Supporting Information

Preprogrammed 2D Folding of Conformationally Flexible Oligoamides: Foldamers with Multiple Turn Elements

Cristian Gobbo[†#], *Min Li*[‡⊥#], *Kunal S. Mali*[‡]*, *Jan H. van Esch*[†]* *and Steven De Feyter*[‡]*

[†]Department of Chemistry, Laboratory of Self-assembling Systems, Delft University of Technology, Julianalaan 136, 2628 BL Delft, The Netherlands, [‡]Division of Molecular Imaging and Photonics, Department of Chemistry, KU Leuven-University of Leuven, Celestijnenlaan 200F, B 3001, Leuven, Belgium.

[#]These authors contributed equally.

[⊥] **Present address:** CAS Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, Institute of High Energy Physics, The Chinese Academy of Sciences, Beijing 100049, China

Corresponding authors: Kunal.Mali@chem.kuleuven.be; J.H.vanEsch@tudelft.nl; Steven.DeFeyter@chem.kuleuven.be

Section 1: Additional STM images and molecular models

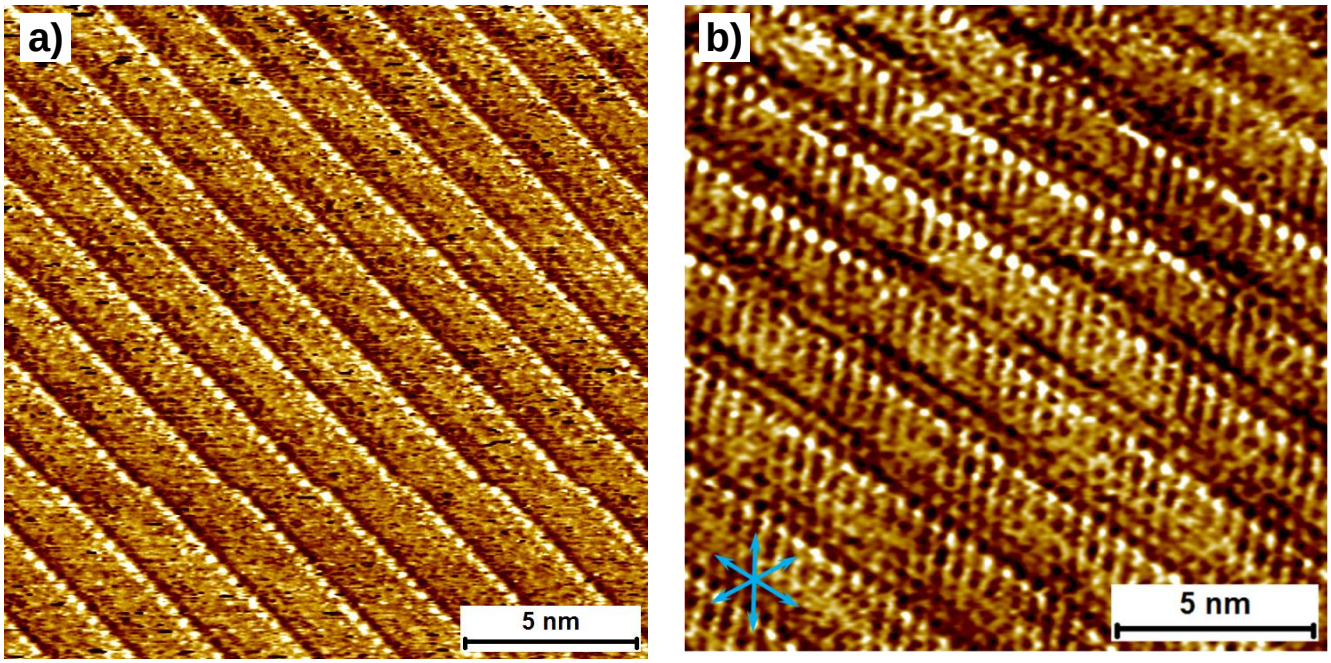


Figure S1: Additional STM image of the monolayer formed by **1.1** at the 1-octanol/HOPG interface. Imaging conditions: I_{set} = *150 pA*, V_{bias} = *–900 mV*.

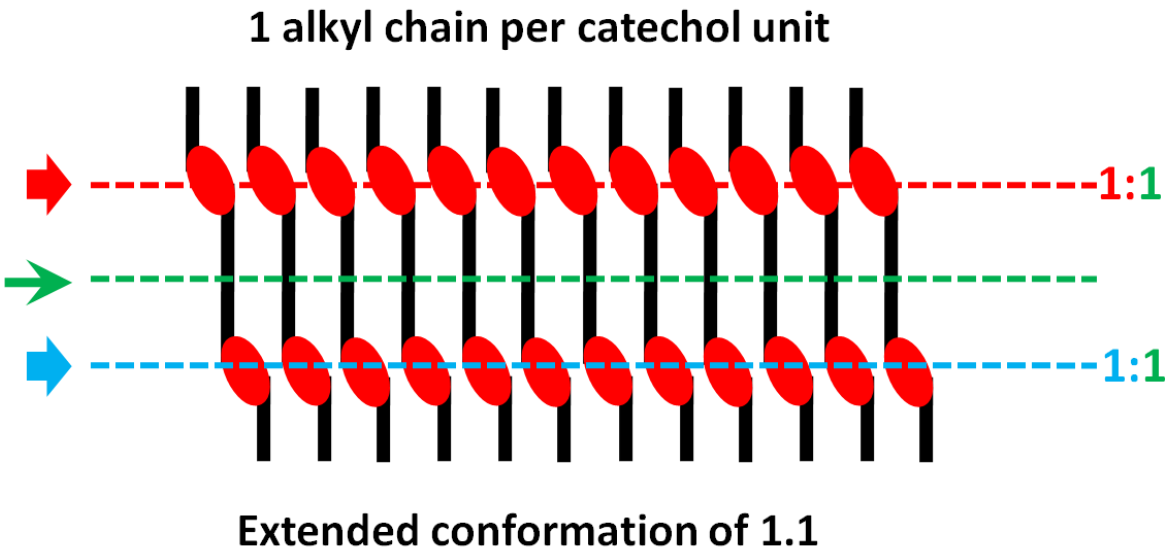


Figure S2: A simple schematic showing the self-assembled structure of **1.1** with extended conformation on the surface of HOPG. It can be easily noticed that the catechol to alkyl chain ratio is **1:1** for the extended conformation in contrast to the **1:2** for the folded conformation.

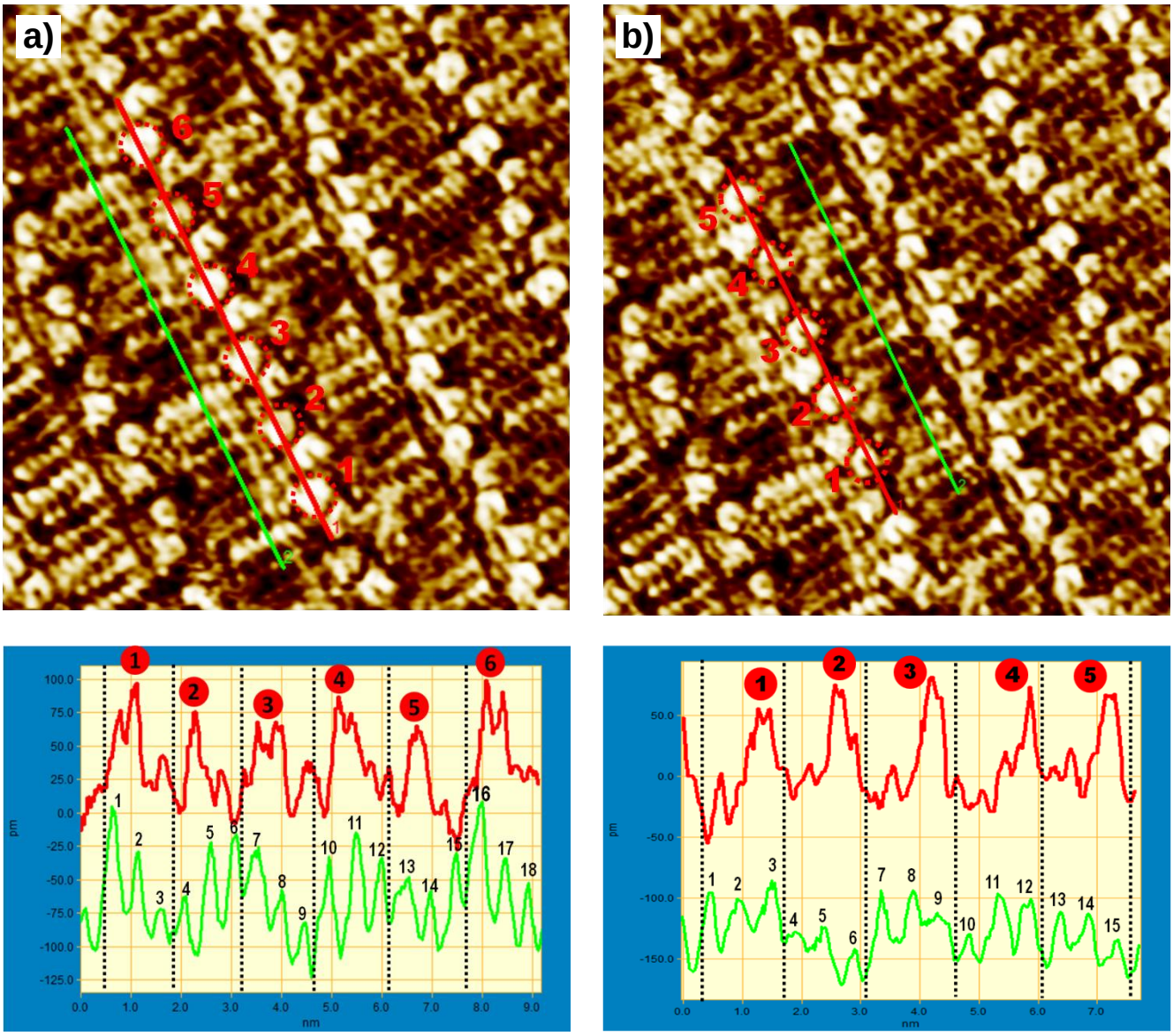


Figure S3: High resolution STM (HR-STM) images of **2.1** at the 1-octanol/HOPG interface with line profiles along the catechol units (red line) and alkyl chains (green line). The line profile analysis clearly shows that there are three alkyl chains per catechol unit present on the surface providing evidence for intramolecular folding. Furthermore, the periodicity in the appearance of three alkyl chains per catechol unit confirms the ordered arrangement of folded molecules on surface. Imaging conditions: I_{set} = *200 pA*, V_{bias} = *–400 mV*.

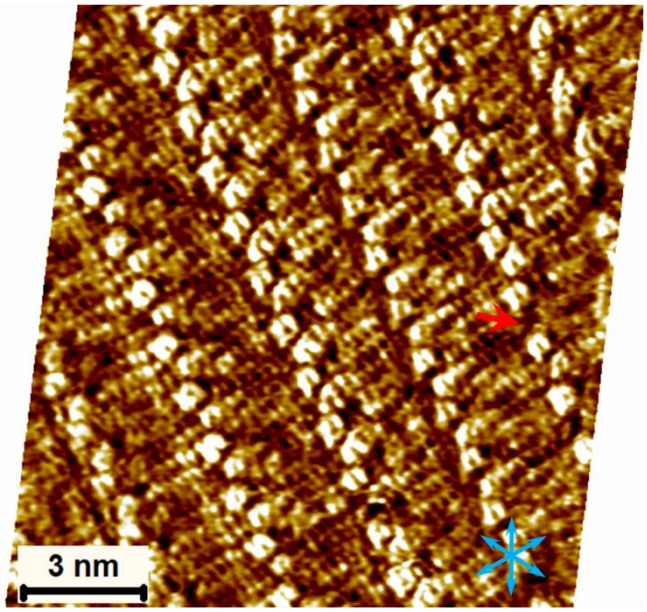


Figure S4: A defect (red arrow) in the self-assembled monolayer of **2.1**. Imaging conditions: I_{set} = *200 pA*, V_{bias} = *–400 mV*.

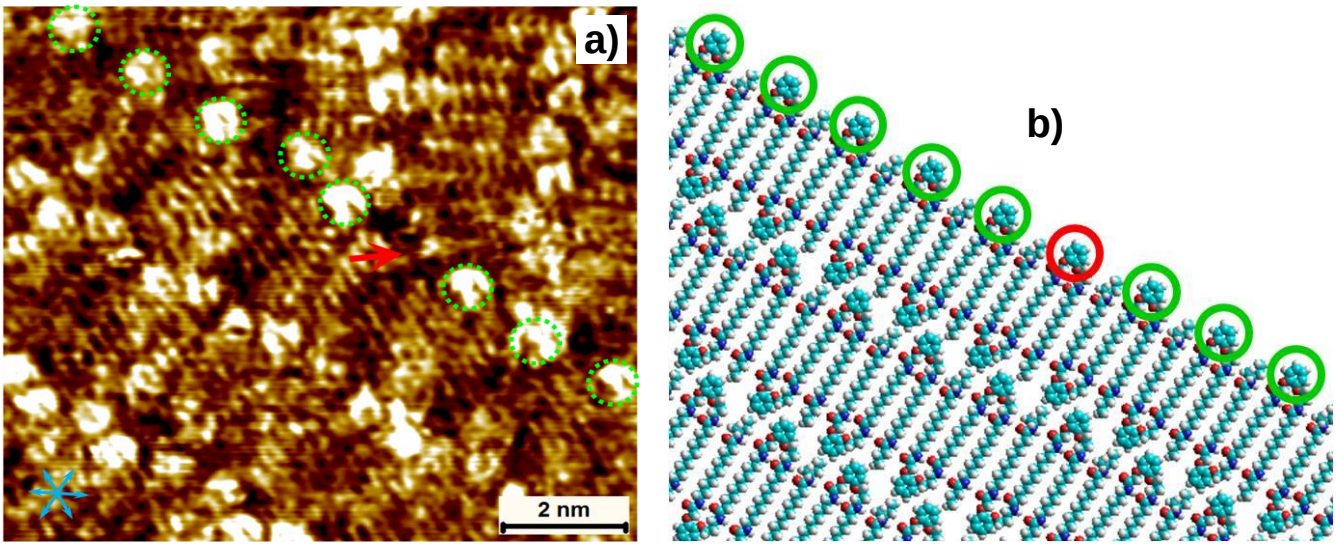


Figure S5. STM image of 2.1 adsorbed on the surface HOPG showing a domain boundary. Note that the catechol units at domain edge (dotted green circles) do not appear in pairs corroborating the molecular model proposed in Figure 5d. (b) A molecular model for an ideally realized domain boundary. A defect pointed by the red arrow plausibly appears due to out of plane twist of the catechol unit shown by the red circle in (b).

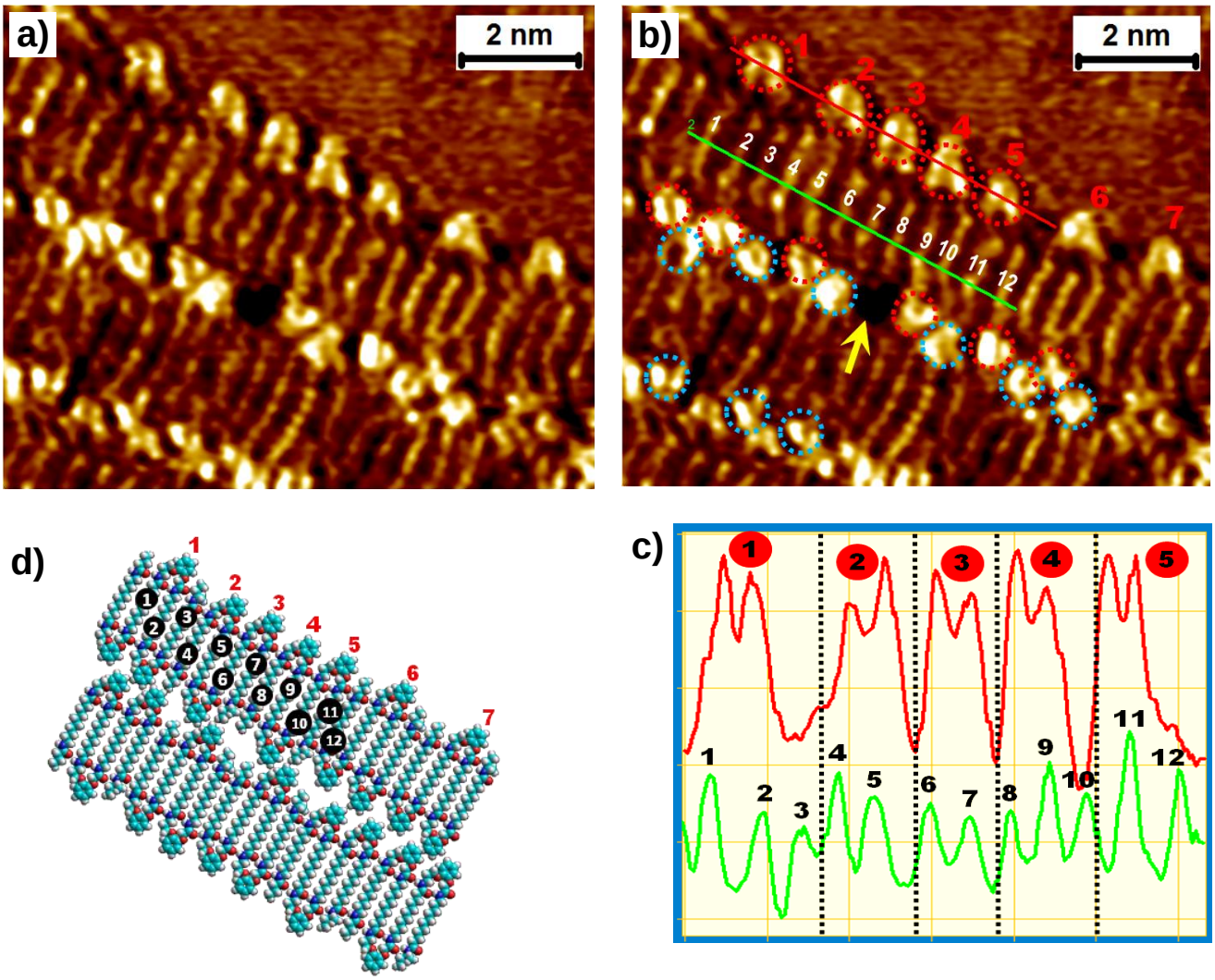
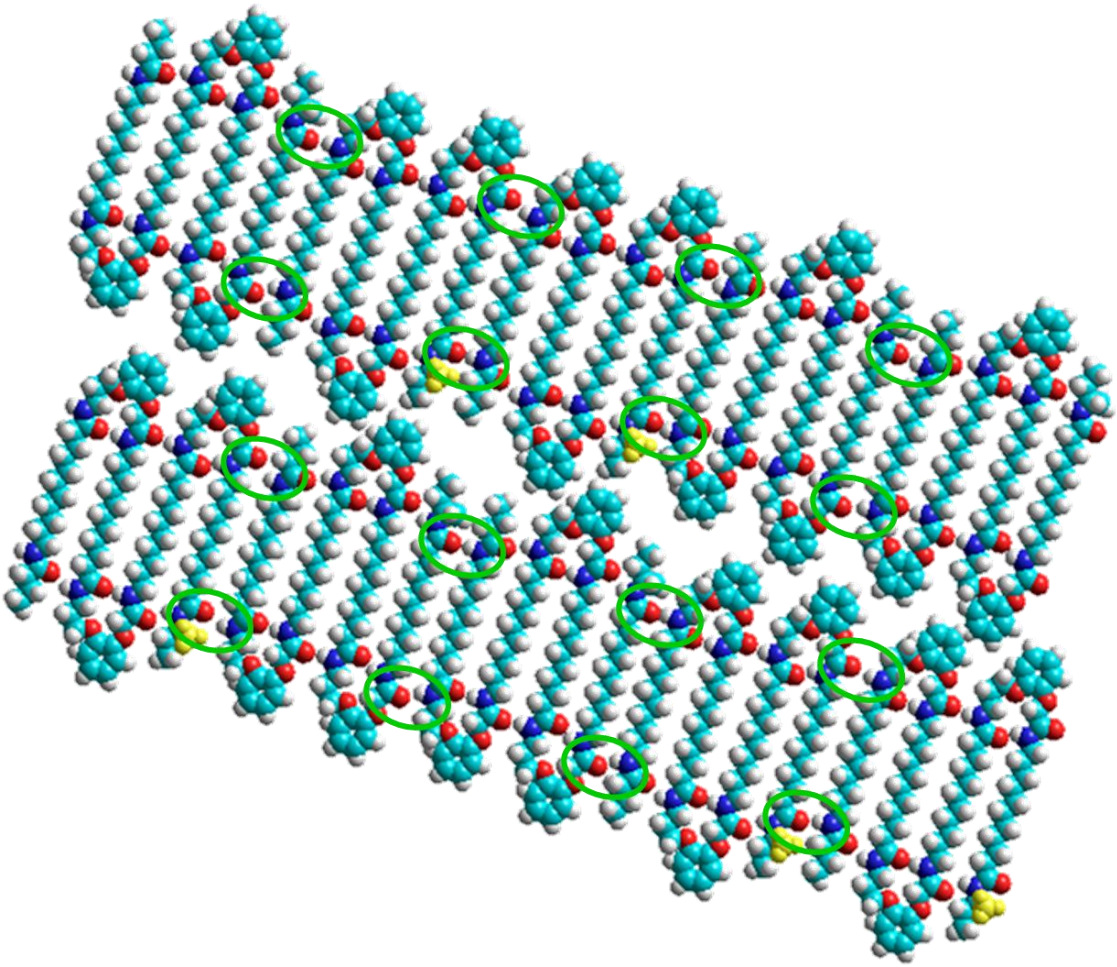


Figure S6. (a) HR-STM image of domain boundary observed in the monolayer of **2.2** at the 1-octanol/HOPG interface. (b) Same image as in (a) with color coded markers to identify molecules for the line profile analysis. Dotted red circles indicate the catechol units of molecules adsorbed in the upper lamella whereas blues circles highlight the probable locations of catechol units of molecules in the adjacent lower column. Yellow arrow in (b) shows a defect. (c) Representative line profile analysis of the domain boundary. (d) Proposed molecular model based on the line profile analysis.



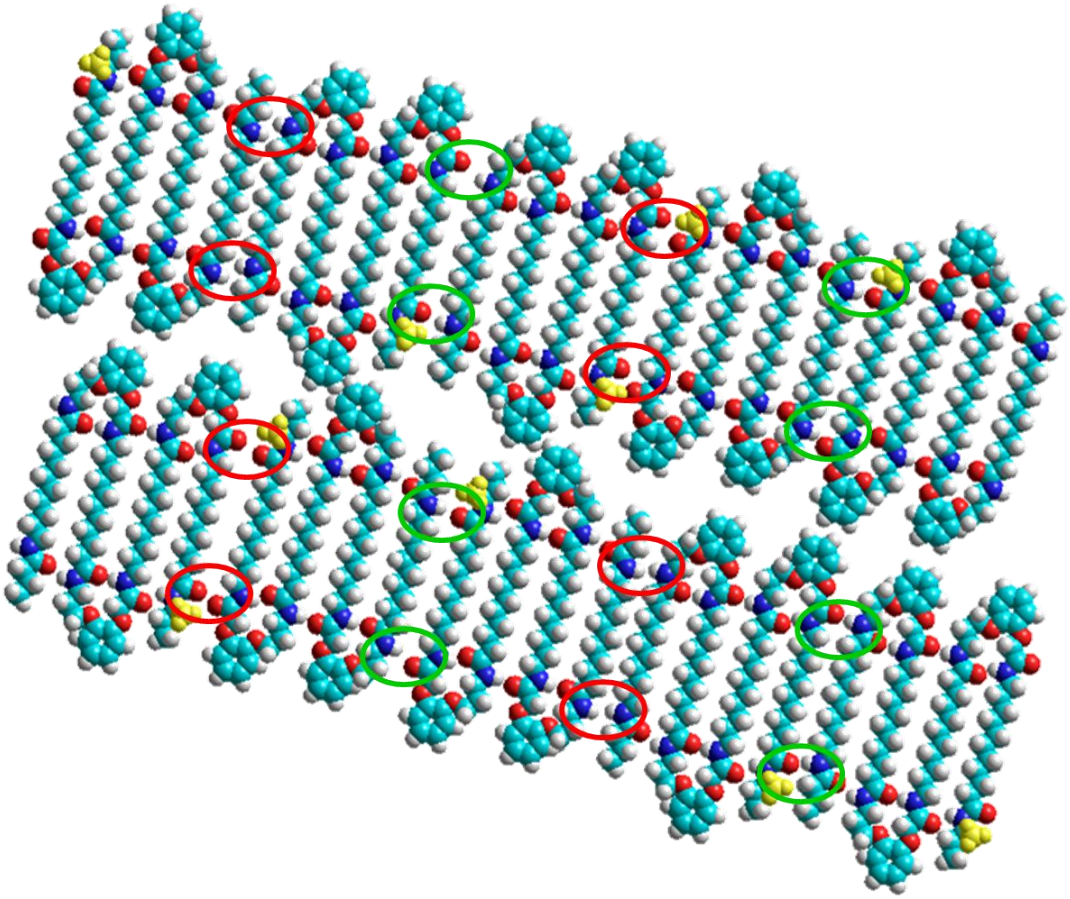


Figure S7: Possible alternative molecular models for the domain boundary depicted in **Figure S5a** in the main text. Only intermolecular (N–H···O=) hydrogen bonding sites are highlighted in the form of ellipses for the sake of clarity. The green ellipses indicate favorable orientation of the hydrogen bonding functionalities whereas the red ones show the arrangement unfavorable for intramolecular hydrogen bonding. Molecular arrangement in model (a) involves all the molecules adsorbed with their methyl groups (shown in yellow color) oriented to the solution phase. It can be easily noticed that such an arrangement leads to unfavorable orientation of hydrogen bonding functionalities of adjacent molecules as highlighted by red ellipses. Molecular arrangement shown in (b) is more feasible since in this arrangement all inter- as well as intramolecular hydrogen bonding valences are satisfied.

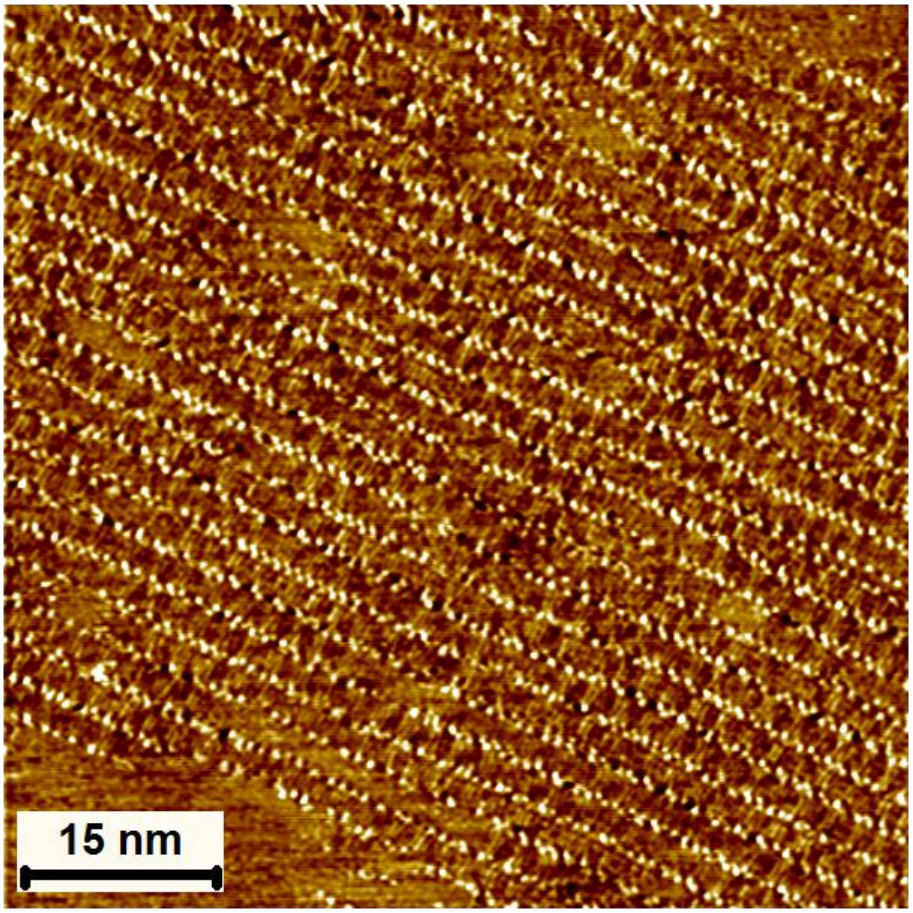


Figure S8: Large scale STM image of the monolayer formed by **2.2** at the 1-octanol/HOPG interface. Imaging conditions: I_{set} = *300 pA,* V_{bias} = *–200 mV*.

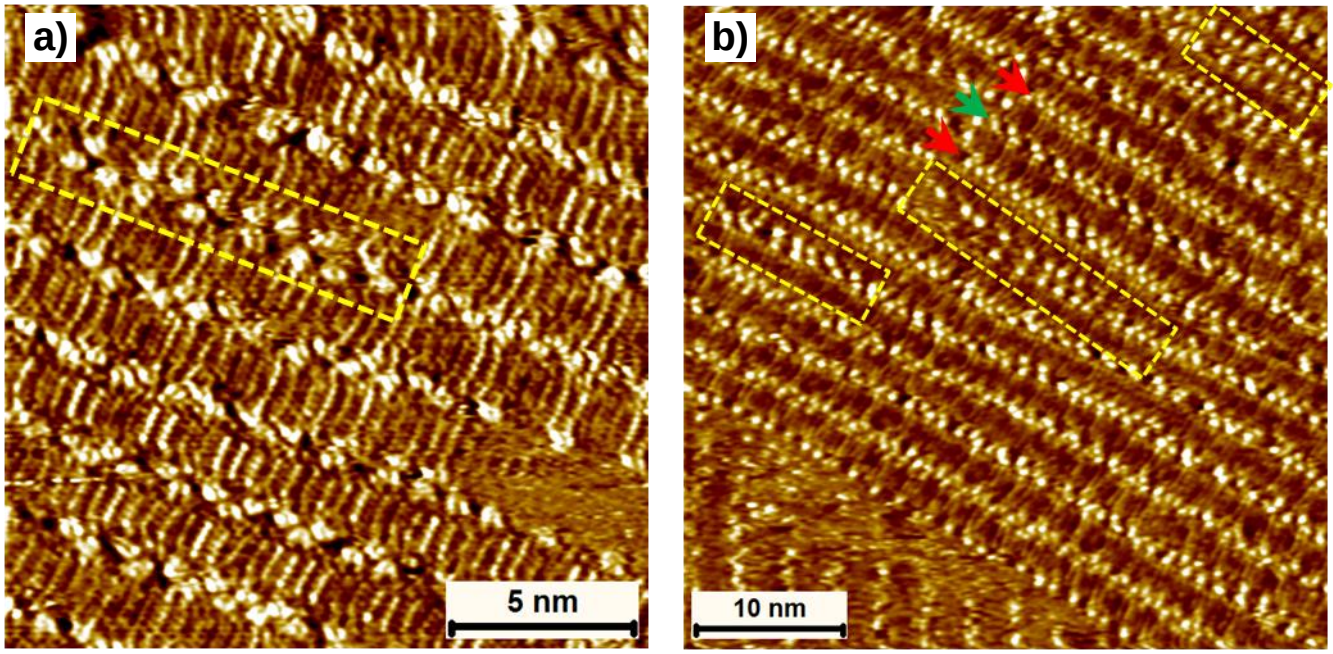


Figure S9: STM images of the monolayer formed by **2.2** at the 1-octanol/HOPG interface. The STM images highlight relatively open structures (dashed yellow rectangles) which are probably formed due to lack of strong intra-columnar forces (*see main text for discussion*). The alternate compact (red arrows) and less-compact (green arrows) arrangement of bright spots is also highlighted. The disorder present in the monolayer can be easily noticed. Imaging conditions: I_{set} = 200 pA, V_{bias} = –300 mV.

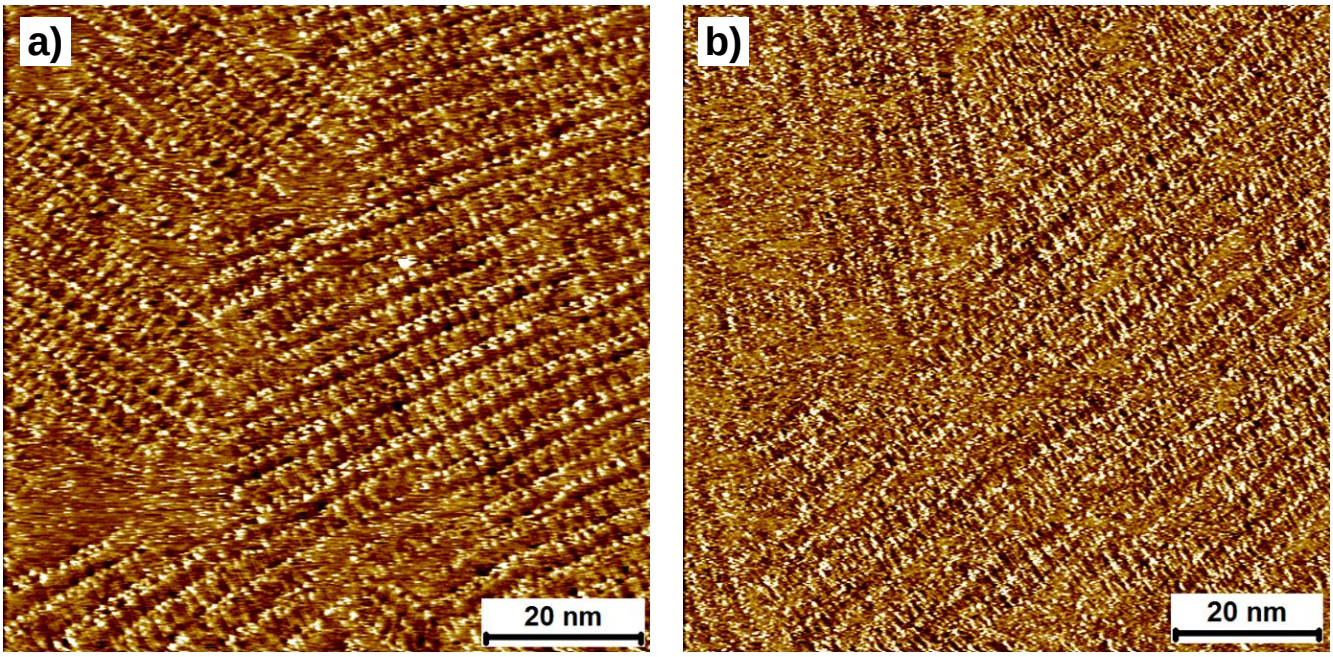


Figure S10: Large scale STM images of the monolayer formed by **2.3** at the 1-octanol/HOPG interface. Imaging conditions: I_{set} = 200 pA, V_{bias} = –250 mV.

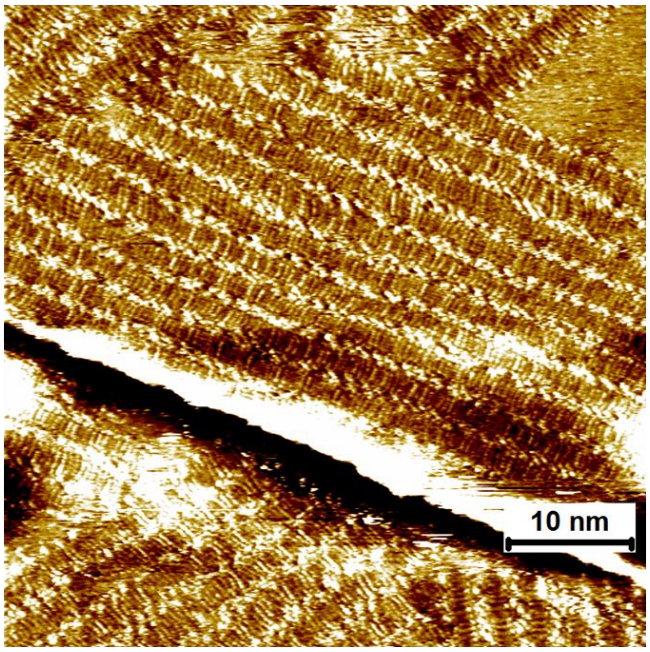


Figure S11. Typical STM image of the monolayer formed by foldamer **2.3** at the 1-octanol/HOPG interface. The alkyl chains are well-resolved whereas the catechol units remain poorly resolved. Imaging conditions: I_{set} = 200 pA, V_{bias} = –250 mV.

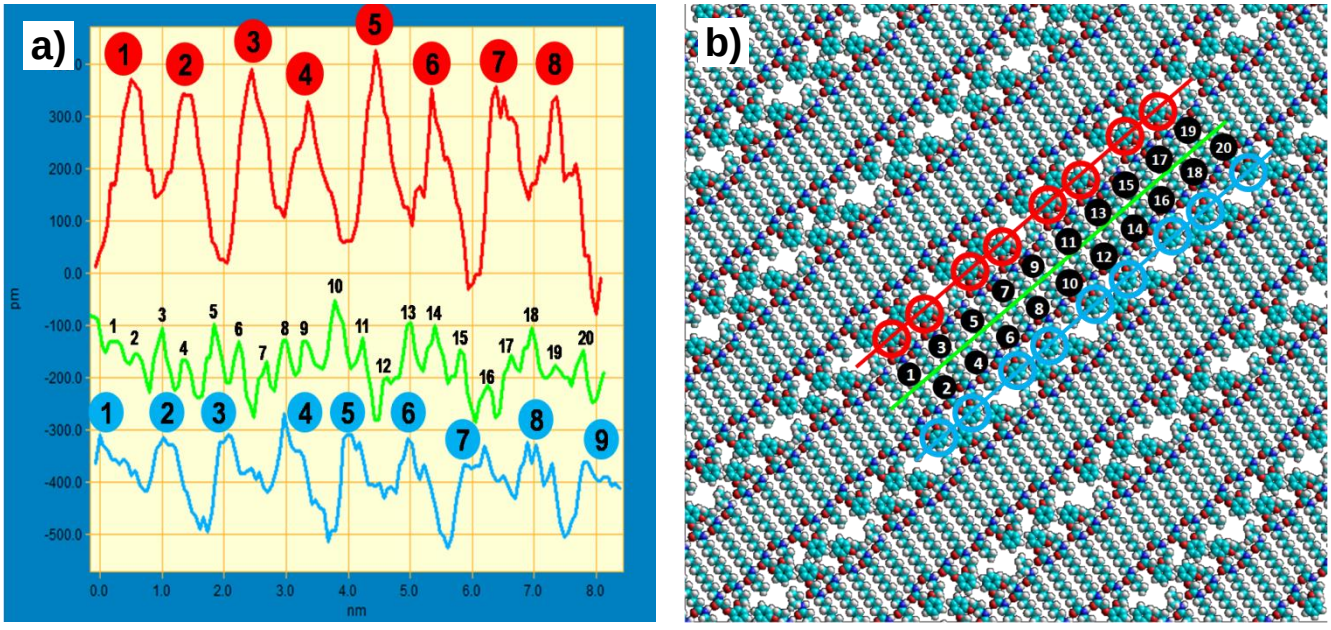


Figure S12. (a) A typical line profile obtained from HR-STM image of **2.3**. (b) A periodic molecular model built from the information obtained from the line profile. The information in the line profile is color coded with the markers shown in the molecular model.

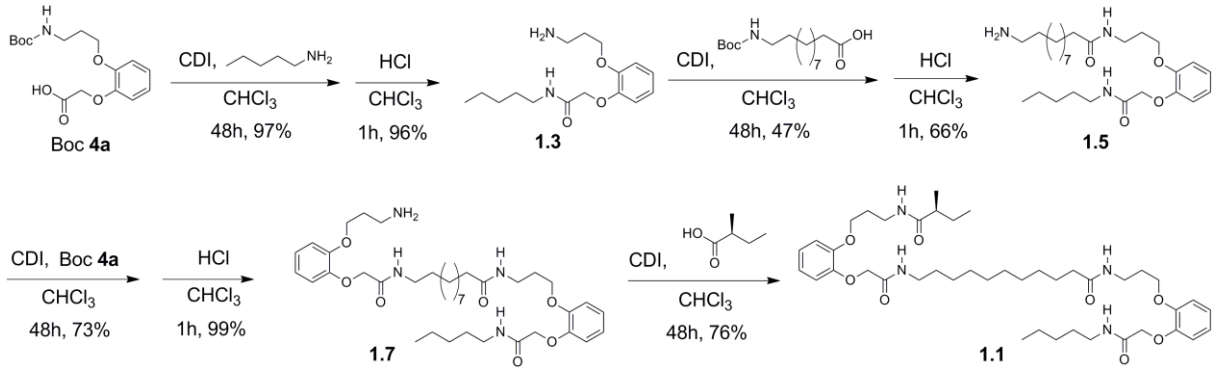
Section 2: Synthesis and Characterization of Foldamers

Materials and Methods:

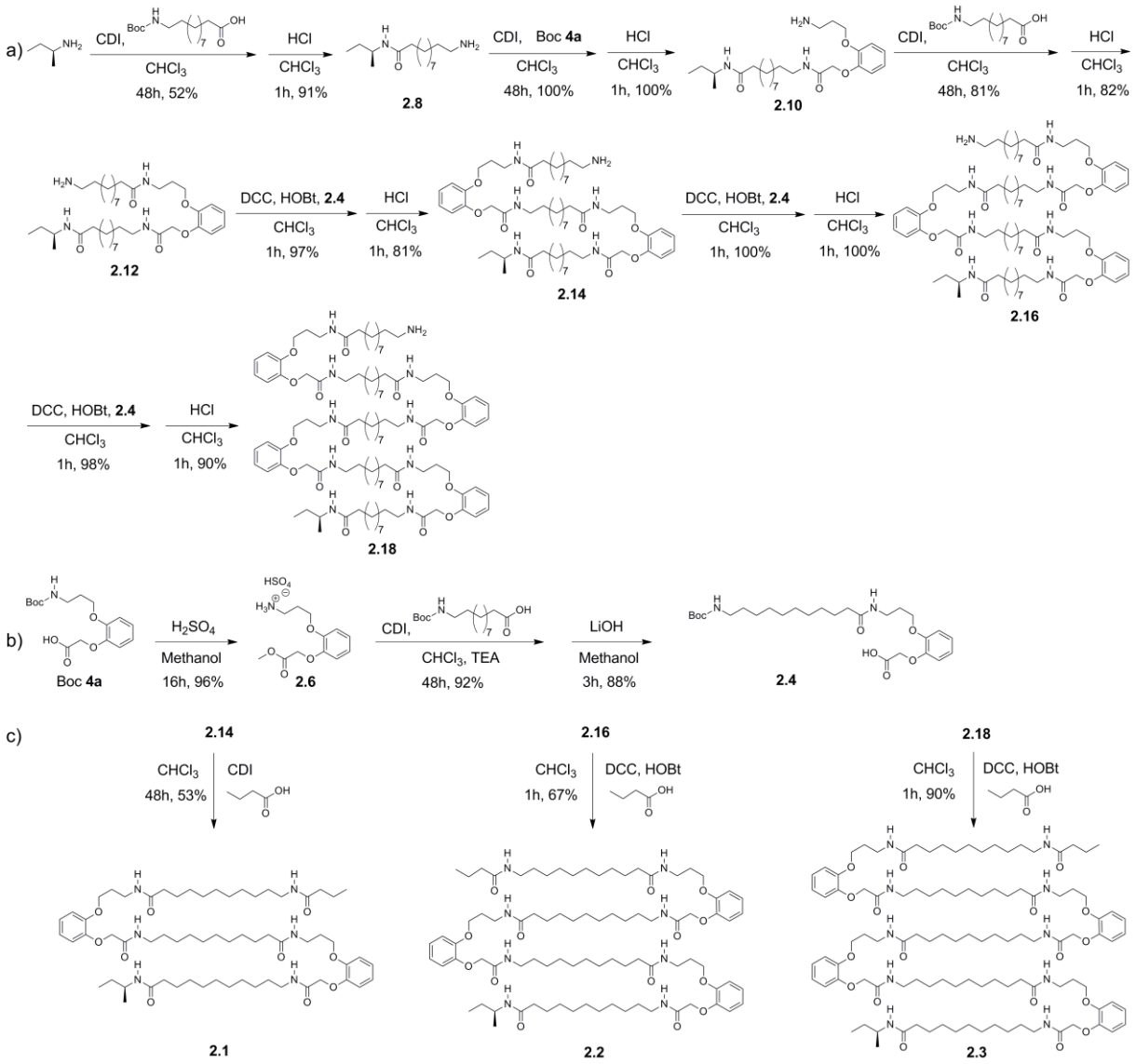
All solvents were dried according to standard procedures. Starting materials were purchased from Aldrich or Acros. Solvent removal (bulk amount), unless differently specified in the procedure, was worked out at 45 ºC, applying different vacuum with regard to the solvent. ^{1}H-NMR and ^{13}C-NMR spectra were recorded at 25 ºC in CDCL3 on a 'Varian Inova-300' (at 300MHz for ^{1}H-NMR and at 75.42 MHz for ^{13}C-NMR) and on a 'Bruker Advance-400' (at 400 MHz for ^{1}H-NMR and at 100.57 MHz for ^{13}C-NMR). Chemical shift were given relative to $CDCl_3$ (7.27 for ^{1}H-NMR and 77.2 for ^{13}C-NMR). The splitting patterns in ^{1}H-NMR spectra are designated as follows: s (singlet), d (doublet), t (triplet), m (multiplet), br (broad). MS (EI ionization) were performed on a 'Shimadzu GCMS-QP2010S' system in EI+ ionization mode. MS (ESI+ ionization) were performed on a 'Shimadzu LCMS-2010A'. Melting points were measured on 'Electrothermal IA9300' apparatus. IR spectra were recorded on 'Perkin Elmer Spectrum One' FT-IR spectrometer. 'Duplo' (double) elemental analysis (C, H and N) was determined using an Euro Vector 3400 CHN-S analyzer. The oxygen content was determined by difference. The data reported in this supporting information are the average of the double measurement.

Synthesis

The amino acidic nature of the building blocks allows applying the well-established step-wise synthesis of peptides towards these oligomeric foldamers that can be considered as peptidomimetics. We followed a N-acylation scheme in solution, in which (i) acylation (coupling) of the terminal amino group in the growing oligomer with an 'activated' acid, and (ii) deprotection of the next amino group (resulting in the new terminal group), were the recursive reactions. The last amine (precursor) was then coupled to an alkyl acid to yield the final product.



Scheme S1. Synthesis of foldamer **1.1** (class 1).



Scheme S2. Synthesis of foldamers **2.1**-**2.3** (class 2). a) Oligomeric step-wise synthesis of foldamer precursors. b) Synthesis of building block **2.4**. c) Final step toward foldamers **2.1**-**2.3**.

Several protocols have been applied for the coupling while tert-butoxycarbonyl (Boc) protected amines were always deprotected in acidic conditions. Carbonyldiimidazole (CDI)-mediated coupling were exclusively applied in the synthesis of class 1 foldamers (Scheme S1). The synthesis starts from the coupling between the turn mimic amino acid Boc **4a**[1] and pentylamine. Subsequent removal of the protecting group led to intermediate **1.3**. This compound, coupled to Boc-11-aminoundecanoic acid (BUA) and deprotected, resulted in compound **1.5**. Hence, coupling/deprotection of this compound involving the turn mimic amino acid Boc **4a** led to the precursor **1.7**. Final coupling of the free amino group to (S)-2-methylbutanoic acid led to foldamer **1.1**.

The synthesis of class 2 foldamers (Scheme S2) was affected by the low solubility of these compounds. We found that branching substitutions increased the solubility, therefore we decided to implement an enantiocenter from the beginning of the oligomeric synthesis (Scheme S2a). (S)-Butan-2-amine was coupled to BUA that, after deprotection, resulted in the compound **2.8**. This material underwent the same treatment (CDI-coupling/deprotection) involving first building block Boc **4a**, and secondly building block BUA, yielding **2.12**. In the meantime, building block **2.4** (Scheme S2b) was obtained from the turn mimic amino acid Boc **4a**. The protection of the latter compound was inverted to the acid side (**2.6**), coupled to BUA, and the acid was deprotected under alkaline conditions. Compound **2.12** (Scheme S2a) was then coupled (and deprotected) for three consecutive times to compound **2.4** in a step-wise fashion. These steps, in which a N,N'-Dicyclohexylcarbodiimide (DCC)/N-

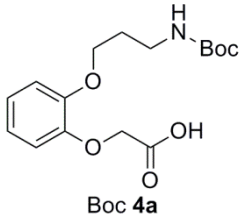
Hydroxybenzotriazole (HOBt) coupling protocol was applied,[2, 3] led to compounds **2.14**, **2.16**, and **2.18** as the precursors of the final foldamers. Finally, these precursors were coupled to butyric acid to yield the final products **2.1**, **2.2**, and **2.3**, respectively (Scheme S2c). The synthesized compounds have been characterized by ^{1}H NMR, ^{13}C NMR, MS, and only for the final products, HPLC-UV trace and elemental analysis.

Technical procedures and characterizations for intermediates and STM analytes

General procedure 1 for the peptide coupling reaction. The carboxylic acid was dissolved in the minimum volume of $CHCl_3$. An equimolar amount of 1,1'-Carbonyldiimidazole (CDI) was added to the solution and the mixture was stirred for 1h. The amine was added and the mixture was stirred for 48 h. The crude compound was purified by flash chromatography using 40−63 μm silica gel (230 - 400 mesh) applying an eluent with increasing polarity gradient (gradient is described in the specifics for any compound). The column was monitored with an UV detector set at 273 nm and 220 nm. The product's peak was collected and the solvent removed to obtain the desired amide.

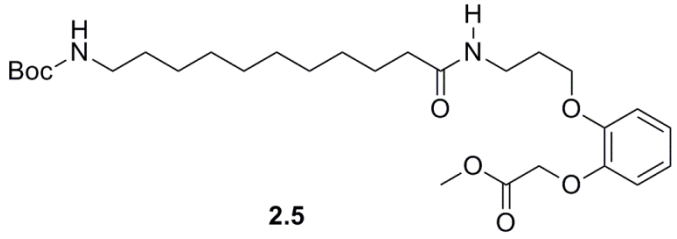
General procedure 2 for the peptide coupling reaction. The carboxylic acid was dissolved in the minimum volume of $CHCl_3$. An equimolar amount of Hydroxybenzotriazole (HOBt) was added to the solution. Immediately after, another equivalent amount *N,N'*-Dicyclohexylcarbodiimide (DCC) was added to the mixture which slowly turns into a clear solution. After 1 h the amine was added and the solution was stirred for 1 h. The crude compound was purified by flash chromatography using 40−63 μm silica gel (230 - 400 mesh) applying an eluent with increasing polarity gradient (gradient is described in the specifics for any compound). The column was monitored with an UV detector set at 273 nm and 220 nm. The product's peak was collected and the solvent removed to obtain the desired amide.

General procedure 3 for deprotection of N-Boc group. The Boc protected amine was dissolved in $CHCl_3$ (V ml) at maximum concentration of 0.05 M. Ethereal HCl (2 M, V/4 ml) was added drop wise to the solution. The mixture was stirred for 1 h and $NaOH_{(aq.)}$ (2 M, V/2 ml) was added. The mixture was extracted twice with $CHCl_3$ (complete dissolution of the material could take up to several minutes) and the combined organic phases were dried over anhydrous $MgSO_4$. The solid was filtered off and the solvent was removed from the clear solution to provide the desired compound.



Boc **4a**

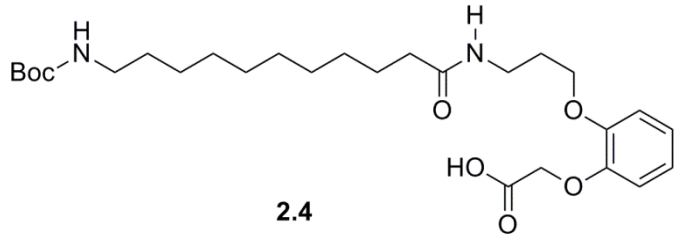
2-(2-(3-(tert-butoxycarbonylamino)propoxy)phenoxy)acetic acid (Boc **4a**). Synthesis of 'turn mimic' amino acid is described somewhere else.[1]



2.5

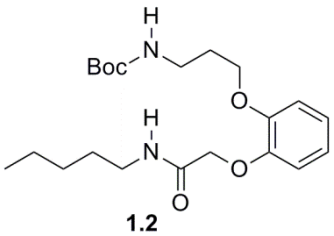
methyl 2-(2-(3-(11-(tert-butoxycarbonylamino)undecanamido)propoxy)phenoxy)acetate (**2.5**). H_2SO_4 (1.25 g, 12.74 mmol) was dissolved in MeOH (16 ml). Boc **4a** (4.00 g, 12.29 mmol) was added to the solution and the mixture was stirred 16h. The resulting product was precipitated pouring the solution into diethyl ether (300 ml). The precipitate was filtered and dried under high vacuum to

provide the intermediate product **2.6** as a white solid. Yield: 3.86 g (5.50 mmol, 96%). Combined ^{1}H-NMR and ESI confirmed formation of the aminium hydrogen sulfate salt and the esterification of the acid moiety. 11-(Boc-amino)-undecanoic acid (1.49 g, 4.94 mmol) was dissolved in the minimum volume of $CHCl_3$. 1,1'-Carbonyldiimidazole (801 mg, 4.94 mmol) was added to the solution and the mixture was stirred for 1h. The aminium hydrogen sulfate salt (1.39 g, 4.13 mmol) was dispersed in the solution and triethylamine (836 mg, 8.26 mmol) was added. The mixture turned into a clear solution which was stirred for 48 h. The solvent was removed and the crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography using 40−63 μm silica gel (230 - 400 mesh) applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 90: 10 in 15 column volumes. The column was monitored with an UV detector set at 273 nm and 220 nm. The product was collected at CH_2Cl_2: MeOH = 97: 3. The compound's peak was collected and the solvent removed to obtain the desired amide. Yield: 1.99 g (3.80 mmol, 92%). ^{1}H-NMR ($CDCl_3$): δ 7.06 - 6.89 (m, 4H), 4.65 - 4.40 (m, 3H), 4.10 (m, 2H), 3.79 (s, 3H), 3.61 - 3.40 (m, 2H), 3.18 - 3.02 (m, 2H), 2.10 (t, ^{3}J = 5.8 Hz, 2H), 2.08 - 2.00 (m, 2H), 1.80 - 1.20 (m, 26H). ^{13}C-NMR ($CDCl_3$): δ 173.4, 173.3, 168.6, 148.7, 147.5, 123.2, 121.7, 115.6, 113.5, 79.2, 69.4, 67.4, 53.5, 50.8, 39.2, 37.0, 30.2, 29.6, 29.3, 29.2, 28.6, 26.9, 25.9, 22.5. MS (ESI+) calcd for $C_{28}H_{46}N_2NaO_7$ $[M+Na]^+$ 545.32, found 545.40.



2.4

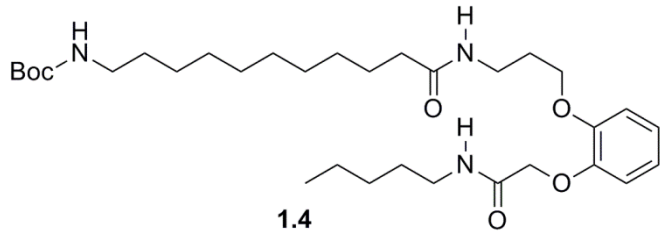
2-(2-(3-(11-(tert-butoxycarbonylamino)undecanamido)propoxy)phenoxy)acetic acid (**2.4**). Compound (1.43 g, 2.73 mmol) was dissolved in MeOH (20 ml). LiOH (317 mg, 13.65 mmol) was added to the solution which was stirred for 3 h. Water (20 ml) was poured into the mixture and $HCl_{(aq.)}$ (1 M) was added to adjust the aqueous layer to pH = 2. The mixture was extracted with $CHCl_3$ (50 ml, 3X) and the combine organic layers were dried over anhydrous $MgSO_4$. The solid was filtered off. The clear solution was concentrated and purified by flash chromatography using 40−63 μm silica gel (230 - 400 mesh) applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 85: 15 in 15 column volumes. The column was monitored with an UV detector set at 273 nm and 220 nm. The compound was collected at CH_2Cl_2: MeOH = 89: 11. The product's peak was collected and the solvent removed to obtain the desired acid. Yield: 1.22 g (2.40 mmol, 88%). ^{1}H-NMR ($CDCl_3$): δ 7.06 - 6.89 (m, 4H), 4.66 (s, 2H), 4.60 (br, 1H), 4.10 (m, 2H), 3.61 - 3.40 (m, 2H), 3.18 - 3.02 (m, 2H), 2.10 (t, ^{3}J = 5.8 Hz, 2H), 2.08 - 2.00 (m, 2H), 1.80 - 1.20 (m, 26H). ^{13}C-NMR ($CDCl_3$): δ 173.4, 171.2, 168.6, 148.7, 147.5, 123.2, 121.7, 115.6, 113.5, 79.2, 69.4, 67.4, 53.5, 39.2, 37.0, 30.2, 29.6, 29.3, 29.2, 28.6, 26.9, 25.9, 22.5. MS (ESI+) calcd for $C_{27}H_{44}N_2NaO_7$ $[M+Na]^+$ 531.30, found 531.35.



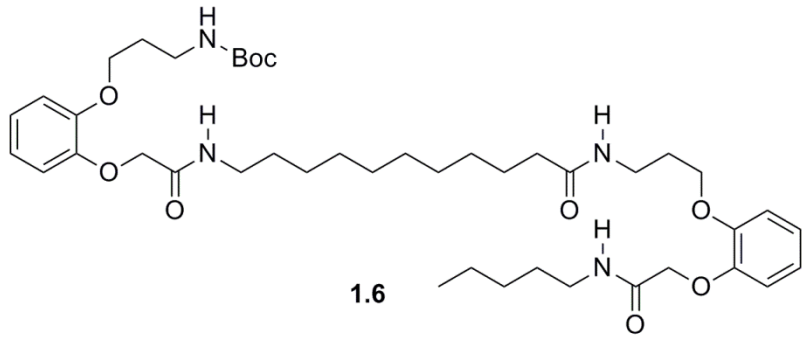
1.2

tert-butyl 3-(2-(2-oxo-2-(pentylamino)ethoxy)phenoxy)propylcarbamate (**1.2**). Pentylamine (0.51 g, 5.89 mmol) and Boc **4a** (2.30 g, 7.07 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 95: 5 in 10 column volumes. The compound was collected at CH_2Cl_2: MeOH = 96: 4. Yield: 2.26 g (5.72 mmol, 97%). ^{1}H-NMR ($CDCl_3$): δ 7.02 - 6.87 (m, 5H), 5.11 (br, 1H), 4.53 (s, 2H), 4.10 (t, ^{3}J = 5.6 Hz, 2H), 3.39 - 3.27 (m, 4H), 2.05 - 1.97 (m, 2H), 1.60 - 1.39 (m, 11H), 1.35 - 1.15 (m, 4H), 0.88 (t, ^{3}J = 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 168.5, 156.0, 148.7,

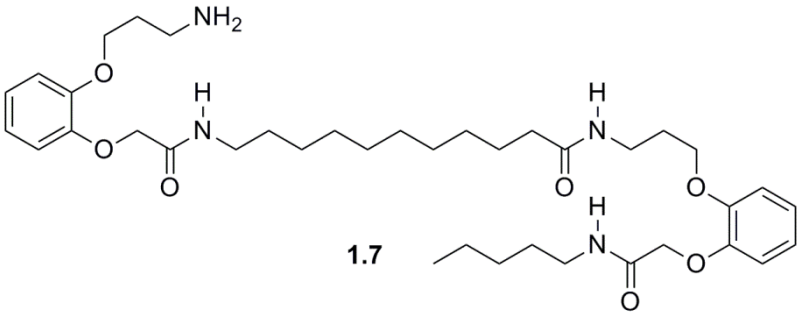
147.5, 122.8, 121.5, 115.1, 113.4, 79.2, 69.4, 67.4, 39.0, 29.6, 29.2, 29.0, 28.4, 25.6, 22.9, 14.3. MS (ESI+) calcd for $C_{16}H_{27}N_2O_3$ $[M\text{-}Boc+2H]^+$ 295.20, $C_{16}H_{26}N_2NaO_3$ $[M\text{-}Boc+H+Na]^+$ 317.18, $C_{21}H_{35}N_2O_5$ $[M+H]^+$ 395.25, $C_{21}H_{34}N_2NaO_5$ $[M+Na]^+$ 417.24, found 295.15, 317.15, 395.25, 417.25.



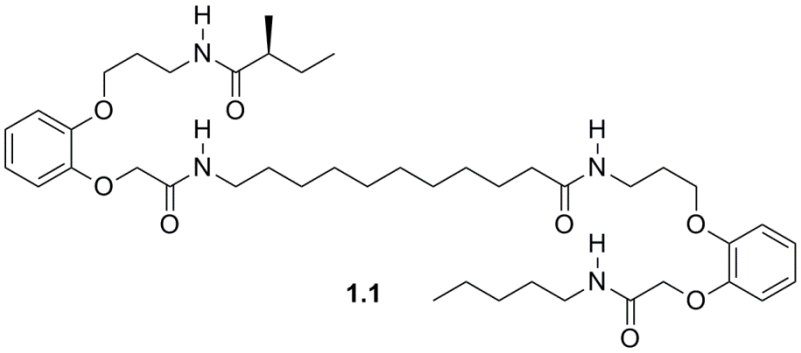
tert-butyl 11-oxo-11-(3-(2-(2-oxo-2-(pentylamino)ethoxy)phenoxy)propylamino)undecylcarbamate (**1.4**). Boc-protected compound **1.2** (2.26 g, 5.72 mmol) was deprotected following general procedure 3. Yield: 1.62 g (5.50 mmol, 96%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group. The deriving free-amino compound **1.3** (1.62 g, 5.50 mmol) and 11-(Boc-amino)-undecanoic acid (1.99 g, 6.60 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 85: 15 in 15 column volumes. The product was collected at CH_2Cl_2: MeOH = 89: 11. Yield: 1.50 g (2.60 mmol, 47%). ^{1}H-NMR ($CDCl_3$): δ 7.10 - 6.84 (m, 5H), 5.98 (br, 1H), 4.65 - 4.40 (m, 3H), 4.09 (t, ^{3}J = 5.8 Hz, 2H), 3.53 - 3.45 (m, 2H), 3.36 - 3.27 (m, 2H), 3.18 - 2.98 (m, 2H), 2.14 (t, ^{3}J = 7.4 Hz, 2H), 2.02 (t, ^{3}J = 5.8 Hz, 2H), 1.70 - 1.18 (m, 31H), 0.88 (t, ^{3}J = 6.9 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 173.4, 168.6, 148.7, 147.5, 123.2, 121.7, 115.6, 113.5, 79.2, 69.4, 67.4, 53.5, 39.2, 37.3, 37.0, 30.2, 29.6, 29.4, 29.3, 29.2, 28.6, 26.9, 25.9, 22.5, 14.1. MS (ESI+) calcd for $C_{27}H_{48}N_3O_4$ $[M\text{-}Boc+2H]^+$ 478.36, $C_{27}H_{47}N_3NaO_4$ $[M\text{-}Boc+H+Na]^+$ 500.35, $C_{32}H_{56}N_3O_6$ $[M+H]^+$ 578.42, $C_{32}H_{55}N_3NaO_6$ $[M+Na]^+$ 600.40, found 478.40, 500.40, 578.50, 600.45.



tert-butyl 3-(2-(2-oxo-2-(11-oxo-11-(3-(2-(2-oxo-2-(pentylamino)ethoxy)phenoxy)propylamino)undecylamino)ethoxy)phenoxy)propylcarbamate (**1.6**). Boc-protected compound **1.4** (1.50 g, 2.60 mmol) was deprotected following general procedure 3. Yield: 0.82 g (1.72 mmol, 66%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group. The deriving free-amino compound **1.5** (0.82 g, 1.72 mmol) and 'turn mimic' amino acid (0.67 g, 2.06 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 85: 15 in 15 column volumes. The compound was collected at CH_2Cl_2: MeOH = 91: 9. Yield: 985 mg (1.25 mmol, 73%). ^{1}H-NMR ($CDCl_3$): δ 7.10 - 6.84 (m, 10H), 5.98 (br, 1H), 5.15 (br, 1H), 4.53 (s, 4H), 4.18 - 4.04 (m, 4H), 3.53 - 3.45 (m, 2H), 3.40 - 3.25 (m, 6H), 2.20 - 2.12 (m, 2H), 2.10 - 1.98 (m, 2H), 1.70 - 1.18 (m, 33H), 0.88 (t, ^{3}J = 6.9 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 173.4, 168.6, 156.2, 148.7, 147.5, 123.2, 121.7, 115.2, 113.5, 79.2, 69.6, 67.3, 50.5, 39.2, 37.2, 37.0, 29.7, 29.4, 29.2, 28.6, 27.0, 25.9, 22.5, 14.1. MS (ESI+) calcd for $C_{38}H_{61}N_4O_7$ $[M\text{-}Boc+2H]^+$ 685.45, $C_{43}H_{69}N_4O_9$ $[M+H]^+$ 785.51, $C_{43}H_{68}N_4NaO_9$ $[M+Na]^+$ 807.49, found 685.50, 785.50, 807.50.



11-(2-(2-(3-aminopropoxy)phenoxy)acetamido)-N-(3-(2-(2-oxo-2-(pentylamino)ethoxy)phenoxy)propyl)undecanamide (**1.7**). Boc-protected compound **1.6** (985 mg, 1.25 mmol) was deprotected following general procedure 3. Yield: 852 mg (1.24 mmol, 99%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group from substrate.

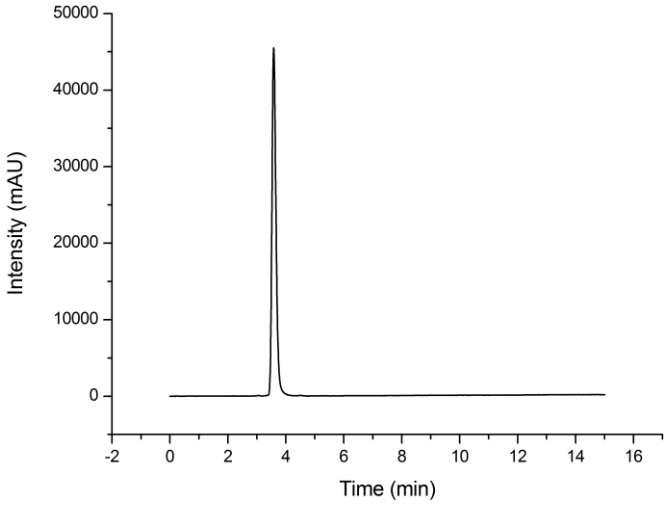


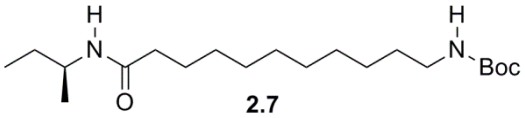
(S)-11-(2-(2-(3-(2-methylbutanamido)propoxy)phenoxy)acetamido)-N-(3-(2-(2-oxo-2-(pentylamino)ethoxy)phenoxy)propyl)undecanamide (**1.1**). The free-amino compound **1.7** (208 mg, 0.31 mmol) and (S)-2-methylbutyric acid (37 mg, 0.36 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 90: 10 in 15 column volumes. The compound was collected at CH_2Cl_2: MeOH = 96: 4. The eluent was removed and the residue dissolved in CH_2Cl_2. The solution was filtered and the compound was precipitated from the clear solution adding an excess of heptane. The precipitate was filtered and dried under high vacuum to provide compound **1.1** as a white solid. Yield: 180 mg (0.23 mmol, 76%). ^{1}H-NMR ($CDCl_3$): δ 7.20 - 6.55 (m, 11H), 6.45 - 6.30 (br, 1H), 4.54 (s, 4H), 4.22 - 4.04 (m, 4H), 3.70 - 3.45 (m, 4H), 3.42 - 3.29 (m, 4H), 2.40 - 1.98 (m, 7H), 1.80 - 1.18 (m, 27H), 0.98 - 0.82 (m, 6H). ^{13}C-NMR ($CDCl_3$): δ 176.8, 173.7, 168.7, 148.8, 147.5, 123.2, 121.7, 115.2, 113.5, 69.5, 67.3, 50.5, 43.4, 39.3, 37.3, 37.1, 36.8, 29.6, 29.5, 29.4, 29.3, 29.2, 27.5, 26.9, 25.9, 22.5, 17.6, 14.1, 12.1. MS (ESI+) calcd for $C_{43}H_{69}N_4O_8$ $[M+H]^+$ 769.51, $C_{43}H_{68}N_4NaO_8$ $[M+Na]^+$ 791.49, $C_{43}H_{68}KN_4O_8$ $[M+K]^+$ 807.47, found 769.45, 791.45, 807.45. Anal. calcd/found for $C_{43}H_{68}N_4O_8$: C, 67.14%/67.09%; H, 8.92%/8.95%; N, 7.29%/7.27%; O, 16.64%/16.68%.

HPLC analysis

Isocratic elution: ACN/H2O = 63/37 (0.1% formic acid)

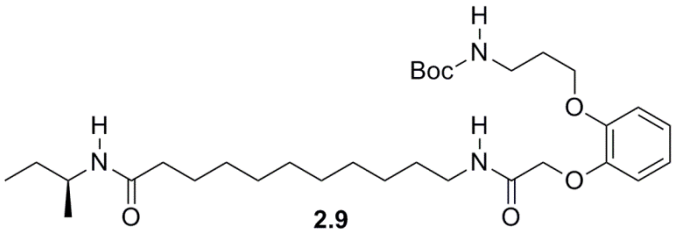
UV detection: 273 nm





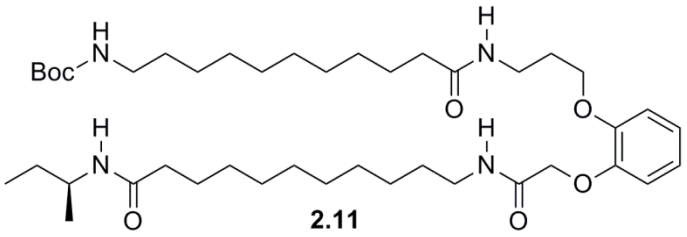
2.7

(S)-tert-butyl 11-(sec-butylamino)-11-oxoundecylcarbamate (**2.7**). (S)-*sec*-butylamine (1.01 g, 13.81 mmol) and 11-(Boc-amino)-undecanoic acid (5.00 g, 16.59 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 95: 5 in 20 column volumes. The compound was collected at CH_2Cl_2: MeOH = 99: 1. Yield: 2.55 g (7.15 mmol, 52%). ^{1}H-NMR ($CDCl_3$): δ 5.22 (br, 1H), 4.52 (br, 1H), 4.00 - 3.85 (m, 1H), 3.18 - 3.04 (m, 2H), 2.18 - 2.10 (m, 2H), 1.70 - 1.56 (m, 2H), 1.55 - 1.38 (m, 13H), 1.37 - 1.20 (m, 12H), 1.11 (d, ^{3}J = 8.6 Hz, 3H), 0.88 (t, ^{3}J = 6.9 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 172.5, 156.1, 79.2, 50.1, 46.5, 37.2, 29.8, 29.6, 29.5, 29.4, 28.6, 26.9, 26.0, 20.6, 10.5. MS (ESI+) calcd for $C_{15}H_{33}N_2O$ $[M\text{-}Boc+2H]^+$ 257.26, $C_{20}H_{41}N_2O_3$ $[M+H]^+$ 357.31, $C_{20}H_{40}N_2NaO_3$ $[M+Na]^+$ 379.29, found 257.40, 357.25, 379.20.

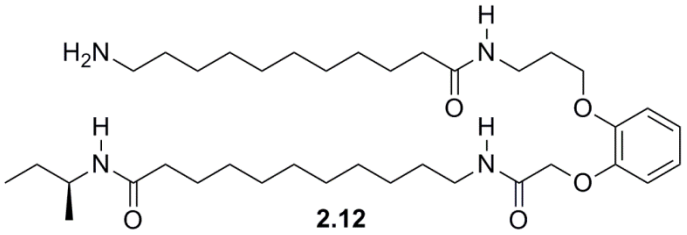


2.9

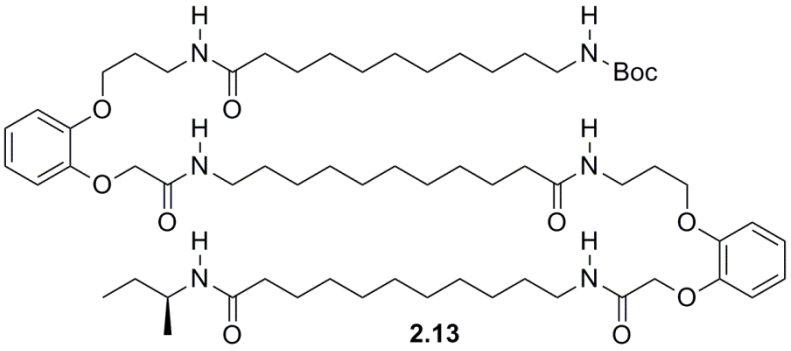
(S)-tert-butyl 3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylcarbamate (**2.9**). Boc-protected compound **2.7** (2.55 g, 7.15 mmol) was deprotected following general procedure 3. Yield: 1.66 g (6.47 mmol, 91%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group. The deriving free-amino compound **2.8** (1.66 g, 6.47 mmol) and Boc **4a** (2.56 g, 7.86 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 95: 5 in 20 column volumes. The compound was collected at CH_2Cl_2: MeOH = 98: 2. Yield: 3.69 g (6.47 mmol, 100%). ^{1}H-NMR ($CDCl_3$): δ 7.10 - 6.87 (m, 5H), 5.40 (br, 1H), 5.11 (br, 1H), 4.53 (s, 2H), 4.10 (t, ^{3}J = 5.6 Hz, 2H), 3.97 - 3.86 (m, 1H), 3.39 - 3.27 (m, 4H), 2.20 - 2.12 (m, 2H), 2.09 - 2.00 (m, 2H), 1.70 - 1.20 (m, 28H), 1.11 (d, ^{3}J = 8.6 Hz, 3H), 0.88 (t, ^{3}J = 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 172.7, 168.5, 156.0, 148.7, 147.5, 122.8, 121.5, 115.1, 113.4, 79.2, 69.4, 67.4, 46.6, 39.2, 37.1, 29.8, 29.6, 29.5, 29.4, 29.3, 28.5, 26.9, 25.9, 20.6, 14.3. MS (ESI+) calcd for $C_{26}H_{46}N_3O_4$ $[M\text{-}Boc+2H]^+$ 464.35, $C_{31}H_{54}N_3O_6$ $[M+H]^+$ 564.40, $C_{31}H_{53}N_3NaO_6$ $[M+Na]^+$ 586.38, found 464.25, 564.35, 586.10.



(S)-tert-butyl 11-(3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylcarbamate (**2.11**). Boc-protected compound **2.9** (3.69 g, 6.54 mmol) was deprotected following general procedure 3. Yield: 3.03 g (6.54 mmol, 100%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group. The deriving free-amino compound **2.10** (3.03 g, 6.54 mmol) and 11-(Boc-amino)-undecanoic acid (2.37 g, 7.86 mmol) were coupled according to general procedure 1. The crude compound was dissolved in CH_2Cl_2 and purified by flash chromatography applying a gradient from pure CH_2Cl_2 to CH_2Cl_2: MeOH = 95: 5 in 20 column volumes. The compound was collected at CH_2Cl_2: MeOH = 97: 3. Yield: 3.95 g (5.29 mmol, 81%). ^{1}H-NMR ($CDCl_3$): δ 7.10 - 6.87 (m, 5H), 6.31 (br, 1H), 5.62 (br, 1H), 4.80 - 4.40 (m, 3H), 4.10 (t, ^{3}J = 5.6 Hz, 2H), 3.97 - 3.86 (m, 1H), 3.62 - 3.42 (m, 2H), 3.39 - 3.27 (m, 2H), 3.21 - 3.00 (m, 2H), 2.20 - 2.12 (m, 4H), 2.09 - 2.00 (m, 2H), 1.70 - 1.20 (m, 43H), 1.11 (d, ^{3}J = 8.6 Hz, 3H), 0.88 (t, ^{3}J = 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 173.0, 172.5, 168.5, 156.0, 148.7, 147.5, 122.8, 121.5, 115.1, 113.4, 79.2, 69.2, 67.0, 46.6, 38.9, 36.9, 36.8, 36.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.3, 26.7, 25.7, 20.4, 10.2. MS (ESI+) calcd for $C_{37}H_{67}N_4O_5$ $[M\text{-}Boc+2H]^+$ 647.51, $C_{42}H_{75}N_4O_7$ $[M+H]^+$ 747.56, $C_{42}H_{74}N_4NaO_7$ $[M+Na]^+$ 769.55, found 647.35, 747.40, 769.35.

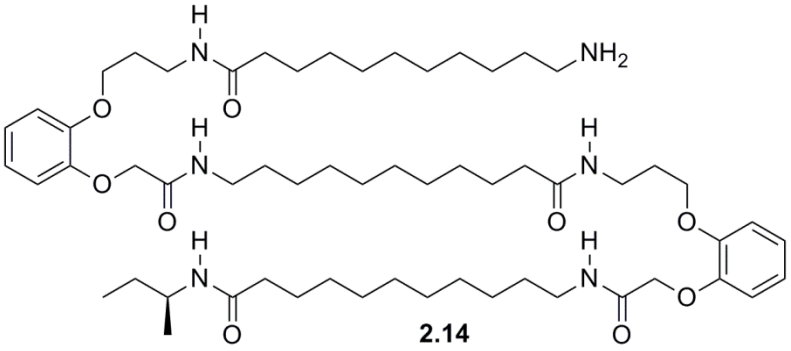


(S)-11-amino-N-(3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propyl)undecanamide (**2.12**). Boc-protected compound **2.11** (3.95 g, 1.25 mmol) was deprotected following general procedure 3. Yield: 2.80 g (4.33 mmol, 82%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group from the substrate.



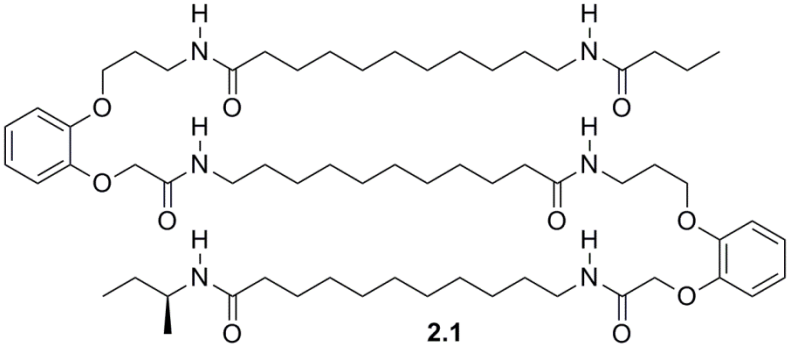
(S)-tert-butyl 11-(3-(2-(2-(11-(3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylcarbamate (**2.13**). The free-amino compound **2.12** (543 mg, 0.84 mmol) and the acid compound **2.4** (519 mg, 1.02 mmol) were coupled according to general procedure 2. The solution was concentrated and purified by flash chromatography applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 94: 6 in 20 column volumes. The compound was collected at $CHCl_3$: MeOH = 97: 3. Yield: 930 mg (0.82 mmol, 97%). ^{1}H-NMR ($CDCl_3$): δ 7.10 - 6.84 (m, 10H), 6.54 (br, 1H), 6.37 (br, 1H), 5.78

(br, 1H), 4.65 - 4.40 (m, 5H), 4.19 - 3.99 (m, 4H), 3.97 - 3.86 (m, 1H), 3.62 - 3.42 (m, 4H), 3.39 - 3.27 (m, 4H), 3.21 - 3.00 (m, 2H), 2.22 - 2.10 (m, 6H), 2.09 - 2.00 (m, 4H), 1.70 - 1.20 (m, 59H), 1.11 (d, ^{3}J = 8.6 Hz, 3H), 0.88 (t, ^{3}J = 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 173.1, 173.0, 172.5, 168.5, 156.0, 148.7, 147.5, 122.8, 121.5, 115.1, 113.4, 79.2, 69.2, 67.0, 46.6, 38.9, 36.9, 36.8, 36.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.3, 26.7, 25.7, 20.4, 10.2. MS (ESI+) calcd for $C_{64}H_{110}N_6O_{11}$ $[M+2H]^{2+}$ (1138.82 / 2 =) 569.41, $C_{64}H_{109}N_6NaO_{11}$ $[M+H+Na]^{2+}$ (1160.81 / 2 =) 580.41, $C_{64}H_{108}N_6Na_2O_{11}$ $[M+2Na]^{2+}$ (1182.79 / 2 =) 591.40, $C_{64}H_{109}N_6O_{11}$ $[M+H]^{+}$ 1137.82, $C_{64}H_{108}N_6NaO_{11}$ $[M+Na]^{+}$ 1159.80, found 569.30, 580.50, 591.50, 1137.40, 1159.45.



2.14

(S)-11-amino-N-(3-(2-(2-(11-(3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propyl)undecanamide (**2.14**). Boc-protected compound **2.13** (900 mg, 0.79 mmol) was deprotected following general procedure 3. Yield: 664 mg (0.64 mmol, 81%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group from the substrate.



2.1

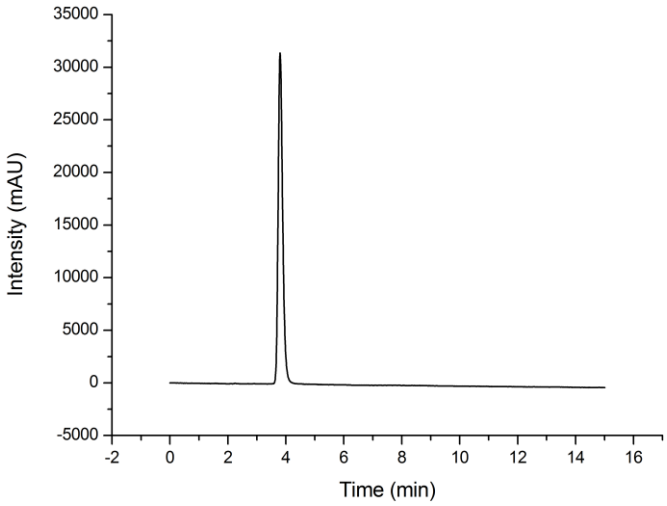
(S)-N-sec-butyl-11-(2-(2-(3-(11-(2-(2-(3-(11-butyramidoundecanamido)propoxy)phenoxy)acetamido)undecanamido)propoxy)phenoxy)acetamido)undecanamide (**2.1**). The free-amino compound **2.14** (170 mg, 0.16 mmol) and butyric acid (17 mg, 0.19 mmol) were coupled according to general procedure 1. The solution was concentrated and purified by flash chromatography applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 90: 10 in 15 column volumes. The compound was collected at $CHCl_3$: MeOH = 96: 4. The eluent was removed and the residue dissolved in $CHCl_3$. The solution was filtered and the compound was precipitated from the clear solution adding an excess of heptane. The precipite was filtered and dried under high vacuum to provide compound **2.1** as a white solid. Yield: 97 mg (0.087 mmol, 53%). ^{1}H-NMR ($CDCl_3$): δ 7.10 - 6.84 (m, 10H), 6.68 - 6.60 (br, 1H), 6.46 - 6.58 (br, 1H), 6.10 -5.70 (m, 2H), 4.53 (s, 4H), 4.19 - 4.02 (m, 4H), 3.93 - 3.80 (m, 1H), 3.54 - 3.40 (m, 4H), 3.37 - 3.10 (m, 6H), 2.30 - 1.90 (m, 18H), 1.70 - 1.20 (m, 48H), 1.11 (d, ^{3}J = 8.6 Hz, 3H), 0.98 - 0.80 (m, 6H). ^{13}C-NMR ($CDCl_3$): δ 173.6, 173.2, 172.8, 168.7, 148.9, 147.5, 123.2, 121.7, 115.5, 113.5, 69.5, 67.3, 67.2, 46.7, 39.7, 39.3, 38.9, 37.1, 36.9, 29.9, 29.8, 29.7, 29.4, 29.3, 27.0, 26.0, 25.9, 20.7, 19.4, 13.9, 13.9, 10.2. MS (ESI+) calcd for $C_{64}H_{110}N_6O_{11}$ $[M+2H]^{2+}$ (1108.81 / 2 =) 554.41, $C_{63}H_{107}N_6NaO_{10}$ $[M+H+Na]^{2+}$ (1130.79 / 2 =) 565.40, $C_{63}H_{106}N_6Na_2O_{10}$ $[M+2Na]^{2+}$ (1152.78 / 2 =) 576.39, $C_{63}H_{106}N_6NaO_{10}$ $[M+Na]^{+}$ 1129.79, found

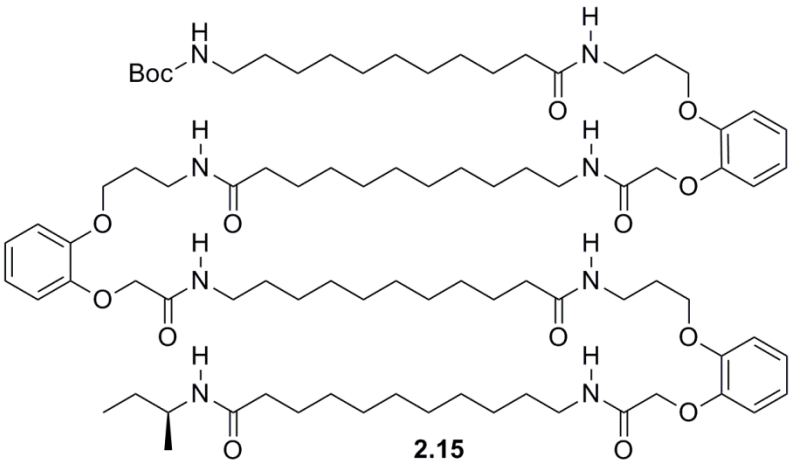
554.80, 565.80, 576.70, 1129.85. Anal. calcd/found for $C_{63}H_{106}N_6O_{10}$: C, 68.32%/68.28%; H, 9.65%/9.68%; N, 7.59%/7.58%; O, 14.45%/14.46%.

HPLC analysis

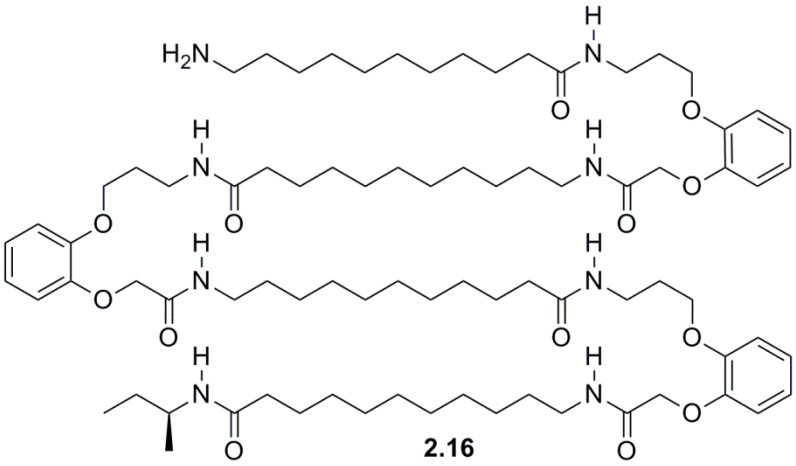
Isocratic elution: ACN/H2O = 63/37 (0.1% formic acid)

UV detection: 273 nm



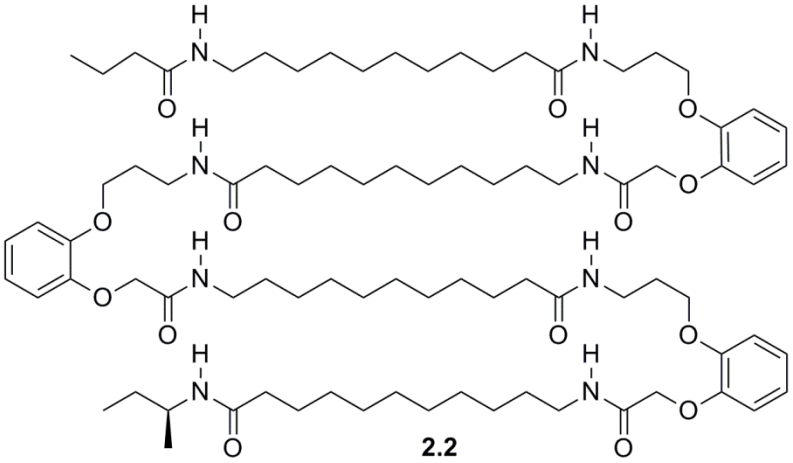


(S)-tert-butyl 11-(3-(2-(2-(11-(3-(2-(2-(11-(3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylcarbamate (2.15). The free-amino compound **2.14** (255 mg, 0.24 mmol) and the acid compound **2.4** (175 mg, 0.34 mmol) were coupled according to general procedure 2. The solution was concentrated and purified by flash chromatography applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 90: 10 in 15 column volumes. The compound was collected at $CHCl_3$: MeOH = 96: 4. Yield: 360 mg (0.24 mmol, 100%). ^{1}H-NMR ($CDCl_3$): δ 7.20 - 6.70 (m, 17H), 6.60 - 6.50 (br, 1H), 6.05 - 5.95 (br, 1H), 4.65 - 4.40 (m, 7H), 4.19 - 4.02 (m, 6H), 3.93 - 3.80 (m, 1H), 3.54 - 3.40 (m, 6H), 3.39 - 3.27 (m, 6H), 3.21 - 3.00 (m, 2H), 2.40 - 2.00 (m, 14H), 1.70 - 1.20 (m, 78H), 0.88 (t, ^{3}J = 6.8 Hz, 3H). ^{13}C-NMR ($CDCl_3$): δ 173.1, 173.0, 172.5, 168.5, 156.0, 148.7, 147.5, 122.8, 121.5, 115.1, 113.4, 79.2, 69.2, 67.0, 46.6, 38.9, 36.9, 36.8, 36.6, 29.5, 29.4, 29.3, 29.2, 29.1, 29.0, 28.3, 26.7, 25.7, 20.4, 10.2. MS (ESI+) calcd for $C_{86}H_{142}N_8Na_3O_{15}$ $[M+3Na]^{3+}$ (1596.03 / 3 =) 532.01, $C_{86}H_{144}N_8O_{15}$ $[M+2H]^{2+}$ (1529.08 / 2 =) 764.54, $C_{86}H_{143}N_8NaO_{15}$ $[M+H+Na]^{2+}$ (1551.06 / 2 =) 775.53, $C_{86}H_{142}N_8Na_2O_{15}$ $[M+2Na]^{2+}$ (1573.04 / 2 =) 786.52, found 532.20, 764.90, 775.10, 786.70.



2.16

(S)-11-amino-N-(3-(2-(2-(11-(3-(2-(2-(11-(3-(2-(2-(11-(sec-butylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propylamino)-11-oxoundecylamino)-2-oxoethoxy)phenoxy)propyl)undecanamide (**2.16**). Boc-protected compound **2.15** (281 mg, 0.18 mmol) was deprotected following general procedure 3. Yield: 257 mg (0.18 mmol, 100%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group from the substrate.



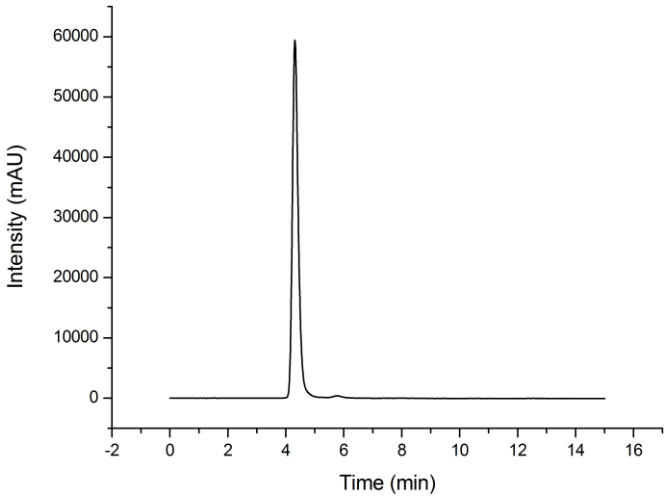
2.2

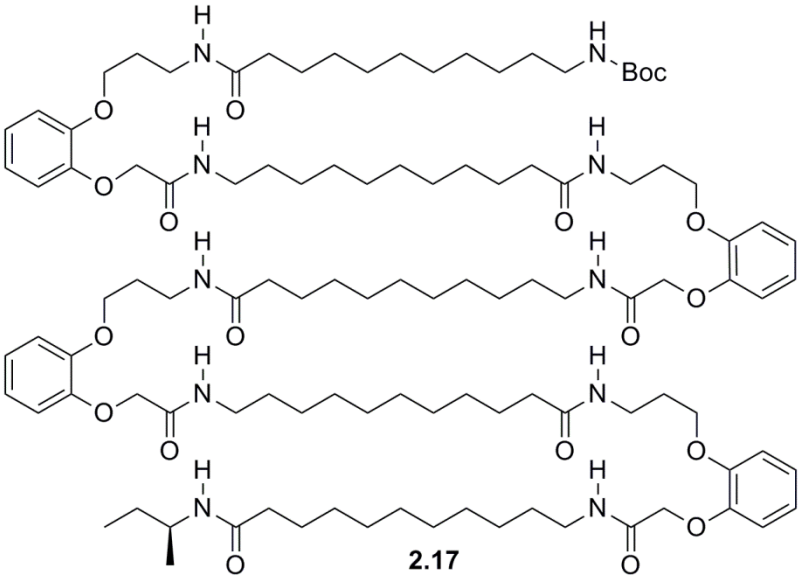
(S)-N-sec-butyl-11-(2-(2-(3-(11-(2-(2-(3-(11-(2-(2-(3-(11-butyramidoundecanamido)propoxy)phenoxy)acetamido)undecanamido)propoxy)phenoxy)acetamido)undecanamido)propoxy)phenoxy)acetamido)undecanamide (**2.2**). The free-amino compound **2.16** (74 mg, 0.052 mmol) and butyric acid (9 mg, 0.102 mmol) were coupled according to general procedure 2. The solution was concentrated and purified by flash chromatography applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 90: 10 in 15 column volumes. The compound was collected at $CHCl_3$: MeOH = 93: 7. The eluent was removed and the residue dissolved in $CHCl_3$. The solution was filtered and the compound was precipitated from the clear solution adding an excess of heptane. The precipitate was filtered and dried under high vacuum to provide compound **2.2** as a white solid. Yield: 52 mg (0.035 mmol, 67%). ^{1}H-NMR ($CDCl_3$): δ 7.20 - 6.70 (m, 18H), 6.50 - 6.10 (m, 2H), 4.53 (s, 6H), 4.19 - 4.02 (m, 6H), 3.93 - 3.80 (m, 1H), 3.54 - 3.40 (m, 6H), 3.37 - 3.10 (m, 8H), 2.40 - 1.90 (m, 16H), 1.70 - 1.20 (m, 71H), 0.98 - 0.80 (m, 6H). MS (ESI+) calcd for $C_{85}H_{143}N_8O_{14}$ $[M+3H]^{3+}$ (1502.08 / 3 =) 500.69, $C_{85}H_{142}N_8NaO_{14}$ $[M+2H+Na]^{3+}$ (1524.07 / 3 =) 508.02, $C_{85}H_{142}N_8O_{14}$ $[M+2H]^{2+}$ (1500.07 / 2 =) 750.03, $C_{85}H_{141}N_8NaO_{14}$ $[M+H+Na]^{2+}$ (1522.05 / 2 =) 761.03, $C_{85}H_{140}N_8Na_2O_{14}$ $[M+2Na]^{2+}$ (1544.03 / 2 =) 772.02, found 500.55, 507.80, 750.30, 761.05, 772.10. Anal. calcd/found for $C_{85}H_{140}N_8O_{14}$: C, 68.15%/68.04%; H, 9.42%/9.45%; N, 7.48%/7.51%; O, 14.95%/15.00%.

HPLC analysis

Isocratic elution: ACN/H2O = 63/37 (0.1% formic acid)

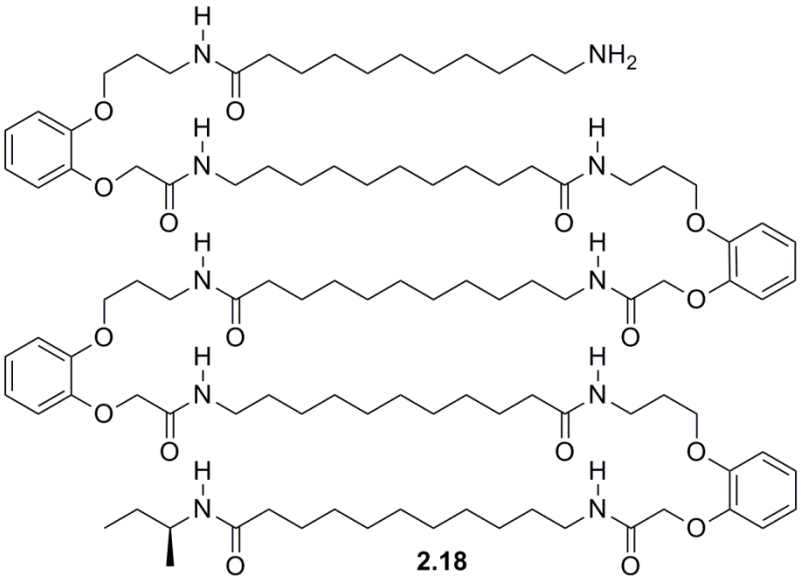
UV detection: 273 nm





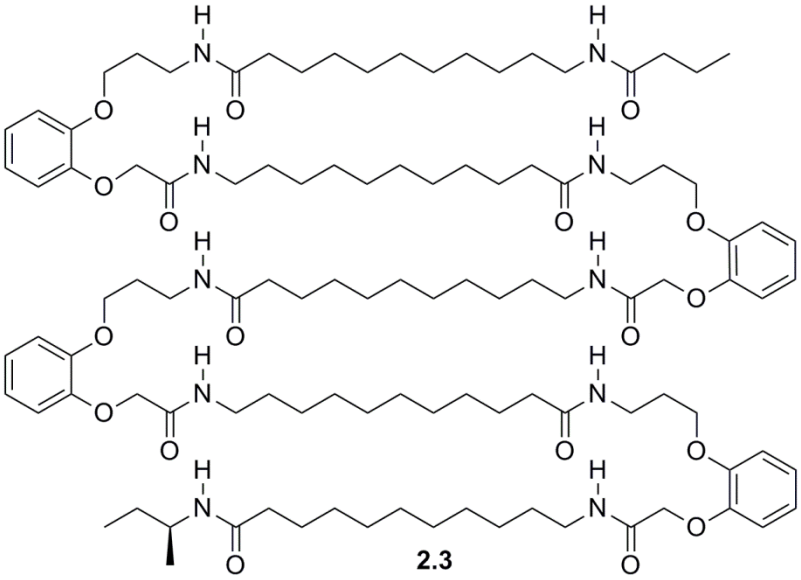
2.17

Compound **2.17**. The free-amino compound **2.16** (146 mg, 0.102 mmol) and the acid compound **2.4** (73 mg, 0.143 mmol) were coupled according to general procedure 2. The solution was concentrated and purified by flash chromatography applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 90: 10 in 15 column volumes. The compound was collected at $CHCl_3$: MeOH = 96: 4. Yield: 192 mg (0.100 mmol, 98%). ^{1}H-NMR ($CDCl_3$): δ 7.20 - 6.70 (m, 23H), 6.60 - 6.50 (br, 1H), 6.05 - 5.95 (br, 1H), 4.65 - 4.40 (m, 9H), 4.19 - 4.02 (m, 8H), 3.93 - 3.80 (m, 1H), 3.54 - 3.40 (m, 8H), 3.39 - 3.27 (m, 8H), 3.21 - 3.00 (m, 2H), 2.40 - 2.00 (m, 18H), 1.70 - 1.20 (m, 94H), 0.88 (t, ^{3}J = 6.8 Hz, 3H). MS (ESI+) calcd for $C_{108}H_{176}N_{10}Na_3O_{19}$ $[M+3Na]^{3+}$ (1987.28 / 3 =) 662.43, $C_{108}H_{176}N_{10}Na_2O_{19}$ $[M+2Na]^{2+}$ (1964.29 / 2 =) 982.14, found 663.05, 982.05.



2.18

Compound **2.18**. Boc-protected compound **2.17** (150 mg, 0.078 mmol) was deprotected following general procedure 3. Yield: 128 mg (0.070 mmol, 90%). Combined ^{1}H-NMR and ESI confirmed removal of the Boc group from the substrate.



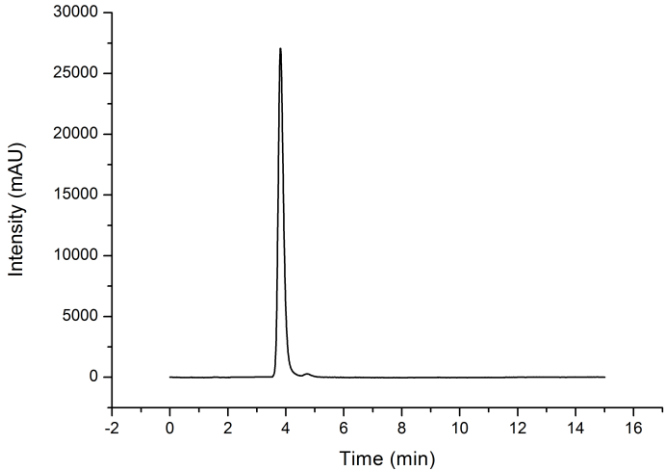
2.3

Compound **2.3**. The free-amino compound **2.18** (30 mg, 0.016 mmol) and butyric acid (7.2 mg, 0.082 mmol) were coupled according to general procedure 2. The solution was concentrated and purified by flash chromatography applying a gradient from pure $CHCl_3$ to $CHCl_3$: MeOH = 80: 20 in 20 column volumes. The compound was collected at $CHCl_3$: MeOH = 84: 16. The eluent was removed and the residue dissolved in $CHCl_3$. The solution was filtered and the compound was precipitated from the clear solution adding an excess of heptane. The precipitate was filtered and dried under high vacuum to provide compound **2.3** as a white solid. Yield: 28 mg (0.014 mmol, 90%). ^{1}H-NMR ($CDCl_3$): δ 7.27 - 6.20 (m, 26H), 4.53 (s, 8H), 4.19 - 4.02 (m, 8H), 3.93 - 3.80 (m, 1H), 3.54 - 3.40 (m, 8H), 3.37 - 3.10 (m, 10H), 2.50 - 1.90 (m, 42H), 1.70 - 1.20 (m, 65H), 0.98 - 0.80 (m, 6H). MS (ESI+) calcd for $C_{107}H_{177}N_{10}O_{18}$ $[M+3H]^{3+}$ (1892.34 / 3 =) 630.78, $C_{107}H_{176}N_{10}NaO_{18}$ $[M+2H+Na]^{3+}$ (1913.31 / 3 =) 637.77, $C_{107}H_{175}N_{10}Na_2O_{18}$ $[M+H+2Na]^{3+}$ (1935.29 / 3 =) 645.09, $C_{107}H_{174}N_{10}Na_3O_{18}$ $[M+3Na]^{3+}$ (1957.27 / 3 =) 652.42, $C_{107}H_{176}N_{10}O_{18}$ $[M+2H]^{2+}$ (1890.32 / 2 =) 945.16, $C_{107}H_{175}N_{10}NaO_{18}$ $[M+H+Na]^{2+}$ (1912.30 / 2 =) 956.15, $C_{107}H_{174}N_{10}Na_2O_{18}$ $[M+2Na]^{2+}$ (1934.28 / 2 =) 967.14, found 630.75, 638.00, 645.15, 652.60, 945.20, 956.35, 966.60. Anal. calcd/found for $C_{107}H_{174}N_{10}O_{18}$: C, 68.05%/67.96%; H, 9.29%/9.32%; N, 7.42%/7.45%; O, 15.25%/15.27%.

HPLC analysis

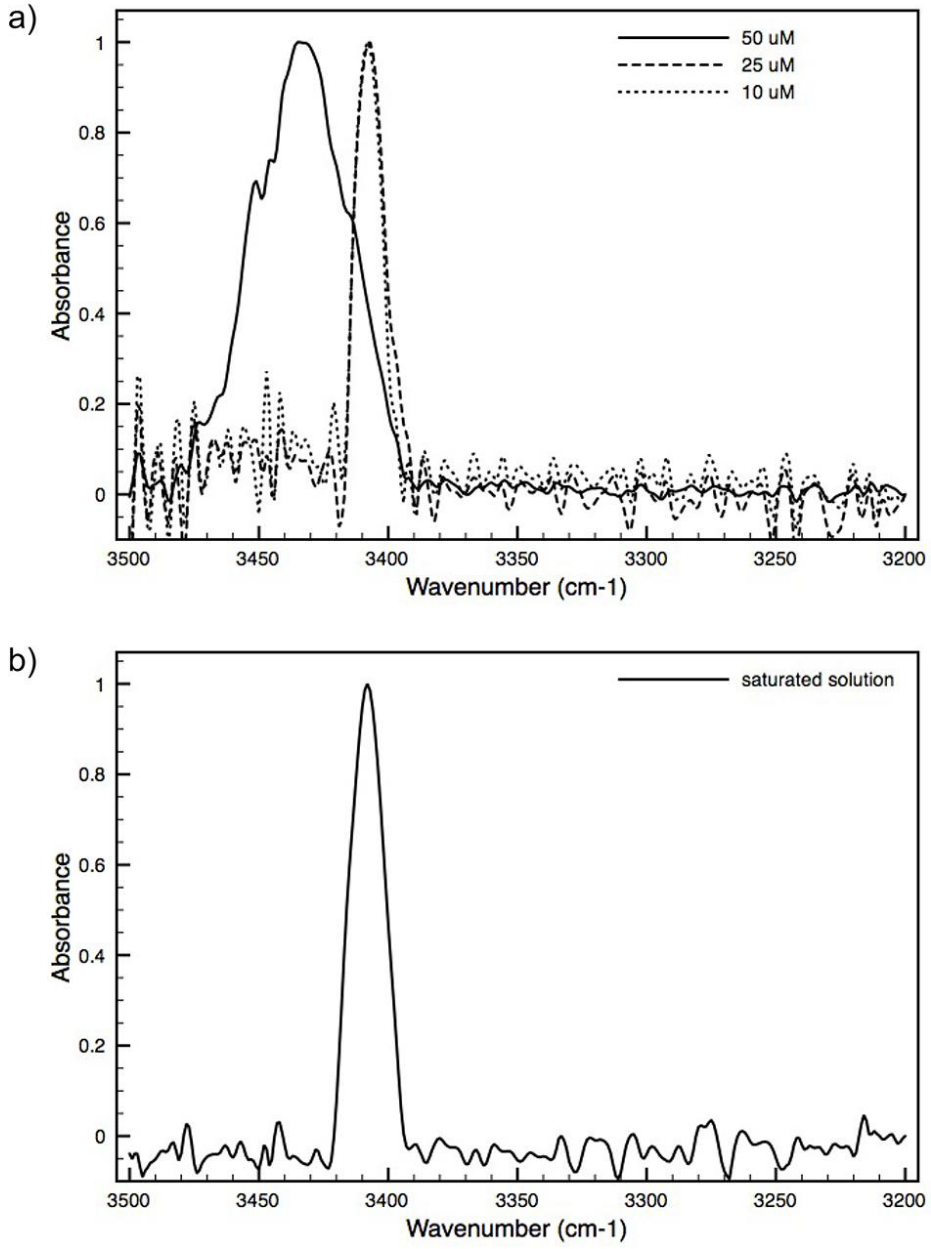
Isocratic elution: ACN/H2O = 65/35 (0.1% formic acid)

UV detection: 273 nm



Section 3: IR absorbance in solution

IR spectra in solution were recorded on 'Perkin Elmer Spectrum One' FT-IR spectrometer using a 3 mm thick cell and a 4 cm^{-1} resolution was applied. Measurements were performed at 25 ºC. Number of scans varied from 512 to 2048 based on the concentration of the sample. Solvent subtraction, baseline correction and normalization of absorbance value to 1 were applied.



IR Absorbance of a dichloromethane solution of foldamers **2.1** (a) and **2.3** (b) in the wavenumber range 3500 - 3200 cm^{-1}. a) 50 μM solutions were prepared by dissolution of compound **2.1** in dichloromethane. Less concentrated solutions were prepared by subsequent dilutions. b) Saturated solution of compound **2.3** was prepared by sonication for 10 minutes and waiting overnight before filtering off the solid residue.

References

1. Li, M., et al., *Molecular Patterning at a Liquid/Solid Interface: The Foldamer Approach.* Langmuir, 2011. **27**(22): p. 13598-13605.
2. Konig, W. and R. Geiger, *A NEW METHOD FOR SYNTHESIS OF PEPTIDES - ACTIVATION OF CARBOXYL GROUP WITH DICYCLOHEXYLCARBODIIMIDE USING 1-HYDROXYBENZOTRIAZOLES AS ADDITIVES.* Chemische Berichte-Recueil, 1970. **103**(3): p. 788-&.
3. Sheehan, J.C. and G.P. Hess, *A NEW METHOD OF FORMING PEPTIDE BONDS.* Journal of the American Chemical Society, 1955. **77**(4): p. 1067-1068.