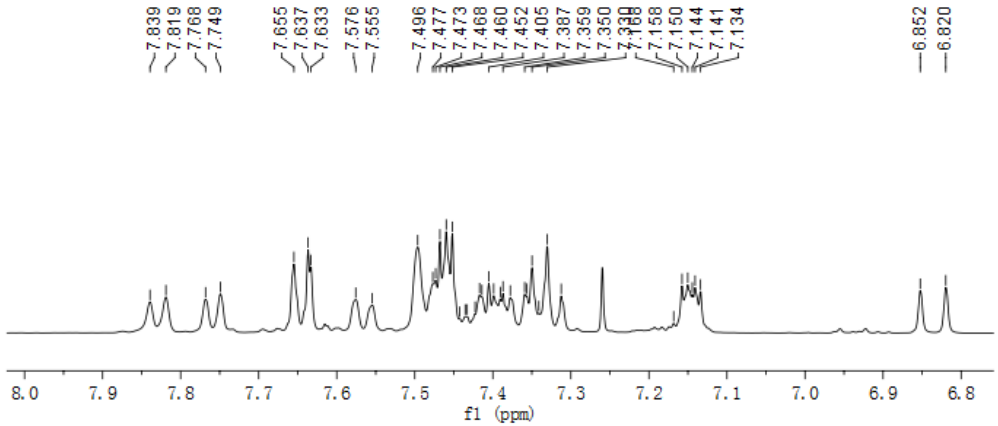
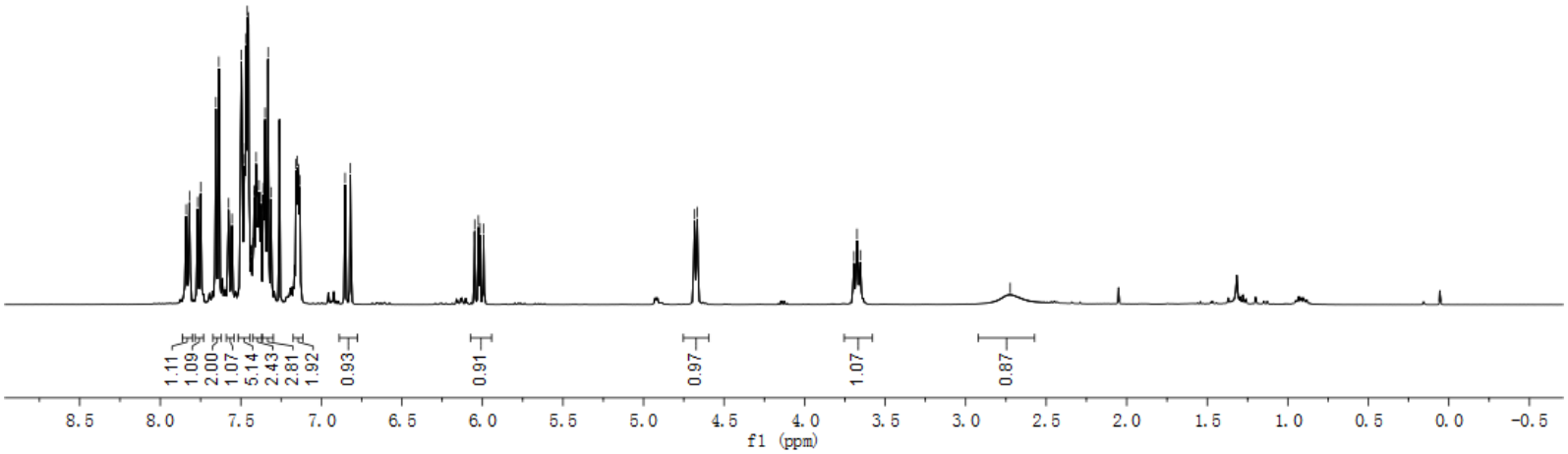


Table 2, entry 7, 8g





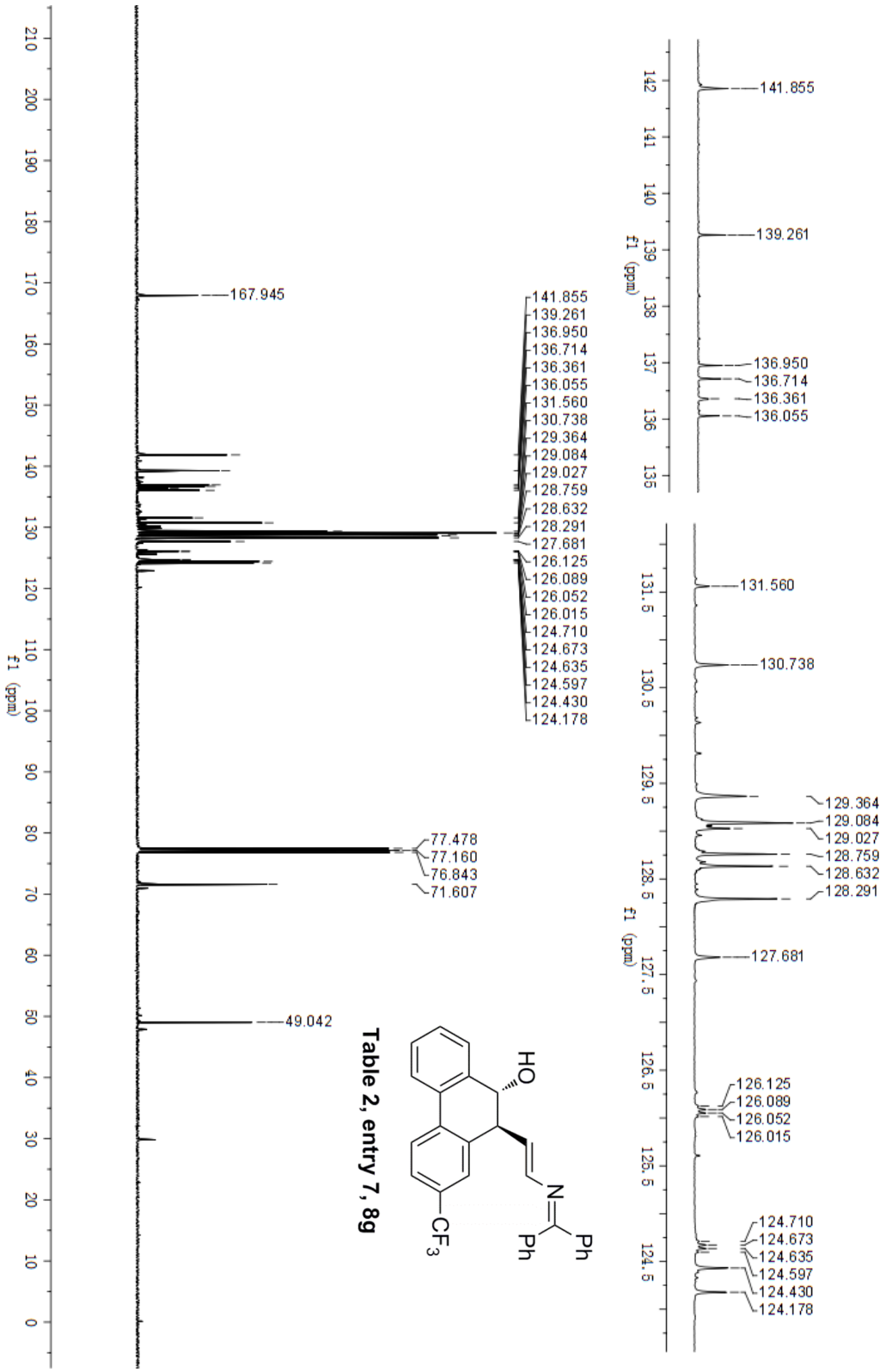


Table 2, entry 7, 8g

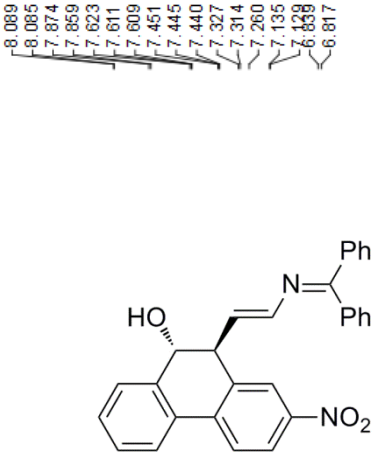
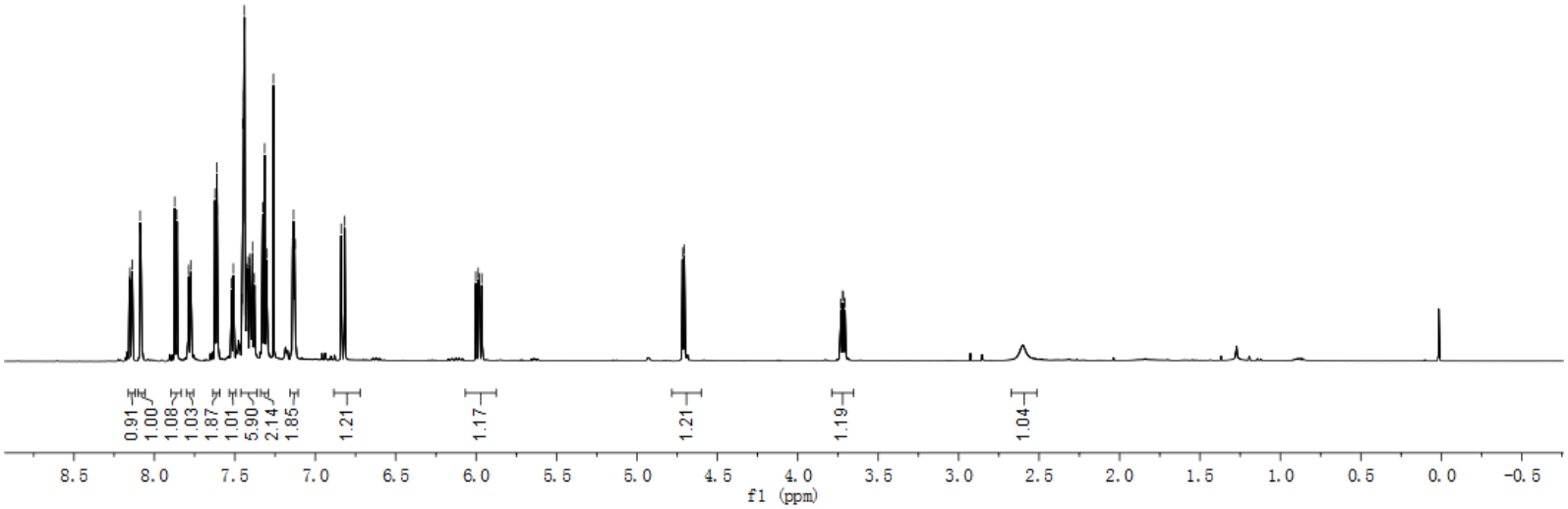


Table 2, entry 8, 8h



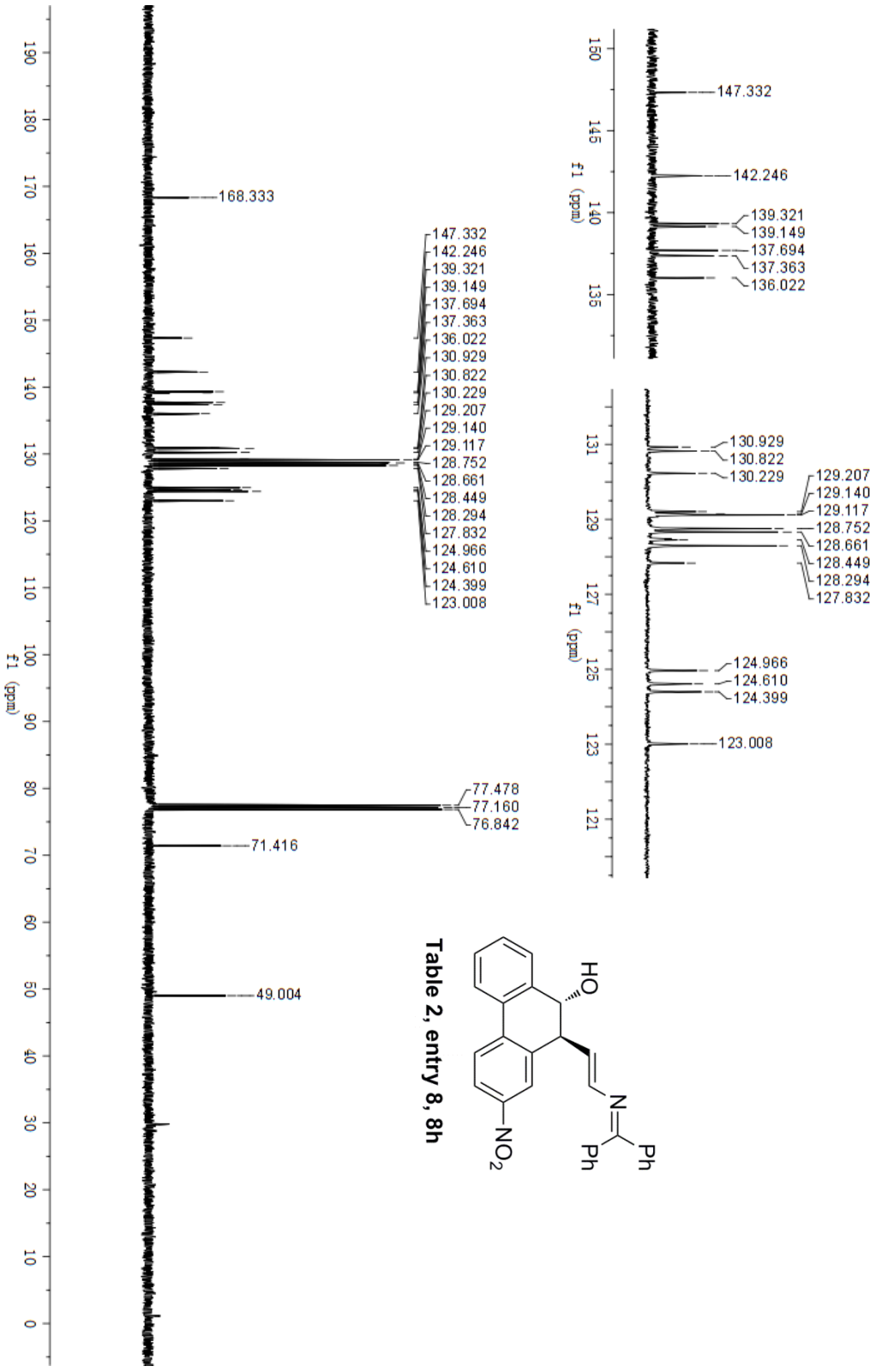


Table 2, entry 8, 8h

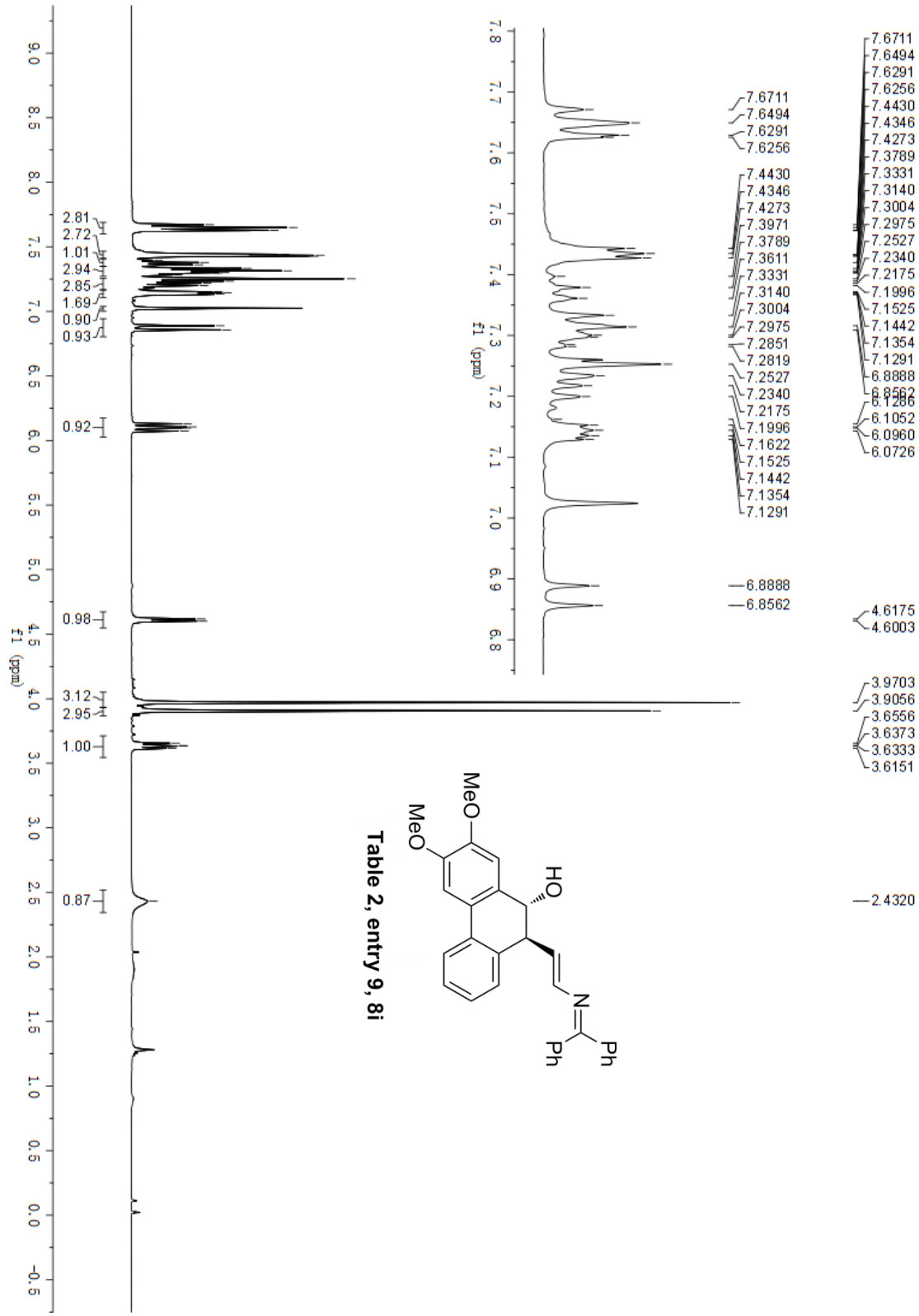
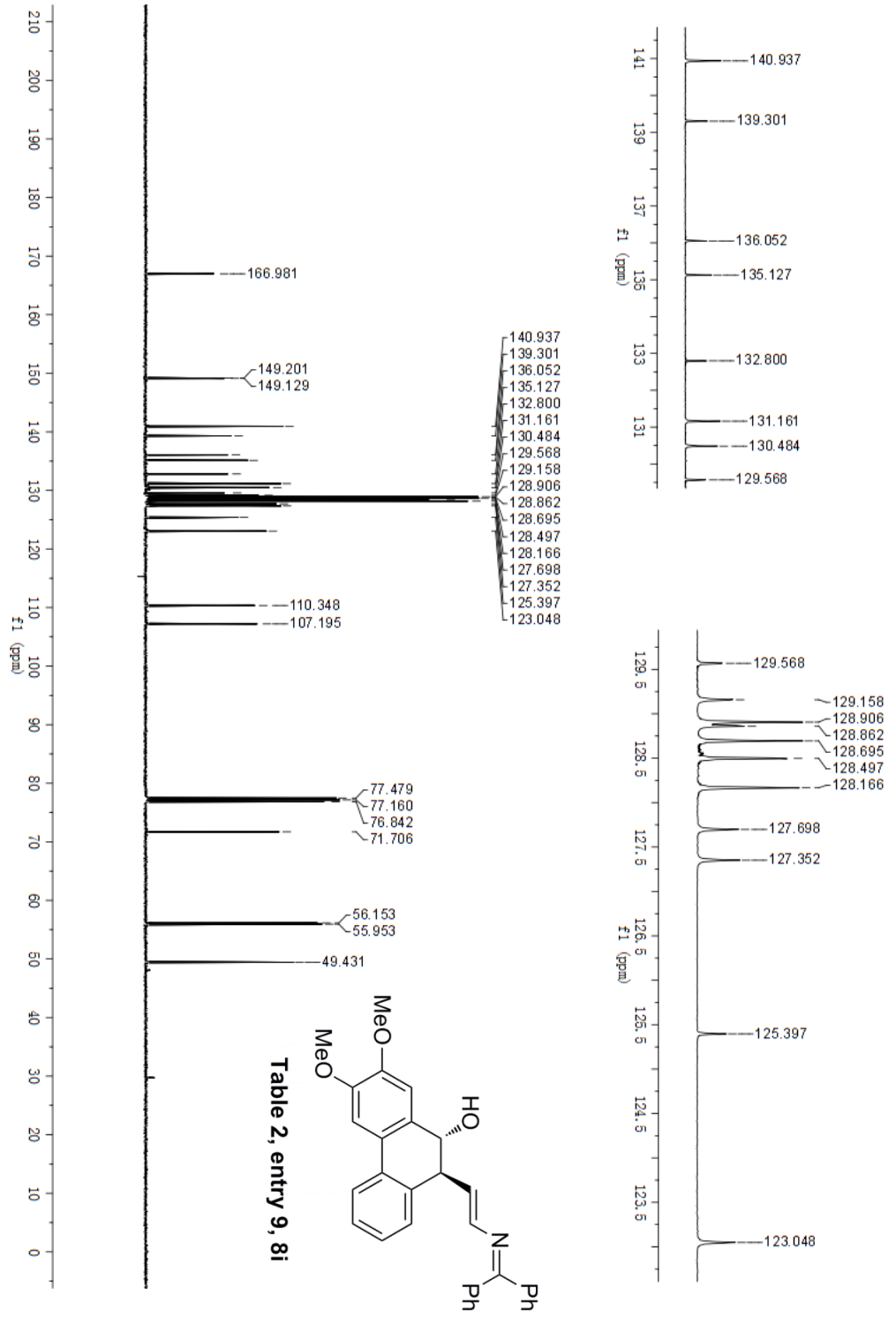


Table 2, entry 9, 8i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149.201
149.129
140.937
139.301
136.052
135.127
132.800
131.161
130.484
129.568
129.158
128.906
128.862
128.695
128.497
128.166
127.698
127.352
125.397
123.048
110.348
107.195
77.479
77.160
76.842
71.706
56.153
55.953
49.431
f1 (ppm)
MeO
MeO
HO
N
Ph
Ph
Table 2, entry 9, 8i

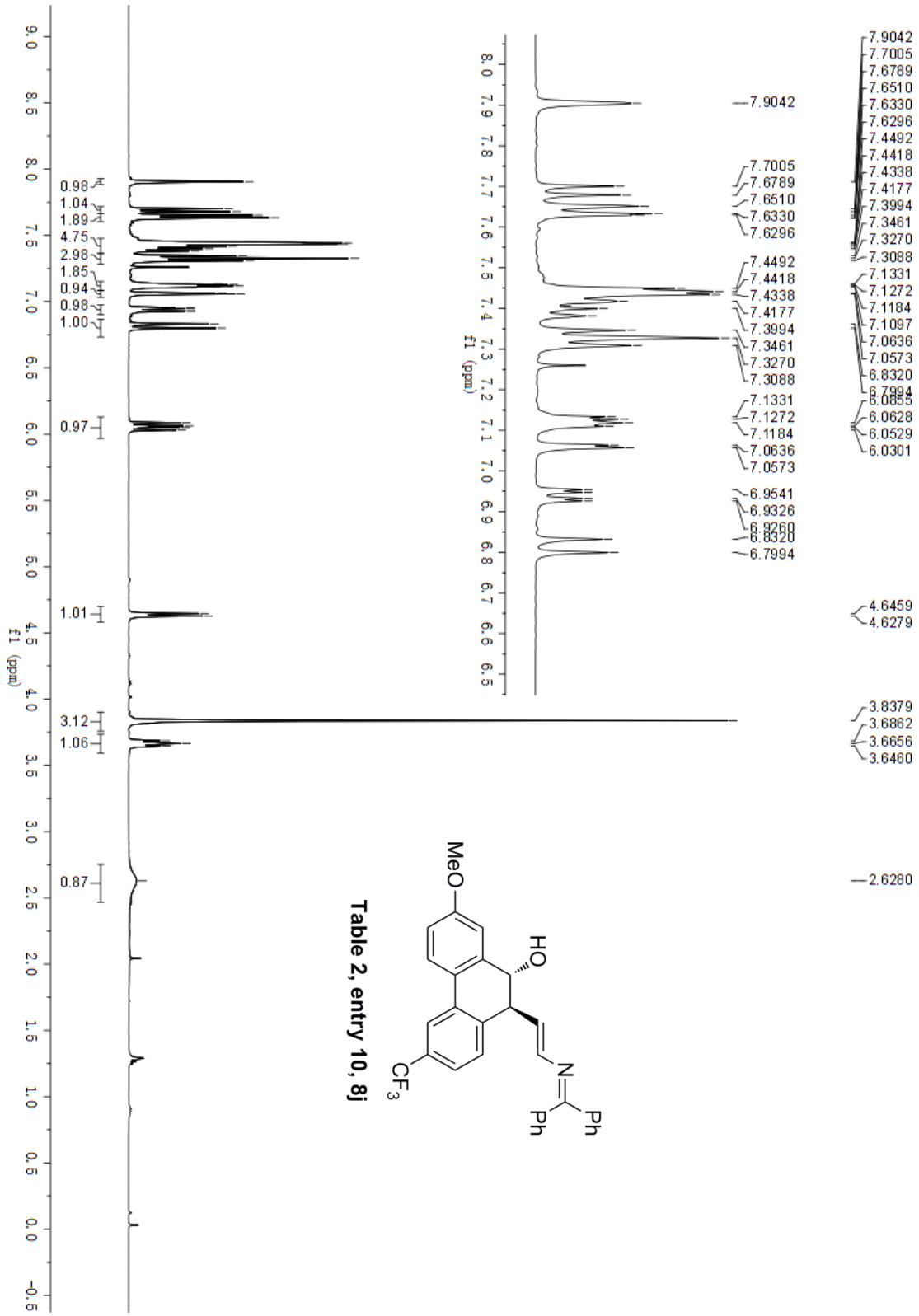
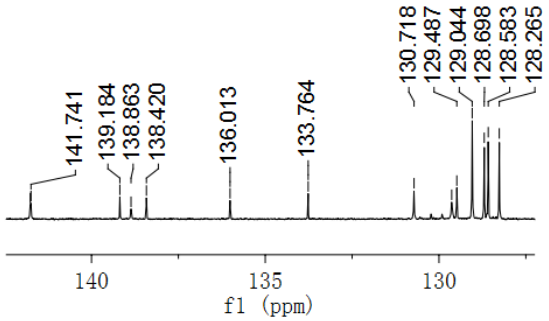
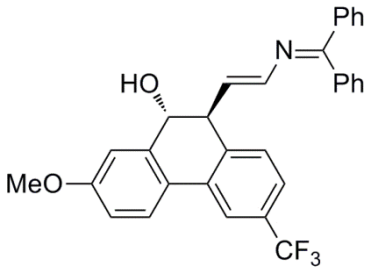


Table 2, entry 10, 8j





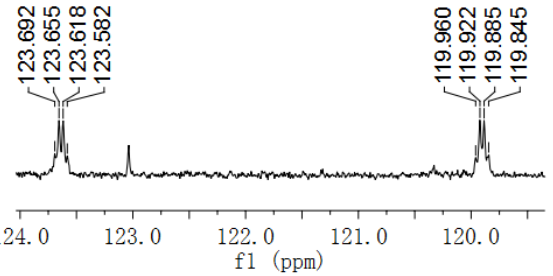
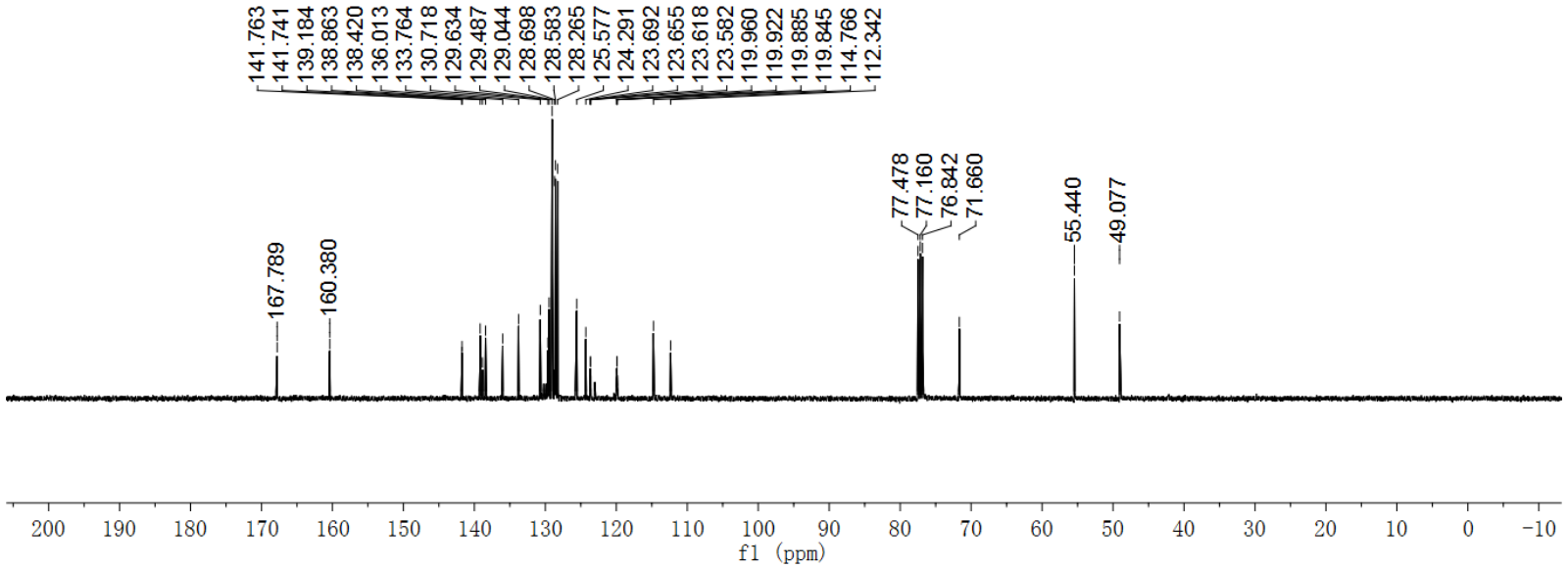
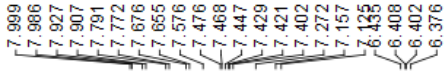


Table 2, entry 10, 8j





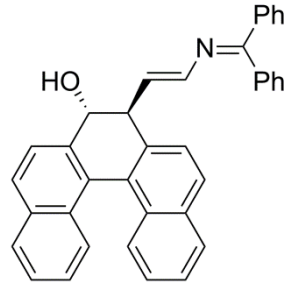
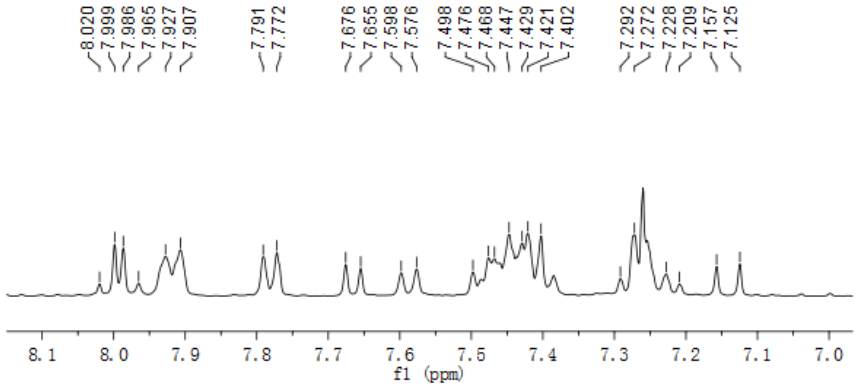
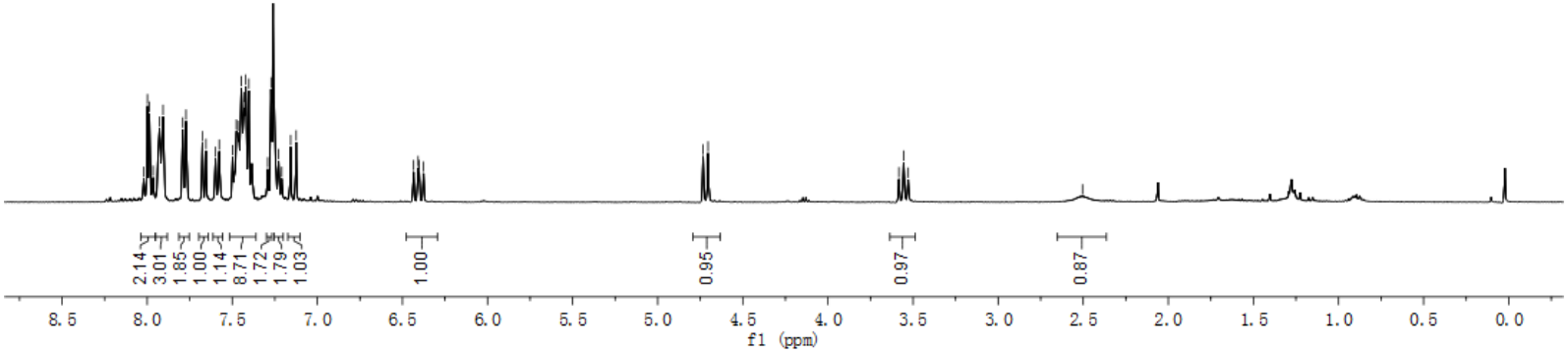
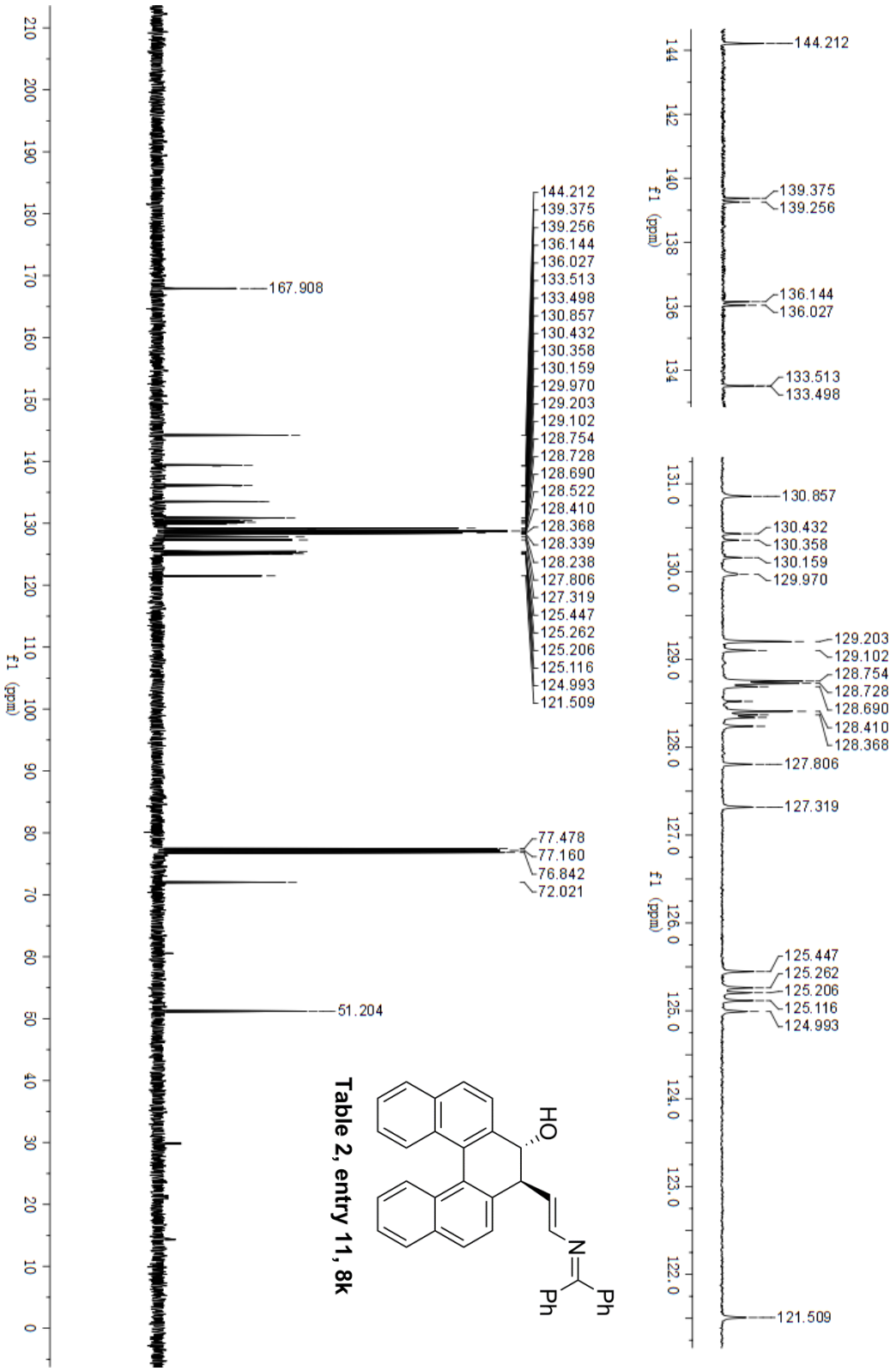


Table 2, entry 11, 8k



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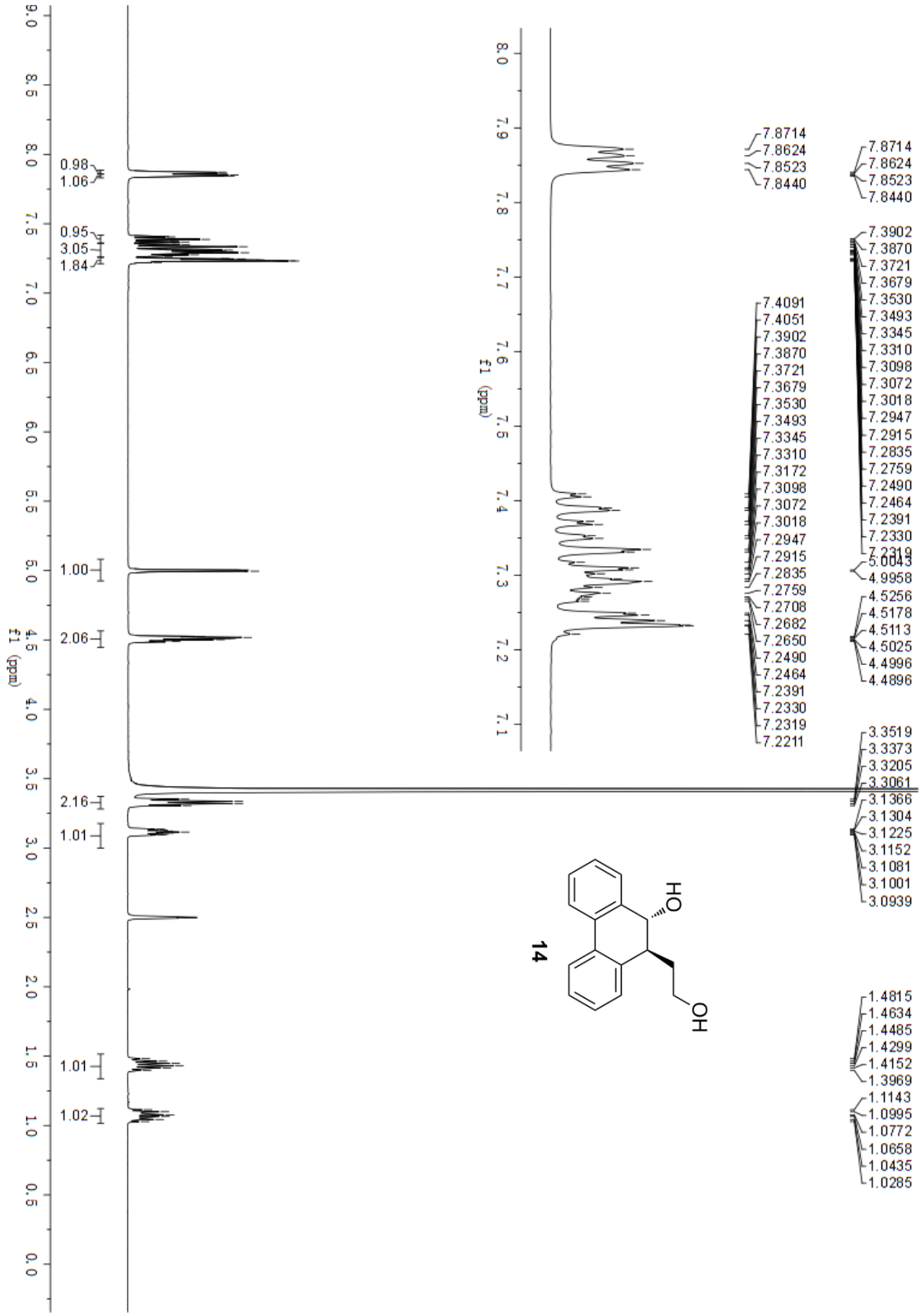
139.256
136.144
136.027
133.513
133.498
130.857
130.432
130.358
130.159
129.970
129.203
129.102
128.754
128.728
128.690
128.522
128.410
128.368
128.339
128.238
127.806
127.319
125.447
125.262
125.206
125.116
124.993
121.509
167.908
77.478
77.160
76.842
72.021
51.204
f1 (ppm)
HO
N
Ph
Ph
Table 2, entry 11, 8k


f1 (ppm)
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1.06
0.95
3.05
1.84
1.00
2.06
2.16
1.01
1.01
1.02
7.8714
7.8624
7.8523
7.8440
7.4091
7.4051
7.3902
7.3870
7.3721
7.3679
7.3530
7.3493
7.3345
7.3310
7.3172
7.3098
7.3072
7.3018
7.2947
7.2915
7.2835
7.2759
7.2708
7.2682
7.2650
7.2490
7.2464
7.2391
7.2330
7.2319
7.2211
5.0043
4.9958
4.5256
4.5178
4.5113
4.5025
4.4996
4.4896
3.3519
3.3373
3.3205
3.3061
3.1366
3.1304
3.1225
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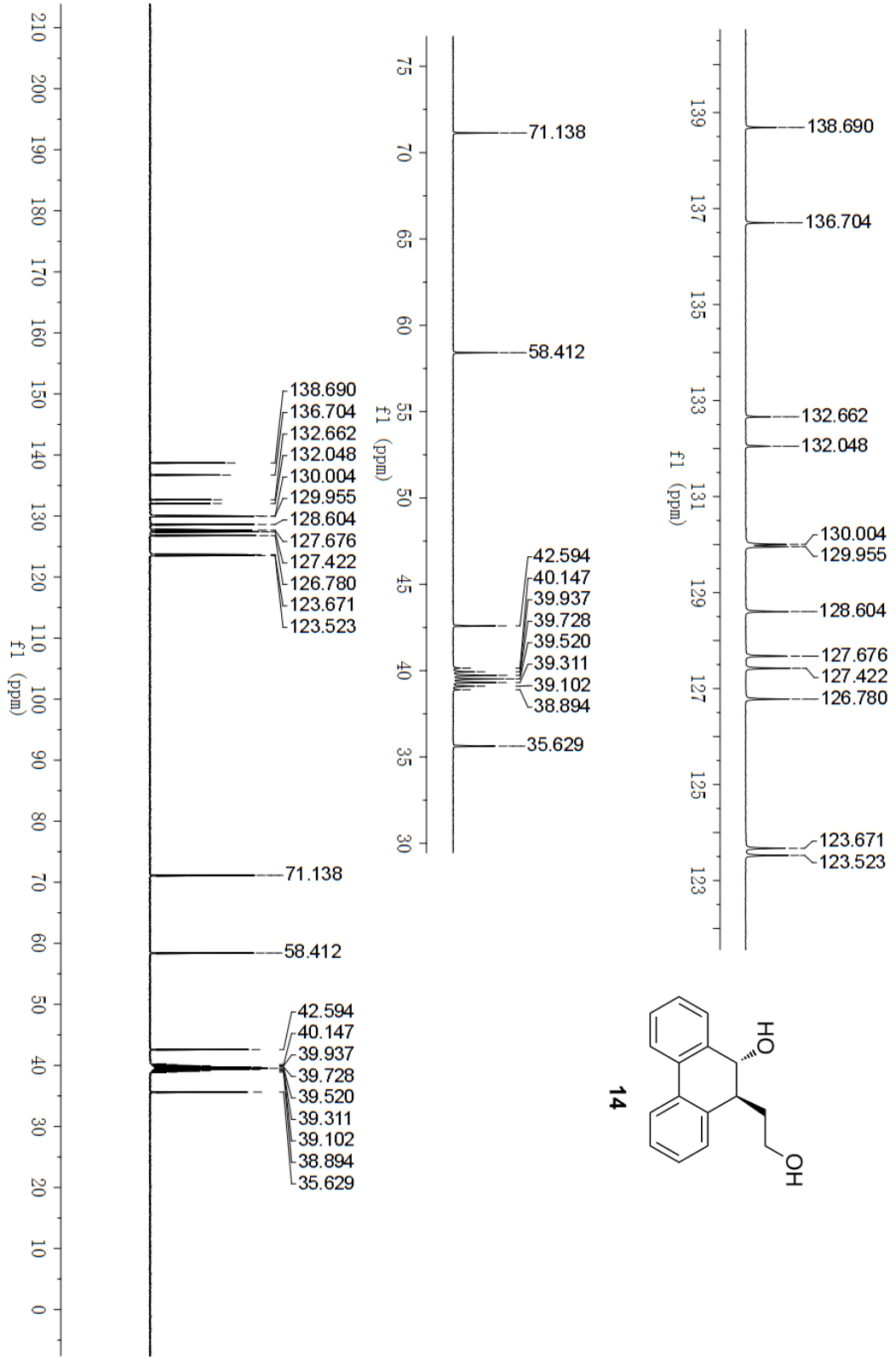
1.1143
1.0995
1.0772
1.0658
1.0435
1.0285
HO
OH
14


f1 (ppm)
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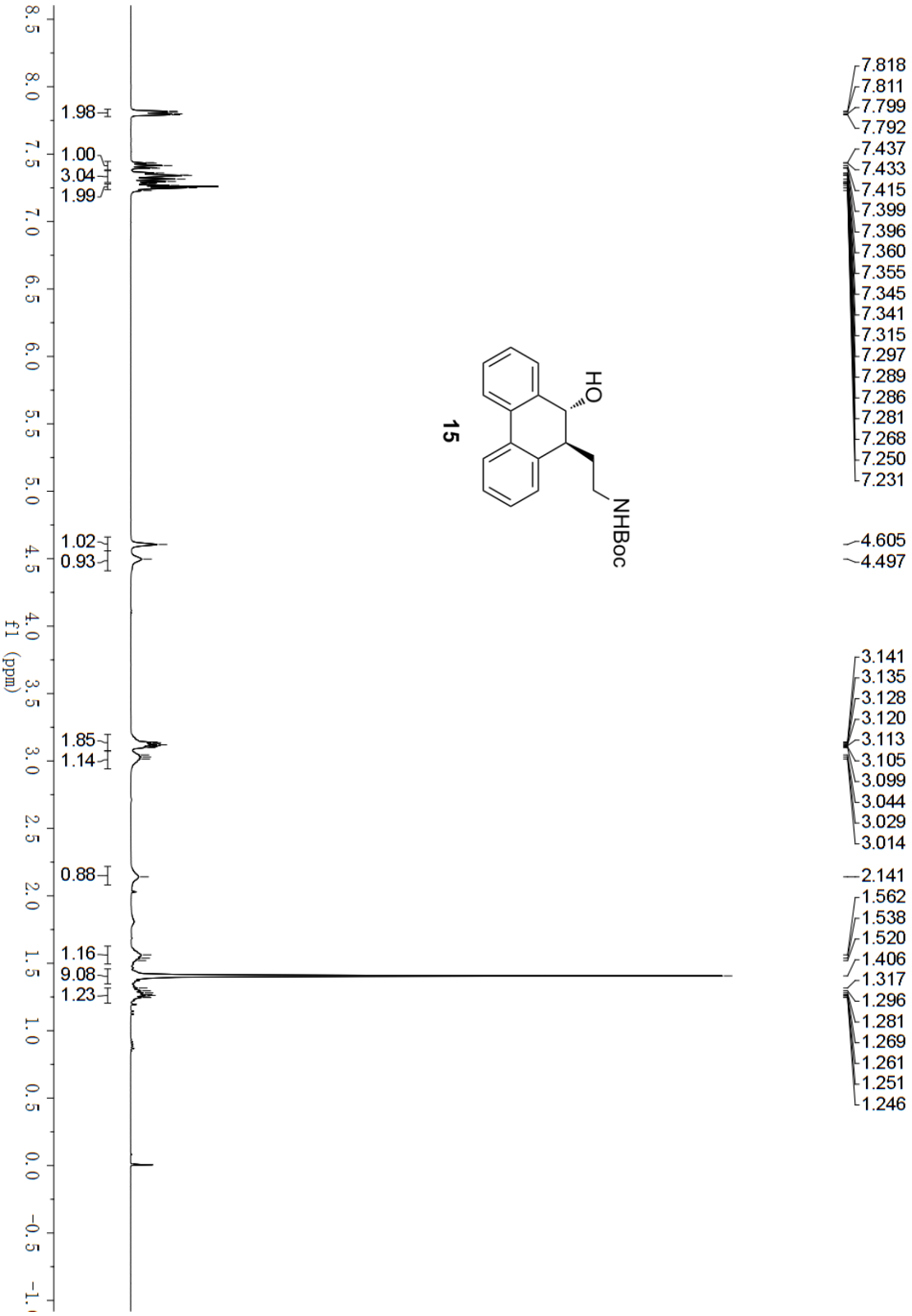
136.704
132.662
132.048
130.004
129.955
128.604
127.676
127.422
126.780
123.671
123.523
71.138
58.412
42.594
40.147
39.937
39.728
39.520
39.311
39.102
38.894
35.629
14
HO
HO


15
HO
NHBoc
f1 (ppm)
1.98
1.00
3.04
1.99
1.02
0.93
1.85
1.14
0.88
1.16
9.08
1.23
7.818
7.811
7.799
7.792
7.437
7.433
7.415
7.399
7.396
7.360
7.355
7.345
7.341
7.315
7.297
7.289
7.286
7.281
7.268
7.250
7.231
4.605
4.497
3.141
3.135
3.128
3.120
3.113
3.105
3.099
3.044
3.029
3.014
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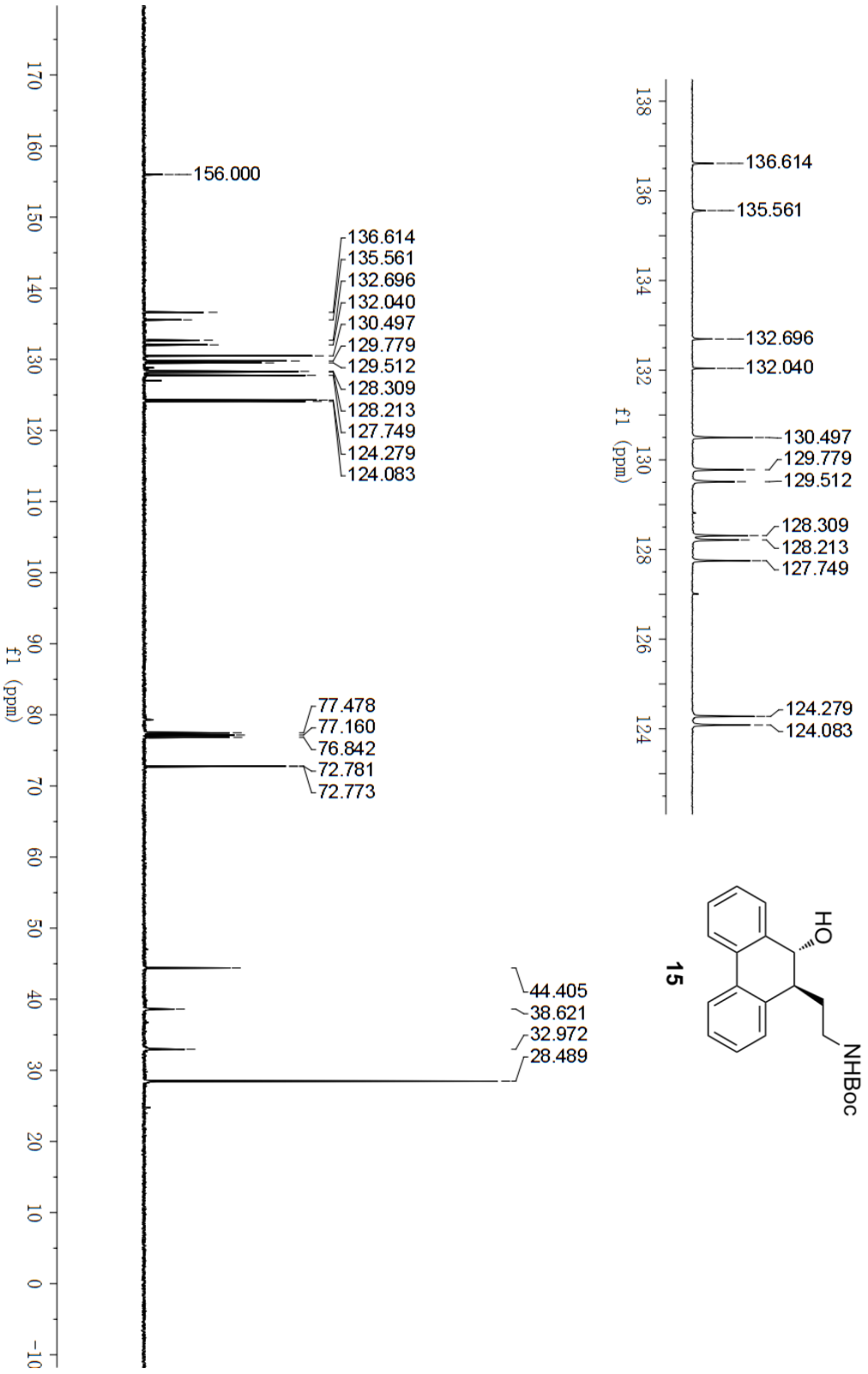
1.261
1.251
1.246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136.614
135.561
132.696
132.040
130.497
129.779
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128.213
127.749
124.279
124.083
77.478
77.160
76.842
72.781
72.773
44.405
38.621
32.972
28.489
f1 (ppm)
136.614
135.561
132.696
132.040
130.497
129.779
129.512
128.309
128.213
127.749
124.279
124.083
f1 (ppm)
HO
NHBoc
15