Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Palladium-Catalyzed ortho-Selective C−H Hydroxylation of Carboxybenzyl-Protected Benzylamines

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Supporting Information

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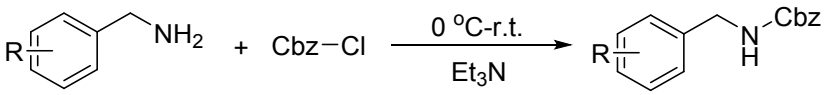
1. Reagents: Unless otherwise noted, all reagents were purchased from Acros, Alfa, Adamas and used without further purification. Column chromatography purifications were performed using 200–300 mesh silica gel.

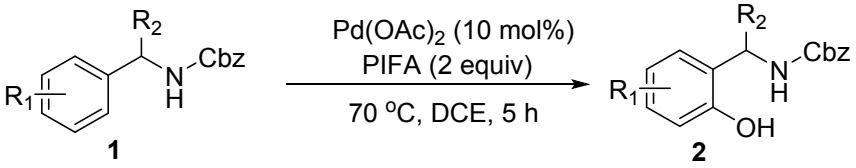
2. Instruments: NMR spectra were recorded on Varian Inova-400 MHz, Inova-300 MHz, Bruker DRX-400 or Bruker DRX-500 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet. HRMS analysis were carried out using TOF-MS instrument with EI source.

3. Procedure for preparation of 1a-1u



A solution of amine derivatives (10 mmol) and Et_3N (1.4 ml, 13 mmol) in CH2Cl2 (10 mL) was added dropwise to a solution of benzyl chloroformate (1.6 ml, 13 mmol) in CH_2Cl_2 (20 mL) at 0 °C. The solution was warmed to room temperature and stirred over night. Then, the reaction was quenched by water (20 mL). The organic layer was separated and extracted with $NaHCO_3$ saturated solution (20 mL × 3), and then dried over anhydrous Na_2SO_4. Evaporation and column chromatography on silica gel afforded corresponding amide substrates as white solid with >90% yield.

4. General procedures for ortho-hydroxylation of benzylamine derivatives.

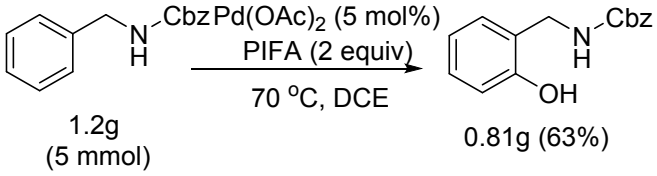


A mixture of **1** (0.2 mmol), PIFA (172 mg, 0.4 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and 2 mL DCE in a 15 mL sealed glass vial was heated at 70 °C under air with vigorous

stirring for 5 hours. The reaction mixture was

cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:20 to 1:10) to give the corresponding product.

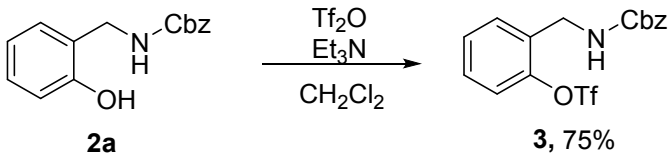
5. Gram scale reaction of 3c



A mixture of **1a** (1.2 g, 5 mmol), PIFA (10 mmol), $Pd(OAc)_2$ (56.1 mg, 5 mol%) and 40 mL DCE in a 100 mL round-bottom flask was heated at 70 °C under air with vigorous stirring for 8 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:25 to 1:10) to give the corresponding product (0.81 g).

6. Further Transformation.

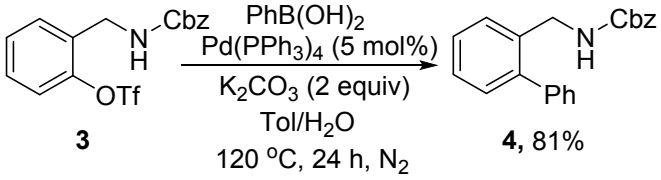
(a) Preparation of 3.



2a **3,** 75%

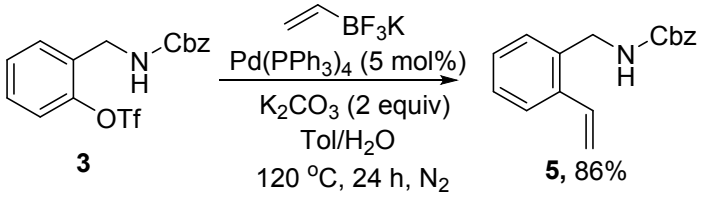
To a solution of **2a** (51.4 mg, 0.2 mmol) and Et_3N (50.6 mg, 0.5 mmol) in DCM (5 mL), Tf_2O (84.6 mg, 0.3 mmol) was added dropwise at 0 °C under nitrogen. After 1 h at 0 °C, the solution was stirred for 12 h at room temperature, and was then was extracted with DCM (10 mL × 3). The combined organic phases were concentrated under vacuum, and purified by column chromatography on silica gel to give the corresponding product **3**.

(b) Preparation of 4.



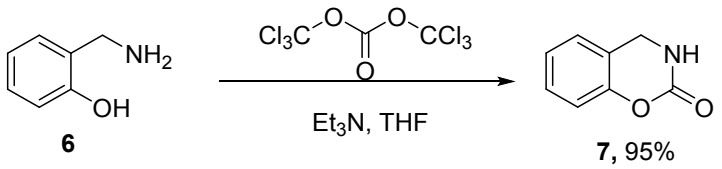
A mixture of **3** (77.8 mg, 0.2 mmol), $PhB(OH)_2$ (36.6 mg, 0.3 mmol), $Pd(PPh_3)_4$ (11.6 mg, 5 mol %), toluene (1.6 mL), H_2O (0.4 mL) and K_2CO_3 (55.2 mg, 0.4 mmol) in a 15 mL sealed glass vial was heated at 120 °C under nitrogen with vigorous stirring for 24 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum, and the residue purified by column chromatography on silica gel to give the corresponding product **4.**

(c) Preparation of 5.



A mixture of **3** (77.8 mg, 0.2 mmol), potassium vinyltrifluoroborate (40.2 mg, 0.3 mmol), $Pd(PPh_3)_4$ (11.6 mg, 5 mol %), toluene (1.6 mL), H_2O (0.4 mL) and K_2CO_3 (55.2 mg, 0.4 mmol) in a 15 mL sealed glass vial was heated at 120 °C under nitrogen with vigorous stirring for 24 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The organic phases were washed with brine, dried over anhydrous Na_2SO_4, and concentrated under vacuum, and the residue purified by column chromatography on silica gel to give the corresponding product **5.**

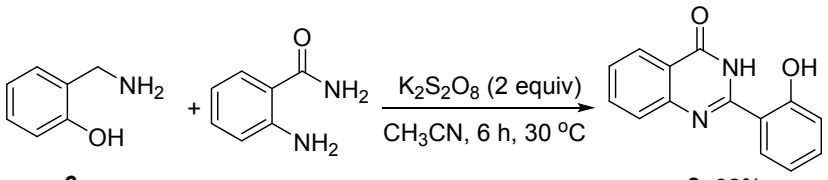
(d) Preparation of 7.



6 **7,** 95%

To a solution of **6** (24.6 mg, 0.2 mmol) and Et_3N (50.5 mg, 0.5 mmol) in anhydrous dichloromethane (5 mL), $CO(OCCl_3)_2$ (29.7 mg, 0.3 mmol) was added dropwise under nitrogen. The solution was stirred for 2 h at 0 °C, then the solution was stirred for 12 h at rt and extracted with DCM (10 mL × 3). The combined organic phases were concentrated under vacuum, and purified by column chromatography on silica gel to give the corresponding product **7**.

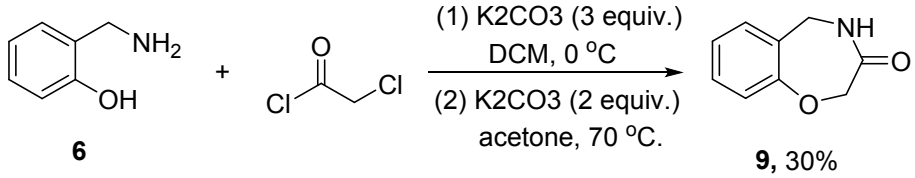
(e) Preparation of 8.



6 **8,** 62%

A mixture of **6** (61.5 mg, 0.5 mmol), anthranilamide (68 mg, 0.5 mmol), $K_2S_2O_8$ (270 mg, 1 mmol) and 1 mL CH_3CN in a 15 mL sealed glass vial was heated at 30 °C under air with vigorous stirring for 6 hours. After the completion of reaction, the reaction mixture was dried on rotator evaporator, dissolved in ethyl acetate and washed with H_2O (3 times). The combined organic phases were concentrated under vacuum, and purified by column chromatography on silica gel to give the corresponding product **8**.

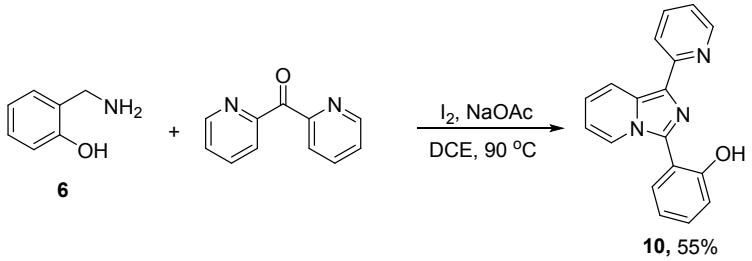
(f) Preparation of 9.



6 **9,** 30%

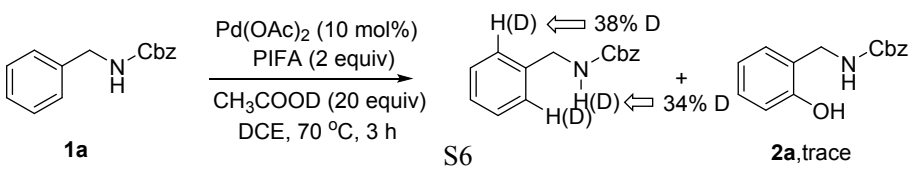
To a stirred mixture of **6** (61.5 mg, 0.5 mmol) and K_2CO_3 (207 mg, 1.5 mmol) in 15 mL CH_2Cl_2 was added dropwise chloroacetyl chloride (62.1 mg, 0.55 mmol) at 0 °C. After being stirred for 30 min, the reaction mixture was diluted with DCM and washed with brine. After being dried over Na_2SO_4, removal of the solvent in vacuo gave a residue. A mixture of this residue and K_2CO_3 (138 mg, 1.0 mmol) in 20 mL acetone was heated at reflux for 6 h. The reaction mixture was concentrated in vacuo, and then a residue was dissolved into DCM and water, The organic phases were dried over anhydrous Na_2SO_4, and concentrated under vacuum, and the residue purified by column chromatography on silica gel to give the corresponding product **9**.

(g) Preparation of 10.

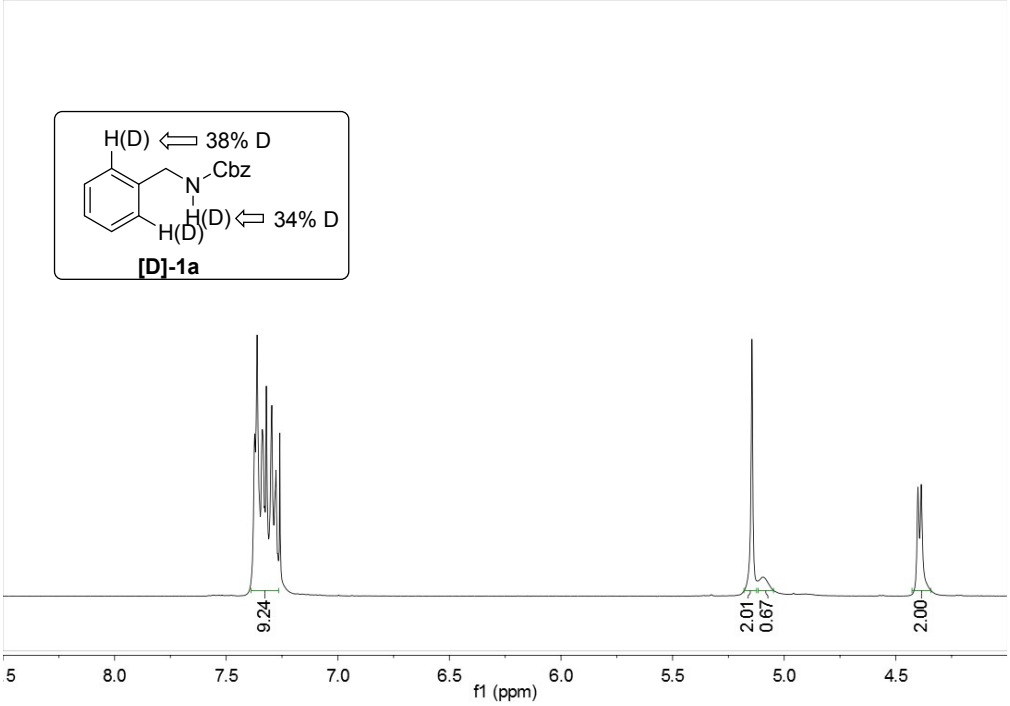


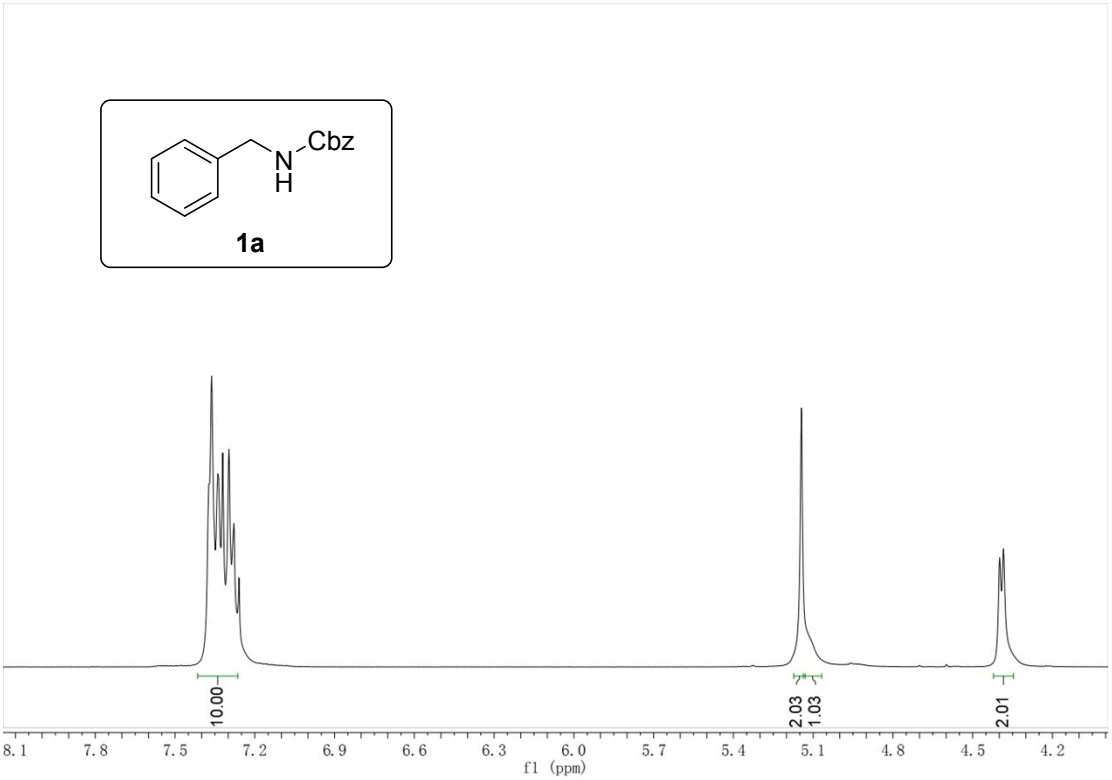
A mixture of **6** (67.6 mg, 0.55 mmol), 2-pyridyl ketone (92 mg, 0.5 mmol), molecular iodine (152 mg, 0.6 mmol), NaOAc (123 mg, 1.5 mmol) and 5 mL DCE in a 15 mL sealed glass vial was heated at 90 °C under air with vigorous stirring for 12 hours. the reaction mixture was allowed to cool down to room temperature, quenched with 5% $Na_2S_2O_3$ (5 mL) and H_2O (15 mL), and extracted with DCM (10 mL × 3). The organic phases were dried over anhydrous Na_2SO_4, and concentrated under vacuum, and the residue purified by column chromatography on silica gel to give the corresponding product **10**.

7. Isotopic Labelling Studies

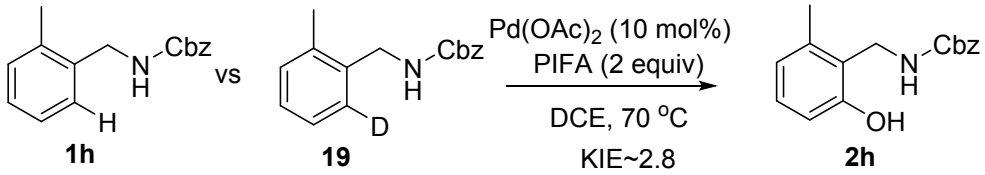


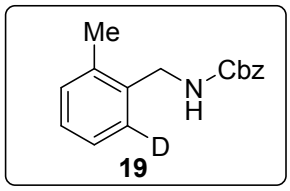
A mixture of **1a** (0.2 mmol), PIFA (0.4 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), 2 mL DCE and deuterium acetate (20 equiv) in a 15 mL sealed glass vial was heated at 70 °C under air with vigorous stirring for 3 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel to give the corresponding product.





8. Kinetic isotope effect

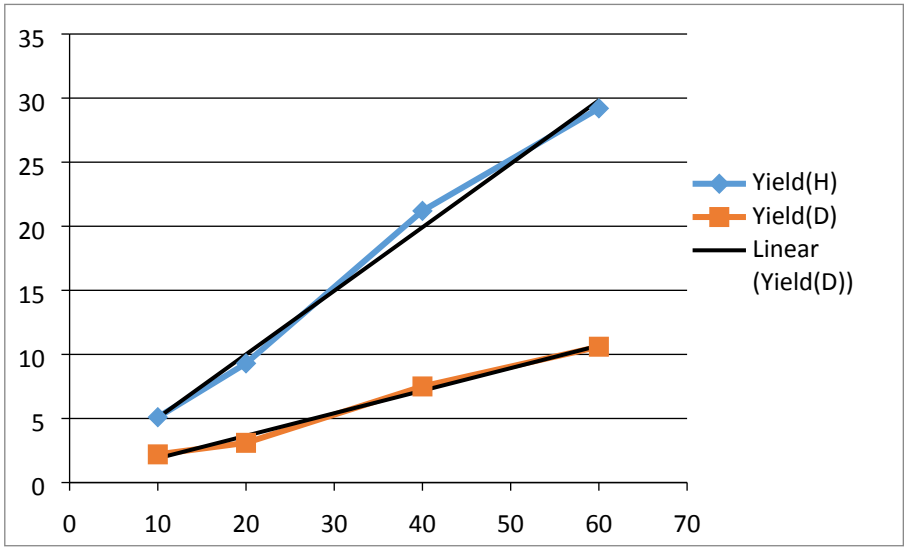




19 ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 – 7.31 (m, 5H), 7.20 – 7.15 (m, 3H), 5.14 (s, 2H), 4.91 (s, 1H), 4.39 (d, J = 5.7 Hz, 2H), 2.33 (s, 3H).

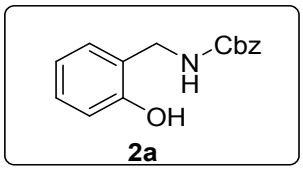
Kinetic isotope effect: A mixture of **1h** (51.0 mg, 0.2 mmol) or **19** (51.2 mg, 0.2 mmol), PIFA (172 mg, 0.4 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and DCE (2.0 mL) in a 15 mL sealed glass vial was heated at 70 °C under air with vigorous stirring for 10, 20, 40, 60 minutes respectively. The yields were determined by GC using tridecane as internal standard.

Time(min)	Yield(H) (%)	Yield(D) (%)
10	5.1	2.2
20	9.3	3.1
40	21.2	7.5
60	29.2	10.6



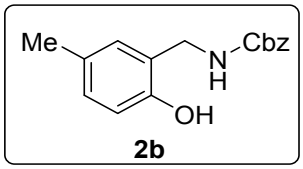
KIE=2.8

Spectroscopic Data of All New Compounds



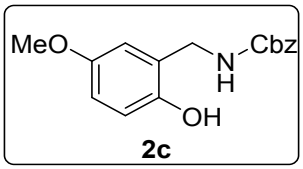
2a

Pale yellow solid; Yield (70%, 35.9 mg); m. p. 50-51 °C; IR (neat, cm^{-1}) 3328, 2921, 1680, 1520, 1254, 1137, 1060, 960, 749, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.36 – 7.32 (m, 5H), 7.24 – 7.18 (m, 1H), 7.10 (d, J = 7.4 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 6.88 – 6.82 (m, 1H), 5.56 (s, 1H), 5.13 (s, 2H), 4.30 (d, J = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 155.4, 135.8, 130.7, 129.9, 128.7, 128.5, 128.3, 124.6, 120.3, 117.6, 67.8, 41.5. HRMS Calcd for $C_{15}H_{15}NO_3$ [M+Na^+]: 280.0950; Found: 280.0945. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8 to 1:5).



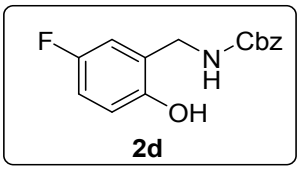
2b

Pale yellow solid; Yield (71%, 38.5 mg); m. p. 91-93 °C; IR (neat, cm^{-1}) 3340, 2918, 1649, 1522, 1466, 1249, 1041, 775, 743, 696; ^1H NMR (400 MHz, $CDCl_3$) δ 8.21 (s, 1H), 7.39 – 7.29 (m, 5H), 7.03 – 6.99 (m, 1H), 6.89 (d, J = 1.9 Hz, 1H), 6.84 (d, J = 8.2 Hz, 1H), 5.45 (s, 1H), 5.12 (s, 2H), 4.26 (d, J = 6.7 Hz, 2H), 2.25 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 153.1, 135.9, 131.1, 130.4, 129.5, 128.7, 128.5, 128.3, 124.4, 117.6, 67.8, 41.5, 20.4. HRMS Calcd for $C_{16}H_{17}NO_3$ [M+Na^+]: 294.1106; Found: 294.1118.



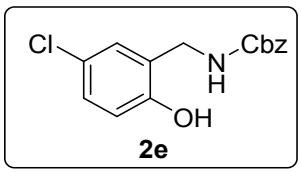
2c

Pale yellow solid; Yield (67%, 38.4 mg); m. p. 84-86 °C; IR (neat, cm^{-1}) 3329, 2938, 1672, 1497, 1253, 1200, 1137, 1045, 743, 697; ^1H NMR (400 MHz, $CDCl_3$) δ 8.06 (s, 1H), 7.38 – 7.30 (m, 5H), 6.88 (d, *J* = 8.7 Hz, 1H), 6.79 – 6.73 (m, 1H), 6.65 (d, *J* = 3.0 Hz, 1H), 5.53 (s, 1H), 5.12 (s, 2H), 4.26 (d, *J* = 6.6 Hz, 2H), 3.74 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.6, 153.3, 149.2, 135.8, 128.7, 128.5, 128.4, 125.4, 118.5, 115.9, 115.0, 67.8, 55.9, 41.6. HRMS Calcd for $C_{16}H_{17}NO_4$ [M+Na^+]: 310.1055; Found: 310.1060. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8 to 1:5).



2d

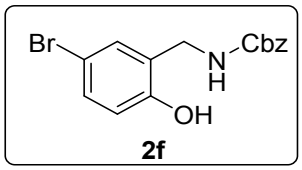
White solid; Yield (43%, 23.6 mg); m. p. 99-100 °C; IR (neat, cm^{-1}) 3364, 2918, 2848, 1666, 1535, 1493, 1287, 1200, 1154, 992, 891, 727, 687; ^1H NMR (400 MHz, $CDCl_3$) δ 8.37 (s, 1H), 7.36 – 7.32 (m, 5H), 6.91 – 6.87 (m, 2H), 6.82 – 6.78 (m, 1H), 5.48 (s, 1H), 5.13 (s, 2H), 4.25 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 156.5 (d, *J* = 238.2 Hz), 151.5 (d, *J* = 4.5 Hz), 135.7, 128.7, 128.5, 128.4, 125.7 (d, *J* = 6.8 Hz), 118.8 (d, *J* = 5.8 Hz), 116.5 (d, *J* = 22.9 Hz), 116.2 (d, *J* = 24.6 Hz), 67.9, 41.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -124.6. HRMS Calcd for $C_{15}H_{14}FNO_3$ [M+Na^+]: 298.0855; Found: 298.0867. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8 to 1:5).



2e

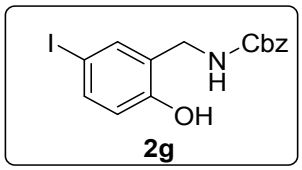
Pale yellow solid; Yield (53%, 30.8 mg); m. p. 89-90 °C; IR (neat, cm^{-1}) 3330, 2801, 1661, 1541, 1486, 1289, 1262, 1222, 1115, 731, 695, 651; ^1H NMR (400 MHz, $CDCl_3$)

δ 8.62 (s, 1H), 7.39 – 7.30 (m, 5H), 7.17 – 7.12 (m, 1H), 7.06 (d, *J* = 2.6 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 5.54 (s, 1H), 5.13 (s, 2H), 4.24 (d, *J* = 6.6 Hz, 2H).^{13}C NMR (101 MHz, $CDCl_3$) δ 153.6, 135.0, 129.6, 129.1, 128.1, 128.0, 127.8, 125.5, 124.1, 118.6, 67.4, 40.6. HRMS Calcd for $C_{15}H_{14}ClNO_3$ [M+Na$^+$]: 314.0560; Found: 314.0559. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8 to 1:5).



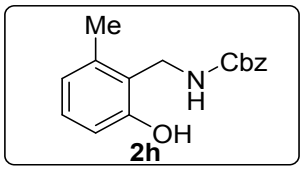
2f

Yellow solid; Yield (51%, 34.2 mg); m. p. 87-89 °C; IR (neat, cm^{-1}) 3345, 2918, 1646, 1524, 1466, 1283, 1248, 1040, 776, 747, 691; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.69 (s, 1H), 7.37 – 7.31 (m, 5H), 7.30 – 7.27 (m, 1H), 7.20 (d, *J* = 2.5 Hz, 1H), 6.82 (d, *J* = 8.5 Hz, 1H), 5.52 (s, 1H), 5.13 (s, 2H), 4.23 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 154.8, 135.6, 133.1, 132.7, 128.7, 128.6, 128.4, 126.7, 119.7, 111.8, 68.0, 41.1. HRMS Calcd for $C_{15}H_{14}BrNO_3$ [M+Na$^+$]: 358.0055; Found: 358.0072. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8 to 1:5).



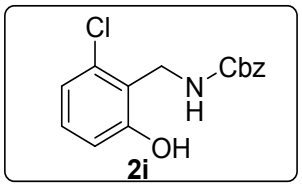
2g

Pale yellow solid; Yield (60%, 46.0 mg); m. p. 110-112 °C; IR (neat, cm^{-1}) 3328, 2919, 2794, 1657, 1542, 1279, 1259, 1226, 1110, 955, 821, 758, 697; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.51 – 7.46 (m, 1H), 7.40 (d, *J* = 2.2 Hz, 1H), 7.39 – 7.34 (m, 5H), 6.74 (d, *J* = 8.5 Hz, 1H), 5.50 (s, 1H), 5.15 (s, 2H), 4.24 (d, *J* = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 155.5, 139.0, 138.6, 135.6, 128.7, 128.6, 128.3, 127.3, 120.2, 81.6, 68.0, 40.9. HRMS Calcd for $C_{15}H_{14}INO_3$ [M+Na$^+$]: 405.9916; Found: 405.9929. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:6 to 1:5).



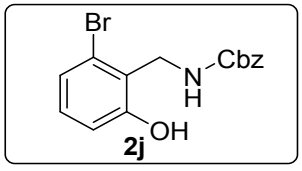
2h

Pale yellow solid; Yield (61%, 33.1 mg); m. p. 106-109 °C; IR (neat, cm^{-1}) 3342, 2952, 1644, 1530, 1466, 1251, 1045, 779, 748, 690; ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.39 – 7.30 (m, 5H), 7.13 – 7.07 (m, 1H), 6.83 (d, *J* = 8.0 Hz, 1H), 6.74 (d, *J* = 7.5 Hz, 1H), 5.47 (s, 1H), 5.11 (s, 2H), 4.36 (d, *J* = 6.6 Hz, 2H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 155.8, 137.6, 135.8, 129.3, 128.7, 128.5, 128.4, 123.7, 122.4, 116.0, 67.9, 37.1, 19.7. HRMS Calcd for $C_{16}H_{17}NO_3$ [M+Na^+]: 294.1106; Found: 294.1109. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



2i

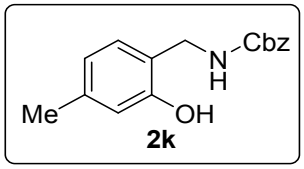
Pale yellow solid; Yield (51%, 29.7 mg); m. p. 62-63 °C; IR (neat, cm^{-1}) 3337, 2921, 1646, 1525, 1453, 1251, 1123, 775, 738, 689; ^1H NMR (400 MHz, $CDCl_3$) δ 9.15 (s, 1H), 7.38 – 7.32 (m, 5H), 7.16 – 7.11 (m, 1H), 6.95 – 6.89 (m, 2H), 5.63 (s, 1H), 5.12 (s, 2H), 4.45 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 157.1, 135.6, 135.0, 130.1, 128.7, 128.6, 128.4, 123.6, 121.2, 117.4, 68.1, 37.9. HRMS Calcd for $C_{15}H_{14}ClNO_3$ [M+Na^+]: 314.0560; Found: 314.0568. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



2j

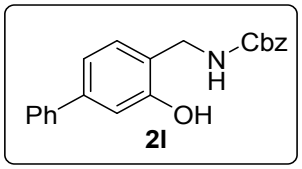
Yellow solid; Yield (41%, 27.5 mg); m. p. 60-61 °C; IR (neat, cm^{-1}) 3337, 2919, 2948, 1677, 1535, 1444, 1269, 1120, 966, 775, 749, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 9.21 (s, 1H), 7.38 – 7.32 (m, 5H), 7.13 – 7.04 (m, 2H), 6.97 – 6.93 (m, 1H), 5.69 (s, 1H), 5.12 (s, 2H), 4.47 (d, *J* = 6.8 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.3, 157.1,

135.6, 130.6, 128.7, 128.6, 128.5, 125.5, 125.2, 124.5, 118.1, 68.1, 40.6. HRMS Calcd for $C_{15}H_{14}BrNO_3$ [M+H$^+$]: 336.0235; Found: 336.0243. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



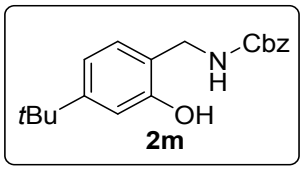
2k

Pale yellow solid; Yield (58%, 31.4 mg); m. p. 93-95 ^{o}C; IR (neat, cm^{-1}) 3346, 2919, 1646, 1525, 1466, 1248, 1040, 776, 747, 691; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.37 – 7.31 (m, 5H), 6.96 (d, *J* = 7.6 Hz, 1H), 6.78 (s, 1H), 6.66 (d, *J* = 7.6 Hz, 1H), 5.43 (s, 1H), 5.12 (s, 2H), 4.26 (d, *J* = 6.7 Hz, 2H), 2.29 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 155.3, 140.3, 135.8, 130.5, 128.7, 128.5, 128.4, 121.7, 121.1, 118.4, 67.8, 41.3, 21.2. HRMS Calcd for $C_{16}H_{17}NO_3$ [M+Na$^+$]: 294.1106; Found: 294.1119. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



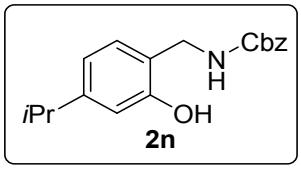
2l

Pale yellow solid; Yield (49%, 32.6 mg); m. p. 81-83 ^{o}C; IR (neat, cm^{-1}) 3393, 3290, 2919, 2848, 1683, 1508, 1410, 1260, 1227, 1114, 960, 907, 762, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.63 (s, 1H), 7.57 (d, *J* = 7.3 Hz, 2H), 7.45 – 7.40 (m, 2H), 7.39 – 7.32 (m, 6H), 7.21 (s, 1H), 7.15 (d, *J* = 7.8 Hz, 1H), 7.09 (d, *J* = 7.8 Hz, 1H), 5.51 (s, 1H), 5.15 (s, 2H), 4.34 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 155.8, 143.2, 140.6, 135.8, 131.1, 128.8, 128.7, 128.5, 128.4, 127.5, 127.1, 123.6, 119.1, 116.5, 67.9, 41.3. HRMS Calcd for $C_{21}H_{19}NO_3$ [M+Na$^+$]: 356.1263; Found: 356.1248. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



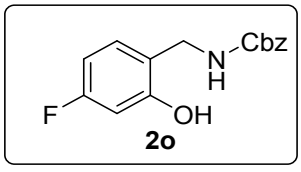
2m

Pale yellow solid; Yield (51%, 31. 9 mg); m. p. 61-63 °C; IR (neat, cm^{-1}) 3317, 2945, 1664, 1560, 1395, 1375, 1240, 1115, 751, 690; ^1H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.36 – 7.31 (m, 5H), 7.04 – 6.99 (m, 2H), 6.89 – 6.86 (m, 1H), 5.49 (s, 1H), 5.12 (s, 2H), 4.27 (d, *J* = 6.6 Hz, 2H), 1.29 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 155.1, 153.8, 135.8, 130.3, 128.7, 128.5, 128.4, 121.6, 117.3, 115.0, 67.8, 41.2, 34.7, 31.3. HRMS Calcd for $C_{19}H_{23}NO_3$ [M+Na^+]: 336.1576; Found: 336.1582. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



2n

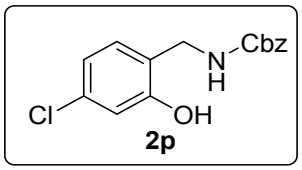
White solid; Yield (55%, 32.9 mg); m. p. 56-58 °C; IR (neat, cm^{-1}) 3310, 2959, 1662, 1551, 1275, 1109, 952, 753, 695, 651; ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 – 7.31 (m, 5H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.84 (s, 1H), 6.73 (dd, *J* = 7.7, 1.7 Hz, 1H), 5.51 (s, 1H), 5.12 (s, 2H), 4.27 (d, *J* = 6.6 Hz, 2H), 2.90 – 2.77 (m, 1H), 1.23 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.8, 155.4, 151.4, 135.8, 130.6, 128.7, 128.5, 128.4, 122.0, 118.5, 115.7, 67.8, 41.3, 33.9, 23.9. HRMS Calcd for $C_{18}H_{21}NO_3$ [M+H^+]: 300.1600; Found: 300.1611. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



2o

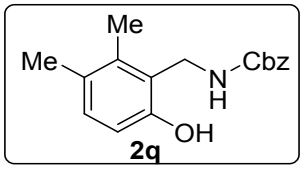
Pale yellow solid; Yield (36%, 19.8 mg); m. p. 57-59 °C; IR (neat, cm^{-1}) 3317, 2920, 1658, 1503, 1282, 1241, 1144, 917, 751, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.40 – 7.30 (m, 5H), 7.03 – 6.99 (m, 1H), 6.66 (dd, *J* = 10.4, 2.5 Hz, 1H), 6.57 –

6.51 (m, 1H), 5.47 (s, 1H), 5.14 (s, 2H), 4.25 (d, J = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.8 (d, J = 245.7 Hz), 159.0, 157.2 (d, J = 12.5 Hz), 135.6, 131.6 (d, J = 10.2 Hz), 128.7, 128.6, 128.4, 120.7 (d, J = 3.0 Hz), 107.0 (d, J = 21.6 Hz), 105.2 (d, J = 24.6 Hz), 68.0, 41.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -112.0. HRMS Calcd for $C_{15}H_{14}FNO_3$ [M+Na$^+$]: 298.0855; Found: 298.0856. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



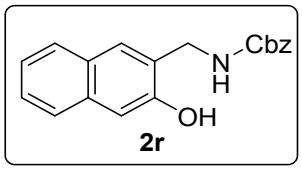
2p

Pale yellow solid; Yield (45%, 26.2 mg); m. p. 96-98 °C; IR (neat, cm^{-1}) 3463, 3313, 2923, 1688, 1518, 1249, 967, 909, 858, 743, 696; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.36 – 7.32 (m, 5H), 6.99 (d, J = 8.1 Hz, 1H), 6.96 (d, J = 1.8 Hz, 1H), 6.83 – 6.80 (m, 1H), 5.46 (s, 1H), 5.13 (s, 2H), 4.25 (d, J = 6.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.9, 156.5, 135.6, 135.1, 131.5, 128.7, 128.6, 128.4, 123.3, 120.3, 118.2, 68.1, 41.1. HRMS Calcd for $C_{15}H_{14}ClNO_3$ [M+Na$^+$]: 314.0560; Found: 314.0560. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



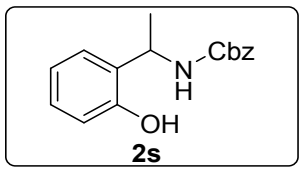
2q

White solid; Yield (60%, 34.2 mg); m. p. 93-95 °C; IR (neat, cm^{-1}) 3320, 2963, 1649, 1529, 1282, 1251, 1040, 810, 751, 693; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.38 – 7.31 (m, 5H), 7.00 (d, J = 8.2 Hz, 1H), 6.76 (d, J = 8.2 Hz, 1H), 5.47 (s, 1H), 5.10 (s, 2H), 4.39 (d, J = 6.5 Hz, 2H), 2.22 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.7, 153.8, 135.8, 135.7, 130.7, 128.7, 128.5, 128.4, 124.1, 123.9, 115.3, 67.8, 37.4, 20.1, 15.8. HRMS Calcd for $C_{17}H_{19}NO_3$ [M+H$^+$]: 286.1443; Found: 286.1437. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



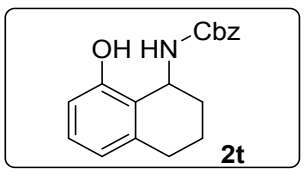
2r

Yellow solid; Yield (52%, 31.9 mg); m. p. 52-53 °C; IR (neat, cm^{-1}) 3312, 2921, 1689, 1517, 1453, 1239, 1157, 1098, 867, 744, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H), 7.69 (d, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.61 (s, 1H), 7.40 – 7.37 (m, 1H), 7.36 – 7.32 (m, 5H), 7.32 – 7.27 (m, 2H), 5.55 (s, 1H), 5.14 (s, 2H), 4.49 (d, *J* = 6.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.4, 153.1, 135.9, 134.9, 129.8, 128.7, 128.5, 128.5, 128.3, 127.5, 127.0, 126.6, 126.3, 123.7, 111.8, 67.8, 41.94. HRMS Calcd for $C_{19}H_{17}NO_3$ [M+Na^+]: 330.1106; Found: 330.1109. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



2s

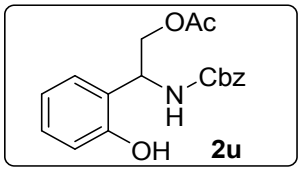
Yellow solid; Yield (62%, 33.6 mg); m. p. 55-57 °C; IR (neat, cm^{-1}) 3311, 2924, 1680, 1517, 1453, 1232, 1060, 749, 694; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.38 – 7.31 (m, 5H), 7.20 – 7.16 (m, 1H), 7.16 – 7.12 (m, 1H), 6.91 – 6.86 (m, 2H), 5.38 (s, 1H), 5.16 (d, *J* = 12.1 Hz, 1H), 5.06 (d, *J* = 12.0 Hz, 2H), 1.55 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.2, 154.3, 136.0, 129.1, 128.8, 128.6, 128.3, 128.2, 126.5, 120.4, 117.3, 67.4, 46.2, 20.6. HRMS Calcd for $C_{16}H_{17}NO_3$ [M+Na^+]: 294.1106; Found: 294.1111. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8 to 1:5).



2t

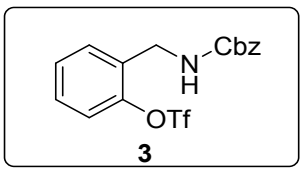
White solid; Yield (56%, 33.3 mg); m. p. 75-77 °C; IR (neat, cm^{-1}) 3311, 2921, 1650, 1536, 1464, 1322, 1244, 1071, 952, 774, 749, 694; ^1H NMR (400 MHz, $CDCl_3$) δ 8.22

(s, 1H), 7.39 – 7.31 (m, 5H), 7.10 (t, *J* = 7.8 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 5.31 (d, *J* = 7.0 Hz, 1H), 5.20 – 5.08 (m, 2H), 5.04 – 4.99 (m, 1H), 2.90 – 2.70 (m, 2H), 2.10 – 2.03 (m, 1H), 1.98 – 1.86 (m, 2H), 1.70 – 1.59 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.9, 155.8, 137.6, 135.8, 128.9, 128.7, 128.5, 128.4, 122.8, 120.9, 114.6, 67.9, 43.5, 29.7, 28.8, 17.9. HRMS Calcd for $C_{18}H_{19}NO_3$ [M+Na$^+$]: 320.1263; Found: 320.1251. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



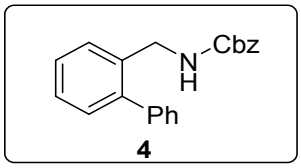
2u

White solid; Yield (66%, 43.4 mg); m. p. 93-96^o C; IR (neat, cm^{-1}) 3459, 3324, 2918, 1726, 1684, 1541, 1291, 1254, 1230, 1213, 1051, 1026, 749, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.39 – 7.30 (m, 5H), 7.15 – 7.11 (m, 1H), 7.10 – 7.07 (m, 1H), 6.83 (t, *J* = 7.4 Hz, 1H), 6.75 (d, *J* = 8.0 Hz, 1H), 5.97 (s, 1H), 5.22 – 5.04 (m, 3H), 4.49 (s, 1H), 4.27 (dd, *J* = 11.2, 4.8 Hz, 1H), 2.00 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.6, 156.9, 154.4, 136.2, 129.4, 128.6, 128.3, 128.2, 120.4, 116.4, 67.4, 65.4, 20.9. HRMS Calcd for $C_{18}H_{19}NO_5$ [M+Na$^+$]: 352.1161; Found: 352.1166. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:8).



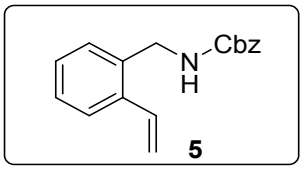
3

White solid; Yield (75%, 58.4 mg); m. p. 62-64 ^{o}C; IR (neat, cm^{-1}) 3317, 2918, 1683, 1517, 1289, 1155, 1045, 760, 695; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.48 (m, 1H), 7.36 – 7.28 (m, 6H), 7.26 – 7.23 (m, 2H), 5.30 (s, 1H), 5.10 (s, 2H), 4.46 (d, *J* = 6.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.56 (s), 147.3, 136.3, 131.7, 130.8, 129.5, 128.8, 128.6, 128.2, 121.5, 120.2, 117.0, 67.2, 39.7. HRMS Calcd for $C_{16}H_{14}F_3NO_5S$ [M+Na$^+$]: 412.0442; Found: 412.0452. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10).



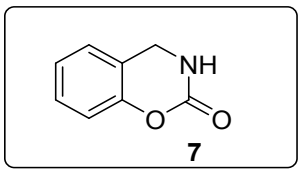
4

White solid; Yield (81%, 51.4 mg); m. p. 83-85 °C; IR (neat, cm^{-1}) 3313, 2945, 1687, 1525, 1243, 1048, 743, 694; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.43 (m, 1H), 7.42 – 7.37 (m, 3H), 7.37 – 7.32 (m, 6H), 7.31 – 7.24 (m, 4H), 5.08 (s, 2H), 4.84 (s, 1H), 4.35 (d, *J* = 5.9 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.3, 141.7, 140.7, 136.6, 135.7, 130.3, 129.1, 128.6, 128.5, 128.5, 128.2, 127.8, 127.5, 127.4, 66.9, 43.1. HRMS Calcd for $C_{21}H_{19}NO_2$ [M+Na^+]: 340.1313; Found: 340.1327. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:15 to 1:10).



5

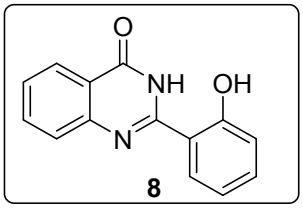
White solid; Yield (86%, 45.9 mg); m. p. 51-53 °C; IR (neat, cm^{-1}) 3356, 2920, 2849, 1696, 1519, 1243, 1041, 751, 736, 695; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, *J* = 7.1 Hz, 1H), 7.38 – 7.31 (m, 5H), 7.30 – 7.24 (m, 3H), 7.01 – 6.91 (m, 1H), 5.67 (d, *J* = 17.3 Hz, 1H), 5.34 (d, *J* = 11.1 Hz, 1H), 5.13 (s, 2H), 4.94 (s, 1H), 4.46 (d, *J* = 5.6 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.1, 136.9, 136.6, 135.0, 133.7, 129.0, 128.6, 128.2, 128.2, 128.1, 126.3, 117.0, 66.9, 43.2. HRMS Calcd for $C_{17}H_{17}NO_2$ [M+Na^+]: 290.1157; Found: 290.1165. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:15 to 1:10).



7

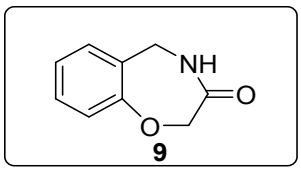
White solid; Yield (95%, 28.3 mg); m. p. 189-191 °C; IR (neat, cm^{-1}) 3246, 3147, 1712, 1476, 1458, 1406, 1264, 1181, 1027, 933, 739, 620; ^1H NMR (400 MHz, DMSO) δ

7.95 (s, 1H), 7.29 – 7.19 (m, 2H), 7.13 – 7.08 (m, 1H), 6.99 (d, J = 8.1 Hz, 1H), 4.39 (s, 2H). ^{13}C NMR (101 MHz, DMSO) δ 150.2, 149.8, 128.4, 126.2, 123.9, 118.1, 115.7, 41.2. HRMS Calcd for $C_8H_7NO_2$ [M+Na$^+$]: 172.0374; Found: 172.0366.



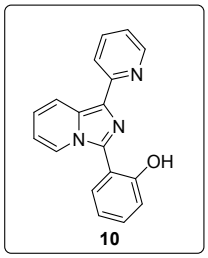
8

Yellow solid; Yield (62%, 73.8 mg); m. p. 251-253 ^{o}C; IR (neat, cm^{-1}) 2920, 2850, 1664, 1605, 1460, 1300, 1251, 1226, 1022, 826, 760, 746, 623; ^{1}H NMR (400 MHz, DMSO) δ 8.29 (dd, J = 8.0, 1.4 Hz, 1H), 8.22 (dd, J = 7.9, 1.2 Hz, 1H), 7.97 – 7.90 (m, 1H), 7.83 (d, J = 7.8 Hz, 1H), 7.66 – 7.59 (m, 1H), 7.55 – 7.47 (m, 1H), 7.12 – 6.99 (m, 2H). HRMS Calcd for $C_{14}H_{10}N_2O_2$ [M+Na$^+$]: 261.0640; Found: 261.0647. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:6).



9

White solid; Yield (30%, 24.5 mg); m. p. 112-113 ^{o}C; IR (neat, cm^{-1}) 3183, 3047, 2916, 1666, 1588, 1236, 1185, 1043, 820, 763, 689; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 7.35 – 7.30 (m, 1H), 7.22 – 7.19 (m, 1H), 7.14 – 7.09 (m, 2H), 4.61 (s, 2H), 4.36 (d, J = 4.7 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.3, 158.1, 131.8, 130.2, 128.5, 124.9, 120.9, 72.9, 42.9. HRMS Calcd for $C_9H_9NO_2$ [M+Na$^+$]: 186.0531; Found: 186.0525. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:1).



10

Yellow solid; Yield (55%, 78.9 mg); m. p. 182-184 ^{o}C; IR (neat, cm^{-1}) 2919, 2850, 1621, 1595, 1451, 1271, 1147, 783, 736, 703; ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.78 (s, 1H), 8.82 – 8.77 (m, 1H), 8.66 – 8.62 (m, 1H), 8.55 (d, J = 7.3 Hz, 1H), 8.12 (d, J = 8.0 Hz, 1H), 7.81 – 7.77 (m, 1H), 7.77 – 7.71 (m, 1H), 7.37 – 7.31 (m, 1H), 7.21 – 7.18 (m, 1H), 7.15 – 7.11 (m, 1H), 7.05 – 6.97 (m, 2H), 6.80 – 6.75 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.6, 159.9, 154.4, 154.2, 141.7, 141.6, 136.8, 136.0, 134.3, 133.9, 129.3, 126.8, 125.6, 124.6, 124.1, 121.7, 121.3, 118.3. HRMS Calcd for $C_{18}H_{13}N_3O$ [M+Na^{+}]: 310.0956; Found: 310.0960. Purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:4).

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3 K. Kamei, N. Maeda, K. Nomura, M. Shibata, R. Katsuragi-Ogino, M. Koyama, M. Nakajima, T. Inoue, T. Ohno, T. Tatsuoka, Synthesis, SAR studies, and Evaluation of 1,4-benzoxazepine Derivatives as Selective 5-HT1A Receptor Agonists with Neuroprotective Effect: Discovery of Piclozotan. *Bioorg. Med. Chem*, 2006, **14**, 1978.

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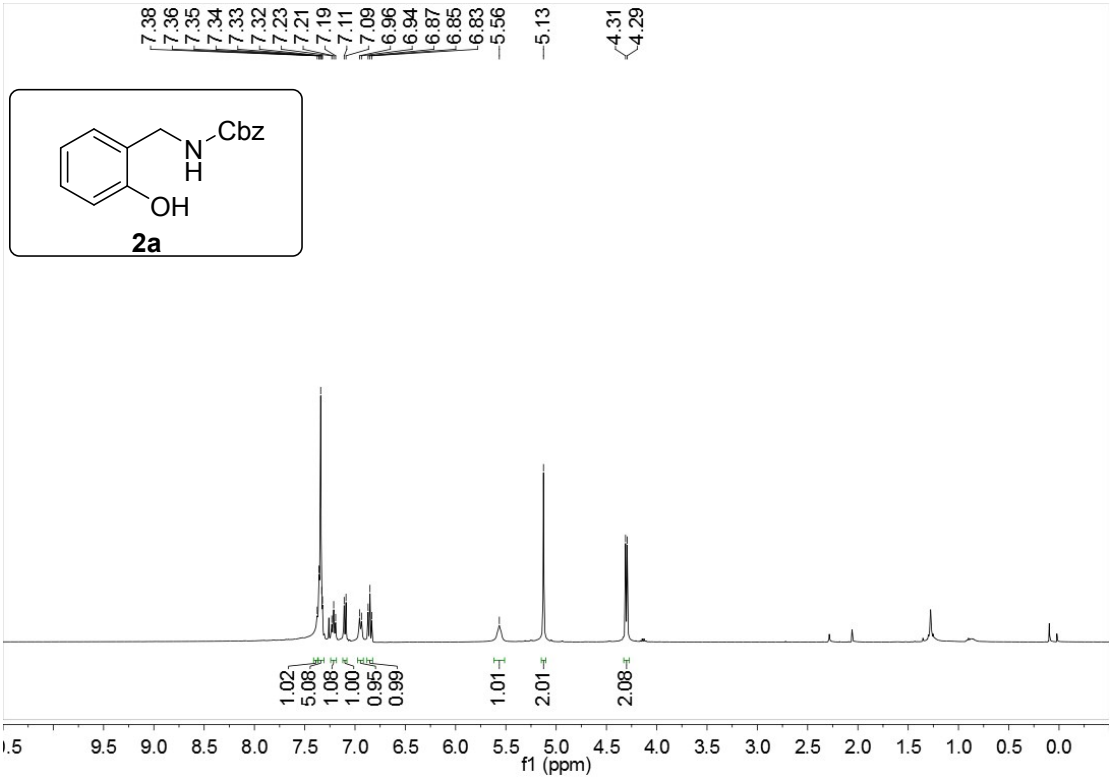
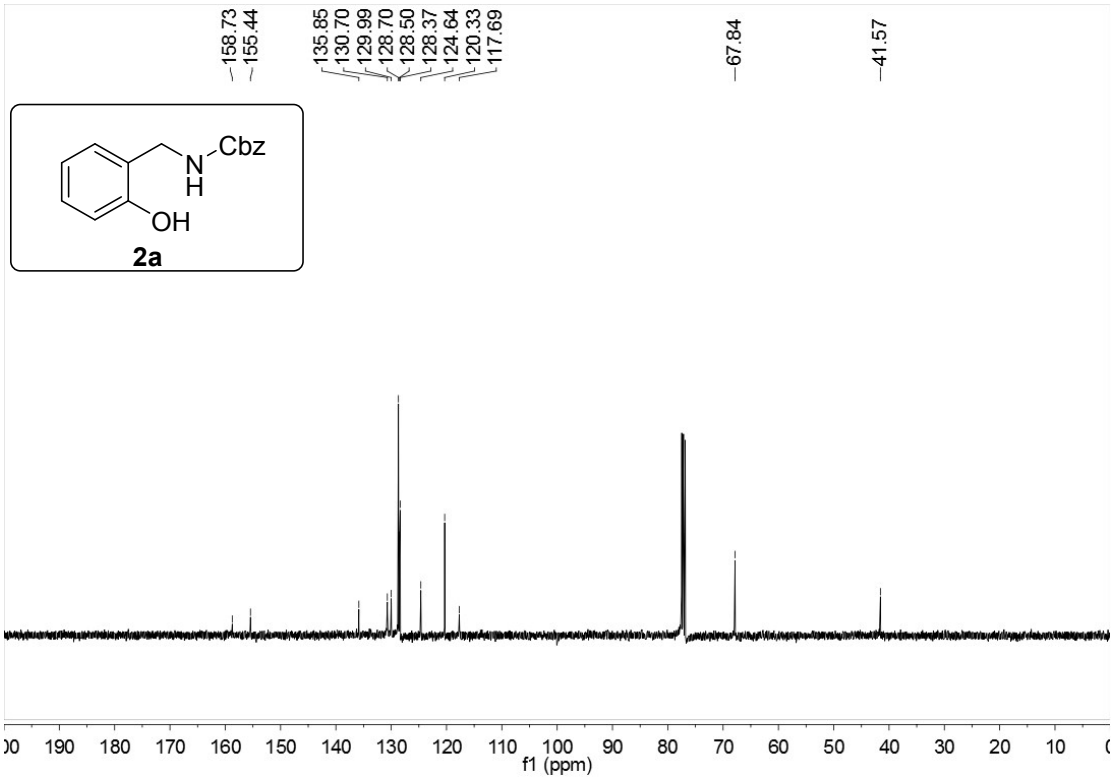
^{1}H NMR and ^{13}C NMR spectra

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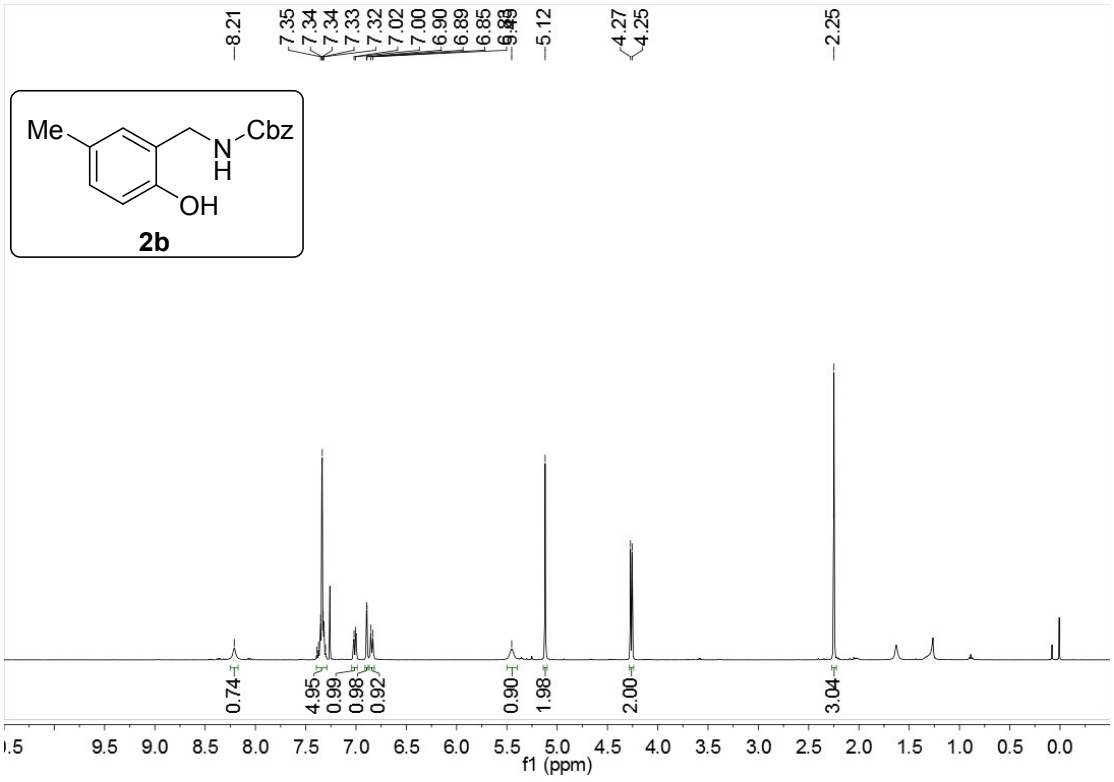
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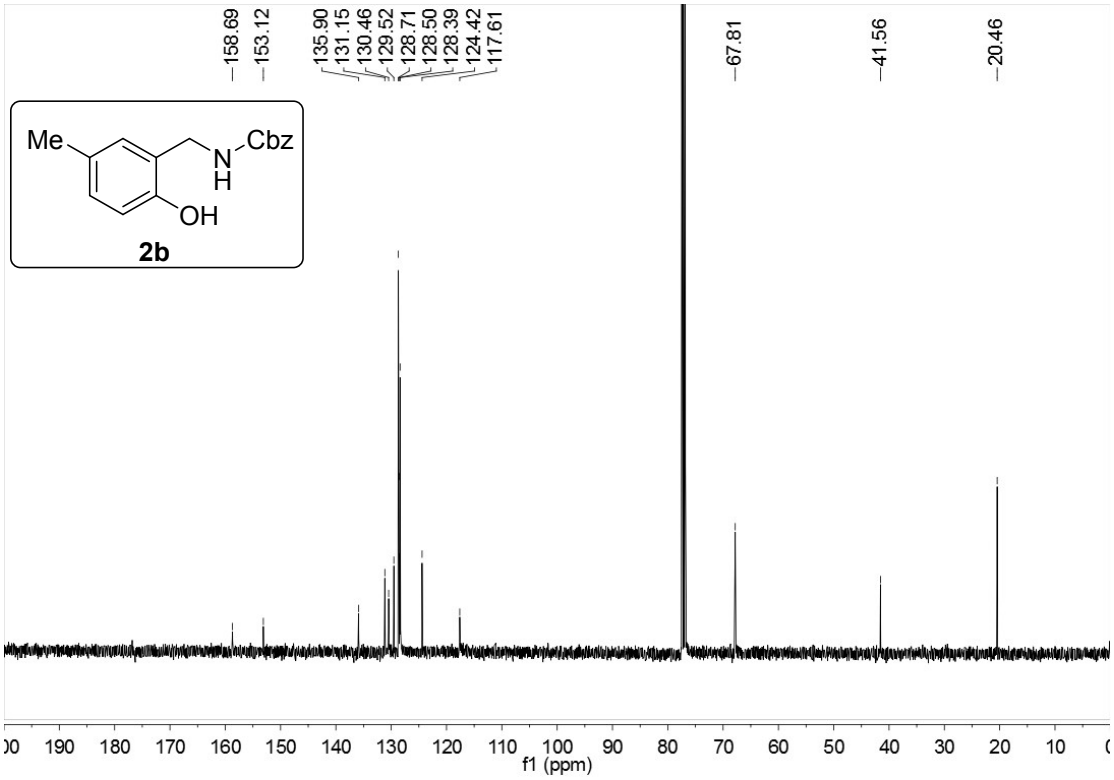
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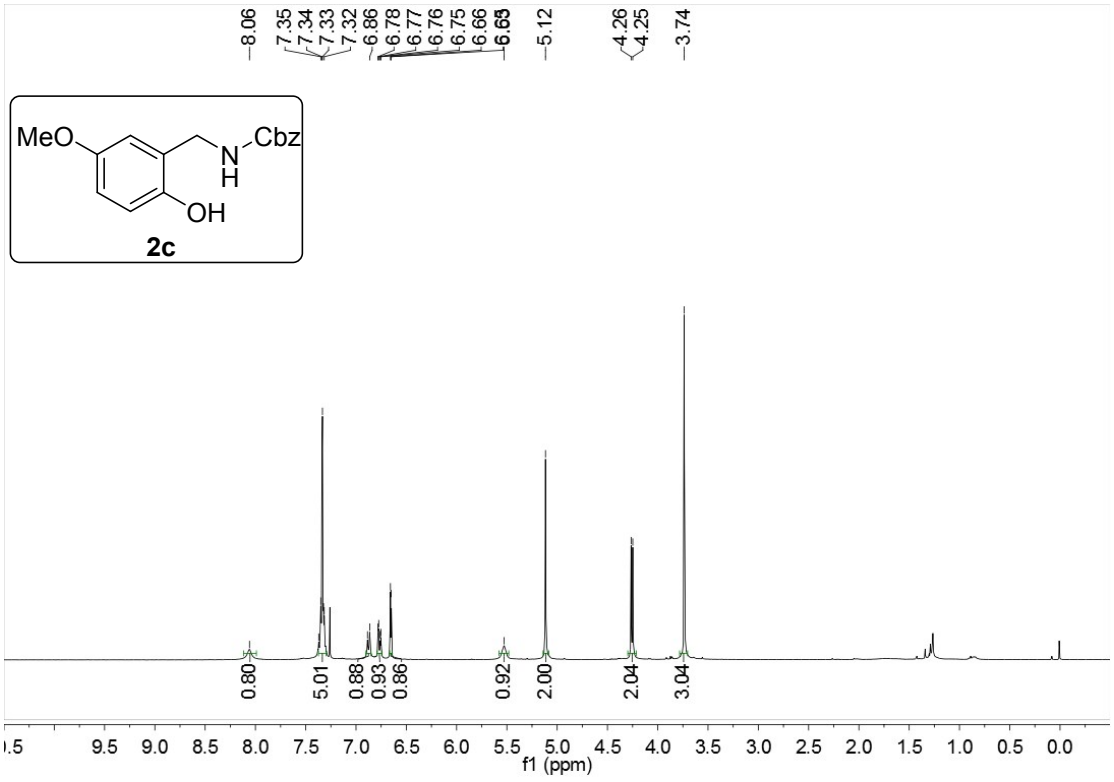
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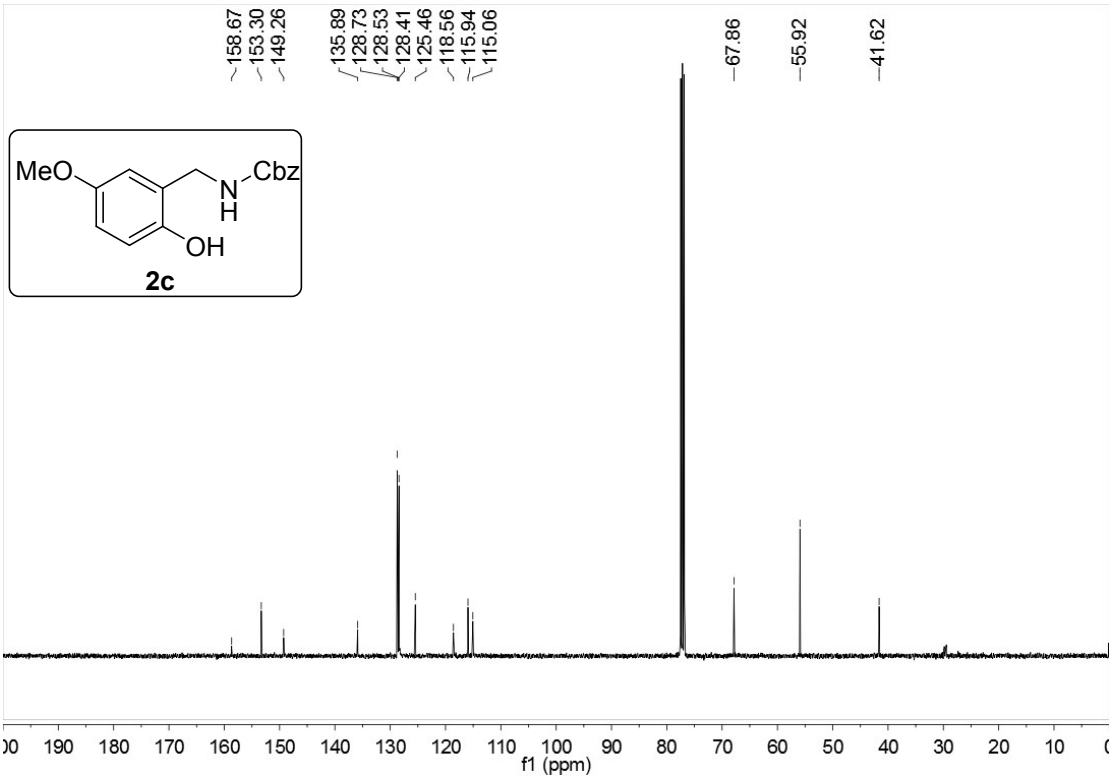
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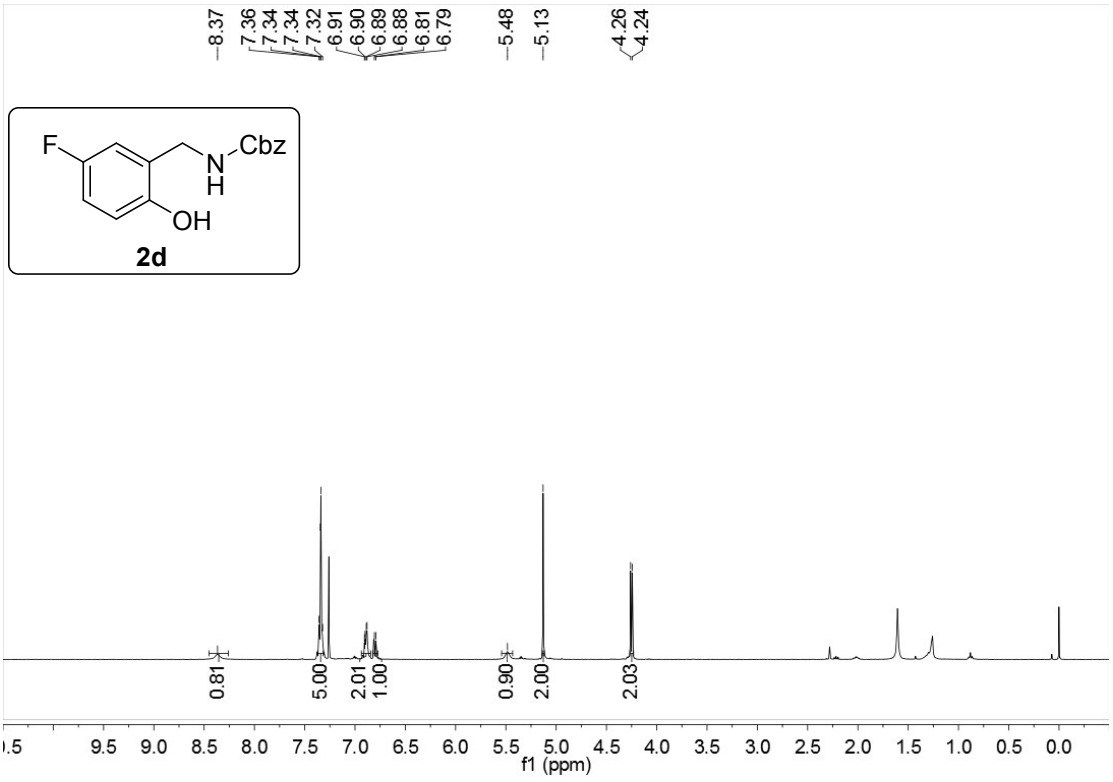
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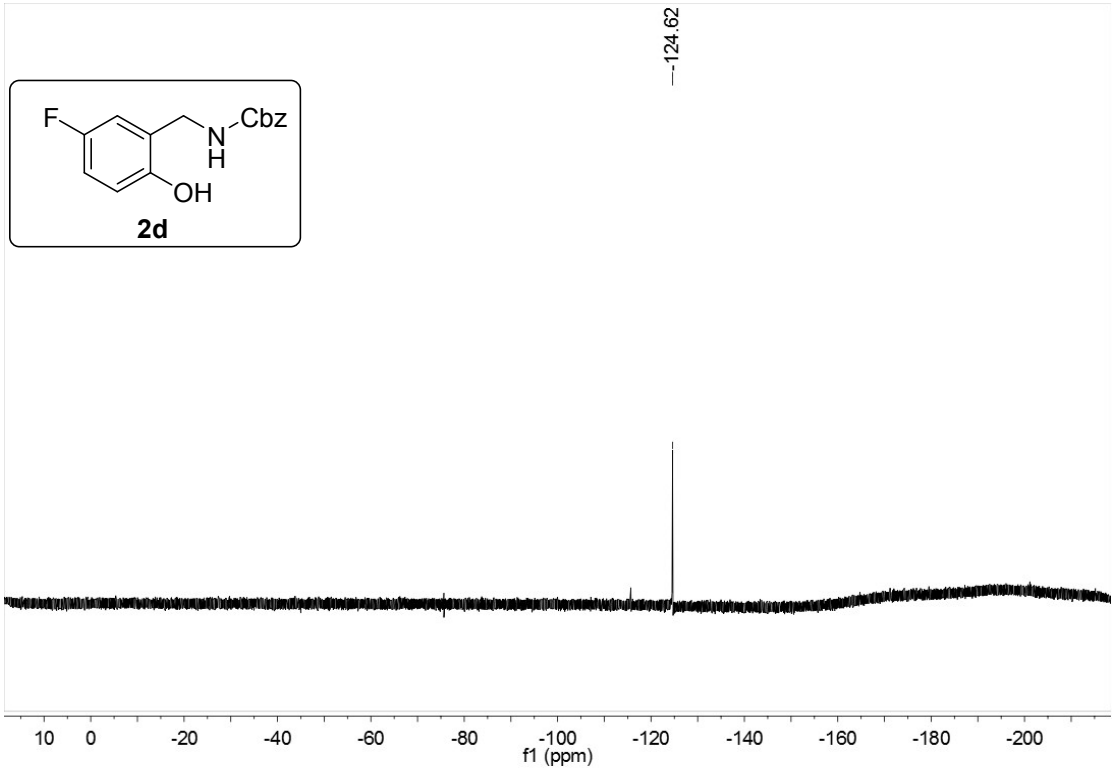
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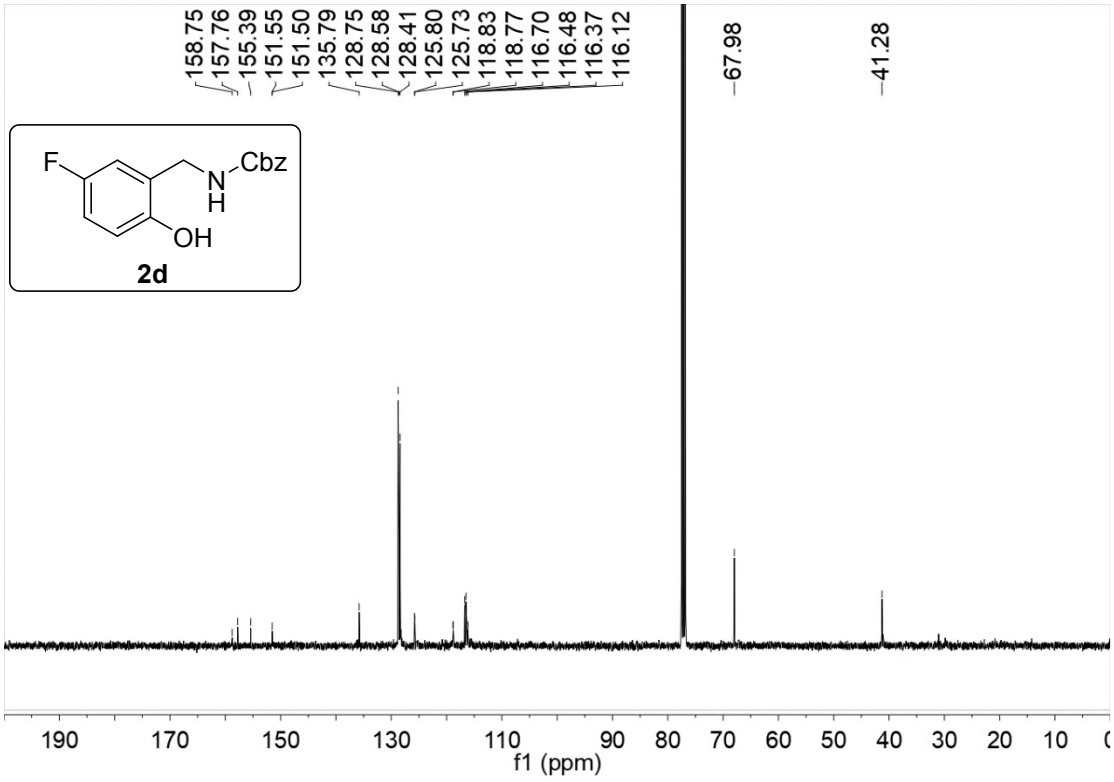
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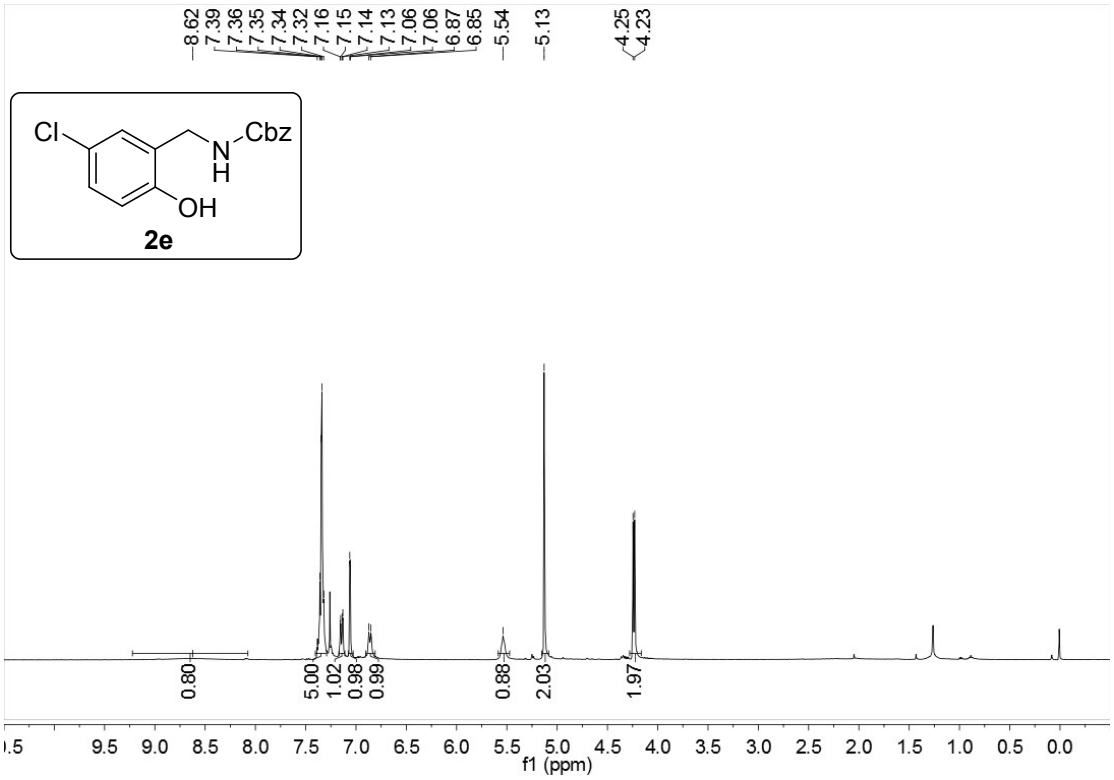
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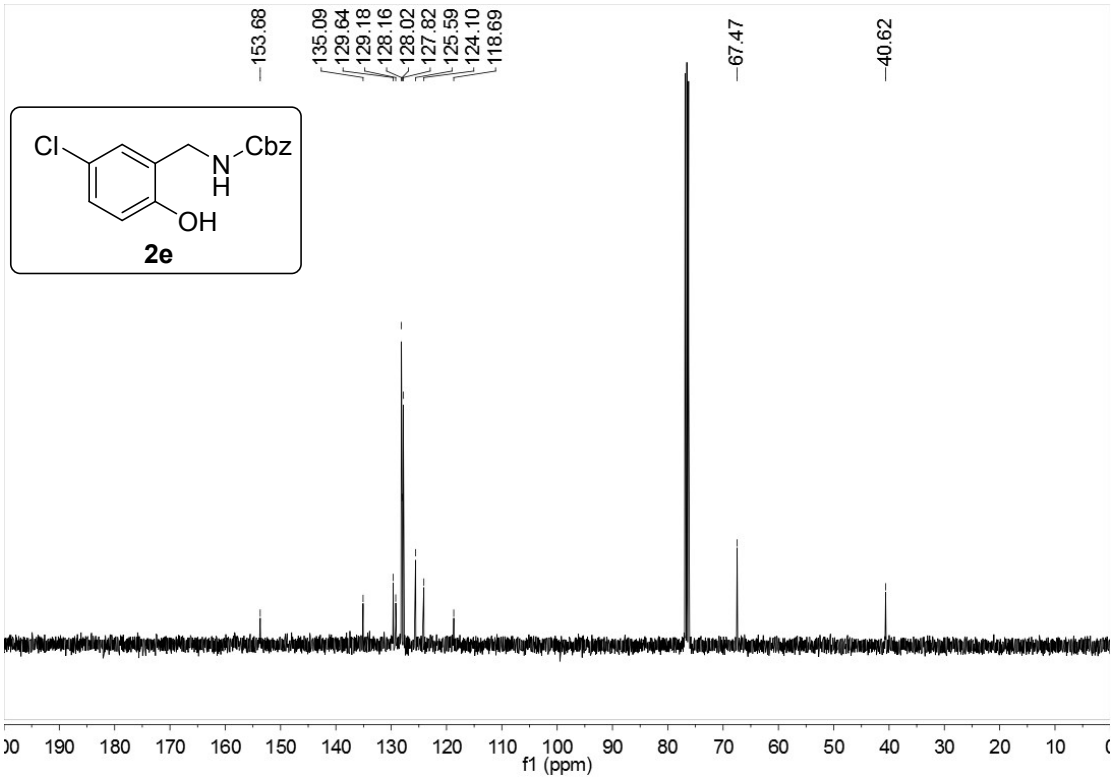
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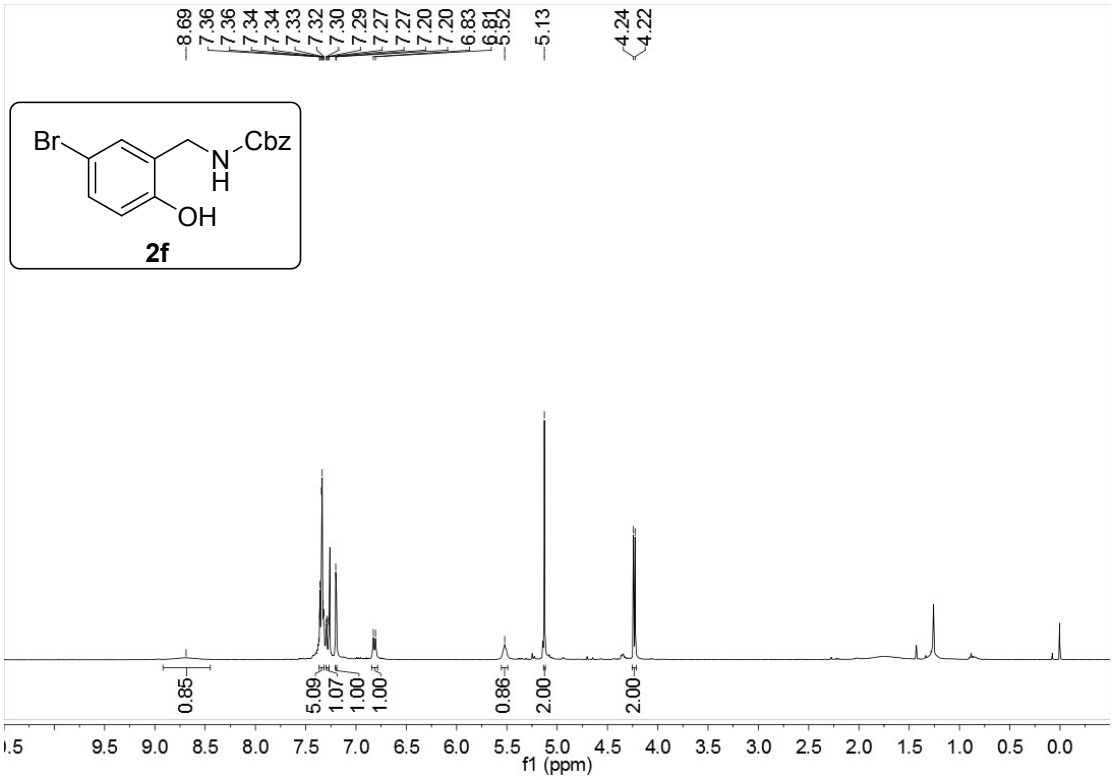
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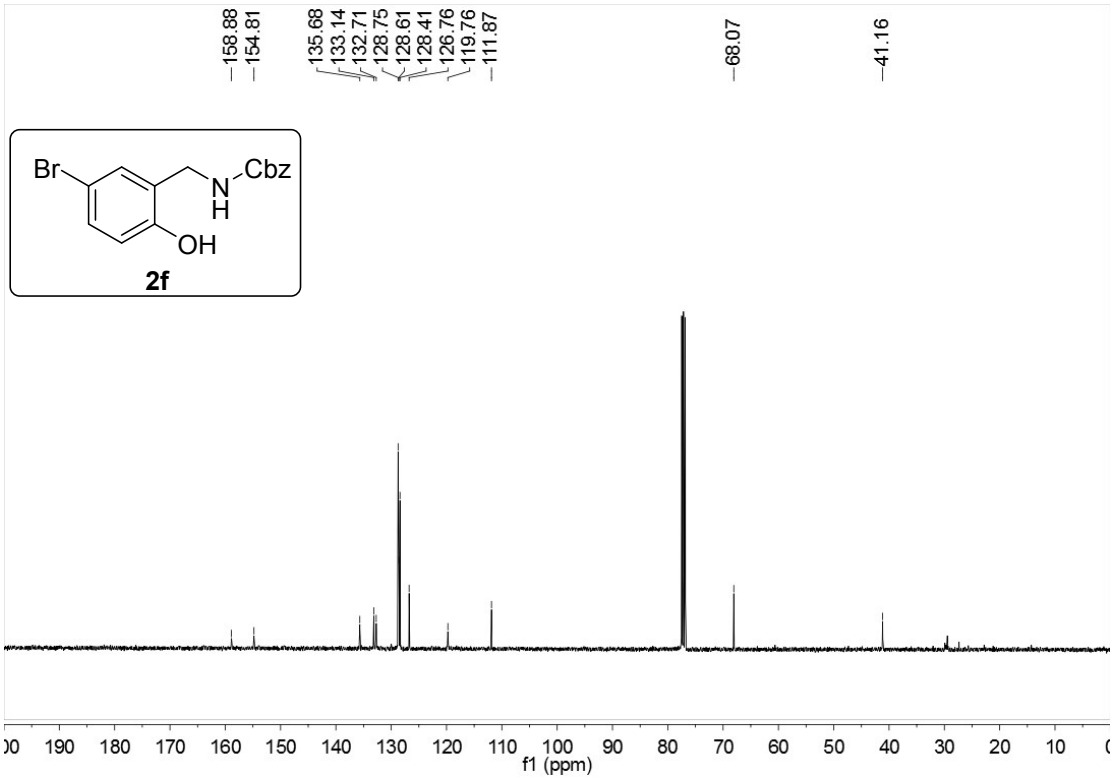
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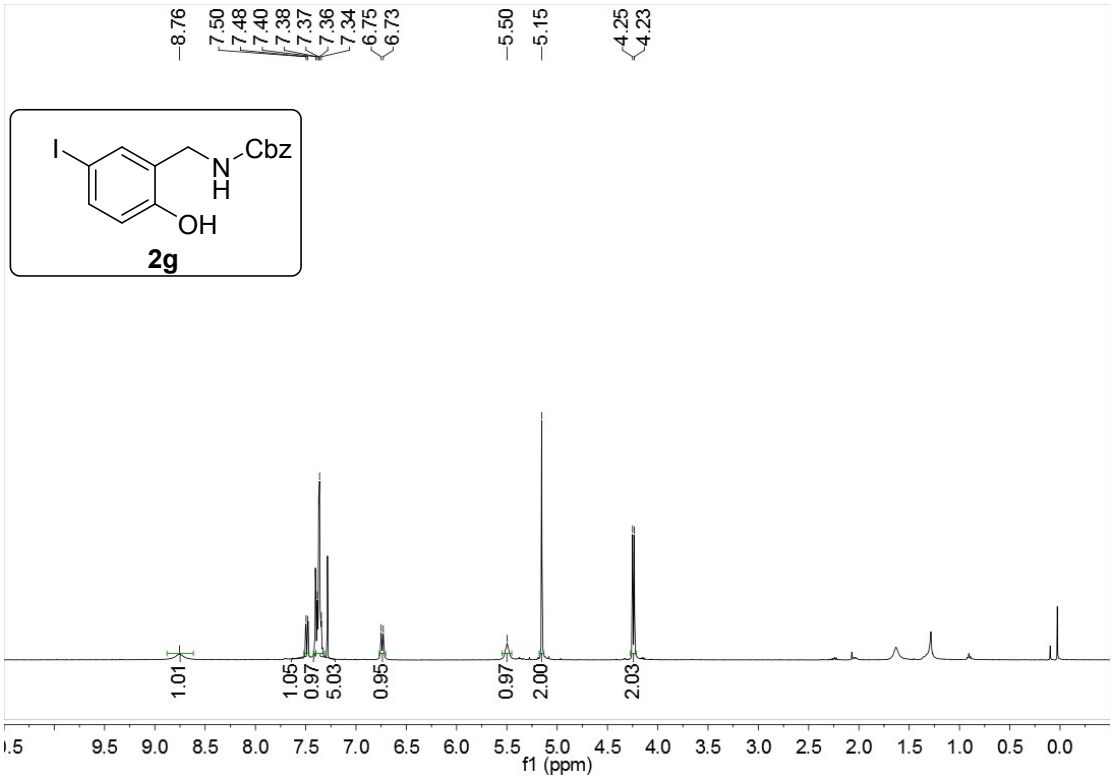
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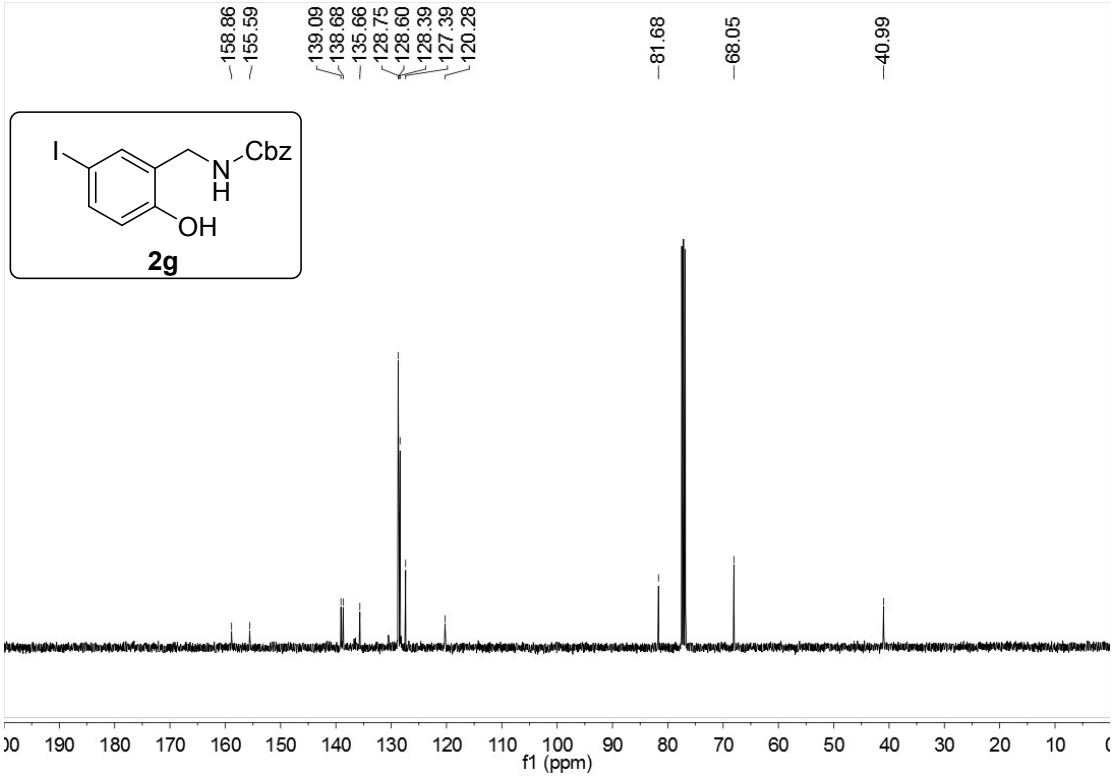
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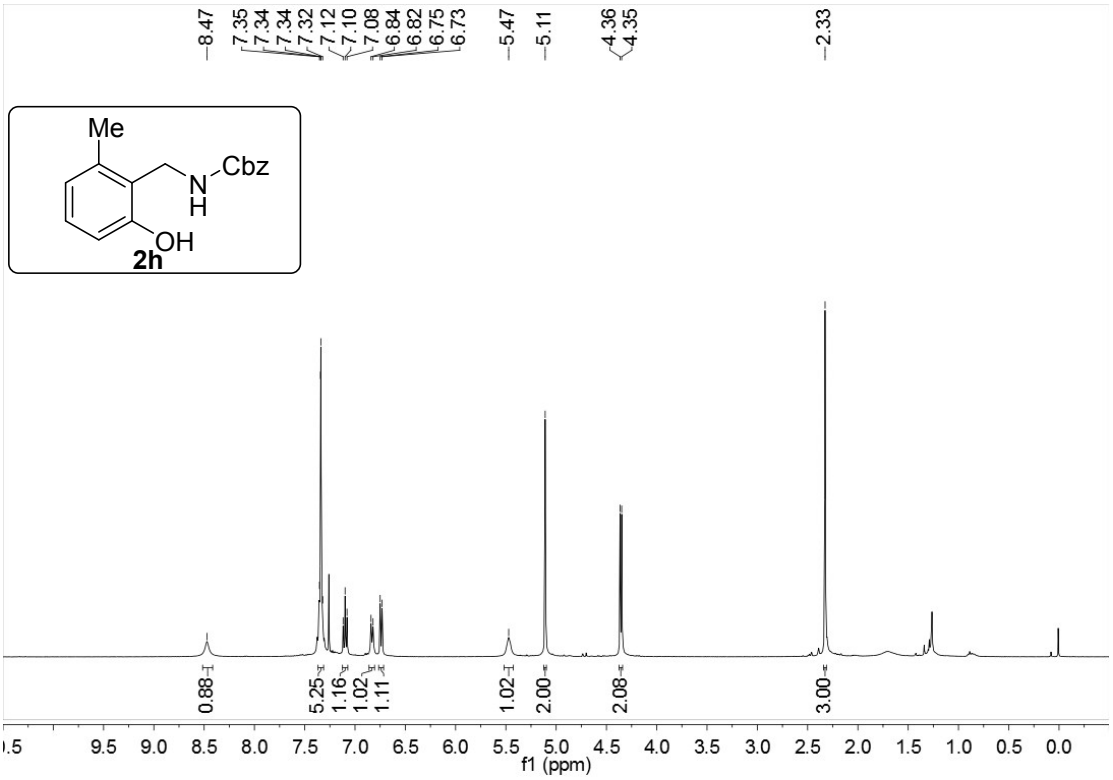
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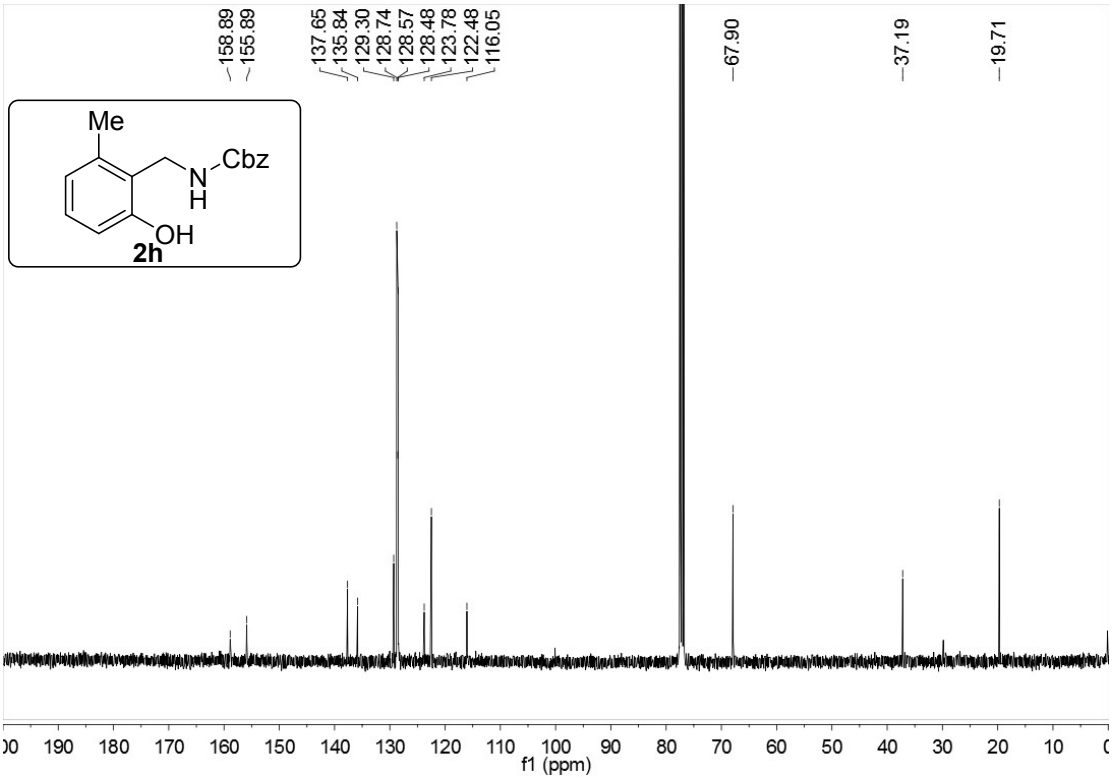
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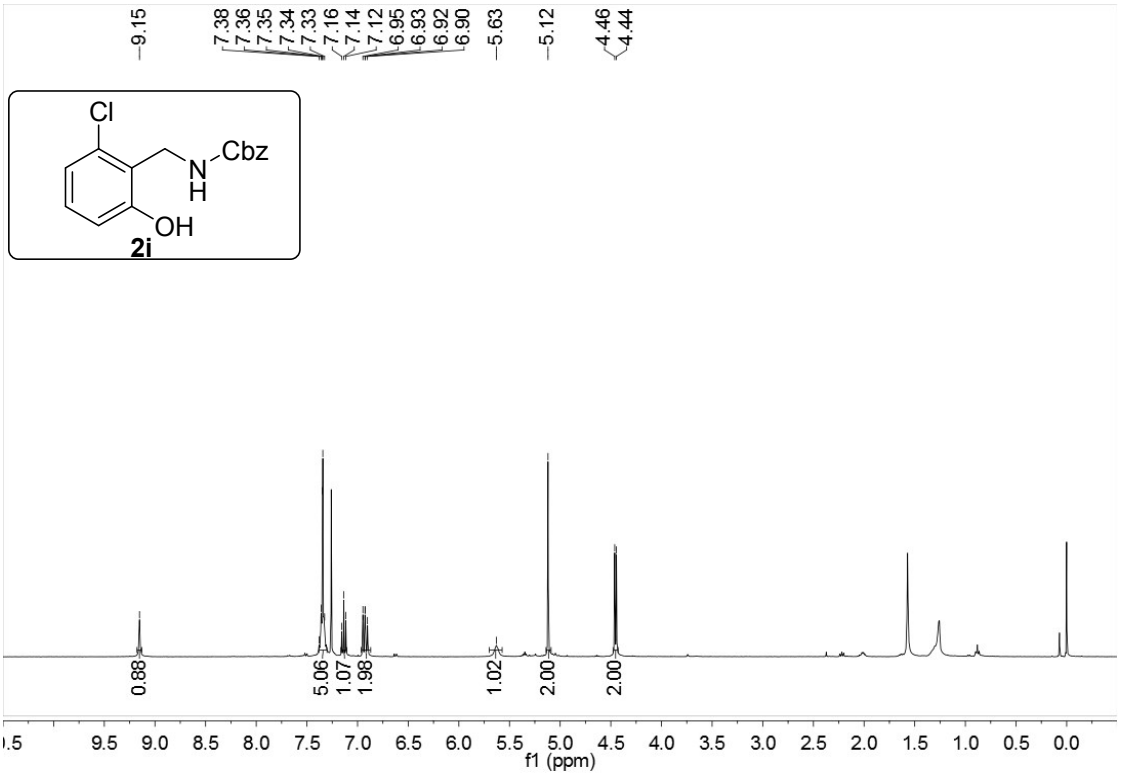
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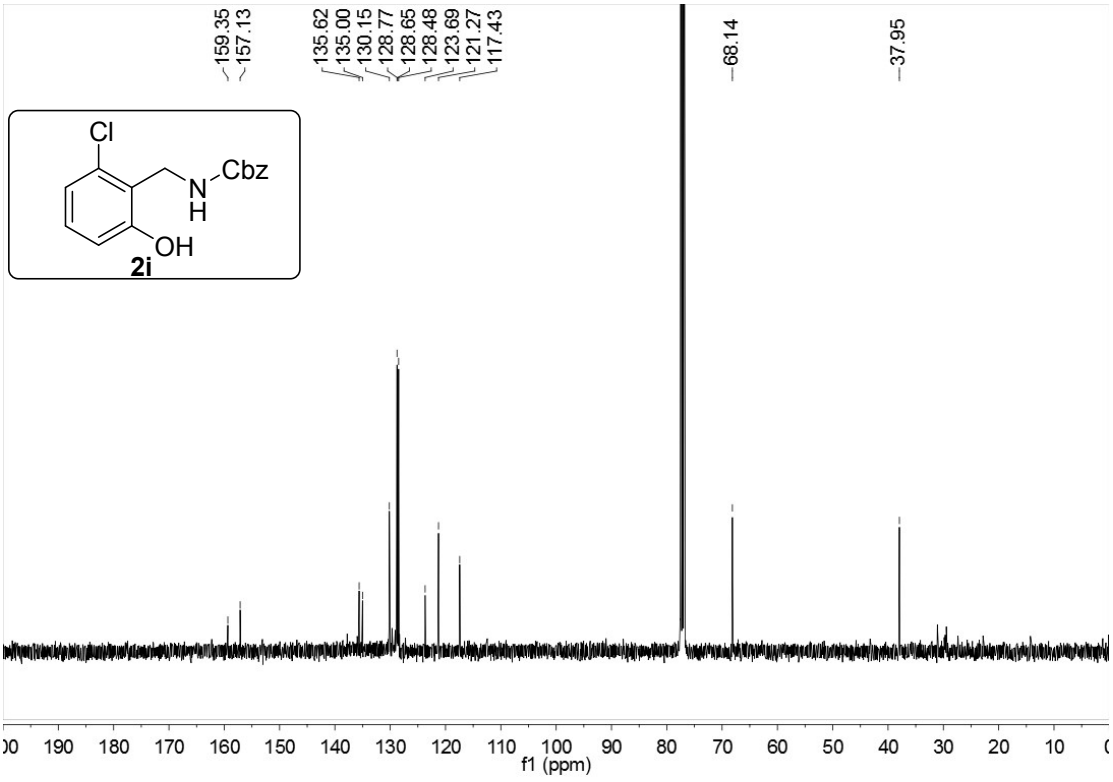
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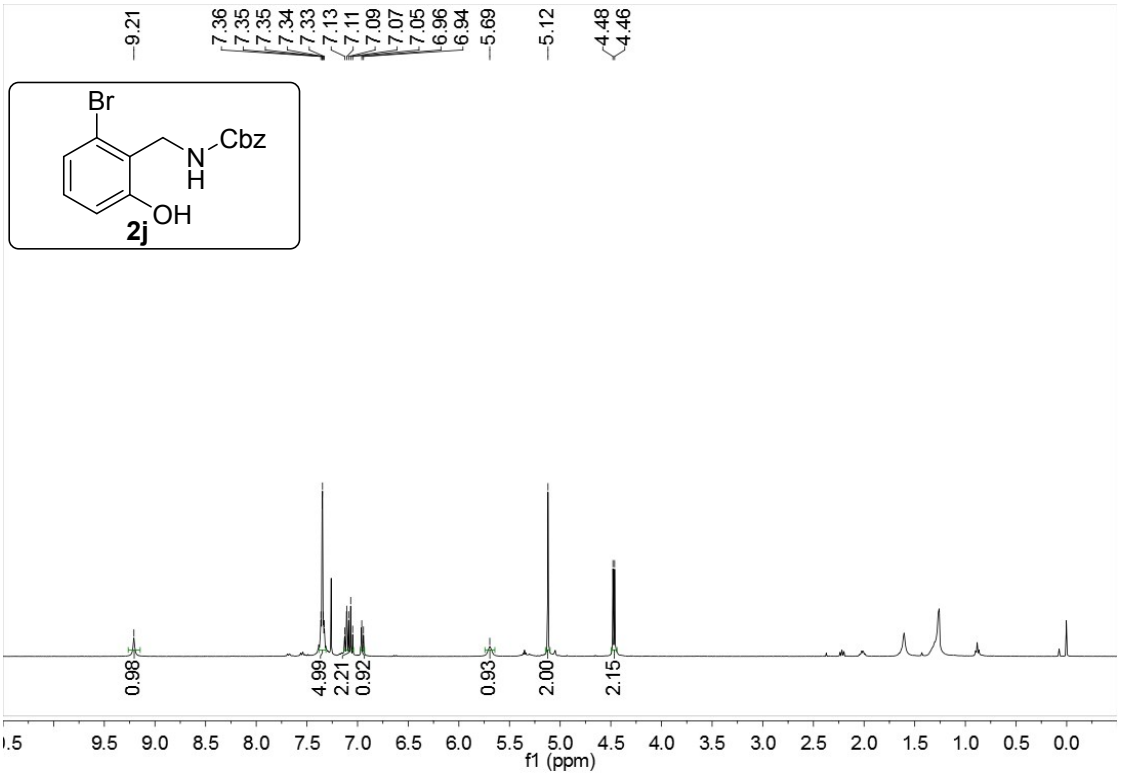
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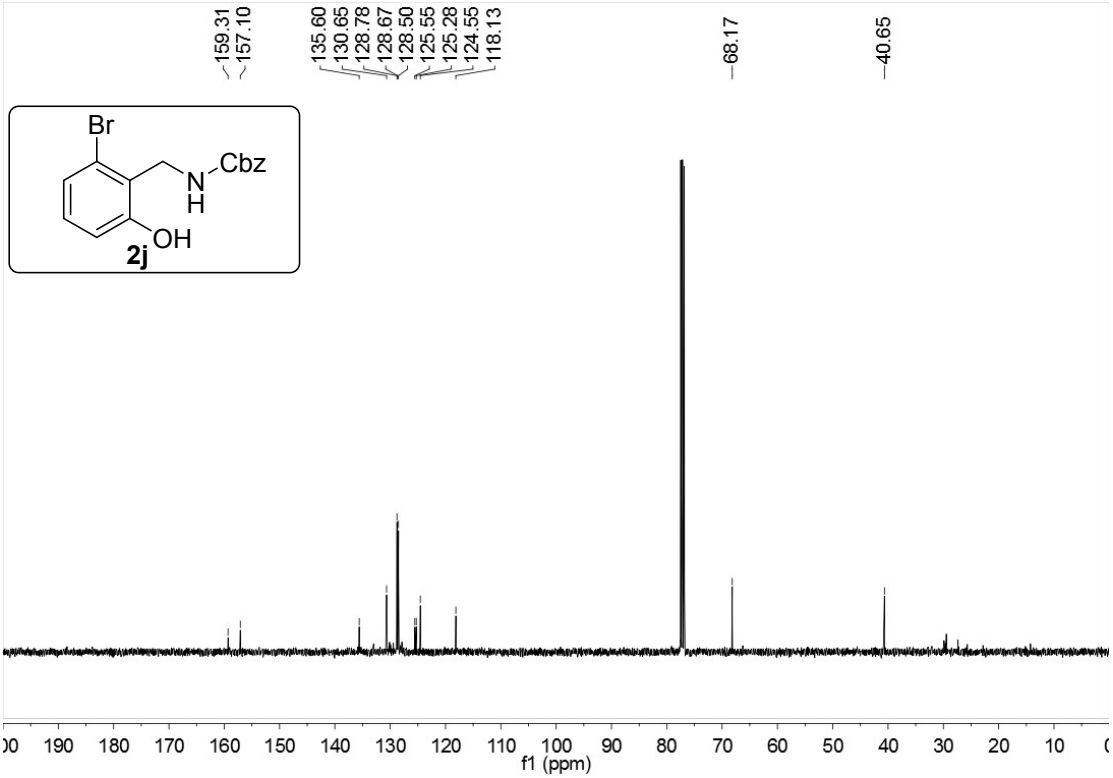
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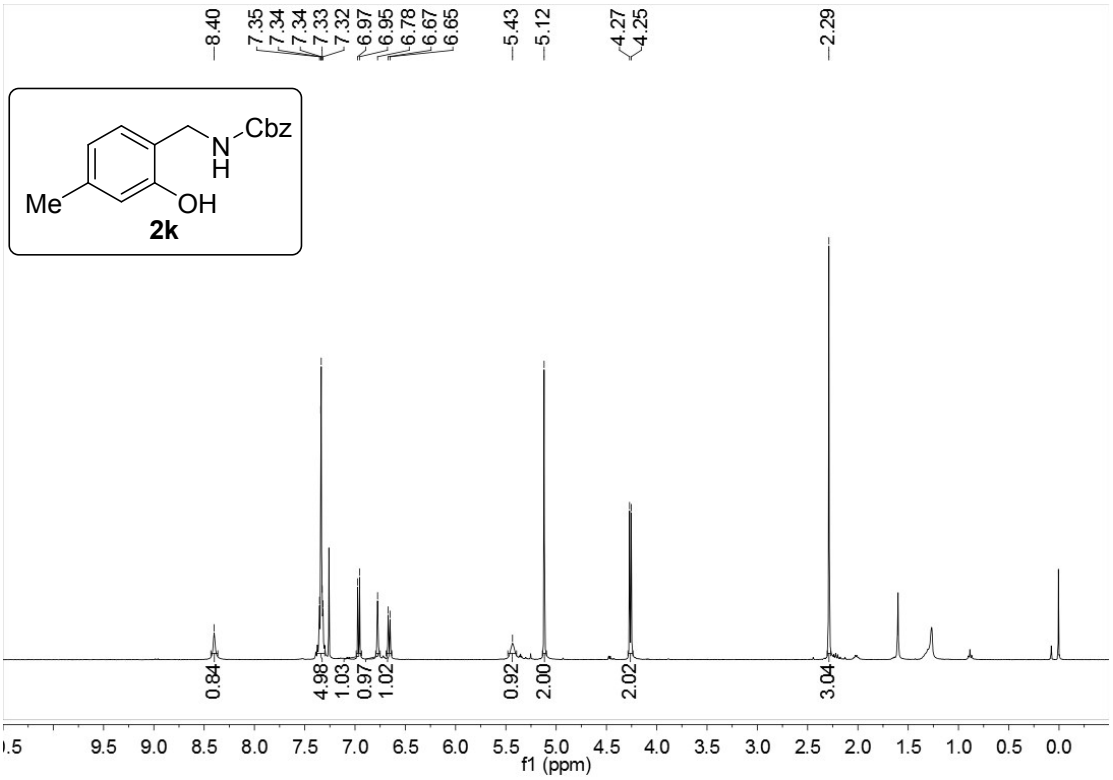
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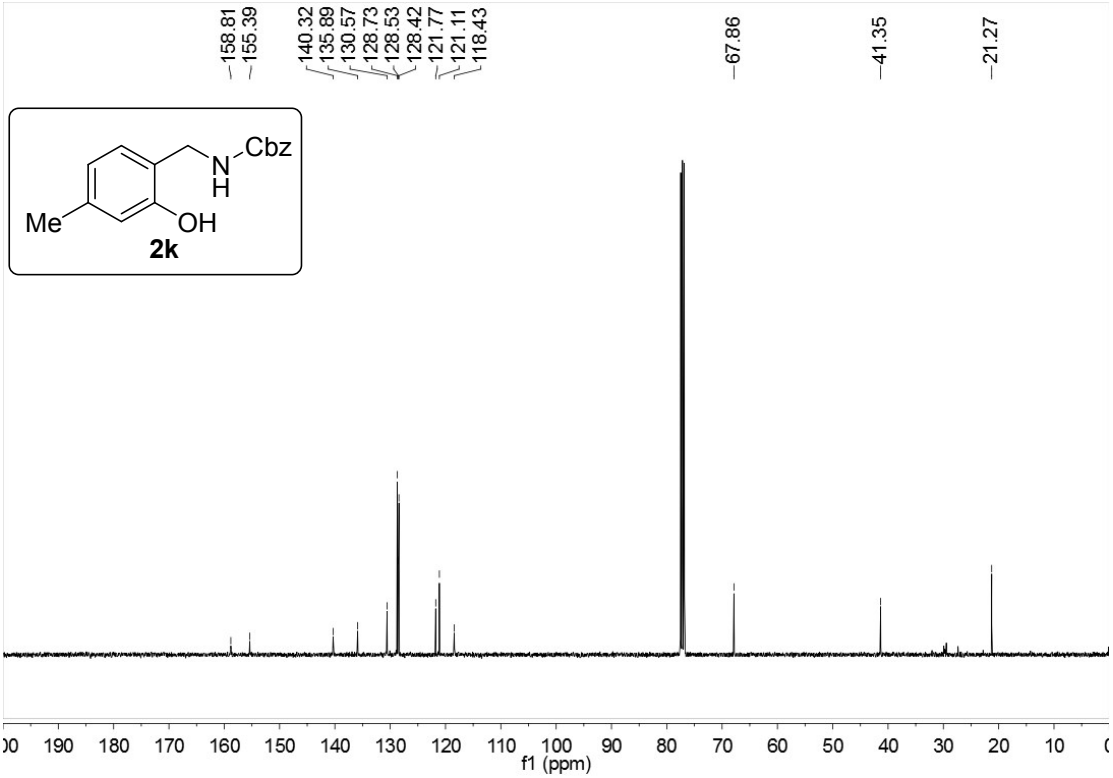
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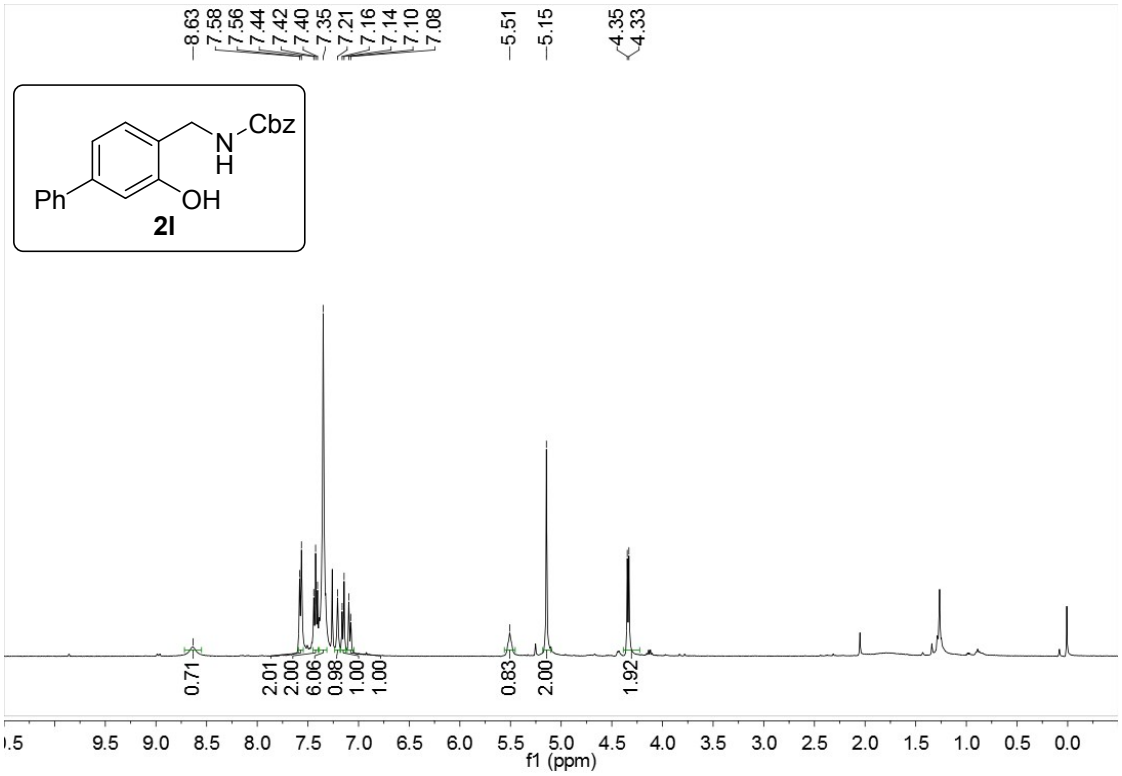
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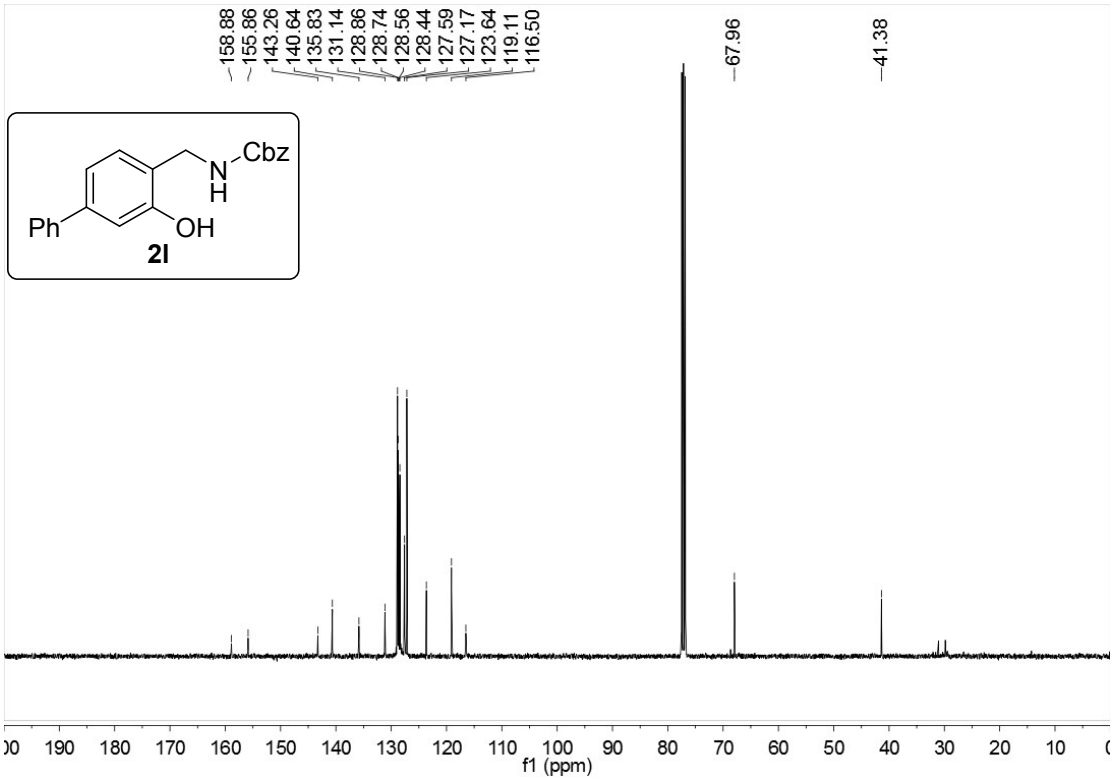
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131.14
128.86
128.74
128.56
128.44
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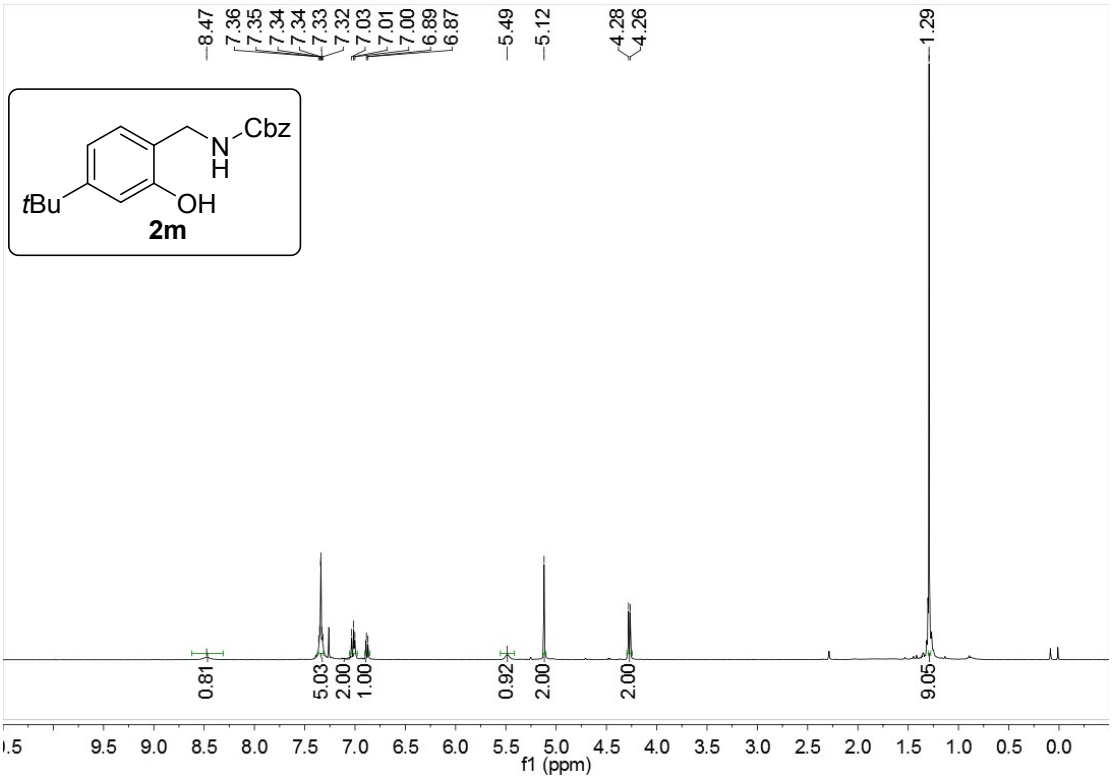
119.11
116.50
67.96
41.38
Cbz
N
H
Ph
OH
2l
f1 (ppm)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7.33
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7.03
7.01
7.00
6.89
6.87
5.49
5.12
4.28
4.26
1.29
Cbz
N
H
tBu
OH
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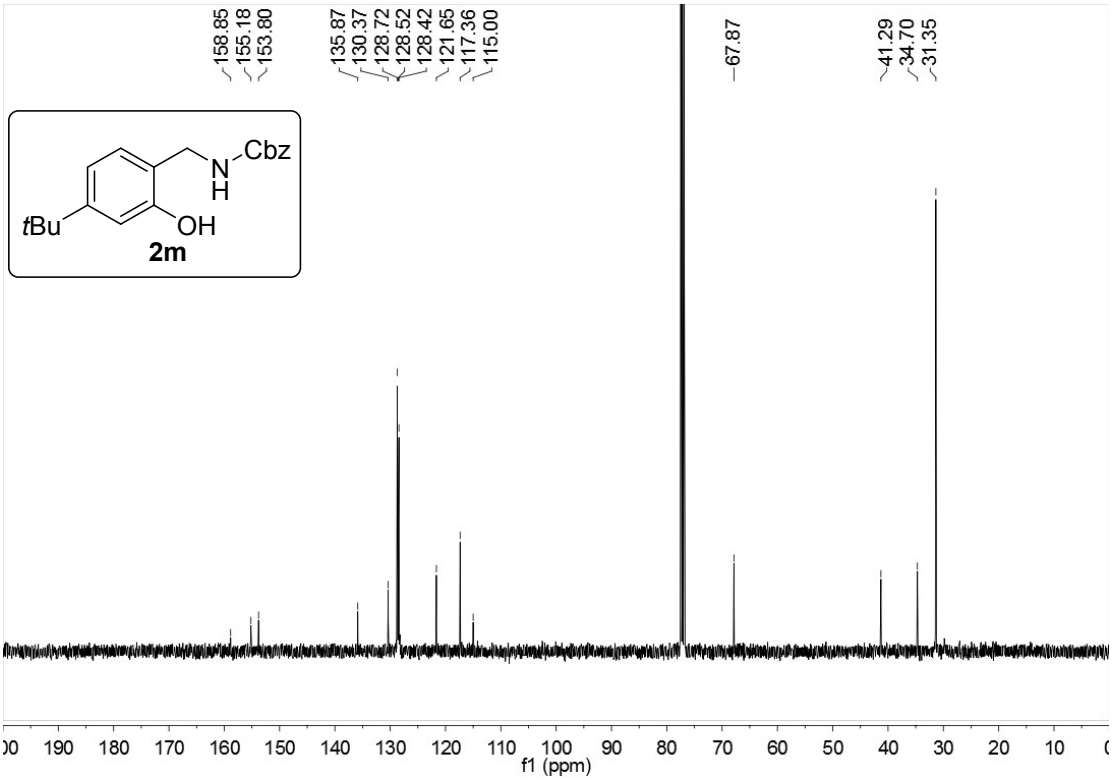
5.03
2.00
1.00
0.92
2.00
2.00
9.05
f1 (ppm)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128.42
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31.35
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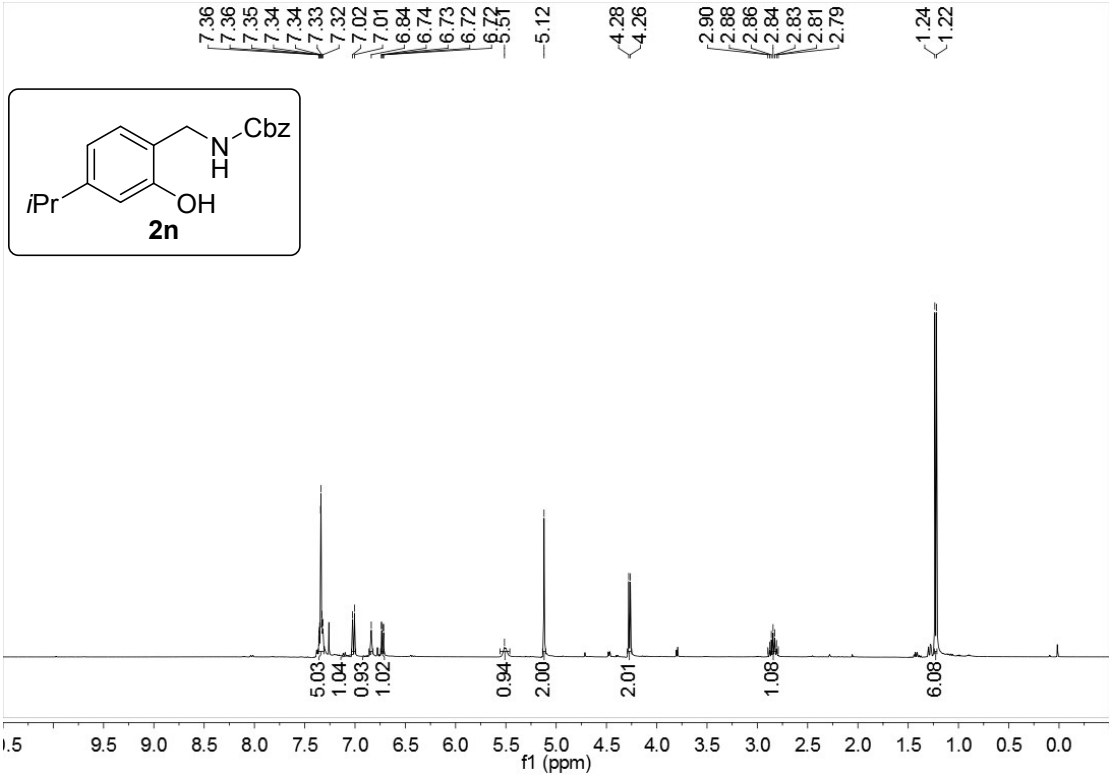
N
H
tBu
OH
2m
f1 (ppm)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7.02
7.01
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6.74
6.73
6.72
6.72
5.51
5.12
4.28
4.26
2.90
2.88
2.86
2.84
2.83
2.81
2.79
1.24
1.22
Cbz
N
H
iPr
OH
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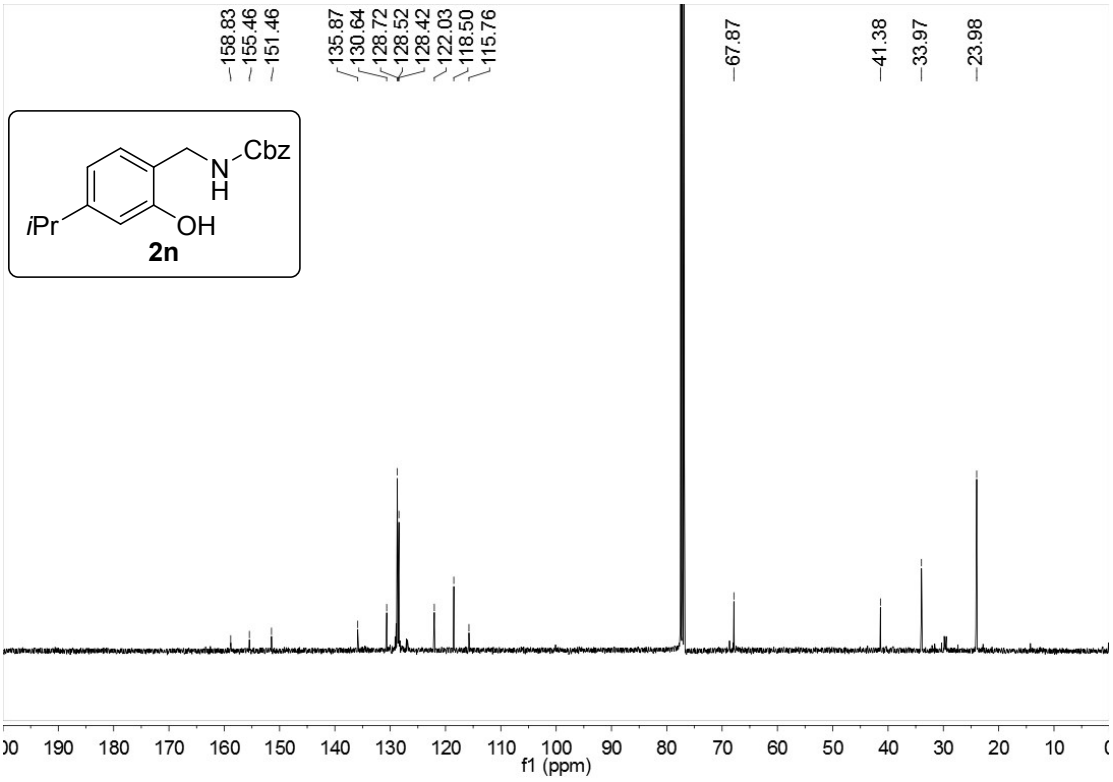
1.02
0.94
2.00
2.01
1.08
6.08
f1 (ppm)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128.42
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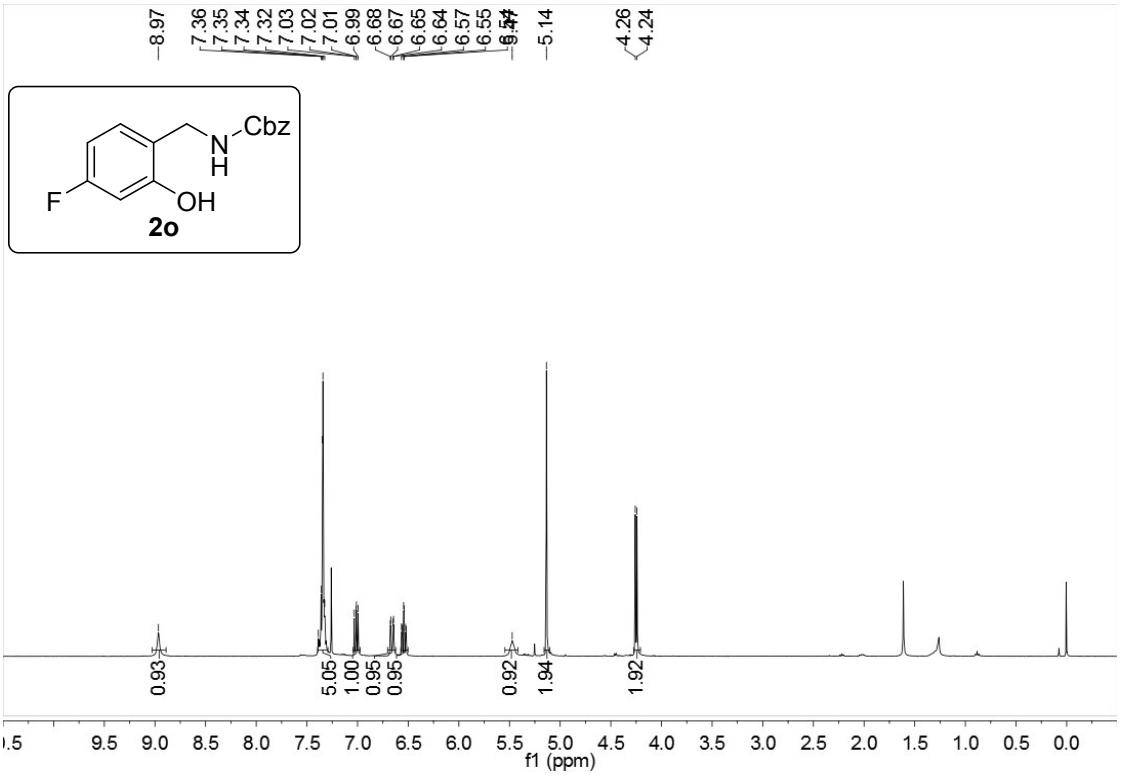
67.87
41.38
33.97
23.98
Cbz
N
H
iPr
OH
2n
f1 (ppm)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7.01
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6.68
6.67
6.65
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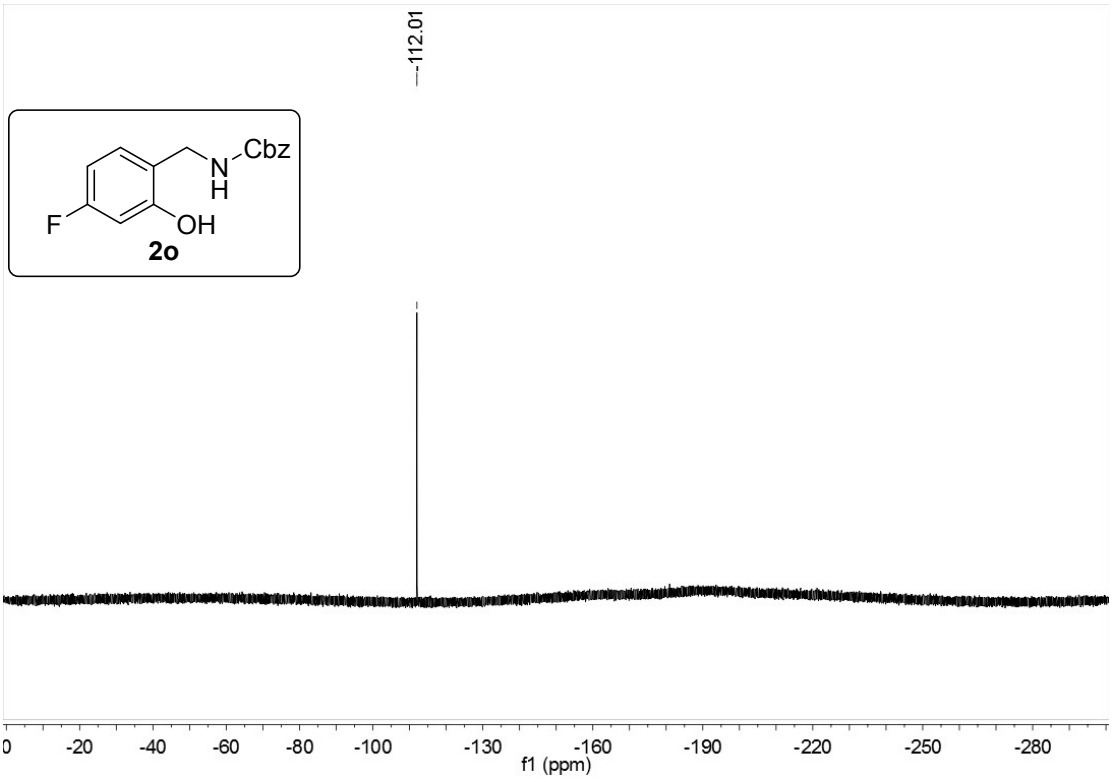
6.57
6.55
5.14
4.26
4.24
Cbz
N
H
F
OH
2o
0.93
5.05
1.00
0.95
0.95
0.92
1.94
1.92
f1 (ppm)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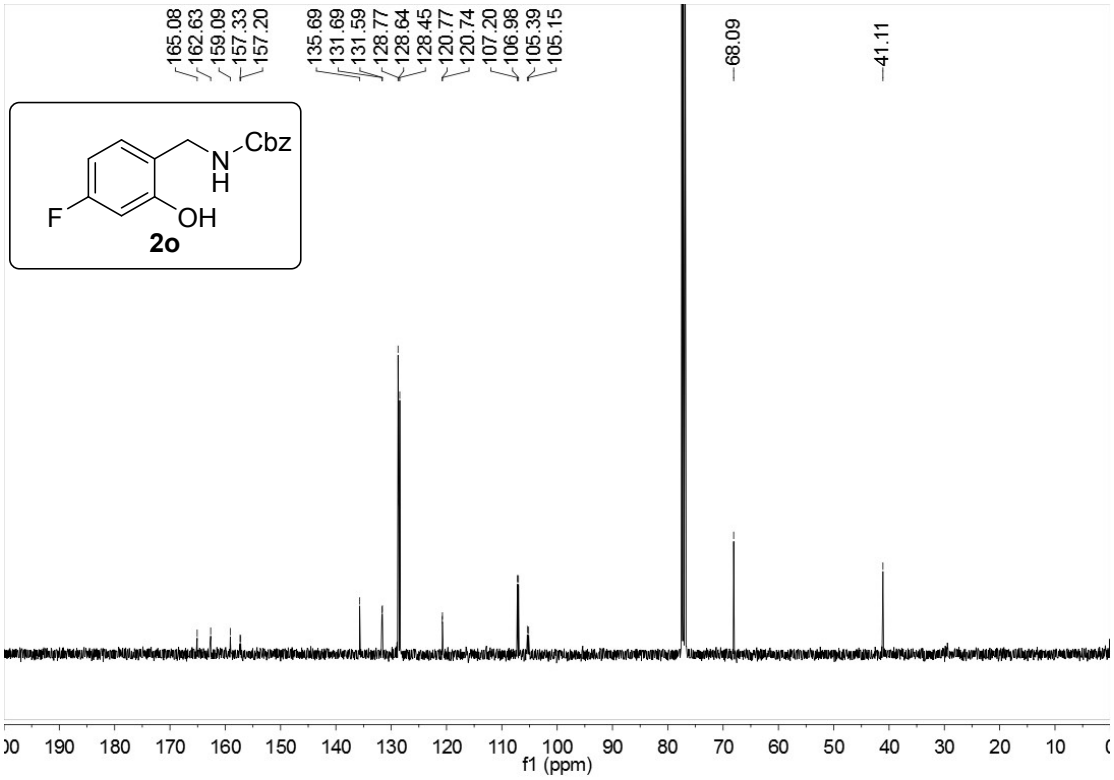
H
F
OH
2o
f1 (ppm)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128.64
128.45
120.77
120.74
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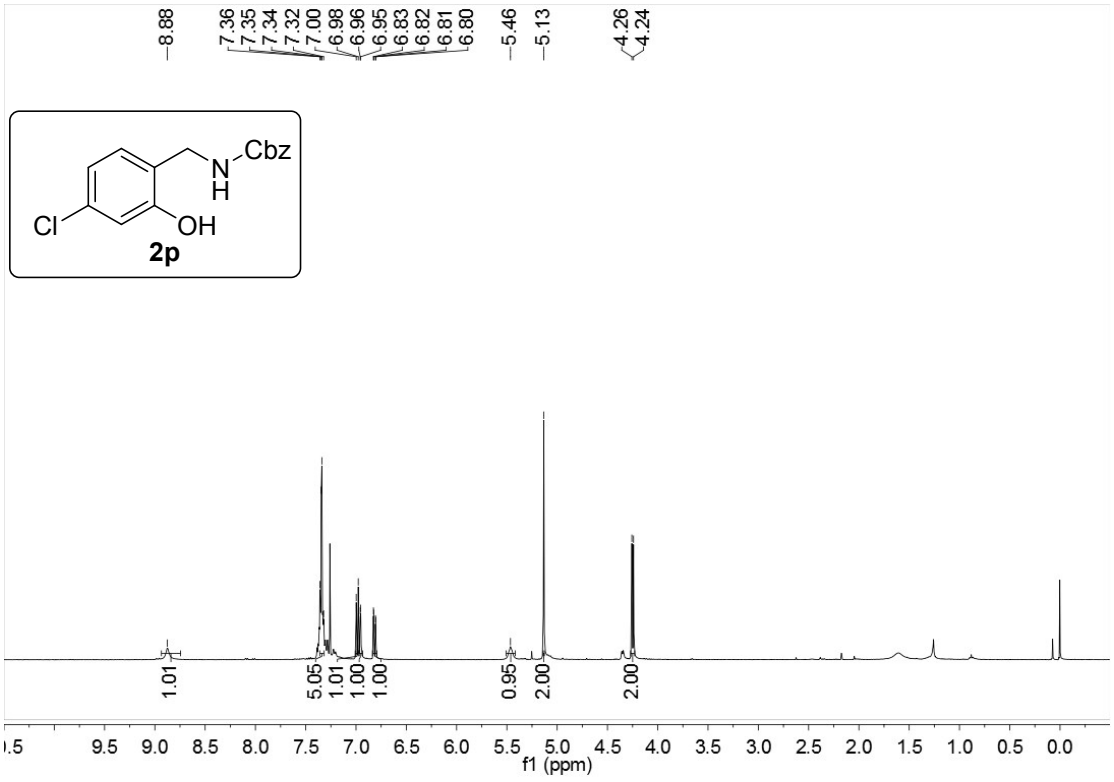
105.39
105.15
68.09
41.11
Cbz
N
H
F
OH
2o
f1 (ppm)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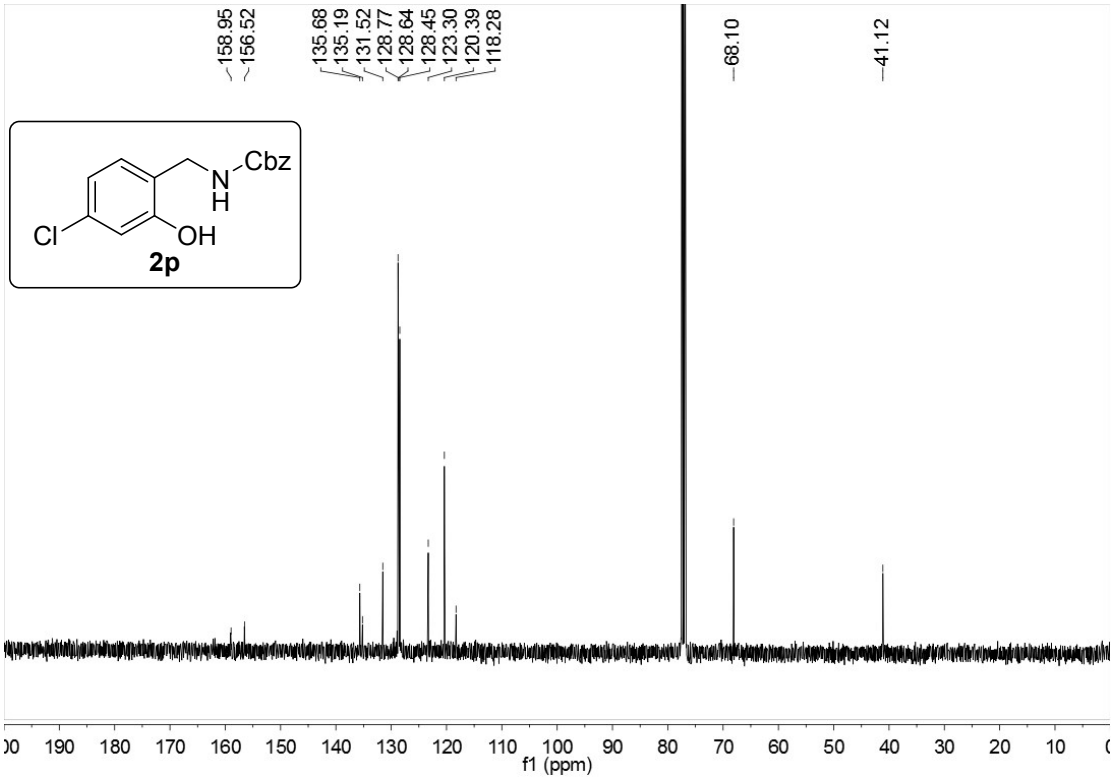
7.32
7.00
6.98
6.96
6.95
6.83
6.82
6.81
6.80
5.46
5.13
4.26
4.24
Cbz
N
H
Cl
OH
2p
1.01
5.05
1.01
1.00
1.00
0.95
2.00
2.00
f1 (ppm)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120.39
118.28
68.10
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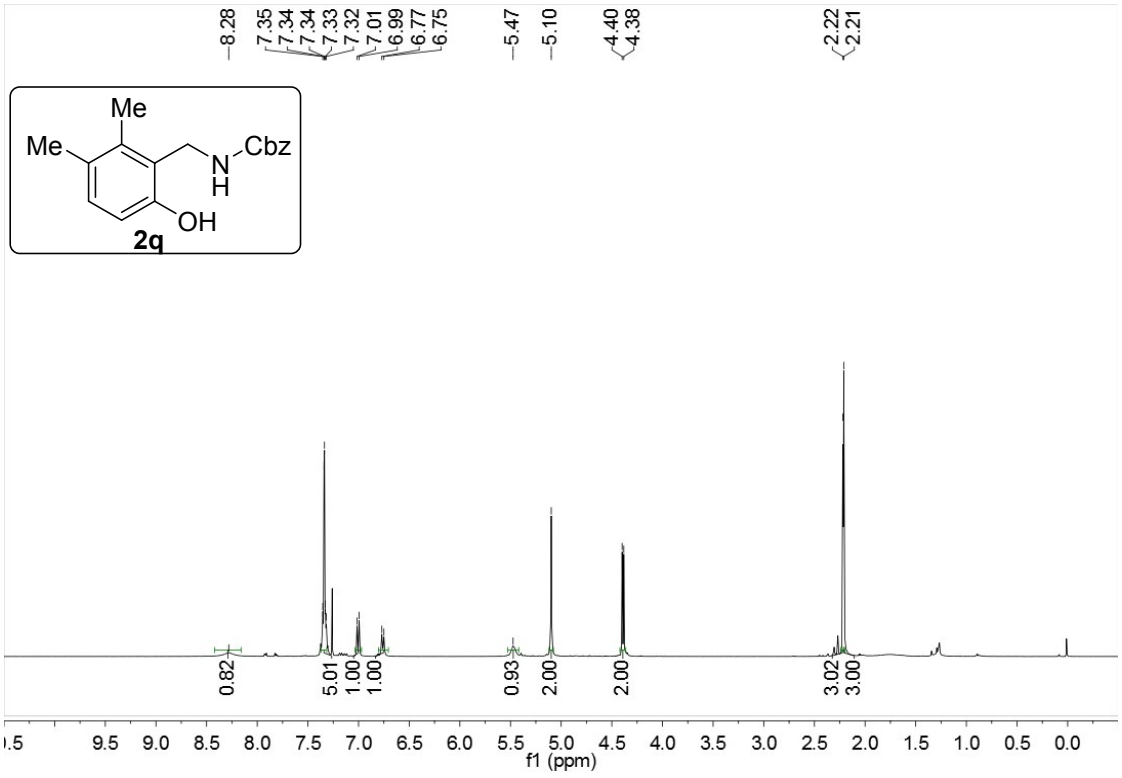
Cbz
N
H
Cl
OH
2p
f1 (ppm)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7.01
6.99
6.77
6.75
5.47
5.10
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4.38
2.22
2.21
Me
Me
Cbz
N
H
OH
2q
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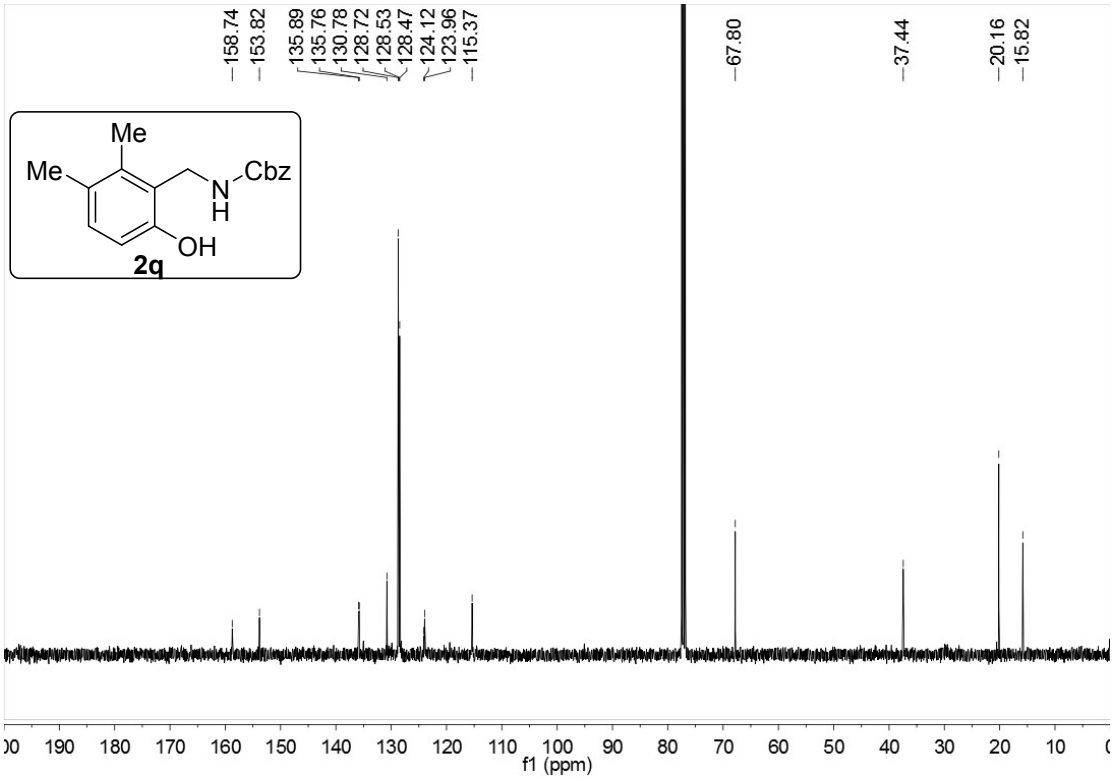
5.01
1.00
1.00
0.93
2.00
2.00
3.02
3.00
f1 (ppm)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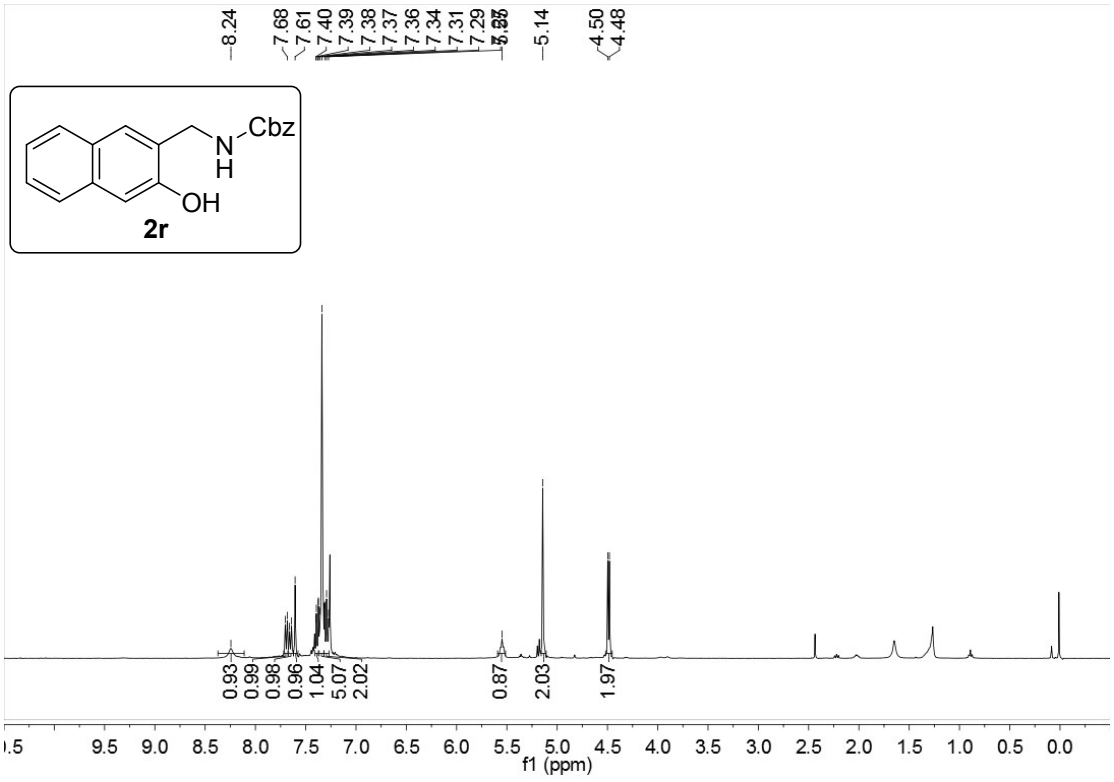
128.72
128.53
128.47
124.12
123.96
115.37
67.80
37.44
20.16
15.82
Me
Me
N
H
Cbz
OH
2q
f1 (ppm)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7.31
7.29
5.14
4.50
4.48
N
H
Cbz
OH
2r
0.93
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0.98
0.96
1.04
5.07
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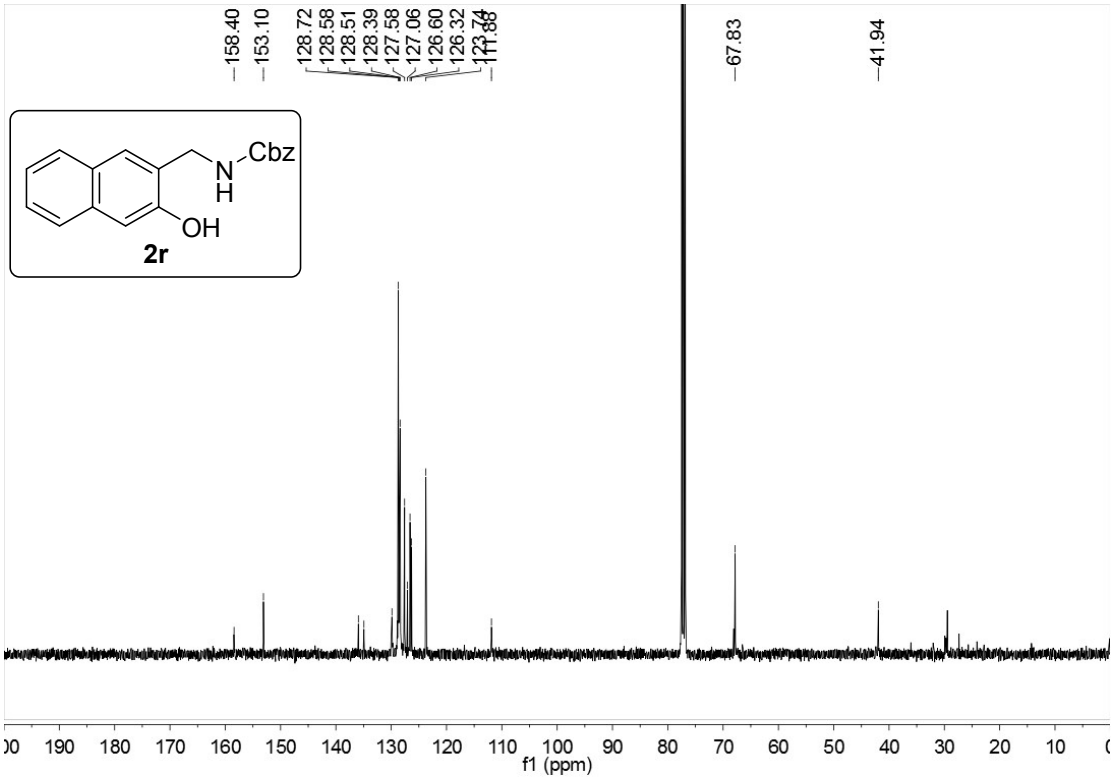
0.87
2.03
1.97
f1 (ppm)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126.32
67.83
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Cbz
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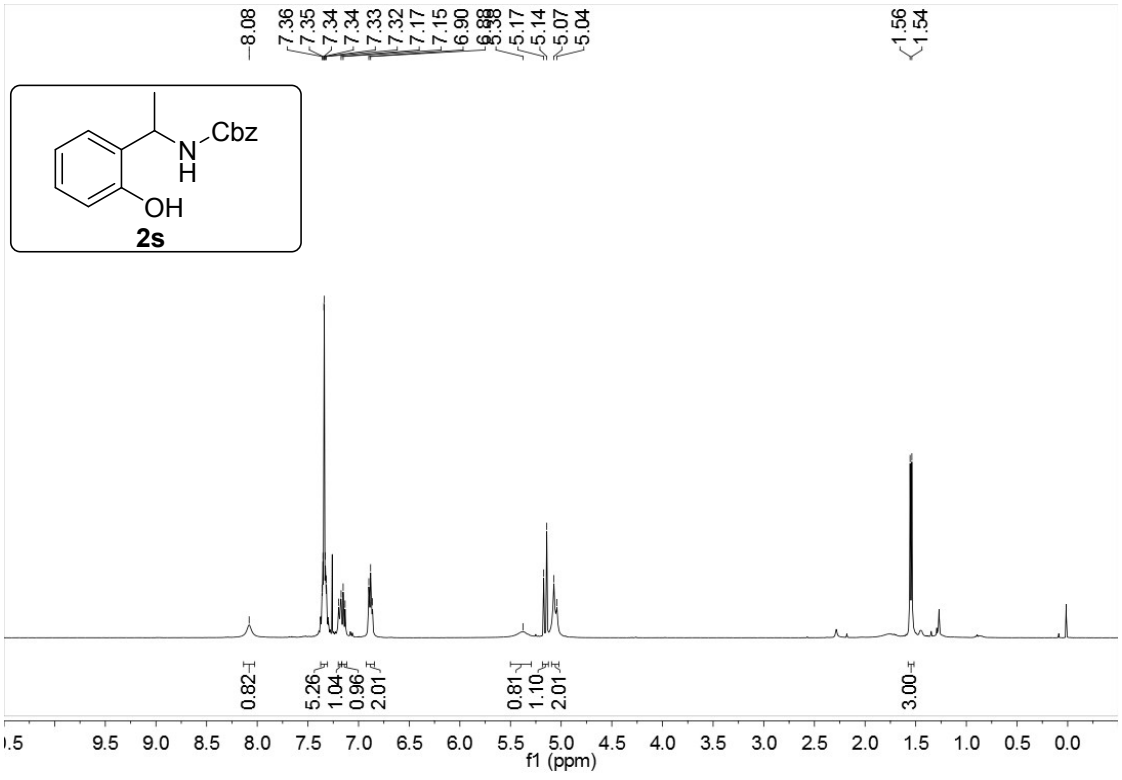
H
OH
2r
f1 (ppm)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7.33
7.32
7.17
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6.90
5.17
5.14
5.07
5.04
1.56
1.54
Cbz
N
H
OH
2s
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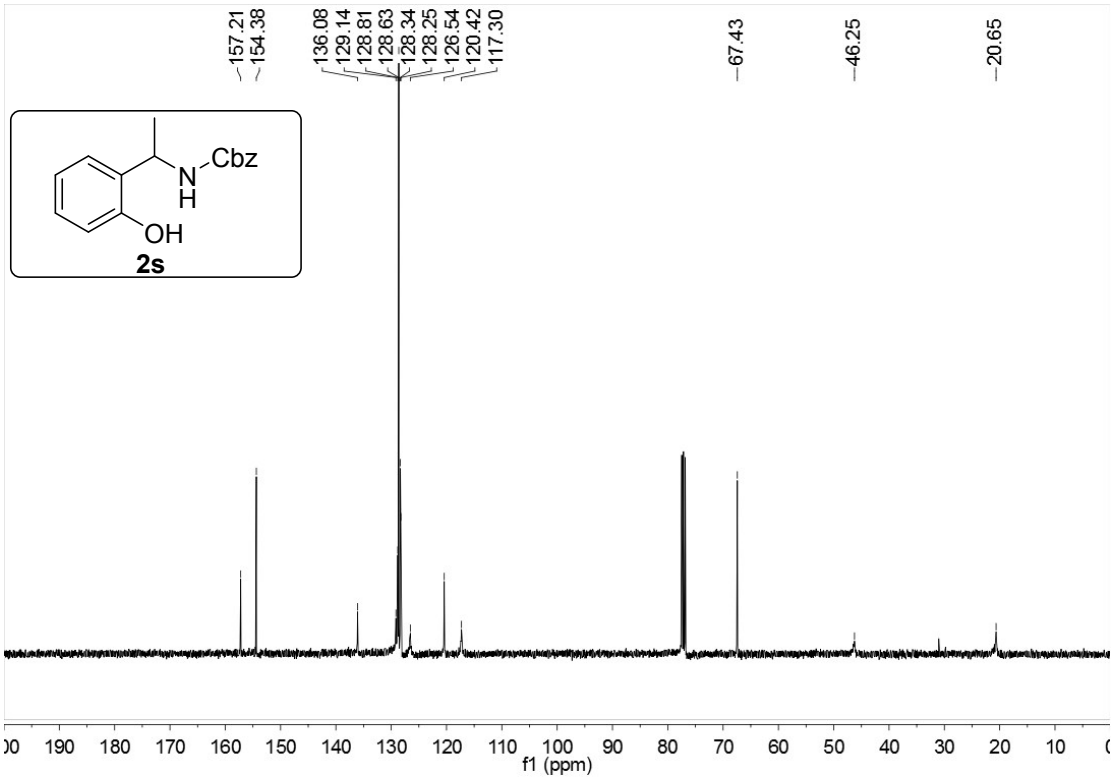
5.26
1.04
0.96
2.01
0.81
1.10
2.01
3.00
f1 (ppm)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Cbz
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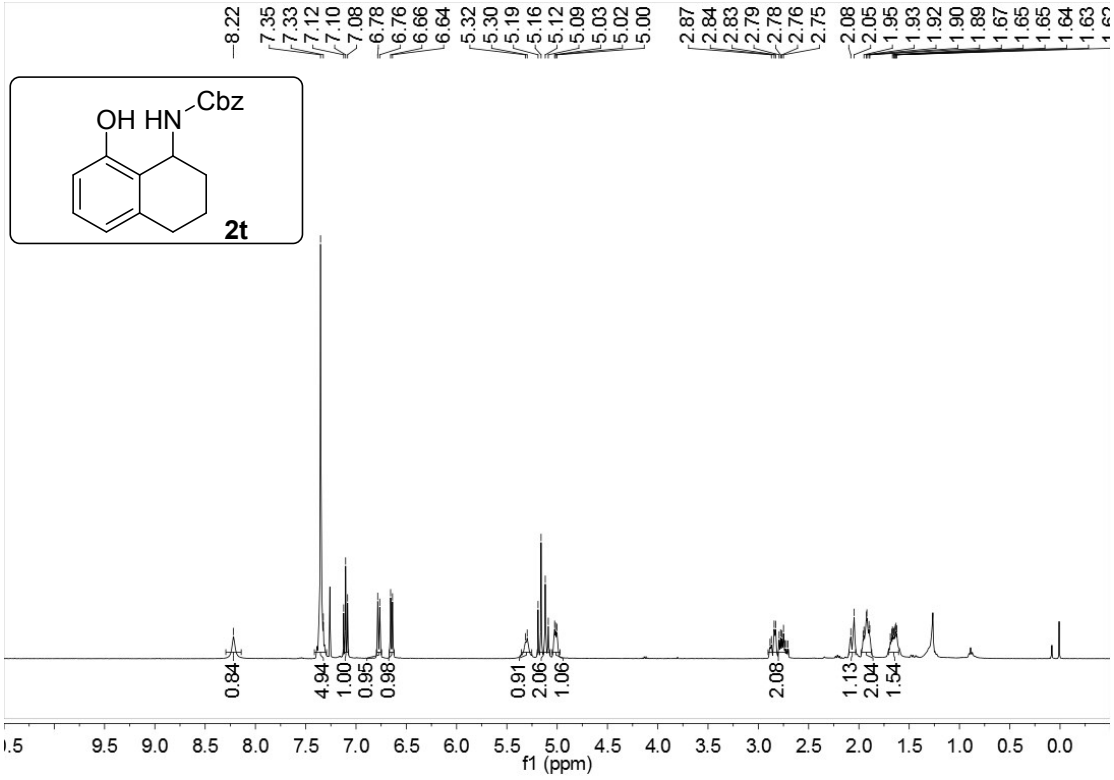
H
OH
2s
f1 (ppm)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5.12
5.09
5.03
5.02
5.00
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2.79
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2.75
2.08
2.05
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1.93
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1.90
1.89
1.67
1.65
1.65
1.64
1.63
OH HN
Cbz
2t
0.84
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0.98
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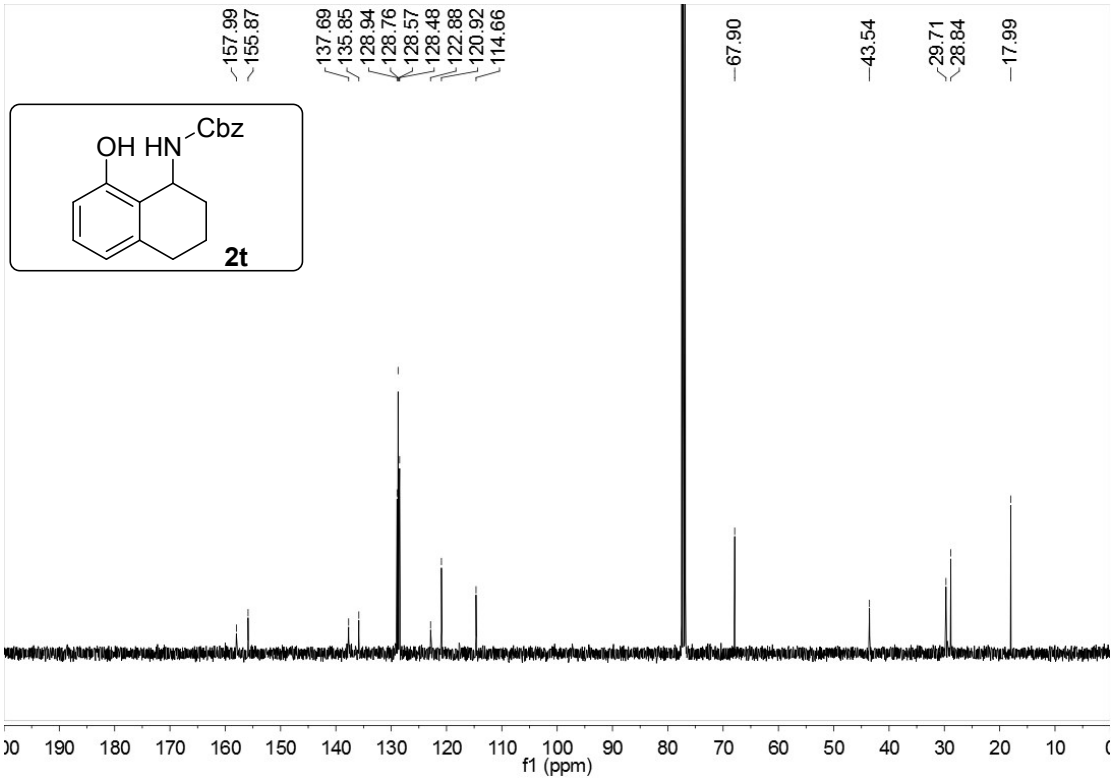
1.06
2.08
1.13
2.04
1.54
f1 (ppm)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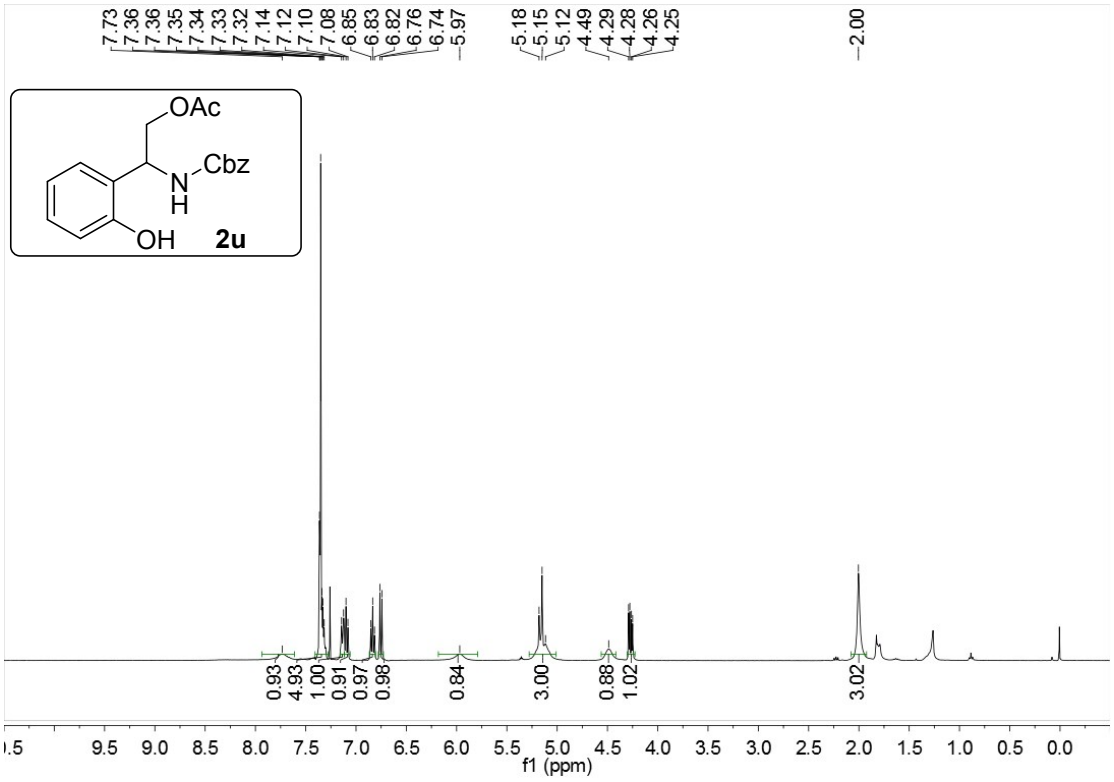
17.99
OH HN
Cbz
2t
f1 (ppm)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7.08
6.85
6.83
6.82
6.76
6.74
5.97
5.18
5.15
5.12
4.49
4.29
4.28
4.26
4.25
2.00
OAc
N
H
Cbz
OH
2u
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4.93
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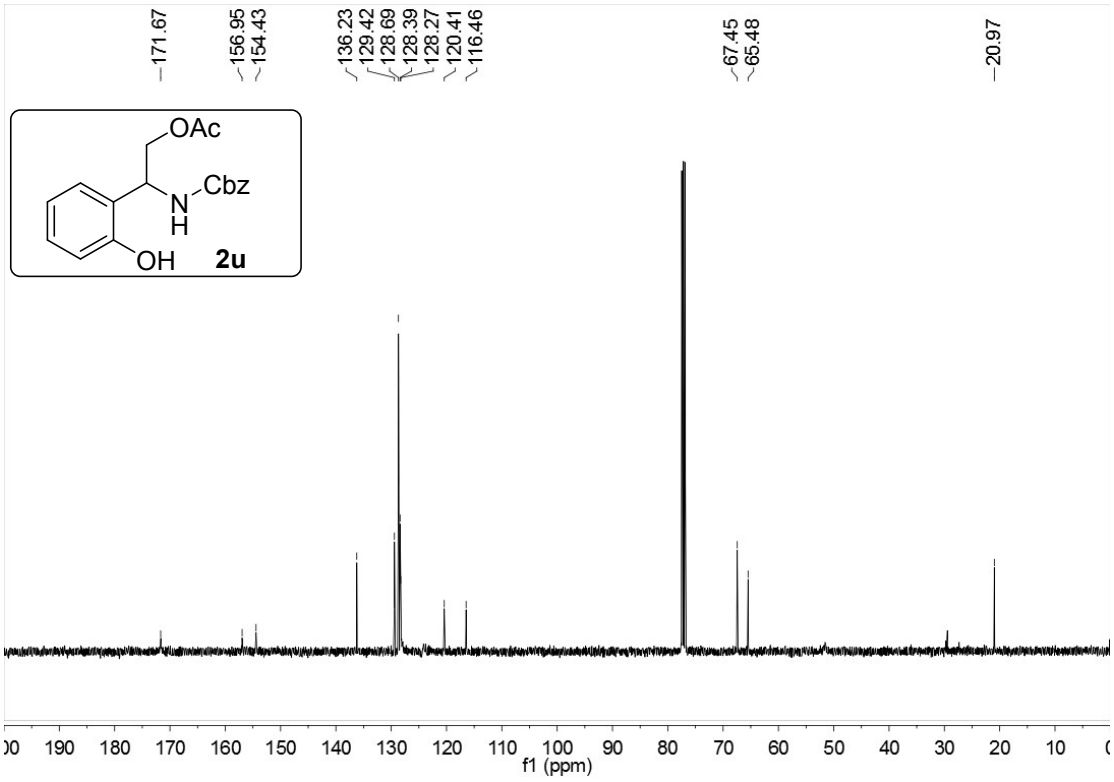
0.91
0.97
0.98
0.84
3.00
0.88
1.02
3.02
f1 (ppm)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128.27
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67.45
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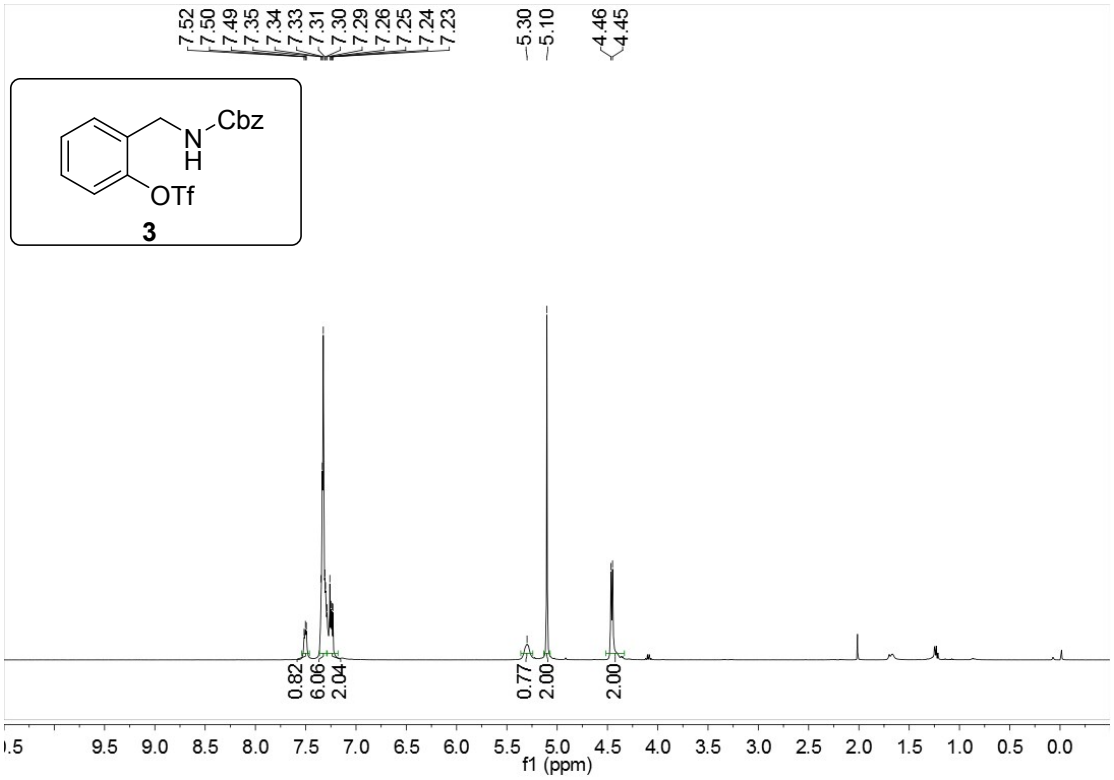
OAc
Cbz
N
H
OH
2u
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)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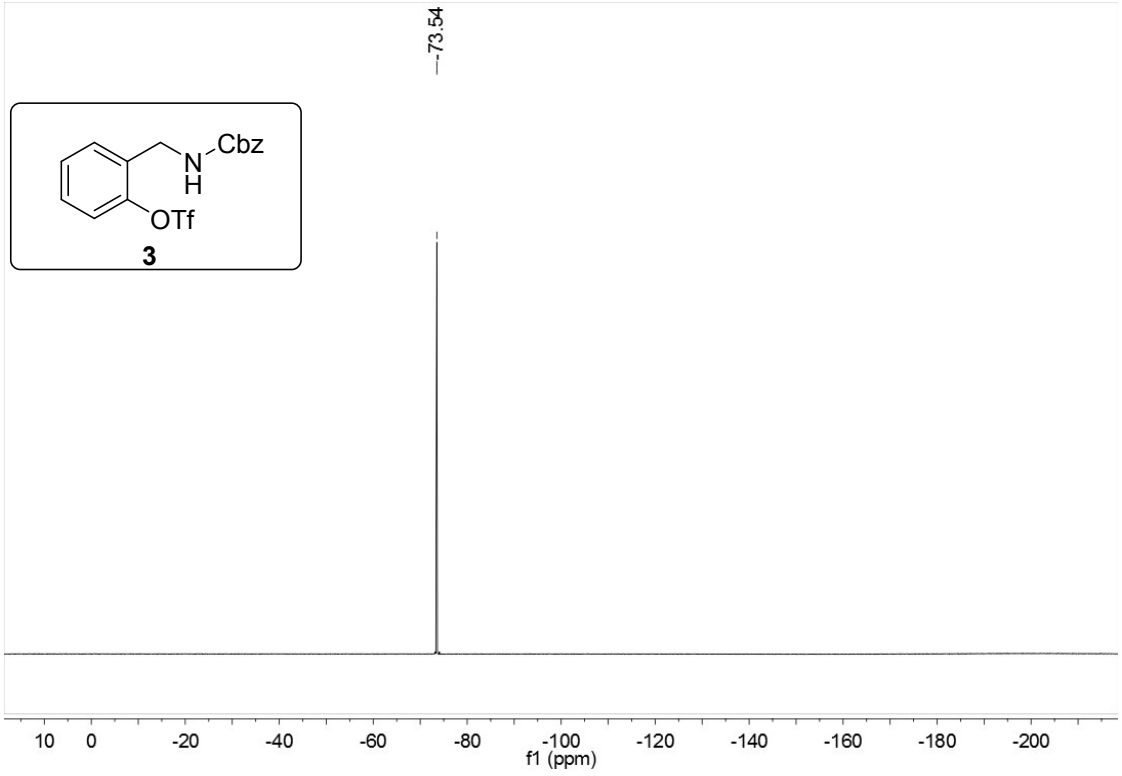
7.24
7.23
5.30
5.10
4.46
4.45
Cbz
N
H
OTf
3
0.82
6.06
2.04
0.77
2.00
2.00
f1 (ppm)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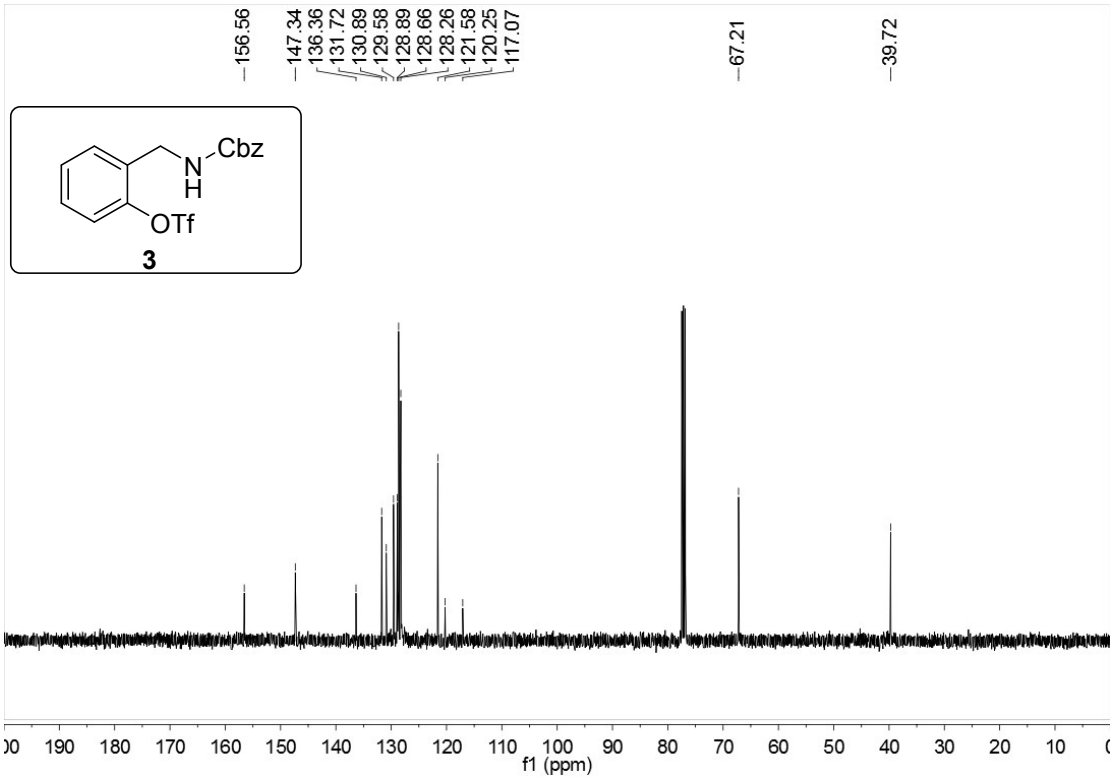
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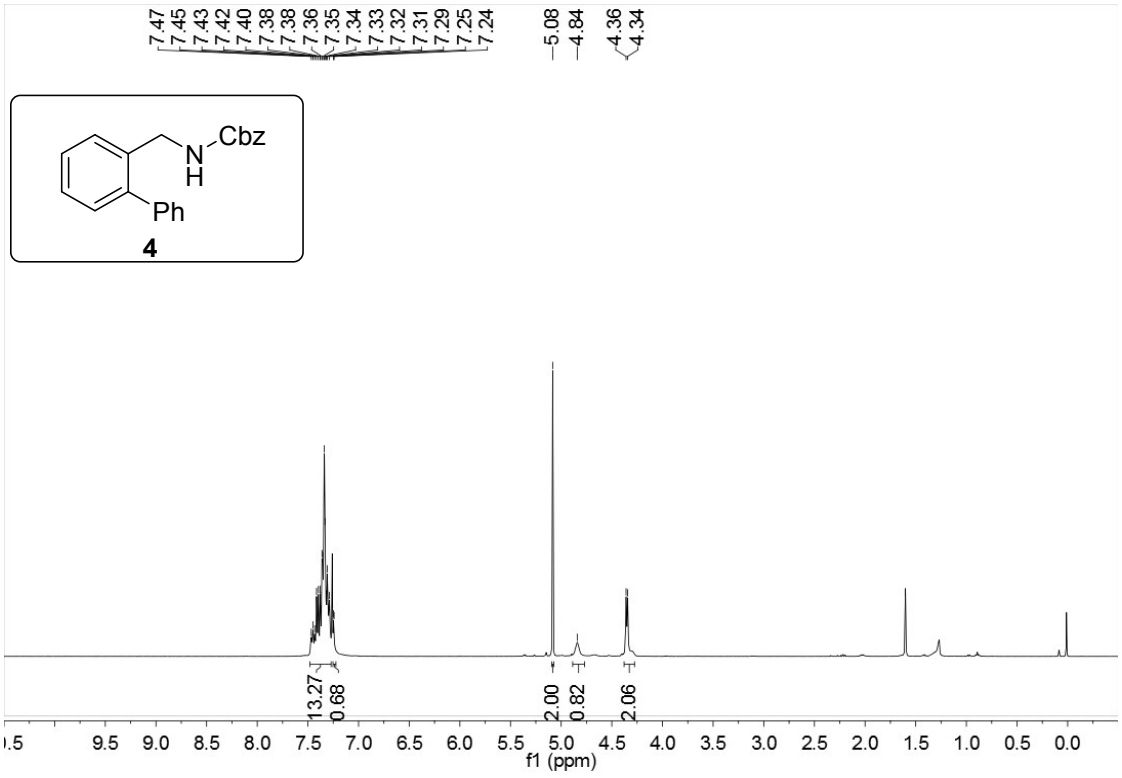
Cbz
N
H
OTf
3
f1 (ppm)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7.32
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7.29
7.25
7.24
5.08
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Cbz
N
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Ph
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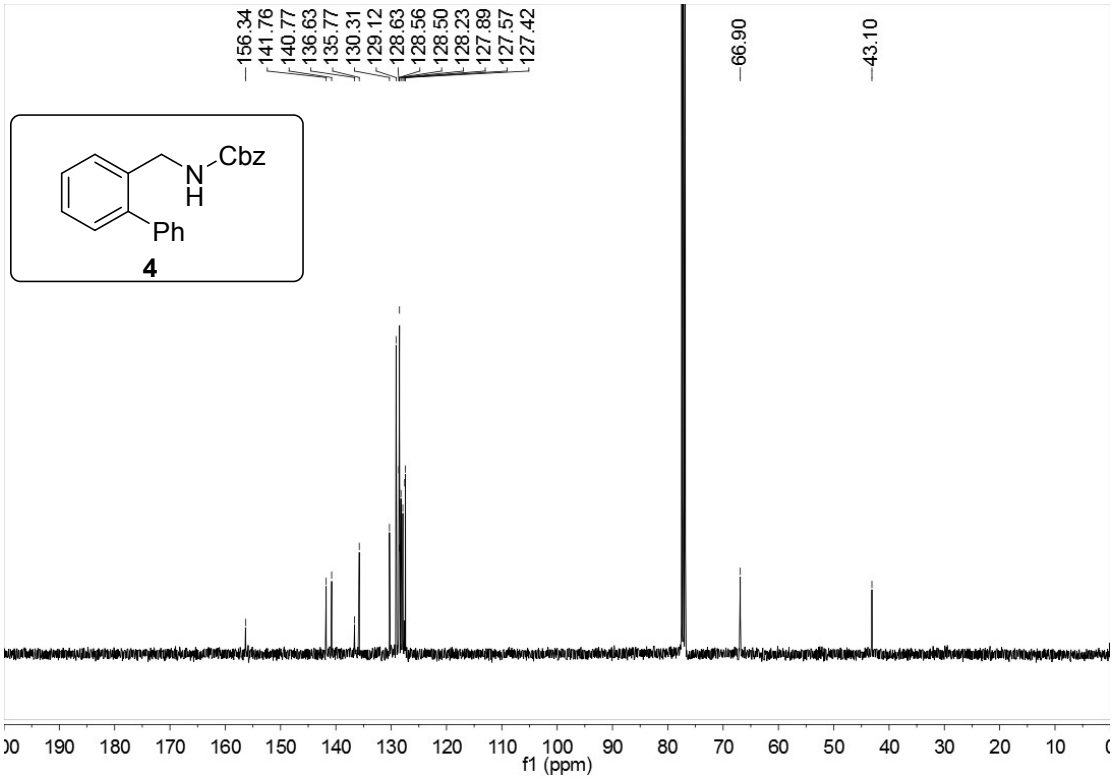
2.06
f1 (ppm)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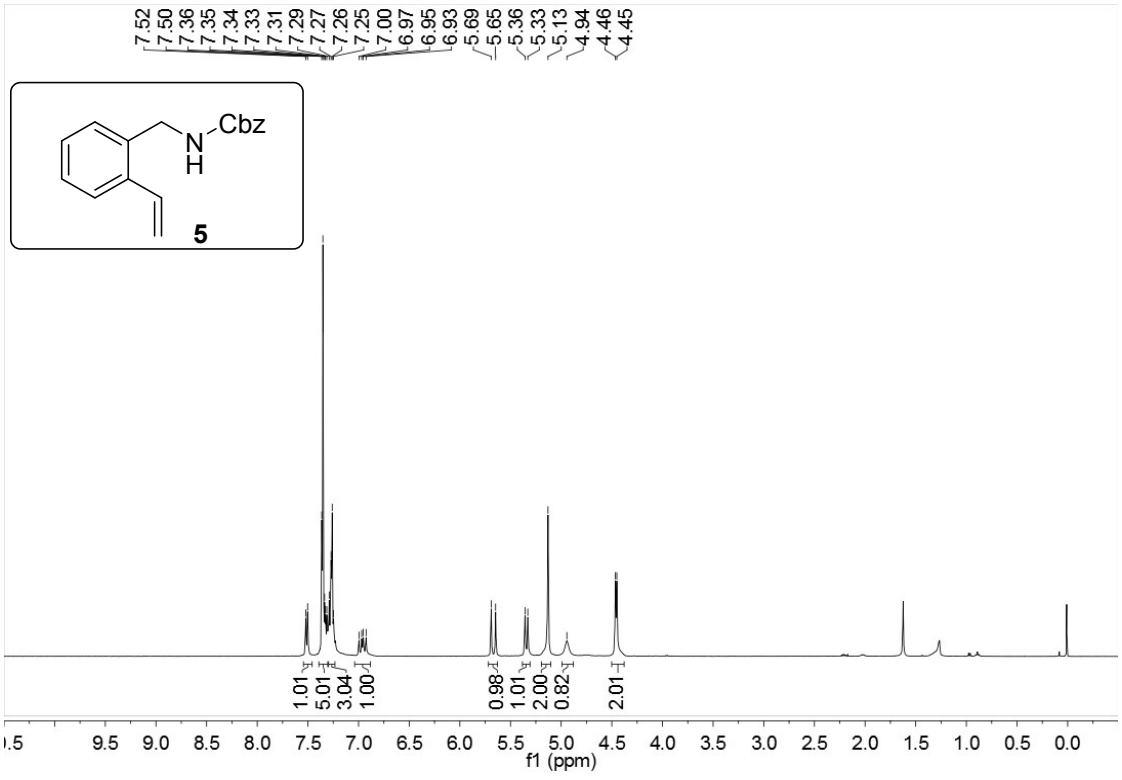
Cbz
N
H
Ph
4
f1 (ppm)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6.95
6.93
5.69
5.65
5.36
5.33
5.13
4.94
4.46
4.45
Cbz
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1.00
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1.01
2.00
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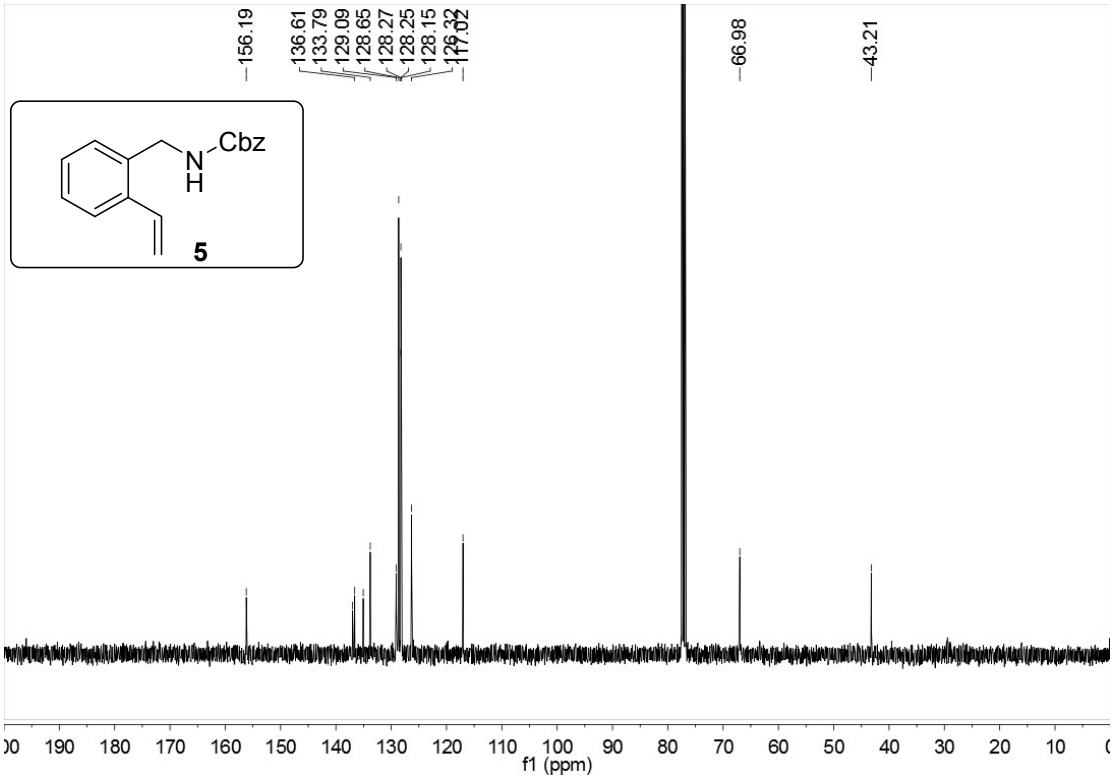
2.01
f1 (ppm)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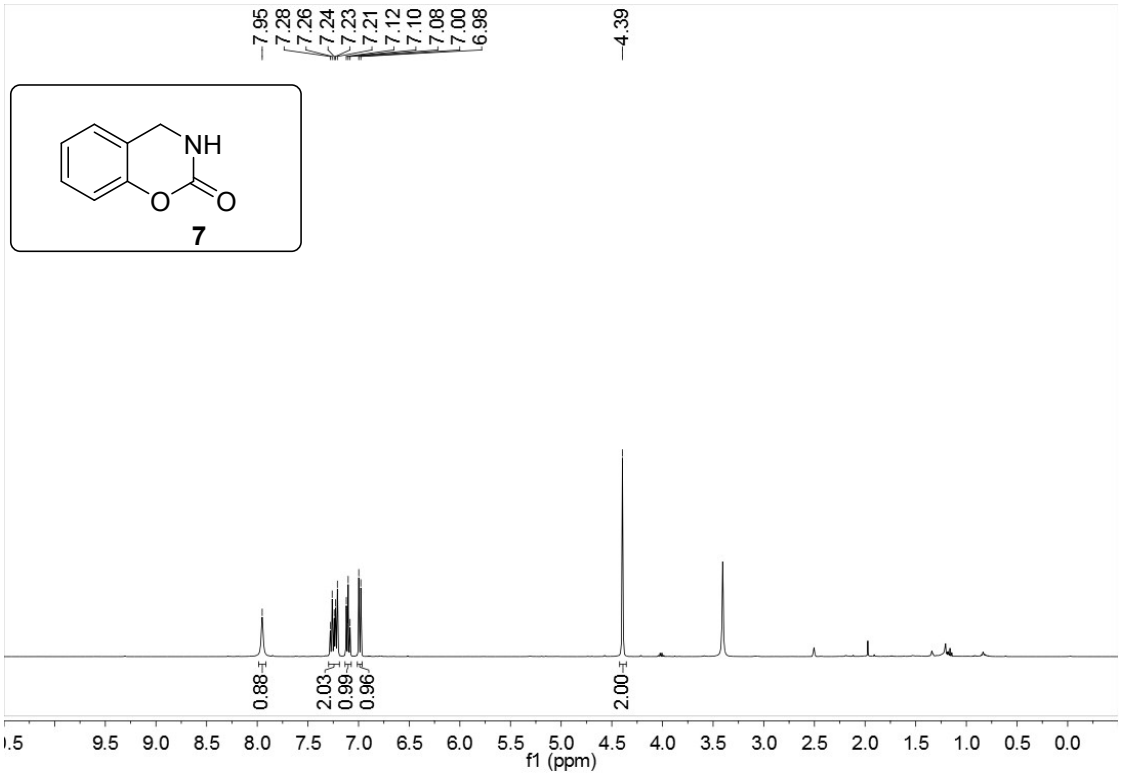
Cbz
5
f1 (ppm)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7.24
7.23
7.21
7.12
7.10
7.08
7.00
6.98
4.39
NH
O
O
7
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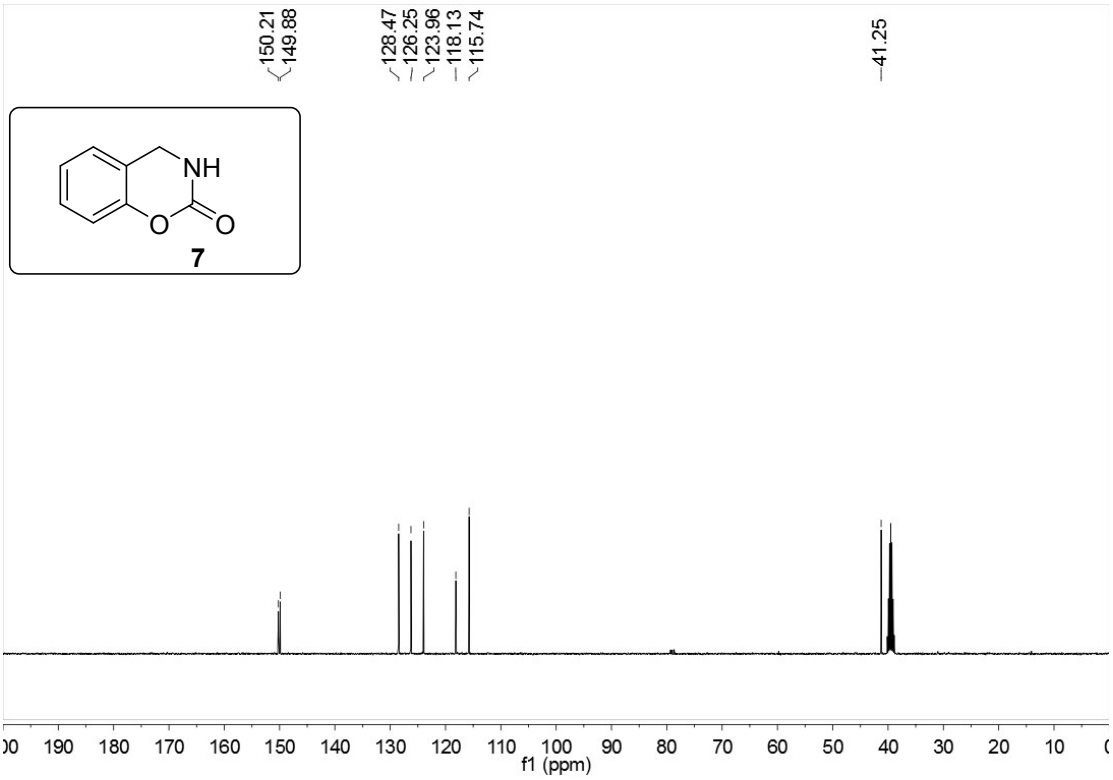
2.03
0.99
0.96
2.00
f1 (ppm)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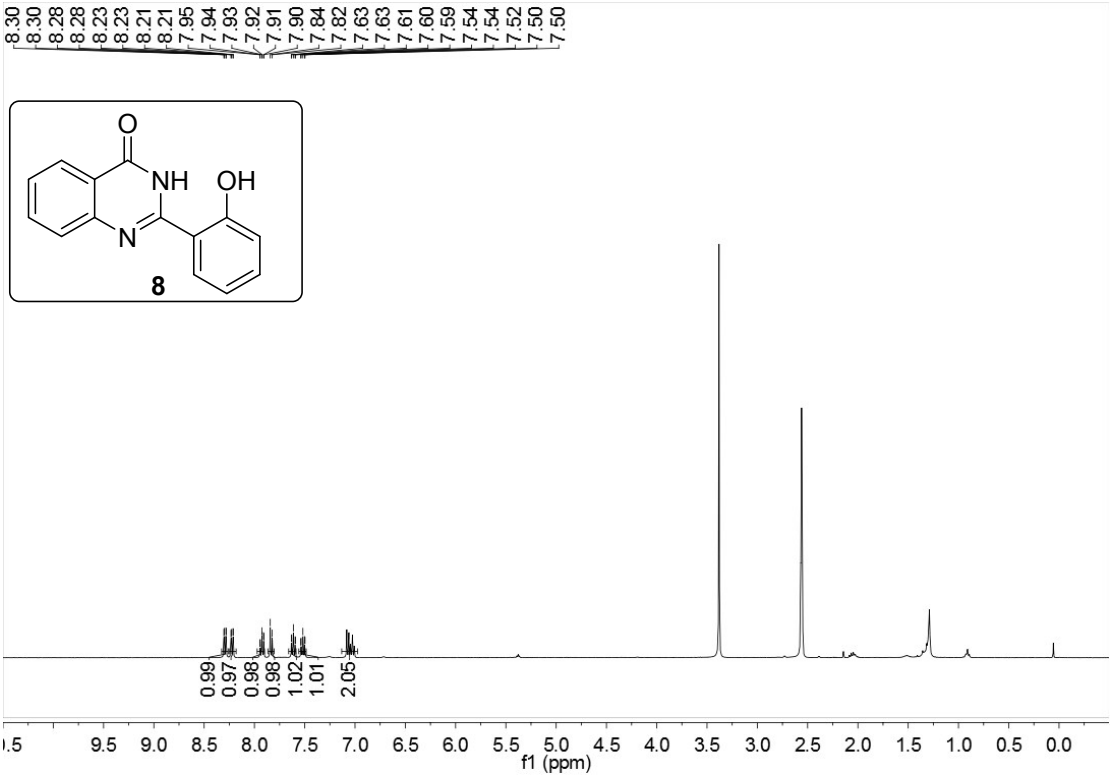
41.25
NH
O
O
7
f1 (ppm)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8.23
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7.92
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7.90
7.84
7.82
7.63
7.63
7.61
7.60
7.59
7.54
7.54
7.52
7.50
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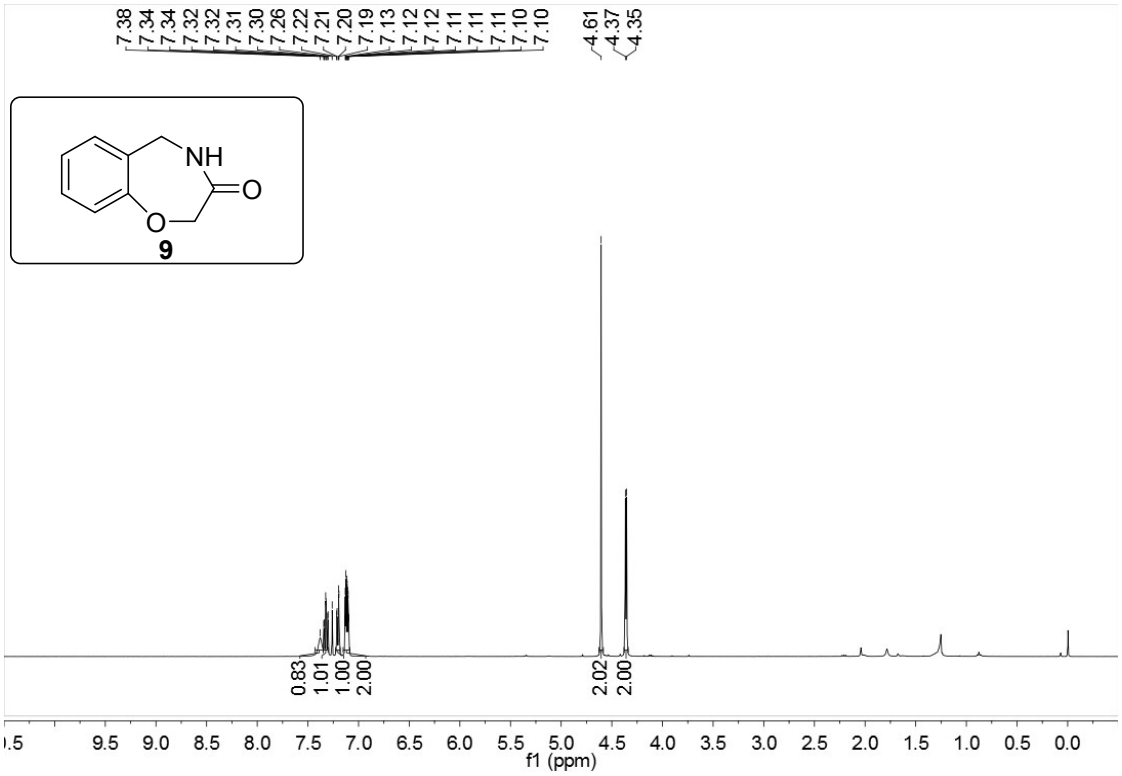
O
NH
OH
N
8
0.99
0.97
0.98
0.98
1.02
1.01
2.05
f1 (ppm)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7.13
7.12
7.12
7.11
7.11
7.11
7.10
7.10
4.61
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O
O
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2.00
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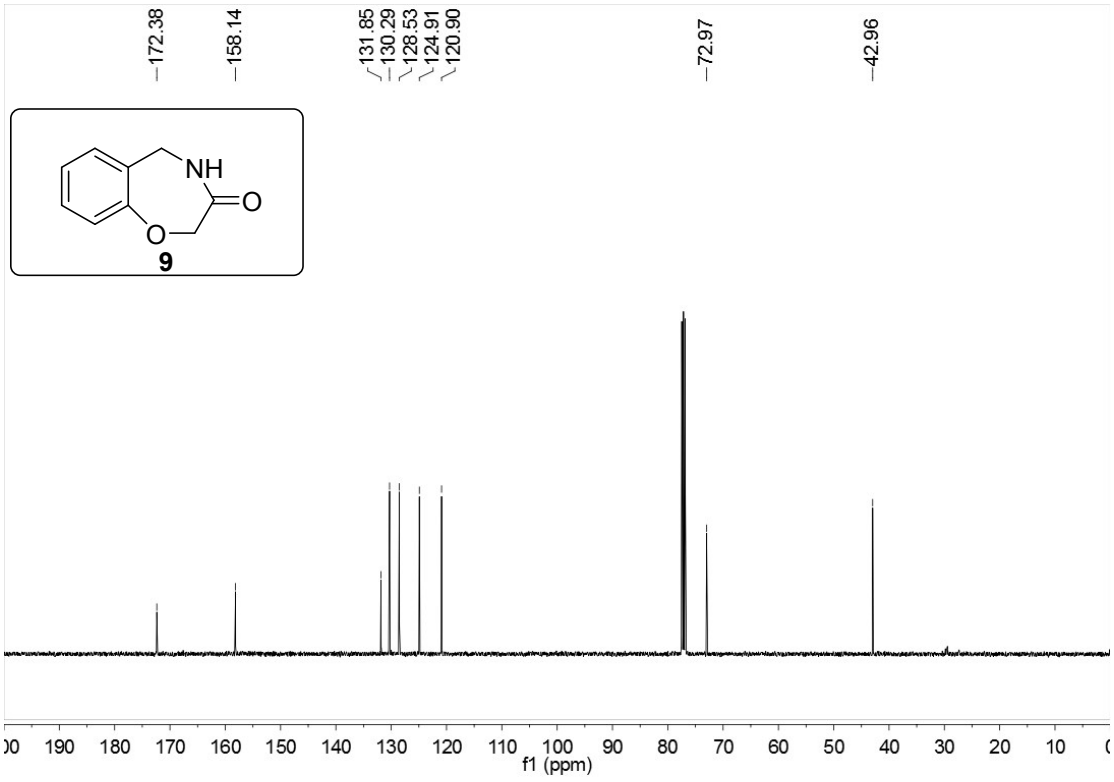
f1 (ppm)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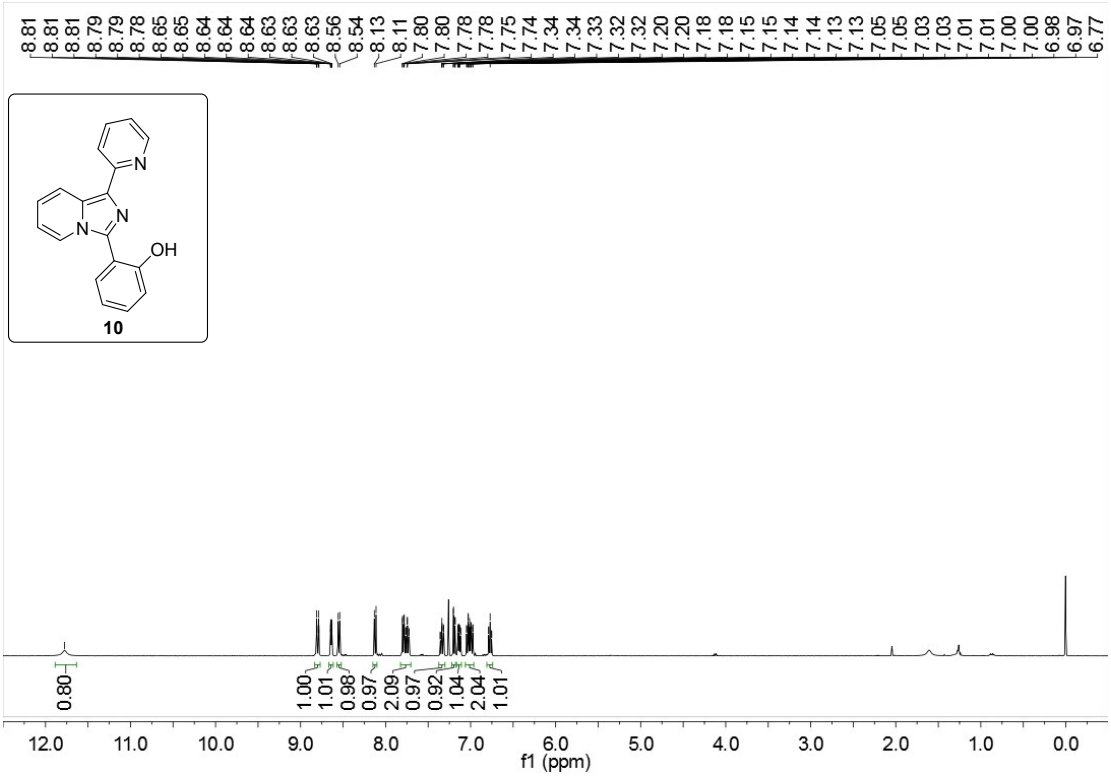
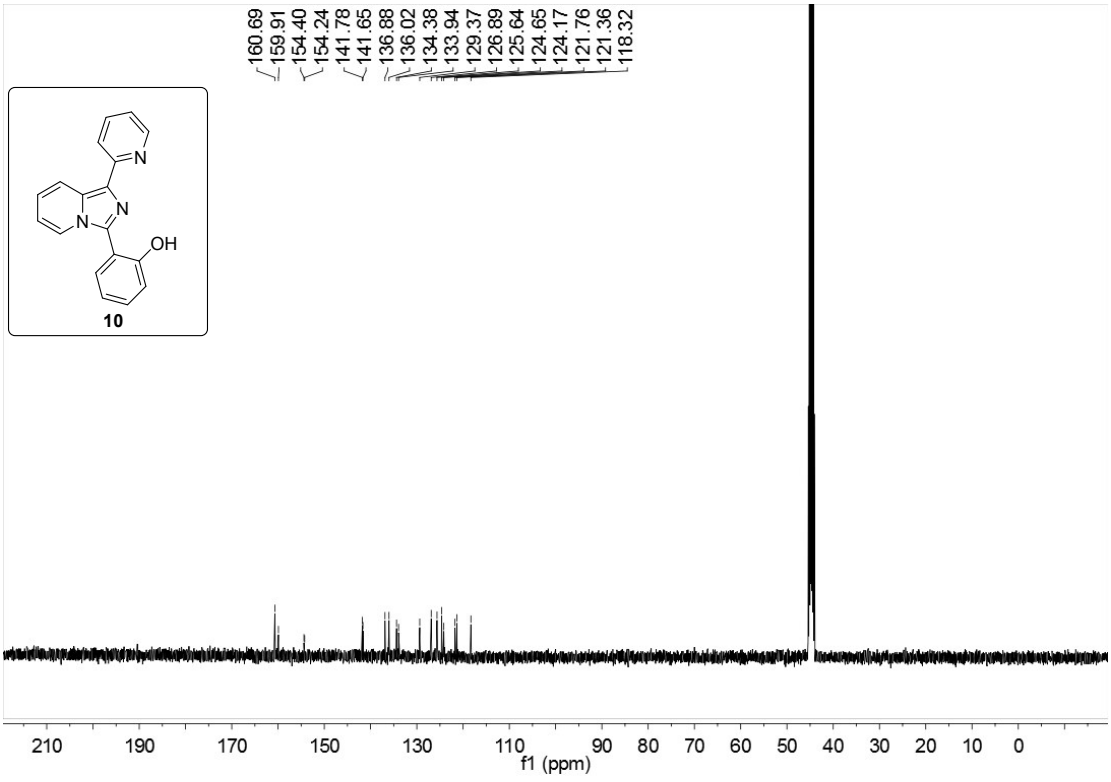
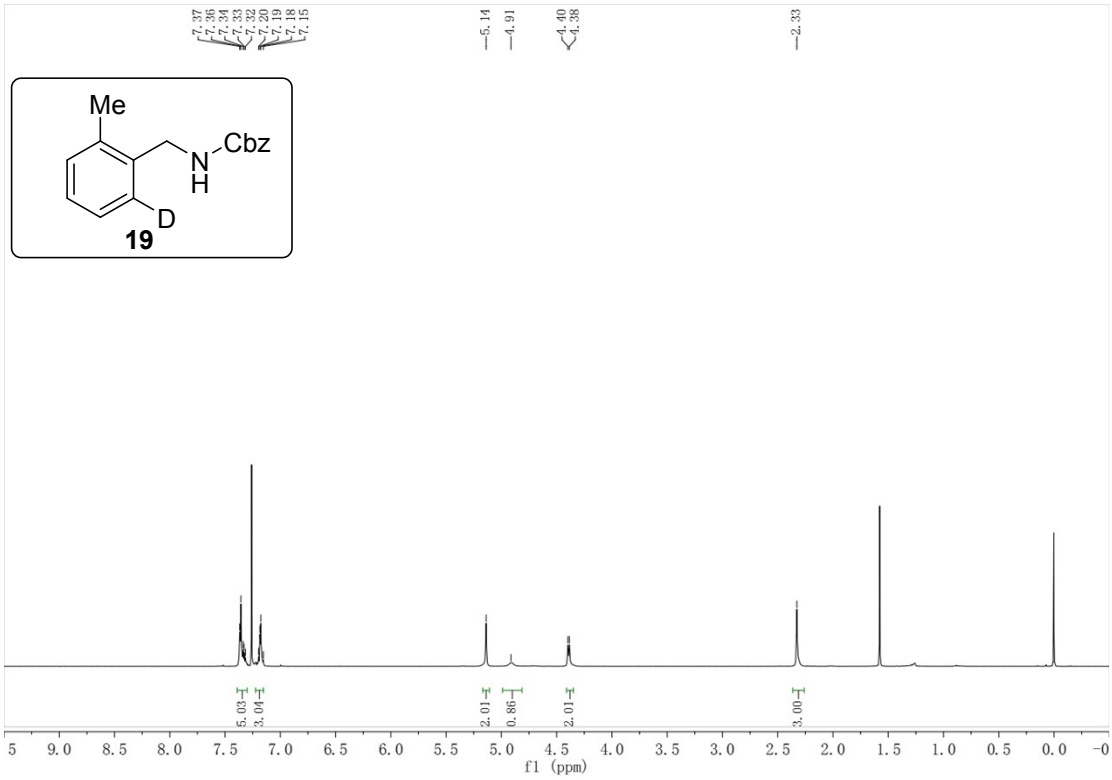
120.90
72.97
42.96
NH
O
O
9
f1 (ppm)


8.81
8.81
8.81
8.79
8.79
8.78
8.65
8.65
8.64
8.64
8.64
8.63
8.63
8.63
8.56
8.54
8.13
8.11
7.80
7.80
7.78
7.78
7.75
7.74
7.34
7.33
7.32
7.32
7.20
7.20
7.18
7.18
7.15
7.15
7.14
7.14
7.13
7.13
7.05
7.05
7.03
7.03
7.01
7.01
7.00
7.00
6.98
6.97
6.77
N
N
N
OH
10
0.80
1.00
1.01
0.98
0.97
2.09
0.97
0.92
1.04
2.04
1.01
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)


160.69
159.91
154.40
154.24
141.78
141.65
136.88
136.02
134.38
133.94
129.37
126.89
125.64
124.65
124.17
121.76
121.36
118.32
N
N
N
OH
10
210
190
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


7.37
7.36
7.34
7.33
7.32
7.20
7.19
7.18
7.15
5.14
4.91
4.40
4.38
2.33
Me
Cbz
N
H
D
19
5.03
3.04
2.01
0.86
2.01
3.00
f1 (ppm)