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1. Material and Methods

1.1. Nuclear Magnetic Resonance and High-Resolution Mass Spectrometry analyses

1D NMR spectra of monomers were recorded on a Bruker Avance II NMR spectrometer (Bruker BioSpin) operating at 300.18 MHz for ^1H observation and 75.48 MHz for ^{13}C observation equipped with a 5mm dual BBFO probe with gradient. 1D NMR spectra of oligomers were recorded on a Bruker Avance NEO NMR spectrometer (Bruker BioSpin) operating at 700.15 MHz for ^1H observation equipped with a 5mm TXI probe with gradient. All NMR experiments were performed at 273 K. Chemical shift values are given in ppm with reference to residual solvent signals: CDCl_3 ($\delta = 7.26$ and 77.2), DMSO-d_6 ($\delta = 2.50$ and 39.4) or to the reference signal of TMS ($\delta = 0.00$ for ^1H) from a $10\ \mu\text{M}$ solution of 3-(trimethylsilyl)-1-propanesulfonic acid sodium salt (TSP- d_4) in $\text{H}_2\text{O}/\text{D}_2\text{O}$ (95/5; v/v). ^1H NMR in $\text{H}_2\text{O}/\text{D}_2\text{O}$ (95/5) were performed with water suppression using an excitation sculpting element from the Bruker pulse program library (noesyfpgpphrs).

HRMS characterization of monomers was performed on an Agilent Technologies 6230 TOF LC/MS spectrometer. The instrument is equipped with an ESI source and experiment were recorded in positive mode. The spray voltage was maintained at 3500 V and the capillary temperature was set at $300\ ^\circ\text{C}$. Samples were introduced by injection through a $20\ \mu\text{L}$ sample loop into a $600\ \mu\text{L}\cdot\text{min}^{-1}$ flow of acetonitrile from the LC pump. HRMS characterizations of oligomers were performed on a Thermo Scientific Exactive Orbitrap spectrometer. The instrument is equipped with an ESI source and experiment were recorded in positive or negative mode. The spray voltage was maintained at 3500 V and capillary temperature set at $220\ ^\circ\text{C}$. Sample were injected in the ESI source using a $250\ \mu\text{L}$ Hamilton syringe at $6\ \mu\text{L}\cdot\text{min}^{-1}$ flow.

1.2. High Performance Liquid Chromatography

HPLC analyses and purification were performed on reverse phase C18 column on Jasco Extrema analytical and preparative systems. Mobile phases were composed of milli-Q water + 0.1% TFA (solvent A) and Acetonitrile + 0.1% TFA (solvent B) for monomers and cationic oligomers. And milli-Q water + triethylammonium acetate buffer (pH = 8.7, solvent A') and Acetonitrile + triethylammonium acetate buffer (pH = 8.7, solvent B') for anionic oligomers. Analyses were done using the following gradient: (0 min): 95 % A, 5 % B then (2 min): 95 % A, 5 % B then (12 min): 0 % A, 100 % B then (15 min): 0 % A, 100 % B.

1.3. Electronic absorption and fluorescence emission

UV-visible absorption spectra were recorded on a UV-1650PC Shimadzu spectrophotometer using a 1 cm pathlength quartz cuvette.

Steady-state emission spectra were recorded on a Horiba Jobin-Yvon Fluorolog-3 spectrofluorometer fitted with a PMT detector and exciting with a 450 W Xe-lamp across a double monochromator and were corrected for instrumental response. The fluorescence and reaction quantum yield were determined in air-equilibrated solutions as follows. The luminescence quantum yield (Φ) was calculated by using the equation $\Phi = \Phi_r(I/I_r)(A_r/A)(\eta^2/\eta_r^2)$ in which Φ_r refers to the quantum yield reference, I is the integrated emission intensity, A is the absorbance at the excitation wavelength and η is the refractive index of the solvent.¹ An optically dilute solution of quinine sulphate ($\lambda_{\text{exc}} = 365\ \text{nm}$) in 1N sulphuric acid was used as the standard, $\Phi_r = 0.54$.

1.4. Circular dichroism and circular polarized luminescence

¹ D. E. Eaton, Handbook of Organic Photochemistry, Vol 1; J. C. Scaiano, Ed.; CRC : Boca Raton, FL, 1989.

CD spectra were recorded on a JASCO J-815 spectropolarimeter using a 1 cm pathlength quartz cuvette. CPL spectra were recorded on a CPL-300 spectrophotometer using a 1 cm pathlength quartz cuvette.

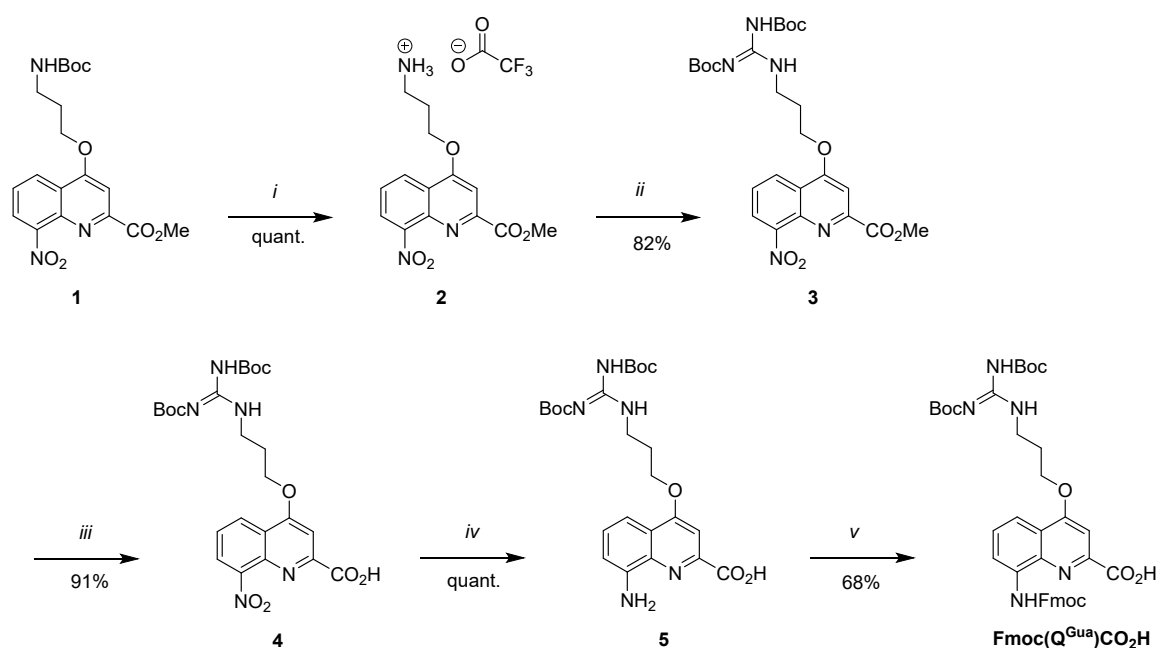
2. Methods for chemical synthesis

Commercial reagents were purchased from Sigma-Aldrich, Alfa-Aesar or TCI and used without further purification. Low-loading ProTide resin was purchased from CEM. Chloroform (CHCl₃), Triethylamine (TEA) and *N,N*-diisopropylethylamine (DIEA) were distilled over calcium hydride prior to use. Dry organic solvents: Tetrahydrofuran (THF) and dichloromethane (DCM), used for solution and solid phase synthesis, were dispensed from a solvent purification system that passes solvents through packed column of dry neutral alumina. Milli-Q water was delivered from a PureLab Prima 7/15/20 system.

2.1. Monomer synthesis

The synthesis of **Fmoc(Q^{Orn})CO₂H** and **Fmoc(Q^{Pho})CO₂H** were performed following reported procedure.^{2,3}

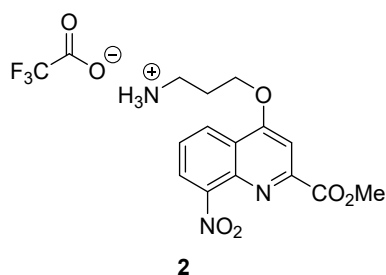
Synthesis of **Fmoc(Q^{Gua})CO₂H**.



Scheme S1: Fmoc(Q^{Gua})CO₂H monomer synthesis. *i*) DCM/TFA, *ii*) *N,N'*-Bis(*tert*-butoxycarbonyl)-1H-pyrazole-1-carboxamidine, DIEA, DCM, *iii*) NaOH, THF/H₂O, *iv*) Pd/C, EtOAc, *v*) Fmoc chloride, NaHCO₃, Dioxane/H₂O.

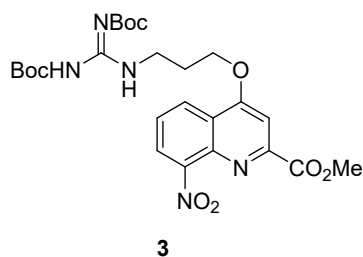
² Vallade M., Sai Reddy P., Fischer L., Huc I., Enhancing aromatic foldamer helix dynamics to probe interactions with protein surfaces, *Eur. J. Org. Chem.*, **2018**, 5489.

³ Corvaglia V., Carbajo D., Prabhakaran P., Ziach K., Mandal P.K., Dos Santos V., Legeay C., Vogel R., Parissi V., Pourquier P., Huc I., Carboxylate-functionalized foldamer inhibitors of HIV-1 integrase and Topoisomerase 1: artificial analogues of DNA mimic proteins, *Nucleic Acids Res.*, **2019**, *47*, 5511.



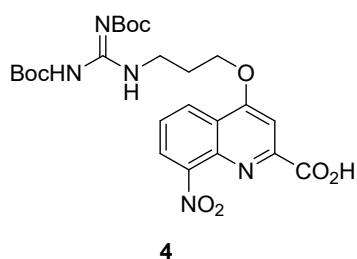
Monomer 2. Compound **1** (3 g, 7.4 mmol) was dissolved in 20 mL of dichloromethane/TFA (1:1; v/v) and stirred for 1.5 h at room temperature. Solvents were evaporated under reduced pressure and the excess of TFA was co-evaporated three times with toluene. The resulting residue was frozen in acetonitrile and freeze-dried. Compound **2** was obtained as a yellow solid (3.1g, quantitative yield).

^1H NMR (300MHz, DMSO- d_6): δ 8.50 (dd, 1H, $^3J_{\text{H-H}} = 8.4$ Hz and $^4J_{\text{H-H}} = 1.3$ Hz), 8.36 (dd, 1H, $^3J_{\text{H-H}} = 7.4$ Hz and $^4J_{\text{H-H}} = 1.3$ Hz), 7.75-7.90 (m, 3H), 7.68 (s, 1H), 4.50 (t, 2H, $^3J_{\text{H-H}} = 5.9$ Hz), 3.95 (s, 3H), 3.10 (t, 2H, $^3J_{\text{H-H}} = 7.0$ Hz), 2.20 (q, 2H, $^3J_{\text{H-H}} = 6.4$ Hz). ^{13}C NMR (75 MHz, DMSO- d_6) δ 165.3, 162.7, 151.4, 148.8, 139.2, 127.5, 126.2, 125.0, 122.7, 103.2, 67.1, 53.5, 36.7, 26.9. HRMS (ESI $^+$) m/z 306.1086 [M] $^+$ (calc. 306.1084 for $\text{C}_{14}\text{H}_{16}\text{N}_3\text{O}_5^+$).



Monomer 3. Compound **2** (2 g, 5 mmol, 1 equiv.) was suspended in 20 mL of dichloromethane. N,N' -bis(*tert*-butoxycarbonyl)-1H-pyrazole-1-carboxamide (3 g, 10 mmol, 2 equiv.) and DIEA (5 mL, 30 mmol, 6 equiv.) were added. The reaction mixture was stirred overnight. After evaporation of the solvent under reduced pressure the crude oil was purified by silica gel chromatography (cyclohexane/ethyl acetate 9:1; v/v) yielding **3** as a white solid (2.26 g, 82 % yield).

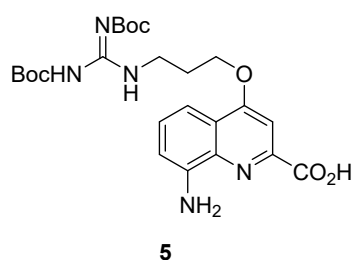
^1H NMR (300MHz, CDCl_3): δ 11.53 (s, 1H), 8.50-8.57 (m, 2H), 8.13 (dd, 1H), $^3J_{\text{H-H}} = 7.4\text{Hz}$ and $^4J_{\text{H-H}} = 1.3$ Hz), 7.63-7.71 (m, 2H), 4.44 (t, 2H, $^3J_{\text{H-H}} = 6.0$ Hz), 4.06 (s, 3H), 3.77 (td, 2H, $^3J_{\text{H-H}} = 6.4$ Hz and $^3J_{\text{H-H}} = 5.6$ Hz), 2.32 (qu, 2H, $^3J_{\text{H-H}} = 6.4$ Hz), 1.45 (s, 18H). ^{13}C NMR (75 MHz, CDCl_3) δ 165.6, 163.5, 162.5, 156.4, 153.4, 151.3, 148.4, 140.1, 126.6, 126.0, 125.2, 123.2, 102.2, 83.4, 79.5, 67.3, 53.4, 38.0, 28.6, 28.3, 28.1, 26.9. HRMS (ESI $^+$) m/z 548.2354 [$\text{M}+\text{H}$] $^+$ (calc. 548.2351 for $\text{C}_{25}\text{H}_{34}\text{N}_5\text{O}_9^+$).



Monomer 4. Compound **3** (2.3 g, 4.1 mmol, 1 equiv.) was dissolved in THF (50 mL) and NaOH (470 mg, 10.3 mmol, 2.5 equiv.) dissolved in 10 mL of water was added. The reaction medium was vigorously stirred at room temperature for 30 min. Then water was added (20 mL) and the mixture was acidified with a 5 % citric acid solution (m/v). The aqueous phase was extracted with dichloromethane

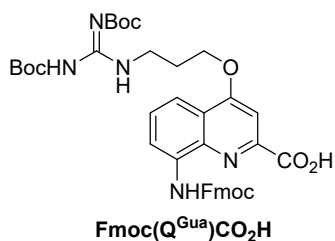
and washed with water and brine. The organic layers were combined, dried with MgSO_4 , filtered and evaporated under reduced pressure yielding **4** as a white solid (2.0 g, 91 % yield).

^1H NMR (300MHz, CDCl_3): δ 11.53 (s, 1H), 8.60 (dd, 1H, $^3J_{\text{H-H}} = 8.5$ Hz and $^4J_{\text{H-H}} = 1.4$ Hz), 8.54 (t, 1H, $^3J_{\text{H-H}} = 5.3$ Hz), 8.26 (dd, 1H, $^3J_{\text{H-H}} = 7.6$ Hz and $^4J_{\text{H-H}} = 1.4$ Hz), 7.71-7.80 (m, 2H), 4.49 (t, 2H, $^3J_{\text{H-H}} = 5.9$ Hz), 3.78 (td, 2H, $^3J_{\text{H-H}} = 6.4$ Hz and $^3J_{\text{H-H}} = 5.3$ Hz), 2.34 (qu, 2H, $^3J_{\text{H-H}} = 6.3$ Hz), 1.50 (s, 9H), 1.47 (s, 9H). ^{13}C NMR (75 MHz, CDCl_3) δ 164.0, 163.6, 163.5, 156.5, 153.4, 149.4, 147.1, 138.4, 127.4, 126.6, 126.2, 123.6, 100.3, 83.4, 79.5, 67.9, 37.8, 28.6, 28.2, 28.1. HRMS (ESI⁺) m/z 534.2207 [M+H]⁺ (calc. 534.2195 for $\text{C}_{24}\text{H}_{32}\text{N}_5\text{O}_9^+$).



Monomer 5. Compound **4** (2 g, 3.8 mmol, 1 equiv.) was dissolved in ethyl acetate (80 mL) and flushed with N_2 gas. Pd/C (10 % w/w, 200 mg) was added, and the reaction mixture was vigorously stirred overnight at 40 °C under H_2 atmosphere. Dichloromethane was added and the mixture was filtered over celite. Solvent were evaporated under reduced pressure yielding **5** as a yellow solid (1.9 g, quantitative yield).

^1H NMR (300 MHz, CDCl_3): δ 11.53 (s, 1H), 8.53 (t, 1H, $^3J_{\text{H-H}} = 4.6$ Hz), 7.57-7.63 (m, 2H), 7.44 (t, 1H, $^3J_{\text{H-H}} = 7.7$ Hz), 7.04 (dd, 1H, $^3J_{\text{H-H}} = 7.6$ Hz and $^4J_{\text{H-H}} = 1.0$ Hz), 4.38 (t, 2H, $^3J_{\text{H-H}} = 5.8$ Hz), 3.75 (td, 2H, $^3J_{\text{H-H}} = 6.5$ Hz and $^3J_{\text{H-H}} = 5.7$ Hz), 2.29 (qu, 2H, $^3J_{\text{H-H}} = 6.4$ Hz), 1.50 (s, 18H). ^{13}C NMR (75 MHz, CDCl_3) δ 164.7, 163.6, 163.5, 156.4, 153.4, 144.6, 143.6, 136.5, 129.1, 123.3, 112.3, 110.6, 98.9, 83.3, 79.4, 66.9, 38.0, 28.7, 28.3, 28.1. HRMS (ESI⁺) m/z 504.2454 [M+H]⁺ (calc. 504.2453 for $\text{C}_{24}\text{H}_{33}\text{N}_5\text{O}_7^+$).

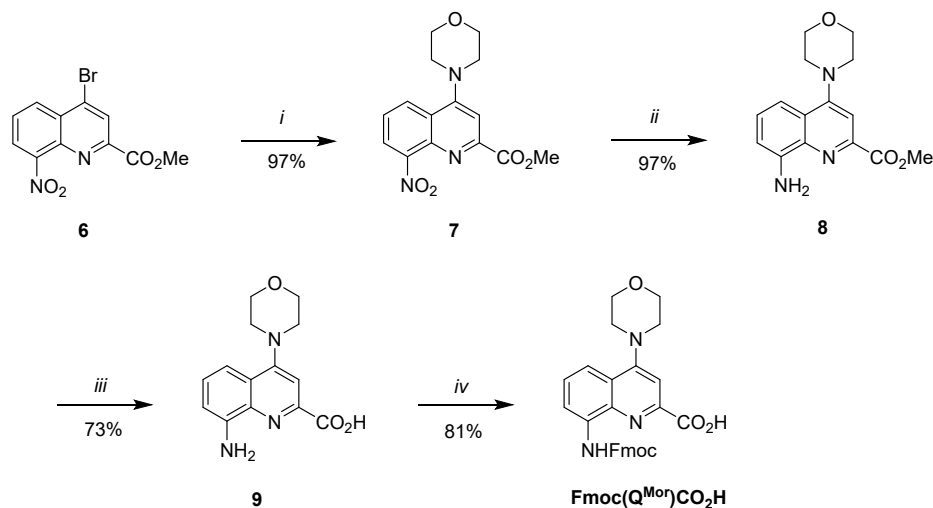


Monomer Fmoc(Q^{Gua})CO₂H. Compound **5** (1.9 g, 3.7 mmol, 1 equiv.) was dissolved in dioxane (67 mL) then NaHCO_3 (6.7 g, 79.7 mmol, 21 equiv.) dissolved in 67 mL of water was added. Fmoc-Cl (1.2 g, 4.8 mmol, 1.3 equiv.) in 22 mL of dioxane was added dropwise and the reaction mixture was stirred overnight at room temperature. Water was added and the mixture was acidified with citric acid 5 % (m/v). to pH = 3-4. Dichloromethane was added and the aqueous phase was extracted with dichloromethane and washed with water and brine. The organic layers were combined, dried with MgSO_4 , filtered and evaporated under reduced pressure. The crude solid was purified by silica gel chromatography (dichloromethane/MeOH) giving the title compound as a yellow solid (1.8 g, 68 % yield).

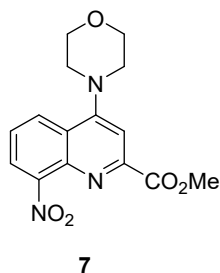
^1H NMR (300MHz, DMSO-d_6): δ 13.51 (s, 1H), 11.47 (s, 1H), 10.45 (s, 1H), 8.50 (t, 1H, $^3J_{\text{H-H}} = 5.3$ Hz), 8.33 (brs, 1H), 7.93 (d, 1H, $^3J_{\text{H-H}} = 7.4$ Hz), 7.76-7.86 (m, 3H), 7.54-7.63 (m, 2H), 7.44 (t, 2H, $^3J_{\text{H-H}} = 7.3$ Hz), 7.36 (td, 2H, $^3J_{\text{H-H}} = 7.3$ Hz and $^4J_{\text{H-H}} = 1.1$ Hz), 4.61 (d, 2H, $^3J_{\text{H-H}} = 6.6$ Hz), 4.37-4.47 (m, 3H), 3.57 (q, 2H, $^3J_{\text{H-H}} = 6.3$ Hz), 2.15 (qu, 2H, $^3J_{\text{H-H}} = 5.9$ Hz), 1.43 (s, 9H), 1.33 (s, 9H). ^{13}C NMR (75 MHz,

CDCl₃) δ 165.1, 163.5, 156.5, 153.3, 146.0, 143.7, 141.4, 137.5, 134.5, 128.7, 127.9, 127.3, 124.9, 122.4, 120.1, 117.3, 115.5, 100.0, 83.4, 79.5, 67.4, 67.1, 47.1, 38.1, 28.6, 28.3, 28.0. HRMS (ESI⁺) m/z 726.3133 [M+H]⁺ (calc. 726.3134 for C₃₉H₄₃N₅O₉⁺).

Synthesis of Fmoc(Q^{Mor})CO₂H.

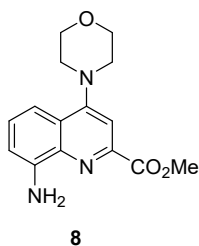


Scheme S2: Fmoc(Q^{Mor})CO₂H monomer synthesis. *i*) Morpholine, TEA, THF; *ii*) Pd/C, EtOAc; *iii*) KOH, Dioxane; *iv*) Fmoc chloride, NaHCO₃, dioxane/H₂O.



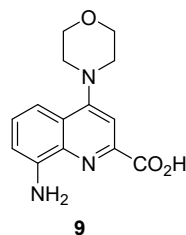
Monomer 7. Compound **6** (300 mg, 0.97 mmol, 1 equiv.) was introduced in a Schlenk flask under nitrogen and dissolved in a mixture of dry triethylamine (2.5 mL) and dry THF (5 mL). Freshly distilled morpholine (1.42 mL, 16.7 mmol, 17 equiv.) was added to the solution and the reaction was allowed to stir at 85 °C overnight. After evaporation of the solvent, the residue was dissolved in dichloromethane, washed with 5 % NH₄Cl solution (*m/v*) and pure water. The organic phases were dried over MgSO₄, filtered and the solvents were removed under reduced pressure to dryness to obtain **7** as a yellow solid (300 mg, 97 % yield).

¹H NMR (CDCl₃, 300 MHz) δ 8.24 (dd, 1H, ³J_{H-H} = 8.8 Hz, ⁴J_{H-H} = 1.4 Hz), 8.03 (dd, 1H, ³J_{H-H} = 7.3 Hz, ⁴J_{H-H} = 1.4 Hz), 7.75 (s, 1H), 7.63 (m, 1H), 4.03 (s, 3H), 4.01 (m, 4H), 3.32 (m, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ 165.9, 158.2, 150.7, 140.9, 127.7, 125.8, 125.3, 124.3, 110.2, 66.8, 53.5, 52.9. HRMS (ESI⁺) m/z 340.0904 [M+Na]⁺ (calc. 340.0903 for C₁₅H₁₅O₅N₃Na).



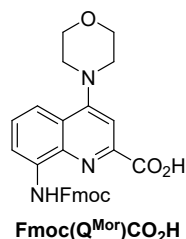
Monomer 8. To a solution of compound **7** (300 mg, 0.97 mmol, 1 equiv.) in degassed EtOAc (45 mL), 10 % Pd/C (10% w/w, 30 mg) was added at RT. The flask was evacuated, filled with hydrogen (1 atm.) and the resulting mixture was stirred overnight at RT. The reaction was monitored by ¹H NMR until completion. The solution was filtered through celite and washed with dichloromethane. The filtrate was evaporated under reduced pressure and the residue dried under vacuum to yield monomer amine **8** as a yellow solid (270 mg, 97 % yield).

¹H NMR (CDCl₃, 300 MHz) δ 7.61 (s, 1H), 7.38-7.26 (m, 2H), 6.89 (dd, 1H, ³J_{H-H} = 7.3 Hz, ⁴J_{H-H} = 1.4 Hz), 5.18 (s, 2H), 4.02 (s, 3H), 3.98 (m, 4H), 3.27 (m, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ 166.6, 157.6, 146.0, 145.3, 139.0, 128.7, 125.0, 111.4, 110.2, 109.0, 67.0, 52.9, 52.6. HRMS (ESI⁺) m/z 288.1340 [M+H]⁺ (calc. 288.1343 for C₁₅H₁₈O₃N₃⁺).



Monomer 9. Compound **8** (270 mg, 0.96 mmol, 1 eq.) was dissolved in a solvent mixture of dioxane/H₂O (14 mL, 6:1, v:v). KOH (161 mg, 2.88 mmol, 3 equiv.) was added to this mixture and the resulting slurry was vigorously stirred for 5 hours at RT. The excess of KOH was subsequently quenched by the addition of 5 % citric acid aqueous solution (m/v). After evaporation of dioxane under reduced pressure, the aqueous phase was extracted with dichloromethane. The organic layers were washed with water, dried over MgSO₄ and evaporated to dryness to obtain **9** as an orange solid (193 mg, 73 % yield).

¹H NMR (CDCl₃, 300 MHz) δ 7.70 (s, 1H), 7.40-7.34 (m, 2H), 6.96 (dd, 1H, ³J_{H-H} = 7.3 Hz, ⁴J_{H-H} = 1.4 Hz), 3.98 (m, 4H), 3.33 (m, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ 144.0, 137.2, 128.8, 112.3, 111.6, 106.8, 89.3, 66.8, 52.4. HRMS (ESI⁺) m/z 274.1183 [M+H]⁺ (calc. 274.1186 for C₁₄H₁₆O₃N₃⁺).



Monomer Fmoc(Q^{Mor})CO₂H. Monomer **9** (193 mg, 0.67 mmol, 1 equiv.) was dissolved in a solvent mixture with a solution of 10 % NaHCO₃ and dioxane (12.5 mL, 4:1; v:v). A solution of Fmoc chloride (207 mg, 0.80 mmol, 1.2 equiv.) in dioxane (10 mL) was added dropwise to the solution at 0 °C and the reaction mixture was stirred at 0 °C for 1 h. Then the reaction was allowed to proceed overnight at RT. The mixture was poured into water (60 mL) and a solution of 1M HCl was added until pH = 2. The aqueous phase was extracted with dichloromethane and the organic layers were washed with water, dried over MgSO₄ and evaporated. The residue was purified by chromatography (silica gel) eluting with dichloromethane/EtOAc (99:1; v:v) to obtain the title compound as a yellow solid (250 mg, 81 % yield). ¹H NMR (CDCl₃, 300 MHz) δ 7.75 (m, 3H), 7.64 (m, 3H), 7.50 (m, 2H), 7.39 (m, 2H), 7.29 (m, 2H), 4.63 (s, 2H), 4.36 (m, 1H), 3.98 (m, 4H), 3.31 (m, 4H). ¹³C NMR (CDCl₃, 75 MHz) δ 158.5, 143.8, 141.3, 138.7, 128.2, 127.9, 127.3, 124.9, 124.3, 120.1, 116.9, 116.3, 108.4, 66.9, 66.8, 52.5, 50.2, 49.9, 49.6, 49.3, 49.0, 48.7, 48.4, 47.2. HRMS (ESI⁺) m/z 518.1682 [M+Na]⁺ (calc. 518.1686 for C₂₉H₂₅O₅N₃Na).

2.2. Oligomer SPS and characterization

2.2.1. General procedures for oligomer synthesis

Resin grafting. On LL ProTide resin (0.17 mmol.g⁻¹), the first Fmoc(Q^R)CO₂H monomer (3 equiv.) was grafted using CsI (5 equiv.) and DIEA (6 equiv.) in dry DMF. The reaction mixture was shaken vigorously overnight. After reaction, the resin was filtered and washed three times with DMF and three times with dichloromethane.

Fmoc deprotection. The grafted resin was washed twice with DMF, suspended in a 20 % piperidine in DMF solution (4 mL) and slowly stirred for 3 min. Resin was then filtered, washed twice with DMF and suspended again in a 20 % piperidine in DMF solution and stirred for 7 min. The resin was then filtered and washed three times with DMF and three times with dry THF.

In situ coupling procedure. The resin was suspended in dry THF and collidine (9 equiv.) was added. A solution of Fmoc(Q^X)CO₂H monomer (3 equiv.), PPh₃ (8 equiv.) and TCAN (9 equiv.) in dry CHCl₃ was added on the resin. The reaction was assisted by microwave irradiation (25W, 50 °C) for 15 min. and repeated once. After reaction, the resin was filtered and washed with dry THF and DMF.

Acid chloride coupling procedure. The resin was suspended in dry THF and DIEA (6 equiv.) was added. Fmoc(Q^X)COCl monomer (3 equiv., scheme S3) was dissolved in dry THF and added to the resin. The reaction was assisted by microwave irradiation (50W, 50 °C) for 15 minutes and repeated once. Resin was then filtered and washed with dry THF and DMF.

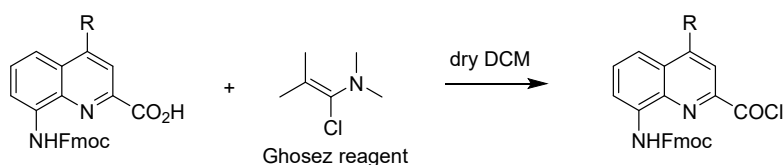
Resin cleavage. The resin was washed three times with DMF and three times with dichloromethane and was suspended in a solution of TFA/TIPS/H₂O, 95:2.5:2.5 (v/v/v). The mixture was vigorously stirred for 4 h. The resin was filtered and the filtrate was evaporated under reduced pressure. The residual solid was suspended in Et₂O and centrifuged at 4 °C for 5 min. Et₂O was removed and the yellow solid was dried under vacuum and then freeze-dried.

Preparative HPLC purification. For sequences containing Q^{Orn} and Q^{Gua} monomers. Crude compounds were purified using solvents A and B. The following gradient was used: (0 min): 95 % A, 5 % B then (2 min): 95 % A, 5 % B then (22 min): 0 % A, 100 % B then (27 min): 0 % A, 100 % B. Collected fractions were analyzed by analytic HPLC and the relevant ones were combined and freeze-dried twice to remove the excess of TFA.

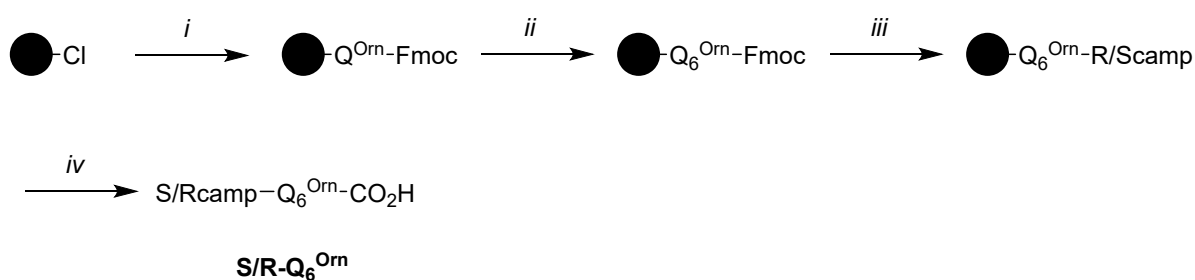
For sequences containing Q^{Pho} monomers. Crude compounds were purified using solvents A' and B'. The following gradient was used: (0 min): 95 % A, 5 % B then (2 min): 95 % A, 5 % B then (22 min): 0 % A, 100 % B then (27 min): 0 % A, 100 % B. Collected fractions were analyzed by analytic HPLC and the relevant ones were combined and freeze-dried twice to remove the excess of triethylammonium acetate.

Ion exchange procedure. Only for sequences containing Q^{Pho} monomers. Exchange of triethylammonium with ammonium cations was performed using Dowex 50W X4 (200-400 Mesh) resin. A 24 mL syringe containing a filter was filled with Dowex resin. The resin preparation/regeneration consisted in washing with 5 volumes of 2 M HCl, then MilliQ water until a neutral pH is reached, then 5 volumes of 2 M NH₄OAc (bio-grade) and then with 5 volumes of MilliQ water. The resin must stay wet all the time. Compounds were introduced as solutions in 300-500 μL of MilliQ water (followed by 2 washings with 300-500 μL of water). Compounds were eluted from the column by washing with 10 mL of MilliQ water. The collected solutions were freeze dried, then remaining solids were dissolved in a small amount of water, transferred to a small vial, and freeze-dried again to afford the ammonium salts of the oligomers. The absence of triethyl-ammonium was confirmed by ¹H NMR. After regeneration, as described above, the resin was used again.⁴

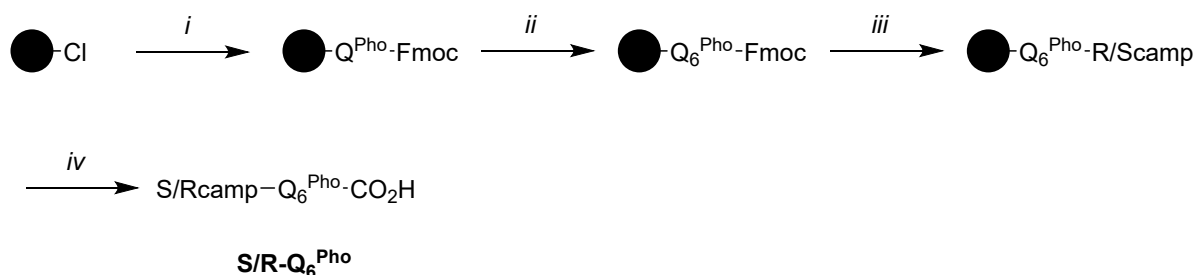
⁴ Ziach K., Chollet C., Parissi V., Prabhakaran P., Marchivie M., Corvaglia V., Bose P. P., Laxmi-Reddy K., Godde F., Schmitter J.-M., Chaignepain S., Pourquier P., Huc I. Single helically folded aromatic oligoamides that mimic the charge surface of double-stranded B-DNA. *Nat. Chem.*, **2018**, *10*, 511.



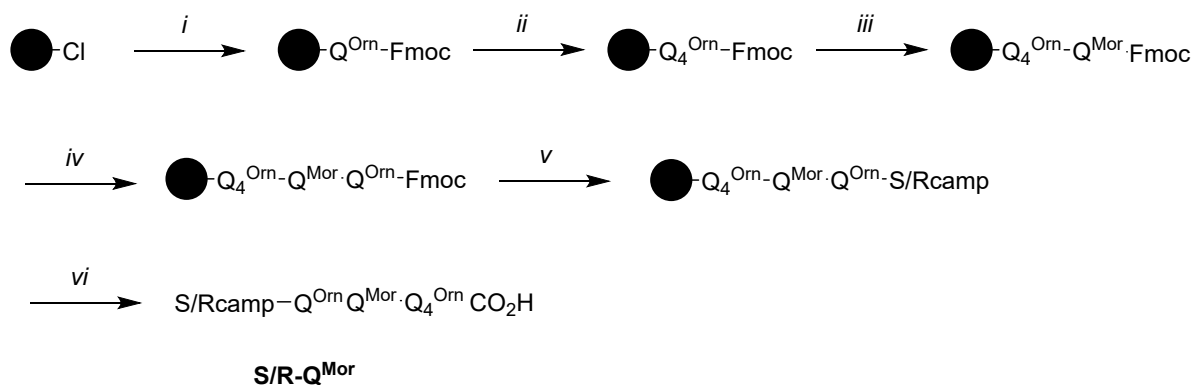
Scheme S3: Acid chloride preparation procedure. Fmoc(Q^X)CO₂H monomer (1 equiv.) was suspended in 1 mL of dry DCM and Ghosez reagent (2 equiv.) was added. The solution was stirred for 2 h, and competition was monitored by ¹H NMR. All volatiles were removed under a vacuum line yielding the corresponding acid chloride Fmoc(Q^X)COCl as a yellow solid (quantitative yield).



Scheme S4: Solid phase synthesis of chiral Q^{Orn} hexamers. *i*) Fmoc(Q^{Orn})CO₂H, CsI, DIEA, dry DMF. *ii*) 5 times [2x(Piperidine/DMF, 2:8; v/v), 2x(Fmoc(Q^{Orn})CO₂H, PPh₃, TCAN, Collidine)]. *iii*) 2x(Piperidine/DMF 2:8 (v/v)), 2x((1R/S)-(+/-)-camphanic acid, PPh₃, TCAN, Collidine). *iv*) TFA/TIPS/H₂O 95:2.5:2.5 (v/v/v).

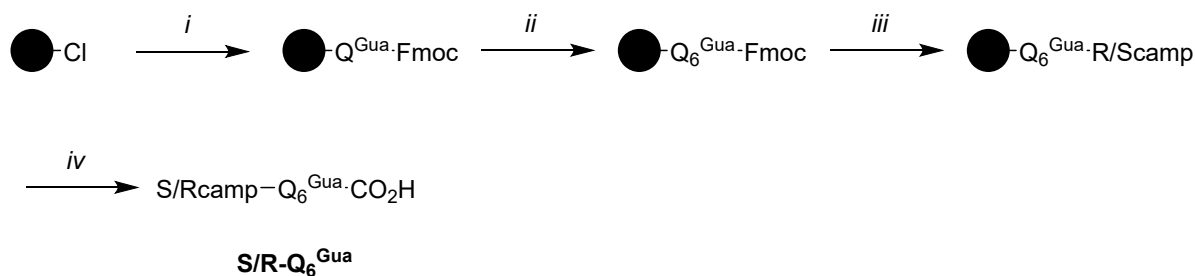


Scheme S5: Solid phase synthesis of chiral Q^{Pho} hexamers. *i*) Fmoc(Q^{Pho})CO₂H, CsI, DIEA, dry DMF. *ii*) 5 times [2x(Piperidine/DMF 2:8 v/v), 2x(Fmoc(Q^{Pho})CO₂H, PPh₃, TCAN, Collidine)]. *iii*) 2x(Piperidine/DMF 2:8 (v/v)), 2x((1R/S)-(+/-)-camphanic acid, PPh₃, TCAN, Collidine). *iv*) TFA/TIPS/H₂O 95:2.5:2.5 (v/v/v).



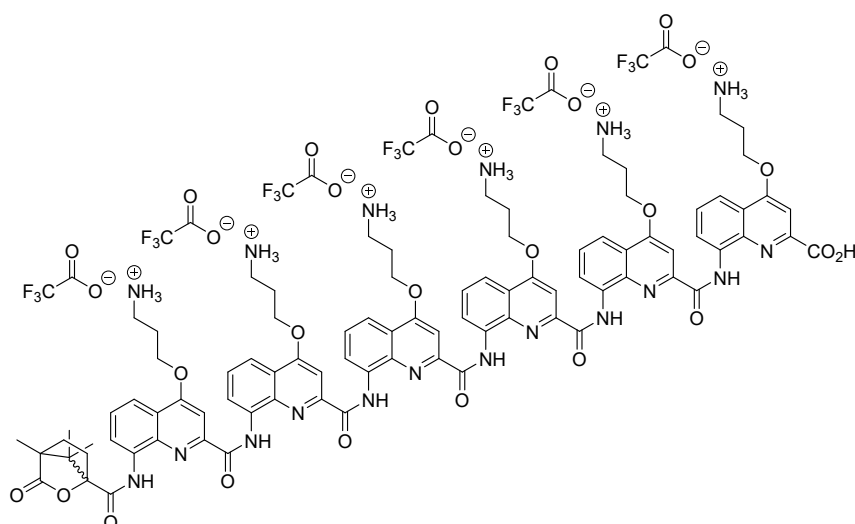
Scheme S6: Solid phase synthesis of chiral Q^{Mor} hexamers. *i*) Fmoc(Q^{Orn})CO₂H, CsI, DIEA, dry DMF. *ii*) 3

times [2x(Piperidine/DMF 2:8 v/v), 2x(Fmoc(Q^{Orn})CO₂H, PPh₃, TCAN, Collidine)]. *iii*) 2x(Piperidine/DMF 2:8 v/v), 2x(Fmoc(Q^{Mor})CO₂H, PPh₃, TCAN, Collidine). *iv*) 2x(Piperidine/DMF 2:8 v/v), 2x(Fmoc(Q^{Orn})CO₂H, PPh₃, TCAN, Collidine). *v*) 2x(Piperidine/DMF 2:8 (v/v)), 2x((1R/S)-(+/-)-camphanic acid, PPh₃, TCAN, Collidine). *vi*) TFA/TIPS/H₂O 95:2.5:2.5 (v/v/v).



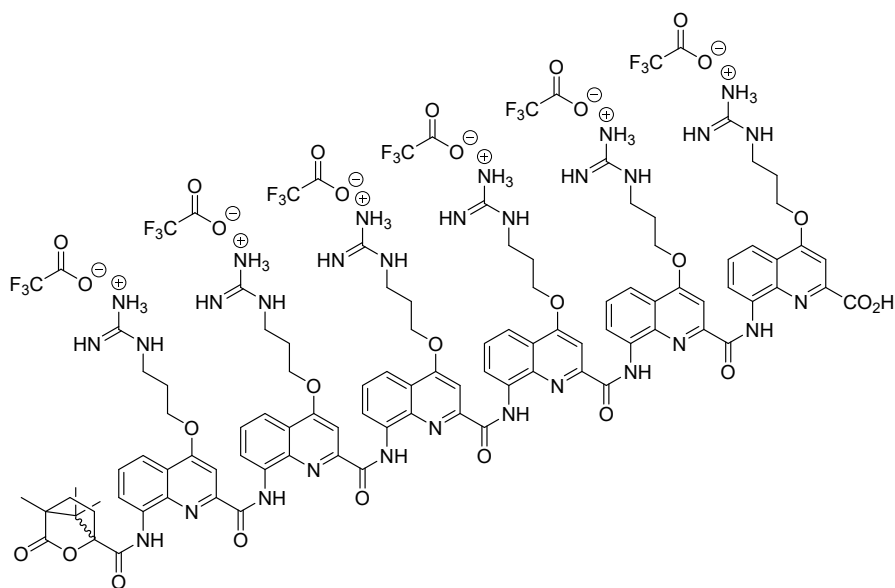
Scheme S7: Solid phase synthesis of chiral Q^{Gua} hexamers. *i*) Fmoc(Q^{Gua})CO₂H, CsI, DIEA, dry DMF. *ii*) 5 times [2x(Piperidine/DMF 2:8 v/v), 2x(Fmoc(Q^{Gua})COCl, DIEA)]. *iii*) 2x(Piperidine/DMF 2:8 (v/v)), 2x((1R/S)-(+/-)-camphanic chloride, DIEA). *iv*) TFA/TIPS/H₂O 95:2.5:2.5 (v/v/v).

2.2.2. Oligomer characterization



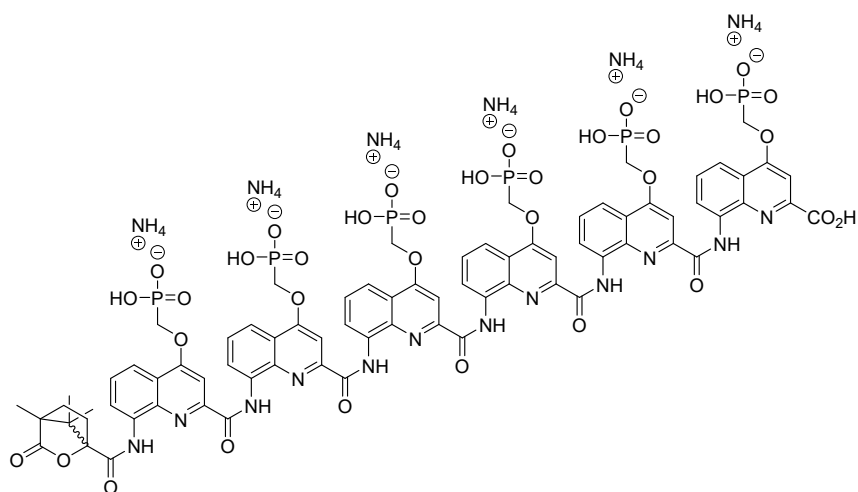
P/M-1: Synthesized on 17 μmol scale following *in situ* coupling procedure. The target compound was obtained as a light yellow solid after purification by preparative HPLC (15 mg for **P-1** and 16 mg for **M-1**, 57 % yield).

¹H NMR (700 MHz, H₂O/D₂O 95:5 (v/v), calibrated with TSP-d₄, ‘watergate’ water suppression applied at 4.76 ppm which may cause errors in the observed peak intensities in the vicinity of the suppressed peak): δ 11.85 (s, 1H), 11.84 (s, 1H), 11.73 (s, 1H), 11.48 (s, 1H), 11.32 (s, 1H), 9.62 (s, 1H), 8.55 (d, 1H, ³J_{H-H} = 7.49 Hz), 8.05-8.08 (m, 1H), 8.03 (d, 2H, ³J_{H-H} = 7.70 Hz), 7.94 (d, 1H, ³J_{H-H} = 7.98 Hz), 7.91 (d, 1H, ³J_{H-H} = 7.63 Hz), 7.89 (d, 1H, ³J_{H-H} = 7.21 Hz), 7.82-7.85 (m, 3H), 7.63-7.68 (m, 4H), 7.55-7.60 (m, 6H), 7.51-7.55 (m, 6H), 7.38-7.51 (m, 7H), 7.33 (s, 1H), 7.27-7.31 (m, 1H), 7.00 (s, 1H), 6.75 (s, 1H), 6.61 (s, 1H), 6.49 (s, 1H), 6.38 (s, 1H), 3.49-3.58 (m, 7H), 3.36-3.46 (m, 12H), 3.28 (t, 2H, ³J_{H-H} = 7.45 Hz), 2.46-2.57 (m, 6H), 2.30-2.46 (m, 7H), 0.80 (s, 3H), 0.60 (s, 3H), 0.56 (s, 3H). HRMS (ESI⁺) m/z 1657.7199 [M+H]⁺ (calc. 1657.7111 for C₈₈H₁₀₃N₁₈O₁₆⁺).



P/M-2: Synthesized on 23 μmol scale following the acid chloride coupling procedure. The target compound was obtained as a light yellow solid after purification by preparative HPLC (3.5 mg for both enantiomers, 7 % yield).

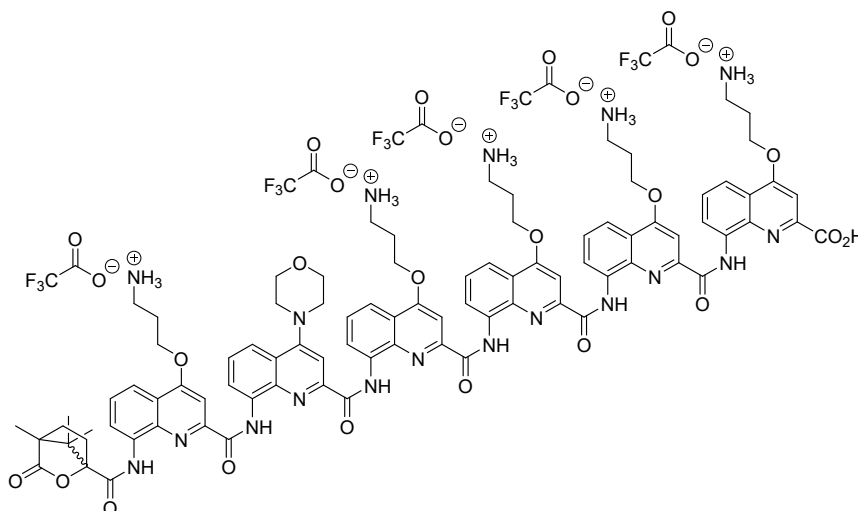
^1H NMR (700MHz, $\text{H}_2\text{O}/\text{D}_2\text{O}$ 95:5 (v/v), calibrated with TSP- d_4 , ‘watergate’ water suppression applied at 4.84 ppm which may cause errors in the observed peak intensities in the vicinity of the suppressed peak): 11.88 (s, 1H), 11.87 (s, 1H), 11.78 (s, 1H), 11.57 (s, 1H), 11.34 (s, 1H), 9.74 (s, 1H), 8.59 (d, 1H, $^3J_{\text{H-H}} = 7.4$ Hz), 8.17 (d, 1H, $^3J_{\text{H-H}} = 8.0$ Hz), 8.12 (d, 1H, $^3J_{\text{H-H}} = 7.9$ Hz), 8.08 (d, 1H, $^3J_{\text{H-H}} = 6.2$ Hz), 8.05 (d, 1H, $^3J_{\text{H-H}} = 8.1$ Hz), 8.01 (d, 1H, $^3J_{\text{H-H}} = 7.8$ Hz), 7.94-7.99 (m, 3H), 7.84-7.90 (m, 3H), 7.76 (d, 1H, $^3J_{\text{H-H}} = 6.4$ Hz), 7.59 (brs, 2H), 7.50-7.56 (m, 6H), 7.44-7.50 (m, 5H), 7.42 (brs, 1H), 7.39 (s, 2H), 7.31-7.35 (m, 2H), 7.18 (s, 1H), 7.11 (s, 2H), 7.03 (s, 1H), 6.84 (s, 1H), 6.71 (s, 1H), 6.56 (s, 1H), 6.46 (s, 1H), 3.46-3.86 (m, 30H), 3.18-3.23 (m, 6H), 2.44-2.60 (m, 10H), 2.32-2.44 (m, 13H), 2.19-2.32 (m, 6H), 1.99 (s, 2H), 1.29 (s, 3H), 1.29 (t, 9H, $^3J_{\text{H-H}} = 7.3\text{Hz}$). HRMS (ESI $^+$) m/z 955.4316 [$\text{M}+2\text{H}$] $^{2+}$ (calc. 955.4196 for $\text{C}_{94}\text{H}_{106}\text{N}_{30}\text{O}_{16}^{2+}$).



P/M-3: Synthesized on 8 μmol scale following the acid chloride coupling procedure. The target compound was obtained as a light yellow solid after purification by preparative HPLC (12 mg for both enantiomers, 80 % yield).

^1H NMR (700 MHz, $\text{H}_2\text{O}/\text{D}_2\text{O}$ 95:5 (v/v) + 50mM NH_4HCO_3 buffer, calibrated with TSP- d_4 , ‘watergate’ water suppression applied at 4.82 ppm which may cause errors in the observed peak intensities in the

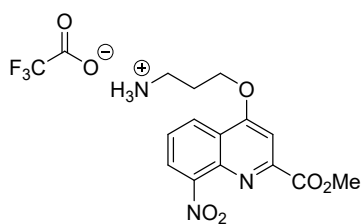
vicinity of the suppressed peak): δ 11.86 (s, 2H), 11.82 (s, 1H), 11.64 (s, 1H), 11.36 (s, 1H), 9.79 (s, 1H), 8.67 (d, 1H, $^3J_{\text{H-H}}=7.49$ Hz), 8.36 (d, 1H, $^3J_{\text{H-H}}=8.26$ Hz), 8.30 (d, 1H, $^3J_{\text{H-H}}=8.33$ Hz), 8.24 (d, 1H, $^3J_{\text{H-H}}=8.05$ Hz), 8.19 (d, 1H, $^3J_{\text{H-H}}=7.98$ Hz), 8.10-8.14 (m, 2H), 8.06 (d, 1H, $^3J_{\text{H-H}}=8.19$ Hz), 8.03 (d, 1H, $^3J_{\text{H-H}}=7.42$ Hz), 7.76 (t, 1H, 7.91 Hz), 7.78-7.80 (m, 1H), 7.59-7.68 (m, 5H), 7.54-7.56 (m, 1H), 7.48 (t, 1H, $^3J_{\text{H-H}}=7.8$ Hz), 7.43 (s, 1H), 7.18 (s, 1H), 6.82 (s, 1H), 6.73 (s, 1H), 6.52 (s, 1H), 6.46 (s, 1H), 4.38-4.46 (m, 0.4H), 4.31-4.36 (m, 0.8H), 4.28 (t, 0.5H, $^3J_{\text{H-H}}=9.94$ Hz), 4.21 (t, 0.6H, $^3J_{\text{H-H}}=9.87$ Hz), 4.10-4.16 (m, 2H), 3.98-4.02 (m, 1H), 3.92-3.96 (m, 1H), 3.16 (q, 2H, $^3J_{\text{H-H}}=7.35$ Hz), 2.01 (s, 1H), 1.92 (s, 6H), 1.25 (t, 4H, $^3J_{\text{H-H}}=7.35$ Hz), 0.67 (s, 3H), 0.64 (s, 3H), 0.16 (s, 3H). HRMS (ESI⁺) m/z 938,1170 [M-2H]²⁻ (calc. 938,1120 for C₇₆H₆₆N₁₂O₃₄P₆²⁻).



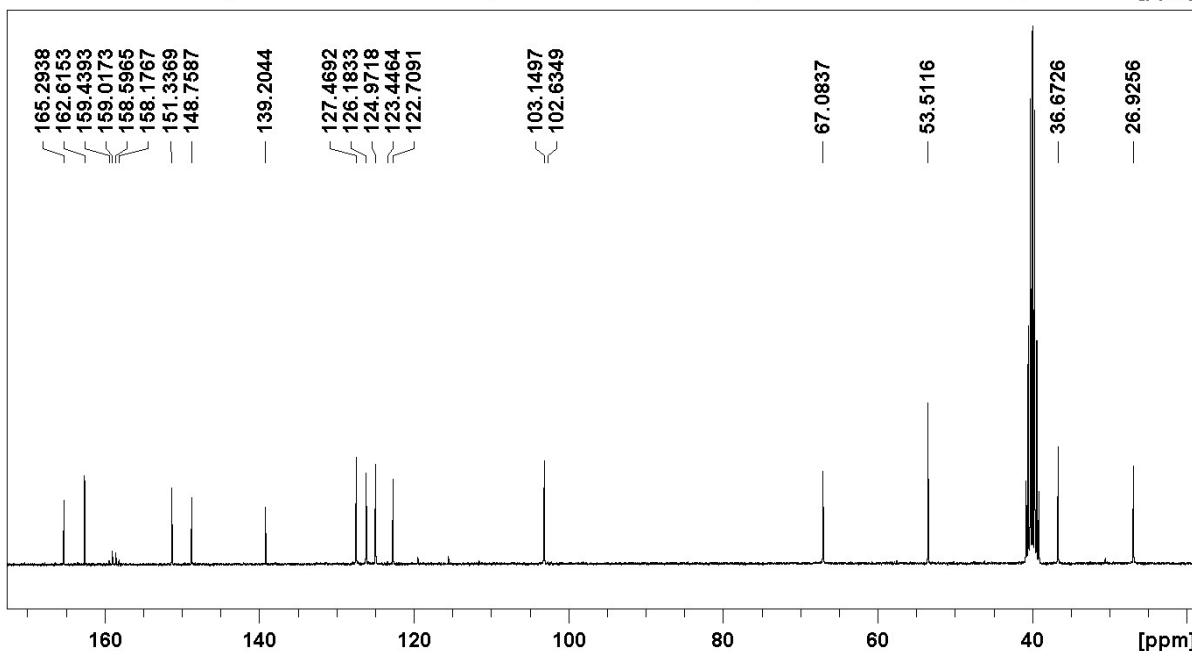
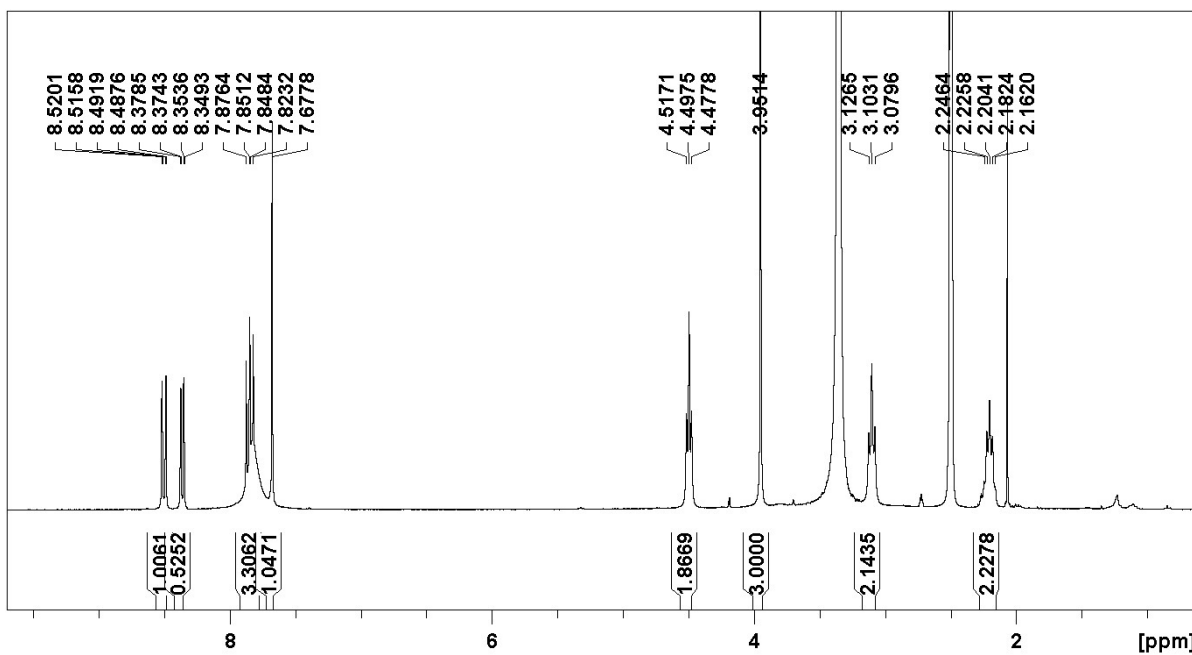
P/M-4: Synthesized on an 11 μmol scale following *in situ* coupling procedure. The target compound was obtained as a light yellow solid after purification by preparative HPLC (10 mg for both enantiomers, 66 % yield).

¹H NMR (700 MHz, H₂O/D₂O 95:5 (v/v), calibrated with TSP-d₄, ‘watergate’ water suppression applied at 4.87 ppm which may cause errors in the observed peak intensities in the vicinity of the suppressed peak): δ 11.92 (s, 1H), 11.91 (s, 1H), 11.77 (s, 1H), 11.64 (s, 1H), 11.43 (s, 1H), 9.73 (s, 1H), 8.60 (d, 1H, $^3J_{\text{H-H}}=7.56$ Hz), 8.14 (d, 1H, $^3J_{\text{H-H}}=7.98$ Hz), 8.11 (d, 1H, $^3J_{\text{H-H}}=7.28$ Hz), 7.95-8.02 (m, 4H), 7.93 (d, 1H, $^3J_{\text{H-H}}=8.12$ Hz), 7.87-7.90 (m, 2H), 7.71 (d, 1H, $^3J_{\text{H-H}}=5.18$ Hz), 7.47-7.58 (m, 8H), 7.37 (t, 1H, $^3J_{\text{H-H}}=7.7$ Hz), 7.13 (s, 1H), 6.87 (s, 1H), 6.57 (s, 1H), 6.46 (s, 1H), 3.70-3.77 (m, 3H), 3.55-3.69 (m, 7H), 3.42-3.53 (m, 6H), 3.35 (t, 3H, $^3J_{\text{H-H}}=7.49$ Hz), 3.21 (q, 2H, $^3J_{\text{H-H}}=7.42$ Hz), 2.38-2.64 (m, 12H), 2.30-2.37 (m, 1H), 2.07-2.12 (m, 1H), 1.93 (s, 1H), 1.82-1.87 (m, 1H), 1.76-1.82 (m, 1H), 1.29 (t, 5H, $^3J_{\text{H-H}}=7.35$ Hz), 0.66 (s, 3H), 0.65 (s, 3H), 0.16 (s, 3H). HRMS (ESI⁺) m/z 1669.7181 [M+H]⁺ (calc. 1669.7011 for C₈₉H₉₃N₁₈O₁₆⁺).

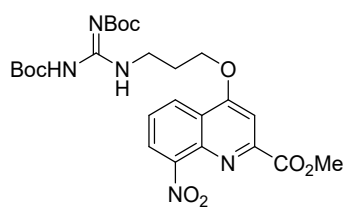
3. NMR, HR-Mass spectra and Chromatograms



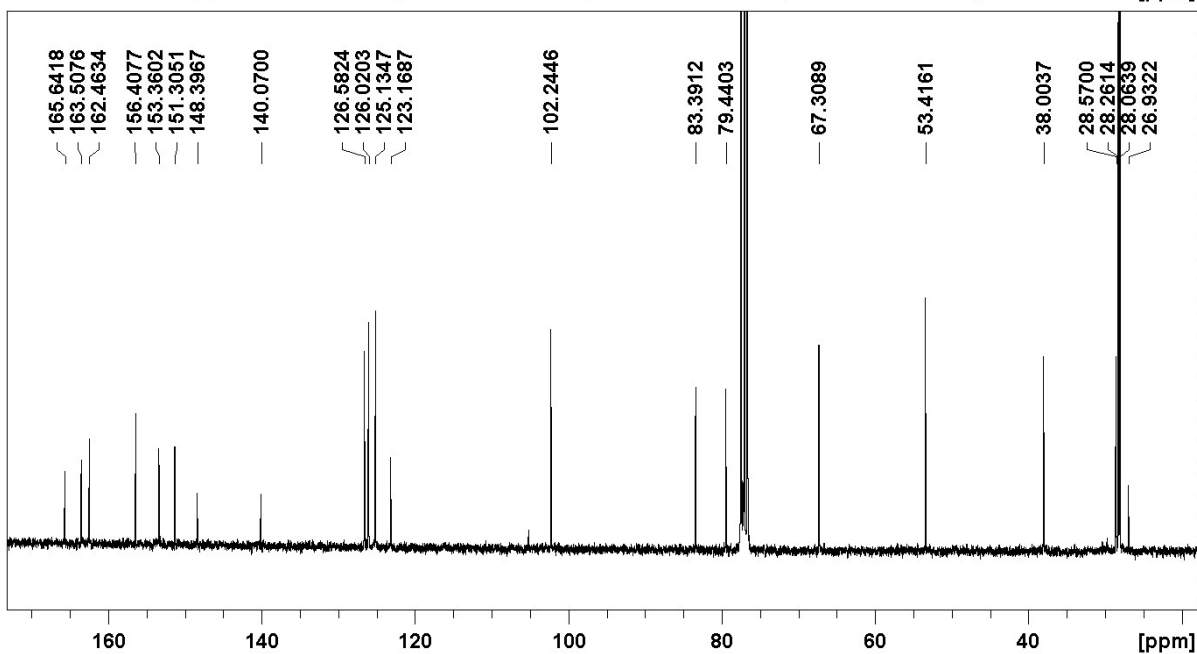
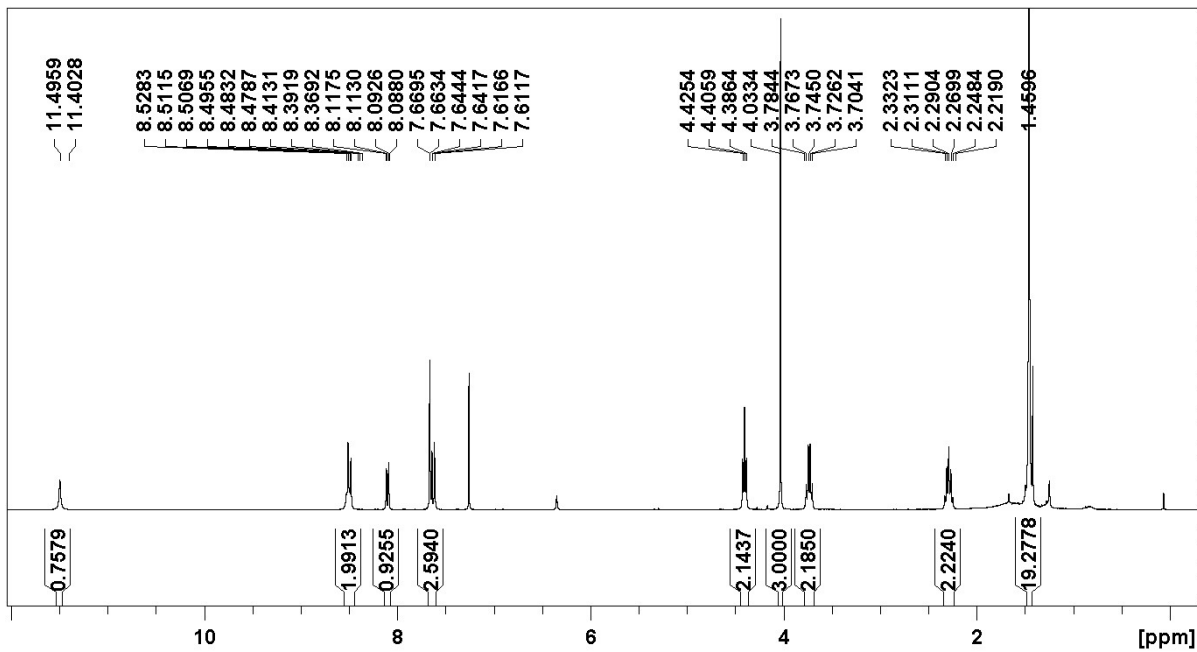
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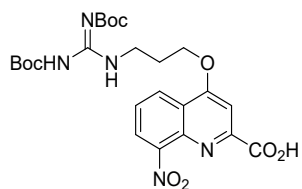


Monomer 3

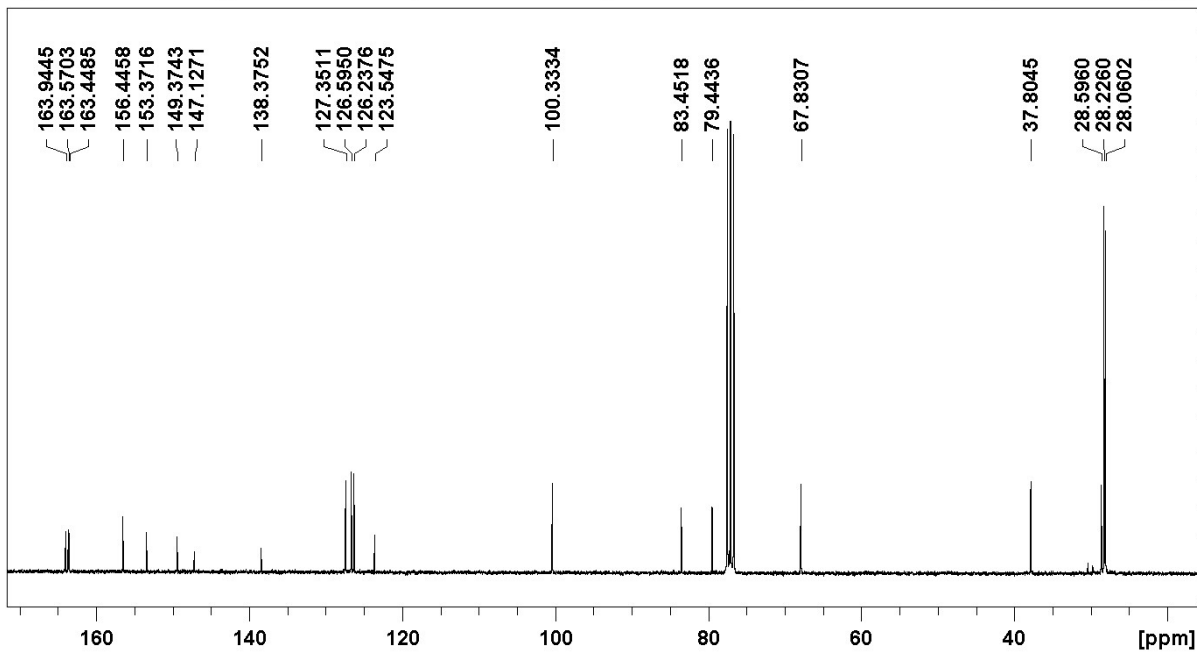
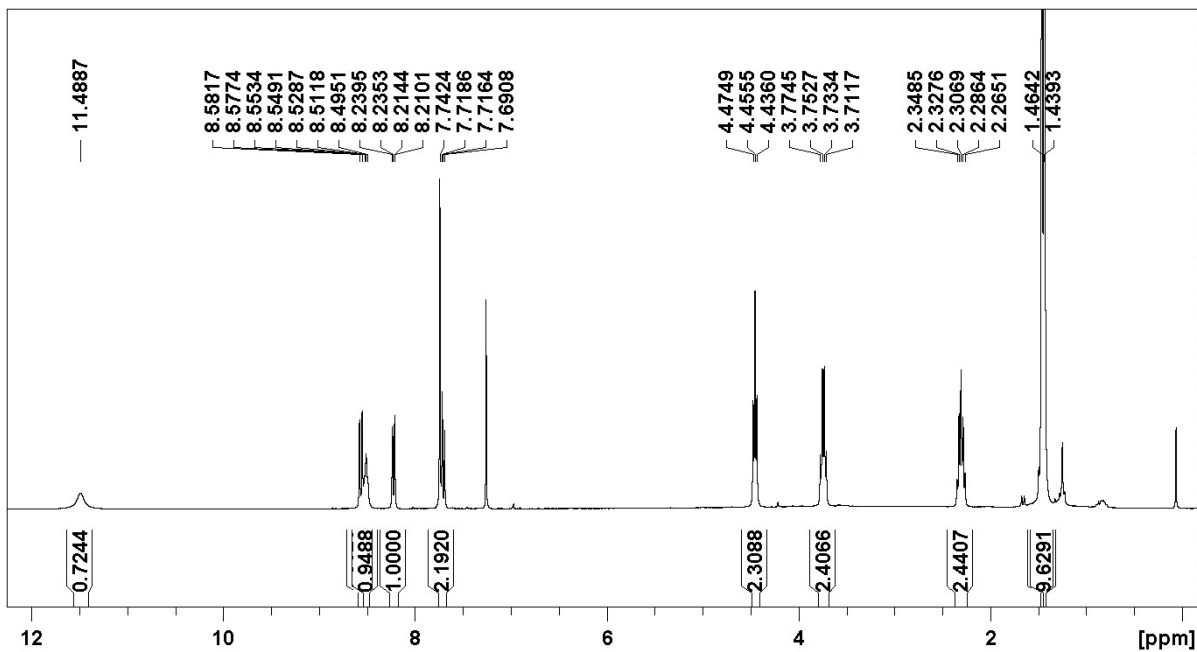


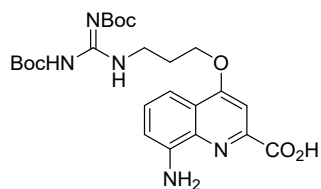
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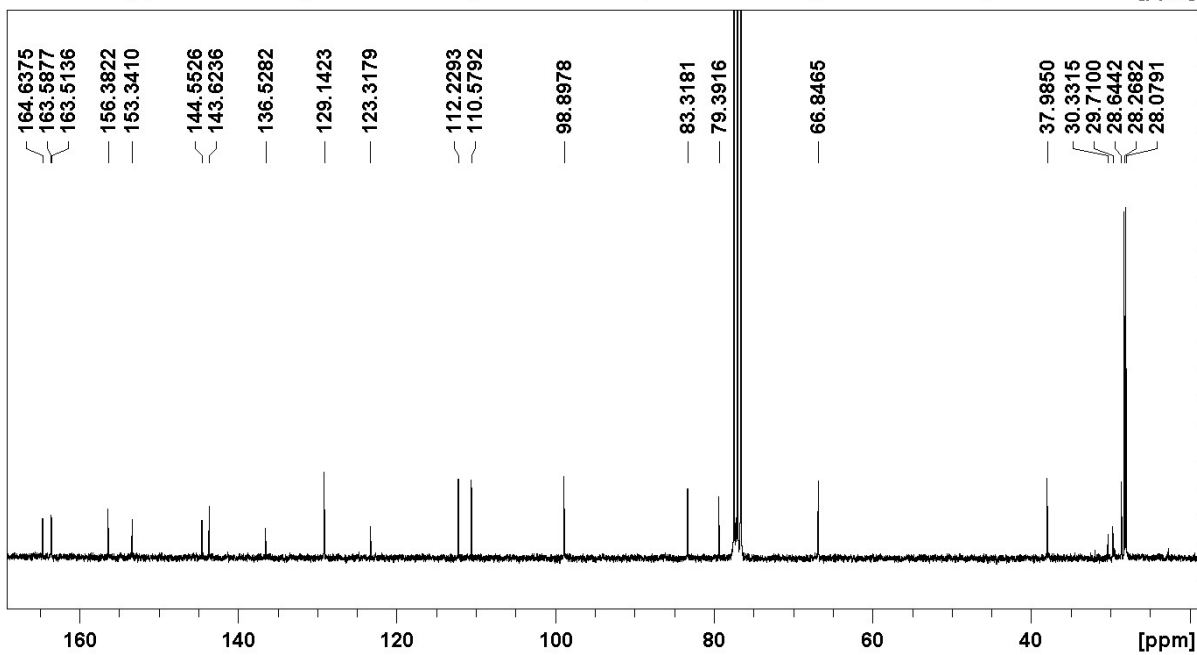
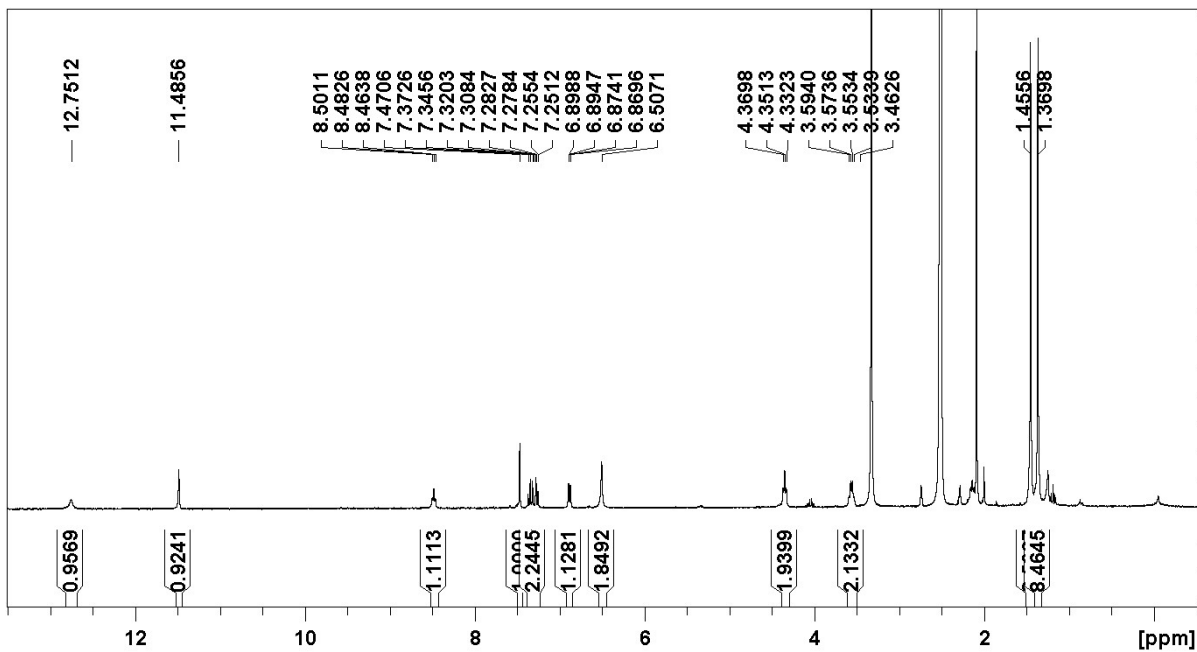


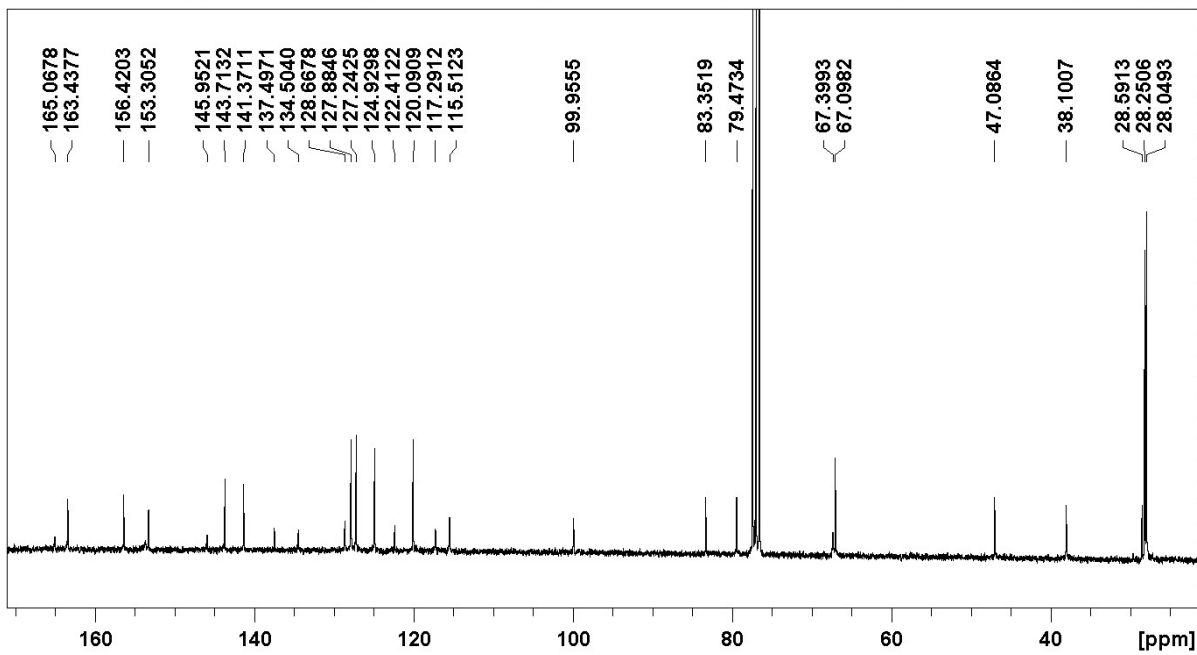
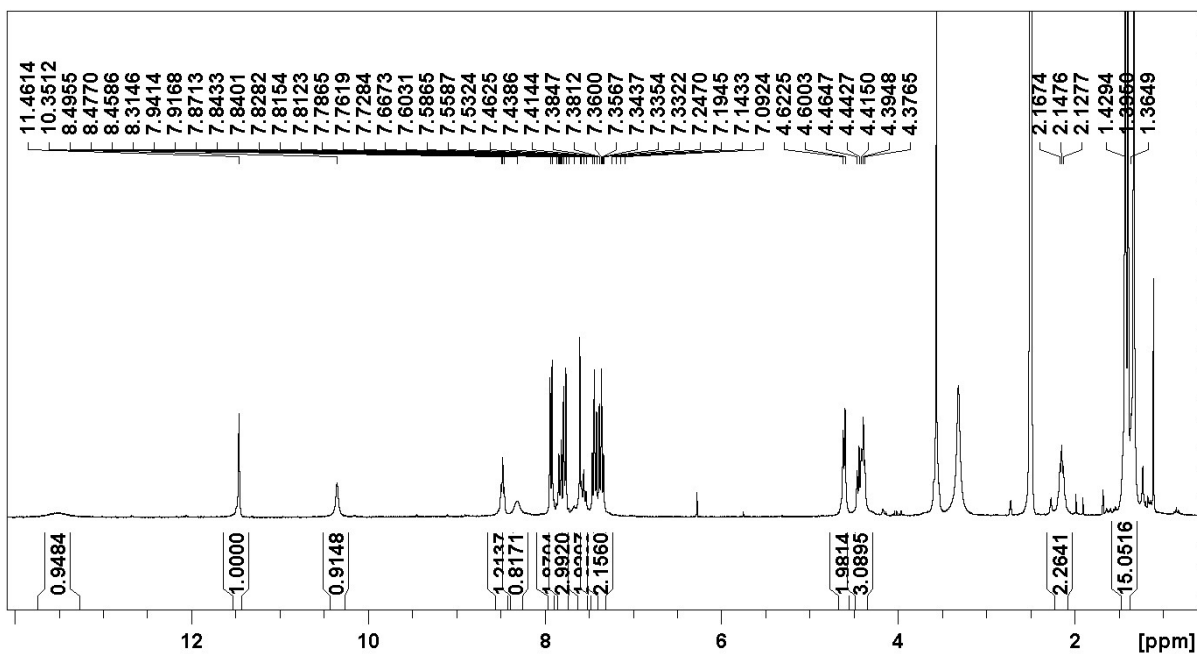
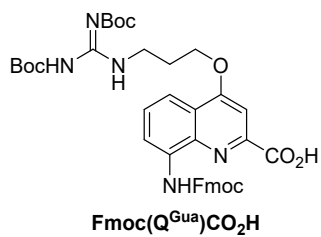
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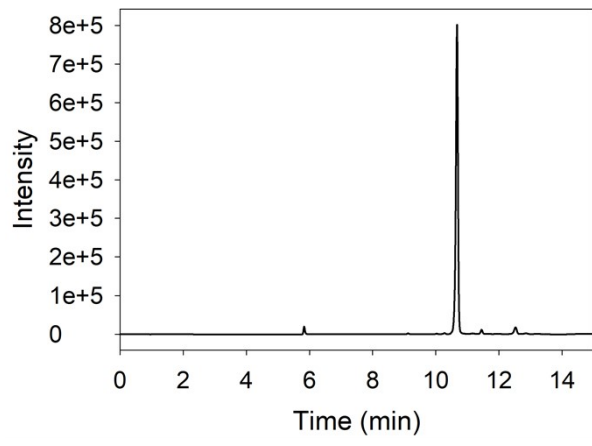


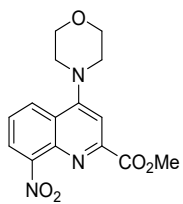


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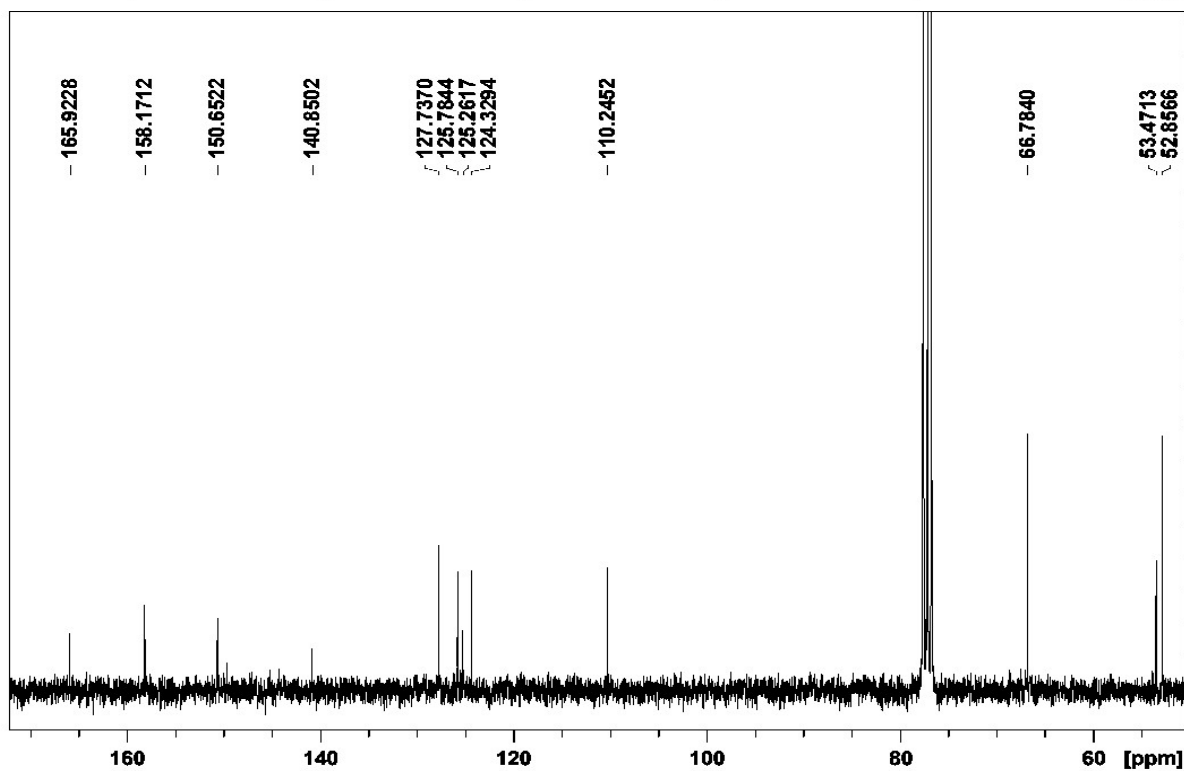
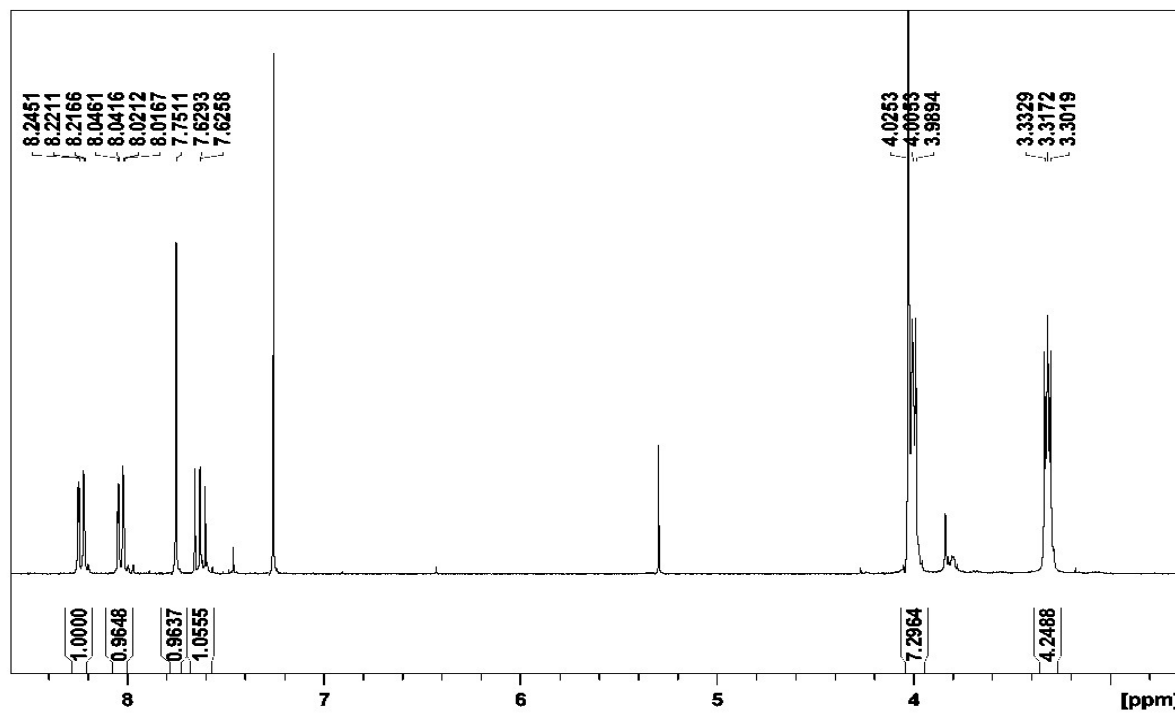


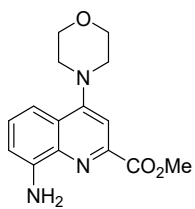




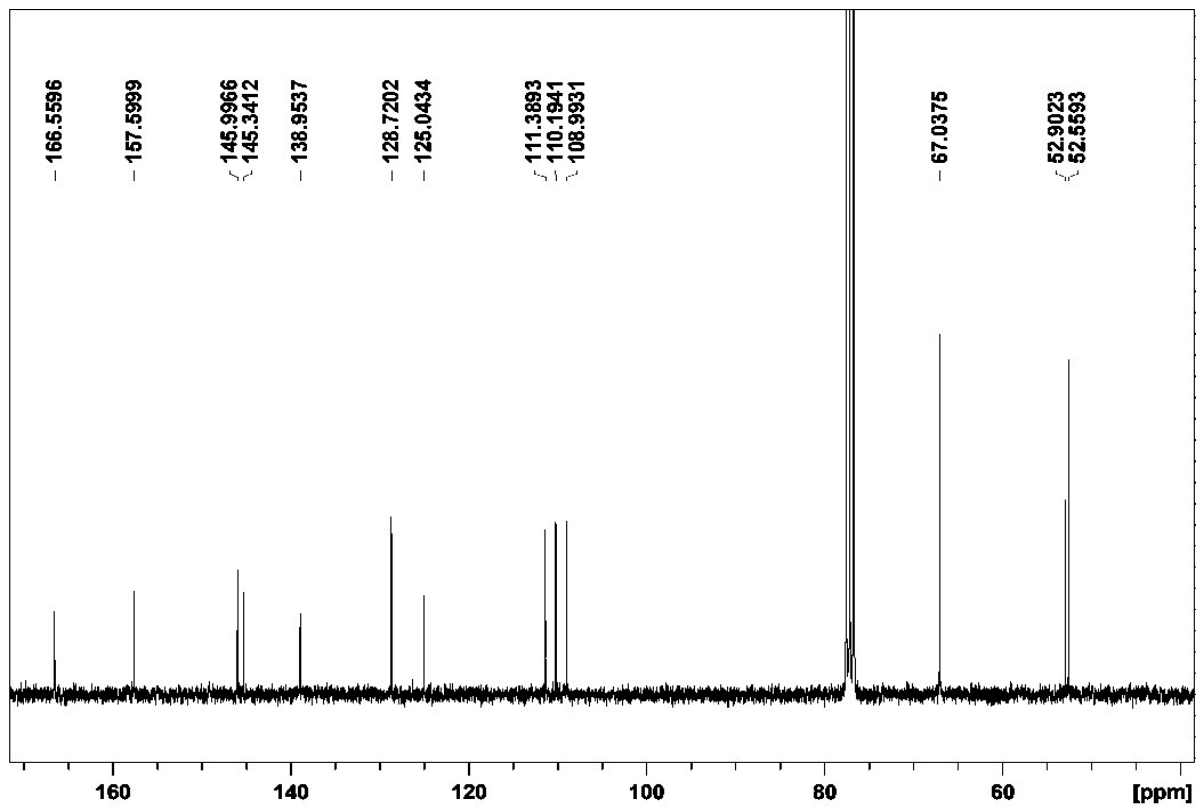
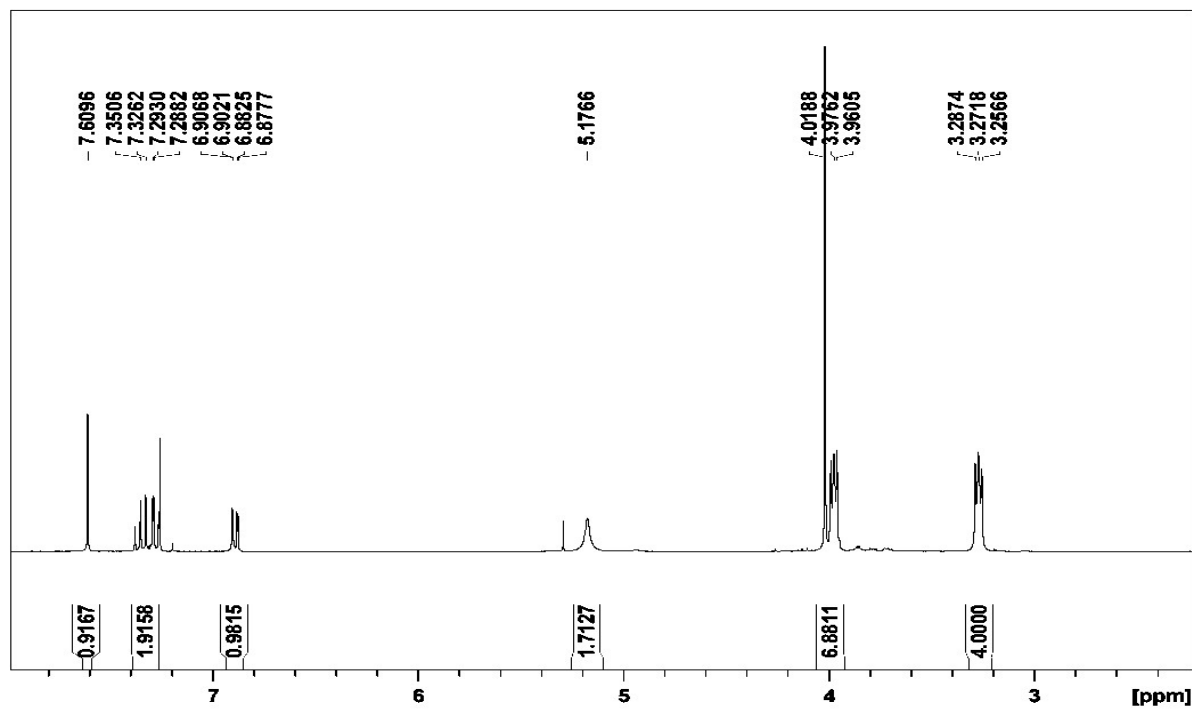


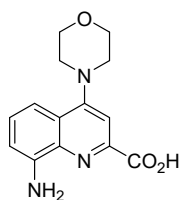
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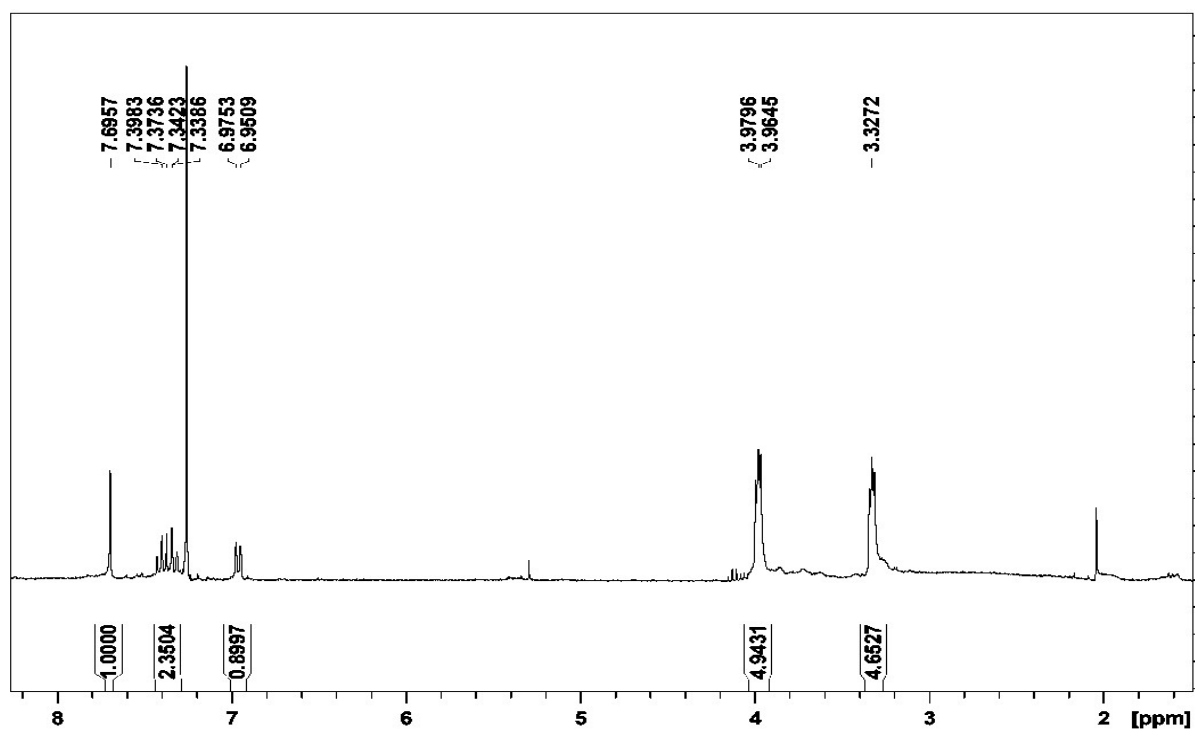


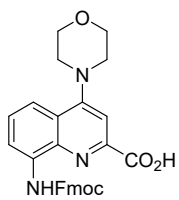
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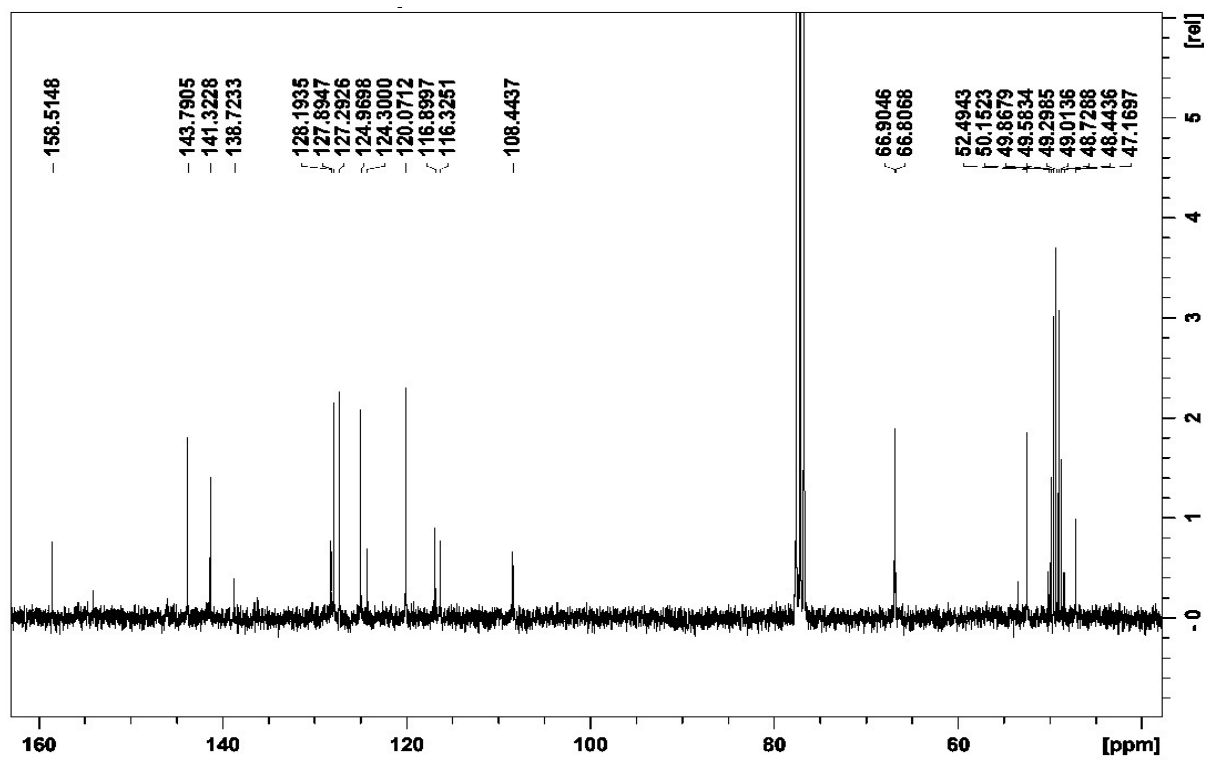
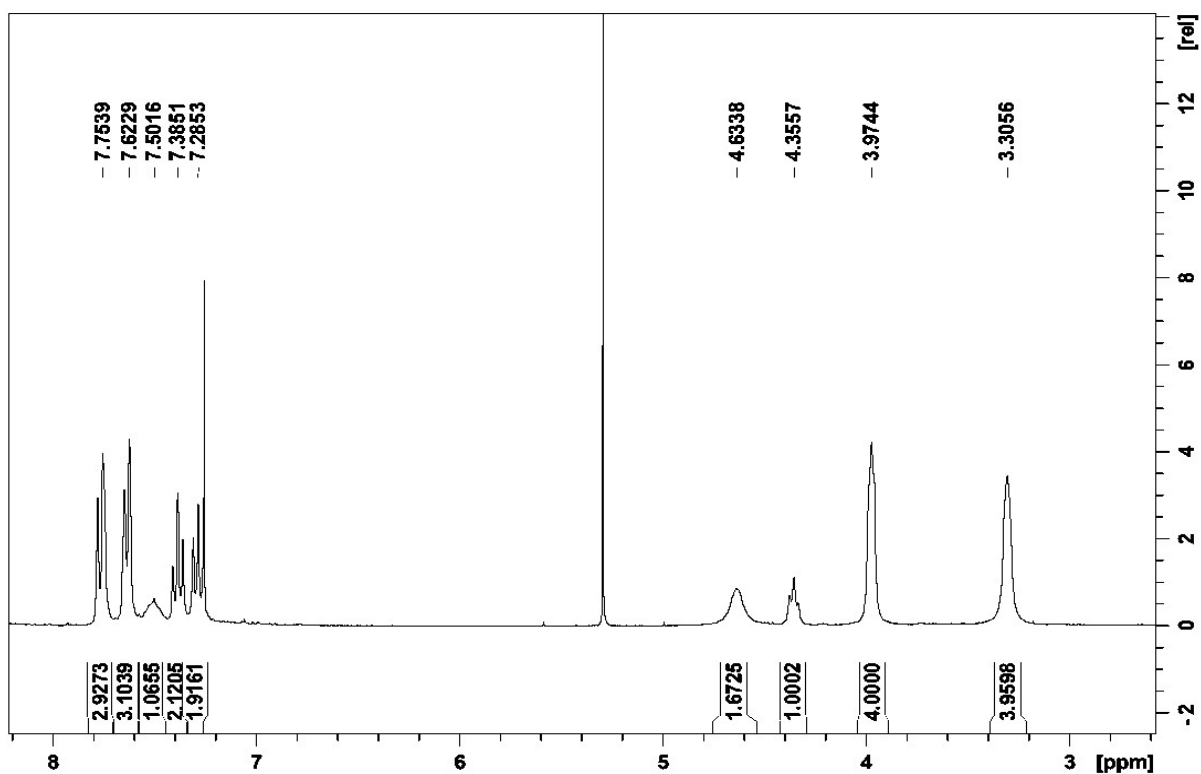


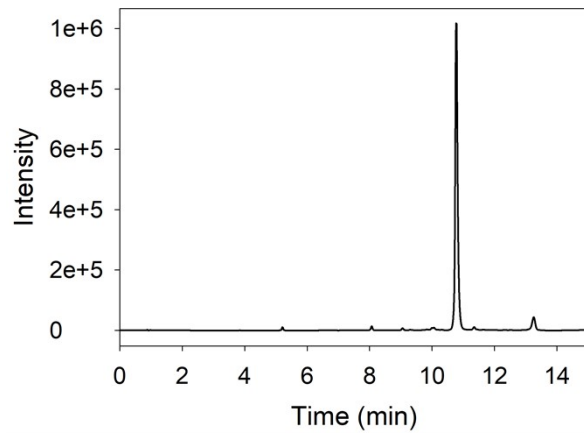
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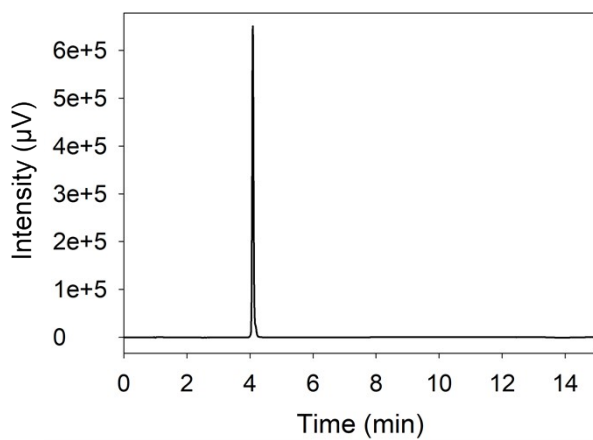
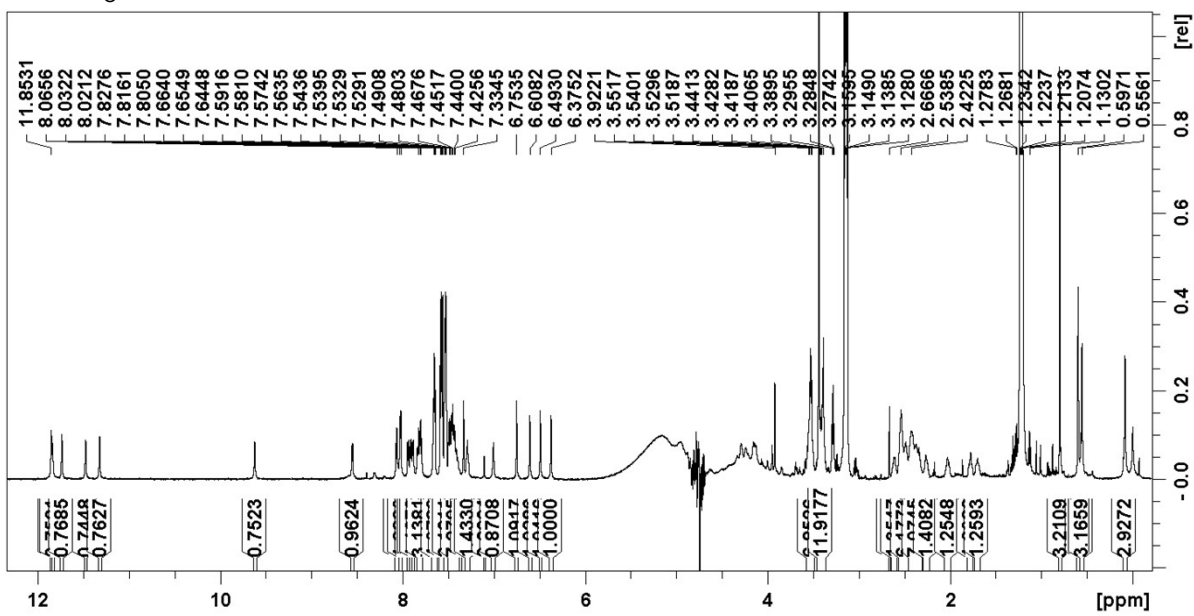
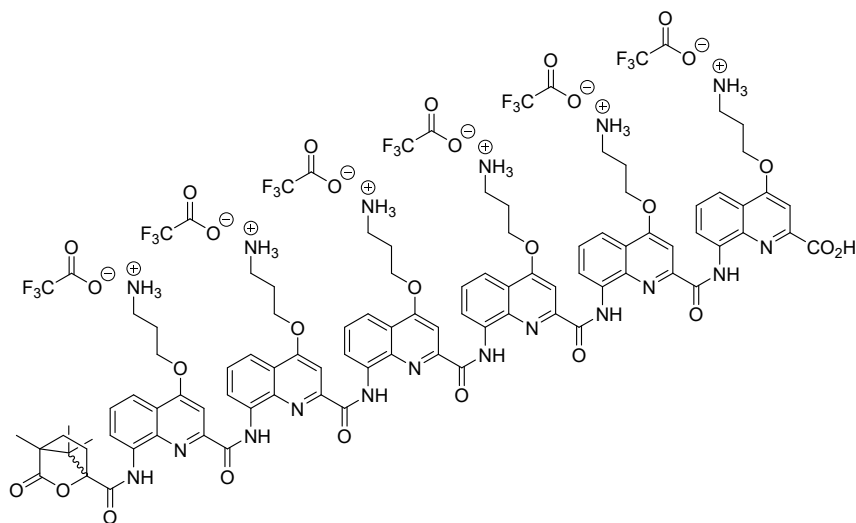


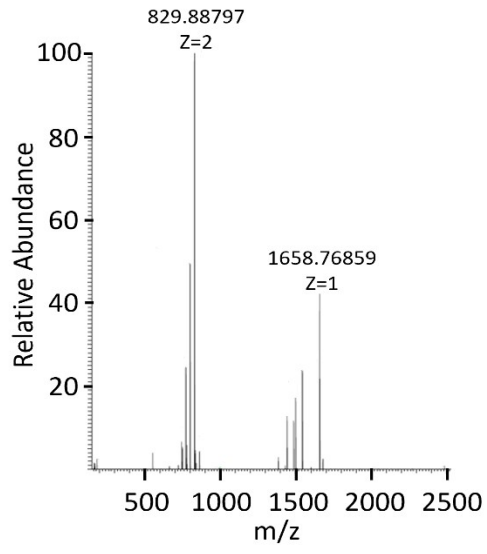
Fmoc(Q^{Mor})CO₂H



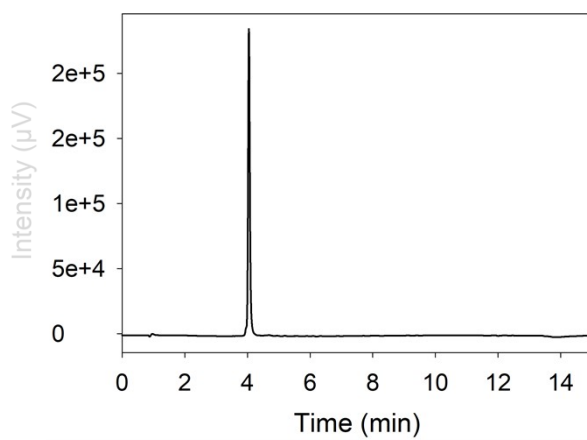
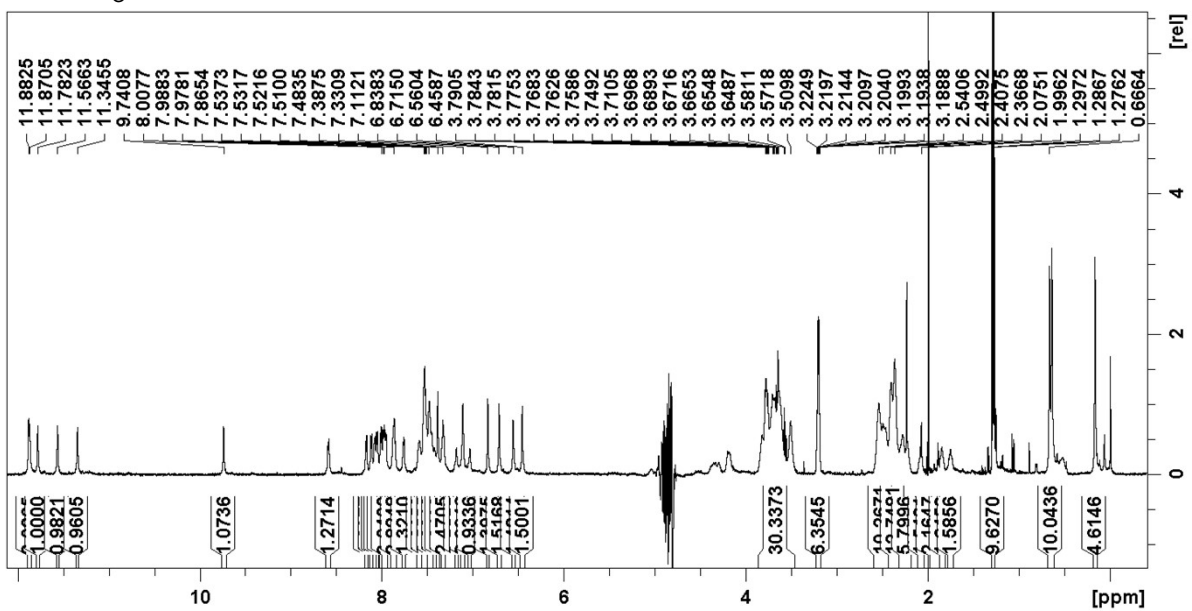
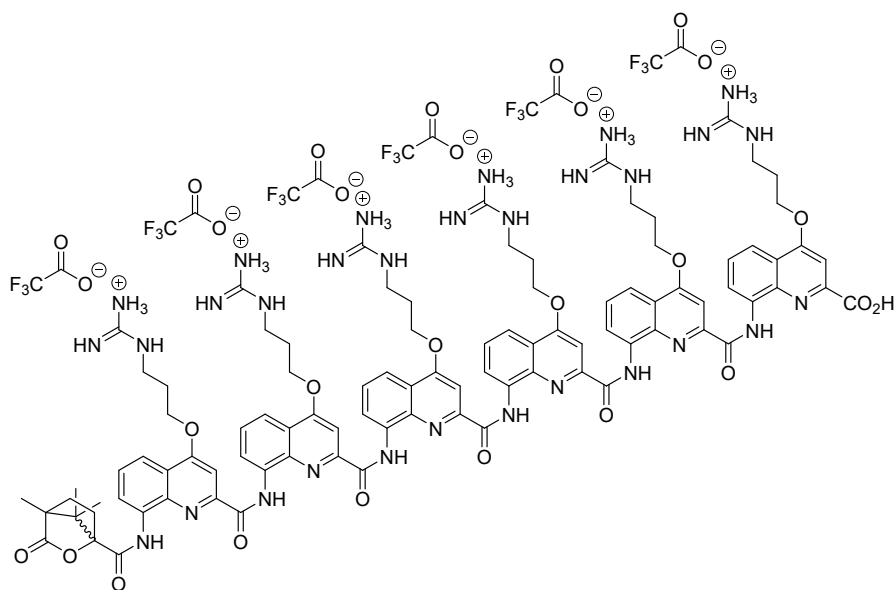


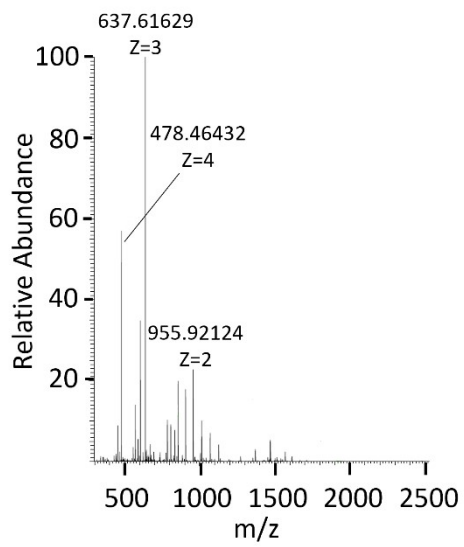
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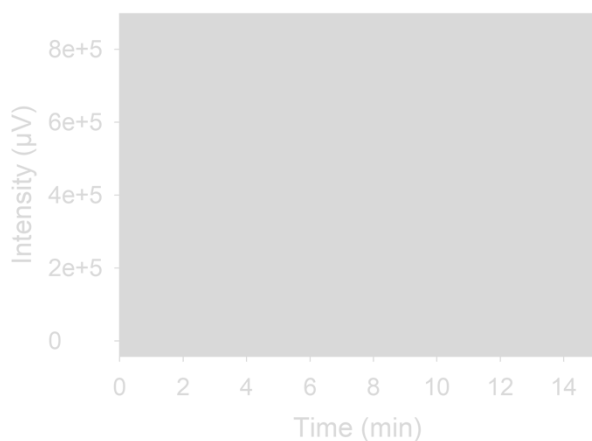
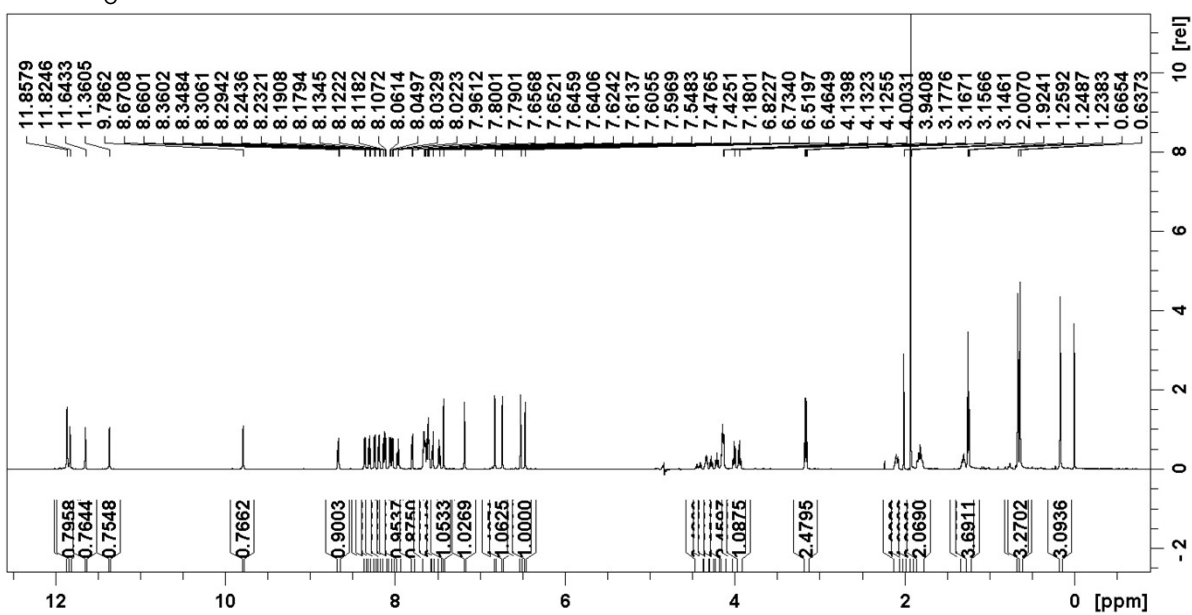
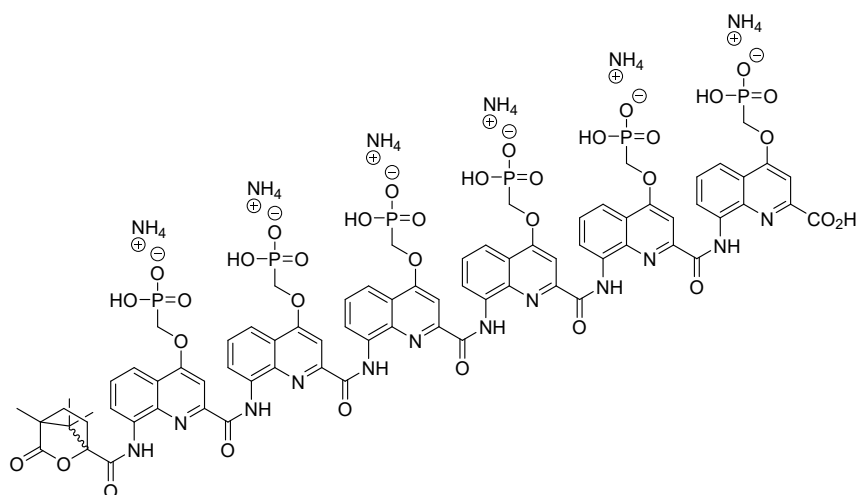


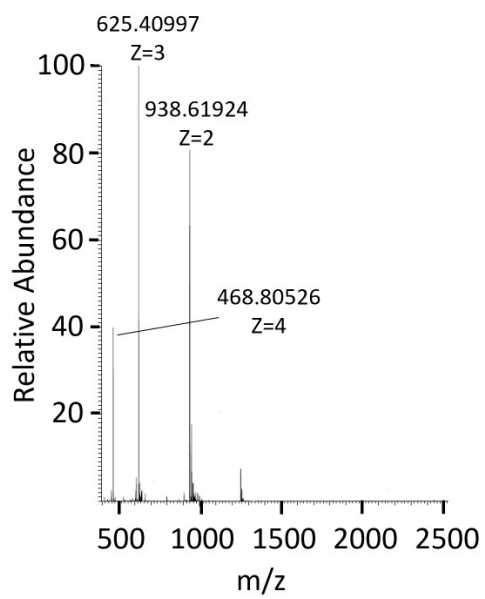


P/M-2









P/M-4

