Supporting Information

Catalytic dehydrative amide bond formation using aqueous ammonia: Synthesis of primary amides utilizing diboronic acid anhydride catalysis

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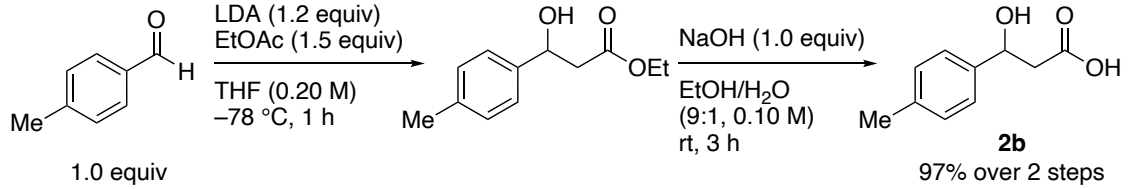
1. General information

IR spectra were recorded on an FT/IR460-plus IR spectrometer and absorbance bands are reported in wavenumber (cm^{-1}). Optical rotation was recorded on a JASCO DIP-1000 polarimeter and reported as follows: $[\alpha]_D$, concentration (g/100 mL), and solvent. NMR spectra were recorded on Agilent Technologies 400-MR DD2 (400 MHz for ^1H, 100 MHz for ^{13}C), 400-MR (400 MHz for ^1H, 100 MHz for ^{13}C), JEOL EX-270 spectrometer (270 MHz for ^1H), JEOL JNM ECP-500 spectrometer (500 MHz for ^1H, 126 MHz for ^{13}C). ^1H NMR data are reported as follows; chemical shift in parts per million (ppm) downfield or upfield from $CDCl_3$ (δ 7.26), DMSO-d_6 (δ 2.50), integration, multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, dd = double doublet, ddd = double double doublet, dt = double triplet, and m = multiplet), and coupling constants (Hz). ^{13}C NMR chemical shifts are reported in ppm downfield or upfield from $CDCl_3$ (δ 77.0) or DMSO-d_6 (δ 39.52). Mass spectra were measured with JEOL JMS-AX505HA, JMS-700 MStation, and JEOL JMS-T100LP spectrometers. Thin-layer chromatography (TLC) was carried out on Merck 60F-254 or Fuji NH KP20610 (NH) precoated silica gel plates and were visualized by fluorescence quenching under UV light. Column chromatography was performed using Silica Gel 60N (spherical, neutral, 63-210 μm) (Kanto Chemical Co., Inc.) and Silica Gel NH (Fuji Silysia Chemical LTD, HU50100, DM1020). Analytical high performance liquid chromatography (HPLC) was performed on a JASCO PU-2089 intelligent HPLC pump with JASCO UV-2075 intelligent UV/VIS detector. Detection was performed at 254 nm. CHIRALPAKR IA (f 0.46 cm × 25 cm) from Daicel were used. Retention times (t_R) and peak ratios were determined with ChromNAV. Air- and/or moisture-sensitive reactions were carried out under nitrogen atmosphere using oven-dried glassware. Aqueous ammonia (**3**) (28% solution), 3-hydroxy-3-phenylpropanoic acid (**2a**), tropic acid (**2l**), 2-hydroxy-2-phenylacetic acid (**5a**), 2-hydroxy-2-(4-methoxyphenyl)acetic acid (**5b**), 2-(4-(benzyloxy)phenyl)-2-hydroxyacetic acid (**5c**), 2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetic acid (**5d**), 2-(4-chlorophenyl)-2-hydroxyacetic acid (**5e**), 2-(3-chlorophenyl)-2-hydroxyacetic acid (**5f**), 2-(2-chlorophenyl)-2-hydroxyacetic acid (**5g**), 2-hydroxy-4-methylpentanoic acid (**5h**), 2-hydroxyoctanoic acid (**5i**), 2-hydroxy-3-phenylpropanoic acid (**5j**), 2-hydroxy-3-(1*H*-indol-3-yl)propanoic acid (**5k**) were commercially available. Diboronic acid anhydride **1**[1] and carboxylic acid **2c**[1], **2d**[1], **2e**[1], **2f**[1], **2g**[2], **2h**[1], **2i**[1], **2j**[2], **2k**[2] were synthesized according to the literatures.

2. Preparation of β-hydroxycarboxylic acid 2b

3-hydroxy-3-(*p*-tolyl)propanoic acid (2b)



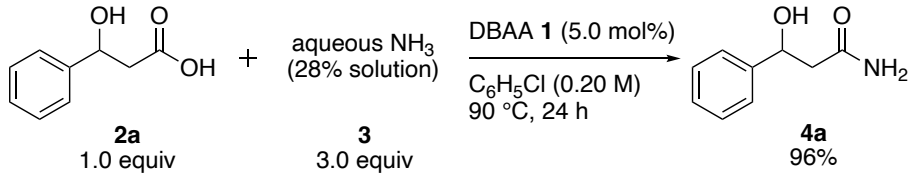
n-BuLi (3.75 mL, 1.6 M in hexane, 6.00 mmol, 1.2 equiv) was added to a stirred solution of *N*,*N*-diisopropylamine (911 μL, 6.50 mmol, 1.3 equiv) in dry THF (25.0 mL, 0.20 M) at –78 °C under nitrogen atmosphere. After stirring for 1 h, EtOAc (737 μL, 7.50 mmol, 1.5 equiv) was added to the solution at –78 °C and stirred for an additional 1 h. To this solution, *p*-tolualdehyde (590 μL, 5.00 mmol, 1.0 equiv) was added. After stirring for 1 h, the reaction was poured into saturated NH_4Cl aq and the mixture was extracted with EtOAc (30.0 mL×3). The combined organic layer was washed with brine (30.0 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was subjected to the next step without further purification.

A solution of 1 M NaOH aq (5.00 mL, 5.00 mmol, 1.0 equiv) was added to a solution of the crude product in EtOH (45.0 mL). After stirring for 3 h at room temperature, organic solvent was removed under reduced pressure and the mixture was washed with Et_2O (5.00 mL×2). Aqueous layer was acidified to pH 2 with 1 M HCl aq and extracted with Et_2O (10.0 mL×3). The combined organic layer was washed with brine (30.0 mL) and dried over Na_2SO_4. Filtration and concentration under reduced pressure furnished crude product, which was purified by trituration with Et_2O/*n*-hexane to give 3-hydroxy-3-(*p*-tolyl)propanoic acid (**2b**) (873 mg, 4.84 mmol, 97%) as a white solid.

Data for **2b**: white solid; R_f = 0.42 ($CHCl_3$/MeOH = 19:1); IR (KBr) ν = 3267, 2925, 2652, 1709, 1421, 1268, 1160, 1053, 1011, 881, 817 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.22 (d, J = 7.6 Hz, 2H), 7.11 (d, J = 7.6 Hz, 2H), 4.88 (t, J = 7.2 Hz, 1H), 2.51–2.48 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 142.2, 136.2, 128.8, 125.9, 69.5, 44.8, 20.8; HRMS (ESI) m/z calcd for $C_{10}H_{11}O_3$ $[M–H]^-$ 179.0708, found 179.0705.

3. Procedure for the catalytic amidation of *β*-hydroxycarboxylic acids and characterization of *β*-hydroxy primary amides (Table 1, Scheme 1A)

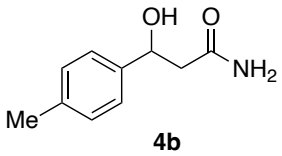
3-hydroxy-3-phenylpropanamide (4a)[3]



Diboronic acid anhydride **1** (5.39 mg, 10.0 μmol, 5.00 mol%) was added to a solution of 3-hydroxy-3-phenylpropanoic acid (**2a**) (33.2 mg, 0.200 mmol, 1.0 equiv) and aqueous NH_3 (**3**) (28% solution, 36.5 mg, 0.600 mmol, 3.0 equiv) in C_6H_5Cl (1.00 mL, 0.20 M) at room temperature. After stirring for 24 h at 90 °C, the reaction mixture was cooled to room temperature. Concentration under reduced pressure furnished the crude product, which was purified by amino silica gel column chromatography (10% MeOH in $CHCl_3$) to give 3-hydroxy-3-phenylpropanamide (**4a**) (31.7 mg, 0.192 mmol, 96%) as a white solid.

Data for **4a**; white solid; R_f = 0.29 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3691, 3337, 3031, 1774, 1623, 889, 802, 747, 703 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.35–7.29 (m, 5H), 7.24–7.19 (m, 1H), 6.82 (br s, 1H), 5.36 (d, J = 4.4 Hz, 1H), 4.94 (dt, J = 8.8, 4.4 Hz, 1H), 2.42 (dd, J = 14.4, 8.8 Hz, 1H), 2.33 (dd, J = 14.4, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 145.5, 128.0, 126.8, 125.7, 69.6, 45.4; HRMS (ESI) m/z calcd for $C_9H_{11}NNaO_2$ $[M+Na]^+$ 188.0688, found 188.0683

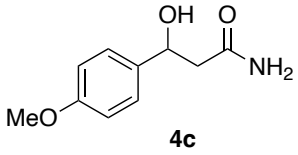
3-hydroxy-3-(*p*-tolyl)propanamide (4b)[4]



4b

Compound **4b** was prepared according to the procedure for **4a** from 3-hydroxy-3-(*p*-tolyl)propanoic acid (**2b**) (36.0 mg, 0.200 mmol) for 48 h. Yield >99% (35.7 mg, 0.199 mmol). Data for **4b**; white solid; R_f = 0.29 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3381, 1658, 1622, 1440, 1402, 916, 891, 813, 612, 580, 523, 434 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.27 (br s, 1H), 7.21 (d, J = 8.0 Hz, 2H), 7.11 (d, J = 8.0 Hz, 2H), 6.80 (br s, 1H), 5.29 (d, J = 4.4 Hz, 1H), 4.90 (dt, J = 8.8, 4.4 Hz, 1H), 2.40 (dd, J = 14.4, 8.8 Hz, 1H), 2.30 (dd, J = 14.4, 4.4 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.4, 142.5, 135.8, 128.6, 125.7, 69.5, 45.4, 20.7; HRMS (ESI) m/z calcd for $C_{10}H_{13}NNaO_2$ $[M+Na]^+$ 202.0844, found 202.0836.

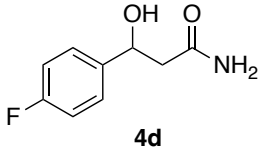
3-hydroxy-3-(4-methoxyphenyl)propanamide (4c)[4]



4c

Compound **4c** was prepared according to the procedure for **4a** from 3-hydroxy-3-(4-methoxyphenyl)propanoic acid (**2c**) (39.2 mg, 0.200 mmol) at 110 °C. Yield 93% (36.3 mg, 0.186 mmol). Data for **4c**; white solid; R_f = 0.34 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3753, 3380, 2959, 1622, 1440, 1402, 1252, 1069, 917, 890, 822, 774, 607, 531, 416 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.25–7.23 (m, 3H), 6.88–6.85 (m, 2H), 6.79 (br s, 1H), 5.25 (d, J = 4.4 Hz, 1H), 4.88 (dt, J = 8.8, 4.4 Hz, 1H), 3.73 (s, 3H), 2.41 (dd, J = 14.4, 8.8 Hz, 1H), 2.30 (dd, J = 14.4, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 158.2, 137.4, 126.9, 113.4, 69.2, 55.0, 45.4; HRMS (ESI) m/z calcd for $C_{10}H_{13}NNaO_3$ $[M+Na]^+$ 218.0793, found 218.0803.

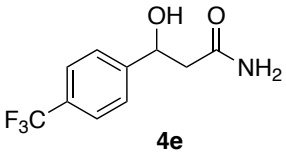
3-(4-fluorophenyl)-3-hydroxypropanamide (4d)[5]



4d

Compound **4d** was prepared according to the procedure for **4a** from 3-(4-fluorophenyl)-3-hydroxypropanoic acid (**2d**) (36.8 mg, 0.200 mmol) for 48 h. Yield 95% (34.8 mg, 0.190 mmol). Data for **4d**; white solid; R_f = 0.37 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3335, 1679, 1621, 1410, 895, 834, 792, 662, 565, 526, 448 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.38–7.34 (m, 2H), 7.29 (br s, 1H), 7.15–7.10 (m, 2H), 6.83 (br s, 1H), 5.42 (d, J = 4.8 Hz, 1H), 4.93 (dt, J = 8.8, 4.8 Hz, 1H), 2.41 (dd, J = 14.4, 8.8 Hz, 1H), 2.32 (dd, J = 14.4, 4.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.2, 161.1 (d, $^1J_{C\text{-}F}$ = 240.3 Hz), 141.6 (d, $^4J_{C\text{-}F}$ = 3.0 Hz), 127.7 (d, $^3J_{C\text{-}F}$ = 8.0 Hz), 114.7 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 69.0, 45.4; HRMS (ESI) m/z calcd for $C_9H_{11}FNO_2$ $[M+H]^+$ 184.0774, found 184.0777.

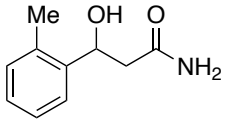
3-hydroxy-3-(4-(trifluoromethyl)phenyl)propanamide (4e)



4e

Compound **4e** was prepared according to the procedure for **4a** from 3-hydroxy-3-(4-(trifluoromethyl)phenyl)propanoic acid (**2e**) (46.8 mg, 0.200 mmol) for 48 h. Yield 78% (36.4 mg, 0.156 mmol). Data for **4e**; white solid; R_f = 0.37 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3427, 2979, 1656, 1515, 1463, 1380, 1263, 1183, 1072, 988, 861, 809, 734, 677, 590 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.68 (d, J = 8.0 Hz, 2H), 7.56 (d, J = 8.0 Hz, 2H), 7.31 (br s, 1H), 6.85 (br s, 1H), 5.59 (d, J = 4.4 Hz, 1H), 5.03 (dt, J = 8.8, 4.4 Hz, 1H), 2.44 (dd, J = 14.4, 8.8 Hz, 1H), 2.37 (dd, J = 14.4, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.7, 150.0, 127.4 (q, $^2J_{C\text{-}F}$ = 31.3 Hz), 127.1 (q, $^1J_{C\text{-}F}$ = 269.7 Hz), 126.5, 124.9 (q, $^3J_{C\text{-}F}$ = 3.6 Hz), 68.9, 45.0; HRMS (ESI) m/z calcd for $C_{10}H_{10}F_3NNaO_2$ $[M+Na]^+$ 256.5613, found 256.0574.

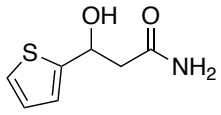
3-hydroxy-3-(*o*-tolyl)propanamide (4f)



4f

Compound **4f** was prepared according to the procedure for **4a** from 3-hydroxy-3-(*o*-tolyl)propanoic acid (**2f**) (36.0 mg, 0.200 mmol). Yield 86% (30.8 mg, 0.172 mmol). Data for **4f**; white solid; R_f = 0.34 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3350, 1675, 1618, 1451, 1409, 888, 826, 766, 728, 698 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.44–7.42 (m, 1H), 7.30 (br s, 1H), 7.19–7.10 (m, 3H), 6.83 (br s, 1H), 5.22 (d, J = 4.4 Hz, 1H), 5.14 (dt, J = 8.8, 4.4 Hz, 1H), 2.34 (dd, J = 14.4, 8.8 Hz, 1H), 2.29 (s, 3H), 2.27 (dd, J = 14.4, 4.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.5, 143.4, 133.8, 129.9, 126.5, 125.7, 125.4, 66.3, 44.0, 18.6; HRMS (ESI) m/z calcd for $C_{10}H_{13}NNaO_2$ $[M+Na]^+$ 202.0844, found 202.0852.

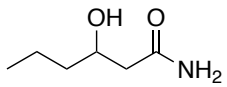
3-hydroxy-3-(thiophen-2-yl)propanamide (4g)[4]



4g

Compound **4g** was prepared according to the procedure for **4a** from 3-hydroxy-3-(thiophen-2-yl)propanoic acid (**2g**) (34.4 mg, 0.200 mmol) at 110 °C. Yield 95% (32.5 mg, 0.190 mmol). Data for **4g**; white solid; R_f = 0.29 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3390, 3187, 1657, 1618, 1438, 1404, 825, 706 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.38–7.36 (m, 1H), 7.34 (br s, 1H), 6.95–6.93 (m, 2H), 6.86 (br s, 1H), 5.74 (d, J = 5.0 Hz, 1H), 5.17 (dt, J = 8.0, 5.0 Hz, 1H), 2.51 (dd, J = 14.5, 8.0 Hz, 1H), 2.44 (dd, J = 14.5, 5.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.8, 150.0, 126.5, 124.1, 122.7, 65.8, 45.4; HRMS (ESI) m/z calcd for $C_7H_{10}NO_2S$ $[M+H]^+$ 172.0432, found 172.0428.

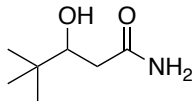
3-hydroxyhexanamide (4h)



4h

Compound **4h** was prepared according to the procedure for **4a** from 3-hydroxyhexanoic acid (**2h**) (26.4 mg, 0.200 mmol) at 110 °C. Yield 81% (21.3 mg, 0.162 mmol). Data for **4h**; colorless oil; R_f = 0.26 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3586, 2964, 2877, 2817, 1667, 1530, 1423 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.25 (br s, 1H), 6.78 (br s, 1H), 4.58 (d, J = 4.5 Hz, 1H), 3.81–3.75 (m, 1H), 2.12 (d, J = 7.0 Hz, 2H), 1.42–1.23 (m, 4H), 0.87–0.84 (m, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.3, 67.1, 43.4, 39.2, 18.3, 14.1; HRMS (ESI) m/z calcd for $C_6H_{13}NNaO_2$ $[M+Na]^+$ 154.0844, found 154.0849.

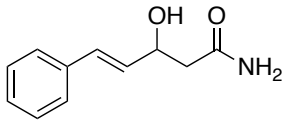
3-hydroxy-4,4-dimethylpentanamide (4i)[3]



4i

Compound **4i** was prepared according to the procedure for **4a** from 3-hydroxy-4,4-dimethylpentanoic acid (**2i**) (29.2 mg, 0.200 mmol). Yield 95% (27.6 mg, 0.190 mmol). Data for **4i**; white solid; R_f = 0.31 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3375, 3191, 1672, 1617, 1389, 1363 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.28 (br s, 1H), 6.81 (br s, 1H), 4.67 (d, J = 5.2 Hz, 1H), 3.49 (ddd, J = 12.0, 5.2, 2.8 Hz, 1H), 2.17 (dd, J = 14.4, 2.8 Hz, 1H), 1.99 (dd, J = 14.4, 12.0 Hz, 1H), 0.81 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.4, 74.8, 37.7, 34.5, 25.8; HRMS (ESI) m/z calcd for $C_7H_{16}NO_2$ $[M+H]^+$ 146.1181, found 146.1184.

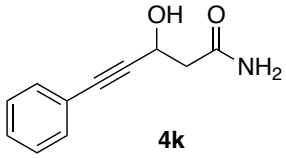
(*E*)-3-hydroxy-5-phenylpent-4-enamide (4j)[6]



4j

Compound **4j** was prepared according to the procedure for **4a** from (*E*)-3-hydroxy-5-phenylpent-4-enoic acid (**2j**) (38.4 mg, 0.200 mmol). Yield 95% (36.3 mg, 0.190 mmol). Data for **4j**; white solid; R_f = 0.45 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3356, 1665, 1619, 877, 746, 692, 627 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.40 (d, J = 8.4 Hz, 2H), 7.34–7.30 (m, 3H), 7.22 (t, J = 7.2 Hz, 1H) 6.84 (br s, 1H), 6.54 (d, J = 16.0 Hz, 1H), 6.30 (dd, J = 16.0, 5.6 Hz, 1H), 5.13 (d, J = 4.8 Hz, 1H), 4.55–4.49 (m, 1H), 2.30 (dd, J = 14.0, 7.6 Hz, 1H), 2.26 (dd, J = 14.0, 6.0 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 172.3, 136.8, 133.4, 128.6, 128.0, 127.3, 126.2, 68.2, 43.6; HRMS (ESI) m/z calcd for $C_{11}H_{14}NO_2$ $[M+H]^+$ 192.1025, found 192.1022.

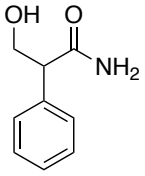
3-hydroxy-5-phenylpent-4-ynamide (4k)



4k

Compound **4k** was prepared according to the procedure for **4a** from 3-hydroxy-5-phenylpent-4-ynoic acid (**2k**) (38.0 mg, 0.200 mmol). Yield 79% (29.9 mg, 0.158 mmol). Data for **4k**; white solid; R_f = 0.42 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3357, 3049, 1952, 1665, 1617, 897, 873, 826, 751, 690, 669 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.40–7.36 (m, 6H), 6.91 (br s, 1H), 5.66 (d, J = 5.6 Hz, 1H), 4.80 (dt, J = 7.6, 5.6 Hz, 1H), 2.51 (dd, J = 14.0, 7.6 Hz, 1H), 2.45 (dd, J = 14.0, 5.6 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 171.0, 131.3, 128.7, 128.5, 122.4, 91.8, 82.9, 58.3, 44.0; HRMS (ESI) m/z calcd for $C_{11}H_{12}NO_2$ $[M+H]^+$ 190.0868, found 190.0870.

3-hydroxy-2-phenylpropanamide (4l)

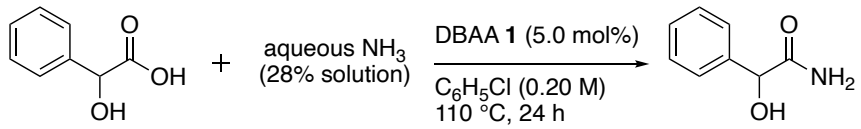


4l

Compound **4l** was prepared according to the procedure for **4a** from 3-hydroxy-2-phenylpropanoic acid (**2l**) (33.2 mg, 0.200 mmol) at 110 °C. Yield 72% (23.8 mg, 0.144 mmol). Data for **4l**; white solid; R_f = 0.21 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3369, 3186, 1679, 1660, 1631, 1244, 885, 835, 753, 708, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.46 (br s, 1H), 7.30–7.24 (m, 4H), 7.23–7.21 (m, 1H), 6.85 (br s, 1H), 4.76 (t, J = 5.2 Hz, 1H), 3.92 (m, 1H), 3.57–3.46 (m, 2H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 173.7, 138.7, 128.2, 128.0, 126.7, 63.3, 54.2; HRMS (ESI) m/z calcd for $C_9H_{12}NO_2$ $[M+H]^+$ 168.0868, found 168.0868.

4. Procedure for the catalytic amidation of α-hydroxycarboxylic acids and characterization of α-hydroxy primary amides (Scheme 1B)

2-hydroxy-2-phenylacetamide (6a)[7]

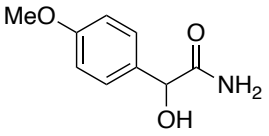


5a 1.0 equiv | **3** 3.0 equiv | **6a** 81%

Diboronic acid anhydride **1** (5.39 mg, 10.0 μmol, 5.00 mol%) was added to a solution of 2-hydroxy-2-phenylacetic acid (**5a**) (30.4 mg, 0.200 mmol, 1.0 equiv) and aqueous NH_3 (**3**) (28% solution, 36.5 mg, 0.600 mmol, 3.0 equiv) in C_6H_5Cl (1.00 mL, 0.20 M) at room temperature. After stirring for 24 h at 110 °C, the reaction mixture was cooled to room temperature. Concentration under reduced pressure furnished the crude product, which was purified by amino silica gel column chromatography (10% MeOH in $CHCl_3$) to give 2-hydroxy-2-phenylacetamide (**6a**) (24.6 mg, 0.163 mmol, 81%) as a white solid.

Data for **6a**; white solid; R_f = 0.26 ($CHCl_3$/MeOH = 10:1); IR (KBr) ν = 3390, 3261, 1640, 1181, 1109, 1059, 923, 752, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.43–7.26 (m, 6H), 7.18 (br s, 1H), 6.01 (d, J = 4.8 Hz, 1H), 4.83 (d, J = 4.8 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 174.6, 141.4, 127.9, 127.3, 126.5, 73.5; HRMS (ESI) m/z calcd for $C_8H_{10}NO_2$ $[M+H]^+$ 152.0712, found 152.0715.

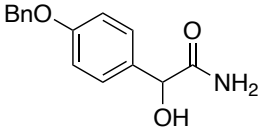
2-hydroxy-2-(4-methoxyphenyl)acetamide (6b)[8]



6b

Compound **6b** was prepared according to the procedure for **6a** from 2-hydroxy-2-(4-methoxyphenyl)acetic acid (**5b**) (36.4 mg, 0.200 mmol) using 10 mol% of **1**. Yield 88% (32.0 mg, 0.177 mmol). Data for **6b**; white solid; R_f = 0.34 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3389, 3262, 1656, 1513, 1254, 1182, 1058, 826, 673 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.33–7.31 (m, 3H), 7.13 (br s, 1H), 6.87 (d, J = 9.0 Hz, 2H), 5.87 (d, J = 4.5 Hz, 1H), 4.77 (d, J = 4.5 Hz, 1H), 3.73 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 174.9, 158.6, 133.5, 127.7, 113.3, 73.0, 55.1; HRMS (ESI) m/z calcd for $C_9H_{11}NNaO_3$ $[M+Na]^+$ 204.0637, found 204.0629.

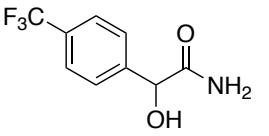
2-(4-(benzyloxy)phenyl)-2-hydroxyacetamide (6c)



6c

Compound **6c** was prepared according to the procedure for **6a** from 2-(4-(benzyloxy)phenyl)-2-hydroxyacetic acid (**5c**) (51.6 mg, 0.200 mmol) using 10 mol% of **1**. Yield 80% (41.0 mg, 0.159 mmol). Data for **6c**; white solid; R_f = 0.14 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3386, 1644, 1420, 1250, 1059, 822, 699 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.43 (d, J = 7.0 Hz, 2H), 7.38 (t, J = 7.0 Hz, 2H), 7.34–7.30 (m, 3H), 7.22 (br s, 1H), 7.13 (br s, 1H), 6.95 (d, J = 9.0 Hz, 2H), 5.89 (d, J = 4.5 Hz, 1H), 5.09 (s, 2H), 4.77 (d, J = 4.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 174.9, 157.7, 137.2, 133.8, 128.5, 127.8, 127.7, 127.6, 114.2, 73.0, 69.2; HRMS (ESI) m/z calcd for $C_{15}H_{15}NNaO_3$ $[M+Na]^+$ 280.0950, found 280.0951.

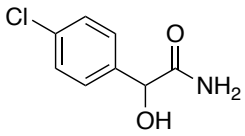
2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetamide (6d)[8]



6d

Compound **6d** was prepared according to the procedure for **6a** from 2-hydroxy-2-(4-(trifluoromethyl)phenyl)acetic acid (**5d**) (44.0 mg, 0.200 mmol). Yield 97% (42.3 mg, 0.193 mmol). Data for **6d**; yellow solid; R_f = 0.33 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3384, 3291, 1648, 1328, 1027, 662 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.70 (d, J = 8.5 Hz, 2H), 7.65 (d, J = 8.5 Hz, 2H), 7.49 (br s, 1H), 7.27 (br s, 1H), 6.27 (d, J = 4.5 Hz, 1H), 4.97 (d, J = 4.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 173.9, 146.0, 128.0 (q, $^2J_{C–F}$ = 31.2 Hz), 127.1, 124.8 (q, $^3J_{C–F}$ = 3.7 Hz), 124.4 (q, $^1J_{C–F}$ = 272.9 Hz), 72.8; HRMS (ESI) m/z calcd for $C_9H_8F_3NNaO_2$ $[M+Na]^+$ 242.0405, found 242.0393.

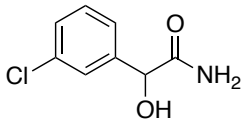
2-(4-chlorophenyl)-2-hydroxyacetamide (6e)[8]



6e

Compound **6e** was prepared according to the procedure for **6a** from 2-(4-chlorophenyl)-2-hydroxyacetic acid (**5e**) (37.3 mg, 0.200 mmol). Yield 85% (31.4 mg, 0.169 mmol). Data for **6e**; white solid; R_f = 0.34 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3401, 3260, 1639, 1409, 1065, 821, 634 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.46–7.43 (m, 3H), 7.38 (d, J = 8.5 Hz, 2H), 7.22 (br s, 1H), 6.13 (br s, 1H), 4.86 (s, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 174.2, 140.4, 131.9, 128.3, 127.9, 72.7; HRMS (ESI) m/z calcd for $C_8H_8ClNNaO_2$ $[M+Na]^+$ 208.0141, found 208.0146.

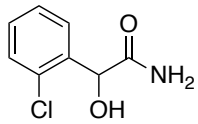
2-(3-chlorophenyl)-2-hydroxyacetamide (6f)[8]



6f

Compound **6f** was prepared according to the procedure for **6a** from 2-(3-chlorophenyl)-2-hydroxyacetic acid (**5f**) (37.3 mg, 0.200 mmol). Yield 87% (32.2 mg, 0.173 mmol) using 10 mol% of **1**. Data for **6f**; yellow solid; R_f = 0.34 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3405, 3264, 1641, 1418, 1190, 1068, 695 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.47–7.45 (m, 2H), 7.38–7.37 (m, 1H), 7.36 (s, 1H), 7.34–7.33 (m, 1H), 7.23 (br s, 1H), 6.17 (d, J = 4.5 Hz, 1H), 4.87 (d, J = 4.5 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 174.0, 143.9, 132.6, 129.8, 127.2, 126.2, 125.1, 72.7; HRMS (ESI) m/z calcd for $C_8H_8ClNNaO_2$ $[M+Na]^+$ 208.0141, found 208.0144.

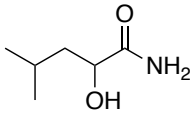
2-(2-chlorophenyl)-2-hydroxyacetamide (6g)[8]



6g

Compound **6g** was prepared according to the procedure for **6a** from 2-(2-chlorophenyl)-2-hydroxyacetic acid (**5g**) (37.3 mg, 0.200 mmol) using 10 mol% of **1**. Yield 86% (31.8 mg, 0.171 mmol). Data for **6g**; yellow solid; R_f = 0.23 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3390, 3228, 1648, 1441, 1320, 1195, 1091, 754, 661 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.47–7.45 (m, 2H), 7.41 (dd, J = 8.0, 1.5 Hz, 1H), 7.35–7.30 (m, 3H), 6.24 (d, J = 5.0 Hz, 1H), 5.24 (d, J = 5.0 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 173.7, 139.2, 132.7, 129.2, 129.1, 128.9, 127.1, 70.3; HRMS (ESI) m/z calcd for $C_8H_8ClNNaO_2$ $[M+Na]^+$ 208.0141, found 208.0140.

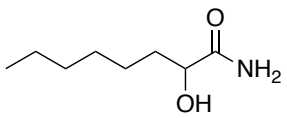
2-hydroxy-4-methylpentanamide (6h)[9]



6h

Compound **6h** was prepared according to the procedure for **6a** from 2-hydroxy-4-methylpentanoic acid (**5h**) (26.4 mg, 0.200 mmol) using 10 mol% of **1**. Yield 88% (23.1 mg, 0.176 mmol). Data for **6h**; white solid; R_f = 0.20 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3395, 2957, 1655, 1324, 1076, 670 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.14 (br s, 1H), 7.03 (br s, 1H), 5.25 (d, J = 5.0 Hz, 1H), 3.78 (dt, J = 9.0, 5.0, 4.0 Hz, 1H), 1.81–1.71 (m, 1H), 1.44–1.32 (m, 2H), 0.88 (d, J = 2.0 Hz, 3H), 0.87 (d, J = 2.0 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 177.2, 69.5, 43.4, 24.0, 23.5, 21.5; HRMS (ESI) m/z calcd for $C_6H_{13}NNaO_2$ $[M+Na]^+$ 154.0844, found 154.0839.

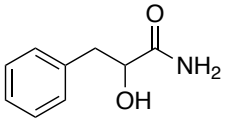
2-hydroxyoctanamide (6i)



6i

Compound **6i** was prepared according to the procedure for **6a** from 2-hydroxyoctanoic acid (**5i**) (32.0 mg, 0.200 mmol) using 10 mol% of **1**. Yield 78% (24.8 mg, 0.156 mmol). Data for **6i**; white solid; R_f = 0.23 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3384, 3288, 2919, 1639, 1424, 1027, 662 cm^{-1}; ^1H NMR (270 MHz, DMSO-d_6) δ 7.11 (br s, 1H), 7.05 (br s, 1H), 5.23 (d, J = 5.4 Hz, 1H), 3.78–3.72 (m, 1H), 1.63–1.54 (m, 1H), 1.47–1.40 (m, 1H), 1.37–1.24 (m, 8H), 0.92 (t, J = 6.2 Hz, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 176.6, 70.8, 34.3, 31.3, 28.6, 24.6, 22.1, 14.0; HRMS (ESI) m/z calcd for $C_8H_{17}NNaO_2$ $[M+Na]^+$ 182.1157, found 182.1150.

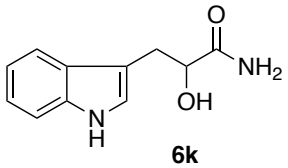
2-hydroxy-3-phenylpropanamide (6j)[8]



6j

Compound **6j** was prepared according to the procedure for **6a** from 2-hydroxy-3-phenylpropanoic acid (**5j**) (33.2 mg, 0.200 mmol) using 10 mol% of **1**. Yield 73% (24.2 mg, 0.146 mmol). Data for **6j**; yellow solid; R_f = 0.48 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3367, 1685, 1578, 1270, 1177, 1088, 1026, 1010, 873, 753, 701 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.28–7.14 (m, 7H), 5.41 (d, J = 5.6 Hz, 1H), 3.99 (ddd, J = 8.4, 5.6, 3.6 Hz, 1H), 2.97 (dd, J = 13.6, 3.6 Hz, 1H), 2.69 (dd, J = 13.6, 8.4 Hz, 1H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 175.8, 138.8, 129.5, 127.9, 126.0, 72.1, 40.3; HRMS (ESI) m/z calcd for $C_9H_{12}NO_2$ $[M+H]^+$ 166.0868, found 166.0862.

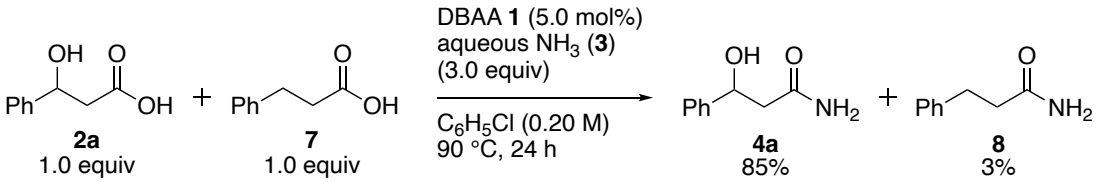
2-hydroxy-3-(1*H*-indol-3-yl)propanamide (6k)



6k

Compound **6k** was prepared according to the procedure for **6a** from 2-hydroxy-3-(1*H*-indol-3-yl)propanoic acid (**5k**) (41.0 mg, 0.200 mmol) using 10 mol% of **1**. Yield 62% (25.3 mg, 0.124 mmol). Data for **6k**; brown solid; R_f = 0.14 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3381, 1649, 1426, 1302, 1025, 741, 663 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 10.8 (br s, 1H), 7.55 (d, *J* = 8.0 Hz, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.20 (br s, 1H), 7.13 (d, *J* = 2.5 Hz, 1H) 7.10 (br s, 1H), 7.06–7.03 (m, 1H), 6.97–6.94 (m, 1H), 5.34 (d, *J* = 6.0 Hz, 1H), 4.06 (ddd, *J* = 8.0, 6.0, 4.0 Hz, 1H), 3.10 (dd, *J* = 10.0, 4.0 Hz, 1H), 2.83 (dd, *J* = 10.0, 8.0 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 176.3, 136.0, 127.7, 123.6, 120.7, 118.7, 118.1, 111.2, 110.9, 71.8, 30.4; HRMS (ESI) m/z calcd for $C_{11}H_{12}N_2NaO_2$ $[M+Na]^+$ 227.0797, found 227.0785.

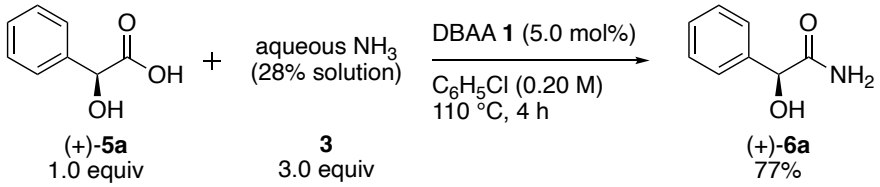
5. Procedure for the crossover experiment (Scheme 2A)



Diboronic acid anhydride **1** (5.39 mg, 10.0 μmol, 5.00 mol%) was added to a solution of 3-hydroxy-3-phenylpropanoic acid (**2a**) (33.2 mg, 0.200 mmol, 1.0 equiv), 3-phenylpropanoic acid (**7**) (29.8 mg, 0.200 mmol, 1.0 equiv) and aqueous NH_3 (**3**) (28% solution, 36.5 mg, 0.600 mmol, 3.0 equiv) in C_6H_5Cl (1.00 mL, 0.20 M) at room temperature. After stirring for 24 h at 90 °C, the reaction mixture was cooled to room temperature. Concentration under reduced pressure furnished the crude product, which was purified by amino silica gel column chromatography (10% MeOH in $CHCl_3$) to amide **4a** (28.1 mg, 0.170 mmol, 85%) and **8**[10] (1.00 mg, 6.70 μmol, 3%)**.**

6. DBAA-catalyzed synthesis of chiral α-hydroxy primary amides (Scheme 2B)

(*S*)-(+)-2-hydroxy-2-phenylacetamide ((+)-6a)

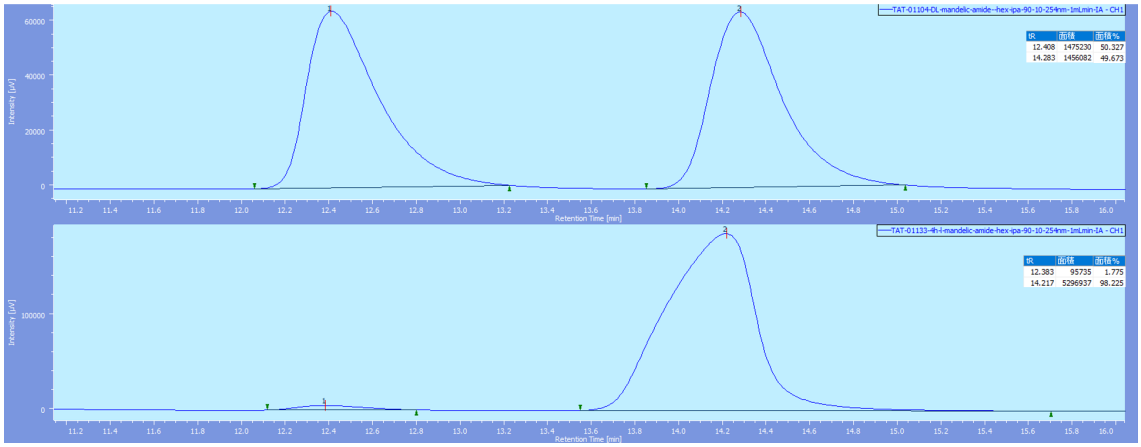


(+)-**5a**
1.0 equiv

3
3.0 equiv

(+)-**6a**
77%

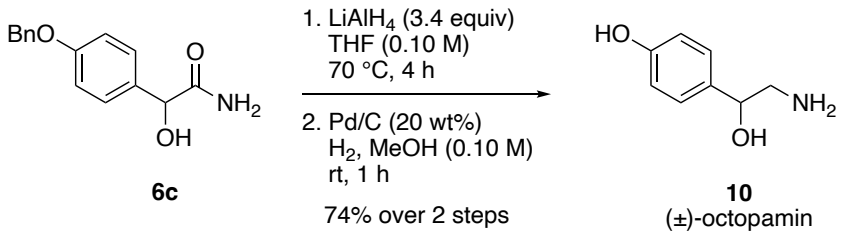
Diboronic acid anhydride **1** (5.39 mg, 10.0 μmol, 5.00 mol%) was added to a solution of (*S*)-2-hydroxy-2-phenylacetic acid ((+)-**5a**) (30.4 mg, 0.200 mmol, 1.0 equiv) and aqueous NH_3 (**3**) (28% solution, 36.5 mg, 0.600 mmol, 3.0 equiv) in C_6H_5Cl (1.00 mL, 0.20 M) at room temperature. After stirring for 4 h at 110 °C, the reaction mixture was cooled to room temperature. Concentration under reduced pressure furnished the crude product, which was purified by amino silica gel column chromatography (10% MeOH in $CHCl_3$) to give (*S*)-(+)-2-hydroxy-2-phenylacetamide ((+)-**6a**) (23.3 mg, 0.154 mmol, 77%, 96% ee, $[\alpha]_D^{23}$ +17.2° (*c* = 1.0, MeOH)) as a white solid.



The ee was determined by chiral HPLC analysis [CHIRALPAK IA(ϕ 0.46 cm × 25 cm), hexane / IPA = 90 : 10, 254 nm, flow rate 1.0 mL/min, t_R = 12.4 min (minor), 14.2 min (major)]

7. Application to the transformation of α-hydroxy primary amides (Scheme 3A)

(±)-octopamine (10)[11]

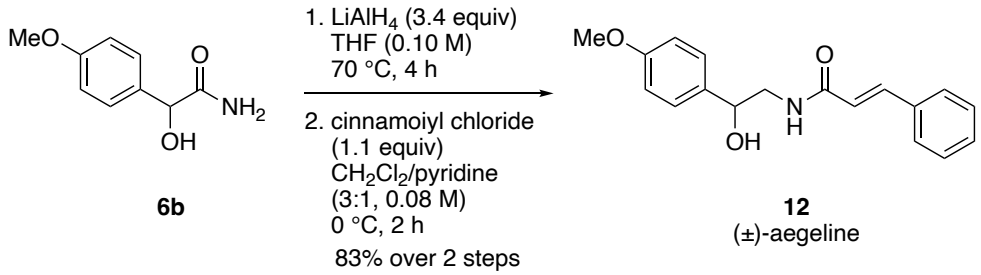


A suspension of $LiAlH_4$ (25.8 mg, 0.680 mmol, 3.4 equiv) in dry THF (1.30 mL, 0.15 M) was added dropwise to a solution of 2-(4-(benzyloxy)phenyl)-2-hydroxyacetamide (**6c**) (51.5 mg, 0.200 mmol, 1.0 equiv) in dry THF (700 μL, 0.30 M, total 0.10 M) at room temperature. After stirring for 4 h at 70 °C, the reaction mixture was cooled to 0 °C and the reaction mixture was quenched with water (25.8 μL), 15% NaOH aq. (25.8 μL), and water (77.4 μL). The resulting mixture was filtered through a pad of Celite® and the resulting filtrate was concentration under reduced pressure to furnish the crude product, which was subjected to the next step without further purification.

5% Pd/C (10.3 mg, 20 wt%, wet) was added to a solution of crude mixture in MeOH (2.00 mL, 0.10 M) and the mixture was stirred at room temperature under hydrogen atmosphere (balloon). After stirring for 1 h, the mixture was filtered through a pad of Celite® and the resulting filtrate was concentrated under reduced pressure to furnish the crude product, which was purified by amino silica gel column chromatography (20% MeOH in $CHCl_3$) to give (±)-octopamine (**10**) (22.7 mg, 0.148 mmol, 74%) as a yellow solid.

Data for **10**; yellow solid; R_f = 0.10 ($CHCl_3$/MeOH = 7:3); IR (KBr) ν = 3337, 1607, 1508, 1254, 1006, 830 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.09 (d, J = 8.0 Hz, 2H), 6.69 (d, J = 8.0 Hz, 2H), 5.10 (br s, 1H), 4.31 (dd, J = 8.0, 4.5 Hz, 1H), 3.33 (br s, 3H), 2.58 (dd, J = 12.5, 4.5 Hz, 1H), 2.53 (dd, J = 12.5, 8.0 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 156.2, 134.6, 127.0, 114.7, 74.2, 50.2; HRMS (ESI) m/z calcd for $C_8H_{11}NNaO_2$ $[M+Na]^+$ 176.0688, found 176.0687.

(±)-aegeline (12)[12]

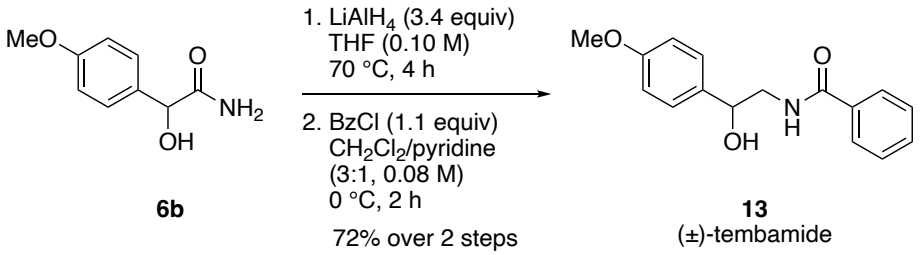


A suspension of $LiAlH_4$ (25.8 mg, 0.680 mmol, 3.4 equiv) in dry THF (1.30 mL, 0.15 M) was added dropwise to a solution of 2-hydroxy-2-(4-methoxyphenyl)acetamide (**6b**) (36.2 mg, 0.200 mmol, 1.0 equiv) in dry THF (700 μL, 0.30 M, total 0.10 M) at room temperature. After stirring for 4 h at 70 °C, the reaction mixture was cooled to 0 °C and the reaction mixture was quenched with water (25.8 μL), 15% NaOH aq. (25.8 μL), and water (77.4 μL). The resulting mixture was filtered through a pad of Celite® and the resulting filtrate was concentrated under reduced pressure to furnish the crude product, which was subjected to the next step without further purification.

Cinnamoyl chloride (36.7 mg, 0.220 mmol, 1.1 equiv) was added to a solution of the crude mixture in CH_2Cl_2/pyridine (3:1, 2.00 mL, 0.08 M) at 0 °C. After stirring for 2 h at 0 °C, the reaction was quenched by H_2O and the resulting mixture was extracted three times with CH_2Cl_2. The combined organic layer was successively washed with 1 M HCl, H_2O, and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was washed by *n*-hexane to give (±)-aegeline (**12**) (49.2 mg, 0.165 mmol, 83%) as a white solid.

Data for **12**; white solid; R_f = 0.19 (hexane/EtOAc = 1:1); IR (KBr) ν = 3369, 3261, 1602, 1510, 1345, 12135, 1075, 979, 830, 767 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 8.16 (t, *J* = 5.0 Hz, 1H), 7.55 (d, *J* = 7.5 Hz, 2H), 7.42–7.35 (m, 4H), 7.27 (d, *J* = 8.5 Hz, 2H), 6.90 (d, *J* = 8.5 Hz, 2H), 6.72 (d, *J* = 16.0 Hz, 1H), 5.45 (br s, 1H), 4.61 (dd, *J* = 8.0, 5.0 Hz, 1H), 3.73 (s, 3H), 3.43–3.38 (m, 1H), 3.23 (ddd, *J* = 13.0, 8.0, 5.0 Hz, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 165.1, 158.4, 138.6, 135.8, 135.0, 129.4, 129.0, 127.5, 127.2, 122.4, 113.5, 71.0, 55.0, 47.1; HRMS (ESI) m/z calcd for $C_{18}H_{19}NNaO_3$ $[M+Na]^+$ 320.1263, found 320.1273.

(±)-tembamide (13)[13]



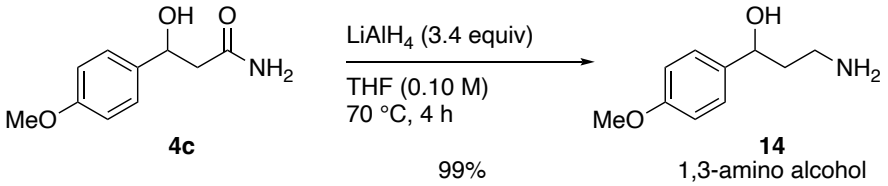
A suspension of $LiAlH_4$ (25.8 mg, 0.680 mmol, 3.4 equiv) in dry THF (1.30 mL, 0.15 M) was added dropwise to a solution of 2-hydroxy-2-(4-methoxyphenyl)acetamide (**6b**) (36.2 mg, 0.200 mmol, 1.0 equiv) in dry THF (700 μL, 0.30 M, total 0.10 M) at room temperature. After stirring for 4 h at 70 °C, the reaction mixture was cooled to 0 °C and the reaction mixture was quenched with water (25.8 μL), 15% NaOH aq. (25.8 μL), and water (77.4 μL). The resulting mixture was filtered through a pad of Celite® and the resulting filtrate was concentrated under reduced pressure to furnish the crude product, which was subjected to the next step without further purification.

Benzoyl chloride (12.8 μL, 0.220 mmol, 1.1 equiv) was added to a solution of the crude mixture in CH_2Cl_2/pyridine (3:1, 2.0 mL, 0.08 M) at 0 °C. After stirring for 2 h at 0 °C, the reaction was quenched by H_2O and the resulting mixture was extracted three times with CH_2Cl_2. The combined organic layer was successively washed with 1 M HCl, H_2O, and brine, dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was washed by *n*-hexane to give (±)-tembamide (**13**) (39.1 mg, 0.144 mmol, 72%) as a white solid.

Data for **13**; white solid; R_f = 0.22 (hexane/EtOAc = 1:1); IR (KBr) ν = 3409, 3317, 1619, 1546, 1244, 1063, 833, 695 cm^{-1}; ^1H NMR (270 MHz, $CDCl_3$) δ 7.77–7.74 (m, 2H), 7.54–7.39 (m, 3H), 7.33 (d, *J* = 8.6 Hz, 2H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.61 (br, 1H), 4.91 (dd, *J* = 7.8, 3.5 Hz, 1H), 3.88 (ddd, *J* = 13.8, 5.2, 3.5 Hz, 1H), 3.81 (s, 3H), 3.56–3.46 (m, 1H), 2.39 (br s, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.5, 159.3, 134.1, 133.8, 131.7, 128.6, 127.1, 127.0, 114.0, 73.3, 55.3, 47.7; HRMS (ESI) m/z calcd for $C_{16}H_{17}NNaO_3$ $[M+Na]^+$ 294.1106, found 294.1109.

8. Application to the transformation of *β*-hydroxy primary amides (Scheme 3B)

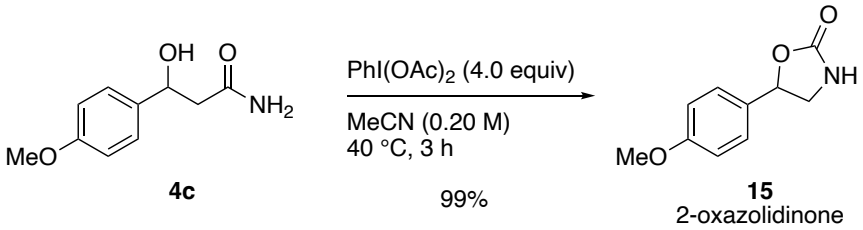
3-amino-1-(4-methoxyphenyl)propan-1-ol (14)[14]



A suspension of $LiAlH_4$ (25.8 mg, 0.680 mmol, 3.4 equiv) in dry THF (1.30 mL, 0.15 M) was added dropwise to a solution of 3-hydroxy-3-(4-methoxyphenyl)acetamide (**4c**) (39.0 mg, 0.200 mmol, 1.0 equiv) in dry THF (700 μL, 0.30 M, total 0.10 M) at room temperature. After stirring for 4 h at 70 °C, the reaction mixture was cooled to 0 °C and the reaction mixture was quenched with water (25.8 μL), 15% NaOH aq. (25.8 μL), and water (77.4 μL). The resulting mixture was filtered through a pad of Celite® and the resulting filtrate was concentrated under reduced pressure to furnish the crude product, which was purified by amino silica gel column chromatography (5% MeOH in $CHCl_3$) to give 3-amino-1-(4-methoxyphenyl)propan-1-ol (**14**) (35.9 mg, 0.198 mmol, 99%) as a white solid.

Data for **14**; white solid; R_f = 0.29 ($CHCl_3$/MeOH = 19:1); IR (KBr) ν = 3354, 2856, 1611, 1510, 1248, 1029, 814 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.22 (d, J = 9.0 Hz, 2H), 6.86 (d, J = 9.0 Hz, 2H), 4.60 (dd, J = 8.0, 4.5 Hz, 1H), 3.72 (s, 3H), 3.27 (br s, 3H), 1.60–1.55 (m, 2H), 1.67–1.58 (m, 2H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 157.9, 138.5, 126.8, 113.3, 71.0, 55.0, 42.5, 39.8; HRMS (ESI) m/z calcd for $C_{10}H_{15}NNaO_2$ $[M+Na]^+$ 204.1001, found 204.0992.

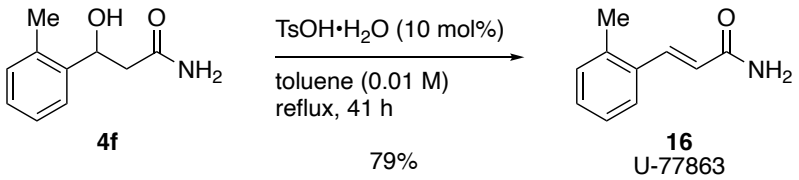
5-(4-methoxyphenyl)oxazolidin-2-one (15)[15]



Iodobenzene diacetate (258 mg, 0.800 mmol, 4.0 equiv) was added to a solution of 3-hydroxy-3-(4-methoxyphenyl)acetamide (**4c**) (39.0 mg, 0.200 mmol, 1.0 equiv) in MeCN (1.00 mL, 0.20 M) at room temperature. After stirring for 3 h at 40 °C, the reaction mixture was cooled to room temperature. Concentration under reduced pressure furnished the crude product, which was purified by silica gel column chromatography (66% EtOAc in hexane) to give 5-(4-methoxyphenyl)oxazolidin-2-one (**15**) (38.1 mg, 0.197 mmol, 99%) as a white solid.

Data for **15**; white solid; R_f = 0.22 (hexane/EtOAc = 1:2); IR (KBr) ν = 3266, 2913, 1752, 1716, 1519, 1389, 1251, 985, 712 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 5.58 (t, *J* = 8.0 Hz, 1H), 5.02 (br, 1H), 3.95–3.91 (m, 1H), 3.82 (s, 3H), 3.56–3.52 (m, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.1, 160.0, 130.2, 127.4, 114.2, 78.0, 55.3, 48.3; HRMS (ESI) m/z calcd for $C_{10}H_{11}NNaO_3$ $[M+Na]^+$ 216.0627, found 216.0638.

U-77863 (**16**)[16]

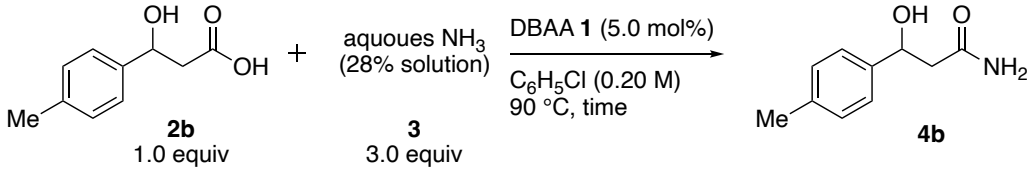


p-Toluenesulfonic acid monohydrate (3.80 mg, 20.0 μmol, 10.0 mol%) was added to a solution of 3-hydroxy-3-(*o*-tolyl)propanamide (**4f**) (39.0 mg, 0.200 mmol, 1.0 equiv) in toluene (20.0 mL, 0.01 M) at room temperature. After stirring for 41 h under reflux, the reaction mixture was cooled to room temperature. Concentration under reduced pressure furnished the crude product, which was purified by silica gel column chromatography (10% MeOH in $CHCl_3$) to give U-77863 (**16**) (25.4 mg, 0.158 mmol, 79%) as a white solid.

Data for **16**; white solid; R_f = 0.23 ($CHCl_3$/MeOH = 9:1); IR (KBr) ν = 3377, 3181, 1667, 1609, 1398, 977, 623 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 7.64 (d, J = 15.5 Hz, 1H), 7.56 (br s, 1H), 7.53 (d, J = 7.0 Hz, 1H), 7.28–7.21 (m, 3H), 7.13 (br s, 1H), 6.50 (d, J = 15.5 Hz, 1H), 2.36 (s, 3H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 166.7, 136.7, 136.6, 133.7, 130.7, 129.2, 126.4, 125.9, 123.5, 19.4; HRMS (ESI) m/z calcd for $C_{10}H_{11}NNaO$ $[M+Na]^+$ 184.0738, found 184.0736.

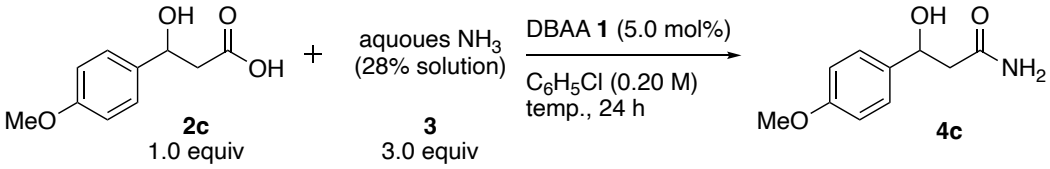
9. Supplemental data for the catalytic amidation of β-hydroxycarboxylic acids

SI-Table 1. Optimization of the reaction conditions for 4b



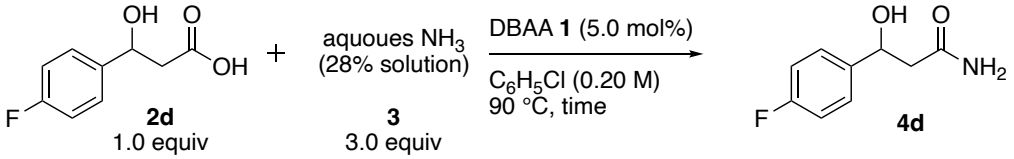
entry	time (h)	yield (%)
1	24	70
2	**48**	**99**

SI-Table 2. Optimization of the reaction conditions for 4c



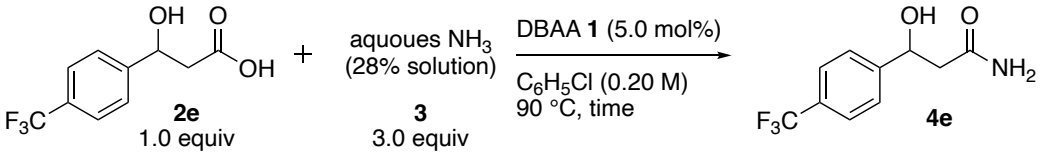
entry	temp. (°C)	yield (%)
1	90	<1
2	**110**	**93**

SI-Table 3. Optimization of the reaction conditions for 4d



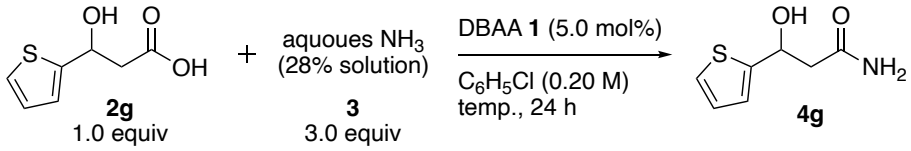
entry	time (h)	yield (%)
1	24	51
2	**48**	**95**

SI-Table 4. Optimization of the reaction conditions for 4e



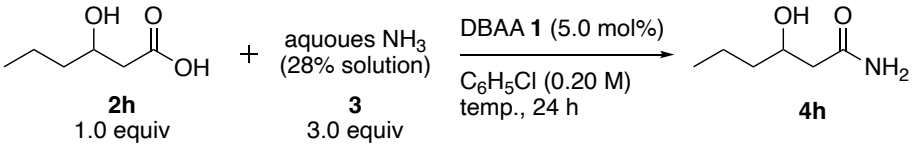
entry	time (h)	yield (%)
1	24	73
2	**48**	**78**

SI-Table 5. Optimization of the reaction conditions for 4g



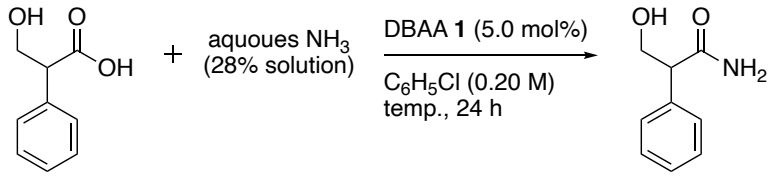
entry	temp. (°C)	yield (%)
1	90	67
2	**110**	**95**

SI-Table 6. Optimization of the reaction conditions for 4h



entry	temp. (°C)	yield (%)
1	90	48
2	**110**	**81**

SI-Table 7. Optimization of the reaction conditions for 4l

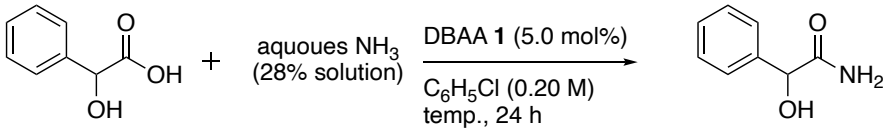


2l 1.0 equiv | **3** 3.0 equiv | **4l**

entry	temp. (°C)	yield (%)
1	90	39
2	**110**	**72**

10. Supplemental data for the catalytic amidation of α-hydroxycarboxylic acids

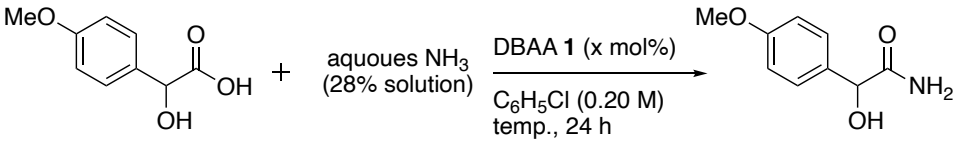
SI-Table 8. Optimization of the reaction conditions for 6a



5a 1.0 equiv | **3** 3.0 equiv | **6a**

entry	temp. (°C)	yield (%)
1	90	59
2	**110**	**81**

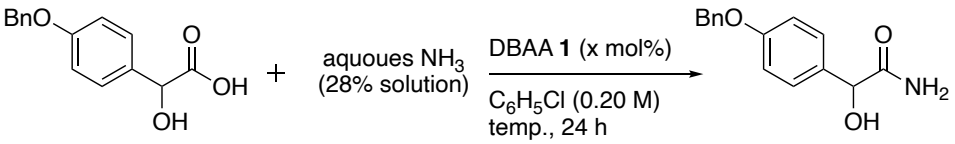
SI-Table 9. Optimization of the reaction conditions for 6b



5b 1.0 equiv | **3** 3.0 equiv | **6b**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	42
2	5.0	110	75
3	**10**	**110**	**88**

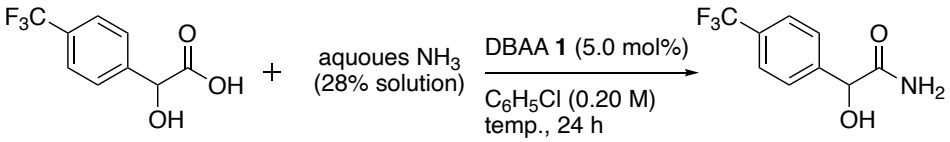
SI-Table 10. Optimization of the reaction conditions for 6c



5c 1.0 equiv | **3** 3.0 equiv | **6c**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	17
2	5.0	110	41
3	**10**	**110**	**80**

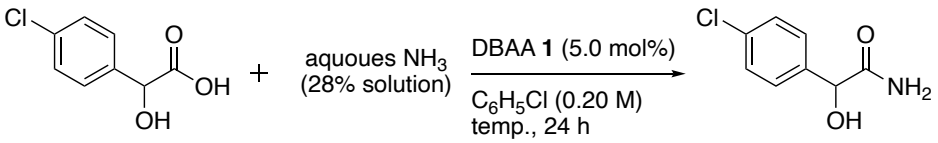
SI-Table 11. Optimization of the reaction conditions for 6d



5d 1.0 equiv | **3** 3.0 equiv | **6d**

entry	temp. (°C)	yield (%)
1	90	27
2	**110**	**97**

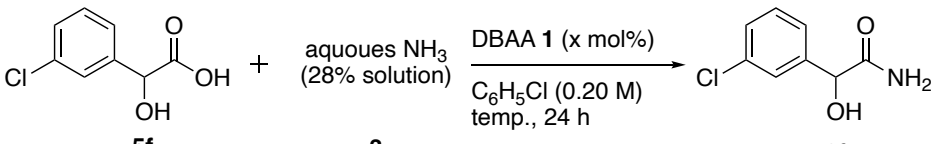
SI-Table 12. Optimization of the reaction conditions for 6e



5e 1.0 equiv | **3** 3.0 equiv | **6e**

entry	temp. (°C)	yield (%)
1	90	33
2	**110**	**85**

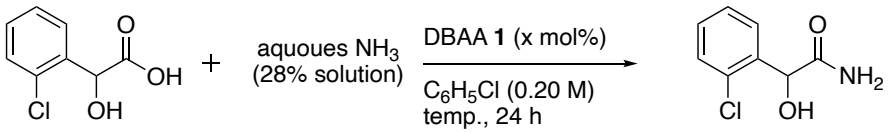
SI-Table 13. Optimization of the reaction conditions for 6f



5f 1.0 equiv | **3** 3.0 equiv | **6f**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	60
2	5.0	110	67
3	**10**	**110**	**87**

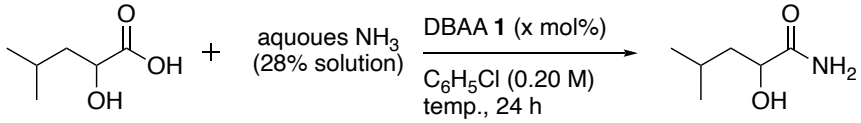
SI-Table 14. Optimization of the reaction conditions for 6g



5g 1.0 equiv | **3** 3.0 equiv | **6g**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	34
2	5.0	110	49
3	**10**	**110**	**86**

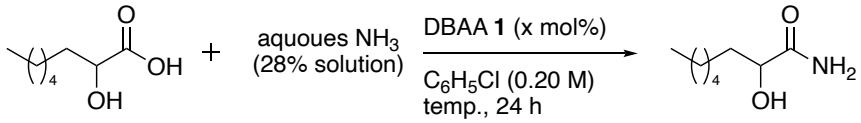
SI-Table 15. Optimization of the reaction conditions for 6h



5h 1.0 equiv | **3** 3.0 equiv | **6h**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	50
2	5.0	110	58
3	**10**	**110**	**88**

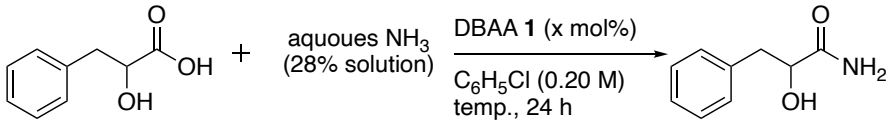
SI-Table 16. Optimization of the reaction conditions for 6i



5i 1.0 equiv | **3** 3.0 equiv | **6i**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	46
2	5.0	110	67
3	**10**	**110**	**78**

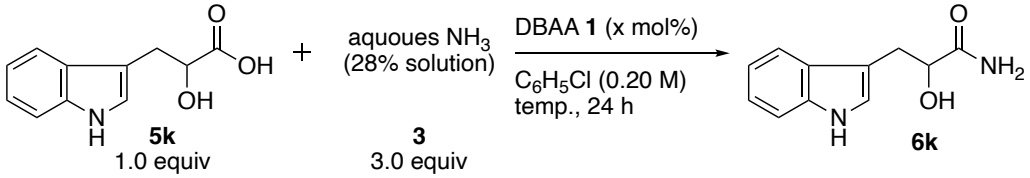
SI-Table 17. Optimization of the reaction conditions for 6j



5j 1.0 equiv | **3** 3.0 equiv | **6j**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	48
2	5.0	110	59
3	**10**	**110**	**73**

SI-Table 18. Optimization of the reaction conditions for 6k



5k 1.0 equiv | **3** 3.0 equiv | **6k**

entry	**1** (mol%)	temp. (°C)	yield (%)
1	5.0	90	25
2	5.0	110	41
3	**10**	**110**	**62**

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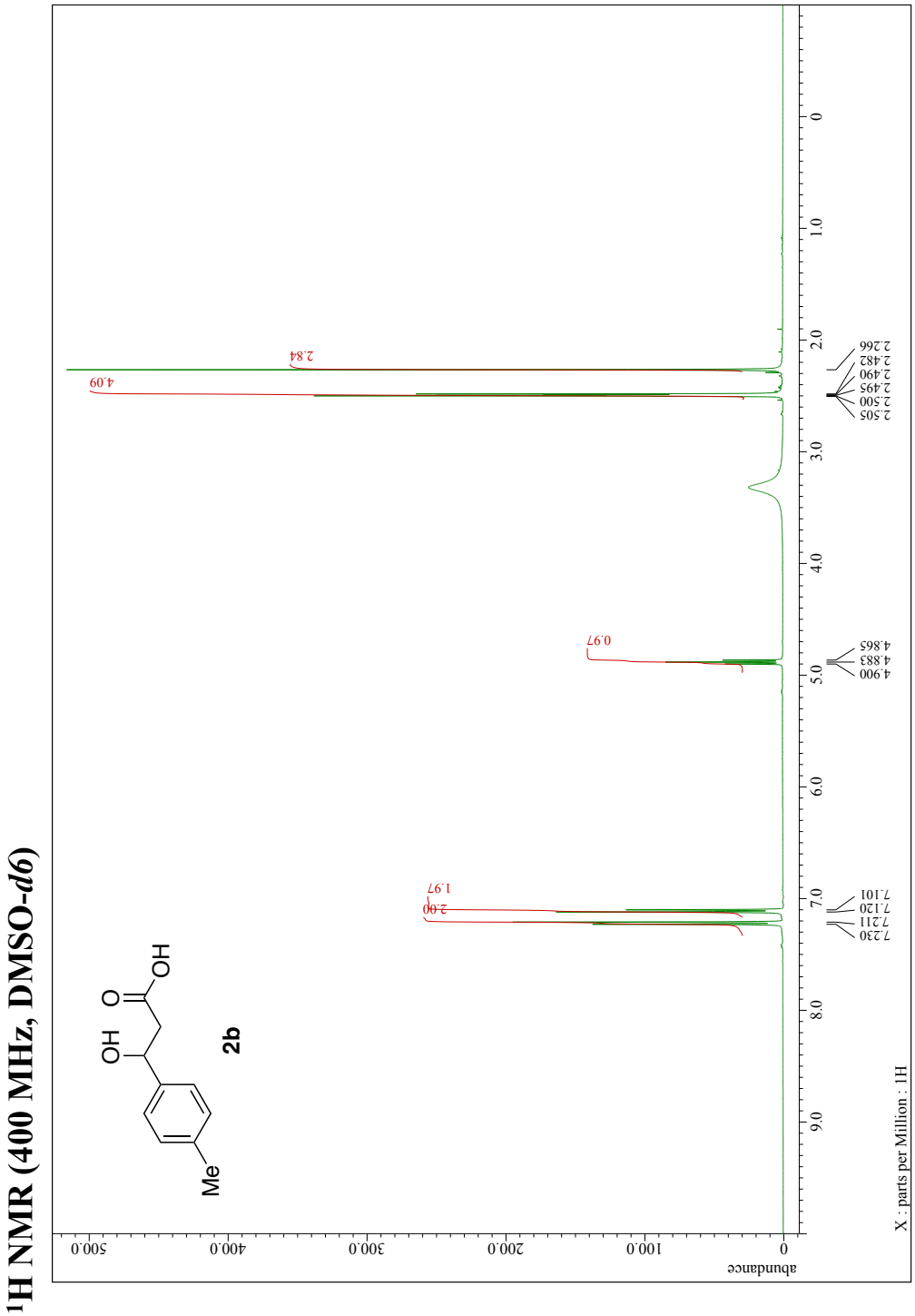
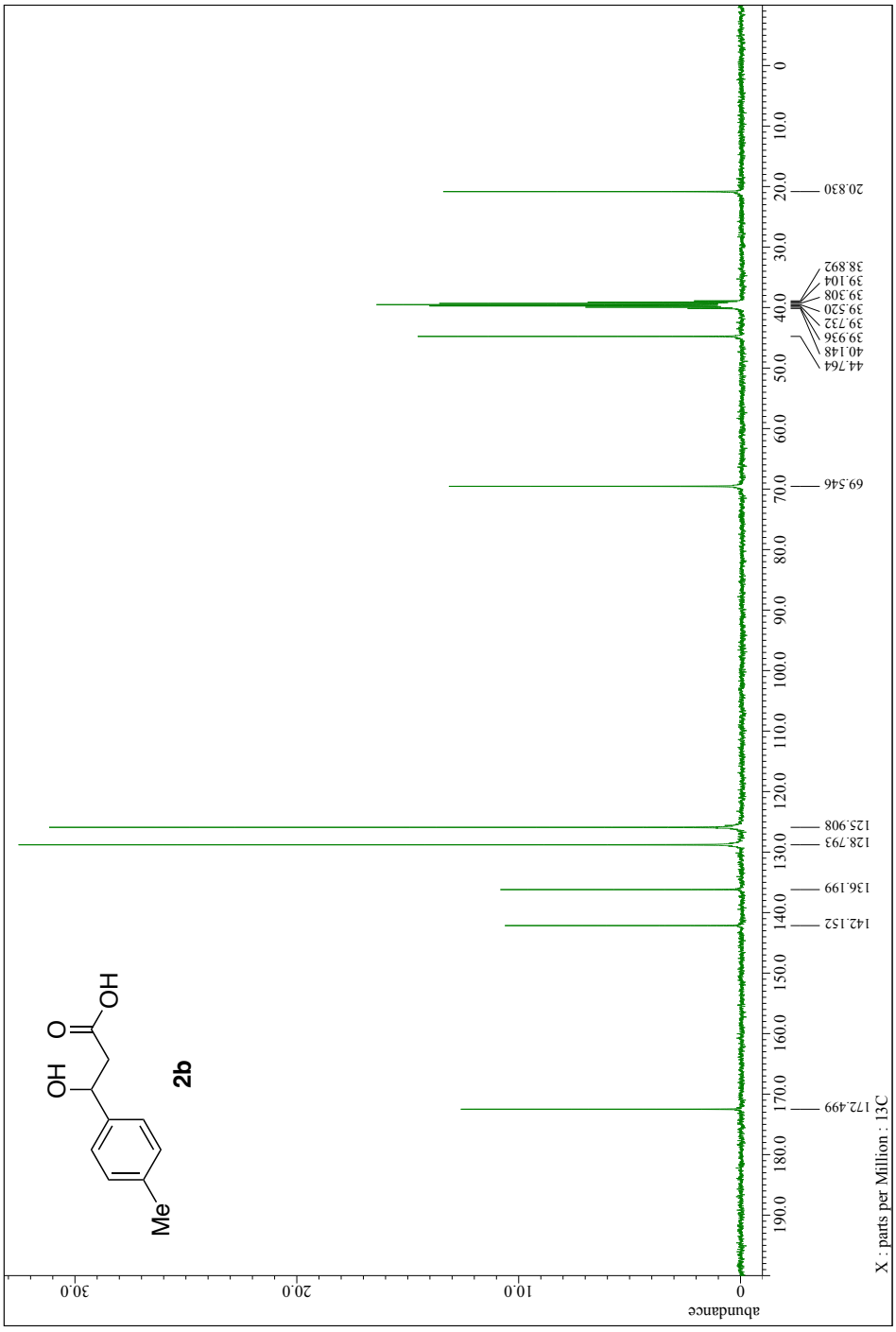
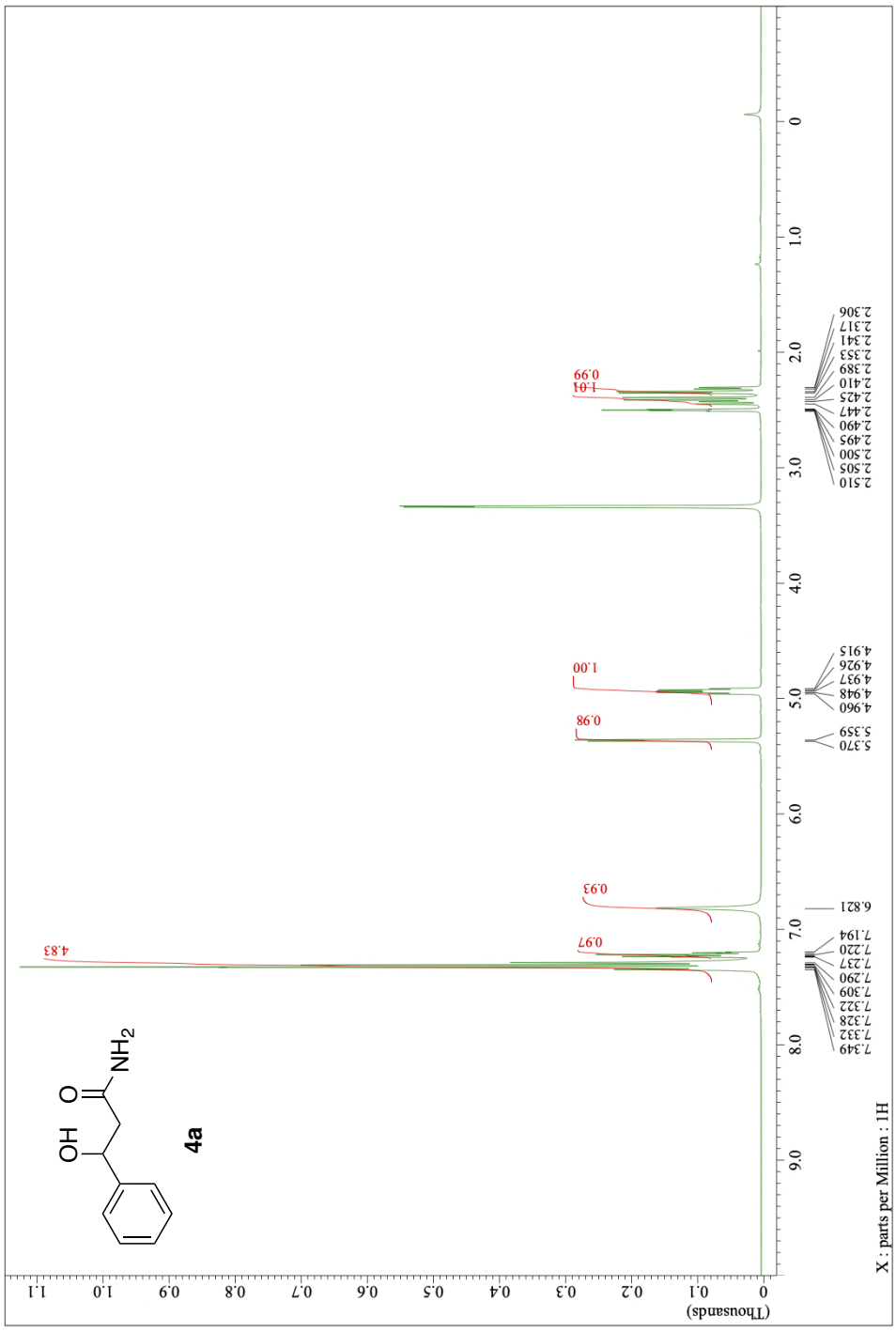
12. ^{1}H and ^{13}C NMR spectra



^{13}C NMR (100 MHz, DMSO-*d6*)



^{1}H NMR (400 MHz, DMSO-*d6*)



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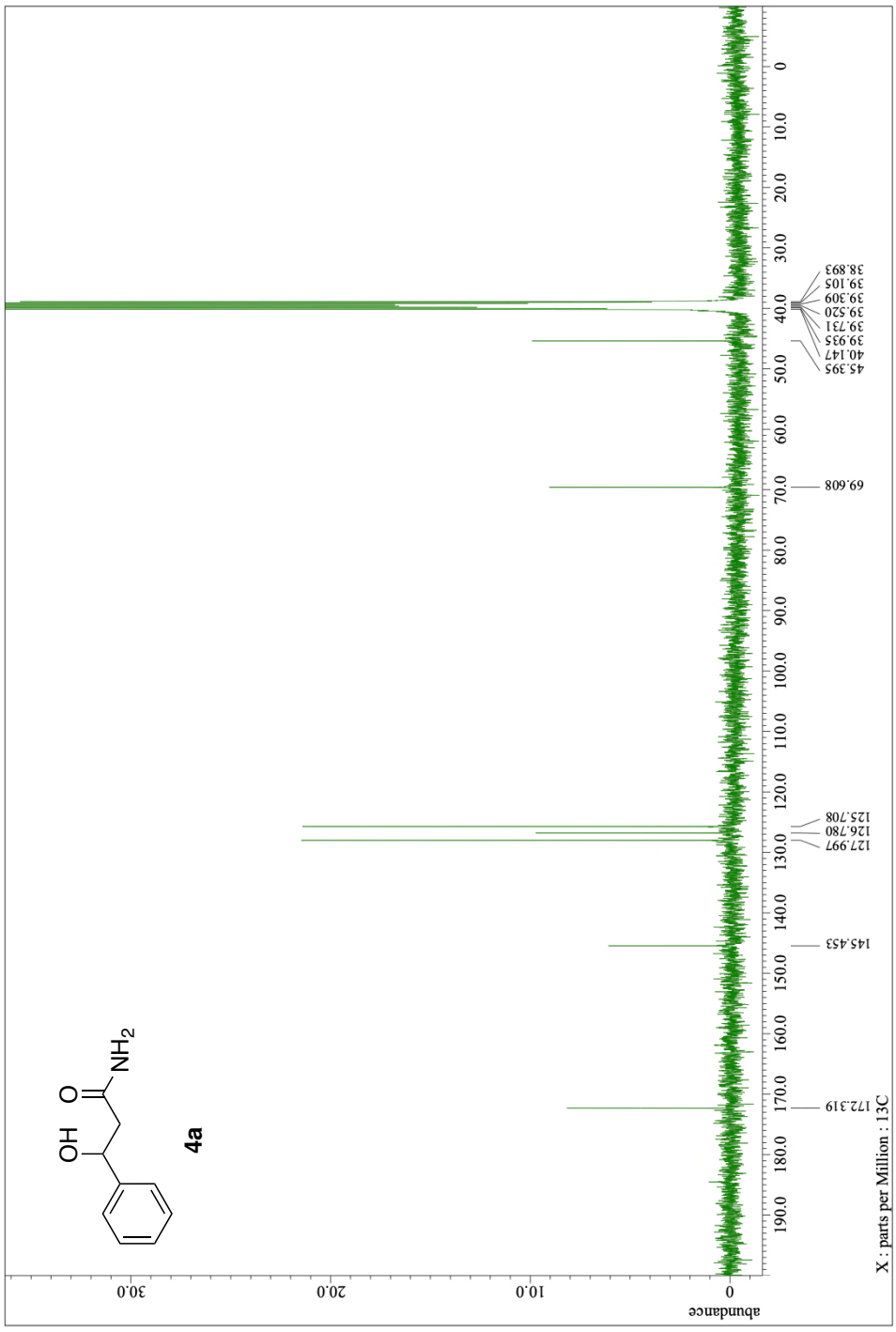
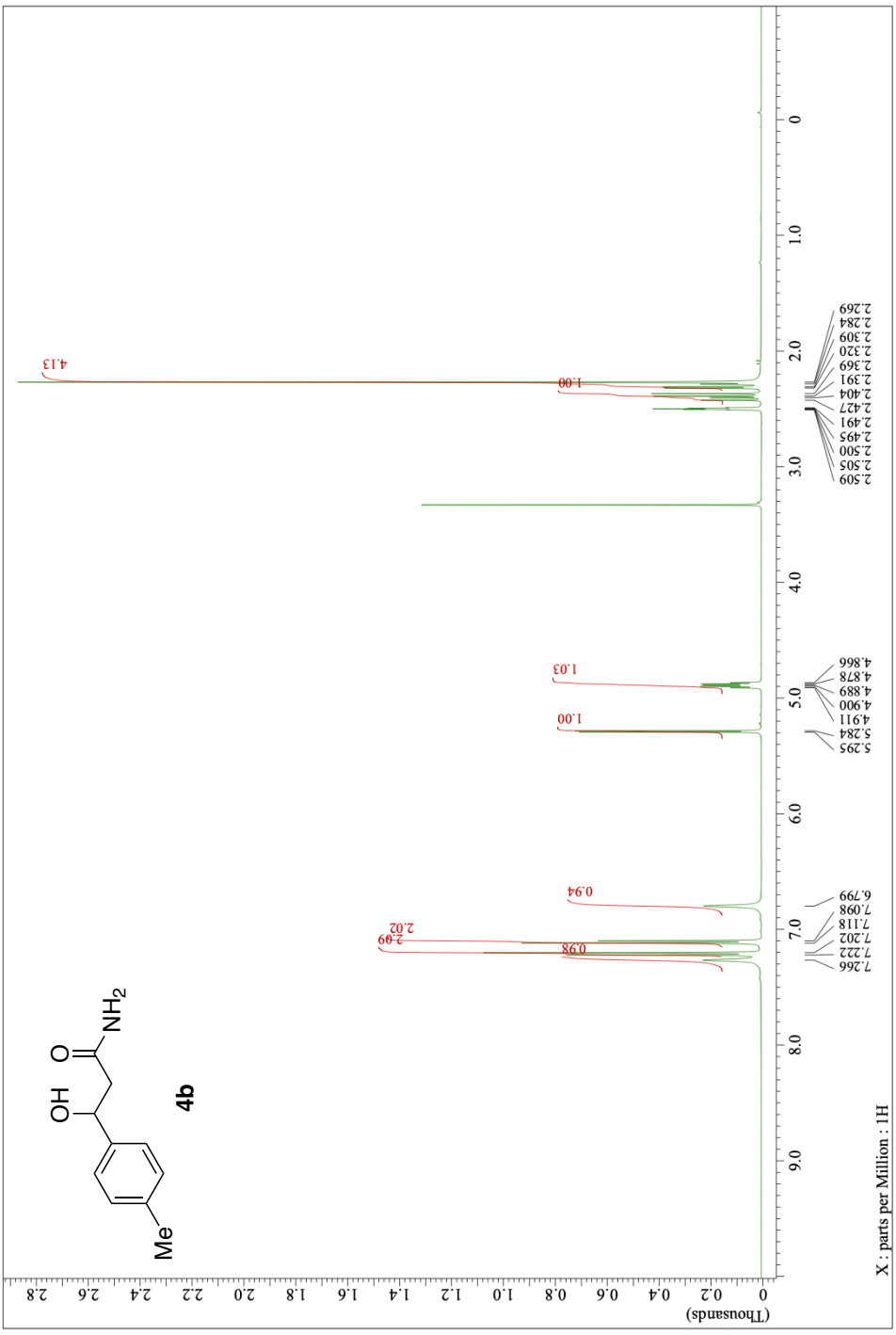
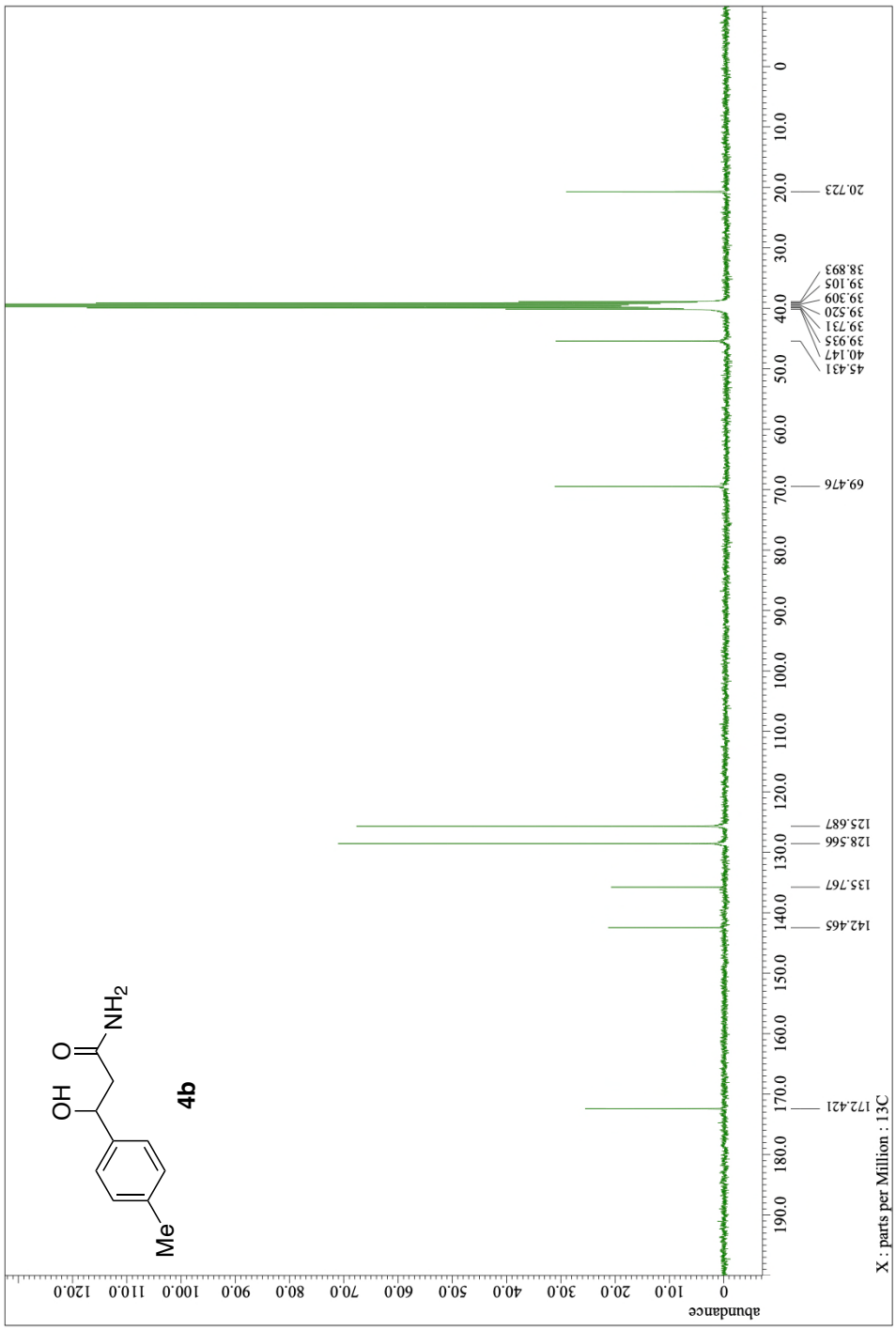


^{1}H NMR (400 MHz, DMSO-*d6*)



^{13}C NMR (100 MHz, DMSO-*d6*)



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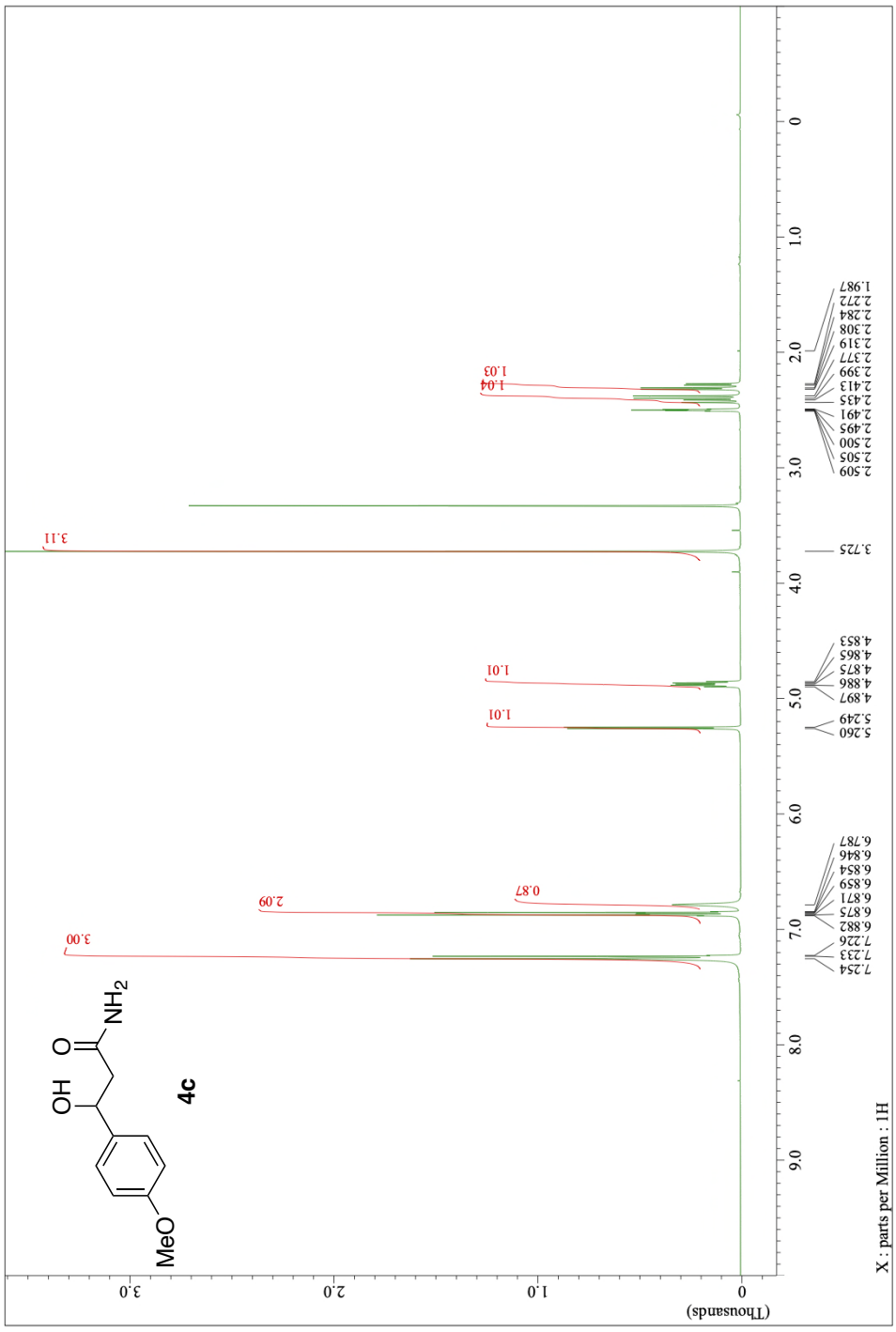
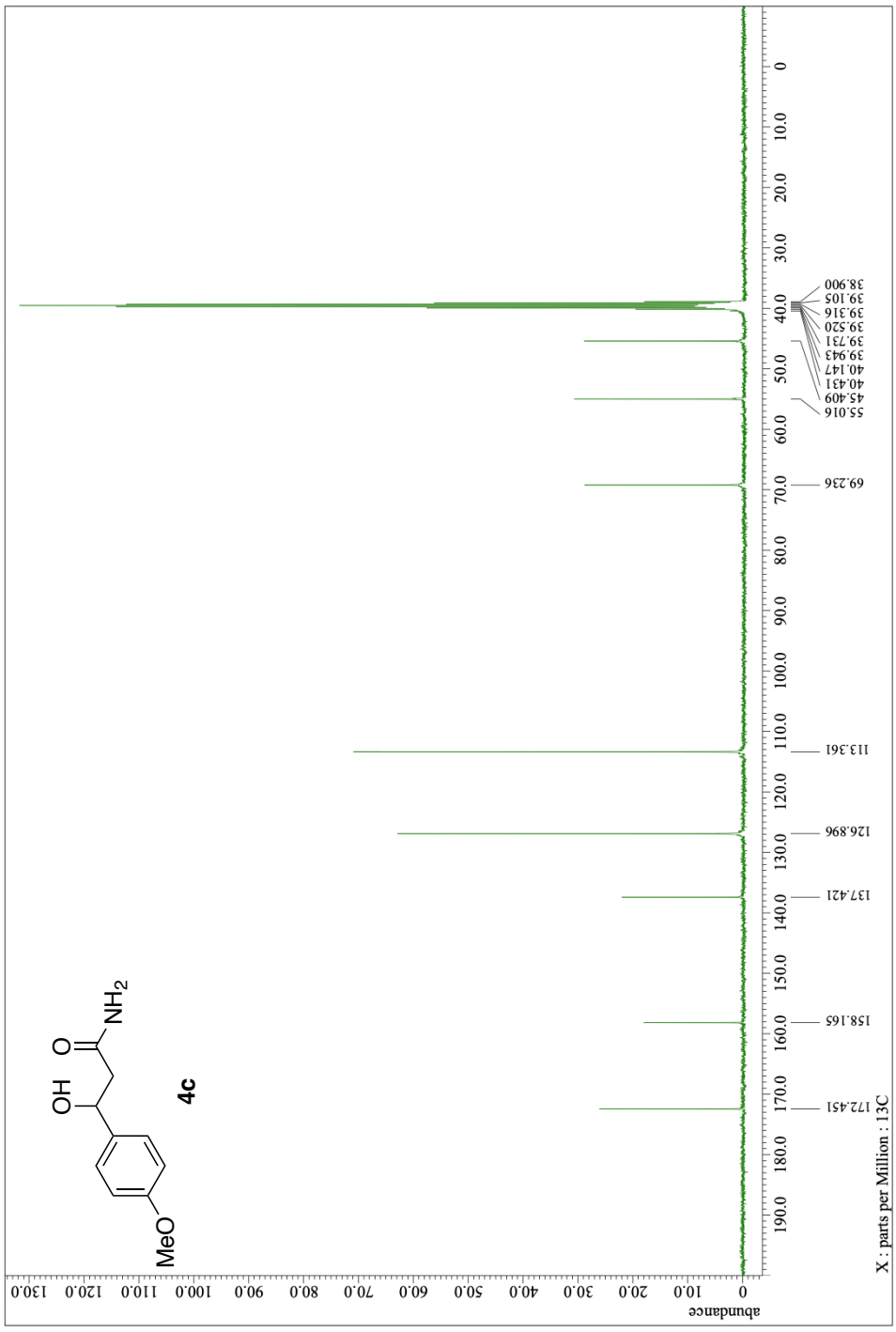
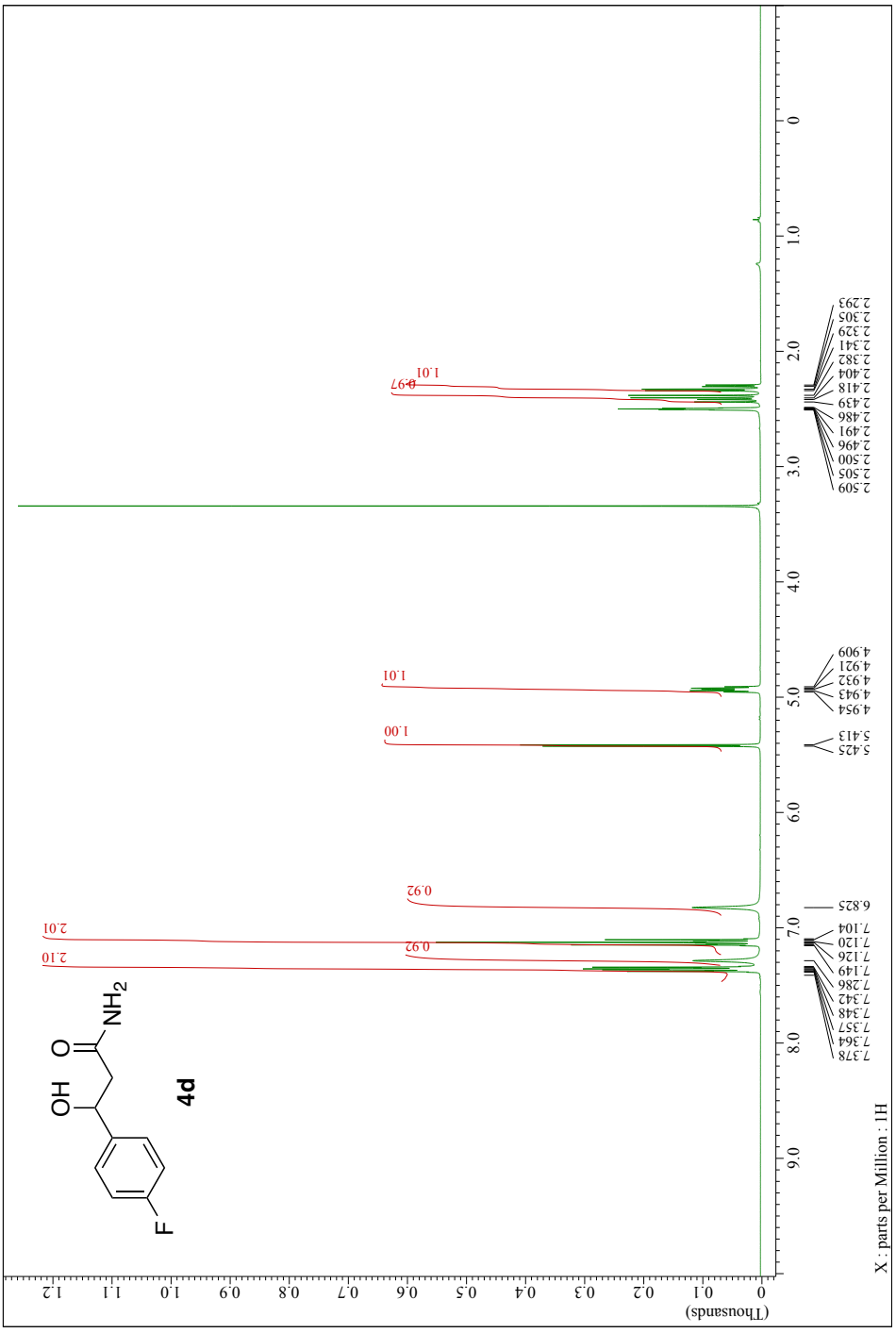


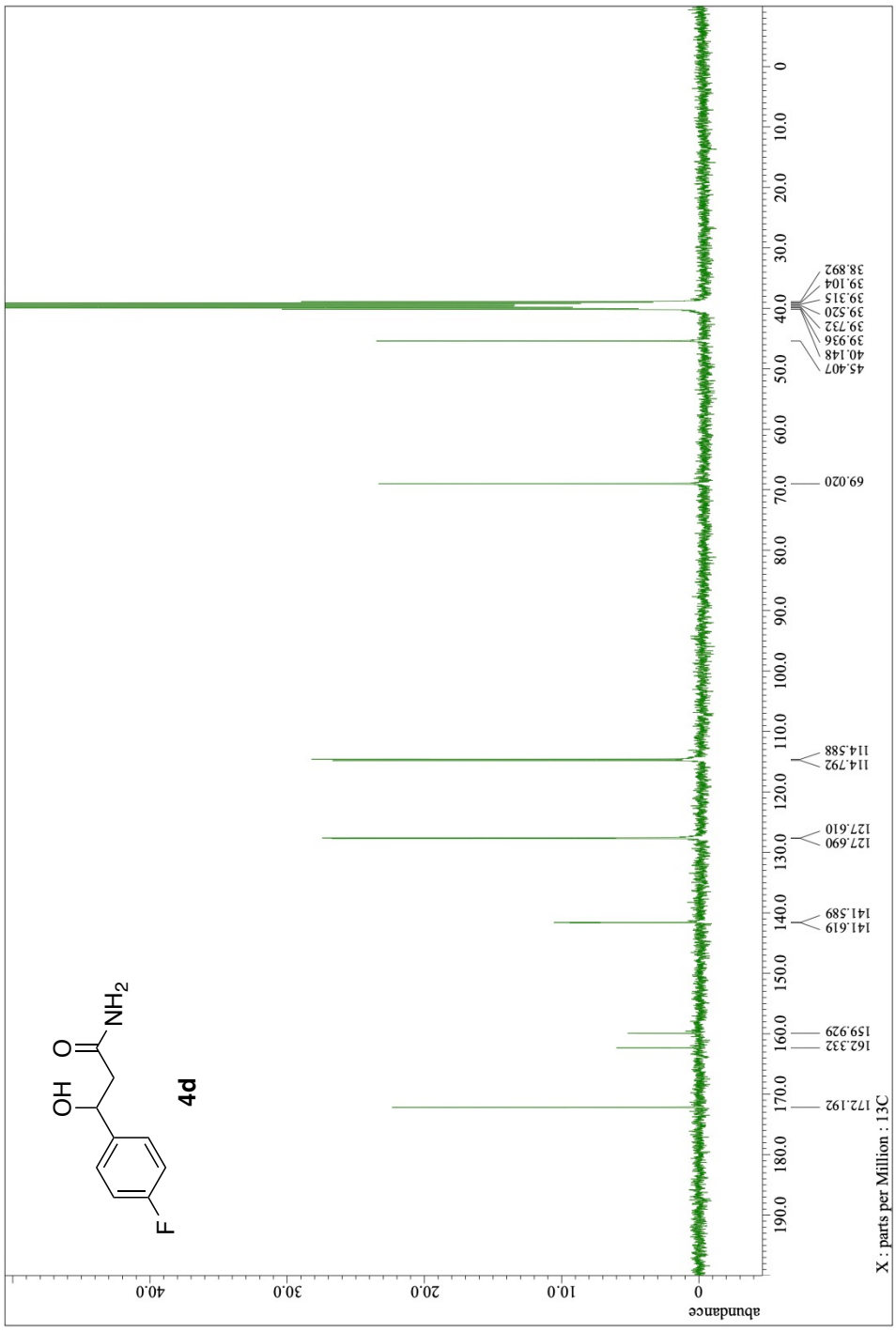
^{13}C NMR (100 MHz, DMSO-*d6*)



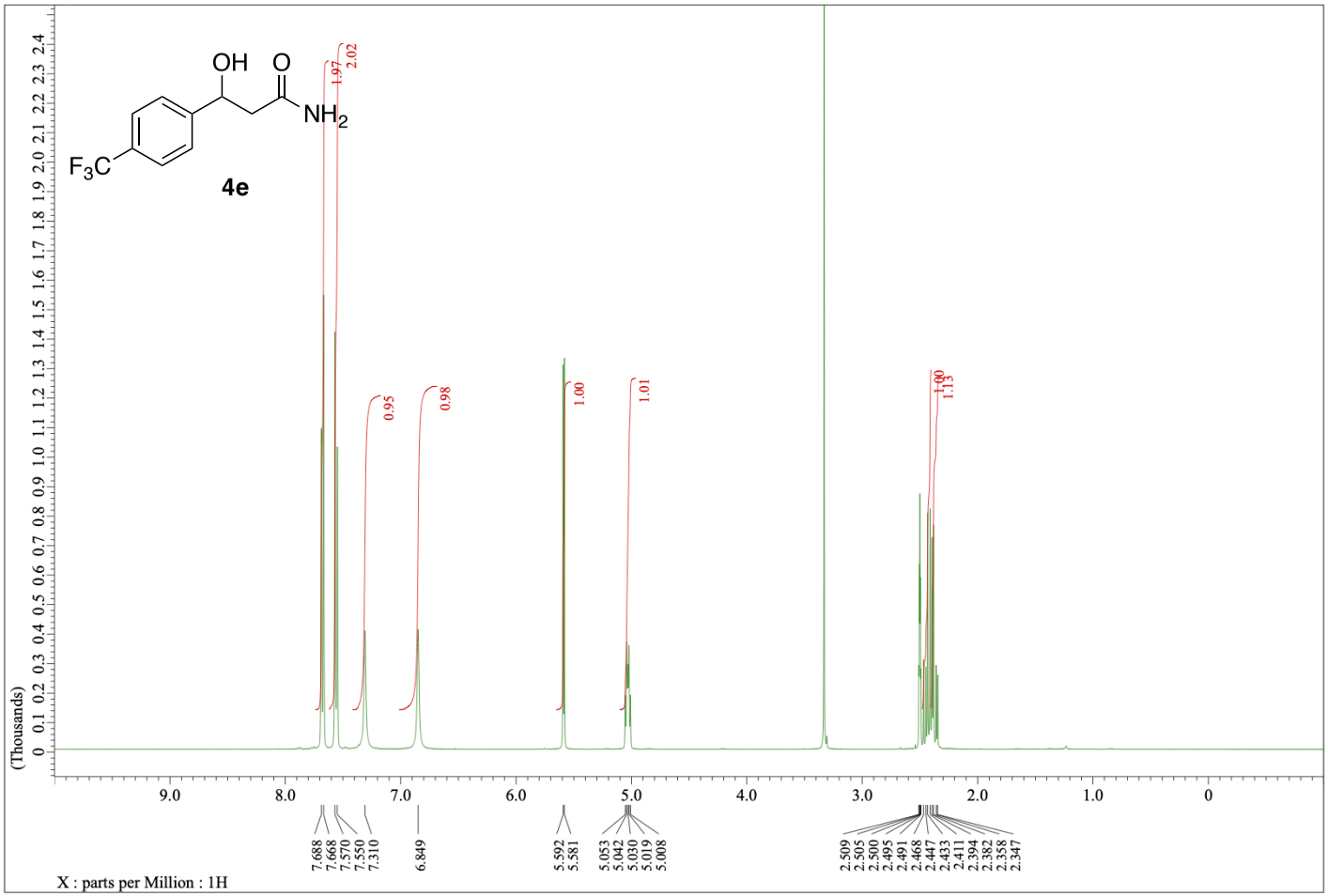
^{1}H NMR (400 MHz, DMSO-*d6*)



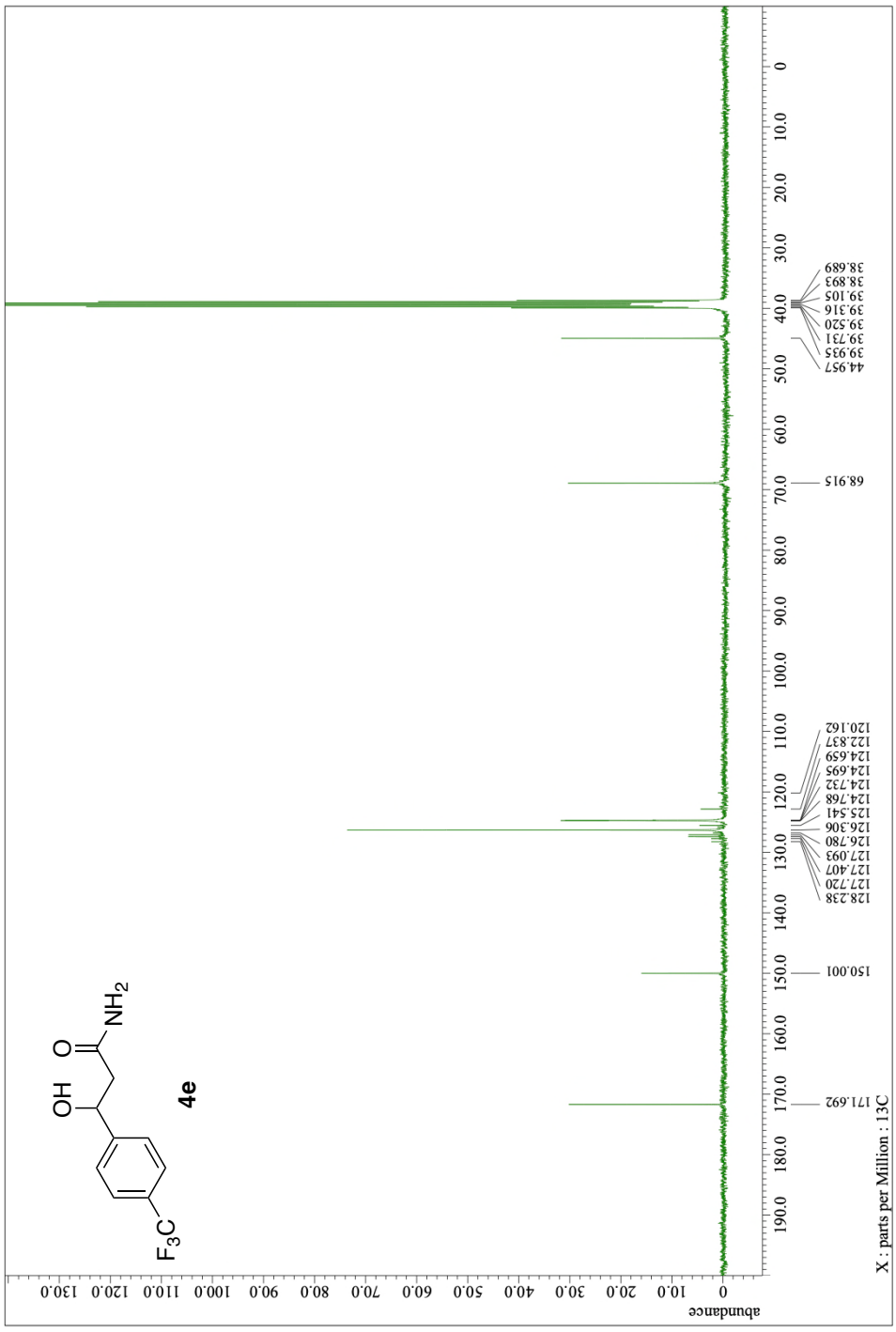
^{13}C NMR (100 MHz, DMSO-*d6*)



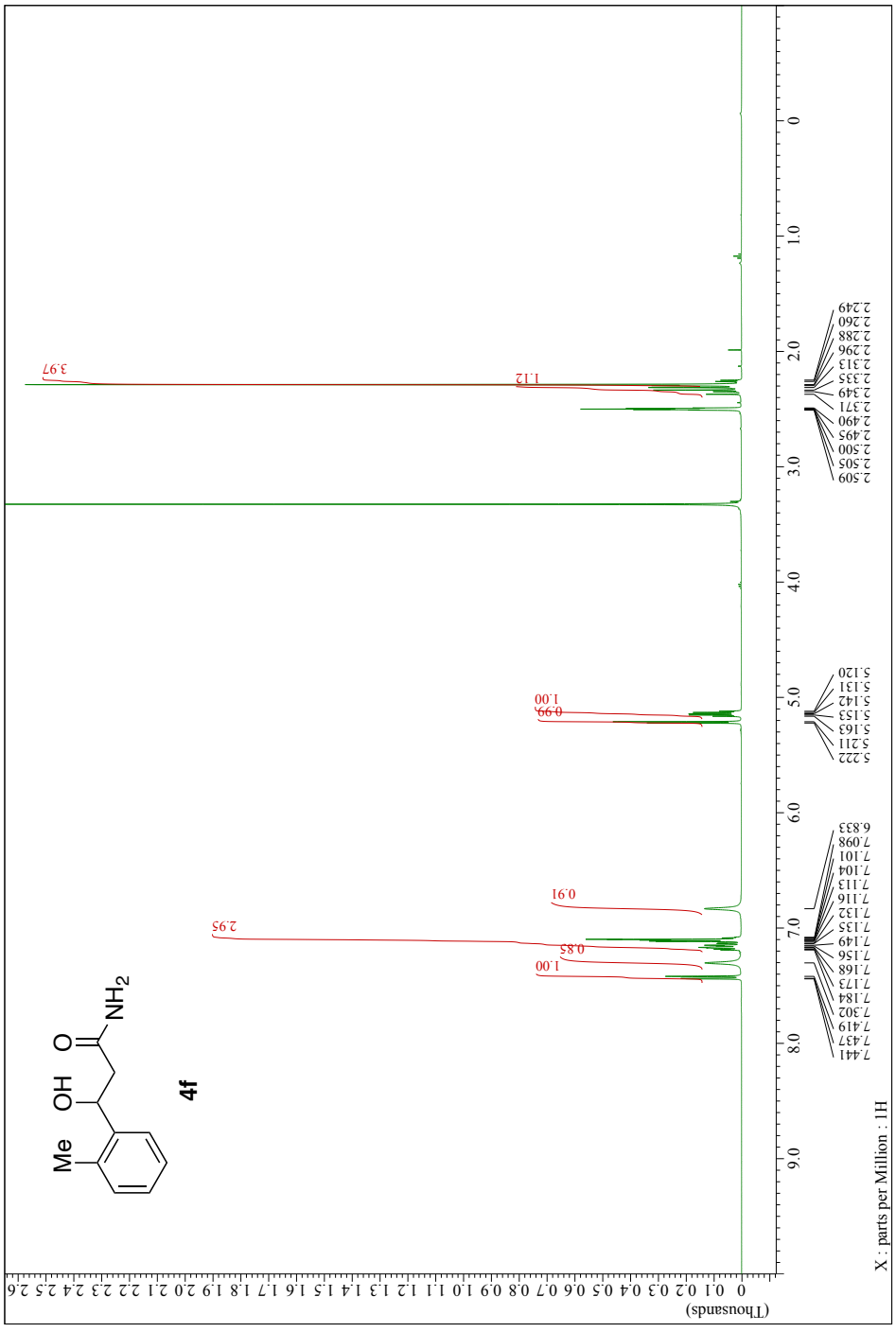
^{1}H NMR (400 MHz, DMSO-*d6*)



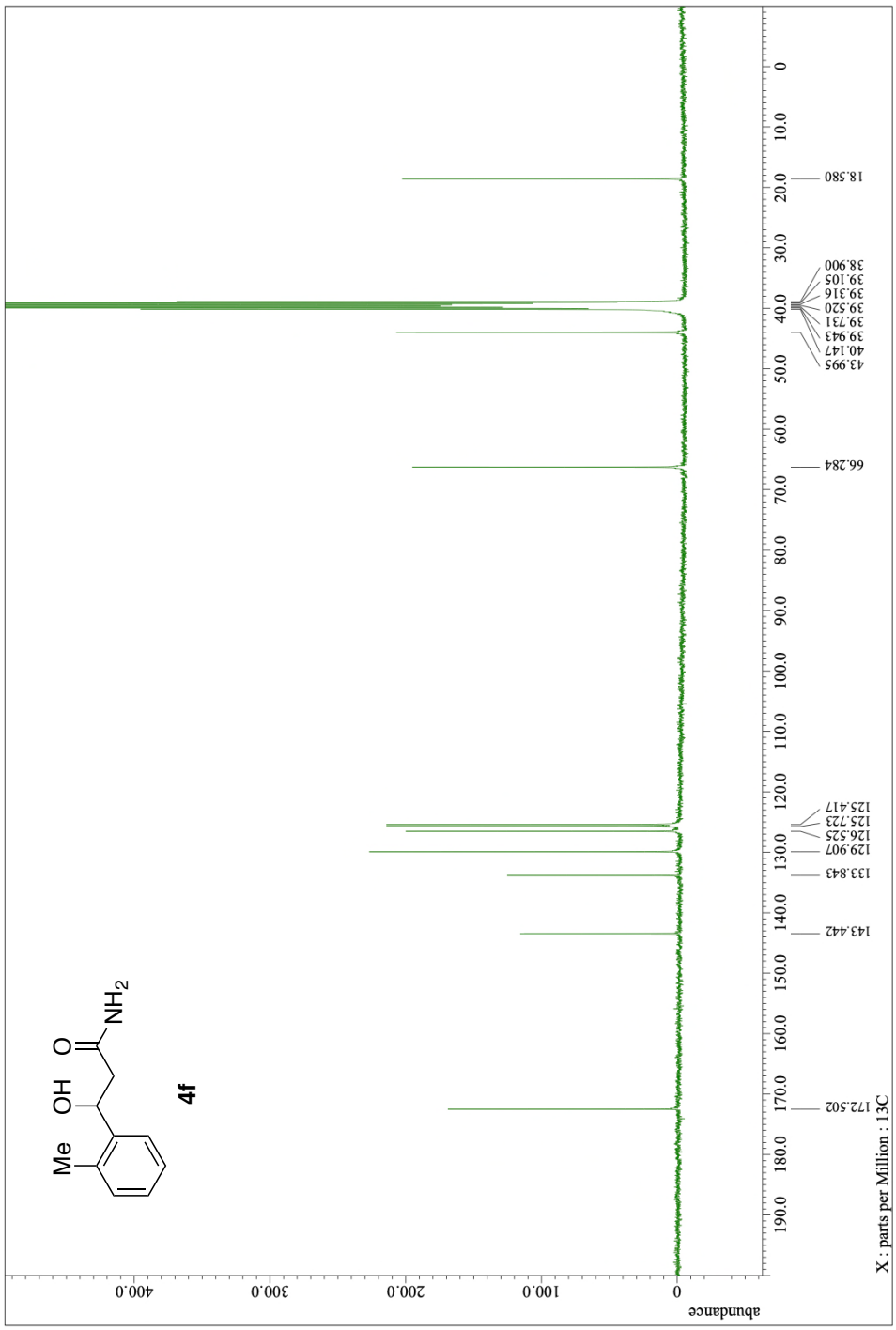
^{13}C NMR (100 MHz, DMSO-*d6*)



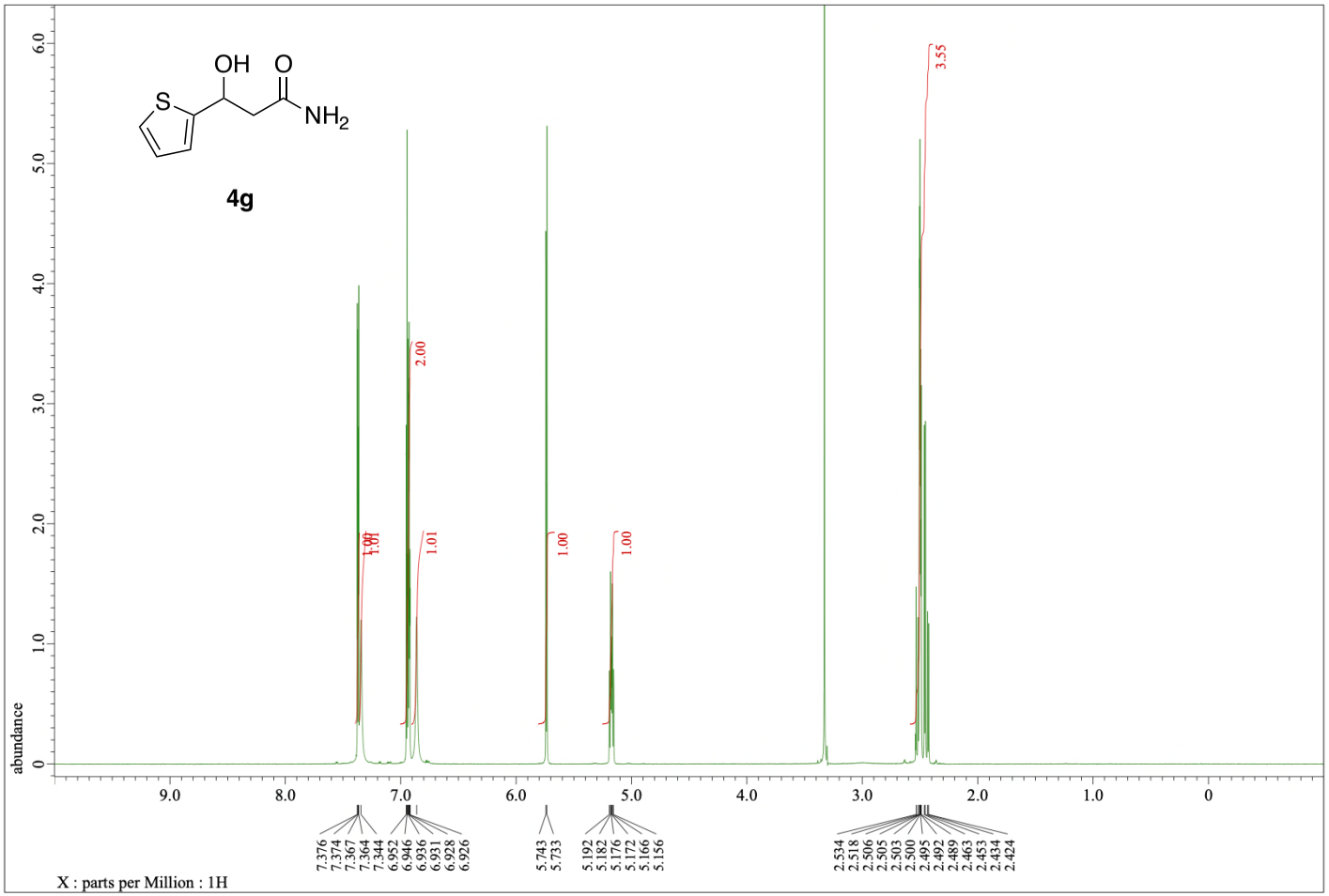
^{1}H NMR (400 MHz, DMSO-*d6*)



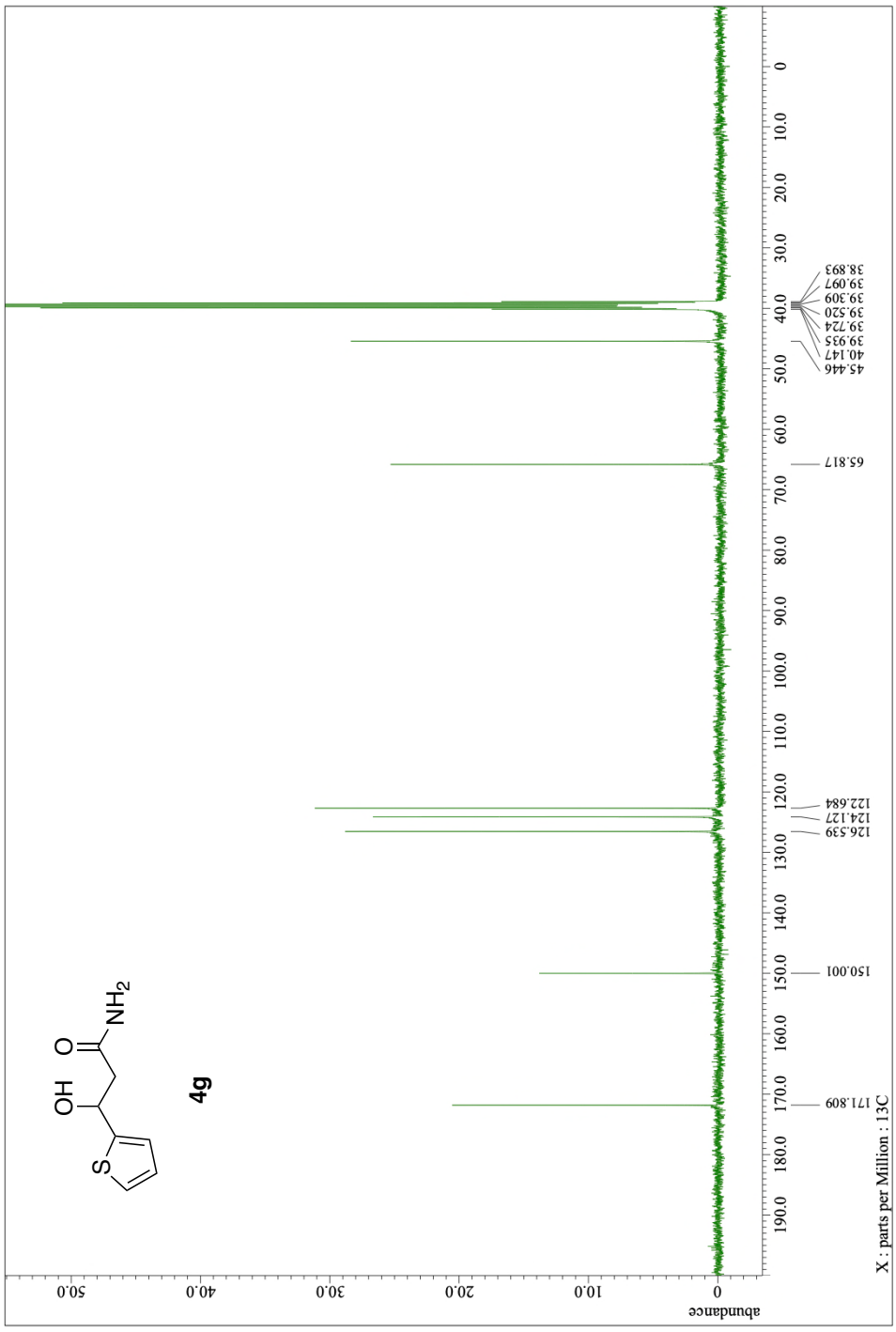
^{13}C NMR (100 MHz, DMSO-*d6*)



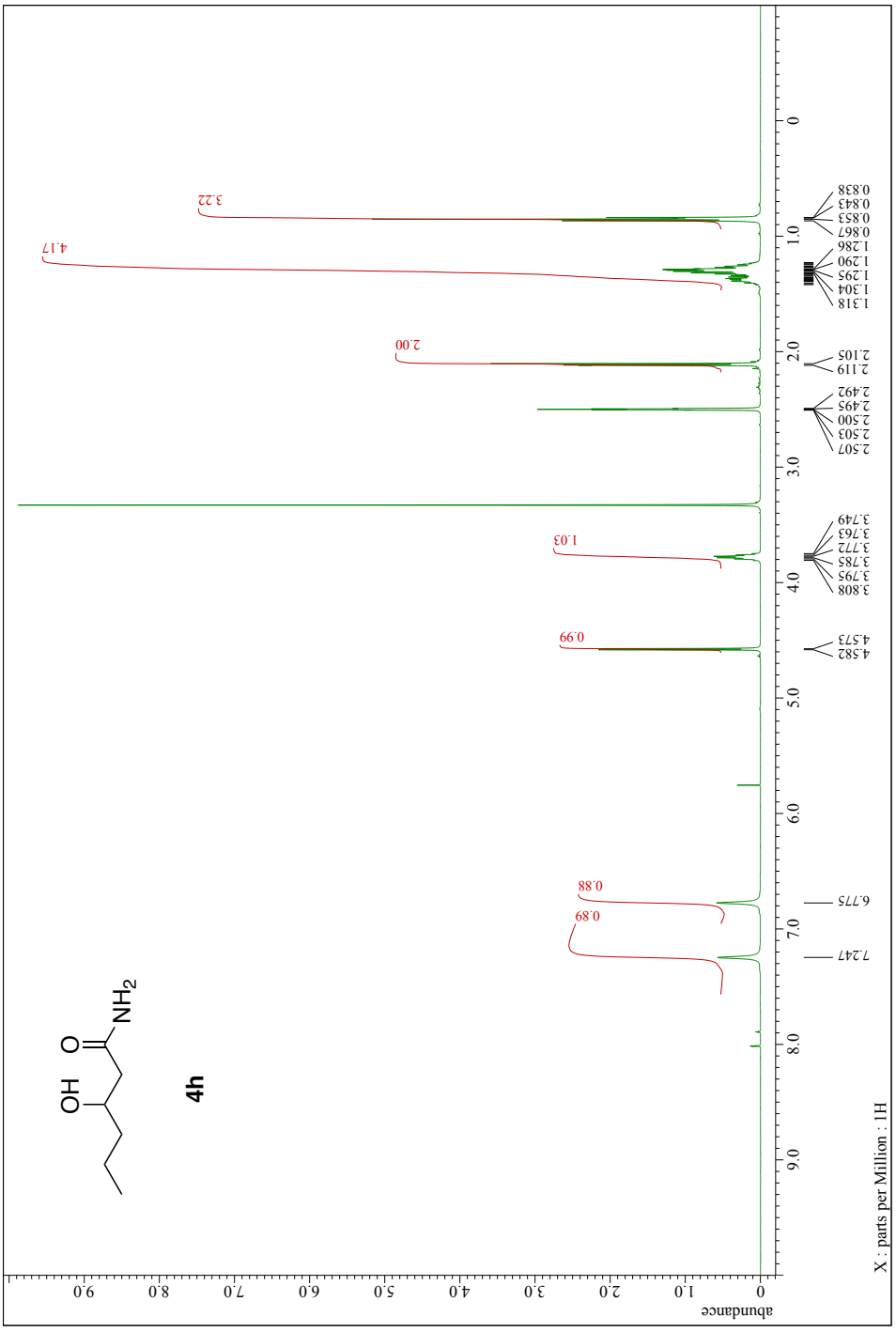
^{1}H NMR (500 MHz, DMSO-*d6*)



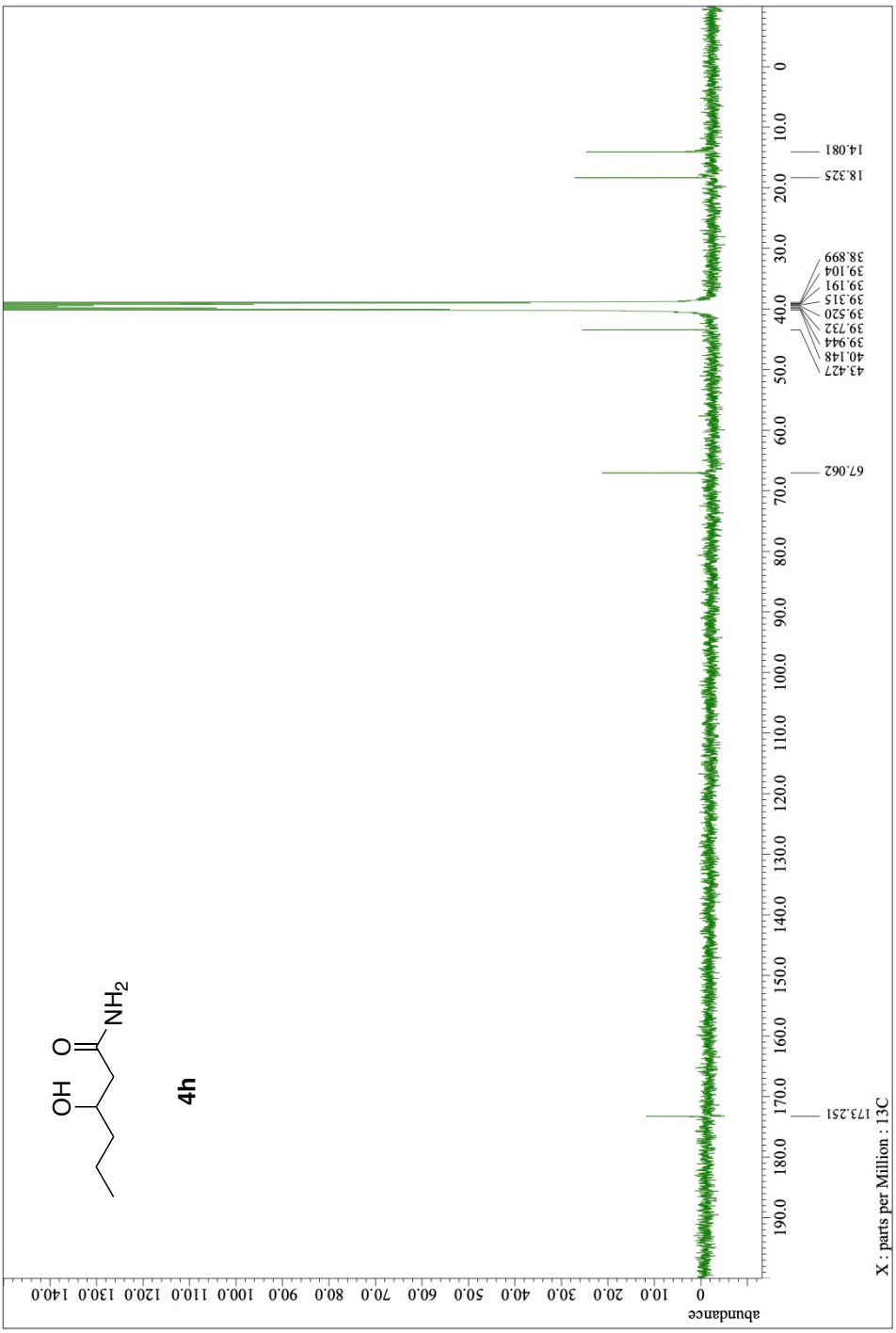
^{13}C NMR (100 MHz, DMSO-*d6*)



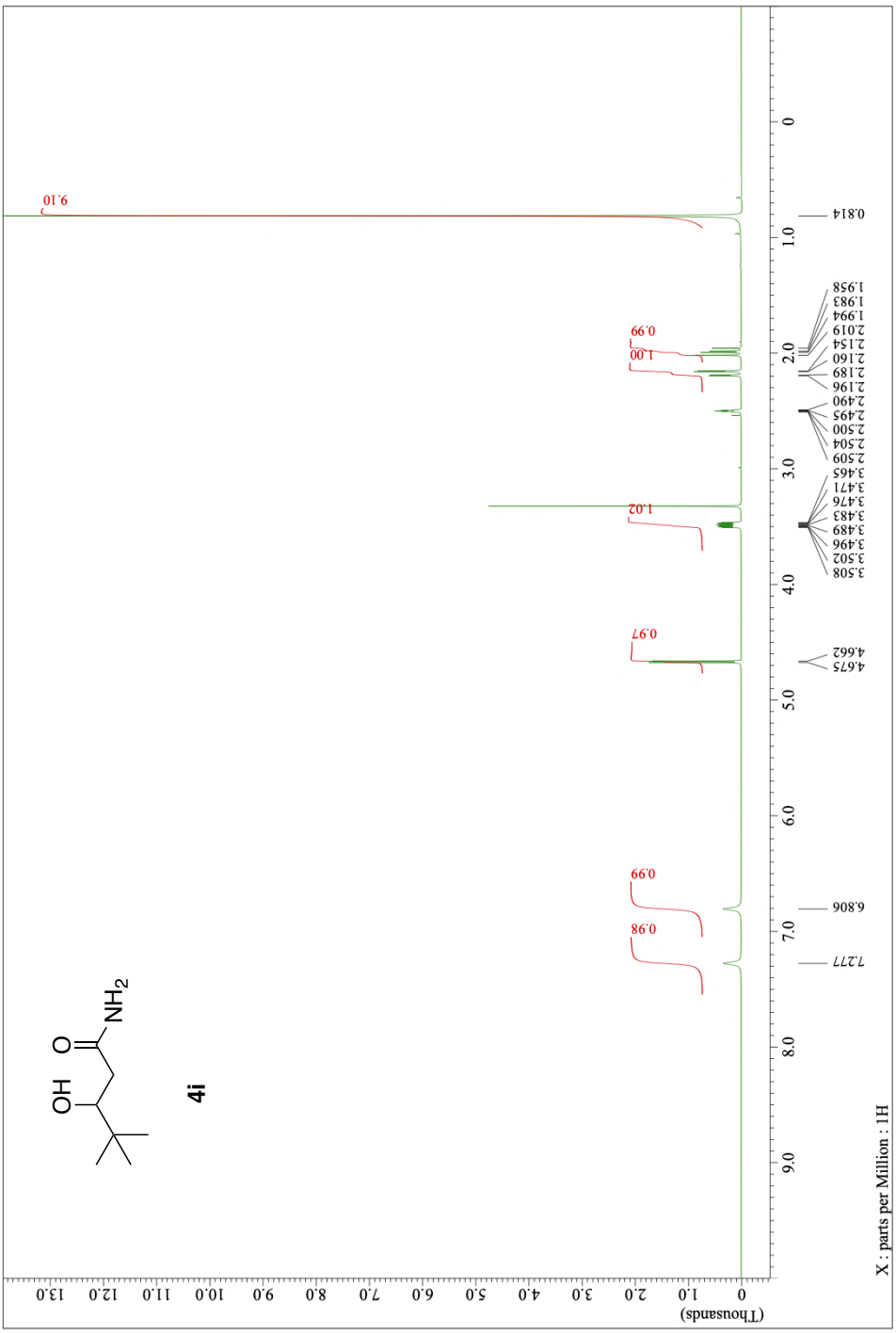
^{1}H NMR (500 MHz, DMSO-*d6*)



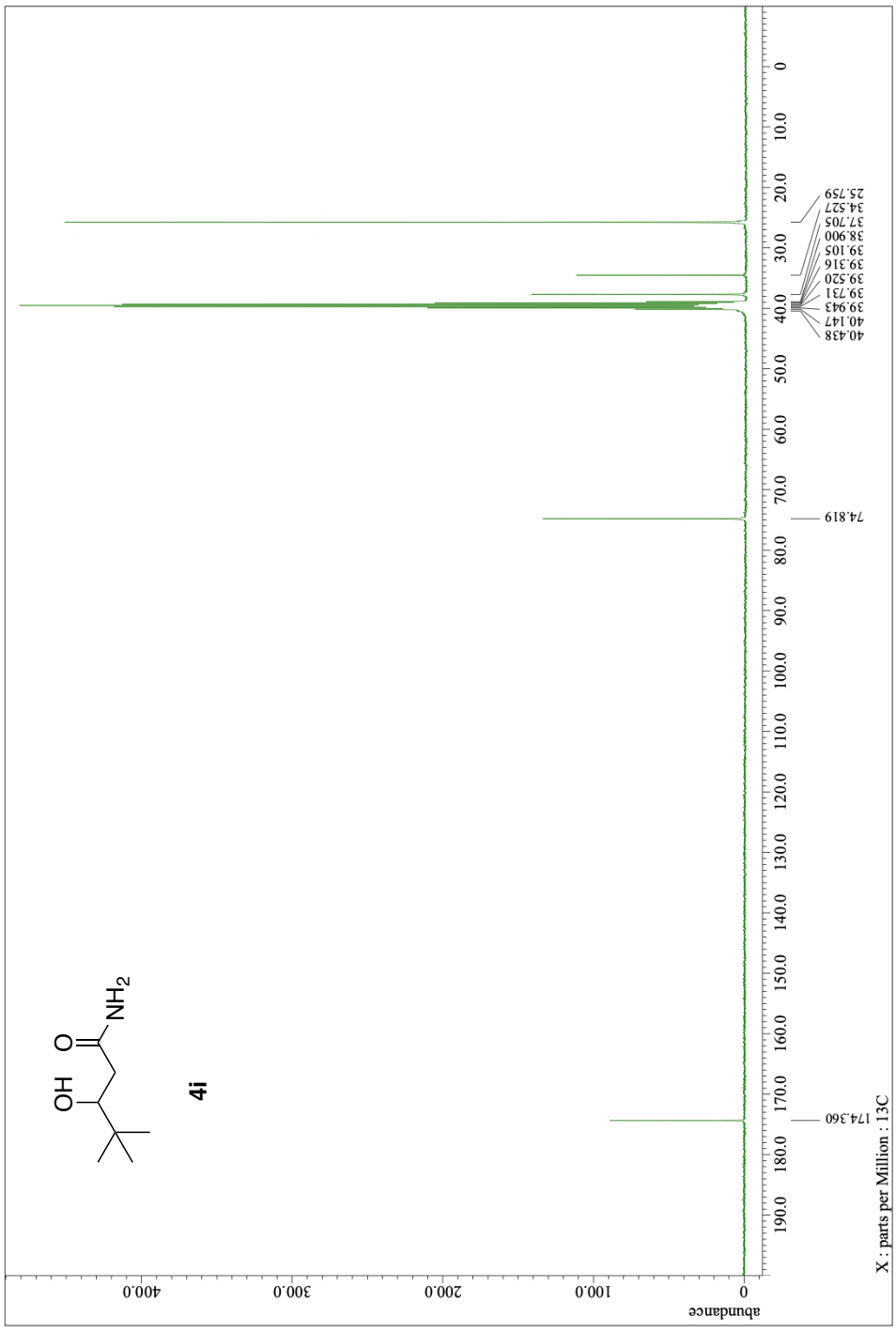
^{13}C NMR (100 MHz, DMSO-*d6*)



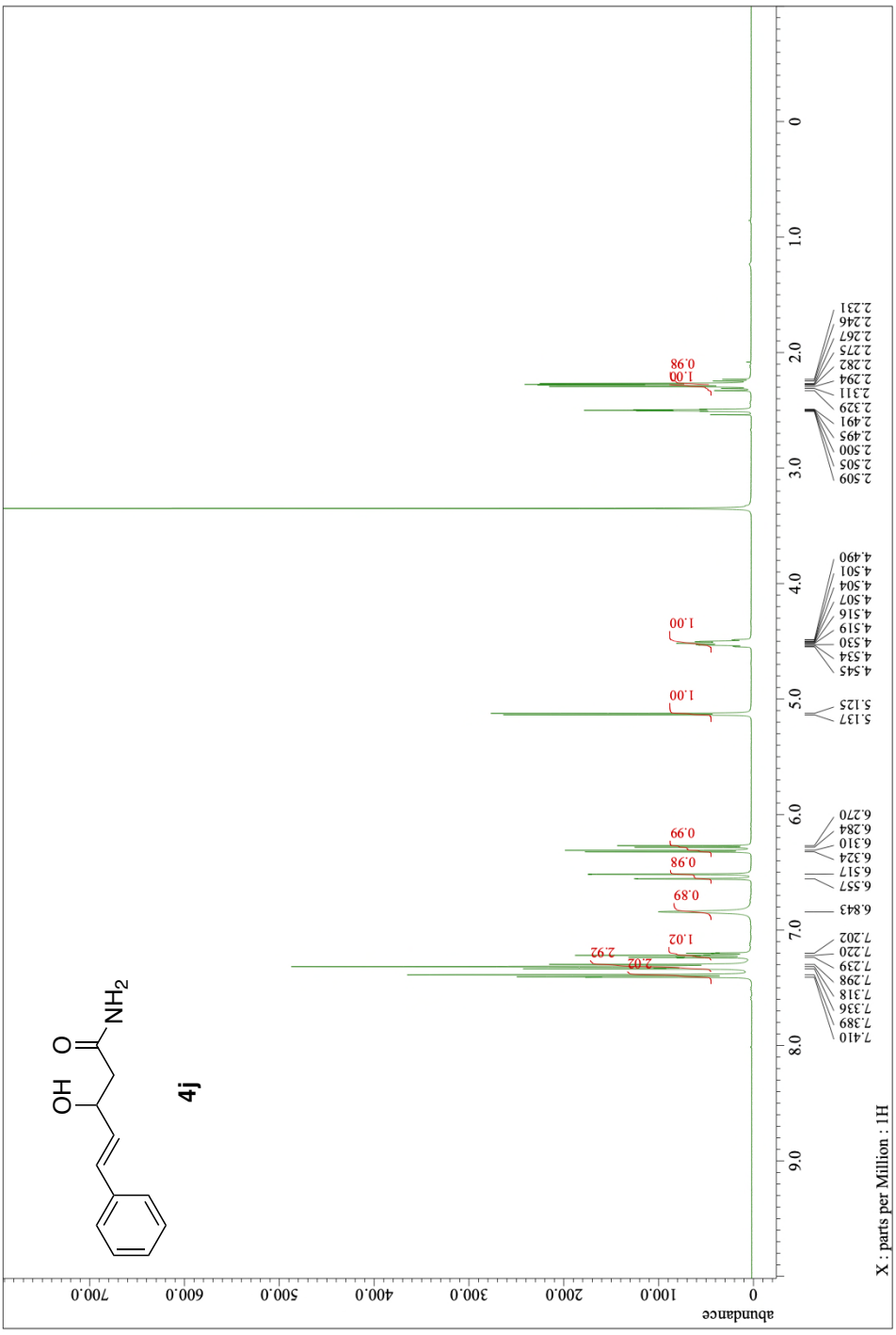
^{1}H NMR (400 MHz, DMSO-*d6*)



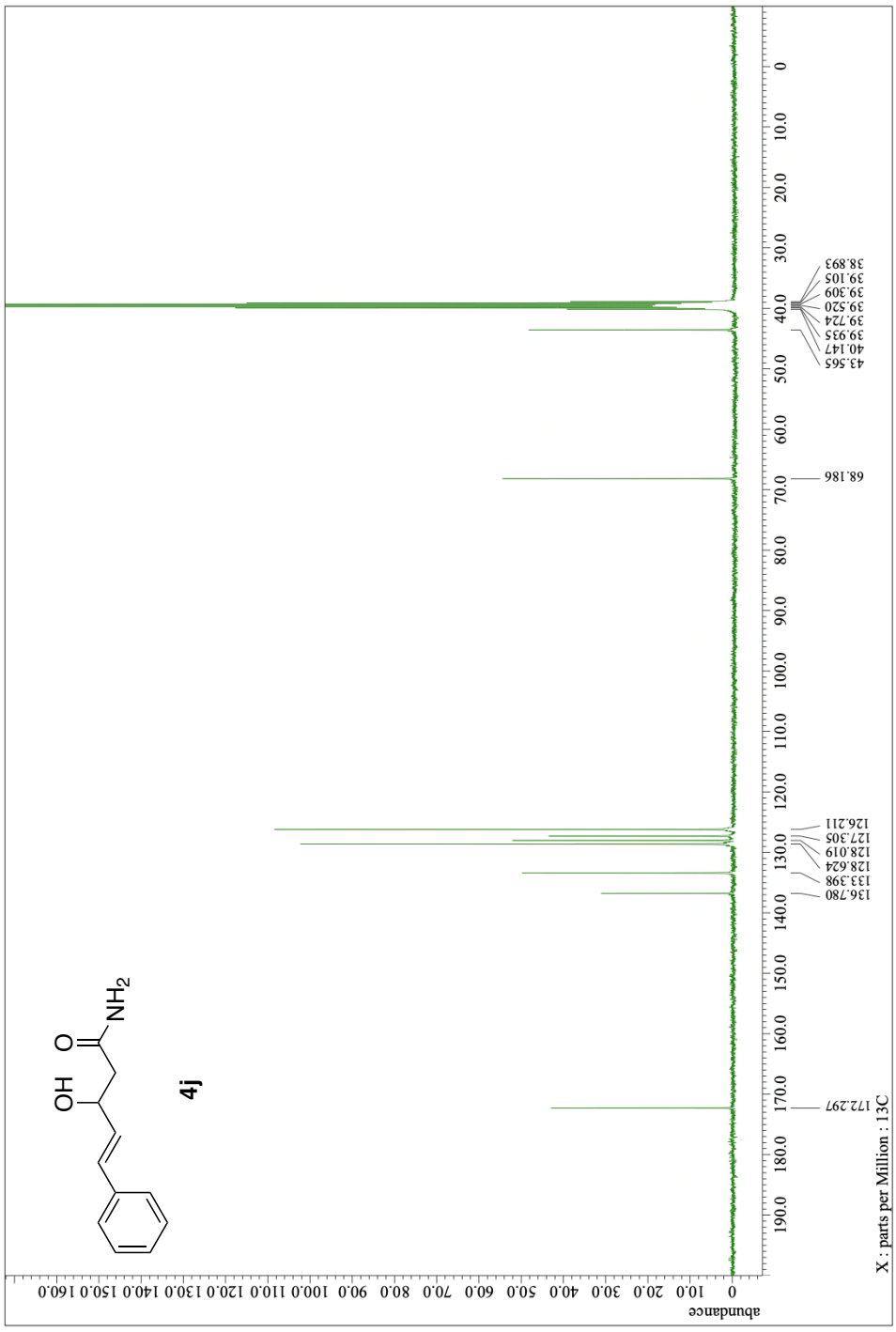
^{13}C NMR (100 MHz, DMSO-*d6*)



^{1}H NMR (400 MHz, DMSO-*d6*)



^{13}C NMR (100 MHz, DMSO-*d6*)



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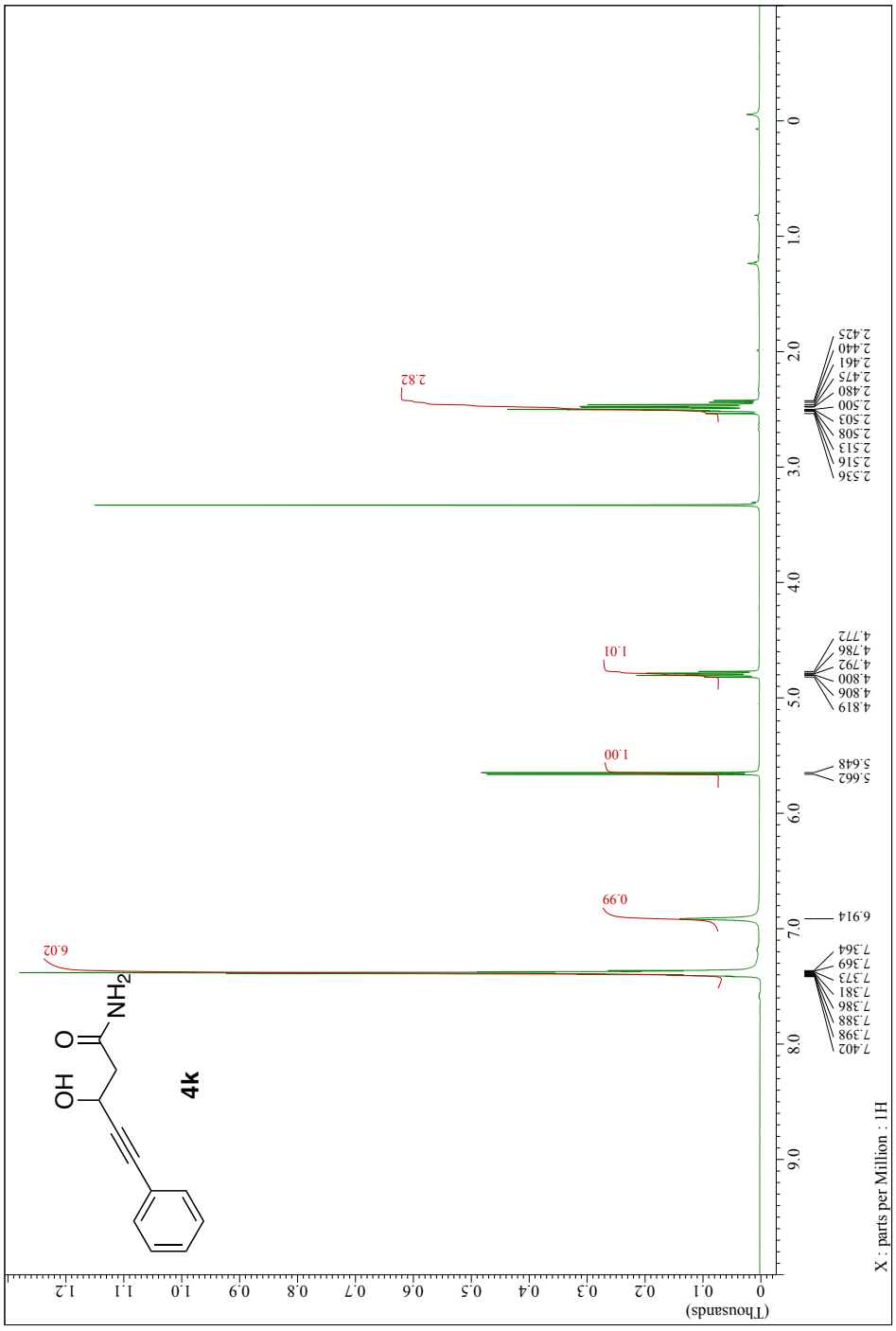

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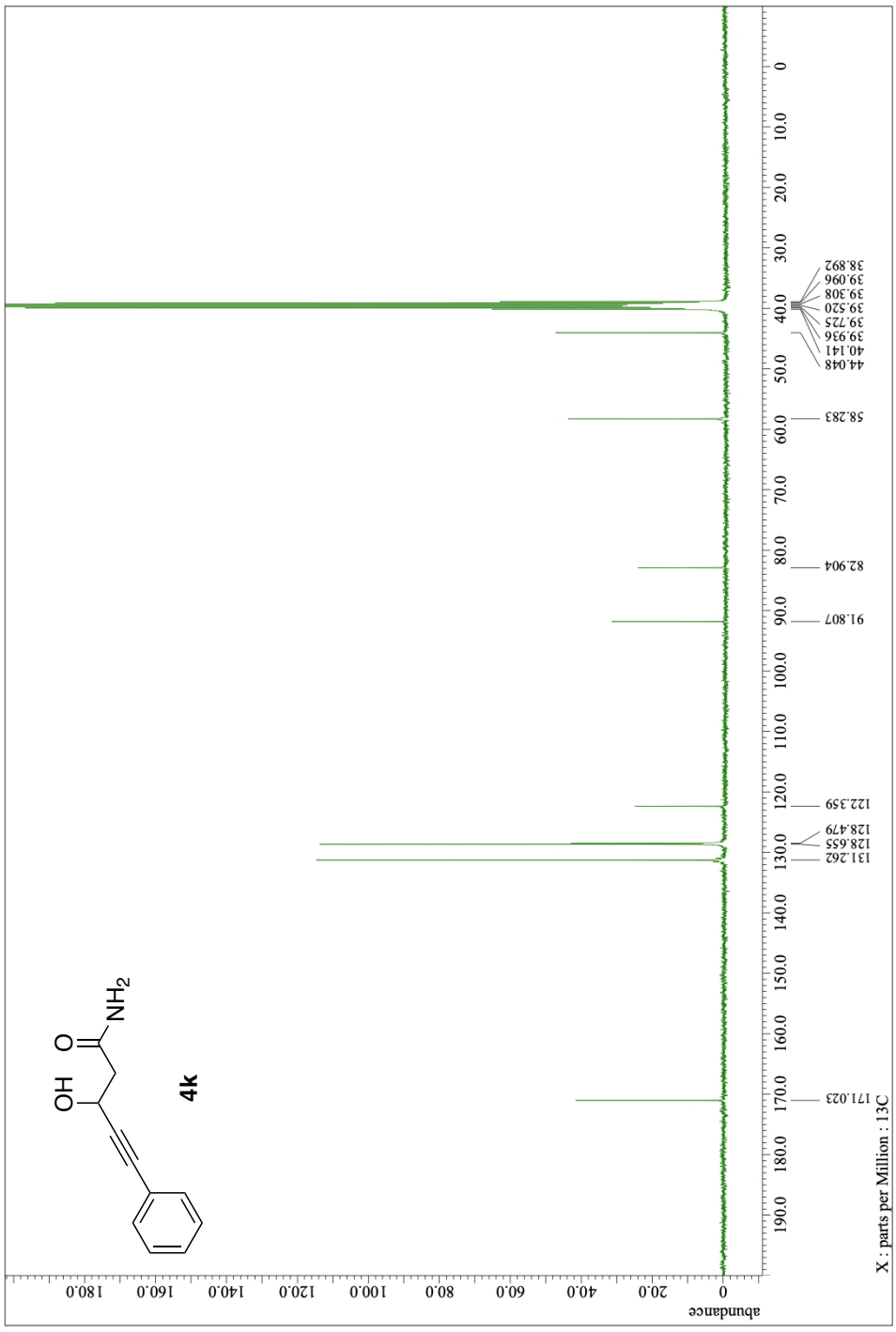
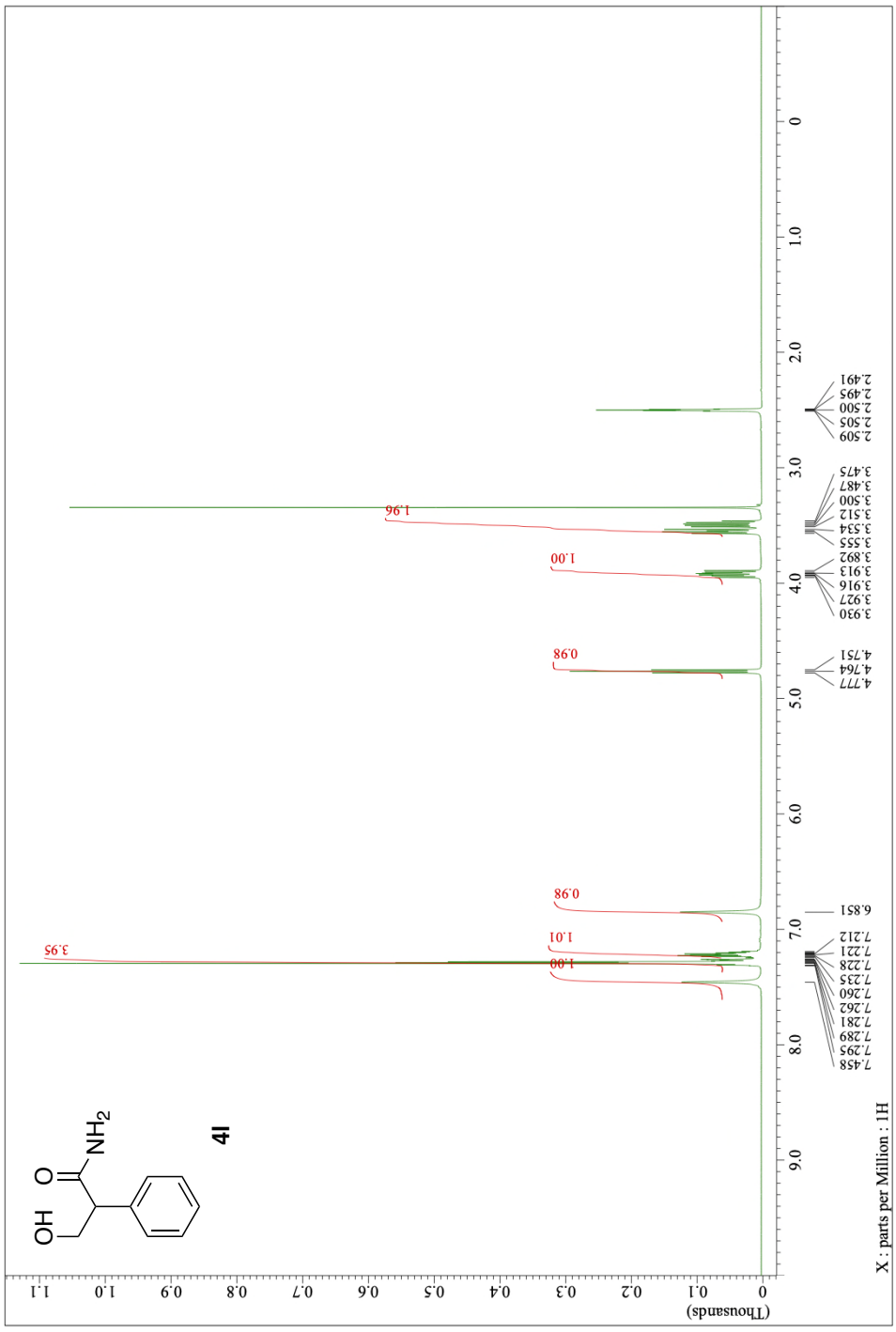
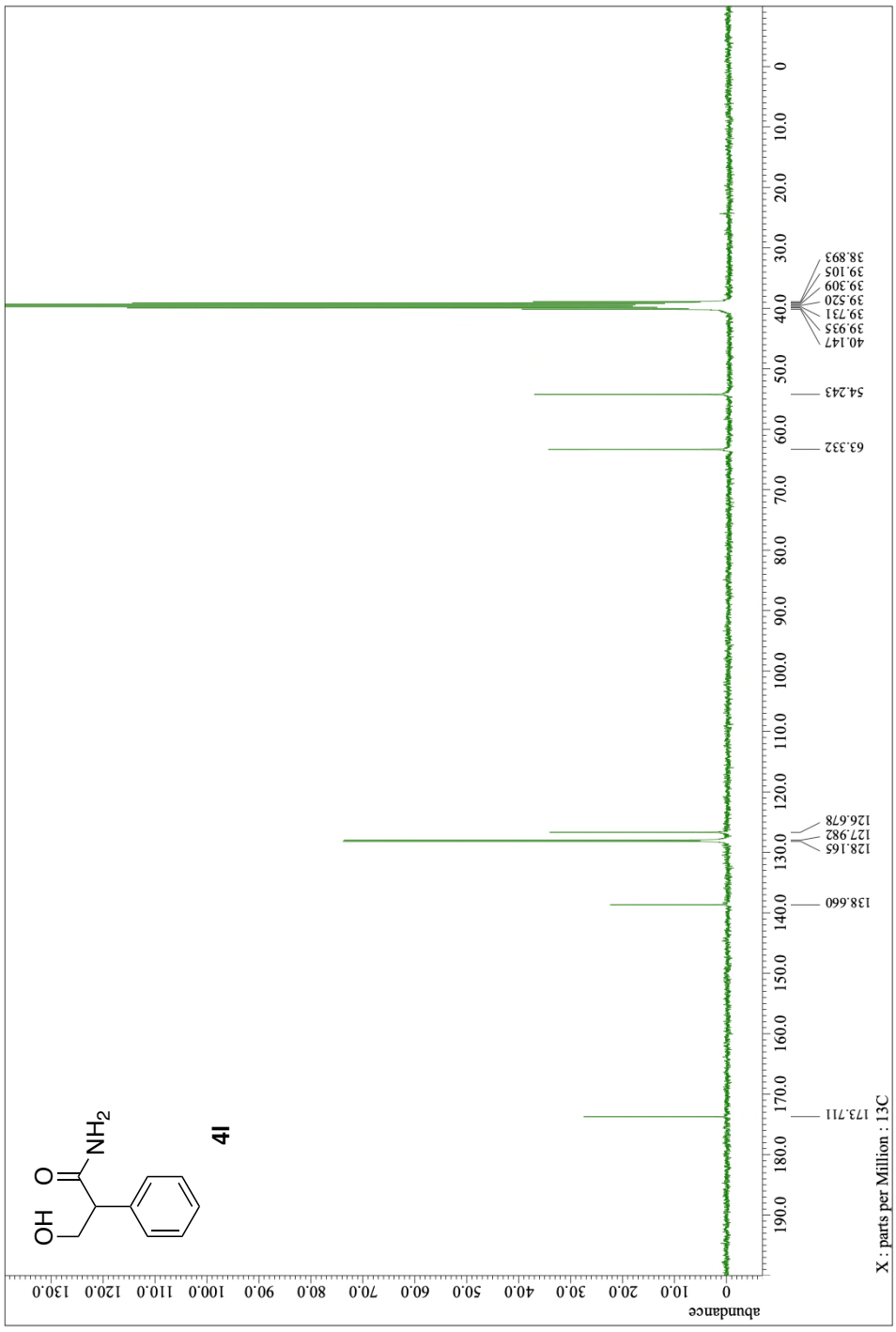


^{1}H NMR (400 MHz, DMSO-*d6*)



^{13}C NMR (100 MHz, DMSO-*d6*)



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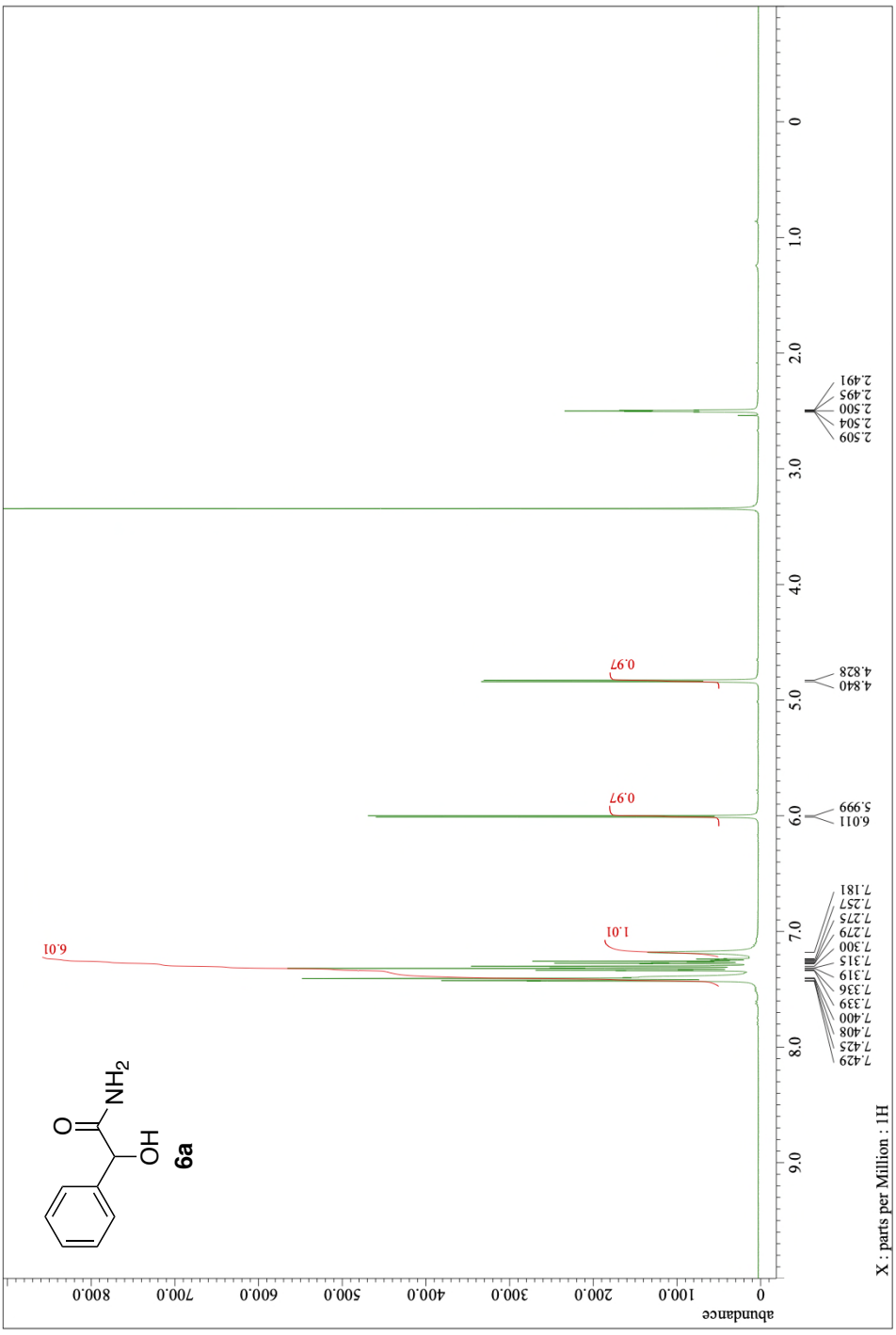

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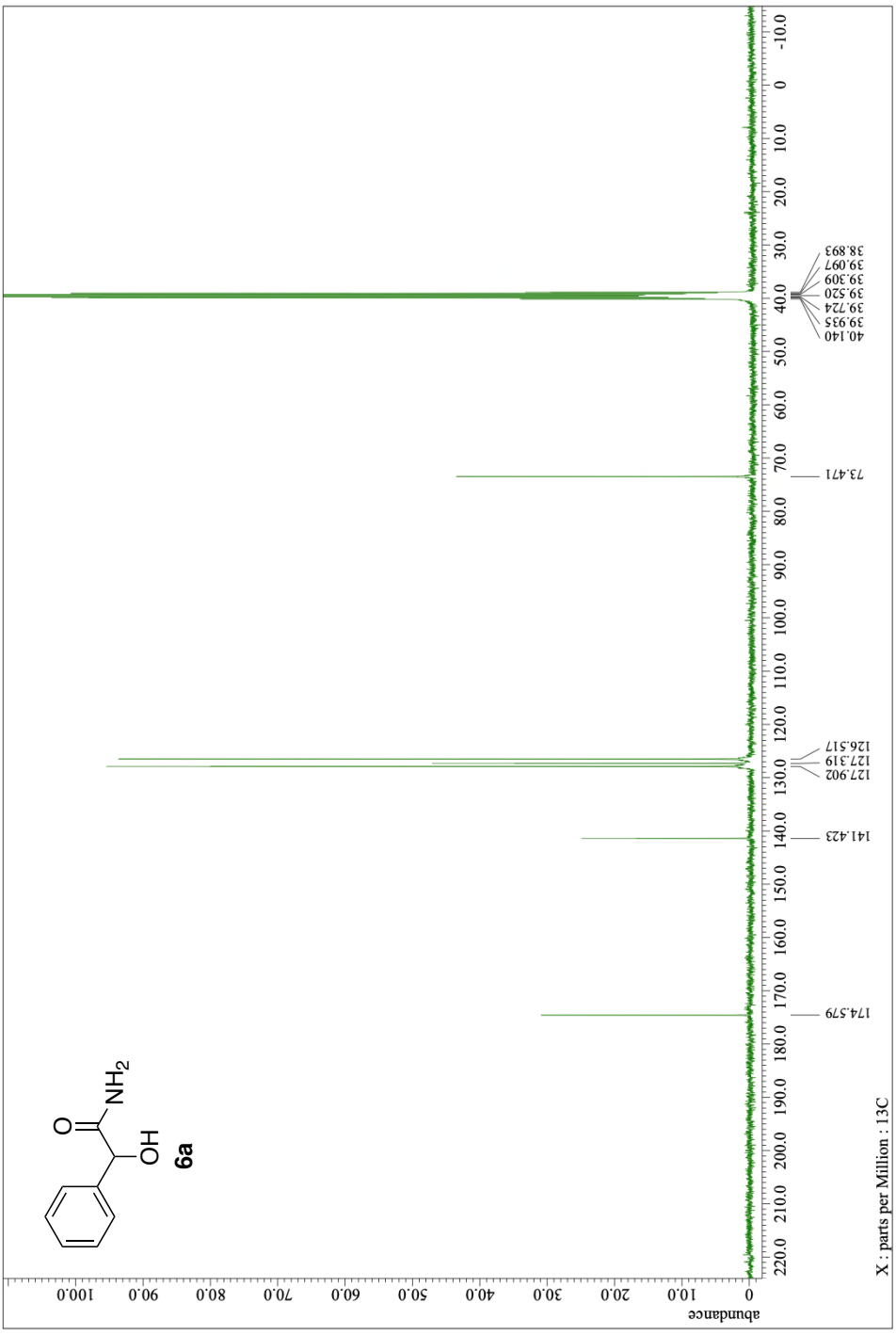
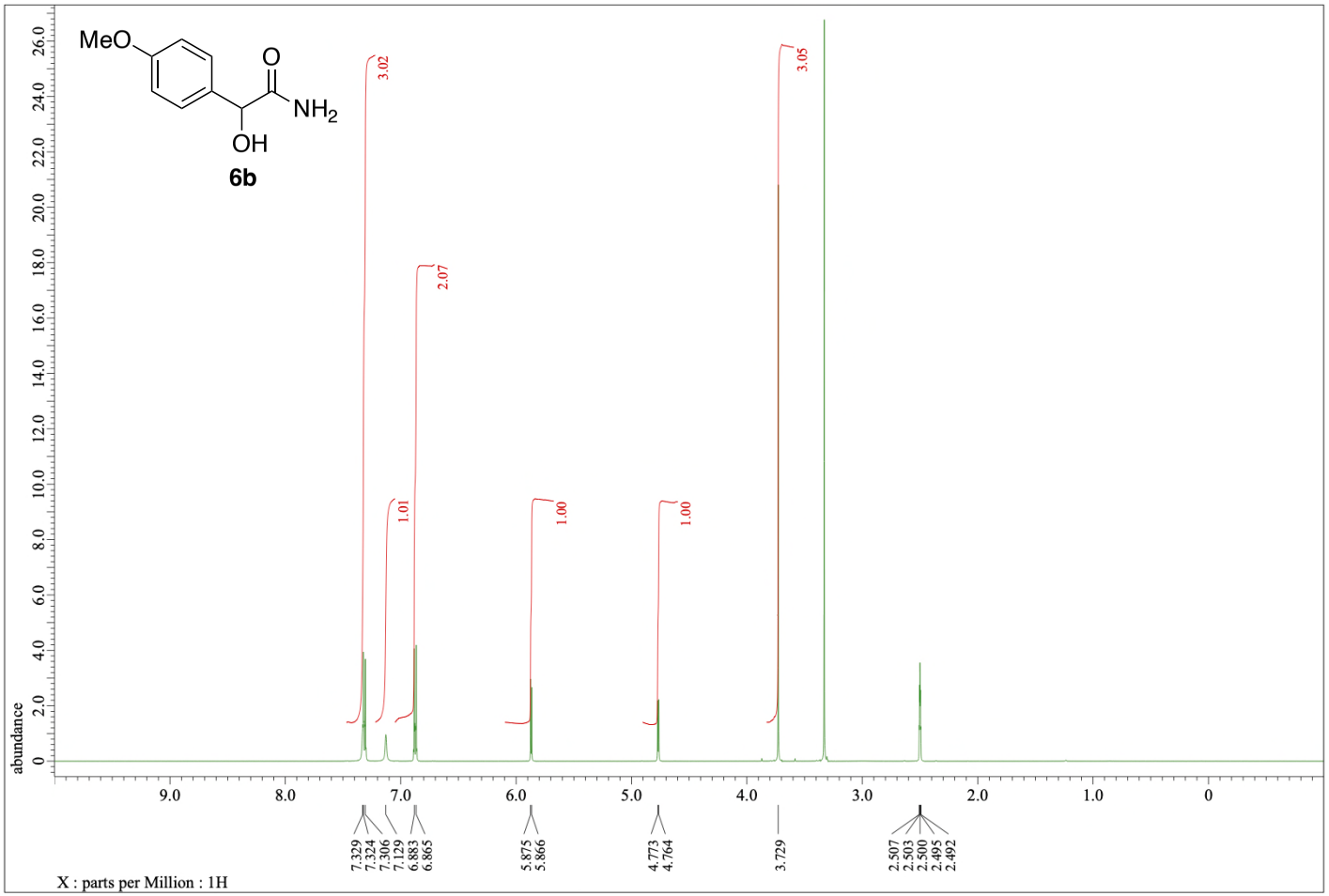
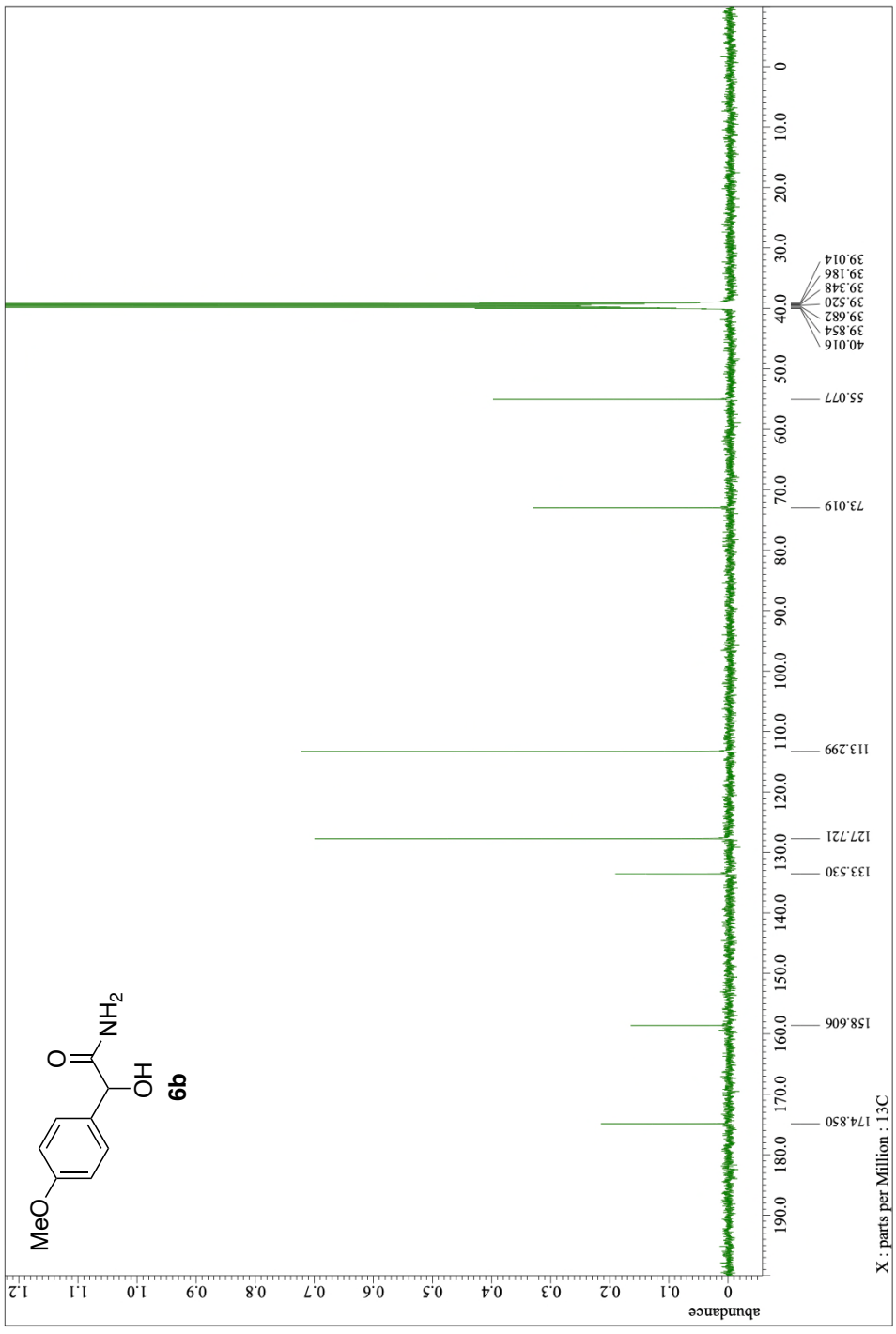


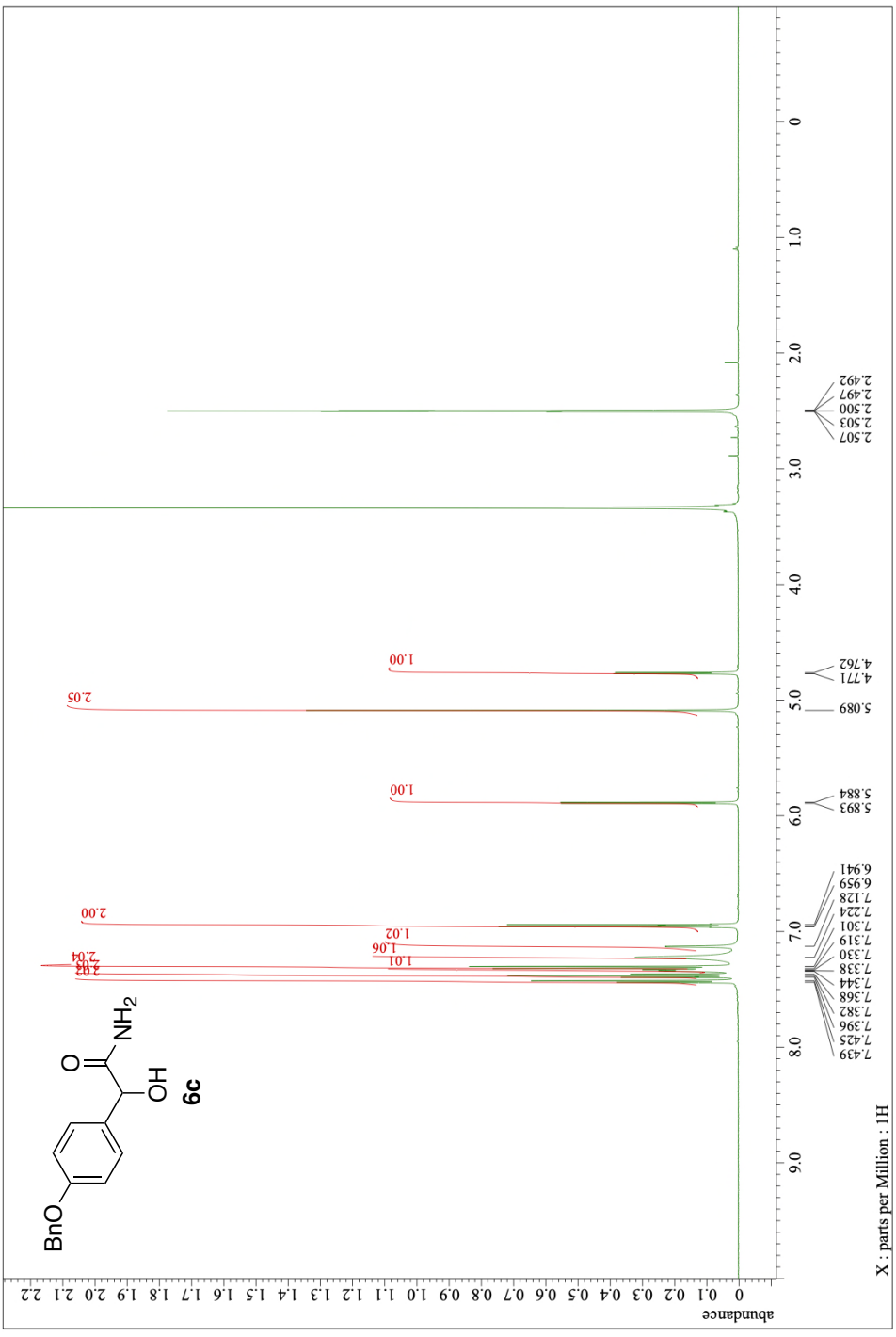
^{1}H NMR (500 MHz, DMSO-*d6*)



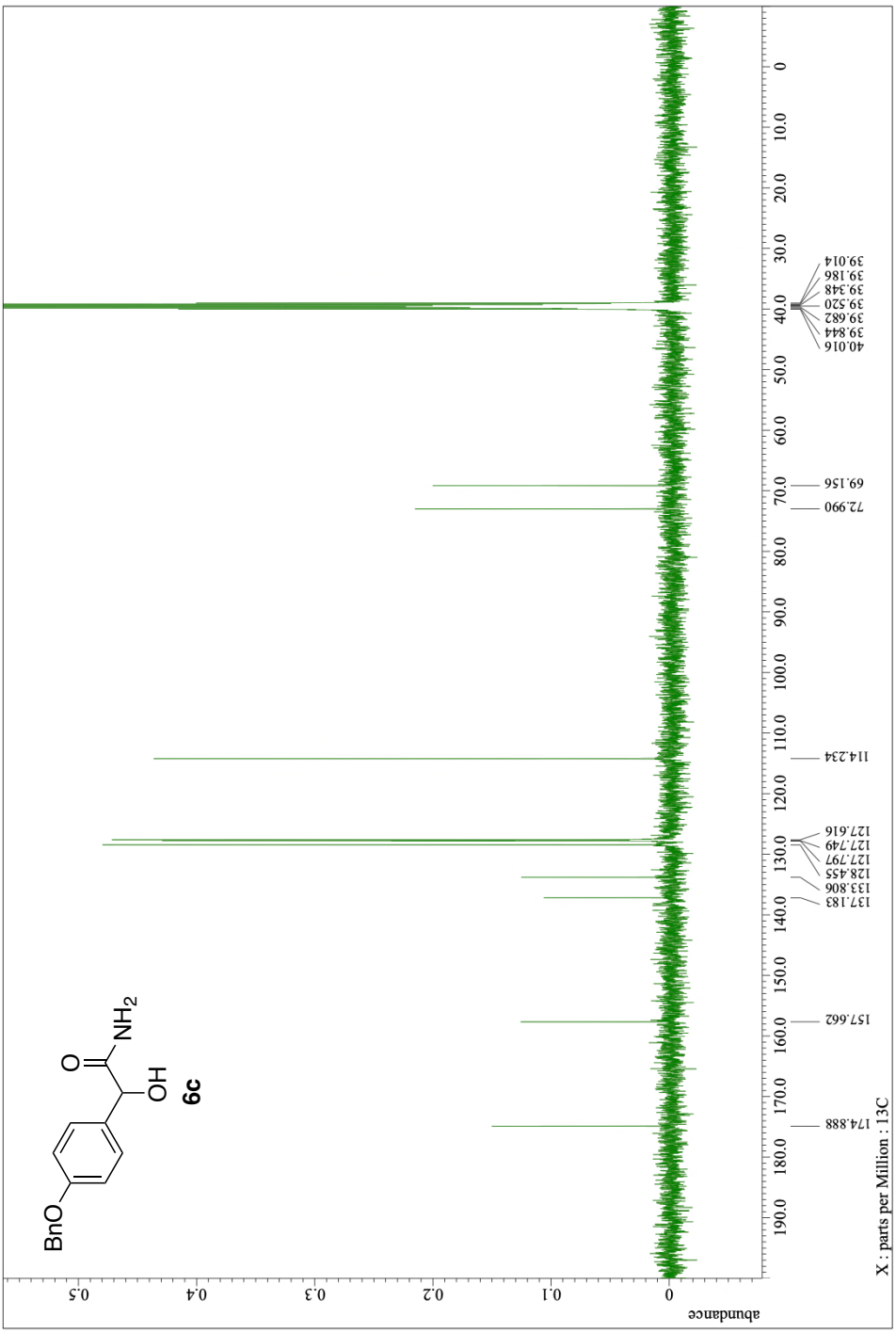
^{13}C NMR (126 MHz, DMSO-*d6*)



^{1}H NMR (500 MHz, DMSO-*d6*)



^{13}C NMR (126 MHz, DMSO-*d6*)



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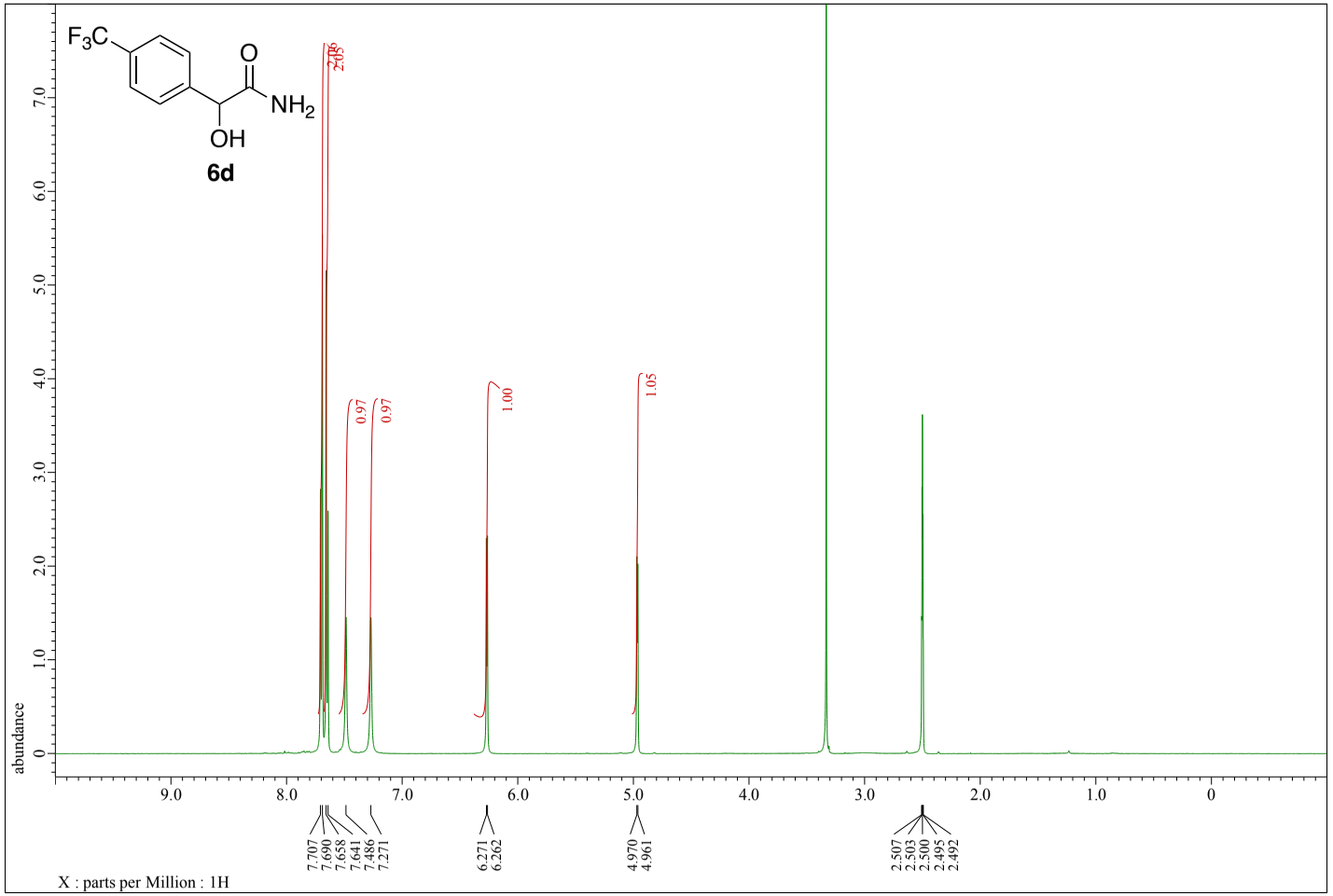

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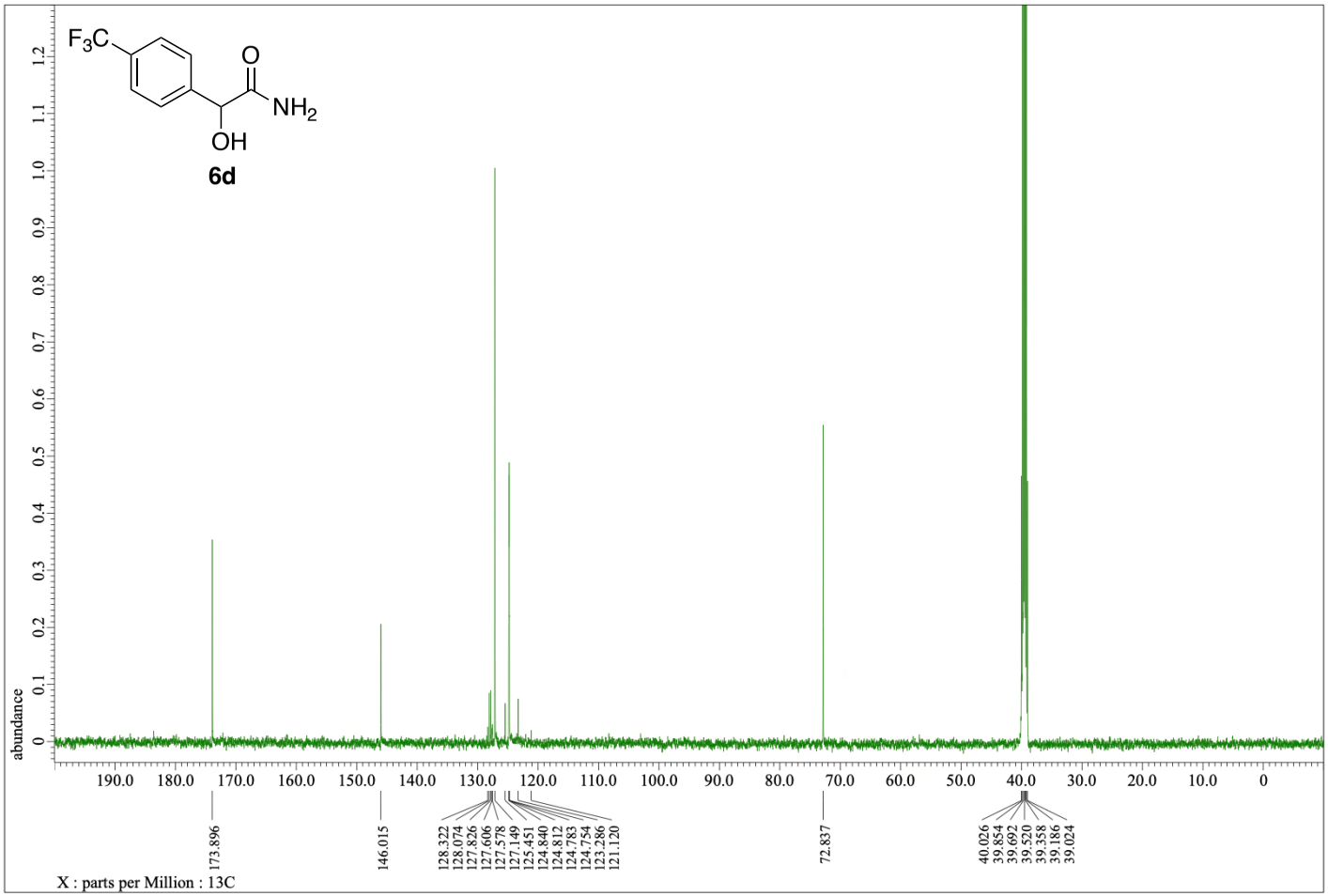
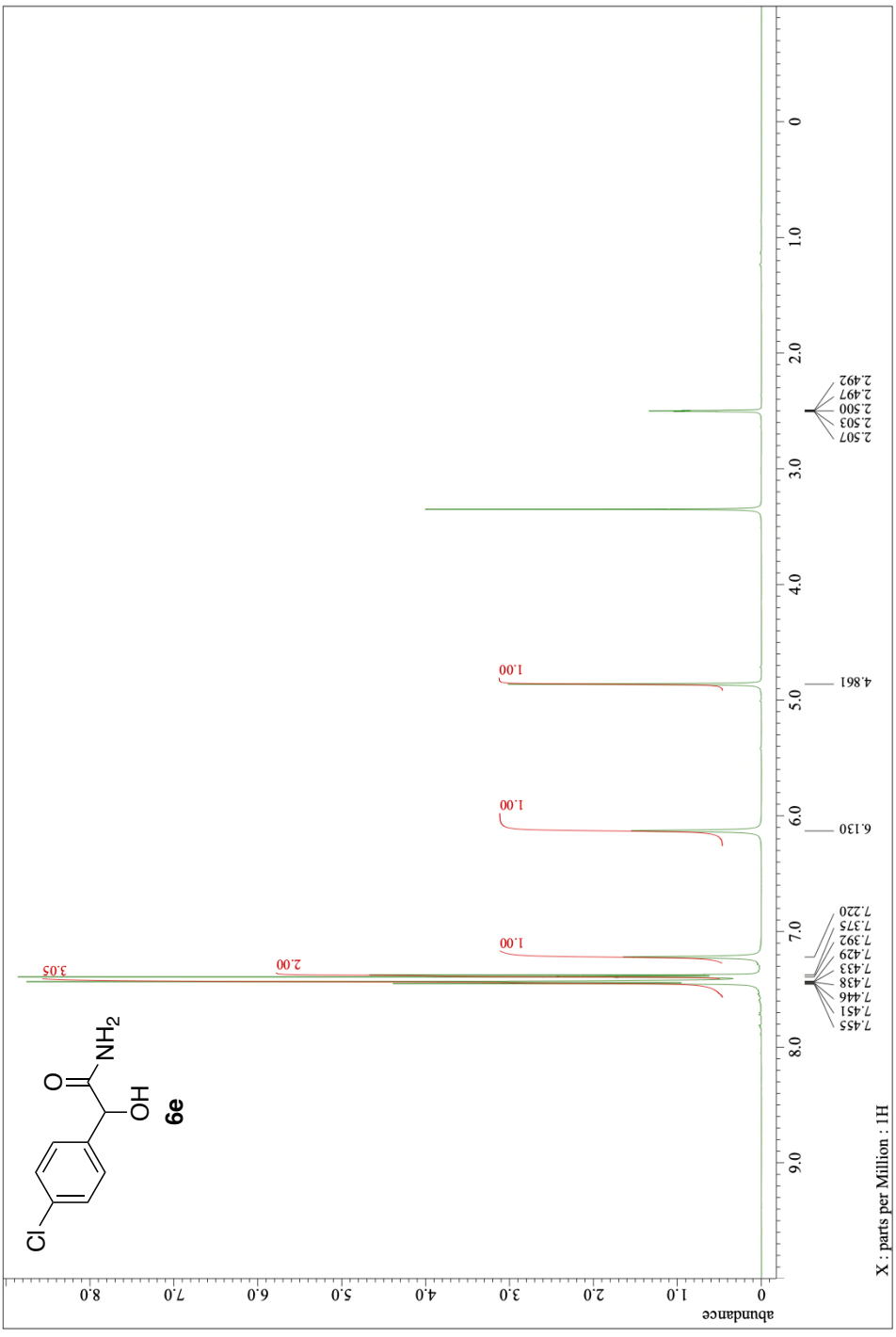


^{1}H NMR (500 MHz, DMSO-*d6*)



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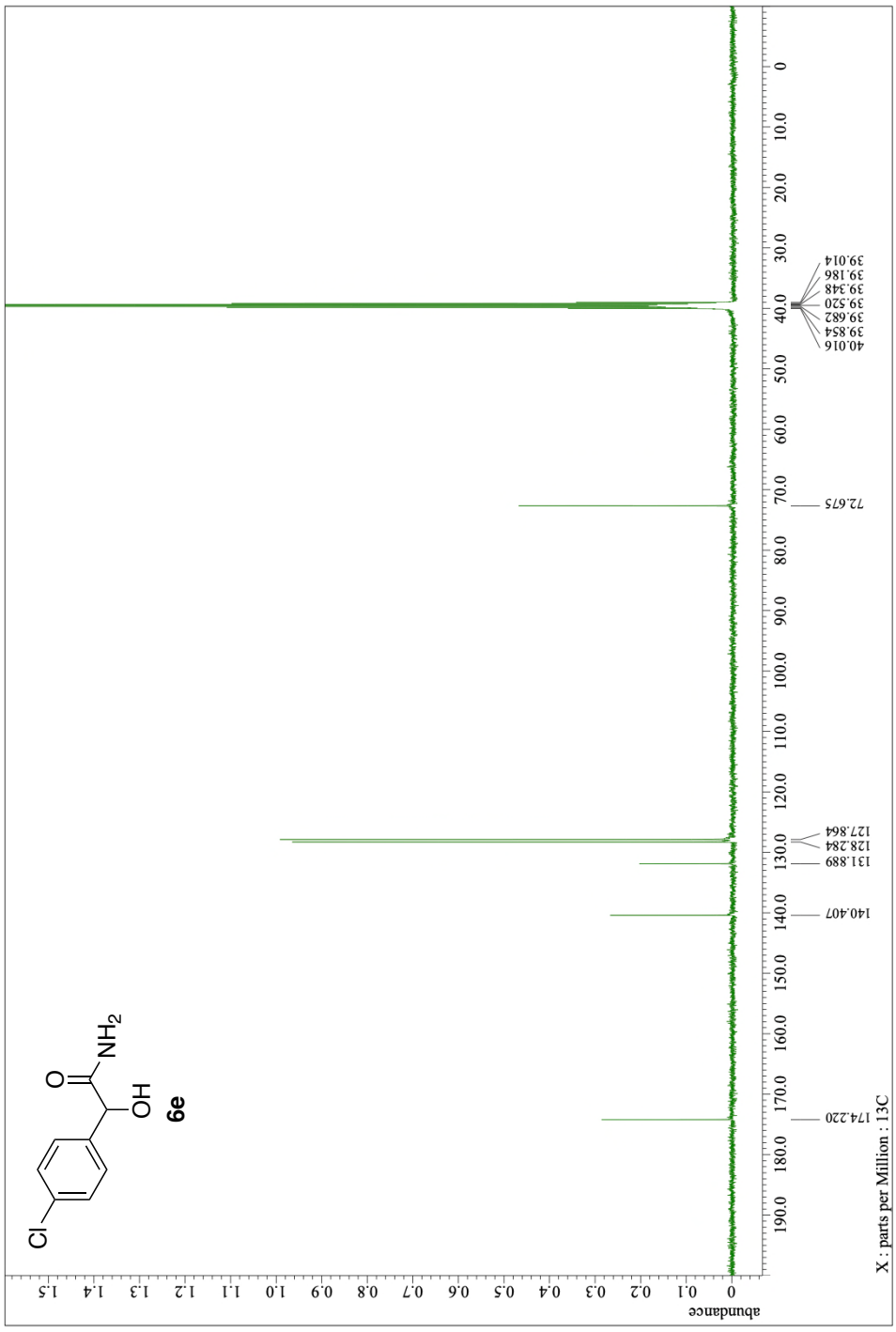

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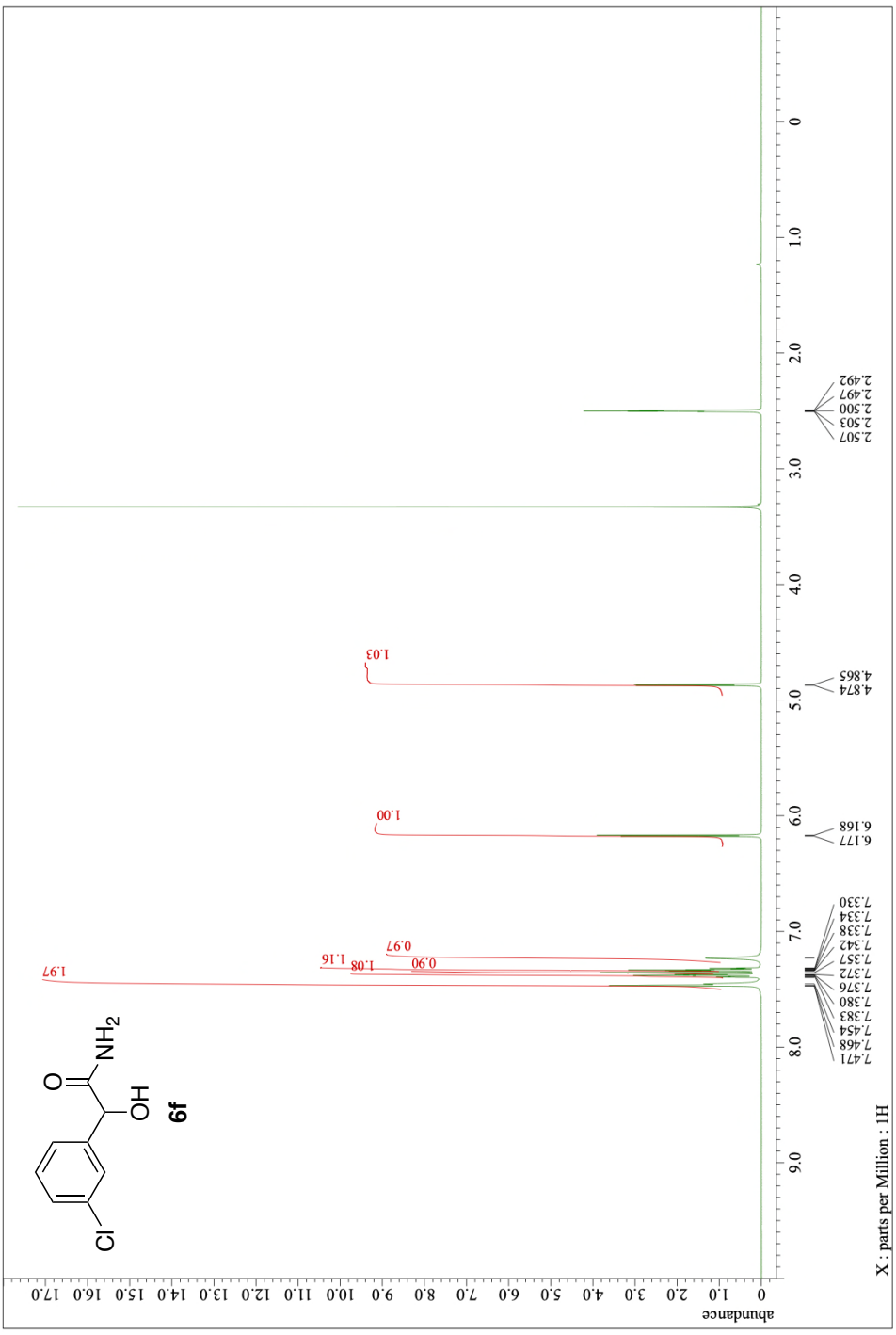

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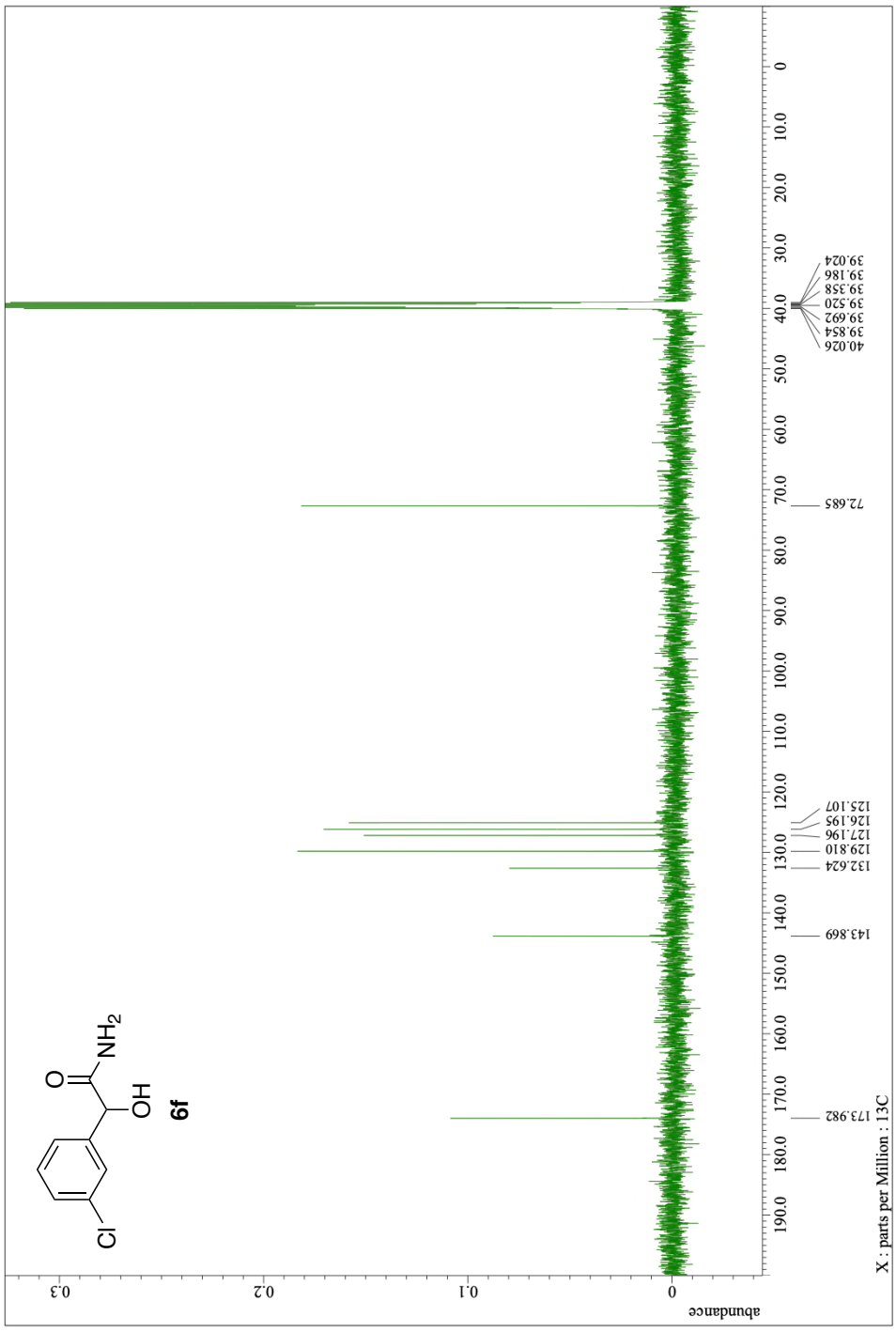

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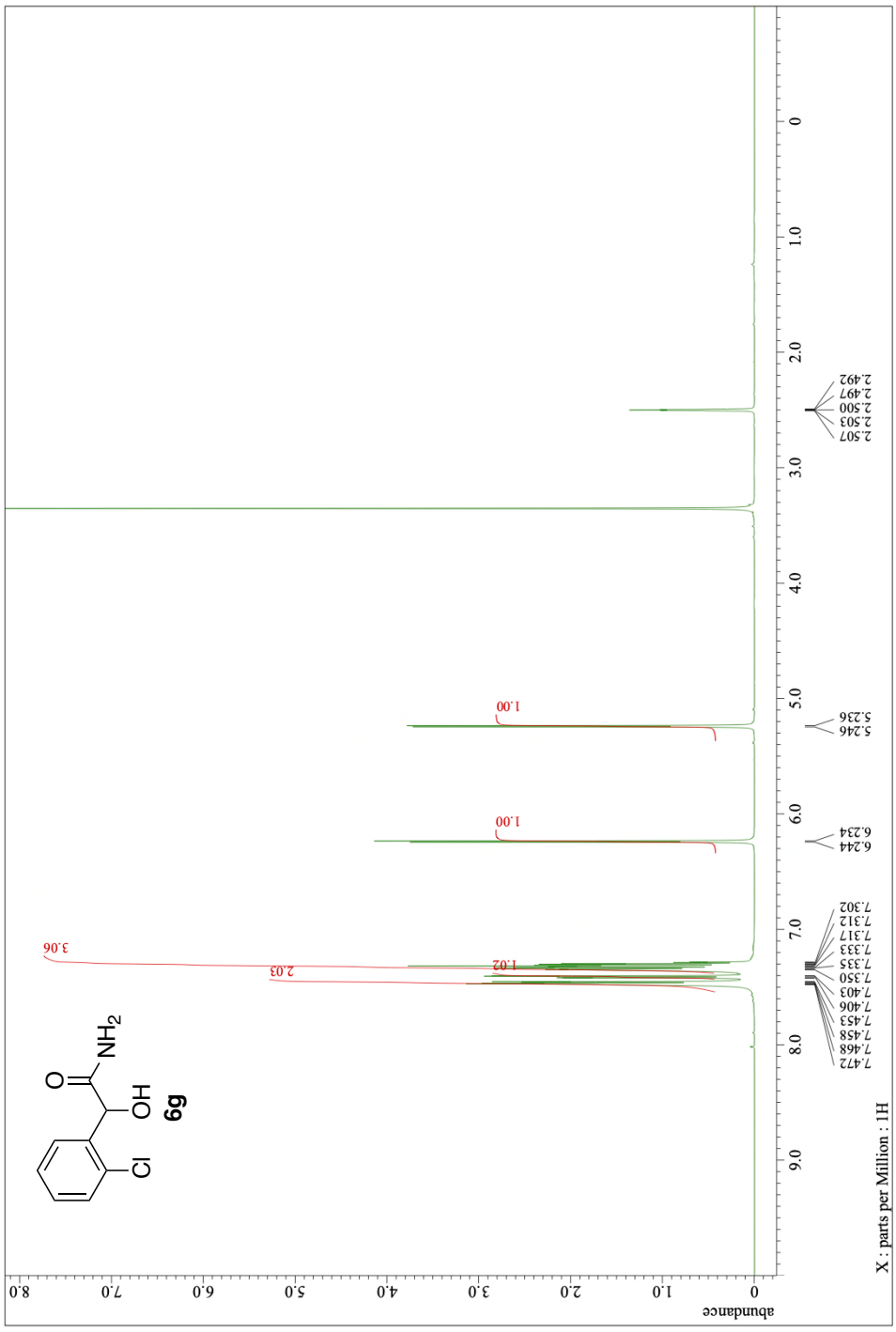
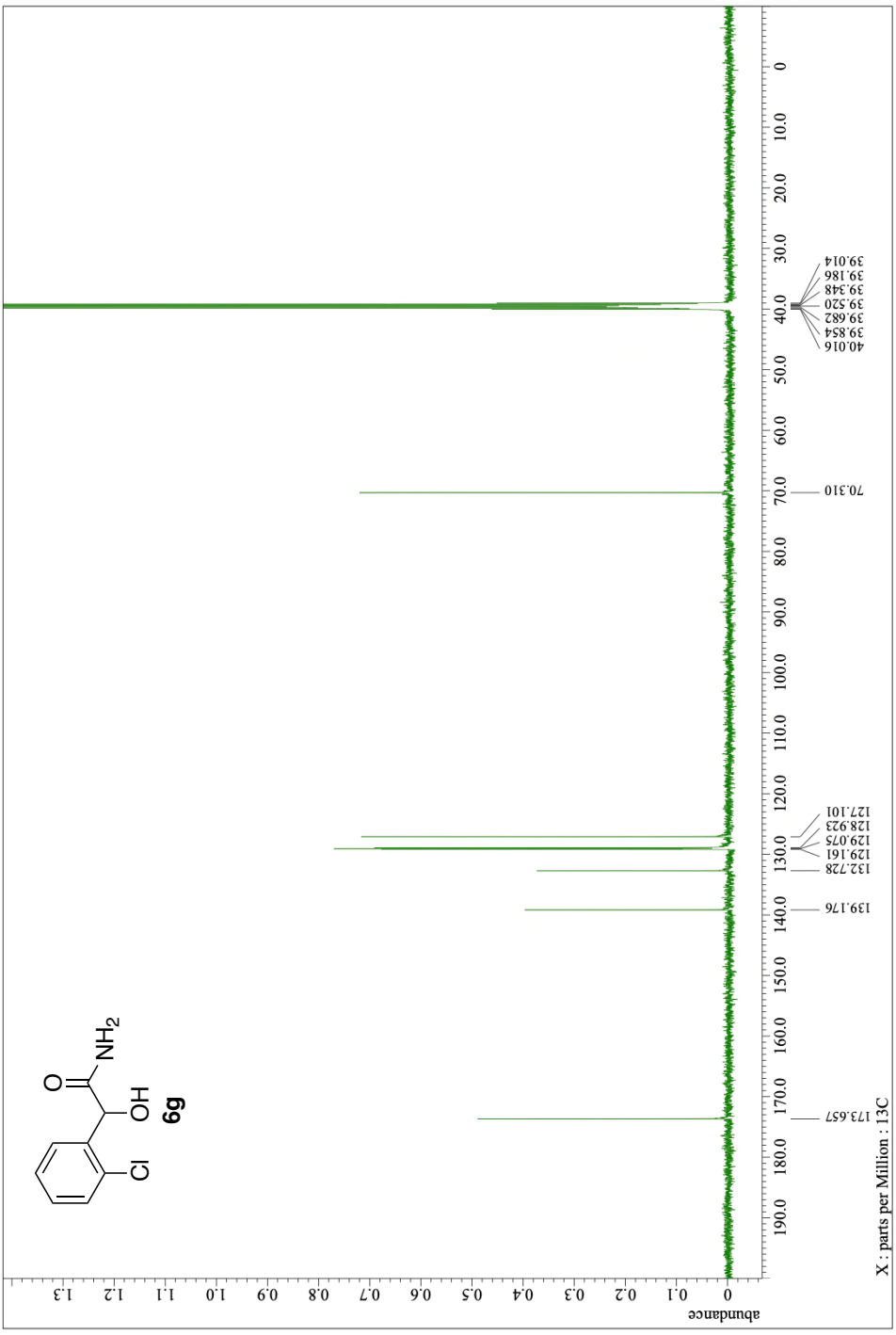


^{13}C NMR (126 MHz, DMSO-*d6*)



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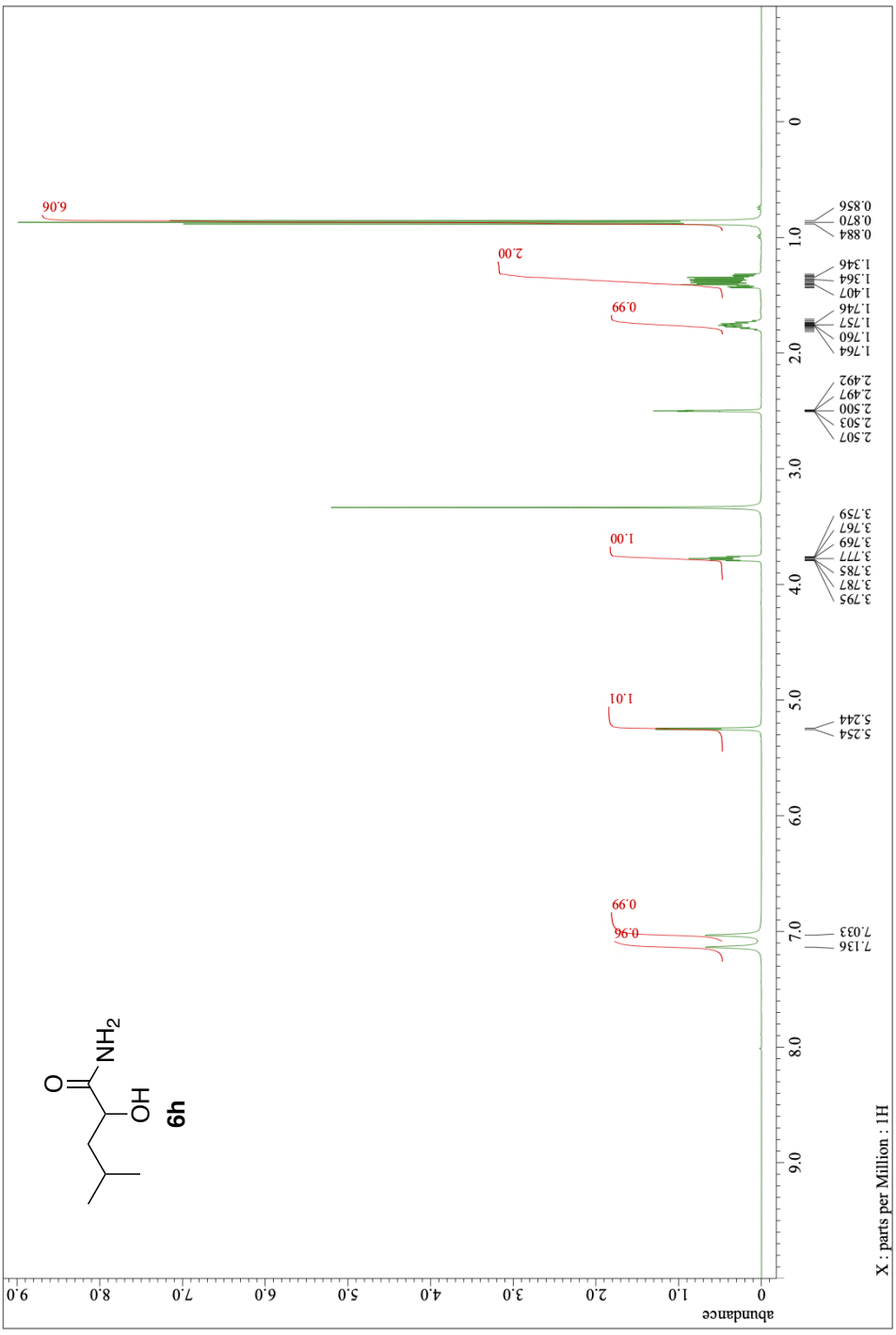
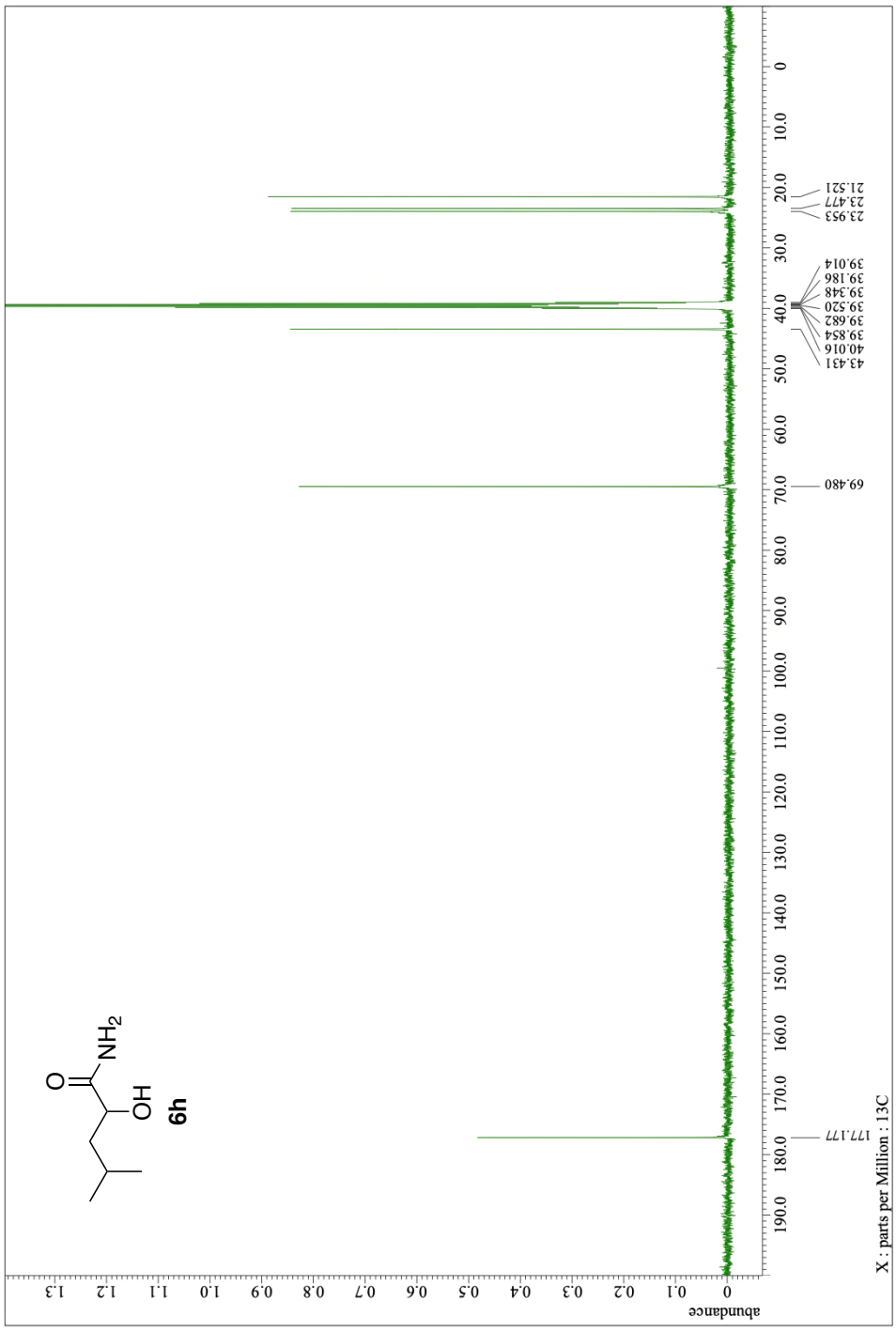
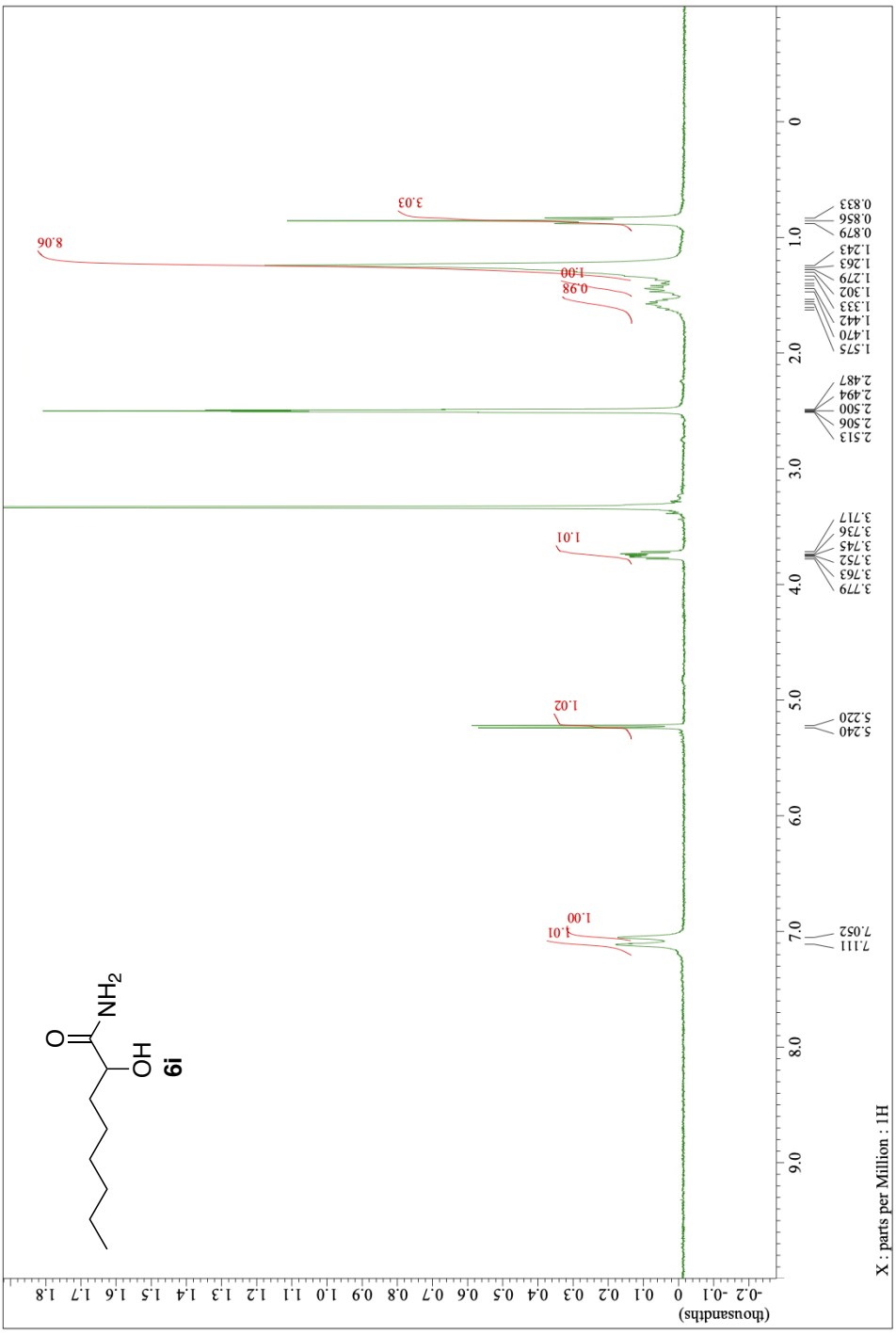


6h

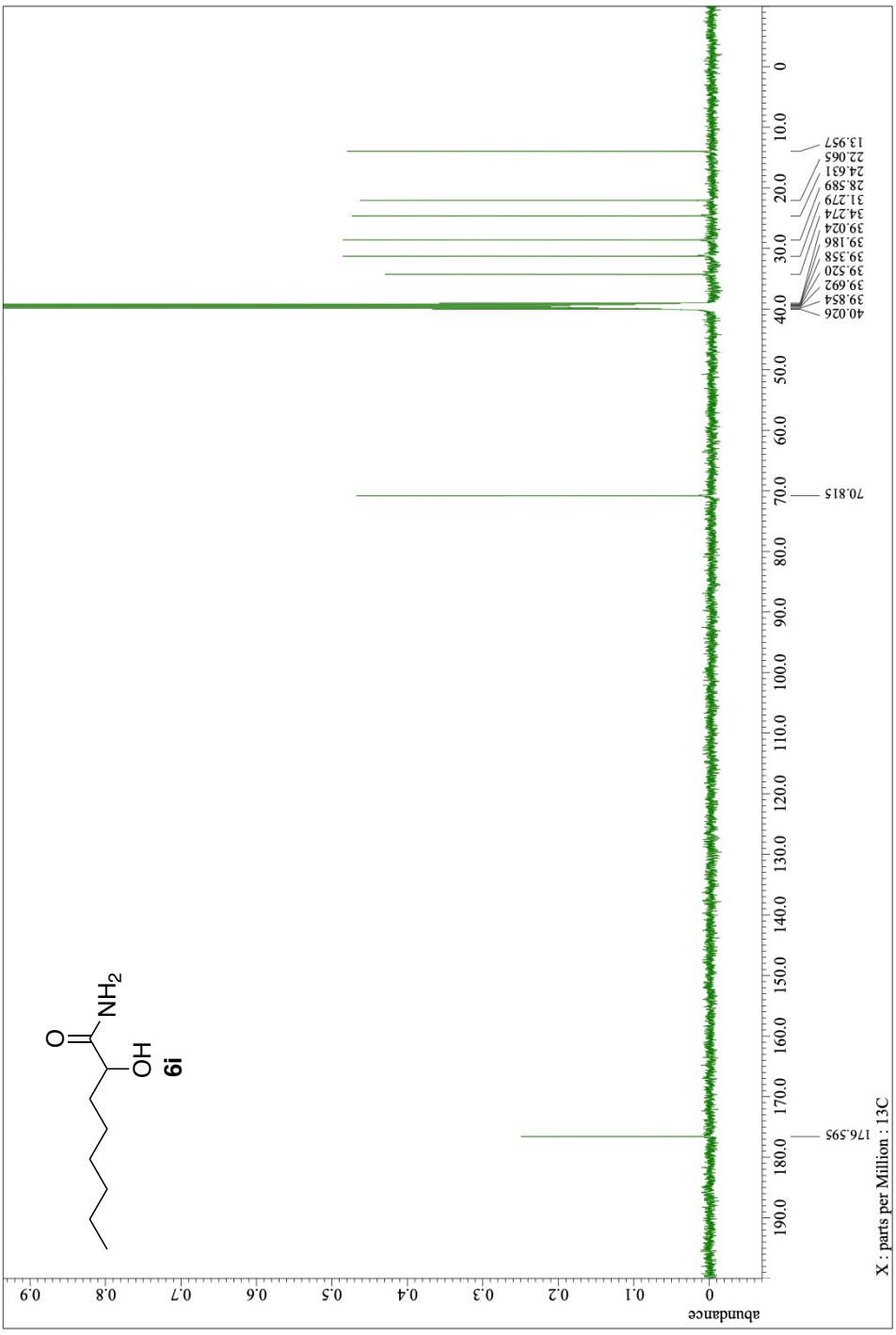
^{13}C NMR (126 MHz, DMSO-*d6*)



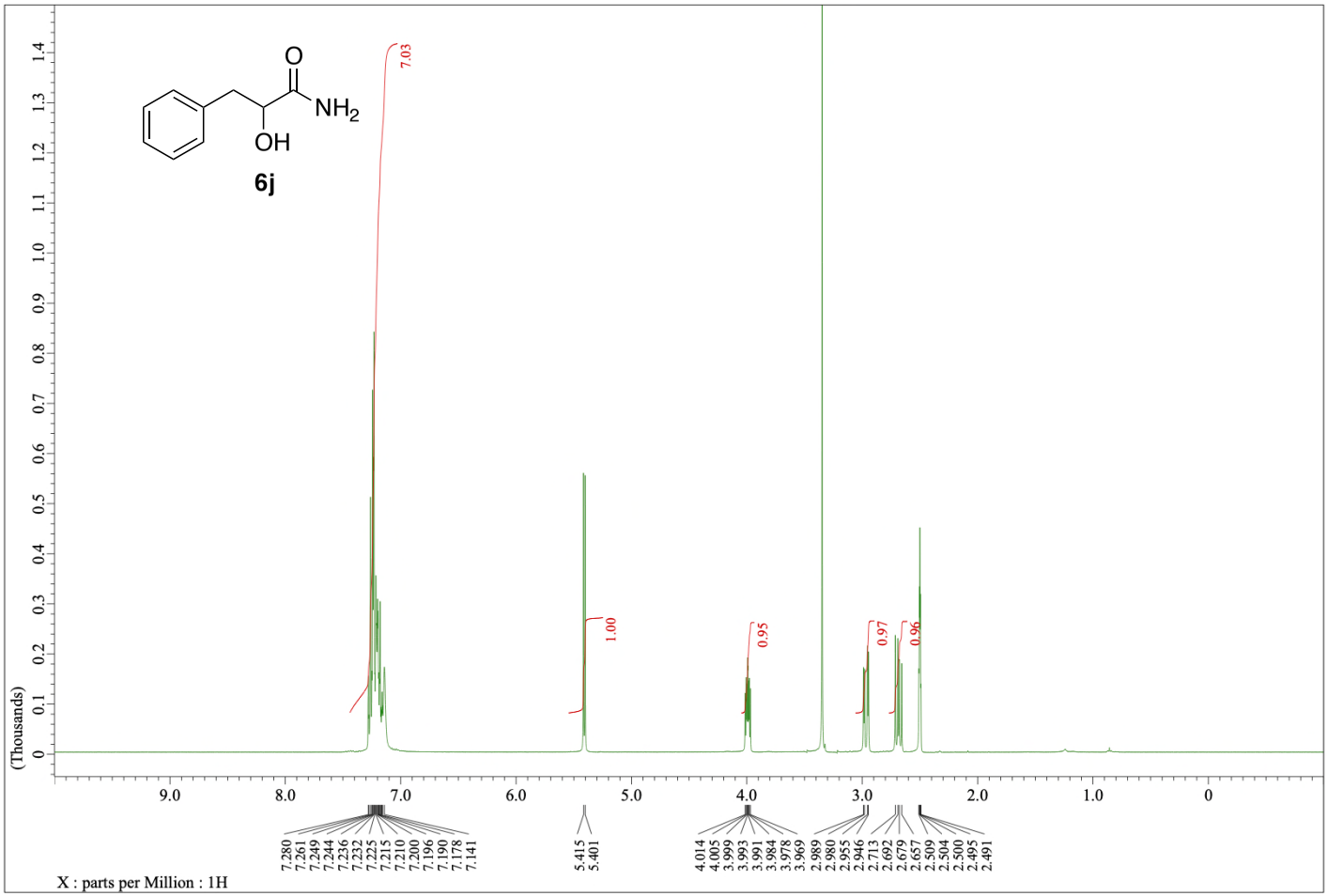
^{1}H NMR (270 MHz, DMSO-*d6*)



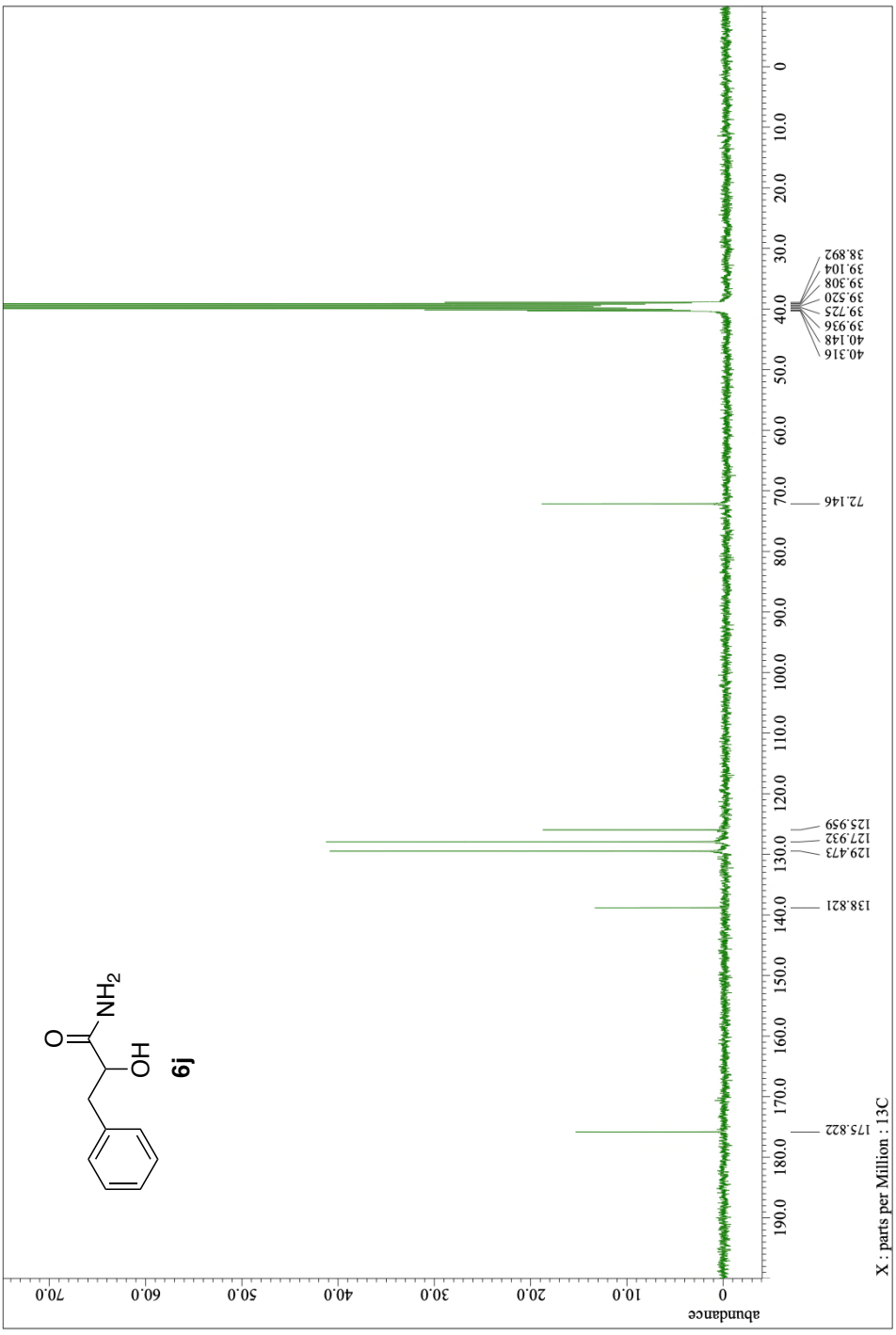
^{13}C NMR (126 MHz, DMSO-*d6*)



^{1}H NMR (400 MHz, DMSO-*d6*)



^{13}C NMR (100 MHz, DMSO-*d6*)



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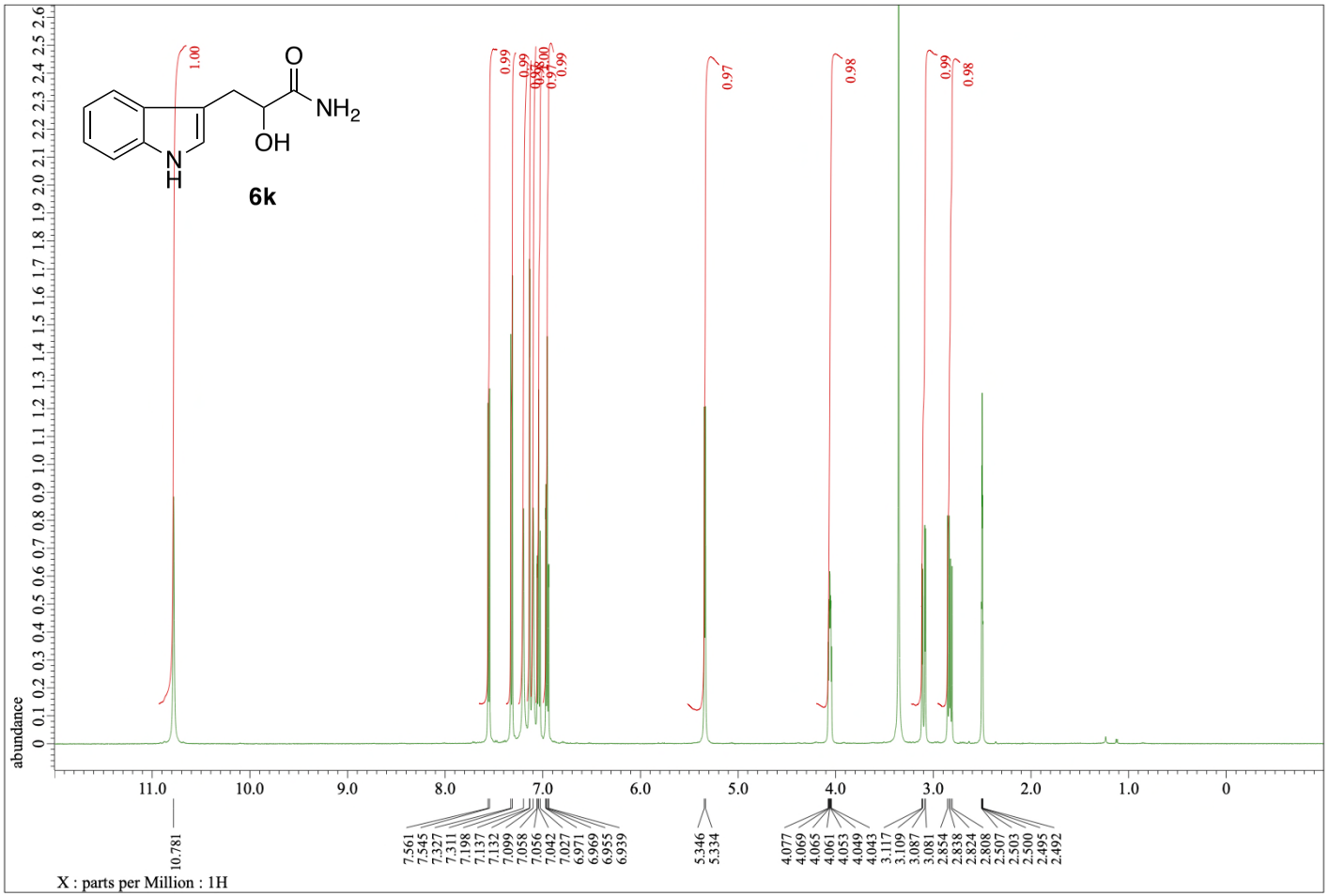
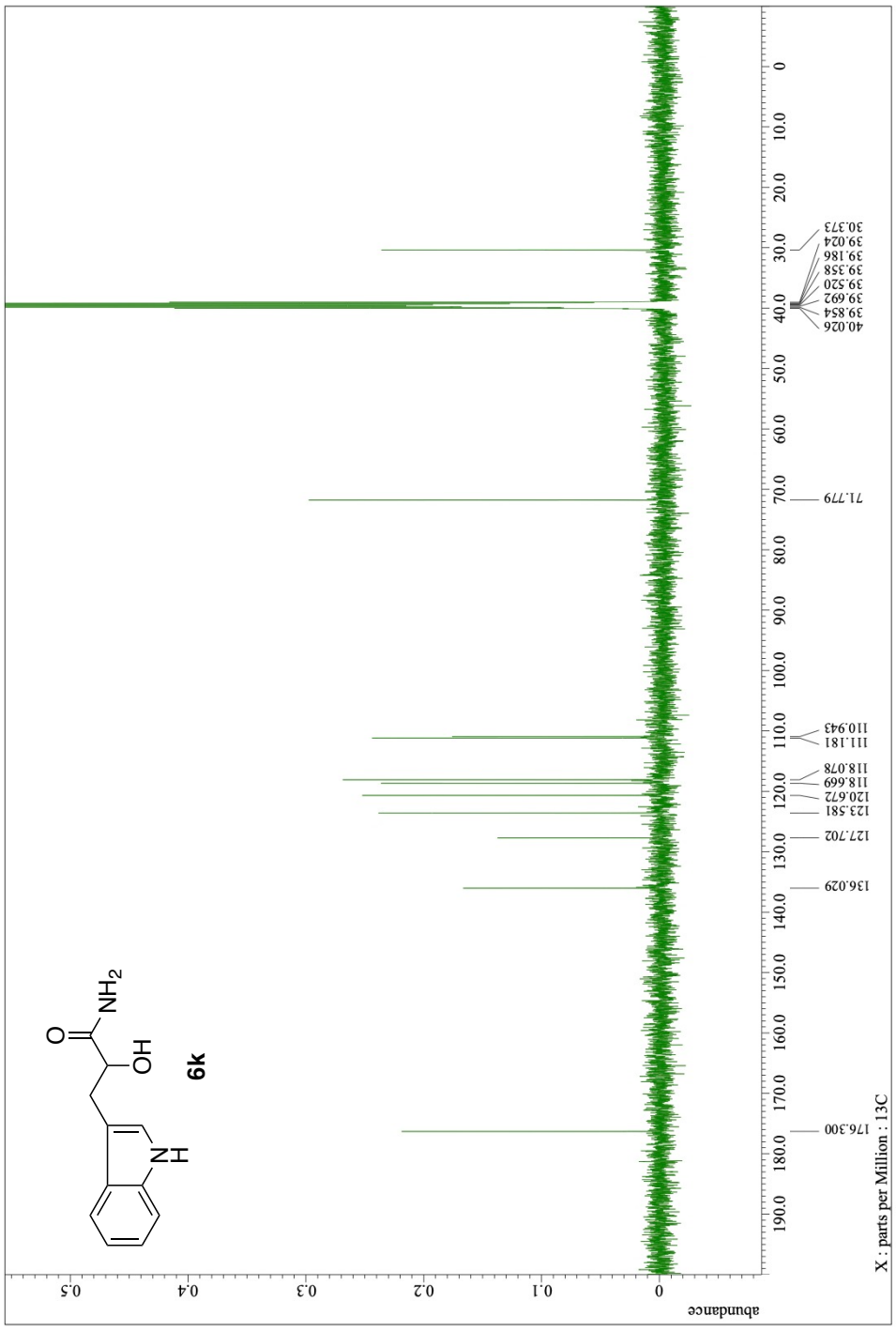
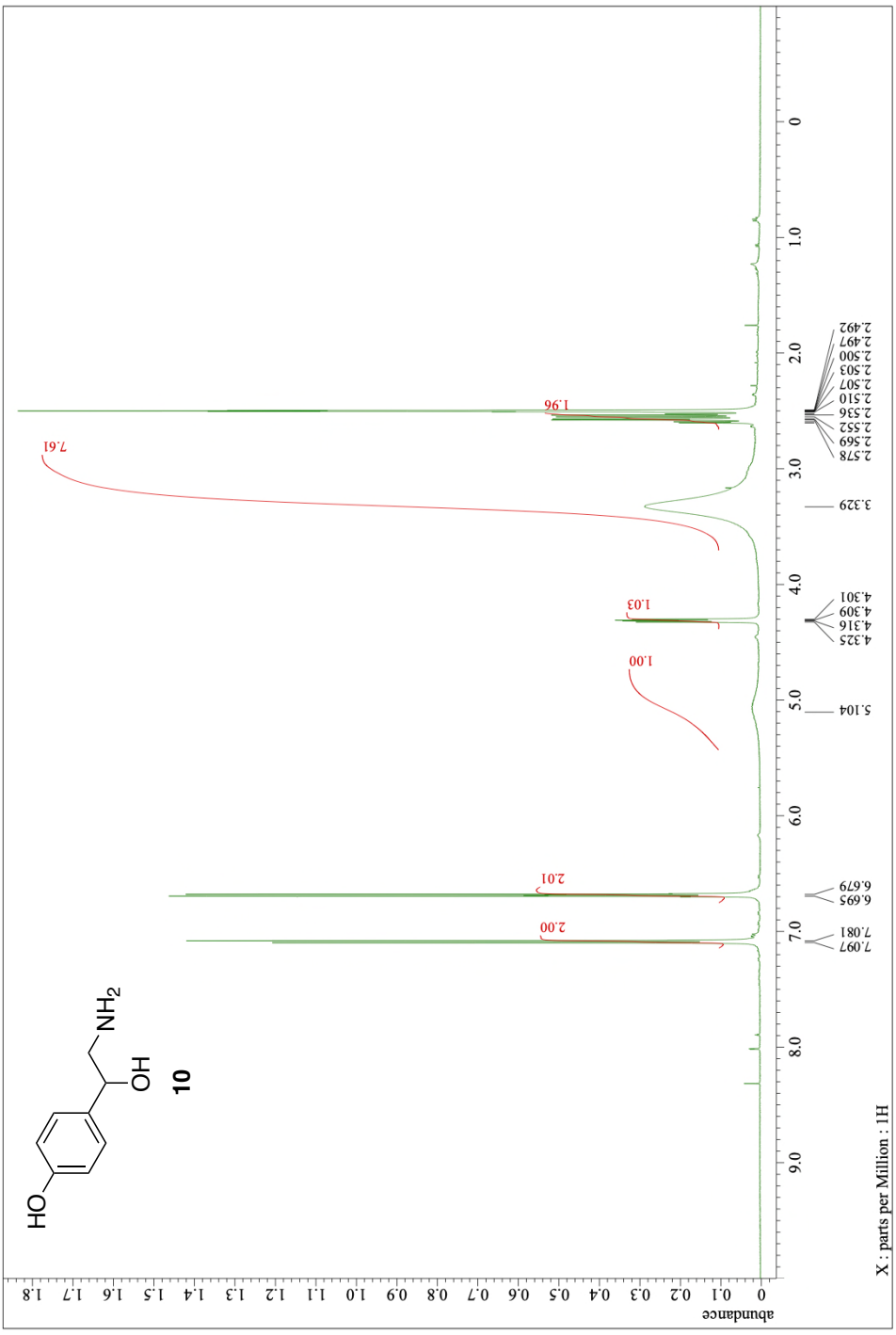


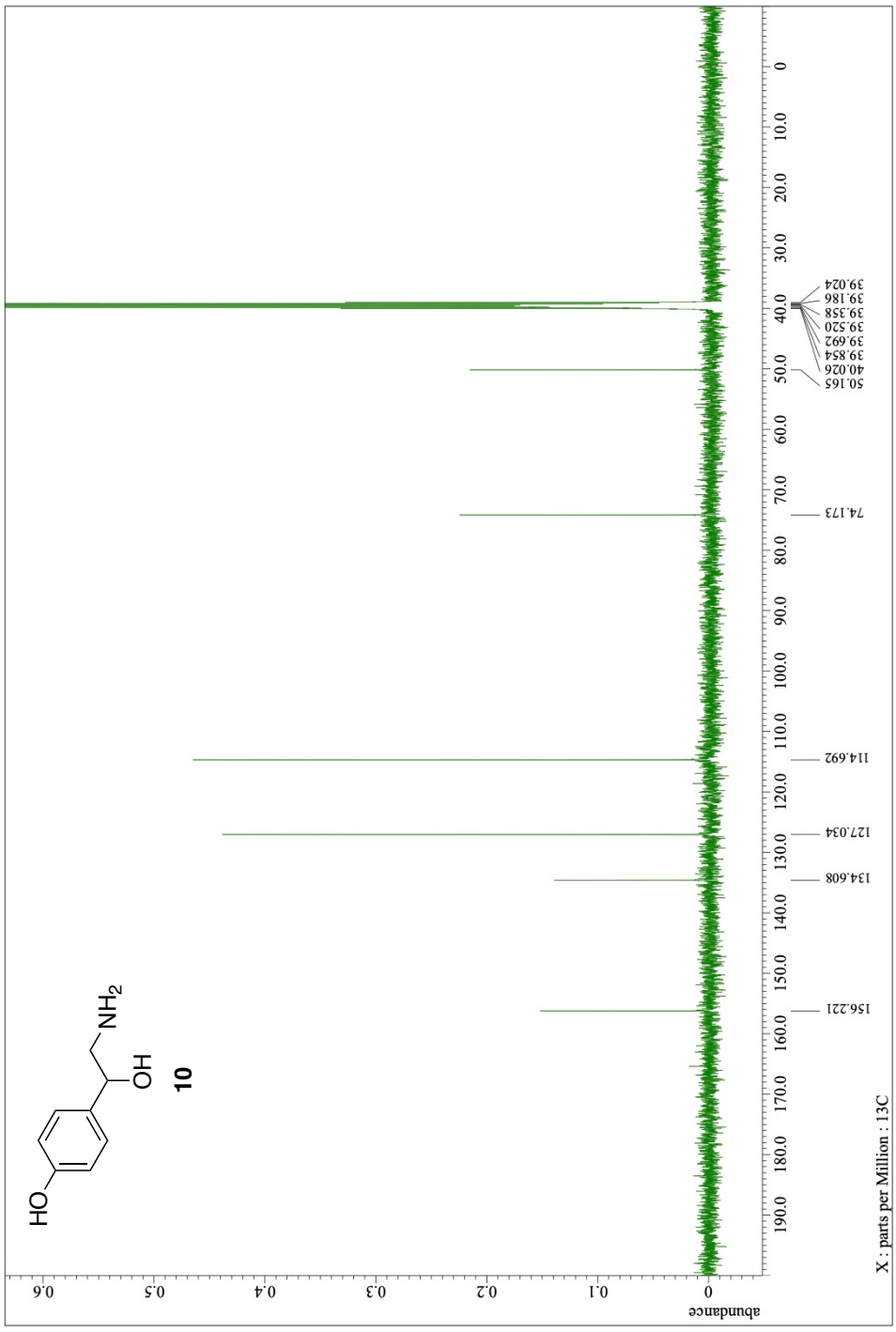
^{13}C NMR (126 MHz, DMSO-*d6*)



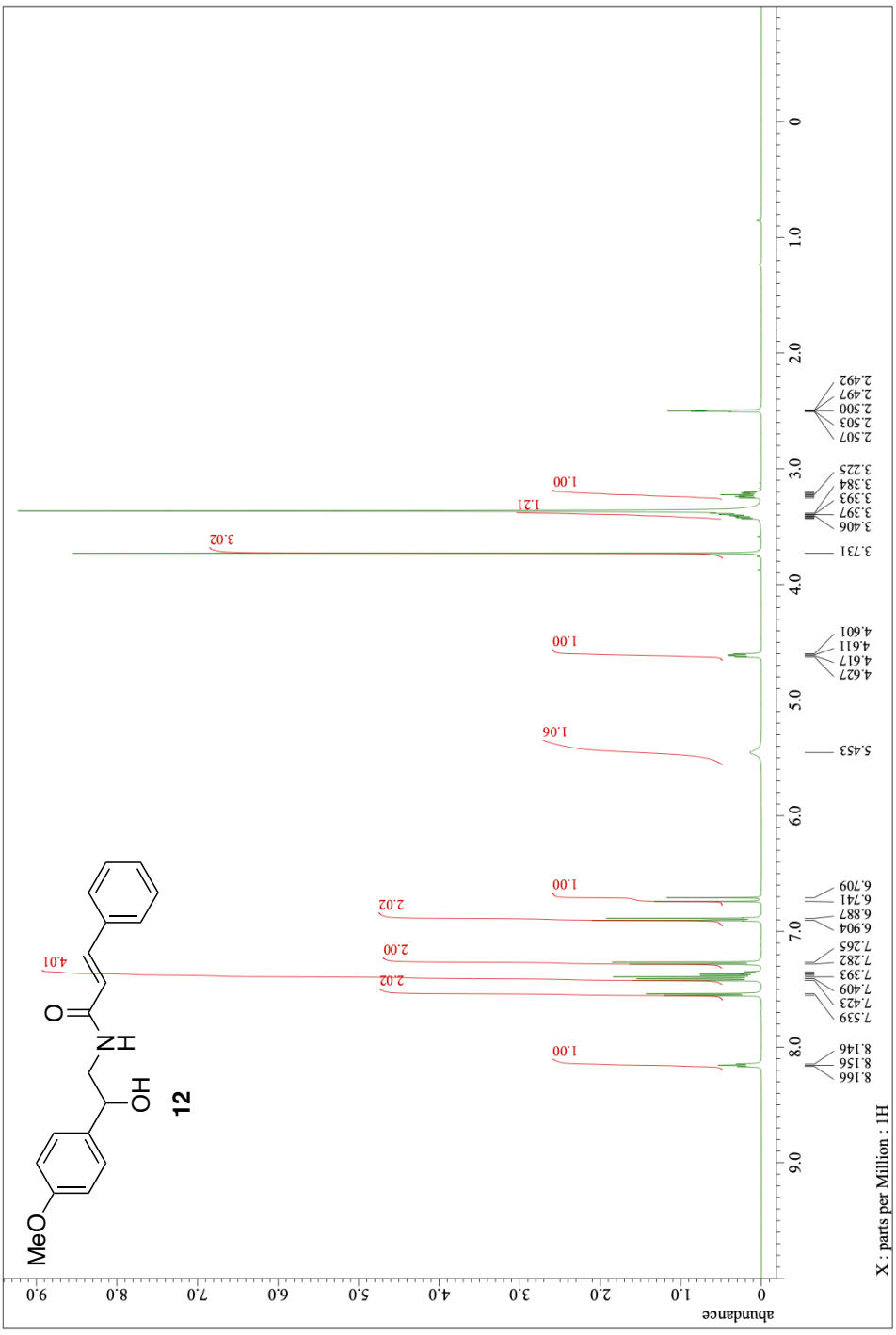
^{1}H NMR (500 MHz, DMSO-*d6*)



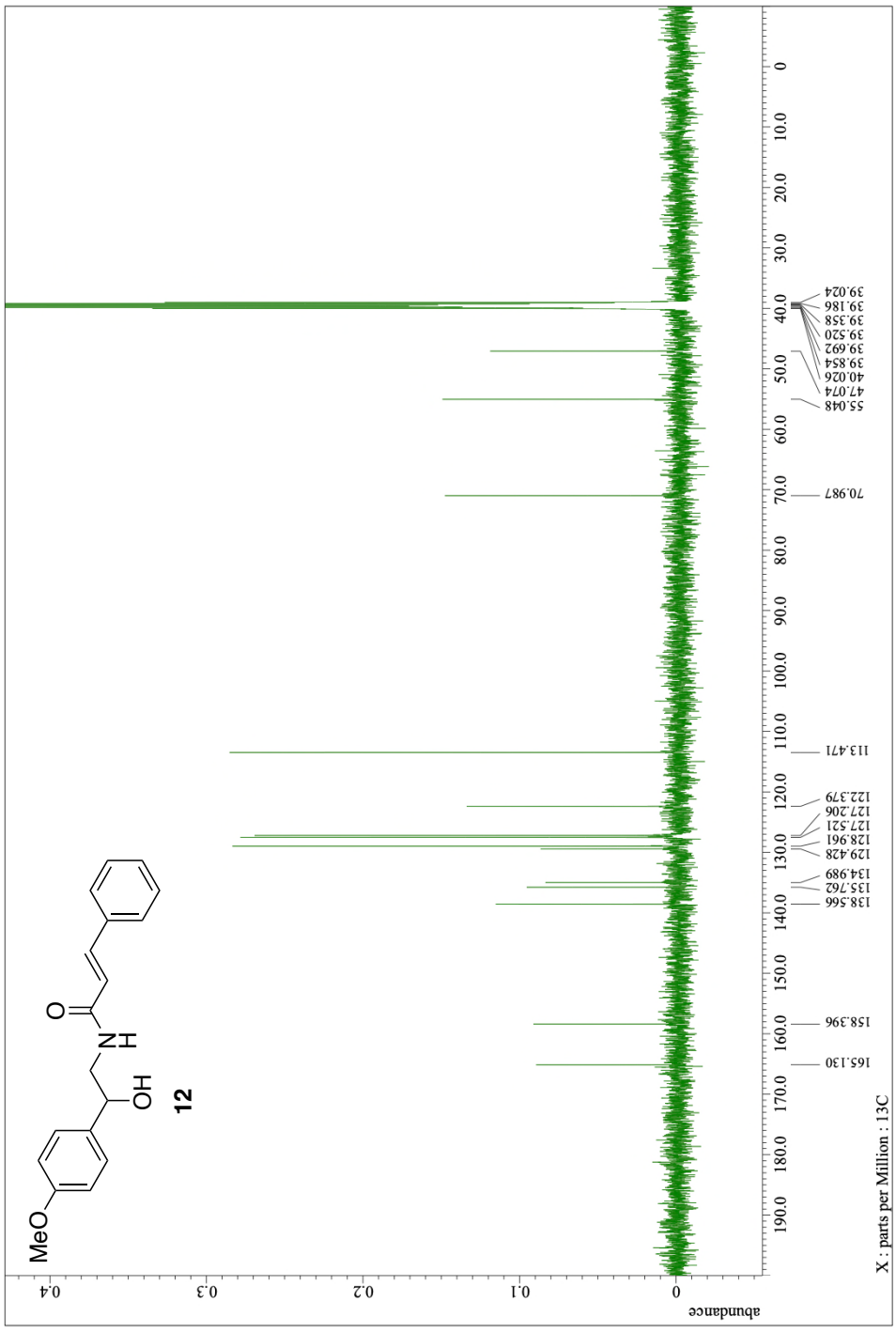
^{13}C NMR (126 MHz, DMSO-*d6*)



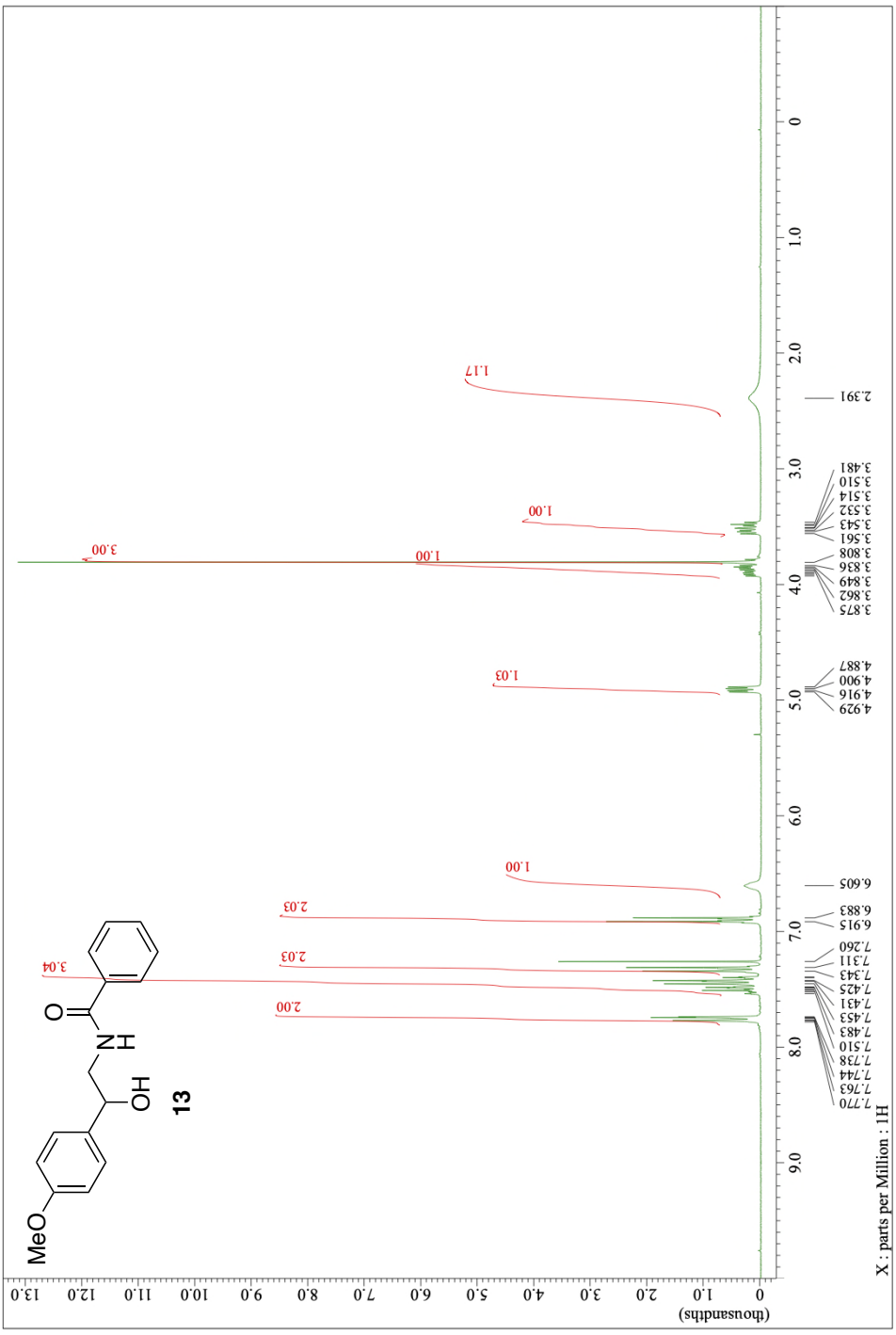
^{1}H NMR (500 MHz, DMSO-*d6*)



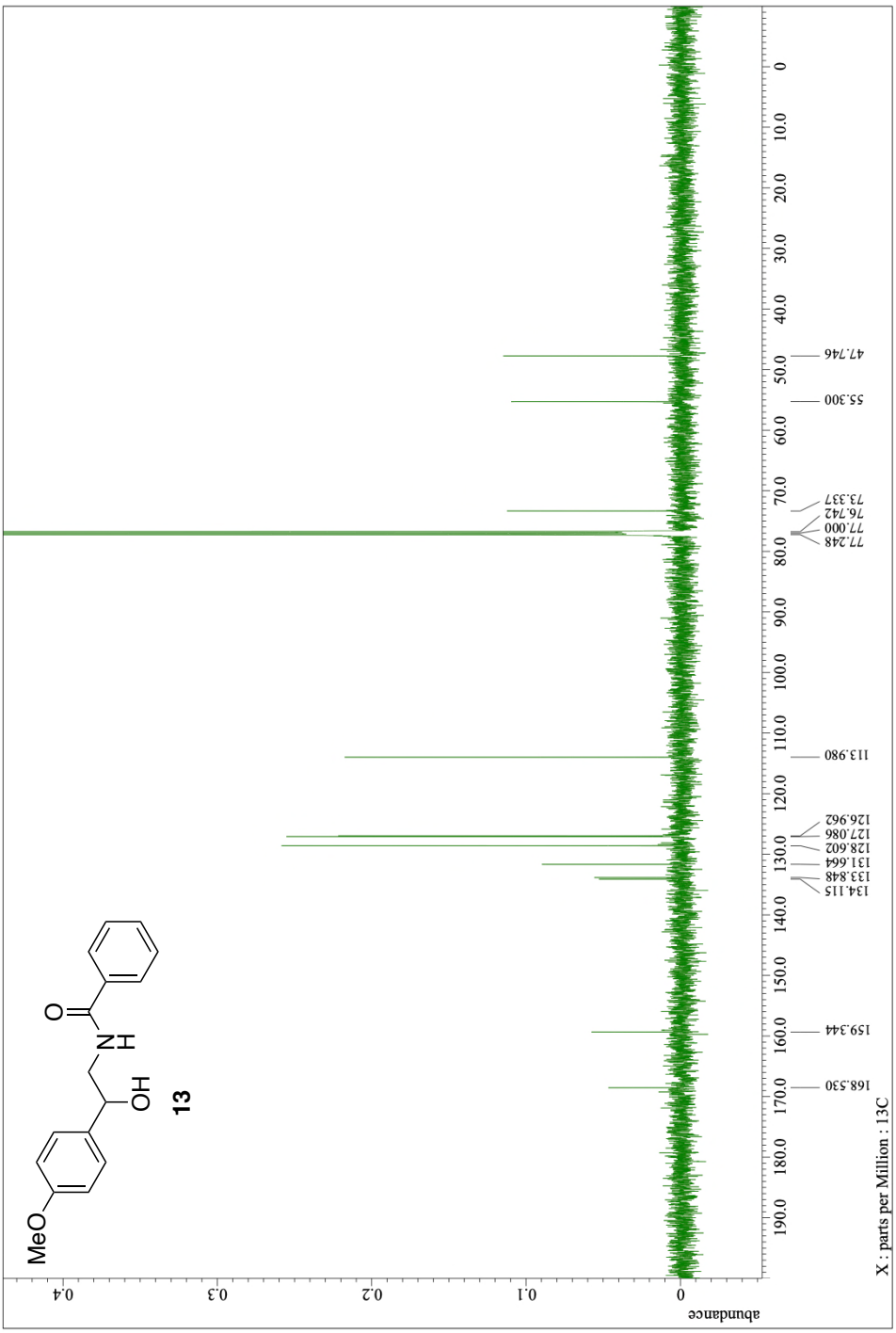
^{13}C NMR (126 MHz, DMSO-*d6*)



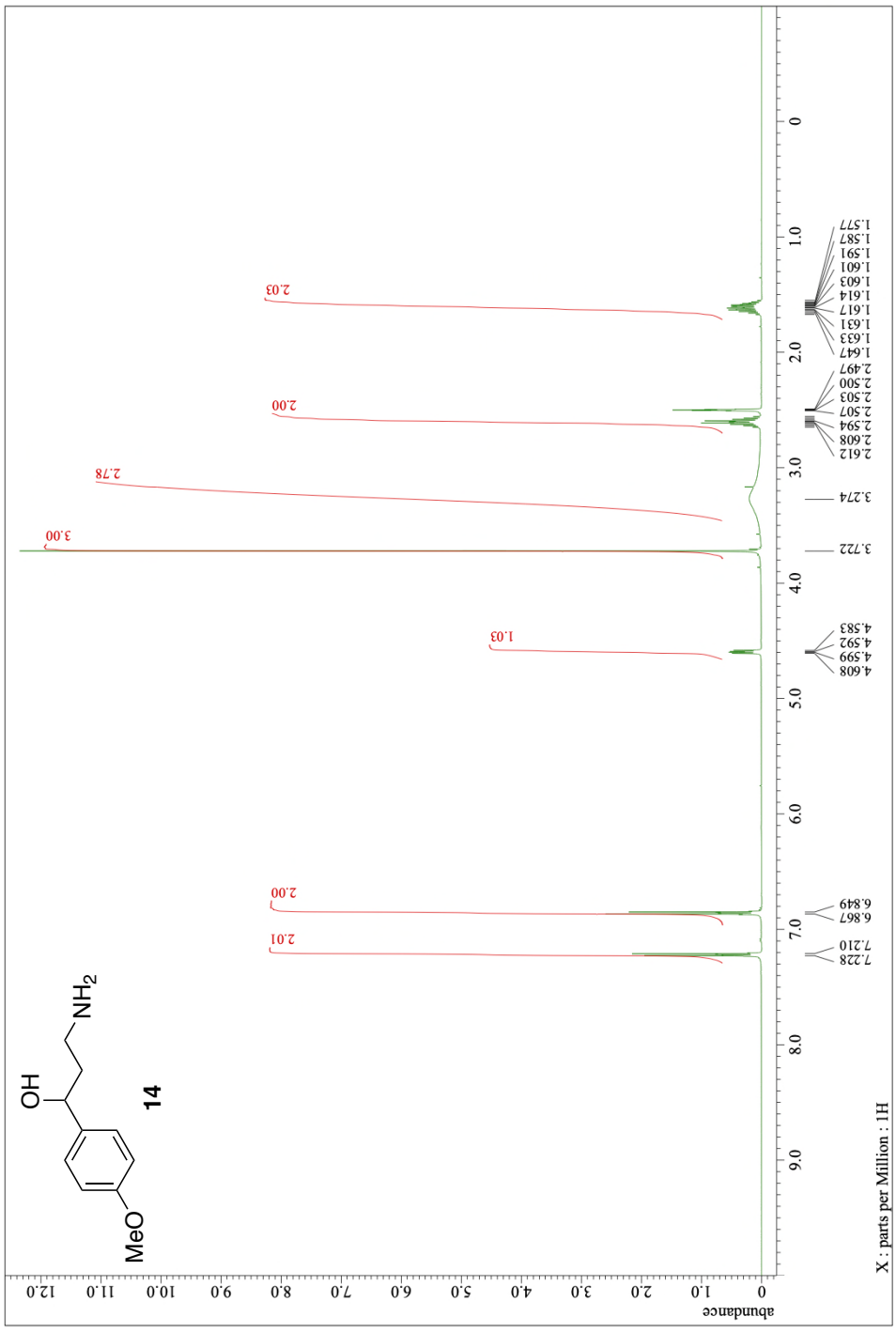
^{1}H NMR (270 MHz, $CDCl_3$)



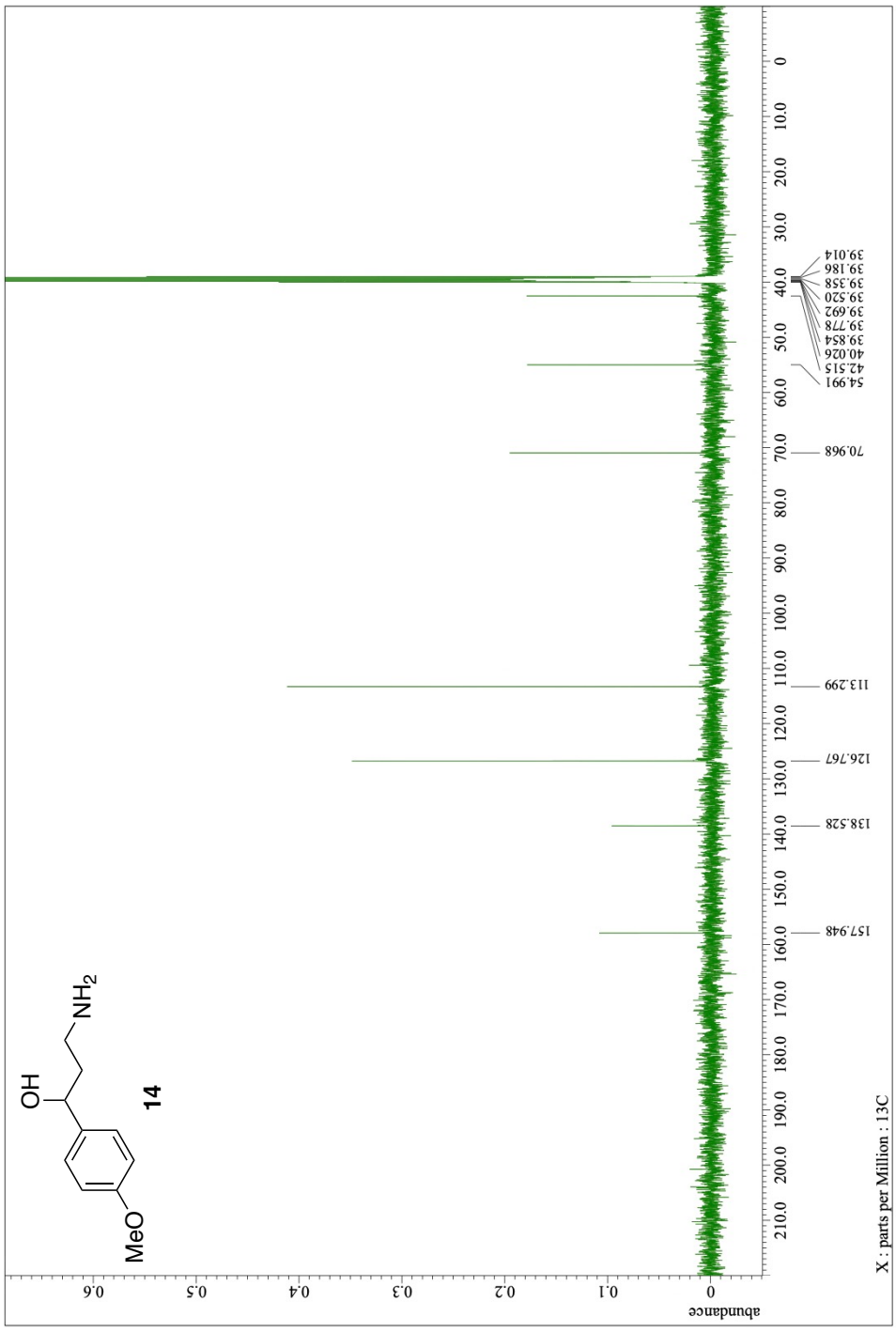
^{13}C NMR (126 MHz, $CDCl_3$)



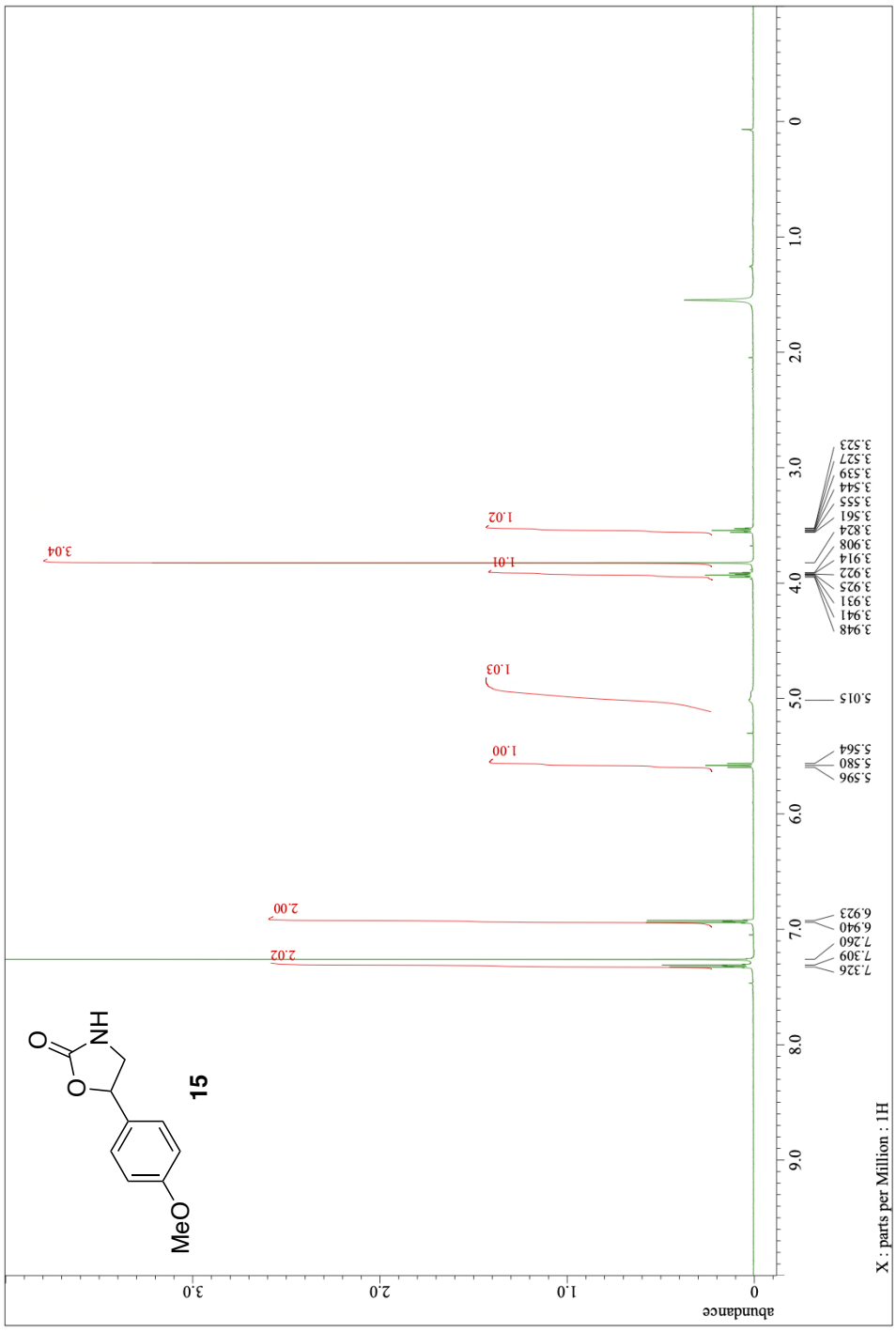
^{1}H NMR (500 MHz, DMSO-*d6*)



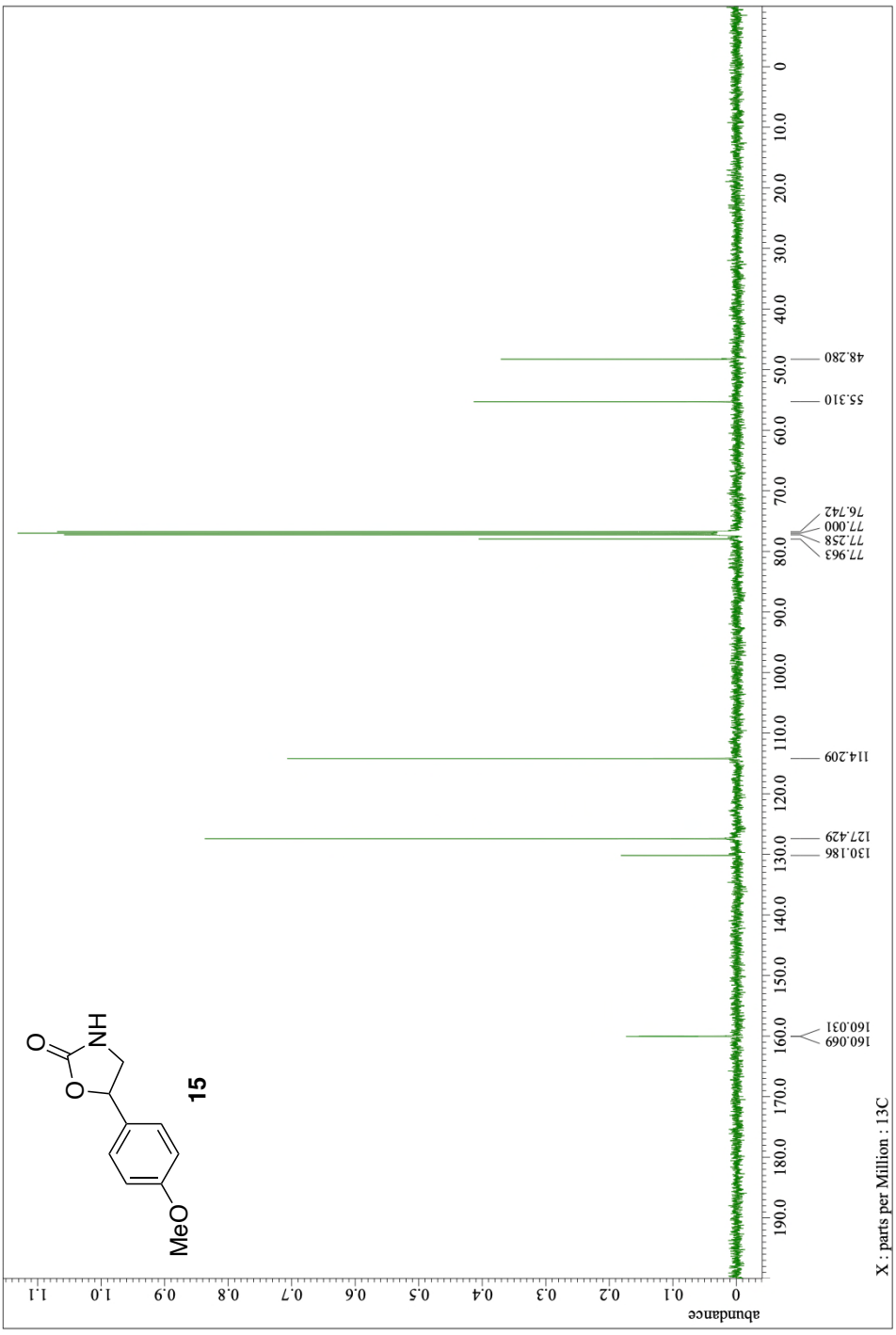
^{13}C NMR (126 MHz, DMSO-*d6*)



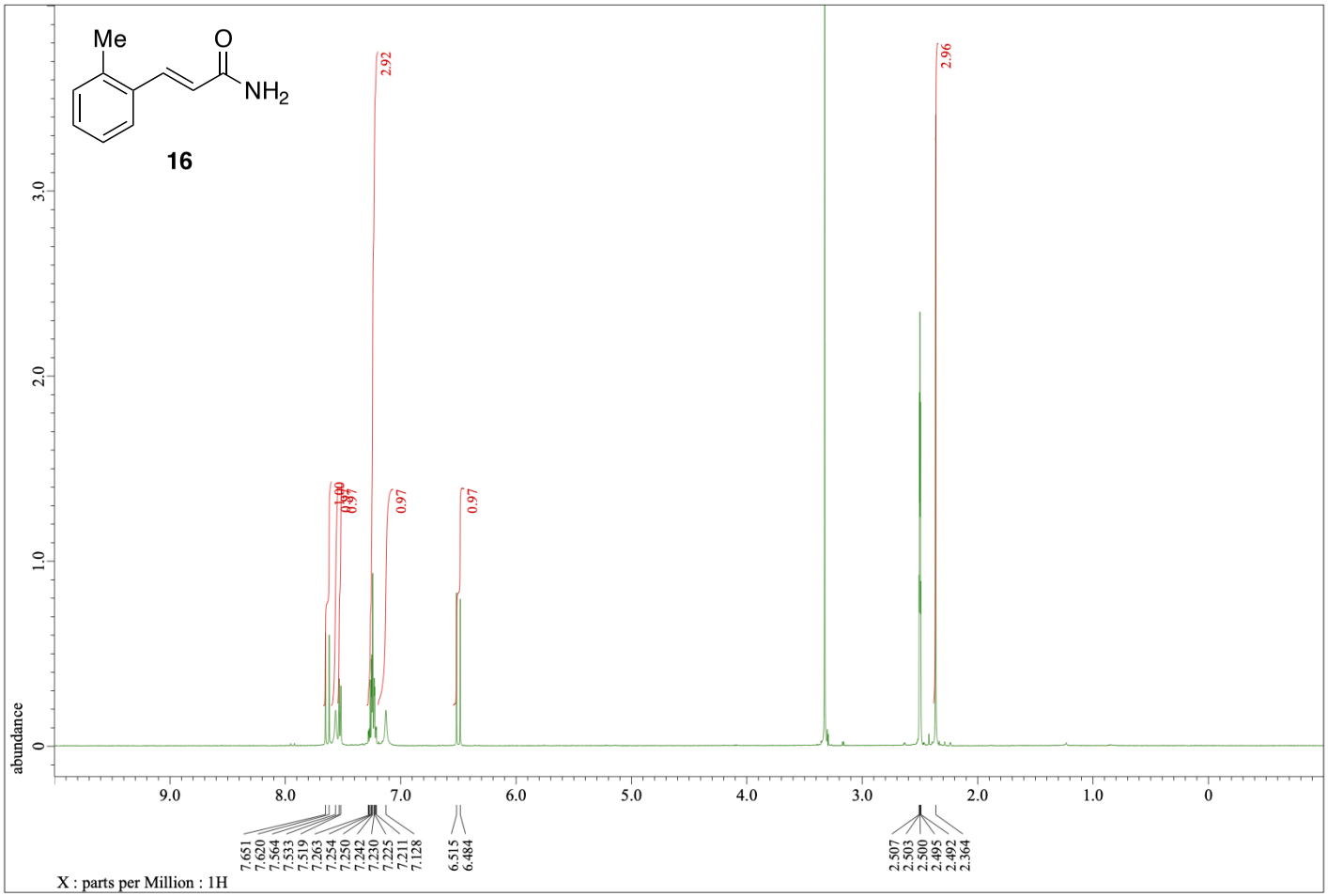
^{1}H NMR (500 MHz, $CDCl_3$)



^{13}C NMR (126 MHz, $CDCl_3$)



^{1}H NMR (500 MHz, DMSO-*d6*)



^{13}C NMR (126 MHz, DMSO-*d6*)