Supporting Information

Precursor-Directed Generation of Amidine Containing Ammosamide Analogs: Ammosamides E-P

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	Page
General Procedures	S3
Collection and phylogenetic analysis of strain SNA-020	S3
Cultivation and extraction	S3
Ammosamide E	S4
General procedure for precursor-derived amidine formation	S4
Ammosamide F-L	S5
Ammosamide M-P	S5
The attempts of the chemical conversion of ammosamide B to ammosamide G	S6
The attempts of the chemical conversion of ammosamide A to ammosamide G	S7
Preparation of synthetic ammosamide C	S7
Conversion of ammosamide C to ammosamide G in bacterial-free media	S7
Cytotoxicity assays	S7
QR2 assay	S8
Table S1. ^{1}H and ^{13}C NMR data for ammosamide E(**1**), F(**2**) and B(**4**) in DMSO-d_6	S9
Table S2. ^{1}H NMR data for aromatic amidine ammosamides (**9**-**13**) in DMSO-d_6	S10
Table S3. ^{1}H NMR data for alkyl amidine ammosamides (**14**-**18**) in DMSO-d_6	S11
Table S4. ^{13}C NMR data for amidine ammosamides (**9**-**17**) in DMSO-d_6	S12
References for supporting information	S12
Ammosamide E (**1**)	
^{1}H NMR spectrum (600 MHz, DMSO-d_6)	S13
^{13}C NMR spectrum (100 MHz, DMSO-d_6)	S13
COSY spectrum (600 MHz, DMSO-d_6)	S14
HMBC spectrum (600 MHz, DMSO-d_6)	S14
HRMS (ESI-TOF)	S15
Ammosamide F (**2**)	
^{1}H NMR spectrum (600 MHz, DMSO-d_6)	S15
^{13}C NMR spectrum (100 MHz, DMSO-d_6)	S16
COSY spectrum (600 MHz, DMSO-d_6)	S16
HMQC spectrum (600 MHz, DMSO-d_6)	S17
HMBC spectrum (600 MHz, DMSO-d_6)	S17
1D NOESY NMR spectrum (excited H-6', δ_H = 7.42) (600 MHz, DMSO-d_6)	S18
HRMS (ESI-TOF)	S18
Ammosamide G (**9**)	
^{1}H NMR spectrum (600 MHz, DMSO-d_6)	S19
^{13}C NMR spectrum (100 MHz, DMSO-d_6)	S19
HRMS (ESI-TOF)	S20
Ammosamide H (**10**)	
^{1}H NMR spectrum (600 MHz, DMSO-d_6)	S20
^{13}C NMR spectrum (100 MHz, DMSO-d_6)	S21
HRMS (ESI-TOF)	S21
Ammosamide I (**11**)	
^{1}H NMR spectrum (600 MHz, DMSO-d_6)	S22
^{13}C NMR spectrum (100 MHz, DMSO-d_6)	S22
HRMS (ESI-TOF)	S23

Ammosamide J (**12**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S23
^{13}C NMR spectrum (100 MHz, DMSO-d_6) S24
HRMS (ESI-TOF) S24

Ammosamide K (**13**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S25
^{13}C NMR spectrum (100 MHz, DMSO-d_6) S25
HRMS (ESI-TOF) S26

Ammosamide L (**14**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S26
^{13}C NMR spectrum (100 MHz, DMSO-d_6) S27
1D NOESY NMR spectrum (excited H-3 δ_H = 8.41) (600 MHz, DMSO-d_6) S27
HRMS (ESI-TOF) S28

Ammosamide M (**15**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S28
^{13}C NMR spectrum (100 MHz, DMSO-d_6) S29
HRMS (ESI-TOF) S29

Ammosamide N (**16**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S30
^{13}C NMR spectrum (100 MHz, DMSO-d_6) S30
HRMS (ESI-TOF) S31

Ammosamide O (**17**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S31
^{13}C NMR spectrum (100 MHz, DMSO-d_6) S32
HRMS (ESI-TOF) S32

Ammosamide P (**18**)
^{1}H NMR spectrum (600 MHz, DMSO-d_6) S33
HRMS (ESI-TOF) S33

General Procedures. UV spectra were recorded on a Shimadzu UV-1601 UV–VIS spectrophotometer. IR spectra were obtained on a Perkin Elmer Spectrum 1000 FT-IR Spectrometer. ^{1}H and 2D NMR spectral data were recorded at 600 MHz in DMSO-d_6 solution on Varian System spectrometer, and chemical shifts were referenced to the corresponding residual solvent signal. ^{13}C NMR spectra were acquired at 100 MHz on a Varian System spectrometer. High resolution ESI-TOF mass spectra were provided by The Scripps Research Institute, La Jolla, CA. Low resolution LC/ESI-MS data were measured using an Agilent 1200 series LC/MS system with a reversed-phase C18 column (Phenomenex Luna, 150 mm × 4.6 mm, 5 μm) at a flow rate of 0.7 mL/min. Preparative HPLC was performed on an Agilent 1200 series instrument with a DAD detector, using a Phenyl-Hexyl column (Phenomenex Luna, 250×10.0 mm, 5 μm). ODS (50 μm, Merck) and Sephadex LH-20 (GE Healthcare) were used for column chromatography. Quinone reductase-2 (QR2) was purchased from Abcam.

Collection and phylogenetic analysis of strain SNA-020. The marine-derived bacterium, strain SNA-020, was isolated from a sediment sample collected at a depth of 1 meter near the prop roots of a mangrove tree in Sweetings Cay, Bahamas (N 26º 33'27", W 77º 51'15''). 2 g of sediment was dried over 24 h in an incubator at 35 ºC and the resulting sediment stamped onto an agar plate made with A1 media; starch (10 g/L), peptone (3 g/L), yeast extract (4 g/L), sH_2O and containing rifampicin (10 mg/L) and cycloheximide (50 mg/L). A colony of SNA-020 was selected from the plate after four weeks and re-streaked on a new A1 agar plate. Genomic DNA of strain SNA-020 was isolated using standard methods and was amplified using PCR with the universal 16S rRNA primers FC27 and RC 1492 using the method of Gontang.[1] The partial 16S rRNA sequence 1472 bp was compared to sequences in available databases using the Basic Local Alignment Search Tool and strain SNA-020 determined to be *Streptomyces variabilis*. The 16S rRNA sequence of SNA-020 was deposited in the NCBI databank as GenBank #JQ815387.

Cultivation and extraction. Bacterium SNA-020 was cultured in 20 × 2.8 L Fernbach flasks each containing 1 L of a seawater based medium (10 g starch, 4 g yeast extract, 2 g peptone, 1 g $CaCO_3$, 40 mg $Fe_2(SO_4)_3$•$4H_2O$, 100 mg KBr) and shaken at 200 rpm at 27 ºC. After seven days of cultivation, sterilized XAD-7-HP resin (20 g/L) was added to adsorb organic products, and the culture and resin were shaken at 200 rpm for 2 h. The resin was filtered through cheesecloth, washed with deionized water, and eluted with methanol. The methanol soluble fraction was dried *in vacuo* to yield 8 g of extract.

Ammosamide E. The extract (8 g) was partitioned with *n*-hexanes, CH_2Cl_2, and MeOH/H_2O. The MeOH/H_2O layer (4.5g) was desalted with Diaion HP20 column. The MeOH portion was fractionated by flash column chromatography on ODS (50 μm, 100 g), eluting with a step gradient of methanol and water with 0.1 % trifluoroacetic acid (10:90–100:0), and six fractions (Fr.1–Fr.6) were collected. Fraction 2 (363 mg) was fractionated by Sephadex LH-20 to afford 10 subfractions (Fr.2-I to Fr. 2-X). Fraction 2-VI (10 mg) was purified by reversed phase HPLC (Phenomenex Luna, Phenyl-Hexyl, 250 × 10.0 mm, 2.0 mL/min, 5 μm) using a gradient solvent system 10%-40% (0.01-20.0 min) CH_3CN/H_2O solution (0.1% trifluoroacetic acid) to afford ammosamide E (**1**, 0.5 mg, t_R = 14.0 min) as a dark red solid: UV (MeOH) λ_{max} nm (log ε) 262 (3.8), 346 (3.6), 423 (3.2), 552 (3.2); IR ν_{max} 3295, 2934, 1670, 1604, 1490, 1354, 1201, 1134 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) see Table 1 and Table S1. ESI-MS m/z 291.0 $[M+H]^+$, 289.0 $[M-H]^-$. HRESIMS m/z 291.0720 $[M+H]^+$ ($C_{12}H_{12}ClN_6O$, calcd 291.0761).

General procedure for precursor-derived amidine formation. 2 g alky/aryl amine was added into bacterium SNA-020 containing seawater culture media (same as mentioned above) in one 2.8 L Fernbach flask and shaken at 200 rpm at 27 °C. Following the above extraction procedure, 2 g obtained extract was partitioned with hexanes and MeOH/H_2O. The MeOH/H_2O layer was desalted with Diaion HP20 column and fractionated with Sephadex LH20. The ammosamide analog containing subfraction was purified by reversed phase HPLC (Phenomenex Luna, Phenyl-Hexyl, 250 × 10.0 mm, 2.0 mL/min, 5 μm) using a gradient solvent system 10%-50% (0.01-27.0min) CH_3CN/H_2O solution (0.1% trifluoroacetic acid) to afford ammosamide F (**2**, 0.3 mg, t_R = 18.0 min), ammosamide G (**9**, 0.4 mg, t_R = 18.9 min), ammosamide H (**10**, 0.6 mg, t_R = 23.0 min), ammosamide I (**11**, 0.4 mg, t_R = 18.1 min), ammosamide J (**12**, 0.5 mg, t_R = 15.9 min), ammosamide K (**13**, 0.4 mg, t_R = 17.0 min), ammosamide L (**14**, 0.3 mg, t_R = 20.6 min), ammosamide M (**15**, 0.4 mg, t_R = 18.5 min), ammosamide N (**16**, 0.4 mg, t_R = 17.3 min), ammosamide O (**17**, 0.5 mg, t_R = 15.0 min), ammosamide P (**18**, 0.4 mg, t_R = 17.9 min), correspondingly.

Ammosamide F. Dark green solid; UV (MeOH) λ_{max} nm (log ε) 206 (2.9), 294 (3.8), 338 (3.5), 424 (3.1), 603 (3.4); IR ν_{max} 3368, 2926, 1676, 1596, 1377, 1204, 1043 cm^{-1}. ^1H NMR (600 MHz, DMSO-d_6) and ^{13}C NMR (100 MHz, DMSO-d_6) see Table 1 and Table S1. ESI-MS m/z 411.1 $[M+H]^+$, 409.0 $[M-H]^-$. HRESIMS m/z 411.0972 $[M+H]^+$ ($C_{19}H_{16}ClN_6O_3$, calcd 411.0972).

Ammosamide G. Blue solid; UV (MeOH) λ_{max} nm (log ε) 208 (3.9), 338 (3.3), 574 (3.0); IR ν_{max} 3334, 2918, 1640 (b), 1604 (b), 1481, 1350, 1089 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S2. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 401.1 $[M+H]^+$, 399.0 $[M-H]^-$. HRESIMS m/z 401.0681 $[M+H]^+$ ($C_{18}H_{15}Cl_2N_6O$, calcd 401.0684).

Ammosamide H. Blue solid; UV (MeOH) λ_{max} nm (log ε) 202 (4.1), 331 (3.3), 571 (2.8); IR ν_{max} 3362, 2926, 1601 (vb), 1475, 1351, 1298, 1145 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S2. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 469.0 $[M+H]^+$, 467.0 $[M-H]^-$. HRESIMS m/z 469.0568 $[M+H]^+$ ($C_{19}H_{14}Cl_2F_3N_6O$, calcd 469.0558).

Ammosamide I. Blue solid; UV (MeOH) λ_{max} nm (log ε) 202 (3.7), 336 (3.1), 568 (2.6); IR ν_{max} 3336, 2922, 1674, 1643, 1615, 1479, 1349, 1227, 1024 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S2. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 381.1 $[M+H]^+$, 379.1 $[M-H]^-$. HRESIMS m/z 381.1223 $[M+H]^+$ ($C_{19}H_{18}ClN_6O$, calcd 381.1231).

Ammosamide J. Blue solid; UV (MeOH) λ_{max} nm (log ε) 209 (3.8), 313 (3.2), 595 (2.8); IR ν_{max} 3397, 2921, 1684, 1608, 1437, 1352, 1207, 1136, 1028 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S2. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 374.1 $[M+H]^+$, 372.0 $[M-H]^-$. HRESIMS m/z 374.0586 $[M+H]^+$ ($C_{15}H_{13}ClN_7OS$, calcd 374.0591).

Ammosamide K. Blue solid; UV (MeOH) λ_{max} nm (log ε) 218 (3.7), 310 (3.2), 598 (2.8); IR ν_{max} 3348, 2920, 1644 (b), 1599 (vb), 1483, 1350, 1292, 1120 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S2. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 407.1 $[M+H]^+$, 405.0 $[M-H]^-$. HRESIMS m/z 407.1125 $[M+H]^+$ ($C_{19}H_{16}ClN_8O$, calcd 407.1136).

Ammosamide L. Blue solid; UV (MeOH) λ_{max} nm (log ε) 212 (3.8), 267 (3.5), 346 (3.2), 427 (2.8), 571 (2.9); IR ν_{max} 3323, 2921, 1603 (vb), 1451, 1352, 1119 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S3. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 375.2 $[M+H]^+$, 373.1 $[M-H]^-$. HRESIMS m/z 375.1695 $[M+H]^+$ ($C_{18}H_{24}ClN_6O$, calcd 375.1700).

Ammosamide M. Blue solid; UV (MeOH) λ_{max} nm (log ε) 207 (3.8), 267 (3.4), 350 (3.0), 429 (2.6), 576 (2.7); IR ν_{max} 3311, 2976, 1683, 1624 (vb), 1496, 1364, 1247, 1120, 1026 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S3. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 333.1 $[M+H]^+$, 331.1 $[M-H]^-$. HRESIMS m/z 333.1229 $[M+H]^+$ ($C_{15}H_{18}ClN_6O$, calcd 333.1231).

Ammosamide N. Blue solid; UV (MeOH) λ_{max} nm (log ε) 213 (3.6), 269 (3.4), 350 (3.0), 429 (2.7), 576 (2.7); IR ν_{max} 3308, 2949, 1607 (vb), 1490, 1355, 1248, 1025 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S3. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 359.1 $[M+H]^+$, 357.1 $[M-H]^-$. HRESIMS m/z 359.1385 $[M+H]^+$ ($C_{17}H_{20}ClN_6O$, calcd 359.1387).

Ammosamide O. Blue solid; UV (MeOH) λ_{max} nm (log ε) 213 (3.7), 269 (3.4), 350 (3.1), 429 (2.7), 576 (2.8); IR ν_{max} 3336, 2925, 1604 (vb), 1450, 1378, 1068 cm^{-1}. ^{1}H NMR (600 MHz, DMSO-d_6) see Table S3. ^{13}C NMR (100 MHz, DMSO-d_6) see Table S4. ESI-MS m/z 373.2 $[M+H]^+$, 371.1 $[M-H]^-$. HRESIMS m/z 373.1532 $[M+H]^+$ ($C_{18}H_{22}ClN_6O$, calcd 373.1544).

Ammosamide P. Blue solid; UV (MeOH) λ_{max} nm (log ε) 213 (4.2), 344 (3.6), 571 (2.9); ^{1}H NMR (600 MHz, DMSO-d_6) see Table S3. ESI-MS m/z 456.1 $[M+H]^+$, 454.1 $[M-H]^-$. HRESIMS m/z 456.1298 $[M+H]^+$ ($C_{19}H_{19}ClN_9O_3$, calcd 456.1299).

Attempts of chemical conversion of ammosamide B (4) to ammosamide G (9).

To a solution of **4** (1.0 mg, 0.0034 mmol) in methanol (0.1 mL) was added DIPEA (1.2 uL, 0.0068mmol) and 2-chloro-*N*-methylpyridinium iodide (1.0 mg, 0.0041 mmol). After stirring for five minutes at 25 ºC, 4-chloroaniline (0.65 mg, 0.0051 mmol) was added and the reaction was stirred for 24 hours. LC-MS analysis of the reaction showed no conversion of **4** to **9**.

To a solution of **4** (0.5 mg, 0.0017 mmol) in neat $POCl_3$ (0.5 mL) was added 4-chloroaniline (0.3 mg, 0.0026 mmol) and stirred at 25 ºC for 1 hour. The reaction mixture (0.1mL) was analyzed by LC-MS and several ammosamide analogs were detected by LC-MS including: **9** (9% yield); **19** (23% yield); and **20** (39% yield).

Attempts of chemical conversion of ammosamide A (3) to ammosamide G (9).

To a solution of **3** (1.0 mg, 0.0032 mmol) in methanol (0.1 mL) was added DIPEA (1.1 uL, 0.0064mmol) and 2-chloro-N-methylpyridinium iodide (1.0 mg, 0.0041 mmol). After stirring for five minutes at 25 ºC, 4-chloroaniline (0.61 mg, 0.0048 mmol) was added and the reaction was stirred for 24 hours. LC-MS analysis showed trace production of **9** (<1%).

To a solution of **3** (0.5 mg, 0.0016 mmol) in methanol (0.2 mL) was added silver tetrafluoroborate (1.6 mg, 0.0082 mmol), 4-chloroaniline (6.1 mg, 0.048 mmol) and $NaHCO_3$ (4.4 mg, 0.016 mmol). The reaction mixture was stirred at 25 ºC for 2 h and concentrated. LC-MS analysis showed no conversion of **3** to **9**.

Preparation of synthetic ammosamide C (5).

Synthetic ammosamide C was obtained according to the procedure of Hughes *et al*.[2] Briefly, to a solution of **3** (4.5 mg, 0.015 mmol) in anhydrous dioxane (2.0 mL) was added MeI (0.10 mL) via syringe. The mixture was heated at 80 °C overnight, allowed to cool, and concentrated to give the crude sulfonium salt. To a solution of the crude sulfonium salt in anhydrous MeOH (2.0 mL) was added $NaBH_4$ (20 mg). The mixture was stirred at room temperature for 2 h, diluted with a saturated $NaHCO_3$ solution (4 mL), and extracted with EtOAc (2 x 3 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated. The product was purified by reversed-phase chromatography using a gradient solvent system 10%-40% (0.01-20.0 min) CH_3CN/H_2O solution (0.1% trifluoroacetic acid) to give 1.0 mg (20%) ammosamide C (t_R = 11.4 min).

Conversion of ammosamide C (5) to ammosamide G (9) in bacterial-free media. To a sample of **5** (3.0 mg) in a 6-dram vial was added A1 media (5 mL) followed by addition 4-chloroaniline (30 mg). The vial was shaken for 12 h (200 rpm, 27 ºC) on a platform shaker. Analysis by LC-MS showed a 20% conversion of **5** to **9**

Cytotoxicity assays. Cell lines were cultured in 10 cm dishes (Corning, Inc.) in NSCLC cell-culture medium: RPMI/L-glutamine medium (Invitrogen, Inc.), 1000 U/mL penicillin (Invitrogen, Inc.), 1 mg/mL streptomycin (Invitrogen, Inc.), and 5% fetal bovine serum (Atlanta Biologicals, Inc.). Cell lines were grown in a humidified environment in the presence of 5% CO_2 at 37 ºC. For cell viability assays, HCC44, HCC4017, Calu-3 and HBEC30KT cells (60 μL) were plated individually at a density of 750 and 500 cells/well, respectively, in 384 well microtiter assay plates (Bio-one; Greiner, Inc.). After incubating the assay plates overnight under the growth conditions described above, purified compounds were dissolved and diluted in DMSO and subsequently added to each plate with final compound concentrations ranging from 40 μM to 1 nM and a final DMSO concentration of 0.5%. After an incubation of 96 h under growth conditions, Cell Titer GloTM reagent (Promega, Inc.) was added to each well and mixed. Plates were incubated for 10 min at room temperature and luminescence was determined for each well using an Envision multi-modal plate reader (Perkin Elmer, Inc.). Relative luminescence units were normalized to the untreated control wells (cells plus DMSO only).

QR2 assay. Steady-state kinetic assays and QR2 IC_{50} determination was accomplished using literature procedures.[3] The enzymatic activity of QR2 was determined using MTT [3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide] and N-methyl dihydronicotinamide as substrates as previously described. Briefly, assays were run in a 96-well plate with a final assay volume of 200 μL, and the appearance of the reduced form of the MTT substrate, formazan, was monitored at 612 nm. The assay was performed at 23 °C using a Spectramax 340PC multimode microplate reader with Softmax Pro software. Each assay mixture contained 10 ng QR2, 25 μM N-methyl dihydronicotinamide, and 200 μM MTT reaction buffer containing 100 mM NaCl, 50 mM Tris, pH 7.5, and 0.1% TritonX-100. All reactions were initiated by the addition of QR2. Initial slopes of the reactions (ΔOD@612 nm/min) were measured and were used to calculate the initial rates of the reaction using a value of 11,300 $M^{-1} cm^{-1}$ for the molar extinction coefficient of MTT. IC_{50} values were determined using method assay as described above with the addition of inhibitor at varying concentrations 1nM to 10 μM (all data points acquired in triplicate). The average and standard deviations in the rate values were used to determine the IC_{50} value by calculating the % inhibition at each inhibitor concentration versus the negative control with zero inhibitor. These data were plotted as the percent inhibition versus inhibitor concentration. All data were fit to the equation: $\% I = (\% I_{max}[1 + [I]/IC_{50})]$ using Excel.

Table S1. ^{1}H and ^{13}C NMR data for ammosamide E (**1**), F (**2**) and B (**4**) in DMSO-d_6

	1			**2**			**4**[a]	
	^{1}H	^{13}C	HMBC	^{1}H	^{13}C	HMBC	^{1}H	^{13}C
1a	3.84 s	32.9	C2, C2a, C8a	3.81 s	32.0	C2, C2a, C8a	3.59 s	28.5
2	-	154.1		-	152.7		-	164.0
2a	-	125.2		-	127.4		-	
3	8.95 s	118.3	C2, C5b, C4, C4a	7.93 s	117.0	C2, C5b, C4, C4a	8.34 s	115.3
4	-	144.2		-	143.9		-	144.7
4a	-	165.8		-	165.8		-	166.2
5a	-	131.8		-	131.8		-	
5b	-	118.9		-	119.7		-	119.0
6	-	138.1		-	134.7		-	
7	-	102.7		-	103.9		-	104.5
8	-	143.6		-	141.5		-	
8a	-	106.3		-	108.5		-	106.3
$CONH_2$-a	7.68 s	-	C4	7.58 s	-	C4	7.66 (br s)	-
$CONH_2$-b	8.90 s	-	C4a	8.82 s	-	C4a	8.91 (br s)	-
NH_2(C-6)	7.23 br s	-		6.77 br s	-		6.73 (br s)	-
NH_2(C-8)	7.00 s	-	C6, C7, C8, C8a	6.37 br s	-		6.18 (br s)	-
=NH	9.46 br s	-		-	-		-	-
1'	-	-		-	147.1		-	-
2'	-	-		-	122.5		-	-
3'	-	-		7.99 (d, 7.7)	131.6	C1', C5', C7'	-	-
4'	-	-		7.21 (t,7.7)	124.0	C2', C3', C5', C6'	-	-
5'	-	-		7.53 (t, 7.7)	133.5	C1', C3'	-	-
6'	-	-		7.42 (d, 7.7)	122.5	C2', C4'	-	-
7'	-	-		-	167.5		-	-

a. C-2a, C-5a, C-6, and C-8 (δ_C = 130.6, 130.8, 132.4, 140.5 ppm) could not be unambiguously assigned.[4]

Table S2. ^{1}H NMR data for aromatic amidine ammosamides (**9**-**13**) in DMSO-d_6

No.	**9**	**10**	**11**	**12**	**13**
1a	3.69 s	3.71 s	3.73 s	3.81 s	3.87 s
2	-	-	-	-	-
2a	-	-	-	-	-
3	7.51 s	7.58 s	7.25 s	9.09 s	9.62 s
4	-	-	-	-	-
4a	-	-	-	-	-
5a	-	-	-	-	-
5b	-	-	-	-	-
6	-	-	-	-	-
7	-	-	-	-	-
8	-	-	-	-	-
8a	-	-	-	-	-
CONH$_2$-a	8.78 (br s)	8.79 (br s)	8.74 (br s)	8.88 (br s)	8.87 (br s)
CONH$_2$-b	7.51 (br s)	7.52 (br s)	7.47 (br s)	7.59 (br s)	7.54 (br s)
NH$_2$(6)	6.45 (br s)	6.53 (br s)	6.38 (br s)	6.82 (br s)	6.73 (br s)
NH$_2$(8)	5.91 (br s)	6.03 (br s)	5.84 (br s)	6.38 (br s)	6.25 (br s)
1'	-	-	-	-	-
2'	7.40 (d,8.5)	7.43 s	-	-	-
3'	7.01 (d,8.5)	-	7.29 (d, 7.4)	7.50 (d,3.8)	-
4'	-	-	7.05 (t, 7.4)	7.24 (d,3.8)	7.42 (d,6.7)
5'	7.01 (d,8.5)	7.67 (d,8.5)	7.19 (t, 7.4)	-	7.06 (t, 6.9)
6'	7.40 (d,8.5)	7.36 (d,8.5)	6.86 (d, 7.4)	-	7.06 (t, 6.9)
7'	-	-	2.05 s	-	7.27 (d,6.7)
8'	-	-	-	-	-
9’	-	-	-	-	-
NH	-	-	-	-	11.70 s

Table S3. ^{1}H NMR data for alkyl amidine ammosamides (**14**-**18**) in DMSO-d_6

No.	**14**	**15**	**16**	**17**	**18**
1a	3.56 s	3.53 s	3.53 s	3.53 s	3.58 s
2	-	-	-	-	-
2a	-	-	-	-	-
3	8.41 s	8.41 s	8.44 s	8.36 s	8.55 s
4	-	-	-	-	-
4a	-	-	-	-	-
5a	-	-	-	-	-
5b	-	-	-	-	-
6	-	-	-	-	-
7	-	-	-	-	-
8	-	-	-	-	-
8a	-	-	-	-	-
$CONH_2$-a	8.88 (br s)	8.88 (br s)	8.88 (br s)	8.88 (br s)	8.88 (br s)
$CONH_2$-b	7.62 (br s)	7.64 (br s)	7.64 (br s)	7.64 (br s)	7.64 (br s)
NH_2(6)	6.31 (br s)	6.26 (br s)	6.29 (br s)	6.28 (br s)	6.32 (br s)
NH_2(8)	5.68 (br s)	5.61 (br s)	5.64 (br s)	5.62 (br s)	5.69 (br s)
=NH	-	-	-	-	-
1'	3.74 (t, 6.9)	4.43m	4.57 (septet, 6.0)	3.99 m	3.98 (t, 6.9)
2'	1.74 m	1.27 (d, 6.1)	2.03m, 1.81m	1.86m, 1.45m	3.77 m
3'	1.34 m	1.27 (d, 6.1)	1.68m, 1.58m	1.83m, 1.45m	-
4'	1.34 m	-	1.68m, 1.58m	1.69m, 1.30m	-
5'	1.50 m	-	2.03m, 1.81m	1.83m, 1.45m	-
6'	0.89 (t, 6.9)	-	-	1.86m, 1.45m	9.09 s
7'	-	-	-	-	-
8'	-	-	-	-	6.62 (d, 6.4)
9’	-	-	-	-	8.09 (d, 6.4)
NH	-	-	-	-	8.40 s

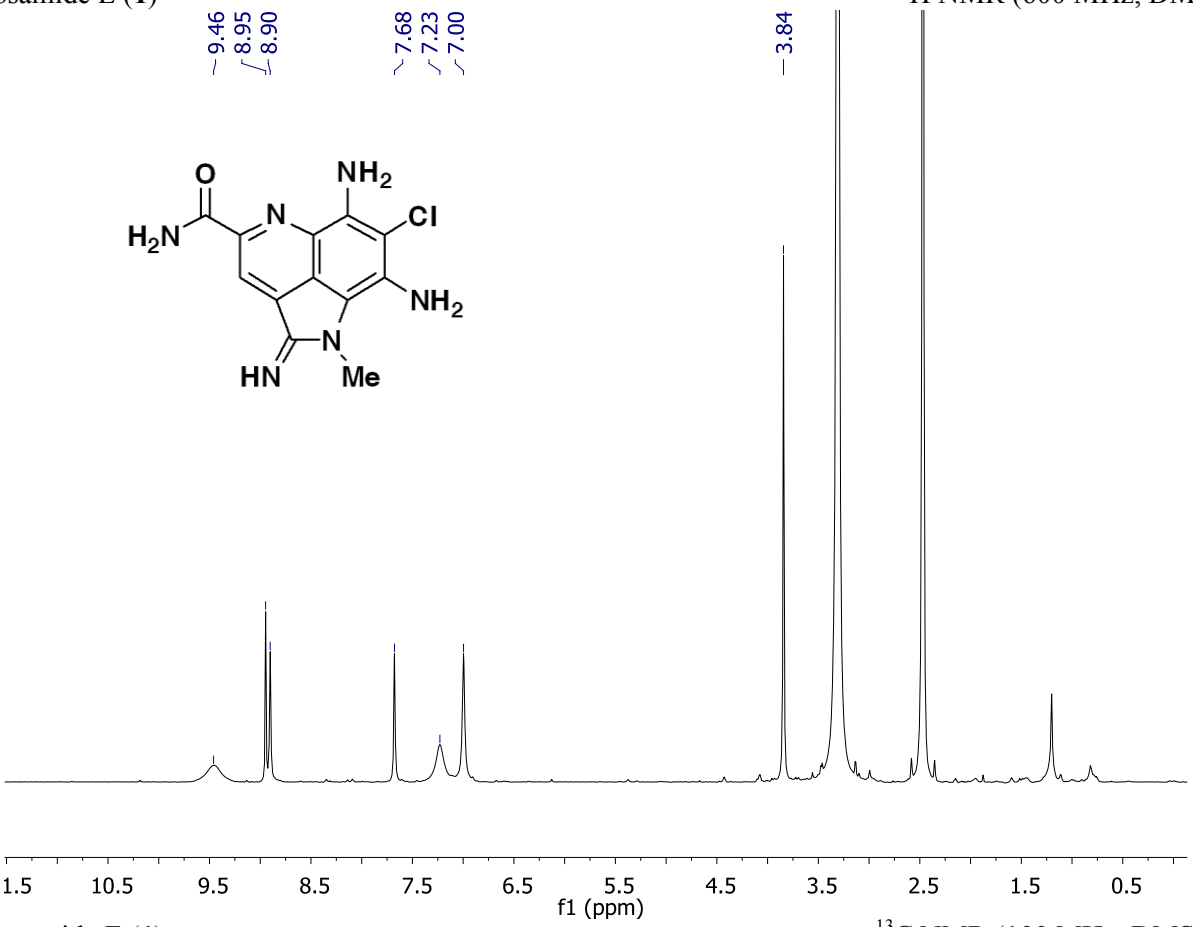
Table S4. ^{13}C NMR data for amidine ammosamides (**9**-**17**) in DMSO-d_6

No.	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**16**	**17**
1a	30.5	30.7	30.5	31.0	31.0	30.4	30.8	30.6	30.3
2	153.1	153.5	152.8	153.1	154.7	153.9	152.6	153.2	152.9
2a	129.7	129.3	129.8	128.9	129.6	128.8	129.5	129.1	128.2
3	115.9	115.9	115.7	114.9	120.8	116.5	116.6	116.4	116.0
4	144.5	144.4	144.9	144.3	144.6	145.2	145.1	145.2	145.4
4a	165.9	165.9	166.0	166.2	166.3	166.4	166.3	166.4	166.4
5a	130.8	131.0	130.6	133.1	131.0	130.4	130.6	130.5	130.5
5b	120.3	120.2	120.3	119.7	119.9	120.1	120.2	120.3	120.4
6	130.3	129.3	130.4	131.1	131.0	130.3	129.6	130.1	130.5
7	105.7	105.5	106.0	104.2	104.2	106.4	106.1	106.4	106.7
8	138.6	139.1	138.2	139.8	140.2	137.3	137.8	137.5	137.0
8a	110.6	110.2	111.2	108.5	108.8	112.4	112.0	112.3	112.8
1'	149.8	150.7	149.4	171.5	155.2	49.7	48.8	59.3	57.3
2'	122.9	120.8	128.3	-	-	31.5	24.3	34.6	34.3
3’	129.5	127.7, 128.0	130.8	119.5	132.5	26.8	24.3	24.0	24.7
4’	126.3	123.2	122.9	140.5	120.8	31.3	-	24.0	25.5
5’	129.5	132.8	127.2	-	120.3	22.2	-	34.6	24.7
6’	122.9	126.8	120.2	-	120.3	14.0	-	-	34.3
7’	-	124.3, 121.6	17.7	-	120.8	-	-	-	-
8’	-	-	-	-	132.5	-	-	-	-

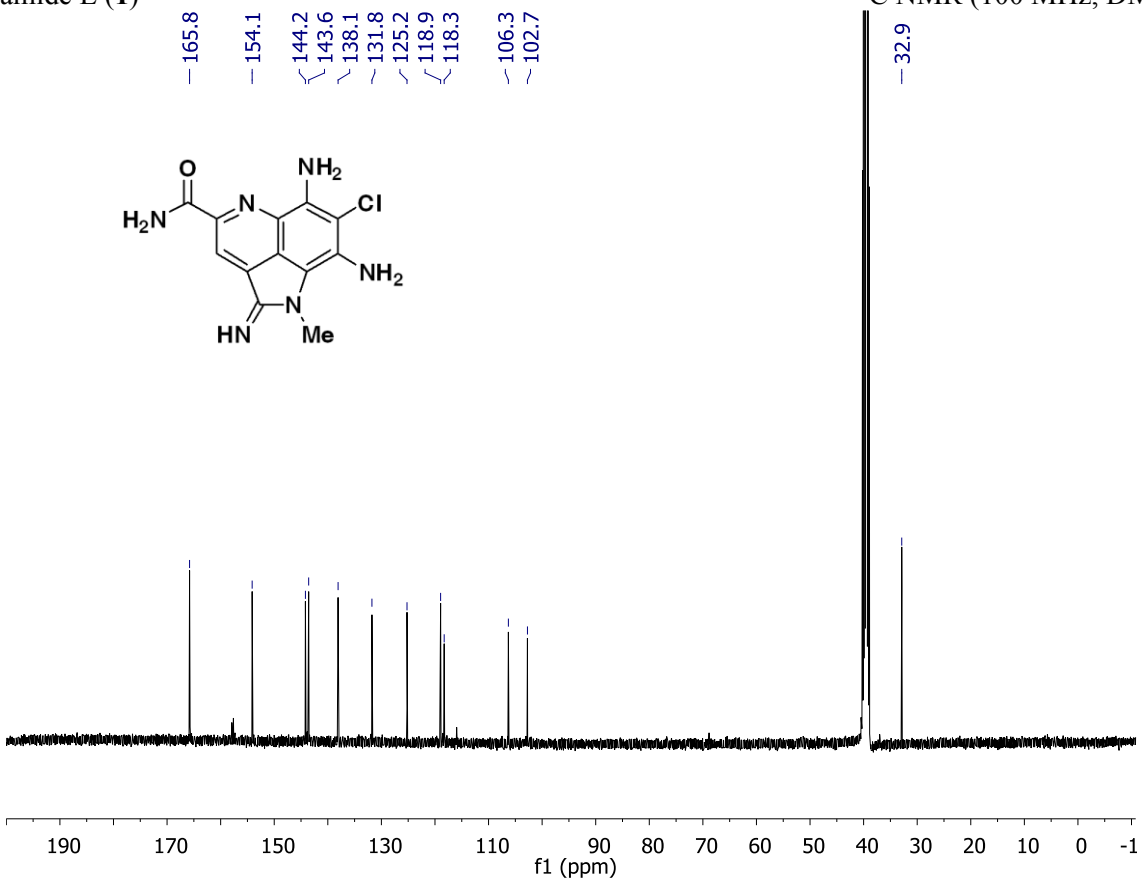
References for supporting information

1. E. A. Gontang, W. Fenical, P. R. Jensen, *Appl. Environ. Microbiol.* **2007**, 73, 3272-3282.
2. C. C. Hughes, W. Fenical, *J. Am. Chem. Soc.* **2010**, 132, 2528-2529.
3. P. V. N. Reddy, K. C. Jensen, A. D. Mesecar, P. E. Fanwick, M. Cushman, *J. Med. Chem.* **2012**, 55, 367-377.
4. C. C. Hughes, J. B. MacMillan, S. P. Gaudencio, P. R. Jensen, W. Fenical, *Angew. Chem. Int. Ed.* **2009**, 48, 725-727.

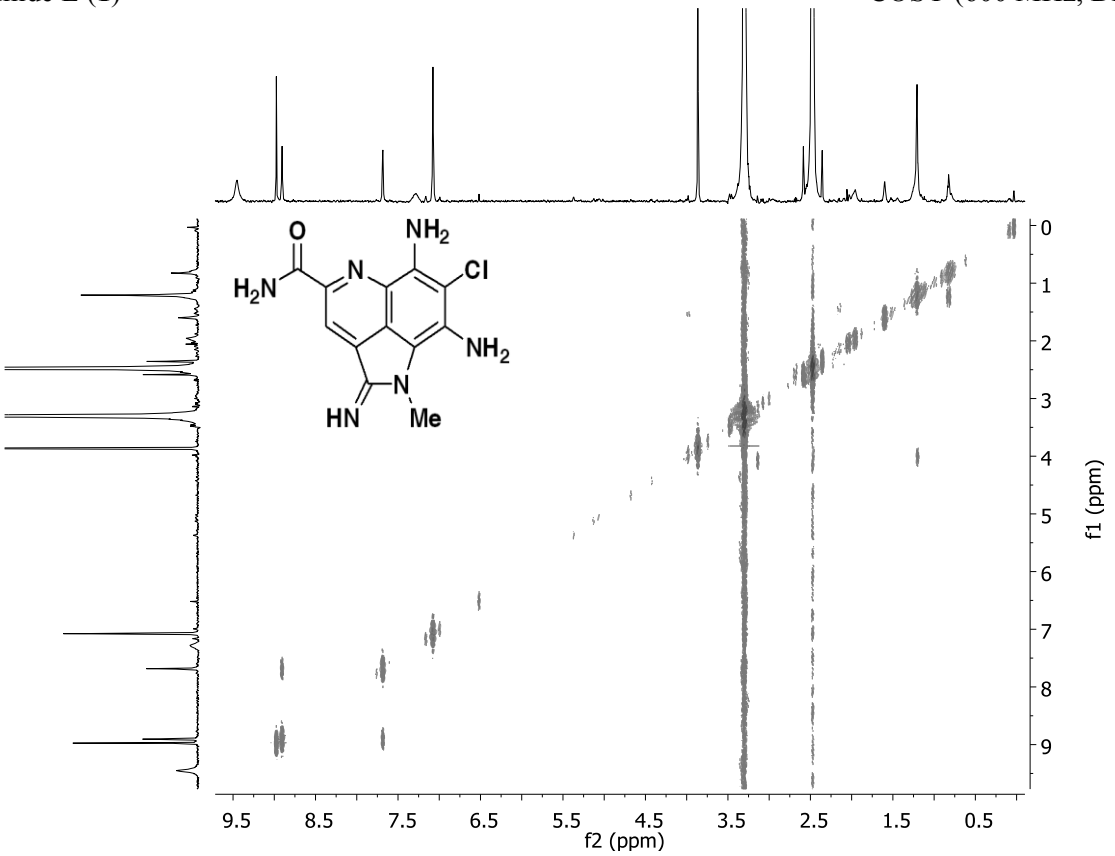
Ammosamide E (**1**) ^{1}H NMR (600 MHz, DMSO-*d*$_6$)



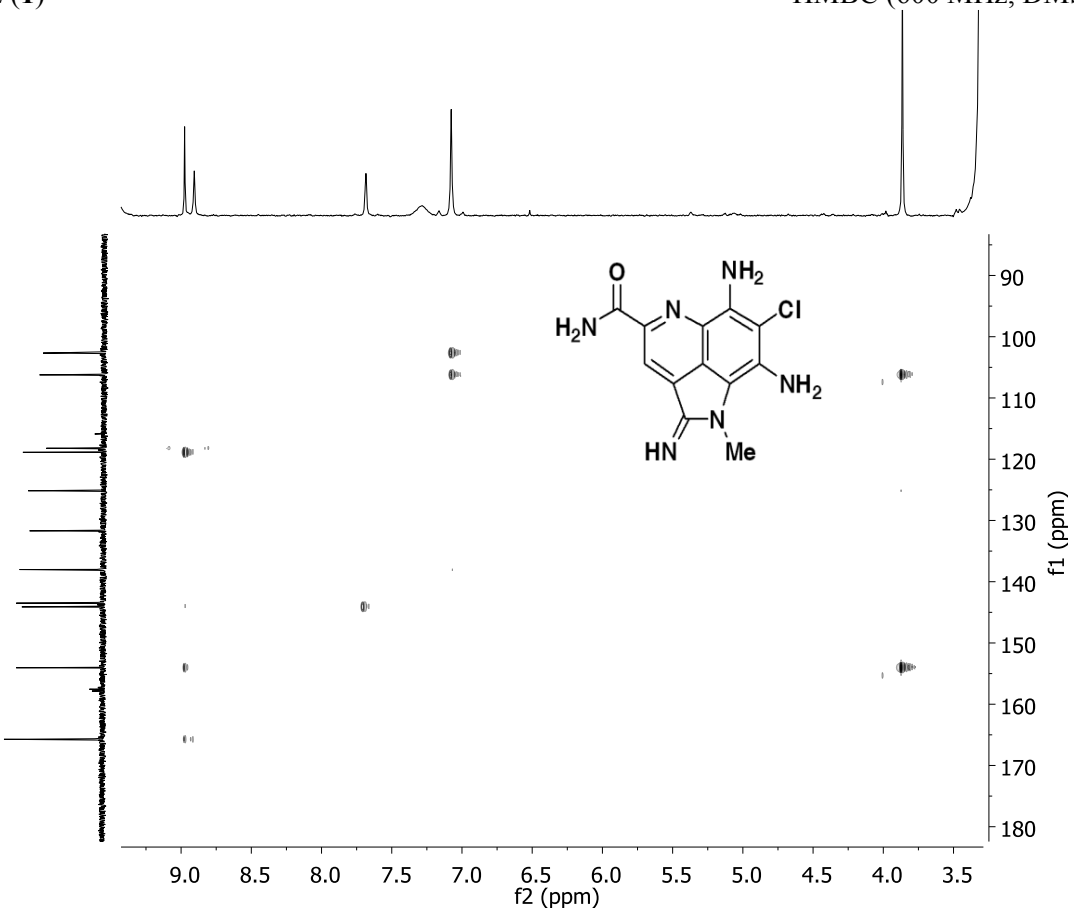
Ammosamide E (**1**) ^{13}C NMR (100 MHz, DMSO-*d*$_6$)



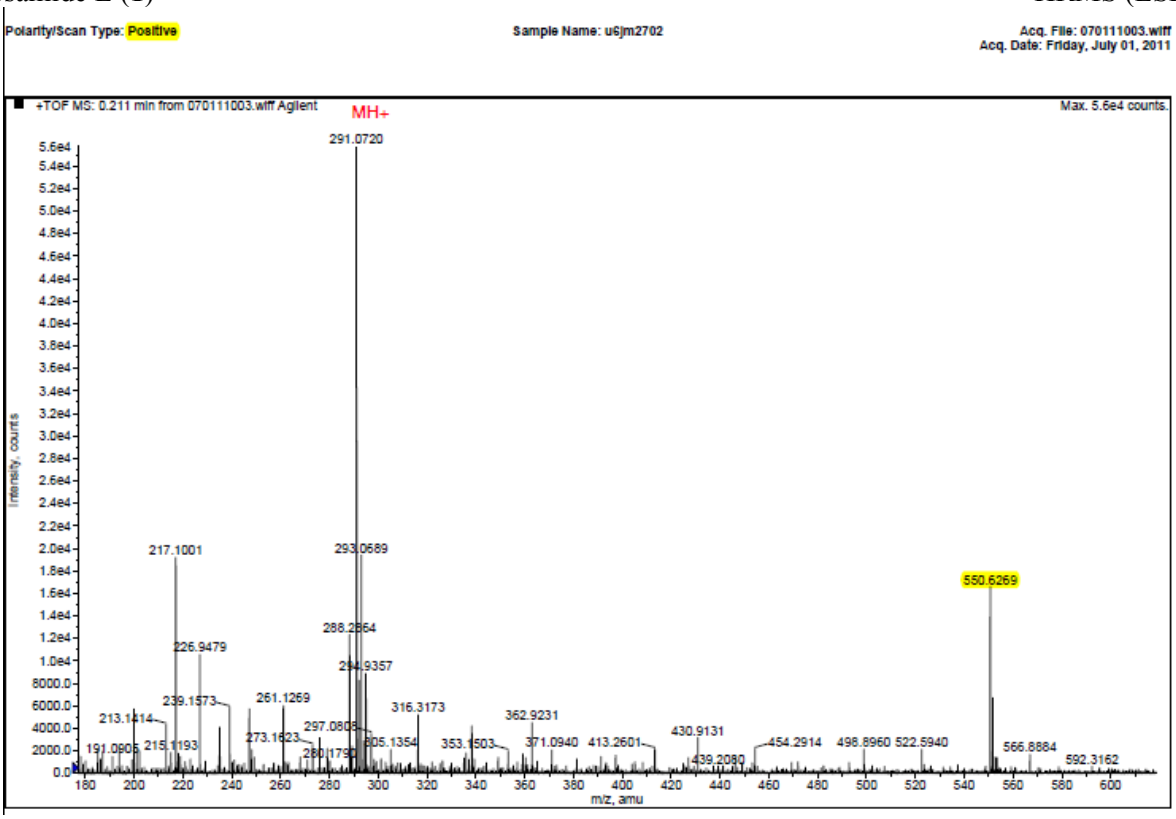
Ammosamide E (**1**) COSY (600 MHz, DMSO-d_6)



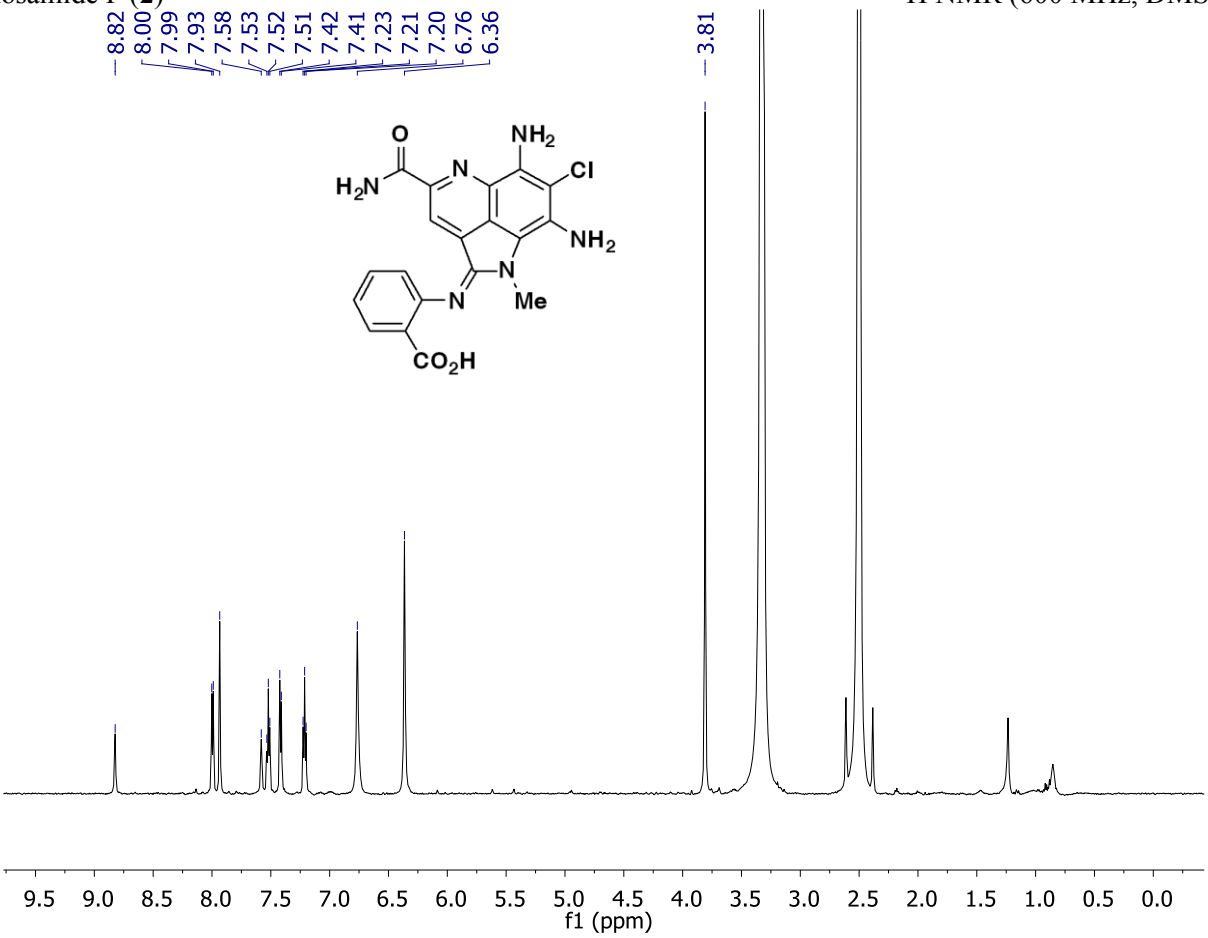
Ammosamide E (**1**) HMBC (600 MHz, DMSO-d_6)



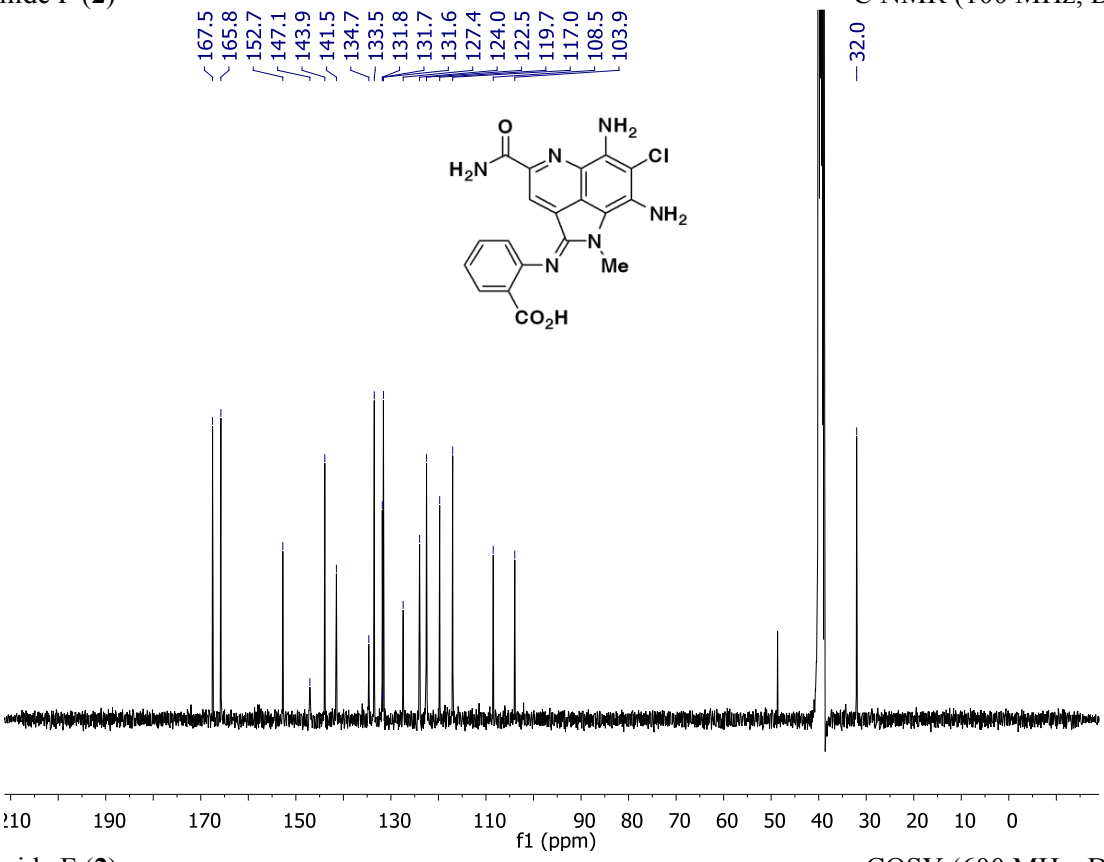
Ammosamide E (**1**) HRMS (ESI-TOF)



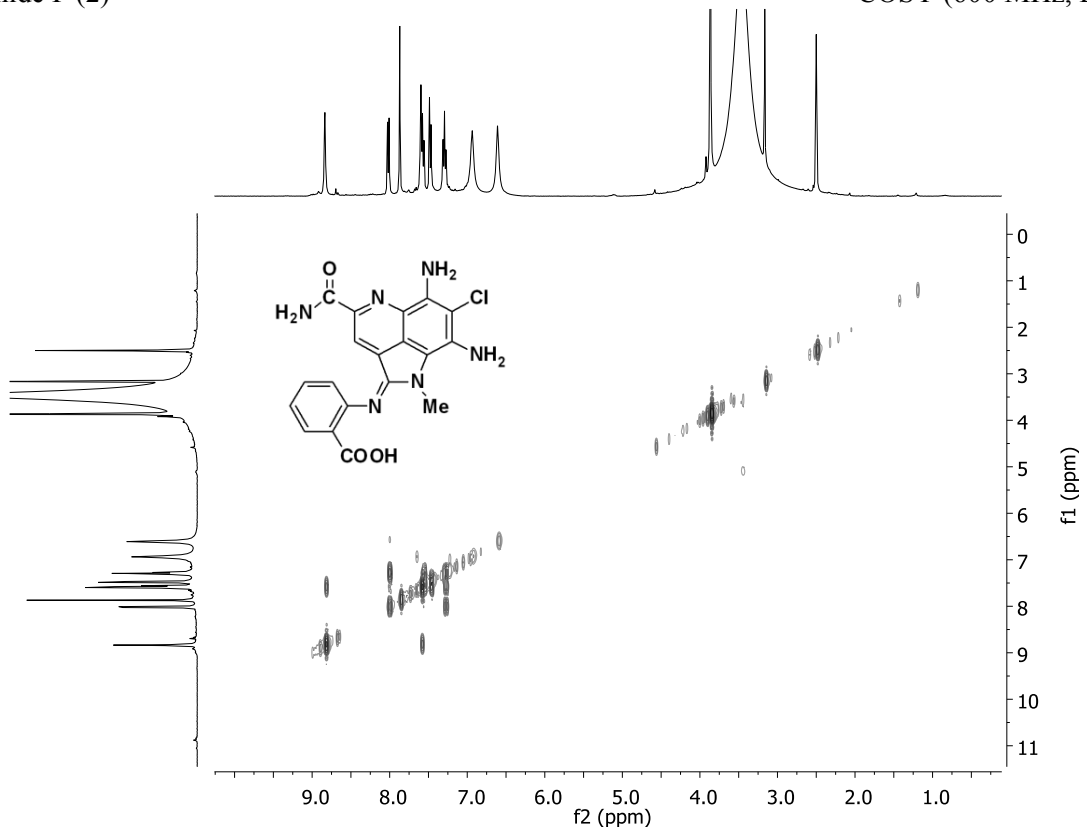
Ammosamide F (**2**) ^{1}H NMR (600 MHz, DMSO-d_6)



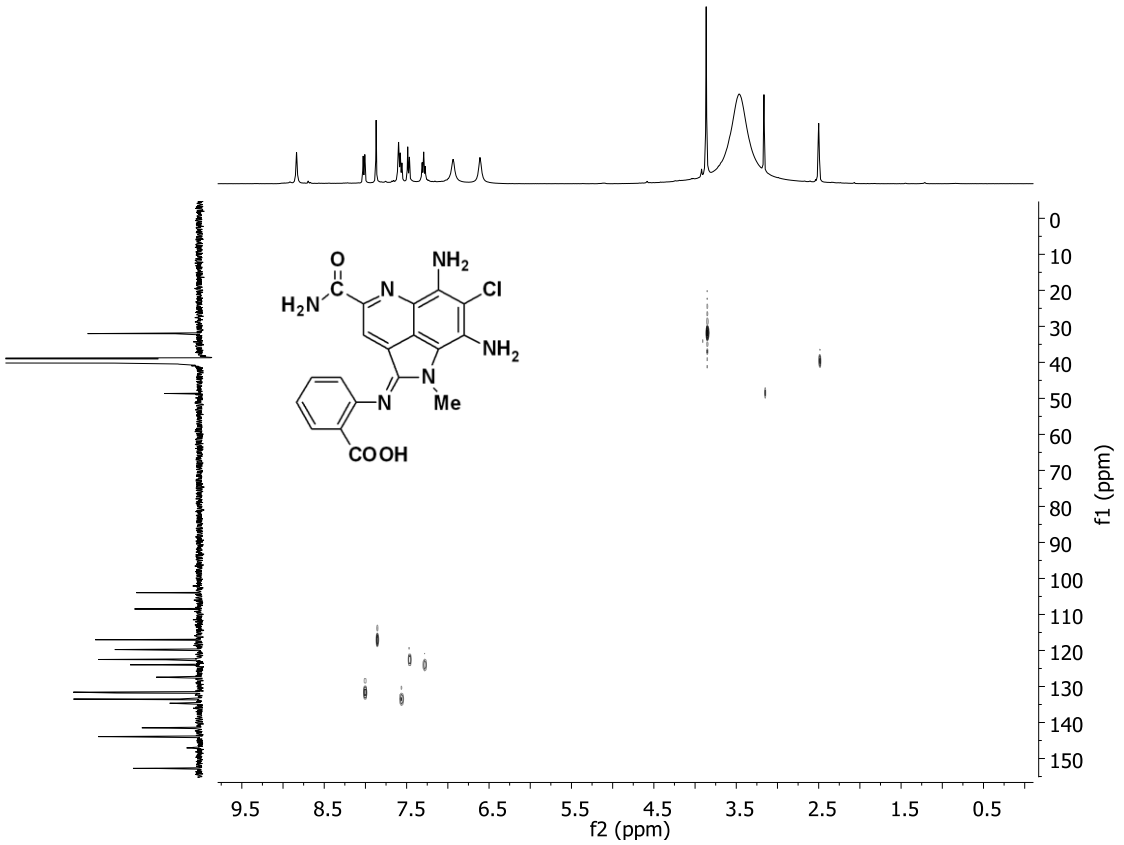
Ammosamide F (**2**) ^{13}C NMR (100 MHz, DMSO-*d*$_6$)



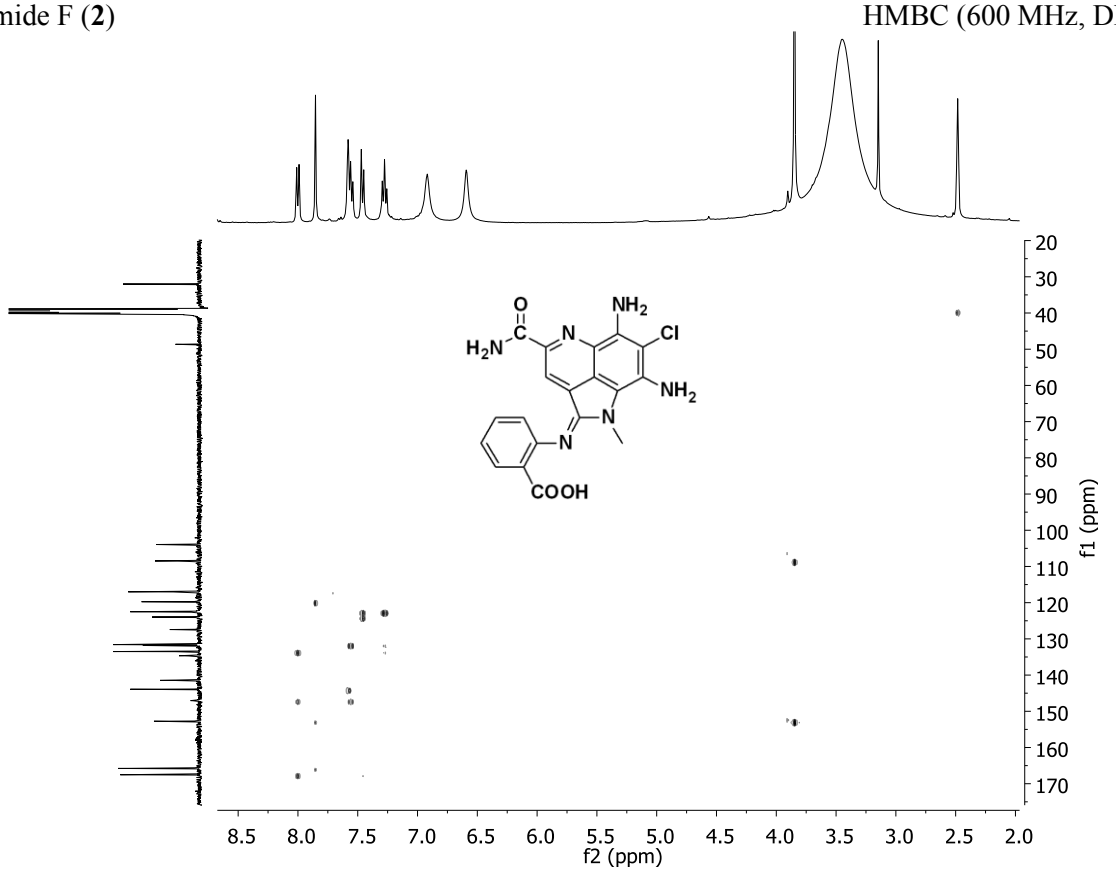
Ammosamide F (**2**) COSY (600 MHz, DMSO-*d*$_6$)



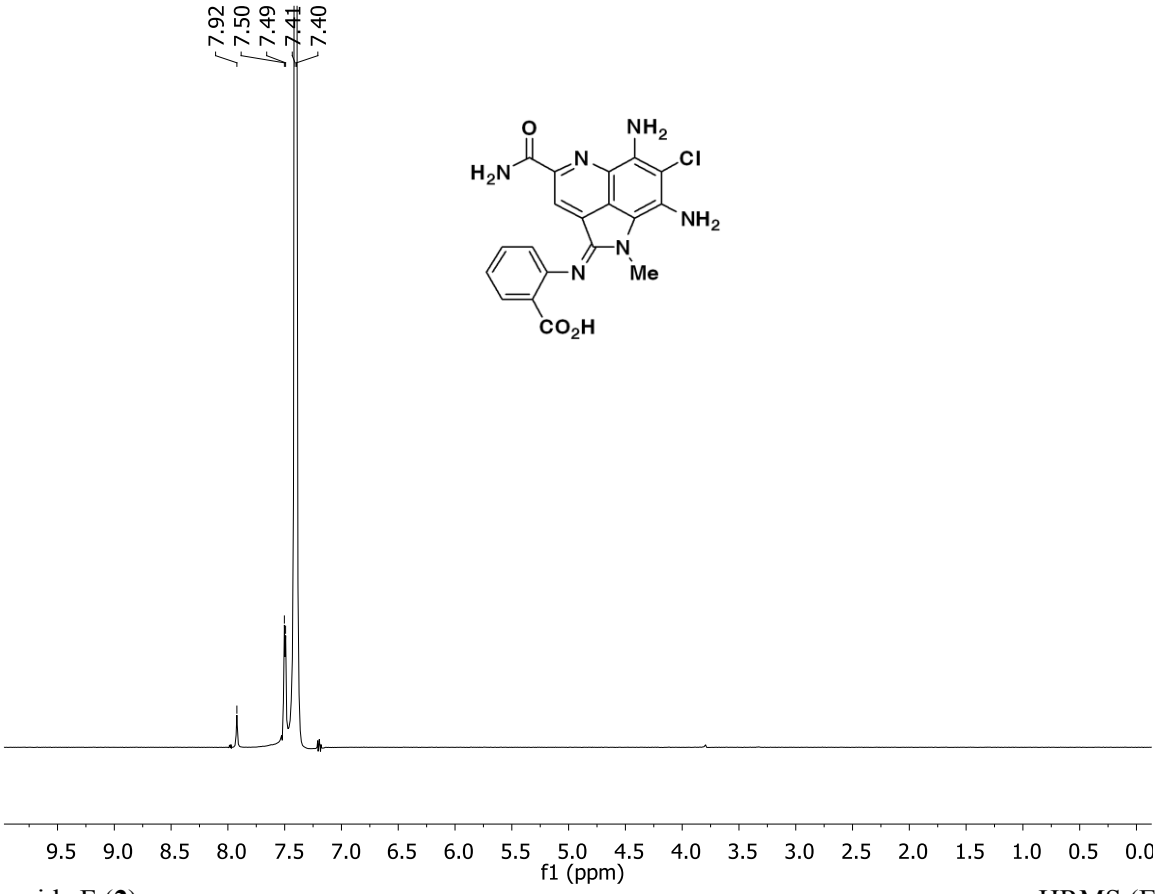
Ammosamide F (**2**) HMQC (600 MHz, DMSO-*d*6)



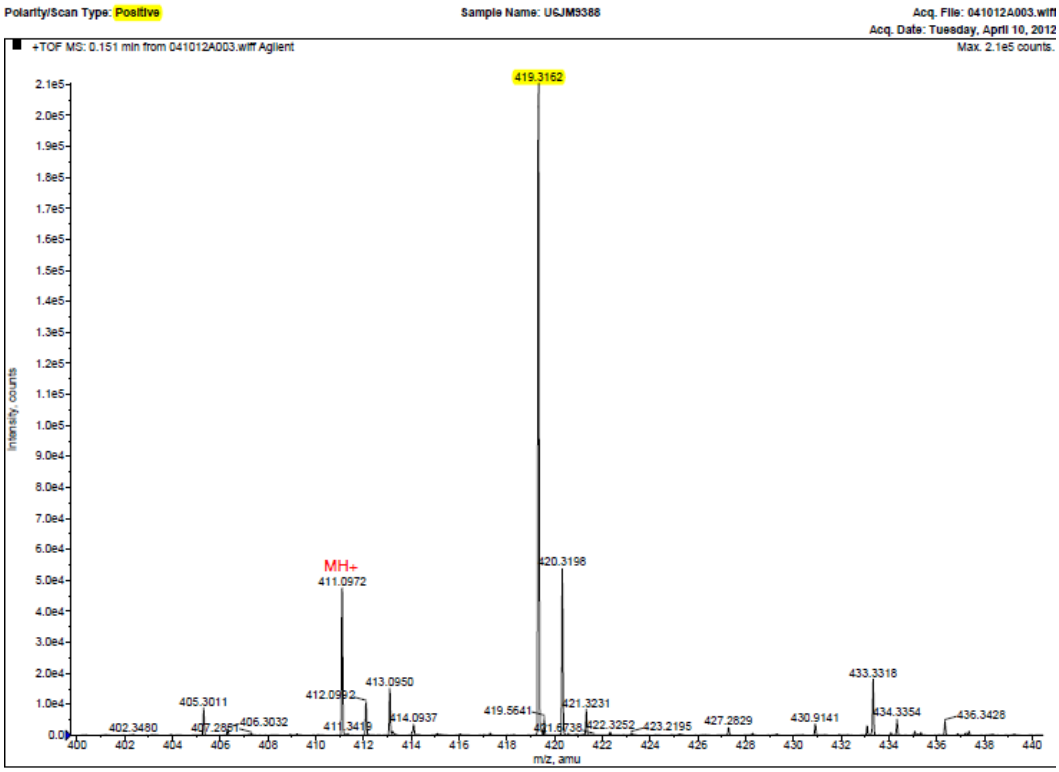
Ammosamide F (**2**) HMBC (600 MHz, DMSO-*d*6)



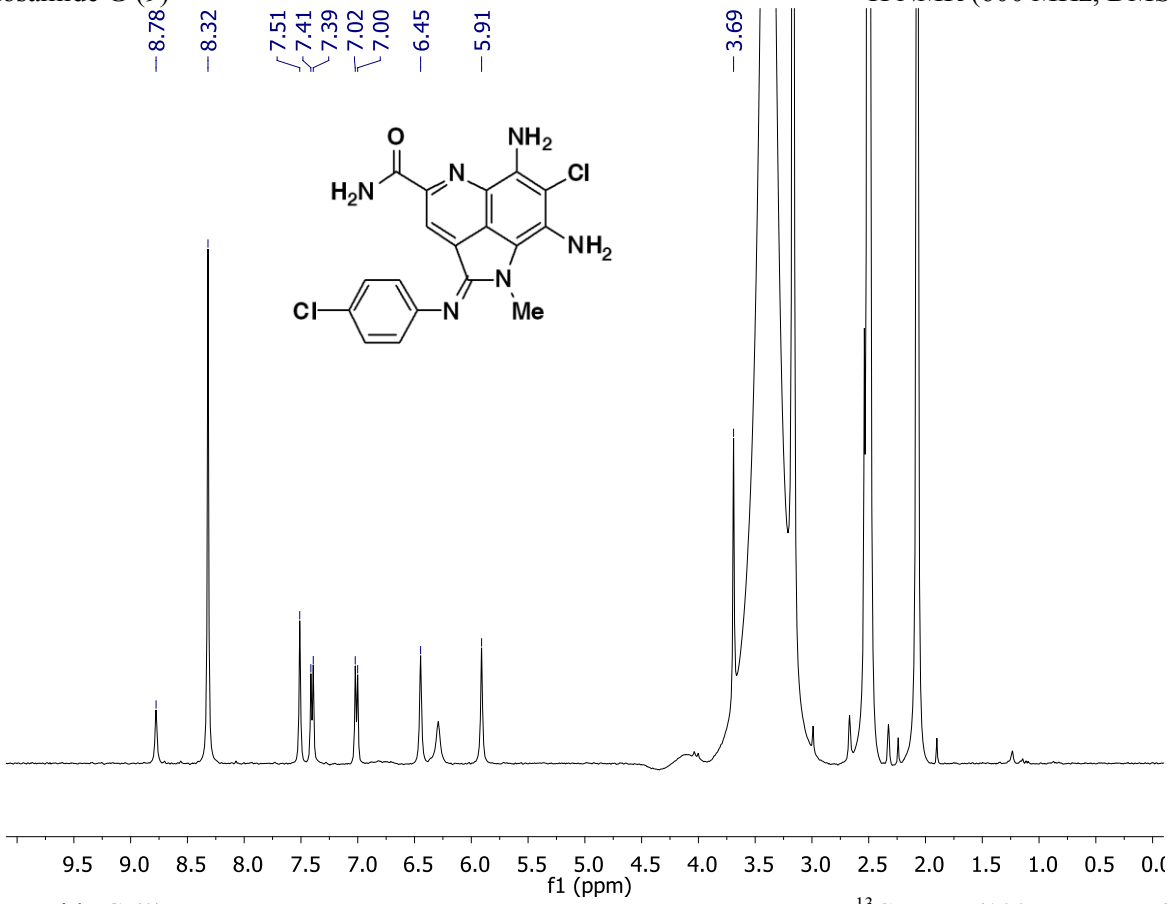
Ammosamide F(**2**) 1D NOESY (excited H-6', δ_H = 7.42) (600 MHz, DMSO-d_6)



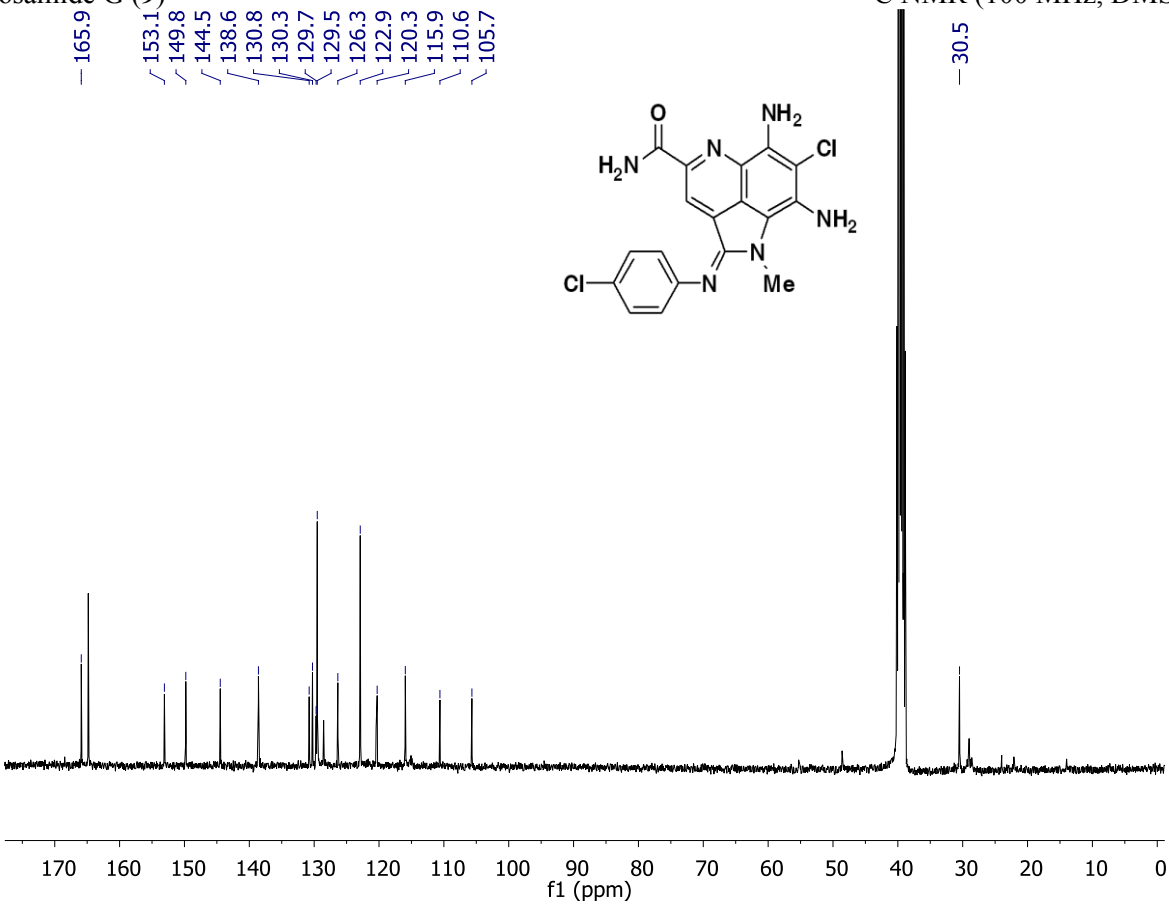
Ammosamide F (**2**) HRMS (ESI-TOF)



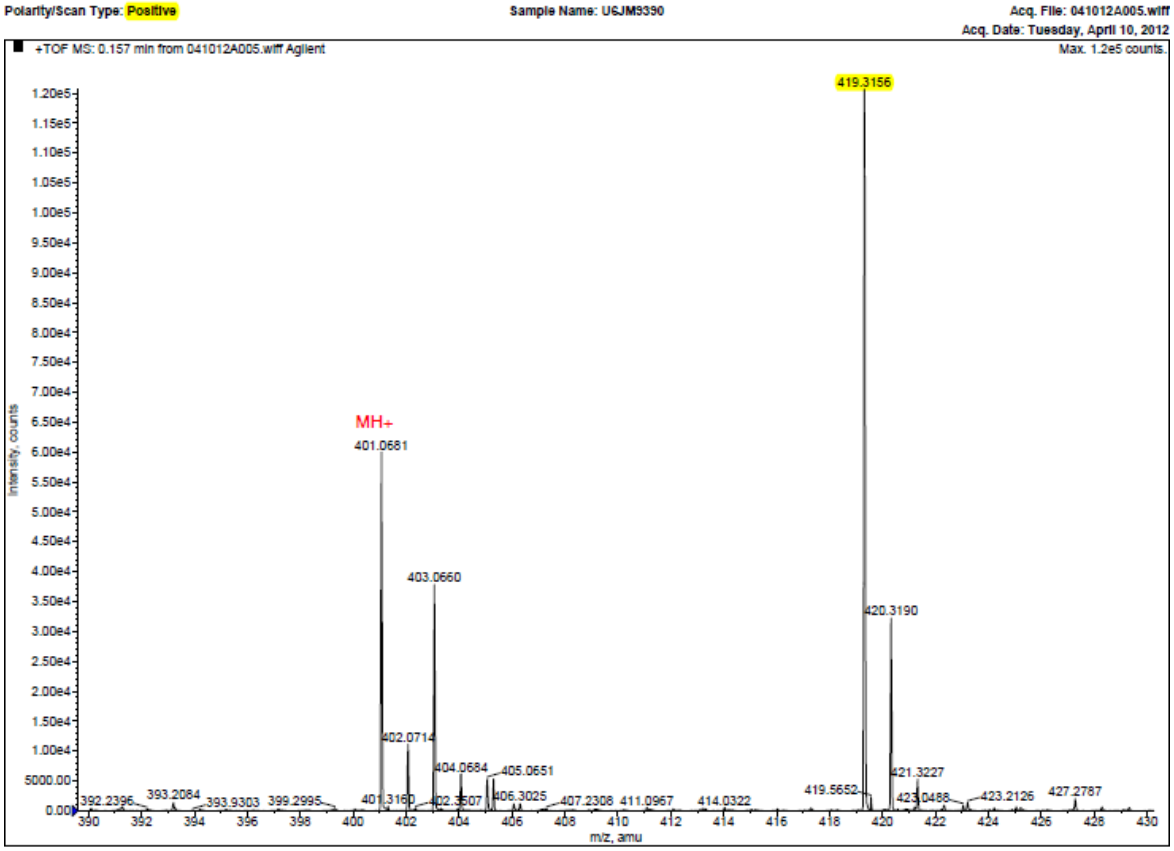
Ammosamide G (**9**) ^{1}H NMR (600 MHz, DMSO-d_6)



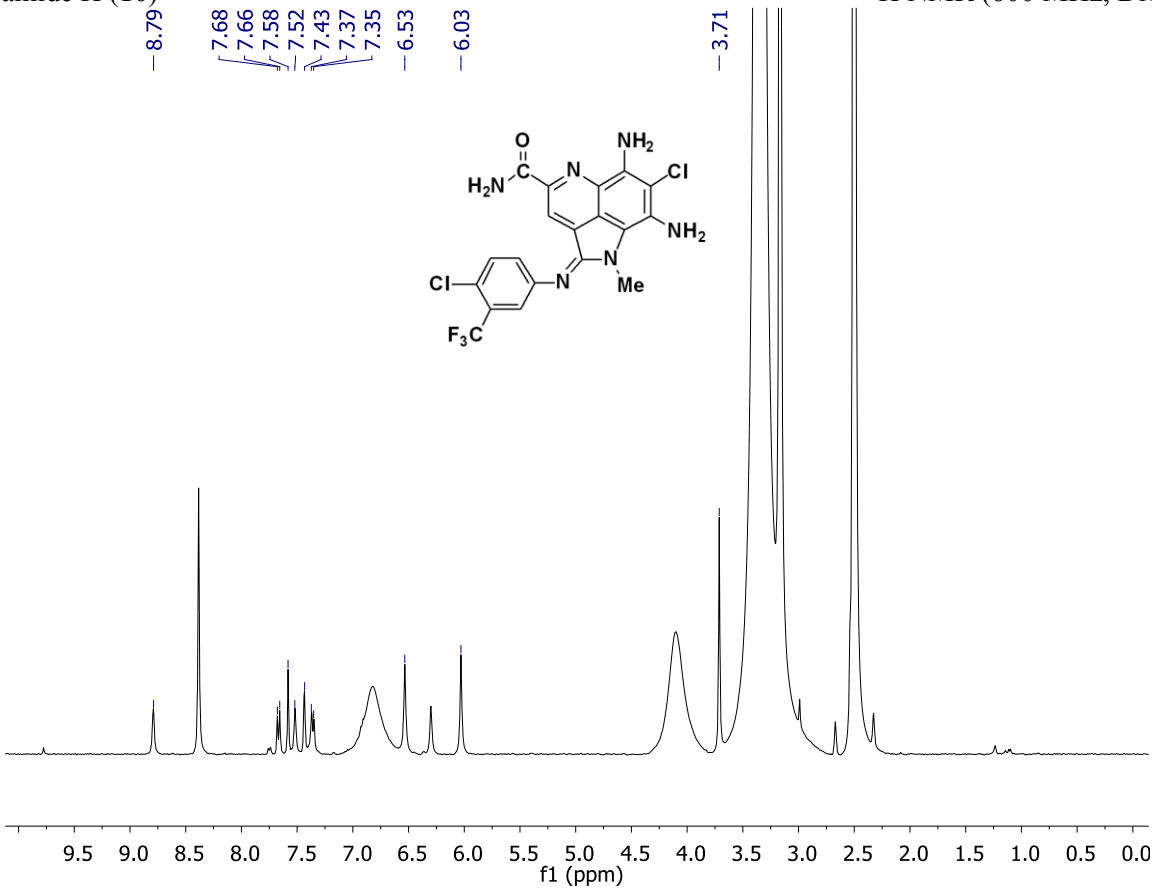
Ammosamide G (**9**) ^{13}C NMR (100 MHz, DMSO-d_6)



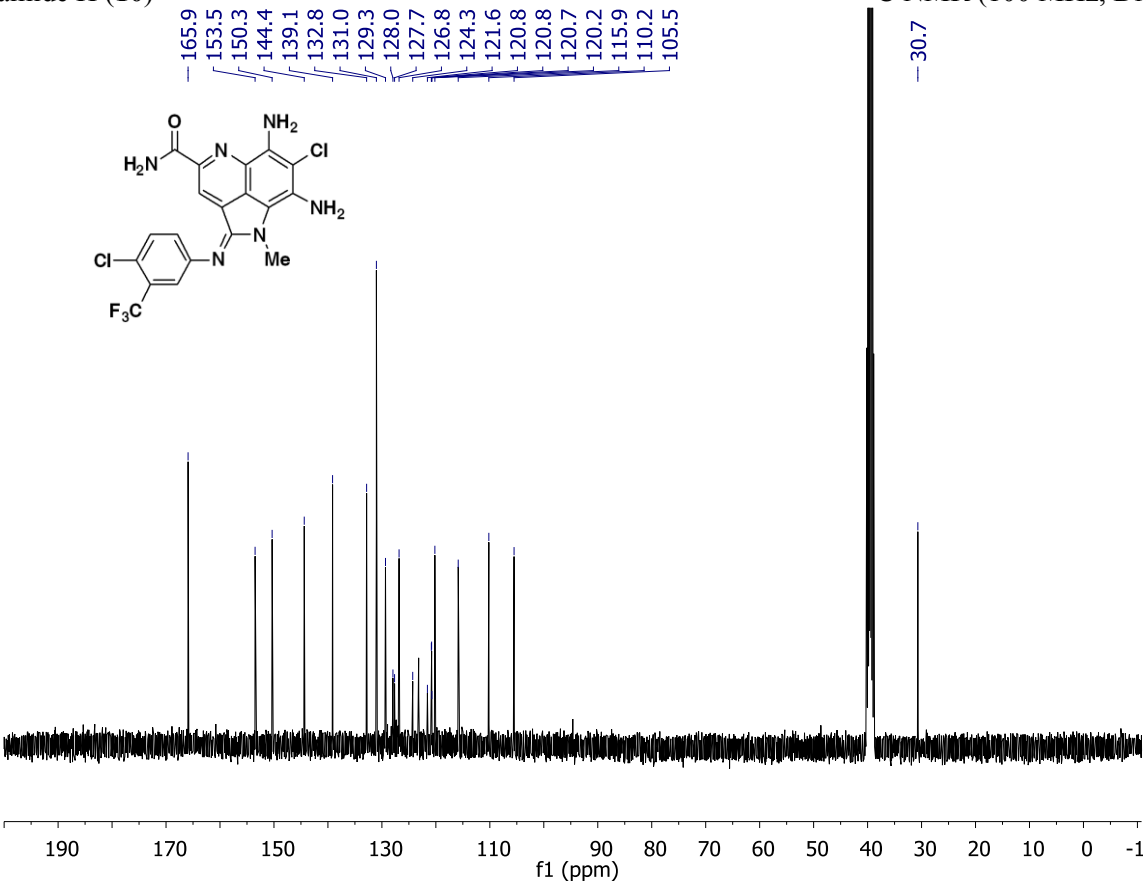
Ammosamide G (**9**) HRMS (ESI-TOF)



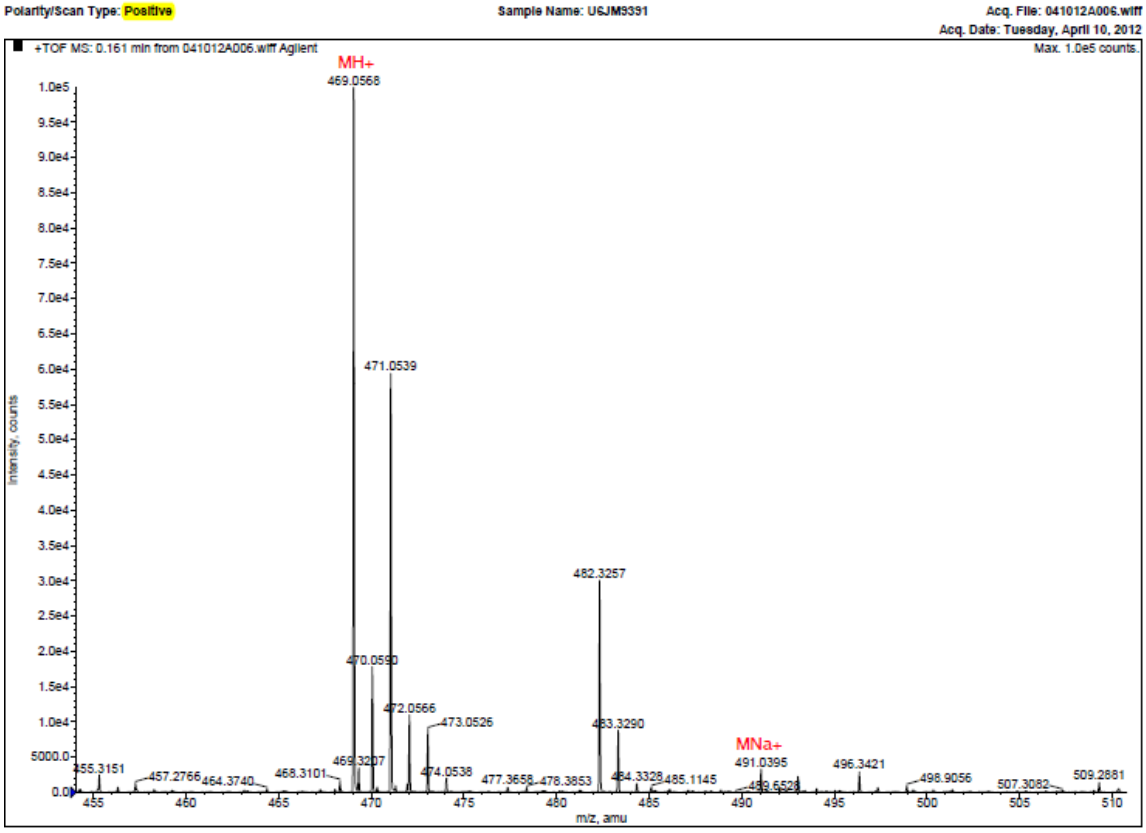
Ammosamide H (**10**) ^{1}H NMR (600 MHz, DMSO-*d*$_6$)



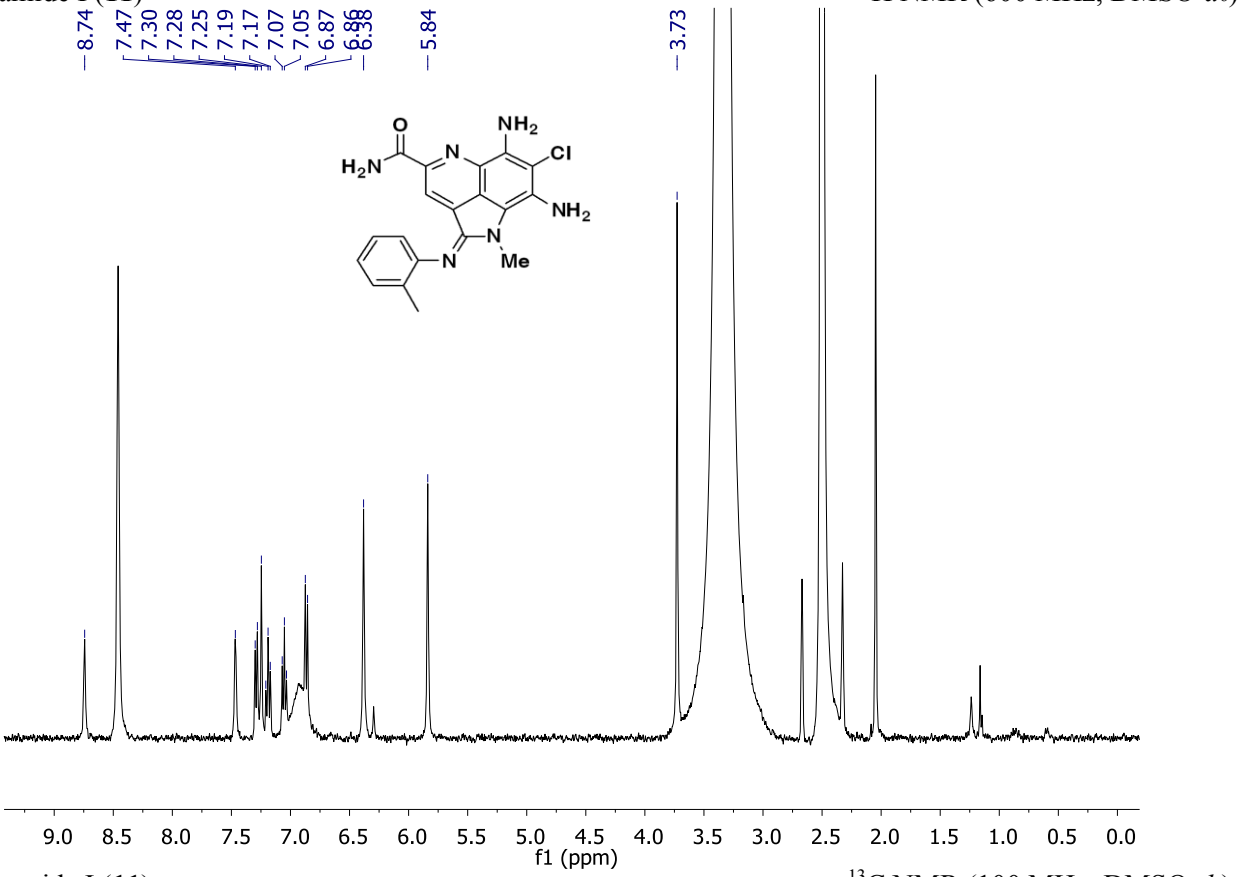
Ammosamide H (**10**) ^{13}C NMR (100 MHz, DMSO-*d*$_6$)



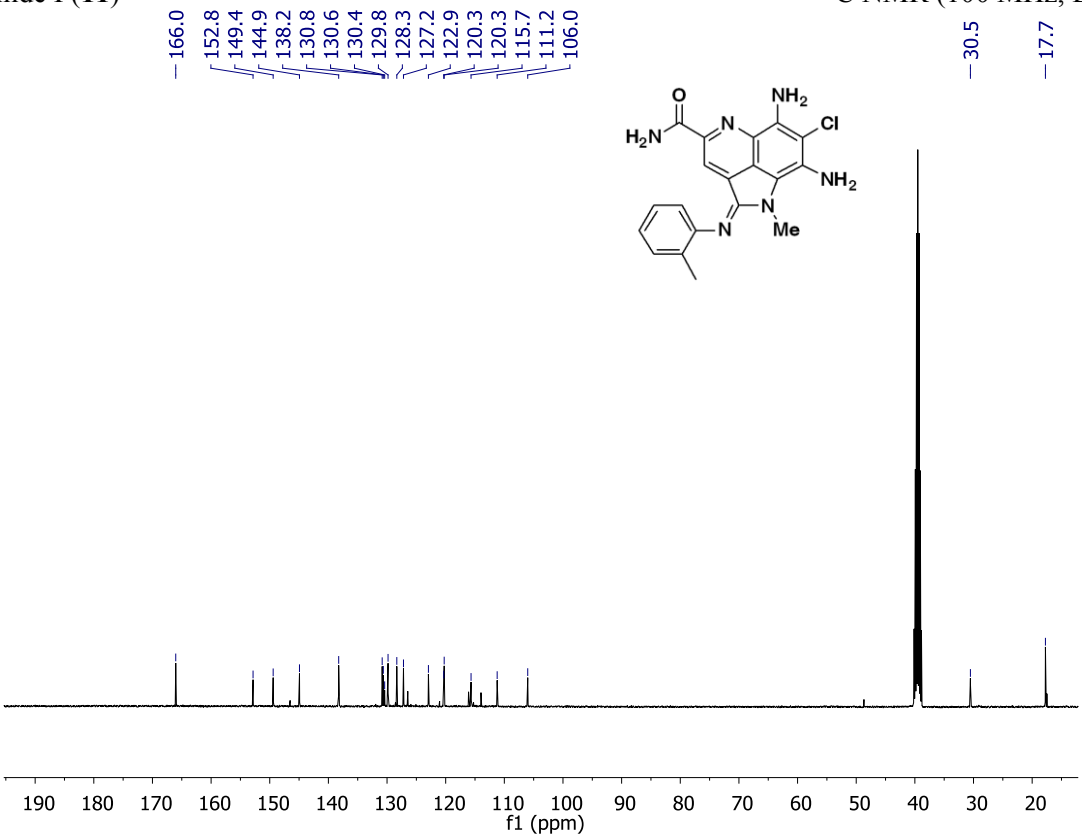
Ammosamide H (**10**) HRMS (ESI-TOF)



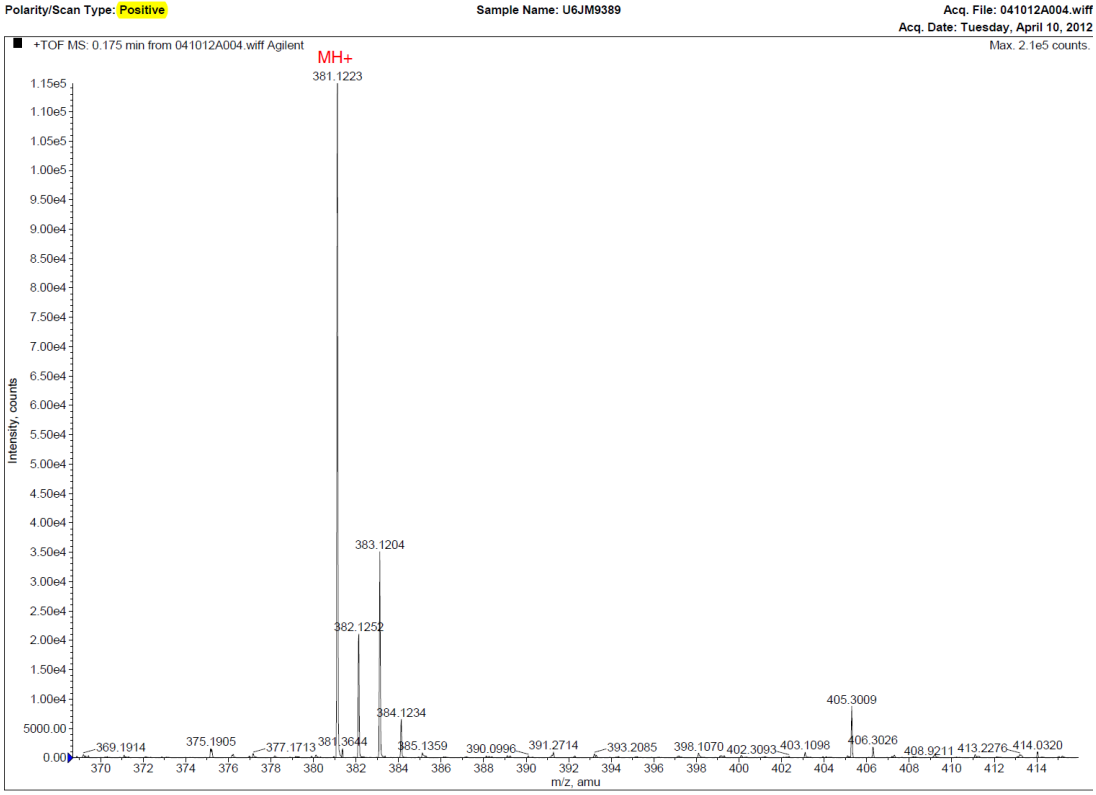
Ammosamide I (**11**) ^{1}H NMR (600 MHz, DMSO-d_6)



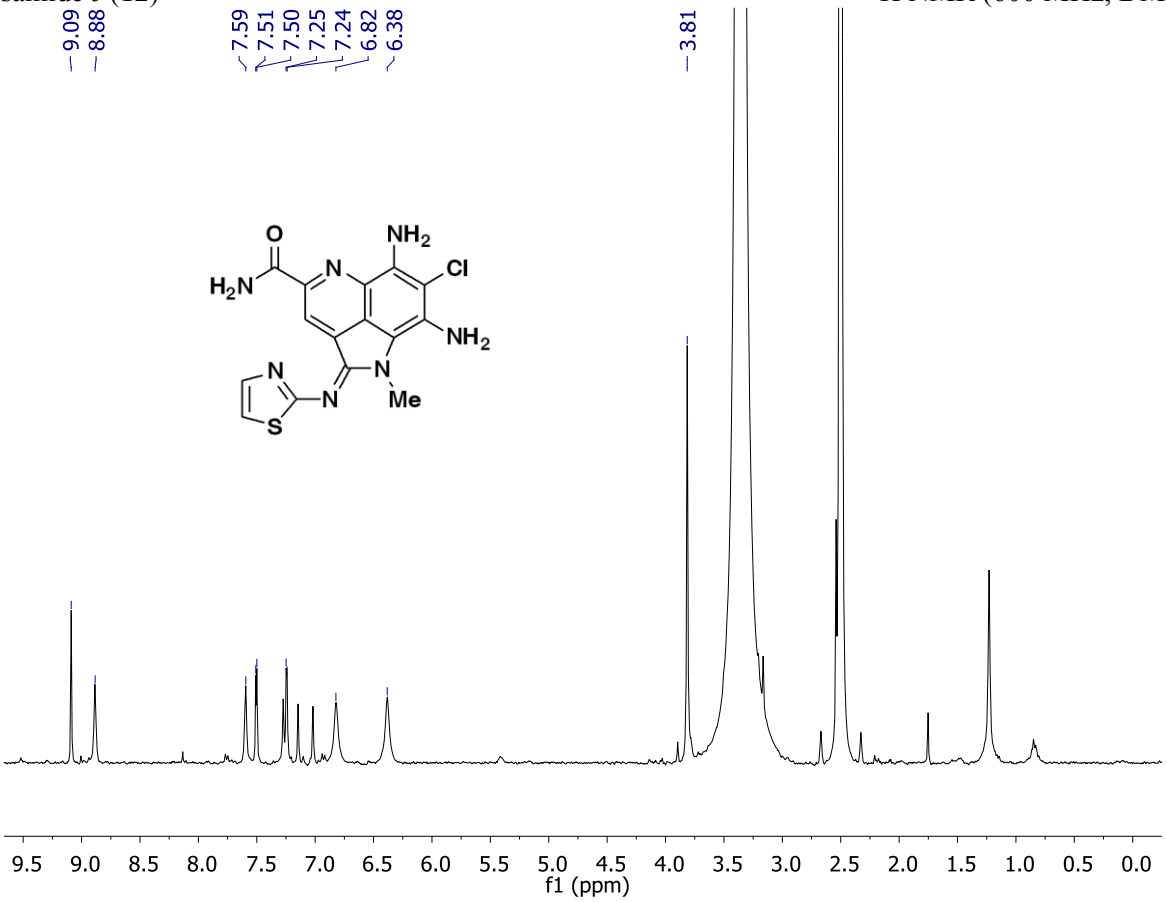
Ammosamide I (**11**) ^{13}C NMR (100 MHz, DMSO-d_6)



Ammosamide I (**11**) HRMS (ESI-TOF)

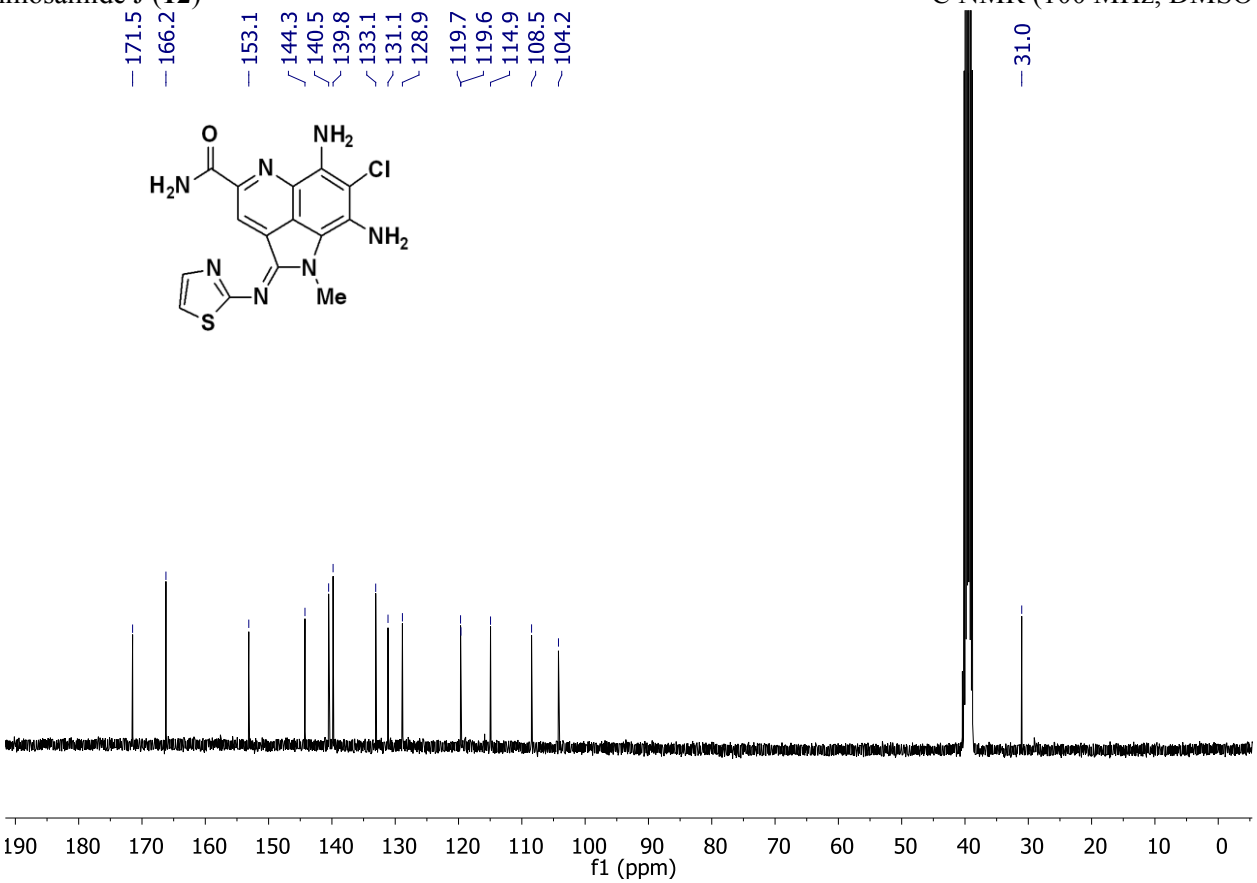


Ammosamide J (**12**) ^{1}H NMR (600 MHz, DMSO-d_6)



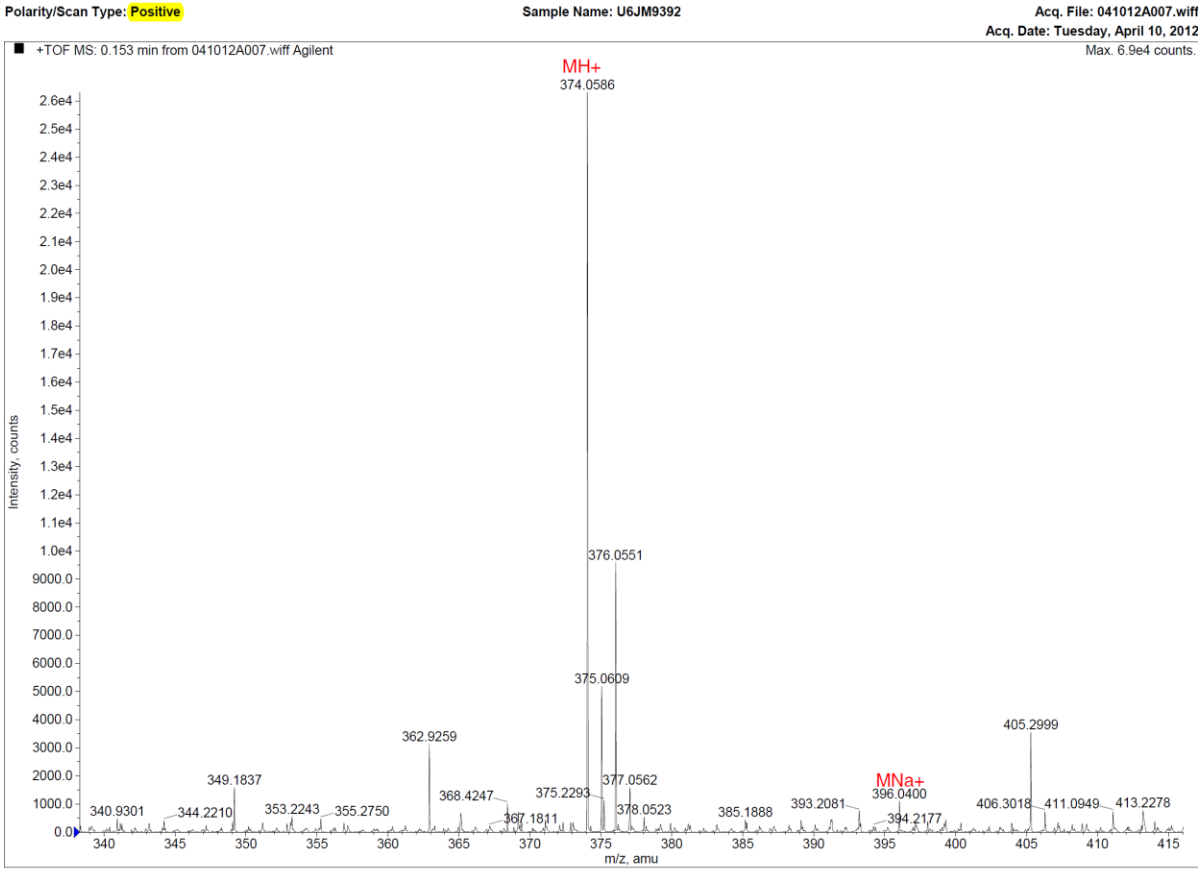
Ammosamide J (**12**)

^{13}C NMR (100 MHz, DMSO-*d*$_6$)

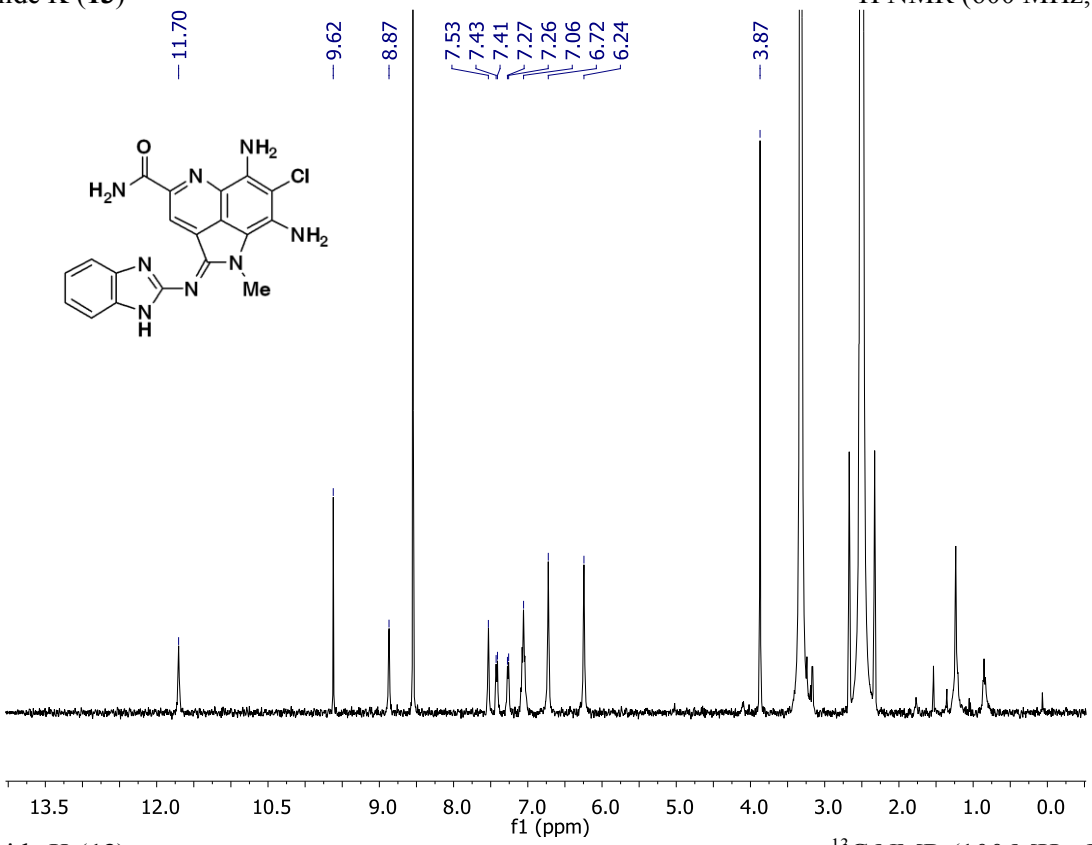


Ammosamide J (**12**)

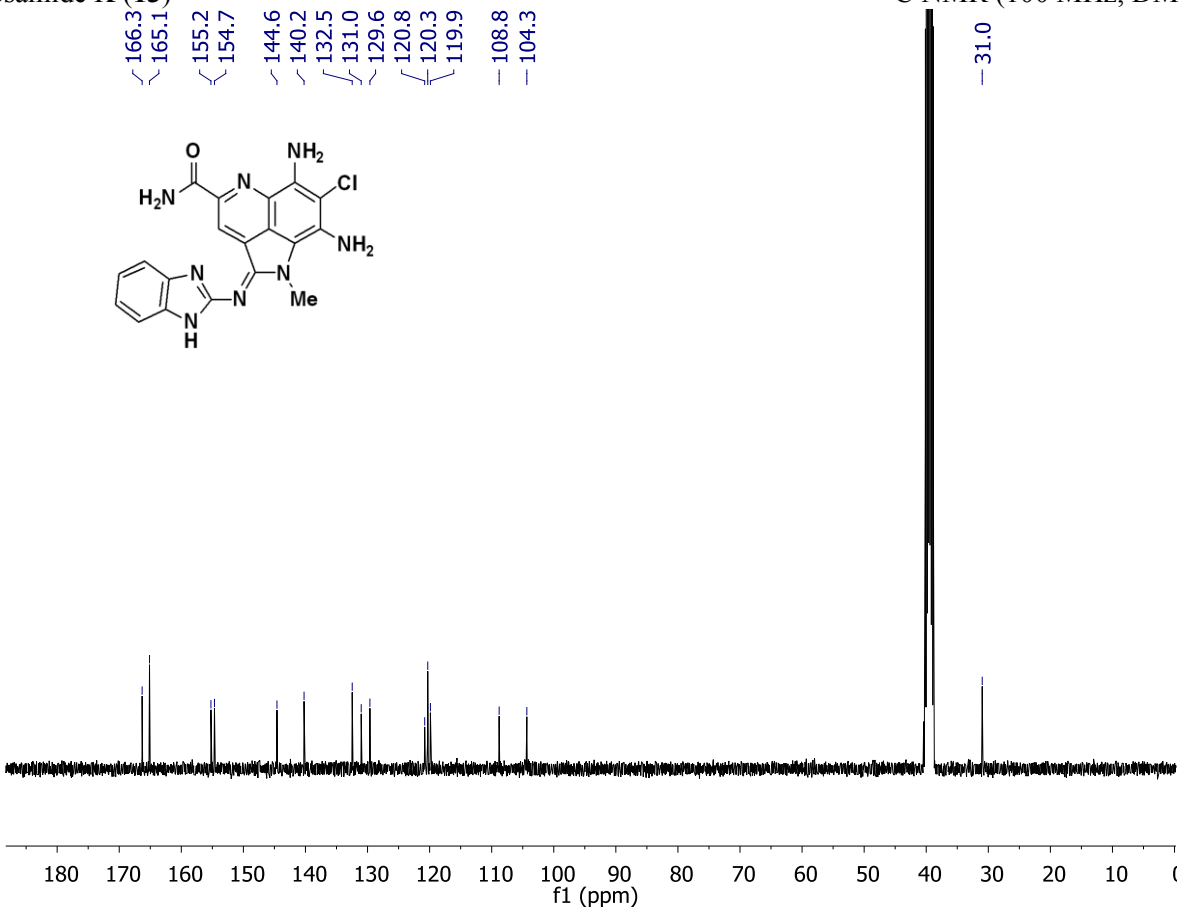
HRMS (ESI-TOF)



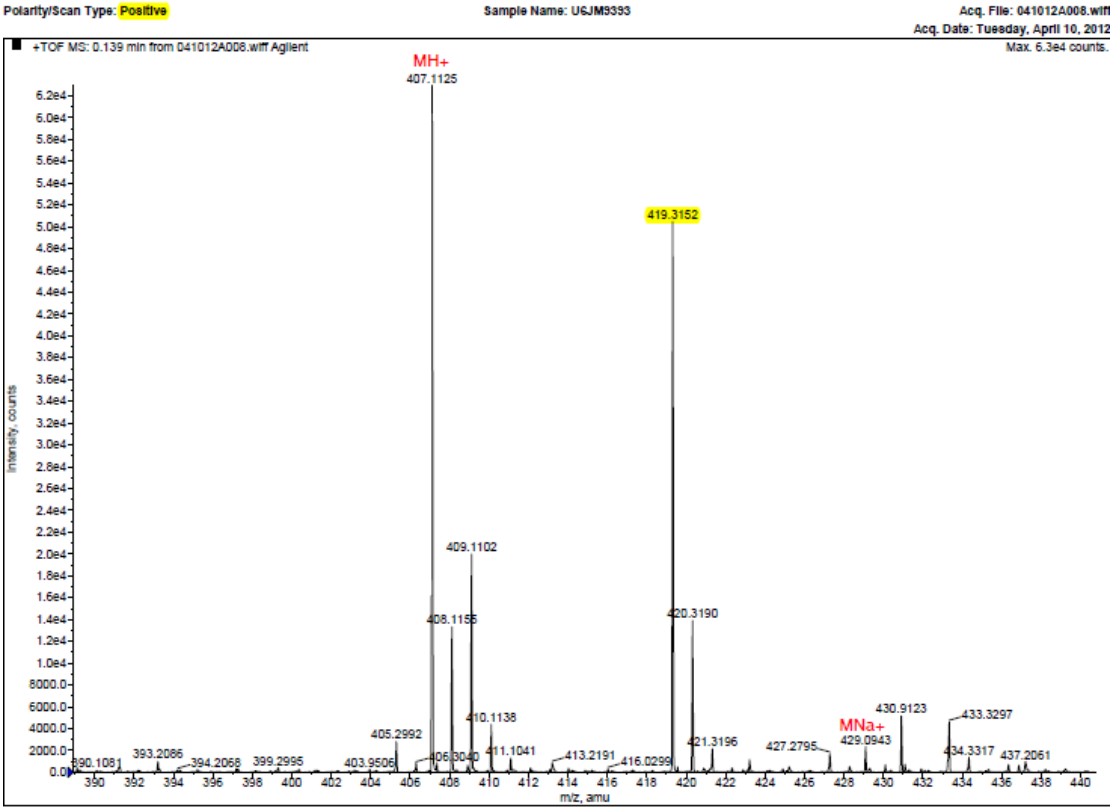
Ammosamide K (**13**) ^{1}H NMR (600 MHz, DMSO-*d*$_6$)



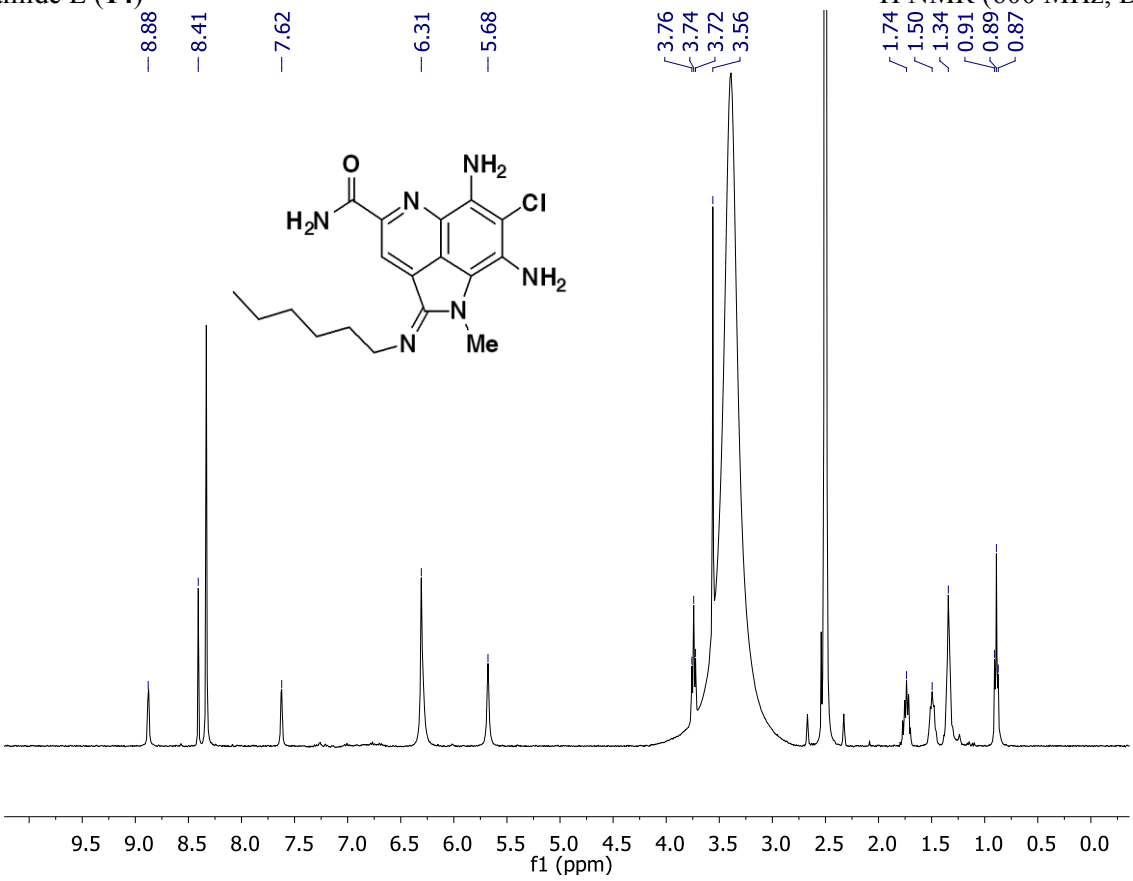
Ammosamide K (**13**) ^{13}C NMR (100 MHz, DMSO-*d*$_6$)



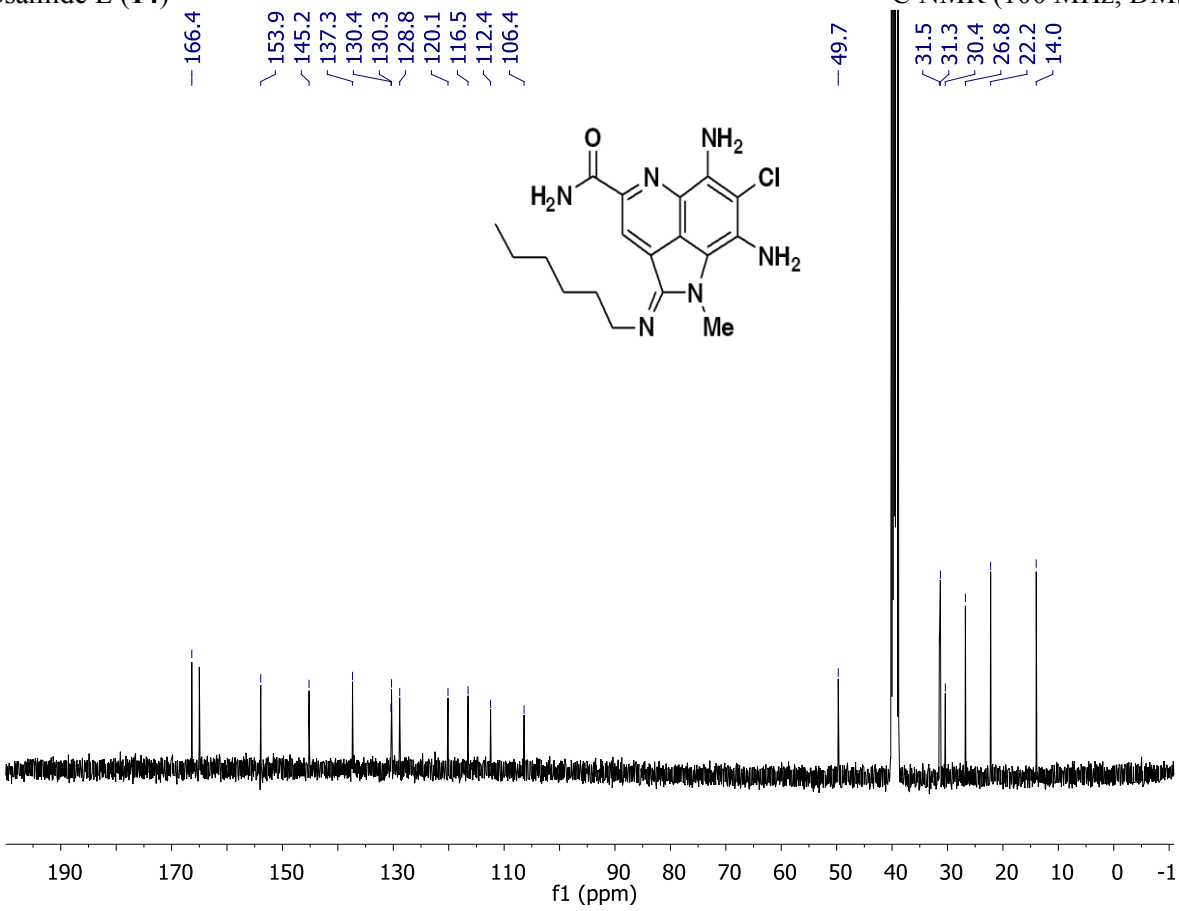
Ammosamide K (**13**) HRMS (ESI-TOF)



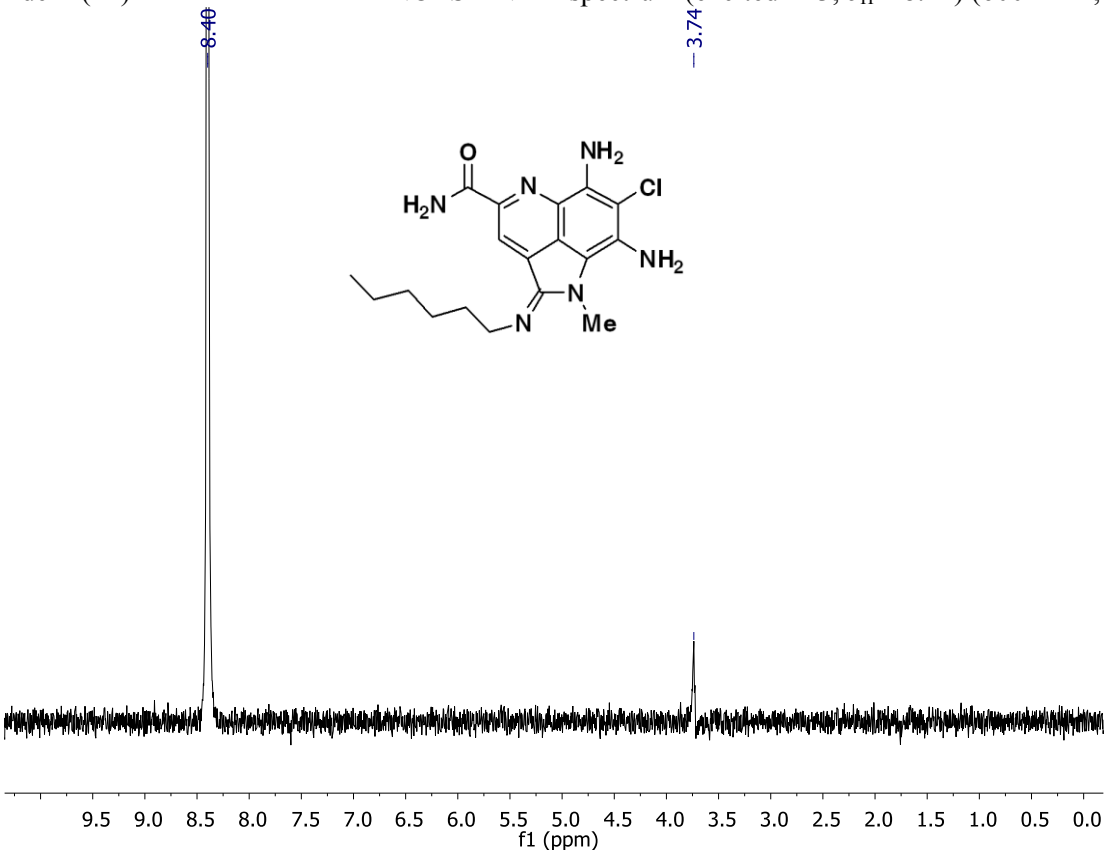
Ammosamide L (**14**) ^{1}H NMR (600 MHz, DMSO-d_6)



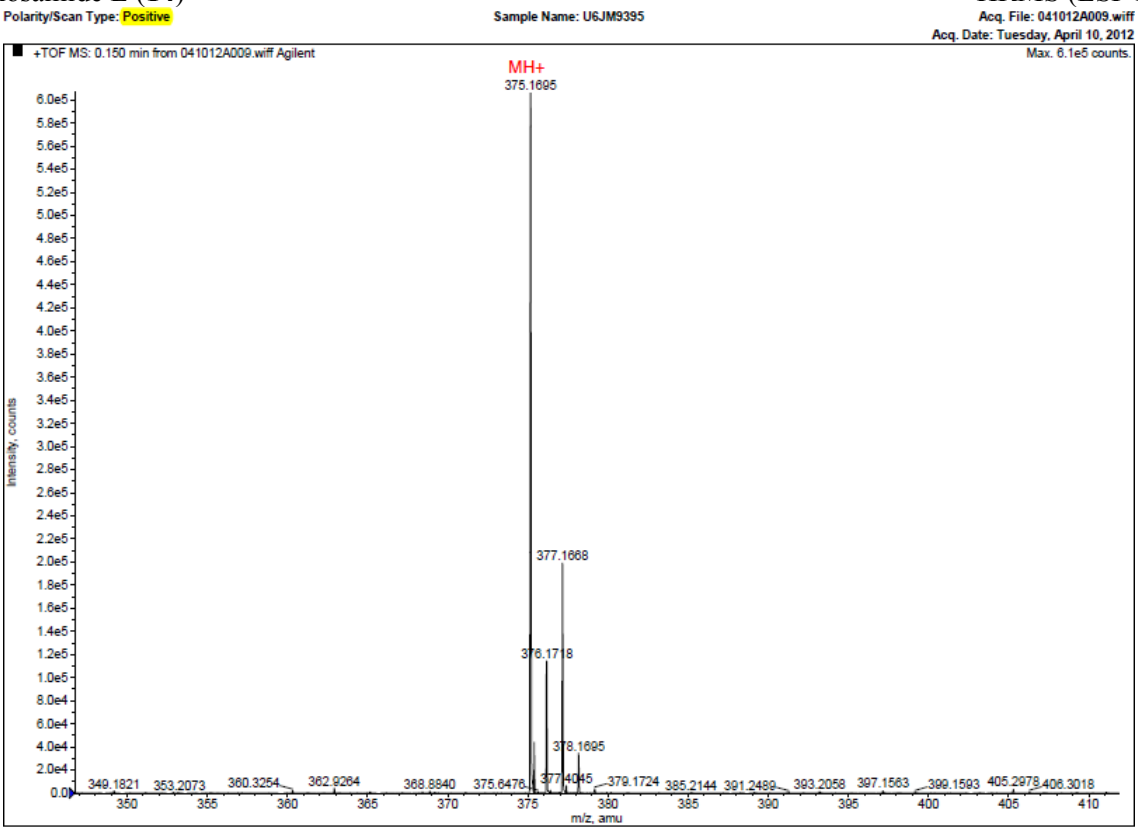
Ammosamide L (**14**) ^{13}C NMR (100 MHz, DMSO-*d*$_6$)



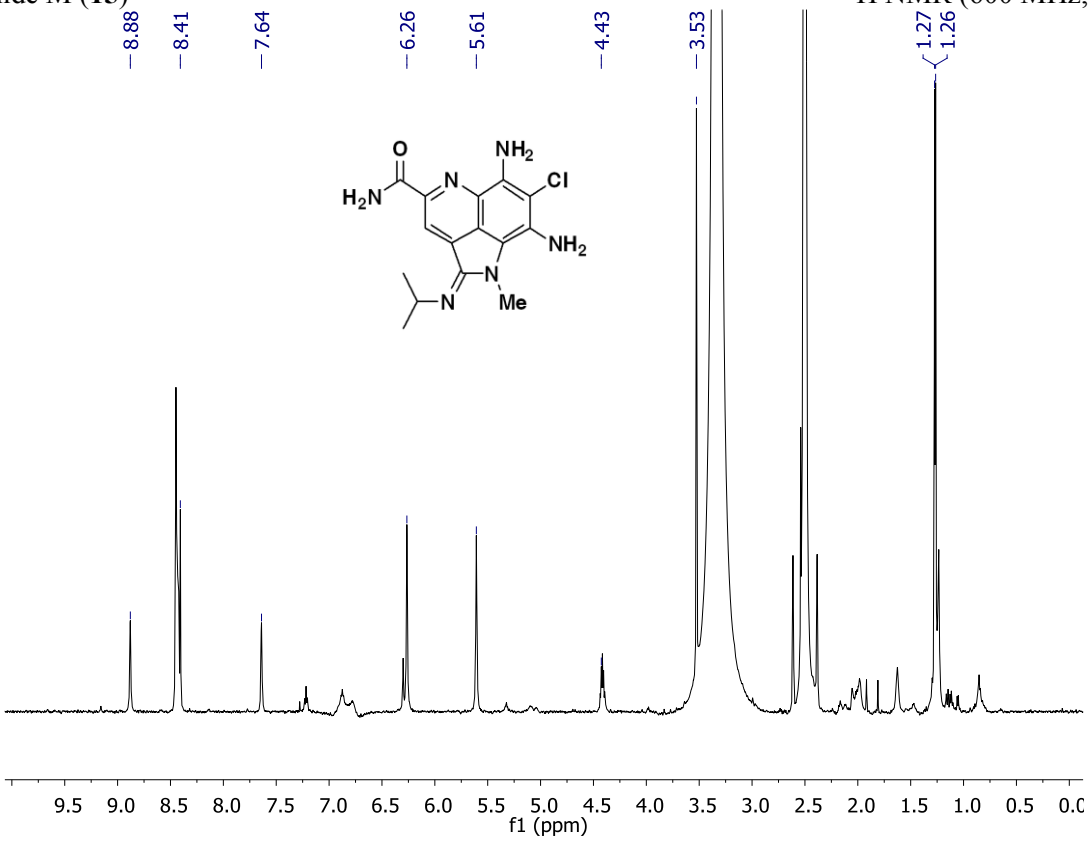
Ammosamide L (**14**) 1D NOESY NMR spectrum (excited H-3, δ_H = 8.41) (600 MHz, DMSO-*d*$_6$)



Ammosamide L (**14**) HRMS (ESI-TOF)

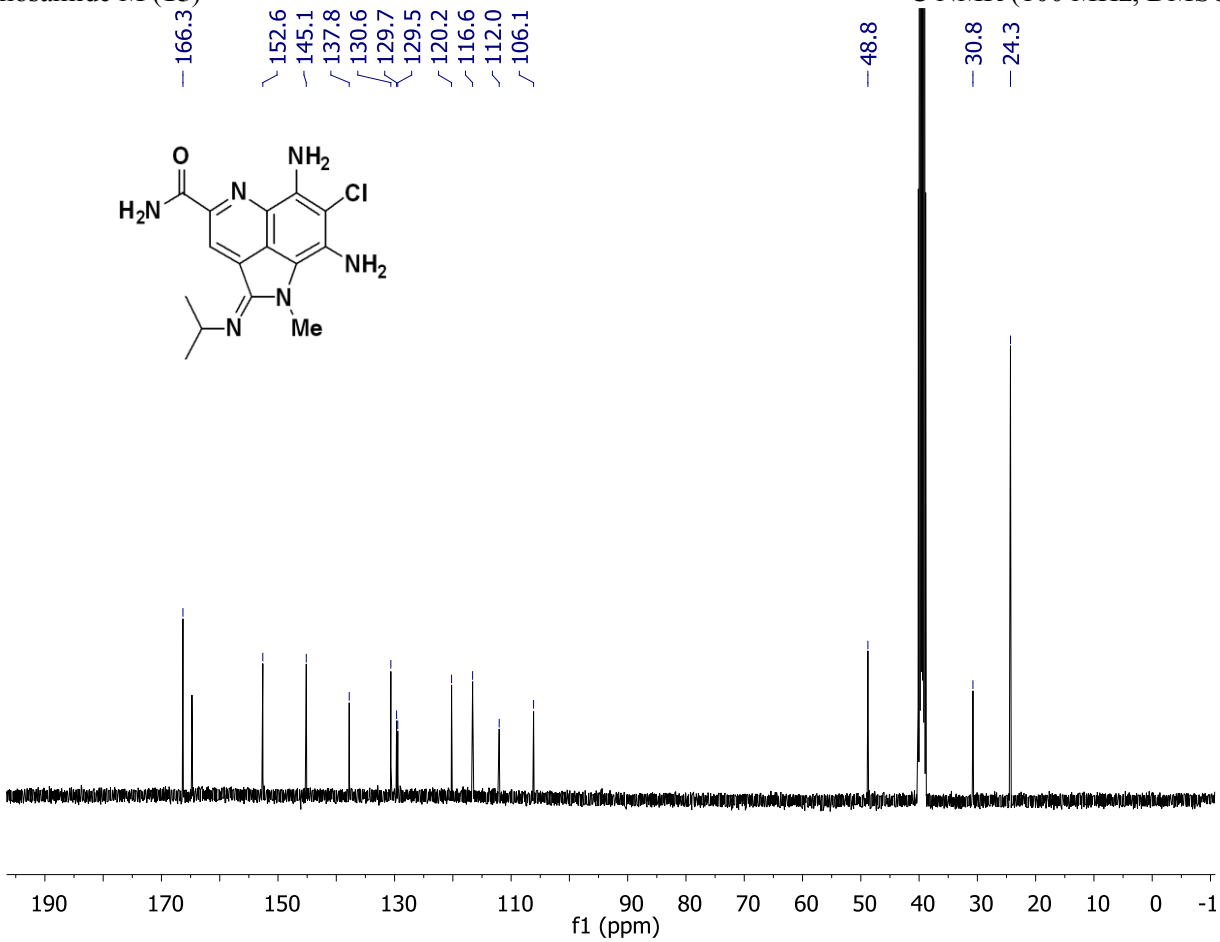


Ammosamide M (**15**) ^{1}H NMR (600 MHz, DMSO-d_6)



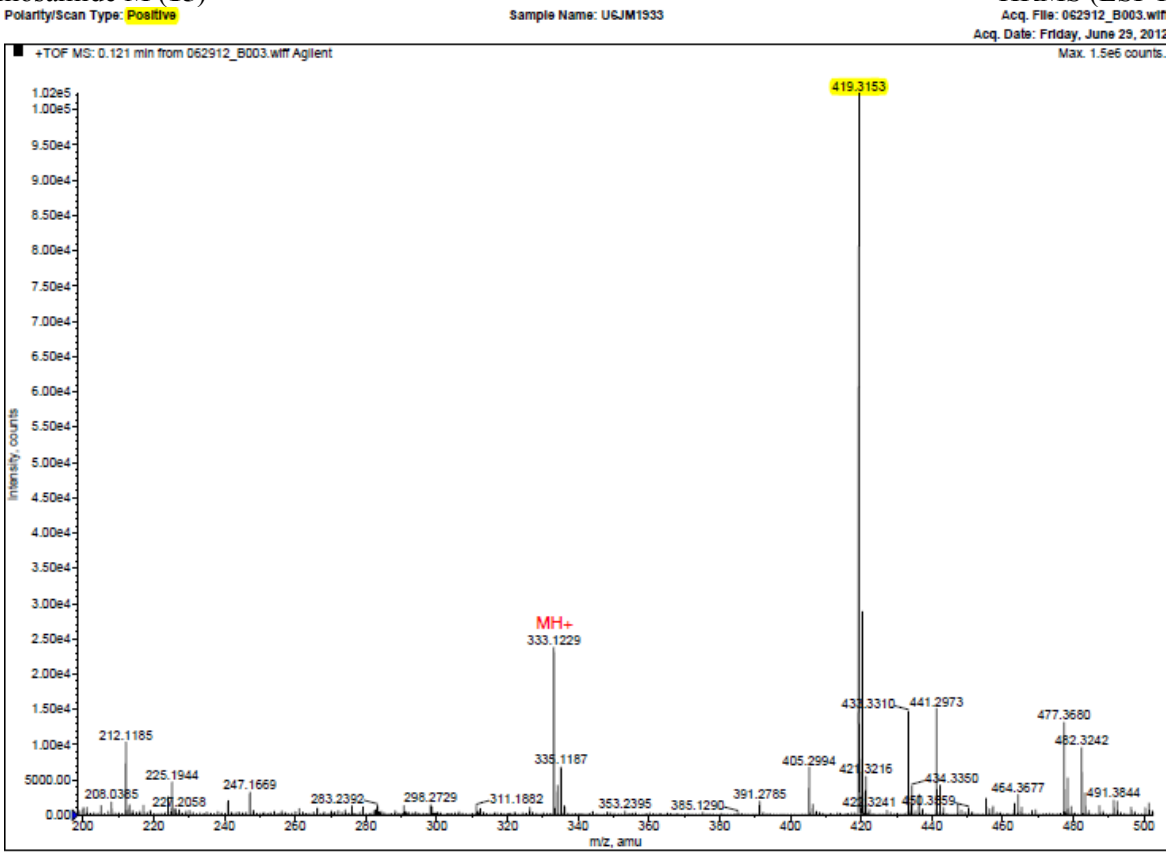
Ammosamide M (**15**)

^{13}C NMR (100 MHz, DMSO-d_6)

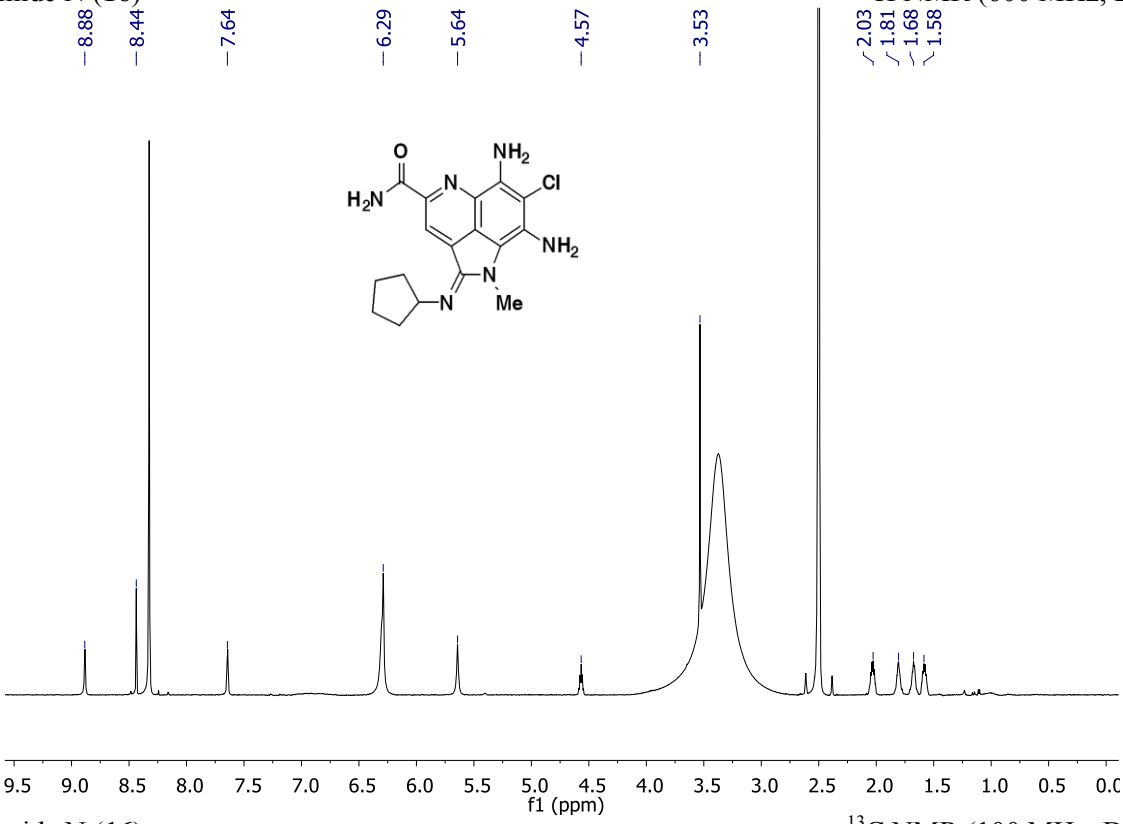


Ammosamide M (**15**)

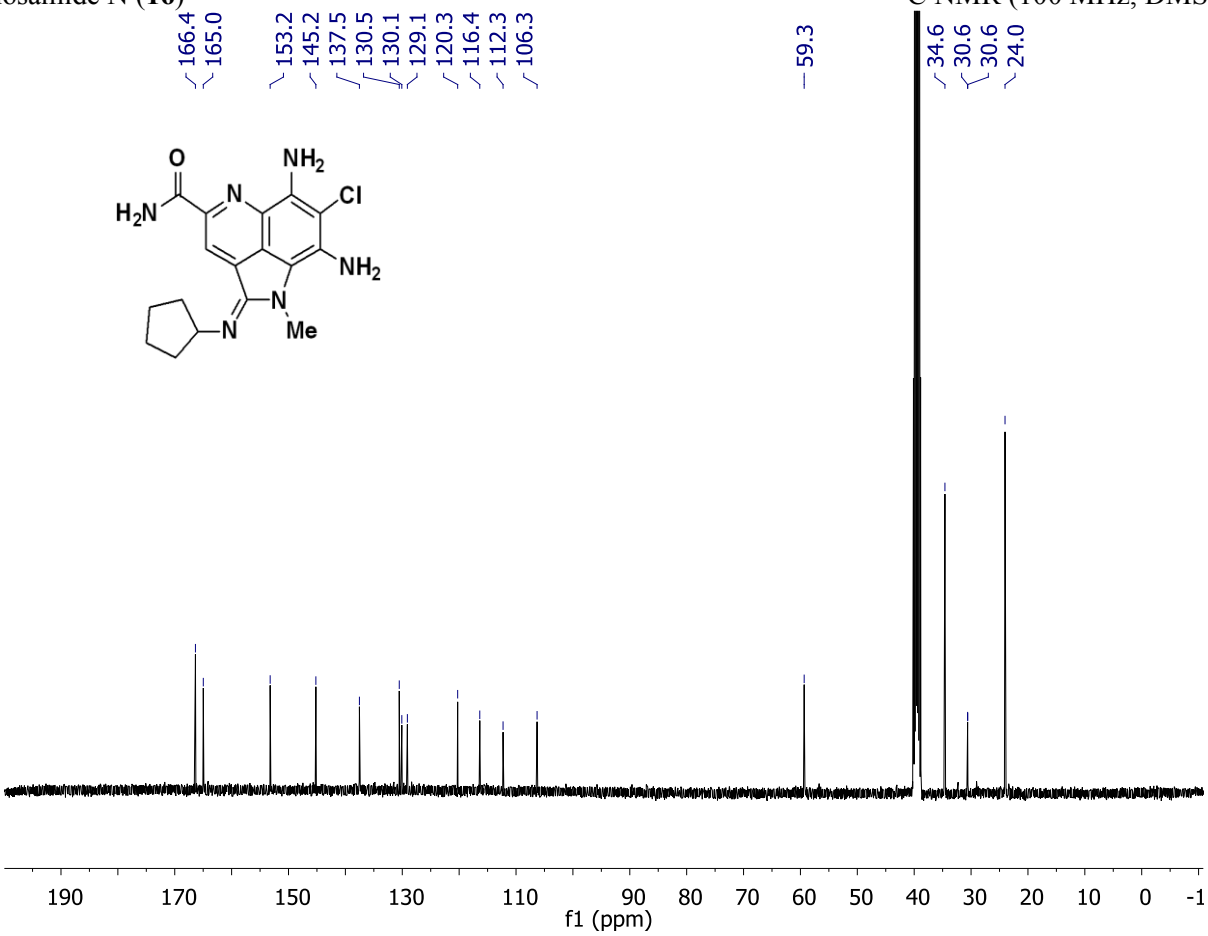
HRMS (ESI-TOF)



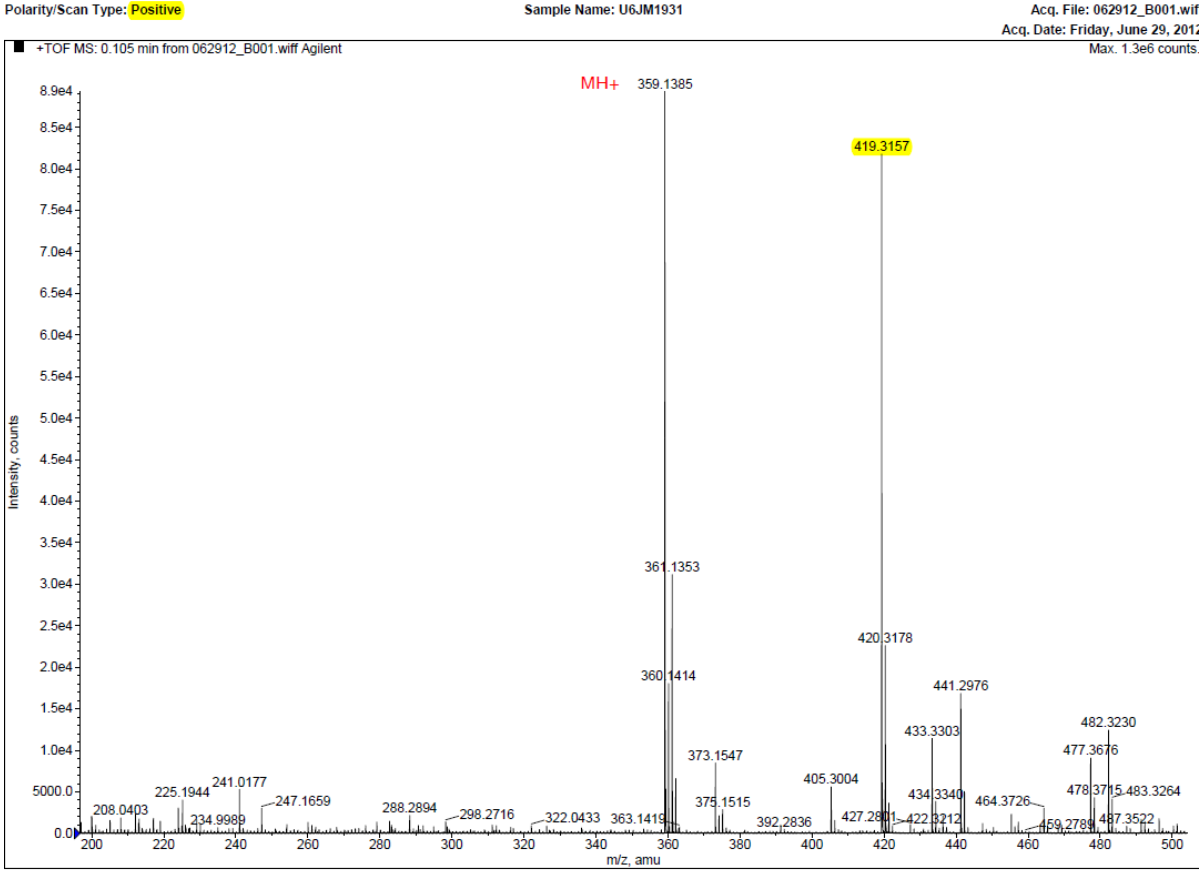
Ammosamide N (**16**) ^{1}H NMR (600 MHz, DMSO-*d*$_6$)



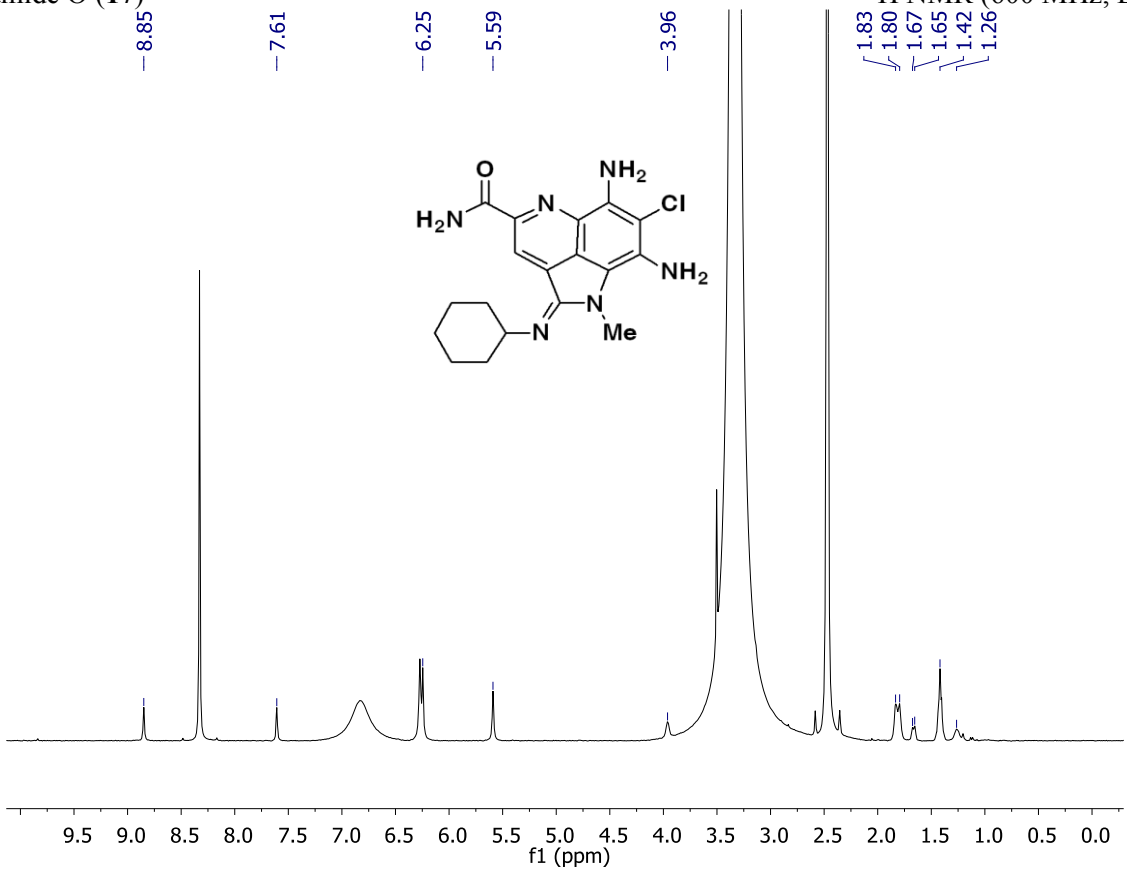
Ammosamide N (**16**) ^{13}C NMR (100 MHz, DMSO-*d*$_6$)



Ammosamide N (**16**) HRMS (ESI-TOF)

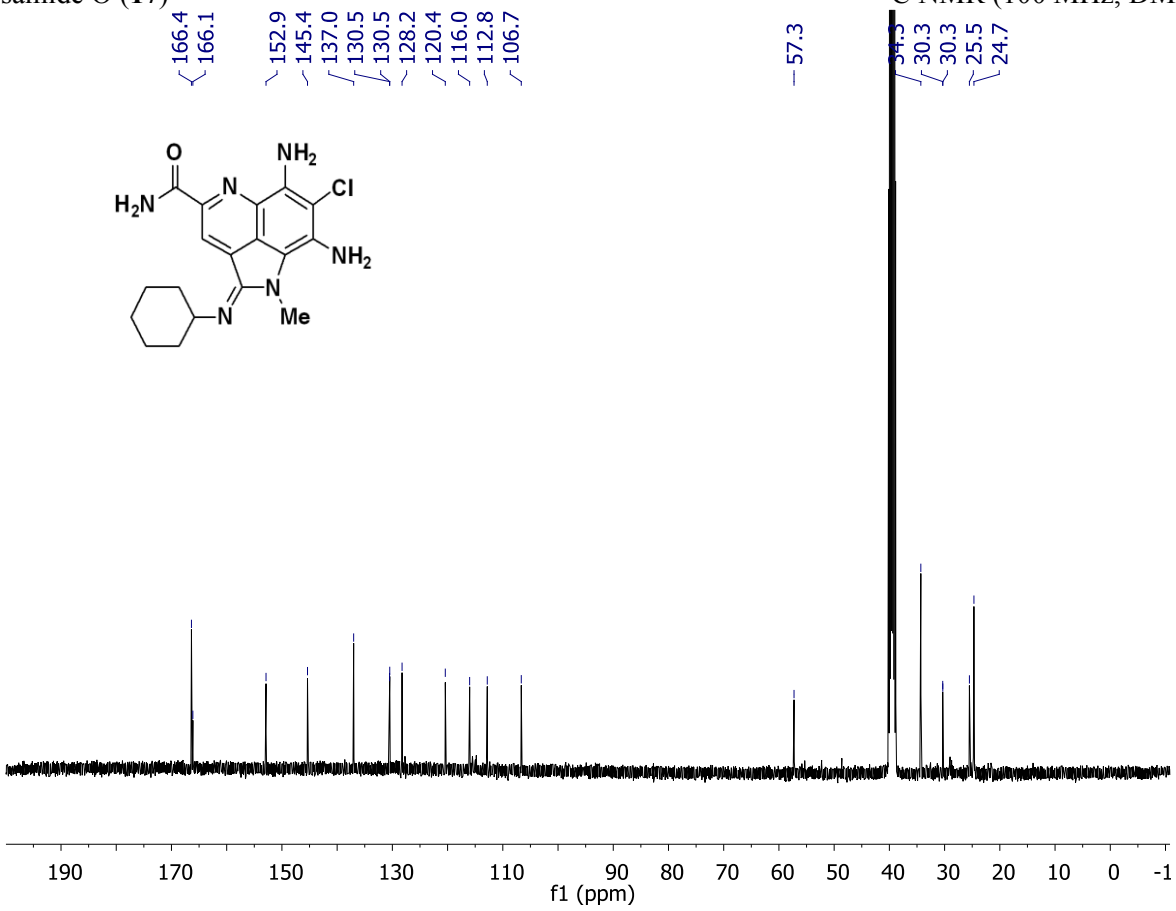


Ammosamide O (**17**) ^{1}H NMR (600 MHz, DMSO-d_6)



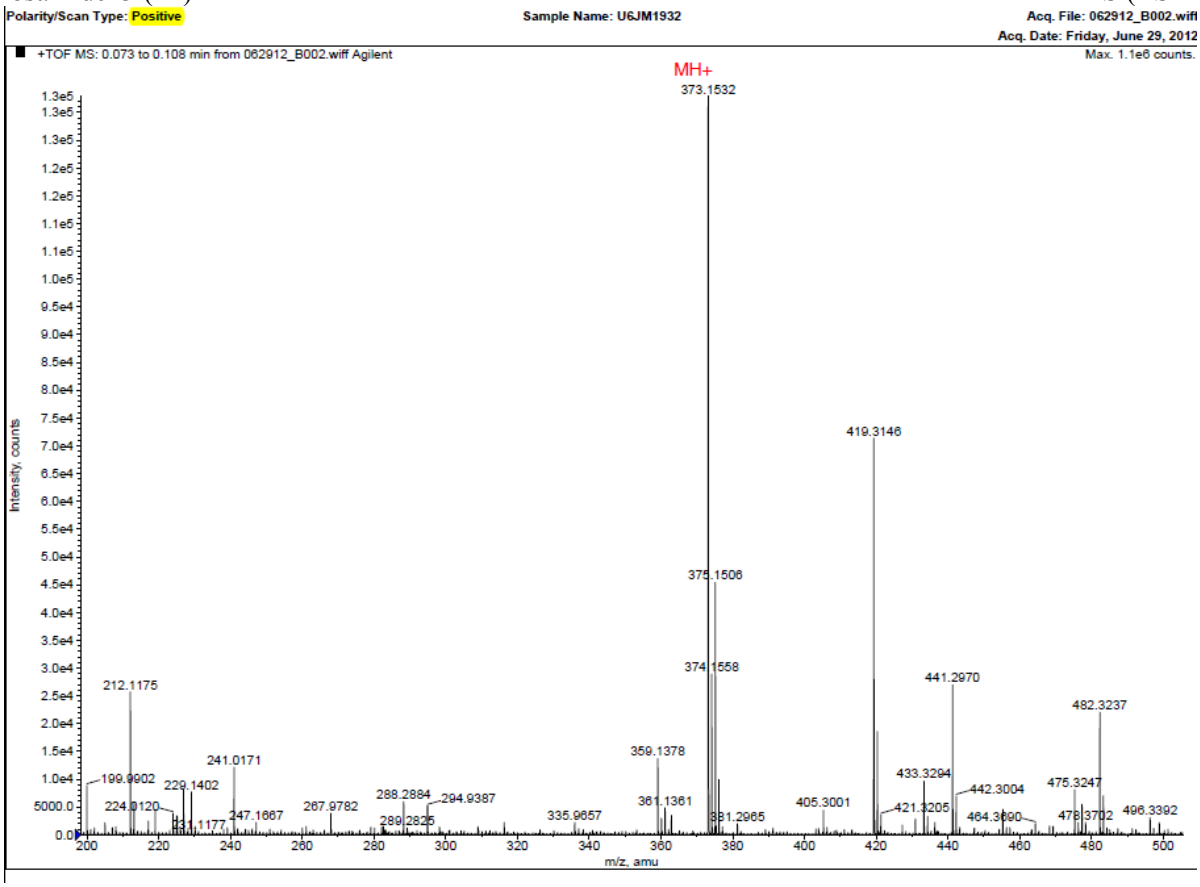
Ammosamide O (**17**)

^{13}C NMR (100 MHz, DMSO-*d*$_6$)

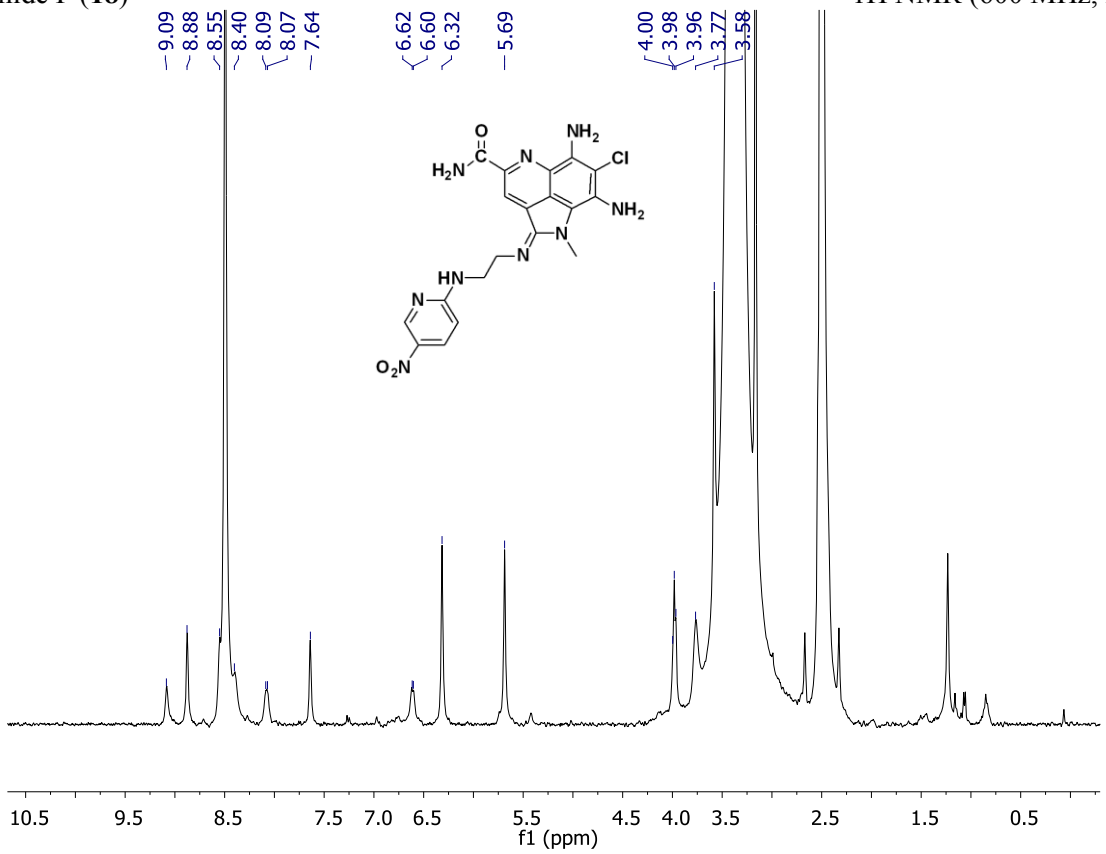


Ammosamide O (**17**)

HRMS (ESI-TOF)



Ammosamide P (**18**) 1H NMR (600 MHz, DMSO-d_6)



Ammosamide P (**18**) HRMS (ESI-TOF)