Supporting Information

Improved Total Synthesis and Biological Evaluation of Coibamide A Analogues

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General Information

Abbreviations: BEP, 2-Bromo-1-ethyl-pyridinium tetrafluoroborate; BOP-Cl, Phosphoric acid bis(2-oxooxazolidide) chloride; BTC, bis-(trichloromethyl)-carbonate; CH_3CN, acetonitrile; DCC, *N,N'*-dicyclohexylcarbodiimide; DCM, dichloromethane; DIC, *N,N'*-diisopropylcarbodiimide; DIAD, diisopropylazodicarboxylate; DIPEA, *N,N'*-diisopropylethylamine; DMAP, 4-dimethylaminopyridine; DMBA, 1,3-dimethylbarbituric acid; DMF, *N,N'*-dimethylformamide; DPPA, diphenylphosphoryl azide; EDCI, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide; HOAt, 1-hydroxy-7-aza-benzotriazole; OxymaPure, ethyl cyanoglyoxylate-2-oxime; PPh_3, triphenylphosphine; PyAOP, (3-Hydroxy-3H-1,2,3-triazolo[4,5-b]pyridinato-O)tri-1-pyrrolidinylphosphonium hexafluorophosphate; PyBOP, benzotriazol-1-yl-oxytripyrrolidinophosphonium-hexafluorophosphate; TFE, 2,2,2-trifluorethanol; TFA, trifluoroacetic acid; THF, tetrahydrofuran.

Dry DMF and dry THF were purchased from Sigma-Aldrich. (*S*)-(+)-2-hydroxy-3-methylbutyric acid, decanoic acid, collidine (2,4,6-collidine) and the HPLC grade solvents (CH_3CN and MeOH) were purchased from J&K Scientific. BTC, DIPEA, formalin, TFE, TFA, sodium triacetoxyborohydride were purchased from Aladdin. 2-CTC (2-chlorotrityl chloride) resin and amino acids such as Fmoc-*N*-Me-Val-OH, Fmoc-*N*-Me-Ser(OtBu)-OH, Cbz-β-Ala-OH, Fmoc-Ala-OH, Fmoc-Tyr(Me)-OH, Fmoc-*N*-Me-Ala-OH, Fmoc-*N*-Me-D-Ala-OH, Fmoc-Tyr(OtBu)-OH, Fmoc-*N*-Me-Leu-OH, Fmoc-*N*-Me-Lys(Boc)-OH, Boc-*N*-Me-Leu-OH, Fmoc-*N*-Me-Thr-OH and Fmoc-*N*-Me-Ile-OH were purchased from GL Biochem.

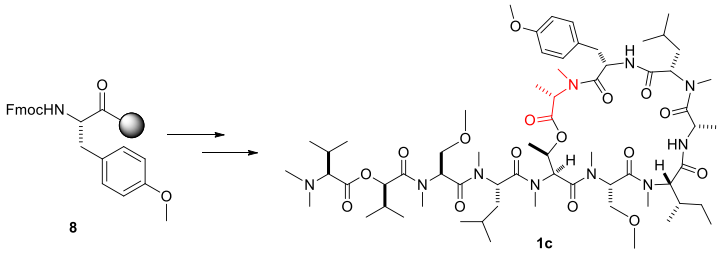
Analytical RP-HPLC was performed on an Agilent 1260 infinity system equipped with a DAD-UV detector using Agilent Poroshell 120, EC-C18 column (4.6x100mm, 2.7um). The RP-HPLC gradient was started at 10% of B (MeCN), then increased to 100% of B over 20 min (A: 0.1% TFA in water) with a flow rate of 0.5 mL/min. The purity of the compounds (>95%) was determined by HPLC. Semi-preparative RP-HPLC was performed on the ULTIMAT 3000 Instrument (DIONEX). UV absorbance was measured using a photodiode array detector at 220 and 254 nm. The RP-HPLC gradient was started at 10% of B (MeCN), then increased to 100% of B over 30 min (A: 0.1% TFA in water). ^{1}H NMR (^{13}C NMR) spectra were recorded with a Bruker AV400 at 400 (100) MHz. Chemical shifts are referenced to either tetramethylsilane as an internal standard or the signals resulting from the residual solvent. High resolution mass spectra

were measured with an ABI Q-star Elite.

Experimental Procedure

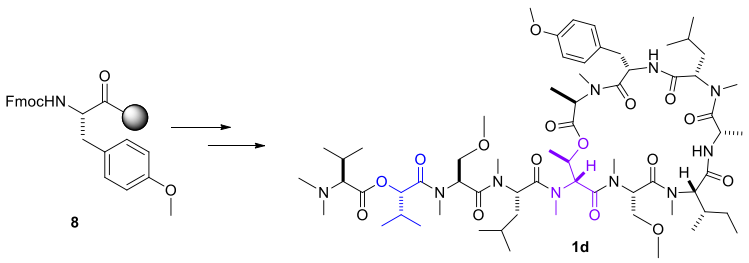
Analogues **1c**-**1r** were prepared using similar procedures for the preparation of compound **1**. All analogues were purified by semi-preparative RP-HPLC.

Preparation of [L-Ala11]-coibamide (1c)



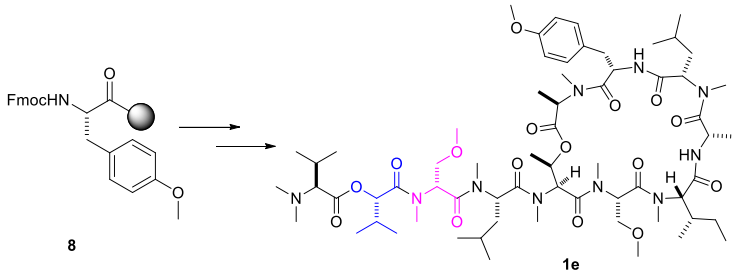
Starting from peptidyl resin **8**, Fmoc-*N*-Me-Ala-OH was used instead of Fmoc-*N*-Me-D-Ala-OH to install residue 11. Following the same procedure used in the synthesis of coibamide A, **1c** was obtained as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.74–0.97 (m, 16H), 1.06 (m, 16H), 1.16–1.66 (m, 17H), 1.77–2.10 (m, 3H), 2.26 (m, 3H), 2.63-2.73(m, 3H), 2.81-2.93(m, 5H), 2.94 (s, 3H), 2.94-2.97 (m, 2H), 2.98 (s, 3H), 2.99 (s, 3H), 3.01-3.07 (m, 2H), 3.08 (s, 3H), 3.11-3.17 (m, 3H), 3.22 (s, 1H), 3.35 (s, 3H), 3.37 (s, 3H), 3.44–3.62 (m, 3H),3.72 (m, 1H), 3.78 (s, 3H), 3.82–3.94 (m, 2H), 4.41 (m, 1H), 4.50–4.84 (m, 3H), 5.07 (d, J = 3.9 Hz, 1H), 5.13 (m, 2H), 5.30-5.37 (m, 1H), 5.38–5.58 (m, 2H), 5.47 (d, J = 20.4 Hz, 2H), 5.66 (m, 1H), 5.74–5.88 (m, 1H), 6.81 (d, J = 8.6 Hz, 2H), 7.18 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 9.4, 13.7, 14.9, 16.3, 16.4, 16.7, 16.7, 18.8, 18.9, 19.2, 20.7, 22.5, 22.9, 23.4, 24.4, 24.5, 25.5, 28.1, 28.9, 28.9, 29.8, 30.0, 30.1, 30.2, 30.4, 30.9, 31.1, 37.2, 37.5, 45.6, 51.7, 52.5, 53.4, 55.2, 55.3, 56.8, 58.4, 58.9, 59.1, 66.4, 68.9, 69.2, 71.2, 113.9, 129.5, 130.2, 158.5, 167.8, 168.6, 169.5, 169.8, 169.9, 170.0, 170.3, 171.5, 172.2, 172.6; HRMS (ESI-TOF) *m/z*: calcd for $C_{67}H_{115}N_{10}O_{16}$ $[M+H]^+$ 1287.8174, found 1287.8148.

Preparation of [L-HIV2-D-*allo*-MeThr5]-coibamide (1d)



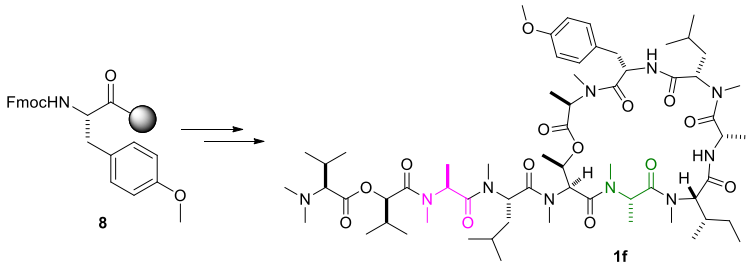
Starting from peptidyl resin **8**, Fmoc-*N*-Me-Val-HIV-OH (**L-7**) was used instead of Fmoc-*N*-Me-Val-D-HIV-OH (**7**), Fmoc-D-*allo*-*N*-Me-Thr-OH was used instead of Fmoc-*N*-Me-Thr-OH, respectively. Following the same procedure used in the synthesis of coibamide A, **1d** was obtained as a white powder. HRMS (ESI-TOF) *m/z*: calcd for $C_{65}H_{111}N_{10}O_{16}$ $[M+H]^+$ 1287.8174, found 1287.8176.

Preparation of [L-HIV2-D-MeSer(Me)3]-coibamide (1e)



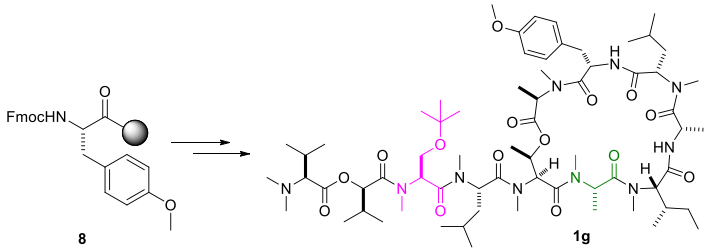
Starting from peptidyl resin **8**, Fmoc-*N*-Me-Val-HIV-OH (**L-7**) was used instead of Fmoc-*N*-Me-Val-D-HIV-OH (**7**), Fmoc-D-*N*-Me-Ser(Me)-OH was used instead of Fmoc-*N*-Me-Ser(Me)-OH, respectively. Following the same procedure used in the synthesis of coibamide A, **1e** was obtained as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 6.4 Hz, 3H), 0.86–1.00 (m, 24H), 1.02–1.16 (m, 11H), 1.20–1.36 (m, 9H), 1.48 (m, 4H), 2.35 (br s, 6H), 2.45 (s, 3H), 2.75 (s, 3H), 2.77–2.83 (m, 1H), 2.89 (s, 3H), 2.91–2.97 (m, 4H), 3.00 (s, 3H), 3.01–3.09 (m, 3H), 3.10 (s, 3H), 3.13 (s, 3H), 3.30 (s, 3H), 3.33 (s, 3H), 3.53–3.64 (m, 2H), 3.69–3.76 (m, 2H), 3.77 (s, 3H), 4.72–4.84 (m, 1H), 5.07–5.16 (m, 2H), 5.21–5.29 (m, 1H), 5.38 (dd, J = 14.3, 7.2 Hz, 1H), 5.51 (m, 1H), 5.59–5.72 (m, 2H), 6.65 (br s, 1H), 6.80 (d, J = 8.7 Hz, 1H), 7.11 (d, J = 8.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 11.8, 13.0, 14.1, 15.7, 17.0, 17.4, 17.9, 18.4, 18.7, 19.2, 19.3, 19.6, 21.2, 22.0, 22.7, 23.4, 24.3, 24.9, 25.1, 25.3, 27.5, 28.9, 29.4, 29.7, 30.0, 30.3, 30.4, 30.9, 32.2, 36.8, 37.6, 38.6, 41.3, 46.6, 46.8, 50.2, 51.5, 52.5, 52.8, 53.2, 55.3, 58.9, 63.6, 64.7, 68.8, 69.4, 74.2, 113.8, 128.3, 130.3, 158.7, 167.3, 168.8, 169.4, 169.5, 169.6, 170.3, 170.6, 171.5, 171.7, 172.3; HRMS (ESI–TOF) *m/z*: calcd for $C_{67}H_{115}N_{10}O_{16}$ $[M+H]^+$ 1287.8174, found 1287.8164.

Preparation of [L-Ala3-L-Ala6]-coibamide (1f)



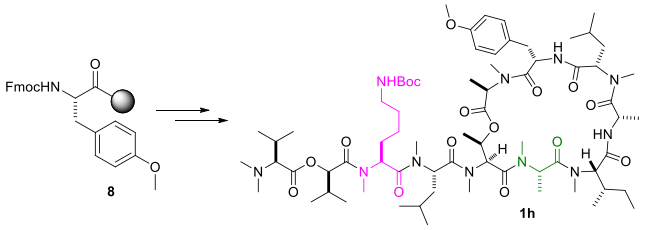
Starting from peptidyl resin **8**, Fmoc-*N*-Me-Ala-OH was used instead of Fmoc-*N*-Me-Ser(Me)-OH. Following the same procedure used in the synthesis of coibamide A, **1f** was obtained as a white powder in an overall yield of 35%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (d, J = 6.5 Hz, 3H), 0.85-0.96 (m, 16H), 0.96-1.03 (m, 8H), 1.03–1.11 (m, 7H), 1.11–1.22 (m, 8H), 1.22–10.33 (m, 9H), 2.46 (m, 2H), 2.74 (s, 3H), 2.84 (m, 1H), 2.85 (s, 3H), 2.92 (s, 9H), 2.93 (m, 2H), 2.95 (s, 6H), 2.97(m, 1H), 3.02 (s, 3H), 3.12 (s, 3H), 3.13 (m, 1H), 3.61 (m, 1H), 3.74 (m, 1H), 3.76 (s, 3H), 3.85 (m, 1H), 4.81 (m, 1H), 4.99 (d, J = 4.6 Hz, 1H), 5.07 (m, 1H), 5.29 (m, 2H), 5.51-5.62 (m, 5H), 6.42 (br s, 1H), 6.79 (d, J = 8.6 Hz, 2H), 7.08 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 12.8, 14.2, 14.5, 15.9, 16.8, 18.6, 18.8, 19.0, 19.1, 21.1, 21.4, 23.1, 23.3, 24.2, 25.2, 25.3, 28.2, 29.0, 29.2, 29.7, 30.0, 30.2, 30.8, 32.2, 36.7, 37.6, 38.4, 46.8, 50.3, 50.4, 51.2, 51.7, 70.9, 113.8, 127.9, 130.3, 158.7, 161.6, 162.0, 167.7, 167.9, 168.6, 169.2, 170.4, 171.6, 172.0, 172.4 ppm; HRMS (ESI-TOF) *m/z*: calcd for $C_{63}H_{107}N_{10}O_{14}$ $[M+H]^+$ 1227.7963, found 1227.8040.

Preparation of [MeSer(tBu)3-MeAla6]-coibamide (1g)



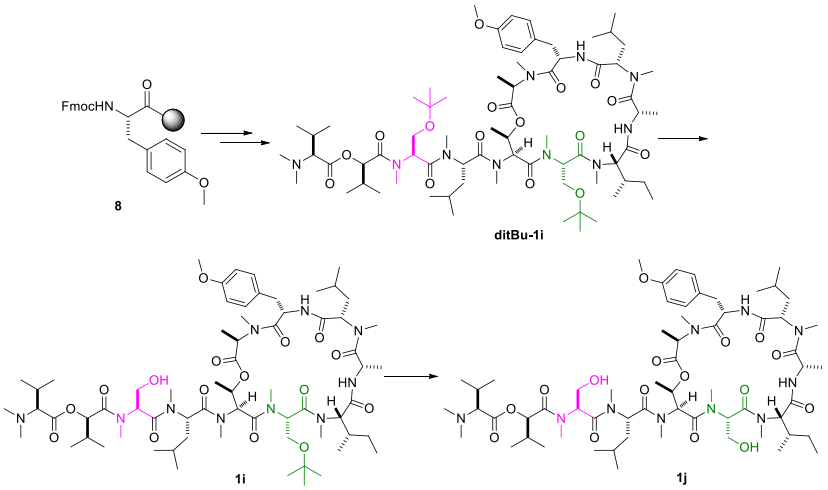
Starting from peptidyl resin **8**, Fmoc-*N*-Me-Ala-OH/Fmoc-*N*-Me-Ser(tBu)-OH was used instead of Fmoc-*N*-Me-Ser(Me)-OH. Following the same procedure used in the synthesis of coibamide A, **1g** was obtained as a white powder. HRMS (ESI-TOF) *m/z*: calcd for $C_{67}H_{115}N_{10}O_{15}$ $[M+H]^+$ 1299.8533, found 1299.8532.

Preparation of [MeLys(Boc)3-MeAla6]-coibamide (1h)



Starting from peptidyl resin **8**, Fmoc-*N*-Me-Ala-OH/Fmoc-*N*-Me-Lys(Boc)-OH was used instead of Fmoc-*N*-Me-Ser(Me)-OH. Following the same procedure used in the synthesis of coibamide A, **1h** was obtained as a white powder. HRMS (ESI-TOF) *m/z*: calcd for $C_{71}H_{122}N_{11}O_{16}$ $[M+H]^+$ 1384.9066, found 1384.9051.

Preparation of [Ser3-Ser(tBu)6]-coibamide (1i) and [Ser3-Ser6]-coibamide (1j)



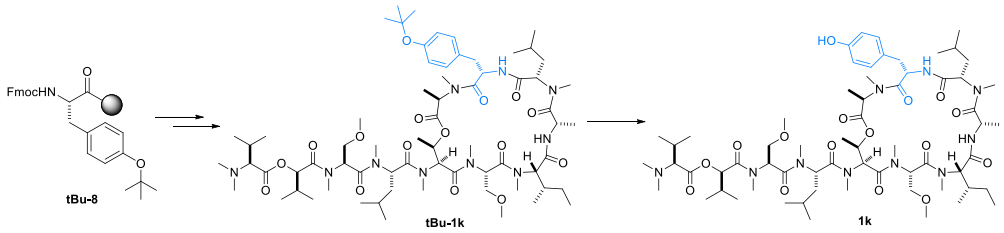
Starting from peptidyl resin **8**, Fmoc-*N*-Me-Ser(tBu)-OH was used instead of Fmoc-*N*-Me-Ser(Me)-OH. Following the same procedure used in the synthesis of coibamide A, **ditBu-1i** was obtained. The tBu protecting group of residue 3 was successfully removed by treating **ditBu-1i** with TFA/DCM (v/v = 1/1) for 30 min at 0°C, **1i** was obtained as a white powder. The tBu protecting group of residue 3 was successfully removed by treating **1i** with TFA/DCM (v/v = 1/1) for 30 min at room temperature, **1j** was obtained as a white powder.

1i: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.86 (d, J = 6.2 Hz, 3H), 0.88-1.01 (m, 13H), 1.04 (m, 7H), 1.08–1.17 (m, 7H), 1.19 (s, 9H), 1.22–1.36 (m, 13H), 1.49 (m, 4H), 2.16–2.34 (m, 4H), 2.49 (s, 3H), 2.57 (m, 2H), 2.77 (s, 3H), 2.84 (m, 1H), 2.94 (s, 6H), 3.01 (s, 3H), 3.03 (s, 3H), 3.07 (s, 3H), 3.17 (s, 3H), 3.61–3.77 (m, 4H), 3.81 (s, 3H),3.83 (br s, 1H), 4.85 (br s, 1H), 5.06 (d, J = 3.8 Hz, 1H), 5.16 (m, 2H), 5.35 –5.45 (m, 2H), 5.55 (br s, 2H), 5.63 (br s, 1H), 6.35 (br s, 2H), 6.84 (d, J = 8.3 Hz, 2H), 7.12 (d, J = 8.3 Hz, 2H); HRMS (ESI-TOF) *m/z*: calcd for

$C_{67}H_{115}N_{10}O_{16}$ $[M+H]^+$ 1315.8487, found 1315.8485.

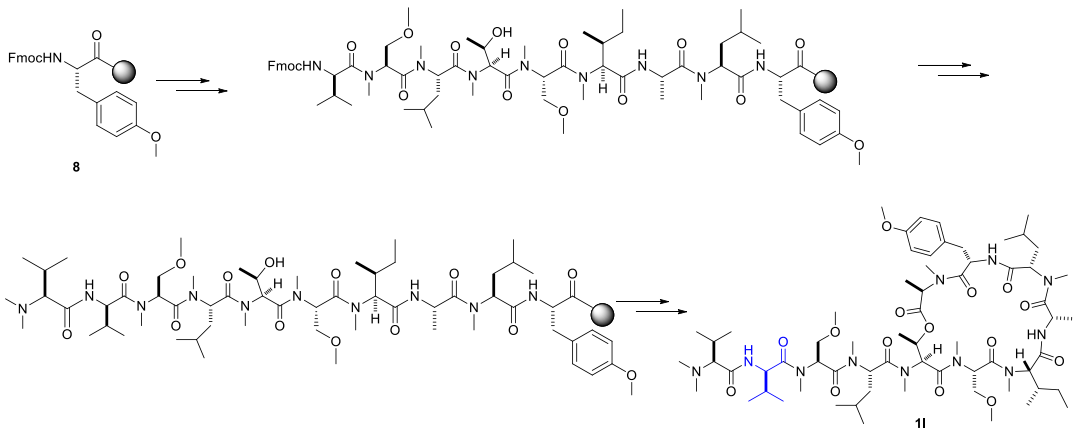
1j: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.83 (d, J = 6.3 Hz, 2H), 0.87–1.05 (m, 21H), 1.09 (d, J = 6.8 Hz, 3H), 1.14 (d, J = 7.2 Hz, 3H), 1.16–1.34 (m, 13H), 1.48 (m, 4H), 1.97–2.10 (m, 2H), 2.23 (m, 2H), 2.48 (s, 3H), 2.51–2.59 (m, 2H), 2.75 (s, 3H), 2.89 (s, 6H), 2.92–3.01 (m, 4H), 3.02 (s, 3H), 3.04 (s, 3H), 3.09 (s, 3H), 3.13 (s, 3H), 3.17 (m, 2H), 3.78 (s, 3H), 3.80–3.87 (m, 2H), 3.91 (br s, 2H), 4.82 (br s, 1H), 5.02 (d, J = 4.1 Hz, 1H),5.08–5.15 (m, 1H), 5.18 (br s, 1H), 5.38 (dd, J = 18.9, 11.7 Hz, 1H), 5.51 (br s, 2H), 5.61 (br s, 1H), 6.32 (br s, 2H), 6.82 (d, J = 8.4 Hz, 2H), 7.10 (d, J = 8.4 Hz, 2H); HRMS (ESI-TOF) *m/z*: calcd for $C_{63}H_{107}N_{10}O_{16}$ $[M+H]^+$ 1259.7861, found 1259.7851.

Preparation of [Tyr10]-coibamide (1k)



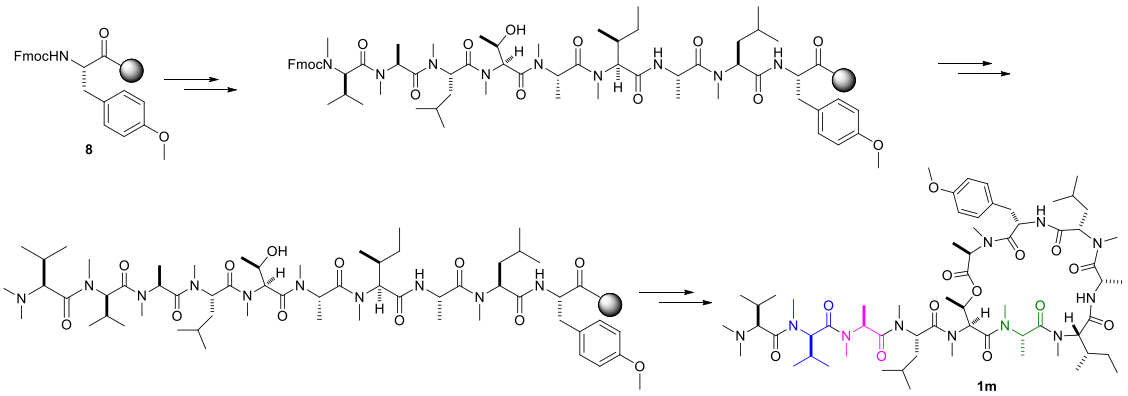
Starting from peptidyl resin **tBu-8**, following the same procedure used in the synthesis of coibamide A, **tBu-1k** was obtained. After removal of tBu group in the presence of TFA, **1k** was obtained as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84 (d, J = 6.3 Hz, 3H), 0.87–0.98 (m, 14H), 0.98–1.05 (m, 7H), 1.06–1.16 (m, 8H), 1.20–1.38 (m, 10H), 1.38–1.56 (m, 4H), 2.50 (br s, 1H), 2.59 (s, 3H), 2.69 (m, 1H), 2.75 (s, 3H), 3.13 (s, 3H), 3.31 (s, 3H), 3.33 (s, 3H), 3.50 (dd, J = 10.8, 4.4 Hz, 1H), 3.60 (dd, J = 10.9, 4.7 Hz, 1H), 3.66–3.92 (m, 5H), 4.70–4.79 (m, 1H), 5.05 (d, J = 4.0 Hz, 1H), 5.13–5.25 (m, 1H), 5.34 (m, 1H), 5.46 (br s, 1H), 5.69 (dt, J = 19.4, 11.9 Hz, 1H), 5.79 (dd, J = 9.7, 4.6 Hz, 1H), 6.24 (br s, 1H), 6.54 (br s, 1H), 6.74 (br s, 1H), 6.80 (d, J = 8.2 Hz, 2H), 6.96 (d, J = 8.2 Hz, 2H); HRMS (ESI-TOF) *m/z*: calcd for $C_{64}H_{109}N_{10}O_{16}$ $[M+H]^+$ 1273.8018, found 1273.8003.

Preparation of [D-Val2]-coibamide (1l)



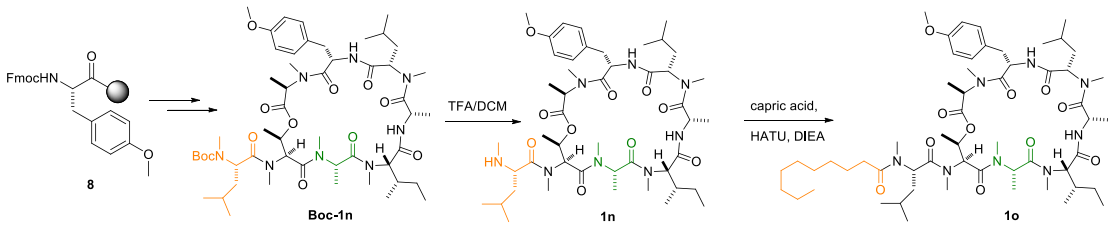
Starting from peptidyl resin **8**, D-Hiv2 residue was replaced by D-Val2. Following the same procedure used in the synthesis of coibamide A, **1l** was obtained as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.84–0.99 (m, 17H), 1.20–1.00 (m, 18H), 1.25–1.40 (m, 6H), 1.42–1.64 (m, 4H), 2.50 (s, 3H), 2.56–2.72 (m, 3H), 2.76 (s, 3H), 2.78-3.18 (m, 27H), 3.33 (s, 3H), 3.34–3.43 (m, 3H), 3.50 (m, 1H), 3.64 (m, 1H), 3.78 (s, 3H), 3.81 (m, 1H), 3.85 (m, 2H), 4.62 (br s, 1H), 4.76–4.83 (m, 1H), 5.08 (br s, 1H), 5.19 (br s, 1H), 5.28 (br s, 1H), 5.52 (br s, 1H), 5.74 (dd, J = 9.7, 4.7 Hz, 1H), 5.91 (br s, 1H), 6.18 (br s, 1H), 6.60 (br s, 1H), 6.79 (d, J = 6.4 Hz, 2H), 7.11 (m, 2H); HRMS (ESI-TOF) *m/z*: calcd for $C_{67}H_{111}N_{11}O_{15}Na$ $[M+Na]^+$ 1308.8153, found 1308.8155.

Preparation of [D-Val2-MeAla3-MeAla6]-coibamide (1m)



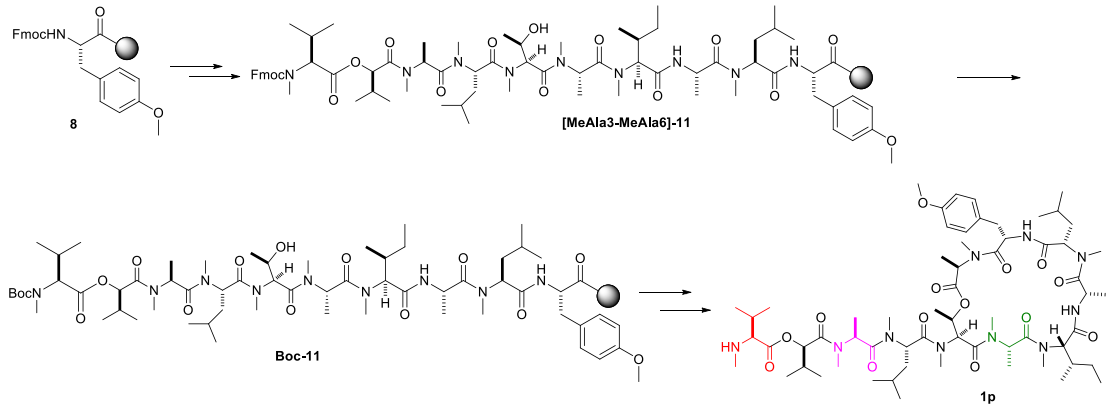
Starting from peptidyl resin **8**, both of two MeSer(Me) residues were replaced by MeAla and D-Hiv2 was replaced by D-MeVal2. Following the same procedure used in the synthesis of coibamide A, **1m** was obtained as a white powder. HRMS (ESI-TOF) *m/z*: calcd for $C_{64}H_{110}N_{11}O_{13}$ $[M+H]^+$ 1240.8279, found 1240.8283.

Preparation of short-[MeAla6]-coibamide (1n) and lipocoibamide (1o)



Starting from peptidyl resin **8**, MeSer(Me)6 residue was replaced by MeAla6. Following the same procedure used in the synthesis of coibamide A, **Boc-1n** was obtained as a white powder. After removal of the Boc protecting group with TFA/DCM (v/v = 1/1) for 30 min at 0°C, short cyclic peptide **1n** was obtained. HATU (1.5 eq.) and DIPEA (10 eq.) were added to a solution of **1n** (1.0 eq.) and capric acid (1.5 eq.) in CH_2Cl_2 at room temperature. After being stirred for 2 h, the reaction mixture was concentrated in vacuo and the residue was purified by semi-preparative RP-HPLC to give **1o** as a white powder. **1n**: HRMS (ESI-TOF) *m/z*: calcd for $C_{47}H_{79}N_8O_{10}$ $[M+H]^+$ 915.5914, found 915.5909. **1o**: HRMS (ESI-TOF) *m/z*: calcd for $C_{59}H_{96}N_8NaO_{11}$ $[M+Na]^+$ 1091.7091, found 1091.7083.

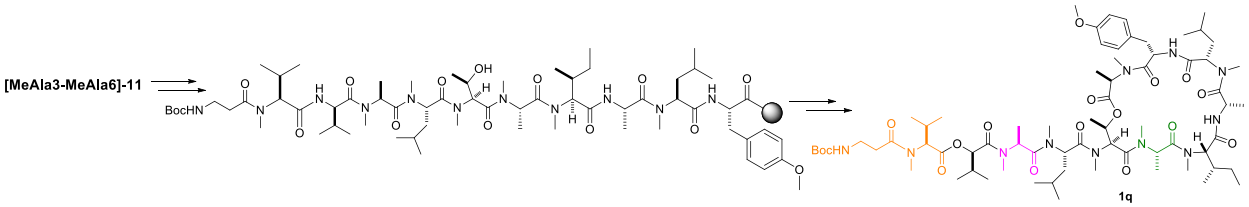
Preparation of [MeVal1-MeAla3-MeAla6]-coibamide (1p)



Starting from peptidyl resin **8**, both of two L-MeSer(Me) residues were replaced by L-MeAla. Following the same procedure used in the synthesis of coibamide A, **11** was obtained. After removal of Fmoc group using 20% piperidine/DMF, the N-terminal was protected with di-tert-butyl dicarbonate and DIPEA to produce **Boc-11**. Following the same procedure used in the synthesis of coibamide A, **1p** was obtained as a white powder. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.85 (d, J = 6.3 Hz, 3H), 0.87–1.01 (m, 15H), 1.02–1.22 (m, 19H), 1.22–1.40 (m, 10H), 1.41–1.65(m, 4H), 2.06 (br s, 1H), 2.24 (m, 1H), 2.49 (s, 3H), 2.53–2.71 (m, 2H), 2.77 (s, 3H), 2.88 (s,

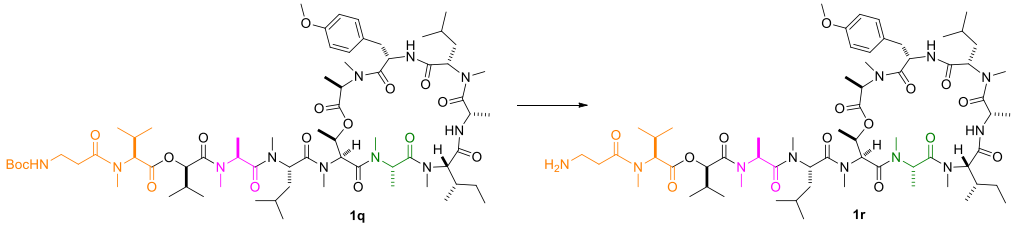
3H), 2.92 (m, 2H), 2.98 (s, 3H), 2.99 (s, 3H), 3.04 (m, 1H), 3.11 (s, 3H), 3.16-3.24 (m, 1H), 3.69 –3.77 (m, 2H), 3.79 (s, 3H), 3.84 (d, J = 4.4 Hz, 1H), 4.71–4.84 (m, 1H), 5.07-5.10 (m, 2H), 5.30 (br s, 2H), 5.53–5.58 (m, 2H), 5.68 (br s, 1H), 6.80 (d, J = 8.65 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 11.6, 12.9, 14.2, 14.5, 15.9, 17.0, 17.3, 18.6, 18.8, 19.1, 20.8, 21.9, 22.4, 23.1,24.2, 25.1, 25.3, 29.0, 29.4, 29.7, 29.8, 29.9, 30.2, 31.0, 32.1, 32.7, 36.8, 37.9, 47.0, 49.9, 50.2, 50.3, 51.0, 52.5, 66.6, 113.8, 128.0, 130.2, 158.6, 161.5, 161.9, 167.7, 167.9, 168.4, 168.8, 169.3, 170.7, 171.8, 172.3 ppm; HRMS (ESI-TOF) *m/z*: calcd for $C_{62}H_{104}N_{10}O_{14}$ $[M+H]^+$ 1213.7806, found 1213.7812.

Preparation of [Boc-β-Ala-MeVal1]-coibamide (1q)



Starting from peptidyl resin **[MeAla3-MeAla6]-11**, the Fmoc group was removed according to *method A*. Boc-β-Ala-OH was coupled to the deprotected resin according to *method C*. Following the same procedure used in the synthesis of coibamide A, **1q** was obtained as a white powder. HRMS (ESI-TOF) *m/z*: calcd for $C_{70}H_{117}N_{11}NaO_{16}$ $[M+Na]^+$ 1406.8521, found 1406.8512.

Preparation of [NH_2-β-Ala-MeVal1]-coibamide (1r)



After removed Boc group of **1q** with TFA/DCM (v/v = 1/1) for 2 h at 0°C, **1r** was obtained as a white powder. HRMS (ESI-TOF) *m/z*: calcd for $C_{65}H_{110}N_{11}O_{15}$ $[M+H]^+$ 1284.8177, found 1284.8162.

^{1}H, ^{13}C NMR, HPLC and HRMS Spectra

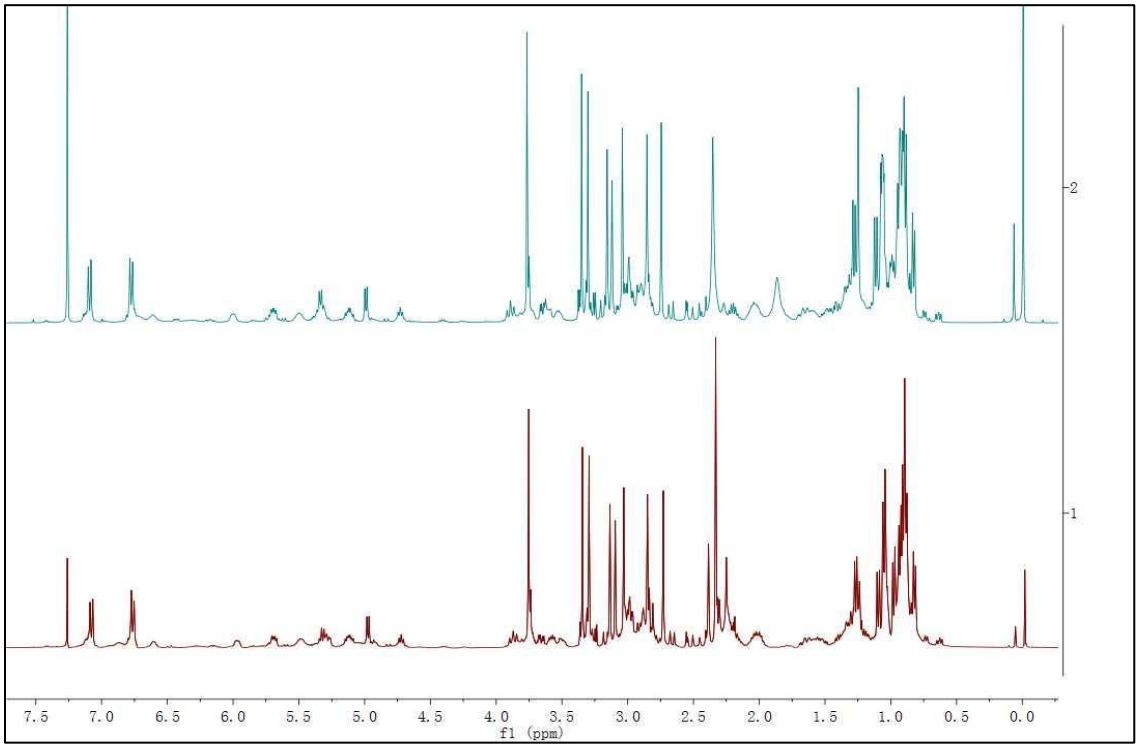
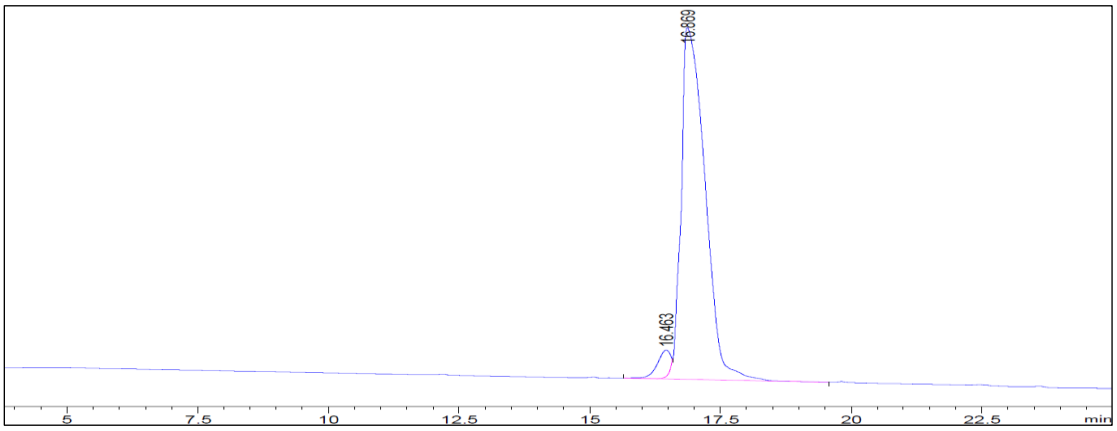


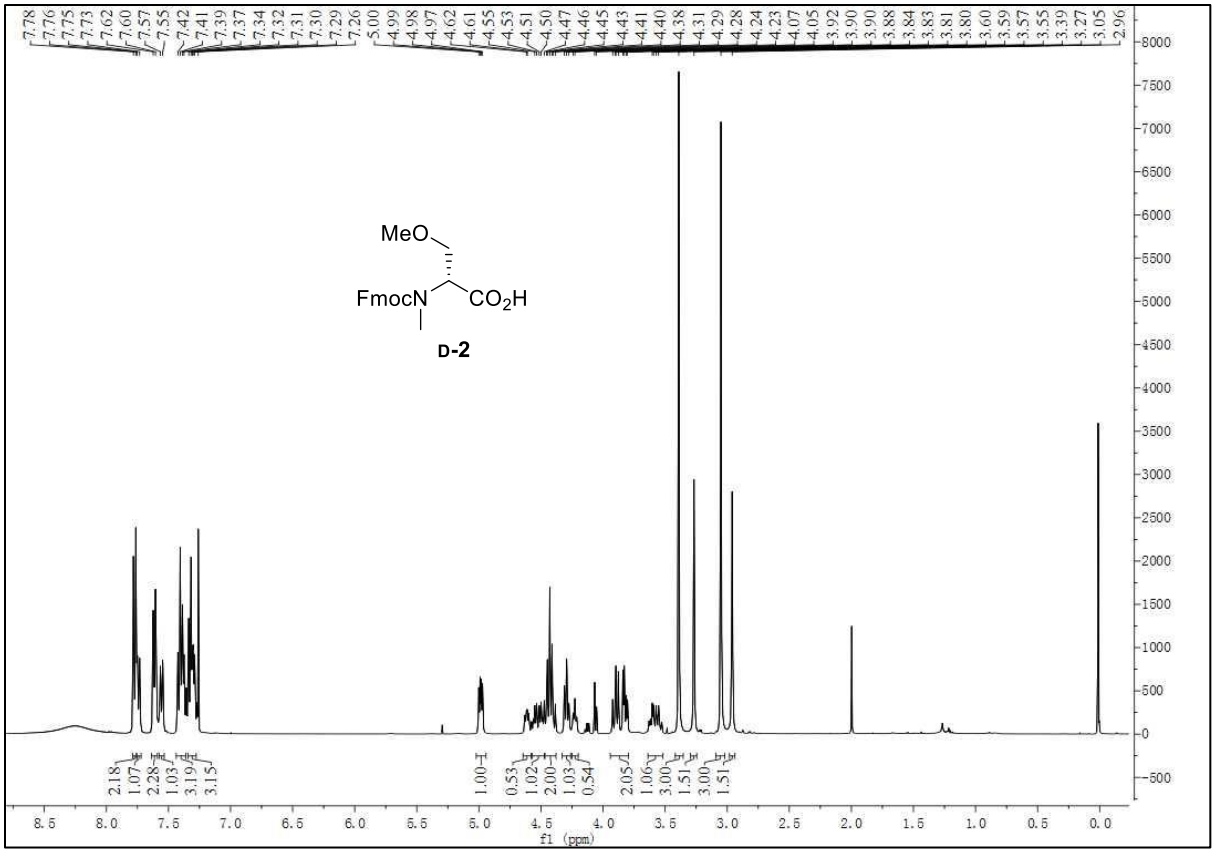
Figure S1. Comparative ^{1}H NMR spectra for our previous reported synthetic coibamide A (upper, 400 MHz) and coibamide A (**1**) synthesized in this study (lower, 400 MHz)

HPLC analysis of **1**:

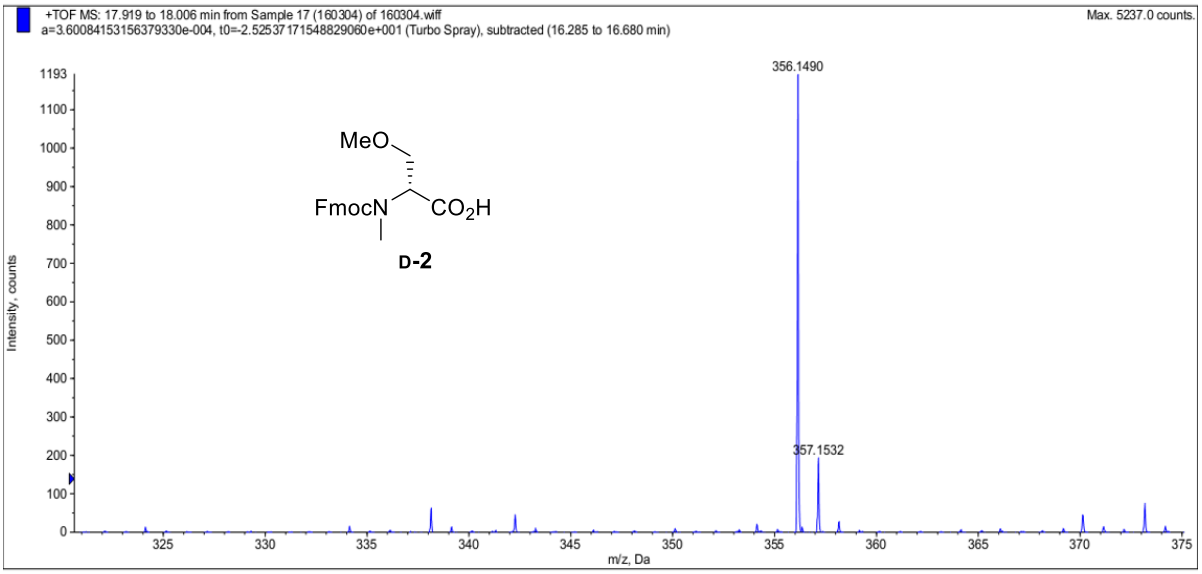


220 nm Result

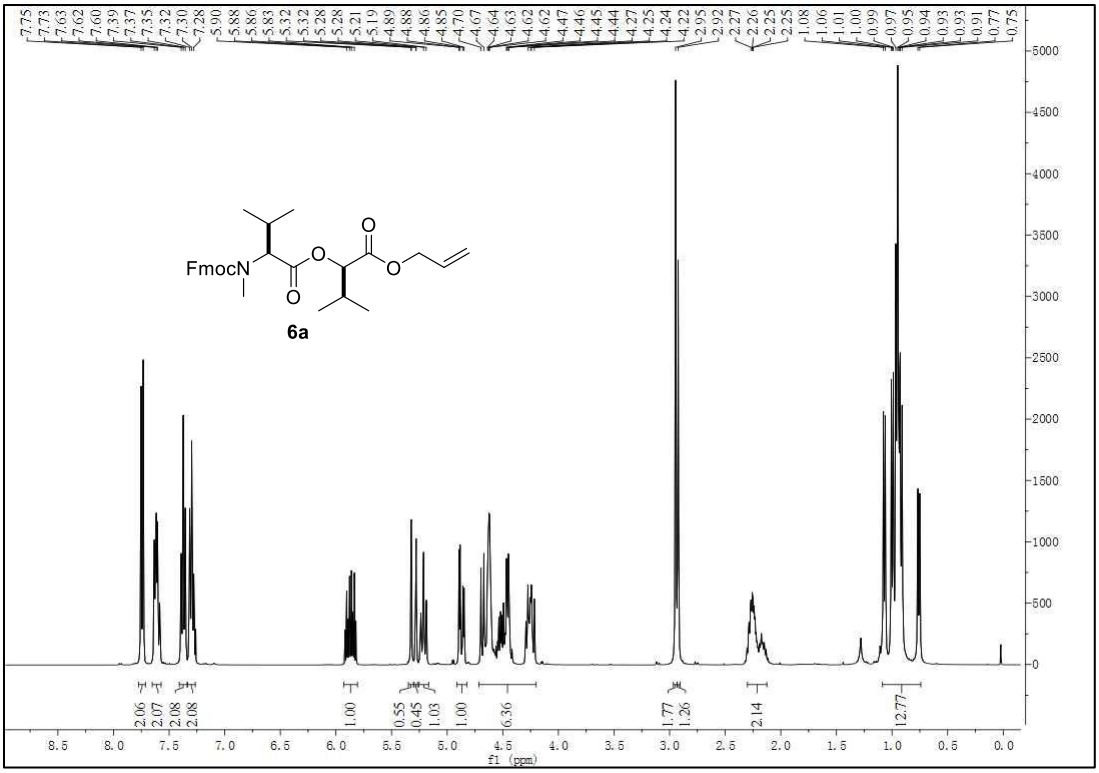
Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	16.463	187.1670	3234.5237	3.8882
2	16.869	2517.7102	7.9955e4	96.1118
Total		2704.8772	8.3189e4	



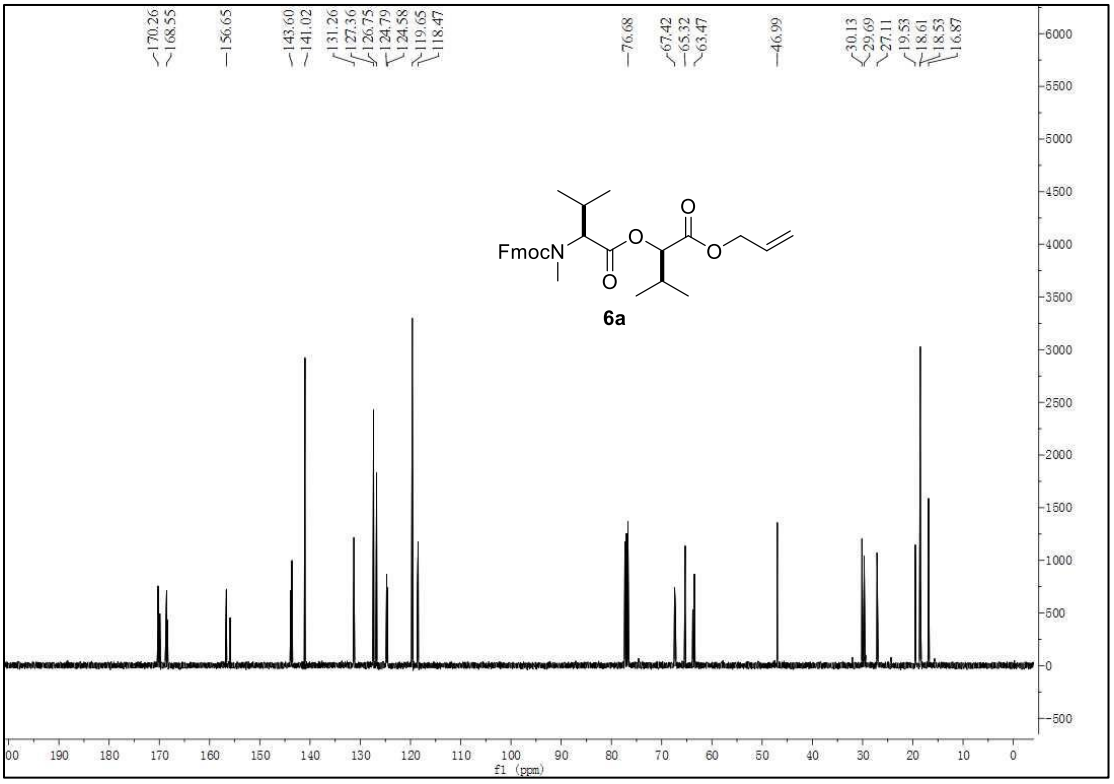
^{1}H NMR spectrum of **D-2**



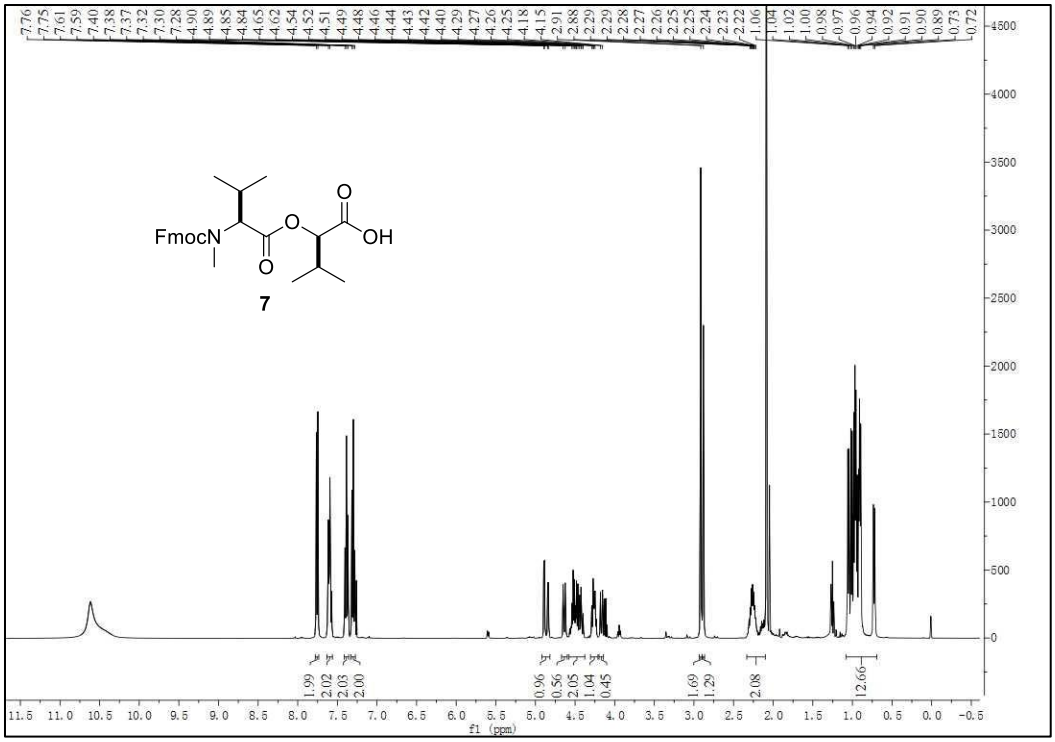
^{13}C NMR spectrum of **D-2**



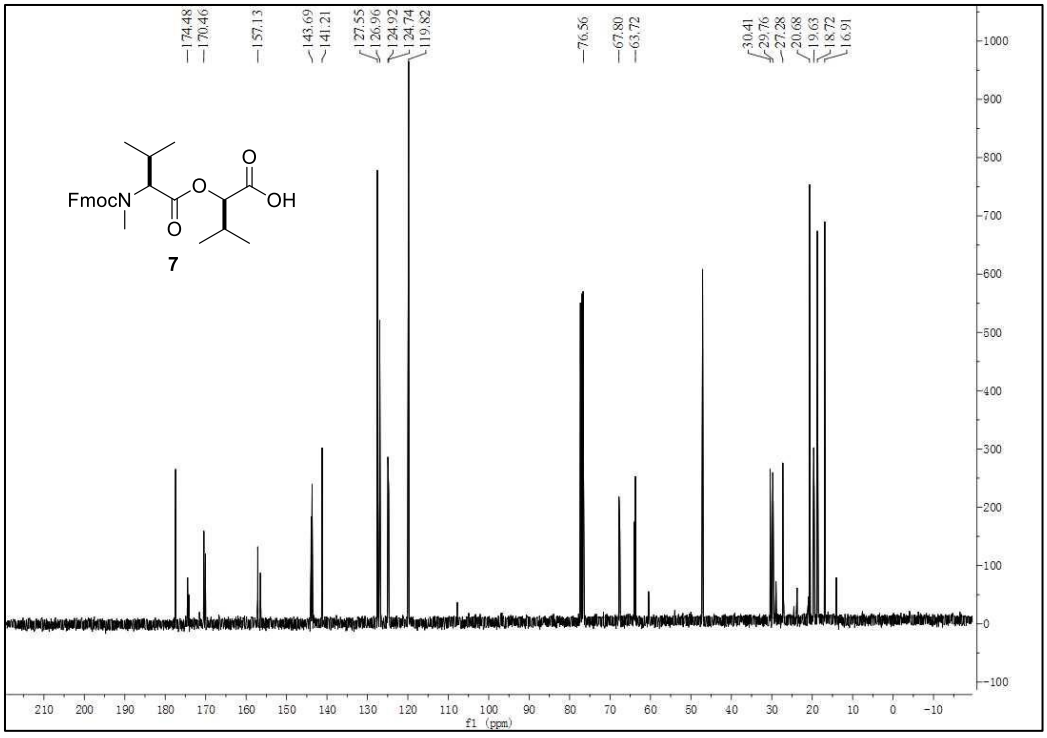
^{1}H NMR spectrum of **6a**



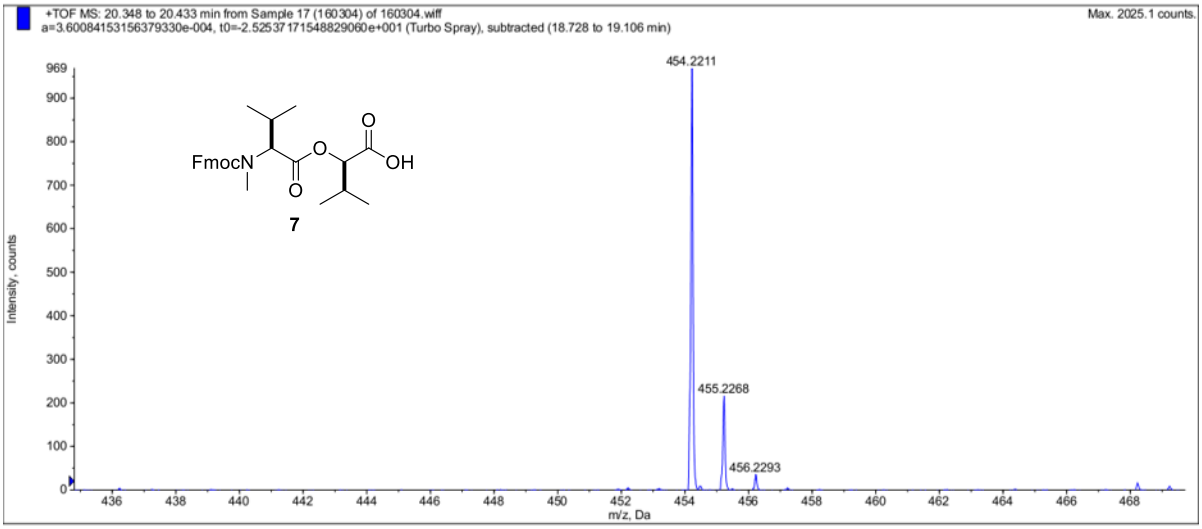
^{13}C NMR spectrum of **6a**



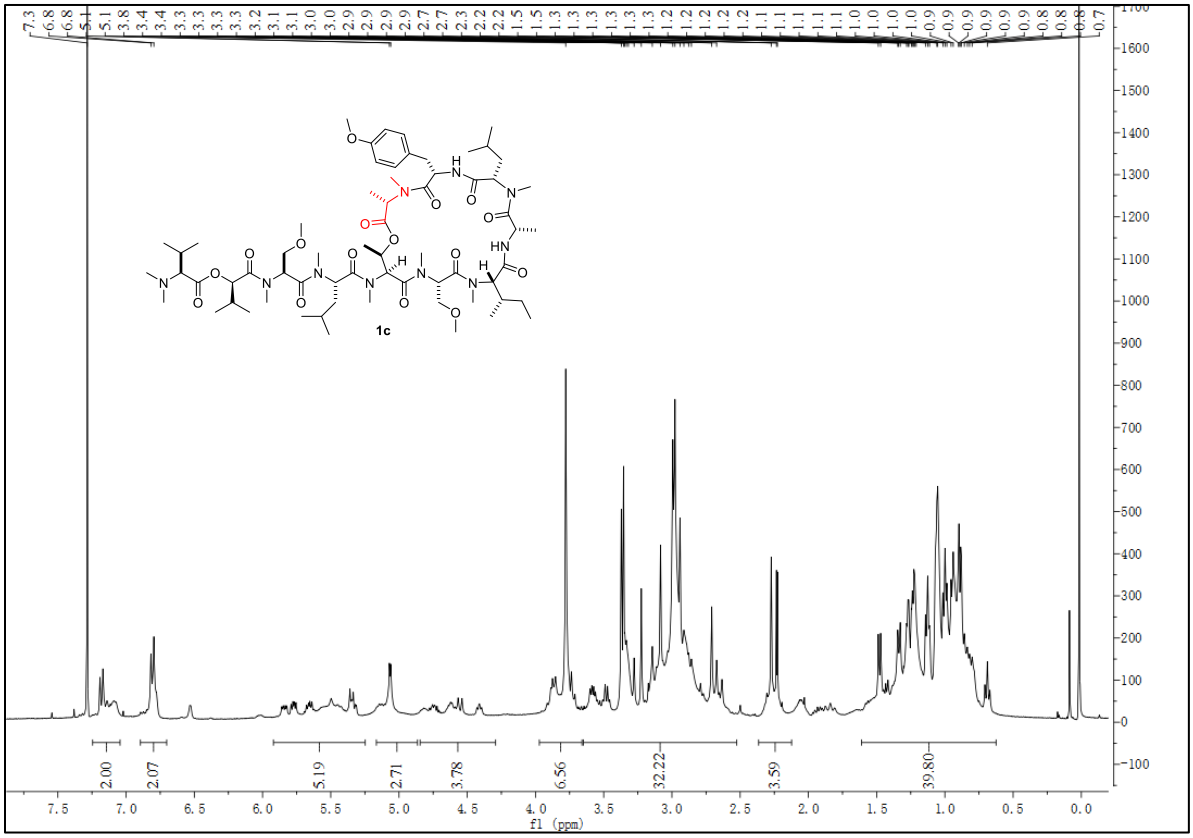
^{1}H NMR spectrum of **7**



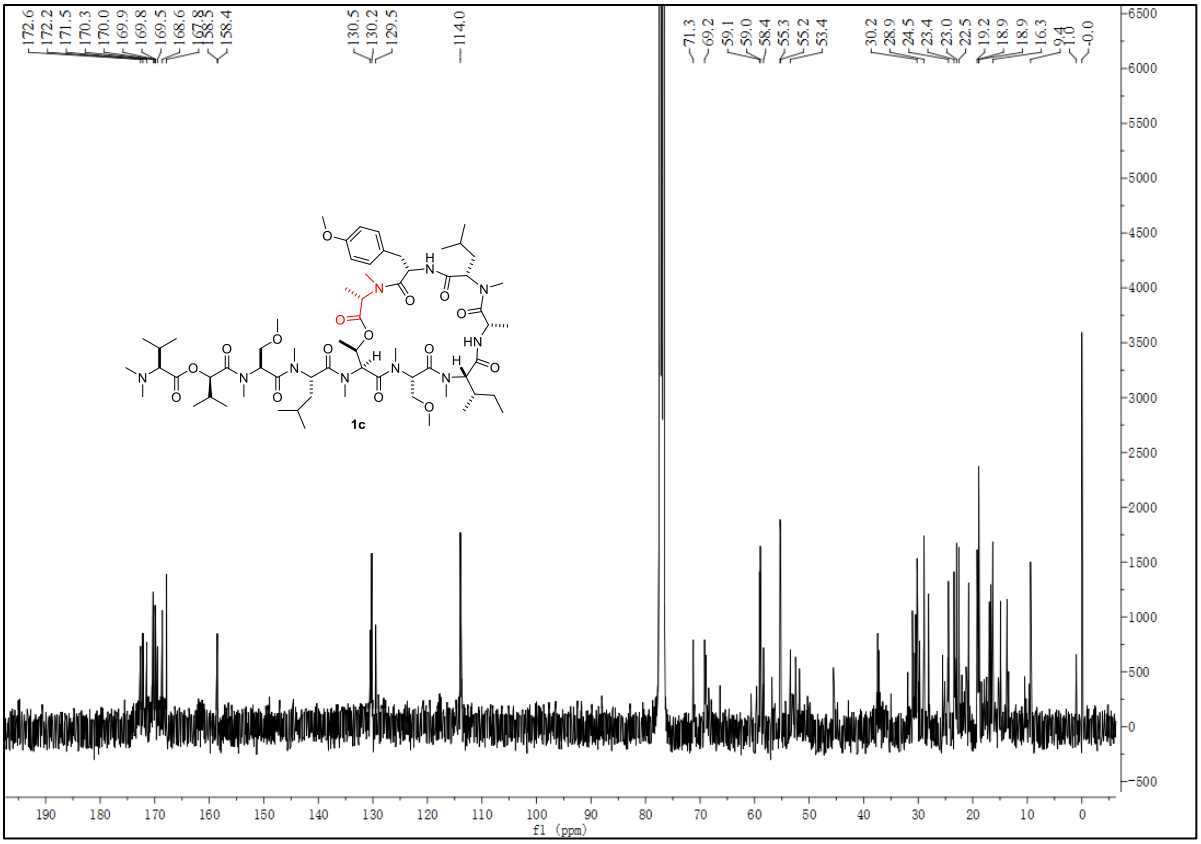
^{13}C NMR spectrum of **7**



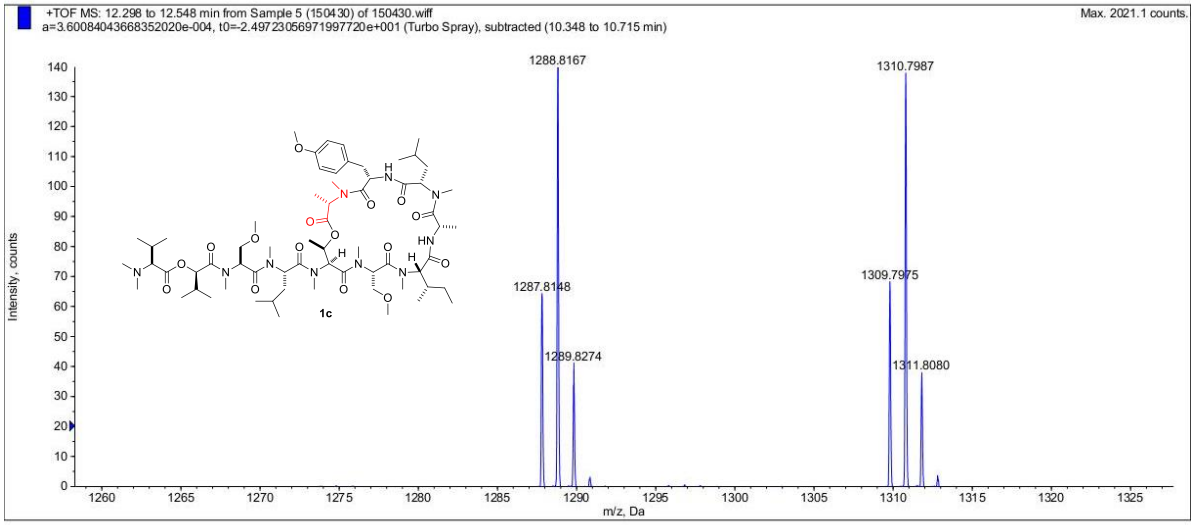
HRMS spectrum of **7**



^{1}H NMR spectrum of **1c**

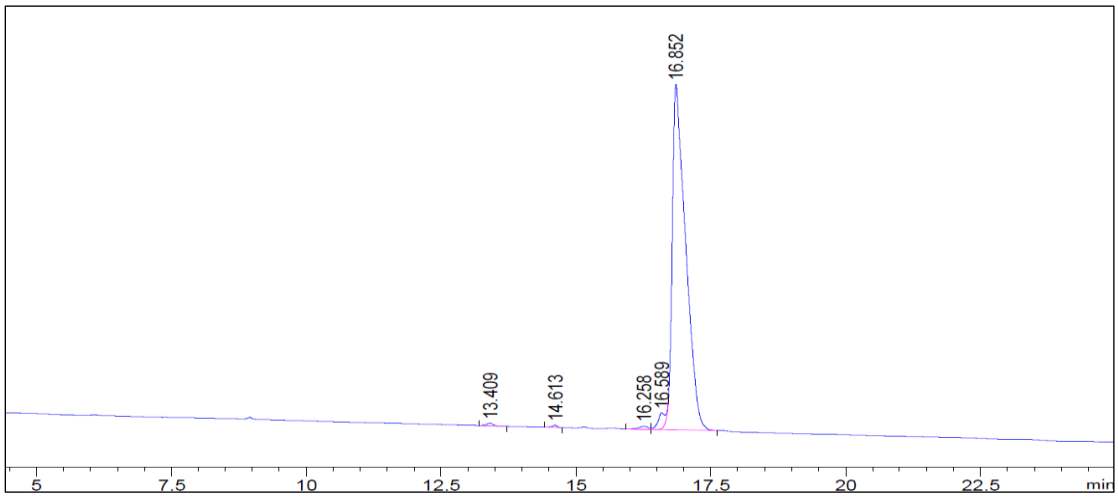


^{13}C NMR spectrum of **1c**



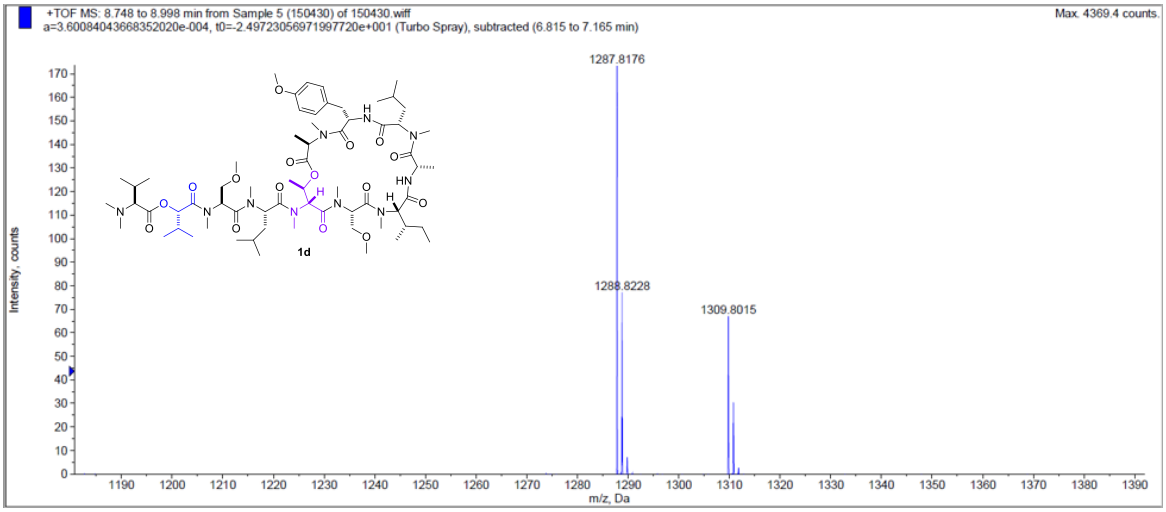
HRMS spectrum of **1c**

HPLC analysis of **1c:**



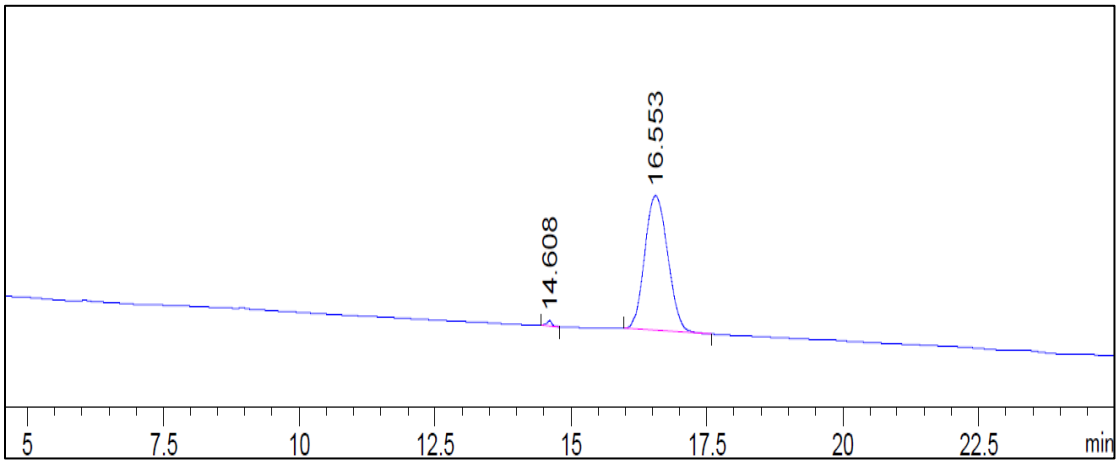
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	13.409	13.8488	119.1098	0.3557
2	14.613	11.8392	78.3555	0.2340
3	16.258	16.0777	203.0629	0.6065
4	16.589	84.3991	738.6790	2.2062
5	16.852	1868.9464	3.2342e4	96.5975
Total		1995.1114	3.3482e4	



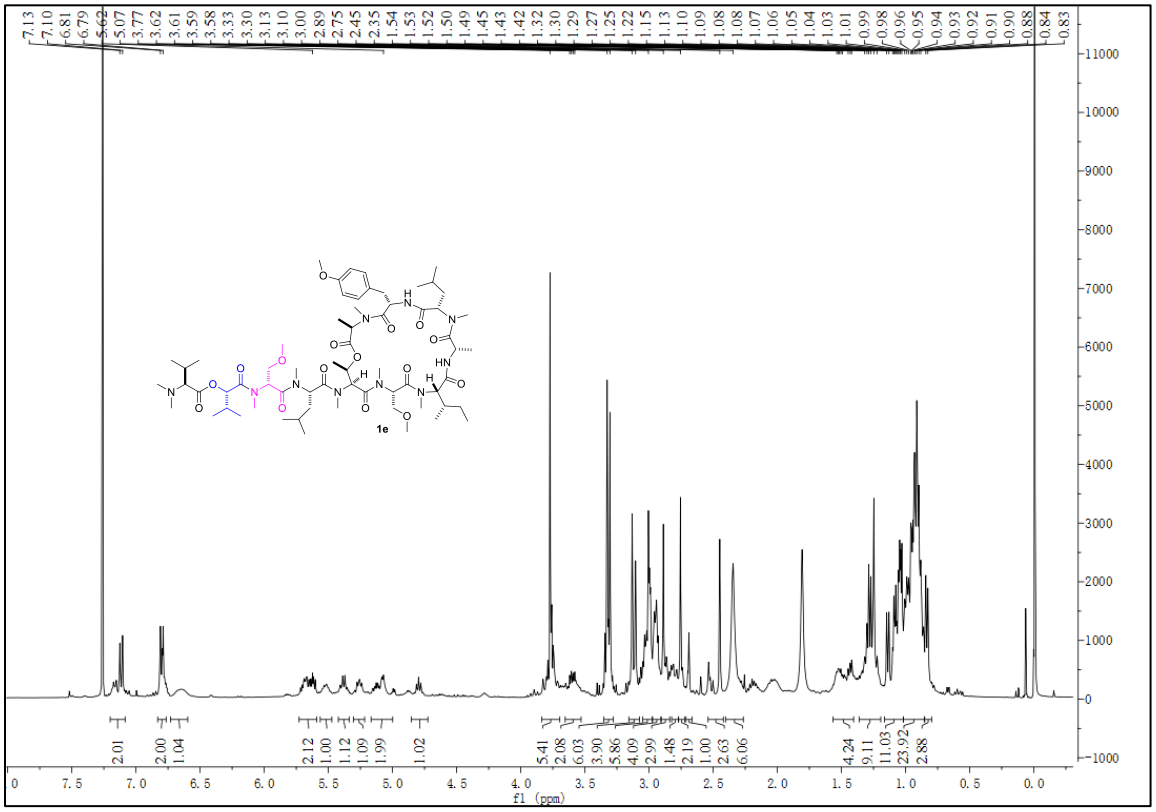
HRMS spectrum of **1d**

HPLC analysis of **1d**:

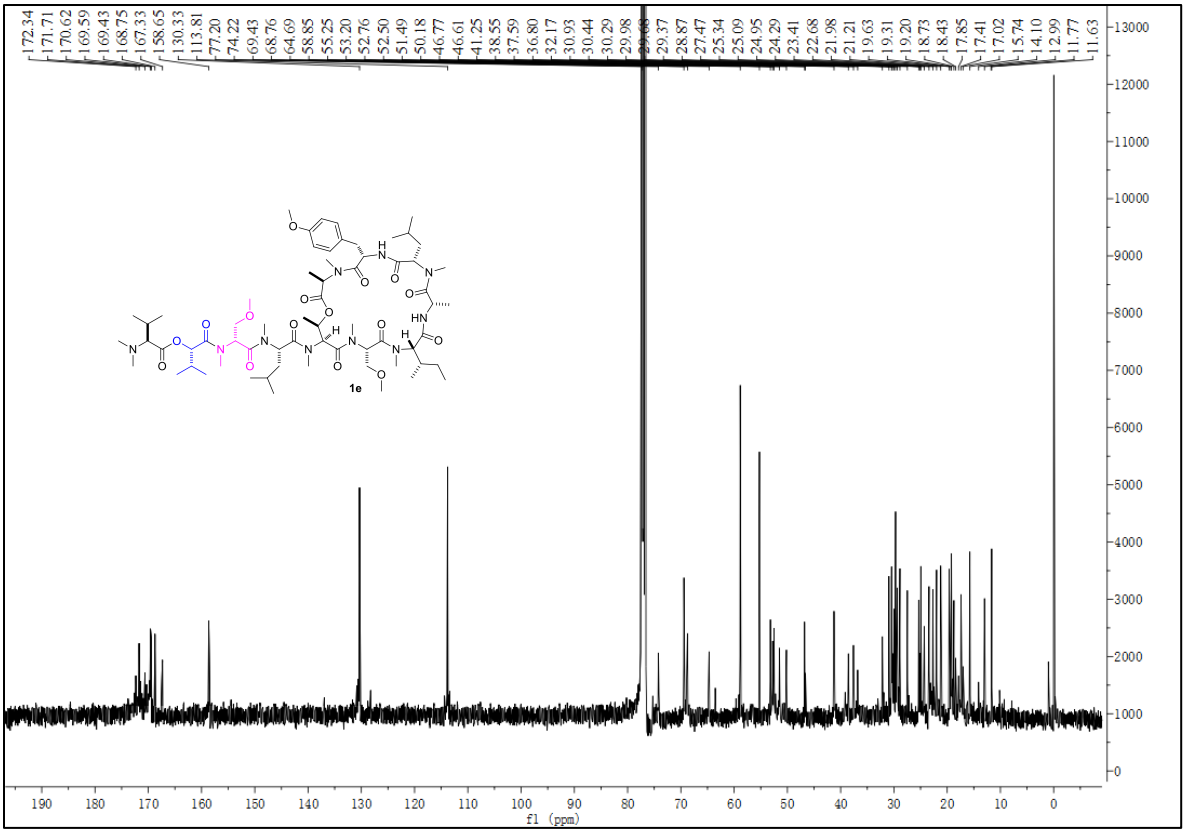


220 nm Result

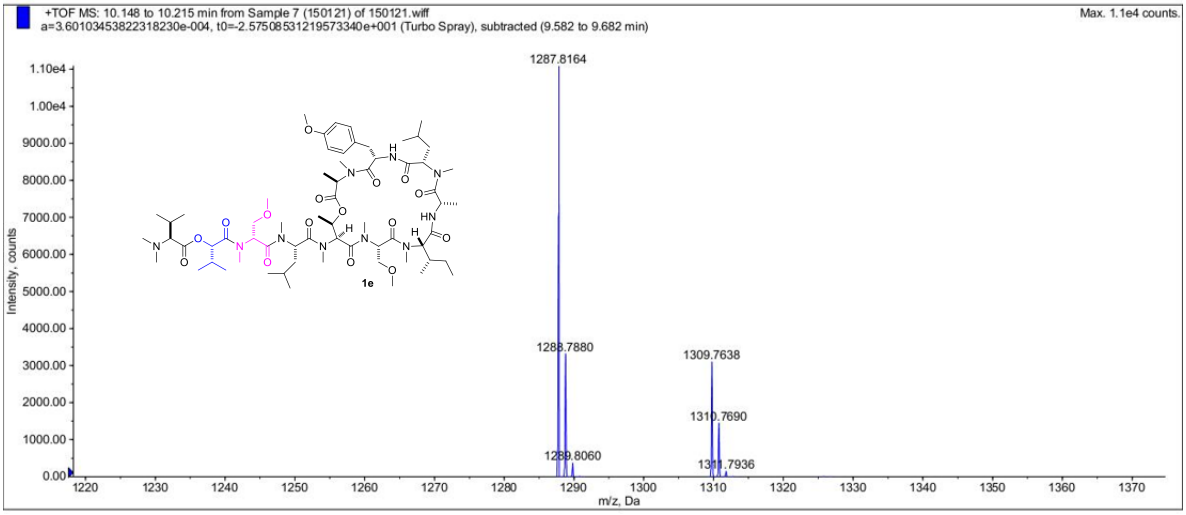
Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	14.608	14.2965	91.8185	0.8688
2	16.553	355.7148	1.0477e4	96.1312
Total		370.0114	1.0569e4	



^{1}H NMR spectrum of **1e**

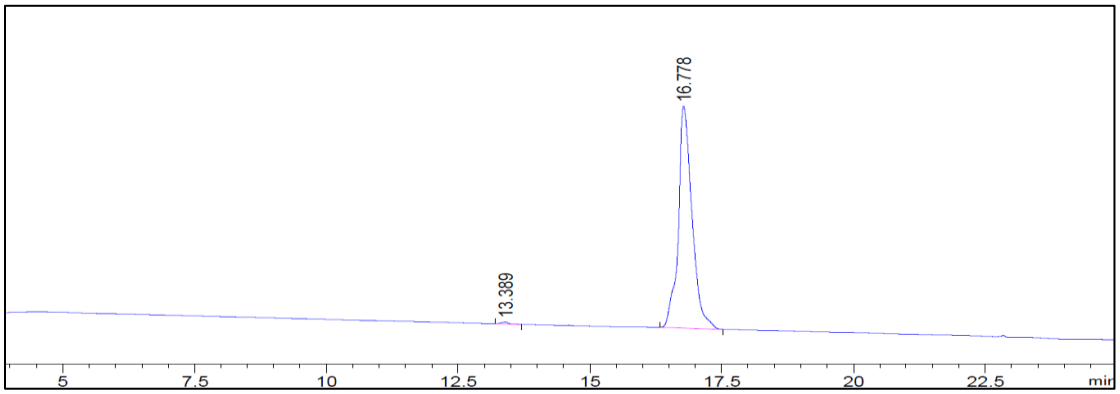


^{13}C NMR spectrum of **1e**



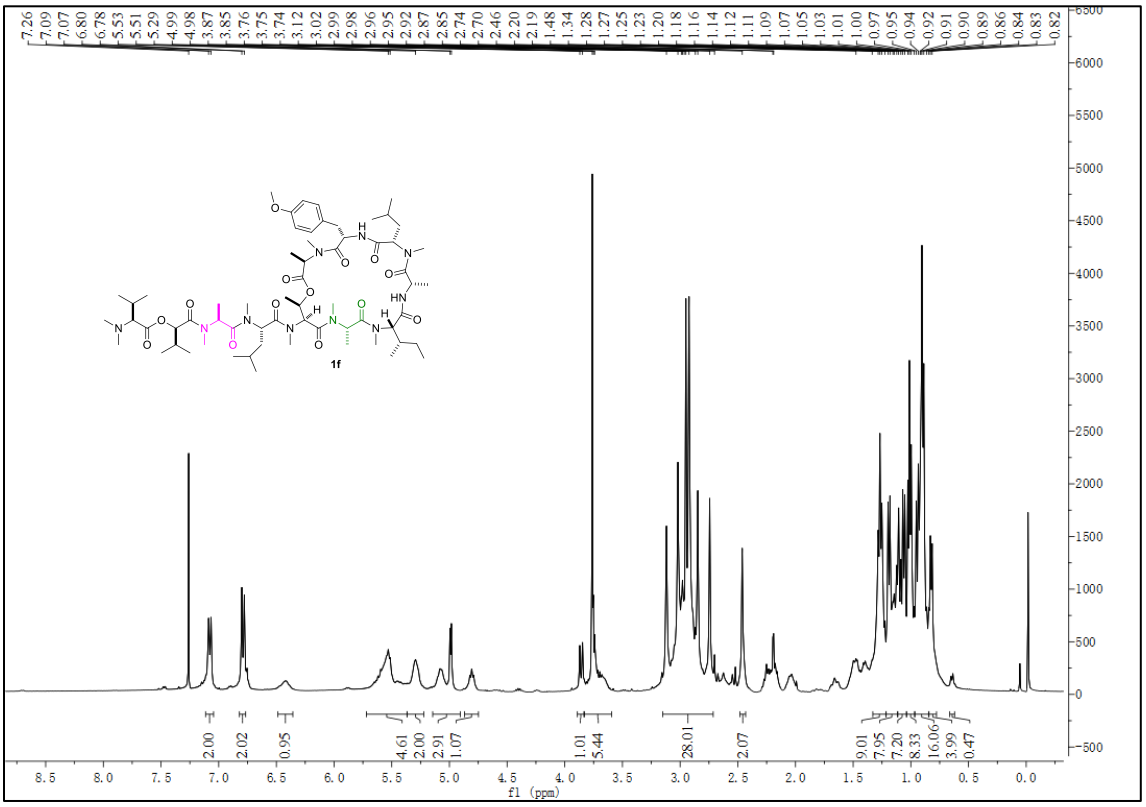
HRMS spectrum of **1e**

HPLC analysis of **1e:**

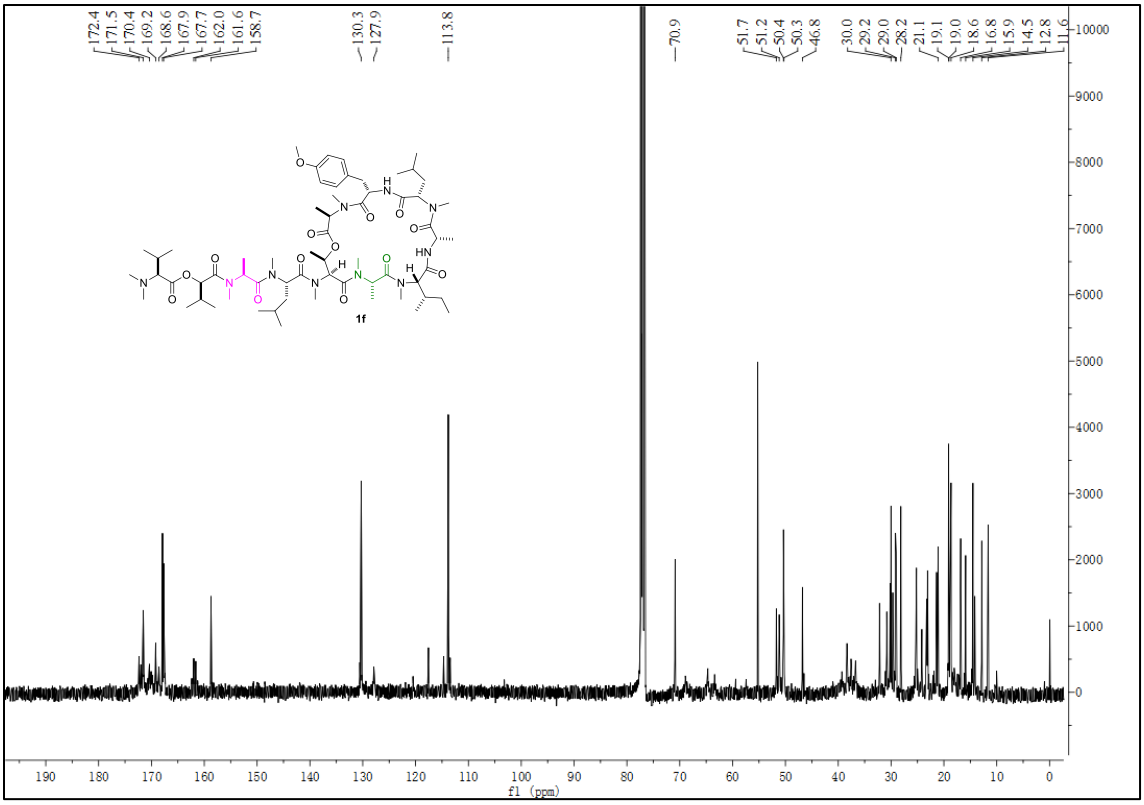


220 nm Result

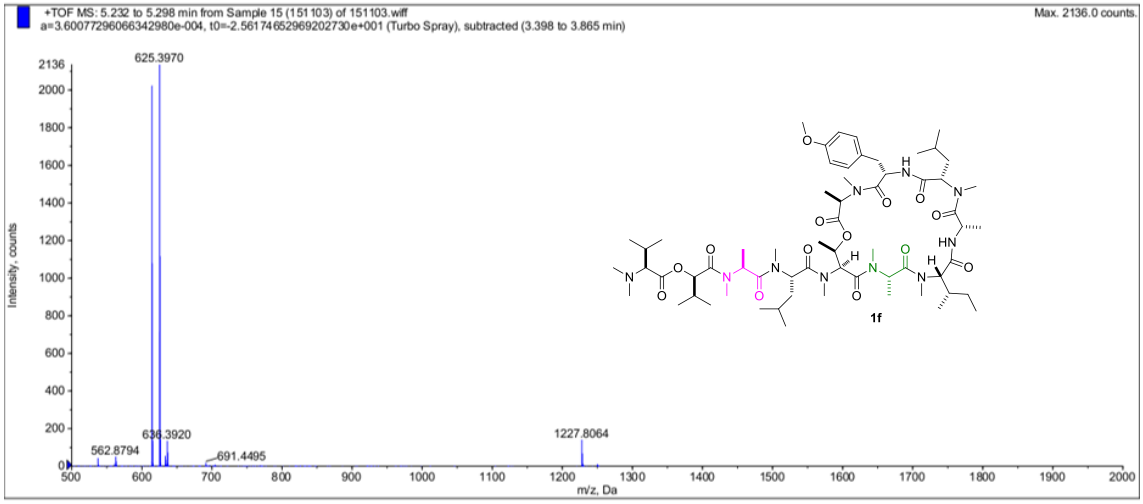
Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	13.389	10.7679	93.6150	0.4250
2	16.778	1208.0380	2.1932e4	99.5750
Total		1218.8060	2.2025e4	



^{1}H NMR spectrum of **1f**

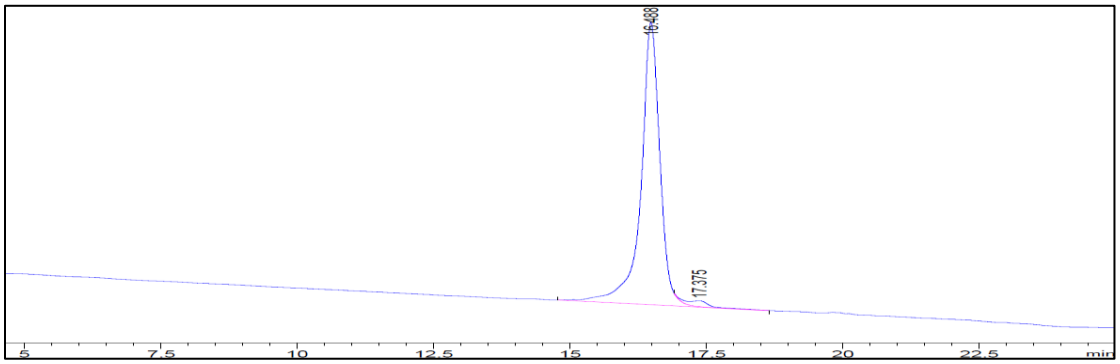


^{13}C NMR spectrum of **1f**



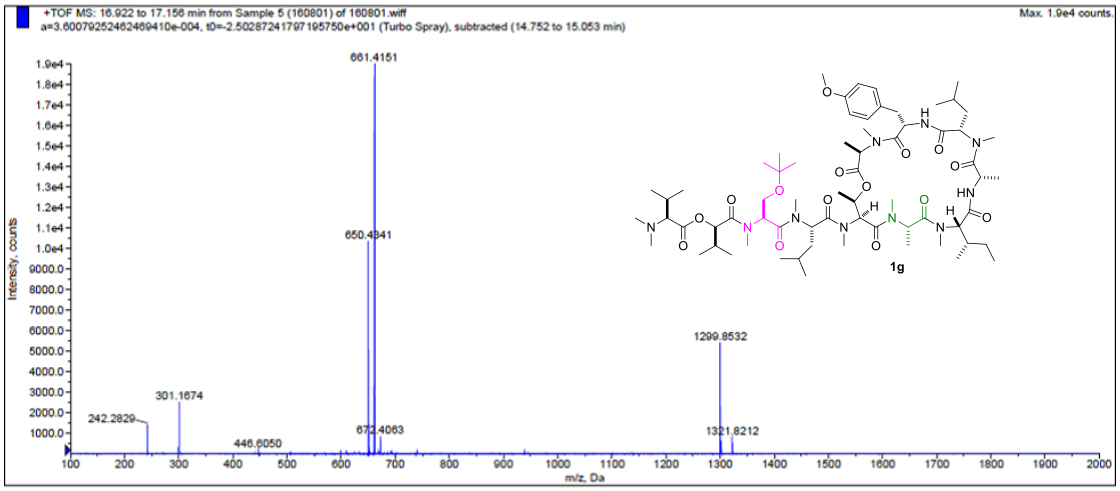
HRMS spectrum of **1f**

HPLC analysis of **1f:**



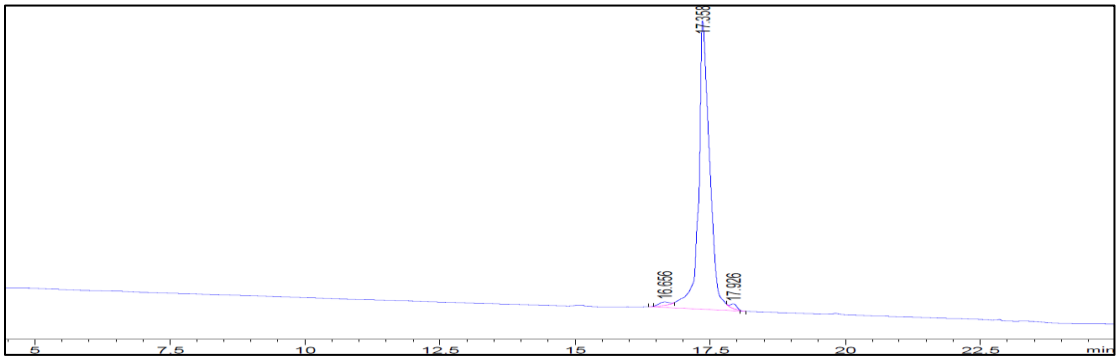
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	16.488	775.8211	1.8916e4	97.6767
2	17.375	16.3924	449.9381	2.3233
Total		792.2135	1.93661e4	



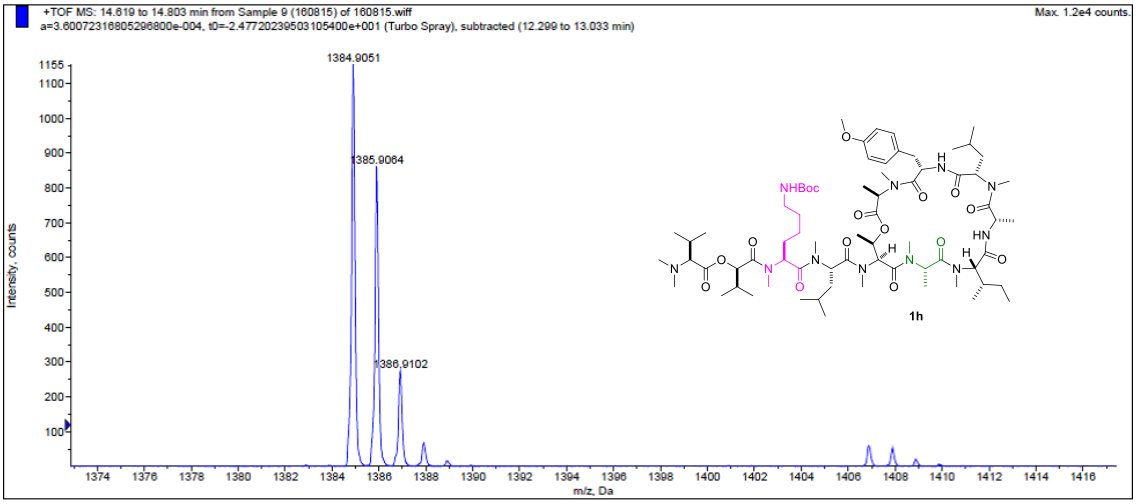
HRMS spectrum of **1g**

HPLC analysis of **1g:**



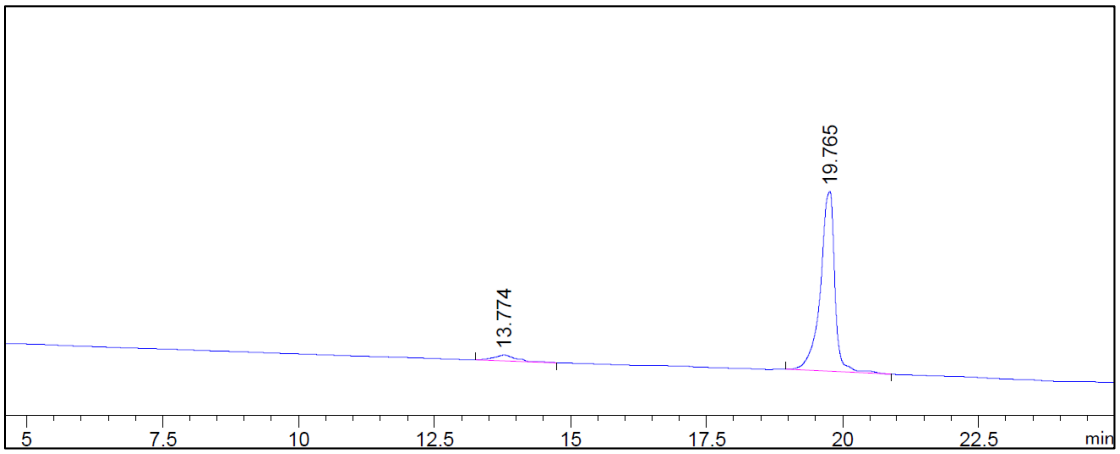
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	16.656	14.8736	187.1558	1.0441
2	17.358	1210.2704	1.7582e4	98.0843
3	17.926	19.6773	156.2403	0.8716
Total		1244.8214	1.7926e4	



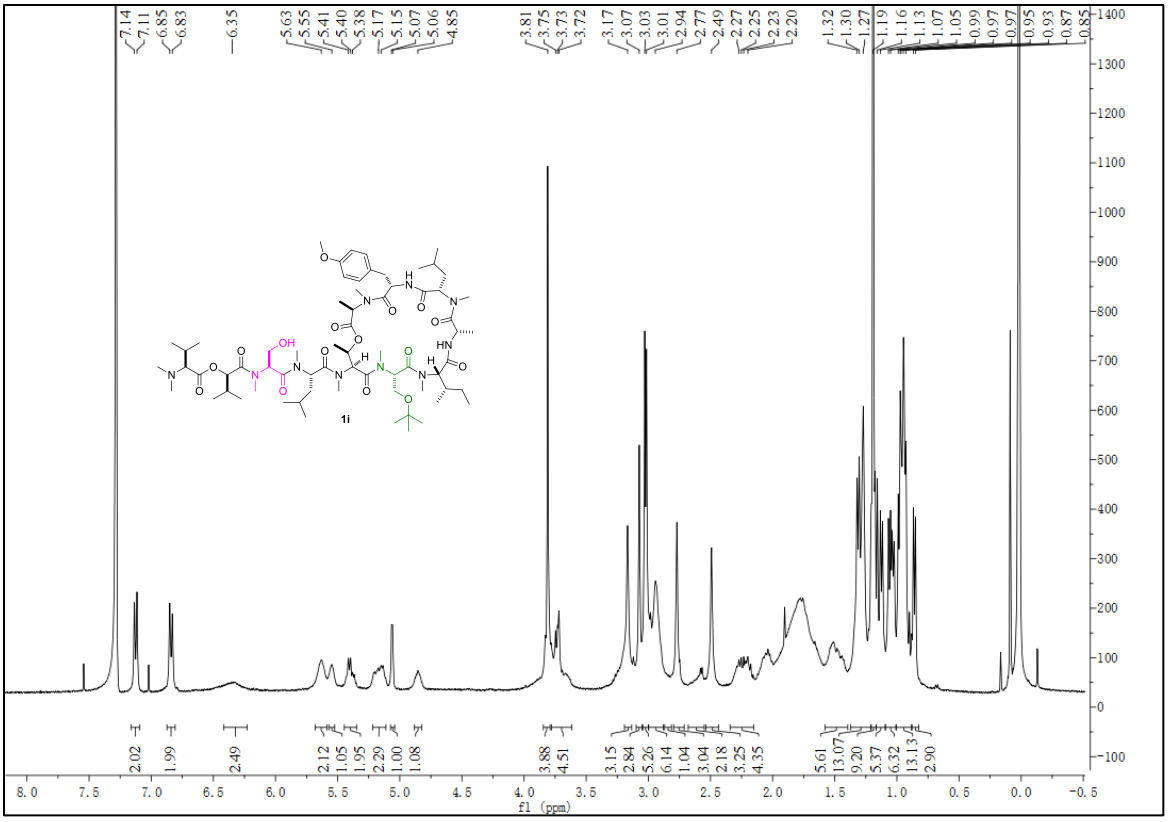
HRMS spectrum of **1h**

HPLC analysis of **1h:**

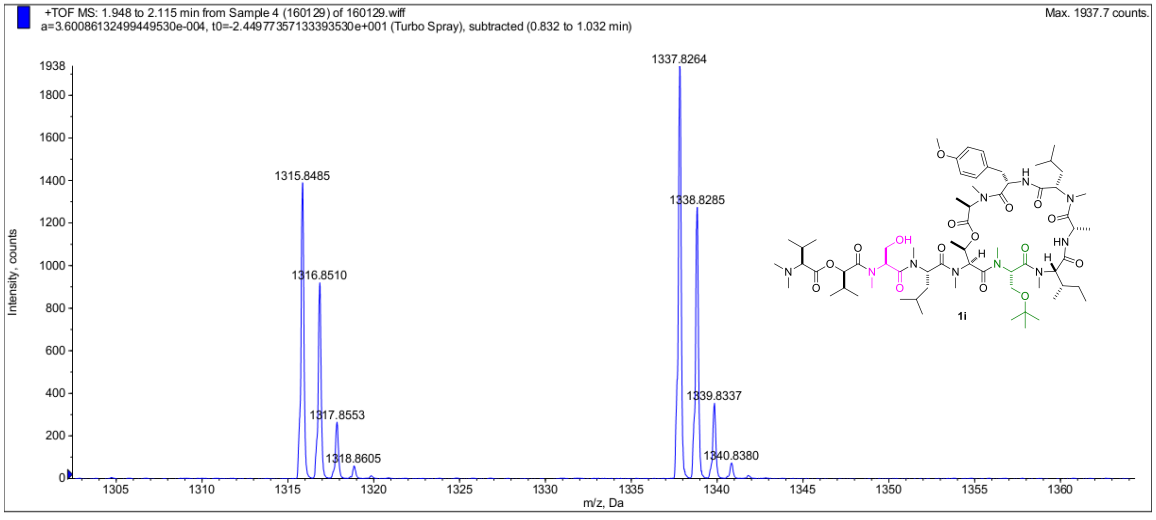


220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	13.774	22.6546	618.4960	4.4947
2	19.765	707.1600	1.3142e4	95.5053
Total		729.8146	1.3761e4	

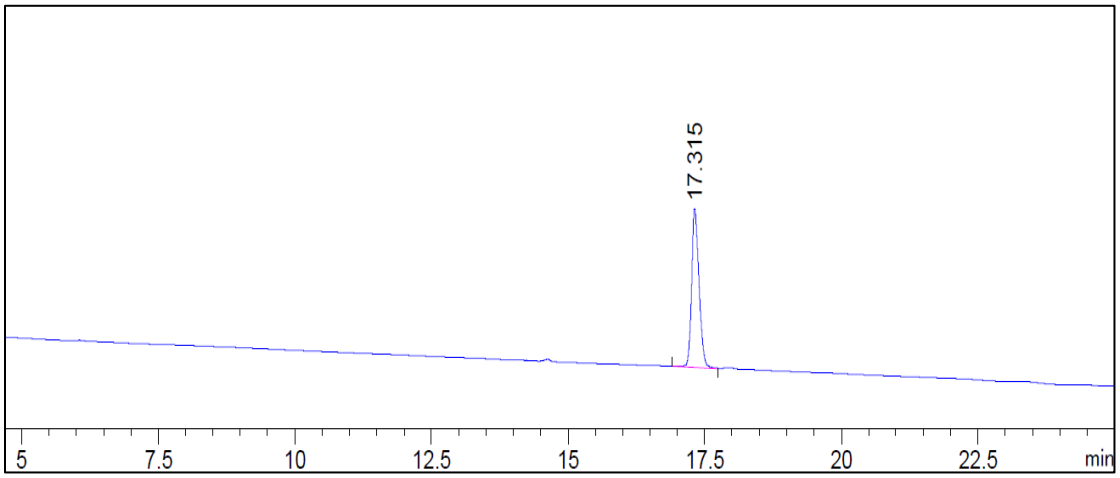


^{1}H NMR spectrum of **1i**



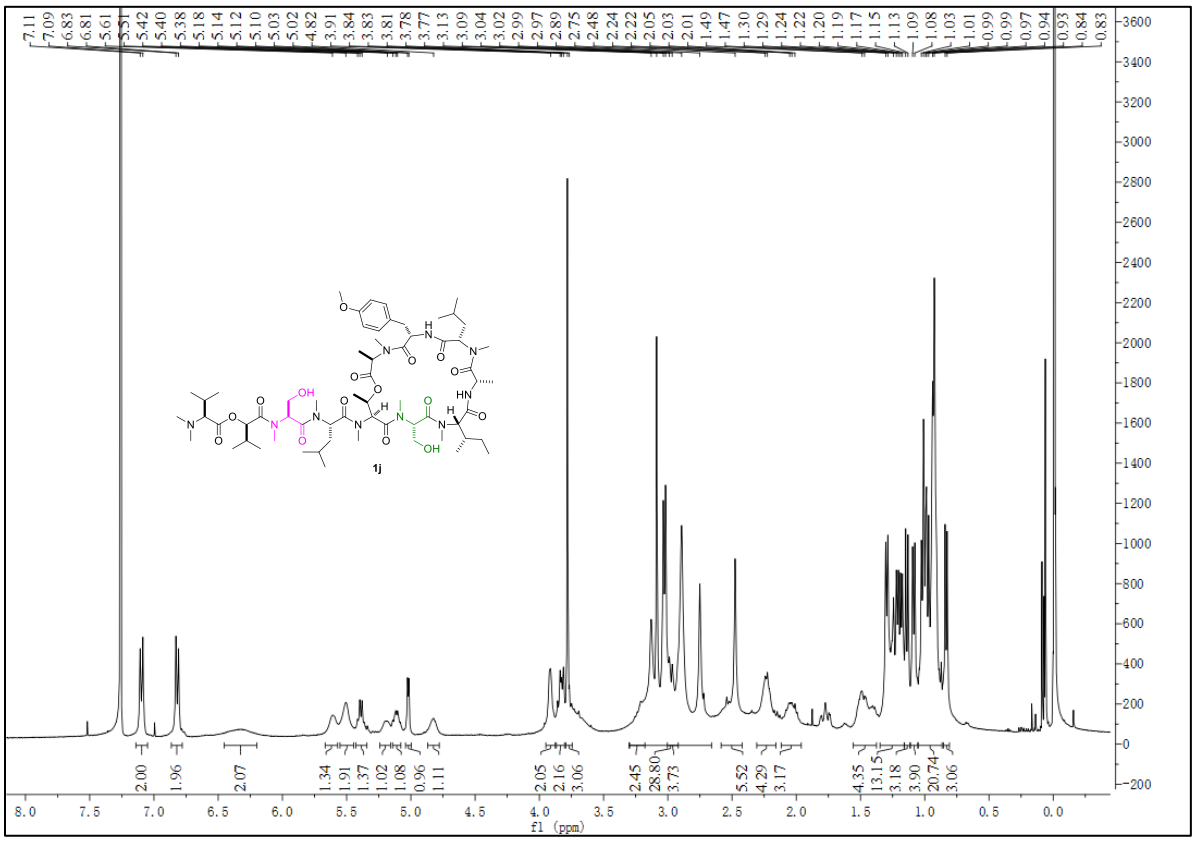
HRMS spectrum of **1i**

HPLC analysis of **1i:**

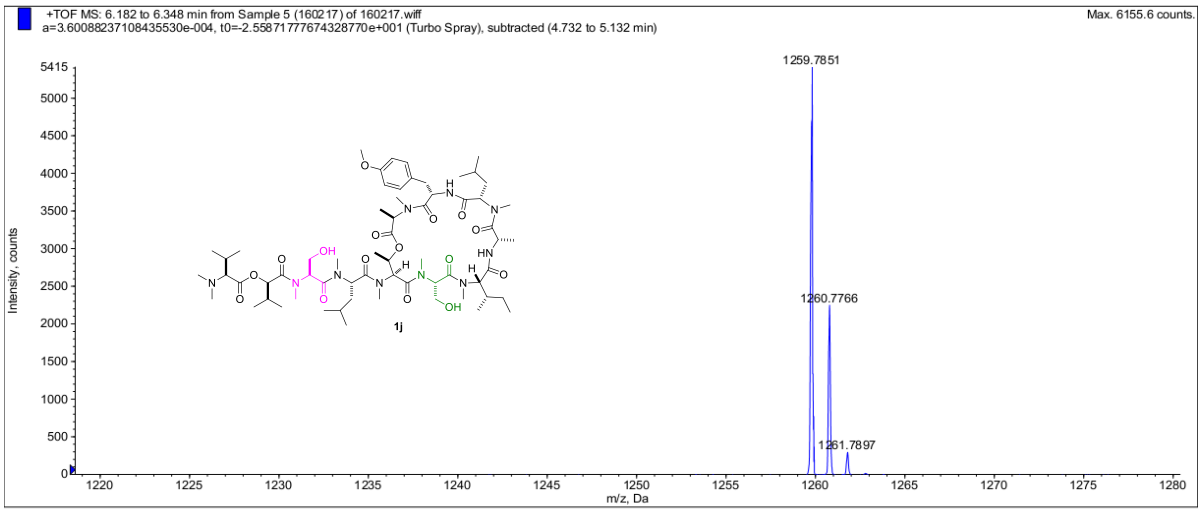


220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	17.315	503.9682	4694.9023	100.0000
Total		503.9682	4694.9023	

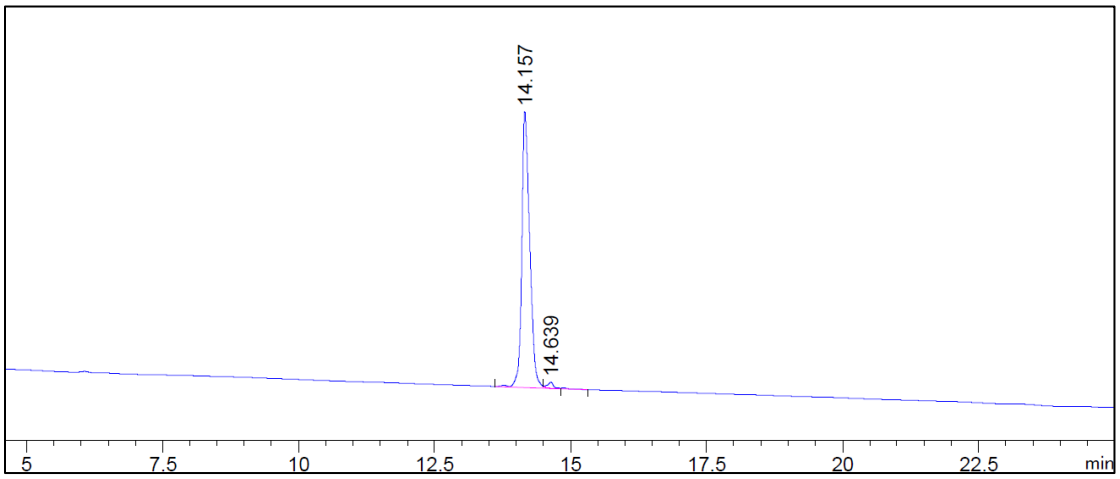


^{1}H NMR spectrum of **1j**



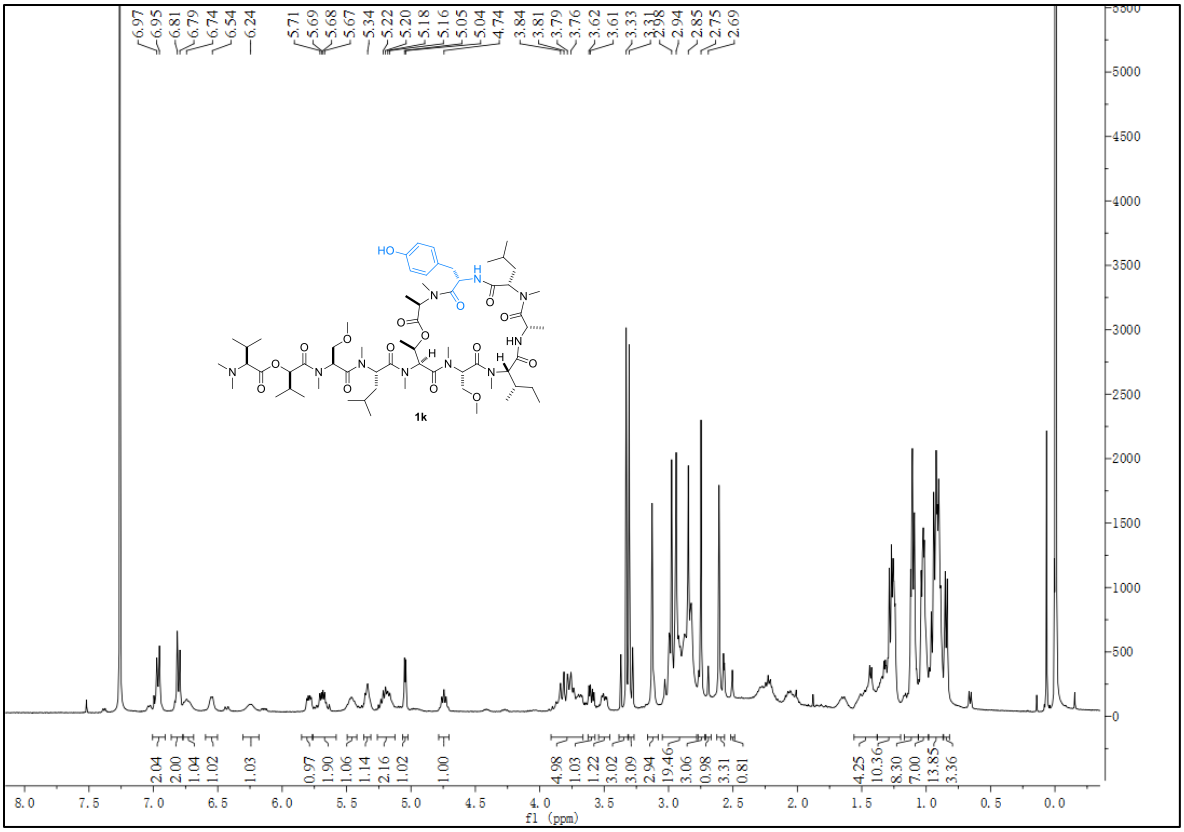
HRMS spectrum of **1j**

HPLC analysis of **1j:**

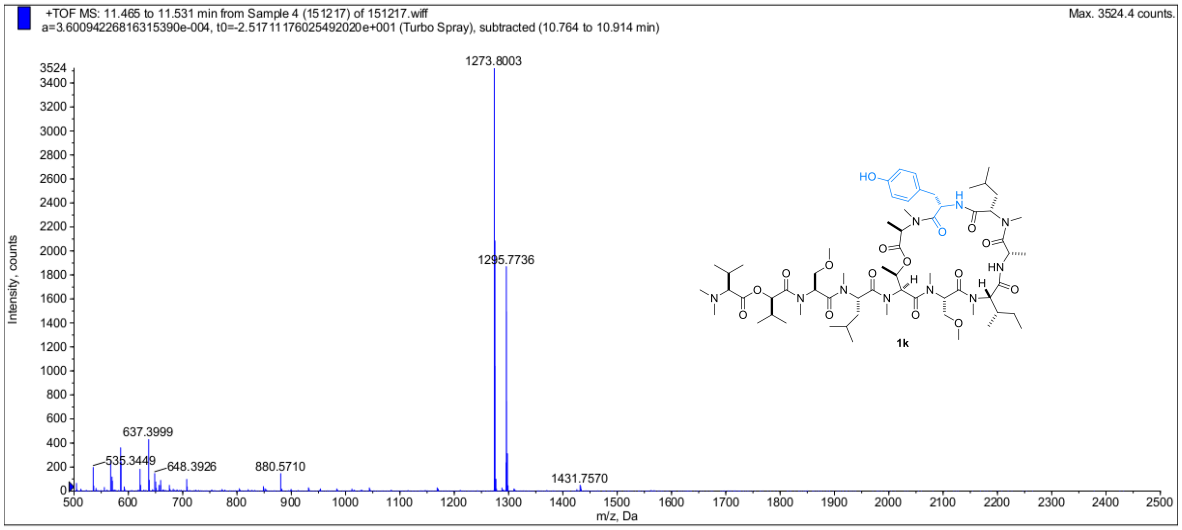


220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	14.157	1137.4020	1.1536e4	98.4650
2	14.639	179.8344	179.8344	1.5350
Total		1162.1264	1.1716e4	

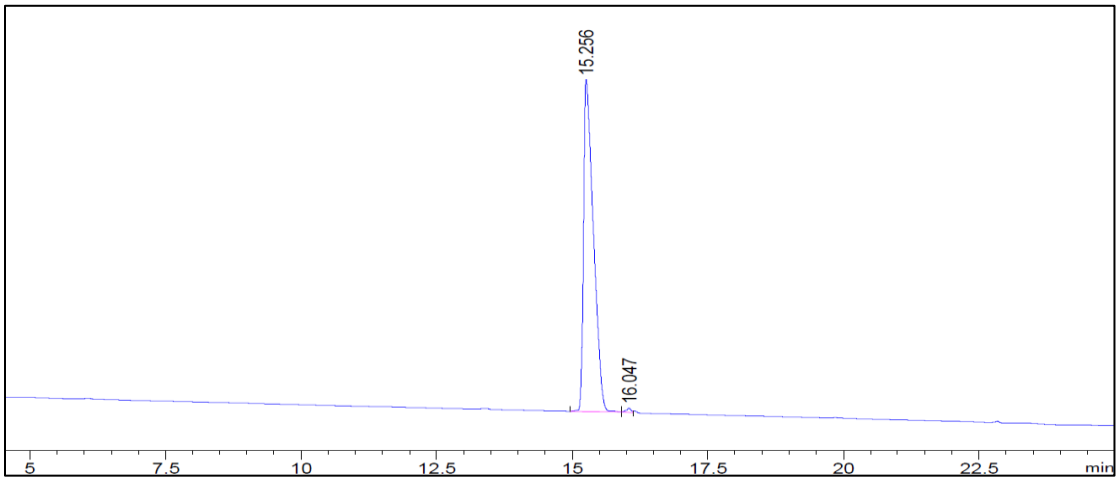


^{1}H NMR spectrum of **1k**



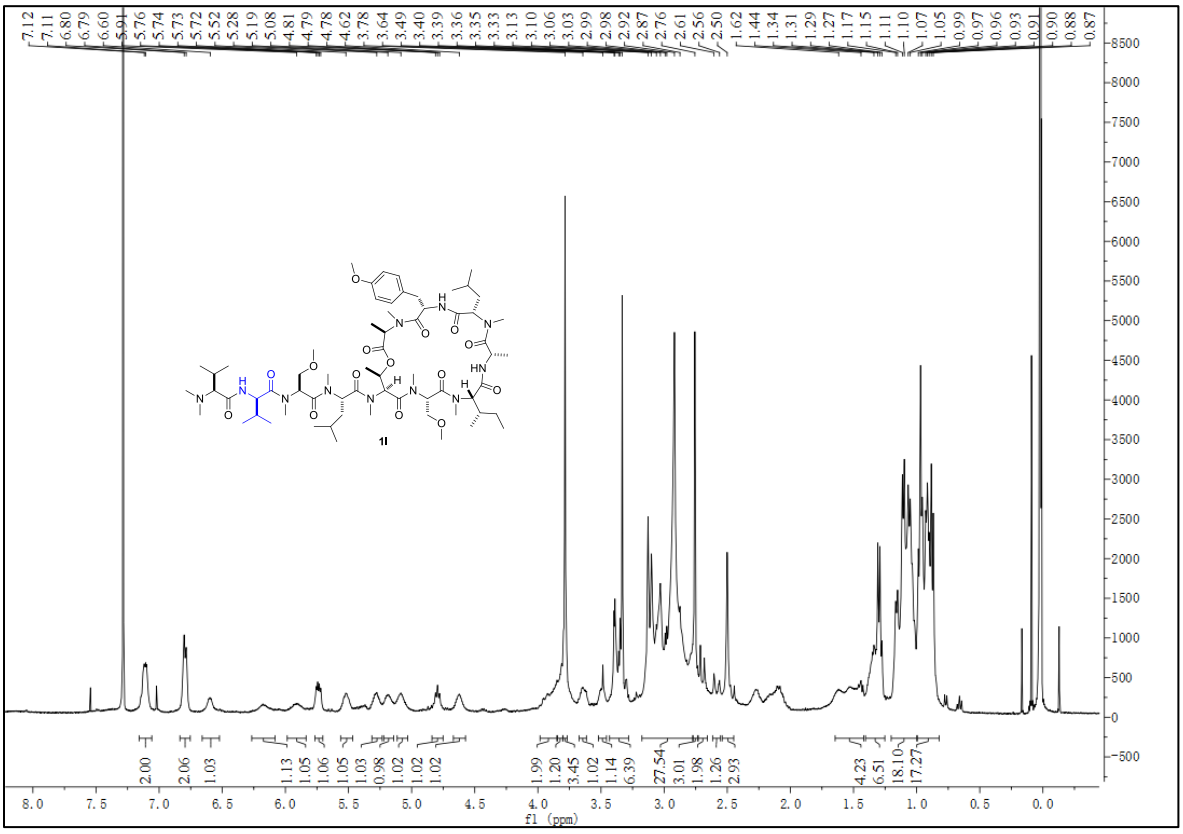
HRMS spectrum of **1k**

HPLC analysis of **1k:**

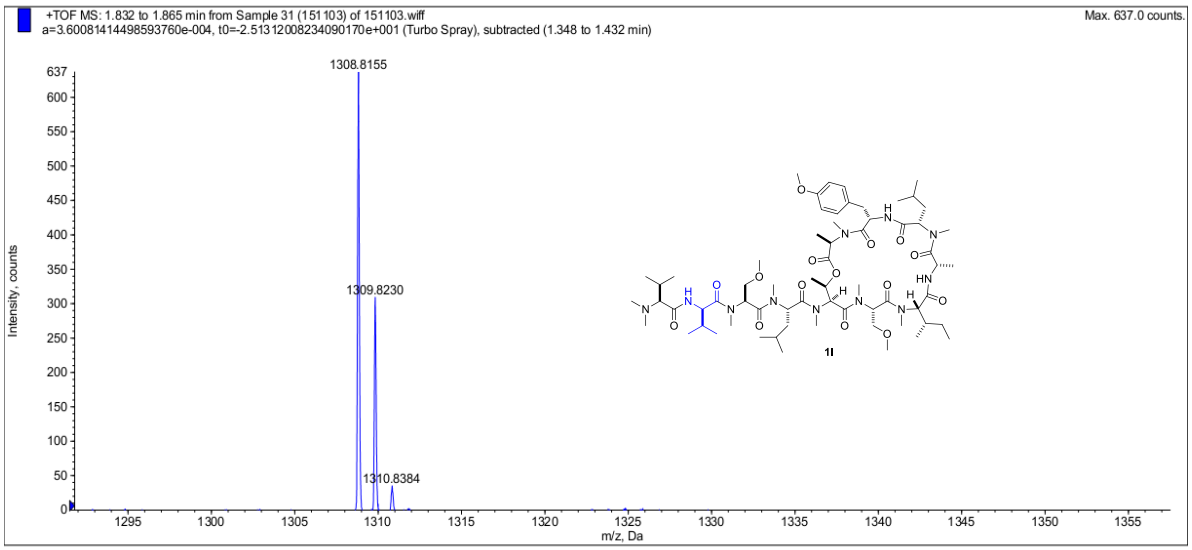


220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	15.256	1775.4265	2.2246e4	99.3701
2	16.047	23.1284	141.0073	0.6299
Total		1798.5549	2.2387e4	

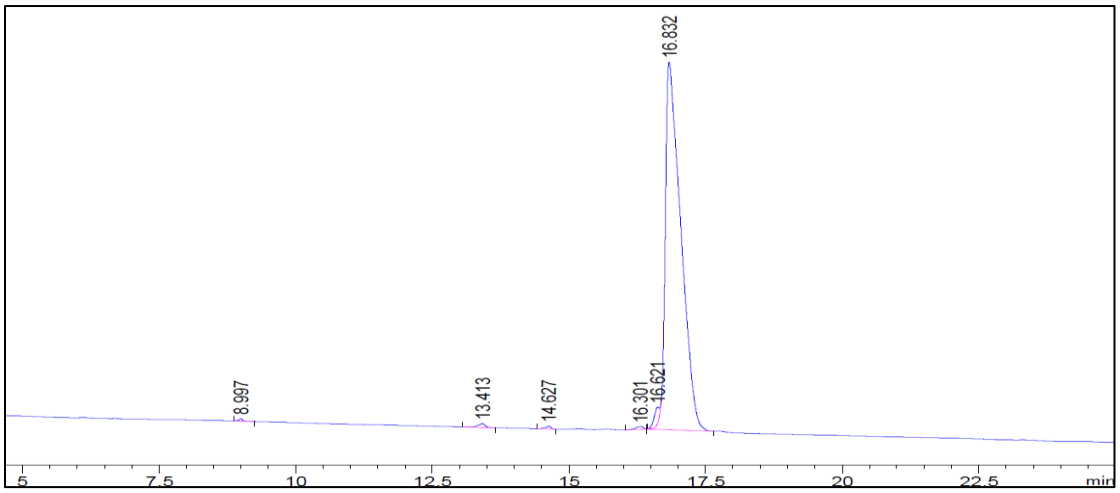


^{1}H NMR spectrum of **1l**



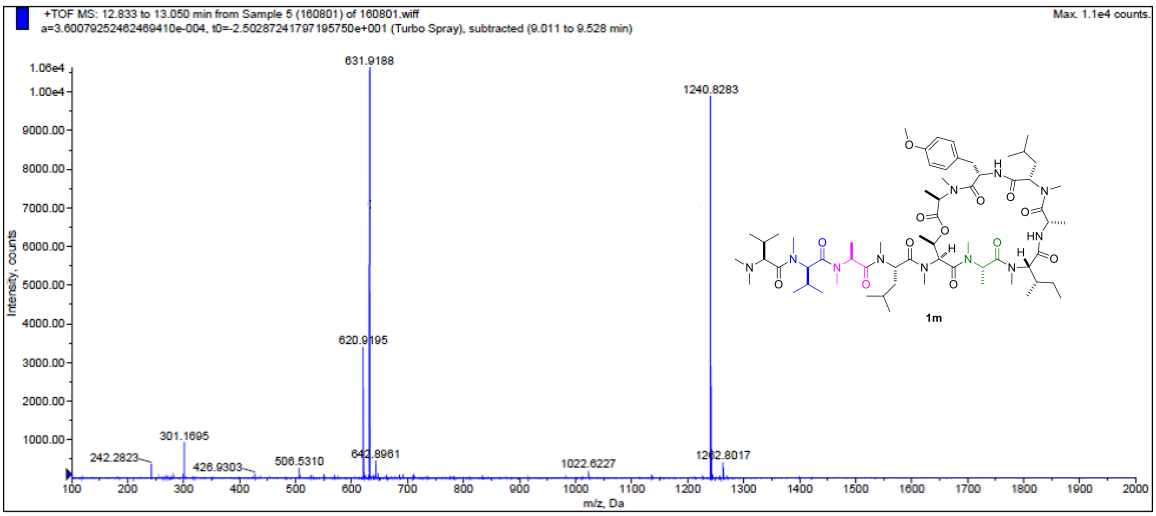
HRMS spectrum of **1l**

HPLC analysis of **1l:**



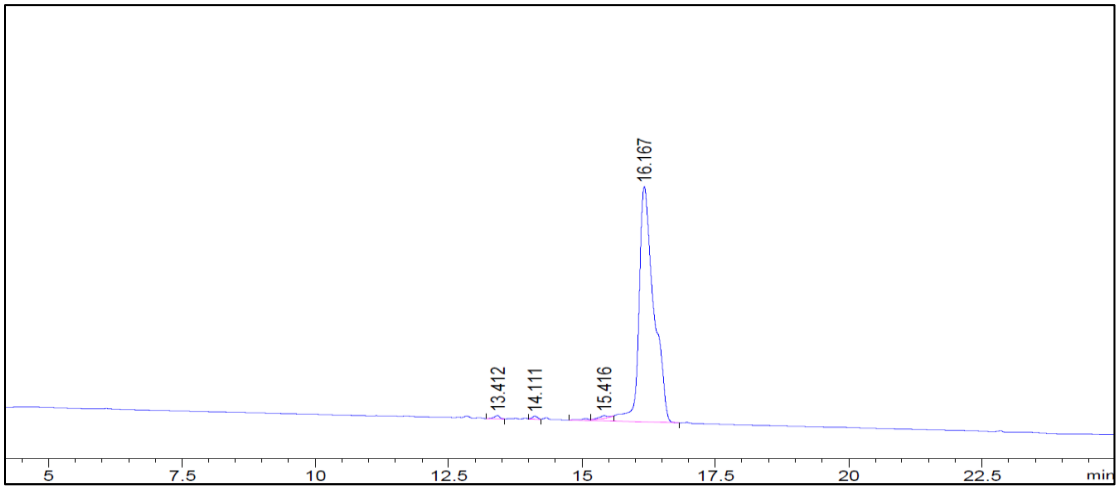
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	8.997	13.8940	63.6537	0.1436
2	13.413	22.2182	202.5929	0.4569
3	14.627	15.6525	108.0623	0.2437
4	16.301	15.7094	153.2405	0.3456
5	16.621	96.2370	666.0664	1.5022
16.832		2186.2065	4.3146e4	97.3080
Total		2349.9176	4.4340e4	



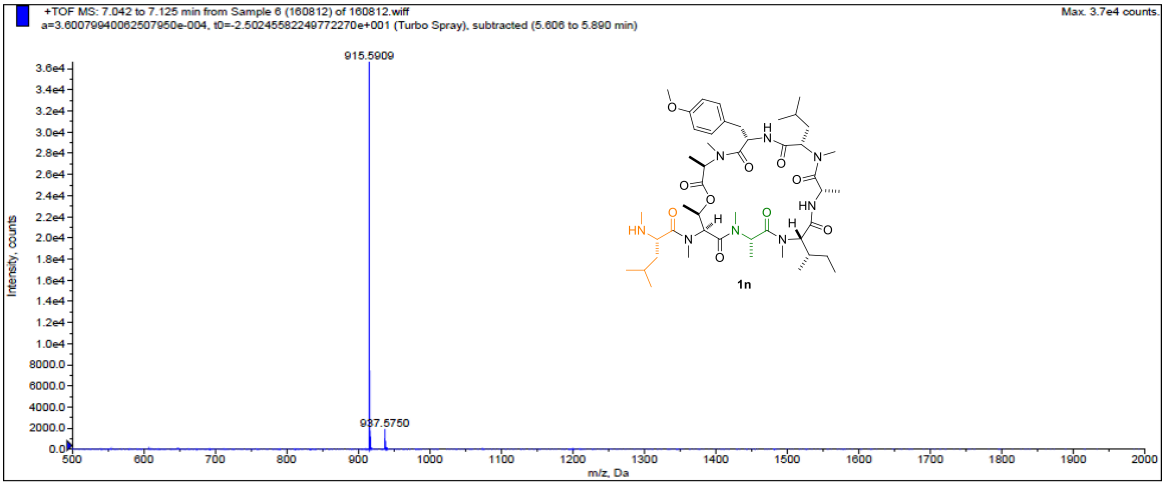
HRMS spectrum of **1m**

HPLC analysis of **1m:**



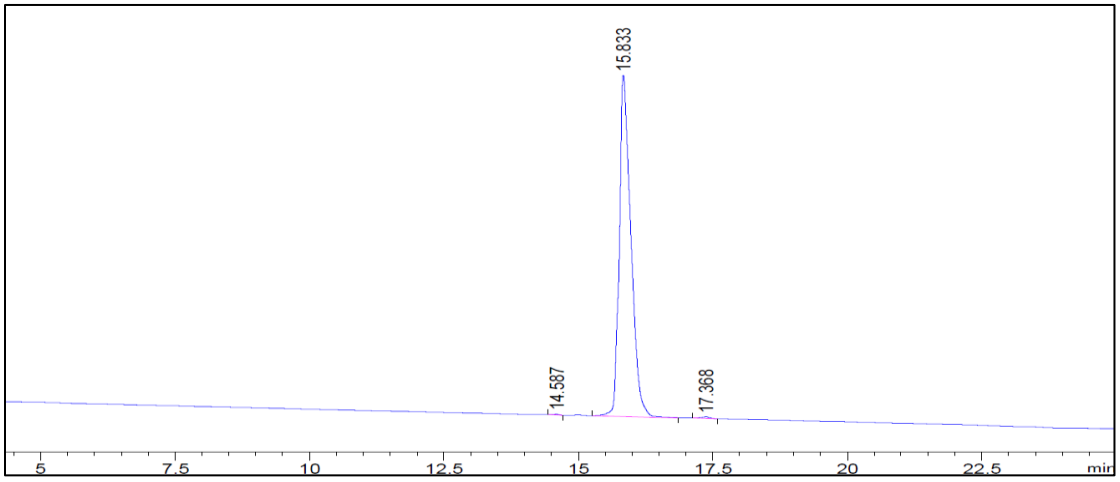
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	13.412	17.8267	124.5102	0.4750
2	14.111	17.8148	131.0461	0.4999
3	15.416	15.6908	175.9565	0.6712
4	16.167	1308.6486	2.5783e4	0.6712
Total		1359.9809	2.6215e4	



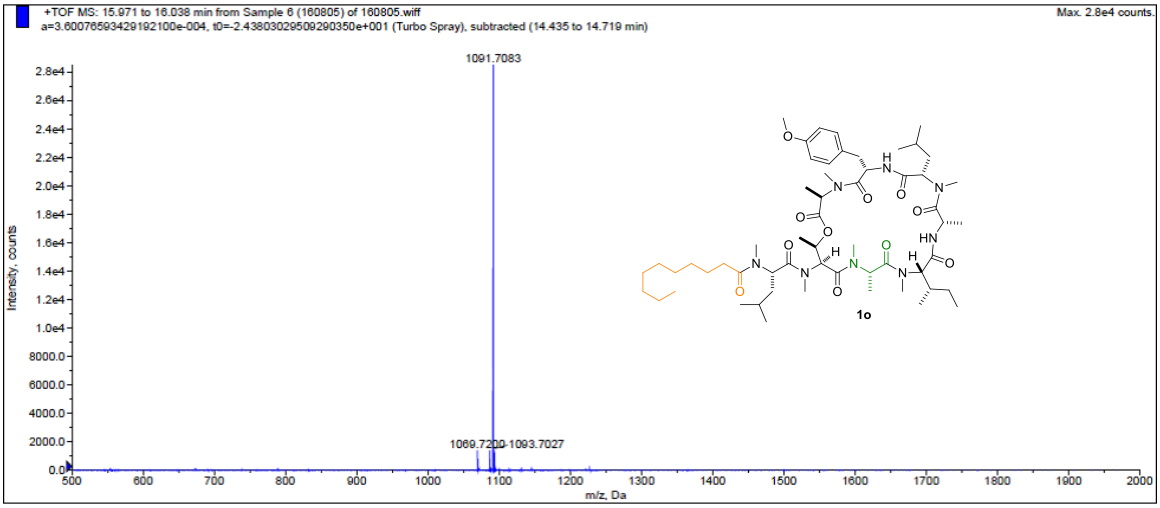
HRMS spectrum of **1n**

HPLC analysis of **1n:**



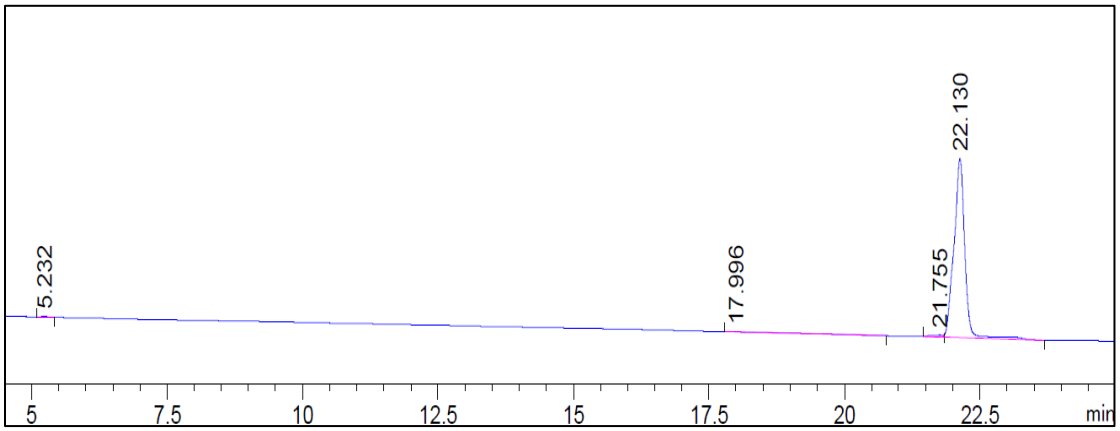
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	14.587	4.4860	33.7224	0.1134
2	15.833	1974.2975	2.9606e4	99.5592
3	17.368	9.4310	97.3571	0.3274
Total		1988.2144	2.9737e4	



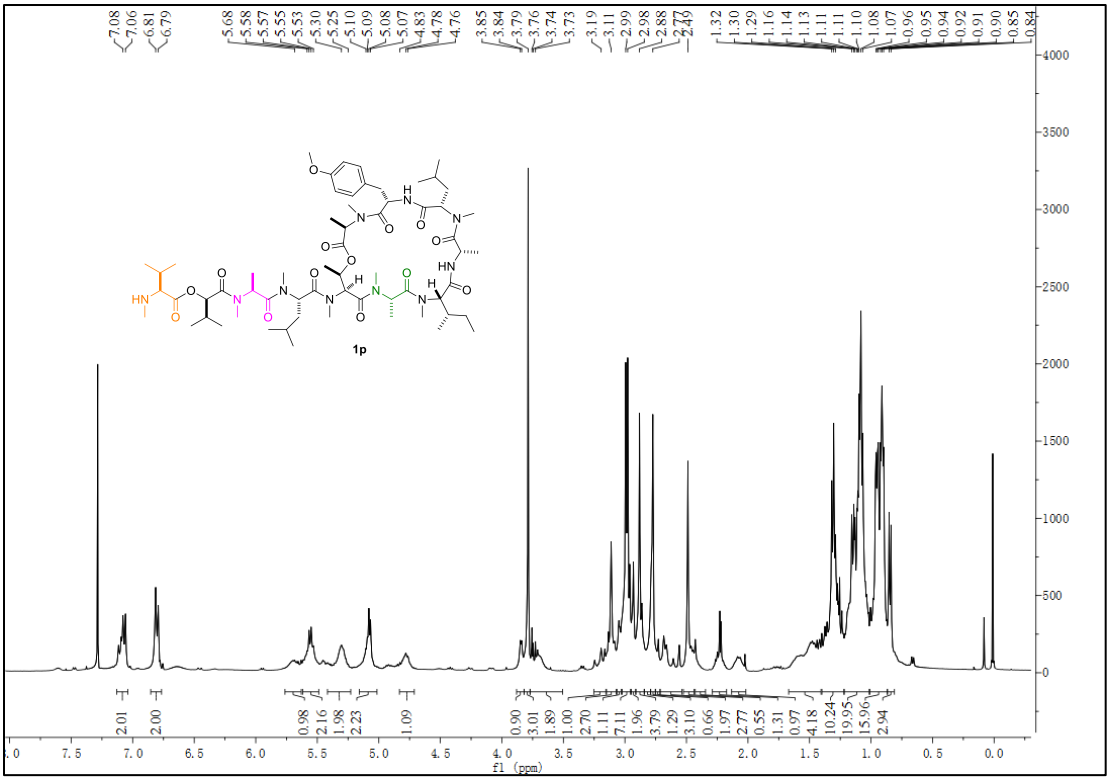
HRMS spectrum of **1o**

HPLC analysis of **1o:**

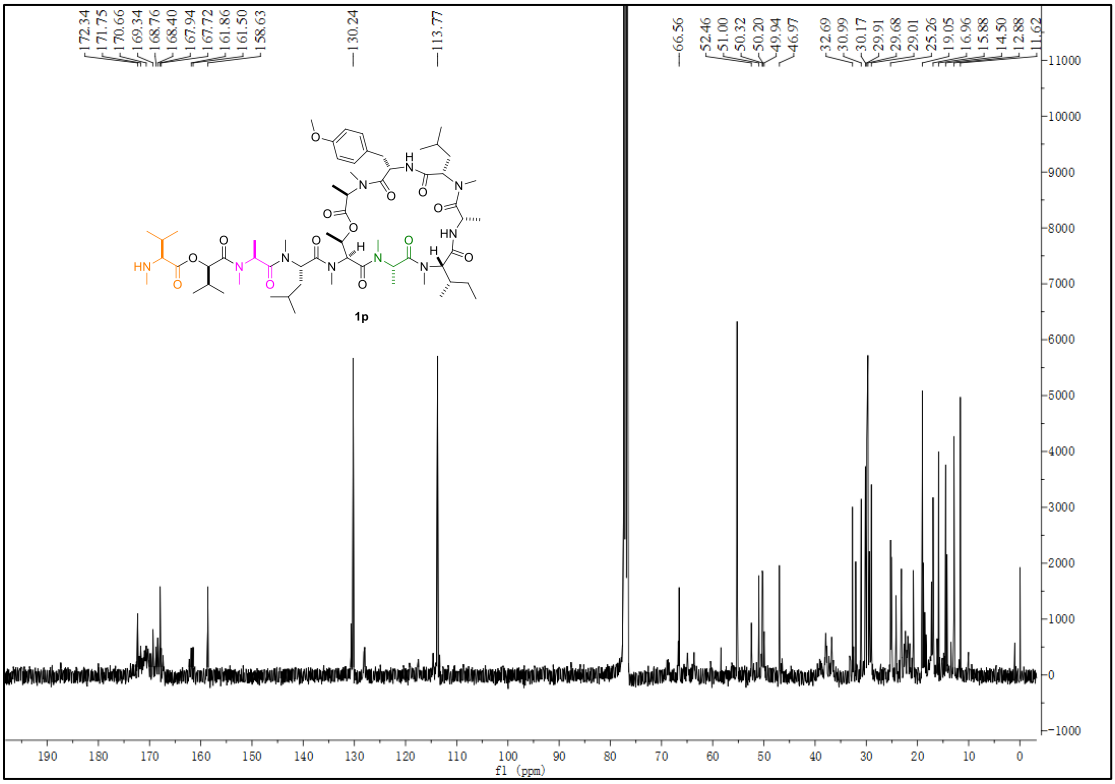


220 nm Result

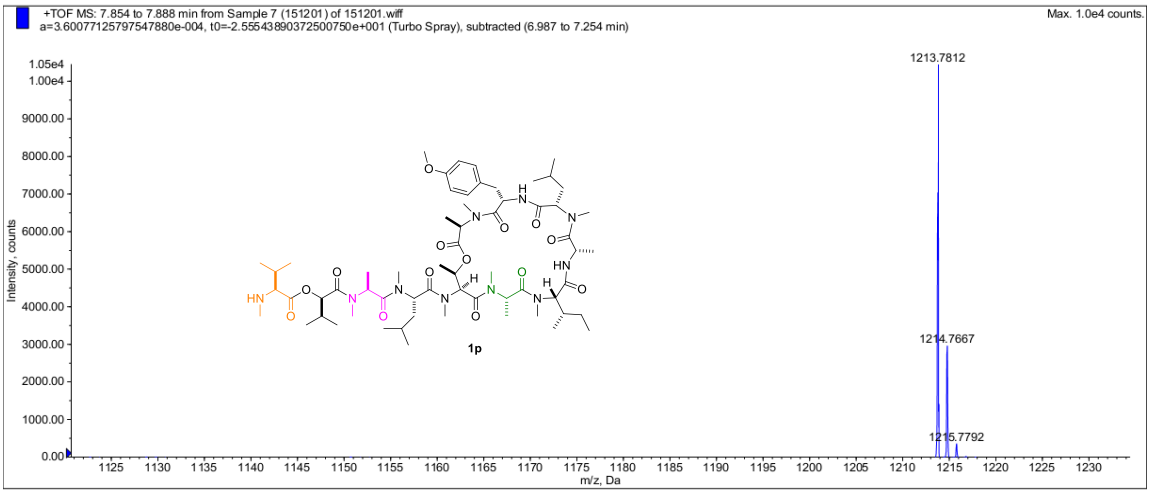
Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	5.232	1.5057	13.6342	0.1734
2	17.996	2.0365	58.2049	0.7404
3	21.755	5.2393	63.6480	0.8096
4	22.130	553.9190	7725.9536	98.2766
Total		562.7005	7861.4407	



^{1}H NMR spectrum of **1p**

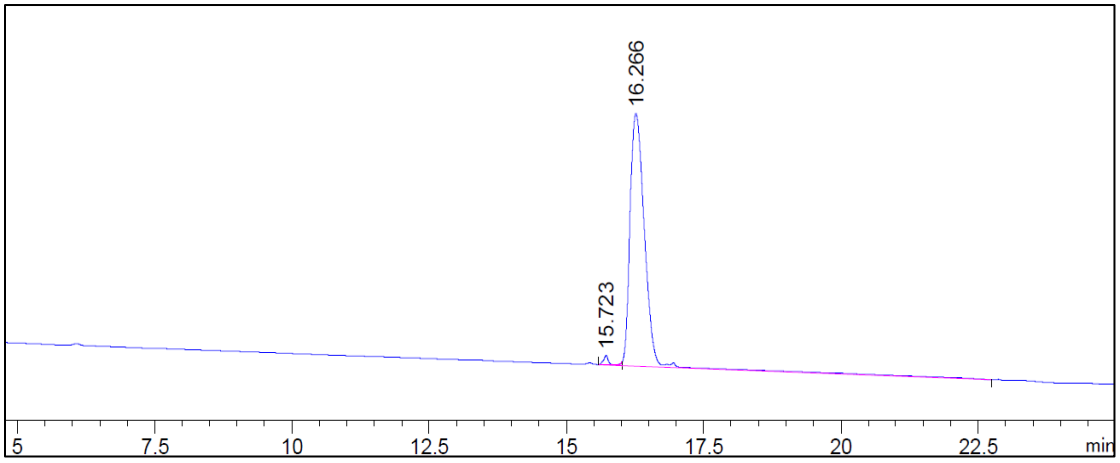


^{13}C NMR spectrum of **1p**



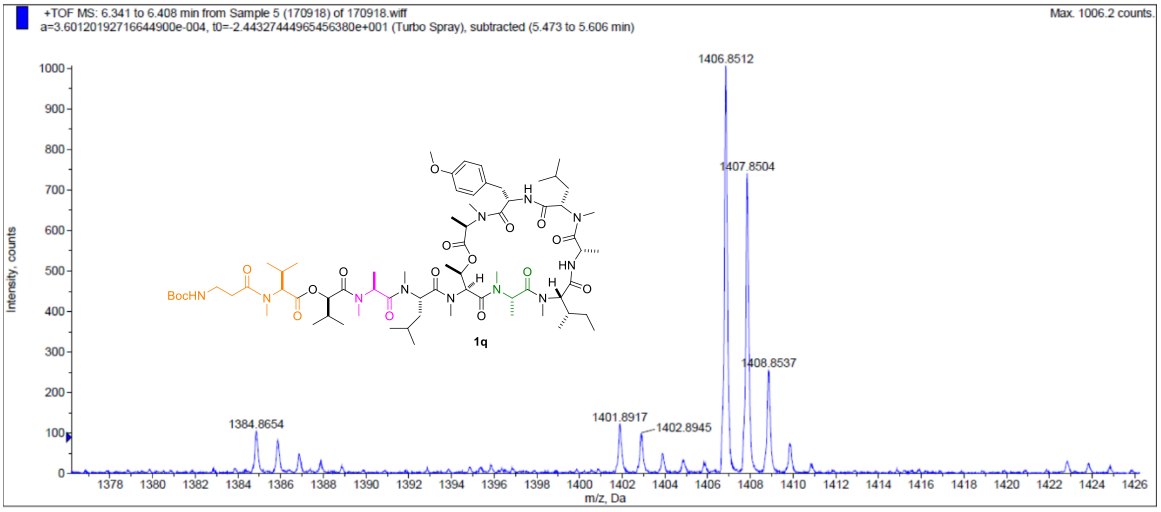
HRMS spectrum of **1p**

HPLC analysis of **1p:**



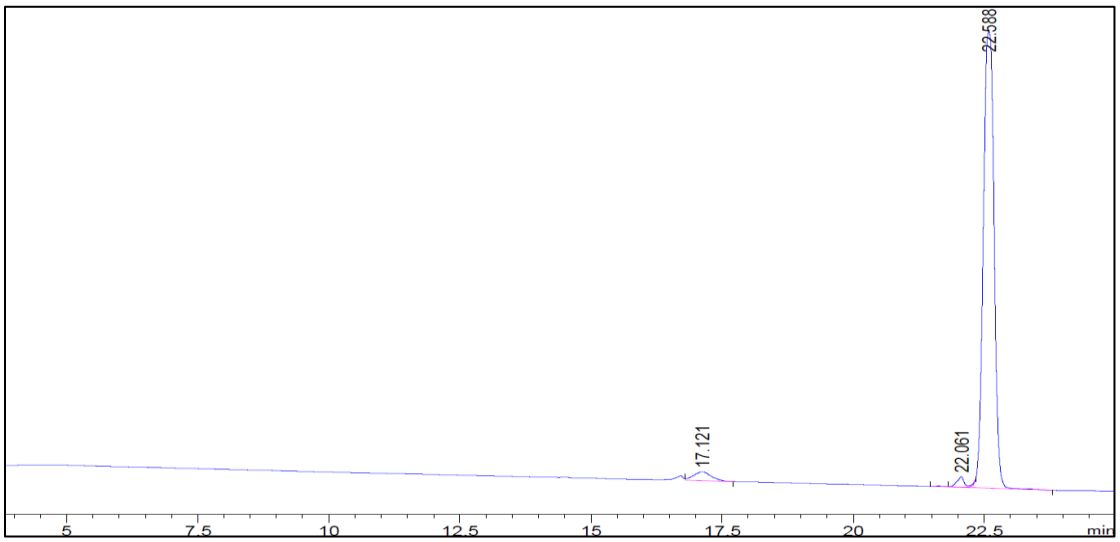
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	15.723	35.0124	218.1017	1.2388
2	16.266	924.8874	1.7388e4	98.7612
Total		959.8998	1.7606e4	



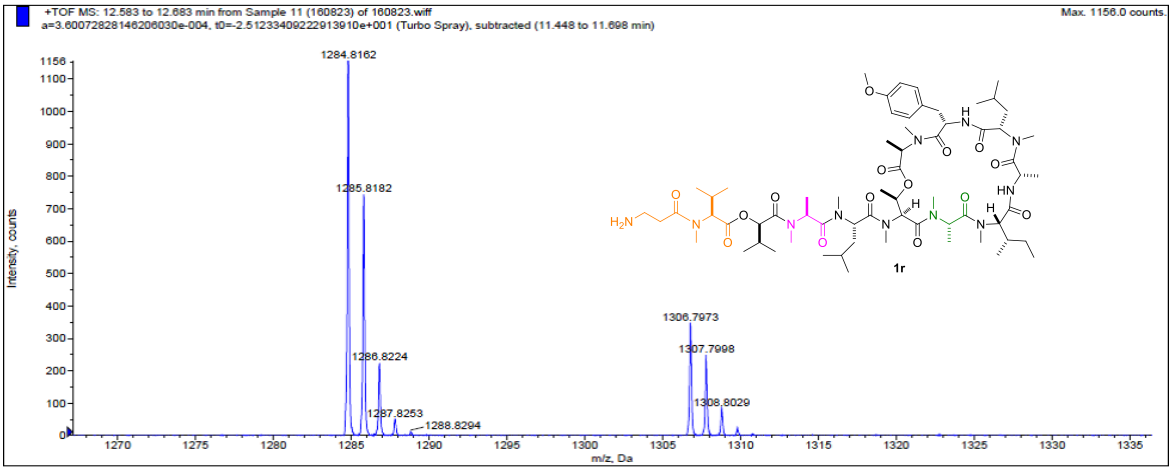
HRMS spectrum of **1q**

HPLC analysis of **1q:**



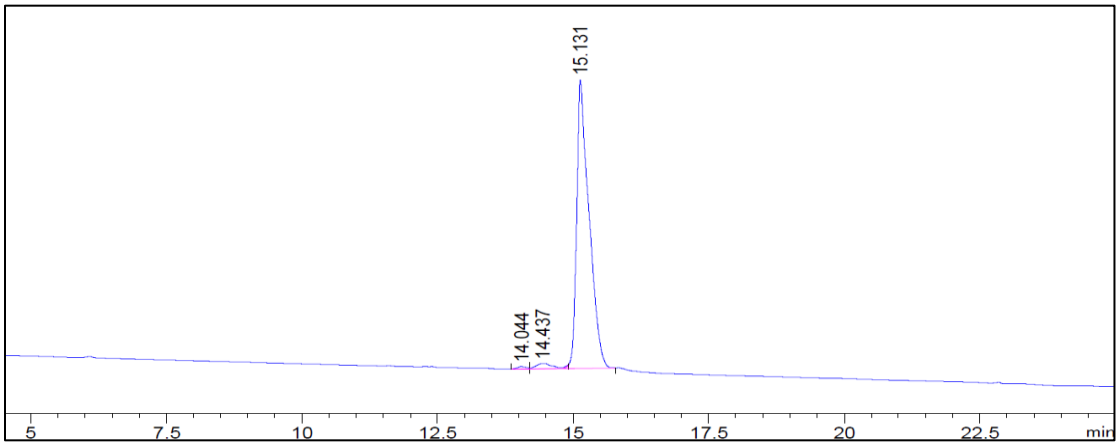
220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	17.121	52.1519	1234.2758	3.1270
2	22.061	60.6584	616.9417	1.5630
3	22.588	2641.8315	3.7620e4	95.3100
Total		2754.6418	3.9472e4	



HRMS spectrum of **1r**

HPLC analysis of **1r:**



220 nm Result

Peak #	Retention Time	Height (mAU)	Area (mAU*s)	Area%
1	14.044	11.7030	133.0496	0.5731
2	14.437	27.2215	558.2685	2.4046
3	15.131	1423.6396	2.2525e4	97.0223
Total		1462.5641	2.3217e4	