Supporting Information

Discovery of a Novel Dipeptidyl Boronic Acid Proteasome Inhibitor for the Treatment of Multiple Myeloma and Triple-negative Breast Cancer

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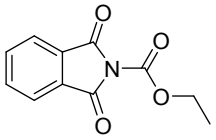
Contents:

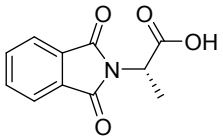
1. ^{1}H NMR and mass spectra of intermediates

N-ethoxycarbonylphthalimide (2a)



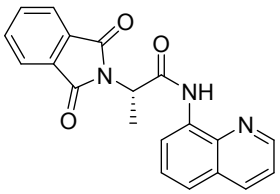
To a solution of phthalimide (7.36 g, 50 mmol) dissolved in anhydrous DMF (25 mL) was added TEA (9 mL, 65 mmol). Then temperature of the reaction system was cooled to 0 °C and ethyl chloroformate (5.7 mL, 60 mmol) was added dropwise. The mixture stirred at room temperature for 2 h and poured into iced water, filtered. The solid was washed with cold water and dried to obtain 8.67 g (79.1% yield) of white solid. mp 81.4-83.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (s, 3H), 4.48 (q, J = 7.1 Hz, 2H), 7.80-7.85 (m, 2H), 7.93-7.99 (m, 2H). MS (ESI) m/z 220.1 $[M+H]^+$.

(S)-2-phthalimidopropionic acid (2b)



To a stirred solution of **2a** in H_2O (100 mL) was added *L*-alanine (8.9 g, 100 mmol) and Na_2CO_3 (10.6 g, 100 mmol). After 1.5 h, the aqueous solution was slowly acidified with aqueous HCl (1N) until pH = 1-2 and filtered to obtain 17.4 g (79.3% yield) of white solid. mp 145.8-146.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.71 (s, 3H), 5.02 (q, J = 7.4 Hz, 1H), 7.69-7.75 (m, 2H), 7.82-7.88 (m, 2H). MS (ESI) m/z 218.2 $[M-H]^-$.

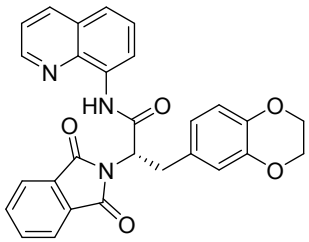
(S)-2-(1,3-dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide (2c)



To a solution of **2b** (17.4 g, 79.3 mmol) in anhydrous CH_2Cl_2 (80 mL) was added thionyl chloride (29 mL, 396 mmol) and the resulting solution was refluxed for 6 h. The solvent was evaporated to give yellow oil. DIPEA (20.5 g, 159 mmol) and 8-aminoquinoline (11.4 g, 79.3 mmol) was dissolved in anhydrous CH_2Cl_2 (103 mL)

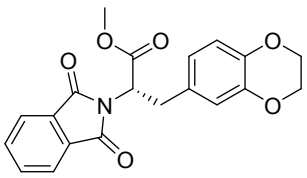
and the obtained yellow oil dissolved in CH_2Cl_2 (30 mL) was added dropwise at -20 °C for 1 h and then allowed to react at room temperature overnight. After evaporation and purification by column chromatography using petroleum ether/EtOAc/CH_2Cl_2 (5:1:1) as eluent, an orange solid (18.7g, 71.9%) was obtained. mp 180.0-181.9°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.98 (s, 3H,), 5.27 (q, J = 7.5 Hz, 1H), 7.42 (dd, J_1 = 4.2 Hz, J_2 = 8.3 Hz, 1H), 7.51 (s, 1H), 7.53 (d, J = 9.0, 1H,), 7.65-7.85 (m, 2H), 7.90 (dd, J_1 = 3.6, J_2 = 7.1 Hz, 2H), 8.15 (d, J = 8.3 Hz, 1H,), 8.69 (d, J = 4.2 Hz, 1H), 8.73 (dd, J_1 = 4.7, J_2 = 8.9 Hz, 1H), 10.33 (s, 1H). MS (ESI) m/z 346.0 $[M+H]^+$.

(S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(1,3-dioxoisoindolin-2-yl)-N-(quinolin-8-yl)propanamide (2d)



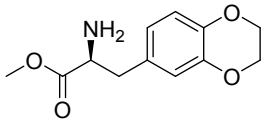
To a solution of **2c** (5.2 g, 15 mmol) in t-BuOH (105 mL) was added 6-iodo-2,3-dihydro-1,4-benzodioxine (5.9 g, 22.5 mmol), $Pd(OAc)_2$ (337 mg, 1.5 mmol) and $AgBF_4$ (3.65 g, 18.8 mmol). The resulting solution was stirred at 85 °C for 24 h. After cooling to room temperature, the reaction was diluted with dichloromethane (100 mL) and triethylamine (6 mL) was added to the mixture. The mixture was maintained for 6 hours and then filtered through a pad of Celite. After evaporation and purification by column chromatography using petroleum ether/EtOAc/CH_2Cl_2 (7:1:1) as eluent, an orange solid (4.8g, 66.7%) was obtained. mp 178.3-179.9 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.54-3.81 (m, 2H), 4.06-4.26 (m, 4H), 5.38 (dd, J_1 = 6.6 Hz, J_2 = 9.9 Hz, 1H), 6.74 (dd, J_1 = 5.0 Hz, J_2 = 16.7 Hz, 2H), 6.83 (d, J = 1.7 Hz, 1H), 7.40 (dd, J_1 = 4.2 Hz, J_2 = 8.3 Hz, 1H), 7.45-7.56 (m, 2H), 7.65-7.79 (m, 2H), 7.80-7.90 (m, 2H), 8.12 (dd, J_1 = 1.5 Hz, J_2 = 8.3 Hz, 1H), 8.63 (dd, J_1 = 1.5 Hz, J_2 = 4.2 Hz, 1H), 8.68-8.78 (m, 1H), 10.29 (s, 1H). MS (ESI) m/z 477.9 $[M-H]^-$.

(S)-methyl3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(1,3-dioxoisoindolin-2-yl)propanoate (2e)



To a 120 mL sealed bottle was added **2d** (2 g, 4.2 mmol), $BF_3 \cdot Et_2O$ (5.3 mL, 42 mmol) and anhydrous methanol (96 mL). The mixture was stirred at 100 °C for 25 hours. After cooling to room temperature, Et_3N (8.8 mL, 63 mmol) was added dropwise. After evaporation of the solvent and dissolved in CH_2Cl_2 (50 mL), the solution was washed with 10% hydrochloric acid, 5% $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4. After evaporation and purification by column chromatography (petroleum ether:EtOAc:CH_2Cl_2 = 7:1:1), 1 g (65.3% yield) of yellow oil was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.35-3.55 (m, 2H), 3.77 (s, 3H), 4.17 (d, J = 7.0 Hz, 4H), 5.09 (dd, J_1 = 5.4 Hz, J_2 = 11.0 Hz, 1H), 6.60 (d, J = 8.2 Hz, 1H), 6.66 (d, J = 8.5 Hz, 1H), 6.68 (s, 1H), 7.71 (d, J = 3.6 Hz, 2H), 7.80 (d, J = 3.4 Hz, 2H). MS (ESI) m/z 368.4 $[M+H]^+$.

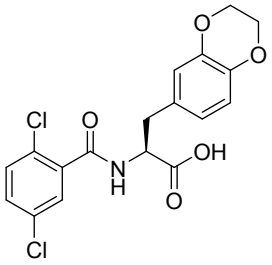
(S)-methyl 2-amino-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)propanoate (2f)



To a solution of **2e** (0.89 g, 2.4 mmol) in anhydrous methanol (23 mL) was added ethylenediamine (0.36 g, 6.1 mmol) and the resulting solution was refluxed for 9 h. The insoluble material was filtered off and the filtrate was evaporated and purified by column chromatography using petroleum ether/EtOAc/CH_2Cl_2 (4:1:1) as eluent to give yellow oil 373 mg (yield 64.9%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.74 (dd, J_1 = 7.9 Hz, J_2 = 13.6 Hz, 1H), 2.98 (dd, J_1 = 5.0 Hz, J_2 = 13.6 Hz, 1H), 3.67 (dd, J_1 = 5.0 Hz, J_2 = 7.9 Hz, 1H), 3.72 (s, 3H), 4.18-4.26 (m, 4H), 6.64 (dd, J_1 = 2.0 Hz, J_2 = 8.2 Hz, 1H), 6.69 (d, J = 2.0 Hz, 1H), 6.78 (d, J = 8.2 Hz, 1H). MS (ESI) m/z 238.2 $[M+H]^+$.

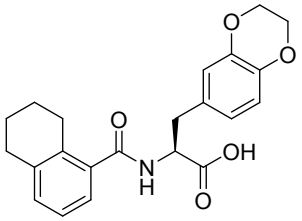
Compounds **3d-3f** were prepared following a similar procedure described for the synthesis of **3a**.

(S)-2-(2,5-dichlorobenzamido)-3-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)propanoic acid (3d)



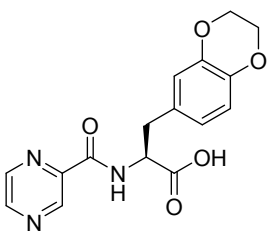
White solid (0.84 g, 88.4%). mp 194.8-196.6 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 2.80 (dd, J_1 = 10.4 Hz, J_2 = 13.8 Hz, 1H), 3.06 (dd, J_1 = 4.6 Hz, J_2 = 13.9 Hz, 1H), 4.20 (s, 4H), 4.48-4.53 (m, 1H), 6.73 (dd, J_1 = 1.8 Hz, J_2 = 8.3 Hz, 1H), 6.76 (d, J = 8.1 Hz, 1H), 6.78 (d, J = 1.7 Hz, 1H), 7.15-7.22 (m, 1H), 7.47-7.57 (m, 2H), 8.84 (d, J = 8.2 Hz, 1H), 12.94 (s, 1H). MS (ESI) m/z 393.8 $[M-H]^-$.

(S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(5,6,7,8-tetrahydronaphthalene-1-carboxamido)propanoic acid (3e)



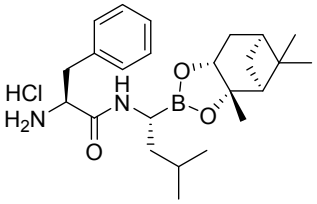
White solid (0.32 g, 84.5%). mp 190.9-192.3 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.54-1.72 (m, 4H), 2.26-2.58 (m, 2H), 2.71 (t, J = 6.1 Hz, 2H), 2.78 (dd, J_1 = 10.6 Hz, J_2 = 13.7 Hz, 1H), 3.04 (dd, J_1 = 4.2 Hz, J_2 = 13.7 Hz, 1H), 4.19 (s, 4H), 4.42-4.54 (m, 1H), 6.71 (d, J = 8.3 Hz, 1H), 6.75 (d, J = 8.2 Hz, 1H), 6.77 (s, 1H), 6.93 (dd, J_1 = 4.3 Hz, J_2 = 8.4 Hz, 1H), 7.04-7.13 (m, 2H), 8.29 (d, J = 7.9 Hz, 1H), 12.91 (s, 1H). MS (ESI) m/z 380.2 $[M-H]^-$.

(S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(pyrazine-2-carboxamido)propanoic acid (3f)



White solid (0.31 g, 90.9%). mp 176.3-178.1 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 3.00-3.16 (m, 2H), 4.09-4.25 (m, 4H), 4.63 (dd, J_1 = 7.1 Hz, J_2 = 13.9 Hz, 1H), 6.66 (dd, J_1 = 1.9 Hz, J_2 = 8.3 Hz, 1H), 6.71 (dd, J_1 = 5.1 Hz, J_2 = 6.7 Hz, 2H), 8.75 (dd, J_1 = 1.5 Hz, J_2 = 2.4 Hz,1H), 8.84 (d, J = 8.1 Hz, 1H), 8.89 (d, J = 2.5 Hz, 1H), 9.15 (d, J = 1.4 Hz, 1H), 13.10 (s, 1H). MS (ESI) m/z 328.2 $[M-H]^-$.

2-amino-N-((R)-3-methyl-1-((3aS,4S,6R,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)-3-phenylpropanamide hydrochloride (6a)

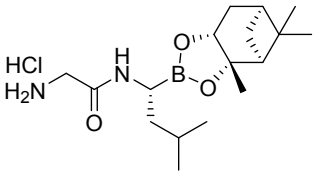


To a cooled solution (-10 °C) of N-Boc-L-phenyl alanine (3.4 g, 12.7 mmol) dissolved in anhydrous CH_2Cl_2 (40 mL) was added HOBt (2.6 g, 19.1 mmol). After 10 min, EDCI (3.7 g, 19.1 mmol) was added. Finally, **5a** (4.8 g, 12.7 mmol) and DIPEA (5.8 g, 44.5 mmol) were added. The mixture stirred at -10 °C for 1 h and at room temperature for 15 h. The mixture was washed with 10% hydrochloric acid, 5% $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4. After filtration and evaporation, the obtained crude product was directly used in the next reaction.

The prepared boronic acid ester was dissolved in ethyl acetate (22 mL) and was dropwise added 4.5 mol/L HCl in ethyl acetate (40 mL) at 0 °C. Then the mixture was stirred for 2 h at room temperature and the ethyl acetate was evaporated under vacuo. MTBE was added to the residue and filtered to obtain glassy solid **6a** (7.05 g, 80.6%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (s, 3H), 0.81-0.86 (m, 6H), 1.20 (d, J = 7.0 Hz, 2H), 1.26 (s, 3H), 1.27-1.31 (m, 1H), 1.33 (s, 3H), 1.48 (d, J = 2.8 Hz, 1H), 1.80 (d, J = 15.2 Hz, 2H), 2.02 (t, J = 5.3 Hz, 1H), 2.06-2.15 (m, 1H), 2.22-2.32 (m, 1H), 2.92-2.95 (m, 1H), 3.31 (dd, J_1 = 13.4 Hz, J_2 = 8.0 Hz, 1H), 3.44 (dd, J_1 = 13.4 Hz, J_2 = 8.1 Hz, 1H), 4.23 (d, J = 8.3 Hz, 1H), 4.67-4.70 (m, 1H), 7.23 (d, J = 7.1 Hz, 1H), 7.26-7.30 (m, 2H), 7.35 (d, J = 7.0 Hz, 2H), 7.66 (s, 1H), 8.27 (s, 3H). MS (ESI) m/z 413.27 $[M+H]^+$.

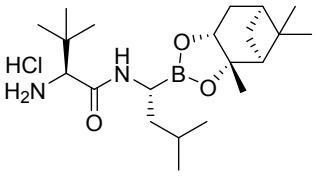
Compounds **6b-6e** were prepared from the corresponding N-boc-carboxylic acids and **5a** following the similar procedure described for the synthesis of **6a**.

2-amino-N-((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)acetamide hydrochloride (6b)



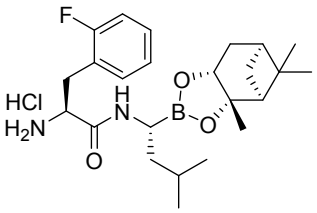
Glassy solid (2.17 g, 66.2%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.84 (dd, J_1 = 8.0 Hz, J_2 = 13.5 Hz, 9H), 1.19 (d, J = 10.6 Hz, 1H), 1.24 (s, 3H), 1.28 (s, 1H), 1.32 (s, 3H),1.37-1.48 (m, 1H), 1.67 (dd, J_1 = 10.4 Hz, J_2 = 21.3 Hz, 2H), 1.84 (s, 1H), 1.94 (t, J = 4.8 Hz, 1H), 2.14 (d, J = 4.9 Hz, 1H), 2.21-2.33 (m, 1H), 3.00 (s, 1H), 3.51 (d, J = 16.4 Hz, 2H), 4.28 (d, J = 8.1 Hz, 1H), 8.14 (s, 3H), 8.52 (s, 1H). MS (ESI) m/z 323.4 $[M+H]^+$.

(S)-2-amino-3,3-dimethyl-N-((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)butanamide hydrochloride (6c)



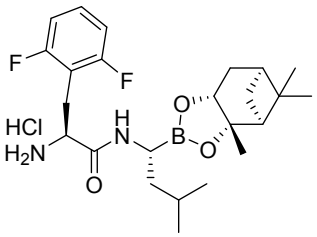
Glassy solid (1.3 g, 87.3%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.80 (s, 3H), 0.87 (dd, J_1 = 3.8 Hz, J_2 = 6.5 Hz, 6H), 0.98 (s, 9H), 1.23 (s, 3H), 1.27 (dd, J_1 = 4.9 Hz, J_2 = 9.4 Hz, 2H), 1.30 (s, 3H), 1.37-1.47 (m, 1H), 1.64-1.74 (m, 2H), 1.80-1.86 (m, 1H), 1.90 (dd, J_1 = 5.1 Hz, J_2 = 6.0 Hz, 1H), 2.02-2.11 (m, 1H), 2.21-2.32 (m, 1H), 2.90-3.00 (m, 1H), 3.57 (s, 1H), 4.26 (dd, J_1 = 1.9 Hz, J_2 = 8.7 Hz, 1H), 8.12-8.26 (m, 3H), 8.58 (d, J = 4.0 Hz, 1H). MS (ESI) m/z 479.4 $[M+H]^+$.

(S)-2-amino-3-(2-fluorophenyl)-N-((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)propanamide hydrochloride (6d)



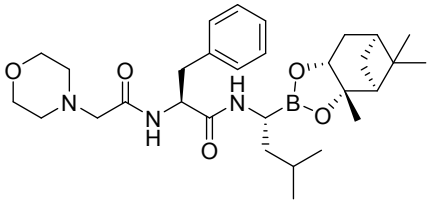
Glassy solid (1.43 g, 82.5%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.78 (d, J = 6.5 Hz, 6H), 0.82 (s, 3H), 1.24 (s, 3H), 1.25-1.30 (m, 2H), 1.31 (s, 3H), 1.32-1.37 (m, 1H), 1.68 (dd, J_1 = 3.3 Hz, J_2 = 8.8 Hz, 1H), 1.79-1.86 (m, 1H), 1.89-1.95 (m, 2H), 2.11 (dd, J_1 = 5.3 Hz, J_2 = 14.8 Hz, 1H), 2.23-2.31 (m, 1H), 2.75-2.84 (m, 1H), 3.00 (dd, J_1 = 8.9 Hz, J_2 = 13.7 Hz, 1H), 3.12 (dd, J_1 = 5.6 Hz, J_2 = 13.8 Hz, 1H), 4.02 (dd, J_1 = 7.2 Hz, J_2 = 14.3 Hz, 1H), 4.25 (dd, J_1 = 1.9 Hz, J_2 = 8.7, 1H), 7.08-7.18 (m, 2H), 7.28-7.35 (m, 2H), 8.51 (s, 3H), 8.55 (d, J = 4.8 Hz, 1H). MS (ESI): observed: m/z 431.8[M+H]$^+$.

(S)-2-amino-3-(2,6-difluorophenyl)-N-((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)propanamide hydrochloride (6e)



Glassy solid (0.58 g, 71.7%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.75 (dd, J_1 = 3.4 Hz, J_2 = 6.5 Hz, 6H), 0.81 (s, 3H), 1.13-1.17 (m, 2H), 1.17-1.21 (m, 1H), 1.24 (s, 3H), 1.30 (s, 3H), 1.65 (d, J = 14.2 Hz, 1H), 1.82 (d, J = 2.6 Hz, 1H), 1.89-1.92 (m, 2H), 2.05-2.13 (m, 1H), 2.20-2.29 (m, 1H), 2.70-2.80 (m, 1H), 3.08 (d, J = 7.5 Hz, 2H), 3.90 (d, J = 22.0 Hz, 1H), 4.21 (dd, J_1 = 1.8 Hz, J_2 = 8.6 Hz, 1H), 7.05 (t, J = 7.9 Hz, 2H), 7.32-7.42 (m, 1H), 8.48 (d, J = 5.2 Hz, 1H), 8.61 (s, 3H). MS (ESI) m/z 449.8 [M+H]$^+$.

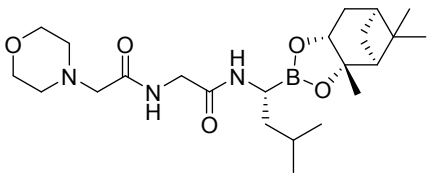
(S)-N-((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)-2-(2-morpholinoacetamido)-3-phenylpropanamide (7a)



TEA (1.35 g, 13.4 mmol) and **6a** (1.0 g, 2.23 mmol) were dissolved in anhydrous CH_2Cl_2 (15 mL) and 2-morpholinoacetyl chloride (0.36 g, 2.23 mmol) was added dropwise at -0 °C and then allowed to react at room temperature for 1 h. The mixture was washed with H_2O and dried over anhydrous Na_2SO_4. After filtration, evaporation and purification by column chromatography using petroleum ether/EtOAc (2:1) as eluent to give a glassy solid 0.84 g (69.8% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (dd, J_1 = 4.2 Hz, J_2 = 8.2 Hz, 9H), 1.28 (s, 3H), 1.40 (s, 3H), 1.41 (d, J = 7.3 Hz, 2H), 1.48 (dd, J_1 = 6.6 Hz, J_2 = 13.1 Hz, 1H), 1.79-1.82 (m, 1H), 1.83-1.86 (m, 1H), 1.87-1.94 (m, 2H), 2.15-2.19 (m, 1H), 2.22 (dd, J_1 = 4.4 Hz, J_2 = 9.6 Hz, 1H), 2.25-2.39 (m, 4H), 3.05-3.08 (m,1H), 3.09 (t, J = 3.7 Hz, 2H), 3.11-3.16 (m, 2H), 3.54-3.63 (m, 4H), 4.30 (dd, J_1 = 2.1 Hz, J_2 = 8.8 Hz, 1H), 4.67 (dd, J_1 = 7.8 Hz, J_2 = 15.3 Hz, 1H), 6.29 (d, J = 4.5 Hz, 1H), 7.19-7.29 (m, 5H), 7.53 (d, J = 7.7 Hz, 1H). MS (ESI) m/z 540.7 $[M+H]^+$.

Compound **7b** was prepared from **6b** following the similar procedure described for the synthesis of **7a**.

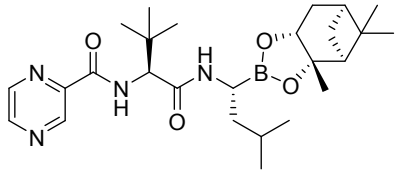
N-((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)-2-(2-morpholinoacetamido)acetamide (7b)



Glassy solid (0.53 g, 41.7%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (s, 3H), 0.90 (dd, J_1 = 2.8 Hz, J_2 = 6.6 Hz, 6H), 1.27 (s, 3H), 1.38 (s, 3H), 1.45 (t, J = 7.3 Hz, 2H), 1.61 (dd, J_1 = 5.9 Hz, J_2 = 12.7 Hz, 1H), 1.78-1.81 (m, 1H), 1.81-1.86 (m, 1H), 2.00-2.04 (m, 2H), 2.14-2.20 (m, 1H), 2.29-2.33 (m, 1H), 2.51-2.55 (m, 4H), 3.21 (dd, J_1 = 7.0 Hz, J_2 = 12.9 Hz, 1H), 3.70-3.74 (m, 4H), 3.96 (t, J = 5.5 Hz, 2H), 4.28 (dd, J_1 =

2.1 Hz, J_2 = 8.8 Hz, 1H), 4.71 (s, 1H), 6.36 (d, J = 3.9 Hz, 1H), 7.75 (s, 1H). MS (ESI) m/z 450.7 $[M+H]^+$.

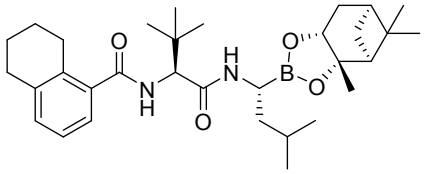
N-((S)-3,3-dimethyl-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxobutan-2-yl)pyrazine-2-carboxamide (7c)



To a cooled solution (-10 °C) of pyrazine-2-carboxylic acid (0.12 g, 0.9 mmol) dissolved in anhydrous CH_2Cl_2 (6 mL) was added HOBt (0.2 g, 1.4 mmol). After 10 min, EDCI (0.3 g, 1.4 mmol) was added. Finally (R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butan-1-amine 2,2,2-trifluoroacetate **6c** (0.4 g, 0.9 mmol) and DIPEA (0.4 g, 3.4 mmol) were added. The mixture stirred at -10 °C for 1 h and at room temperature overnight. The mixture was washed with 1N HCl, 5% $NaHCO_3$, and brine, dried over anhydrous Na_2SO_4. After filtered, evaporation and purification with chromatography (petroleum ether/EtOAc = 3:1), 0.38 g (81.6%) of glassy solid was obtained. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (s, 3H), 0.89 (dd, J_1 = 4.7 Hz, J_2 = 6.5 Hz, 6H), 1.07 (s, 9H), 1.25 (d, J = 1.8 Hz, 1H), 1.27 (s, 3H), 1.36 (s, 3H), 1.46 (t, J = 7.4 Hz, 2H), 1.58-1.68 (m, 2H), 1.87-1.93 (m, 1H), 1.98 (t, J = 5.5 Hz, 1H), 2.12-2.19 (m, 1H), 2.32 (m, 1H), 3.26 (dd, J_1 = 7.6 Hz, J_2 = 13.1 Hz, 1H), 4.30 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 4.39 (d, J = 9.7 Hz, 1H), 5.95 (d, J = 5.1 Hz, 1H), 8.49 (d, J = 9.7 Hz, 1H), 8.55 (dd, J_1 = 2.4, J_2 = 1.5 Hz, 1H), 8.74 (d, J = 2.4 Hz, 1H), 9.37 (d, J = 1.4 Hz, 1H). MS (ESI) m/z 485.6 $[M+H]^+$.

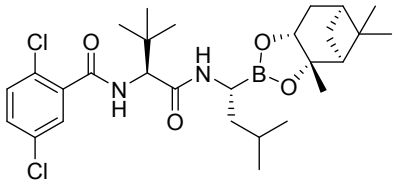
Compounds **7d-7h** were prepared from the corresponding carboxylic acids and boric acid ester hydrochloride following the similar procedure described for the synthesis of **7c**.

N-((S)-3,3-dimethyl-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxobutan-2-yl)-5,6,7,8-tetrahydronaphthalene-1-carboxamide (7d)



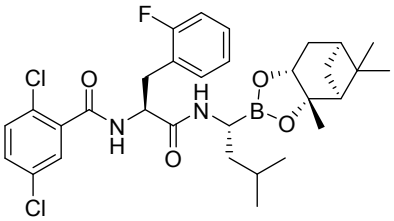
Glassy solid (0.48 g, 81.3%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (dd, J_1 = 5.9 Hz, J_2 = 19.8 Hz, 9H), 1.06 (s, 9H), 1.27 (s, 3H), 1.29 (d, J = 6.4 Hz, 2H), 1.37 (s, 3H), 1.40 (d, J = 7.4 Hz, 1H), 1.57 (dd, J_1 = 6.7 Hz, J_2 = 13.3 Hz, 1H), 1.77 (d, J = 4.4 Hz, 4H), 1.86 (d, J = 12.8 Hz, 2H), 2.00 (t, J = 5.5 Hz, 1H), 2.1-2.19 (m, 1H), 2.35-2.27 (m, 1H), 2.83 (d, J = 35.3 Hz, 4H), 3.12 (dd, J_1 = 7.5 Hz, J_2 = 12.3 Hz, 1H), 4.23-4.28 (m, 1H), 4.60 (d, J = 9.6 Hz, 1H), 6.51 (d, J = 9.5 Hz, 1H), 6.75 (d, J = 3.9 Hz, 1H), 7.12 (dd, J_1 = 7.0 Hz, J_2 = 11.9 Hz, 3H). MS (ESI) m/z 537.5$[M+H]^+$.

2,5-dichloro-N-((S)-3,3-dimethyl-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxobutan-2-yl)benzamide (7e)



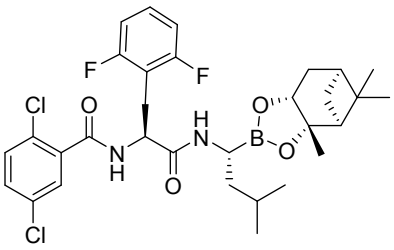
Glassy solid (0.31 g, 57.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (s, 3H), 0.87 (dd, J_1 = 6.6 Hz, J_2 = 8.8 Hz, 6H), 1.08 (s, 9H), 1.24 (d, J = 6.6 Hz, 2H), 1.27 (s, 3H), 1.30 (t, J = 8.1 Hz, 1H), 1.37 (s, 3H), 1.62 (dd, J_1 = 6.6 Hz, J_2 = 13.4 Hz, 1H), 1.81-1.90 (m, 2H), 2.00 (t, J = 5.5 Hz, 1H), 2.11-2.19 (m, 1H), 2.28-2.37 (m, 1H), 3.22 (dd, J_1 = 7.6 Hz, J_2 = 13.0 Hz, 1H), 4.28 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 4.51 (d, J = 9.3 Hz, 1H), 6.30 (d, J = 4.9 Hz, 1H), 6.88 (d, J = 9.2 Hz, 1H), 7.33 (d, J = 1.9 Hz, 2H), 7.56 (dd, J_1 = 1.0 Hz, J_2 = 1.8 Hz, 1H). MS (ESI) m/z 551.3$[M+H]^+$.

2,5-dichloro-N-((S)-3-(2-fluorophenyl)-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxopropan-2-yl)benzamide (7f)



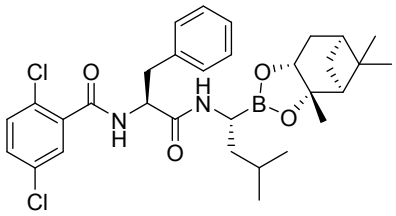
Glassy solid (0.94 g, 53.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (s, 3H), 0.87 (dd, J_1 = 3.6 Hz, J_2 = 6.5 Hz, 6H), 1.28 (s, 3H), 1.32-1.37 (m, 1H), 1.39 (s, 3H), 1.40-1.45 (m, 2H), 1.53 (dd, J_1 = 6.5 Hz, J_2 = 19.4 Hz, 1H), 1.80-1.86 (m, 1H), 1.88-1.93 (m, 1H), 2.01-2.05 (m, 1H), 2.14-2.23 (m, 1H), 2.28-2.37 (m, 1H), 3.19 (dd, J_1 = 7.8 Hz, J_2 = 14.1 Hz, 1H), 3.25 (dd, J_1 = 6.7 Hz, J_2 = 13.9 Hz, 2H), 4.30 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H), 4.84-4.94 (m, 1H), 6.23 (d, J = 5.6 Hz, 1H), 6.84 (d, J = 8.0 Hz, 1H), 7.00-7.10 (m, 2H), 7.20-7.25 (m, 1H), 7.27-7.33 (m, 3H), 7.43 (dd, J_1 = 0.7 Hz, J_2 = 1.9 Hz, 1H). MS (ESI) m/z 603.7 $[M+H]^+$.

2,5-dichloro-N-((S)-3-(2,6-difluorophenyl)-1-(((R)-3-methyl-1-((3aS,4S,6S, 7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxopropan-2-yl)benzamide (7g)



Glassy solid (0.37 g, 50.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (-CH_3, s, 3H), 0.90 (-CH_3, dd, J_1 = 3.9 Hz, J_2 = 6.5 Hz, 6H), 1.33 (-CH_3, s, 3H), 1.37 (-CH_2, dd, J_1 = 5.8 Hz, J_2 = 11.2 Hz, 2H), 1.40 (-CH_3, s, 3H), 1.46-1.49 (-CH, m, 1H), 1.80-1.88 (-CH, m, 1H), 1.89- 1.94 (-CH, m, 1H), 1.99-2.07 (-CH_2, m, 2H), 2.17-2.23 (-CH_2, m, 1H), 2.29-2.38 (-CH_2, m, 1H), 3.19 (-CH, dd, J_1 = 9.7 Hz, J_2 = 14.2 Hz, 1H), 3.24-3.34 (-CH_2, m, 2H), 4.31 (-CH, dd, J_1 = 1.9 Hz, J_2 = 8.8 Hz, 1H), 4.92 (-CH, dd, J_1 = 5.2 Hz, J_2 = 9.3 Hz, 1H), 6.31 (-CONH, d, J = 5.7 Hz, 1H), 6.85 (-CONH, d, J = 8.3 Hz, 1H), 6.89 (-Ph, d, J = 7.7 Hz, 1H), 7.17-7.25 (-Ph, m, 1H), 7.26-7.55 (-Ph, m, 4H). MS (ESI) m/z 619.8 $[M-H]^-$.

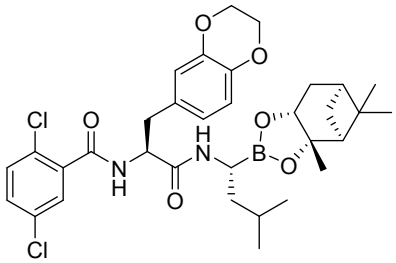
2,5-dichloro-N-((S)-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethyl hexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxo-3-phenylpropan-2-yl)benzamide (7h)



Glassy solid (0.71 g, 76.8%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (dd, J_1 = 2.2 Hz, J_2 = 4.0 Hz, 9H), 1.29 (s, 3H), 1.39 (s, 3H), 1.47 (dd, J_1 = 6.6 Hz, J_2 = 13.9 Hz, 1H), 1.61-1.67 (m, 2H), 1.78-1.94 (m, 3H), 2.01-2.05 (m, 1H), 2.16-2.21 (m, 1H), 2.30-2.37 (m, 1H), 3.13 (dd, J_1 = 7.8 Hz, J_2 = 13.7 Hz, 1H), 3.17-3.27 (m, 2H), 4.30 (dd, J_1 =2.0 Hz, J_2 = 8.8 Hz, 1H), 4.82 (dd, J_1 = 6.2 Hz, J_2 = 7.8 Hz, 1H), 5.93 (d, J = 4.7 Hz, 1H), 6.89 (d, J = 7.6 Hz, 1H), 7.22-7.34 (m, 8H), 7.48 (dd, J_1 = 1.0 Hz, J_2 = 1.9 Hz, 1H). MS (ESI) m/z 585.7$[M+H]^+$.

Compounds **7k-7m** and **7o-7p** were prepared following a similar procedure described for the synthesis of **7i**.

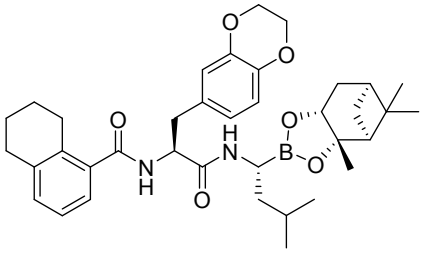
2,5-dichloro-N-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxopropan-2-yl)benzamide (7k)



Glassy solid (0.14 g, 74.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (d, J = 5.4 Hz, 3H), 0.87 (d, J = 6.7 Hz, 6H), 1.19 (d, J = 12.5 Hz, 1H), 1.28 (s, 3H), 1.29-1.36 (m, 1H), 1.41 (s, 3H), 1.44-1.52 (m, 1H), 1.85 (dd, J_1 = 12.0 Hz, J_2 = 19.5 Hz, 2H), 1.99 (dd, J_1 = 8.9 Hz, J_2 = 14.9 Hz, 1H), 2.04 (d, J = 3.2 Hz, 1H), 2.12-2.25 (m, 1H), 2.33 (dd, J_1 = 8.5 Hz, J_2 = 14.2 Hz, 1H), 2.92-3.06 (m, 1H), 3.07-3.36 (m, 2H), 4.23 (s,

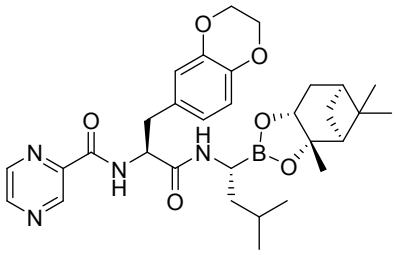
4H), 4.27-4.37 (m, 1H), 4.67-4.80 (m, 1H), 5.90 (dd, J_1 = 5.1 Hz, J_2 = 56.0 Hz, 1H), 6.70-6.83 (m, 3H), 6.86 (t, J = 7.9 Hz, 1H), 7.30 (d, J = 8.5 Hz, 2H), 7.45-7.58 (m, 1H). MS (ESI) m/z 643.2 $[M+H]^+$.

N-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxopropan-2-yl)-5,6,7,8-tetrahydronaphthalene-1-carboxamide (7l)



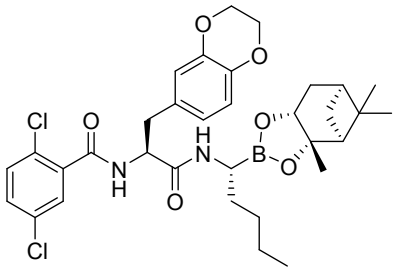
Glassy solid (0.15 g, 85.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (t, J = 3.5 Hz, 3H), 0.85-0.94 (m, 6H), 1.25 (d, J = 2.6 Hz, 1H), 1.27 (s, 3H), 1.34 (dd, J_1 = 4.6 Hz, J_2 = 11.2 Hz, 1H), 1.43 (s, 3H), 1.52 (dd, J_1 = 7.3 Hz, J_2 = 13.6 Hz, 1H), 1.59-1.67 (m, 1H), 1.74 (s, 4H), 1.80-1.96 (m, 2H), 1.98-2.06 (m, 1H), 2.12–2.25 (m, 1H), 2.26-2.38 (m, 1H), 2.67-2.78 (m, 4H), 2.93-3.11 (m, 2H), 3.14-3.23 (m, 1H), 4.22 (s, 4H), 4.31 (dd, J_1 = 4.4 Hz, J_2 = 9.1 Hz, 1H), 4.66-4.83 (m, 1H), 6.12 (dd, J_1 = 5.3 Hz, J_2 = 49.1 Hz, 1H), 6.27-6.42 (m, 1H), 6.70-6.76 (m, 1H), 6.76-6.83 (m, 2H), 6.99-7.14 (m, 3H). MS (ESI) m/z 627.3 $[M-H]^-$.

N-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-(((R)-3-methyl-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)butyl)amino)-1-oxopropan-2-yl)pyrazine-2-carboxamide (7m)



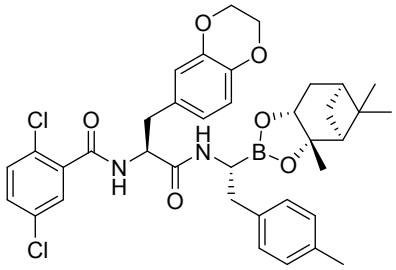
Glassy solid (0.56 g, 85.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (d, J = 2.2 Hz, 3H), 0.85 (d, J = 6.3 Hz, 6H), 0.93 (s, 1H), 1.22 (d, J = 10.8 Hz, 1H), 1.28 (s, 3H), 1.40 (s, 3H), 1.46 (dd, J_1 = 6.8 Hz, J_2 = 13.2 Hz, 1H), 1.66 (s, 1H), 1.79-1.93 (m, 2H), 2.02 (dd, J_1 = 7.3 Hz, J_2 = 12.6 Hz, 1H), 2.14-2.23 (m, 1H), 2.27-2.38 (m, 1H), 2.96-3.07 (m, 1H), 3.07-3.26 (m, 2H), 4.21 (s, 4H), 4.24-4.37 (m, 1H), 4.74 (dd, J_1 = 7.8 Hz, J_2 = 14.3 Hz, 1H), 5.90 (dd, J_1 = 5.1 Hz, J_2 = 39.8 Hz, 1H), 6.71-6.85 (m, 3H), 8.38 (dd, J_1 = 8.3 Hz, J_2 = 14.3 Hz, 1H), 8.54 (d, J = 5.1 Hz, 1H), 8.74 (d, J = 2.2 Hz, 1H), 9.35 (s, 1H). MS (ESI) m/z 575.3 $[M-H]^-$.

2,5-dichloro-N-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-oxo-1-(((R)-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)pentyl)amino)propan-2-yl)benzamide (7o)



The obtained crude product was directly used in the next reaction without purification.

2,5-dichloro-N-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1-oxo-1-(((R)-2-(p-tolyl)-1-((3aS,4S,6S,7aR)-3a,5,5-trimethylhexahydro-4,6-methanobenzo[d][1,3,2]dioxaborol-2-yl)ethyl)amino)propan-2-yl)benzamide (7p)

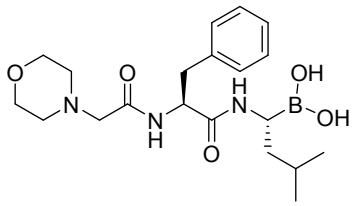


The obtained crude product was directly used in the next reaction without purification.

2. ^{1}H NMR, ^{13}C NMR and mass spectra of target compounds 8a-8m, 8o-8p

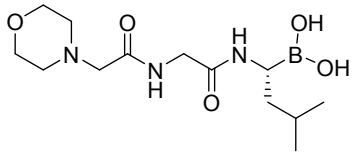
Compounds **8a-8m** and **8o-8p** were prepared from the corresponding starting materials described for the synthesis of **8n**.

((R)-3-methyl-1-((S)-2-(2-morpholinoacetamido)-3-phenylpropanamido) butyl)boronic acid (8a)



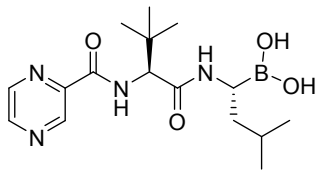
Yellow foam solid (0.49 g, 84.6%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.85 (dd, J_1 = 4.8 Hz, J_2 = 6.5 Hz, 6H), 1.17 (t, J = 7.3 Hz, 2H), 1.40 (dd, J_1 = 6.7 Hz, J_2 = 13.4 Hz, 1H), 2.69 (t, J = 7.4 Hz, 1H), 3.03-3.21 (m, 4H), 3.23 (d, J = 7.3 Hz, 1H), 3.49 (d, J = 12.0 Hz, 1H), 3.73-3.87 (m, 2H), 3.94-4.09 (m, 4H), 4.87 (d, J = 8.0 Hz, 1H), 7.22-7.36 (m, 5H). ^{13}C NMR (100 MHz, CD_3OD) δ 22.14, 23.67, 26.64, 38.51, 40.63, 47.87, 52.84, 58.02, 64.62, 128.29, 129.75, 130.54, 136.86, 165.12, 176.92. MS (ESI) m/z 404.6 $[M-H]^-$. HRMS (ESI): calcd for $C_{20}H_{32}BN_3NaO_5$ $[M+Na]^+$, 428.2330; found, 428.2337.

(R)-(3-methyl-1-(2-(2-morpholinoacetamido)acetamido)butyl)boronic acid (8b)



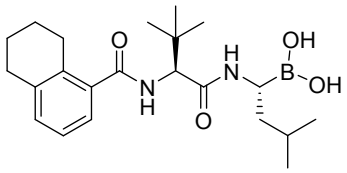
Yellow foam solid (0.25 g, 69.1%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.93 (d, J = 6.6 Hz, 6H), 1.32-1.39 (m, 2H), 1.63-1.70 (m, 1H), 2.78 (t, J = 7.5 Hz, 1H), 3.19-3.29 (m, 2H), 3.56 (d, J = 12.4 Hz, 2H), 3.81-3.89 (m, 2H), 4.06 (d, J = 17.1 Hz, 4H), 4.15 (s, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 22.49, 23.54, 26.73, 40.75, 53.93, 54.30, 58.20, 64.69, 166.05, 166.13. MS (ESI) m/z 314.1 $[M-H]^-$. HRMS (ESI): calcd for $C_{13}H_{26}BN_3NaO_5$ $[M+Na]^+$, 338.1860; found, 338.1864.

((R)-1-((S)-3,3-dimethyl-2-(pyrazine-2-carboxamido)butanamido)-3-methylbutyl)boronic acid (8c)



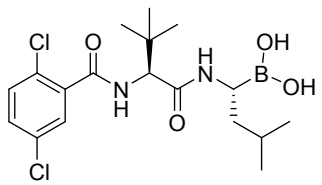
Yellow foam solid (0.15 g, 56.3%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.93 (dd, J_1 = 1.5 Hz, J_2 = 6.5 Hz, 6H), 1.12 (s, 9H), 1.33-1.39 (m, 2H), 1.65 (dd, J_1 = 6.6 Hz, J_2 = 13.4 Hz, 1H), 2.74 (dd, J_1 = 6.5 Hz, J_2 = 8.8 Hz, 1H), 4.72 (d, J = 6.2 Hz, 1H), 8.73 (s, 1H), 8.85 (d, J = 2.3 Hz, 1H), 9.25 (s, 1H). ^{13}C NMR (100 MHz, CD_3OD) δ 22.27, 23.80, 26.88, 27.02, 35.93, 41.15, 58.64, 144.84, 144.87, 145.24, 149.19, 164.70, 176.00. MS (ESI) m/z 349.4 $[M-H]^-$. HRMS (ESI) calcd for $C_{16}H_{27}BN_4NaO_4$ $[M+Na]^+$, 373.2021; found, 373.2014.

((R)-1-((S)-3,3-dimethyl-2-(5,6,7,8-tetrahydronaphthalene-1-carboxamido)butanamido)-3-methylbutyl)boronic acid (8d)



Yellow foam solid (0.19 g, 56.7%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.94 (dd, J_1 = 1.0 Hz, J_2 = 6.5 Hz, 6H), 1.10 (s, 9H), 1.34-1.39 (m, 2H), 1.62-1.71 (m, 1H), 1.78 (d, J = 13.0 Hz, 4H), 2.75 (dd, J_1 = 6.0 Hz, J_2 = 9.3 Hz, 1H), 2.80 (d, J = 5.3 Hz, 4H), 4.70 (s, 1H), 7.09-7.17 (m, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 22.15, 23.91, 23.94, 24.09, 27.05, 27.12, 27.84, 30.69, 35.49, 41.30, 59.04, 125.34, 126.40, 131.86, 135.27, 137.72, 139.06, 173.59, 176.97. MS (ESI) m/z 401.5 $[M-H]^-$. HRMS (ESI) calcd for $C_{22}H_{35}BN_2NaO_4$ $[M+Na]^+$, 425.2586; found, 425.2577.

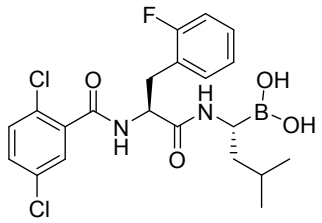
((R)-1-((S)-2-(2,5-dichlorobenzamido)-3,3-dimethylbutanamido)-3-methylbutyl)boronic acid (8e)



White foam solid (0.15 g, 68.9%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.96 (dd, J_1 = 2.1 Hz, J_2 = 6.6 Hz, 6H), 1.13 (s, 9H), 1.32 (dd, J_1 = 7.9 Hz, J_2 = 15.5 Hz, 2H), 1.65-

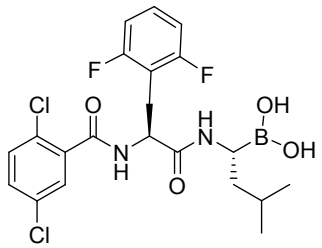
1.73 (m, 1H), 2.78 (dd, J_1 = 6.1 Hz, J_2 = 9.3 Hz, 1H), 4.73 (s, 1H), 7.45–7.50 (m, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ 22.14, 23.91, 27.04, 27.08, 35.66, 41.27, 59.15, 129.8, 130.46, 132.14, 132.43, 133.89, 138.63, 168.61, 176.45. MS (ESI) m/z 415.3[M-H]$^-$. HRMS (ESI) calcd for $C_{18}H_{27}BCl_2N_2NaO_4$ $[M+Na]^+$, 439.1336; found, 439.1346.

((R)-1-((S)-2-(2,5-dichlorobenzamido)-3-(2-fluorophenyl)propanamido)-3-methylbutyl)boronic acid (8f)



White foam solid (0.46 g, 62.8%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.85 (t, J = 6.2 Hz, 6H), 1.17 (t, J = 7.3 Hz, 2H), 1.34-1.43 (m, 1H), 2.72 (t, J = 7.6 Hz, 1H), 3.22 (d, J = 8.0 Hz, 2H), 5.05 (t, J = 8.0 Hz, 1H), 7.13 (dd, J_1 = 8.2 Hz, J_2 =14.8 Hz, 2H), 7.32 (dd, J_1 = 7.6 Hz, J_2 = 14.7 Hz, 3H), 7.42-7.48 (m, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 21.99, 23.89, 26.70, 32.07, 40.93, 51.59, 116.32, 116.54, 123.88, 125.52, 129.86, 130.64, 132.32, 132.56, 133.12, 133.88, 138.10, 161.57, 164.01, 168.11, 176.51. MS (ESI) m/z 467.7 [M-H]$^-$. HRMS (ESI): calcd for $C_{21}H_{24}BCl_2FN_2NaO_4$ $[M+Na]^+$, 491.1086; found, 491.1095.

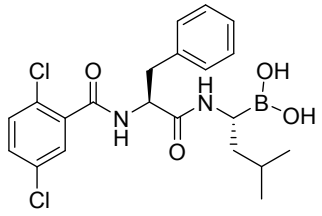
((R)-1-((S)-2-(2,5-dichlorobenzamido)-3-(2,6-difluorophenyl)propanamido)-3-methylbutyl)boronic acid (8g)



White foam solid (0.11 g, 55.5%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.88 (dd, J_1 = 1.9 Hz, J_2 = 6.5 Hz, 6H), 1.22 (t, J = 7.4 Hz, 2H), 1.40-1.48 (m, 1H), 2.75 (t, J = 7.6 Hz, 1H), 3.23 (dd, J_1 = 8.1 Hz, J_2 = 13.8 Hz, 1H), 3.28-3.36 (m, 1H), 5.09 (t, J = 7.9 Hz, 1H), 6.95-7.04 (m, 2H), 7.31-7.41 (m, 2H), 7.43-7.48 (m, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 23.85, 25.69, 26.73, 30.71, 40.93, 50.93, 112.33, 112.39, 112.52,

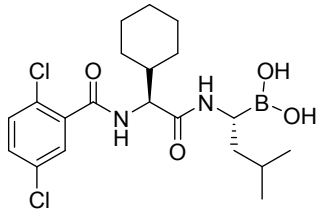
112.58, 129.84, 130.63, 130.79, 132.35, 132.58, 133.88, 137.99, 161.94, 162.02, 164.40, 164.48, 168.07, 176.21. MS (ESI) m/z 485.6 $[M-H]^-$. HRMS (ESI): calcd for $C_{21}H_{23}BCl_2F_2N_2NaO_4$ $[M+Na]^+$, 509.0992; found, 509.1001.

((R)-1-((S)-2-(2,5-dichlorobenzamido)-3-phenylpropanamido)-3-methylbutyl)boronic acid (8h)



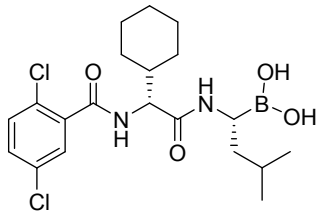
White foam solid (0.31 g, 61.9%). ^{1}H NMR (400 MHz, CD_3OD) δ 0.85 (t, J = 6.8 Hz, 6H), 1.26-1.33 (m, 2H), 1.37 (dd, J_1 = 7.0 Hz, J_2 = 13.6 Hz, 1H), 2.65-2.73 (m, 1H), 3.12-3.19 (m, 2H), 4.94-5.01 (m, 1H), 7.24-7.37 (m, 6H), 7.45 (d, J = 1.1 Hz, 2H). ^{13}C NMR (100 MHz, CD_3OD) δ 21.92, 23.91, 26.67, 38.55, 40.88, 53.03, 128.30, 129.73, 129.87, 130.55, 130.62, 132.28, 132.53, 133.84, 136.98, 138.13, 168.14, 176.83. MS (ESI) m/z 449.6$[M-H]^-$. HRMS (ESI): calcd for $C_{21}H_{25}BCl_2N_2NaO_4$ $[M+Na]^+$, 473.1180; found, 473.1188.

((R)-1-((S)-2-cyclohexyl-2-(2,5-dichlorobenzamido)acetamido)-3-methylbutyl)boronic acid (8i)



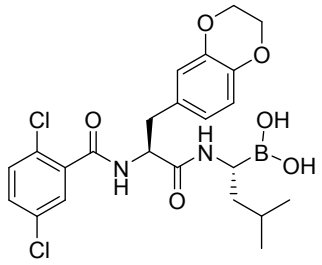
Yellow foam solid (0.16 g, 71.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.65-0.83 (m, 3H), 0.83-0.96 (m, 3H), 1.01-1.27 (m, 5H), 1.31-1.51 (m, 2H), 1.52-1.62 (m, 1H), 1.67 (d, J = 11.3 Hz, 1H), 1.75 (s, 5H), 2.80-3.09 (m, 1H), 4.39-4.75 (m, 1H), 7.29-7.43 (m, 2H), 7.50-7.62 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.05, 25.83, 28.85, 29.35, 29.64, 39.98, 40.62, 56.60, 58.10, 129.02, 129.62, 131.34, 133.10, 135.82, 135.98, 165.34, 172.59. MS (ESI) m/z 441.2 $[M-H]^-$. HRMS (ESI) calcd for $C_{20}H_{29}BCl_2N_2NaO_4$ $[M+Na]^+$, 465.1493; found, 465.1497.

((R)-1-((R)-2-cyclohexyl-2-(2,5-dichlorobenzamido)acetamido)-3-methylbutyl)boronic acid (8j)



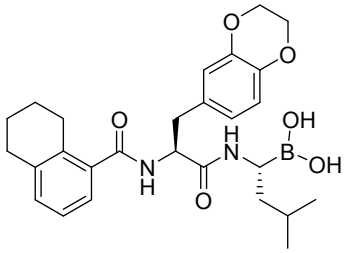
Yellow foam solid (0.17 g, 68.5%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (d, J = 8.1 Hz, 3H), 0.82-0.90 (m, 3H), 1.13-1.29 (m, 5H), 1.29-1.45 (m, 2H), 1.47-1.58 (m, 1H), 1.68 (s, 1H), 1.83 (dd, J_1 = 23.0 Hz, J_2 = 26.6 Hz, 5H), 3.09 (d, J = 109.8 Hz, 1H), 4.50-4.81 (m, 1H), 7.28-7.88 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 23.08, 25.65, 25.77, 26.09, 29.65, 39.86, 39.92, 57.29, 57.37, 129.17, 129.77, 131.17, 132.91, 136.00, 165.32, 172.40. MS (ESI) m/z 441.3 $[M-H]^-$. HRMS (ESI) calcd for $C_{20}H_{29}BCl_2N_2NaO_4$ $[M+Na]^+$, 465.1493; found, 465.1495.

((R)-1-((S)-2-(2,5-dichlorobenzamido)-3-(2,3-dihydrobenzo[*b*][1,4]dioxin-6-yl)propanamido)-3-methylbutyl)boronic acid (8k)



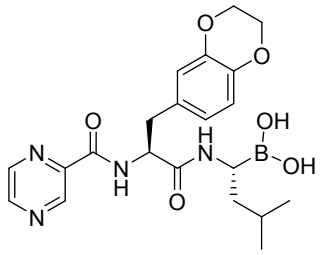
Yellow foam solid (0.85 g, 52.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.76-0.83 (m, 3H), 0.83-0.91 (m, 3H), 1.29 (dd, J_1 = 8.8 Hz, J_2 = 15.0 Hz, 1H), 1.39-1.56 (m, 2H), 2.92 (d, J = 35.0 Hz, 1H), 3.09 (t, J = 6.2 Hz, 2H), 4.21 (d, J = 5.5 Hz, 4H), 4.91 (t, J = 19.8 Hz, 1H), 6.66 (dd, J_1 = 12.5 Hz, J_2 = 27.4 Hz, 1H), 6.71-6.80 (m, 2H), 7.21-7.59 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.98, 25.82, 37.32, 39.90, 50.52, 52.82, 64.25, 117.35, 118.30, 122.46, 128.74, 129.09, 129.48, 131.25, 132.94, 135.75, 142.68, 143.36, 165.24, 172.64. MS (ESI) m/z 507.2 $[M-H]^-$. HRMS (ESI) calcd for $C_{23}H_{27}BCl_2N_4NaO_6$ $[M+Na]^+$, 531.1325; found, 531.1246.

((R)-1-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(5,6,7,8-tetrahydronaphthalene-1-carboxamido)propanamido)-3-methylbutyl)boronic acid (8l)



Yellow foam solid (0.47 g, 59.2%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 4.7 Hz, 3H), 0.86 (d, J = 10.6 Hz, 3H), 1.41-1.51 (m, 2H), 1.52-1.64 (m, 1H), 1.73 (s, 4H), 2.50-2.67 (m, 2H), 2.73 (s, 2H), 2.88-2.98 (m, 1H), 2.99-3.15 (m, 2H), 4.11-4.31 (m, 4H), 4.82-4.99 (m, 1H), 6.44-6.62 (m, 1H), 6.63-6.82 (m, 3H), 6.99-7.10 (m, 3H), 7.37-7.97 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.41, 22.54, 22.87, 25.82, 26.54, 29.71, 31.88, 39.97, 52.20, 52.69, 64.25, 117.23, 118.17, 122.18, 124.03, 125.12, 129.14, 131.09, 134.83, 135.61, 138.02, 142.49, 143.37, 170.43, 173.44. MS (ESI) m/z 493.2 $[M-H]^-$. HRMS (ESI) calcd for $C_{23}H_{27}BCl_2N_2NaO_6$ $[M+Na]^+$, 517.2485; found, 517.2480.

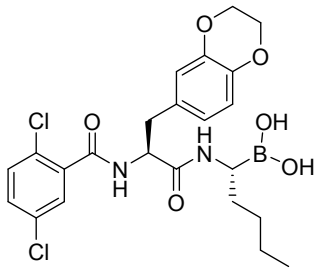
((R)-1-((S)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-(pyrazine-2-carboxamido)propanamido)-3-methylbutyl)boronic acid (8m)



Yellow foam solid (0.14 g, 63.2%). ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.74 (d, J = 5.4 Hz, 3H), 0.84 (m, 3H), 1.02-1.21 (m, 1H), 1.30-1.41 (m, 1H), 1.51 (dd, J_1 = 6.6 Hz, J_2 = 13.1 Hz, 1H), 2.82-3.01 (m, 2H), 3.02-3.15 (m, 1H), 4.14 (d, J = 5.5 Hz, 4H), 4.62-4.88 (m, 1H), 6.64 (d, J = 10.7 Hz, 2H), 6.71 (d, J = 4.2 Hz, 1H), 8.62 (t, J = 8.3 Hz, 1H), 8.68-8.78 (m, 1H), 8.79-8.93 (m, 2H), 9.05-9.17 (m, 1H). ^{13}C NMR (100MHz, DMSO-d_6) δ 22.96, 25.89, 31.88, 37.60, 52.41, 58.34, 64.21, 117.30,

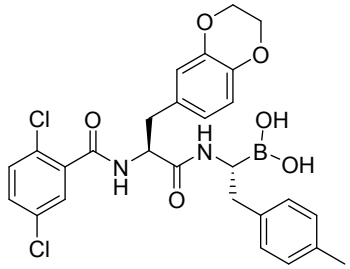
118.18, 122.35, 128.72, 142.68, 142.74, 143.44, 143.78, 144.22, 147.44, 162.94, 172.84. MS (ESI) m/z 441.1 $[M-H]^-$. HRMS (ESI) calcd for $C_{21}H_{27}BN_4NaO_6$ $[M+Na]^+$, 465.1919; found, 469.1932.

((R)-1-((S)-2-(2,5-dichlorobenzamido)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)propanamido)pentyl)boronic acid (8o)



Yellow foam solid (0.03 g, 46.4%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (s, 3H), 1.25 (s, 2H), 1.27-1.38 (m, 2H), 1.52-2.07 (m, 2H), 2.60-3.00 (m, 1H), 3.06 (s, 2H), 4.20 (d, J = 5.4 Hz, 4H), 4.86 (d, J = 68.6 Hz, 1H), 6.71 (dd, J_1 = 13.6 Hz, J_2 = 29.0 Hz, 3H), 7.04 (d, J = 38.7 Hz, 1H), 7.17-7.25 (m, 1H), 7.27-7.44 (m, 2H), 7.47-7.86 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.25, 22.49, 22.82, 29.83, 36.05, 55.36, 64.44, 117.64, 118.41, 122.53, 129.21, 129.27, 130.05, 131.45, 133.18, 133.32, 142.88, 143.69, 165.12, 171.26. MS (ESI) m/z 507.1 $[M-H]^-$. HRMS (ESI): calcd for $C_{23}H_{27}BCl_2N_2NaO_6$ $[M+Na]^+$, 531.1236; found, 531.1239.

((R)-1-((S)-2-(2,5-dichlorobenzamido)-3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)propanamido)-2-(p-tolyl)ethyl)boronic acid (8p)

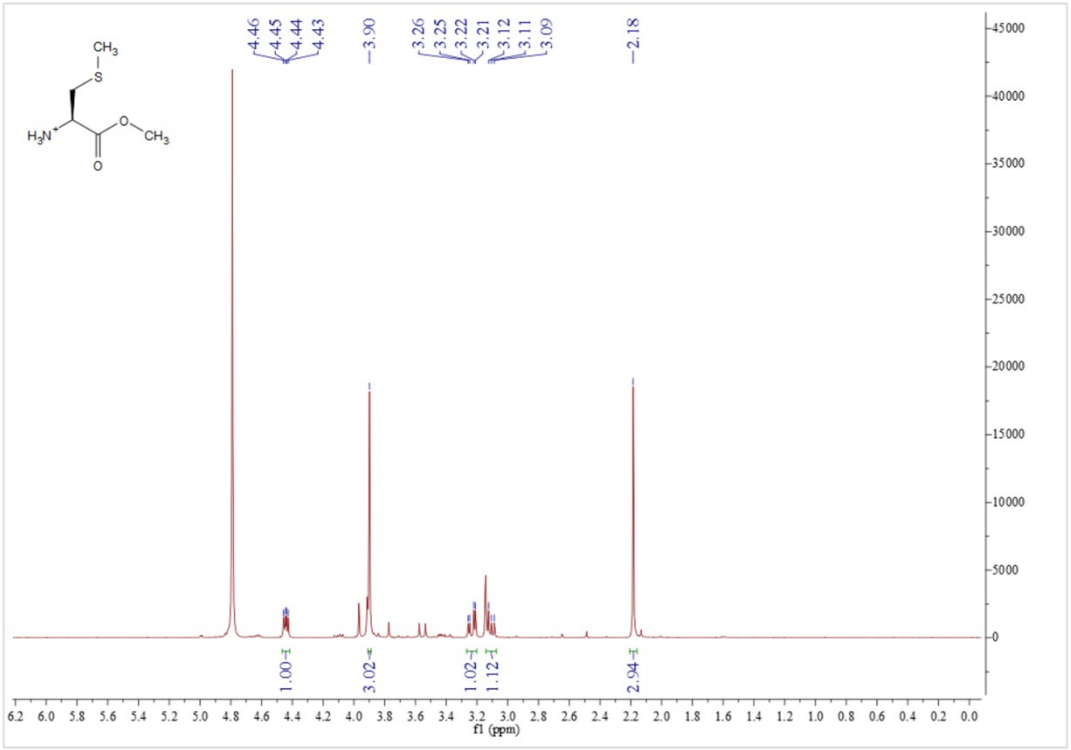


Yellow foam solid (0.03 g, 27.9%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.23 (s, 3H), 2.73 (d, J = 23.3 Hz, 2H), 2.91-3.05 (m, 2H), 3.05-3.23 (m, 1H), 3.97-4.33 (m, 4H), 4.71-5.02 (m, 1H), 6.26-6.46 (m, 1H), 6.58-6.86 (-Ph, m, 4H), 6.85-7.00 (-Ph, m, 3H), 7.01-7.11 (-Ph, m, 3H), 7.32-7.93 (-CONH, m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.52, 29.74, 36.13, 46.62, 52.26, 64.27, 117.34, 118.17, 122.19, 128.82, 134.91,

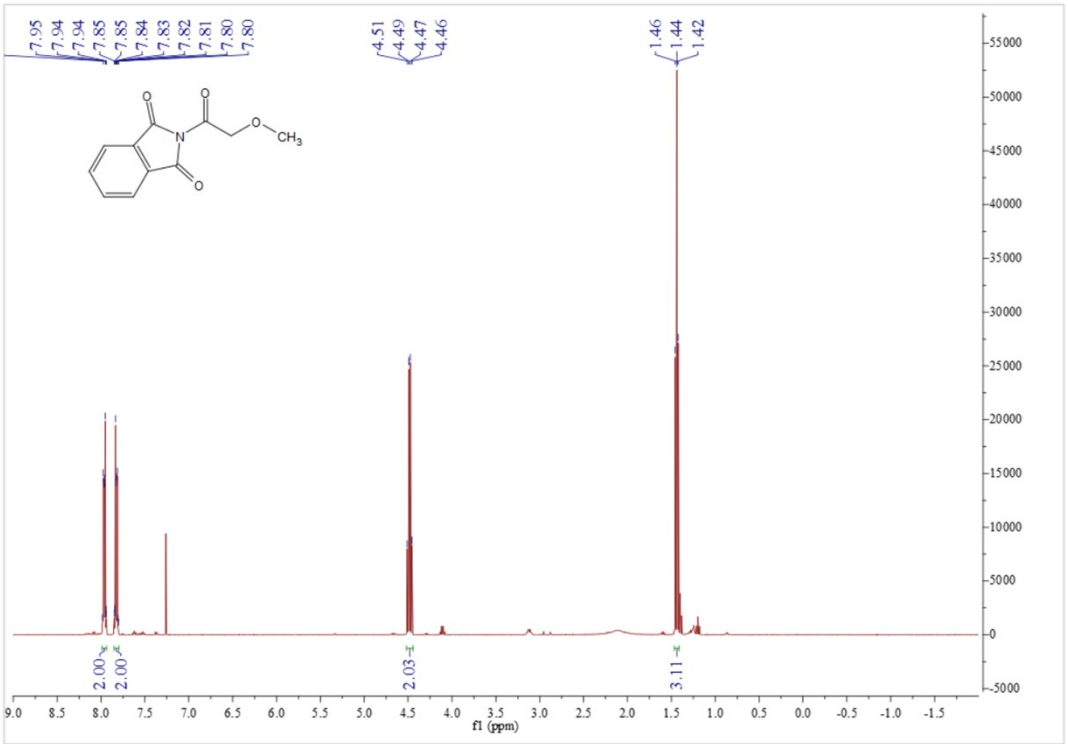
135.20, 137.50, 138.07, 143.56, 170.20, 174.00. MS (ESI) m/z 555.4 $[M-H]^-$. HRMS (ESI): calcd for $C_{27}H_{27}BN_2NaO_6$ $[M+Na]^+$, 579.1236; found, 579.1237.

3. ^{1}H NMR spectra of intermediate compounds

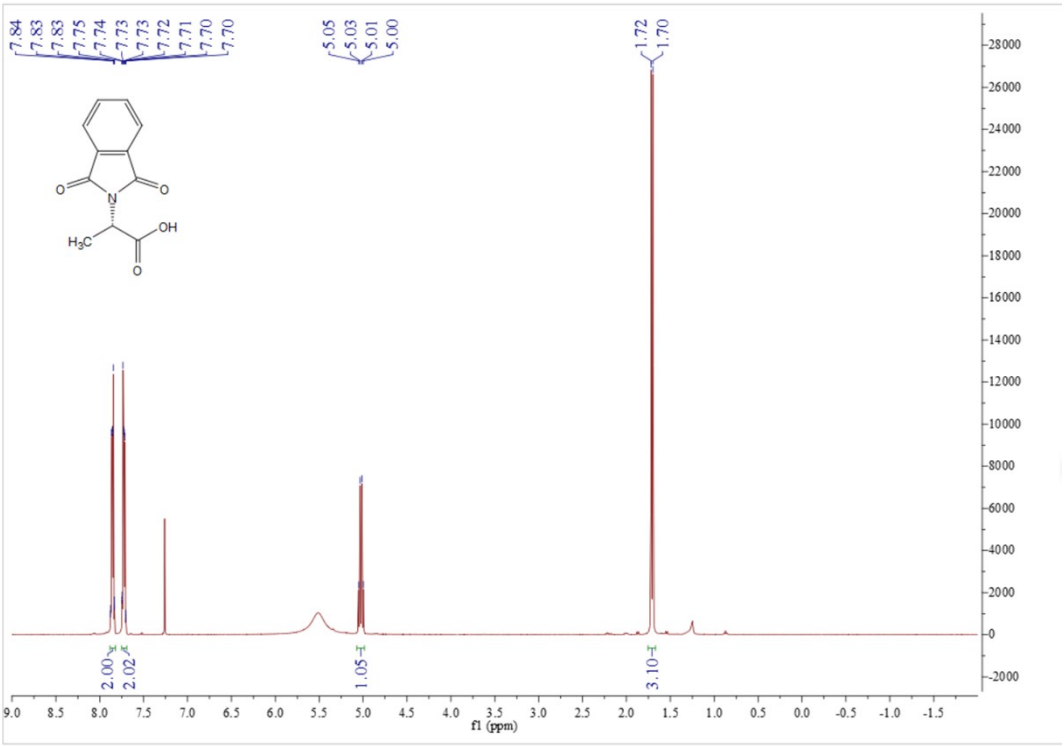
Compound **1c**



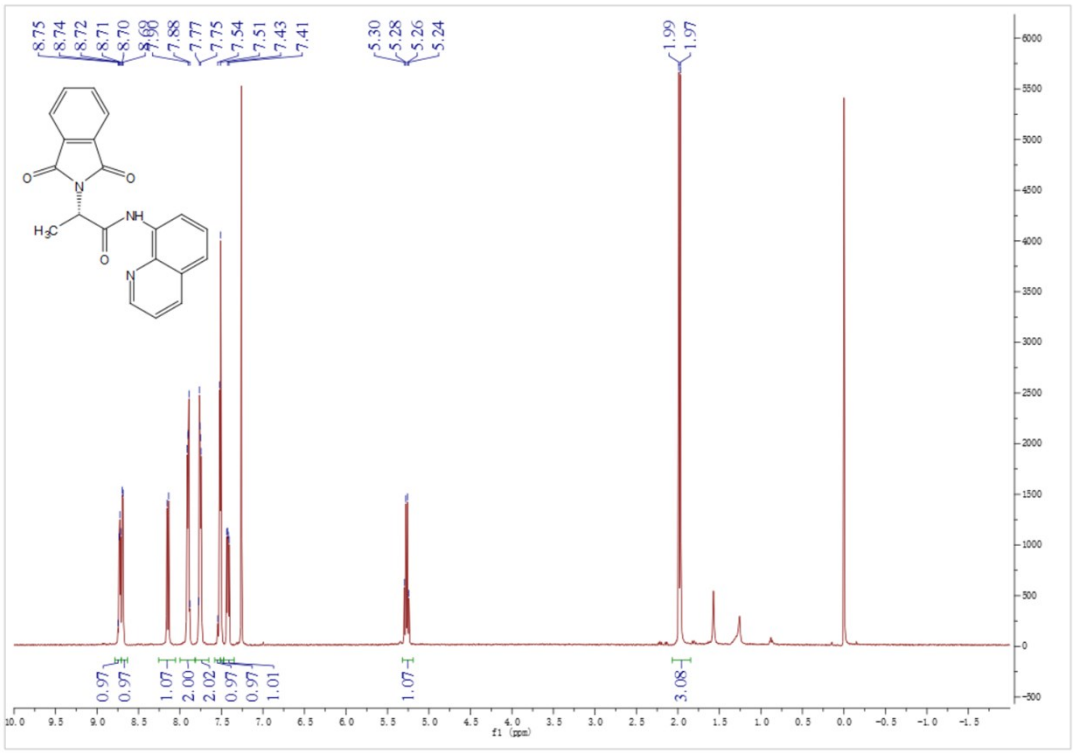
Compound **2a**



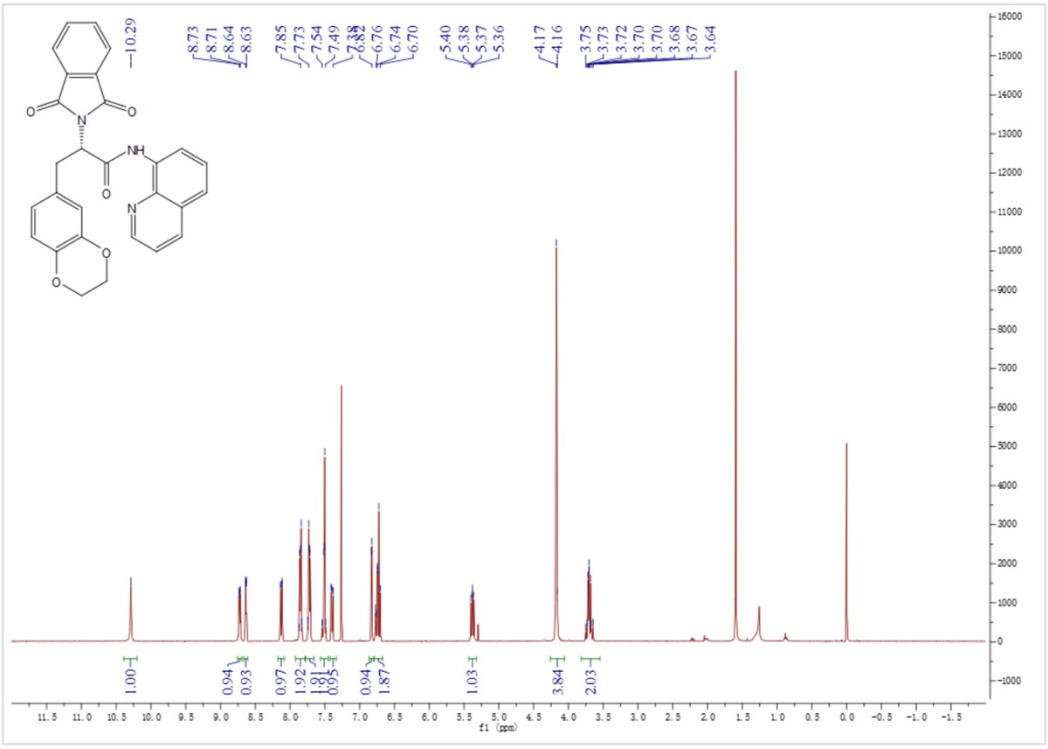
Compound **2b**



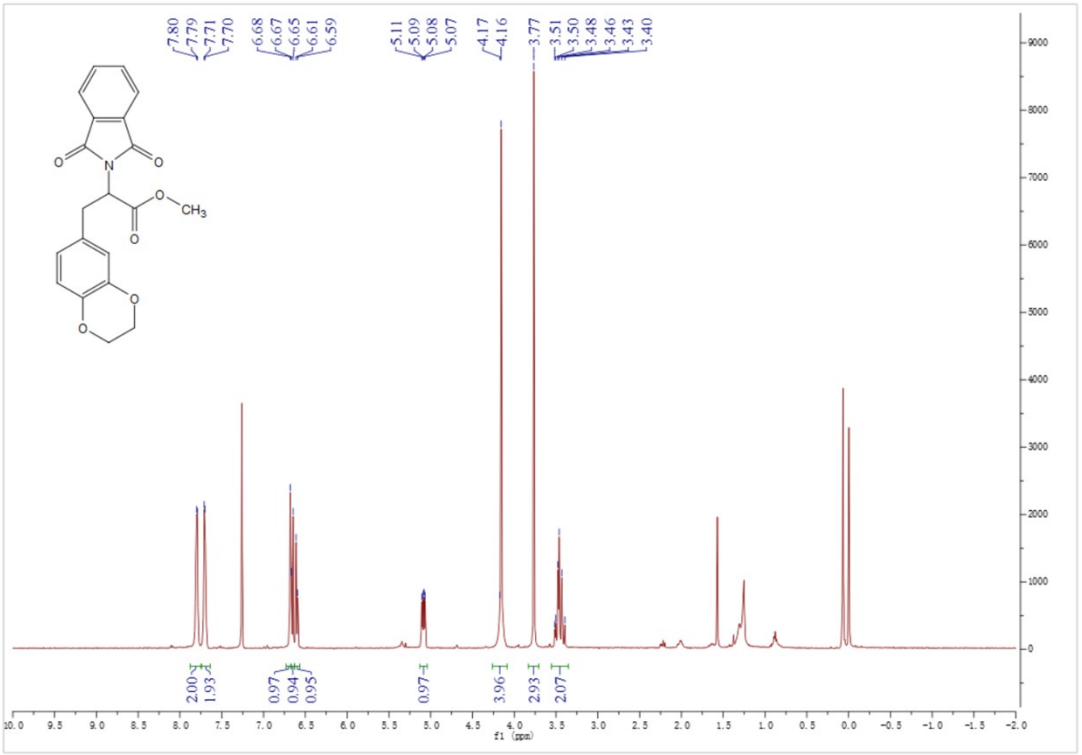
Compound **2c**



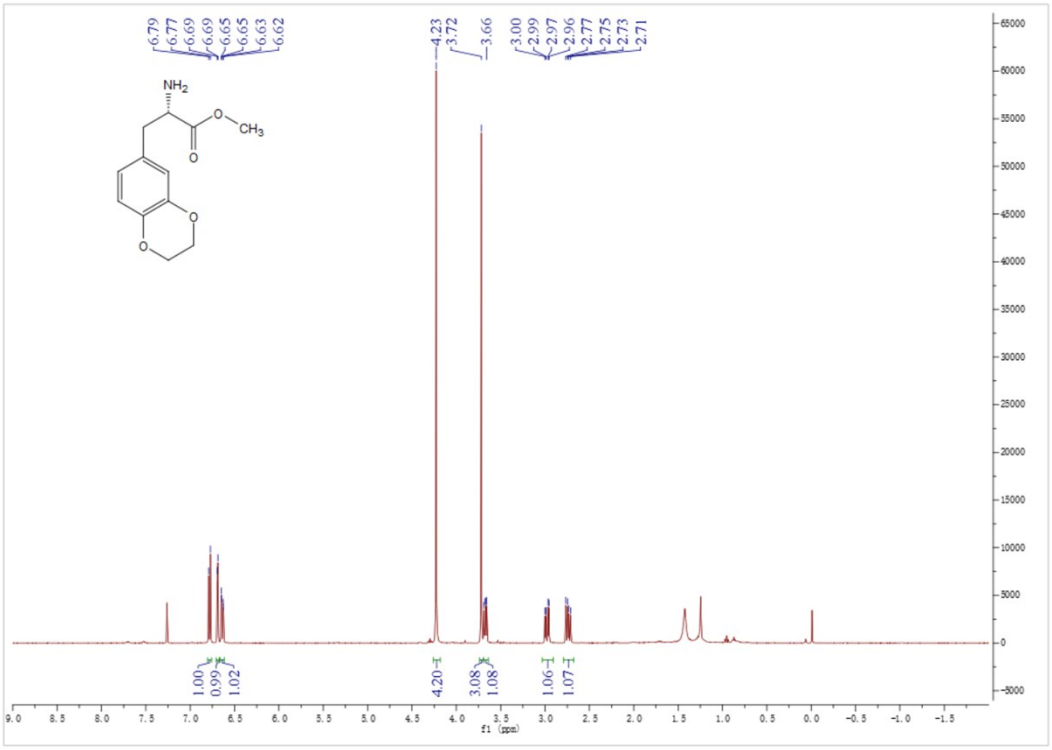
Compound **2d**



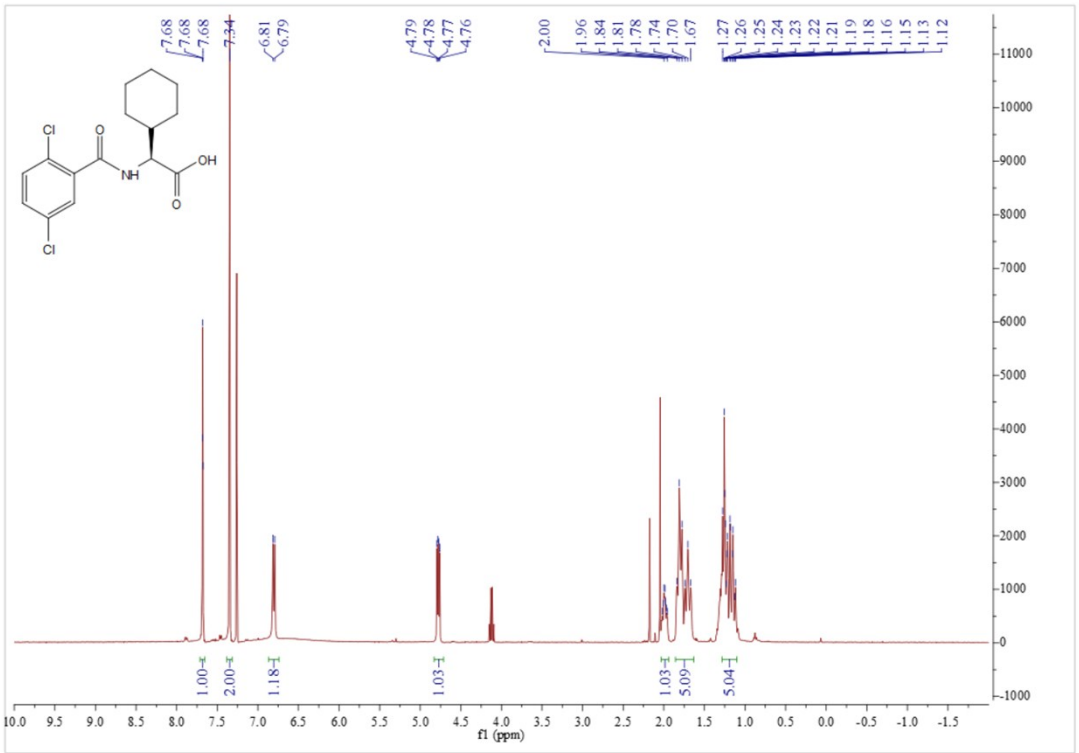
Compound **2e**



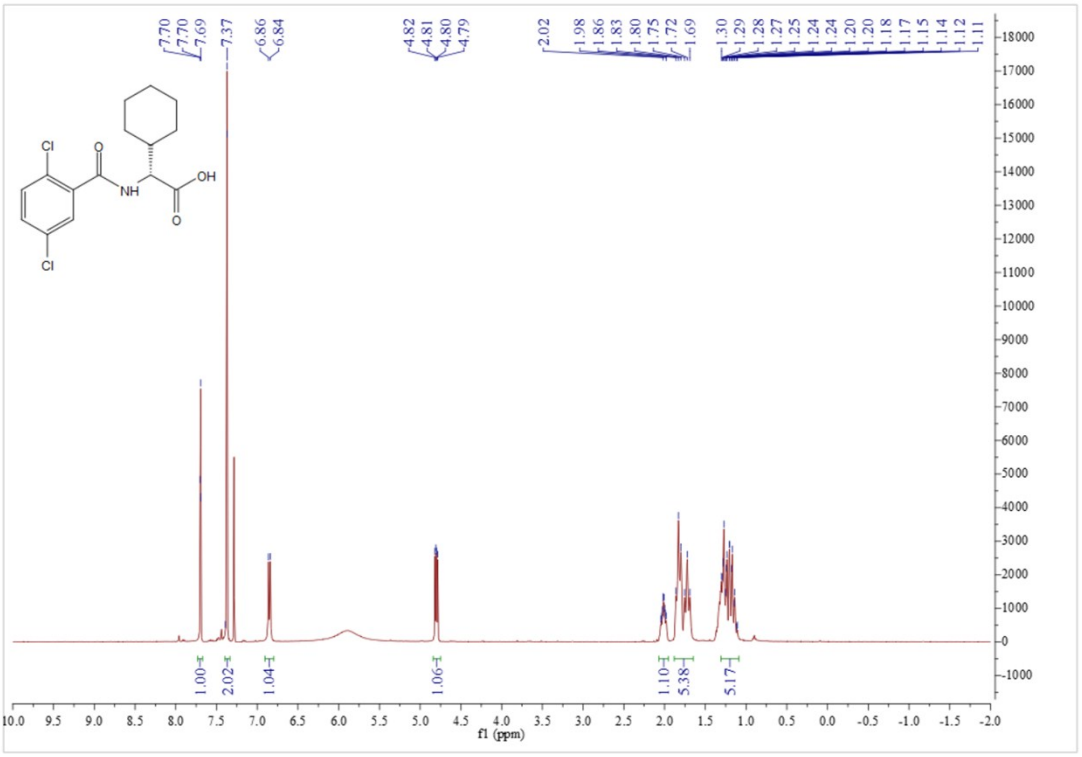
Compound **2f**



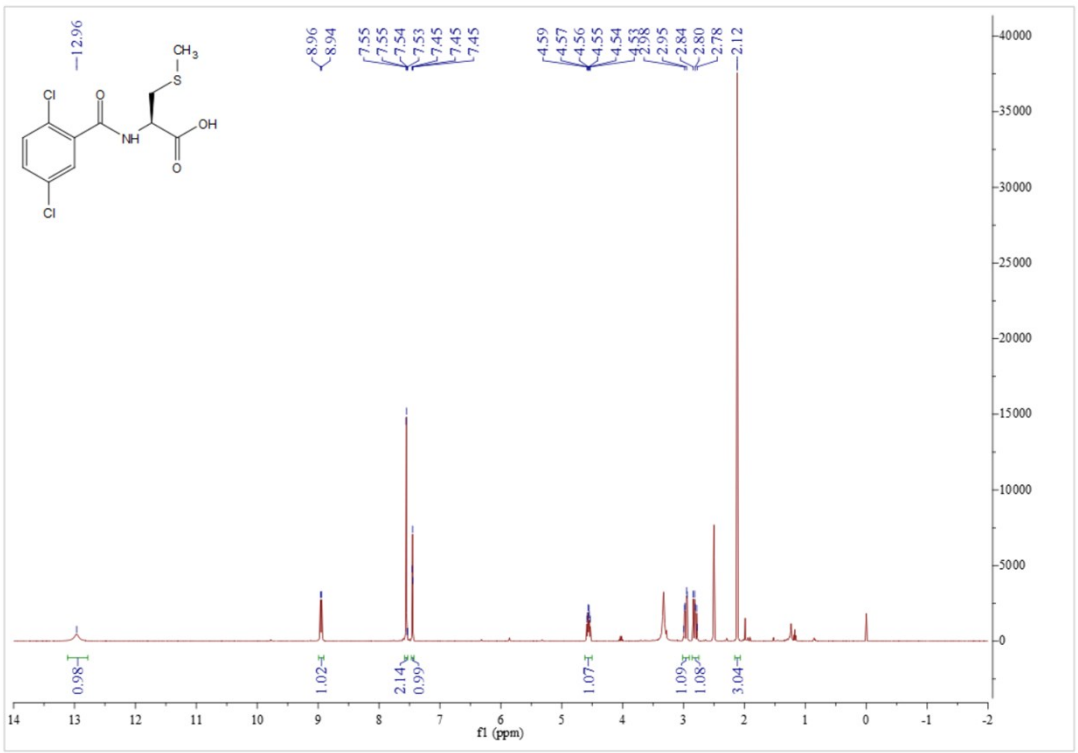
Compound **3a**



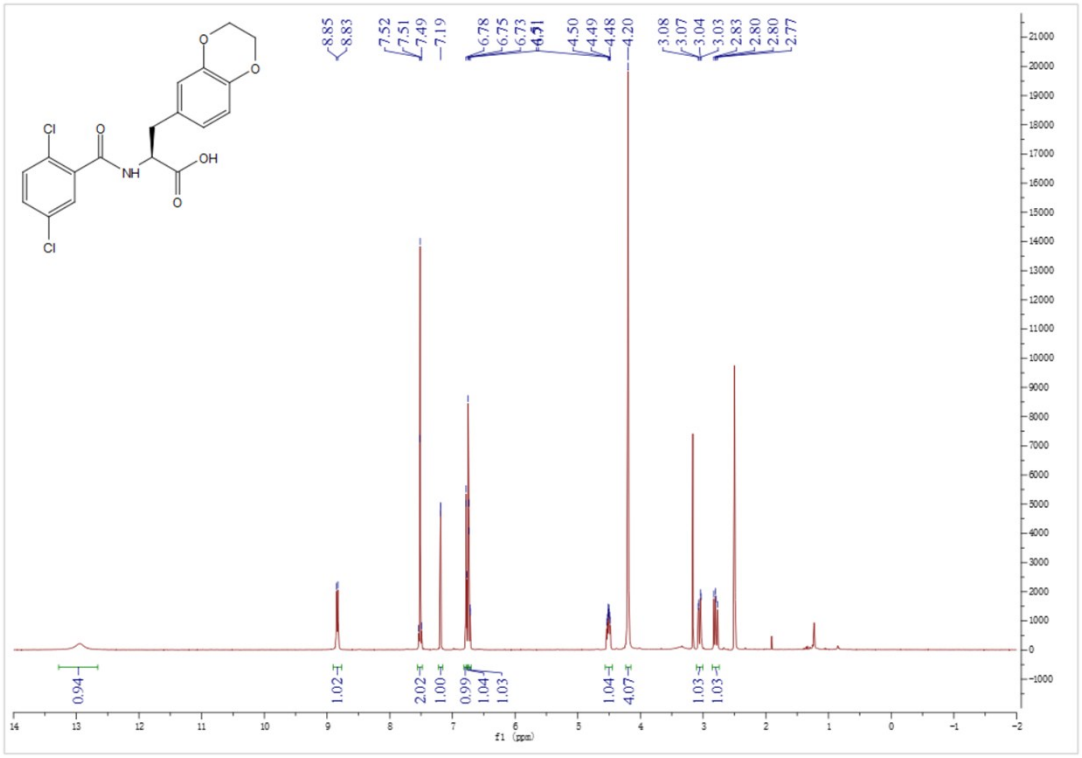
Compound **3b**



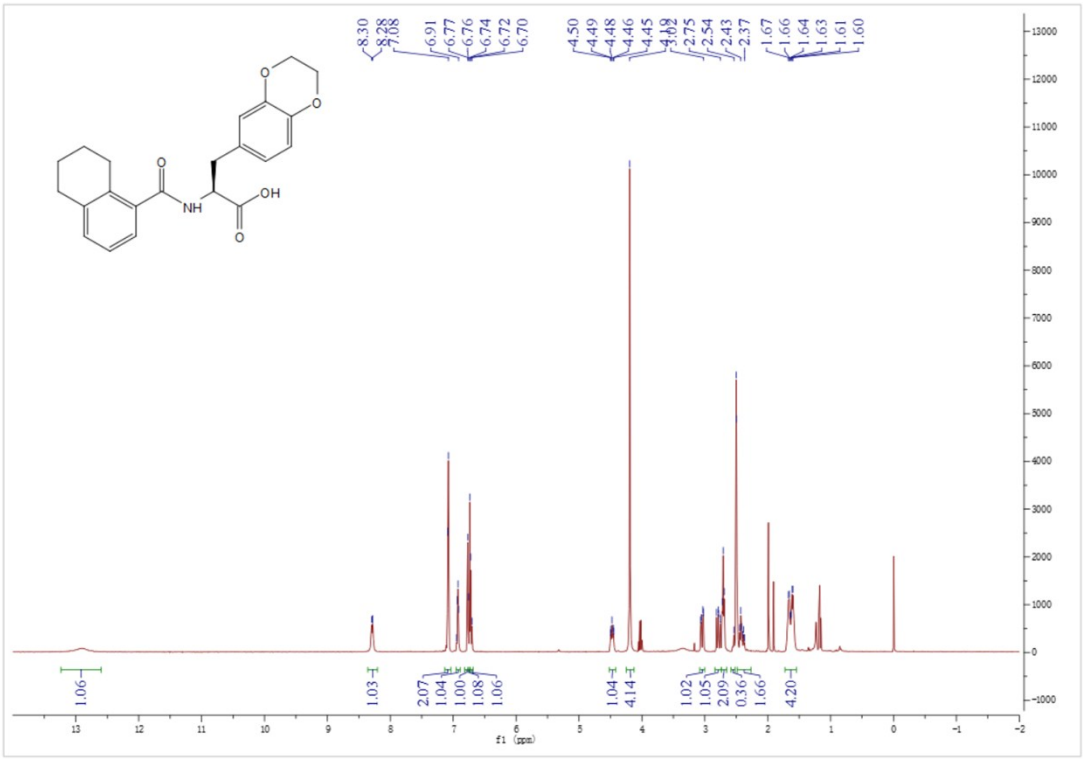
Compound **3c**



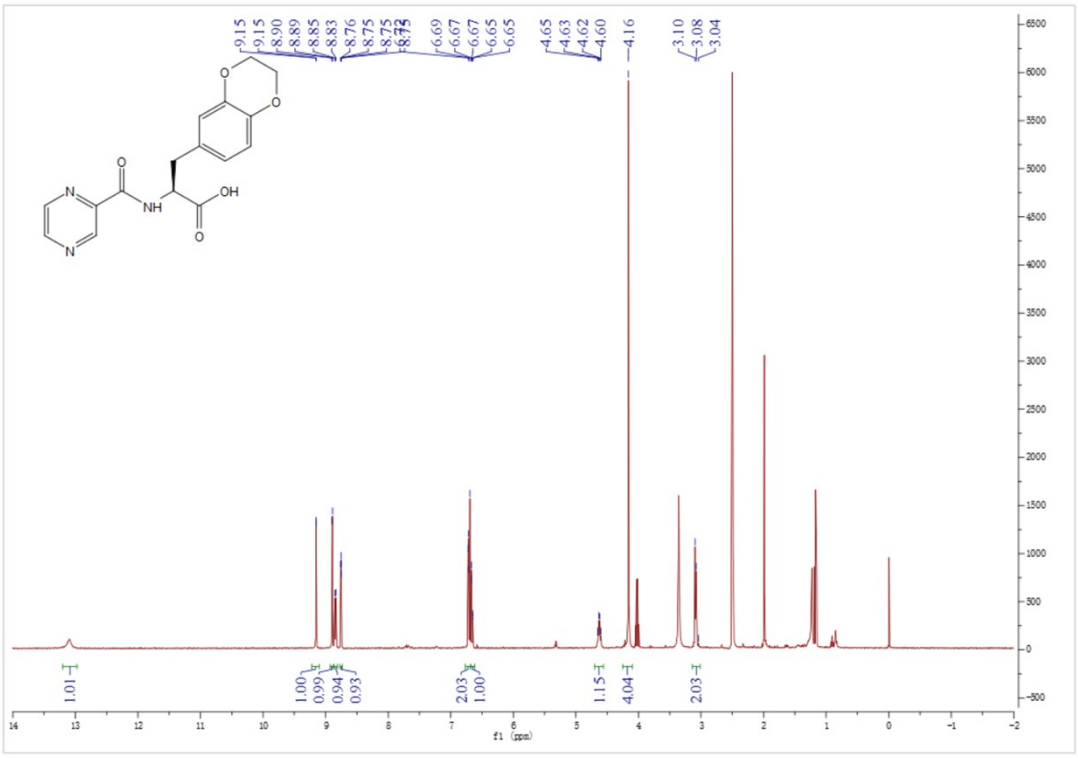
Compound **3d**



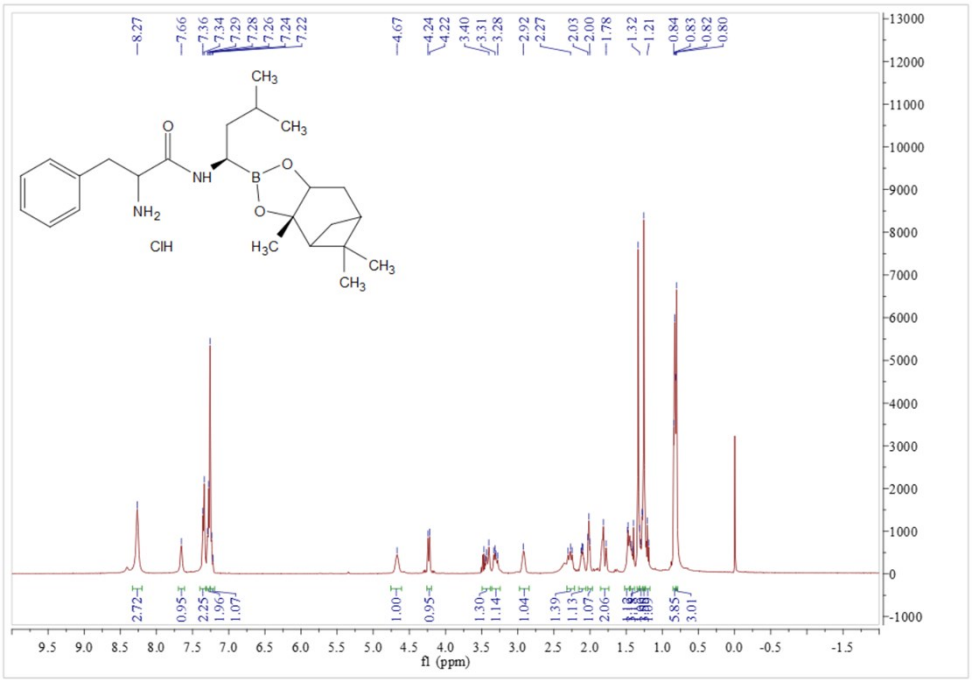
Compound **3e**



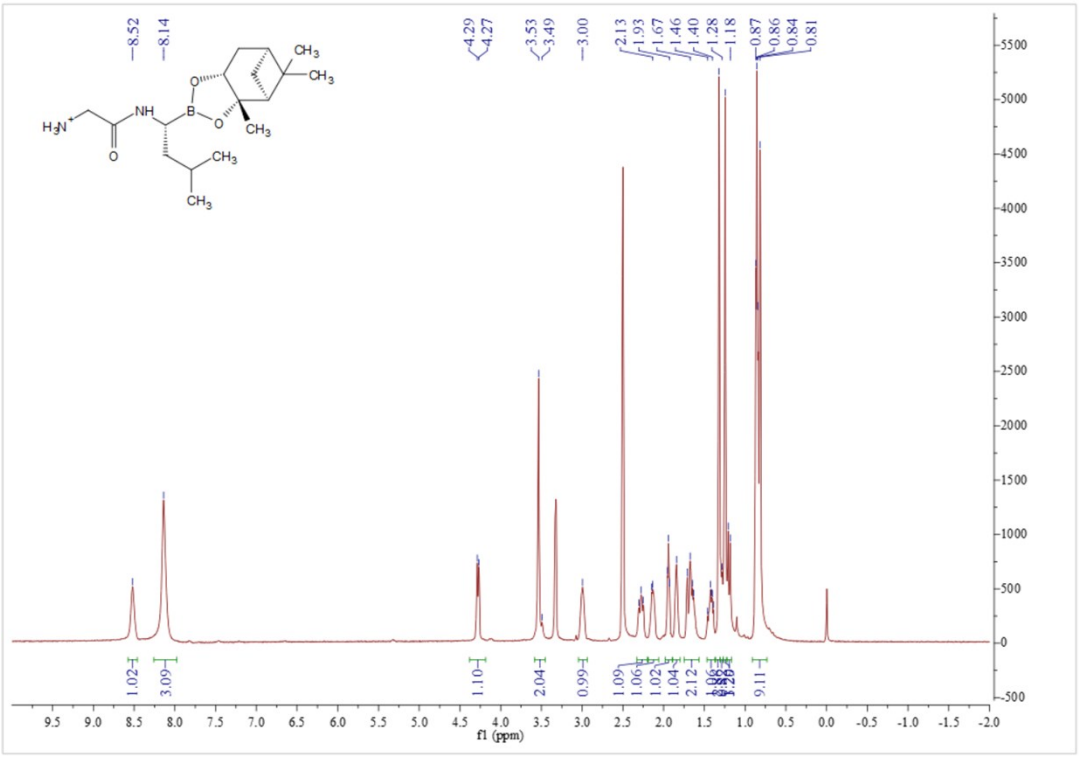
Compound **3f**



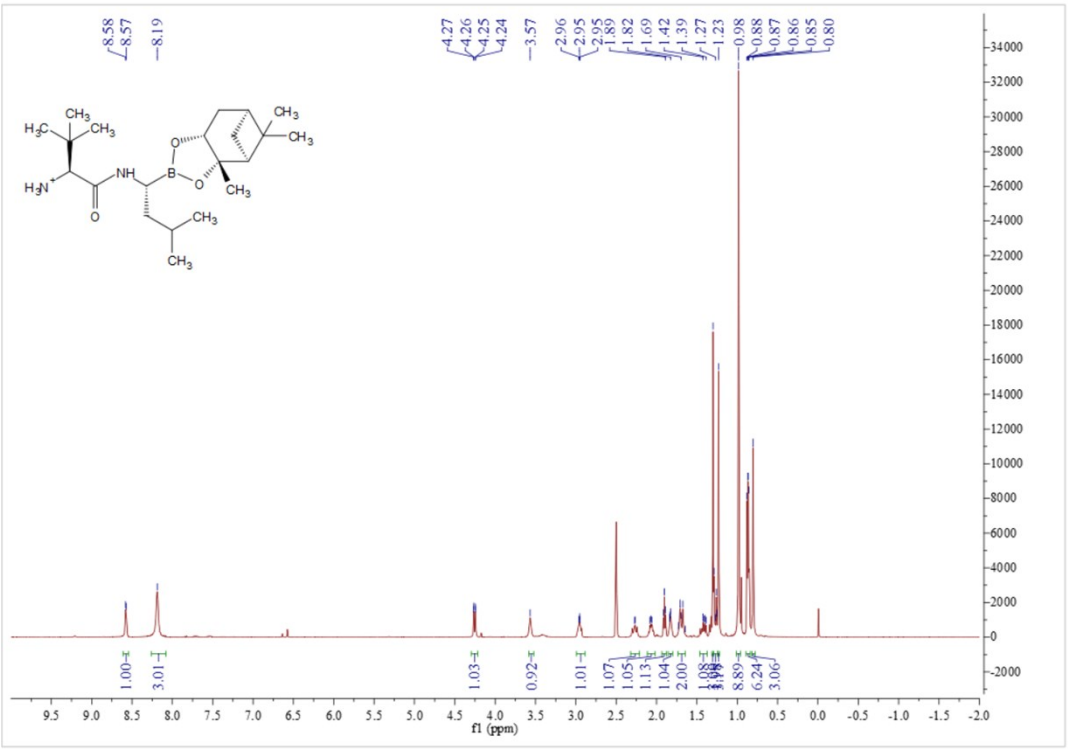
Compound **6a**



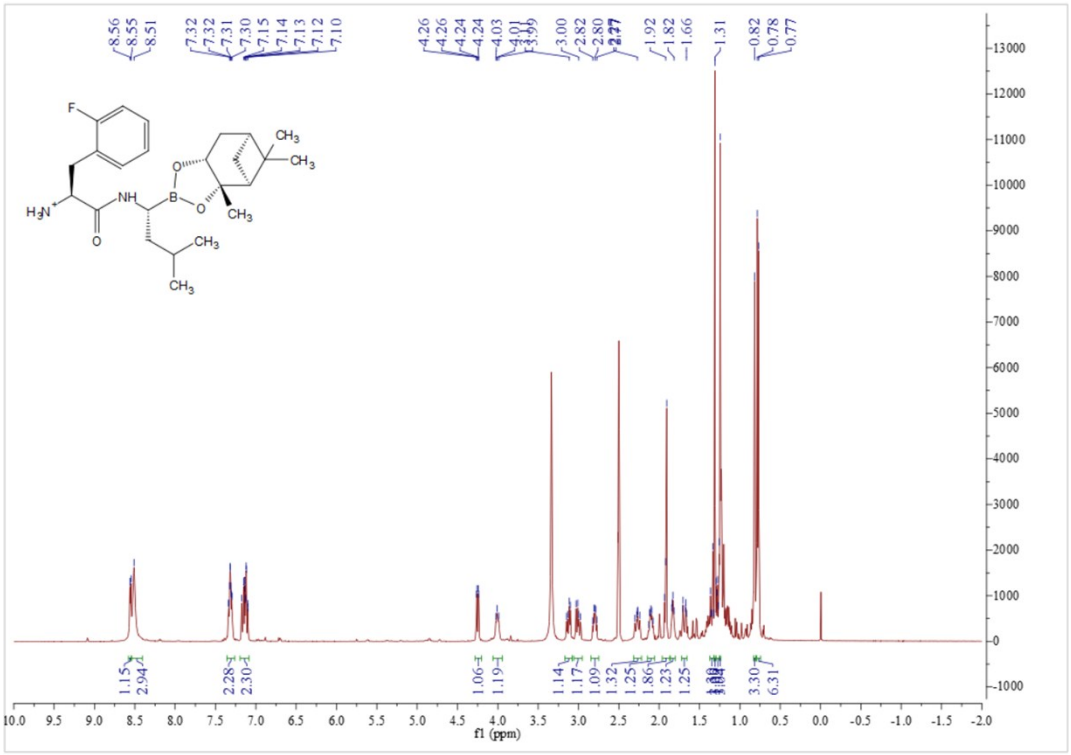
Compound **6b**



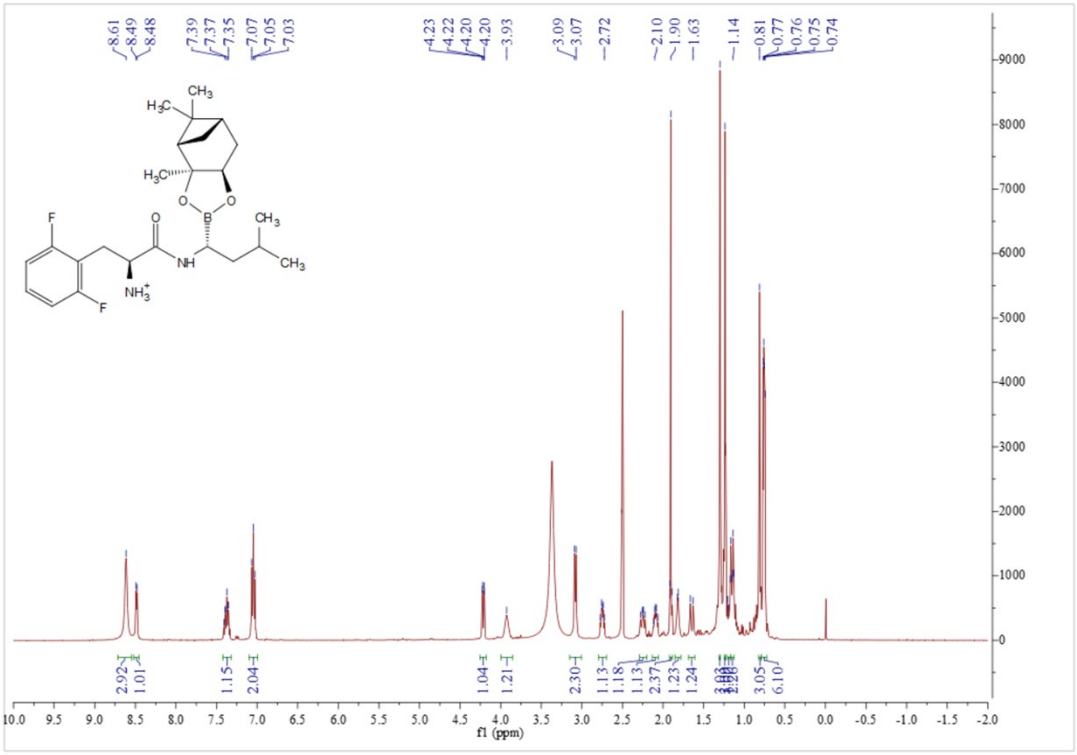
Compound **6c**



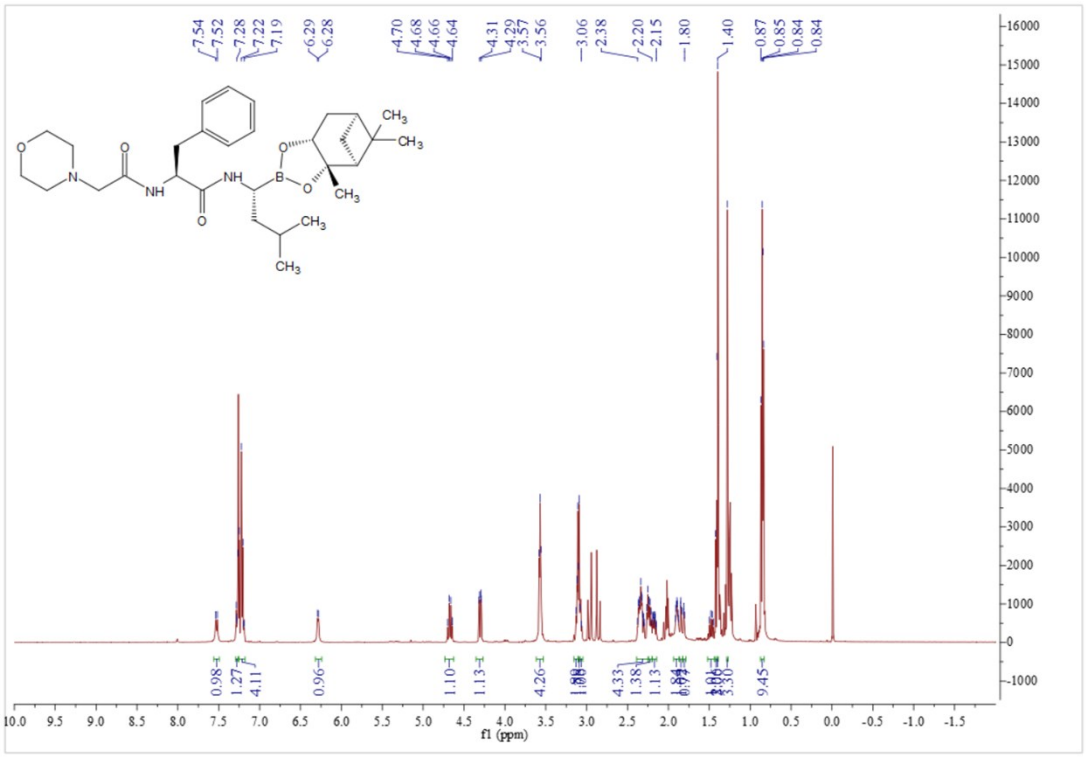
Compound **6d**



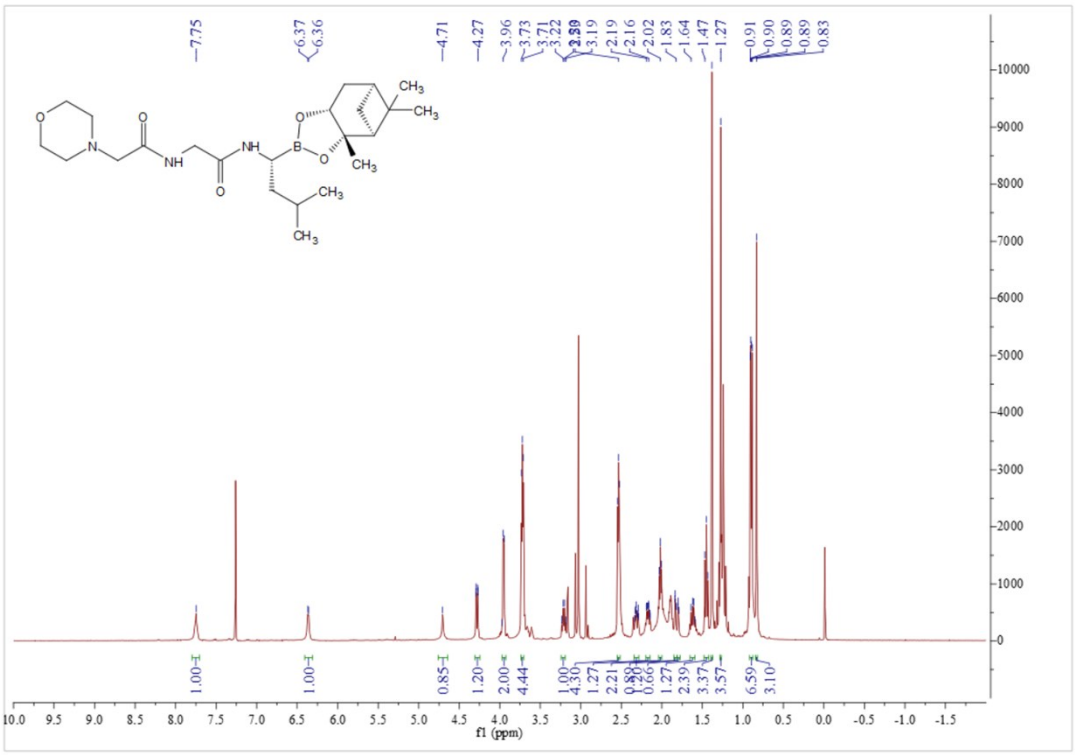
Compound **6e**



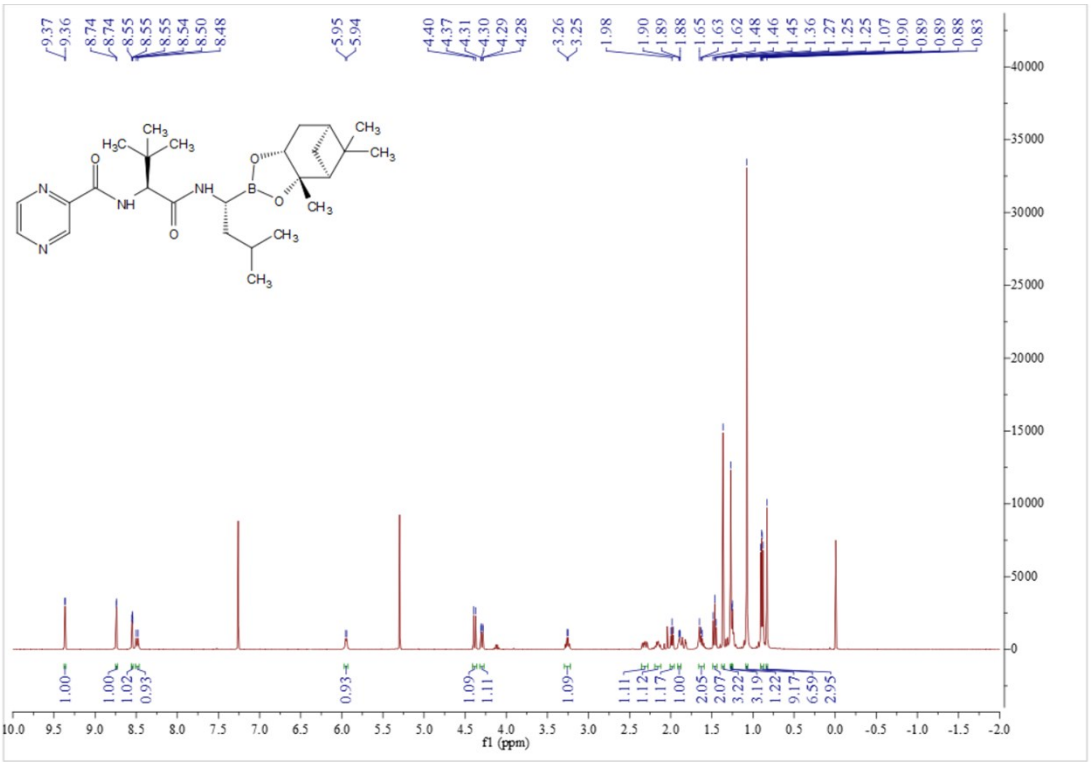
Compound **7a**



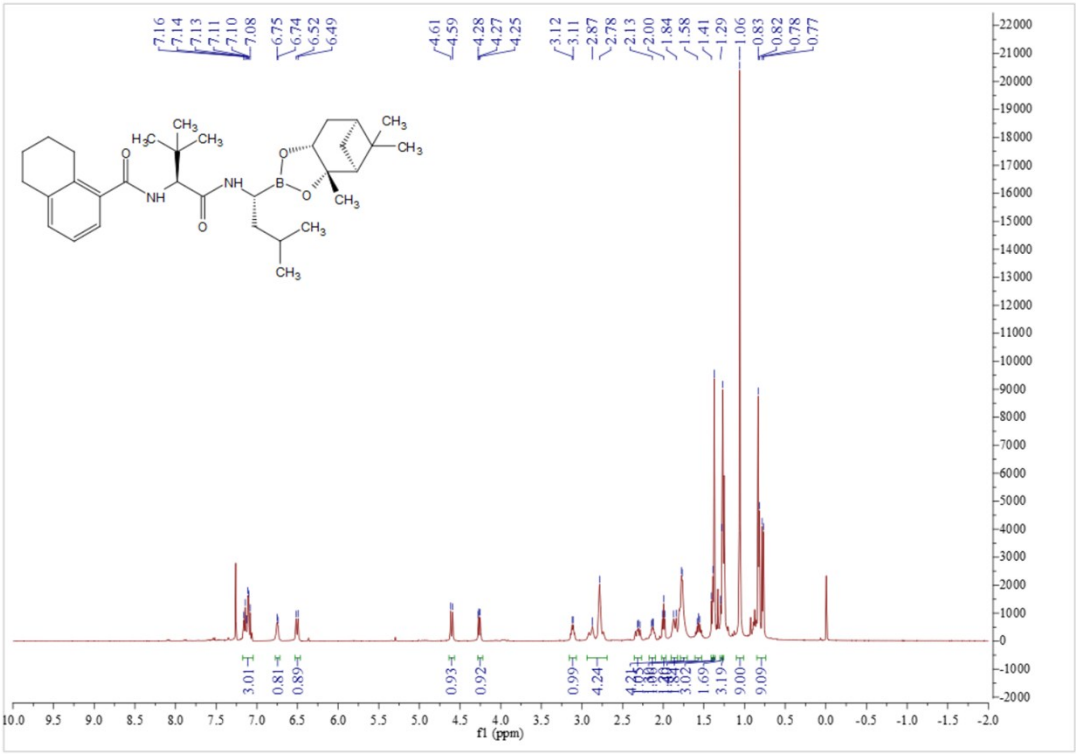
Compound **7b**



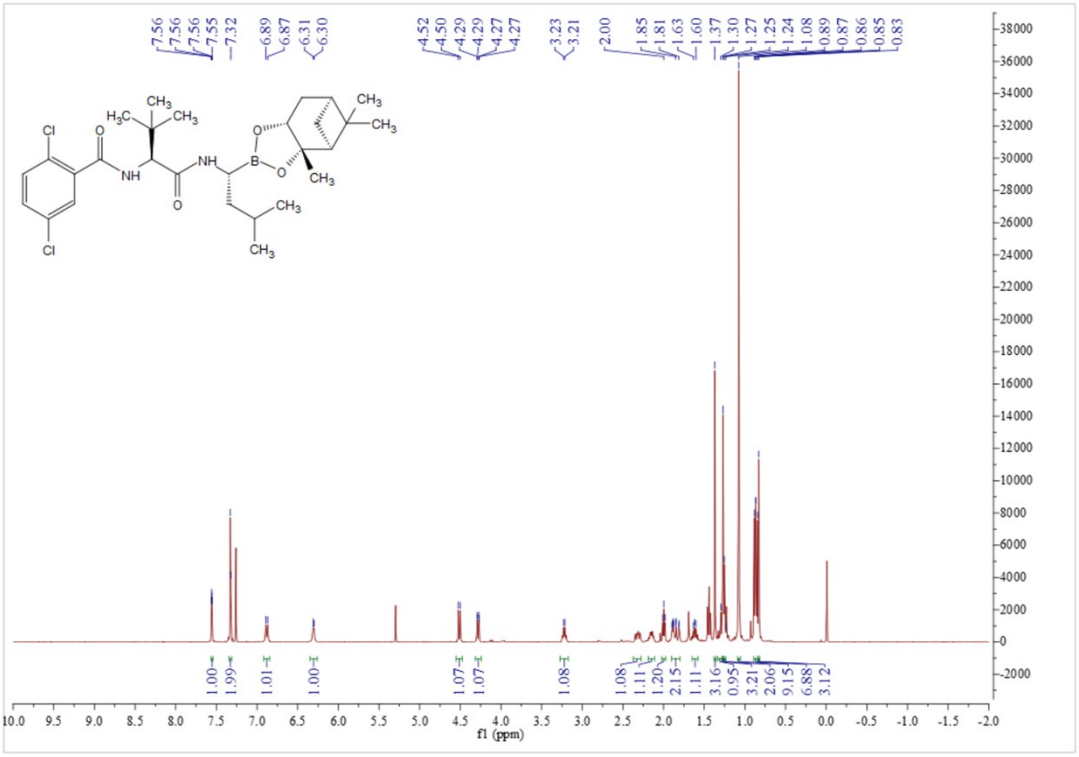
Compound **7c**



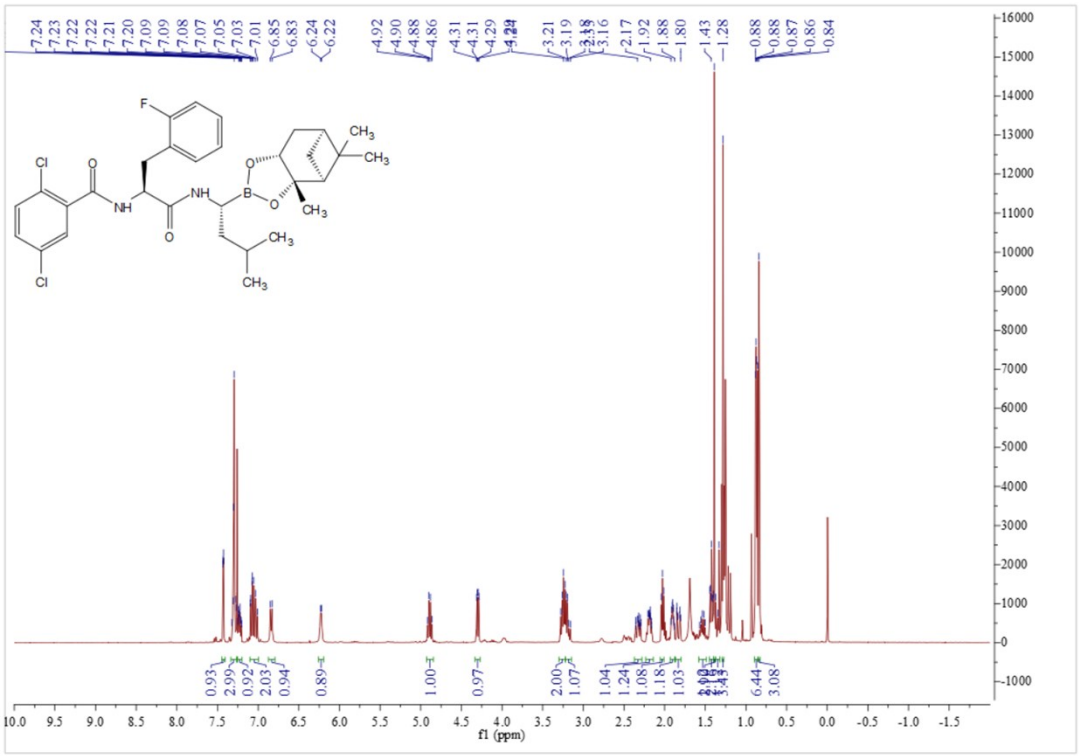
Compound **7d**



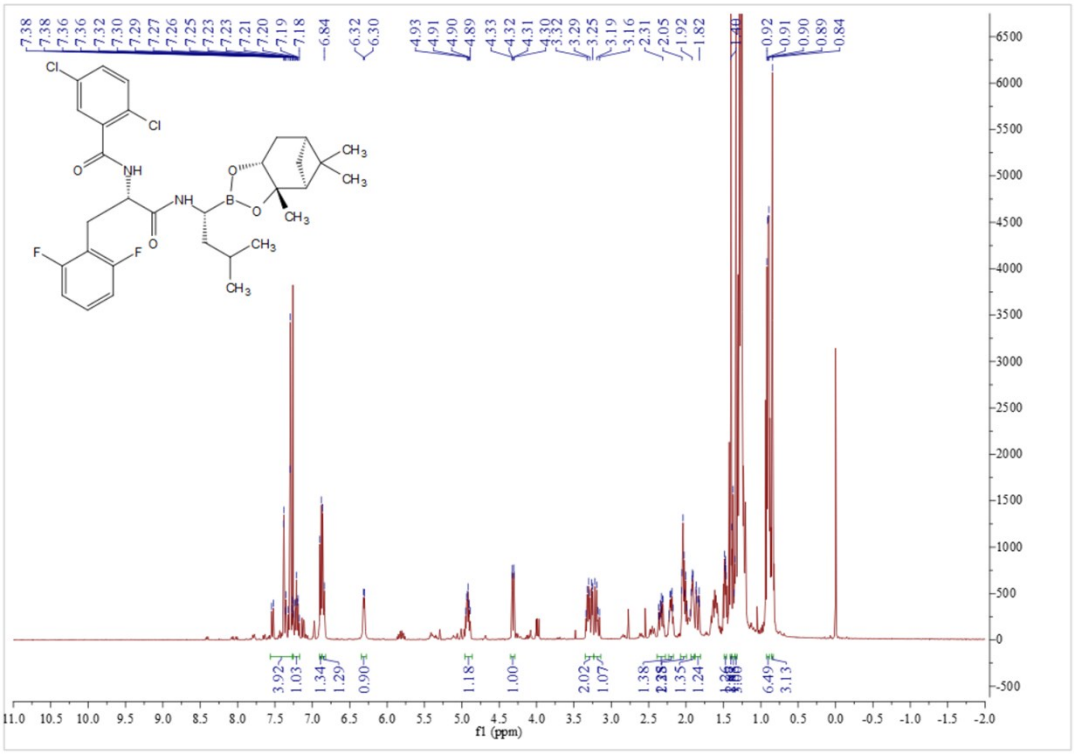
Compound **7e**



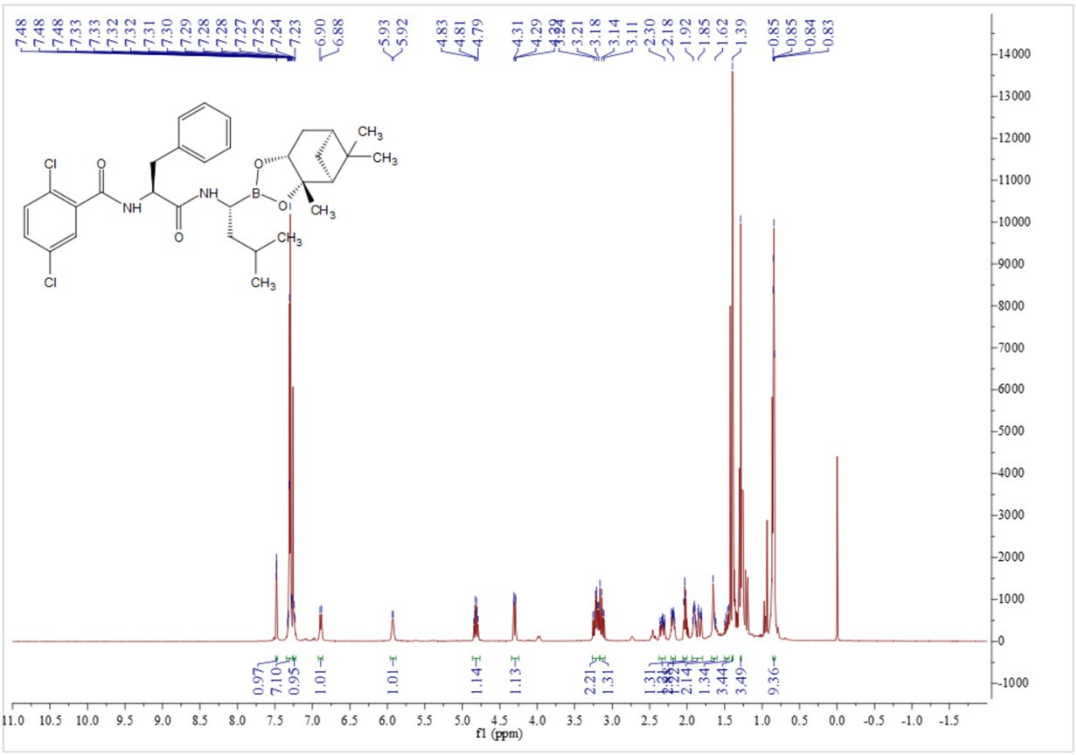
Compound **7f**



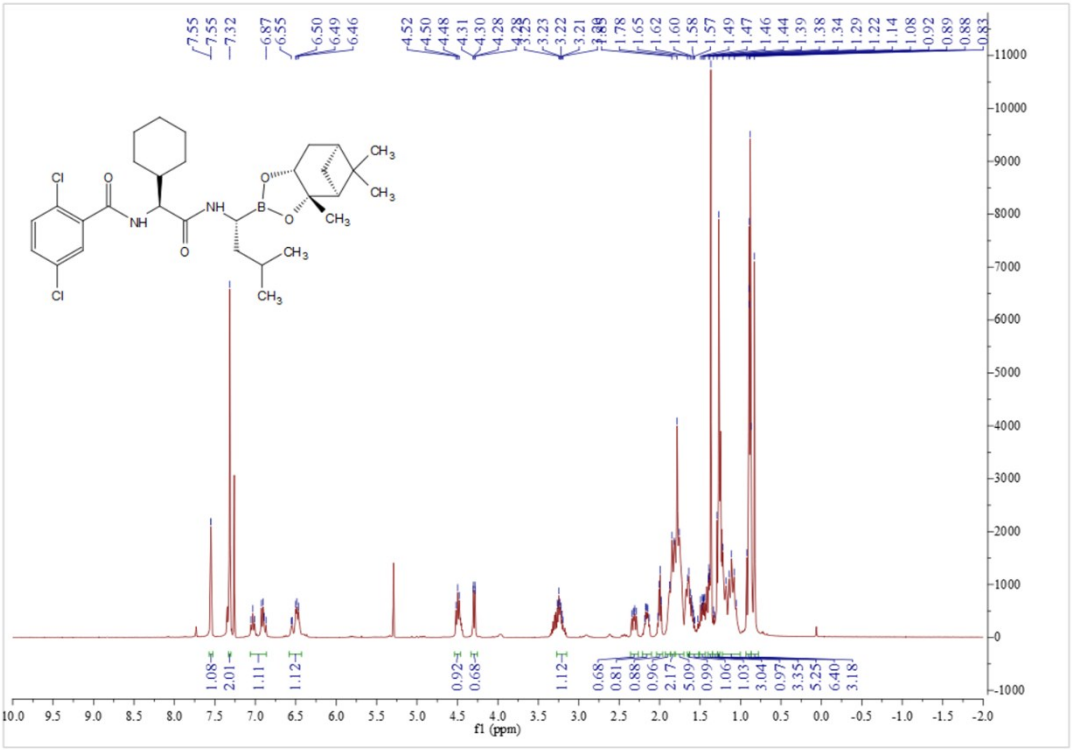
Compound **7g**



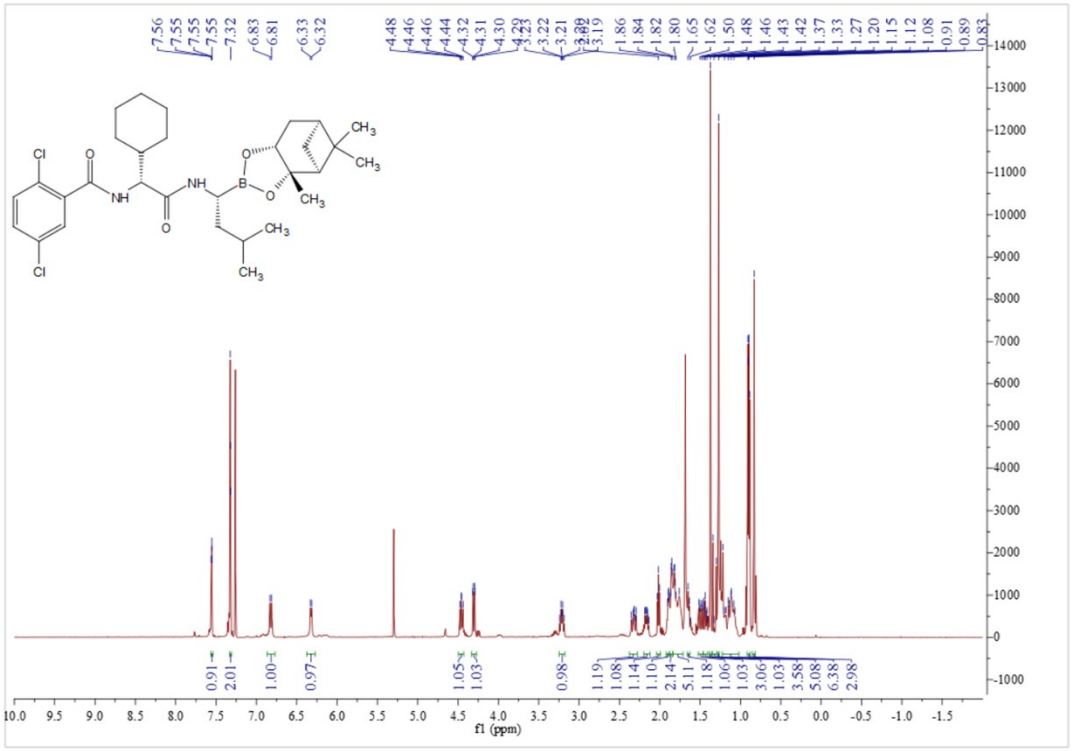
Compound **7h**



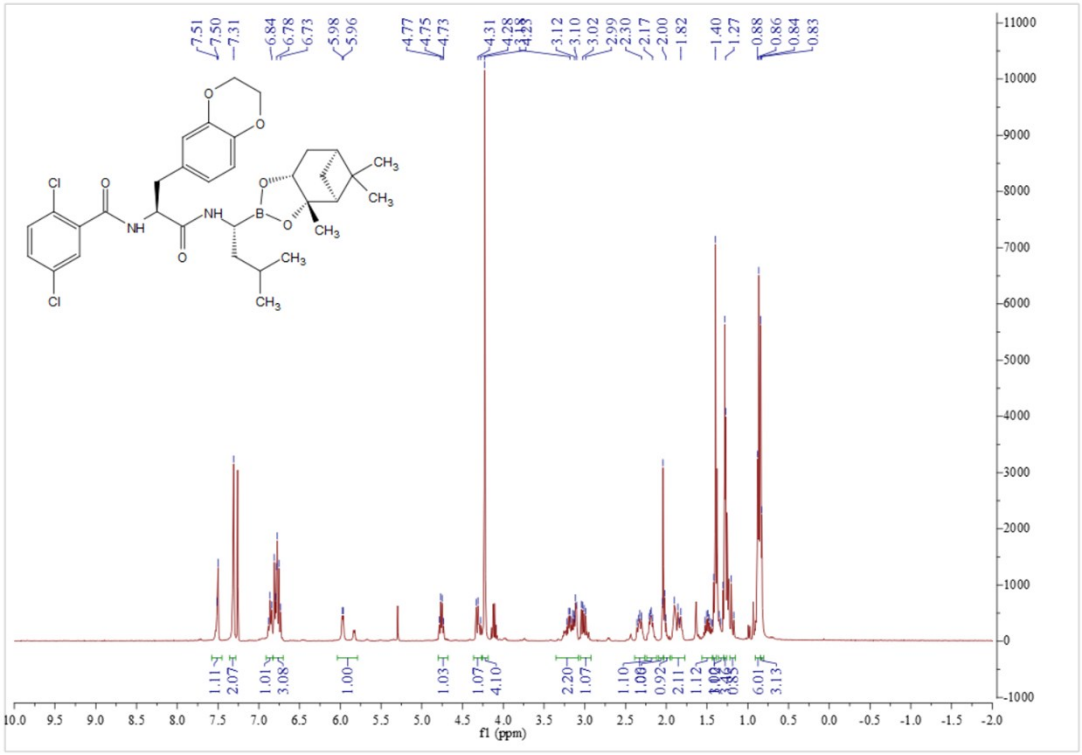
Compound **7i**



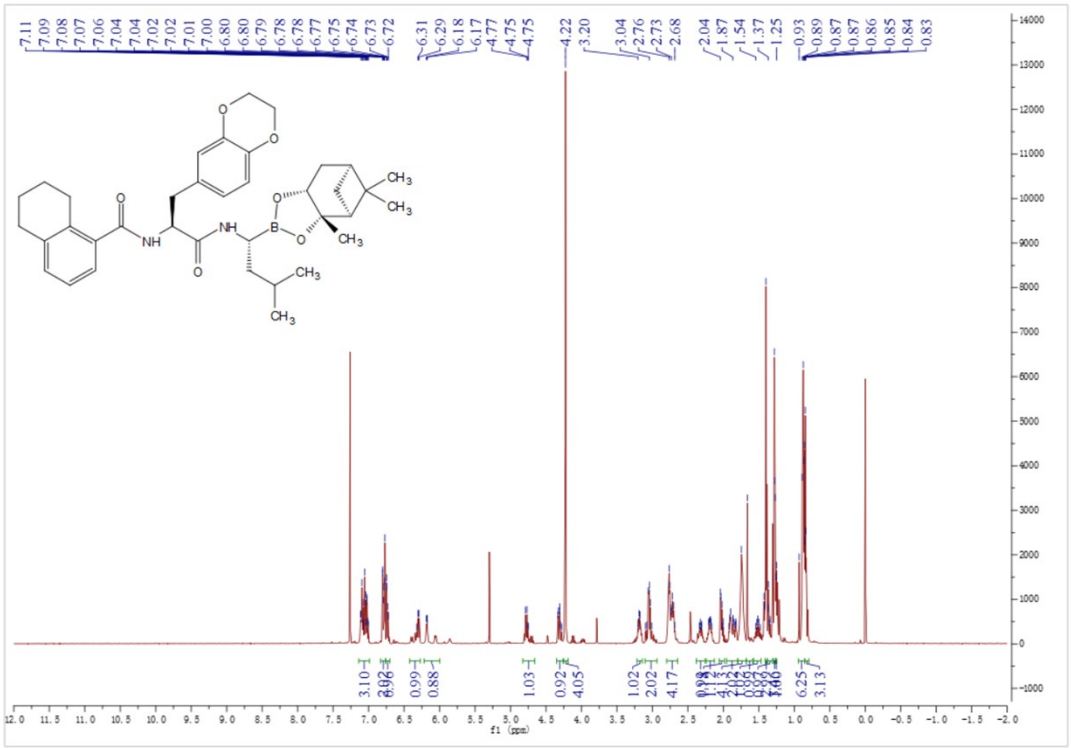
Compound **7j**



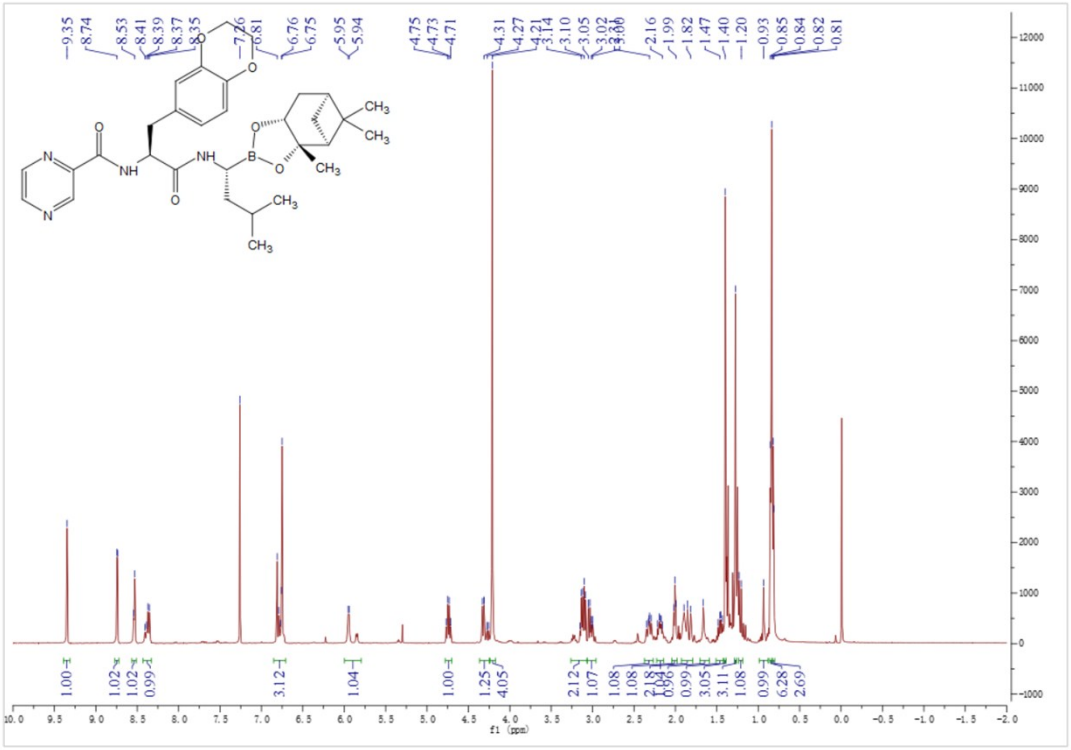
Compound **7k**



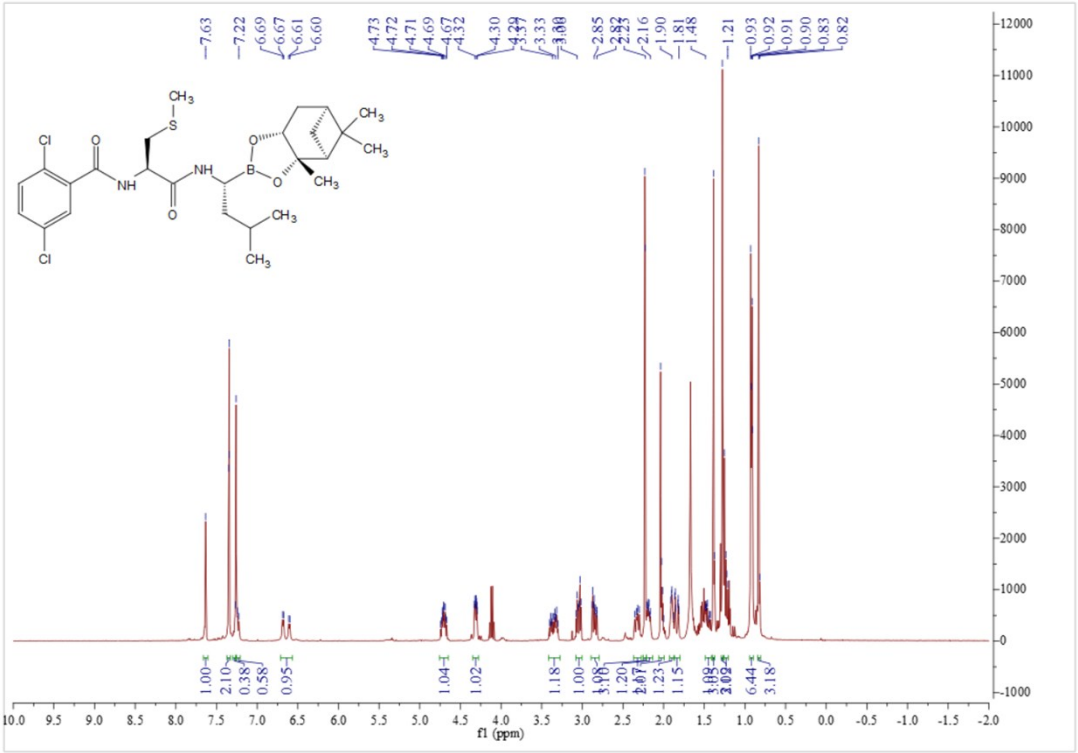
Compound **7l**



Compound **7m**

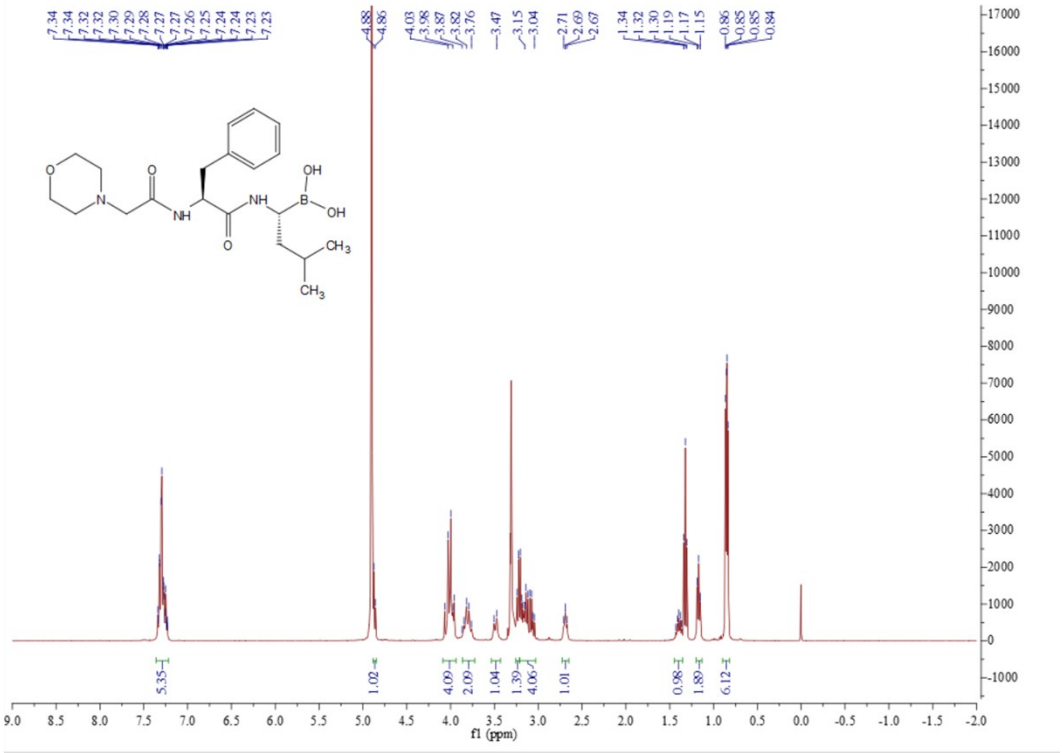


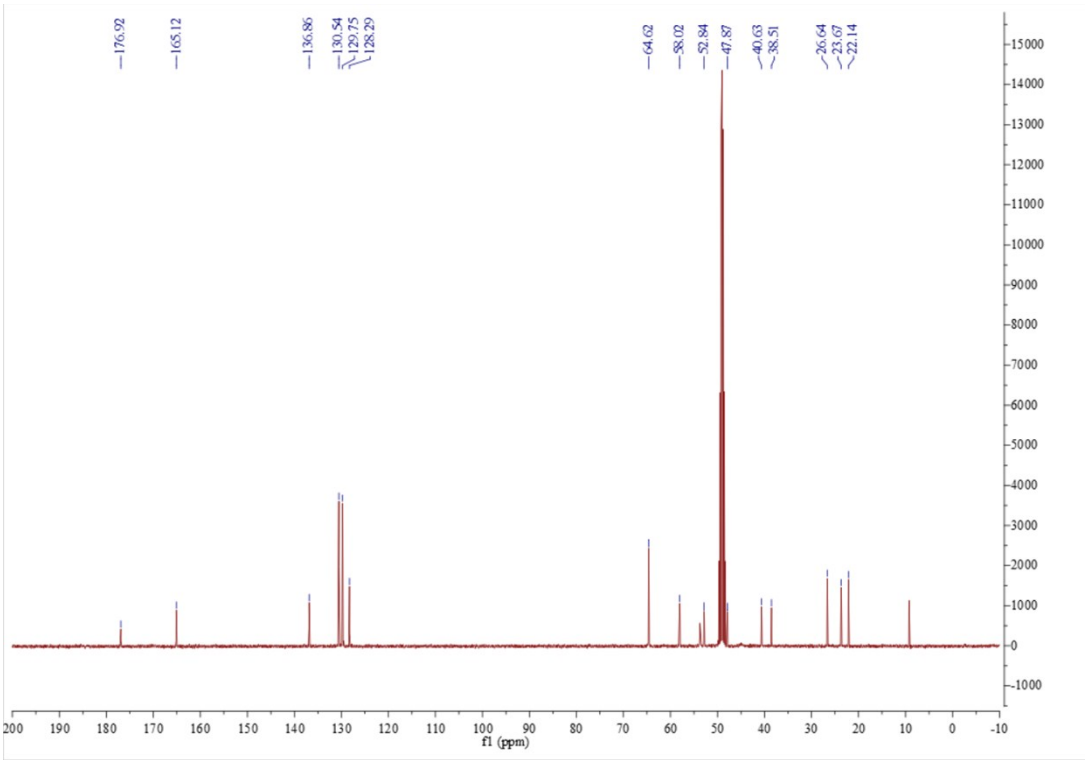
Compound **7n**



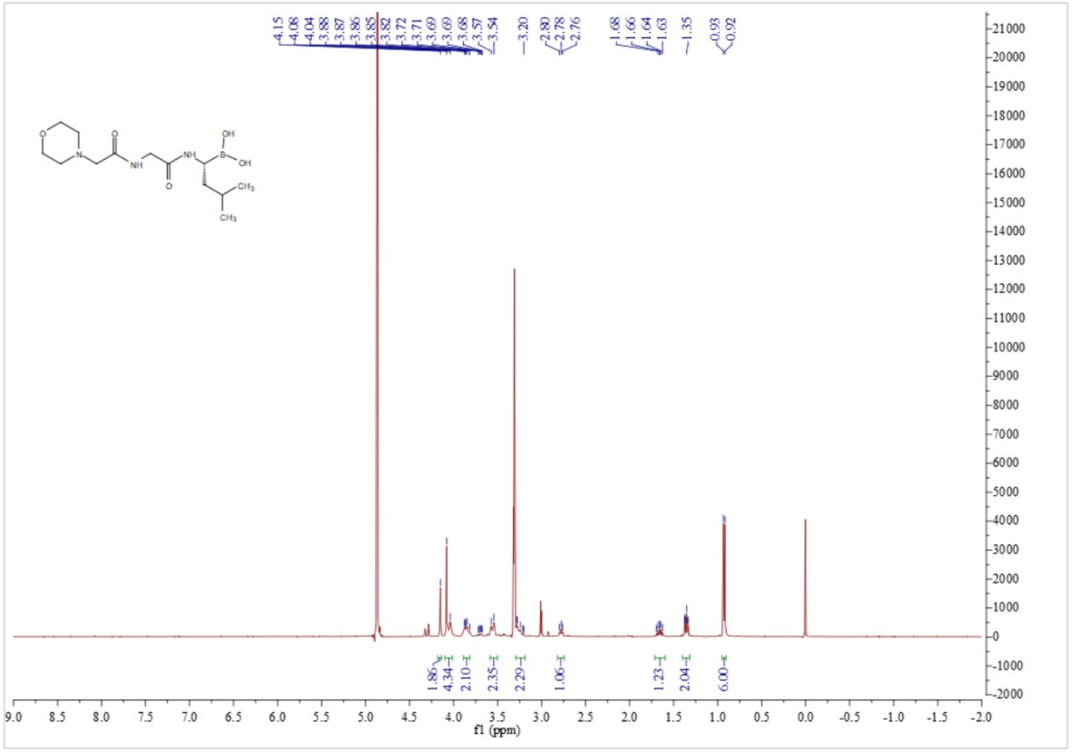
4. ^{1}H NMR and ^{13}C NMR spectra of final compounds

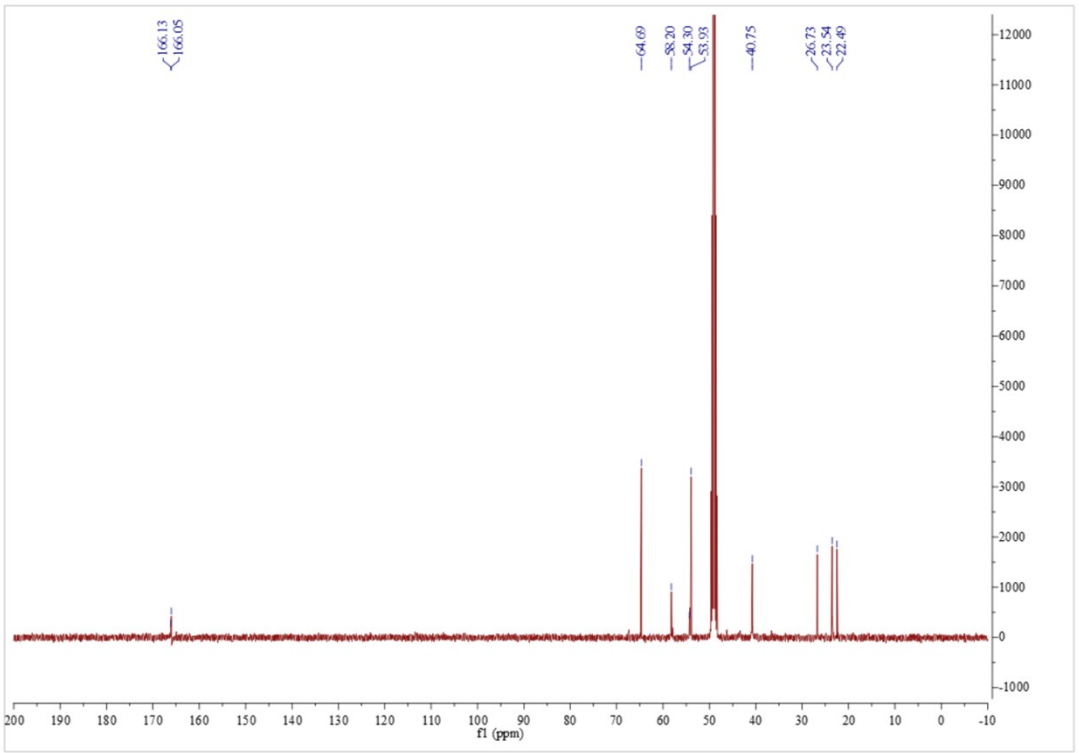
Compound **8a**



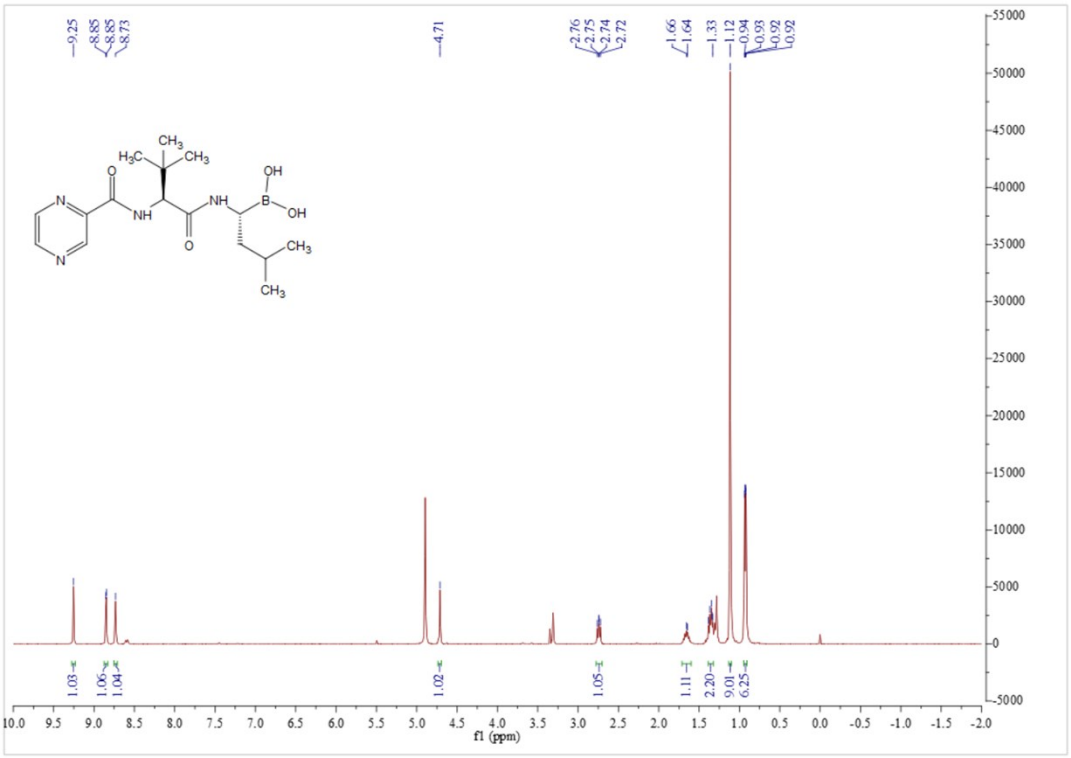


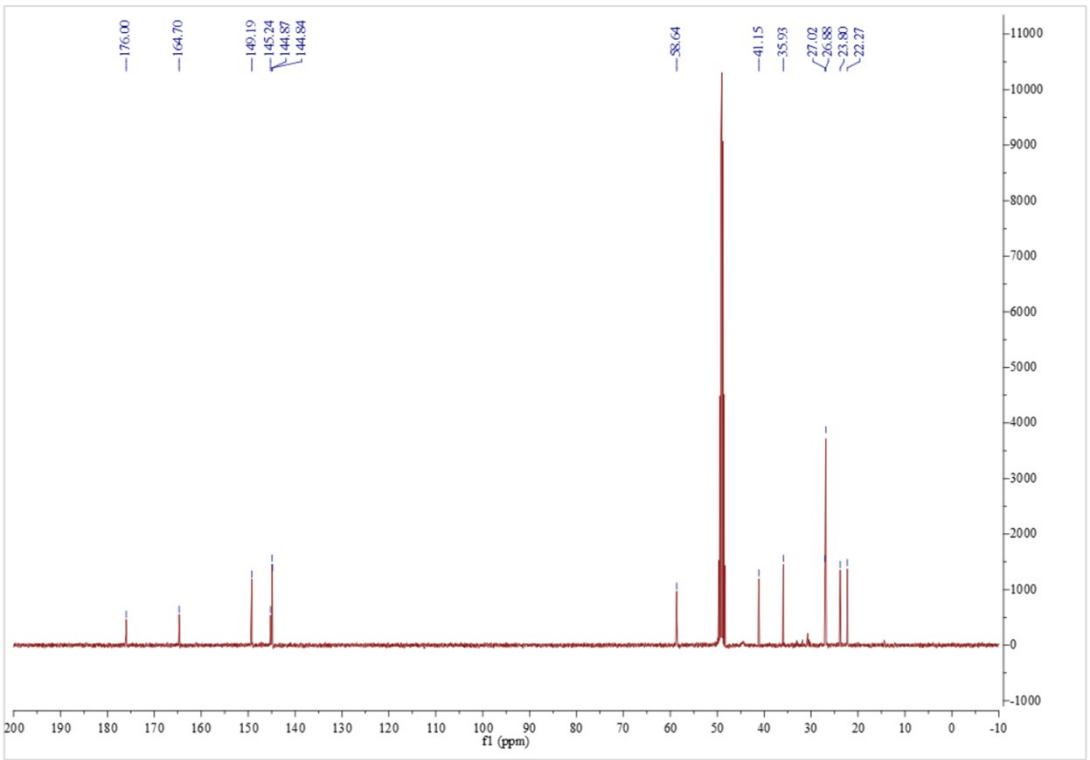
Compound **8b**


4.15
4.08
4.04
3.88
3.87
3.86
3.85
3.82
3.72
3.71
3.69
3.69
3.68
3.57
3.54
3.20
2.80
2.78
2.76
1.68
1.66
1.64
1.63
1.35
0.93
0.92
1.86
4.34
2.10
2.35
2.29
1.06
1.23
2.04
6.00
f1 (ppm)

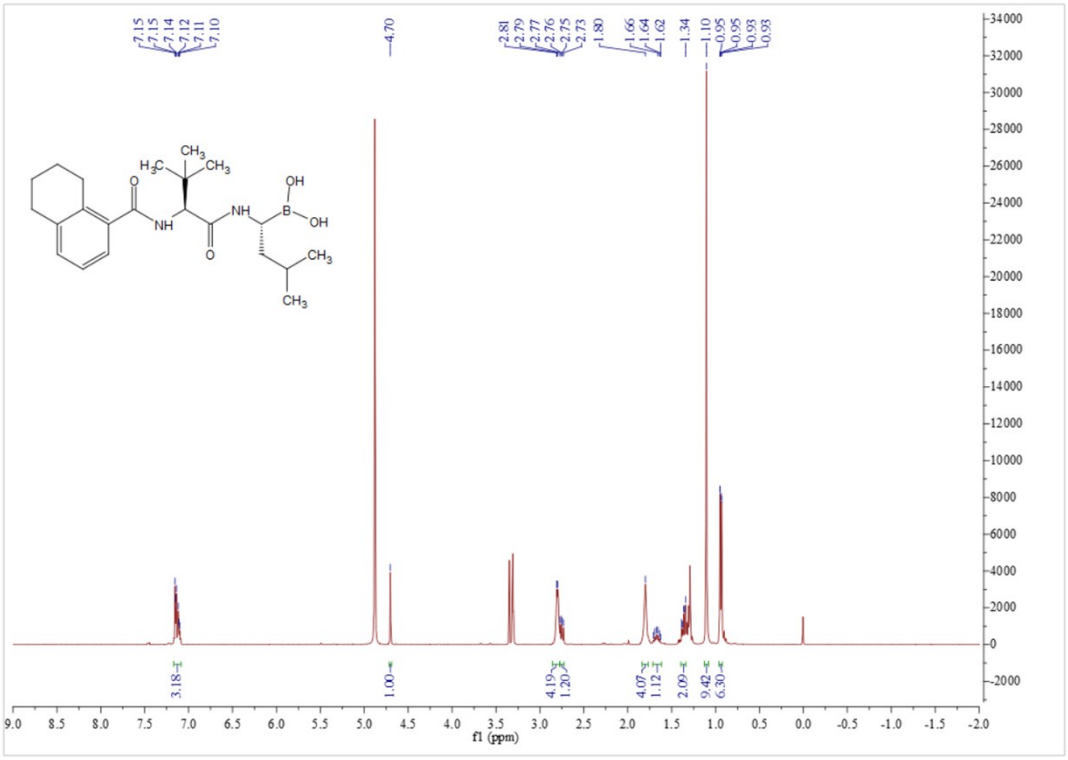

166.13
166.05
64.69
58.20
54.30
53.93
40.75
26.73
23.54
22.49
f1 (ppm)

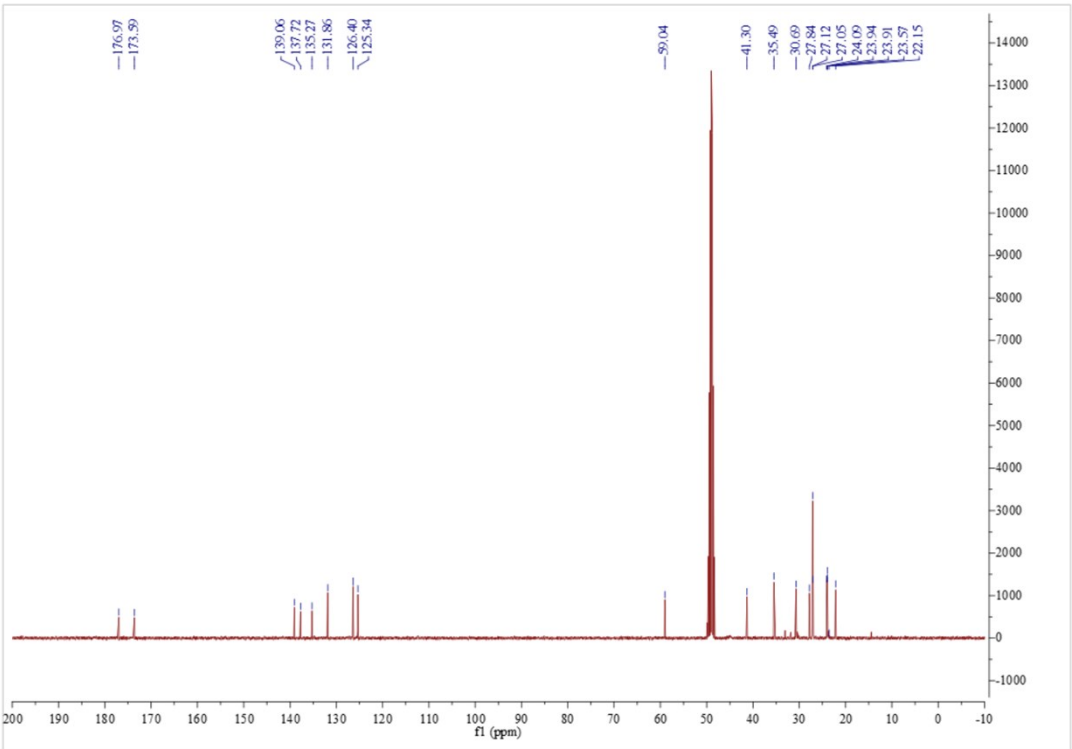
Compound **8c**


9.25
8.85
8.85
8.73
4.71
2.76
2.75
2.74
2.72
1.66
1.64
1.33
1.12
0.94
0.93
0.92
0.92
1.03
1.06
1.04
1.02
1.05
1.11
2.20
9.01
6.25
f1 (ppm)

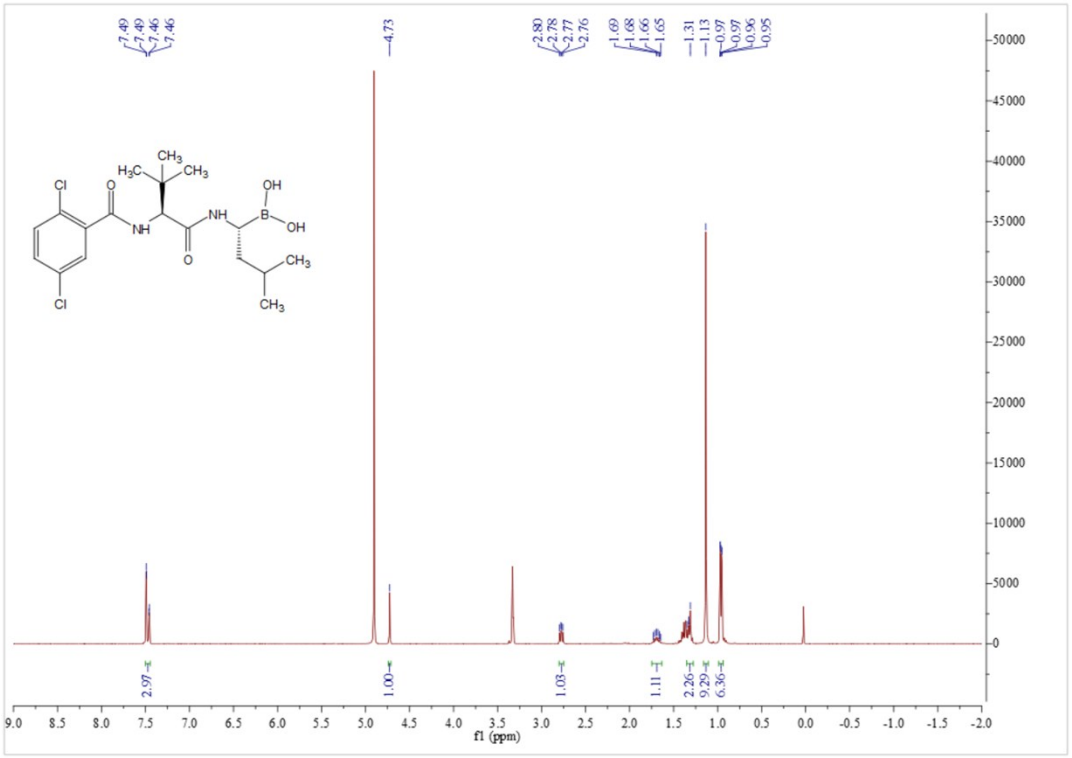

176.00
164.70
149.19
145.24
144.87
144.84
58.64
41.15
35.93
27.02
26.88
23.80
22.27
f1 (ppm)

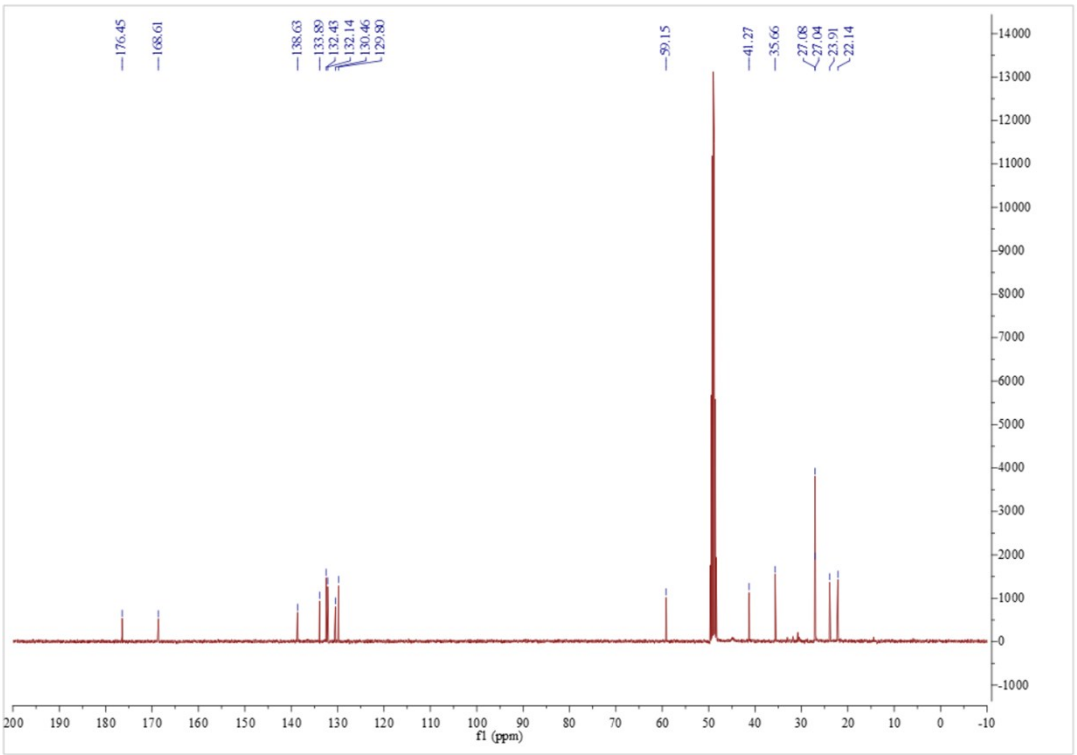
Compound **8d**


7.15
7.15
7.14
7.12
7.11
7.10
4.70
2.81
2.79
2.77
2.76
2.75
2.73
1.80
1.66
1.64
1.62
1.34
1.10
0.95
0.95
0.93
0.93
CH3
H3C
CH3
O
NH
NH
B
OH
OH
O
CH3
CH3
3.18
1.00
4.19
1.20
4.07
1.12
2.09
9.42
6.30
f1 (ppm)

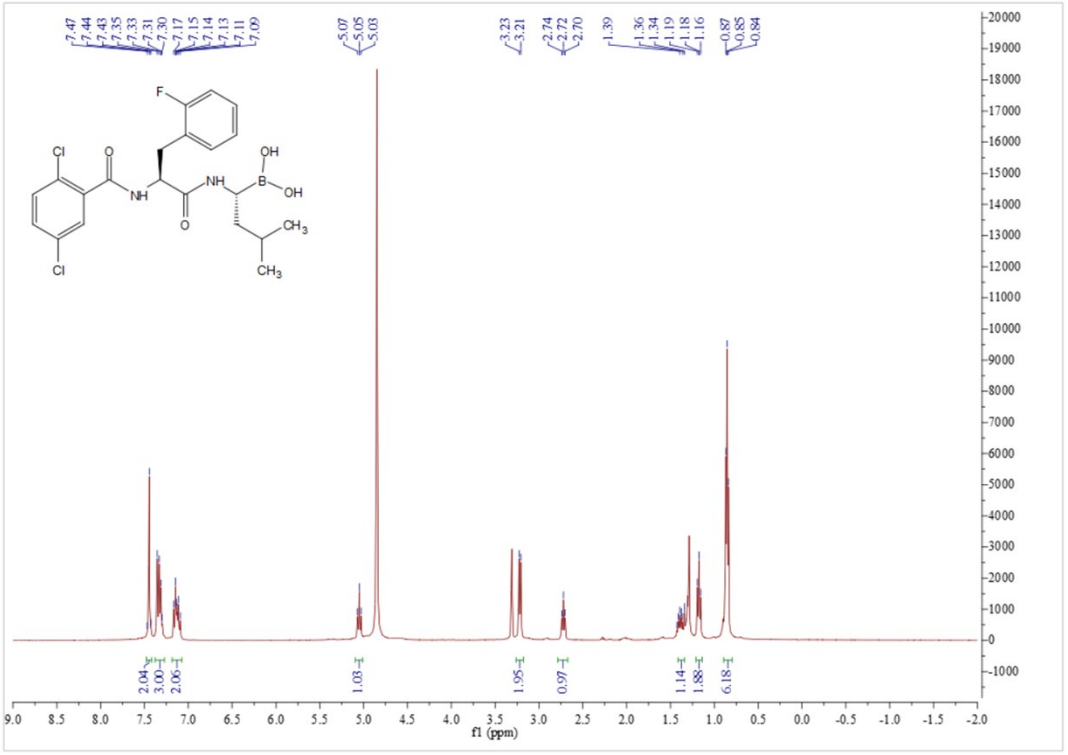

176.97
173.59
139.06
137.72
135.27
131.86
126.40
125.34
59.04
41.30
35.49
30.69
27.84
27.12
27.05
24.09
23.94
23.91
23.57
22.15
f1 (ppm)

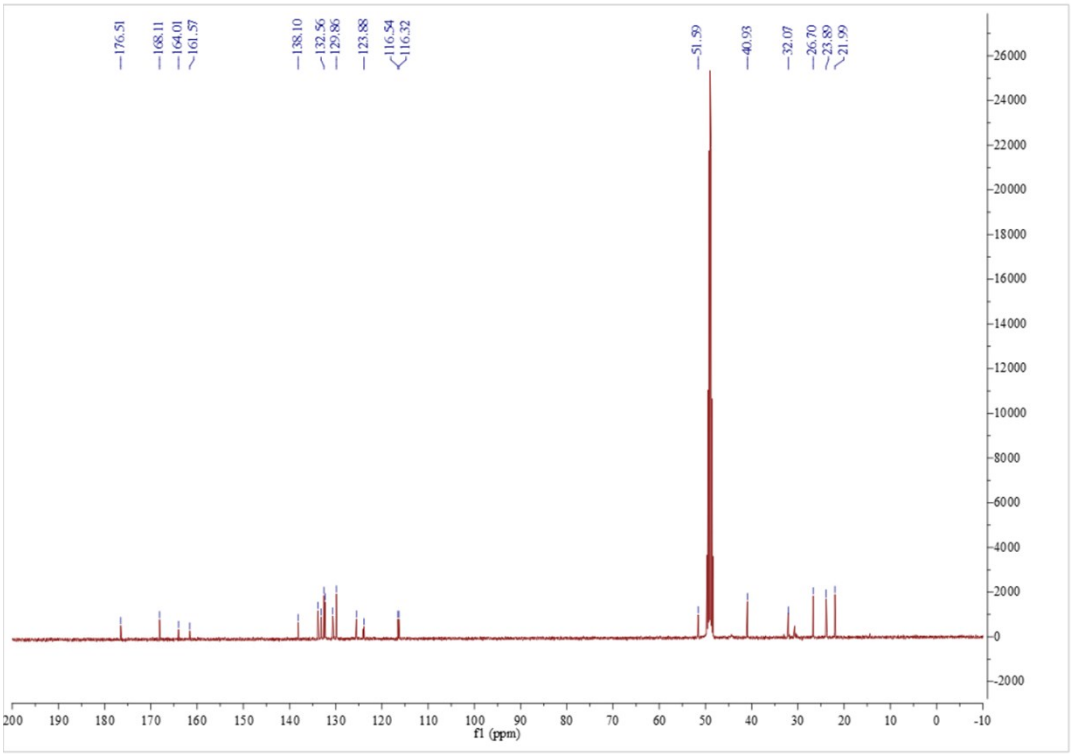
Compound **8e**


7.49
7.49
7.46
7.46
4.73
2.80
2.78
2.77
2.76
1.69
1.68
1.66
1.65
1.31
1.13
0.97
0.97
0.96
0.95
2.97
1.00
1.03
1.11
2.26
9.29
6.36
f1 (ppm)

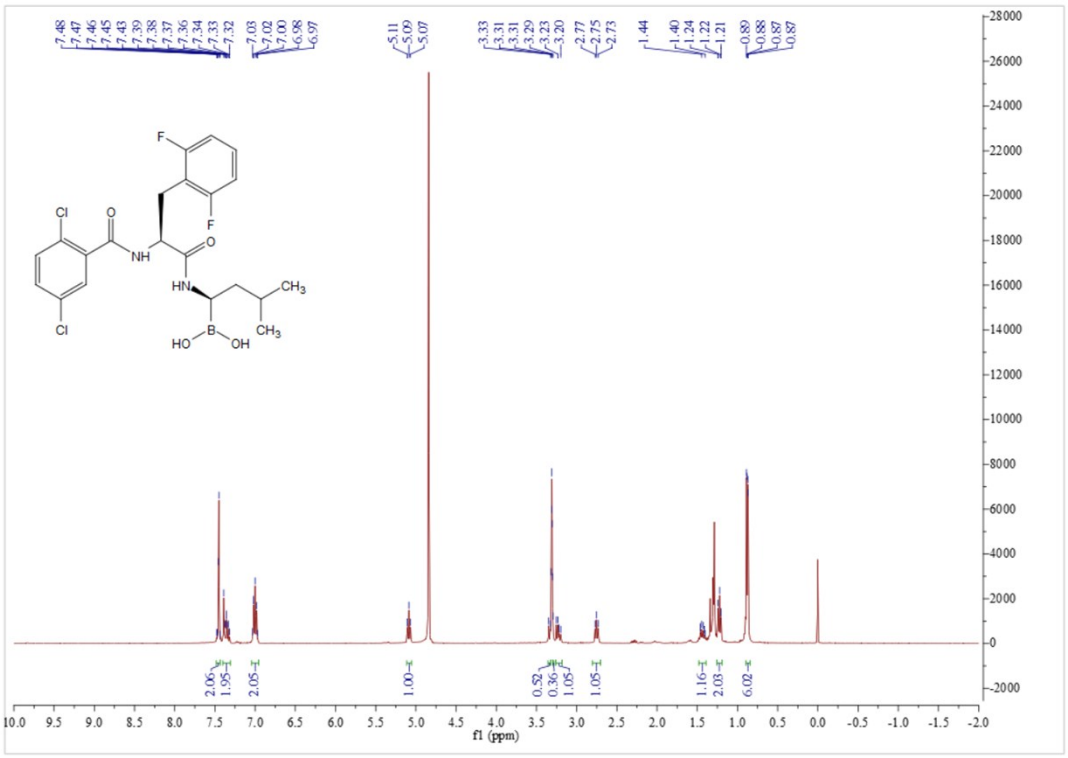

176.45
168.61
138.63
133.89
132.43
132.14
130.46
129.80
59.15
41.27
35.66
27.08
27.04
23.91
22.14
f1 (ppm)

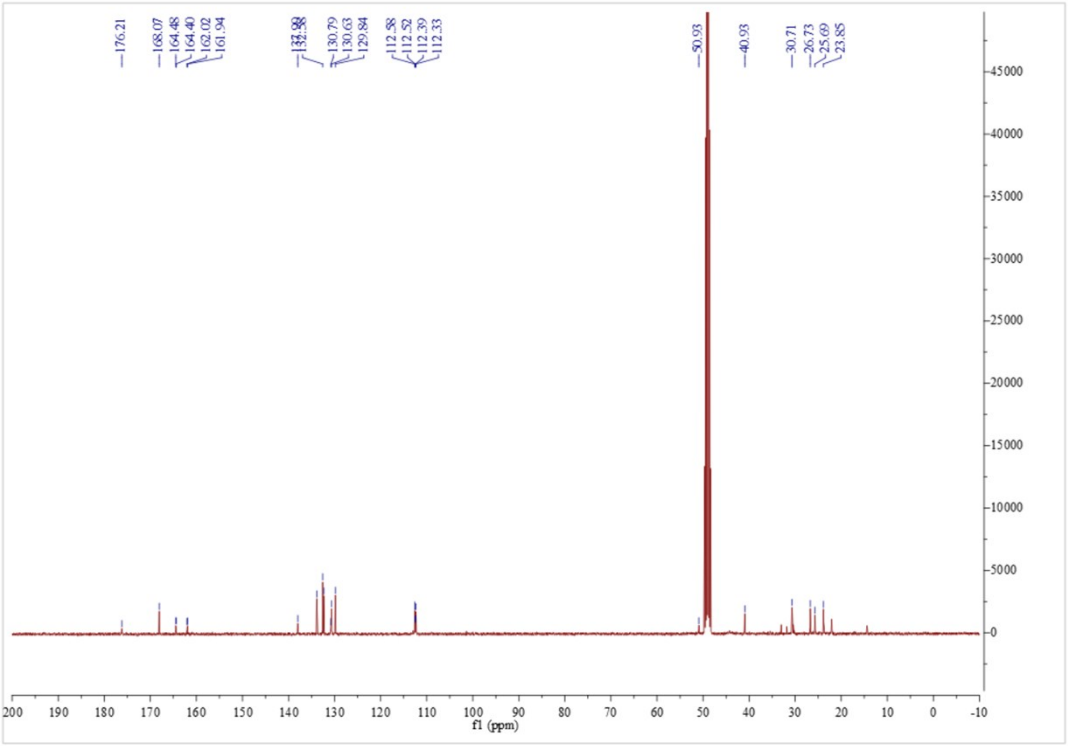
Compound **8f**


7.47
7.44
7.43
7.35
7.33
7.31
7.30
7.17
7.15
7.14
7.13
7.11
7.09
5.07
5.05
5.03
3.23
3.21
2.74
2.72
2.70
1.39
1.36
1.34
1.19
1.18
1.16
0.87
0.85
0.84
F
Cl
O
NH
NH
O
OH
B
OH
CH3
CH3
Cl
2.04
3.00
2.06
1.03
1.95
0.97
1.14
1.88
6.18
f1 (ppm)


176.51
168.11
164.01
161.57
138.10
132.56
129.86
123.88
116.54
116.32
51.99
40.93
32.07
26.70
23.89
21.99
f1 (ppm)

Compound **8g**


7.48
7.47
7.46
7.45
7.43
7.39
7.38
7.37
7.36
7.34
7.33
7.32
7.03
7.02
7.00
6.98
6.97
5.11
5.09
5.07
3.33
3.31
3.31
3.29
3.23
3.20
2.77
2.75
2.73
1.44
1.40
1.24
1.22
1.21
0.89
0.88
0.87
0.87
F
F
Cl
Cl
O
NH
O
HN
CH3
CH3
HO
B
OH
2.06
1.95
2.05
1.00
0.52
0.36
1.05
1.05
1.16
2.03
6.02
f1 (ppm)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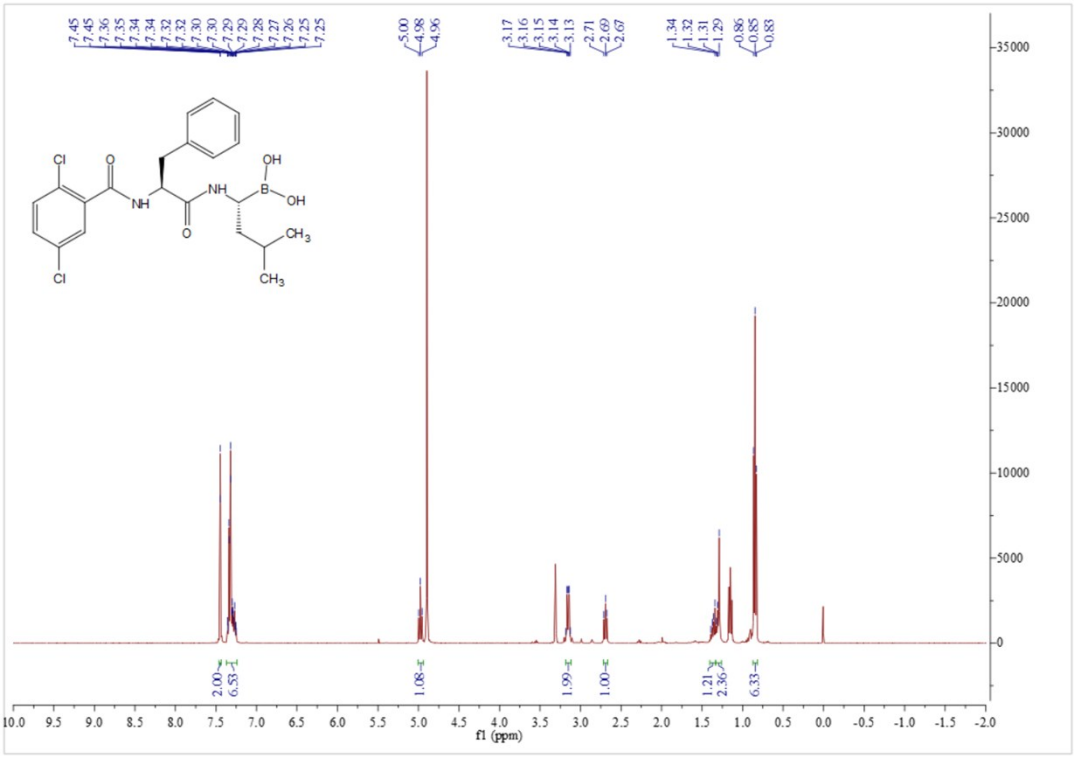
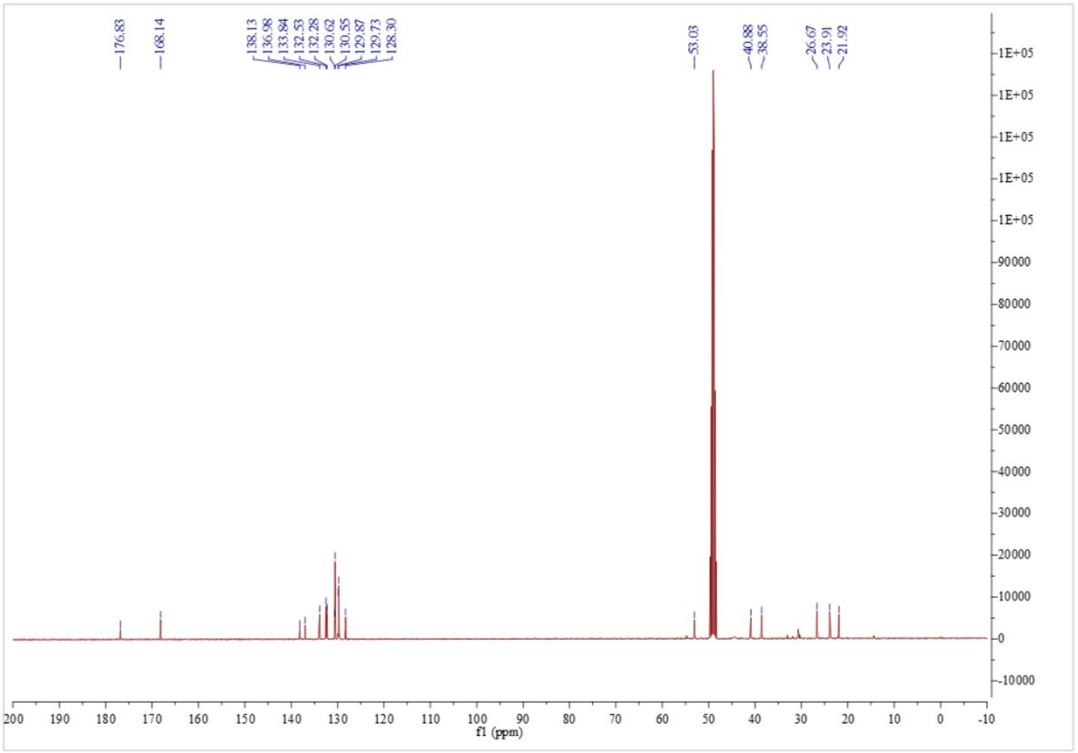
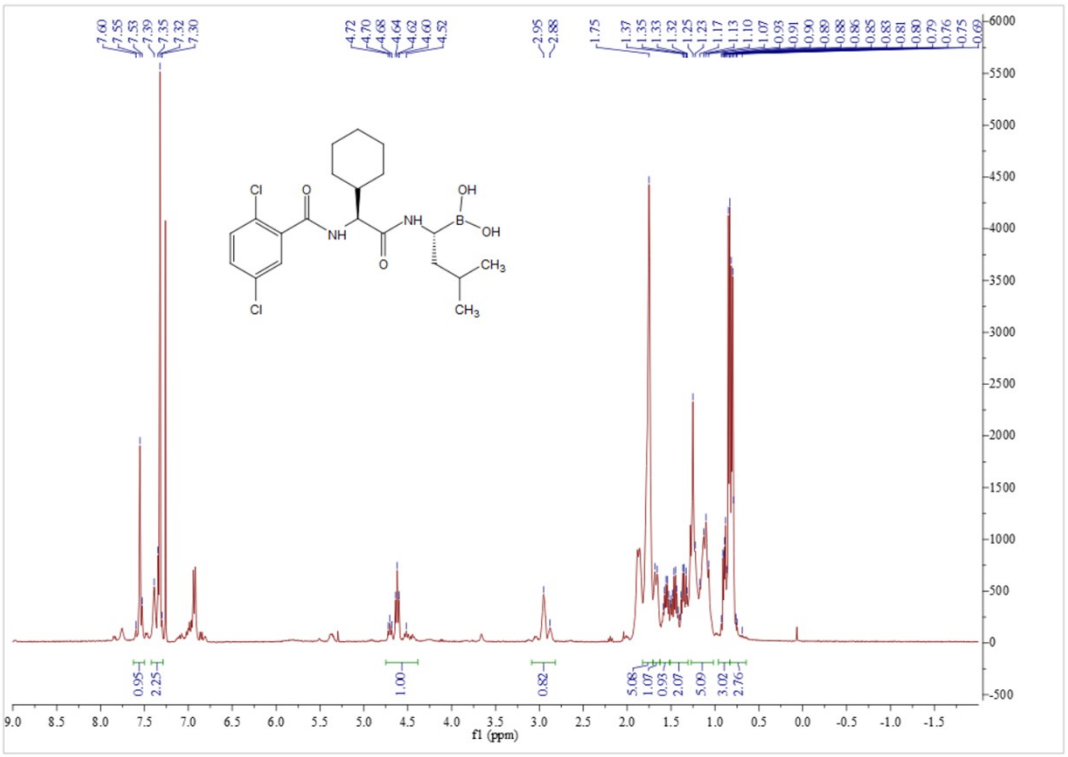
168.07
164.48
164.40
162.02
161.94
130.79
130.63
129.84
112.58
112.52
112.39
112.33
50.93
40.93
30.71
26.73
25.69
23.85
f1 (ppm)

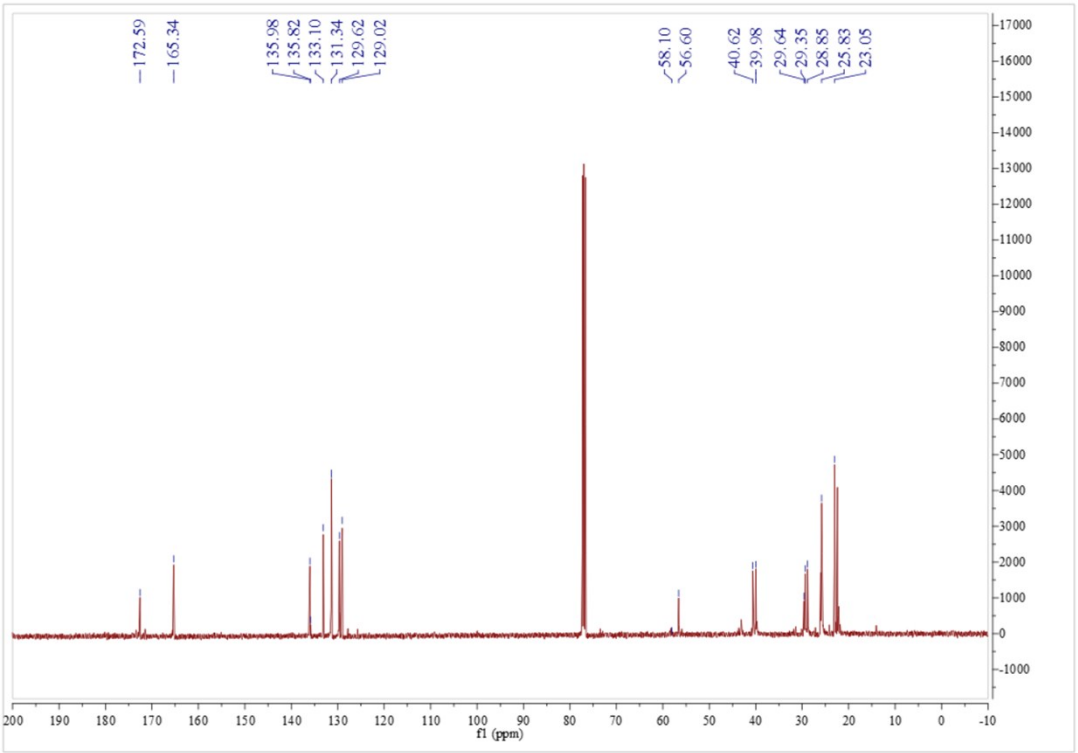
Compound **8h**


7.45
7.45
7.36
7.35
7.34
7.34
7.32
7.32
7.30
7.30
7.29
7.29
7.28
7.27
7.26
7.25
7.25
5.00
4.98
4.96
3.17
3.16
3.15
3.14
3.13
2.71
2.69
2.67
1.34
1.32
1.31
1.29
0.86
0.85
0.83
Cl
O
NH
NH
O
OH
B
OH
CH3
CH3
Cl
2.00
6.53
1.08
1.99
1.00
1.21
2.36
6.33
f1 (ppm)

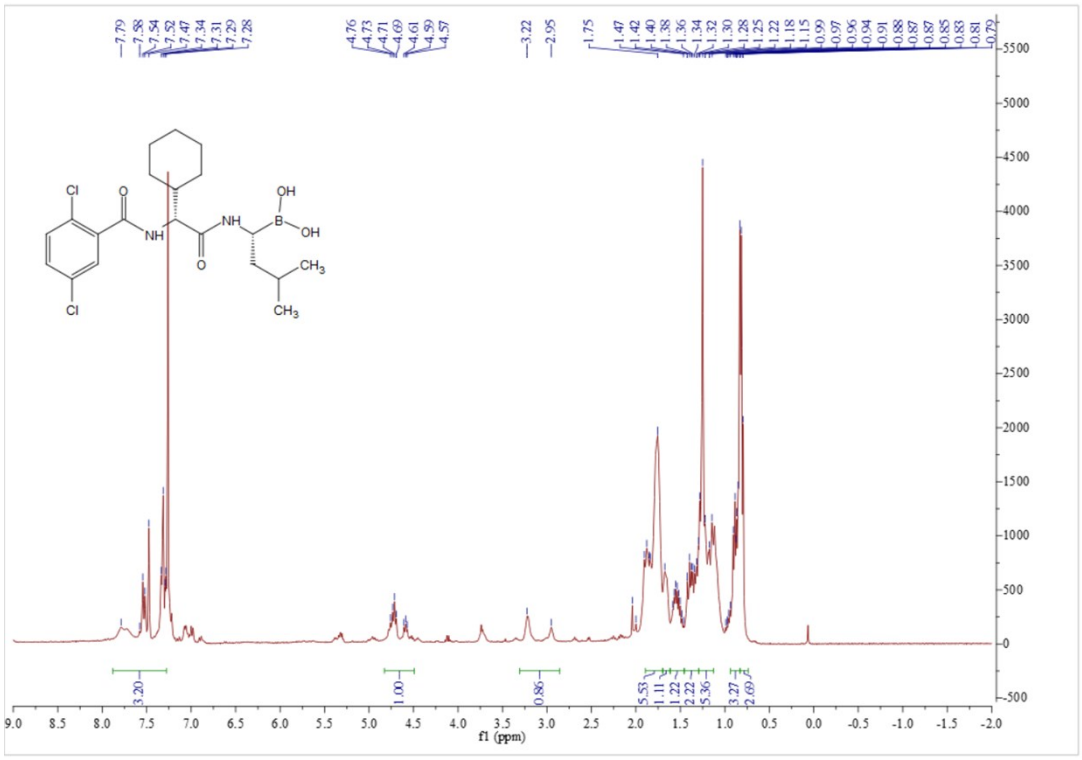

176.83
168.14
138.13
136.98
133.84
132.53
132.26
130.62
130.55
129.87
129.73
128.30
53.03
40.88
38.55
26.67
23.91
21.92
f1 (ppm)

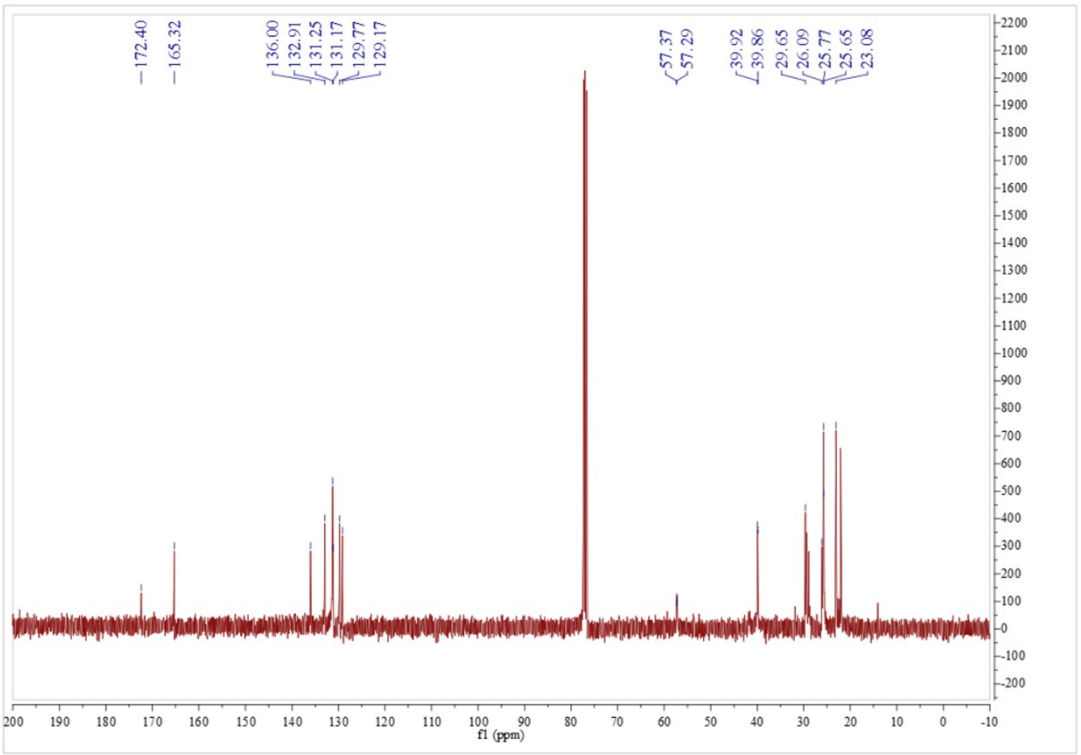
Compound **8i**


7.60
7.55
7.53
7.39
7.35
7.32
7.30
4.72
4.70
4.68
4.64
4.62
4.60
4.52
2.95
2.88
1.75
1.37
1.35
1.33
1.32
1.25
1.23
1.17
1.13
1.10
1.07
0.93
0.91
0.90
0.89
0.88
0.86
0.85
0.83
0.81
0.80
0.79
0.76
0.75
0.69
Cl
O
NH
NH
B
OH
OH
O
CH3
CH3
Cl
0.95
2.25
1.00
0.82
5.08
1.07
0.93
2.07
5.09
3.02
2.76
f1 (ppm)

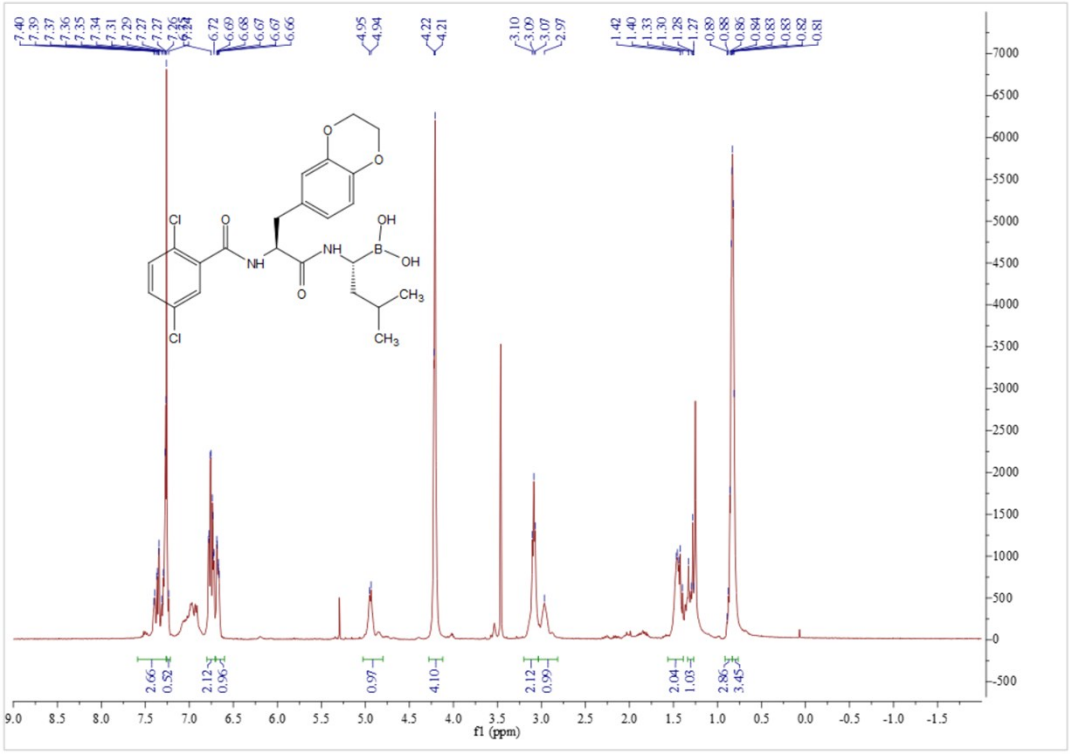

172.59
165.34
135.98
135.82
133.10
131.34
129.62
129.02
58.10
56.60
40.62
39.98
29.64
29.35
28.85
25.83
23.05
f1 (ppm)

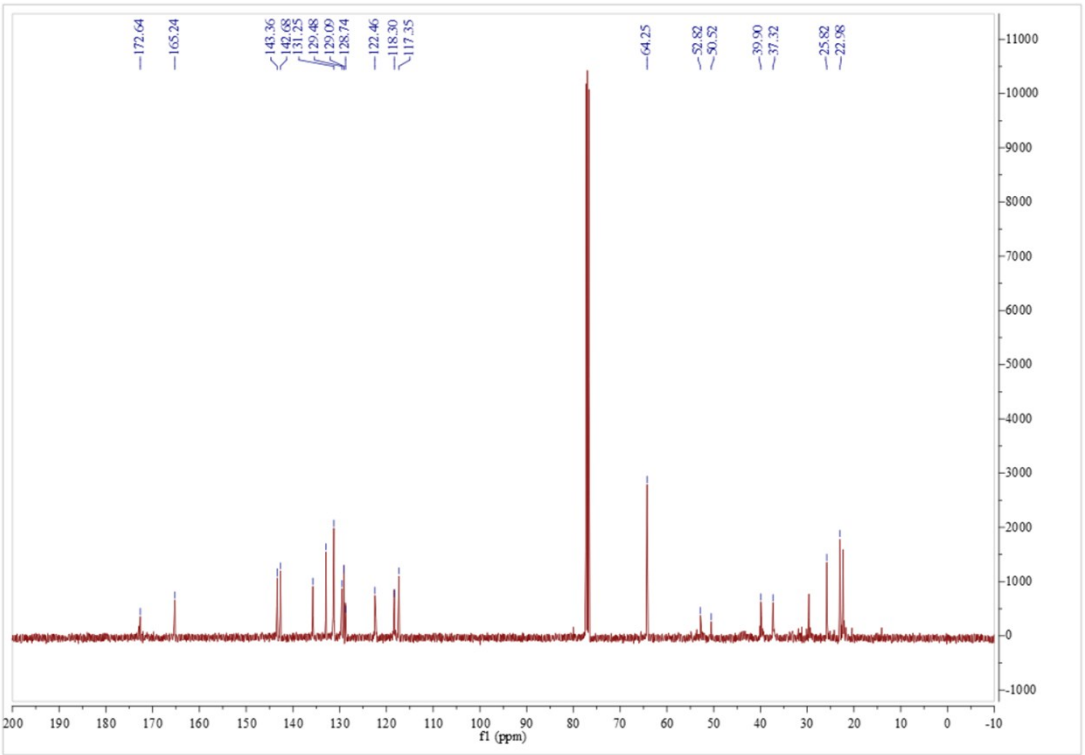
Compound **8j**


7.79
7.88
7.54
7.52
7.47
7.34
7.31
7.29
7.28
4.76
4.73
4.71
4.69
4.61
4.59
4.57
3.22
2.95
1.75
1.47
1.42
1.40
1.38
1.36
1.34
1.32
1.30
1.28
1.25
1.22
1.18
1.15
0.99
0.97
0.96
0.94
0.91
0.88
0.87
0.85
0.83
0.81
0.79
Cl
O
NH
O
NH
B
OH
OH
CH3
CH3
Cl
3.20
1.00
0.86
5.53
1.11
1.22
2.22
5.36
3.27
2.69
f1 (ppm)

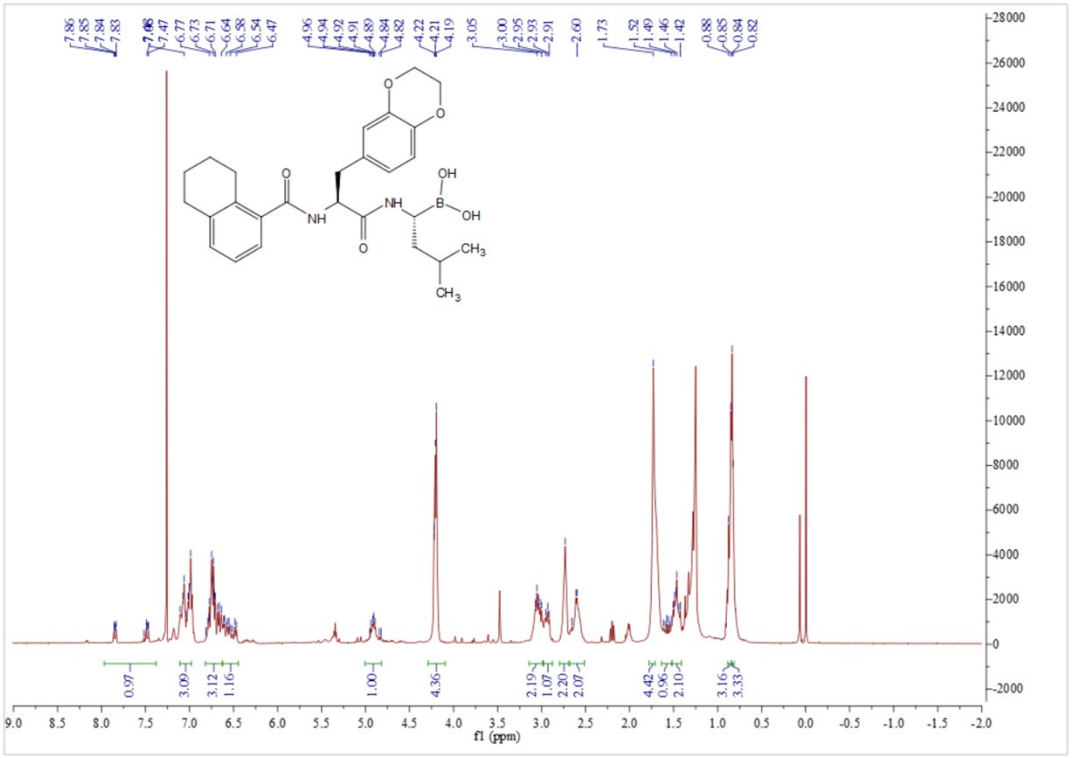

172.40
165.32
136.00
132.91
131.25
131.17
129.77
129.17
57.37
57.29
39.92
39.86
29.65
26.09
25.77
25.65
23.08
f1 (ppm)

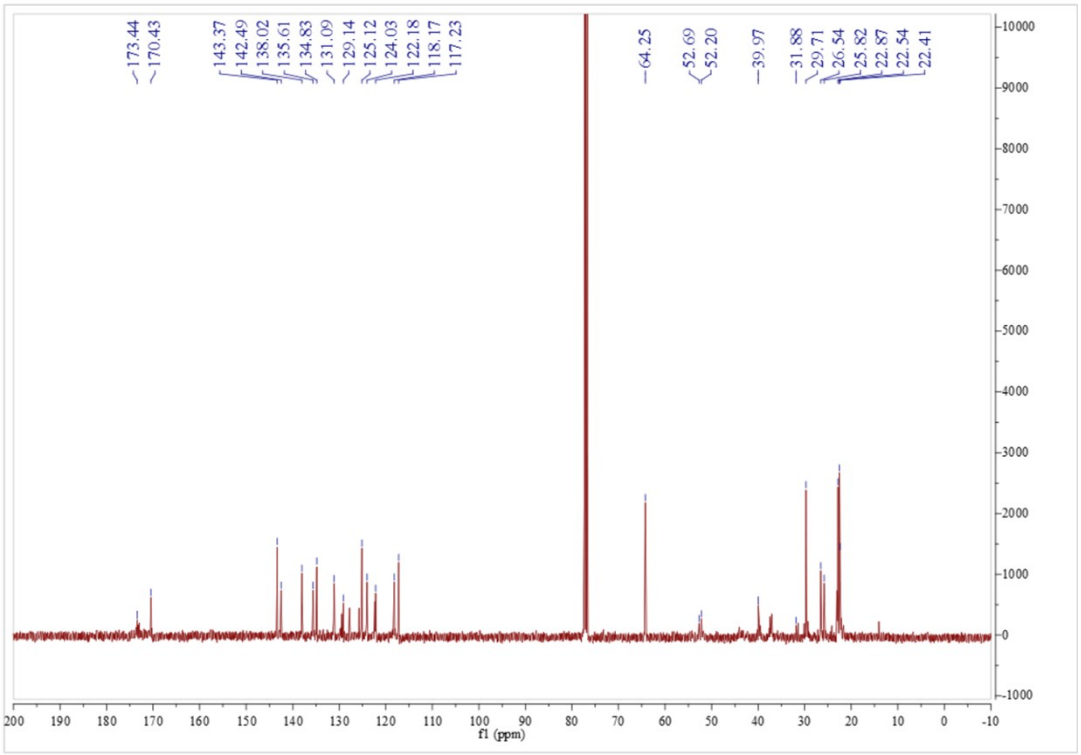
Compound **8k**


7.40
7.39
7.37
7.36
7.35
7.34
7.31
7.29
7.27
7.27
7.26
6.72
6.69
6.68
6.67
6.67
6.66
4.95
4.94
4.22
4.21
3.10
3.09
3.07
2.97
1.42
1.40
1.33
1.30
1.28
1.27
0.89
0.88
0.86
0.84
0.83
0.83
0.82
0.81
Cl
O
NH
O
NH
OH
B
OH
CH3
CH3
Cl
O
O
2.66
0.52
2.12
0.96
0.97
4.10
2.12
0.99
2.04
1.03
2.86
3.45
f1 (ppm)

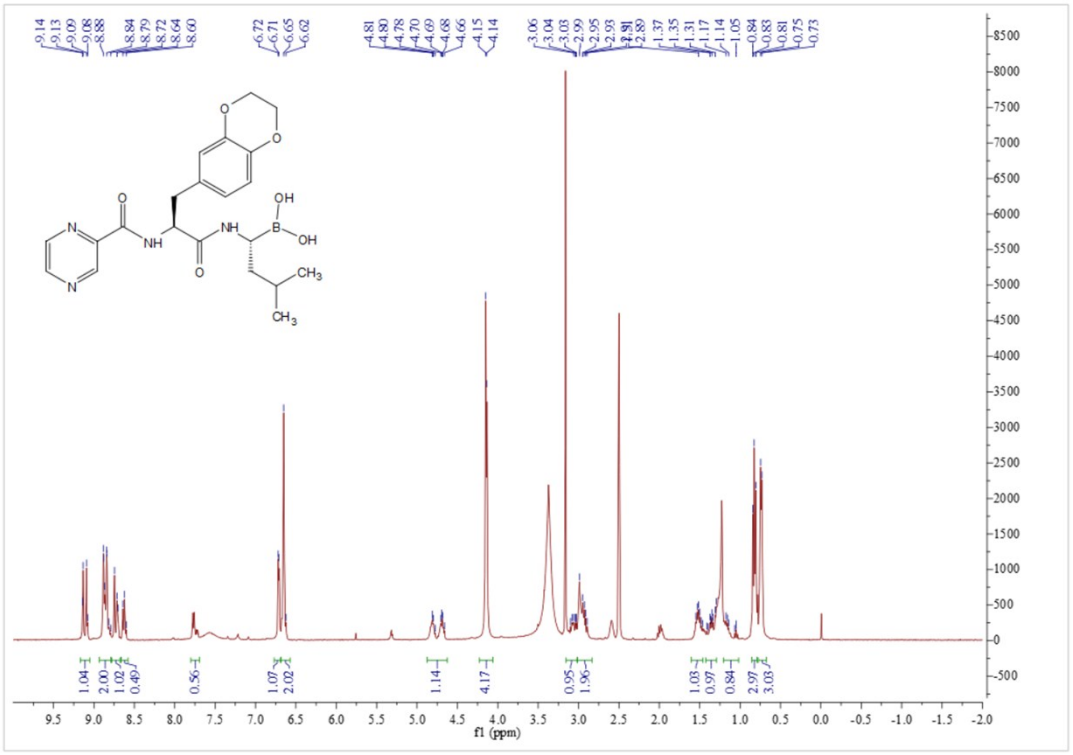

172.64
165.24
143.36
142.68
131.25
129.48
129.09
128.74
122.46
118.30
117.35
64.25
52.82
50.52
39.90
37.32
25.82
22.98
f1 (ppm)

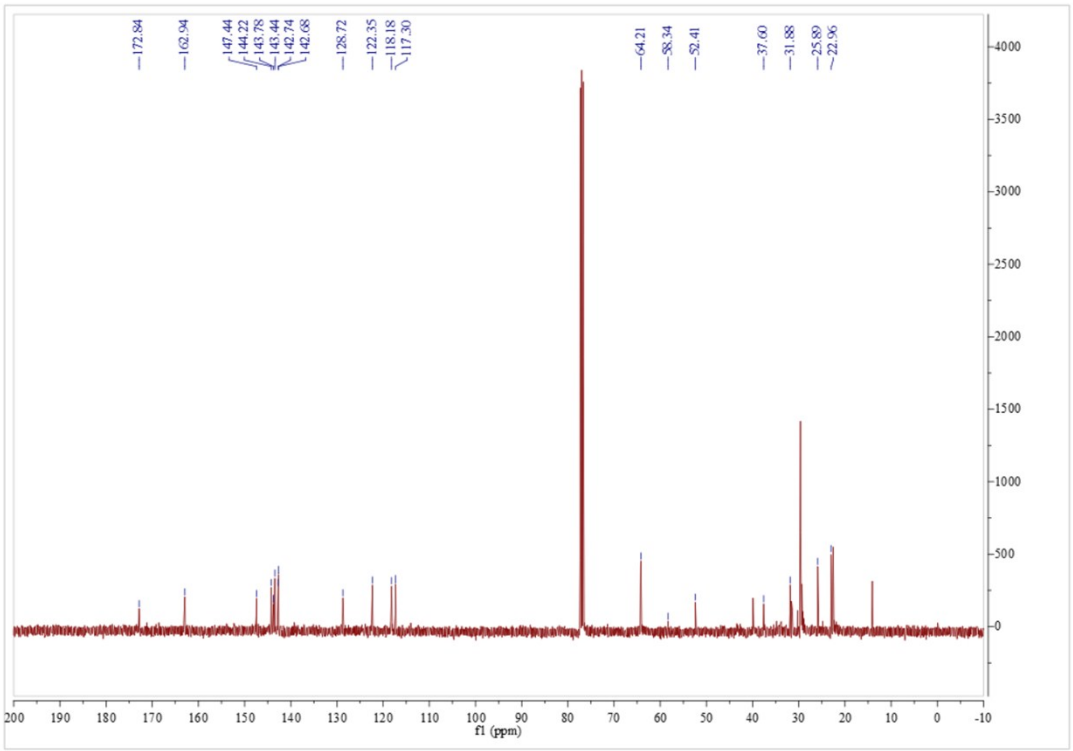
Compound **8l**


7.86
7.85
7.84
7.83
7.47
6.77
6.73
6.71
6.64
6.58
6.54
6.47
4.96
4.94
4.92
4.91
4.89
4.84
4.82
4.22
4.21
4.19
3.05
3.00
2.95
2.93
2.91
2.60
1.73
1.52
1.49
1.46
1.42
0.88
0.85
0.84
0.82
O
O
O
NH
NH
OH
B
OH
O
CH3
CH3
0.97
3.09
3.12
1.16
1.00
4.36
2.19
1.07
2.20
2.07
4.42
0.96
2.10
3.16
3.33
f1 (ppm)

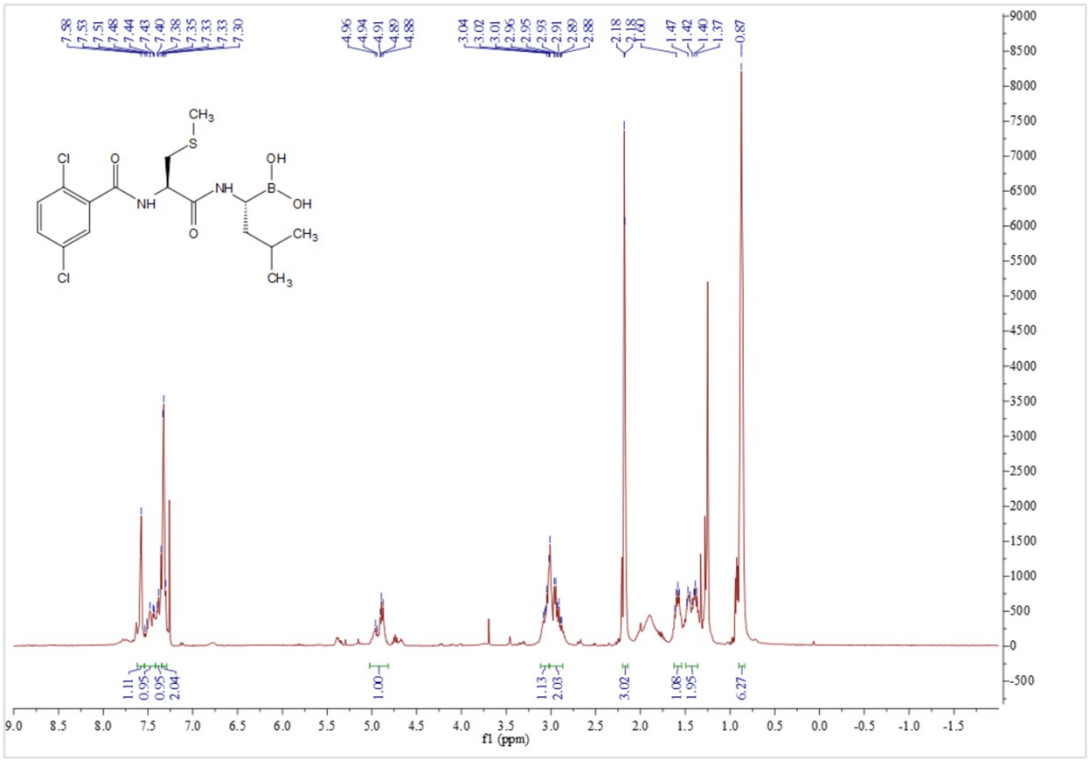

173.44
170.43
143.37
142.49
138.02
135.61
134.83
131.09
129.14
125.12
124.03
122.18
118.17
117.23
64.25
52.69
52.20
39.97
31.88
29.71
26.54
25.82
22.87
22.54
22.41
f1 (ppm)

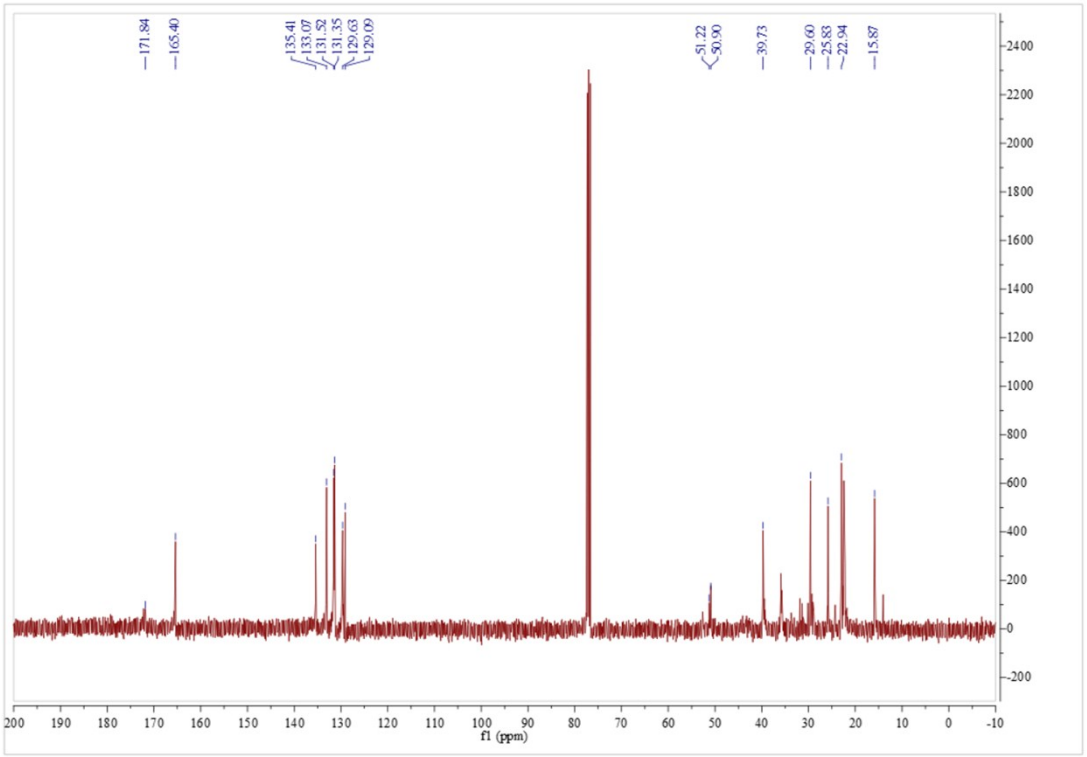
Compound **8m**


9.14
9.13
9.09
9.08
8.88
8.84
8.79
8.72
8.64
8.60
6.72
6.71
6.65
6.62
4.81
4.80
4.78
4.70
4.69
4.68
4.66
4.15
4.14
3.06
3.04
3.03
2.99
2.95
2.93
2.91
2.89
1.37
1.35
1.31
1.17
1.14
1.05
0.84
0.83
0.81
0.75
0.73
1.04
2.00
1.02
0.49
0.56
1.07
2.02
1.14
4.17
0.95
1.96
1.03
0.97
0.84
2.97
3.03
f1 (ppm)

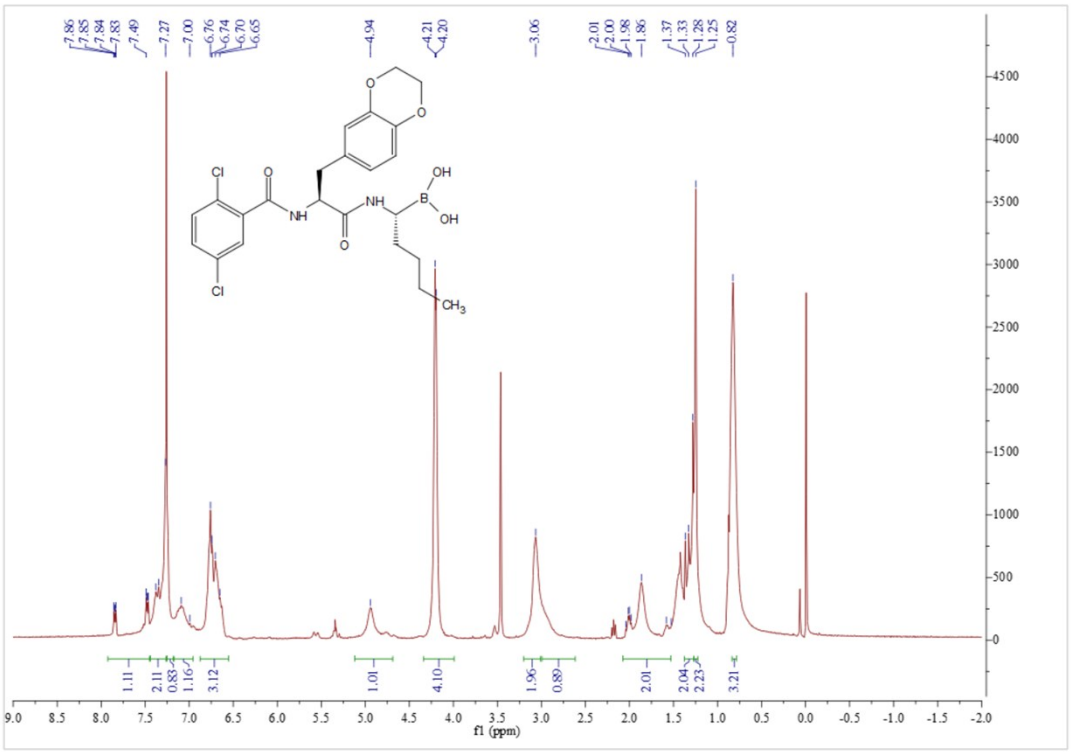

172.84
162.94
147.44
144.22
143.78
143.44
142.74
142.68
128.72
122.35
118.18
117.30
64.21
58.34
52.41
37.60
31.88
25.89
22.96
f1 (ppm)

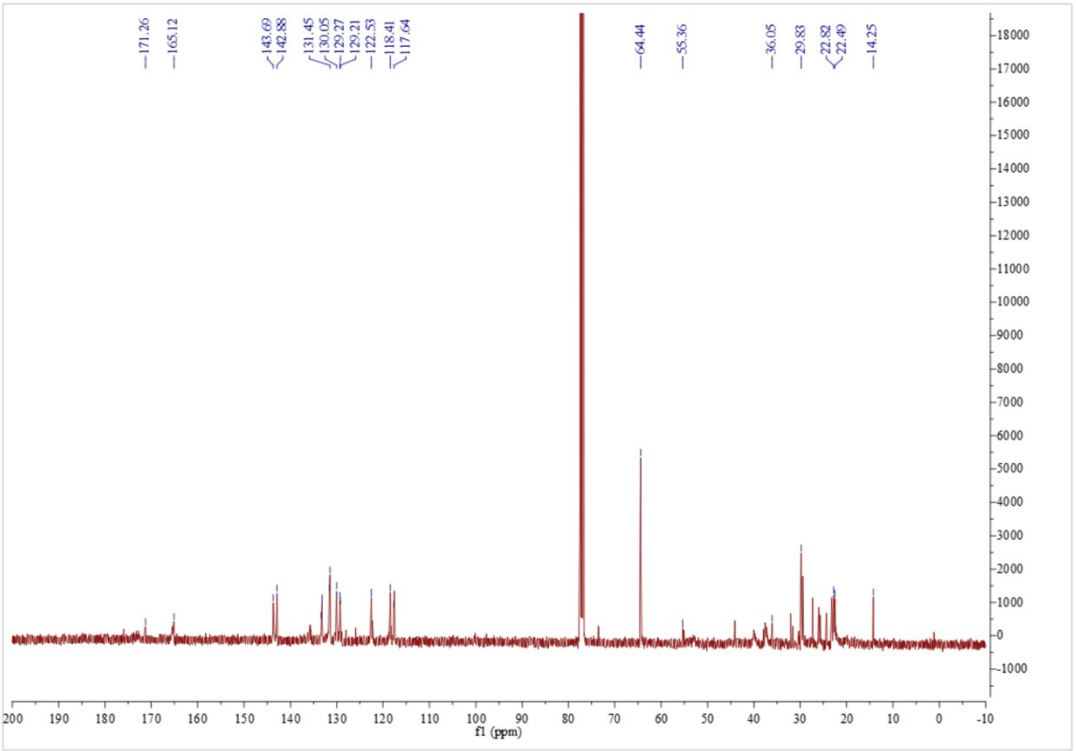
Compound **8n**


7.58
7.53
7.51
7.48
7.44
7.43
7.40
7.38
7.35
7.33
7.30
4.96
4.94
4.91
4.89
4.88
3.04
3.02
3.01
2.96
2.95
2.93
2.91
2.89
2.88
2.18
2.18
1.60
1.47
1.42
1.40
1.37
0.87
CH3
S
Cl
O
OH
NH
NH
B
OH
CH3
O
Cl
CH3
1.11
0.95
0.95
2.04
1.00
1.13
2.03
3.02
1.08
1.95
6.27
f1 (ppm)

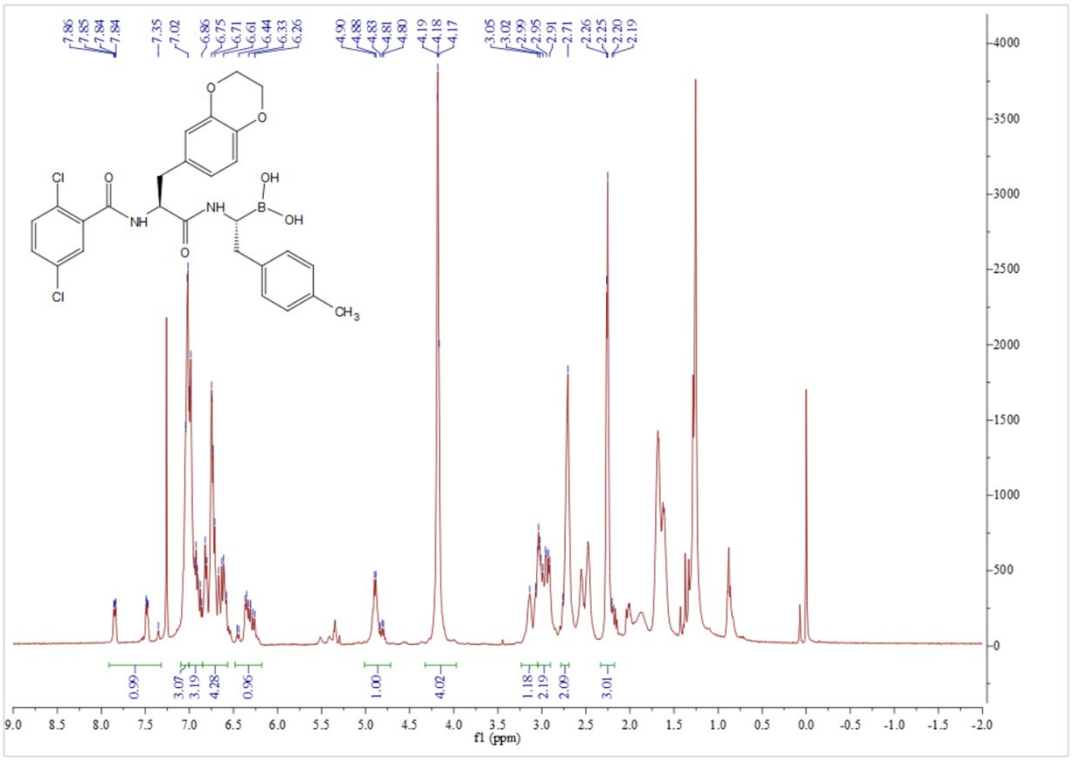

171.84
165.40
135.41
133.07
131.52
131.35
129.63
129.09
51.22
50.90
39.73
29.60
25.83
22.94
15.87
f1 (ppm)

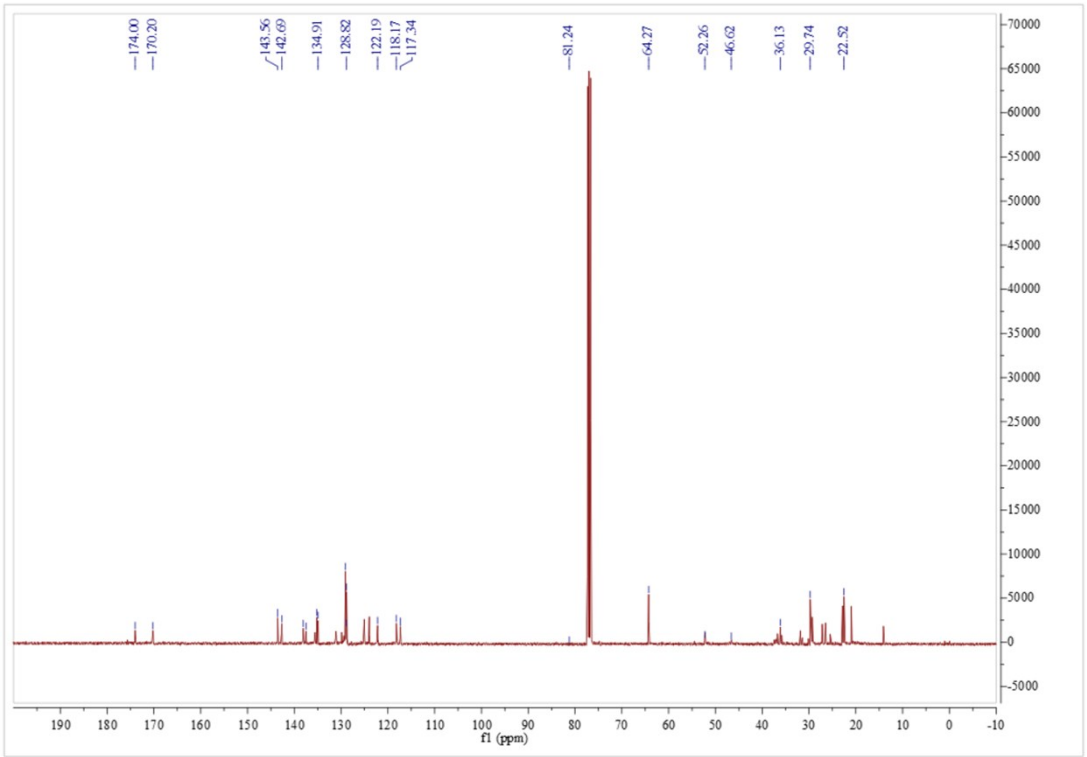
Compound **8o**


7.86
7.85
7.84
7.83
7.49
7.27
7.00
6.76
6.74
6.70
6.65
4.94
4.21
4.20
3.06
2.01
2.00
1.98
1.86
1.37
1.33
1.28
1.25
0.82
Cl
O
O
NH
NH
B
OH
OH
O
Cl
CH3
1.11
2.11
0.83
1.16
3.12
1.01
4.10
1.96
0.89
2.01
2.04
2.23
3.21
f1 (ppm)

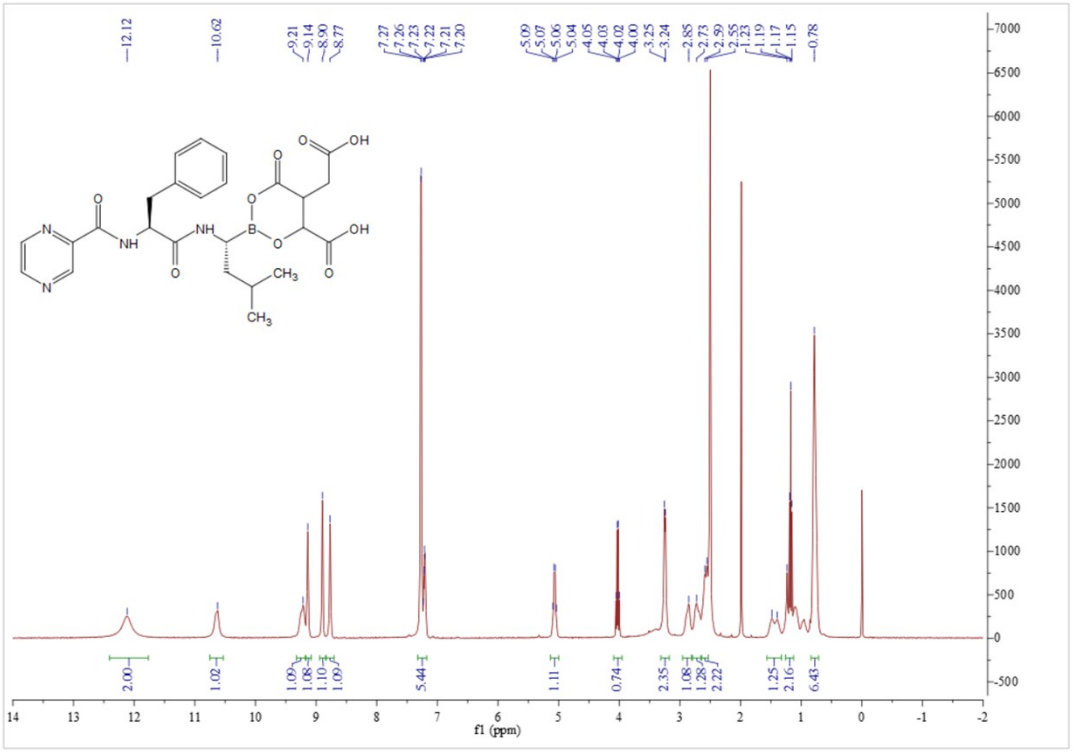

171.26
165.12
143.69
142.88
131.45
130.05
129.27
129.21
122.53
118.41
117.64
64.44
55.36
36.05
29.83
22.82
22.49
14.25
f1 (ppm)

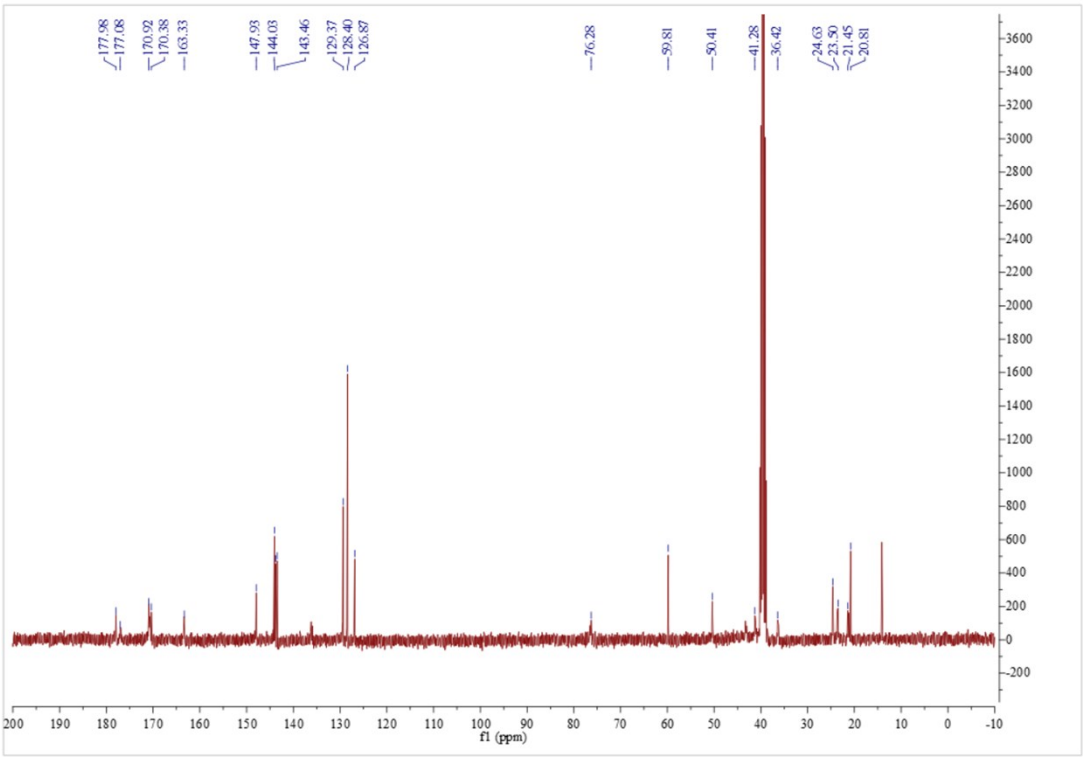
Compound **8p**


7.86
7.85
7.84
7.84
7.35
7.02
6.86
6.75
6.71
6.61
6.44
6.33
6.26
4.90
4.88
4.83
4.81
4.80
4.19
4.18
4.17
3.05
3.02
2.99
2.95
2.91
2.71
2.26
2.25
2.20
2.19
Cl
O
NH
NH
B
OH
OH
O
O
O
Cl
CH3
0.99
3.07
3.19
4.28
0.96
1.00
4.02
1.18
2.19
2.09
3.01
f1 (ppm)

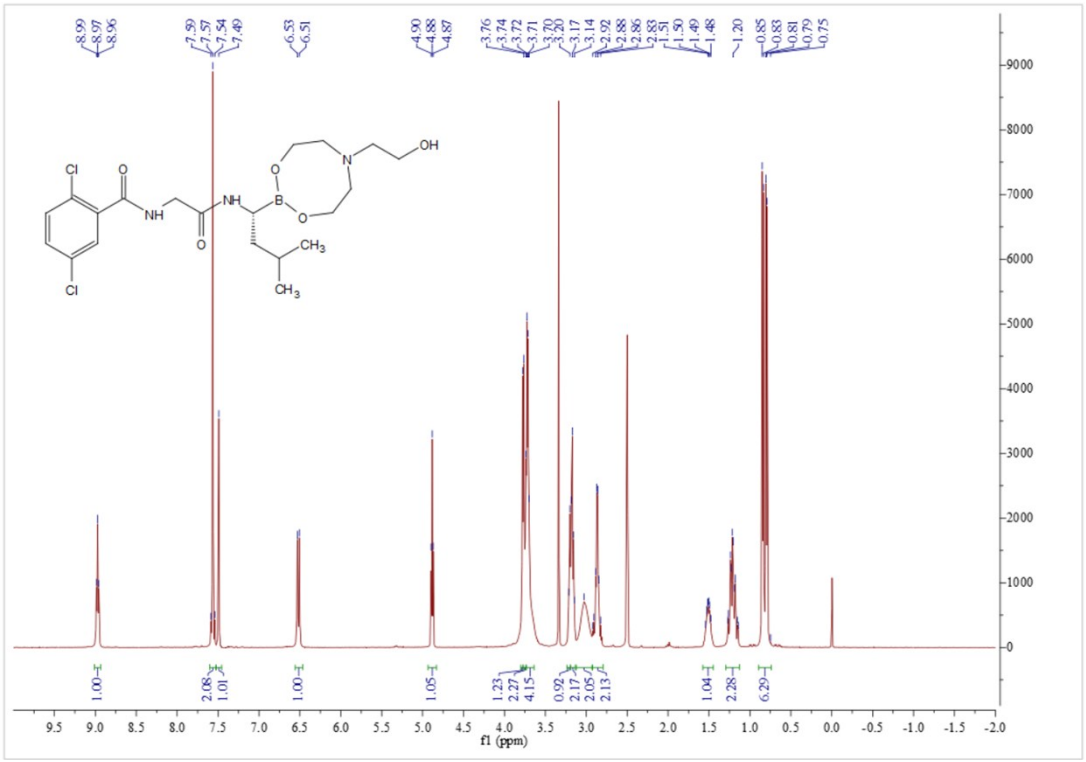

174.00
170.20
143.56
142.69
134.91
128.82
122.19
118.17
117.34
81.24
64.27
52.26
46.62
36.13
29.74
22.52
f1 (ppm)

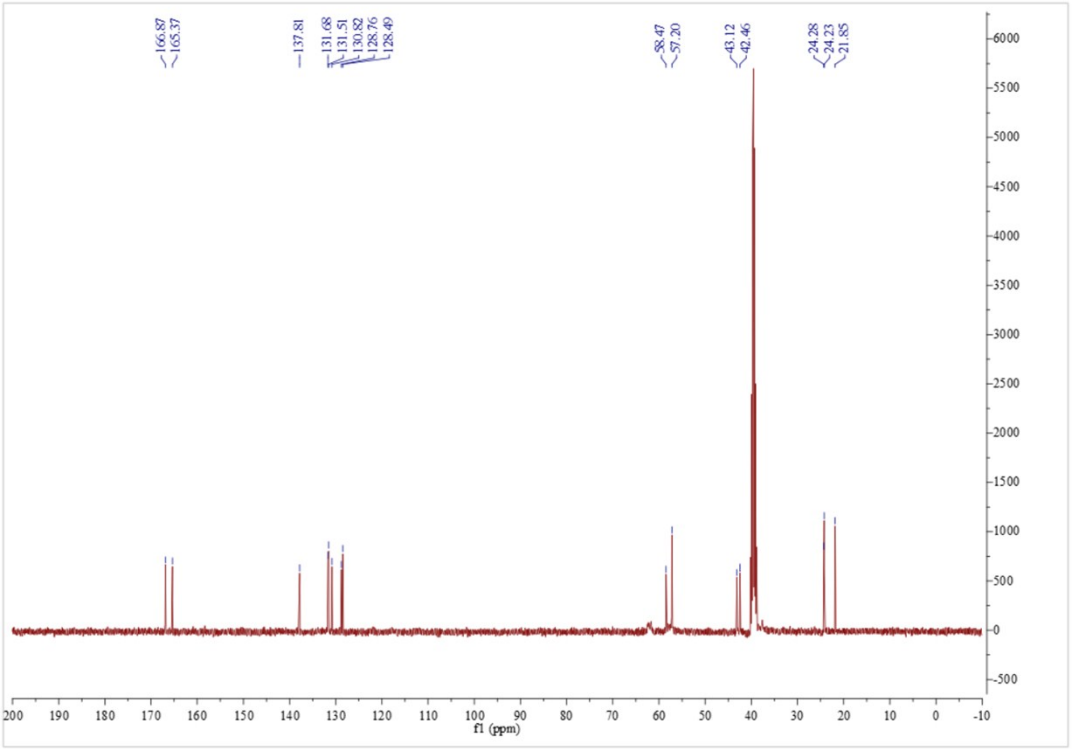
Compound **8q**


12.12
10.62
9.21
9.14
8.90
8.77
7.27
7.26
7.23
7.22
7.21
7.20
5.09
5.07
5.06
5.04
4.05
4.03
4.02
4.00
3.25
3.24
2.85
2.73
2.59
2.55
1.23
1.19
1.17
1.15
0.78
2.00
1.02
1.09
1.08
1.10
1.09
5.44
1.11
0.74
2.35
1.08
1.28
2.22
1.25
2.16
6.43
f1 (ppm)

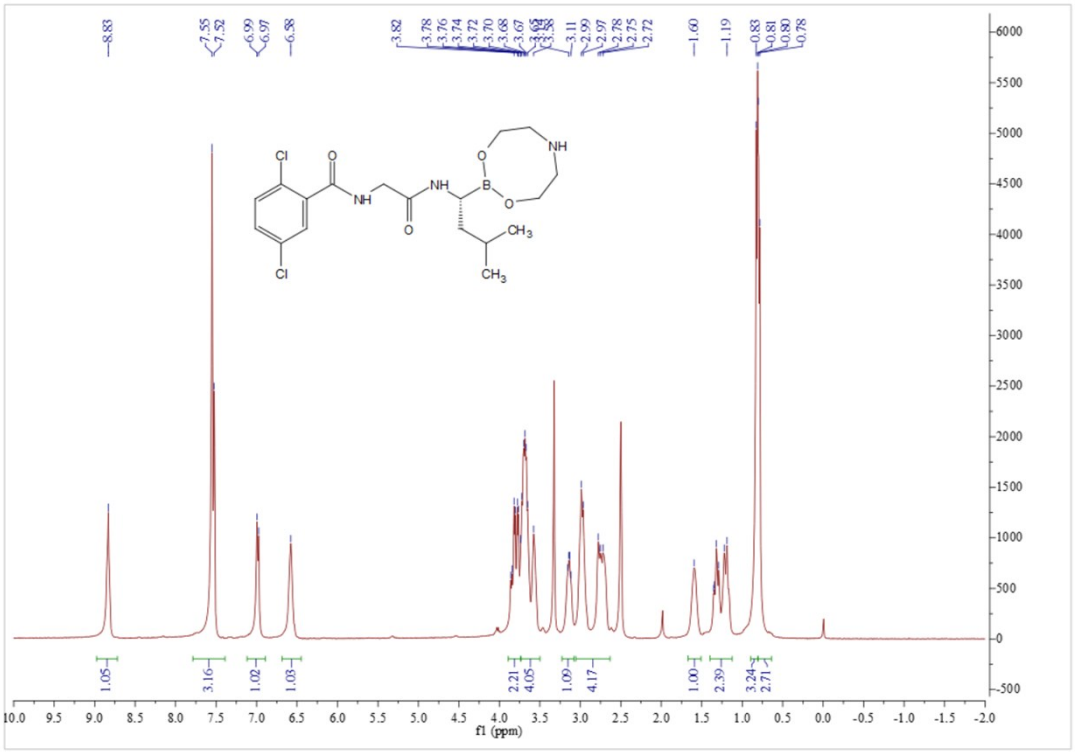

177.58
177.08
170.92
170.38
163.33
147.93
144.03
143.46
129.37
128.40
126.87
76.28
59.81
50.41
41.28
36.42
24.63
23.50
21.45
20.81
f1 (ppm)

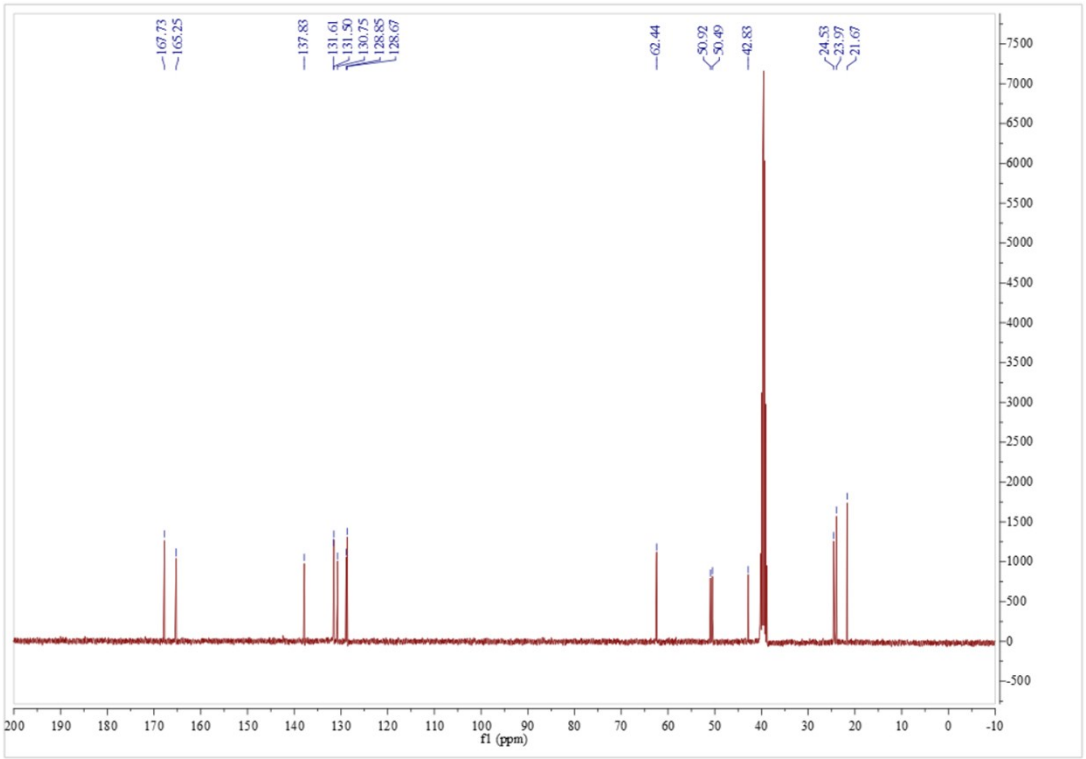
Compound **8r**


8.99
8.97
8.96
7.59
7.57
7.54
7.49
6.53
6.51
4.90
4.88
4.87
3.76
3.74
3.72
3.71
3.20
3.17
3.14
2.92
2.88
2.86
2.83
1.51
1.50
1.49
1.48
1.20
0.85
0.83
0.81
0.79
0.75
Cl
O
NH
O
NH
B
O
O
N
OH
CH3
CH3
Cl
1.00
2.08
1.01
1.00
1.05
1.23
2.27
4.15
0.92
2.17
2.05
2.13
1.04
2.28
6.29
f1 (ppm)

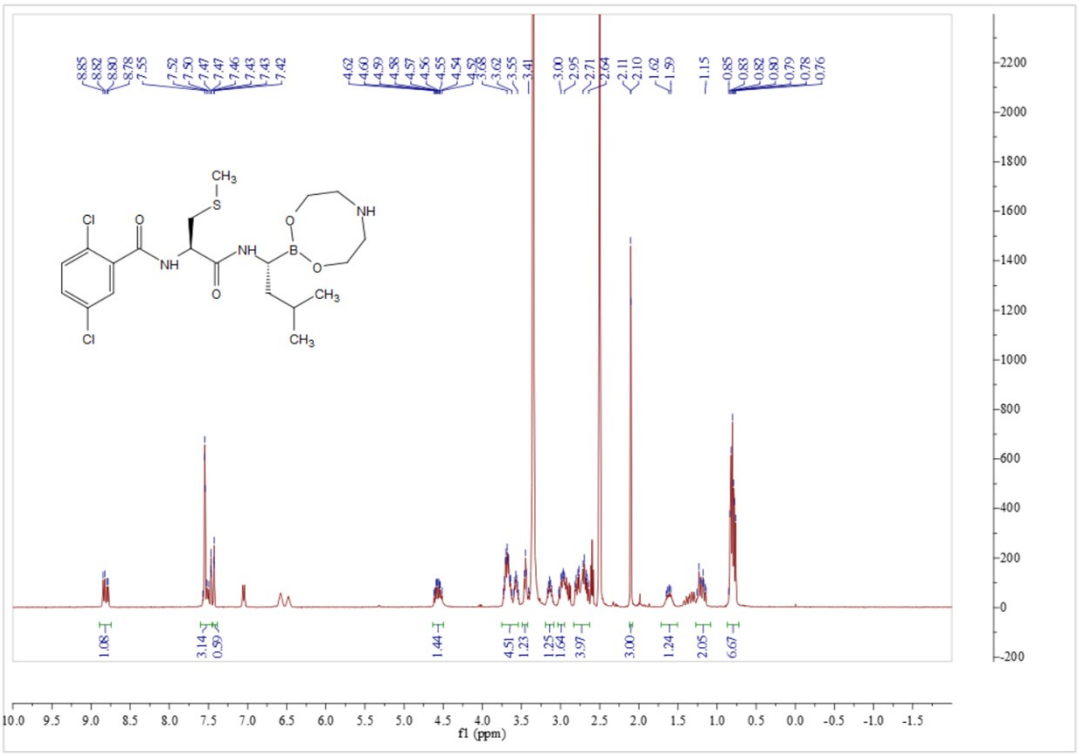

166.87
165.37
137.81
131.68
131.51
130.82
128.76
128.49
58.47
57.20
43.12
42.46
24.28
24.23
21.85
f1 (ppm)

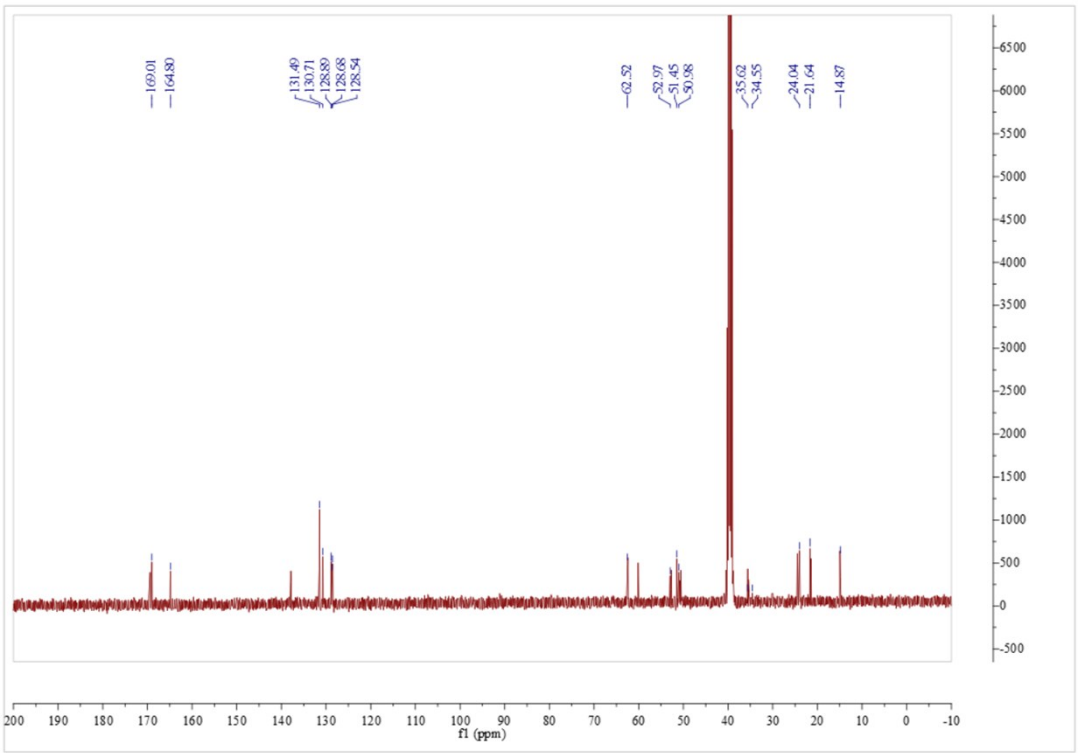
Compound **8s**


8.83
7.55
7.52
6.99
6.97
6.38
3.82
3.78
3.76
3.74
3.72
3.70
3.68
3.67
3.11
2.99
2.97
2.78
2.75
2.72
1.60
1.19
0.83
0.81
0.80
0.78
Cl
O
NH
NH
B
O
O
NH
O
CH3
CH3
Cl
1.05
3.16
1.02
1.03
2.21
4.05
1.09
4.17
1.00
2.39
3.24
2.71
f1 (ppm)


167.73
165.25
137.83
131.61
131.50
130.75
128.85
128.67
62.44
50.92
50.49
42.83
24.53
23.97
21.67
f1 (ppm)

Compound **8t**


8.85
8.82
8.80
8.78
7.55
7.52
7.50
7.47
7.47
7.46
7.43
7.43
7.42
4.62
4.60
4.59
4.58
4.57
4.56
4.55
4.54
4.52
3.68
3.62
3.55
3.41
3.00
2.95
2.71
2.64
2.11
2.10
1.62
1.59
1.15
0.85
0.83
0.82
0.80
0.79
0.78
0.76
1.08
3.14
0.59
1.44
4.51
1.23
1.25
1.64
3.97
3.00
1.24
2.05
6.67
f1 (ppm)


169.01
164.80
131.49
130.71
128.89
128.68
128.54
62.52
52.97
51.45
50.98
35.62
34.55
24.04
21.64
14.87
f1 (ppm)