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Supporting Information

Supporting Information

Deciphering C-H···O/X Weak Hydrogen Bonding and Halogen Bonding Interactions in Aromatic Peptoids

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1. Materials and Experiment Methods

General Experimental: All starting material and reagents were brought from a commercial source (Alfa-Aesar, Sigma-Aldrich, Fisher Scientific, and TCI) and used without further purification. Dichloromethane and THF solvents were purchased from commercial sources (Spectrochem, Rankem) and used without further distillation. The reaction was monitored by thin-layer chromatography (TLC) experiments were done using (Merck Silica gel 60, F254) aluminum sheets and the chromatogram was accompanied by UV visualization. Flash chromatography was performed using silica gel 60 Å, mesh size 40-63 microns (230-400 mesh) from Sisco research laboratories Pvt. Ltd (SRL).

Instrumentation: NMR (^{1}H NMR) spectra and carbon nuclear magnetic resonance (^{13}C NMR) spectra were recorded in $CDCl_3$ using Bruker AMX-400 (400 MHz) spectrometer. Sample preparation: 10 mg of sample dissolved in $CDCl_3$ to make ~800 µl of total volume for NMR. Liquid chromatography coupled to mass spectrometry (LC-MS) analysis was carried out using the Agilent 1200 series LC system (Agilent Technologies, Santa Clara, California, USA), hyphenated to quadrupole time of flight (Q-TOF) mass spectrometer (6540 series, Agilent Technologies). The study was carried out in positive mode under electrospray ionization (ESI). The typical operating source conditions for MS scan were set as the frag mentor voltage was set at 175 V, the capillary at 4000 V, the skimmer at 65 V, and nitrogen was used as the drying (325 °C, 12 L/min) and nebulizing gas (40 psi). All the spectra were recorded under identical experimental conditions. Before analysis, internal calibration was carried out using an ESI-L tuning mix (Agilent Technologies). Then, the data were acquired and evaluated using Mass Hunter Workstation software.

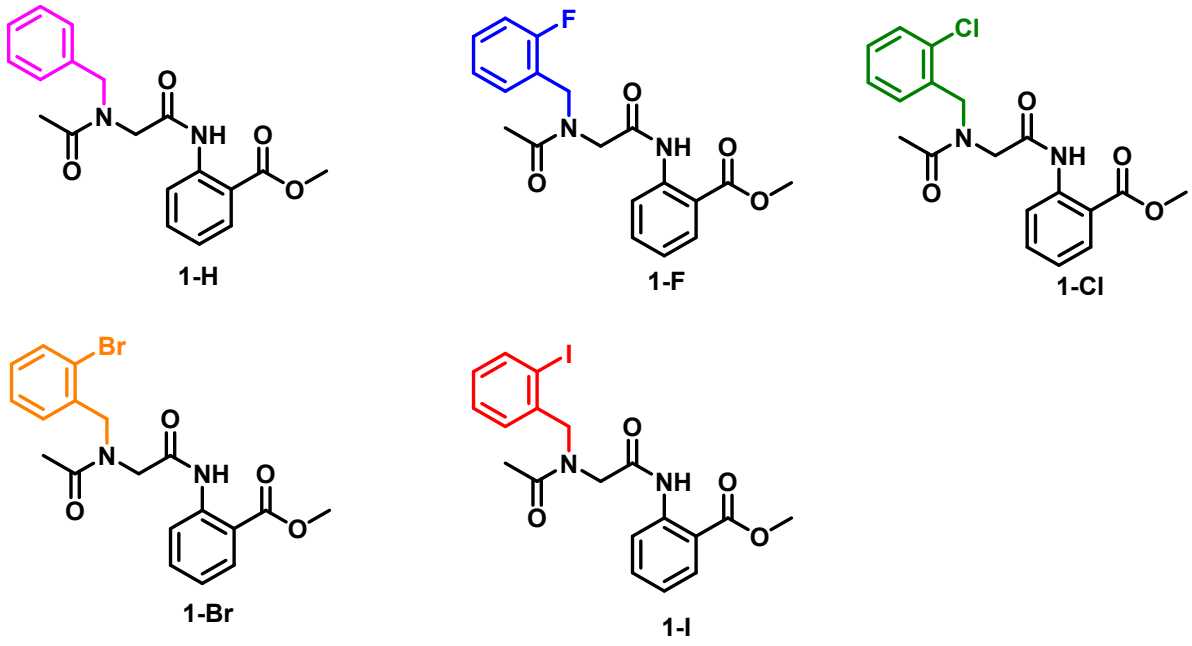
NMR experiments were carried out on Bruker Avance 500 MHz spectrometer. NMR spectra were recorded for the peptoids at a concentration of ~6 mM at 300 K temperature in $CDCl_3$, DMSO-D6, CD_3CN and CD_3OD solutions to determine the cis/trans equilibrium constant and Gibbs free energy. For the determination of the thermodynamic parameters for cis/trans equilibrium about

tertiary amide linkages in the peptoid backbone, conformer populations were determined as a function of temperature over the range 260 K-300 K in acetonitrile and 300 K-340 K in DMSO-D6 solutions at 10 K intervals and determined the population of *cis* and *transforms* in both the solvents at each temperature.

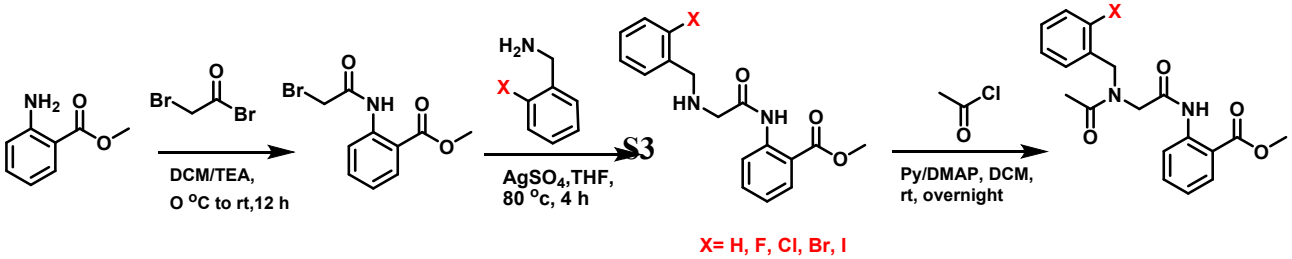
A chromatographic run was performed on Agilent Zorbax Eclipse plus C18 (4.6 mm × 250 mm, 5 µm) column. The mobile phase components water and acetonitrile were used in the linear gradient elution method of 20% acetonitrile to 100% acetonitrile in 30 mins followed by 15 min of equilibration. The flow rate was set at 1 mL/min, and the column temperature was 10 ± 2 °C. Auto-sampler temperature and injection volume were set as 5 ± 2 °C and 2 µL, respectively. The samples were identified at 230 nm using Waters HPLC System (Model: e2695 Separations Module with 2998 PDA Detector, Milford, Massachusetts, United States).

2. Chemical Structures

Scheme 1. Structure of ortho-substituted peptoid dimers



3. Scheme 2. General Synthetic scheme and protocol for peptoid model systems



Synthetic steps:

a). Bromo acetylation step. Methyl anthranilate (5 g, 33.0 mmol) has been dissolved in DCM followed by the addition of triethylamine (4.66 mL, 33.0 mmol) under nitrogen at 0 ºC. The mixture was stirred at 0 °C for 15 min then added bromoacetyl bromide (4.66 mL, 52.9 mmol) dropwise over 10 min. The reaction mixture changed from the colourless suspension immediately turned yellow-orange solution and the reaction was left at room temperature overnight. The solvent was evaporated under reduced pressure. The resulting crude oil has been purified by column chromatography. The gradient of the solvent was (100% hexane to 90/10 hexane/EtOAc) to yield the desired compound as a white crystalline solid (7.9 g, 88 %).

b). Displacement step: To a solution of N-(2-phenyl)bromoacetamide (1 g, 3.676 mmol) was treated with an ortho-substituted benzylamine (4.044 mmol) in THF followed by the addition of $AgSO_4$ (11.029 mmol). The reaction was allowed for reflux at 80 ºC for 4 h. The solvent was removed under reduced pressure. The crude mixture was then subjected to silica gel column chromatography in an n-hexane/ EtOAc solvent in which the gradient of the solvent was from (100% hexane to 85/15 hexane/EtOAc), depending upon the polarity of the compounds. The desired compounds were isolated yield **1-H** (0.94 g, 87 %), **1-F** (1.01 g, 87 %), **1-Cl** (1.08 g, 88 %), **1-Br** (1.22 g, 88 %) and **1-I** (1.34 g, 86 %).

c). Acetylation step: The next step was acetylation of N-termini of peptoids (1 mmol) by reacting with acetyl chloride with pyridine (1.2 mmol) followed by a catalytic amount of DMAP (~ 0.5 mg) in DCM. The acetyl chloride (2.5 mmol) was then added dropwise over 10 min. The reaction mixture was allowed to stir overnight at room temperature. The solvent was removed under reduced pressure to afford a crude compound, which was purified by column chromatography to yield the desired compound.

Synthesis of 1-H: The title compound has been prepared from methyl 2-(2-(N-benzylacetamido)acetamido)benzoate (0.5 g, 1.67 mmol) effected using the general procedure as

mentioned above for the preparation of **1-H** and purification was conducted *via* column chromatography (SiO_2; 100% hexane to 60/40 hexane/EtOAc) to yield **1-H**, as a colourless solid, (0.38 g, 67 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.53 (1H, s, N*H*), 8.77 (1H, dd, *J* = 8.0 Hz, NH-Ar-*H*), 8.08 (1H, dd, *J* = 4.0 Hz, 8.0 Hz, NH-Ar-*H*), 7.61-7.56 (1H, m, NH-Ar-*H*), 7.42 (2H, t, *J* = 8.0 Hz, N-Ar-*H*), 7.34 (2H, dd, *J* = 4.0 Hz, 12.0 Hz, N-Ar-*H*), 7.25 (1H, d, *J* = 8.0 Hz, NH-Ar-*H*), 7.21-7.12 (1H, m, N-Ar-*H*), 4.79 (2H, s, β-CH_2), 4.27 (2H, s, α-CH_2), 3.97 (3H, s, OCH_3), 2.40 (3H, s, CH_3); **^{13}C NMR (100 MHz, $CDCl_3$):** 171.11, 167.70, 166.55, 139.96, 134.79, 133.69, 129.81, 128.07, 126.93, 125.50, 121.80, 119.24, 114.23, 52.12, 51.29, 49.38, 20.37; **HRMS:** m/z Calculated for $[M+H]^+$. $[C_{19}H_{20}N_2O_4 + H]^+$ = 341.1496 Found = 341.1495.

Synthesis of 1-F: The title compound has been prepared from methyl 2-(2-(N-(2-fluorobenzyl)acetamido)acetamido)benzoate (0.5 g, 1.58 mmol) effected using the general procedure as mentioned above for the preparation of **1-F** and purification was conducted *via* column chromatography (SiO_2; 100% hexane to 60/40 hexane/EtOAc) to yield **1-F**, as a colourless solid, (0.37 g, 68 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.53 (1H, s, N*H*), 8.75 (1H, d, *J* = 8.0 Hz, NH-Ar-*H*), 8.07 (1H, dd, *J* = 4.0 Hz, 8.0 Hz, NH-Ar-*H*), 7.62-7.55 (1H, m, NH-Ar-*H*), 7.46-7.32 (1H, m, N-Ar-*H*), 7.28-7.18 (2H, m, NH-Ar-*H,* N-Ar-*H*), 7.15-7.02 (2H, m, N-Ar-*H*), 4.81 (2H, s, β-CH_2), 4.26 (2H, s, α-CH_2), 3.97 (3H, s, OCH_3), 2.41 (3H, s, CH_3); **^{13}C NMR (100 MHz, $CDCl_3$):** 171.05, 167.68, 166.39, 161.02, 139.91, 133.67, 129.80, 128.87, 128.79, 127.42, 127.38, 123.58, 121.81, 119.23, 114.92, 51.31, 49.25, 46.53, 20.26; **HRMS:** m/z Calculated for $[M+H]^+$. $[C_{19}H_{19}FN_2O_4 + H]^+$ = 359.1402 Found = 359.1400.

Synthesis of 1-Cl: The title compound has been prepared from methyl 2-(2-(N-(2-chlorobenzyl)acetamido)acetamido)benzoate (0.5 g, 1.50 mmol) effected using the general procedure as mentioned above for the preparation of **1-Cl** and purification was conducted *via* column chromatography (SiO_2; 100% hexane to 70/30 hexane/EtOAc) to yield **1-Cl**, as a colourless solid, (0.365 g, 65 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.58 (1H, s, N*H*), 8.77 (1H, d, *J* = 8.0 Hz, NH-Ar-*H*), 8.08 (1H, dd, *J* = 8.0 Hz, NH-Ar-*H*), 7.61-7.57 (1H, m, NH-Ar-*H*), 7.46 (1H, dd, *J* = 8.0 Hz, N-Ar-*H*), 7.39-7.32 (2H, m, N-Ar-*H*), 7.26-7.13 (2H, m, NH-Ar-*H,* N-Ar-*H*), 4.85 (2H, s, β-CH_2), 4.28 (2H, s, α-CH_2), 3.98 (3H, s, OCH_3), 2.34 (3H, s, CH_3); **^{13}C NMR (100 MHz, $CDCl_3$):** 171.36, 167.74, 166.27, 139.92, 133.70, 132.31, 129.82, 129.06, 128.58, 128.14, 126.43, 126.03, 121.86, 119.28, 114.30, 51.34, 50.14, 49.61, 20.24; **HRMS:** m/z Calculated for $[M+H]^+$. $[C_{19}H_{19}ClN_2O_4+ H]^+$ = 375.1106 Found = 375.1103.

Synthesis of 1-Br: The title compound has been prepared from methyl 2-(2-(N-(2-bromobenzyl)acetamido)acetamido)benzoate (0.5 g, 1.32 mmol) effected using the general procedure as mentioned above for the preparation of **1-Br** and purification was conducted *via* column chromatography (SiO_2; 100% hexane to 70/30 hexane/EtOAc) to yield **1-Br**, as a colourless solid, (0.368 g, 66 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.58 (1H, s, N*H*), 8.77 (1H, dd, *J* = 8.0 Hz, NH-Ar-*H*), 8.08 (1H, dd, *J* = 4.0 Hz, NH-Ar-*H*), 7.66-7.56 (2H, m, NH-Ar-*H*, N-Ar-*H*), 7.43-7.39 (1H, m, N-Ar-*H*), 7.27-7.23 (1H, m, N-Ar-*H*), 7.20-7.13 (2H, m, NH-Ar-*H,* N-Ar-*H*), 4.81 (2H, s, β-CH_2), 4.28 (2H, s, α-CH_2), 3.98 (3H, s, OCH_3), 2.33 (3H, s, CH_3); **^{13}C NMR (100 MHz, $CDCl_3$):** 171.38, 167.75, 166.24, 139.92, 133.70, 132.37, 129.82, 128.84, 128.39, 127.06, 126.04, 122.30, 121.86, 119.30, 114.32, 52.62, 51.34, 49.68, 20.24; **HRMS:** m/z Calculated for $[M+H]^+$. $[C_{19}H_{19}BrN_2O_4+ H]^+$ = 419.0601 Found = 419.0597.

Synthesis of 1-I: The title compound has been prepared from methyl 2-(2-(N-(2-iodobenzyl)acetamido)acetamido)benzoate (0.5 g, 1.17 mmol) effected using the general procedure as mentioned above for the preparation of **1-I** and purification was conducted *via* column chromatography (SiO_2; 100% hexane to 75/25 hexane/EtOAc) to yield **1-I**, as a colourless solid, (0.36 g, 65 %).

^{1}H NMR (400 MHz, $CDCl_3$): δ 11.58 (1H, s, N*H*), 8.77 (1H, dd, *J* = 8.0 Hz, NH-Ar-*H*), 8.09 (1H, dd, *J* = 8.0 Hz, NH-Ar-*H*), 7.93 (1H, dd, *J* = 8.0 Hz, N-Ar-*H*), 7.62-7.58 (1H, m, NH-Ar-*H*), 7.44 (1H, t, *J* = 8.0 Hz, N-Ar-*H*), 7.18-7.14 (2H, m, NH-Ar-*H,* N-Ar-*H*), 7.09 (1H, t, *J* = 8.0 Hz, N-Ar-*H*), 4.72 (2H, s, β-CH_2), 4.28 (2H, s, α-CH_2), 3.99 (3H, s, OCH_3), 2.32 (3H, s, CH_3); **^{13}C**

NMR (100 MHz, $CDCl_3$): 171.39, 167.76, 166.21, 139.92, 139.07, 136.57, 133.71, 129.82, 128.59, 127.91, 125.61, 121.88, 119.35, 114.35, 96.61, 57.55, 51.37, 49.75, 20.30; **HRMS:** m/z Calculated for $[M+H]^+$. $[C_{19}H_{19}IN_2O_4 + H]^+$ = 467.0462 Found = 467.0455.

4. Characterization Data

Table S1. Characterization of N-benzyl Peptoid dimers by LC-HRMS

N-benzyl Peptoid dimers	Theoretical mass $(M+H)^+$	Observed mass $(M+H)^+$	Mass Error (in ppm)
1-H	341.1496	341.1495	-0.293127
1-F	359.1402	359.1400	-0.556886
1-Cl	375.1106	375.1103	-0.799764
1-Br	419.0601	419.0597	-0.954517
1-I	467.0462	467.0455	-1.498781

5. Nuclear Magnetic Resonance (NMR) Spectra

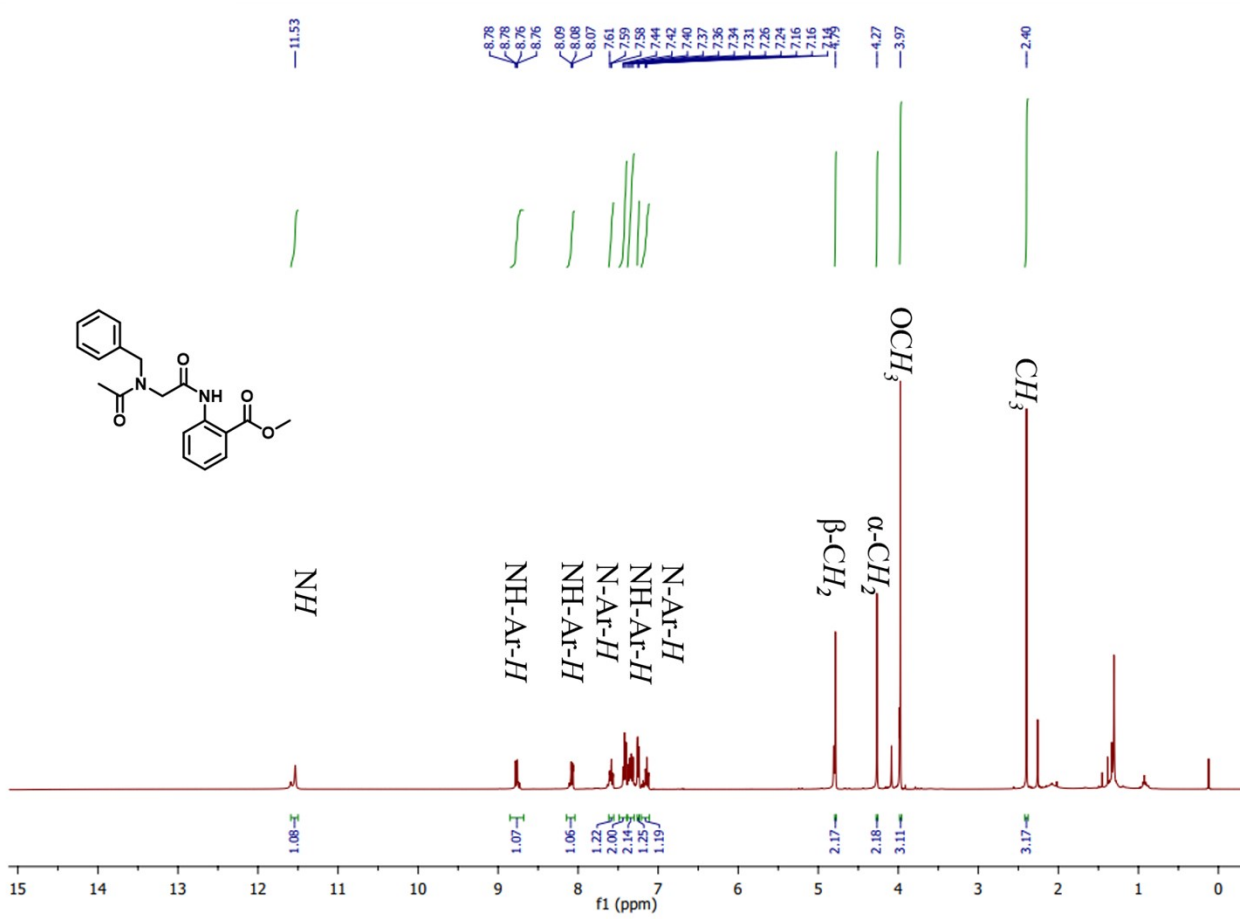


Figure S1. ^{1}H-NMR Spectra of Peptoid **1-H** in $CDCl_3$.

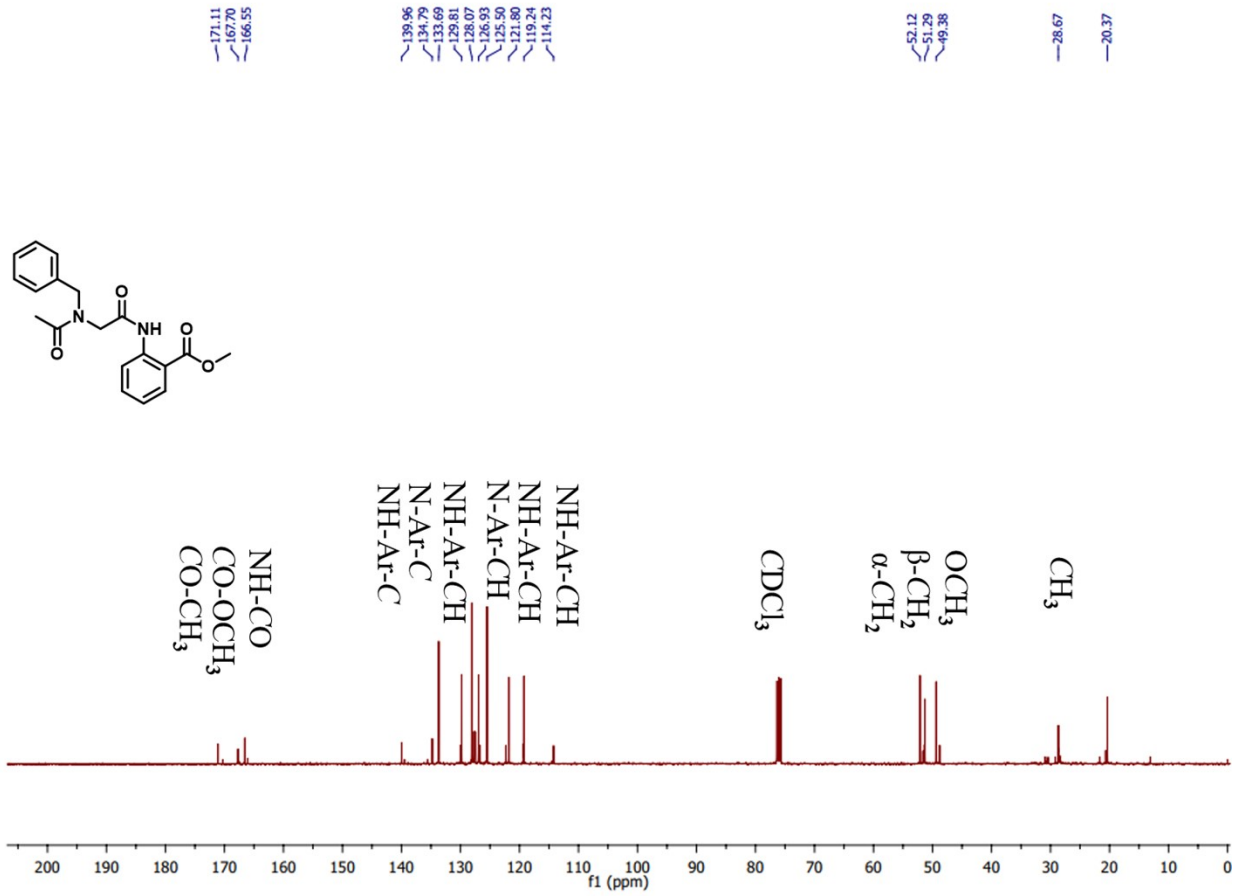


Figure S2. ^{13}C-NMR Spectra of Peptoid **1-H** in $CDCl_3$.

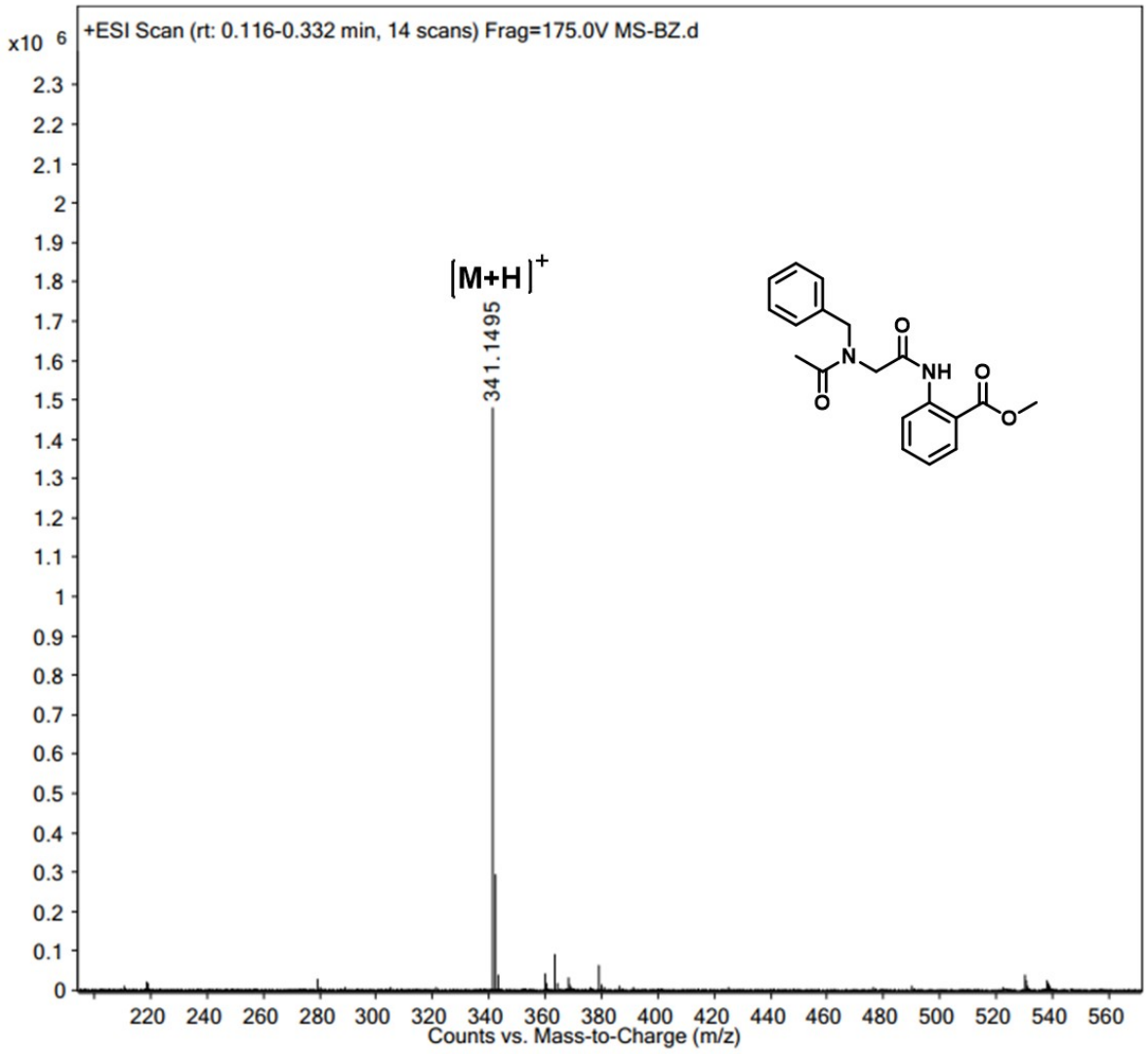


Figure S3. Mass spectra of peptoid **1-H**.

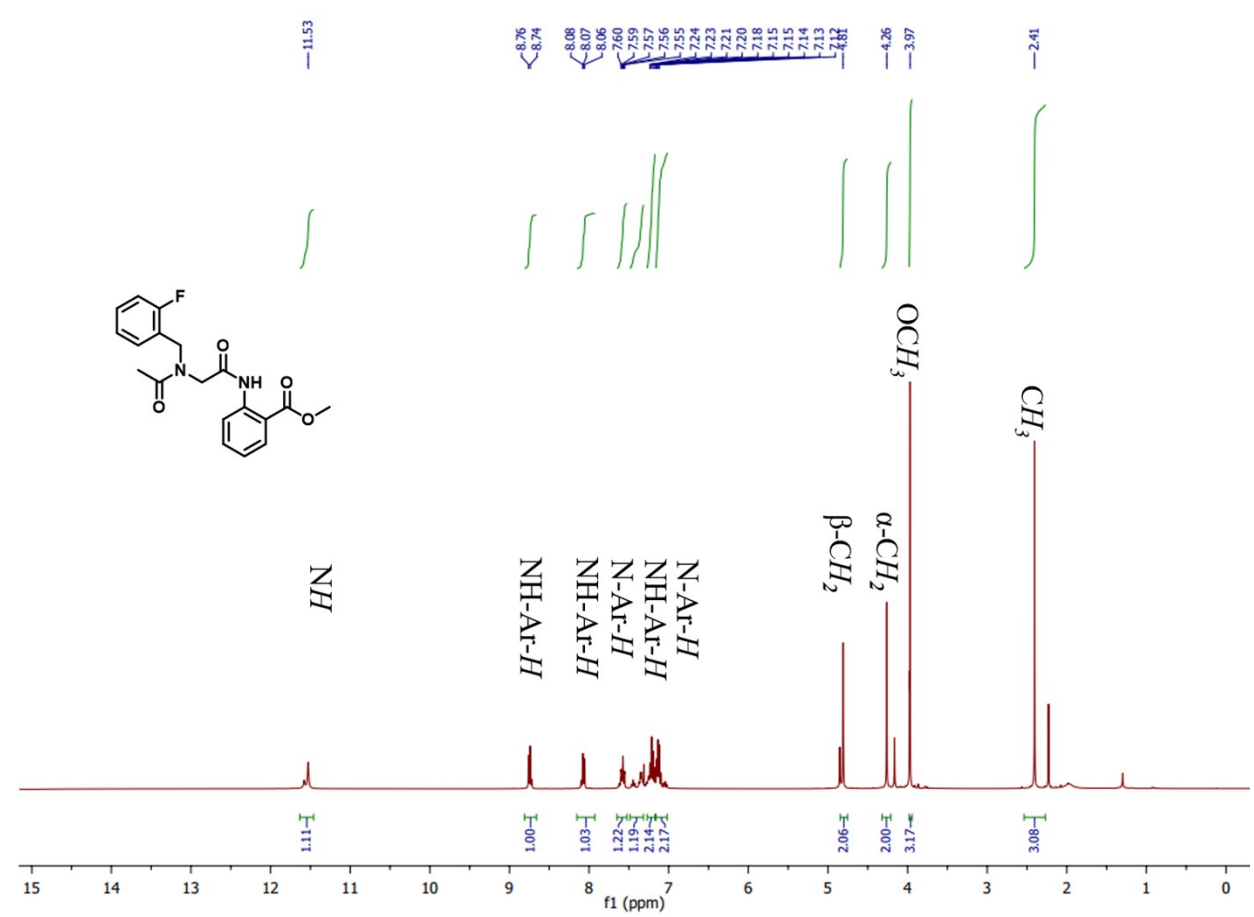


Figure S4. ^{1}H-NMR Spectra of Peptoid **1-F** in $CDCl_3$.

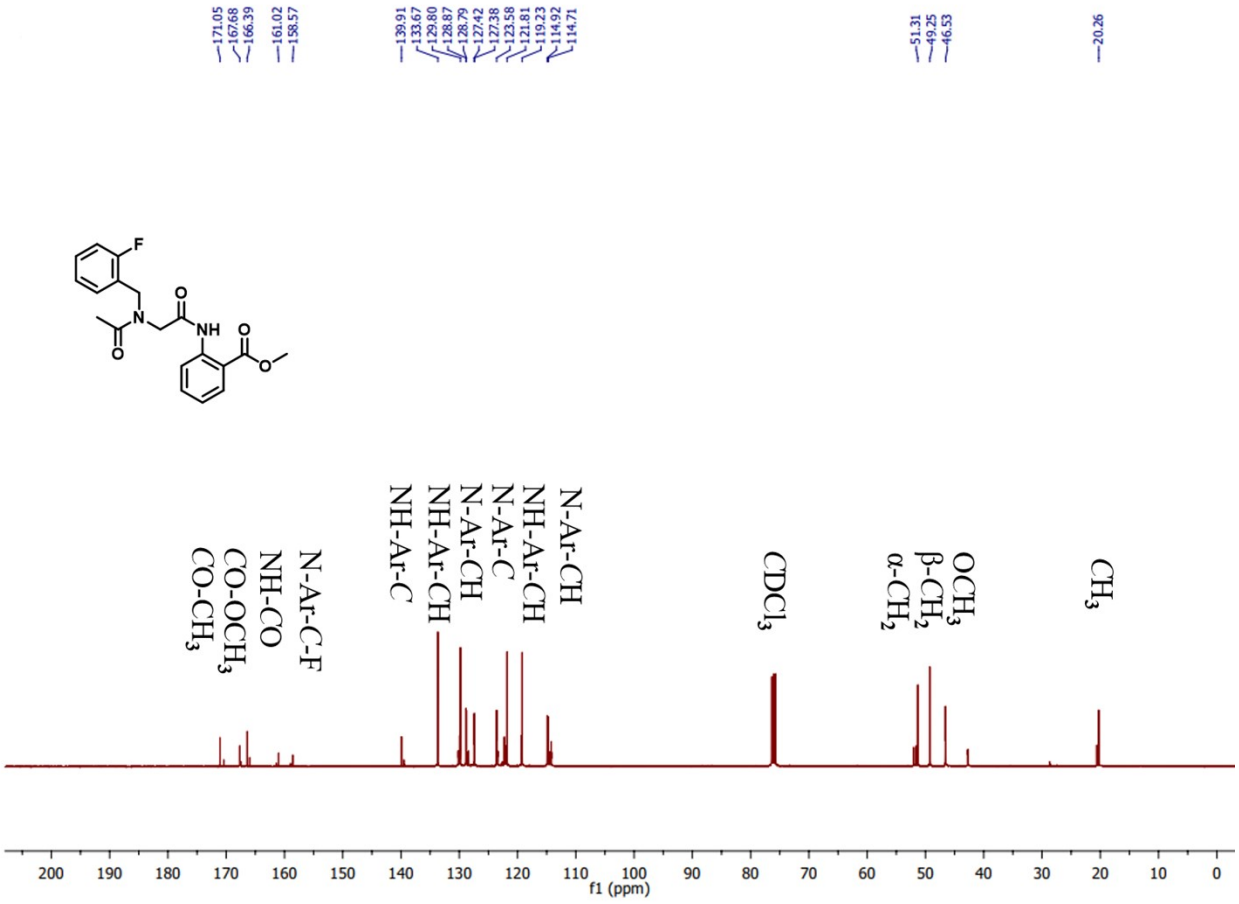


Figure S5. ^{13}C-NMR Spectra of Peptoid **1-F** in $CDCl_3$.

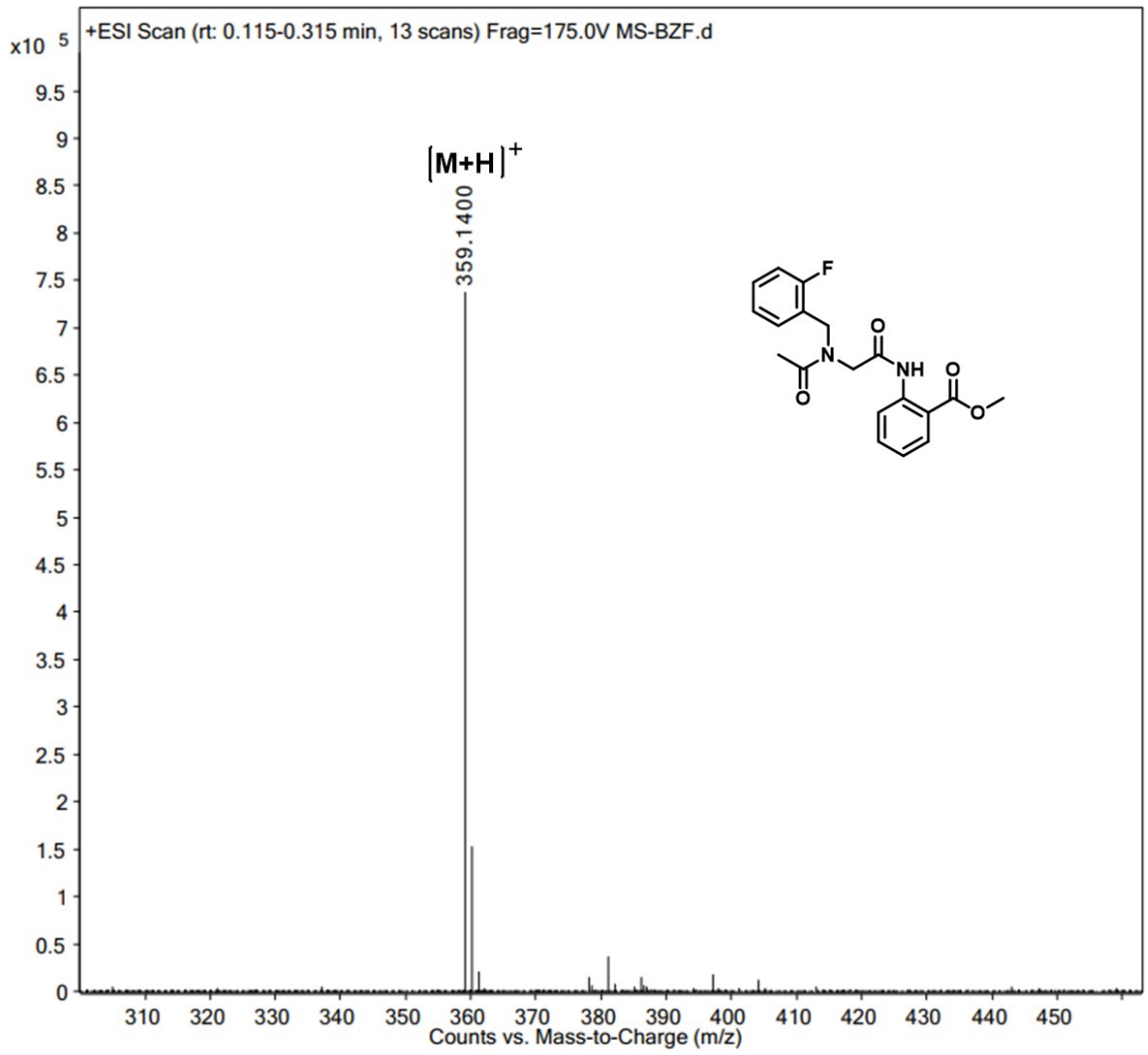


Figure S6. Mass spectra of peptoid **1-F**.

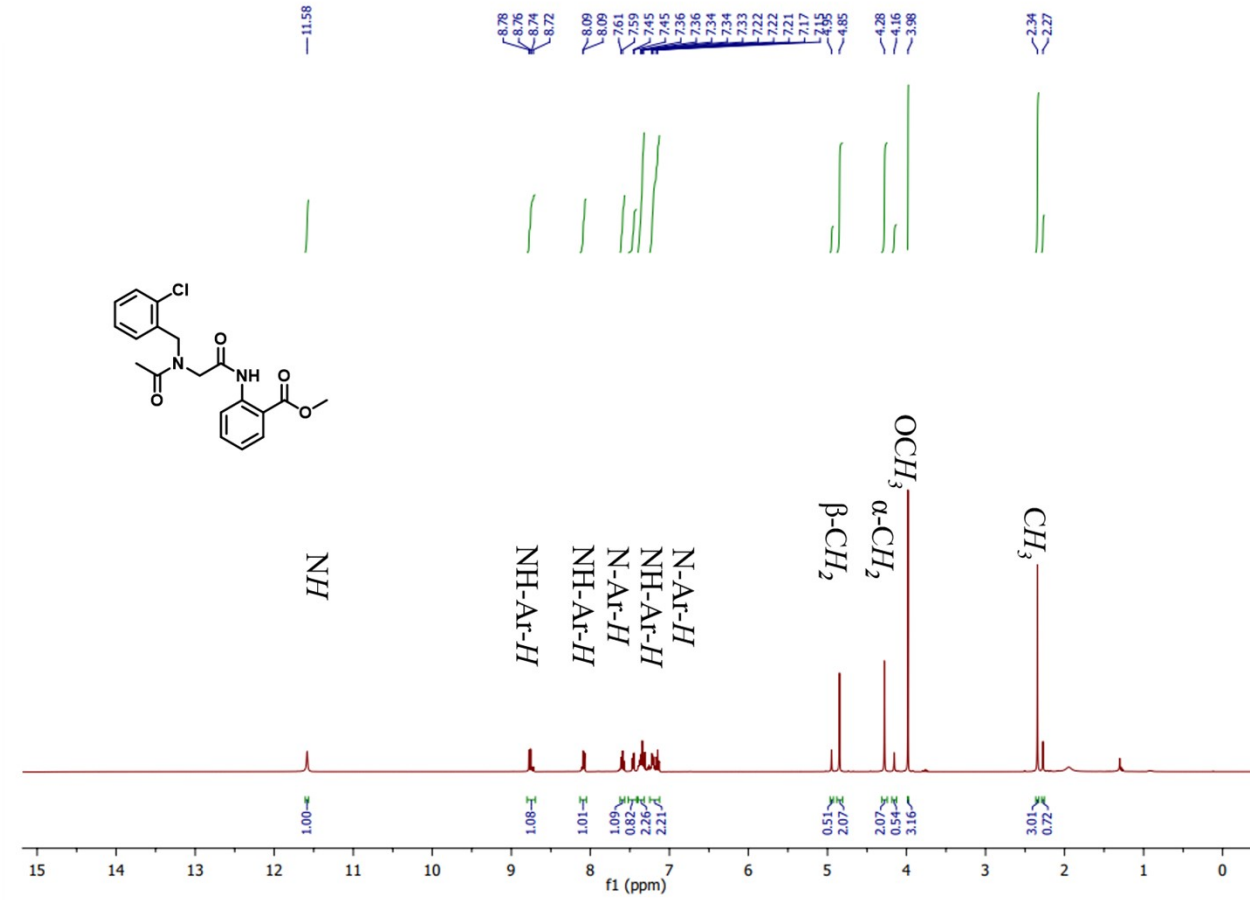


Figure S7. ^{1}H-NMR Spectra of Peptoid **1-Cl** in $CDCl_3$.

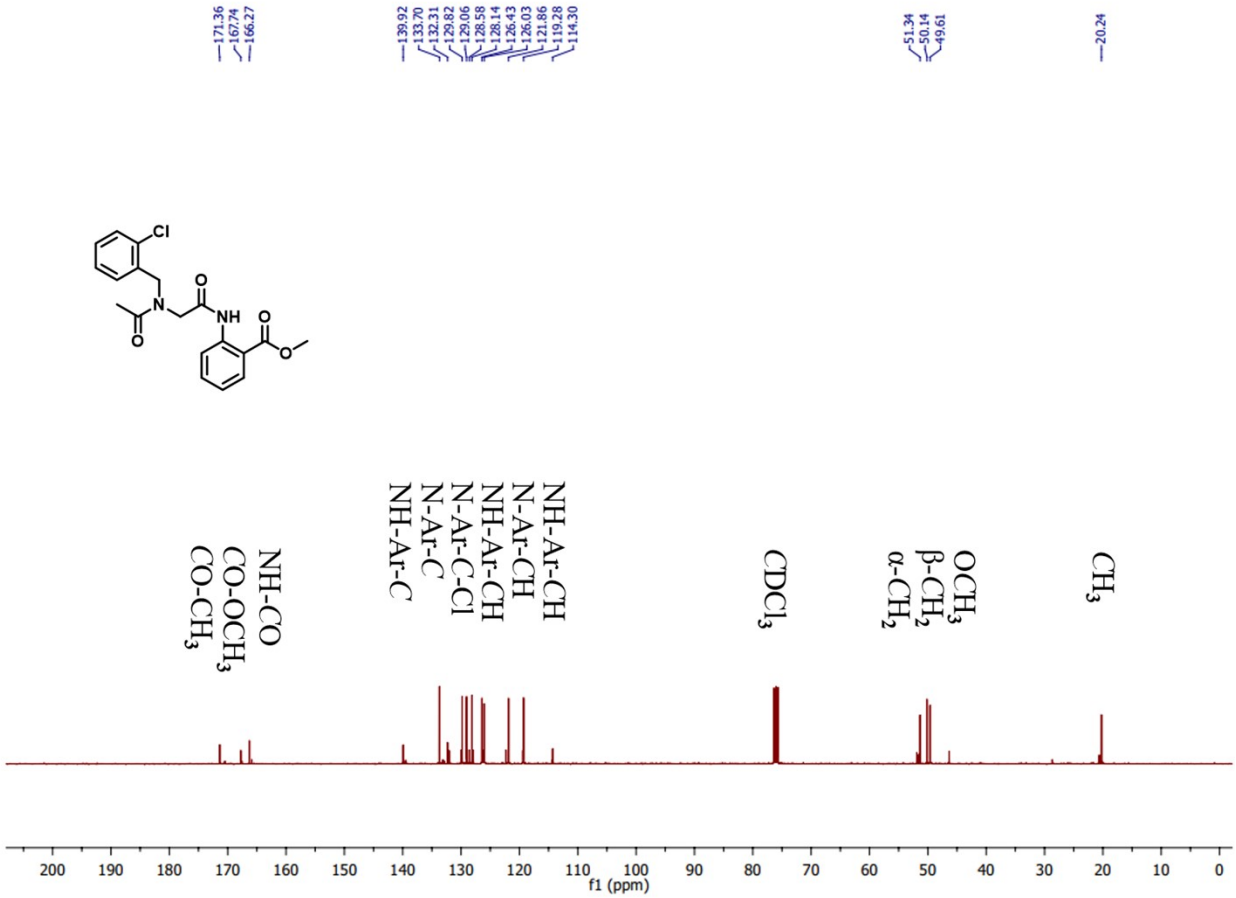


Figure S8. ^{13}C-NMR Spectra of Peptoid **1-Cl** in $CDCl_3$.

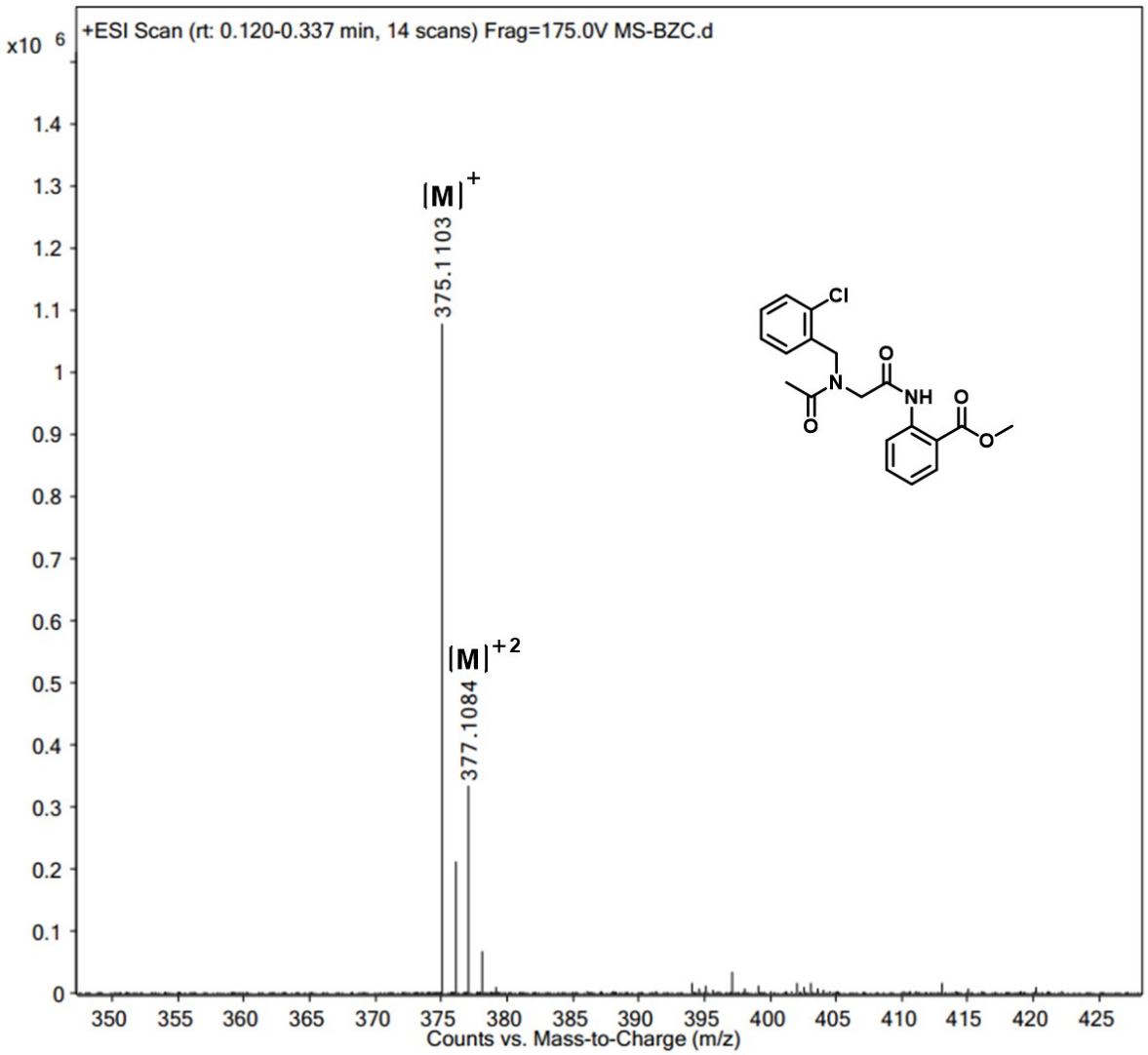


Figure S9. Mass spectra of peptoid **1-Cl**.

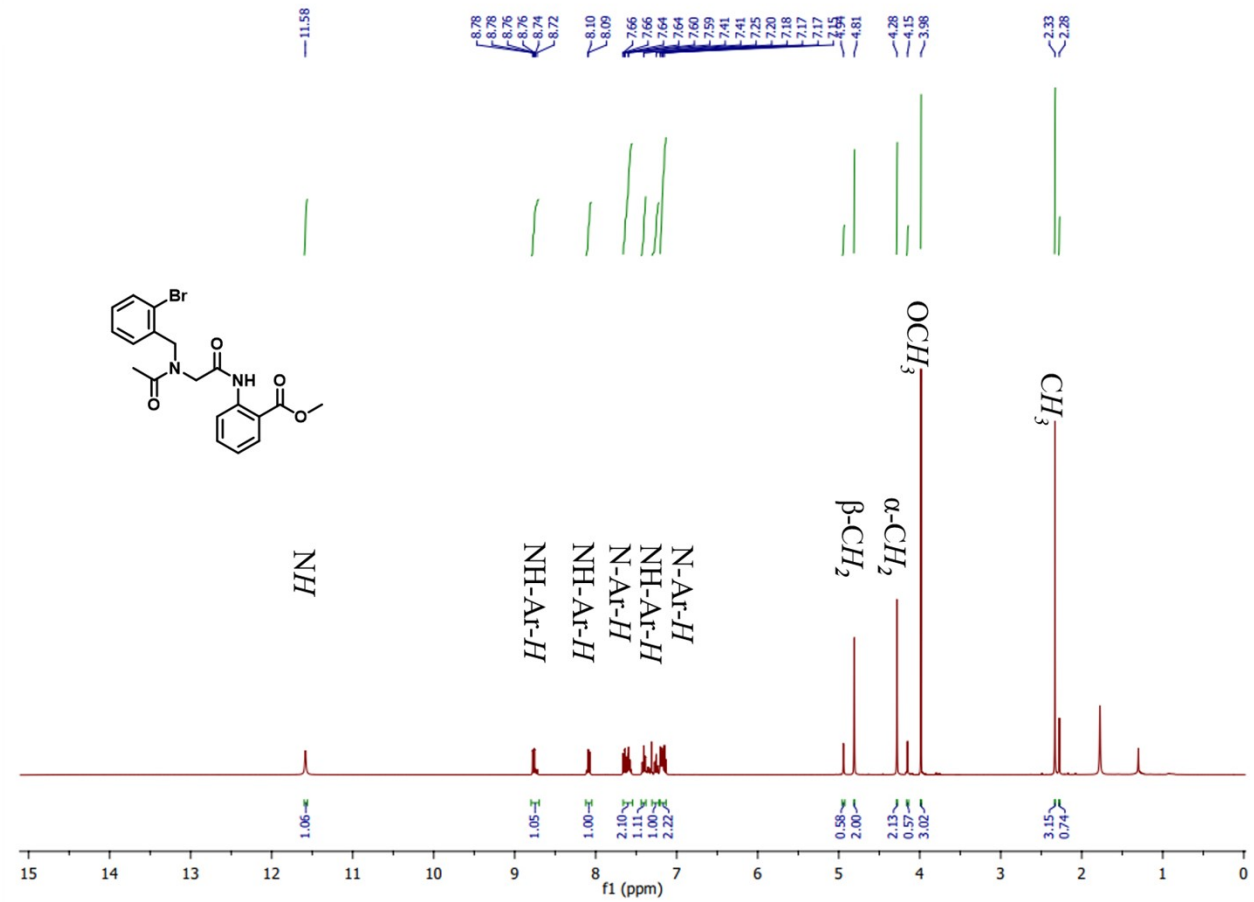


Figure S10. ^{1}H-NMR Spectra of Peptoid **1-Br** in $CDCl_3$.

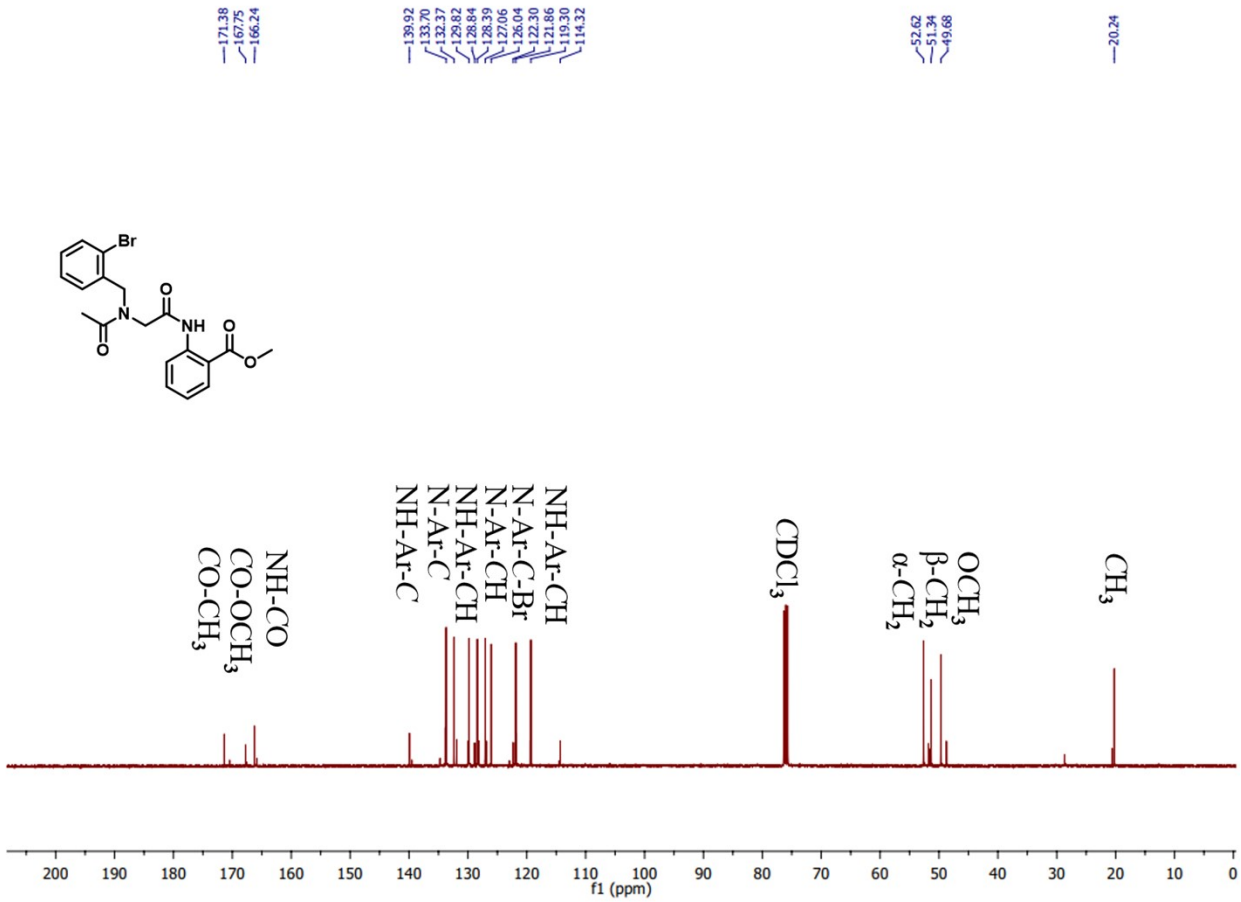


Figure S11. ^{13}C-NMR Spectra of Peptoid **1-Br** in $CDCl_3$.

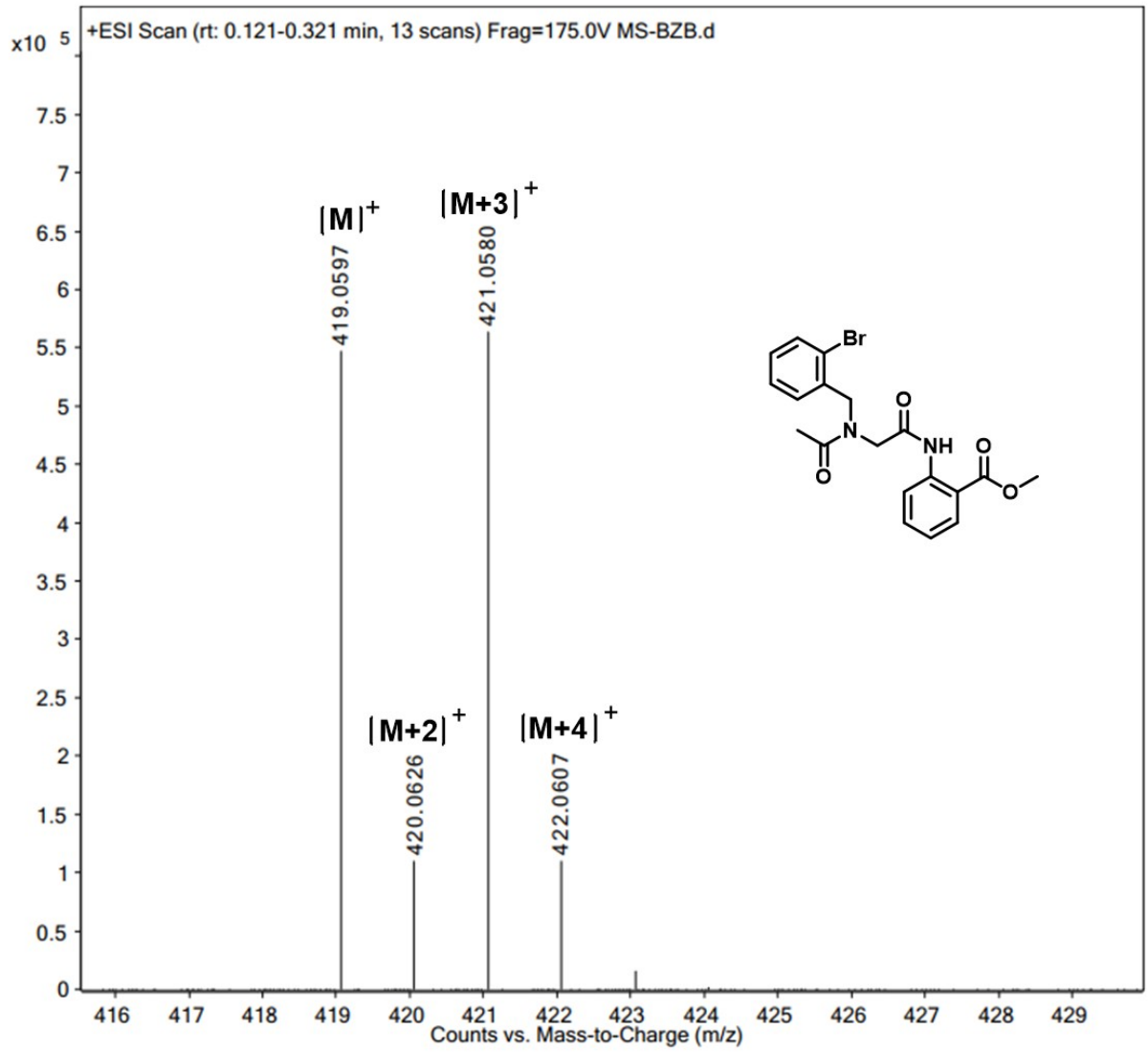


Figure S12. Mass spectra of peptoid **1-Br**.

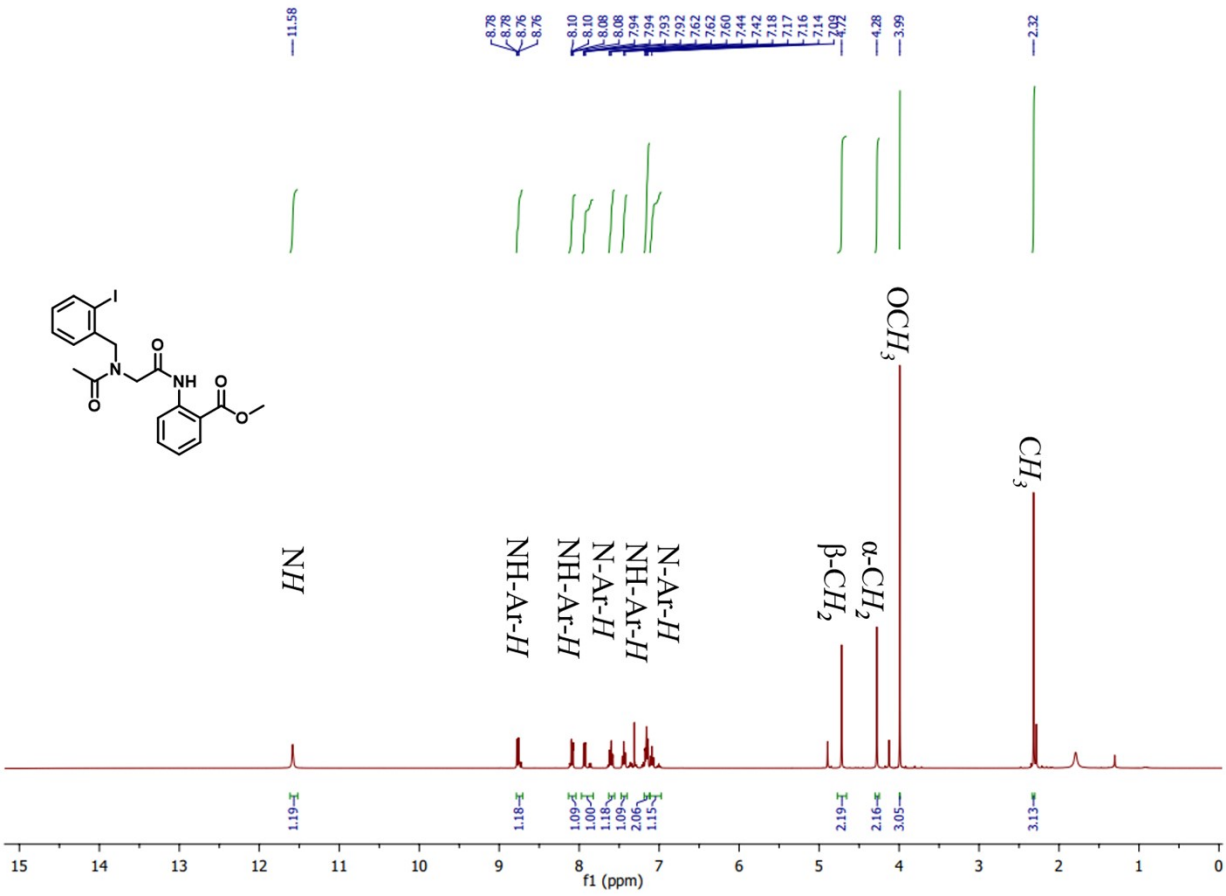


Figure S13. ^{1}H-NMR Spectra of Peptoid **1-I** in $CDCl_3$.

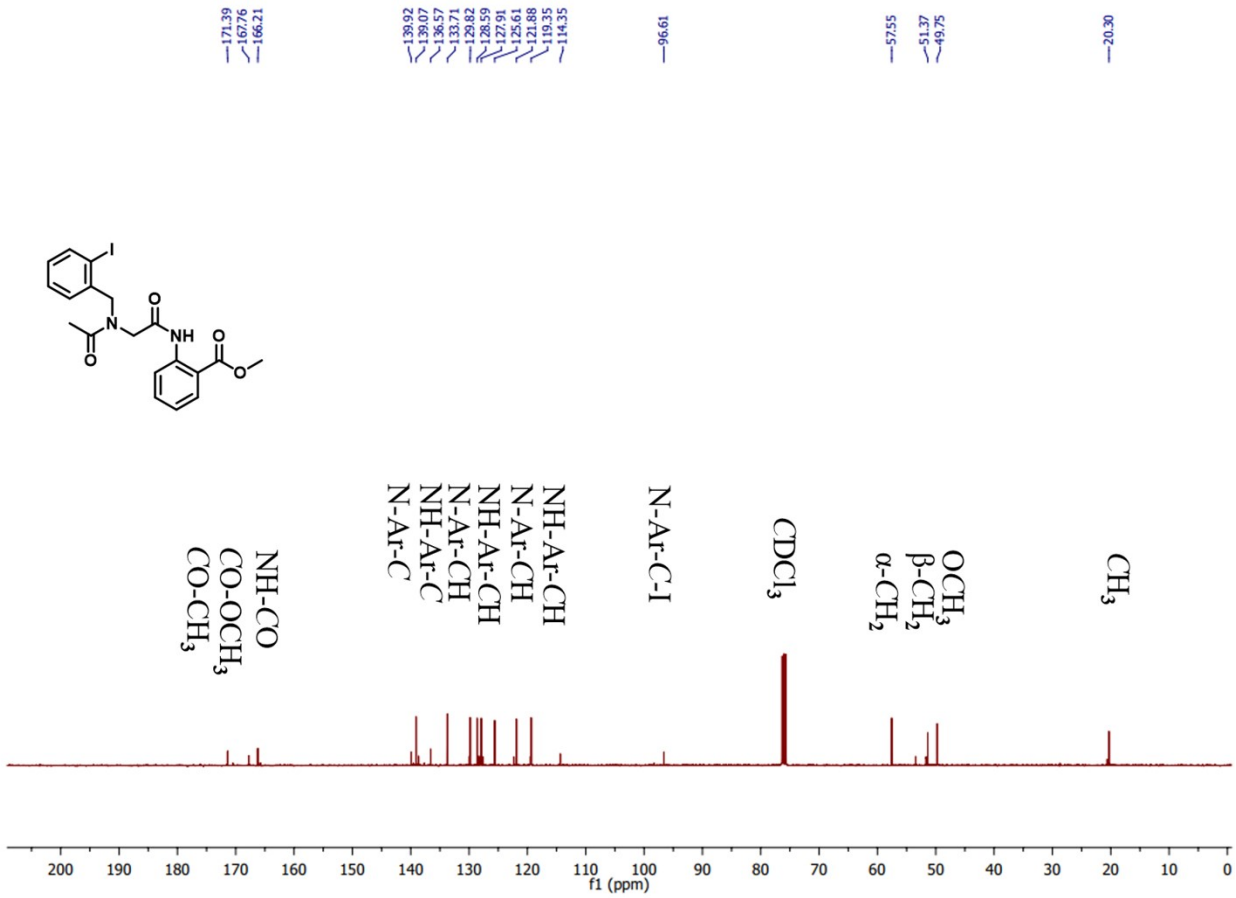


Figure S14. ^{13}C-NMR Spectra of Peptoid **1-I** in $CDCl_3$.

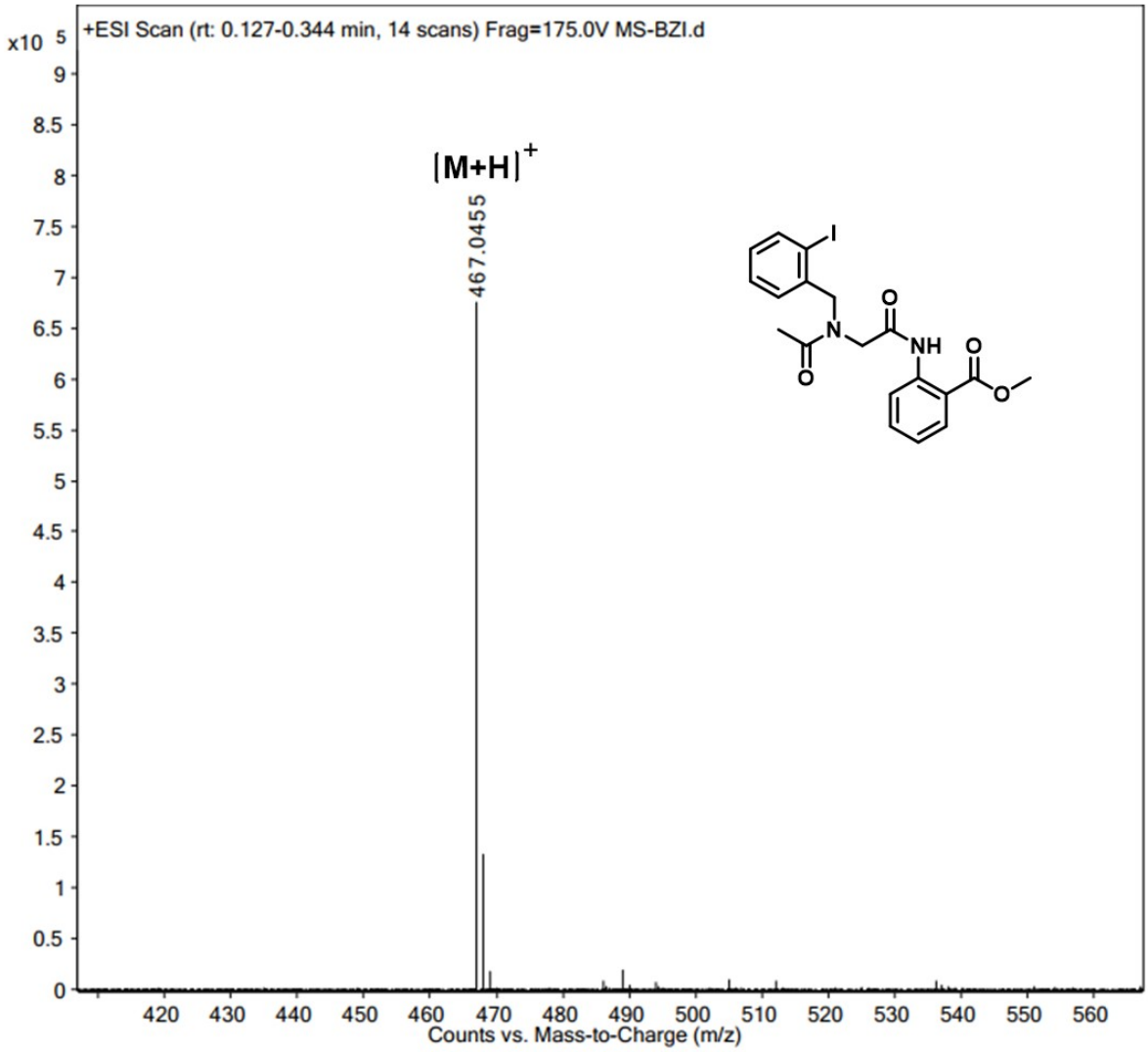


Figure S15. Mass spectra of peptoid **1-I**.

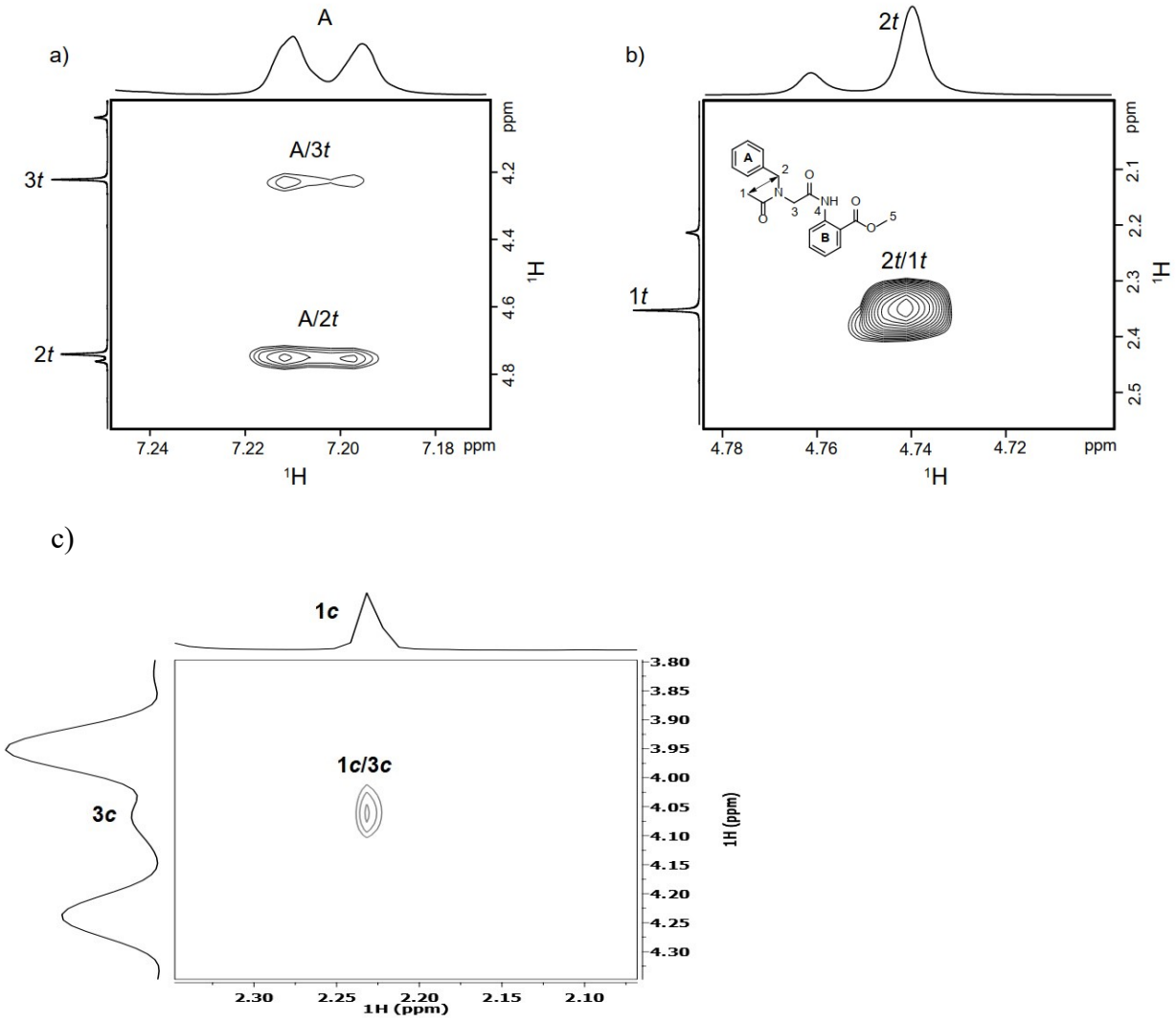


Figure S16. Partial 2D ^{1}H-^{1}H ROSEY spectra of **1-H** peptoid in $CDCl_3$ highlighting ROEs in 500 MHz at 300 K: a) Aromatic ring A↔2t. b) Major conformer 2*t*↔1*t*. c) Minor conformer 1*c*↔3*c*. Note: The double head arrow inserted represents the ROE contours of **1-H**.

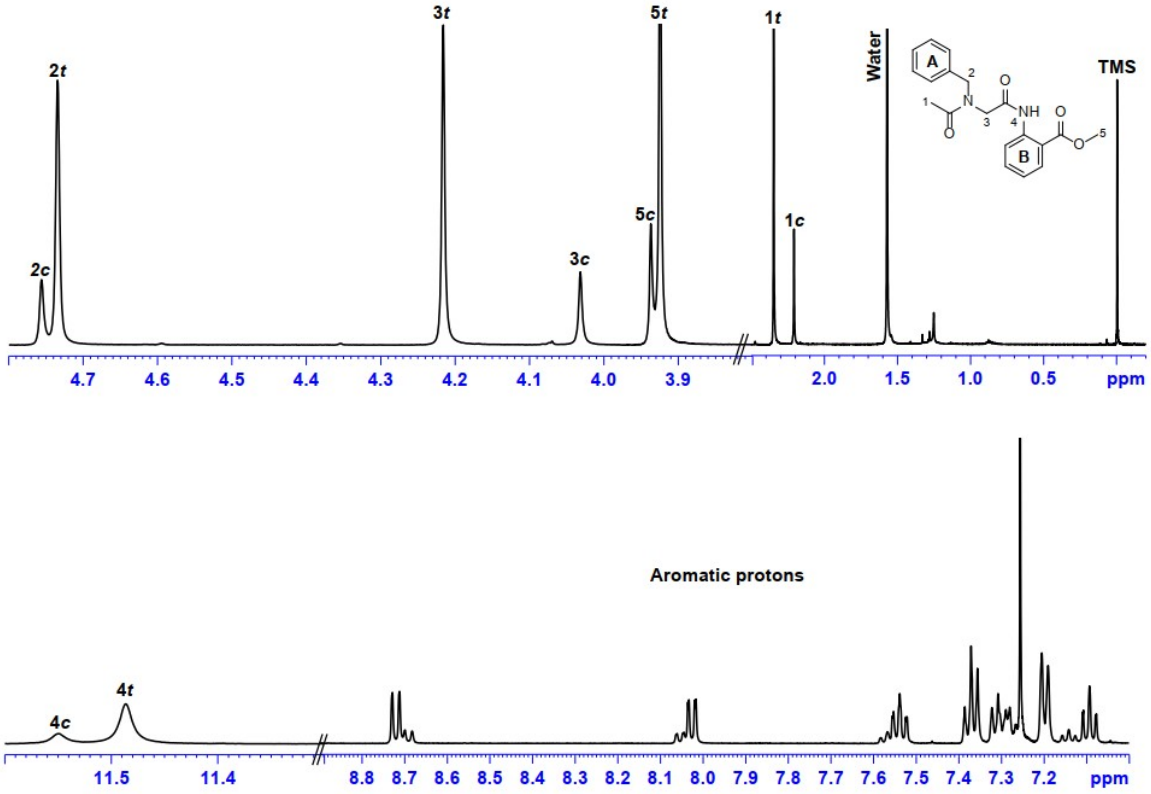


Figure S17. The ^{1}H-NMR Spectra of Peptoid **1-H** in $CDCl_3$ at 300 K.

Backbone benzylic CH_2 groups show cis-trans isomerization as observed by ^{1}H-NMR in $CDCl_3$." with "two sets of resonances. Selective 1D ROESY NMR experiments confirm trans isomer to be more populated".

Table S2: ^{1}H NMR chemical shift values for **1-H** peptoid.

Position	Chemical shift (ppm)
1	**2.3465**, 2.2074
3	**4.2160**, 4.0316
2	**4.7343**, 4.7559
4	**11.4865**, 11.5497
5	**3.9245**, 3.9369

Note: chemical shift values for *trans* isomer were shown in bold.

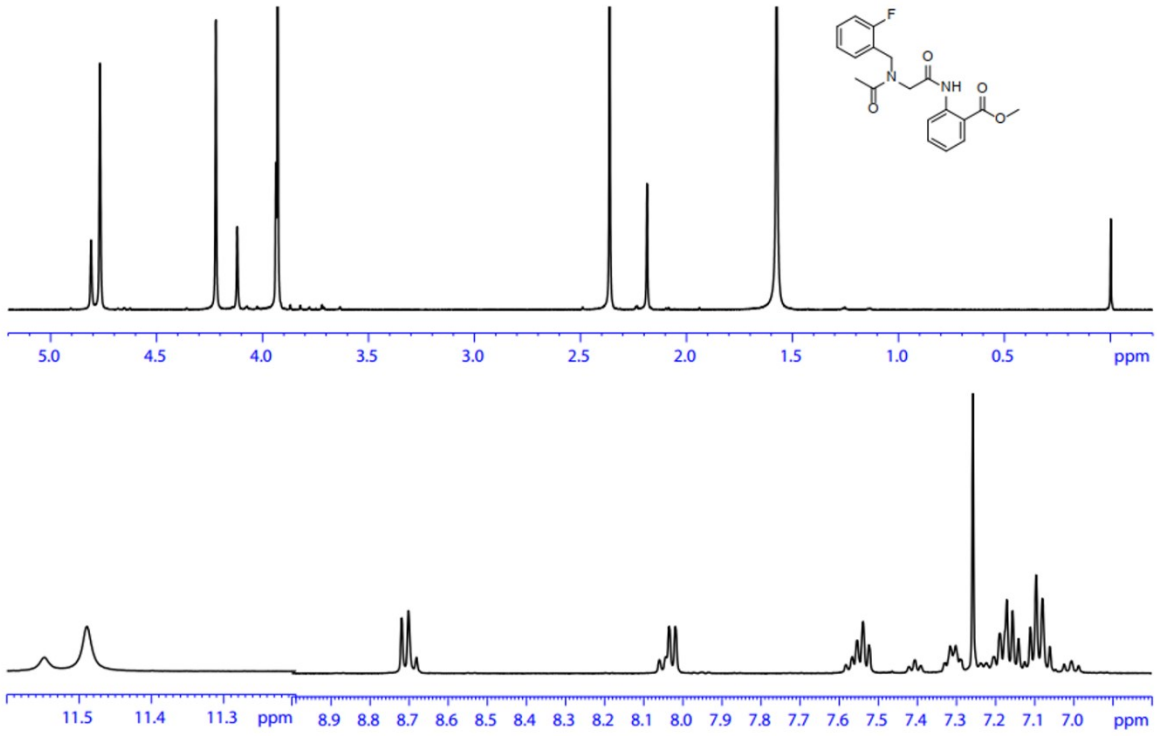


Figure S18. ^{1}H-NMR Spectra of Peptoid **1-F** in $CDCl_3$ at 300 K.

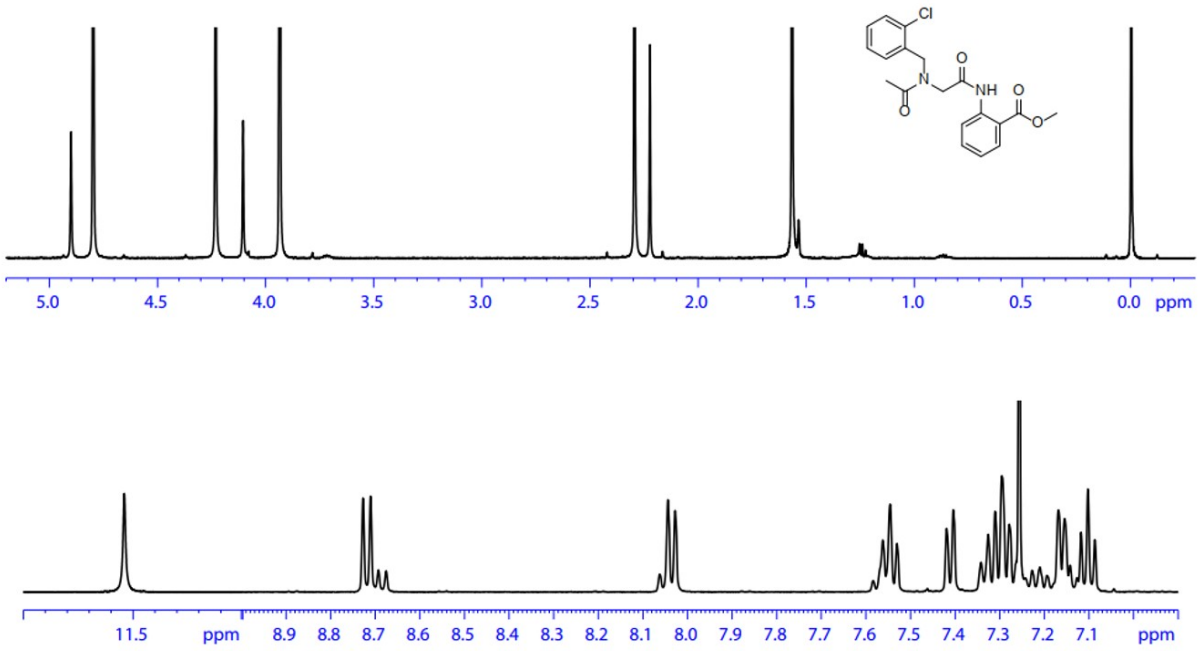


Figure S19. ^{1}H-NMR Spectra of Peptoid **1-Cl** in $CDCl_3$ at 300 K.

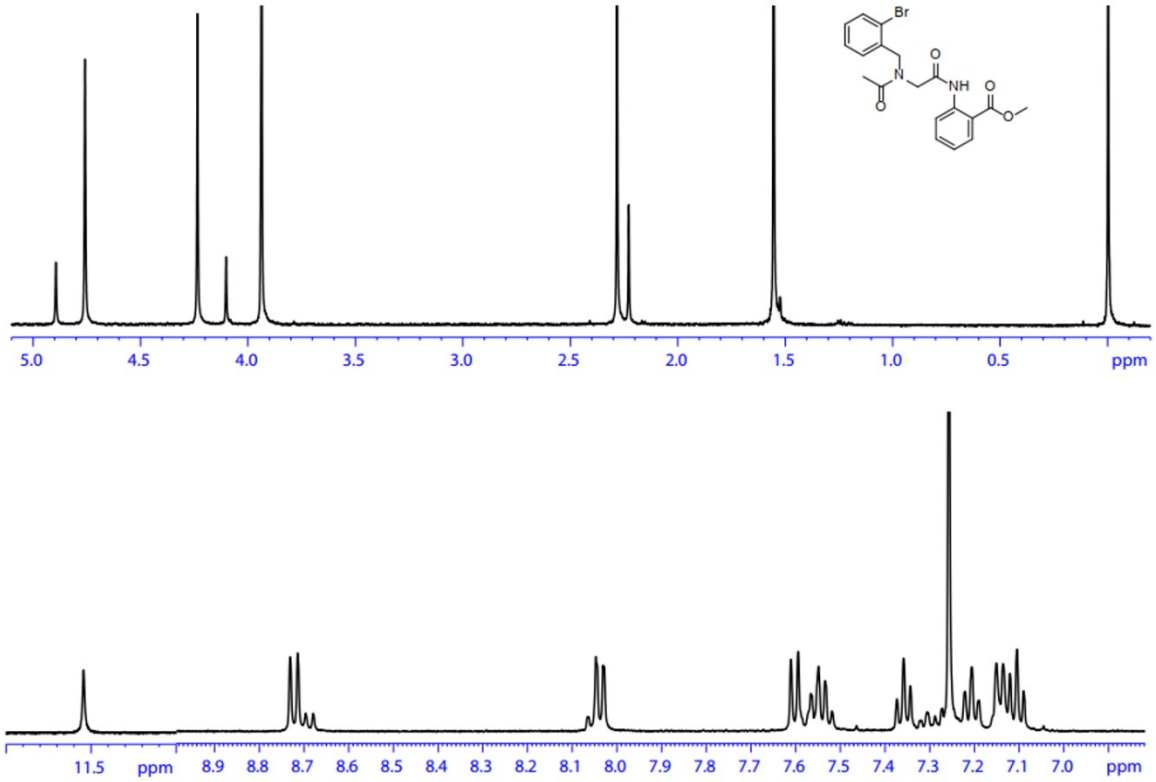


Figure S20. ^{1}H-NMR Spectra of Peptoid **1-Br** in $CDCl_3$ at 300 K.

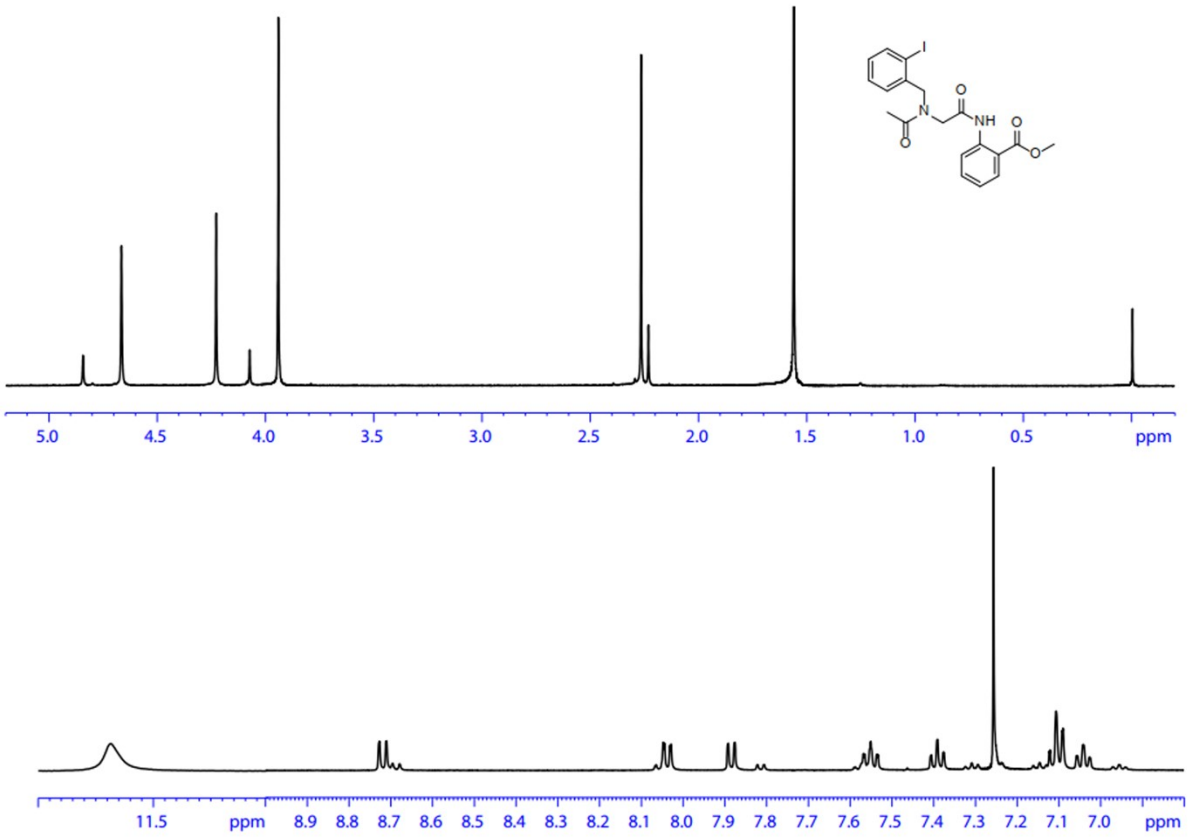


Figure S21. ^{1}H-NMR Spectra of Peptoid **1-I** in $CDCl_3$ at 300 K.

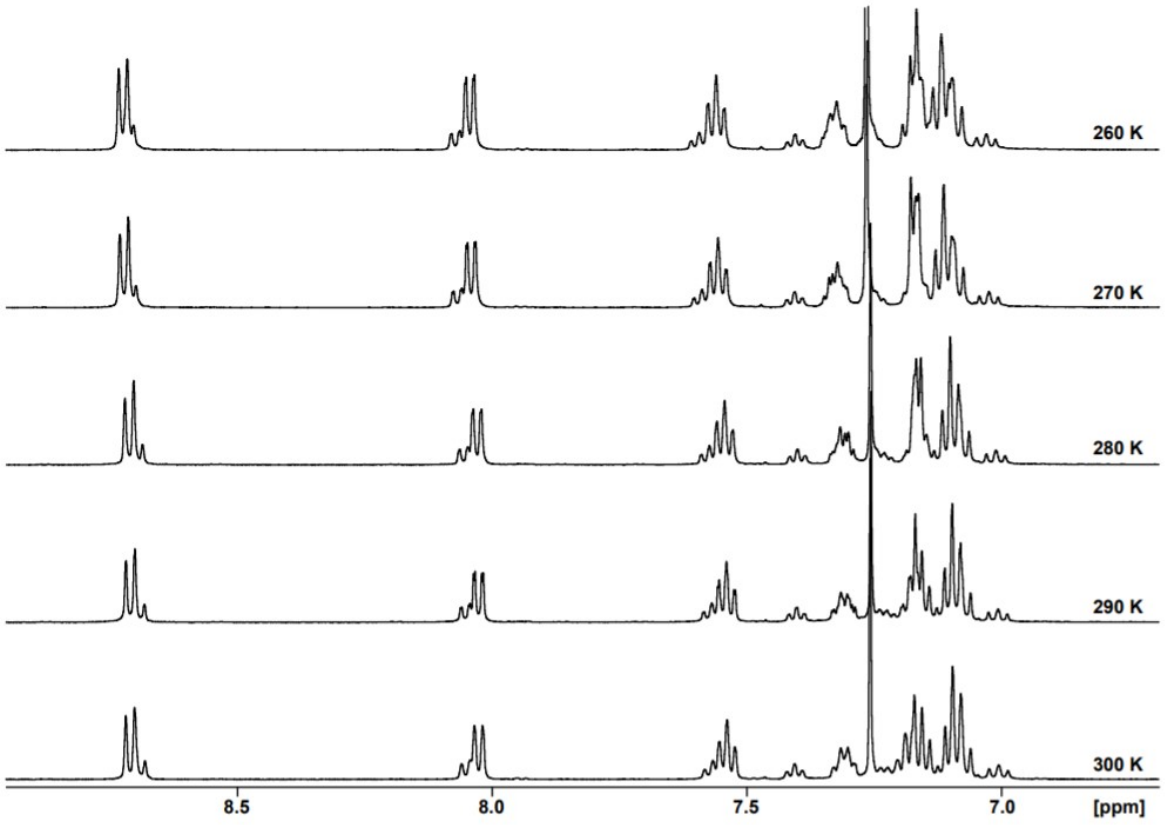


Figure S22. Variable Temperature Expanded Aromatic Region ^{1}H-NMR Spectra of Peptoid **1-F** in $CDCl_3$.

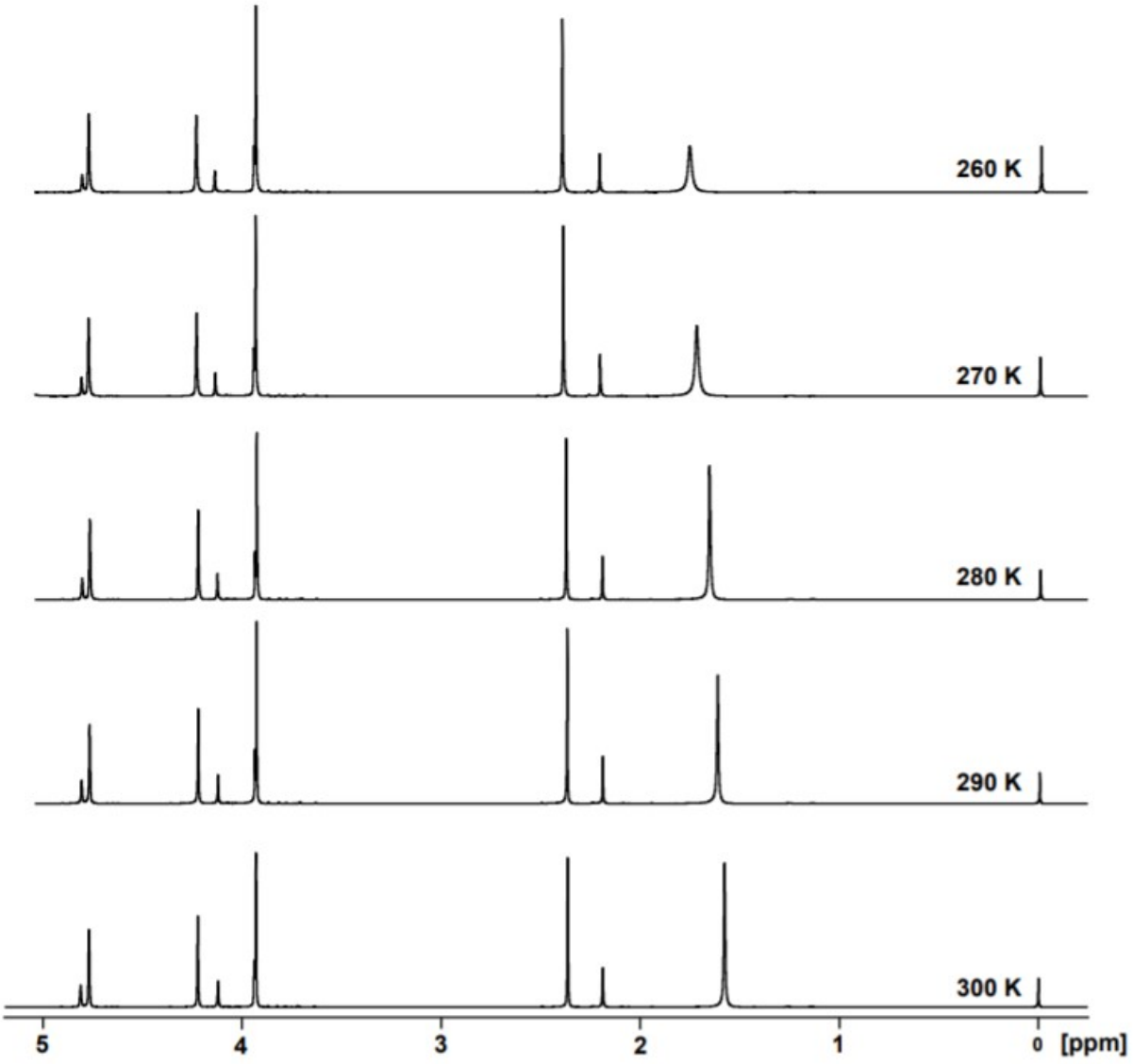


Figure S23. Variable Temperature Expanded Aliphatic Region ^{1}H-NMR Spectra of Peptoid **1-F** in $CDCl_3$.

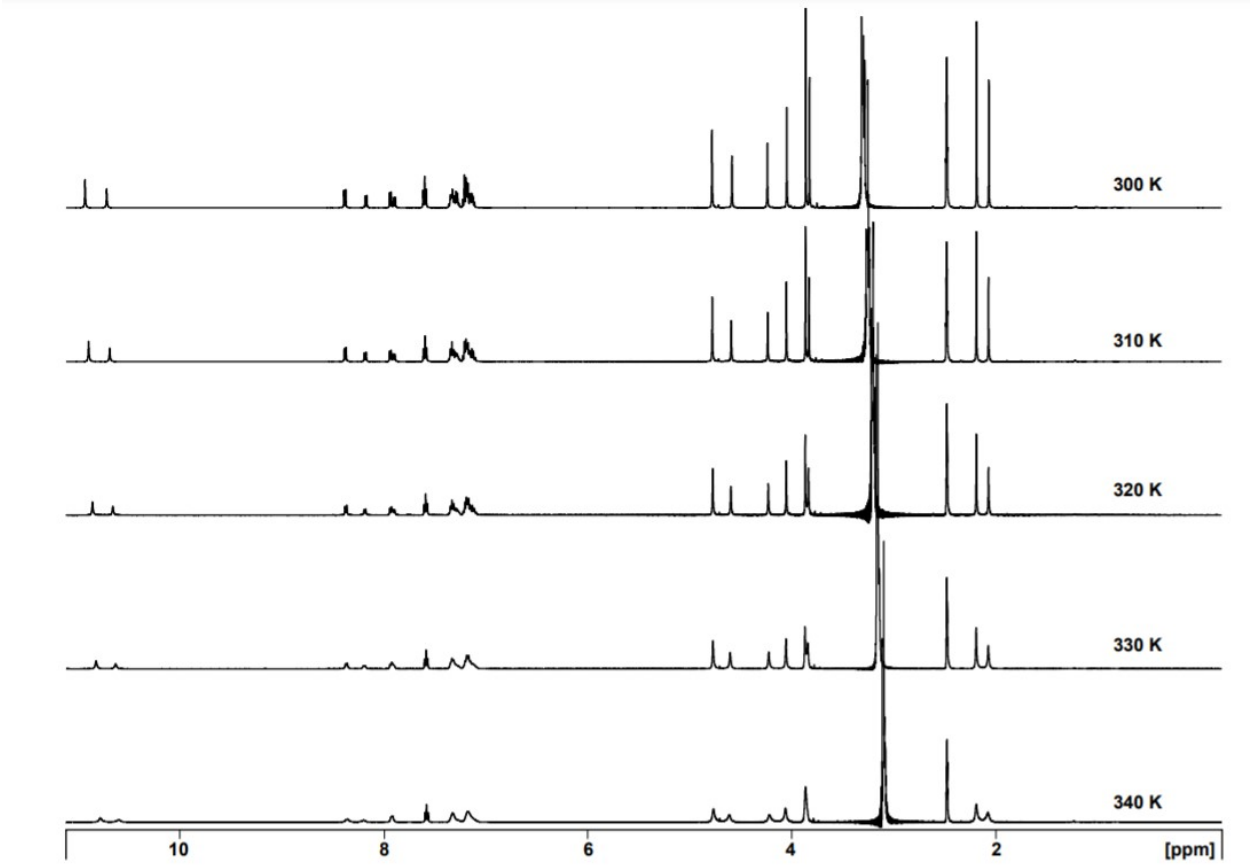


Figure S24. Variable Temperature ^{1}H-NMR Spectra of Peptoid **1-F** in DMSO.

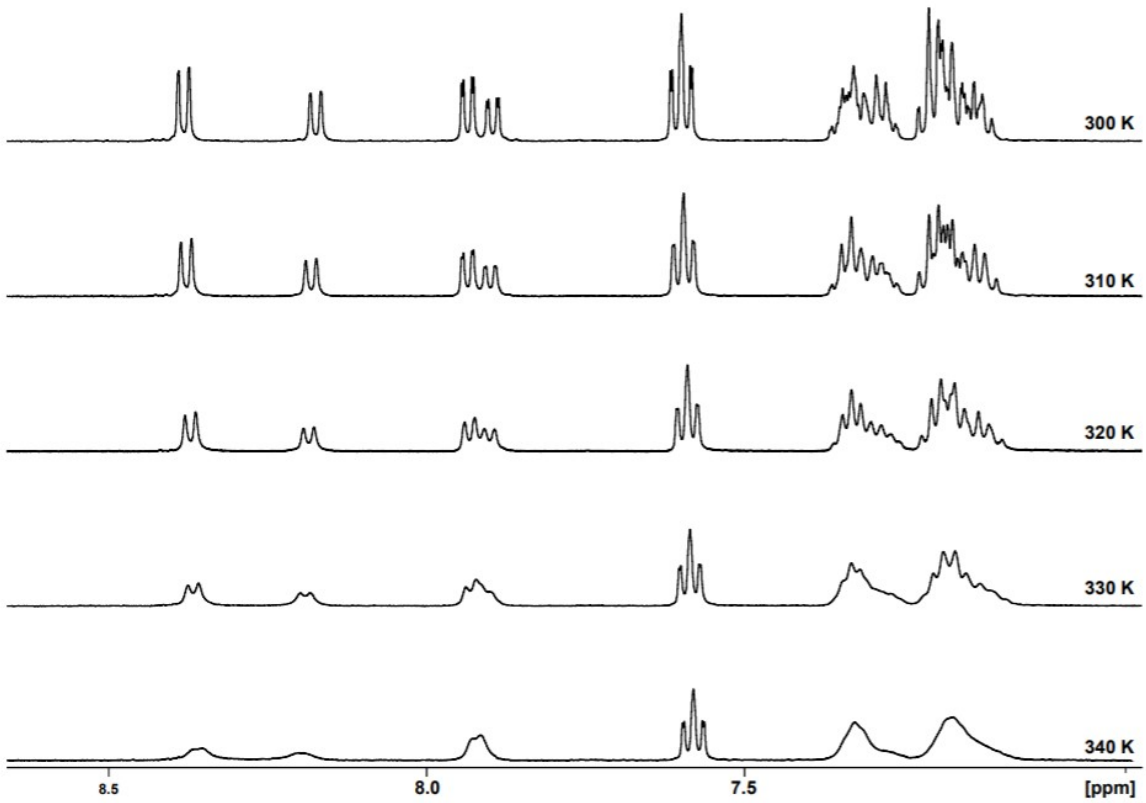


Figure S25. Variable Temperature Expanded Aromatic Region ^{1}H-NMR Spectra of Peptoid **1-F** in DMSO.

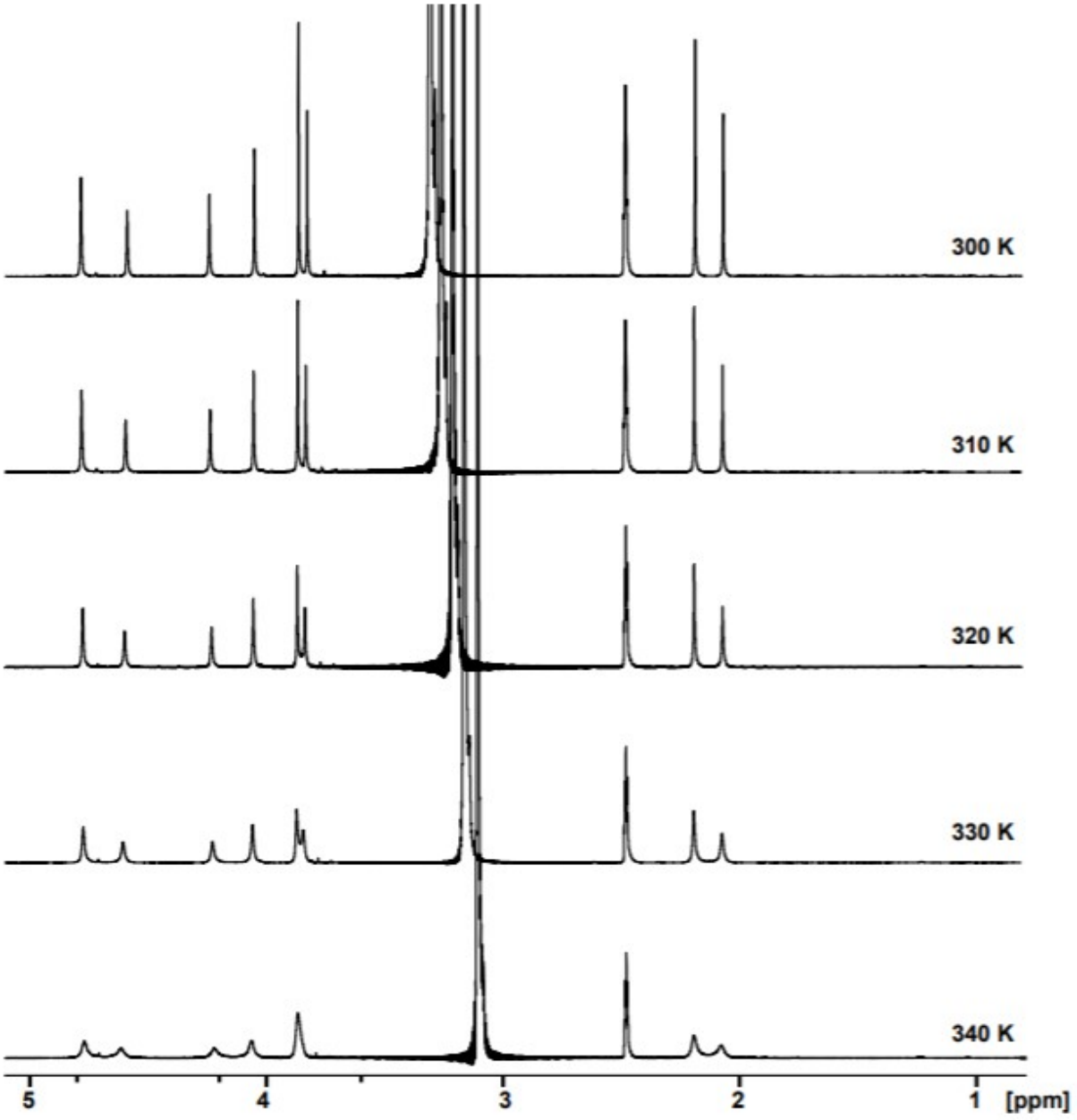


Figure S26. Variable Temperature Expanded Aliphatic Region ^{1}H-NMR Spectra of Peptoid **1-F** in DMSO.

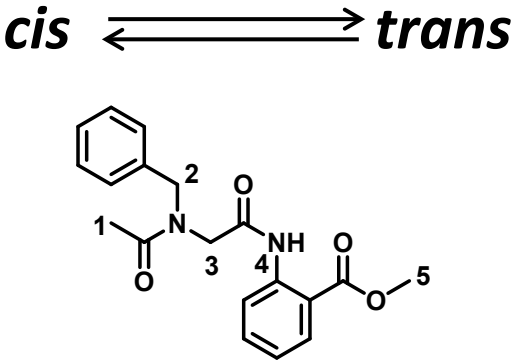


Table S3: Thermodynamic parameters for the *trans/cis* equilibrium (K_{eq})[a] of peptoids in $CDCl_3$.

Peptoid	ΔH (J) × 10^3	ΔS (J/K)	ΔG (kcal/mol)
1-H	-5.63	-7.97	-0.85
1-F	-5.87	-9.80	-0.79
1-Cl	-7.53	-13.44	-0.96
1Br	-7.21	-11.96	-0.98
1-I	-4.76	-3.87	-0.90

[a]K_{eq} = [*trans*/*cis*]

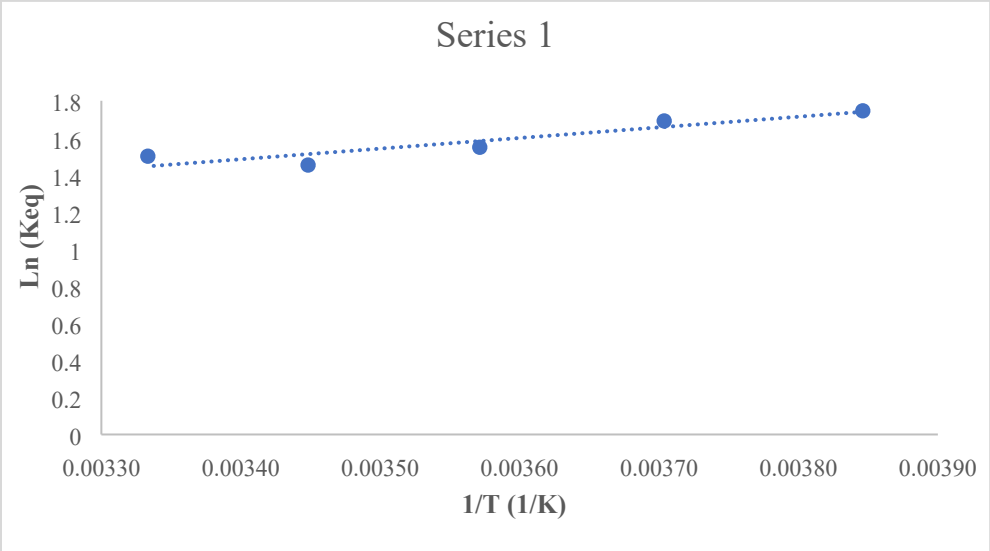
Table S4: *Cis-trans* ratio in solvents

Compound	Temperature (K)	%*trans*	%*cis*	k_{eq}	ln (k_{eq})	R (J/K·mol)	ΔG (J/mol)	ΔG (kcal/mol)
1-H	300	73.32	26.68	2.75	1.010876174	8.314462618	-2521.467649	-0.60
1-F	300	71.69	28.31	2.53	0.929122711	8.314462618	-2317.546814	-0.55
1-Cl	300	70.13	29.87	2.35	0.853315933	8.314462618	-2128.459027	-0.51
1-Br	300	70.63	29.37	2.40	0.877310432	8.314462618	-2188.309438	-0.52
1-I	300	71.11	28.89	2.46	0.90090963	8.314462618	-2247.173832	-0.54

Table S5: van't Hoff plot

Temperature,T (K)	*%trans*	*%cis*	K_{eq}	1/T	ln (K_{eq})
260	85.14	14.86	5.73	0.00385	1.745830537
270	84.44	15.56	5.43	0.00370	1.691190414
280	82.48	17.52	4.71	0.00357	1.54928399
290	81.05	18.95	4.28	0.00345	1.45328923
300	81.77	18.23	4.49	0.00333	1.501032039

Slope (m), $-\Delta H/R$	Y-intercept, $\Delta S/R$	ΔH (J)	ΔS (J/K)	ΔG (J/mol)	ΔG (kcal/mol)
573.58	-0.4656	-4769.01	-3.87	-3762.493882	-0.90



6. HPLC Data

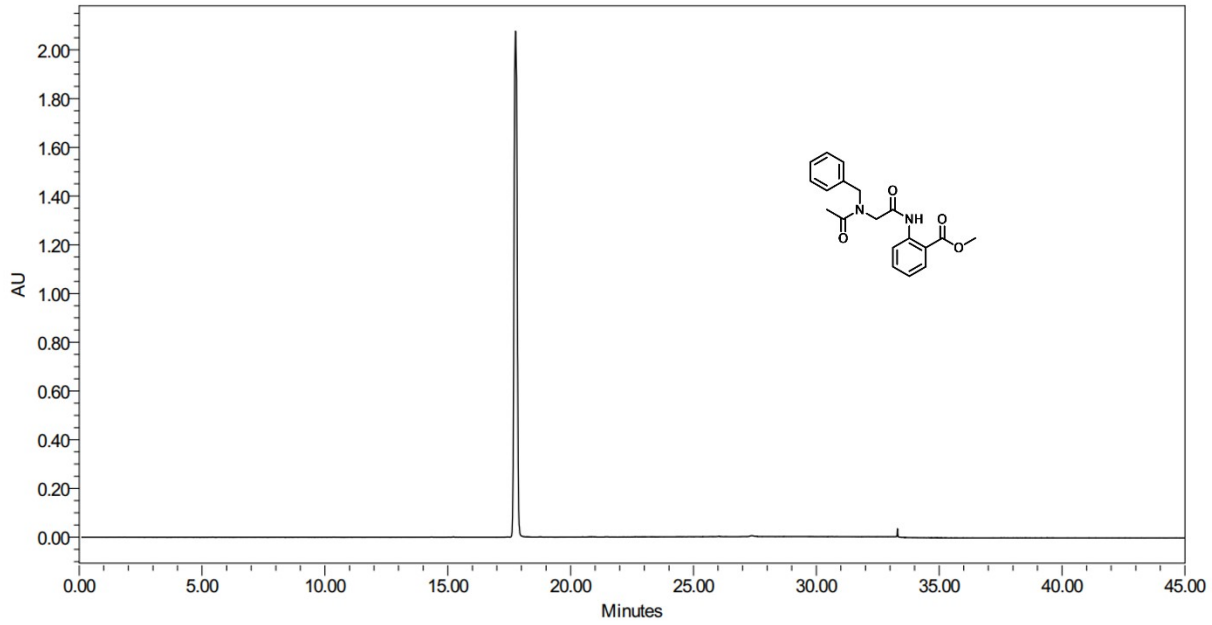


Figure S27. Characterization of peptoid **1-H** by RP-HPLC.

Analytical HPLC Condition: Luna C18 (4.6 × 150 mm column, 5 µm particle size), Acetonitrile (solvent A), Water (solvent B), Gradient 20 % solvent A to 100 % solvent B in 45 min, the flow rate of 1mL min^{-1}, Injection volume 2µL, Column temperature 5-10 ºC, Detection wavelength= 221 nm. No separation of cis and transforms of peptoids was observed by RP-HPLC.

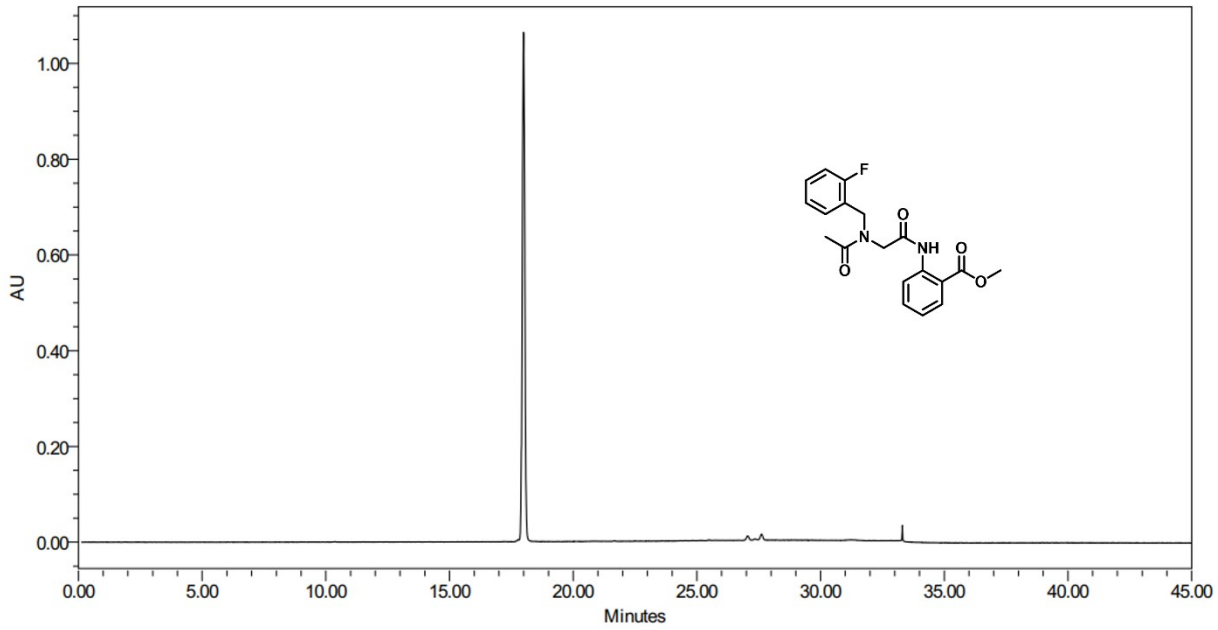


Figure S28. Characterization of ortho-substituted peptoid **1-F** by RP-HPLC.

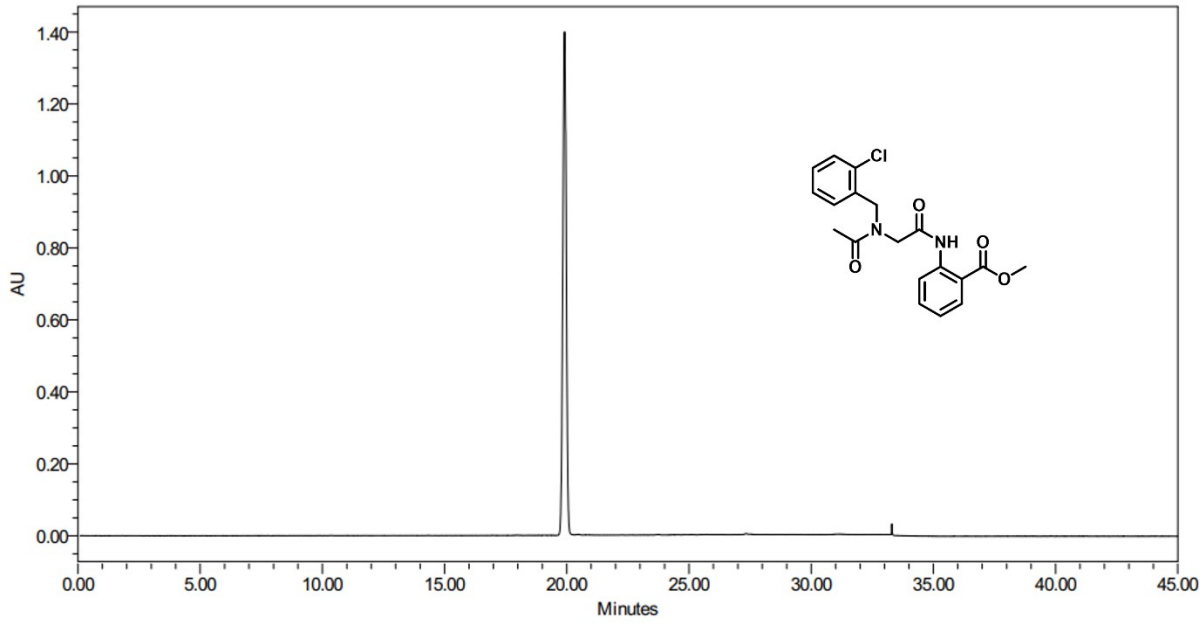


Figure S29. Characterization of ortho-substituted peptoid **1-Cl** by RP-HPLC.

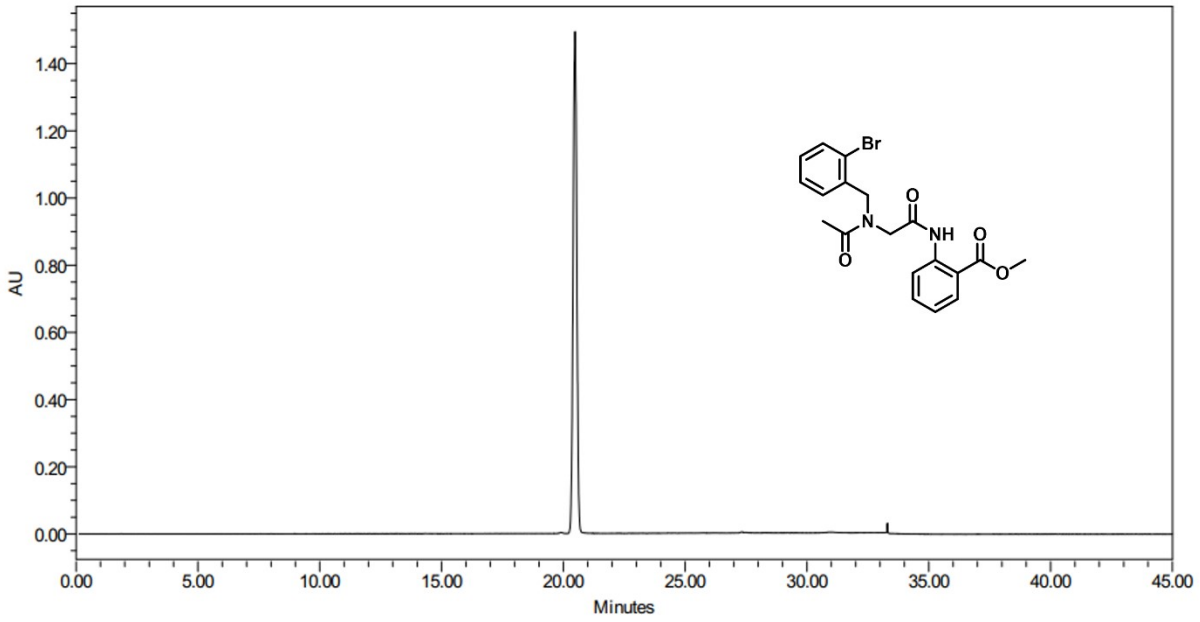


Figure S30. Characterization of ortho-substituted peptoid **1-Br** by RP-HPLC.

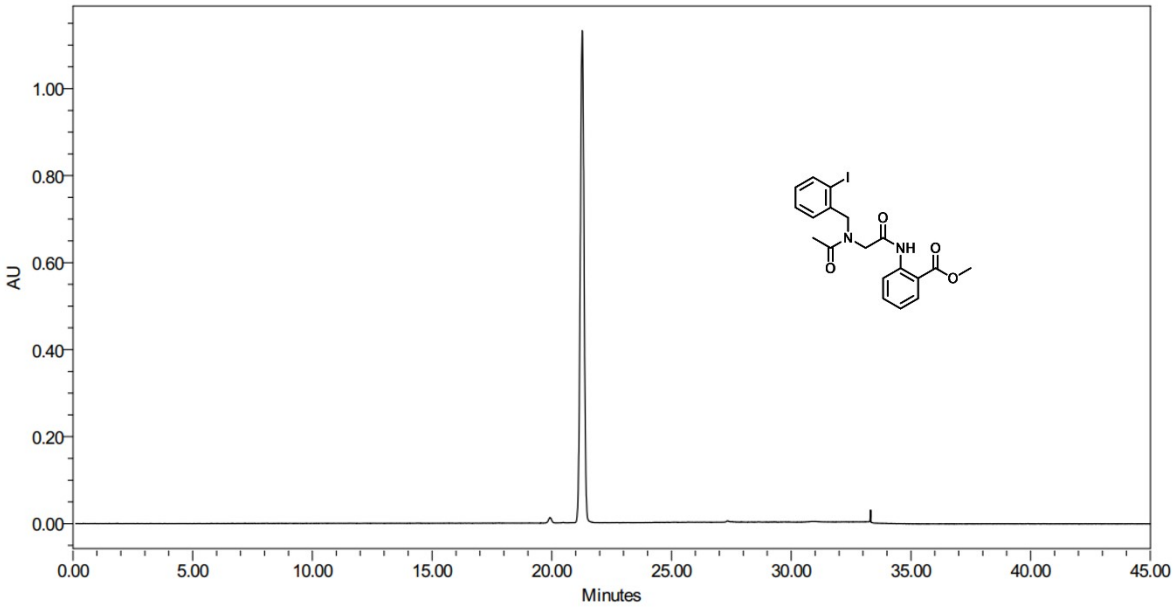
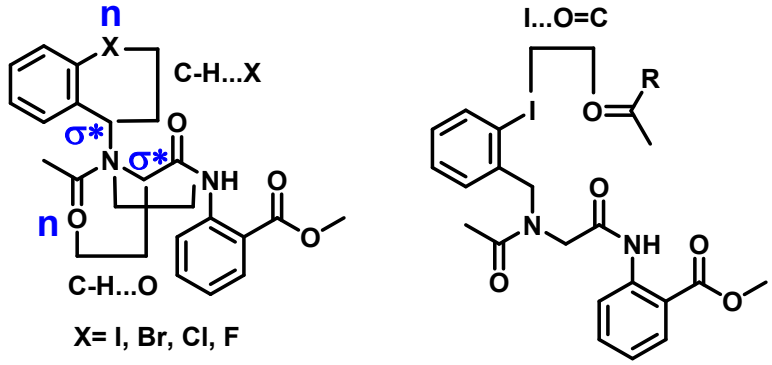


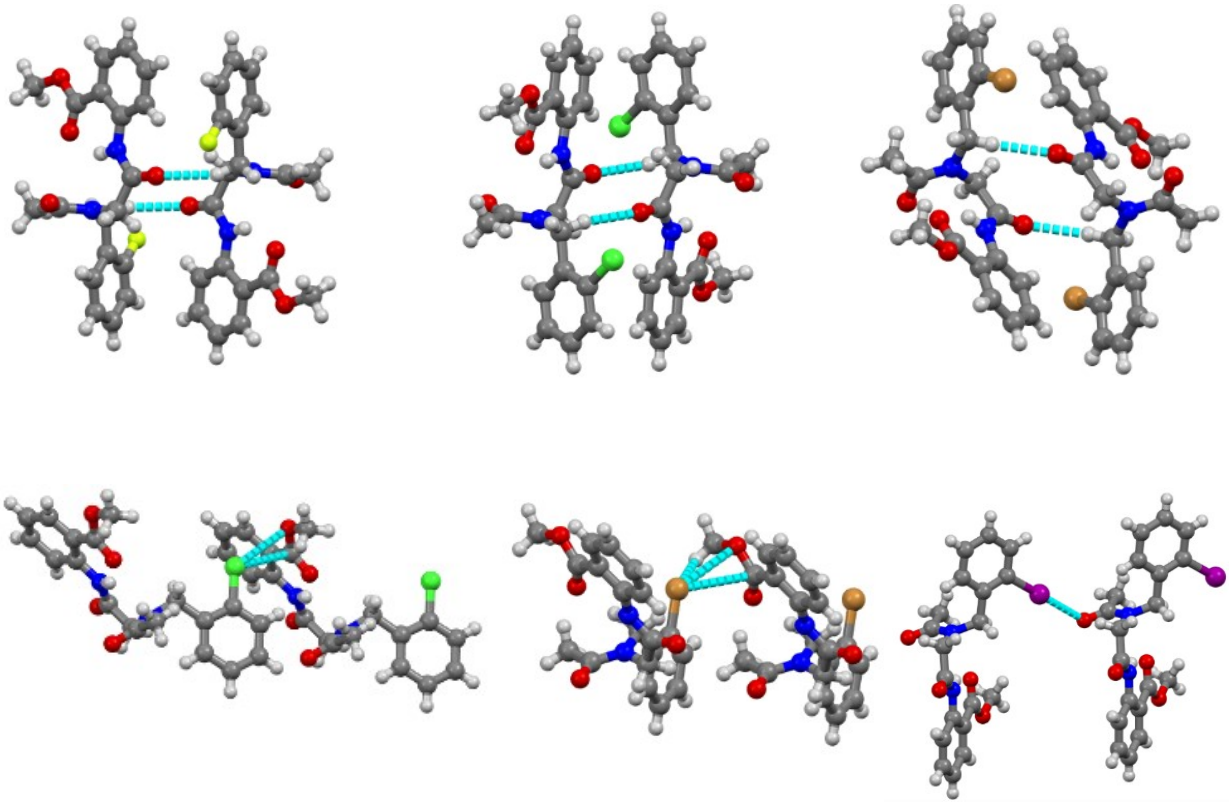
Figure S31. Characterization of ortho-substituted peptoid **1-I** by RP-HPLC.

7. Crystallographic Data



Scheme 3. Noncovalent interaction depicting C-H---O, C-H---X (Hydrogen Bonding), and C_{aryl}-X---O=C (Halogen Bonding).

We further investigated the crystal structures of N-benzyl peptoid model systems: **1-H, 1-F**, **1-Cl**, **1-Br** and **1-I**.



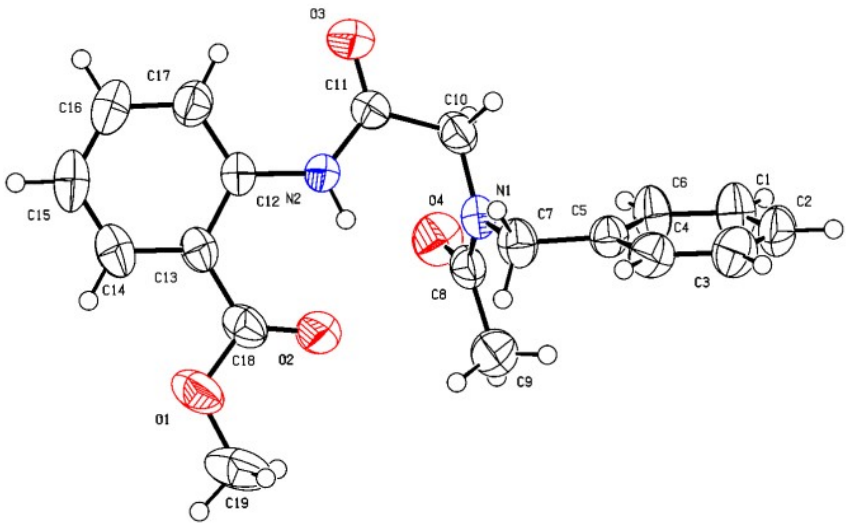


Figure S33. Crystal structure ORTEP diagram of ortho-substituted peptoid **1-H**.

Table S6. Crystallographic data and structure refinement of peptoid **1-H**

Empirical formula	$C_{19}H_{20}N_2O_4$
Formula Weight	340.3790
Crystal system	triclinic
Space group	P -1
Temperature	296 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 8.4482(19) Å, α = 101.727(12)
	b = 10.535(3) Å, β = 97.628(11)
	c = 10.731(3) Å, γ = 104.253(13)

Volume	889.4(4) Å^3
Z, Calculated density	2
Absorption coefficient μ (mm^{-1})	0.090 mm^-1
F(000)	360.0
Crystal size	0.20 mm
D_{cal} (g/cm^{-3})	1.271
Refinement method	SHELXT
Reflections collected	4499
R_1[I> 2 sigma(I)]	0.0611
wR_2 (all data)	0.1678
Goodness of Fit	0.960

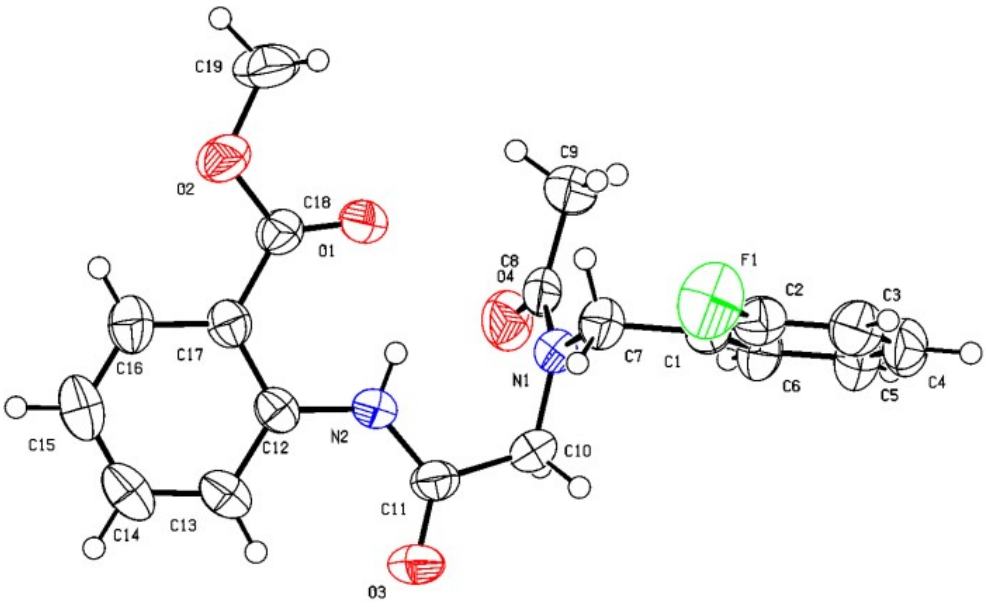


Figure S34. Crystal structure ORTEP diagram of ortho-substituted peptoid **1-F**.

Table S7. Crystallographic data and structure refinement of peptoid **1-F**

Empirical formula	$C_{19}H_{19}F\,N_2O_4$
Formula Weight	358.3694
Crystal system	triclinic
Space group	P -1
Temperature	296 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 9.5349(6) Å, α = 76.135(3)
	b = 10.5406(7) Å, β = 66.751(3)
	c = 10.6231(7) Å, γ = 64.827(3)
Volume	884.49(10) Å^3
Z, Calculated density	2
Absorption coefficient μ (mm^{-1})	0.102 mm^-1
F(000)	376.0
Crystal size	0.20 mm
D_{cal} (g/cm^{-3})	1.346
Refinement method	SHELXT
Reflections collected	5426
R_1[I> 2 sigma(I)]	0.0502
wR_2 (all data)	0.1589
Goodness of Fit	0.992

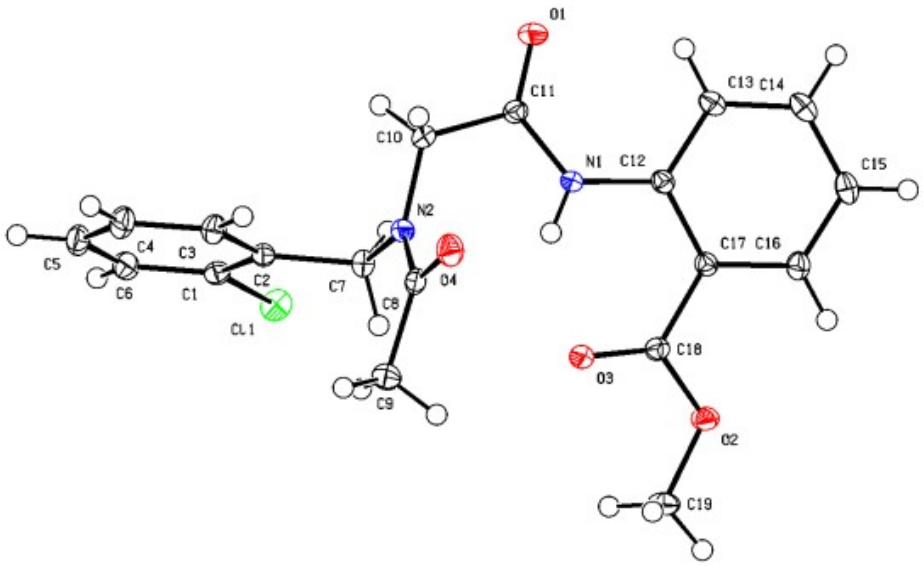


Figure S35. Crystal structure ORTEP diagram of ortho-substituted peptoid **1-Cl**.

Table S8. Crystallographic data and structure refinement of peptoid **1-Cl**

Empirical formula	$C_{19}H_{19}Cl\,N_2O_4$
Formula Weight	374.8210
Crystal system	triclinic
Space group	P -1
Temperature	100 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 9.5811(3) Å, α = 74.919(2)
	b = 10.4629(4) Å, β = 66.039(2)
	c = 10.6719(4) Å, γ = 64.784(2)
Volume	879.53(6) Å^3
Z, Calculated density	2

Absorption coefficient μ (mm^{-1})	0.245 mm^-1
F(000)	392.0
Crystal size	0.20 mm
D_{cal} (g/cm^{-3})	1.415
Refinement method	SHELXT
Reflections collected	5363
R_1[I> 2 sigma(I)]	0.0381
wR_2 (all data)	0.1116
Goodness of Fit	0.995

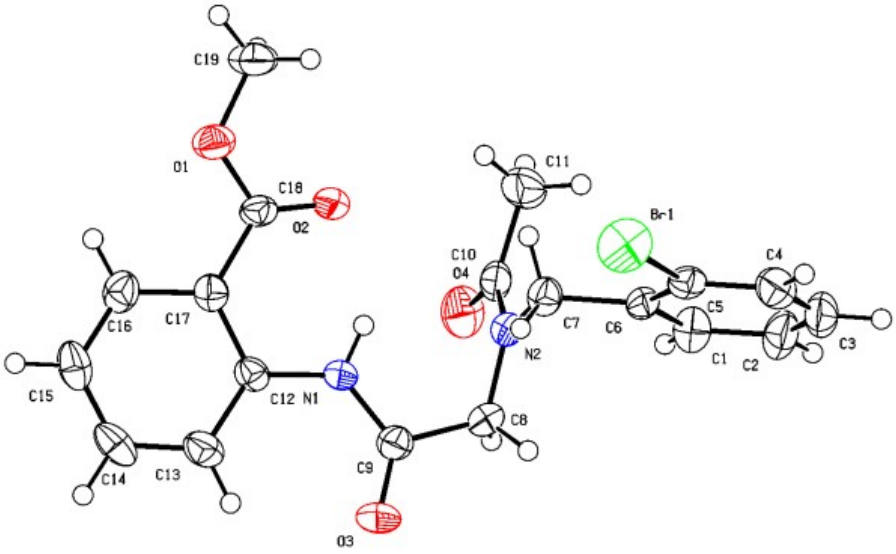


Figure S36. Crystal structure ORTEP diagram of ortho-substituted peptoid **1-Br**.

Table S9. Crystallographic data and structure refinement of peptoid **1-Br**

Empirical formula	$C_{19}H_{19}Br\,N_2O_4$

Formula Weight	419.2750
Crystal system	triclinic
Space group	P -1
Temperature	296 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 9.6335(9) Å, α = 74.967(4)
	b = 10.5541(11) Å, β = 66.776(4)
	c = 10.7463(9) Å, γ = 66.004(4)
Volume	910.89(15) Å^3
Z, Calculated density	2
Absorption coefficient μ (mm^{-1})	2.283 mm^-1
F(000)	428.0
Crystal size	0.500 mm
D_{cal} (g/cm^{-3})	1.529
Refinement method	SHELXT
Reflections collected	4545
R_1[I> 2 sigma(I)]	0.0620
wR_2 (all data)	0.2054
Goodness of Fit	0.951

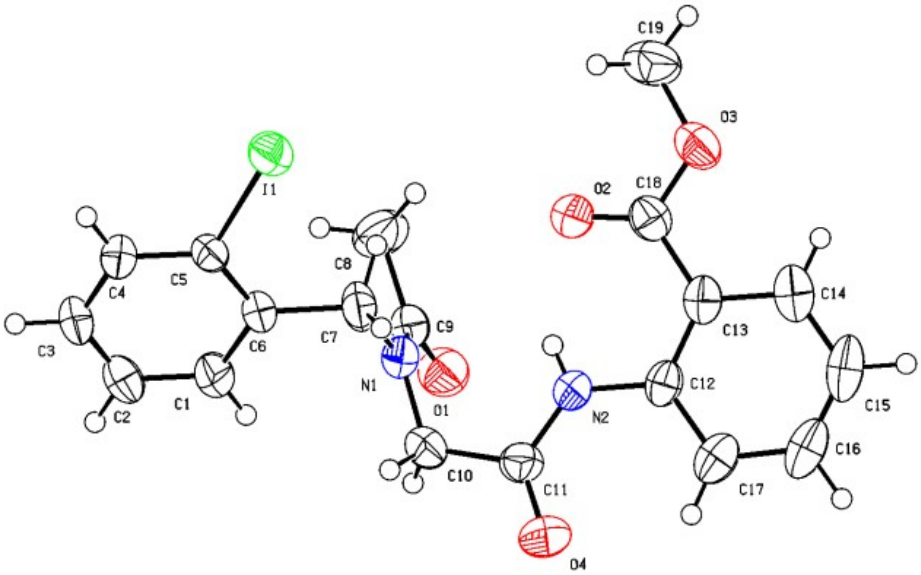


Figure S37. Crystal structure ORTEP diagram of ortho-substituted peptoid **1-I**.

Table S10. Crystallographic data and structure refinement of peptoid **1-I**

Empirical formula	$C_{19}H_{19}IN_2O_4$
Formula Weight	466.2755
Crystal system	triclinic
Space group	P -1
Temperature	296 K
Wavelength	0.71073 Å
Unit cell dimensions	a = 8.7203(5) Å, α = 74.064(3)
	b = 9.1769(7) Å, β = 88.893(3)
	c = 13.4991(9) Å, γ = 71.669(3)
Volume	983.38(12) Å^3
Z, Calculated density	2

Absorption coefficient μ (mm^{-1})	1.653 mm^-1
F(000)	464.0
Crystal size	0.350 mm
D_{cal} (g/cm^{-3})	1.575
Refinement method	SHELXT
Reflections collected	4925
R_1[I> 2 sigma(I)]	0.0309
wR_2 (all data)	0.0867
Goodness of Fit	0.971

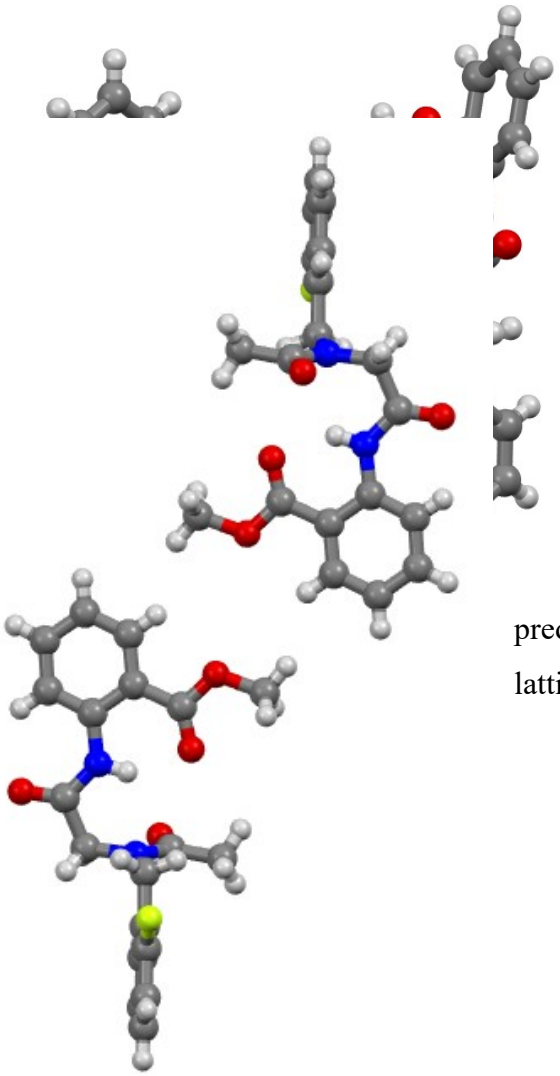


Figure S38. The predominant structure was observed in the lattice of Peptoid **1-H**.

Figure S39. The predominant structure was observed in the lattice of Peptoid **1-F**.

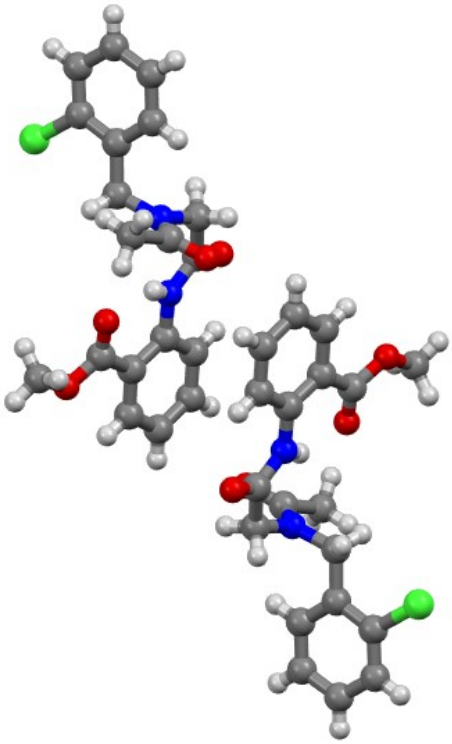


Figure S40. The predominant structure was observed in the lattice of Peptoid **1-Cl**.

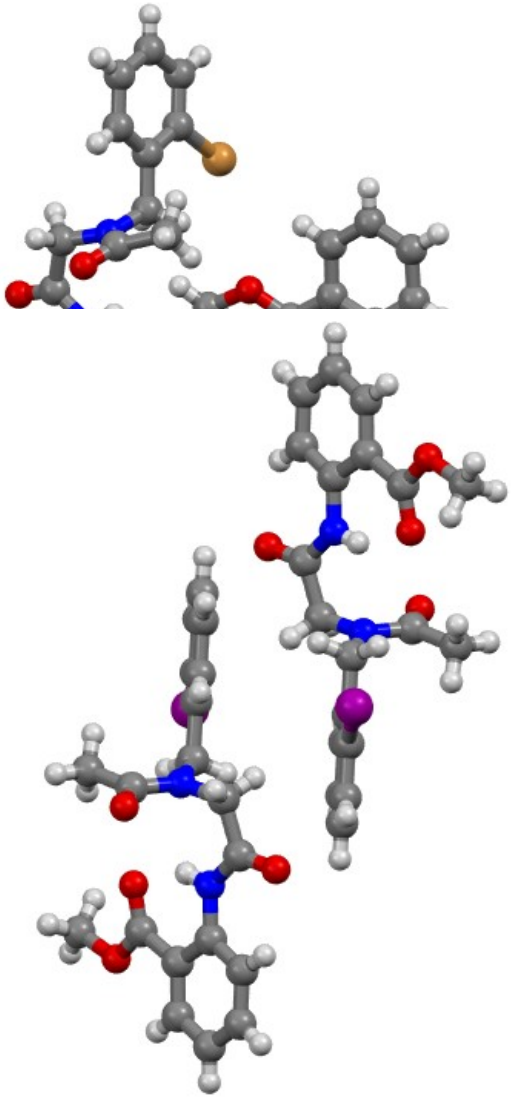
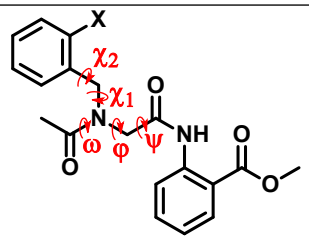


Figure S41. The predominant structure observed in the lattice of Peptoid **1-Br**.

Figure S42. The predominant structure is observed in the lattice of Peptoid **1-I**.

8. Computational Details

Table S11. Comparison of dihedral angles observed from the X-ray Crystallography and Optimized structures of 1-F, 1-Cl, 1-Br and **1-I.**



Comp.	Method	ω (°)	φ (°)	ψ (°)	χ_1 (°)	χ_2 (°)
1-H		-176.24	-89.01	3.13	-84.67	
1-F	Crystal	-176.8	-94.6	12.9	87.0	-171.4
	Optimized	-177.6	-101.1	10.8	86.8	-175.5
1-Cl	Crystal	-175.5	-95.4	15.3	86.8	-171.1
	Optimized	-177.9	-100.9	10.7	87.7	-177.7
1-Br	Crystal	-176.2	-95.3	15.8	88.5	173.6

	Optimized	-178.0	-100.7	10.3	88.3	-178.1
1-I	Crystal	178.0	87.4	-2.7	-91.9	-165.8
	Optimized	178.1	100.7	-10.2	-88.5	178.7

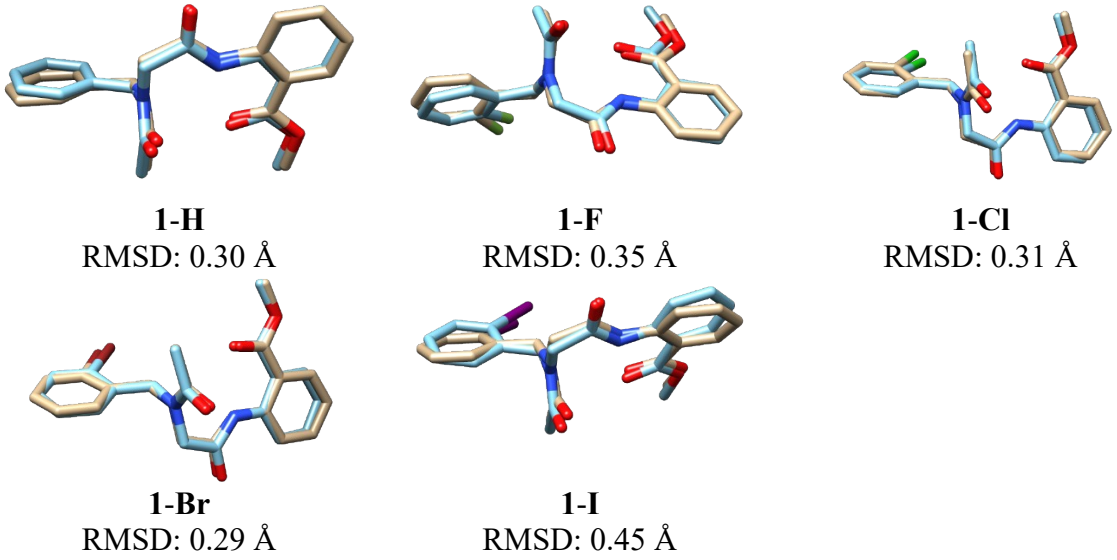
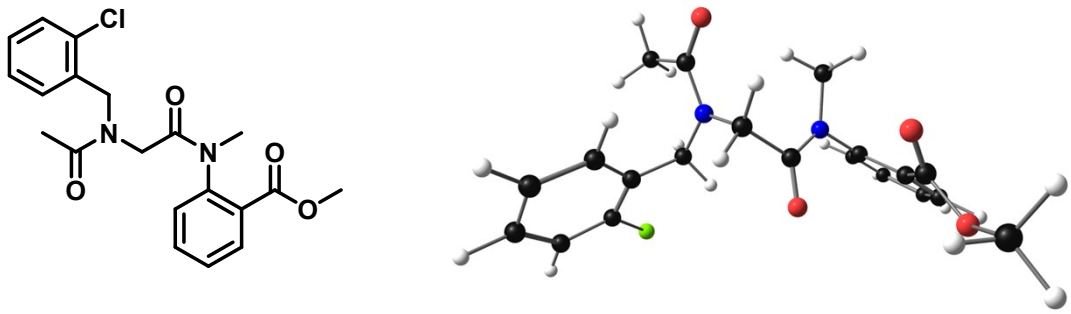


Figure S43. Overlay diagram for structural similarity of X-ray crystal structure and DFT optimised structure. All non-hydrogen atoms were used to calculate the RMSD.



NBO E^2 ($n_O \rightarrow \sigma^*_{C\text{-}H}$) = 0.24 kcal/mol

Figure S44. Chemdraw and Optimised structure of **1-Cl-Me**.

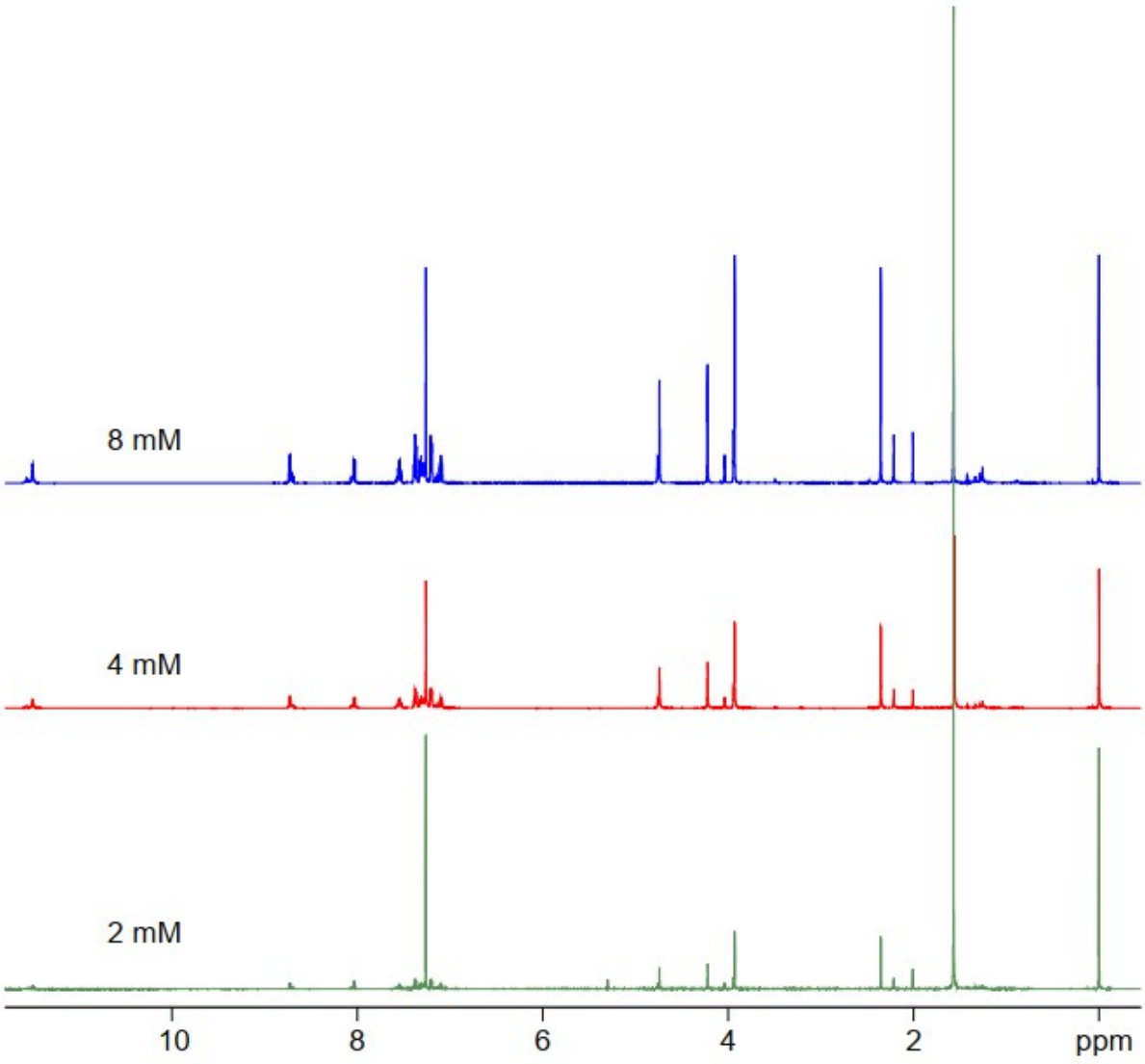


Figure S45. 1D ^{1}H Overlay of **1-H** at varying concentrations.

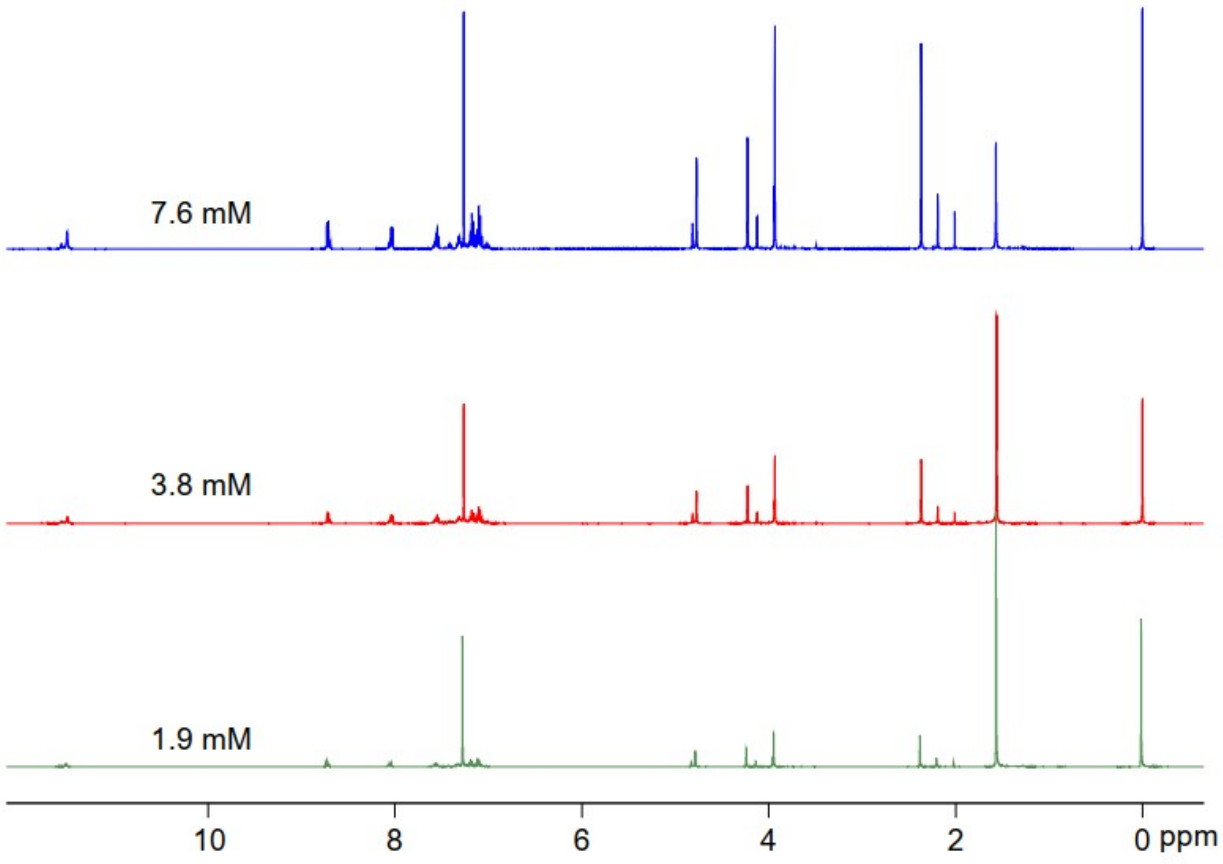
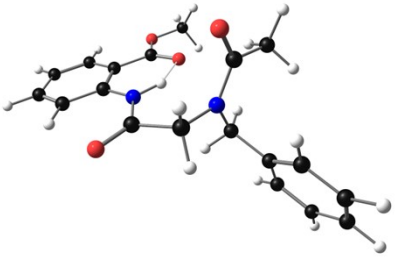


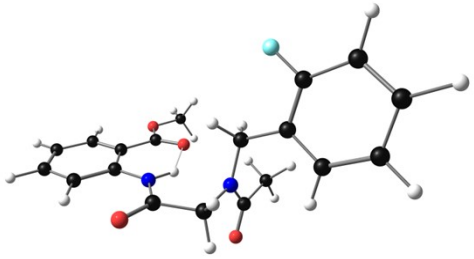
Figure S46. 1D ^{1}H Overlay of **1-F** at varying concentrations.

9. Optimized Cartesian coordinates, number of imaginary frequencies and total energy (E in a.u.) of the optimised structures



1-H
M062X/6-311+G(2d,p)
E = -1146.40366702 au

-ve frequency = nil			
6	5.481275	-0.418549	0.020938
1	6.159356	-0.733951	0.803950
6	5.968986	-0.118453	-1.241468
1	7.028339	-0.197623	-1.449488
6	5.088529	0.281599	-2.240937
1	5.460539	0.514584	-3.230774
6	3.732576	0.378673	-1.972578
1	3.047358	0.686719	-2.755628
6	3.235885	0.082233	-0.704579
6	4.119798	-0.318175	0.289240
1	3.746712	-0.556733	1.278617
6	1.746260	0.223923	-0.451195
1	1.446824	1.266755	-0.561467
1	1.197545	-0.324630	-1.222989
6	1.236964	0.509956	1.971322
6	1.624020	1.962989	1.822771
1	0.864012	2.484749	1.237543
1	2.588319	2.076164	1.324910
1	1.668255	2.391925	2.819419
6	1.004830	-1.681413	0.938868
1	1.092529	-1.991417	1.979842
1	1.715220	-2.259299	0.343999
6	-0.397497	-2.079669	0.471971
6	-2.556128	-1.004295	-0.152487
6	-3.196753	0.237176	-0.372320
6	-4.535913	0.257077	-0.770331
1	-5.013173	1.212835	-0.931836
6	-5.243093	-0.913257	-0.958318
1	-6.278851	-0.880285	-1.267886
6	-4.604934	-2.129520	-0.742312
1	-5.146761	-3.056658	-0.883219
6	-3.281793	-2.185056	-0.343970
1	-2.793319	-3.130712	-0.174272
6	-2.479244	1.523181	-0.198034
6	-2.620075	3.854933	-0.237036
1	-2.229446	3.952926	0.774597
1	-3.390515	4.596373	-0.424667
1	-1.803947	3.959232	-0.950305
7	1.303857	-0.269171	0.838878
7	-1.226869	-1.015650	0.255768
1	-0.822573	-0.099147	0.410249
8	-3.259170	2.588064	-0.398563
8	-1.304720	1.649802	0.091814
8	-0.683478	-3.247144	0.329251
8	0.870179	0.047010	3.032449



1-F

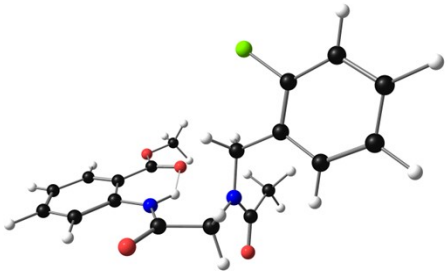
M062X/6-311+G(2d,p)

E = -1245.64884780 au

-ve frequency = nil

6	-3.969849	-0.547640	0.461904

1	-3.561567	-0.964128	1.375474
6	-5.335643	-0.623587	0.212185
1	-5.987215	-1.099886	0.932726
6	-5.860827	-0.092134	-0.956417
1	-6.923142	-0.150353	-1.154198
6	-5.022123	0.518494	-1.881134
1	-5.393503	0.944514	-2.803621
6	-3.673872	0.576525	-1.602986
6	-3.110444	0.056919	-0.447264
6	-1.615416	0.178749	-0.236395
1	-1.093677	-0.248002	-1.097853
1	-1.322825	1.228891	-0.214681
6	-0.802639	-1.894721	0.839276
1	-1.515941	-2.399534	0.184277
1	-0.851954	-2.355681	1.825359
6	0.593714	-2.181594	0.280827
6	-1.061195	0.114883	2.190858
6	-1.476329	1.565714	2.262883
1	-0.742964	2.181690	1.738553
1	-1.499738	1.846625	3.311534
1	-2.456299	1.729003	1.811723
6	2.701088	-0.965851	-0.252123
6	3.450378	-2.086248	-0.626219
1	2.995984	-3.061723	-0.565704
6	4.753211	-1.934400	-1.064643
1	5.314555	-2.816141	-1.348211
6	5.346538	-0.679423	-1.142456
1	6.366703	-0.571278	-1.484928
6	4.614976	0.431939	-0.774941
1	5.057307	1.416220	-0.828005
6	3.295546	0.314744	-0.330712
6	2.548864	1.541766	0.038620
6	2.608845	3.866044	0.266406
1	3.340449	4.654793	0.121151
1	2.280688	3.831324	1.304046
1	1.745909	4.017928	-0.380060
7	1.390531	-1.075560	0.201170
1	0.971480	-0.202455	0.500153
7	-1.137863	-0.491592	0.956805
8	3.278470	2.653014	-0.080092
8	1.392082	1.585930	0.412552
8	0.900170	-3.307540	-0.040849
8	-0.665044	-0.491341	3.165164
9	-2.849697	1.167408	-2.490422



1-Cl

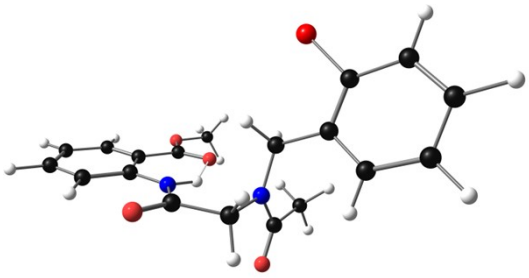
M062X/6-311+G(2d,p)

E = -1606.00821394 au

-ve frequency = nil

6	-3.800996	-0.896096	0.490724
1	-3.331366	-1.530634	1.232968
6	-5.173617	-0.963782	0.291910

1	-5.767661	-1.652414	0.878390
6	-5.778671	-0.151252	-0.655055
1	-6.847730	-0.197882	-0.816465
6	-5.009603	0.729582	-1.402317
1	-5.458631	1.374713	-2.145475
6	-3.642939	0.781234	-1.189818
6	-3.008217	-0.023163	-0.247302
6	-1.508896	0.070681	-0.045599
1	-1.006236	-0.117712	-0.999040
1	-1.231909	1.089848	0.226439
6	-0.609888	-2.178475	0.459580
1	-1.326239	-2.530253	-0.285922
1	-0.616374	-2.871798	1.300201
6	0.777343	-2.266851	-0.182408
6	-0.885963	-0.579091	2.275661
6	-1.334874	0.794639	2.715481
1	-0.632072	1.543892	2.345392
1	-1.335852	0.805628	3.801311
1	-2.330646	1.034790	2.339590
6	2.827938	-0.878464	-0.448397
6	3.601967	-1.845384	-1.098271
1	3.183504	-2.824979	-1.262158
6	4.883332	-1.539988	-1.519403
1	5.464583	-2.304775	-2.019616
6	5.430497	-0.279246	-1.308861
1	6.434284	-0.050611	-1.640318
6	4.674158	0.681356	-0.668109
1	5.080434	1.667373	-0.494888
6	3.375322	0.407340	-0.232460
6	2.600240	1.478767	0.438877
6	2.583718	3.685601	1.205194
1	3.278314	4.519642	1.224500
1	2.302706	3.394898	2.216204
1	1.688249	3.943332	0.641860
7	1.537785	-1.147023	-0.002819
1	1.101494	-0.389943	0.510717
7	-0.984002	-0.862162	0.931159
8	3.282616	2.619118	0.561481
8	1.459395	1.381288	0.849863
8	1.107622	-3.266622	-0.779425
8	-0.446334	-1.395598	3.058991
17	-2.691580	1.899485	-2.138583



1-Br

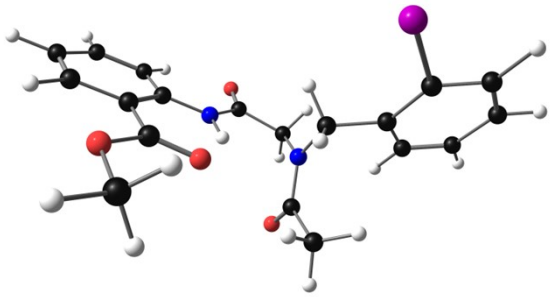
M062X/6-311+G(2d,p)

E = -3719.97475282 au

-ve frequency = nil

6	-3.453632	-1.535145	0.371776
1	-2.898098	-2.351209	0.818399
6	-4.828660	-1.641185	0.213273
1	-5.338175	-2.540303	0.534452
6	-5.543849	-0.597957	-0.354561

1	-6.615976	-0.671149	-0.482596
6	-4.881338	0.551317	-0.762714
1	-5.421845	1.376283	-1.206549
6	-3.509655	0.636897	-0.596717
6	-2.765086	-0.394343	-0.031156
6	-1.264004	-0.266839	0.141403
1	-0.807109	-0.069057	-0.832970
1	-1.032291	0.608950	0.748574
6	-0.194595	-2.470215	-0.215372
1	-0.925429	-2.592059	-1.017665
1	-0.109952	-3.414246	0.322130
6	1.158988	-2.213770	-0.883915
6	-0.472486	-1.643101	2.058550
6	-0.984157	-0.554019	2.971857
1	-0.353220	0.331604	2.872559
1	-0.925185	-0.927076	3.989932
1	-2.012668	-0.277048	2.735388
6	3.090533	-0.652164	-0.703306
6	3.896304	-1.268130	-1.666448
1	3.541717	-2.165387	-2.147020
6	5.127630	-0.727269	-1.989107
1	5.735333	-1.222084	-2.736658
6	5.592219	0.428266	-1.371138
1	6.557529	0.842294	-1.628949
6	4.803563	1.043350	-0.419802
1	5.145812	1.942601	0.071605
6	3.553571	0.525356	-0.072022
6	2.739732	1.231916	0.946784
6	2.595559	3.045047	2.412767
1	3.220719	3.888521	2.688720
1	2.403338	2.409482	3.275734
1	1.648446	3.387065	1.998459
7	1.849356	-1.167130	-0.343523
1	1.391723	-0.674081	0.414589
7	-0.628893	-1.440824	0.704897
8	3.335725	2.325817	1.425331
8	1.638257	0.893981	1.337519
8	1.524334	-2.911991	-1.802637
8	0.063206	-2.644939	2.486104
35	-2.634397	2.230902	-1.166263



1-I

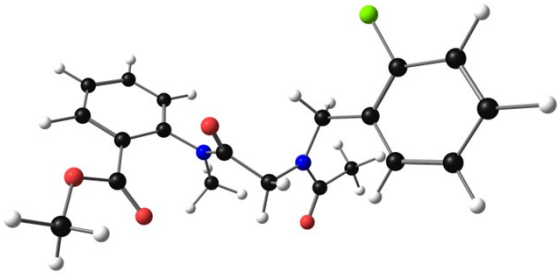
M062X/6-311+G(2d,p)

E = -1157.14248537 au

-ve frequency = nil

6	-3.080638	2.081055	0.221531
1	-2.444161	2.907678	0.514079
6	-4.444791	2.283272	0.068469
1	-4.864600	3.266156	0.238807

6	-5.262608	1.227102	-0.300775
1	-6.328238	1.371617	-0.423285
6	-4.712027	-0.029066	-0.514839
1	-5.343674	-0.859115	-0.801156
6	-3.347139	-0.215684	-0.359357
6	-2.504364	0.830678	0.009761
6	-1.011695	0.618253	0.182572
1	-0.829910	-0.163050	0.921579
1	-0.594499	0.232400	-0.752736
6	-0.641087	1.330562	2.924539
1	-0.526286	1.854354	3.868763
1	-0.086945	0.390427	2.961024
1	-1.694360	1.106883	2.747910
6	-0.066886	2.213997	1.842011
6	0.219261	2.641434	-0.538795
1	0.394384	3.648422	-0.161235
1	-0.519543	2.695479	-1.341279
6	1.529246	2.167563	-1.174539
6	3.323910	0.487440	-0.777468
6	3.693061	-0.625666	0.012498
6	4.881983	-1.302738	-0.270289
1	5.152599	-2.150475	0.342483
6	5.700131	-0.906336	-1.308980
1	6.617374	-1.441234	-1.514587
6	5.327724	0.187233	-2.082538
1	5.959803	0.511244	-2.900132
6	4.158826	0.881139	-1.828245
1	3.875593	1.729310	-2.429920
6	2.843096	-1.099813	1.131496
6	2.562426	-2.671457	2.836861
1	2.460029	-1.907611	3.606049
1	3.108327	-3.529081	3.217545
1	1.573982	-2.967457	2.488825
7	-0.273729	1.812429	0.540457
7	2.143861	1.163035	-0.483423
8	0.557770	3.223224	2.096169
8	1.792744	-0.600654	1.488554
8	3.341068	-2.173753	1.747630
8	1.927250	2.678074	-2.197253
53	-2.577874	-2.150351	-0.695358
1	1.665308	0.835440	0.347682



1-Cl-Me

M062X/6-311+G(2d,p)

E = -1645.28799191 au

-ve frequency = nil

6	-3.668881	-1.159442	-0.590359
1	-3.121450	-1.992004	-0.163902
6	-4.766953	-1.406130	-1.403414
1	-5.065310	-2.426233	-1.606971

6	-5.476005	-0.348184	-1.952217
1	-6.332264	-0.531638	-2.588038
6	-5.086918	0.956121	-1.683818
1	-5.625406	1.798325	-2.097166
6	-3.989227	1.181082	-0.870882
6	-3.255847	0.139281	-0.309844
6	-2.062847	0.437729	0.578704
1	-1.350161	1.048936	0.018886
1	-2.382590	1.048904	1.423030
6	-0.368679	-1.297965	0.146502
1	-0.808140	-1.450400	-0.841518
1	-0.032273	-2.253496	0.542939
6	0.792497	-0.333058	-0.075399
6	-1.798169	-1.481016	2.124152
6	-2.936103	-0.902860	2.936358
1	-2.624786	0.019680	3.429493
1	-3.205125	-1.637464	3.689209
1	-3.801975	-0.678888	2.311504
6	2.783339	0.714111	0.731864
6	2.938018	1.883027	1.461003
1	2.168542	2.155543	2.172962
6	4.049581	2.691999	1.269573
1	4.159769	3.600362	1.848136
6	5.004827	2.344114	0.325974
1	5.868226	2.976090	0.164174
6	4.846609	1.184545	-0.418275
1	5.578524	0.907664	-1.164977
6	3.749734	0.354401	-0.211846
6	3.628601	-0.921882	-0.976265
6	4.130370	-2.031760	-2.961616
1	4.645447	-1.806700	-3.890496
1	3.086409	-2.277966	-3.149199
1	4.608004	-2.862648	-2.444459
7	1.630914	-0.094683	0.977242
7	-1.365544	-0.743064	1.052699
8	4.214949	-0.843358	-2.174251
8	3.098941	-1.923245	-0.567976
8	0.917601	0.226595	-1.147694
8	-1.280165	-2.540664	2.425376
17	-3.523854	2.831860	-0.537102
6	1.722162	-0.961493	2.150703
1	2.016613	-0.359322	3.009650
1	0.766458	-1.428480	2.368466
1	2.472183	-1.737989	1.980373

10. References

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