Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

DMF/NaOH/H_2O: a metal-free system for efficient and chemoselective reduction of α-ketoamides

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Contents

General information:

^{1}H and ^{13}C NMR spectra were collected on 400 MHz NMR spectrometers (Bruker AVANCE) in $CDCl_3$ with TMS as internal standard. High-resolution mass spectra (HRMS) were acquired with an LTQ-Orbitrap XL mass spectrometer (Thermo Scientific) equipped with an Electrospray ionization (ESI) source. Infrared spectra were obtained on an FTIR spectrometer. Unless otherwise noted, all solvents and commercially available reagents were purchased from commercial sources and used directly. Anhydrous DMF and DMSO were handled with CaH_2, distillated under vacuum and preserved in seal bottle containing activated 4A molecular sieve. Toluene and 1,4-dioxane were distilled from Na. α-Ketoamide substrates were prepared according to the known procedure[1].

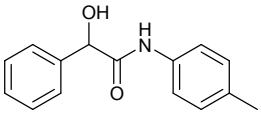
General procedure for chemoselective reduction of α-ketoamides.

An oven-dried reaction vessel was charged with NaOH (0.36 mmol), H_2O (1.2 mmol) and DMF (1mL) under argon. The combined mixture was heated to 120°C for 1 h. After being cooled to room temperature, α-ketoamide (**1**, 0.3 mmol) was added and the reaction mixture was then reacted at 120°C under Ar for 18 h. The solvent was removed under vacuum, water was added, and the aqueous phase was extracted with CH_2Cl_2 (3×5 mL). The combined organic layer was dried over Na_2SO_4 and concentrated to dryness under vacuum. The crude product was then purified by flash chromatography to afford product **2**.

General procedure for the reduction reaction with HCOONa as hydrogen source.

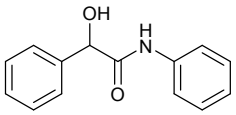
An oven-dried reaction vessel was charged with aldehyde or α-ketoamide (0.3 mmol), HCOONa (0.36 mmol), H_2O (1.2 mmol) and DMSO (1 mL) under argon. The resultant mixture was stirred at 120 ℃ for 12 h. Then, the mixture was cooled to the room temperature, and water (5 mL) was added. The obtained mixture was extracted with CH_2Cl_2 (3 × 5 mL) and dried over Na_2SO_4. After concentration under reduced pressure, the residue was then purified by flash chromatography to afford the desired product.

The spectroscopic data of compounds



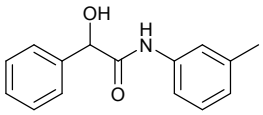
2aa

White solid[2], yield: 98%, mp: 171.4-172.6 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 9.88 (s, 1H), 7.58-7.66 (m, 2H), 7.58-7.51 (m, 2H), 7.35-7.42 (m, 2H), 7.27-7.35 (m, 1H), 7.12 (d, J = 8.4 Hz, 2H), 6.46 (d, J = 4.7 Hz, 1H), 5.12 (d, J = 4.7 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.4, 141.4, 136.5, 132.9, 129.4, 128.5, 128.0, 127.0, 120.1, 74.4, 20.9; IR (KBr): 3324, 3161, 2920, 2898, 2851, 1652, 1597, 1544, 1514, 1456, 1407, 1062, 820, 702 cm^{-1}.



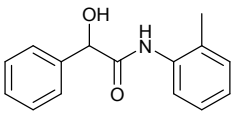
2ab

White solid[2], yield: 97%, mp: 149.6-151.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (br s, 1H), 7.50-7.57 (m, 2H), 7.50-7.45 (m, 2H),7.44-7.35 (m, 3H), 7.35-7.28 (m, 2H), 7.17-7.08 (m, 1H), 5.18 (d, J = 2.7 Hz, 1H), 3.46 (d, J = 3.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.9, 139.0, 137.0, 129.1, 129.0, 129.0, 126.9, 124.7, 119.8, 74.7; IR (KBr): 3302, 3227, 1659, 1602, 1556, 1498, 1447, 1067, 754, 692 cm^{-1}.



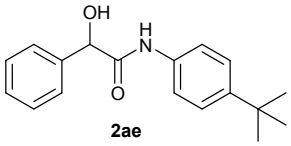
2ac

White solid[3], yield: 96%, mp: 170.7-172.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (br s, 1H), 7.52-7.45 (m, 2H), 7.45-7.33 (m, 4H), 7.30 (d, J = 8.2 Hz, 1H), 7.20 (t, J = 7.8 Hz, 1H), 6.94 (d, J = 7.5 Hz, 1H), 5.19 (s, 1H), 3.39 (br s, 1H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 139.1, 139.0, 137.0, 129.1, 129.0, 128.9, 126.9, 125.5, 120.4, 116.8, 74.7, 21.5; IR (KBr): 3308, 3208, 2921, 2885, 1656, 1613, 1567, 1494, 1455, 1304, 1070, 779, 691 cm^{-1}.



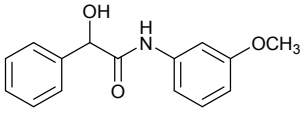
2ad

White solid[4], yield: 98%, mp: 80.7-82.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (br s, 1H), 7.87 (d, *J* = 8.0Hz, 1H), 7.51-7.44 (m, 2H), 7.43-7.32 (m, 3H), 7.23-7.12 (m, 2H), 7.02-7.10 (m, 1H), 5.17 (s, 1H), 3.80 (s, 1H), 2.13 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 139.1, 134.9, 130.4, 129.0, 128.9, 128.4, 126.8, 126.8, 125.2, 122.0, 74.7, 17.4 IR (KBr): 3312, 3234, 3025, 2924, 2849, 1655, 1603, 1519, 1491, 1447, 1064, 754, 693 cm^{-1}.



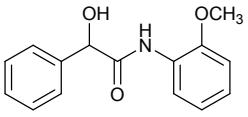
2ae

White solid (CAS: 1285041-79-3), yield: 96%, mp: 129.1-130.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): 8.01 (br s, 1H), 7.51-7.44 (m, 3H), 7.44-7.35 (m, 4H), 7.35-7.30 (m, 2H), 5.18 (d, *J* = 3.4 Hz, 1H), 3.42 (d, *J* = 3.4 Hz, 1H), 1.29 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 147.8, 139.1, 134.4, 129.0, 128.9, 126.9, 125.9, 119.5, 74.7, 34.4, 31.3; IR (KBr): 3313, 3206, 2962, 2904, 2867, 1655, 1597, 1541, 1496, 1456, 1410, 1061, 836, 698 cm^{-1}. HRMS (ESI/TOF) Calcd for $C_{18}H_{21}NO_2Na$ [$(M+Na)^+$]: 306.147~~0~~065, found 306.1474.



2af

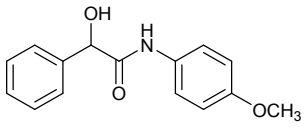
White solid[4], yield: 96%, mp: 153.6-154.9 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (br s, 1H), 7.52-7.45 (m, 2H), 7.44-7.34 (m, 3H), 7.33 (t, *J* = 2.3 Hz, 1H), 7.21 (t, *J* = 8.1 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.67 (d, *J* = 8.1 Hz, 1H), 5.19 (s, 1H), 3.79 (s, 3H), 3.37 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 160.2, 138.9, 138.3, 129.7, 129.1, 129.0, 126.9, 111.8, 110.7, 105.3, 74.7, 55.3; IR (KBr): 3329, 3273, 3069, 2958, 2834, 1659, 1609, 1562, 1498, 1452, 1266, 1062, 766 cm^{-1}.



2ag

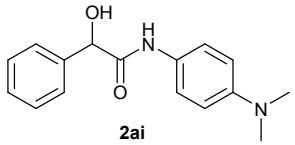
White solid[5], yield: 98%, mp: 120.5-122.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.73 (br s, 1H),

8.31 (dd, J = 8.0, 1.7 Hz, 1H), 7.52-7.43 (m, 2H), 7.42-7.29 (m, 3H), 7.04 (td, J = 7.8, 1.6 Hz, 1H), 6.93 (td, J = 7.8, 1.4 Hz, 1H), 6.85 (dd, J = 8.2, 1.4 Hz, 1H), 5.16 (s, 1H), 3.83 (s, 3H), 3.79 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 148.2, 139.2, 128.9, 128.7, 126.9, 126.8, 124.3, 121.1, 119.7, 110.1, 74.8, 55.8; IR (KBr): 3366, 3230, 3033, 2893, 2840, 1667, 1596, 1530, 1250, 1063, 755, 697 cm^{-1}.



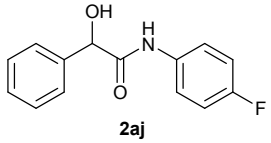
2ah

White solid[2], yield: 98%, mp: 152.3-154.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (br s, 1H), 7.50-7.45 (m, 2H), 7.32-7.44 (m, 5H), 6.90-6.78 (m, 2H), 5.16 (d, J = 2.6 Hz, 1H), 3.78 (s, 3H), 3.52 (d, J = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.7, 156.7, 139.1, 130.2, 129.0, 128.9, 126.9, 121.6, 114.2, 74.6, 55.5; IR (KBr): 3294, 3240, 3064, 2949, 2837, 1647, 1601, 1553, 1513, 1454, 1252, 1067, 841 cm^{-1}.



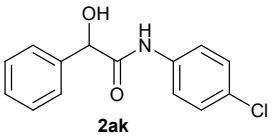
2ai

White solid, yield: 96%, mp: 173.3-174.2 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (br s, 1H), 7.51-7.43 (m, 2H), 7.43-7.30 (m, 5H), 6.69 (d, J = 8.5 Hz, 2H), 5.14 (s, 1H), 3.65 (br s, 1H), 2.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.6, 139.3, 128.9, 128.8, 127.0, 121.5, 116.4, 113.1, 96.1, 74.5, 41.0; IR (KBr): 3309, 3218, 2797, 1640, 1594, 1547, 1520, 1454, 1326, 1068, 821, 754 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{16}H_{17}N_2O_2$ [(M-H)$^-$]: 269.129~~06~~, found 269.1290.



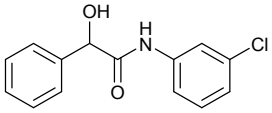
2aj

White solid[6], yield: 95%, mp: 161.8-163.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (br s, 1H), 7.45-7.55 (m, 4H), 7.44-7.33 (m, 3H), 7.01 (t, J = 8.6 Hz, 2H), 5.20 (d, J = 3.1 Hz, 1H), 3.33 (d, J = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 74.7, 115.7 (d, $^2J_{CF}$ = 22.0 Hz), 121.6 (d, $^3J_{CF}$ = 8.0 Hz), 126.8, 129.0, 129.04, 133.1, 138.9, 159.6 (d, $^1J_{CF}$ = 243.0 Hz), 169.8; IR (KBr): 3304, 3247, 1656, 1560, 1513, 1454, 1411, 1308, 1237, 1064, 834, 773, 505 cm^{-1}.



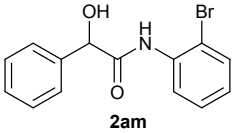
2ak

White solid[2], yield: 96%, mp: 162.7-165.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.14 (s, 1H), 7.85-7.74 (m, 2H), 7.60-7.49 (m, 2H), 7.44-7.28 (m, 5H), 6.53 (d, J = 4.5 Hz, 1H), 5.14 (d, J = 4.5 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.8, 141.1, 138.0, 128.9, 128.6, 128.1, 127.6, 127.0, 121.8, 74.5; IR (KBr): 3317, 3158, 2896, 1652, 1596, 1544, 1493, 1456, 1402, 1092, 1060, 829, 759, 700 cm^{-1}.



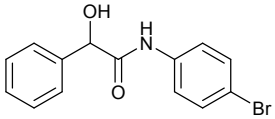
2al

White solid[7], yield: 94%, mp: 178.0-179.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.18 (s, 1H), 7.95 (s, 1H), 7.69 (d, J = 8.2 Hz, 1H), 7.55 (d, J = 7.3 Hz, 2H), 7.45-7.28 (m, 4H), 7.15 (d, J = 7.8 Hz, 1H), 6.55 (d, J = 4.5 Hz, 1H), 5.15 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.1, 141.0, 140.5, 133.4, 130.8, 128.6, 128.2, 127.0, 123.7, 119.6, 118.6, 74.5; IR (KBr): 3295, 3208, 3060, 2882, 1659, 1599, 1556, 1483, 1455, 1404, 1100, 1069, 878, 775, 761, 697 cm^{-1}.



2am

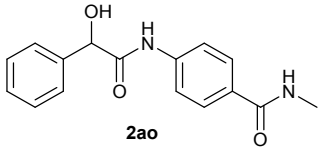
White solid[7], yield: 82%, mp: 85.0-87.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (s, 1H), 7.40-7.56 (m, 4H), 7.21-7.40 (m, 4H), 7.11 (t, J = 7.4 Hz, 1H), 5.10 (d, J = 3.3 Hz, 1H), 3.80 (d, J = 3.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 138.7, 135.0, 132.3, 129.1, 129.0, 128.4, 126.9, 125.6, 121.5, 113.7, 75.0; IR (KBr): 3355, 3298, 3029, 1675, 1663, 1588, 1578, 1529, 1438, 1407, 1301, 1059, 1024, 751, 695 cm^{-1}.



2an

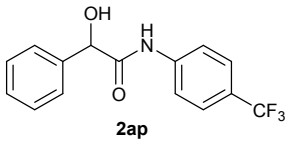
White solid[5], yield: 93%, mp: 168.3-169.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.25 (br s, 1H), 7.55-7.30 (m, 9H), 5.18 (d, J = 3.3 Hz, 1H), 3.34 (d, J = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.8, 138.8, 136.2, 132.0, 129.0, 129.0, 126.8, 121.3, 117.3, 74.8; IR (KBr): 3297,

3231, 2892, 2835, 1659, 1597, 1547, 1490, 1455, 1398, 1068, 849, 752, 699, 498 cm^{-1}.



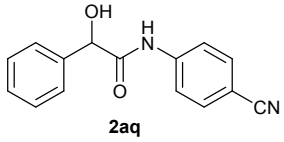
2ao

White solid, yield: 99%, mp: 203.9-205.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.18 (br s, 1H), 8.35 (q, J = 4.6 Hz, 1H), 7.81 (s, 4H, overlap), 7.56 (d, J = 7.4 Hz, 2H), 7.24-7.46 (m, 3H), 6.56 (br s, 1H), 5.16 (br s, 1H), 2.79 (d, J = 4.4 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.0, 166.5, 141.4, 141.1, 129.8, 128.6, 128.2, 128.1, 127.0, 119.4, 74.5, 26.6; IR (KBr): 3377, 3277, 1676, 1628, 1608, 1522, 1454, 1303, 851, 762 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{16}H_{15}N_2O_3$ [(M-H)$^-$]: 283.108~~3~~8, found 283.1082.



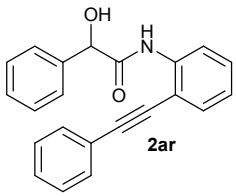
2ap

White solid[2], yield: 86%, mp: 207.3-209.1 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δ 10.32 (s, 1H), 7.95 (d, J = 8.5 Hz, 2H), 7.66 (d, J = 8.6 Hz, 2H), 7.53 (d, J = 7.2 Hz, 2H), 7.25-7.43 (m, 3H), 6.54 (d, J = 4.5 Hz, 1H), 5.15 (d, J = 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.4, 142.6, 141.0, 128.6, 128.2, 127.0, 126.3 (q, $^3J_{CF}$ = 3.5 Hz), 124.8 (q, J = 269.8 Hz), 124.0 (q, $^2J_{CF}$ = 31.8 Hz), 120.1, 74.5; IR (KBr): 3295, 3206, 1665, 1605, 1556, 1455, 1413, 1339, 1115, 1073, 847, 700 cm^{-1}.



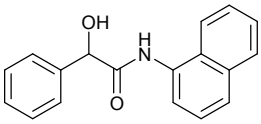
2aq

White solid[2], yield: 60%, mp: 145.1-146.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.65 (s, 1H), 7.68 (d, J = 8.7 Hz, 2H), 7.58 (d, J = 8.7 Hz, 2H), 7.43-7.49 (m, 2H), 7.42-7.32 (m, 3H), 5.21 (d, J = 3.1 Hz, 1H), 3.49 (d, J = 3.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 172.6, 143.3, 140.8, 133.6, 128.6, 128.2, 127.0, 120.2, 119.5, 105.8, 74.6; IR (KBr): 3293, 2228, 1668, 1646, 1597, 1543, 1454, 843 cm^{-1}.



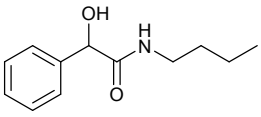
2ar

White solid, yield: 80%, mp: 134.7-135.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.30 (br s, 1H), 8.40 (d, *J* = 8.3 Hz, 1H), 7.52-7.60 (m, 2H), 7.51-7.42 (m, 3H), 7.34-7.42 (m, 3H), 7.34-7.24 (m, 4H), 7.08 (t, *J* = 7.6 Hz, 1H), 5.18 (d, J = 2.6 Hz, 1H), 3.86 (d, J = 2.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.3, 138.9, 138.2, 131.6, 131.6, 129.7, 128.9, 128.9, 128.8, 128.5, 126.9, 123.9, 122.4, 119.1, 112.6, 96.7, 84.0. 75.0; IR (KBr): 3331, 3219, 1674, 1661, 1579, 1533, 1491, 1452, 1309, 1063, 703, 753 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{22}H_{16}NO_2$ [(M-H)$^-$]: 326.1181~~7~~, found 326.1181.



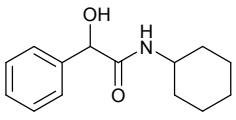
2as

White solid[2], yield: 75%, mp: 136.9-139.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.74 (br s, 1H), 7.95 (d, *J* = 7.4 Hz, 1H), 7.89-7.79 (m, 1H), 7.61-7.71 (m, 2H), 7.55-7.33 (m, 8H), 5.24 (d, *J* = 2.8 Hz, 1H), 3.96 (d, *J* = 3.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.7, 139.2, 134.0, 131.4, 129.0, 128.9, 128.8, 126.9, 126.7, 126.4, 126.0, 125.9, 125.7, 120.2, 120.0, 74.9; IR (KBr): 3367, 3258, 3051, 1659, 1595, 1521, 1502, 1449, 1278, 1060, 795, 772, 725 cm^{-1}.



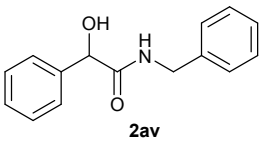
2at

White solid[7], yield: 98%, mp: 59.4-62.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ7.45-7.28 (m, 5H), 6.12 (br s, 1H), 4.99 (s, 1H), 3.75 (br s, 1H), 3.18-3.32 (m, 2H), 1.49-1.40 (m, 2H), 1.32-1.23 (m, 2H), 0.88 (t, J = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 139.6, 128.9, 128.6, 126.9, 74.1, 39.4, 31.5, 19.9, 13.7; IR (KBr): 3289, 2958, 2930, 2862, 1654, 1544, 1497, 1450, 750, 697 cm^{-1}.



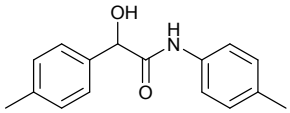
2au

White solid[4], yield: 98%, mp: 95.1-96.7 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42-7.28 (m, 5H), 6.10 (br s, 1H), 4.94 (d, *J* = 3.0 Hz, 1H), 3.98-3.79 (m, 1H), 3.79-3.62 (m, 1H), 1.78-1.92 (m, 2H), 1.71-1.52 (m, 3H), 1.43-1.21 (m, 2H), 1.21-0.98 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.2, 139.7, 128.8, 128.6, 126.9, 74.0, 48.4, 32.9, 32.8, 25.4, 24.7, 24.7; IR (KBr): 3341, 3261, 3064, 3030, 2936, 2852, 1640, 1601, 1544, 1492, 1452, 702, 738, 780 cm^{-1}.



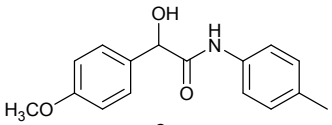
2av

White solid[8], yield: 93%, mp: 99.1-100.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44-7.23 (m, 8H), 7.21-7.14 (m, 2H), 6.50 (br s, 1H), 5.06 (s, 1H), 4.53-4.31 (m, 2H), 3.64 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.0, 139.4, 137.7, 128.9, 128.8, 128.7, 127.6, 127.6, 126.9, 74.2, 43.5; IR (KBr): 3277, 3228, 3062, 3030, 2873, 1620, 1536, 1492, 1454, 1090, 1064, 698 cm^{-1}.



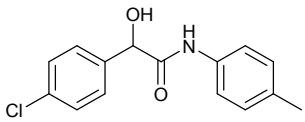
2aw

White solid[9], yield: 93%, mp: 146.3-148.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 (br s, 1H), 7.39 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.1 Hz, 2H), 7.20 (d, *J* = 7.9 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 5.12 (d, *J* = 1.7 Hz, 1H), 3.43 (d, *J* = 2.5 Hz, 1H), 2.35 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.0, 138.8, 136.1, 134.6, 134.3, 129.7, 129.5, 126.9, 119.8, 74.5, 21.2, 20.9; IR (KBr): 3390, 2917, 1637, 1594, 1528, 1502, 1409, 1069, 821 cm^{-1}.



2ax

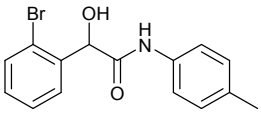
White solid[10], yield: 94%, mp: 135.2-136.6 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.03 (br s, 1H), 7.39 (d, *J* = 7.0 Hz, 2H), 7.37 (d, *J* = 7.2 Hz, 2H), 7.11 (d, *J* = 8.3 Hz, 2H), 6.91 (d, *J* = 8.7 Hz, 2H), 5.11 (d, *J* = 2.5 Hz, 1H), 3.80 (s, 3H), 3.44 (d, J = 3.1 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 170.1, 160.0, 134.6, 134.3, 131.2, 129.5, 128.4, 119.8, 114.4, 74.3, 55.4, 20.9; IR (KBr): 3276, 2996, 2954, 2835, 1651, 1637, 1610, 1595, 1533, 1512, 1449, 1408, 1250, 1059, 1033, 824 cm^{-1}.



2ay

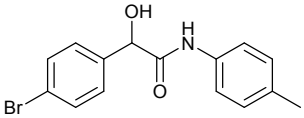
White solid (CAS: 1267573-27-2), yield: 90%, mp: 160.2-162.1 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.17 (br s, 1H), 7.30-7.45 (m, 6H), 7.11 (d, *J* = 8.2 Hz, 2H), 5.12 (s, 1H), 3.67 (br s, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.3, 137.5, 134.7, 134.6, 134.3, 129.6,

129.1, 128.2, 119.8, 73.9, 20.9; IR (KBr): 3288, 3043, 1670, 1636, 1594, 1533, 1490, 1409, 1088, 1070, 820 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{15}H_{14}NO_2NaCl$ [$(M+Na)^+$]: 298.06~~11~~05, found 298.0614.



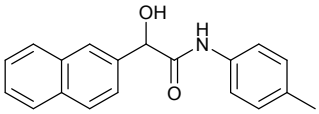
2az

White solid[9], yield: 81%, mp: 150.3-152.4 °C; ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (br s, 1H), 7.60 (dd, *J* = 8.0, 0.9 Hz, 1H), 7.49 (dd, *J* = 7.8, 1.6 Hz, 1H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.38-7.31 (m, 1H), 7.21 (td, *J* = 7.9, 1.7 Hz, 1H), 7.12 (d, *J* = 8.2 Hz, 2H), 5.63 (d, *J* = 4.4 Hz, 1H), 4.07 (d, *J* = 4.6 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.2, 138.7, 134.6, 134.4, 133.1, 130.3, 129.6, 128.9, 128.4, 122.9, 119.9, 72.7, 20.9; IR (KBr): 3346, 3143, 1655, 1595, 1537, 1406, 1075, 1023, 808, 764 cm^{-1}.



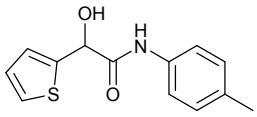
2ba

White solid, mp: 162.9-163.8 °C, yield: 88%; ^1H NMR (400 MHz, DMSO-d_6): δ 9.89 (s, 1H), 7.65-7.55 (m, 4H), 7.50 (d, *J* = 8.4 Hz, 2H), 7.13 (d, *J* = 8.2 Hz, 2H), 6.55 (d, *J* = 4.8 Hz, 1H), 5.12 (d, *J* = 4.8 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 170.9, 140.8, 136.4, 133.02, 131.4, 129.5, 129.2, 121.2, 120.2, 73.7, 20.9; IR (KBr): 3292, 3040, 2904, 1636, 1593, 1530, 1487, 1405, 1070, 820, 512 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{15}H_{13}NO_2Br$ [$(M-H)^-$]: 318.013~~0~~5, found 318.0131.



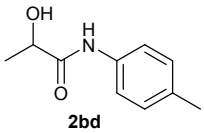
2bb

White solid, mp: 209.2-209.9 °C, yield: 90%; ^1H NMR (400 MHz, DMSO-d_6): δ 9.89 (br s, 1H), 8.00 (s, 1H), 7.93-7.85 (m, 3H), 7.65 (d, *J* = 7.6 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 7.44-7.53 (m, 2H), 7.07 (d, *J* = 8.3 Hz, 2H), 6.55 (br s, 1H), 5.25 (s, 1H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, DMSO-d_6): δ 171.3, 138.9, 136.5, 133.1, 133.0, 132.9, 129.5, 128.3, 128.1, 128.0, 126.7, 126.4, 125.8, 125.2, 120.2, 74.6, 20.9; IR (KBr): 3275, 2919, 2851, 1638, 1594, 1530, 1408, 1073, 823, 814, 745 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{19}H_{16}NO_2$ [$(M-H)^-$]: 290.118~~1~~7, found 290.1182.



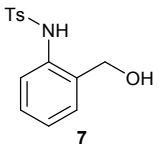
2bc

White solid, yield: 76%, mp: 169.9-171.5 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (br s, 1H), 7.41 (d, *J* = 8.4 Hz, 2H), 7.33 (dd, *J* = 5.1, 1.3 Hz, 1H), 7.20 (dt, *J* = 3.5, 1.0 Hz, 1H), 7.13 (d, *J* = 8.2 Hz, 2H), 7.02 (dd, *J* = 5.1, 3.5 Hz, 1H), 5.46 (d, *J* = 3.7 Hz, 1H), 3.66 (d, *J* = 3.8 Hz, 1H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.6, 141.9, 134.6, 134.3, 129.6, 127.1, 126.5, 126.3, 119.9, 70.6, 20.9; IR (KBr): 3310, 3146, 2921, 2841, 1651, 1598, 1545, 1513, 1433, 1408, 1160, 1059, 819, 717 cm^{-1}; HRMS (ESI/TOF) Calcd for $C_{13}H_{13}NO_2NaS$ [$(M+Na)^+$]: 270.05~~65~~59, found 270.0567.



2bd

Colorless oil (solidified after storage, mp: 93.2-94.5 °C) [6], 35% yield; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.55 (br s, 1H), 7.39 (d, *J* = 8.3 Hz, 2H), 7.10 (d, *J* = 8.3 Hz, 2H), 4.28 (q, *J* = 6.8 Hz, 1H), 3.94 (br s, 1H), 2.30 (s, 3H), 1.47 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 134.5, 134.3, 129.6, 120.0, 68.7, 21.1, 20.9; IR (KBr): 3298, 3030, 2981, 2928, 1655, 1594, 1541, 1454, 1279, 817 cm^{-1}.



7

White solid[11], 75% yield, mp: 147.9-149.0 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89 (br s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.1 Hz, 1H), 7.30-7.18 (m, 3H), 7.12-7.05 (m, 2H), 4.39 (s, 2H), 2.38 (s, 3H), 2.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ143.8, 136.9, 136.4, 131.7, 129.6, 129.2, 129.0, 127.1, 125.4, 123.4, 63.9, 21.6; IR (KBr): 3440, 3071, 2918, 2876, 2809, 1594, 1458, 1334, 1153, 1032, 762 cm^{-1}.

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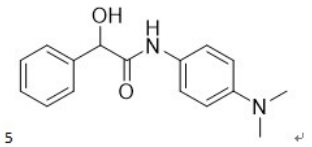
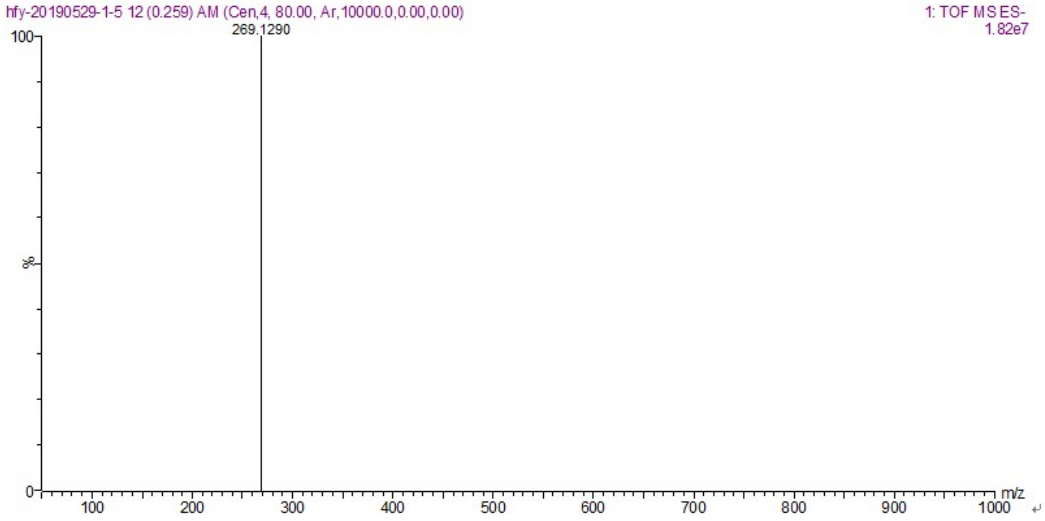
The original HRMS

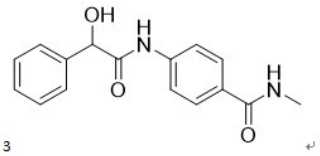


5

Chemical Formula: C16H18N2O2

Exact Mass: 270.14

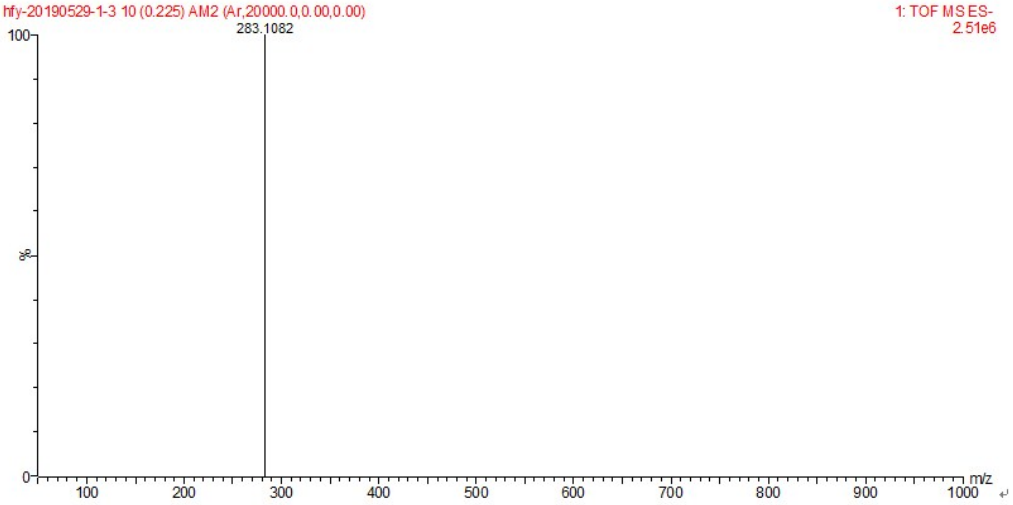


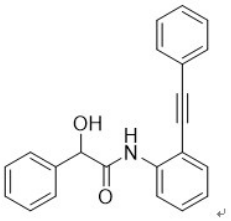


3

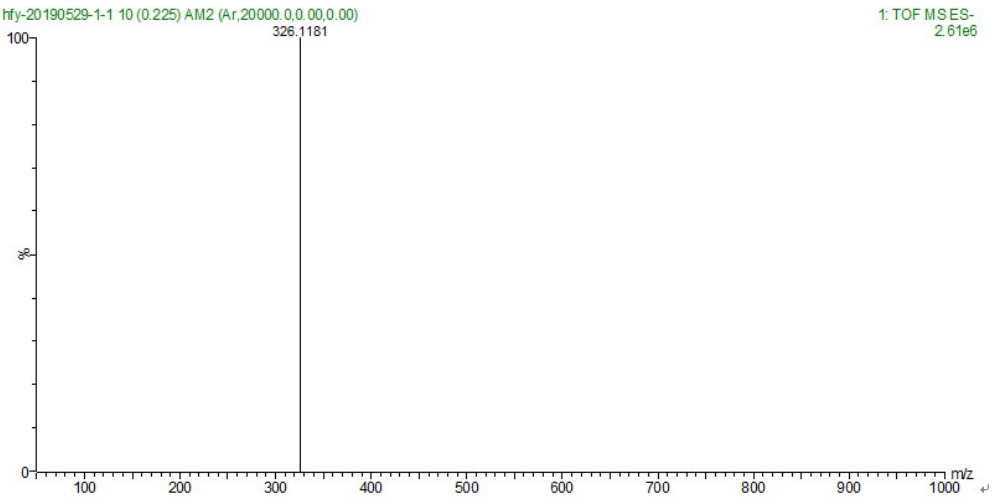
Chemical Formula: C16H16N2O3

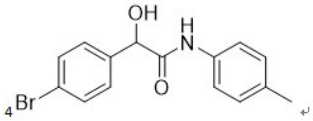
Exact Mass: 284.12





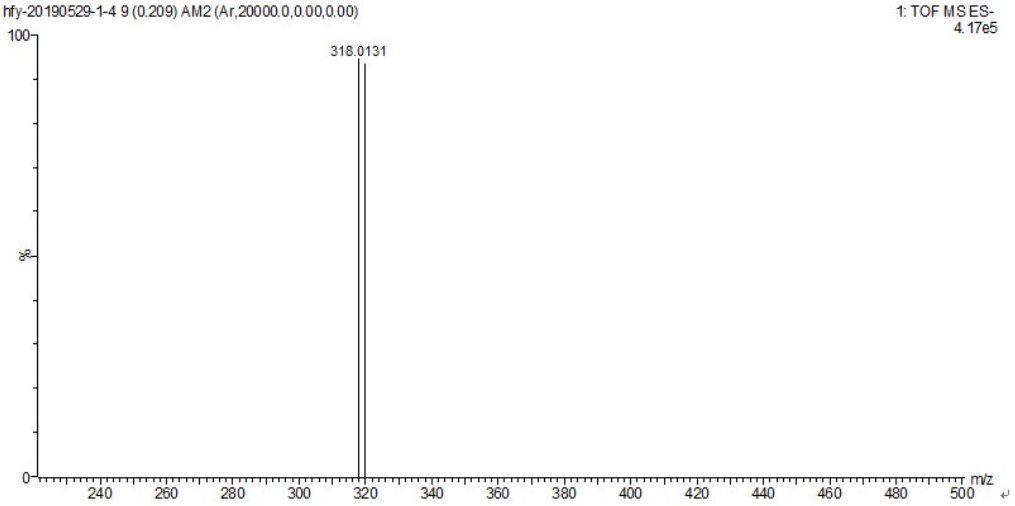
Chemical Formula: C22H17NO2 Exact Mass: 327.13

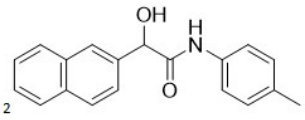




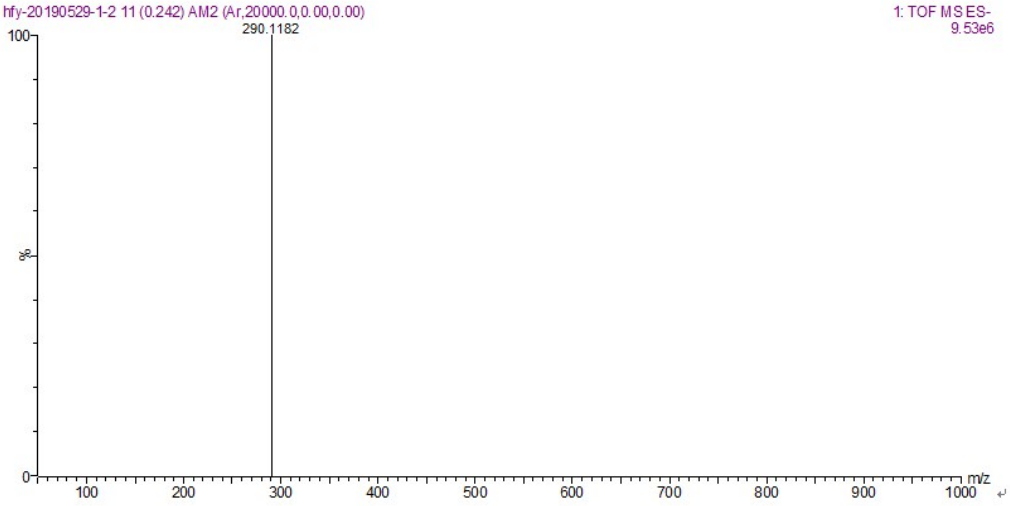
Chemical Formula: C15H14BrNO2

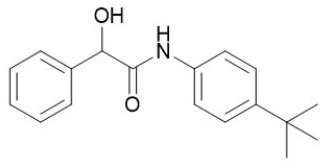
Exact Mass: 319.02



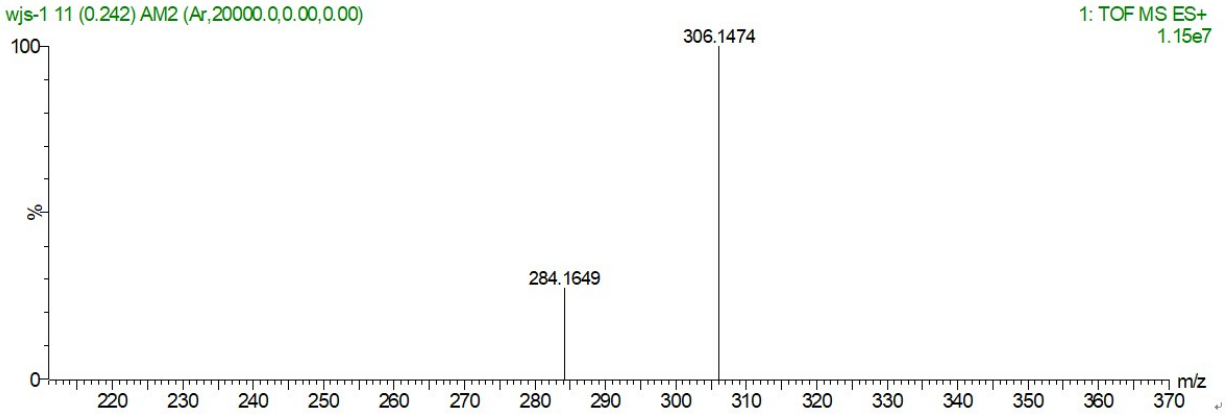


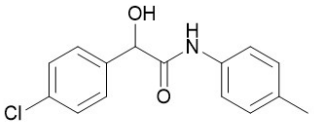
Chemical Formula: C19H17NO2 Exact Mass: 291.13



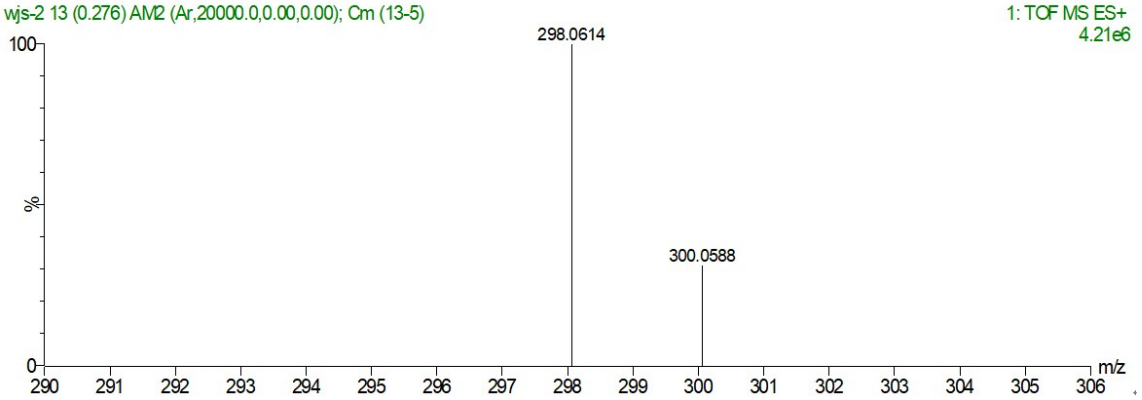


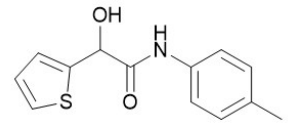
Chemical Formula: $C_{18}H_{21}NO_2$
Exact Mass: 283.16



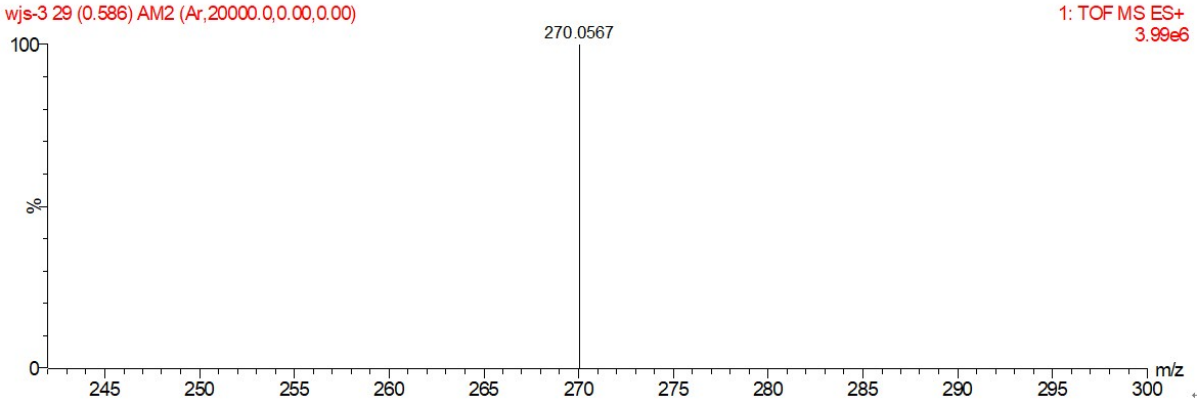


Chemical Formula: $C_{15}H_{14}ClNO_2$
Exact Mass: 275.07



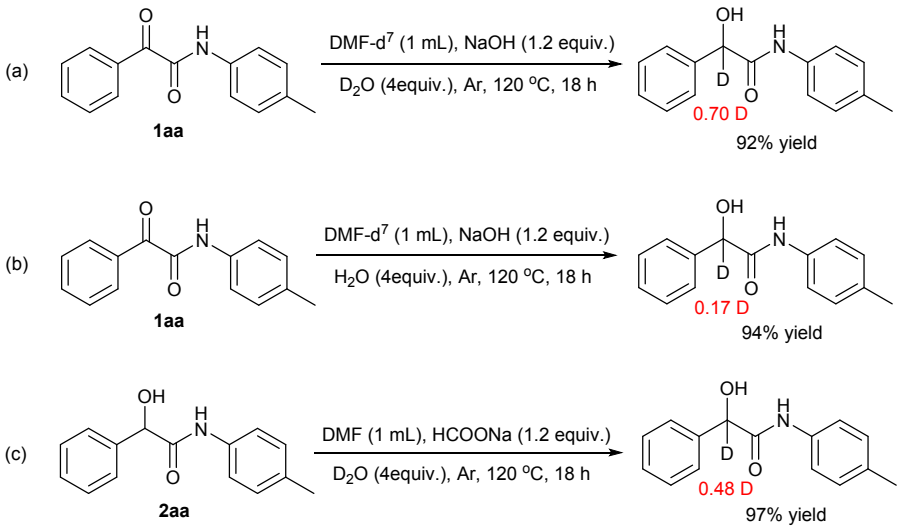


Chemical Formula: $C_{13}H_{13}NO_2S$
Exact Mass: 247.07

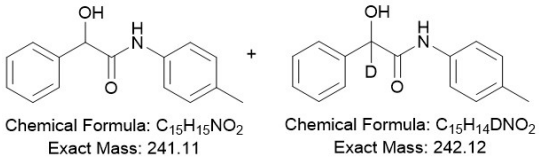


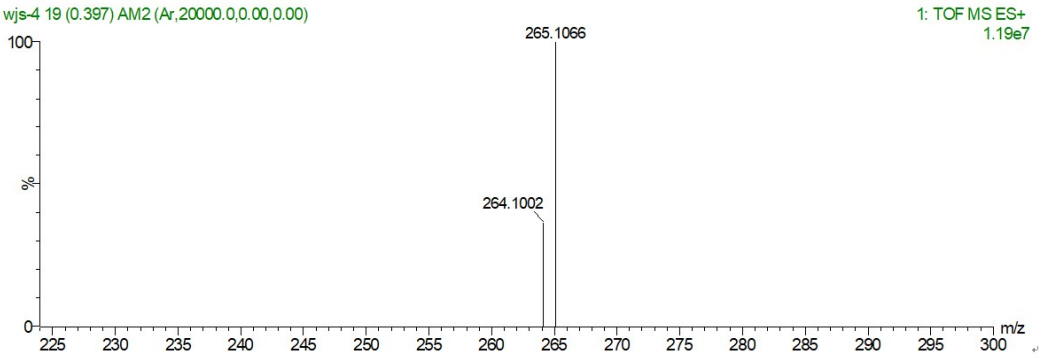
Deuterium labelling experiments

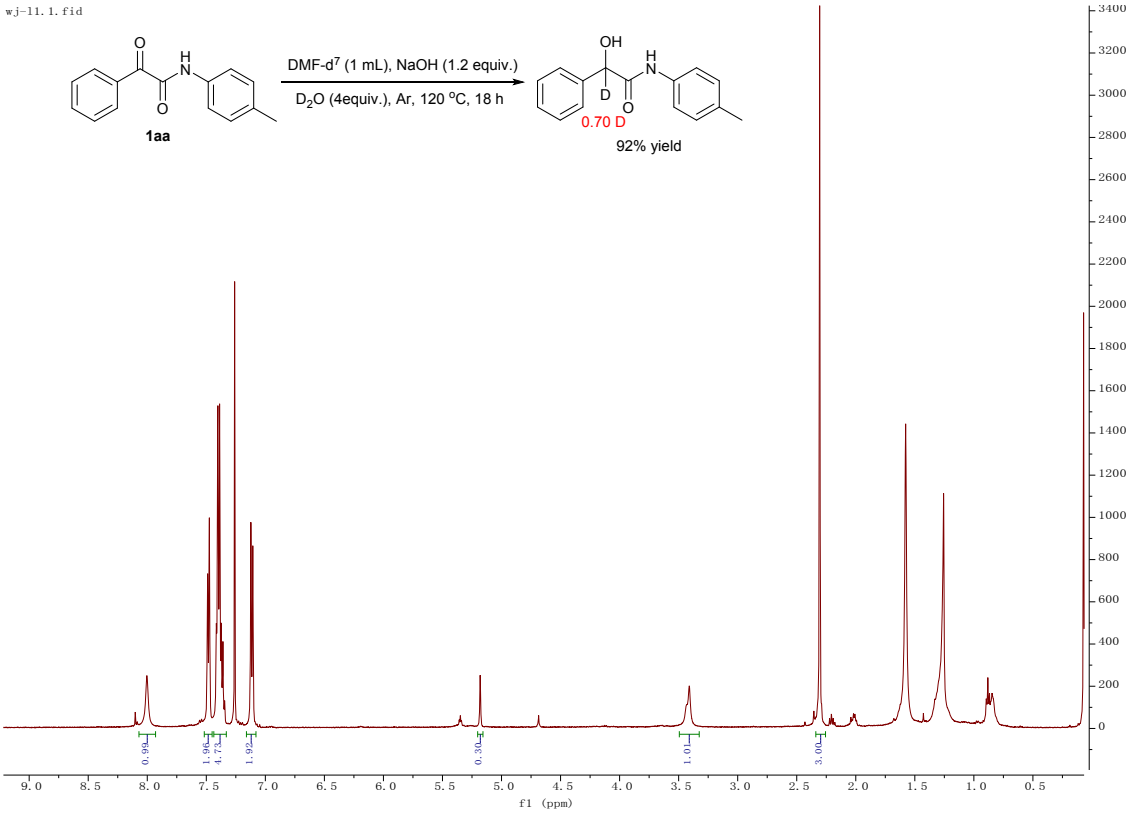
In order to gain more information on the reaction mechanism, several deuterium labelling experiments were carried out to support the proposed mechanism in Scheme 4. First, replacing the DMF and H_2O by DMF-d^7 (99.5% D) and D_2O (99.9% D), the product contained 0.70 D at α position (Scheme S1a). Second, replacing the DMF by DMF-d^7, only 0.17 D at α position of the product was observed (Scheme S1b). The low deuteration ratio can be explained by the acidity of α-hydrogen of **2aa** which facilitate the proton exchange with H_2O under basic condition. Indeed, when **2aa** was treated with D_2O in the presence of HCOONa in DMF at 120 °C, the deuterated product (0.48 D) was isolated (Scheme S1c).

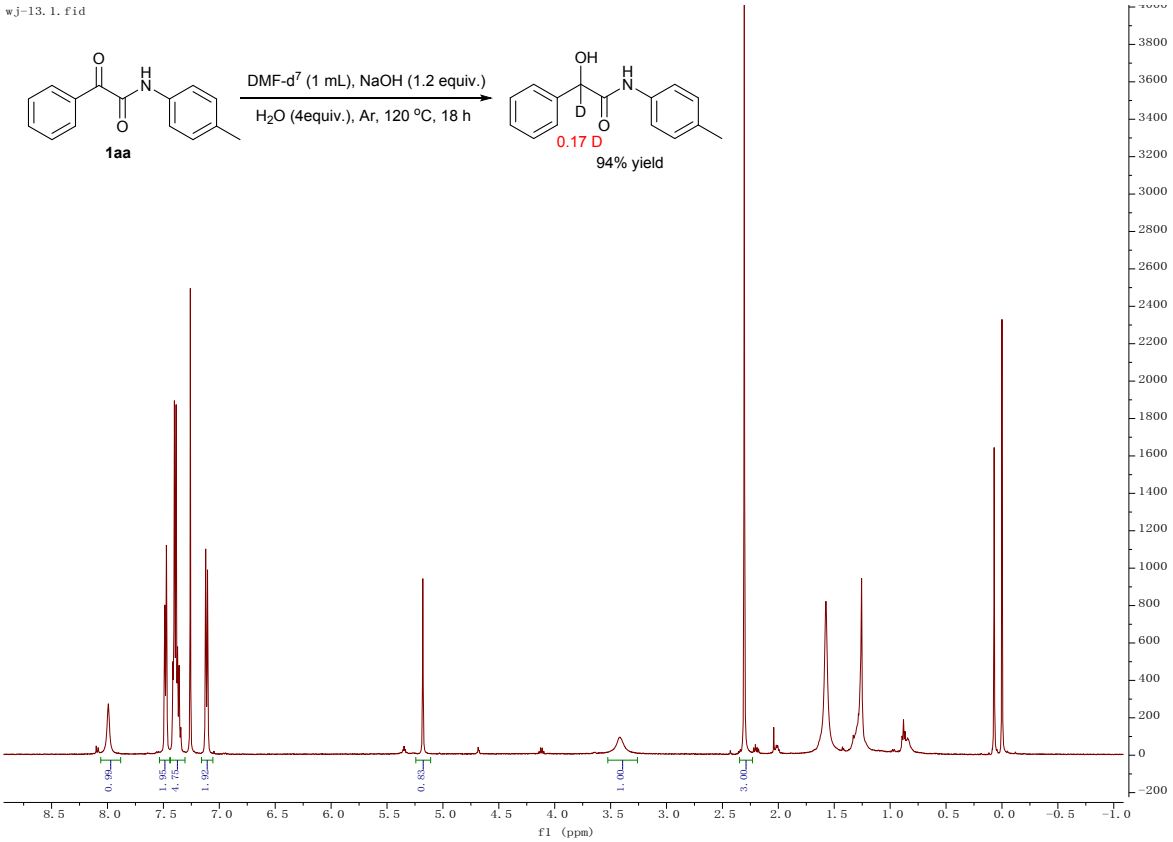

(a)
DMF-d7 (1 mL), NaOH (1.2 equiv.)
D2O (4equiv.), Ar, 120 °C, 18 h
1aa
0.70 D
92% yield
(b)
DMF-d7 (1 mL), NaOH (1.2 equiv.)
H2O (4equiv.), Ar, 120 °C, 18 h
1aa
0.17 D
94% yield
(c)
DMF (1 mL), HCOONa (1.2 equiv.)
D2O (4equiv.), Ar, 120 °C, 18 h
2aa
0.48 D
97% yield

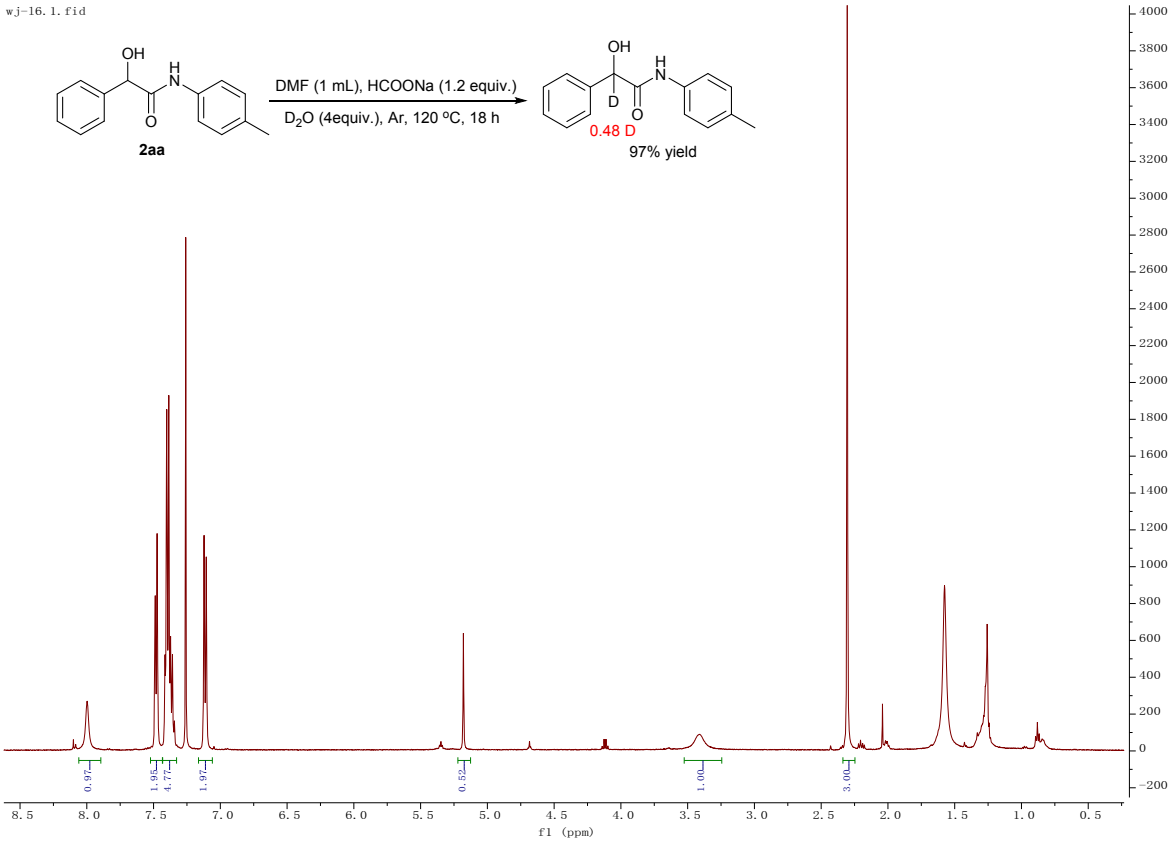
Scheme S1


Chemical Formula: C15H15NO2
Exact Mass: 241.11
Chemical Formula: C15H14DNO2
Exact Mass: 242.12

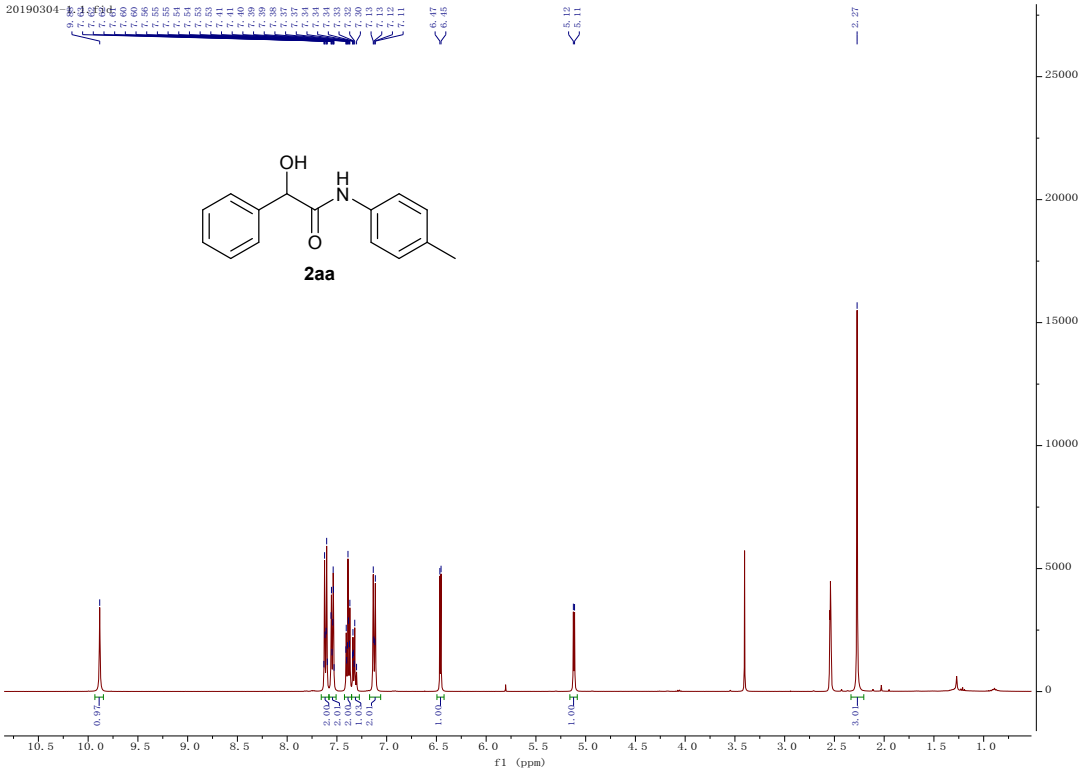

wjs-4 19 (0.397) AM2 (Ar,20000.0,0.00,0.00)
1: TOF MS ES+
1.19e7
265.1066
264.1002
100
%
0
225
230
235
240
245
250
255
260
265
270
275
280
285
290
295
300
m/z

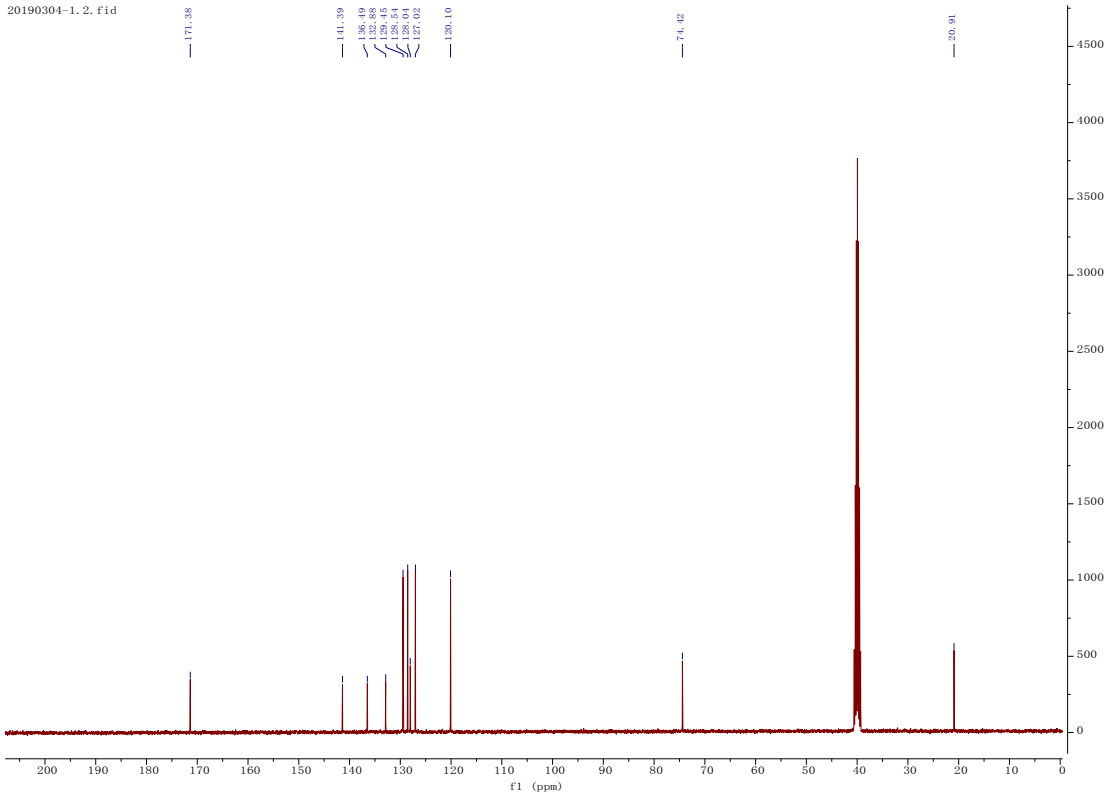

wj-11.1.fid
1aa
DMF-d7 (1 mL), NaOH (1.2 equiv.)
D2O (4equiv.), Ar, 120 °C, 18 h
0.70 D
92% yield
f1 (ppm)

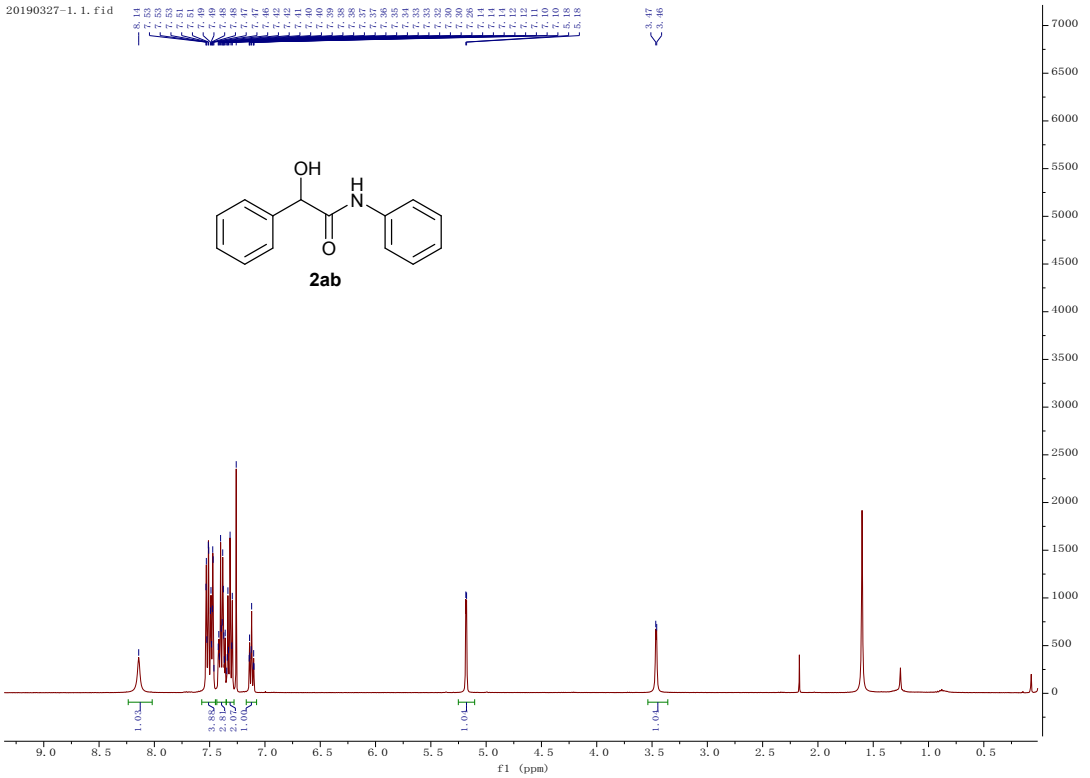

wj-13.1.fid
1aa
DMF-d7 (1 mL), NaOH (1.2 equiv.)
H2O (4equiv.), Ar, 120 °C, 18 h
0.17 D
94% yield
f1 (ppm)

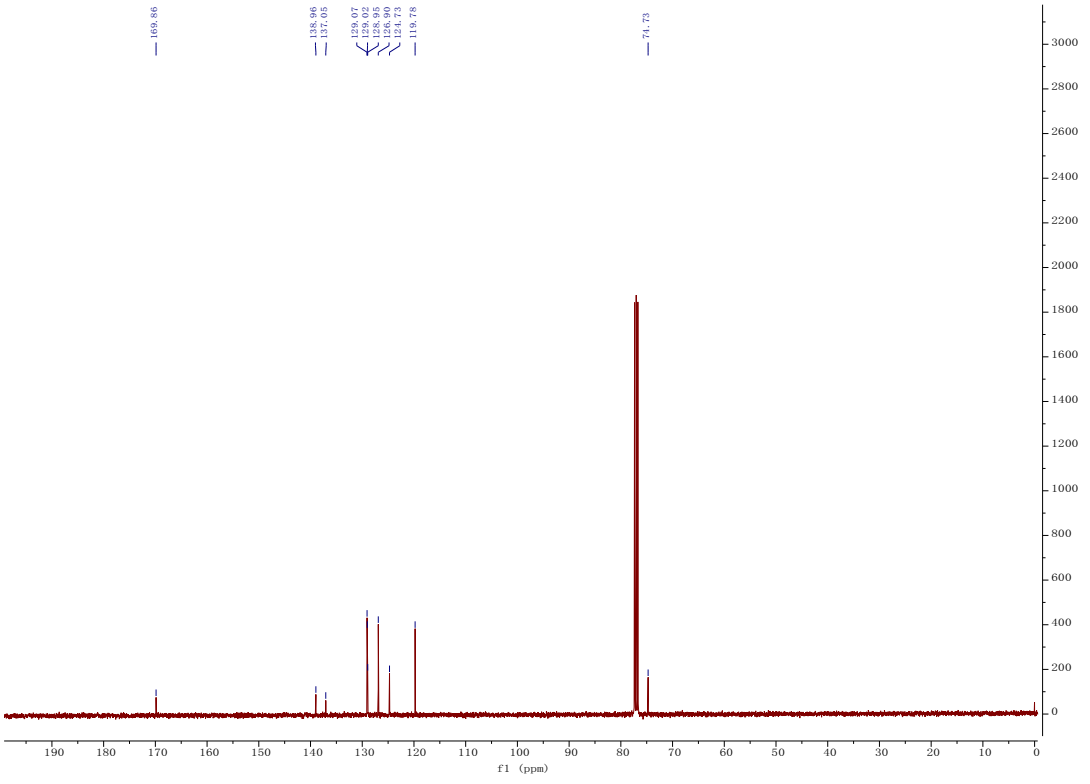

wj-16.1.fid
OH
H
N
O
2aa
DMF (1 mL), HCOONa (1.2 equiv.)
D2O (4equiv.), Ar, 120 °C, 18 h
OH
H
N
D
O
0.48 D
97% yield
0.97
1.96
4.77
1.97
0.52
1.00
3.00
f1 (ppm)

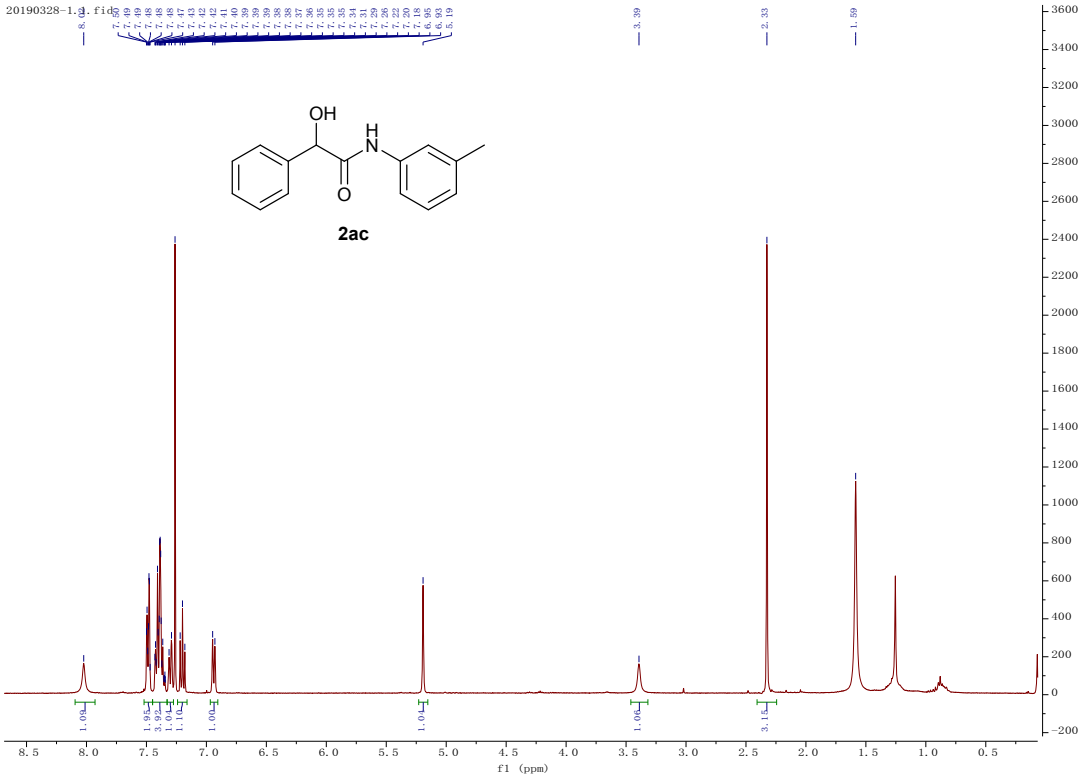
The ^{1}H and ^{13}C NMR spectra of compounds

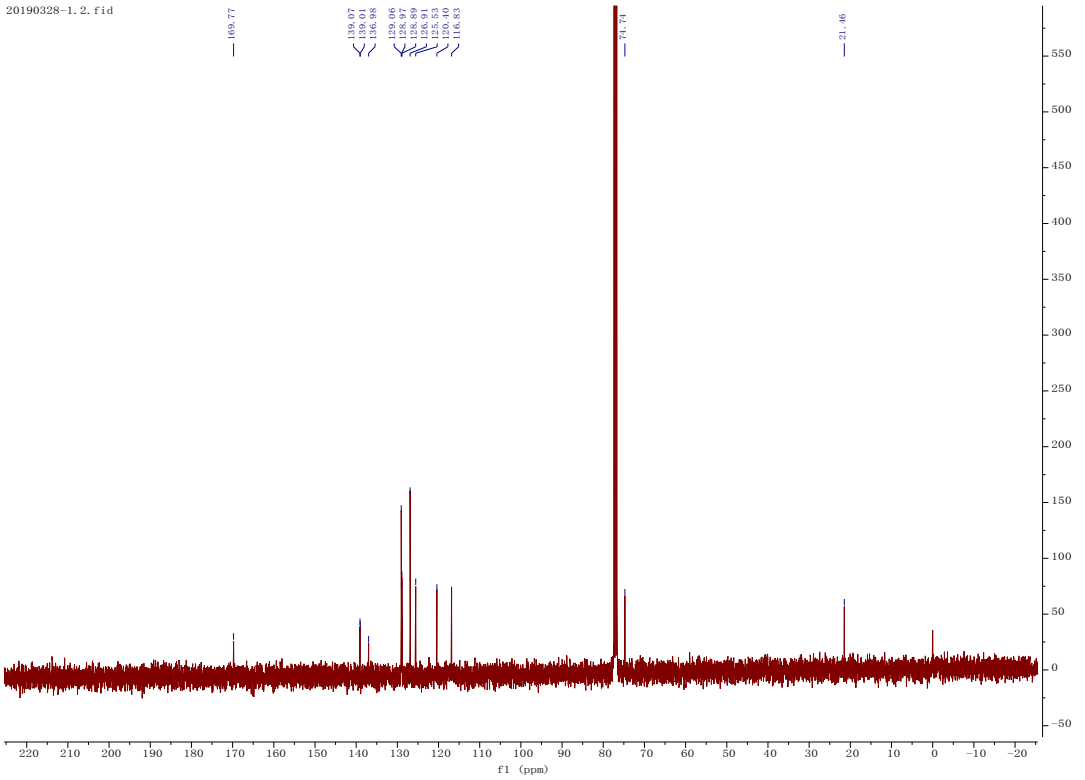


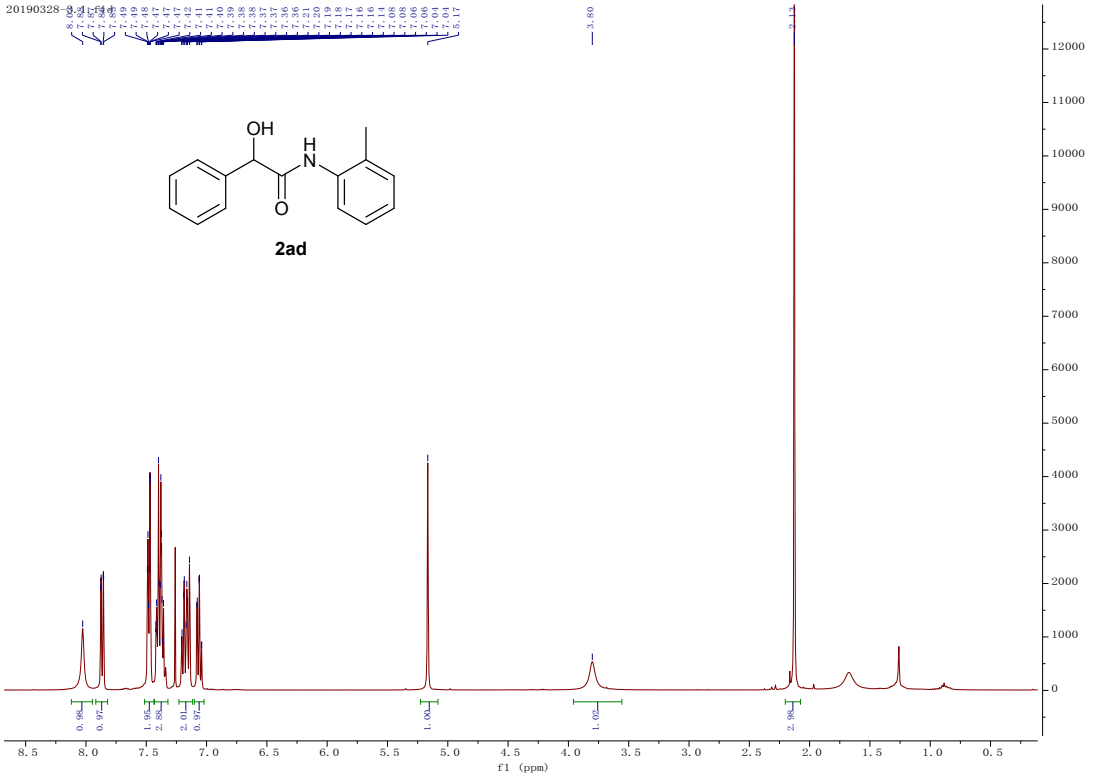


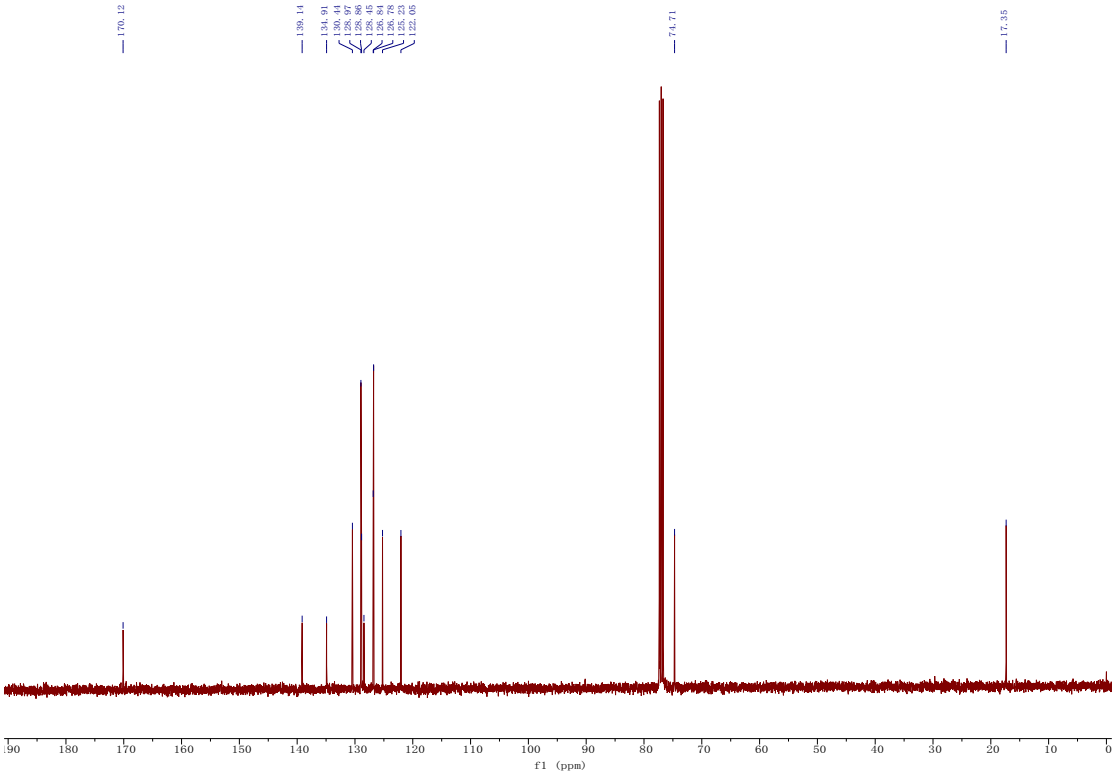

20190327-1.1.fid
OH
H
N
O
2ab
f1 (ppm)

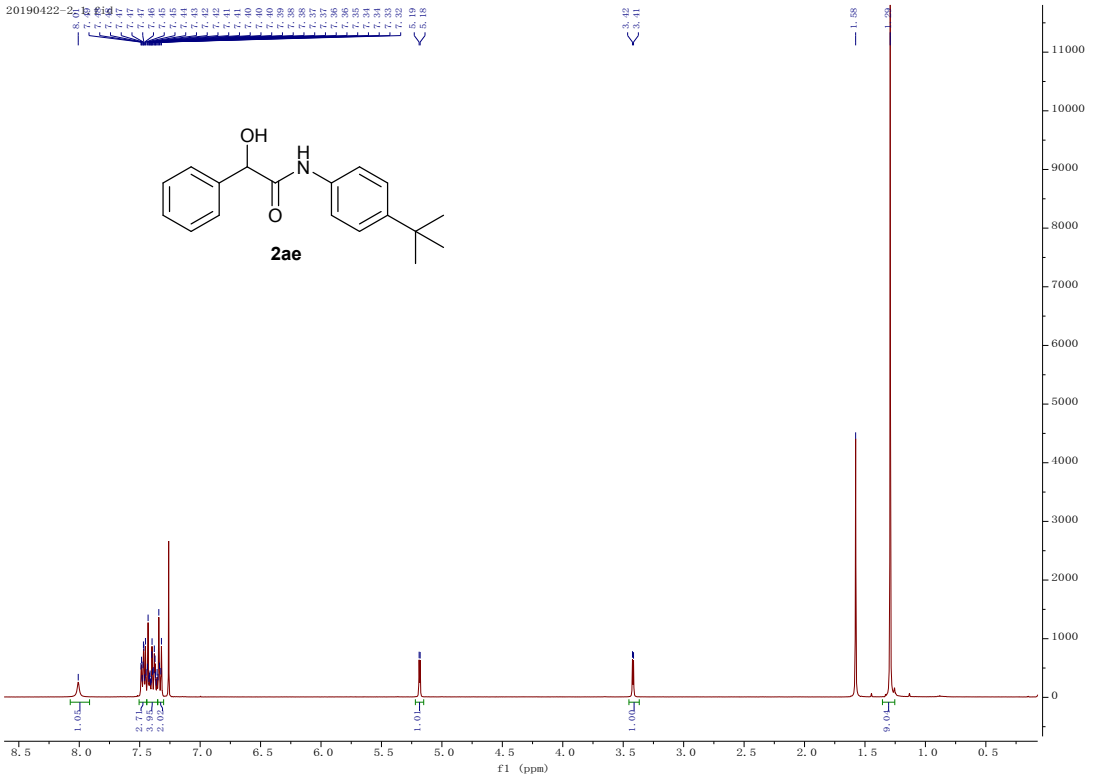

169.86
138.96
137.05
129.07
129.02
128.95
126.90
124.73
119.78
71.73
f1 (ppm)

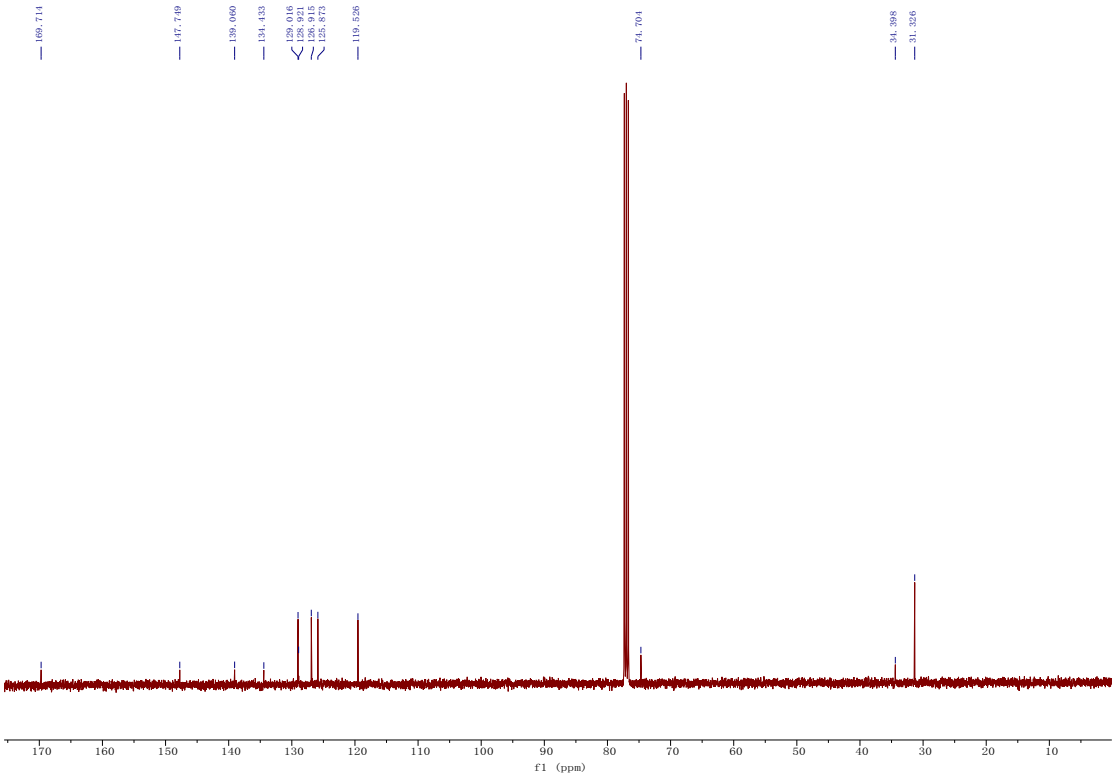

20190328-1.1.fid
OH
H
N
O
2ac
f1 (ppm)

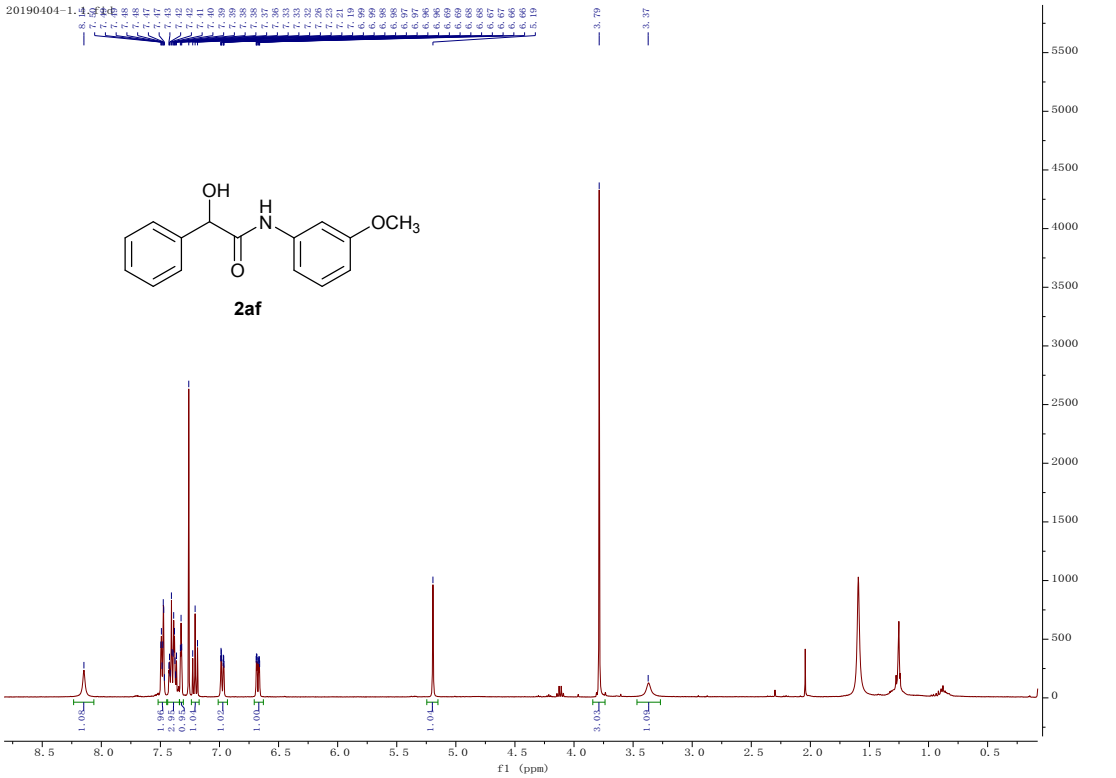

20190328-1.2.fid
f1 (ppm)

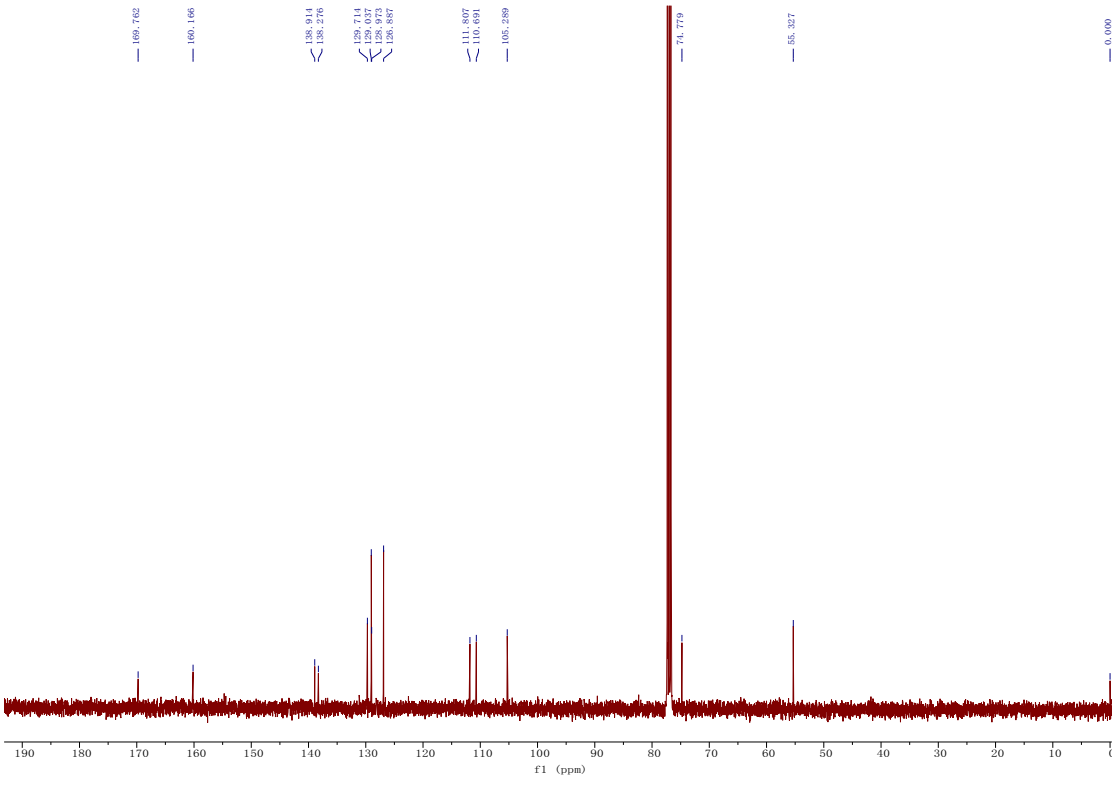

OH
H
N
O
2ad
f1 (ppm)

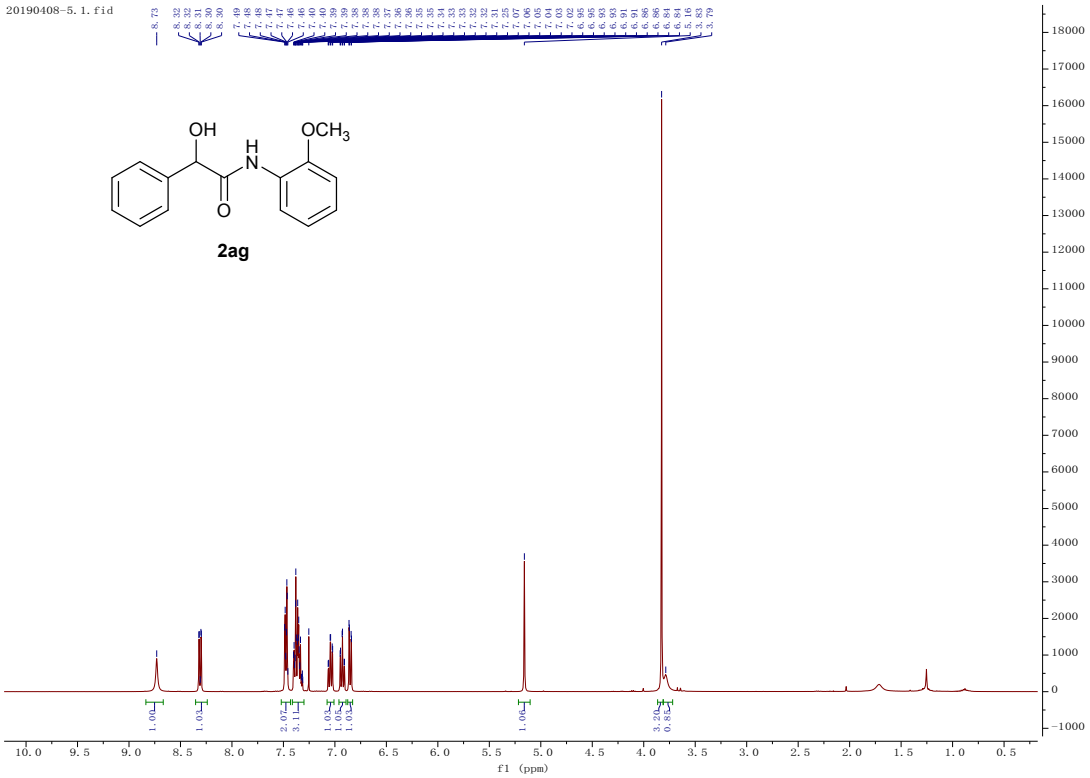

f1 (ppm)

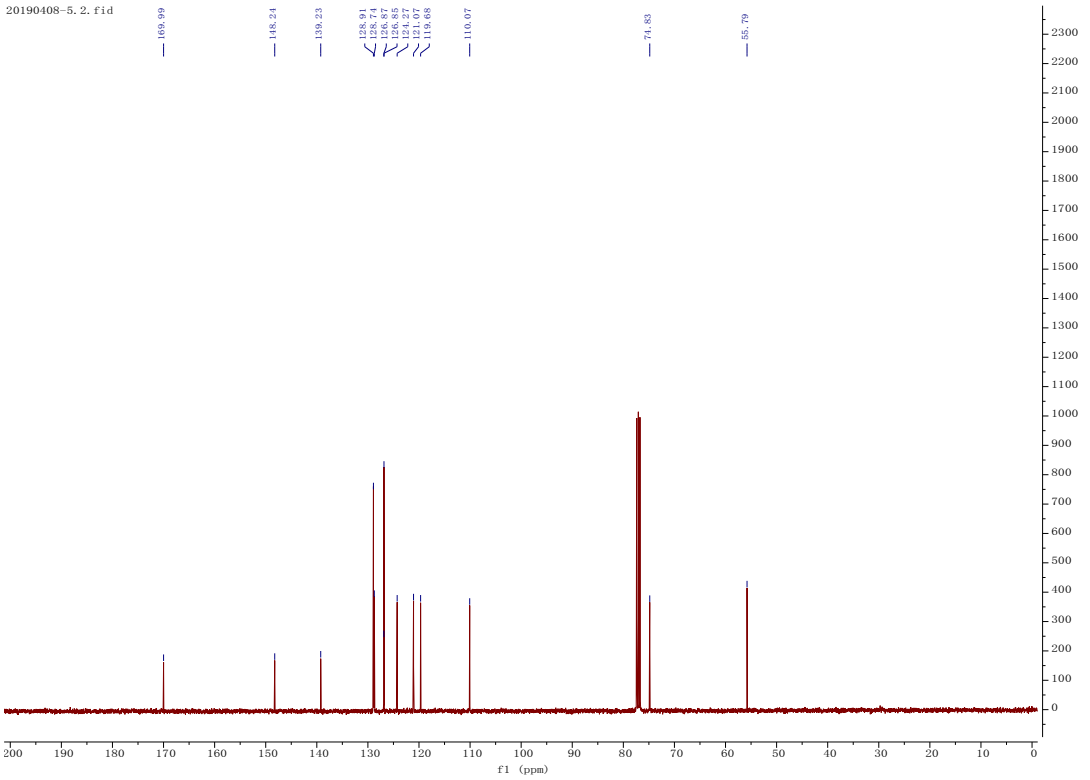

OH
H
N
O
2ae
f1 (ppm)

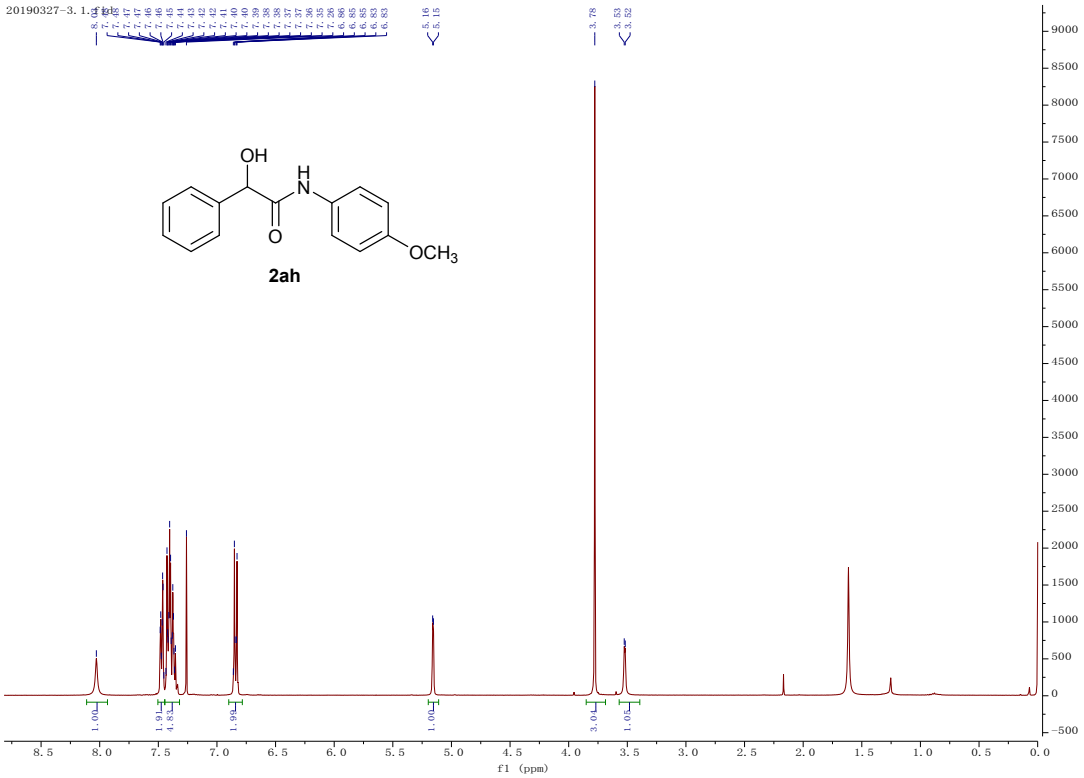

f1 (ppm)

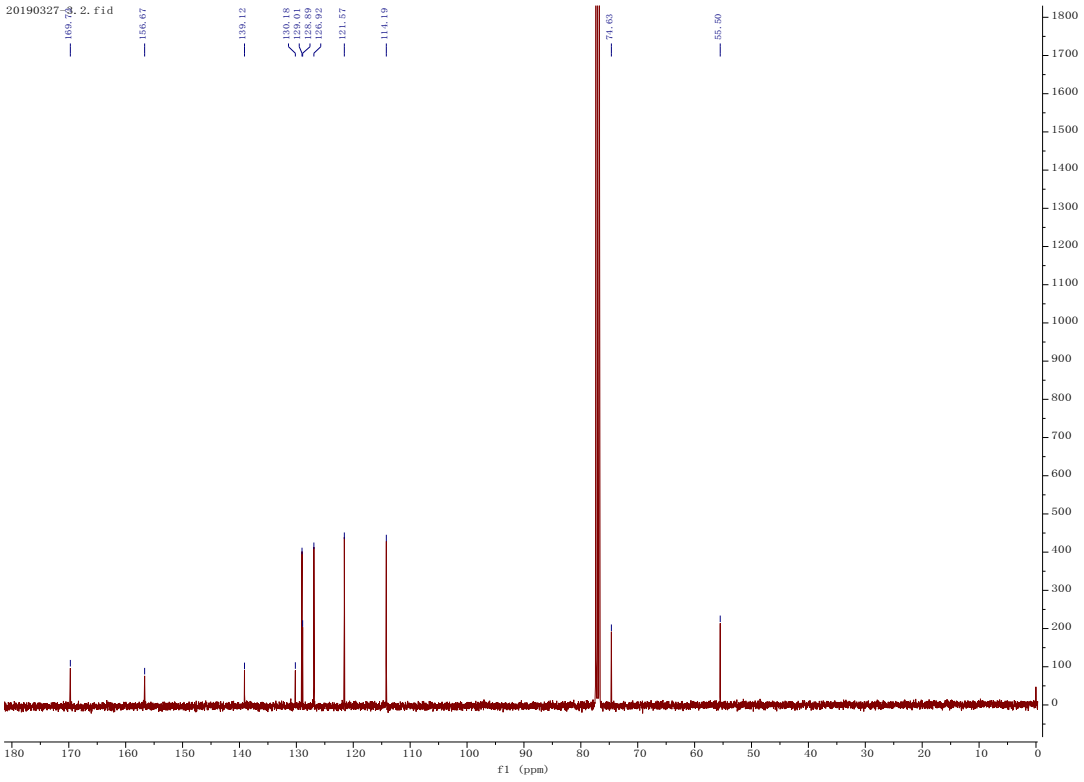

OH
H
N
O
OCH3
2af
f1 (ppm)

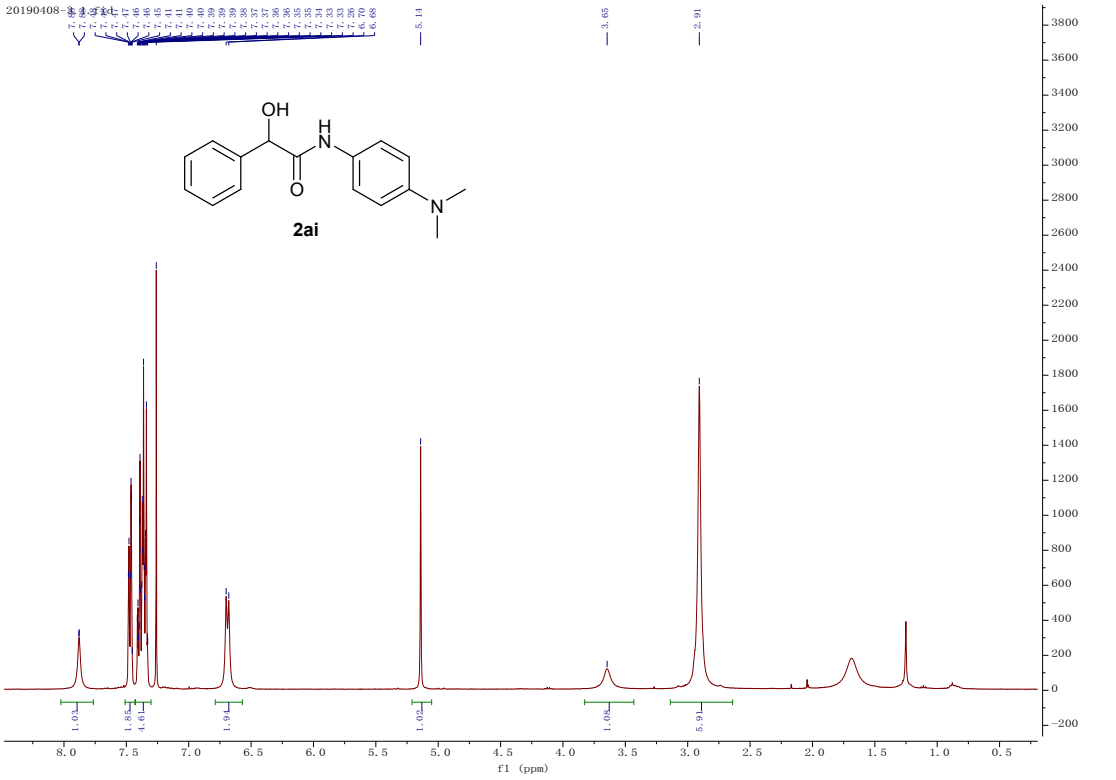

f1 (ppm)

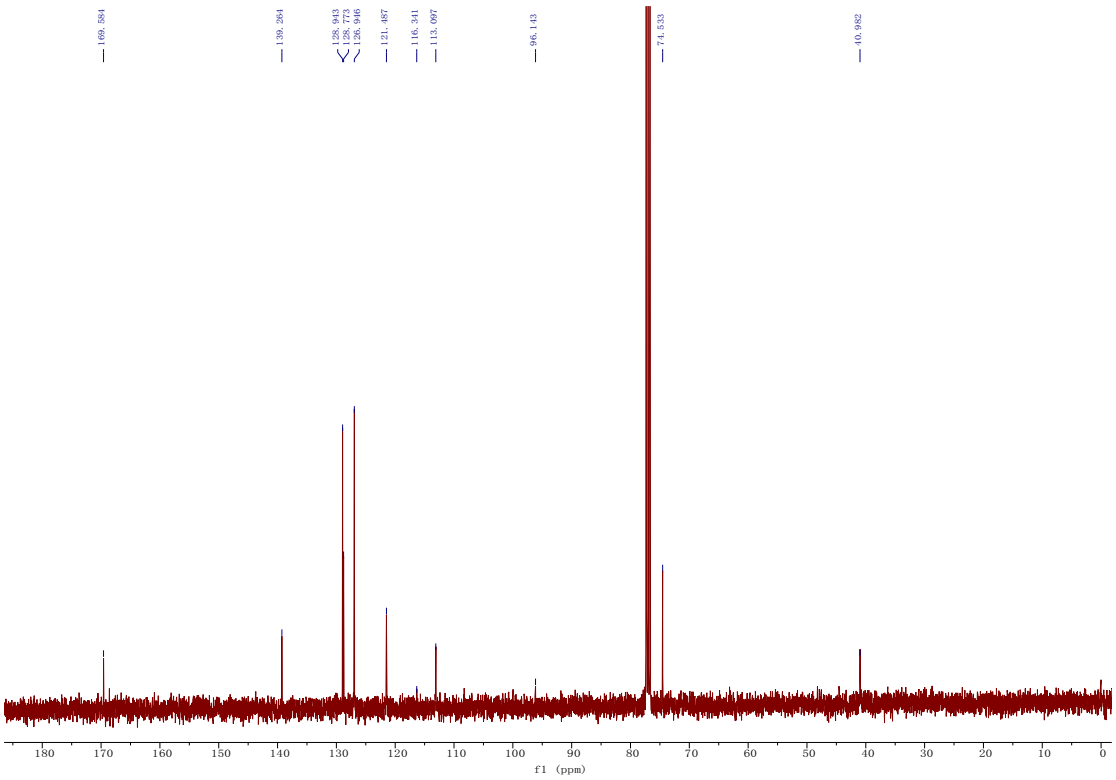

20190408-5.1.fid
OH
H
N
OCH3
O
2ag
f1 (ppm)

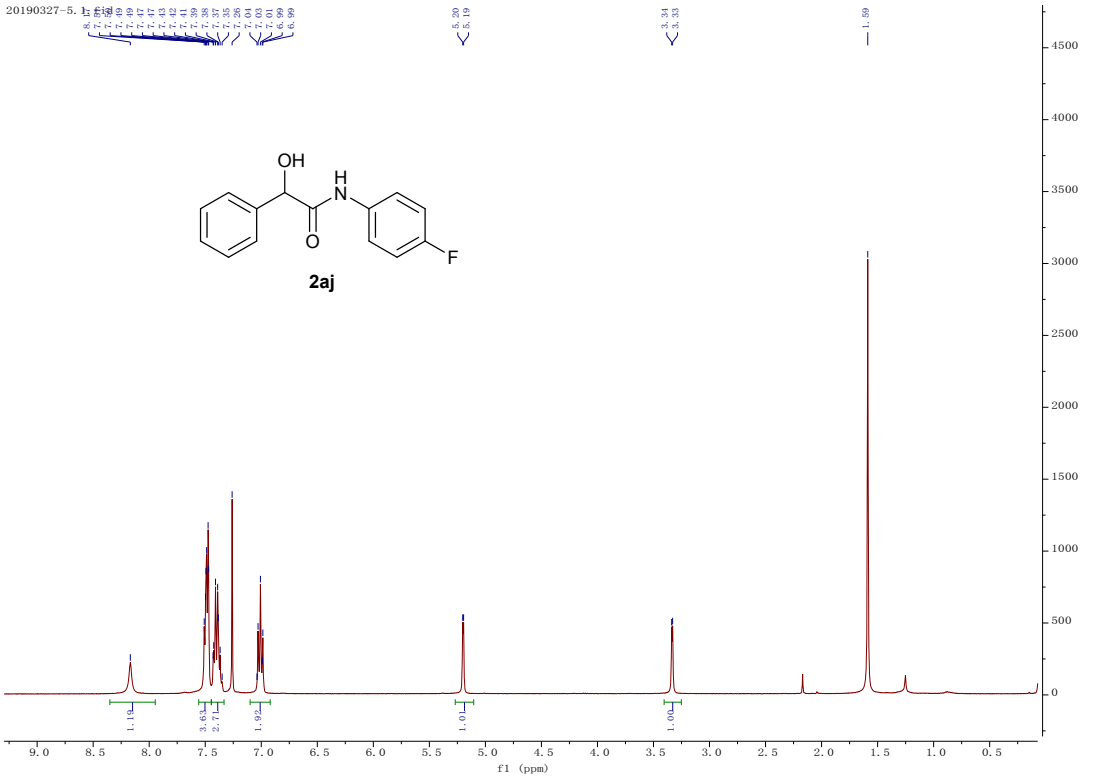

20190408-5.2.fid
169.99
148.24
139.23
128.91
128.74
126.87
126.85
124.27
121.07
119.68
110.07
74.83
55.79
f1 (ppm)

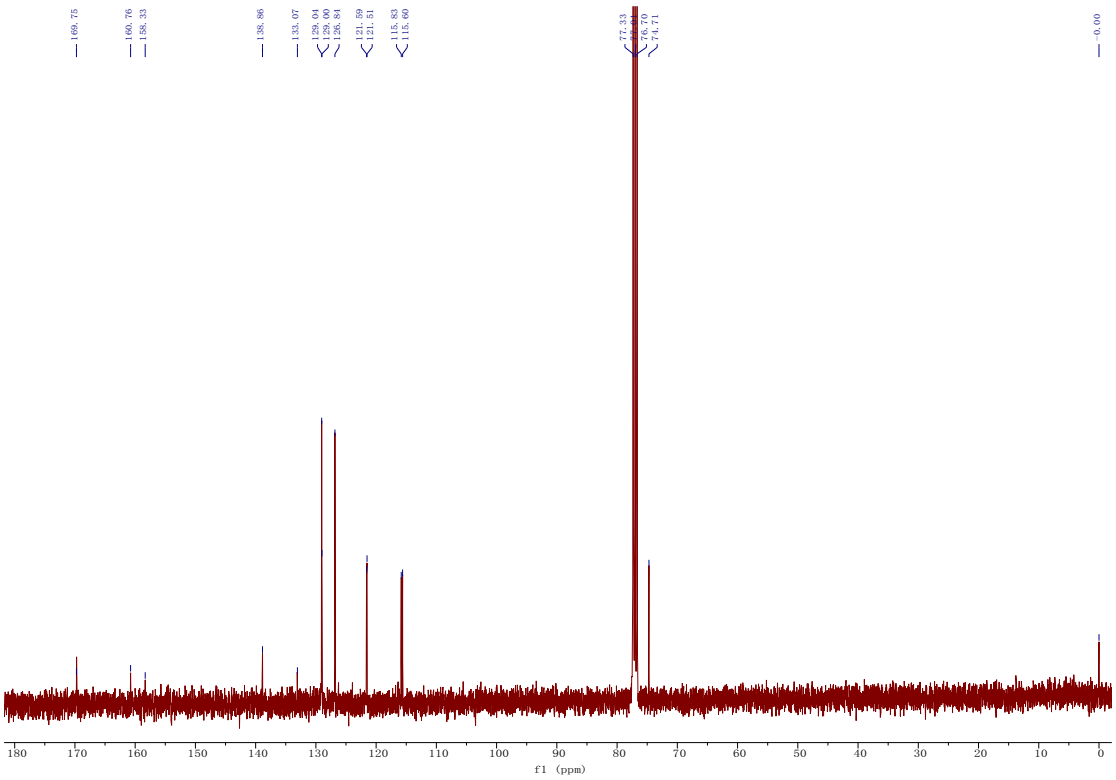

OH
H
N
O
OCH3
2ah
f1 (ppm)

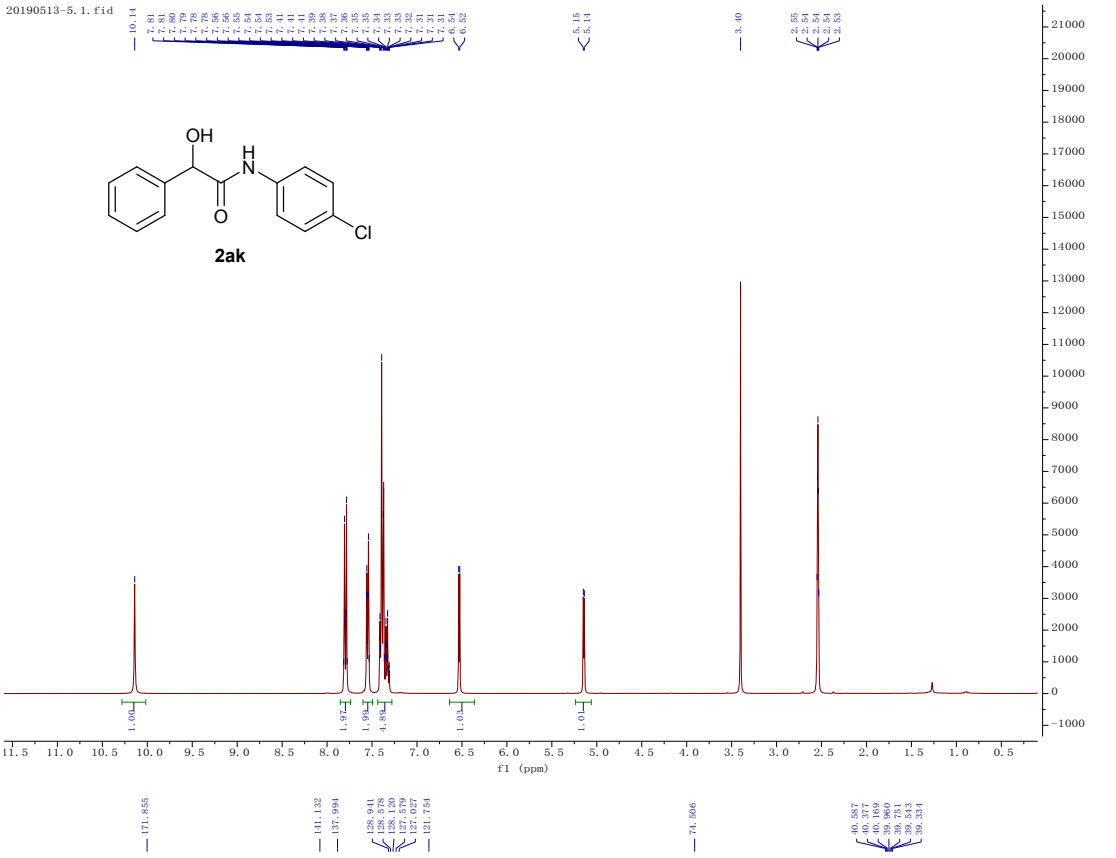

169.74
156.67
139.12
130.18
129.01
128.89
126.92
121.57
114.19
74.63
55.50
f1 (ppm)

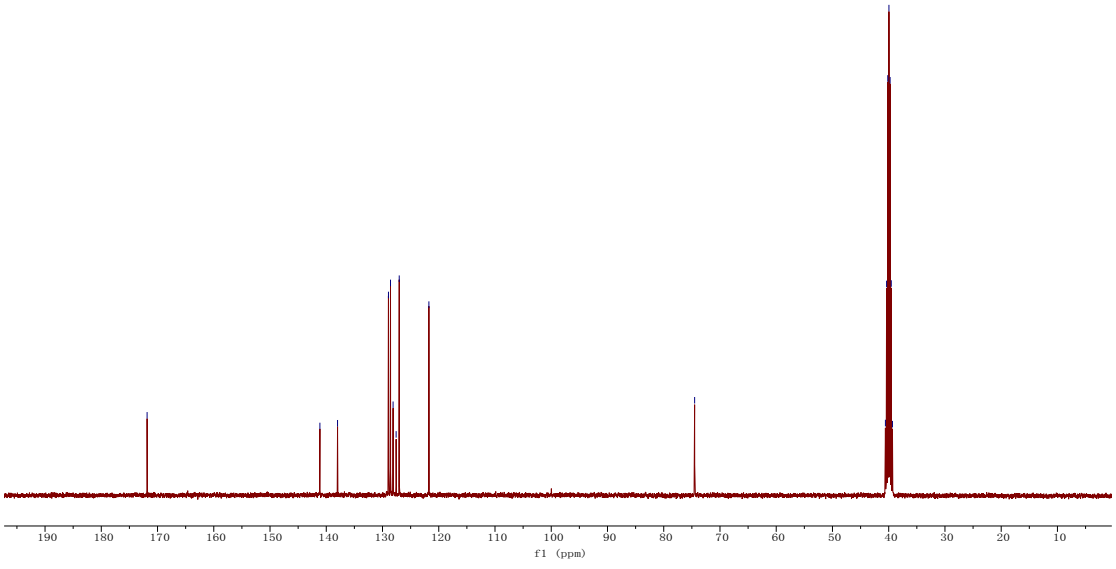

OH
H
N
O
N
2ai
5.14
3.65
2.91
f1 (ppm)

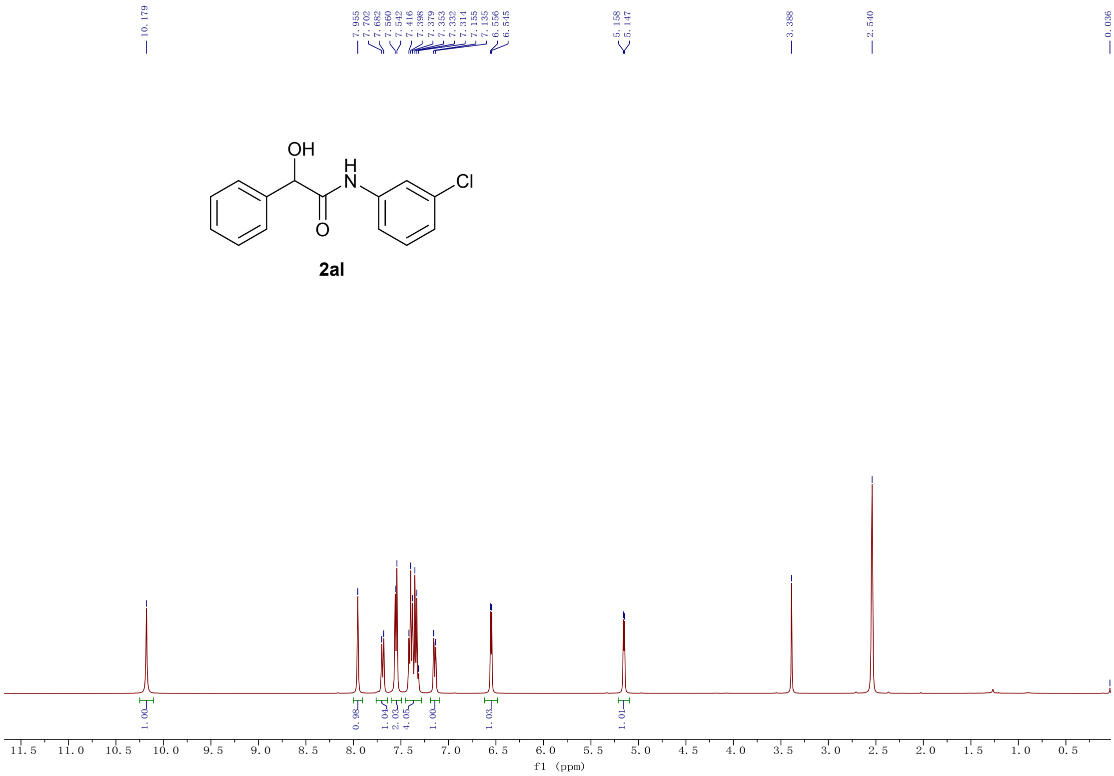

169.584
139.264
128.943
128.772
126.946
121.487
116.341
113.097
96.143
74.533
40.982
f1 (ppm)


OH
H
N
O
F
2aj
f1 (ppm)

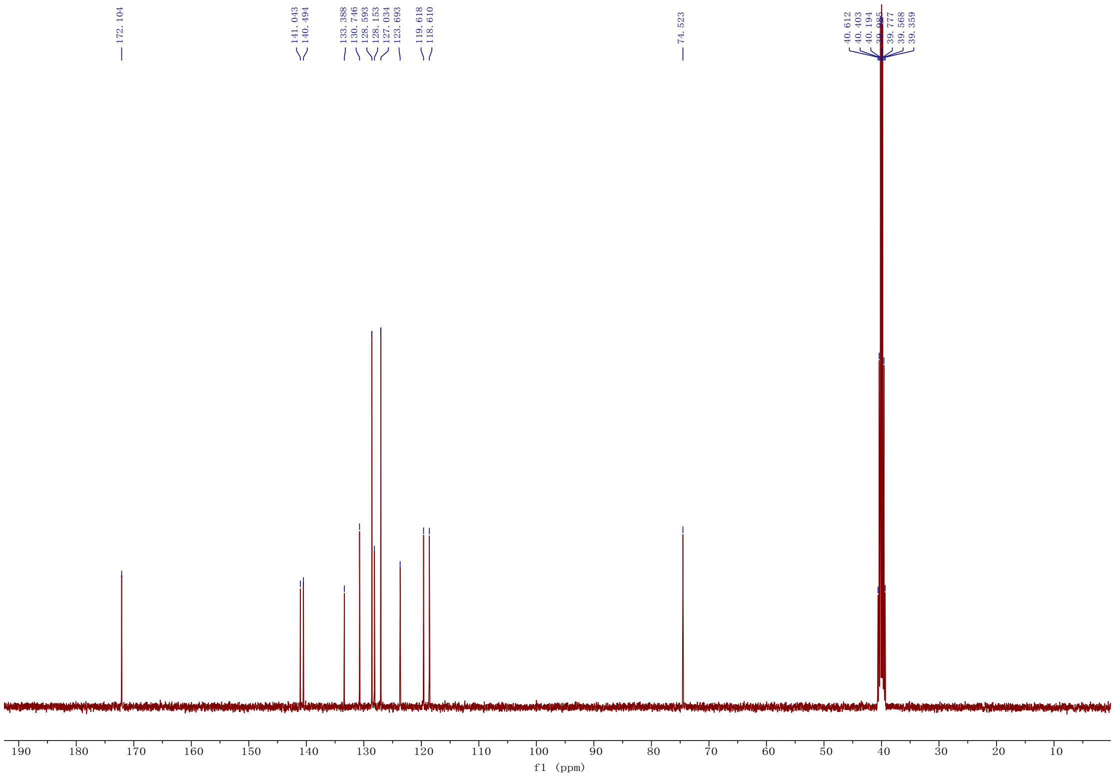

f1 (ppm)


20190513-5.1.fid
OH
H
N
O
Cl
2ak
f1 (ppm)

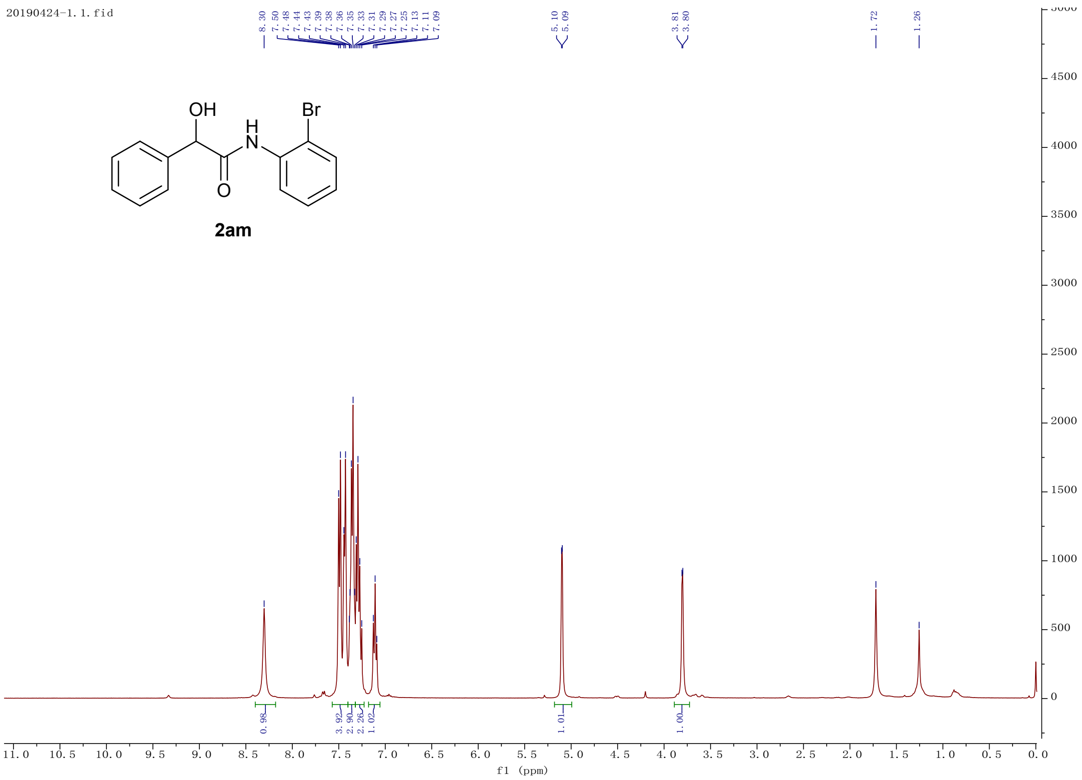

f1 (ppm)

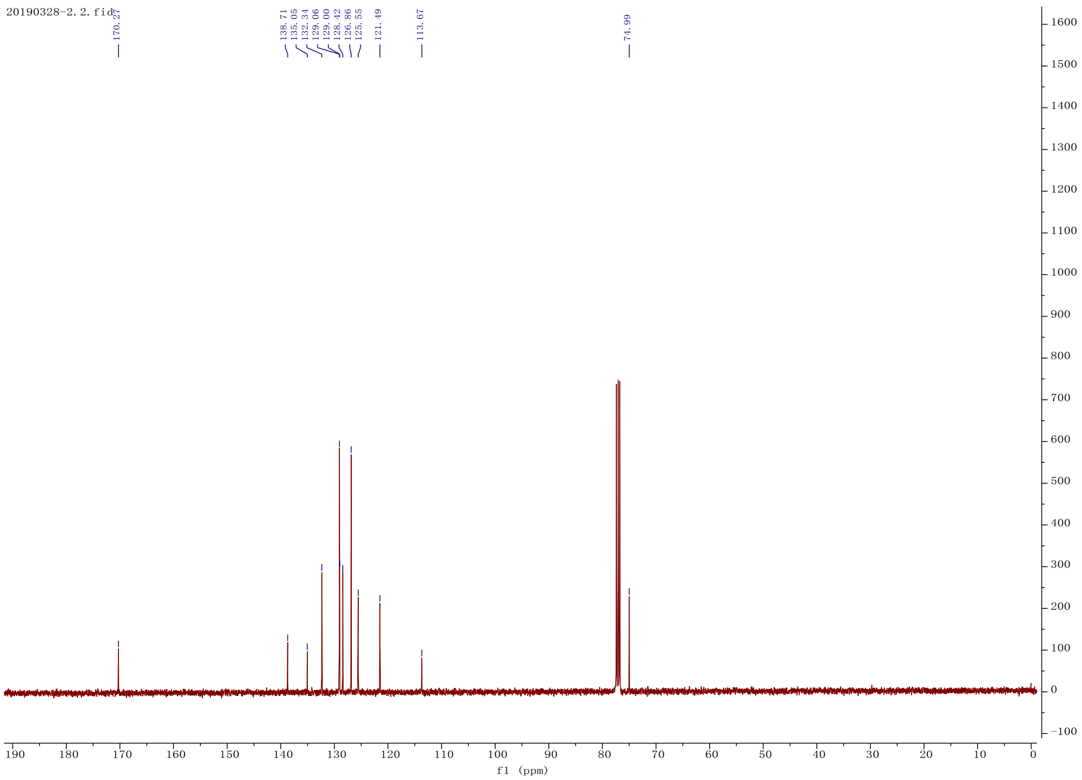


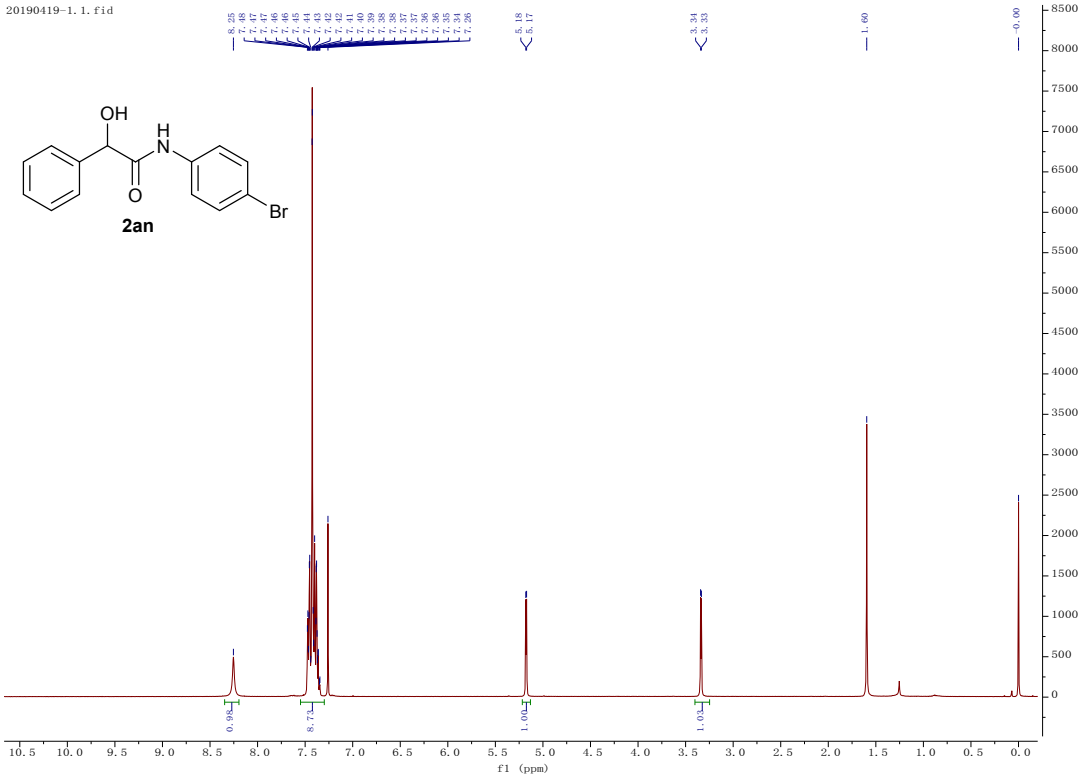
10.179
7.955
7.702
7.682
7.560
7.542
7.416
7.398
7.379
7.353
7.332
7.314
7.155
7.135
6.556
6.545
5.158
5.147
3.388
2.540
0.036
OH
H
N
Cl
O
2al
1.00
0.98
1.04
2.03
4.05
1.00
1.03
1.01
f1 (ppm)

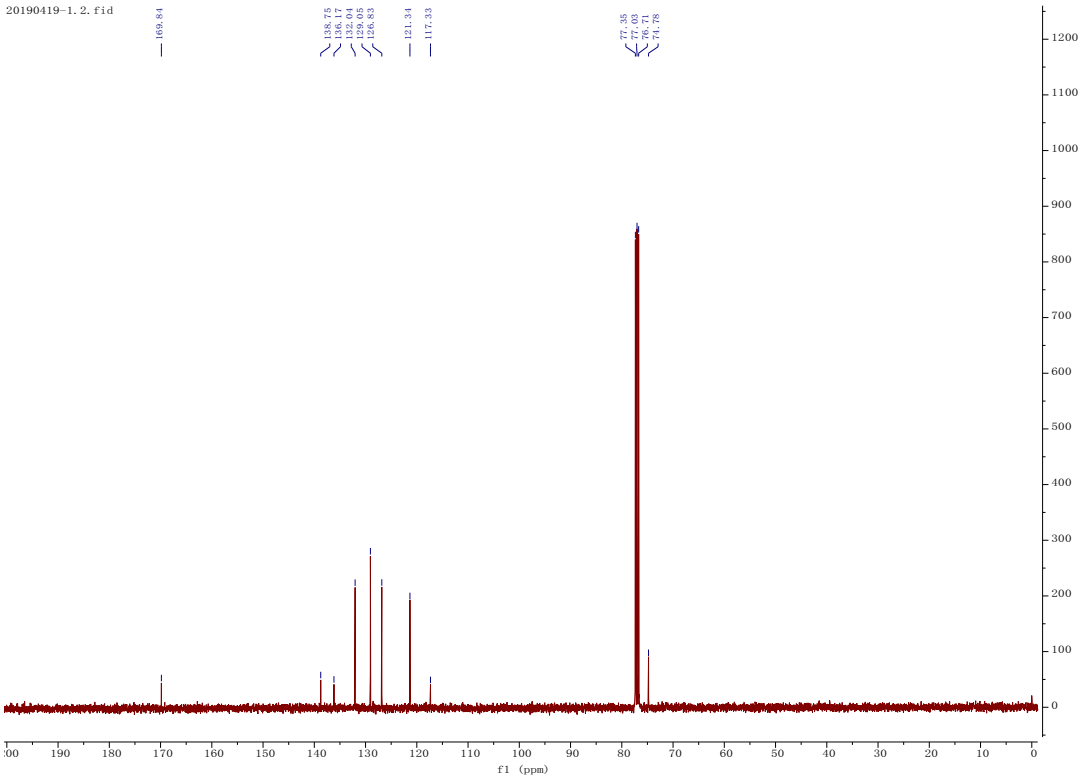


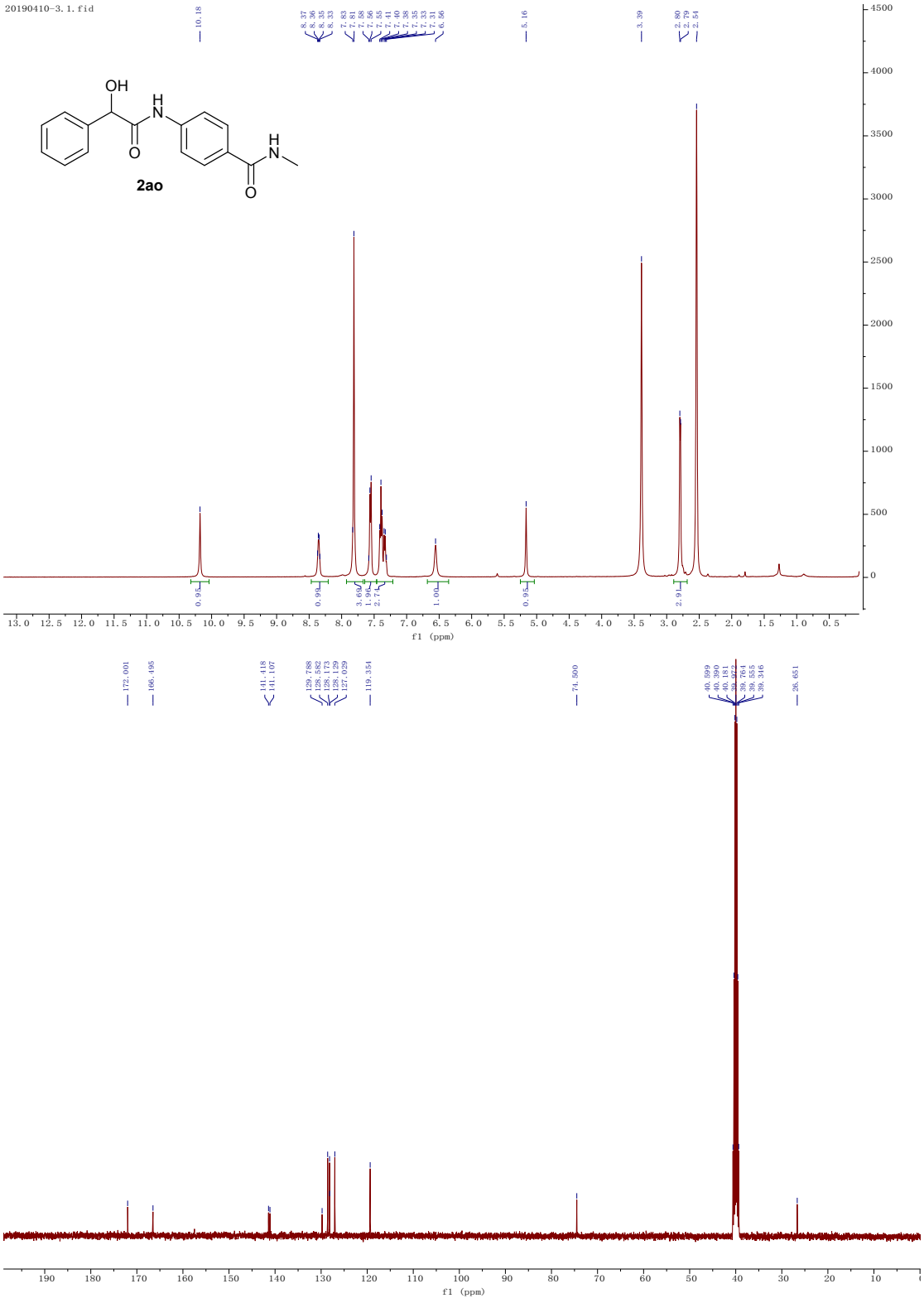
172.104
141.043
140.494
133.388
130.746
128.593
128.153
127.034
123.693
119.618
118.610
74.523
40.612
40.403
40.194
39.985
39.777
39.568
39.359
f1 (ppm)

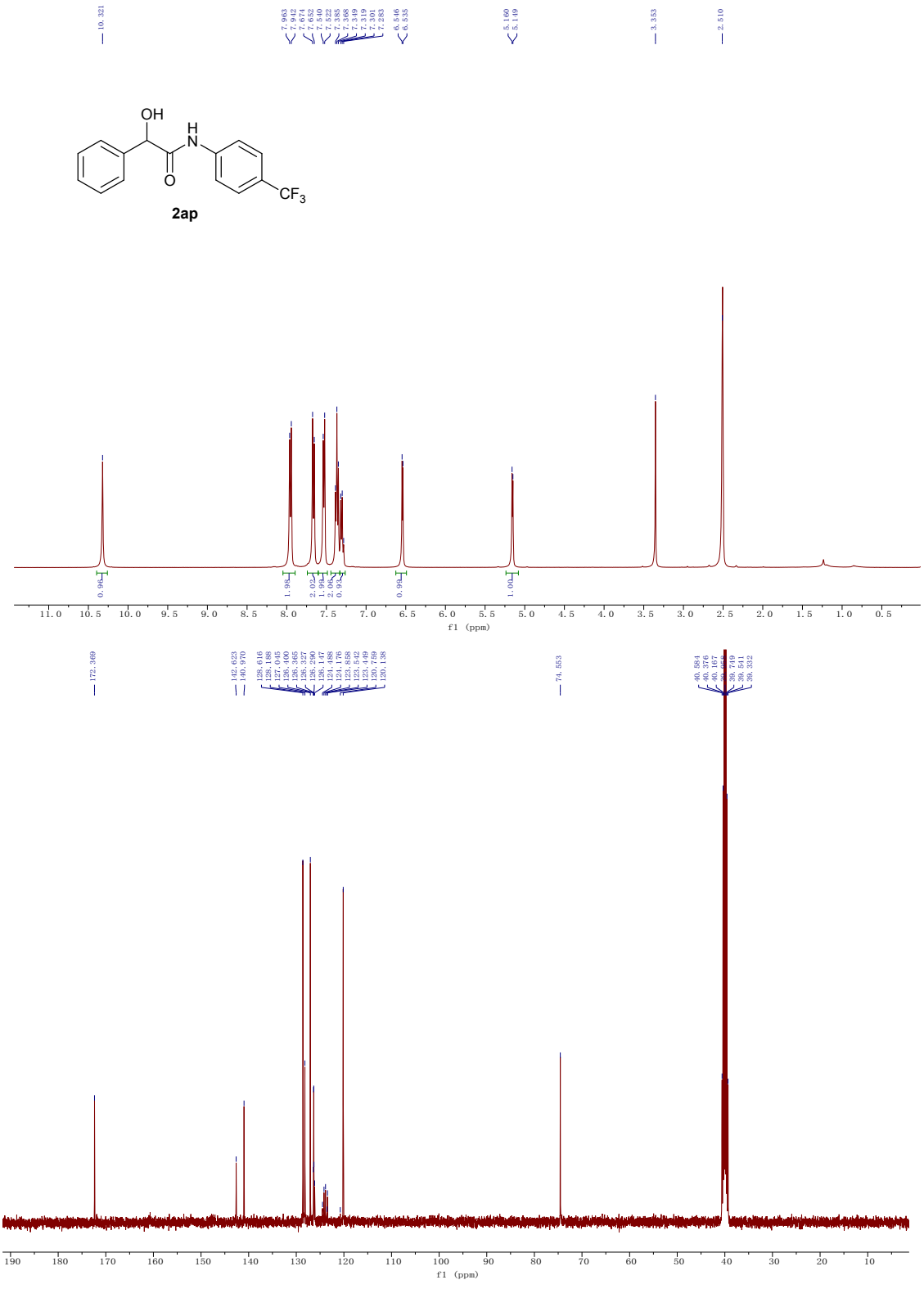

20190424-1.1.fid
8.30
7.50
7.48
7.44
7.43
7.39
7.38
7.36
7.35
7.33
7.31
7.29
7.27
7.25
7.13
7.11
7.09
5.10
5.09
3.81
3.80
1.72
1.26
OH
H
N
Br
O
2am
0.98
3.92
2.90
2.20
1.02
1.01
1.00
f1 (ppm)


20190328-2.2.fid
170.27
138.71
135.05
132.34
129.06
129.00
128.42
126.86
125.55
121.49
113.67
74.99
f1 (ppm)


20190419-1.1.fid
OH
H
N
O
Br
2an
f1 (ppm)


20190419-1.2.fid
f1 (ppm)


20190410-3.1.fid
OH
H
N
O
H
N
O
2ao
f1 (ppm)
f1 (ppm)


10.321
7.963
7.942
7.674
7.652
7.540
7.522
7.385
7.368
7.349
7.319
7.301
7.283
6.546
6.535
5.166
5.149
3.353
2.510
OH
H
N
O
CF3
2ap
0.96
1.98
2.05
1.98
2.05
0.98
1.00
f1 (ppm)
172.369
142.623
140.970
128.616
128.188
127.045
126.400
126.345
126.327
126.290
126.147
124.188
124.176
123.858
123.542
123.449
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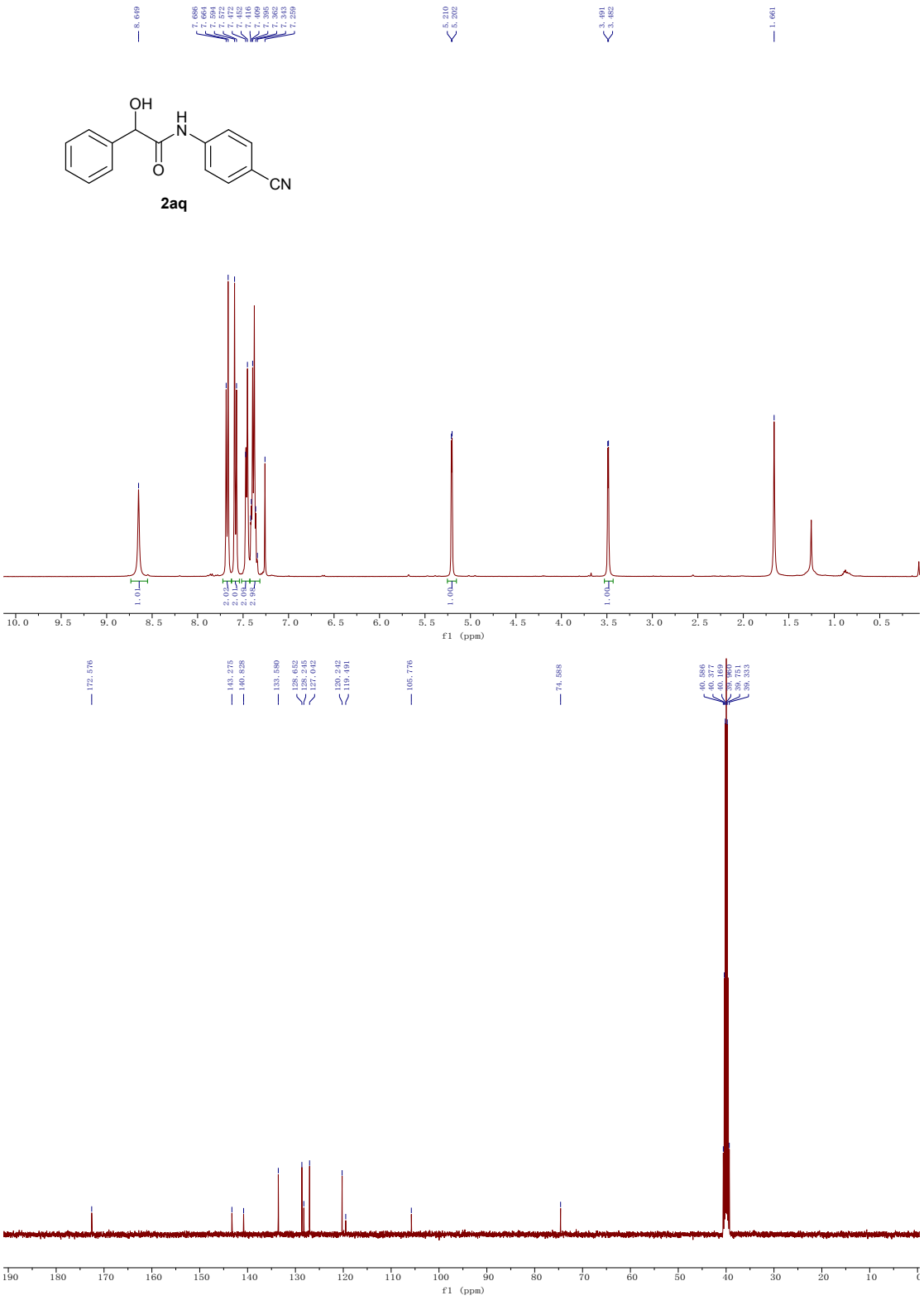
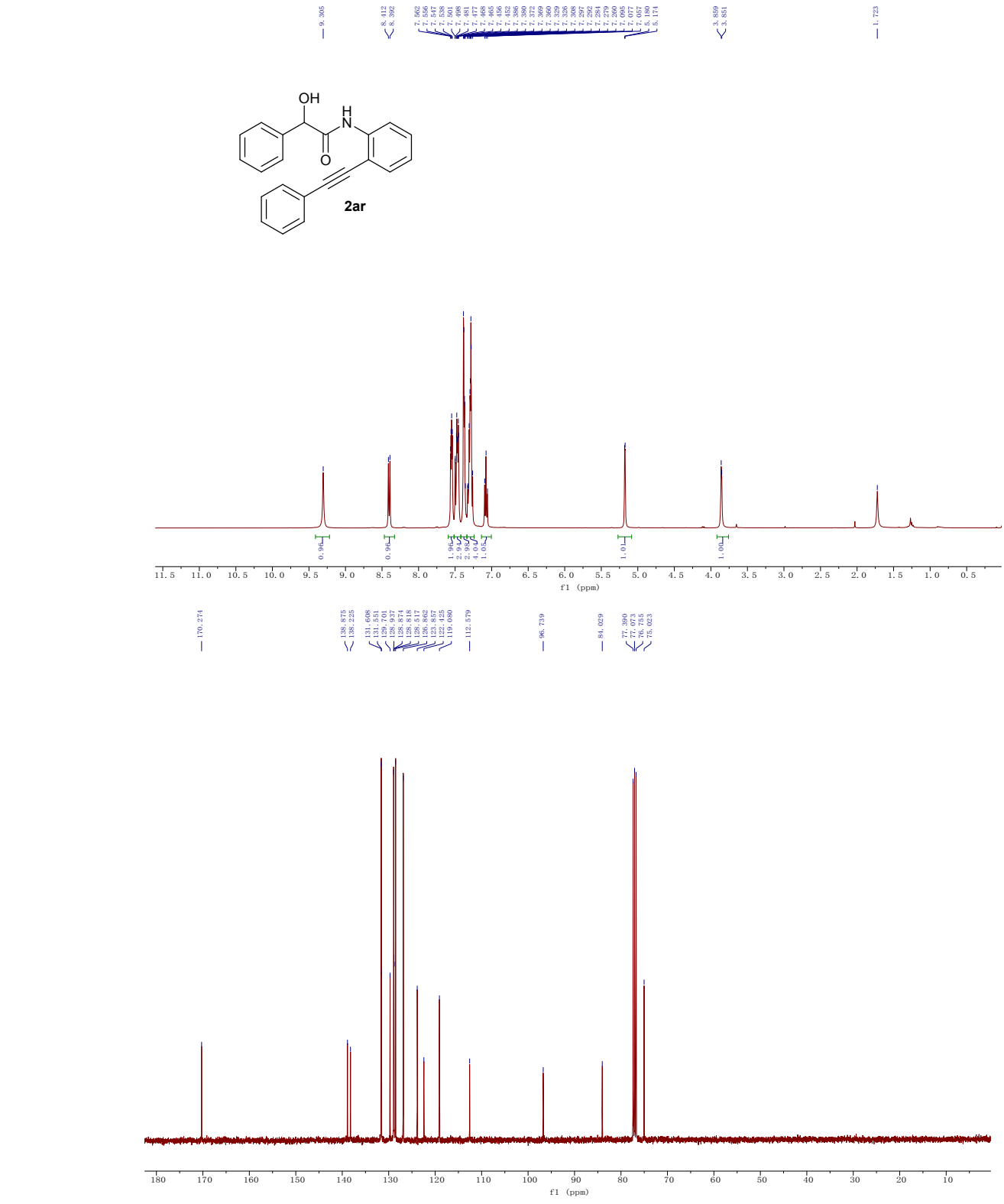
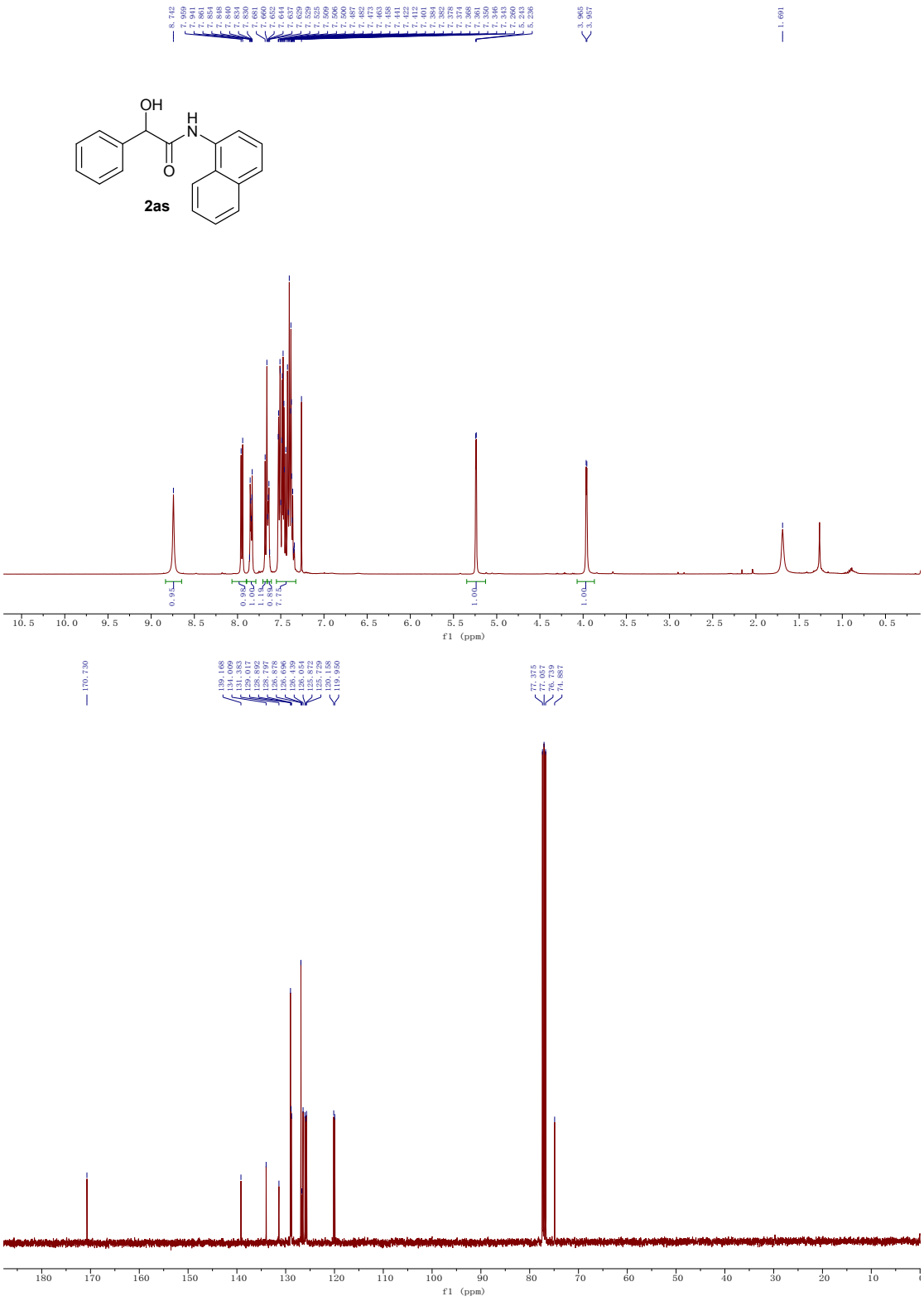
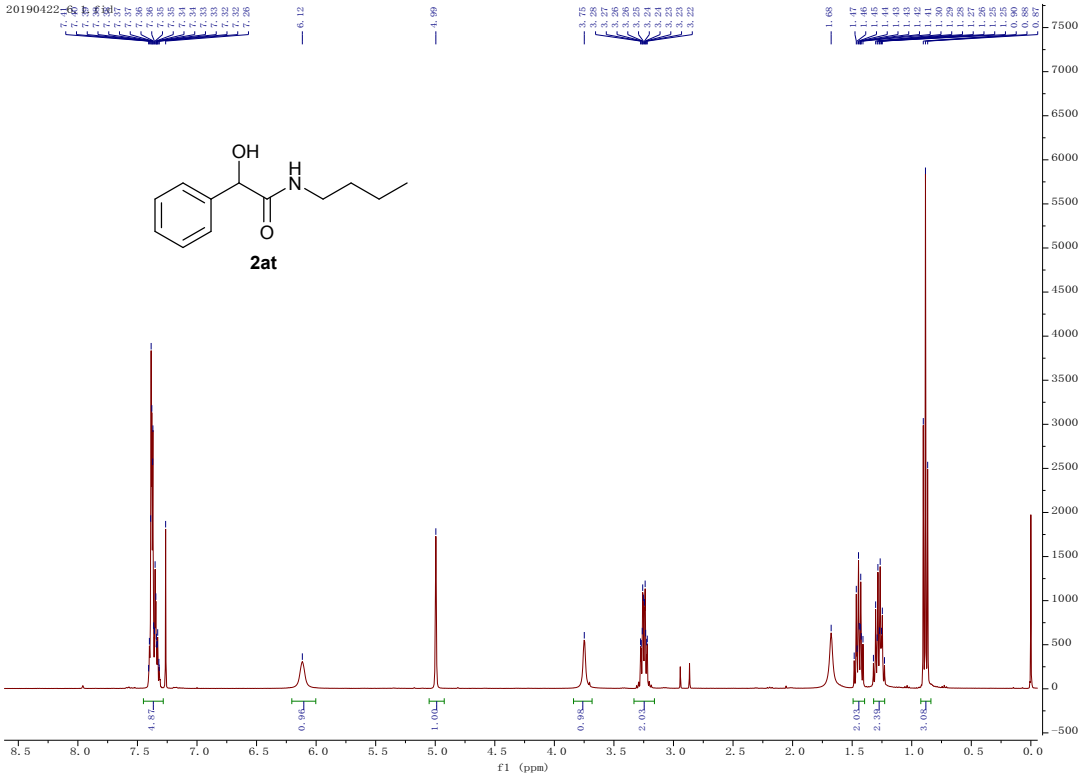
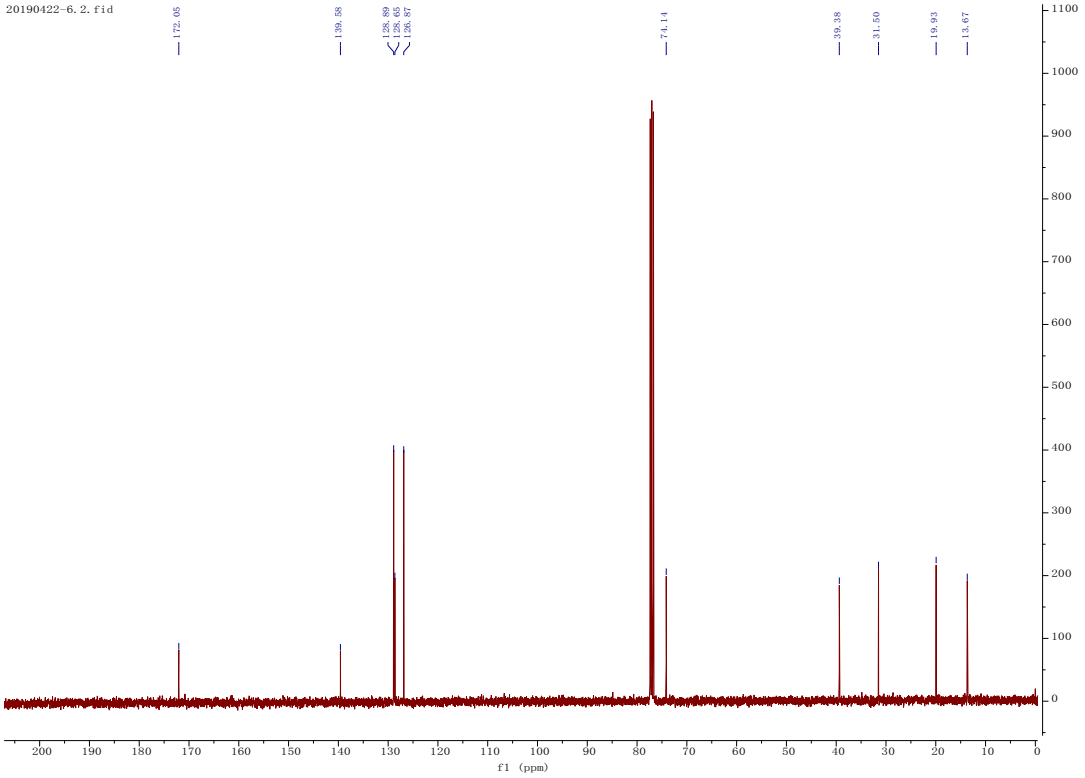
120.138
74.853
40.584
40.376
40.167
39.749
39.541
39.332
f1 (ppm)

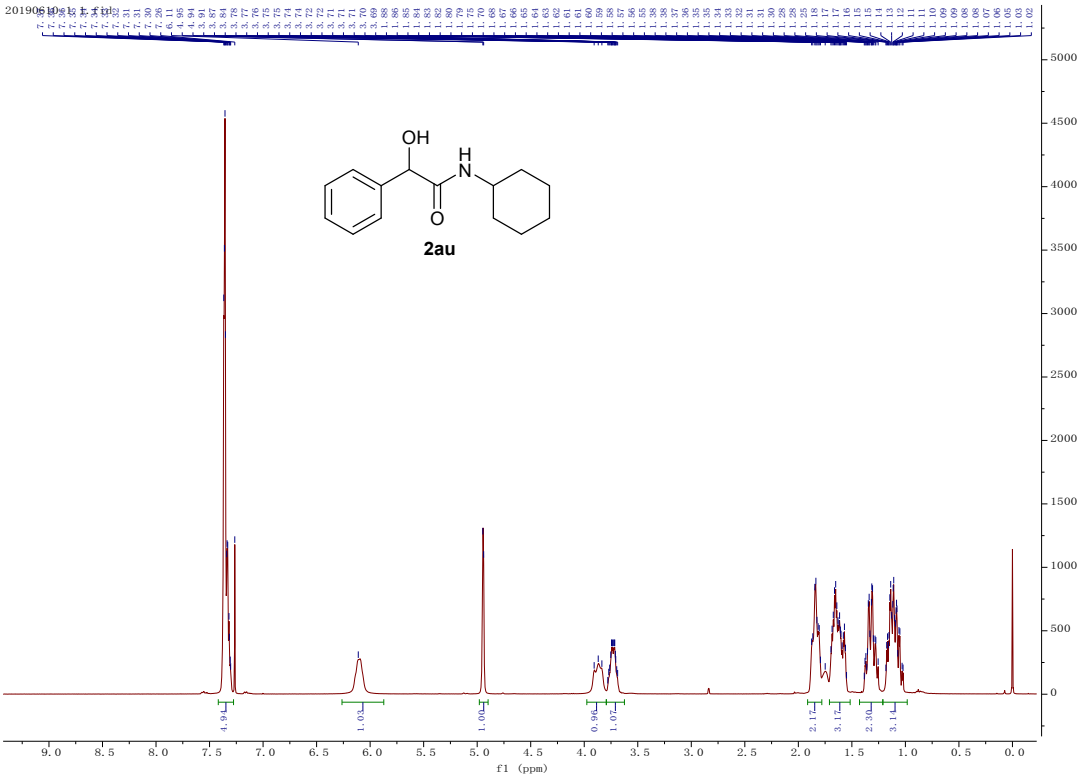

8.649
7.698
7.684
7.594
7.572
7.472
7.452
7.416
7.409
7.395
7.382
7.343
7.259
5.210
5.202
3.491
3.482
1.661
OH
H
N
O
CN
2aq
1.00
2.02
2.01
2.00
2.98
1.00
1.00
f1 (ppm)
172.576
143.275
140.828
133.580
128.652
128.245
127.042
120.242
119.491
105.776
74.588
40.586
40.377
40.169
39.960
39.751
39.333
f1 (ppm)

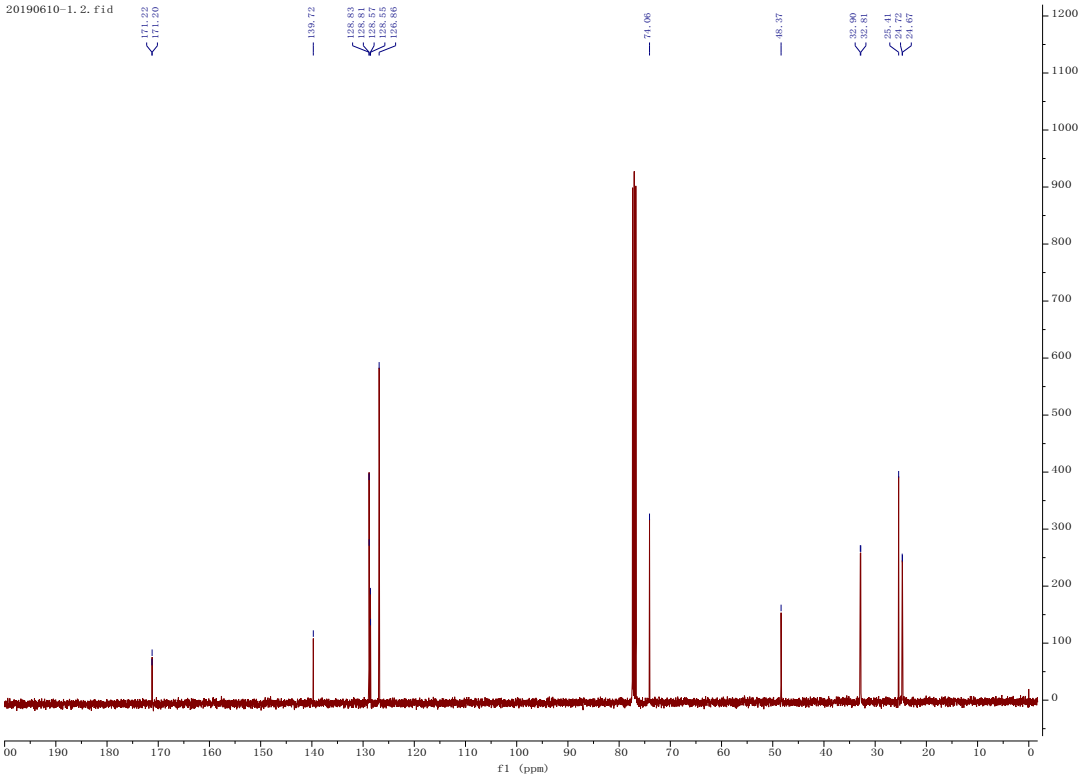

9.305
8.412
8.392
7.562
7.556
7.547
7.538
7.501
7.498
7.481
7.477
7.468
7.465
7.456
7.452
7.386
7.380
7.372
7.369
7.360
7.339
7.335
7.308
7.297
7.282
7.264
7.279
7.260
7.095
7.077
7.057
5.180
5.174
3.859
3.851
1.723
OH
H
N
O
2ar
0.96
0.90
1.94
2.92
4.00
1.05
1.01
1.00
11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)
170.274
138.875
138.225
131.668
131.551
129.701
128.937
128.874
128.818
128.117
126.862
123.857
122.425
119.080
112.579
96.739
84.029
77.390
77.073
76.755
75.023
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

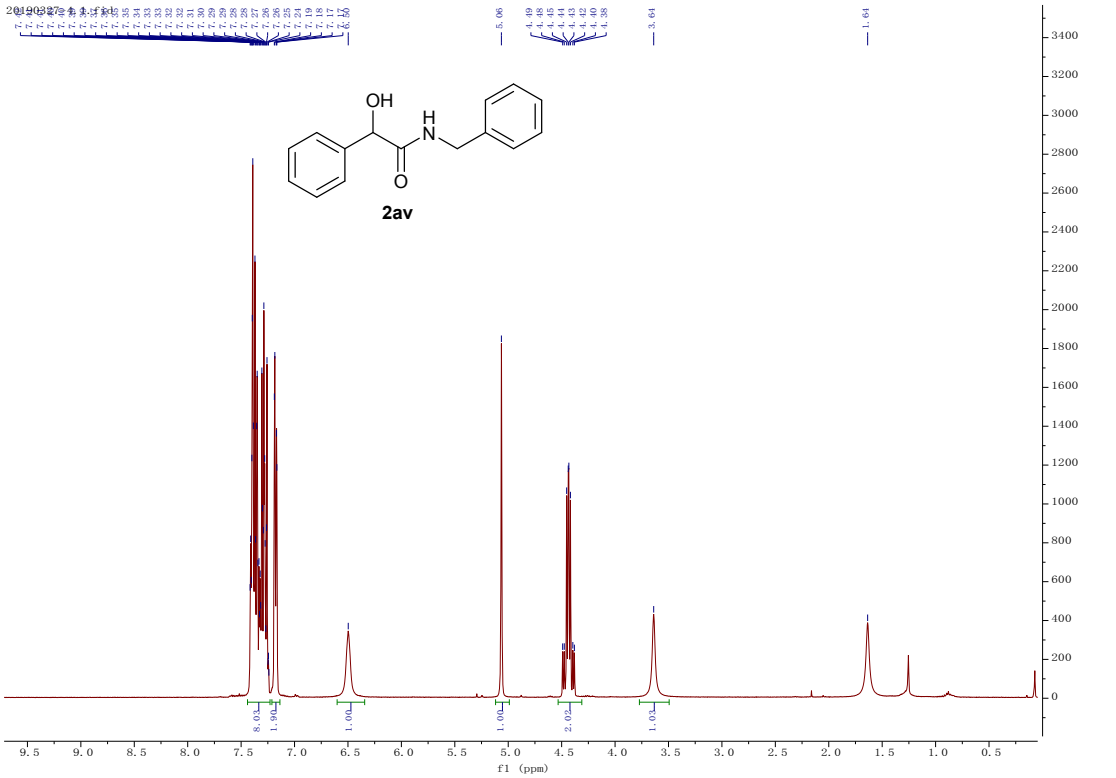

OH
H
N
O
2as
f1 (ppm)
f1 (ppm)

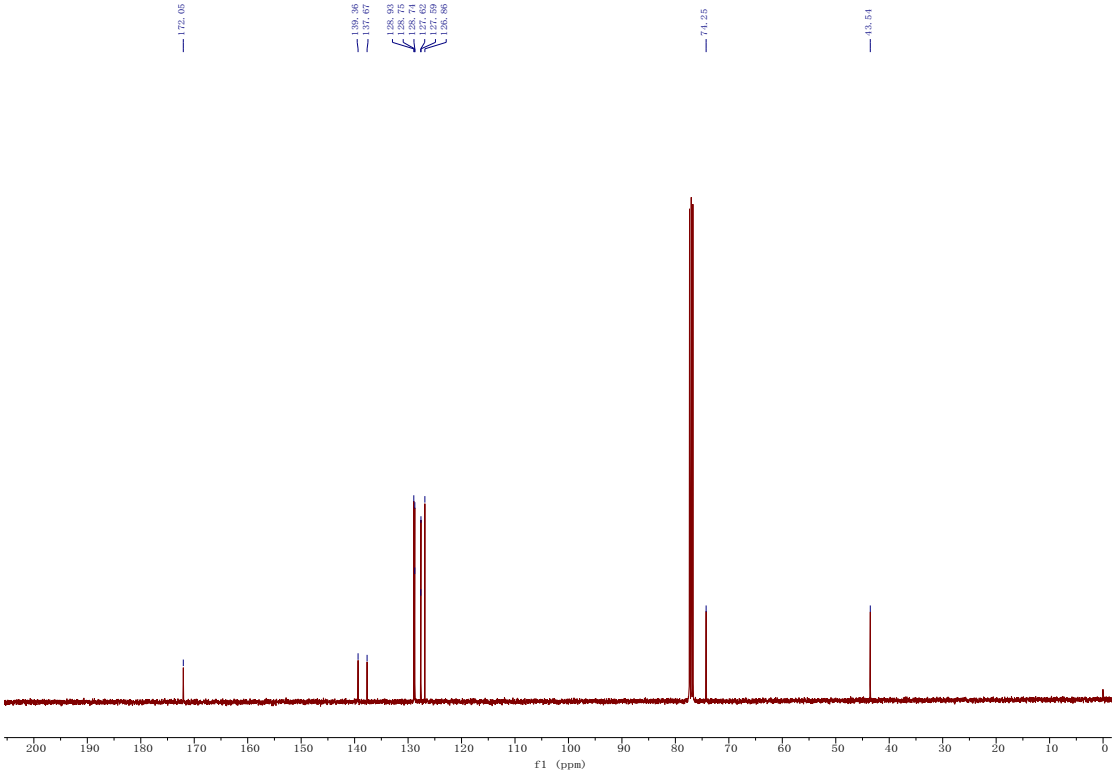

OH
H
N
O
2at
f1 (ppm)

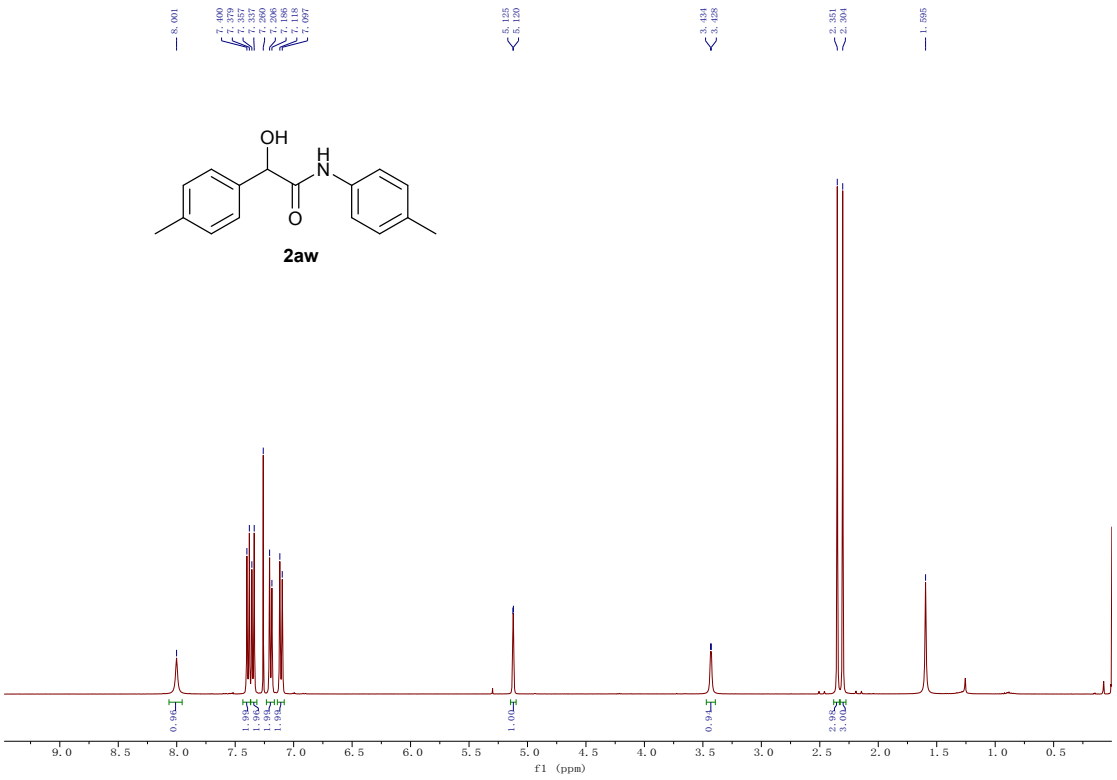

20190422-6.2.fid
f1 (ppm)

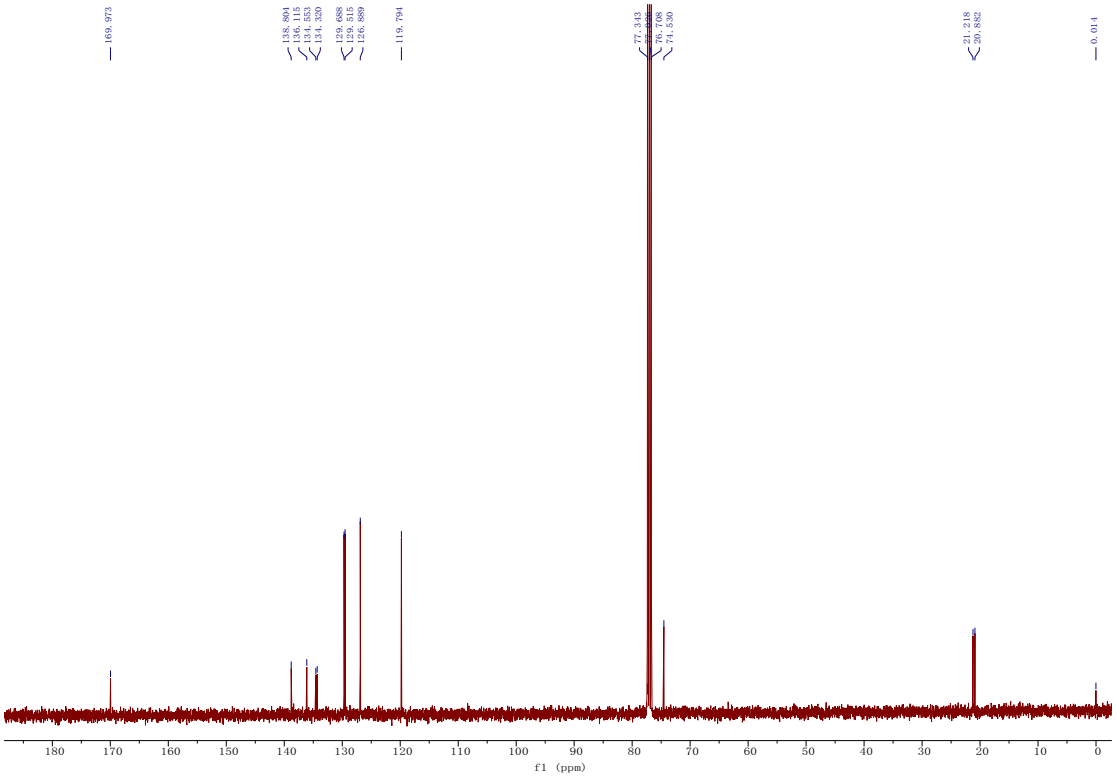

OH
H
N
O
2au
f1 (ppm)

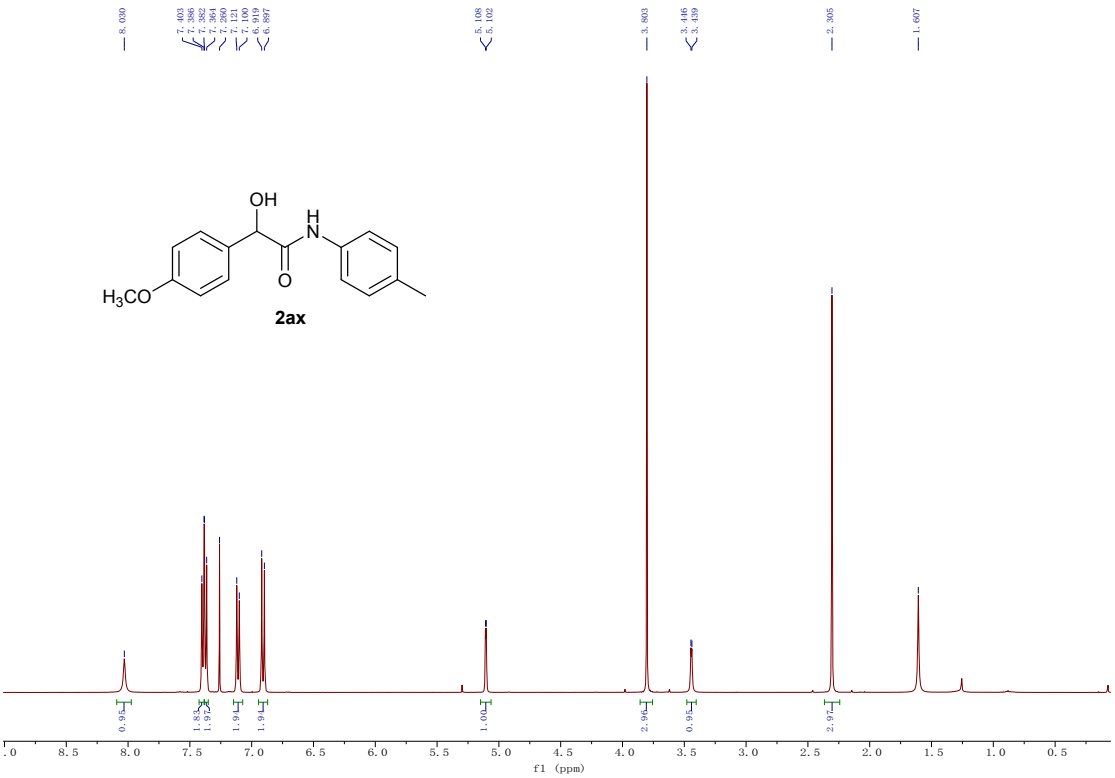

20190610-1.2.fid
f1 (ppm)

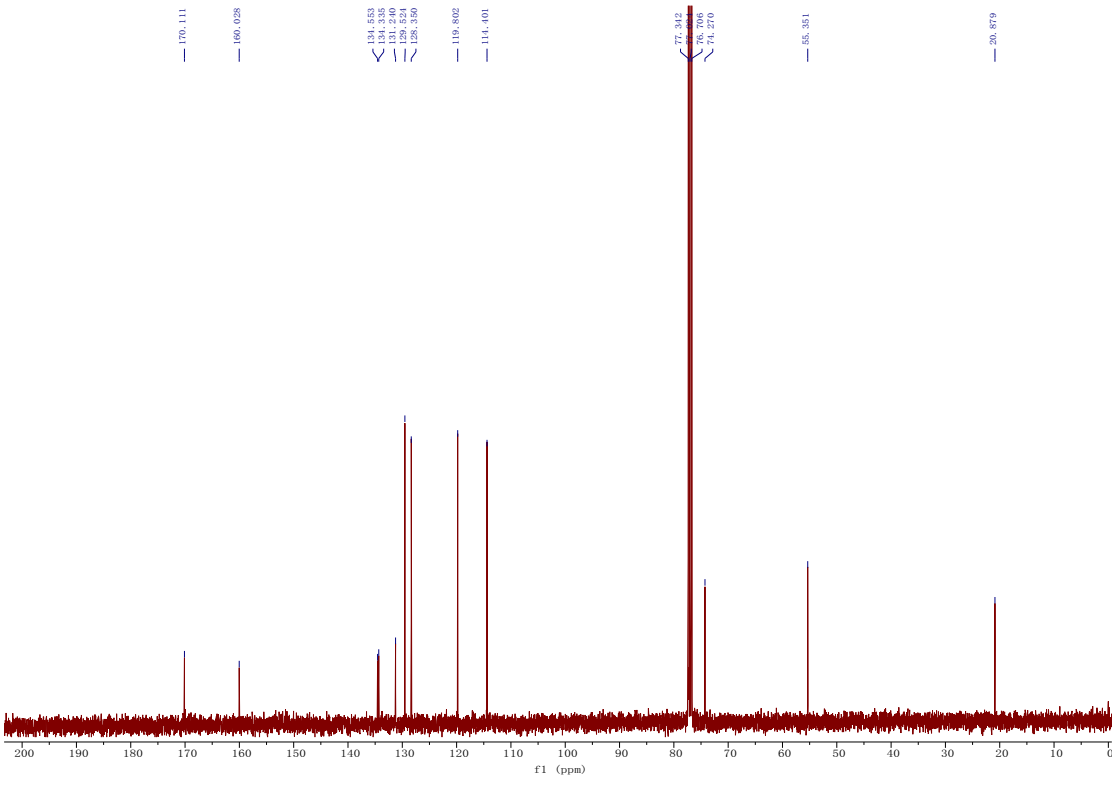

OH
H
N
O
2av
f1 (ppm)

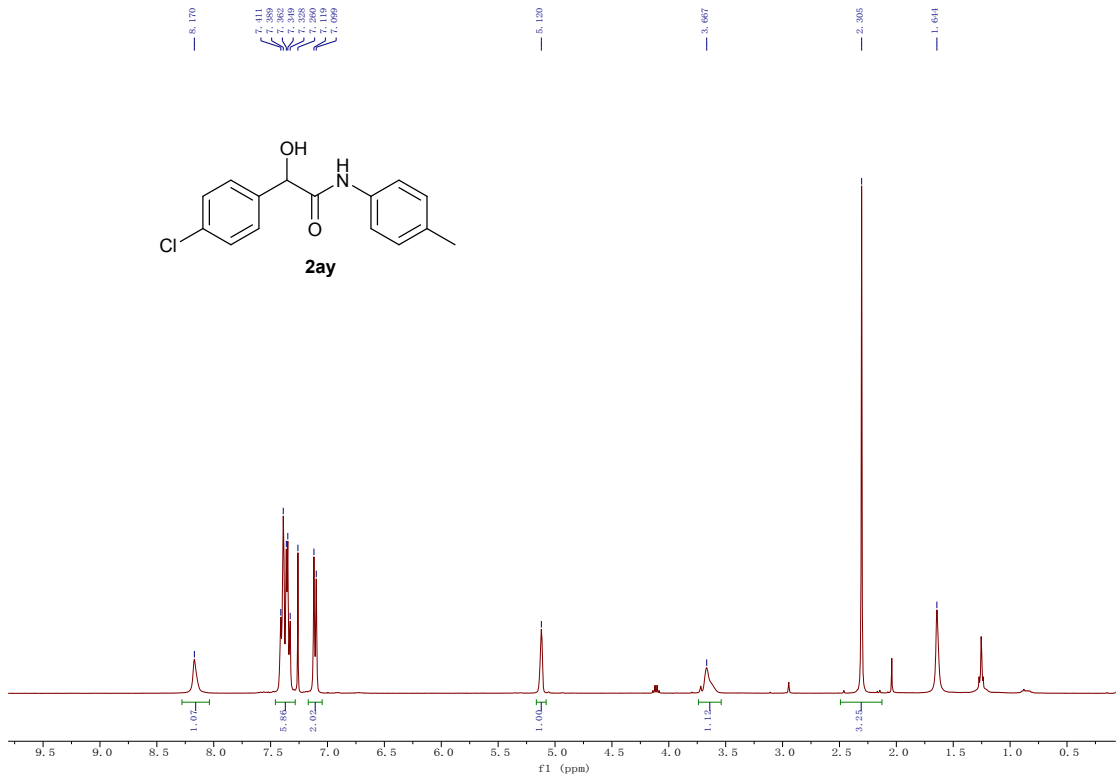

f1 (ppm)

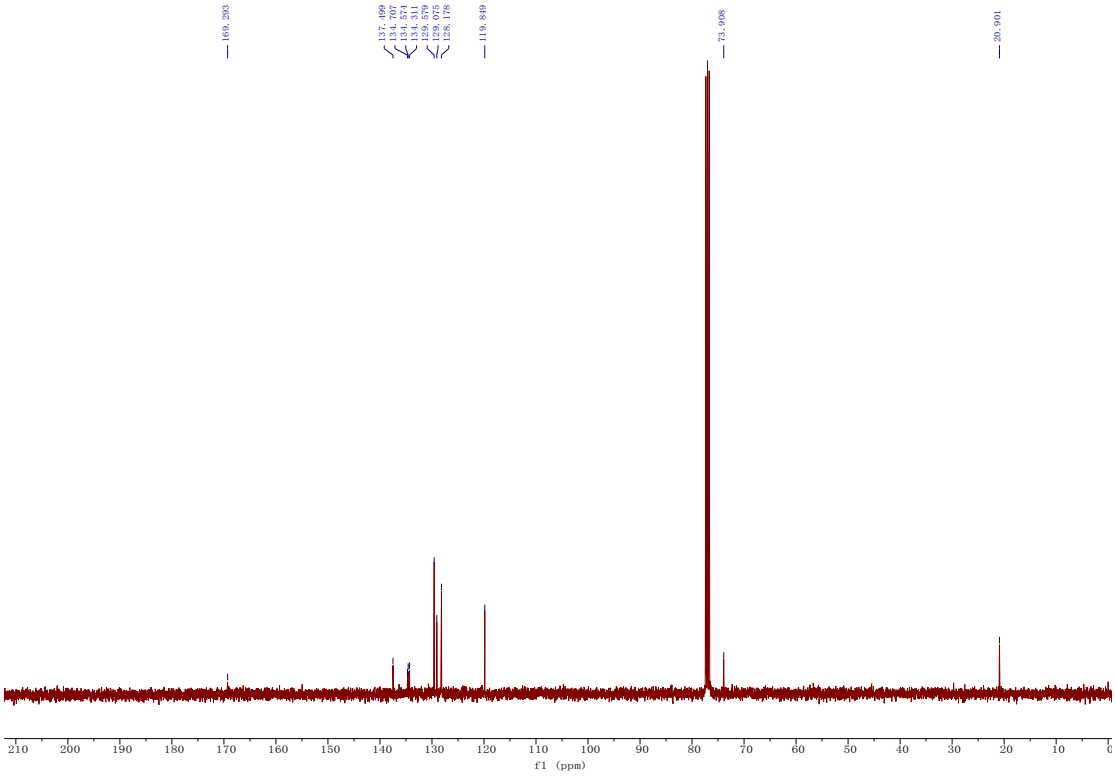

8.001
7.400
7.379
7.357
7.337
7.269
7.206
7.186
7.118
7.097
5.125
5.120
3.434
3.428
2.351
2.304
1.595
OH
H
N
O
2aw
0.96
1.92
1.92
1.94
1.94
1.00
0.94
2.98
3.00
f1 (ppm)

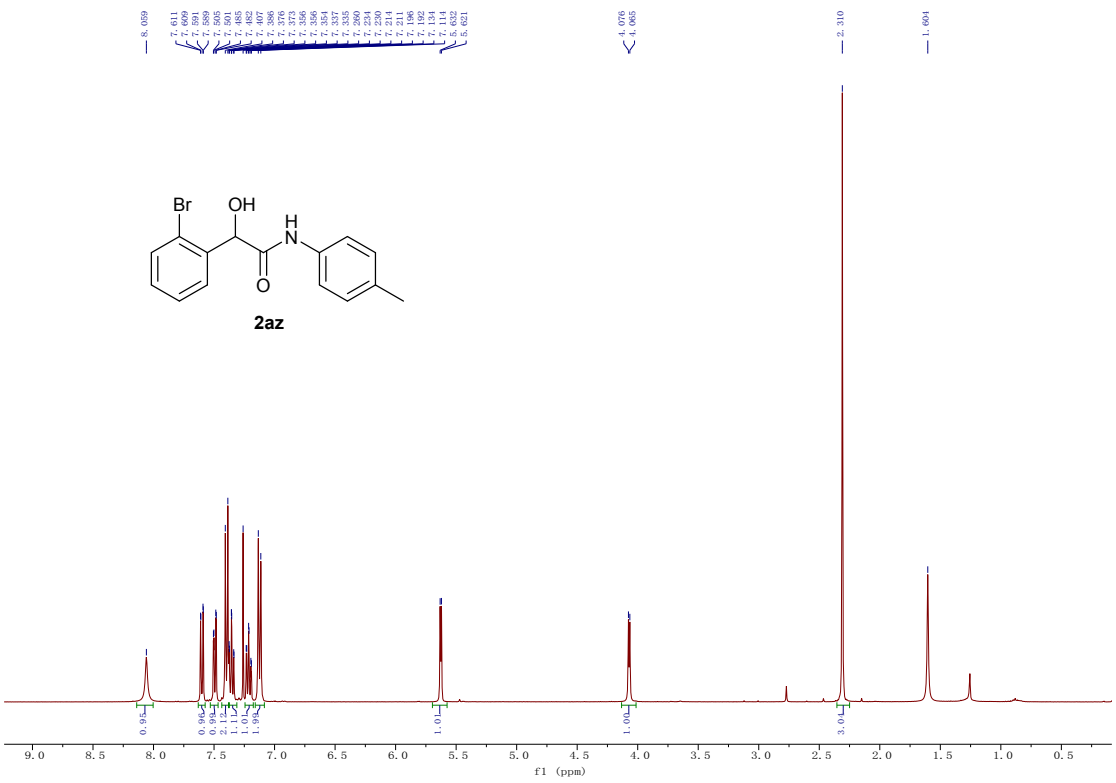

169.973
138.804
136.115
134.553
134.320
129.688
129.515
126.889
119.794
77.343
76.708
71.530
21.218
20.882
0.014
f1 (ppm)

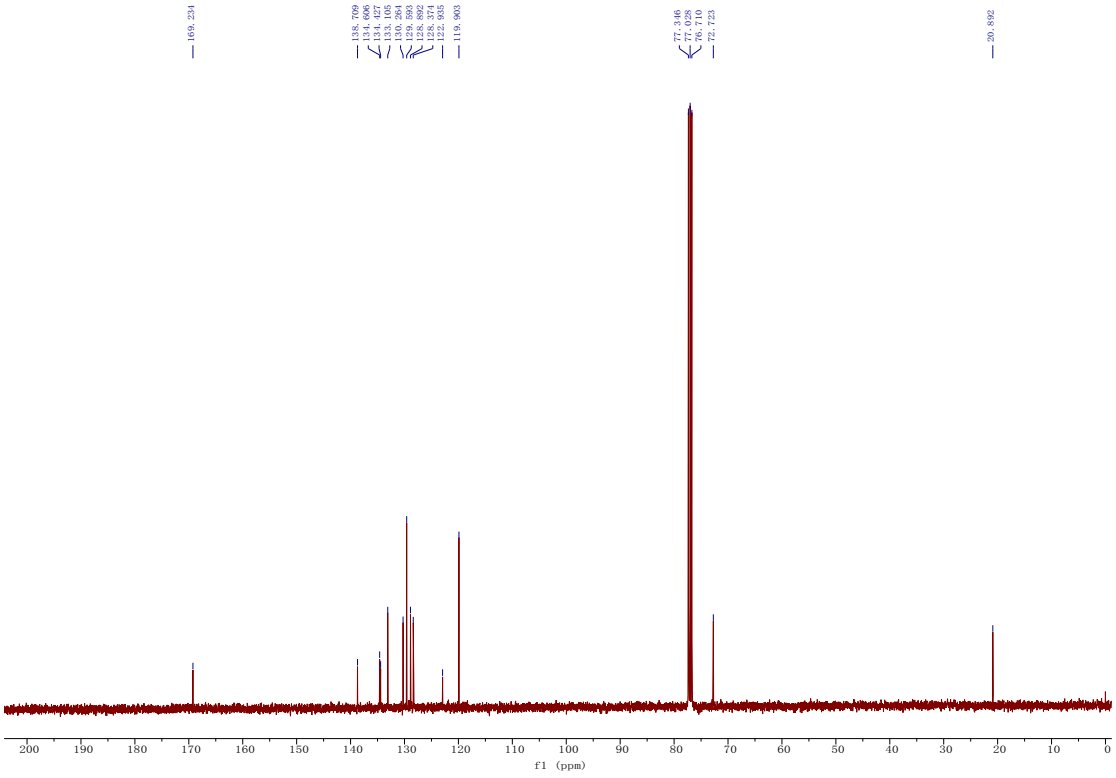

8.030
7.403
7.396
7.382
7.364
7.290
7.171
7.150
6.919
6.897
5.108
5.102
3.803
3.446
3.439
2.305
1.697
OH
H
N
O
H3CO
2ax
f1 (ppm)


170.111
160.028
134.553
134.335
131.240
129.534
128.350
119.802
114.401
77.342
76.706
76.270
55.351
20.879
f1 (ppm)


8.170
7.411
7.389
7.382
7.349
7.328
7.299
7.119
7.099
5.120
3.667
2.305
1.644
OH
H
N
O
Cl
2ay
1.07
5.84
2.05
1.00
1.12
3.25
f1 (ppm)

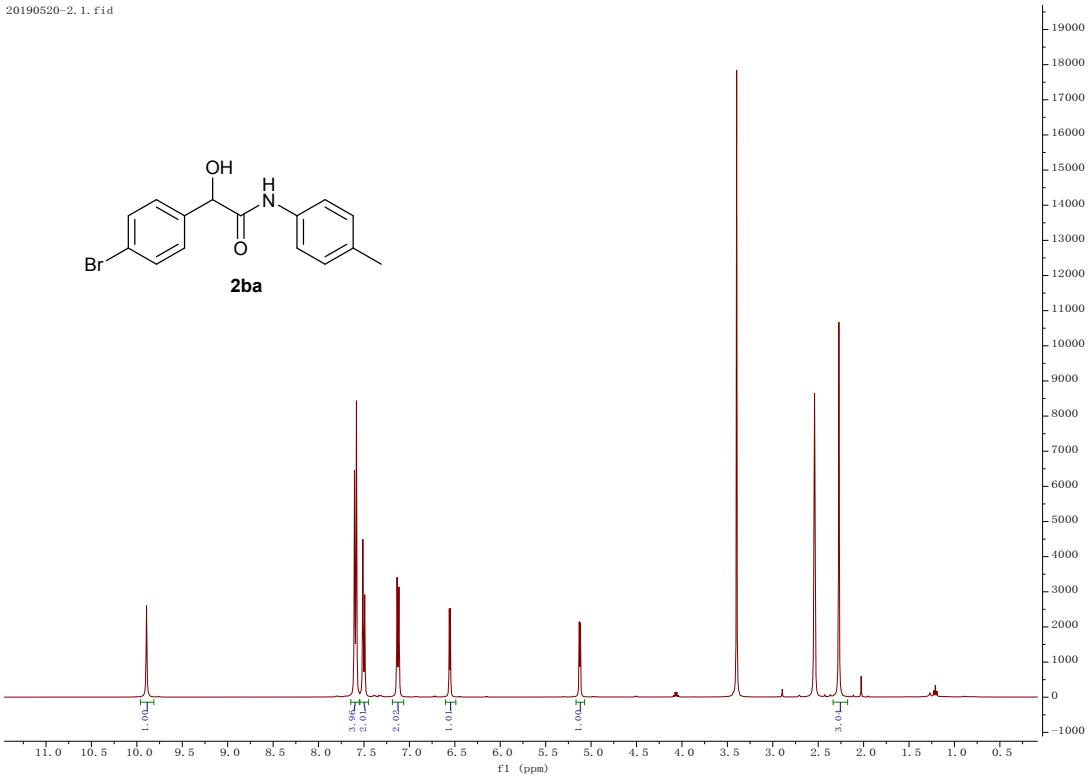

169.293
137.499
134.707
134.574
134.311
129.579
129.075
128.178
119.849
73.908
20.901
f1 (ppm)


8.059
7.611
7.609
7.591
7.588
7.505
7.501
7.485
7.482
7.407
7.386
7.376
7.373
7.356
7.356
7.354
7.337
7.335
7.260
7.234
7.230
7.214
7.211
7.196
7.192
7.134
7.114
5.632
5.621
4.076
4.065
2.310
1.604
Br
OH
H
N
O
2az
0.96
0.98
0.98
2.15
1.14
1.00
1.98
1.00
1.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

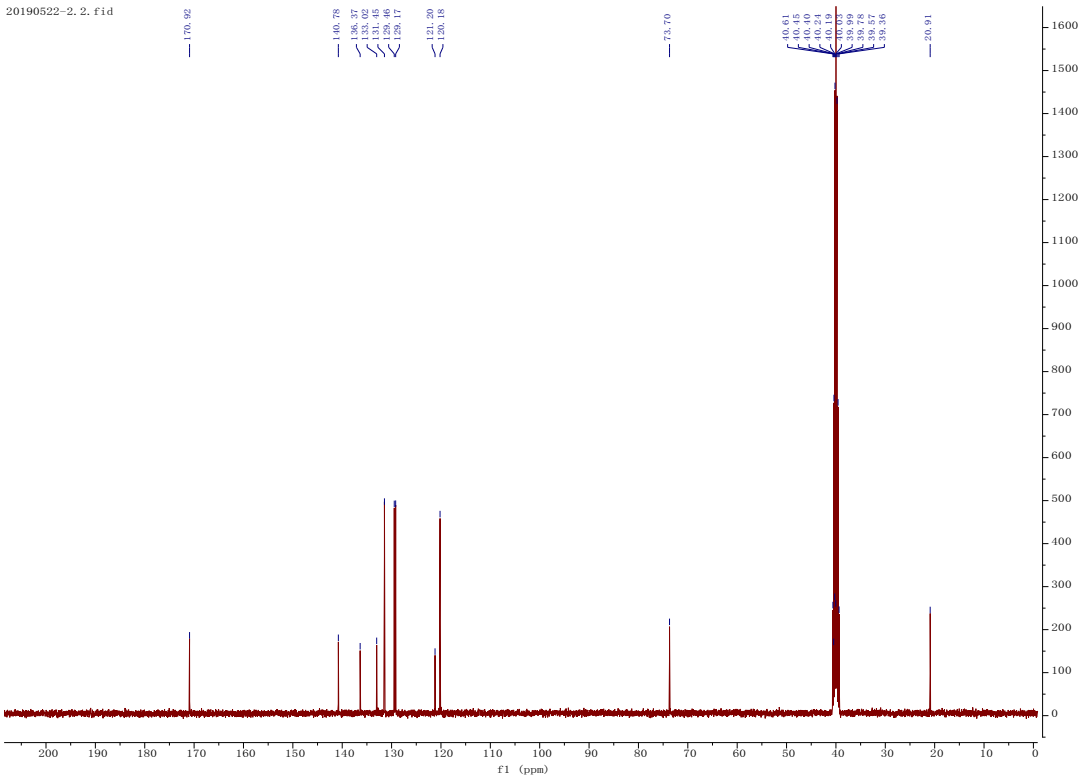

169.234
138.709
134.606
134.427
133.105
130.264
129.593
128.892
128.374
122.935
119.903
77.346
77.028
76.710
72.723
20.892
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

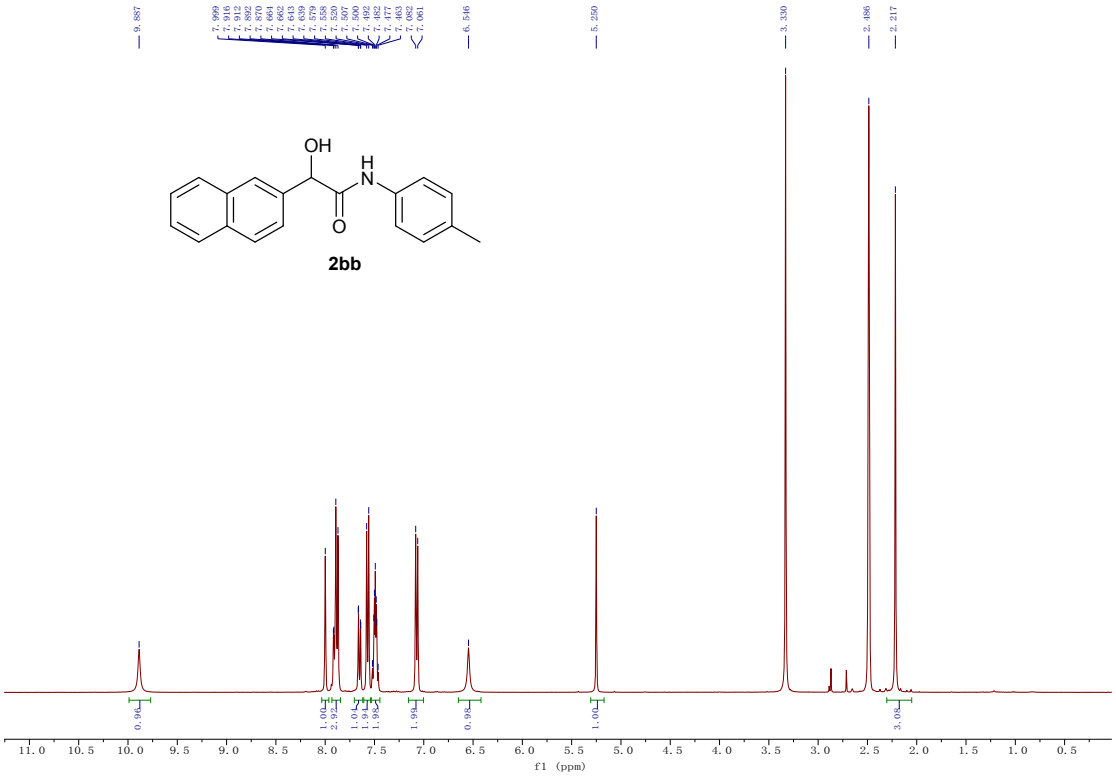
20190520-2.1.fid

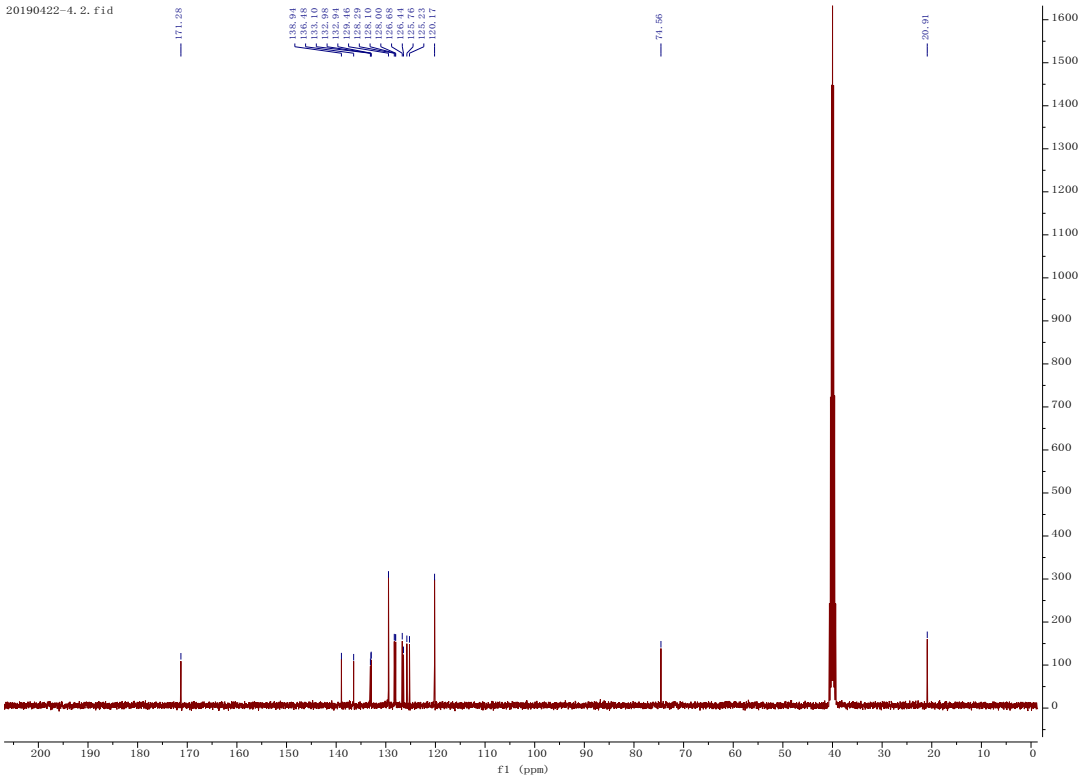
2ba

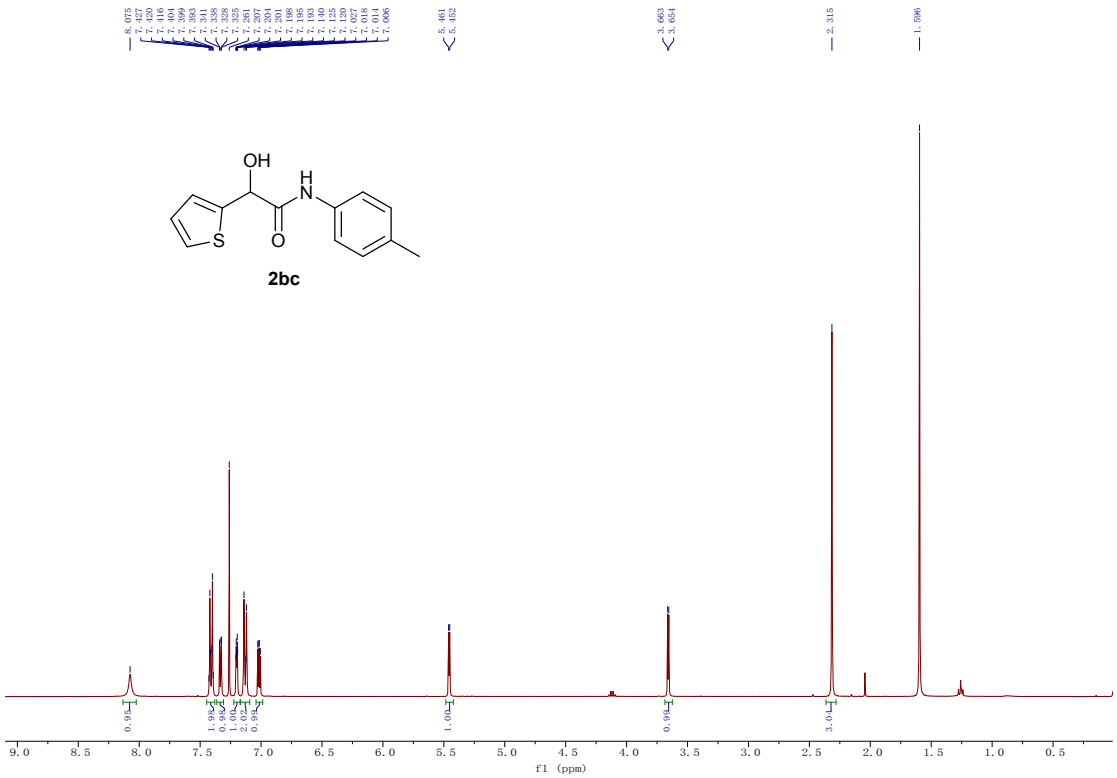


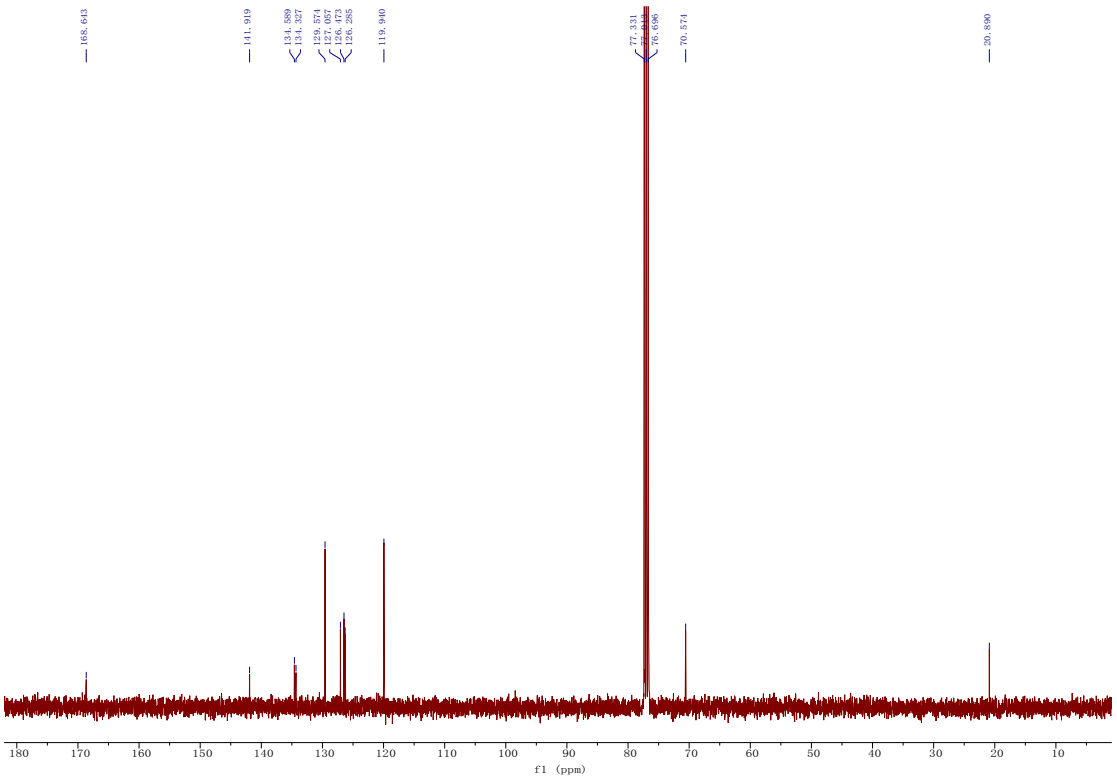
20190522-2.2.fid

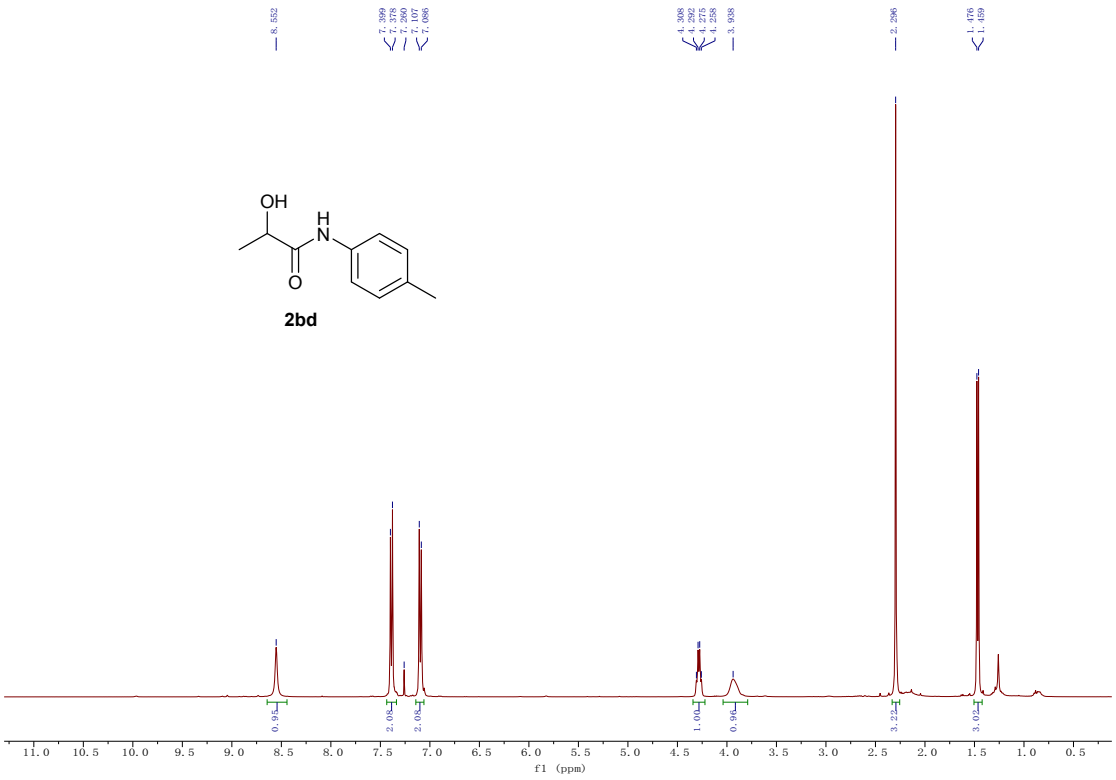


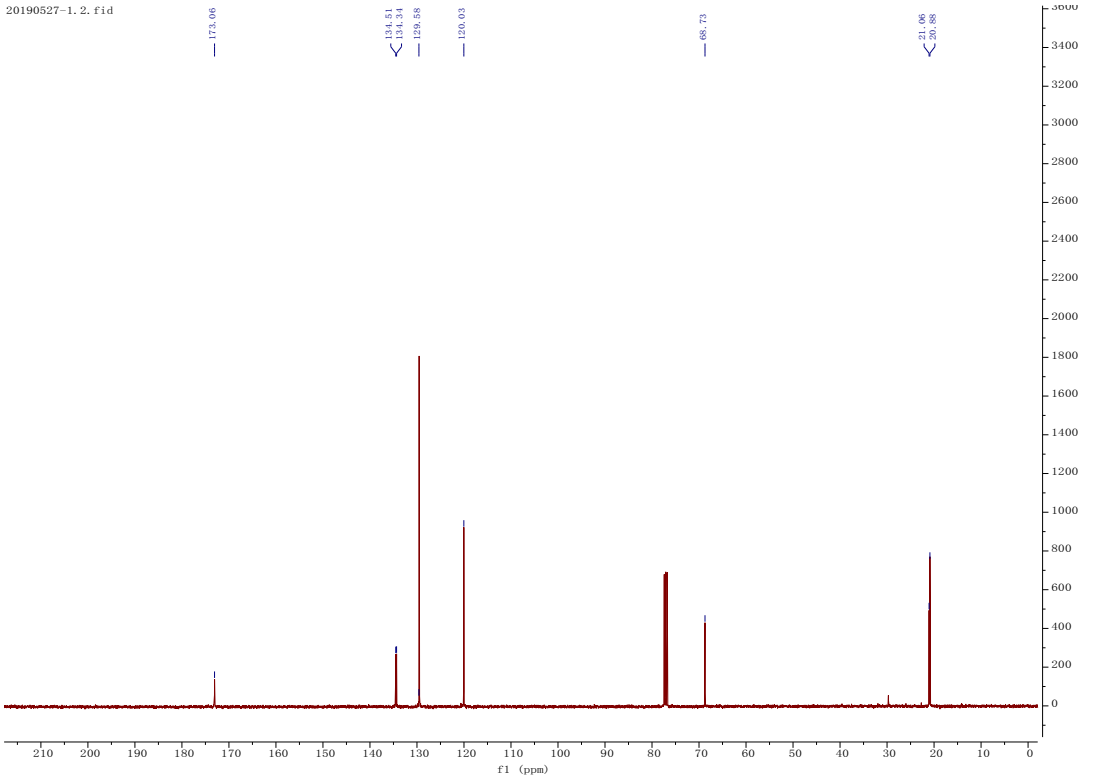

9.887
7.999
7.916
7.912
7.892
7.870
7.664
7.662
7.643
7.639
7.579
7.558
7.539
7.507
7.500
7.492
7.482
7.477
7.463
7.082
7.061
6.546
5.250
3.330
2.486
2.217
OH
H
N
O
2bb
0.96
1.00
2.92
1.01
1.94
1.98
0.98
1.00
3.08
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)


20190422-4.2.fid
171.28
138.94
136.48
133.10
132.98
132.94
130.46
128.29
128.10
128.00
126.68
126.44
125.76
125.23
120.17
74.56
20.91
1600 1500 1400 1300 1200 1100 1000 900 800 700 600 500 400 300 200 100 0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


OH
H
N
S
O
2bc
f1 (ppm)


f1 (ppm)


8.552
7.399
7.378
7.109
7.107
7.086
4.308
4.292
4.275
4.258
3.938
2.296
1.476
1.459
OH
H
N
O
2bd
0.95
2.00
2.04
1.00
0.96
3.22
3.02
f1 (ppm)


20190527-1.2.fid
173.06
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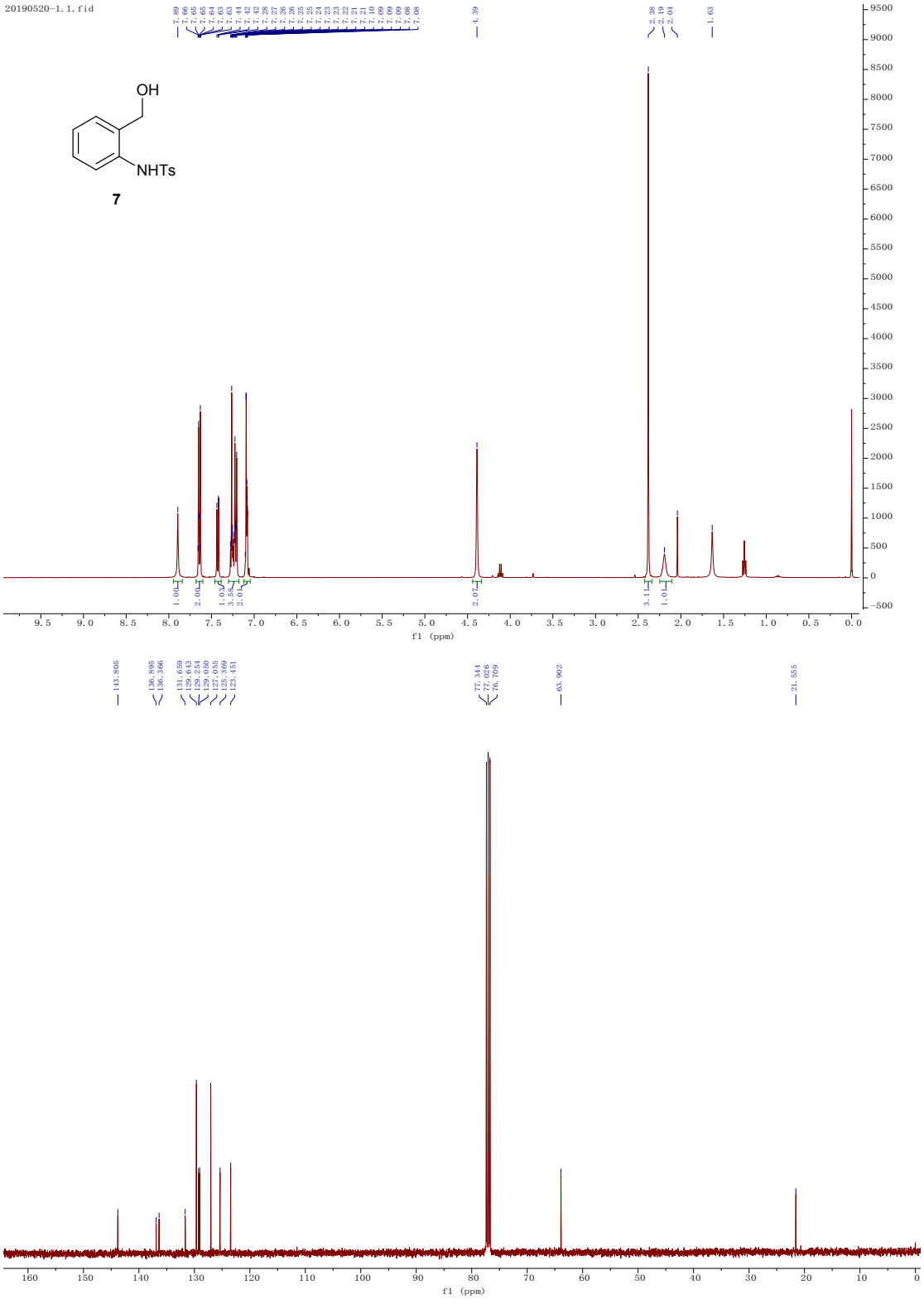
134.34
129.58
120.03
68.73
21.06
20.88
f1 (ppm)


20190520-1.1.fid
OH
NHTs
7
f1 (ppm)
f1 (ppm)