Supporting Information for

Measurement of the Persistence Length of Helical and Non-helical Polypeptoids in Solution

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Semi-flexible Cylinder Model Equations

The following equations are used to fit the scattering data and calculate a persistence length.

$$S_{SB}(q,L,b) = S_{exv}(q,L,b) + \left[\frac{4}{15} + \frac{7}{15u} - \left(\frac{11}{15} + \frac{7}{15u}\right)\exp(-u)\right] b/L$$

$$S_{exv}(q) = w(qR_g)S_{Debye}(q,L,b) + [w(qR_g)]\left[C_1(qR_g)^{-1/\vartheta} + C_2(qR_g)^{-2/\vartheta} + C_3(qR_g)^{-3/\vartheta}\right]$$

$$w(qR_g) = \left[1 + (\frac{qR_g}{3.12})^2 + (\frac{qR_g}{8.67})^3\right]^{\frac{0.176}{3}}$$

$$S_{Debye}(q,L,b) = 2[exp(-u) + u - 1]/u^2$$

$$u = R_g^2 q^2$$

$$\vartheta = 0.585$$

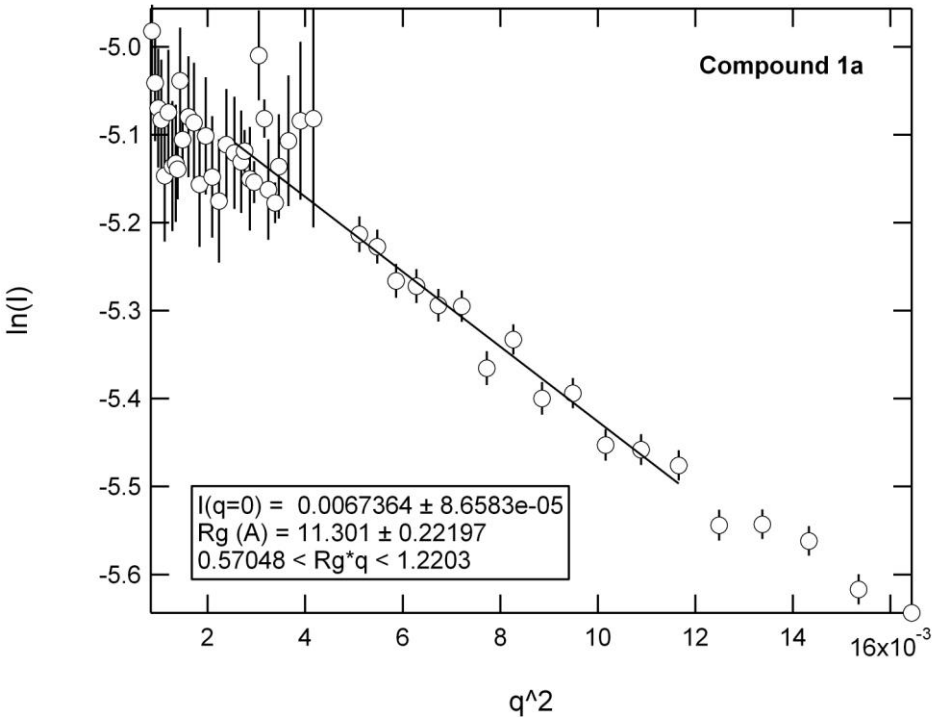
$$b = statistical\ segement\ (Kuhn) length = 2l_p$$

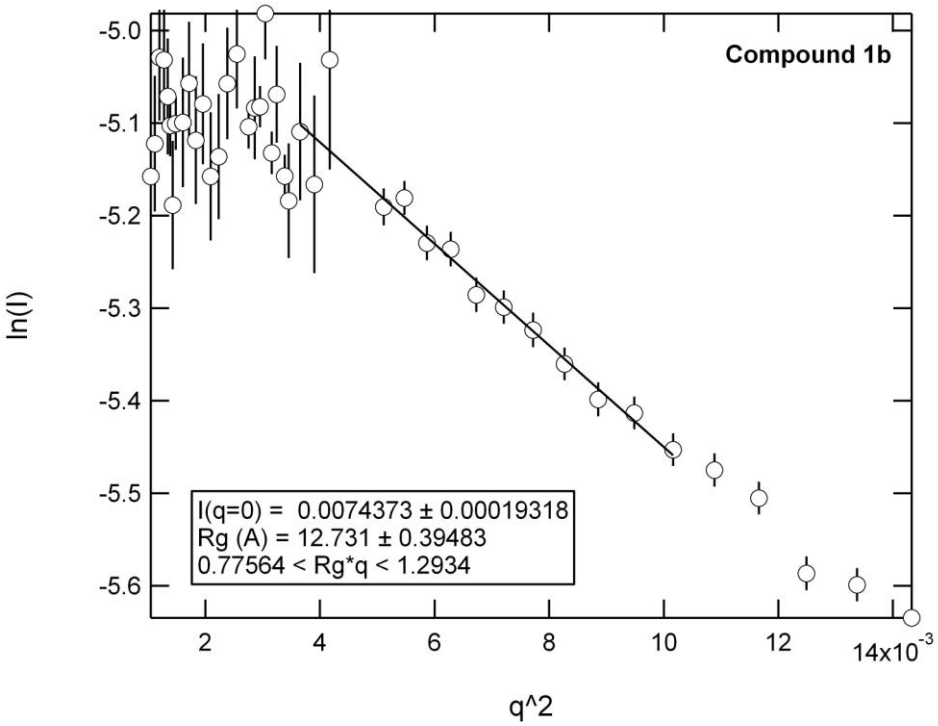
$$l_p = persistence\ length$$

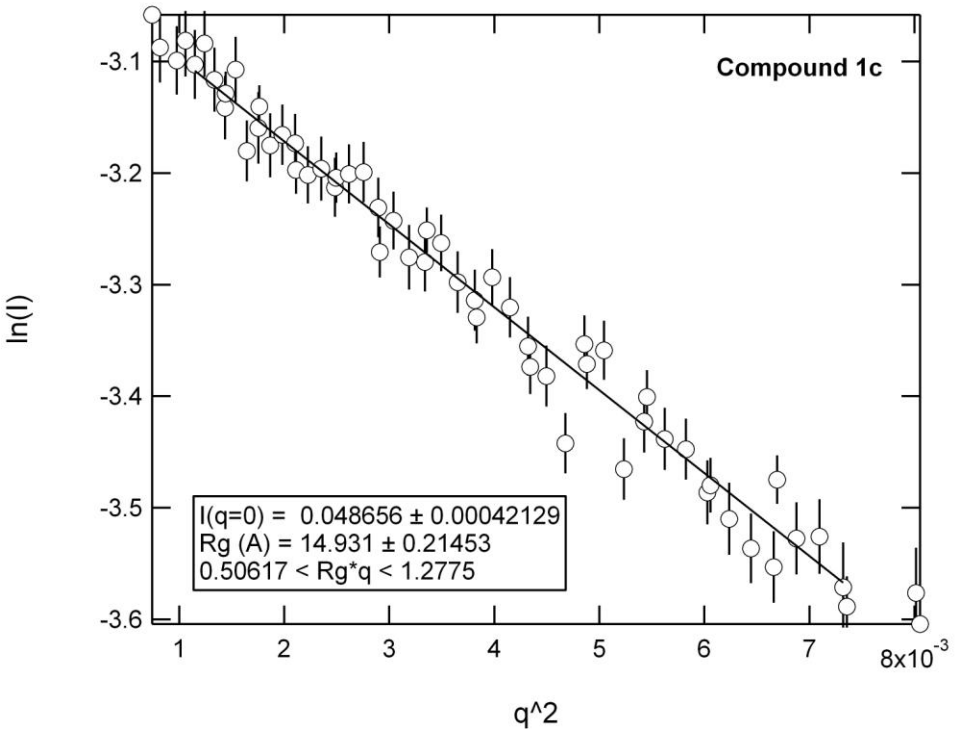
$$L = contour\ length$$

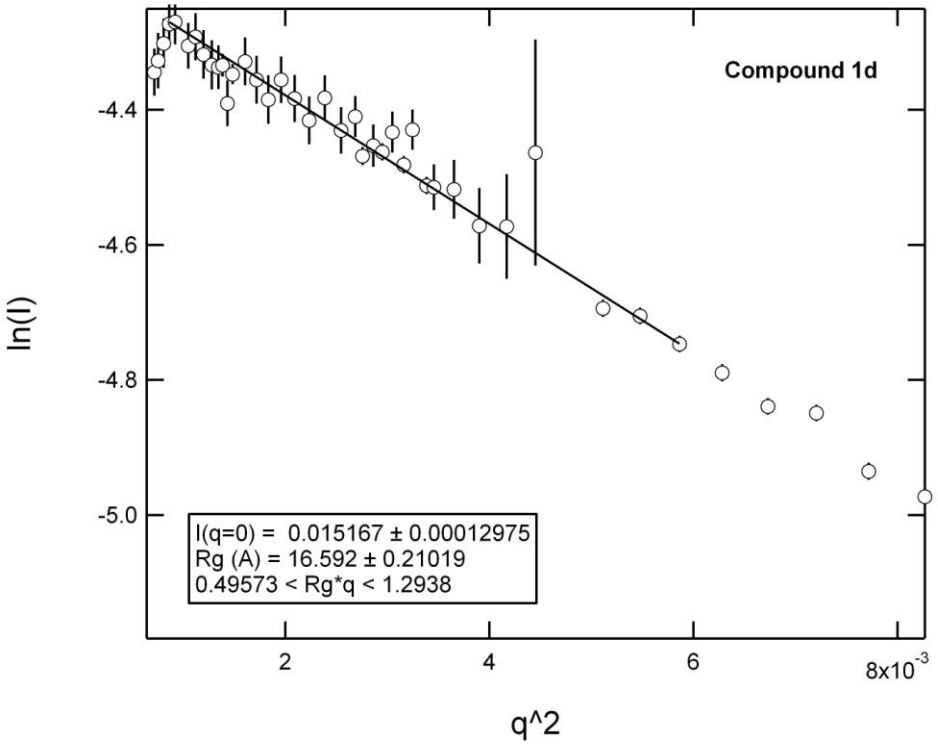
Guinier Plots

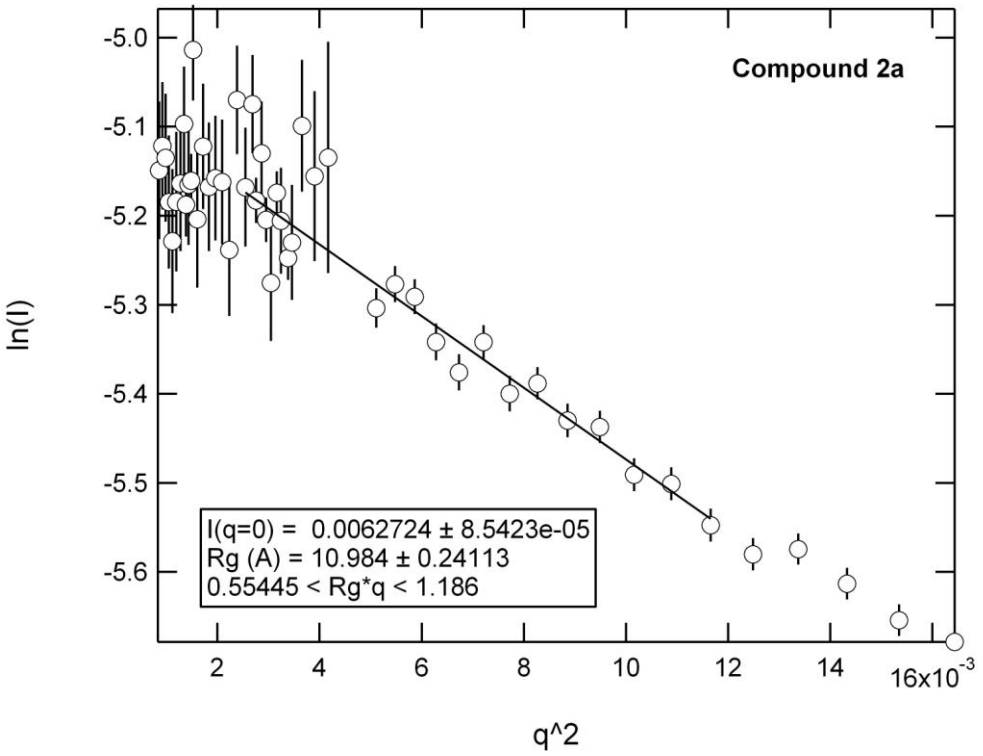
The following plots were used to deduce the R_g's of Compounds **1** and **2**.

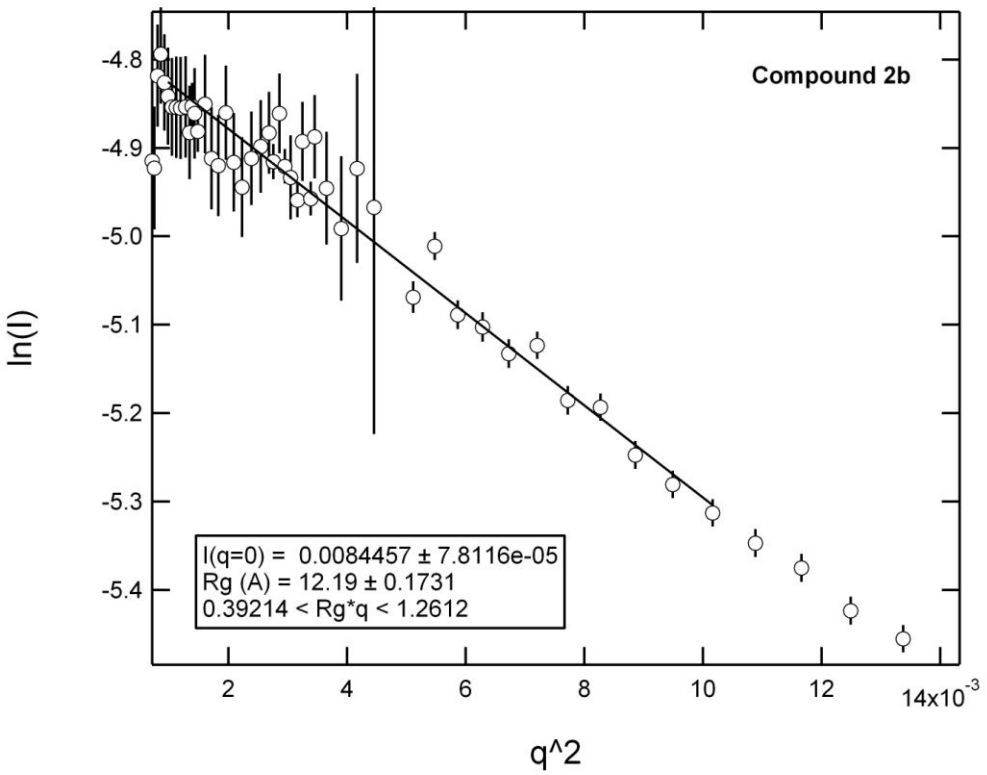


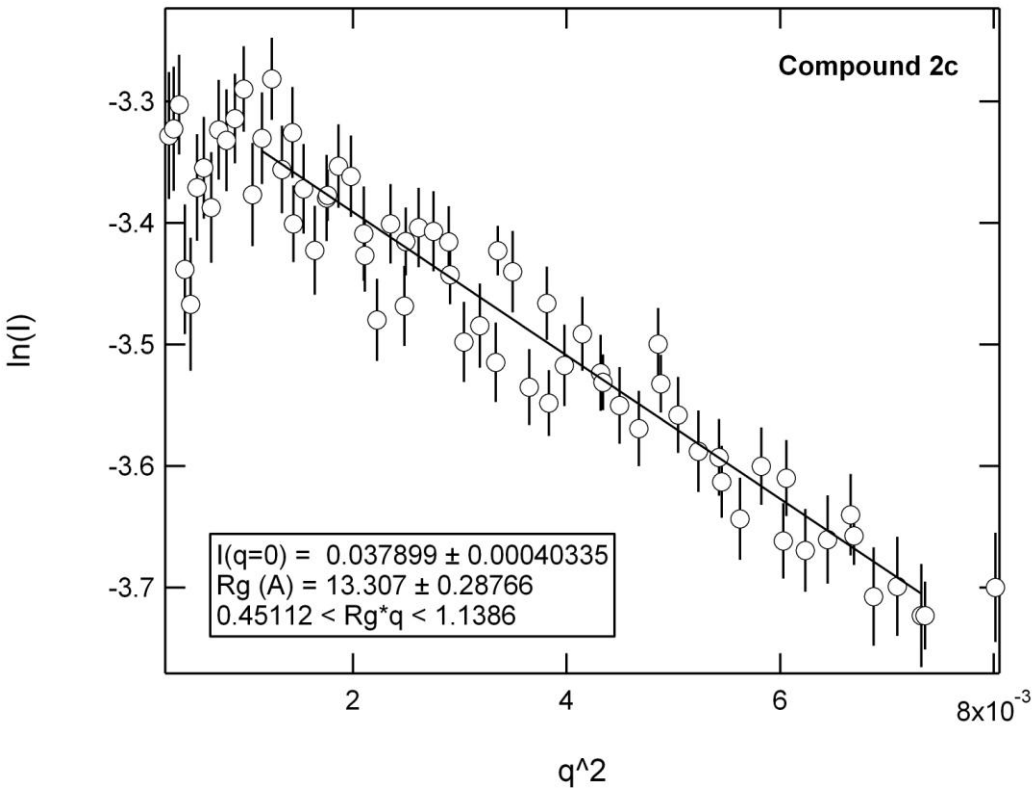


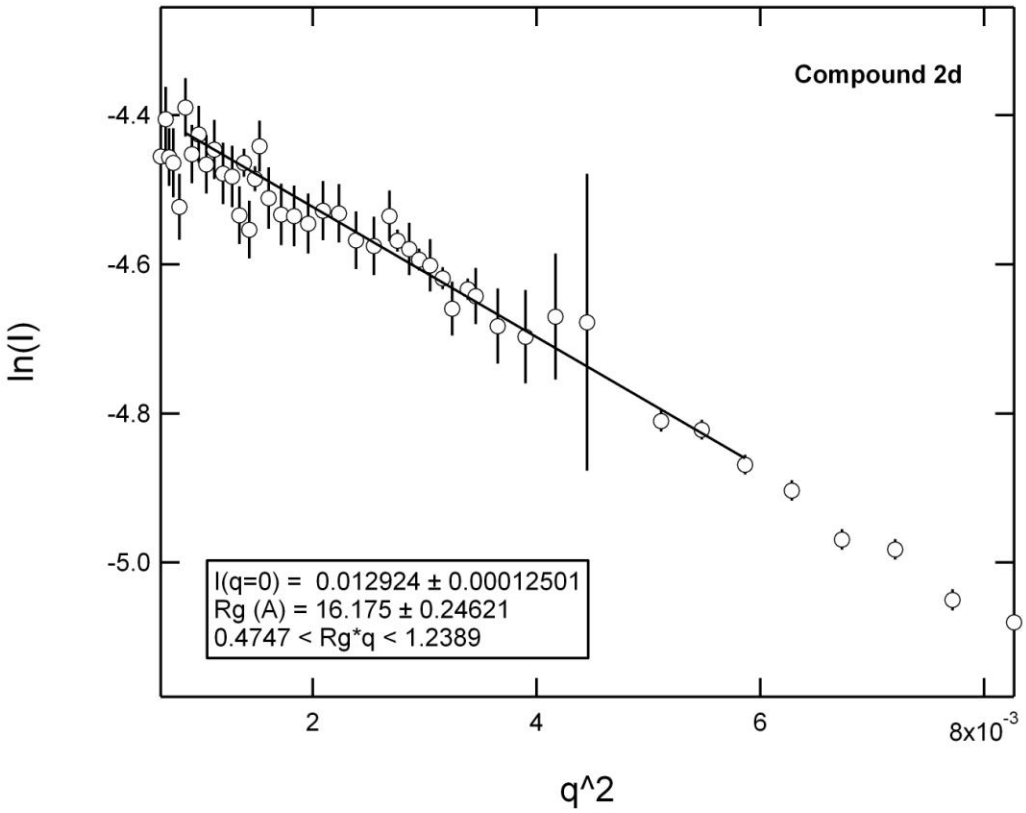












Wormlike Chain Analysis for Different Polypeptoid Chain Lengths

The radius of gyration (R_g) for polypeptoids 18, 24, 36, and 48 monomers long were obtained using a Guinier analysis on the SANS scattering curves for each polypeptoid (above). This molecular weight series was measured for both the non-helical (**1**) and the helical (**2**) compound. For compound **1**, the contour length was calculated as product of the number of monomers and the length of each monomer, and the wormlike chain equation was fit to the data by changing the persistence length, L_p. For compound **2**, the contour length was calculated using the helical pitch (0.6 nm) previously measured by 2D solution NMR experiments in acetonitrile. The fitted L_p was 0.6 nm for **1** and 1.1 nm for **2**, which agrees well with the values obtained from the semiflexible cylinder model fit.

Despite the good agreement, the wormlike chain equation does not quite fit the data, especially at lower polypeptoid chain lengths for both **1** and **2**. As stated in the manuscript, this error is due to the 18 and 24-mers simply being too short to be modeled by this equation.

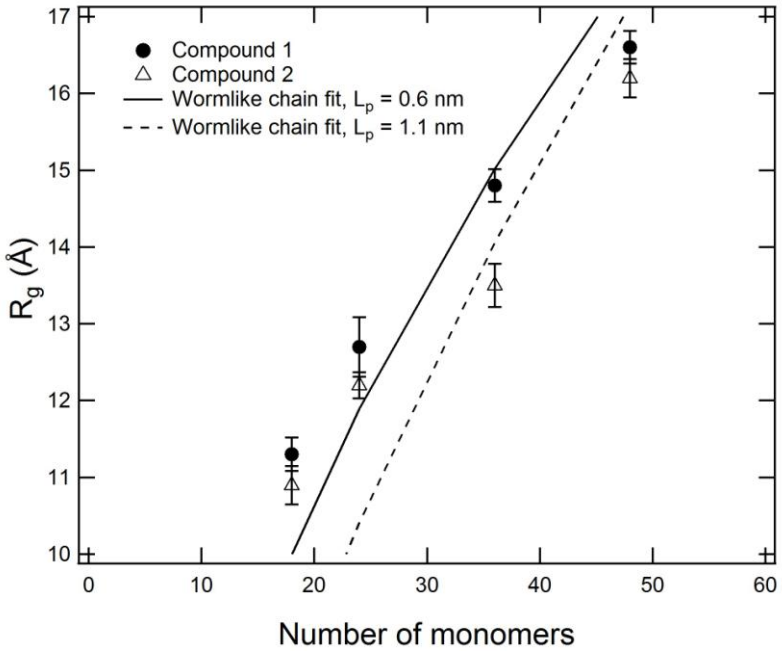


Figure S1. Fitted persistence lengths using the wormlike chain equation over a series of polypeptoid chain lengths. The fitted L_p of **2** is longer than that of **1**, indicating it is indeed stiffer.

Persistence Length of a Polypeptoid with a Racemic Mixture of Monomers

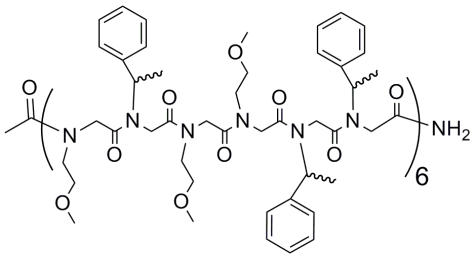


Figure S2. **3** contains a racemic mixture of α-chiral side chains and is proposed to be non-helical.

As another point of comparison, a 36-mer polypeptoid was synthesized using the same monomers as **2** but with a racemic mixture instead of an enantiomerically pure mixture of the α-methylbenzyl side chain. The structure for this compound (compound **3**) is given in Figure S3. Circular dichroism data is provided in Figure S4, showing that **3** is truly racemic and that there is no net ellipticity due to an equal mixture of *R* and *S* enantiomers. The helical structure of **2** results from the steric hindrance of the bulky side chains with the same chirality; thus, the racemic nature of **3** should disrupt any helical structure. SANS measurements probed the structure of **3** in the same way as for **1** and **2**. A Guinier analysis of the scattering curve yields an R_g of 14.5 ± 0.1 Å, which is closer to the value of the R_g for **1** (14.7 Å) than **2** (13.3 Å). In addition, using the wormlike chain formula and the semiflexible cylinder model to calculate a persistence length for **3** yields a value of (results indicate that **3** is quite flexible, which is similar to **1** and **2**.

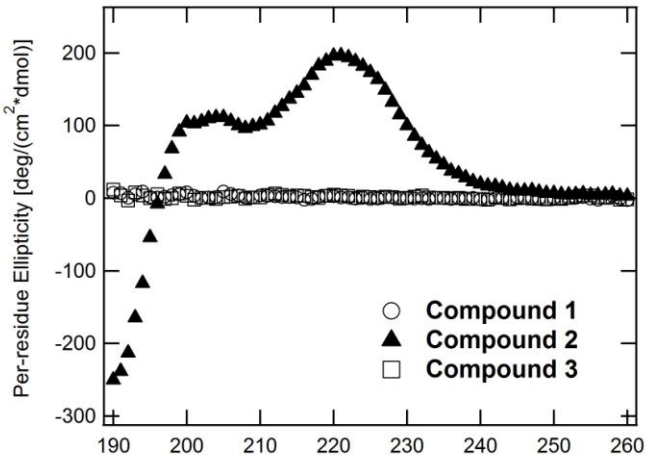


Figure S3. Compound **3** shows no net ellipticity, confirming its racemic nature.

Semiflexible Cylinder Model of the 36-mer Polypeptoids Using a Fitted Contour Length

The semiflexible cylinder model was allowed to fit the contour length, persistence length, and cylinder radius simultaneously. Using this model, the non-helical sequence, **1**, has a much longer contour length than the chiral sequence, **2**. The secondary structure of **2c** is thought to cause the contour length to be much shorter as the polymer is adopting a helix conformation with the majority of the amide bonds in the *cis* geometry. This fitted value is less than the value estimated by NMR (7.2 nm) by about 2 nm. The fitted contour length for **1c** is less than the calculated fully extended (all-*trans*) chain length (13 nm), which is reasonable given that the flexible polypeptoid backbone chain likely exists with both *cis* and *trans* amide bonds at any given moment. Furthermore, a contour length of 8.5 ± 0.6 nm is obtained for compound **3**, suggesting that **3** is not as compact as **2c**. The

fitted persistence length is also smaller for **3** (0.9 ± 0.02 nm) than **2c** (1.97 ± 0.17 nm), supporting the idea that the racemic nature of **3** results in a more flexible molecule. The results of this model fit are consistent with the trends identified from the semiflexible cylinder fit with a fixed contour length and the wormlike chain equation fit, but there is a larger error in the persistence length.

Polypeptoid	**Contour Length (nm)***	**Persistence Length* (nm)**	**Radius (nm)***
1	10.58 ± 4.8	0.66 ± 0.03	0.93 ± 0.2
2	4.93 ± 2.8	1.97 ± 0.17	0.99 ± 0.3
3	8.5 ± 0.6	0.9 ± 0.02	0.96 ± 0.2

Table S1. The contour length and the persistence length have been fitted using the semiflexible cylinder model. Consistent with other analyses explored in this paper, the helical compound has a slightly higher persistence length than the non-helical version.

Circular Dichroism Measurements

Extensive CD measurements have been taken at various temperatures and solvents. The most relevant graphs have been included in the manuscript. The remaining data is summarized here.

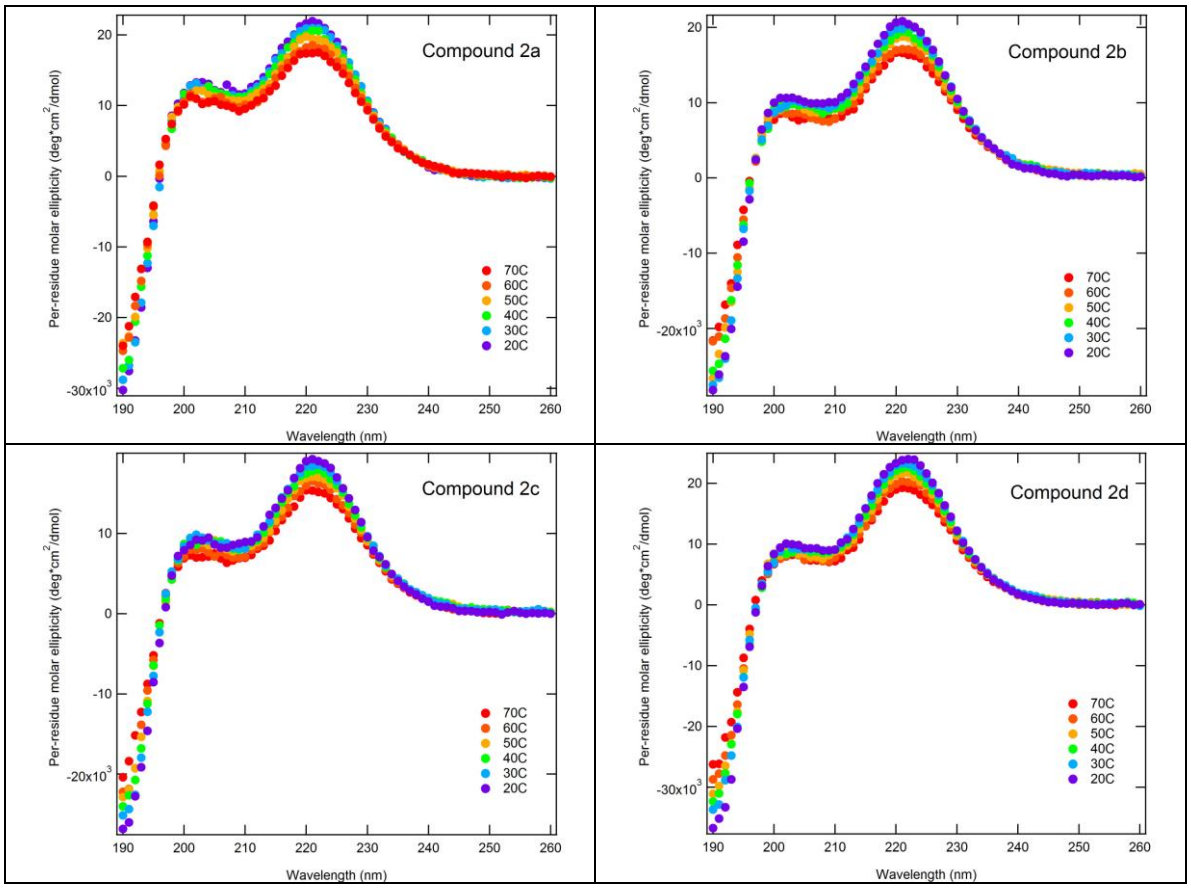


Figure S4. Circular dichroism at varying temperatures for each helical polypeptoid.