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Supplementary Information

Metal-free quinolylation of the primary amino groups of amino acid derivatives and peptides with dihydrooxazolo[3,2-a]quinoliniums

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1. Supporting figure

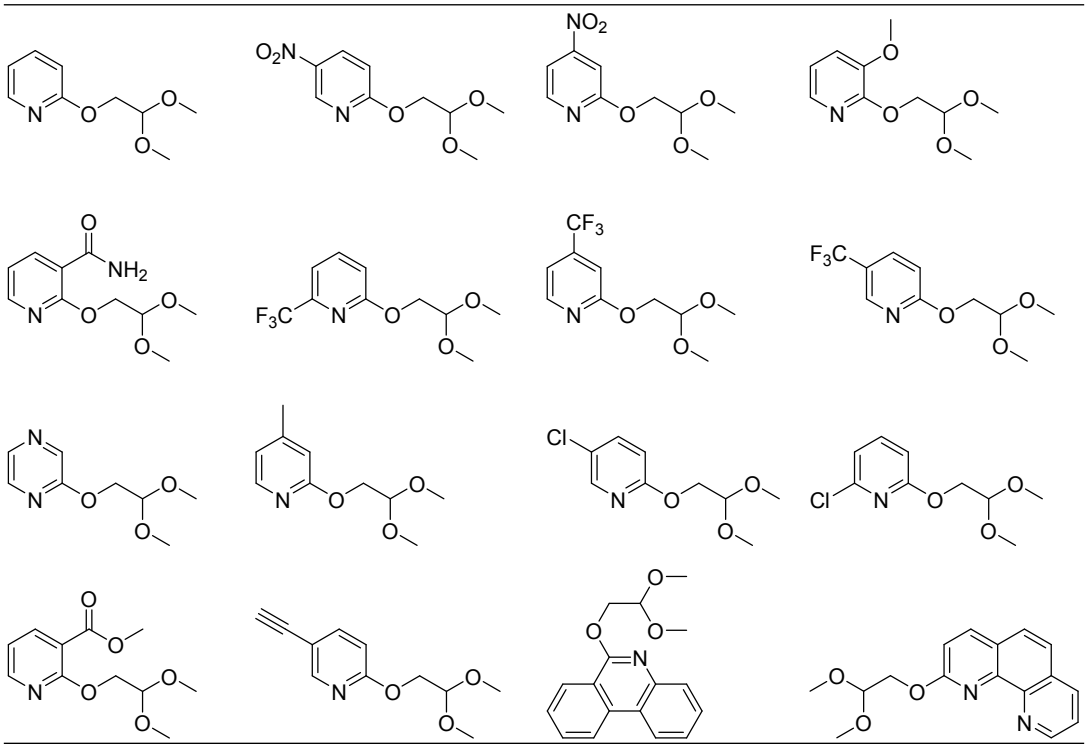


Figure S1. Screened substrates that can't react with N-terminus of amino acid

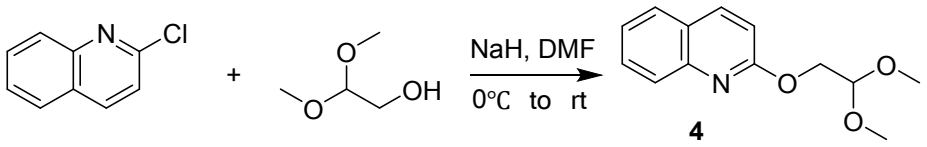
2. Chemical experiments

2.1 General information

All reactions were carried out at room temperature under anhydrous atmosphere. Yields were determined by HPLC. All materials and solvents were purchased from commercial suppliers and used without further purification. The LRMS and HRMS were recorded on Finnigan LCQ/DECA and Micromass Ultra Q-TOF (ESI) spectrometer, respectively.

The ^{1}H and ^{13}C spectra were taken on Bruker Avance - 400 and 500 NMR spectrometer operating at 400 MHz for ^{1}H NMR and 125 MHz for ^{13}C NMR, respectively, using TMS as the internal standard and $CDCl_3$, MeOD-d_4, Acetone-d_6 or DMSO-d_6 as the solvent. Chemical shifts are given in δ values of ppm. The abbreviations s is singlet, d is doublet, t is triplet and m is multiplet. Coupling constants (J) were measured in hertz (Hz).

2.2 Substrate synthesis



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2-(2,2-Dimethoxyethoxy)quinoline (4). 2,2-dimethoxyethan-1-ol (3.89 g, 36.6 mmol) was charged into a 250 ml round-bottom flask containing anhydrous DMF (50 ml). Sodium hydride (1.76 g, 73.2 mmol) was added. After 30 minutes, 2-chloroquinoline (4 g, 24.4 mmol) was added and the reaction was stirred at room temperature for 24 h. The grey solution was quenched with

ice water (200 ml), extracted with EtOAc (200 ml × 2), washed with brine (200 ml × 2) and dried over Na_2SO_4, and purified by column chromatography to afford **4** as a white solid in 81% yield (4.608 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 1H), 7.85 (d, *J* = 8.5 Hz, 1H), 7.74 (d, *J* = 7.9 Hz, 1H), 7.64 (ddd, *J* = 8.3, 6.8, 1.5 Hz, 1H), 7.43 – 7.38 (m, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 4.86 (t, *J* = 5.3 Hz, 1H), 4.58 (d, *J* = 5.3 Hz, 2H), 3.51 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.41, 146.29, 138.81, 129.46, 127.37, 127.26, 125.18, 124.11, 113.07, 101.84, 64.58, 53.95. HRMS (ESI) $[M+H]^+$ found 234.1127, calcd for $C_{13}H_{16}NO_3$ 234.1125.

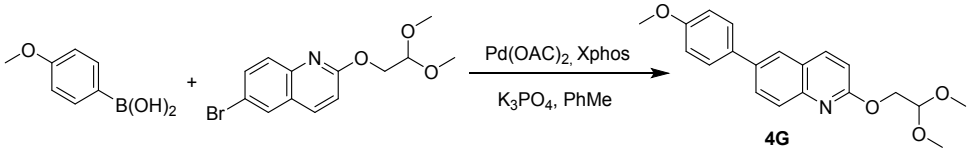
Alternative preparation method for compound **4**: quinolin-2-ol (10.0 mmol) was charged into a round-bottom flask containing anhydrous acetone (50 ml). Sodium carbonate (12.0 mmol) was added. After 30 minutes, 2-bromo-1,1-dimethoxyethane (11.0 mmol) was added and the reaction was stirred at reflux temperature for 48 h. The reaction mixture was quenched with ice water and filtered. After washing by water, the precipitate was dried to give the compound **4** in almost quantitative yield.

2-(2,2-Dimethoxyethoxy)-4-methylquinoline (4A). Following the procedure of **4** starting from 2-chloro-4-methylquinoline, the product **4A** was obtained as a white solid in 39% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 8.2 Hz, 1H), 7.85 (d, *J* = 8.3 Hz, 1H), 7.63 (ddt, *J* = 8.2, 7.0, 1.3 Hz, 1H), 7.42 (ddt, *J* = 8.0, 7.0, 1.2 Hz, 1H), 6.85 (d, *J* = 1.3 Hz, 1H), 4.85 (td, *J* = 5.2, 1.0 Hz, 1H), 4.56 (dd, *J* = 5.3, 1.0 Hz, 2H), 3.50 (d, *J* = 1.0 Hz, 6H), 2.64 (d, *J* = 1.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.26, 146.92, 146.28, 129.20, 127.74, 125.48, 123.86, 123.61, 112.98, 101.87, 64.30, 53.93, 18.65. HRMS (ESI) $[M+H]^+$ found 248.1277, calcd for $C_{14}H_{18}NO_3$ 248.1281.

2-(2,2-Dimethoxyethoxy)-8-methylquinoline (4B). Following the procedure of **4** starting from 2-chloro-8-methylquinoline, the product **4B** was obtained as a white solid in 64% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, *J* = 8.8 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H), 7.53 – 7.49 (m, 1H), 7.33 – 7.29 (m, 1H), 6.99 (d, *J* = 8.8 Hz, 1H), 4.92 (t, *J* = 5.4 Hz, 1H), 4.59 (d, *J* = 5.4 Hz, 2H), 3.52 (s, 6H), 2.71 (s, 3H). HRMS (ESI) $[M+H]^+$ found 248.1277, calcd for $C_{14}H_{18}NO_3$ 248.1281.

6-Chloro-2-(2,2-dimethoxyethoxy)quinoline (4C). Following the procedure of **4** starting from 2,6-dichloroquinoline, the product **4C** was obtained as a white solid in 81% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.8 Hz, 1H), 7.78 (d, *J* = 8.9 Hz, 1H), 7.72 (d, *J* = 2.3 Hz, 1H), 7.57 (dd, *J* = 8.9, 2.4 Hz, 1H), 7.01 (d, *J* = 8.9 Hz, 1H), 4.85 (t, *J* = 5.3 Hz, 1H), 4.55 (d, *J* = 5.3 Hz, 2H), 3.50 (s, 6H). HRMS (ESI) $[M+H]^+$ found 268.0734, calcd for $C_{13}H_{15}ClNO_3$ 268.0735.

8-Bromo-2-(2,2-dimethoxyethoxy)quinoline (4D). Following the procedure of **4** starting from 8-bromo-2-chloroquinoline and heating to 80 °C, the product **4D** was obtained as a white solid in 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 8.00 (m, 1H), 7.98 – 7.96 (m, 1H), 7.73 – 7.70 (m, 1H), 7.27 – 7.25 (m, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 4.99 (d, *J* = 5.4 Hz, 1H), 4.66 (d, *J* = 5.4 Hz, 2H), 3.53 (s, 6H). HRMS (ESI) $[M+H]^+$ found 312.016, calcd for $C_{13}H_{15}BrNO_3$ 312.018.



2-(2,2-Dimethoxyethoxy)-6-(4-methoxyphenyl)quinoline (4G). (4-methoxyphenyl)boronic acid (73 mg, 0.64 mmol), 6-bromo-2-(2,2-dimethoxyethoxy)quinoline (100 mg, 0.32 mmol), $Pd(OAC)_2$ (1.5 mg, 0.64 mmol%), Xphos (12 mg, 2.56 mmol%) and K_3PO_4 (136 mg, 0.64 mmol)

were charged into a 50 ml round-bottom flask containing toluene (20 ml). The reaction was nitrogen-flushed and then stirred at 100 °C overnight. Upon completion, the reaction mixture was cooled and evaporated to dryness. The residue was diluted in water and extracted twice with EtOAc, washed with brine and dried over Na_2SO_4, and purified by column chromatography to afford **4G** as white solid in 67% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J* = 8.8 Hz, 1H), 7.89 – 7.83 (m, 3H), 7.62 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 8.8 Hz, 2H), 6.98 (d, *J* = 8.8 Hz, 1H), 4.85 (t, *J* = 5.3 Hz, 1H), 4.57 (d, *J* = 5.3 Hz, 2H), 3.87 (s, 3H), 3.50 (s, 6H). HRMS (ESI) $[M+H]^+$ found 340.147, calcd for $C_{20}H_{22}NO_4$ 340.150.

2-(2,2-Dimethoxyethoxy)-6-(4-(trifluoromethyl)phenyl)quinoline (4H). Following the procedure of **4G**, the product **4H** was obtained as a white solid in 90% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.01 (m, 1H), 7.97 – 7.83 (m, 3H), 7.83 – 7.68 (m, 4H), 7.07 – 6.97 (m, 1H), 4.90 – 4.80 (m, 1H), 4.63 – 4.52 (m, 2H), 3.52 (s, 3H), 3.49 (s, 3H). HRMS (ESI) $[M+H]^+$ found 378.1315, calcd for $C_{20}H_{19}F_3NO_3$ 378.1312.

4-(2-(2,2-Dimethoxyethoxy)quinolin-6-yl)benzonitrile (4I). Following the procedure of **4G**, the product **4I** was obtained as a white solid in 85% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (d, *J* = 8.9 Hz, 1H), 7.93 (s, 1H), 7.92 (d, *J* = 4.8 Hz, 1H), 7.87 – 7.83 (m, 1H), 7.80 – 7.73 (m, 4H), 7.02 (d, *J* = 8.8 Hz, 1H), 4.85 (t, *J* = 5.3 Hz, 1H), 4.57 (d, *J* = 5.3 Hz, 2H), 3.50 (s, 6H). HRMS (ESI) $[M+H]^+$ found 335.1324, calcd for $C_{20}H_{19}N_2O_3$ 335.1326.

Methyl 4-(2-(2,2-dimethoxyethoxy)quinolin-6-yl)benzoate (4J). Following the procedure of **4G**, the product **4J** was obtained as a white solid in 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.4 Hz, 2H), 8.05 (d, *J* = 8.9 Hz, 1H), 7.95 (s, 1H), 7.92 – 7.89 (m, 2H), 7.75 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 1H), 4.85 (t, *J* = 5.3 Hz, 1H), 4.57 (d, *J* = 5.3 Hz, 2H), 3.95 (s, 3H), 3.50 (s, 6H). HRMS (ESI) $[M+H]^+$ found 368.1423, calcd for $C_{21}H_{22}NO_5$ 368.1424.

2-(2,2-Dimethoxyethoxy)-7-(2-fluorophenyl)-4-methylquinoline (4K). Following the procedure of **4G**, the product **4K** was obtained as a white solid in 87% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.94 (d, *J* = 8.5 Hz, 1H), 7.65 (d, *J* = 8.5 Hz, 1H), 7.60 (t, *J* = 7.7 Hz, 1H), 7.42 – 7.35 (m, 1H), 7.29 (d, *J* = 7.3 Hz, 1H), 7.25 – 7.19 (m, 1H), 6.87 (s, 1H), 4.87 (t, *J* = 5.2 Hz, 1H), 4.58 (d, *J* = 5.2 Hz, 2H), 3.51 (s, 6H), 2.66 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 157.3, 156.5, 142.4, 142.0, 132.5, 126.6, 124.9, 124.3, 123.5, 120.6, 120.4, 120.1, 119.3, 111.7, 108.9, 97.5, 60.1, 49.6, 14.2. HRMS (ESI) $[M+H]^+$ found 342.1499, calcd for $C_{20}H_{21}FNO_3$ 342.15.

2.3 Experimental data

N-methyl-2-(quinolin-2-ylamino)acetamide (6). 2-(2,2-dimethoxyethoxy)quinoline (200 mg, 0.86 mmol) reacted with hydrochloric acid in diethyl ether (5 mL). After that the solvent was evaporated under anhydrous atmosphere. The residue was dissolved in anhydrous n-butanol (10 mL) directly without further purification and treated with 2-amino-N-methylacetamide (151 mg, 1.71 mmol) and Et_3N (237 μL, 1.71 mmol). After stirring overnight at room temperature, the reaction mixture was concentrated. H_2O was added to the reaction mixture and the mixture was extracted twice with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by reverse-phase silica gel column chromatography (MeOH/H_2O = 0% to 80%) to give **6** as a white solid in 95% yield (172 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, J = 8.9 Hz, 1H), 7.72 (d, J = 8.4 Hz, 1H), 7.63 (d, J = 8.0 Hz, 1H), 7.57 (t, J = 7.5 Hz, 1H), 7.31 – 7.25 (m, 1H), 6.96 (s, 1H), 6.71 (d, J = 8.9 Hz, 1H), 5.67 (s, 1H), 4.24 (s, 2H), 2.84 (d, J = 4.9 Hz, 3H), 2.24 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.3,

156.0, 147.4, 137.8, 129.8, 127.5, 126.2, 123.7, 122.8, 111.9, 45.9, 26.2. HRMS (ESI) $[M+H]^+$ found m/z 216.1006, calcd for $C_{12}H_{14}N_3O$ 215.1058.

Alternative quaternary ammonium salt preparation method: Concentrated sulfuric acid is added dropwise to the sodium chloride solid to produce hydrogen chloride gas. This gas is then passed to the acetone solution containing the 2-(2,2-dimethoxyethoxy)quinoline for reaction. After the reaction is completed, the solvent is distilled for recovery. The obtained residue is a quaternary ammonium salt for further amino coupling reaction.

(R)-N-methyl-2-(quinolin-2-ylamino)propanamide (6a). Following the procedure of **6** starting from (S)-2-amino-N-methylpropanamide, the product **6a** was obtained as a white solid (yield 92% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.8 Hz, 1H), 7.67 (d, J = 8.3 Hz, 1H), 7.59 (d, J = 7.9 Hz, 1H), 7.53 (t, J = 7.3 Hz, 1H), 7.27 – 7.21 (m, 1H), 7.10 (s, 1H), 6.61 (d, J = 8.8 Hz, 1H), 5.28 (d, J = 5.9 Hz, 1H), 4.72 (p, J = 6.7 Hz, 1H), 2.78 (d, J = 4.9 Hz, 3H), 1.52 (d, J = 7.0 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.3, 155.8, 147.4, 137.6, 129.7, 127.5, 126.1, 123.6, 122.6, 112.0, 50.7, 26.1, 18.1. HRMS (ESI) $[M+H]^+$ found m/z 230.1284, calcd for $C_{13}H_{16}N_3O$ 230.1288. $[\alpha]_D^{20}$ -141.5 (c = 0.188, CH_3OH).

(S)-N,3,3-trimethyl-2-(quinolin-2-ylamino)butanamide (6b). Following the procedure of **6** starting from 2-amino-N,3,3-trimethylbutanamide, the product **6b** was obtained as a white solid (yield 66% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, J = 8.9 Hz, 1H), 7.69 (d, J = 8.4 Hz, 1H), 7.61 (s, 1H), 7.57 – 7.52 (m, 1H), 7.25 (t, J = 8.0 Hz, 1H), 6.70 (d, J = 8.9 Hz, 1H), 6.44 (s, 1H), 5.68 (s, 1H), 4.50 (d, J = 7.8 Hz, 1H), 2.80 (d, J = 4.9 Hz, 3H), 1.14 (s, 9H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.6, 156.3, 147.1, 137.8, 129.7, 127.5, 125.7, 123.6, 122.5, 112.0, 34.4, 27.0, 26.1. HRMS (ESI) $[M+H]^+$ found m/z 272.1756, calcd for $C_{16}H_{22}N_3O$ 272.1757. $[\alpha]_D^{20}$ -178.7 (c = 0.075, CH_3OH).

(S)-N-methyl-2-phenyl-2-(quinolin-2-ylamino)acetamide (6c). Following the procedure of **6** starting from (S)-2-amino-N-methyl-2-phenylacetamide, the product **6c** was obtained as a white solid (yield 63% for 2 steps). ^{1}H NMR (400 MHz, MeOD-d_4) δ 7.88 (d, J = 8.9 Hz, 1H), 7.66 – 7.60 (m, 2H), 7.57 – 7.47 (m, 3H), 7.42 – 7.36 (m, 2H), 7.36 – 7.30 (m, 1H), 5.69 (s, 1H), 2.77 (s, 3H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 173.8, 156.1, 147.5, 138.6, 136.8, 128.9, 128.3, 127.7, 127.5, 127.1, 125.6, 123.7, 122.0, 112.4, 59.7, 25.1. HRMS (ESI) $[M+H]^+$ found m/z 292.145, calcd for $C_{18}H_{18}N_3O$ 292.144. $[\alpha]_D^{20}$ -4.0 (c = 0.121, CH_3OH).

(S)-N-methyl-3-phenyl-2-(quinolin-2-ylamino)propanamide (6d). Following the procedure of **6** starting from (S)-2-amino-N-methyl-3-phenylpropanamide, the product **6d** was obtained as a white solid (yield 72% for 2 steps). ^{1}H NMR (400 MHz, Acetone-d_6) δ 7.86 (s, 1H), 7.63 (d, J = 8.3 Hz, 2H), 7.50 (t, J = 7.5 Hz, 1H), 7.41 (s, 1H), 7.33 (d, J = 7.5 Hz, 2H), 7.25 (t, J = 7.5 Hz, 2H), 7.17 (s, 2H), 6.88 (d, J = 8.9 Hz, 1H), 6.50 (s, 1H), 5.11 – 5.02 (m, 1H), 3.30 (dd, J = 13.8, 5.9 Hz, 1H), 3.13 (dd, J = 13.7, 7.8 Hz, 1H), 2.70 (d, J = 4.7 Hz, 3H). ^{13}C NMR (125 MHz, Acetone-d_6) δ 205.2, 172.3, 156.2, 147.8, 138.5, 136.7, 129.3, 129.0, 128.1, 127.4, 126.2, 126.1, 123.6, 121.8, 113.1, 56.0, 38.0, 25.2. HRMS (ESI) $[M+H]^+$ found m/z 306.1597, calcd for $C_{19}H_{20}N_3O$ 306.1601. $[\alpha]_D^{20}$ 29.9 (c = 0.126, CH_3OH).

Methyl quinolin-2-ylphenylalaninate (6e). Following the procedure of **6** starting from methyl L-phenylalaninate, the product **6e** was obtained as a white solid (yield 61% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.75 (d, *J* = 8.1 Hz, 1H), 7.62 (d, *J* = 7.7 Hz, 1H), 7.60 – 7.54 (m, 1H), 7.35 – 7.26 (m, 4H), 7.21 (d, *J* = 7.3 Hz, 2H), 6.65 (dd, *J* = 8.8, 2.7 Hz, 1H), 5.27 – 5.21 (m, 1H), 5.19 (s, 1H), 3.77 (d, *J* = 2.8 Hz, 3H), 3.39 (ddd, *J* = 13.7, 5.5, 2.4 Hz, 1H), 3.27 (ddd, *J* = 13.9, 5.7, 2.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.3, 155.1, 147.1, 137.6, 136.6, 130.4, 129.6, 129.4, 128.5, 127.4, 126.9, 126.2, 123.6, 122.6, 112.1, 55.1, 52.2. HRMS (ESI) $[M+H]^+$ found m/z 307.1437, calcd for $C_{19}H_{19}N_2O_2$ 307.1441. $[\alpha]_D^{20}$ -2.9 (c = 0.105, CH_3OH).

(R)-2-(quinolin-2-ylamino)butanamide (6f). Following the procedure of **6** starting from 2-aminobutanamide, the product **6f** was obtained as a white solid (yield 85% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.85 (d, *J* = 8.9 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.48 – 7.43 (m, 3H), 7.15 (ddd, *J* = 8.1, 4.8, 3.2 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 6.99 (s, 1H), 6.93 (d, *J* = 8.9 Hz, 1H), 4.54 (q, *J* = 6.9 Hz, 1H), 1.90 – 1.76 (m, 1H), 1.76 – 1.63 (m, 1H), 0.94 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 175.1, 157.0, 148.0, 136.6, 129.4, 127.9, 126.0, 123.5, 121.7, 113.9, 55.4, 25.8, 10.8. HRMS (ESI) $[M+H]^+$ found m/z 230.1288, calcd for $C_{13}H_{16}N_3O$ 230.1288. $[\alpha]_D^{20}$ -66.3 (c = 0.080, CH_3OH).

Methyl quinolin-2-ylglycinate (6g). Following the procedure of **6** starting from methyl glycinate, the product **6g** was obtained as a white solid (yield 95% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.9 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.57 – 7.51 (m, 1H), 7.23 (t, 1H), 6.72 (d, 1H), 5.24 (s, 1H), 4.38 (d, *J* = 5.1 Hz, 2H), 3.80 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 155.7, 147.6, 137.4, 129.5, 127.4, 126.4, 123.7, 122.5, 112.1, 52.3, 43.3, 29.7. HRMS (ESI) $[M+H]^+$ found m/z 217.0973, calcd for $C_{12}H_{13}N_2O_2$ 217.0972.

Methyl quinolin-2-yl-L-alaninate (6h). Following the procedure of **6** starting from methyl D-alaninate, the product **6h** was obtained as a white solid (yield 93% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.25 – 7.21 (m, 1H), 6.67 (d, *J* = 8.8 Hz, 1H), 5.27 (s, 1H), 4.90 (p, *J* = 7.1 Hz, 1H), 3.77 (s, 3H), 1.56 (d, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.0, 155.3, 147.4, 137.4, 129.5, 127.4, 126.4, 123.6, 122.5, 112.0, 52.3, 49.7, 18.6. HRMS (ESI) $[M+H]^+$ found m/z 231.1129, calcd for $C_{13}H_{15}N_2O_2$ 231.1128. $[\alpha]_D^{20}$ –23.7 (c = 0.114, CH_3OH).

Methyl quinolin-2-yl-L-valinate (6i). Following the procedure of **6** starting from methyl D-valinate, the product **6i** was obtained as a white solid (yield 91% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.8 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 1H), 7.56 (d, *J* = 8.8 Hz, 1H), 7.54 – 7.49 (m, 1H), 7.24 – 7.19 (m, 1H), 6.67 (d, *J* = 8.8 Hz, 1H), 5.21 (d, *J* = 7.5 Hz, 1H), 4.87 (dd, *J* = 8.3, 5.4 Hz, 1H), 3.75 (s, 3H), 1.05 (dd, *J* = 6.8, 3.4 Hz, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.1, 156.1, 147.7, 137.2, 129.4, 127.3, 126.5, 123.7, 122.3, 112.1, 59.0, 51.9, 31.3, 19.1, 18.5. $[\alpha]_D^{20}$ -145.6(c = 0.148, CH_3OH).

Methyl quinolin-2-yl-L-isoleucinate (6j). Following the procedure of **6** starting from methyl D-isoleucinate, the product **6j** was obtained as a white solid (yield 82% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (dd, *J* = 8.9, 2.2 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H),

7.54 (t, *J* = 7.7 Hz, 1H), 7.23 (t, *J* = 7.3 Hz, 1H), 6.71 (dd, *J* = 8.9, 2.0 Hz, 1H), 5.02 (s, 1H), 4.83 (s, 1H), 3.77 (s, 3H), 2.14 – 2.01 (m, 1H), 1.70 – 1.53 (m, 1H), 1.03 (d, *J* = 3.0 Hz, 3H), 1.02 – 0.99 (m, 3H). HRMS (ESI) $[M+H]^+$ found m/z 273.1603, calcd for $C_{16}H_{21}N_2O_2$ 273.1598. [α] -8.1 (c = 0.078, CH_3OH).

Methyl quinolin-2-yl-L-serinate (6k). Following the procedure of **6** starting from methyl D-serinate, the product **6k** was obtained as a white solid (yield 88% for 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.9 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.59 – 7.53 (m, 1H), 7.28 – 7.25 (m, 1H), 6.77 (d, *J* = 8.9 Hz, 1H), 5.87 (s, 1H), 4.97 (s, 1H), 4.26 (dd, *J* = 10.9, 2.6 Hz, 1H), 3.98 (dd, *J* = 10.9, 6.2 Hz, 1H), 3.85 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.8, 155.6, 146.2, 138.2, 130.0, 127.5, 125.6, 123.5, 123.0, 112.5, 65.5, 58.0, 52.9. HRMS (ESI) $[M+H]^+$ found m/z 247.1081, calcd for $C_{13}H_{15}N_2O_3$ 247.1077. [α] 5.8 (c = 0.136, CH_3OH).

Methyl quinolin-2-yl-L-threoninate (6l). Following the procedure of **6** starting from methyl L-threoninate, the product **6l** was obtained as a white solid (yield 66% for 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.62 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.55 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.28 – 7.24 (m, 1H), 6.77 (d, *J* = 8.8 Hz, 1H), 5.51 (s, 1H), 4.96 (dd, *J* = 7.3, 3.8 Hz, 1H), 4.40 (qd, *J* = 6.4, 3.7 Hz, 1H), 3.82 (s, 3H), 1.35 (d, *J* = 6.4 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.8, 156.0, 147.1, 137.6, 129.6, 127.4, 126.3, 123.8, 122.7, 112.4, 69.3, 59.9, 52.5, 20.4. HRMS (ESI) $[M+H]^+$ found m/z 261.1228, calcd for $C_{14}H_{17}N_2O_3$ 261.1234. [α] -113.8 (c = 0.052, CH_3OH).

Methyl quinolin-2-yl-L-tyrosinate (6m). Following the procedure of **6** starting from methyl L-tyrosinate, the product **6m** was obtained as a white solid (yield 63% for 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.9 Hz, 1H), 7.73 (d, *J* = 8.5 Hz, 1H), 7.61 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.54 (ddd, *J* = 8.4, 7.0, 1.5 Hz, 1H), 7.26 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 6.97 (d, *J* = 8.5 Hz, 2H), 6.68 (d, *J* = 8.5 Hz, 2H), 6.64 (d, *J* = 8.9 Hz, 1H), 5.47 (s, 1H), 5.03 (s, 1H), 3.75 (s, 3H), 3.25 (dd, *J* = 13.9, 5.3 Hz, 1H), 3.13 (dd, *J* = 13.9, 6.4 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.6, 155.5, 155.5, 147.0, 138.1, 130.4, 129.9, 127.5, 127.3, 125.8, 123.6, 122.7, 115.6, 111.5, 55.5, 52.3, 37.2. HRMS (ESI) $[M+H]^+$ found m/z 323.1388, calcd for $C_{19}H_{19}N_2O_3$ 323.1390. [α] 12.4 (c = 0.106, CH_3OH).

Methyl quinolin-2-yl-L-tryptophanate (6n). Following the procedure of **6** starting from methyl L-tryptophanate, the product **6n** was obtained as a white solid (yield 70% for 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.80 (d, *J* = 8.9 Hz, 1H), 7.76 (d, *J* = 8.4 Hz, 1H), 7.61 (d, *J* = 7.9 Hz, 2H), 7.59 – 7.54 (m, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.20 (t, *J* = 7.1 Hz, 1H), 7.13 (t, *J* = 7.5 Hz, 1H), 7.01 (d, *J* = 2.1 Hz, 1H), 6.57 (d, *J* = 8.8 Hz, 1H), 5.34 – 5.29 (m, 1H), 5.27 (d, *J* = 8.2 Hz, 1H), 3.73 (s, 3H), 3.54 (dd, *J* = 14.6, 5.2 Hz, 1H), 3.45 (dd, *J* = 14.6, 5.6 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 155.4, 147.5, 137.4, 136.2, 129.5, 127.8, 127.4, 126.4, 123.6, 122.9, 122.5, 122.1, 119.6, 118.8, 112.2, 111.2, 110.7, 54.6, 52.2, 27.9. HRMS (ESI) $[M+H]^+$ found m/z 346.1560, calcd for $C_{21}H_{20}N_3O_2$ 346.1550. [α] 2.5 (c = 0.120, CH_3OH).

Methyl quinolin-2-yl-D-methioninate (6p). Following the procedure of **6** starting from methyl L-methioninate, the product **6p** was obtained as a white solid (yield 96% for 2 steps). ^1H

NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 8.4 Hz, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.24 (t, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 8.8 Hz, 1H), 5.42 (s, 1H), 5.06 (q, *J* = 7.2 Hz, 1H), 3.78 (s, 3H), 2.65 (td, *J* = 7.9, 3.4 Hz, 2H), 2.35 (dq, *J* = 13.5, 7.4 Hz, 1H), 2.16 (dd, *J* = 14.3, 7.5 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.9, 155.4, 147.3, 137.5, 129.6, 127.4, 126.4, 123.7, 122.6, 112.0, 53.2, 52.4, 32.0, 30.3, 15.5. HRMS (ESI) $[M+H]^+$ found m/z 291.1167, calcd for $C_{15}H_{19}N_2O_2S$ 291.1162. [α] -4.2 (c = 0.095, CH_3OH).

Methyl N^6-(quinolin-2-yl)lysinate (6r). Following the procedure of **6** starting from methyl lysinate, the product **6r** was obtained as a white solid (yield 53% for 2 steps). ^1H NMR (400 MHz, D_2O) δ 7.94 (s, 1H), 7.63 (t, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.53 (s, 1H), 7.35 (t, *J* = 7.6 Hz, 1H), 6.76 (s, 1H), 4.06 (t, *J* = 6.4 Hz, 1H), 3.70 (s, 3H), 3.33 (t, *J* = 6.7 Hz, 2H), 2.00 – 1.80 (m, 2H), 1.67 (p, *J* = 7.2 Hz, 2H), 1.55 – 1.34 (m, 2H). ^{13}C NMR (125 MHz, D_2O) δ 170.6, 152.5, 141.9, 135.6, 132.5, 128.7, 125.4, 121.1, 117.0, 113.8, 53.6, 52.7, 41.6, 29.4, 26.9, 21.7. HRMS (ESI) $[M+H]^+$ found m/z 288.17, calcd for $C_{16}H_{22}N_3O_2$ 288.1707.

2-Amino-N-methyl-6-(quinolin-2-ylamino)hexanamide (6s). Following the procedure of 6 starting from 2-(2,2-dimethoxyethoxy)-4-methylquinoline, the product 6A was obtained as a white solid (yield 50% for 2 steps). ^1H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.9 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 1H), 7.57 (d, *J* = 7.9 Hz, 1H), 7.54 – 7.46 (m, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 6.63 (d, *J* = 8.9 Hz, 1H), 3.56 – 3.49 (m, 2H), 3.40 – 3.33 (m, 1H), 2.80 (d, *J* = 4.9 Hz, 3H), 1.73 – 1.67 (m, 2H), 1.61 – 1.57 (m, 2H), 1.54 – 1.48 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 175.5, 156.9, 147.8, 137.3, 129.5, 127.4, 125.8, 123.2, 121.9, 111.2, 77.2, 76.9, 76.7, 55.0, 41.3, 34.7, 29.3, 25.7, 23.1. HRMS (ESI) $[M+H]^+$ found m/z 287.1864, calcd for $C_{16}H_{23}N_4O$ 287.1866.

N-methyl-2-((4-methylquinolin-2-yl)amino)acetamide (6A). Following the procedure of **6** starting from 2-(2,2-dimethoxyethoxy)-4-methylquinoline, the product **6A** was obtained as a white solid (yield 91% for 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.73 (s, 1H), 7.58 (s, 1H), 7.30 (s, 1H), 7.05 (s, 1H), 6.55 (s, 1H), 5.63 (s, 1H), 4.21 (s, 2H), 2.83 (d, *J* = 4.5 Hz, 3H), 2.56 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.9, 156.7, 147.8, 144.1, 129.3, 126.4, 124.2, 123.8, 121.9, 113.5, 44.3, 26.0, 18.7. HRMS (ESI) $[M+H]^+$ found m/z 230.1291, calcd for $C_{13}H_{16}N_3O$ 230.1288.

N-methyl-2-((8-methylquinolin-2-yl)amino)acetamide (6B). Following the procedure of **6** starting from 2-(2,2-dimethoxyethoxy)-8-methylquinoline, the product **6B** was obtained as a white solid (yield 45% for 2 steps). ^1H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.8 Hz, 1H), 7.50 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.46 (d, *J* = 7.1 Hz, 1H), 7.24 (s, 2H), 7.19 (dd, *J* = 7.9, 7.1 Hz, 1H), 6.72 (d, *J* = 8.8 Hz, 1H), 5.50 (s, 1H), 4.22 (d, *J* = 5.2 Hz, 2H), 2.83 (d, *J* = 4.9 Hz, 3H), 2.65 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.9, 155.2, 146.1, 138.0, 134.0, 130.1, 125.5, 123.4, 122.5, 111.6, 46.5, 26.0, 17.9. HRMS (ESI) $[M+H]^+$ found m/z 230.1282, calcd for $C_{13}H_{16}N_3O$ 230.1288.

2-((6-Chloroquinolin-2-yl)amino)-N-methylacetamide (6C). Following the procedure of **6** starting from 6-chloro-2-(2,2-dimethoxyethoxy)quinoline, the product **6C** was obtained as a white solid (yield 53% for 2 steps). ^1H NMR (400 MHz, MeOD-d_4) δ 7.86 (d, *J* = 9.0 Hz, 1H), 7.65 (s, 1H), 7.59 (d, *J* = 9.0 Hz, 1H), 7.46 (d, *J* = 8.9 Hz, 1H), 6.88 (d, *J* = 8.8 Hz, 1H), 4.13 (s, 2H), 2.76 (s, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.6, 157.3, 146.6, 135.9, 129.6, 128.0, 126.6, 125.6, 124.4, 114.9, 44.3, 26.0. HRMS (ESI) $[M+H]^+$ found m/z 250.0739, calcd for $C_{12}H_{13}ClN_3O$ 250.0742.

2-((8-Bromoquinolin-2-yl)amino)-N-methylacetamide (6D). Following the procedure of **6** starting from 8-bromo-2-(2,2-dimethoxyethoxy)quinoline, the product **6D** was obtained as a white solid (yield 42% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.81 (d, *J* = 8.9 Hz, 1H), 7.59 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 1H), 6.76 (d, *J* = 8.9 Hz, 1H), 6.10 (s, 1H), 4.23 (d, *J* = 6.0 Hz, 2H), 2.85 (d, *J* = 4.9 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5, 156.7, 144.4, 137.9, 133.1, 127.3, 124.8, 123.0, 121.2, 113.2, 46.8, 26.0. HRMS (ESI) $[M+H]^+$ found m/z 294.0245, calcd for $C_{12}H_{13}BrN_3O$ 294.0237.

2-((3-Chloroisoquinolin-1-yl)amino)-N-methylacetamide (6E). Following the procedure of **6** starting from 3-chloro-1-(2,2-dimethoxyethoxy)isoquinoline, the product **6E** was obtained as a white solid (yield 52% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 8.4 Hz, 1H), 7.65 – 7.58 (m, 2H), 7.50 – 7.42 (m, 1H), 7.01 (s, 1H), 6.49 (s, 1H), 6.39 (s, 1H), 4.29 (d, *J* = 5.0 Hz, 2H), 2.91 (d, *J* = 4.8 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 154.7, 143.8, 138.7, 130.8, 126.4, 126.2, 122.0, 116.6, 109.4, 45.4, 26.3. HRMS (ESI) $[M+H]^+$ found m/z 250.0739, calcd for $C_{12}H_{13}ClN_3O$ 250.0742.

N-methyl-2-((6-phenylquinolin-2-yl)amino)acetamide (6F). Following the procedure of **6** starting from 2-(2,2-dimethoxyethoxy)-6-phenylquinoline, the product **6F** was obtained as a white solid (yield 75% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.8 Hz, 1H), 7.82 (t, 2H), 7.76 (d, *J* = 9.1 Hz, 1H), 7.67 (d, *J* = 8.0 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.36 (t, *J* = 7.4 Hz, 1H), 6.83 (s, 1H), 6.72 (d, *J* = 8.8 Hz, 1H), 5.50 (s, 1H), 4.23 (d, *J* = 5.1 Hz, 2H), 2.84 (d, *J* = 4.9 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.2, 156.0, 146.7, 140.7, 138.0, 135.7, 129.3, 128.9, 127.1, 127.1, 126.5, 125.4, 123.9, 112.3, 45.9, 26.2. HRMS (ESI) $[M+H]^+$ found m/z 292.1449, calcd for $C_{18}H_{18}N_3O$ 292.1444.

2-((6-(4-Methoxyphenyl)quinolin-2-yl)amino)-N-methylacetamide (6G). Following the procedure of **6** starting from 2-(2,2-dimethoxyethoxy)-6-(4-methoxyphenyl)quinoline, the product **6G** was obtained as a white solid (yield 54% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.91 (d, *J* = 9.0 Hz, 1H), 7.87 (d, *J* = 1.9 Hz, 1H), 7.75 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.65 (d, *J* = 8.7 Hz, 2H), 7.51 (d, 1H), 7.28 (t, *J* = 5.5 Hz, 1H), 7.01 (d, *J* = 8.7 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 1H), 4.00 (d, *J* = 5.5 Hz, 2H), 3.78 (s, 3H), 2.60 (d, *J* = 4.0 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.8, 159.0, 157.0, 147.1, 136.9, 133.3, 132.8, 128.1, 128.0, 126.6, 124.7, 123.8, 114.8, 114.1, 55.6, 44.5, 26.0. HRMS (ESI) $[M+H]^+$ found m/z 322.1549, calcd for $C_{19}H_{20}N_3O_2$ 322.155.

N-methyl-2-((6-(4-(trifluoromethyl)phenyl)quinolin-2-yl)amino)acetamide (6H). Following the procedure of **6** starting from 2-(2,2-dimethoxyethoxy)-6-(4-(trifluoromethyl)phenyl)quinoline, the product **6H** was obtained as a white solid (yield 65% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.06 (d, *J* = 1.8 Hz, 1H), 7.96 (t, 3H), 7.86 (dd, *J* = 8.7, 2.0 Hz, 1H), 7.80 (d, *J* = 8.3 Hz, 2H), 7.57 (d, 1H), 7.41 (t, *J* = 5.8 Hz, 1H), 6.93 (d, *J* = 8.9 Hz, 1H), 4.02 (d, *J* = 5.4 Hz, 2H), 2.60 (d, *J* = 3.9 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.6, 157.5, 148.1, 144.4, 137.1, 131.7, 128.3, 127.5, 126.8, 126.3, 126.2, 126.2, 126.2, 123.8, 114.5, 44.4, 26.0. HRMS (ESI) $[M+H]^+$ found m/z 360.1317, calcd for $C_{19}H_{17}FN_3O$ 360.1318.

2-((6-(4-Cyanophenyl)quinolin-2-yl)amino)-N-methylacetamide (6I). Following the procedure of **6** starting from 4-(2-(2,2-dimethoxyethoxy)quinolin-6-yl)benzonitrile, the product **6I** was obtained as a white solid (yield 78% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.11 (s, 1H), 7.94 (dt, *J* = 19.1, 9.6 Hz, 7H), 7.59 (d, *J* = 8.8 Hz, 1H), 7.49 (t, *J* = 5.6 Hz, 1H), 6.96 (d, *J* = 9.1 Hz, 1H), 4.04 (d, *J* = 5.2 Hz, 2H), 2.62 (d, *J* = 4.4 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ

170.6, 157.6, 148.3, 144.9, 137.1, 133.3, 131.3, 128.2, 127.6, 126.9, 126.5, 123.7, 119.5, 114.5, 109.7, 44.4, 26.0. HRMS (ESI) $[M+H]^+$ found m/z 317.1401, calcd for $C_{19}H_{17}N_4O$ 317.1397.

Methyl 4-(2-((2-(methylamino)-2-oxoethyl)amino)quinolin-6-yl)benzoate (6J). Following the procedure of **6** starting from methyl 4-(2-(2,2-dimethoxyethoxy)quinolin-6-yl)benzoate, the product **6J** was obtained as a white solid (yield 57% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.09 (d, J = 2.0 Hz, 1H), 8.05 (d, J = 8.4 Hz, 2H), 7.98 (d, J = 8.9 Hz, 1H), 7.94 – 7.88 (m, 4H), 7.59 (d, J = 8.7 Hz, 1H), 7.44 (t, J = 5.5 Hz, 1H), 6.95 (d, J = 8.9 Hz, 1H), 4.04 (d, J = 5.6 Hz, 2H), 3.88 (s, 3H), 2.62 (d, J = 4.6 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 170.7, 166.6, 157.5, 148.1, 145.0, 137.1, 131.9, 130.3, 128.3, 128.2, 127.0, 126.8, 126.3, 123.8, 114.4, 56.5, 52.6, 26.0. HRMS (ESI) $[M+H]^+$ found m/z 350.1501, calcd for $C_{20}H_{20}N_3O_3$ 350.1499.

2-((7-(2-Fluorophenyl)-4-methylquinolin-2-yl)amino)-N-methylacetamide (6K). Following the procedure of **6** starting from 2-(2,2-dimethoxyethoxy)-7-(2-fluorophenyl)-4-methylquinoline, the product **6K** was obtained as a white solid (yield 70% for 2 steps). ^{1}H NMR (400 MHz, MeOD-d_4) δ 7.83 (d, J = 8.5 Hz, 1H), 7.80 (s, 1H), 7.54 (t, J = 7.8 Hz, 1H), 7.41 (d, J = 8.5 Hz, 1H), 7.39 – 7.35 (m, 1H), 7.27 (d, J = 7.5 Hz, 1H), 7.25 – 7.20 (m, 1H), 6.70 (s, 1H), 4.14 (s, 2H), 2.76 (s, 3H), 2.56 (s, 3H). ^{13}C NMR (126 MHz, MeOD) δ 172.4, 160.3, 158.4, 156.5, 146.9, 144.3, 136.1, 130.1, 128.6, 125.4, 123.8, 123.0, 122.7, 122.3, 115.3, 112.2, 43.7, 24.5, 16.8. HRMS (ESI) $[M+H]^+$ found m/z 324.1507, calcd for $C_{19}H_{19}FN_3O$ 324.1507.

N-(2-(2,5-dimethoxyphenyl)-2-hydroxyethyl)-2-(quinolin-2-ylamino)acetamide (8a). Following the procedure of **6** starting from midodrine hydrochloride, the product **8a** was obtained as a white solid (yield 72% for 2 steps). ^{1}H NMR (400 MHz, MeOD-d_4) δ 7.88 (d, J = 8.9 Hz, 1H), 7.62 (t, J = 8.0 Hz, 2H), 7.53 – 7.48 (m, 1H), 7.24 (t, 1H), 7.00 (d, 1H), 6.81 (d, 1H), 6.75 (d, 1H), 6.70 (dd, J = 8.9, 3.1 Hz, 1H), 5.08 (dd, J = 7.1, 4.3 Hz, 1H), 4.12 (s, 2H), 3.72 (s, 3H), 3.68 (s, 3H), 3.56 (dd, 1H), 3.39 (dd, 1H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 172.5, 156.8, 153.8, 150.3, 147.3, 137.2, 131.1, 129.1, 127.2, 125.4, 123.7, 122.0, 112.5, 112.3, 111.1, 66.7, 54.9, 54.6, 45.1, 44.6. HRMS (ESI) $[M+H]^+$ found m/z 382.1761, calcd for $C_{21}H_{24}N_3O_4$ 382.1761.

(1S,3S,5S)-2-((S)-2-((1s,3S,5R,7S)-3-hydroxyadamantan-1-yl)-2-(quinolin-2-ylamino)acetyl)-2-azabicyclo[3.1.0]hexane-3-carbonitrile (8b). Following the procedure of 6 starting from saxagliptin, the product **8b** was obtained as a white solid (yield 46% for 2 steps). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 – 7.46 (m, 5H), 7.22 (t, J = 7.3 Hz, 1H), 6.65 (d, J = 8.7 Hz, 1H), 5.94 (d, J = 9.5 Hz, 1H), 5.27 (d, J = 9.4 Hz, 1H), 5.00 (dd, J = 10.6, 2.4 Hz, 1H), 4.63 (td, J = 6.2, 2.6 Hz, 1H), 2.75 (s, 1H), 2.51 (ddd, J = 13.8, 10.7, 5.8 Hz, 1H), 2.36 (dd, J = 13.7, 2.4 Hz, 1H), 2.32 – 2.23 (m, 3H), 2.07 (d, J = 11.6 Hz, 1H), 2.00 – 1.92 (m, 2H), 1.86 (dd, J = 25.7, 12.0 Hz, 2H), 1.73 (q, J = 14.1 Hz, 6H), 1.59 (d, J = 14.3 Hz, 3H), 1.28 (s, 2H), 1.18 (s, 1H), 1.17 – 1.11 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.7, 156.6, 147.5, 136.9, 129.2, 127.5, 126.1, 123.8, 122.2, 119.5, 113.2, 68.7, 58.9, 46.2, 45.3, 44.6, 44.2, 40.7, 38.3, 38.0, 37.7, 35.5, 30.6, 30.4, 30.3, 17.5, 13.7. HRMS (ESI) $[M+H]^+$ found m/z 443.2432, calcd for $C_{27}H_{31}N_4O_2$ 443.2442. [α] -111.0 (c = 0.091, CH_3OH).

Methyl quinolin-2-yl-L-tyrosyl-L-seryl-L-leucinate (8c). Following the procedure of **6** starting from methyl tyroserleutide, the product **8c** was obtained as a white solid (yield 56% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.16 (s, 1H), 8.20 (d, J = 7.9 Hz, 1H), 7.98 (d, J = 7.9 Hz, 1H), 7.84 (d, J = 8.9 Hz, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.50 – 7.42 (m, 2H), 7.21 (d, J = 7.6 Hz, 1H), 7.17 (s, 1H), 7.13 (d, J = 7.6 Hz, 2H), 6.85 (d, J = 8.9 Hz, 1H), 6.62 (d, J = 7.6 Hz, 2H), 4.84

(t, J = 5.0 Hz, 1H), 4.76 (s, 1H), 4.31 (dd, J = 14.0, 7.0 Hz, 2H), 4.15 (d, J = 5.0 Hz, 1H), 3.61 (s, 3H), 3.19 – 3.17 (m, 3H), 1.58 – 1.44 (m, 2H), 1.41 – 1.35 (m, 2H), 0.81 – 0.75 (m, 6H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 173.1, 173.1, 170.5, 156.8, 156.1, 147.9, 136.8, 130.6, 129.4, 129.0, 127.9, 126.2, 123.5, 121.9, 115.3, 113.6, 62.1, 56.7, 55.3, 52.3, 50.6, 49.1, 37.2, 24.5, 23.1, 21.7. HRMS (ESI) $[M+H]^+$ found m/z 523.2554, calcd for $C_{28}H_{35}N_4O_6$ 523.2551. [α] -7.2 (c = 0.107, CH_3OH).

(S)-N-(4-(hydroxymethyl)phenyl)-2-((S)-3-methyl-2-(quinolin-2-ylamino)butanamido)-5-ureidopentanamide (8d). Following the procedure of **6** starting from Val-Cit-PAB-OH, the product **8d** was obtained as a white solid (yield 56% for 2 steps). ^{1}H NMR (400 MHz, MeOD-d_4) δ 7.87 (d, J = 8.9 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.47 (ddd, J = 8.4, 7.0, 1.4 Hz, 1H), 7.39 (d, J = 8.5 Hz, 2H), 7.25 (d, J = 8.6 Hz, 2H), 7.22 – 7.17 (m, 1H), 6.91 (d, J = 8.9 Hz, 1H), 4.58 – 4.53 (m, 3H), 4.49 (d, J = 7.5 Hz, 1H), 3.37 (s, 2H), 3.09 (dt, J = 13.3, 6.7 Hz, 1H), 2.99 (dt, J = 13.5, 6.7 Hz, 1H), 2.30 – 2.19 (m, 1H), 1.94 – 1.84 (m, 1H), 1.80 – 1.68 (m, 1H), 1.60 – 1.43 (m, 2H), 1.11 (d, J = 6.9 Hz, 3H), 1.09 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 174.4, 170.9, 160.8, 157.0, 147.4, 137.4, 137.0, 136.9, 129.0, 127.1, 127.1, 125.4, 123.6, 121.9, 120.0, 112.6, 63.4, 60.9, 53.4, 48.4, 30.4, 29.3, 26.3, 18.7, 17.9. HRMS (ESI) $[M+H]^+$ found m/z 507.2724, calcd for $C_{27}H_{35}N_6O_4$ 507.2714. [α] -186.3 (c = 0.096, CH_3OH).

(S)-2-((S)-2-((7-(2-fluorophenyl)-4-methylquinolin-2-yl)amino)-3-methylbutanamido)-N-(4-(hydroxymethyl)phenyl)-5-ureidopentanamide (8e). Following the procedure of **6** starting from Val-Cit-PAB-OH, the product **8e** was obtained as a white solid (yield 52% for 2 steps). ^{1}H NMR (500 MHz, MeOD-d_4) δ 7.88 (d, J = 8.4 Hz, 1H), 7.80 (s, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.44 (d, J = 8.4 Hz, 1H), 7.42 – 7.37 (m, 1H), 7.33 (d, J = 8.5 Hz, 2H), 7.28 (t, J = 7.5 Hz, 1H), 7.24 – 7.21 (m, 1H), 7.20 (d, J = 8.4 Hz, 2H), 6.82 (s, 1H), 4.56 (dd, J = 9.0, 5.1 Hz, 1H), 4.52 (s, 2H), 4.48 (d, J = 7.4 Hz, 1H), 3.11 – 3.04 (m, 1H), 3.01 – 2.94 (m, 1H), 2.61 (s, 3H), 2.31 – 2.22 (m, 1H), 1.89 (dt, J = 14.3, 6.6 Hz, 1H), 1.78 – 1.68 (m, 1H), 1.57 – 1.47 (m, 2H), 1.13 (d, J = 6.8 Hz, 3H), 1.11 (d, J = 6.8 Hz, 3H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 175.8, 172.3, 162.2, 160.3, 158.7, 148.8, 146.2, 138.8, 138.3, 137.9, 132.1, 130.5, 130.4, 128.4, 127.4, 125.7, 124.8, 124.6, 124.1, 121.5, 117.2, 117.0, 114.2, 64.8, 62.4, 54.8, 31.7, 30.7, 27.7, 20.1, 19.3, 18.7. HRMS (ESI) $[M+H]^+$ found m/z 615.3081, calcd for $C_{34}H_{40}FN_6O_4$ 615.309. [α] -0.8 (c = 0.105, CH_3OH).

(S)-1-((4R,7S,10S,13S,16S,19S)-7-(2-amino-2-oxoethyl)-10-(3-amino-3-oxopropyl)-13-((S)-sec-butyl)-16-(4-hydroxybenzyl)-6,9,12,15,18-pentaoxo-19-(quinolin-2-ylamino)-1,2-dithia-5,8,11,14,17-pentaazacycloicosane-4-carbonyl)-N-((S)-1-((2-amino-2-oxoethyl)amino)-4-methyl-1-oxopentan-2-yl)pyrrolidine-2-carboxamide (8f). Following the procedure of **6** starting from oxytocin, the product **8f** was obtained as a white solid (yield 42% for 2 steps). ^{1}H NMR (400 MHz, MeOD-d_4) δ 8.36 (d, J = 9.2 Hz, 1H), 7.96 (d, J = 7.8 Hz, 1H), 7.89 (t, J = 7.8 Hz, 1H), 7.74 (d, J = 8.3 Hz, 1H), 7.61 (t, J = 7.4 Hz, 1H), 7.00 (d, 4H), 6.18 (s, 1H), 5.17 (s, 1H), 4.87 (d, J = 6.8 Hz, 2H), 4.50 – 4.42 (m, 1H), 4.31 (dd, J = 9.4, 5.4 Hz, 1H), 4.07 (d, J = 6.5 Hz, 1H), 3.95 (d, J = 7.6 Hz, 1H), 3.91 (d, J = 17.1 Hz, 1H), 3.81 (d, J = 8.4 Hz, 1H), 3.76 (d, J = 17.0 Hz, 1H), 3.68 (dt, J = 10.4, 5.7 Hz, 1H), 3.42 (dt, J = 13.6, 4.3 Hz, 2H), 3.37 (s, 4H), 2.91 (s, 1H), 2.71 (s, 1H), 2.39 (t, J = 6.9 Hz, 2H), 2.31 – 2.14 (m, 3H), 2.03 – 1.83 (m, 4H), 1.68 (qd, J = 9.7, 9.3, 5.1 Hz, 4H), 1.37 – 1.24 (m, 1H), 1.05 (d, J = 6.7 Hz, 3H), 1.00 (t, J = 7.4 Hz, 3H), 0.94 (d, J = 6.3 Hz,

3H), 0.91 (d, J = 6.1 Hz, 3H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 176.6, 173.7, 173.5, 173.2, 172.9, 172.1, 168.4, 167.7, 157.7, 157.4, 155.6, 133.1, 129.8, 128.7, 127.2, 125.9, 121.8, 117.7, 115.8, 114.4, 113.5, 61.0, 60.8, 55.8, 54.9, 53.6, 53.0, 52.3, 50.6, 48.5, 48.2, 41.9, 39.7, 37.7, 35.7, 31.4, 29.0, 25.6, 24.5, 24.5, 22.1, 20.5, 14.6, 10.2. HRMS (ESI) $[M+H]^+$ found m/z 1132.4742, calcd for $C_{52}H_{70}N_{13}O_{12}S_2$ 1132.4742. [α] -110.2(c = 0.077, CH_3OH).

(S)-N-((S)-1-amino-3-hydroxy-1-oxopropan-2-yl)-1-(quinolin-2-yl-D-tyrosyl-L-alanyl-D-phenylalanylglycyl-D-tyrosyl)pyrrolidine-2-carboxamide (8g). Following the procedure of 6 starting from dermorphin, the product **8g** was obtained as a white solid (yield 47% for 2 steps). ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.25 (s, 1H), 9.17 (s, 1H), 8.27 (d, J = 8.0 Hz, 1H), 8.20 (s, 1H), 8.12 (d, J = 8.6 Hz, 1H), 8.00 (d, J = 6.9 Hz, 1H), 7.82 (d, J = 8.9 Hz, 1H), 7.75 (d, J = 7.4 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.49 (d, J = 7.8 Hz, 1H), 7.46 – 7.38 (m, 1H), 7.18 (dd, J = 13.4, 5.1 Hz, 5H), 7.12 (d, J = 7.5 Hz, 3H), 7.10 – 7.05 (m, 3H), 6.85 (d, J = 8.9 Hz, 1H), 6.66 (d, J = 8.2 Hz, 2H), 6.62 (d, J = 8.0 Hz, 2H), 4.91 (t, J = 5.3 Hz, 1H), 4.74 (d, J = 4.4 Hz, 1H), 4.60 (s, 1H), 4.47 (s, 1H), 4.35 (d, J = 6.0 Hz, 1H), 4.26 – 4.04 (m, 2H), 3.78 – 3.69 (m, 1H), 3.68 – 3.54 (m, 4H), 2.97 (d, J = 10.9 Hz, 3H), 2.87 – 2.76 (m, 1H), 2.69 – 2.60 (m, 1H), 2.57 (d, J = 12.8 Hz, 1H), 1.93 (d, J = 51.9 Hz, 4H), 0.82 (d, J = 6.9 Hz, 3H). ^{13}C NMR (125 MHz, DMSO-d_6) δ 172.5, 172.3, 172.3, 171.6, 171.6, 171.0, 168.8, 156.6, 156.3, 156.1, 147.9, 138.2, 136.8, 130.7, 130.6, 129.6, 129.5, 128.8, 128.4, 128.1, 127.8, 126.6, 126.2, 123.5, 121.9, 115.5, 115.3, 113.6, 62.0, 60.4, 56.5, 55.5, 54.1, 53.1, 48.5, 47.4, 42.0, 38.1, 37.5, 36.7, 29.3, 24.9, 18.8. HRMS (ESI) $[M+H]^+$ found m/z 928.3993, calcd for $C_{49}H_{54}N_9O_{10}$ 928.3999. [α] -19.9 (c = 0.098, CH_3OH).

(4R,7S,10S,13R,16S,19R)-13-((1H-indol-3-yl)methyl)-10-(4-aminobutyl)-16-benzyl-N-(1,3-dihydroxybutan-2-yl)-7-((R)-1-hydroxyethyl)-6,9,12,15,18-pentaoxo-19-((R)-3-phenyl-2-(quinolin-2-ylamino)propanamido)-1,2-dithia-5,8,11,14,17-pentaazacycloicosane-4-carboxamide (8h). Following the procedure of **6** starting from otreotide, the product **8h** was obtained as a white solid (yield 41% for 2 steps). ^{1}H NMR (500 MHz, Methanol-d_4) δ 8.27 (d, J = 9.4 Hz, 1H), 7.85 (d, J = 7.9 Hz, 1H), 7.78 (dd, J = 14.4, 7.1 Hz, 2H), 7.52 (t, J = 7.8 Hz, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.40 – 7.35 (m, 3H), 7.27 – 7.22 (m, 3H), 7.19 (t, J = 7.9 Hz, 4H), 7.16 – 7.10 (m, 3H), 7.04 (t, J = 7.4 Hz, 1H), 7.00 (s, 1H), 5.25 (d, J = 9.4 Hz, 2H), 4.68 (dd, J = 8.8, 6.2 Hz, 1H), 4.49 (d, J = 5.6 Hz, 1H), 4.38 – 4.32 (m, 1H), 4.23 (dd, J = 11.0, 5.3 Hz, 1H), 4.17 (dd, J = 6.4, 2.8 Hz, 1H), 4.02 (dd, J = 10.9, 3.2 Hz, 1H), 3.89 – 3.85 (m, 1H), 3.74 (s, 2H), 3.50 (d, J = 9.2 Hz, 1H), 3.33 (s, 2H), 3.18 – 2.90 (m, 8H), 2.86 (dd, J = 13.8, 5.2 Hz, 1H), 2.61 (dq, J = 18.7, 12.4, 9.4 Hz, 2H), 1.35 – 1.23 (m, 9H), 0.62 – 0.43 (m, 2H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 173.9, 173.2, 171.2, 171.0, 170.9, 168.8, 152.3, 136.3, 136.2, 135.4, 129.0, 128.7, 128.2, 128.1, 127.6, 126.9, 126.7, 126.1, 125.3, 123.1, 121.1, 120.8, 118.3, 117.7, 110.7, 108.4, 66.8, 61.2, 59.3, 57.0, 56.1, 55.8, 54.5, 53.3, 53.0, 52.2, 48.2, 38.8, 38.6, 38.5, 29.5, 26.0, 25.5, 21.5, 18.7, 18.4. HRMS (ESI) $[M+H]^+$ found m/z 1146.4891, calcd for $C_{58}H_{72}N_{11}O_{10}S_2$ 1146.49. [α] -31.8 (c = 0.067, CH_3OH).

(4R,7S,10S,13R,16S,19R)-13-((1H-indol-3-yl)methyl)-10-(4-aminobutyl)-16-benzyl-N-(1,3-dihydroxybutan-2-yl)-7-((R)-1-hydroxyethyl)-19-((R)-2-((6-methoxyquinolin-2-yl)amino)-3-phenylpropanamido)-6,9,12,15,18-pentaoxo-1,2-dithia-5,8,11,14,17-pentaazacycloicosane-4-carboxamide (8i).Following the procedure of **6** starting from otreotide, the product **8i** was

obtained as a white solid (yield 46% for 2 steps). ^{1}H NMR (500 MHz, Methanol-d_4) δ 8.35 (d, J = 9.4 Hz, 1H), 8.23 (d, J = 8.7 Hz, 1H), 8.14 – 8.00 (m, 2H), 7.84 (d, J = 27.0 Hz, 1H), 7.71 – 7.64 (m, 2H), 7.51 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 7.6 Hz, 2H), 7.39 (d, J = 8.1 Hz, 1H), 7.31 (t, J = 7.5 Hz, 2H), 7.27 – 7.19 (m, 5H), 7.18 – 7.13 (m, 2H), 7.08 (dd, J = 8.4, 6.7 Hz, 3H), 7.02 (s, 1H), 5.30 (t, J = 12.2 Hz, 2H), 4.71 (dd, J = 8.9, 6.0 Hz, 1H), 4.54 – 4.47 (m, 1H), 4.44 – 4.33 (m, 1H), 4.25 (dd, J = 10.9, 5.4 Hz, 1H), 4.23 – 4.16 (m, 1H), 4.06 (dd, J = 11.0, 3.5 Hz, 1H), 3.89 (s, 4H), 3.77 (d, J = 5.2 Hz, 2H), 3.54 (dd, J = 14.0, 5.0 Hz, 1H), 3.39 (s, 2H), 3.23 – 2.94 (m, 8H), 2.89 (dd, J = 13.8, 5.3 Hz, 1H), 2.65 (tt, J = 20.1, 10.6 Hz, 2H), 1.28 (m, 9H), 0.69 – 0.50 (m, 2H). ^{13}C NMR (125 MHz, MeOD-d_4) δ 174.2, 173.6, 171.6, 171.3, 169.2, 160.0, 152.5, 138.6, 136.6, 136.5, 135.8, 131.2, 129.5, 129.4, 129.3, 129.0, 128.4, 128.0, 127.8, 127.2, 127.1, 126.4, 125.2, 123.4, 122.0, 121.1, 118.6, 118.0, 114.2, 110.9, 108.8, 67.1, 59.7, 57.3, 56.4, 54.8, 54.4, 53.5, 53.3, 52.6, 48.4, 38.8, 31.6, 28.9, 26.3, 25.5, 22.3, 19.0, 13.0. HRMS (ESI) $[M+H]^+$ found m/z 1252.5299, 20

calcd for $C_{65}H_{78}N_{11}O_{11}S_2$ 1252.5318. [α] 1.8 (c = 0.055, CH_3OH).

3. Biological studies

3.1 Cell prolifation inhibition assay

The cancer cell lines BEL-7402 and SMMC-7721 were purchased from the American Type Culture Collection (Manassas, VA, USA). All cell lines were maintained in DMEM containing 10% fetal bovine serum at 37 °C and 5% CO_2 in a humid environment.

Tumor cells were seeded in the 96-wells plates overnight and then were treated with increasing doses of compounds in triplicate for 72 h. The anti-proliferative activities were accessed by SRB assay. Then the OD was measured at 510 nm wavelength using Synergy H4 Hybrid reader (BioTek, Winooski, VT, USA) using Gen5.0 software (BioTek). The IC_{50} values were calculated using the software Prism 5 (GraphPad Software, Inc). The test results are shown in the following table.

Table S1. Liver cancer cell proliferation inhibition assays of selected compounds

Compound	Proliferation inhibition IC_{50} (μM)	
	BEL-7402	SMMC-7721
YSL	>100	>100
YSL-M	>100	>100
8c	52.57±2.47	63.30±6.35

3.2 [^{35}S]GTP$_\gamma$S Binding Assay

Transfer 10μl standard protein to a centrifuge tube (final concertration 0.5 mg/ml). Transfer the sample and 0, 1, 2, 4, 8, 12, 16, 20 μl bovine serum albumin (BSA) standard protein into the wells of a 96-well plate. The solution was supplemented to 20 μl using diluted standard. 200 μl of BCA working solution was added to each well then the plate was placed at 37 °C for 30 min. Meanwhile, set the plate reader to read absorption at 560 nm. The protein concentration was calculated from the standard curve.

The prepared membrane receptor is diluted to the desired concentration with a reaction buffer (R.B). Load according to the following table (unit: μl).

	R.B	[^{35}S]GTP$_\gamma$S 0.1-0.2nM	GTP$_\gamma$S 20μM	GDP 40μM	Agonist	Protein 20-30μg
NS binding	30	10	10	0	0	50
Basal	30	10	0	10	0	50
Agonist	20	10	0	10	10	50

The reaction tube was incubated for 1 hour in a 27 °C water bath, filtered under reduced pressure on a glass fiber membrane, and flash-counted. Calculate according to the following formula: [^{35}S]GTP$_\gamma$S binding rate=100 × (cpm_{sample}-$cpm_{non\text{-}specific}$) / (cpm_{basal}-$cpm_{non\text{-}specific}$)

Table S2. μ-opioid receptor (MOR) agonist activity assays

Compound	(MOR) (mean±sem)	
	EC_{50}(nM)	Emax(%)
Dermorphin	61.3±10.6	218.8±7.1
8g	223.9±25.1	202.7±5.1

3.3 *In vitro* liver stability assessment

Adhering fat and connective tissue were removed from 5 g fresh pig liver. Wash it with cold saline, blot water on the surface with filter paper and weigh it. Add appropriate PBS buffer, cut the pig liver with scissor and make a 20 ml homogenate with a homogenizer with a frequency of 30/s for 4 min. Tested compound (final concentration 1 mg/ml and co-solvent (1% DMSO)) were added to 20 ml of pig liver homogenate, stir well and stand. Take 1 ml of the sample twice in the six time periods of 0.25 h, 0.5 h, 1 h, 1.5 h, 2 h and 3 h respectively and methanol (500μl) was added to terminate the reaction. After centrifugation (1000 rpm, 6 min), the supernatant was separated and extracted twice with 750 μl of water-saturated n-butanol. Then extracted samples were analyzed by HPLC. Reversed phase HPLC was carried out on an Agilent Zorbax SB-C18 column (5 μm, 4.6 × 250 mm) from Agilent, with a flow rate of 1 mL/min at 25 °C. The gradient conditions used are 50% A (MeOH), 50% B (H_2O + 0.2% CH_3COOH), to 95% A and 5% B in 16 min. Acquisition for the UV-DAD detector was set to 210, 254, and 280 nm.

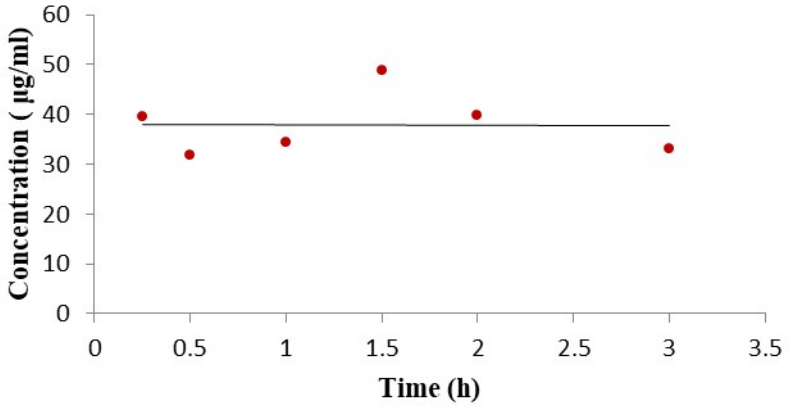


Figure S2. The concentration of 8e changes with time

4. DFT Studies

4.1 Computational Methods

All computations were performed with the Gaussian 09 [1] series of programs. All the structures were optimized using the density functional M06-2*X* methods [2] at the 6-311+G(d) level. A Solvent effects of 1-butanol were considered by using the SMD model [3]. Frequencies calculations were performed to judge them as local minima or transition states and obtain the thermal corrections to the Gibbs free energies and enthalpies. The Gibbs free energies were used to describe the reaction energies.

4.2 M06-2X calculated energies for reported complexes and transition states

Geometry	E[1]	H[2]	G[3]	IF[4]
5a	-669.441609	-669.204898	-669.255131	
7	-303.8408662	-303.71088	-303.749907	
TS	-973.2815993	-972.914091	-972.981862	-297.80
9	-973.288612	-972.918828	-972.986512	

[1]Single point energies calculated by M06-2*X* at the 6-311+g(d) level in 1-butanol solvent.
[2]Enthalpies calculated by M06-2*X* at the 6-311+g(d) level in 1-butanol solvent.
[3]Gibbs free energies calculated by M06-2*X* at the 6-311+g(d) level in 1-butanol solvent.
[4]M06-2*X*/6-311+g(d) calculated imaginary frequencies for transition states.
The unit of energy values in the above table are Hartree/Particle (a.u.).

4.3 Cartesian coordinates of minimum energy structures

5a
C 2.385000 -2.003000 0.303000
C 1.076000 -1.576000 0.371000
C 0.807000 -0.217000 0.166000
C 1.840000 0.700000 -0.121000
C 3.166000 0.225000 -0.184000
C 3.434000 -1.107000 0.028000
H 2.606000 -3.053000 0.463000
H 0.274000 -2.277000 0.572000
C 1.510000 2.070000 -0.345000
H 3.962000 0.930000 -0.400000
H 4.453000 -1.472000 -0.019000
C 0.224000 2.521000 -0.284000
C -0.768000 1.573000 0.020000
H 2.314000 2.763000 -0.568000
H -0.060000 3.551000 -0.449000
O -2.047000 1.838000 0.119000
C -2.725000 0.649000 0.608000
C -1.714000 -0.486000 0.415000
H -2.959000 0.822000 1.657000
H -3.627000 0.507000 0.018000
N -0.479000 0.291000 0.239000
O -1.894000 -1.226000 -0.750000
C -2.798000 -2.314000 -0.572000
H -3.777000 -1.961000 -0.237000
H -2.900000 -2.794000 -1.543000
H -2.398000 -3.028000 0.154000
H -1.635000 -1.131000 1.294000

7
C 0.062000 0.527000 -0.008000
O 0.642000 1.615000 0.081000
N 0.707000 -0.641000 -0.051000
H 0.141000 -1.474000 -0.146000
C 2.154000 -0.724000 -0.004000
H 2.443000 -1.772000 -0.026000
H 2.604000 -0.214000 -0.859000
H 2.538000 -0.270000 0.911000
C -1.452000 0.462000 -0.096000
H -1.844000 1.175000 0.637000
H -1.715000 0.848000 -1.085000
N -1.977000 -0.892000 0.044000
H -2.116000 -1.116000 1.024000
H -2.885000 -0.960000 -0.400000

TS
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C -3.012000 1.247000 -0.097000

C -2.222000 0.136000 0.204000
C -2.737000 -1.171000 0.103000
C -4.069000 -1.339000 -0.302000
C -4.856000 -0.243000 -0.602000
H -4.938000 1.907000 -0.739000
H -2.601000 2.248000 -0.028000
C -1.886000 -2.287000 0.454000
H -4.469000 -2.345000 -0.374000
H -5.883000 -0.380000 -0.919000
C -0.585000 -2.120000 0.758000
C -0.049000 -0.778000 0.694000
H -2.326000 -3.279000 0.473000
H 0.082000 -2.931000 1.022000
O 1.071000 -0.448000 1.336000
C 1.057000 0.983000 1.585000
C -0.182000 1.507000 0.848000
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H 1.983000 1.404000 1.202000
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H 6.027000 -0.880000 0.712000
H 5.718000 0.296000 -0.581000
H 4.964000 0.510000 1.011000
C 2.013000 -1.464000 -1.226000
H 2.279000 -1.767000 -2.244000
H 1.985000 -2.364000 -0.607000
N 0.714000 -0.800000 -1.190000
H 0.803000 0.173000 -1.490000
H 0.041000 -1.263000 -1.797000

9

C -4.369000 1.009000 -0.523000
C -3.043000 1.228000 -0.171000
C -2.230000 0.136000 0.136000
C -2.744000 -1.174000 0.094000
C -4.081000 -1.365000 -0.264000
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C -1.871000 -2.274000 0.484000
H -4.476000 -2.376000 -0.287000
H -5.928000 -0.443000 -0.853000
C -0.560000 -2.103000 0.698000
C 0.036000 -0.759000 0.463000
H -2.320000 -3.253000 0.621000
H 0.101000 -2.902000 1.013000
O 1.076000 -0.412000 1.306000
C 0.963000 0.992000 1.641000
C -0.219000 1.515000 0.816000
H 0.764000 1.066000 2.709000
H 1.902000 1.484000 1.391000
N -0.908000 0.288000 0.542000
O 0.163000 2.087000 -0.421000
C 0.702000 3.396000 -0.301000
H 1.623000 3.402000 0.289000
H 0.927000 3.737000 -1.310000
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H -0.847000 2.213000 1.378000
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H 5.132000 0.398000 0.969000
H 6.157000 -0.951000 0.437000
H 5.673000 0.304000 -0.720000
C 1.966000 -1.480000 -1.082000
H 2.113000 -1.783000 -2.120000
H 1.930000 -2.371000 -0.456000
N 0.683000 -0.747000 -0.990000
H 0.853000 0.239000 -1.249000
H -0.002000 -1.126000 -1.649000

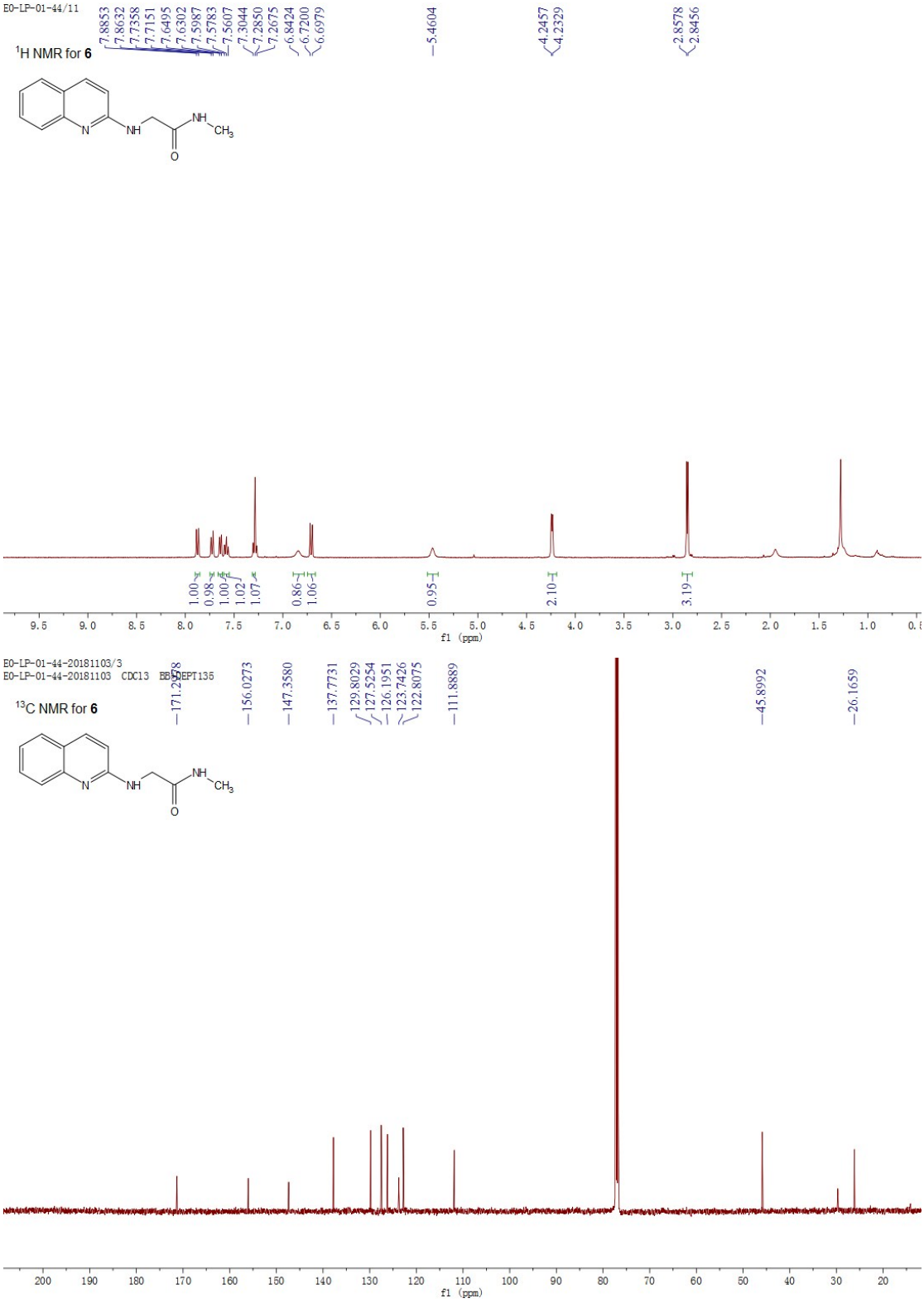
5. References

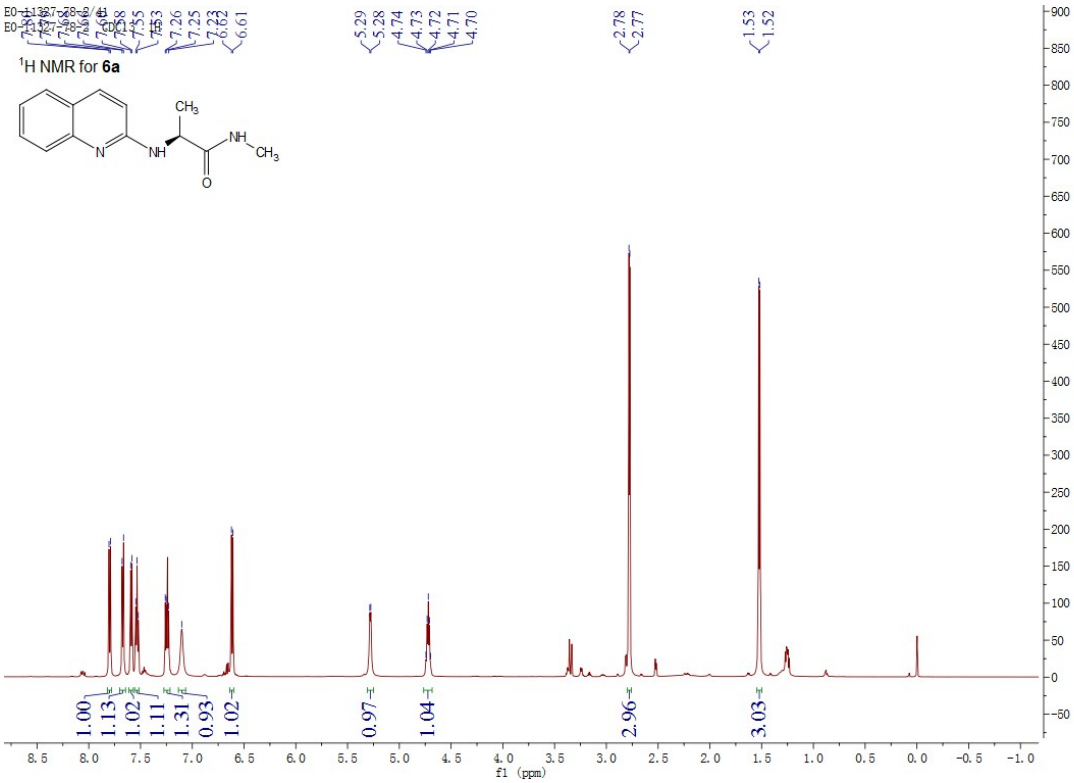
[1] Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Keith, T.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*, Revision D.01; Gaussian, Inc.: Wallingford, CT, 2013.

[2] Zhao Y., Truhlar D. G.; Theoretical Chemistry Accounts, **2008**, 120, 215-241.

[3] Marenich A. V., Cramer C. J., Truhlar D. G. *J. Phys. Chem. B,* **2009**, 113, 6378-6396.

6. NMR spectra of products

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6.61
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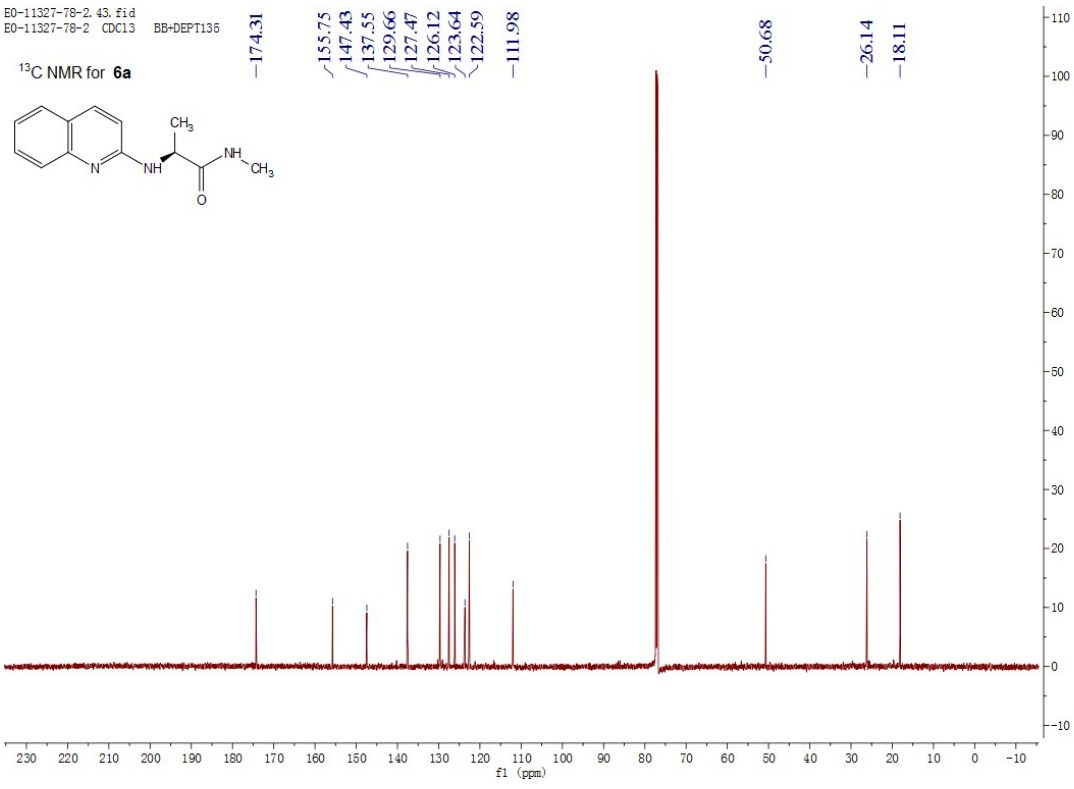
5.28
4.74
4.73
4.72
4.71
4.70
2.78
2.77
1.53
1.52
1.00
1.13
1.02
1.11
1.31
0.93
1.02
0.97
1.04
2.96
3.03
f1 (ppm)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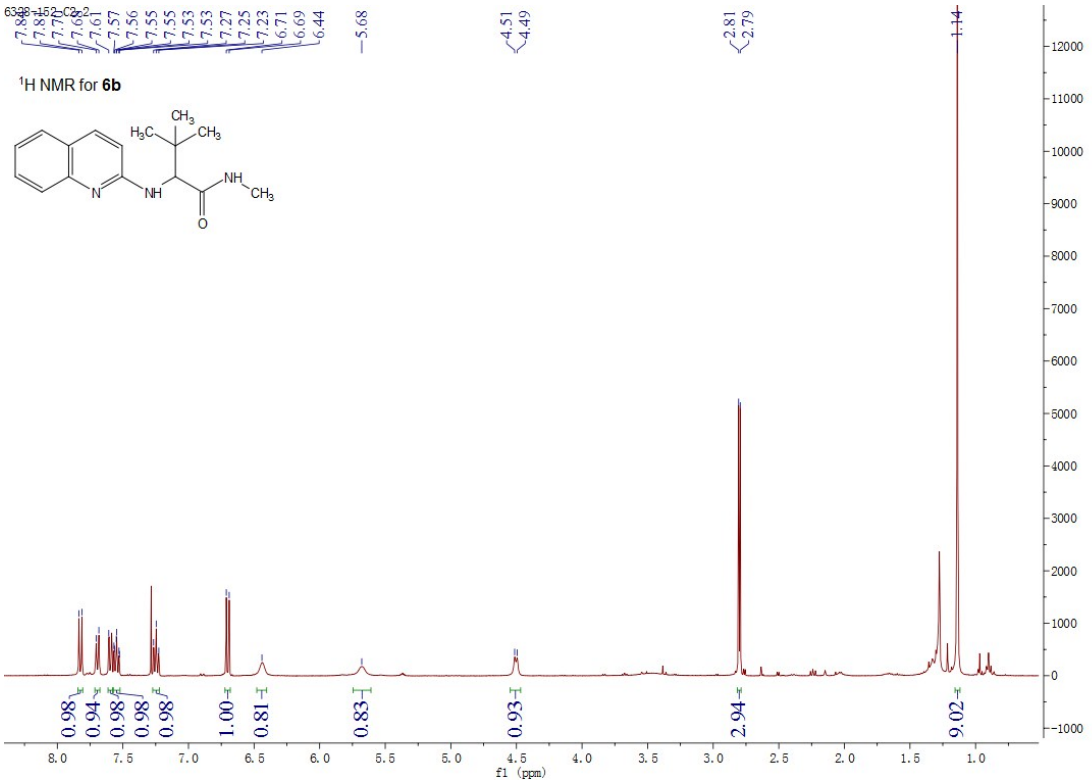
f1 (ppm)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7.78
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7.23
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6.69
6.44
5.68
4.51
4.49
2.81
2.79
1.14
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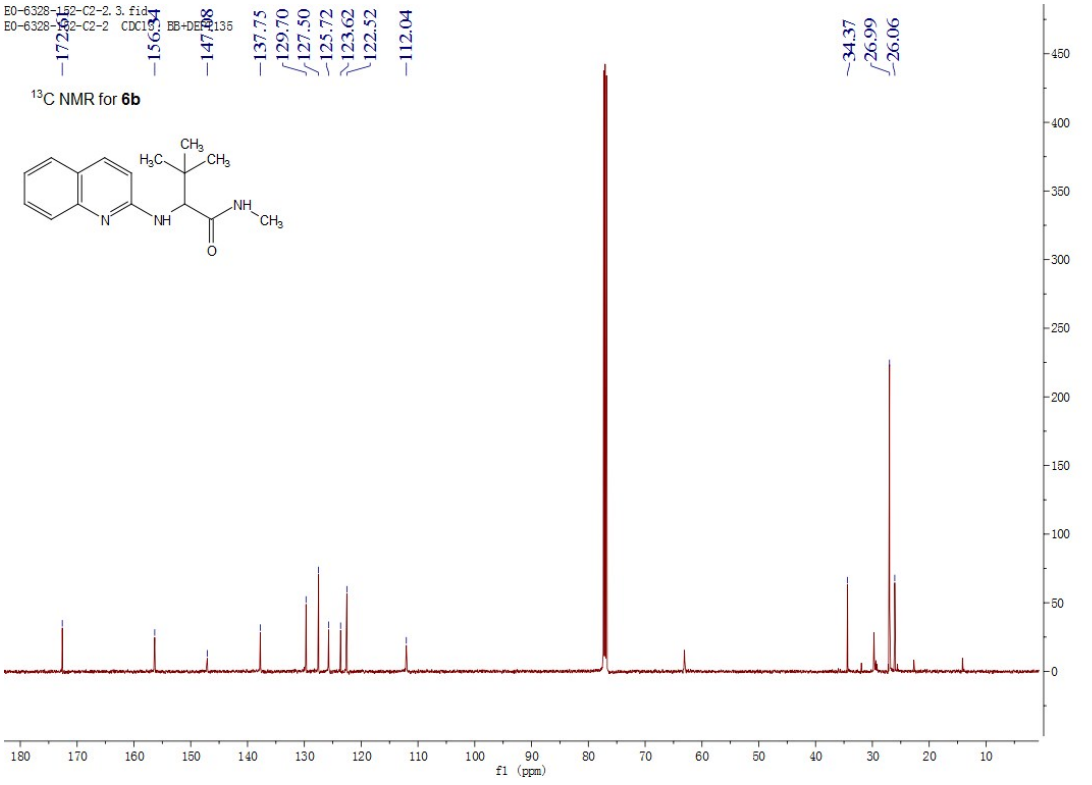
9.02
f1 (ppm)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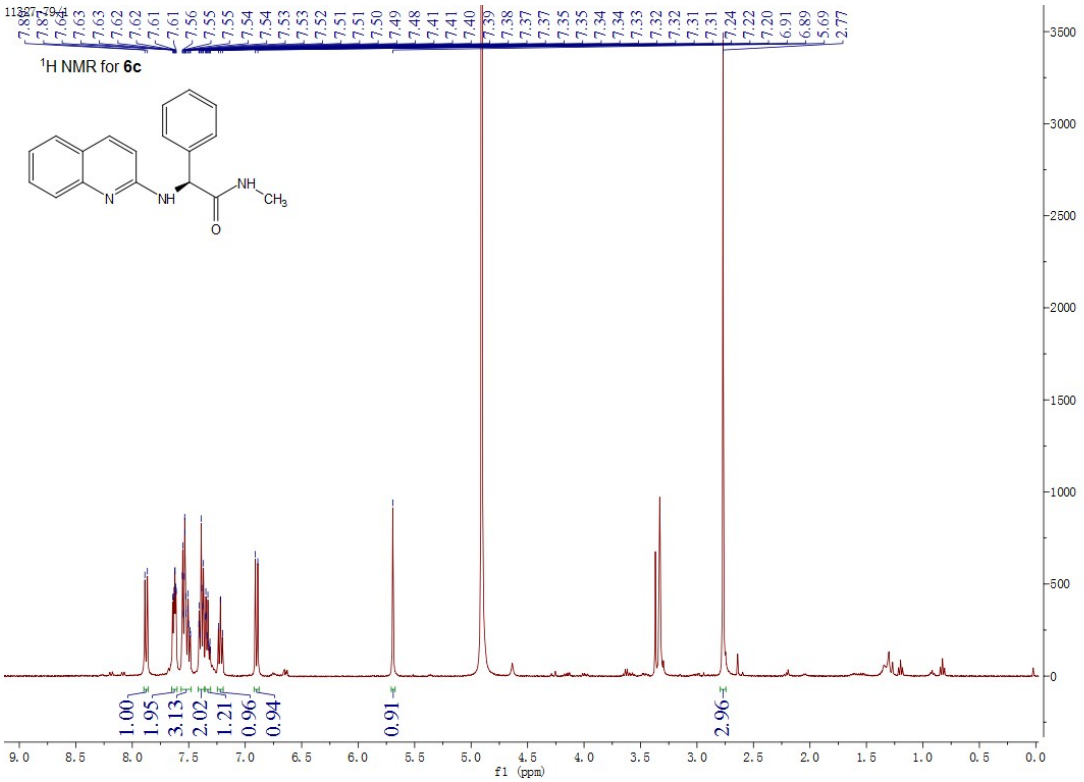
123.62
122.52
112.04
34.37
26.99
26.06
f1 (ppm)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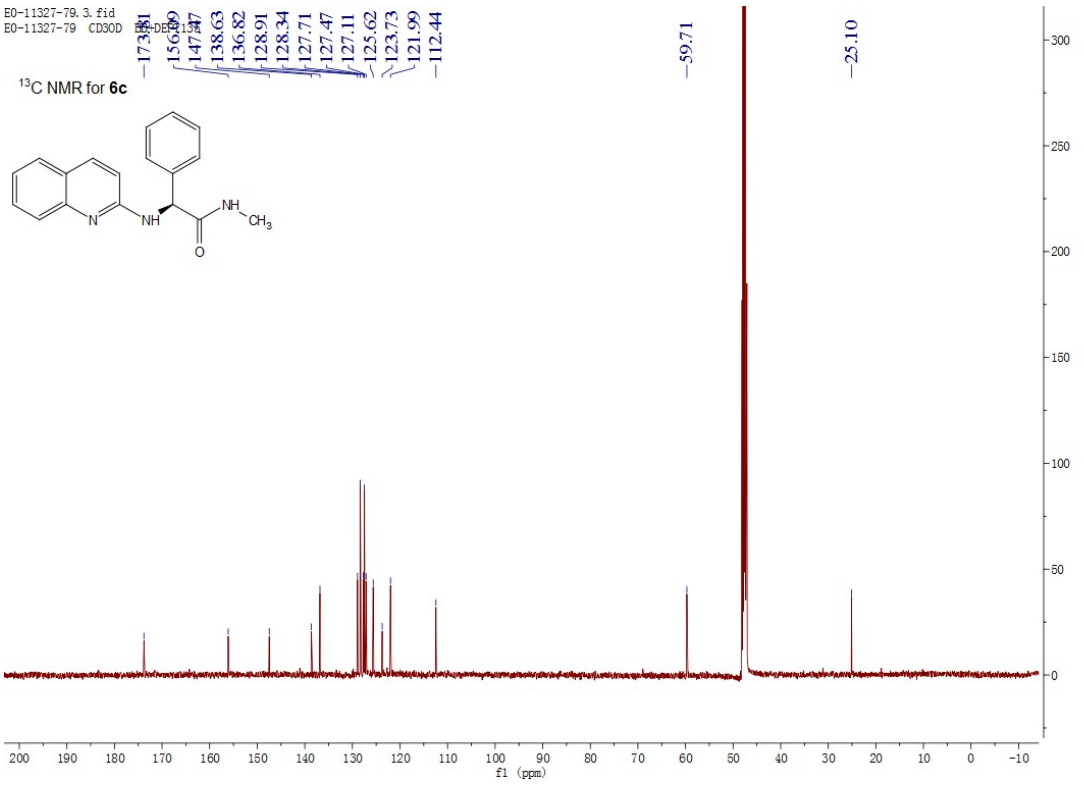
2.02
1.21
0.96
0.94
0.91
2.96
f1 (ppm)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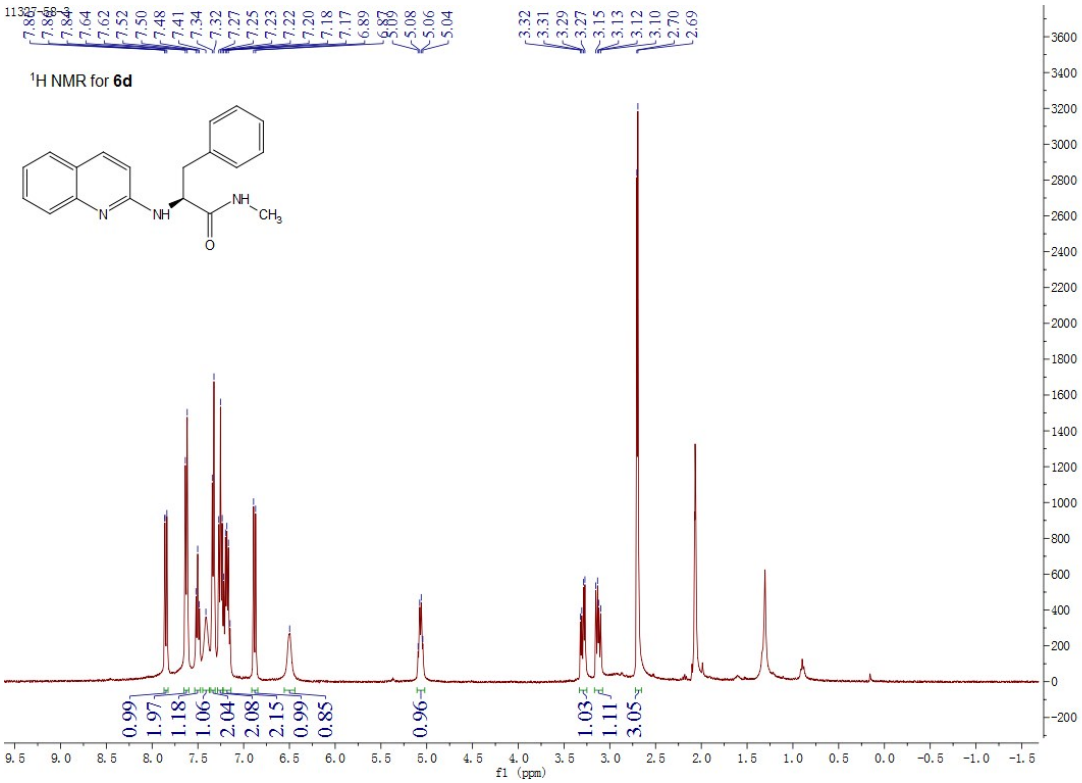
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7.25
7.23
7.22
7.20
7.18
7.17
6.89
5.08
5.06
5.04
3.32
3.31
3.29
3.27
3.15
3.13
3.12
3.10
2.70
2.69
1H NMR for 6d
NH
CH3
O
N
0.99
1.97
1.18
1.06
2.04
2.08
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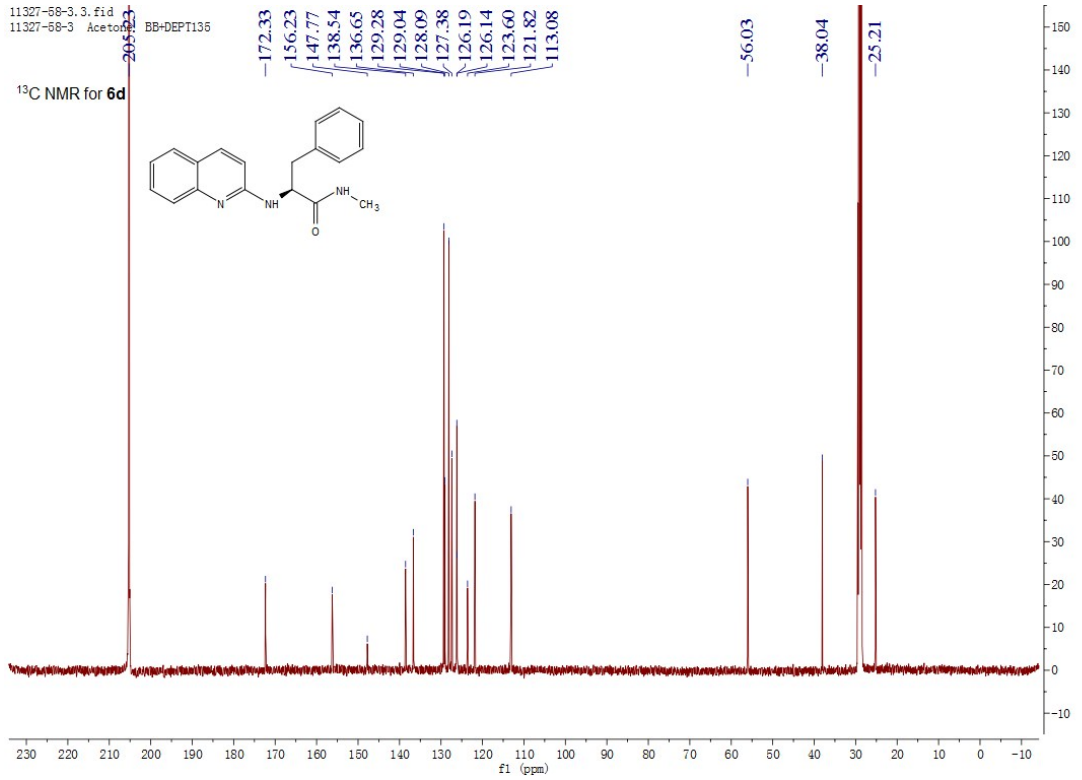
0.99
0.85
0.96
1.03
1.11
3.05
f1 (ppm)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129.28
129.04
128.09
127.38
126.19
126.14
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113.08
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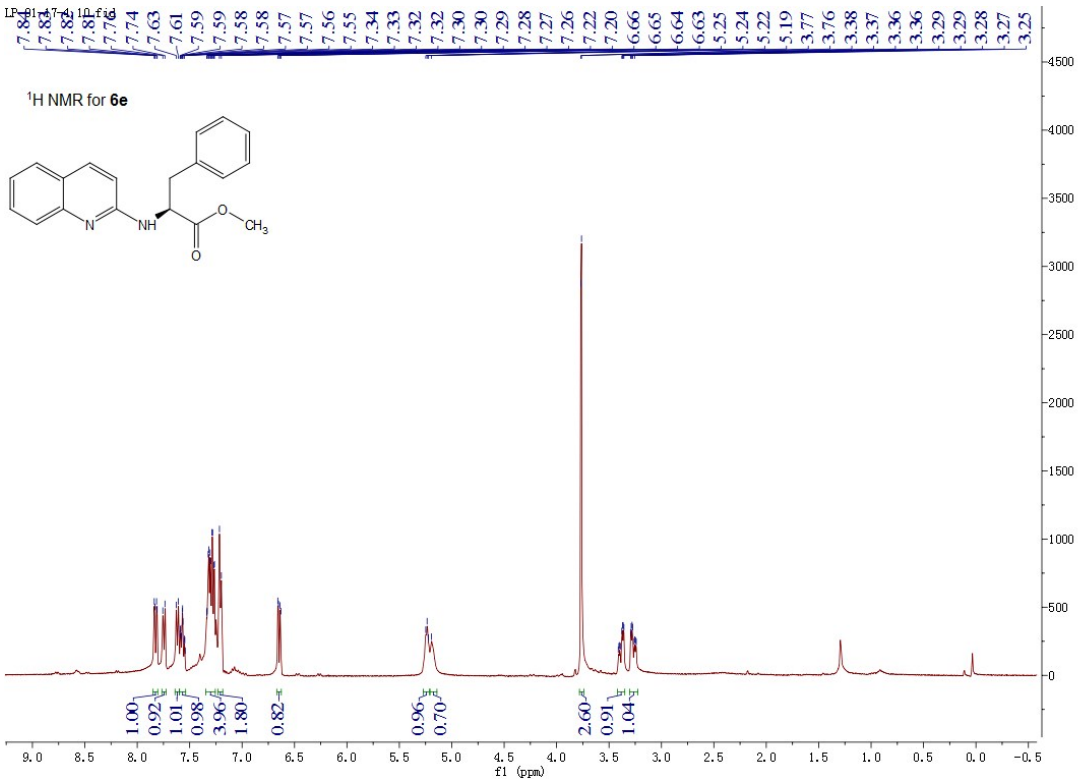
25.21
13C NMR for 6d
NH
CH3
O
N
f1 (ppm)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7.82
7.81
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7.61
7.59
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7.55
7.34
7.33
7.32
7.32
7.30
7.30
7.29
7.28
7.27
7.26
7.22
7.20
6.66
6.65
6.64
6.63
5.25
5.24
5.22
5.19
3.77
3.76
3.38
3.37
3.36
3.36
3.29
3.29
3.28
3.27
3.25
1H NMR for 6e
NH
O
CH3
1.00
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0.96
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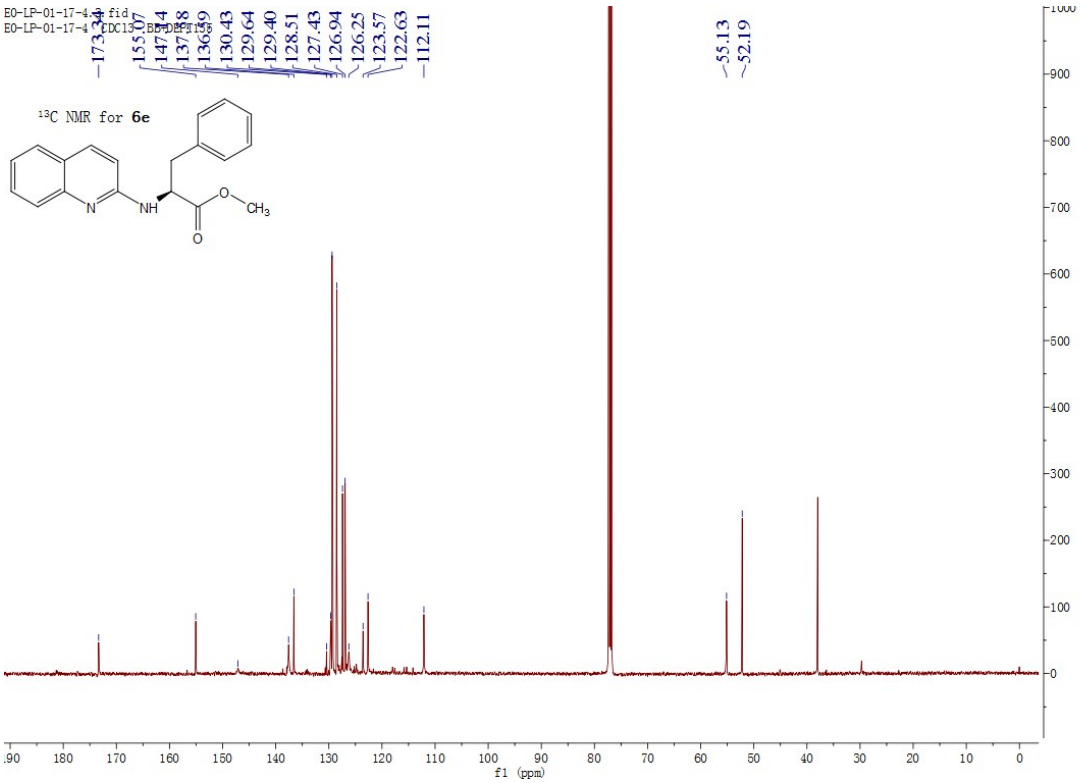
0.91
1.04
f1 (ppm)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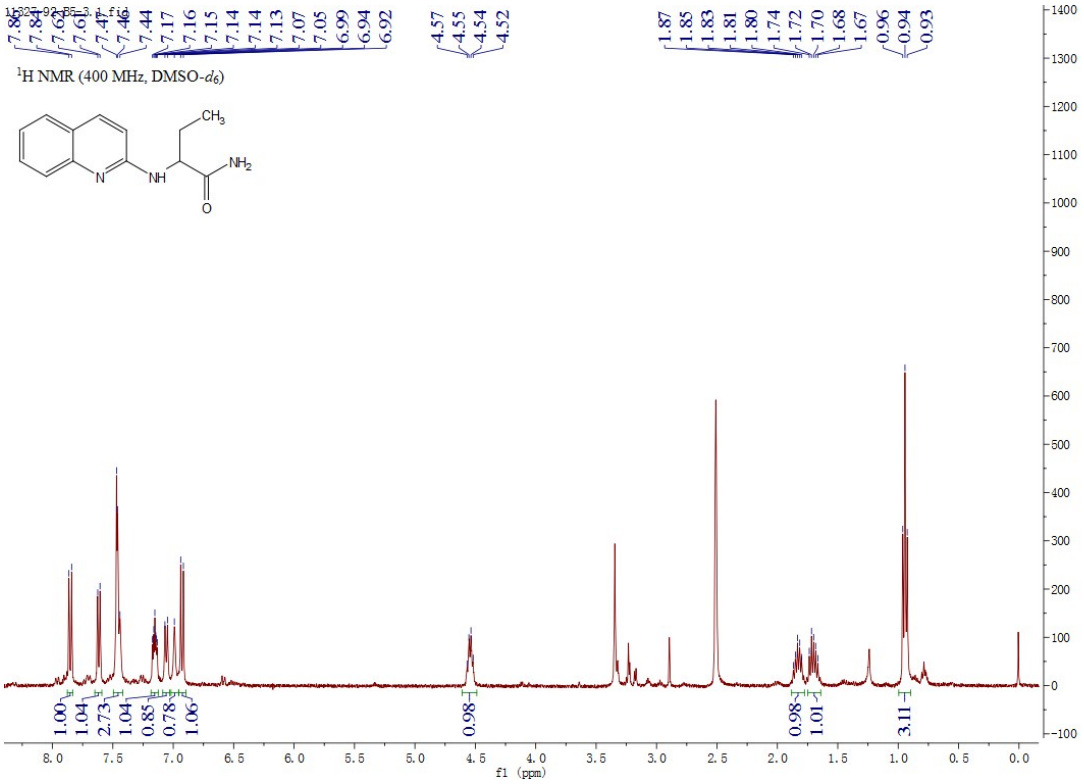
52.19
13C NMR for 6e
NH
O
CH3
f1 (ppm)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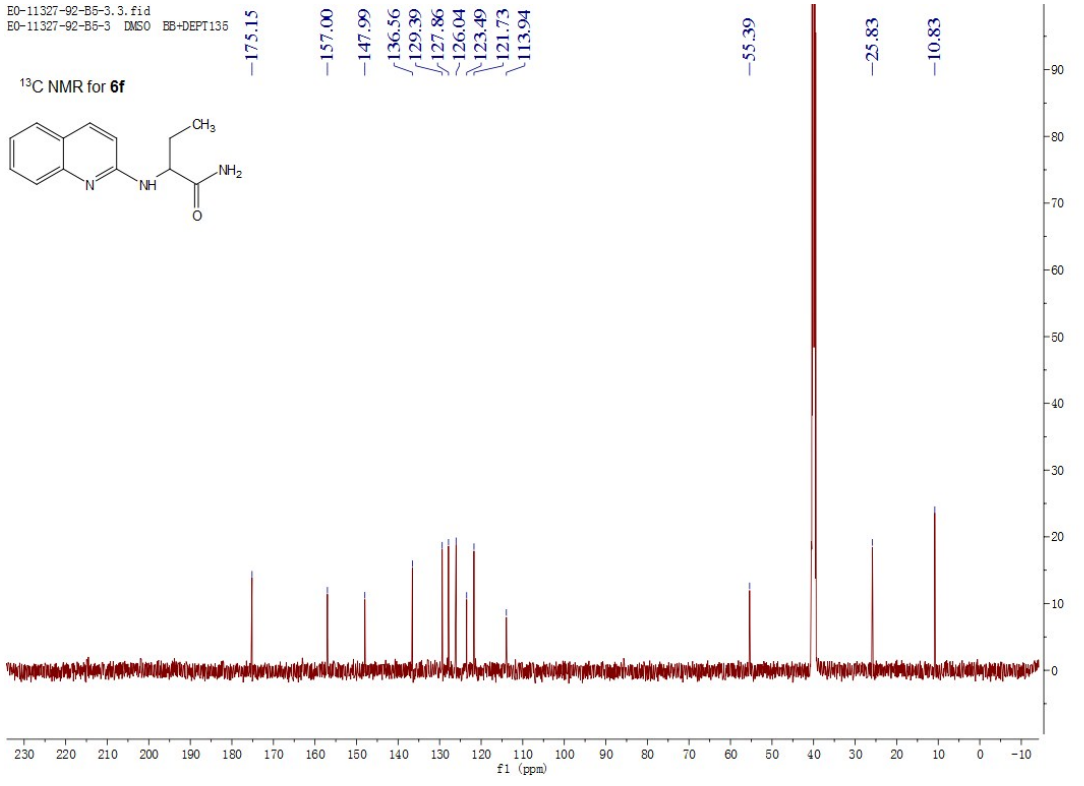
NH2
N
NH
O
f1 (ppm)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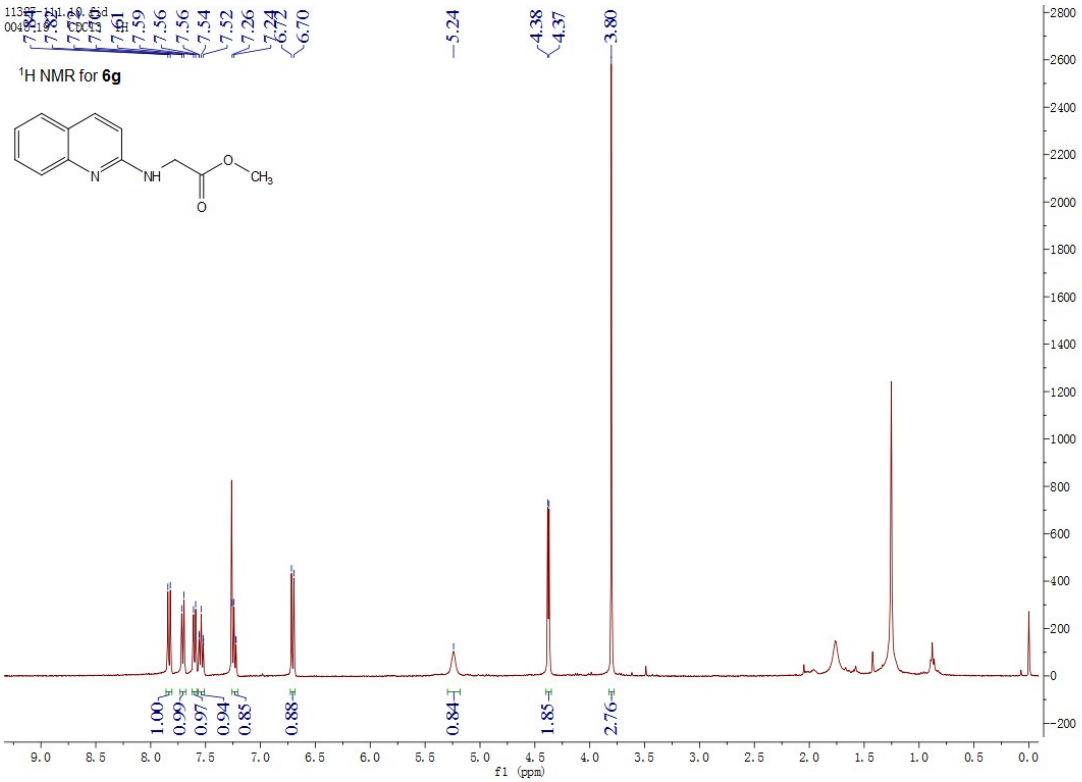
NH2
N
NH
O
f1 (ppm)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7.59
7.56
7.56
7.54
7.52
7.26
7.24
6.72
6.70
5.24
4.38
4.37
3.80
1H NMR for 6g
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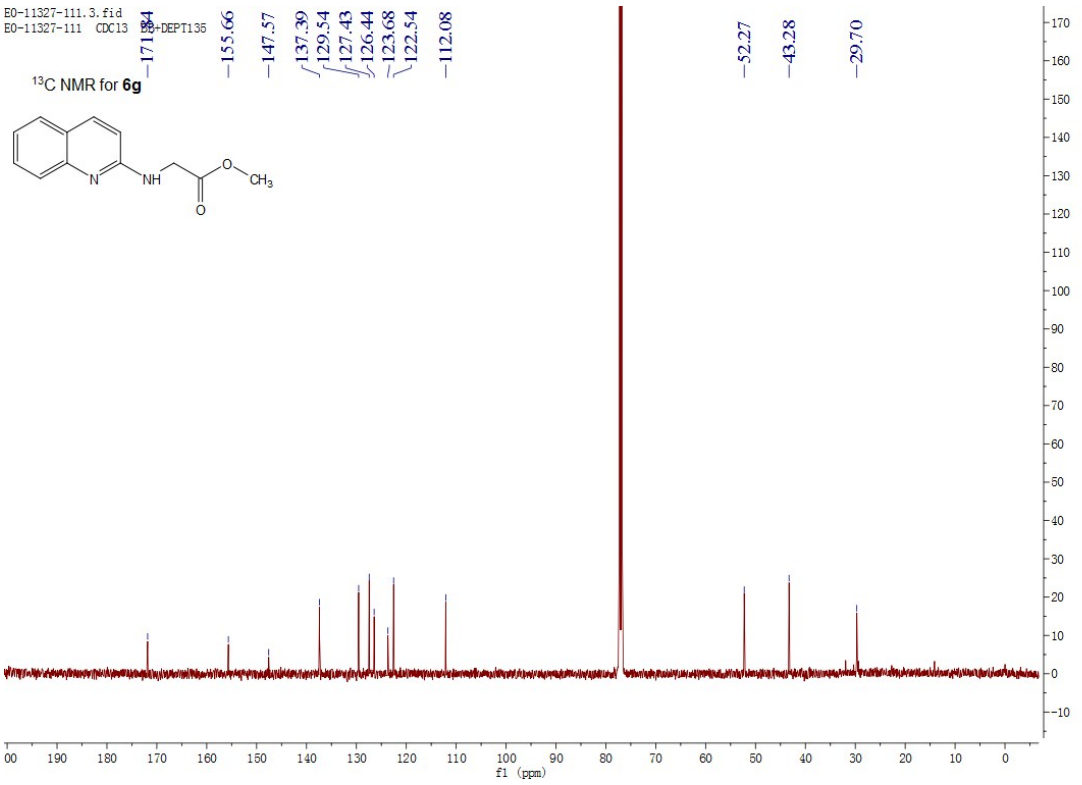
0.99
0.97
0.94
0.85
0.88
0.84
1.85
2.76
f1 (ppm)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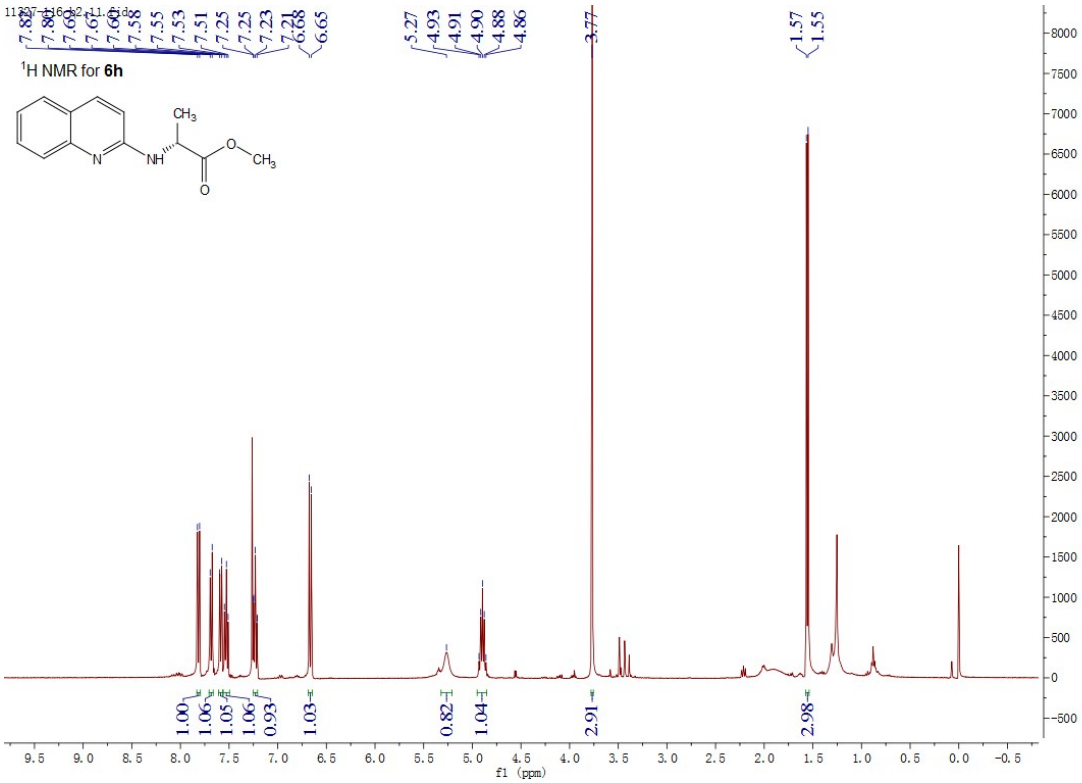
13C NMR for 6g
f1 (ppm)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4.93
4.91
4.90
4.88
4.86
3.77
1.57
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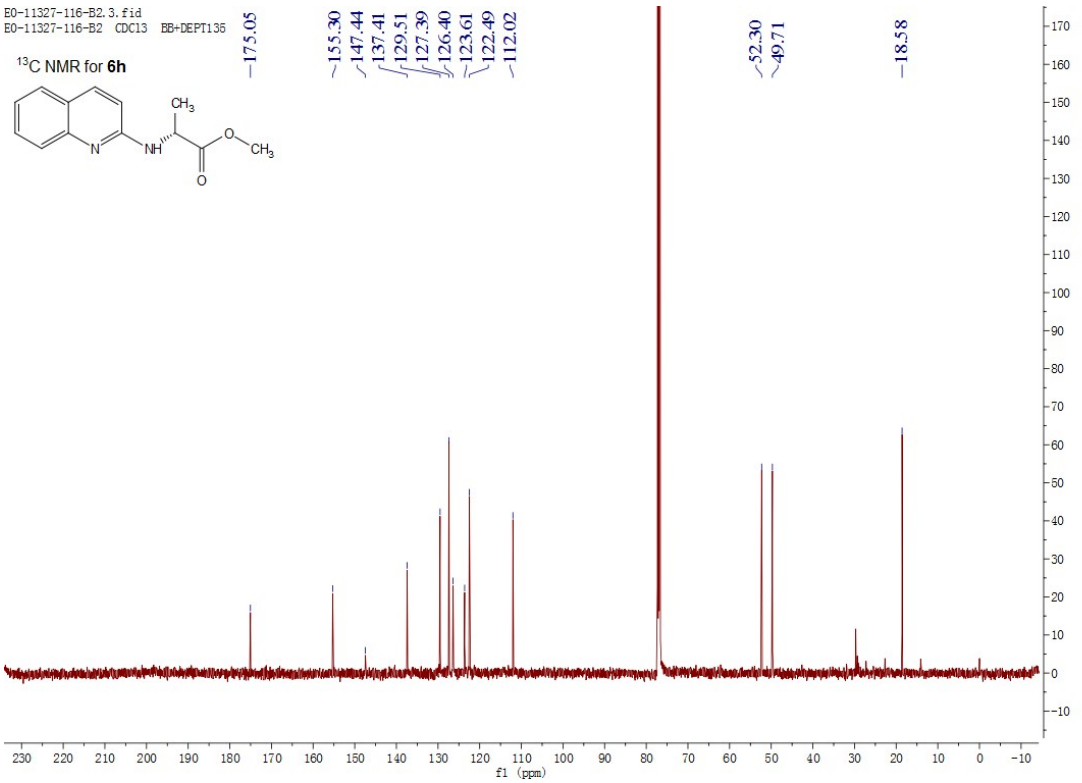
f1 (ppm)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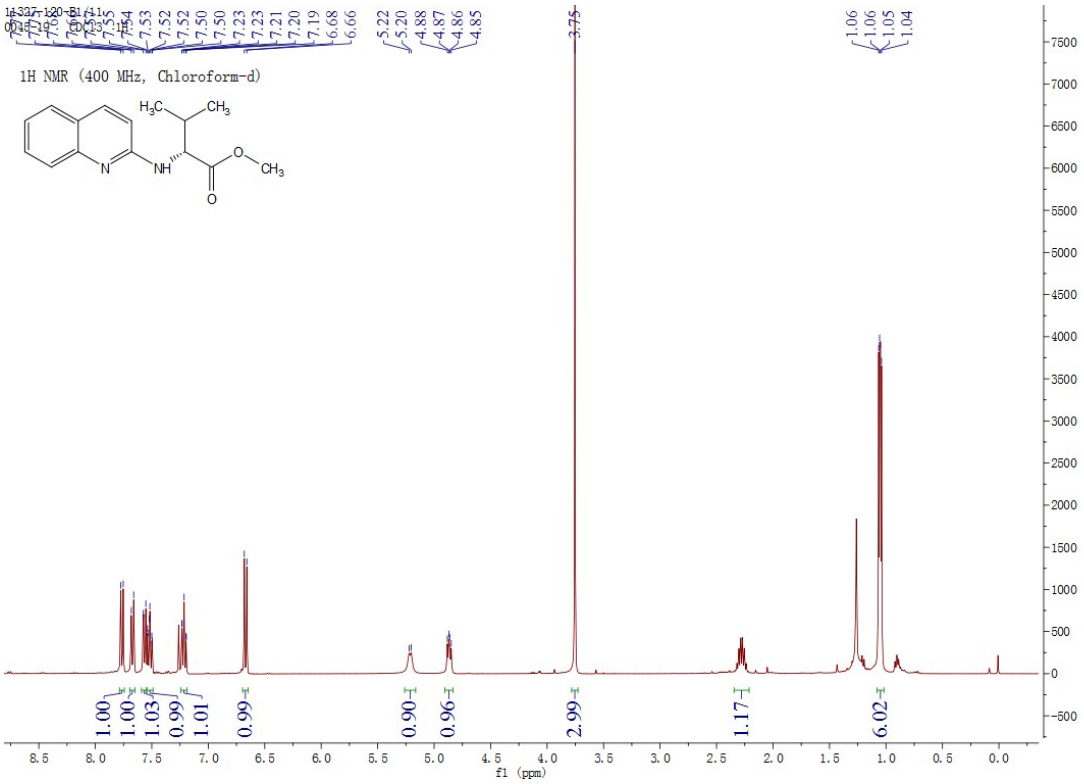
f1 (ppm)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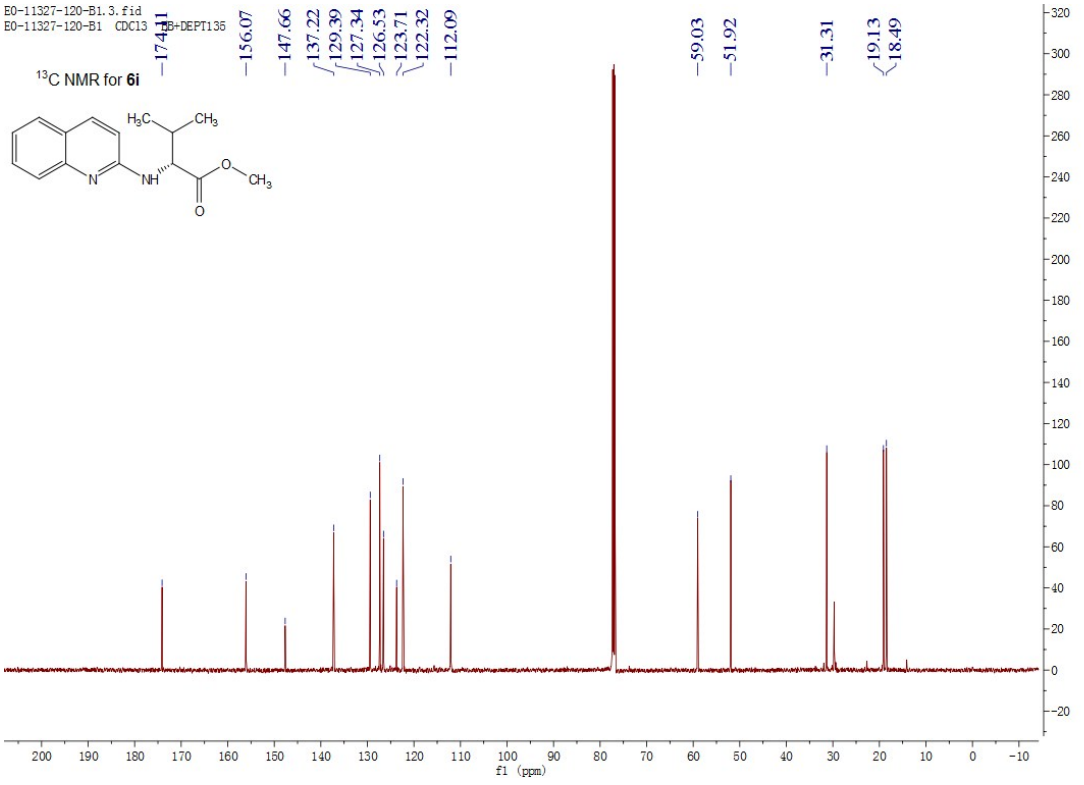
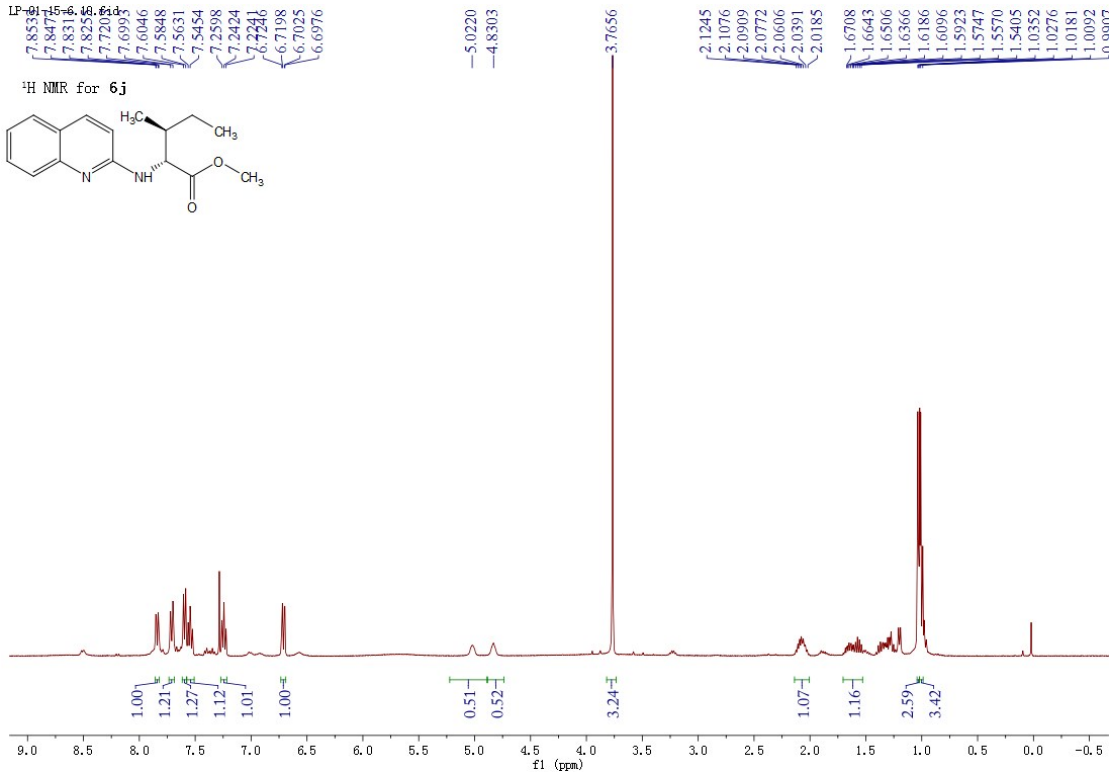
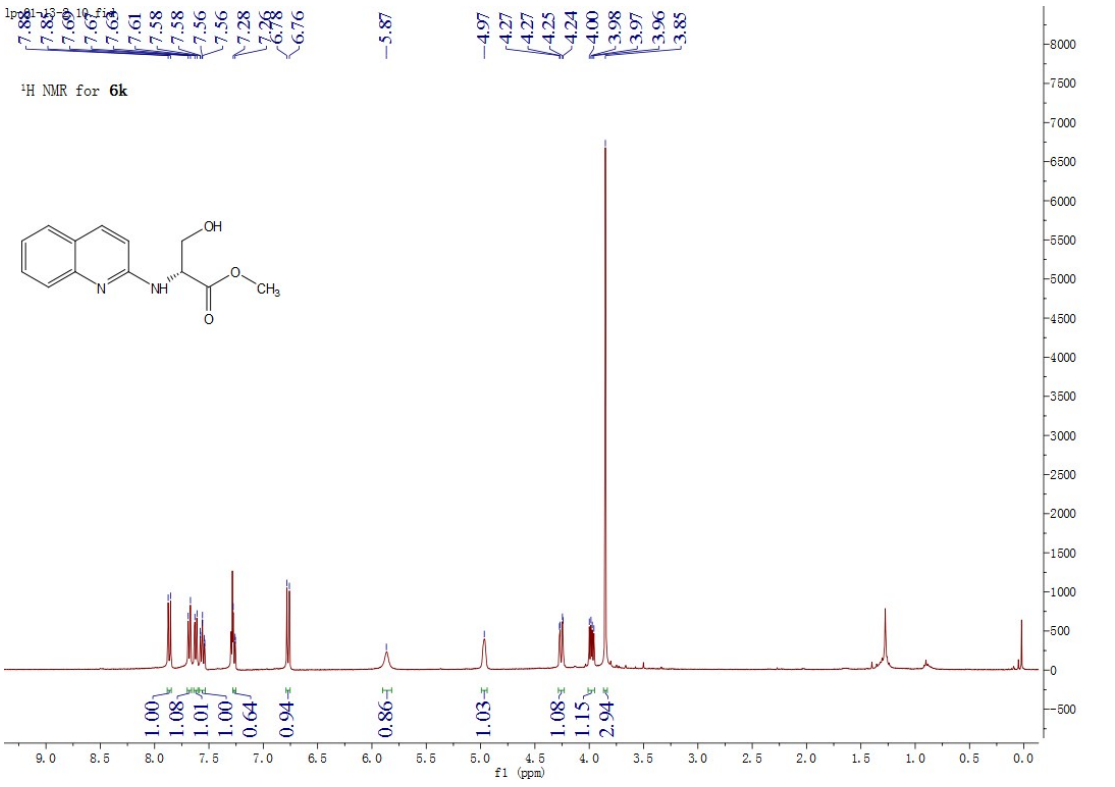
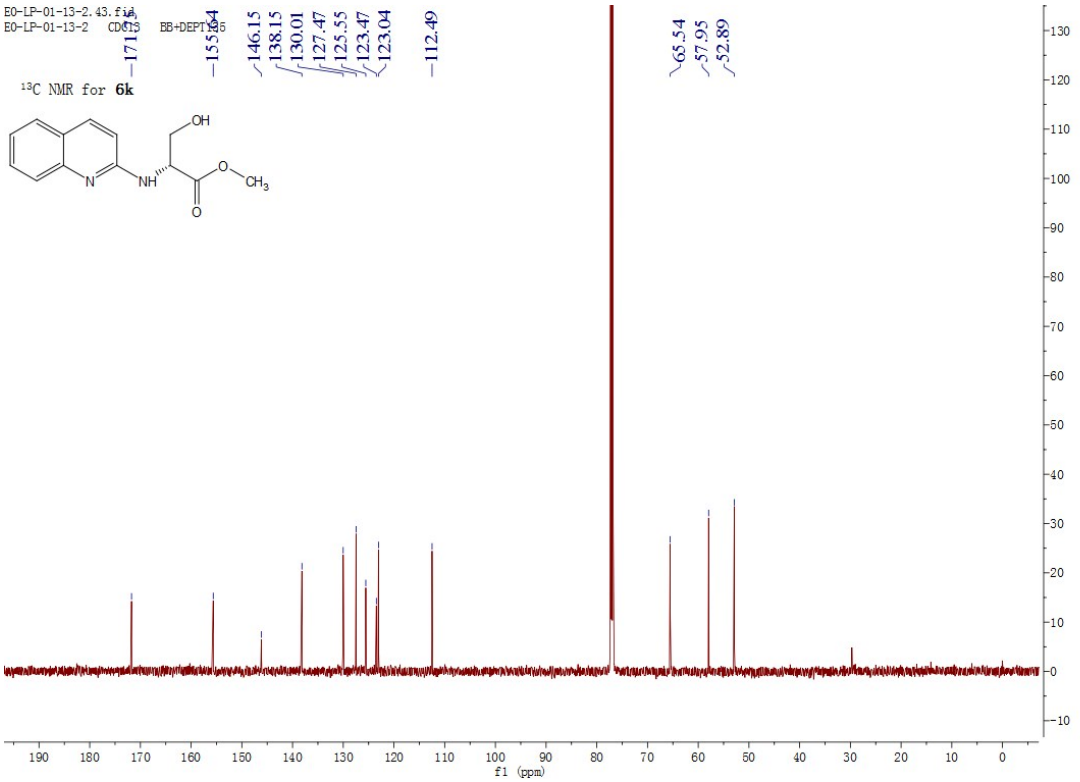
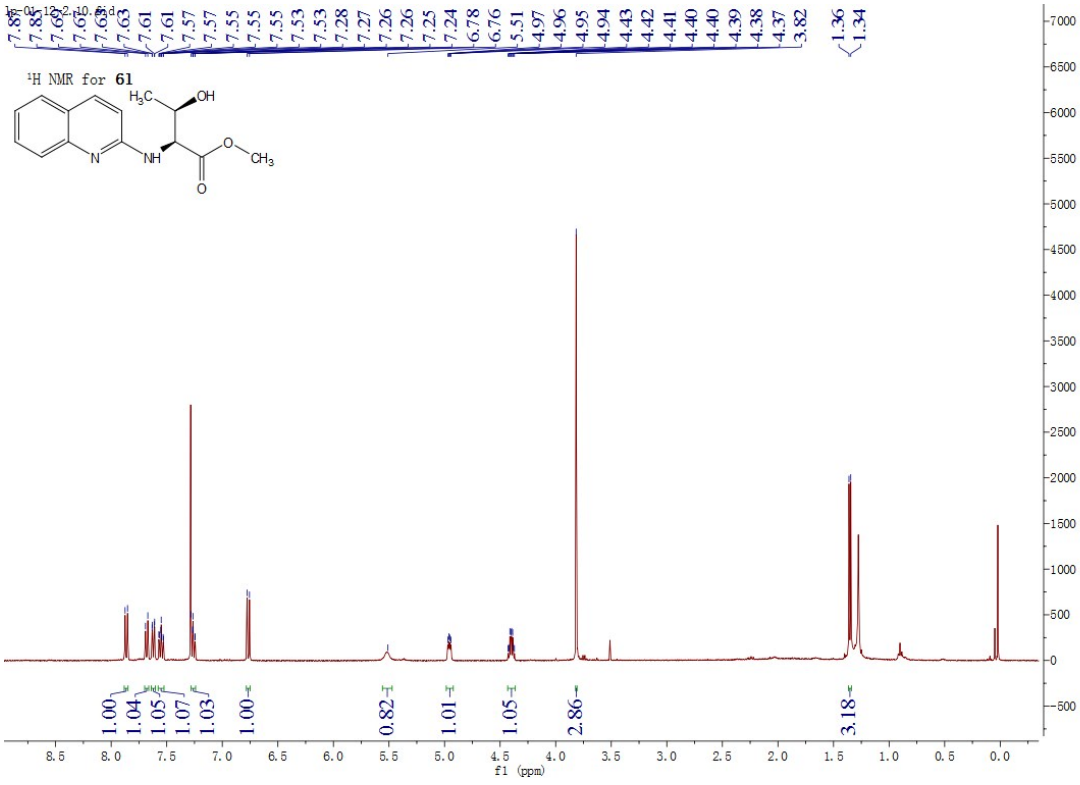
7.50
7.50
7.23
7.23
7.21
7.20
7.19
6.68
6.66
5.22
5.20
4.88
4.87
4.86
4.85
3.75
1.06
1.06
1.05
1.04
1.00
1.00
1.03
0.99
1.01
0.99
0.90
0.96
2.99
1.17
6.02
f1 (ppm)


13C NMR for 6i
174.11
156.07
147.66
137.22
129.39
127.34
126.53
123.71
122.32
112.09
59.03
51.92
31.31
19.13
18.49
f1 (ppm)


LP-01-15-6.10.fid
7.8533
7.8477
7.8317
7.8255
7.7205
7.6995
7.6046
7.5848
7.5631
7.5454
7.2598
7.2424
7.2241
7.2046
6.7198
6.7025
6.6976
5.0220
4.8303
3.7656
2.1245
2.1076
2.0909
2.0772
2.0606
2.0391
2.0185
1.6708
1.6643
1.6506
1.6366
1.6186
1.6096
1.5923
1.5747
1.5570
1.5405
1.0352
1.0276
1.0181
1.0092
¹H NMR for 6j
H3C
CH3
N
NH
O
CH3
O
1.00
1.21
1.27
1.12
1.01
1.00
0.51
0.52
3.24
1.07
1.16
2.59
3.42
f1 (ppm)


7.88
7.85
7.69
7.63
7.61
7.58
7.58
7.56
7.56
7.28
7.26
6.78
6.76
5.87
4.97
4.27
4.27
4.25
4.24
4.00
3.98
3.97
3.96
3.85
¹H NMR for 6k
OH
N
NH
O
CH3
O
1.00
1.08
1.01
1.00
0.64
0.94
0.86
1.03
1.08
1.15
2.94
f1 (ppm)


EO-LP-01-13-2.43.fid
EO-LP-01-13-2 CDCl3 BB+DEPT135
171.13
155.34
146.15
138.15
130.01
127.47
125.55
123.47
123.04
112.49
65.54
57.95
52.89
13C NMR for 6k
OH
NH
O
CH3
O
N
f1 (ppm)


1c-01-12-2-10.fid
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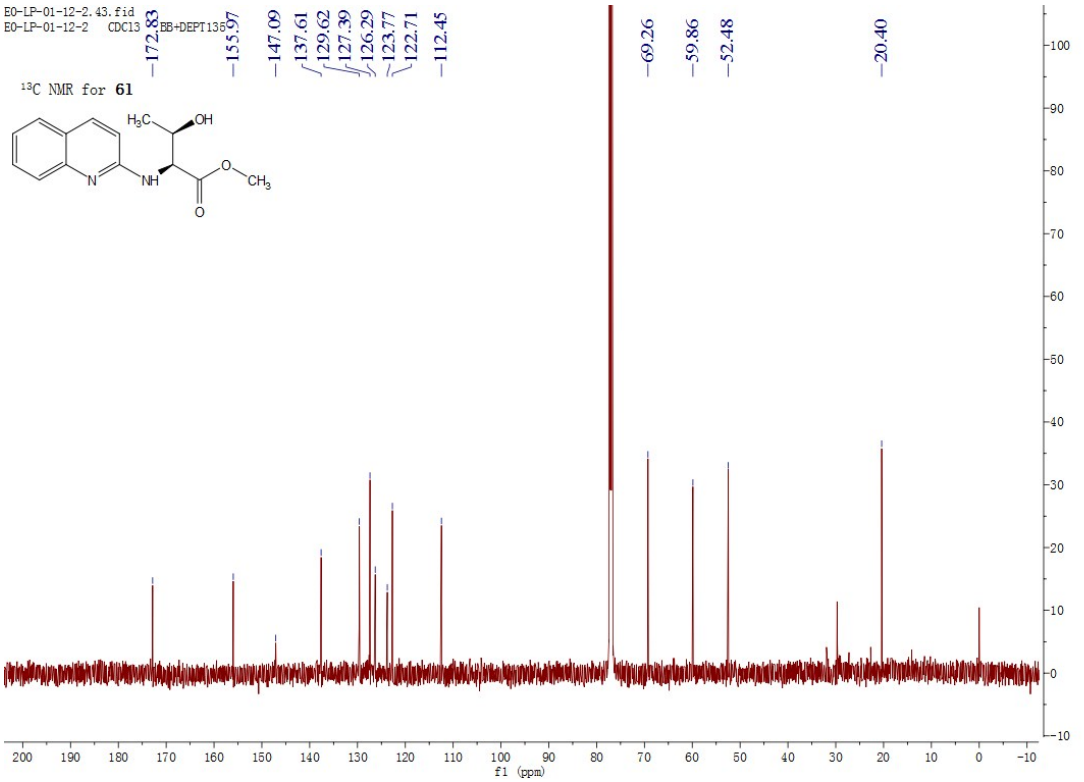
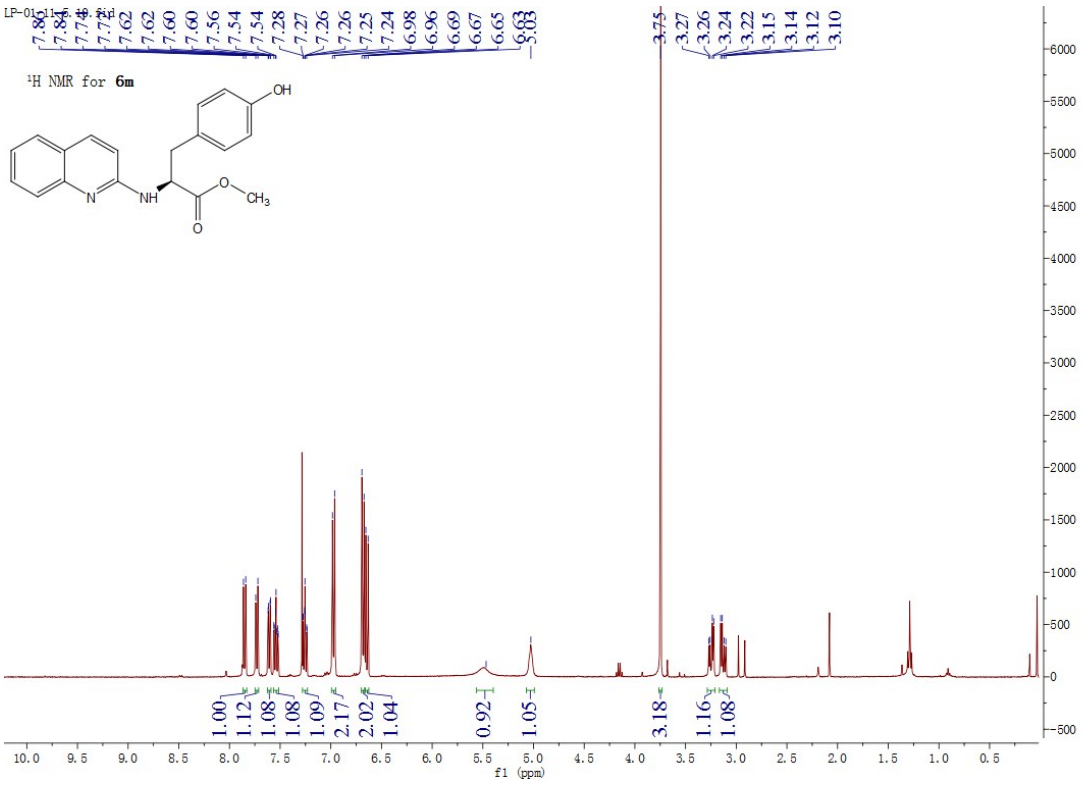
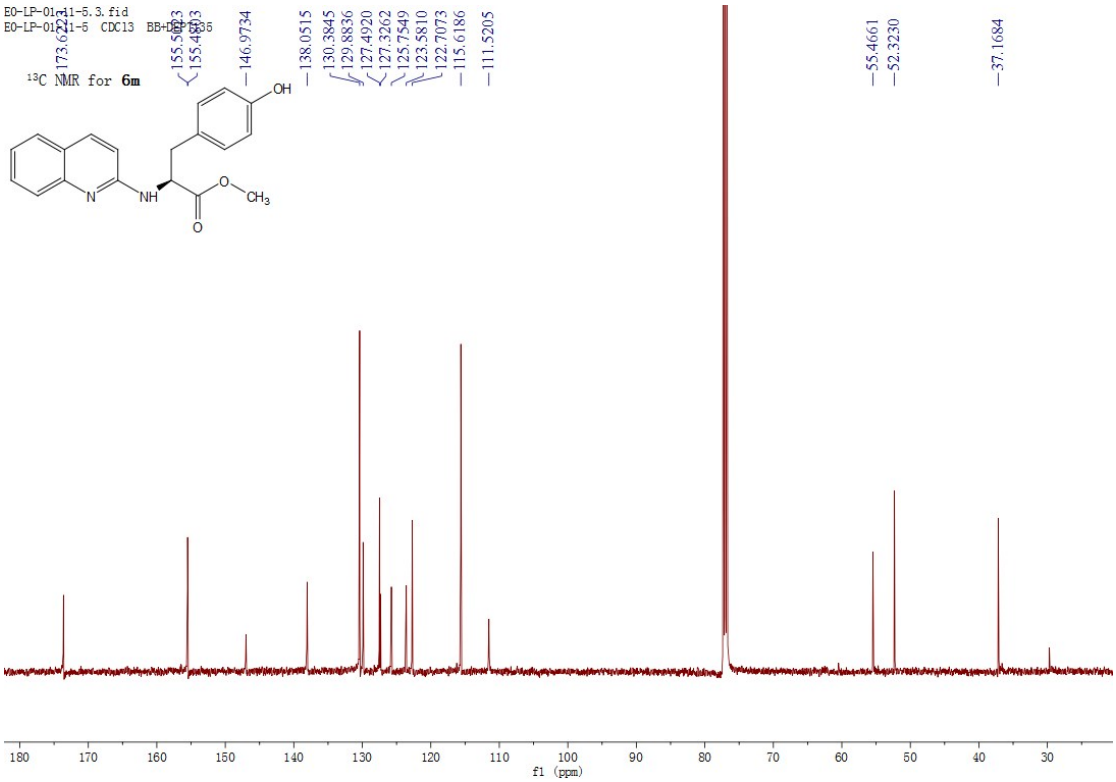
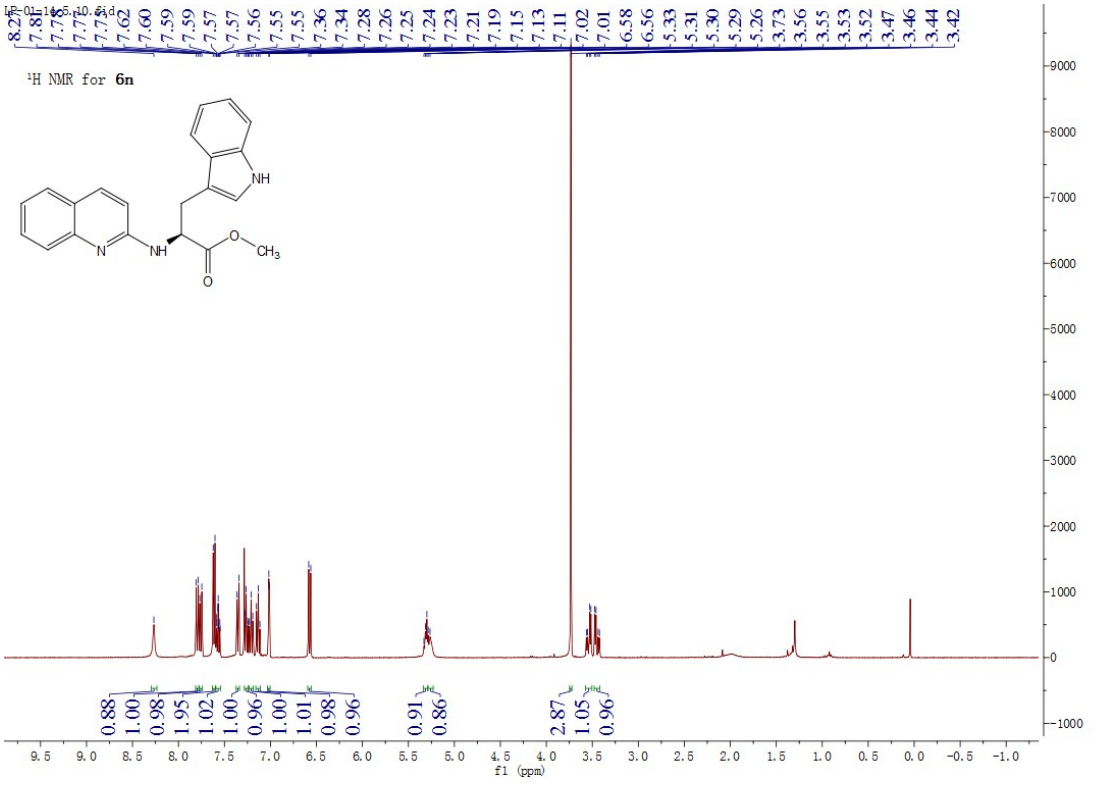
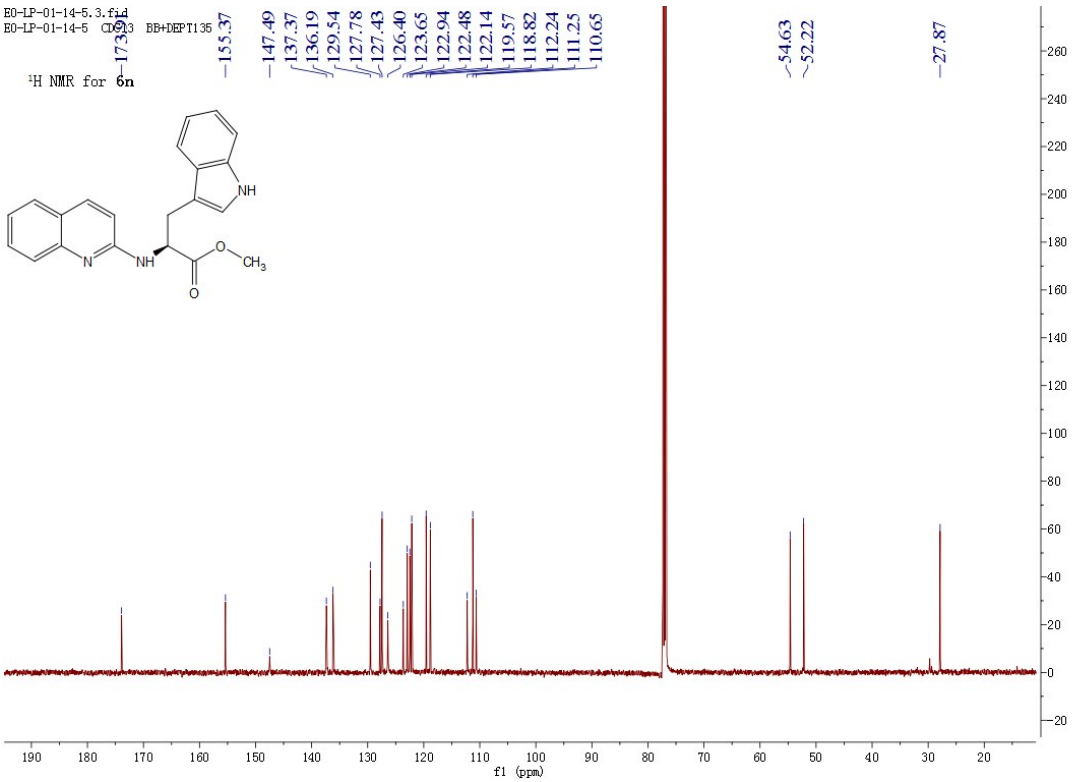
7.83
7.65
7.63
7.61
7.57
7.55
7.53
7.28
7.27
7.26
7.25
7.24
6.78
6.76
5.51
4.97
4.96
4.95
4.94
4.43
4.42
4.41
4.40
4.39
4.38
4.37
3.82
1.36
1.34
1H NMR for 61
H3C
OH
NH
O
CH3
O
N
1.00
1.04
1.05
1.07
1.03
1.00
0.82
1.01
1.05
2.86
3.18
f1 (ppm)

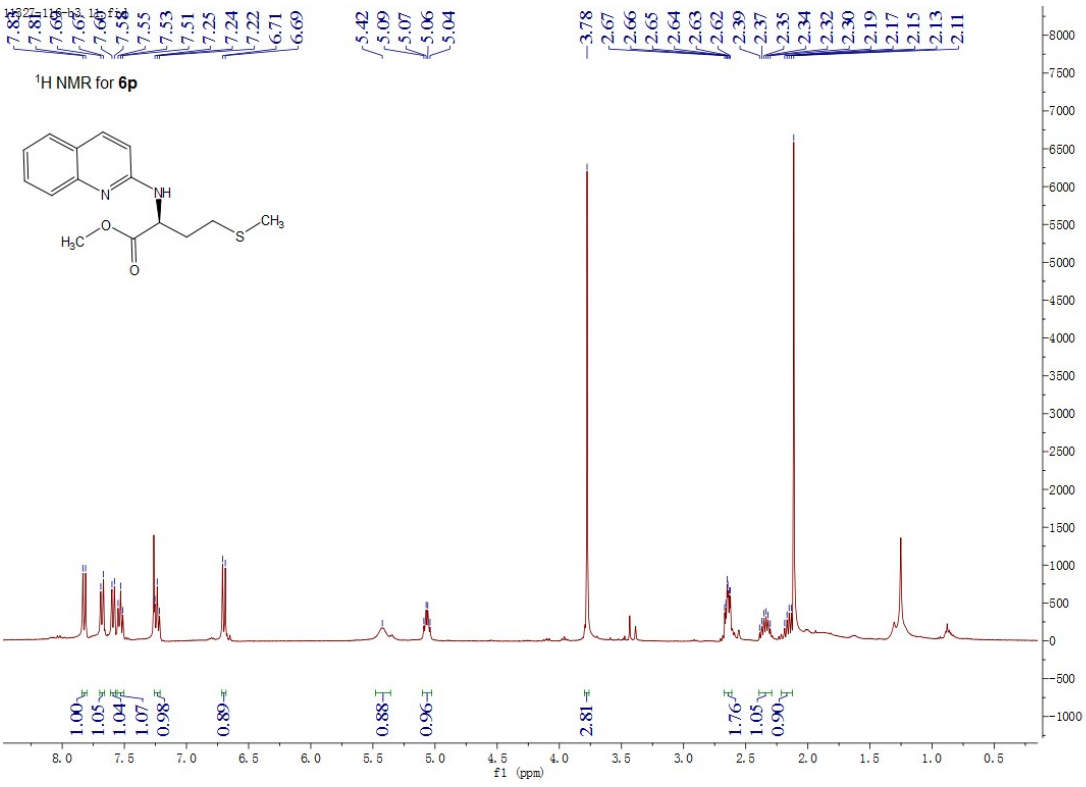

EO-LP-01-12-2.43.fid
EO-LP-01-12-2 CDC13 BB+DEPT135
172.83
155.97
147.09
137.61
129.62
127.39
126.29
123.77
122.71
112.45
69.26
59.86
52.48
20.40
13C NMR for 61
f1 (ppm)

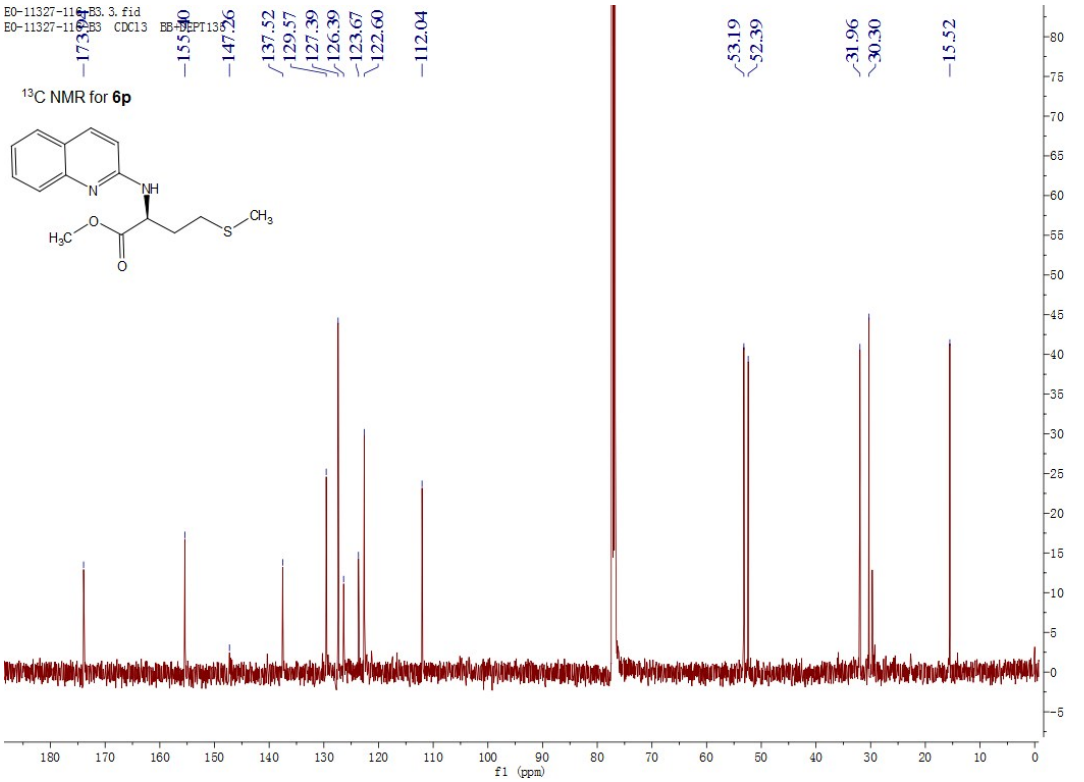

7.87
7.74
7.62
7.60
7.56
7.54
7.28
7.27
7.26
7.25
7.24
6.98
6.96
6.69
6.67
6.65
6.63
5.03
3.75
3.27
3.26
3.24
3.22
3.15
3.14
3.12
3.10
1.00
1.12
1.08
1.08
1.09
2.17
2.02
1.04
0.92
1.05
3.18
1.16
1.08
1H NMR for 6m
f1 (ppm)

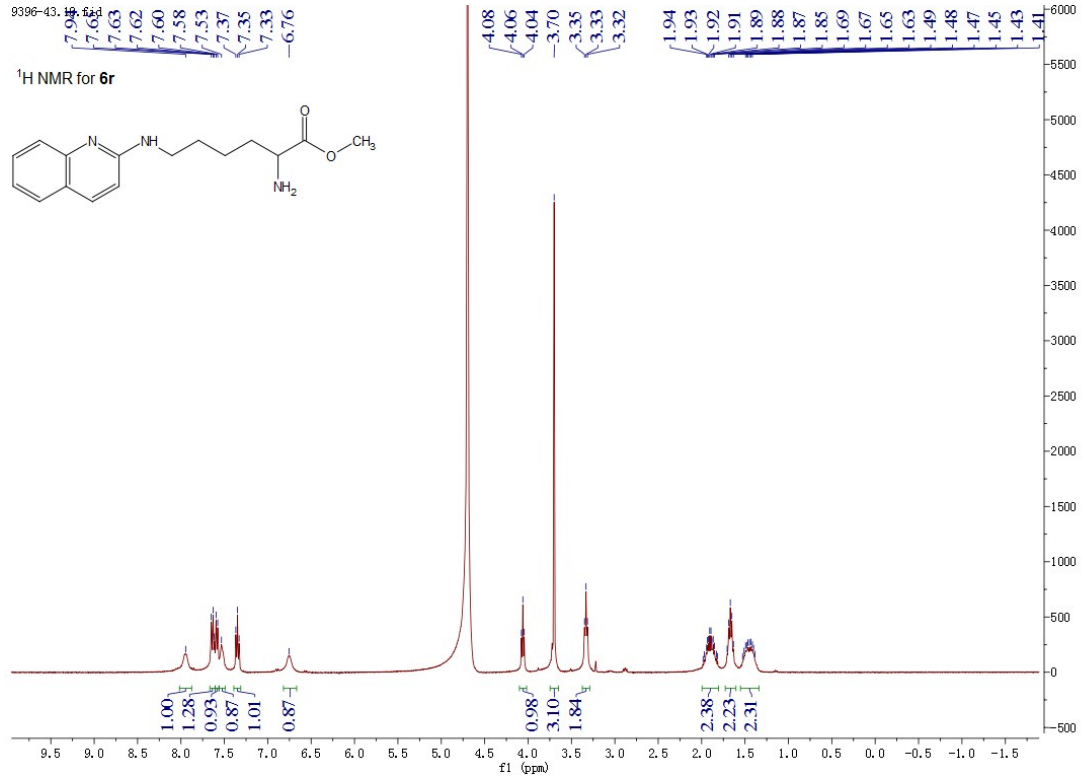

EO-LP-01-11-5.3.fid
EO-LP-01-11-5 CDC13 BB+DEPT135
173.6221
155.5013
155.4813
146.9734
138.0515
130.3845
129.8836
127.4920
127.3262
125.7549
123.5810
122.7073
115.6186
111.5205
55.4661
52.3230
37.1684
13C NMR for 6m
OH
NH
O
CH3
O
N
f1 (ppm)

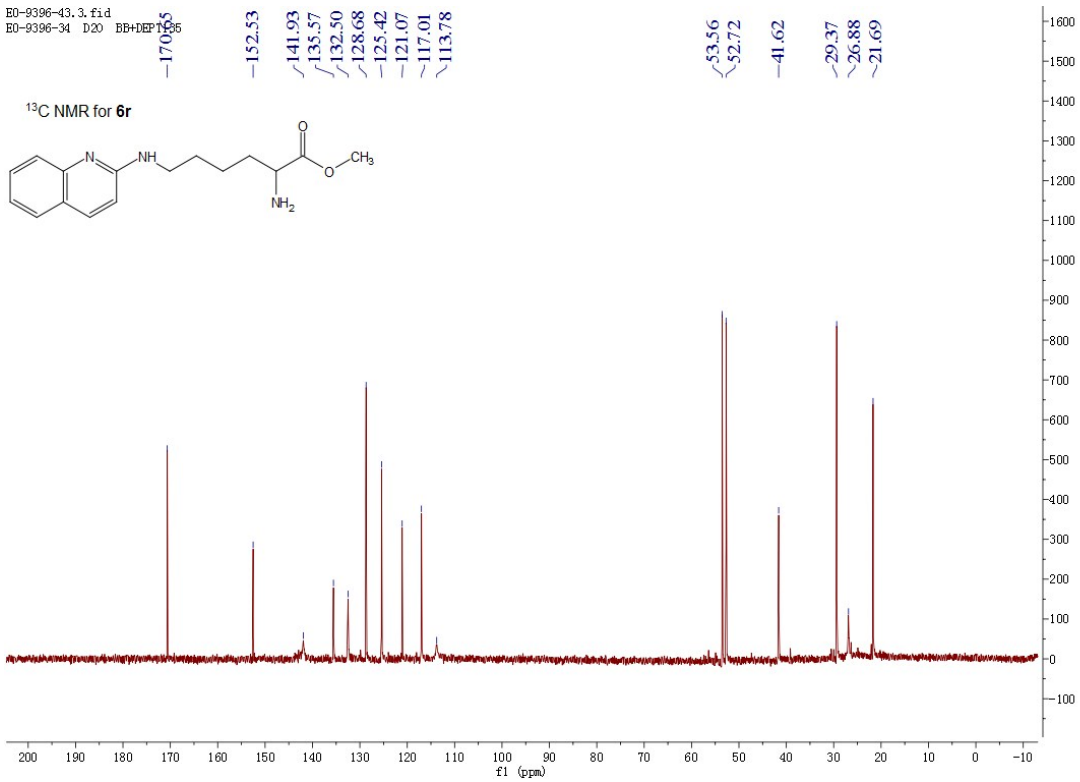

8.25
7.81
7.77
7.62
7.60
7.59
7.59
7.57
7.57
7.56
7.55
7.55
7.36
7.34
7.28
7.26
7.25
7.24
7.23
7.21
7.19
7.15
7.13
7.11
7.02
7.01
6.58
6.56
5.33
5.31
5.30
5.29
5.26
3.73
3.56
3.55
3.53
3.52
3.47
3.46
3.44
3.42
1H NMR for 6n
NH
NH
O
CH3
O
N
0.88
1.00
0.98
1.95
1.02
1.00
0.96
1.00
1.01
0.98
0.96
0.91
0.86
2.87
1.05
0.96
f1 (ppm)

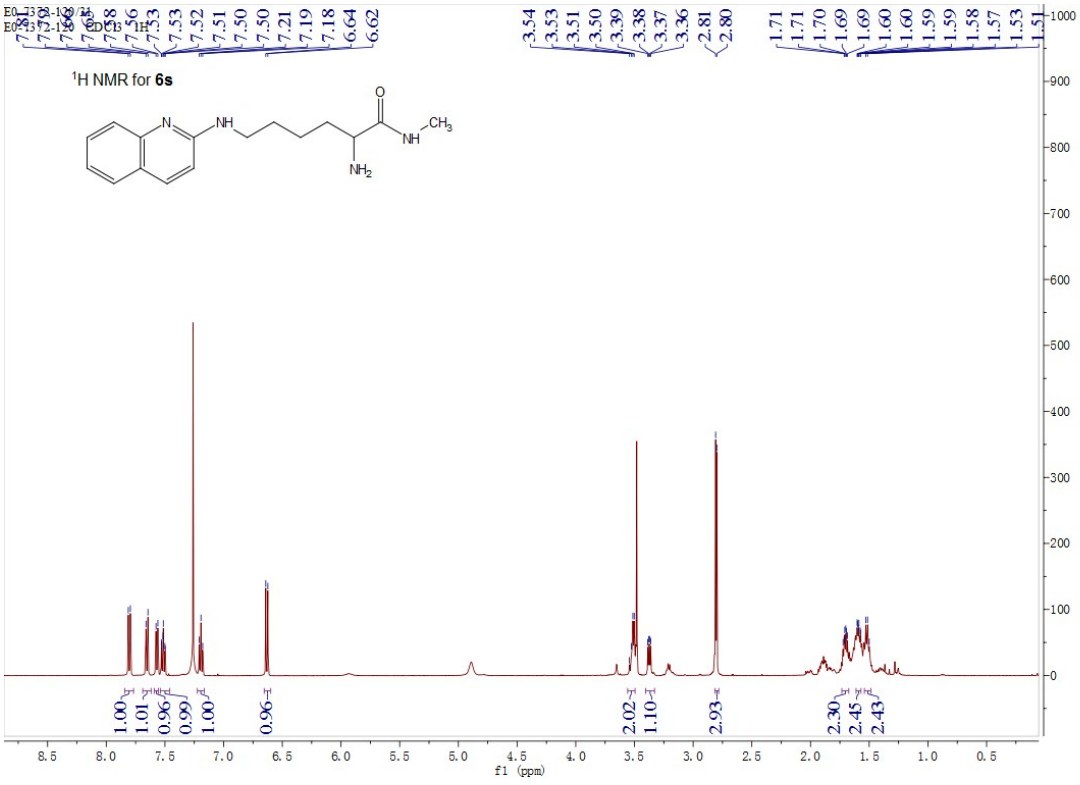

E0-LP-01-14-5.3.fid
E0-LP-01-14-5 CDCl3 BB+DEPT135
173.21
155.37
147.49
137.37
136.19
129.54
127.78
127.43
126.40
123.65
122.94
122.48
122.14
119.57
118.82
112.24
111.25
110.65
54.63
52.22
27.87
¹H NMR for 6n
NH
N
NH
O
O
CH3
f1 (ppm)

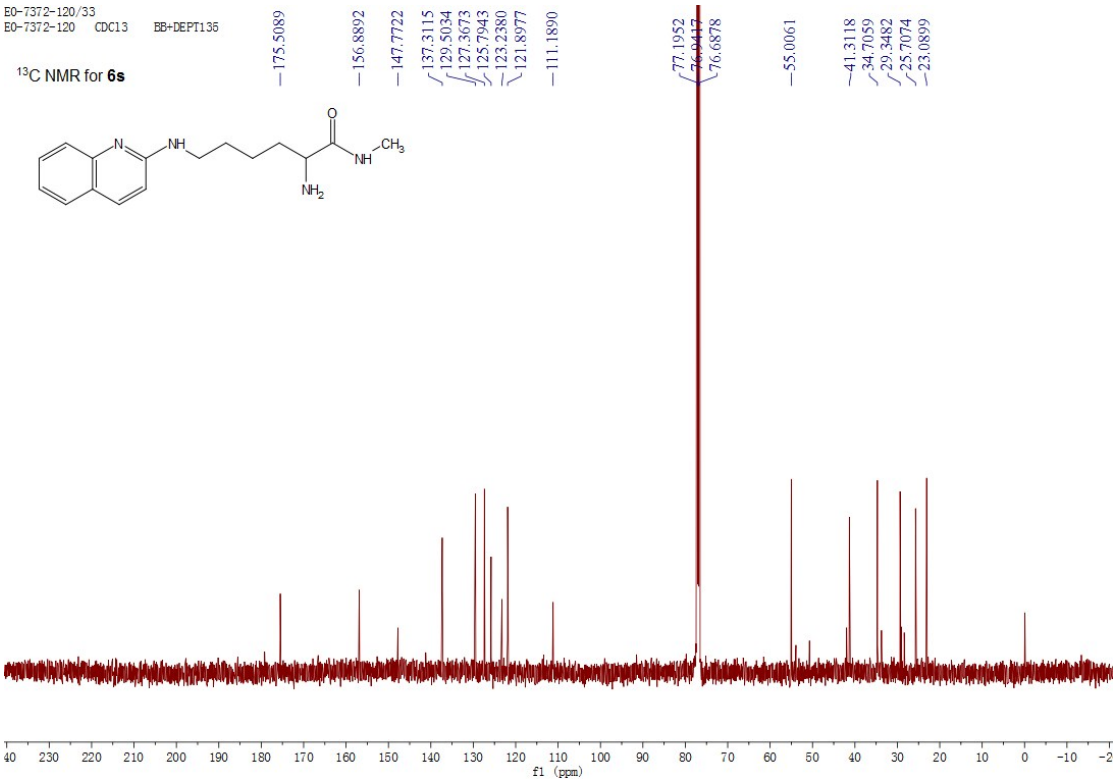

7.82
7.81
7.68
7.67
7.66
7.58
7.55
7.53
7.51
7.25
7.24
7.22
6.71
6.69
5.42
5.09
5.07
5.06
5.04
3.78
2.67
2.66
2.65
2.64
2.63
2.62
2.39
2.37
2.35
2.34
2.32
2.30
2.19
2.17
2.15
2.13
2.11
¹H NMR for 6p
N
NH
H3C
O
O
S
CH3
1.00
1.05
1.04
1.07
0.98
0.89
0.88
0.96
2.81
1.76
1.05
0.90
f1 (ppm)

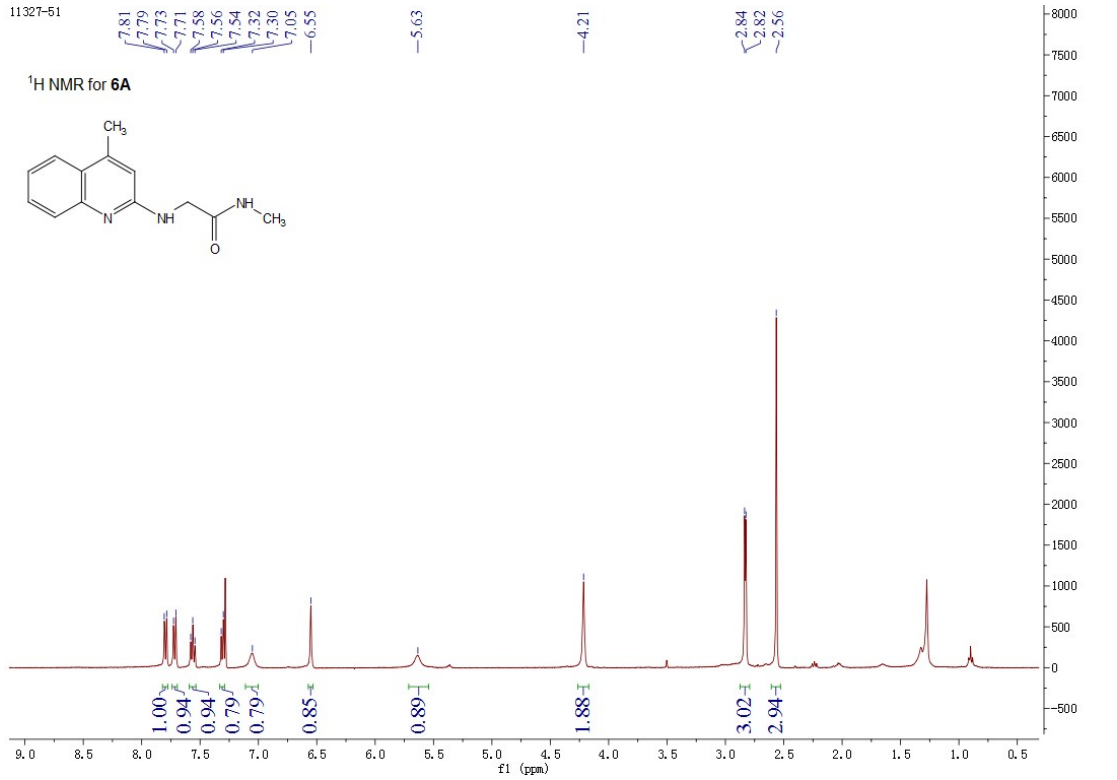

13C NMR for 6p
173.17
155.10
147.26
137.52
129.57
127.39
126.39
123.67
122.60
112.04
53.19
52.39
31.96
30.30
15.52
f1 (ppm)

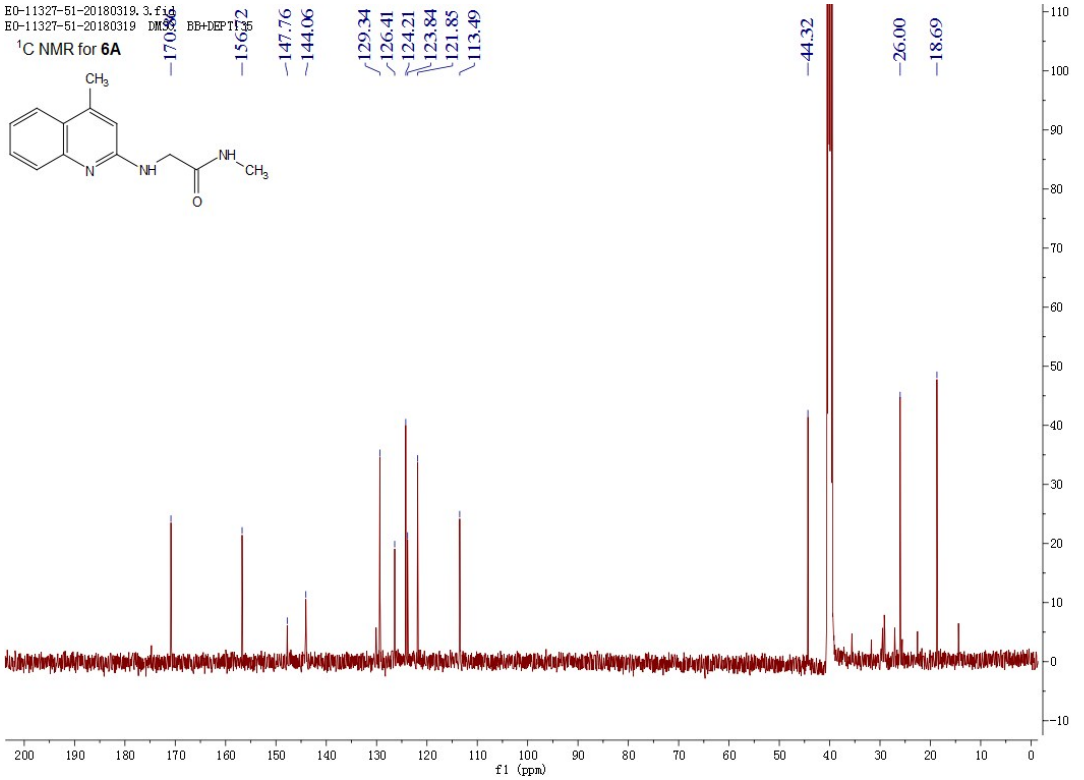

1H NMR for 6r
7.99
7.65
7.63
7.62
7.60
7.58
7.53
7.37
7.35
7.33
6.76
4.08
4.06
4.04
3.70
3.35
3.33
3.32
1.94
1.93
1.92
1.91
1.89
1.88
1.87
1.85
1.69
1.67
1.65
1.63
1.49
1.48
1.47
1.45
1.43
1.41
1.00
1.28
0.93
0.87
1.01
0.87
0.98
3.10
1.84
2.38
2.23
2.31
f1 (ppm)

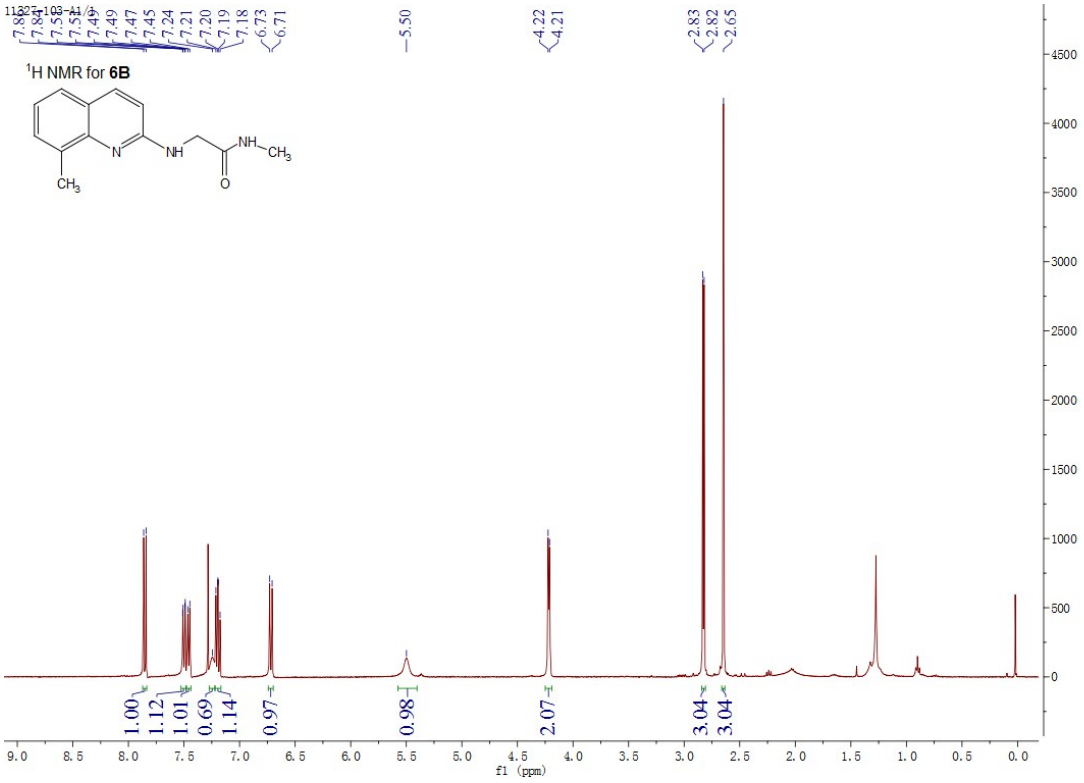

E0-9396-43.3.fid
E0-9396-34 D2O BB+DEPT135
170.95
152.53
141.93
135.57
132.50
128.68
125.42
121.07
117.01
113.78
53.56
52.72
41.62
29.37
26.88
21.69
13C NMR for 6r
f1 (ppm)

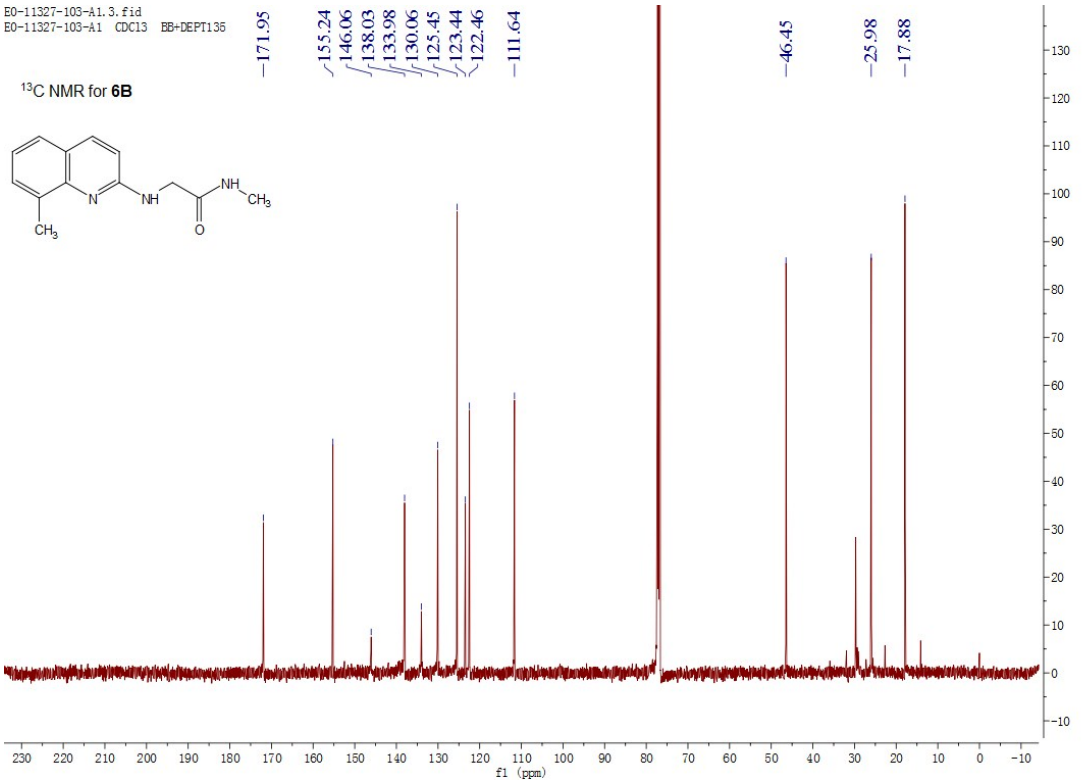

3.54
3.53
3.51
3.50
3.39
3.38
3.37
3.36
2.81
2.80
1.71
1.71
1.70
1.69
1.69
1.60
1.60
1.59
1.59
1.58
1.57
1.53
1.51
1H NMR for 6s
1.00
1.01
0.96
0.99
1.00
0.96
2.02
1.10
2.93
2.30
2.45
2.43
f1 (ppm)

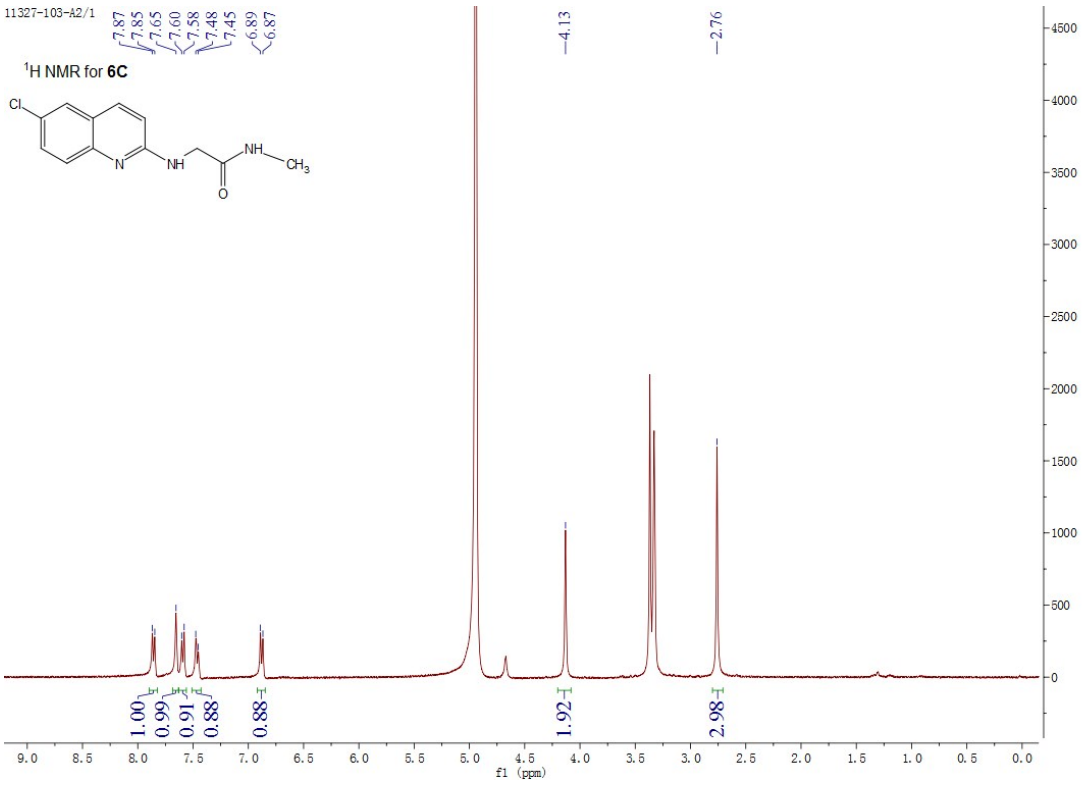

E0-7372-120/33
E0-7372-120 CDCl3 BB+DEPT135
13C NMR for 6s
175.5089
156.8892
147.7722
137.3115
129.5034
127.3673
125.7943
123.2380
121.8977
111.1890
77.1952
76.6878
55.0061
41.3118
34.7059
29.3482
25.7074
23.0899
f1 (ppm)

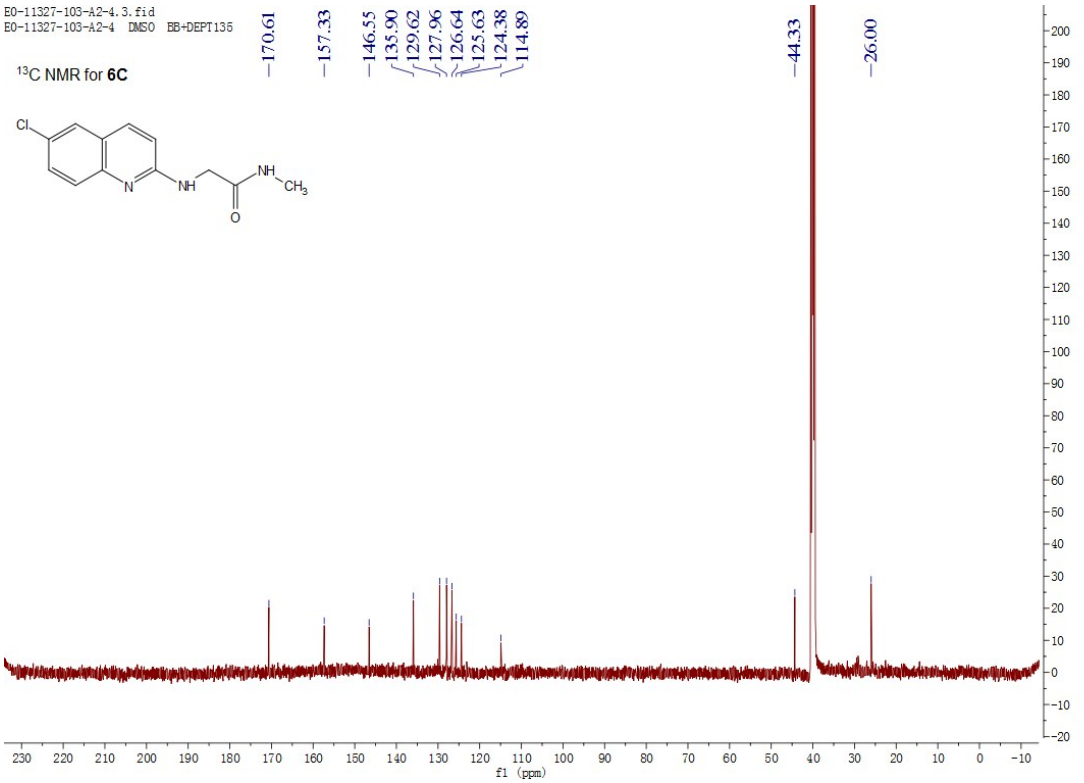

11327-51
1H NMR for 6A
7.81
7.79
7.73
7.71
7.58
7.56
7.54
7.32
7.30
7.05
6.55
5.63
4.21
2.84
2.82
2.56
1.00
0.94
0.94
0.79
0.79
0.85
0.89
1.88
3.02
2.94
f1 (ppm)

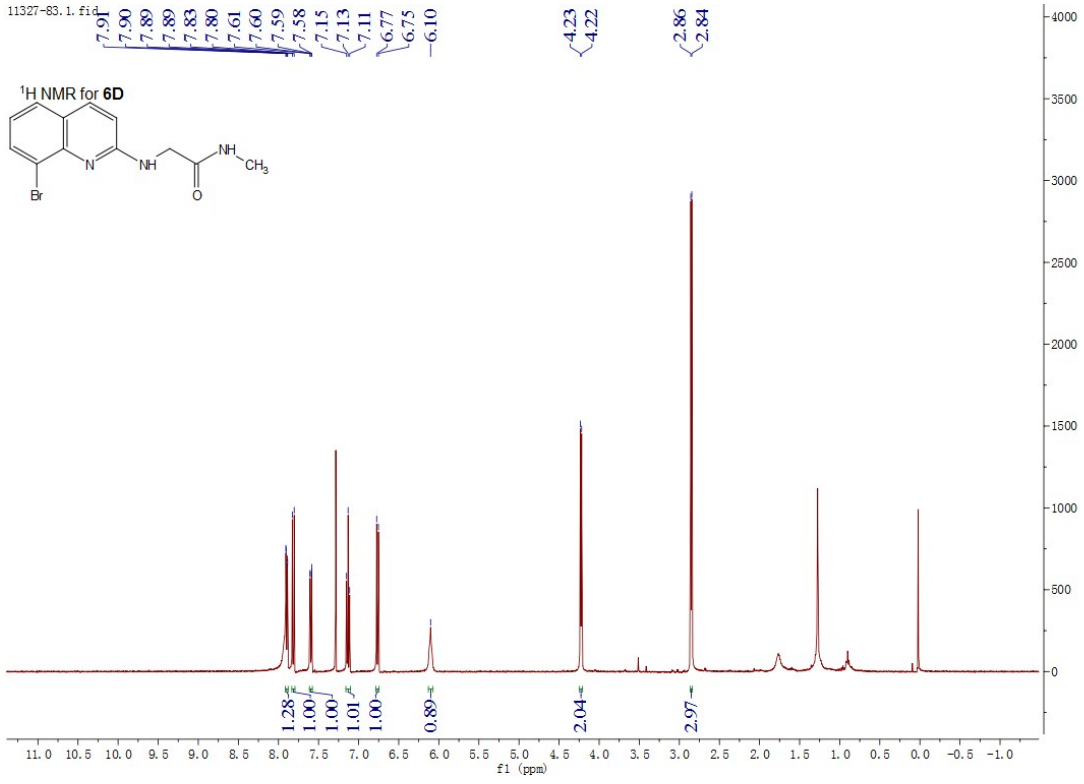

EO-11327-51-20180319.3.fid
EO-11327-51-20180319 DMSO BB+DEPT135
^{1}C NMR for **6A**
170.86
156.62
147.76
144.06
129.34
126.41
124.21
123.84
121.85
113.49
44.32
26.00
18.69
f1 (ppm)

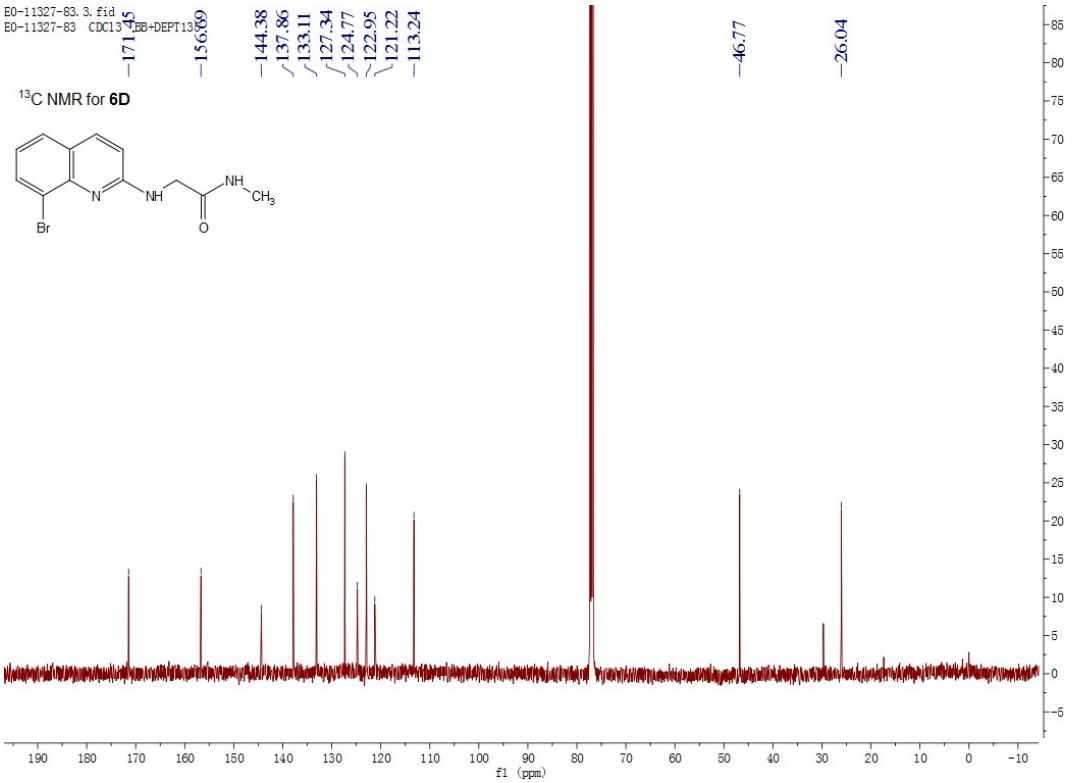

^{1}H NMR for **6B**
7.84
7.55
7.49
7.47
7.45
7.24
7.21
7.20
7.19
7.18
6.73
6.71
5.50
4.22
4.21
2.83
2.82
2.65
1.00
1.12
1.01
0.69
1.14
0.97
0.98
2.07
3.04
3.04
f1 (ppm)

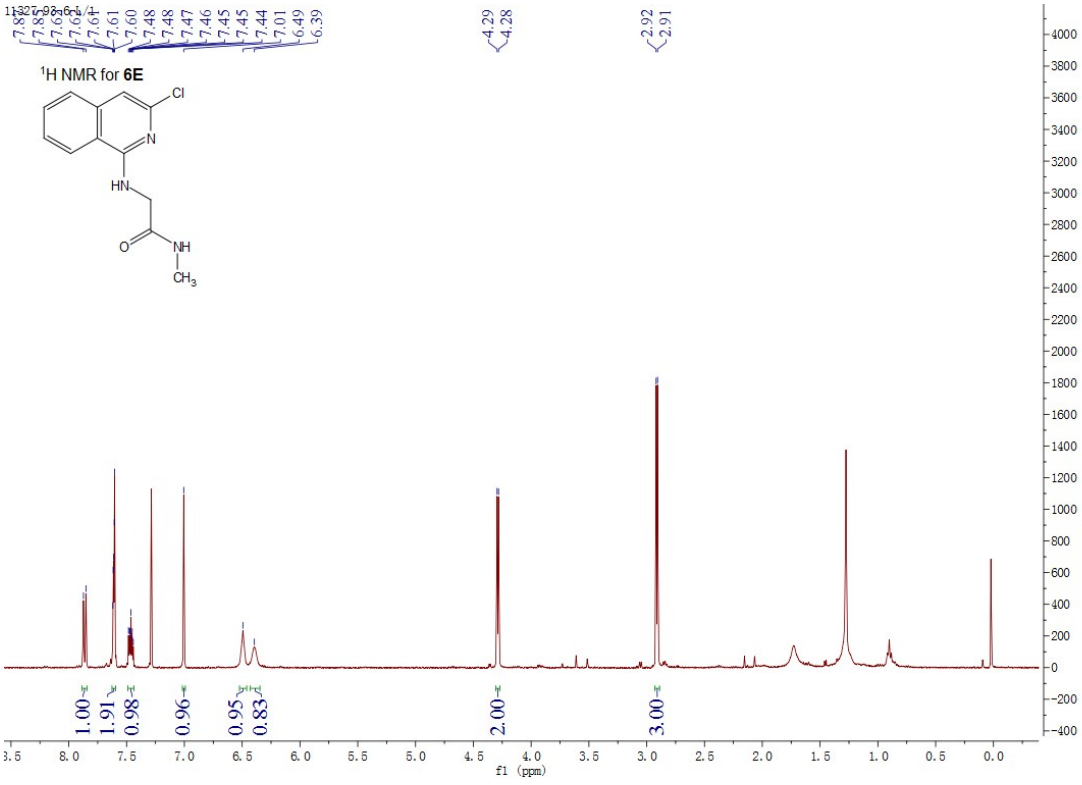

E0-11327-103-A1.3.fid
E0-11327-103-A1 CDCl3 BB+DEPT135
171.95
155.24
146.06
138.03
133.98
130.06
125.45
123.44
122.46
111.64
46.45
25.98
17.88
13C NMR for 6B
f1 (ppm)

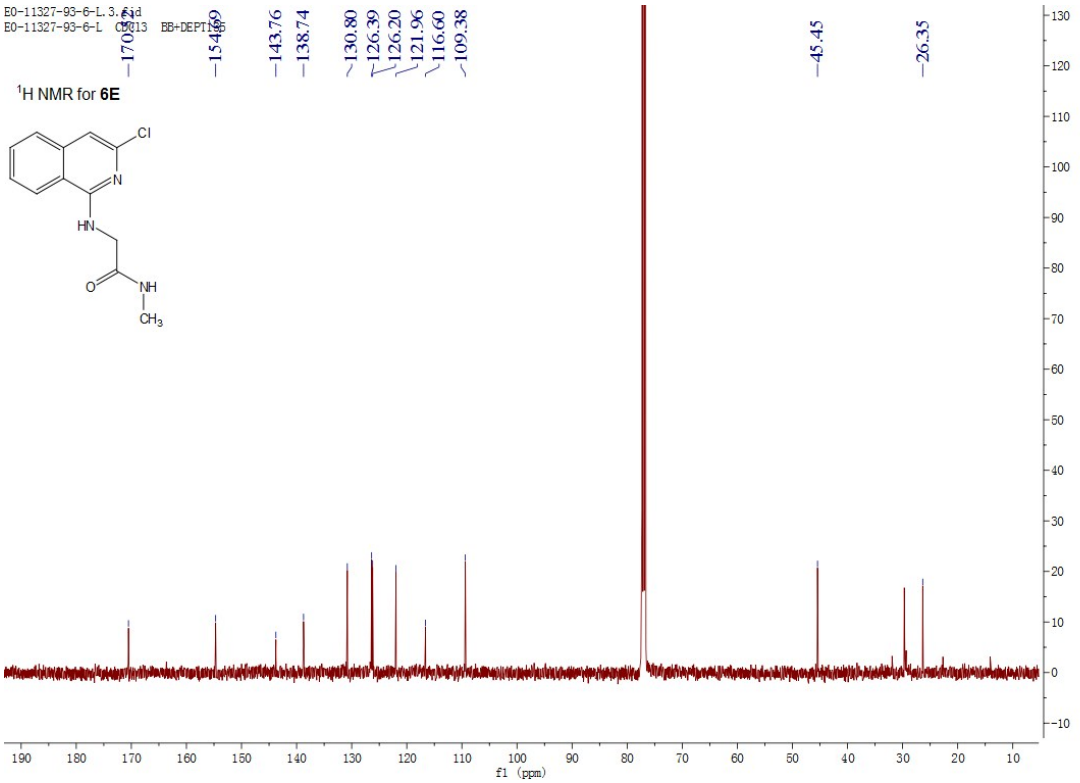

11327-103-A2/1
7.87
7.85
7.65
7.60
7.58
7.48
7.45
6.89
6.87
4.13
2.76
1H NMR for 6C
1.00
0.99
0.91
0.88
0.88
1.92
2.98
f1 (ppm)

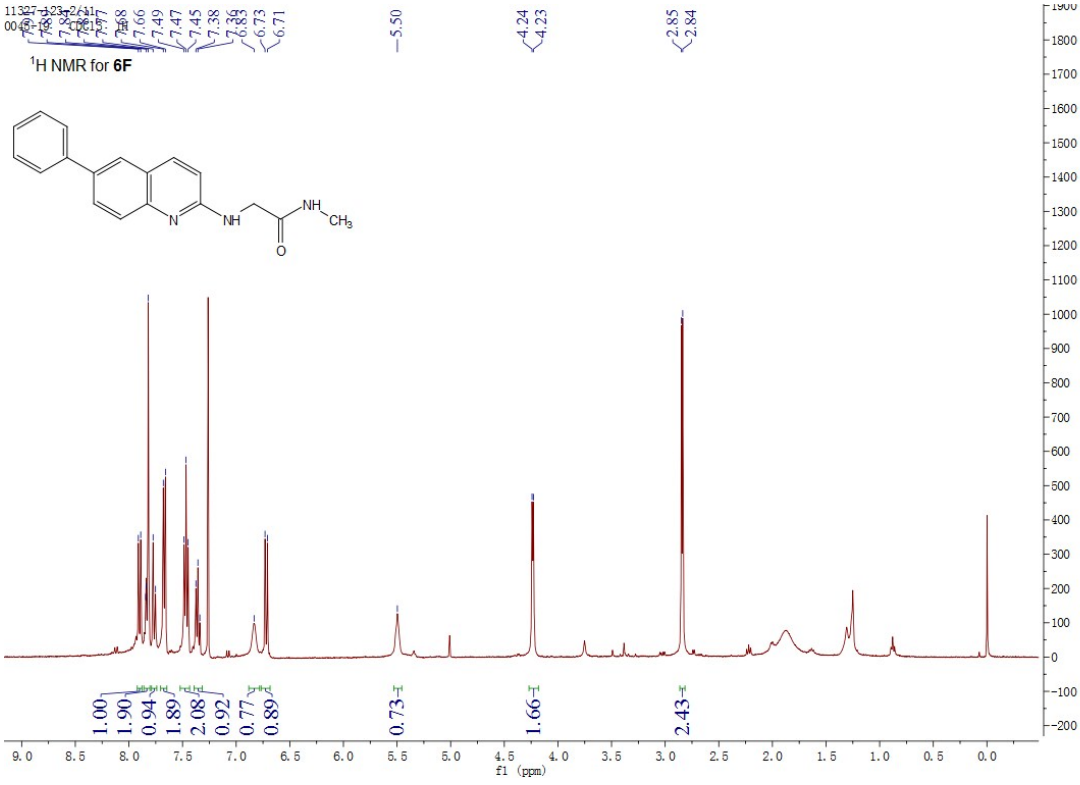

E0-11327-103-A2-4.3.fid
E0-11327-103-A2-4 DMSO BB+DEPT135
170.61
157.33
146.55
135.90
129.62
127.96
126.64
125.63
124.38
114.89
44.33
26.00
13C NMR for 6C
Cl
N
NH
NH
CH3
O
f1 (ppm)

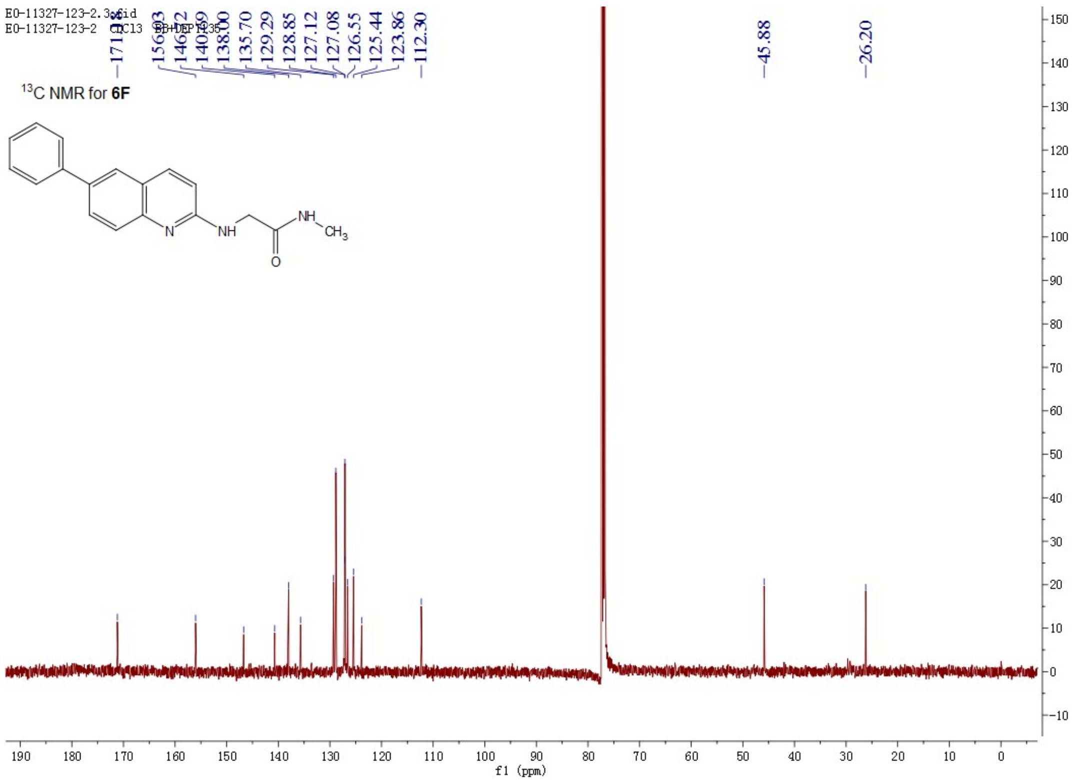

11327-83.1.fid
7.91
7.90
7.89
7.89
7.83
7.80
7.61
7.60
7.59
7.58
7.15
7.13
7.11
6.77
6.75
6.10
4.23
4.22
2.86
2.84
1H NMR for 6D
N
NH
NH
CH3
Br
O
1.28
1.00
1.00
1.01
1.00
0.89
2.04
2.97
f1 (ppm)

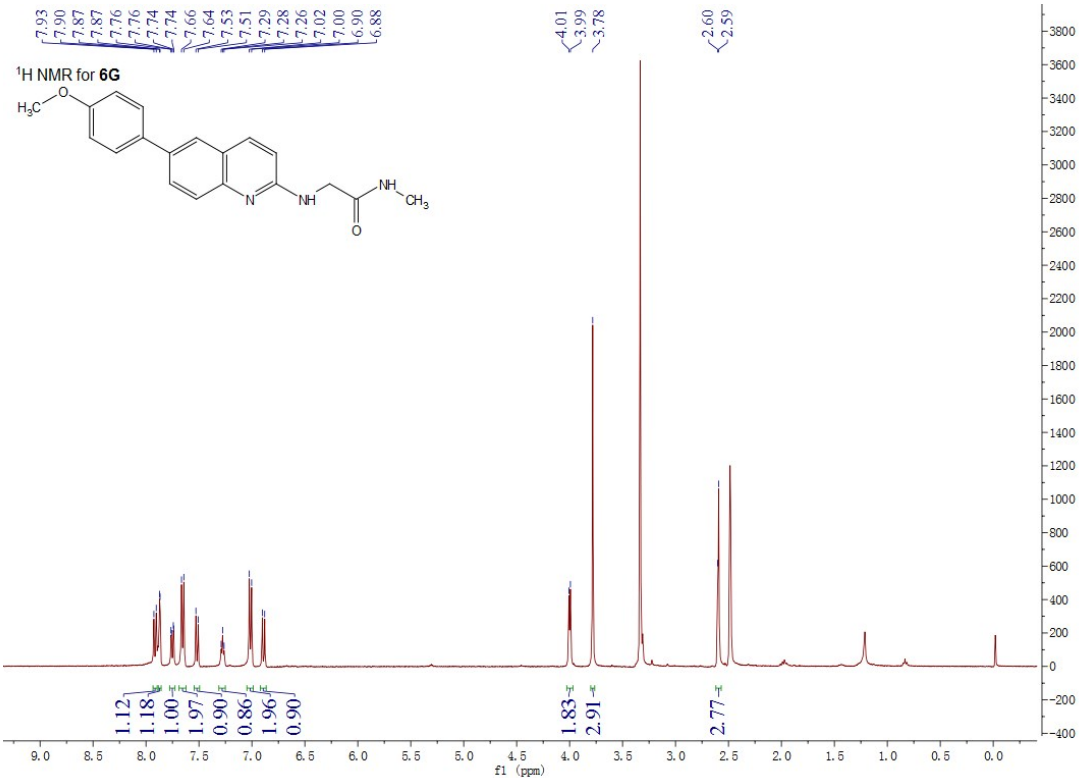

E0-11327-83.3.fid
E0-11327-83 CDCl3 1BB+DEPT135
171.15
156.89
144.38
137.86
133.11
127.34
124.77
122.95
121.22
113.24
46.77
26.04
13C NMR for 6D
N
NH
NH
CH3
Br
O
f1 (ppm)

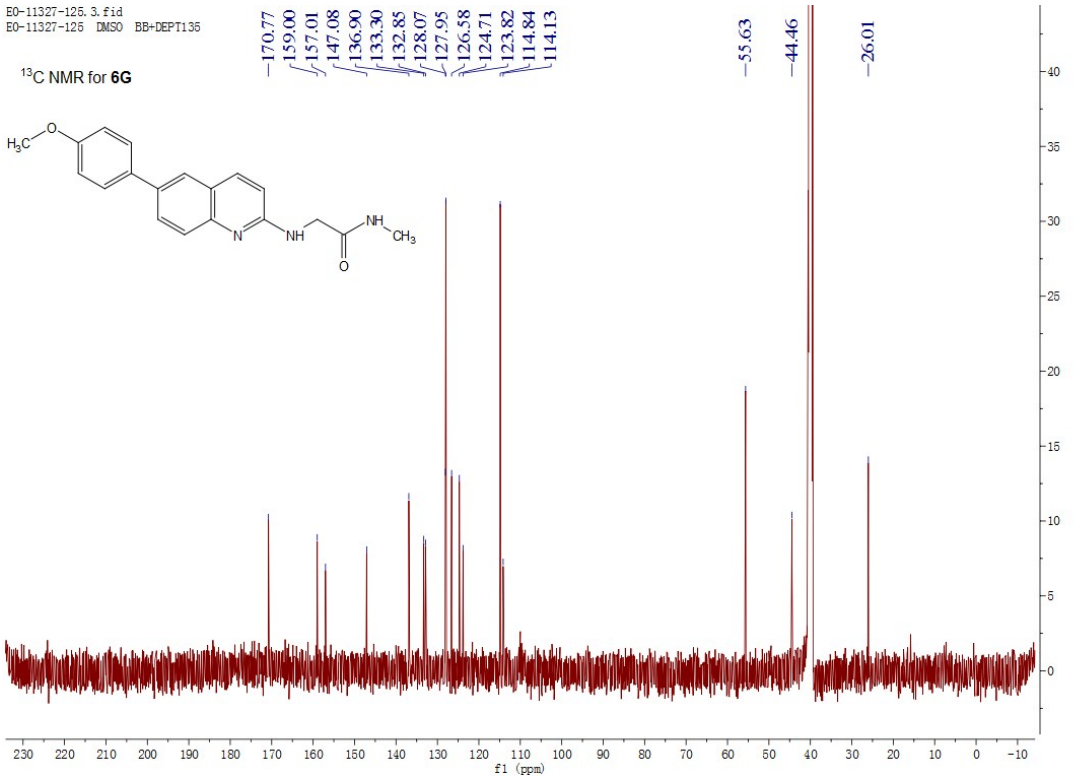

7.85
7.63
7.61
7.60
7.48
7.47
7.46
7.45
7.44
7.01
6.49
6.39
4.29
4.28
2.92
2.91
1H NMR for 6E
Cl
N
HN
O
NH
CH3
1.00
1.91
0.98
0.96
0.95
0.83
2.00
3.00
f1 (ppm)

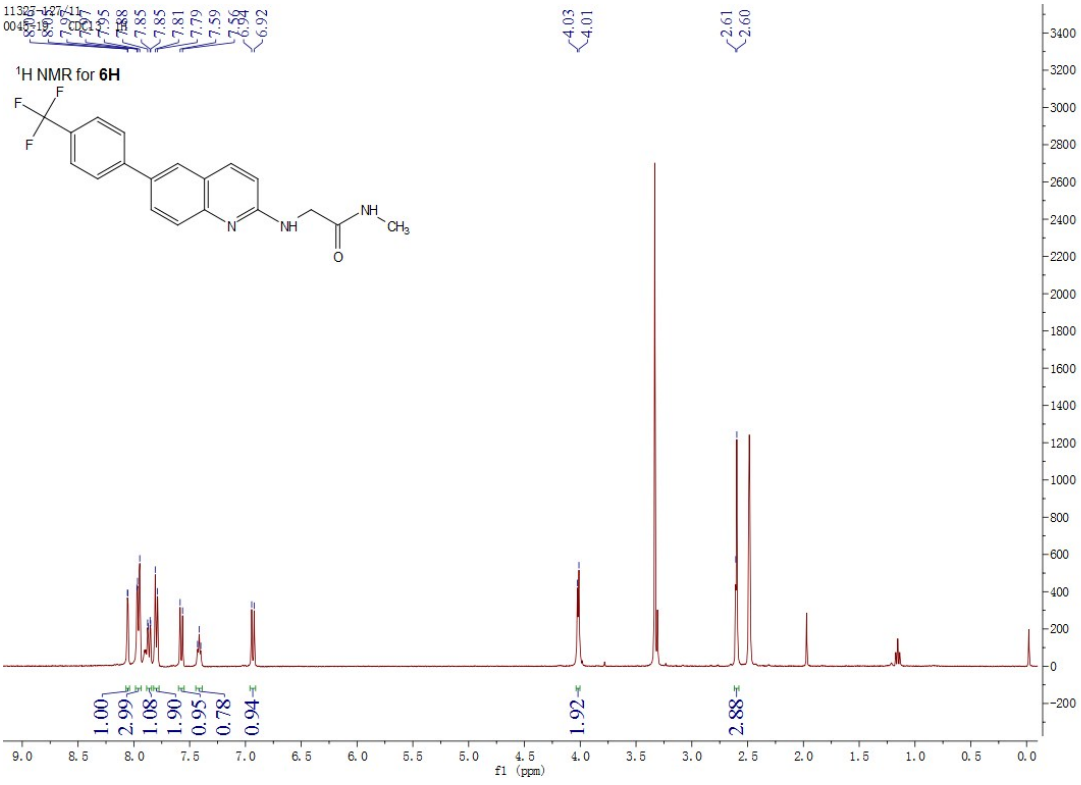

EO-11327-93-6-L.3.fid
EO-11327-93-6-L CDCl3 BB+DEPT135
170.61
154.29
143.76
138.74
130.80
126.39
126.20
121.96
116.60
109.38
45.45
26.35
1H NMR for 6E
Cl
N
HN
O
NH
CH3
f1 (ppm)

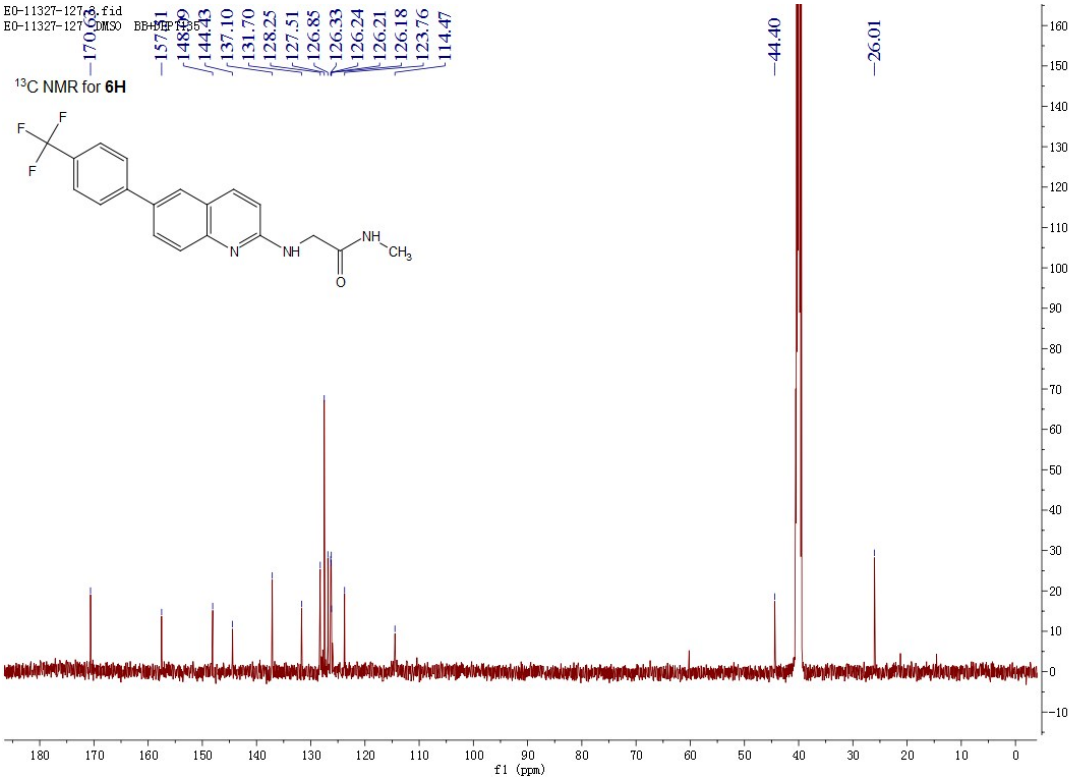

7.68
7.66
7.49
7.47
7.45
7.38
6.83
6.73
6.71
5.50
4.24
4.23
2.85
2.84
1H NMR for 6F
N
NH
NH
CH3
O
1.00
1.90
0.94
1.89
2.08
0.92
0.77
0.89
0.73
1.66
2.43
f1 (ppm)

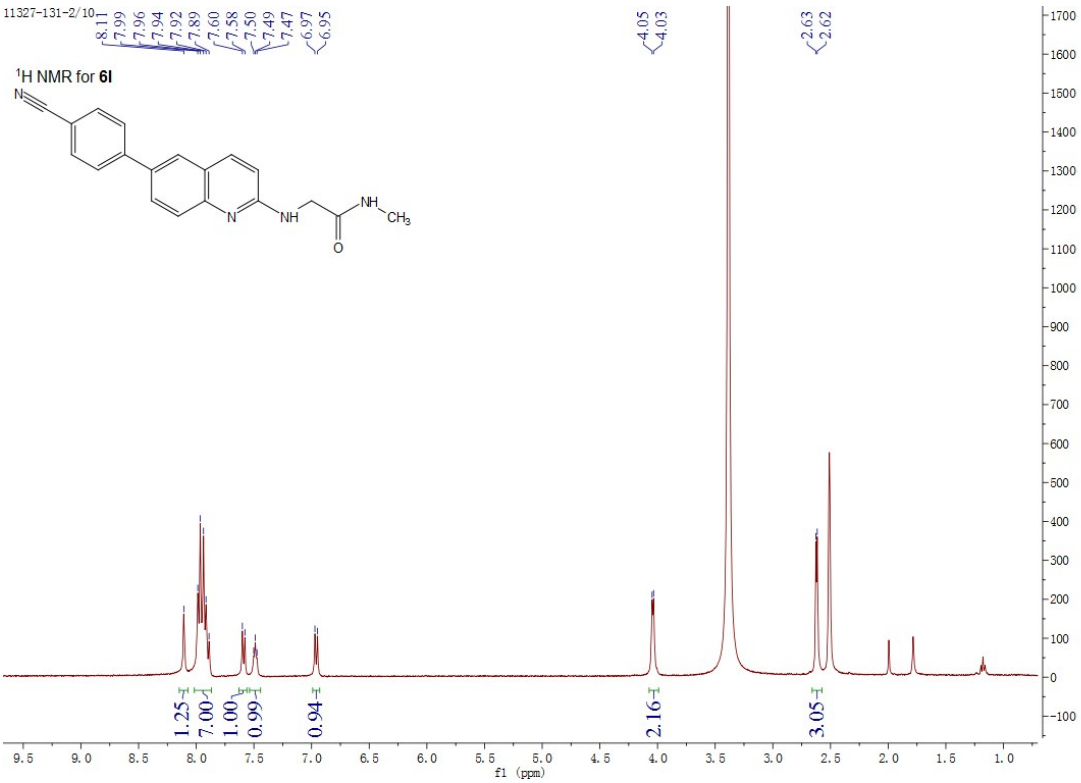

E0-11327-123-2.3.fid
E0-11327-123-2 13C13 BB+DEPT135
^{13}C NMR for **6F**
171.14
156.03
146.72
140.99
138.00
135.70
129.29
128.85
127.12
127.08
126.55
125.44
123.86
112.30
45.88
26.20
NH
N
NH
O
CH$_3$
f1 (ppm)

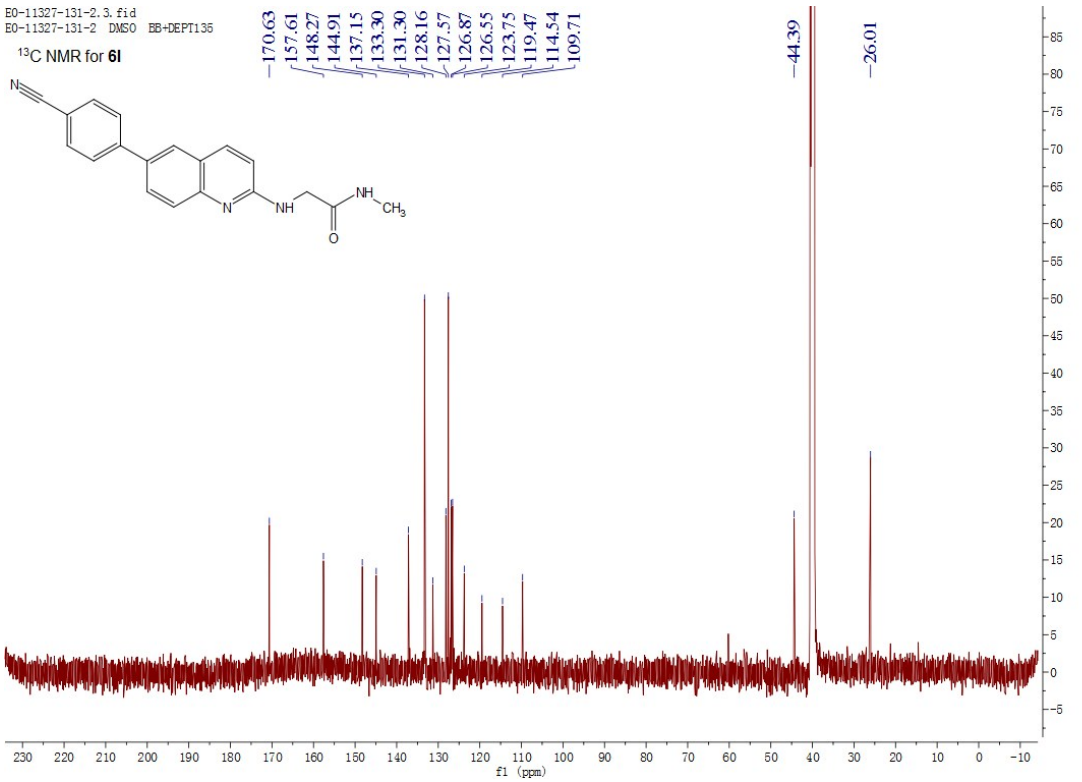

^{1}H NMR for **6G**
7.93
7.90
7.87
7.87
7.76
7.76
7.74
7.74
7.66
7.64
7.53
7.51
7.29
7.28
7.26
7.02
7.00
6.90
6.88
4.01
3.99
3.78
2.60
2.59
H$_3$C
O
N
NH
NH
O
CH$_3$
1.12
1.18
1.00
1.97
0.90
0.86
1.96
0.90
1.83
2.91
2.77
f1 (ppm)

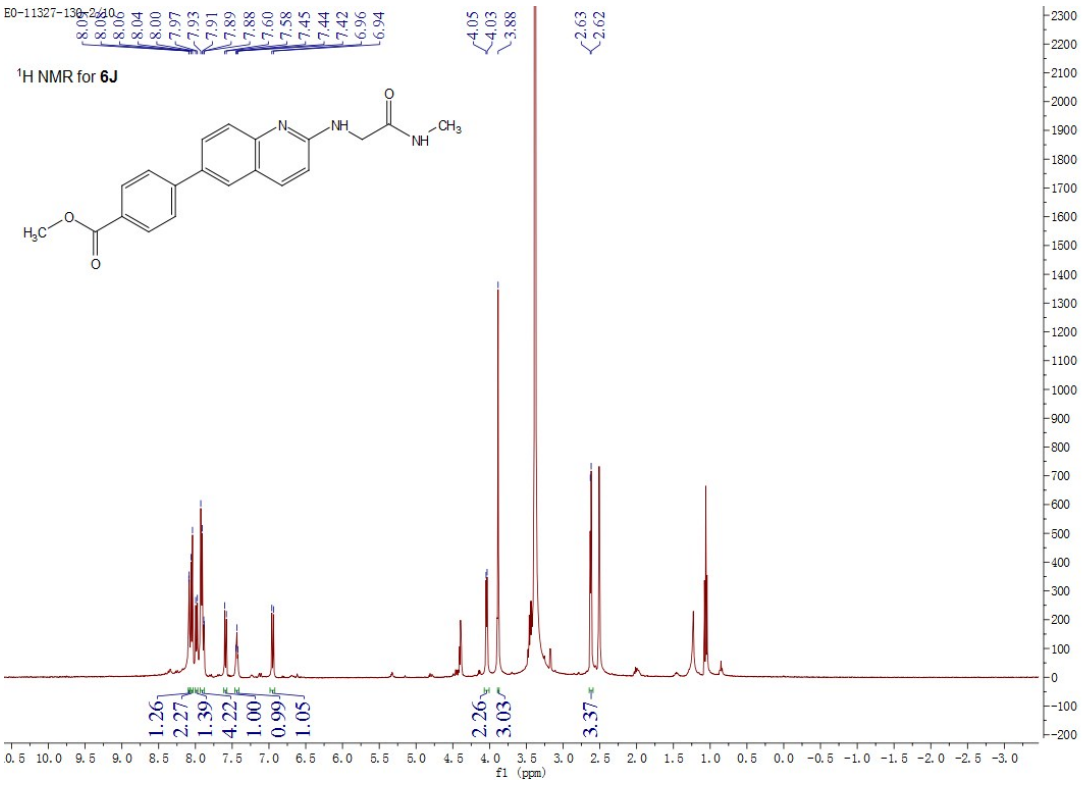

E0-11327-125.3.fid
E0-11327-125 DMSO BB+DEPT135
13C NMR for 6G
170.77
159.00
157.01
147.08
136.90
133.30
132.85
128.07
127.95
126.58
124.71
123.82
114.84
114.13
55.63
44.46
26.01
f1 (ppm)

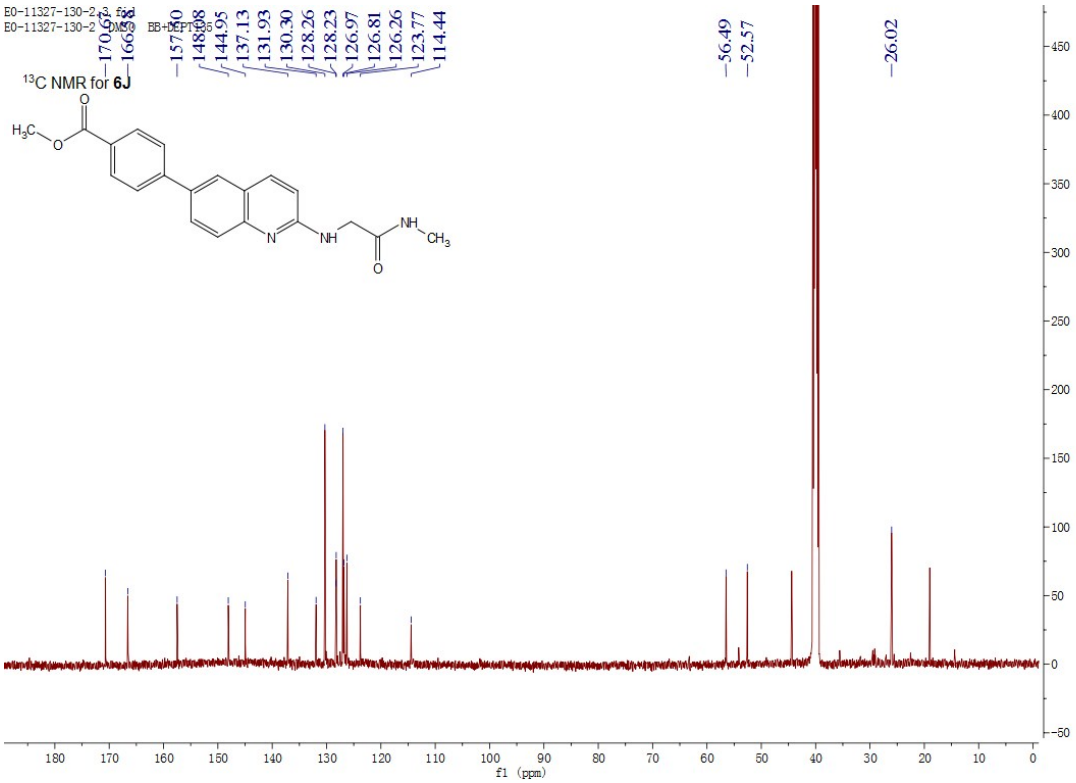

1H NMR for 6H
8.40
7.97
7.95
7.88
7.85
7.85
7.81
7.79
7.59
7.56
6.94
6.92
4.03
4.01
2.61
2.60
1.00
2.99
1.08
1.90
0.95
0.78
0.94
1.92
2.88
f1 (ppm)

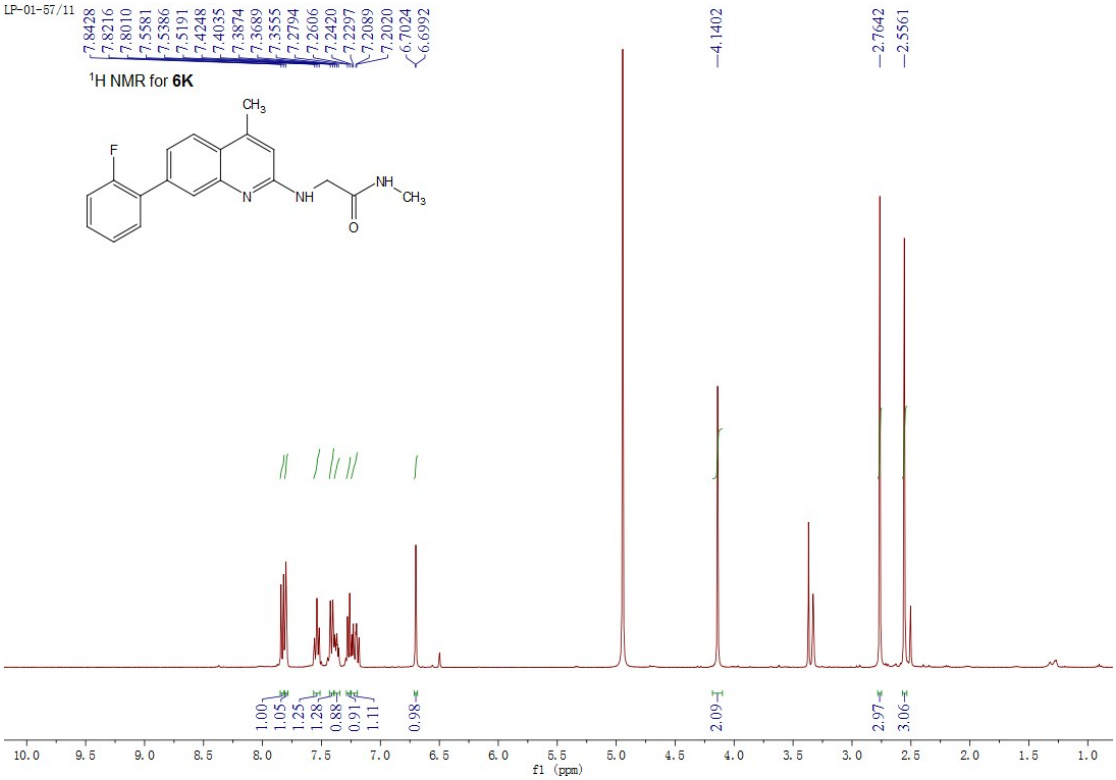

EO-11327-127c8.fid
EO-11327-127c8 DMSO BB+MEPTAB
170.63
157.41
148.89
144.43
137.10
131.70
128.25
127.51
126.85
126.33
126.24
126.21
126.18
123.76
114.47
44.40
26.01
13C NMR for 6H
F
F
F
N
NH
NH
CH3
O
f1 (ppm)

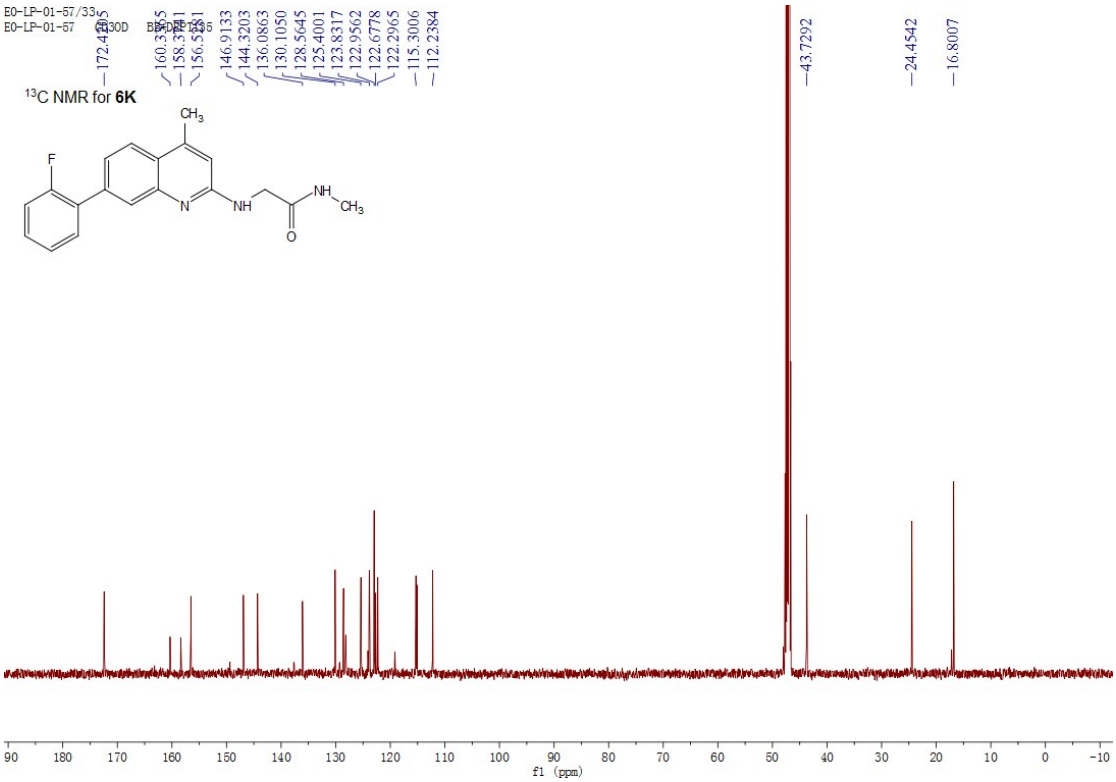

11327-131-2/10
8.11
7.99
7.96
7.94
7.92
7.89
7.60
7.58
7.50
7.49
7.47
6.97
6.95
4.05
4.03
2.63
2.62
1H NMR for 6I
N
NH
NH
CH3
O
1.25
7.00
1.00
0.99
0.94
2.16
3.05
f1 (ppm)

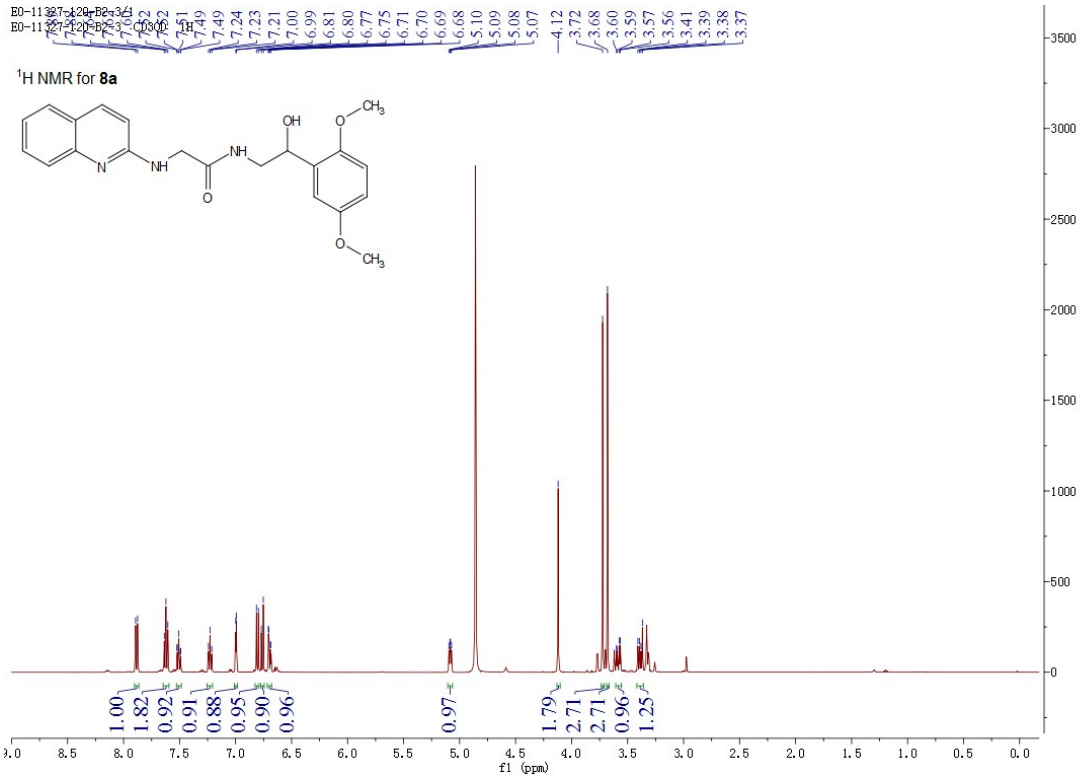

E0-11327-131-2.3.fid
E0-11327-131-2 DMSO BB+DEPT135
^{13}C NMR for **6I**
170.63
157.61
148.27
144.91
137.15
133.30
131.30
128.16
127.57
126.87
126.55
123.75
119.47
114.54
109.71
44.39
26.01
f1 (ppm)

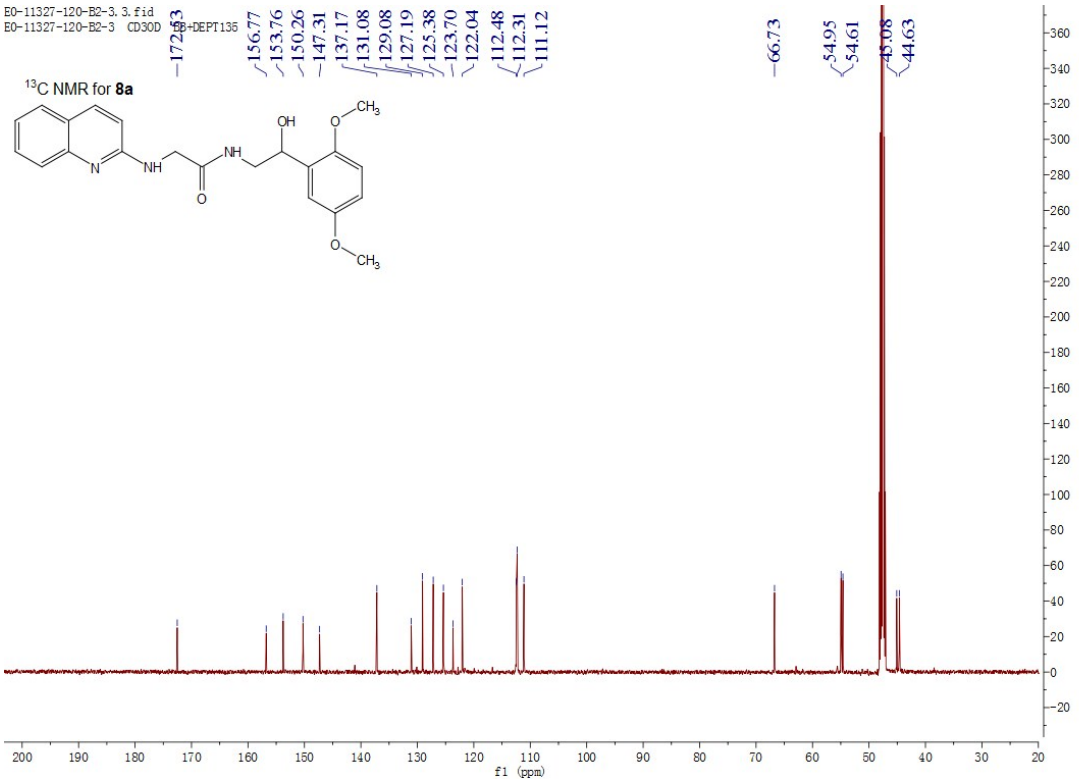

E0-11327-136-2.10
^{1}H NMR for **6J**
8.07
8.05
8.04
8.00
7.97
7.93
7.91
7.89
7.88
7.60
7.58
7.45
7.44
7.42
6.96
6.94
4.05
4.03
3.88
2.63
2.62
1.26
2.27
1.39
4.22
1.00
0.99
1.05
2.26
3.03
3.37
f1 (ppm)

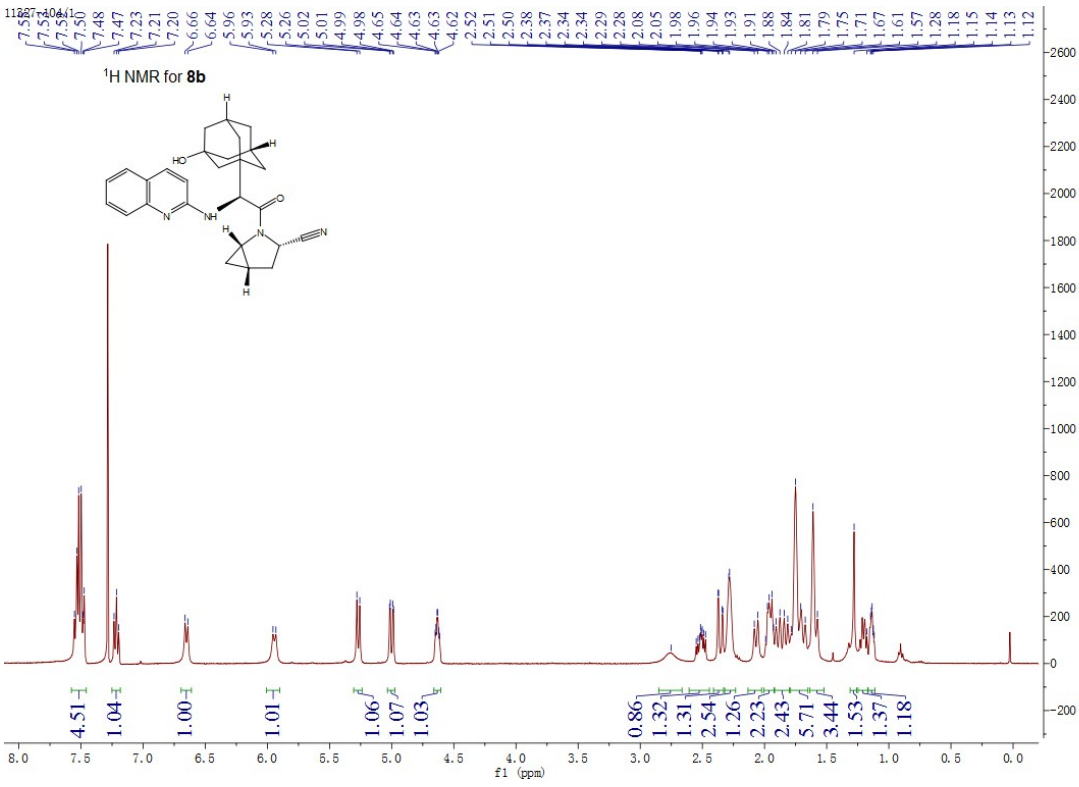

E0-11327-130-2-3.fid
E0-11327-130-2 DMSO BB+DEPT135
170.67
166.33
157.10
148.98
144.95
137.13
131.93
130.30
128.26
128.23
126.97
126.81
126.26
123.77
114.44
56.49
52.57
26.02
13C NMR for 6J
f1 (ppm)

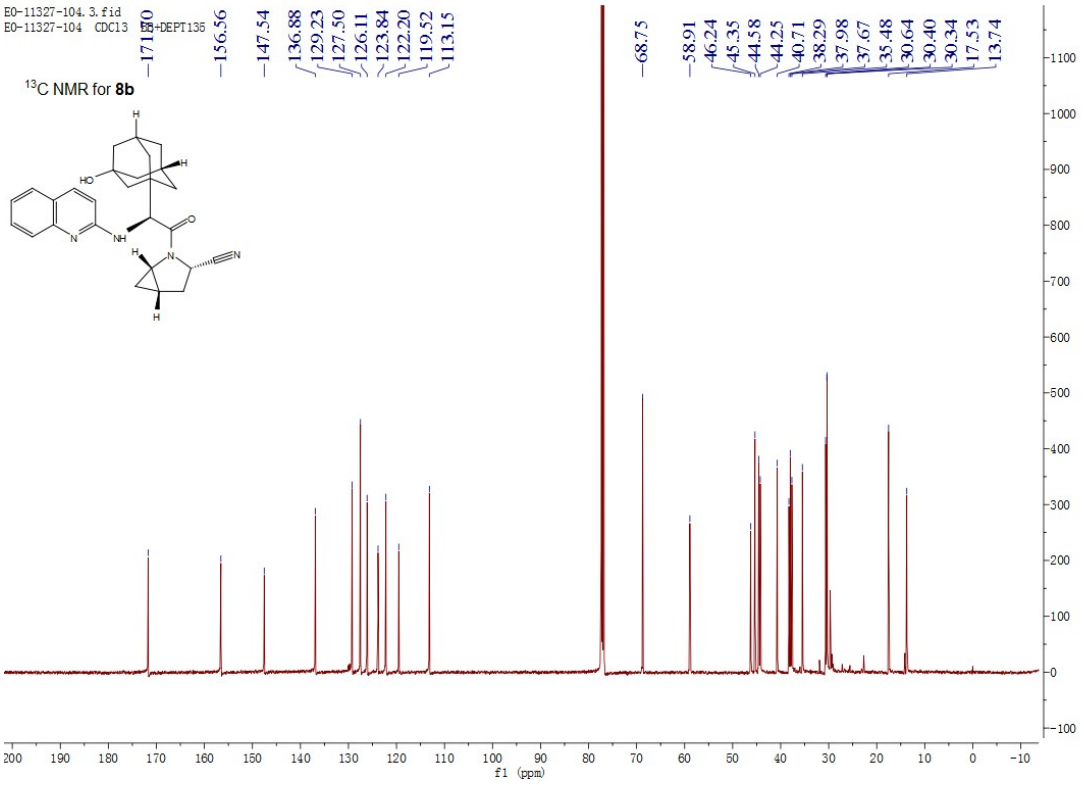

LP-01-57/11
7.8428
7.8216
7.8010
7.5581
7.5386
7.5191
7.4248
7.4035
7.3874
7.3689
7.3555
7.2794
7.2606
7.2420
7.2297
7.2089
7.2020
6.7024
6.6992
4.1402
2.7642
2.5561
1H NMR for 6K
1.00
1.05
1.25
1.28
0.88
0.91
1.11
0.98
2.09
2.97
3.06
f1 (ppm)

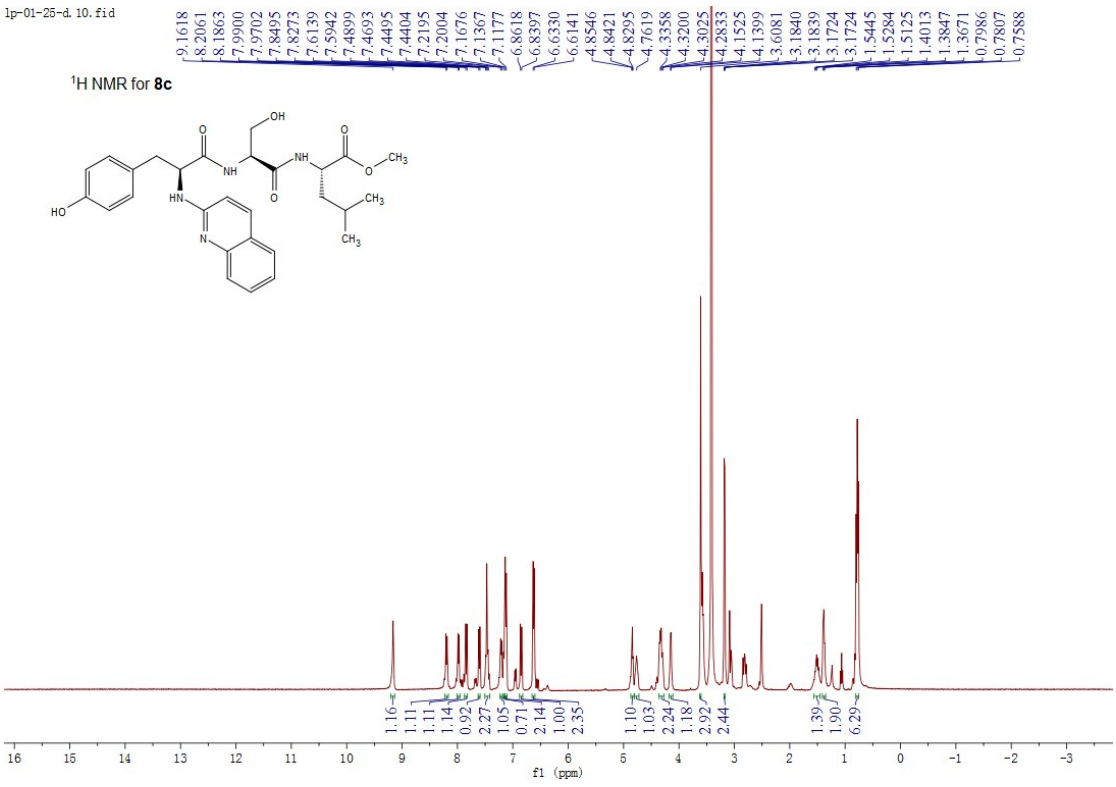

13C NMR for 6K
F
CH3
N
NH
NH
CH3
O
f1 (ppm)

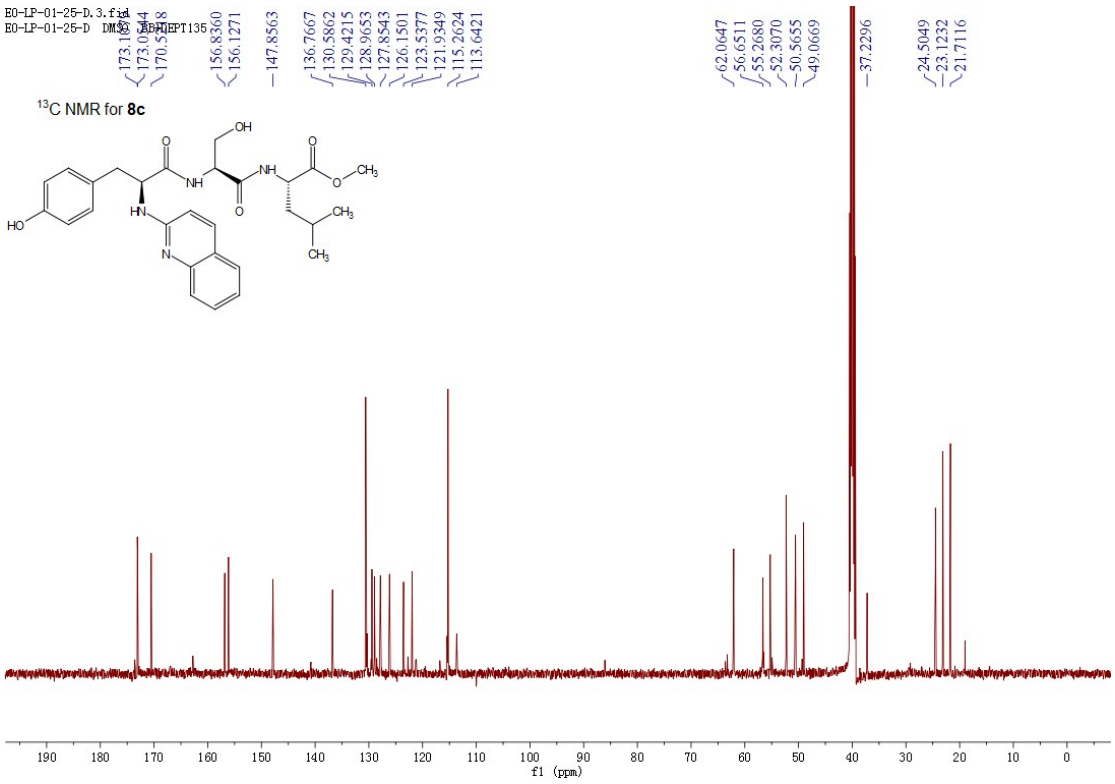

1H NMR for 8a
OH
O
CH3
NH
N
NH
O
O
CH3
1.00
1.82
0.92
0.91
0.88
0.95
0.90
0.96
0.97
1.79
2.71
2.71
0.96
1.25
f1 (ppm)

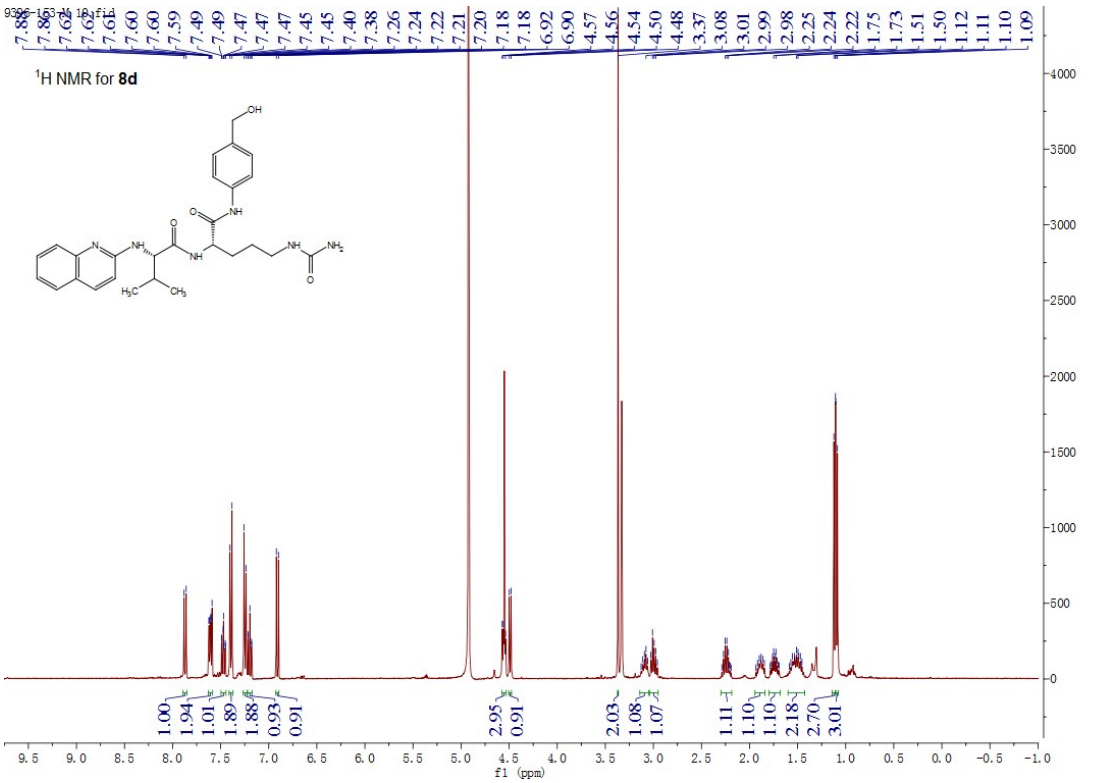

E0-11327-120-B2-3.3.fid
E0-11327-120-B2-3 CD3OD 13C+DEPT135
172.33
156.77
153.76
150.26
147.31
137.17
131.08
129.08
127.19
125.38
123.70
122.04
112.48
112.31
111.12
66.73
54.95
54.61
45.08
44.63
13C NMR for 8a
f1 (ppm)


1H NMR for 8b
4.51
1.04
1.00
1.01
1.06
1.07
1.03
0.86
1.32
1.31
2.54
1.26
2.23
2.43
5.71
3.44
1.53
1.37
1.18
f1 (ppm)


EO-11327-104.3.fid
EO-11327-104 CDC13 BB+DEPT135
171.50
156.56
147.54
136.88
129.23
127.50
126.11
123.84
122.20
119.52
113.15
68.75
58.91
46.24
45.35
44.58
44.25
40.71
38.29
37.98
37.67
35.48
30.64
30.40
30.34
17.53
13.74
13C NMR for 8b
f1 (ppm)


lp-01-25-d.10.fid
9.1618
8.2061
8.1863
7.9900
7.9702
7.8495
7.8273
7.6139
7.5942
7.4899
7.4693
7.4495
7.4404
7.2195
7.2004
7.1676
7.1367
7.1177
6.8618
6.8397
6.6330
6.6141
4.8546
4.8421
4.8295
4.7619
4.3358
4.3200
4.3025
4.2833
4.1525
4.1399
3.6081
3.1840
3.1839
3.1724
3.1724
1.5445
1.5284
1.5125
1.4013
1.3847
1.3671
0.7986
0.7807
0.7588
1H NMR for 8c
1.16
1.11
1.11
1.14
0.92
2.27
1.05
0.71
2.14
1.00
2.35
1.10
1.03
2.24
1.18
2.92
2.44
1.39
1.90
6.29
f1 (ppm)


EO-LP-01-25-D.3.fid
EO-LP-01-25-D DMSO 13CDEPT135
173.1
173.0
170.5
156.8360
156.1271
147.8563
136.7667
130.5862
129.4215
128.9653
127.8543
126.1501
123.5377
121.9349
115.2624
113.6421
62.0647
56.6511
55.2680
52.3070
50.5655
49.0669
37.2296
24.5049
23.1232
21.7116
13C NMR for 8c
f1 (ppm)


9386-153-N 1H.fid
7.88
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7.61
7.60
7.60
7.60
7.59
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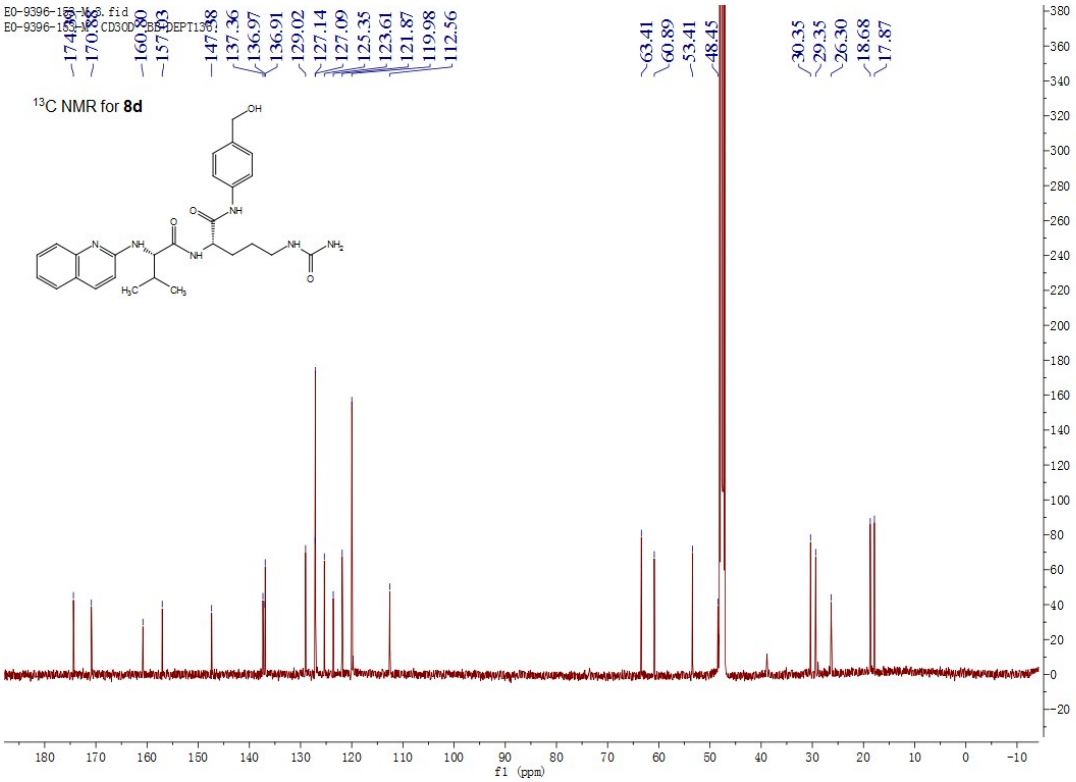
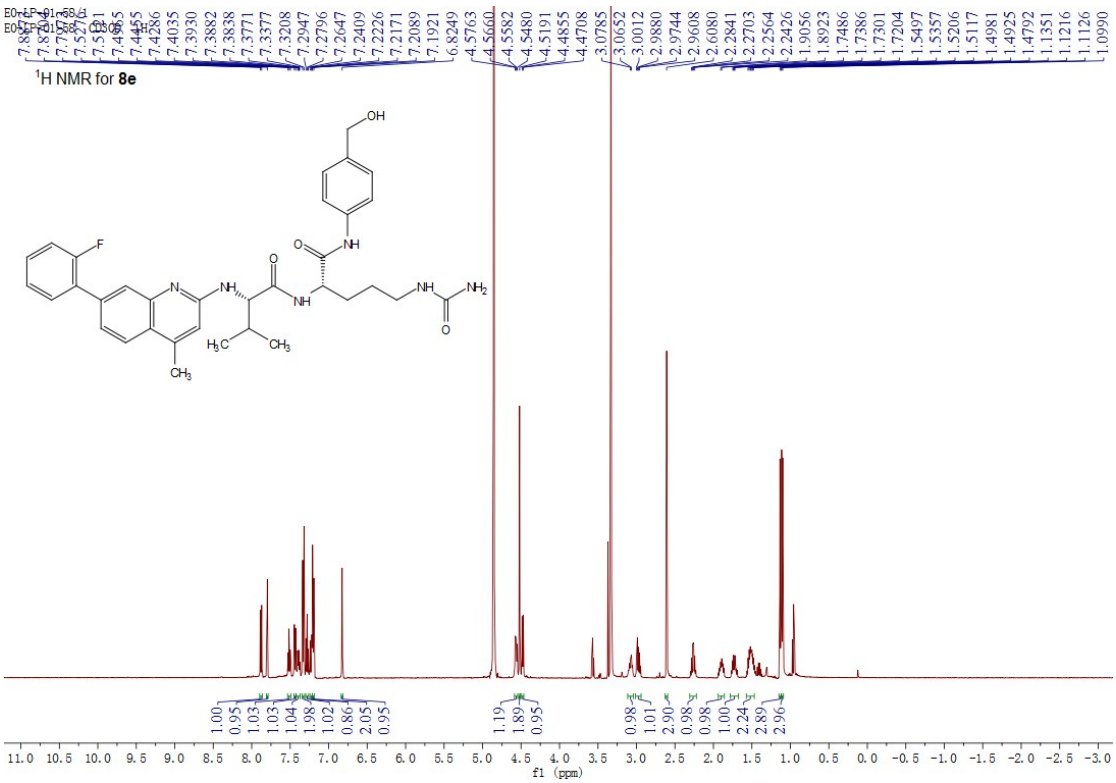
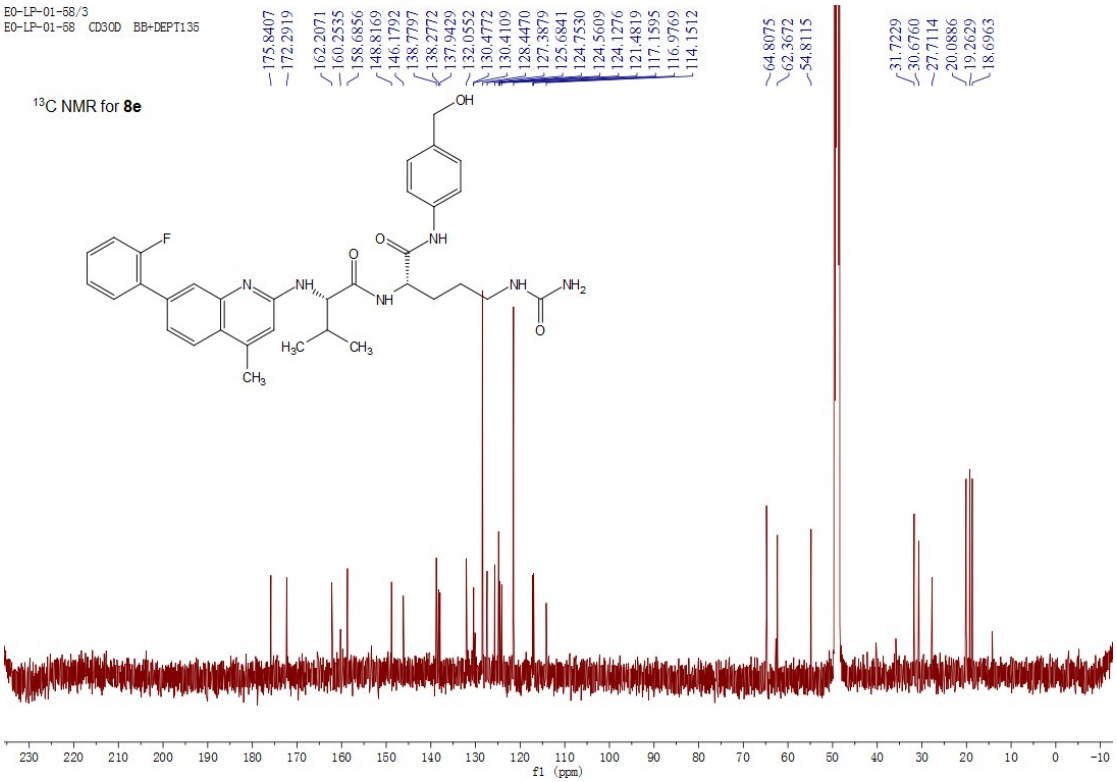
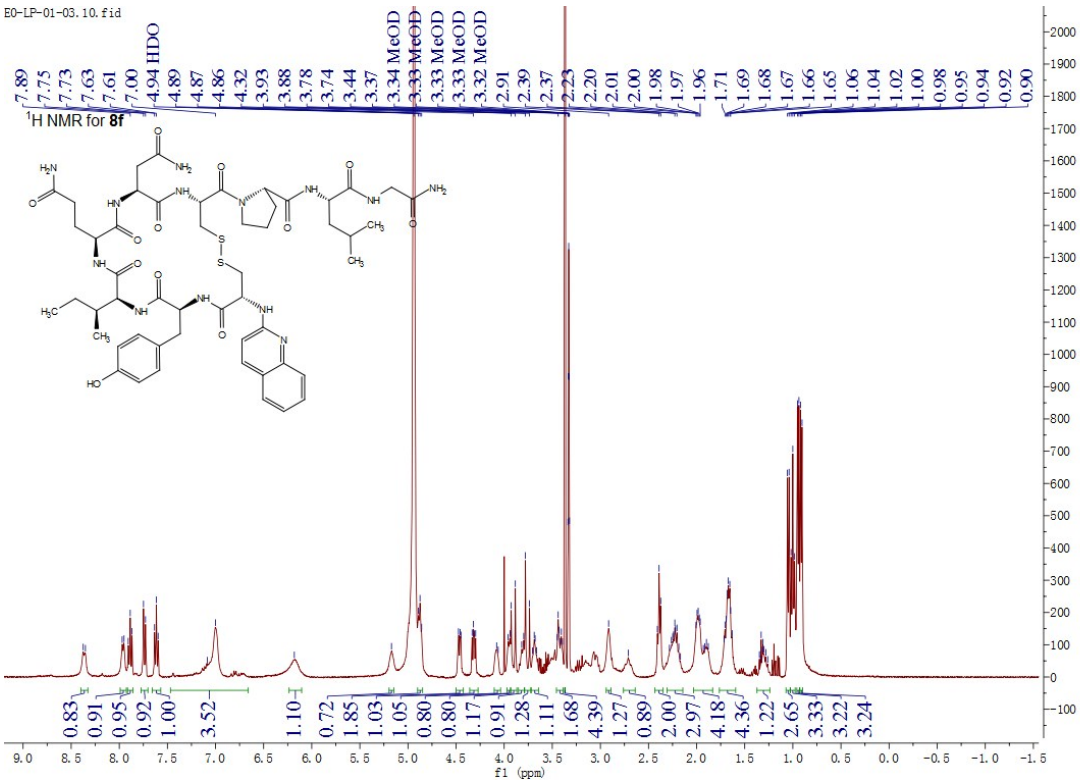
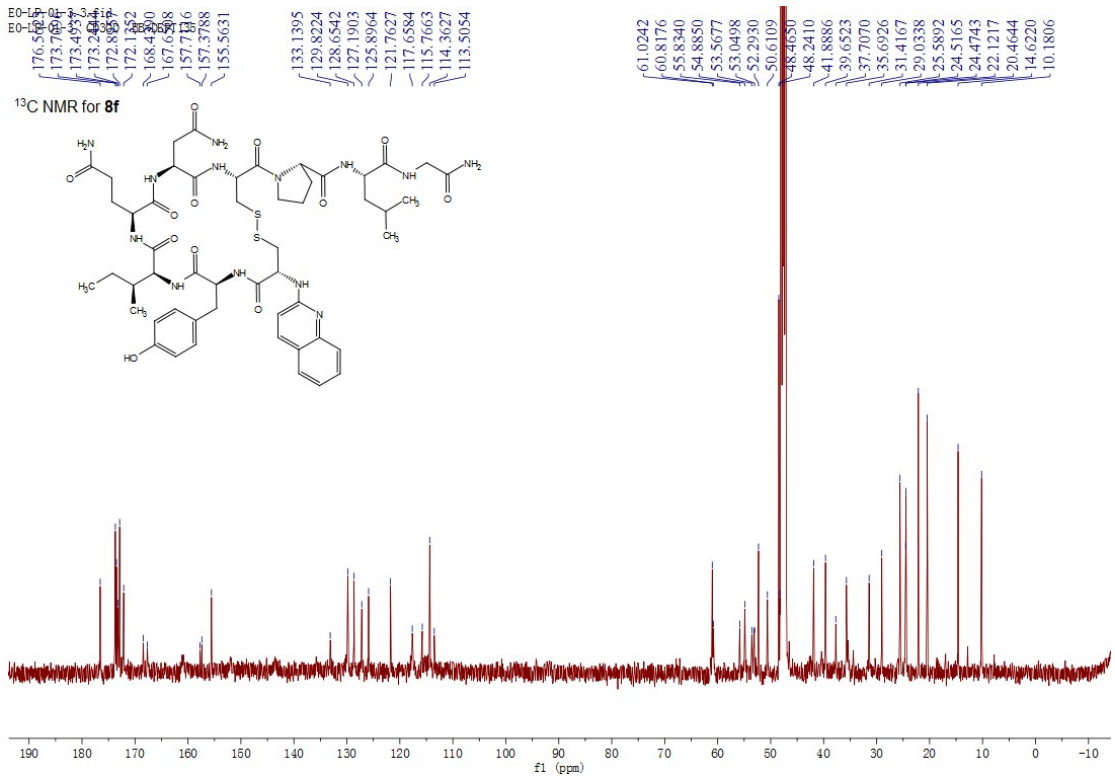
7.49
7.47
7.47
7.47
7.45
7.45
7.40
7.38
7.26
7.24
7.22
7.21
7.20
7.18
7.18
6.92
6.90
4.57
4.56
4.54
4.50
4.48
3.37
3.08
3.01
2.99
2.98
2.25
2.24
2.22
1.75
1.73
1.51
1.50
1.12
1.11
1.10
1.09
1H NMR for 8d
1.00
1.94
1.01
1.89
1.88
0.93
0.91
2.95
0.91
2.03
1.08
1.07
1.11
1.10
1.10
2.18
2.70
3.01
f1 (ppm)

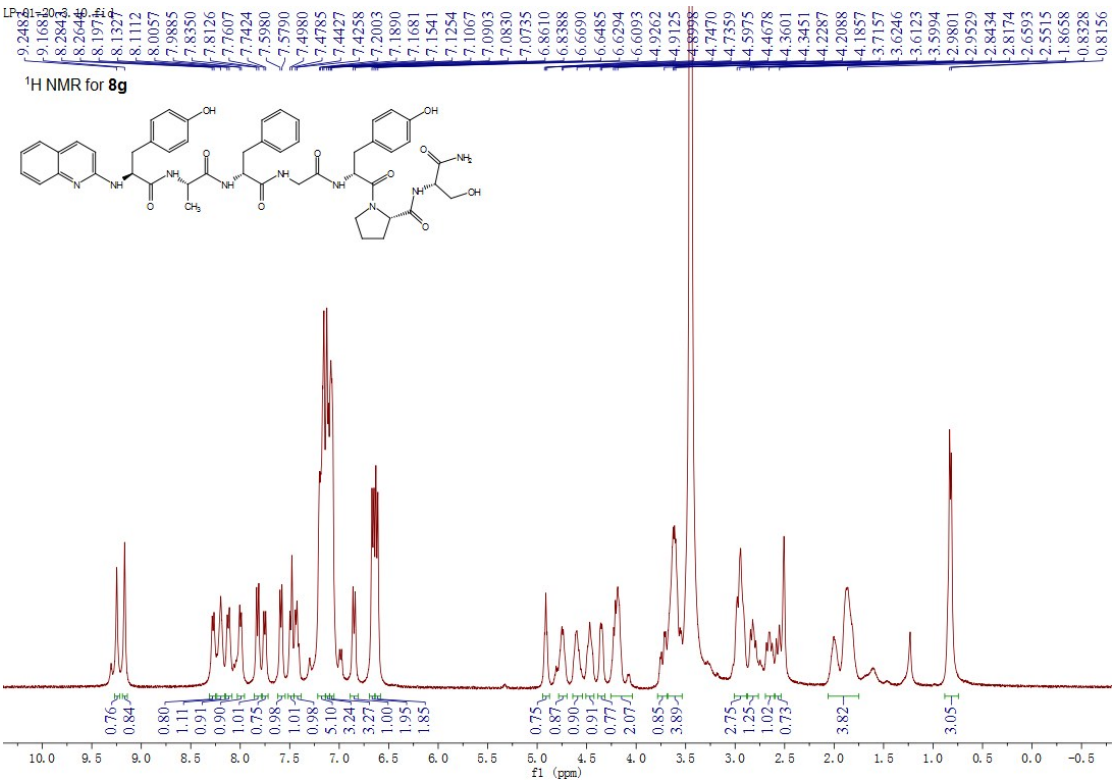

13C NMR for 8d
f1 (ppm)

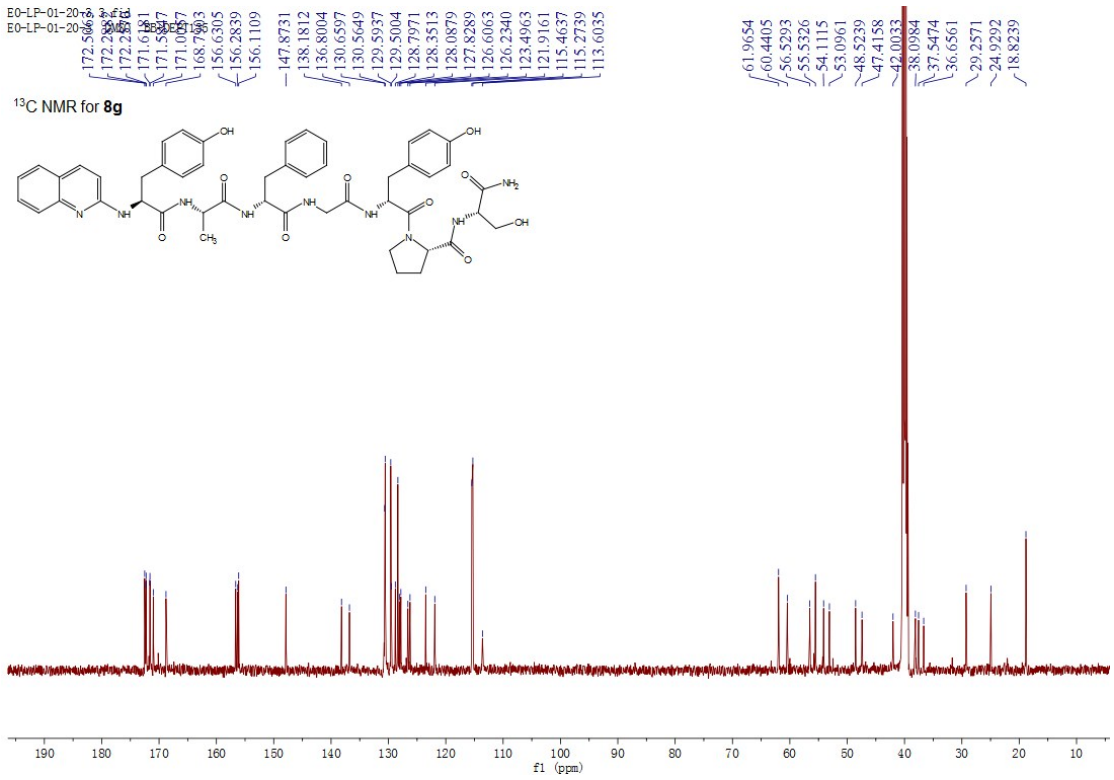

1H NMR for 8e
f1 (ppm)

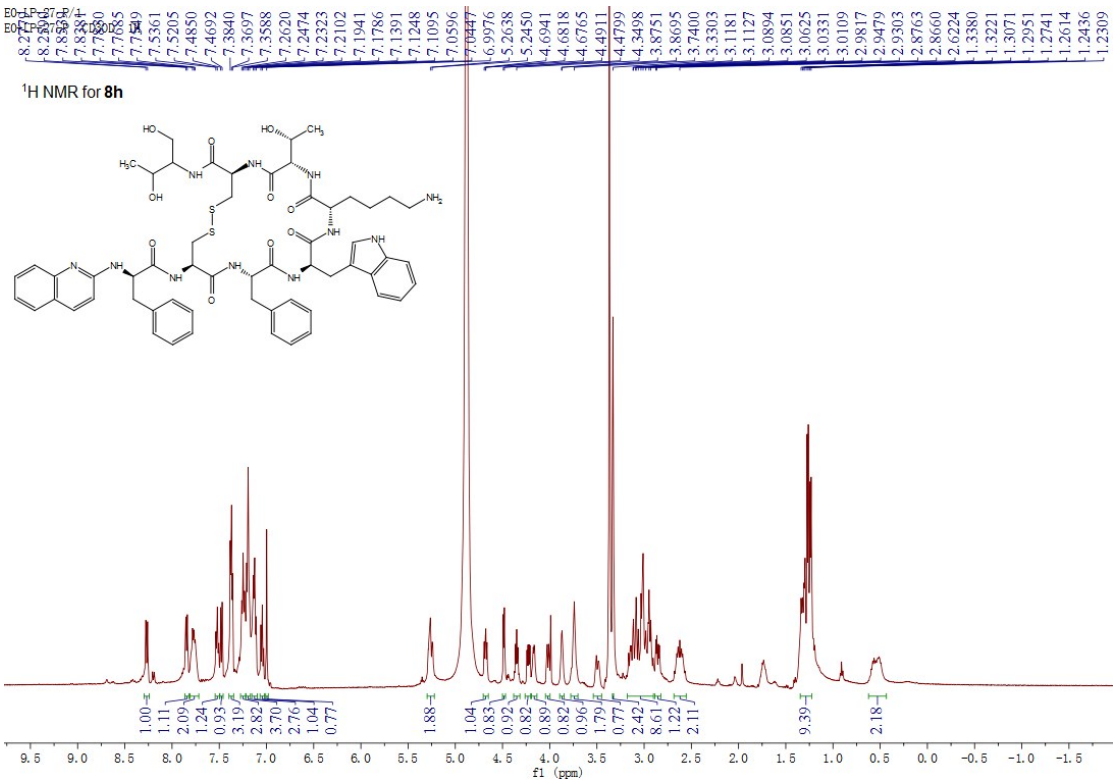

E0-LP-01-58/3
E0-LP-01-58 CD3OD BB+DEPT135
175.8407
172.2919
162.2071
160.2535
158.6856
148.8169
146.1792
138.7797
138.2772
137.9429
132.0552
130.4772
130.4109
128.4470
127.3879
125.6841
124.7530
124.5609
124.1276
121.4819
117.1595
116.9769
114.1512
64.8075
62.3672
54.8115
31.7229
30.6760
27.7114
20.0886
19.2629
18.6963
13C NMR for 8e
f1 (ppm)

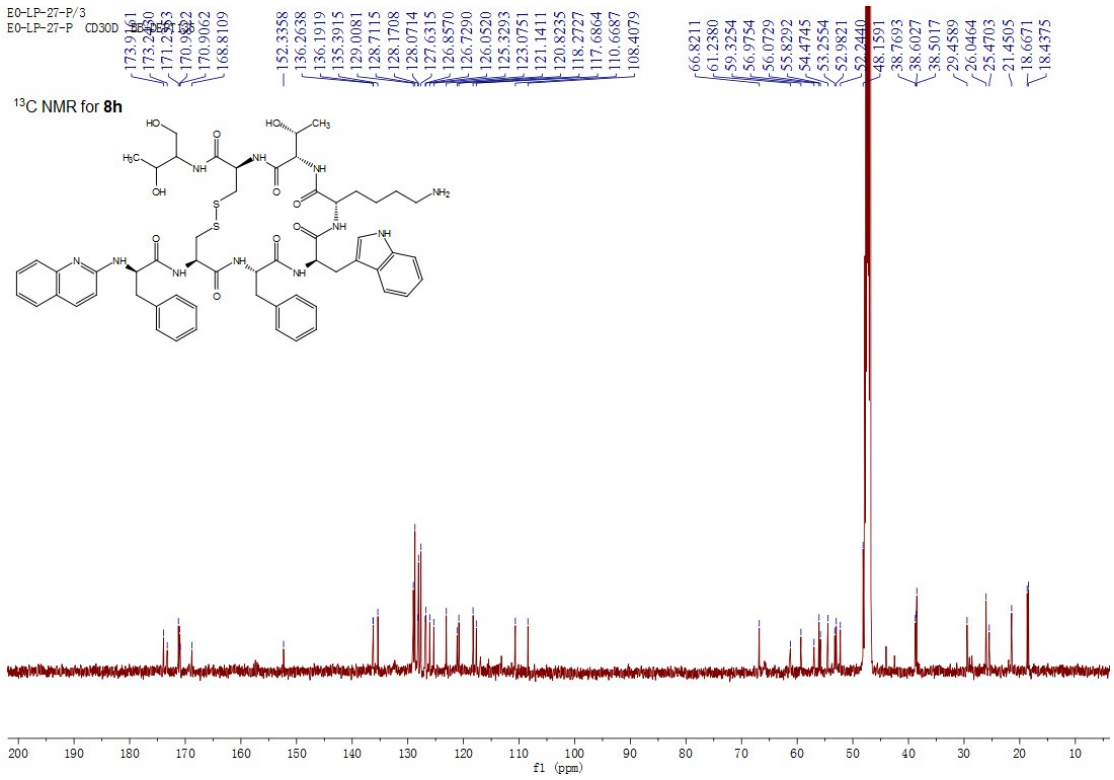

E0-LP-01-03.10.fid
7.89
7.75
7.73
7.63
7.61
7.00
4.94 HDO
4.89
4.87
4.86
4.32
3.93
3.88
3.78
3.74
3.44
3.37
3.34 MeOD
3.33 MeOD
3.33 MeOD
3.32 MeOD
2.91
2.39
2.37
2.23
2.20
2.01
2.00
1.98
1.97
1.96
1.71
1.69
1.68
1.67
1.66
1.65
1.06
1.04
1.02
1.00
0.98
0.95
0.94
0.92
0.90
1H NMR for 8f
0.83
0.91
0.95
0.92
1.00
3.52
1.10
0.72
1.85
1.03
1.05
0.80
0.80
1.17
0.91
1.28
1.11
1.68
4.39
1.27
0.89
2.00
2.97
4.18
4.36
1.22
2.65
3.33
3.22
3.24
f1 (ppm)

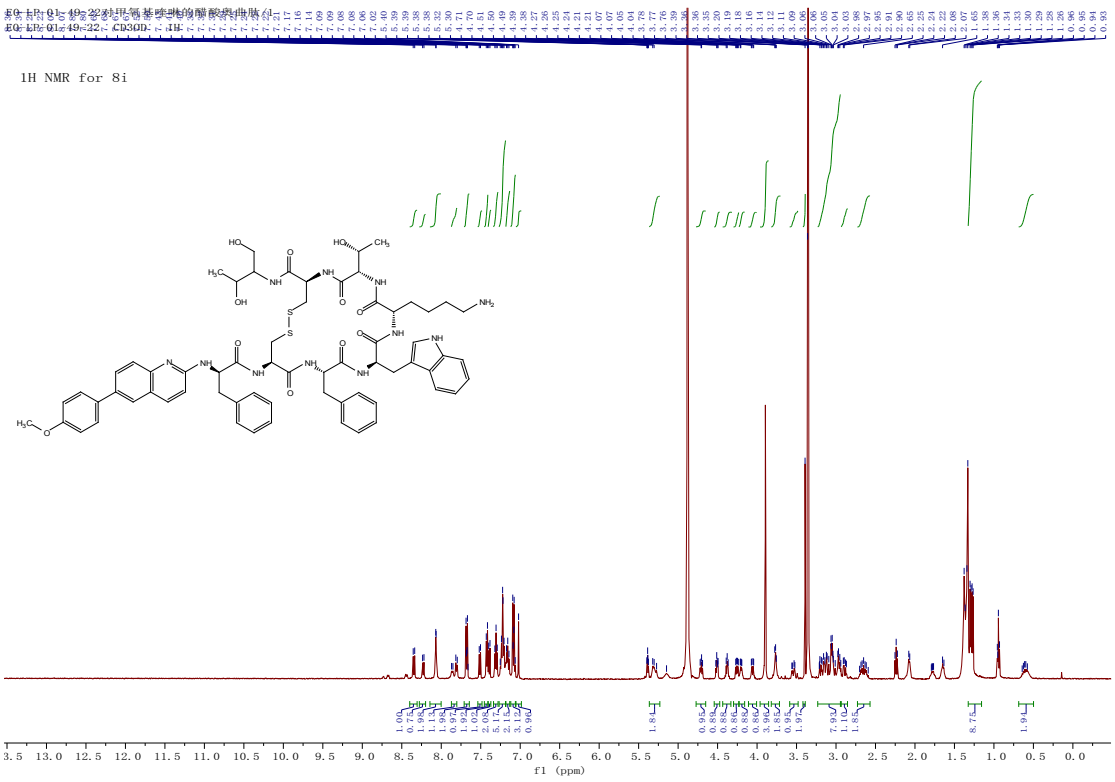

^{13}C NMR for **8f**
f1 (ppm)

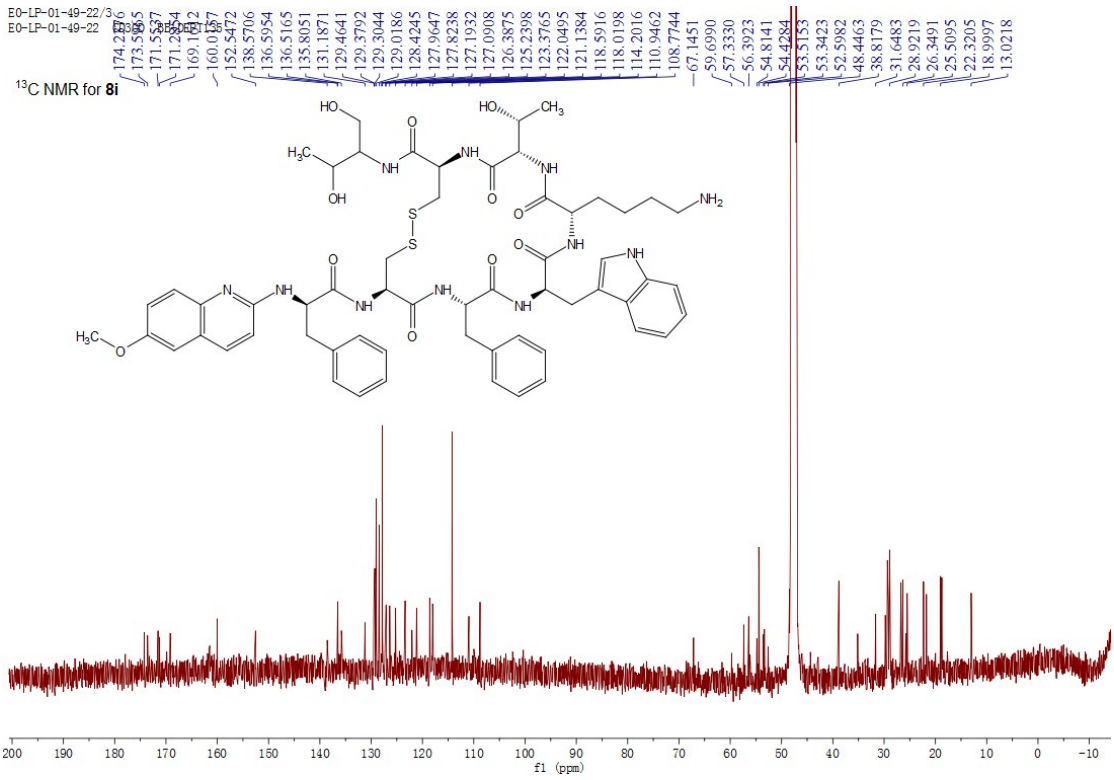

^{1}H NMR for **8g**
f1 (ppm)


^{13}C NMR for **8g**
f1 (ppm)


^{1}H NMR for **8h**
f1 (ppm)


E0-LP-27-P/3
E0-LP-27-P CD3OD
13C NMR for 8h
f1 (ppm)


1H NMR for 8i
f1 (ppm)


E0-LP-01-49-22/3
E0-LP-01-49-22
174.2776
173.5965
171.5537
171.3854
171.2642
169.1112
160.0167
152.5472
138.5706
136.5954
136.5165
135.8051
131.1871
129.4641
129.3792
129.3044
129.0186
128.4245
127.9647
127.8238
127.1932
127.0908
126.3875
125.2398
123.3765
122.0495
121.1384
118.5916
118.0198
114.2016
110.9462
108.7744
67.1451
59.6990
57.3330
56.3923
54.8141
54.4284
53.5153
53.3423
52.5982
48.4463
38.8179
31.6483
28.9219
26.3491
25.5095
22.3205
18.9997
13.0218
13C NMR for 8i
f1 (ppm)