Supporting information

Helical peptoid ions in the gas phase:

Thwarting the charge solvation effect by H-bond compensation

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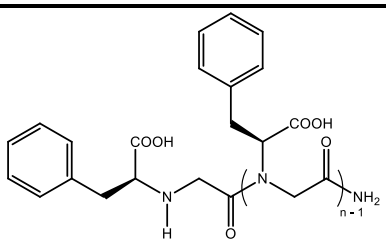
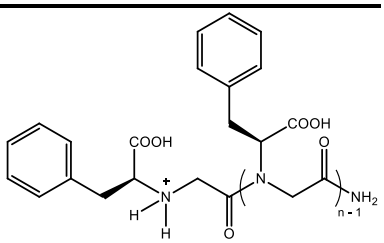
Peptoid synthesis

Table S1. Monoisotopic mass of each *N*scp peptoids and their monoisotopic mass-to-charge ratio for the protonated species obtained during the analyses.

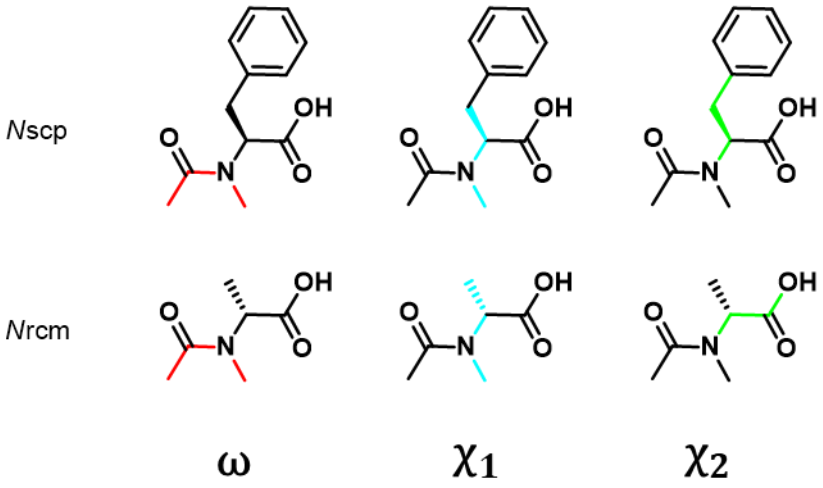
Degree of polymerization (n)	Monoisotopic mass (Da) [M]	Mass-to-charge ratio (*m*/*z*) $[M+H]^+$
		
3	632.248	633.280
4	837.322	838.362
5	1042.396	1043.454
6	1247.470	1248.526
7	1452.544	1453.616
8	1658.618	1658.636
9	1863.692	1863.705
10	2068.765	2068.792
15	3094.138	3094.122

Ion Mobility Mass Spectrometry

Peptoids are cleaved from the resin using a 95/5 (v/v) trifluoroacetic/water solution. The cleavage solution is diluted in 50/50 (v/v) methanol/water solution for *N*scp$_{3\text{-}9}$ (10 µl) or in acetonitrile for *N*scp$_{10\text{-}15}$ (50 µl). The IMS samples are prepared with 50 µl of these diluted solutions in acetonitrile or in 50/50 (v/v) methanol/acetonitrile solution to study the solvent influence on the adopted structure in gas phase.

During the ion mobility measurements, typical ion source conditions are: capillary voltage, 3.1 kV; sampling cone, 30V; source offset, 80V; source temperature, 100°C; desolvation temperature, 200°C; and desolvation gas flow, 600 L/h. The typical IMS parameters are: wave height 40 V; wave velocity (350, 600 and 800) $m.s^{-1}$; mass to charge range m/z 50 to 4000; Nitrogen IMS flow 60 $ml.min^{-1}$; Helium Cell Gas flow 180 $ml.min^{-1}$; Trap bias 45 V.

Computational chemistry



Scheme S1. Dihedrals related to the side chains *N*scp and *N*rce. χ_2 dihedrals of *N*rce are also involved in the *N*scp side chain.

All geometrical parameters are optimized, except for the denoted dihedrals which adopt their minimum energy configuration when building each torsional profile, as described in Ref. 41. For sake of example, the ω angle torsion profile is built by step of 10° while the two other angles are constrained to their MP2/cc-pVDZ-calculated equilibrium values and all other parameters are free to relax (**Figure S1**). These energy profiles are converted into normalized population distributions according to the Boltzmann equation at 298K:

$$Normalized\ population\ fraction = \frac{e^{-E_i/kT}}{\sum_i e^{-E_i/kT}} \qquad Eq.1$$

$$E_{dihedral} = \sum_{n=1}^{6} \frac{1}{2} B_n [1 - d \cos(n\,\theta)] \qquad Eq.2$$

The same procedure is achieved at the molecular mechanics level. The default energy profiles provided by DREIDING largely deviate from the MP2 profiles. We therefore fitted the dihedral parameters B_n, d and n from Eq. 2, which are respectively the barrier height, the phase factor (only integer, -1 or 1), and the periodicity (only integer from 1 to 6), to reproduce the MP2 population profiles. They were adjusted systematically to promote the lower RMSD (**Table S2**).

Table S2. RMSD values obtained between QM and MM torsional scans for the optimized dihedral parameters (B_n barrier height, d phase factor and n periodicity).

Dihedral angle	RMSD (%)
*N*sce	
ω	2.81
χ_1	2.04
χ_2	2.58
*N*scp	
ω	1.60
χ_1	1.04
χ_2	1.24

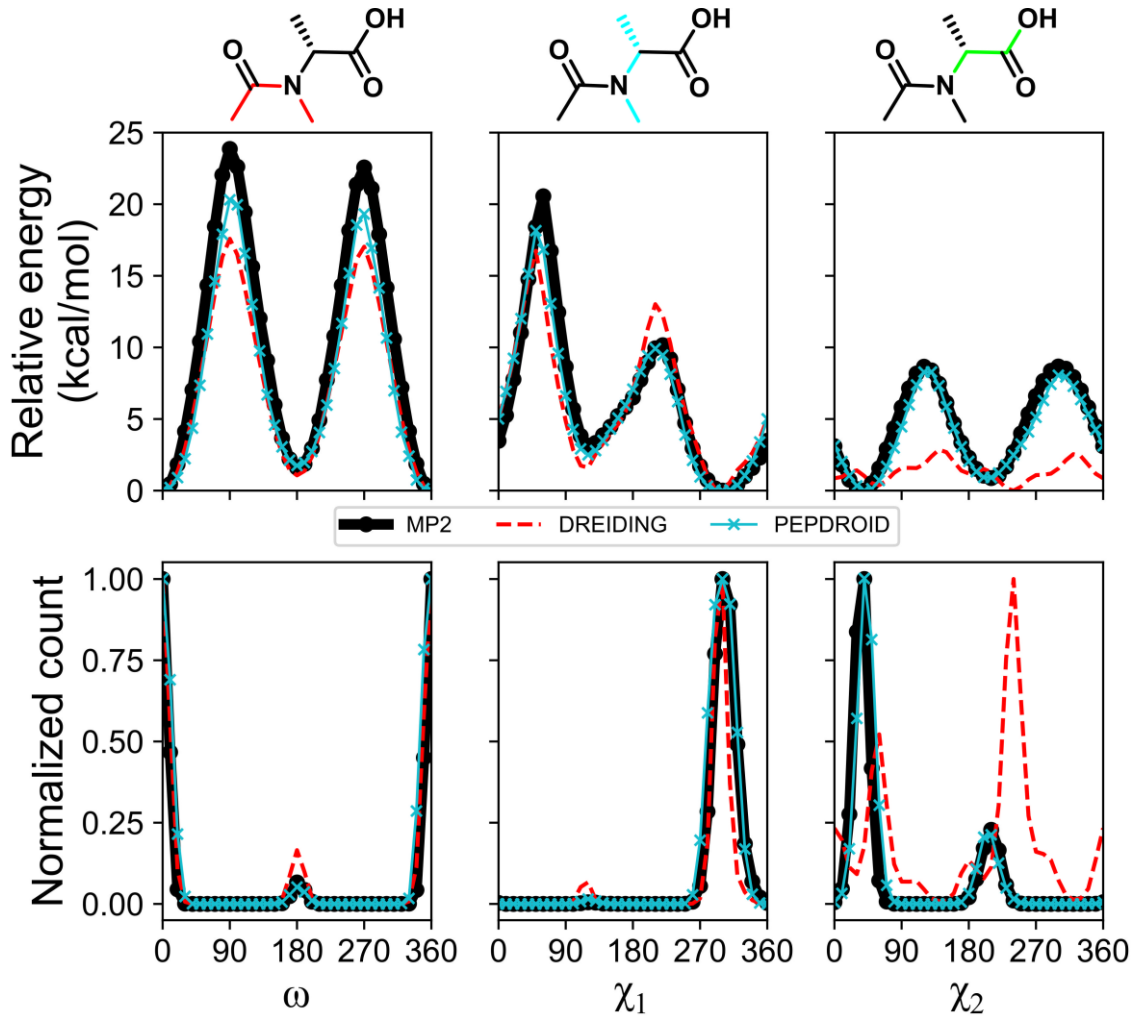


Figure S1. Torsion energy (top) and relative population (at 298K, bottom) profiles for *N*sce dihedrals, as calculated at the QM level (MP2/cc-pVDZ) (black curve), with the default DREIDING parameters (red dashed curve) and with the fitting procedure of the dihedral parameters PEPDROID (cyan curve).

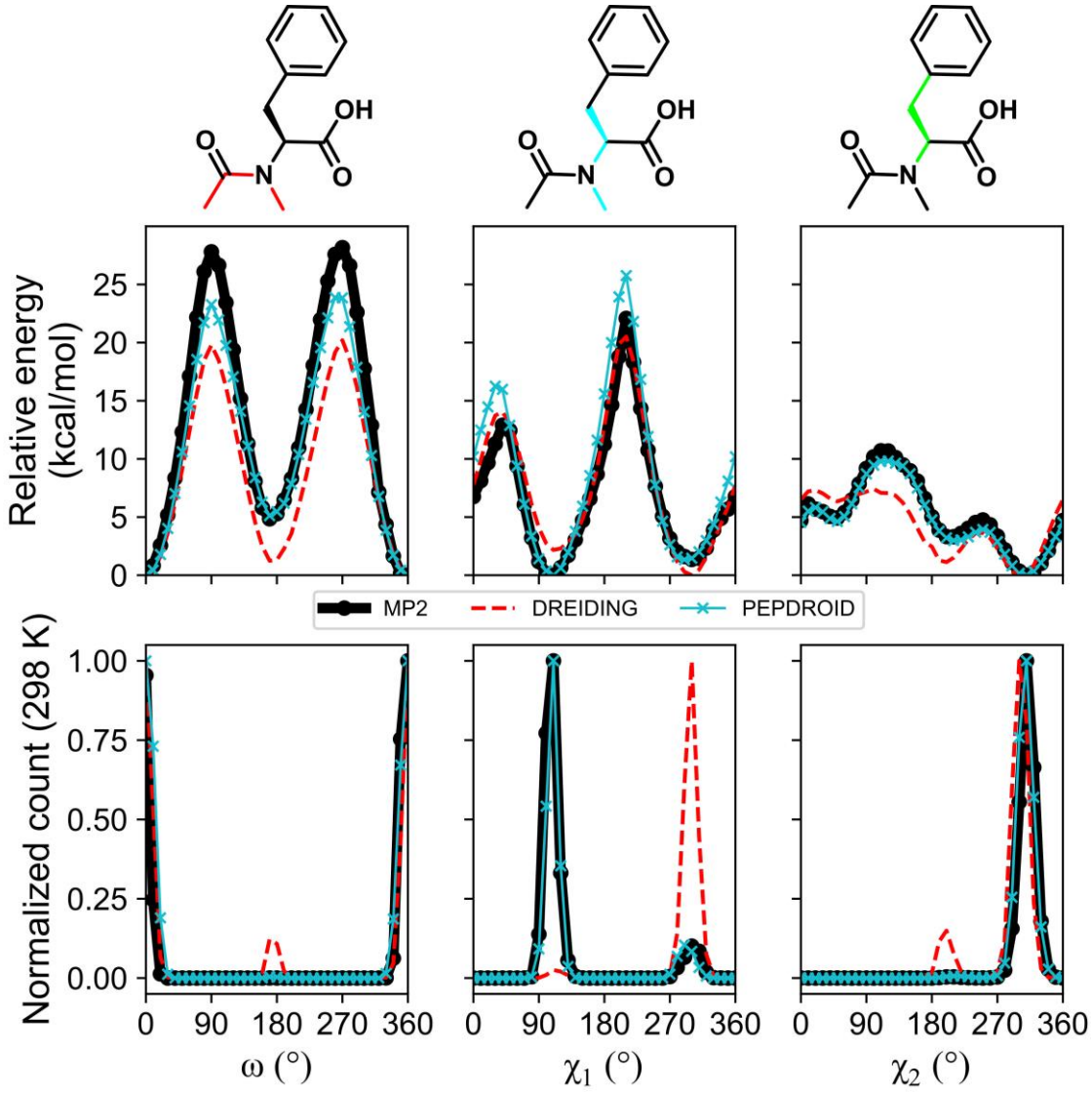


Figure S2. Torsion energy (top) and relative population (at 298K, bottom) profiles for *N*scp dihedrals, as calculated at the QM level (MP2/cc-pVDZ) (black curve), with the default DREIDING parameters (red dashed curve) and with the fitting procedure of the dihedral parameters PEPDROID (cyan curve).

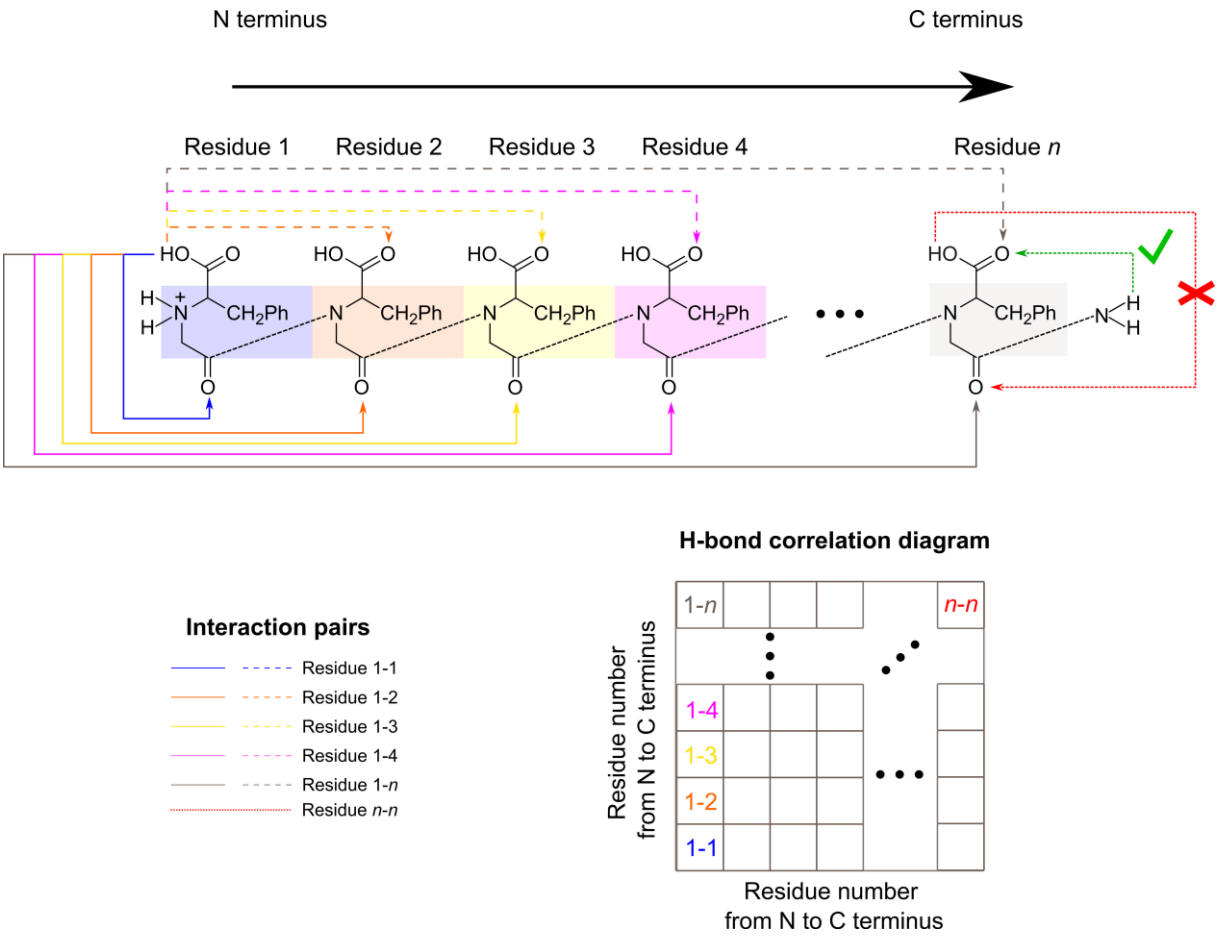


Figure S3. Primary structure of the peptoid chain bearing *N*scp side chains. Each residue is highlighted using a unique color. The hydrogen bond donor used in the H-bond correlation diagram is always the hydroxyl moiety from the carboxylic acid side chains, while the acceptors are the oxygen from the carbonyl amide and the oxygen from the carbonyl of the carboxylic acid. For a given donor, *i.e.*, Residue 1, the H-bond is monitored in each residue pair. For residue pairs on the diagonal, *i.e.*, Residue 1-1, a H-bond can only be formed between the hydroxyl and the amide oxygen (plain color line). For every other off-diagonal pairs, a maximum of one H-bond can be formed, either with the amide oxygen or the carboxylic acid oxygen (dashed color line). In general, the last diagonal term (Residue *n*-*n*) does not form H-bond based on the constrains defined (red dotted line). It rather forms a H-bond between the hydrogen from the amide at the C terminus (acting now as the donor) and the carbonyl of the carboxylic acid (acting as the acceptor, green dotted line). However, this type of H-bond is not accounted for in the H-bond correlation diagrams.

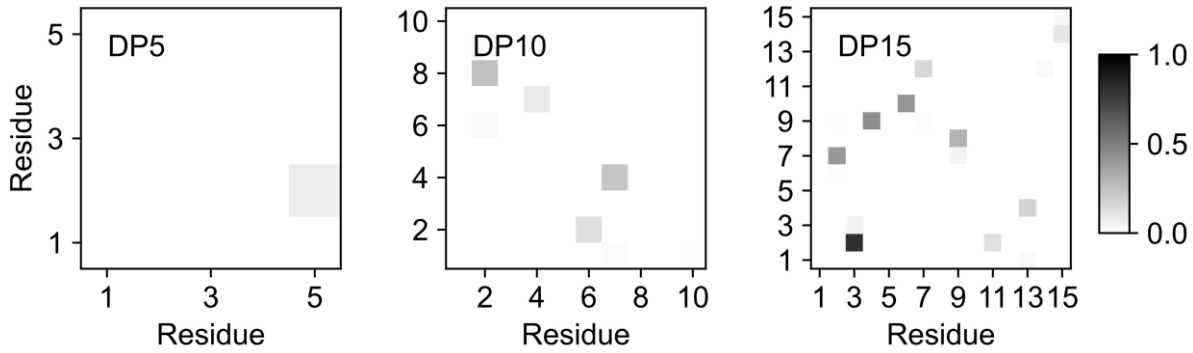


Figure S4. Hydrogen bond correlation matrices for *N*rce peptoids (DP 5, 10, 15) generated from 50 ns MD simulations. The X and Y axes correspond to the residue number starting from the N terminus. The hydrogen bonds are monitored between the hydrogen from the carboxylic acid moieties and the oxygen from the backbone carbonyls and the carboxylic acid carbonyls.

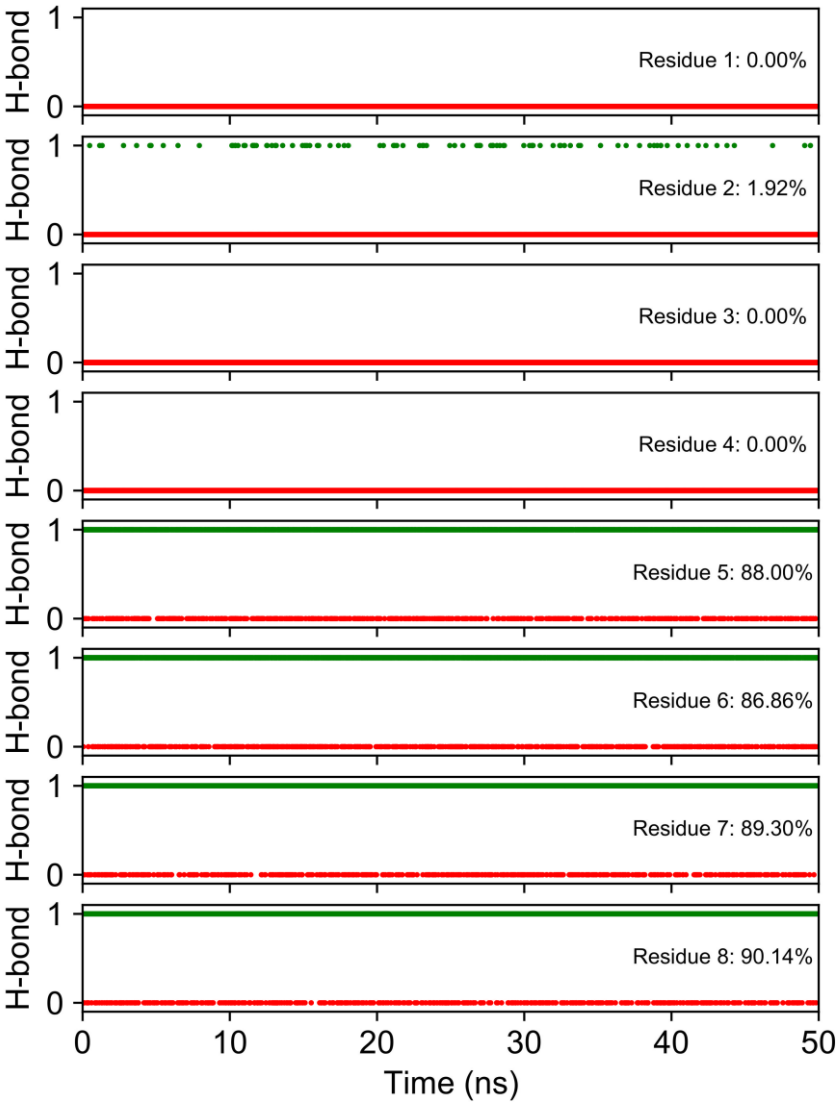


Figure S5. Evolution of the number of intra-residue hydrogen bonds along the 50 ns MD simulation of *N*scp$_8$. A value of 1 is attributed when the distance between the donor (hydroxyl from the carboxylic acid moiety) and the acceptor (either the amide oxygen or the carboxylic acid oxygen) is lower than 3.5 Å and the angle formed between the donor – hydrogen and acceptor is larger than 150° (green points), otherwise no hydrogen bond is counted (red points). The percentage value corresponds to the fraction of hydrogen bonds formed during the MD, which is the value reported in the matrix of Figure 3.

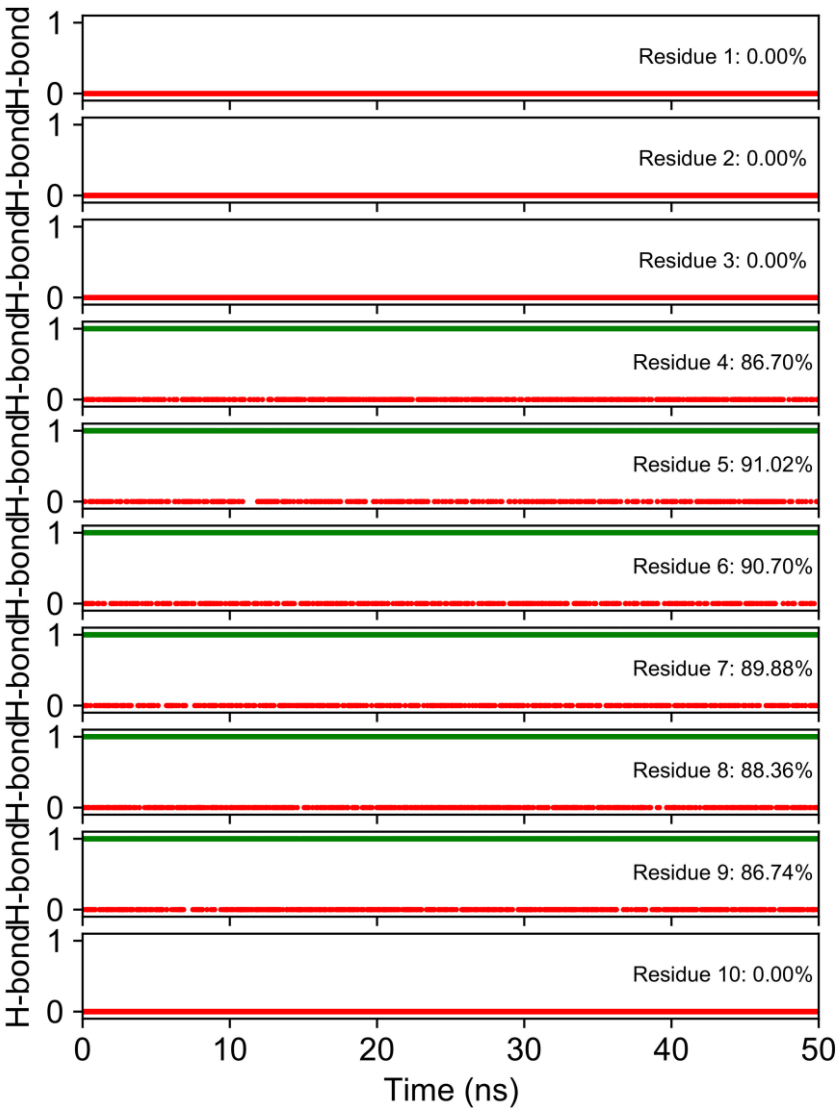


Figure S6. Evolution of the number of intra-residue hydrogen bonds along the 50 ns MD simulation of *N*scp$_{10}$. A value of 1 is attributed when the distance between the donor (hydroxyl from the carboxylic acid moiety) and the acceptor (either the amide oxygen or the carboxylic acid oxygen) is lower than 3.5 Å and the angle formed between the donor – hydrogen and acceptor is larger than 150° (green points), otherwise no hydrogen bond is counted (red points). The percentage value corresponds to the fraction of hydrogen bonds formed during the MD, which is the value reported in the matrix of Figure 3.

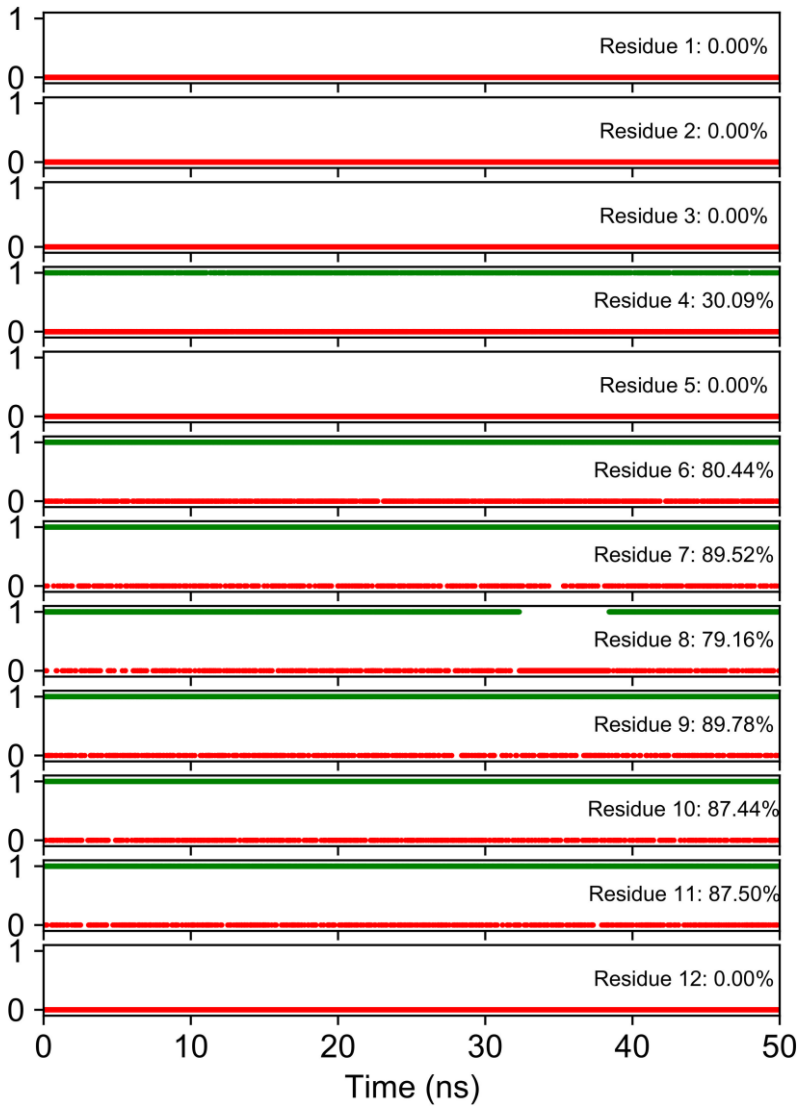


Figure S7. Evolution of the number of intra-residue hydrogen bonds along the 50 ns MD simulation of *N*scp$_{12}$. A value of 1 is attributed when the distance between the donor (hydroxyl from the carboxylic acid moiety) and the acceptor (either the amide oxygen or the carboxylic acid oxygen) is lower than 3.5 Å and the angle formed between the donor – hydrogen and acceptor is larger than 150° (green points), otherwise no hydrogen bond is counted (red points). The percentage value corresponds to the fraction of hydrogen bonds formed during the MD, which is the value reported in the matrix of Figure 3.

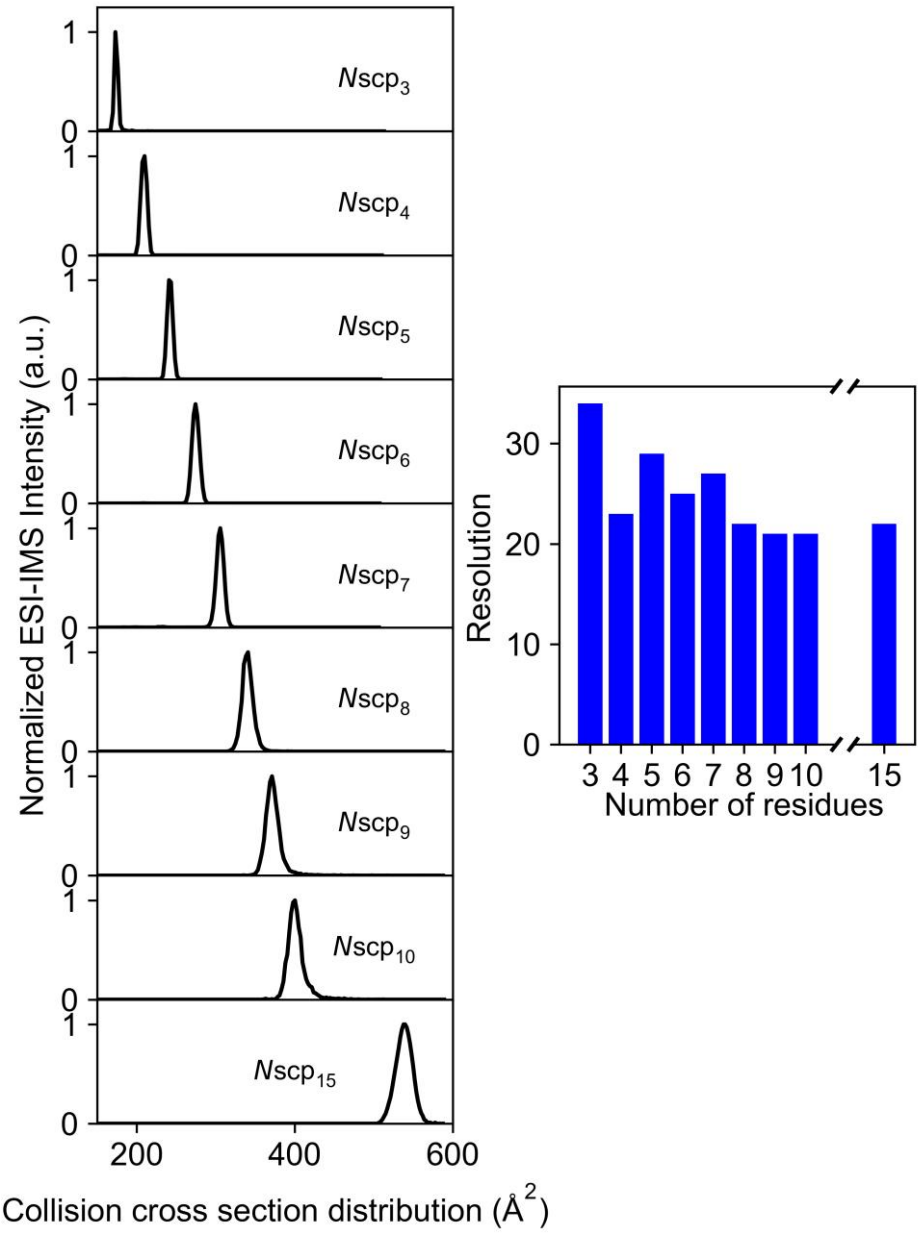


Figure S8. Experimental collision cross section distributions for each $[N\text{scp}+\text{H}]^+$ peptoid chain length (left) and the associated resolution (right). The resolution is computed by dividing the apex of the distribution by the width at 50% intensity of the distribution.

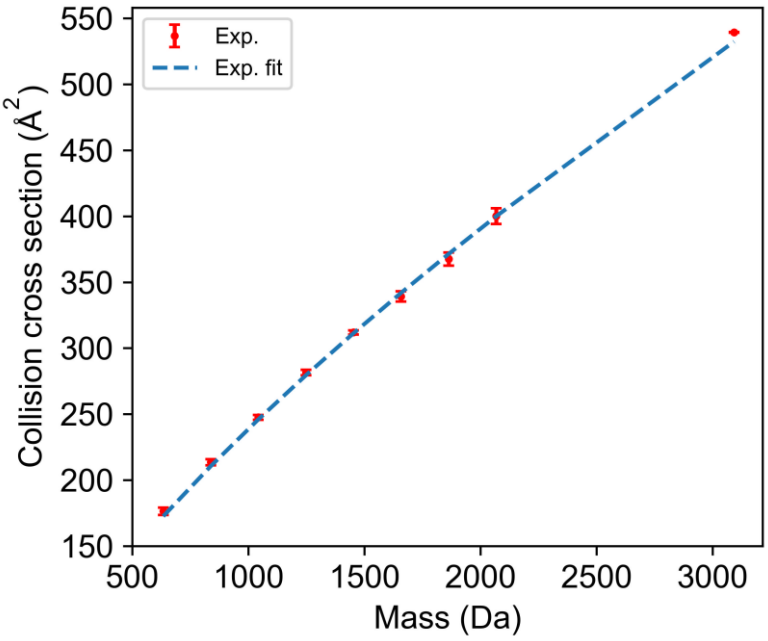


Figure S9. Experimental and theoretical collision cross sections (CCS) of singly protonated *N*scp peptoids (red points) with the associated error bars and the fitting of the data using $\Omega = A.M^B$.